Stony Brook University

Part 1. Synthesis and Bioassay of SNF Analogues

Part 2. 1,2-Addition of Organometallic Reagents to Unprotected Juglones and Progress Toward the Synthesis of Ravidomycins

Part 3. Synthesis of Cis-Alkenes via a Novel Copper-Mediated Cross-Coupling of 1,1-Dibromoalkenes and Halides

A Dissertation Presented

By

Pei Wang

The Graduate School

in Partial Fulfillment of the

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in

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Pei Wang

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Abstract of the Dissertation

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Part 1. Multidrug resistance (MDR), one of the major clinical problems in cancer chemotherapy, is a condition enabling a disease-causing organism to resist distinct drugs or chemicals of a wide variety of structure and function targeted at eradicating the organism. One of the mechanisms is an overexpression of P-glycoprotein, the product of the mdr-1 gene in human cells. SNF (the code name of Snow Brand Milk Prod. Co.)

compounds showed a potent immunosuppressive activity in vitro by suppressing B-cell proliferation (induced by lipopolysaccharide) and T-cell proliferation (induced by concanavalin A) in non-cytotoxic concentrations. They also showed a multidrug resistance (MDR) reversal activity in tumor cells by inhibition of P-glycoprotein. In order to obtain MDR reversal agents with better activities, 14 SNF analogs were designed and prepared. During the bioassay of the SNF analogs, some of the compounds exhibited very good multidrug resistance (MDR) reversal effects. In particular, SNF analog **11** was the most active in modulating sensitivity to Paclitaxel (99% reduction in IC50 at 1.0 μM in MCF7-R). SNF analog **12** also showed a good activity by reducing 99% of Paclitaxel IC_{50}. Moreover, a new strategy for the synthesis of the tricyclic core of spatol, a potent inhibitor of cancer cell replication, was developed based on the SNF bicyclo[4,2,0] structure.

Part 2. *p*-Quinols can undergo mild reductions to form *p*-phenols. Oxidations of *p*-phenols can reverse these reductions back to give corresponding *p*-quinols. Some biochemical compounds in nature contain *p*-quinol substructures, such as coenzyme Q. *p*-Quinols have a variety of uses principally associated with their actions as reduction or oxidation agents. We developed a new synthetic methodology for the preparation of quinol-containing nature products, in which organometallic reagents regioselectively added to the non-hydrogen bonding carbonyl groups. Ravidomycin is a potent antitumor and antibiotic, which has attracted the attention of chemists for many years. The new synthetic methodology for the synthesis of quinols was applied to the total synthesis of ravidomycin and a series of models were established. The total synthesis of ravidomycin is still in progress.

Part 3. Organo-copper reagents are very frequently applied in organic syntheses because of this selective reactivity and lower nucleophilicity for carbon. However,

organo-copper compounds are thermally unstable. Thus they can not undergo consecutive cross-coupling processes like some other transition organometals. A new highly stereoselective olefination methodology for preparation of cis-alkenes is developed based on a novel copper-mediated cross-coupling. This is the first example of consecutive cross-couplings of organocopper intermediates and aryl/vinyl halides in a one-pot reaction.

Dedicated to those whom I love and those who love me

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List of abbreviations

α	alpha
[α]	specific optical rotation
β	beta
δ	delta, or chemical shift
γ	gamma
Δ	heat
σ	sigma bond
π	pi bond, or orbital
π*	antibonding orbital
n	nonbonding orbital
Å	angström
Ac	Acetyl
AcOH	Actetic acid
Ac_2O	Acetic anhydride
aq.	Aqueous
Ar	Aryl
Atm	Atmosphere
ATP	Adenosine triphosphate
b	broad
bd	Broad doublet
Bn	Benzyl
bp	Boiling point
bs	Broad singlet
t-Bu	*tert*-Butyl
n-BuLi	n-Butyllithium
Bz	Benzoyl
Calcd	Calculated
CDI	1,1'-carbonyldiimidazole
CI	Chemical ionization
cm^{-1}	Reciprocal Centimeter
COSY	Homonuclear (^1H-^1H) correlated spectroscopy
d	Doublet
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
dd	Doublet of doublet
DIBALH	Diisobutylaluminum hydride
DIPA	Diisopropylamine
DIPEA	Diisopropylethylamine
DMAP	Dimethylaminopyridine
DMDO	Dimethyldioxirane
DME	Dimethoxyethane

DMF	N,N-Dimethylformamide
ee	Enantiomeric excess
EI	Electron-impact
Eq.	Equivalent(s)
Et	Ethyl
Et_2O	Diethyl ether
EtOAc	Ethyl acetate
g	Gram
h	Hour(s)
HMDS	1,1,1,3,3,3-Hexanmethyldisilazane
HMPA	Hexamethylphosphramide
HOMO	Highest occupied molecular orbital
Hz	Hertz
IC_{50}	Concentration for 50% inhibition
i-Pr	Isopropyl
IR	Infrared spectroscopy
in vacuo	Under vaccum
J	First order coupling constant of NMR
KHMDS	Potassium 1,1,1,3,3,3-hexamethyldisilazide
L	liter
LAH	Lithium aluminum hydride
LDA	Lithium diisopropylamide
LiHMDS	Lithium 1,1,1,3,3,3-hexamethyldisilazide
LUMO	Lowest occupied molecular orbital
m	Multiplet
MDR	Multi-drug Resistance
Me	Methyl
mg	Milligram
MHz	Megahertz
Min	Minute(s)
mL	Milliliter
mol	mole
mp	Melting point
MS	Mass spectrometry
Ms	Methanesulfonyl (mesyl)
m/z	Mass-charge ratio
NaHMDS	Sodium 1,1,1,3,3,3-hexamethyldisilazide
NMR	Nuclear magnetic resonance

p	pentet
Ph	Phenyl
Pip	piperidine
p-gp	P-glycoprotein
ppm	Parts per million
Py	Pyridine
q	Quartet
r.t.	Room temperature
s	singlet
t	triplet
TBAF	Tetra-N-butylammonium fluoride
TBS	Tert-Butyldimethylsilyl
Tf	Trifluoromethane sulfonate
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
Ts	para-Toluenesuflfonyl (tosyl)
wt	weight

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Chapter 1. Synthesis and Bioassay of SNF Analogues

1.1 Introduction

1.1.1 Background of SNF 4435C and D

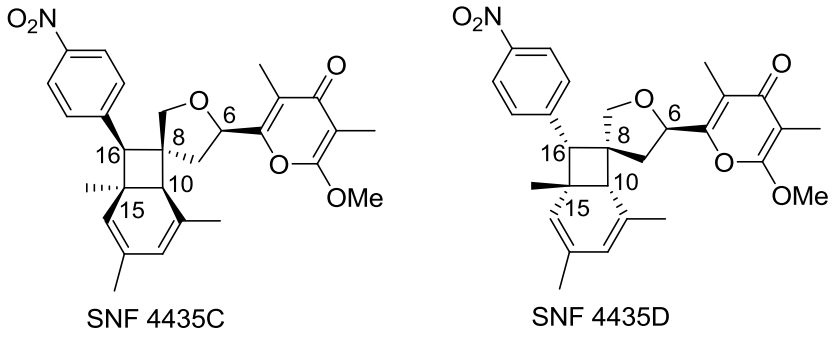

Figure **1.** SNF 4435C and SNF 4435D

SNF 4435 C and SNF 4435 D, two diastereomeric natural products in which four of the five chiral centers have the same stereochemistry relative to each other and the fifth chiral center is epimeric, was discovered in the culture broth of a strain of *Streptomyces spectabilis* originally isolated from a soil sample collected in the main island of Okinawa, Japan in 2001 (Figure 1).[1] The structures of SNF 4435 C and D were elucidated to be novel nitrophenyl pyrones containing a tricyclic ring system by NMR. Their novel bicycle[4,2,0] structures attract attention of many chemists. In 2004, Parker

group finished the first total syntheses of SNF 4435 C and D in which the key step was a tandem 8π/6π electrocyclization.[2]

1.1.2 Biological Activities of SNF 4435C and D

1.1.2.1 Immunosuppressive Activities

SNF 4435C and D not only own the novel structures which present interesting questions of biosynthetic origins and biomimetic synthetic approaches but also they exhibit immunosuppressive activity *in vitro* at submicromolar concentrations. Kurosawa and coworkers reported that SNF 4435C and D selectively suppressed B-cell proliferation induced by lipopolysaccharide (LPS) and T-cell proliferation induced by concanavalin A (Con A) in non-cytotoxic concentrations.[3, 4]

SNF 4435 C and D exhibited antimicrobial activities against *Candida albicans*, *Mycobacterium phlei*, and *Pyricularia oryzae.* In particular, SNF 4435D was active against *Bacillus subtilis*, *Staphylococcus aureus*, and *Trichophyton rubrum.* However, they did not show any remarkable cytotoxicities against KB, K-562, HL-60, and rat hepatocytes. In comparison with tacrolimus (FK-506)[5], SNF 4435 C and D did not suppress the production of IL-2 but the productions of IL-6 and IFN-γ. In the experiment of the effects of delayed addition to the culture on the inhibition of mouse mixed lymphocyte reaction (MLR), the potent inhibitory activities of SNF 4435 C and D were still observed when FK-506 exhibited very little inhibitory activity.

The results suggested that the mechanism by which SNF 4435 C and D act is different from those of FK-506 and cyclosporin A (CsA)[6] which have been developed as

pharmaceuticals. SNF 4435C and D have potential to be effective means for immunosuppressive therapy.[5]

1.1.2.2 Reversal of Multidrug Resistance

Multidrug resistance (MDR), one of the major clinical problems in cancer chemotherapy, is a condition enabling a disease-causing organism to resist distinct drugs or chemicals of a wide variety of structure and function targeted at eradicating the organism. One of the mechanisms is an overexpression of P-glycoprotein, the product of the mdr-1 gene in human cells.[7] Kurosawa and coworkers also reported that SNF 4435C and D effectively overcame MDR in an almost nontoxic dose range by direct binding to P-glycoprotein and inhibiting the pump activity.[8] During their experiments, SNF 4435C and D completely reversed the resistance to vincristine (VCR) *in vitro* in several cell lines, such as mouse leukemia P388 (P388/VCR and P388/ADM, vincristine- and adriamycin-resistant), human myelogenous leukemia K562 (K562/VCR and K562/ADM, vincristine- and adriamycin-resistant) and human ovarian cancer A2780 (adriamycin-resistant AD10), at micromolar concentrations. In addition, SNF 4435C showed positive effects in vincristine-treated mice that bore VCR-resistant P388 leukemia. Furthermore, since the immunosuppressive activity of SNF 4435C and D might limit the clinical use of them for conquering MDR and non-immunosuppressive analogues of CsA exhibited abilities of reversing MDR, Kurosawa and coworkers suggested that non-immunosuppressive SNF4435 derivatives might be potential agents for cancer chemotherapy.

1.1.3 Drug Development for MDR Reversal

1.1.3.1 Multidrug Resistance (MDR)

Multidrug resistance (MDR) is the ability of a disease-causing organism to resist distinct drugs or chemicals of a wide variety of structure and function targeted at eradicating the organism. The organisms can be pathologic cells, including bacterial and neoplastic (tumor, cancer) cells. Thus, multidrug resistance is a serious clinical problem. Because efflux of drugs by the MDR proteins including P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), lung resistance-related protein (LRP) and multidrug resistance protein (MRP-1) is a significant contributor to multidrug resistance in cancer cells, current research is aimed at inhibiting those specific efflux proteins. P-gp, BCRP, LRP, and MRP-1 are membrane-bound ATP-binding cassette transporters which utilize the energy of ATP hydrolysis to transport various substrates across membranes.[9] These proteins have different selectivities for different drugs.[10] People are interested in both selective inhibition[11] and broad spectrum inhibition of these proteins.[12]

1.1.3.2 The Structure of P-gp

P-gp is a 170 kDa transmembrane glycoprotein with a 10-15 kDa of N-terminal glycosylation site. Six transmembrane domains and a large cytoplasmic domain with an ATP-binding site constitute the N-terminal half of P-gp, and the other six transmembrane domains and an ATP-binding site constitute the C-terminal half of P-gp. The two sections share over 65% amino acid similarity.[13] A number of recent contributions described the general features of the protein. A coherent presentation of the functioning of P-gp was recently published by Clarke and Loo.[14] Seigneuret and Kerr respectively designed the different models for P-gp.[15, 16] On the basis of molecular modeling of known P-gp inhibitors and the competitive binding relationships, Orlowski et al. generated a model for part of the interior binding surface of P-gp.[17] However the functioning of P-gp is

complex and still not well understood. A high resolution x-ray structure had not been produced until a structure of mouse P-gp, which has 87% sequence identity to human P-gp, was solved at 3.8 angstroms in 2009.[18]

A nucleotide-free inward-facing conformation arrayed as two "halves" with pseudo two-fold molecular symmetry in the plane of the bilayer was showed in the X-ray structure of P-gp (Figure 2). Two bundles of six transmembrane helices (TMs 1 to 3, 6, 10, 11 and TMs 4, 5, 7 to 9, 12) formed the inward-facing conformation which led to a large internal cavity, so that the nucleotide-binding domains (NBDs) were separated by ~30 Å.

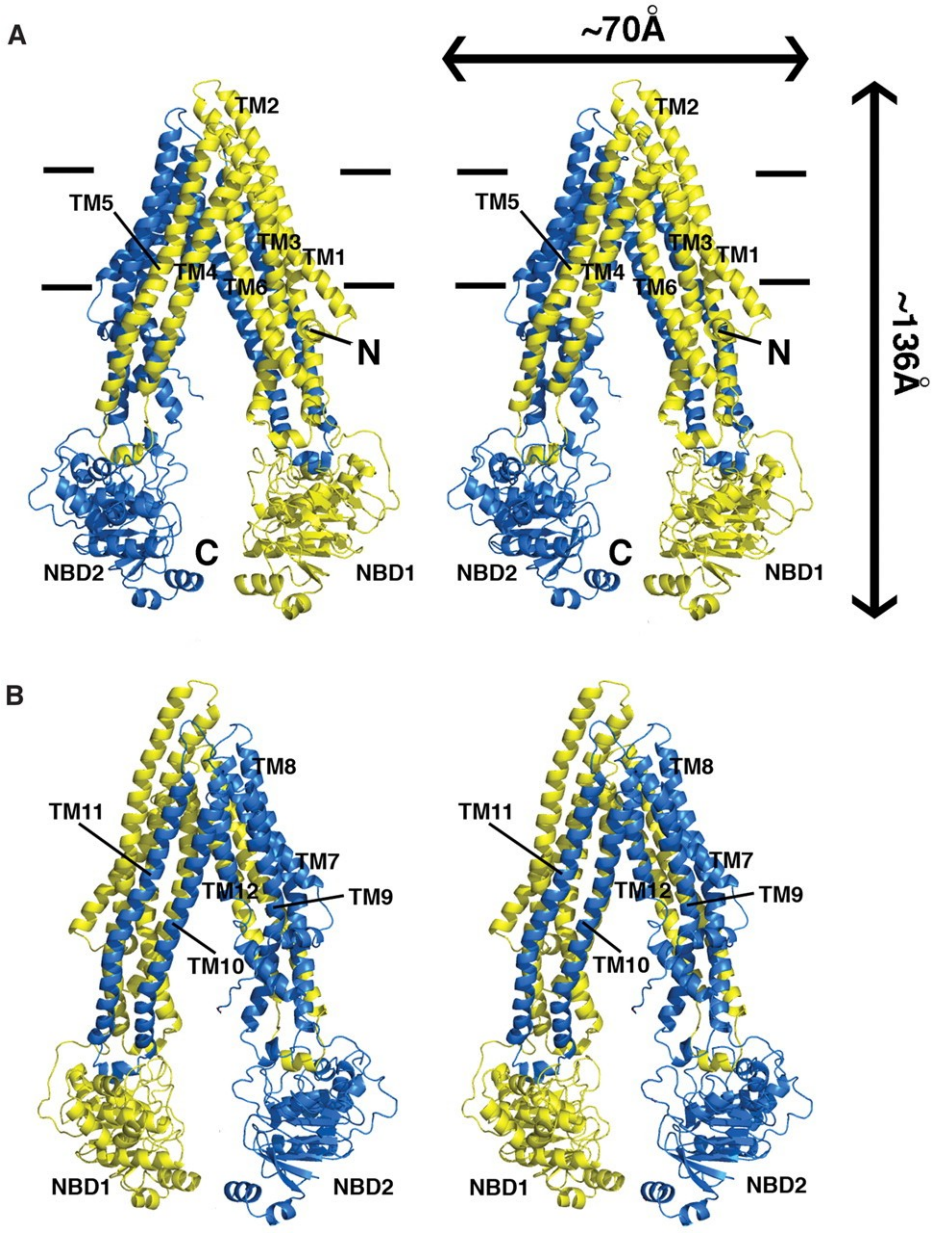

Figure **2.** The X-ray Structure of P-gp.[18] (A) Front and (B) back stereo views of P-gp.

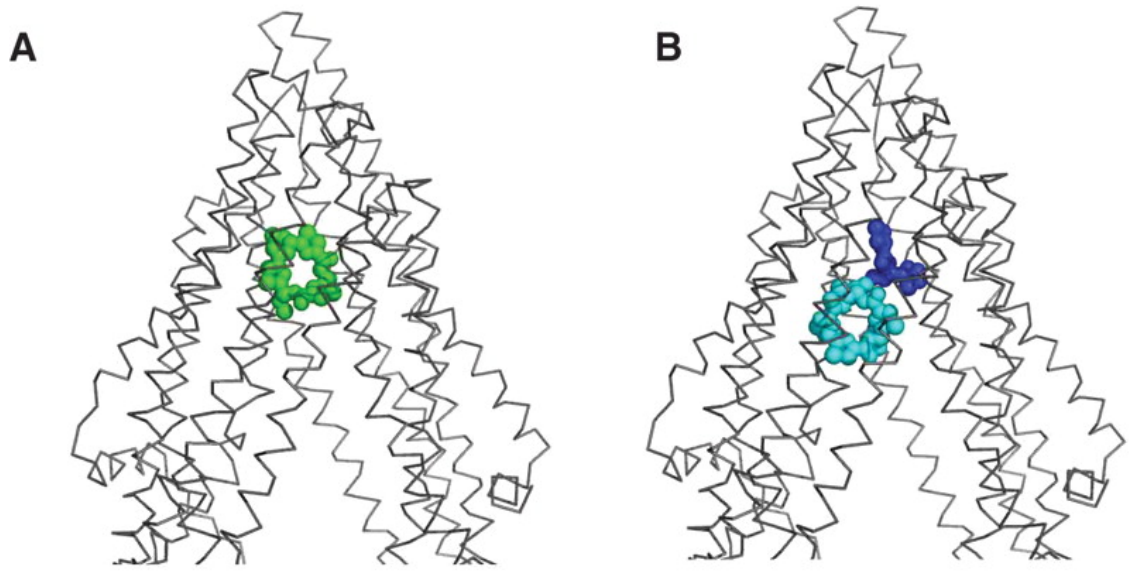

Figure **3.** The X-ray Structure of P-gp.[18] (A) Location of one QZ59-RRR (green spheres) and (B) two QZ59-SSS (blue and cyan spheres) molecules in the P-gp internal cavity.

In the cocrystal structures of P-gp with cyclic-valineselena (QZ59), the inward-facing conformation exhibited the capability to bind drugs (Figure 3). P-gp also showed the ability to distinguish between stereoisomers. The appearance of many residues that interacted with drugs in the drug-binding pocket suggests a common mechanism of poly-specific drug recognition (Figure 4). The upper half of the pocket is predominantly hydrophobic and aromatic; the lower half is polar and charged so that hydrophobic polar substrates might bind.

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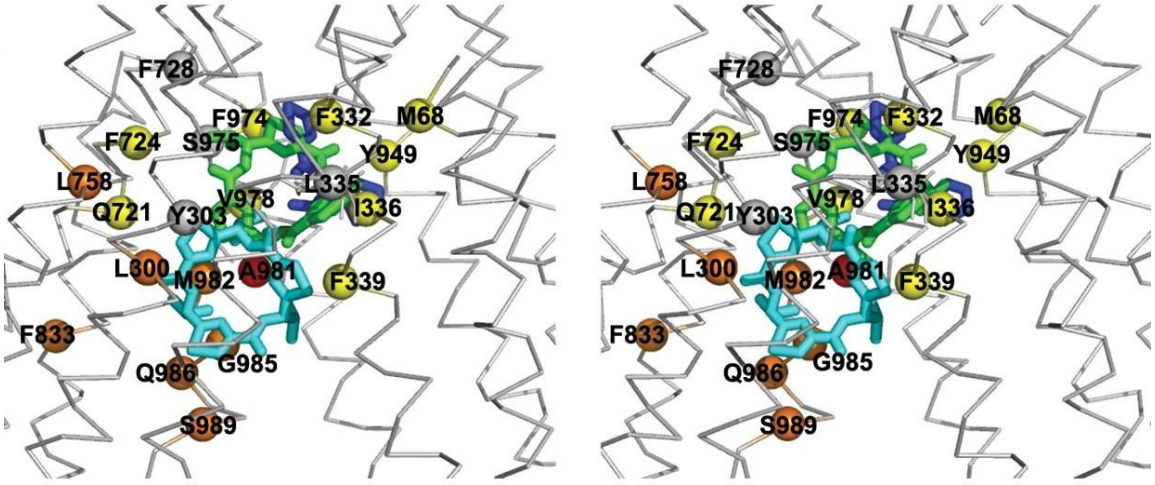


Figure **4.** Stereo view of drug-binding residues of P-gp.[18]

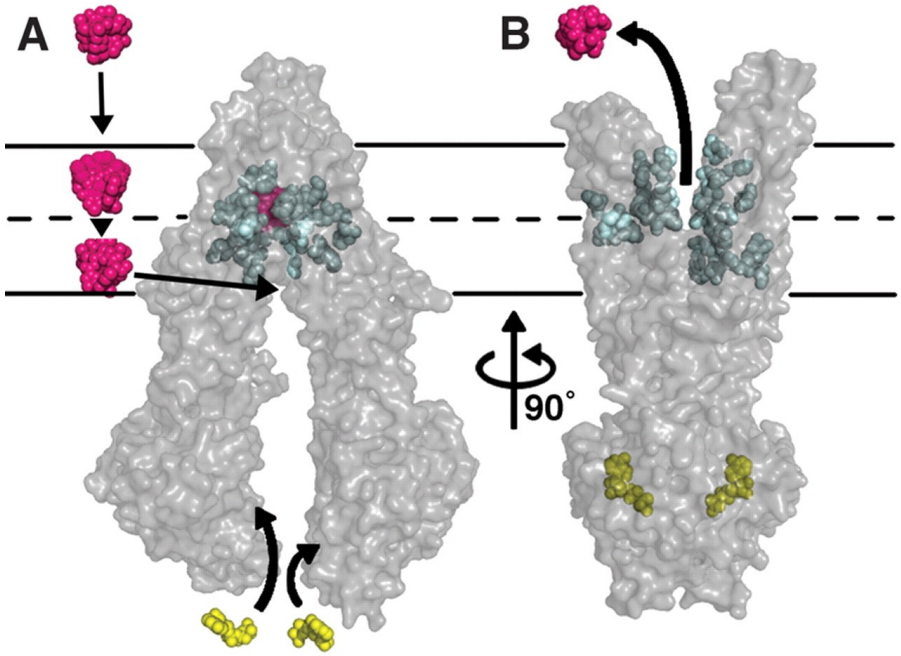


Figure **5**. Model of substrate transport by P-gp.[18]

The drug-binding pocket of P-gp is much larger than those of some other multidrug transporters.[18] In order to accommodate hydrophobic molecules and phospholipids in the pocket, the inward-facing conformation of P-gp has to open two portals wide. According to the literature,[18] the substrate (magenta) entered the internal

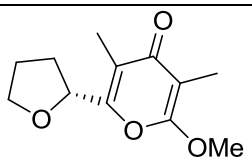
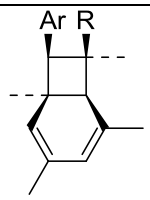
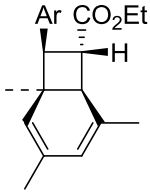
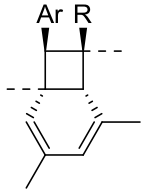
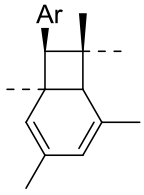
drug-binding pocket through the open portal and then bound with the residues (cyan) in the pocket during transportation (Figure 5). The binding of ATP (yellow) to the NBDs resulted in a big conformational change in which the substrate and drug-binding site(s) exposed to the outer leaflet or extra cellular space.

1.1.3.3 Inhibition of P-gp

Recently, since the importance of P-gp as drug target was realized, some inhibitors against P-gp have been accepted as drugs and a number of specific assays for P-gp inhibition have been developed. Because of SNF compounds' rigid and well understood structures, they provide a very attractive platform for rational drug design.

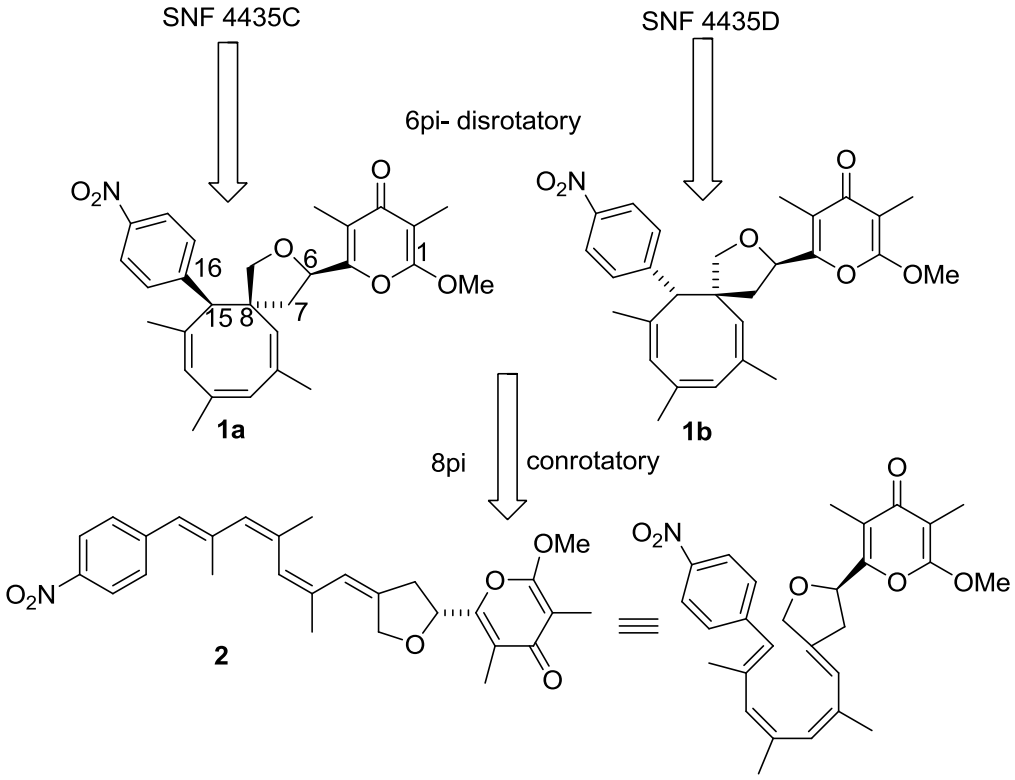
Seelig has approached the problem of a general P-gp pharmacophore by identifying two elements appearing on the surface of P-gp substrates.[19] There were two hydrogen bond acceptor patterns termed type **I** and type **II**. It was claimed that type **I** units with a negative charge, including nitro groups, were unfavorable for the interaction with P-gp. Some structural features appear to be common to many of the substrates and inhibitors that interacted with P-gp. First, a pair of flat hydrophobic surfaces, close in space and with a distance to approximately 5 Å from the center of the hydrophobic region, appear to be important. Again, additional aromatic ring and hydrogen bond donors and acceptors are thought to be advantageous, leading to tighter binding.

Table **1.** MDR Test Result.[20]

Structure	R	IC50 (μM) MCF7-S	MCF7-R	With Paclitaxel (μM)[2]	% Paclitaxel IC50 Reduction
		>100	>100	10 1.0	10 10
 Ar = *p*-nitrophenyl	CH_2OH CO_2Et CN	>50 >10	>50 >10	10 1.0 10 1.0 1.0	23 9 79 22 40
 Ar = *p*-nitrophenyl		>10	>10	10 1.0	90 26
 Ar = *p*-nitrophenyl	CH_2OH CO_2Et CN	>10 >10	>10 >10	10 1.0 10 1.0 1.0	49 5 46 17 12
 endo:exo 50:50 Ar = *p*-nitrophenyl		>10	>10	10 1.0	54 17

A number of SNF analogs were prepared by Yeon-Hee Lim and tested for MDR reversal (Table 1).[20] The IC50 reduction values of some analogs were higher than those of SNF 4435C and D, but the differences are small. The results suggested that SNF compounds' rigid bicyclic structures were very important to inhibit P-gp. Because the action of these SNF analogs has now been validated as inhibition of P-glycoprotein, these compounds may provide an additional tool for the study of the target, for the design of improved inhibitors, and for the design of primary drugs which are not subject to efflux.

1.1.4 The Biomimetic Synthesis of SNF 4435 C and D



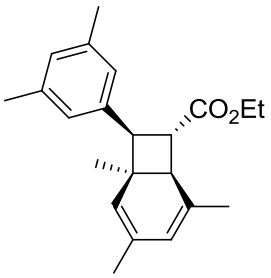
Scheme **1.** Suggested biomimetic synthesis of SNF4435C and D.[2]

The bicyclo[4,2,0]-substructure of SNF4435C and D presents interesting questions of biosynthetic origins and biomimetic synthetic approaches (Scheme 1). The Parker group proposed and finished a biomimetic total synthesis of SNF4435C and D

based on the proposed biosynthesis.[2] The precursor **2**, a linear (1E,3Z,5Z,7E)-1,3,5,7-tetraene, could bend to a helical transition state. Therefore, it carried out a tandem 8π/6π electrocyclization in which a thermal 8π-conrotatory ring closure occurred first to form 2,4,6,- cyclooctatriene intermediates **1a** and **1b**. Because of the higher Gibbs free energies, these intermediates were individually transformed to SNF 4435C and D with lower Gibbs free energies by a thermal 6π-electrocyclic disrotatory ring closure at room temperature. The linear (1E,3Z,5Z,7E)-1,3,5,7-tetraene 2 was suggested to form by a polypropionate synthase from six units of propionyl coenzyme A, one acetyl coenzyme A, and p-aminobenzoic acid as the source of the nitrophenyl ring.[2, 21]

1.2 Results and Discussion

Seelig mentioned that negatively charged groups were unfavorable for the interaction with P-gp.[19] Therefore, the analog **3** with a non-polar 3,5-dimethylphenyl group was designed and synthesized for MDR reversal tests (Figure 6). Seelig also maintained that primary and secondary amines and amides didn't serve as recognition elements for P-gp.[19] The previous SNF 4435 analogues made by Parker and Lim don't contain the commonly observed P-gp type **I** and type **II** hydrogen bond acceptors. Furthermore, almost ubiquitous tertiary amine or amide moieties were absent. Thus it seems likely that tighter binders can be produced by adding functionality to the core structure. The SNF 4435 analog **5,** with tertiary amide group, was expected to have much better MDR reversal activity. In order to examine Seelig's hypothesis that primary and secondary amine and amide do not serve as recognition elements for P-gp,[19] SNF analogue **6**, containing (3-aminopropyl)formamide at C8, was designed and synthesized. SNF 4435 analogue **4** was prepared first as the precursor to SNF analogues **5** and **6**.



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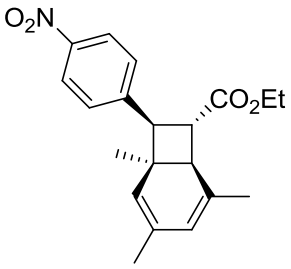

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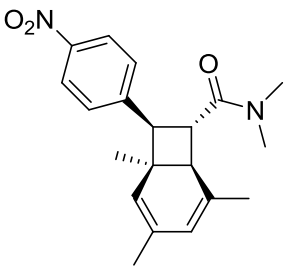

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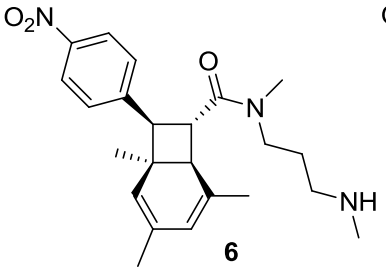

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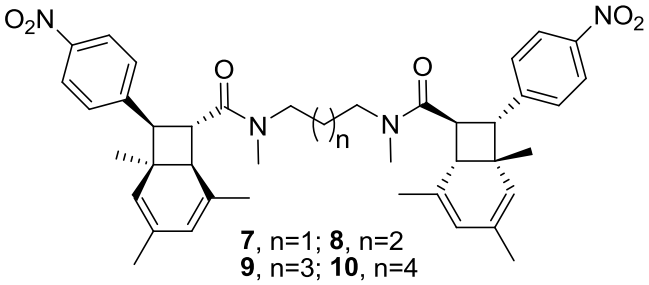
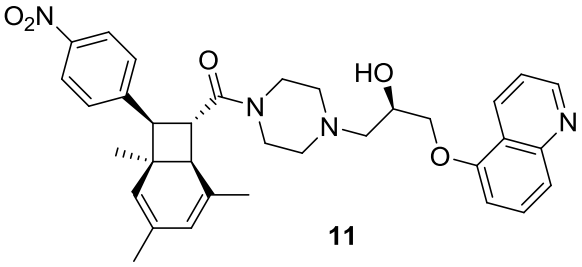


7, n=1; **8**, n=2
9, n=3; **10**, n=4



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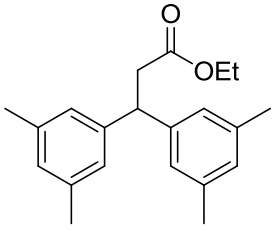

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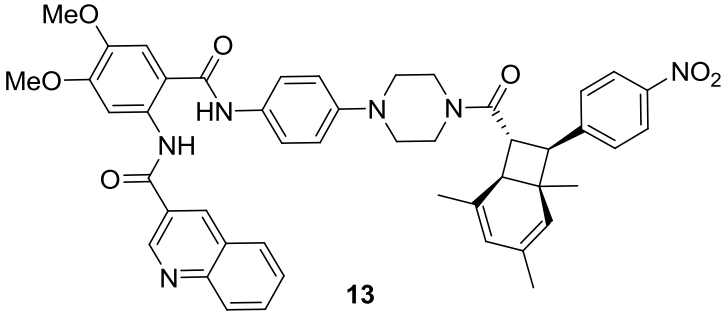

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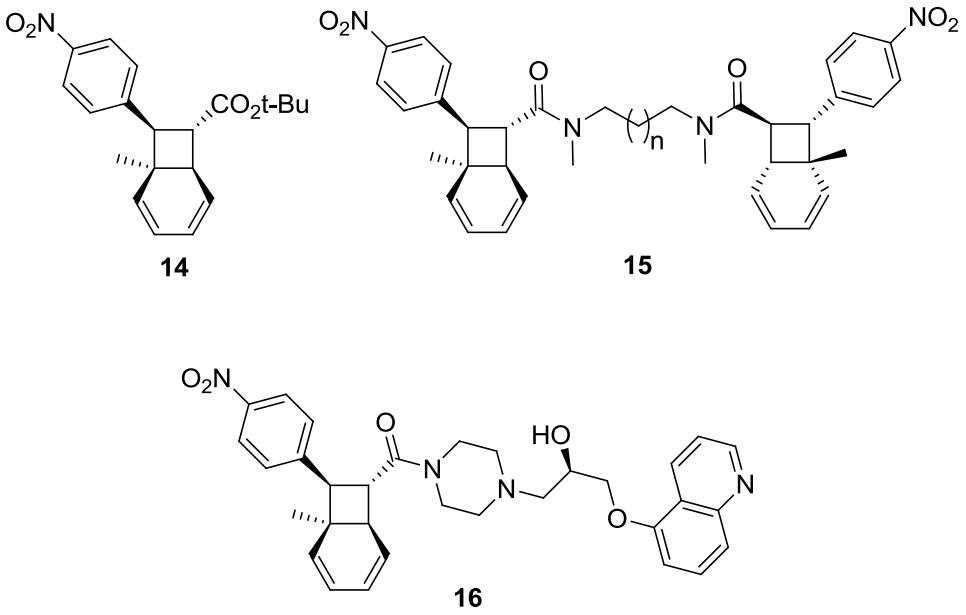


Figure **6.** The SNF analogues designed and made.

SNF analogues **7**, **8**, **9**, and **10** contain two endo-bicyclo[4,2,0]-SNF substructures (Figure 6). At the same concentration, these compounds provide more active units than the previous SNF analogues. Thus, SNF analogues **7**, **8**, **9**, and **10** are expected to show outstanding MDR reversal activities.

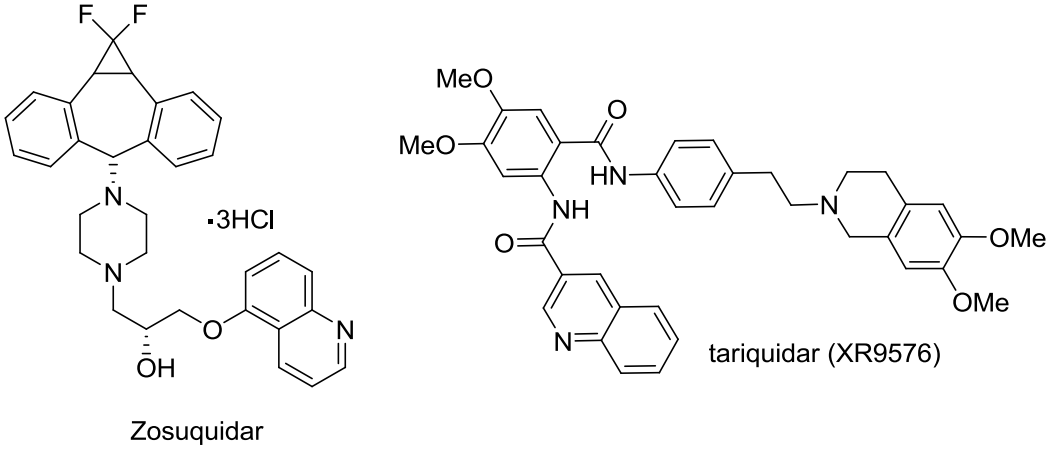


Figure **7**. Zosuquidar[22, 35] and Tariquidar[42]

Zosuquidar[22, 35] and Tariquidar[42] are P-glycoprotein inhibitors undergoing research for treatment of cancer (Figure **7)**. The endo-bicyclo[4,2,0]-SNF substructures were coupled with the 1-piperazin-3-quinolinyloxy-propanol unit of Zosuquidar (LY335979) and the arylpiperazinyl unit of Tariquidar (XR9576) derivatives, individually, to form SNF analogues **11** and **13**.

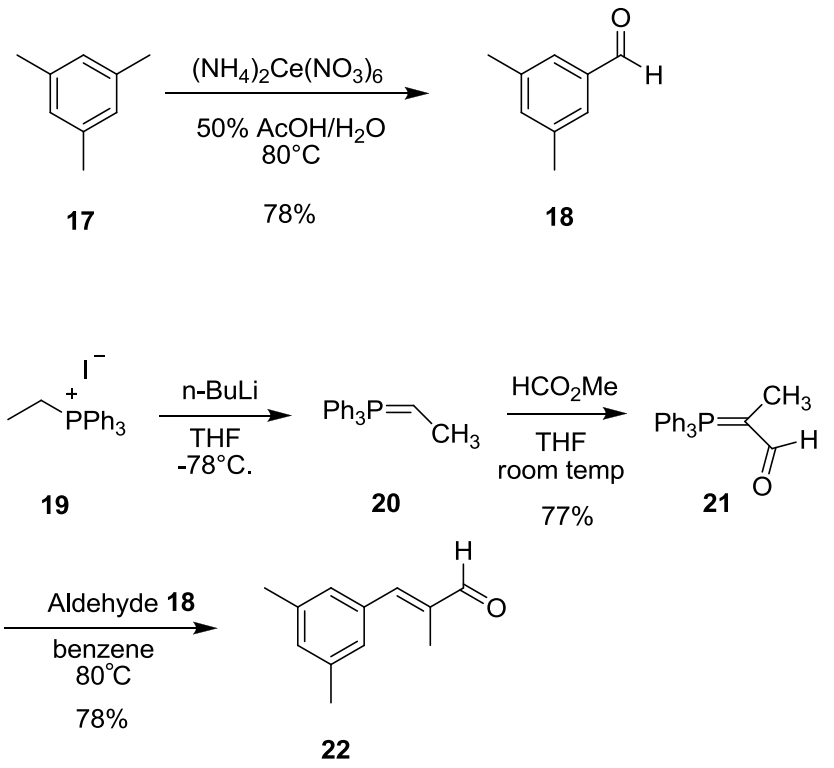
To improve the efficiency of organic synthesis of the SNF analogues, SNF analogue **12**, a mimic compound of SNF analogue **3**, was prepared (Figure 6); a new synthetic methodology for endo-bicyclo[4,2,0] substructure was applied to synthesize SNF analogue **14**. The new endo-bicyclo[4,2,0] substructures of SNF analogue **14** were connected by a diamide linker to form SNF analogue **15**. SNF analogue **16** consisting of a new endo-bicyclo[4,2,0] substructure and a 1-piperazin-3-quinolinyloxy-propanol unit of Zosuquidar was prepared for MDR reversal tests.

1.2.1 The Synthesis of the SNF Analogue 3

The analogue **3** in which the nitrophenyl group is replaced by 3,5-dimethylphenyl was designed and synthesized to examine Seelig's hypothesis of type **I** acceptor (Figure 6). [19]

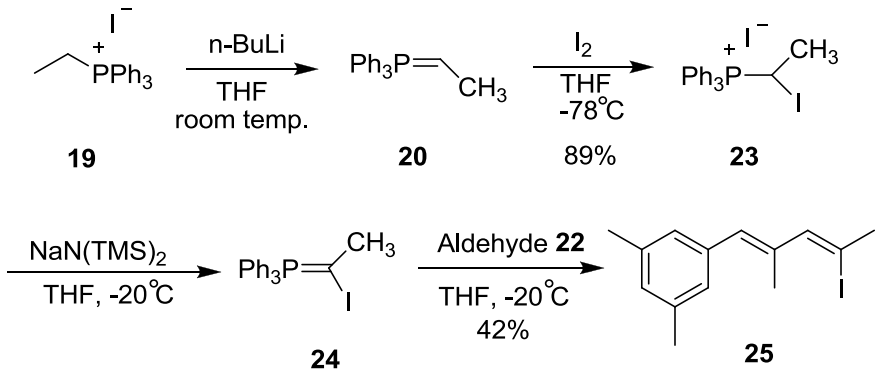
The synthetic strategy for the analogue **3** is coupling of iododiene and vinyl stannane as demonstrated by Parker and Lim.[2] The iododiene **25** was efficiently prepared by a Stork-Zhao reaction[22] which prefered to give the (Z)-olefinic product. (*E*)-2-Methyl-3-(3,5-dimethylphenyl)-propenal **22**, the precursor of **25**, had not reported previously. We expected it was prepared by a cross aldol condensation or a Wittig reaction with aldehyde **18**. Gaspar et al. reported that ammonium cerium (IV) nitrate ($(NH4)_2Ce(NO_3)_6$) could selectively oxidize one methyl group on an aromatic ring to an aldehyde.[23] Thus, compound **18** was prepared in 78% yield by oxidizing only one methyl group of

mesitylene **17** with $(NH4)_2Ce(NO_3)_6$. The cross aldol condensation of the aldehyde **18** and propanal did not work. Thus the Wittig reaction preferring (E)-olefinic product became the better choice.



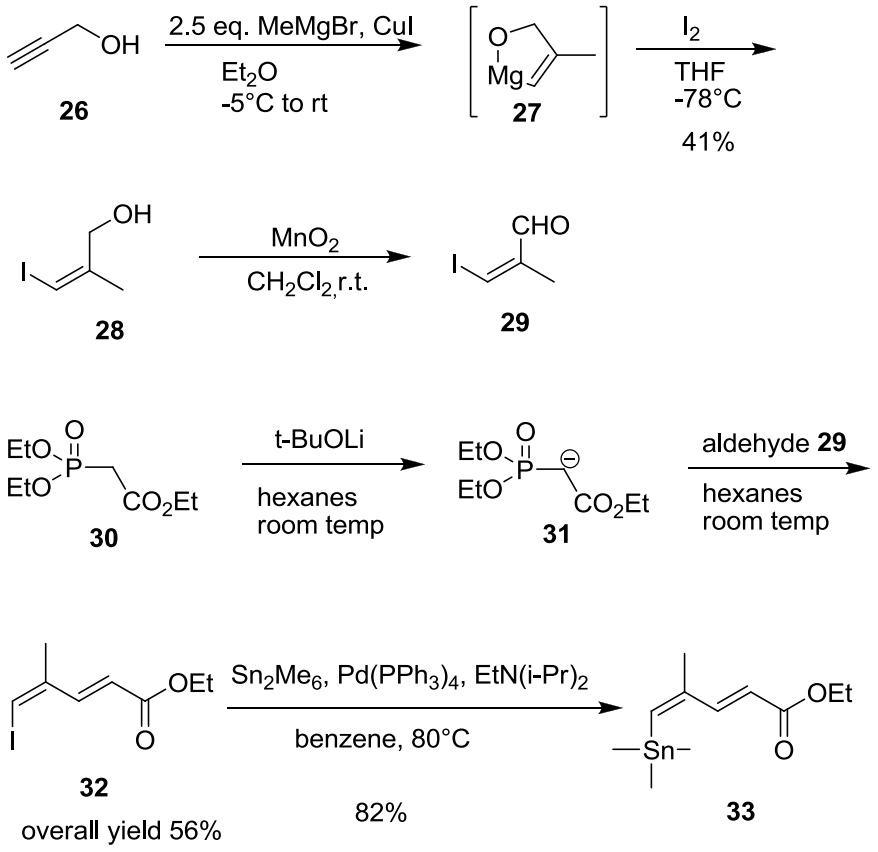
Scheme **2.** Preparation of aldehyde **22**

The stable deprotonated Wittig reagent **21** was prepared in 77% yield from deprotonated ethyltriphenylphosphonium iodide **19** and methyl formate; a second Wittig reaction produced (E)-α,β-unsaturated aldehyde **22** in 78% yield (Scheme 2).[24] Then the Stork-Zhao reagent, (1-iodoethyl)triphenyl-phosphonium iodide **23**, was synthesized by deprotonation of compound **19** with n-butyllithium and subsequent halogenation of the resulted ylide **20**. Treatment of compound **23** with sodium hexamethyldisilazane at – 20 °C afforded the ylide **24**. Reaction with aldehyde **22** produced the desired iodoolefin **25** in 42% yield (Scheme 3).



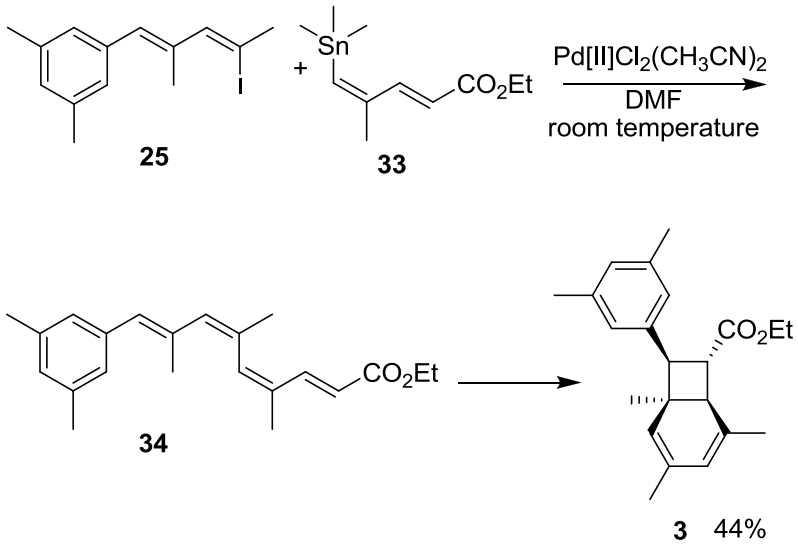
Scheme **3**. Preparation of Iododiene **25**

The stannyl ester **33** was prepared as demonstrated by Parker and Lim.[19] First, the (Z)-iodoallylic alcohol **28** was obtained in 42% yield from propargyl alcohol **26** through a stereoselective carbocupration/iodination sequence (Scheme 4).[25] The intermediate of this reaction was supposed to be a five-member ring **27** which controls the stereoselectivity of the reaction. Oxidation of (Z)-iodoallylic alcohol **28** with MnO_2 afforded a very unstable (Z)-iodovinyl aldehyde **29** which was transferred into a Horner-Wadsworth-Emmons reaction system as soon as possible after filtration and concentration.[26] In the immediate Horner-Wadsworth-Emmons reaction, Wadsworth-Emmons reagent **30** was deprotonated by lithium tert-butoxide (t-BuOLi) to produce an enolate which reacted with aldehyde **29** to give an iododiene **32** in overall 56% yield. This reaction specifically formed the (E)-isomer.[27] The (1Z,3E)-iododiene **32** was converted to the corresponding proton-sensitive vinyl stannane **33** in 82% yield by treatment with hexamethylditin under the Pd(0)-catalysis in benzene.



Scheme **4.** Preparation of vinyl stannane **33**

A tandem process consisting of a cross coupling and electrocyclizations is shown in Scheme 5. The coupling reaction of vinyl stannane **33** and iododiene **25** in the presence of catalytic amounts of bisacetonitrile-palladium(II) chloride $(CH_3CN)_2PdCl_2$ in diisopropylethylamine and DMF at room temperature afforded the intermediate **34** which underwent a 8π/6π electrocyclization to form the endo-bicyclo[4,2,0]-SNF analog **3** in overall yield 44% . This stereoselective tandem reaction only gave the endo product in which the phenyl unit and cyclohexadiene unit were cis on the cyclobutane ring

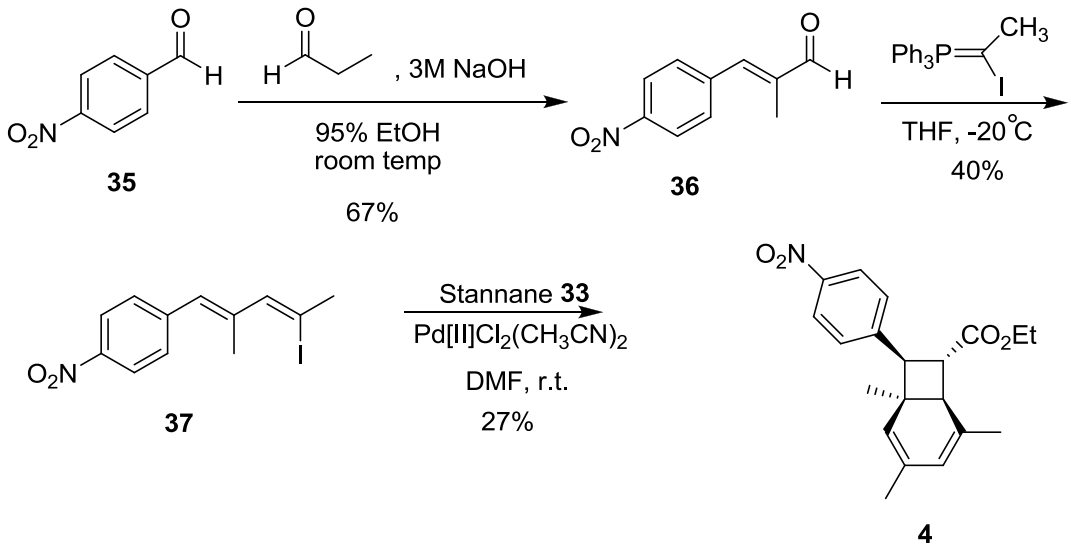


Scheme **5.** Preparation of SNF analogue **3**.

1.2.2 The Synthesis of SNF Analogue 4

According to Kurosawa, modified SNF analogues with lower immunosuppressive activity might be more effective for reversal of multiple drug resistance.[8] In order to make various SNF analogues, SNF analogue **4** was prepared.

The iododiene **29** was also prepared by a Stork-Zhao reaction (Scheme 6). Under catalysis by sodium hydroxide, the cross aldol condensation of 4-nitro-benzaldehyde **27** and propionaldehyde specifically gave the (E)-1,3-unsaturated aldehyde **28** in 67% yield.[28] The ylide **24** reacted with aldehyde **36** to produce the desired iodoolefin **37** in 40% yield.



Scheme **6.** Preparation of SNF analogue **4**.

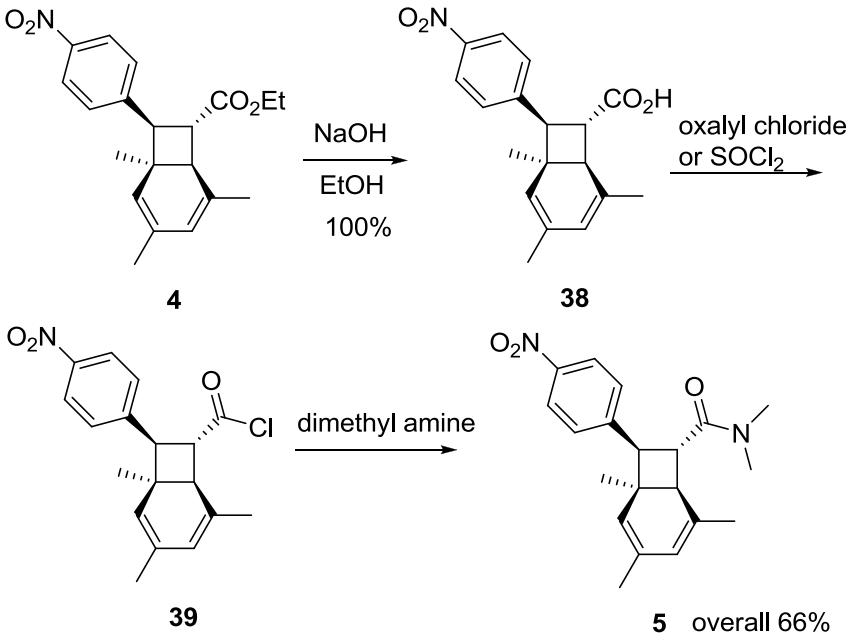
The Stille cross coupling reaction of vinyl stannane **33** and iododiene **37** in the presence of catalytic amounts of $(CH_3CN)_2PdCl_2$ in diisopropylethylamine and DMF at room temperature stereospecifically afforded the endo-bicyclo[4,2,0] SNF analogue **4** in overall yield 27%.

1.2.3 The Synthesis of SNF Analogue 5

Seelig maintained that primary and secondary amines and amides do not serve as recognition elements for P-gp.[19] Analogues **3** and **4** do not contain the commonly observed P-gp type **I** and type **II** hydrogen bond acceptors. Also common tertiary amine or amide moieties were absent. Thus it seems likely that tighter binders can be produced by adding functionality to the core structure. SNF 4435 analogue **5** with tertiary amide group was expected to have much better MDR reversal activities.

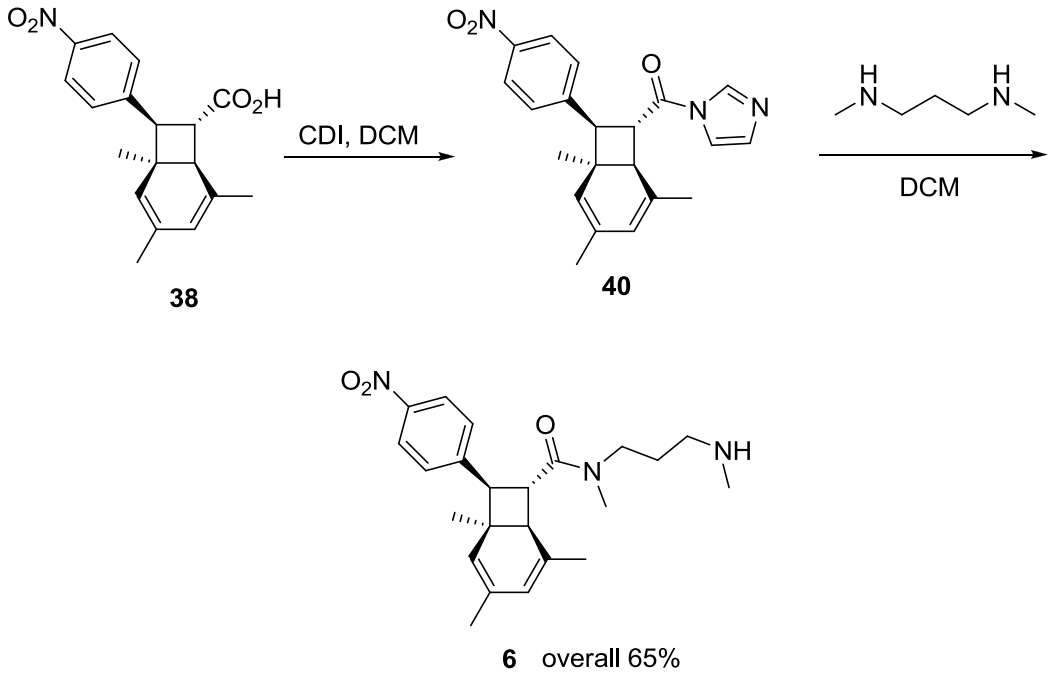
SNF analog **5** was derived from SNF analog **4** (Scheme 7). The ester group of SNF analog **4** was hydrolyzed by sodium hydroxide in ethanol to give the acid **38** in 100% yield. Treatment of the acid **38** with excess oxalyl chloride or thionyl chloride in

dichloromethane (DCM) afforded the acid chloride **39**. An excess 50% solution of dimethyl amine in water and acetone was directly added to the acid chloride **39** to produce SNF analogue **5** in overall yield of 66%.[29]



Scheme **7.** Preparation of SNF analogue **5**.

1.2.4 The Synthesis of SNF Analogue 6



Scheme **8.** Preparation of SNF analogue **6**

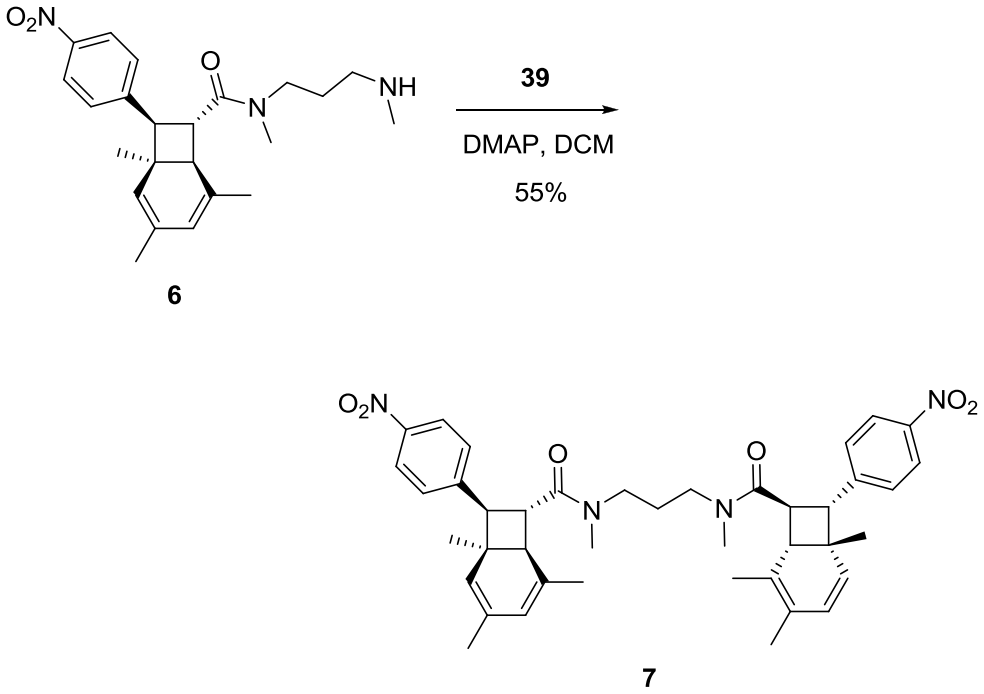
Dr. Eryk Stolarzewicz of the Parker group studied modeling for inhibition of P-gp based on Geoffrey Chang's work.[30] The modeling showed that SNF analogues substituted with an aminoamide at the C8 position might have better inhibitive activities against P-gp. The length the chain between the amide functional group and the amine function group could affect the activity. In order to examine Seelig's hypothesis that primary and secondary amines and amides do not serve as recognition elements for P-gp,[19] SNF analogue **6**, substituted by (3-aminopropyl)formamide at C8, was designed and synthesized (Scheme 7).

First, the acid **38** which was produced by hydrolyzing SNF analogue **5** with sodium hydroxide was added by carbonyl diimidazole (CDI) in methylene chloride (DCM) to lead to the carbonyl imidazole intermediate **40**. Then the solution of carbonyl

imidazole **40** was added quickly to an excess solution of N,N'-dimethylpropyldiamine in methylene chloride to give a momoacylation diamine **6** in overall yield 65%.[31]

1.2.5 The Synthesis of SNF Analogue 7

SNF analogue **7** consisting of two endo-bicyclo[4,2,0]-SNF substructures can increase the effective concentration of the inhibitive units against P-gp. Moreover, according to the X-ray structure of P-gp, the upper half of the pocket is predominantly hydrophobic and aromatic; the lower half is polar and charged. Thus SNF analogue **7** contains more hydrophobic cyclohexadiene units and more polar nitrophenyl units than the previous SNF analogs. Thus, SNF analog **7** is expected to show an outstanding MDR reversal activity.



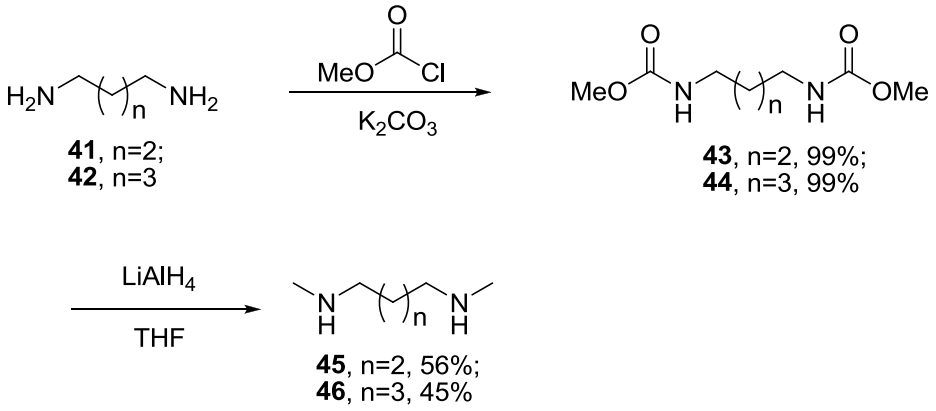
Scheme **9.** Preparation of SNF analogue **7**

The amine group of SNF analogue **6** was acylated by the second portion of the acid chloride **39** under the presence of 4-(dimethylamino)pyridine (DMAP) in methylene

chloride to form SNF analog **7** , a mixture of two enantiomers and one diastereomer, in 55% yield (Scheme 9).[32]

1.2.6 The Synthesis of SNF Analogues 8, 9, and 10

Considering that the length of the diamide chain linking two endo-bicyclo[4,2,0]-SNF substructures of analogue **7** could effect the inhibitive activities against P-gp, SNF analogues **8**, **9**, **10** with diamide linker of different lengths were designed and synthesized.

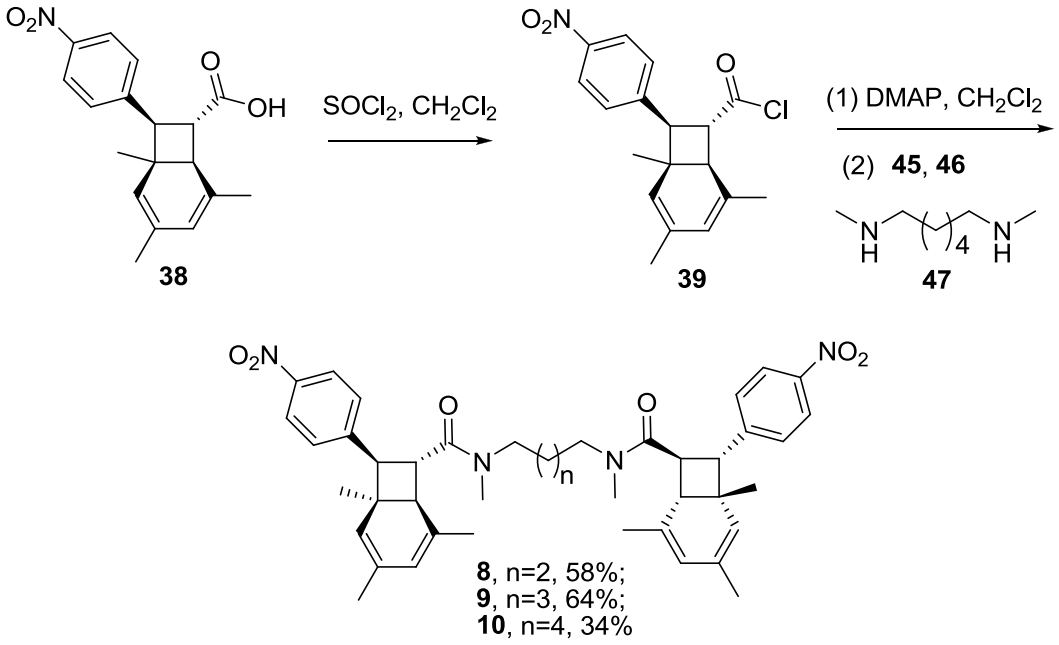


Scheme **10.** Preparation of N,N'-dimethyldiamines **45** and **46**

Unlike N,N'-dimethylpropyldiamine, N,N'-dimethyldiamines **45** and **46** are not commercially available. Treatment with methyl chloroformate and potassium carbonate converted diamines **41** and **42** to dicarbamates **43** and **44** in very high yields.[33] Then lithium aluminum hydride ($LiAlH_4$) in tetrahydrofuran (THF) reduced the dicarbamates **43** and **44** to the desired N,N'-dimethyldiamines **45** and **46** in about 50% yields.[34]

Treatment of the acid **38** with excess thionyl chloride in dichloromethane (DCM) afforded the acid chloride **39** (Scheme 11). In the presence of 4-(dimethylamino)pyridine (DMAP), a solution of 0.5 equivalent of N,N'-dimethyldiamine **45** in dichloromethane (DCM) was added to the acid chloride **39** to produce SNF analogue **8** in overall 58%

yields. Analogs **9** and **10** were prepared by the same method in overall 64% and 34% yields, respectively.



Scheme **11.** Preparation of SNF analogues **8**, **9**, and **10**.

1.2.7 The Synthesis of SNF Analogue 11

1.2.7.1 Another Modulator of Multiple Drug Resistance, LY335979.

Compound LY335979 3HCl has been found to be a clinically useful modulator of *P*-glycoprotein-mediated multiple drug resistance in the research by Syntex Corporation and Lilly Research Laboratories (Figure 7).[22, 35] LY335979 3HCl contains a rigid bicycle[5,1,0] substructure in the upper part of the molecule. Now, Zosuquidar, the commercial name of LY335979 3HCl, is under development in "Phase 3" of clinical trial in the United States.

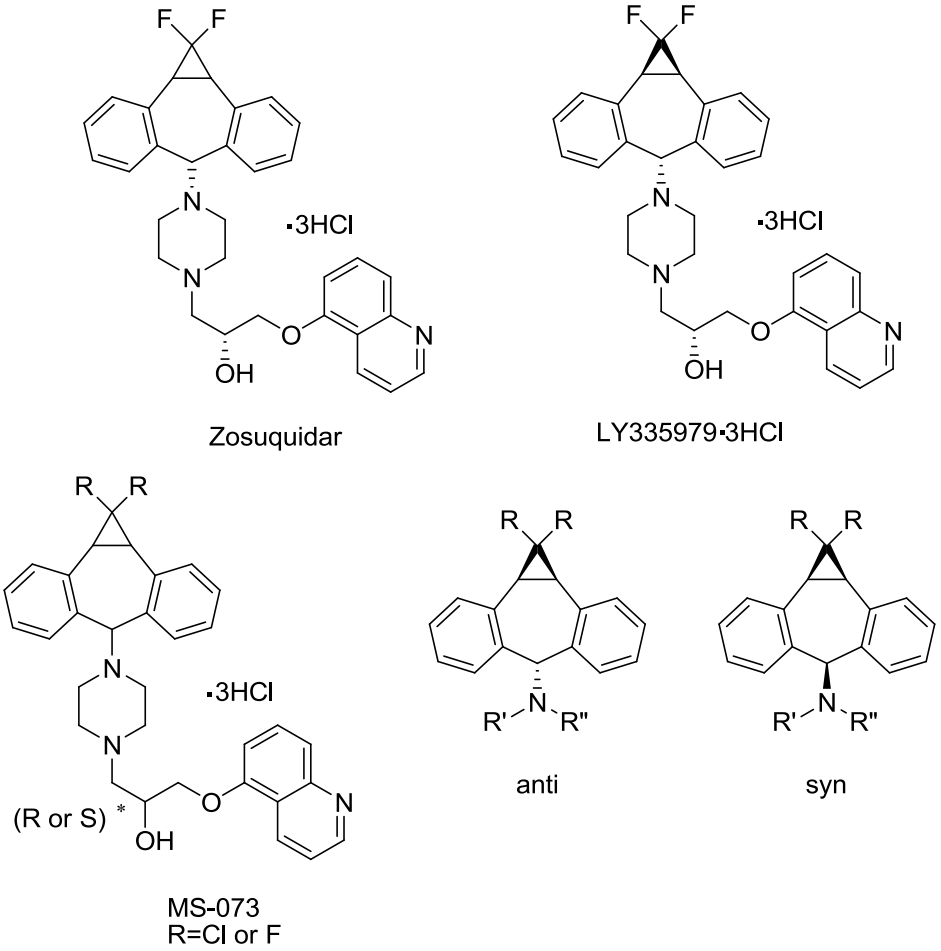


Figure **8**. Zosuquidar, LY335979 3HCl and MS-073

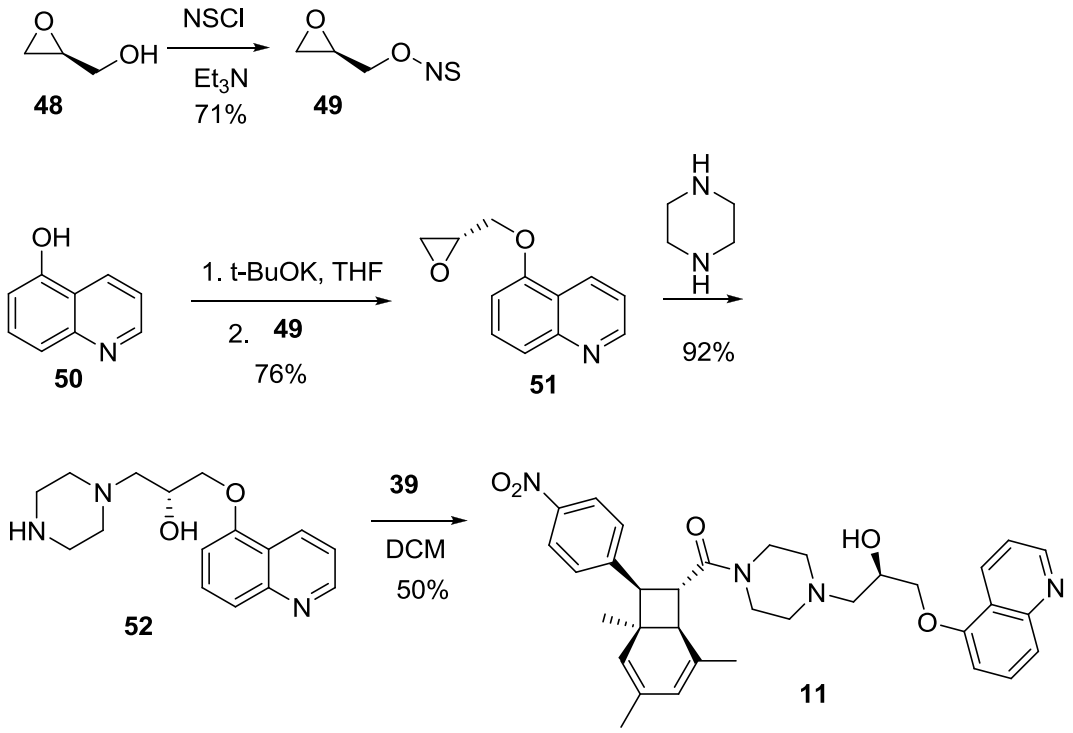
Syntex Corporation tested various MS-073 compounds (Figure 7) with extensive structural modifications on MDR (Table 2).[35] These data in Table 2 show that the anti-compounds (piperazine and cyclopropane axial) are more potent than their syn-counterparts.[35] Furthermore, the compounds with the (R)-configuration in the hydroxylpropoxy spacer unit are more potent than the (S)-enantiomer.[35] LY335979, an anti-(R)-MS073 compound, holds the best MDR activities. According to the literature,[35] the drug molecule would partition to a well-defined, energetically favorable location, orientation and conformation in the membrane bilayer pathway for binding of MDR reversal agents to P-gp.

Table **2.** MDR reversal EC_{50} *values in vitro*[35]

Ex.	R	Stereochemistry	EC_{50}(nM)
MS-073	F	anti-(R,S)	50
		anti-(R)	20.7±3.8
		anti-(S)	60
		syn-(R)	200
		syn -(S)	180
		syn -(R,S)	190
	Cl	anti-(R,S)	70
		anti-(R)	55
		anti-(S)	100
	H	anti-(R,S)	40
S 9788			290
Ro 11-2933			540
Verapamil			1200

Since both LY335979 and the SNF analogues contain rigid bicyclic substructures and show good inhibitive activities, we wondered whether the combination of these two kinds of *P*-glycoprotein inhibitors could afford a more biologically active compound. Verapamil analogs and 1,4-dihydropyridines which differ in their potencies as calcium entry blockers are effective in modulating drug transport by P-gp, and SNF's arylbicyclo[4,2,0]-substructure may replace LY335979's bicyclo[5,1,0]-substructure. Thus the 1-piperazin-3-quinolinyloxy-propanol unit of LY335979, which contains several hydrogen bond acceptors and donors, was chosen for a structural component of the new designed SNF analogue **11**.

1.2.7.2 Preparation of SNF Analogue 11.

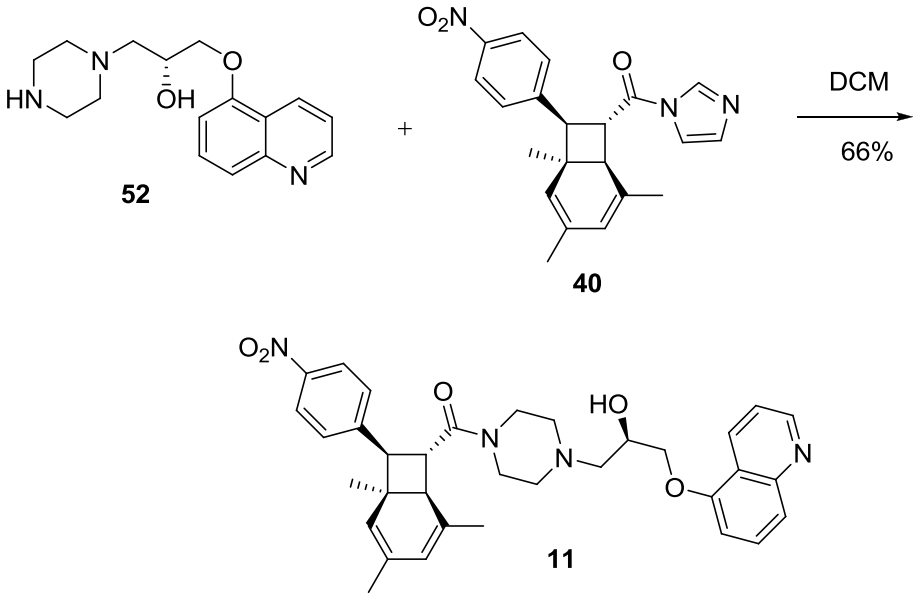


Scheme **12.** Preparation of SNF analogues **11.**

Following Dr. Charles J. Barnett's work, piperazine moiety **52** was synthesized selectively (Scheme 12).[22] (-)-D-Glycidol **48** was protected by 4-nitrobenzenesulfonyl chloride in the presence of trimethylamine in methylene chloride to form epoxide **49** in 71 % yield. 5-Quinolinol **50** was deprotonated by potassium t-butoxide in THF. The resulting nucleophilic quinolinyl-5-oxyl replaced the 4-nitrobenzenesulfonate group of epoxide **49** by a S_N2 reaction to produce quinolinylglycidol **51** in 76% yield. Excess piperazine opened the epoxide ring of quinolinylglycidol **51** in ethanol to give N-monosubstituted piperazine **52** in 92% yield .[36]

Piperazine **52** was added to acid chloride **39** in methylene chloride to afford SNF analogue **11** in 50% yield (Scheme 12). Alternatively, the coupling of acid and amine by

carbonyldiimidazole (CDI) was applied. In methylene chloride, the piperazine **52** coupled with SNF imidazole **40** to give SNF analog **11** in 66% yield (Scheme 13). The analogue **11** is a mixture of two diastereomers.



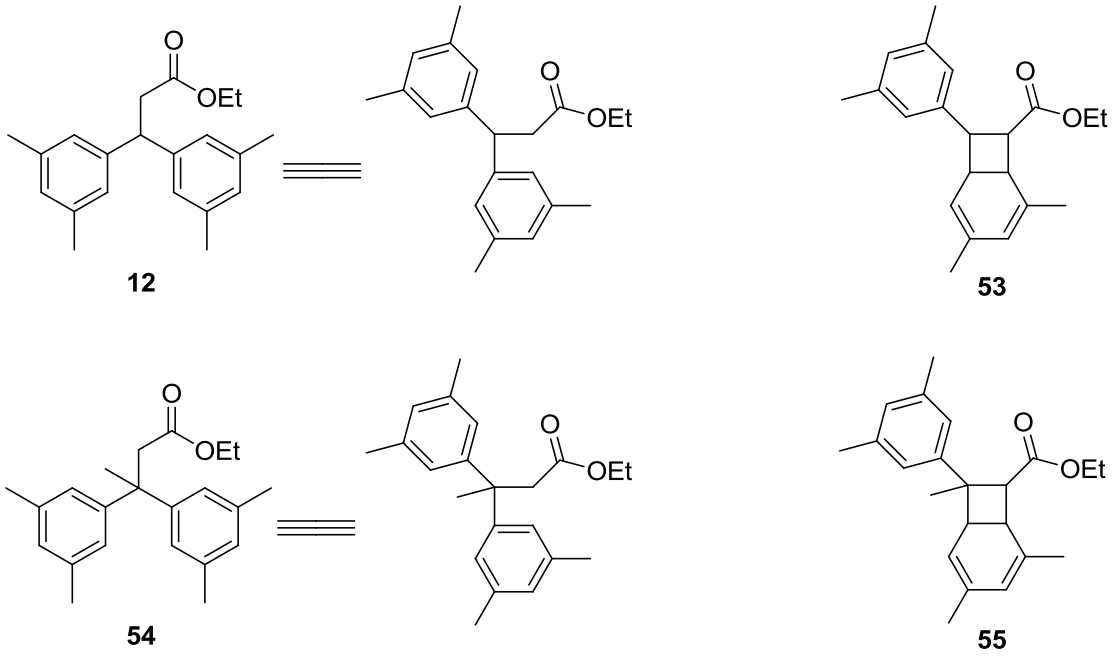
Scheme **13.** Plan B for preparation of SNF analogues **11.**

1.2.8 The Synthesis of 3,3'-Dixylylpropionic Ester 12

In the syntheses of SNF analogues, there are several disadvantages. First, the Stork-Zhao reaction and Stille cross coupling gave the products in low yield. Second, the key Stille cross coupling utilized tin reagents which are toxic and are not acceptable for pharmaceutical intermediates. Third, to make stereospecific olefins, the reaction conditions are limited. Thus the bicyclic structure of SNF compounds was redesigned.

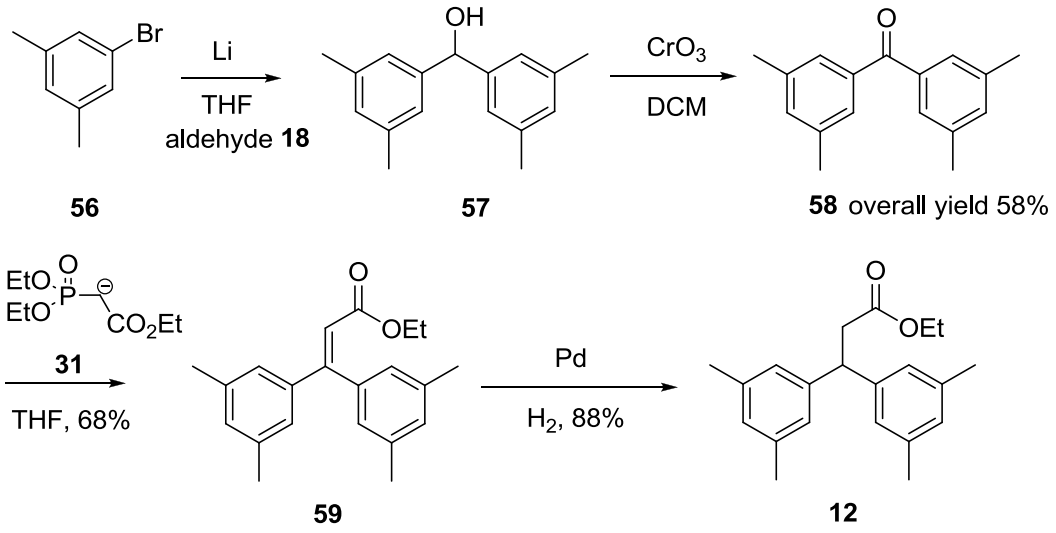
The ethyl 3,3'-dixylylpropionates **12** and **54** might form mimic conformations of compounds **53** and **55,** respectively. Therefore, we expected that compounds **12** and **54**

might occupy the same volume as SNF analogue **3** does in P-glycoprotein. Compounds **12** and **54** would be much easier to make and they do not have any stereoisomer pattern.

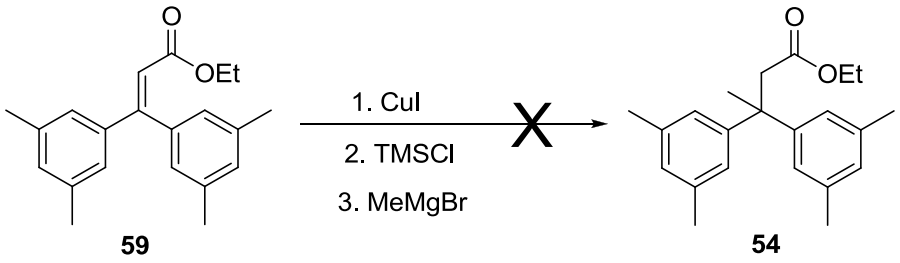


Scheme **14.** A proposed cyclization in biological systems**.**

A mixture of 5-bromo-m-xylene **56** and aldehyde **18** was stirred with lithium wire in THF to give the adduct **57** (Scheme 15).[37] The resulting alcohol **57** was oxidized by chromium(VI) oxide in a mixture of methylene chloride and acetic acid to give ketone **58** in 58% overall yield.[38] Horner-Wadsworth-Emmons reagent **31** was added to the ketone **58** in THF to afford α,β-unsaturated ester **59** in 68% yield.[39] The α,β-double bond of ester **59** was reduced by Pd-mediated catalytic hydrogenation in methanol to give the desired dixylylpropionic ester **12** in 88% yield.[39]



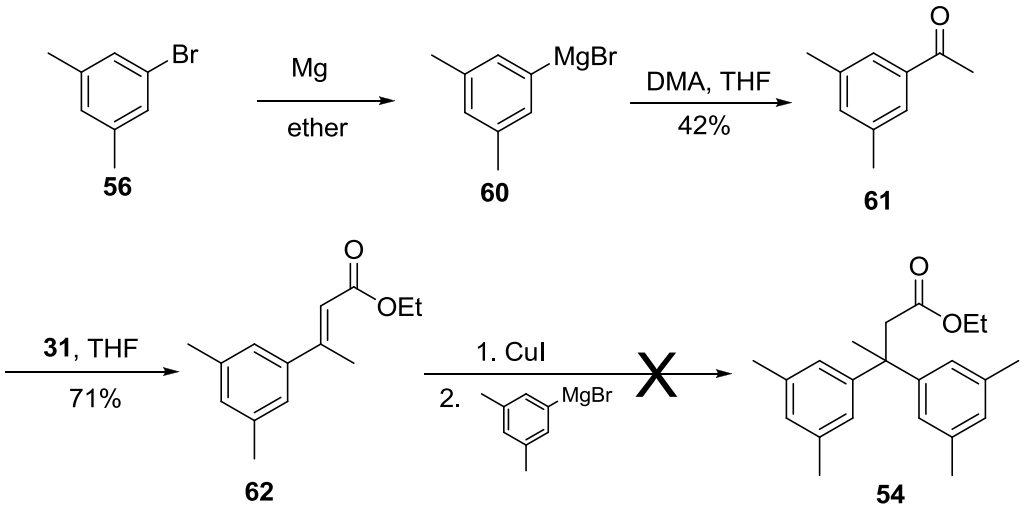
Scheme **15.** Preparation of 3,3'-dixylylpropionic ester **12.**



Scheme **16.** Attempt at preparation of 3,3'-dixylylpropionic ester **56.**

We attempted to synthesize the dixylylpropionic ester **54** (Scheme 16). First, copper(I) iodide (CuI) and chlorotrimethylsilane (TMSCl) were added to a solution of α,β-unsaturated ester **59** in THF. Then methylmagnesium bromide (MeMgBr) was added to the suspension.[40] However, compound **54** was not produced, and the reaction only gave back the starting material **59**. A possible reason that the addition did not work is the big steric effect of 3,5-dimethylphenyl function groups. Another synthetic route to ester **54** was tried (Scheme 17): 5-Bromo-m-xylene **56** was treated with magnesium to prepare 3,5-dimethylphenylmagnesium bromide **60**, which was added to N,N'-dimethylacetamide to form the ketone **61** in 42% yield.[41] Horner-Wadsworth-Emmons reagent **31** converted

the ketone **61** to a trans-α,β-unsaturated ester **62** in 71% yield.[39] The suspension of α,β-unsaturated ester **62** and copper (I) iodide in THF was added 3,5-dimethylphenylmagnesium bromide **60**.[40] Still because of the big steric effects, the desired compound **54** was not obtained and the reaction only gave the starting material **62** back.



Scheme **17.** The second attempt at preparation of 3,3'-dixylylpropionic ester **54**

1.2.9 The Synthesis of SNF Analogue 13

1.2.9.1 Backgroud: Anthranilamide Derivatives as Modulators of Multiple Drug Resistance

Tariquidar (XR9576, Figure 8) is one of the third generation of the inhibitors of P-gp. Recently, because of a significant proportion of adverse events, the progress of clinical trials of Tariquidar slowed down.[42] Therefore, a new generation of inhibitors of P-gp based on anthranilamide derivatives was developed (Figure 9).[43]

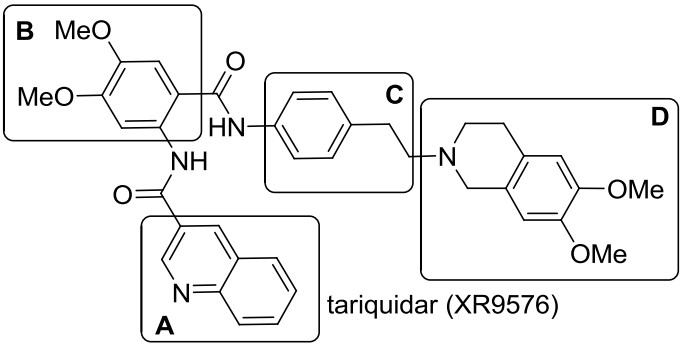


Figure **9**. Tariquidar (XR9576). **A**, **B**, **C**, and **D** define the four regions of XR9576

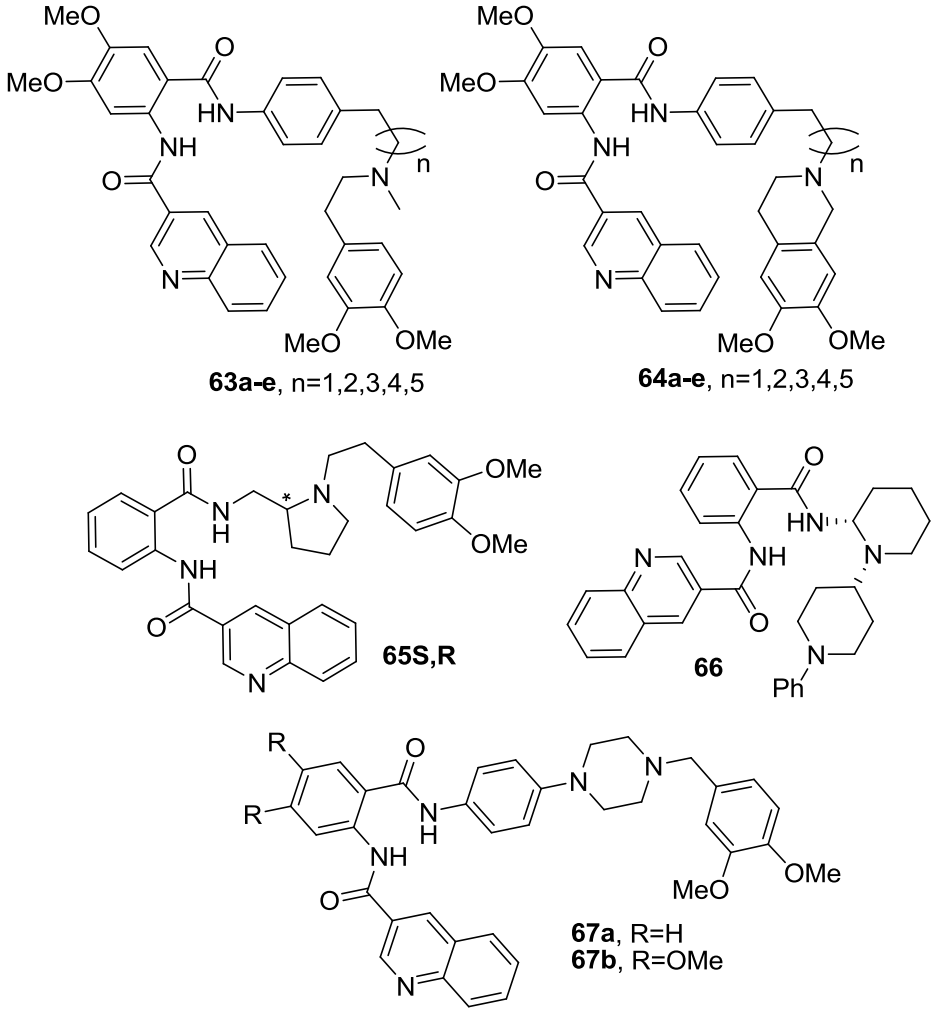


Figure **10**. Anthranilamide derivatives

The P-gp inhibition potencies of compounds **63a–e**, **64a–e**, **65S/R**, **66**, and **67a-b** in combinations respectively with daunorubicin (DNR) and vinblastine (VBL), were assessed using CEM/VLB500 human leukemia cells. These compounds exhibited more potent MDR reversal activities than verapamil did (Table 3). In particular, compounds **67a** and **b** were respectively 9- and 20-fold more potent than verapamil (VRP); they were almost equipotent to XR9576. These compounds also exhibited minimal cytotoxicity at concentrations up to 10 μM while XR9576 was significantly toxic at this concentration

The metabolism of drugs by cytochrome P-450 (CYP) initiates many drug–drug interactions.[43] In addition, P-gp can act synergistically with cytochrome P450 (CYP) 3A4 to enhance drug metabolism and elimination.[44] CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 are involved in the metabolism and the drug–drug interactions. Compounds **63a**, **67a-b,** and XR9576 were examined in a CYP450 inhibition assay to evaluate their ability to inhibit catalytic activities (Table 4). The results showed that compound **67b** exhibited the best inhibition of CYPs.

According to the effect of the modifications on the regions B-C-D versus the P-gp/CYPs inhibition and the cytotoxicity, an arylpiperazinyl group instead of an alkyl chain in region C may led to significant inhibitive activities against P-gp and CYPs; and the addition of two methoxy groups to the anthralinidyl moiety (region B compound **67a**) increased by 200% the P-gp inhibition activity and completely inhibited CYP-450. In comparison with other compounds, compound **67b** was considered as the most active P-gp inhibitor at nM.[43]

Table **3**. In vitro inhibition activities of new anthranilamide derivatives on CEM/VBL500 cells incubated in the presence of vinblastine and their cytotoxic activity.[43]

Compound	**Inhibitory activity on CEM/VLB$_{500}$ EC$_{50}$ (nM)**	**Cytotoxicity activity on CEM/VLB$_{500}$ GI$_{50}$ (nM)**
63a	270 ± 84	27707 ± 15909
63b	490 ± 90	29177 ± 13401
63c	781 ± 177	19063 ± 7858
63d	1345 ± 113	17845 ± 10300
63e	904 ± 384	10201 ± 2147
64a	899 ± 127	42298 ± 4588
64b	500 ± 147	29339 ± 11787
64c	945 ± 346	26353 ± 4588
66d	1274 ± 27	17210 ±4952
64e	1084 ± 255	17060 ± 9197
65R	329 ± 138	>15000
65S	482 ± 226	>15000
66	648 ± 208	11500 ± 1400
67a	124 ± 76	>15000
67b	59 ± 35	⩾15000
XR9576	68 ± 40	13500 ± 3100
VRP	1041 ± 443	>15000

Table **4**. Cytochrome-P450 inhibition assays of compounds **63a, 67a-b**, and XR9576.[43]

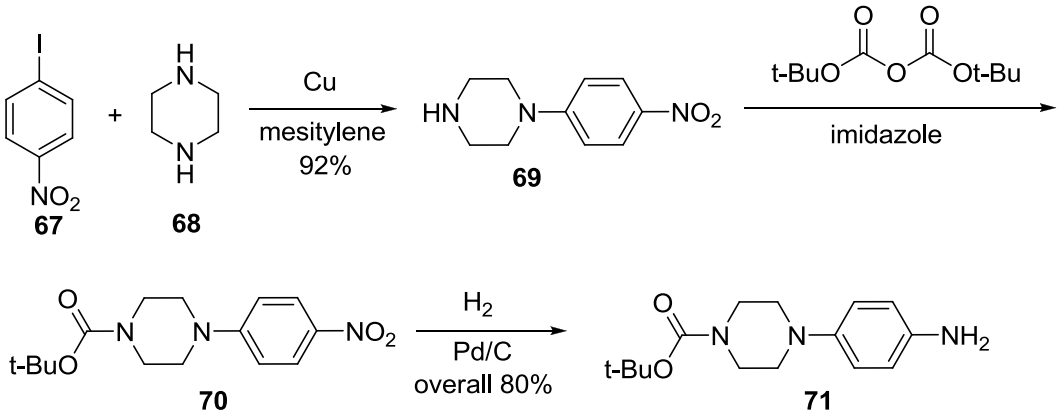
P-450 subunit	**Inhibitor Ref.**	**Ref. IC_{50} (μM)**	**XR9576 IC_{50}(μM)**	**63a IC_{50} (μM)**	**67a IC_{50} (μM)**	**67b IC_{50} (μM)**
CYP1A2	Furafylline	4.98	27.2	>100	>100	6.68
CYP2A6	Tranylcypromine	0.98	>100	>100	>100	n/a
CYP2B6	Tranylcypromine	10.3	>100	>100	>100	100
CYP2C8	Quercetin	1.56	45.3	5.82	13.3	1.08
CYP2C9	Sulfaphenazole	0.56	7.1	2.08	>10	0.0968
CYP2C19	Tranylcypromine	8.74	>10	14.7	23	0.393
CYP2D6	Quinidine	0.0074	100	>100	>100	17.3
CYP2E1	DDTC	17.1	>100	>100	>100	n/c
CYP3A4/BFC	Ketoconazole	0.096	>100	1.62	20.2	0.195
CYP3A4/BQ	Ketoconazole	0.26	>100	7.75	3.58	2.48

Compound **69b** inhibited both CYP3A4 and P-gp, while XR9576 and LY335979 selectively inhibited P-gp. Therefore, the new SNF analogue based on compound **67b** was designed. Since regions B and C significantly affect the activities, we decided to replace region D with SNF substructure. SNF analogue **13** with a SNF unit and an arylpiperazinyl unit of Tariquidar was expected to inhibit not only P-gp, but also CYP450.

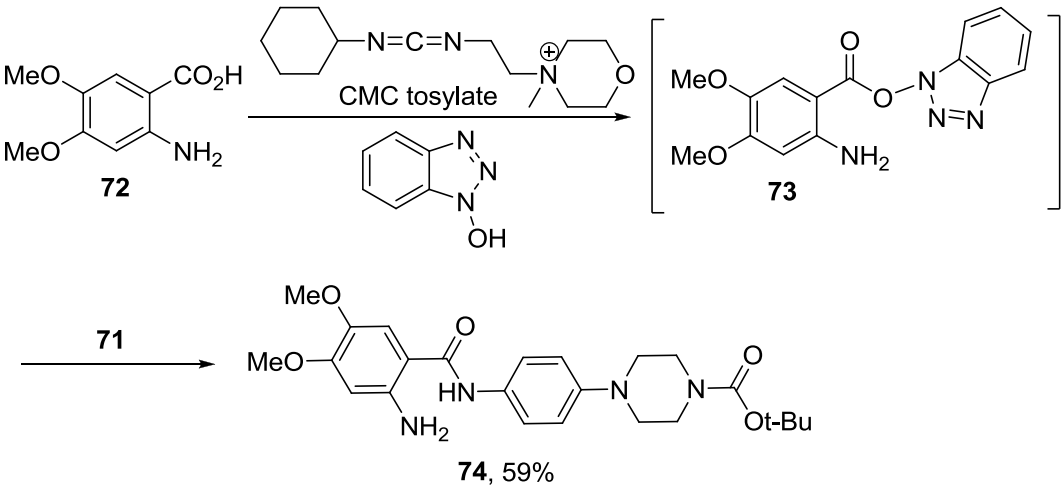
1.2.9.2 Preparation of SNF Analogue 13.

N-tert-Butoxycarbonyl (t-Boc) protected arylpiperazine **71** was prepared (Scheme 18). Under the catalysis of copper, p-nitroiodobenzene coupled with piperazine in mesitylene to afford compound **69** in 92% yield.[45] The protection of compound **69** with di-tert-butyl dicarbonate led to compound **70**.[46] The following selective hydrogenation

under the catalysis of palladium reduced the nitrophenyl group to give the desired compound **71** in overall 80% yield.[47]



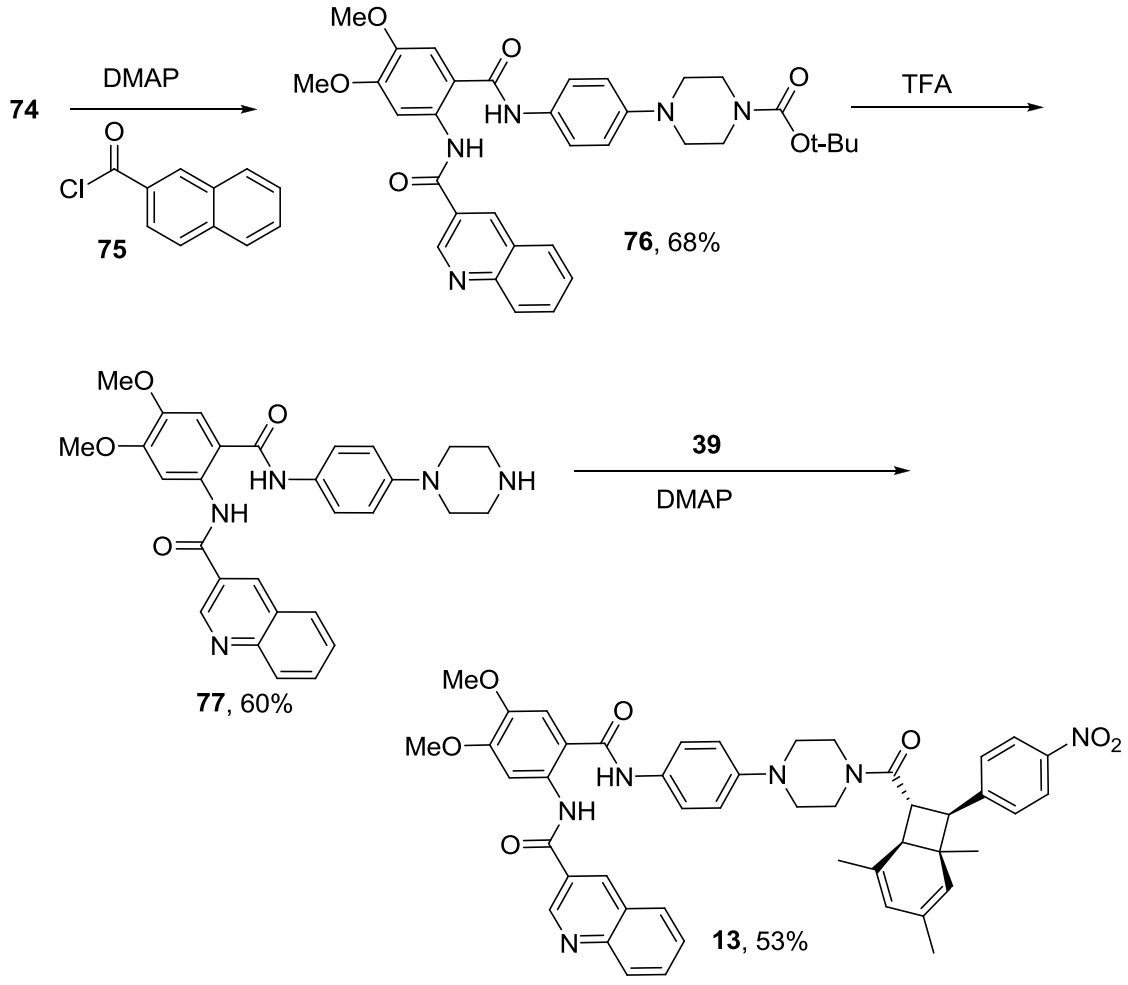
Scheme **18**. Preparation of arylpiperazine **71**.



Scheme **19**. Preparation of compound **74**

A special procedure was employed to couple compound **71** and 2-amino-4,5-dimethoxybenzoic acid **72** together (Scheme 19). First, 1-hydroxybenzotriazole (HOBt) and CMC tosylate activated the amino acid **72** to form an intermediate **73**. Then

compound **71** substituted the benzotriazole of the intermediate to afford the product **74** in 59% yield.[43]

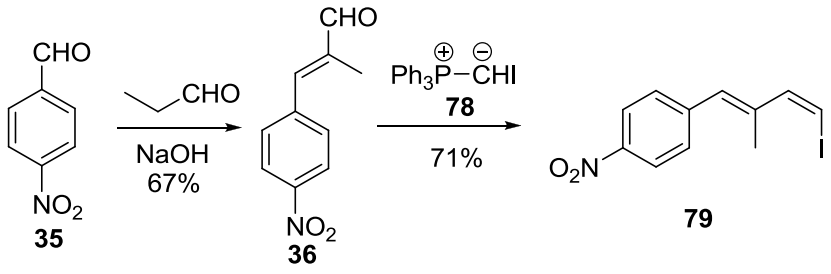


Scheme **20**. Preparation of SNF analogue **13**

The acylation of compound **74** with acid chloride **75** in the presence of 4-dimethylaminopyridine (DMAP) resulted in compound **76** in 68% yield. Treatment with trifluoroacetic acid (TFA) selectively removed the t-Boc protection group to give the piperazine **77** in 60% yield. In the presence of DMAP, SNF acid chloride **39** was added piperazine **77** to give the desired SNF analogue **13**, which contains the active regions of **67b** and a rigid SNF substructure, in 53% yield (Scheme 20).

1.2.10 The Synthesis of SNF Analogue 14

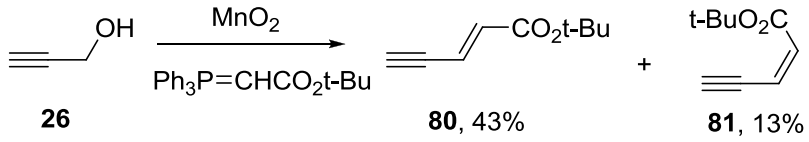
The synthetic route to SNF's bicyclo[4,2,0] system is not efficient. It takes seven steps to prepare the basic SNF analogue **4**, and the overall yield is 5% based on propargyl alcohol. The reason is that several low-yield reactions such as the Stork-Zhao reaction and the addition of methylmagnesium bromide to propargyl alcohol were used to make stereospecific olefins. Furthermore, the key Stille cross-coupling reaction utilizes toxic tin starting materials and also gives the products in low yield. Considering that the rigid bicyclic structure of SNF analogues plays an important role in mult-drug resistance reversal, we proposed that SNF analogues without two methyl group respectively on C-11 and C13 might also exhibit good activities against MDR. Therefore we developed a new strategy for the syntheses of SNF analogues, which does not require the vinyltin reagents.



Scheme **21**. Preparation of iododiene **79**.

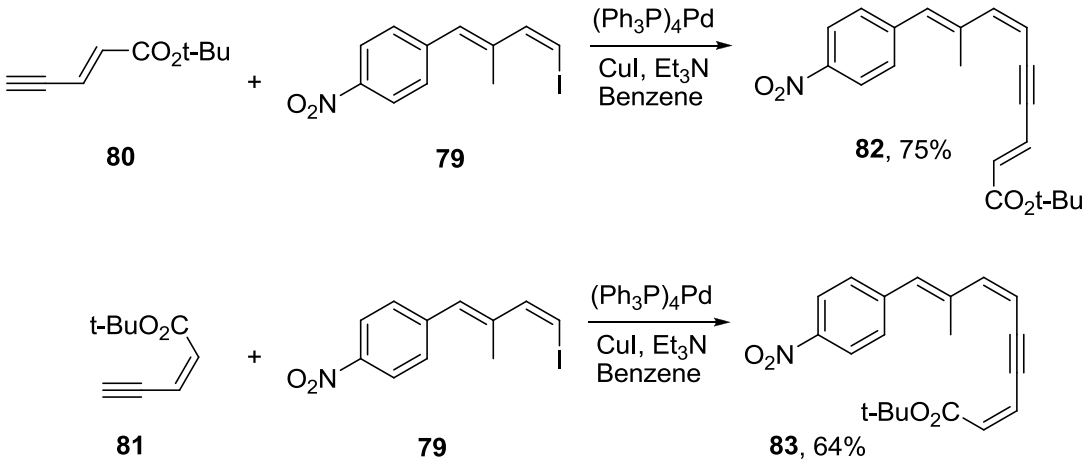
The cross-Aldol condensation of 4-nitrobenzaldehyde **35** and propionaldehyde afforded the aldehyde **36** in 67% yield (Scheme 21). Treatment with iodo-Wittig reagent **78**[48] converted the aldehyde **36** to (1Z,3E)-iododiene **79** in 71% yield.[49]

In a one-pot oxidation-olefination reaction, propargyl alcohol **26** was oxidized and then the resulting aldehyde was treated with a Wittig reagent to produce two isomers **80** and **81** in 43% and 13% yield, respectively (Scheme 22).[50]



Scheme **22**. Preparation of esters **80** and **81**.

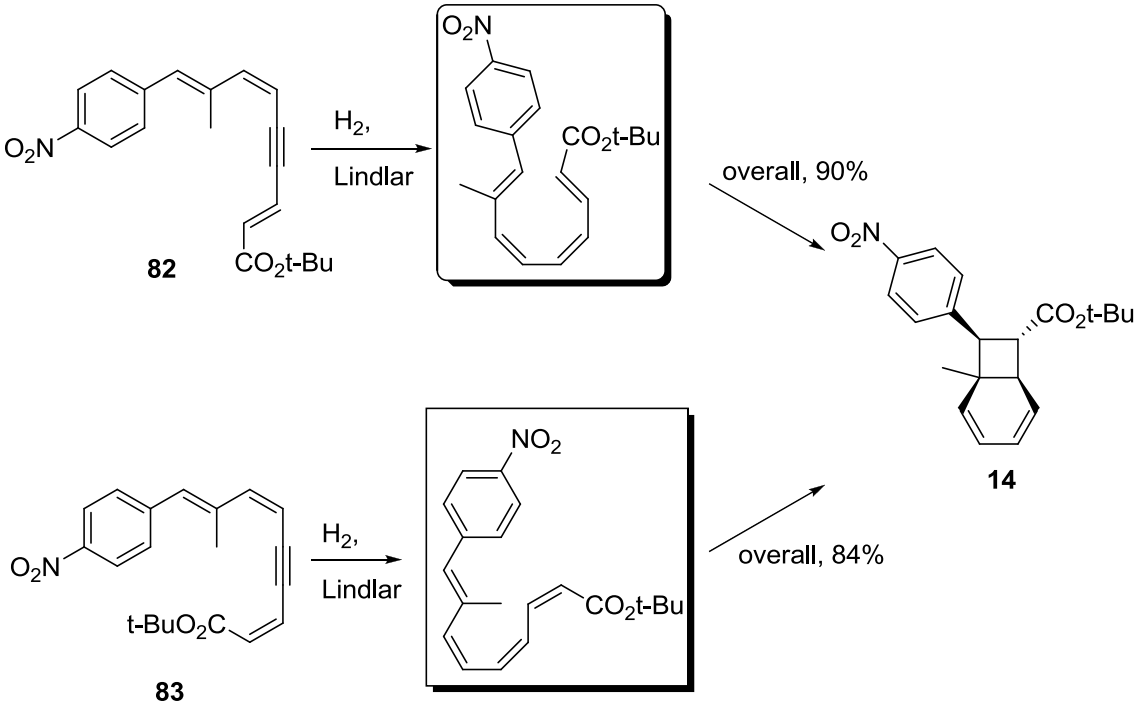
Sonogashira coupling of the trans-isomer **80** and iododiene **79** in the presence of tetrakis(triphenylphosphine)palladium ($(Ph_3P)_4Pd$) and copper(I) iodide (CuI) led to compound **82** in 75% yield (Scheme 23).[51] The cis-isomer **81** and iododiene **79** coupled to afford compound **83** in 64% yield. In the transition state of the reaction, since the cis-starting material **81** might cause a big steric effect, the yield of the corresponding product is lower.



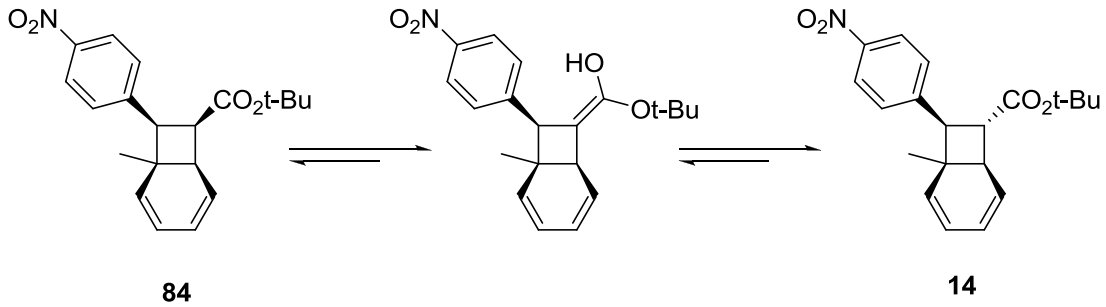
Scheme **23**. Preparation of esters **82** and **83**.

The hydrogenation of the triple bonds of isomer **82** in the presence of Lindlar catalyst gave the trans-endo product, SNF analogue **14**, in 90% yield (Scheme 24)[52]. The reduction of isomer **83** afforded the same product in 84% yield. The results suggest that the cis-endo product **84,** which resulted from epimerization of cis-isomer **83** to the

thermodynamically stable trans-endo product **14,** which was also made directly from trans-isomer **82** (Scheme 25).

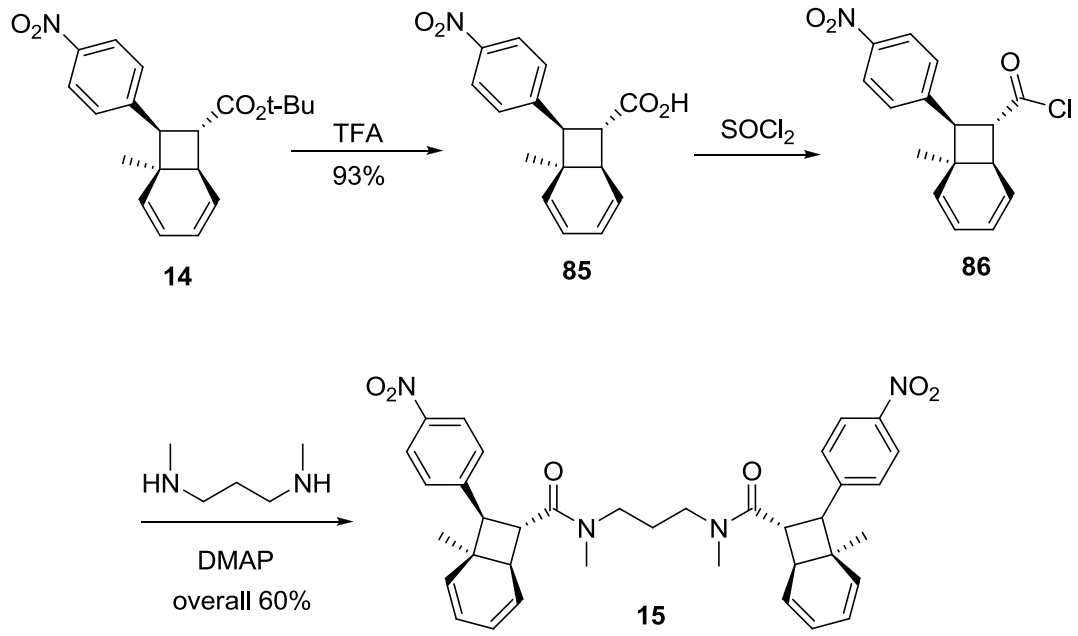


Scheme **24**. Preparation of SNF analogue **14**.



Scheme **25**. Epimerization of **84** to **14.**

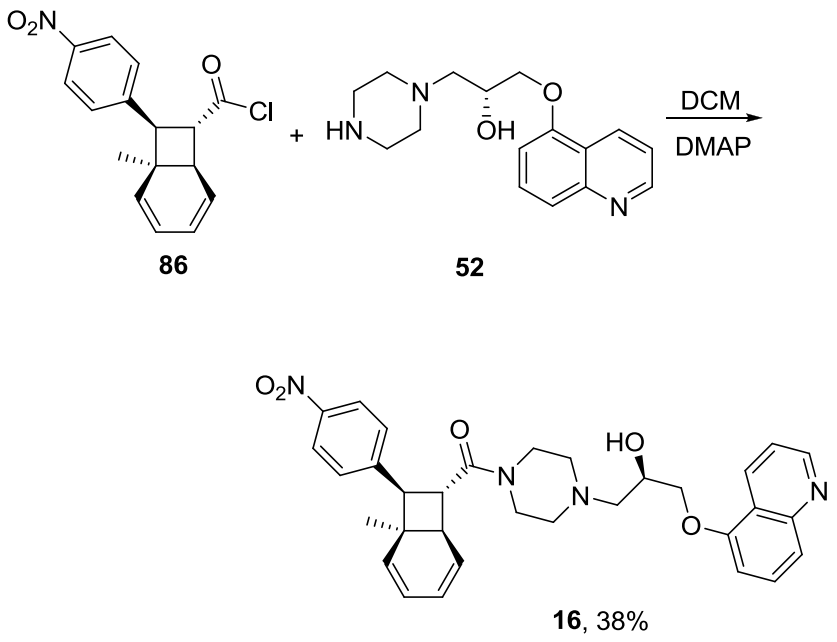
1.2.11 the Synthesis of SNF Analogue 15



Scheme **26**. Preparation of SNF analogue **15**.

SNF analogue **7** exhibited a good MDR reversal activity. In order to thoroughly investigate the P-gp inhibition of the new bicyclic coupound **14**, analogue **15** with two new bicyclic(4,2,0) units was prepared. Treatment with trifluoroacetic acid (TFA) removed the t-butyl group of SNF analogue **14** to afford acid **85** in 93% yield (Scheme 26). Excess thionyl chloride ($SOCl_2$) converted acid **85** to acid chloride **86**. In the presence of excess 4-(dimethylamino)pyridine (DMAP), 0.5 equivalent of N,N'-dimethylpropyldiamine was added to the acid chloride **86** to give SNF analogue **15** in 60% yield. Like SNF analogues **7**-**10**, analogue **15** was obtained as a pair of enantiomers and a meso-diastereomer.

1.2.12 the Synthesis of SNF Analogue 16



Scheme **27**. Preparation of SNF analogue **16**.

In biological tests, SNF analog **11** consisting of a functional unit of LY335979 and a SNF bicyclic unit showed an outstanding MDR reversal ability. We wondered whether anaolg **16** with a LY335979 unit and the new bicyclic substructure of **14** could possess a good activity as **11** does (Scheme 27). In the presence of excess 4-(dimethylamino)pyridine (DMAP), the piperazine **52** was acetylated by the acid chloride **86** to give SNF analogue **16** in 38% yield (Scheme 27).

1.2.13 Biological Activity of SNF Analogues

Dr. Ralph J. Bernacki and Dr. Paula Pera of Experimental Therapeutics Department at Roswell Park Cancer Institute tested some of the SNF analogues for reversal of multidrug resistance in the paired drug-sensitive and drug-resistant cell lines

MCF7 and MCF7 Adr(R), a drug-selected NCI cell line that has high levels of P-glycoprotein.[10] The protocol is that described in the literature.[12]

Table **5.** Effect of Modulators on Sensitivity to Taxol in MCF7-R Human Mammary Cells

Compound	IC50(μM) MCF7-S[1]	IC50(μM) MCF7-R[1]	Compound Tested in Combination With Paclitaxel (μM)	Paclitaxel IC_{50} (nM) MCF7-R	% Paclitaxel IC_{50} Reduction [4]
paclitaxel			none	1000	
3			10	90	91
4	>10	>10	10 and 1.0	100 and 740	90 and 26
5			10	270	73
6	>10 (0)[2]	>10 (0)[2]	1.0 [3]	861	14
7	>10 (0)[2]	>10 (0)[2]	1.0 [3]	329	67
11	>10 (42)[2]	>10 (42)[2]	1.0 [3]	5.1	99
12	>10 (0)[2]	>10 (0)[2]	1.0 [3]	825	18

[1]Human mammary carcinoma – MCF7-S – sensitive cell line, MCF7-R – multidrug resistant cell line.
[2]The IC50 value was greater than 10 μM for all reversal agents tested, however the % growth inhibition seen at 10 μM is indicated in parentheses.
[3]Reversal agent alone (at 1.0 μM) resulted in 0% growth inhibition
[4][100 - (IC_{50} reversal agent + paclitaxel/IC_{50} paclitaxel x100)]

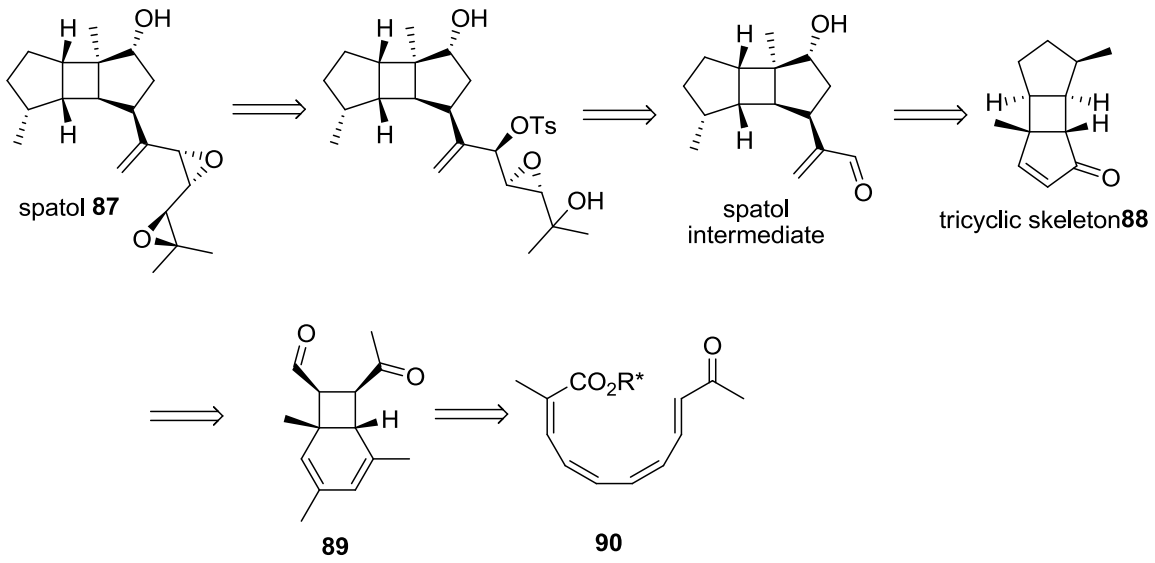
The biological results are showed in Table 5. The growth inhibitory effect of each compound alone is indicated in columns 2 and 3. Analog **11** inhibited cell growth by 42% at 10 μM in both cell lines and 0% at 1.0 μM in MCF7-R. For combination studies (performed in MCF7-R cells) with taxol, a concentration of compound which had no effect on cell growth (1 μM for analogs **4, 6, 7, 11,** and **12;** 10 μM for analogs **3**-**5**) was combined with varying concentrations of taxol. Columns 5 and 6 indicate the results of

this combination. Analog **11** was the most active in modulating sensitivity to taxol (99% reduction in IC50), followed by analog **12** (67% reduction in IC50). Analogs **5**, **6,** and **7** showed very little modulating activity. Ester analog **3**, in which the p-nitrophenyl substituent has been replaced by a 3,5-dimethylphenyl group is almost as active as ester **4**, indicating that the nitro group is not a significant contributor to activity.

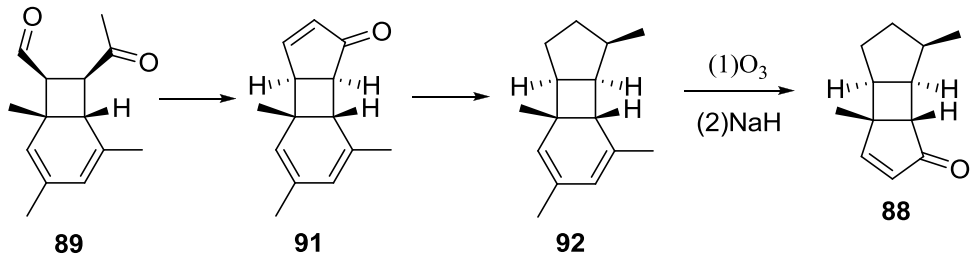
1.2.14 A Model for Synthesis of Spatol

Spatol **87**, a diterpene isolated from the brown algae *Spatoglossum howleii* (Scheme 28),[53] attracted much attention from chemists not only because of its relatively unique structure but also because of its biological activity. Spatol was considered as a potent inhibitor of cancer cell replication.[53] It was reported that spatol inhibited synchronous cell division in the fertilized sea urchin egg *(Lytechinus pictus*) at 1.2 μg/mL. Spatol was also found to inhibit human T242 melanoma and 224C astrocytoma cell lines in vitro with activity ranging from 1 to 5 μg/mL. A number of synthetic studies directed toward spatol and other spatane diterpenes have appeared.[54] The synthetic challenges include the stereoselective preparation of the cis,anti,cis-tricyclo[5.3.0.0]decane skeleton, as well as the labile diepoxide functionality.[55]

We proposed a new strategy for the synthesis of spatol tricyclic core **88**, which starts from the SNF bicyclic skeleton (Scheme 28). The spatol intermediate could be made from ketone **88** sequentially by reduction, Sharpless epoxidation, and further transformations. The synthetic route from the spatol intermediate to spatol has been reported.[56] The process consists of 1,2-addition, epoxidation, and cyclization.[57]



Scheme **28**. A proposal of the synthesis of spatol from a SNF bicyclic skeleton.

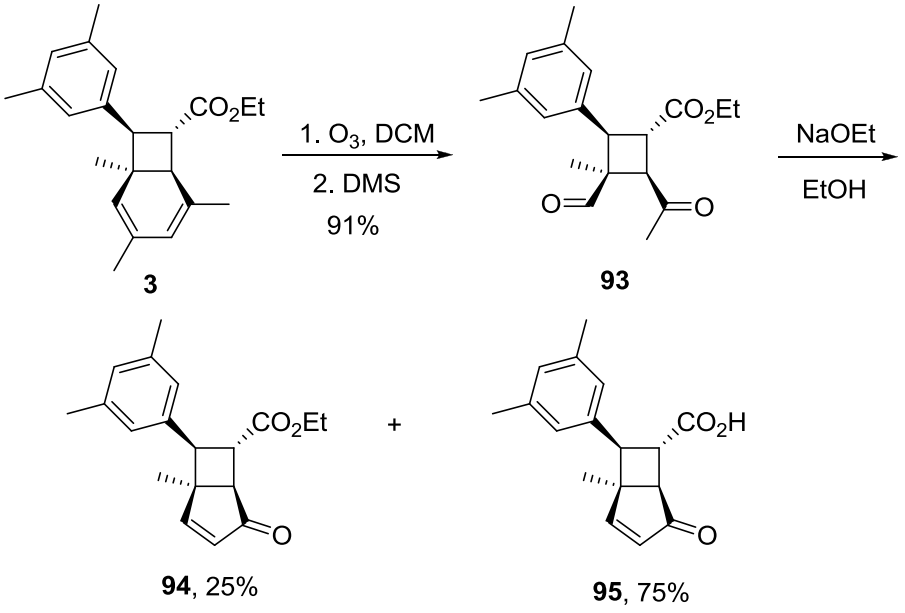


Scheme **29**. A proposed transformation from the compound **89** to ketone **88.**

Ketone **89** might cyclize by an intramolecular aldol condensation to the α,β-unsaturated ketone **91** (Scheme 29). The ketone **91** could be reduced to tricyclo[4,3,0,0] system **92**. Ozonolysis might open the six-membered ring of sesquiterpene **92** to form a cis-acetylcyclobutylcarbaldehyde intermediate which could cyclize by a following intramolecular aldol condensation to the desired spatol precursor **88**.[58]

In order to examine the proposal, a model based on SNF analog **3** was built (Scheme 30). The ozonolysis in the presence of dimethyl sulfide (DMS) cleaved the cyclohexadiene substructure of SNF analogue **3** to give cis-acetylcyclobutylcarbaldehyde

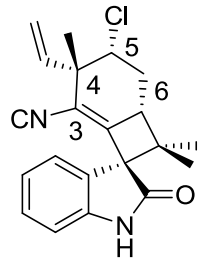
93 in yield 91%. Base-catalyzed intramolecular aldol condensation led to bicyclo[3.2.0]heptones **94** and **95** in yields 25% and 75%, respectively. Ester **94** underwnt a partial hydrolysis to the acid **95** during the aldol condensation.



Scheme **30**. Model reactions for spatol synthesis

1.2.15 Application of 8π/6π –Electrocyclization to the Synthesis of Welwitindolinone A Isonitrile

1.2.15.1 Background: Welwitindolinone A Isonitrile



welwitindolinone A isonitrile
96

Figure **11**. Welwitindolinone A isonitrile.

Several related oxindole-containing alkaloids, including hapalindole, fischerindole, ambiguine, and welwitindolinone, were isolated from marine blue-green algae *Hapalosiphon welwitschii* and *Westiella intricata* Borzi by Moore and co-workers.[59] Among the known welwitindolinones, the only one comprised of a highly functionalized spirocyclobutane oxindole carbon skeleton is welwitindolinone A isonitrile **96**. Consequently, this compound has been postulated to serve as the biosynthetic precursor to the remaining congeners.[59,60] Welwitindolinone A isonitrile **96** is a densely functionalized oxindole harboring three all-carbon quaternary centers, a neopentyl chlorine atom, and a striking spiro-fused cyclobutane that appears to be strained to exist upon cursory inspection.[61]

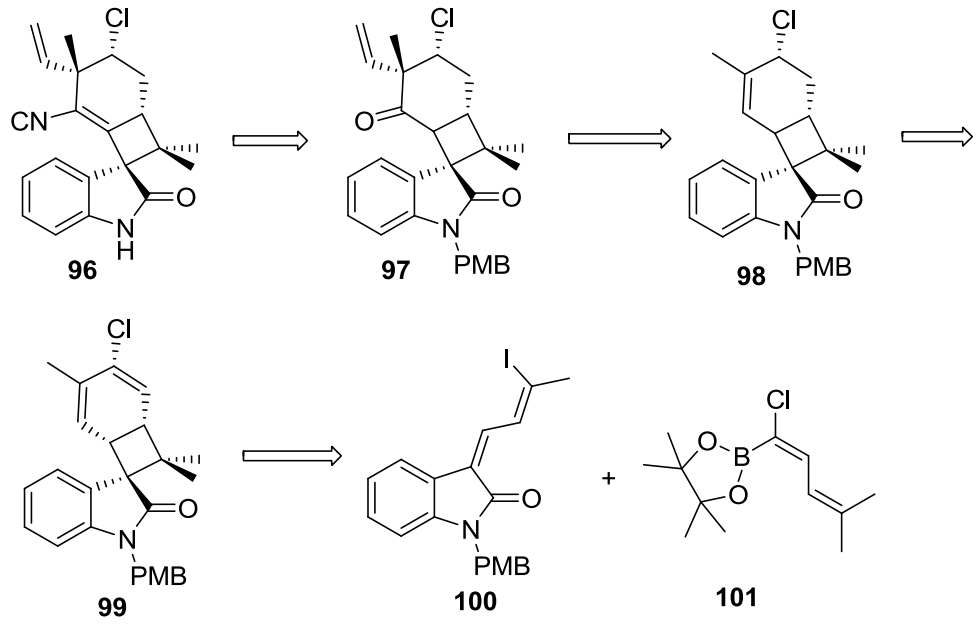
1.2.15.2 Biological Activity

Welwitindolinone A displays diverse and valuable biological activity, including reversal of P-glycoprotein-mediated multiple drug resistance (MDR), antifungal activity,

larvacidal activities, and inhibition of cancer cell proliferation. Similar to the effects of verapamil, welwitindolinone might attenuate the resistance of MCF-7/ADR cells to anticancer drugs, such as vinblastine, taxol, actinomycin D, daunomycin, and colchicine. These effects are apparent at doses as low as 0.1 μM, without affecting the cytotoxicity of cisplatin. Therefore it was considerably more potent than verapamil for reversal of MDR.[62]

1.2.15.3 Retrosynthetic Analysis of Welwitindolinone A Isonitrile

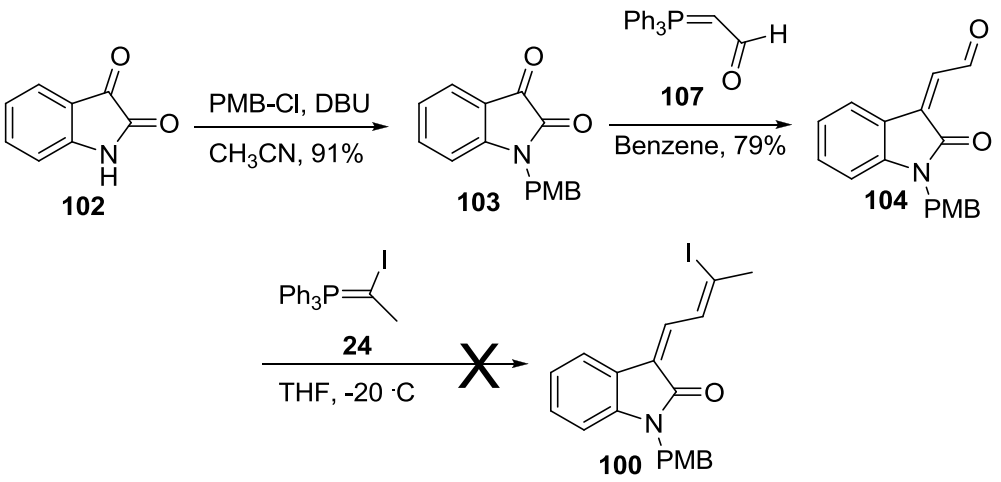
The synthetic method of the vinyl isonitrile region in welwitindolinone A isonitrile **96** from a ketone **97** has been reported (Scheme 31).[63] The carbonyl group of compound **97** could be converted to a formamide. The dehydration of the formamide by trifluoroacetic anhydride could form the target **96**. Bicyclo[4,2,0]octane **98** could be converted to the key intermediate **97** by a formation of cyclobutanone on C3,C4 double bond and a following ring opening.[64] Hydrazine might selectively hydrogenate the double bond of the vinyl chloride region (C5,C6) of cyclohexadiene **99** to give bicyclo[4,2,0]octane **98**.[65] The stability of the C3,C4 double bond and lower electron density of the C5,C6 double bond might provide the selectivity in the reduction. Pd-catalyzed Suzuki cross coupling of iododiene **100** and dienylborate **101** could lead to a tetraene.[66] The consequent tandem 8π, 6π-electonic cyclization could result in bicycle[4,2,0]octadiene **99**.



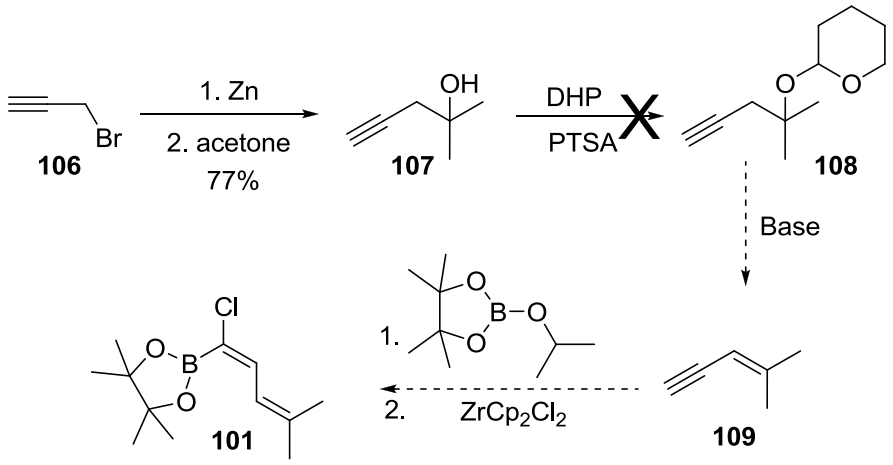
Scheme **31**. Retrosynthetic analysis of welwitindolinone A isonitrile.

1.2.15.4 Toward the Synthesis of Welwitindolinone A Isonitrile

The amide group of isatin **102** was protected by p-methoxybenzylchloride (PMB-Cl) to afford PMB-isatin **103** in 91% yield (Scheme 32).[67] Wittig reagent **105** transformed PMB-protected isatin to the aldehyde **104** in 79% yield.[68] However, Stork-Zhao reaction of the aldehyde **104** with ylide **24** did not produce iododiene **100** and the starting material **104** decomposed.

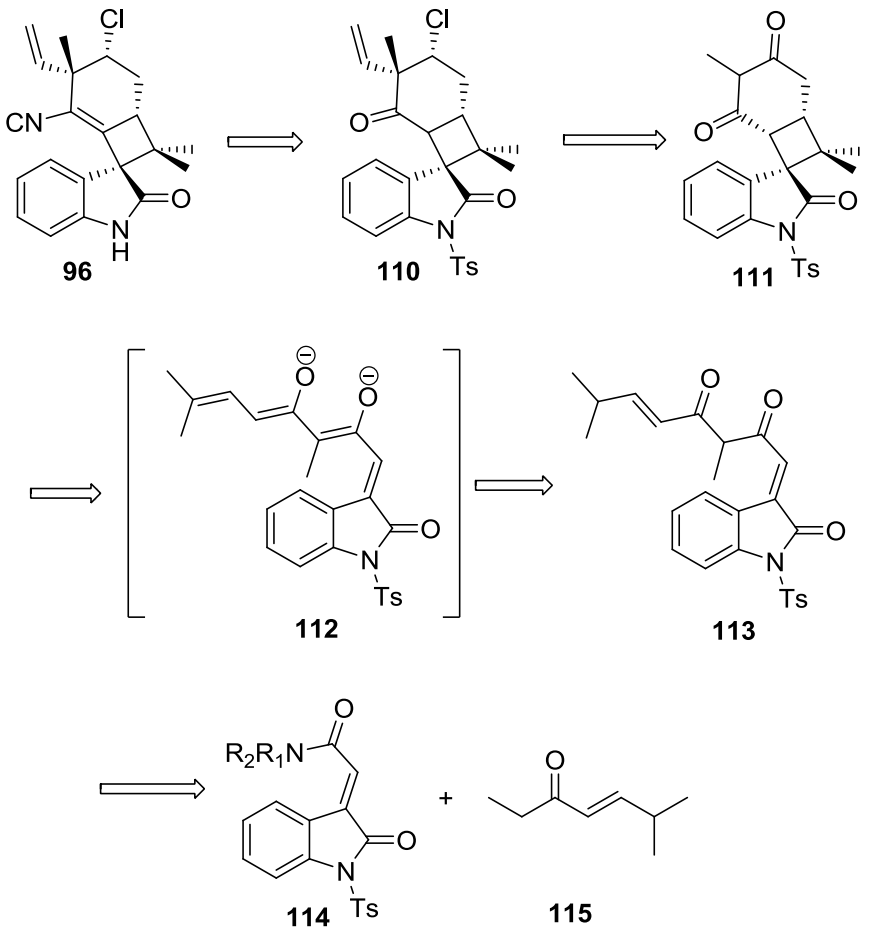


Scheme **32**. Attempt at preparation of iododiene **100**.



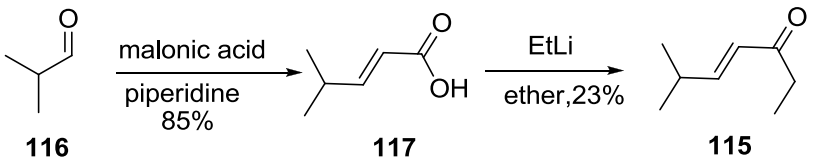
Scheme **33**. Attempt at preparation of dienylborate **101**.

Zinc-mediated addition of propargyl bromide **106** to acetone gave the tertiary alcohol **107** in 77% yield (Scheme 33).[69] Acid-catalyzed addition of **107** to 2,3-dihydropyran (DHP) did not afford desired 2-alkoxytetrahydrofuran **108** which was supposed to be transformed to a conjugated 4-methylpentenyne **109** by base-catalyzed elimination.[70]



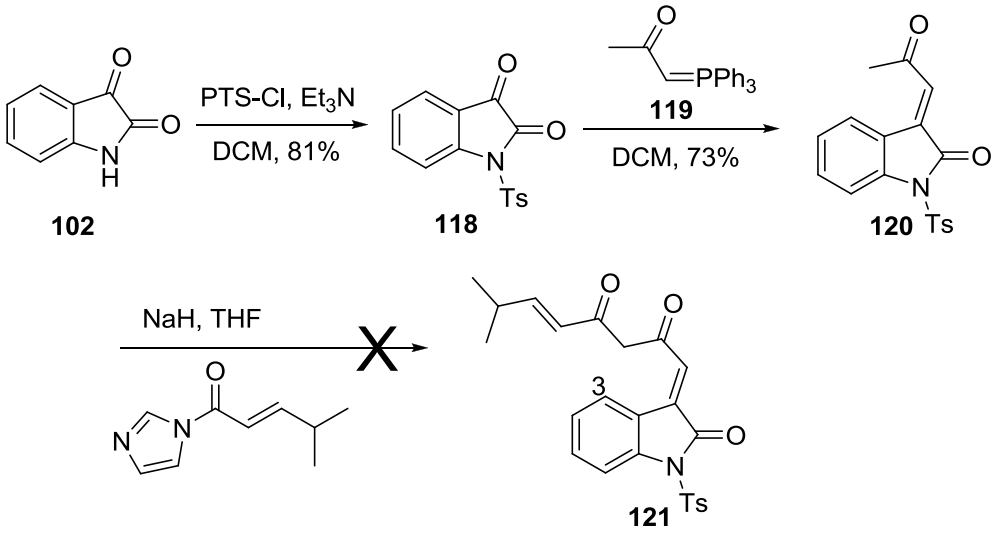
Scheme **34**. Revised synthetic route for welwitindolinone A isonitrile **96**.

Due to the absence of iododiene **100**, the proposed route (Scheme 31) for the synthesis of welwitindolinone A isonitrile **96** was revised (Scheme 34). The system of triphenylphosphine and tetrachloromethane might tranform β-diketone **111** to β-chloro-α,β-unsaturated ketone.[71] Reduction and further transformations of the β-chloroketone might produce the welwitindolinone intermediate **110**. Base catalysis might move the γ,δ-double bond of β-diketone **113** to δ,ε-position and result in a dienolate intermediate **112**. [72] The tandem 8π,6π-electonic cyclization of **112** could lead to bicycle[4,2,0]octadione **111**.[73] The cross condensation of ketone **115** and amide **114** might afford β-diketone **113**.[74]



Scheme **35**. Preparation of ketone **115**.

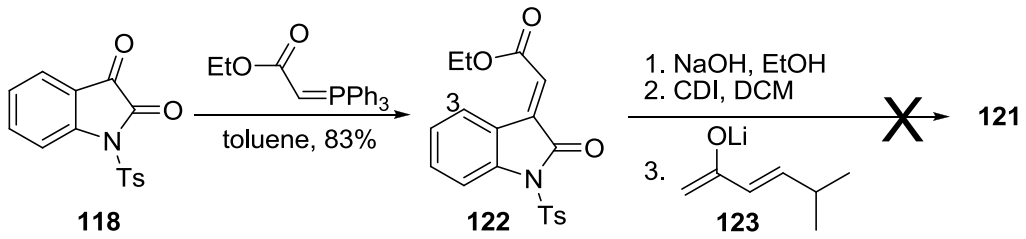
Isobutanal **116** condensed with malonic acid in the presence of piperidine to produce (E)-α,β-unsaturated acid **117** in 85% yield (Scheme 35). The addition of two equivalents of ethyl lithium (EtLi) to the acid **117** resulted in α,β-unsaturated ketone **115** in 23% yield.[75]



Scheme **36**. Attempt at preparation of β-diketone **121**.

Isatin **102** was protected by p-toluenesulfonic chloride (PTS-Cl) to form N-tosylisatin **118** in 81% yield (Scheme 36).[76] Wittig reaction **119** transformed the tosylisatin **118** to α,β-unsaturated ketone **120** in 73% yield.[77] The NMR spectrum of ketone **120** showed that the proton on C3 of the benzene ring is deshielded by the C=O double bond and has a larger down-field chemical shift than that of compound **118** do. Thus, compound **120** is the (E)-isomer. Condensation of the ketone **120** was subjecteded

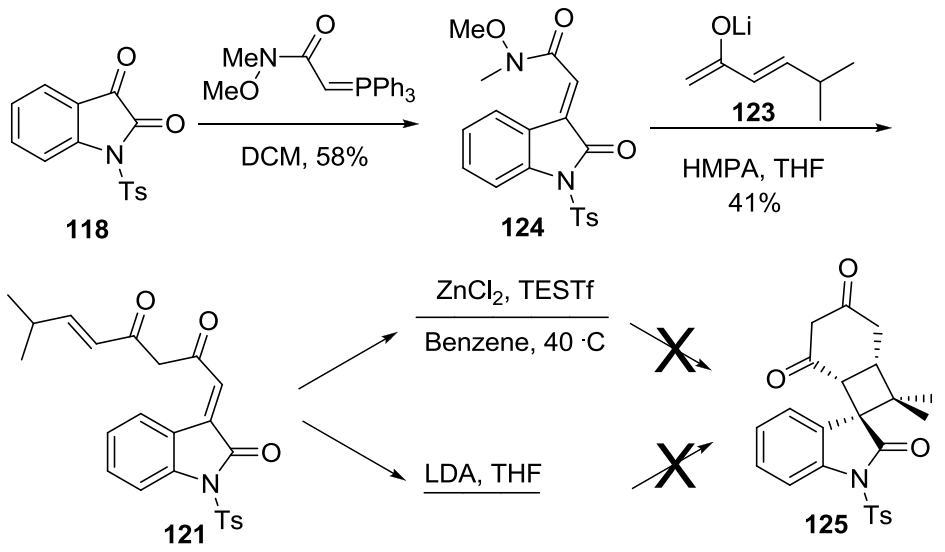
to the acyl imidazole derived from the acid **117**.[78] However, the desired compound **121** was not produced.



Scheme **37**. The second attempt at preparation of β-diketone **121**.

(E)-α,β-Unsaturated ester **122** was derived from tosylisatin **118** by a Wittig reaction in 83% yield (Scheme 37). The NMR spectrum of the product also showed that the proton on C3 of benzene ring has a larger down-field chemical shift, which means the compound has the (E)-configuration.[77] The ester **122** was hydrolyzed and then the acid was transformed to an acyl imidazole. The addition of an enolate of (E)-5-methylhex-3-en-2-one **123** to the acyl imidazole failed to lead to the diketone product **121** and gave the starting material back.

Weinreb amide **124** was provided by a Wittig reaction of tosylisatin **118** in 58% yield (Scheme 38). The NMR spectrum indicated only the (E)-isomer was present.[77] The cross condensation of Weinreb amide **124** and (E)-5-methylhex-3-en-2-one **123** afforded the target diketone **121** in 41% yield.[74] Two attempts failed to transform the diketone **121** to bicyclo[4,2,0]octadione **125**. First, treatment of the diketone **121** with zinc chloride and trimethylsilyl triflate in benzene was tried, but the target product **125** was not obtained and the starting material was recovered. Second, the diketone **121** was deprotonated by excess lithium diisopropylamide (LDA); however, the resulting dienolate did not cyclize to bicyclo[4,2,0]octadione **125** and the starting material was recovered.



Scheme **38**. Attempt at electrocyclization of β-diketone **125**.

1.3 Experimental Section

General

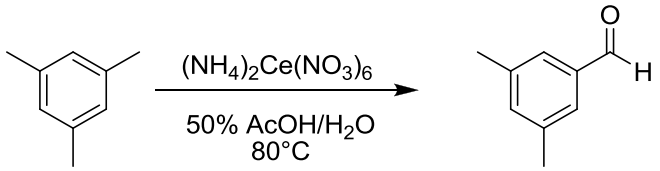
For all compounds, ^{1}H, ^{13}C and NOE NMR spectra were recorded on Varian Gemini 2300 (300 MHz), Inova 400 (400 MHz), Inova 500 (500 MHz), Inova 600 (600 MHz) spectrometer. Chemical shifts were measured relative to the residual solvent resonance for ^{1}H and internal reference. IR spectra were recorded on a Mattson Galaxy Series FTIR 3000 or 2020 spectrophotometer.

Reagents and solvents were purchased from Aldrich Chemical Company, Fisher Scientific or Acros Organics. Liquid reagents were purified by distillation prior to use. Unless otherwise noted, solid reagents were used without further purification. Methylene chloride, acetonitrile, cyclohexane, and toluene were distilled from CaH_2 under Ar atmosphere. Diethyl ether and THF were distilled from Na and benzophenone under Ar atmosphere.

All reactions unless otherwise noted were performed in oven-dried glassware under positive pressure of Ar. All yields are isolated yields.

Chromatographic separations were performed using Fisher grade 1740 type 60 Å silica gel (170-400 mesh). Analytical thin layer chromatography was performed using Analtech Uniplate pre-coated glass 250 micron silica gel GHLF plates with 254 nm fluorescent indicator. Preparative thin layer chromatography was performed using Analtech Uniplate pre-coated glass 1000 or 2000 micron silica gel GHLF plates with 254 nm fluorescent indicator.

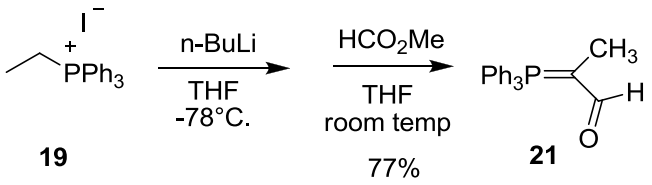
3,5-Dimethylbenzaldehyde 18.[23]



In a two-necked round bottom flask, 2 mL (14 mmol) of mesitylene **17** was mixed with 70 mL of 50% acetic acid in H_2O. The reaction mixture was heated to 80 °C. 31.37 g (57 mmol) ammonium cerium(IV) nitrate in 140 mL of 50% acetic acid/ H_2O was added dropwise into the reaction mixture. The color of the reaction system was always yellow. After the addition of the oxidant, the mixture was refluxed for 120 minutes till the reaction mixture turned colorless. The reaction system was cooled down and diluted by water. The solution was extracted three times with CH_2Cl_2. The organic layers were combined and dried by Na_2SO_4. After concentration by rotovap, the organic products were separated by a silica gel column with 30:1 hexanes and AcOEt to give 1.493 g (11 mmol) of colorless liquid **18** in 78% yield.

^{1}HNMR ($CDCl_3$): δ 9.93 (d, 1H, ^4J = 0.6 Hz), 7.48 (dd, 2H, ^4J = 0.6 Hz, ^4J = 0.3 Hz), 6.96 (m, 1H), and 2.39 (dd, 6H, ^4J = 2.4 Hz, ^4J = 0.3 Hz). IR (KBr): υmax 3031, 2969, 1738, 1698, 1598, and 1463 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature.[23]

2-(Triphenylphosphoranylidene)propionaldehyde 21.[24]

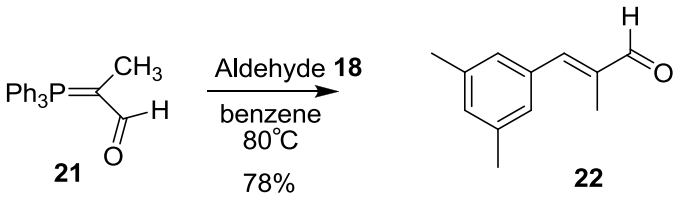


19 **21**

In 250 mL round bottom flask, 22 g (53 mmol) of ethyltriphenylphosphonium iodide **19** was mixed with 125 mL of THF. The 20 mL of 2.5 M n-BuLi was added dropwise to the suspension. The reaction turned into a red transparent solution. After the addition of n-BuLi, the reaction solution was stirred for 20 minutes. Then the red solution was transferred to a suspension of 6.5 g (68 mmol) of t-BuONa and 30 mL of THF. The reaction mixture was allowed to cool to 0 °C. After stirring for 10 minutes, 5 mL (83mmol) of methyl formate was added to this suspension rapidly. The reaction mixture turned white from red quickly. After stirring for 7 hours, when this mixture was completely white, the reaction was quenched by 1M HCl. The pH value was adjusted to 8.0. Then the solution was extracted by CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvent was removed by rotovap, 19 g of pale yellow solid was gotten. It was recrystallized in CH_2Cl_2 and Et_2O to give 17.1 g (42 mmol) of white solid **21** in 77% yield.

