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Synthetic Approaches to a Bis-Thiol based Arsenic Receptor and a Potential Pi-Stacking based Polyamide Foldamer

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Dana Castro

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Abstract of the Thesis

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Arsenic is a known harmful chemical, causing cancer and other adverse health effects if consumed in even modest amounts. Arsenic is found in drinking water at levels higher than deemed safe in many parts of the world. Current detection methods for arsenic in water have many limitations. A low-cost, safe, and efficient alternative would make arsenic detection simpler and human lives safer. As arsenic is known to have a high affinity to sulfur, the Drueckhammer group has designed a compound with two protruding thiol groups that may provide the basis for fluorescence-based detection. In this study, preliminary steps in the proposed synthesis of the designed arsenic receptor have been performed. An initial intermediate has been synthesized via reaction that forms a Grignard intermediate and generates benzyne *in situ*, followed by a Diels Alder reaction. An additional intermediate has also been synthesized via a Grubbs II-catalyzed reaction of the aforementioned Diels Alder product to yield a less strained alkene that may be more reactive in the subsequent steps. Various methods of double-bond ring cleavage and alkene oxidation have been explored. Ozonolysis seemed most promising in its efficiency and yield but unfortunately no success was seen with either starting material. Another approach of oxidative cleavage was explored with much success and has allowed the proposed synthetic pathway to progress further.

In conjunction with this project, additional work was performed on a separate project in hopes of developing a pi-stacking polyamide oligomer. A synthetic pathway toward nucleic acid mimics is being pursued by another student in the lab, and it is possible for this pathway to branch off into another synthesis to possibly develop a foldamer molecule. Foldamer chemistry strives to understand how proteins fold and maintain certain structures, and how that can be reproduced synthetically. Being able to synthetically replicate interactions such as protein folding is a thriving field as its success can be used for the cure and treatment of diseases, most notably, cancer.

Dedication Page

This thesis is dedicated to my friends and family for their never-ending support in my pursuit of knowledge.

Frontispiece

Table of Contents

List of Schemes/Figures

Acknowledgments

I am forever indebted to the mentorship and support offered by James Liao, James Marecek, Eleanor Castracane, Karlee Archer, and my departmental colleagues.

Chapter 1

A Synthetic Approach to a Bis-Thiol based Arsenic Receptor

Background

Arsenic Toxicity

Arsenic can be found in pesticides and herbicides, and is a by-product of the smelting industry. Today, arsenic is commonly used in the electronics industry: gallium arsenide and arsine gas are components of semiconductor devices.[1] Arsenic is widely accepted as a chemical harmful to human health if ever ingested or inhaled. Arsenic poisoning is referred to as arsenicosis and manifests itself initially with skin lesions and discoloration, stomach pain, nausea, and can escalate to partial paralysis and blindness. The prolonged exposure can then lead to even more serious conditions.[2] Arsenic is a known cause of cancer, diabetes, developmental and reproductive problems, neurological complications, and cardiovascular disease.[3] Arsenic-contaminated drinking water is a worldwide problem, especially affecting countries lacking sanitation while having a high abundance of arsenic in the land.[4] The World Health Organization (WHO) lists an estimated 35 to 77 million people out of the 125 million in Bangladesh alone are at risk for arsenic exposure due to contaminated drinking water.[5] As much as other countries are affected, exposure to arsenic has also been reported in America. More than 40 million Americans drink from private wells that access deep groundwater, and these often contain high levels of arsenic. According to the U.S. Geological Survey, as many as 3 million people are drinking water that would not meet the current Environmental Protection Agency (EPA) standard of 10 ppb. Arsenic is especially common throughout the western United States and there are hot spots in other states, such as Michigan's "thumb" region, as well as Maine.[6] In nature, arsenic is found most commonly as As(III) and As(V). As(III) is considered the most toxic form of arsenic and is predominately found in deep-well water, whereas As(V) is found in more shallow waters. The form arsenic takes is dependent upon the concentration of oxygen present.[7] Groundwater may contain elevated concentrations of arsenic due to agricultural runoff and improperly disposed waste chemicals.[1]

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[1] ATSDR Case Studies in Environmental Medicine: Arsenic Toxicity, **2009**, 11-13
[2] "US EPA." Chemical Contaminant Rules. US EPA, Web. **2016**.
[3] Hughes, M. et al. *Toxicological Sciences*, **2011**, *123*, (2), 305–332
[4] Nordstrom, *D. K. Science*, **2002**, *296*, 2143-2144
[5] *World Health Organization*, Water Sanitation Health: Arsenicosis
[6] *Center for Public Integrity*, "What to Do If Your Drinking Water Contains Arsenic", **2014**.
[7] *Oregon.gov*,"Drinking Water Program Fact Sheet: Recommendations for Arsenic Removal from Private Drinking Water Wells in Oregon"

Detection Methods

Currently, water is tested to make sure that arsenic levels are safe for human consumption. The World Health Organization (WHO) suggests the maximum arsenic concentration in drinking water is 10 ppb. In many areas, those levels are exceeded.[8] The Environmental Protection Agency (EPA) stated there is no safe level of the toxin but due to fears and backlash about the cost to maintain arsenic-free water, the agency set the standard at 10 ppb after it had previously been set to 50 ppb.[9] Current detection methods have many limitations. One inexpensive but less accurate detection method uses a test strip in water that converts the inorganic arsenic into arsine gas, which is then reduced to a compound that sticks to the test strip and generates a color change. Some recently developed test strips can detect from 0 ppb up to 500 ppb but their sensitivities in concentration detection are low where only broad ranges can be determined and rely on the human eye to compare to a color chart.[10] The testing chemicals, such as zinc powder[11], also reduce sulfides, which generate toxic hydrogen sulfide gas, in addition to the already dangerous arsine gas.[12] Another more expensive but accurate method of detection is Inductively Coupled Plasma Mass Spectrometry (ICP-MS).[13] This method is used to detect metals and some non-metals at concentrations at or below the single part per trillion. A drawback of this method is that arsenic gas is still produced during analysis and can escape the instrument, exposing those conducting the analysis to a risk of breathing in this toxic gas.[14] Another drawback is that it is not a method that would be simple to use on-site at a water source as it requires machinery that is not portable. It is seen that accurate and sensitive arsenic detection requires expensive and advanced laboratory equipment. Otherwise, cheaper alternatives cannot measure specific concentrations (just broad ranges) and use toxic chemicals as reagents.[10] Not every country or state even has the resources to employ these detection methods, so a cheap and safe alternative would not only replace methods

[8] ATSDR Case Studies in Environmental Medicine: Arsenic Toxicity, **2009**, 11-13
[9] *Center for Public Integrity*, "What to Do If Your Drinking Water Contains Arsenic", **2014**.
[10] *Manufactures Water Quality Testing and Analytical Instruments & Reagents*, "Arsenic Low Range Test Kit",
[11] *Water & Wastes Digest*, "Arsenic Testing the Easy Way"
[12] a) Das, J. et al., *Journal of Environmental Science and Health*, Part A: Toxic/Hazardous Substances and Environmental Engineering, **2014**, 49, (1), p108-115 b) Baghel, A. et al. *Analytical Sciences*, **2007**, 23
[13] Grosser, Z., *Water Technology* "The Challenge: Measure Arsenic in Drinking Water"
[14] *Perkin Elmer*, The 30-Minute Guide to ICP-MS, p. 1.

already being used, but introduce a viable, affordable option for those that don't currently have detection in place.

Experimental Design

The Drueckhammer group has designed a compound that would exploit arsenic's high affinity for thiol groups to aid in arsenic detection. As(III) is found in nature typically bound to sulfur in minerals such as realgar.[15] It has been seen that the As(III)-sulfur bond is much more resistant to hydrolysis than an As(III)-oxygen bond.[16]

One way As(III) compounds disrupt cellular activity is by binding two proximal thiol groups of a protein[15], as seen in **Figure 1**[16]. Molecular modeling with HostDesigner was performed by Professor Drueckhammer to determine that structure **a (Fig. 2)** would bind favorably to arsenic and was chosen for experimental synthesis by a previous student. **Scheme 1** was the initial proposed pathway to synthesizing a compound like **a**.

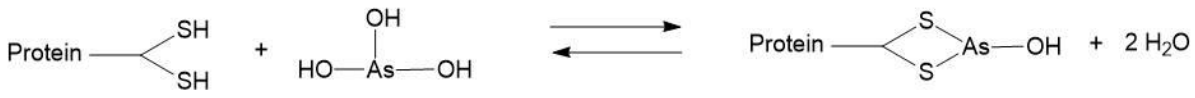


Figure 1: Protein-Arsenic(III) interaction

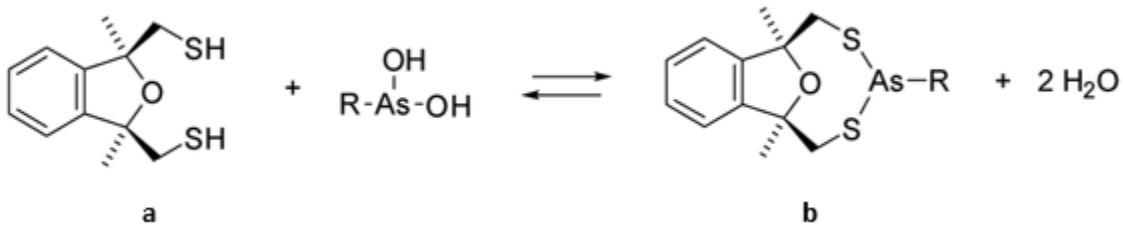


Figure 2: Basic receptor structure and its reaction with arsenic

[15] Hughes, M. et al. *Toxicological Sciences*, **2011**, 123, (2), 305–332

[16] *The National Academies Press*, "Chemistry and Analysis of Arsenic Species in Water and Biological Materials." Arsenic in Drinking Water: **1999,** 31-32.

Fluorescence Resonance Energy Transfer (FRET)

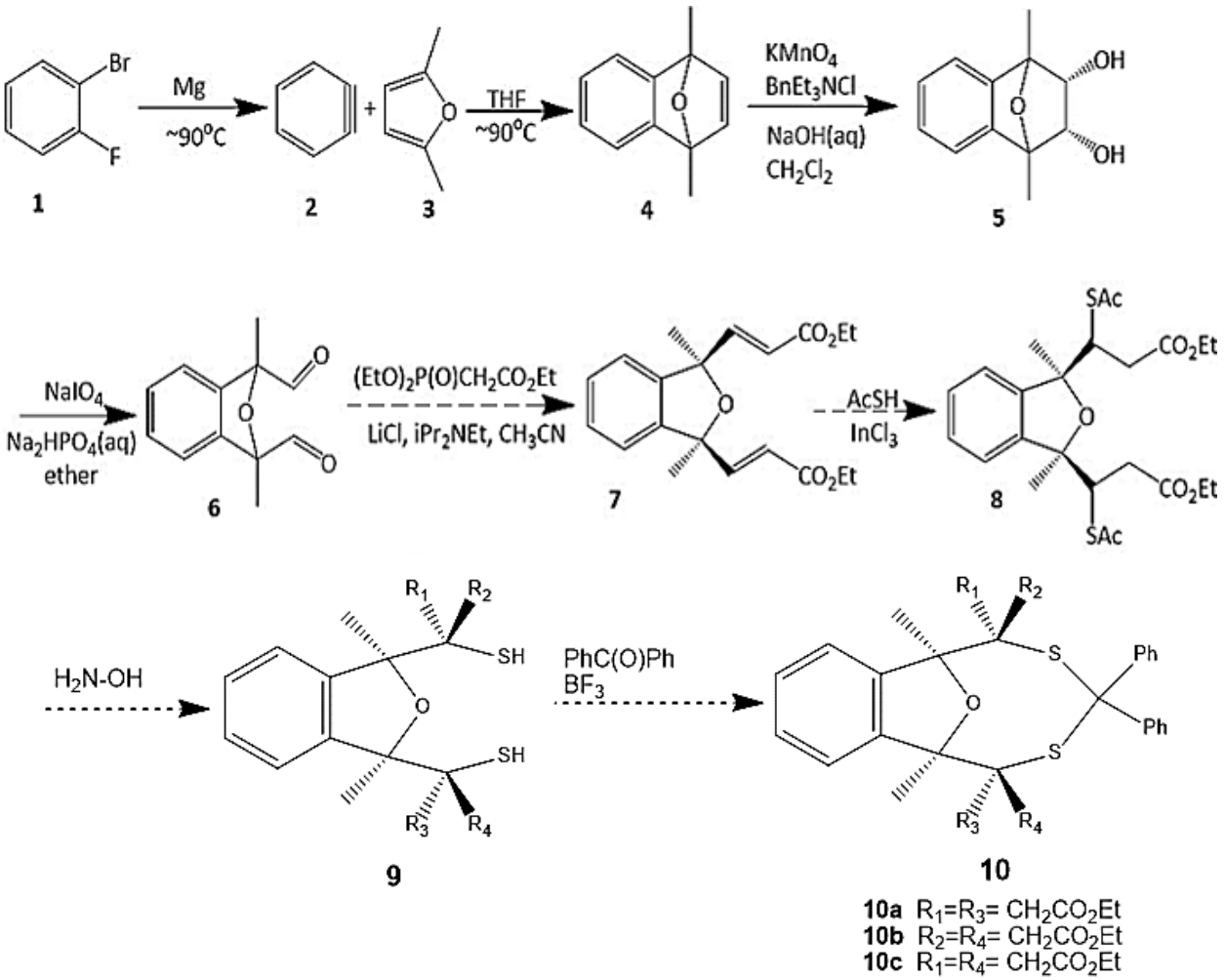
In FRET, a donor fluorophore is excited by light and if an acceptor fluorophore is close enough, the energy can be donated or transferred to the acceptor. The donor fluorophore's fluorescent intensity and excited state lifetime is reduced whereas the acceptor's emission intensity is increased. Förster proved that this process's efficiency (***E***) relies on the inverse sixth-distance between the donor and acceptor fluorophores, as shown by the below equation.