^{1}HNMR ($CDCl_3$): δ 8.06 (d, 1H, ^4J = 4.8 Hz), 7.6 (m, 15H), and 1.87 (d, 3H, ^4J = 13.5 Hz). The spectroscopic and other physical data reported are consistent with values reported in the literature. [24]

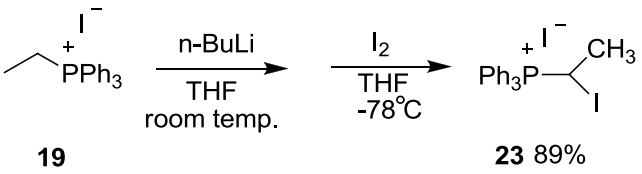
(*E*)-2-Methyl-3-(3,5-dimethylphenyl)-propenal 22.



249 mg (0.94 mmol) of 2-(triphenylphosphoranylidene)propionaldehyde **21** and 105 mg (0.783 mmol) of aldehyde **18** were mixed in 20 mL of dry benzene.[24] The reaction was refluxed at 80 °C. The NMR of the reaction mixture was check every five hours. After two days, the reaction was quenched by water. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed by rotovap, the organic products were separated by a silica gel column with 30:1 hexanes and AcOEt to give 90 mg (0.61 mmol) of yellow liquid **22** in yield 78%.

^{1}HNMR ($CDCl_3$): δ 9.57 (s, 1H), 7.16 (s, 2H), 7.05 (s, 1H), 6.98 (s, 1H), 2.37 (s, 6H), and 2.09 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 195.9, 150.6, 138.5, 135.3, 131.6, 130.1, 128.1, 126.3, 21.5, and 11.2. IR (KBr): υmax 3010, 2930, 2875, 2710, 1745, 1710, and 1610 cm^{-1}

(1-Iodoethyl)triphenyl-phosphonium iodide 24.[20]

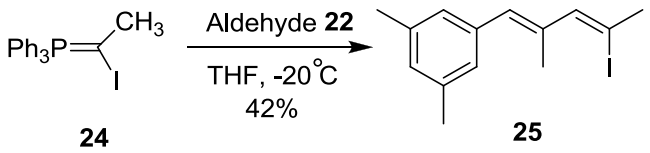


In 250 mL round bottom flask, 11 g (26 mmol) of ethyltriphenylphosphonium iodide **19** was mixed with 125 mL of THF. 10 mL of 2.5 M n-BuLi was added dropwise to the suspension. The reaction turned into a red transparent solution. After the addition of n-BuLi, the reaction solution was stirred for 20 minutes. The red solution was transferred to 21 mL of 1.1 M I_2/THF solutions at -78 °C by a cannula. The reaction

turned white from red. After addition of the red ylide, the reaction was stirred at room temperature for 5 hours. Then this mixture was quenched by 1 M HCl and a yellow solid was filtered off. This solid was washed by Et_2O till it turned white. 12 g (23 mmol) of white solid **23** was given (89%).

^{1}HNMR ($CDCl_3$): δ 7.8 (m, 15H), 6.93 (m, 1H), and 2.2 (d, 2H, ^3J = 7.2 Hz). The spectroscopic and other physical data reported are consistent with values reported in the literature. [20]

(E,Z)-Iodo-1,3-pentadiene 25.



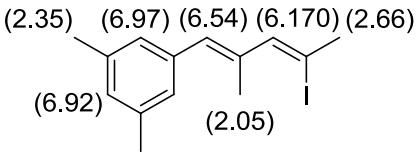
24 **25**

In 100 mL round bottom flask, 602 mg (1.1 mmol) of (1-iodoethyl)triphenyl-phosphonium iodide **24** was mixed with 20 mL of THF. The reaction was cooled down to -20 °C. The 1.8 mL of 1 M NaHMDS was added dropwise to the reaction. The yellow mixture turned into dark red and transparent. After stirring for 15 minutes, 150 mg (0.86 mmol) of aldehyde **22** in 5 mL of THF was added dropwise to the red solution. The dark red reaction solution turned into a brown black mixture. After stirring for 4 hours, this reaction was quenched by saturated NH_4Cl solution. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed by rotovap, the organic products were separated by a silica gel column with hexanes to give 64 mg (0.36 mmol) of yellow liquid **25** in 42% yield.

^{1}HNMR ($CDCl_3$): δ 6.94 (s, 2H), 6.89 (s, 1H), 6.51 (s, 1H), 6.14 (s, 1H), 2.63 (s, 3H), 2.33 (s, 6H), and 2.02 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 138.8, 137.8, 137.5, 136.0,

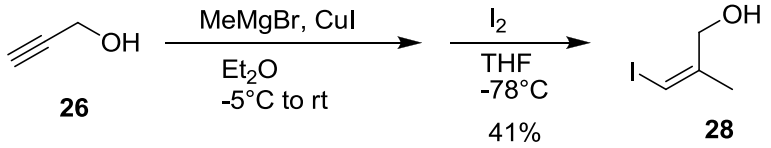
131.6, 128.7, 127.2, 127.1, 97.8, 35.4, 29.9, 21.6, and 18.2. IR (KBr): υmax 3010, 2980, 2885, 2810, 1620, and 1420 cm^{-1}

NOE:



Irradiated (saturated) peak	Enhanced peaks
2.66ppm	6.17ppm
6.17ppm	6.54, 2.66ppm
6.54ppm	6.97, 6.17ppm

(2Z)-3-Iodo-2-methyl-2-propen-1-ol 28. [25]

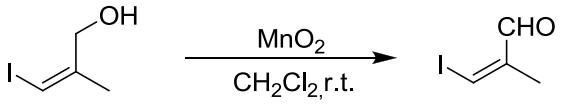


In 1 L round bottom flask, 1.5 mL (26.8 mmol) of propargyl alcohol **26** and 2 g (10.4 mmol) of dry CuI were mixed in 200 mL of Et_2O. 14 mL of 2.5 M methyl magnesium bromide (MeMgBr) was added dropwise to the reaction at 0 °C. The first 6 mL was added very carefully. After the CH_4 bubbling stopped, the left 8 mL was added a little bit fast. After addition of MeMgBr, the reaction became very viscid. After 20 hour continuous stirring, the reaction mixture turned dark green. 15 mL of 1.1 M I_2 solution in THF was added dropwise to the reaction mixture at -78 °C. The color of the reaction mixture first turned red from dark green, and then became yellow. The reaction mixture was stirred over night and quenched by the saturated NH_4Cl solution. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed by rotovap,

the organic products were separated by a silica gel column with 5:1 hexanes and AcOEt to give 2.1714 g (11 mmol) of yellow liquid **28** in 41% yield.

^{1}HNMR ($CDCl_3$): δ 5.98 (s, 1H), 4.25 (s, 2H), and 1.98 (s, 3H). IR (KBr): υmax 3455, 2920, 2950, 1721, 1460, 1379, 1138, and 1085 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [25]

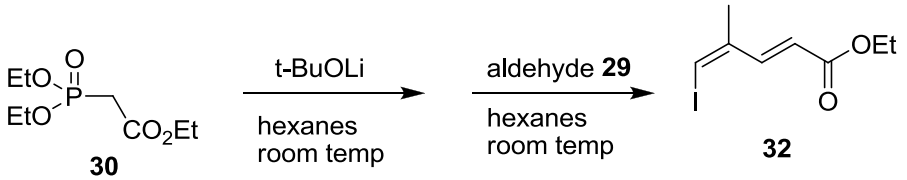
(2Z)-3-Iodo-2-methyl-2-propenal 29.[29]



28 **29**

In 50 mL round bottom flask, 200 mg (1 mmol) of alcohol **28** was mixed with 30 mL of dry CH_2Cl_2. 2 g (23 mmol) of MnO_2 was added into the reaction solution rapidly. The black reaction suspension was stirred for 3 hours. The extra MnO_2 was filtered off. The solvents were removed by rotovap. This aldehyde is not stable, so it was used in the next step as soon as possible.

(2E,4Z)-5-Iodo-diene ester 32. [27]



30 **32**

overall yield 56%

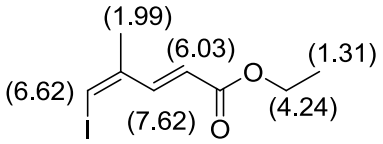
In 50 mL round bottom flask, 0.16 mL (0.71 mmol) of triethyl phosphonoacetate **30** was mixed with 20 mL of hexanes. 1 mL of 1 M lithium tert-butoxide was added dropwise to the solution. The reaction solution turned pale yellow from colorless. After 15 minutes stirring, 172 mg (0.65 mmol) of 2-(Z)-3-iodo-2-methyl-2-propenal **29** produced in the last step in 10 mL of hexanes was added dropwise to the reaction solution by syringe. The reaction solution turned orange. After 8 hours stirring, some small

insoluble oil drops appeared. The reaction was quenched by water. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed by rotovap, the organic products were separated by a silica gel column with 20:1 hexanes and AcOEt to give 141 mg (0.36 mmol) of yellow liquid **32** in 56% yield.

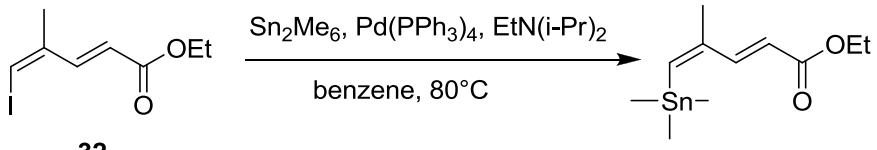
^{1}HNMR ($CDCl_3$): δ 7.62 (d, 1H, ^3J = 15.6 Hz), 6.62 (s, 1H), 6.03 (d, 1H, ^3J = 15.6 Hz), 4.23 (q, 2H, ^3J = 7.2 Hz), 1.99 (s, 3H), and 1.31(t, 3H, ^3J = 7.2 Hz). The spectroscopic and other physical data reported are consistent with values reported in the literature. [27]

NOE:

Irradiated (saturated) peak	Enhanced peaks
6.62ppm	1.99ppm



(2E,4Z)-5-(Trimethylstannyl)-diene ester 33. [20]



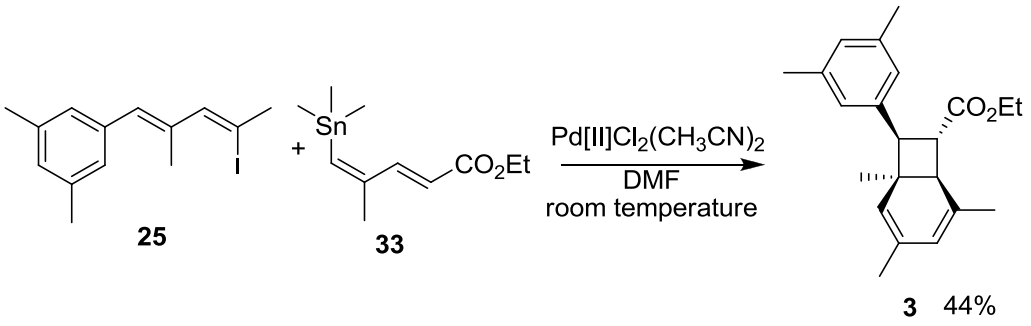
32 **33**

In 50 mL two-necked RBF, 130 mg (0.49 mmol) of (2E,4Z)-5-iodo-diene ester **32** was mixed with 30 mL of benzene. Then, 30 mg of catalyst tetrakis(triphenylphosphine)palladium(0) and 30 μL of N,N-diisopropylethylamine were added to the reaction solution. Finally, 200 μL of hexamethylstannane was added to the reaction solution. The reaction solution was refluxed at 80°C overnight. The pale yellow

reaction solution became a black mixture. After 15 hours refluxing, the reaction was cooled down to room temperature and stirred with KF and celite. The resulted insoluble matters were filtered off by celite. The residues were purified by a basic alumina column with benzene to give 120 mg (0.41 mmol) of pale yellow liquid **33** (82%).

^{1}HNMR (C_6D_6): δ 7.69 (d, 1H, ^3J = 15.6 Hz), 6.23 (s, 1H), 5.96 (d, 1H, ^3J = 15.6 Hz), 4.03 (q, 2H, ^3J = 7.2 Hz), 1.77 (s, 3H), 0.98 (t, 3H, ^3J = 7.2 Hz), and 0.19 (s, 9H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [20]

SNF analog 3.



25 **33** **3** 44%

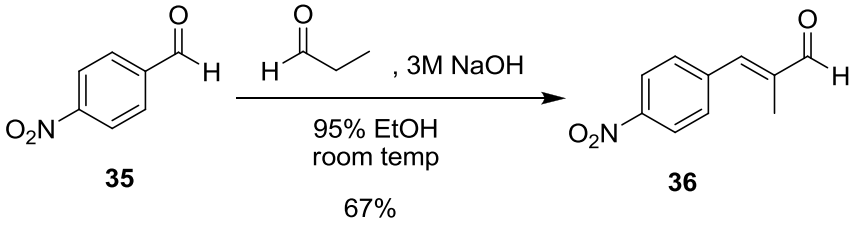
In a 50 mL round bottom flask, 40 mg (0.132 mmol) of (2E,4Z)-5-(trimethylstannyl)-diene ester **33** was mixed with 30 mL of dry DMF. Then 40 mg (128 mmol) of (E,Z)-iodo-1,3-pentadiene **25** and 3 mg of bis(acetonitrile)dichloropalladium(II) were added into the reaction solution. The reaction mixture was stirred in dark for 24 hours. 1 mg of catalyst $PdCl_2(CH_3CN)_2$ was added. After 5 hours stirring, the reaction was quenched by potassium fluoride (KF) and Celite. The resulted insoluble matters were filtered off by Celite. The residues were washed by saturated $NaHCO_3$. The solution was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed by rotovap, the organic products were separated by a silica gel column with 200:1 hexanes and AcOEt to give 21 mg (0.058 mmol) of yellow liquid **3** (44%).

^{1}HNMR ($CDCl_3$): δ 6.86 (s, 1H), 6.81 (s, 2H), 5.44 (s, 1H), 4.58 (s, 1H), 4.13 (m, 2H), 3.59 (d, 1H, ^{3}J = 10.8 Hz), 3.42 (dd, 1H, ^{3}J = 10.8 Hz, ^{3}J = 9.0 Hz), 2.63 (d, 1H, ^{3}J = 9.0 Hz), 2.30 (s, 6H), 1.78 (s, 3H), 1.64 (s, 3H), 1.23 (t, 3H, ^{3}J = 6.6 Hz), and 1.22 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 174.0, 137.7, 134.1, 129.7, 128,1, 122.2, 60.3, 56.0, 46.2, 46.2, 43.4, 29.7, 28.4, 21.9, 21.6, and 14.2. IR (KBr): υmax 2950, 2855, 1740, 1600, 1440, 1380, and 1005 cm^{-1}

NOE:

Irradiated (saturated) peak	Enhanced peaks
5.455 ppm	1.793, 1.645 ppm
4.602 ppm	1.645 ppm
3.42 ppm	6.822 ppm
3.608 ppm	6.813 ppm
2.64 ppm	3.617 ppm

(*E*)-2-Methyl-3-(4-nitro-phenyl)-propenal 36.[28]

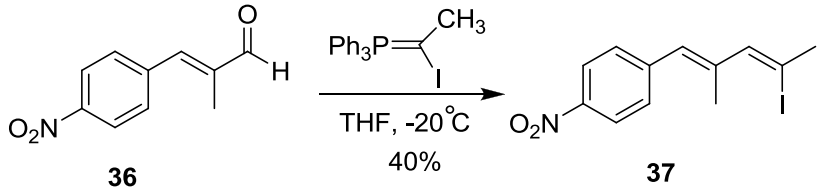


In a 50 mL round bottom flask, 2 g (13.2 mmol) of 4-nitrobenzaldehyde **35** and propionaldehyde were mixed in 95% ethyl alcohol. 2 mL of 3 M NaOH was added into the reaction mixture at room temperature. The reaction mixture became dark red. After 4 hours stirring, the reaction was quenched by 1 M HCl. The pH value was adjusted to 8.0. The reaction mixture was extracted three times with Et_2O. The organic layers were combined and dried over Na_2SO_4. After the solvents were removed in vacuo, the organic products were separated by a silica gel column with 2:1 hexanes and AcOEt. The product

was recrystallized in a mixture of EtOH and hexanes to give 1.7 g (8.8 mmol) of yellow solid **36** (67%).

^{1}HNMR ($CDCl_3$): δ 9.65 (s, 1H), 8.30 (d, 2H, ^{3}J = 8.8 Hz), 7.66 (d, 2H, ^{3}J = 8.8 Hz), 7.32 (s, 1H), and 2.09 (s, 3H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [28]

(E,Z)-1-(4-Nitro-phenyl)-2-methyl-4-iodo-1,3-pentadiene 37.[20]



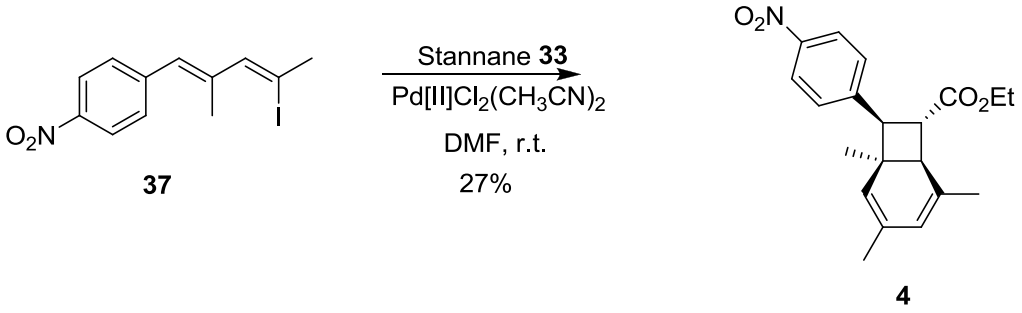
36 **37**

In 50 mL round bottom flask, 3 g (5.5 mmol) of (1-iodoethyl)triphenyl-phosphonium iodide was added to 25 mL of THF. The reaction suspension was cooled down to -20 °C. Then 4 mL of 1 M NaHMDS was added dropwise to the reaction suspension. The yellow mixture became dark red and transparent. After 15 minutes stirring, 1 g (5.3 mmol) of (*E*)-2-methyl-3-**(**4-nitro-phenyl)-propenal **36** in 5 mL of THF was added dropwise to the red solution. The dark red reaction solution turned into a brown black mixture. After 4 hours stirring, this reaction was quenched by the saturated NH_4Cl solution. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed in vacuo, the organic products were separated by a silica gel column with 50:1 hexanes and AcOEt to give 703 mg (2.2 mmol) of yellow liquid **37** (40%).

^{1}HNMR ($CDCl_3$): δ 8.20 (d, 2H, ^{3}J = 8.0 Hz), 7.44 (d, 2H, ^{3}J = 8.0 Hz), 6.59 (s, 1H), 6.17 (s, 1H), 2.65 (s, 3H), and 2.01 (s, 3H). IR (KBr): υmax 3071, 3000, 2961, 2913,

1592, 1514, 1491, and 1434 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [20]

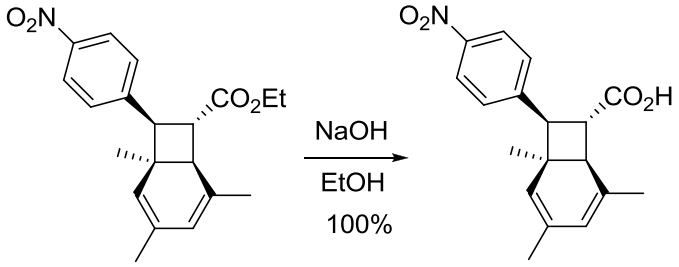
SNF analog 4.[20]



In a 50 mL round bottom flask, 35 mg (0.127 mmol) of (2E,4Z)-5-(trimethylstannyl)-pentadiene ester **33** was dissolved in 30 mL of dry DMF. Then 42 mg (0.138 mmol) of compound **37** and 3 mg of bis(acetonitrile) dichloropalladium(II) were added into the reaction solution. The reaction mixture was stirred in dark for 24 hours. 1 mg of catalyst $PdCl_2(CH_3CN)_2$ was added. After extra 5 hours stirring, the reaction was quenched by KF and Celite. The resulted insoluble matters were filtered off by Celite. The residues were washed by saturated $NaHCO_3$. The solution was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed in vacuo, the organic products were separated by a silica gel column with 40:1 hexanes and AcOEt to give 10 mg (0.034 mmol) of yellow liquid **4** (27%).

^{1}HNMR ($CDCl_3$): δ 8.17 (d, 2H, ^3J = 8.0 Hz), 7.23 (d, 2H, ^3J = 8.0 Hz), 5.47 (s, 1H), 4.43 (s, 1H), 4.14 (m, 2H), 3.75 (d, 1H, ^3J = 10.8 Hz), 3.44 (dd, 1H, ^3J = 10.8 Hz, ^3J = 9.0 Hz), 2.74 (d, 1H, ^3J = 9.0 Hz), 1.80 (s, 3H), 1.62 (s, 3H), 1.26 (s, 3H), and 1.24 (t, 3H, ^3J = 6.6 Hz). ^{13}CNMR ($CDCl_3$): δ 173.5, 146.9, 145.9, 134.3, 131.1, 128.3, 123.6, 122.4, 121.372, 60.8, 56.0, 46.1, 44.3, 28.5, 22.1, 21.7, and 14.3. IR (KBr): υmax 2966, 2941, 2913, 1727, 1620, 1518, 1445, and 1178 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [20]

SNF acid 38.

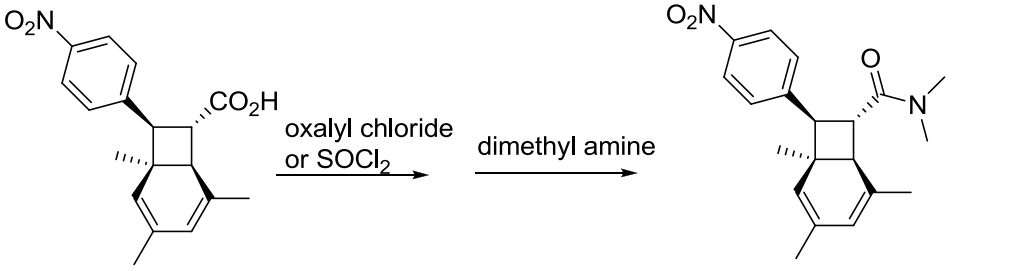


4 **38**

The ester (**4**, 6 mg, 0.0175 mmol) was dissolved in ethanol (95%, 1 mL). KOH/EtOH (0.05 M, 1 mL) solution was added to the mixture dropwise. The yellow solution was stirred at r.t. over night. The reaction was quenched by HCl/H_2O (1 M, 5 mL). The water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo to give 6mg crude product. The NMR showed that the crude product was pure enough.

^{1}HNMR ($CDCl_3$): δ 8.17 (d, 2H, ^3J = 8.5 Hz), 7.34 (d, 2H, ^3J = 8.5 Hz), 5.47 (s, 1H), 4.42 (s, 1H), 3.74 (d, 1H, ^3J = 10 Hz), 3.49 (t, 1H, ^3J = 10 Hz, ^3J = 9.5 Hz), 2.76 (d, 1H, ^3J = 9.5 Hz), 1.80 (s, 3H), 1.62 (s, 3H), and 1.26 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 179.1, 147.0, 145.6, 134.2, 131.4, 128.4, 123.7, 122.7, 121.2, 56.1, 46.0, 44.4, 29.9, 28.7, 22.2, and 21.7. IR (KBr): υmax 3500, 2945, 2825, 1662, 1619, 1474, and 1258cm^{-1}.

SNF dimethyl amide 5.



38 **5** overall 66%

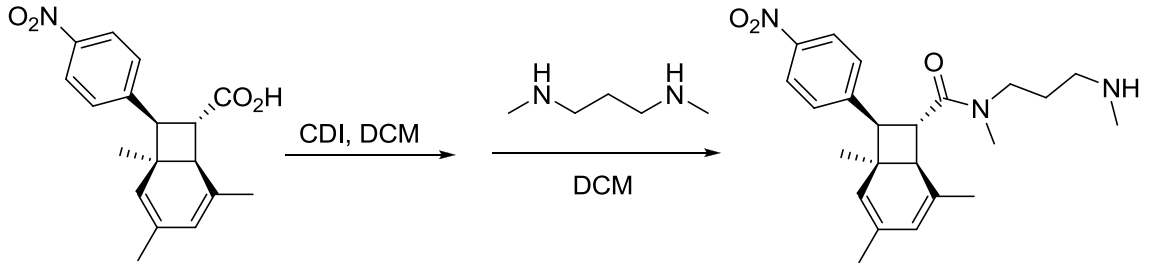
The acid (**38**, 6 mg, 0.019 mmol) was dissolved in dry benzene (2 mL). Dimethylformamide (1 drop) was added to the solution. Oxalyl chloride (0.05 mL) was added to the mixture at 0 °C.[31] The reaction was stirred at 0 °C for 2 hours and at r.t. for 1 hour. The mixture was concentrated in vacuo. Dimethyl amine (40% in water, 0.5 mL) in acetone (0.5 mL) was added to the acid chloride at 0 °C. The reaction was stirred at r.t. overnight and quenched by HCl (1 M in water, 2 mL). The water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was purified by a TLC plate with ethyl acetate and hexanes (1:2) to give the amide **5** (4 mg, 0.012 mmol, 66%).

^{1}HNMR ($CDCl_3$): δ 8.16 (d, 2H, ^3J = 9.0 Hz), 7.33 (d, 2H, ^3J = 9.0 Hz), 5.49 (s, 1H), 4.50 (s, 1H), 3.87 (d, 1H, ^3J = 9.6 Hz), 3.71 (dd, 1H, ^3J = 9.6 Hz, ^3J = 9.0 Hz), 2.94 (d, 6H, ^3J = 7.2 Hz), 2.81 (d, 1H, ^3J = 9.0 Hz), 1.74 (s, 3H), 1.68 (s, 3H), and 1.24 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 161.9, 134.5, 132.8, 130.0, 128.7, 123.6, 56.0, 54.1, 46.5, 44.4, 36.2, 29.9, 28.3, and 22.2. IR (KBr): υmax 3390, 3290, 2985, 2810, 1715, 1382, and 1149 cm^{-1}.

NOE:

Irradiated (saturated) peak	Enhanced peaks
5.492 ppm	1.744, 1.675 ppm
4.502 ppm	1.677 ppm
3.8 ppm	3.81, 1.237, 7.33 ppm
3.69 ppm	2.936, 7.33 ppm
2.81 ppm	3.87, 1.746, 1.238 ppm

SNF analog 6.

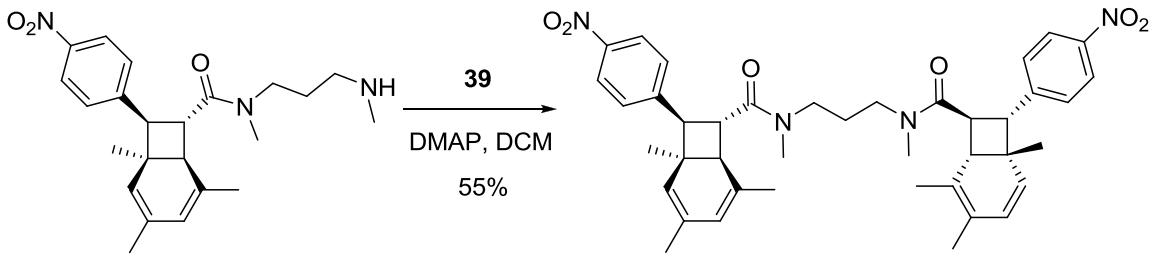


38 **6** overall 65%

The acid (**38**, 50 mg, 0.16 mmol) and carbonyl diimidazole (40 mg, 0.25 mmol) were dissolved in dry methylene chloride (2 mL).[31] The mixture was stirred at r.t. for one hour. A little gas was released. The N,N'-dimethyl-1,3-propanediamine (0.2 mL) in dry methylene chloride (1 mL) was added to the mixture. The reaction was stirred at r.t. for 18 hours. The solution was diluted with 10ml methylene chloride. The mixture was washed by water. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a TLC plate with methanol and methylene chloride (1:10) to give yellow oil **6** (42 mg, 10 mmol, 65%)

^{1}HNMR ($CDCl_3$): δ 8.15 (d, 2H, ^3J = 8.0 Hz), 7.31 (d, 2H, ^3J = 8.0 Hz), 5.48 (s, 1H), 4.74 (s, 1H), 3.77 (d, 1H, ^3J = 9.6 Hz), 3.70 (t, 1H, ^3J = 9.6 Hz, ^3J = 8.4 Hz), 3.49 (m, 2H), 2.94 (s, 3H), 2.81 (m, 2H), 2.72 (d, 1H, ^3J = 8.4 Hz), 2.60 (s, 3H), 2.09 (m, 3H), 1.70 (s, 3H), 1.65 (s, 3H), and 1.21 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 174.2, 147.0, 145.7, 133.5, 131.1, 128.5, 123.7, 123.3, 122.2, 70.6, 55.8, 46.8, 46.6, 45.1, 44.3, 44.2, 35.9, 33.3, 28.3, 24.0, 22.1, and 22.1. IR (KBr): υmax 3390, 2985, 1740, 1630, 1515, 1345, 1275, and 1115 cm^{-1}. ESI-MS ($M-H^+$): 398.14, 399.19, and 400.22 g/mol.

SNF analog 7.

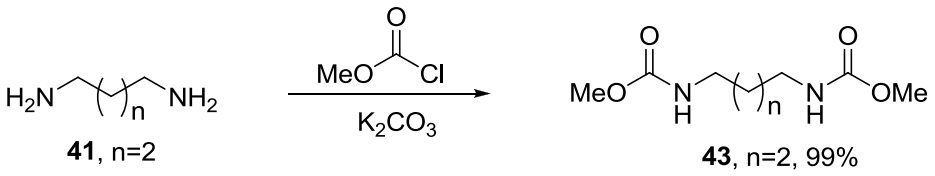


6 7

The acid (**38**, 29 mg, 0.09 mmol) was dissolved in dry methylene chloride. Thionyl chloride (0.1 mL) was added dropwise to the mixture at 0 °C.[32] The reaction was stirred for half an hour and then concentrated in vacuo. The residues were placed in high vacuo for 2 hours to remove extra thionyl chloride. 4-Dimethylaminopyridine (12 mg, 0.1 mmol) and the amine (**6**, 15 mg, 0.1 mmol) were mixed in methylene chloride (2 mL). The residues were added dropwise to the mixture by a pipet at 0 °C. The reaction was stirred at r.t. for 3 hours and quenched by N,N'-dimethyl-1,3-propanediamine (0.1 mL). The mixture was washed by sat. ammonium chloride solution. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a TLC plate with ethyl acetate and hexanes (1:1) to give yellow oil **7** (15 mg, 0.05 mmol, 55%).

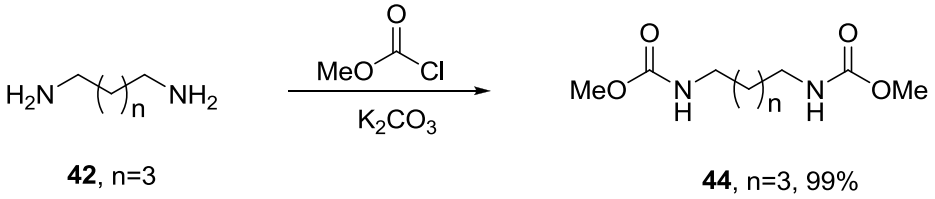
^{1}HNMR ($CDCl_3$, mixture): δ 8.14 (m, 4H), 7.33 (m, 4H), 5.47 (d, 2H), 4.50 (d, 2H), 3.84 (m, 2H), 3.66 (m, 2H), 2.91 (m, 6H), 2.74 (m, 2H), 1.68 (m, 15H), and 1.22 (m, 6H). ^{13}CNMR ($CDCl_3$): δ 172.5, 146.9, 146.3, 134.1, 131.0, 128.8, 128.5, 127.9, 123.6, 123.0, 122.4, 55.8, 47.6, 46.7, 46.6, 45.9, 44.4, 35.7, 34.0, 28.4, 26.7, 24.9, 22.2, and 22.0. IR (KBr): υmax 2945, 1770, 1640, 1600, 1520, and 1135 cm^{-1}. ESI-MS ($M-H^+$): 693.27, and 694.37 g/mol.

Dicarbamates 43.[33]



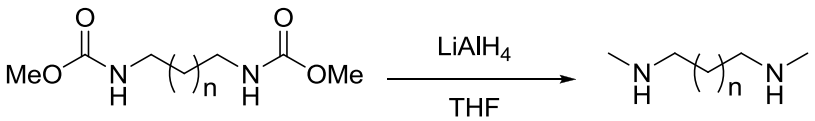
1,4-Butanediamine (2 g, 22.7 mmol) in water (30 mL) and methylene chloride (30 mL) was added potassium carbonate (3.2 g). Ethyl chloroformate (6.5 mL, 66 mmol) was added to the reaction at 0 °C. The reaction was stirred for 4 hours at room temperature. The solution was poured in 250 mL of 1 M ice cold hydrochloric acid solution. The solution was extracted three times with methylene chloride. The organic solution was concentrated to give a pure white solid **43** (4.54 g, 22.5 mmol, 99%) which was used directly in reduction.

Dicarbamates 44.[33]



1,5-Pentanediamine (2 mL, 20 mmol) in water (40 mL) and methylene chloride (40 mL) was added potassium carbonate (3.0 g). Methyl chloroformate (5.5 mL, 60 mmol) was added to the reaction at 0 °C. The reaction was stirred for 4 hours at room temperature. The solution was poured in 250 mL of 1 M ice cold hydrochloric acid solution. The solution was extracted three times with methylene chloride. The organic solution was concentrated to give a pure white solid **44** (5.92 g, 20 mmol, 99%) which was used directly in reduction.

N,N'-Dimethyldiamines 45.[34]

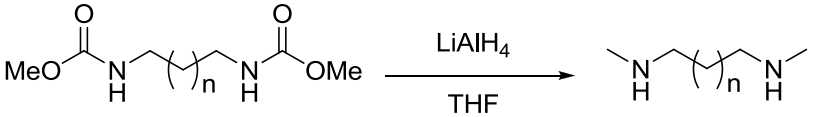


43, n=2 **45**, n=2, 56%

4.54 g (28.4 mmol)of **43** in 120 mL of THF was added 2.0 g of $LiAlH_4$ very slowly at 0 °C. The reaction was warmed up to room temperature and refluxed for 3 hours. Celite was added to the reaction and the suspension was stirred for 15 minutes. The solids were filtered off. The filtrate was quenched by methanol. The solution was concentrated. The resulting liquid was distilled to give 1.143 g (15.9 mmol) of **45** (56%).

^{1}HNMR ($CDCl_3$): δ 2.47 (t, 4H, ^{3}J = 6.0 Hz), 2.34 (s, 6H), 1.41 (m, 2H), and 1.36 (b, 2H). ^{13}CNMR ($CDCl_3$): δ 52.036, 36.480, and 27.677. The spectroscopic and other physical data reported are consistent with values reported in the literature. [34]

N,N'-Dimethyldiamines 46.

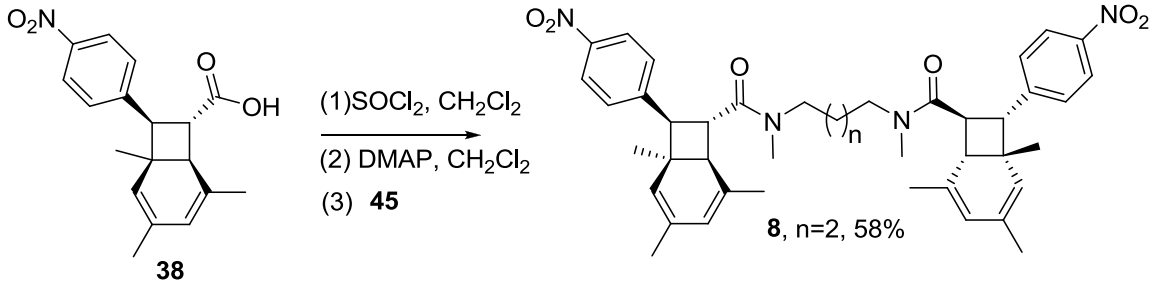


44, n=3 **46**, n=3, 45%

5.92 g (31.1 mmol) of **44** in 120 mL of THF was added 2.0 g (52.6 mmol) of $LiAlH_4$ very slowly at 0 °C. The reaction was warmed up to room temperature and refluxed for 3 hours. Celite was added to the reaction and the suspension was stirred for 15 minutes. The solids were filtered off. The filtrate was quenched by methanol. The solution was concentrated. The resulting liquid was distilled to give 1.21 g (14 mmol) of **46** (45%).

^{1}HNMR ($CDCl_3$): δ 2.49 (t, 4H, ^{3}J = 7.8 Hz), 2.34 (s, 6H), 1.91 (b, 2H), 1.42 (tt, 4H, ^{3}J = 7.8 Hz, ^{3}J = 6.6 Hz), and 1.28 (m, 2H). ^{13}CNMR ($CDCl_3$): δ 52.0, 36.5, 29.8, and 25.1. IR (KBr): υmax 3296, 2931, 2855, 2796, 1660, 1547, 1474, 1380, and 1116 cm^{-1}.

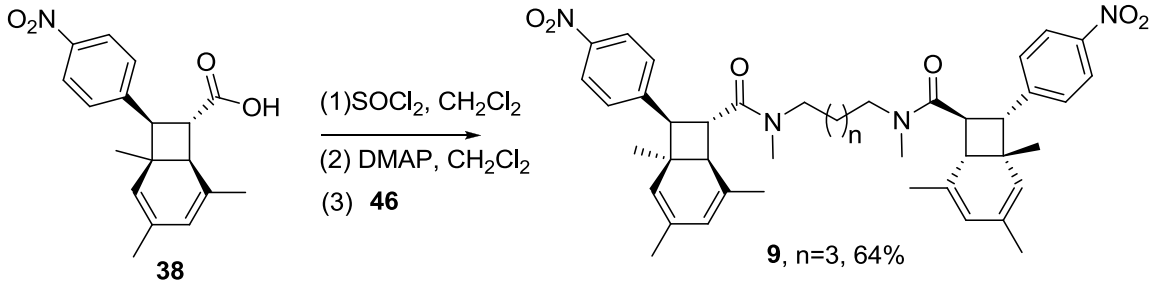
SNF analogue 8.



SNF acid (19 mg, 0.06 mmol) in 3 mL of methylene chloride was added 0.1 mL of thionyl chloride at 0 °C. The mixture was stirred for half an hour at room temperature. The solution was concentrated in vacuo. 1 mL of methylene chloride was added to the resulting acid chloride and then of 7 mg of 4-dimethylaminopyridine was added. 3.3 mg (0.03 mmol) of diamine **45** was added to the solution. The reaction was stirred for 24 hours and then quenched by water. The water solution was extracted three times with methylene chloride. The organic solutions were combined, dried over $MgSO_4$, and concentrated in vacuo. The residues were separated by a TLC plate with 1:1 hexanes and ethyl acetate to offer 12 mg (0.035 mmol) of compound **8** (58%).

Mixture of diastereomers ^{1}HNMR ($CDCl_3$, mixture): δ 8.16 (m, 4H), 7.34 (m, 4H), 5.48 (m, 2H), 4.50 (m, 2H), 3.84 (m, 2H), 3.65 (m, 4H), 3.45 (m, 2H), 2.86 (m, 6H), 2.75 (m, 2H), 1.68 (m, 12H), 1.44 (m, 4H), and 1.23 (m, 6H). ^{13}CNMR ($CDCl_3$): δ 172.4, 146.991, 134.0, 131.0, 129.9, 128.8, 128.6, 123.6, 122.7, 62.9, 56.6, 49.3, 47.7, 46.6, 44.7, 35.5, 28.3, 22.2, and 22.2. IR (KBr): υmax 2963, 2929, 2875, 1640, 1603, 1514, 1462, 1379, and 1108 cm^{-1}. ESI-MS ($M-H^{+}$): 707.3, and 708.3 g/mol.

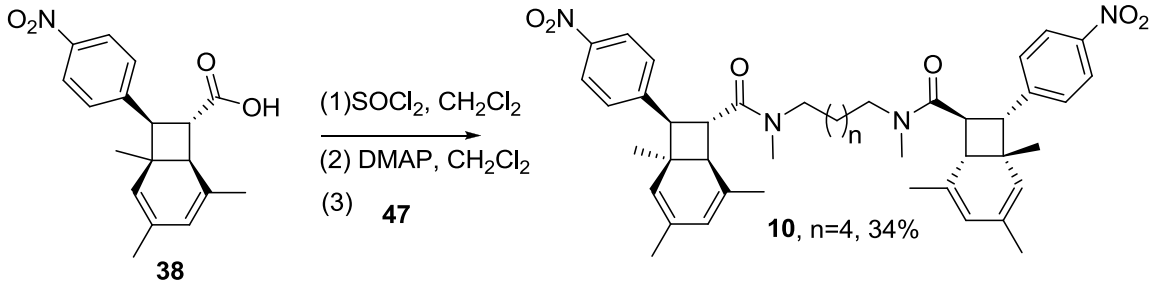
SNF analogue 9.



SNF acid (20 mg, 0.06 mmol) in 3 mL of methylene chloride was added 0.1 mL of thionyl chloride at 0 °C. The mixture was stirred for half an hour at room temperature. The solution was concentrated in vacuo. 1 mL of methylene chloride followed by 7 mg of 4-dimethylaminopyridine was added to the acid chloride. 4.6 mg (0.03 mmol) of diamine **46** was added to the solution. The reaction was stirred for 24 hours and quenched by water. The water solution was extracted three times with methylene chloride. The organic solutions were combined, dried over $MgSO_4$, and concentrated in vacuo. The residues were separated by a TLC plate with 1:1 hexanes and ethyl acetate to offer 14 mg (0.038 mmol) of compound **9** (64%).

Mixture of diastereomers ^{1}HNMR ($CDCl_3$, mixture): δ 8.16 (m, 4H), 7.34 (m, 4H), 5.48 (m, 2H), 4.50 (m, 2H), 3.84 (m, 2H), and 3.66 (m, 4H), 3.40 (m, 2H), 2.87 (m, 6H), 2.77 (m, 2H), 1.69 (m, 12H), 1.50 (m, 6H), and 1.23 (m, 6H). ^{13}CNMR ($CDCl_3$): δ 172.3, 147.0, 134.3, 131.0, 129.9, 128.8, 128., 123.7, 122.9, 56.3, 49.8, 47.9, 46.5, 44.3, 35.5, 34.0, 28.3, 26.8, 26.9, and 22.2. IR (KBr): υmax 2963, 2877, 1631, 1514, 1484, 1346, 1267, and 1108 cm^{-1}. ESI-MS ($M-H^{+}$): 721.4 g/mol.

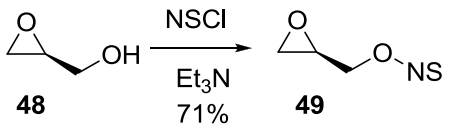
SNF analogue 10.



SNF acid (30 mg, 0.09 mmol) in 3 mL of methylene chloride was added 0.1 mL of thionyl chloride at 0 °C. The mixture was stirred for half an hour at room temperature. The solution was concentrated under vacuum. 1 mL of methylene chloride followed by 7 mg of 4-dimethylaminopyridine was added to the acid chloride. 0.010 mL (0.045 mmol) of *N*,*N*′-dimethyl-1,6-hexanediamine was added to the solution. The reaction was stirred for 24 hours and quenched by water. The water solution was extracted three times with methylene chloride. The organic solution was combined, dried over $MgSO_4$, and concentrated in vacuo. The residues were separated by a TLC plate with 1:1 hexanes and ethyl acetate to offer 12 mg (0.03 mmol) of compound **10** (34%).

Mixture of diastereomers ^{1}HNMR ($CDCl_3$, mixture): δ 8.16 (m, 4H), 7.33 (m, 4H), 5.48 (m, 2H), 4.48 (m, 2H), 3.83 (m, 2H), 3.62 (m, 4H), 3.42 (m, 2H), 2.88 (m, 6H), 2.78 (m, 2H), 1.69 (m, 12H), 1.50 (m, 8H), and 1.23 (m, 6H). ^{13}CNMR ($CDCl_3$): δ 172.2, 146.437, 134.7, 131.0, 129.9, 128.6, 123.6, 122.9, 122.5, 172.3, 147.0, 134.3, 131.0, 129.9, 128.8, 128.6, 123.7, 122.9, 62.9, 55.9, 49.7, 48.0, 46.5, 44.4, 35.5, 28.4, 27.2, 26.7, and 22.2. IR (KBr): υmax 2963, 2876, 1640, 1603, 1514, 1484, 1451, 1414, 1381, and 1346 cm^{-1}. ESI-MS ($M-H^+$): 735.5 g/mol.

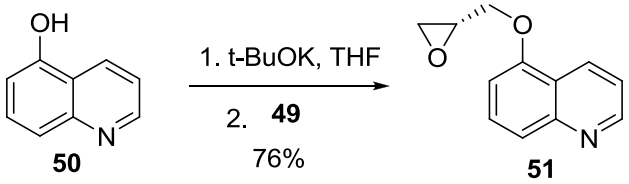
Protected glycidol 49 .[22]



Triethyl amine (0.4 mL) was added to the mixture of (-)-D-glycidol (**48**, 200 mg, 2.7 mmol) and dry methylene chloride (20 mL) at 0 °C under nitrogen. 4-nitrobenzenesulfonyl chloride (700 mg, 3 mmol) in methylene chloride (10 ml) was added dropwise to the mixture at 0 °C. The reaction was stirred for 2 hours and quenched by dilute HCl/H_2O. The organic phase was separated; the water phase was extracted three times by ether. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a silica gel column with ethyl acetate and hexanes (1:10) to give the protected (-)-D-glycidol **49** (607 mg, 1.9 mmol, 71%).

^{1}HNMR ($CDCl_3$): δ 8.39 (d, 2H, ^3J = 8.5 Hz), 8.11 (d, 2H, ^3J = 8.5 Hz), 4.46 (dd, 1H, ^2J = 11 Hz, ^3J = 2.5 Hz), 4.01 (dd, 1H, ^2J = 12 Hz, ^3J = 6.0 Hz), 3.20 (d, 1H, ^3J = 2.5 Hz), 2.83 (dd, 1H, ^3J = 4.0 Hz, ^3J = 4.0 Hz), and 2.60 (dd, 1H, ^3J = 2.0 Hz, ^3J = 2.0 Hz). ^{13}CNMR ($CDCl_3$): δ 151.1, 141.8, 129.5, 124.7, 71.9, 48.9, and 44.7. IR (KBr): Vm υmax ax 3516, 3108, 2921, 1607, 1532, 1404, 1351, 1186, and 1095 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [22]

5-Quinolinol 51.[22]



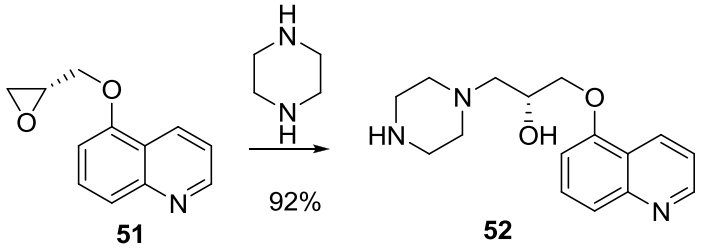
50 **51**

Potassium t-butoxide (1 M in ether, 0.78 mL, 0.78 mmol) was added dropwise to the mixture of 5-quinolinol (**50**, 100 mg, 0.69 mmol) and THF (10 mL) at 0 °C. The reaction was stirred for an hour at r.t. to give a yellow suspension. Then the protected (-)-D-glycidol (**31**, 170 mg, 1.42 mmol) in THF (5 mL) was added dropwise to the suspension. The reaction was stirred for two hours at r.t. and quenched by sat. ammonium

chloride solution (1 mL). The organic phase was separated; the water phase was extracted three times by ether. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a silica gel column with methanol and methylene chloride (1:150) to give the ether **51** (99 mg, 0.53 mmol, 76%).

^{1}HNMR ($CDCl_3$): δ 8.84 (dd, 1H, ^3J = 4.8 Hz, ^4J = 2.4 Hz), 8.54 (dd, 1H, ^3J = 7.2 Hz, ^4J = 0.6 Hz), 7.65 (d, 1H, ^3J = 8.4 Hz), 7.51 (dd, 1H, ^3J = 7.8 Hz, ^3J = 7.8 Hz), 7.31 (dd, 1H, ^3J = 8.4 Hz, ^3J = 4.2 Hz), 4.35 (d, 1H, ^3J = 7.8 Hz), 4.01 (dd, 1H, ^2J = 12 Hz, ^3J = 6.0 Hz), 3.40(dd, 1H, ^2J = 10.8 Hz, ^3J = 6.0 Hz), 2.89 (dd, 1H, ^3J = 9.6 Hz, ^3J = 4.8 Hz), and 2.76 (dd, 1H, ^3J = 10.8 Hz, ^3J = 2.4 Hz). ^{13}CNMR ($CDCl_3$): δ 153.6, 150.5, 148.8, 130.6, 129.0, 121.9, 120.5, 120.1, 105.1, 69.0, 49.8, and 44.3. The spectroscopic and other physical data reported are consistent with values reported in the literature. [22]

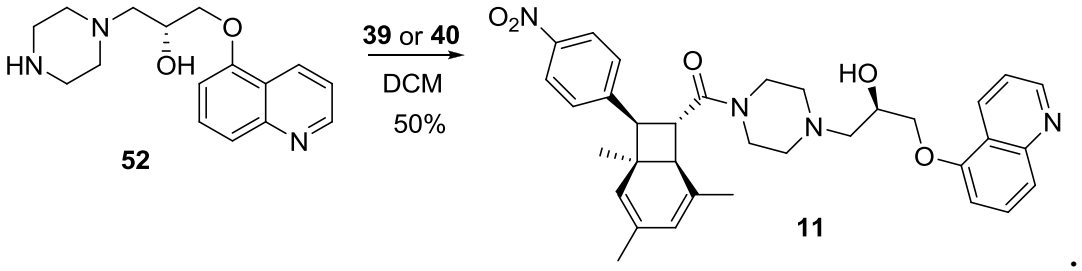
Piperazine 52.[36]



The quinolinol (**51**, 188 mg, 0.94 mmol) was mixed with piperazine (3.7 g, 43 mmol) and ethanol (20 ml). The mixture was refluxed at 85 °C for 24 hours. Then potassium carbonate (200 mg) was added to the mixture. The reaction was refluxed at 85 °C for 2 more days. The solid was filtered off. The filtrate was concentrated in vacuo. The residues were separated by a silica gel column with methanol and methylene chloride (1:5) to give yellow oil **52** (264 mg, 0.86 mmol, 92%).

^{1}HNMR ($CDCl_3$): δ 8.80 (d, 1H, ^{3}J = 4.0 Hz), 8.48 (d, 1H, ^{3}J = 9.5 Hz), 7.62 (d, 1H, ^{3}J = 9.5 Hz), 7.50 (dd, 1H, ^{3}J = 8.0 Hz, ^{3}J = 8.0 Hz), 7.27 (dd, 1H, ^{3}J = 8.0 Hz, ^{3}J = 4.0 Hz), 4.18 (t, 1H, ^{3}J = 4.0 Hz, ^{3}J = 4.0 Hz), 4.08 (t, 2H, ^{3}J = 4.0 Hz, ^{3}J = 4.0 Hz), 3.74 (s, 2H), 2.87 (m, 4H), 2.61 (d, 2H, ^{3}J = 5.0 Hz), 2.55 (d, 2H, ^{3}J = 7.0 Hz), and 2.44 (d, 2H, ^{3}J = 5.5 Hz). ^{13}CNMR ($CDCl_3$): δ 153.7, 149.9, 148.2, 130.5, 129.0, 120.8, 120.3, 119.7, 104.9, 70.7, 65.4, 61.1, 53.8, 49.2, 45.4, 45.2, and 44.9. IR (KBr): υmax 3383, 3298, 1268, 1170, 1097, 1048, and 887 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [36]

SNF analog 11

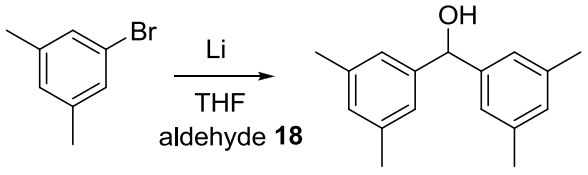


Method one: The acid (**38**, 40 mg, 0.13 mmol) was dissolved in dry methylene chloride. Thionyl chloride (0.2 mL) was added dropwise to the mixture at 0 °C. The reaction was stirred for an hour and then concentrated in vacuo. The residues were placed in high vacuo for 2 hours to remove extra thionyl chloride. 4-Dimethylaminopyridine (20 mg, 0.3 mmol) and the piperazine (**52**, 40mg, 0.14 mmol) were dissolved in methylene chloride (2 mL). The residues were added dropwise to the mixture by a pipet at 0 °C. The reaction was stirred for 3 hours at r.t. and quenched by water. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a TLC plate with methanol and methylene chloride (1:10) to give yellow oil **11** (40 mg, 0.065 mmol, 50%)

Method two: the acid (**38**, 50 mg, 0.16 mmol) and carbonyl diimidazole (30 mg, 0.19 mmol) were dissolved in dry methylene chloride (2 mL). The mixture was stirred at r.t. for one hour. A little gas was release. The piperazine (**52**, 40 mg, 0.014 mmol) in dry methylene chloride (1 mL) was added to the mixture. The reaction was stirred at r.t. for 18 hours. The solution was diluted with 10 mL of methylene chloride. The mixture was washed by water. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined, dried over Na_2SO_4, and concentrated in vacuo. The residue was separated by a TLC plate with methanol and methylene chloride (1:10) to give yellow oil **11** (56 mg, 0.096 mmol, 66%)

^{1}HNMR ($CDCl_3$): δ 8.80 (s, 1H), 8.51 (d, 1H, ^3J = 8.5 Hz), 8.13 (d, 2H, ^3J = 7.5 Hz), 7.69 (d, 1H, ^3J = 7.0 Hz), 7.56 (t, 1H, ^3J = 7.5 Hz), 7.32 (d, 2H, , ^3J = 8.0 Hz), 6.83 (d, 1H, ^3J = 7.5 Hz), 5.49 (s, 1H), 4.49 (s, 1H), 4.272 (m, 1H), 4.15 (s, 2H), 3.83 (d, 2H, ^3J = 8.0 Hz)), 3.64 (t, 2H, ^3J = 9.0 Hz), 3.45 (s, 2H), 2.85 (d, 1H, ^3J = 6.5 Hz)), 2.65 (m, 4H), 1.74 (s, 3H), 1.67 (s, 3H), and 1.23 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 154.1, 147.0, 145.9, 134.2, 131.0, 130.9, 129.5, 128.6, 123.6, 122.9, 122.4, 122.0, 120.4, 105.5, 70.7, 65.8, 60.9, 60.8, 56.1, 56.2, 46.1, 46.0, 45.5, 44.3, 44.2, 42.1, 28.3, 22.2, and 22.0. IR (KBr): υmax 3480, 3080, 2920, 2780, 1630, 1585, 1475, 1345, and 1265 cm^{-1}. ESI-MS (M-H$^+$): 583.31, 584.42, and 585.46 g/mol.

Alcohol 57.



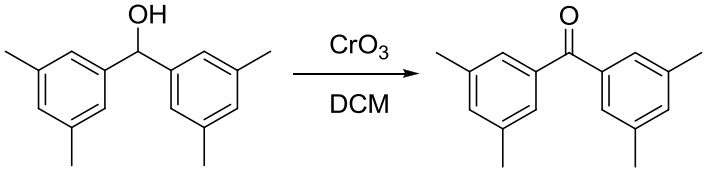
56 **57**

In a two necked RBF, 1-bromo-3, 5-xylene (**56**, 120 mg, 0.65 mmol) and mesitylenaldehyde (**18**, 50 mg, 0.37 mmol) were added to lithium (200 mg) in THF (25

mL) at 0 °C. [37] A mixture of bromide (1.08 g, 9.7 mmol) and aldehyde (470 mg, 3.5 mmol) in THF (25 mL) were added dropwise to the reaction system during 2 hours. After the addition, the reaction was stirred for one hour and then quenched by sat. NH_4Cl solution (10 mL) at 0 °C. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined, dried over Na_2SO_4, and concentrated in vacuo to give a crude product **57** (810 mg, 3.37 mmol, 87%).

^{1}HNMR ($CDCl_3$): δ 7.000 (s, 4H), 6.902 (s, 2H), 5.700 (s, 1H), and 2.302 (s, 12H). ^{13}CNMR ($CDCl_3$): δ 144.1, 138.2, 129.3, 124.4, 76.5, and 21.5. IR (KBr): υmax 3380, 3005, 2910, 1601, 1460, 1151, 1052, and 852 cm^{-1}.

Ketone 58.

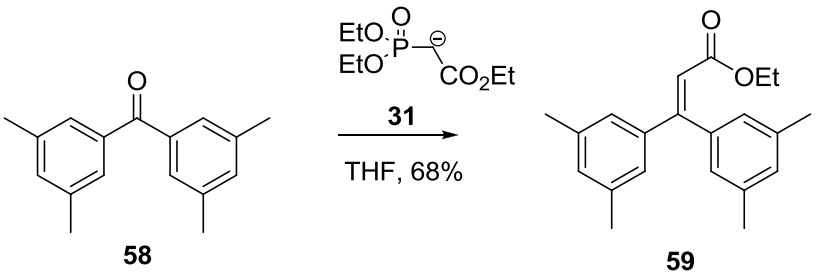


57 **58** overall yield 58%

The crude product **57** (810 mg, 3.37 mmol) was dissolved in acetic acid (25 mL). Chromium oxide (2.5 g, 16.4 mmol) was added to the mixture at 0 °C. [38] The reaction was stirred at r.t. for 2 hours and quenched by ice cold water. The water phase was extracted three times by ether. The organic phases were combined and concentrated. The residue was separated by a TLC plate with ethyl acetate and hexanes (1:15) to give a white solid **58** (523 mg, 1.95 mmol, 58%).

^{1}HNMR ($CDCl_3$): δ 7.393 (s, 4H), 7.217 (s, 2H), 2.378 (s, 12H). ^{13}CNMR ($CDCl_3$): δ 183.4, 138.2, 138.0, 134.1, 127.9, and 21.4. IR (KBr): 2990, 2810, 1590, and 1205 cm^{-1}.

Ester 59.

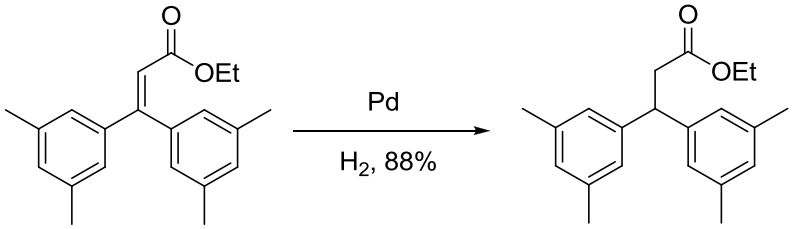


58 59

Lithium t-butoxide (1 M in ether, 1.4 mL, 1.4 mmol) was added dropwise to a mixture of triethyl phosphoacetate (200 mg, 0.89 mmol) and benzene (10 mL) at r.t. [39] The mixture was stirred for half an hour at r.t.. The ketone (**58**, 104 mg, 0.44 mmol) in benzene (2 mL) was added dropwise to the reaction. The reaction was refluxed for 18 hours and quenched by sat. NH_4Cl solution (10 mL). The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a silica gel column with ethyl acetate and hexanes (1:200) to give a white solid **59** (89 mg, 0.30 mmol, 68%).

^{1}HNMR ($CDCl_3$): δ 7.00 (s, 2H), 6,91 (s, 2H), 6.81 (s, 2H), 6.29 (s, 1H), 3.49 (q, 2H, ^3J = 7.0 Hz), 2.31 (s, 6H), 2.28 (s, 6H), and 1.16 (t, 3H, ^3J = 7.0 Hz). ^{13}CNMR ($CDCl_3$): δ 166.5, 157.3, 141.4, 139.2, 138.0, 137.3, 131.2, 129.9, 127.0, 126.4, 117.3, 117.3, 60.1, 21.5, 21.5, and 14.2. IR (KBr): υmax 2985, 2915, 1740, 1605, 1495, 1395, 1190, 1075, and 880. GC-MS (M^+): 308, 293, 263, 262, 235, 221, 202, 178, 165, 133, 115, 105, 77, 63, and 46 g/mol.

Ester 12.

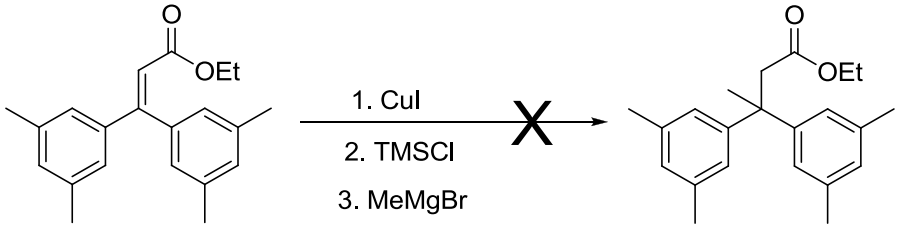


59 **12**

The 25 mL RBF containing palladium (10% 10mg) was connected with vacuo to remove air. [36] And then hydrogen was injected. The operation was repeated five times. Hydrogen in a balloon was pumped to the RBF; and then ethanol (95%, 10 mL) was added. The ester (**59**, 48 mg, 0.16 mmol) in ethanol (95%, 2 mL) was added to the RBF. The reaction was stirred at r.t. overnight. The solid was filtered off and the solution was concentrated in vacuo to give a pure solid **12** (42 mg, 14 mmol, 88%).

^{1}HNMR ($CDCl_3$): δ 6.76 (s, 4H), 6.73 (s, 2H, ^{3}J = 7.0 Hz), 4.31 (t, 1H, ^{3}J = 7.0 Hz), 3.95 (t, 2H, ^{3}J = 7.0 Hz), 2.91 (d, 2H, ^{3}J = 8.5 Hz), 2.18 (s, 12H), and 1.03 (t, 3H, ^{3}J = 7.0 Hz). ^{13}CNMR ($CDCl_3$): δ 172.2, 143.8, 138.0, 128.3, 125.7, 60.5, 47.1, 41.1, 21.6, and 14.3. IR (KBr): υmax 2995, 2940, 1730, 1590, 1455, 1380, 1260, and 1160 cm^{-1}. GC-MS (M^{+}): 310, 236, 223, 193, 165, 131, 115, 91, 77, and 53 g/mol.

Attempt at ester 54 .

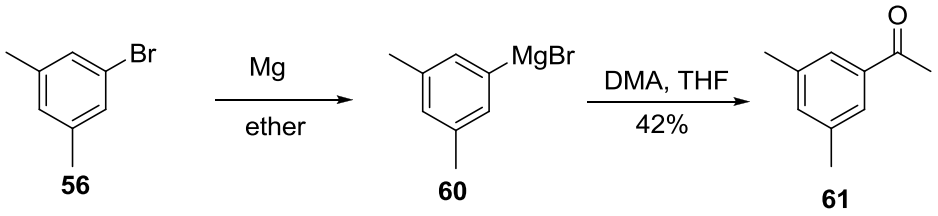


59 **54**

The ester (**59**, 41 mg, 0.13 mmol) was mixed with copper(I) iodide (10 mg, 0.05 mmol) and THF (10 mL). Chlorotrimethylsilane (21 mg, 0.2 mmol) was added to the suspension at r.t.; and then the suspension was stirred for half an hour. It was allowed to

cool down to -15 °C. Methylmagnesium bromide (3M in THF, 0.070 mL, 0.21 mmol) was added dropwise to the suspension at -15 °C. The reaction was stirred for 8 hours and quenched by sat. NH_4Cl solution (10 mL). The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. An NMR of the residues showed that no reaction occurred and the starting material was obtained.

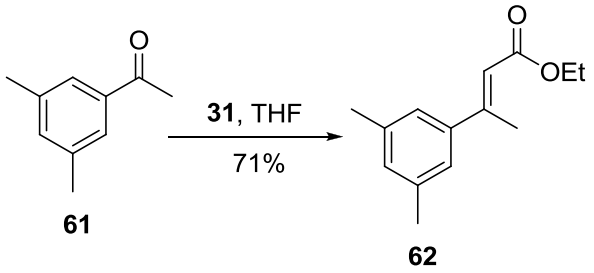
Ketone 61.



1-Bromo-3, 5-xylene (2 mL, 14.7 mmol) in THF (15 mL) was added dropwise to the suspension of magnesium and THF (10 mL) during an hour to give a dark brown solution.[41] The solution was transferred to the other RBF. Dimethylacetamide in THF (5 mL) was added dropwise to the dark solution at 0 °C. The solution was stirred at r.t. overnight and then quenched by sat. NH_4Cl solution (10 mL) at 0 °C. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a silica gel column with ethyl acetate and hexanes (1:50) to give oil **61** (1.09 g, 6.0 mmol, 42%).

^{1}HNMR ($CDCl_3$): δ 7.57 (s, 2H), 7.20 (s, 1H), 2.57 (s, 3H), and 2.37 (s, 6H). The spectroscopic and other physical data reported are consistent with values reported in the literature.[41]

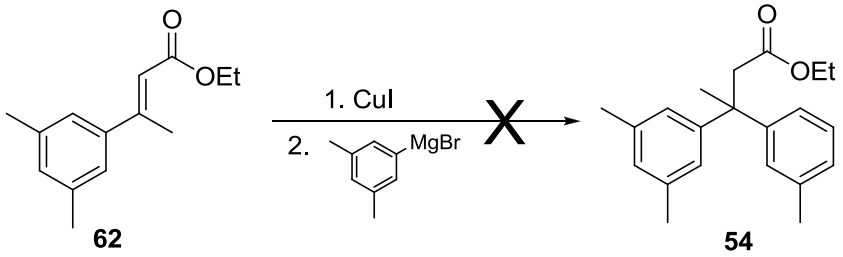
Ester 62.



Lithium t-butoxide (1 M in ether, 2.5 mL, 2.5 mmol) was added dropwise to the mixture of triethyl phosphoacetate (400 mg, 1.79 mmol) and THF (10 mL) at r.t.[37] The mixture was stirred at r.t. for half an hour. The ketone (**61**, 207 mg, 1.4 mmol) in THF (5 mL) was added dropwise to the reaction system. The reaction was refluxed overnight and quenched by sat. NH_4Cl solution (10 mL). The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residue was separated by a silica gel column with ethyl acetate and hexanes (1:40) to give a white solid **62** (197 mg, 1.0 mmol, 71%).

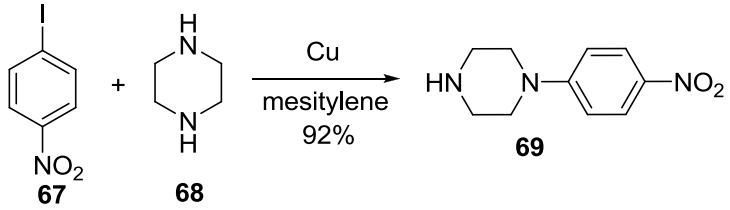
^{1}HNMR ($CDCl_3$): δ 7.11 (s, 2H), 7.02 (s, 1H), 6.13 (s, 1H), 4.23 (q, 2H, ^3J = 7.0 Hz), 2.57 (s, 3H), 2.36 (s, 6H), and 1.34 (t, 3H, ^3J = 7.0 Hz). ^{13}CNMR ($CDCl_3$): δ 167.2, 156.2, 142.6, 138.2, 134.9, 130.8, 126.4, 124.8, 124.4, 117.0, 60.0, 21.5, 18.2, and 14.6. IR (KBr): υmax 2980, 2837, 1702, 1630, 1572, 1511, 1463, 1366, 1303, and 1252 cm^{-1}.

The second attempt at ester 54.



1-Bromo-3, 5-xylene (250 mg, 1.35 mmol) in THF (10 mL) was added dropwise to the suspension of magnesium (1.3 g, 54 mmol) and THF (25 mL) during an hour to give a dark brown solution. [36] The solution was transferred to the suspension of copper iodide (30 mg, 0.15 mmol), the ester (**62**, 250 mg, 1.15 mmol) and THF (10 mL) at 0 °C. The reaction was stirred at r.t. overnight and quenched by sat. NH_4Cl solution (10 mL). The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The crude NMR showed that no reaction occurred and the starting material was obtained.

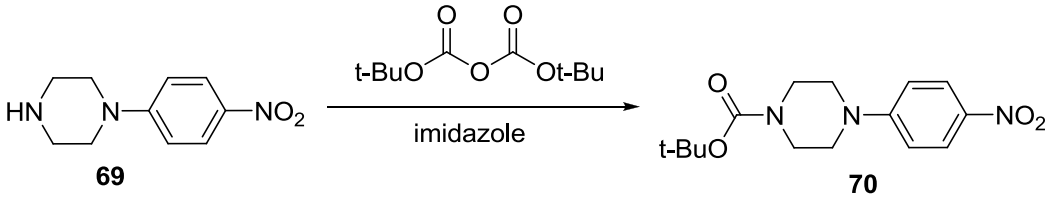
Arylpiperazine 69.



6.5 g (76 mmol) of piperazine and 1.2 g (4.8 mmol) of 1-iodo-4-nitrobenzene were mixed in 30 mL of mesitylene. 3.7 g (56 mmol) of copper, 3 g (21 mmol) of potassium carbonate, and 1.4 g (5.3 mmol) of 18-crown-6 were added to the mixture. The reaction was refluxed at 185 °C for 24 hours. Then the reaction was cooled down to room temperature and was added celite. The solid was filtered off, the filtrate was concentrated. The residue was separated by a silica gel column with 1:1 hexanes and ethyl acetate to give 965 mg (4.4 mmol) of product (92%). The product was recrystallized from acetone to give 358 mg (1.6 mmol) of yellow solid **69**.

^{1}HNMR ($CDCl_3$): δ 8.00 (d, 2H, ^3J = 9.6 Hz), 6.72 (d, 2H, ^3J = 9.6 Hz), 3.30 (t, 4H, ^3J = 5.2 Hz), and 2.93 (t, 4H, ^3J = 5.2 Hz). The spectroscopic and other physical data reported are consistent with values reported in the literature. [45]

t-Boc protected arylpiperazine 70.[46]

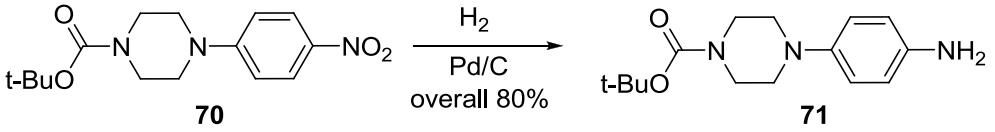


69 **70**

358 mg (1.73 mmol) of **69** was dissolved in THF. 600 mg (2.75 mmol) of di-tert-butyldicarbonate and 600 mg of triethylamine were added to the solution at 0 °C. The reaction was refluxed overnight. The reaction mixture was washed by 1 M sodium hydroxide solution. The aqueous solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. The extraction was concentrated to give 596 mg (1.94 mmol) of crude product **70** which was used directly in the next step.

^{1}HNMR ($CDCl_3$): δ 8.15 (d, 2H, ^{3}J = 9.6 Hz), 6.81 (d, 2H, ^{3}J = 9.6 Hz), 3.60 (t, 4H, ^{3}J = 5.2 Hz), 3.42 (t, 4H, ^{3}J = 5.2 Hz), and 1.49 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 155.0, 138.4, 126.0, 112.7, 80.5, 70.7, 50.9, 48.1, and 47.1. The spectroscopic and other physical data reported are consistent with values reported in the literature. [46]

t-Boc protected arylpiperazine 71.[47]

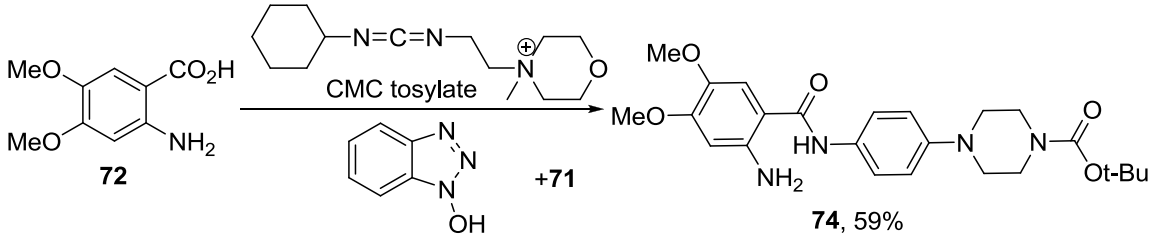


70 **71**

In a 50 mL RBF, 10% Pd/C was connected to vacuum for 5 minutes. And then hydrogen was flushed to the RBF. 595 mg (1.94 mmol) of compound **70** in 15 mL ethanol was added to the reaction under hydrogen. The reaction was stirred overnight under hydrogen. The solid was filtered off. The filtrate was concentrated to give 442 mg (1.59 mmol) of product **71** (80%).

^{1}HNMR ($CDCl_3$): δ 6.79 (d, 2H, ^{3}J = 6.4 Hz), 6.63 (d, 2H, ^{3}J = 6.4 Hz), 3.54 (t, 4H, ^{3}J = 4.8 Hz), 2.94 (t, 4H, ^{3}J = 4.8 Hz), and 1.46 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 154.9, 144.5, 140.7, 119.3, 116.2, 79.9, 58.4, 51.5, and 28.5. IR (KBr): υmax 3329, 2976, 2817, 1697, 1594, 1518, 1478, 1416, and 1317 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [47]

Amine 74.

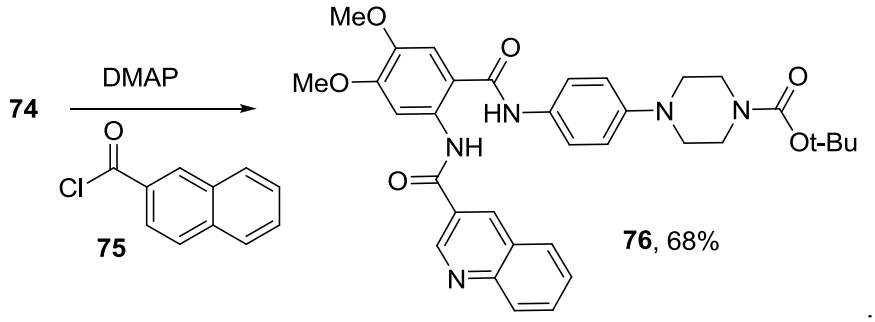


234 mg (1.18 mmol) of 2-amino-4,5-dimethoxybenzoic acid and 297 mg (1.07 mmol) of **71** were mixed in dry methylene chloride. 423 mg (1.2 mmol) of 4-methyl morpholine N-oxide monohydrate followed by 135 mg (1.0 mmol) of 1-hydroxybenzotriazole was added to the reaction. The black solution was stirred for 24 hours and then washed by 1 M sodium hydroxide solution. The water solution was extracted three times with methylene chloride. The organic solution was dried over magnesium sulfate and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 methylene chloride and methanol to give 386 mg of product **74** (0.61 mmol, 59%).

^{1}HNMR ($CDCl_3$): δ 7.91 (s, 1H), 7.41 (d, 2H, ^{3}J = 8.0 Hz), 6.98 (s, 1H), 6.88 (d, 2H, ^{3}J = 8.0 Hz), 6.19 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.55 (t, 4H, ^{3}J = 4.0 Hz), 3.05 (t, 4H, ^{3}J = 4.0 Hz), and 1.47 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 167.3, 154.8, 153.6, 148.4, 145.0, 141.1, 131.1, 122.4, 117.3, 111.4, 107.8, 101.1, 80.0, 57.2, 55.8, 49.9, and 28.5. IR (KBr):

υmax 3351, 2974, 1753, 1692, 1642, 1572, 1515, 1422, and 1286 cm^{-1}. ESI-MS ($M-H^+$): 457.4 g/mol.

Amide 76

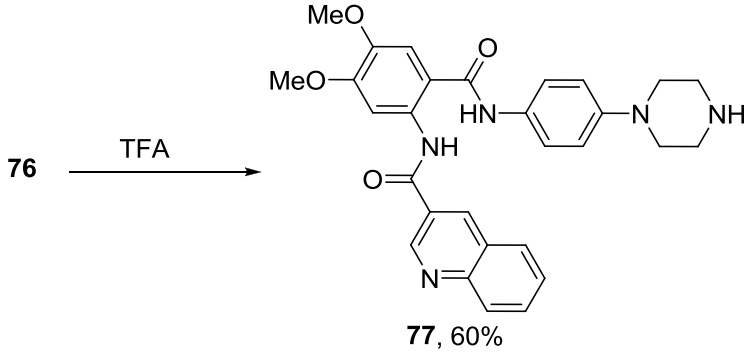


60 mg (0.32 mmol) of 3-quinolinecarboxylic acid in 10 mL of methylene chloride was added 1 mL of thionyl chloride at room temperature. The reaction was refluxed overnight. The solvent and extra thionyl chloride were removed in vacuo. 43 mg (0.35 mmol) of 4-dimethylaminopyridine in 10 mL of methylene chloride was added to the reaction. Then 100 mg (0.158 mmol) of **7**4 in 1 mL of methylene chloride was added to the reaction. The reaction was stirred overnight and quenched by water. The water solution was extracted three times with methylene chloride. The organic solution was dried over magnesium sulfate and concentrated in vacuo. The residues were crystallized in 95% ethanol to give 97 mg of product **76** (0.137 mmol, 68%).

^{1}HNMR ($CDCl_3$): δ 12.51 (s, 1H), 9.51 (s, 1H), 8.73 (s, 1H), 8.54 (s, 1H), 8.30 (s, 1H), 8.15 (d, 1H, ^3J = 8.8 Hz), 7.97 (d, 1H, ^3J = 8.0 Hz), 7.81 (dd, 1H, ^3J = 8.8 Hz, ^3J = 7.2 Hz), 7.62 (dd, 1H, ^3J = 8.0 Hz, ^3J = 7.2 Hz), 7.53 (d, 2H, ^3J = 8.8 Hz), 7.10 (s, 1H), 6.93 (d, 2H, ^3J = 8.8 Hz), 5.29 (s, 1H), 3.93 (s, 3H), 3.77 (s, 3H), 3.58 (t, 4H, ^3J = 4.2 Hz), 3.10 (t, 4H, ^3J = 4.2 Hz), and 1.48 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 167.5, 164.0, 154.9, 152.8, 149.5, 149.0, 149.0, 144.7, 135.9, 135.7, 131.6, 130.2, 129.5, 129.3, 127.6, 127.4, 127.0, 122.8, 117.2, 112.4, 109.8, 105.1, 80.2, 56.5, 56.3, 49.7, and 28.6. IR (KBr): υmax

3365, 2975, 2916, 2849, 1749, 1694, 1622, 1558, 1475, 1418, 1366, and 1264 cm^{-1}. ESI-MS ($M-H^+$): 612.4, and 613.4 g/mol.

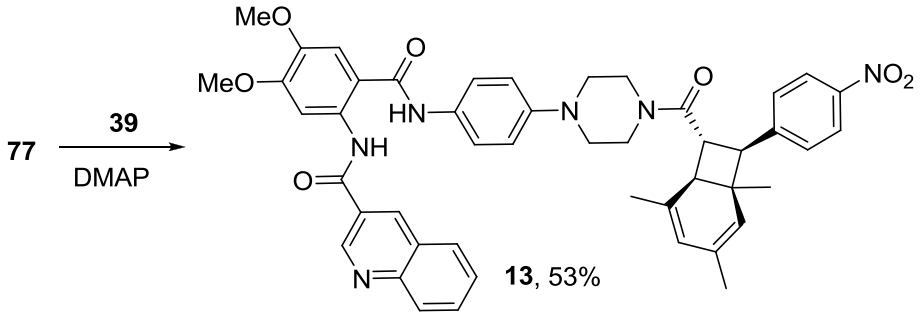
Piperazine 77.



90 mg (0.128 mmol) of **76** was dissolved in 10 mL of methylene chloride. 2 mL of trifluoroacetic acid was added to the solution at 0 °C. The reaction was stirred for 5 hours at room temperature and then quenched with 1 M sodium hydroxide solution. The water solution was extracted three times with methylene chloride. The organic solutions were combined, dried over magnesium sulfate, and concentrated in vacuo. The residues were crystallized in 95% ethanol to give 45 mg of yellow solid **77** (0.077 mmol, 60%).

^{1}HNMR ($CDCl_3$): δ 12.51 (s, 1H), 9.53 (s, 1H), 8.75 (s, 1H), 8.59 (s, 1H), 8.15 (d, 1H, ^3J = 8.0 Hz), 7.98 (d, 1H, ^3J = 8.0 Hz), 7.81 (dd, 1H, ^3J = 8.0 Hz, ^3J = 7.2 Hz), 7.63 (dd, 1H, ^3J = 8.0 Hz, ^3J = 7.2 Hz), 7.51 (d, 2H, ^3J = 8.8 Hz), 7.08 (s, 1H), 6.95 (d, 2H, ^3J = 8.8 Hz), 5.29 (s, 1H), 3.98 (s, 3H), 3.84 (s, 3H), 3.15 (t, 4H, ^3J = 4.2 Hz), and 3.05 (t, 4H, ^3J = 4.2 Hz). ^{13}CNMR ($CDCl_3$): δ 167.4, 164.1, 152.9, 149.7, 149.5, 149.0, 144.8, 135.9, 131.0, 129.5, 129.5, 129.4, 127.6, 127.5, 127.1, 122.7, 116.7, 112.4, 109.7, 105.2, 56.6, 56.3, 50.7, and 46.3. IR (KBr): υmax 3455, 2975, 2827, 1678, 1589, 1514, 1414, 1366, 1319, 1251, and 1165 cm^{-1}. ESI-MS ($M-H^+$): 512.4, 513.4, and 514.4 g/mol.

SNF analogue 13.



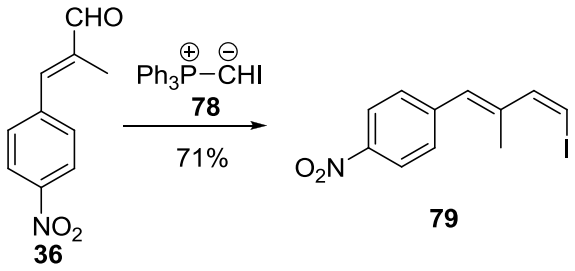
40 mg (0.132 mmol) of SNF acid in 5 mL of methylene chloride was added 0.5 mL of thionyl chloride. The mixture was stirred for half an hour. Then the solvent and extra thionyl chloride were removed in vacuo. 30 mg (0.059 mmol) of compound **77** and 10 mg (0.082 mmol) of 4-dimethylaminopyridine in 5 mL of methylene chloride was added to the reaction. The reaction was stirred for 24 hours and then quenched by 1 M sodium hydroxide solution. The water solution was extracted three times with methylene chloride. The organic solutions were combined, dried over magnesium sulfate, and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 methylene chloride and methanol to give 25 mg of product **13** (0.031 mmol, 53%).

^{1}HNMR ($CDCl_3$): δ 12.52 (s, 1H), 9.52 (s, 1H), 8.75 (s, 1H), 8.58 (s, 1H), 8.17 (m, 3H), 7.97 (d, 1H, ^{3}J = 8.4 Hz), 7.82 (dd, 1H, ^{3}J = 8.0 Hz, ^{3}J = 6.8 Hz), 7.63 (dd, 1H, ^{3}J = 8.0 Hz, ^{3}J = 6.8 Hz), 7.51 (d, 2H, ^{3}J = 8.4 Hz), 7.33 (d, 2H, ^{3}J = 8.4 Hz), 7.12 (s, 1H), 6.86 (d, 2H, ^{3}J = 8.8 Hz), 5.51 (s, 1H), 4.51 (s, 1H), 3.96 (s, 3H), 3.82 (s, 3H), 3.85 (d, 1H, ^{3}J = 9.6 Hz), 3.74 (dd, 1H, ^{3}J = 9.6 Hz, ^{3}J = 8.8 Hz), 3.55 (m, 4H), 3.08 (m, 4H), 2.87 (d, 1H, ^{3}J = 8.8 Hz), 1.76 (s, 1H), 1.69 (s, 1H), and 1.24 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 171.2, 167.5, 164.0, 153.0, 149.5, 148.9, 148.4, 147.0, 146.0, 144.8, 136.0, 134.3, 132.2, 131.6, 131.1, 130.5, 129.5, 129.3, 128.6, 127.6, 127.5, 127.1, 123.8, 123.0, 122.8, 122.4, 117.2, 112.2, 109.9, 105.2, 56.7, 56.3, 56.2, 50.4, 49.7, 46.1, 45.7, 44.3, 44.2, 28.4, 22.2, and 22.1. IR (KBr): υmax 3305, 2970, 2857, 1667, 1589, 1519, 1412, 1346, and 1277 cm^{-1}.ESI-MS (M-H^{+}): 807.3, and 808.3 g/mol.

Iodomethyltriphenylphosphonium iodide 78.[48]

5 g (18.6 mmol) of diiodomethane was added to a solution of 5 g (19 mmol) of triphenylphosphine in 50 mL of benzene at room temperature. The reaction was stirred overnight. The solid was filtered off and then was washed three times with ether to yield 9.21 g of compound **78** (17.1 mmol, 92%).

Iododiene 79.

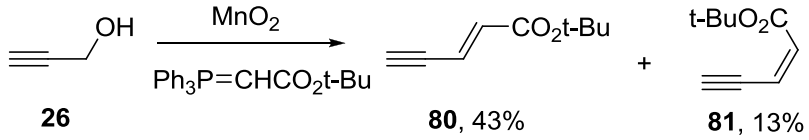


In a 100 mL round bottom flask, 5 g (11.6 mmol) of iodomethyltriphenylphosphonium iodide **78** was mixed with 50 mL of THF. The reaction mixture was cooled down to -20 °C. Then 12 mL of 1 M NaHMDS (12 mmol) was added dropwise to the reaction mixture. The yellow suspension became red. After 15 minutes stirring, 2.0 g (10.4 mmol) of (*E*)-2-methyl-3-(4-nitro-phenyl)-propenal **36** in 10 mL of THF was added dropwise to the reaction. The reaction gave a brown suspension. After 4 hours stirring at -20 °C, this reaction was quenched by a saturated NH_4Cl solution. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over $MgSO_4$. After solvents were removed in vacuo, the organic products were separated by a silica gel column with 50:1 hexanes and AcOEt to give 2.03 g of yellow liquid **79** (7.4 mmol, 71%).

^{1}HNMR ($CDCl_3$): δ 8.21 (d, 1H, ^3J = 9.0 Hz), 7.46 (d, 1H, ^3J = 9.0 Hz), 6.92 (d, 1H, ^3J = 8.5 Hz), 6.74 (s, 1H), 6.44 (d, 1H, ^3J = 8.5 Hz), and 2.16 (s, 3H). ^{13}CNMR

($CDCl_3$): δ 146.2, 143.7, 141.8, 138.6, 130.3, 129.6, 123.4, 79.2, and 17.8. IR (KBr): υmax 3419, 2929, 2855, 1706, 1652, 1594, 1558, 1456, 1393, 1256, and 1156 cm^{-1}.

Ester 80 and 81.



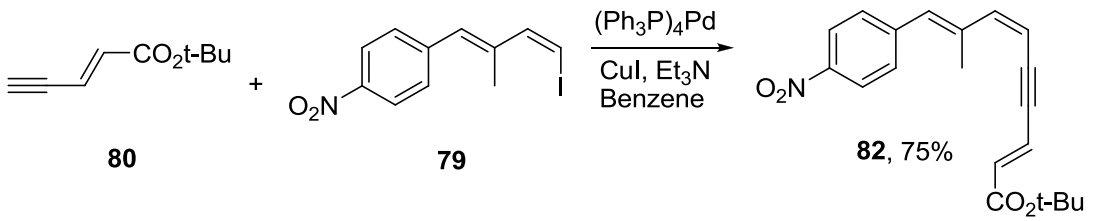
26 **80**, 43% **81**, 13%

In a 250 mL round bottom flask, 3 g (54 mmol) of propargyl alcohol was dissolved in 170 mL of dry CH_2Cl_2. 45 g (517 mmol) of MnO_2 was added to the reaction solution rapidly. After 10 minutes stirring, 15 g (40 mmol) of (tert-butoxycarbonylmethylene)triphenylphosphorane was added to the reaction. The black reaction suspension was stirred for 3 hours. The solid was filtered off. After solvents were removed in vacuo, the organic products were separated by a silica gel column with 20:1 hexanes and AcOEt to give 2.64g of trans-product **80** (17.2 mmol, 43%) and 0.79 g of cis-product **81** (6.2 mmol, 13%).

Cis **80** ^{1}HNMR ($CDCl_3$): δ 6.09 (d, 1H, ^3J = 12.0 Hz), 6.04 (d, 1H, ^3J = 12.0 Hz), 3.55 (s, 1H), and 1.50 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 163.8, 132.9, 120.8, 88.7, 81.5, 79.9, and 28.2. IR (KBr): υmax 3273, 2979, 2934, 1716, 1476, 1394, 1313, 1256, 1154, and 979 cm^{-1}

Trans **81** ^{1}HNMR ($CDCl_3$): δ 6.62 (d, 1H, ^3J = 16.0 Hz), 6.23 (d, 1H, ^3J = 16.0 Hz), 3.28 (s, 1H), and 1.47 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 164.8, 134.6, 123.0, 85.3, 81.4, 80.5, and 28.2. δ. IR (KBr): υmax 3273, 2979, 2934, 1716, 1476, 1394, 1313, 1256, 1154, and 979 cm^{-1}

(E)-ester 82.

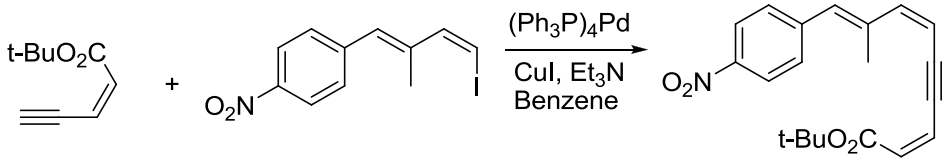


80 **79** **82**, 75%

In a 25 mL round bottom flask, 300 mg (0.95 mmol) of iododiene **79** was added to a solution of 174 mg (1.14 mmol) of ester **80** in 10 mL of benzene at room temperature. Then 40 mg of tetrakis(triphenylphosphine)palladium and 10 mg of triethylamine were added individually under argon. After 14 mg of copper iodide was added to the reaction, the yellow solution became dark brown immediately. The reaction was stirred for 12 hours at room temperature. The solid was filtered off. The filtrate was concentrated in vacuo. The residues were separated by a silica gel column with 10:1 hexane/ethyl acetate to afford 274 mg of compound **82** (0.80 mmol, 75%).

^{1}HNMR ($CDCl_3$): δ 8.21 (d, 1H, ^{3}J = 8.8 Hz), 7.45 (d, 1H, ^{3}J = 8.8 Hz), 6.84 (dd, 1H, ^{3}J = 15.6 Hz, ^{4}J = 2.8 Hz), 6.74 (s, 1H), 6.47 (d, 1H, ^{3}J = 12.0 Hz), 6.14 (d, 1H, ^{3}J = 15.6 Hz), 5.763 (dd, 1H, ^{3}J = 12.0 Hz, ^{4}J = 2.8 Hz), 2.34 (s, 3H), and 1.49 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 165.1, 147.6, 146.5, 144.8, 143.9, 139.9, 132.9, 132.0, 130.1, 123.7, 108.1, 96.4, 94.2, 81.3, 28.2, and 17.0. IR (KBr): υmax 3401, 2976, 2856, 2175, 1712, 1593, 1519, 1392, and 1259 cm^{-1}

(Z)-ester 83.



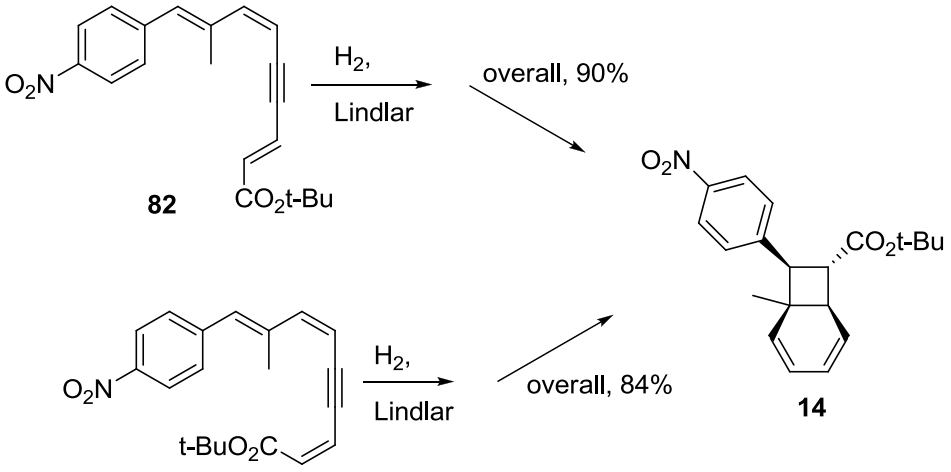
81 **79** **83**, 64%

In a 25 mL round bottom flask, 150 mg (0.48 mmol) of iododiene **79** was added to a solution of 134 mg (0.88 mmol) of ester **81** in 10 mL of benzene at room temperature.

Then 30 mg of tetrakis(triphenylphosphine)palladium and 10 mg of triethylamine were added individually under argon. After 8 mg of copper iodide was added to the reaction, the yellow solution became dark brown immediately. The reaction was stirred for 12 hours at room temperature. The solid was filtered off. The filtrate was concentrated in vacuo. The residues were separated by a silica gel column with 10:1 hexane/ethyl acetate to afford 107 mg of compound **83** (0.31 mmol, 64%).

^{1}HNMR ($CDCl_3$): δ 8.20 (d, 1H, ^{3}J = 7.2 Hz), 7.45 (d, 1H, ^{3}J = 7.2 Hz), 6.83 (s, 1H), 6.44 (d, 1H, ^{3}J = 12.0 Hz), 6.23 (dd, 1H, ^{3}J = 11.2 Hz, ^{4}J = 2.8 Hz), 6.01 (d, 1H, ^{3}J = 12.0 Hz), 5.86 (dd, 1H, ^{3}J = 11.2 Hz, ^{4}J = 2.8 Hz), 2.34 (s, 3H), and 1.49 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 165.2, 147.6, 146.6, 144.8, 143.9, 139.9, 132.9, 132.0, 130.2, 124.0, 108.2, 96.4, 94.3, 81.3, 28.2, 163.8, 132.9, 120.8, 88.7, 81.5, 79.9, and 28.2. IR (KBr): υmax 3405, 2977, 2932, 2179, 1707, 1594, 1519, 1455, 1368, 1258, and 1150 cm^{-1}.

SNF analogue 14.



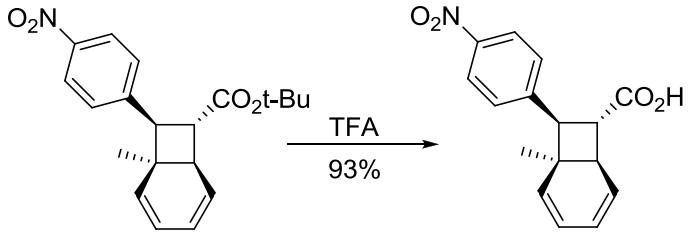
(a) From **82**: Under hydrogen, a solution of 340 mg (1 mmol) of ester **82** in 5 mL of ethyl acetate was added to 100 mg of Lindlar catalyst in a 25 mL round bottom flask. The reaction was stirred for half an hour under H_2 in the darkness at room temperature. Then the reaction was flushed with Argon. The reaction was stirred for a day at room

temperature. The solid was filtered off. The filtrate was concentrated in vacuo. The residues were separated by a TLC plate with 20:1 hexanes/ ethyl acetate to afford 305 mg of compound **14** (0.9 mmol, 90%)

(b) From **83**: Under hydrogen, a solution of 80 mg (24 mmol) of ester **83** in 5 mL of ethyl acetate was added to 34 mg of Lindlar catalyst in a 25 mL round bottom flask. The reaction was stirred for half an hour under H_2 in the darkness at room temperature. Then the reaction was flushed with Argon. The reaction was stirred for a day at room temperature. The solid was filtered off. The filtrate was concentrated in vacuo. The residues were separated by a TLC plate with 20:1 hexanes/ ethyl acetate to afford 67 mg of compound **14** (20 mmol, 84%)

^{1}HNMR ($CDCl_3$): δ 8.17 (d, 2H, ^3J = 9.2 Hz), 7.37 (d, 2H, ^3J = 9.2 Hz), 5.79 (m, 3H), 4.89 (d, 1H, ^3J = 10.0 Hz), 3.76 (d, 2H, ^3J = 10.5 Hz), 3.53 (dd, 2H, ^3J = 10.5 Hz, ^3J = 10.0 Hz), 2.91 (dd, 2H, ^3J = 9.6 Hz, ^3J = 6.0 Hz), 1.41 (s, 9H), and 1.30 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 172.7, 147.0, 145.7, 130.2, 128.3, 124.8, 123.7, 123.6, 123.5, 81.0, 57.8, 47.1, 42.8, 41.3, 28.2, and 28.1. IR (KBr): υmax 2916, 1724, 1592, 1515, 1444, 1341, 1181, and 962 cm^{-1}.

Acid 85.



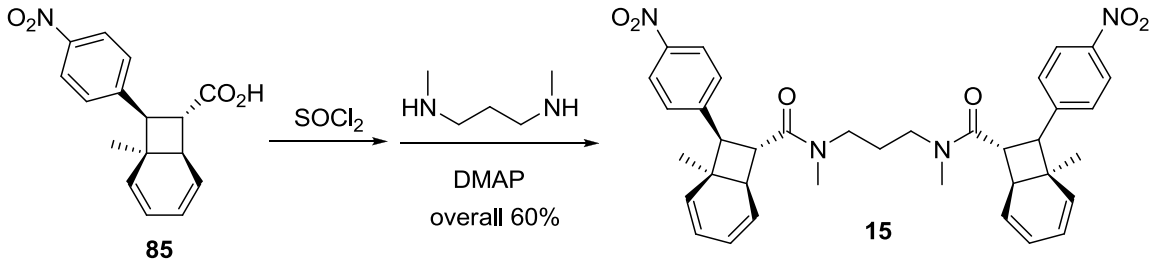
14 **85**

80 mg (24 mmol) of ester in 10 mL of THF was treated with 1 mL of TFA at 0 °C. The reaction was warmed up to room temperature and stirred overnight. The reaction was quenched with 10 mL of water. The solution was extracted three times with methylene

chloride. The organic layers were combined and dried over $MgSO_4$, concentrated in vacuo to afford 62mg of crude acid **85** (22 mmol, 93%).

^{1}HNMR ($CDCl_3$): δ 8.18 (d, 2H, ^3J = 8.8 Hz), 7.38 (d, 2H, ^3J = 8.8 Hz), 5.84 (m, 2H), 5.75 (dd, 1H, ^3J = 8.8 Hz, ^3J = 5.6 Hz), 4.91 (d, 1H, ^3J = 9.6 Hz), 3.85 (d, 2H, ^3J = 10.4 Hz), 3.65 (dd, 2H, ^3J = 10.4 Hz, ^3J = 9.2 Hz), 3.00 (dd, 2H, ^3J = 9.2 Hz, ^3J = 6.0 Hz), and 1.31 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 179.0, 147.1, 144.9, 130.1, 128.2, 124.1, 123.9, 123.8, 123.7, 57.4, 45.8, 43.2, 41.4, and 29.8. IR (KBr): υmax 3401, 2922, 2851, 1702, 1598, 1518, 1455, and 1345 cm^{-1}.

SNF analogue 15.

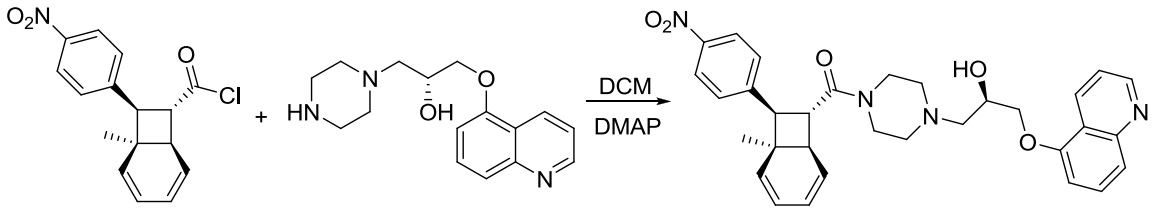


85 **15**

At 0 °C, 0.5 mL of thionyl chloride was added to a solution of 62 mg (0.22 mmol) of acid **85** in 5 mL of methylene chloride. The reaction was stirred for half an hour. The solvent and extra thionyl chloride was removed in vacuo. The crude product was used directly. 11 mg (0.11 mmol) of N,N'-dimethylpropane-1,3-diamine and 25 mg (0.2 mmol) of DMAP in 2 mL of methylene chloride were added to the acid chloride at 0 °C. The reaction was warmed up to room temperature and stirred overnight. The reaction was quenched with saturated NH_4Cl. The solution was extracted three times with methylene chloride. The organic layers were combined and dried over $MgSO_4$. After solvents were removed in vacuo, the residues were separated by a TLC plate with 2:1 hexanes and ethyl acetate to afford 42 mg of compound **15** (0.13 mmol, 60%).

Mixture ^{1}HNMR ($CDCl_3$): δ 8.15 (m, 2H), 7.35 (m, 2H), 5.86 (m, 2H), 5.75 (m, 1H), 4.98 (d, 1H, ^{3}J = 10.6 Hz), 4.04 (m, 1H), 3.83 (dd, 1H, ^{3}J = 10.0 Hz, ^{3}J = 8.8 Hz), 2.98 (m, 6H), 2.89 (m, 5H), 1.71 (m, 2H), and 1.29 (m, 6H). ^{13}CNMR ($CDCl_3$): δ 172.2, 147.0, 145.9, 131.4, 128.6, 124.6, 124.1, 123.7, 123.0, 56.3, 47.8, 45.7, 44.9, 42.6, 42.6, 36.0, and 27.8. IR (KBr): υmax 3032, 2946, 1633, 1603, 1517, 1493, 1452, 1346, and 1109 cm^{-1}.

SNF analogue 16.



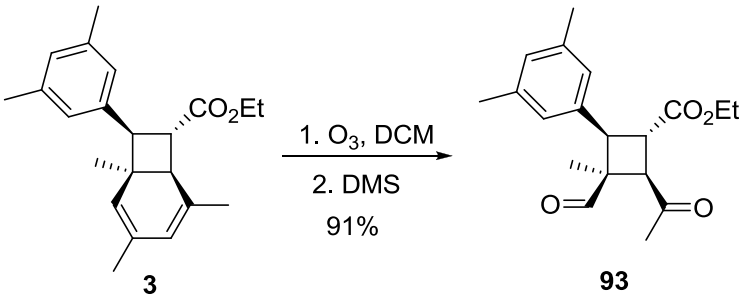
86 **52** **16**, 38%

At 0 °C, 0.5 mL of thionyl chloride was added to a solution of 60 mg (0.21 mmol) of acid **85** in 5 mL of methylene chloride. The reaction was stirred for half an hour. The solvent and extra thionyl chloride was removed in vacuo. The crude product was used directly. 31 mg (0.11 mmol) of amine **52** and 12 mg (0.1 mmol) of DMAP in 2 mL of methylene chloride were added to the residues at 0 °C. The reaction was warmed up to room temperature and stirred overnight. The reaction was quenched with saturated NH_4Cl. The solution was extracted three times with methylene chloride. The organic layers were combined and dried over $MgSO_4$. After solvents were removed in vacuo, the residues were separated by a TLC plate with 2:1 hexanes and ethyl acetate to afford 44 mg of compound **16** (0.079 mmol, 71%).

Mixture of diastereomers ^{1}HNMR ($CDCl_3$): δ 8.90 (d, 1H, ^{3}J = 3.2 Hz), 8.55 (d, 1H, ^{3}J = 8.0 Hz), 8.16 (d, 2H, ^{3}J = 8.8 Hz), 7.71 (d, 1H, ^{3}J = 8.4 Hz), 7.59 (dd, 1H, ^{3}J = 8.4 Hz, ^{3}J = 7.6 Hz), 7.36 (m, 3H), 6.87 (d, 1H, ^{3}J = 7.6 Hz), 5.89 (m, 2H), 5.72 (m, 1H),

5.02 (dd, 1H, ^{3}J = 9.6 Hz), 4.28 (m, 1H), 4.19 (m, 2H), 4.10 (d, 1H, ^{3}J = 10.0 Hz), 3.78 (dd, 1H, ^{3}J = 10.0 Hz, ^{3}J = 9.6 Hz), 3.60 (m, 4H), 2.91 (dd, 1H, ^{3}J = 7.6 Hz, ^{3}J = 7.2 Hz), 2.68 (m, 4H), 2.50 (m, 2H), and 1.27 (d, 3H). ^{13}CNMR ($CDCl_3$): δ 170.7, 154.1, 150.9, 149.2, 147.0, 145.6, 131.5, 130.8, 129.5, 128.5, 124.5, 124.1, 123.7, 123.0, 122.3, 120.9, 120.4, 105.5, 70.8, 65.9, 60.9, 56.0, 46.0, 44.6, 42.8, 42.5, 42.1, and 27.9. IR (KBr): υmax 3397, 3035, 2923, 2854, 1634, 1589, 1516, 1456, 1407, 1345, and 1266 cm^{-1}.

Cyclobutane 93.



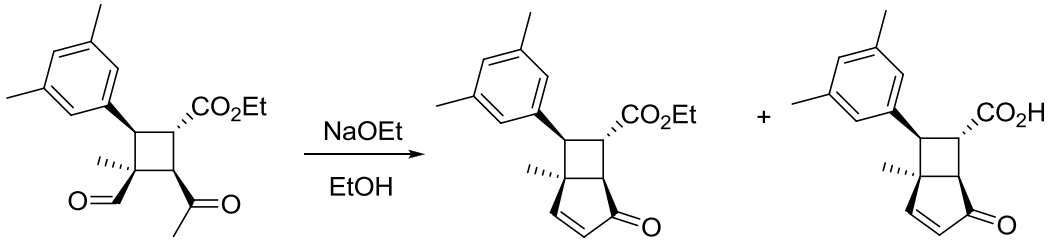
3 **93**

A solution of the ester (**3**, 9.1 mg, 0.028 mmol) in methylene chloride (15 mL) was cooled down to -78 °C under nitrogen. Oxygen was flushed through the mixture at -78 °C for 5 minutes. Then ozone was pumped to the mixture for 3 minutes to give a blue solution. After the ozone stream was continued for 3 more minutes, an oxygen stream was flushed through the mixture for 10 minutes. Nitrogen was passed through the mixture for half an hour to remove oxygen and ozone. Dimethyl sulfide was added to the mixture. Then the mixture was stirred overnight at room temperature. The mixture was concentrated in vacuo. The residues were separated by a TLC plate with ethyl acetate and hexanes (1:10) to give pure oil **93** (8.1 mg, 0.026 mmol, 91%).

^{1}HNMR ($CDCl_3$): δ 9.24 (s, 1H), 6.87 (s, 1H), 6.79 (s, 2H), 4.19 (q, 2H, ^{3}J = 7.5 Hz), 3.98 (t, 1H, ^{3}J = 10.5 Hz), 3.57 (d, 1H, ^{3}J = 10.5 Hz), 3.27 (d, 1H, ^{3}J = 10.5 Hz), 2.25 (s, 6H), 2.12 (s, 3H), 1.69 (s, 3H), and 1.28 (t, 3H, ^{3}J = 7.5 Hz). ^{13}CNMR ($CDCl_3$): δ

209.5, 193.0, 168.3, 138.3, 135.2, 129.2, 125.0, 50.8, 50.4, 49.6, 40.9, 23.8, and 21.5. IR (KBr): υmax 3410, 2975, 2960, 1730, 1605, and 1160 cm^{-1}

Bicyclo[3.2.0]hept-2-ene 94 and **95**.



93 **94**, 25% **95**, 75%

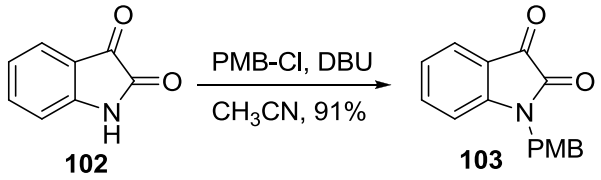
Sodium (200 mg) was added to dry ethanol (2 mL). The reaction was stirred for 3 hours to give a sodium ethoxide solution. The solution was added to a solution of cyclobutane (**93**, 8.1 mg, 0.026 mmol) in dry ethanol (2 mL). The reaction was stirred overnight at room temperature; and then it was quenched by HCl (1M, 10 mL). The water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. The organic solution was concentrated in vacuo. The residues were separated by a TLC plate with ethyl acetate and hexanes (1:10) to give the acid **95** (6.4 mg, 0.019 mmol, 75%) and the ester **94** (2.1 mg, 0.007 mmol, 25%).

94 ^{1}HNMR ($CDCl_3$): δ 7.12 (d, 1H, ^{3}J = 6.0 Hz), 6.88 (s, 1H), 6.71 (s, 2H), 6.25 (d, 1H, ^{3}J = 6.0 Hz), 4.18 (t, 2H, ^{3}J = 7.5 Hz), 3.77 (d, 1H, ^{3}J = 9.0 Hz), 3.10 (dd, 1H, ^{3}J = 9.0 Hz, , ^{3}J = 9.0 Hz), 2.92 (d, 1H, ^{3}J = 5.5 Hz), 2.29 (s, 6H), 1.56 (s, 3H), and 1.26 (t, 3H, ^{3}J = 7.5 Hz). IR (KBr): υmax 2950, 2905, 1730, 1709, 1460, and 1378 cm^{-1}

95 ^{1}HNMR ($CDCl_3$): δ 7.16 (d, 1H, ^{3}J = 5.0 Hz), 6.89 (s, 1H), 6.71 (s, 2H), 6.27 (d, 1H, ^{3}J = 5.0 Hz), 3.81 (s, 1H), 3.15 (s, 1H), 3.00 (s, 1H), 2.29 (s, 6H), and 1.50 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 173.3, 168.0, 138.3, 135.2, 130.8, 129.0, 125.1, 124.9, 61.5, 50.5,

41.3, 29.9, 21.5, and 14.4. IR (KBr): υmax 3455, 2960, 2935, 2806, 1730, 1709, 1460, and 1378 cm^{-1}

PMB protected isatin 103.

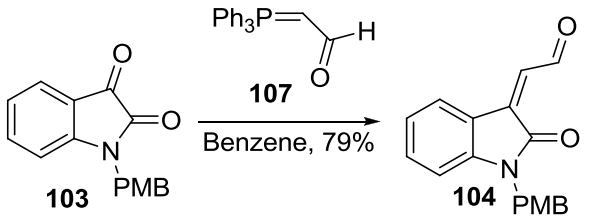


102 **103**

Isatin (**102**, 540 mg, 3.67 mmol) and p-methoxybenzyl chloride (0.54 mL, 4.2 mmol) in dry acetonitrile (20 mL) was added by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 1.0mL) dropwise at room temperature. [67] The solution was stirred for half an hour at 60 °C. Then the reaction was cooled down to 0 °C. HCl (1M, 10 mL) was added to quench the reaction. The organic phase was separated, and the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residues were separated by a silica gel column with ethyl acetate and hexanes (1:10) to give protected isatin **103** (960 mg, 3.34 mmol, 91%).

^{1}HNMR ($CDCl_3$): δ 7.60 (d, 1H, ^3J = 7.5 Hz), 7.48 (t, 2H, ^3J = 7.5 Hz), 7.26 (d, 2H, ^3J = 6.6 Hz), 7.09 (t, 1H, ^3J = 7.5 Hz), 6.85 (t, 1H, ^3J = 6.9 Hz), 4.82 (s, 2H), and 3.83 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 183.2, 159.3, 158.1, 150.6, 138.2, 128.8, 126.3, 125.2, 123.6, 117.5, 114.2, 110.8, 55.1, and 43.3. IR (KBr): υmax 2955, 1737, 1691, 1612, 1513, 1467, 1246, and 1175 cm^{-1}

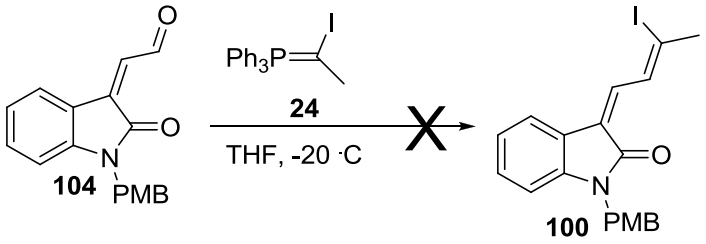
Aldehyde 104.[68]



A solution of PMB protected isatin (**103**, 130 mg, 0.5 mmol) in dry benzene (10 mL) was added by a solution of (formylmethylene)triphenylphosphorane (200 mg, 0.75 mmol) in dry benzene (5 mL). The solution was refluxed for 3 hours at 75 °C. The mixture was concentrated in vacuo. The residues were separated by a silica gel column with ethyl acetate and hexanes (1:4) to give the red aldehyde **104** (120 mg, 39 mmol, 79%).

^{1}HNMR ($CDCl_3$): δ 11.12 (d, 1H, ^{3}J = 7.8 Hz), 7.46 (d, 1H, ^{3}J = 7.5 Hz), 7.30 (m, 4H), 7.02 (t, 1H, ^{3}J = 7.5 Hz), 6.85 (d, 2H, ^{3}J = 6.6 Hz), 6.74 (d, 1H, ^{3}J = 8.1 Hz), 6.71 (d, 1H, ^{3}J = 7.5 Hz), 4.86 (s, 2H), and 3.78 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 192.1, 165.9, 159.2, 144.5, 139.5, 132.9, 129.2, 128.7, 127.1, 122.8, 122.4, 121.2, 114.2, 109.7, 55.2, and 43.1. IR (KBr): υmax 2958, 2867, 1791, 1718, 1664, 1615, 1470, 1341, 1215, and 1182 cm^{-1}

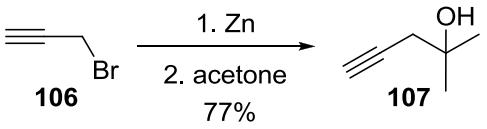
Attempt at iodo-diene 100.



A suspension of (iodoethyl)triphenylphosphonium iodide (25 mg, 0.046 mmol) in THF (5 mL) was cooled down to -20 °C. Sodium hexamethyldisilazane (1 M, 0.05 mL) was added dropwise to the suspension by a syringe to give a red solution. After the solution was stirred for 10 minutes, a solution of the aldehyde (**104**, 13 mg, 0.044 mmol)

in THF (5 mL) was added dropwise to the mixture at -20 °C to give a green solution. After the reaction was stirred for 2 hours at -20 °C, it was quenched by sat. ammonium chloride solution (0.2 mL). The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residues were separated by a silica gel column with ethyl acetate and hexanes (1:3). No desired product was given and the starting material was obtained.

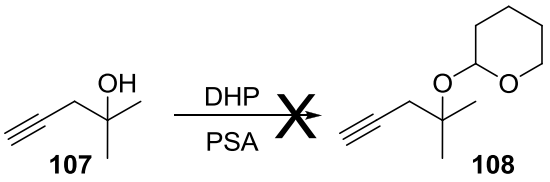
2-Methylpent-4-yn-2-ol 107.[69]



Acetone was distilled off from calcium chloride. Zinc was washed with HCl (0.2 g/L) and then ether. Propargyl bromide (**106**, 5 mL, 89 mmol) was added dropwise to zinc in THF at 0 °C. The reaction was stirred for 4 hours. Then acetone in THF was added the reaction at 0 °C. The reaction was stirred overnight and then the solid was filtered off. HCl (3M, 10 mL) was added to the filtrate. The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, oil **107** (4.9 g, 69 mmol, 77%) was distilled out.

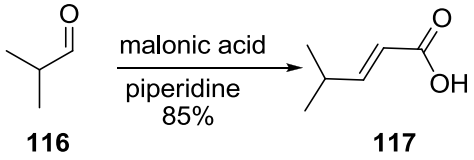
^{1}HNMR ($CDCl_3$): δ 2.37 (d, 2H, ^3J = 2.7 Hz), 2.08 (t, 1H, ^3J = 2.4 Hz), and 1.32 (s, 6H). IR (KBr): υmax 3399, 2976, 2915, 2884, 1680, 1617, 1466, 1367, and 1299 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [69]

Attempt at THP protected alcohol 108.



p-Toluenesulfonic acid (61 mg, 0.35 mmol) was added to a mixture of the alcohol (**107**, 430 mg, 4.38 mmol) and dihydropyran (1.2 mL) in methylene chloride (25 mL). The mixture was stirred overnight to give a dark red solution. Then the reaction was quenched by sat. sodium bicarbonate solution (10 mL). The organic phase was separated; the water phase was extracted three times by ether. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residues were separated by a silica gel column with ethyl acetate and hexanes (1:15) to give the starting material back.

(E)-4-Methylpent-2-enoic acid 117.[75]

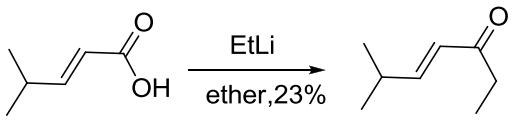


iso-Butanal (**116**, 5 mL, 64 mmol) was mixed with malonic acid (5.8 g, 58 mmol) and piperidine (20 mL). The mixture was stirred at 60 °C overnight and quenched by HCl (3 M, 100 mL). The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residues were separated by a silica gel column with acetone and hexanes (1:2) to give the liquid **117** (5.41 g, 54.4 mmol, 85%).

^{1}HNMR ($CDCl_3$): δ 7.02 (dd, 1H, ^3J = 15.9 Hz, ^3J = 6.6 Hz), 5.76 (d, 1H, ^3J = 15.9 Hz), 2.43 (m, 1H), and 1.04 (d, 6H, ^3J = 6.6 Hz,). ^{13}CNMR ($CDCl_3$): δ 171.9, 157.6, 118.5, 31.1, and 21.2. IR (KBr): υmax 3414, 3092, 2966, 2874, 1701, 1656, 1467, 1387,

and 1214 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [75]

Ketone 115.[75]

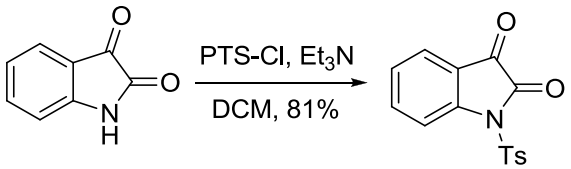


117 **115**

Under nitrogen, ethyl lithium (0.5 M, 20 mL, 10 mmol) was added dropwise to a mixture of the acid (**117**, 507 mg, 4.44 mmol) and dry ether (30 mL) at -78 °C. The reaction was stirred for an hour at -78 °C and then for 3 hours at room temperature. The reaction was quenched by sat. NH_4Cl solution (5 mL). The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residue was separated by a silica gel column with ethyl acetate and hexanes (1:20) to give oil **115** (131 mg, 1.0 mmol, 23%).

^{1}HNMR ($CDCl_3$): δ 6.78 (dd, 1H, ^{3}J = 15.9 Hz, ^{3}J = 6.6 Hz), 6.03 (d, 1H, ^{3}J = 15.9 Hz), 2.53 (dd, 2H, ^{3}J = 7.5 Hz), 2.43 (m, 1H), and 1.05 (m, 9H). ^{13}CNMR ($CDCl_3$): δ 201.662, 153.244, 127.360, 33.365, 31.210, 21.459, and 8.286. IR (KBr): υmax 2995, 2905, 2815, 1736, 1460, 1373, and 1188 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [75]

p-Toluenesulfonyl protected isatin 118.



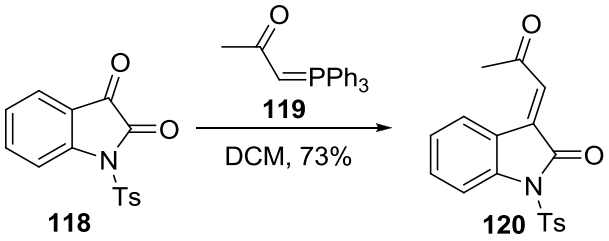
102 **118**

p-Toluenesulfonyl chloride was added to a mixture of isatin (**102**, 2 g, 13.6 mmol), triethylamine (10 mL) and methylene chloride (15 mL). [76] The mixture was stirred

overnight at room temperature to form a lot of yellow solid. Then the solid was filtered off. The yellow solid was washed with toluene once and ether twice. The solid was recrystallized in methylene chloride to give a yellow crystal **118** (3.9g, 11 mmol, 81%).

^{1}HNMR ($CDCl_3$): δ 8.08 (d, 1H, ^{3}J = 8.0 Hz), 8.01 (d, 2H, ^{3}J = 8.5 Hz), 7.72 (m, 2H), 7.36 (d, 2H, ^{3}J = 7.5 Hz), 7.28 (t, 1H, ^{3}J = 7.5 Hz), and 2.44 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 179.1, 155.8, 147.7, 146.7, 139.5, 134.6, 130.3, 128.9, 128.1, 126.1, 119.0, 115.3, and 21.9. IR (KBr): υmax 2978, 2738, 2604, 2530, 1774, 1605, 1475, 1397, 1232, and 1202 cm^{-1}.

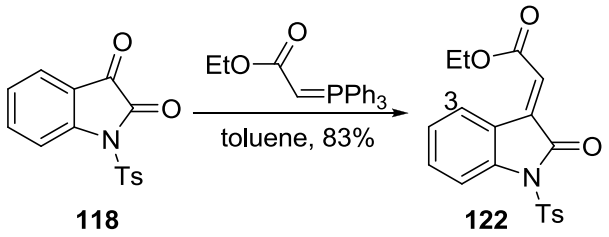
Ketone 120.[77]



A mixture of 1-(triphenylphosphoranylidene)-2-propanone (2.00 g, 6.3 mmol) and protected isatin (**118**, 3.06 g, 10 mmol) in methylene chloride (15 mL) was stirred overnight at room temperature. The solution was concentrated in vacuo. The residues were separated by a silica gel column with ethyl acetate and hexanes (3:1) to give an orange solid **120** (1.46 g, 4.6 mmol, 73%)

^{1}HNMR ($CDCl_3$): δ 8.56 (d, 1H, ^{3}J = 3.0 Hz), 7.98 (dd, 3H, ^{3}J = 3.0 Hz, ^{3}J = 8.5 Hz), 7.48 (dt, 1H, ^{3}J = 8.5 Hz, ^{3}J = 7.5 Hz), 7.32 (d, 2H, ^{3}J = 7.5 Hz), 7.20 (dt, 1H, ^{3}J = 8.5 Hz, ^{3}J = 12.5 Hz), 7.09 (s, 1H), 2.44 (s, 3H), and 2.42 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 166.7, 146.1, 141.4, 135.3, 133.8, 133.1, 130.0, 129.2, 128.3, 128.1, 125.2, 120.7, 113.7, 32.4, and 21.9. IR (KBr): υmax 3022, 2995, 1748, 1613, 1596, 1454, 1380, and 1086 cm^{-1}

Ester 122.

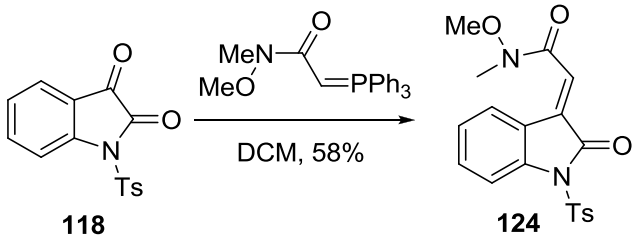


118 **122**

A mixture of (carbethoxymethylene)triphenylphosphorane (260 mg, 0.75 mmol) and protected isatin (**118**, 200 mg, 0.66 mmol) in toluene (20 mL) was stirred overnight at 70 °C. The mixture was concentrated in vacuo. The residues were separated by a silica gel column with ethyl acetate and hexanes (3:1) to give a lot of orange solid **122** (208 mg, 0.81 mmol, 83%)

^{1}HNMR ($CDCl_3$): δ 8.60 (d, 1H, ^{3}J = 7.8 Hz), 7.32 (d, 1H, ^{3}J = 3.0 Hz), 7.28 (d, 2H, ^{3}J = 8.1 Hz), 7.04 (dd, 1H, ^{3}J = 7.5 Hz), 6.90 (d, 2H, ^{3}J = 8.1 Hz), 6.76 (d, 1H, ^{3}J = 8.1 Hz), 4.39 (q, 2H, ^{3}J = 4.2 Hz), 3.79 (s, 3H), and 1.43 (t, 3H, ^{3}J = 4.2 Hz). ^{13}CNMR ($CDCl_3$): δ 167.8, 165.8, 145.3, 137.9, 132.5, 129.0, 127.7, 122.9, 120.2, 114.4, 109.3, 55.4, 43.5, and 14.4. IR (KBr): υmax 2990, 2851, 1741, 1643, 1513, 1460, 1351, and1246 cm^{-1}.

Weinreb amide 124.[74]

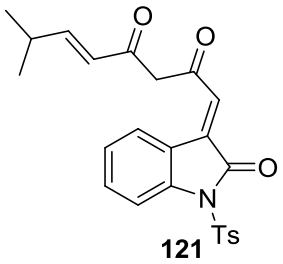


118 **124**

A mixture of N-methoxy-N-methyl(triphenylphosphoranylidene)acetamide (1.006 g, 2.77 mmol) and protected isatin (**118**, 1.54 g, 5 mmol) in dry methylene chloride (15 mL) was stirred overnight at room temperature. The mixture was concentrated and the residues were separated by a silica gel column with ethyl acetate and hexanes (1:2) to give a lot of white solid **124** (580 mg, 1.6 mmol, 58%).

^{1}HNMR ($CDCl_3$): δ 8.41 (d, 1H, ^{3}J = 7.6 Hz), 7.99 (m, 3H), 7.43 (t, 1H, ^{3}J = 8.0 Hz), 7.32 (m, 3H), 7.17 (t, 2H, ^{3}J = 7.6 Hz), 3.72 (s, 3H), 3.33 (s, 3H), 2.42 (s, 3H), and 1.56 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 166.1, 165.0, 145.9, 140.5, 135.1, 133.2, 132.4, 129.9, 127.9, 124.9, 124.3, 120.3, 113.4, 62.3, 32.3, and 21.7. IR (KBr): υmax 2933, 2919, 1711, 1607, 1513, 1466, 1378, 1247, 1178, and 1031 cm^{-1}

Diketone 121.[71]



121

1st try: The acid (**117**, 268 mg, 2.35 mmol) and carbonyl diimidazole (380 mg, 2.5 mmol) were mixed in dry THF (5 mL). The mixture was stirred for one hour at room temperature. A little gas was released. The ketone (**120**, 653 mg, 2.4 mmol) was added dropwise to a suspension of sodium hydride (120 mg) in dry THF (5 mg) in 15 minutes at 0 °C. The suspension was stirred for 15 minutes at room temperature and then was cooled down to 0 °C. The suspension was added dropwise by the solution of imidazole made in the first step. The reaction was stirred for 2 hours and quenched by water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the crude product's NMR showed that only the starting materials were given.

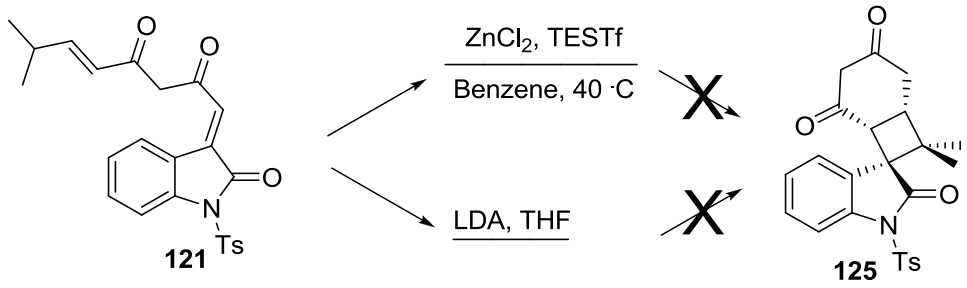
2nd try: A mixture of the ester (**122**, 0.81g, 2.2 mmol) and 1 M KOH in ethanol was stirred for an hour and quenched by 1M HCl. The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residue was separated by a silica gel column with ethyl acetate and hexanes (1:1) to give an acid (157 mg, 21%). The acid (21 mg, 0.062 mmol) and carbonyl diimidazole (26 mg, 0.1 mmol) were dissolved in dry THF (5 mL). The mixture was stirred for one hour at room temperature. A little gas was released. 5-Methyl-3-hexen-2-one (**123**, 37 mg, 0.37 mmol) was added dropwise to a

mixture of lithium diisopropylamide (2 M, 0.2 mL) and hexamethylphosphoramide (0.2 mL) in THF (5 mL) at -78 °C. The reaction was stirred for half an hour at -78 °C to give a light red solution. The carbonyl imidazole solution made in the first step was added dropwise to the reaction in 15 minutes to give a dark yellow mixture. The mixture was stirred for 2 hours at -78 °C and quenched by sat. NH_4Cl solution (5 mL). The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the crude product's NMR showed that only the starting materials were given.

3rd try: Lithium diisopropylamide (2 M, 0.7 mL, 1.4 mmol) was added to a mixture of hexamethylphosphoramide (0.2 mL) and THF (5 mL) at -78 °C. 5-Methyl-3-hexen-2-one (75%, 88 mg, 0.88 mmol) in THF (2 mL) was added dropwise to the mixture in 15 minutes at -78 °C. The reaction was stirred for half an hour at -78 °C to give a light red solution. Winreb amide (**124**, 123 mg, 0.32 mmol) in THF (5 mL) was added dropwise to the reaction during 15 minutes to give a dark yellow mixture. The mixture was stirred for 6 hours at -78 °C and quenched by sat. NH_4Cl solution (5 mL). The organic phase was separated; the water phase was extracted three times by methylene chloride. The organic phases were combined and dried over Na_2SO_4. After concentration of organic solution, the residue was separated by a silica gel column with ethyl acetate and hexanes (1:6) to give yellow oil **121** (57 mg, 0.13 mmol, 41%).

^{1}HNMR ($CDCl_3$): δ 7.99 (m, 2H), 7.92 (d, 1H, ^3J = 8.0 Hz), 7.32 (m, 3H), 7.13 (t, 1H, ^3J = 7.5 Hz), 6.68 (d, 2H, ^3J = 16 Hz), 5.87 (d, 1H, ^3J = 16.5 Hz), 3.80 (s, 2H), 3.14 (s, 2H), 2.79 (m, 1H), 2.55 (m, 1H), 2.40 (s, 1H), and 1.02 (d, 6H, ^3J = 7.5 Hz). ^{13}CNMR ($CDCl_3$): δ 197.7, 174.6, 154.1, 145.6, 139.7, 129.9, 129.7, 129.1, 128.0, 126.7, 125.4, 124.7, 124.5, 113.6, 113.1, 61.6, 45.2, 38.7, 37.1, 31.1, 21.7, and 31.2. IR (KBr): υmax 2975, 1770, 1660, 1460, 1370, 1230, 1180, and 1085 cm^{-1}.

3,5-Dioxobicyclo[4.2.0]octane 125.



1st try: Zinc chloride powder (2 mg, 0.015 mmol) and triethyl amine (1 mL) were stirred together for an hour at room temperature to give a suspension. A solution of the diketone (**121**, 21 mg, 0.048 mmol) in benzene (1 mL) was added to the suspension. Then triethylsilyl triflate was added to this suspension at room temperature. The reaction was allowed to warm up to 40 °C in half an hour. The reaction was stirred for two days. The mixture was concentrated in vacuo. The residues were separated by a TLC plate with ethyl acetate and hexanes to give 3 fractions, but all of them were not the desired product.

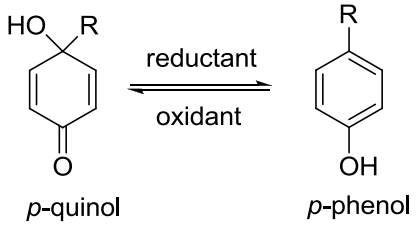
2nd try: A solution of the diketone (**121**, 36.8 mg, 0.084 mmol) in dry THF (5 mL) was cooled down to -78 °C. LDA (2 M, 0.7 mL, 1.4 mmol) was added dropwise to the mixture. Then the reaction was allowed to warm up to room temperature and stirred in the darkness for a day. The reaction was quenched by sat. NH_4Cl solution (5 mL). The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution, the residue was separated by a TLC plate with ethyl acetate and hexanes (1:2) to give 3 fractions, but all of them were not the product wanted and the starting material was recovered.

Chapter 2. 1,2-Addition of Organometallic Reagents to Unprotected Juglones and Progress Toward the Synthesis of Ravidomycins

2.1 Introduction

2.1.1 Addition to Juglone Derivatives

p-Quinols can undergo mild reductions to form *p*-phenols. Oxidations of *p*-phenols can reverse this reduction back to give the corresponding *p*-quinol (Scheme 39). Some biochemical compounds in nature such as coenzyme Q contain *p*-quinol substructures. *p*-Quinols have a variety of uses, principally associated with their actions as reduction or oxidation agents which are soluble in water. Thus *p*-quinols are very important synthetic precursors, pharmaceuticals, metabolic and biosynthetic intermediates, and chemical photoresists. [79] Quinols have been the subject of investigations, both synthetic and mechanistic, for many years.



Scheme **39**. Redox reaction of the system of *p*-quinol and *p*-phenol.

The oxidation of *p*-phenols has been used in the synthesis of *p*-quinols. This transformation can be accomplished by a variety of reagents including peracetic acid, thallium(III) salts, and hypervalent iodine.[80] Most of these procedures suffer from limitations, such as poor yields and various side reactions. The other direct access to quinols is 1,2-addition of an organometallic reagent to a quinone. Alkyllithium and Grignard reagents have been used most frequently for this purpose and organocadmium reagents have been used, recently.[79]

Although 1,2 addition to quinones by organometallic reagents has potential for the synthesis of quinols, its utility is complicated by the formation of double 1,2-addition products, Michael addition products, and/or electron-transfer products (hydroquinones).[81] Electronic or steric differences between the two carbonyl groups in an unsymmetrical quinone may result in the formation of a single *p*-quinol; however, 1,2-addition to these systems usually produces mixtures of regioisomers.[82] Approaches which employ protected quinones or masked quinones such as quinone monoketals and silylcyanohydrins have alleviated the above problems of direct quinine alkylation, but multistep procedures generally give low overall yields from commercially available materials.[79,83]

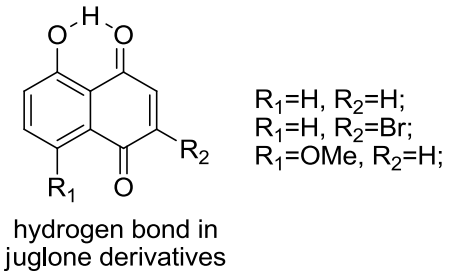
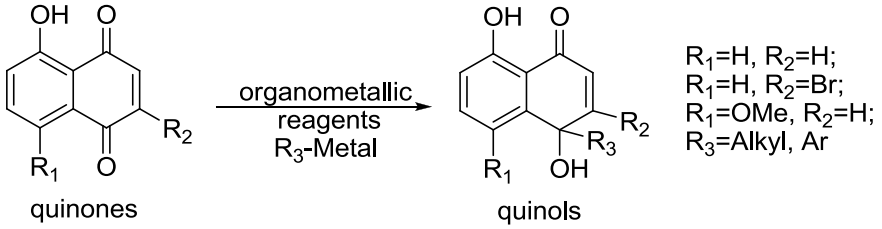


Figure **12**. Juglone and derivatives.

Juglone and bromojuglone contain strong intramolecular hydrogen bonds (Figure 11). The intramolecular hydrogen bonds will be broken in Grignard or alkyllithium

reaction systems, but this process may be slower than addition of the organometallics to the non-hydrogen bonding carbonyl groups. Therefore, treatment of juglone or bromojuglone with one equivalent of Grignard reagent or alkyllithium could lead to a regioselective mono 1,2-adduct at the C-1 position (Scheme 40). 1,2-Addition to a 5-alkoxy naphthoquinone could also give a regioselective monoadduct due to a strong intramolecular hydrogen bond. The regioselective monoadducts of juglone derivatives are seen as key intermediates for the preparation of complex aryl C-glycosides such as gilvocarcins, pluramycins, and griseusins.[84]



Scheme **40**. Additions of organometallics to juglone derivatives.

2.1.1 Ravidomycin

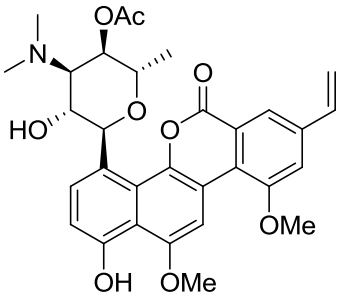


Figure **13**. Ravidomycin.

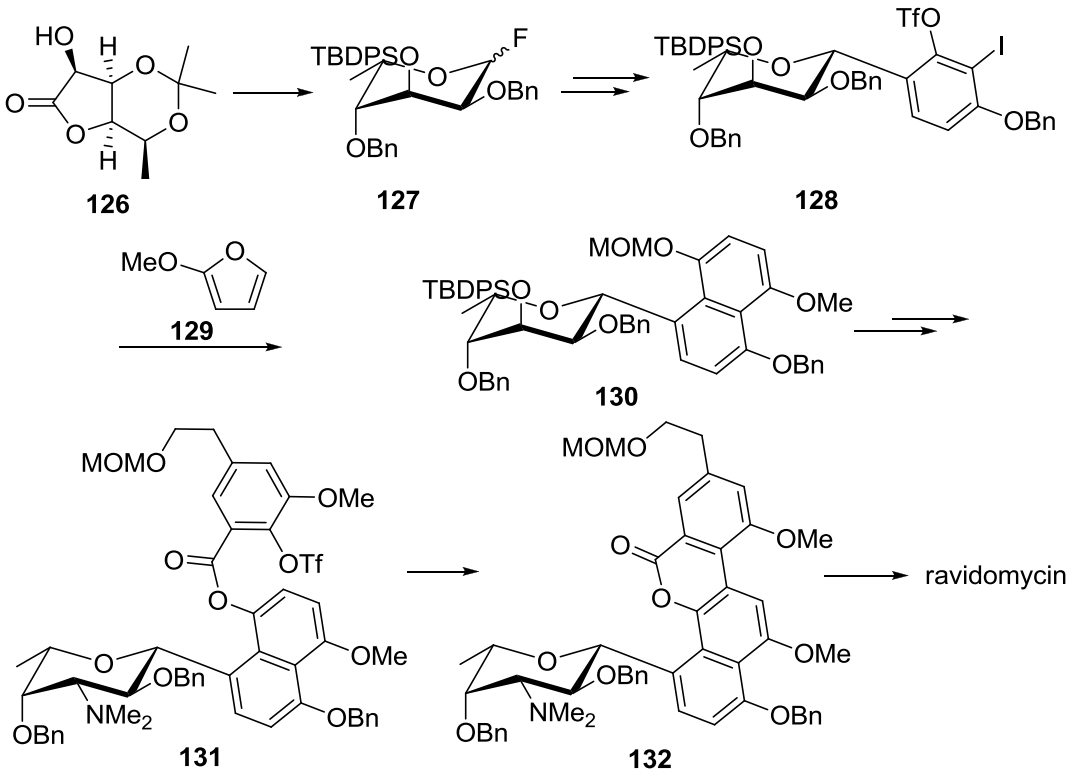
Ravidomycin was isolated from the mycelium of a streptomycete which was obtained from a soil sample from Guatemala (Figure 12). [85] Ravidomycin is an amino sugar congener of the gilvocarcin antibiotics.[86] It contains an amino sugar moiety, 3,6-dideoxy-3-N,N-dimethylamino pseudo altropyranose. The remaining aglycone moiety of

ravidomycin is identical with those of toromycinz and gilvocarcin. Since the complex polycyclic structure is a challenge to synthesize, ravidomycin attracted attention.

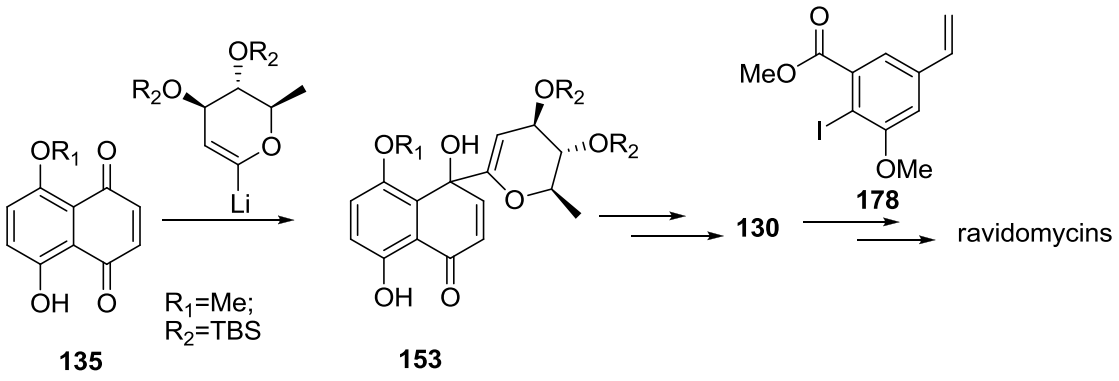
Ravidomycin exhibits strong activity against Gram-positive bacteria, weak activity against Gram-negative bacteria, and no activity against fungi.[86] It also shows strong activity against P388 lymphocytic leukemia, Colon 38 tumor, and CD8F1 mammary tumor in mice. The mechanism of action of ravidomycin is that it selectively inhibits DNA and RNA synthesis at low concentration.[87]

Suzuki and coworkers finished a total synthesis of ravidomycin (Scheme 41).[88] The total synthesis of twenty-six steps started from making compound **126**. The overall yield from **126** is 2%. Actually, if the steps for making **126** are counted in, the synthesis took more than thirty two steps. Since compound **127** containing a fluorine atom was difficult to make, it took 17 steps to get the key intermediate **129**. Therefore, the synthetic route was not efficient. Thus development of a new strategy for preparation of ravidomycin is necessary (Scheme 42). Lithiated rhamnal could be added to quinone **135** to give the regioselective monoadduct **153**. The further transformations give **130** from **153**. Phenyl iodide could couple with **130** to offer the target compound.

The key steps of Suzuki's synthesis of ravidomycin



New strategy for preparation of ravidomycin



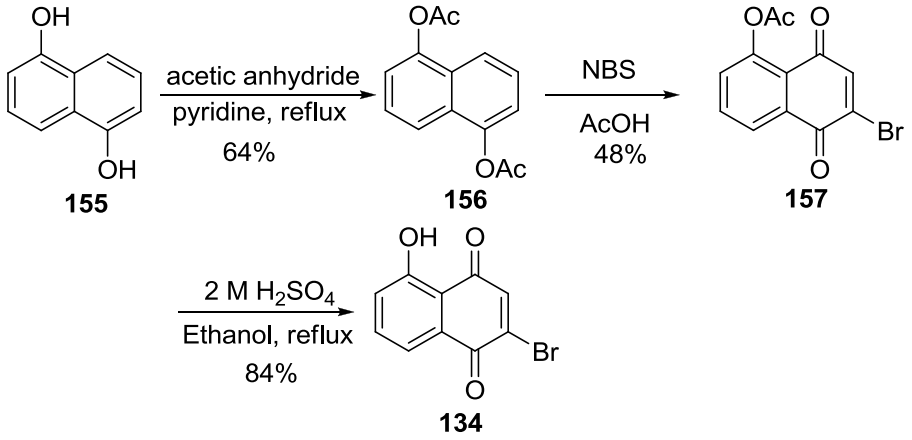
Scheme **41**. The key steps of Suzuki's synthesis of ravidomycin and proposed new strategy for preparation of ravidomycin.

2.2 Results and Discussion

2.2.1 The Syntheses of Substrates for 1,2-Addition

2.2.1.1 The Preparation of Bromojuglone 134

Juglone is commercially available, but 2-bromojuglone (**134)** is not. In order to prepare compound **134**, first the hydroxyl groups of 1,5-dihydroxynaphthalene **155** were acylated by acetic anhydride to 1,5-diacetoxynaphthalene **156** in 64% yield (Scheme 42).[89] Then treatment of 1,5-diacetoxynaphthalene **156** with NBS in acetic acid afforded acetyl-protected bromojuglone **157** in 48% yield.[89] According to Grunwell's procedures, the acetyl protecting group was removed by strong acid to give bromojuglone **134** in 84% yield.[89]

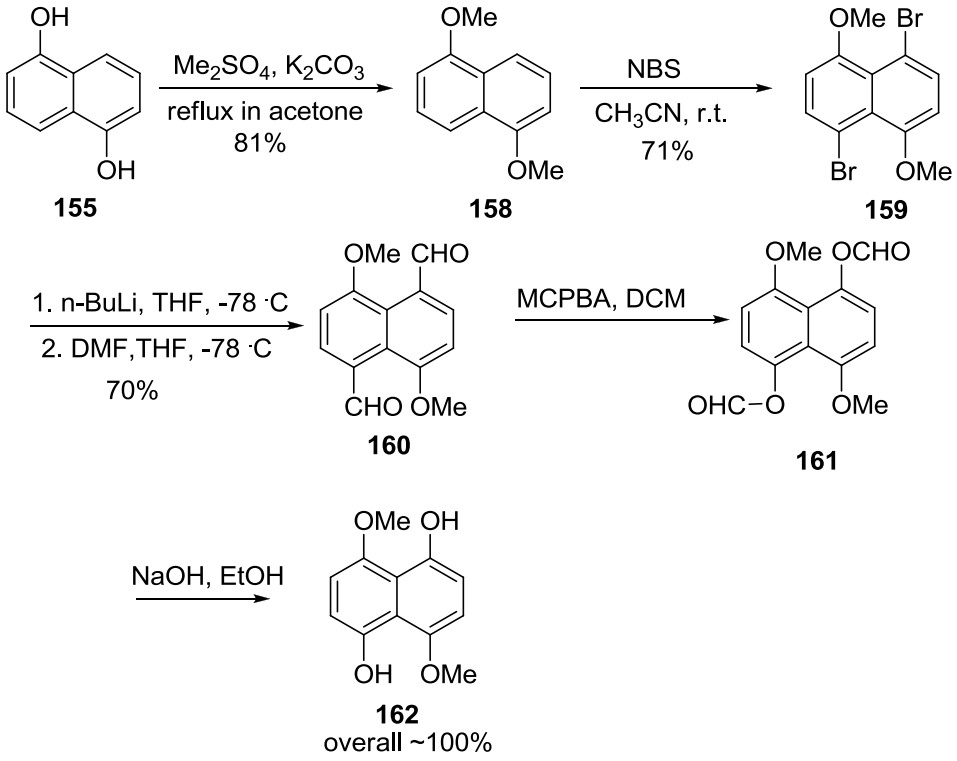


Scheme **42**. Preparation of bromojuglone **134**.

2.2.1.2 The Preparation of 8-Hydroxy-5-methoxy-1,4-naphthoquinone 135

In order to synthesize 8-hydroxy-5-methoxy-1,4-naphthoquinone **135**, its precursor, 4,8-dimethoxynaphthalene-1,5-diol **162**, was prepared first (Scheme 43). The hydroxyl groups of 1,5-dihydroxynaphthalene **155** were methylated by dimethyl sulfate

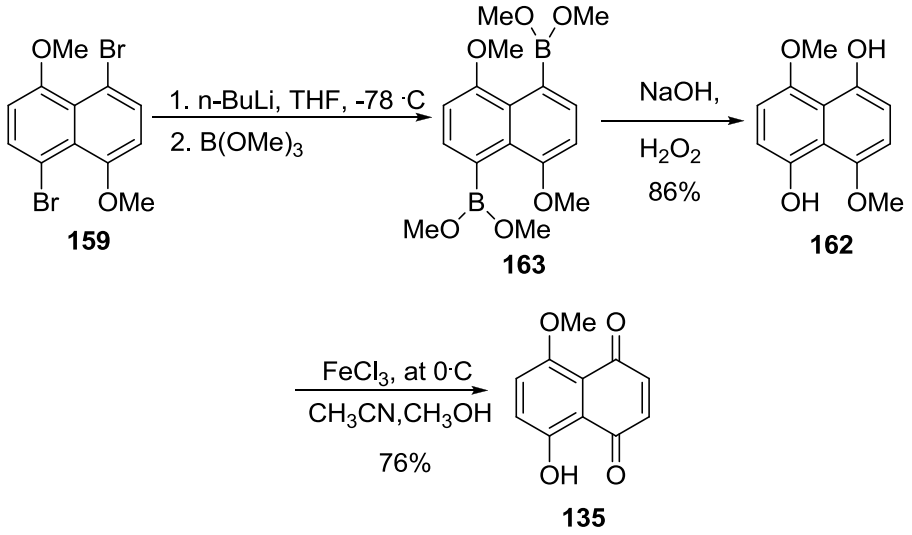
to 1,5-dimethoxynaphthalene **158** in 81% yield. [90] Treatment of 1,5-dimethoxynaphthalene **158** with NBS in acetonitrile afforded 1,5-dibromo-4,8-dimethoxynaphthalene **159** in 71% yield. Dibromide **159** was transformed to a dicarbanion by two equivalents of n-butyl lithium. Addition of the dicarbanion to DMF produced 4,8-dimethoxy-diformylnaphthalene **160** in 70% yield.[91] According to Wipf's procedures, Baeyer-Villiger oxidation of **160** by 3-chloroperoxybenzoic acid yielded a diformate **161** which was hydrolyzed by sodium hydroxide to form 4,8-dimethoxynaphthalene-1,5-diol **162** in quantitative overall yield.[92]



Scheme **43**. Preparation of compound **162**.

A more convenient synthetic route for dimethoxynaphthalenediol **162** was developed (Scheme 44). 1,5-Dibromo-4,8-dimethoxynaphthalene **159** was transformed to a dicarbanion by two equivalents of n-butyl lithium. The reaction was quenched by trimethylborate to afford a dimethoxynaphthalenylborane; then the borane was oxidized

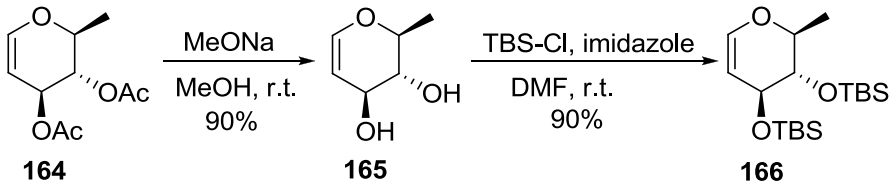
by hydrogen peroxide to yield a naphthalenyldimethoxyborate.[93] The resulting borate was hydrolyzed by sodium hydroxide to produce dimethoxynaphthalenediol **162** in overall 86% yield.[94] According to Wipf's procedures, oxidation of dimethoxynaphthalenediol **162** by iron(III) chloride afforded 8-hydroxy-5-methoxy-1,4-naphthoquinone **135** in 76% yield.[95]



Scheme **44**. Preparation of juglone **135** and the other method for preparation of compound **162**.

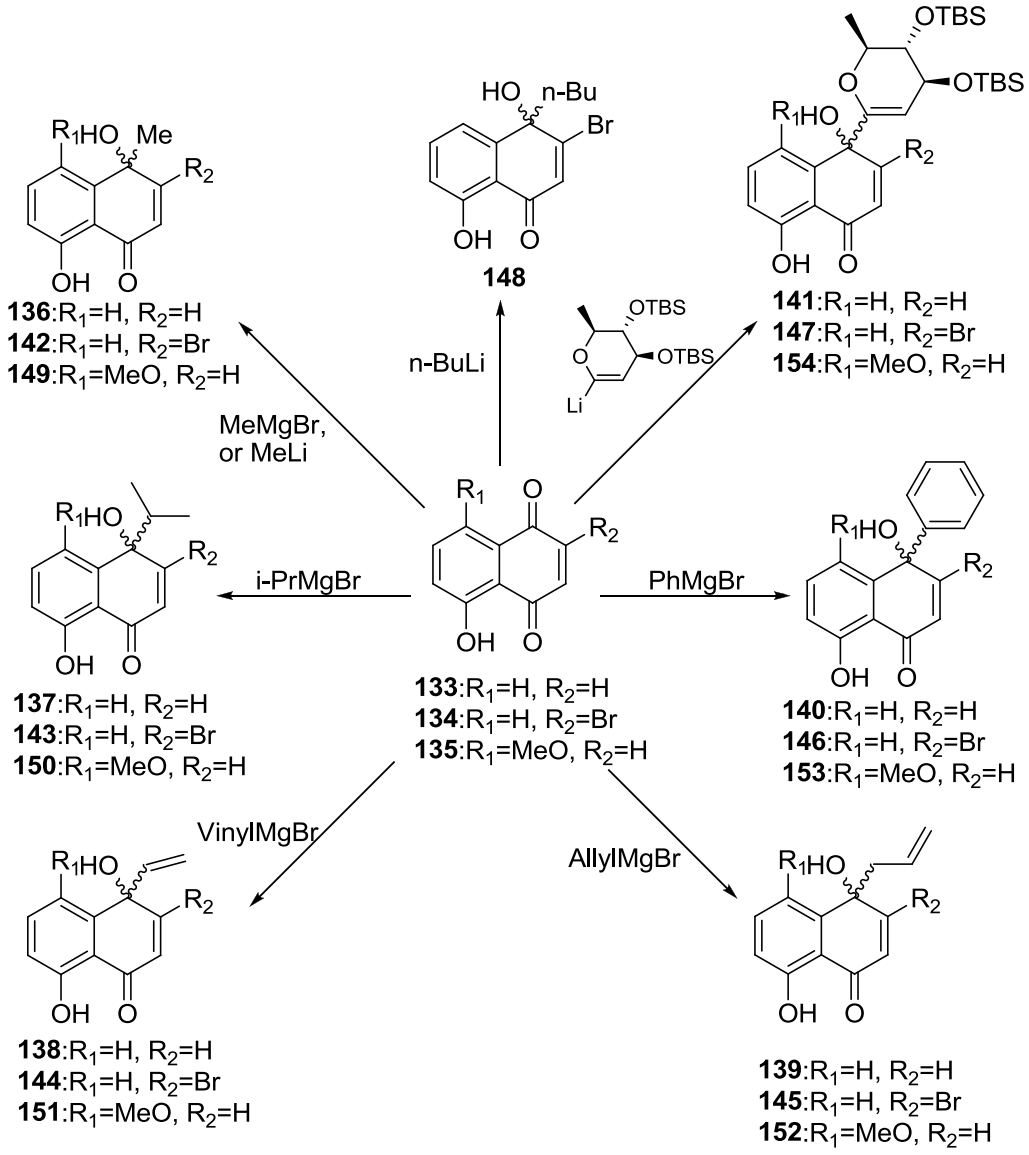
2.2.1.3 The Preparation of TBS-L-Rhamnal 166

3,4-Di-O-acetyl-6-deoxy-L-glucal **164** was hydrolyzed by sodium methoxide to give L-rhamnal **165** in 90% yield (Scheme 45).[96] Treatment of L-rhamnal **165** with imidazole and t-butyldimethylsilyl chloride afforded TBS protected L-rhamnal **166** in 90% yield.[96]



Scheme **45**. Preparation of TBS protected L-rhamnal **166**.

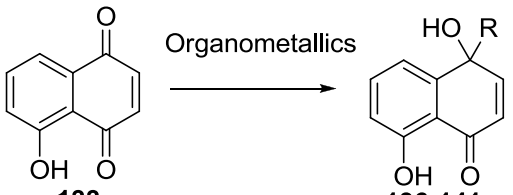
2.2.2-Addition to Juglone Derivatives.



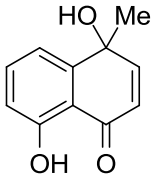
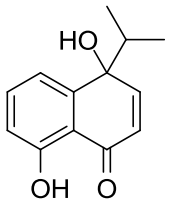
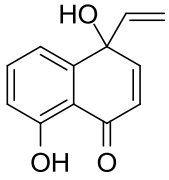
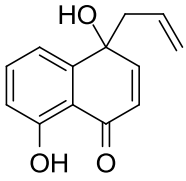
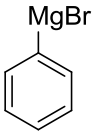
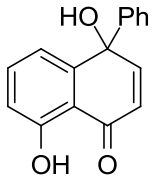
Scheme **46**. 1,2-Additions to juglone derivatives

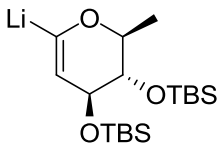
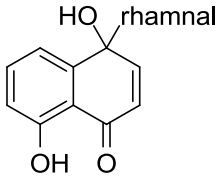
Juglone **133** was added 1.2 equivalents of Grignard reagents or alkyllithium under various reaction conditions to give the monoaddition products in modest yields (Scheme 46 and Table 6.) The organometallic reagents included methylmagnesium bromide, methyl lithium, isopropylmagnesium bromide, phenylmagnesium bromide, vinylmagnesium bromide, allylmagnesium bromide, and lithiated glycal **166**.

Table **6**. 1,2-Additions to juglone **133**



133 **136-141**

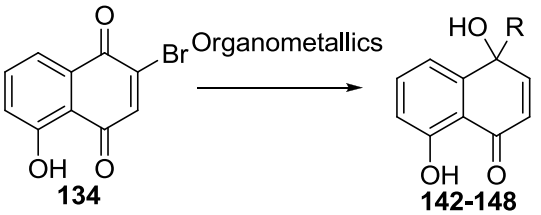
Organometallics	Yields and Conditions	Adducts
MeMgBr	46% 8 hours at -78°C	 **136**
iPrMgBr	41% 8 hours at -78°C	 **137**
 MgBr	8% 0.5 hours at -95°C	 **138**
 MgBr	19% 8 hours at -78°C	 **139**
 MgBr	25% 8 hours at -78°C	 **140**

Organometallics	Yields and Conditions	Adducts
 **166**	0% 48 hours at -78°C	 **141**

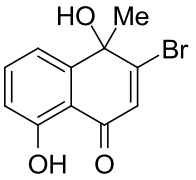
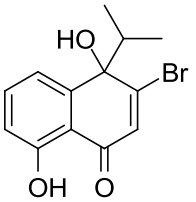
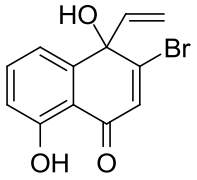
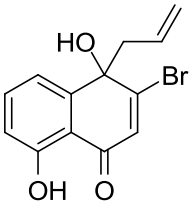
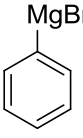
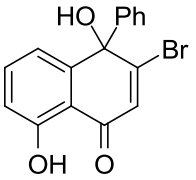
The results showed that methyl and isopropyl magnesium bromide offered a moderate yield of around 45%. However phenyl, vinyl, and allyl magnesium bromide gave low yields of adducts; and lithiated glycal **166** could not give the desired product.

Similar procedures were applied to substrate **134** (Table 7) and **135** (Table 8). Organometallic reagents usually add to 2-haloquinones at the C-4 carbonyl group which is nonadjacent to the halogenated carbon.[108] But when 2-bromojuglone **134** was the substrate, organometallic reagents added to the carbonyl group adjacent to the halo substituent. When bromojuglone **134** was the substrate, lithiated glycal **166** was added to the non-hydrogen bonding carbonyl group to produce compound **154** in 51%yield.

Table **7**. 1,2-Additions to 2-bromojuglone **134**



134 **142-148**

Organometallics	Yields and Conditions	Adducts
MeMgBr	41% 40 minutes at -93°C	 **142**
iPrMgBr	37% 8 hours at -78°C	 **143**
 MgBr	8% 0.5 hours at -95°C	 **144**
 MgBr	0% 8 hours at -78°C	 **145**
 MgBr	16% 8 hours at -78°C 47% 48 hours at -78°C	 **146**

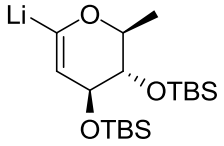
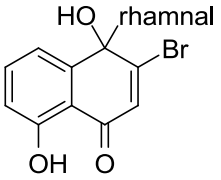
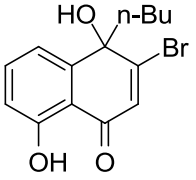
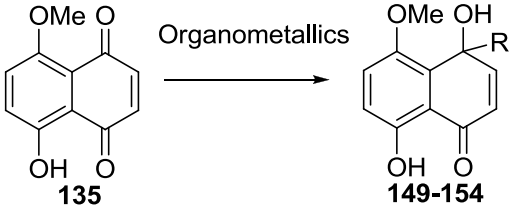
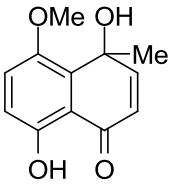
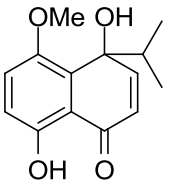
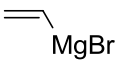
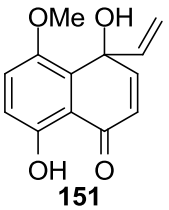
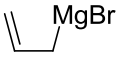
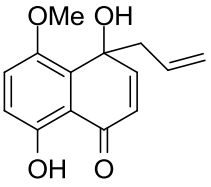
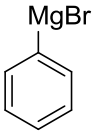
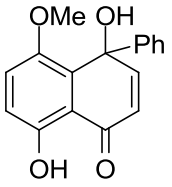
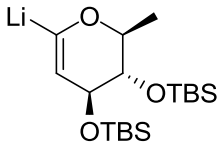
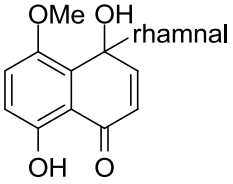
Organometallics	Yields and Conditions	Adducts
 **166**	0% 48 hours at -78°C	 **147**
n-BuLi	46% 0.5 hour at -93°C	 **148**

Table **8**. 1,2-Additions to 8-hydroxy-5-methoxy-1,4-naphthoquinone **135**



Organometallics	Yields and Conditions	Adducts
MeMgBr	57% 12 hours at -72°C	 **149**
iPrMgBr	19% 12 hours at -78°C	 **150**

Organometallics	Yields and Conditions	Adducts
	31% 48 hours at -78°C	 **151**
	20% 12 hours at -78°C	 **152**
	46% 12 hours at -78°C	 **153**
 **166**	51% 48 hours at -78°C	 **154**

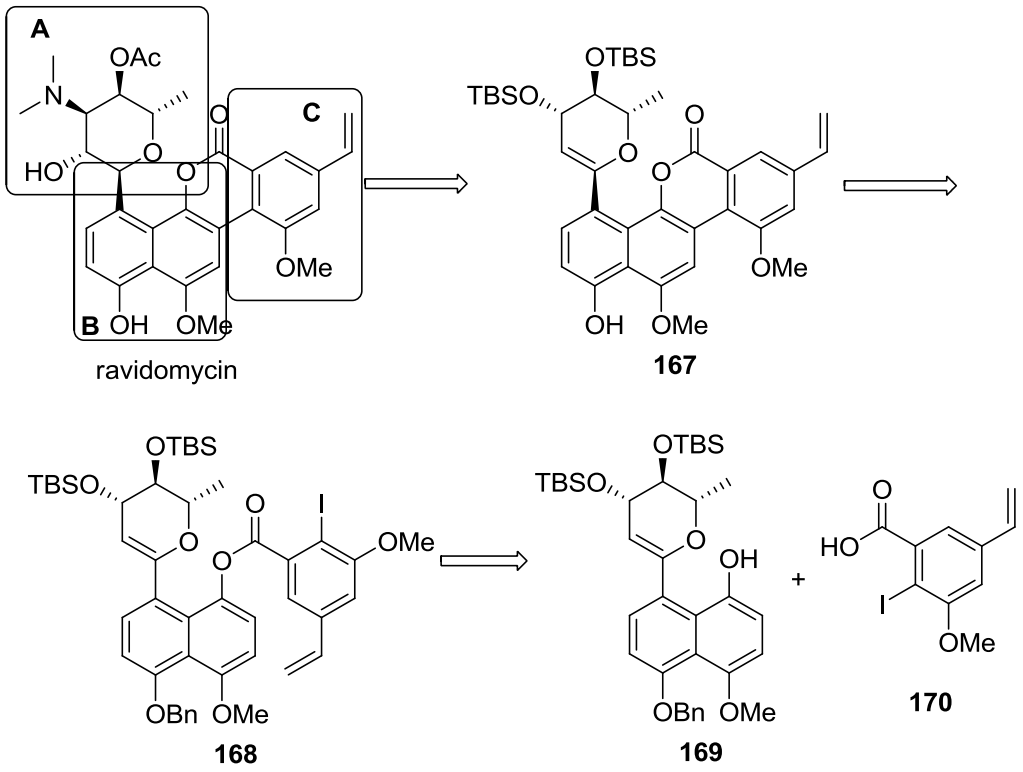
In summary, methylmagnesium bromide afforded the addition products in about 50% yields. With increasing steric effects for the organometallic reagents, the yields decreased. As a result, isopropylmagnesium bromide gave the adducts in about 40% yield. The yields of 1,2-additions of vinylmagnesium bromide and allylmagnesium bromide were low. Phenylmagnesium bromide gave about 20% yields. But when reaction times were lengthened, 1,2-addition of phenylmagnesium bromide gave much better yields. Lithiated rhamnal **165** only added to naphthoquinone **135**. In most cases, 1,2-additions to 8-hydroxy-5-methoxy-1,4-naphthoquinone **135** afforded better yields.

The results suggest that the addition reaction is more rapid than deprotonation of the hydroxyl group donating the intramolecular hydrogen bond. This hydrogen bonding hydroxyl group was involved in distinguishing the two carbonyl groups. Although the methoxy group on C-5 of 8-hydroxy-5-methoxy-1,4-naphthoquinone **135** has a steric effect, organometallic reagents regioselectively added to the carbonyl close to the methoxy group, and the addition to **135** produced higher yields than those to **133** and **134**. The result suggest that the hydrogen bond of 8-hydroxy-5-methoxy-1,4-naphthoquinone **135** may be stronger than those of **133** and **134**.

The strong intramolecular hydrogen bonding of juglone derivatives has not gone unrecognized and it has been the subject of a number of spectroscopic investigations.[97] Its effect as a director of regiochemistry in Diels-Alder reactions has been reported.[98] However, the hydrogen bond has not previously been applied for the control of regiochemistry in the addition of organometallic reagents. The regioselective addition of organometallic reagents to juglone derivatives could be the method of choice for the synthesis of densely functionalized naphthoquinols.

2.2.3 Progress toward the Synthesis of Ravidomycins.

As an application of the regioselective 1,2-additions of organometallic reagents to juglone derivatives, a new synthetic route for ravidomycin was proposed (Scheme 37). Ravidomycin intermediate **167** could be easily transformed to ravidomycin by treatment with trichloroacetonitrile and a subsequent borohydration.[99] Pd(II)-catalyzed intramolecular biaryl coupling of the naphthalenol ester **168** might lead to the polycyclic intermediate **167**.[100] Naphthalenol **169** might couple with the acid **170** to produce the ester **168**.

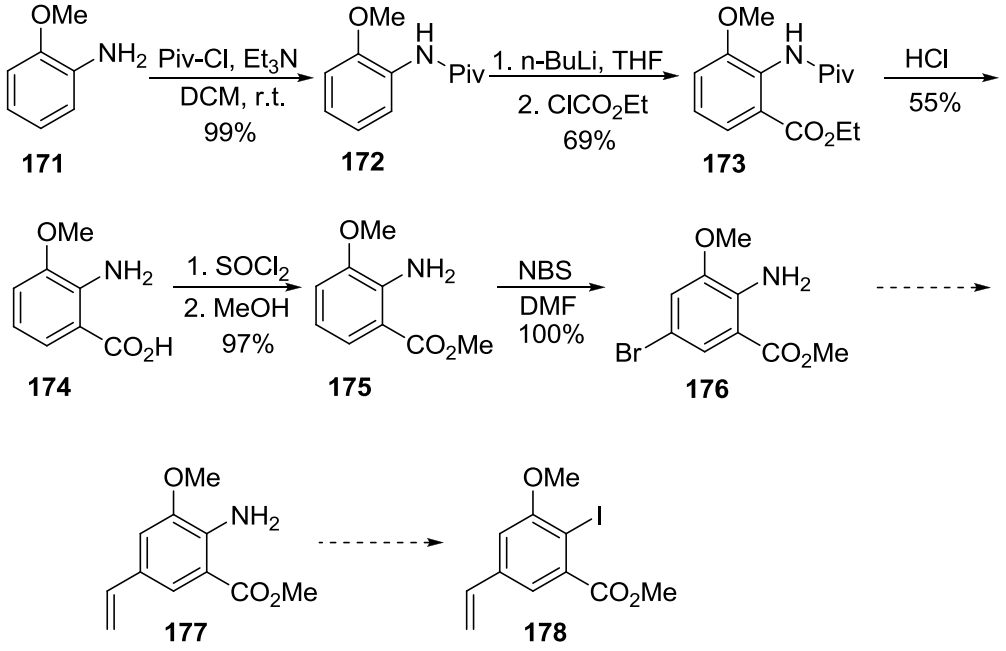


Scheme **47**. Proposed synthetic route for ravidomycin

2.2.3.1 Toward Preparation of Iodide 178, Region C.

We planned to prepare phenyl iodide **178** to build the region C by the method shown in Scheme 48. The amino group of o-anisidine **171** was protected by pivaloyl chloride to produce compound **172** in 99% yield.[101] n-Butyllithium deprotonated the Piv-protected o-anisidine **172** at C-3 position; and then the resulting carbanion was quenched by ethyl chloroacetate to form 2-amino-3-methoxybenzoic ester **173** in 69% yield.[102] The Piv protecting group was removed by HCl to provide the amino acid **174** in 55% yield. Treatment with thionyl chloride converted the amino acid **174** to an acid chloride which was methoxylated to give the amino ester **175** in 97% yield. The amino ester **175** was oxidized by NBS at C-5 position to bromide **176** quantitatively.[101] The bromide **176** was supposed to couple with tetravinyltin to produce the ester **177**. The amino group of **177**

could be oxidized to a diazo group which could be substituted by iodine to form m-iodobenzoic ester **178**.[100]

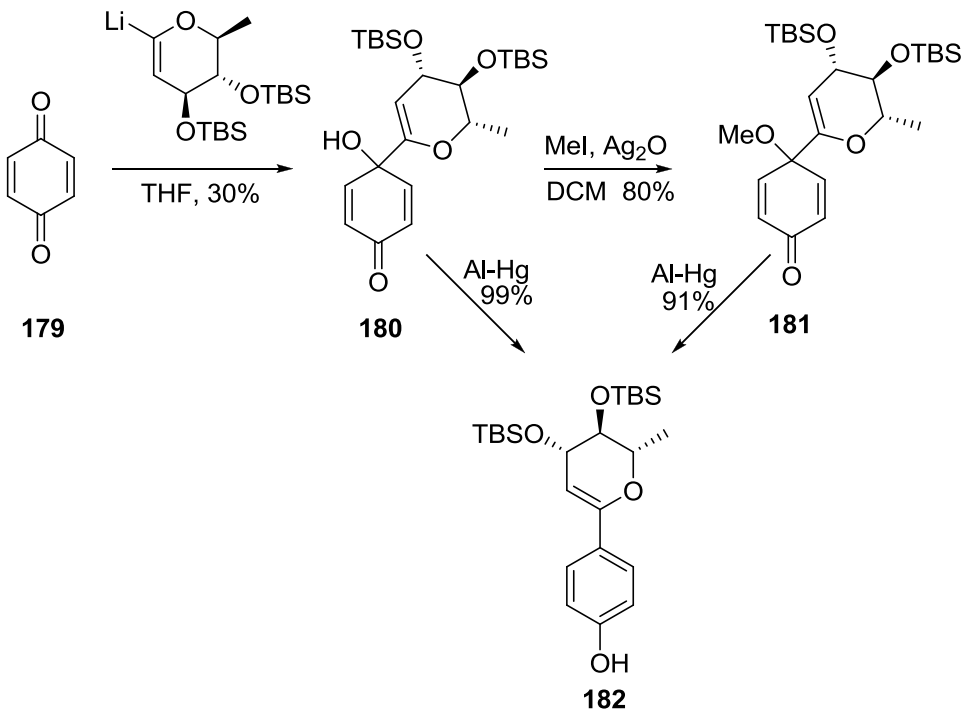


Scheme **48**. Toward preparation of iodide **178**.

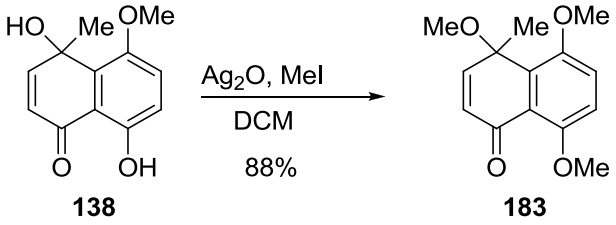
2.2.3.2 Models for Construction of Region A and B of Ravidomycin

2.2.3.2.1 Reduction of Quinols (Region B).

In order to build the region B of ravidomycin, a model system for preparing a carbohydrate substituted phenol was examined (Scheme 49). Lithiated rhamnal was added to quinone **179** to give the monoadduct **180** in 30% yield.[99] According to past work from Parker's group, mercury-aluminum amalgam reduced the *p*-quinol **180** to the phenol **182** quantitatively.102 The methylated quinol **181** was also reduced by mercury-aluminum amalgam to the phenol **182** in 91% yield.[103]

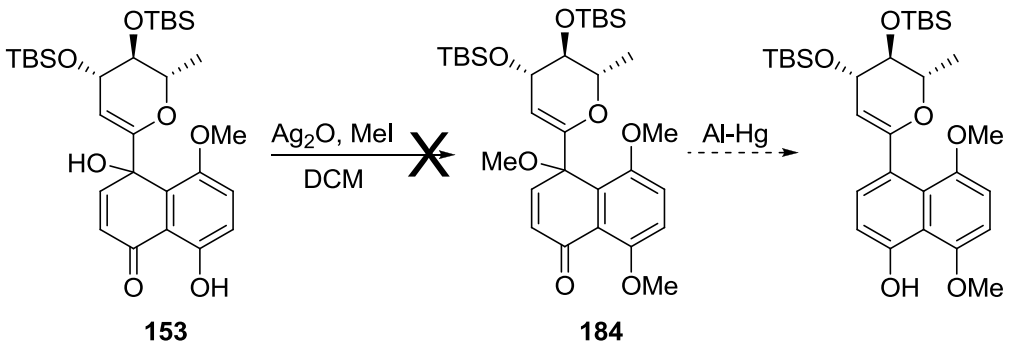


Scheme **49**. A model for reduction of quinols.

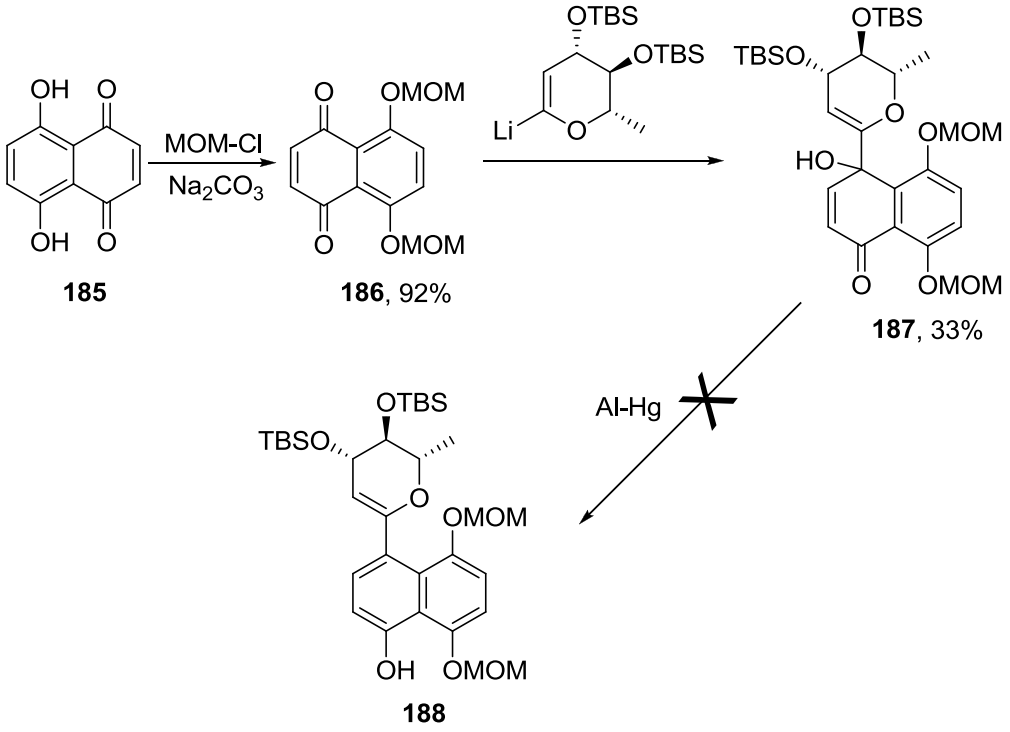


Scheme **50**. Methylation of quinol **138**.

In order to examine the reduction method in the 5,8-dimethoxy-4-naphthoquinol system, methylation of carbohydrate substituted quinol **153** was studied. Treatment of L-rhamnal **165** with silver(I) oxide and iodomethane afforded the methylated quinol **183** in 88% yield (Scheme 50). Methylation of quinol **153** was also attempted inusing silver(I) oxide and iodomethane (Scheme 51). However, the target methylated quinol **184** was not obtained.



Scheme **51**. Attempt at methylation of naphthylquinol **153**.

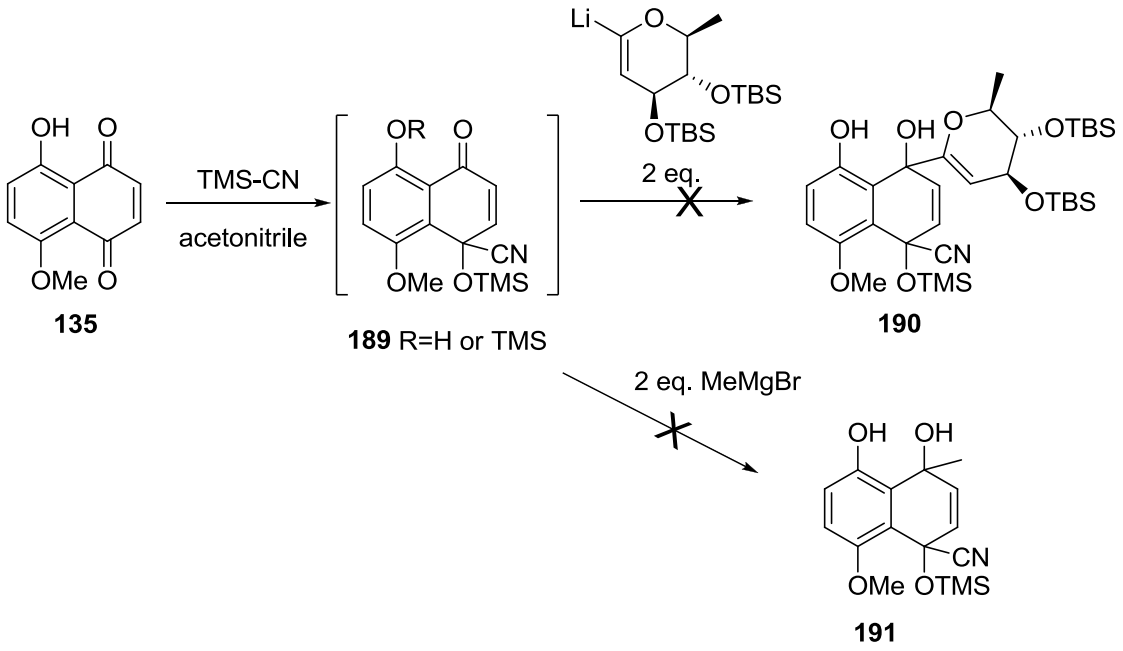


Scheme **52**. Attempt at reduction of naphthylquinol **187**.

Since methylation of naphthylquinol **153** did not work, a direct reduction of **187** without methylation was tried (Scheme 52). Compound **186** was obtained in 92% yield by treatment of **185** with chloromethylmethylether (MOM-Cl) in the presence of sodium carbonate.[104] Then addition of lithiated rhamnal to **186** afforded compound **187** in 33%

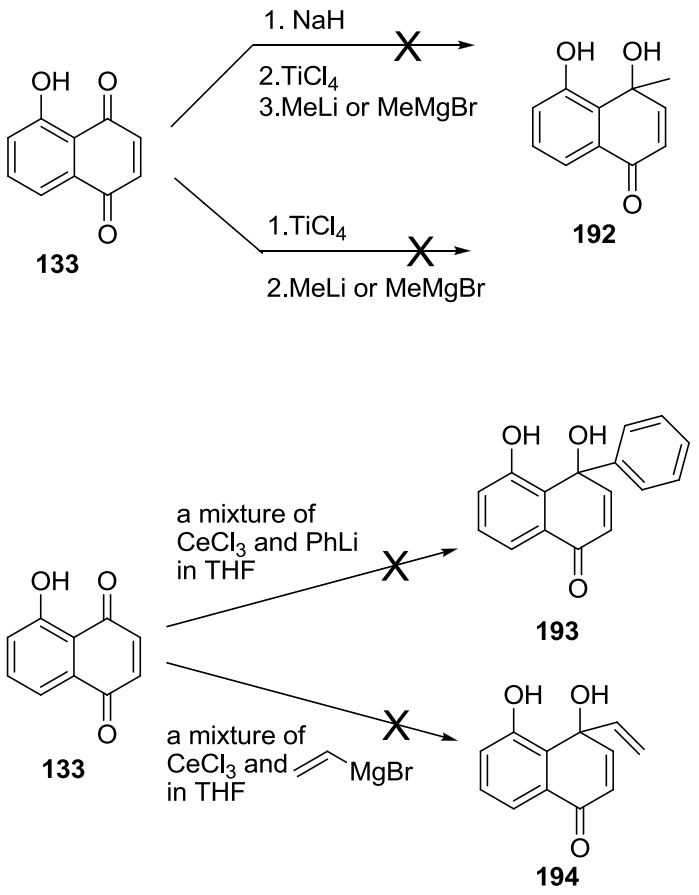
yield. However mercury-aluminum amalgam did not give any desired compound but the starting material.

2.2.3.2.2 Attempts at 1,2-Additions to the Hydrogen Bonded Carbonyl Groups of Juglone Derivatives (Region B).



Scheme **53**. An umpolung strategy.

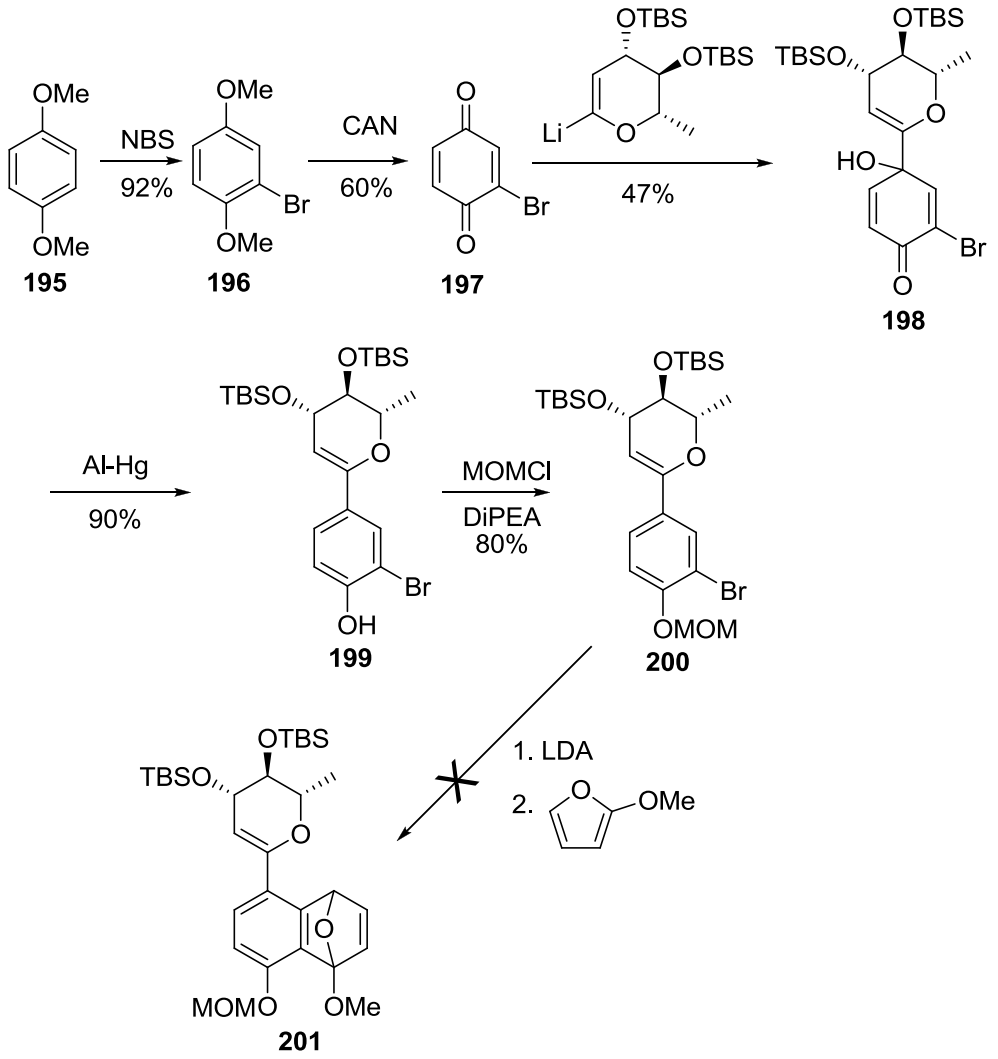
Selective 1,2-addition to hydrogen bonding C1 carbonyls of juglone derivatives might shorten the proposed synthetic route for ravidomycin. An umpolung strategy which is different from the previously described 1,2-addition was attempted (Scheme 53). The C5 carbonyl group of compound **135** was protected by trimethylsilyl cyanide to form an intermediate **189**.[105] Then **189** was treated with lithiated rhamnal or methylmagnesium bromide. However, the desired product **190** or **191** was not obtained.



Scheme **54**. Lewis acids mediated 1,2-additon attempts.

In order to get addition products at the C-4 position rather than the C-1 position, a series of models for Lewis acid-mediated 1,2-addition to the hydrogen bonded carbonyl of juglone **133** were tried (Scheme 54). In the presence of titanium(IV) chloride,[106] additions of methyllithium or methylmagnesium bromide to juglone **133** and deprotonated juglone did not afford the desired product **192**. When cerium(III) chloride was used as the Lewis acid,[107] addition of phenyl lithium or vinylmagnesium bromide to juglone did not give the corresponding adduct, either.

2.2.3.2.3 Diels-Alder Strategy.

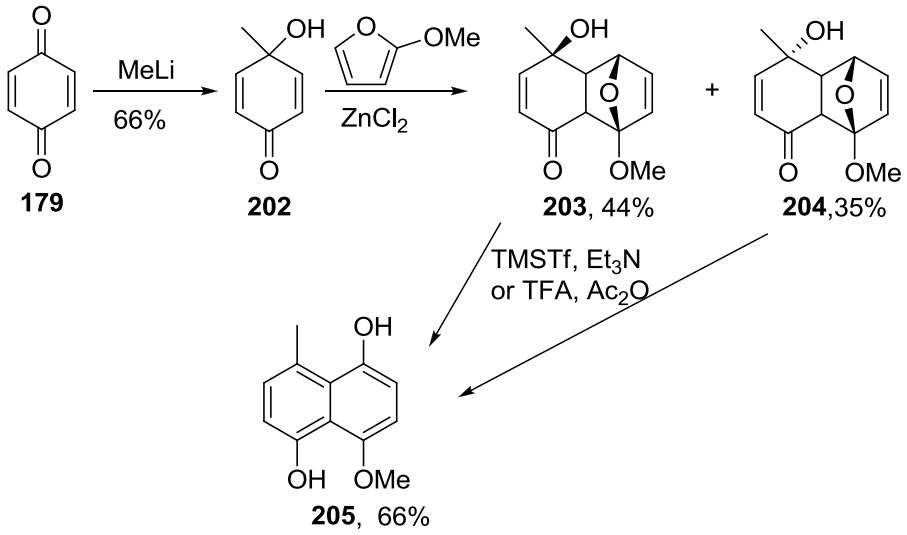


Scheme **55**. Diels-Alder reaction of benzyne and 2-methoxyfuran.

Since the reduction of naphthylquinol to naphthalenol has not been solved, a Diels-Alder strategy was employed to construct the regions A and B of ravidomycin (Scheme 47 and 55). 1,4-Dimethoxybenzene **195** was oxidized by NBS to 2-bromo-1,4-dimethoxybenzene **196** in 92% yield. The further oxidation of **196** by ceric ammonium nitrate (CAN) gave the 2-bromoquinone **197** in 60% yield.[108] Then compound **198** was obtained in 47% yield by selective 1,2-addition of lithiated rhamnal to **197**. The presence

of the bromo group caused the selectivity. Mercury-aluminum amalgam reduced quinol **198** to phenol **199** in 90% yield. Chloromethylmethylether (MOMCl) was used to protect the hydroxyl group of **199**. However, the following Diels-Alder reaction did not work. Because the proton at the C3 position of compound **200** was distant to the MOMO group, it was not acidic enough to be deprotonated to form a benzyne by strong bases such as LDA.

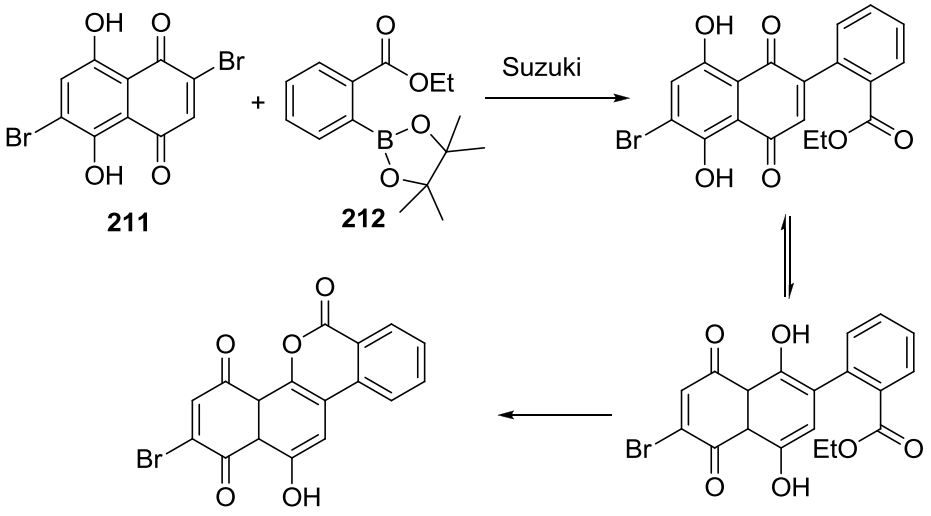
After two oxidations and two reductions, the oxidation state from compound **195** to **199** did not change (Scheme 55). The presence of the bromo group requests two more steps, one oxidation and one reduction. Therefore the bromo group was not necessary for the Diels-Alder strategy. A new model of Diels-Alder strategy was built (Scheme 56). Compound **202** was obtained by addition of methyllithium to benzoquinone **179**.[109] **202** was in the same oxidation state as compound **195**. In the presence of zinc chloride ($ZnCl_2$), a Diels-Alder cyclization between compound **202** and 2-methoxyfuran produced two isomers **203** and **204** in 44% and 35% yields, respectively. Treatment with trimethylsilyl triflate (TMSTf) or trifluoroacetic acid (TFA) opened the furan rings of both isomers to give the product **205.**



Scheme **56**. Diels-Alder reaction of *p*-methylquinol and 2-methoxyfuran

2.2.3.3 A Model for Regions B and C of Ravidomycin, Suzuki Cross Coupling between Dibromo Juglone Derivatives and 2-Ethoxycarbonylphenylborate.

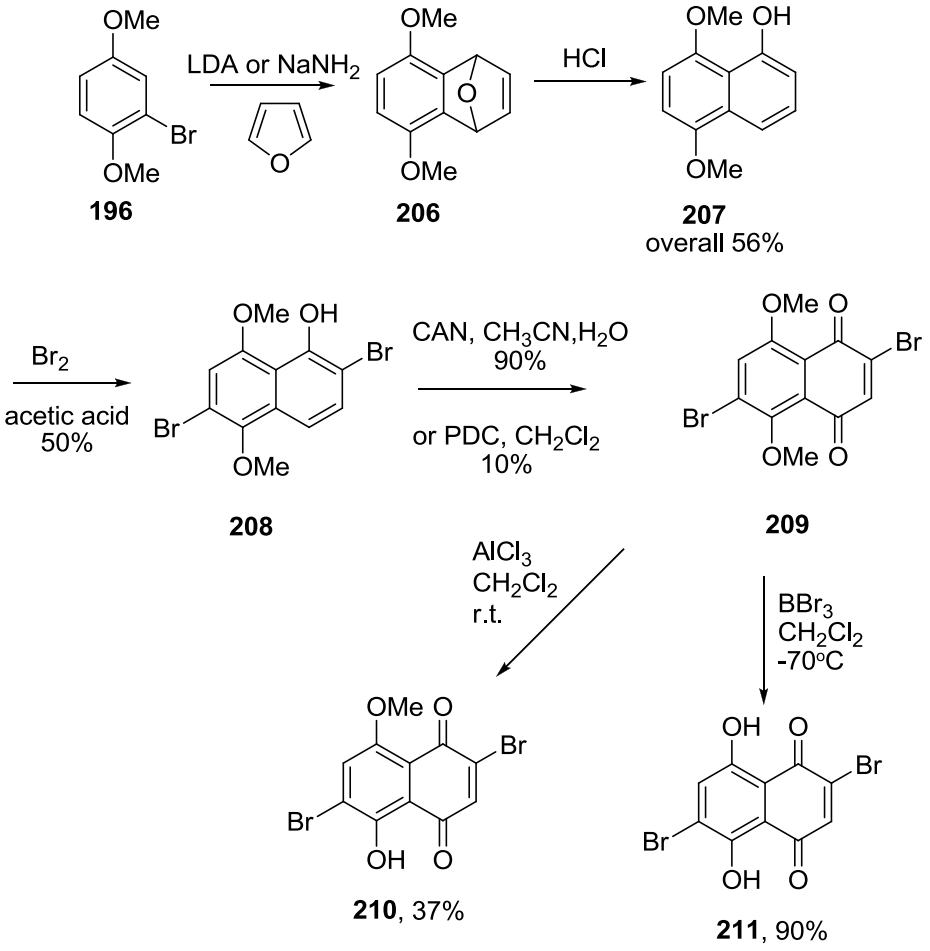
Suzuki cross coupling[110] between a bromojuglone derivative and borate might shorten the proposed synthetic route for regions B and C of ravidomycin (Scheme 57). Considering that the presence of a bromo group might result in selective 1,2-addition of organometallics to the C-4 carbonyl of the naphthylquinone, a model of the Suzuki coupling between dibromo dibromonaphthylquinones and 2-ethoxycarbonylphenylborate was built.



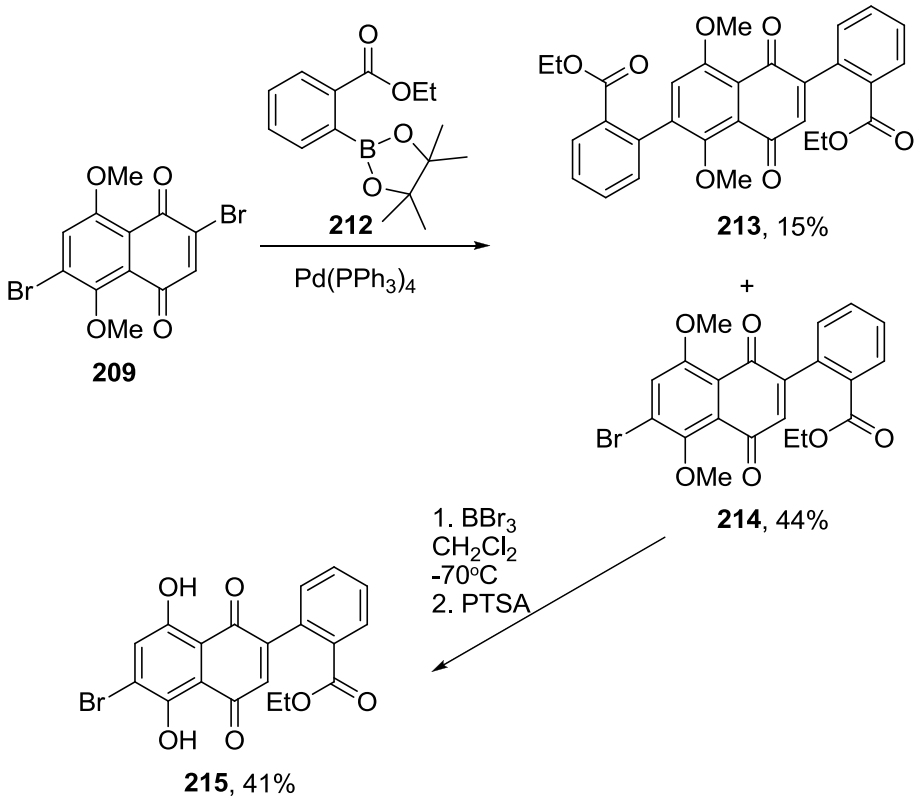
Scheme **57**. Proposed Suzuki strategy.

A strong base removed the proton at the C3 position of **196** to form a benzyne which underwent a Diels-Alder cyclization with furan to yield compound **206** (Scheme 58).[111] Treatment with acid opened the furan ring of **206** to afford the compound **207** in overall 56% yield.[112] The oxidation of **207** by bromine in acetic acid gave the dibromo compound **208** in 50% yield.[113] The further oxidation by pyridinium dichromate (PDC) transformed **208** to naphthylquinone **209** in very low yield. Ceric ammonium nitrate (CAN) as the oxidant increased the yield of the transformation to 90%.[114] One of the two

methyl groups of naphthylquinone **209** was removed by aluminum chloride to produce monoprotected dibromonaphthylquinone **210** in 37% yield. Treatment with boron bromide deprotected both methoxy groups to give the dibromonaphthylquinone **211** in 90% yield.[115]

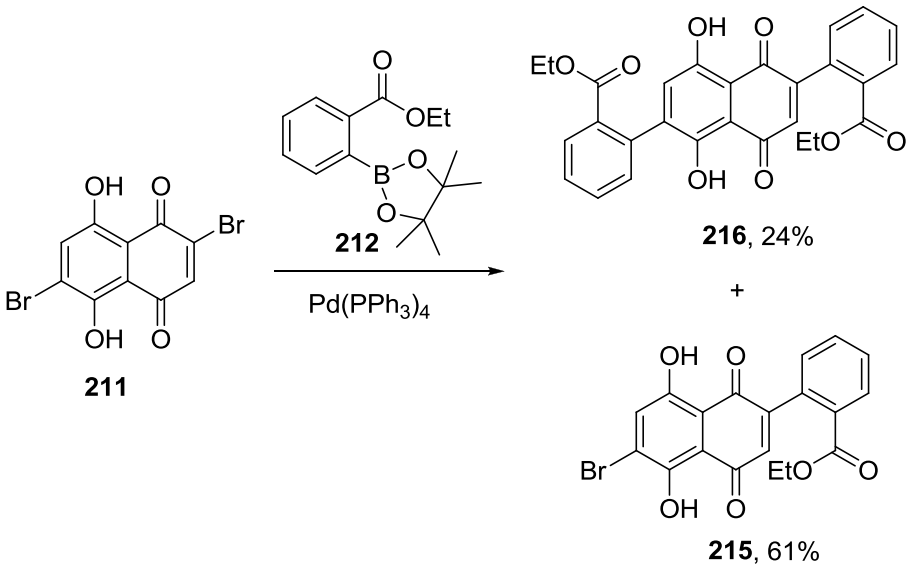


Scheme **58**. Preparation of dibromo juglone derivatives **209**, **210**, and **211**.



Scheme **59**. Suzuki coupling of **209** and 2-ethoxycarbonylphenylborate **212**.

Under the catalysis of tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$), dibromonaphthylquinone **209** and 2-ethoxycarbonylphenylborate **212** coupled together to afford mono-coupling product **214** and di-coupling product **213** in 44% and 15% yields, respectively (Scheme 59). After demethylation of compound **200** by boron bromide, treatment with p-toluenesulfonic acid (PTSA) did not yield a lactone product but the deprotected compound **215** in 41% yield.



Scheme **60**. Suzuki coupling of **211** and 2-ethoxycarbonylphenylborate **212**.

Under the catalysis of tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$), dibromonaphthylquinone **211** and 2-ethoxycarbonylphenylborate **212** coupled together to afford mono-coupling product **215** and di-coupling product **216** in 61% and 24% yields, respectively (Scheme 60). The yields were much better than the coupling between **209** and **212**.

2.3 Experimental Section

General

For all compounds, ^{1}H, ^{13}C and NOE NMR spectra were recorded on Varian Gemini 2300 (300 MHz), Inova 400 (400 MHz), Inova 500 (500 MHz), Inova 600 (600 MHz) spectrometer. Chemical shifts were measured relative to the residual solvent resonance for ^{1}H and internal reference. IR spectra were recorded on a Mattson Galaxy Series FTIR 3000 or 2020 spectrophotometer.

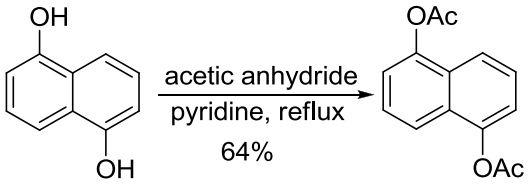
Reagents and solvents were purchased from Aldrich Chemical Company, Fisher Scientific or Acros Organics. Liquid reagents were purified by distillation prior to use.

Unless otherwise noted, solid reagents were used without further purification. Methylene chloride, acetonitrile, cyclohexane, and toluene were distilled from CaH_2 under Ar atmosphere. Diethyl ether and THF were distilled from Na and benzophenone under Ar atmosphere.

All reactions unless otherwise noted, were performed in oven dried glassware under positive pressure of Ar. All yields are isolated yields.

Chromatographic separations were performed using Fisher grade 1740 type 60 Å silica gel (170-400 mesh). Analytical thin layer chromatography was performed using Analtech Uniplate pre-coated glass 250 micron silica gel GHLF plates with 254 nm fluorescent indicator. Preparative thin layer chromatography was performed using Analtech Uniplate pre-coated glass 1000 or 2000 micron silica gel GHLF plates with 254 nm fluorescent indicator.

1,5-Dihydroxynaphthalene ester 156.[89]

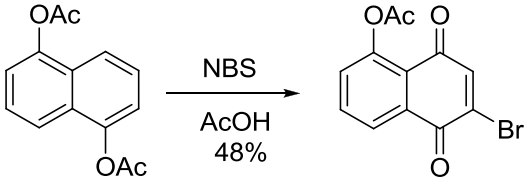


155 **156**

1,5-Dihydroxynaphthalene **155** (21 g, 131 mmol), acetic anhydride (30 mL, 27mmol), and piperidine (25 mL) were mixed together in methylene chloride. After the mixture was refluxed overnight, it was poured into ice cold water (800 mL). The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution, the residue was recrystallized in acetone to give a brown solid **156** (20.4 g, 83 mmol, 64%).

^{1}H-NMR ($CDCl_3$): δ 7.78 (dd, 2H, ^3J = 7.7 Hz, ^3J = 0.9 Hz), 7.50 (dd, 2H, ^3J = 7.7 Hz, ^3J = 0.9 Hz), 7.29 (dd, 2H, ^3J = 7.7 Hz, ^3J = 0.9 Hz), and 2.47 (s, 6H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [89]

Acetyl bromojuglone 157.[82]

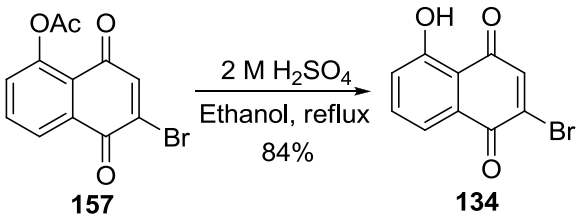


156 **157**

A solution of NBS (12.0 g, 67 mmol) in a mixture of acetic acid (50 mL) and water (120 mL) was warmed up to 55 °C. A solution of 1,5-dihydroxynaphthalene ester **156** (4.2 g, 17 mmol) in warm acetic acid (70 mL) was added dropwise to the NBS solution in 15 minutes at 55 °C. The reaction was stirred for 80 minutes and then it was poured into cold water (800 mL). The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was recrystallized in ethanol to give a yellow solid **157** (2.41 g, 8.3 mmol, 48%).

^{1}H-NMR ($CDCl_3$): δ 8.14 (dd, 1H, ^3J = 8.0 Hz, ^3J = 1.0 Hz), 7.77 (dd, 1H, ^3J = 7.5 Hz, ^3J = 8.0 Hz), 7.41 (d, 1H, ^3J = 7.0 Hz), 7.39 (s, 1H), and 2.44 (s, 3H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [82]

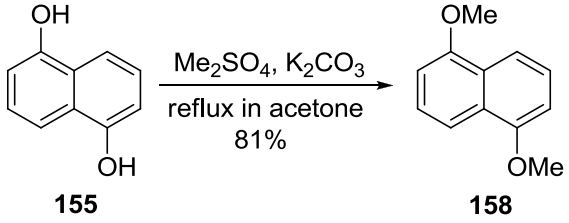
Bromojuglone 134.[82]



A solution of acetyl bromojuglone **157** (2.41 g, 8.3 mmol) in ethanol (95%, 120 mL) was added by sulfuric acid (30%, 30 mL). The reaction was refluxed carefully for 3 hours and then it was poured into ice cold water (400 mL). The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution, the residues were separated by a silica gel column with ethyl acetate and hexanes (1:10) to give the yellow aldehyde **134** (1.74 g, 6.9 mmol, 84%).

^{1}H-NMR ($CDCl_3$): δ 11.77 (s, 1H), 7.73(d, 1H, ^3J = 7.0 Hz), 7.63 (d, 1H, ^3J = 8.0 Hz), 7.50 (s, 1H), and 7.31 (d, 1H, ^3J = 8.0 Hz). ^{13}CNMR ($CDCl_3$): δ 189.6, 187.7, 177.4, 161.9, 141.1, 140.5, 136.6, 130.9, 125.3, 121.1, and 114.8. IR (KBr): υmax 1674, 1584, 1452, 1244, 1198, and 1088 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [82]

1,5-Dimethoxynaphthalene 158.[90]

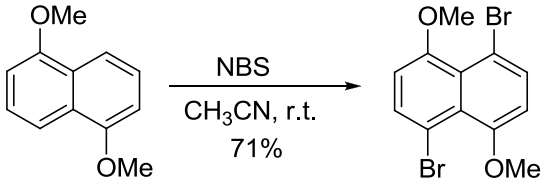


1,5-Dihydroxynaphthalene **155** (2.0 g, 13 mmol) and K_2CO_3 (4.0 g, 29 mmol) were mixed in 50 mL of dry acetone. Dimethyl sulfate (3.4 mL, 36 mmol) was added to the suspension at room temperature. After 12 hours reflux, the solid was filtered off. The

filtrate was concentrated in vacuo. The recrystallization of the residues gave 1.9 g of a yellow solid **158** (10.5 mmol, 81%).

^{1}H-NMR ($CDCl_3$): δ 7.87 (d, 2H, ^{3}J = 8.5 Hz), 7.41(dd, 2H, ^{3}J = 8.5 Hz, ^{3}J = 7.5 Hz), 6.87 (d, 2H, ^{3}J = 7.5 Hz), and 4.01 (s, 6H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [90]

1,5-Dibromo-4,8-dimethoxynaphthalene 159.[91]

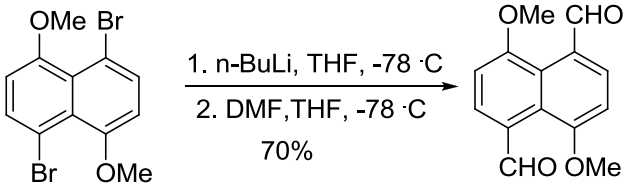


158 **159**

1,5-Dimethoxynaphthalene **158** (1.89 g, 10.0 mmol) was dissolved in 30 mL of CH_3CN. N-Bromosuccinimide (4.05 g, 22.8 mmol) in 20 mL of CH_3CN was added to the solution at 0 °C. After addition, the reaction was allowed to warm to room temperature and it was stirred for 4 hours. Then 20 mL of CH_3CN was removed from the dark red solution by rotovap and the residue was crystallized at 0 °C. The crystal was filtered off and washed with 10 mL of CH_3CN and 5 mL of methanol to give a brown solid **159** (2.48 g, 7.1 mmol, 71%).

^{1}H-NMR ($CDCl_3$): δ 7.70 (d, 2H, ^{3}J = 8.0 Hz), 6.74(d, 2H, ^{3}J = 8.0 Hz), and 3.92 (s, 6H). ^{13}CNMR ($CDCl_3$): δ 155.3, 133.9, 126.4, 108.6, 107.3, and 55.9. IR (KBr): υmax 2963, 2934, 1588, 1509, 1365, 1250, 1179, and 1060 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [91]

4,8-Dimethoxynaphthalene-1,5-dicarbaldehyde 160.[91]

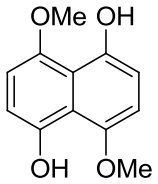


159 **160**

A solution of 1,5-dibromo-4,8-dimethoxynaphthalene **159** (580 mg, 1.69 mmol) in 20 mL of THF was cooled down to -78 °C. n-BuLi (2.5 M in hexanes, 1.8 mL, 4.5 mmol) was added to the solution at -78 °C and the reaction was stirred for 2 hours at -78 °C. Then the dark yellow suspension was added dimethylformamide (1.2 mL) dropwise. After the mixture was stirred for 3 hours, the reaction was allowed to warm to 0 °C and quenched by 1 M HCl. The yellow solid was filtered off and washed with ether to give the product (286 mg, 1.18 mmol, 70%).

^{1}H-NMR ($CDCl_3$): δ 10.90 (s, 2H), 8.01 (d, 2H, ^3J = 8.0 Hz), 7.06 (d, 2H, ^3J = 8.0 Hz), and 4.08 (s, 6H). IR (KBr): υmax 2969, 2902, 2854, 1671, 1543, 1411, 1375, and 1271 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature.[91]

4,8-Dimethoxy-1,5-naphthalenediol 162.[92, 94]



162

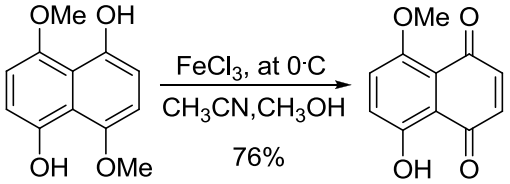
Method one:[92] A solution of 4,8-dimethoxynaphthalene-1,5-dicarbaldehyde **160** (213 mg, 0.87 mmol) in 15 mL of methylene chloride was cooled down to 0 °C. A solution of m-chloroperbenzoic acid (520 mg, 3 mmol) in 6 mL of methylene chloride was added to the solution at 0 °C. After the reaction was stirred for 18 hours at room

temperature, it was quenched by sat. $NaHCO_3$. The organic phase was separated; the water phase was extracted three times by ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were added a solution of NaOH (1 g) in EtOH (15 mL) and water (2 mL). The mixture was stirred overnight and poured into 1M HCl. The yellow solid was filtered off and washed with ether to give the crude product **162** (319 mg, 0.87 mmol, ~100%).

Method two:[93, 94] A solution of 1,5-dibromo-4,8-dimethoxynaphthalene **159** (510 mg, 1.47 mmol) in 20 mL of THF was cooled down to -78 °C. n-BuLi (2.5 M in hexanes, 1.4 mL, 3.5 mmol) was added to the mixture at -78 °C. The reaction was stirred for 2 hours at -78 °C. The dark yellow suspension was added trimethyl borate (1.7 mL, 15.2 mmol) dropwise. The dark mixture resulted was stirred overnight. Then the reaction was allowed to warm to 0 °C. A solution of NaOH (290 mg 7.25 mmol) in 2.9 mL of H_2O and 0.8 mL of H_2O_2 was added to the reaction. The mixture was stirred for 4 hours to give a lot of yellow solid. The suspension was poured into 50 mL of 1 M HCl. The yellow solid was filtered off and washed with ether to give the compound **162** (287 mg, 1.26 mmol, 86%).

^{1}H-NMR ($CDCl_3$): δ 9.47 (s, 2H), 6.82 (d, 2H, ^3J = 3.0 Hz), and 4.06 (s, 6H). IR (KBr): υmax 2964, 2921, 2850, 1662, 1523, 1324, and 1224 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [92, 94]

5-Hydroxy-8-methoxy-1,4-naphthalenedione 135.[95]

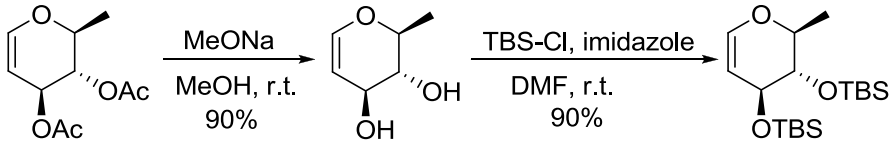


162 **135**

A solution of 4,8-dimethoxy-1,5-naphthalenediol **162** (256 mg, 1.16 mmol) in 22 mL of 1:1 MeCN and MeOH was cooled down to 0 °C in an ice bath. Iron (III) chloride hexahydrate (1.26 g, 4.66 mmol) in 2 mL of 4 N HCl was added to the mixture. The reaction was stirred for 15 minutes at 0 °C; and then it was quenched with 8 mL of 1 N NaOH. The red solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with methylene chloride and ethyl acetate (10:1) to give a red solid **135** (192 mg, 0.88 mmol, 76%).

^{1}H-NMR ($CDCl_3$): δ 12.44 (s, 1H), 7.37 (d, 1H, ^3J = 8.5 Hz), 7.31 (d, 1H, ^3J = 8.5 Hz), 6.88 (s, 2H), and 3.98 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 190.6, 183.4, 156.6, 154.1, 141.8, 136.5, 126.9, 123.6, 117.4, 114.9, and 57.0. IR (KBr): υmax 2745, 1636, 1620, 1475, 1435, 1250, and 845 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature.[95]

Rhamnal 166.[96]



164 **165** **166**

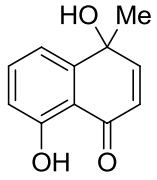
A solution of 3,4-di-O-acetyl-6-deoxy-L-glucal **164** (0.50 mL, 2.6 mmol) in 20 mL of methanol was added 3 drops of sodium methoxide. The reaction was stirred overnight at room temperature. The solvent was removed in vacuo, a white crystal **165** (298 mg, 2.3 mmol, 90%) was given.

A mixture of L-rhamnal **165** (290 mg, 2.23 mmol) and imidazole (570 mg, 8.38 mmol) in 20 mL of DMF was added t-butyl(chloro)dimethylsilane (790 mg, 5.27 mmol) at 0 °C. The reaction was stirred for 18 hours, and then quenched by $CuSO_4$ solution in

water. The water phase was extracted three times with ether; the organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ether (100:1) to give a lot transparent crystal **166** (715 mg, 2.0 mmol, 90%).

^{1}H-NMR ($CDCl_3$): δ 6.27 (d, 1H, ^3J = 6.0 Hz), 4.65 (dd, 1H, ^3J = 6.0 Hz, ^3J = 3.0 Hz), 4.08 (dd, 1H, ^3J = 5.0 Hz, ^3J = 4.0 Hz), 3.92 (dt, 1H, ^3J = 6.5 Hz, ^3J = 7.0 Hz), 3.55 (dd, 1H, ^3J = 5.5 Hz, ^3J = 6.5 Hz), 1.31 (d, 3H, ^3J = 6.5 Hz), 0.90 (s, 18H), and 0.09 (m, 12H). IR (KBr): υmax 2955, 2887, 2858, 1251, 1115, and 1073 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [96]

Quinol 136.



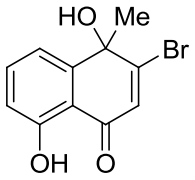
136

Juglone **133** (103 mg, 0.75 mmol) was dissolved in 20 mL of dry THF. Methylmagnesium bromide (3.0 M in diethyl ether, 0.30 mL, 0.9 mmol) was added to the red solution at -78 °C. After the solution was stirred for eight hours, the reaction was quenched with 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **136** (51 mg, 3.4 mmol, 46%).

^{1}H-NMR ($CDCl_3$): δ 12.26 (s, 1H), 7.44 (bt, 1H, ^3J = 8.0 Hz), 7.15 (dd, 1H, ^3J = 7.7 Hz, ^4J = 0.9 Hz), 6.96 (d, 1H, ^3J = 10.2 Hz), 6.80 (dd, 1H, ^3J = 8.3 Hz, ^4J = 0.9 Hz),

6.16 (d, 1H, ^{3}J = 10.2 Hz), 2.88 (s, 1H), and 1.50 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 190.3, 162.0, 154.8, 149.2, 136.3, 126.6, 117.5, 116.8, 114.1, 68.8, and 31.3. IR (KBr): υmax 3405, 2980, 2920, 1655, 1605, 1455, 1345, 1240, 1050, 850, and 750 cm^{-1}.

Bromoquinol 142.

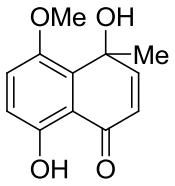


142

A solution of bromojuglone **134** (155 mg, 0.62 mmol) in 20 mL of dry THF was cooled down to -93 °C. Methylmagnesium bromide (3.0 M in diethyl ether, 0.25 mL, 0.75 mmol) was added to the red solution at -93 °C. After the solution was stirred for 40 minutes, the reaction was quenched with 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **142** (68 mg, 26 mmol, yield 41%).

^{1}H-NMR ($CDCl_3$): δ 12.05 (s, 1H), 7.52 (dt, 1H, ^{3}J = 7.5 Hz, ^{3}J = 8.5 Hz), 7.29 (t, 1H, ^{3}J = 8.0 Hz, ^{3}J = 6.0 Hz), 6.92 (d, 1H, ^{3}J = 9.0 Hz), 6.73 (s, 1H), 2.88 (s, 1H), and 1.69 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 187.0, 161.8, 157.2, 147.7, 136.2, 130.9, 118.2, 117.2, 113.108, 72.4, and 33.0. IR (KBr): υmax 3428, 3418, 1641, 1590, 1485, 1325, and 1240 cm^{-1}

Quinol 149.

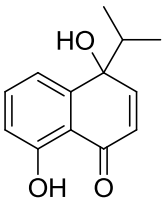


149

A solution of 5-hydroxy-8-methoxy-1,4-naphthalenedione **135** (77 mg, 0.37 mmol) in 25 mL of dry THF was cooled down to -72 °C. Methylmagnesium bromide (3.0 M in diethyl ether, 0.15 mL, 0.45 mmol) was added to the red solution at -72 °C. The solution was stirred for 18 hours. The reaction was quenched with 1 mL of saturated aq. NH_4Cl . The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (20:1) to give a red solid **149** (47 mg, 21 mmol, 57%).

^{1}HNMR ($CDCl_3$): δ 12.13 (s, 1H), 7.16 (d, 1H, ^3J = 9.2 Hz), 7.99 (d, 1H, ^3J = 10.4 Hz), 6.91 (d, 1H, ^3J = 9.2 Hz), 6.24 (d, 2H, ^3J = 10.4 Hz), 4.63 (s, 1H), 3.93 (s, 3H), and 1.68 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 190.3, 156.7, 154.3, 151.9, 148.9, 134.0, 130.1, 125.6, 119.9, 117.1, 113.8, 69.8, 56.5, and 29.5. ^{1}HNMR ($CDCl_3$, D_2O): δ 12.13 (s, 1H), 7.16 (d, 1H), 7.99 (d, 1H), 6.91 (d, 1H), 6.24 (d, 2H), 3.93 (s, 3H), 1.68 (s, 1H). IR (KBr): υmax 3545, 2965, 2805, 1665, 1570, 1480, 1275, and 1070 cm^{-1}. ESI-MS ($M\text{-}H^+$): 219.11, and 220.13, g/mol.

Quinol 137.

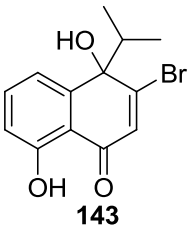


137

A solution of juglone **133** (186.4 mg, 1.1 mmol) in 20 mL of dry THF was cooled down to -78 °C. iso-Propylmagnesium bromide (2.0 M in diethyl ether, 0.7 mL, 1.4 mmol) was added to the red solution at -78 °C. The solution was stirred for eight hours. The reaction was quenched with 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **137** (96 mg, 0.45 mmol, 41%).

^{1}HNMR ($CDCl_3$): δ 12.30 (s, 1H), 7.45 (dt, 1H, ^3J = 9.2 Hz, ^3J = 7.2 Hz), 7.15 (d, 1H, ^3J = 10.4 Hz), 6.97 (d, 1H, ^3J = 9.2 Hz), 6.92 (d, 1H, ^3J = 7.2 Hz), 6.32 (d, 1H, ^3J = 10.4 Hz), 2.64 (s, 1H), 2.17 (m, 1H), 1.09 (d, 3H, ^3J = 6.8 Hz), and 0.52 (d, 3H, ^3J = 6.8 Hz). ^{13}CNMR ($CDCl_3$): δ 189.9, 161.7, 151.4, 148.4, 136.0, 128.9, 117.0, 116.8, 115.2, 74.2, 41.3, 17.4, and 17.0. IR (KBr): υmax 3410, 2925, 1650, 1605, 1460, 1365, 1275, and 1220 cm^{-1}.

Bromoquinol 143.

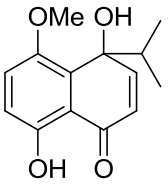


143

A solution of bromojuglone **134** (165 mg, 0.65 mmol) in 20 mL of dry THF was cooled down to -78 °C. iso-Propylmagnesium bromide (2.0 M in diethyl ether, 0.40 mL, 0.8 mmol) was added to the red solution at -78 °C. The solution was stirred for eight hours. The reaction was quenched with 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give the starting material back (37 mg, 0.15 mmol, 23%) and yellow oil **143** (73 mg, 0.24 mmol, 37%).

^{1}HNMR ($CDCl_3$): δ 12.01 (s, 1H), 7.47 (d, 1H, ^3J = 8.0 Hz), 7.21 (d, 1H, ^3J = 8.0 Hz), 6.94 (d, 1H, ^3J = 8.0 Hz), 6.86 (s, 1H), 2.69 (s, 1H), 2.33 (m, 1H), 1.00 (d, 3H, ^3J = 7.0 Hz), and 0.61 (d, 3H, ^3J = 6.5 Hz). ^{13}CNMR ($CDCl_3$): δ 187.5, 161.9, 156.4, 143.6, 134.8, 132.7, 129.9, 119.3, 117.5, 115.2, 78.4, 39.0, 17.6, and 15.7. IR (KBr): υmax 3429, 1639, 1604, 1452, and 1248 cm^{-1}

Quinol 150.



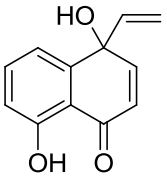
150

A solution of 5-hydroxy-8-methoxy-1,4-naphthalenedione **135** (160 mg, 0.78 mmol) in 25 mL of dry THF was cooled down to -78 °C. iso-Propylmagnesium bromide (2.0 M in diethyl ether, 0.36 mL, 0.72 mmol) was added to the red solution at -78 °C. The solution was stirred overnight. Then the reaction was allowed to warm up to -65 °C and stirred for 2 days. The reaction was quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The

organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **150** (36 mg, 0.15 mmol, 19%).

^{1}HNMR ($CDCl_3$): δ 12.15 (s, 1H), 7.15 (d, 1H, ^3J = 9.2 Hz), 6.95 (d, 1H, ^3J = 16.4 Hz), 6.91 (d, 1H, ^3J = 14 Hz), 6.41 (d, 1H, ^3J = 10.8 Hz), 4.63 (s, 1H), 3.91 (s, 3H), 2.55 (m, 1H), 1.15 (d, 3H, ^3J = 6.8 Hz), and 0.52 (d, 3H, ^3J = 7.2 Hz). ^{13}CNMR ($CDCl_3$): δ 190.4, 156.6, 150.5, 133.8, 128.3, 119.9, 117.1, 115.5, 76.1, 56.5, 38.5, 18.1, and 17.4. IR (KBr): υmax 3520, 2965, 1655, 1470, 1220, and 1040 cm^{-1}. ESI-MS (M^-): 247.15 g/mol.

Quinol 138.



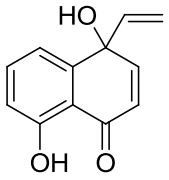
138

A solution of juglone **133** (85 mg, 0.49 mmol) in 10 mL of dry THF was cooled down to -95 °C. Vinylmagnesium bromide (1.0 M in diethyl ether, 0.60 mL, 0.6 mmol) was added to the red solution at -95 °C. The solution was stirred for half an hour. Then the reaction was allowed to warm up to -78 °C and stired for 2 hours. The reaction was quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **138** (8 mg, 0.04 mmol, 8%).

^{1}HNMR ($CDCl_3$): δ 12.30 (s, 1H), 7.49 (dt, 1H, ^3J = 7.0 Hz, ^3J = 8.5 Hz), 7.08 (d, 1H, ^3J = 7.0 Hz), 6.98 (m, 2H), 6.31 (d, 1H, ^3J = 10.5 Hz), 5.80 (dd, 1H, ^3J = 17.5 Hz, ^3J

= 10.5 Hz), 5.46 (d, 1H, ^{3}J = 17 Hz), 5.23 (d, 1H, ^{3}J = 10.5 Hz), and 2.51 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 190.0, 177.5, 162.1, 157.6, 151.5, 139.7, 136.2, 127.0, 118.6, 117.3, 115.2, 114.0, and 71.3. IR (KBr): υmax 3409, 3054, 1653, 1606, 1454, 1345, and 1234cm^{-1}

Bromoquinol 144.



144

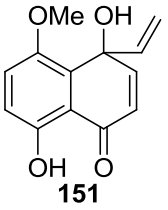
A solution of bromojuglone **134** (102 mg, 0.41 mmol) in 10 mL of dry THF was cooled down to -78 °C. Vinylmagnesium bromide (1.0 M in diethyl ether, 0.50 mL, 0.50 mmol) was added to the red solution at -78 °C. The solution was stirred for eight hours. The reaction was quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give the starting material back (69 mg, 0.27 mmol, 66%) and yellow oil **144** (28.3 mg, 0.1 mmol, 25%).

A solution of bromojuglone **134** (103 mg, 0.41 mmol) in 10 mL of dry THF was cooled down to -78 °C. Vinylmagnesium bromide (1.0 M in diethyl ether, 0.55 mL, 0.55 mmol) was added to the red solution at -78 °C. The solution was stirred for a day. Then the reaction was allowed to warm up to -68 °C for a day. The reaction was quenched with 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a

silica gel column with hexanes and ethyl acetate (15:1) to give the starting material back (61 mg, 0.24 mmol, 59%) and yellow oil **144** (24 mg, 0.085 mmol, 21%).

^{1}HNMR ($CDCl_3$): δ 12.04 (s, 1H), 7.50 (dt, 1H, ^{3}J = 8.0 Hz, ^{3}J = 8.0 Hz), 7.16 (d, 1H, ^{3}J = 7.5 Hz), 6.96 (d, 1H, ^{3}J = 8.5 Hz), 6.86 (s, 1H), 5.78 (dd, 1H, ^{3}J = 16.5 Hz, ^{3}J = 11.5 Hz), 5.53 (d, 1H, ^{3}J = 17 Hz), 5.33 (d, 1H, ^{3}J = 10.5 Hz), and 2.77 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 187.1, 162.1, 153.7, 144.9, 140.0, 137.2, 136.2, 131.7, 125.7, 119.5, 117.6, 115.9, and 75.0. IR (KBr): υmax 2910, 2845, 1642, 1607, 1453, 1359, and 1250 cm^{-1}

Quinol 151.



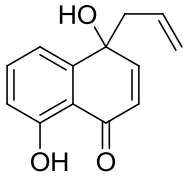
151

A solution of 5-hydroxy-8-methoxy-1,4-naphthalenedione **135** (80 mg, 39 mmol) in 10 mL of dry THF was cooled down to -78 °C. Vinylmagnesium bromide (1.0 M in diethyl ether, 0.5 mL, 0.5 mmol) was added to the red solution at -78 °C. The solution was stirred for 2 days and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **151** (32 mg, 0.14 mmol, 35%).

^{1}HNMR ($CDCl_3$): δ 12.11 (s, 1H), 7.16 (d, 1H, ^{3}J = 11.5 Hz), 6.95 (d, 1H, ^{3}J = 11.5 Hz), 6.81 (d, 1H, ^{3}J = 12.5 Hz), 6.27 (d, 1H, ^{3}J = 12.5 Hz), 5.89 (dd, 1H, ^{3}J = 16.5 Hz, ^{3}J = 13 Hz), 5.33 (d, 1H, ^{3}J = 16.5 Hz), 5.20 (d, 1H, ^{3}J = 13 Hz), 4.78 (s, 1H), and 3.85 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 190.4, 156.8, 151.3, 149.2, 140.2, 132.2, 125.9, 120.8,

117.7, 114.9, 113.9, 72.4, and 56.9. IR (KBr): υmax 3435, 1657, 1480, 1395, 1265, 1220, 1160, and 1040 cm^{-1}

Quinol 139.

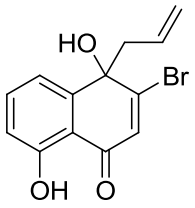


139

A solution of juglone **133** (100 mg, 57 mmol) in 25 mL of dry THF was cooled down to -78 °C. Allylmagnesium bromide (1.0 M in diethyl ether, 0.7 mL, 0.7 mmol) was added to the red solution at -78 °C. The black solution was stirred for eight hours and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **139** (24 mg, 11 mmol, 19%).

^{1}HNMR ($CDCl_3$): δ 12.32 (s, 1H), 7.51 (dt, 1H, ^3J = 16 Hz, ^3J = 8.0 Hz), 7.19 (d, 1H, ^3J = 8.0 Hz), 6.96 (d, 1H, ^3J = 12 Hz), 6.90 (d, 1H, ^3J = 8.4 Hz), 6.30 (d, 1H, ^3J = 10.4 Hz), 5.42 (m, 1H), 5.01 (m, 2H), and 2.61 (m, 2H). ^{13}CNMR ($CDCl_3$): δ 190.0, 162.1, 153.0, 147.3, 136.3, 136.1, 131.1, 127.8, 120.5, 117.2, 117.2, 114.7, 71.3, and 48.8. IR (KBr): υmax 3420, 3040, 2915, 1740, 1675, 1630, 1420, 1240, and 1150 cm^{-1}.

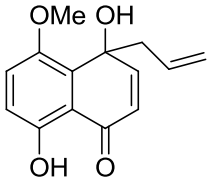
Bromoquinol 145.



145

A solution of bromojuglone **134** (158 mg, 0.63 mmol) in 20 mL of dry THF was cooled down to -78 °C. Allylmagnesium bromide (1.0 M in diethyl ether, 0.87 mL, 0.87 mmol) was added to the red solution at -78 °C. The solution was stirred for eight hours and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give the starting material back (43 mg, 17 mmol, 0.26%).

Quinol 152.



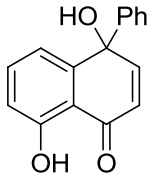
152

A solution of 5-hydroxy-8-methoxy-1,4-naphthalenedione **135** (110 mg, 0.54 mmol) in 25 mL of dry THF was cooled down to -78 °C. Allylmagnesium bromide (1.0 M in diethyl ether, 0.69 mL, 0.69 mmol) was added to the red solution at -78 °C. The solution was stirred overnight. Then the reaction was allowed to warm up to -65 °C and stirred for 12 hours. The reaction was quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic

solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **152** (27 mg, 11 mmol, 20%).

^{1}HNMR ($CDCl_3$): δ 12.12 (s, 1H), 7.17 (d, 1H, ^{3}J = 8.8 Hz), 6.90 (dd, 2H, ^{3}J = 10 Hz, ^{3}J = 8.4 Hz), 6.32 (d, 1H, ^{3}J = 10 Hz), 6.39 (m, 1H), 4.92 (d, 1H, ^{3}J = 10.4 Hz), 4.85 (d, 1H, ^{3}J = 17.2 Hz), 4.75 (s, 1H), 3.95 (s, 3H), 2.86 (dd, 1H, ^{3}J = 13.2 Hz, ^{3}J = 7.6 Hz), and 2.72 (dd, 1H, ^{3}J = 13.2 Hz, ^{3}J = 7.2 Hz). ^{13}CNMR ($CDCl_3$): δ 190.5, 156.7, 152.6, 148.8, 132.5, 131.8, 127.0, 119.8, 119.5, 117.4, 114.8, 72.8, 56.5, and 46.4. IR (KBr): υmax 3320, 3070, 2980, 2820, 1705, 1662, 1440, and 1340 cm^{-1}. ESI-MS ($M-H^-$): 245.14 g/mol.

Quinol 140.



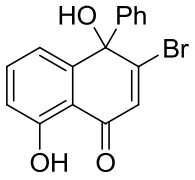
140

A solution of juglone **133** (167.3 mg, 0.95 mmol) in 25 mL of dry THF was cooled down to -78 °C. Phenylmagnesium bromide (3.0 M in diethyl ether, 0.39 mL, 1.2 mmol) was added to the red solution at -78 °C. The solution was stirred for eight hours and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **140** (61 mg, 0.24 mmol, 25%).

^{1}HNMR ($CDCl_3$): δ 12.36 (s, 1H), 7.32 (m, 6H), 6.95 (d, 1H, ^{3}J = 6.0 Hz), 6.90 (m, 2H), 6.27 (d, 1H, ^{3}J = 10 Hz), and 3.07 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 190.5, 161.8,

152.9, 147.8, 142.2, 136.5, 128.8, 128.7, 128.0, 125.6, 125.6, 119.7, 117.2, 114.3, and 72.2. IR (KBr): υmax 3435, 3040, 2945, 1650, 1490, 1400, 1360, 1230, and 1145 cm^{-1}.

Bromoquinol 146.



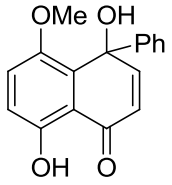
146

A solution of bromojuglone **134** (136 mg, 0.54 mmol) in 20 mL of dry THF was cooled down to -78 °C. Phenylmagnesium bromide (3.0 M in diethyl ether, 0.2 mL, 0.6 mmol) was added to the red solution at -78 °C. The black solution resulted was stirred for eight hours and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **146** (29 mg, 0.09 mmol, 16%) and the starting material (69 mg, 0.27 mmol, 50%).

A solution of bromojuglone **134** (104 mg, 0.41 mmol) in 20 mL of dry THF was cooled down to -78 °C. Phenylmagnesium bromide (3.0 M in diethyl ether, 0.2 mL, 0.6 mmol) was added to the red solution at -78 °C. The solution was stirred for 2 days and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give yellow oil **146** (64 mg, 19 mmol, 47%) and the starting material (22 mg, 0.086 mmol, 21%).

^{1}HNMR ($CDCl_3$): δ 12.10 (s, 1H), 7.30 (m, 6H), 6.94 (m, 3H), and 3.03 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 187.6, 161.7, 155.3, 147.2, 141.7, 136.5, 131,3, 129.8, 129.8, 128.8, 128.3, 125.2, 120.8, 120.5, 117.3, and 75.8. IR (KBr): υmax 3440, 1640, 1607, 1452, 1340, 1253, 1230, and 1195cm^{-1}.

Quinol 153.

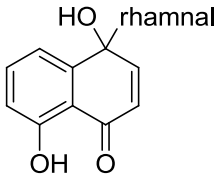


153

A solution of 5-hydroxy-8-methoxy-1,4-naphthalenedione **135** (100 mg, 0.50 mmol) in 25 mL of dry THF was cooled down to -78 °C. Phenylmagnesium bromide (3.0 M in diethyl ether, 0.2 mL, 0.6 mmol) was added to the red solution at -78 °C. The solution was stirred overnight. Then the reaction was allowed to warm up to -65 °C and stirred for 36 hours. The reaction was quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes chloride and ethyl acetate (15:1) to give yellow oil **153** (63 mg, 23 mmol, 46%).

^{1}HNMR ($CDCl_3$): δ 12.18 (s, 1H), 7.28 (m, 5H), 7.13 (d, 1H, ^{3}J = 9.2 Hz), 7.00 (d, 1H, ^{3}J = 9.2 Hz), 6.87 (d, 1H, ^{3}J = 10 Hz), 6.20 (d, 1H, ^{3}J = 10 Hz), 4.92 (s, 1H), and 3.46 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 190.7, 156.7, 152.6, 149.1, 143.7, 134.1, 128.6, 127.9, 125.326, 124.4, 122.0, 118.0, 114.6, 73.2, and 57.1. IR (KBr): υmax 3520, 1665, 1590, 1480, 1435, 1285, 1220, and 1640 cm^{-1}. ESI-MS ($M-H^-$): 281.16, and 283.31 g/mol.

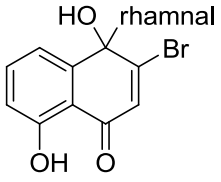
Quinol 141.



141

A solution of rhamnal **166** (309 mg, 0.86 mmol) in 10 mL of dry THF was added t-BuLi (1.7 M, 0.7 mL, 1.2 mmol) dropwise at -78 °C. After addition, the yellow solution was allowed to warm up to 0 °C and stirred for 100 minutes. The pale yellow solution was cooled down to -78 °C again. Then it was transferred to a solution of juglone **133** (166 mg, 0.95 mmol) in 5 mL of dry THF by a cannula at -78 °C. The reaction was stirred for 24 hours at -78 °C and 24 hours at -70 °C to form a dark green mixture. The reaction was quenched by 1 mL of water. The organic phase was separated; the water phase was extracted three times with diethyl ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give the starting juglone (96 mg, 55 mmol, 58%) back.

Bromoquinol 147.

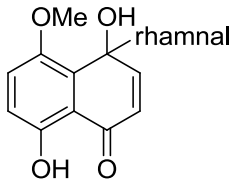


147

A solution of rhamnal **166** (355 mg, 1 mmol) in 10 ml of dry THF was added t-BuLi (1.7 M, 0.8 mL, 1.4 mmol) dropwise at -78 °C. After addition, the yellow solution was allowed to warm up to 0 °C and stirred for 2 hours. The pale yellow solution was cooled down to -78 °C again. Then it was transferred to a solution of bromojuglone **134** (131 mg, 0.52 mmol) in 5 mL of dry THF by a cannula at -78 °C. The reaction was

stirred for 24 hours at -78 °C and 24 hours at -70 °C to form a dark green mixture. The reaction was quenched by 1 mL of water. The organic phase was separated; the water phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (15:1) to give the starting juglone (82 mg) back.

Quinol 154.



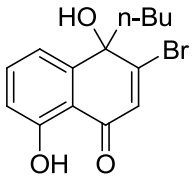
154

A solution of rhamnal **166** (370 mg, 1.03 mmol) in 15 mL of dry THF was added t-BuLi (1.7 M, 1.4 mL, 2.38 mmol) dropwise at -78 °C. After addition, the yellow solution was allowed to warm up to 0 °C and stirred for 2 hours. The pale yellow solution resulted was cooled down to -78 °C again. Then it was transferred to a solution of 5-hydroxy-8-methoxy-1,4-naphthalenedione **135** (135 mg, 0.661 mmol) in 10 mL of dry THF by a cannula at -78 °C. The reaction was stirred for 12 hours at -78 °C and 48 hours at -60 °C to form a dark green mixture. The reaction was quenched by 1 mL of water. The organic phase was separated; the water phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (10:1) to give a yellow solid **154** (190 mg, 0.33 mmol, 51%).

^{1}HNMR ($CDCl_3$): δ 12.07 (s, 1H), 7.11 (dd, 1H, ^3J = 6.8 Hz, ^3J = 3.0 Hz), 6.93 (dd, 1H, ^3J = 9.0 Hz, ^3J = 2.5 Hz), 6.75 (d, 1Hz, ^3J = 9.5 Hz), 6.29 (dd, 1H, ^3J = 10 Hz, ^3J = 4.0 Hz), 5.18 (d, 1H, ^3J = 4.0 Hz), 4.90 (s, 1H), 3.93 (d, 1H, ^3J = 3.5 Hz), 3.82 (s, 3H),

3.51 (s, 1H), 1.08 (s, 3H), 0.85 (m, 18H), and 0.10 (m, 12H). ^{13}CNMR ($CDCl_3$): δ 190.9, 156.8, 153.0, 152.5, 150.4, 149.2, 132.0, 127.3, 121.7, 120.2, 117.8, 115.3, 98.0, 76.0, 73.8, 72.1, 68.9, 67.9, 58.1, 57.0, 26.0, 18.2, 16.1, 15.5, and -4.2. IR (KBr): υmax 3505, 2945, 2810, 1665, 1610, 1470, 1250, 1105, and 1060 cm^{-1}. ESI-MS ($M-H^-$): 561.26, 562.33, and 563.31 g/mol.

Bromophenol 148.

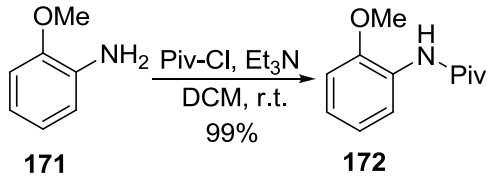


148

A solution of bromojuglone **134** (104 mg, 0.41 mmol) in 20 mL of dry THF was cooled down to -93 °C. n-Butyl lithium (1.6 M in diethyl ether, 0.30 mL, 0.48 mmol) was added to the red solution at -93 °C. The black solution resulted was stirred for half an hour and then quenched by 0.4 mL of water. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with methylene chloride and ethyl acetate (15:1) to give yellow oil **148** (52 mg, 19 mmol, yield 46%).

^{1}HNMR ($CDCl_3$): δ 12.10 (s, 1H), 7.53 (dt, 1H, ^3J = 8.0 Hz, ^3J = 8.0 Hz), 7.27 (s, 1H), 6.95 (d, 1H, ^3J = 8.5 Hz), 6.87 (s, 1H), 2.56 (s, 1H), 2.22 (m, 1H), 1.91 (m, 1H), 1.17 (m, 2H), 0.93 (m, 2H), and 0.77 (t, 3H, ^3J = 7.0 Hz). ^{13}CNMR ($CDCl_3$): δ 188.9, 163.8, 157.6, 147.9, 137.5, 134.2, 119.7, 118.6, 116.1, 77.1, 45.8, 27.3, and 23.9. IR (KBr): υmax 3393, 2998, 1642, 1608, 1453, 1362, 1251, and 1040 cm^{-1}.

Protected anisidine 172.[101]

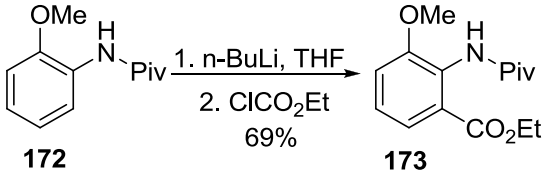


171 **172**

A solution of o-anisidine **171** (21 g, 170 mmol) and trimethylamine (12 g, 1.2 mmol) in methylene chloride was cooled down to 0 °C. Pivaloyl chloride (15 g, 1.25 mmol) was added to the mixture at 0 °C. The reaction was stirred overnight at room temperature and then quenched by 1M HCl. The organic phase was separated; the water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give a lot crystal **172** (35 g, 99%).

^{1}HNMR ($CDCl_3$): δ 7.53 (d, 1H, ^3J = 7.2 Hz), 6.89 (dd, 1H, ^3J = 8.4 Hz), 6.77 (m, 2H), 3.73 (s, 3H), and 1.24 (s, 9H). IR (KBr): υmax 3442, 2961, 2870, 1680, 1601, 1522, 1460, 1334, 1249, and 1160 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [101]

Amino ester 173.[102]



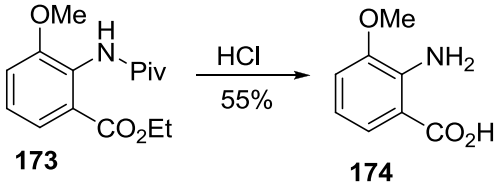
172 **173**

n-BuLi (1.6 M, 11.7 mL, 18.7 mmol) was added to a solution of the protected anisidine **172** (1.53 g, 7.3 mmol) in THF (20 mL) at room temperature. The mixture was stirred for 2 hours at room temperature to give a lot yellow solid. The reaction was allowed to cool down to 0 °C and then quenched by ethyl chloroformate (1.7 mL). After the solution was stirred for 2 hours at room temperature, it was poured into sat. NH_4Cl solution. The organic phase was separated; the water phase was extracted three times by

methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (6:1) to give a crystal **173** (1.43g, 12.9 mmol, 69%).

^{1}HNMR ($CDCl_3$): δ 7.55 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.6 Hz), 7.30 (dd, 2H, ^3J = 8.0 Hz, ^4J = 1.6 Hz), 7.06 (dd, 2H, ^3J = 8.4 Hz, ^4J = 1.6 Hz), 4.10 (q, 2H, ^3J = 7.2 Hz), 3.77 (s, 3H), and 1.11 (t, 3H, ^3J = 7.2 Hz). ^{13}CNMR ($CDCl_3$): δ 183.4, 165.4, 129.2, 128.4, 122.7, 120.7, 115.4, 111.8, 62.5, 61.1, 56.0, 27.7, and 14.1. IR (KBr): υmax 2967, 2909, 2841, 1794, 1584, 1474, 1393, 1263, and 1059 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [102]

Amino acid 174.

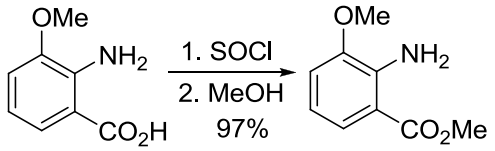


173 **174**

Amino ester **173** (700 mg, 2.5 mmol) was added a mixture of concentrated hydrochloric acid (12 mL) and water (3 mL). The mixture was refluxed overnight and then quenched by sat. $NaHCO_3$ solution. The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (3:1) to give oil **174** (230 mg, 1.38 mmol, 55%).[102]

^{1}HNMR ($CDCl_3$): δ 7.55 (dd, 1H, ^3J = 8.4 Hz, ^4J = 1.2 Hz), 6.88 (d, 1H, ^3J = 7.2 Hz), 6.60 (dt, 1H, ^3J = 8.0 Hz, ^3J = 1.2 Hz), and 3.88 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 173.7, 147.2, 142.7, 123.4, 114.9, 113.7, 109.0, and 55.9. IR (KBr): υmax 3455, 2960, 1680, 1595, 1465, 1410, and 1270 cm^{-1}.

Amino ester 175.[102]

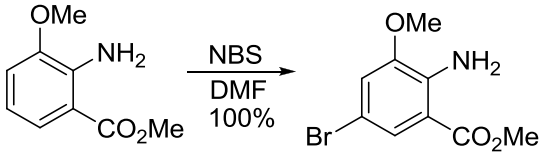


174 **175**

Amino acid **174** (119 mg, 0.71 mmol) was added by thionyl chloride (5 mL). The mixture was refluxed for 3 hours. Then extra thionyl chloride was removed in vacuo. The residues were added dry methanol (25 mL). The reaction was stirred overnight and quenched by water. The water phase was extracted three times by methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give a crystal **175** (125 mg, 0.69 mmol, 97%).

^{1}HNMR ($CDCl_3$): δ 7.47 (d, 1H, ^3J = 8.0 Hz), 6.85 (d, 1H, ^3J = 7.6 Hz), 6.58 (dt, 1H, ^3J = 8.0 Hz, ^3J = 8.0 Hz), and 3.87 (s, 6H). ^{13}CNMR ($CDCl_3$): δ 185.4, 173.9, 147.2, 142.7, 123.4, 114.9, 113.7, 109.2, 55.9, 38.8, 27.2, and 22.8. IR (KBr): υmax 3455, 2960, 1680, 1595, 1465, 1410, and 1270 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [102]

Bromobenzoic ester 176.

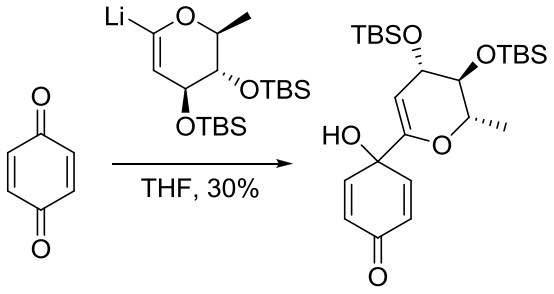


175 **176**

Amino ester **175** (100 mg, 0.55 mmol) and NBS (111 mg, 0.66 mmol) were dissolved in DMF (5 mg) at 0 °C. Then the mixture was stirred for 4 hours at room temperature. The mixture was washed with a copper sulfate solution. The water phase was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give a crystal **176** (144 mg, 0.55 mmol, 100%).[98]

^{1}HNMR ($CDCl_3$): δ 7.59 (d, 1H, ^{3}J = 1.5 Hz), 6.89 (d, 1H, ^{3}J = 2.0 Hz), 6.01 (brand, 2H), 3.85 (s, 3H), and 3.84 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 167.8, 147.9, 141.1, 124.6, 116.1, 105.9, 56.1, and 51.8. IR (KBr): υmax 3497, 1695, 1547, 1477, 1439, 1301, 1264, and 1230 cm^{-1}.

Quinol 180.[96]



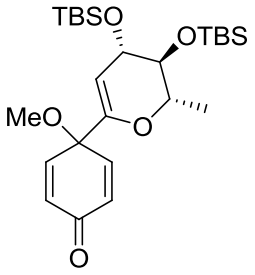
179 **180**

A solution of rhamnal **166** (954 mg, 2.7 mmol) in 30 mL of dry THF was added t-BuLi (1.7 M, 3.1 mL, 5.2 mmol) dropwise at -78 °C. The yellow solution was allowed to warm up to 0 °C. After the pale yellow solution was stirred for 2 hours at 0 °C, it was cooled down to -78 °C; and then it was transferred to a solution of quinone **179** (660 mg, 0.661 mmol) in 30 mL of dry THF at -78 °C by a cannula. The reaction was stirred overnight at -78 °C and then quenched by 1 mL of water. The organic phase was separated; the water phase was extracted three times with diethyl ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (7:3) to give a solid **180** (366 mg, 0.81 mmol, 30%).

^{1}HNMR ($CDCl_3$): δ 6.82 (m, 2H), 6.20 (m, 2H), 4.94 (d, 1H, ^{3}J = 4.0 Hz), 4.12 (m, 1H), 3.98 (dt, 1H, ^{3}J = 1.0 Hz, ^{3}J = 1.0 Hz), 3.58 (dd, 1H, ^{3}J = 5.0 Hz, ^{3}J = 3.5 Hz), 2.98 (s, 1H), 1.31 (d, 1H, ^{3}J = 7.0 Hz), 0.86 (s, 18H), and 0.80 (m, 12H). ^{13}CNMR ($CDCl_3$): δ 185.5, 150.0, 147.8, 131.5, 100.1, 74.0, 52.5, 26.1, 18.1, 16.4, -3.8, -4.00, and -4.3. IR (KBr): υmax 3315, 2954, 2886, 1602, 1514, 1255, 1169, and 1098 cm^{-1}. The

spectroscopic and other physical data reported are consistent with values reported in the literature. [96]

Methylated quinol 181.

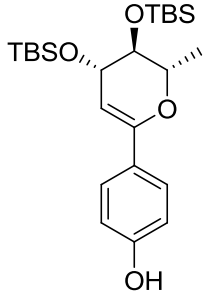


181

A solution of quinol **180** (230 mg, 0.5 mmol) in methylene chloride was added silver oxide (360 mg) and iodomethane (400 mg). The reaction was stirred for 5 hours at 40 °C. The solid was filtered off; the filtrate was concentrated in vacuo to give oil **181** (194 mg, 0.4 mmol, 80%).[103]

^{1}HNMR ($CDCl_3$): δ 6.76 (m, 2H), 6.36 (m, 2H), 5.05 (d, 1H, ^{3}J = 3.9 Hz), 4.02 (m, 1H), 3.54 (dd, 1H, ^{3}J = 4.8 Hz, ^{3}J = 4.2 Hz), 3.28 (s, 3H), 1.25 (d, 1H, ^{3}J = 6.6 Hz), 0.84 (m, 18H), and 0.61 (m, 12H). ^{13}CNMR ($CDCl_3$): δ 185.6, 150.0, 148.3, 147.8, 143.2, 131.5, 128.8, 100.1, 76.2, 74.9, 74.0, 69.0, 52.6, 26.0, 18.1, 16.6, and -3.9. IR (KBr): υmax 3432, 2953, 2889, 1669, 1472, 1386, 1254, 1105, and 1069 cm^{-1}.

Quinol 182.[99]



182

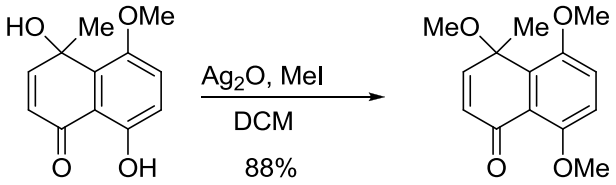
(a) Aluminum was merged in a 2% solution of mercury(II) chloride in water for 10 sec. The aluminum was cut into small pieces. Methylated quinol **181** (110 mg, 0.24) in

a mixture of 2 mL of THF and 0.3 mL of water was added by mercury-aluminum amalgam (60 mg). The reaction was refluxed for 2 hours. The solid was filtered off; the filtrate was concentrated in vacuo to give oil (93mg, 0.22 mmol, 91%)

(b) Quinol **180** (104 mg, 0.23 mmol) in a mixture of 2 mL of THF and 0.3 mL of water was added by the mercury-aluminum amalgam (60 mg). The reaction was refluxed for 2 hours. The solid was filtered off; the filtrate was concentrated in vacuo to give oil **182** (97mg, 0.23 mmol, 99%)

^{1}HNMR ($CDCl_3$): δ 7.44 (dd, 2H, ^{3}J = 6.8 Hz, ^{4}J = 2.0 Hz), 6.79 (dd, 2H, ^{3}J = 6.8 Hz, ^{4}J = 2.0 Hz), 5.10 (d, 1H, ^{3}J = 3.6 Hz), 4.30 (dd, 1H, ^{3}J = 5.2 Hz, ^{4}J = 3.6 Hz), 4.08 (dd, 1H, ^{3}J = 6.8 Hz, ^{3}J = 6.8 Hz), 3.64 (dd, 1H, ^{3}J = 6.8 Hz, ^{3}J = 5.2 Hz), 1.42 (d, 3H, ^{3}J = 6.4 Hz), 0.86 (m, 18H), and 0.18 (m, 12H). ^{13}CNMR ($CDCl_3$): δ 185.9, 150.3, 148.6, 148.3, 128.7, 128.3, 116.3, 98.9, 76.6, 69.3, 68.7, 25.9, 18.1, 16.5, and -4.0. IR (KBr): υmax 3396, 2930, 2888, 1669, 1512, 1472, 1388, 1255, 1104, and 1071 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [99]

Quinol 183.



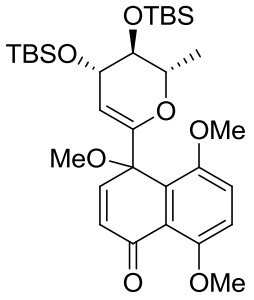
138 **183**

A solution of quinol **138** (30 mg, 0.14 mmol) in methylene chloride was added silver oxide (320 mg) and iodomethane (0.40 mL). The reaction was stirred for 24 hours at 40 °C. The solid was filtered off; the filtrate was concentrated in vacuo to give the methylation product **183** (26mg, 0.12 mmol, 88%)[103]

^{1}HNMR ($CDCl_3$): δ 7.09 (d, 1H, ^{3}J = 9.2 Hz), 6.93 (d, 1H, ^{3}J = 9.2 Hz), 6.56 (d, 1H, ^{3}J = 10.4 Hz), 6.28 (d, 1H, ^{3}J = 10.4 Hz), 3.84 (s, 3H), 3.82 (s, 3H), 2.94 (s, 3H), and

1.67 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 150.8, 130.5, 117.8, 113.2, 74.3, 56.8, 56.7, 52.7, and 26.0. IR (KBr): υmax 2930, 2865, 1680, 1490, 1277, and 1092 cm^{-1}.

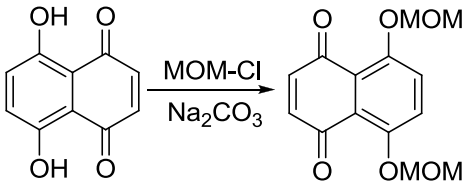
Attempt at quinol 184.



184

A solution of quinol **153** (60 mg, 0.11 mmol) in methylene chloride was added silver oxide (200 mg) and iodomethane (0.30 mL). The reaction was stirred for 5 hours at 40 °C. The solid was filtered off; the filtrate was concentrated in vacuo. The NMR of crude product showed that the starting material decomposed.

Naphthylquinone 186.

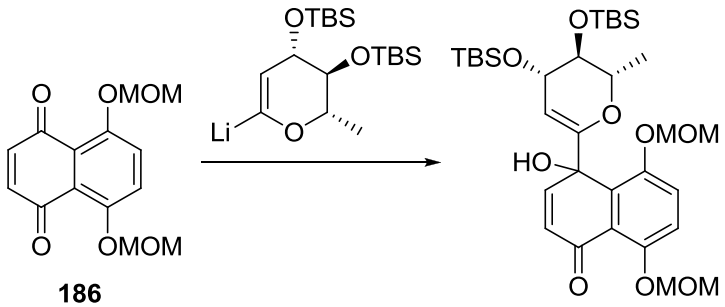


185 **186**, 92%

A solution of naphthylquinone **185** (200 mg, 1.05mmol) in 10 mL of methylene chloride was added 300 mg of sodium carbonate and 200 mg of chloromethylmethyl ether at 0 °C. The reaction was stirred overnight at 0 °C. The solid was filtered off; the filtrate was concentrated in vacuo to give the MOM protected product (260 mg, 0.93 mmol, 92%).

^{1}HNMR ($CDCl_3$): δ 7.43 (s, 2H), 6.73 (s, 2H), 5.21 (s, 4H), and 3.49 (s, 6H). ^{13}CNMR ($CDCl_3$): δ 184.5, 152.2, 138.4, 125.2, 96.0, and 56.6. IR (KBr): υmax 3384, 2935, 2836, 1736, 1612, 1586, 1463, 1363, 1247, and 1175 cm^{-1}.

Naphthylquinol 187.

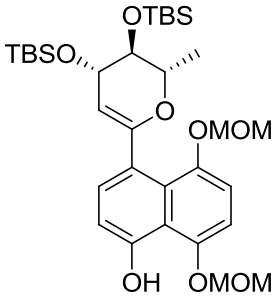


186 **187**, 33%

A solution of rhamnal **166** (370 mg, 1.03 mmol) in 15 mL of dry THF was added t-BuLi (1.7 M, 1.4 mL, 2.38 mmol) dropwise at -78 °C. After addition, the yellow solution was allowed to warm up to 0 °C and stirred for 2 hours. The pale yellow solution was cooled down to -78 °C again. Then it was transferred to a solution of naphthalenedione **187** (260 mg, 0.94 mmol) in 10 mL of dry THF by a cannula at -78 °C. The reaction was stirred for 12 hours at -78 °C and 48 hours at -60 °C to form a dark green mixture. The reaction was quenched by 1 mL of water. The organic phase was separated; the water phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (10:1) to give a yellow solid (196 mg, 0.31 mmol, 33%).

^{1}HNMR ($CDCl_3$, diastereomers): δ 7.30 (m, 1H), 7.14 (m, 1H), 6.58 (m, 1H), 6.23 (m, 1H), 5.23 (s, 1H), 5.17 (s, 1H), 5.06(m, 1H), 4.99 (s, 1H), 4.95(s, 1H), 3.91 (m, 2H), 3.54 (m, 1H), 3.51 (d, 6H), 1.05 (q, 3H), 0.83 (q, 18H), and 0.00 (q, 12H). ^{13}CNMR ($CDCl_3$): δ 184.6, 153.1, 150.0, 145.9, 135.0, 129.0, 122.6, 120.5, 119.1, 98.4, 96.4, 76.3, 75.6, 74.3, 74.0, 71.8, 70.0, 67.9, 56.5, 26.1, 25.9, 18.1, -4.0, and -4.5. IR (KBr): υmax 3399, 2954, 2856, 1715, 1597, 1463, 1254, and 1102 cm^{-1}.

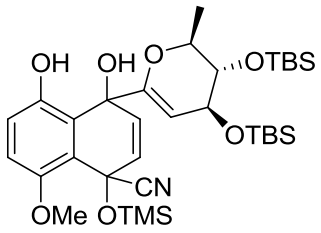
Attempt at naphthol 188.



188

Aluminum was merged in a 2% solution of mercury(II) chloride in water for 10 sec. The mercury-aluminum amalgam was cut into small pieces. A solution of naphthylquinol **187** (50 mg, 0.078 mmol) in a mixture of 2 mL of THF and 0.3 mL of water was added the mercury-aluminum amalgam (30 mg). The reaction was refluxed for 2 hours. The solid was filtered off; the filtrate was concentrated in vacuo. The NMR of crude product showed that the desired product was not obtained.

Attempt at naphthylquinol 190.

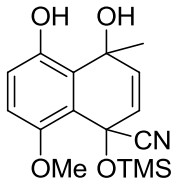


190

t-Butyl lithium (1mL, 1.7 M, 1.7 mmol) was added to a solution of 420 mg (1.17 mmol) of TBS protected rhamnal **166** in THF at -78 °C. The mixture was allowed to warm up to room temperature and it was stirred for 2 hours to give a yellow solution. 0.350 mL of trimethylsilyl cyanide was added to a solution of 103 mg (0.51 mmol) of quinone **135** in 5 mL of acetonitrile under argon. The reaction was stirred for an hour. The solution was concentrated in vacuo. The residues were dissolved in 50 mL of THF. The solution was added the lithiated rhamnal solution prepared in the first step at -78 °C. The reaction was stirred for 24 hours at -78 °C and then it was quenched by water. The water solution was extracted three times with diethyl ether. The organic phases were

combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate. The desired product was not obtained.

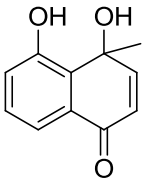
Attempt at naphthylquinol 191.



191

0.300 mL of trimethylsilyl cyanide was added to a solution of 88 mg (0.44 mmol) of quinone **135** in 25 mL of acetonitrile under argon at 0 °C. The reaction was stirred for an hour. The solution was concentrated in vacuo. The residues were dissolved in 20 mL of THF. The solution was added by 0.400 mL of 3 M methylmagnesium bromide (1.2 mmol) at -78 °C. The reaction was stirred for 24 hours at -78 °C and then it is quenched with water. The water solution was extracted three times with diethyl ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate. The desired product was not obtained.

Attempt at quinol 192.



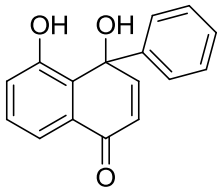
192

(a) 23 mg (1 mmol) of sodium hydride was added to a solution of 174 mg (1 mmol) of juglone in 10 mL of THF. 0.070 mL of titanium chloride was added to the black solution. Some solid appeared. The reaction was stirred for half an hour at -30 °C. Then the reaction was cooled down to -78 °C. 1.2 mL of 1.6 M (1.9 mmol) methyl lithium was added to the reaction. The reaction was tracked by TLC. After 4 hours, there

was not reaction occurred. 3.6 mL of 1.6 M (5.8 mmol) methyl lithium was added. The reaction was stirred overnight. The TLC shown there was still much starting material in the reaction. The reaction was quenched with water. The water solution was extracted three times with ethyl acetate. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 15: 1 hexanes and ethyl acetate to give starting material back.

(b) 0.06 mL of titanium chloride was added to a solution of 174 mg (1.0 mmol) of juglone in THF. The reaction turned black. The reaction was stirred for 1 hour at room temperature. The solution was cooled down to -78 °C. 10 equivalents of methylmagnesium bromide were added to the reaction. The reaction became dark yellow. The reaction was allowed to warm up to room temperature and stirred for 24 hours. The reaction was quenched by water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 15:1 hexanes and ethyl acetate to give starting material back.

Attempt at quinol 193

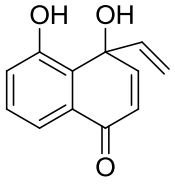


193

1.5 mL (1.5 mmol) of 1M phenyl lithium was added to a solution of 246 mg (1 mmol) of $CeCl_3$ in 5 mL of THF at -78 °C. Then, the solution was allowed to warm up to room temperature and stirred for 2 hours to give a black solution. The solution was cooled down to -78 °C. A solution of 87 mg (0.5 mmol) of juglone in 5 mL of THF was added to the reaction. The reaction was stirred overnight and then it was warmed up to 0 °C. After the reaction was stirred for 2 more hours at 0 °C, it was quenched with sat.

NH_4Cl solution. The water solution was extracted three times with diethyl ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate to give 74 mg of starting material.

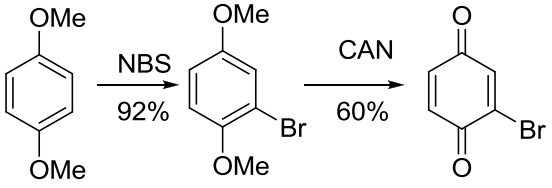
Attempt at quinol 194.



194

1.5 mL (1.5 mmol) of 1M vinylmagnesium bromide was added to a solution of 298 mg (1.2 mmol) of dry $CeCl_3$ in 8 mL of THF at -78 °C. Then, the solution was warmed up to -20 °C and stirred for 2 hours to give a brown solution. The solution was cooled down to -78 °C. A solution of 87 mg (0.5 mmol) of juglone in 1 mL of THF was added to the reaction. The reaction was stirred overnight and then it was warmed up to 0 °C. After the reaction was stirred for 2 more hours at 0 °C, it was quenched by sat. NH_4Cl solution. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the organic solutions were dried, combined and concentrated. The residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate to give 77 mg of starting material back.

Bromoquinone 197.[108]



195 **196** **197**

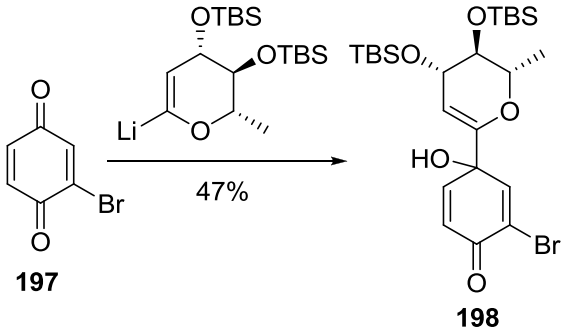
84 g (0.61 mol) of 1,4-dimethoxybenzene and 114 g (0.64 mmol) of N-bromosuccinimide were dissolved in 700 mL methylene chloride at room temperature. The mixture was stirred for 48 hours at room temperature. The solution was washed with a solution of sodium thiosulfate in water. The organic solution was separated and dried

over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 30:1 hexanes and ethyl acetate to give 122 g of compound **196** (0.56 mmol, 92%).

In a 100 mL round bottom flask, 30 g of silica gel was added a solution of 11.25 g (20.5 mmol) of ammonium cerium (IV) nitrate in 2.5 mL of water. The powder was stirred to a free flowing yellow solid. A solution of 1.86 g (8.6 mmol) of 2-bromo-1,4-dimethoxybenzene **196** in 10 mL of methylene chloride was added to the solid. The reaction was stirred for 15 minutes. The solid was filtered off; the filtrate was concentrated in vacuo. The residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate to give 1.10 g of compound **197** (7.8 mmol, 90%).

^{1}HNMR ($CDCl_3$): δ 7.30 (d, 1H, ^{4}J = 2.4 Hz), 6.96 (d, 1H, ^{3}J = 20.0 Hz), and 6.82 (dd, 1H, ^{3}J = 20.0 Hz, ^{4}J = 2.4 Hz). ^{13}CNMR ($CDCl_3$): δ 184.7, 179.3, 138.3, 137.7, 136.8, and 136.0. The spectroscopic and other physical data reported are consistent with values reported in the literature. [108]

Quinol 198.

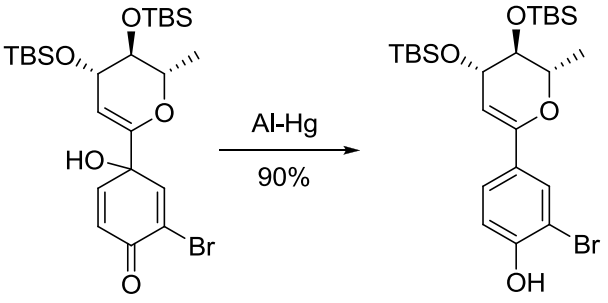


A solution of rhamnal **166** (622 mg, 2.06 mmol) in 1 mL of dry THF was added t-BuLi (1.7 M, 2.8 mL, 4.8 mmol) dropwise at -78 °C. After addition, the yellow solution was allowed to warm up to 0 °C and it was stirred for 2 hours. The pale yellow solution resulted was cooled down to -78 °C again. Then it was transferred to a solution of bromoquinone **197** (711 mg, 3.82 mmol) in 10 mL of dry THF by a cannula at -78 °C. The reaction was stirred for 4 hours at -78 °C to form a dark green mixture. The reaction

was quenched by 1 mL of water. The organic phase was separated; the water phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (10:1) to give a yellow solid **198** (723 mg, 1.3 mmol, 63%).

Mixture of diastereomers ^{1}HNMR ($CDCl_3$): δ 7.25 (m, 1H), 6.85 (m, 1H), 6.30 (m, 1H), 5.10 (m, 1H), 4.09 (m, 1H), 3.98 (m, 1H), 3.57 (m, 1H), 1.26 (m, 3H), 0.863 (m, 18H), and 0.06 (m, 12H).

Phenol 199.



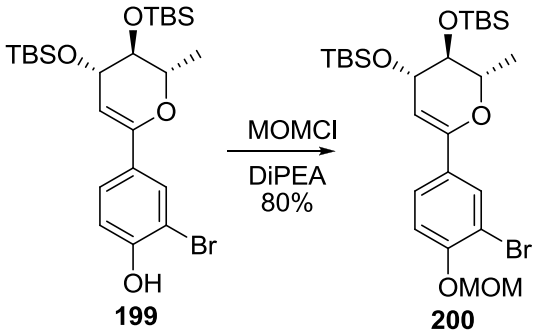
198 **199**

Aluminum was merged in a 2% solution of mercury(II) chloride in water for 10 sec. The mercury-aluminum amalgam was cut into small pieces. Quinol **187** (364 mg, 0.34 mmol) in a mixture of 2 mL of THF and 0.3 mL of water was added mercury-aluminum amalgam (130 mg). The reaction was stirred for 2 hours at room temperature. The solid was filtered off; the filtrate was concentrated in vacuo. The residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give a yellow solid **199** (314 mg, 0.31 mmol, 90%).

^{1}HNMR ($CDCl_3$): δ 8.14 (d, 1H, ^4J = 2.0 Hz), 7.87 (dd, 1H, ^3J = 8.8 Hz, ^4J = 2.0 Hz), 7.05 (d, 1H, ^3J = 8.8 Hz), 4.60 (dd, 1H, ^3J = 8.0 Hz, ^3J = 4.0 Hz), 3.98 (m, 1H), 3.48 (dd, 1H, ^3J = 8.8 Hz, ^3J = 4.0 Hz), 3.35 (dd, 1H, ^3J = 16.0 Hz, ^3J = 8.8 Hz), 1.25 (d, 3H, ^3J = 6.0 Hz), 0.86 (d, 18H), and 0.10 (d, 12H). ^{13}CNMR ($CDCl_3$): δ 196.2, 157.1, 133.3, 131.8, 129.9, 116.1, 110.9, 81.2, 75.5, 73.5, 70.0, 25.9, 25.8, 21.0, -4.0, -4.4, -4.5, and -

4.7. IR (KBr): υmax 3391, 2955, 2895, 1733, 1683, 1596, 1496, 1361, 1290, 1170, and 1055 cm^{-1}.

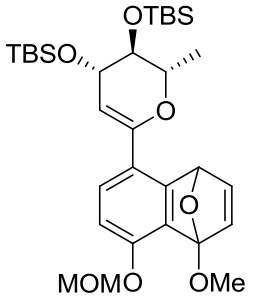
MOM-phenol 200.



A solution of phenol **199** (59 mg, 0.11 mmol) in 2 mL of methylene chloride was added 30.8 mg of diisopropylethylamine and 11.8 mg (0.15 mmol) of chloromethylmethyl ether at 0 °C. The reaction was stirred overnight at 0 °C. The solution was concentrated in vacuo. The residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give the MOM protected compound **200** (52mg, 0.088 mmol, 80%).

^{1}HNMR ($CDCl_3$): δ 7.76 (d, 1H, ^{4}J = 2.4 Hz), 7.44 (dd, 1H, ^{3}J = 8.8 Hz, ^{4}J = 2.4 Hz), 7.09 (d, 1H, ^{3}J = 8.8 Hz), 5.25 (s, 2H), 5.12 (d, 1H, ^{3}J = 3.2 Hz), 4.25 (dd, 1H, ^{3}J = 4.0 Hz, ^{3}J = 4.0 Hz), 4.10 (dq, 1H, ^{3}J = 6.4 Hz, ^{3}J = 6.4 Hz), 3.63 (dq, 1H, ^{3}J = 6.4 Hz, ^{3}J = 4.0 Hz), 3.51 (s, 1H), 1.41 (d, 3H, ^{3}J = 6.4 Hz), 0.93 (s, 9H), 0.91 (s, 9H), 0.14 (s, 6H), and 0.11 (s, 6H). ^{13}CNMR ($CDCl_3$): δ 153.9, 149.6, 130.4, 115.7, 112.8, 99.1, 95.2, 75.9, 75.0, 70.7, 56.5, 26.2, 26.1, 18.4, 18.2, 17.3, -3.4, and -3.7. IR (KBr): υmax 2927, 2854, 1713, 1650, 1463, 1257, 1140, and 1088 cm^{-1}.

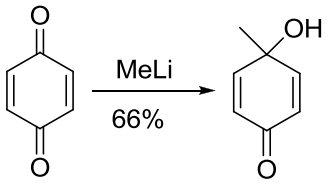
Attempt at MOM-phenol 201.



201

1.5 mL of 2M LDA (3 mmol) was added to a solution of 23 mg (0.04 mmol) of MOM-phenol **200** in 2 mL of THF at -78 °C. After the reaction was stirred for 1 hour at -78 °C, it was allowed to warm up to room temperature. The reaction was stirred for 24 hours and then quenched with water. The organic phase was separated; the water phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give the starting material back.

p-Methylquinol 202.[109]



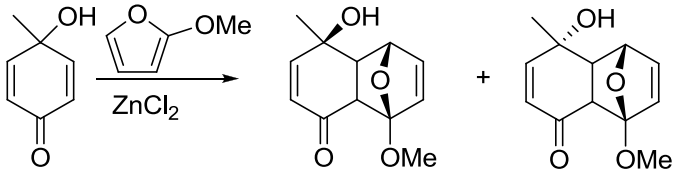
179 **202**

4.7 mL (8 mmol) of 1.7 M solution of methyl lithium in diethyl ether was added to a solution of 660 mg (6.1 mmol) of benzoquinone **179** in THF at -95 °C. After the reaction was stirred for an hour, it was quenched by water. The organic phase was separated; the water phase was extracted three times with diethyl ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a silica gel column with hexanes and ethyl acetate (5:1) to give 500 mg of compound **202** (4.0 mmol, 66 %).

^{1}HNMR ($CDCl_3$): δ 6.81 (d, 2H, ^3J = 10.5 Hz), 7.87 (d, 2H, ^3J = 10.5 Hz), 4.07 (s, 1H), and 1.37 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 186.0, 153.3, 126.6, 67.0, and 26.8. IR (KBr):

υmax 3387, 2978, 1666, 1620, 1396, 1306, 1246, 1177, and 1092 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature.[109]

Compound 203 and 204.



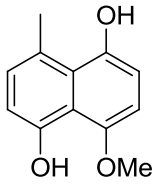
202 **203**, 44% **204**,35%

A solution of 150 mg (1.2 mmol) of p-methylquinol **202** in 2 mg of benzene was added 143 mg (1.46 mmol) of furan and 15 mg (0.11 mmol) of zinc chloride at room temperature. The reaction was stirred overnight at 45-50 °C in a well-sealed vial. The solution was concentrated in vacuo. The residue was separated by a silica gel column with hexanes and ethyl acetate (10:1) to give 119 mg of compound **203** (0.54 mmol, 44%) and 95 mg of compound **204** (0.43 mmol, 35%).

^{1}HNMR ($CDCl_3$): δ 6.41 (d, 1H, ^{3}J = 10.4 Hz), 5.80 (d, 1H, ^{3}J = 11.2 Hz), 5.78 (d, 1H, ^{3}J = 10.4 Hz), 5.57 (dd, 1H, ^{3}J = 11.2 Hz, ^{3}J = 10.4 Hz), 3.68 (s, 3H), 3.38 (s, 1H), 3.33 (dd, 1H, ^{3}J = 10.4 Hz, ^{3}J = 8.0 H), 2.09 (d, 2H, ^{3}J = 8.0 Hz), and 1.50 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 194.8, 166.8, 149.2, 147.8, 126.3, 120.0, 66.6, 51.4, 36.4, 33.9, 29.2, and 27.0. IR (KBr): υmax 3453, 2952, 1778, 1715, 1666, 1444, 1370, 1203, and 1006 cm^{-1}.

^{1}HNMR ($CDCl_3$): δ 6.44 (d, 1H, ^{3}J = 10.4 Hz), 5.84 (m, 2H), 5.66 (d, 1H, ^{3}J = 10.4 Hz), 3.76 (s, 1H), 3.69 (s, 3H), 3.11 (dd, 1H, ^{3}J = 10.4 Hz, ^{3}J = 4.4 Hz), 2.16 (m, 1H), 1.97 (m, 1H), and 1.47 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 194.0, 167.6, 151.8, 148.0, 124.0, 120.9, 67.5, 51.7, 34.5, 33.8, 29.6, and 27.5. IR (KBr): υmax 3453, 2952, 1778, 1715, 1666, 1444, 1370, 1203, 1006, and 922 cm^{-1}.

Naphthol 205.



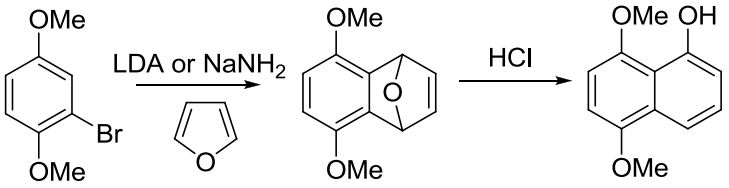
205, 66%

(a) A solution of 40 mg (0.18 mmol) of **203** or **204** in methylene chloride was added 80 mg of triethylamine and 200 μL of trimethylsilyl triflate at 0 °C. The reaction was stirred overnight at room temperature. Then the reaction was quenched with 1 M HCl solution. The organic phase was separated; the water phase was extracted three times with diethyl ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a TLC plate with hexanes and ethyl acetate (10:1) to give 23 mg of compound **205** (0.12 mmol, 66 %).

(b) A solution of 40 mg (0.18 mmol) of **203** or **204** in methylene chloride was added 100 μL of trifluoroacetic acid and 200 μL of acetic anhydride at 0 °C. The reaction was stirred overnight at room temperature. Then the reaction was quenched by water. The organic phase was separated; the water phase was extracted three times with ether. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was separated by a TLC plate with hexanes and ethyl acetate (10:1) to give 21 mg of product (10.8 mmol, 60 %).

^{1}HNMR ($CDCl_3$): δ 7.31 (d, 1H, ^3J = 10.4 Hz), 7.31 (s, 1H), 7.05 (d, 1H, ^3J = 10.4 Hz), 6.55 (s, 1H), 3.82 (s, 2H), 3.75 (s, 3H), and 2.42 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 169.5, 153.5, 148.2, 132.3, 129.9, 128.8, 125.3, 120.8, 110.7, 105.0, 52.6, and 34.7. IR (KBr): υmax 3453, 2954, 2854, 1742, 1677, 1546, 1491, 1262, 1121, and 1014 cm^{-1}. GC-MS (M^+): 205.12, 204.04, 146.10, 144.96, 116.06, 115.01, 91.03 and 72.14 g/mol.

Compound 207.[112]

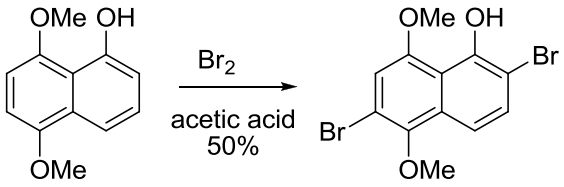


196 **206** **207**
overall 56%

50 g of sodium amide was added to a mixture of 200 mL of furan and 300 mL of THF at room temperature. The reaction was allowed to warm up to 50 °C. 122 g (0.56 mol) of bromoquinone **197** in 200 mL of THF was added to the reaction. After the reaction was stirred for 24 hours, it was cooled down to room temperature. The solid was filtered off and the filtrate was concentrated in vacuo. 350 mL of methanol was added to the crude product at 0 °C. Then 15 mL of concentrated HCl was added. The solution was stirred for 12 hours at room temperature and refluxed for 3 hours. The reaction was poured into ice cold water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate to give 64 g of compound **207** (0.31 mmol, 56%).

^{1}HNMR ($CDCl_3$): δ 9.46 (s, 1H), 7.71 (d, 1H, ^3J = 8.4 Hz), 7.37 (dd, 1H, ^3J = 8.4 Hz, ^3J = 8.0 Hz), 6.93 (d, 1H, ^3J = 8.4 Hz), 6.66 (m, 2H), 4.01 (s, 3H), and 3.94 (s, 3H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [112]

Dibromonaphthol 208.



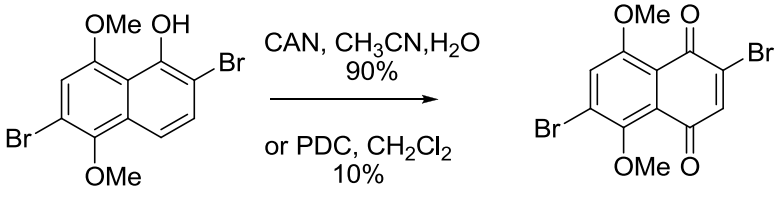
207 **208**

A solution of 21 g (0.13 mol) of bromine in 50 mL of acetic acid was added to a solution of 14 g (68 mmol) of compound **207** in 150 mL of acetic acid at 60 °C. The

reaction was stirred for 3 hours and then quenched by water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were crystallized in methanol to give 12.54 g of compound **208** (34 mmol, 50%).

^{1}HNMR ($CDCl_3$): δ 9.89 (s, 1H), 7.61 (d, 1H, ^3J = 9.2 Hz), 7.46 (d, 1H, ^3J = 9.2 Hz), 6.92 (s, 1H), 4.07 (s, 3H), and 3.91 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 151.9, 151.2, 148.1, 132.6, 130.4, 115.6, 114.4, 112.2, 109.3, 105.8, 61.5, and 57.1. IR (KBr): υmax 3431, 2963, 1634, 1588, 1498, 1330, 1265, 1164, and 1064 cm^{-1}

Compound 209



208 **209**

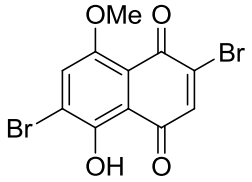
(a) A solution of 818 mg (1.5 mmol) of ammonium cerium (IV) nitrate in 2 mL of water was added to a solution of 130 mg (0.36 mmol) of **208** in 20 mL of acetonitrile at room temperature. The reaction was stirred for 15 minutes and then quenched by ice cold water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 8:1 hexanes and ethyl acetate to give 121 mg of compound **209** (0.32 mmol, 90%).

(b) 1g (4.6 mmol) of pyridinium dichromate was added to a solution of 312 mg (0.86 mmol) of **208** in 20 mL of methylene chloride at 0 °C. The reaction was stirred for 2 hours at room temperature. The solid was filtered off. The organic solution was washed with sodium bisulfite. Then it was dried over $MgSO_4$ and concentrated in vacuo. The

residues were separated by a silica gel column with 8:1 hexanes and ethyl acetate to give 34 mg of compound **209** (0.086 mmol, 10%).

^{1}HNMR ($CDCl_3$): δ 7.55 (s, 1H), 7.35 (s, 1H), 3.98 (s, 1H), and 3.89 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 181.2, 176.2, 156.8, 150.8, 140.3, 139.4, 129.2, 128.4, 126.3, 123.3, 62.0, and 57.2. IR (KBr): υmax 2942, 1758, 1665, 1565, 1466, 1379, 1216, 1191, and 1089 cm^{-1}.

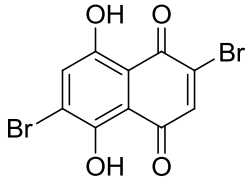
Compound 210.



A solution of 100 mg (0.27 mmol) of compound **209** in 5 mL of methylene chloride was cooled down to 0 °C. 54 mg (0.4 mmol) of aluminum chloride was added to the solution at 0 °C. The reaction was stirred overnight at room temperature and then quenched by water. The water solution was extracted three times with methylene chloride. The organic solution was washed with sodium bisulfite. Then it was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 3:1 hexanes and ethyl acetate to give 36 mg of compound **210** (0.1 mmol, 37%).

^{1}HNMR ($CDCl_3$): δ 12.94 (s, 1H), 7.64 (s, 1H), 7.47 (s, 1H), and 3.99 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 187.7, 175.1, 154.7, 153.8, 143.9, 138.1, 126.4, 122.2, 115.7, 114.8, and 57.4. IR (KBr): υmax 3399, 3059, 1662, 1587, 1450, 1355, 1266, 1192, and 1094 cm^{-1}.

Dibromonaphthylquinone 211.[115]

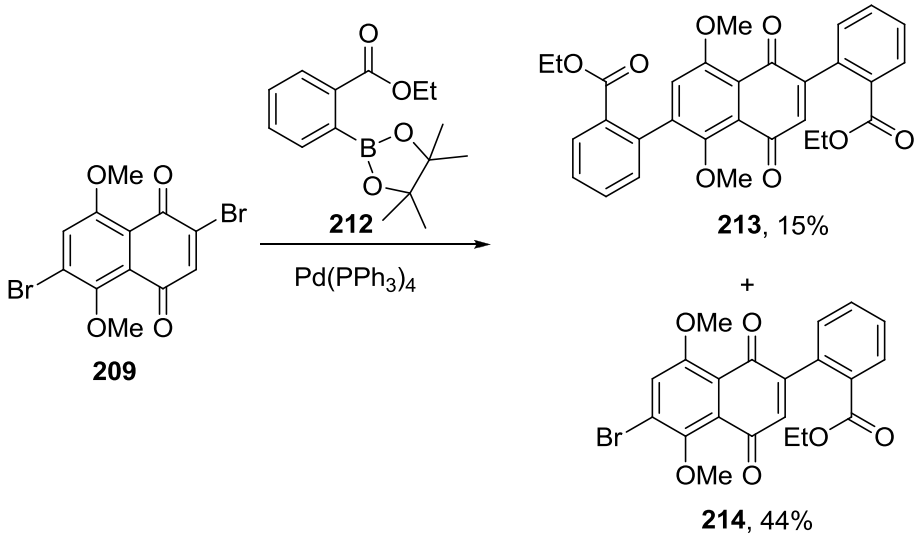


211, 90%

A solution of 29 mg (0.078 mmol) of compound **209** in 5 mL of methylene chloride was cooled down to -70 °C. 0.1 mL of boron bromide was added to the solution at -70 °C. The reaction was stirred for 2 hours at -70 °C and then it was allowed to warm up to room temperature. The reaction was quenched by water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate to give 24 mg of product (0.07 mmol, 90%).

^{1}HNMR ($CDCl_3$): δ 12.57 (s, 2H), and 7.61 (s, 2H). The spectroscopic and other physical data reported are consistent with values reported in the literature. [115]

Naphthylquinone 213 and **214**.



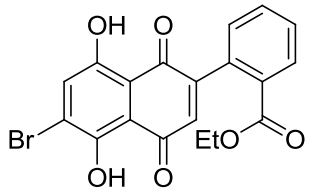
1 g (10 mmol) of sodium carbonate was added to a solution of 147 mg (0.4 mmol) of compound **209** in a mixture of 8 mL of benzene, 3 mL of 1,4-dioxane, and 4 mL of water. Then 89 mg (0.53 mmol) of 2-ethoxycarbonylphenylboronic acid pinacol ester was added to the reaction. Finally, 80 mg of tetrakis(triphenylphosphine)palladium was added. After the reaction was stirred for 48 hours at 55 °C, it was poured into water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 5:1 hexanes and ethyl acetate to

give 76 mg of compound **214** (0.18 mmol, 44%) and 32 mg of compound **213** (0.06 mmol, 15%).

213 ^{1}HNMR ($CDCl_3$): δ 8.05 (d, 1H, ^{3}J = 7.6 Hz), 7.58 (dd, 1H, ^{3}J = 7.6 Hz, ^{3}J = 6.4 Hz), 7.52 (s, 1H), 7.49 (dd, 1H, ^{3}J = 7.2 Hz, ^{3}J = 6.4 Hz), 7.32 (d, 1H, ^{3}J = 7.2 Hz), 6.73 (s, 1H), 4.19 (q, 2H, ^{3}J = 7.2 Hz), 3.90 (s, 6H), and 1.23 (t, 3H, ^{3}J = 7.2 Hz). ^{13}CNMR ($CDCl_3$): δ 184.0, 183.1, 166.5, 156.0, 152.4, 150.2, 135.5, 132.6, 131.8, 130.4, 130.3, 129.6, 127.4, 126.9, 123.2, 121.5, 61.8, 61.4, 57.0, and 14.1. IR (KBr): υmax 3515, 2978, 1721, 1659, 1586, 1467, 1390, 1284, 1135, and 1085 cm^{-1}

214 ^{1}HNMR ($CDCl_3$): δ 8.06 (d, 1H, ^{3}J = 8.0 Hz), 8.01 (d, 1H, ^{3}J = 7.6 Hz) 7.59 (dd, 2H, ^{3}J = 8.0 Hz, ^{3}J = 7.6 Hz), 7.50 (dd, 2H, ^{3}J = 8.0 Hz, ^{3}J = 7.6 Hz), 7.37 (d, 1H, ^{3}J = 8.0 Hz), 7.34 (d, 1H, ^{3}J = 7.6 Hz), 7.18 (s, 1H), 6.75 (s, 1H), 4.21 (q, 2H, ^{3}J = 7.2 Hz), 4.14 (q, 2H, ^{3}J = 7.2 Hz), 3.90 (s, 3H), 3.43 (s, 3H), 1.25 (t, 3H, ^{3}J = 7.2 Hz), and 1.09 (t, 3H, ^{3}J = 7.2 Hz). ^{13}CNMR ($CDCl_3$): δ 184.9, 183.5, 167.2, 166.6, 155.9, 152.2, 150.7, 145.1, 137.3, 135.8, 132.7, 132.5, 131.7, 131.3, 130.9, 130.6, 130.3, 130.2, 129.4, 128.5, 126.0, 121.1, 120.3, 61.4, 61.2, 61.2, 56.9, 14.1, and 13.9. IR (KBr): υmax 3389, 2930, 1711, 1659, 1467, 1382, 1264, 1194, 1138, and 1097 cm^{-1}.

Naphthylquinone 215.



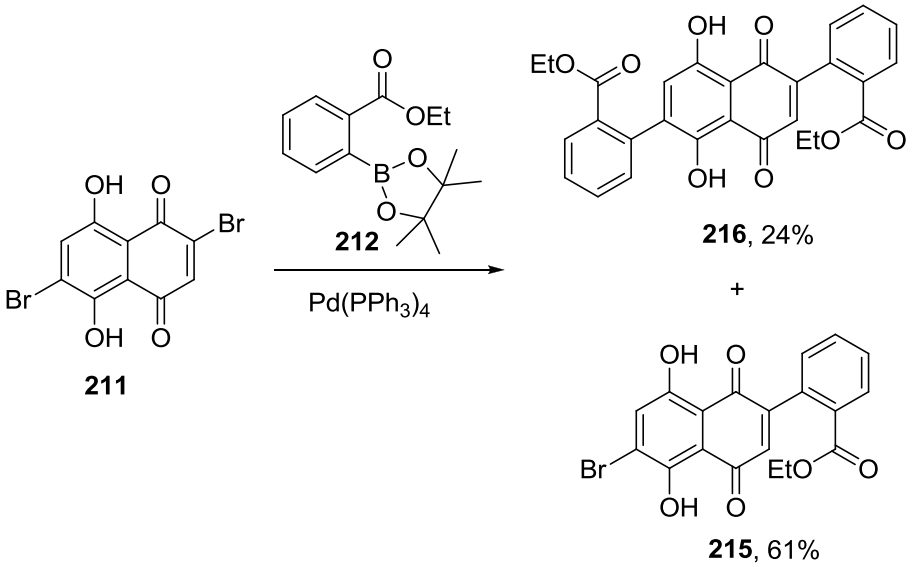
215

A solution of 12 mg (0.027 mmol) of **214** in 3 mL of methylene chloride was cooled down to -70 °C. 0.1 mL of boron bromide was added to the solution at -70 °C. The reaction was stirred for 2 hours at -70 °C and then quenched by water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residue was dissolved in methylene chloride. The solution was added 4 mg of p-

toluenesulfonic acid. The reaction was stirred overnight at room temperature and quenched by water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues were separated by a silica gel column with 5:1 hexanes and ethyl acetate to 5 mg of compound **215** (0.012 mmol, 45%).

^{1}HNMR ($CDCl_3$): δ 12.98 (d, 1H), 12.28 (d, 1H), 8.16 (d, 1H, ^3J = 7.6 Hz), 7.64 (m, 3H), 7.31 (d, 1H, ^3J = 7.6 Hz), 7.03 (d, 1H), 4.23 (m, 2H), and 1.26 (m, 3H). ^{13}CNMR ($CDCl_3$): δ 181.7, 179.5, 166.6, 160.8, 159.5, 157.7, 153.3, 135.7, 134.2, 133.5, 132.9, 132.0, 130.8, 130.3, 129.9, 129.4, 128.7, 61.7, and 14.2. IR (KBr): υmax 3451, 2923, 2852, 1720, 1658, 1481, 1366, 1262, 1188, and 1096 cm^{-1}.

Naphthylquinone 215 and **216**.



1 g (10 mmol) of sodium carbonate was added to a solution of 98 mg (0.28 mmol) of **211** in a mixture of 6 mL of benzene, 2 mL of 1,4-dioxane, and 3 mL of water. Then 64 mg (0.23 mmol) of 2-ethoxycarbonylphenylboronic acid pinacol ester was added to the reaction. Finally, 70 mg of tetrakis(triphenylphosphine)palladium was added. After the reaction was stirred for 48 hours at 55 °C, it was washed by water. The water solution was extracted three times with methylene chloride. The organic phases were combined and dried over $MgSO_4$. After concentration of organic solution in vacuo, the residues

were separated by a silica gel column with 5:1 hexanes and ethyl acetate to give 72 mg of **215** (0.17 mmol, 61%) and 33 mg of **216** (0.068 mmol, 24%).

216 ^{1}HNMR ($CDCl_3$): δ 12.81 (s, 2H), 8.09 (d, 2H, ^{3}J = 7.6 Hz), 7.64 (dd, 2H, ^{3}J = 7.6 Hz, ^{3}J = 7.6 Hz), 7.55 (dd, 2H, ^{3}J = 7.6 Hz, ^{3}J = 7.6 Hz), 7.34 (d, 2H, ^{3}J = 7.6 Hz), 7.10 (s, 2H), 4.24 (q, 4H, ^{3}J = 7.2 Hz), and 1.25 (t, 6H, ^{3}J = 7.2 Hz). ^{13}CNMR ($CDCl_3$): δ 173.2, 171.4, 166.8, 148.8, 135.1, 132.5, 131.3, 130.5, 130.3, 129.5, 128.4, 61.4, and 14.1. IR (KBr): υmax 3372, 3053, 2923, 1721, 1590, 1481, 1392, 1258, 1183, and 1074 cm^{-1}.

Chapter 3. Synthesis of Cis-Alkenes via a Novel Copper-Mediated Cross-Coupling of 1,1-Dibromoalkenes with Halides.

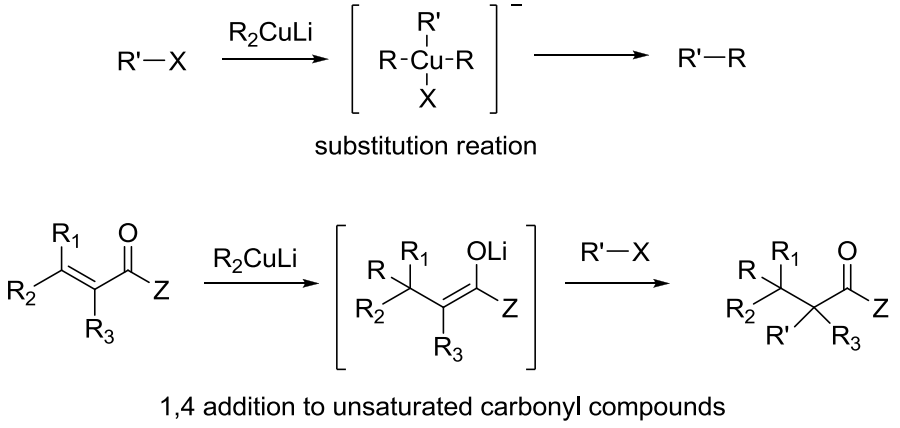
3.1 Introduction

3.1.1 Background: Organocopper Reagents

Since the first organo-copper compound, copper(I) acetylide, was synthesized by Bottger in 1859,[116] various organo-copper compounds and their reactions have been studied by chemists. Methylcopper was prepared by Henry Gilman in 1936.[117] In 1941 Kharash discovered 1,4-addition instead of 1,2-addition of a Grignard reagent to cyclohexenone in presence of Cu(I).[118] In 1952 Gilman synthesized dialkylcuprates for the first time.[119] Now organo-copper reagents are very frequently used in organic syntheses because of selective reactivity and lower nucleophilicity for carbon.[120] However, organo-copper compounds are thermally unstable.[121] Thus they can not undergo consecutive cross-coupling processes like some other transition metal complexes.

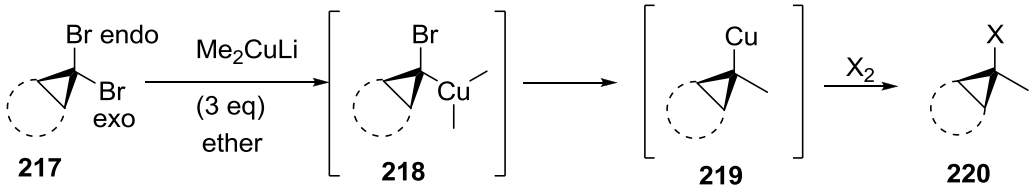
Because of the instability of organocopper reagents, they are usually prepared in situ by adding organolithium reagents or Grignard reagents to copper(I) halides. Divalent cuprates R_2CuLi are also known as Gilman reagents. In diethyl ether, lithium dimethyl cuprate, a Gilman reagent, is a dimer forming an eight-membered ring with two lithium atoms coordinating between two methyl groups.[122] In different solvent, the Gilman reagent exhibits different structures.[123]

Organocopper reagents are mainly involved in two kinds of reactions. One is substitution with halides; the other is 1,4-addition to α,β-unsaturated carbonyl compounds (Scheme 61). In various organocopper reactions, the oxidation state of copper can be changed from +1 to +2. In an organocopper intermediate, the oxidation state of copper can be +3.