$$E = \frac{1}{1 + \left(\frac{R}{R_0}\right)^6}$$

R represents the separation distance between the donor and acceptor, while $\boldsymbol{R_0}$ represents the distance where the energy transfer is 50% efficient.[17] The range the energy transfer can typically take place over is about 10 nm (100 Å). Since the efficiency of this energy transfer is extremely sensitive to donor-acceptor separation, FRET can be a useful tool in following molecular interactions.[18] Since the distances referred to are rather small, FRET is better for use in following relative changes in distance and conformations rather than determining absolute distances. This is because ***E*** depends on the orientation of the dyes and that is typically poorly measured.[18]

The coupling of sulfur to arsenic in a compound like **b** may allow it to participate in fluorescence-based detection. Compound **a** has the thiol groups not held in a particular conformation, allowing them to rotate freely around their single bonds. Once bound to arsenic, as in **b**, the thiol groups would be locked in place, no longer free to rotate. This distance is what could be used as the source of detection using FRET once fluorophores are attached to each thiol position.

[17] Selvin, Paul. *Nature America*, "The renaissance of fluorescence resonance energy transfer", **2000,** *7(9)*, 730.
[18] *Olympus Microscopy Resource Center*, "Fluorescence Resonance Energy Transfer (FRET) Microscopy." **2012**



Scheme 1: First proposed synthesis of a bis-thiol-based arsenic receptor

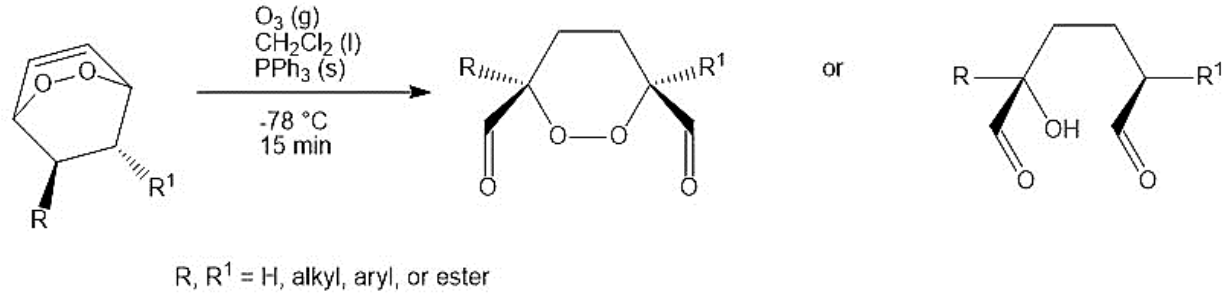
Results & Discussion

Scheme 1 is the proposed synthesis of a bis-thiol-based arsenic receptor. Generation of benzyne from 2-bromofluorobenzene, **1**, in the presence of 2,5-dimethylfuran, **3**, formed the known product **4** in a cycloaddition reaction. [19] This proceeded without much difficulty as long as the reaction system was dry. It was also found that sometimes the reaction begins noticeably during the dropwise addition step, but sometimes it does not visually seem to react. Yet, if the mixture is continually stirred at room temperature after the heating portion is complete, the reaction will

[19] Sawama, Y., et al.; *Synlett*. "Regioselective Gold-Catalyzed Allylative Ring Opening of 1,4-Epoxy-1,4-dihydronaphthalenes". **2010,** (14), 2151-2155.

eventually initiate over time with no noticeable loss in yield. This stirring can go on as long as a week with no detriment to the product, so it is a stable product.

By a previous student, **4** was converted to the glycol **5** using $KMnO_4$ under phase-transfer conditions.[20] This step is difficult in that **4** is very sensitive to acidic environments due to formation of a tertiary benzyllic/allylic cation and is also easily oxidized to 1,2-diacetyl benzene (**Fig. 7**). Only about 20% yield of the product **5** has been obtained in the past. The resulting glycol **5** could be converted to the dialdeyde **6** by oxidation with a periodate cleavage, but also suffered from low yields. However, another option was pursued which is an ozonolysis of **4** to directly yield **6**, given the success rates and convenience of ozonolysis experiments.[21] Ozonolysis reactions are one-pot and some reaction mixtures use simple solvents like acetone and water, making them easy to conduct, aside from the need for an ozone source. It is known as a relatively straightforward way of cleaving alkenes into aldehydes, and if this could be done on compound **4**, the proposed synthesis could be condensed. The first piece of literature found to employ required ozone to be bubbled into the desired alkene dissolved in dichloromethane (DCM) in a -78° C bath until the reaction mixture turned a pale blue, followed by a reductive workup with triphenylphosphine. The molecule reacted on in the literature is shown in **Figure 3**.[22]



R, R^1 = H, alkyl, aryl, or ester

Figure 3: Ozonolysis procedure by Cain et al

[20] Weber, W. P., et al; *Tetrahedron Letters*. "Improved Procedure for $KMNO_4$ Oxidation of Olefins to Cis-1,2-Glycols by Use of Phase Transfer Catalysis. **1972,** (48), 4907-&.
[21] Veysoglu, T.; Mitscher, L.; Swayze, J.; *Communications,"*A Convenient Method for the Control of Selective Ozonizations of Olefins". **1980,** 87.
[22] Cain, N. et al; *J. Org. Chem.*, **2012,** *77*, 3808-3819.

The pale blue color indicates excess unreacted ozone is present, which in turn means the alkene starting material has fully reacted.[23] The H-NMR spectrum of this reaction done on compound **4** gave no shifts in the aldehyde region and the aromatic region came back noisy as well as a mixture of peaks upfield. While this experiment was being done, another literature procedure was found that used an easy solvent mixture of 95% acetone in water and did not require reductive workup to yield an aldehyde and used an added indicator to show when the reaction has gone to completion. The molecule reacted on in the literature is shown in **Figure 4** [24].

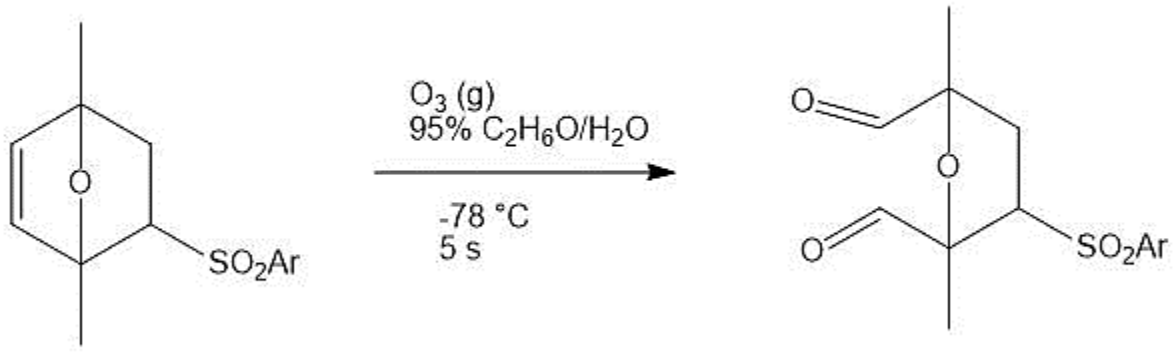


Figure 4: Ozonolysis procedure by Benjamin et al

This procedure was more attractive so further ozonolysis experiments were carried out using this procedure. At first, the lab did not have the Sudan Red III indicator required, but the literature also reported that their reaction times were about 60 seconds, so an experiment was attempted without the indicator to see how the reaction would progress. The HNMR spectrum for this experiment showed a very small peak in the aldehyde region, gave a messy aromatic region, and did seem to show the presence of methyl groups. It was concluded that starting material remained so the reaction did not go to completion in 60 seconds. The next reactions should then be done with the indicator to make sure the reaction goes to completion. Sudan Red III reacts with ozone a lot more slowly than with the desired alkene starting material and once that alkene is completely consumed only then will ozone completely react with the indicator, as seen when the red color disappears.[25]

[23] Research Group, ADT, et al; *J. Appl. Chem.,* **2015,** *4(5),* 1308-1312.
[24] Benjamin, N.; Martin, S.; *Org. Lett.,***2011,** *13(3),* 450-453.
[25] Veysoglu, T.; Mitscher, L.; Swayze, J.; *Communications*,"A Convenient Method for the Control of Selective Ozonizations of Olefins". **1980,** *87.*

When indicator was added to the reaction mixture of compound **4**, it turned a clear, blood red. After about two minutes of pumping ozone gas into the stirring reaction mixture, the color disappeared and the mixture was removed from the -78 °C bath. HNMR showed a slight peak in the aldehyde region with a messy aromatic region and a possible methyl peak. A spectrum of the Sudan Red III indicator was taken to see the chemical shifts of the indicator itself. The indicator does have a peak in the same region the methyl shift would be that characterizes the hydrogens neighboring the nitrogens as seen in the structure of Sudan Red III in **Figure 5**. There are also lots of resolved peaks in the aromatic region that aren't obviously present in the spectrum of the reaction product so it was unclear as to whether this was starting material still present, Sudan Red III present, or a mixture of both.

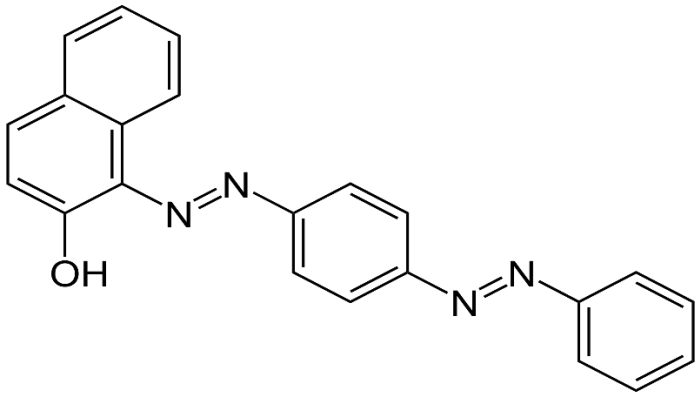


Figure 5: Sudan Red III indicator structure[26]

Since these reactions were unsuccessful, one possible reason is that the double bond is very stable and unreactive-- maybe if it were an alkene not in a ring, then it would more easily cleave. In this case, a Grubbs II-catalyzed olefin metathesis of **4** was considered. This would yield two non-cyclic alkenes that ozonolysis could target, as seen in **Figure 6**[27].

[26] *Chemical Land 21,* Sudan III MSDS, *http*://www.chemicalland21.com/specialtychem/finechem/SUDAN%20III.htm
[27] Finnegan, D.; Seigal, B.; Snapper, M.; *Org. Lett.*, **2006**, *8(12),* 2603-2606.