Scheme **61**. Coupling and 1,4 addition reactions of organocopper reagents.

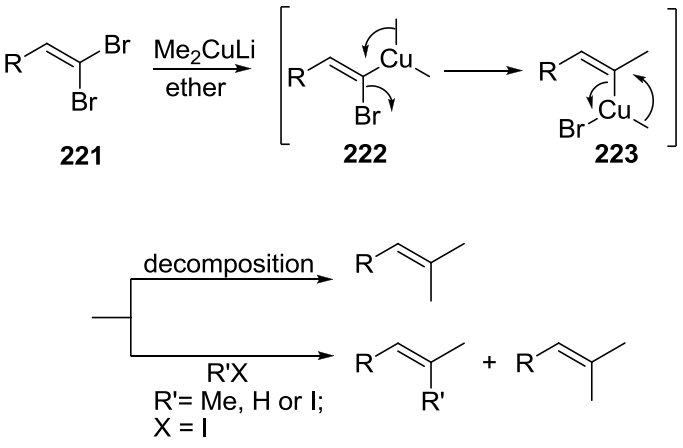
3.1.2 A New Method to Generate (Z)-Vinylcopper Species from 1,1-Dibromoalkenes



Scheme **62**. The reaction of Gilman reagent and 1,1-dibromocyclopropane.

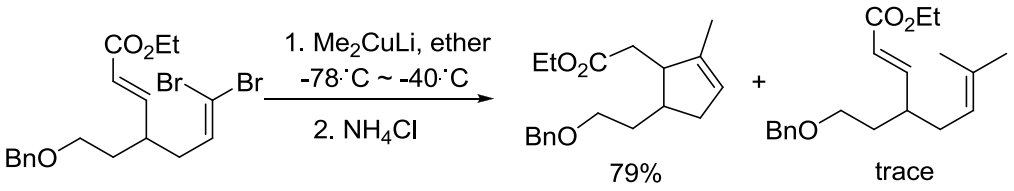
Lithium dimethyl cuprate may replace the less hindered exo-bromo group of a 1,1-dibromocyclopropane **217** to give the intermediate **218** (Scheme 62).[124] Then a 1,2-shift of the alkyl group with inversion of configuration affords an endo cyclopropyl

copper intermediate **219** which can be quenched by halogen to form an endo cyclopropyl halide **220**.



Scheme **63**. The reaction of Gilman reagent and 1,1-dibromoalkene.

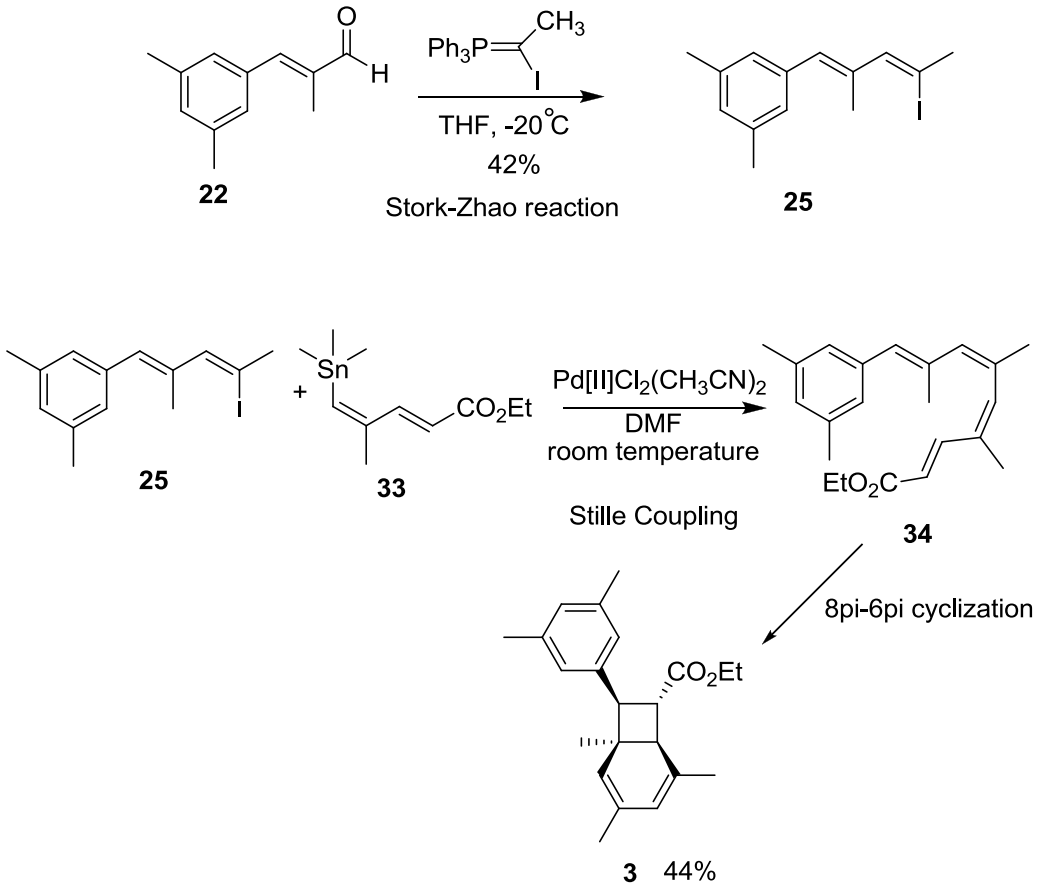
According to the literature, [125] lithium dimethyl cuprate may act as a nucleophile to substitute the less hindered (E)-bromo group of a 1,1-dibromoalkene (Scheme 63). Then a 1,2-shift of the methyl group gives a (Z)-vinyl copper intermediate **223.** The intermediate may decompose to the dimethylalkene product. Quenching the reaction with MeI may improve the yield of dimethyl product.[126] Recently, Masaaki Miyashita reported that a (Z)-vinylcopper intermediate undergos an intramolecular 1,4-addition to an α,β-unsaturated ester moiety (Scheme 64).[127] Additionally, the vinylcopper intermediate was quenched with iodine to prepare (Z)-1-iodo-1-methylalkenes (Scheme 63).



Scheme **64**. (Z)-vinylcopper intermediate involved 1,4-addion.

In one of the key steps for the synthesis of SNF analogues, the low-yield Stork-Zhao reaction has been used to make a (Z)-iodoalkene (Scheme 65). The other key step is Stille cross-coupling for the preparation of tetraenes. The Stille reaction not only afforded

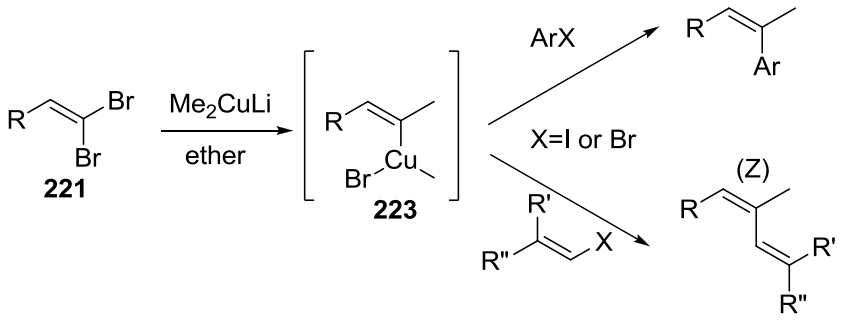
a product in low yield but also used a toxic tin starting material. We investigated some new olefination strategies to avoid the low-yield Stork-Zhao reaction and the toxic Stille coupling. We wondered whether the vinylcopper intermediates could be trapped by coupling with an aryl halide or a vinyl halide.



Scheme **65**. Low-yield Stork-Zhao reaction and Stille cross-coupling in the synthesis of SNF analogs.

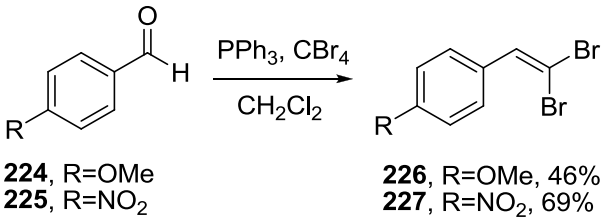
3.2 Results and Discussion

Thus, we proposed a new synthetic route for polyenes (Scheme 66). Lithium dimethyl cuprate replaces the less hindered exo-bromo group of a 1,1-dibromoalkene **221**. Then a 1,2-shift of the methyl group affords an (Z)-vinyl copper intermediate **223**. The intermediate may couple with aryl halide to provide a (Z)-1-aryl-1-methylalkene; the intermediate also may couple with vinyl halide to give a (Z)-polyene.



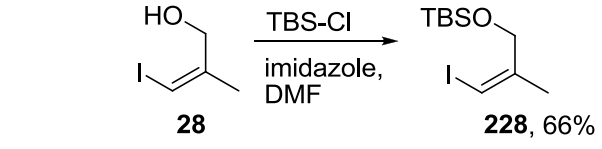
Scheme **66**. A new proposed synthetic route for polyenes.

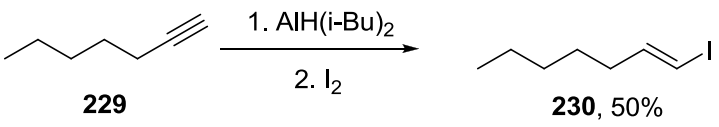
3.2.1 The Syntheses of Substrates



Scheme **67**. Preparation of 1,1-dibromoalkene **226** and **227**.

To examine the proposed methodology, 1,1-dibromoalkene **226** and **227** were designed as the substrates (Scheme 67). Treatment with tetrabromomethane and triphenylphosphine transformed *p*-methoxybenzaldehyde or *p*-nitrobenzaldehyde to the corresponding dibromoalkene.[128]

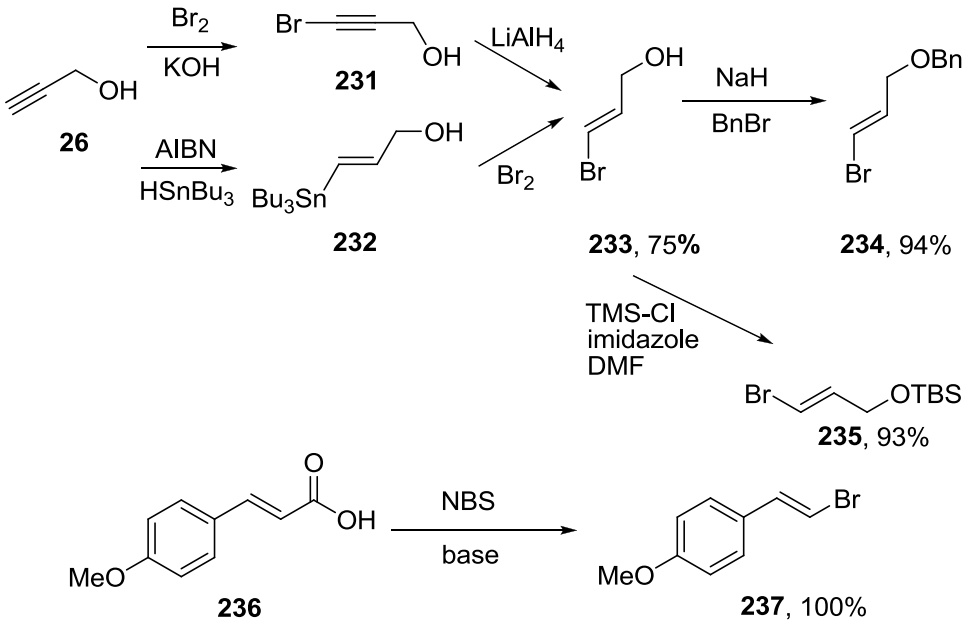




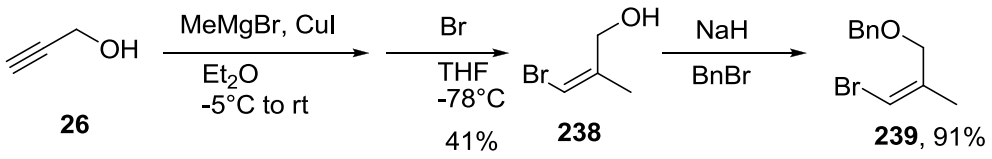
Scheme **68**. Preparation of vinyl iodide **228** and **230**.

In order to examine the proposed coupling of the vinylcopper intermediate **223** and vinyl iodides, two vinyl iodides were prepared. TBS protection of (Z)-iodoallylic alcohol **28** provided the vinyl iodide **228** (Scheme 68).[129] 1-Heptyne **228** was reduced by diisobutylaluminum hydride to form a trans-vinylaluminum intermediate.[130] Treatment with iodine quenched the intermediate to give the (E)-vinyl iodide **230** in 50% yield.

In order to examine the proposed coupling of the vinylcopper intermediate **223** and vinyl bromides, several vinyl bromides were prepared. Bromoallylic alcohol **233** was synthesized in two ways (Scheme 69).[131] Propargyl alcohol was oxidized by bromine in the presence of strong base to compound **231**. Reduction of **231** by lithium aluminum hydride produced compound **233** in 75% yield.[132] In the other synthetic route, propargyl alcohol **26** was reduced by tributylstannane to compound **232**. The bromine oxidized **232** to bromoallylic alcohol **233** in 46% yield.[133] Benzyl protection of **233** provided the vinyl bromide **234** in 91% yield.[134] Treatment of bromoallylic alcohol **233** with tert-butyldimethylsilyl chloride afforded the TBS-protected (E)-vinyl bromide **235** in 93% yield.[135] Base catalyzed decarboxylation of acid **236** and subsequent oxidation by NBS gave the (E)-vinyl bromide **237** in 94% yield (Scheme 69).[136]



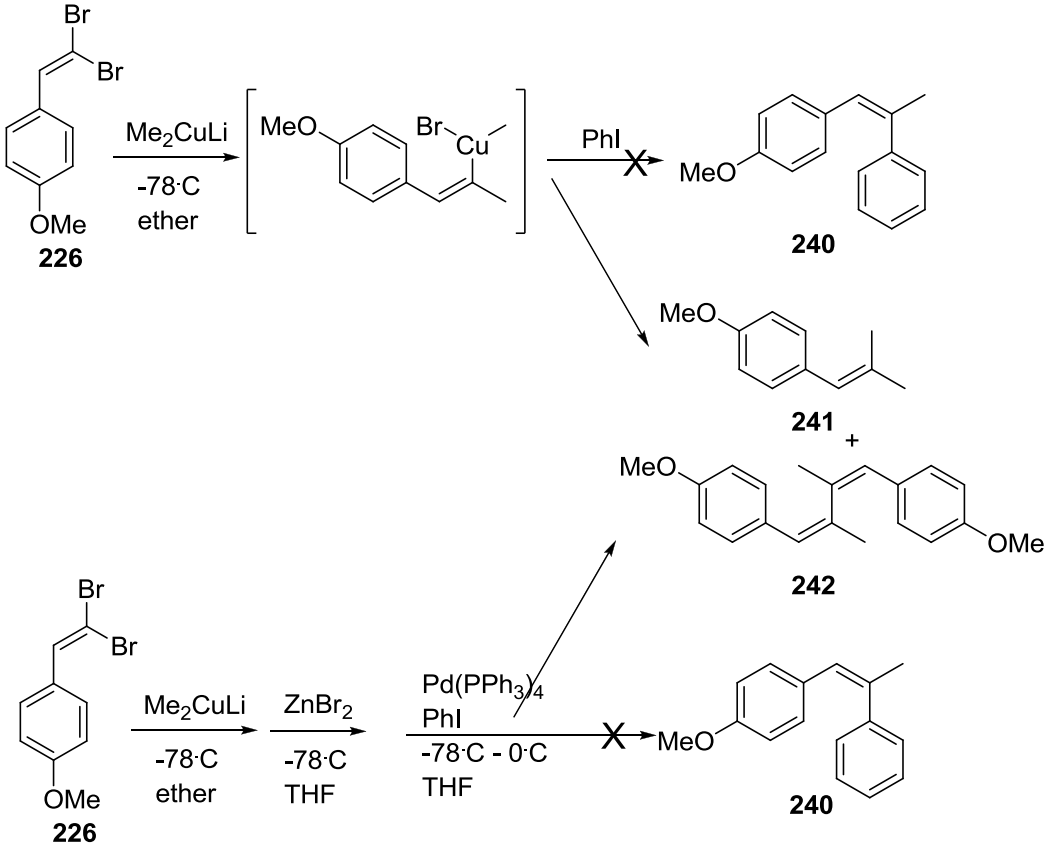
Scheme **69**. Preparation of (E)-vinyl bromides **234, 235,** and **237**.



Scheme **70**. Preparation of (Z)-vinyl bromide **239**.

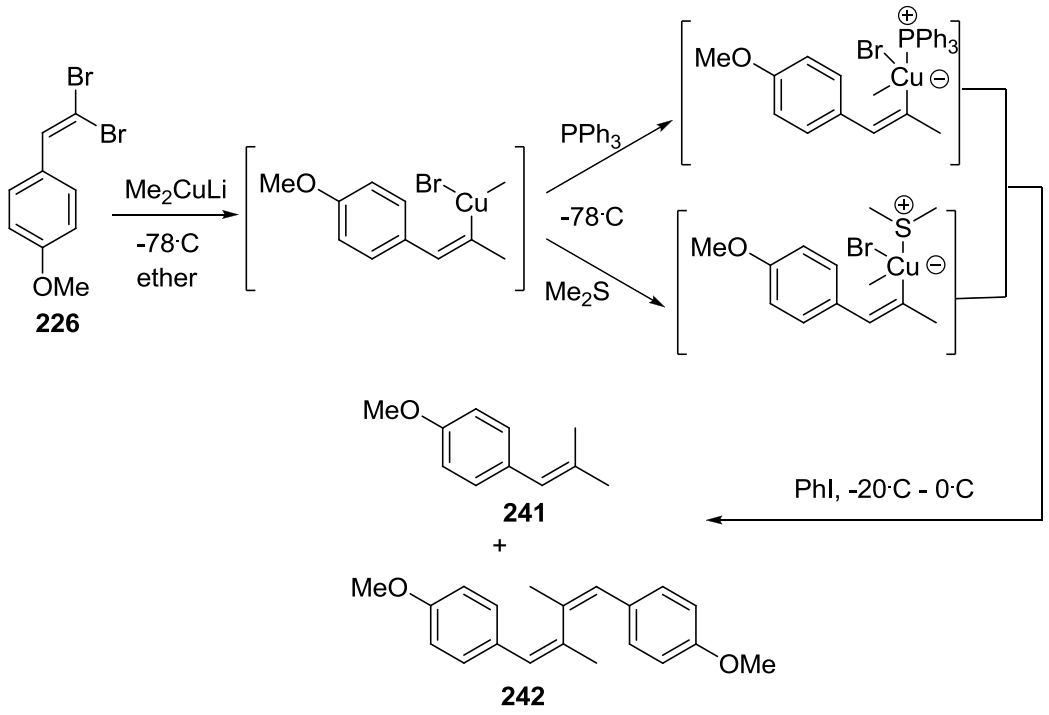
The (Z)-bromoallylic alcohol **238** was obtained in 41% yield from propargyl alcohol **26** through a stereoselective carbocupration/bromination sequence (Scheme 70).[137] Benzyl protection of **238** provided the (Z)-vinyl bromide **239** in 91% yield.

3.2.2 A New One-Pot Coupling Reaction via Organocopper Intermediates



Scheme **71**. Attempt at coupling of dibromoalkene **226** and iodobenzene.

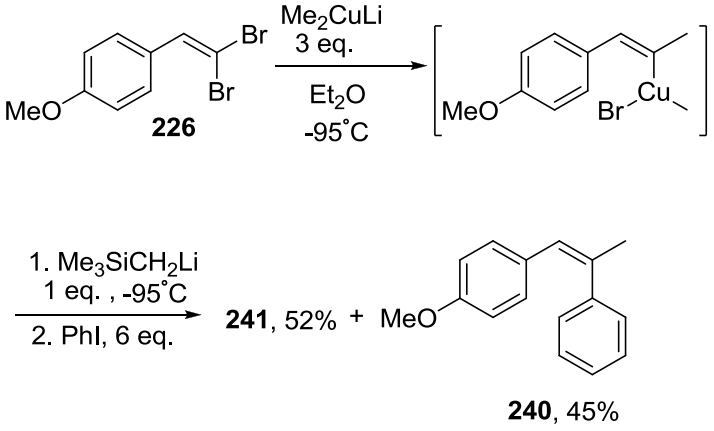
The substrate **226** was treated with lithium dimethyl cuprate to form a copper intermediate. Iodobenzene was added directly to the reaction mixture at low temperature (Scheme 71). Since nothing happened at -95 °C, the reaction was allowed to warm up to -20 °C. With increasing temperature, the decomposition of the intermediate accelerated to give lots of black solid. The reaction did not produce the desired 1-phenyl-1-methylalkene **240** but 1,1-dimethylalkene **241** [138] as the major product and a little dimerized product **242**. A Negishi strategy also was employed. Addition of zinc bromide to the copper intermediate was supposed to offer a (Z)-vinyl zinc reagent. However, Negishi condition only gave dimethylalkene **241** and dimerized product **242**. The results suggested that the Cu(I) intermediates were not stable enough to make a cross-coupling.



Scheme **72**. Attempt at coupling of dibromoalkene **226** and iodobenzene in the presence of ligands.

Dimethyl sulfide, triphenylphosphine, and cyanide are known as good ligands for stabilizing organocopper reagents.[139] In order to stabilize the proposed (Z)-vinylcopper intermediates, dimethyl sulfide or triphenylphosphine was added as ligand to the reaction (Scheme 72). However, the reaction also only gave compounds **241** and **242** as products.

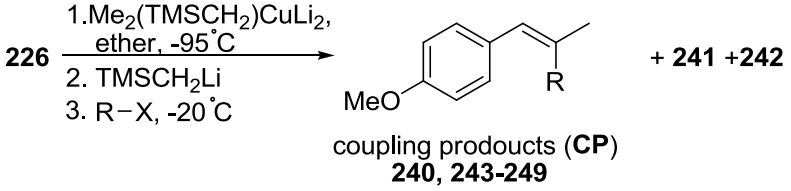
The results showed that dimethyl sulfide and triphenylphosphine as ligands could not make the copper intermediates thermally stable enough for a further coupling. In addition, those ligands could not activate the intermediates so well that the desired coupling of the copper intermediate and phenyl iodide could not compete with the decomposition of the copper intermediate.

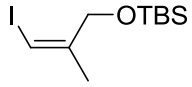
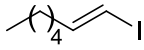
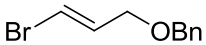
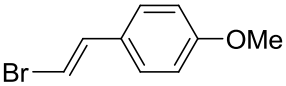
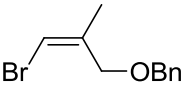
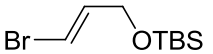


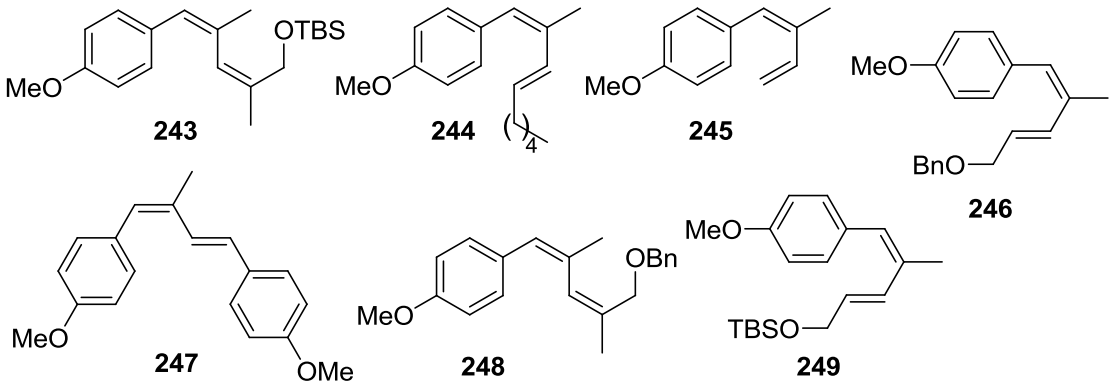
Scheme **73**. Coupling of dibromoalkene **226** and iodobenzene in the presence of (trimethylsilyl)methyl lithium.

Since (trimethylsilyl)methyl group (TMS-CH_2-) can stabilize and activate cuprate reagents, (trimethylsilyl)methyl was chosen as the ligand.[140] The procedures described above were modified by adding 1 equivalent of (trimethylsilyl)methyl lithium to the reaction at -95 °C after 1,1-dibromoalkene was added to dimethyl cuprate. The reaction was allowed to slowly warm up to -20 °C and then 6 equivalents of iodobenzene was added (Scheme 73). After work-up, 1,1-dimethylalkene **241** and the coupling product, 1-methyl-1-phenylalkene **240,** were obtained in 52% and 45% yields, respectively. The chemical shifts of NMR spectra of compound **240** are different from those of trans-1-(4-methoxyphenyl)-2-phenylpropene. [141] In addition, the NOE spectra indicated that compound **240** is cis.

Table **9**. (Trimethylsilyl)methyl stabilizing coupling reactions.



entry	R-X		yields% 241,242,CP	coupling products (CP)
a	PhI		27, 0, 68	**240**
b	$PhOSO_2CF_3$		80, 17, 0	**240**
c	PhBr		85, 14, 0	**240**
d		**228**	88, 12, 0	**243**
e		**230**	85, 0, 13	**244**
f			49, 0, 43	**245**
g		**234**	38, 0, 56	**246**
h		**237**	35, 0, 57	**247**
i		**239**	60, 10, 29	**248**
j		**235**	81, 0, 12	**249**



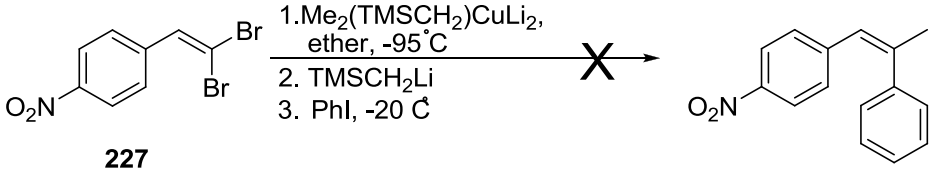
In order to keep copper intermediates stable from the beginning of the reaction, a mixed 2:1:1 cuprate, dimethyl (trimethylsilyl)methyl cuprate ($Me_2(TMS\text{-}CH_2)CuLi_2$), was used instead of dimethylcuprate.[142] Compound **226** was added to 3 equivalents of $Me_2(TMS\text{-}CH_2)CuLi_2$ at -95°C. After the reaction was warmed up to -20 °C, one more equivalent of $TMS\text{-}CH_2Li$ followed by 6 equivalents of various halides was added to the reaction mixture (Table 9).

The results showed that iodobenzene (entry a) gave the relatively best yield of the consecutive cross-coupling product **240** at 68% and 1,1-dimethyl product **241** in 27% yield. However, phenyl triflate (entry b), bromobenzene (entry c), and TBS protected cis-iodoallyl alcohol (entry d) did not produce cross-coupling products; they only yielded 1,1-dimethyl product **241** as major product and dimerized product **242** as the minor poduct. When trans-1-iodoalkene (entry e) was used as the vinyl halide to examine the reaction, the yield of compound **244** was low.

A series of bromoalkenes were employed to examine the copper mediated reaction. Vinyl bromide (entry f) and trans-bromoalkenes (entry g, h) offered coupling products **245**, **246,** and **247** in about 50% yields. The benzyl protected (Z)-3-bromo-2-methallyl alcohol (entry i) gave the product **248** in low yield at 29% presumably because of the steric effect of (Z,Z)-transition state. Little of coupling product **249** was obtained when TBS-protected (E)-bromoallylic alcohol (entry j) was the substrate.

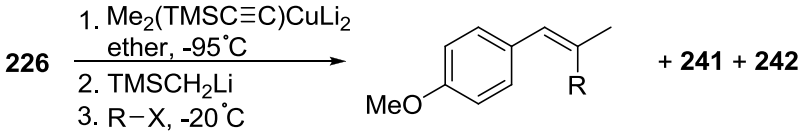
The results suggested that phenyl iodide has a better activity in the reaction than phenyl bromide does; however, vinyl bromides worked better in the reaction than vinyl iodide. Presumably because of steric effects, cis-vinyl bromides do not give good yields of cross coupling products. TBS protection of allylic alcohol may also lower the yield.

The dibromo compound **227** was also used as a substrate to examine the reaction (Scheme 74). Under the conditions that produced **240** from **226**, the reaction did not successfully afford the coupling product and the starting material decomposed. We concluded that the nitro group is not compatible with this reaction.

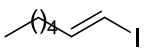


Scheme **74**. Attempt at coupling using 1,1-dibromoalkene **227** as the substrate.

Table **10**. (Trimethylsilyl)ethynyl stabilizing coupling reactions.



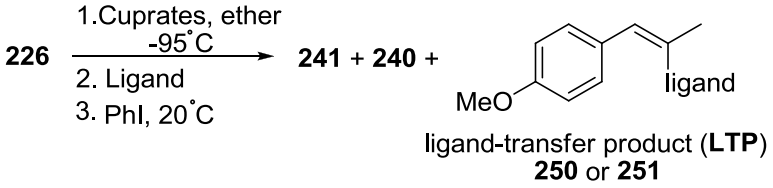
coupling prodoucts (**CP**)
240, 244, and **245**

entry	R-X	yields% **241**,**242**,**CP**	coupling products (**CP**)
a	PhI	46, 0, 43	**240**
b	$PhOSO_2CF_3$	86, 10, 0	**240**
c	PhBr	84, 14, 0	**240**
d	 **230**	89, 0, 10	**244**
e		65, 0, 31	**245**

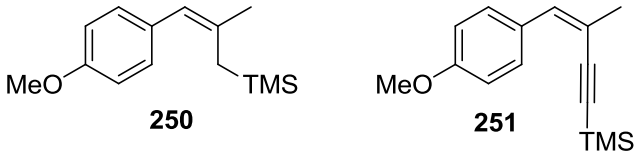
(Trimethylsilyl)ethynyl group (TMS-C≡C-) is also known as a ligand that stabilizes mixed cuprate reagents.[143] (Trimethylsilyl)ethynyllithium was applied to make dimethyl (trimethylsilyl)ethynyl cuprate (Me_2(TMS-C≡C)$CuLi_2$) which was examined in consecutive cross-coupling reactions (Table 10). (Trimethylsilyl)ethynyl ligand acted as trimethylsilyl ligand but was not very good. The (trimethylsilyl)ethynyl coordinated copper intermediate did not couple with phenyl triflate (entry b) and bromobenzene (entry c), either; but it coupled with iodobenzene (entry a), cis-iodoallyl alcohol (entry d), and vinyl bromide (entry f) to offer coupling products **240**, **244**, and **245** in lower yields than (trimethylsilyl)methyl copper intermediates did.

We wondered whether or not the reaction gave a better yield of the coupling product when we reduced the proportion of methyl group in the mixed cuprate reagents. Two mixed 1:2:1 cuprates, $Me(TMS\text{-}CH_2)_2CuLi_2$ and $Me(TMSC{\equiv}C)_2CuLi_2$, were studied in the reaction (Table 11). Both of them produced ligand-transfer products **250** and **251**; and only $Me(TMSCH_2)_2CuLi_2$ gave the desired product **240** in 33% yield.

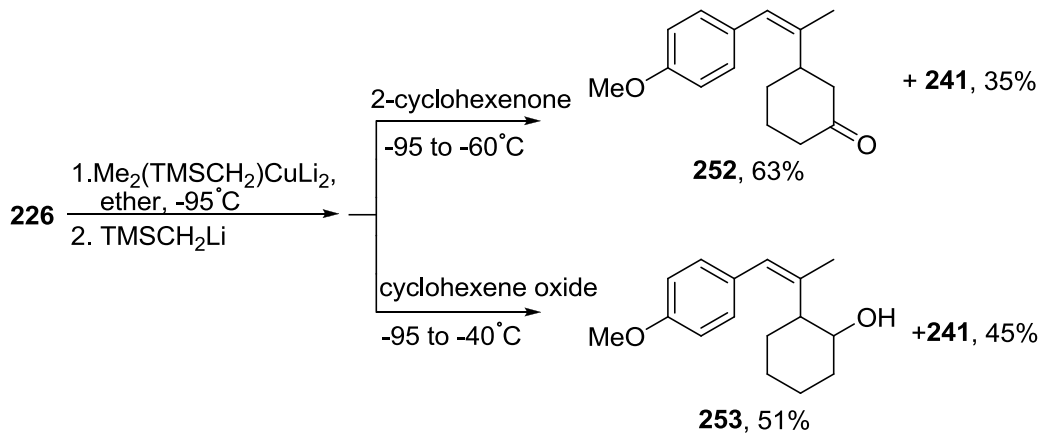
Table **11**. Coupling using $Me(TMSCH_2)_2CuLi_2$ and $Me_2(TMSC{\equiv}C)_2CuLi_2$.



Cuprates	Ligand	yields% 241,240,LTP	LTP
$Me(TMSCH_2)_2CuLi_2$	$TMSCH_2Li$	33, 33, 33	**250**
$Me(TMSC{\equiv}C)_2CuLi_2$	$TMSC{\equiv}CLi$	76, 0, 20	**251**



We expected that the (trimethylsilyl)methyl stabilized copper intermediate **223** was able to carry out an intermolecular 1,4-additon to α,β-unsaturated ketones. At -60 °C, 6 equivalents of 2-cyclohexen-1-one was added to the (trimethylsilyl)methyl stabilizing intermediate (Scheme 75). After work-up, ketone **252** was obtained in 63% yield. The intermolecular epoxide-opening was also invested. The addition of 6 equivalents of cyclohexene oxide to the reaction gave alcohol **253** in 51% yield.



Scheme **75**. Intermolecular 1,4 addition to α,β-unsaturated ketone and intermolecular ring-opening of epoxide.

The new copper mediated consecutive cross-coupling may stereospecifically produce (Z)-2-methyl-alkenes in moderate yields in two steps from aldehydes.[144] It can potentially be applied in syntheses of polyene natural products, such as SNF 4435 C/D and superstolides.[145]

3.3 Experimental Section

General

For all compounds, ^{1}H, ^{13}C and NOE NMR spectra were recorded on Varian Gemini 2300 (300 MHz), Inova 400 (400 MHz), Inova 500 (500 MHz), Inova 600 (600 MHz) spectrometer. Chemical shifts were measured relative to the residual solvent resonance for ^{1}H and internal reference. IR spectra were recorded on a Mattson Galaxy Series FTIR 3000 or 2020 spectrophotometer.

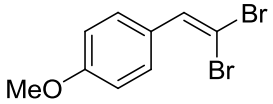
Reagents and solvents were purchased from Aldrich Chemical Company, Fisher Scientific or Acros Organics. Liquid reagents were purified by distillation prior to use. Unless otherwise noted, solid reagents were used without further purification. Methylene chloride, acetonitrile, cyclohexane, and toluene were distilled from CaH_2 under Ar

atmosphere. Diethyl ether and THF were distilled from Na and benzophenone under Ar atmosphere.

All reactions unless otherwise noted, were performed in oven dried glassware under positive pressure of Ar. All yields are isolated yields.

Chromatographic separations were performed using Fisher grade 1740 type 60 Å silica gel (170-400 mesh). Analytical thin layer chromatography was performed using Analtech Uniplate pre-coated glass 250 micron silica gel GHLF plates with 254 nm fluorescent indicator. Preparative thin layer chromatography was performed using Analtech Uniplate pre-coated glass 1000 or 2000 micron silica gel GHLF plates with 254 nm fluorescent indicator.

1,1-Dibromoalkene 226.[128]



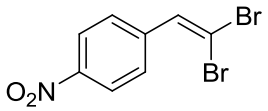
226

2.0 g (6.6 mmol) of tetrabromomethane was added to a solution of 4.0 g (15 mmol) of triphenylphosphine in 50 mL of methylene chloride at 0 °C. The mixture was stirred for 15 minutes at 0 °C. Then 5.0 g (37 mmol) of 4-methoxybenzaldehyde was added to the reaction. The reaction was stirred for an hour at 0 °C and half an hour at room temperature. The reaction was quenched by ice cold water. The water solution was extracted three times with methylene chloride. The organic solutions were combined, dried over Mg_2SO_4, and concentrated in vacuo. The residues were separated by a silica gel column with 40:1 hexanes and ethyl ether to give 1.89 g of compound **226** (98%).

^{1}HNMR ($CDCl_3$): δ 7.37 (d, 2H, ^3J = 8.8 Hz), 7.41(s, 1H), 6.75 (d, 2H, ^3J = 8.8 Hz), and 3.66 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 159.7, 136.4, 129.9, 127.8, 113.8, 87.3, and 55.3. IR (KBr): υmax 3056, 3023, 1948, 1885, 1594, 1444, 1337, 1267, 1157, and 1029,

cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [128]

1,1-Dibromoalkene 227.[128]

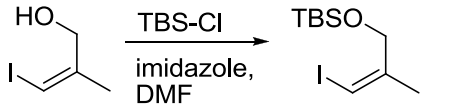


227

2.0 g (6.6 mmol) of tetrabromomethane was added to a solution of 4 g (15 mmol) of triphenylphosphine in 50 mL of methylene chloride at 0 °C. The mixture was stirred for 15 minutes at 0 °C. Then 4.0 g (26 mmol) of 4-nitro-benzaldehyde was added to the reaction. The reaction was stirred for an hour at 0 °C and half an hour at room temperature. The reaction was quenched by ice cold water. The water solution was extracted three times with methylene chloride. The organic solutions were combined, dried over Mg_2SO_4, and concentrated in vacuo. The residues were separated by a silica gel column with hexanes and ethyl acetate (10:1) to give 1.6 g of compound **227** (79%).

^{1}HNMR ($CDCl_3$): δ 8.22 (d, 2H, ^3J = 9.0 Hz), 7.69 (d, 2H, ^3J = 9.0 Hz), and 7.55 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 147.4, 141.6, 135.1, 129.3, 123.9, and 94.2. IR (KBr): υmax 3029, 2968, 2729, 1633, 1596, 1494, 1346, 1248, 1178, and 1054 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [128]

TBS protected iodoallylic alcohol 228.[129]



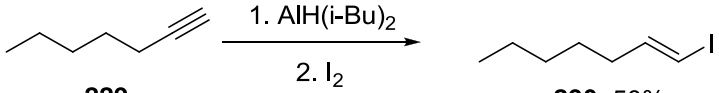
28 **228**, 66%

1.8 g (12 mmol) of t-butyldimethylchlorosilane was added to a mixture of 1.45 g (7.3 mmol) of iodoallylic alcohol **28** and 2.2 g (32 mmol) of imidazole in 15 mL of DMF at 0 °C. The reaction was stirred overnight and then it was quenched by water. The water solution was extracted three times with diethyl ether. The organic solutions were combined, dried over Mg_2SO_4, and concentrated in vacuo. The residues were separated

by a silica gel column with 100:1 hexanes and diethyl ether to give 1.89 g of compound **228** (4.9 mmol, 66%).

^{1}HNMR ($CDCl_3$): δ 5.86 (s, 1H), 4.25 (s, 2H), 1.91 (s, 3H), 0.91 (s, 9H), and 0.10 (s, 6H). ^{13}CNMR ($CDCl_3$): δ 146.9, 136.1, 68.8, 26.0, 21.6, 18.5, and -5.0. The spectroscopic and other physical data reported are consistent with values reported in the literature. [129]

Vinyl iodide 230.[130]

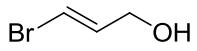


229 **230**, 50%

45 mL (45 mmol) of 1 M solution of diisobutylaluminum hydride in hexanes was added to 4.6 g (47 mmol) of heptyne at 0 °C. Then the reaction was allowed to warm up to 50 °C and stirred overnight. The reaction was cooled down to -50 °C and quenched by a solution of 11.4 g (0.045 mol) of iodine in 25 mL of THF. The solution was warmed up to 0 °C. 200 mL of 20% sulfuric acid was added to the solution. The water solution was extracted three times with diethyl ether. The organic solutions were washed with sodium thiosulfate solution. The organic solution was separated, dried over Mg_2SO_4, and concentrated in vacuo. The residues were distilled at 120 °C in vacuo to give 5.34 g of compound **230** (23 mmol, 50%). Red copper was added to stabilize the product.

^{1}HNMR ($CDCl_3$): δ 6.51 (dt, 1H, ^{3}J = 15.0 Hz, ^{3}J = 7.0 Hz), 5.97 (d, 1H, ^{3}J = 15.0 Hz), 2.05 (dt, 2H, ^{3}J = 8.0 Hz, ^{3}J = 7.0 Hz), 1.39 (tt, 2H, ^{3}J = 8.0 Hz, ^{3}J = 7.0 Hz), 1.29 (m, 4H), and 0.89 (t, 3H, ^{3}J = 6.8 Hz). ^{13}CNMR ($CDCl_3$): δ 147.0, 74.4, 36.2, 31.3, 28.2, 22.6, and 14.1. The spectroscopic and other physical data reported are consistent with values reported in the literature. [130]

(*E*)-3-Bromo-2-propene-1-ol 233.[131]

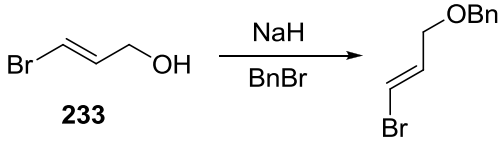


233

Br_2 (12.00 g, 75 mmol) was added to a vigorously stirring solution of KOH (11.00 g, 0.2 mol) in water (40 mL) at -5 °C. The yellow solution was kept at 0 °C and added dropwise for 3 h to a solution of propargyl alcohol (4.5 g, 80 mmol, 1.06 equiv; freshly distilled) in water (10 mL) at -7 °C - 0 °C. The reaction mixture was warmed up to 10 °C and then extracted 4 times with diethyl ether. The organic layer was washed with $Na_2S_2O_3$, dried over K_2CO_3. The solvent was removed to provide the crude 1-bromopropyne-3-ol. A 500 mL flask charged with $LiAlH_4$ (5.1 g, 150 mmol, 2.0 equiv) was carefully added anhydrous ether (50 mL) at -5 °C with stirring. Then a solution of $AlCl_3$ (13.50 g, 75 mmol, 1.0 equiv) in anhydrous ether (50 mL) was carefully added. The crude 1-bromopropyne-3-ol, prepared in the first step, was added dropwise and the mixture was refluxed for 4 h. The reaction was quenched with wet ether (water saturated, 200 mL), followed by water (20 mL) and 5 % NaOH (20 mL) at -10 °C. Then water (60 mL) was added to break up the solid mass. The liquid was decanted and extracted with ether. The combined organic layer was dried over K_2CO_3 and concentrated. The residue was distilled at reduced pressure to yield the alcohol **233** (7.46 g, 60 mmol, 75 % from propargyl alcohol).

^{1}HNMR ($CDCl_3$): δ 6.35 (m, 2H), and 4.09 (m, 2H). ^{13}CNMR ($CDCl_3$): δ 136.6, 107.979, and 63.0. The spectroscopic and other physical data reported are consistent with values reported in the literature.[131]

Benzyl protected allylic alcohol 234.[134]



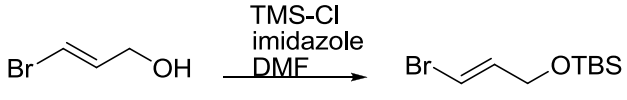
233 **234**, 94%

NaH (0.55 g, 60 %, 13.8 mmol) was added to a solution of (*E*)-3-bromo-2-propene-1-ol **233** (1.33 g, 10 mmol) in THF (20 mL) at 0 °C. After the mixture was stirred for 30 minutes, benzyl bromide (1.96 g, 11.5 mmol) and trace amounts of iodine was added. The reaction mixture was stirred for 4 hours at room temperature and it was

poured into water. The mixture was extracted with dichloromethane. The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes : ethyl acetate = 20:1) to give the ether **234** (2.07 g, 9.4 mmol, 94 %).

^{1}HNMR ($CDCl_3$): δ 7.37 (m, 5H), 6.37 (m, 2H), 4.54 (s, 2H), and 4.00 (d, 2H, ^3J = 5.0 Hz). IR (KBr): υmax 3063, 2855, 1721, 1619, 1453, 1357, 1269, 1108, and 1071 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [134]

TBS protected allylic alcohol 235.[135]

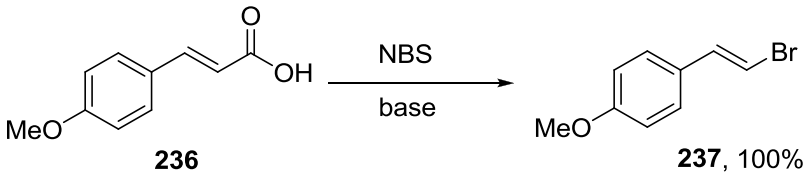


233 **235**, 93%

5 g of t-butyldimethylchlorosilane (33.3 mmol, 1.5 eq.) was added to a mixture of 3.00 g (22 mmol) of bromoallylic alcohol and 2.50 g (37 mmol) of imidazole in 20 mL of DMF at 0 °C. The reaction was stirred overnight and then quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 5.17 g of compound **235** (20.5 mmol, 93%).

^{1}HNMR ($CDCl_3$): δ 6.28 (m, 2H), 4.12 (m, 2H), 0.89 (s, 9H), and 0.07 (s, 6H). ^{13}CNMR ($CDCl_3$): δ 136.9, 106.2, 63.4, 26.0, and -5.1. The spectroscopic and other physical data reported are consistent with values reported in the literature. [135]

(E)-Vinyl bromide 237.[136]

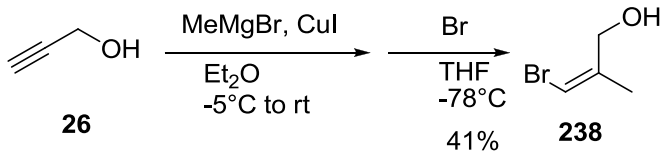


236 **237**, 100%

Triethylamine (3.0 mL, 27 mmol) was added to a solution of 4-methoxycinnamic acid (3.0 g, 17 mmol) in 20 mL of dichloromethane. After the mixture was stirred for 5 minutes at room temperature, *N*-bromosuccinimide (3.0 g, 17 mmol) was added. The solution was stirred for 5 minutes, and then the solvent was removed in vacuo. The mixture was subjected to column chromatography over silica gel (eluent 1% ethyl acetate in hexane) to afford the halostyrenes **237** (3.6 g, 17 mmol, 100%).

^{1}HNMR ($CDCl_3$): δ 7.22 (d, 2H, ^{3}J = 7.6 Hz), 7.05 (d, 1H, d, 2H, ^{3}J = 9.0 Hz), 6.86 (d, 2H, ^{3}J = 7.6 Hz), 6.62 (d, 1H, d, 2H, ^{3}J = 9.0 Hz), and 3.81 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 159.8, 136.7, 128.9, 127.5, 114.3, 104.1, and 55.5. IR (KBr): υmax 3066, 2957, 2836, 1605, 1512, 1441, 1305, 1254, 1181, and 1029 cm^{-1}. The spectroscopic and other physical data reported are consistent with values reported in the literature. [136]

(2Z)-3-Bromo-2-methyl-2-Propen-1-ol 238.



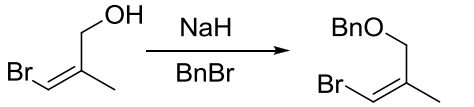
26 41% **238**

In 1 L round bottom flask, 1.5 mL (27 mmol) of propargyl alcohol **26** and 2 g (10.5 mmol) of dry CuI were mixed in 200 mL of Et_2O. 14 mL (35 mmol) of 2.5 M methyl magnesium bromide solution in diethyl ether (MeMgBr) was added dropwise to the reaction at 0 °C.[137] The first 6 mL was added very carefully. After the CH_4 bubbling stopped, the left 8 mL was added a little bit fast. After addition of MeMgBr, the reaction became very viscid. After 20 hours continuous stirring, the reaction mixture turned dark

green. 15 mL (16.5) of 1.1 M Br_2 solution in THF was added dropwise to the reaction mixture at -78 °C. The color of the reaction mixture first turned red from dark green, and then became yellow. The reaction mixture was stirred over night and then it was quenched by the saturated NH_4Cl solution. The organic layer was separated and the water layer was extract three times with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. After solvents were removed by rotovap, the organic products were separated by a silica gel column with 5:1 hexanes and AcOEt to give 1.67 g (11 mmol) of yellow liquid **238** in 41% yield.

^{1}HNMR ($CDCl_3$): δ 5.947 (s, 1H), 4.21 (s, 2H), and 1.95 (s, 1H). ^{13}CNMR ($CDCl_3$): δ 146.2, 108.8, 68.2, and 21.7. IR (KBr): υmax 3337, 2912, 1629, 1432, 1375, 1223, 1134, and 1063 cm^{-1}.

Benzyl protected allylic alcohol 239.



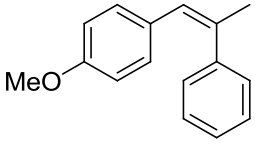
238 **239**, 91%

NaH (0.800 g, 60%, 20 mmol) was added to a solution of alcohol **238** (2.00 g, 13 mmol) in THF (50 mL) at 0 °C. After the mixture was stirred for 30 minutes, benzyl bromide (2.50 g, 14.6 mmol) and trace amounts of iodine were added. The mixture was stirred for 4 hours at room temperature and then it was poured into water. The mixture was extracted with diethyl ether. The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexanes: ethyl acetate = 20:1) to give the benzyl ether **239** (2.92 g, 11.8 mmol, 91 %).

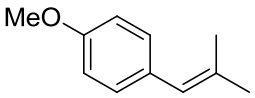
^{1}HNMR ($CDCl_3$): δ 7.35 (m, 5H), 6.09 (s, 1H), 4.51 (s, 2H), 4.19 (s, 2H), and 1.98 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 144.4, 138.2, 128.5, 127.9, 127.8, 76.2, 75.0, 72.3, and

22.0. IR (KBr): υmax 3062, 2913, 2855, 1699, 1558, 1454, 1352, 1281, 1139, and 1093 cm^{-1}.

Coupling with iodobenzene to generate 240.



240



241

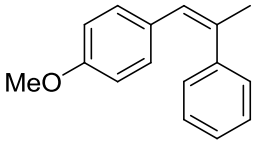
To a suspension of 275 mg (1.44 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 2 mL (3.2 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 1.5 mL (1.5 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 146 mg (0.50 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.5 mL (0.5 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 760 mg of iodobenzene was added to the reaction. The reaction solution turned white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 76 mg of compound **240** (0.34 mmo, 68%) and 22 mg of compound **241** (0.13 mmol, 27%).

240 ^{1}HNMR ($CDCl_3$): δ 7.53 (d, 2H, ^{3}J = 7.6 Hz), 7.35 (m, 5H), 6.93 (d, 1H, ^{3}J = 7.6 Hz), 6.80 (s, 1H), 3.85 (s, 3H), and 2.30 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 158.4, 144.4,

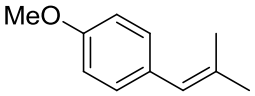
126.1, 131.1, 130.5, 128.5, 127.4, 127.1, 126.1, 113.8, 55.4, and 17.6. IR (KBr): υmax 2953, 2835, 1677, 1573, 1463, 1378, 1297, 1108, and 1034 cm^{-1}.

241 ^{1}HNMR ($CDCl_3$): δ 7.18 (d, 2H, ^{3}J = 8.8 Hz), 6.89 (d, 2H, ^{3}J = 8.8 Hz), 6.24 (s, 1H), 3.82 (s, 3H), 1.91 (s, 3H), and 1.88 (s, 3H).

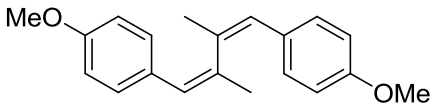
Attempt at coupling with phenyl triflate to produce 240.



240



241

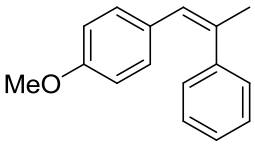


242

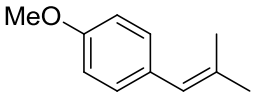
To a suspension of 275 mg (1.44 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 2 mL (3.2 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 1.5 mL (1.5 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 146 mg (0.5 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.5 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 780 mg phenyl triflate was added to the reaction. The reaction solution became white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 65 mg of dimethyl substitution compound **241** (0.4 mmol, 80%) and 13 mg of dimerized compound **242** (0.08 mmol, 17%).

242 ^{1}HNMR ($CDCl_3$): δ 7.26 (d, 4H, ^{3}J = 8.8 Hz), 6.91 (d, 4H, ^{3}J = 8.8 Hz), 6.72 (s, 2H), 3.87 (s, 6H), and 2.13 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 158.2, 138.0 131.4, 130.7, 126.53, 113.7, 55.4, and 15.9. IR (KBr): υmax 2952, 2835, 1604, 1509, 1462, 1371, 1248, 1178, and 1030 cm^{-1}.

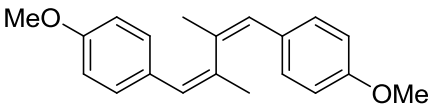
Attempt at coupling with bromobenzene to generate 240.



240



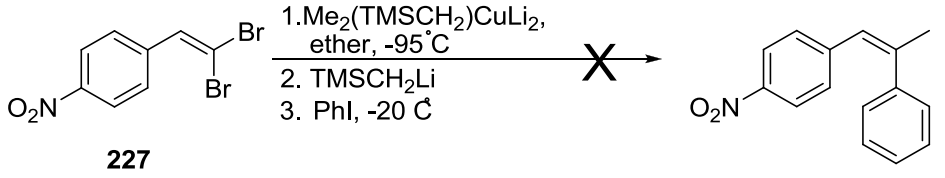
241



242

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 350 mg of bromobenzene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 34 mg dimethyl substitution compound **241** (0.21 mmol, 85%) and 5 mg dimerized compound **242** (0.04 mmol, 14%).

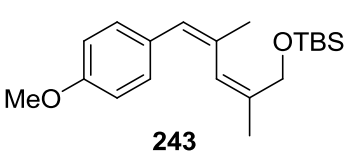
Attempt at coupling using 1-(2,2-dibromovinyl)-4-nitrobenzene 227 as the substrate.



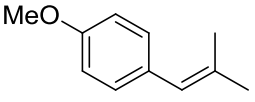
227

To a suspension of 275 mg (1.44 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 2 mL (3.2 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 1.5 mL (1.5 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 169 mg (0.5 mmol) of nitro-dibromide in 1 mL of diethyl ether was added to the reaction dropwise to give a green intermediate. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.5 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 760 mg of iodobenzene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 10:1 hexanes and ethyl acetate. The starting material decomposed.

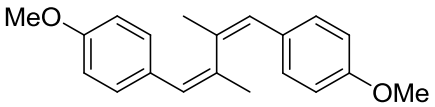
Attempt at coupling with TBS protected iodoallylic alcohol 228 to generate 243.



243



241

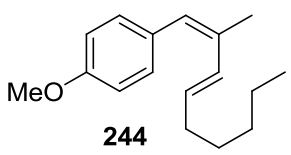


242

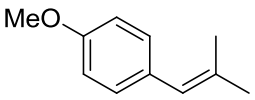
To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution

was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 480 mg of TBS iodoallylic alcohol **228** was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 36 mg of dimethyl substitution compound **241** (0.22 mmol, 88%) and 4.5 mg of dimerized compound **242** (0.3 mmol, 12%).

Diene 244.



244



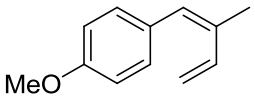
241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 400 mg of iodo-heptene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in

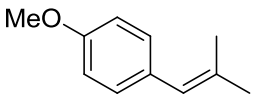
vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 44 mg of mixture of dimethyl substitution compound **241** and methyl vinyl product compound in ratio 6:1. After further purification, 6.5 mg of compound **244** (0.033 mmol, 13%) and 36 mg of compound (21 mmol, 85%) were obtained.

^{1}HNMR ($CDCl_3$): δ 7.21 (d, 2H, ^{3}J = 9.0 Hz), 6.87 (d, 2H, ^{3}J = 9.0 Hz), 6.36 (s, 1H), 6.22 (d, 1H, ^{3}J = 16.0 Hz), 5.75 (dt, 1H, ^{3}J = 8.0 Hz, ^{3}J = 7.0 Hz), 3.81 (s, 3H), 2.15 (dt, 2H, 1H, ^{3}J = 16.0 Hz, ^{3}J = 8.0 Hz), 1.97 (s, 3H), 1.31 (m, 6H), and 0.91 (t, 3H, ^{3}J = 7.0 Hz). ^{13}CNMR ($CDCl_3$): δ 158.1, 135.3, 134.6, 130.9, 130.6, 129.9, 128.8, 113.7, 55.5, 33.2, 31.7, 30.6, 29.6, 22.8, and 14.3. IR (KBr): υmax 2955, 2855, 1606, 1573, 1464, 1294, 1105, and 1037 cm^{-1}.

Diene 245.



245



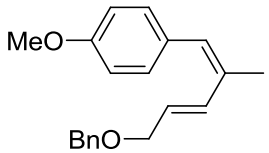
241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 300 mg of vinylbromide was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in

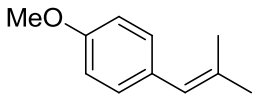
vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 43mg of mixture of dimethyl substitution compound **241** and vinyl substitution compound **245**. The further separation by TLC gave 19 mg of compound **245** (0.108 mmol, 43%) and 19 mg of compound **241** (0.123 mmol, 49%).

^{1}HNMR ($CDCl_3$): δ 7.28 (d, 2H, ^{3}J = 8.8 Hz), 6.91 (d, 2H, ^{3}J = 8.8 Hz), 6.57 (dd, 1H, ^{3}J = 17.2 Hz, ^{3}J = 10.8 Hz), 6.50 (s, 1H), 5.28 (d, 1H, ^{3}J = 17.2 Hz), 5.12 (d, 1H, ^{3}J = 10.8 Hz), 3.84 (s, 3H), and 2.02 (d, 3H, ^{4}J = 1.2 Hz). ^{13}CNMR ($CDCl_3$): δ 158.4, 142.1, 133.9, 133.7, 131.3, 130.5, 128.6, 113.7, 55.4, and 13.4. IR (KBr): υmax 3001, 2953, 2835, 1605, 1572, 1441, 1376, 1299, 1110, and 1035 cm^{-1}.

Diene 246.



246



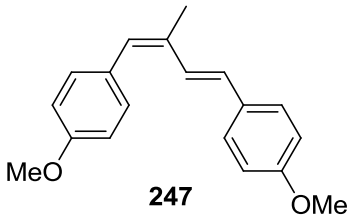
241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 350 mg of vinylbromide **234** was added to the reaction. The reaction solution turned white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined

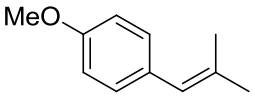
organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 41 mg of vinyl methyl substitution compound **246** (0.14 mmol, 56%) and 15 mg of dimethyl substitution compound **241** (0.095 mmol, 38%).

^{1}HNMR ($CDCl_3$): δ 7.37 (m, 5H), 7.25 (d, 2H, ^{3}J = 9.0 Hz), 6.89 (d, 2H, ^{3}J = 9.0 Hz), 6.47 (s, 1H), 6.44 (d, 1H, ^{3}J = 15.5 Hz), 5.85 (dt, 1H, ^{3}J = 15.5 Hz, ^{3}J = 6.0 Hz), 4.56 (s, 2H), 4.15 (d, 1H, ^{3}J = 6.0 Hz), 3.82 (s, 3H), and 2.01 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 158.5, 138.5, 133.8, 131.5, 130.7, 130.6, 130.5, 128.6, 128.0, 127.8, 124.6, 113.8, 72.3, 71.2, 55.4, and 14.0. IR (KBr): υmax 3425, 3029, 2931, 2854, 1606, 1509, 1453, 1249, 1176, and 1090 cm^{-1}.

Diene 247.



247



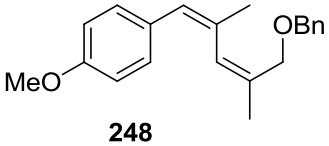
241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 350 mg of vinylbromide **237** was added to the reaction. The reaction solution turned white and then yellow. The

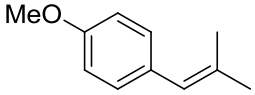
reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 27 mg of vinyl methyl substitution compound **247** (0.14 mmol, 57%) and 14 mg of dimethyl substitution compound **241** (0.087 mmol, 35%).

^{1}HNMR ($CDCl_3$): δ 7.40 (d, 2H, ^{3}J = 8.8 Hz), 7.28 (d, 2H, ^{3}J = 8.8 Hz), 6.89 (m, 5H), 6.58 (d, 1H, ^{3}J = 15.6 Hz), 6.47 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H), and 2.12 (d, 3H, ^{4}J = 0.8 Hz). ^{13}CNMR ($CDCl_3$): δ 159.1, 158.4, 134.7, 132.7, 131.1, 130.9, 130.8, 130.6, 127.6, 126.9, 114.3, 113.8, 55.53, 55.50, and 14.1. IR (KBr): υmax 3375, 2954, 1604, 1510, 1462, 1303, 1255, 1178, and 1029 cm^{-1}.

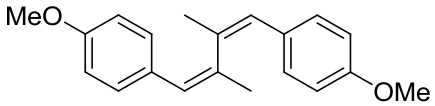
Diene 248.



248



241



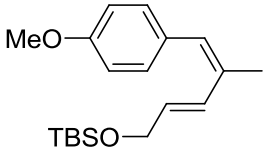
242

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 400 mg of vinylbromide **239** was added to the reaction. The reaction solution turned white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by

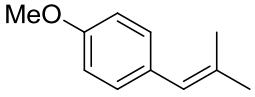
water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 22 mg of vinyl methyl substitution compound **248** (0.073 mmol, 29%), 24 mg of dimethyl substitution compound **241** (0.15 mmol, 60%), and 4 mg of dimerized compound **242** (0.025 mmol, 10%).

^{1}HNMR ($CDCl_3$): δ 7.32 (m, 5H), 7.18 (2H, ^{3}J = 8.8 Hz), 6.88 (d, 2H, ^{3}J = 8.8 Hz), 6.23 (s, 1H), 6.01 (s, 1H), 4.48 (s, 2H), 4.21 (s, 2H), 3.83 (s, 3H), 1.93 (s, 3H), and 1.92 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 158.3, 138.7, 134.3, 134.0, 133.2, 130.7, 130.4, 128.9, 128.5, 128.0, 127.7, 113.7, 72.3, 69.7, 55.4, 22.3, and 19.0. IR (KBr): υmax 2930, 2852, 1605, 1547, 1452, 1296, 1176, and 1035 cm^{-1}.

Diene 249.



249



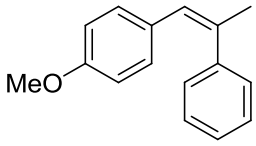
241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1 M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 420 mg of vinylbromide **235** was added to the reaction. The reaction solution turned white and then yellow. The

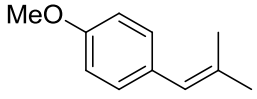
reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 47 mg mixture of vinyl methyl substitution product and dimethyl substitution product. The mixture was dissolved in 2 mL of THF and then the solution was added 1 mL of 1 M tetrabutylammonium fluoride solution in tetrahydrofuran at 0 °C. The reaction was stirred for 6 hours at 0 °C and then it was quenched by water. The water solution was extracted three times with diethyl ether. The organic solutions were combined and dried over $MgSO_4$. The solution was concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 6.1 mg of deprotected vinyl methyl substitution compound **249** (deprotected compound, 0.03 mmol, 12%) and 33 mg of dimethyl substitution compound **241** (0.2 mmol, 81%).

^{1}HNMR ($CDCl_3$): δ 7.22 (d, 2H, ^3J = 8.8 Hz), 6.86 (d, 2H, ^3J = 8.8 Hz), 6.45 (s, 1H), 6.40 (d, 1H, ^3J = 16.0 Hz), 5.87 (dt, 1H, ^3J = 16.0 Hz, ^3J = 5.6 Hz), 4.25 (d, 2H, ^3J = 5.6 Hz), 3.79 (s, 3H), and 2.00 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 197.0, 185.8, 137.3, 131.6, 130.6, 127.1, 113.8, 94.6, 64.1, 55.4, and 20.4. IR (KBr): υmax 3388, 2956, 2919, 1708, 1665, 1510, 1462, 1364, 1299, 1175, and 1035 cm^{-1}.

(Trimethylsilyl)acetyl stabilizing coupling to generate 240.



240



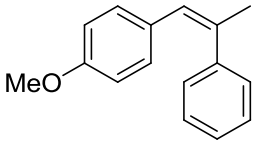
241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of lithium

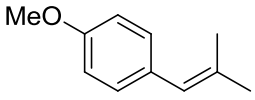
(trimethylsilyl)acetylide in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added. After the reaction was slowly warmed up to -20 °C, 400 mg of iodobenzene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 19 mg of dimethyl substitution compound **241** (0.12 mmol, 46%) and 24 mg of methyl phenyl compound **240** (0.11 mmol, 43%).

^{1}HNMR ($CDCl_3$): δ 7.53 (d, 2H, ^3J = 7.6 Hz), 7.35 (m, 5H), 6.93 (d, 1H, ^3J = 7.6 Hz), 6.80 (s, 1H), 3.85 (s, 3H), and 2.30 (s, 3H). ^{13}CNMR ($CDCl_3$): δ 158.4, 144.4, 136.1, 131.1, 130.5, 128.5, 127.4, 127.1, 126.1, 113.8, 55.4, and 17.6. IR (KBr): υmax 2953, 2835, 1677, 1509, 1463, 1378, 1249, 1176, and 1034 cm^{-1}.

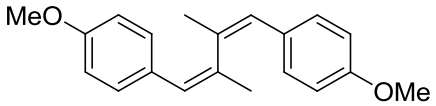
Attempt at (trimethylsilyl)acetyl stabilizing coupling with phenyl triflate to generate 240.



240



241

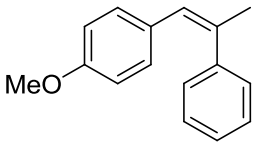


242

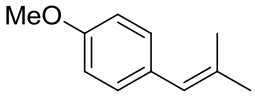
To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added to the reaction at 0 °C. The solution was

stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added. After the reaction was slowly warmed up to -20 °C, 380 mg of phenyl triflate was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 31 mg of dimethyl substitution compound **241** (0.18 mmol, 72%) and 6 mg of dimerized compound **242** (0.04 mmol, 16%).

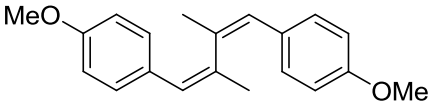
Attempt at (trimethylsilyl)acetyl stabilizing coupling with bromobenzene to generate 240.



240



241

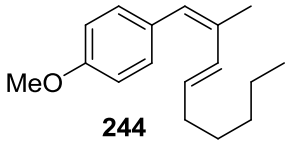


242

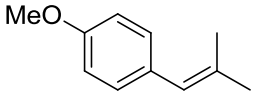
To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added. After the reaction was slowly warmed up to -20 °C, 350 mg of bromobenzene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The

reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 34 mg of dimethyl substitution compound **241** (0.21 mmol, 84%) and 5 mg of dimerized compound **242** (0.035 mmol, 14%).

(Trimethylsilyl)acetyl stabilizing coupling to generate 244.



244

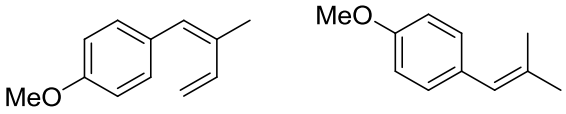


241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added. After the reaction was slowly warmed up to -20 °C, 400 mg of trans 1-iodo-1-heptene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 43 mg of a mixture of dimethyl substitution compound **241** and methyl vinyl compound **244** in ratio 9:1. The further purification by TLC gave 4.6 mg of compound **244** (0.025 mmol, 10%) and 37 mg of compound **241** (0.22 mmol, 89%).

^{1}HNMR ($CDCl_3$): δ 7.21 (d, 2H, ^{3}J = 9.0 Hz), 6.87 (d, 2H, ^{3}J = 9.0 Hz), 6.36 (s, 1H), 6.22 (d, 1H, ^{3}J = 16.0 Hz), 5.75 (dt, 1H, ^{3}J = 8.0 Hz, ^{3}J = 7.0 Hz), 3.81 (s, 3H), 2.15 (dt, 2H, 1H, ^{3}J = 16.0 Hz, ^{3}J = 8.0 Hz), 1.97 (s, 3H), 1.31 (m, 6H), and 0.91 (t, 3H, ^{3}J = 7.0 Hz). ^{13}CNMR ($CDCl_3$): δ 158.1, 135.3, 134.6, 130.9, 130.6, 129.9, 128.8, 113.7, 55.5, 33.2, 31.7, 30.6, 29.6, 22.8, and 14.3. IR (KBr): υmax 2955, 2855, 1606, 1573, 1441, 1294, 1105, and 1037 cm^{-1}.

(Trimethylsilyl)acetyl stabilizing coupling to generate 245.

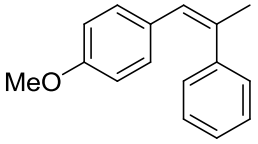


245 **241**

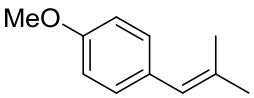
To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added. After the reaction was slowly warmed up to -20 °C, 300 mg of vinylbromide was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 41 mg of a mixture of dimethyl substitution compound **241** and vinyl substitution compound **245**. The further separation by TLC gave 14 mg of compound **245** (0.078 mmol, 31%) and 26 mg of compound **241** (0.12 mmol, 49%).

^{1}HNMR ($CDCl_3$): δ 7.28 (d, 2H, ^{3}J = 8.8 Hz), 6.91 (d, 2H, ^{3}J = 8.8 Hz), 6.57 (dd, 1H, ^{3}J = 17.2 Hz, ^{3}J = 10.8 Hz), 6.50 (s, 1H), 5.28 (d, 1H, ^{3}J = 17.2 Hz), 5.12 (d, 1H, ^{3}J = 10.8 Hz), 3.84 (s, 3H), and 2.02 (d, 3H, ^{4}J = 1.2 Hz). ^{13}CNMR ($CDCl_3$): δ 158.4, 142.1, 133.9, 133.7, 131.3, 130.5, 128.6, 113.7, 55.4, and 13.4. IR (KBr): υmax 3001, 2835, 1605, 1572, 1463, 1376, 1299, 1176, and 1035 cm^{-1}.

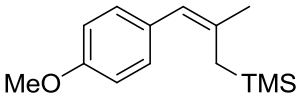
Ligand-transfer coupling product 250.



240



241

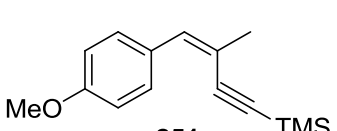


250

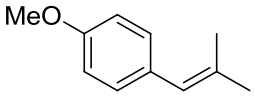
To a suspension of 275 mg (1.44 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (3.2 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 3.0 mL (3.0 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 146 mg (0.75 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.5 mL of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -20 °C, 760 mg of iodobenzene was added to the reaction. The reaction solution became white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give a mixture of dimethyl substitution compound **241**, methyl TMS-methylene substitution compound **250**, and methyl phenyl substitution compound **240** in total 99% yield. The ratio determined by NMR is 1:1:1. Futher purification by TLC gave 30 mg of compound **250** (0.25 mmol, 33%), 29 mg of compound **240** (0.25 mmol, 33%), and 21 mg of compound **241** (0.25 mmol, 33%).

^{1}HNMR ($CDCl_3$): δ 7.14 (d, 2H, ^{3}J = 8.8 Hz), 6.85 (d, 2H, ^{3}J = 8.8 Hz), 6.036 (s, 1H), 3.81 (s, 3H), 1.84 (s, 3H), 1.26 (s, 2H), and 0.06 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 158.8, 129.8, 127.5, 126.3, 122.1, 113.6, 55.4, 29.9, 19.7, and -1.2. IR (KBr): υmax 2953, 1727, 1607, 1509, 1464, 1287, 1174, and 1037 cm^{-1}.

Ligand-transfer coupling product 251.



251

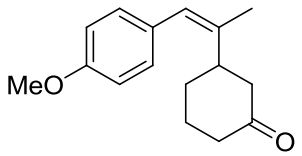


241

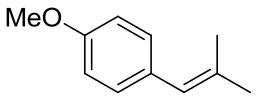
To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 0.5 mL (0.8 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 1.5 mL (1.5 mmol) of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL of 1M solution of lithium (trimethylsilyl)acetylide in hexanes was added. After the reaction was slowly warmed up to -20 °C, 400 mg of iodobenzene was added to the reaction. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 100:1 hexanes and diethyl ether to give 43 mg of a mixture of dimethyl substitution compound **241** and ligand-transfer compound **251** in ratio 4:1 (NMR). The further separation by TLC gave 11 mg of compound **251** (0.05 mmol, 20%**)** and 31 mg of compound **241** (0.19 mmol, 76%).

^{1}HNMR ($CDCl_3$): δ 7.23 (d, 2H, ^{3}J = 8.7 Hz), 6.88 (d, 2H, ^{3}J = 8.7 Hz), 6.85 (s, 1H), 3.81 (s, 3H), 2.06 (s, 3H), and 0.21 (s, 9H). ^{13}CNMR ($CDCl_3$): δ 158.8, 136.7, 130.4, 129.5, 117.9, 113.8, 109.6, 92.2, 55.5, 19.4, and 0.3. IR (KBr): υmax 2957, 2835, 2139, 1604, 1509, 1464, 1250, 1177, and 1036 cm^{-1}.

Ketone 252.



252

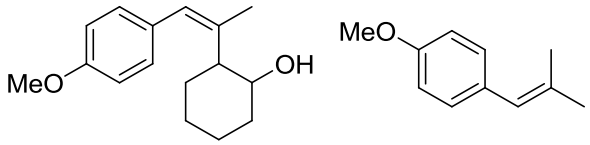


241

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL (0.25 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -40 °C, 400 mg of 1-cyclohexenone was added to the reaction. The reaction solution turned white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 40:1 hexanes and diethyl ether to give 38 mg of 1,4-adduct **252** (0.16 mmol, 63%) and 14 mg of dimethyl substitution compound **241** (0.087 mmol, 35%).

^{1}HNMR ($CDCl_3$): δ 7.16 (d, 1H, ^{3}J = 8.8 Hz), 6.86 (d, 1H, ^{3}J = 8.8 Hz), 6.25 (s, 1H), 3.80 (s, 3H), 2.47 (m, 3H), 2.35 (m, 1H), 2.20 (m, 1H), 1.98 (m, 1H), 1.85 (s, 3H), 1.84(m, 1H), and 1.71 (m, 2H). ^{13}CNMR ($CDCl_3$): δ 211.7, 158.1, 139.0, 130.7, 130.2, 124.4, 113.7, 55.4, 48.5, 47.0, 41.5, 30.3, and 25.4. IR (KBr): υmax 2927, 2855, 1737, 1263, 1201, 1121, and 1017 cm^{-1}

Alcohol 253.



253 **241**

To a suspension of 145 mg (0.75 mmol) of copper (I) iodide in 1.5 mL of diethyl ether, 1 mL (1.6 mmol) of 1.6 M solution of methyl lithium in diethyl ether was added at 0 °C till a transparent solution was given. 0.75 mL (0.75 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added to the reaction at 0 °C. The solution was stirred for 15 min at 0 °C and then cooled down to -95 °C. A solution of 73 mg (0.25 mmol) of compound **226** in 1 mL of diethyl ether was added to the reaction dropwise to give a pale yellow solution. The reaction was allowed to slowly warm up to -79 °C for 15 min and then 0.25 mL (0.25 mmol) of 1M solution of trimethylsilylmethyl lithium in hexanes was added. After the reaction was slowly warmed up to -60 °C, 400 mg of cyclohexene oxide was added to the reaction. The reaction solution turned white and then yellow. The reaction was stirred for 4 hours to give a black suspension. The reaction was quenched by water. The water solution was extracted three times with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residues were separated by a silica gel column with 10:1 hexanes and diethyl ether to give 31 mg of ring-opening compound **253** (0.13 mmol, 51%) and 14 mg of dimethyl substitution compound **241** (0.11 mmol, 45%).

^{1}HNMR ($CDCl_3$): δ 7.21 (d, 2H, ^{3}J = 8.4 Hz), 6.87 (d, 2H, ^{3}J = 8.4 Hz), 6.38 (s, 1H), 3.81s (s, 3H), 3.54 (m, 1H), 2.06 (m, 2H), 1.84 (s, 3H), 1.77 (m, 2H), 1.42 (m, 2H), and 1.35 (m, 3H). ^{13}CNMR ($CDCl_3$): δ 158.2, 137.8, 130.5, 130.3, 127.5, 113.7, 70.8, 57.3, 55.4, 34.3, 30.3, 25.9, 25.1, and 14.5. IR (KBr): υmax 3425, 2929, 2855, 1607, 1573, 1449, 1295, 1109, and 1062 cm^{-1}

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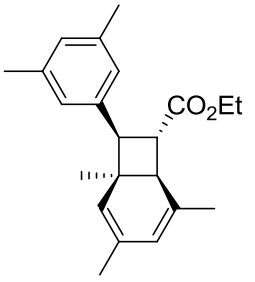
Appendix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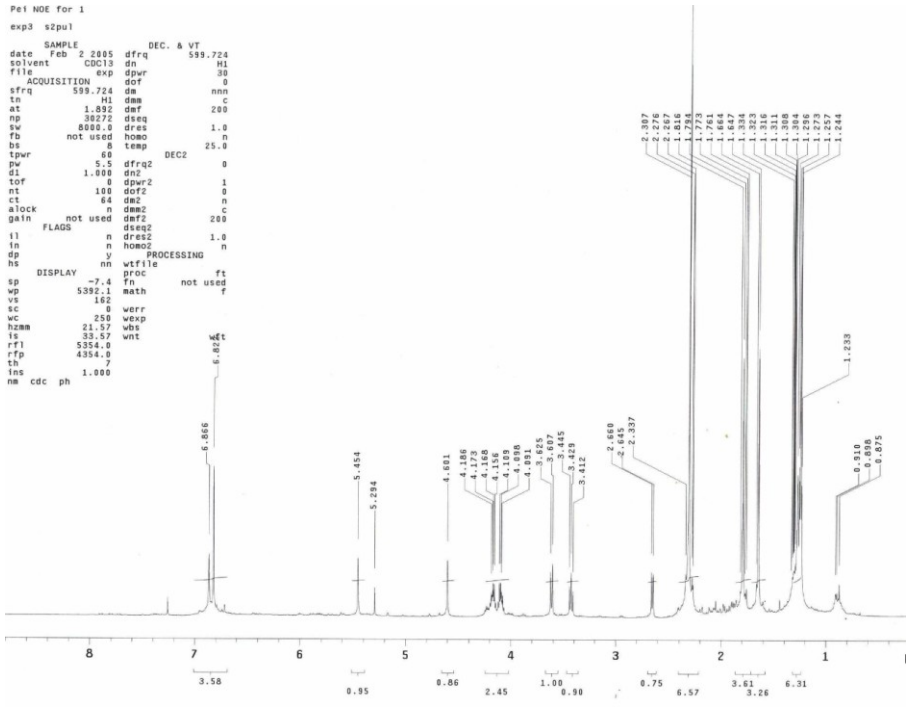
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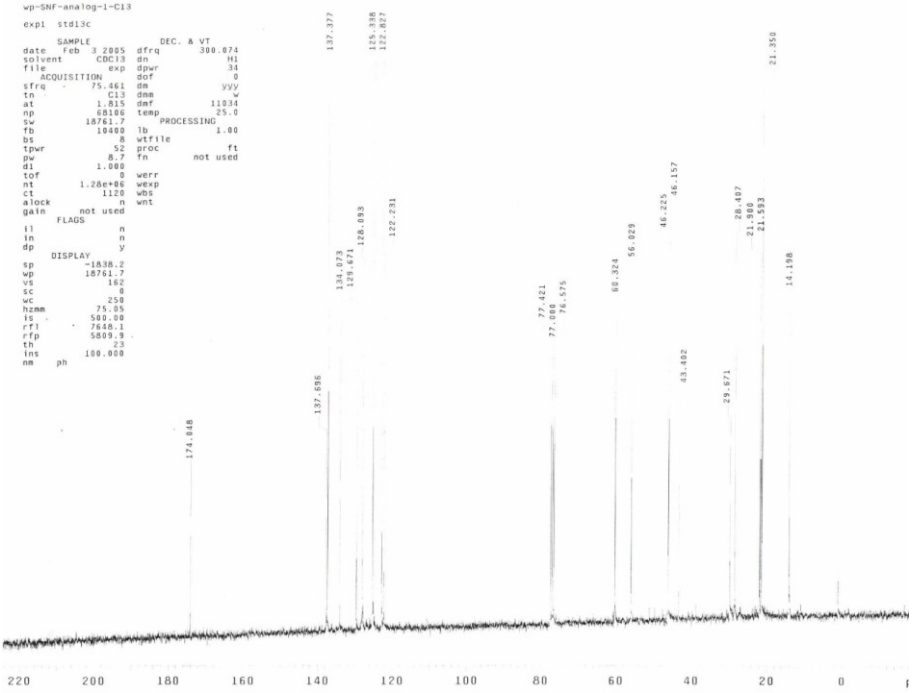
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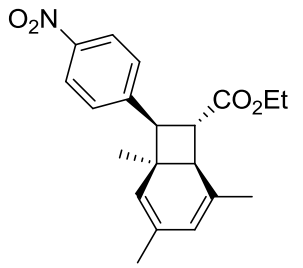
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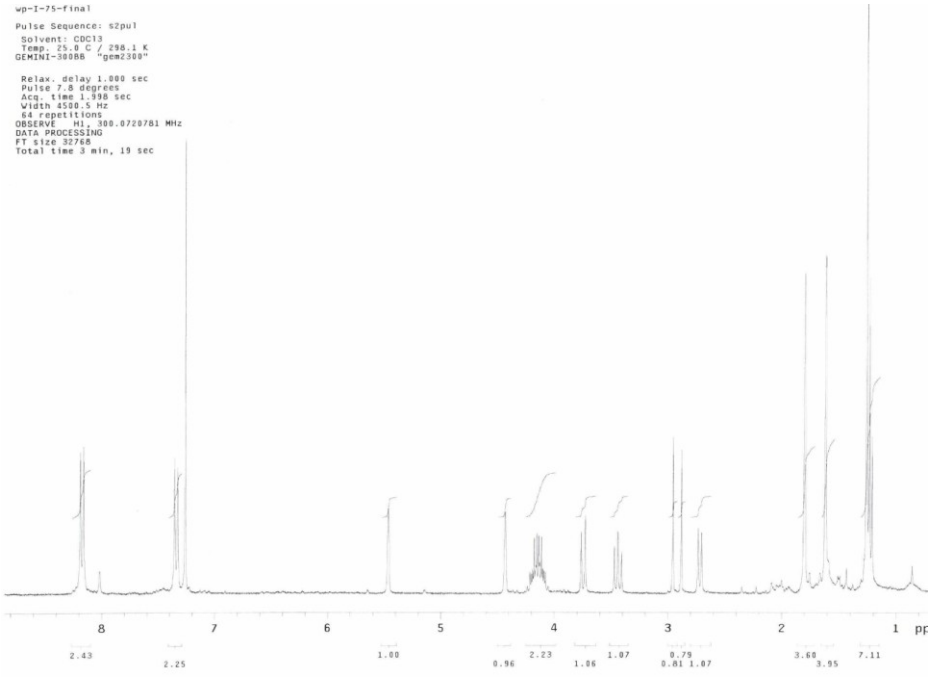
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Width 4500.5 Hz
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7
6
5
4
3
2
1
ppm
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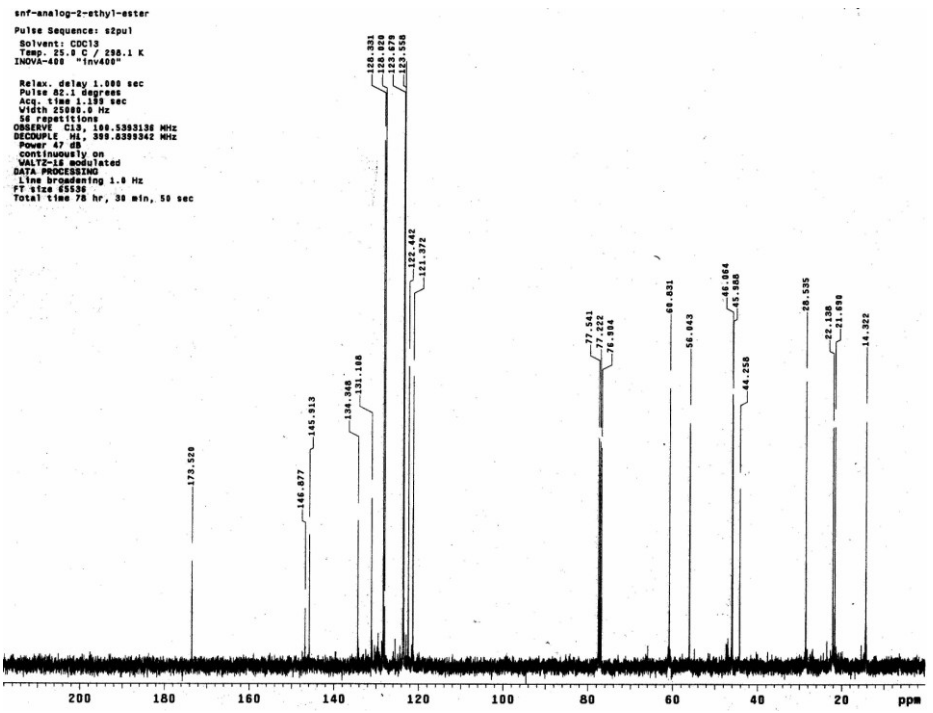
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DECOUPLE H1, 399.8393342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
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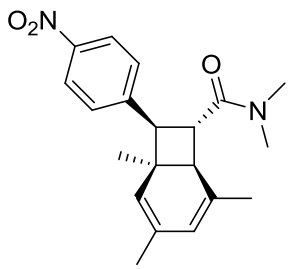

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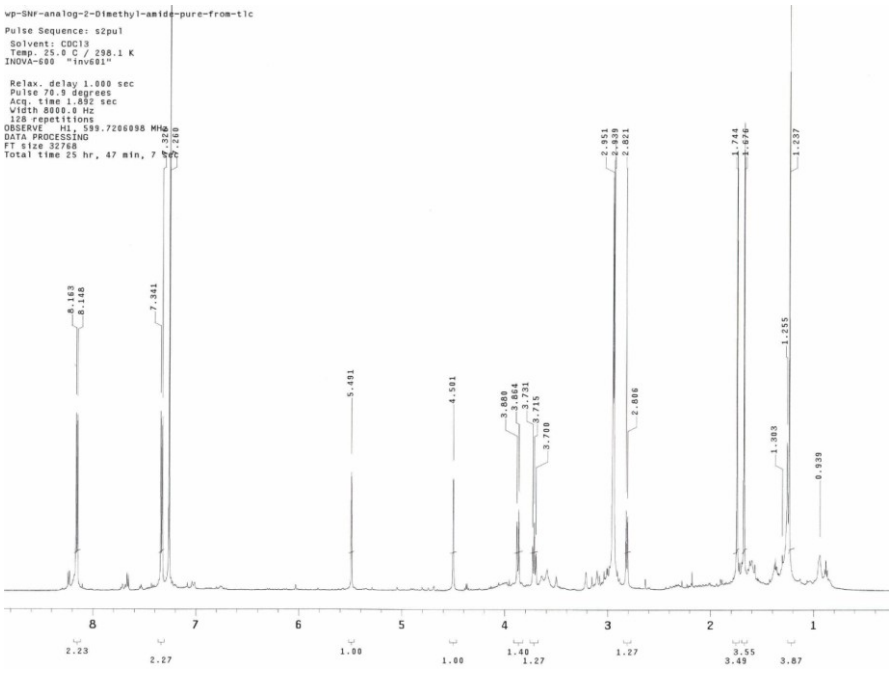
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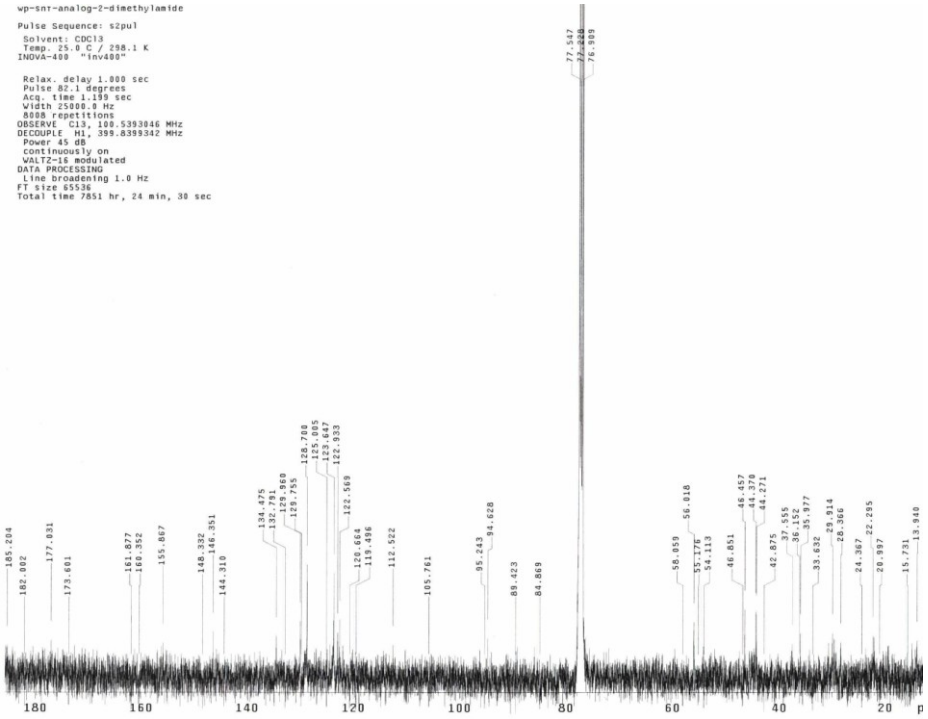
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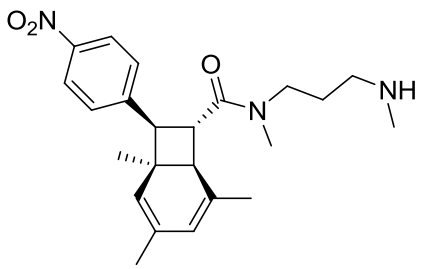
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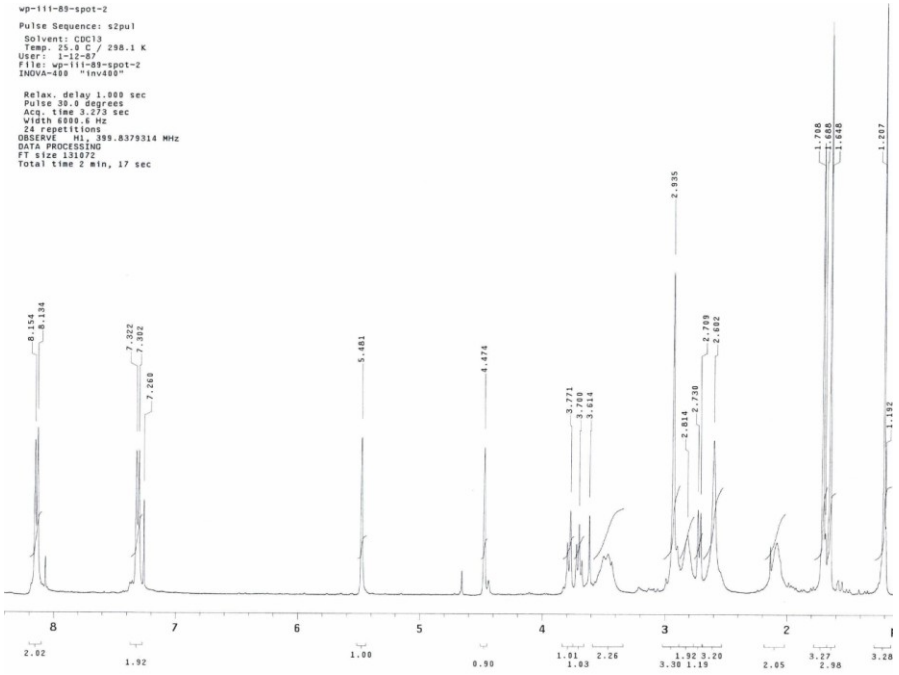
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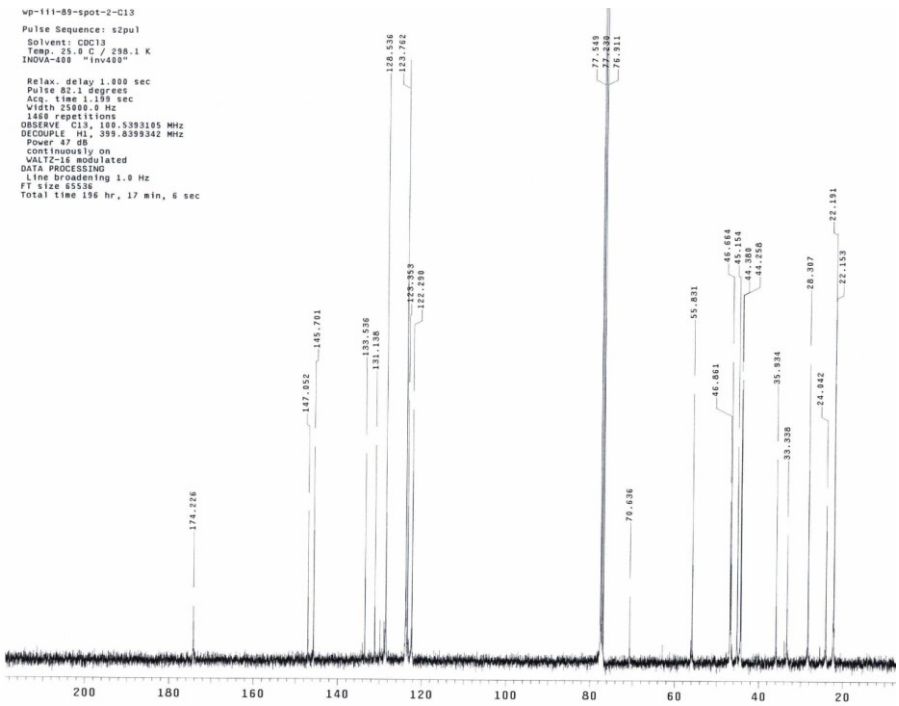
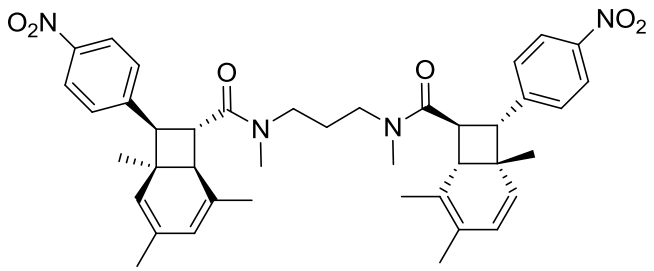
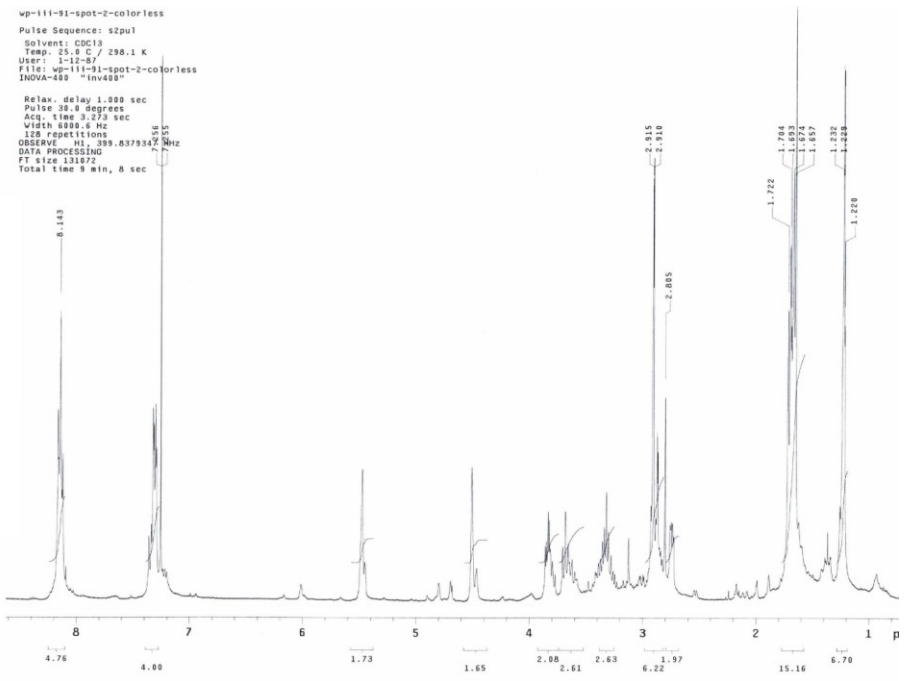
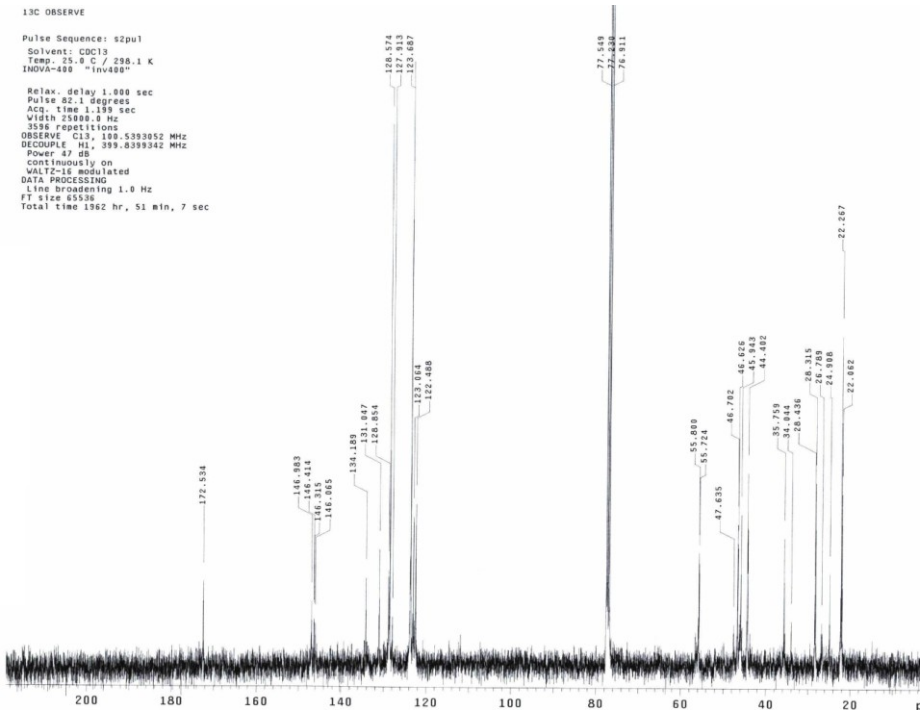
3.771
3.760
3.744
2.935
2.814
2.730
2.709
2.692
1.708
1.688
1.668
1.648
1.207
1.192
8
7
6
5
4
3
2
2.02
1.92
1.00
0.90
1.01
1.03
2.26
1.92
3.30
3.20
1.19
2.05
3.27
2.98
3.28

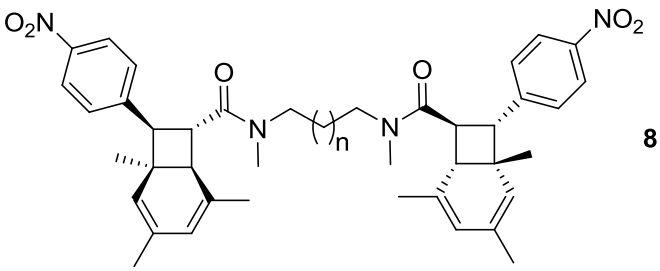

wp-iii-89-spot-2-C13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1460 repetitions
OBSERVE C13, 100.5393105 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 196 hr, 17 min, 6 sec
174.226
147.052
145.701
133.536
131.138
128.536
123.762
77.549
77.230
76.911
70.636
55.831
46.861
46.664
45.154
44.380
44.056
35.934
33.338
28.307
24.042
22.191
22.153
200
180
160
140
120
100
80
60
40
20


O2N
NO2
O
O
N
N

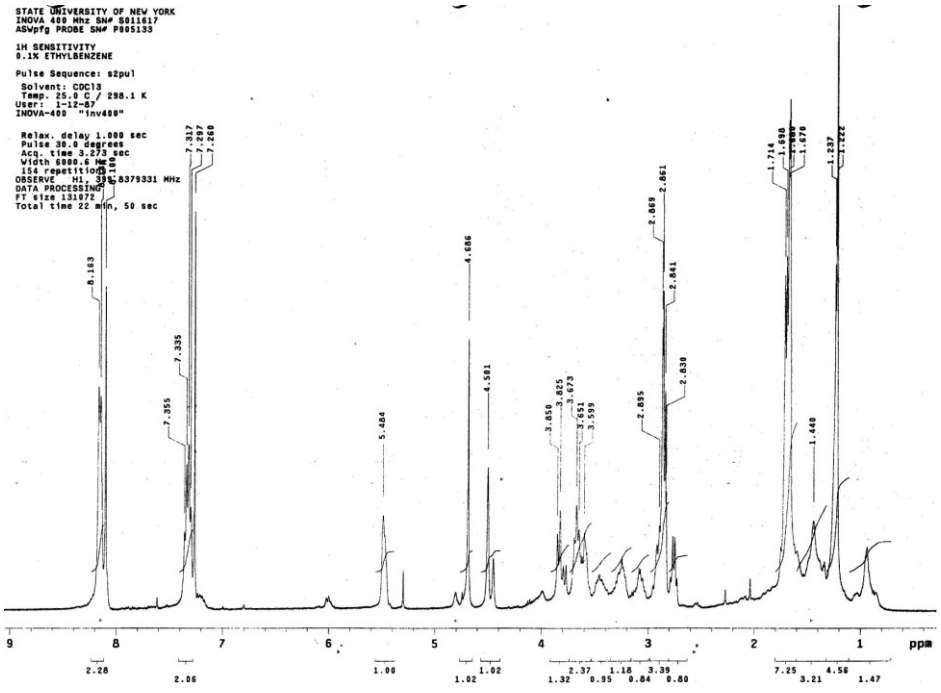
7

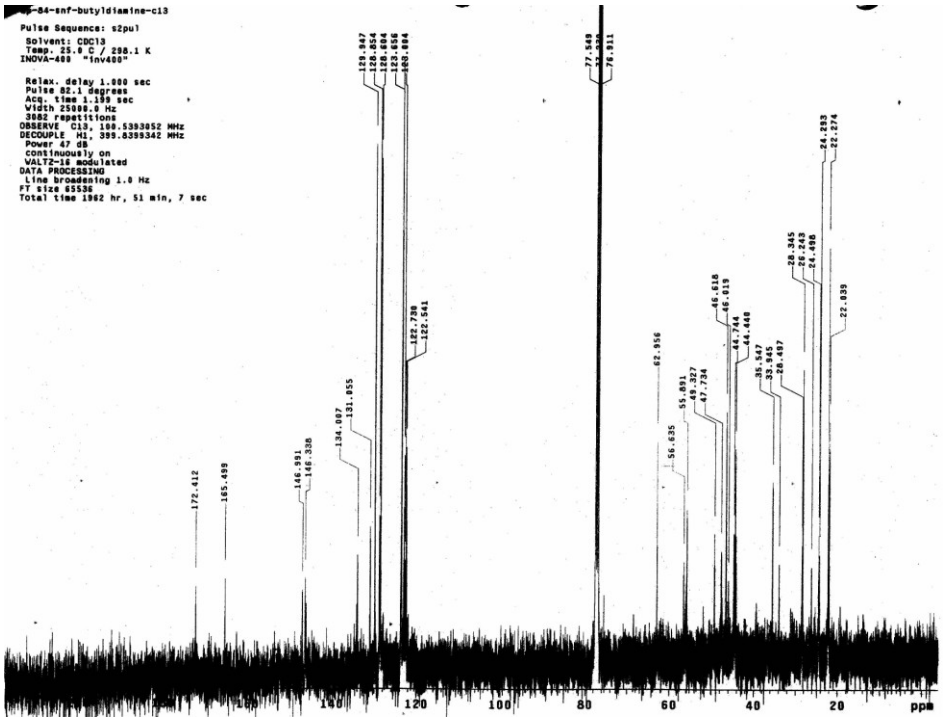

wp-iii-91-spot-2-colorless
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
File: wp-iii-91-spot-2-colorless
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
128 repetitions
OBSERVE H1, 399.8379347 MHz
DATA PROCESSING
FT size 131072
Total time 9 min, 8 sec
8.143
7.556
7.555
2.915
2.910
2.085
1.722
1.704
1.693
1.674
1.657
1.232
1.220
8 7 6 5 4 3 2 1 p
4.76
4.00
1.73
1.65
2.08
2.61
2.63
6.22
1.97
15.16
6.70

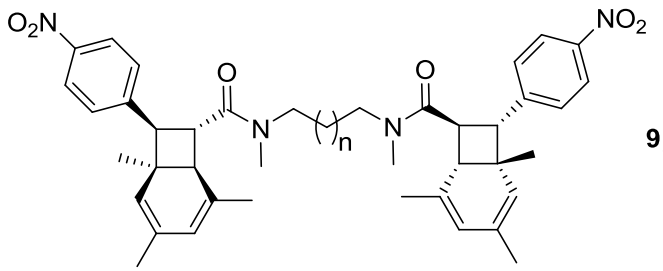

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
3596 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1962 hr, 51 min, 7 sec
172.534
146.883
146.414
146.315
146.065
134.188
131.847
128.854
128.574
127.913
123.687
123.064
122.488
77.549
77.228
76.911
55.880
55.724
47.635
46.782
46.626
45.943
44.492
35.759
34.444
28.436
28.315
26.789
24.908
22.862
22.267
200 180 160 140 120 100 80 60 40 20


O2N
NO2
O
O
N
N
n

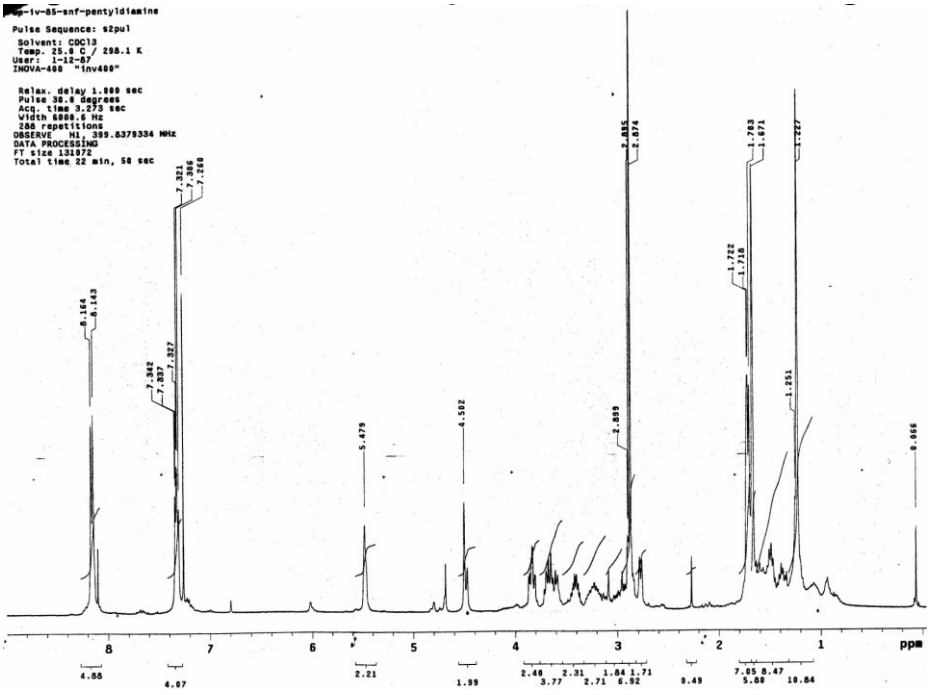
8, n=2

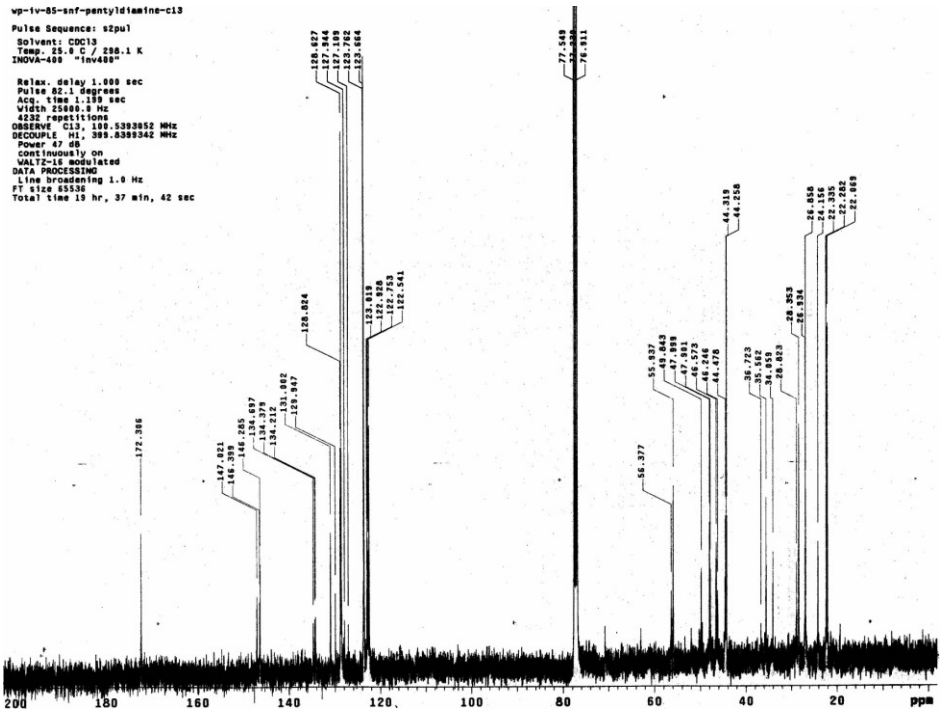

STATE UNIVERSITY OF NEW YORK
INOVA 400 MHz SN# 5011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
154 repetitions
OBSERVE H1, 399.8379331 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

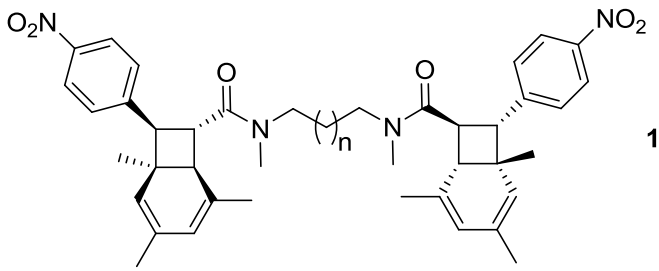

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.8 Hz
3082 repetitions
OBSERVE C13, 100.5393852 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1962 hr, 51 min, 7 sec
ppm


O2N
NO2
O
O
N
N
n

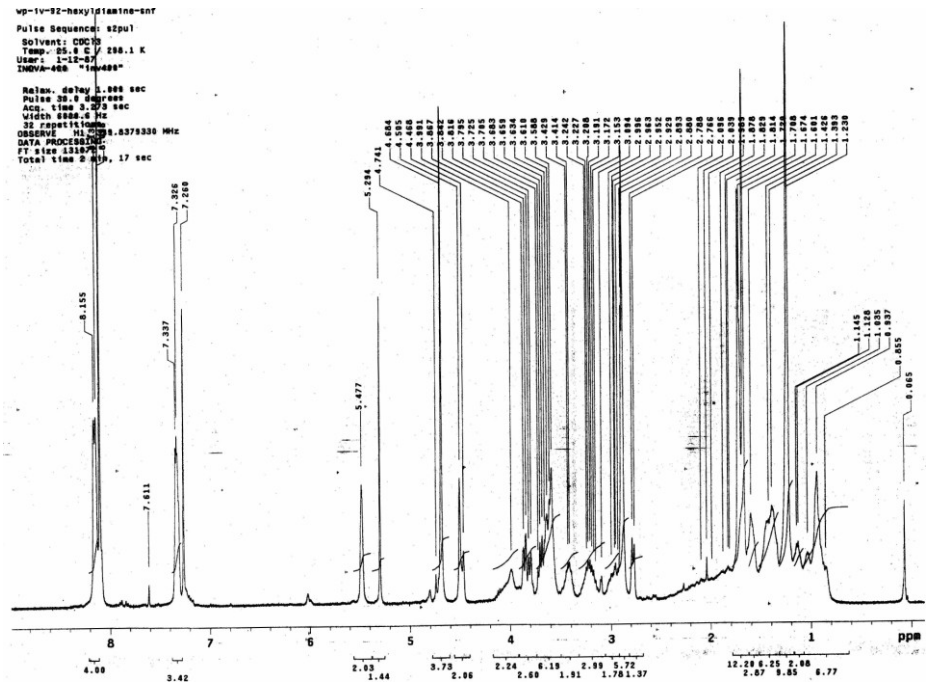
9, n=3

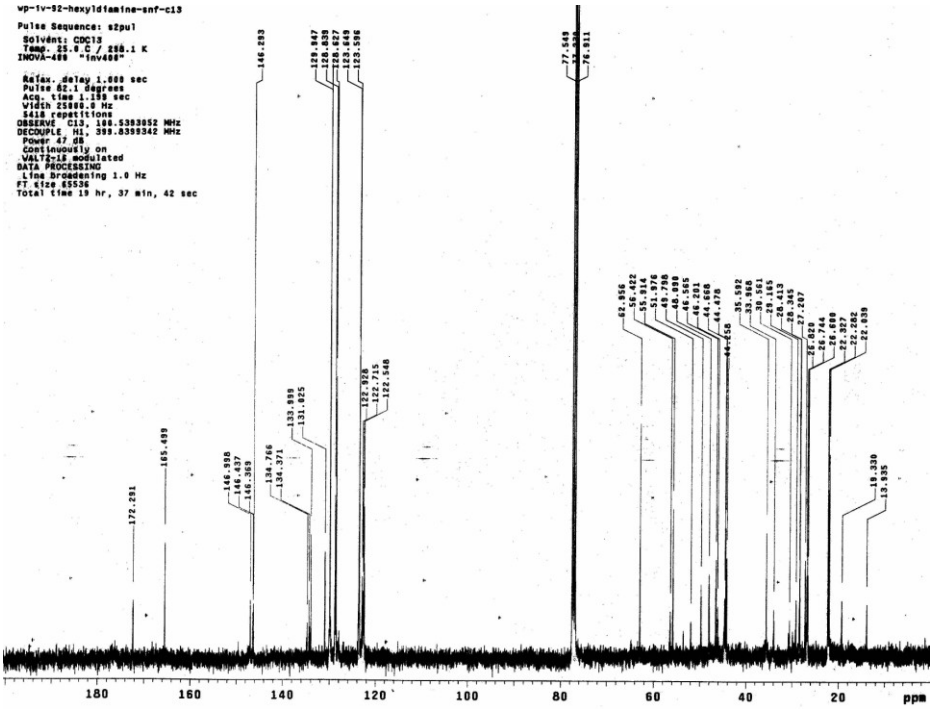

wp-iv-85-snf-pentyldiamine
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
288 repetitions
OBSERVE H1, 399.8379334 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
8.164
8.143
7.342
7.337
7.327
7.321
7.306
7.288
5.479
4.592
2.835
2.674
2.659
1.763
1.671
1.722
1.718
1.251
1.227
0.666
ppm

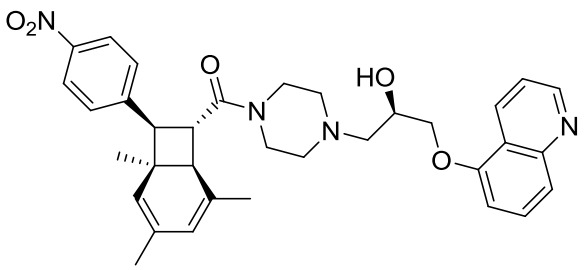

wp-iv-85-snf-pentyldiamine-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.8 Hz
4232 repetitions
OBSERVE C13, 100.5393852 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
172.306
147.821
146.399
146.285
135.647
134.379
134.212
131.892
129.947
128.824
126.827
127.844
127.338
127.192
123.684
123.619
122.928
122.755
122.541
77.548
77.231
76.911
56.377
55.937
49.843
47.999
47.831
46.573
46.246
44.478
44.319
44.256
36.723
35.562
35.455
28.853
28.353
28.334
26.858
24.156
22.335
22.282
22.069
ppm



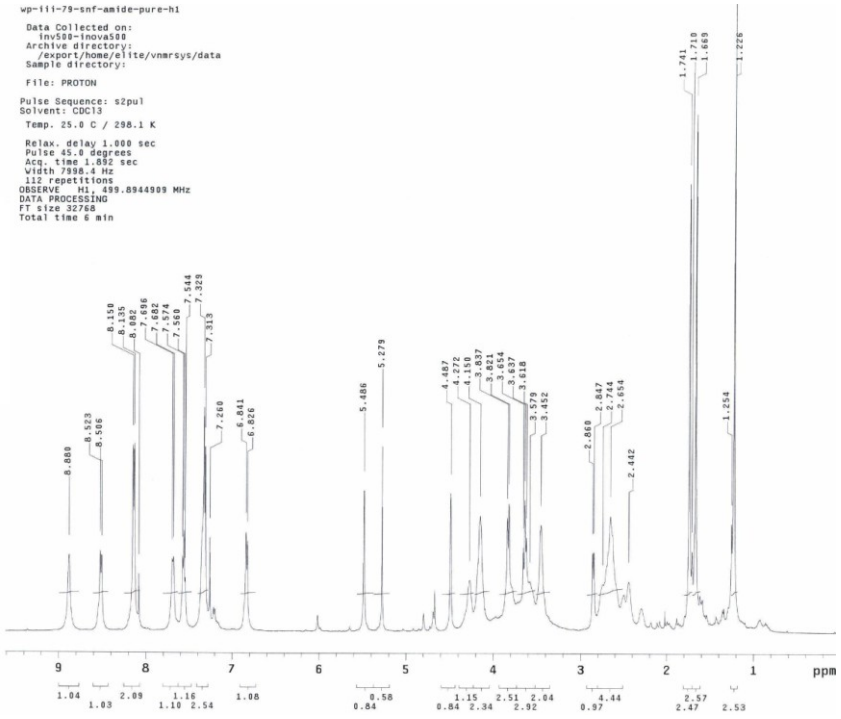
10, n=4

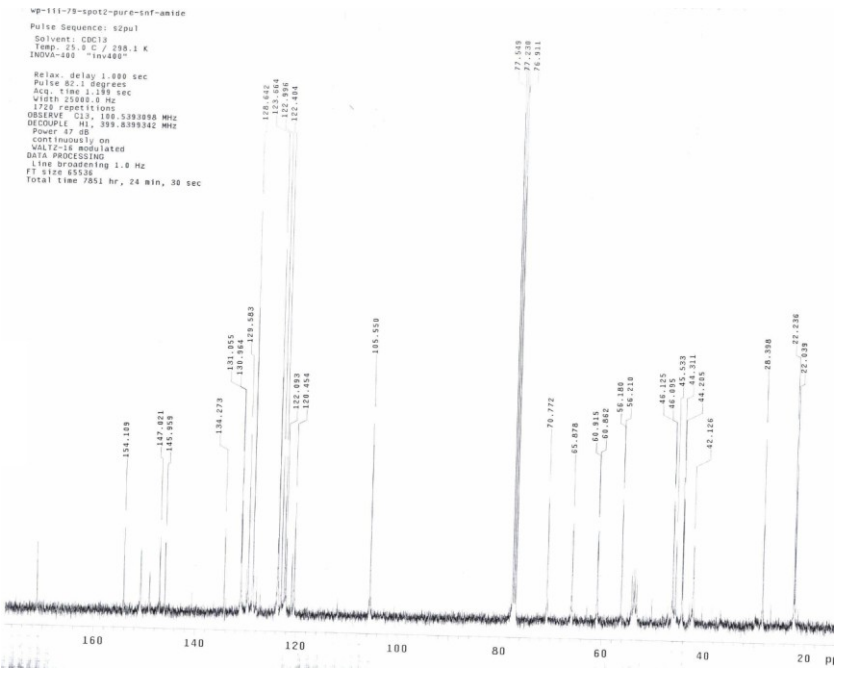


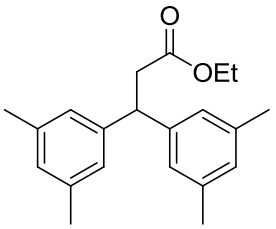



O2N
O
N
N
HO
O
N

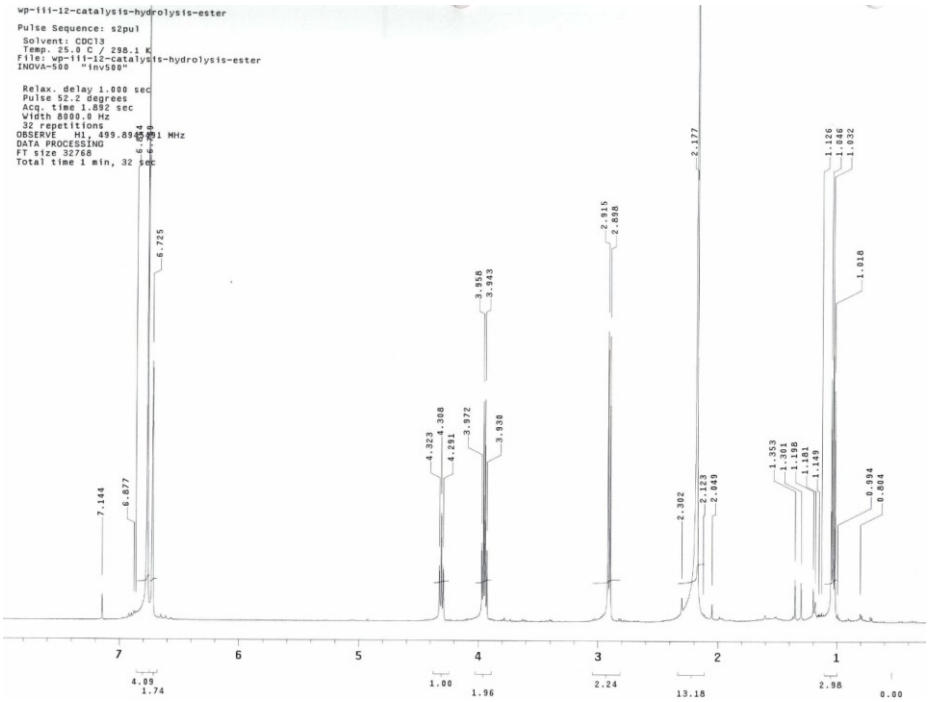
11

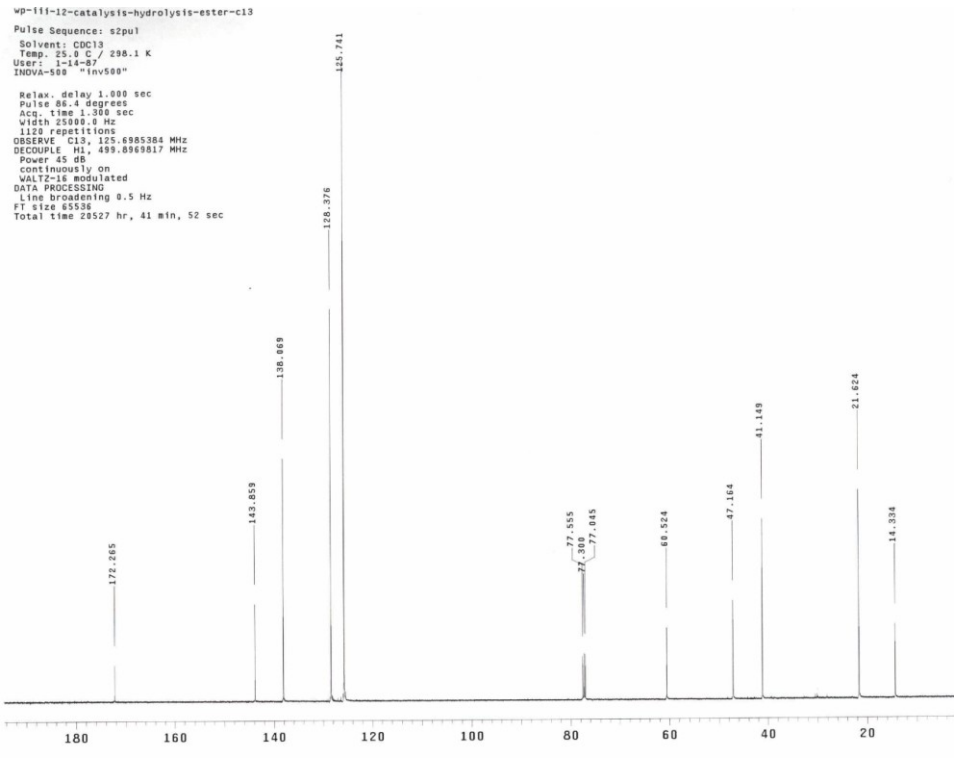

wp-iii-79-snf-amide-pure-h1
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
112 repetitions
OBSERVE H1, 499.8944909 MHz
DATA PROCESSING
FT size 32768
Total time 6 min
ppm

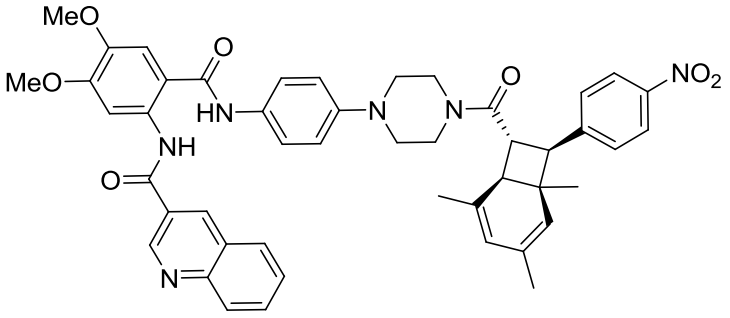

wp-iii-79-spot2-pure-snf-amide
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1720 repetitions
OBSERVE C13, 100.5393858 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7851 hr, 24 min, 30 sec


O
OEt

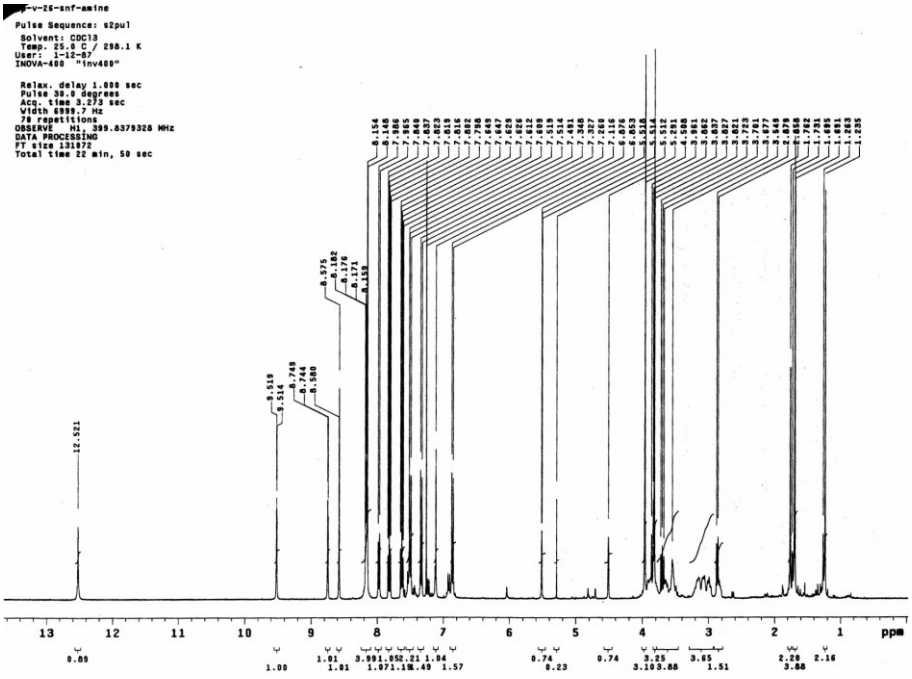
12

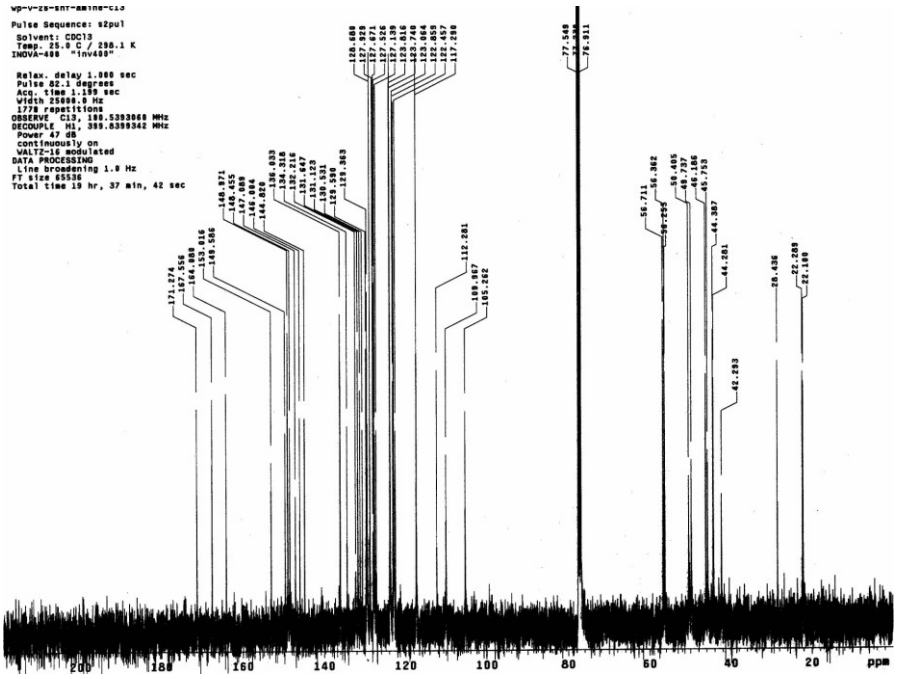

wp-iii-12-catalysis-hydrolysis-ester
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: wp-iii-12-catalysis-hydrolysis-ester
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 52.2 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8954091 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
7.144
6.877
6.725
4.323
4.308
4.291
3.972
3.958
3.943
3.938
2.915
2.898
2.302
2.177
2.123
2.049
1.353
1.301
1.198
1.181
1.149
1.126
1.046
1.032
1.018
0.994
0.864
4.09
1.74
1.00
1.96
2.24
13.18
2.98
0.00

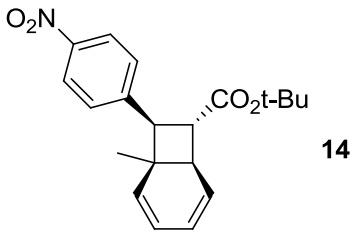

wp-iii-12-catalysis-hydrolysis-ester-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-07
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 86.4 degrees
Acq. time 1.300 sec
Width 25000.0 Hz
1120 repetitions
OBSERVE C13, 125.6985384 MHz
DECOUPLE H1, 499.8969817 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 20527 hr, 41 min, 52 sec
172.265
143.859
136.069
128.376
125.741
77.555
77.360
77.045
60.524
47.164
41.149
21.624
14.334


MeO
MeO
O
HN
NH
O
N
N
O
NO2
N

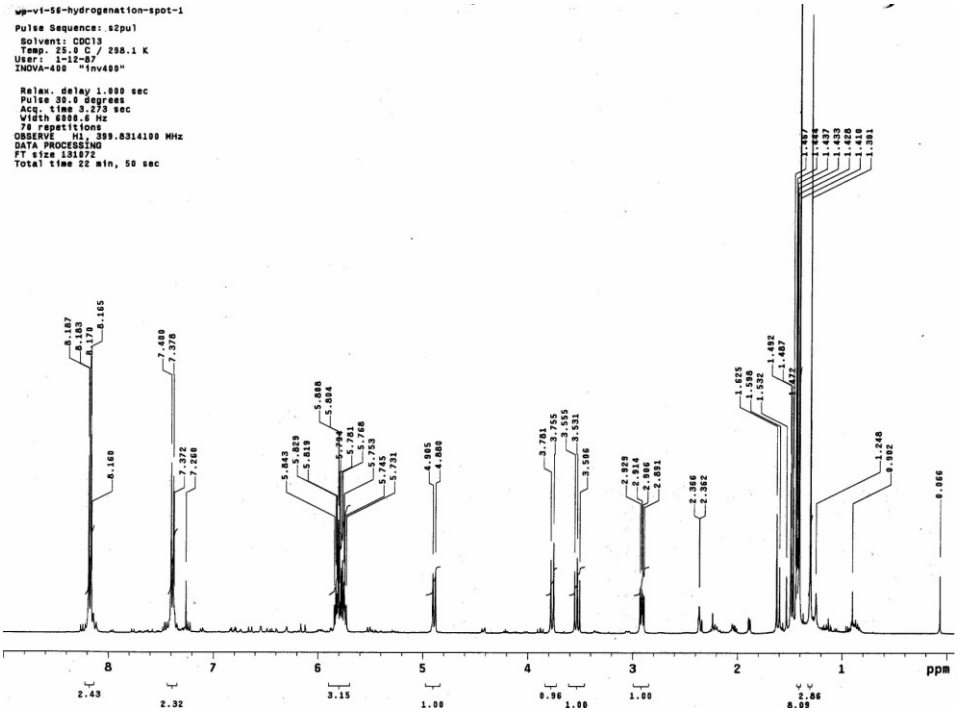
13

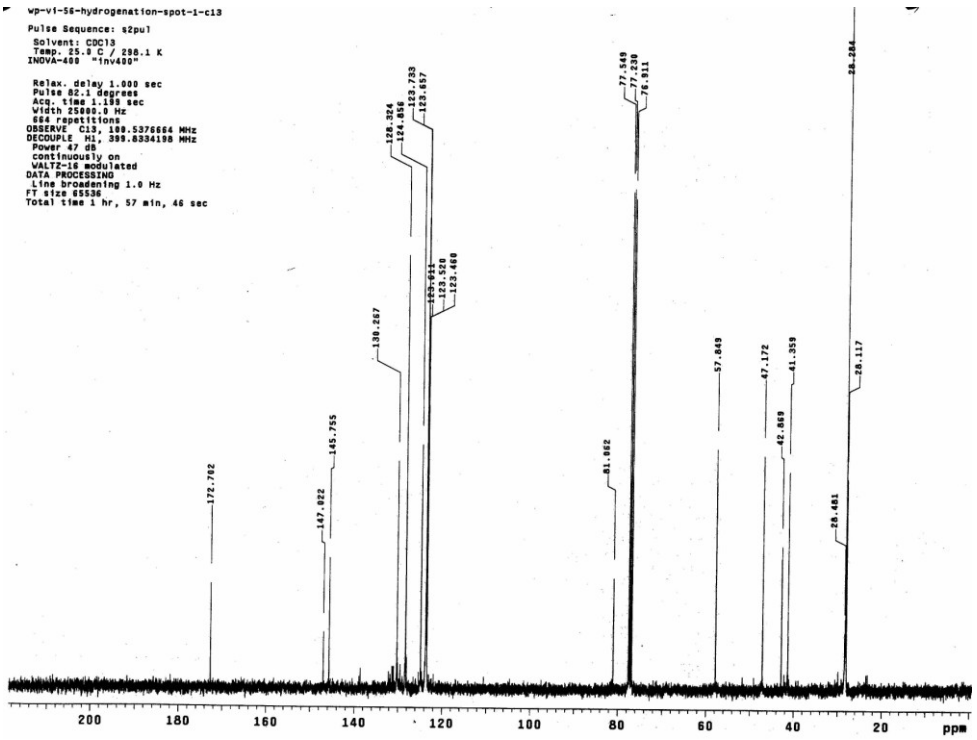

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6998.7 Hz
76 repetitions
OBSERVE H1, 399.8379328 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
12.521
9.519
9.514
8.749
8.744
8.580
8.575
8.162
8.158
8.171
8.153
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

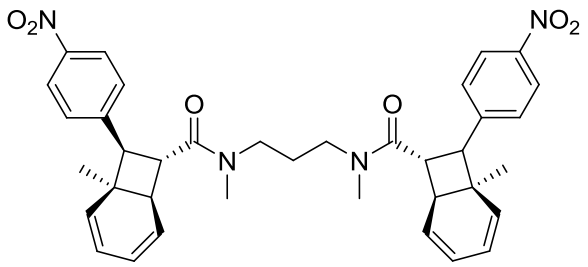

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25898.8 Hz
1778 repetitions
OBSERVE C13, 100.5383068 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
171.274
167.556
164.888
153.516
148.586
148.455
147.888
146.884
144.828
138.383
136.353
132.216
131.647
131.173
130.532
129.590
129.383
128.680
127.929
127.671
127.336
127.138
123.816
123.748
123.466
122.959
122.457
117.298
112.281
109.967
105.262
77.548
77.232
76.911
56.711
56.382
56.055
50.495
49.737
46.156
45.758
44.387
44.261
42.293
28.436
22.289
22.189
200
180
160
140
120
100
80
60
40
20
ppm


O_2N
CO_2t-Bu

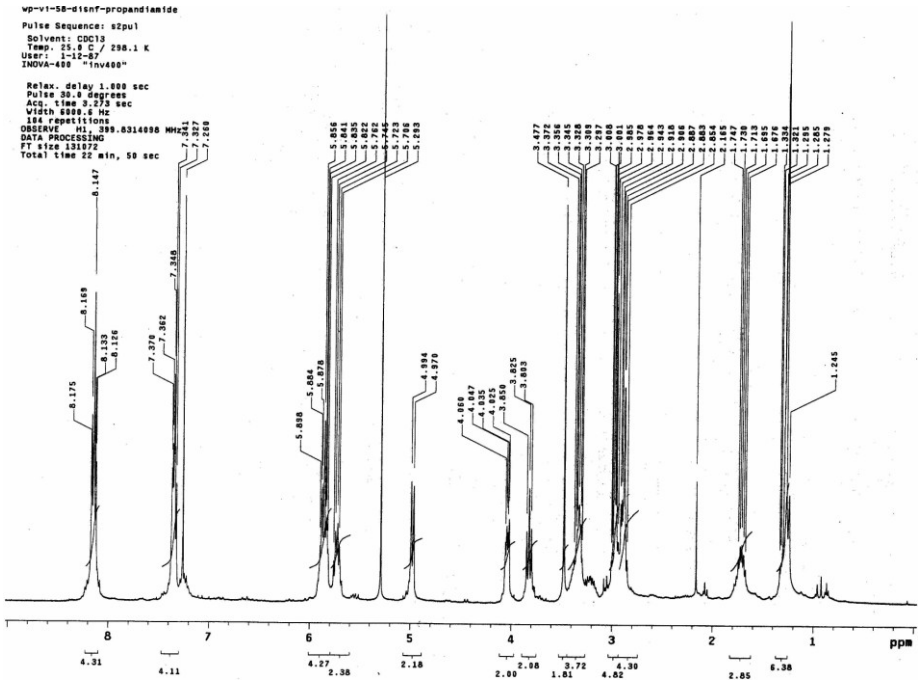
14

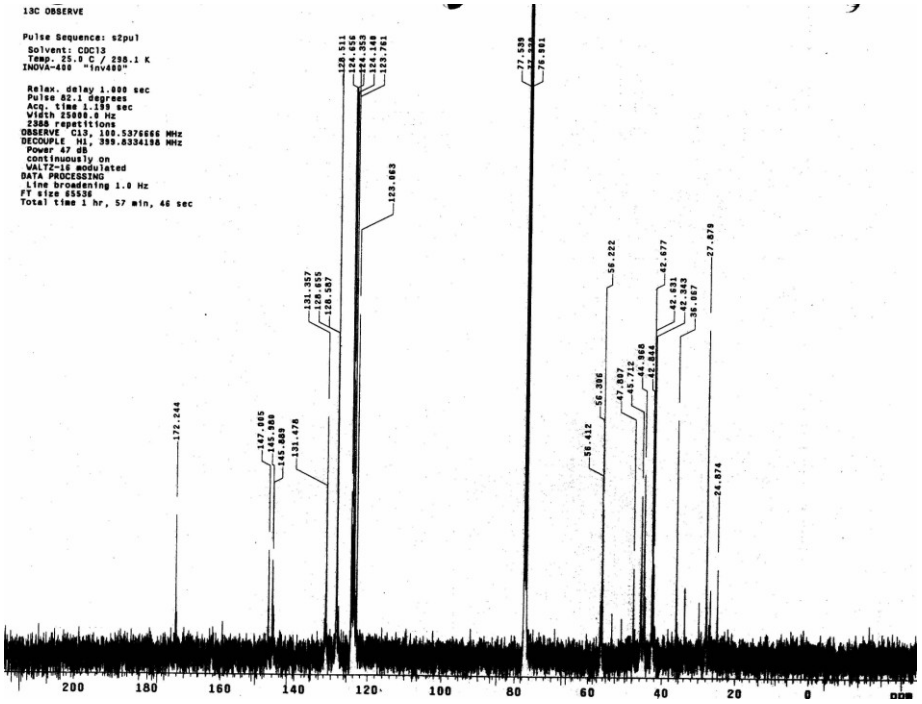

wp-vi-56-hydrogenation-spot-1
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6006.6 Hz
70 repetitions
OBSERVE H1, 399.8314100 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

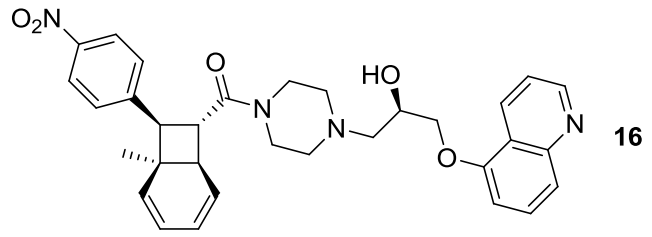

wp-vi-56-hydrogenation-spot-1-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.9 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.198 sec
Width 25000.0 Hz
664 repetitions
OBSERVE C13, 100.5376664 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


O2N
NO2
O
O
N
N

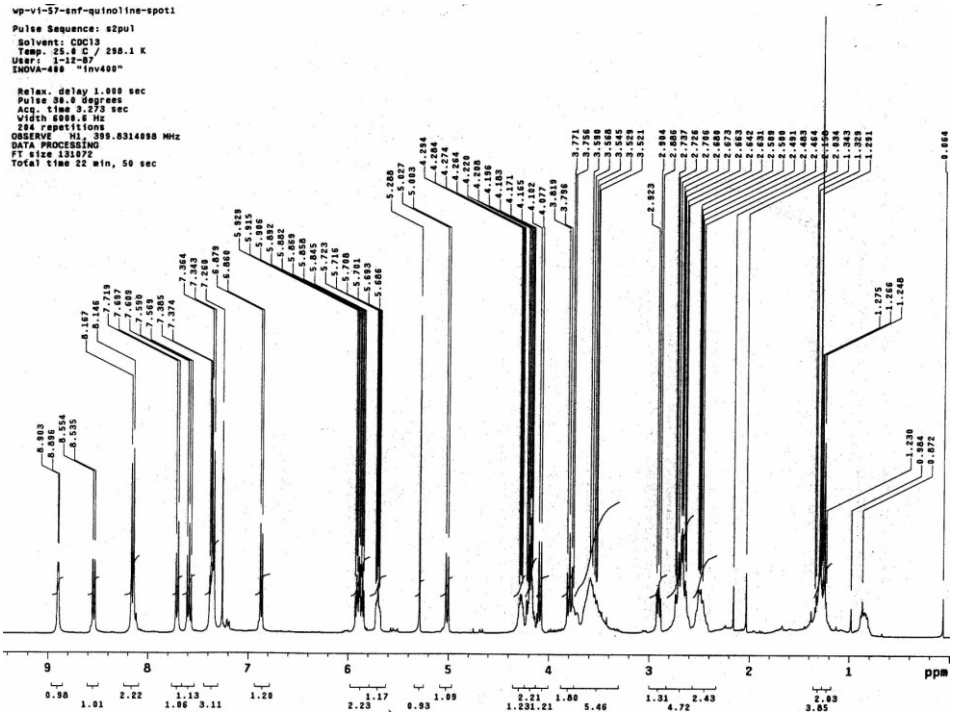
15

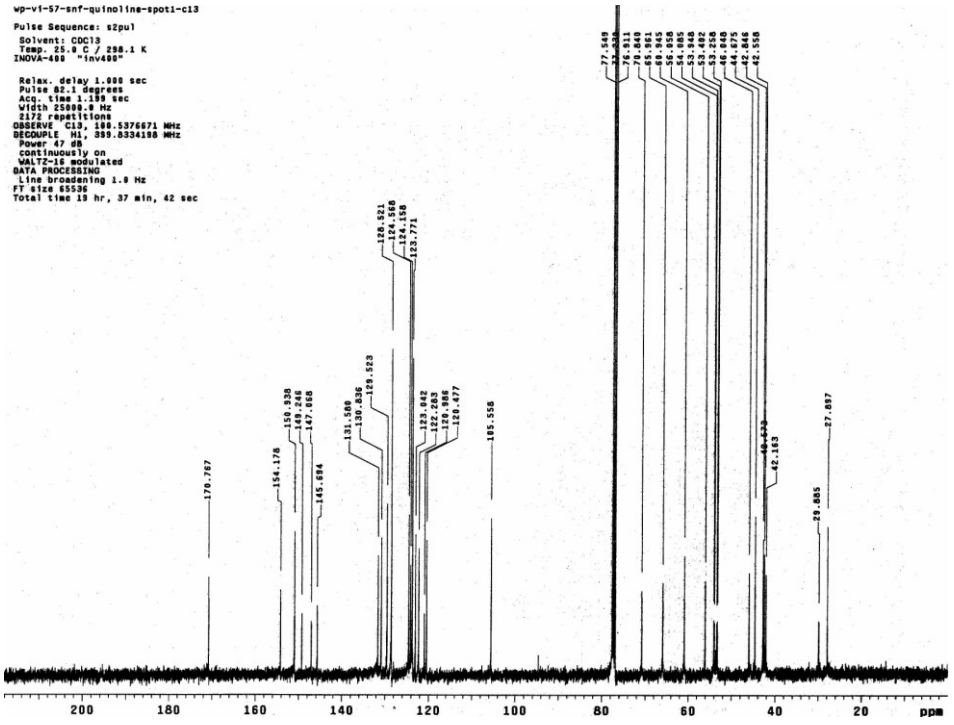

wp-v1-58-disnf-propandiamide
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 5988.6 Hz
184 repetitions
OBSERVE H1, 399.8314098 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

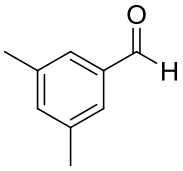

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.155 sec
Width 25000.8 Hz
2388 repetitions
OBSERVE C13, 100.5376666 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec


O2N
O
N
N
HO
O
N

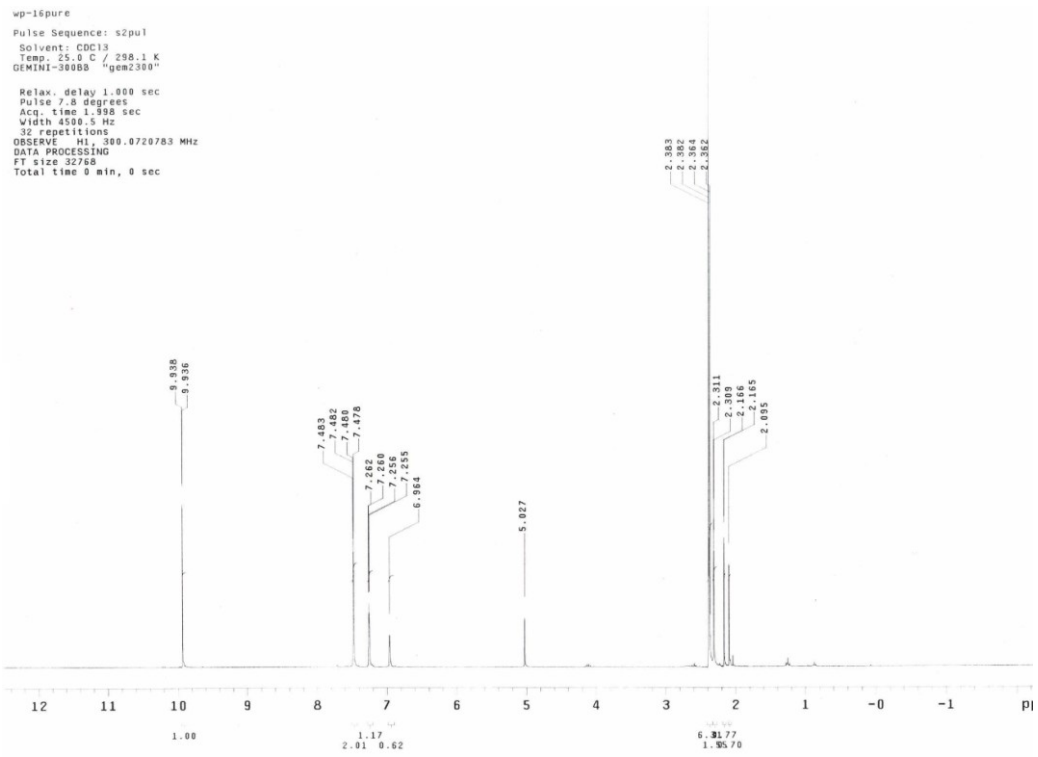
16

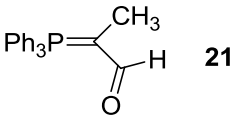

wp-v1-57-snf-quinoline-spot1
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6009.6 Hz
284 repetitions
OBSERVE H1, 399.8314098 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm


wp-v1-57-snf-quinoline-spot1-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2172 repetitions
OBSERVE C13, 100.5376671 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
ppm