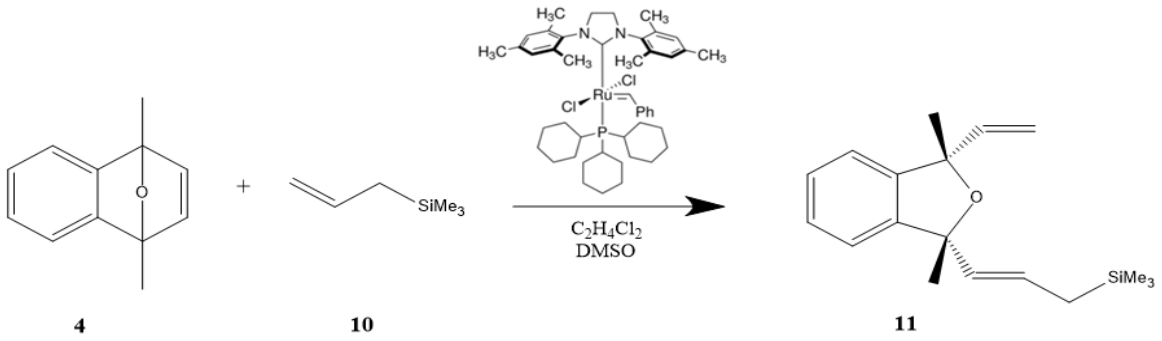


Figure 6: Grubbs II-catalyzed olefin metathesis of **4**

This reaction proceeded easily with no major changes from the literature procedure.[30] Monitoring by TLC gave a reaction time of about 4 hours. It was unknown whether the allyltrimethylsilane group would add twice and yield a symmetrical molecule but HNMR revealed that the allyltrimethylsilane group only added once and the other carbon contained a terminal alkene. This compound might respond better to ozonolysis than the cyclic alkene did. The next attempt was the Benjamin ozonolysis procedure on compound **11**. For this experiment, it took about 8 minutes until the indicator color disappeared. After removing the mixture from the ozonolysis setup to remove the solvent by rotoevaporation as done in every trial so far, the red indicator color seemed to reappear. It was unclear as to whether there may have been some undissolved indicator on the flask that made its way into the reaction mixture or if the indicator somehow reverted back to its unreacted state. HNMR of the crude product was very dilute and only showed solvent peaks. A separation with DCM and water was done to remove any aqueous soluble impurities and solvents. HNMR analysis of the washed organic layer still only showed solvent peaks as though no qualitative amount of either starting material or reacted starting material was present. Since this reaction showed indicator color after the reaction, it was worth repeating. In the next attempt, the indicator color disappeared in about 2 minutes—much shorter than the previous attempt. One drawback of ozonolysis, though, is the machine must be fully warmed up before it successfully pumps ozone, so there is a chance that even though it was on and pumping for a certain amount of time, it does not necessarily mean that ozone was being pumped through once the stopwatch began. HNMR of this product showed a desired aldehyde peak, peaks in the aromatic region, and peaks in the methyl region but the spectrum is noisy enough where purification was required to fully confirm the identity of the resulting compound. As such, the product mixture was loaded onto a

column for flash chromatography using a gradient of 5-30% ethyl acetate in hexanes. The first few fractions were colored as though they contained indicator, and remaining fractions did not spot on TLC so they needed to be concentrated before they could be characterized by TLC. Once concentrated, spots were able to be seen, and did not match the spotting pattern of compound **11** so conducting HNMR analysis would give more information on those fractions. Each fraction that spotted only showed solvent peaks. Even combining all of the fractions that spotted for one spectrum did not contain enough material to yield signal. There is a possibility that the ozonolysis reaction yielded o-diacetyl benzene, a further undesired oxidation of **4**. The chemical shifts of o-diacetyl benzene agree with the shifts in the spectrum but also contain solvent peaks so this is not definite.

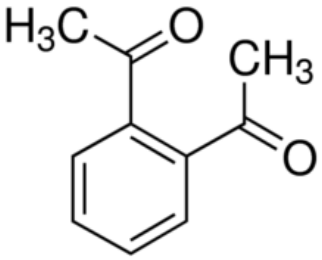


Figure 7: o-diacetylbenzene; δ_H 2.54 (s, 6H, CH_3), 7.56, 7.57 (m, 4H, ArH)[28]

Since none of these spectra were helpful, performing this experiment on a larger scale was considered; this would eliminate the problem of concentration of product being too small for analysis. The starting material **11** was scaled up from using 0.10 mmol to using 1 mmol. The reaction proceeded smoothly with an ozone pump time of about 5 minutes. The HNMR of the crude showed a very slight peak in the aldehyde region but still small. After the separation with DCM and water, the dried organic layer seemed to show some crystal formation. These crystals were isolated for HNMR and still gave the same spectrum as before the separation. An attempt was made to combine all previously synthesized residues from the same procedure to get a spectrum that would be concentrated enough but there was still no evidence of desired product nor any starting material. After reevaluating the experiments, it was thought that even though crude **4** and **11** were mostly pure, they should be purified prior to further experimentation. Once each

[28] Spectral Database for Organic Compounds, o-diacetylbenzene, http://sdbs.db.aist.go.jp/sdbs/cgi-bin/direct_frame_top.cgi

compound was successfully purified by flash column chromatography, the ozonolysis was attempted again. The ozonolysis of purified **4** gave a spectrum that was noisy upfield, in the aromatic region, and barely had a peak in the aldehyde region, which was also surrounded by bumpy signal. This spectrum resembled what was seen when the ozonolysis was done on impure **4**. Repeating the experiment on pure **11** gave interesting results. The indicator color did not disappear at all, and pumping ozone was allowed to go for 35 minutes. Typically, under 10 minutes was the expected time necessary. The HNMR of this product gave a less noisy spectrum as compared to the ozonolysis of purified **4** with a more intense peak in the aldehyde region, peak in the aromatic region, and peak in the methyl region along with other trace peaks. After separation by DCM and water, more solvent peaks were present as well as peaks in the aromatic region, but the aldehyde had competing intensity. To determine if this was really the desired product, it was purified by flash column chromatography. The gold column stained purple by the end of the separation. A sequence of fractions that spotted on TLC were collected for HNMR analysis and showed a very slight peak in the aldehyde region but nowhere near the intensity that was seen in the crude. To try and flush the column of any other components left behind, 100% acetone was eluted through. HNMR of all the acetone fractions only showed overpowering solvent and an occasional blip in the aldehyde region but nothing more. Even combining all of these acetone fractions gave no evidence of desired product. At this point, ozonolysis was considered insufficient for cleaving **4** or **11** to the dialdehyde. Experimental conditions may provide insight as to why ozonolysis did not work on either reagent. Both the potassium permanganate oxidation and ozonolysis reactions involve biphasic reaction mixtures. For potassium permanganate, the oxidant was in a solid/aqueous phase whereas the reactant was in an organic phase. This makes stirring and agitation essential for both phases to ensure constant interaction for a reaction to be successful. For ozonolysis, there are gas and liquid phases, and the ozone has to move to the liquid phase to ensure reaction success. These strict reaction conditions may explain their failure, although does not explain the lack of evidence of starting material in some cases. In this regard, other methods of cleaving to the dialdehyde were explored. Osmium tetroxide has been commonly used in catalyzed dihydroxylations. Since the goal was still to minimize the steps taken to get to the dialdehyde, a procedure was found that gave a one-pot synthesis from the alkene **4** straight to the aldehyde. This procedure (as seen in **Figure 8**) noted the effectiveness of 2,6-lutidine or pyridine

for speeding up reaction times and providing better yields than typical osmium tetroxide-catalyzed oxidations.[29]

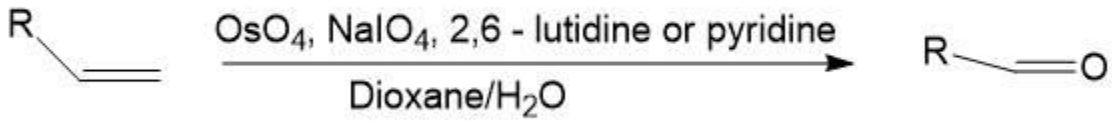
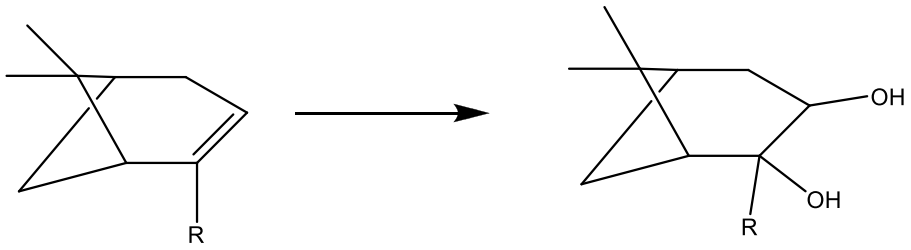


Figure 8: Procedure for the osmium tetroxide oxidative cleavage

Since osmium tetroxide is a dangerous, volatile chemical, potassium osmate was used as a source of osmium tetroxide instead. This experiment was first performed on **4** with hopes of condensing the synthesis as the ozonolysis would have if it were successful. 2,6-lutidine was used rather than pyridine because the reference noted that most extensively. This paper mostly did reactions on terminal alkenes and reaction times took up to 24 hours. Conducting the reaction on **4** was monitored by both TLC and NMR. The first attempt was done for about 22 hours, and starting material was recovered with no evidence of reaction initiation. Repeating this reaction with a longer running time of about 74 hours gave full consumption of starting material and a small peak that could have possibly been desired product but after purification, no evidence of desired product was seen. Using the same logic as was used for ozonolysis, this reaction was repeated but using **11** as the starting material instead. Following the same reaction procedure previously, this experiment was conducted for a reaction time of 72 hours. This gave no evidence of reaction, only unreacted starting material. Then, an attempt was made using pyridine instead of 2,6-lutidine as the literature recommends it as well. This reaction was also allowed to proceed for 72 hours. Based on HNMR, a reaction did occur that most closely resembles that the disubstituted alkene underwent oxidation while the terminal alkene did not. The reaction also took long to initiate (beyond 40 hours), but once it began, the rate increased. Based on these results, it is unknown as to whether both alkenes would have cleaved if given more time, or if this is a selective reaction. The pH could attribute to the rate phenomenon—sodium periodate is acidic and protonates pyridine, leaving behind basic sodium iodate to deprotonate pyridine. As the pH increases, the rate may start to pick up. With this consideration, the same reaction was conducted with double the amount of pyridine

[29] Yu, W.; Mei. Y.; Kang, Y.; Hua, Z., Jin, Z.; *Org. Lett.*, **2004**, *6(19)*, 3217-3219.

to hopefully speed up the initiation of this reaction. After about 48 hours of stirring, HNMR showed only starting material was present. Yet, after allowing to stir for about 8 days, crude HNMR shows convincing evidence that **6** was obtained. This experiment was put to the side because in the meantime, another reference was found that does a dihydroxylation with osmium tetroxide with a cyclic alkene.[30]