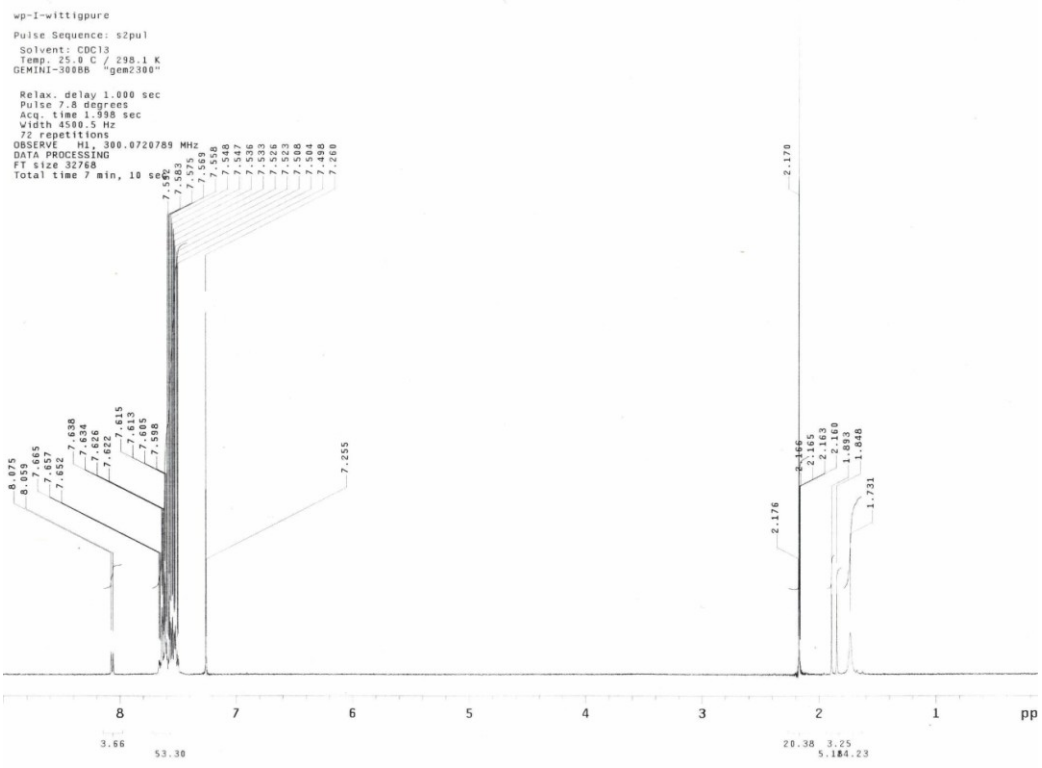

O
H

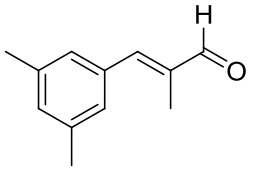
18


wp-16pure
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720783 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 0 sec
9.938
9.936
7.483
7.482
7.480
7.478
7.262
7.260
7.256
7.255
6.964
5.027
2.383
2.382
2.364
2.362
2.311
2.309
2.166
2.165
2.095
12
11
10
9
8
7
6
5
4
3
2
1
-0
-1
1.00
1.17
2.01
0.62
6.31
77
1.95
70

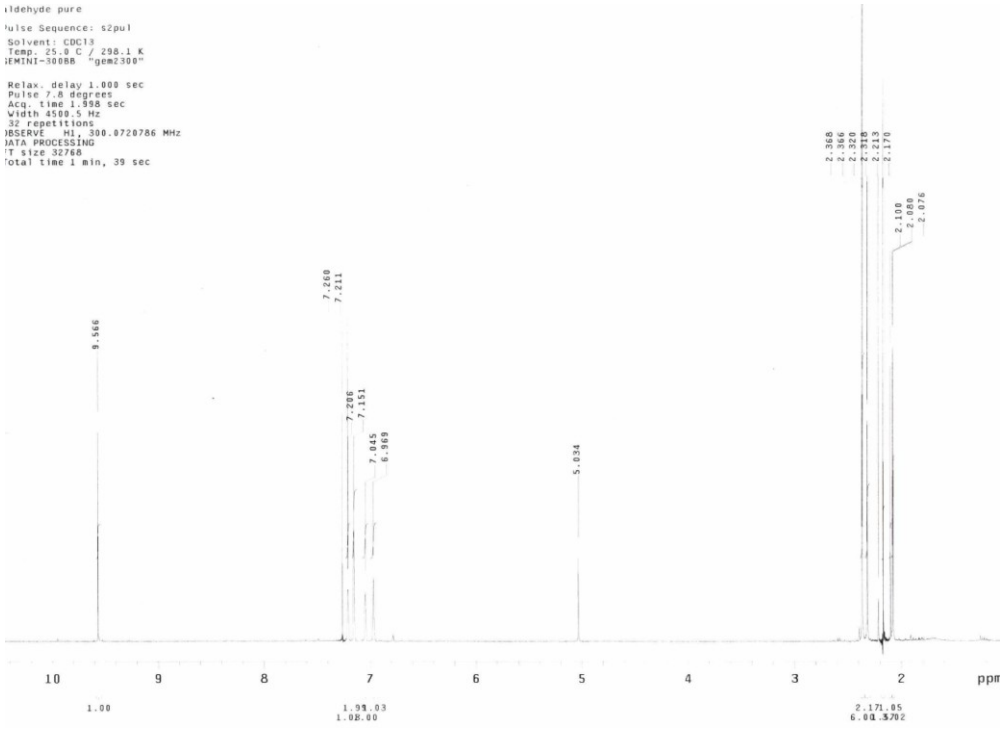

CH3
Ph3P
H
O

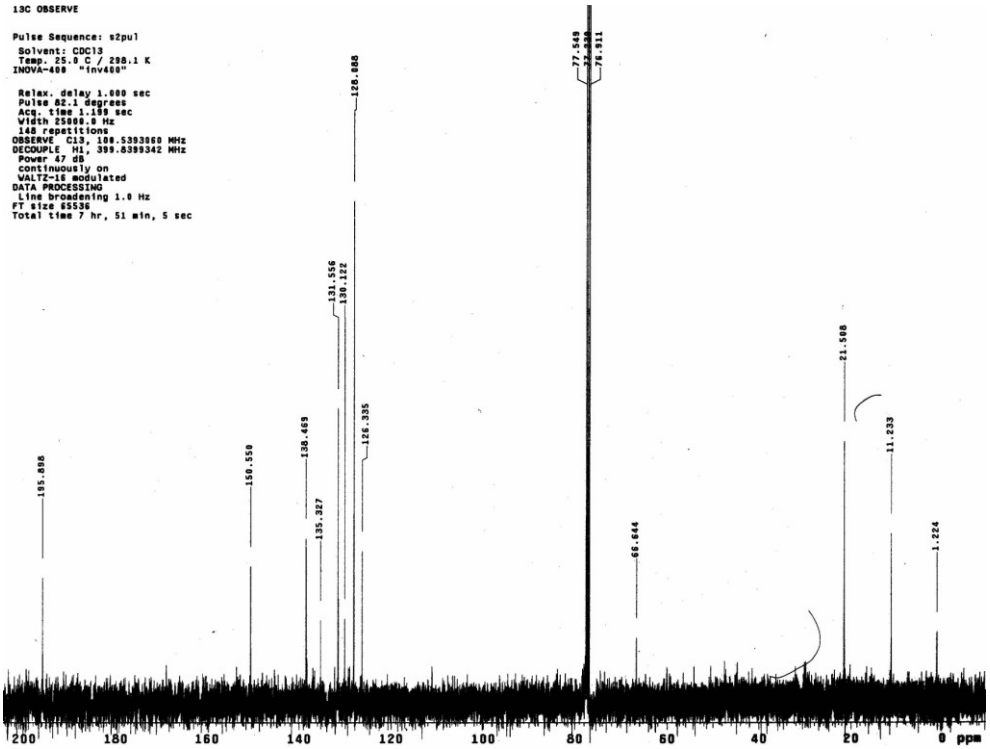
21

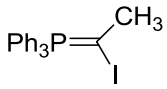

wp-I-wittigpure
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4580.5 Hz
72 repetitions
OBSERVE H1, 300.0720789 MHz
DATA PROCESSING
FT size 32768
Total time 7 min, 10 sec
8.075
8.059
7.665
7.657
7.652
7.638
7.634
7.626
7.622
7.615
7.613
7.605
7.598
7.592
7.583
7.578
7.559
7.558
7.548
7.547
7.536
7.533
7.526
7.523
7.508
7.504
7.498
7.260
7.255
2.170
2.176
2.166
2.165
2.163
2.160
1.653
1.648
1.731
8
7
6
5
4
3
2
1
pp
3.66
53.30
20.38
3.25
5.18
4.23


H
O

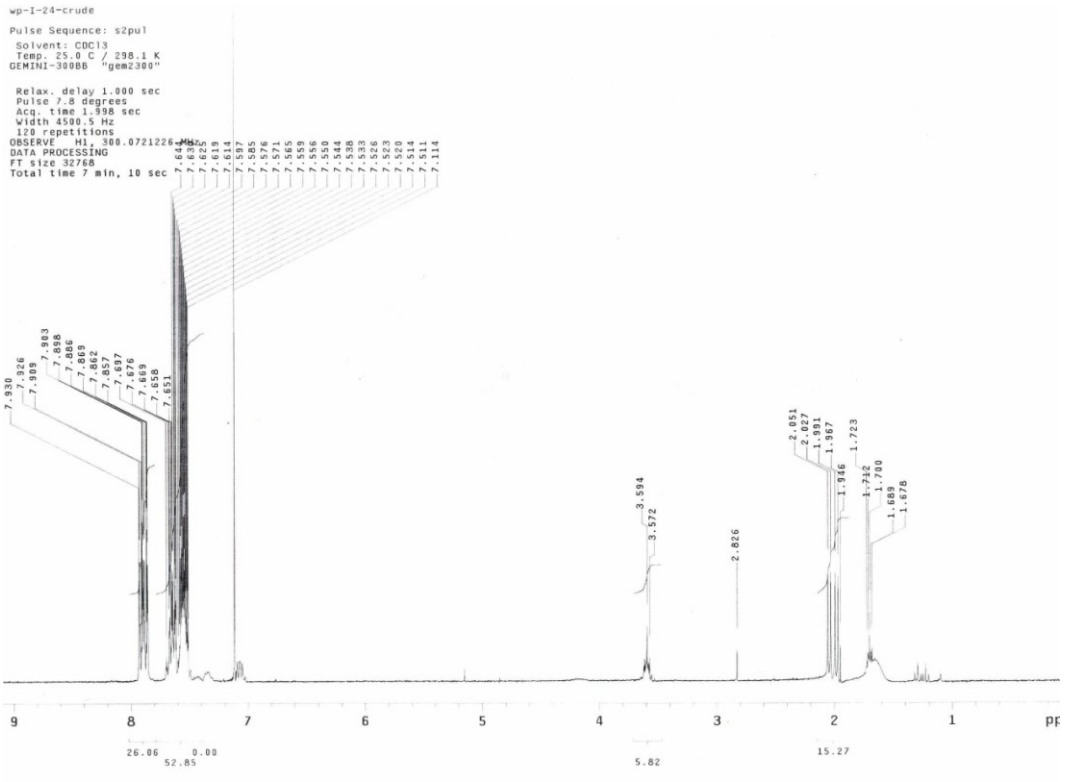
22

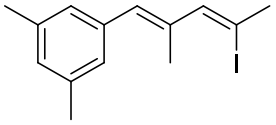

ildehyde pure
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
EMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
BSERVE H1, 300.0720786 MHz
ATA PROCESSING
T size 32768
otal time 1 min, 39 sec
9.566
7.260
7.211
7.206
7.151
7.045
6.969
5.034
2.368
2.366
2.320
2.318
2.213
2.170
2.108
2.080
2.076
10
9
8
7
6
5
4
3
2
ppm
1.00
1.95.03
1.08.00
2.171.05
6.00 3.702


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
148 repetitions
OBSERVE C13, 100.5393060 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
195.898
150.550
138.469
135.327
131.556
130.122
126.886
126.335
77.549
77.230
76.911
66.644
21.508
11.233
1.224
200
180
160
140
120
100
80
60
40
20
0 ppm

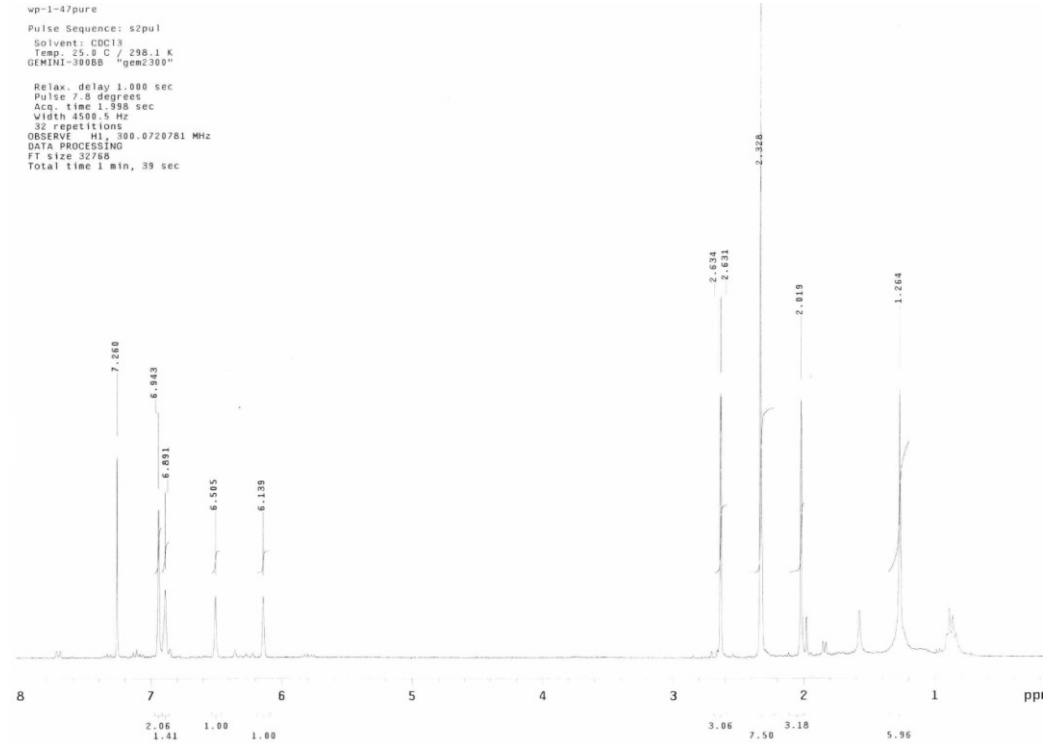

Ph3P
CH3
I

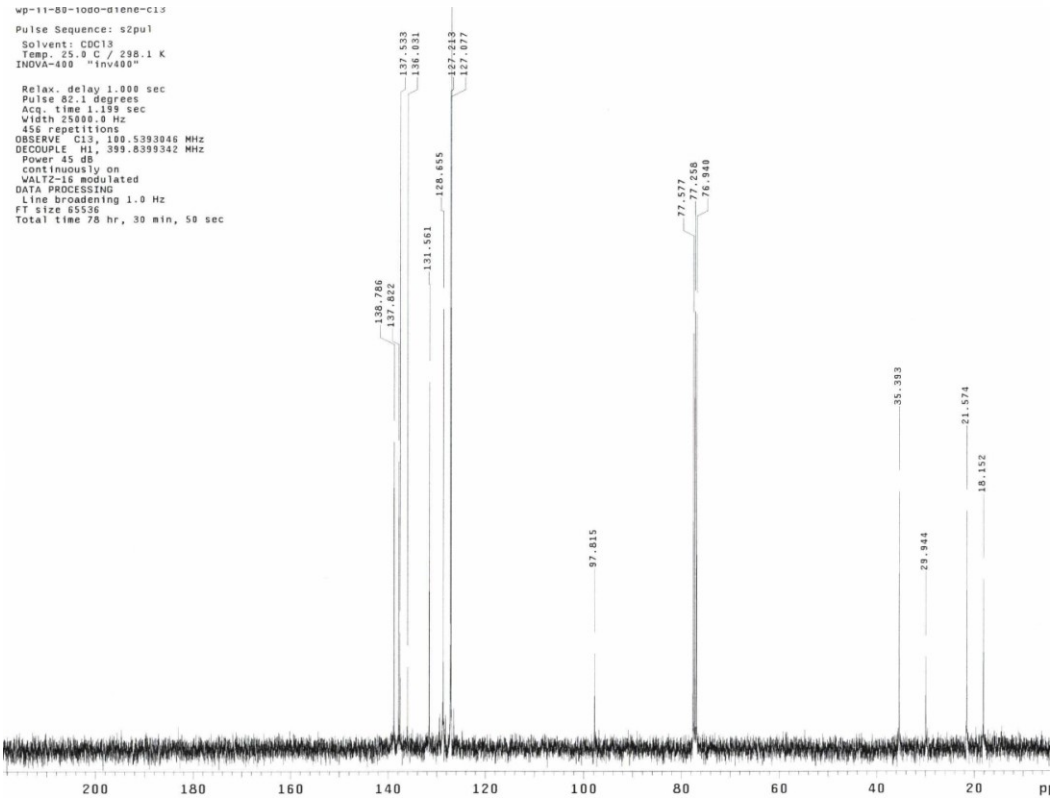
24

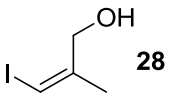

wp-I-24-crude
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
120 repetitions
OBSERVE H1, 300.0721226 MHz
DATA PROCESSING
FT size 32768
Total time 7 min, 10 sec
7.930
7.926
7.909
7.903
7.898
7.886
7.869
7.862
7.857
7.697
7.676
7.669
7.658
7.651
3.594
3.572
2.826
2.051
2.027
1.991
1.967
1.946
1.723
1.742
1.700
1.689
1.678
9
8
7
6
5
4
3
2
1
ppm
26.06
0.00
52.85
5.82
15.27



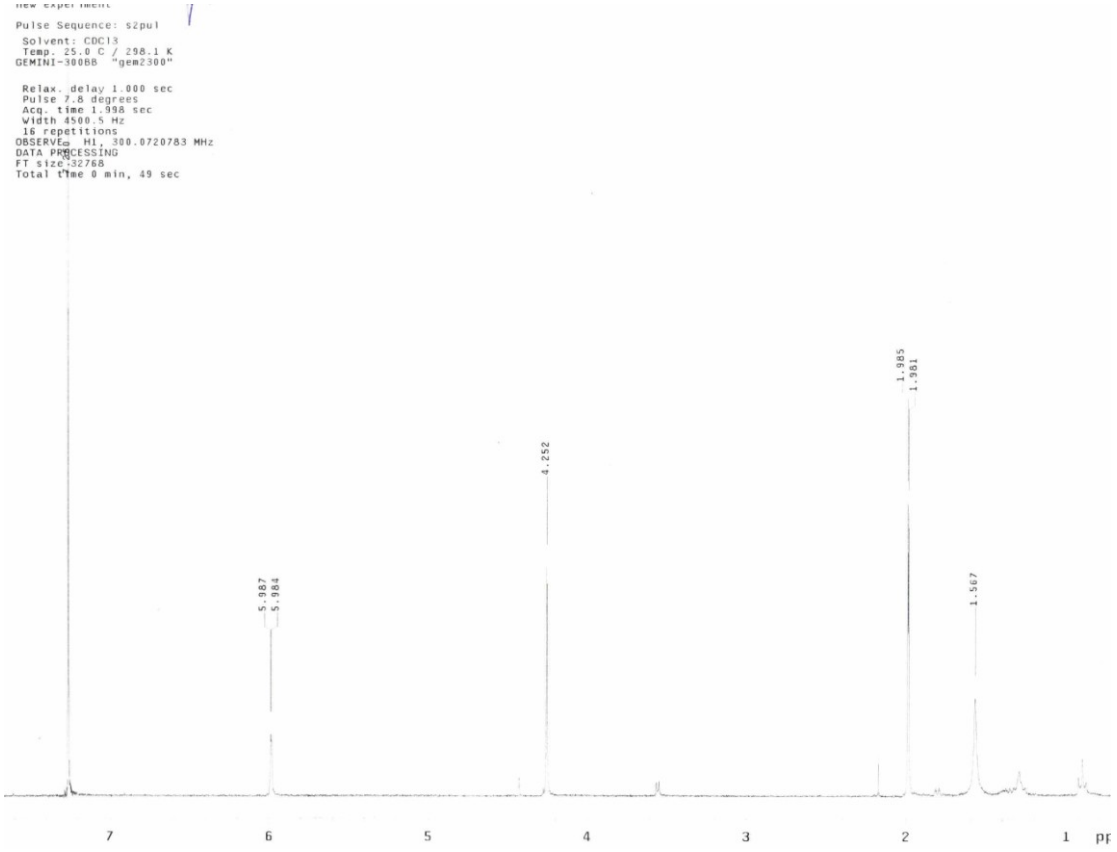
25

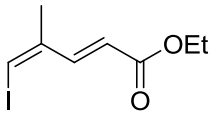

wp-1-47pure
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4508.5 Hz
32 repetitions
OBSERVE H1, 300.0720781 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
7.268
6.943
6.891
6.505
6.139
2.634
2.631
2.328
2.019
1.264
2.06
1.41
1.00
1.00
3.06
7.50
3.18
5.96
ppm


wp-11-80-iodo-diene-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
456 repetitions
OBSERVE C13, 100.5393046 MHz
DECOUPLE H1, 399.8399342 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 50 sec
137.533
136.831
127.213
127.077
128.655
131.561
138.786
137.822
77.577
77.258
76.940
97.815
35.393
29.944
21.574
18.152
200
180
160
140
120
100
80
60
40
20
ppm

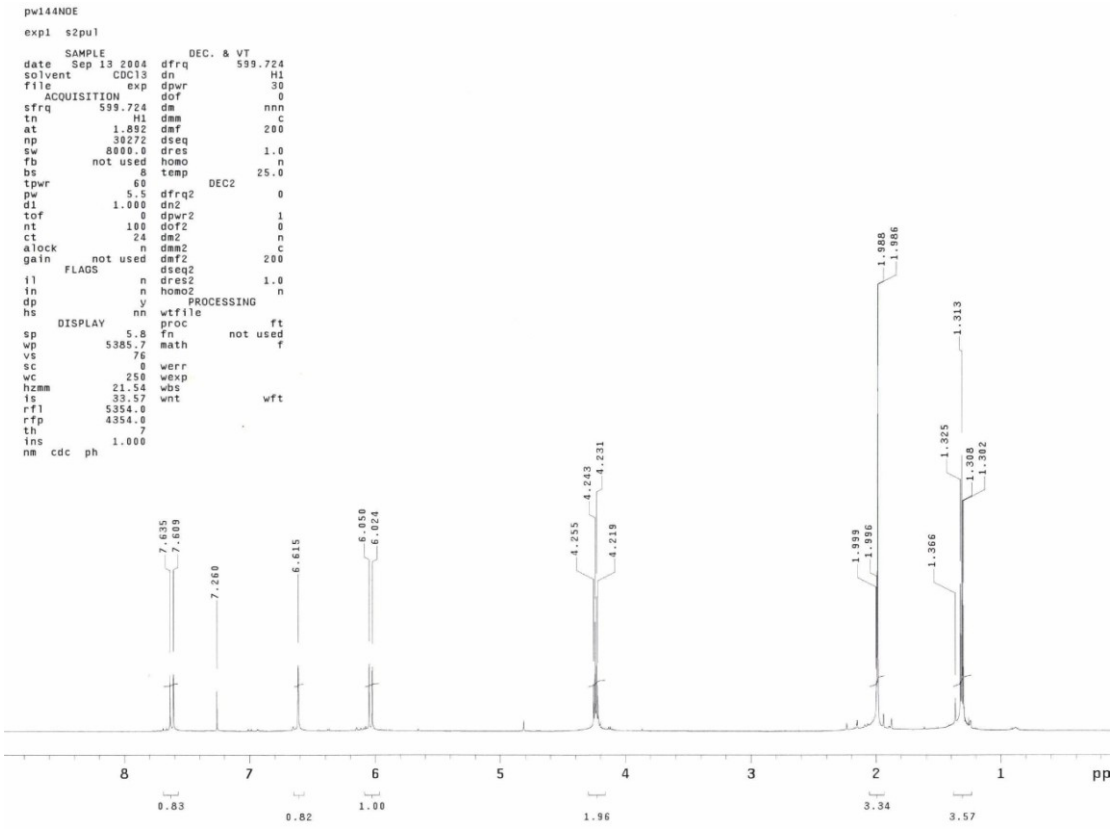

OH
I

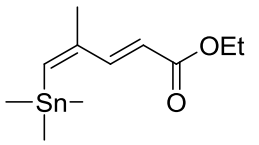
28


New Experiment
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
16 repetitions
OBSERVE H1, 300.0720783 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 49 sec
5.987
5.984
4.252
1.985
1.981
1.567
7
6
5
4
3
2
1
ppm

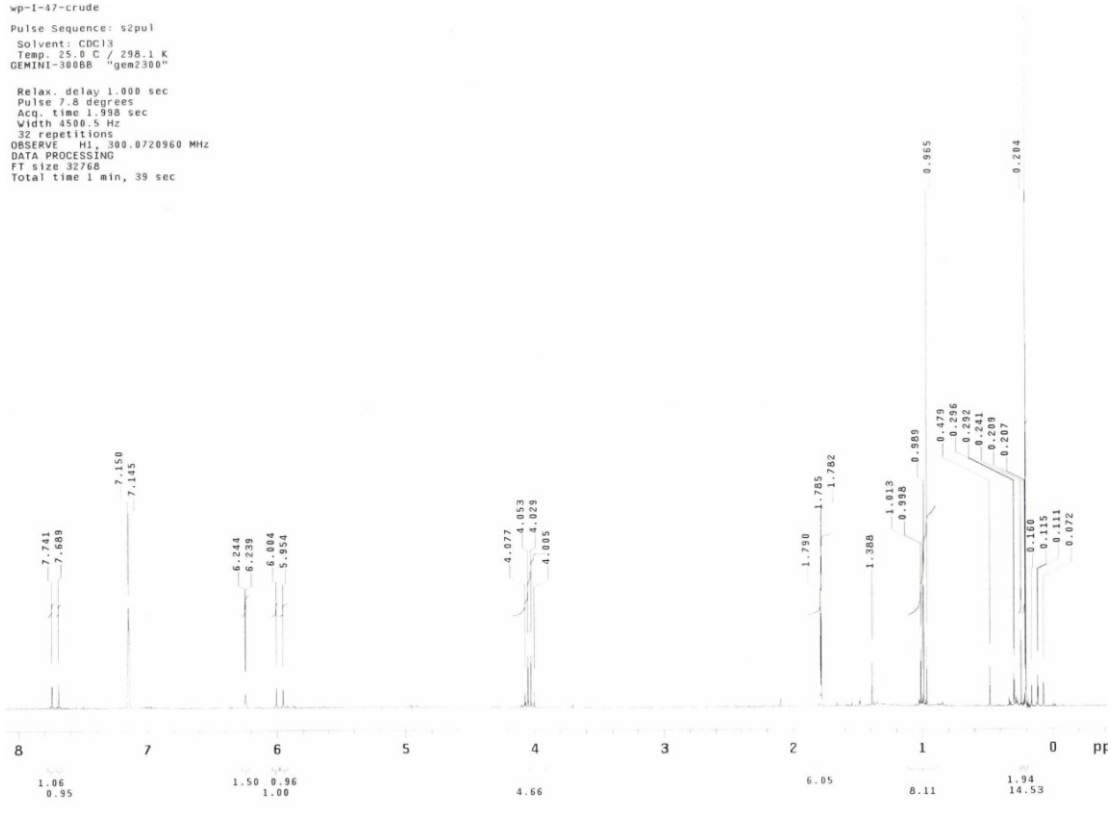

OEt
I
O

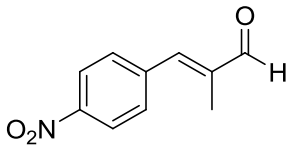
32


pw144NOE
exp1 s2pul
SAMPLE
date Sep 13 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 599.724
tn H1
at 1.892
np 30272
sw 8000.0
fb not used
bs 8
tpwr 60
pw 5.5
d1 1.000
tof 0
nt 100
ct 24
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp 5.8
wp 5385.7
vs 76
sc 0
wc 250
hzmm 21.54
is 33.57
rfl 5354.0
rfp 4354.0
th 7
ins 1.000
nm cdc ph
DEC. & VT
dfrq 599.724
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
temp 25.0
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
7.635
7.609
7.260
6.615
6.050
6.024
4.255
4.243
4.231
4.219
1.999
1.988
1.986
1.366
1.325
1.313
1.308
1.302
8
7
6
5
4
3
2
1
pp
0.83
0.82
1.00
1.96
3.34
3.57

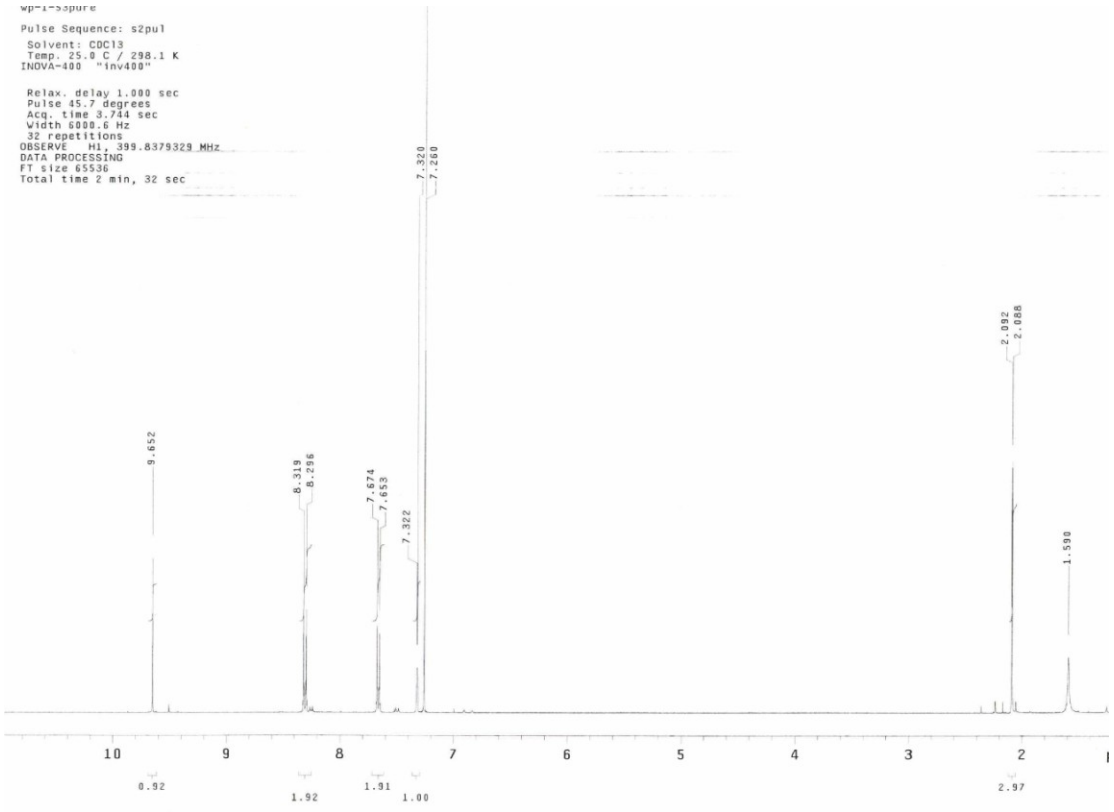

OEt
Sn
O

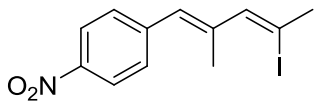
33


wp-I-47-crude
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720960 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
7.741
7.689
7.150
7.145
6.244
6.239
6.084
5.954
4.077
4.053
4.029
4.005
1.790
1.785
1.782
1.388
1.013
0.998
0.989
0.965
0.479
0.296
0.292
0.241
0.209
0.207
0.204
0.160
0.115
0.111
0.072
8
7
6
5
4
3
2
1
0
ppm
1.06
0.95
1.50
0.96
1.00
4.66
6.05
8.11
1.94
14.53

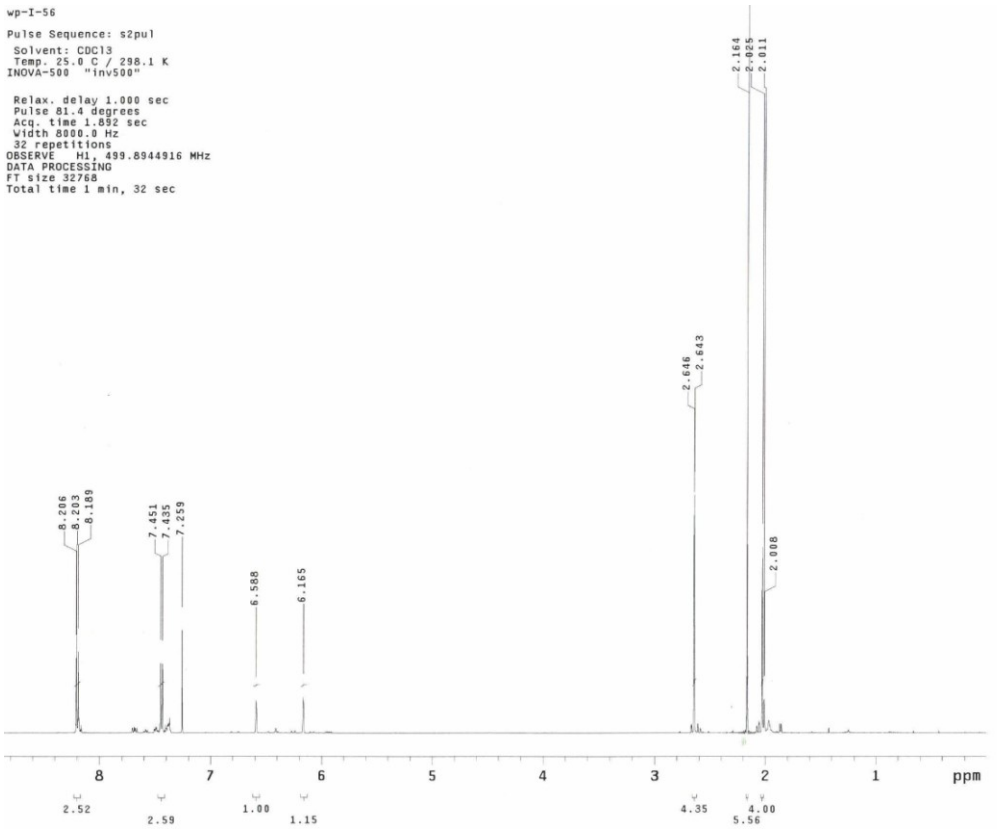

O
H
O2N

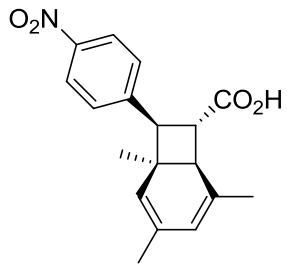
36


Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 45.7 degrees
Acq. time 3.744 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379329 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 32 sec
9.652
8.319
8.296
7.674
7.653
7.322
7.320
7.260
2.092
2.088
1.598
10
9
8
7
6
5
4
3
2
0.92
1.92
1.91
1.00
2.97

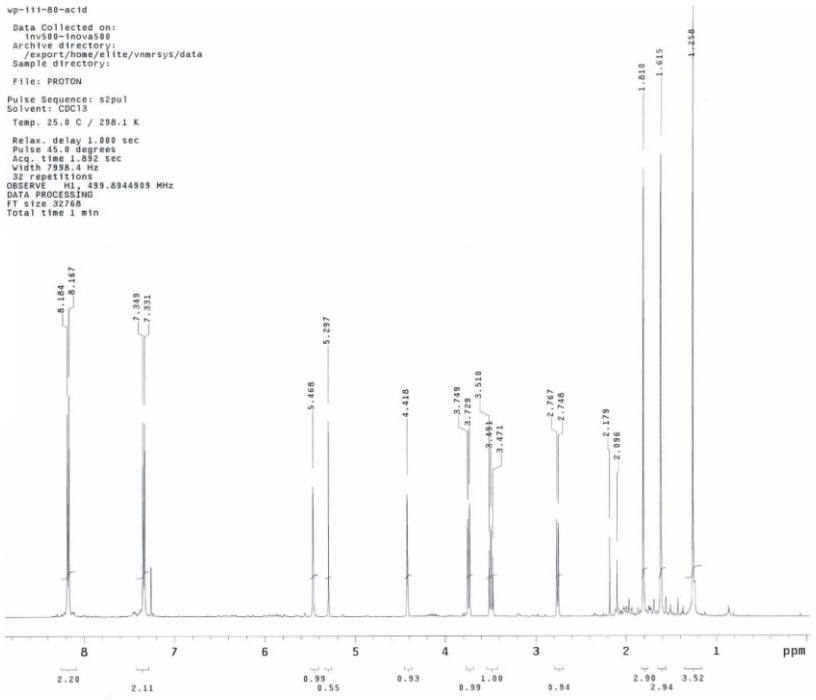

O2N
I

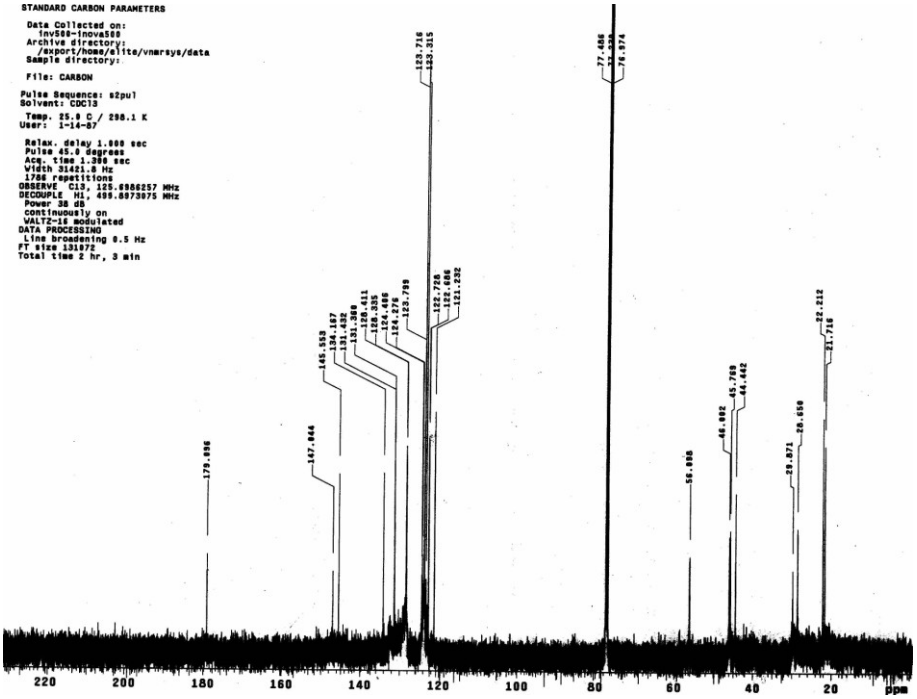
37

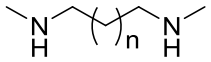

wp-I-56
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 81.4 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944916 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
8.206
8.203
8.189
7.451
7.435
7.259
6.588
6.165
2.646
2.643
2.164
2.025
2.011
2.008
8
7
6
5
4
3
2
1
ppm
2.52
2.59
1.00
1.15
4.35
4.00
5.56



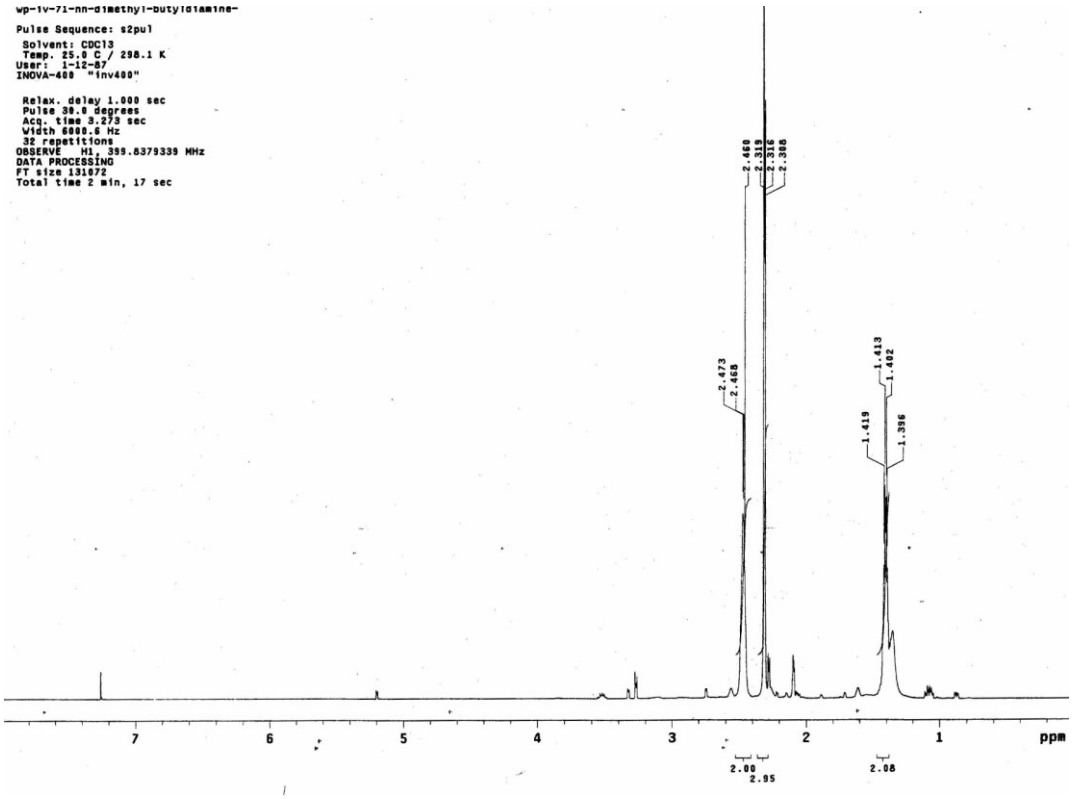
38

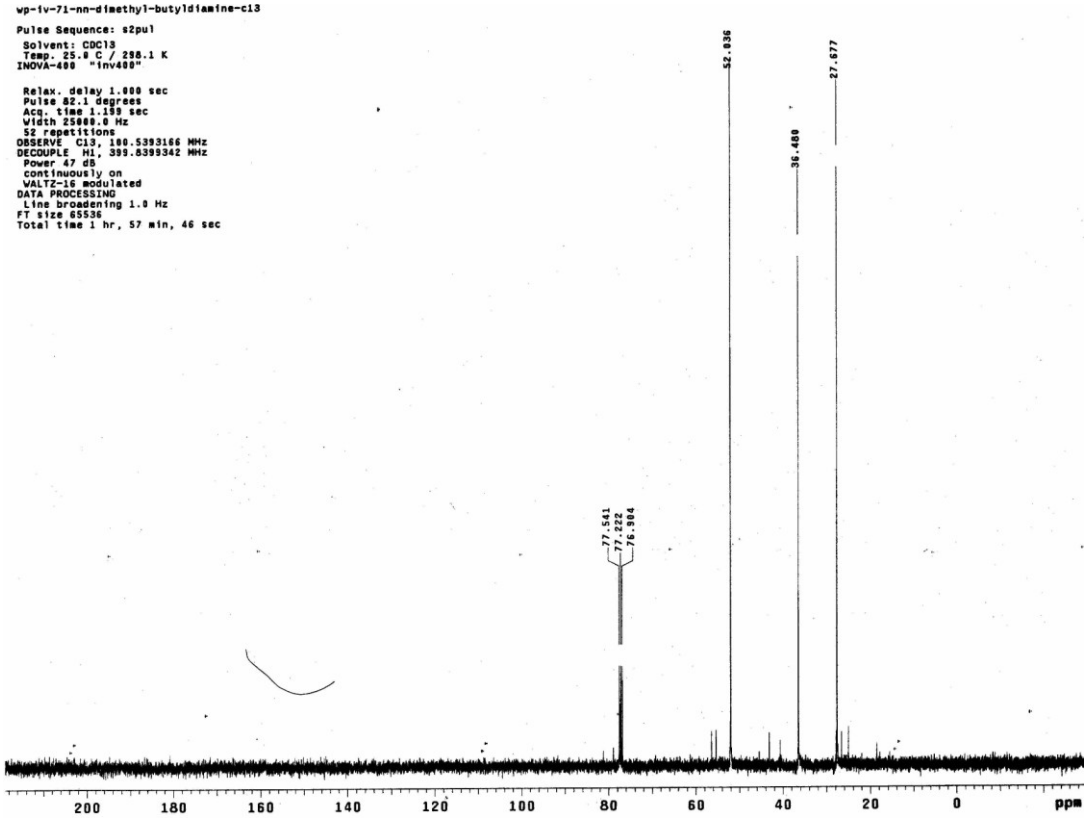

wp-iii-80-acid
Data Collected on:
inv580-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944989 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
8.184
8.167
7.349
7.331
5.468
5.297
4.418
3.749
3.728
3.510
3.491
3.471
2.767
2.748
2.179
2.096
1.810
1.615
1.258
ppm
2.20
2.11
0.99
0.55
0.93
0.99
1.00
0.94
2.90
2.94
3.52

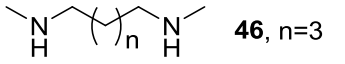

STANDARD CARBON PARAMETERS
Data Collected on:
inv580-inova580
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-97
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 31421.8 Hz
1788 repetitions
OBSERVE C13, 125.6986257 MHz
DECOUPLE H1, 499.8973075 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 2 hr, 3 min
183.716
153.315
77.486
76.974
179.096
147.944
146.569
134.167
131.432
131.380
128.355
124.486
124.274
123.799
122.728
121.486
121.292
55.096
46.892
45.789
44.442
29.871
28.659
22.212
21.716
ppm



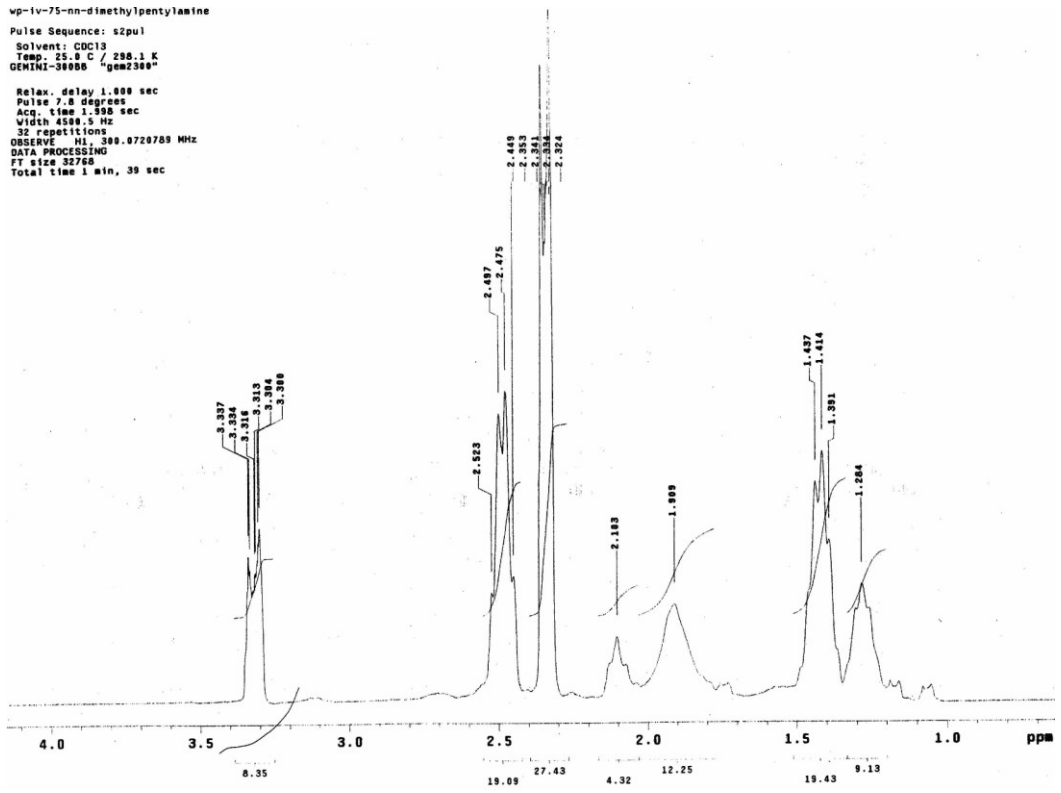
45, n=2

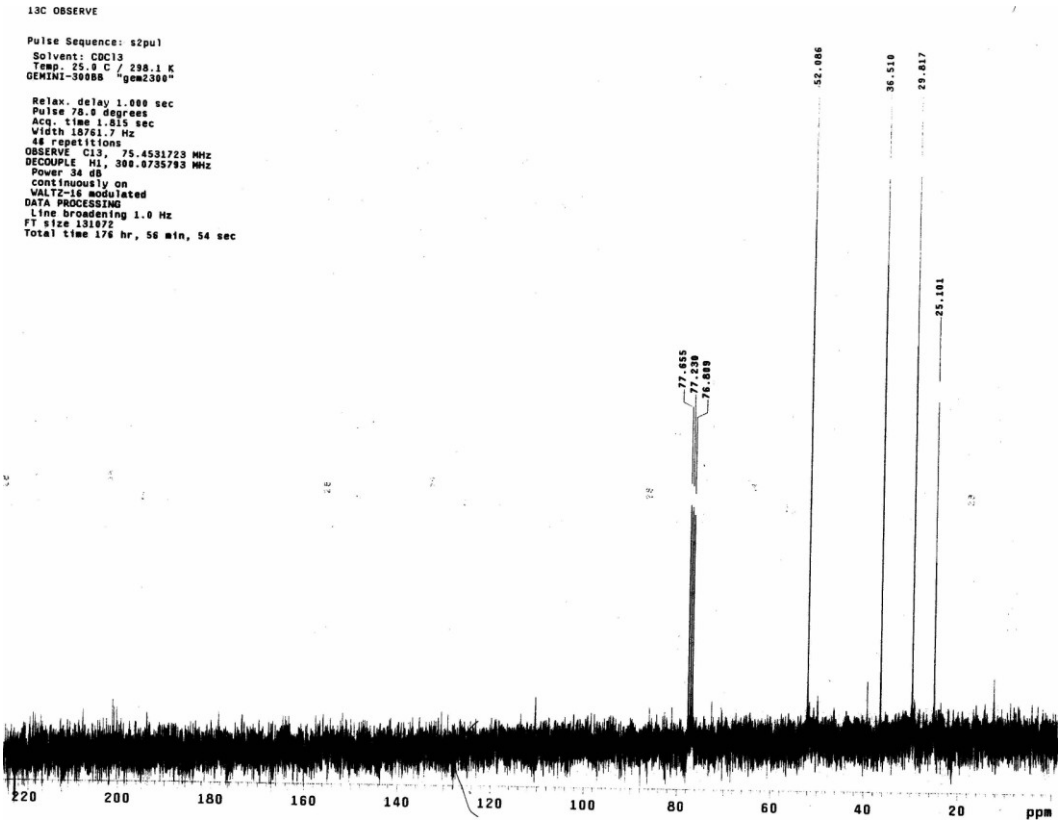

wp-iv-71-nn-dimethyl-butyldiamine-
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: i-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379339 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
2.469
2.319
2.316
2.308
2.473
2.468
1.413
1.402
1.419
1.396
7
6
5
4
3
2
1
ppm
2.00
2.95
2.08

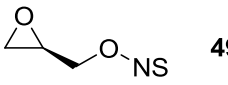

wp-iv-71-nn-dimethyl-butyldiamine-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
52 repetitions
OBSERVE C13, 100.5393166 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
52.836
36.489
27.677
77.541
77.222
76.904
200
180
160
140
120
100
80
60
40
20
0
ppm



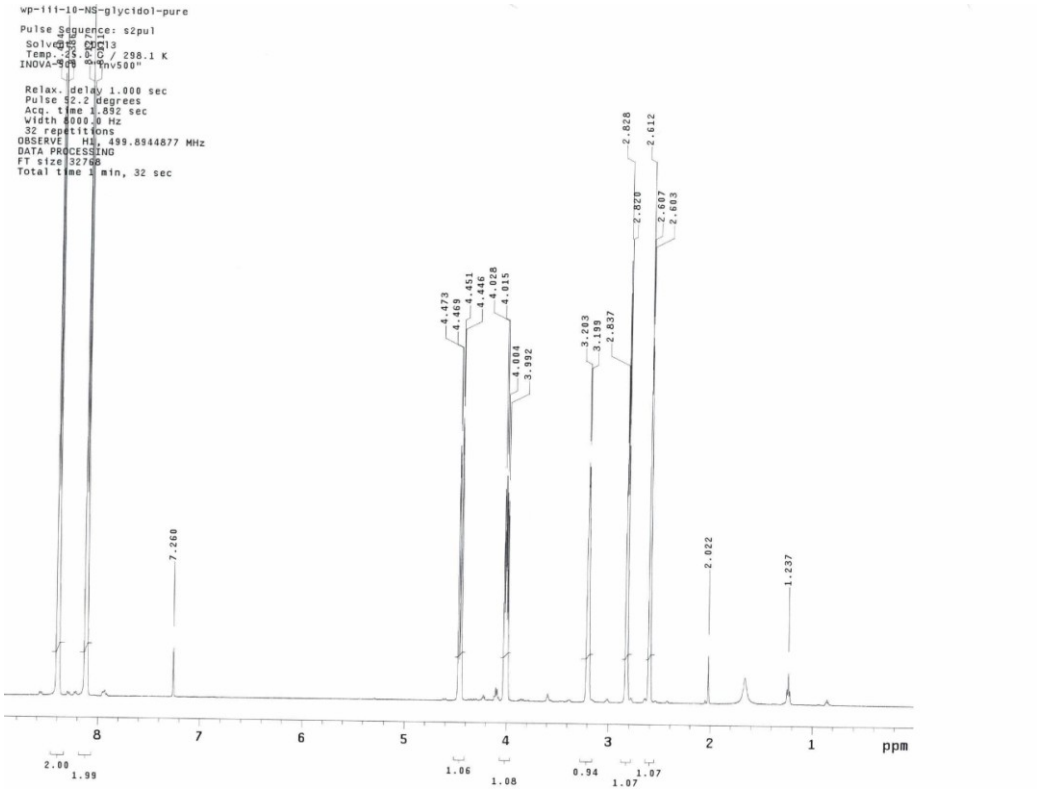
46, n=3

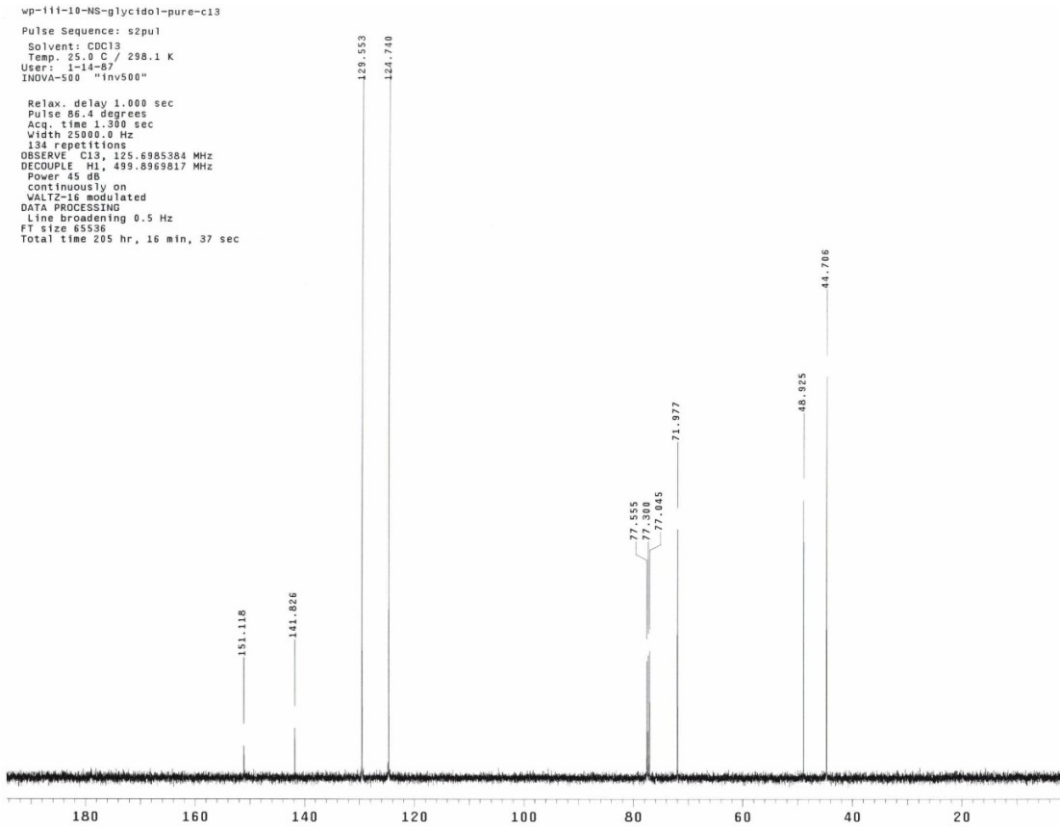

wp-iv-75-nn-dimethylpentylamine
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.598 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720789 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
3.337
3.334
3.316
3.313
3.304
3.300
2.523
2.497
2.475
2.449
2.353
2.334
2.324
2.183
1.969
1.437
1.414
1.391
1.284
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
8.35
19.09
27.43
4.32
12.25
19.43
9.13

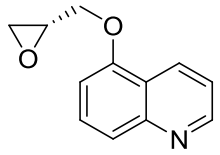

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 78.0 degrees
Acq. time 1.815 sec
Width 16761.7 Hz
48 repetitions
OBSERVE C13, 75.4531723 MHz
DECOUPLE H1, 300.0735793 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 176 hr, 56 min, 54 sec
52.086
36.510
29.817
25.101
77.655
77.230
76.809
220
200
180
160
140
120
100
80
60
40
20
ppm


O
O
NS

49


wp-iii-10-NS-glycidol-pure
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 52.2 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944877 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
7.260
4.473
4.469
4.461
4.446
4.028
4.015
4.004
3.992
3.203
3.199
2.837
2.828
2.820
2.612
2.607
2.603
2.022
1.237
ppm
2.00
1.99
1.06
1.08
0.94
1.07
1.07


wp-iii-10-NS-glycidol-pure-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-07
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 86.4 degrees
Acq. time 1.300 sec
Width 25000.0 Hz
134 repetitions
OBSERVE C13, 125.6985384 MHz
DECOUPLE H1, 499.8969817 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 205 hr, 16 min, 37 sec
151.118
141.826
129.553
124.740
77.555
77.300
77.045
71.977
48.925
44.706



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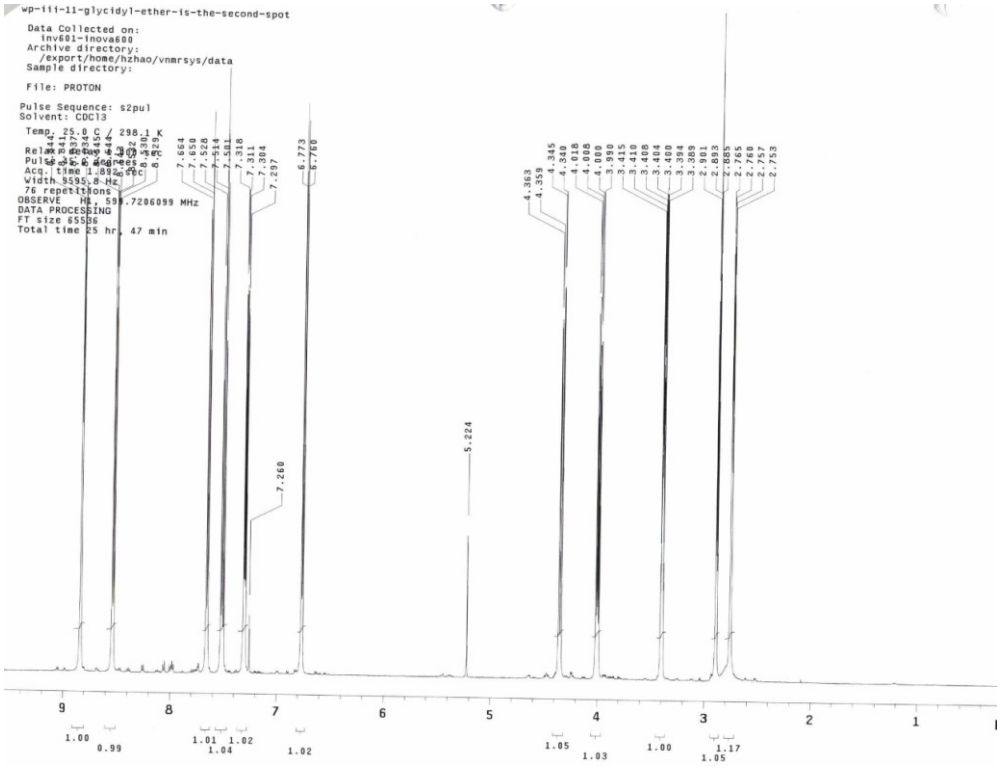
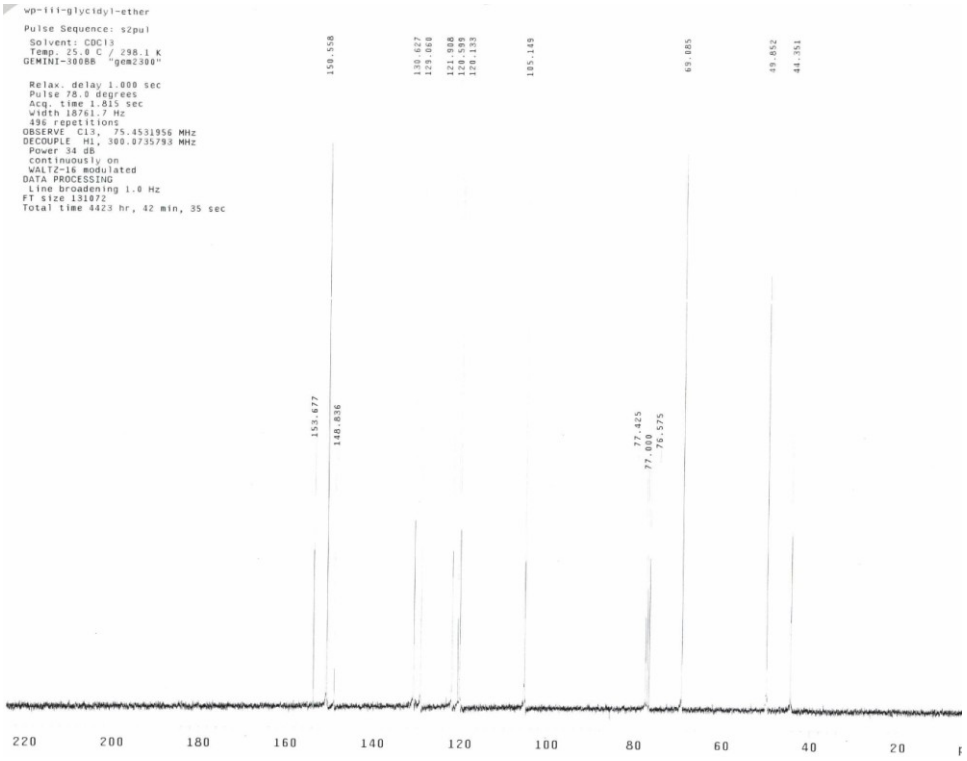
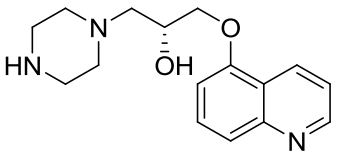
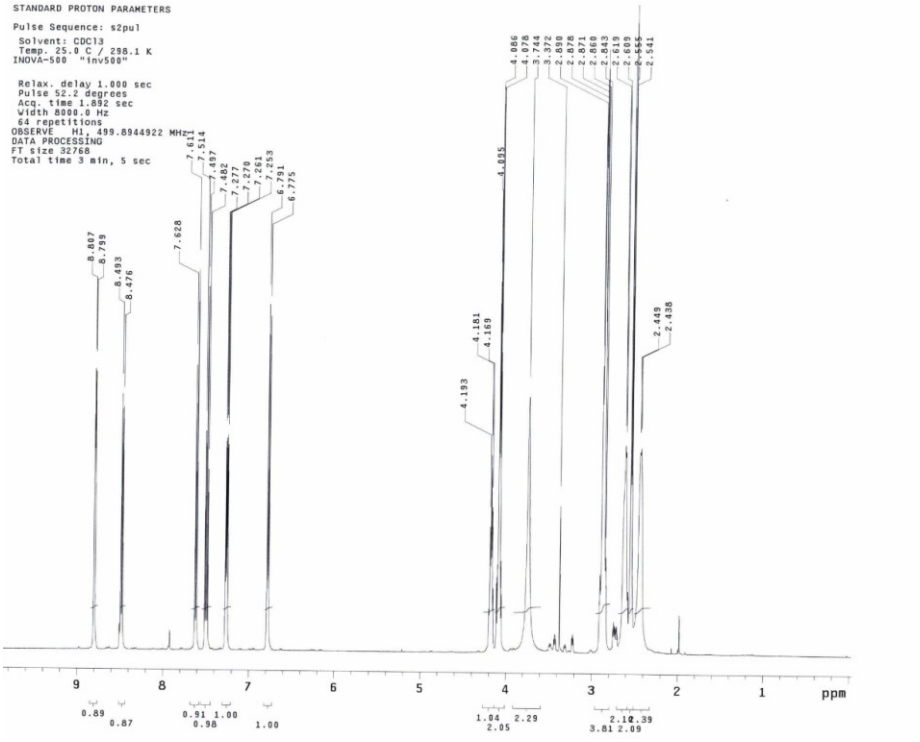
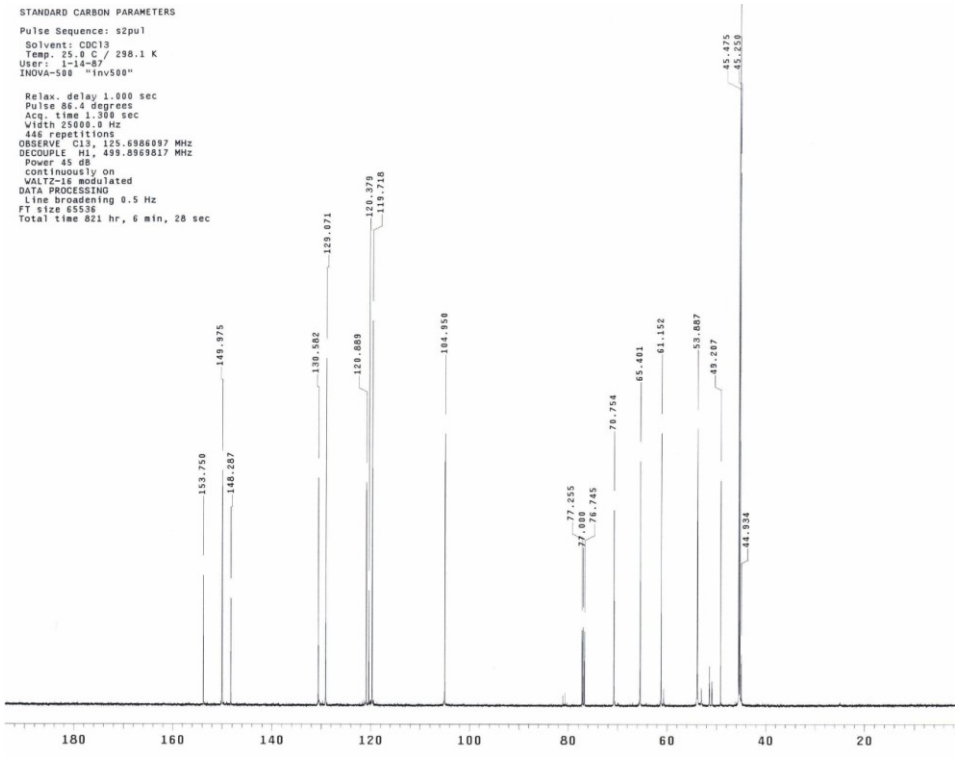

wp-iii-11-glycidyl-ether-is-the-second-spot
Data Collected on:
inv601-inova600
Archive directory:
/export/home/hzhao/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Acq. time 1.892 sec
Width 9595.8 Hz
76 repetitions
OBSERVE H1, 599.7206099 MHz
DATA PROCESSING
FT size 65536
Total time 25 hr, 47 min
8.329
7.664
7.650
7.528
7.514
7.316
7.311
7.304
7.297
6.773
6.760
5.224
7.260
4.363
4.359
4.345
4.340
4.018
4.004
4.000
3.990
3.415
3.410
3.408
3.404
3.400
3.394
3.389
2.901
2.893
2.885
2.765
2.760
2.757
2.753
1.00
0.99
1.01
1.04
1.02
1.02
1.05
1.03
1.00
1.17
1.05

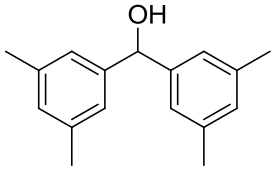

wp-iii-glycidyl-ether
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 78.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
496 repetitions
OBSERVE C13, 75.4531956 MHz
DECOUPLE H1, 300.0735793 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 4423 hr, 42 min, 35 sec
150.558
130.627
129.468
121.908
120.599
120.133
105.149
69.085
49.652
44.351
153.677
140.836
77.425
77.000
76.575


HN
N
OH
O
N

52


STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 52.2 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
64 repetitions
OBSERVE H1, 499.8944922 MHz
DATA PROCESSING
FT size 32768
Total time 3 min, 5 sec
ppm


STANDARD CARBON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-07
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 86.4 degrees
Acq. time 1.300 sec
Width 25000.0 Hz
446 repetitions
OBSERVE C13, 125.6986097 MHz
DECOUPLE H1, 499.8969817 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 821 hr, 6 min, 28 sec


OH

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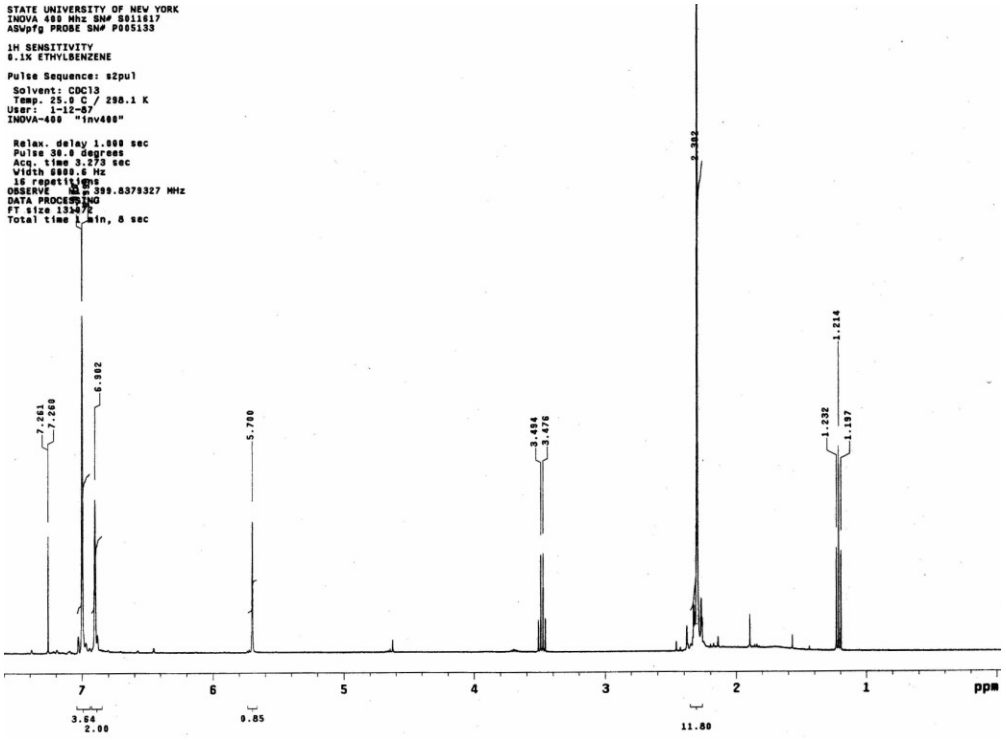
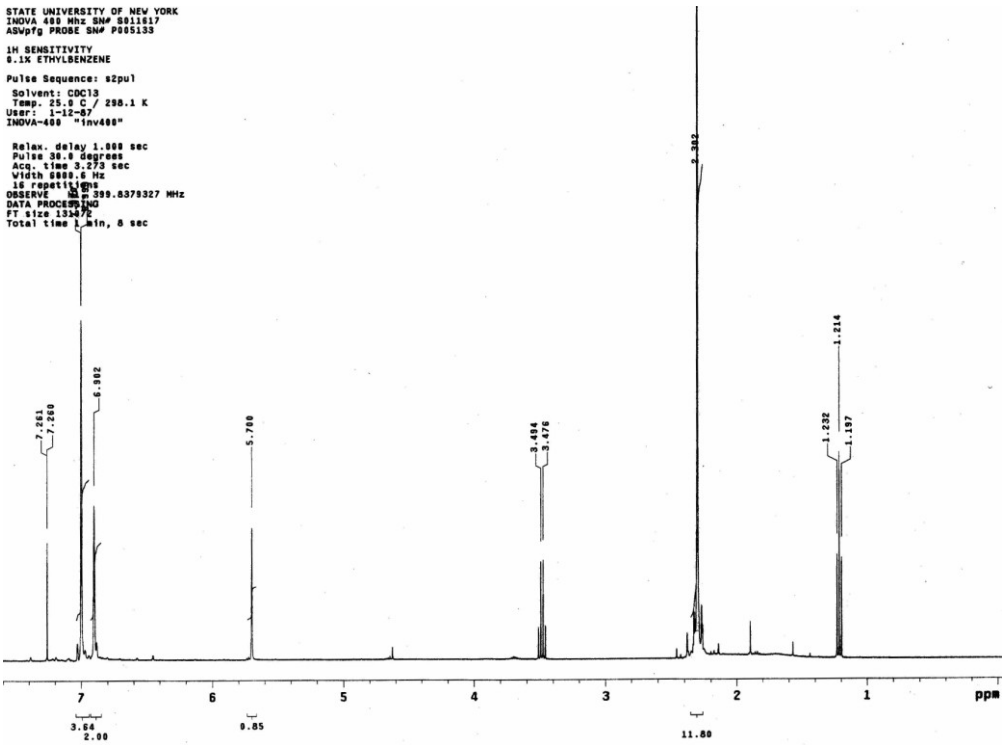
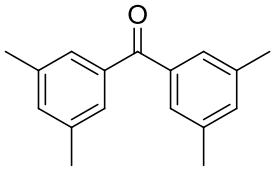

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6888.6 Hz
16 repetitions
OBSERVE
DATA PROCESSING
FT size 131072
Total time 1 min, 8 sec
7.261
7.260
6.982
5.700
3.484
3.476
2.382
1.214
1.232
1.197
7
6
5
4
3
2
1
ppm
3.64
2.00
0.85
11.80


STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6888.6 Hz
16 repetitions
OBSERVE
DATA PROCESSING
FT size 131072
Total time 1 min, 8 sec
7.261
7.260
6.982
5.700
3.484
3.476
2.382
1.214
1.232
1.197
7
6
5
4
3
2
1
ppm
3.64
2.00
0.85
11.80



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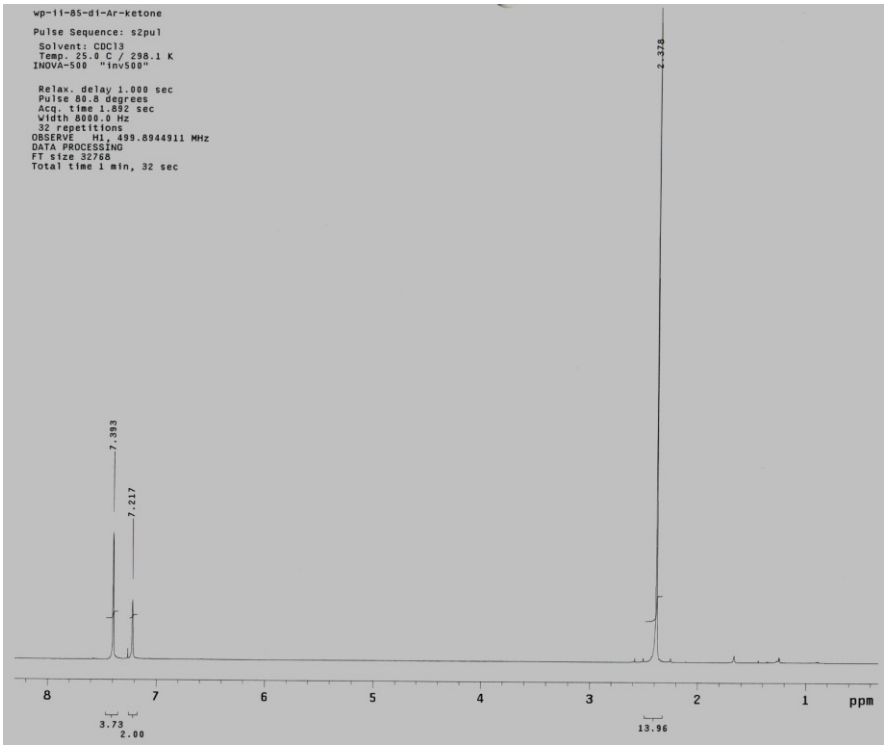
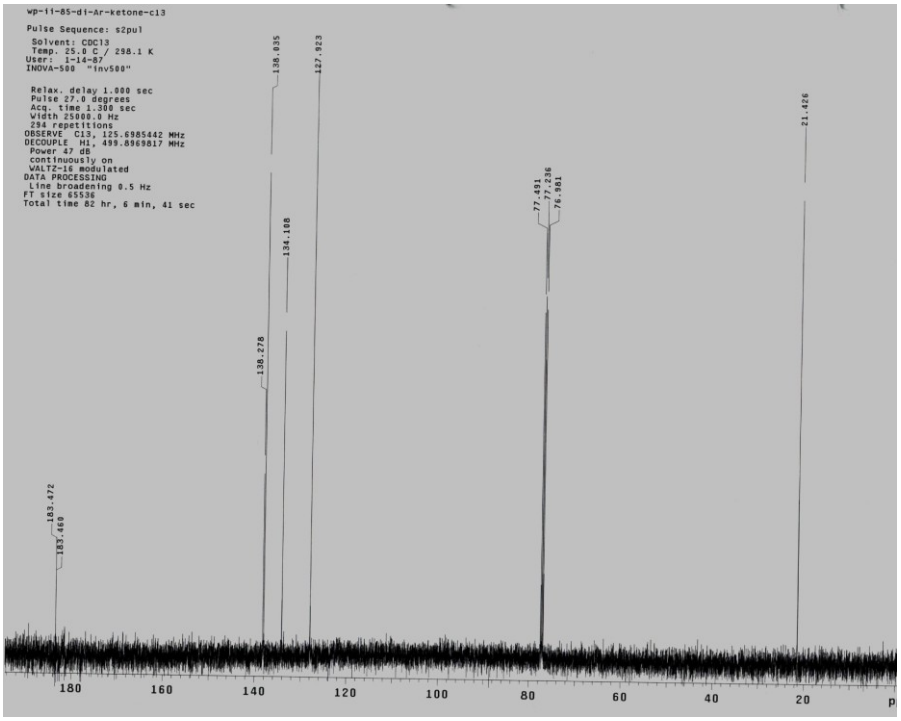
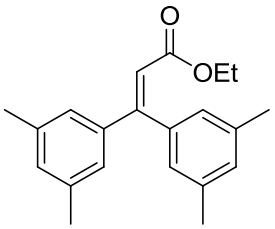
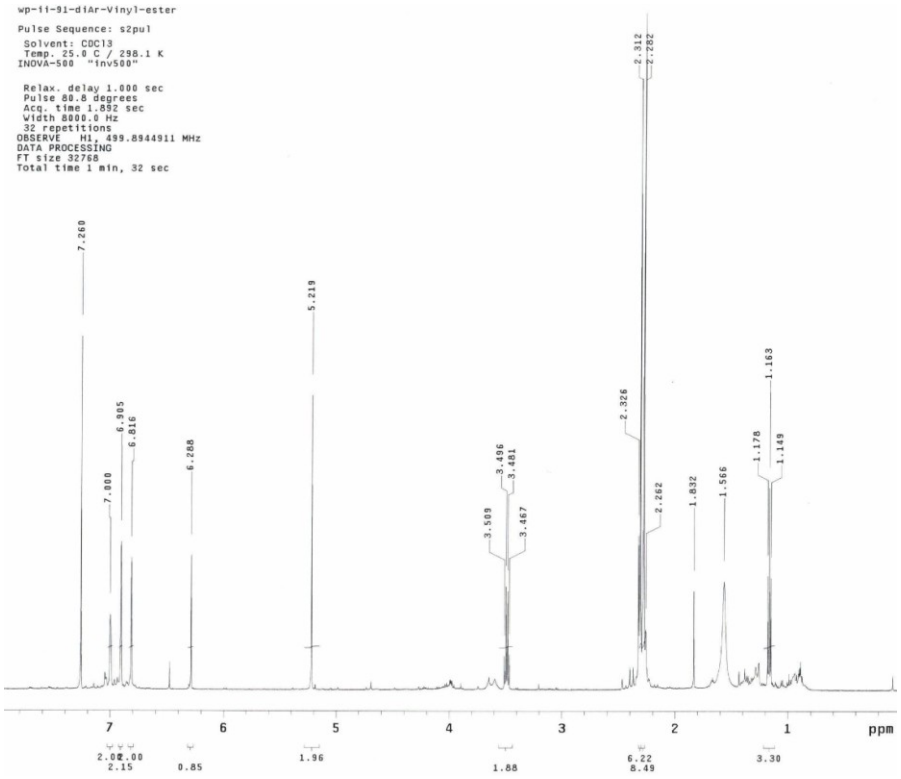
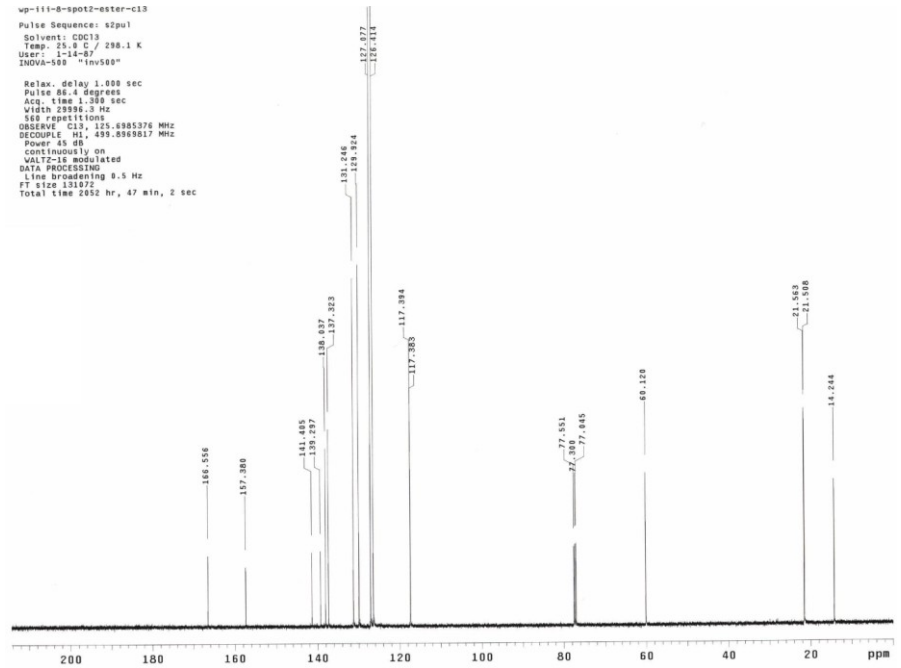

wp-ii-85-d1-Ar-ketone
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944911 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
2.378
7.393
7.217
8
7
6
5
4
3
2
1
ppm
3.73
2.00
13.96

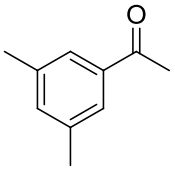

wp-ii-85-d1-Ar-ketone-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 27.0 degrees
Acq. time 1.300 sec
Width 25000.0 Hz
294 repetitions
OBSERVE C13, 125.6985442 MHz
DECOUPLE H1, 499.8969817 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 82 hr, 6 min, 41 sec
138.035
127.923
134.108
136.278
77.491
77.236
76.981
21.426
183.472
183.468
180
160
140
120
100
80
60
40
20


O
OEt

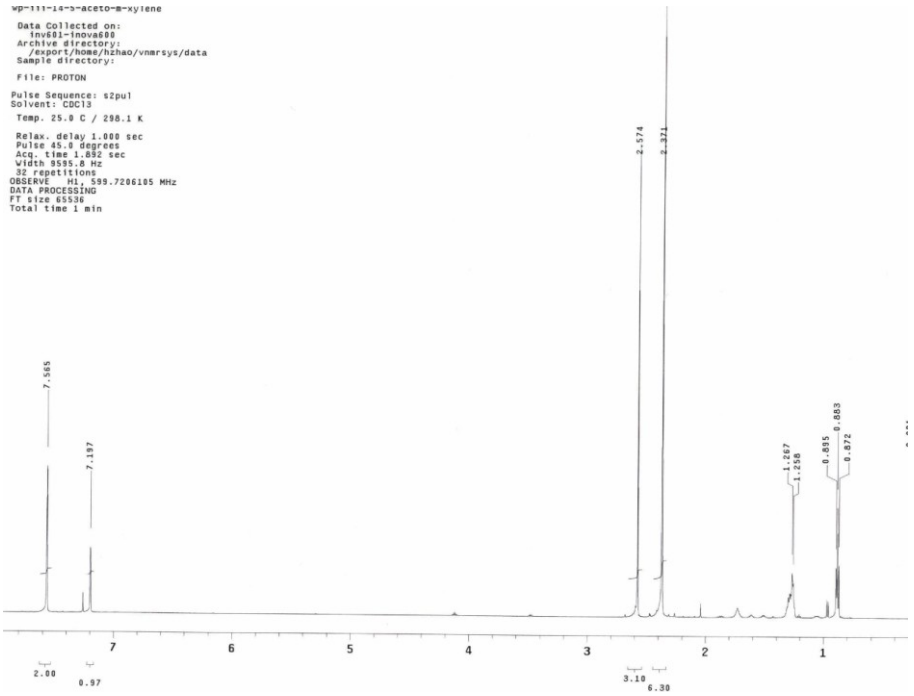
59

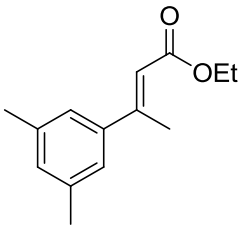

wp-ii-91-diAr-Vinyl-ester
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944911 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
7.260
7.000
6.985
6.816
6.288
5.219
3.496
3.481
3.509
3.467
2.326
2.312
2.262
1.832
1.566
1.178
1.163
1.149
7
6
5
4
3
2
1
ppm
2.00
2.15
0.85
1.96
1.88
6.22
8.49
3.30


wp-iii-8-spot2-ester-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 86.4 degrees
Acq. time 1.388 sec
Width 29996.3 Hz
560 repetitions
OBSERVE C13, 125.6985376 MHz
DECOUPLE H1, 499.8969817 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 2052 hr, 47 min, 2 sec
166.556
157.380
141.495
138.257
138.037
137.323
131.246
131.024
127.977
126.414
117.384
117.383
77.551
77.380
77.045
60.120
21.583
21.508
14.244
200
180
160
140
120
100
80
60
40
20
ppm

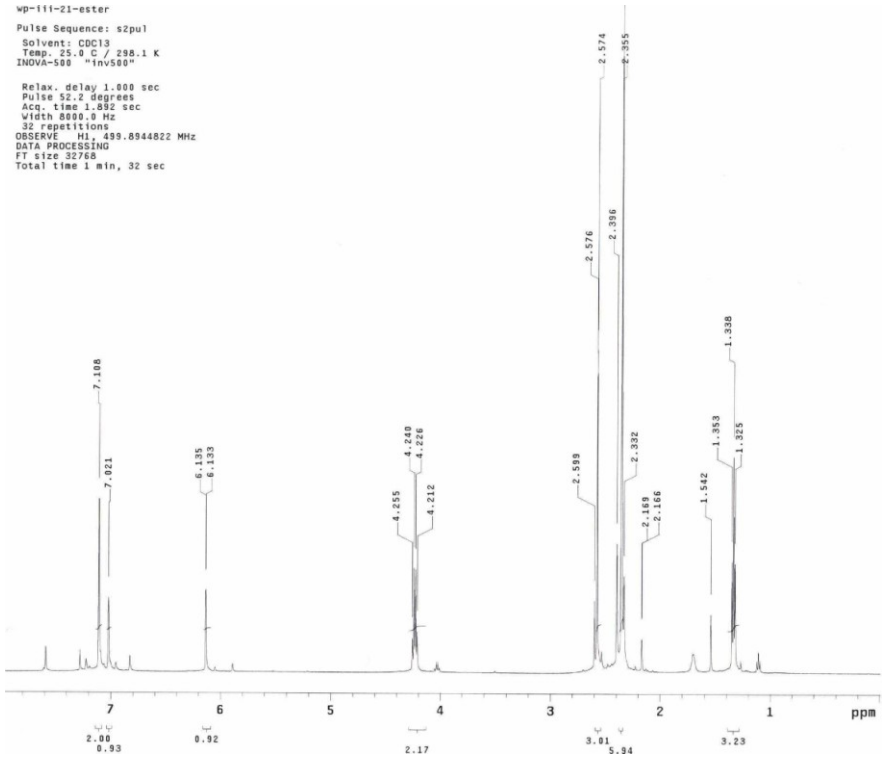


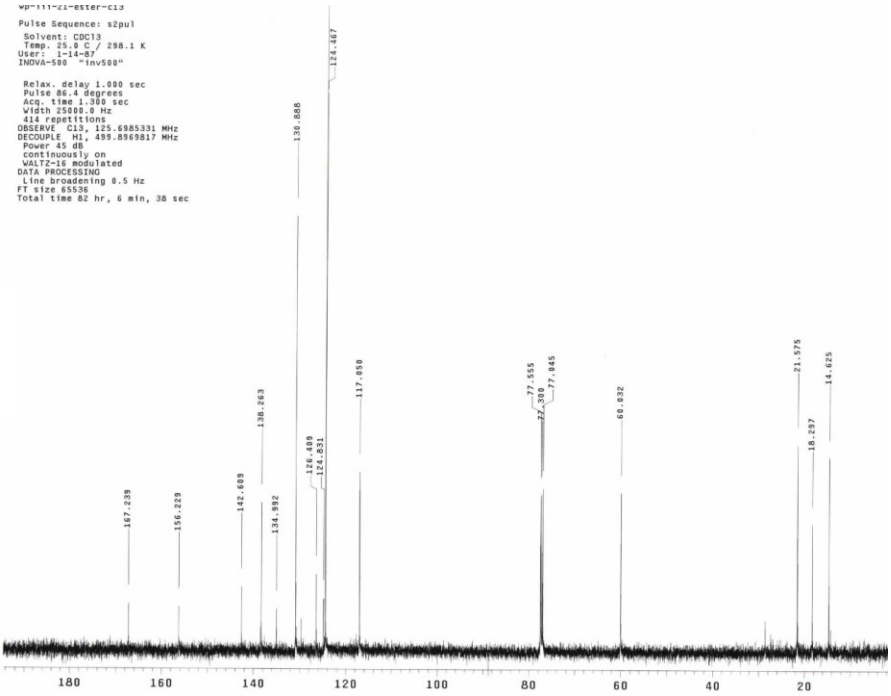
61

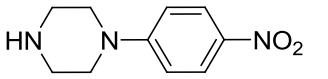

wp-111-14-5-aceto-m-xylene
Data Collected on:
inv601-inova600
Archive directory:
/export/home/hzhao/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 9595.8 Hz
32 repetitions
OBSERVE H1, 599.7206185 MHz
DATA PROCESSING
FT size 65536
Total time 1 min
7.565
7.197
2.574
2.321
1.267
1.258
0.895
0.883
0.872
7
6
5
4
3
2
1
2.00
0.97
3.10
6.30


O
OEt

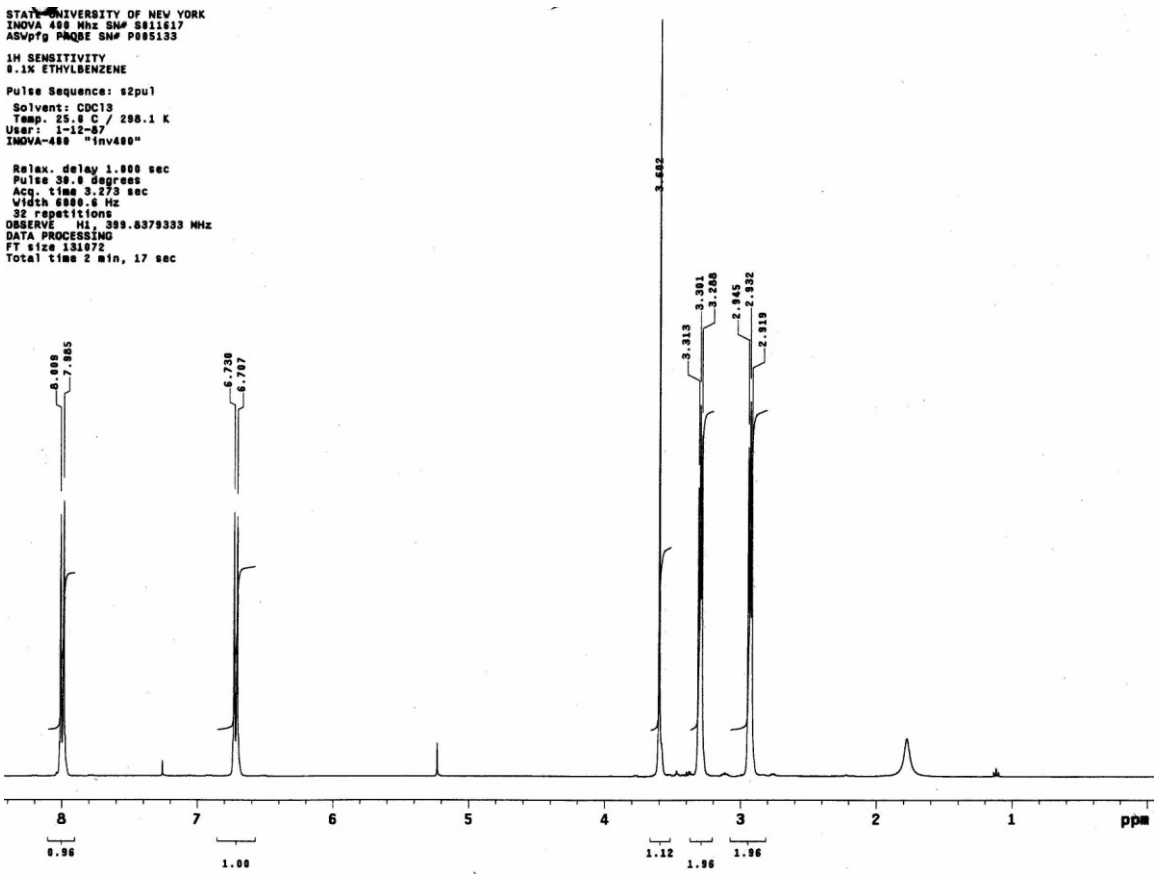
62

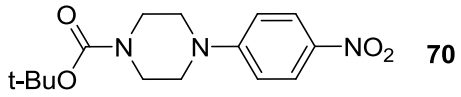

wp-iii-21-ester
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 52.2 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944822 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
7.108
7.021
6.135
6.133
4.240
4.226
4.255
4.212
2.599
2.574
2.576
2.386
2.355
2.332
2.168
2.166
1.542
1.353
1.338
1.325
7
6
5
4
3
2
1
ppm
2.00
0.93
0.92
2.17
3.01
5.94
3.23


wp-iii-21-ester-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: l-14-87
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 86.4 degrees
Acq. time 1.300 sec
Width 25000.0 Hz
414 repetitions
OBSERVE C13, 125.6985331 MHz
DECOUPLE H1, 499.8969817 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 82 hr, 6 min, 38 sec
167.239
156.229
142.689
130.263
134.992
130.886
126.489
124.831
124.467
117.050
77.555
77.300
77.045
60.632
21.575
18.297
14.625
180
160
140
120
100
80
60
40
20

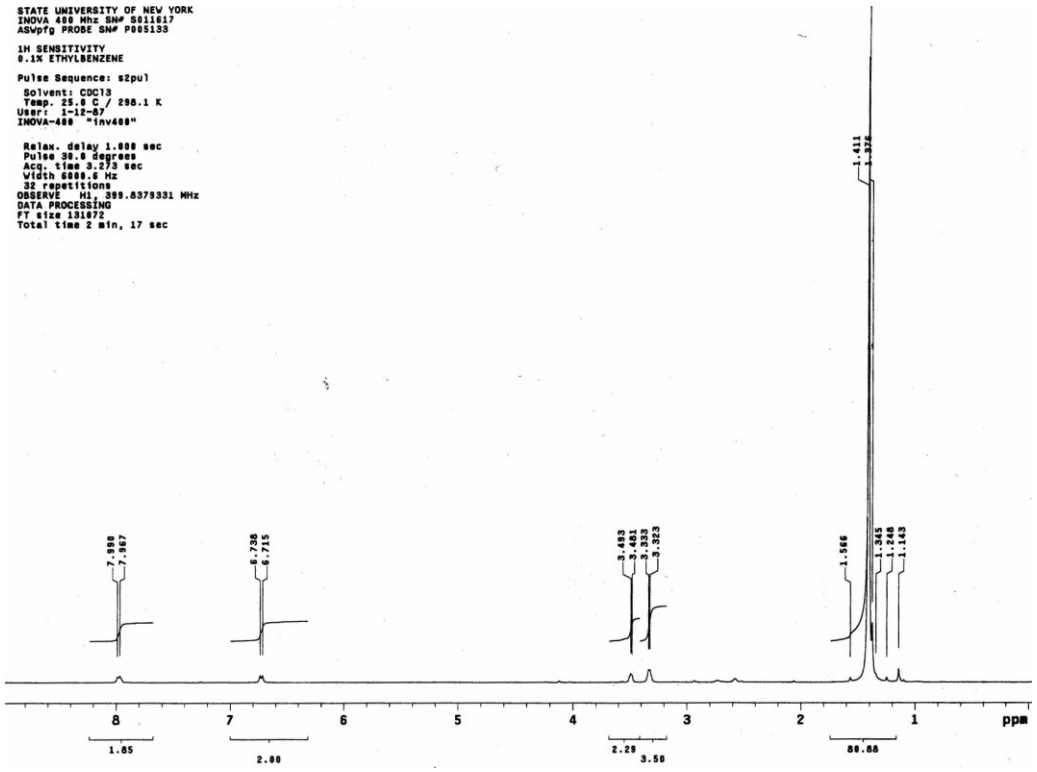

HN
N
NO2

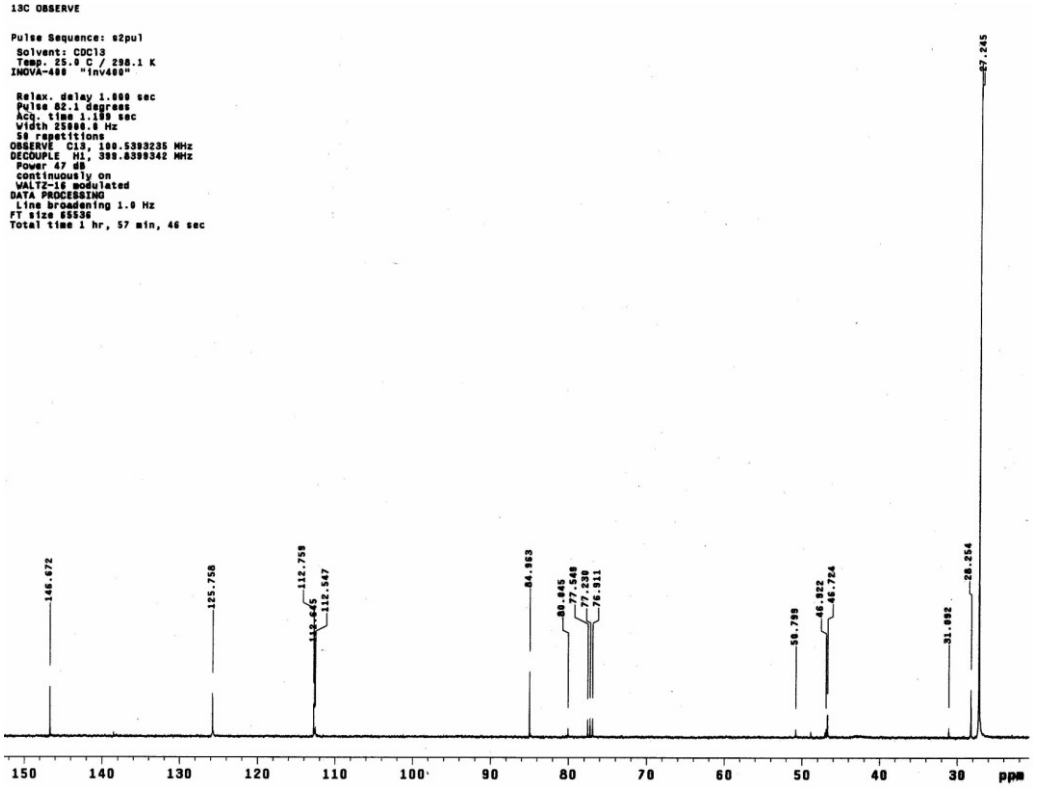
69

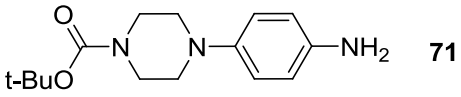

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S811617
ASVpfg PROBE SN# P085133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Usar: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379333 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
8.008
7.985
6.738
6.707
3.682
3.313
3.301
3.288
2.945
2.932
2.919
8
7
6
5
4
3
2
1
ppm
0.96
1.00
1.12
1.96
1.96


O
N
N
NO2
t-BuO

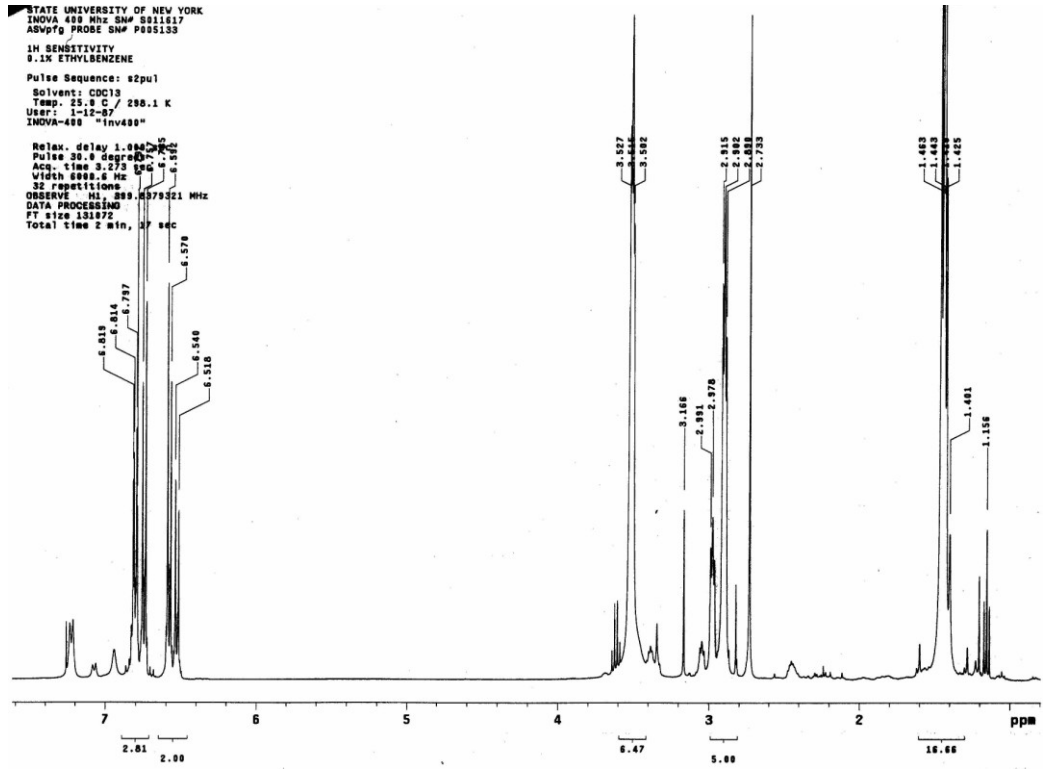
70

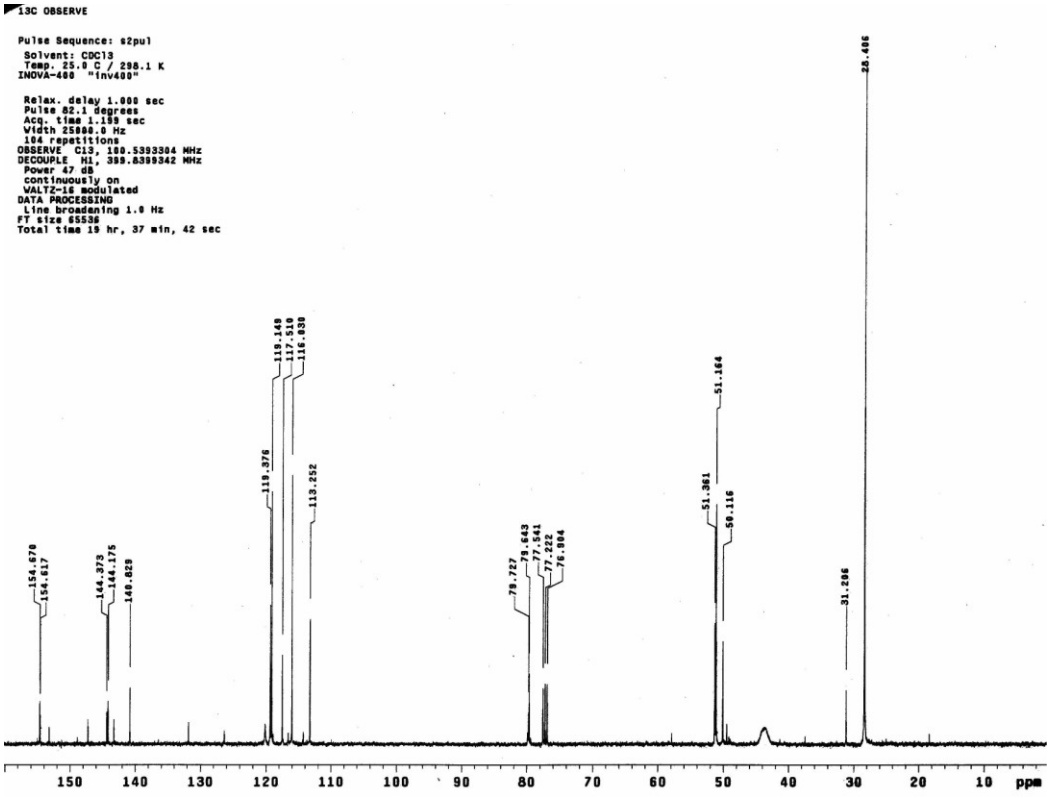

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-97
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379331 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
7.998
7.987
6.738
6.715
3.483
3.465
3.333
3.323
1.566
1.411
1.376
1.345
1.246
1.143
8
7
6
5
4
3
2
1
ppm
1.85
2.00
2.29
3.50
80.88

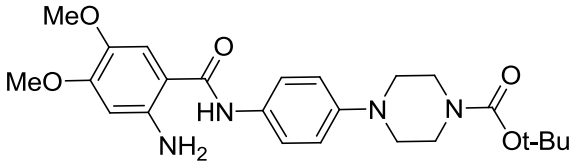

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
59 repetitions
OBSERVE C13, 100.5383235 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
146.672
125.758
112.759
112.445
112.547
84.963
80.845
77.548
77.230
76.911
50.758
46.822
46.724
31.092
28.254
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm


O
N
N
NH2
t-BuO

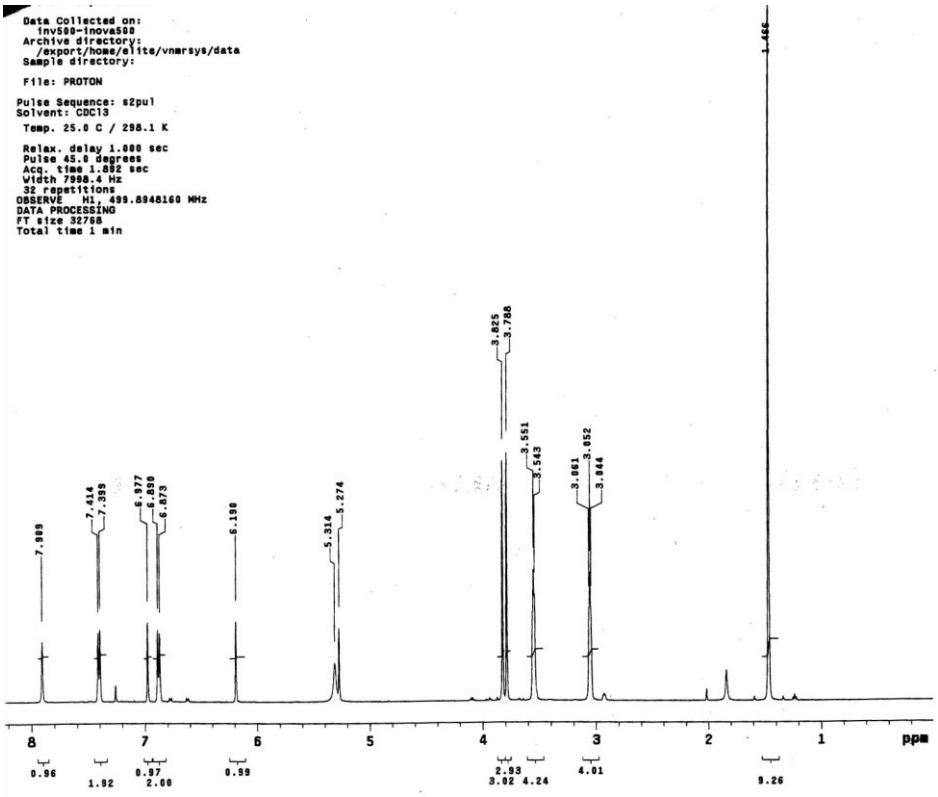
71

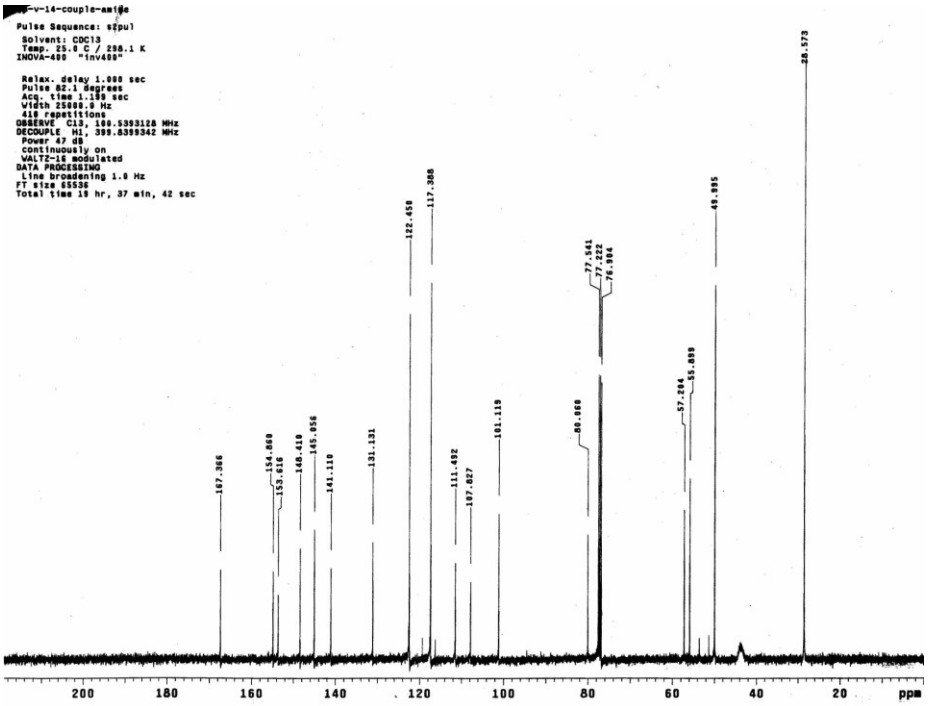

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASVpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6868.6 Hz
32 repetitions
OBSERVE H1, 399.8379321 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
6.819
6.814
6.797
6.578
6.540
6.516
3.527
3.502
3.166
2.991
2.978
2.915
2.902
2.888
2.733
1.463
1.425
1.401
1.156
ppm
2.81
2.00
6.47
5.89
16.66

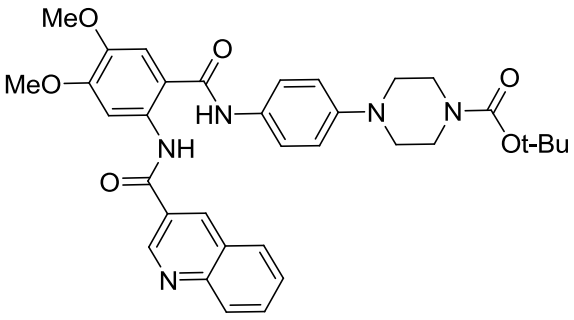

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.155 sec
Width 25888.0 Hz
104 repetitions
OBSERVE C13, 100.5393384 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.8 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
154.670
154.617
144.373
144.175
140.028
119.376
113.252
79.727
79.643
77.541
77.222
76.804
51.381
51.164
50.116
31.286
28.486
ppm


MeO
MeO
O
HN
NH2
N
N
O
Ot-Bu

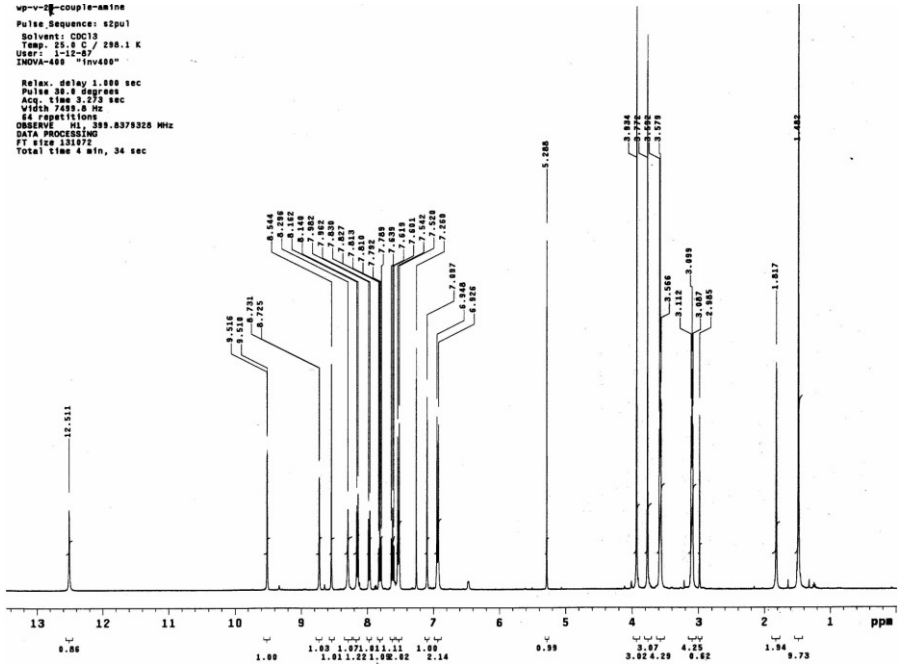
74

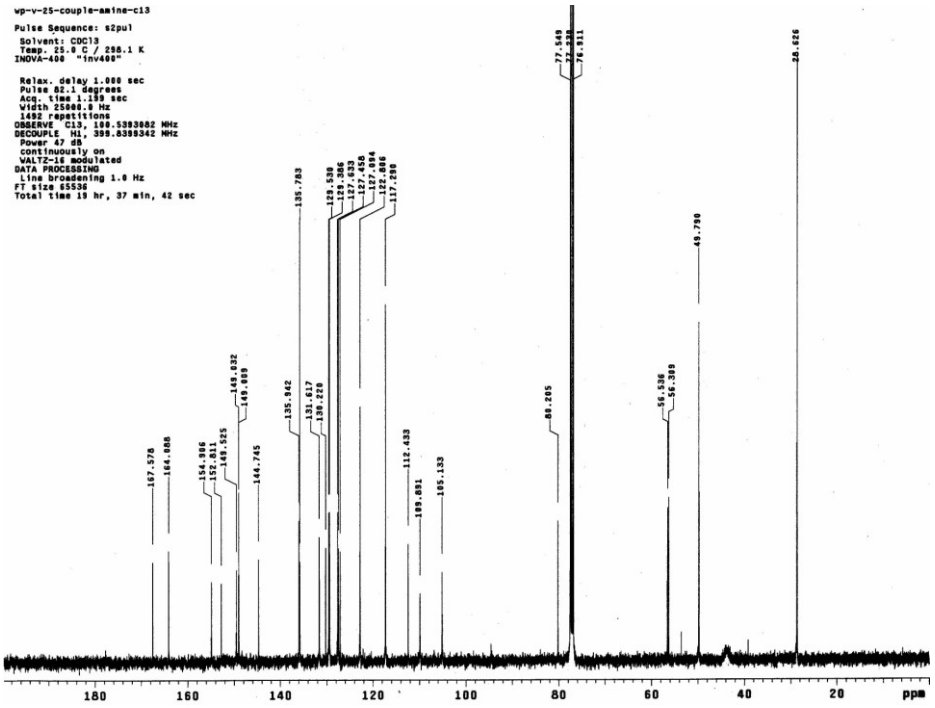

Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.882 sec
Width 7988.4 Hz
32 repetitions
OBSERVE H1, 499.8848160 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
7.989
7.414
7.399
6.877
6.859
6.873
6.198
5.314
5.274
3.825
3.788
3.551
3.543
3.061
3.052
3.044
1.466
8
7
6
5
4
3
2
1
ppm
0.96
1.92
0.97
2.00
0.99
2.93
3.02
4.24
4.01
9.26

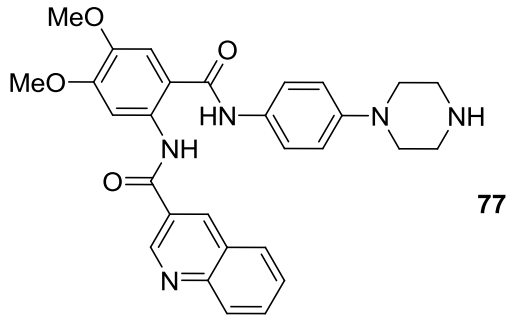

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
418 repetitions
OBSERVE C13, 100.5393128 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 13 hr, 37 min, 42 sec
167.366
154.660
153.616
148.419
145.956
141.110
131.131
122.458
117.388
111.492
107.027
101.119
86.068
77.541
77.222
76.904
67.284
65.899
49.895
28.573
200
180
160
140
120
100
80
60
40
20
ppm


MeO
MeO
O
HN
N
N
O
Ot-Bu
NH
O
N

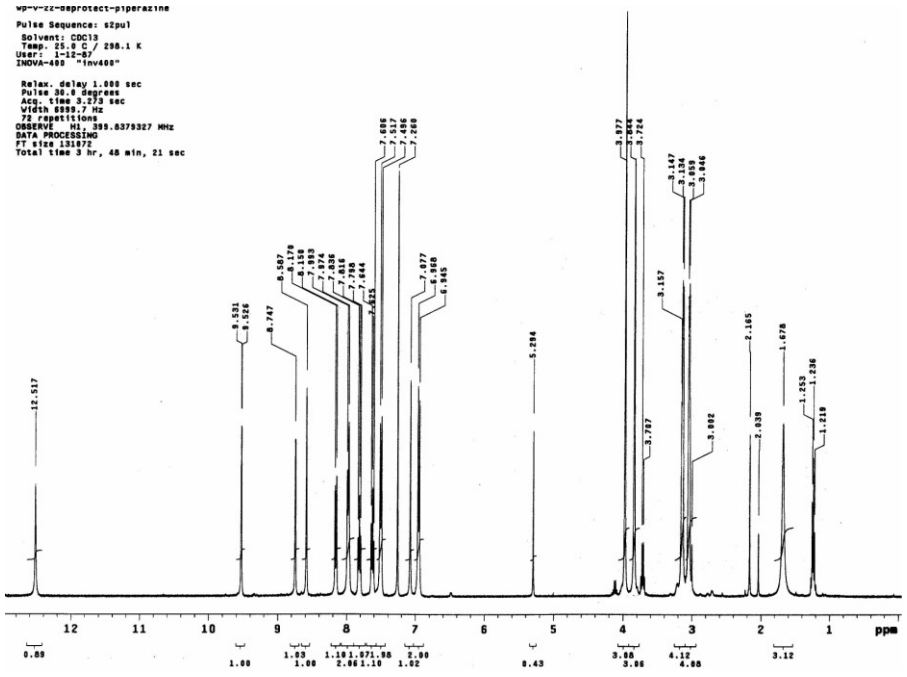
76

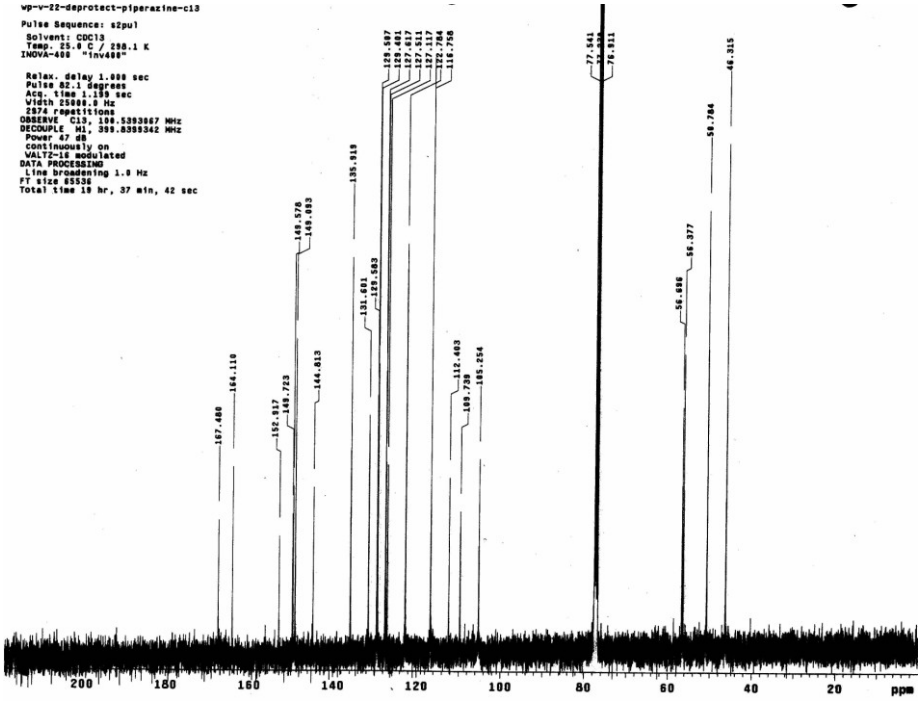

wp-v-25-couple-amine
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: i-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 7499.8 Hz
64 repetitions
OBSERVE H1, 399.8379328 MHz
DATA PROCESSING
FT size 131072
Total time 4 min, 34 sec
ppm

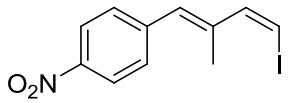

wp-v-25-couple-amine-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1492 repetitions
OBSERVE C13, 100.5383682 MHz
DECOUPLE H1, 399.8389342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
ppm


MeO
MeO
O
HN
N
NH
NH
O
N

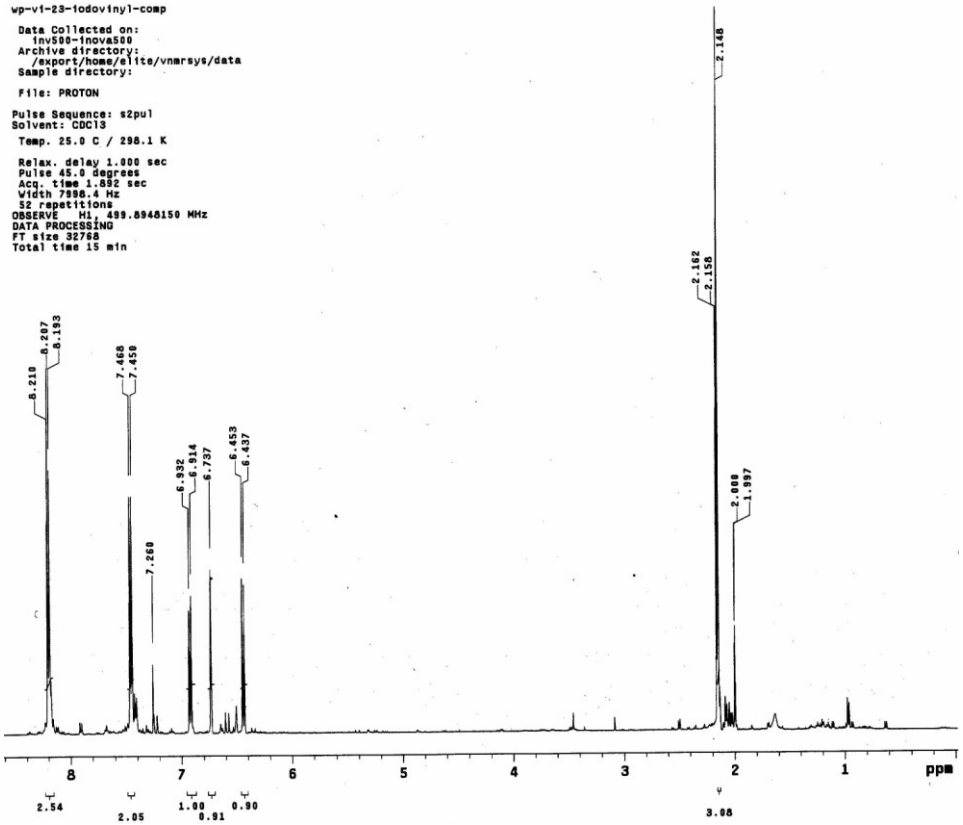
77

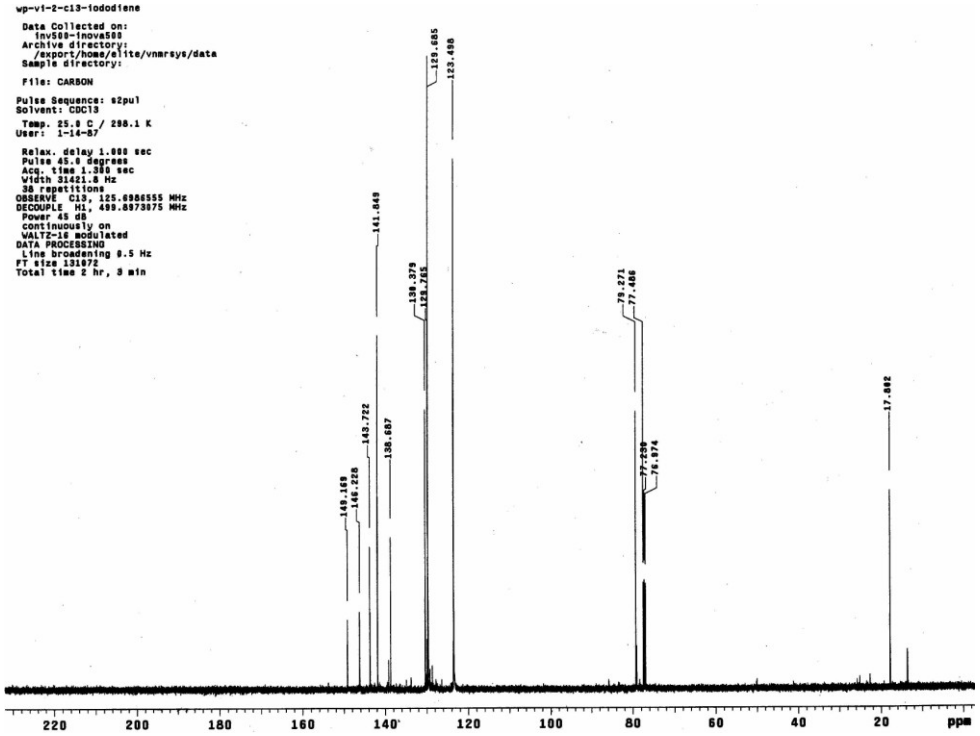

wp-v-22-deprotect-piperazine
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 8999.7 Hz
72 repetitions
OBSERVE H1, 399.8379327 MHz
DATA PROCESSING
FT size 131072
Total time 3 hr, 48 min, 21 sec
12.517
8.531
8.526
8.747
8.587
8.179
8.158
7.993
7.974
7.838
7.816
7.798
7.644
7.623
7.696
7.517
7.496
7.488
7.077
6.960
6.945
5.294
3.977
3.964
3.784
3.157
3.147
3.134
3.059
3.046
3.787
3.092
2.165
2.039
1.678
1.253
1.236
1.219
ppm

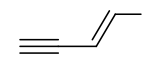

wp-v-22-deprotect-piperazine-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
2974 repetitions
OBSERVE C13, 100.5393867 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
167.480
164.110
152.917
149.723
148.578
148.493
144.813
135.918
131.681
129.583
129.587
129.481
129.417
127.611
127.117
122.784
116.758
112.463
109.738
105.254
77.541
77.311
76.911
58.784
56.377
56.098
46.315
ppm


O2N
I

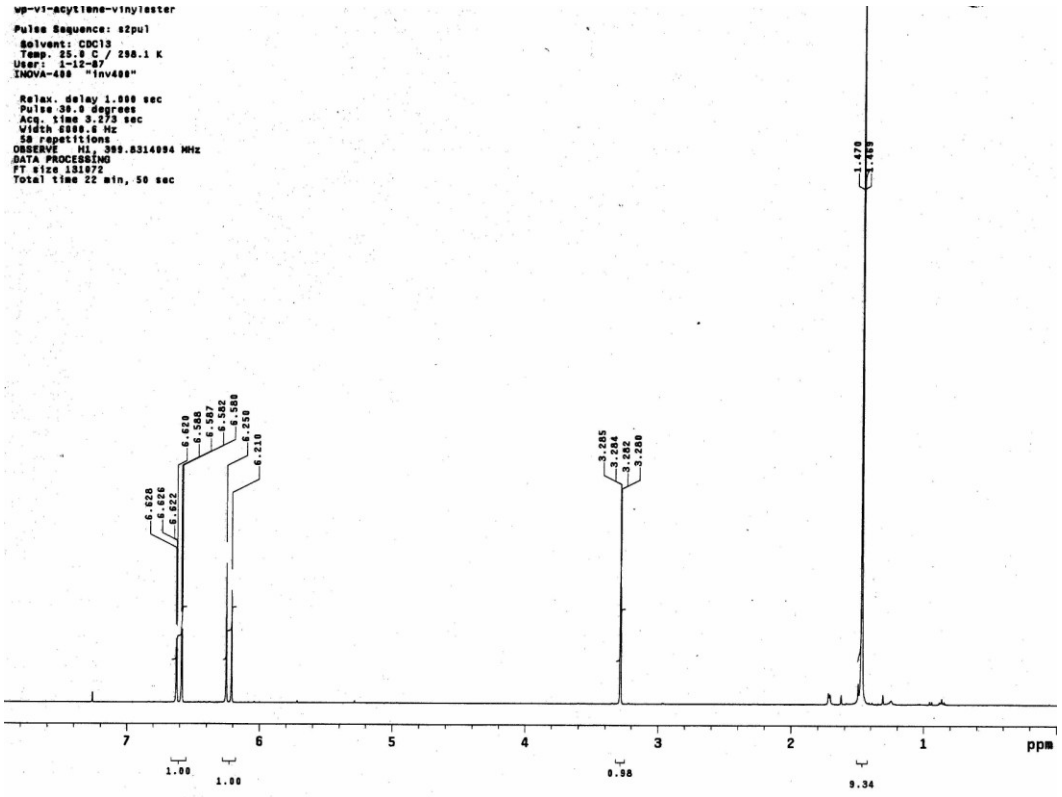
79

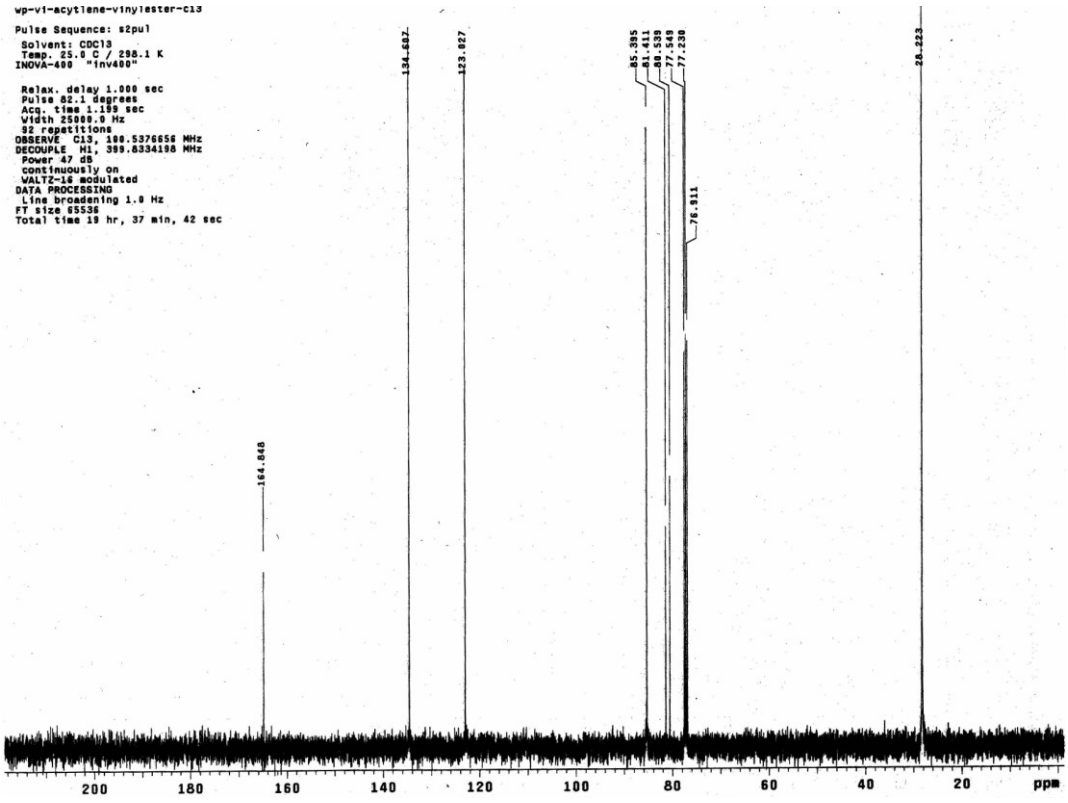

wp-vi-23-iodovinyl-comp
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
52 repetitions
OBSERVE H1, 499.8948150 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
8.219
8.207
8.193
7.468
7.459
7.260
6.932
6.914
6.737
6.453
6.437
2.162
2.158
2.148
2.009
1.997
ppm
2.54
2.05
1.00
0.91
0.90
3.08

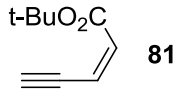

wp-vi-2-c13-iododiene
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
38 repetitions
OBSERVE C13, 125.6986555 MHz
DECOUPLE H1, 499.8973875 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 2 hr, 8 min
149.169
146.228
143.722
141.849
138.687
138.379
131.765
129.685
128.498
79.271
77.466
77.039
76.974
17.892
ppm


CO2t-Bu

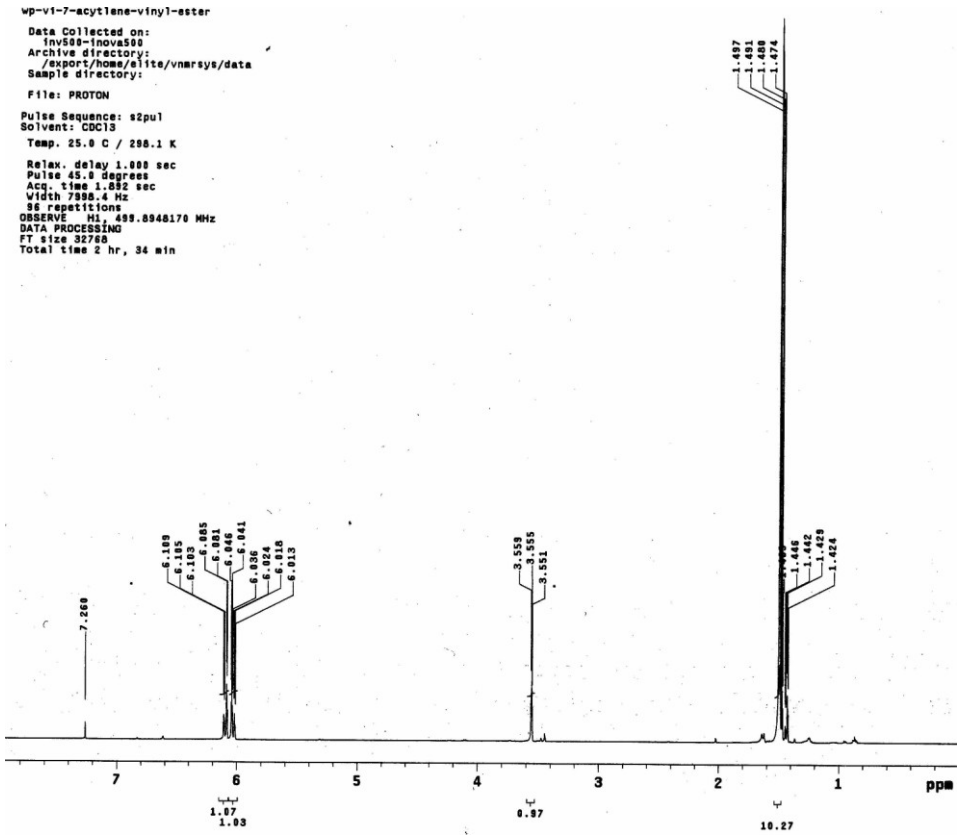
80

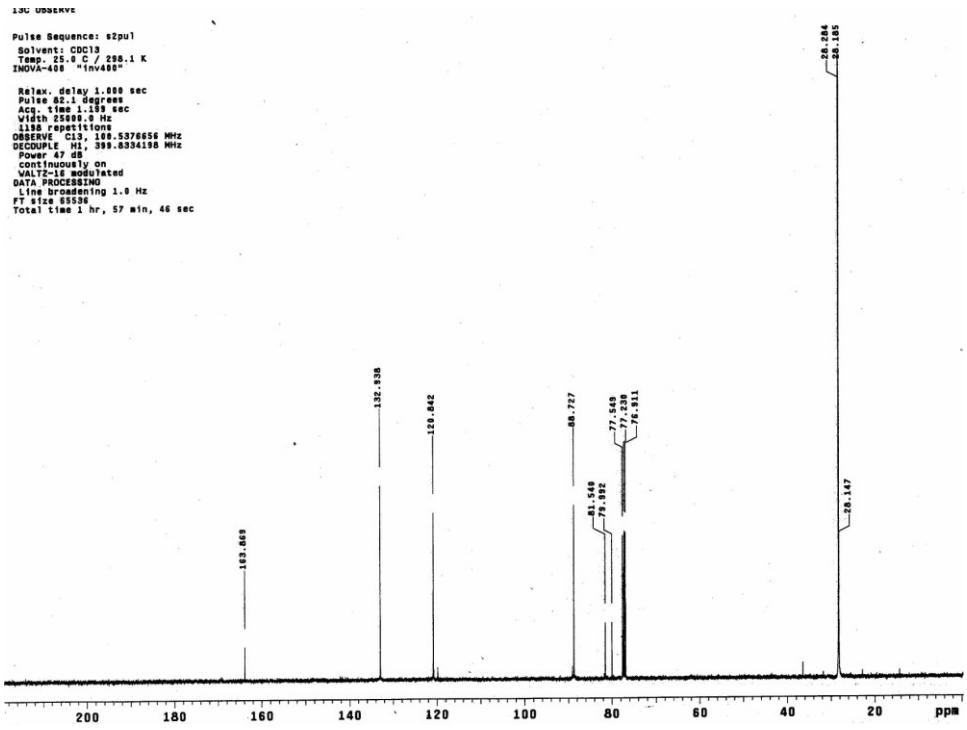

wp-v1-acytlene-vinylester
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
58 repetitions
OBSERVE H1, 399.8314094 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
6.628
6.626
6.622
6.588
6.587
6.582
6.580
6.259
6.210
3.285
3.284
3.282
3.280
1.479
1.469
7
6
5
4
3
2
1
ppm
1.00
1.00
0.98
9.34

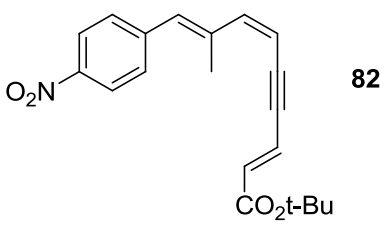

wp-v1-acytlene-vinylester-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
92 repetitions
OBSERVE C13, 100.5376656 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
164.648
134.687
123.027
85.395
81.411
80.539
77.549
77.230
76.911
28.223
200
180
160
140
120
100
80
60
40
20
ppm


t-BuO2C

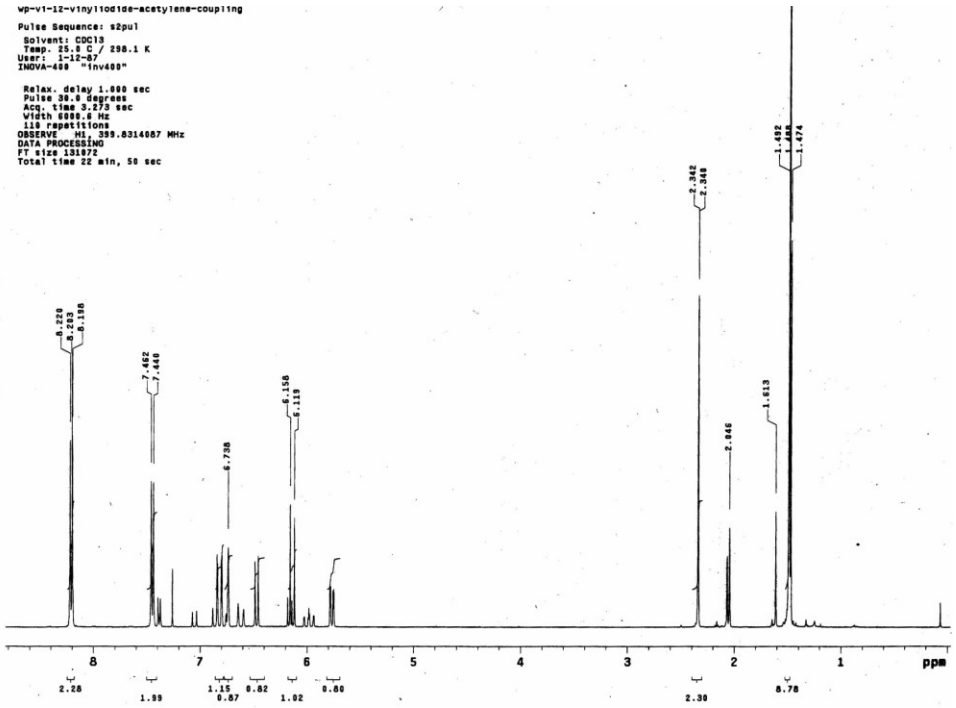
81

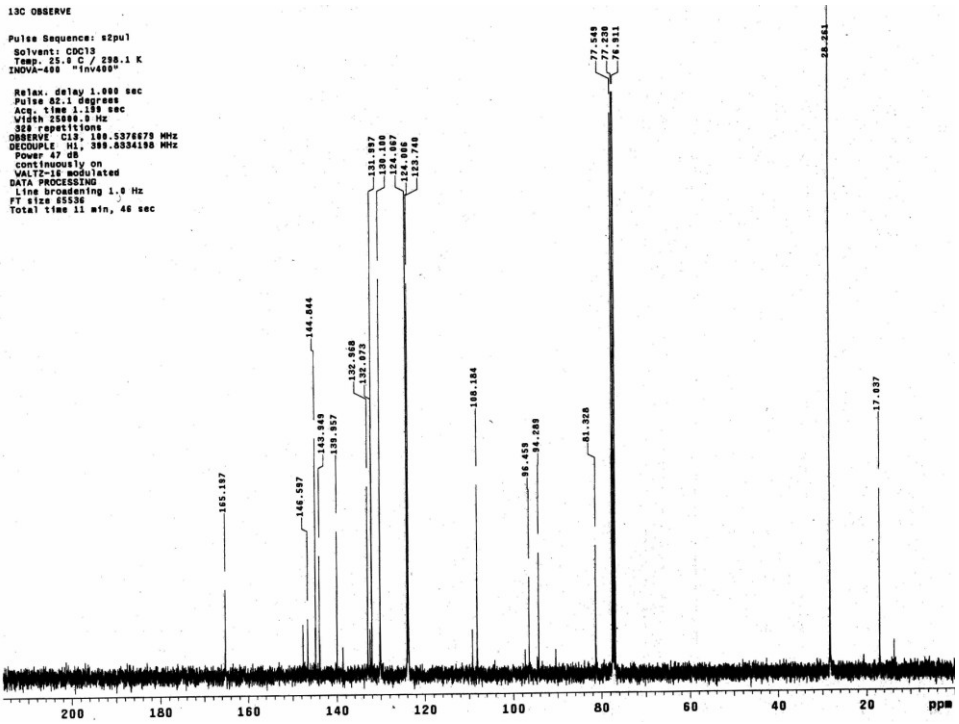

wp-v1-7-acytlene-vinyl-ester
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
96 repetitions
OBSERVE H1, 499.8948170 MHz
DATA PROCESSING
FT size 32768
Total time 2 hr, 34 min
7.269
6.169
6.165
6.103
6.085
6.081
6.046
6.041
6.036
6.024
6.018
6.013
3.559
3.555
3.551
1.497
1.491
1.488
1.474
1.446
1.442
1.428
1.424
7
6
5
4
3
2
1
ppm
1.07
1.03
0.97
10.27

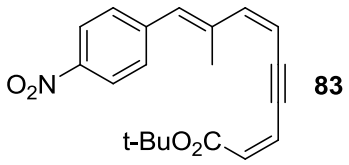

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1198 repetitions
OBSERVE C13, 100.5376656 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
163.869
132.938
120.842
88.727
81.548
79.892
77.569
77.230
76.911
28.284
28.165
28.147
200
180
160
140
120
100
80
60
40
20
ppm


O2N
CO2t-Bu

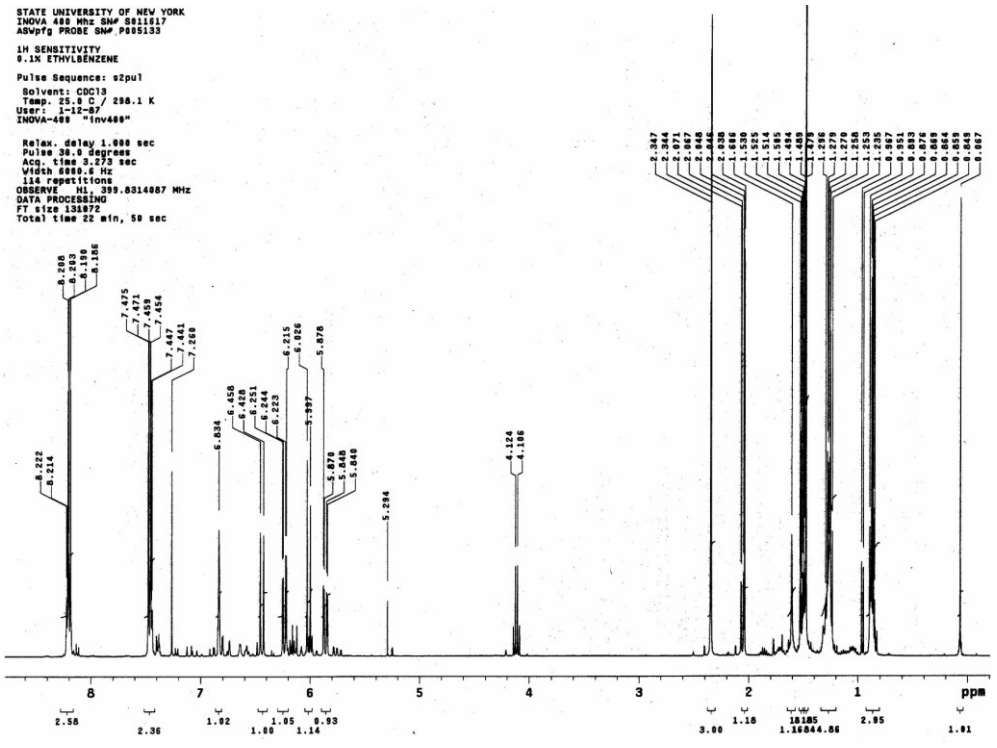
82

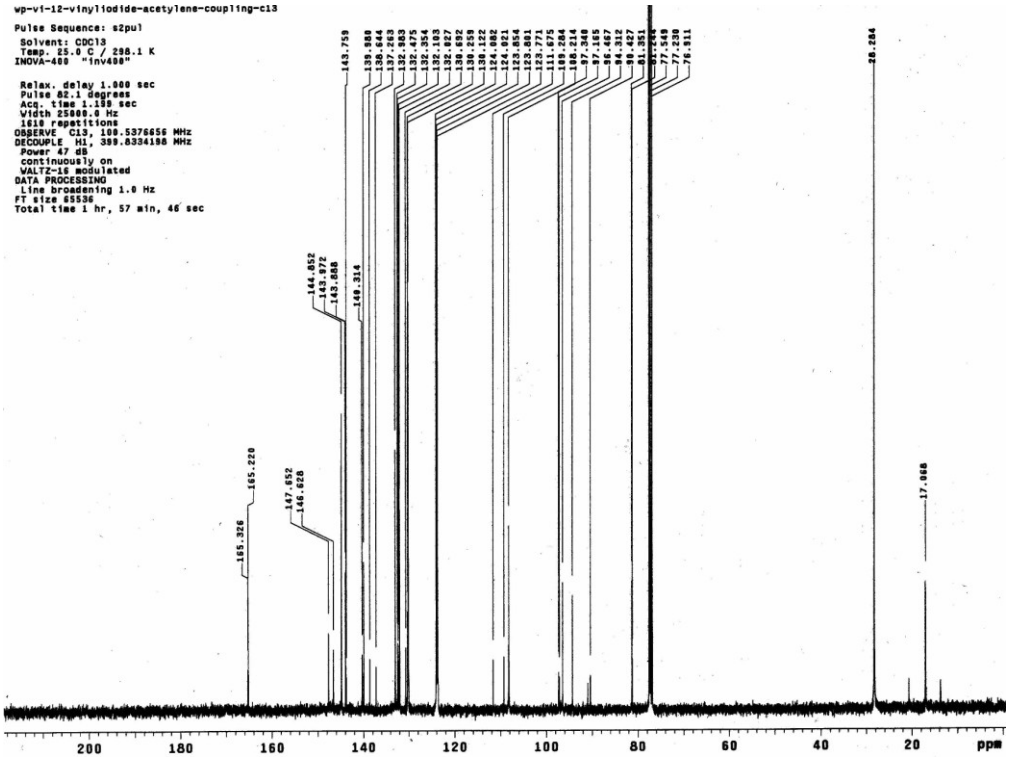

wp-v1-12-vinyliodide-acetylene-coupling
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
118 repetitions
OBSERVE H1, 399.8314887 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
8.259
8.253
8.158
7.462
7.446
6.738
6.158
6.119
2.342
2.348
2.046
1.613
1.492
1.488
1.474
ppm