R= $CH_2CH_2OCH_2OCH_2CH_2OCH_3$

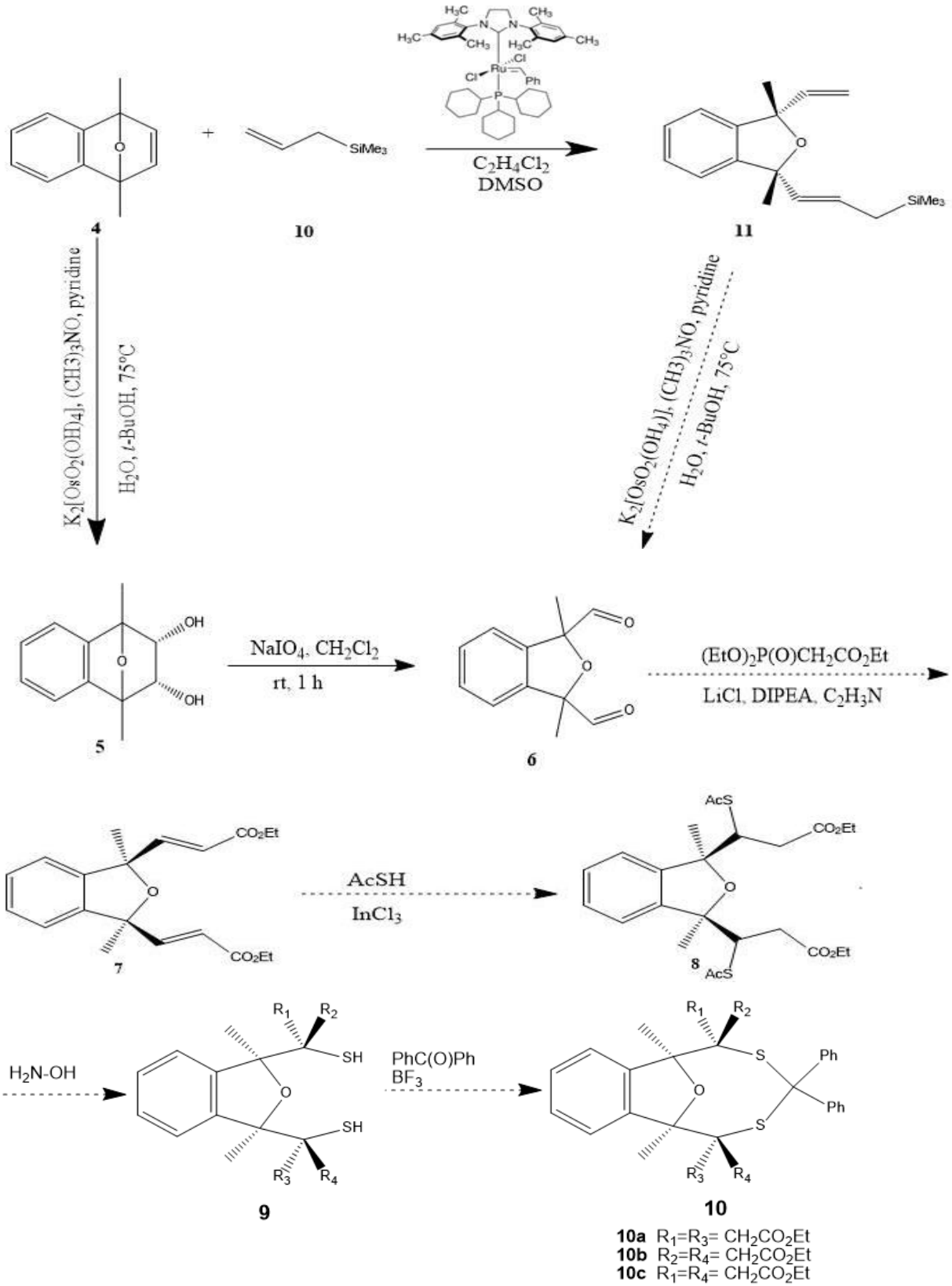
R= $CH_2CH_2OCH_3$

R=CH_3

Figure 9: Literature molecule for osmium tetroxide dihydroxylation

Even though this would not yield a dialdehyde, it would save the Grubbs-catalyzed step if it was successful. The literature procedure was closely followed with the exception of the use of potassium osmate instead of osmium tetroxide. This swap also required the catalyst to be suspended in water instead of t-BuOH since potassium osmate is not soluble in t-BuOH. This reaction proceeded for about 28 hours and yielded a very clean NMR spectrum without need for purification. The desired diol was successfully synthesized with a crude yield of 75%. Previous oxidation steps, such as the potassium permanganate oxidation, gave very low yields. This experimental procedure itself is also simpler than potassium permanganate oxidation and yields a very pure product without purification. This success eliminates the need for the Grubbs-catalyzed reaction and allowed the synthetic pathway to progress into forming the dialdehyde as shown in the modified **Scheme 2.**

[30] Ray, R.; Matteson, D.; *Tet. Lett.*, **1980**, *21*, 449-450.



Scheme 2: Modified approach to obtaining the dialdehyde

A former group member performed a very small-scale sodium periodate cleavage to the dialdehyde on the diol in the past and achieved an impure product in low yield, so another procedure was found. This procedure was an improved version of sodium periodate cleavage. It called for the adsorption of sodium periodate onto silica-gel for improved cleavage yields.[31] This reaction was simple and also gave much cleaner yields than past procedures. One reason could again be the issue of phases. In past procedures, sodium periodate was dissolved in an aqueous phase and the starting material in an organic phase, again requiring these two phases to mix strongly for any reaction to occur. Adsorbing the sodium periodate onto the silica gel eliminated the need for an aqueous phase and may have allowed the sodium periodate to come in contact with the starting material much more efficiently. Since the dialdehyde was successfully obtained, an attempt at performing the next step of the synthesis was done. Previously in the group, this reaction was performed on an impure, small amount of compound **6** and it required a minimum of 24 hours to give evidence of reaction.[32] A hopefully improved procedure was found and conducted, taking the first NMR after 25 hours[33]. At this point, reaction evidence was seen, but starting material **6** was still present. It seemed both desired product and the product with one aldehyde converted to the alkene were present based on the spectrum. There were two peaks in the aldehyde region, and two doublets in the alkene region to support the development of the single and double alkene conversion. The mixture was allowed to stir with another HNMR taken at the 70-hour mark. At that time, the spectrum showed no further reaction progress as compared to the 25-hour mark. After reevaluation of the reaction conditions, it is likely that the reaction mixture became less basic throughout reaction leaving more protonated amine (N,N-Diisopropylethylamine, DIPEA) than unprotonated, causing the reaction to come to a standstill. In addition, referring back to the literature procedure that was followed, the starting material used only contained a single aldehyde whereas **6** is a dialdehyde. In this case, the starting molar equivalents should have been adjusted accordingly. To account for this alteration, 2 more equivalents of all reagents (excluding **6**) were added to the already stirring mixture. After about 25 hours of stirring, the reaction mixture with the additional reagents showed further reaction progress but still showed presence of the starting

[31] Zhong, Y.; Shing, T.; *J. Org. Chem.*, **1997**, *62*, 2622-2624.
[32] Rathke, M.W., et al; *J. Org. Chem.*, "The Horner-Wadsworth-Emmons Modification of the Wittig Reaction Using Triethylamine and Lithium or Magnesium Salts.", **1985,** 50, (15), 2624-2626.
[33] Blanchette, M. et al; *Tet. Lett.*, **1984**, *25(21)*, 2183-2186.

material **6**. At the 40-hour mark, no obvious evidence of progression from 25 hours was seen. These spectra showed one of the aldehyde peaks became smaller as well as one of the doublets. But between the 25 and 40-hour marks, there seemed to be no change in their intensities again. Adding another two equivalents of the amine was attempted, and at the 44-hour mark, no reaction evidence past the previous addition was seen. Since the literature mentions the use of another base also, 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), this procedure would be worth trying. Once **6** is converted to the bis-olefin **7** by a Horner-Wadsworth-Emmons (HWE) reaction, conjugate addition of sulfur groups will yield **8**. One complication with this approach, though, is that two new stereocenters will be introduced following the conjugate addition step (compound **9**), yielding diastereomers. To address this, the final step of the scheme converts the dithiol to a cyclic thioacetal. This should hopefully allow separation of the achiral isomers (**10a** and **10b**) from the racemic mixture. NMR should allow the chiral isomer to be assigned as it lacks the plane of symmetry found in **10a** and **10b**.

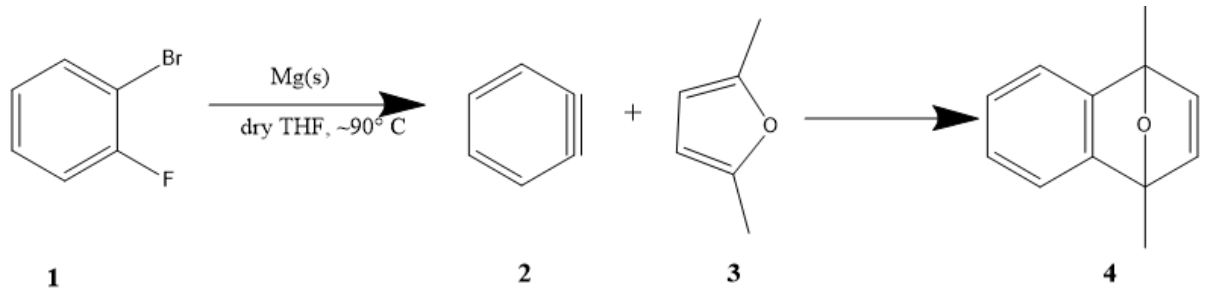
Future Study

As compound **4** has been successfully oxidized to a dialdehyde and the Horner-Wadsworth-Emmons reaction has shown correct reaction progression, future work would involve optimizing the conversion to the dialdehyde for better yields, but otherwise continuing the synthesis to find the highest yielding procedure to obtain the proposed desired product, **9**. The HWE reaction was referenced from literature and also suggested 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) could be used instead of DIPEA and reported faster reaction times, so this procedure should be attempted. Once this can be accomplished, the remainder of the proposed synthesis should proceed smoothly. Continued improvement of experiment **7b** can also be pursued to somewhat condense the original synthesis by skipping over the dihydroxylation. The ester groups in a successfully synthesized compound **9** will provide a location to attach fluorophores, and with high hopes, the final product can be tested with arsenic to determine its effectiveness as an As(III) receptor using fluorescence-based detection. Stereochemistry complications will have to be treated sensitively. Limitations on detection will have to be addressed. For example, interferences by other substances commonly present in drinking water will have to be addressed. In addition, it would be ideal to be able to expand the detection to other forms of arsenic, such as As(V) to make this detection method more sensitive and useful.

Experimental Procedures

Solvents unless specified to be anhydrous, were used directly from purchase without special treatment or storage after bottle opening. Dichloromethane was purchased from EMD Millipore as HPLC grade. Chloroform was purchased from J.T.Baker as HPLC grade. Ethyl acetate was purchased from EMD Millipore as GR ACS grade. Methanol was purchased from BDH as ACS grade. Acetone was purchased from BDH as ACS grade. Hexanes was purchased from Avantor Materials as ACS grade. Ethyl ether was purchased from EMD Millipore as GR ACS grade. Tetrahydrofuran was purchased from Sigma-Aldrich as spectrophotometric grade. HNMR data were collected from a Bruker 300MHz spectrometer with deuterated chloroform as the reference standard.. Additional chemicals were purchased from various sources. Ozonolysis done with Ozone Services, A Division of Yanco Industries, Ltd. as made graciously available by the Ojima group. This information applies to both chapters.

Experiment 1: Grignard intermediate followed by Diels Alder *in situ*

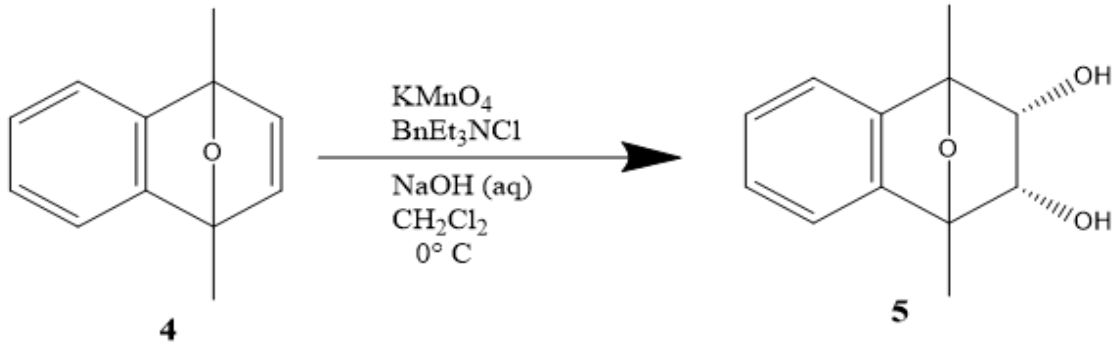


1 **2** **3** **4**

A flake of 1,2-diiodoethane and a stir bar was added to scratched magnesium turnings (0.81 g, 34 mmol) in a 50-mL 2-neck flask under nitrogen. This reaction flask was heated to 85 °C for 5 minutes to activate the magnesium. Then, a condenser and pressure equalizing addition funnel were attached and the system was evacuated with a vacuum pump for 5 minutes and refilled with $N_2(g)$. Dimethylfuran (0.50 mL, 4.5 mmol) and dry THF (12.5 mL) were added via syringe to the flask through the addition funnel. With the addition funnel stopcock closed, dimethylfuran (2.4 mL, 22 mmol), 2-bromofluorobenzene (2.4 mL, 22 mmol), and 12.5 mL dry THF were added to the funnel. The flask was heated in an oil bath at 95 °C and the solution from the addition funnel was added at a rate of about 1 drop/s and heating was continued for about 15 minutes after addition was complete at 90 °C. The reaction mixture was allowed to cool to room temperature and ether (50 mL) was added. The solution was filtered by vacuum and the filtrate was evaporated to give crude product **4**. Crude oil was loaded onto column for flash purification with a gradient of 100% hexanes to 19:1 hexanes/ethyl acetate to give a 90% yield.

δ_H 1.93 (s, 6H, CH_3), 6.80 (s, 2H, CH), 7.00 (m, 2H, ArH), 7.13 (m, 2H, ArH)

Experiment 2: Potassium Permanganate Oxidation of **4**

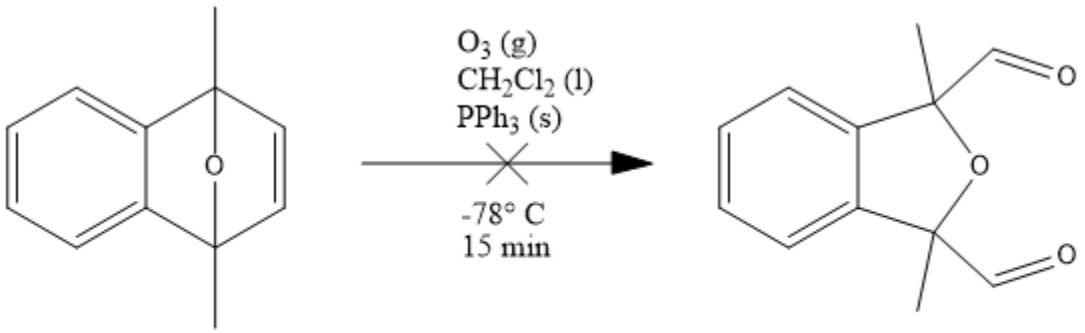


4 **5**

A 125-mL Erlenmeyer flask containing **4** (0.625 g, 3.60 mmol if pure, but actually less) and benzyltriethylammonium chloride (0.1 g) in dichloromethane (2.5 mL) was cooled in an ice bath. While stirring vigorously, 10 mL 40% aq. NaOH solution was added in one portion followed by addition of $KMnO_4$ (0.275 g, 1.75 mmol) in four portions over 10 minutes. Stirring was continued in ice bath for one hour after addition was complete. A solution of 0.75 g sodium bisulfate in 7.5 mL water was added. After 10 minutes, 2.375 mL 36% HCl was added over about 2 minutes. The solution was immediately extracted with ether (3 x 12.5 mL). The combined ether layers were dried over $MgSO_4$ and evaporated to give crude product.

δ_H 1.77 (s, 6H, CH_3), 3.12 (br s, 2H, OH), 3.77 (s, 2H, CH), 7.19 (m, 2H, ArH), 7.24 (m, 2H, ArH)

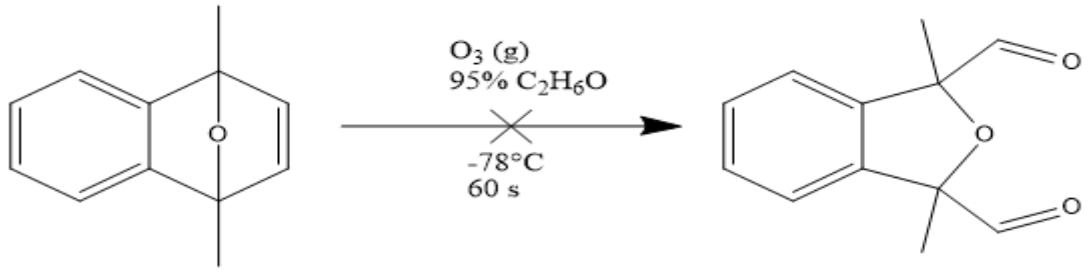
Experiment 3a*:* Alternative route to dialdehyde **6** via ozonolysis[34]



4 **6**

To a 50-mL double-necked round bottom flask, 1.12 mmol (0.192 g) of crude **4**, 17 mL dichloromethane, and a stir bar were added. This mixture was evacuated with nitrogen while stirring. The sealed container was cooled with liquid nitrogen in ethyl acetate to -78 °C. The ozone source needle was submerged into the reaction mixture for 15 min. The reaction was allowed to reach room temperature over a period of 45 min. PPh_3 (0.330 g, 1.258 mmol) was added to the reaction flask while stirring. This was left to stir overnight. The mixture was evaporated to yield crude product. This NMR spectrum did not show any aldehyde evidence and showed possible remaining starting material.

Experiment 3b: Modified ozonolysis of **4**[35]

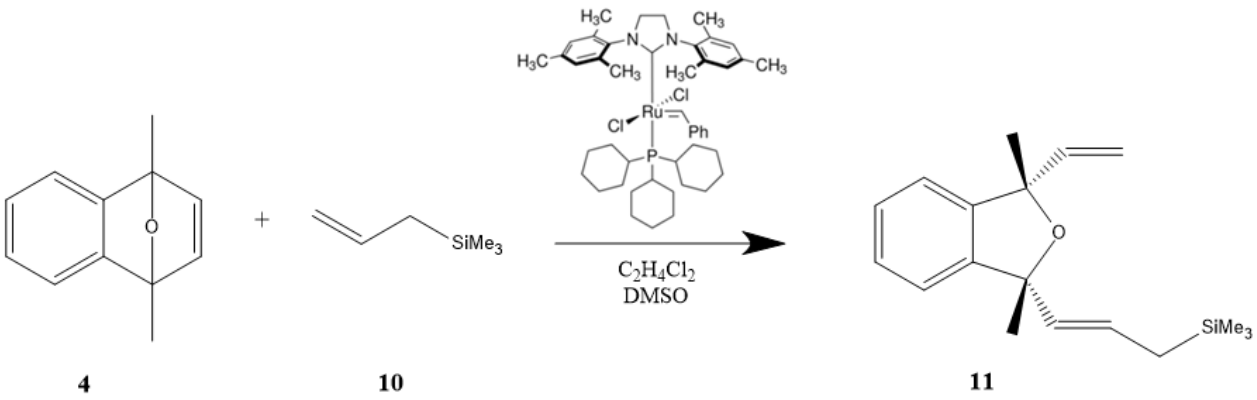


4 **6**

[34] Cain, N., et al. *J. Org. Chem.*, 2012,77,3816
[35] Benjamin, N., et al. *Org. Let*. 2011, 13(3), 450-453

Crude **4** (0.023 g, 0.10 mmol) and 3 mL of 95% acetone was added to a 25-mL 3-necked round bottom flask. The reaction flask was evacuated and refilled with nitrogen. The flask was submerged in dry ice and ethyl acetate to reach and maintain -78 °C. Ozone was administered for 60 s. The flask was then evacuated with nitrogen again and allowed to reach room temperature overnight. The mixture was evaporated and then 3 mL of dichloromethane was added. This was separated and the organic layer was dried over $MgSO_4$ for crude analysis. HNMR showed a tiny peak in the aldehyde region and presence of starting material. When Sudan Red III indicator was used, ozone was pumped for no more than 10 minutes and always gave crude HNMR spectra with tiny aldehyde-region peaks and possible starting material peaks.

Experiment 4: Grubbs catalyzed olefin metathesis of **4**

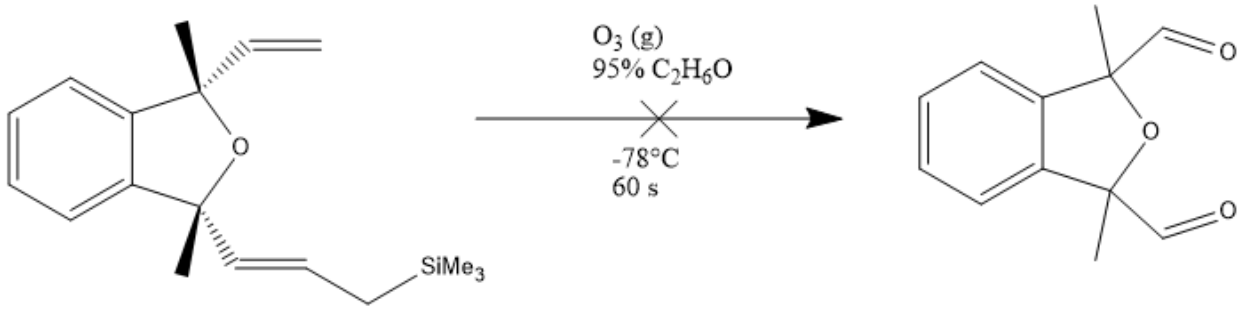


4 **10** **11**

A solution of 6 mg of Grubbs 2nd generation catalyst in 1 mL of 1,2-dichloroethane was prepared. Compound **4** (0.14 mmol) was added to a 5-mL round bottom flask. 1,2-dichloroethane (0.8 µL), allyltrimethylsilane (222 µL, 1.4 mmol), and 200 µL of the Grubbs catalyst solution were added. The solution was heated to 70 °C with stirring. Dimethyl sulfoxide (80 µL) was added and mixture was heated with stirring for twelve hours. The reaction was monitored by TLC, hourly. The reaction mixture was concentrated to remove solvent and a separation was performed with addition of dichloromethane and water. Washed organic layers were combined and dried over $MgSO_4$. Solvent was removed again for crude analysis. When purified on pipette column with a gradient of 100% hexanes to 9:1 hexanes/ethyl acetate, a 69% yield is seen.

δ_H 0.014 (s, 18H, CH_3), 1.43 (d, 2H, CH_2), 1.63 (s, 6H, CH_3), 5.04 (d, 2H, RC=CH_2), 5.20 (d, 1H, CH), 5.56 (m, 1H, CH), 6.01 (q, 1H, CH), 7.07 (m, 4H, ArH)

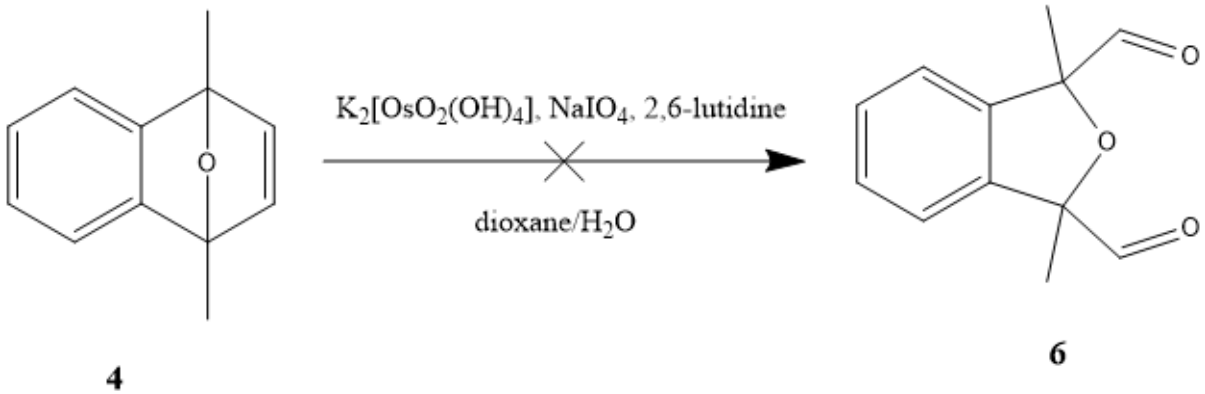
Experiment 5: Benjamin Ozonolysis of **11**



11 **6**

Crude **11** (0.10 mmol, 28.63 mg) was added to a 3-necked 25-mL round bottom flask. A solution of of 95% acetone/water (3 mL) was added to the rbf, along with a spatula-tip of Sudan Red III indicator and a stir bar. The flask was sealed, evacuated, and refilled with N_2 (*g*). With dry ice or N_2(*l*) and ethyl acetate, the flask was brought to -78 °C with stirring. Once at proper temperature, ozone was pumped in until red indicator color disappeared. The solution was removed from the ozonolysis setup and refilled with N_2 (*g*) and allowed to return to room temperature. Solvent was removed for crude analysis. During solvent removal, red indicator color reappeared. NMR showed solvent only, not enough product or starting material present to give signal.