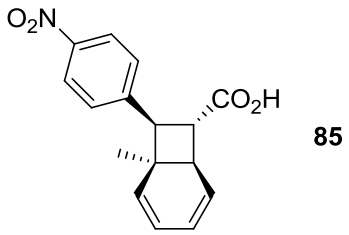

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.155 sec
Width 25000.0 Hz
320 repetitions
OBSERVE C13, 100.5376679 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 11 min, 46 sec
77.548
77.230
76.911
28.261
17.037
81.328
86.459
84.289
100.184
131.997
131.568
131.139
124.487
124.066
123.748
132.568
132.073
144.644
143.949
139.957
146.597
165.197
ppm


O_2N
t-BuO_2C

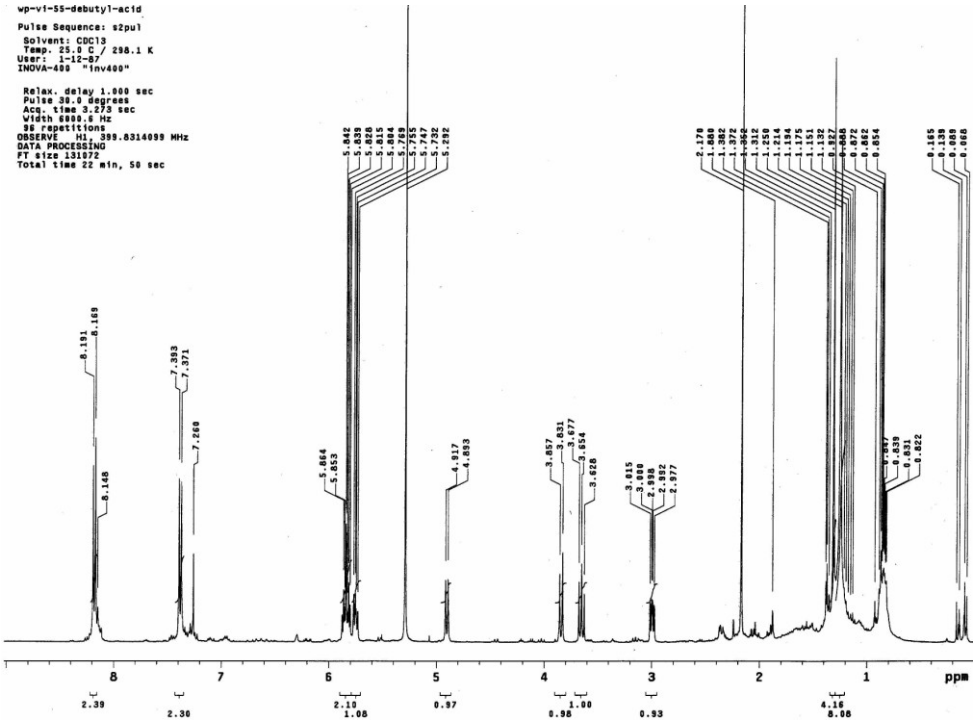
83

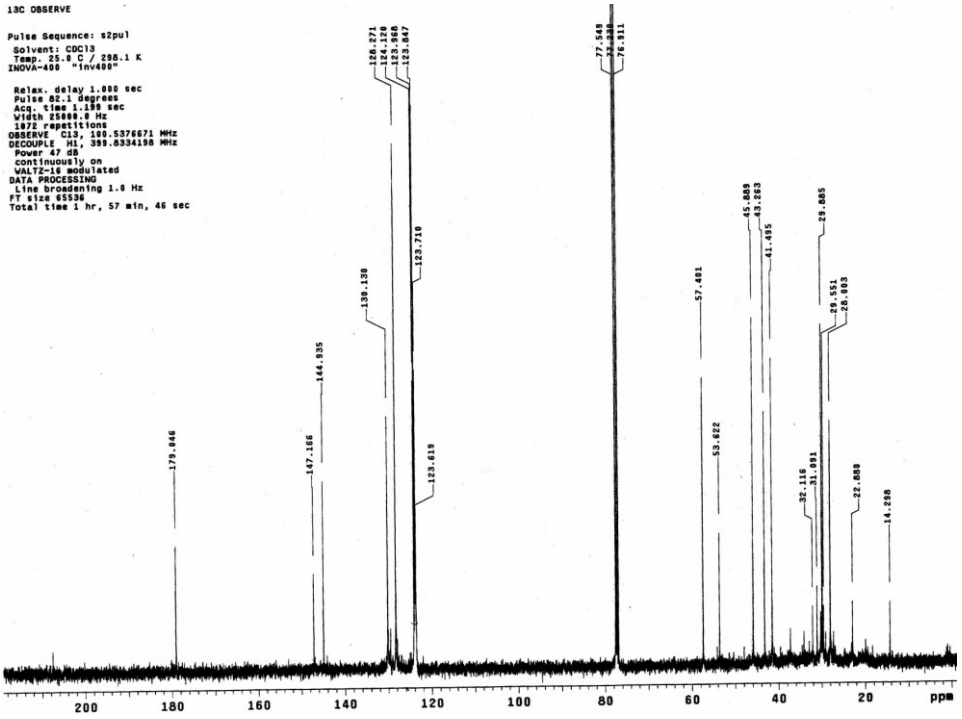

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# 5011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-97
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
114 repetitions
OBSERVE H1, 399.8314887 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

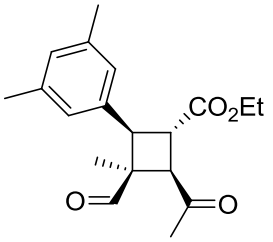

wp-vi-12-vinyliodide-acetylene-coupling-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1616 repetitions
OBSERVE C13, 100.5376656 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


O2N
CO2H

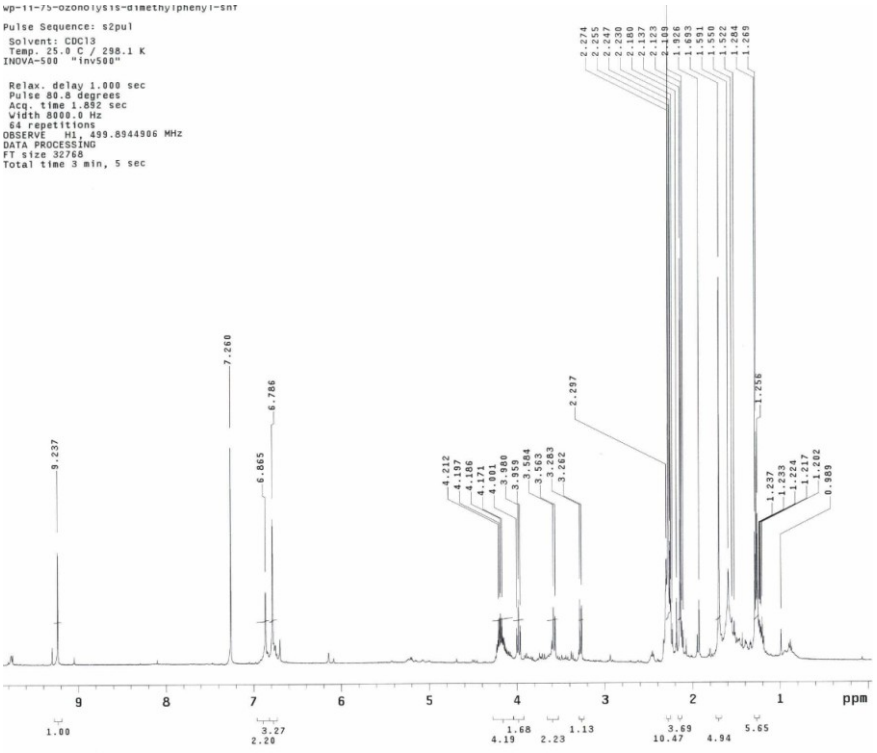
85

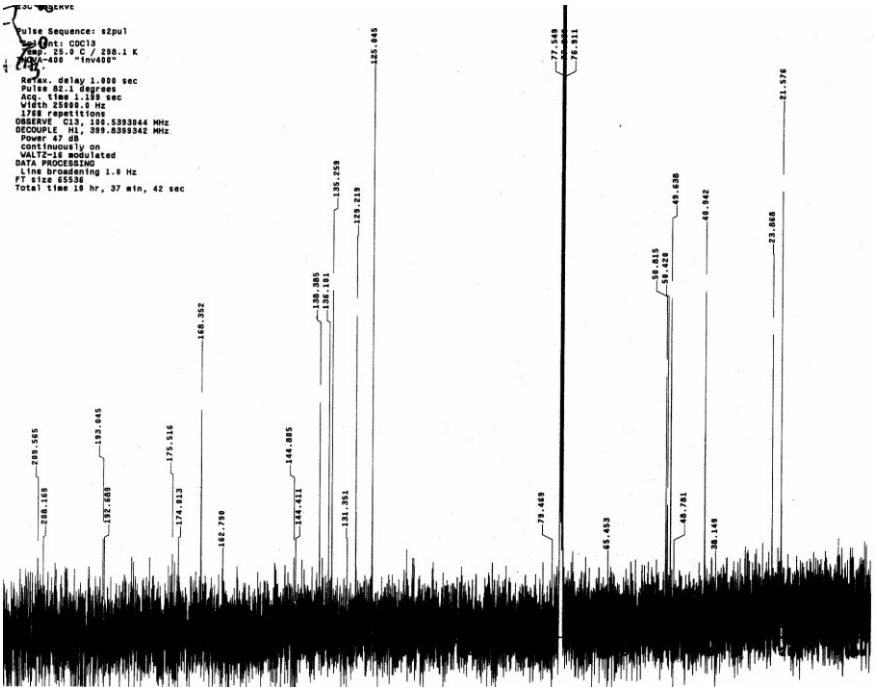

wp-v1-55-debutyl-acid
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6980.6 Hz
96 repetitions
OBSERVE H1, 399.8314099 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
ppm

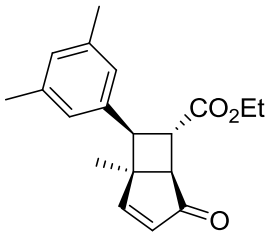

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25888.8 Hz
1072 repetitions
OBSERVE C13, 100.5376671 MHz
DECOUPLE H1, 399.8334198 MHz
Power 57 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.8 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


CO2Et
O
O

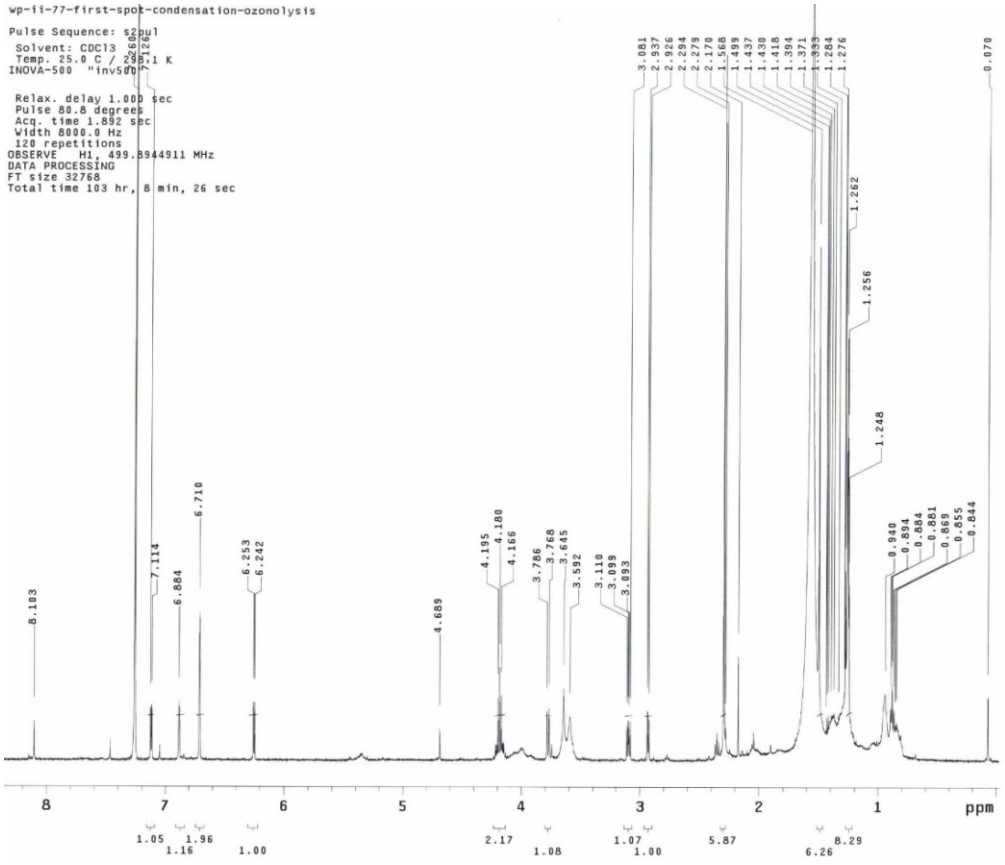
93

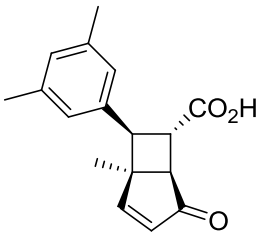

wp-11-75-ozonolysis-dimethylphenyl-snf
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
64 repetitions
OBSERVE H1, 499.8944906 MHz
DATA PROCESSING
FT size 32768
Total time 3 min, 5 sec
9.237
7.260
6.865
6.786
4.212
4.197
4.186
4.171
4.001
3.980
3.959
3.684
3.565
3.283
3.262
2.297
2.274
2.255
2.247
2.230
2.180
2.137
2.123
2.108
1.926
1.693
1.591
1.550
1.522
1.504
1.269
1.258
1.237
1.233
1.224
1.217
1.202
0.989
9
8
7
6
5
4
3
2
1
ppm
1.00
3.27
2.20
1.68
4.19
2.23
1.13
3.69
10.47
4.94
5.65


Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25880.0 Hz
1768 repetitions
OBSERVE C13, 100.5393044 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
200.565
198.169
193.645
192.669
175.516
174.813
168.352
162.799
144.805
144.411
138.385
138.181
135.259
131.351
129.219
125.945
77.148
76.831
79.469
65.453
59.815
59.418
49.638
48.781
40.842
38.148
23.868
21.576

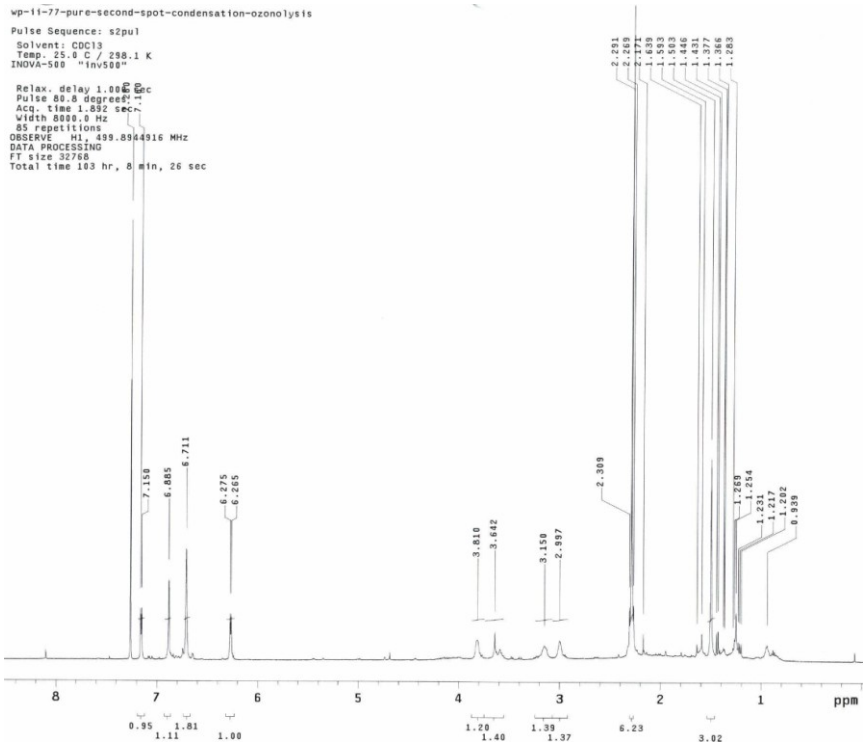

CO2Et
O

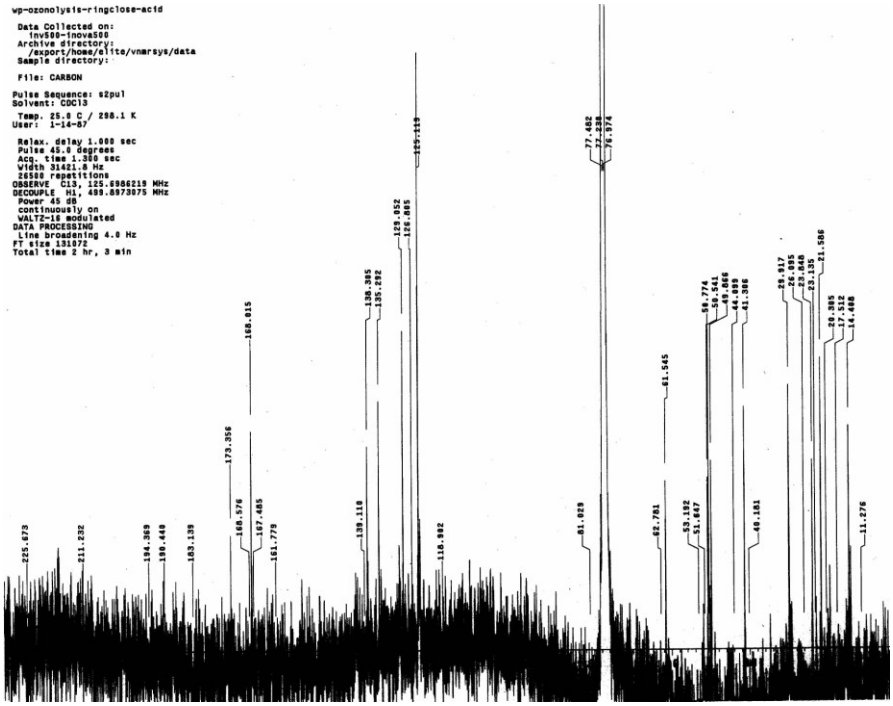
94

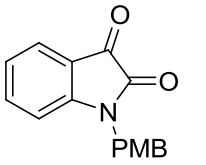

wp-ii-77-first-spot-condensation-ozonolysis
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
120 repetitions
OBSERVE H1, 499.8944911 MHz
DATA PROCESSING
FT size 32768
Total time 103 hr, 8 min, 26 sec
8.103
7.114
6.884
6.710
6.253
6.242
4.689
4.195
4.180
4.166
3.786
3.768
3.645
3.592
3.110
3.099
3.093
3.061
2.937
2.926
2.294
2.279
2.170
1.568
1.499
1.437
1.430
1.418
1.384
1.371
1.333
1.284
1.276
1.262
1.256
1.248
0.940
0.894
0.884
0.881
0.869
0.855
0.844
0.070
8
7
6
5
4
3
2
1
ppm
1.05
1.96
1.16
1.00
2.17
1.08
1.07
1.00
5.87
8.29
6.26


CO2H
O

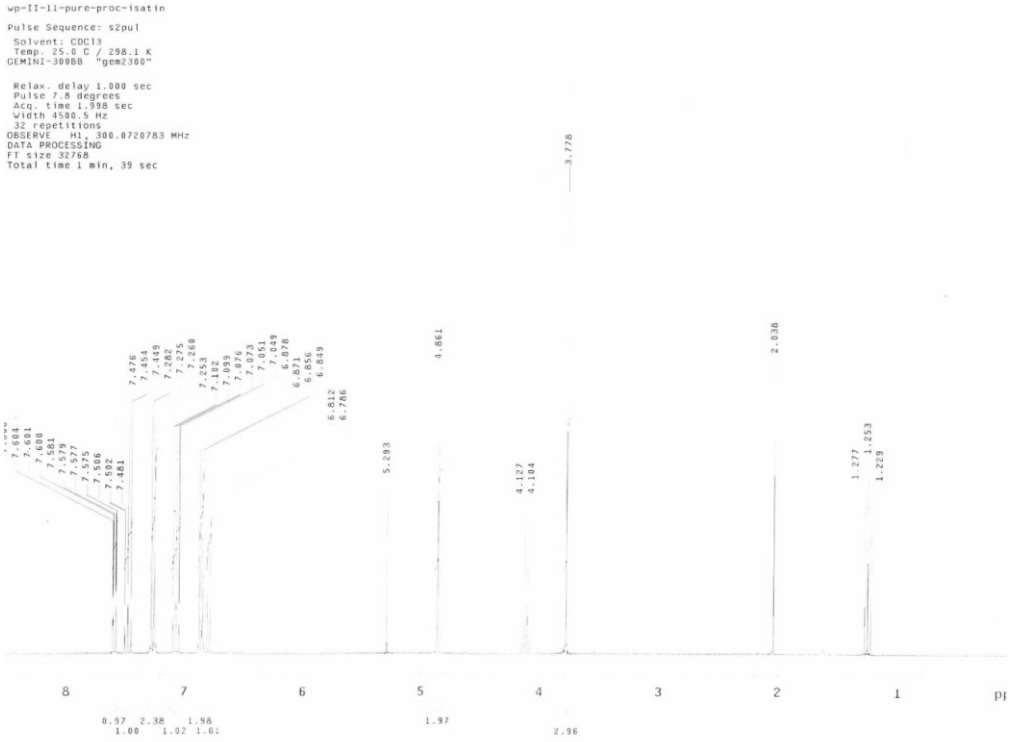
95

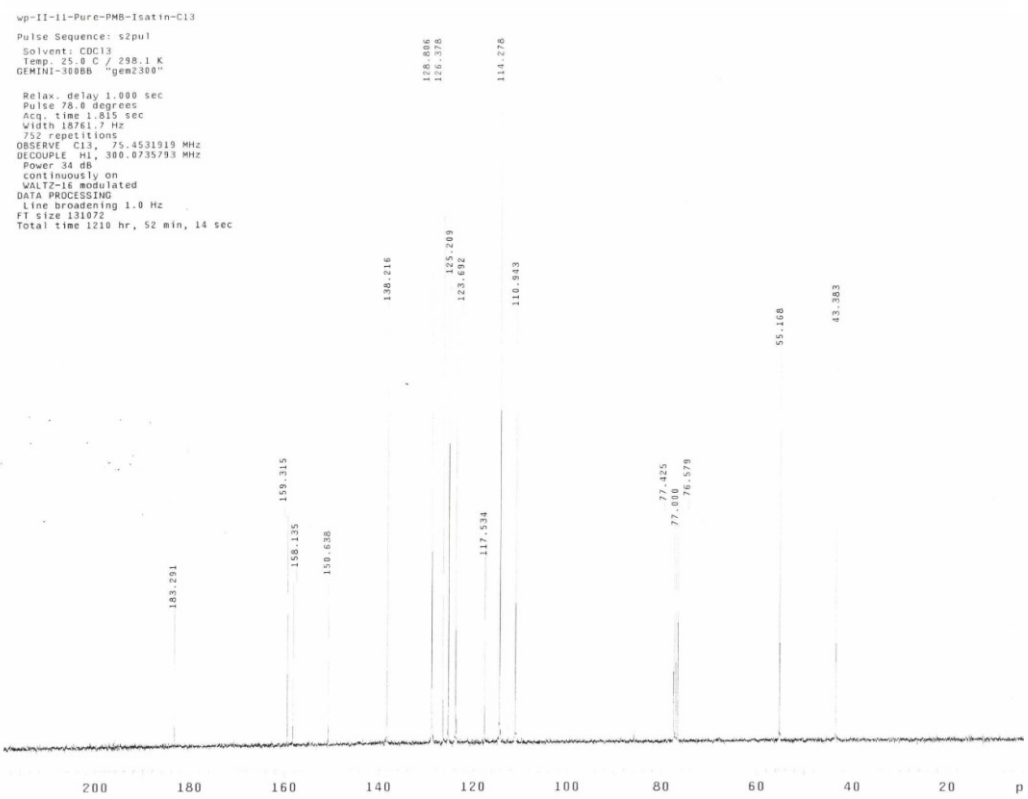

wp-ii-77-pure-second-spot-condensation-ozonolysis
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
85 repetitions
OBSERVE H1, 499.8944916 MHz
DATA PROCESSING
FT size 32768
Total time 103 hr, 8 min, 26 sec
7.159
6.885
6.711
6.275
6.265
3.810
3.642
3.150
2.997
2.309
2.291
2.269
2.171
1.639
1.583
1.503
1.446
1.431
1.377
1.366
1.268
1.269
1.254
1.231
1.217
1.202
0.939
8
7
6
5
4
3
2
1
ppm
0.95
1.11
1.81
1.00
1.20
1.40
1.39
1.37
6.23
3.02

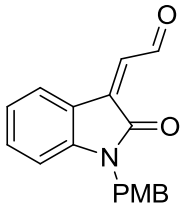

wp-ozonolysis-ringclose-acid
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 31421.8 Hz
26580 repetitions
OBSERVE C13, 125.6986218 MHz
DECOUPLE H1, 499.8973075 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 4.0 Hz
FT size 131072
Total time 2 hr, 3 min
225.673
211.232
194.369
190.440
183.139
173.356
168.915
168.578
167.485
161.778
139.110
130.395
130.202
129.352
129.085
125.119
116.982
77.482
77.228
76.974
61.545
62.781
53.192
51.647
49.181
44.899
41.386
11.276


O
O
N
PMB

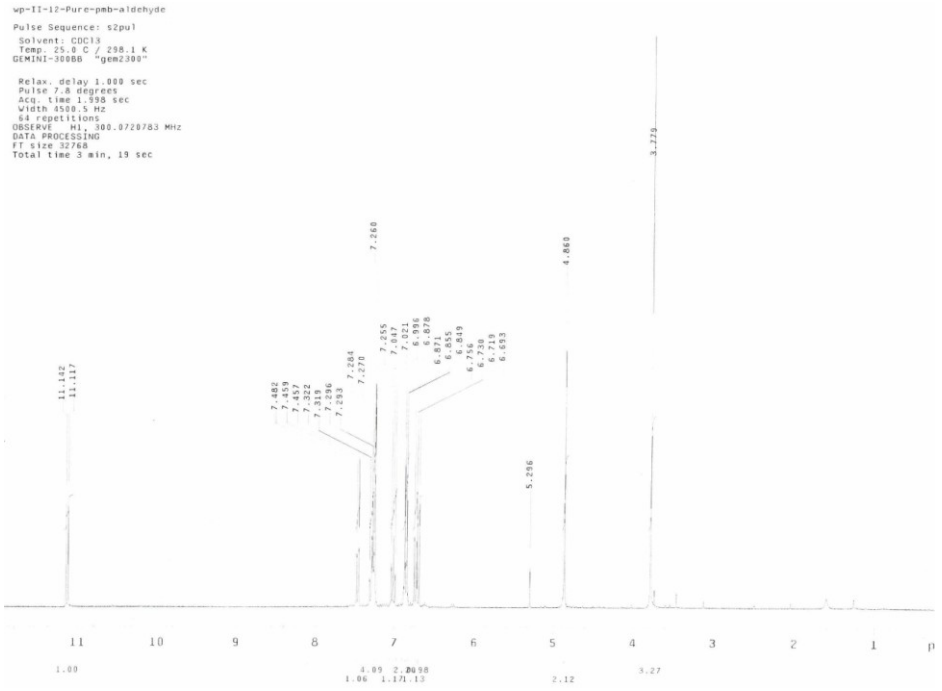
103

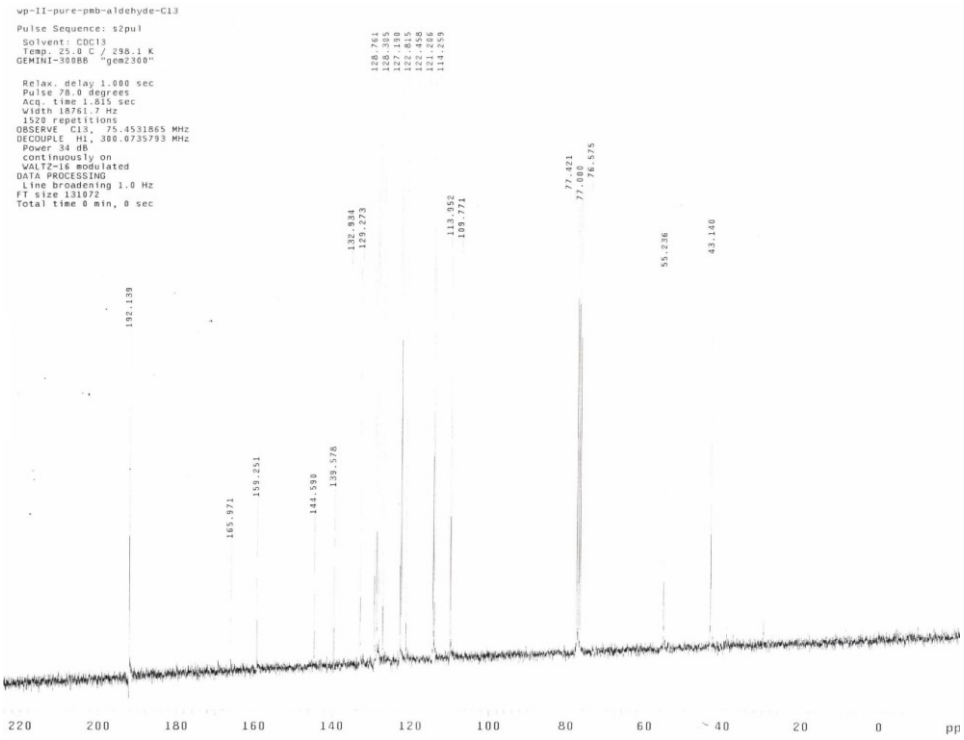

wp-II-11-pure-proc-isatin
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720783 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
7.604
7.601
7.600
7.581
7.579
7.577
7.575
7.506
7.502
7.461
7.476
7.464
7.449
7.282
7.275
7.260
7.253
7.102
7.089
7.076
7.073
7.051
7.049
6.878
6.871
6.856
6.849
6.812
6.766
5.293
4.861
4.127
4.104
3.778
2.038
1.277
1.253
1.229
8
7
6
5
4
3
2
1
0.97
2.38
1.98
1.00
1.02
1.01
1.97
2.96

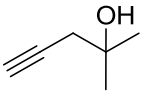

wp-II-11-Pure-PMB-Isatin-C13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 78.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
752 repetitions
OBSERVE C13, 75.4531919 MHz
DECOUPLE H1, 300.0735793 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1210 hr, 52 min, 14 sec
183.291
159.315
158.135
150.638
138.216
128.886
126.378
125.209
123.692
117.534
114.278
110.943
77.425
77.000
76.579
55.168
43.383
200
180
160
140
120
100
80
60
40
20


O
O
N
PMB

104


wp-II-12-Pure-pmb-aldehyde
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4508.5 Hz
64 repetitions
OBSERVE H1, 300.0720783 MHz
DATA PROCESSING
FT size 32768
Total time 3 min, 19 sec
11.142
11.117
7.482
7.459
7.457
7.322
7.318
7.296
7.293
7.284
7.270
7.266
7.255
7.047
7.021
6.876
6.871
6.855
6.849
6.756
6.730
6.719
6.693
5.296
4.860
3.279
1.00
4.09
2.28
1.06
1.17
1.13
2.12
3.27


wp-II-pure-pmb-aldehyde-C13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 78.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
1528 repetitions
OBSERVE C13, 75.4531865 MHz
DECOUPLE H1, 300.0735793 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 0 min, 0 sec
192.139
165.971
159.251
144.598
139.578
132.934
129.273
128.761
128.365
127.190
122.815
122.458
121.256
114.259
113.952
109.771
77.421
77.000
76.575
55.236
43.148


OH

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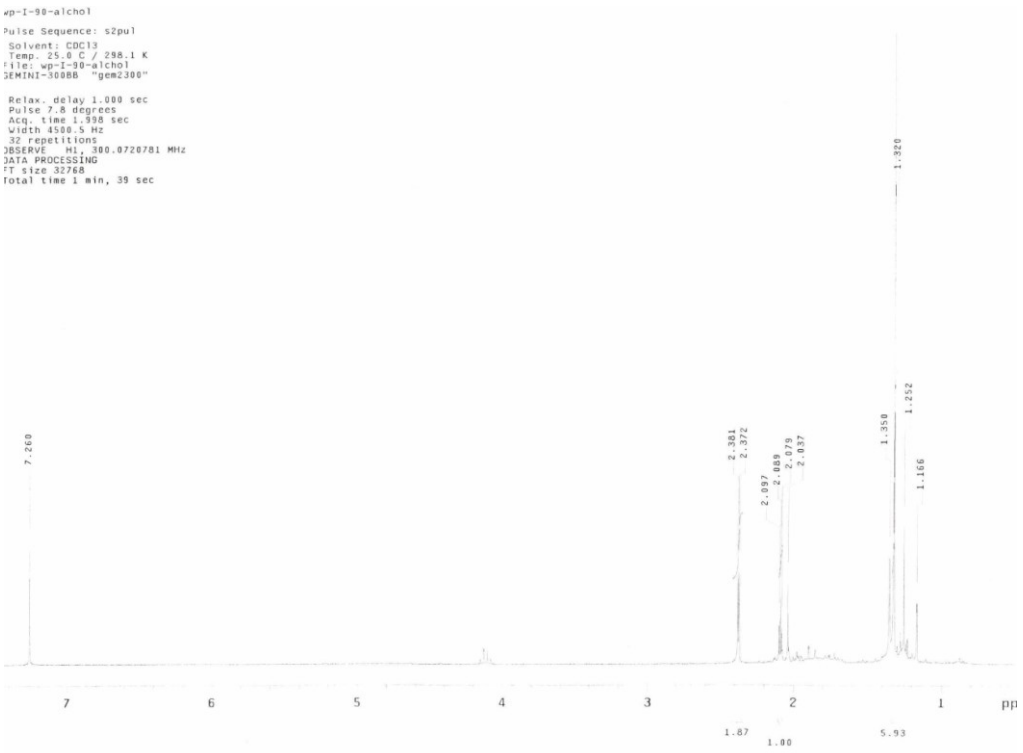
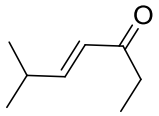

wp-I-90-alchol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: wp-I-90-alchol
SEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720781 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
7.260
2.381
2.372
2.097
2.089
2.079
2.037
1.350
1.320
1.252
1.166
7
6
5
4
3
2
1
ppm
1.87
1.00
5.93



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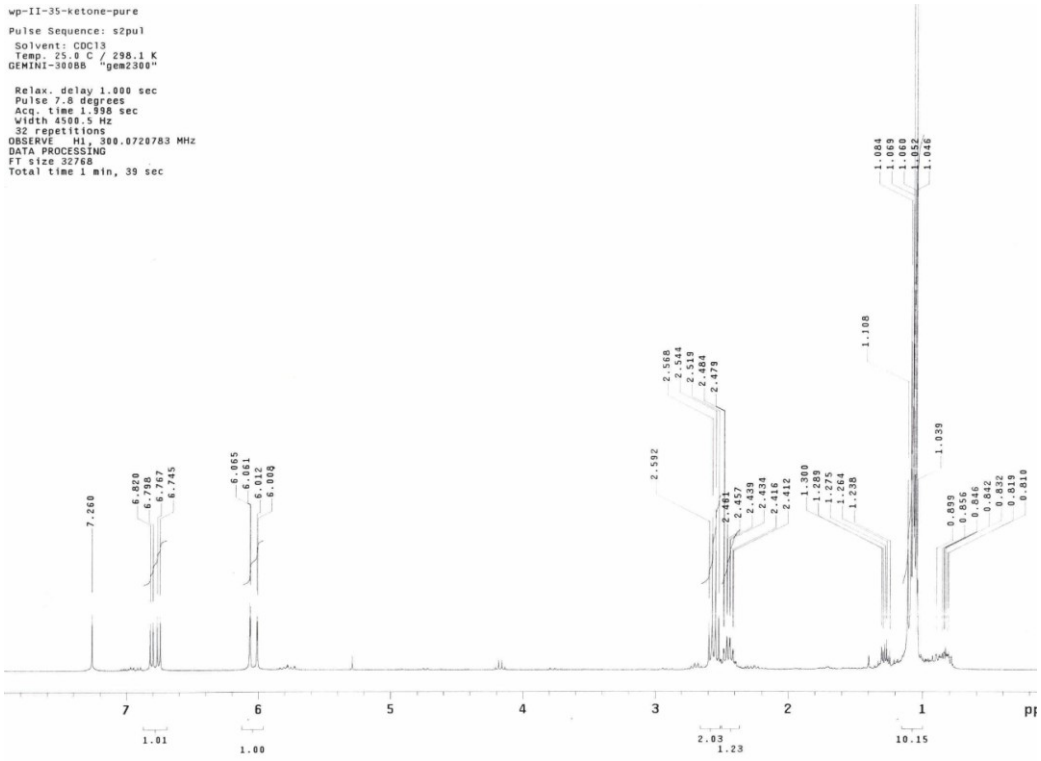
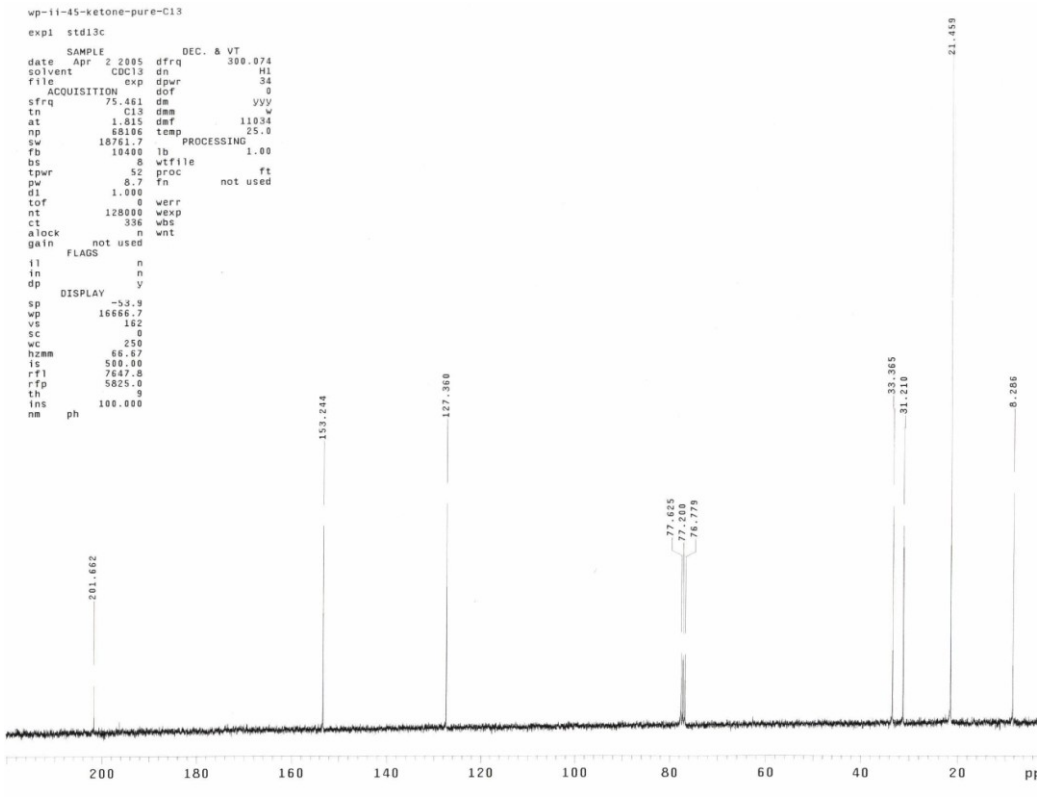
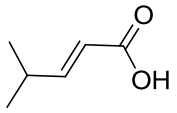
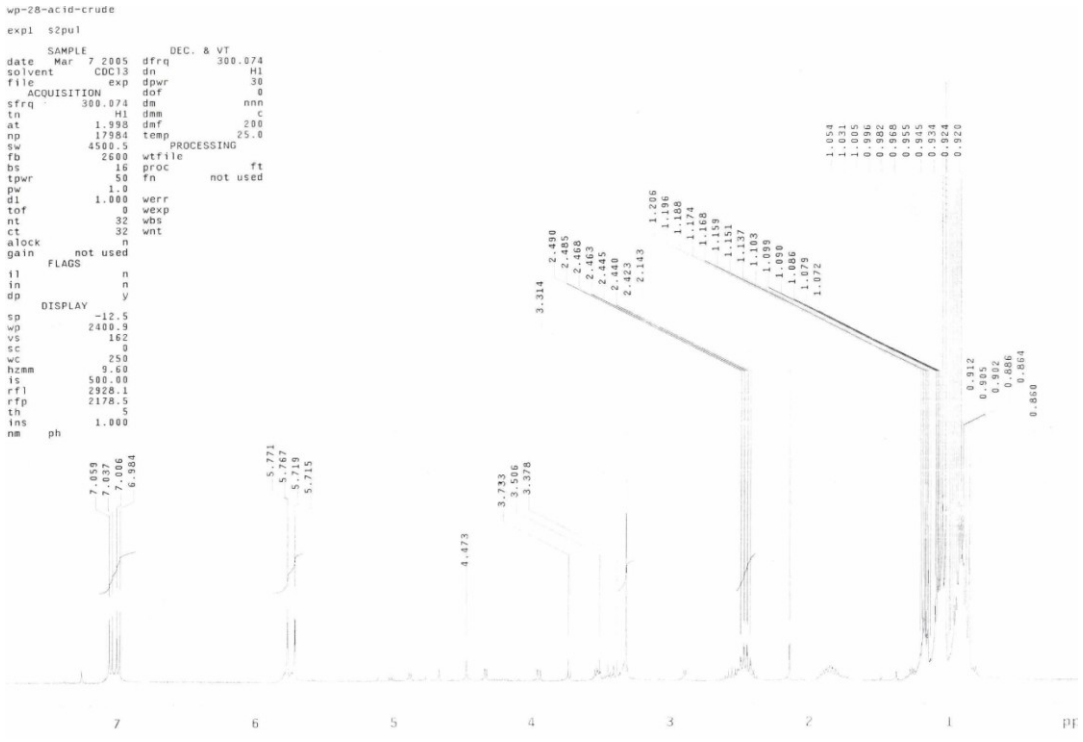
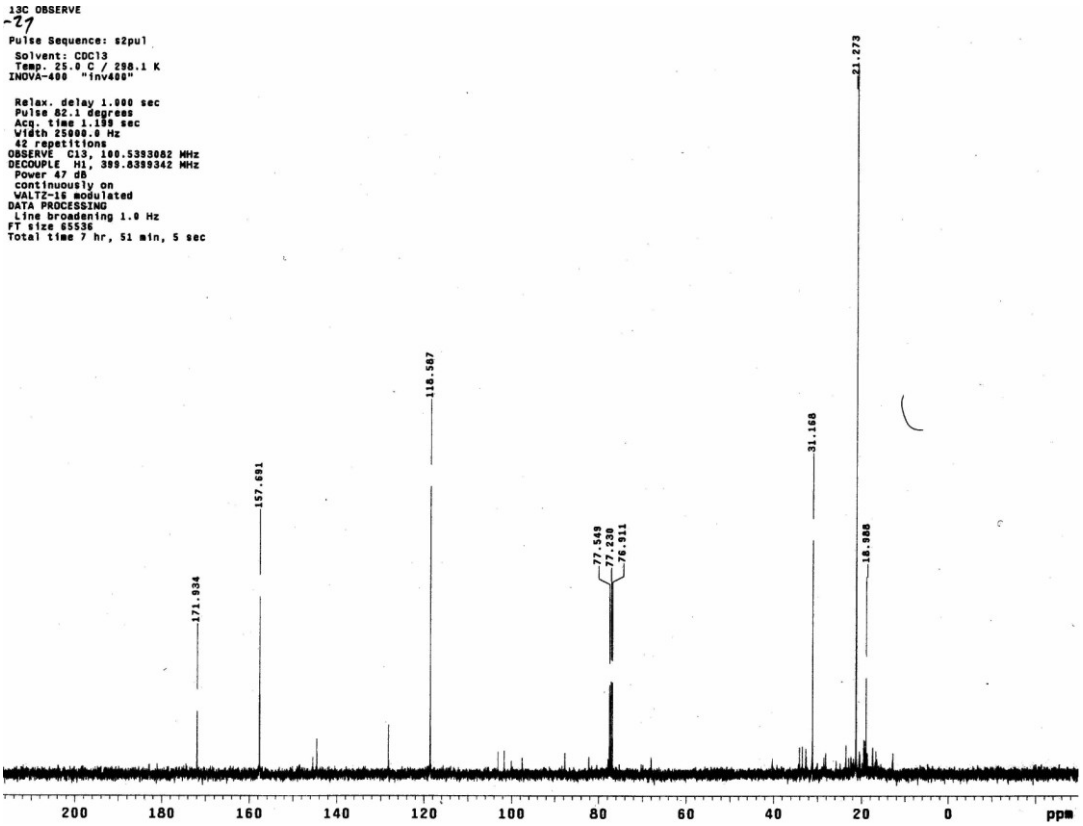

wp-II-35-ketone-pure
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720783 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
7.260
6.820
6.798
6.787
6.745
6.665
6.661
6.612
6.604
2.592
2.568
2.544
2.518
2.484
2.479
2.461
2.457
2.439
2.434
2.416
2.412
1.300
1.288
1.275
1.264
1.238
1.108
1.084
1.069
1.065
1.052
1.046
1.039
0.899
0.856
0.846
0.842
0.832
0.819
0.810
1.01
1.00
2.03
1.23
10.15

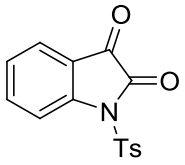

wp-ii-45-ketone-pure-C13
exp1 stdi3c
SAMPLE
date Apr 2 2005
solvent CDCl3
file exp
ACQUISITION
sfrq 75.461
tn C13
at 1.815
np 68106
sw 18761.7
fb 10400
bs 8
tpwr 52
pw 8.7
d1 1.000
tof 0
nt 128000
ct 336
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -53.9
wp 16666.7
vs 162
sc 0
wc 250
hzmm 66.67
is 500.00
rfl 7647.8
rfp 5825.0
th 9
ins 100.000
nm ph
DEC. & VT
dfrq 300.074
dn H1
dpwr 34
dof 0
dm yyy
dmm w
dmf 11034
temp 25.0
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
201.662
153.244
127.360
77.625
77.208
76.779
33.365
31.210
21.459
8.266


O
OH

117


wp-28-acid-crude
exp1 s2pul
SAMPLE
date Mar 7 2005
solvent CDCl3
file exp
ACQUISITION
sfrq 300.074
tn H1
at 1.998
np 17984
sw 4500.5
fb 2600
bs 16
tpwr 50
pw 1.0
dl 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -12.5
wp 2400.9
vs 162
sc 0
wc 250
hzmm 9.60
is 580.80
rfl 2928.1
rfp 2178.5
th 5
ins 1.000
nm ph
DEC. & VT
dfrq 300.074
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
temp 25.0
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
7.059
7.037
7.006
6.984
5.771
5.767
5.719
5.715
4.473
3.733
3.506
3.378
3.314
2.490
2.485
2.468
2.463
2.445
2.440
2.423
2.143
1.296
1.196
1.188
1.174
1.168
1.159
1.151
1.137
1.103
1.099
1.050
1.086
1.079
1.072
1.054
1.031
1.005
0.986
0.982
0.968
0.955
0.945
0.934
0.924
0.920
0.912
0.905
0.892
0.886
0.864
0.860
7
6
5
4
3
2
1
PF


13C OBSERVE
-27
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.185 sec
Width 25000.0 Hz
42 repetitions
OBSERVE C13, 100.5393082 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
171.934
157.691
118.567
77.549
77.230
76.911
31.168
21.273
18.986
200
180
160
140
120
100
80
60
40
20
0
ppm



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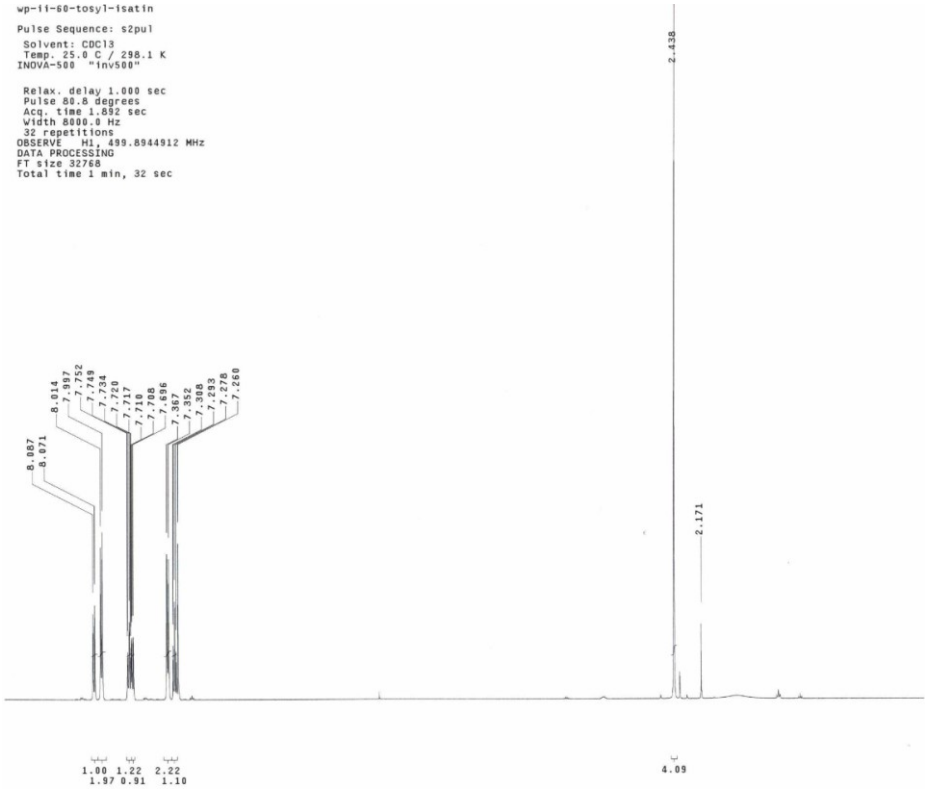
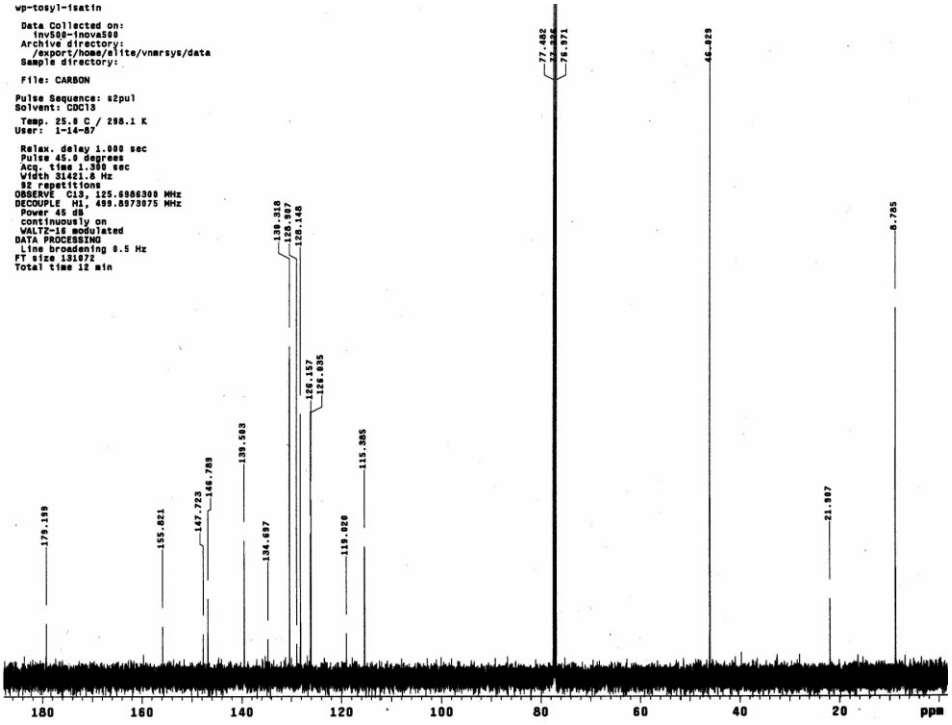
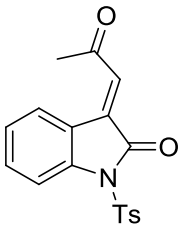
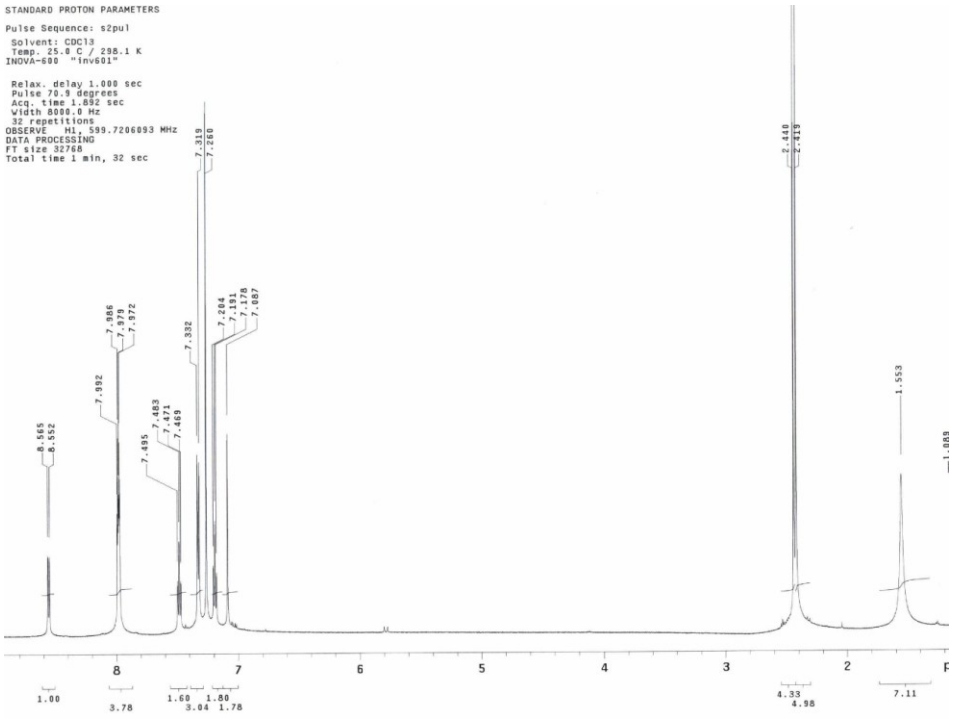
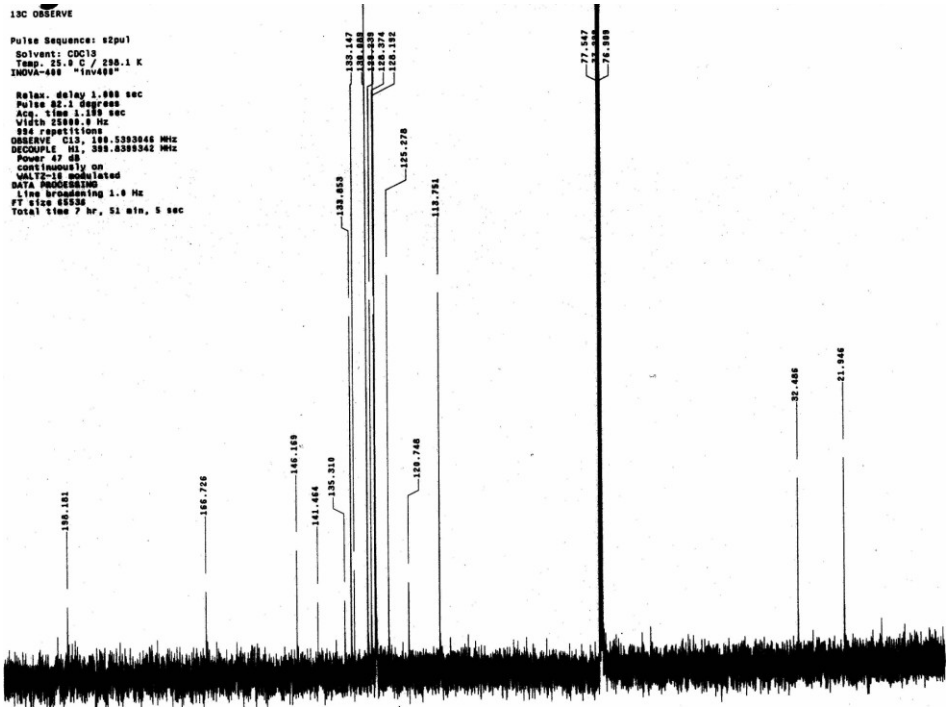

wp-ii-60-tosyl-isatin
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944912 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
8.087
8.071
8.014
7.997
7.752
7.748
7.734
7.729
7.717
7.710
7.708
7.696
7.367
7.362
7.308
7.293
7.278
7.260
2.438
2.171
1.00 1.22 2.22
1.97 0.91 1.10
4.09

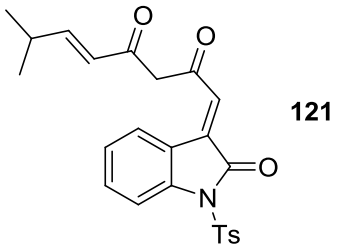

wp-tosyl-isatin
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.8 C / 298.1 K
User: l-14-87
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
82 repetitions
OBSERVE C13, 125.6986308 MHz
DECOUPLE H1, 499.8973075 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 12 min
179.199
155.021
147.723
146.709
139.593
134.687
130.310
128.997
128.148
126.157
124.035
119.026
115.355
77.482
77.056
76.971
46.429
21.987
8.785
180
160
140
120
100
80
60
40
20
ppm



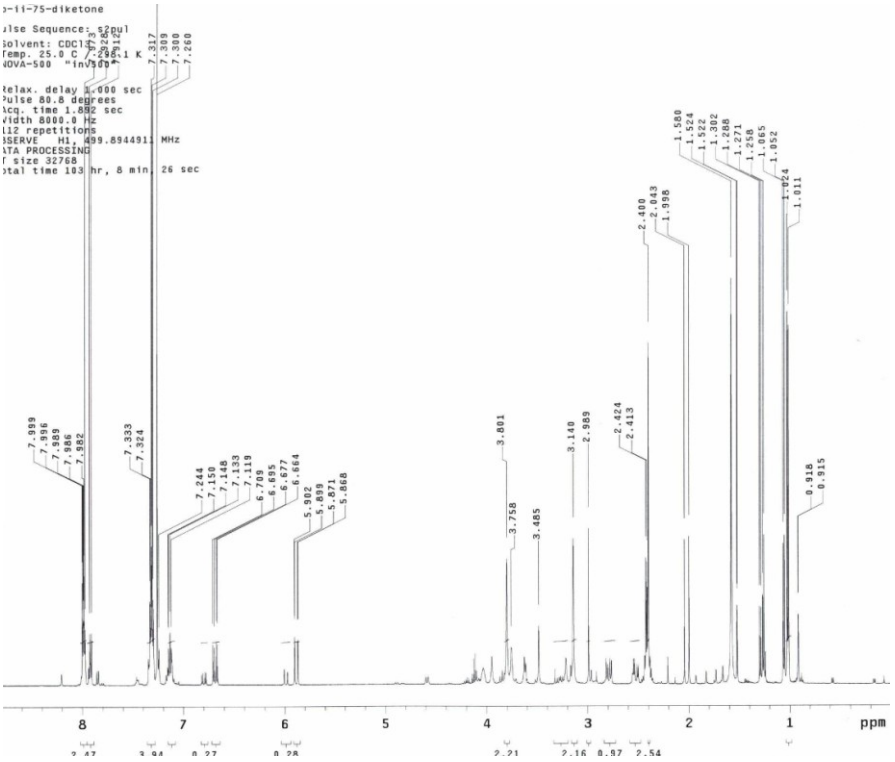
120

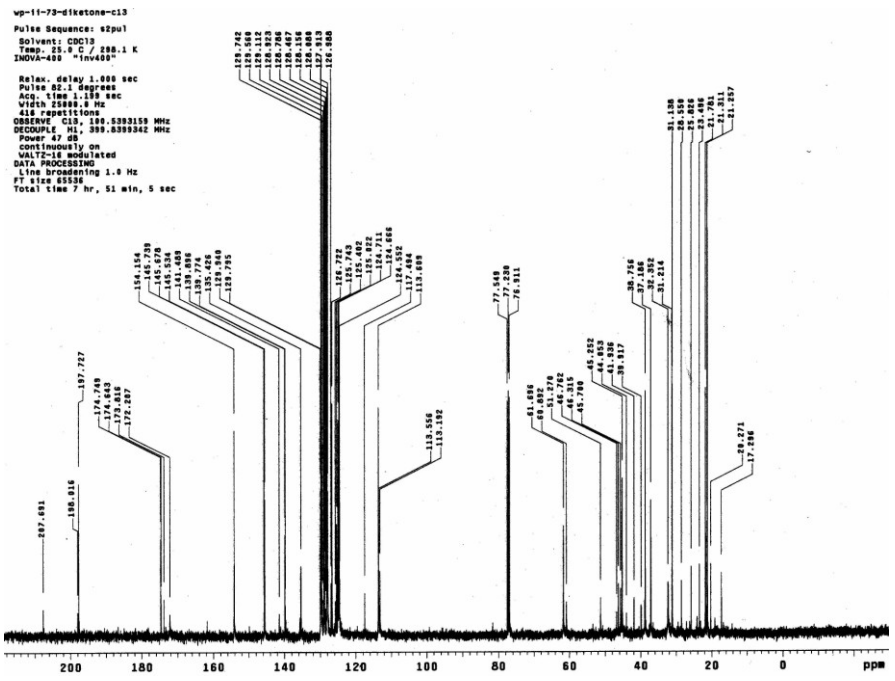

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-600 "inv601"
Relax. delay 1.000 sec
Pulse 70.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 599.7206093 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
8.565
8.552
7.992
7.986
7.979
7.972
7.495
7.483
7.471
7.469
7.332
7.319
7.260
7.204
7.191
7.178
7.087
2.440
2.419
1.553
1.00
3.78
1.60
1.80
3.04
1.78
4.33
4.98
7.11

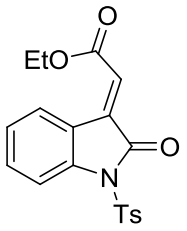

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
934 repetitions
OBSERVE C13, 100.5393046 MHz
DECOUPLE H1, 399.8393342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
133.147
130.888
128.839
128.374
126.152
125.278
119.751
77.547
77.000
76.189
32.486
21.946
166.726
146.169
141.464
135.310
129.748


O
O
O
N
Ts

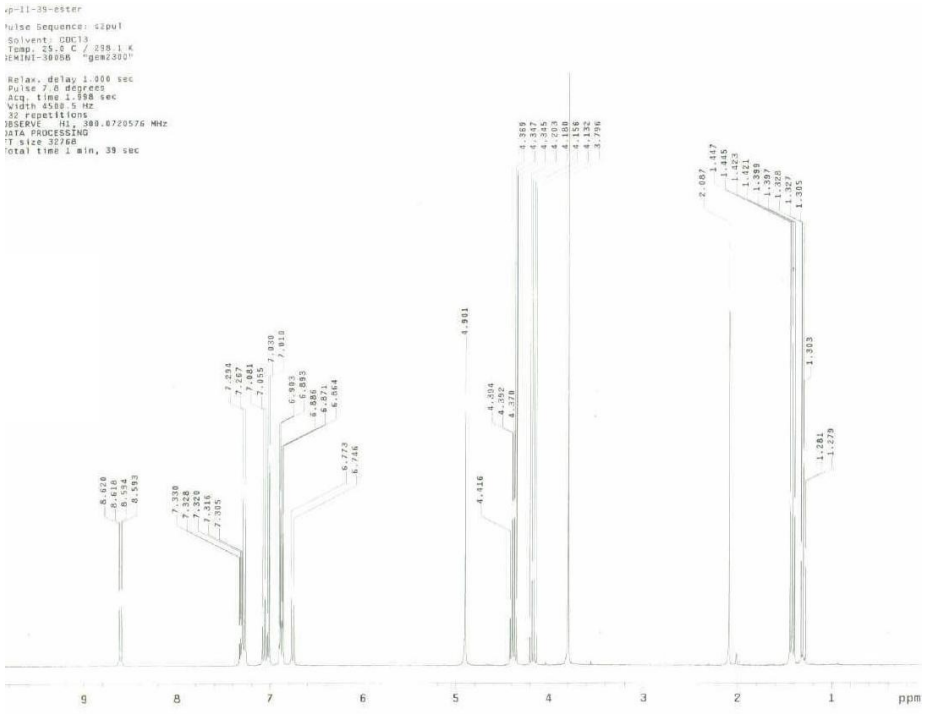
121

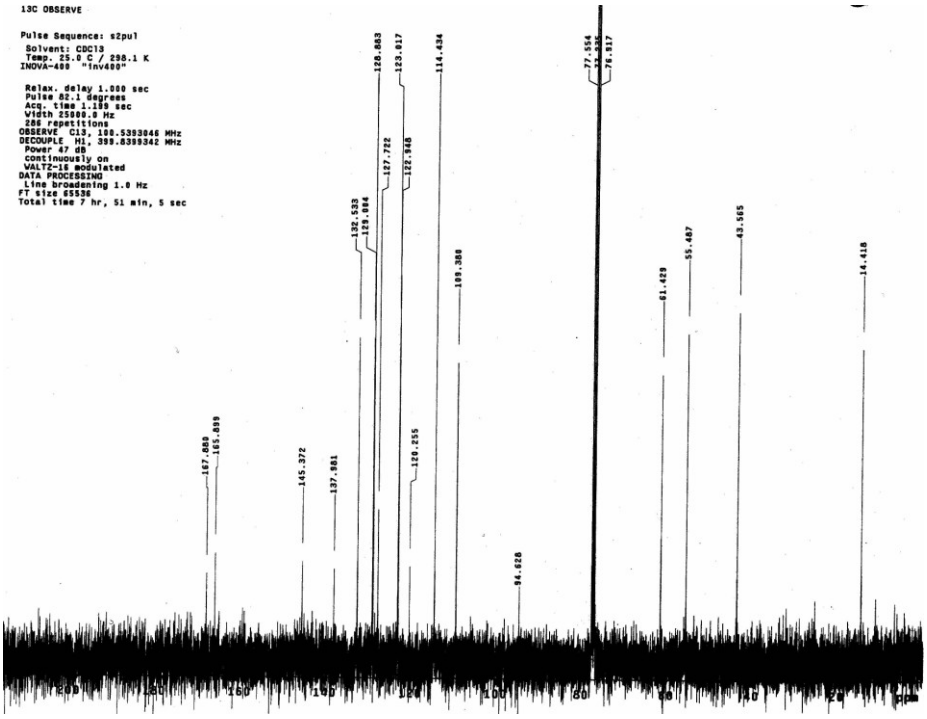

wp-ii-75-diketone
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 80.8 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
112 repetitions
OBSERVE H1, 499.8944911 MHz
DATA PROCESSING
FT size 32768
Total time 183 hr, 8 min, 26 sec
ppm

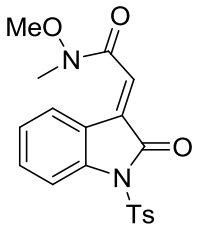

wp-ii-73-diketone-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.188 sec
Width 25000.0 Hz
416 repetitions
OBSERVE C13, 100.5383159 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
ppm


O
EtO
O
N
Ts

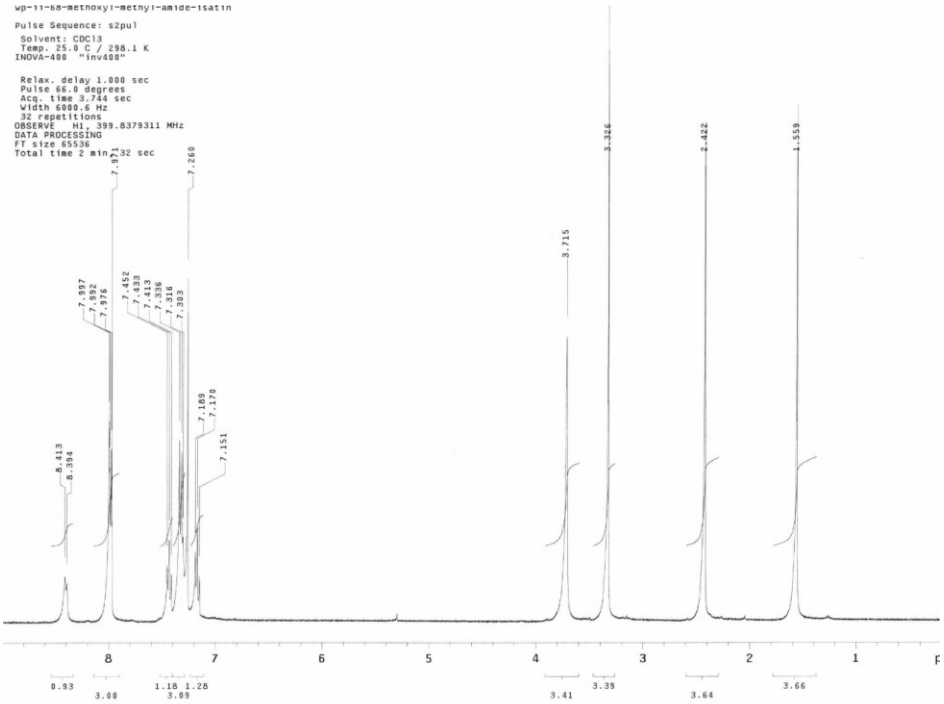
122

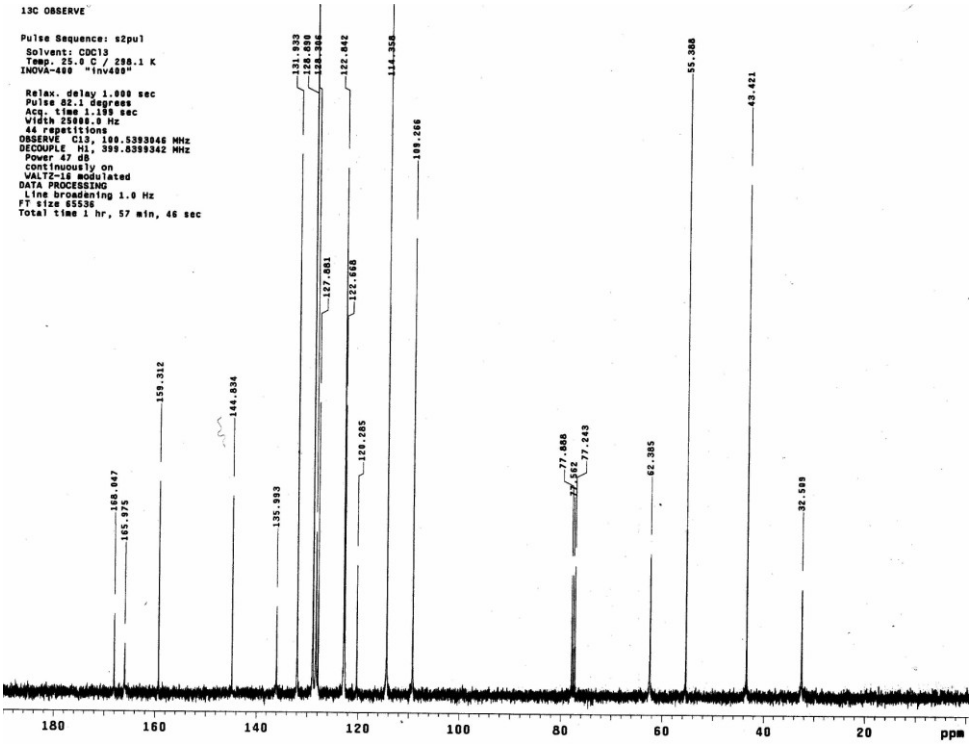

ep-II-39-ester
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 7.0 degrees
Acq. time 1.598 sec
Width 4588.5 Hz
32 repetitions
OBSERVE H1, 399.8399342 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 39 sec
8.620
8.616
8.594
8.593
7.338
7.328
7.320
7.316
7.305
7.084
7.067
7.061
7.055
7.030
7.010
6.983
6.893
6.886
6.871
6.564
6.773
6.746
4.961
4.416
4.384
4.382
4.378
4.369
4.347
4.345
4.203
4.188
4.156
4.132
3.796
2.687
1.447
1.445
1.423
1.421
1.399
1.397
1.328
1.327
1.305
1.303
1.281
1.279
9
8
7
6
5
4
3
2
1
ppm

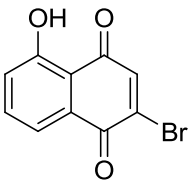

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
286 repetitions
OBSERVE C13, 100.5393846 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously ON
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
167.084
165.899
145.372
137.981
132.533
129.084
120.683
127.722
123.817
122.948
120.255
114.434
109.388
94.628
77.554
77.236
76.917
61.429
55.487
43.565
14.418
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
N
O
O
N
Ts

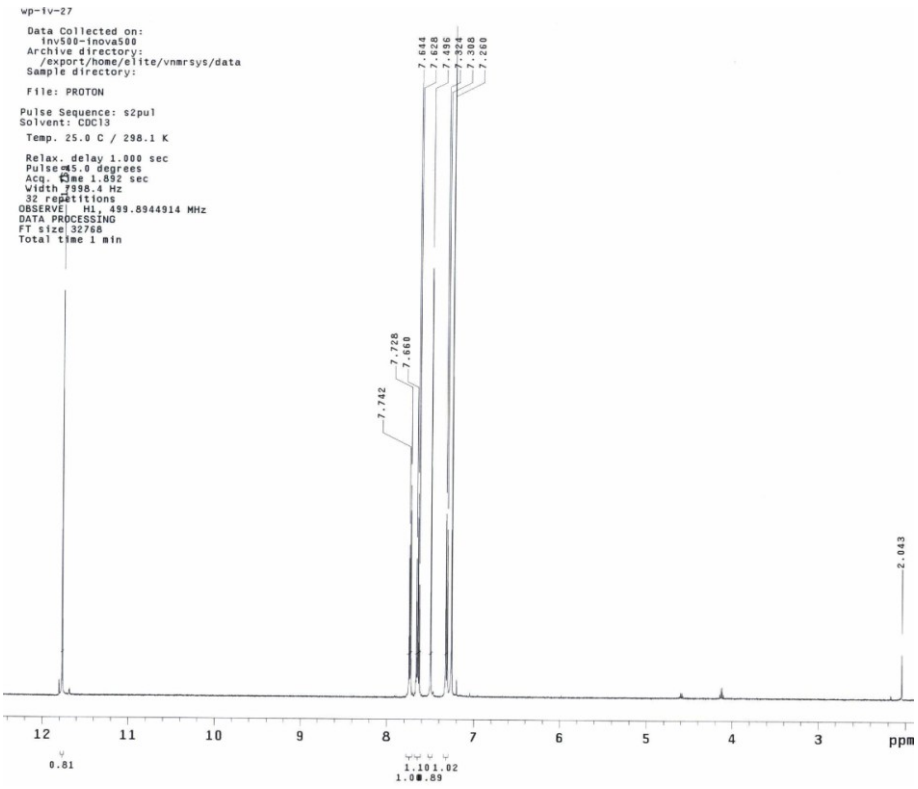
124

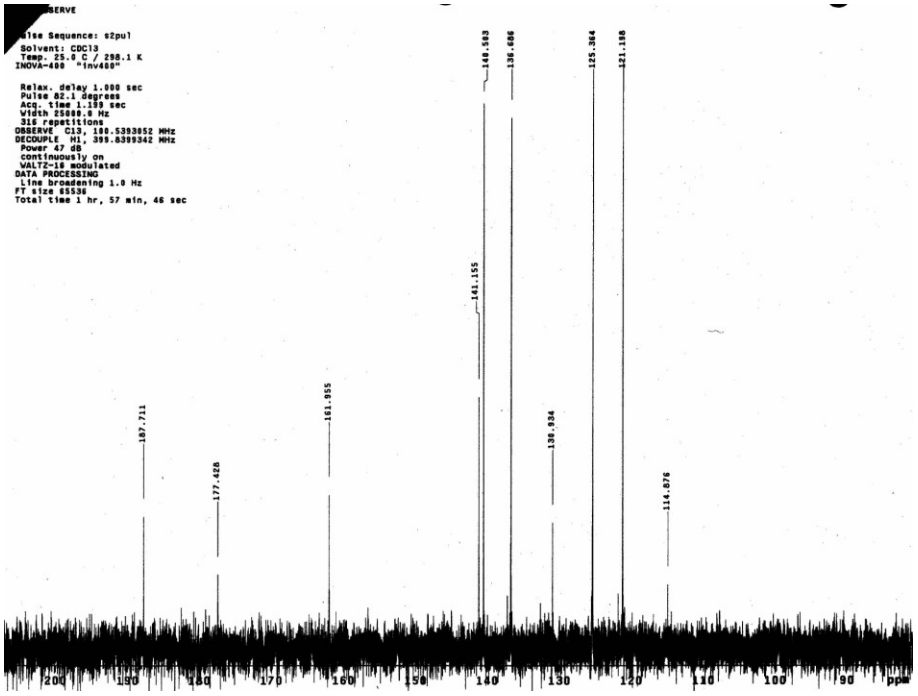

wp-11-68-methoxyl-methyl-amide-isatin
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 66.0 degrees
Acq. time 3.744 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379311 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 32 sec
8.413
8.394
7.997
7.992
7.976
7.971
7.452
7.438
7.413
7.336
7.316
7.308
7.260
7.189
7.178
7.151
3.715
3.326
2.422
1.559
0.93
3.00
1.18
1.28
3.09
3.41
3.39
3.64
3.66

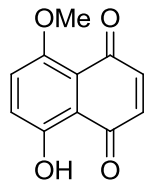

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.180 sec
Width 25000.0 Hz
44 repetitions
OBSERVE C13, 100.5393046 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
168.047
165.975
159.312
144.634
135.993
131.933
129.488
128.386
127.861
122.842
122.668
120.285
114.358
109.266
77.488
77.243
62.385
55.386
43.421
32.588


OH
O
Br
O

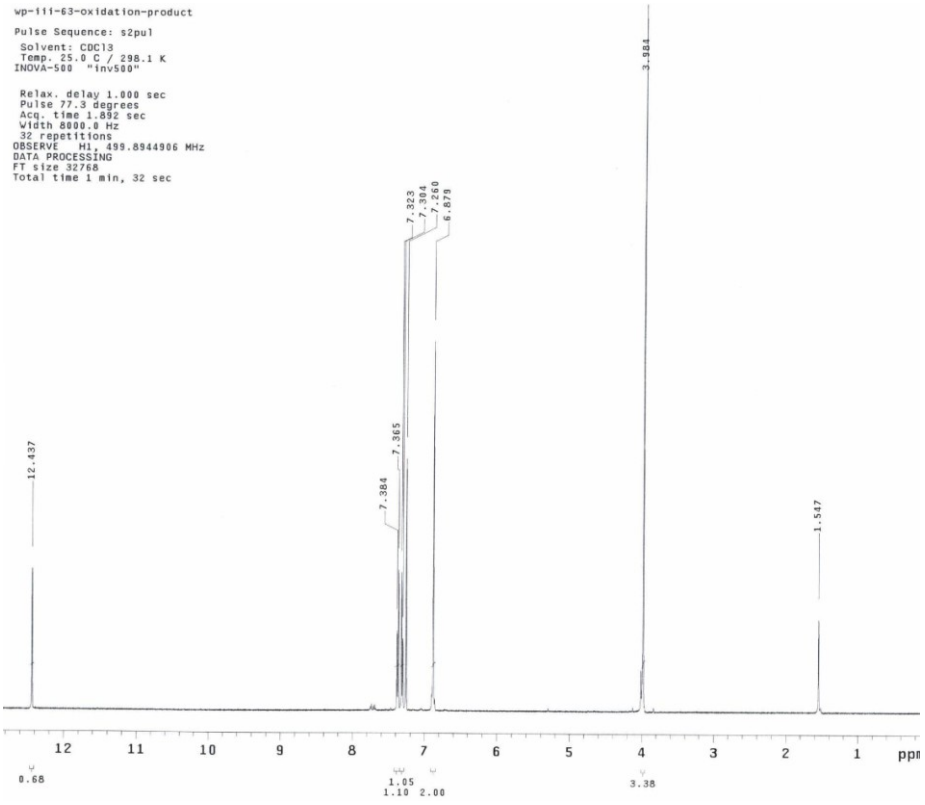
134

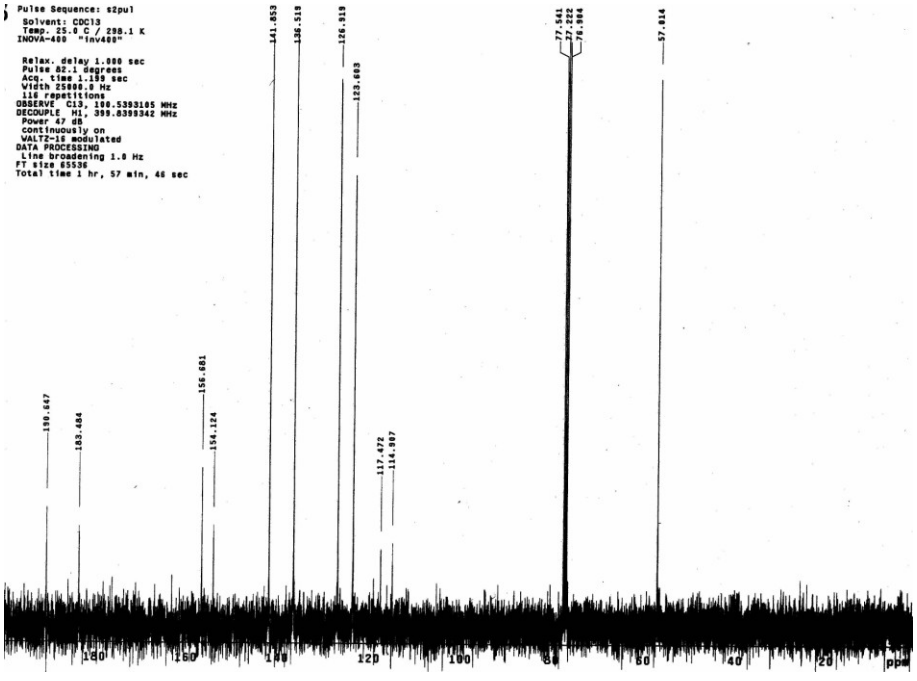

wp-iv-27
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944914 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
7.644
7.638
7.466
7.324
7.308
7.260
7.728
7.660
7.742
2.043
12
11
10
9
8
7
6
5
4
3
ppm
0.81
1.10
1.02
1.00
0.89

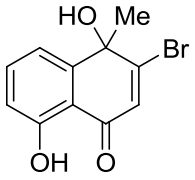

OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.139 sec
Width 25000.0 Hz
316 repetitions
OBSERVE C13, 100.5393852 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
140.593
136.686
125.384
121.196
141.155
187.711
177.426
161.955
130.934
114.876
200
190
180
170
160
150
140
130
120
110
100
90
ppm


OMe O
OH O

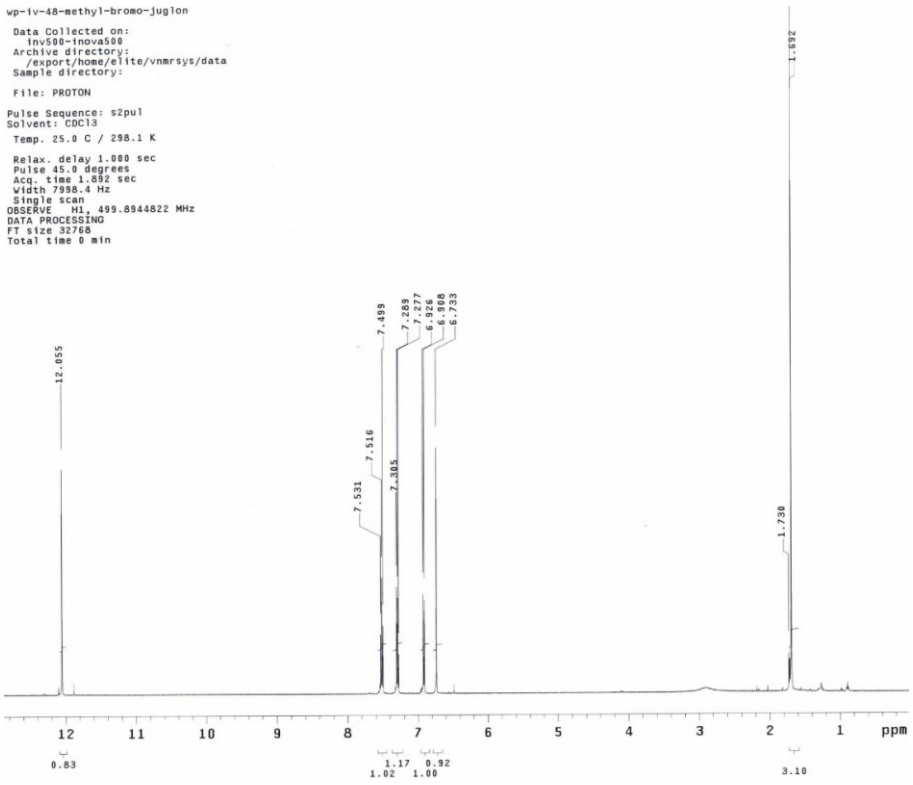
135

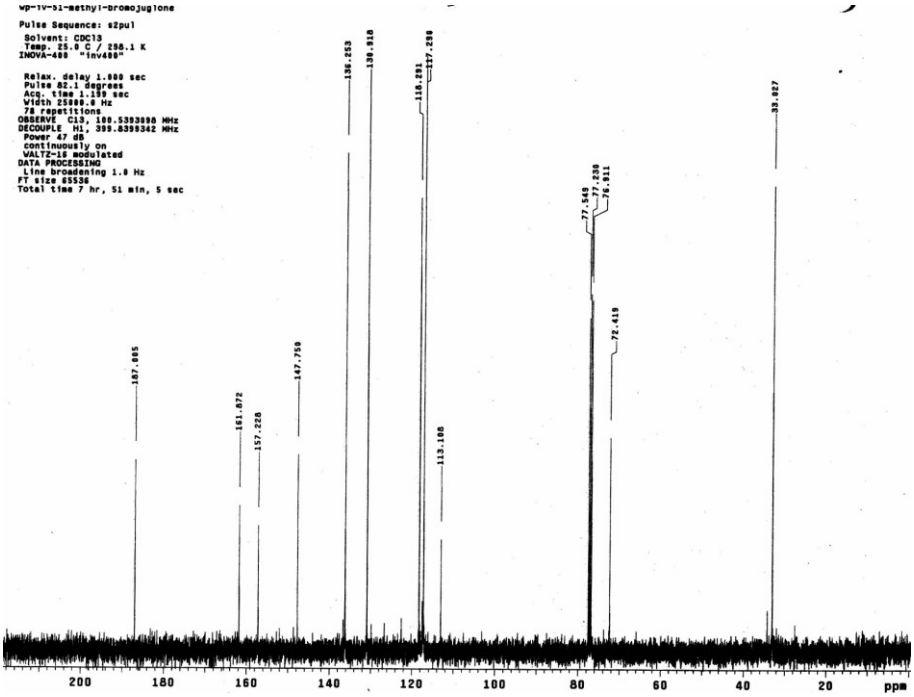

wp-iii-63-oxidation-product
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 77.3 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944906 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
12.437
7.384
7.365
7.323
7.304
7.280
6.879
3.984
1.547
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.68
1.05
1.10
2.00
3.38

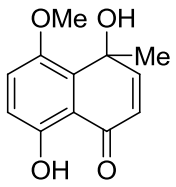

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
116 repetitions
OBSERVE C13, 100.5393105 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
190.647
183.484
156.681
154.124
141.653
136.518
126.519
123.693
117.472
114.097
77.541
77.222
76.904
57.614
160
140
120
100
80
60
40
20
ppm


HO
Me
Br
OH
O

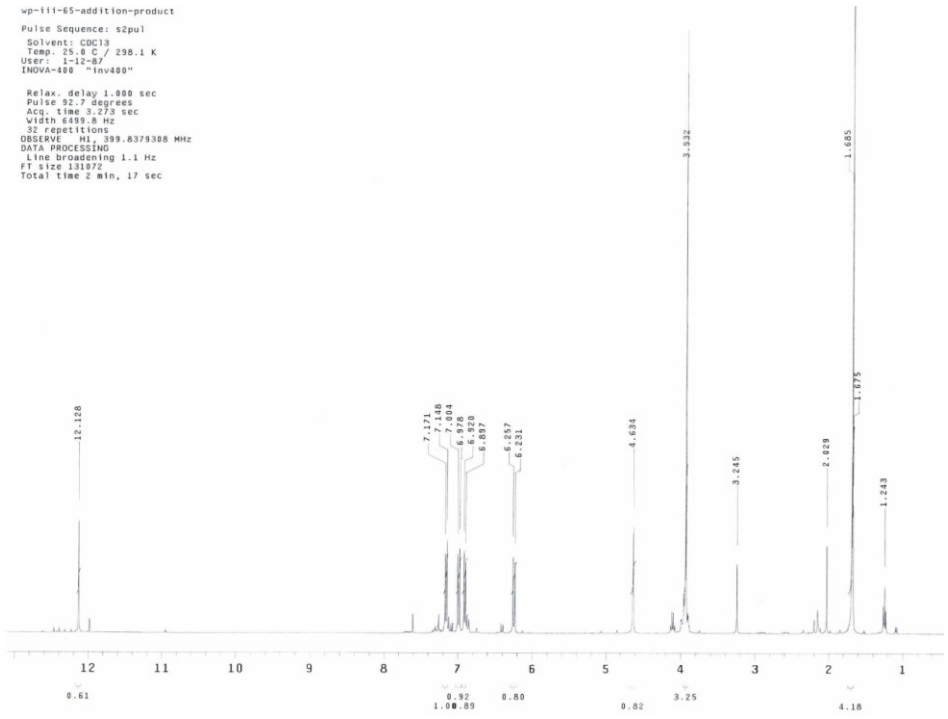
137

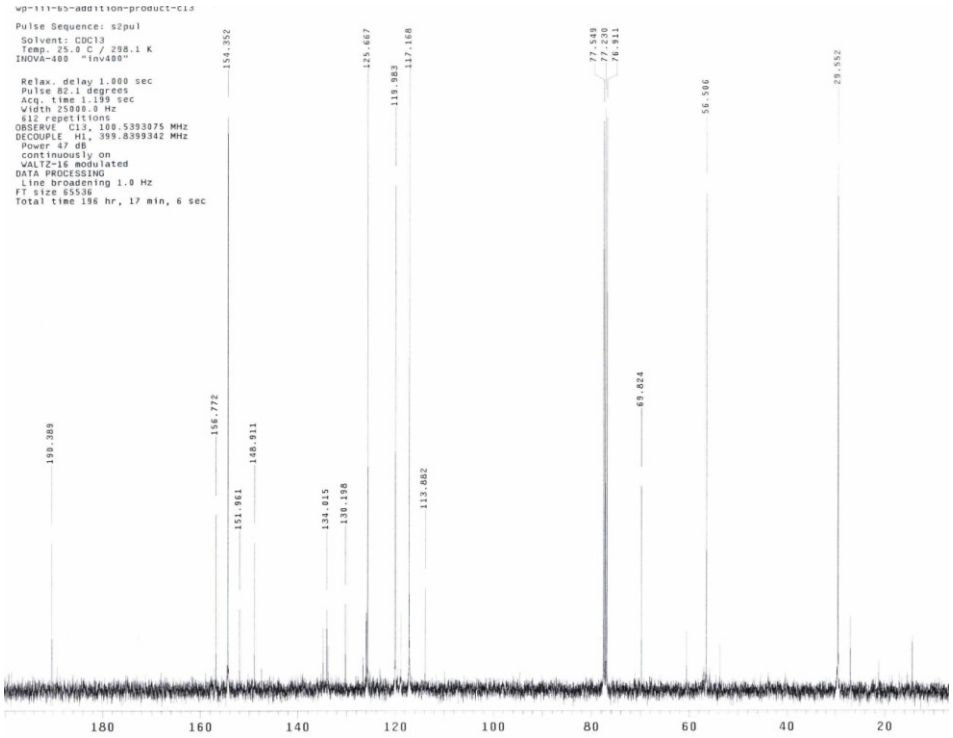

wp-iv-48-methyl-bromo-juglon
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
Single scan
OBSERVE H1, 499.8944822 MHz
DATA PROCESSING
FT size 32768
Total time 0 min
12.055
7.531
7.516
7.385
7.289
7.277
6.926
6.908
6.733
1.692
1.738
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.83
1.17
1.02
0.92
1.00
3.10

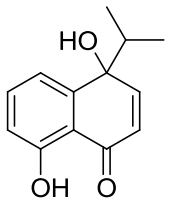

wp-iv-51-methyl-bromojuglone
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25988.6 Hz
78 repetitions
OBSERVE C13, 100.5393898 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
187.665
161.872
157.226
147.750
136.253
130.910
118.891
117.298
113.105
77.549
77.238
76.911
72.419
33.027
200
180
160
140
120
100
80
60
40
20
ppm


OMe
OH
Me
OH
O

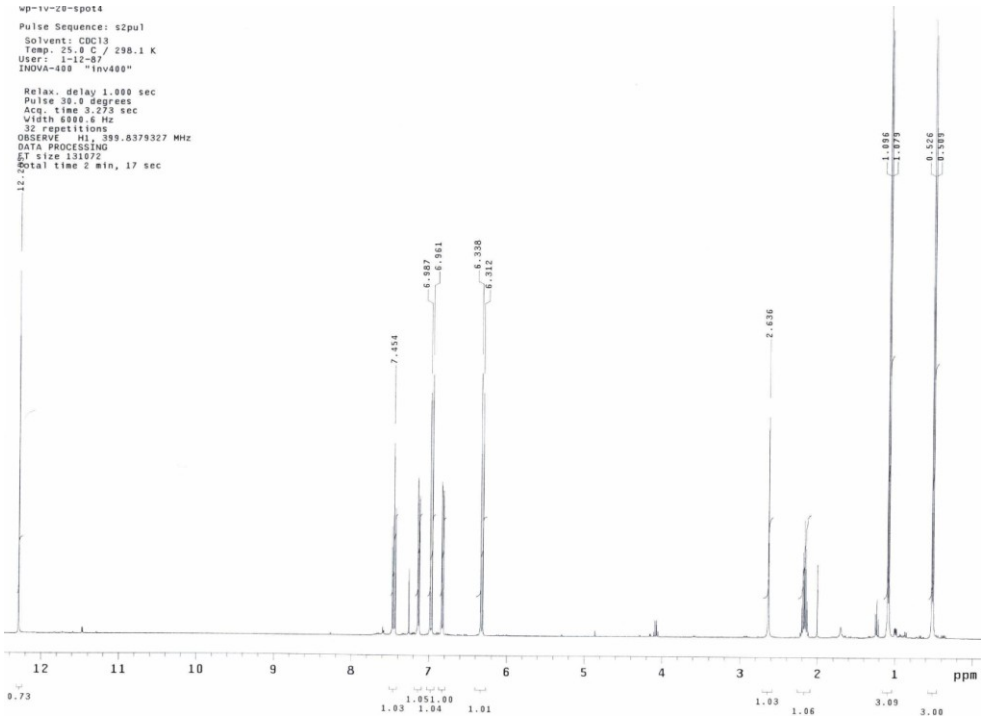
138

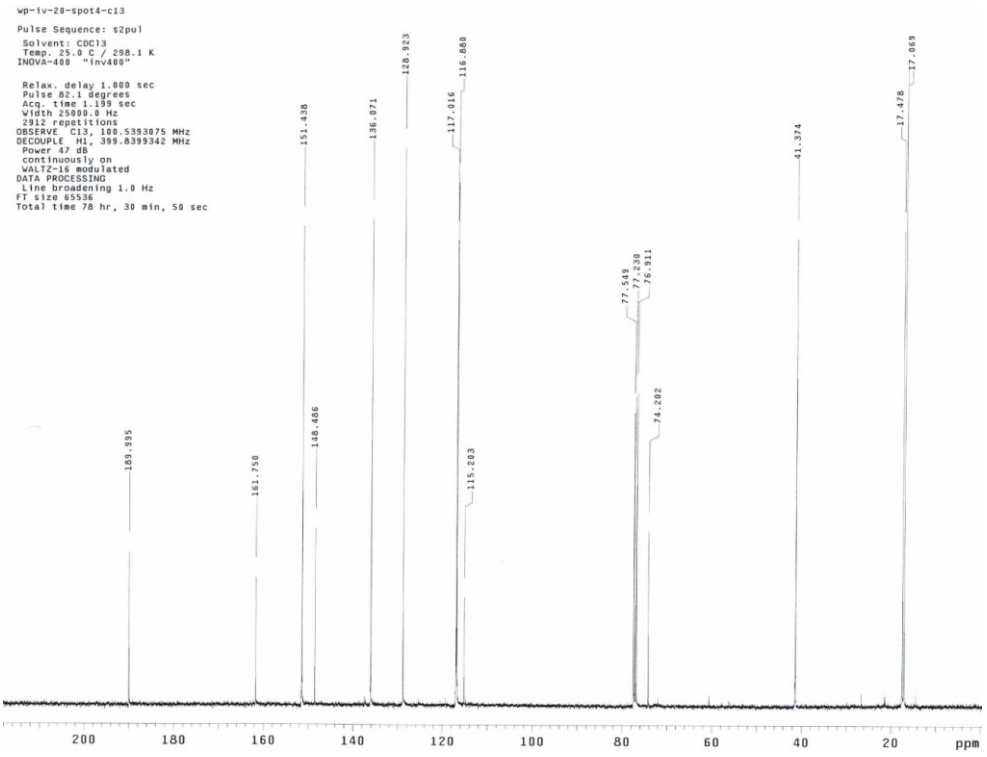

wp-iii-65-addition-product
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.6 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 92.7 degrees
Acq. time 3.273 sec
Width 6499.8 Hz
32 repetitions
OBSERVE H1, 399.8379308 MHz
DATA PROCESSING
Line broadening 1.1 Hz
FT size 131072
Total time 2 min, 17 sec
12.128
7.171
7.148
7.104
6.978
6.920
6.897
6.257
6.231
4.634
3.932
3.245
2.829
1.685
1.675
1.243
0.61
0.92
1.00
0.89
0.80
0.82
3.25
4.18

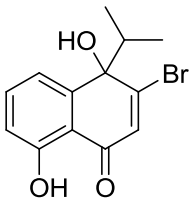

wp-iii-65-addition-product-C13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
612 repetitions
OBSERVE C13, 100.5393075 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 196 hr, 17 min, 6 sec
154.352
156.772
151.961
148.911
134.015
130.198
125.667
119.983
117.168
113.882
77.548
77.230
76.911
69.824
56.506
29.552
190.389


HO
OH
O

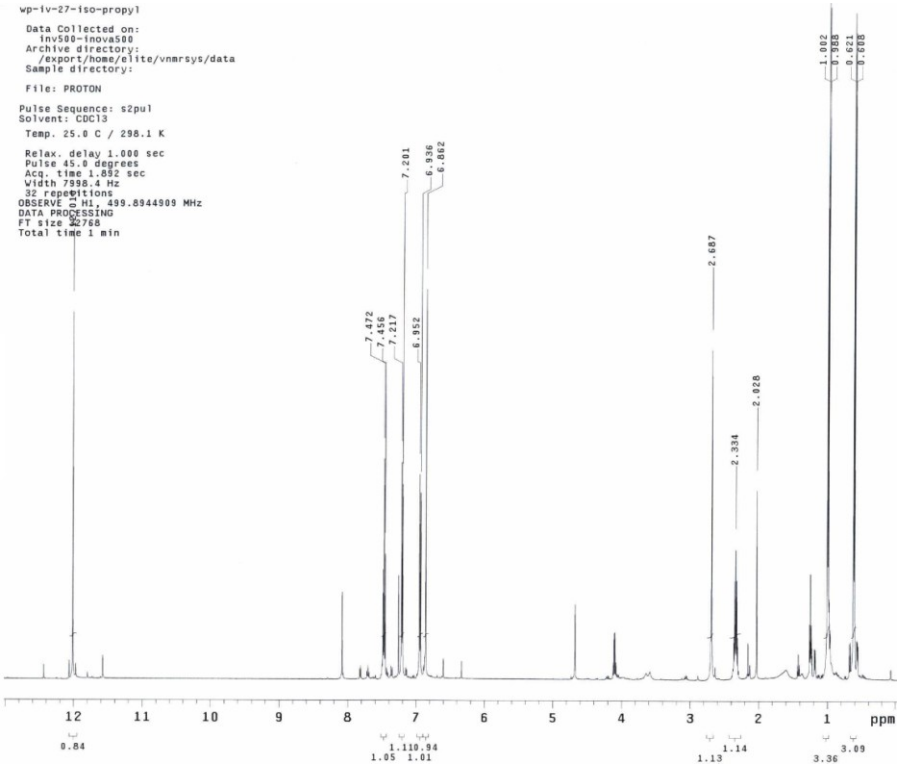
139

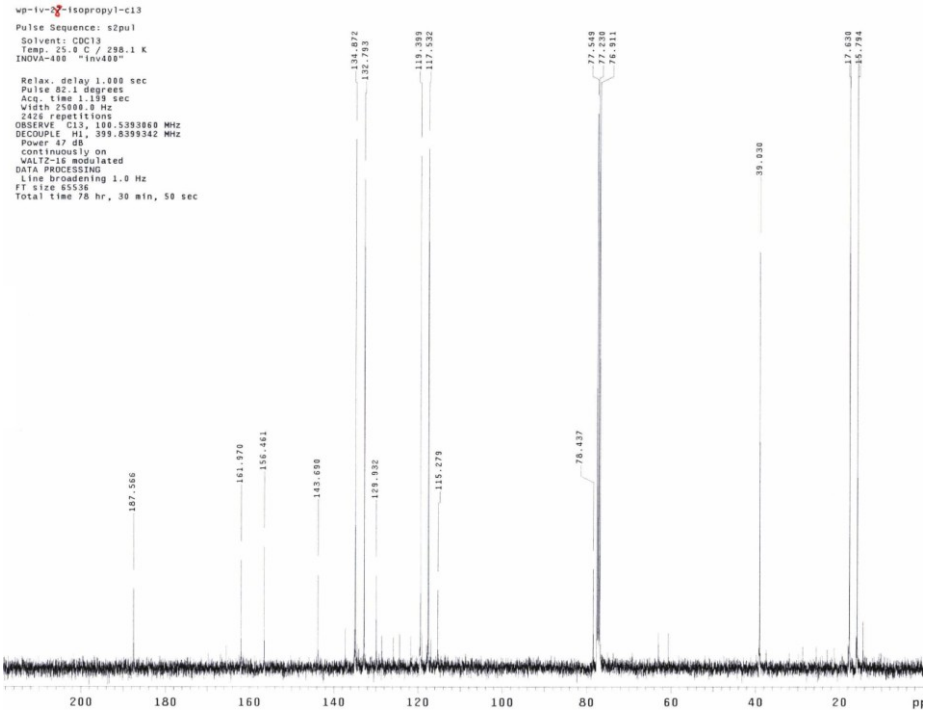

wp-iv-28-spot4
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: i-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379327 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
12.
7.454
6.987
6.961
6.338
6.312
2.636
1.086
1.079
0.526
0.509
ppm
0.73
1.03
1.051.00
1.04
1.01
1.03
1.06
3.09
3.00

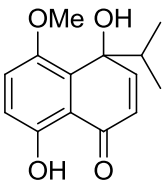

wp-iv-28-spot4-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2912 repetitions
OBSERVE C13, 100.5393875 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 59 sec
189.995
161.750
151.438
148.486
136.871
128.923
117.016
116.880
115.203
77.549
77.238
76.911
74.282
41.374
17.478
17.069
ppm


HO
Br
OH
O

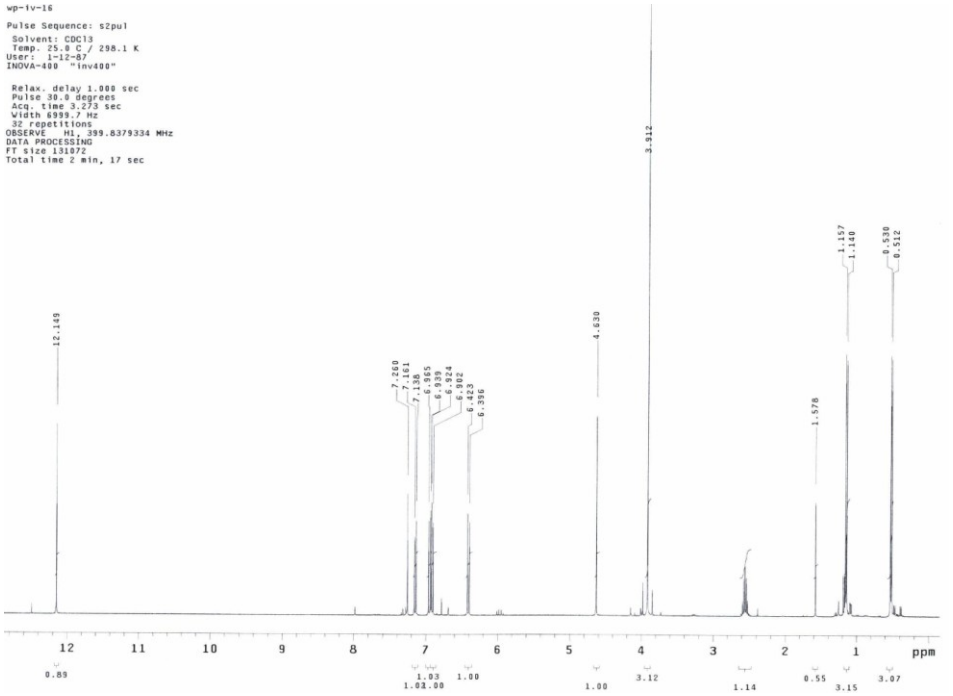
140

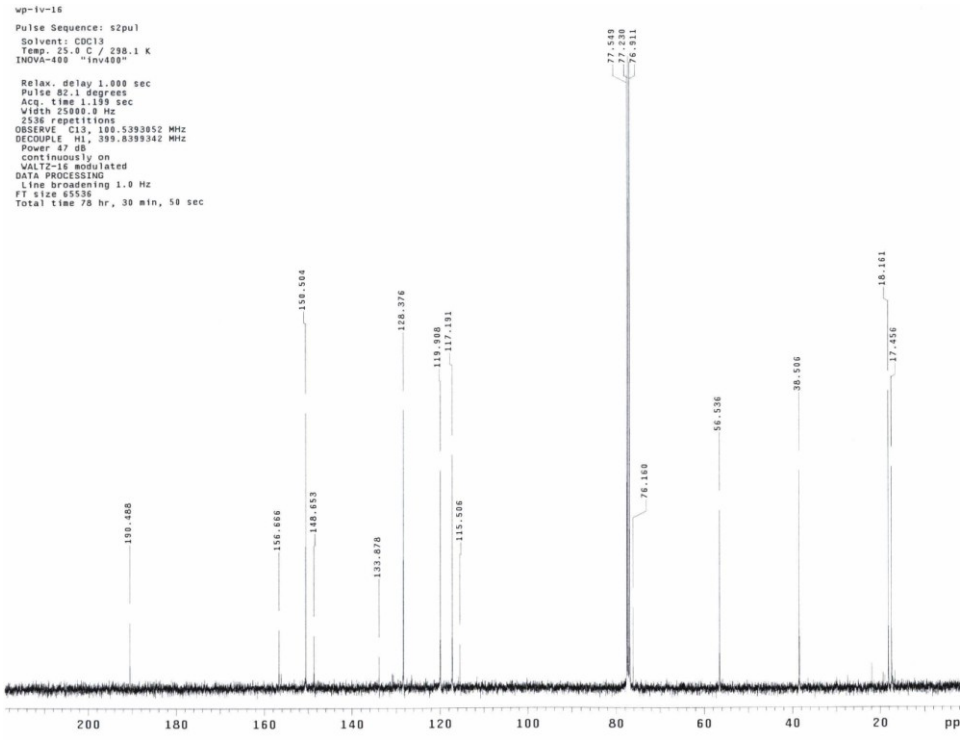

wp-iv-27-iso-propyl
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.852 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944909 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
7.472
7.456
7.217
7.201
6.952
6.936
6.862
2.687
2.334
2.026
1.002
0.988
0.621
0.608
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.84
1.11
0.94
1.05
1.01
1.13
1.14
3.36
3.09

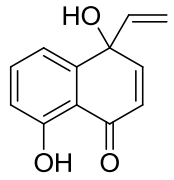

wp-iv-27-isopropyl-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2426 repetitions
OBSERVE C13, 100.5393860 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 50 sec
134.872
132.793
119.399
117.532
77.549
77.230
76.911
17.630
15.794
39.038
187.566
161.970
156.461
143.698
128.932
115.279
78.437
200
180
160
140
120
100
80
60
40
20


OMe OH
OH O

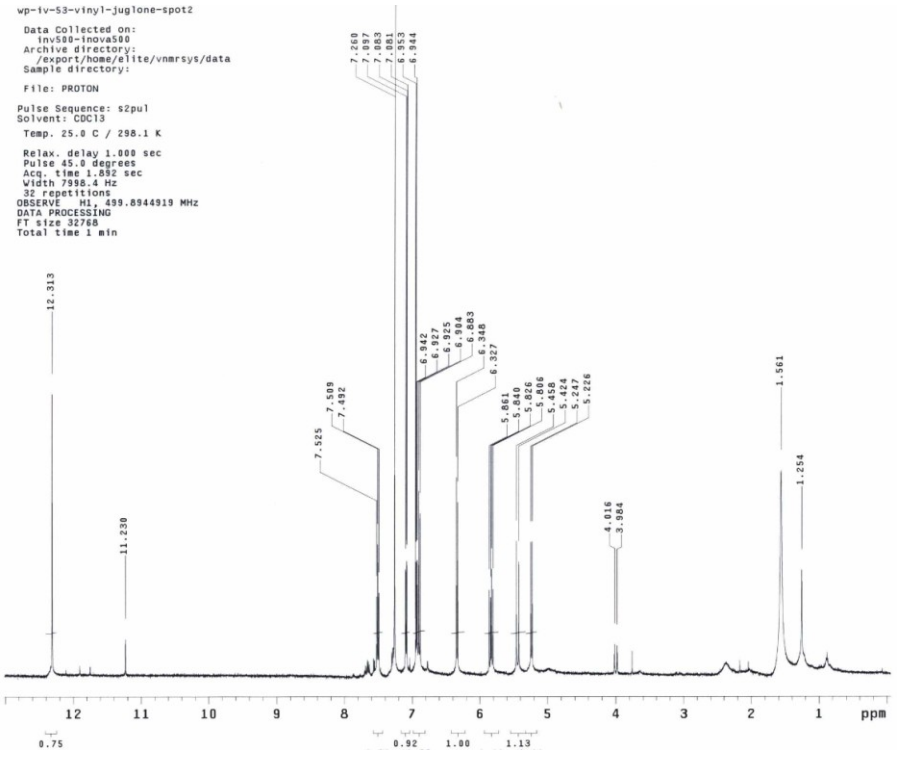
141

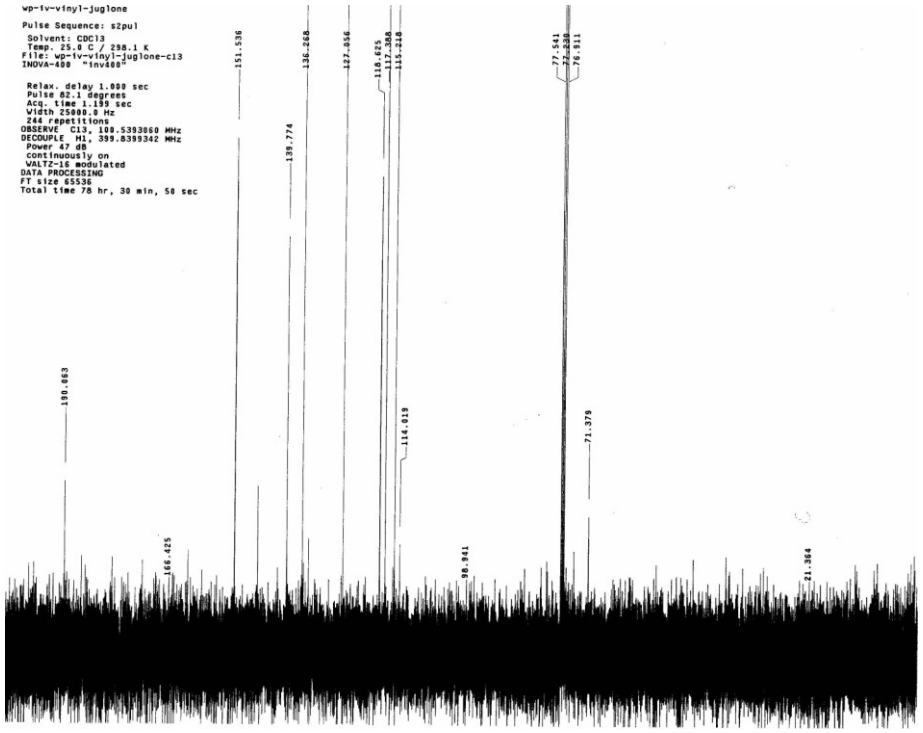

wp-iv-16
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: i-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
32 repetitions
OBSERVE H1, 399.8379334 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
12.149
7.260
7.161
7.138
6.965
6.939
6.924
6.902
6.423
6.396
4.630
3.912
1.578
1.157
1.140
0.530
0.512
ppm

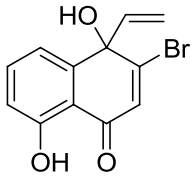

wp-iv-16
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2536 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 50 sec
77.549
77.230
76.911
76.160
190.488
156.666
150.584
148.653
133.878
128.376
119.908
117.191
115.506
56.536
38.506
18.161
17.456
pp


HO
OH
O

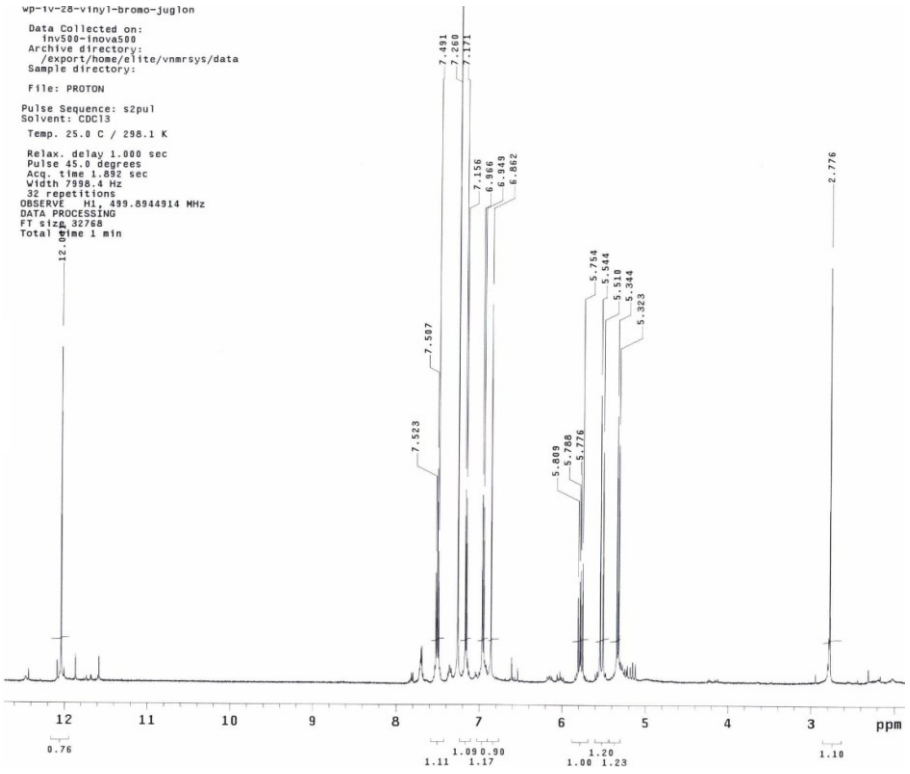
142

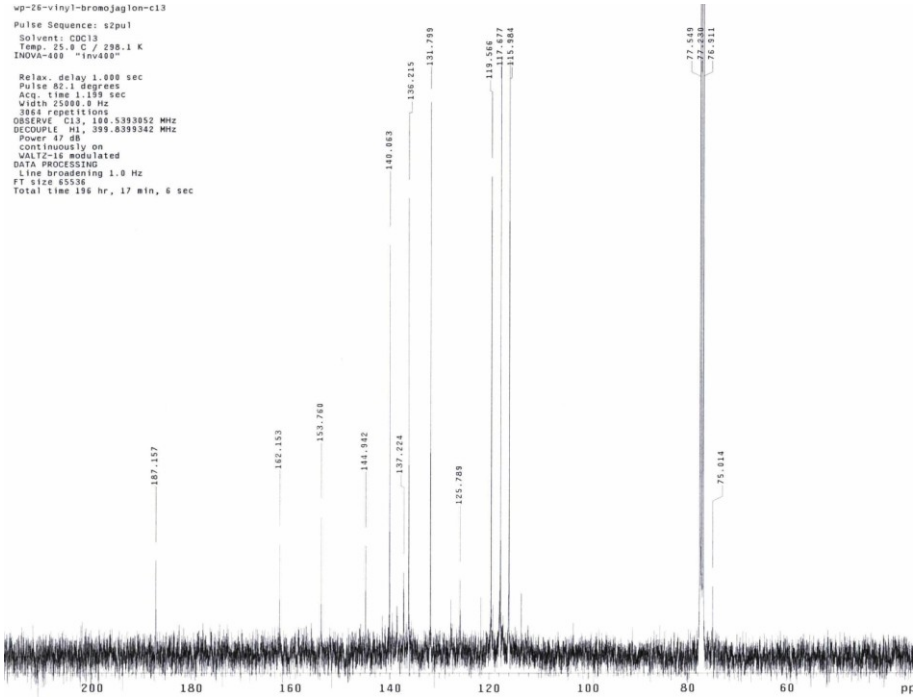

wp-iv-53-vinyl-juglone-spot2
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944919 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
12.313
11.230
7.525
7.509
7.492
7.060
7.057
7.053
7.051
6.953
6.944
6.942
6.927
6.925
6.904
6.883
6.348
6.327
5.861
5.840
5.826
5.806
5.458
5.444
5.247
5.226
4.016
3.984
1.561
1.254
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.75
0.92
1.00
1.13

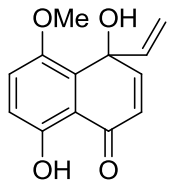

wp-iv-vinyl-juglone
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: wp-iv-vinyl-juglone-c13
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.8 Hz
244 repetitions
OBSERVE C13, 100.5393860 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
FT size 65536
Total time 78 hr, 30 min, 58 sec
190.663
166.425
151.536
139.774
136.268
127.656
118.625
117.388
115.218
114.019
98.941
77.541
77.230
76.911
71.379
21.364


HO
Br
OH
O

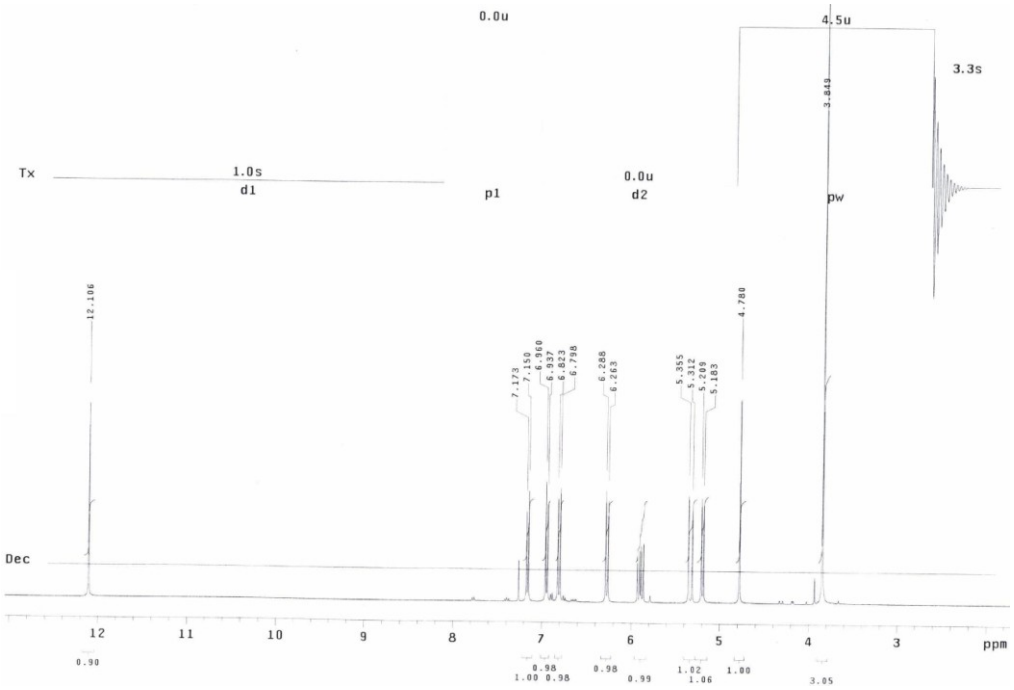
143

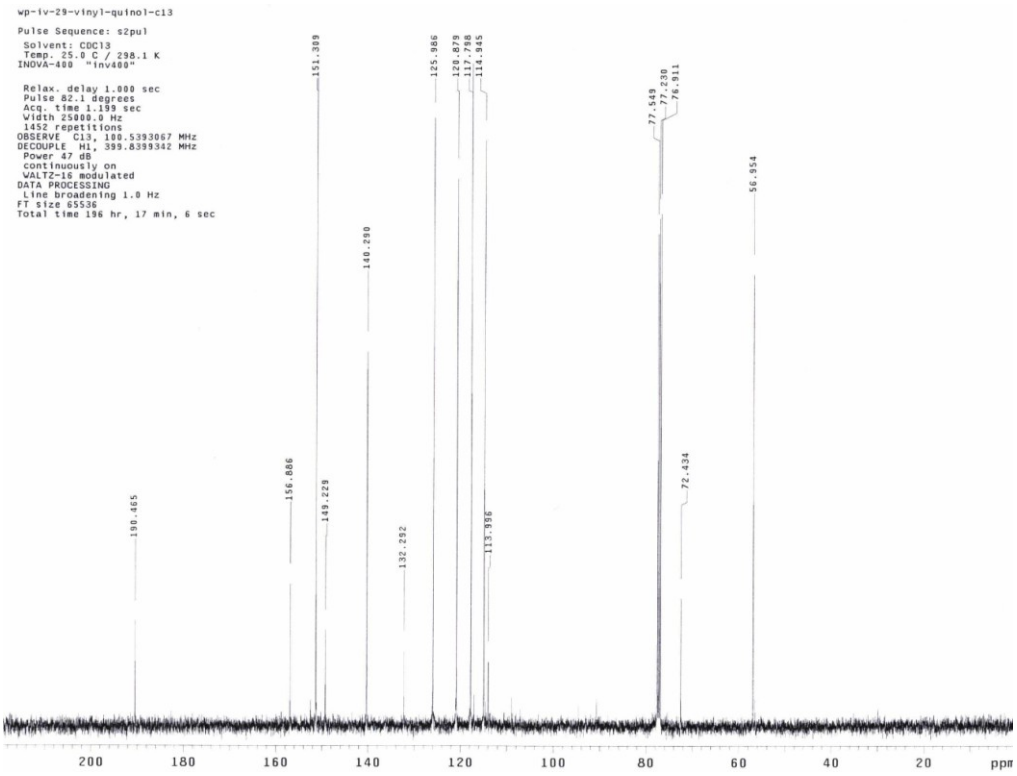

wp-1v-28-vinyl-bromo-juglon
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944914 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
12.049
7.587
7.523
7.491
7.260
7.171
7.156
6.966
6.949
6.862
5.809
5.788
5.776
5.754
5.544
5.510
5.344
5.323
2.776
12
11
10
9
8
7
6
5
4
3
ppm
0.76
1.11
1.09
0.90
1.17
1.00
1.20
1.23
1.10

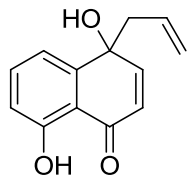

wp-28-vinyl-bromojaglon-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
3064 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 196 hr, 17 min, 6 sec
187.157
162.153
153.769
144.942
140.863
137.224
136.215
131.799
125.789
119.566
117.677
115.984
77.549
77.231
76.911
75.614
200
180
160
140
120
100
80
60


OMe
OH
OH
O

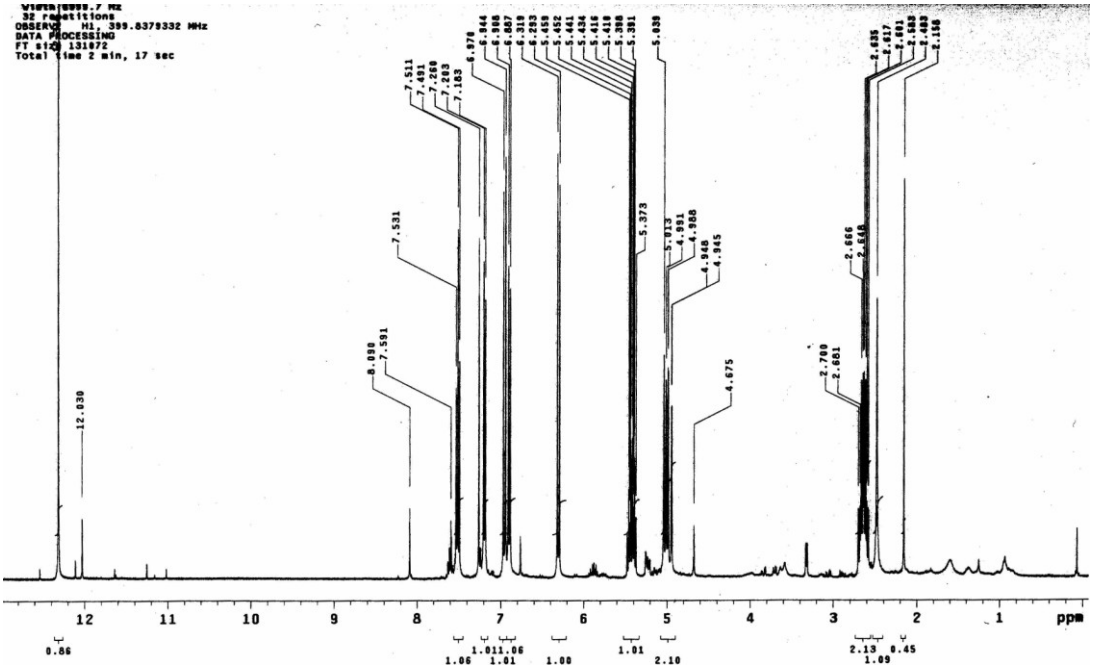
144

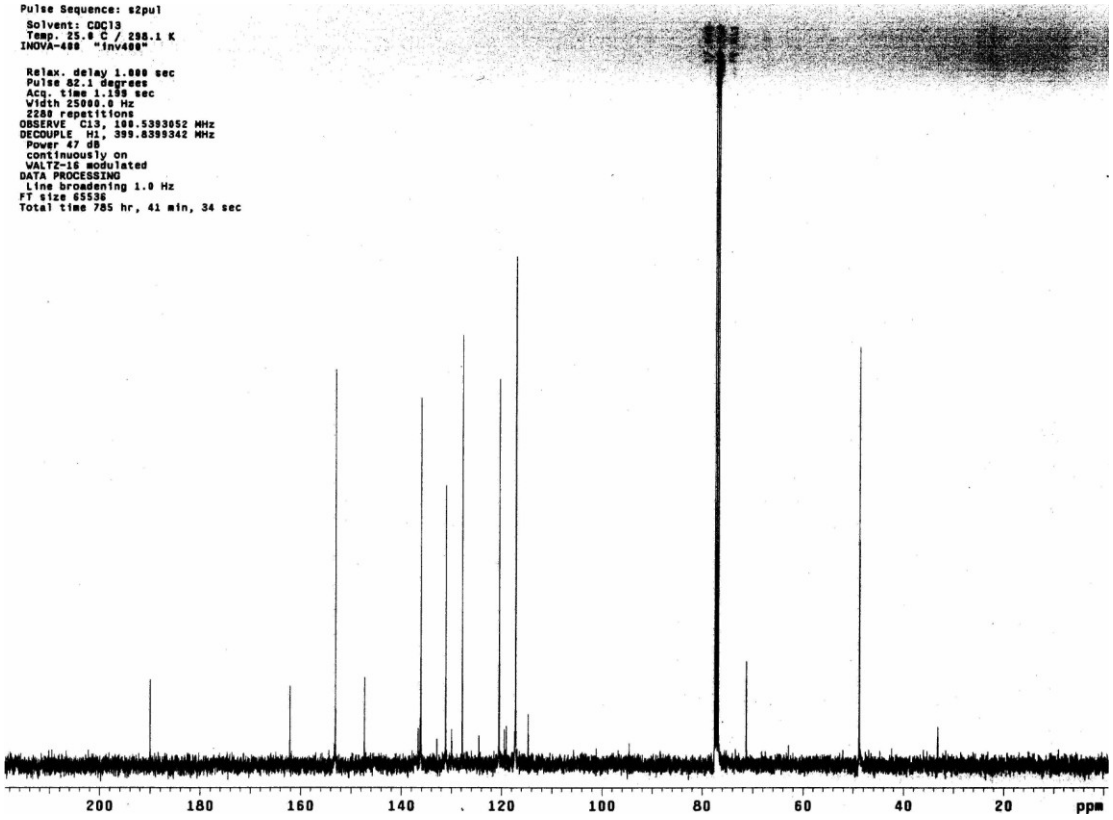

0.0u
4.5u
3.3s
3.849
Tx
1.0s
d1
p1
0.0u
d2
pw
12.106
7.173
7.150
6.360
6.337
6.823
6.798
6.288
6.263
5.355
5.332
5.208
5.183
4.780
Dec
12
11
10
9
8
7
6
5
4
3
ppm
0.90
0.98
1.00 0.98
0.98
0.99
1.02
1.06
1.00
3.05

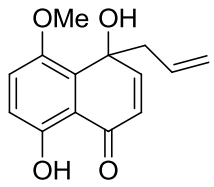

wp-iv-29-vinyl-quinol-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1452 repetitions
OBSERVE C13, 100.5393067 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 196 hr, 17 min, 6 sec
190.465
156.086
151.389
149.229
140.290
132.292
125.986
120.879
117.748
114.945
113.986
77.549
77.230
76.911
72.434
56.954
200
180
160
140
120
100
80
60
40
20
ppm


HO
OH
O

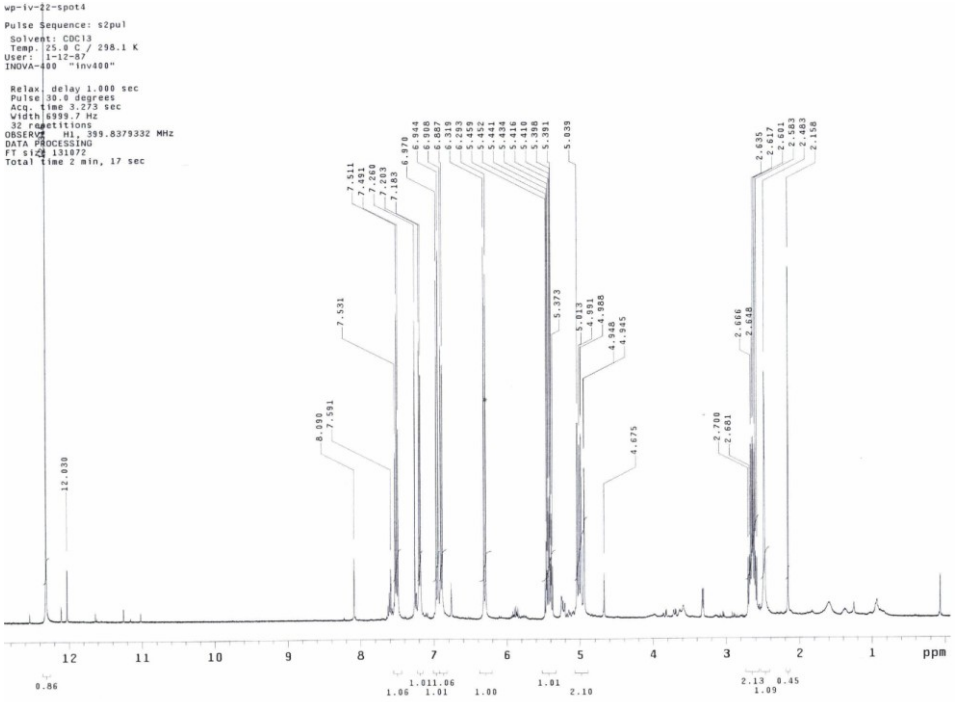
145

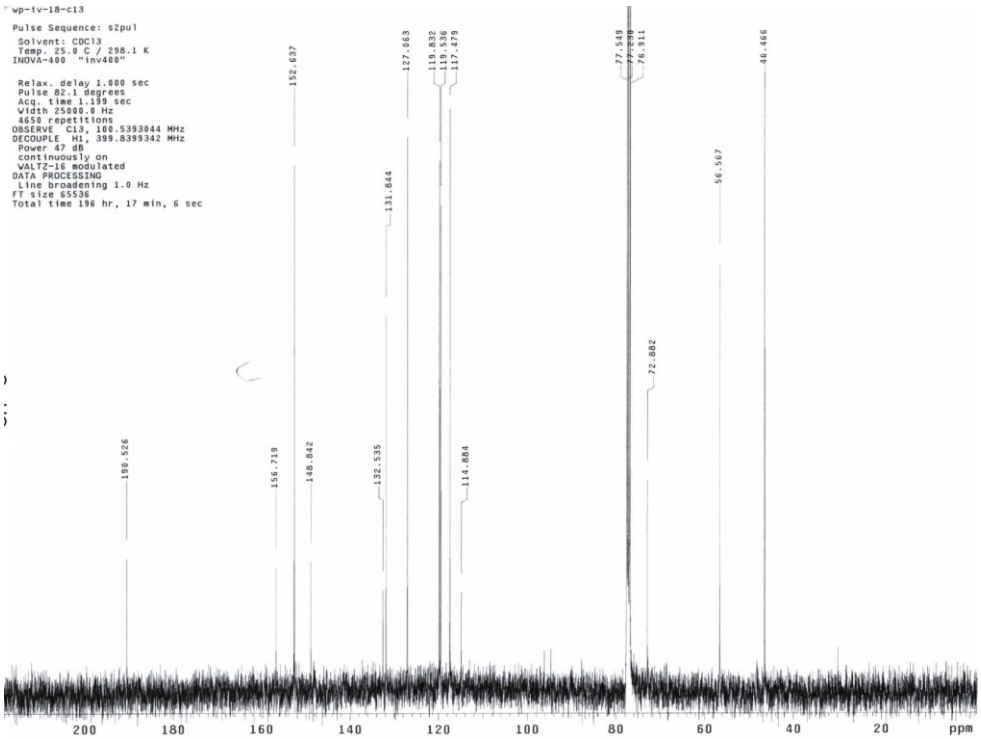

32 repetitions
OBSERVE H1, 399.8379332 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
12.030
8.098
7.591
7.531
7.511
7.491
7.269
7.203
7.163
6.878
6.844
6.808
6.687
6.653
6.283
5.459
5.452
5.441
5.434
5.418
5.411
5.388
5.381
5.039
5.373
5.013
4.991
4.988
4.948
4.945
4.675
2.700
2.681
2.666
2.648
2.635
2.617
2.601
2.583
2.483
2.158
ppm
0.86
1.06
1.01
1.06
1.01
1.00
1.01
2.10
2.13
1.09
0.45

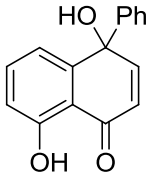

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2280 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 785 hr, 41 min, 34 sec
200
180
160
140
120
100
80
60
40
20
ppm


OMe
OH
OH
O

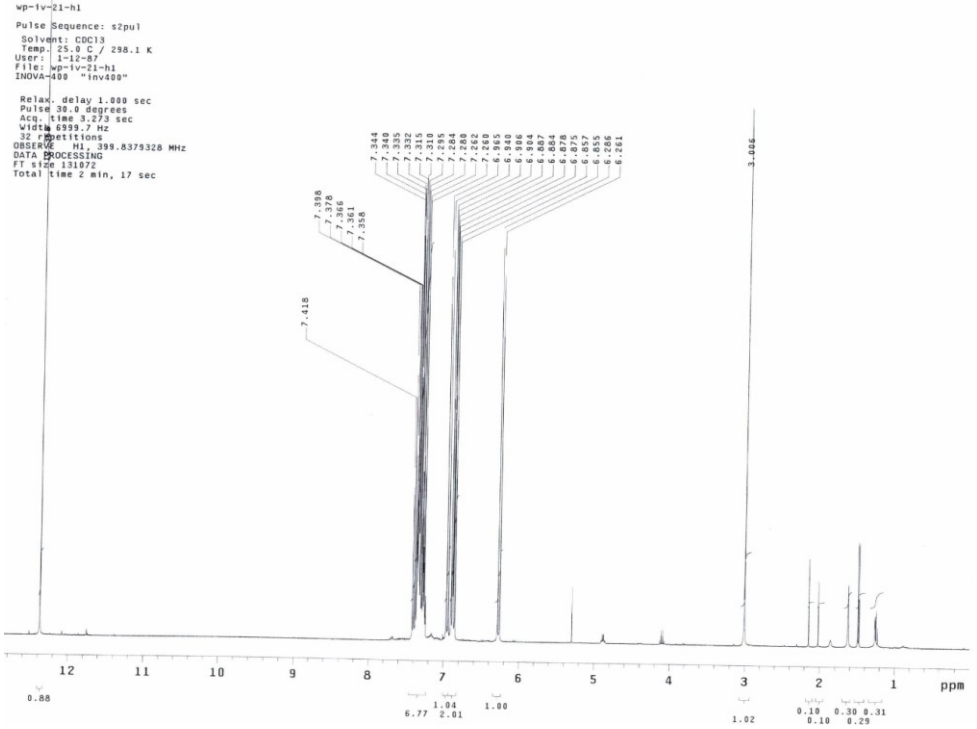
147

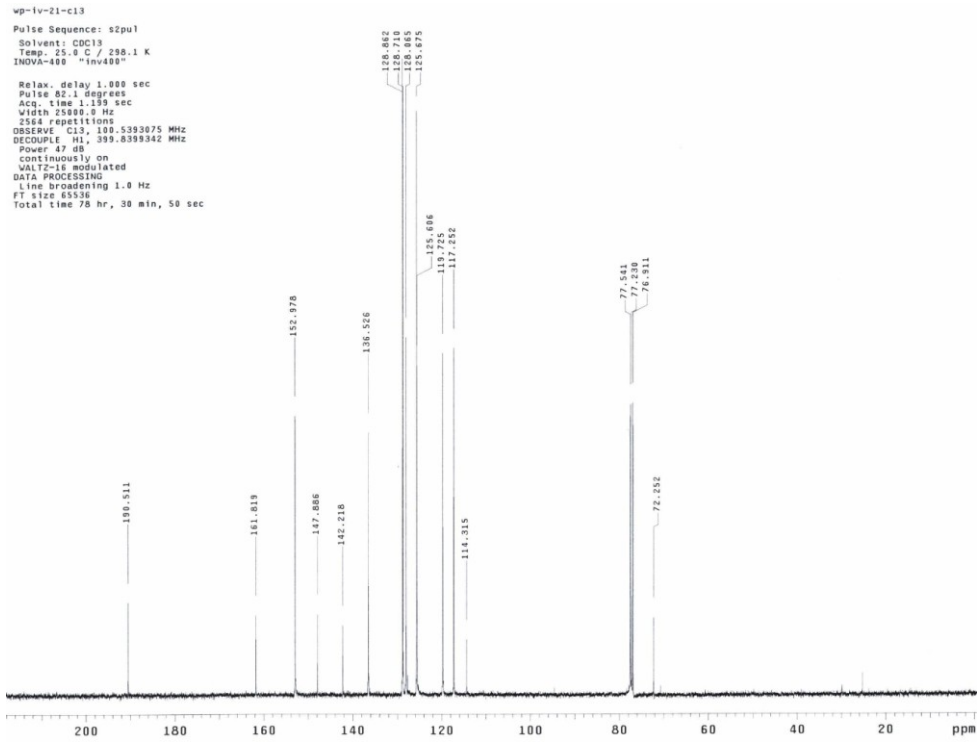

wp-iv-22-spot4
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
32 repetitions
OBSERVE H1, 399.8379332 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
12.038
8.599
7.591
7.531
7.511
7.491
7.269
7.245
7.183
6.970
6.944
6.906
6.887
6.319
6.293
5.455
5.452
5.441
5.434
5.416
5.408
5.398
5.391
5.038
5.373
5.013
4.991
4.988
4.948
4.945
4.675
2.700
2.681
2.666
2.638
2.635
2.617
2.601
2.483
2.480
2.158
ppm

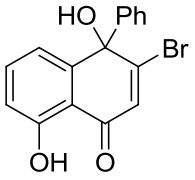

wp-iv-18-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
4650 repetitions
OBSERVE C13, 100.5393044 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 196 hr, 17 min, 6 sec
190.526
156.719
152.637
148.842
132.535
131.644
127.063
119.832
119.536
117.479
114.884
77.549
77.230
76.911
72.682
56.567
46.466
ppm


HO
Ph
OH
O

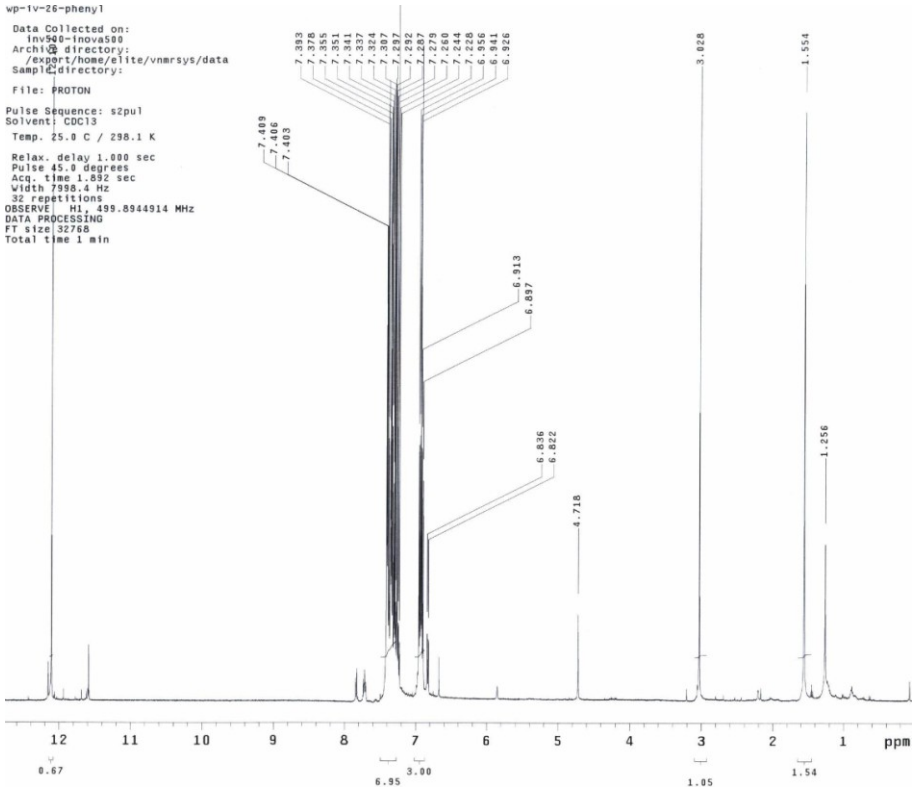
148

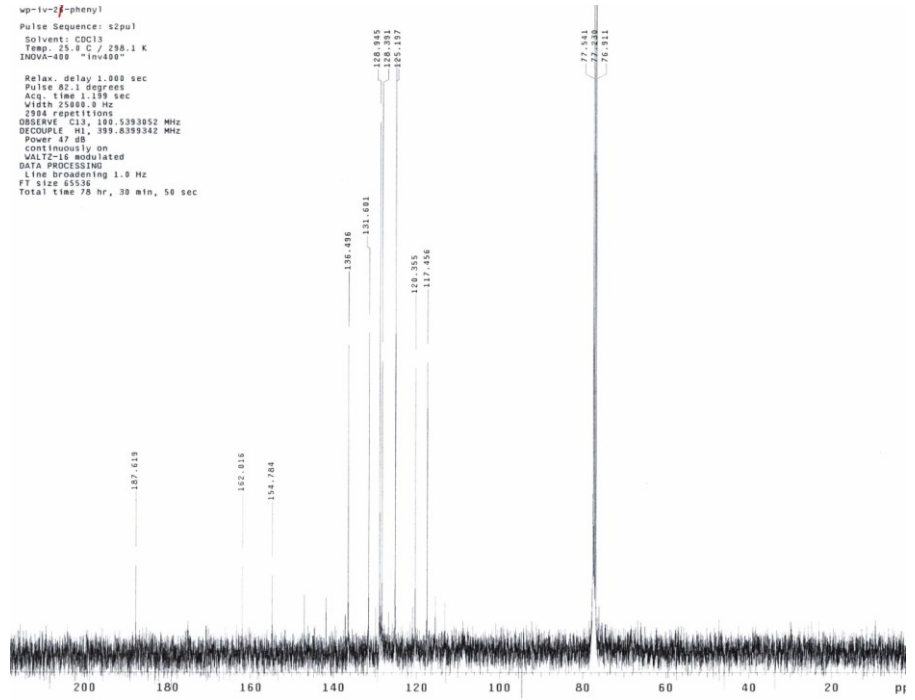

wp-iv-21-h1
Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
User: 1-12-87
File: wp-iv-21-h1
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
32 repetitions
OBSERVE H1, 399.8379328 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
7.418
7.396
7.378
7.366
7.361
7.358
7.344
7.340
7.335
7.332
7.315
7.310
7.295
7.284
7.280
7.262
6.965
6.960
6.906
6.904
6.887
6.884
6.880
6.875
6.857
6.855
6.266
6.261
3.066
ppm
0.88
6.77
1.04
2.01
1.00
1.02
0.10
0.10
0.30
0.29
0.31

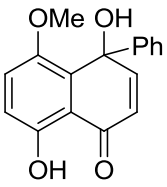

wp-iv-21-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2564 repetitions
OBSERVE C13, 100.5393075 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 50 sec
128.662
128.210
126.065
125.675
125.686
119.725
117.292
77.541
77.208
76.911
152.978
136.526
190.511
161.819
147.686
142.218
114.315
72.252
ppm