Experiment 6a: Potassium Osmate Oxidation of **4**

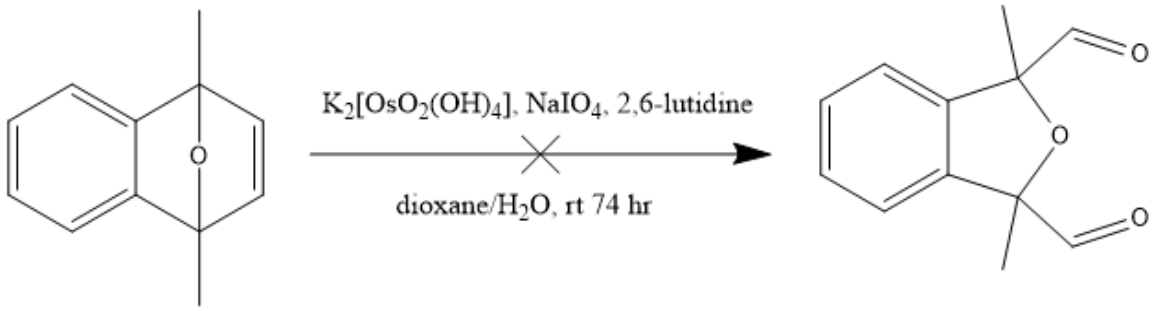


4 **6**

Pure **4** (0.5 mmol) was dissolved in 5 mL of a 3:1 dioxane:water solution. 2,6-lutidine (0.116 mL), potassium osmate (0.00368 g), and sodium periodate (0.4278 g) were added to reaction flask. The

reaction was stirred at room temperature and monitored by TLC. It was allowed to stir overnight for a reaction time of about 22 hours. When the reaction was completed, a separation was done by adding dichloromethane and water. All organic layers were combined and a final wash was done with brine and the final organic layer dried over Na_2SO_4. HNMR showed unreacted starting material.

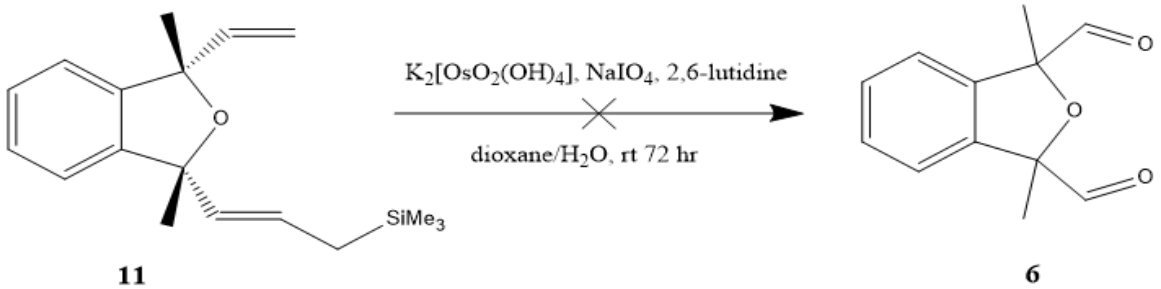
Experiment 6b: Potassium Osmate Oxidation of **4**



4 **6**

Pure **4** (0.5 mmol) was dissolved in 5 mL of a 3:1 dioxane:water solution. 2,6-lutidine (0.116 mL), potassium osmate (0.00368 g), and sodium periodate (0.4278 g) were added to reaction flask. The reaction was stirred at room temperature and monitored by TLC. It was allowed to stir for 74 hours, followed by a separation using dichloromethane and water. All organic layers were combined and a final wash was done with brine and the final organic layer dried over Na_2SO_4. HNMR showed mixture of solvents and starting material, no aldehyde evidence.

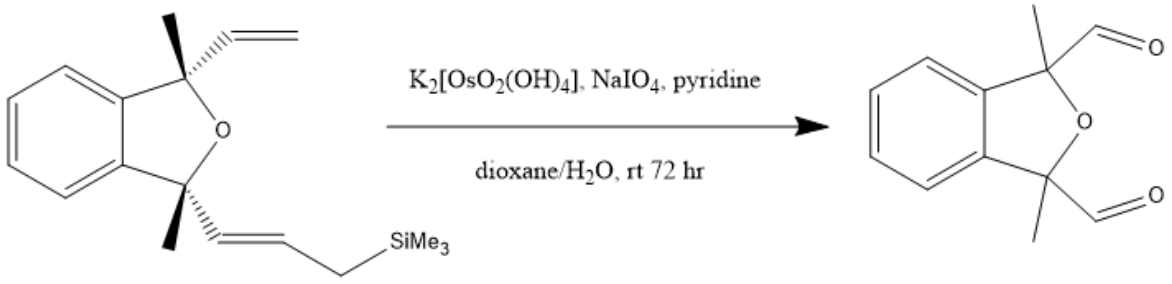
Experiment 7a: Potassium Osmate Oxidation of Grubbs product



11 **6**

Pure **11** (0.5 mmol) was dissolved in 5 mL of a 3:1 dioxane:water solution. 2,6-lutidine (0.116 mL), potassium osmate (0.00368 g), and sodium periodate (0.4278 g) were added to reaction flask. The reaction was stirred at room temperature and monitored by TLC. It was allowed to stir for about 96 hours. When the reaction was completed, a separation was done by adding dichloromethane and water. All organic layers were combined and a final wash was done with brine and the final organic layer dried over $NaSO_4$. HNMR showed unconsumed starting material with the slightest blip in the aldehyde region.

Experiment 7b: Potassium Osmate Oxidation of **11** (pyridine instead of lutidine)

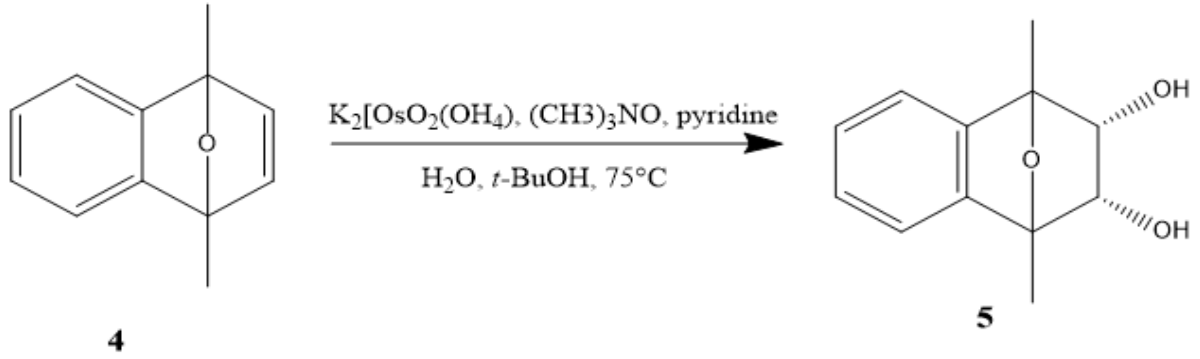


11 **6**

The same procedure was followed for this experiment as in **Experiment 7a**, with pyridine replacing 2,6-lutidine. The literature focused more on 2,6-lutidine but advised pyridine to be successful as well. The reaction was allowed to proceed for about 72 hours before it was fully characterized. Pipette column purification gave evidence of unreacted starting material and a relatively intense aldehyde peak as compared to past reactions.

Experiment 8: The same procedure was followed for this experiment as in **Experiment 7b**, with 2 more molar equivalents of pyridine. HNMR showed mixture of solvents and evidence of an aldehyde after 44 hours. After 8 days of stirring, crude HNMR supported the presence of desired product.

Experiment 9: Potassium Osmate Catalyzed Hydroxylation of **4**

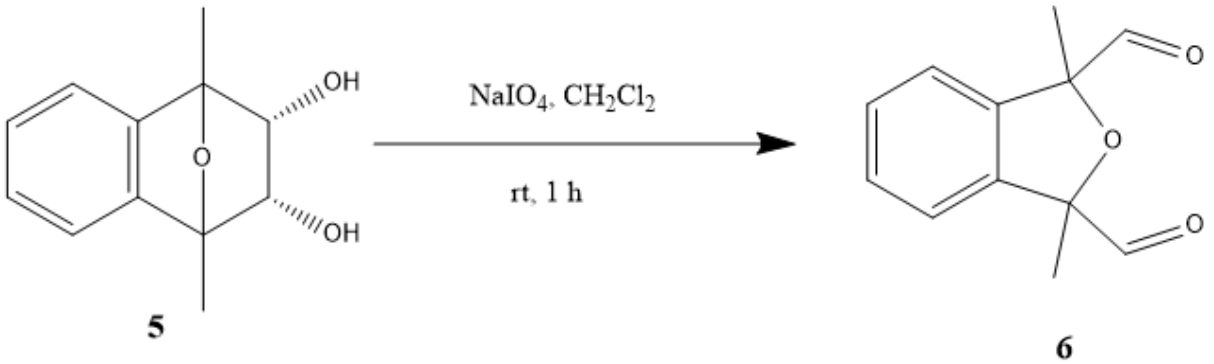


4 **5**

A solution of 20 mg of potassium osmate in 1 mL of water was prepared. This solution (0.1 mL) was added to 2.5 mmol **4**, along with trimethylamine N-oxide dihydrate (3.4 mmol), 0.2 mL of pyridine, 1.4 mL of water, and 5.1 mL of t-BuOH. The system was vacuumed and refilled with $N_2(g)$, refluxed at 75 °C, and monitored by TLC hourly. Solution was cooled to room temperature after a 28-hour reaction time. Once cooled, the reaction mixture was treated with 20% aqueous sodium bisulfite and concentrated under vacuum to remove t-BuOH. Then, an extraction was performed with saturated sodium chloride and ether to collect the organic layer. The organic layer was concentrated under vacuum to characterize the crude product. Gave 75% yield.

δ_H 1.79 (s, 6H, CH_3), 3.79 (s, 2H, CH), 7.20 (m, 4H, ArH)

Experiment 10: Silica Gel-Supported Sodium Metaperiodate cleavage of **5** to the dialdehyde **6**



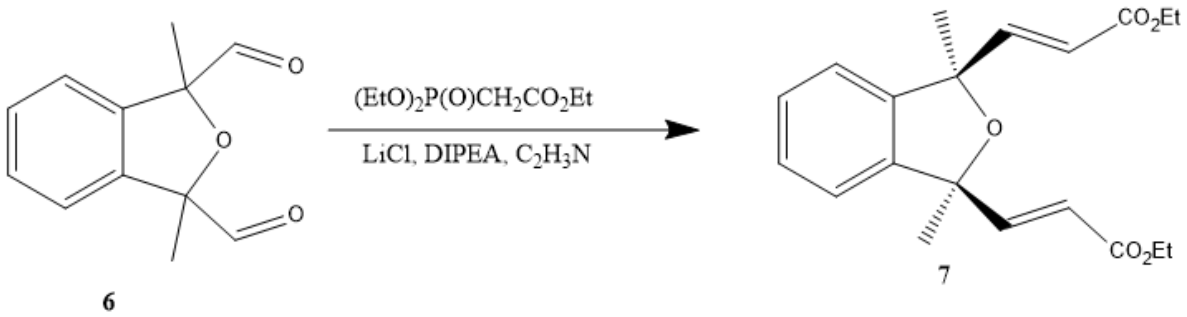
5 **6**

Sodium periodate (12 mmol, 2.6 g) was dissolved in 5 mL of hot water at about 70 °C in a 25 mL round bottom flask. Once fully dissolved, 10 g of silica gel was added with vigorous swirling and shaking to yield a free-flowing powder. From this 10 g mixture, 1 g was suspended in 2.5 mL of

dichloromethane in a 10-mL rbf. Diol **5** (0.5 mmol) in 2.5 mL of dichloromethane was added to the 10 mL rbf, along with a stir bar. The solution was stirred vigorously and monitored by TLC every 10 minutes. After 60 minutes, the reaction mixture was filtered through a sintered glass funnel and the silica gel was thoroughly washed with chloroform. Evacuation under vacuum yielded nearly pure dialdehyde. Crude yield of 65%.

δ_H 1.70 (s, 6H, CH_3), 7.44 (m, 4H, ArH), 9.77 (s, 2H, OCH)

Experiment 11a: Horner-Wadsworth-Emmons bis-olefin conversion of **6**



6 **7**

Lithium chloride (0.49 mmol, 21 mg) was added to 5 mL of dry acetonitrile under nitrogen for stirring at room temperature. Triethylphosphonoacetate (0.49 mmol, 98 µL), N,N-diisopropylethylamine (DIPEA) (0.41 mmol, 71 µL), and **6** (0.50 mmol, 0.167 g) were added via syringe. The mixture was allowed to stir with monitoring by HNMR. HNMR after 25 hours showed reaction evidence with both desired product peaks and peaks that agreed with one aldehyde converted to the alkene. Allowing to stir for additional 15 hours showed no more reaction progress.

Experiment 11b and c: Modification of **11a**

Added two more equivalents of LiCl, dry acetonitrile, triethylphosphonoacetate, and DIPEA to the already stirring reaction mixture. HNMR showed evidence of reaction with peaks showing desired product and one aldehyde converted to the alkene but the ratios shifted toward the desired product by the 25-hour mark. Allowing to proceed to the 44-hour mark showed no more reaction evidence. One final addition of 2 more equivalents of DIPEA showed no more reaction progress after another 44 hours.