HO
Ph
Br
OH
O

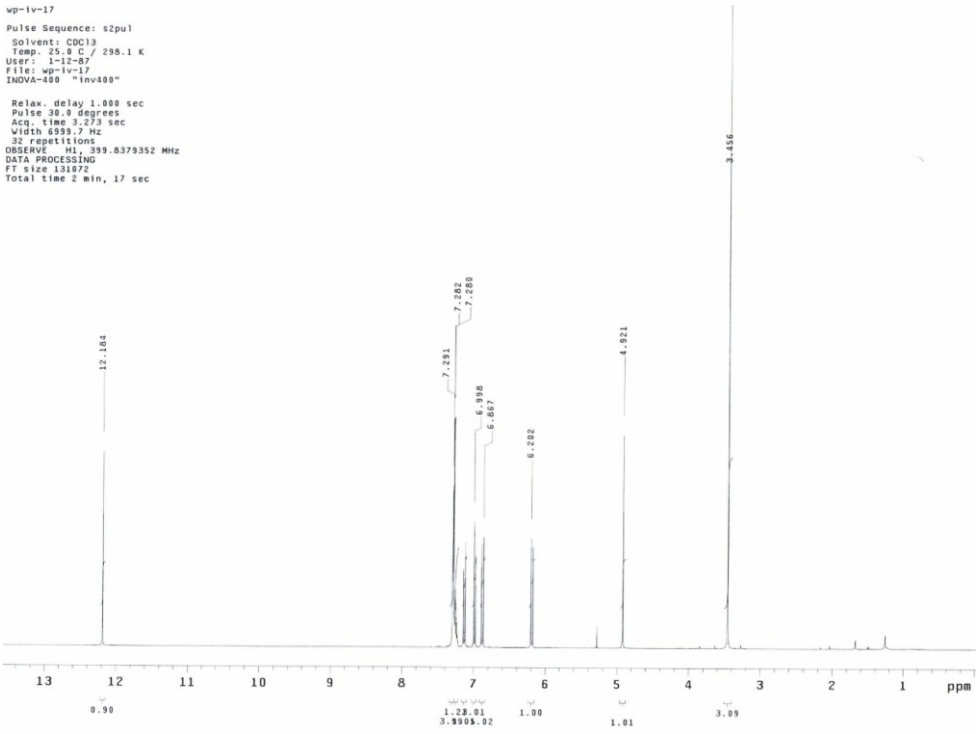
149

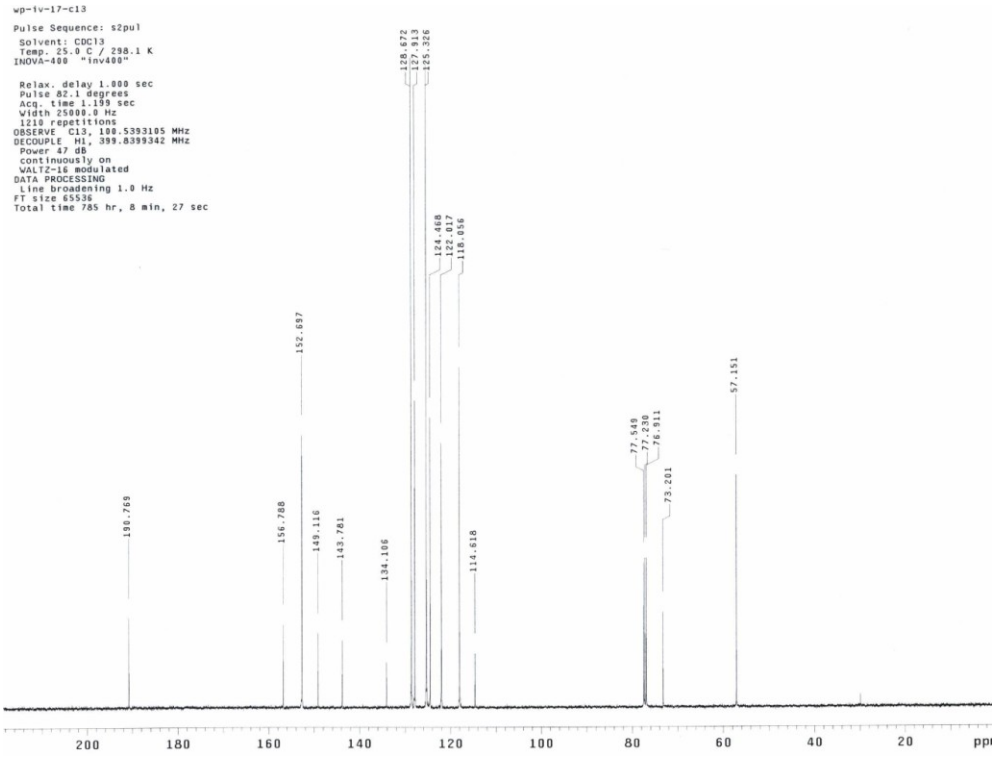

wp-1v-26-phenyl
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944914 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
7.409
7.406
7.403
6.913
6.897
6.836
6.822
4.718
3.028
1.554
1.256
ppm
0.67
6.95
3.00
1.05
1.54

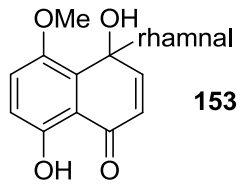

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2304 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 50 sec
128.945
128.391
125.197
77.541
77.230
76.911
136.496
131.601
120.355
117.456
187.619
162.016
154.784


OMe
OH
Ph
OH
O

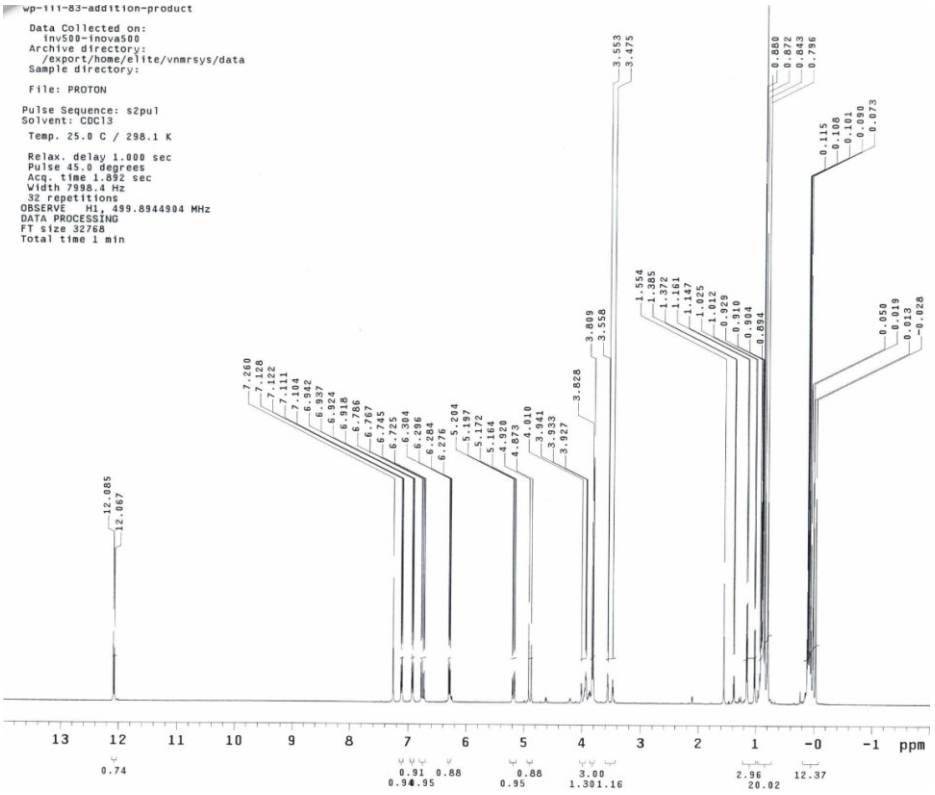
150

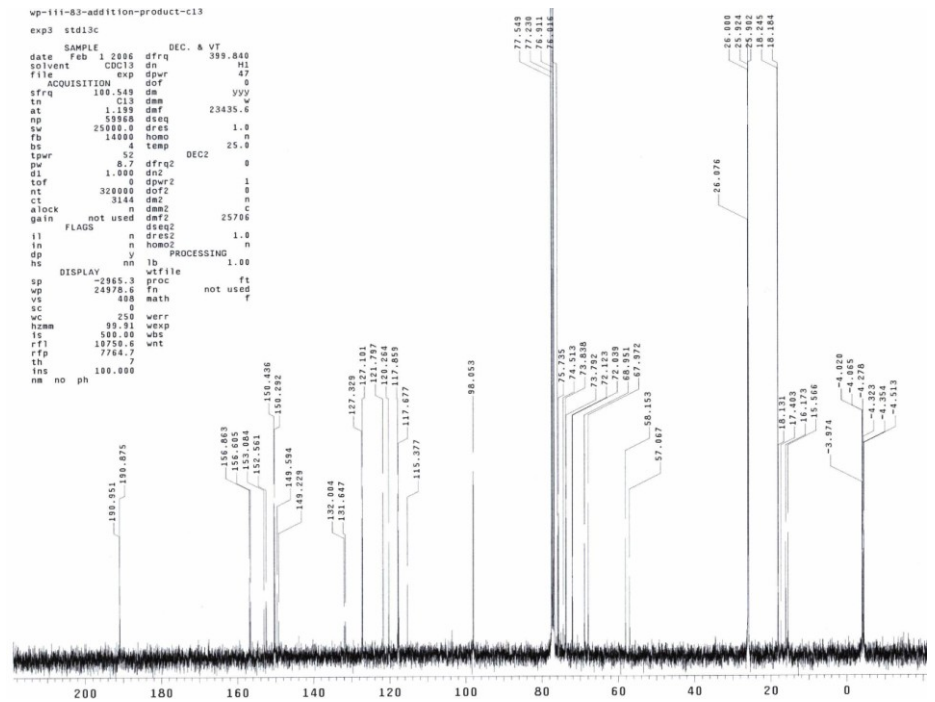

wp-iv-17
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
File: wp-iv-17
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
32 repetitions
OBSERVE H1, 399.8379352 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
12.184
7.282
7.280
7.291
6.998
6.867
6.282
4.921
3.456
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.90
1.28
3.99
5.02
1.00
1.01
3.09

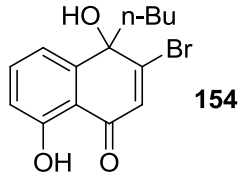

wp-iv-17-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1210 repetitions
OBSERVE C13, 100.5393105 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 785 hr, 8 min, 27 sec
190.769
156.788
152.697
149.116
143.761
134.106
128.672
127.913
125.326
124.468
122.017
118.056
114.618
77.549
77.230
76.911
73.201
57.151
200
180
160
140
120
100
80
60
40
20


OMe OH
rhamnal
OH O

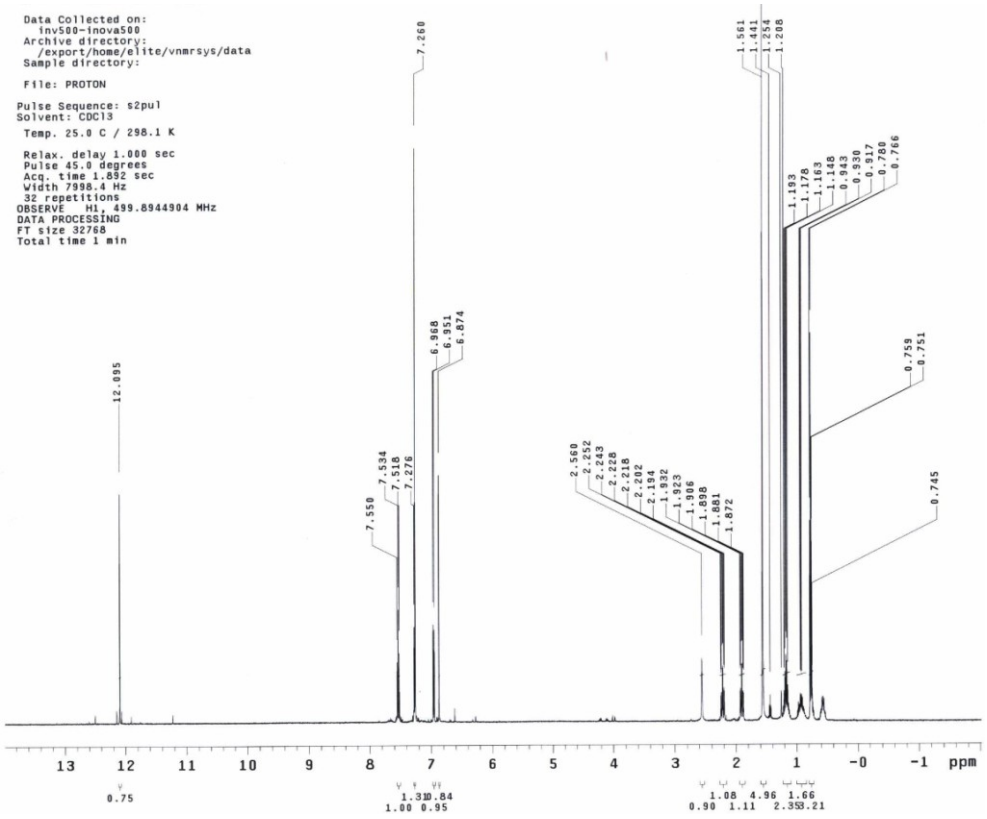
153

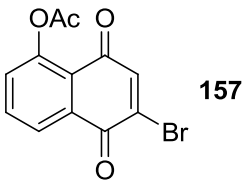

wp-iii-83-addition-product
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944904 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
ppm
0.74
0.91
0.94
0.95
0.88
0.95
0.88
1.30
3.00
1.16
2.96
20.02
12.37


wp-iii-83-addition-product-c13
exp3 std13c
SAMPLE
date Feb 1 2006
solvent CDCl3
file exp
ACQUISITION
sfrq 100.549
tn C13
at 1.199
np 59968
sw 25000.0
fb 14000
bs 4
tpwr 52
pw 8.7
d1 1.000
tof 0
nt 320000
ct 3144
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -2965.3
wp 24978.6
vs 408
sc 0
wc 250
hzmm 99.91
is 500.00
rfl 10758.6
rfp 7764.7
th 7
ins 100.000
nm no ph
DEC. & VT
dfrq 399.840
dn H1
dpwr 47
dof 0
dm yyy
dmm w
dmf 23435.6
dseq
dres 1.0
homo n
temp 25.0
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 25706
dseq2
dres2 1.0
homo2 n
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbt
wnt
200
180
160
140
120
100
80
60
40
20
0

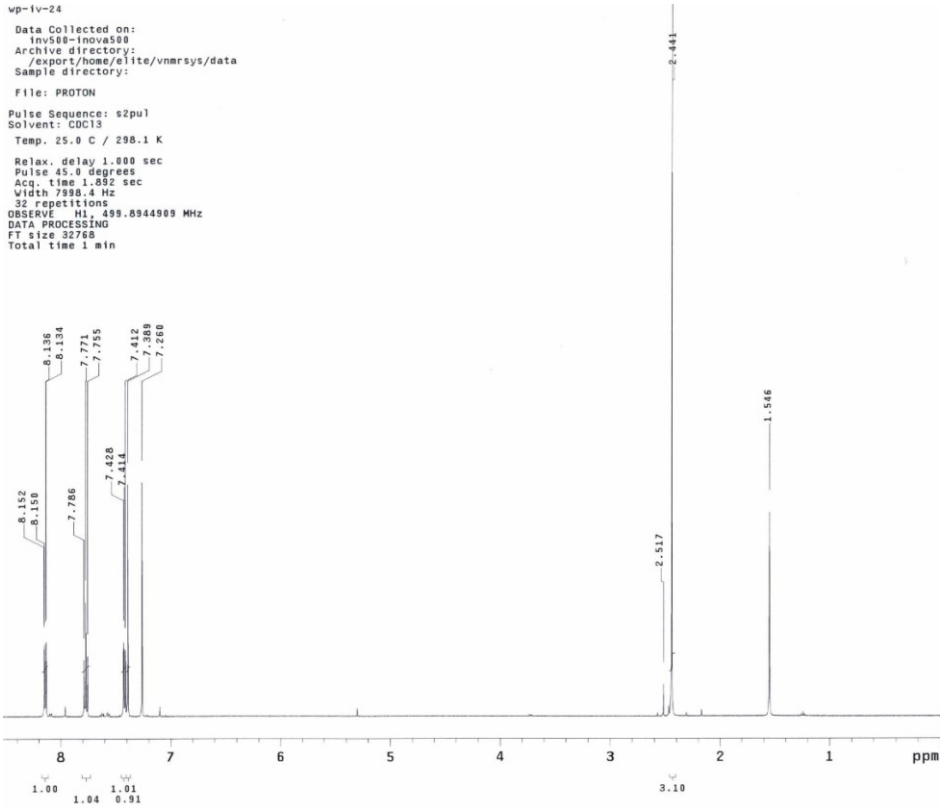

HO
n-Bu
Br
OH
O

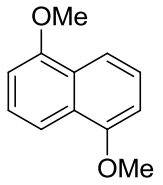
154


Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944904 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
12.095
7.550
7.534
7.518
7.276
7.260
6.968
6.951
6.874
2.560
2.252
2.243
2.228
2.218
2.202
2.194
2.183
1.923
1.906
1.898
1.881
1.872
1.561
1.441
1.254
1.208
1.193
1.178
1.163
1.148
0.943
0.930
0.917
0.780
0.766
0.759
0.751
0.745
13 12 11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm
0.75
1.00 0.95
1.08 4.96 1.66
0.90 1.11 2.35 3.21

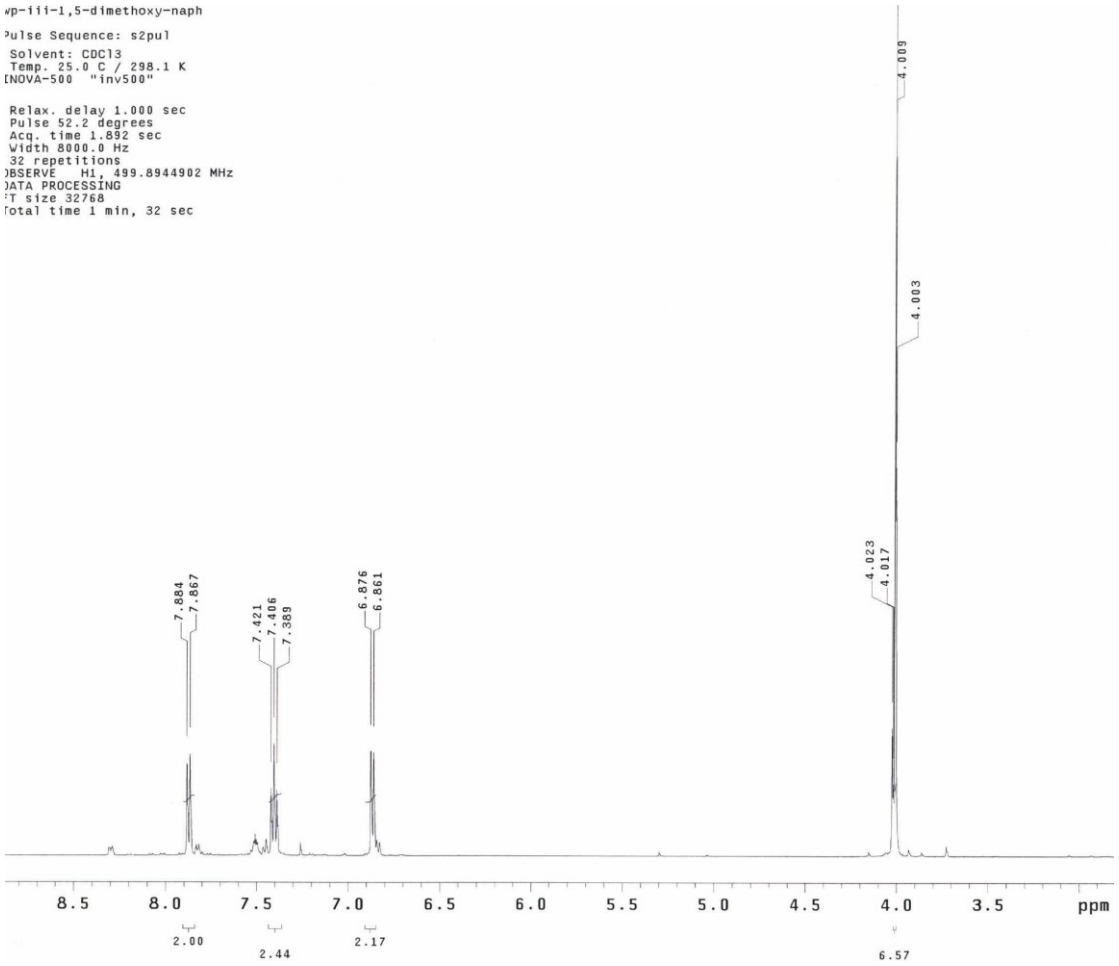

OAc
O
Br
O

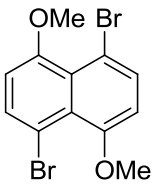
157


wp-iv-24
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7988.4 Hz
32 repetitions
OBSERVE H1, 499.8944989 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
8.441
8.136
8.134
7.771
7.755
7.412
7.389
7.260
1.546
8.152
8.150
7.786
7.428
7.414
2.517
8
7
6
5
4
3
2
1
ppm
1.00
1.04
1.01
0.91
3.10

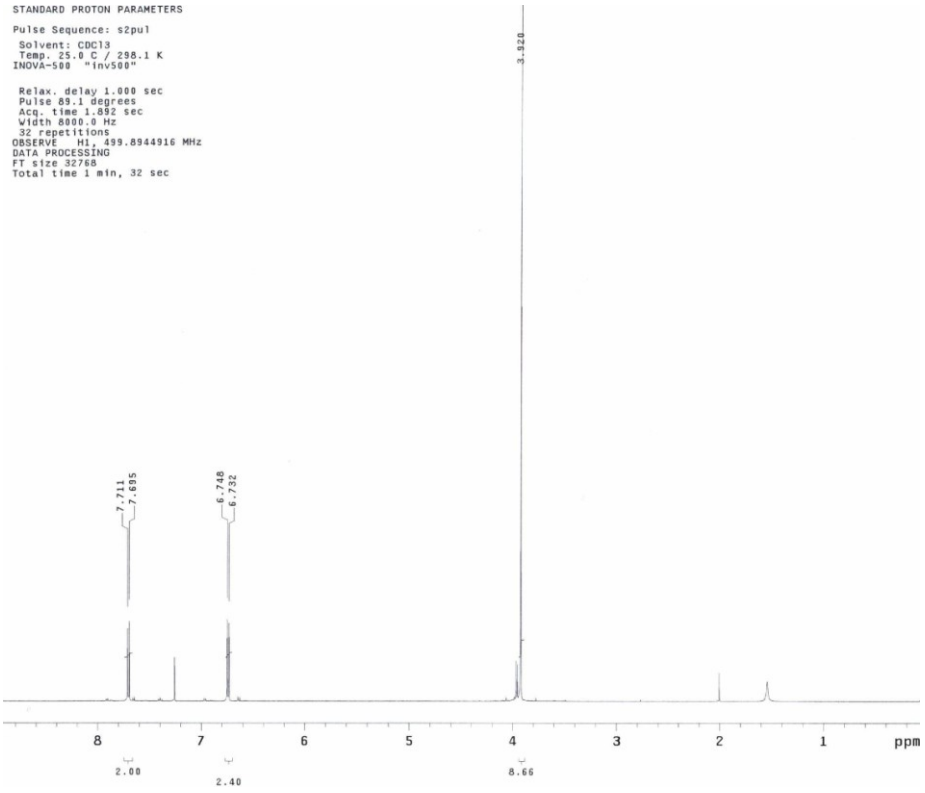

OMe
OMe

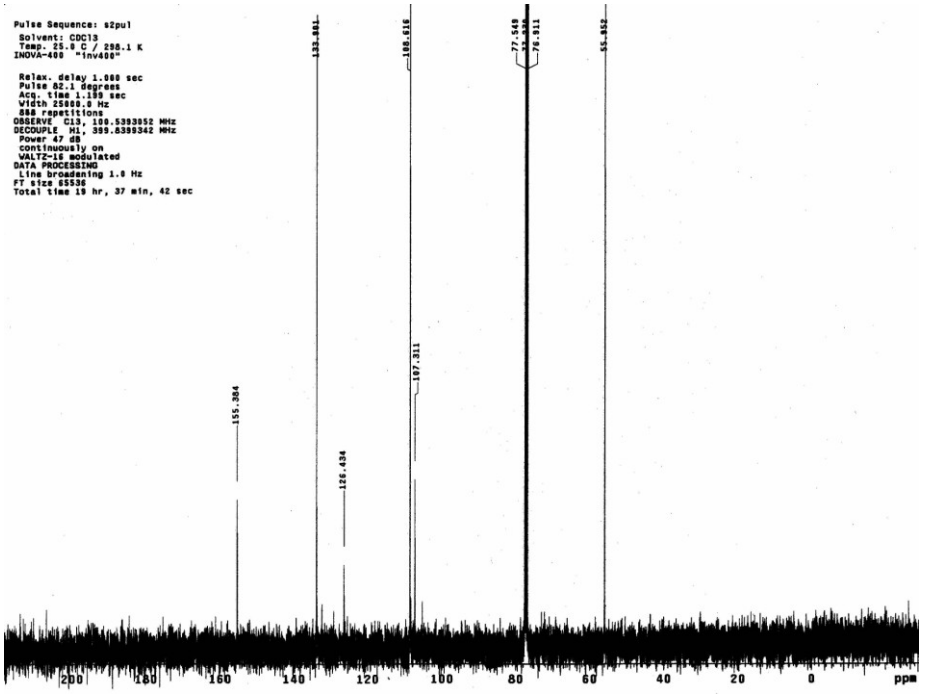
158

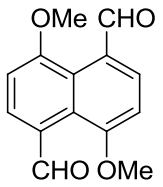

wp-iii-1,5-dimethoxy-naph
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 52.2 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944902 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
4.009
4.003
4.023
4.017
7.884
7.867
7.421
7.406
7.389
6.876
6.861
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
2.00
2.44
2.17
6.57


OMe Br
Br OMe

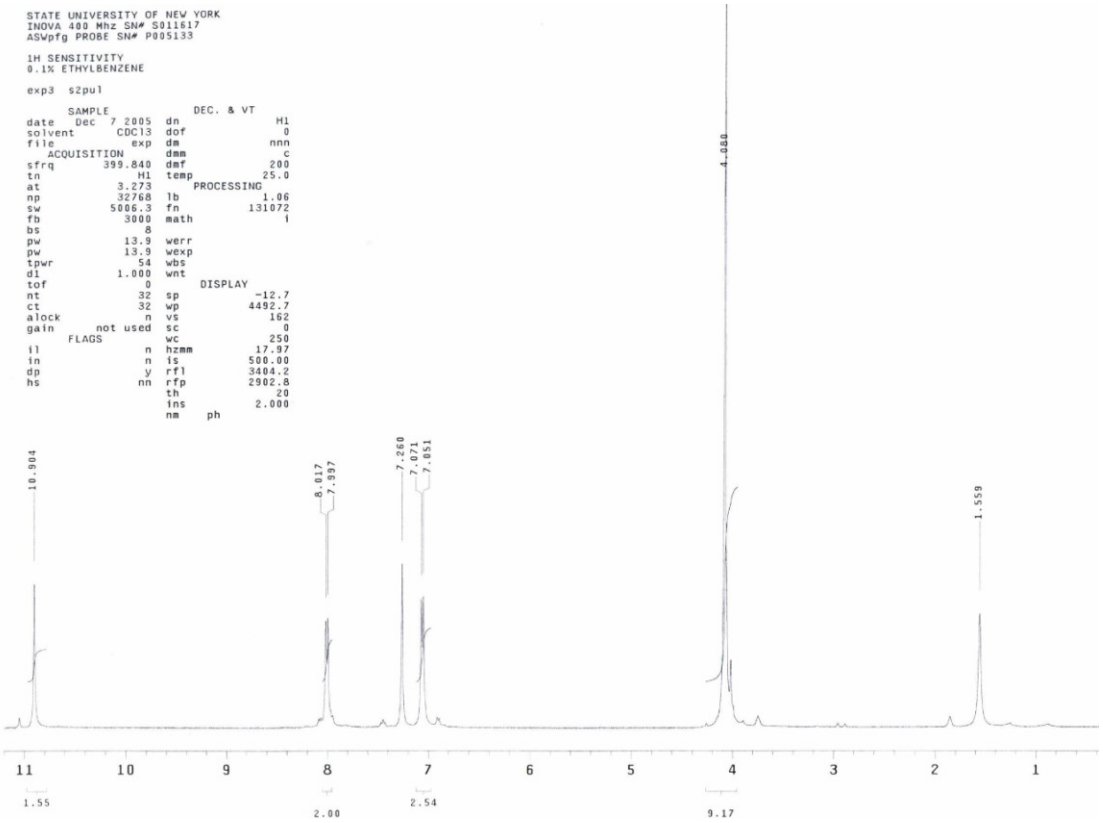
159

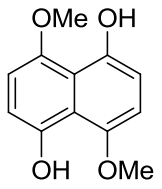

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-500 "inv500"
Relax. delay 1.000 sec
Pulse 89.1 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.8944916 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 32 sec
7.711
7.695
6.748
6.732
3.920
8
7
6
5
4
3
2
1
ppm
2.00
2.40
8.66


Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.8 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25680.8 Hz
886 repetitions
OBSERVE C13, 100.5393852 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously ON
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
155.384
133.881
126.434
108.616
97.811
77.549
77.232
76.911
55.452
200
180
160
140
120
100
80
60
40
20
0
ppm

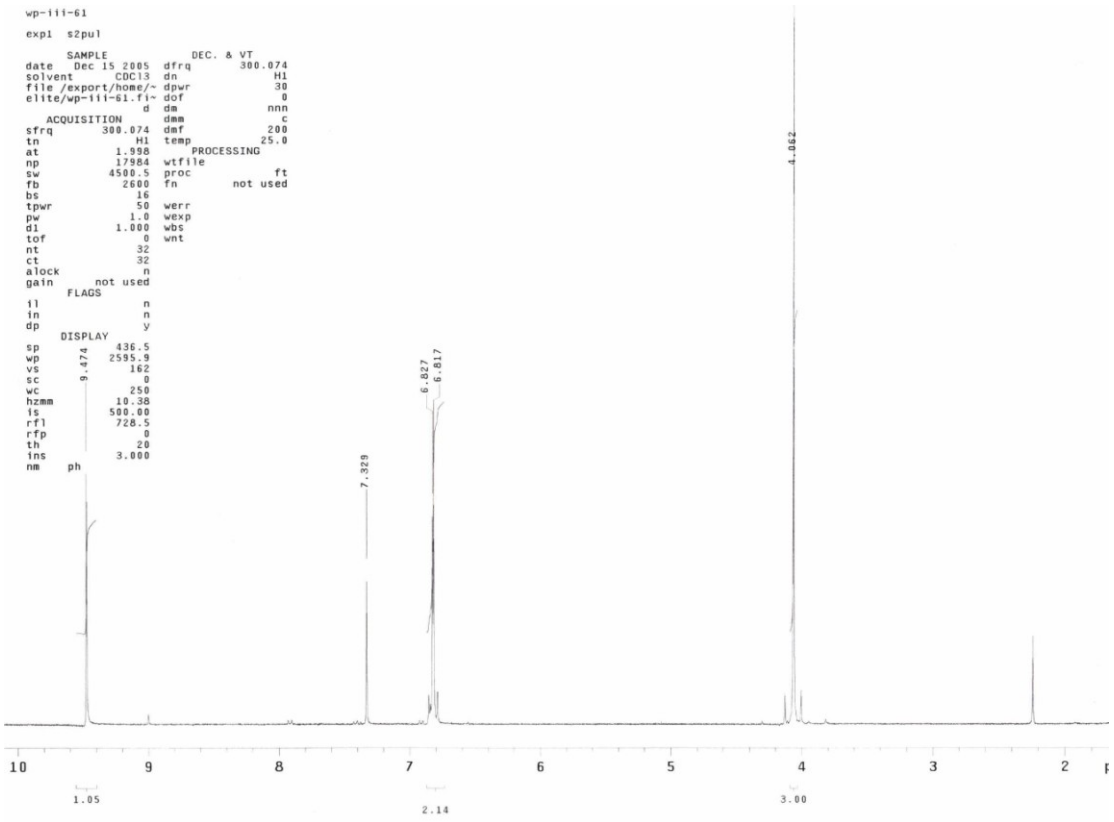

OMe CHO
CHO OMe

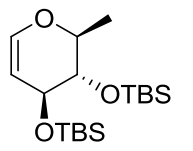
160


STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
exp3 s2pul
SAMPLE
date Dec 7 2005
solvent CDCl3
file exp
ACQUISITION
sfrq 399.840
tn H1
at 3.273
np 32768
sw 5006.3
fb 3000
bs 8
pw 13.9
pw 13.9
tpwr 54
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DEC. & VT
dn H1
dof 0
dm nnn
dmm c
dmf 200
temp 25.0
PROCESSING
lb 1.06
fn 131072
math i
werr
wexp
wbs
wnt
DISPLAY
sp -12.7
wp 4492.7
vs 162
sc 0
wc 250
hzmm 17.97
is 500.00
rfl 3404.2
rfp 2902.8
th 20
ins 2.000
nm ph
10.904
8.017
7.997
7.260
7.071
7.051
4.080
1.559
11
10
9
8
7
6
5
4
3
2
1
1.55
2.00
2.54
9.17

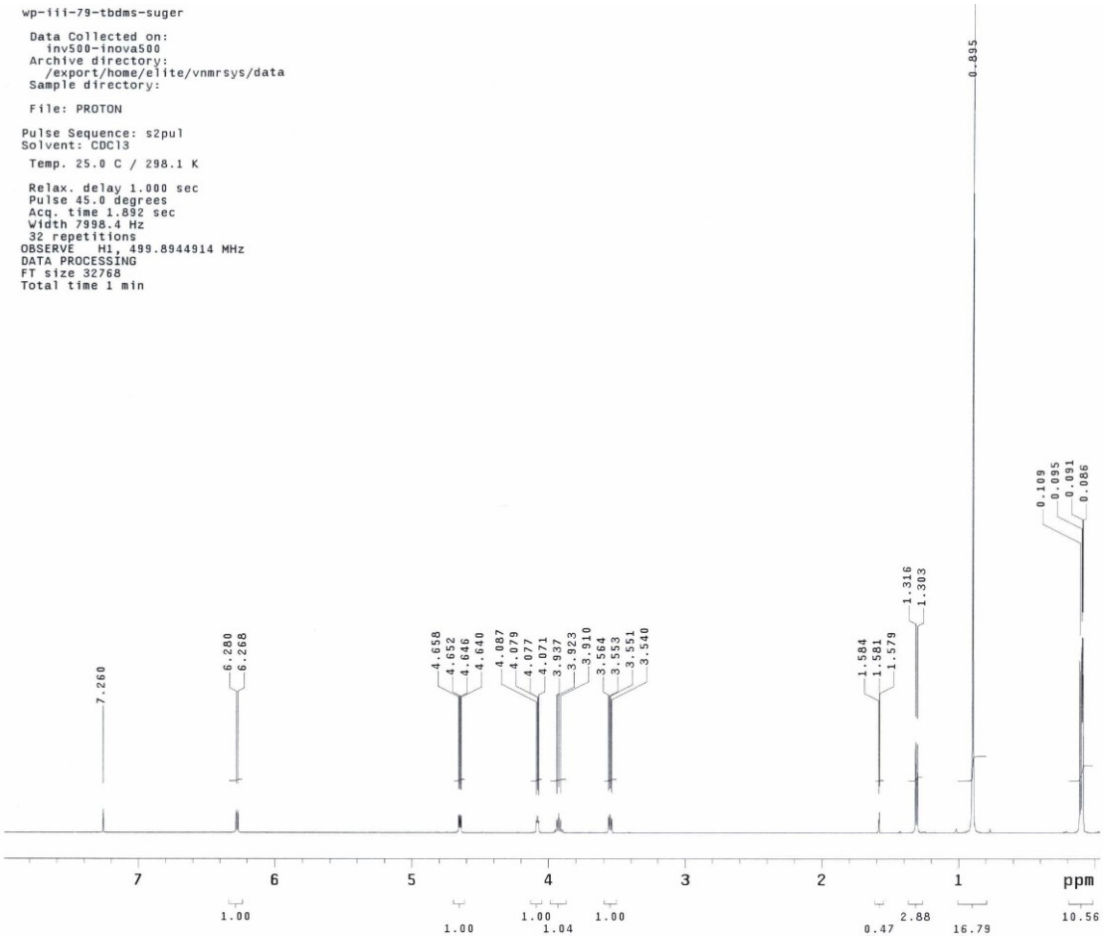

OMe OH
OH OMe

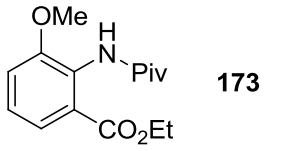
162


wp-iii-61
exp1 s2pul
SAMPLE
date Dec 15 2005
solvent CDCl3
file /export/home/~
elite/wp-iii-61.fi~
d
ACQUISITION
sfrq 300.074
tn H1
at 1.998
np 17984
sw 4500.5
fb 2600
bs 16
tpwr 50
pw 1.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp 436.5
wp 2595.9
vs 162
sc 0
wc 250
hzmm 10.38
is 500.00
rfl 728.5
rfp 0
th 20
ins 3.000
nm ph
DEC. & VT
dfrq 300.074
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
temp 25.0
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
9.474
7.329
6.827
6.817
4.062
10
9
8
7
6
5
4
3
2
1.05
2.14
3.00

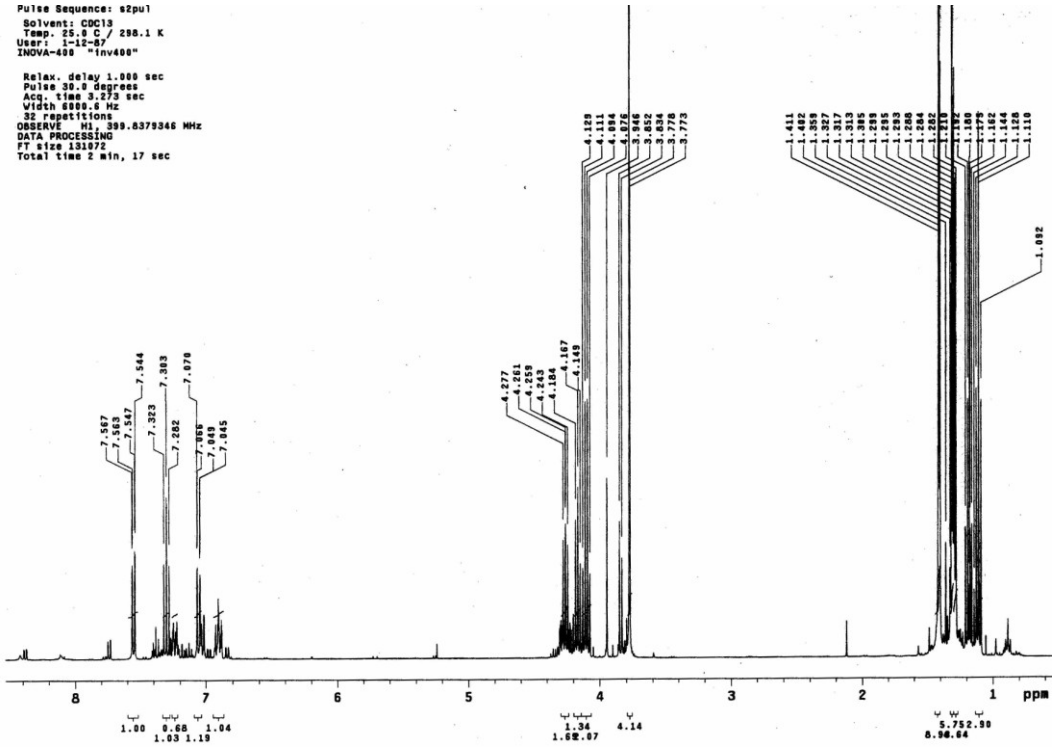

O
OTBS
OTBS

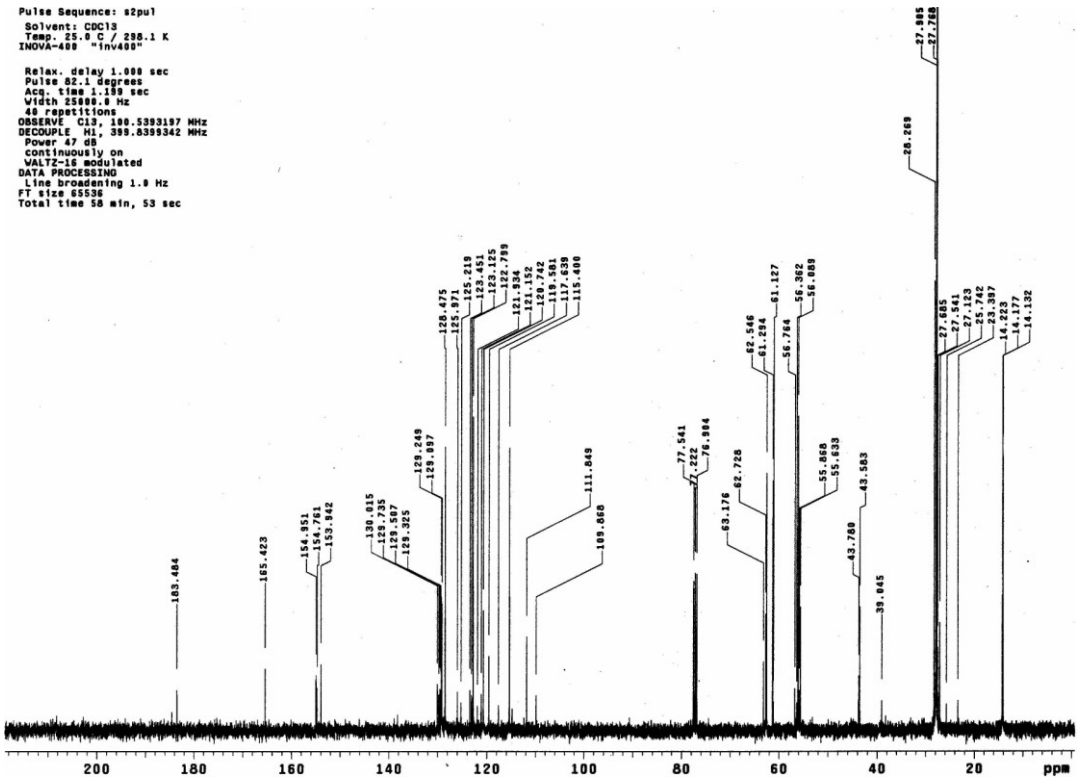
166

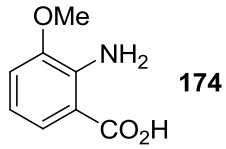

wp-iii-79-tbdms-suger
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944914 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
7.260
6.280
6.268
4.658
4.652
4.646
4.640
4.087
4.079
4.077
4.071
3.937
3.923
3.910
3.564
3.553
3.551
3.540
1.584
1.581
1.579
1.316
1.303
0.895
0.109
0.095
0.091
0.086
7
6
5
4
3
2
1
ppm
1.00
1.00
1.00
1.04
1.00
0.47
2.88
16.79
10.56


OMe
H
N
Piv
CO2Et

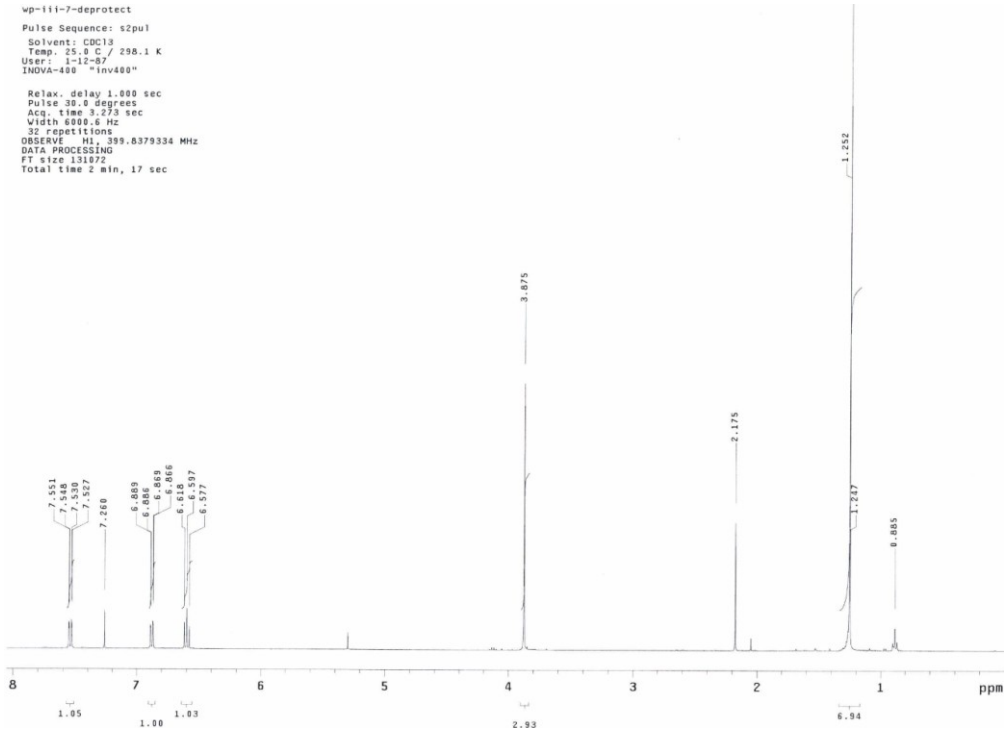
173

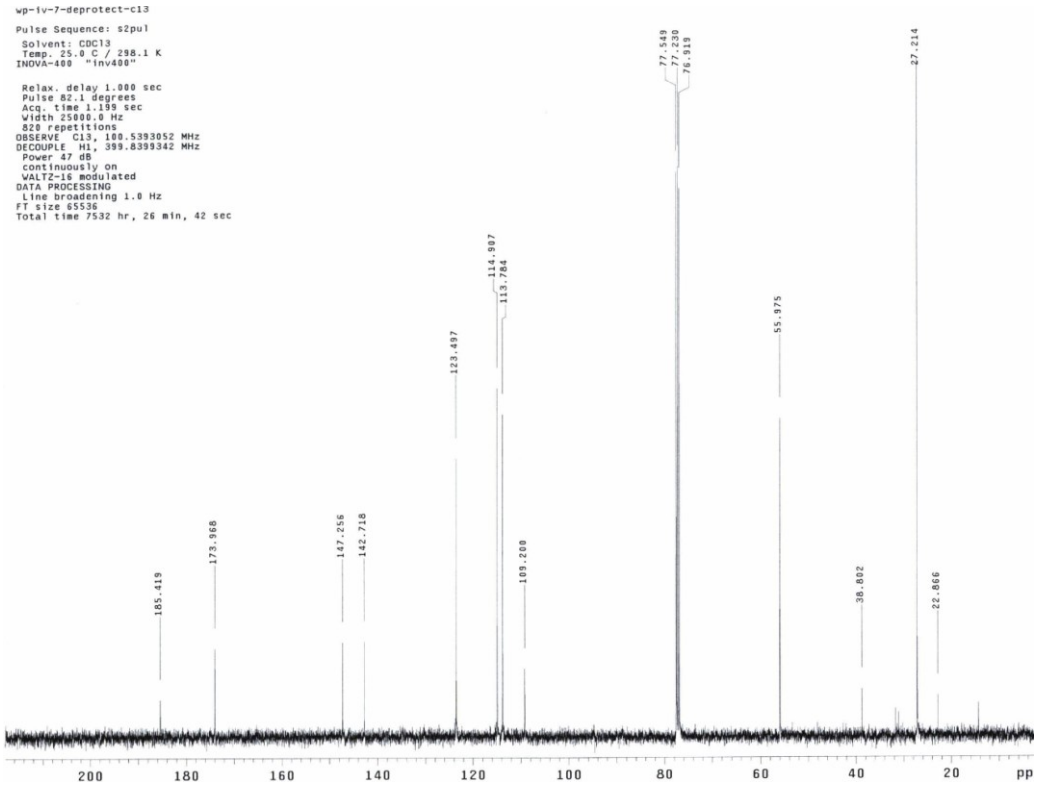

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379346 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
ppm

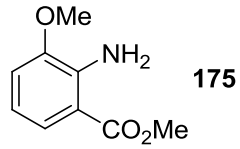

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
48 repetitions
OBSERVE C13, 100.5393187 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 58 min, 53 sec
ppm


OMe
NH2
CO2H

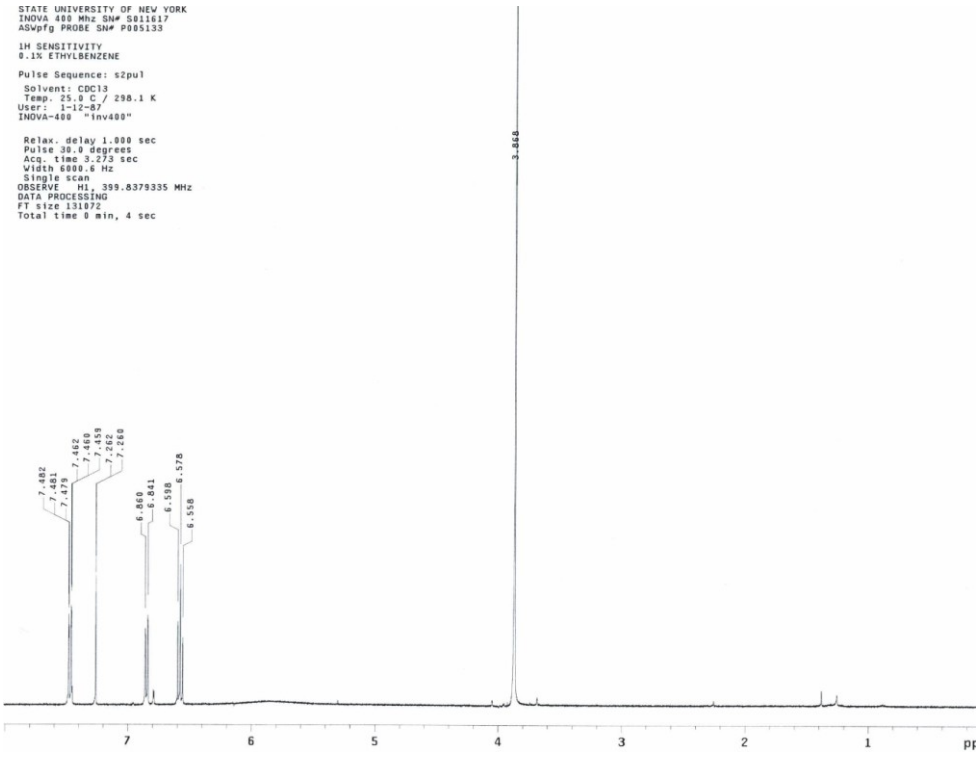
174

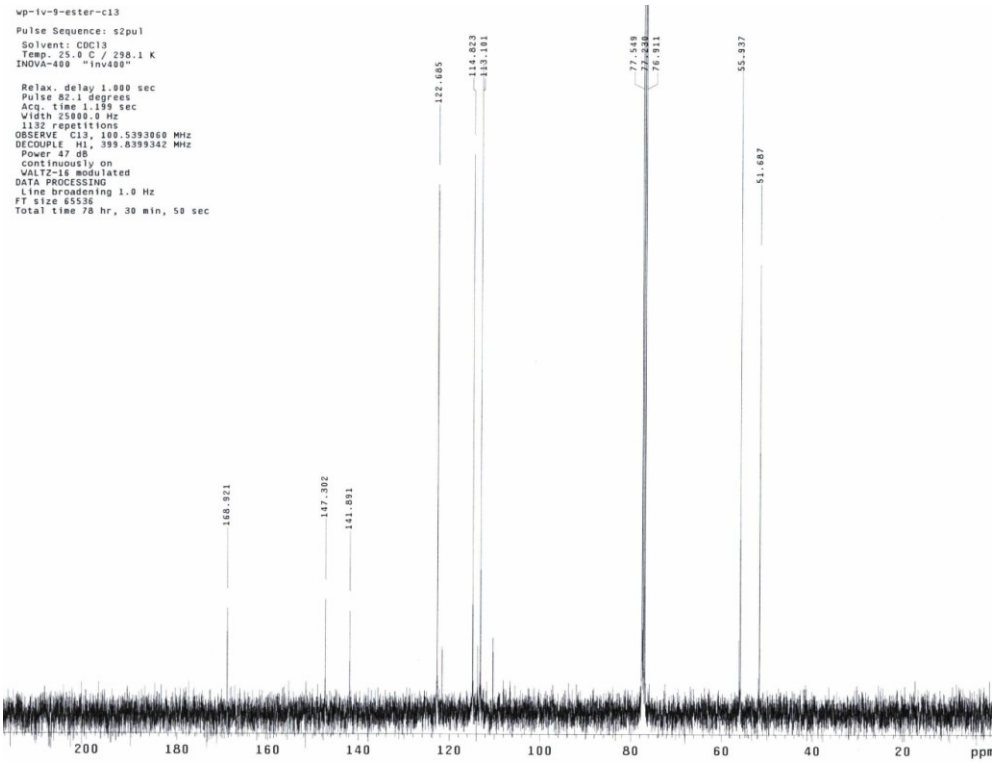

wp-iii-7-deprotect
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379334 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
7.551
7.548
7.539
7.527
7.260
6.889
6.886
6.869
6.866
6.618
6.597
6.577
3.875
2.175
1.252
1.247
0.885
ppm
1.05
1.00
1.03
2.93
6.94

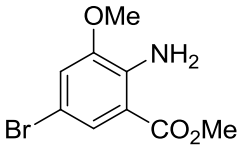

wp-iv-7-deprotect-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.195 sec
Width 25000.0 Hz
820 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7532 hr, 26 min, 42 sec
77.549
77.230
76.910
27.214
114.987
113.784
123.497
55.975
185.419
173.968
147.256
142.718
109.200
38.802
22.866
200
180
160
140
120
100
80
60
40
20
pp


OMe
NH2
CO2Me

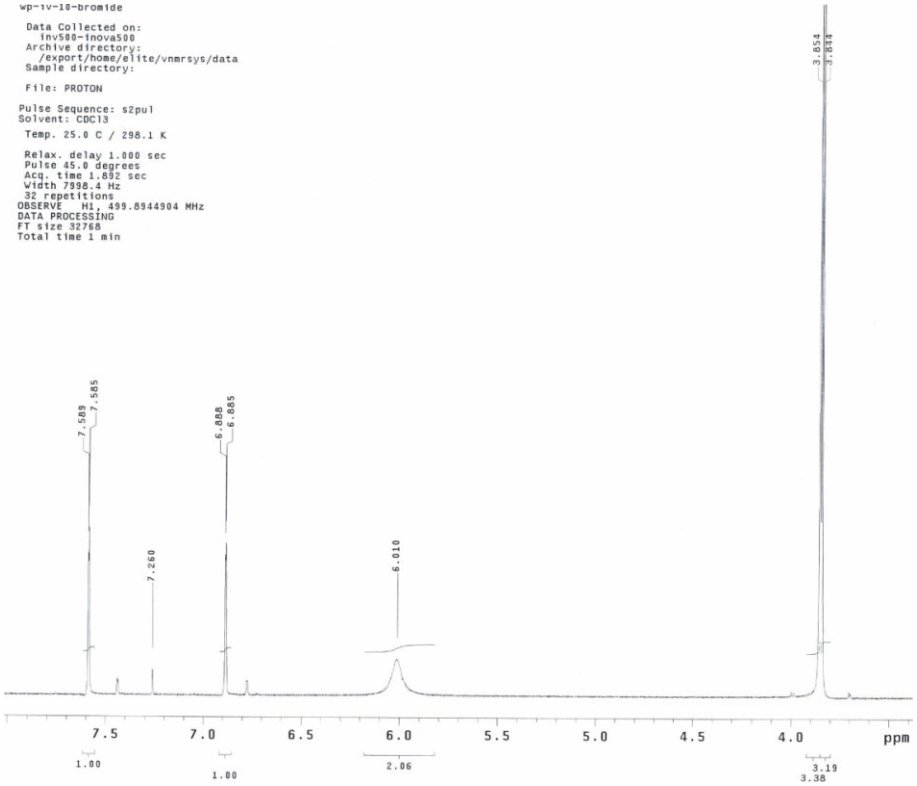
175

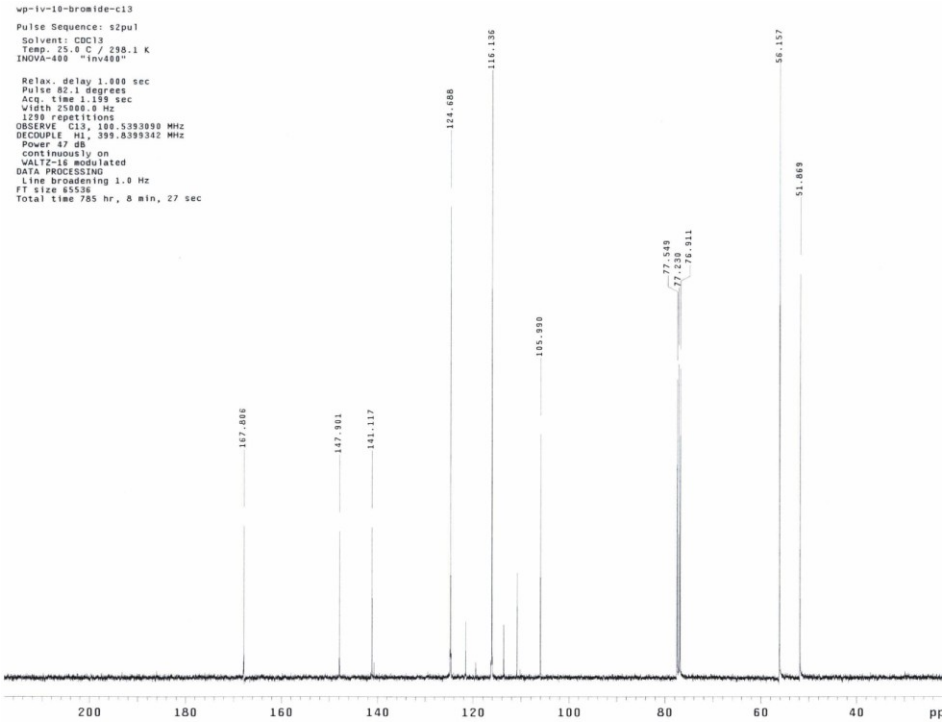

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
Single scan
OBSERVE H1, 399.8379335 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 4 sec
7.482
7.481
7.479
7.468
7.466
7.459
7.262
7.260
6.860
6.841
6.598
6.578
6.558
3.868
7
6
5
4
3
2
1
ppm

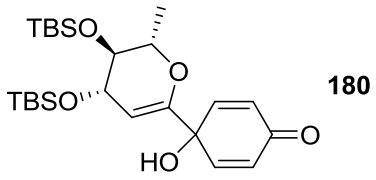

wp-iv-9-ester-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1132 repetitions
OBSERVE C13, 100.5393060 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 58 sec
168.921
147.302
141.891
122.685
114.823
113.101
77.549
77.230
76.911
55.937
51.687
200
180
160
140
120
100
80
60
40
20
ppm


OMe
NH2
Br
CO2Me

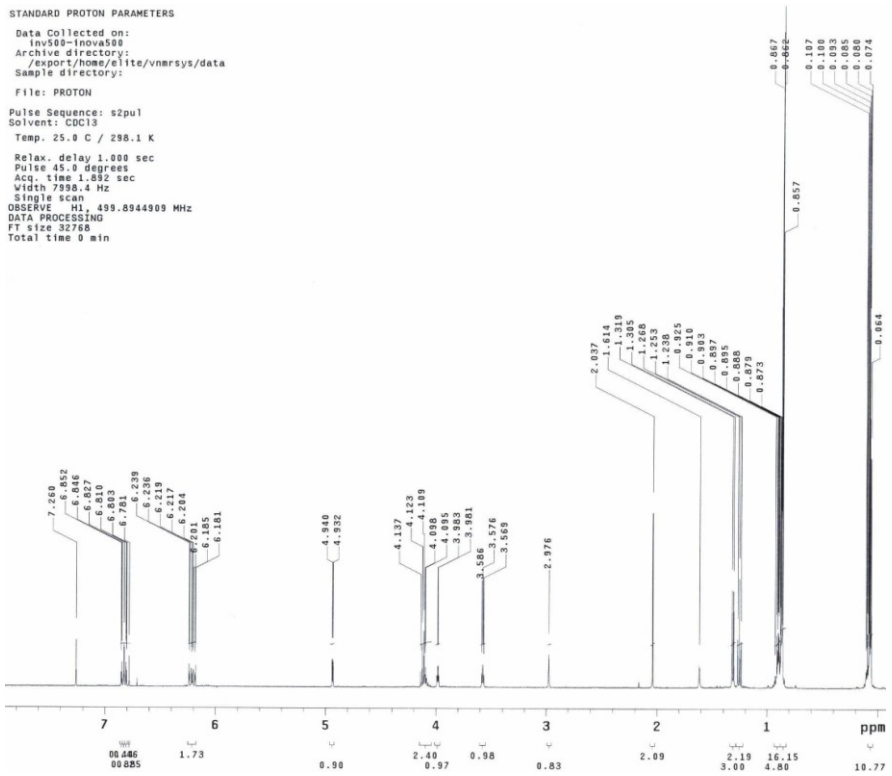
176

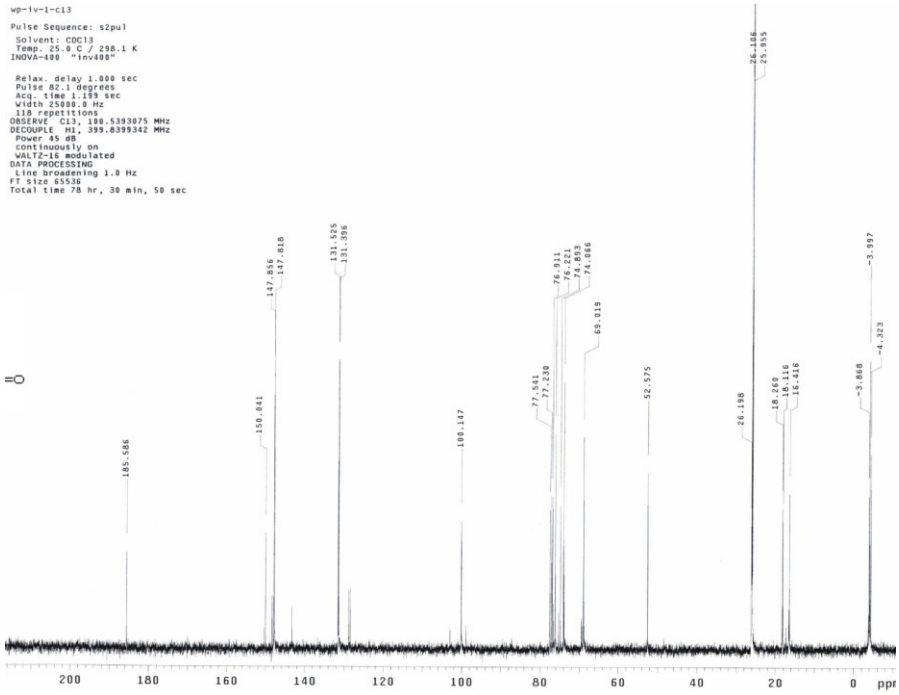

wp-iv-10-bromide
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
32 repetitions
OBSERVE H1, 499.8944904 MHz
DATA PROCESSING
FT size 32768
Total time 1 min
7.589
7.585
6.888
6.885
7.260
6.010
3.654
3.644
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm
1.00
1.00
2.06
3.19
3.38

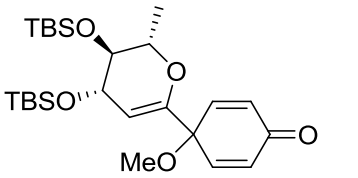

wp-iv-10-bromide-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1290 repetitions
OBSERVE C13, 100.5393098 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 785 hr, 8 min, 27 sec
167.806
147.901
141.117
124.688
116.136
105.990
77.549
77.230
76.911
56.157
51.869
200
180
160
140
120
100
80
60
40


TBSO
TBSO
O
O
HO

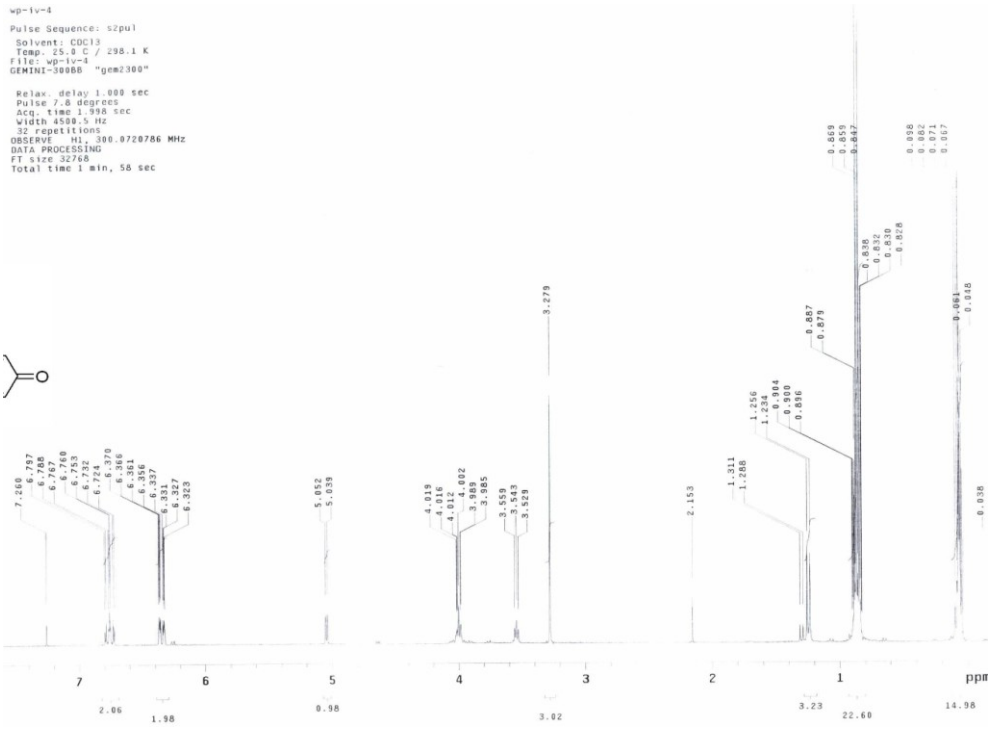
180

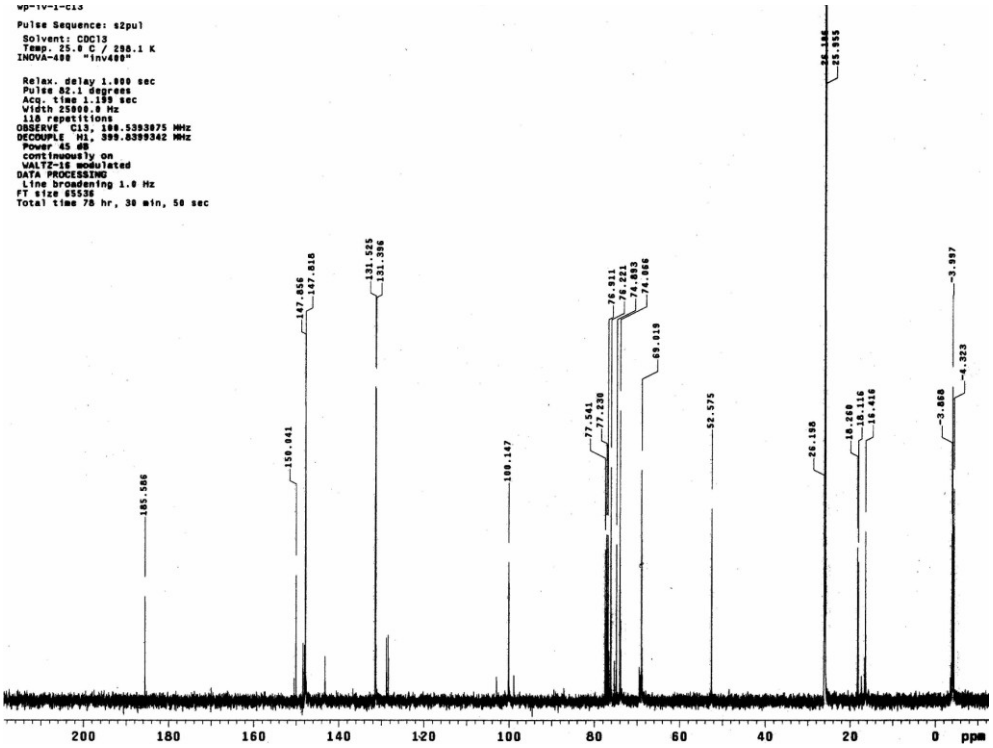

STANDARD PROTON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
Single scan
OBSERVE H1, 499.8944909 MHz
DATA PROCESSING
FT size 32768
Total time 0 min
ppm

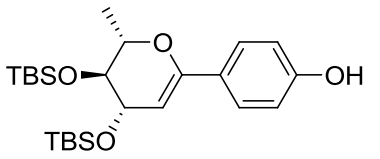

wp-iv-1-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
118 repetitions
OBSERVE C13, 100.5393075 MHz
DECOUPLE H1, 399.8399342 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 30 min, 50 sec
ppm


TBSO
TBSO
O
O
MeO

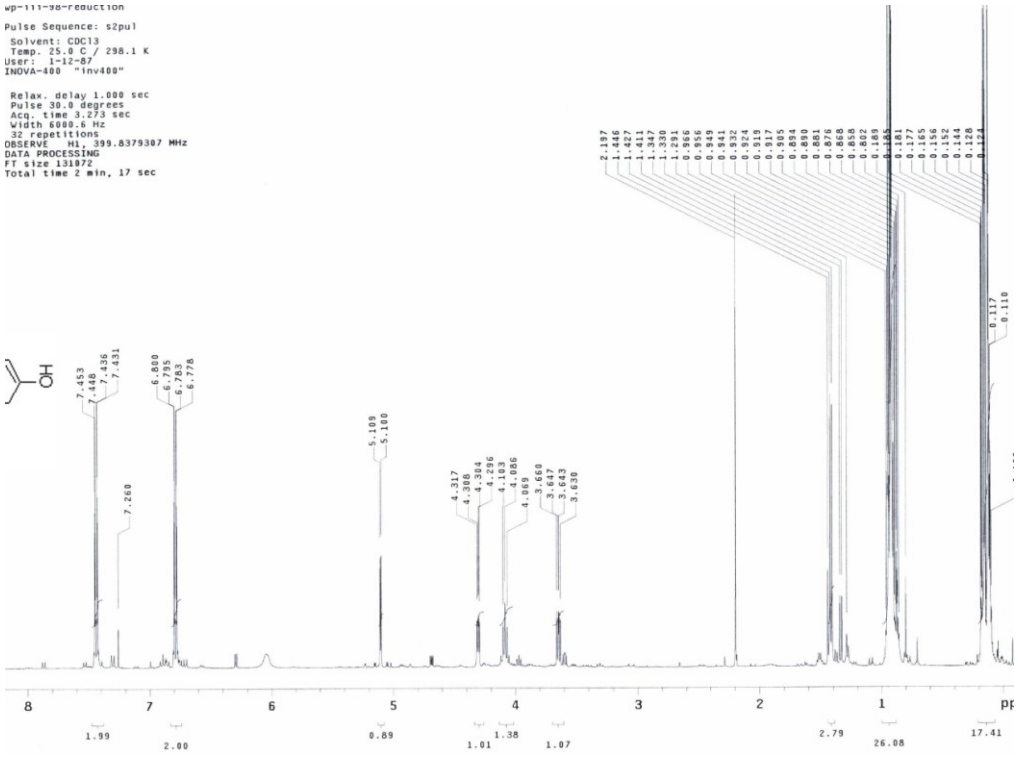
181

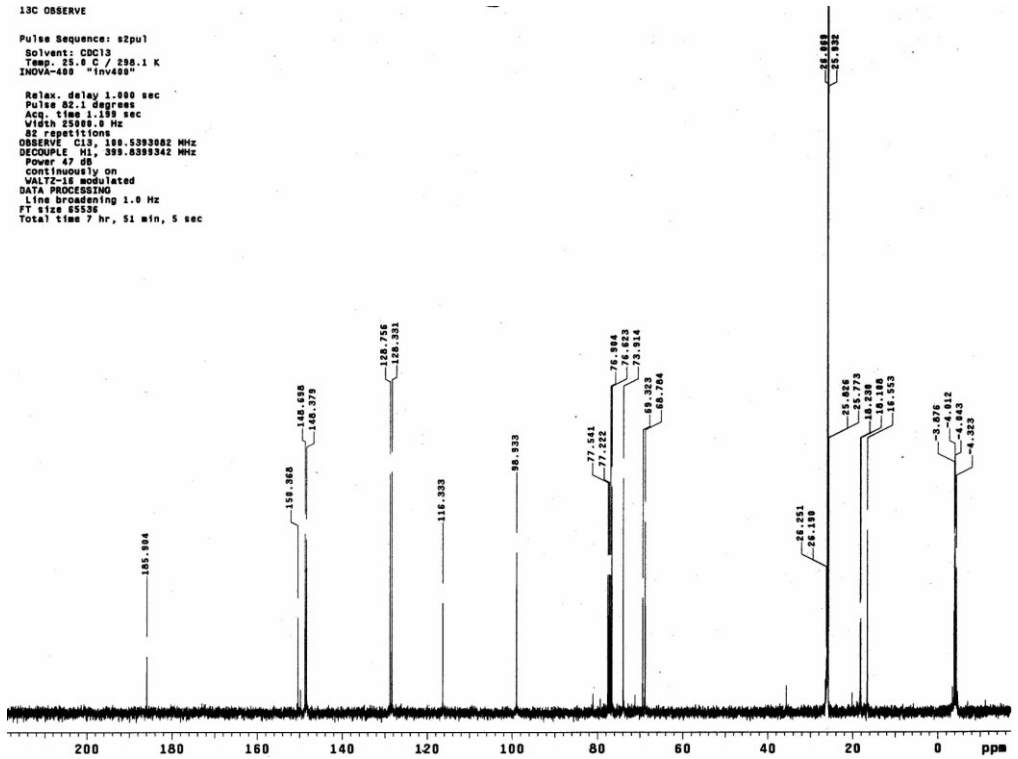

wp-iv-4
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: wp-iv-4
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
32 repetitions
OBSERVE H1, 300.0720786 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 58 sec
ppm

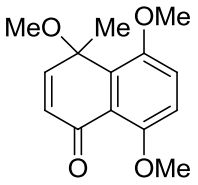

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
118 repetitions
OBSERVE C13, 100.5353875 MHz
DECOUPLE H1, 399.8399342 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 78 hr, 38 min, 58 sec
ppm


TBSO
O
OH
TBSO

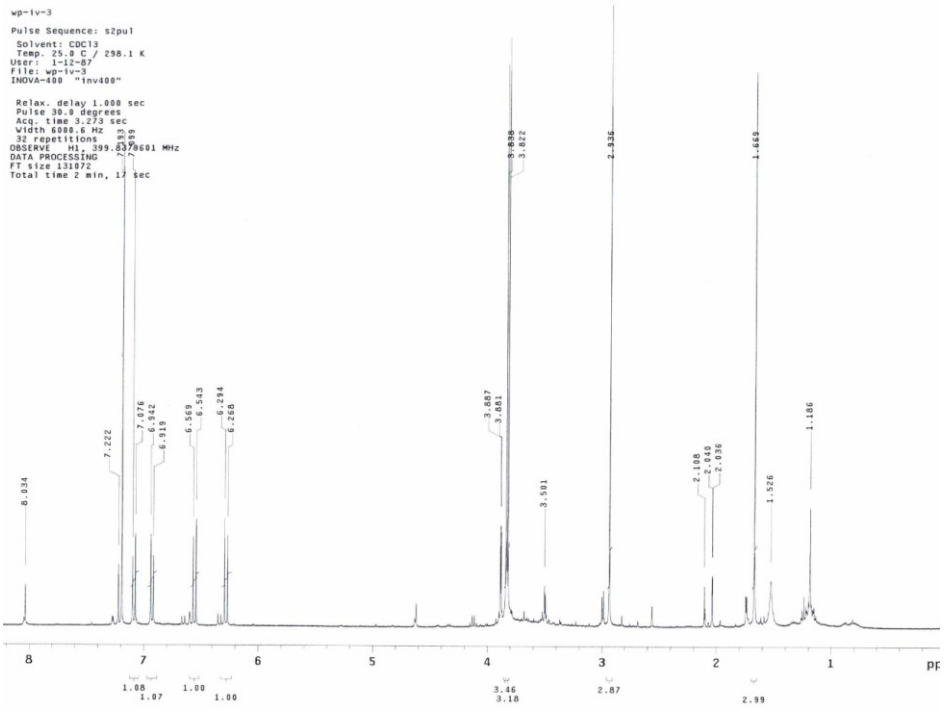
182

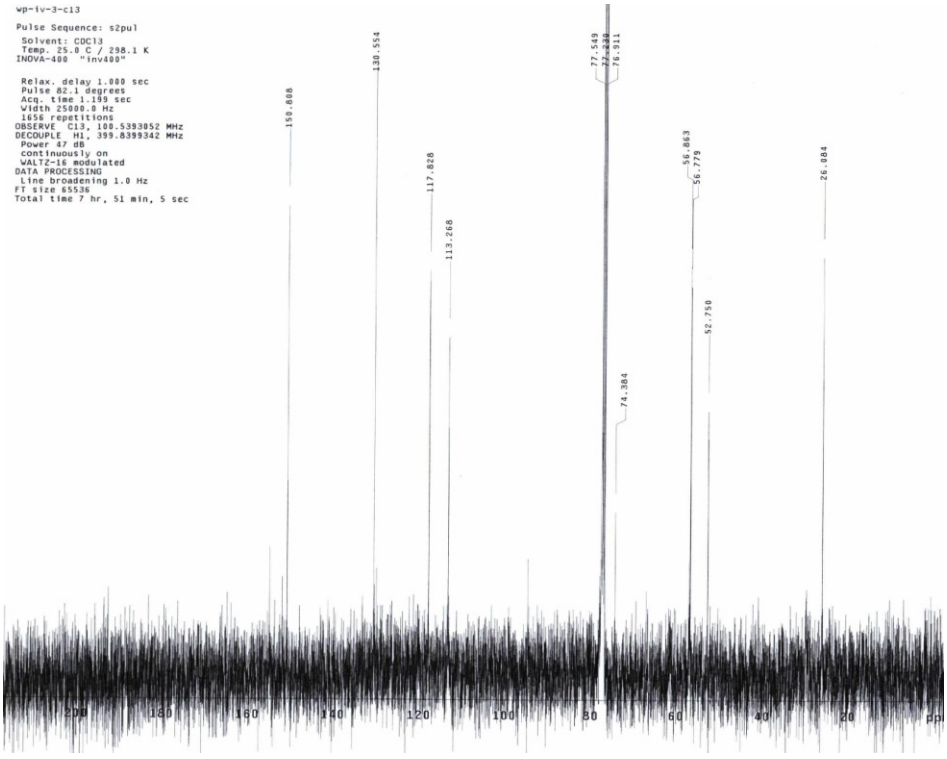

wp-111-98-reduction
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379307 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
7.453
7.448
7.436
7.431
6.800
6.795
6.783
6.778
7.260
5.108
5.100
4.317
4.308
4.304
4.296
4.103
4.086
4.069
3.660
3.647
3.643
3.630
2.197
1.446
1.427
1.411
1.347
1.330
1.291
0.966
0.956
0.949
0.941
0.932
0.924
0.919
0.917
0.905
0.896
0.890
0.881
0.876
0.868
0.858
0.852
0.845
0.181
0.177
0.165
0.156
0.152
0.144
0.128
0.124
0.117
0.110
8
7
6
5
4
3
2
1
1.99
2.00
0.89
1.01
1.38
1.07
2.79
26.08
17.41

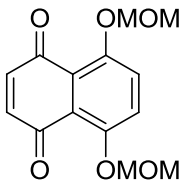

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
82 repetitions
OBSERVE C13, 100.5393682 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
185.904
159.368
148.698
148.379
128.756
128.331
116.333
98.933
77.541
77.222
76.984
76.673
76.364
73.514
69.323
68.764
26.251
26.190
25.826
25.773
18.238
18.118
18.053
-3.676
-4.044
-4.412
-4.463
-4.823
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
Me
OMe
O
OMe

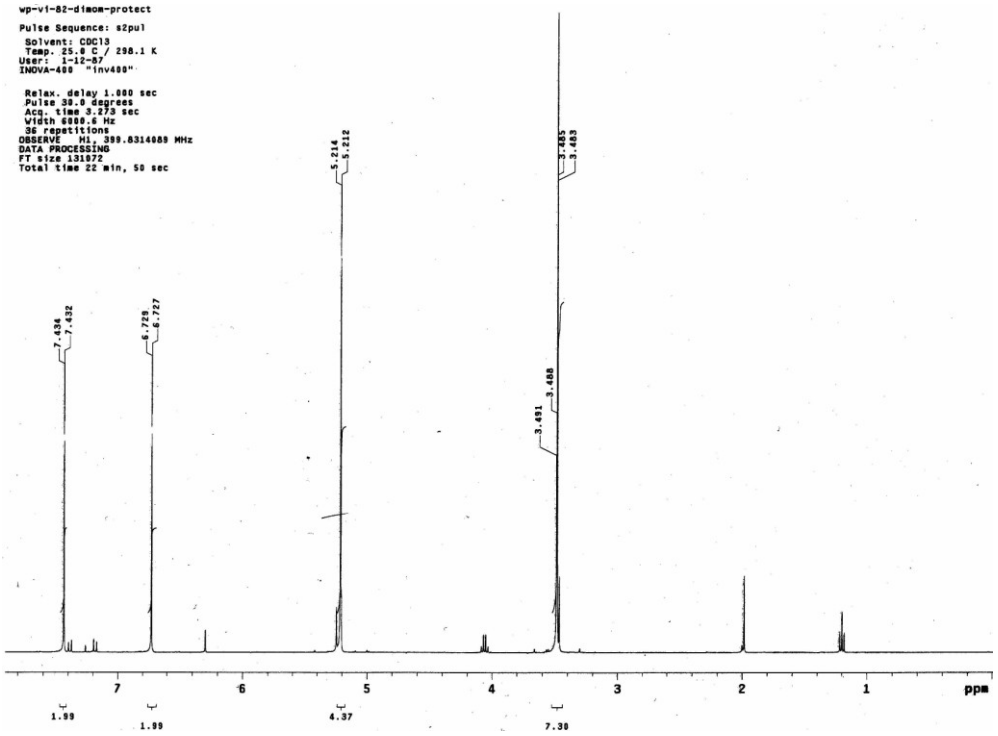
183

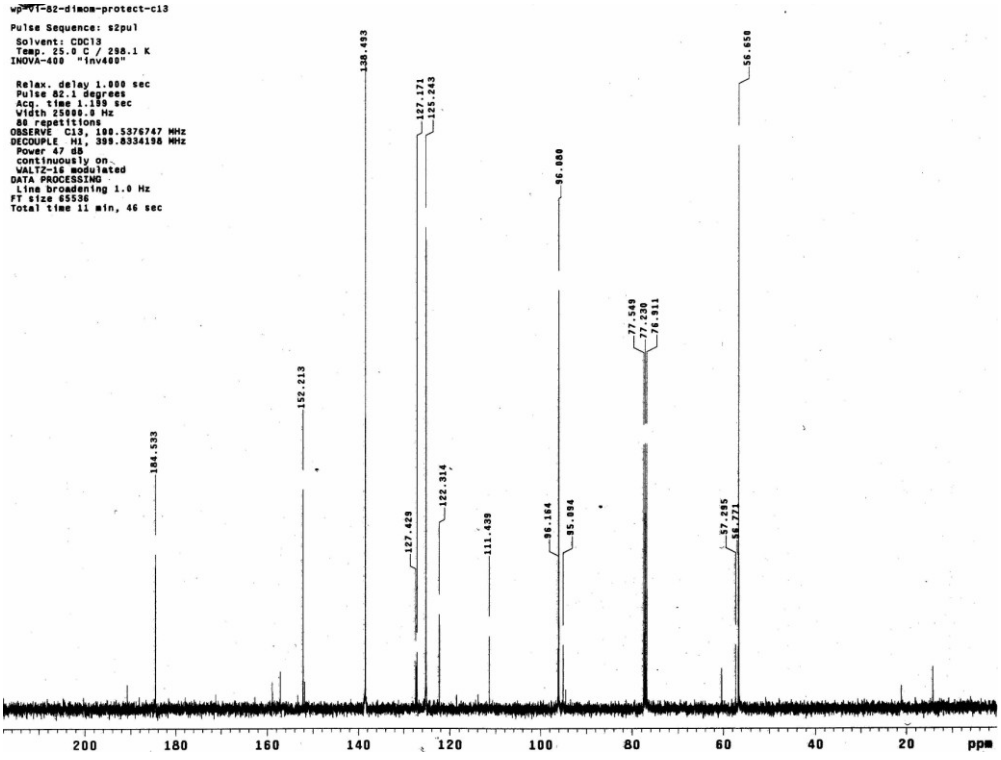

wp-iv-3
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
File: wp-iv-3
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8378601 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 1 sec
8.034
7.222
7.076
6.942
6.919
6.569
6.543
6.294
6.266
3.887
3.801
3.591
2.936
2.108
2.040
2.036
1.526
1.186
8
7
6
5
4
3
2
1
1.08
1.07
1.00
1.00
3.46
3.18
2.87
2.99

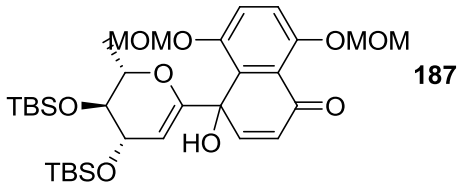

wp-iv-3-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1656 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 7 hr, 51 min, 5 sec
150.608
130.554
117.828
113.268
77.549
77.232
76.911
74.384
56.863
56.779
52.750
26.084
200
180
160
140
120
100
80
60
40
20


O
OMOM
O
OMOM

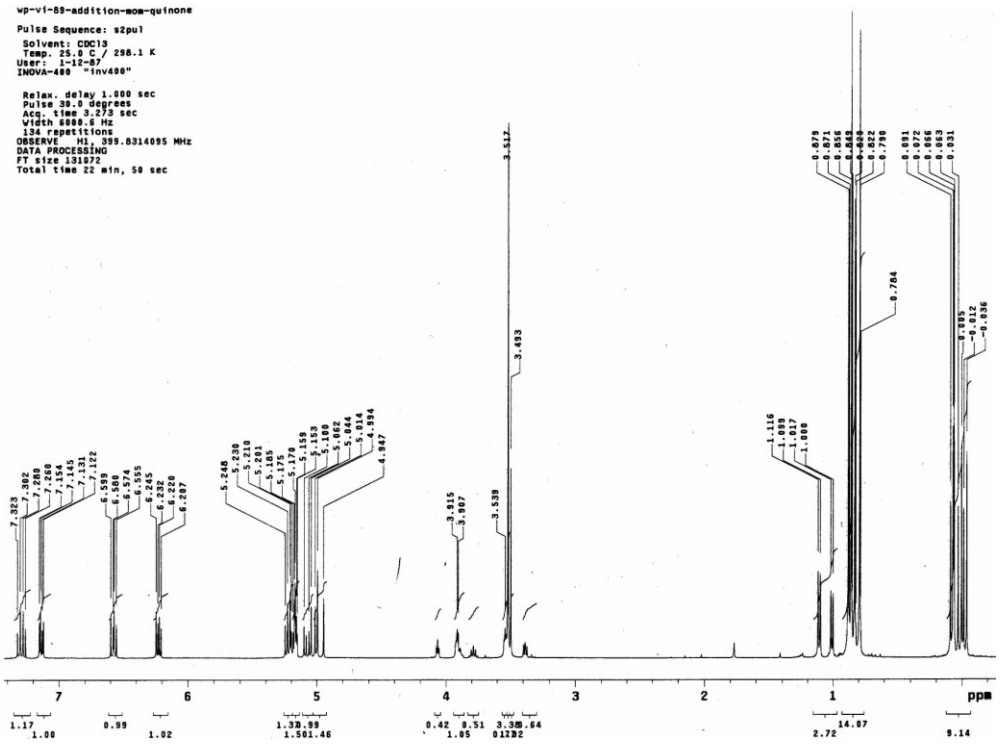
186

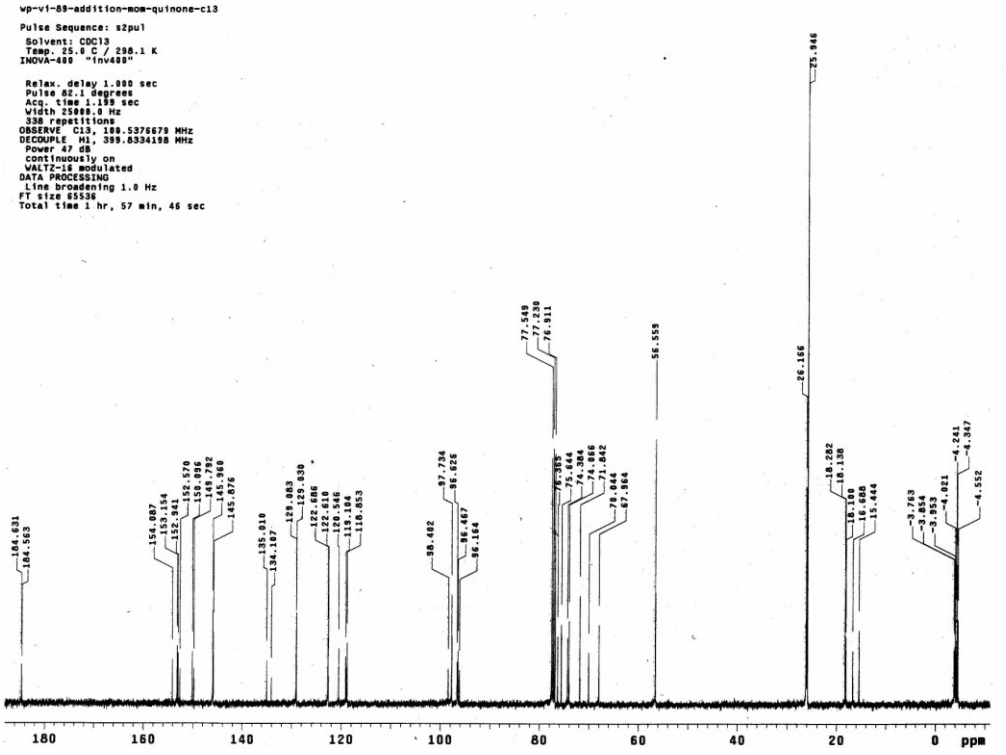

wp-vi-82-dimom-protect
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
36 repetitions
OBSERVE H1, 399.8314089 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
7.434
7.432
6.729
6.727
5.214
5.212
3.485
3.483
3.491
3.488
1.99
1.99
4.37
7.38
ppm

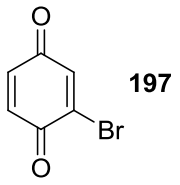

wp-vi-82-dimom-protect-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
80 repetitions
OBSERVE C13, 100.5376747 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 11 min, 46 sec
184.533
152.213
138.493
127.429
127.171
125.243
122.314
111.439
96.060
96.164
85.894
77.549
77.230
76.911
57.295
56.650
ppm


MOMO
OMOM
O
TBSO
O
HO
TBSO

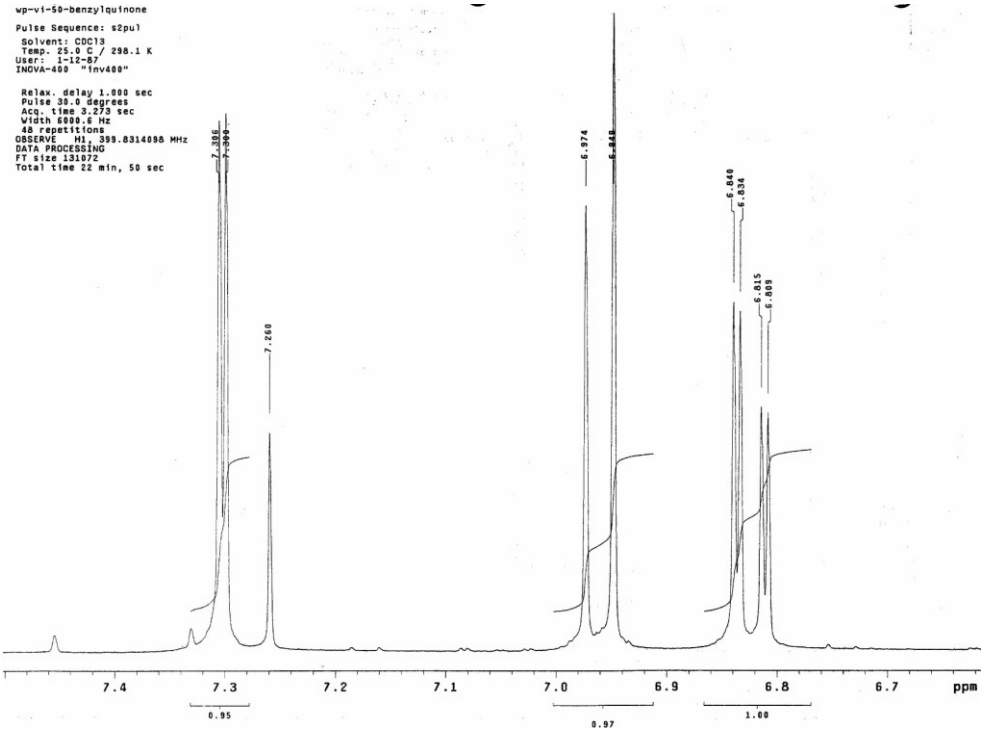
187

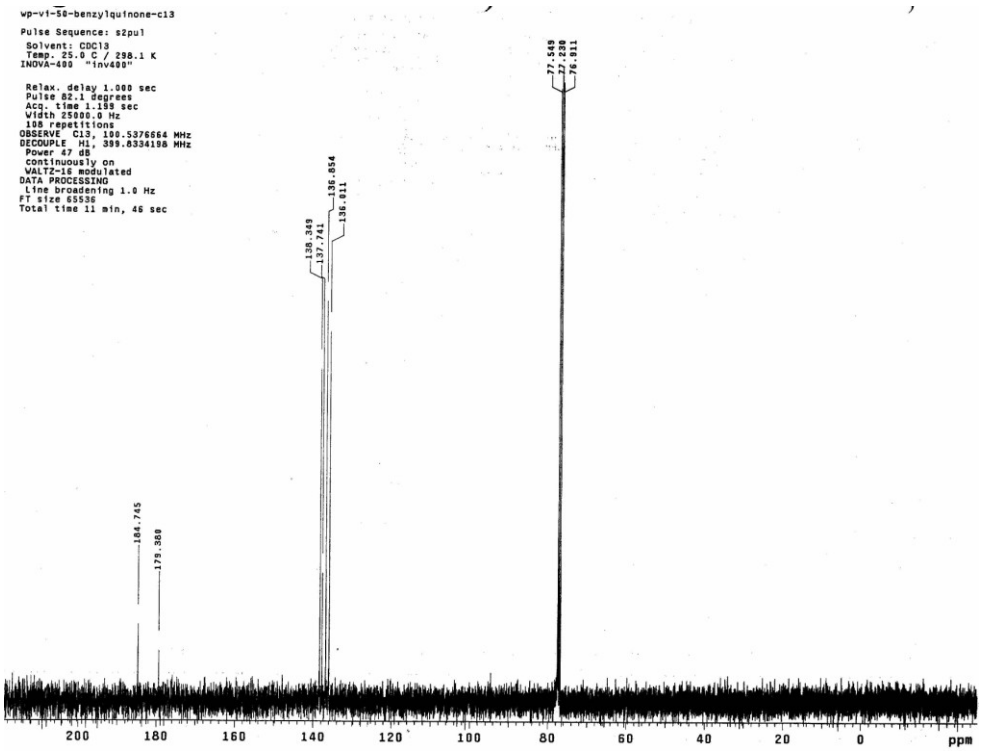

wp-vi-89-addition-mom-quinone
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
134 repetitions
OBSERVE H1, 399.8314095 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
ppm

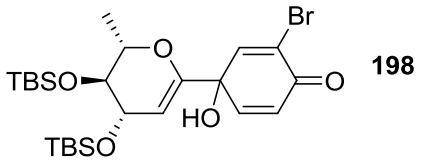

wp-vi-89-addition-mom-quinone-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
338 repetitions
OBSERVE C13, 100.5376679 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


O
O
Br

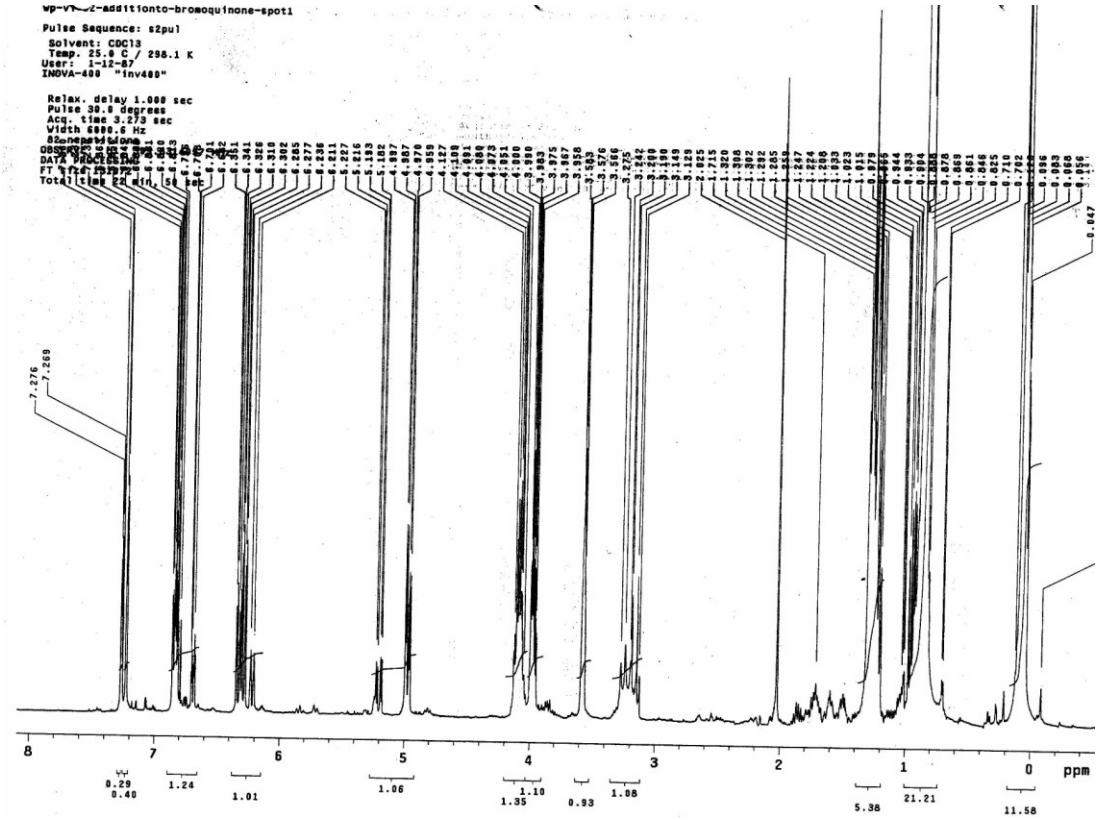
197

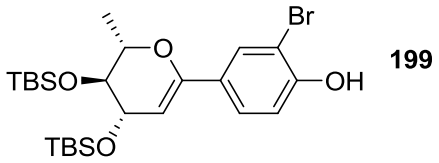

wp-vi-50-benzylquinone
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
48 repetitions
OBSERVE H1, 399.8314098 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
7.386
7.369
7.260
6.974
6.848
6.840
6.834
6.815
6.809
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
ppm
0.95
0.97
1.00


wp-vi-50-benzylquinone-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
108 repetitions
OBSERVE C13, 100.5376664 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 11 min, 46 sec
184.745
179.388
138.369
137.741
136.854
136.611
77.545
77.238
76.911
200
180
160
140
120
100
80
60
40
20
0
ppm

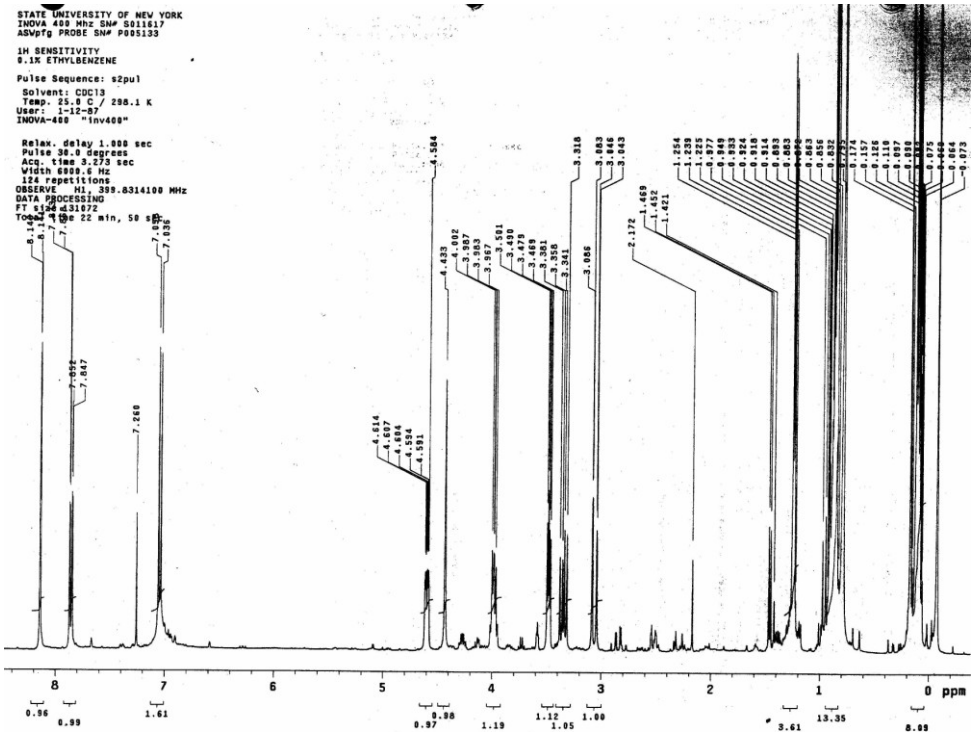

Br
O
TBSO
O
HO
TBSO

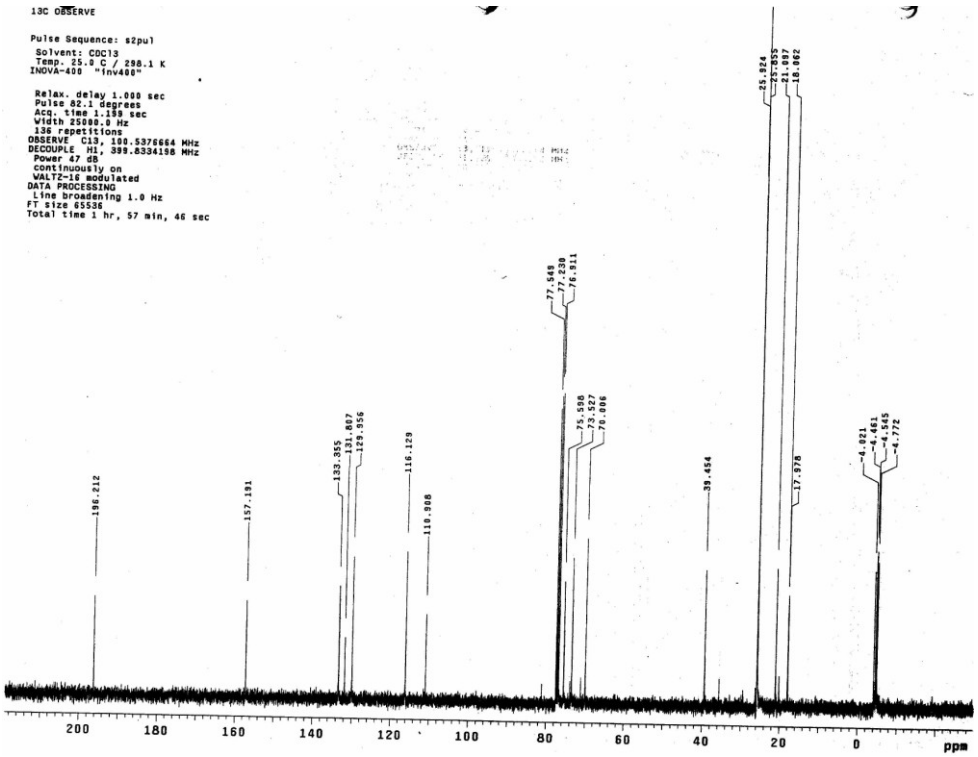
198

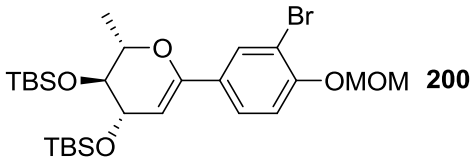

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: i-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
7.276
7.269
0.647
8
7
6
5
4
3
2
1
0
ppm
0.29
0.40
1.24
1.01
1.06
1.10
1.35
0.93
1.08
5.38
21.21
11.58


Br
O
TBSO
OH
TBSO

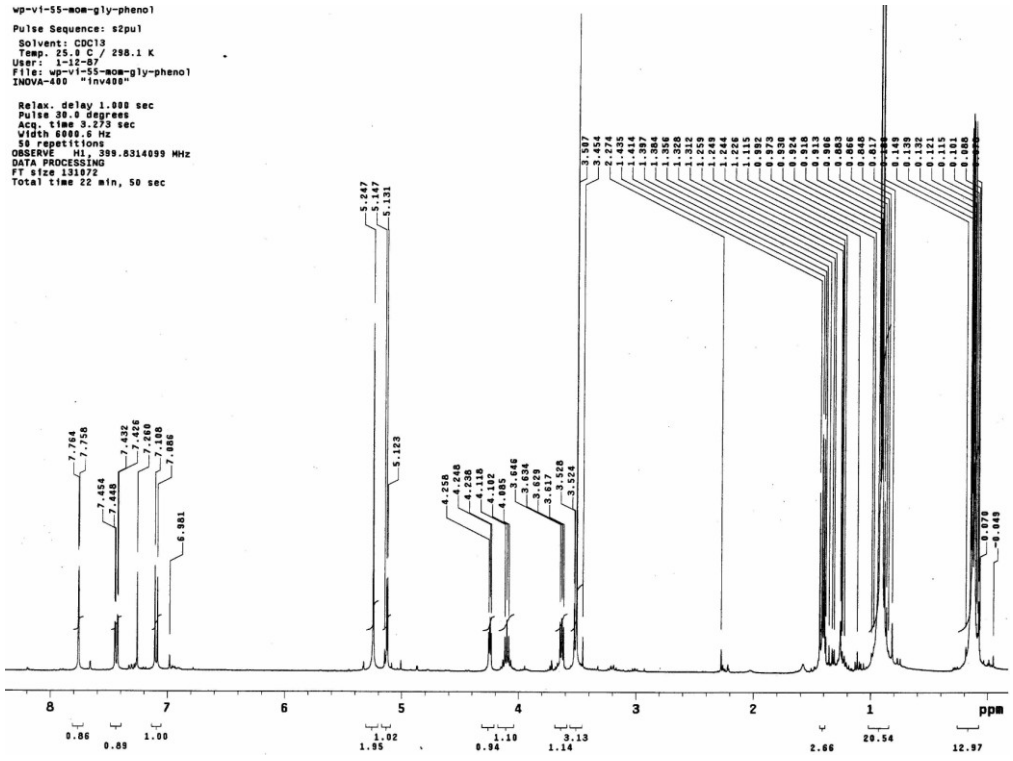
199

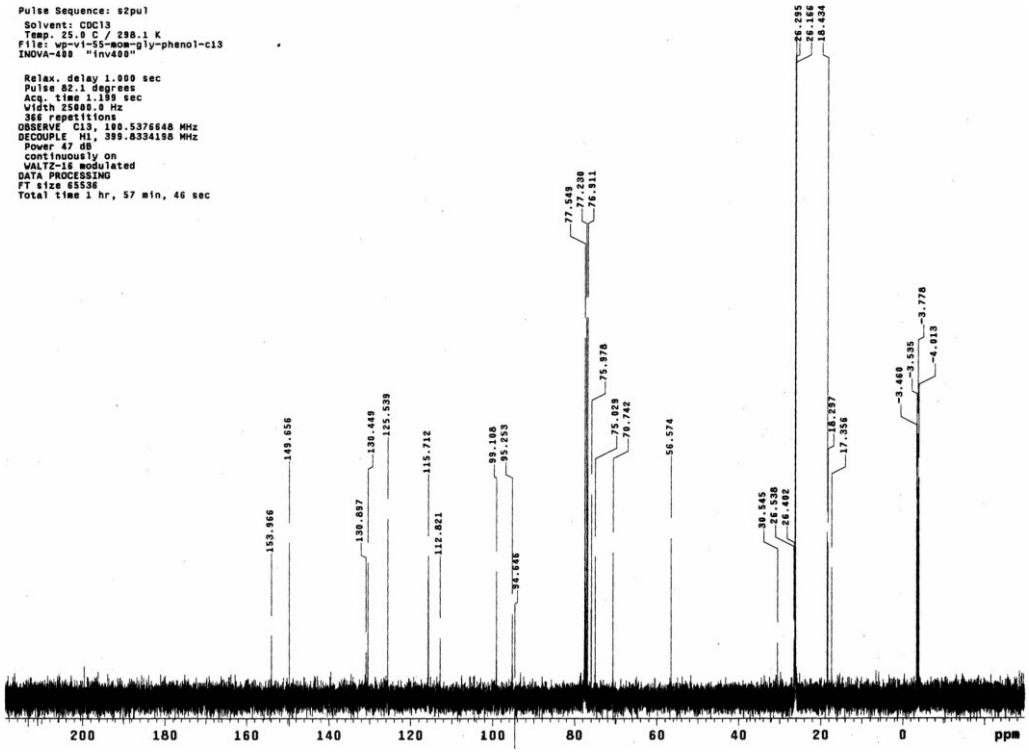

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# S011617
ASVpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
124 repetitions
OBSERVE H1, 399.8314100 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

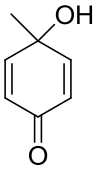

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
136 repetitions
OBSERVE C13, 100.5376664 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


Br
O
TBSO
OMOM
TBSO

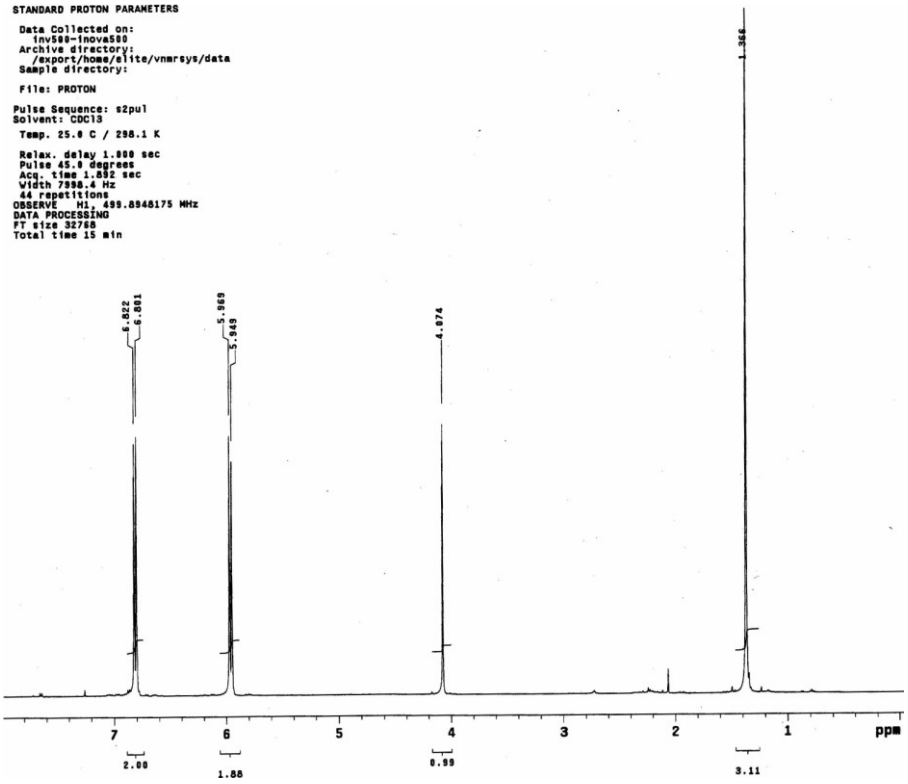
200

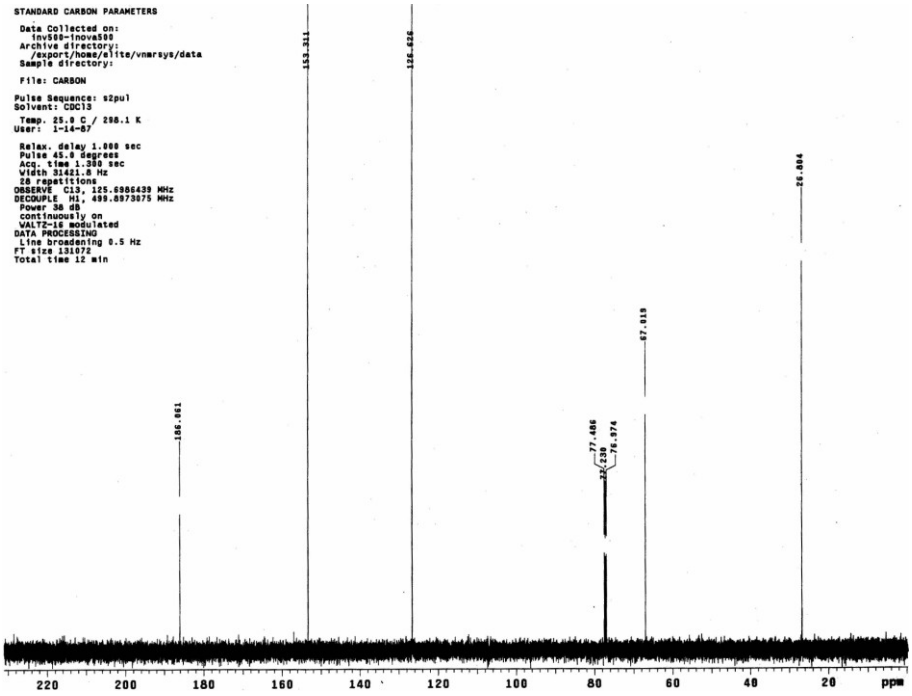

wp-vi-55-mom-gly-phenol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
File: wp-vi-55-mom-gly-phenol
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
50 repetitions
OBSERVE H1, 399.8314099 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

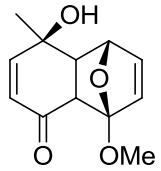

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: wp-vi-55-mom-gly-phenol-c13
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
366 repetitions
OBSERVE C13, 100.5376648 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


OH
O

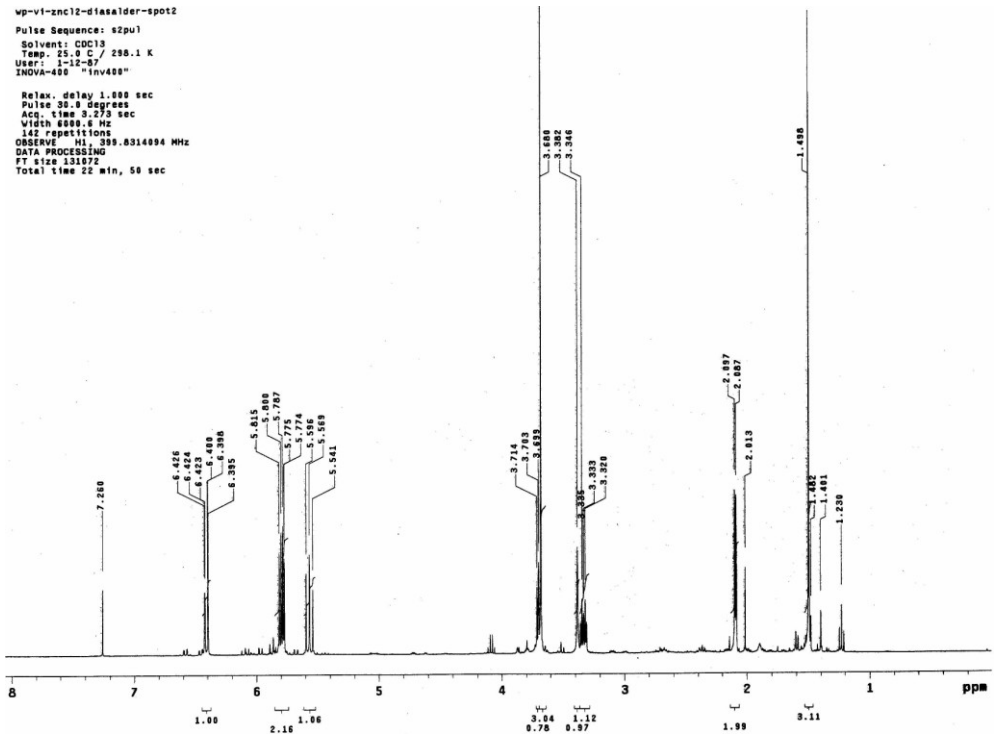
202

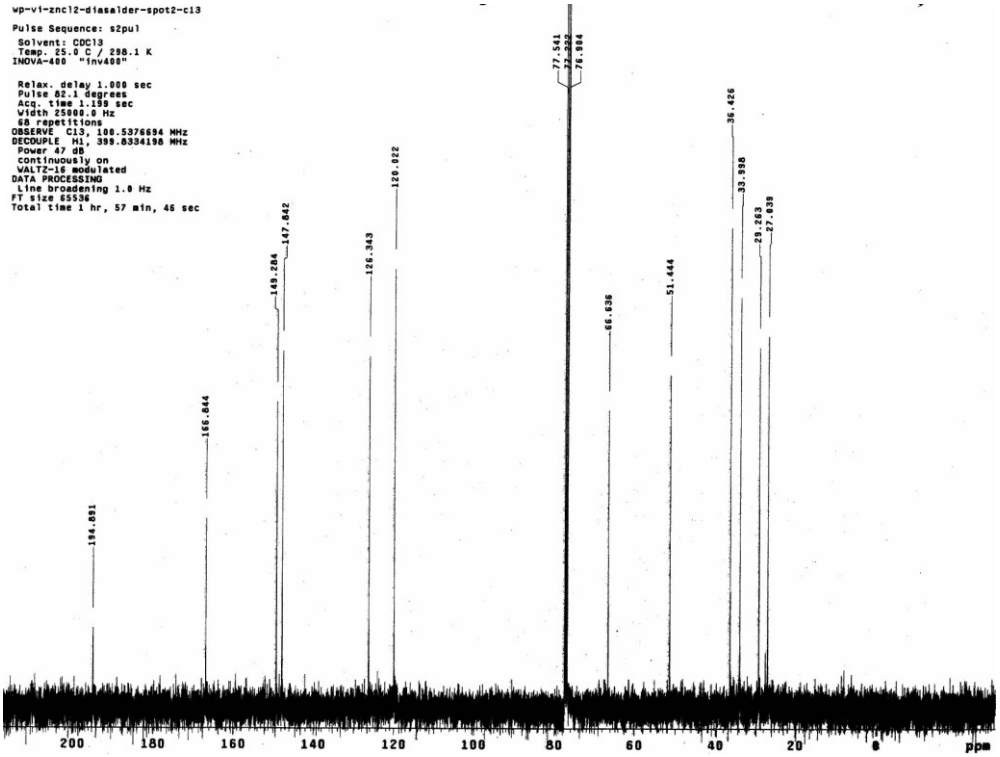

STANDARD PROTON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
44 repetitions
OBSERVE H1, 499.8948175 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
6.822
6.801
5.969
5.949
4.074
1.366
7
6
5
4
3
2
1
ppm
2.00
1.88
0.99
3.11

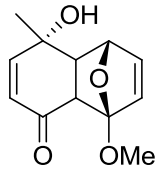

STANDARD CARBON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 31421.8 Hz
28 repetitions
OBSERVE C13, 125.6986439 MHz
DECOUPLE H1, 499.8973875 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 12 min
153.311
126.626
77.486
77.230
76.974
67.019
26.864
186.861
220
200
180
160
140
120
100
80
60
40
20
ppm


OH
O
O
OMe

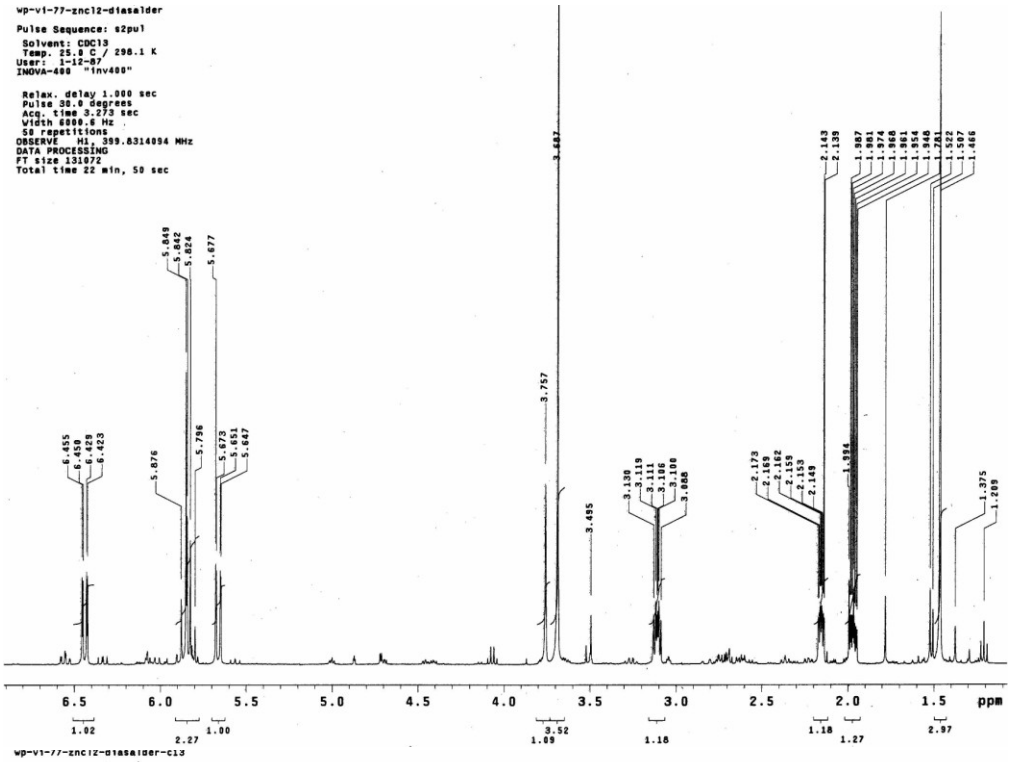
203

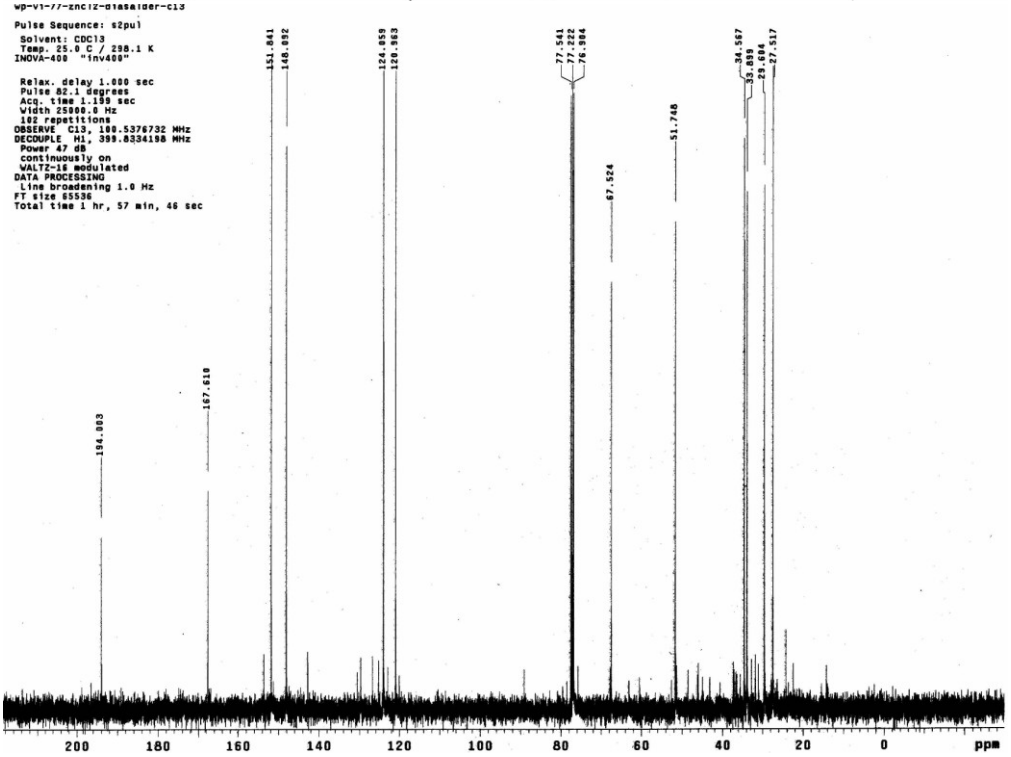

wp-v1-zncl2-diasalder-spot2
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
142 repetitions
OBSERVE H1, 399.8314094 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
7.260
6.426
6.424
6.423
6.408
6.398
6.395
5.815
5.808
5.787
5.775
5.774
5.556
5.569
5.541
3.714
3.703
3.693
3.680
3.362
3.346
3.333
3.320
2.897
2.887
2.813
1.488
1.482
1.461
1.230
8
7
6
5
4
3
2
1
ppm
1.00
2.16
1.06
3.04
0.78
1.12
0.97
1.99
3.11

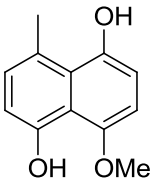

wp-v1-zncl2-diasalder-spot2-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
68 repetitions
OBSERVE C13, 100.5376694 MHz
DECOUPLE H1, 399.8334196 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
194.691
166.844
149.284
147.842
126.343
120.022
77.541
77.232
76.924
66.636
51.444
36.426
33.938
29.263
27.933
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
O
O
OMe

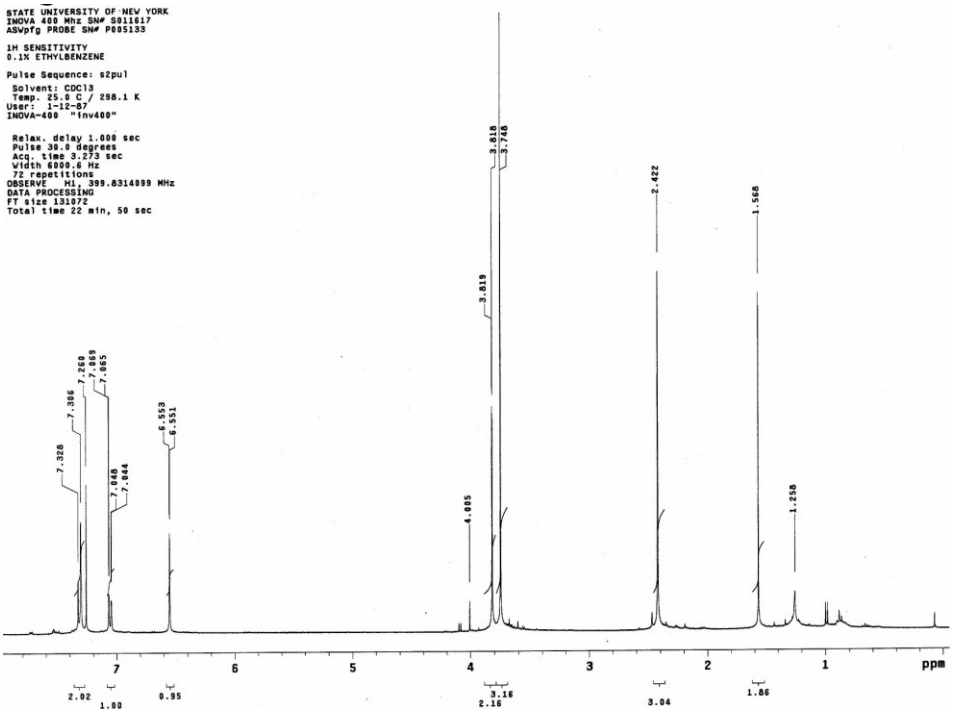
204

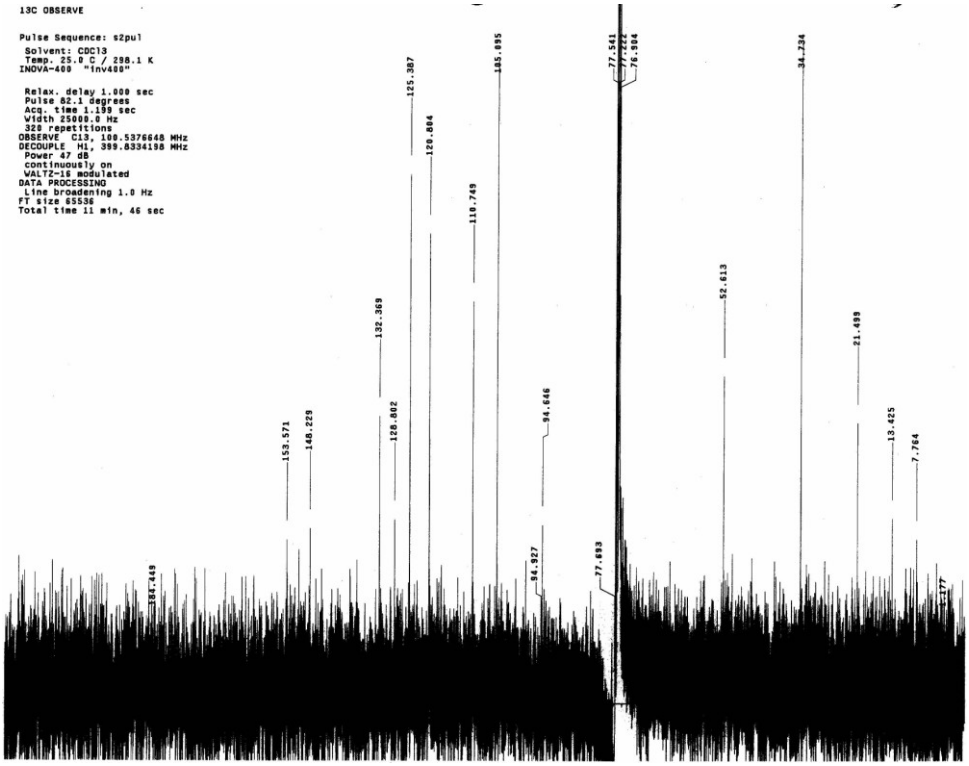

wp-v1-77-zncl2-diasalder
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
50 repetitions
OBSERVE H1, 399.8314094 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

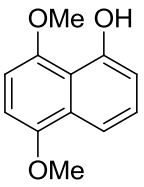

wp-v1-77-zncl2-diasalder-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
102 repetitions
OBSERVE C13, 100.5376732 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously On
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
OH
OMe

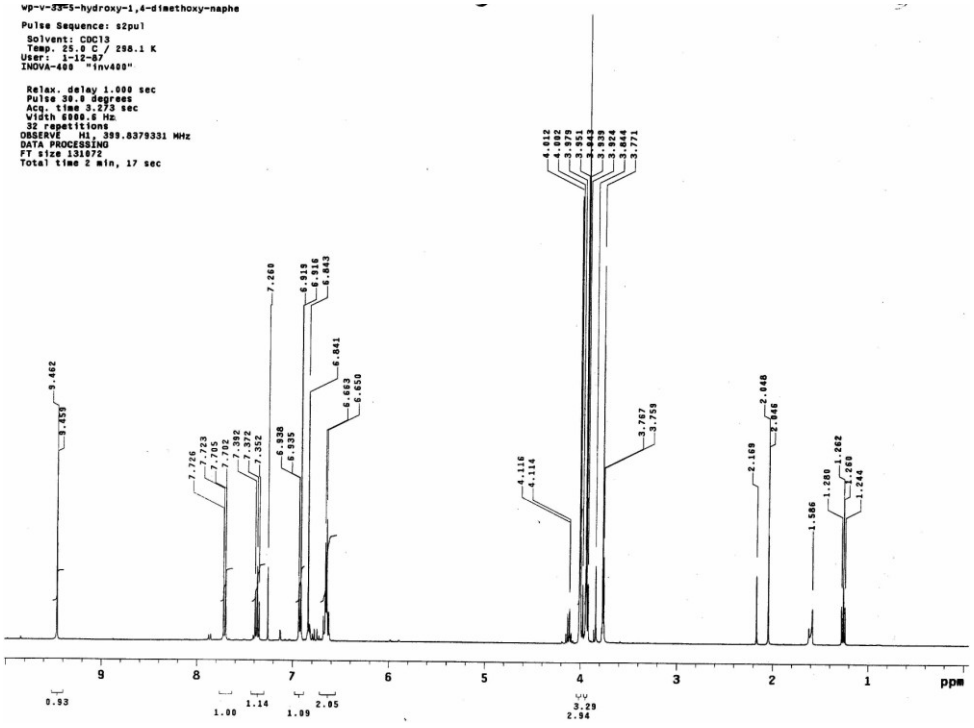
205

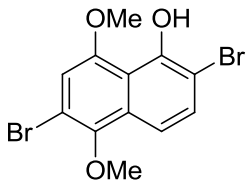

STATE UNIVERSITY OF NEW YORK
INOVA 400 Mhz SN# 5011617
ASWpfg PROBE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
72 repetitions
OBSERVE H1, 399.8314999 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
7.328
7.386
7.260
7.069
7.065
7.048
7.044
6.559
6.551
4.095
3.819
3.816
3.746
2.422
1.568
1.258
7
6
5
4
3
2
1
ppm
2.02
1.00
0.95
3.16
2.16
3.04
1.86


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.139 sec
Width 25000.0 Hz
328 repetitions
OBSERVE C13, 100.5376648 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 11 min, 46 sec
153.571
148.229
132.369
128.802
125.387
120.884
110.749
105.095
94.646
77.541
77.222
76.904
52.613
34.734
21.499
13.425
7.764

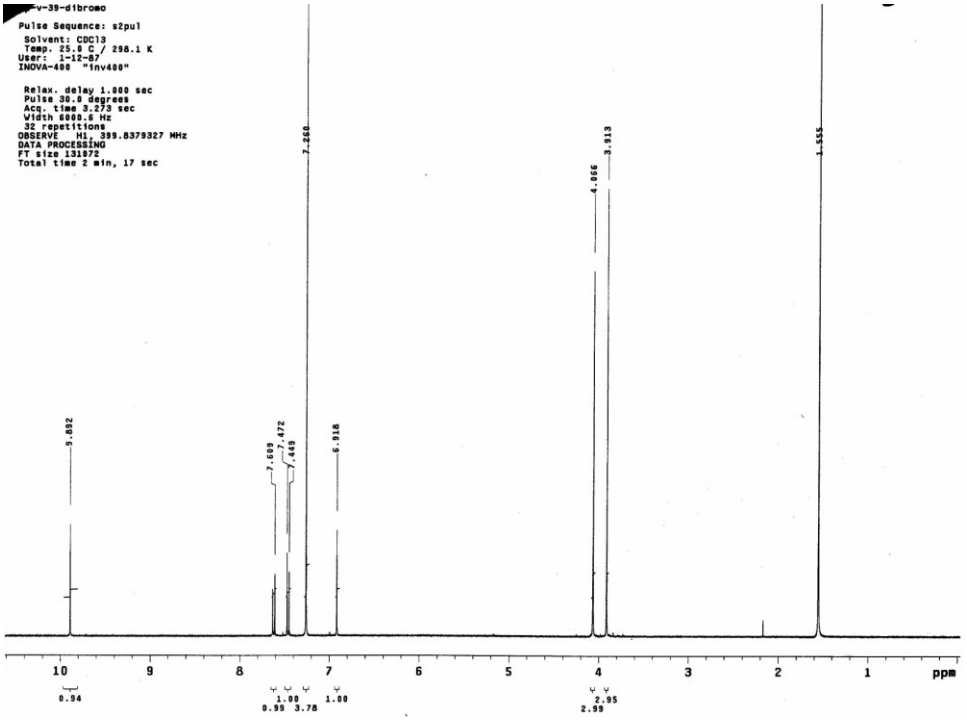

OMe OH
OMe

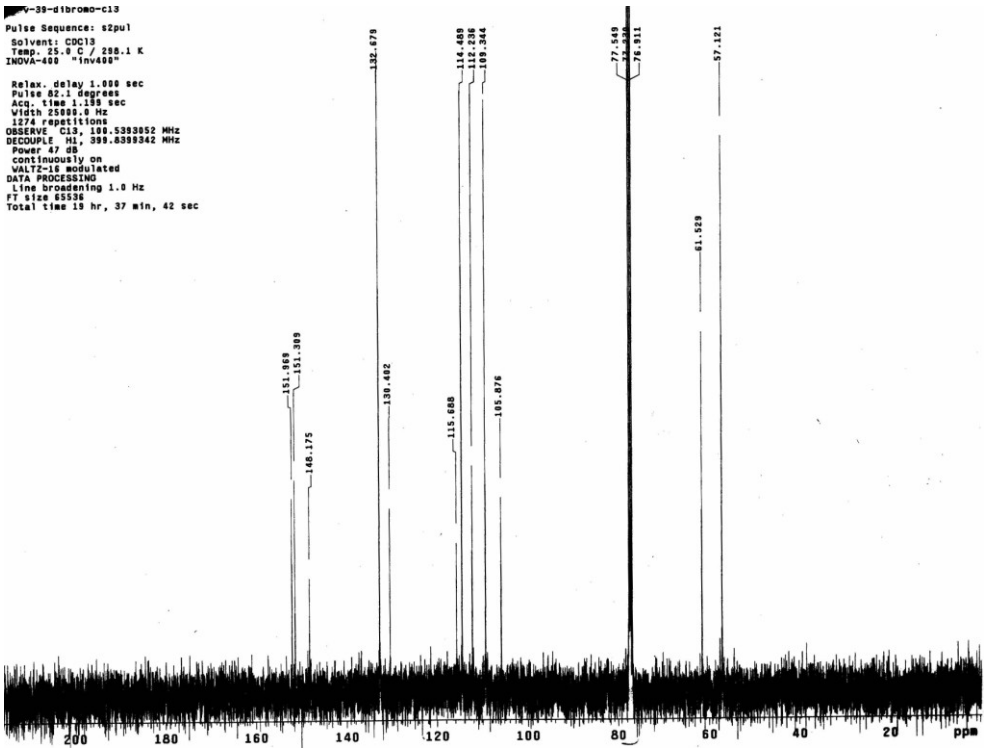
207

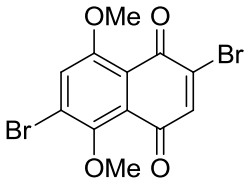

wp-v-33-5-hydroxy-1,4-dimethoxy-naphe
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379331 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
9.462
9.459
7.726
7.723
7.705
7.702
7.372
7.352
7.266
6.938
6.935
6.919
6.916
6.843
6.841
6.663
6.650
4.116
4.114
4.012
4.002
3.979
3.951
3.943
3.939
3.924
3.844
3.771
3.767
3.759
2.169
2.048
2.046
1.586
1.266
1.262
1.259
1.244
9
8
7
6
5
4
3
2
1
ppm
0.93
1.00
1.14
1.09
2.05
3.29
2.94


OMe
OH
Br
Br
OMe

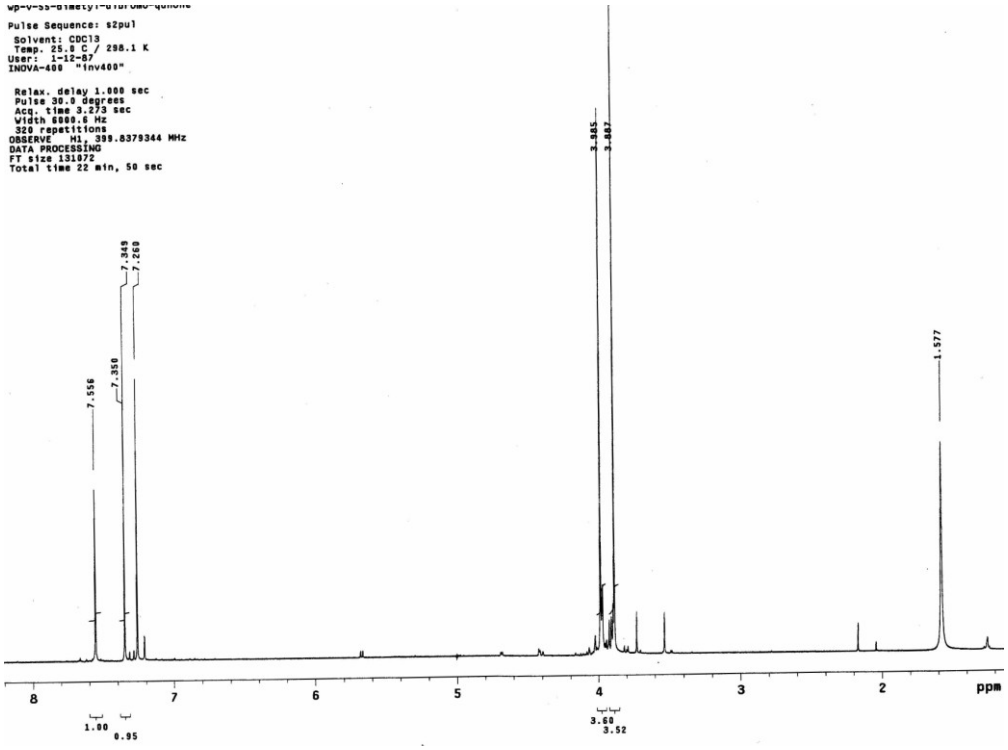
208

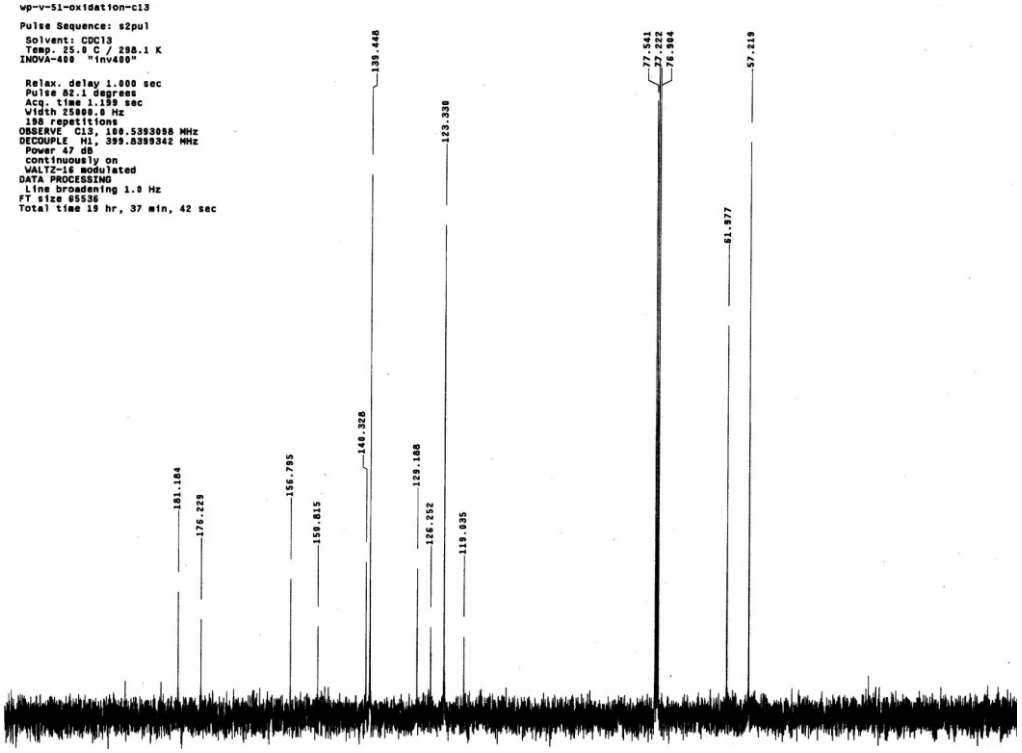

v-39-dibromo
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379327 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
9.892
7.669
7.472
7.449
7.260
6.918
4.066
3.913
1.555
10
9
8
7
6
5
4
3
2
1
ppm
0.94
1.00
0.99
3.78
1.00
2.95
2.99

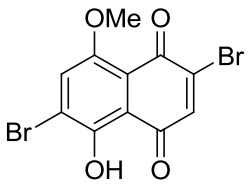

v-39-dibromo-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
1274 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
132.879
114.488
112.336
109.044
77.549
77.231
76.911
57.121
61.529
151.969
151.309
146.175
130.402
115.688
105.876
200
180
160
140
120
100
80
60
40
20
ppm


OMe O
Br
Br
OMe O

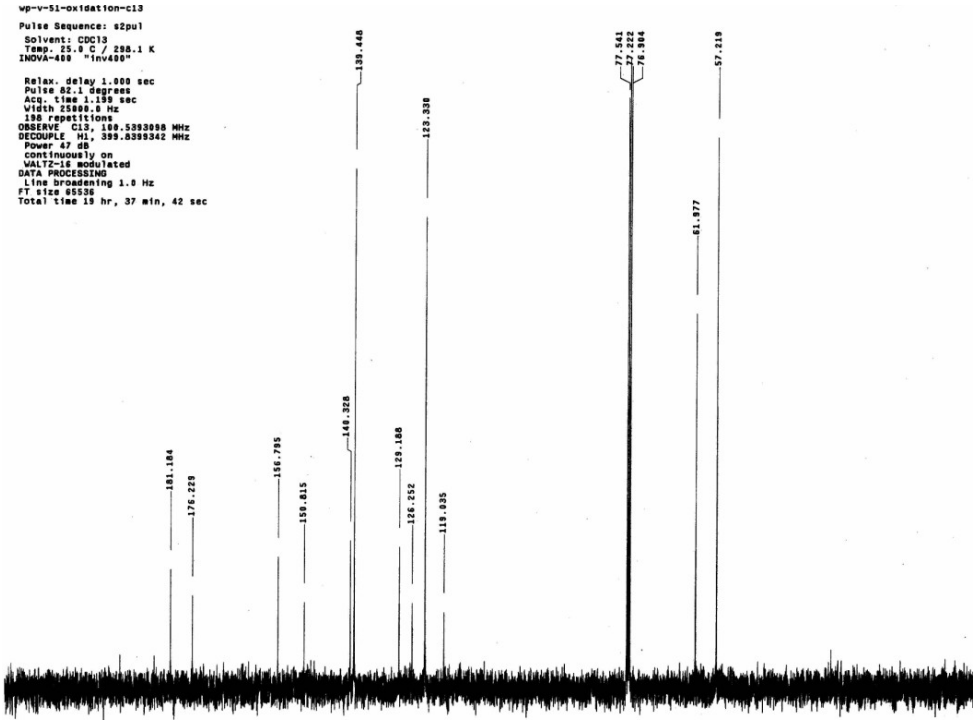
209

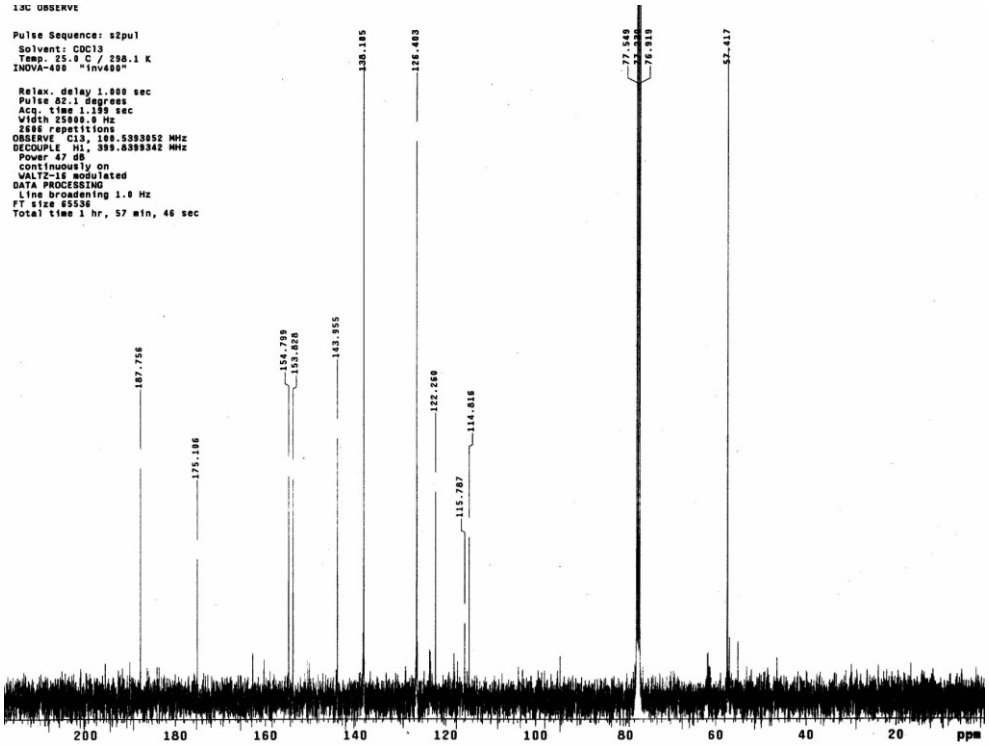

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.8 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
320 repetitions
OBSERVE H1, 399.8379344 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
7.556
7.350
7.349
7.260
3.885
3.867
1.577
8
7
6
5
4
3
2
ppm
1.00
0.95
3.68
3.52

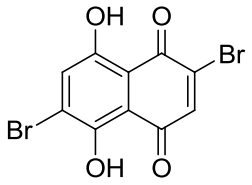

wp-v-51-oxidation-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.159 sec
Width 25000.0 Hz
198 repetitions
OBSERVE C13, 100.5393098 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
181.184
176.229
156.795
150.615
140.328
139.448
129.188
126.252
123.338
119.035
77.541
77.222
76.904
61.977
57.219


OMe
O
Br
Br
OH
O

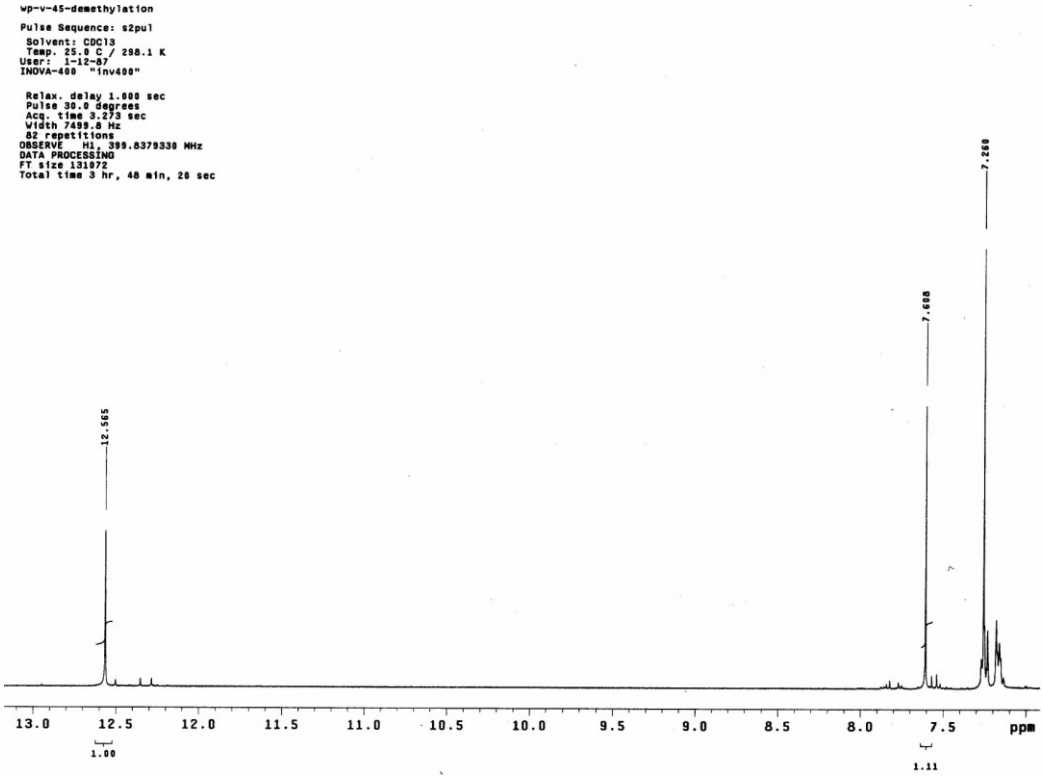
210

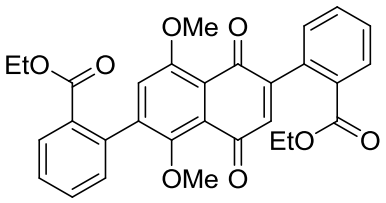

wp-v-51-oxidation-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
198 repetitions
OBSERVE C13, 100.5393098 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
181.184
176.229
156.795
150.615
140.328
139.448
129.188
126.252
123.338
119.035
77.541
77.232
76.924
61.977
57.219


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2688 repetitions
OBSERVE C13, 100.5393052 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
187.756
175.186
154.799
153.828
143.555
130.195
126.403
122.260
115.787
114.618
77.549
77.240
76.919
57.417
200
180
160
140
120
100
80
60
40
20
ppm

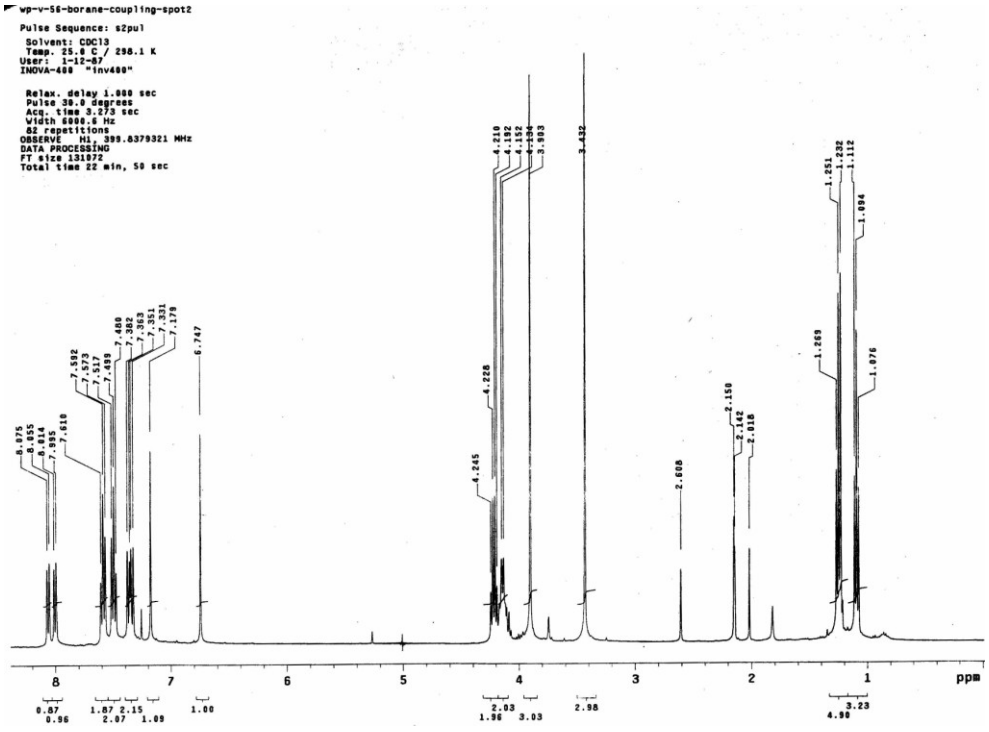

OH
O
Br
Br
OH
O

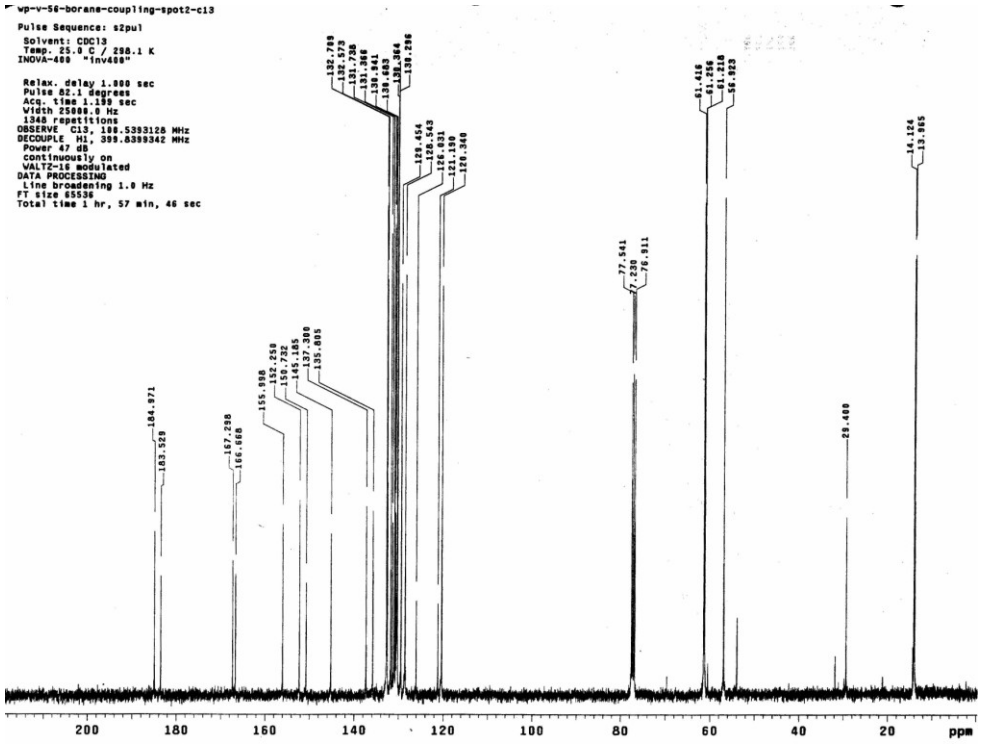
211

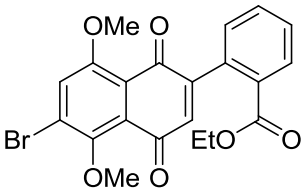

wp-v-45-demethylation
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 7499.8 Hz
82 repetitions
OBSERVE H1, 399.8379330 MHz
DATA PROCESSING
FT size 131072
Total time 3 hr, 48 min, 28 sec
12.565
7.608
7.269
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
ppm
1.00
1.11


OMe O
EtO O
EtO O
OMe O

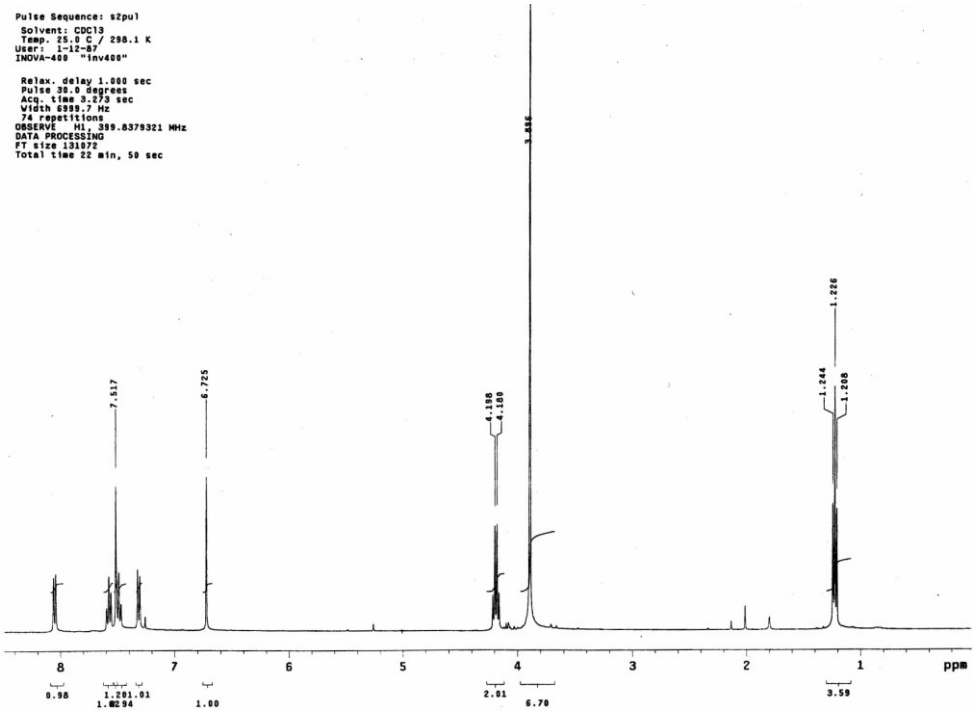
213

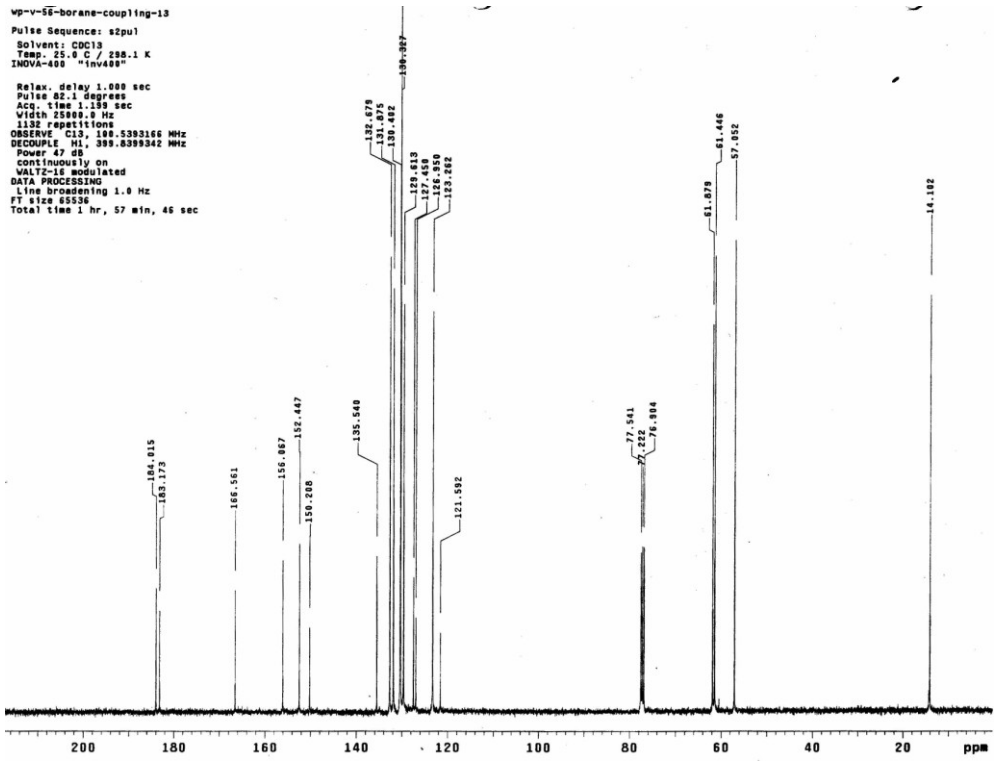

wp-v-56-borane-coupling-spot2
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
82 repetitions
OBSERVE H1, 399.8379321 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

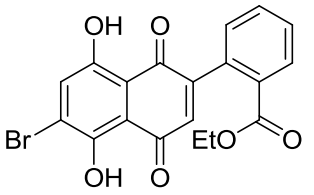

wp-v-56-borane-coupling-spot2-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 62.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1348 repetitions
OBSERVE C13, 100.5393128 MHz
DECOUPLE H1, 399.8389342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


OMe O
Br
EtO
O
OMe O

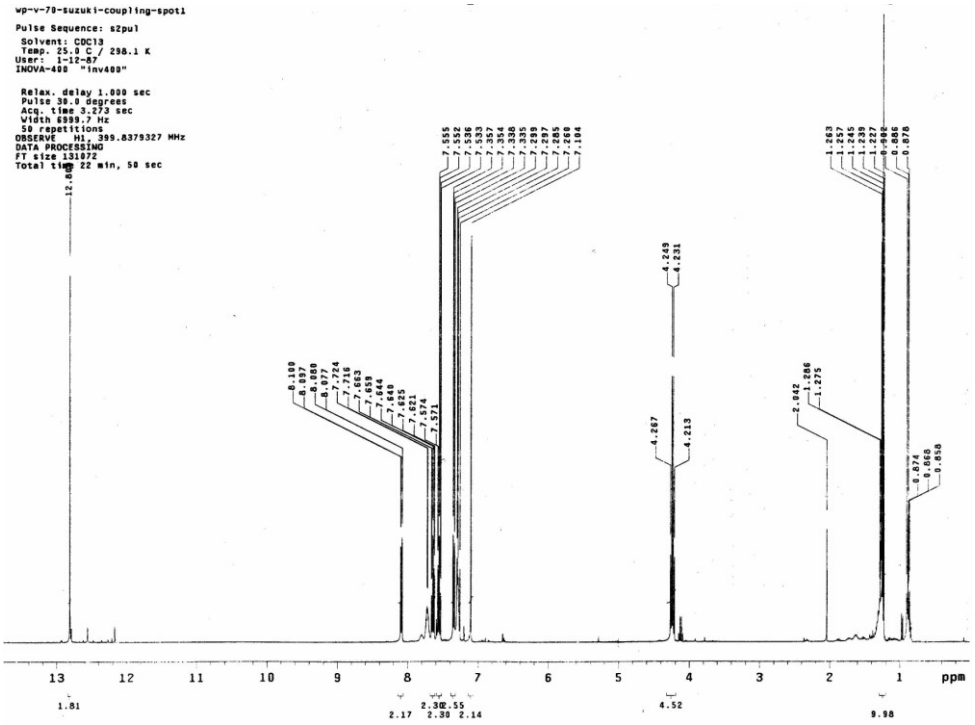
214

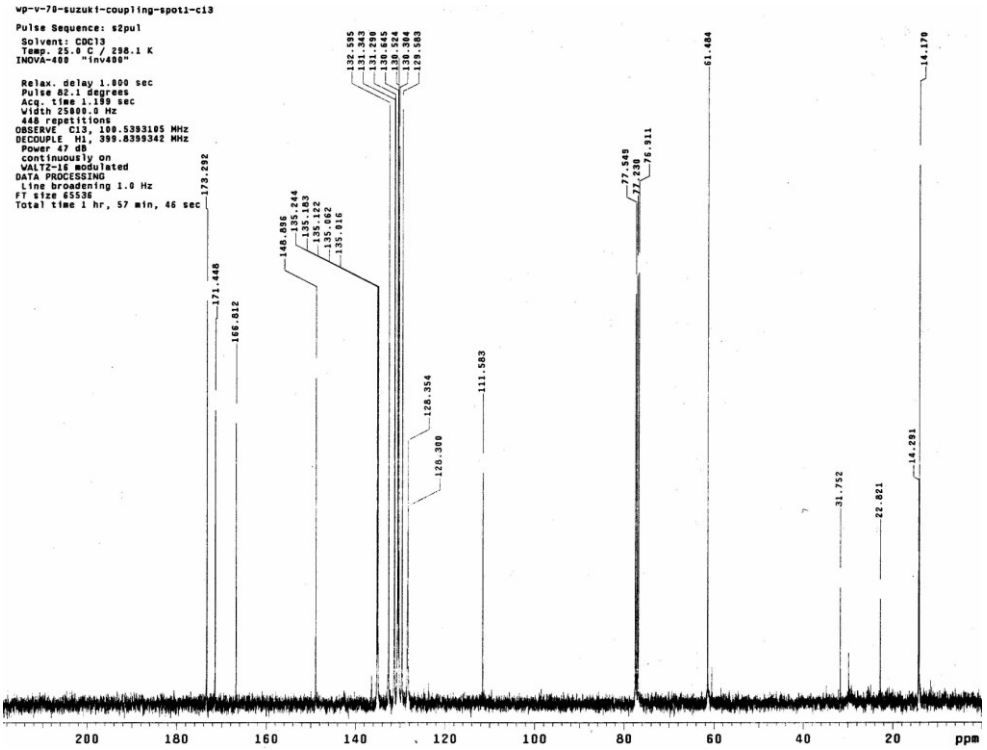

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
74 repetitions
OBSERVE H1, 399.8379321 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
7.517
6.725
4.198
4.180
1.244
1.226
1.208
ppm
0.98
1.01
1.00
2.01
6.70
3.59

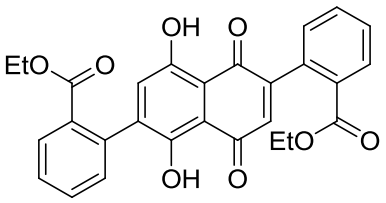

wp-v-56-borane-coupling-13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1132 repetitions
OBSERVE C13, 100.5393166 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
184.015
183.173
166.561
156.067
152.447
150.208
135.540
132.679
131.875
130.482
130.307
129.613
127.459
126.950
123.282
121.592
77.541
77.232
76.804
61.879
61.446
57.052
14.182
ppm


OH
O
Br
EtO
O
OH
O

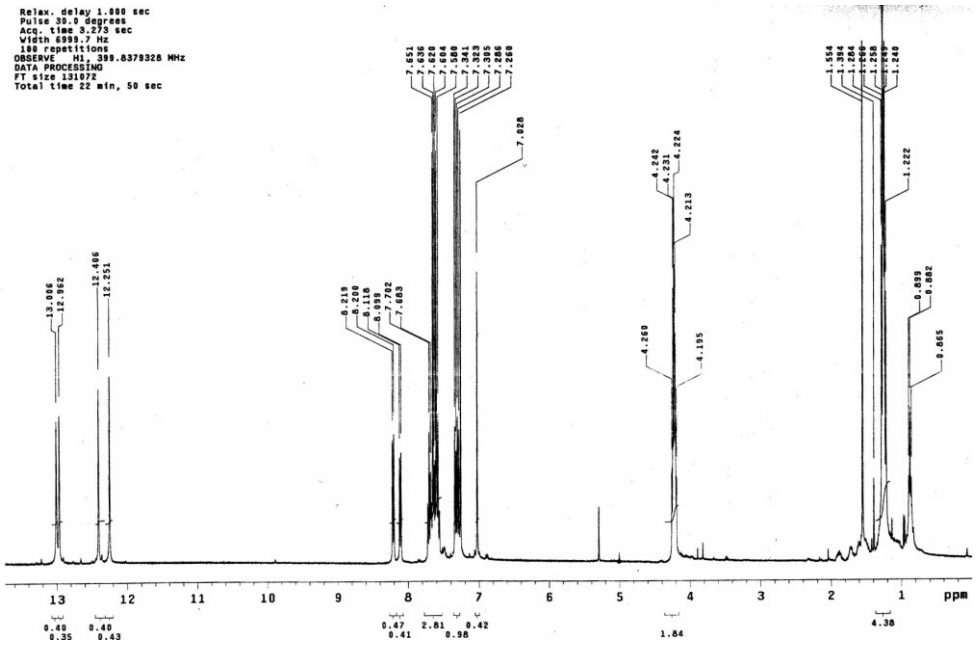
215

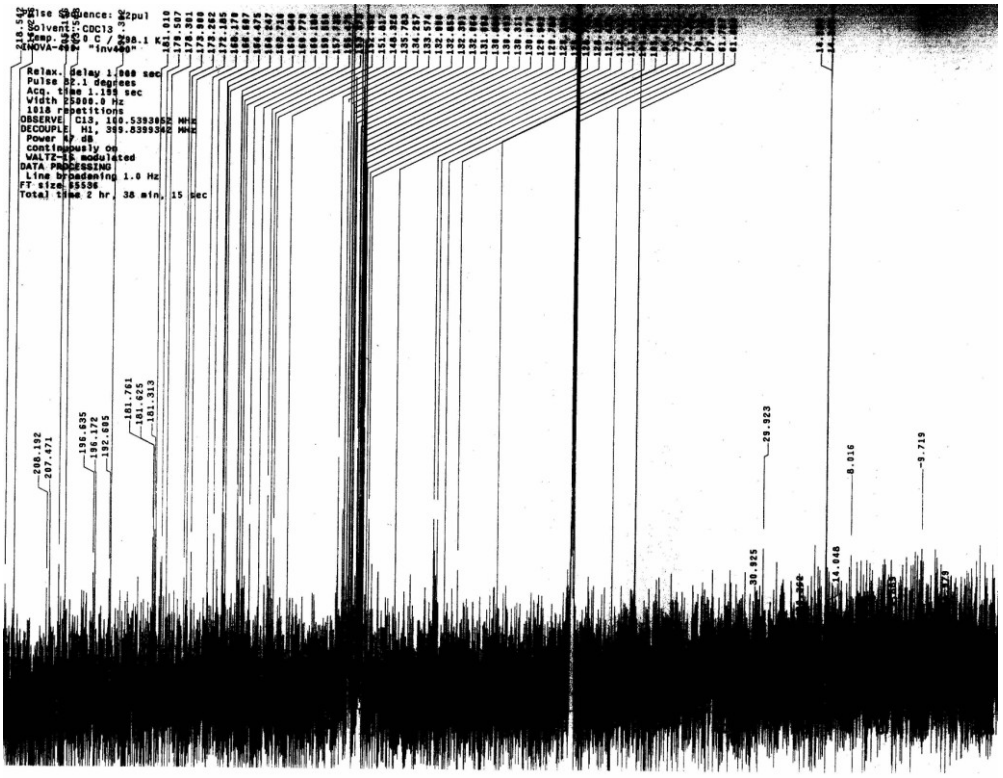

wp-v-78-suzuki-coupling-spot1
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
50 repetitions
OBSERVE H1, 399.8379327 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

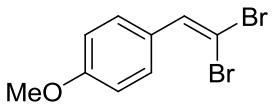

wp-v-78-suzuki-coupling-spot1-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
448 repetitions
OBSERVE C13, 100.5393105 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


OH
O
EtO
O
EtO
O
OH
O

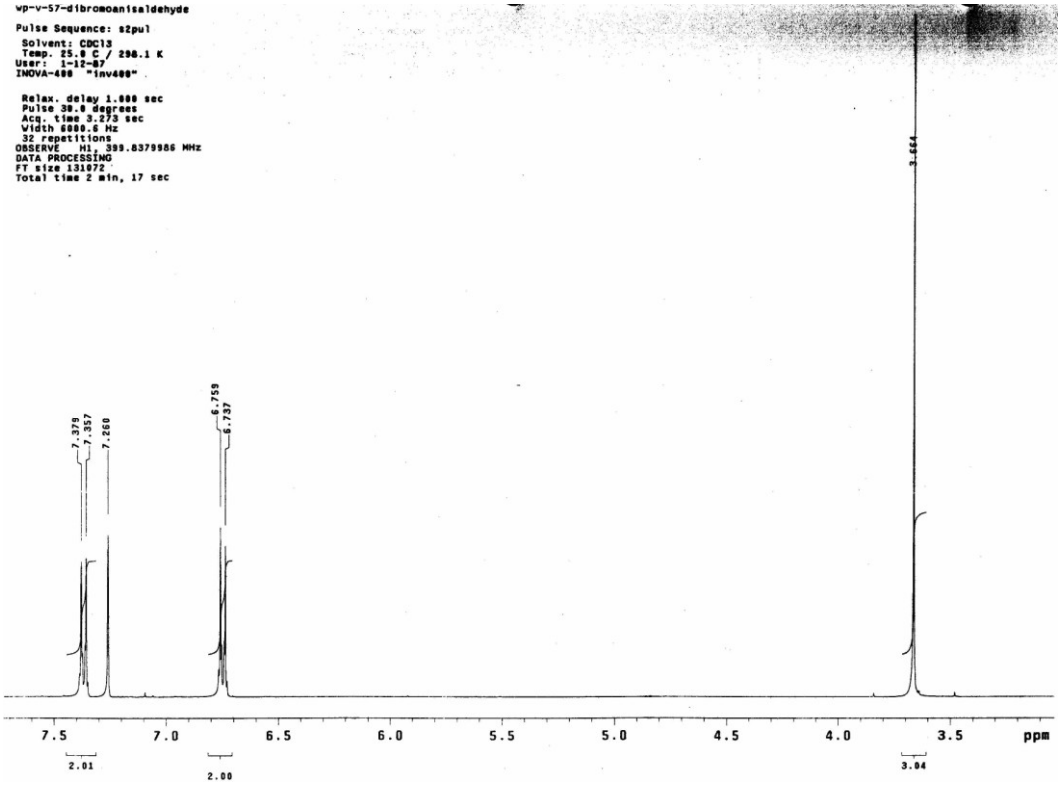
216

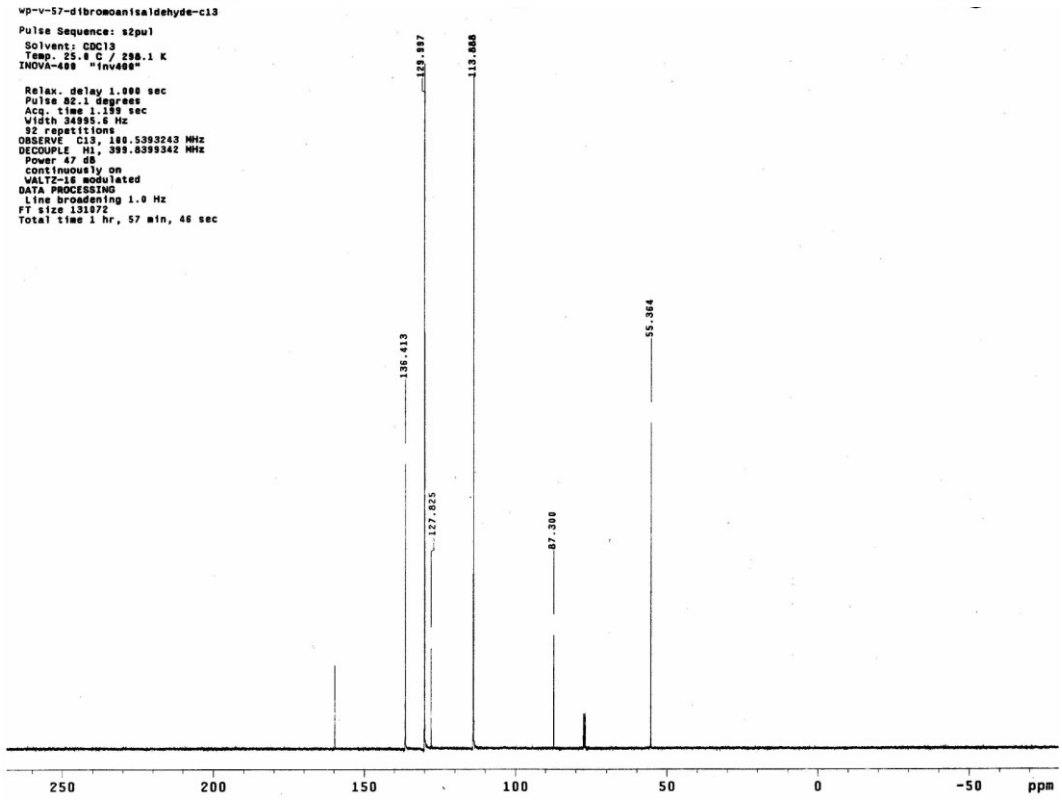

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6999.7 Hz
100 repetitions
OBSERVE H1, 399.8379328 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

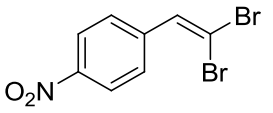

Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.184 sec
Width 25000.0 Hz
1018 repetitions
DECOUPLE H1, 399.8399362 MHz
Power 47 dB
continuously ON
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 38 min, 15 sec


Br
Br
MeO

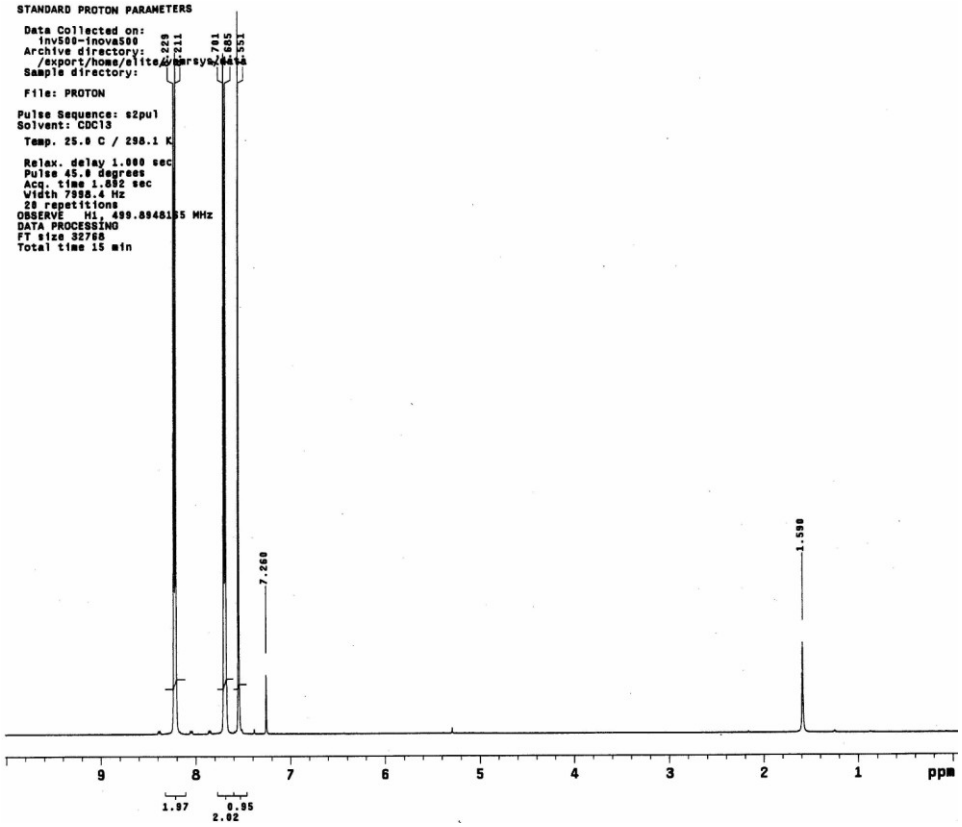
226

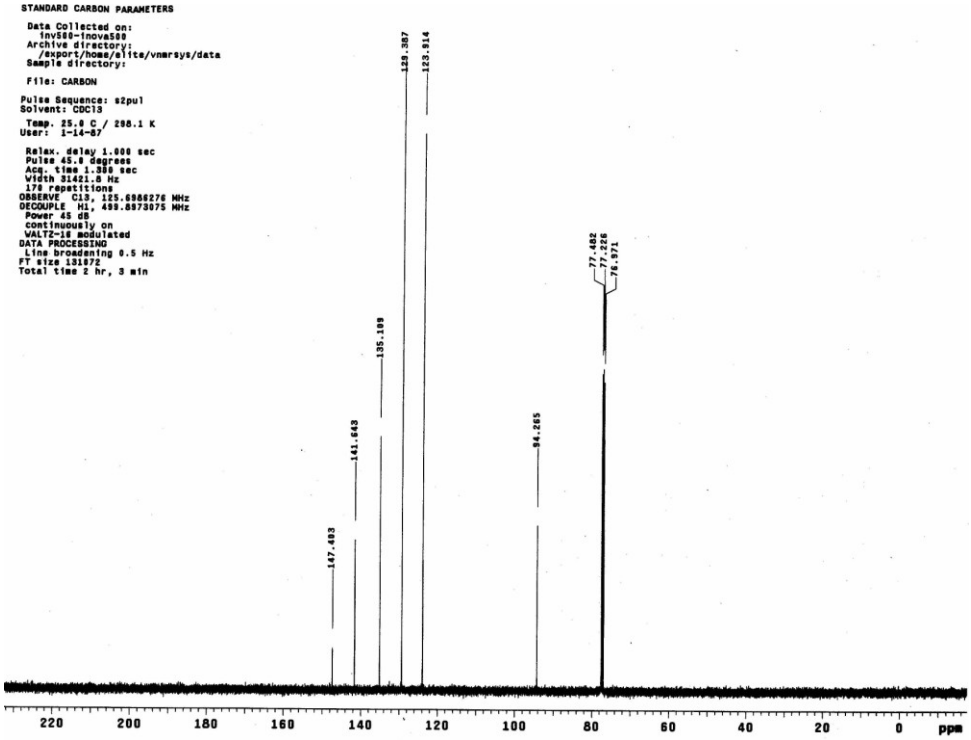

wp-v-57-dibromoanisaldehyde
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
32 repetitions
OBSERVE H1, 399.8379986 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 17 sec
7.379
7.357
7.260
6.759
6.737
3.664
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
2.01
2.00
3.04

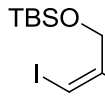

wp-v-57-dibromoanisaldehyde-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 34995.8 Hz
32 repetitions
OBSERVE C13, 100.5393243 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 57 min, 46 sec
129.987
113.688
136.413
127.625
87.300
55.364
250
200
150
100
50
0
-50
ppm


Br
Br
O_2N

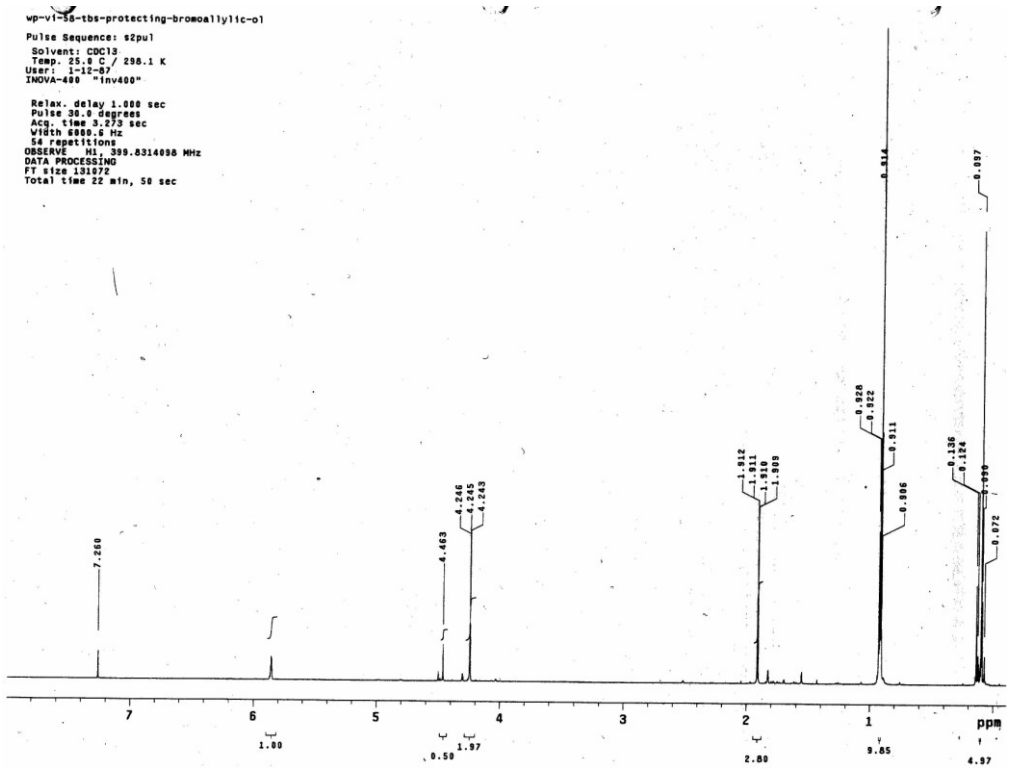
227

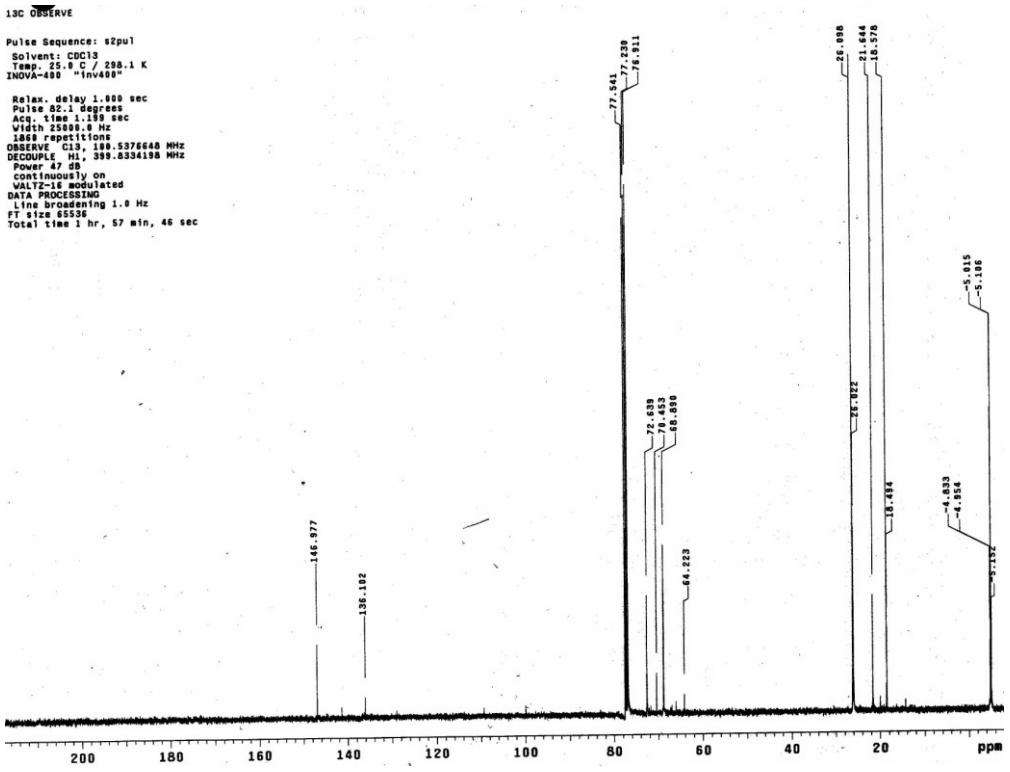

STANDARD PROTON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
28 repetitions
OBSERVE H1, 499.8948135 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
7.229
7.211
7.701
7.685
7.551
7.260
1.590
9
8
7
6
5
4
3
2
1
ppm
1.97
0.95
2.02

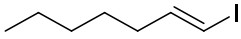

STANDARD CARBON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-07
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 31421.9 Hz
176 repetitions
OBSERVE C13, 125.6866276 MHz
DECOUPLE H1, 499.8873075 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 2 hr, 3 min
147.493
141.643
135.109
128.387
123.914
94.265
77.482
77.226
76.971
220
200
180
160
140
120
100
80
60
40
20
0
ppm


TBSO
I

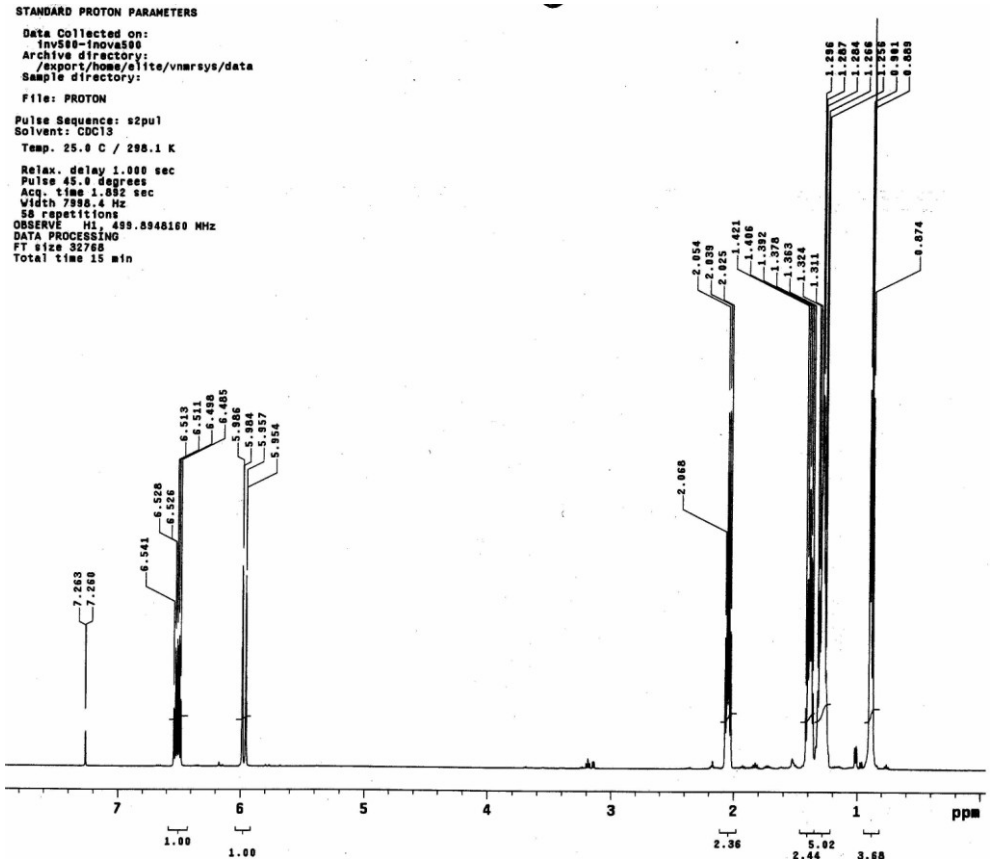
228

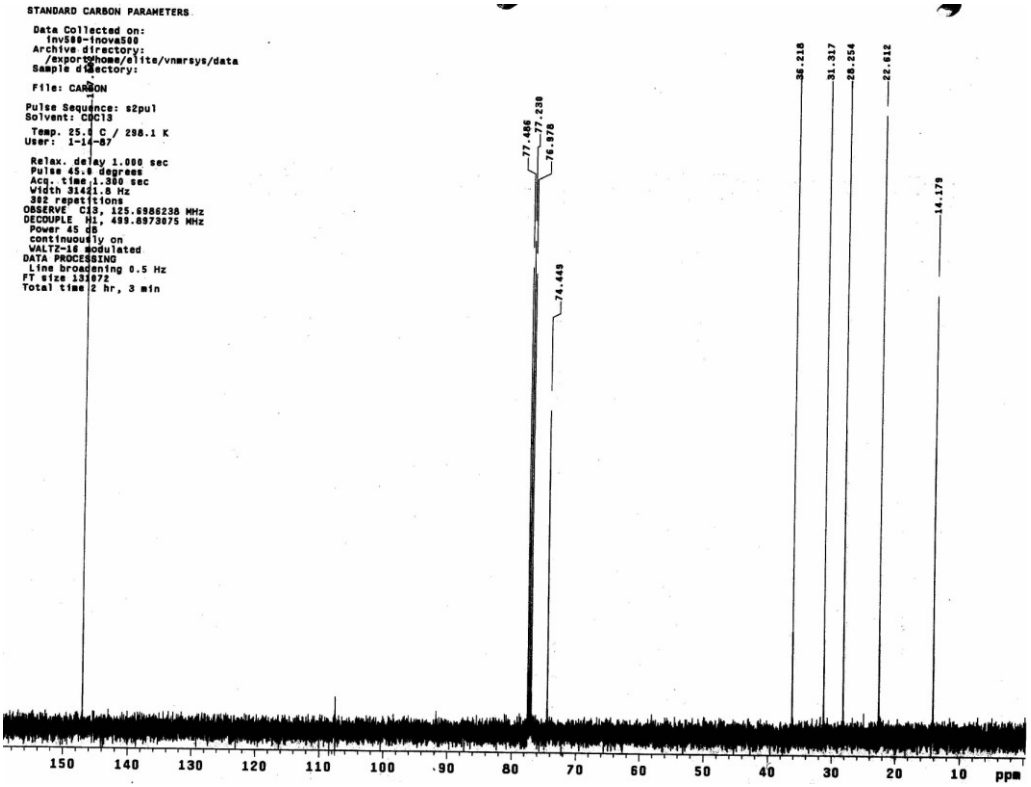

wp-vi-58-tbs-protecting-bromoallylic-ol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
54 repetitions
OBSERVE H1, 399.8314098 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
7.260
4.463
4.246
4.245
4.243
1.912
1.911
1.910
1.909
0.928
0.922
0.911
0.906
0.136
0.124
0.097
0.072
ppm
1.00
0.50
1.97
2.80
9.85
4.97

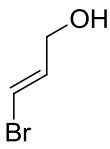

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
1860 repetitions
OBSERVE C13, 100.5376648 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
146.977
136.102
77.541
77.239
76.911
72.639
70.458
68.898
64.223
26.098
26.022
21.644
18.576
18.494
-4.833
-4.954
-5.015
-5.106
ppm



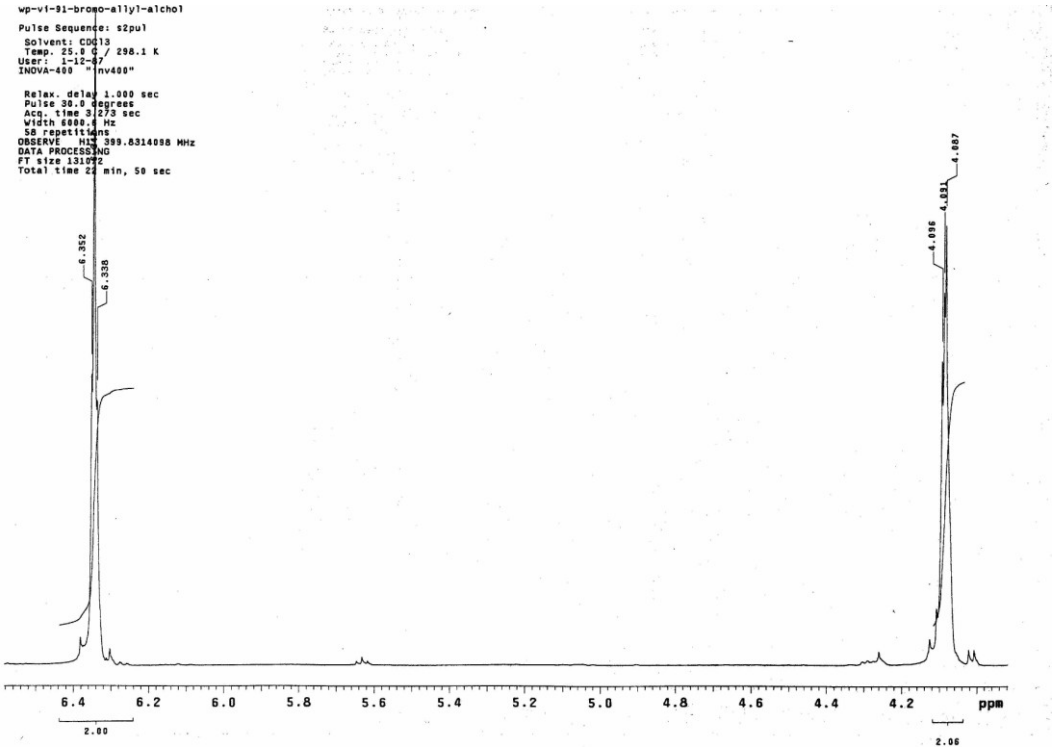
230

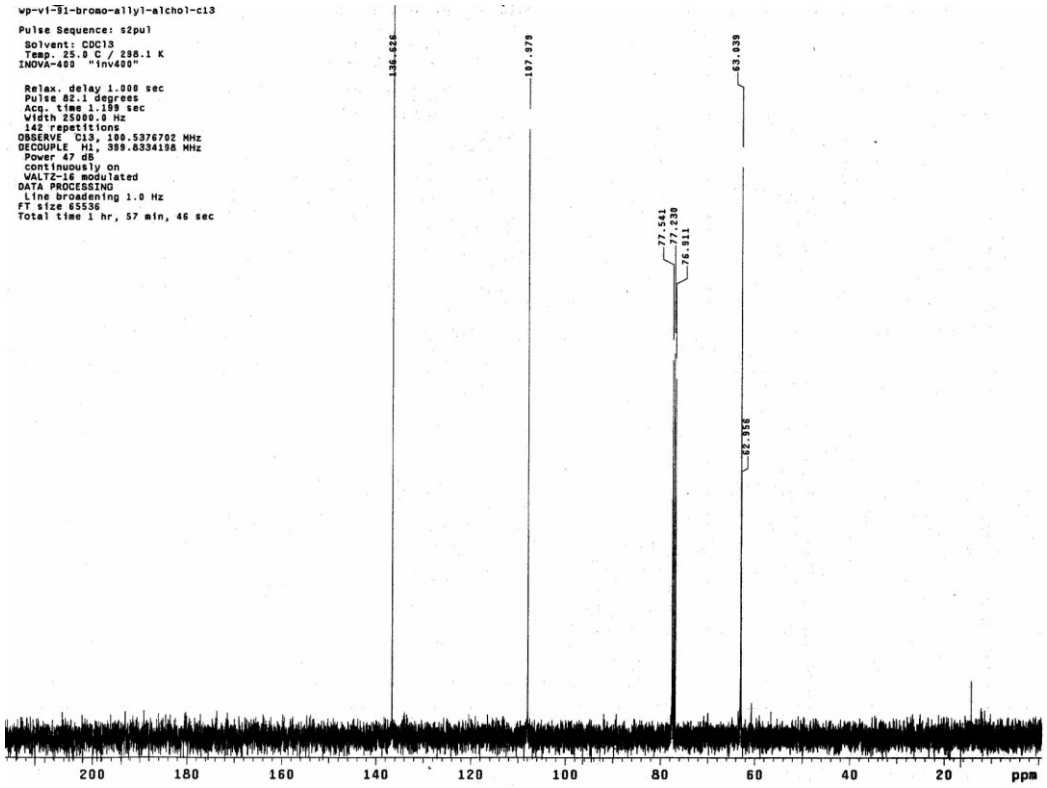

STANDARD PROTON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.852 sec
Width 7998.4 Hz
58 repetitions
OBSERVE H1, 499.8948160 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
7.263
7.260
6.541
6.528
6.526
6.513
6.511
6.498
6.485
5.986
5.984
5.557
5.554
2.066
2.054
2.039
2.025
1.421
1.406
1.392
1.378
1.363
1.324
1.311
1.296
1.287
1.284
1.266
1.255
0.881
0.869
0.874
ppm
1.00
1.00
2.36
5.02
2.44
3.68

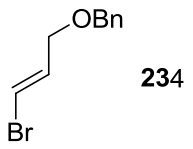

STANDARD CARBON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
382 repetitions
OBSERVE C13, 125.6986238 MHz
DECOUPLE H1, 499.8973875 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 2 hr, 3 min
77.486
77.230
76.978
74.449
36.218
31.917
29.254
22.612
14.179
ppm


OH
Br

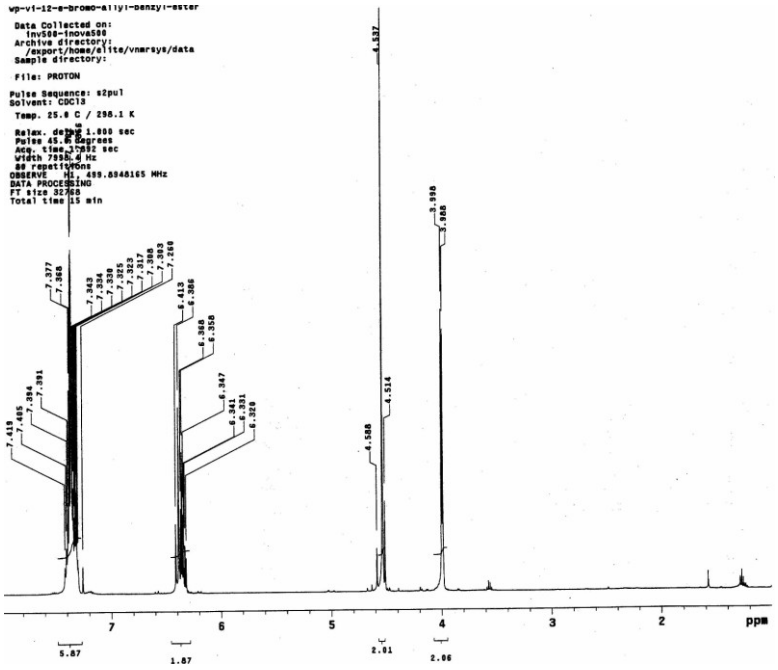
233


wp-vi-91-bromo-allyl-alchol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
58 repetitions
OBSERVE H1, 399.8314088 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
6.352
6.338
4.096
4.087
4.081
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
ppm
2.00
2.06

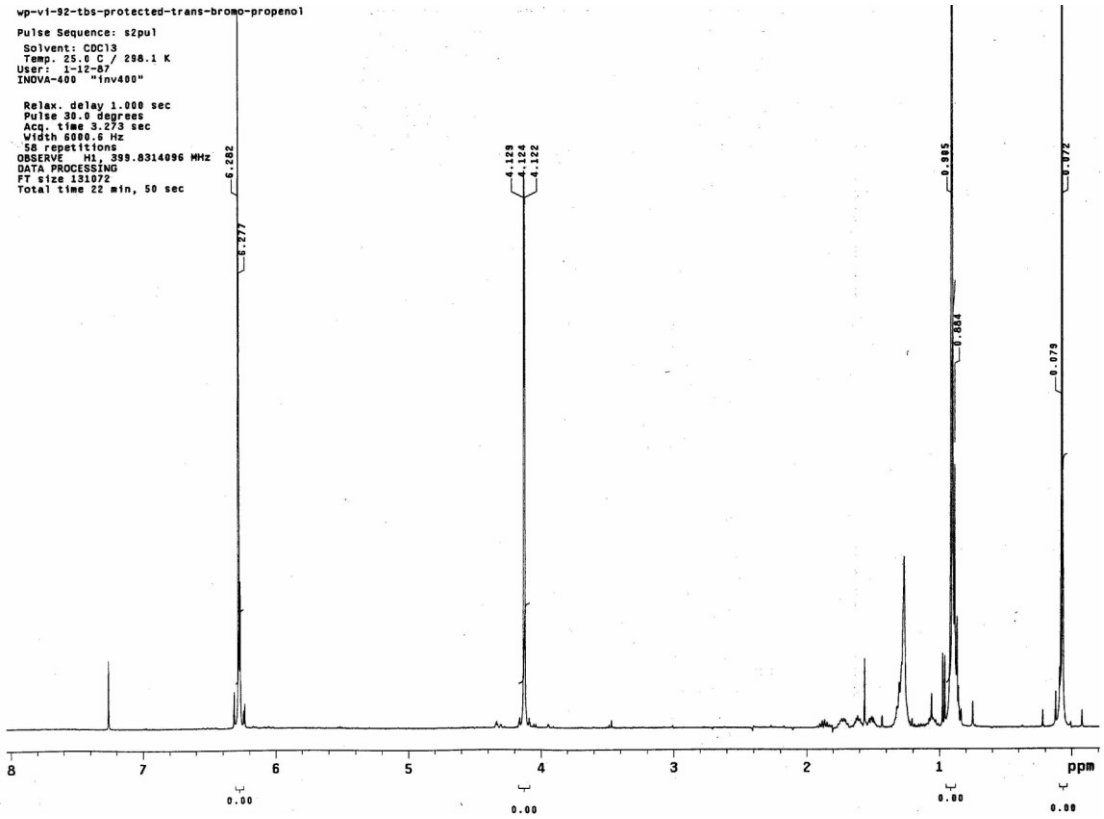

wp-vi-91-bromo-allyl-alchol-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
142 repetitions
OBSERVE C13, 100.5376702 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
136.626
117.079
77.541
77.239
76.911
63.039
62.958
200
180
160
140
120
100
80
60
40
20
ppm

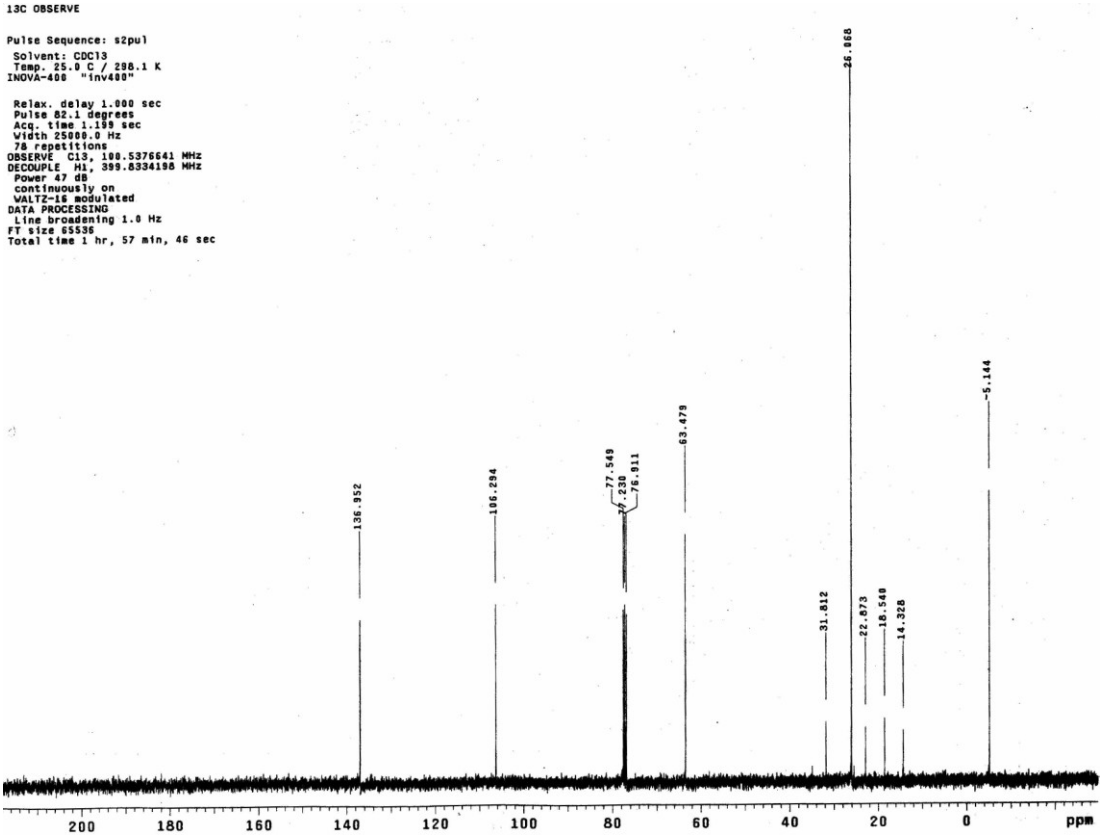

OBn
Br

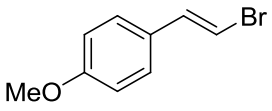
234


wp-vi-12-e-bromo-allyl-benzyl-ester
Data Collected on:
Inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.092 sec
Width 7995.4 Hz
80 repetitions
OBSERVE H1, 499.8848165 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
7.419
7.405
7.394
7.391
7.377
7.368
7.343
7.336
7.330
7.325
7.323
7.317
7.308
7.303
7.269
6.413
6.386
6.368
6.350
6.347
6.341
6.331
6.326
4.588
4.537
4.514
3.998
3.988
7
6
5
4
3
2
ppm
5.87
1.87
2.01
2.06

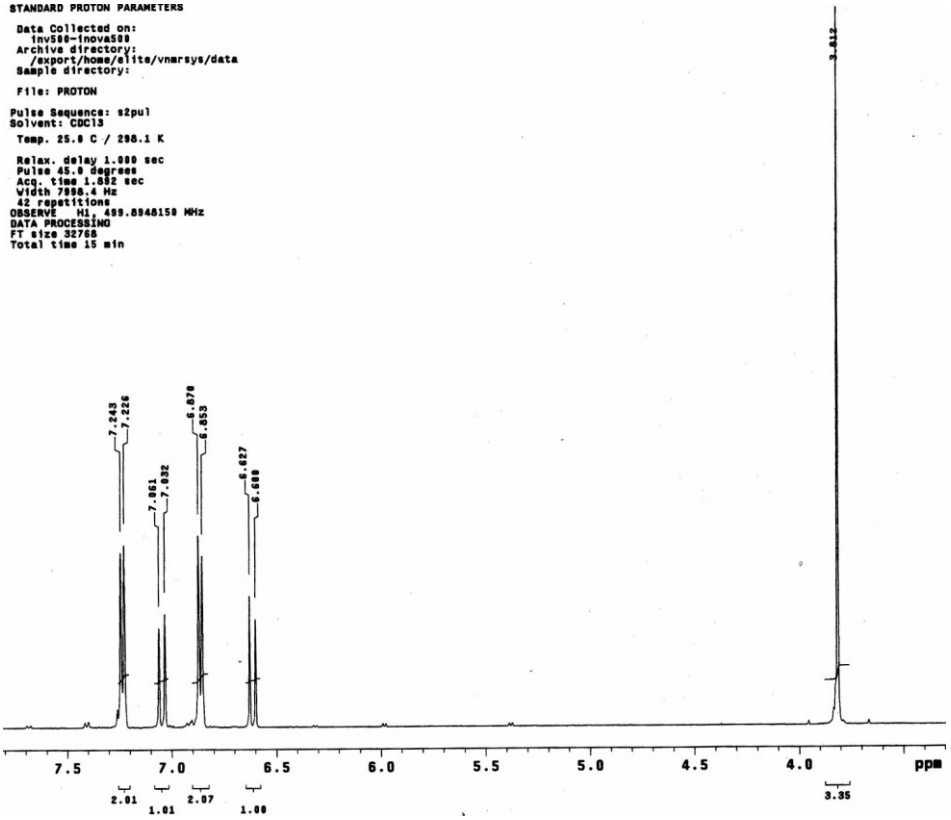
Br OTBS **235**

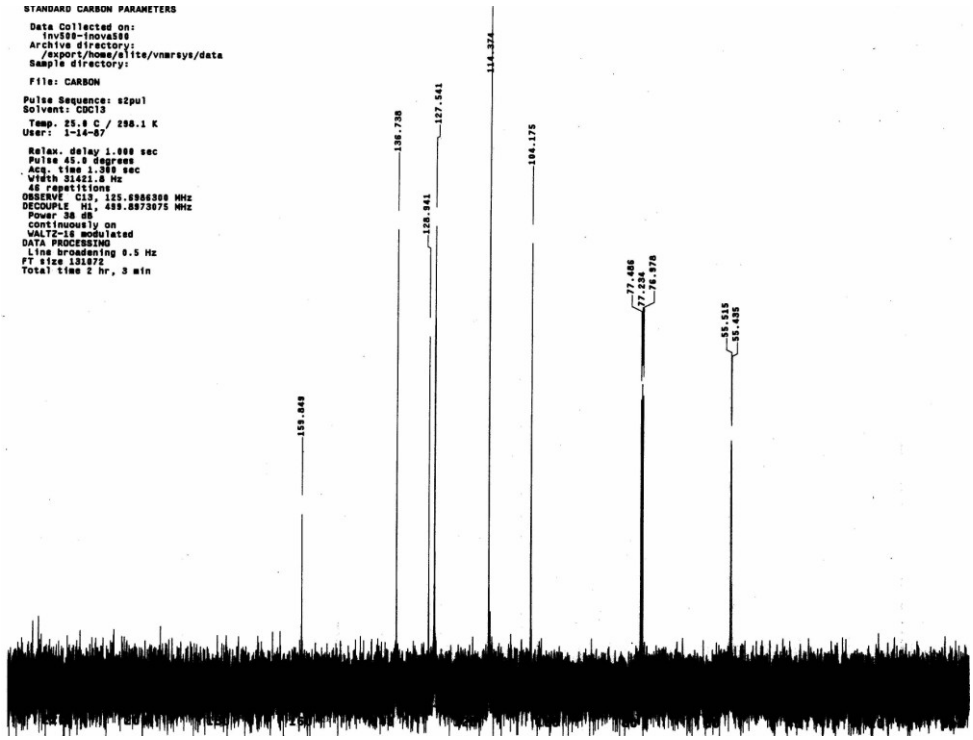

wp-vi-92-tbs-protected-trans-bromo-propenol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-IZ-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 5080.6 Hz
58 repetitions
OBSERVE H1, 399.8314096 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
6.282
6.277
4.129
4.124
4.122
0.885
0.884
0.079
0.072
8
7
6
5
4
3
2
1
ppm
0.00
0.00
0.00
0.00

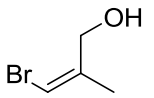

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
78 repetitions
OBSERVE C13, 100.5376641 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
136.952
106.294
77.549
77.238
76.811
63.479
31.812
26.068
22.873
18.549
14.328
-5.144
200
180
160
140
120
100
80
60
40
20
0
ppm


Br
MeO

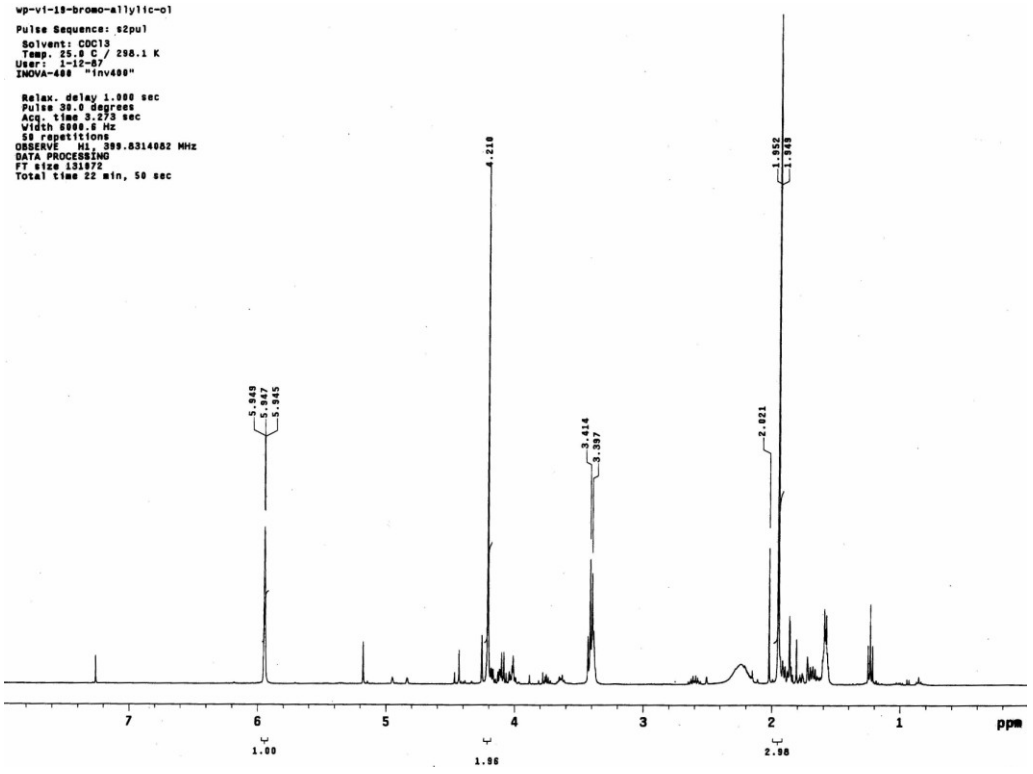
237

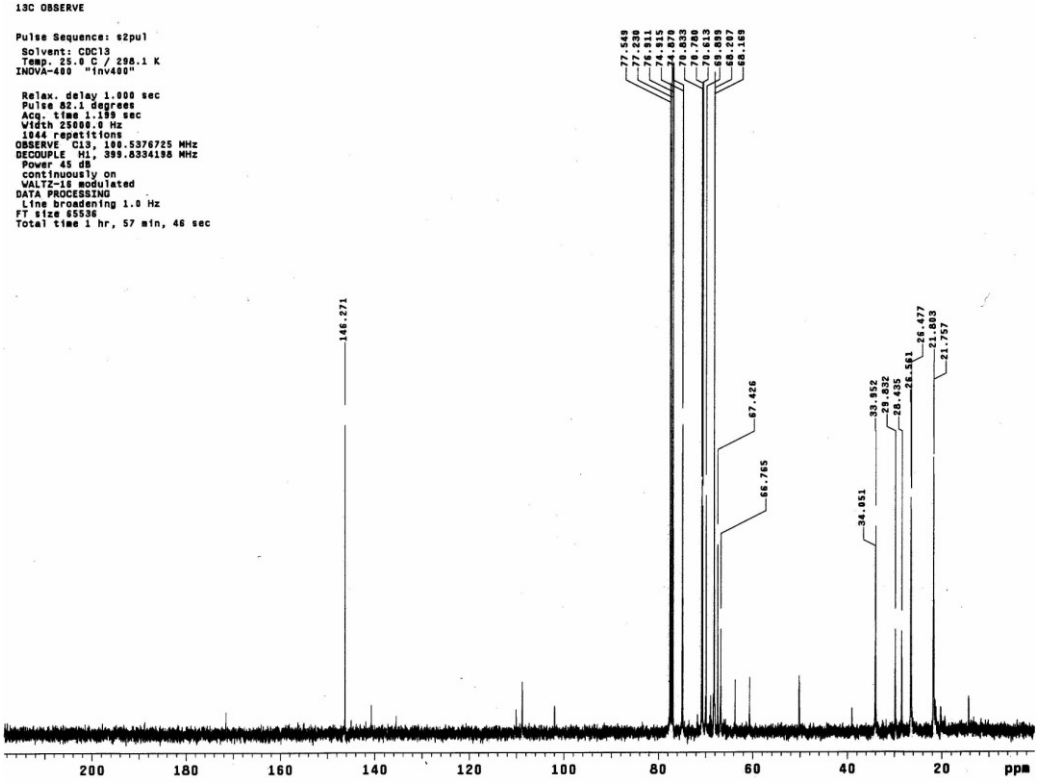

STANDARD PROTON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.882 sec
Width 7986.4 Hz
42 repetitions
OBSERVE H1, 499.8948158 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
7.243
7.226
7.861
7.832
6.678
6.653
6.627
6.608
3.812
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm
2.01
1.01
2.07
1.88
3.35

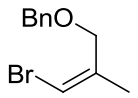

STANDARD CARBON PARAMETERS
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-07
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 31421.8 Hz
48 repetitions
OBSERVE C13, 125.6986308 MHz
DECOUPLE H1, 499.8973075 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 2 hr, 3 min
159.849
138.738
128.941
127.541
114.374
104.175
77.466
77.254
76.978
55.515
55.435


OH
Br

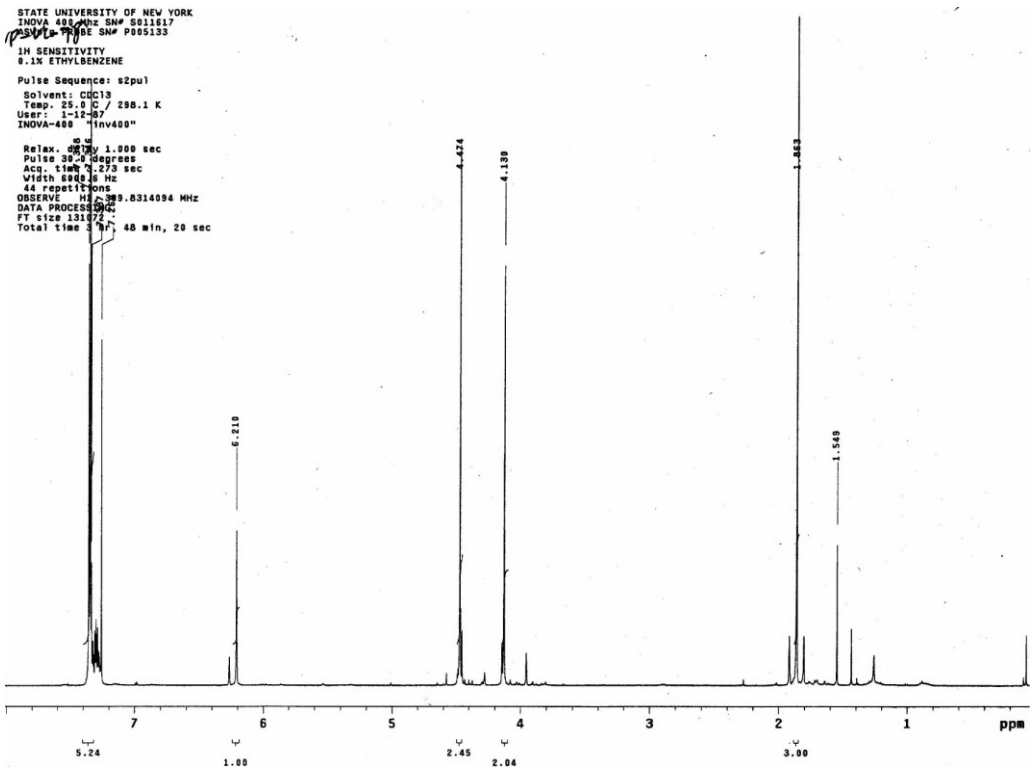
238

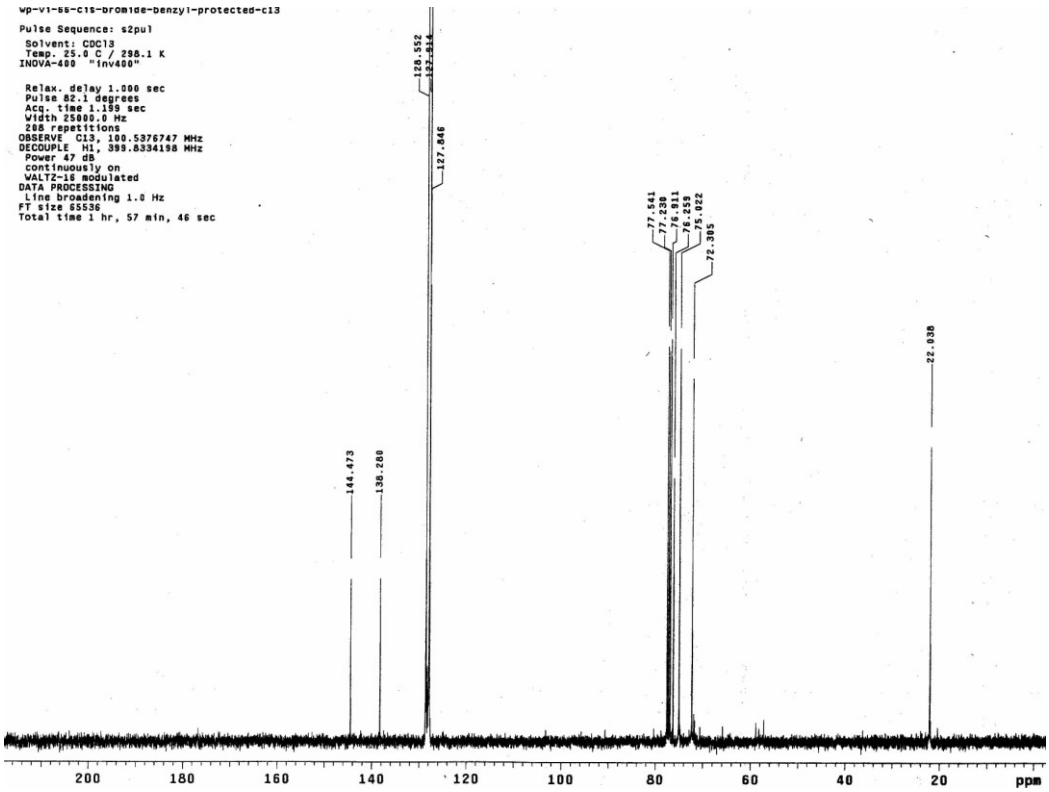

wp-vi-18-bromo-allylic-ol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
56 repetitions
OBSERVE H1, 399.8314082 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
5.949
5.947
5.945
4.216
3.414
3.397
2.021
1.952
1.948
1.00
1.96
2.98
ppm

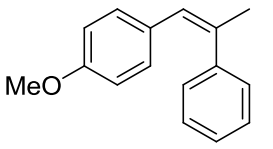

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1644 repetitions
OBSERVE C13, 100.5376725 MHz
DECOUPLE H1, 399.8334198 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
77.548
77.230
76.911
74.915
74.870
70.833
70.780
70.613
68.809
68.287
68.169
146.271
67.426
66.765
34.051
33.952
28.832
28.435
26.561
26.477
21.883
21.757
ppm


BnO
Br

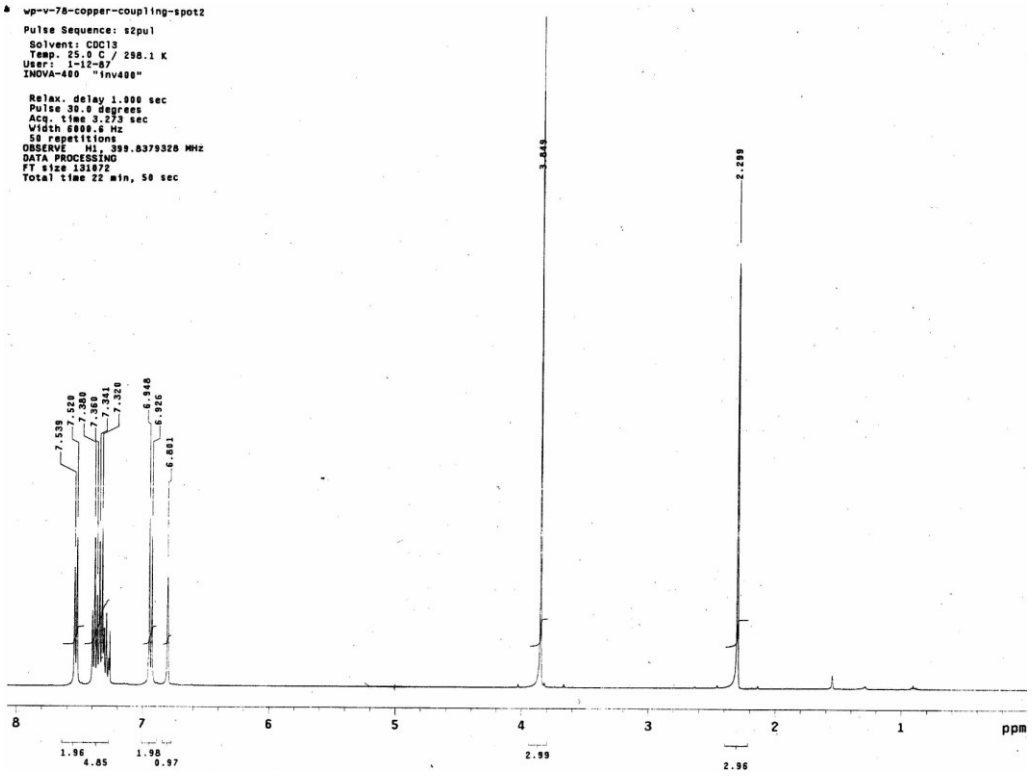
239

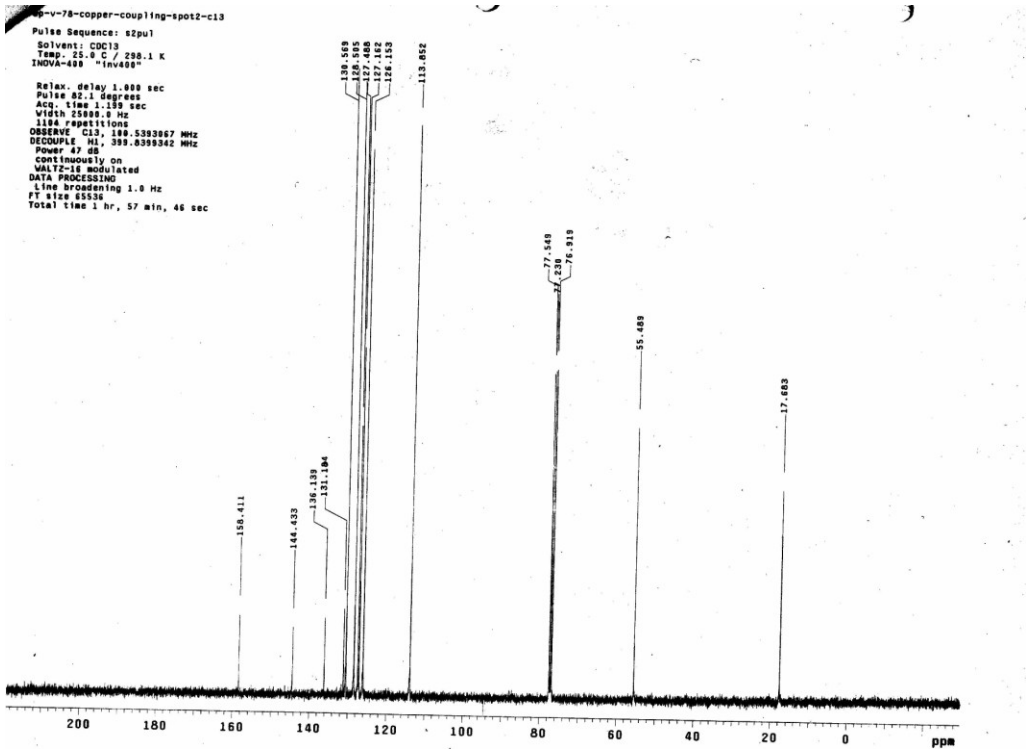

STATE UNIVERSITY OF NEW YORK
INOVA 400 MHz SN# S011617
PASVE-TUNE SN# P005133
1H SENSITIVITY
0.1% ETHYLBENZENE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
44 repetitions
OBSERVE H1, 399.8314094 MHz
DATA PROCESSING
FT size 131072
Total time 3 hr, 48 min, 20 sec
6.218
4.424
4.139
1.863
1.549
ppm
5.24
1.00
2.45
2.04
3.00

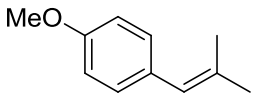

wp-v1-ss-cis-bromide-benzyl-protected-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
288 repetitions
OBSERVE C13, 100.5376747 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
144.473
138.288
128.552
127.844
127.646
77.541
77.238
76.911
76.259
75.022
72.385
22.038
ppm


MeO

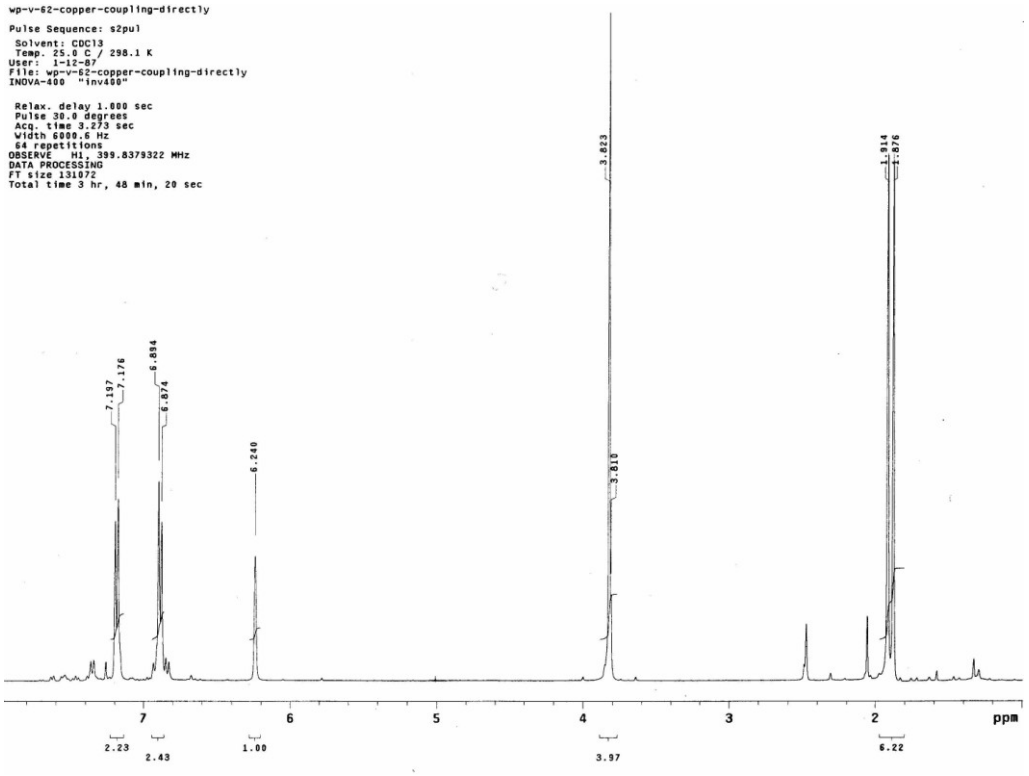
240

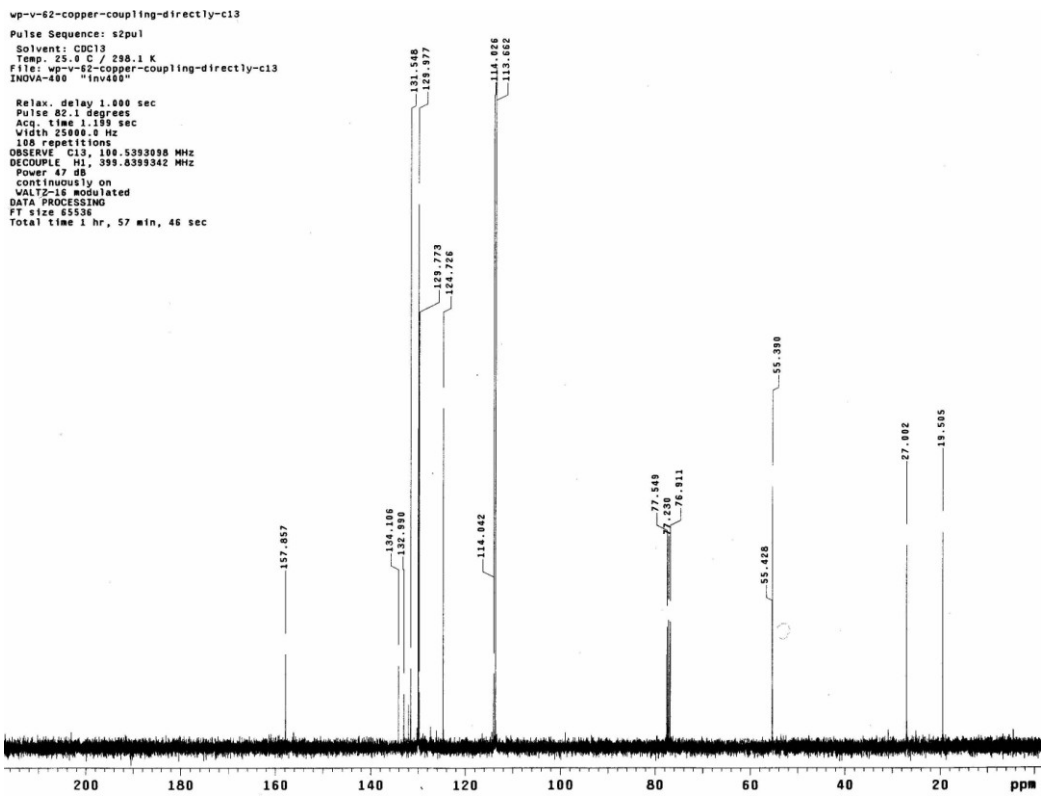

wp-v-78-copper-coupling-spot2
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
58 repetitions
OBSERVE H1, 399.8379328 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 58 sec
7.539
7.538
7.388
7.369
7.341
7.320
6.946
6.926
6.881
3.849
2.289
8
7
6
5
4
3
2
1
ppm
1.96
4.85
1.98
0.97
2.99
2.96

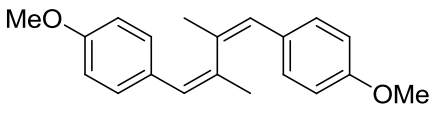

wp-v-78-copper-coupling-spot2-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1184 repetitions
OBSERVE C13, 100.5393867 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
158.411
144.433
136.139
131.184
130.569
128.595
127.488
127.152
126.153
113.852
77.549
77.230
76.910
55.489
17.683
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO

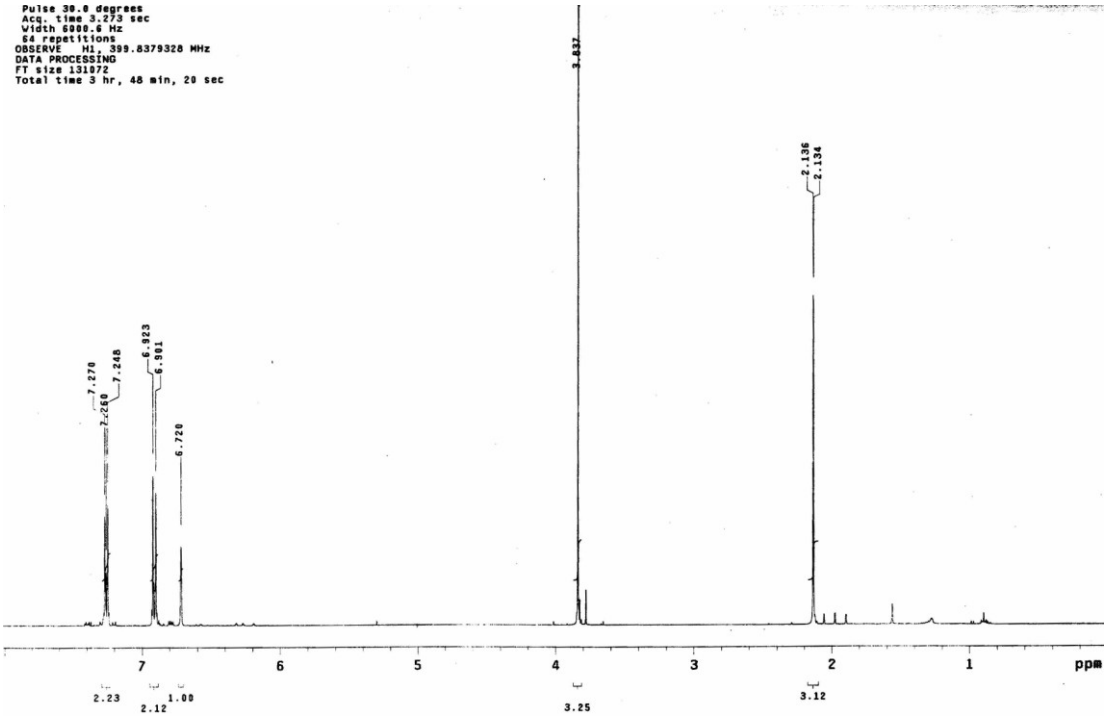
241

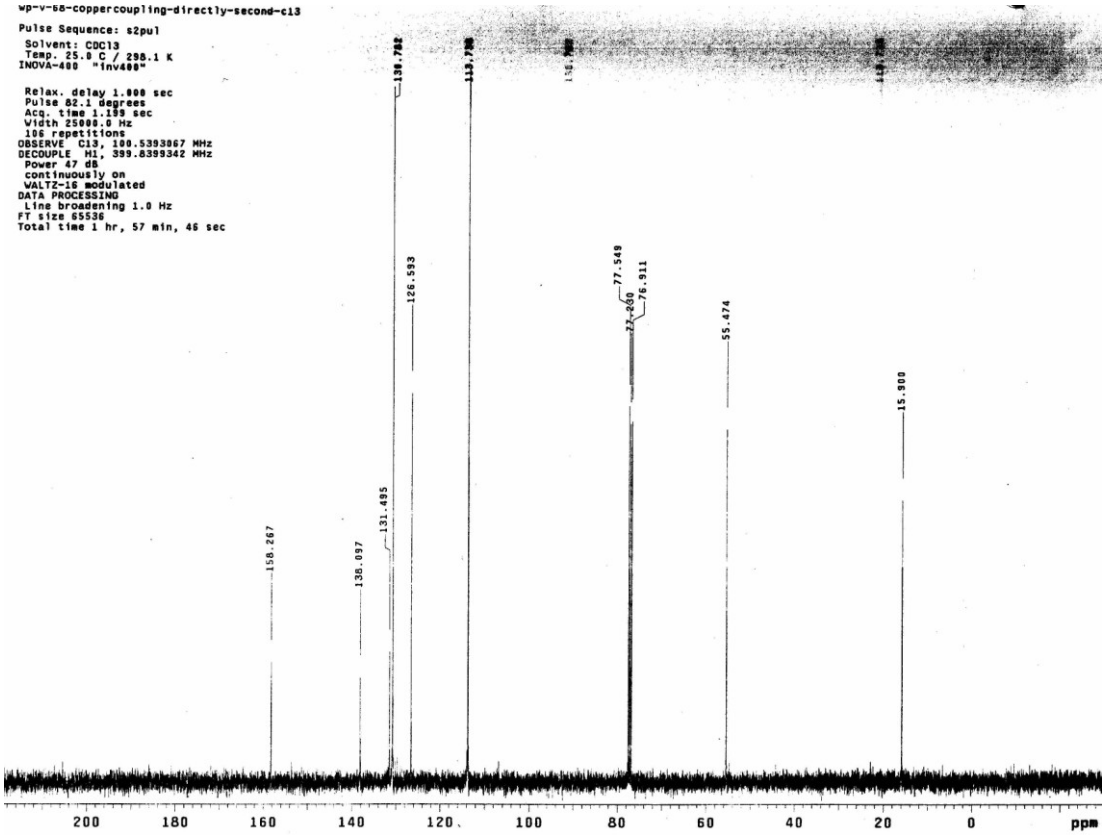

wp-v-62-copper-coupling-directly
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
File: wp-v-62-copper-coupling-directly
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
64 repetitions
OBSERVE H1, 399.8379322 MHz
DATA PROCESSING
FT size 131072
Total time 3 hr, 48 min, 20 sec
7.197
7.176
6.884
6.874
6.240
3.823
3.810
1.914
1.876
7
6
5
4
3
2
ppm
2.23
2.43
1.00
3.97
6.22

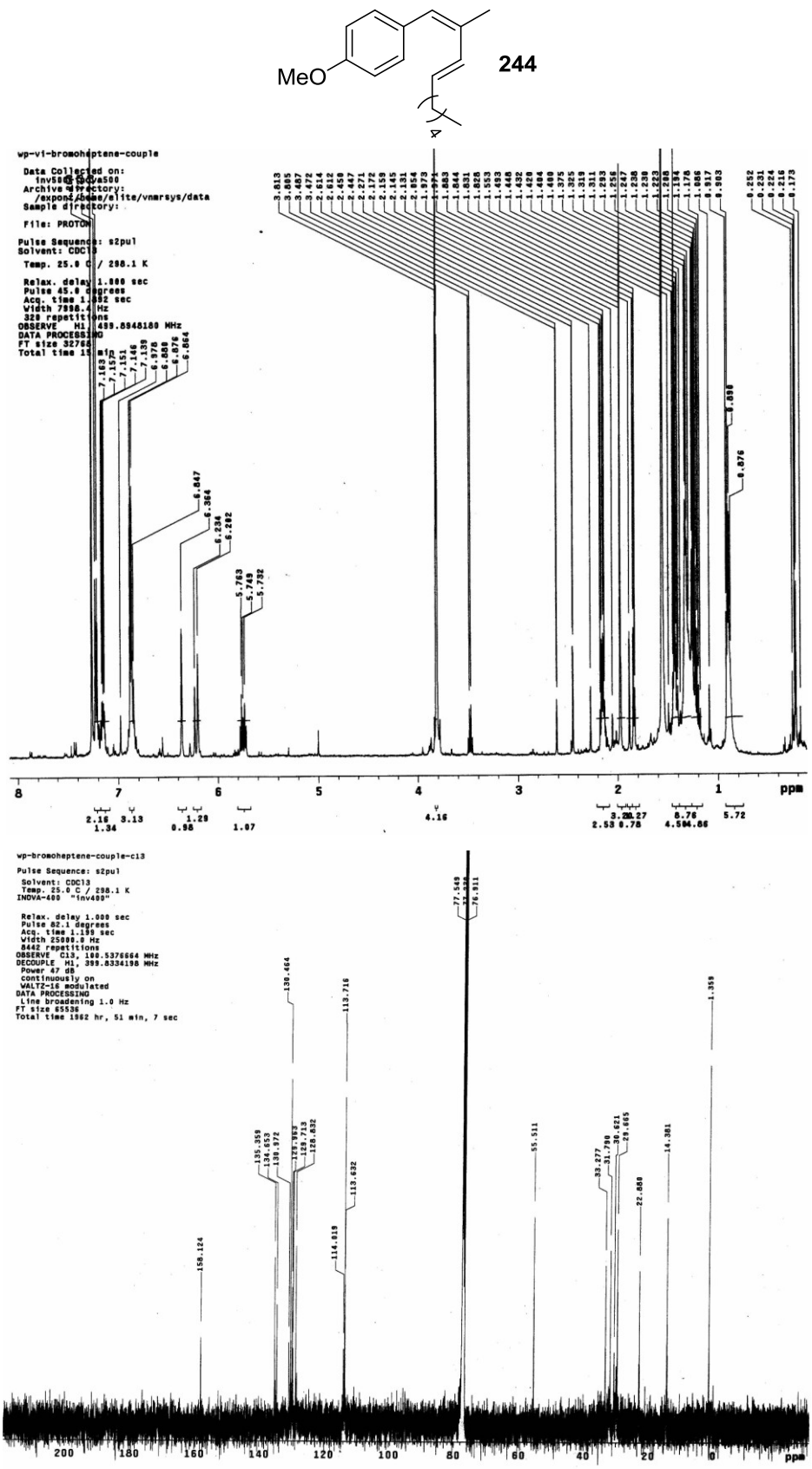

wp-v-62-copper-coupling-directly-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: wp-v-62-copper-coupling-directly-c13
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
108 repetitions
OBSERVE C13, 100.5393098 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
FT size 65536
Total time 1 hr, 57 min, 46 sec
157.857
134.106
132.990
131.548
129.977
129.773
124.726
114.042
114.026
113.662
77.549
77.230
76.911
55.390
55.428
27.002
19.585
200
180
160
140
120
100
80
60
40
20
ppm

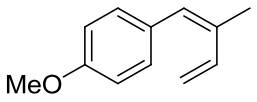

MeO
OMe

242

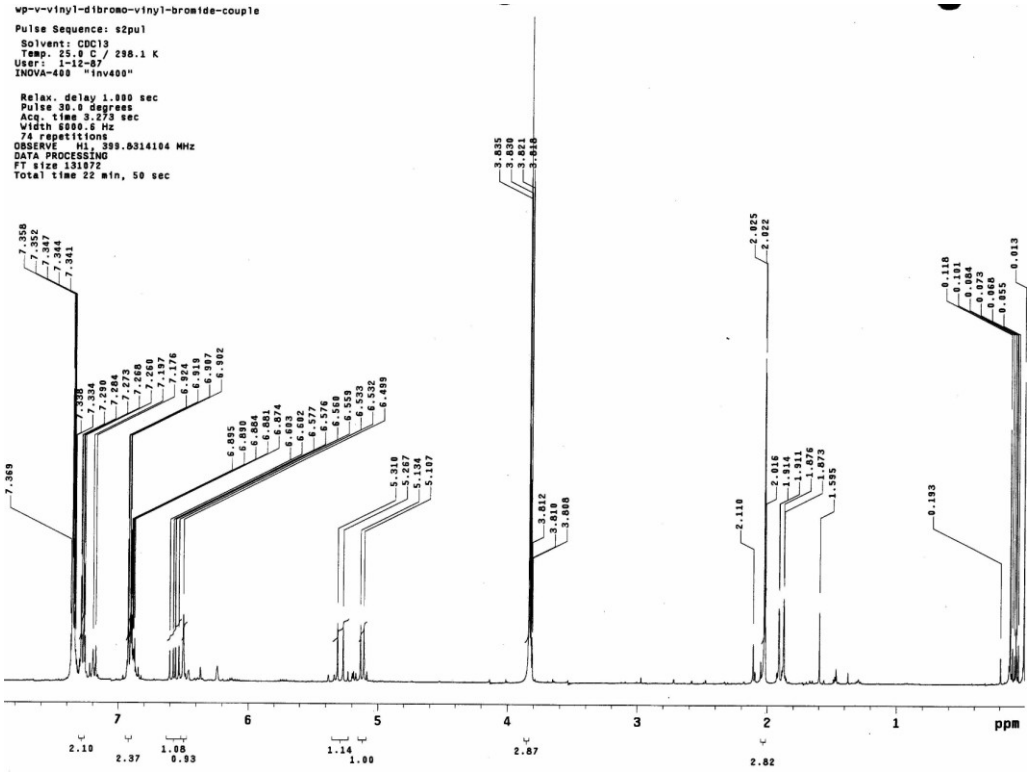

Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
64 repetitions
OBSERVE H1, 399.8379328 MHz
DATA PROCESSING
FT size 131072
Total time 3 hr, 48 min, 20 sec
7.270
7.260
7.248
6.923
6.901
6.720
3.837
2.136
2.134
2.23
2.12
1.00
3.25
3.12
ppm

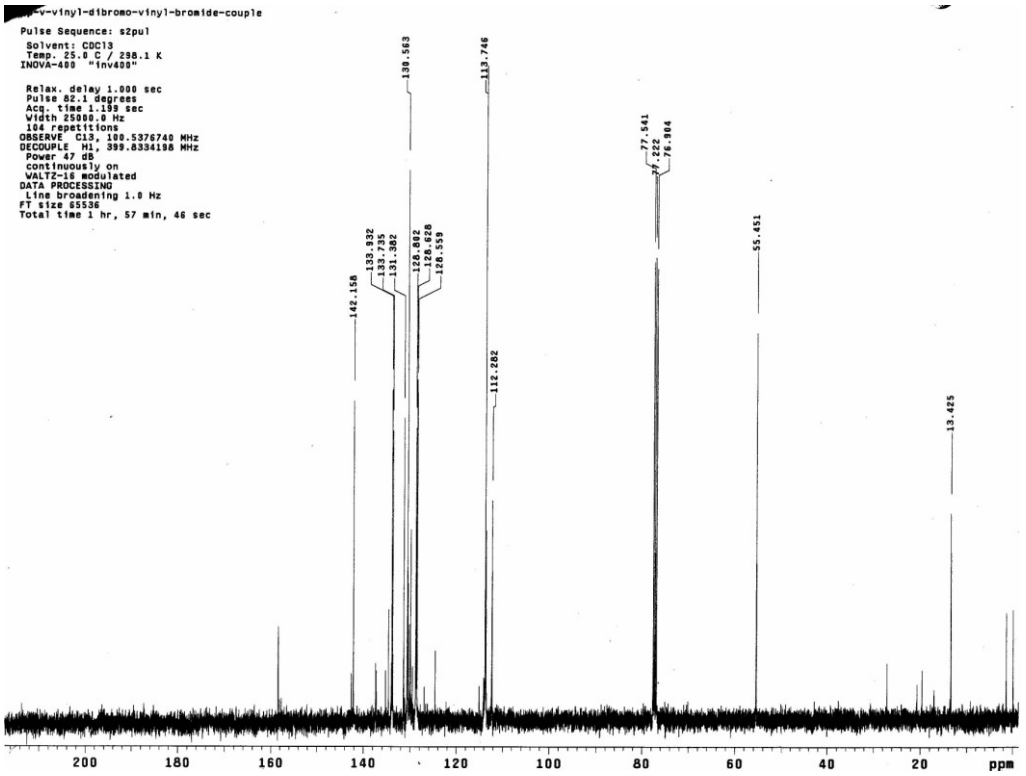

wp-v-58-coppercoupling-directly-second-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.139 sec
Width 25000.0 Hz
106 repetitions
OBSERVE C13, 100.5393867 MHz
DECOUPLE H1, 399.8399342 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
158.267
138.097
131.495
126.593
77.548
77.200
76.911
55.474
15.900
ppm

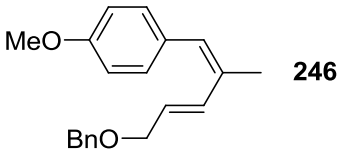

MeO
244
wp-vi-bromoheptene-couple
Data Collected on:
Archive directory:
/expont/dmae/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7986.4 Hz
32 repetitions
OBSERVE H1, 499.8948189 MHz
DATA PROCESSING
FT size 32768
Total time 1
wp-bromoheptene-couple-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
8442 repetitions
OBSERVE C13, 100.5376664 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1962 hr, 51 min, 7 sec
ppm


MeO

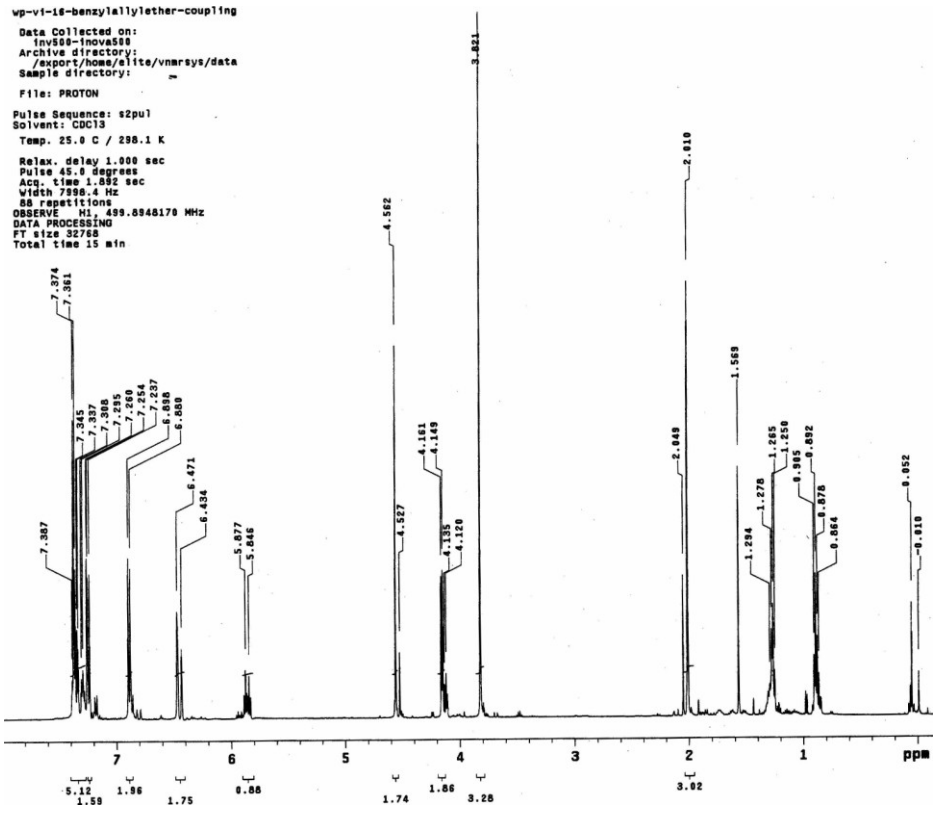
245

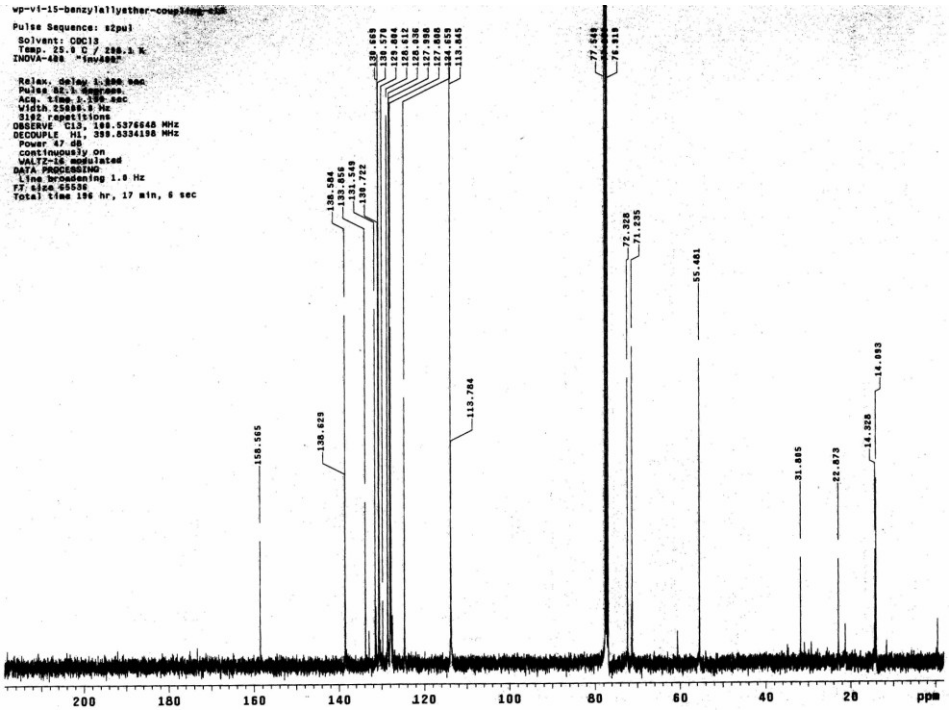

wp-v-vinyl-dibromo-vinyl-bromide-couple
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 5880.6 Hz
74 repetitions
OBSERVE H1, 399.8314104 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm

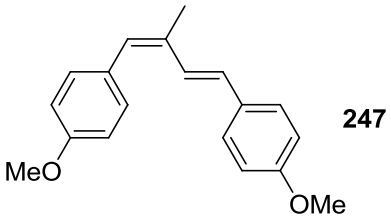

wp-v-vinyl-dibromo-vinyl-bromide-couple
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
104 repetitions
OBSERVE C13, 100.5376740 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


MeO
BnO

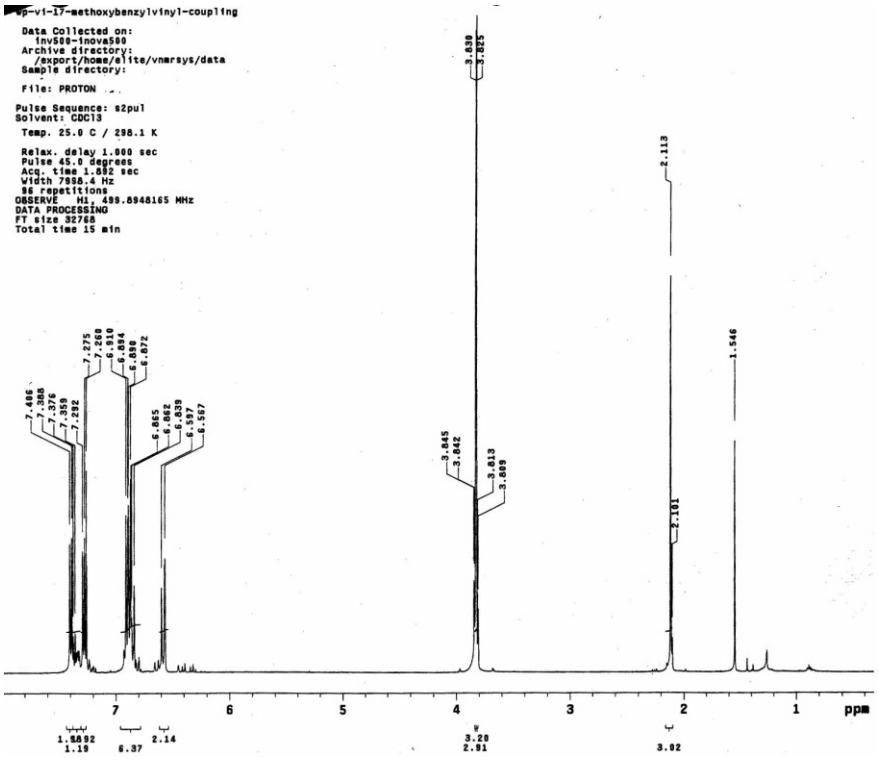
246

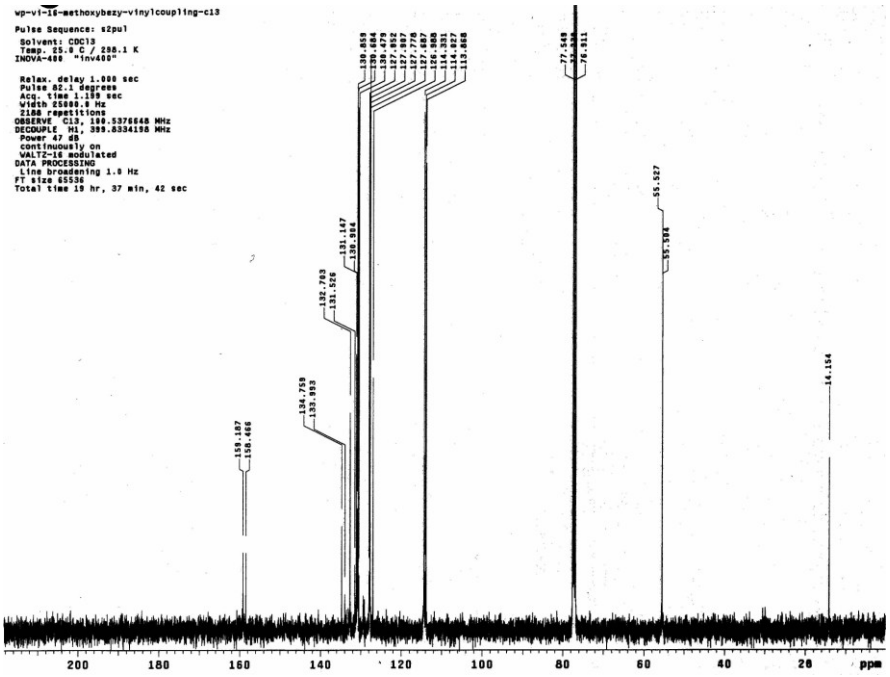

wp-vi-16-benzylallylether-coupling
Data Collected on:
inv500-inova500
Archive directory:
/export/home/alite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
88 repetitions
OBSERVE H1, 499.8848170 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
7.374
7.361
7.345
7.337
7.308
7.295
7.260
7.254
7.237
6.898
6.889
6.471
6.434
5.877
5.846
4.562
4.527
4.161
4.149
4.135
4.120
3.821
2.610
2.049
1.569
1.285
1.278
1.250
1.294
0.985
0.892
0.878
0.864
0.852
0.810
7.387
ppm

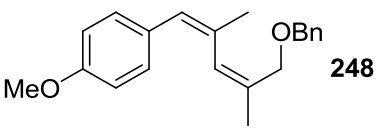

wp-vi-15-benzylallylether-coupling-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.196 sec
Width 25000.0 Hz
3102 repetitions
OBSERVE C13, 100.5376648 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 196 hr, 17 min, 6 sec
139.669
138.579
138.448
128.612
128.336
127.998
127.698
127.650
114.555
113.845
77.548
77.232
76.916
138.584
138.054
137.945
137.722
72.328
71.235
55.481
150.565
138.629
113.784
31.865
22.673
14.328
14.093
ppm


MeO
OMe

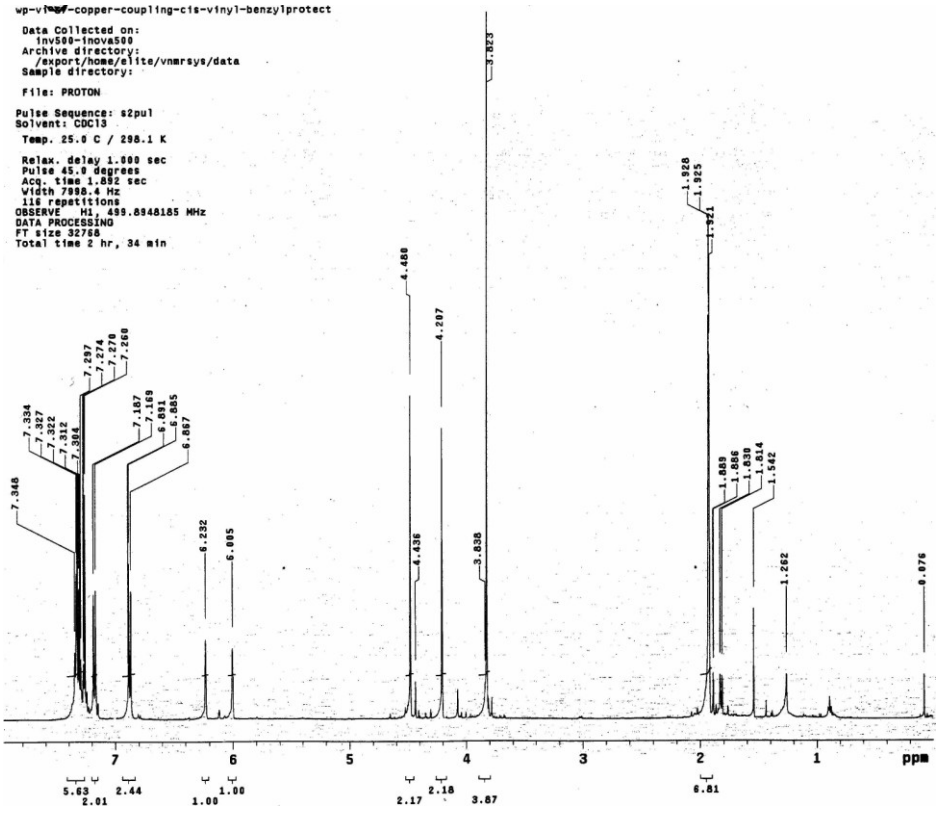
247

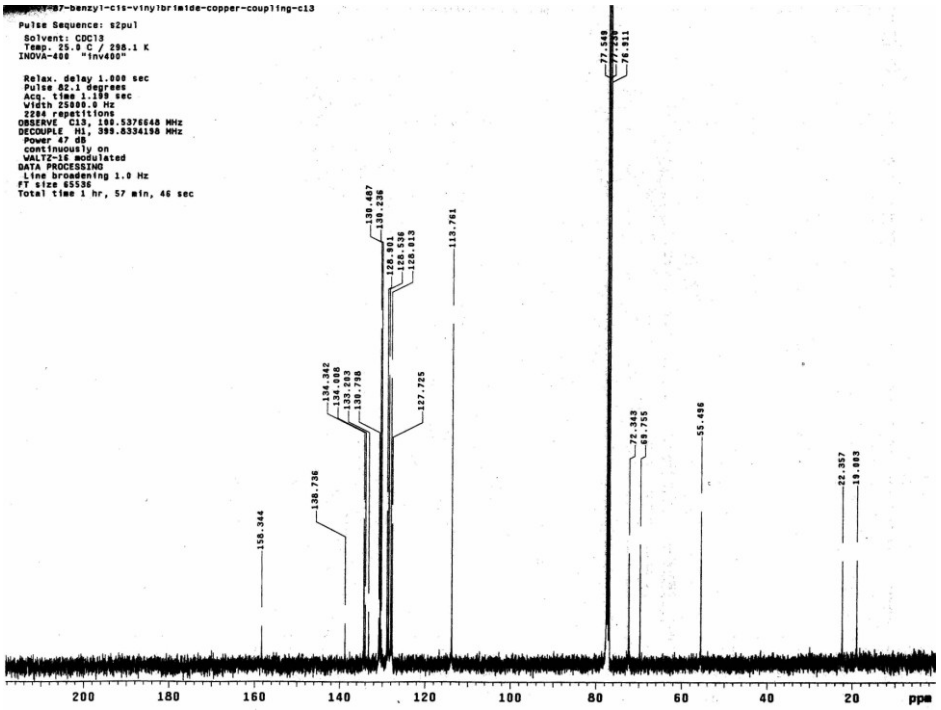

wp-vi-17-methoxybenzylvinyl-coupling
Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.852 sec
Width 7998.4 Hz
96 repetitions
OBSERVE H1, 499.8948165 MHz
DATA PROCESSING
FT size 32768
Total time 15 min
7.496
7.388
7.376
7.359
7.292
7.275
7.269
6.910
6.894
6.888
6.872
6.865
6.842
6.839
6.597
6.567
3.839
3.825
3.645
3.642
3.613
3.589
2.113
2.101
1.546
ppm
1.5892
1.19
6.37
2.14
3.20
2.91
3.02

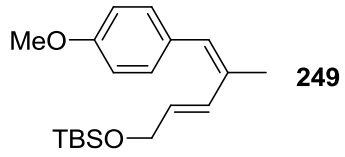

wp-vi-16-methoxybezy-vinylcoupling-c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2168 repetitions
OBSERVE C13, 100.5376648 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
159.187
158.466
134.758
133.993
130.783
131.526
131.147
130.984
130.859
130.684
130.479
127.892
127.805
127.778
127.687
127.568
114.331
114.027
113.868
77.548
77.316
76.911
55.527
55.384
14.154
ppm


OBn
MeO

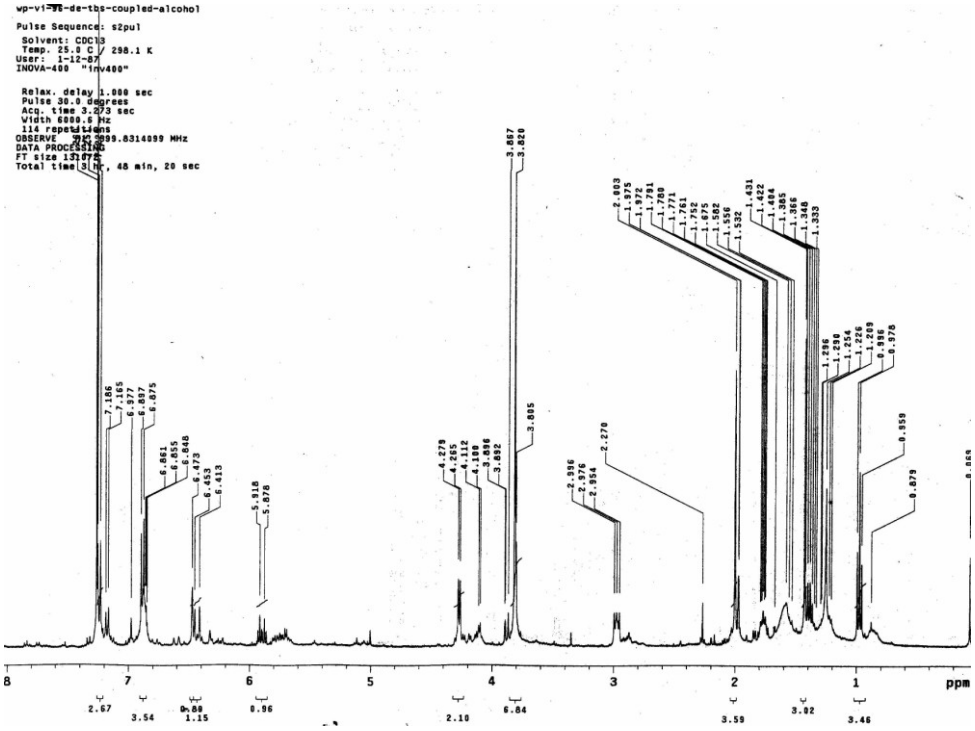
248

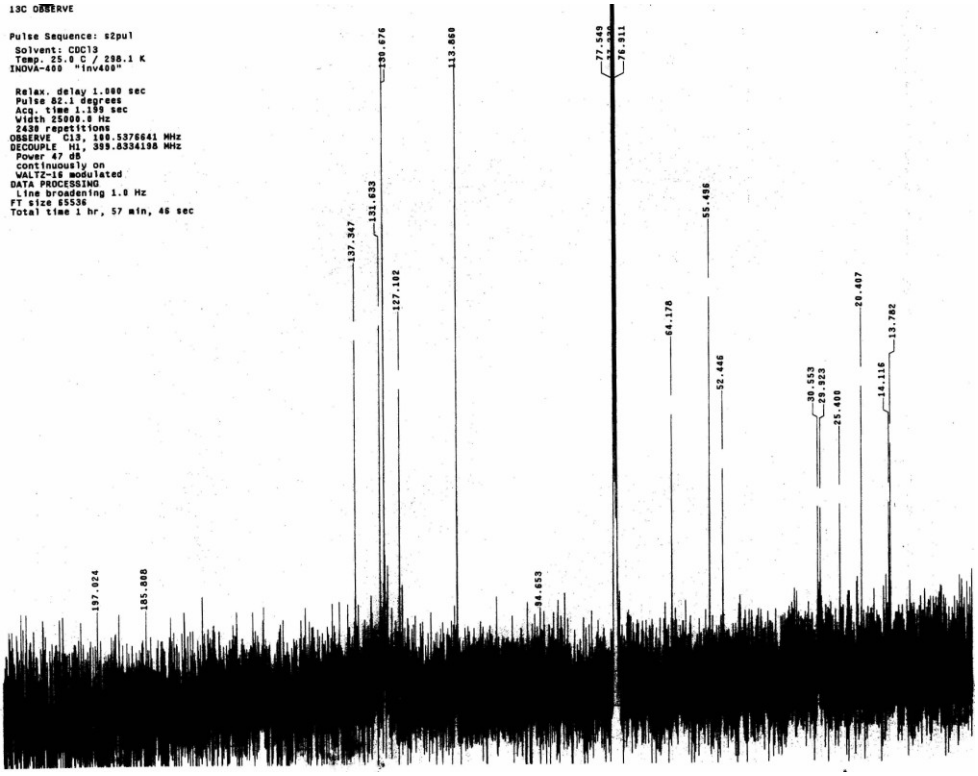

Data Collected on:
inv500-inova500
Archive directory:
/export/home/elite/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7998.4 Hz
116 repetitions
OBSERVE H1, 499.8848185 MHz
DATA PROCESSING
FT size 32768
Total time 2 hr, 34 min
ppm

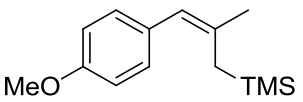

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
7264 repetitions
OBSERVE C13, 100.5376648 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm


MeO
TBSO

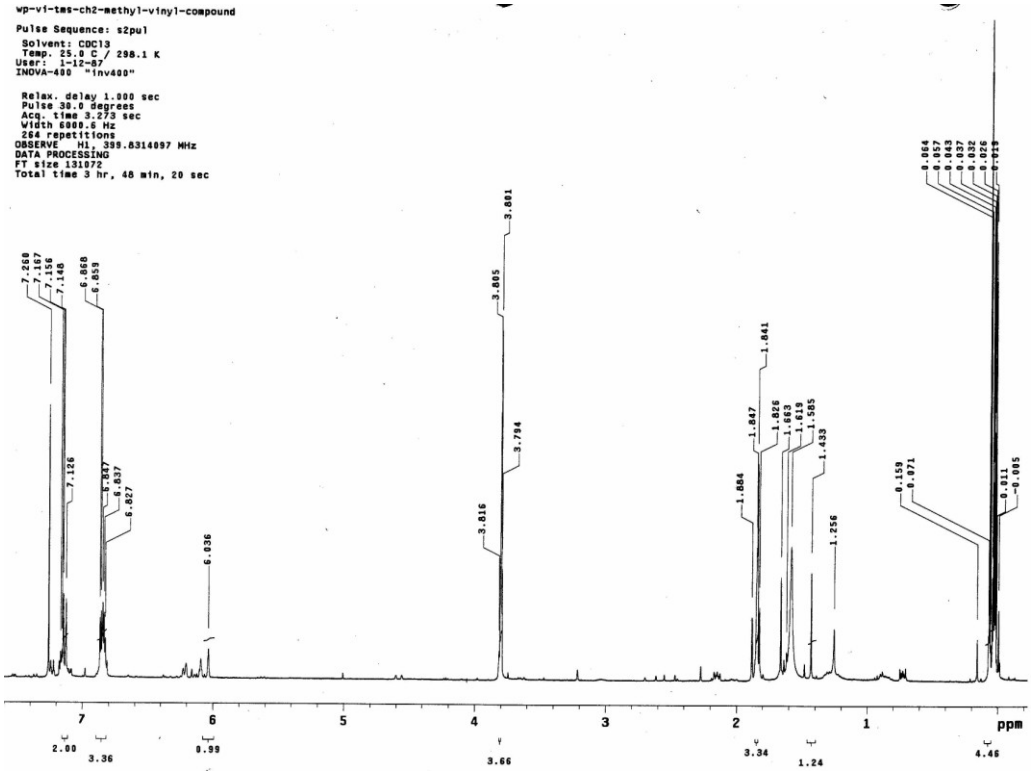
249

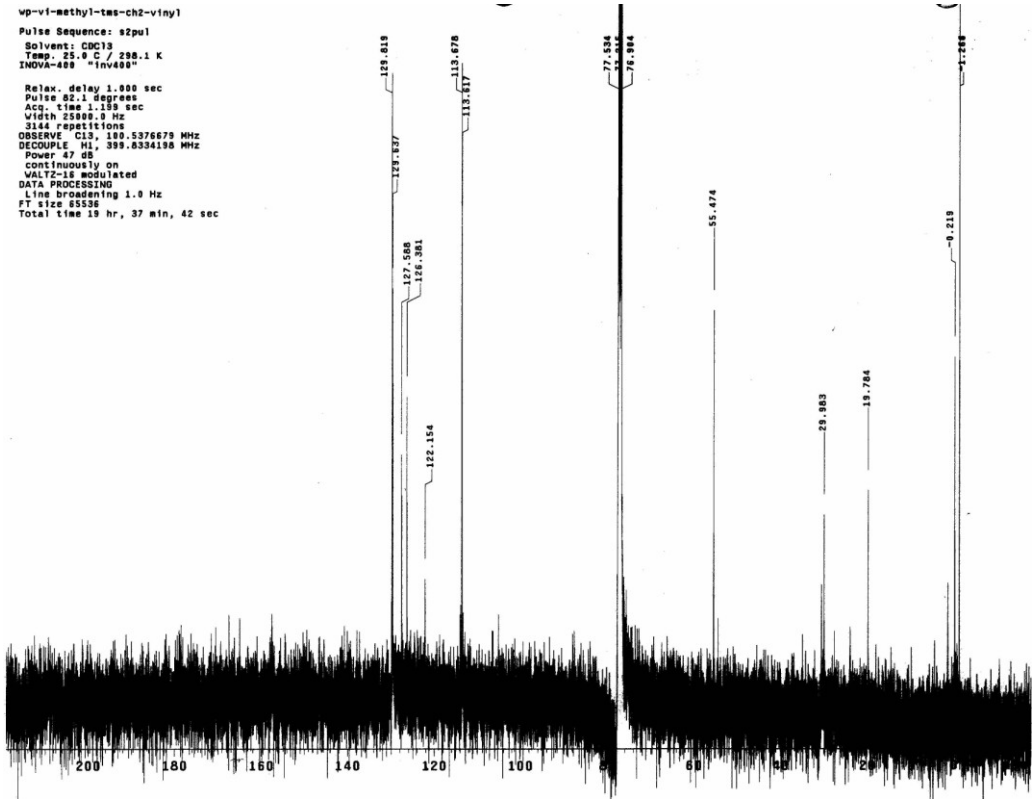

wp-vi-96-de-tbs-coupled-alcohol
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
114 repetitions
OBSERVE H1, 399.8314099 MHz
DATA PROCESSING
FT size 131072
Total time 9 hr, 48 min, 20 sec
ppm

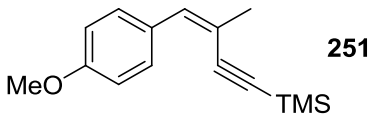

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
2430 repetitions
OBSERVE C13, 100.5376641 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec


MeO
TMS

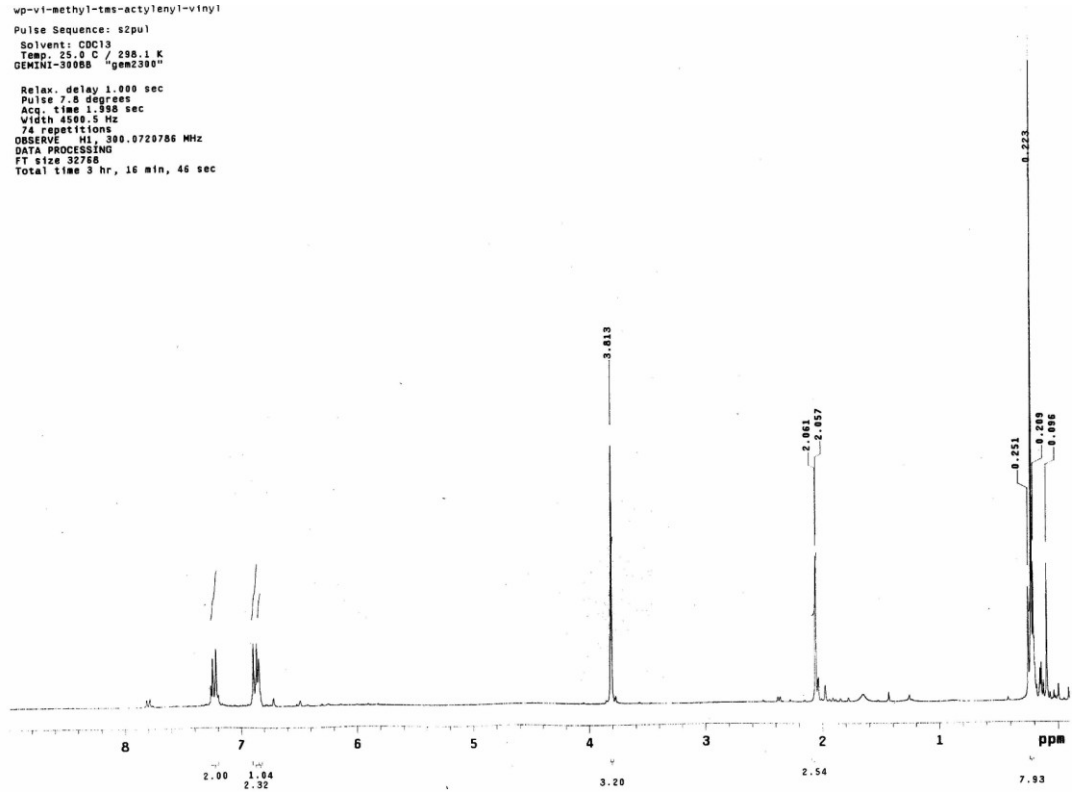
250

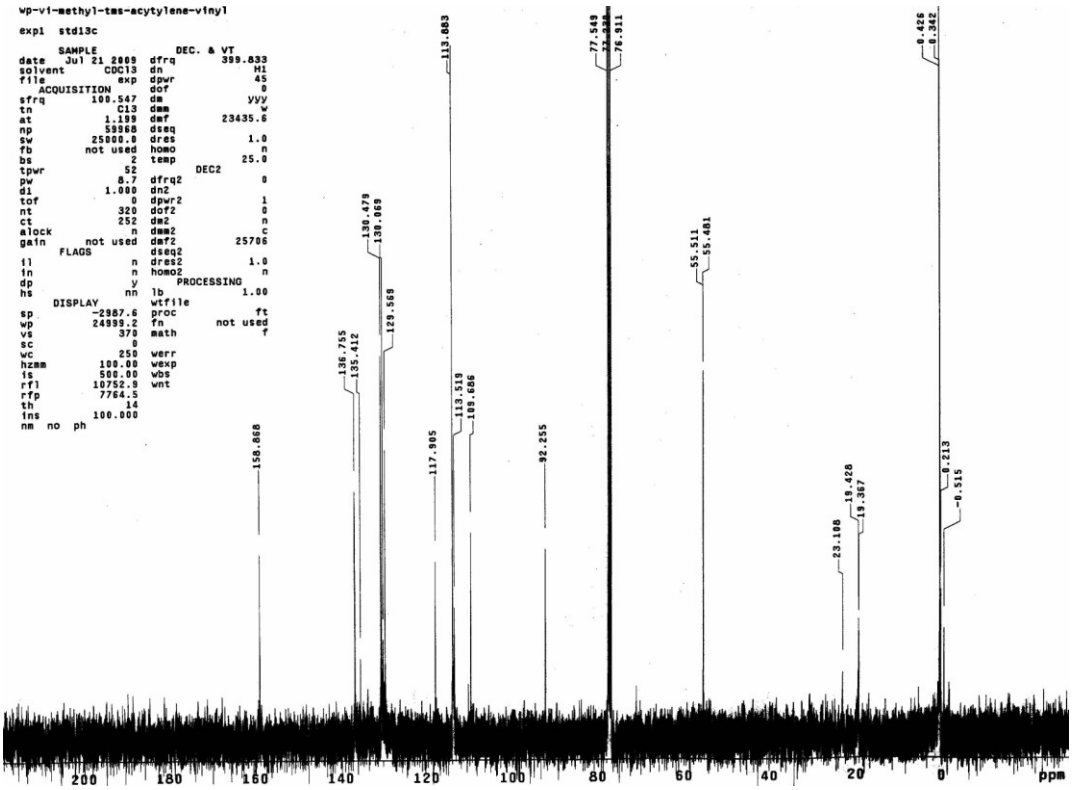

wp-vi-tms-ch2-methyl-vinyl-compound
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-87
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
264 repetitions
OBSERVE H1, 399.8314097 MHz
DATA PROCESSING
FT size 131072
Total time 3 hr, 48 min, 20 sec
7.269
7.167
7.156
7.148
6.868
6.859
7.126
6.847
6.837
6.827
6.036
3.891
3.885
3.794
3.816
1.841
1.847
1.826
1.585
1.433
1.256
1.684
0.159
0.071
0.011
-0.005
0.064
0.057
0.043
0.037
0.032
0.026
0.019
ppm
2.00
3.36
0.99
3.66
3.34
1.24
4.46

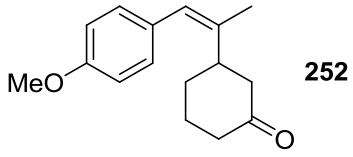

wp-vi-methyl-tms-ch2-vinyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.138 sec
Width 25000.0 Hz
3144 repetitions
OBSERVE C13, 100.5376679 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 19 hr, 37 min, 42 sec
129.619
129.037
127.568
126.381
122.154
113.678
113.617
77.534
77.216
76.904
55.474
29.983
19.784
-0.219
200
180
160
140
120
100
80
60
40
20


MeO
TMS

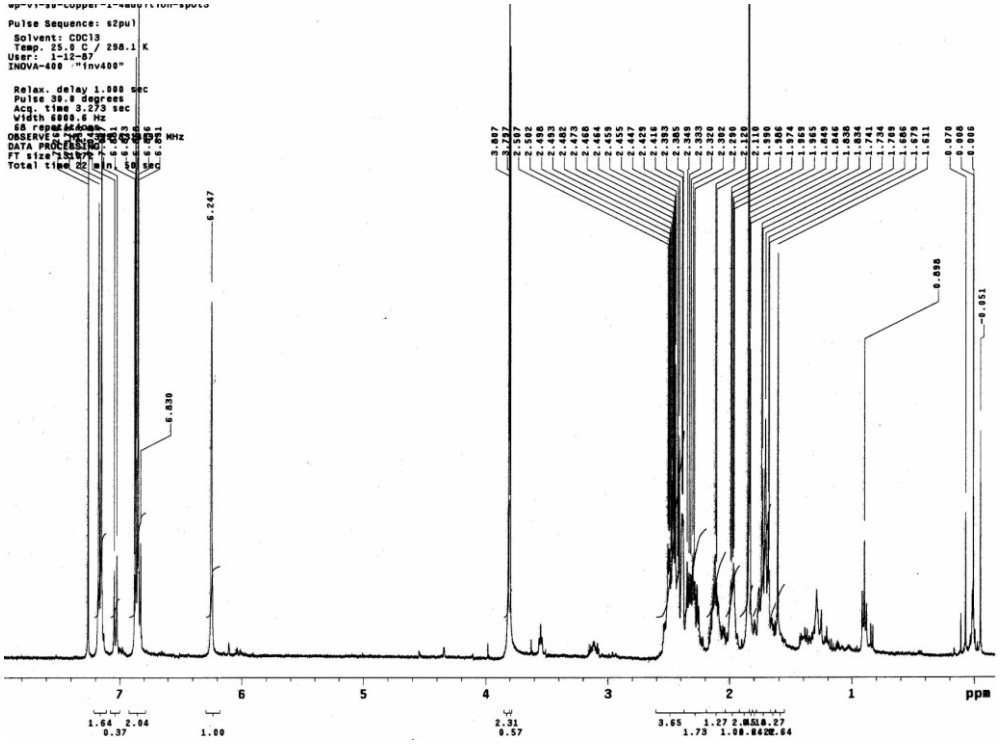
251

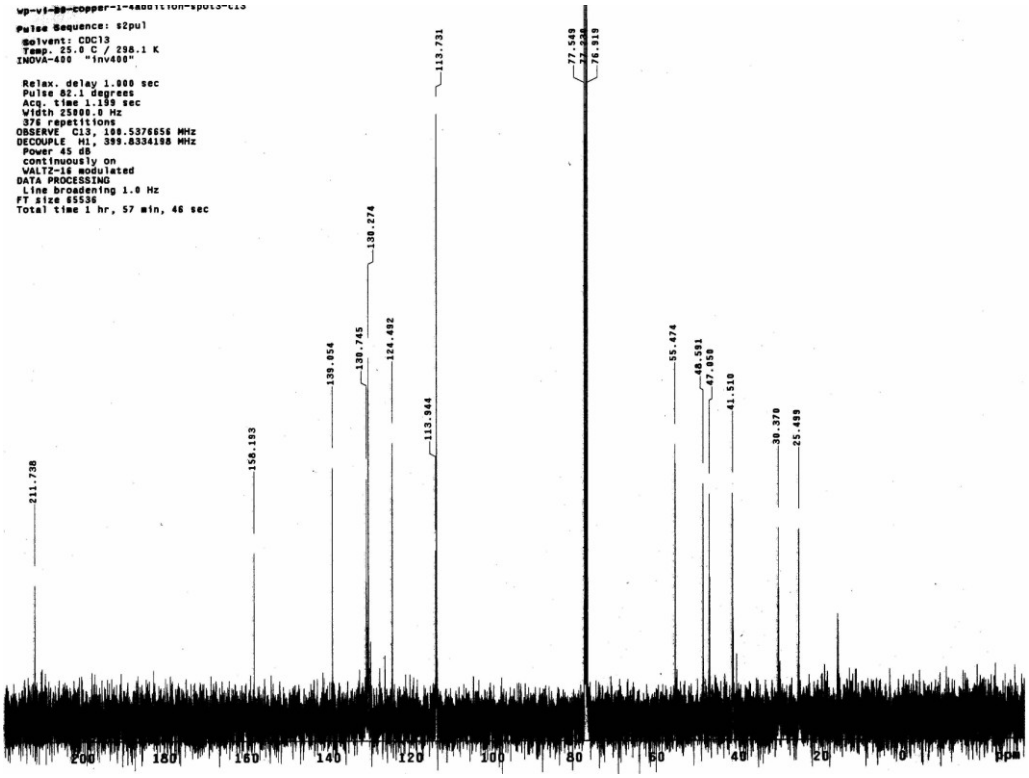

wp-vi-methyl-tms-actylenyl-vinyl
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
GEMINI-300BB "gem2300"
Relax. delay 1.000 sec
Pulse 7.8 degrees
Acq. time 1.998 sec
Width 4508.5 Hz
74 repetitions
OBSERVE H1, 300.0720786 MHz
DATA PROCESSING
FT size 32768
Total time 3 hr, 16 min, 46 sec
3.813
2.061
2.057
0.251
0.223
0.209
0.096
ppm
2.00
1.04
2.32
3.20
2.54
7.93

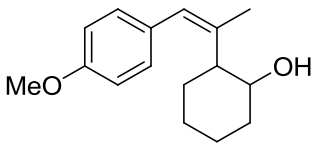

wp-vi-methyl-tms-acytylene-vinyl
expl std13c
SAMPLE
date Jul 21 2009
solvent CDCl3
file exp
ACQUISITION
sfrq 100.547
tn C13
at 1.199
np 59968
sw 25000.0
fb not used
bs 2
tpwr 52
pw 8.7
d1 1.000
tof 0
nt 320
ct 252
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -2987.6
wp 24999.2
vs 370
sc 0
wc 250
hzmm 100.00
is 500.00
rfl 10752.9
rfp 7764.5
th 14
ins 100.000
nm no ph
DEC. & VT
dfrq 399.833
dn H1
dpwr 45
dof 0
dm yyy
dmm w
dmf 23435.6
dseq
dres 1.0
homo n
temp 25.0
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 25706
dseq2
dres2 1.0
homo2 n
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
158.868
136.755
135.412
130.479
130.069
129.568
117.905
113.883
113.519
109.686
92.255
77.549
77.228
76.911
55.511
55.481
23.188
19.428
19.367
0.428
0.342
0.213
0.515
ppm


MeO
O

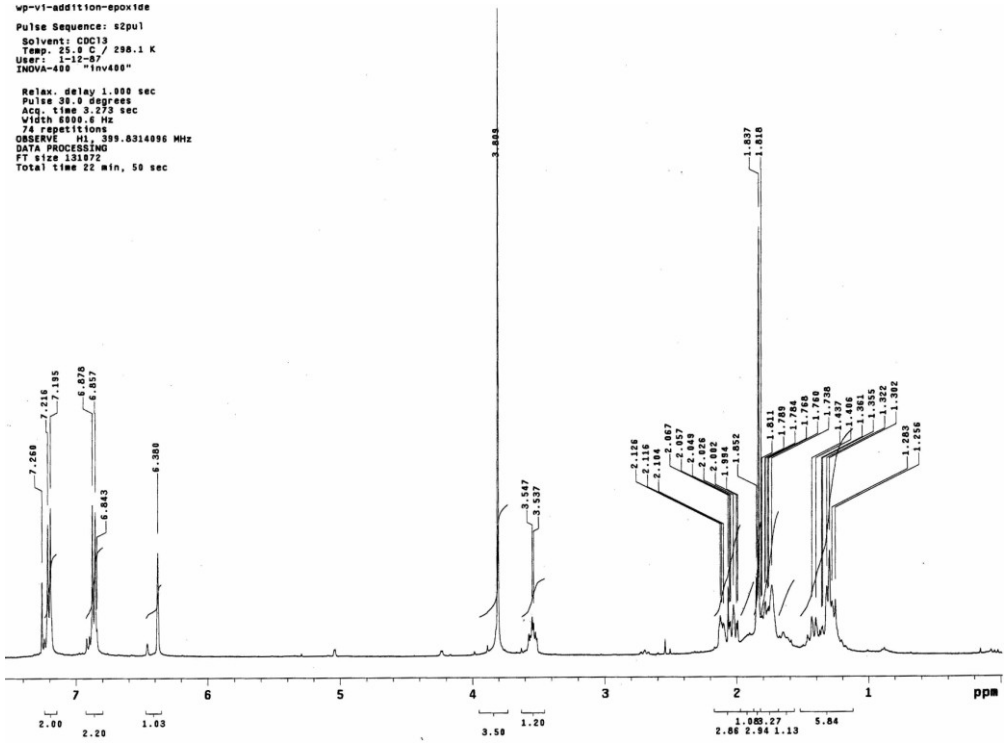
252

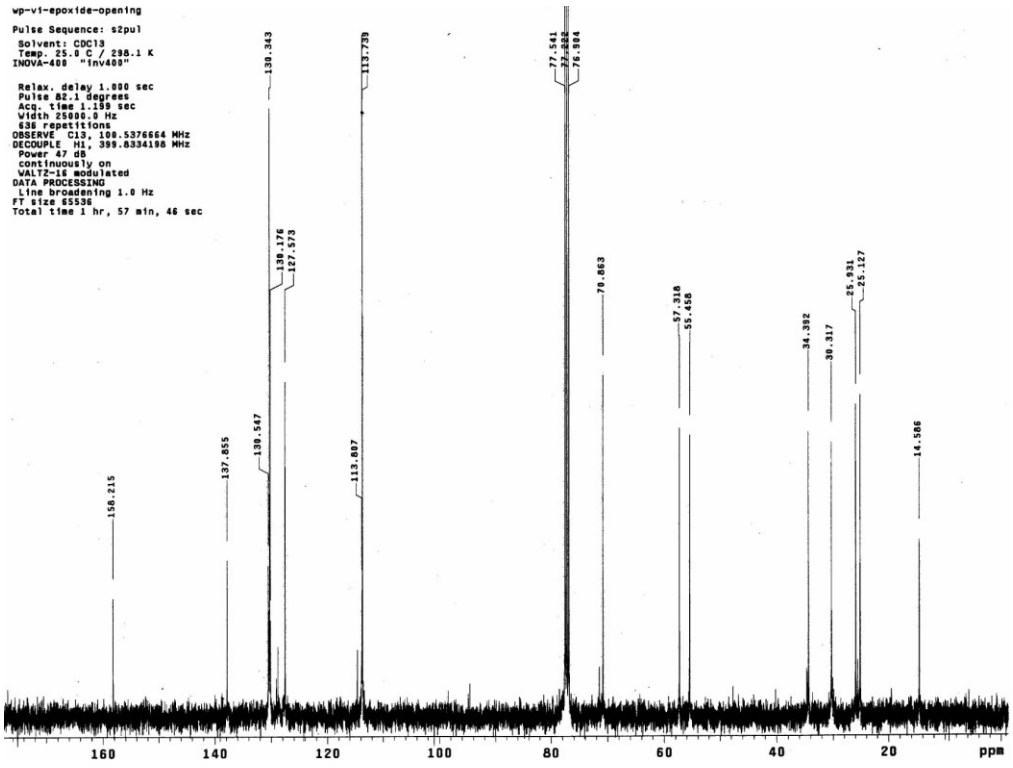

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
6.247
6.838
6.898
6.851
7
6
5
4
3
2
1
ppm
1.64
2.04
0.37
1.00
2.31
0.57
3.65
1.27
1.73
1.00
0.42
2.64


Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.139 sec
Width 25000.0 Hz
376 repetitions
OBSERVE C13, 100.5376656 MHz
DECOUPLE H1, 399.8334198 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
211.738
156.183
139.654
130.745
130.274
124.492
113.944
113.731
77.549
77.238
76.919
55.474
48.591
47.058
41.510
30.370
25.489
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
OH

253


wp-vi-addition-epoxide
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-12-07
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 3.273 sec
Width 6000.6 Hz
74 repetitions
OBSERVE H1, 399.8314096 MHz
DATA PROCESSING
FT size 131072
Total time 22 min, 50 sec
ppm


wp-vi-epoxide-opening
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "inv400"
Relax. delay 1.000 sec
Pulse 82.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
636 repetitions
OBSERVE C13, 100.5376664 MHz
DECOUPLE H1, 399.8334198 MHz
Power 47 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 57 min, 46 sec
ppm