Chapter 2

A Synthetic Approach to a Potential Pi-Stacking based Polyamide Foldamer

Background

Proteins are an essential part of life. Their existence plays a role in gene expression and disease, among other basic functions of life. Their behavior has been long studied in order to fully understand how they work, and then to ultimately use that knowledge for improving quality of life, such as finding cures and treatments for diseases. One major field of study revolves around nucleic acid mimics, or PNAs. PNAs mimic the behavior of DNA and bind complementary nucleic acid strands. Two of the most important properties of DNA are its specificity and the ability of the hydrogen bonds between complementary nucleobases to reverse which allow the double helix strands to be unwound and rewound in exactly the same configuration. If individual strands of DNA could be synthesized, then base sequences of genes can be studied and manipulated for multiple benefits, most notably a cure for cancer. [36] The growing field of synthetic molecules that can mimic the functions and behaviors of molecules like proteins that are unrecognizable to protease digestion has changed the name of the game. PNAs have an intrinsic resistance to protease and nuclease digestion, with a stability of at least 48 hours as compared to 15 minutes for natural nucleic acids.[37] With advantages like this, these synthetic molecules show great promise for anti-sense and anti-gene drugs and therapy. One study showed a successful insertion of PNA into a cell while bound to a strand of DNA, and once inside the cell, the inhibition of human telomerase with anticancer activities.[38] There is so much promise in this field of synthetic nucleic acid analog development that the field itself has expanded to include the study of *foldamers*. "Foldamers are sequence-specific oligomers akin to peptides, proteins and oligonucleotides that fold into well-defined three-dimensional structures."[39] Foldamer chemistry strives to understand how proteins fold and maintain certain structures, and how that can be reproduced synthetically. Thus far, the central challenge is to mimic proteins by finding a way to design a sequence of building blocks that will fold like a particular α-peptide.[40] The major issue is being able to replicate these folds and interactions with unnatural, modified backbones.[41] As the Drueckhammer lab has successfully

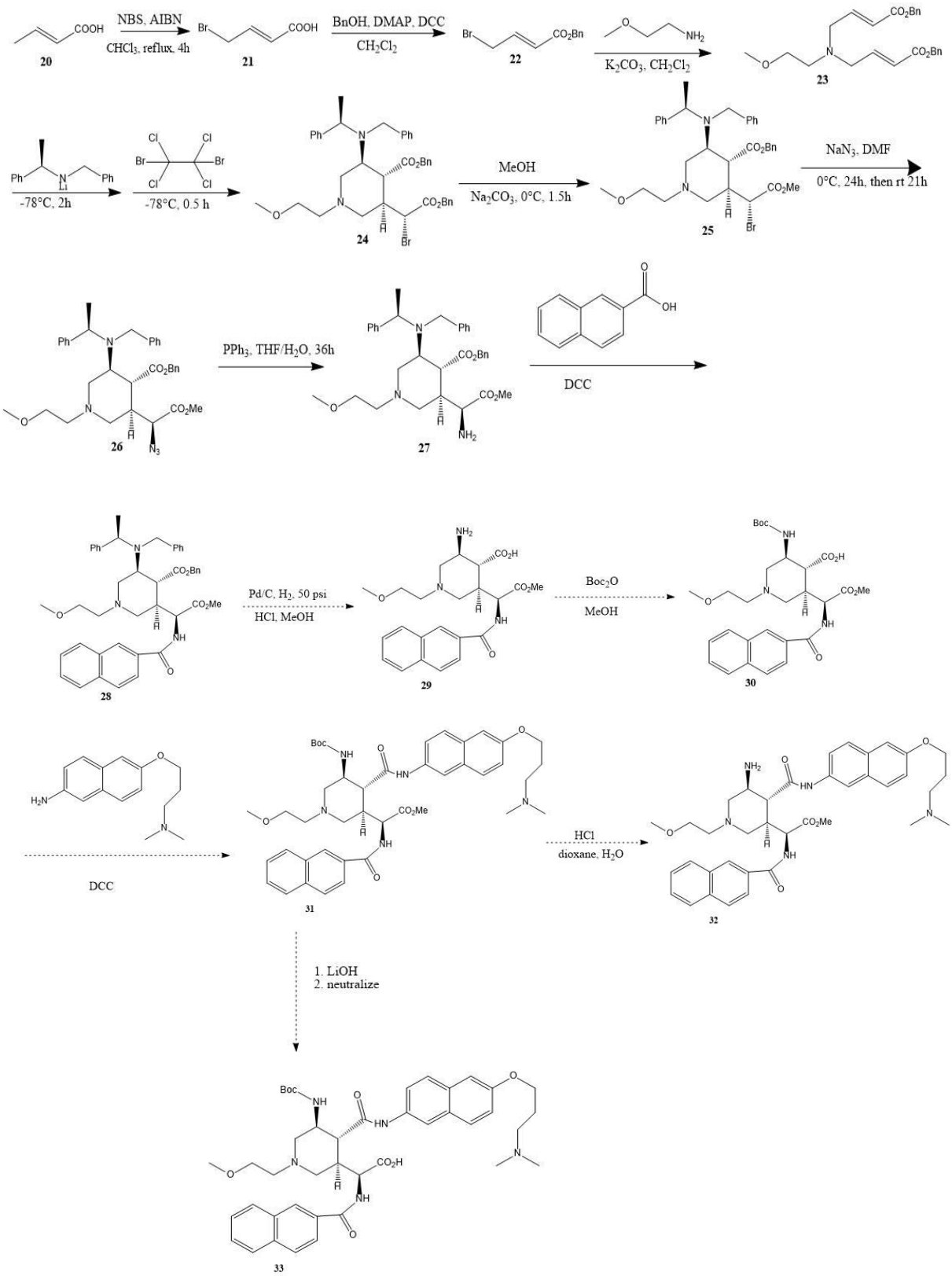
[36] Nielsen, P.; Egholm, M.; *Current Issues Molec. Bio.,* **1999**, *1(2)*, 89-104
[37] Hamilton, S. E.; Simmons, C. G.; Kathiriya, I. S.; Corey, D. R., *Chemistry & Biology*, "Cellular delivery of peptide nucleic acids and inhibition of human telomerase", **1999**, *6*, 343-351.
[38] Nastruzzi, C.; Cortesi, R.; Esposito, E.; Gambari, R.; Borgatti, M.; Bianchi, N.; Feriotto, G.; Mischiati, C.; *J. Control Release*, "Liposomes as carriers for DNA–PNA hybrids", **2000**, *68*, 237-249.
[39] Saido, T.; Leissring, M.; *Cold Spring Harb. Perspect. Med.*, **2012**, *2:a006379.*
[40] Reinert, Z.; Lengyel, G.; Horne, S.; *J. Am. Chem. Soc.*, **2013**, *135*, 12528-12531.
[41] Reinert, Z.; Horne, S.; *Chem. Sci.*, **2014**, *5*, 3325.

synthesized nucleic acid mimics, part of that synthetic route was worth branching off into a new project with hopes of dipping our toe into this foldamer field.

Experimental Design

The proposed synthesis for a stackable backbone foldamer is shown below in **Scheme 3.** The first seven steps have been performed successfully by the Drueckhammer group previously to form compound **27** in a proposed synthesis of a nucleic acid mimic. From that point, the nucleic acid project followed an alternate synthesis route, whereas the foldamer proposed route is represented in **Scheme 3**. This route came about during the group's initial project to see how the synthesized singular molecular strand that had this modified backbone would behave structurally. Successful production of compounds **32** and **33** will be used as building blocks for the synthesis of a polyamide oligomer. It is predicted that the oligomer will adopt a helical folded state as driven by the pi-stacking of the naphthalene groups. If successful, they can be important factors in drug design and other types of therapy.[42] This chapter follows the replication of the first 7 experiments and initiation of the foldamer route.

[42] Babine, R.E.; Bender, S.L.; *Chem. Rev.* " Molecular Recognition of Protein−Ligand Complexes: Applications to Drug Design". **1997,** *97 (5),* 1359–1472.



Scheme 3: Proposed foldamer synthetic route

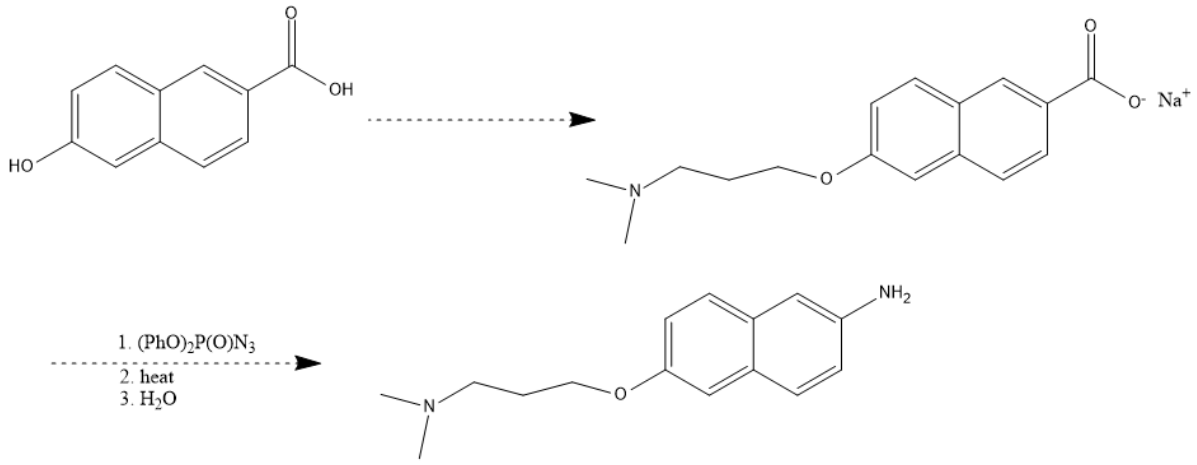
Results and Discussion

Each reaction in the synthesis of **27** was replicated with success to yield desired products in high yields and purity. Bromination of crotonic acid is very reproducible but is temperature sensitive. If the reflux reaction temperature is below 70 °C, the reaction does not proceed. The crude product is pure enough to be used in the next step without any detriment to yields, although when using pure **21**, purity of **22** is more likely to be higher. In addition, the reaction does require a full overnight of stirring after the DCC addition to give good yields, shorter reaction times have shown low yields. The bis-alkylation reaction to form **23** is time sensitive. Allowing the reaction to go beyond 22 hours or not purifying immediately caused severe detriment in yield. The key addition/cyclization reaction of **23** and trapping of the enolate resulting with the mild brominating agent 1,2-dibromotetrachloroethane to give **24** proceeded without any difficulties, as long as the reaction environment was dry. The selective transesterification reaction of the more reactive α-bromoester to give **25** is the most straightforward of the experiments, and easily gave high yields. Displacement of the bromide with azide to give **26** gave more difficulties and low yields. The reduction of the azide **26** to give the amine **27** is very solvent sensitive, as impure THF resulted in consumption of the triphenylphosphine before it reacted with **27** and decomposition of the starting material. It is unclear what the decomposition pathway and decomposition products are, but this problem was avoided when newly purchased THF was used. The naphthanoic acid attachment to form **28** has only been done on a very small scale for qualitative purposes, but HNMR showed the desired product.

Future Study

As these synthetic steps are perfected, future work will proceed with the proposed synthesis to create the desired foldamer and analyze its structural behavior.

The reagent proposed for attachment to compound **30** will have to be synthesized as well, and a synthesis has been proposed for that pathway, as seen in **Scheme 4**.



Scheme 4: Proposed scheme for synthesis of required reagent for attachment to **11**

Future work will be conducting not only the foldamer synthetic procedure but perfecting the synthesis of compound **27** for use in the foldamer synthesis. Once **32** and **33** can be successfully synthesized, observing their folding behavior and pi-stacking interactions will follow and confirm the hypothesis, their pi-stacking interactions represented in 2D and 3D below.

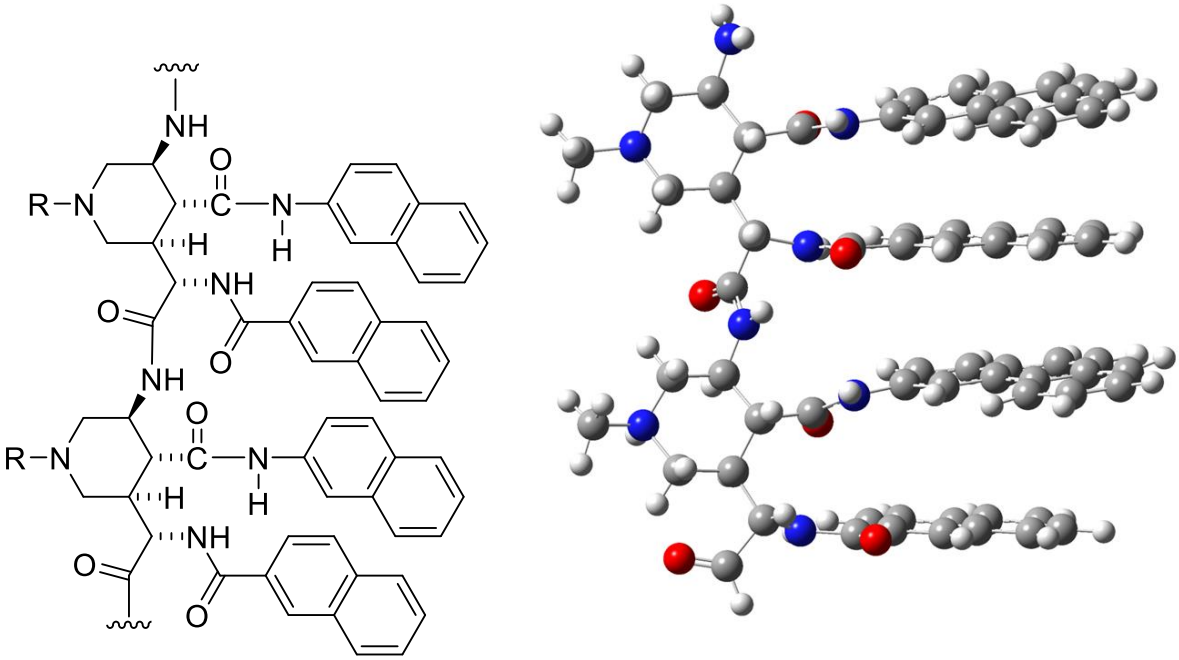
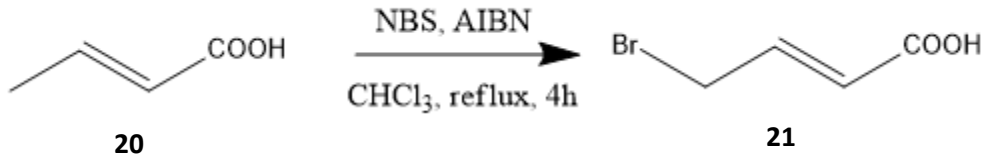


Figure 10: Pi-stacking interaction prediction for molecules **32** and **33**

Experimental Procedures:

4-Bromo Crotonic acid

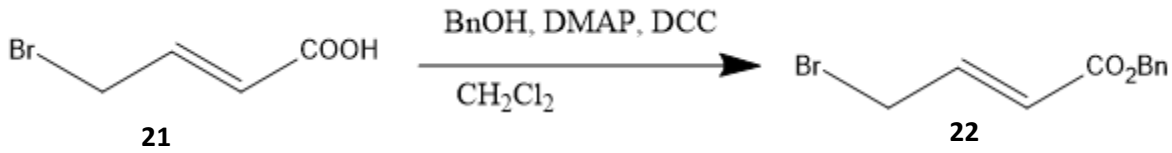


20 **21**

Crotonic acid (10.0 g, 116 mmol) was added to a round bottom flask, followed by an addition of N-bromosuccimide (NBS) (20.7 g, 116 mmol), chloroform (116 mL), and AIBN (1.16 g, 7.00 mmol). The mixture was refluxed for 4 hours. After 4 hours, another 0.3 equivalents of NBS and AIBN were added to the reaction mixture and allowed to reflux for another 4 hours. The flask was cooled to room temperature and solvent removed via rotovap. The crude oil is used in the next step without purification, but can be purified with flash chromatography with a gradient of 5% to 20% acetone in hexanes. The desired product came out at 20% acetone as a white solid. Obtained 15.06 g, 79% yield.

δ_H 4.03 (dd, 2H, $BrCH_2$, J= 7.3 Hz), 6.04 (d, 1H, COCH=, J=15.3 Hz), 7.13 (dt, 1H, CH, J=15.3 Hz, 7.3 Hz)

Benzyl 4-bromo-crotonate



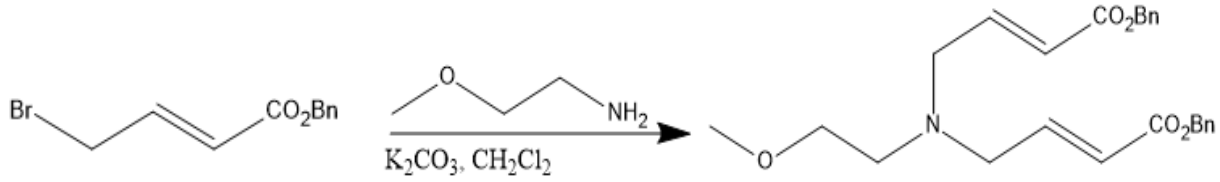
21 **22**

Crude 4-bromo crotonic acid (8.065 g, 48.90 mmol) and benzyl alcohol (5.280 g, 48.90 mmol) were mixed with 100 mL of dichloromethane in a round bottom flask. Dimethylaminopyridine (DMAP) (0.597 g, 4.89 mmol) was added subsequently, and the rbf chilled in an ice bath and stirred for 30 minutes. During the 30 minutes, N,N'-dicyclohexylcarbodiimide (DCC) was dissolved in a total of 45.5 mL of dichloromethane and added to the rbf. The reaction was allowed to warm to room temperature over the course of about 2 hours. The solid was removed via vacuum filtration. The solvent was removed via rotary evaporation, and the residual oil was loaded onto a

column. A gradient of 0% to 5% acetone in hexanes was used to elute. Obtained 6.134 g of product, 48% yield. This reaction should be stirred about overnight to obtain yields in the 70% range. The product is initially a yellow oil, which turns into a waxy solid upon cooling down from rotary evaporation.

δ_H 4.04 (dd, 2H, $BrCH_2$, J=7.3 Hz), 5.21 (s, 2H, $PhCH_2$), 6.07(d, 1H, COCH=, J= 15.3 Hz), 7.05 (dt, 1H, CH, J=15.3 Hz, 7.3 Hz), 7.38 (s, 5H, PhH)

Compound 23

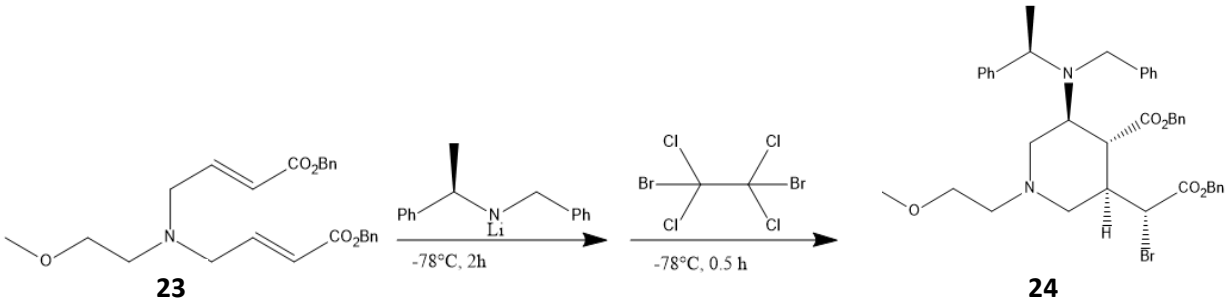


22 **23**

Benzyl 4-bromo-crotonate (6.426 g, 21.84 mmol) was added to a round bottom flask, followed by addition of potassium carbonate (3.014 g, 21.84 mmol). 2-methoxyethylamine (0.819 g, 10.9 mmol) was dissolved in 11 mL of dichloromethane, and added into to flask. The reaction was stirred for 22 hours. Then the solvent was removed directly via rotovap and at the same time the residue mixed with silica for loading onto column. A gradient of 5% to 10% acetone in hexanes gave the desired product (3.02 g, 7.14 mmol, 68%) at 10% acetone.

δ_H 2.68 (t, 2H, N**CH**$_2$$CH_2$, J= 4.15 Hz), 3.30 (s, 3H, CH_3), 3.47 (t, 2H, OCH_2, J= 4.15 Hz), 5.19 (s, 4H, $PhCH_2$), 6.05 (d, 2H, COCH=, J=15.7 Hz), 6.98 (dt, 2H, CH, J= 15.7 Hz, J= 5.36 Hz), 7.31-7.40 (br, 10H, PhH)

Compound 24

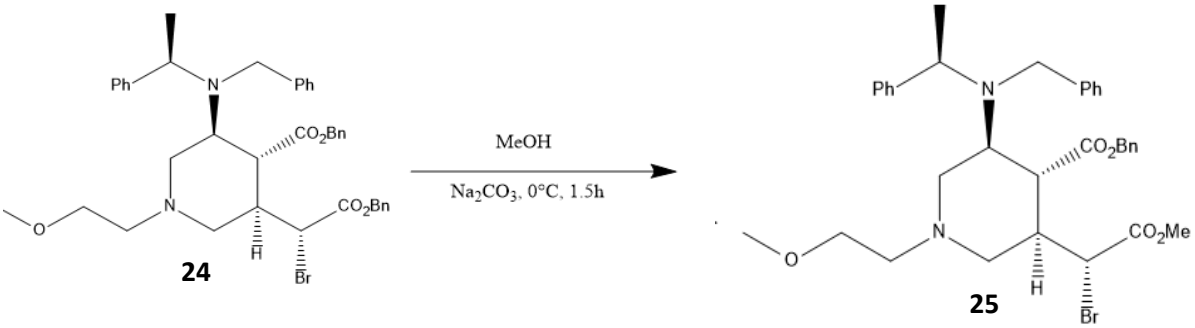


23 **24**

A 2-neck flask was vacuumed and refilled with $N_2(g)$. R-(+)-N-benzyl-phenylethylamine (2.109 g, 9.995 mmol) was injected, followed by addition of anhydrous THF (20 mL) and stirred. The flask was cooled to -78 °C, and n-BuLi (1.6 M in hexanes, 7.139 mL, 11.42 mmol) was added slowly. The reaction was stirred for 30 min, then **23** (3.02 g, 7.14 mmol) dissolved in anhydrous THF (21.4 mL) was added slowly and further stirred for 2 hours at -78 °C. 1,2-dibromotetrachloroethane (2.328 g, 7.139 mmol) dissolved in anhydrous THF (14 mL) was added slowly, and stirred for another 30 minutes. Finally, 10% aqueous ammonium chloride was poured into flask to quench the reaction, and the reaction was allowed to warm up to room temperature. Ethyl ether was added, and the contents transferred to a separatory funnel. The layers were separated, and the aqueous layer was washed one more time with ethyl ether. The combined organic layers were dried over magnesium sulfate, the solvent removed via rotovap, and residue loaded onto column. A gradient of 5% to 10% acetone in hexanes gave the desired product (3.67 g, 5.15 mmol, 72%) at 10% acetone.

δ_H 1.34 (d, 3H, CH**C**$\mathbf{H_3}$, J= 6.89 Hz), 1.99 (t, 1H, $C^6H_{ax}H_{eq}$, J= 11.2 Hz), 2.08 (t, 1H, $C^2H_{ax}H_{eq}$, J= 11.2 Hz), 2.34-2.63 (m, 1H, C^5H; m, 2H, NC$\mathbf{H_2}CH_2$), 2.75 (t, 1H, C^4H, J= 11.0 Hz), 2.89 (dd, 1H, $C^6H_{ax}H_{eq}$ J= 11.3 Hz, J= 1.90 Hz), 3.16 (dd, 1H, $C^2H_{ax}H_{eq}$, J=11.3 Hz, J= 1.90 Hz), 3.4-3.5(m, 1H, C^3H; 3.36 s, 3H, OCH_3; 3.43, t, 2H, OCH_2, J= 5.40 Hz), 3.95(m, 2H, C^7H_2), 3.90-4.04 (q, 1H, CH_3*CH*, J= 6.89 Hz), 4.01 (d, 1H, BrCH, J = 2.51 Hz), 5.02 (d, 2H, C^8H_2, J= 11.0 Hz), 5.15 (m, 2H, C^9H_2), 7.15-7.46 (m, 20H, PhH)

Compound 25

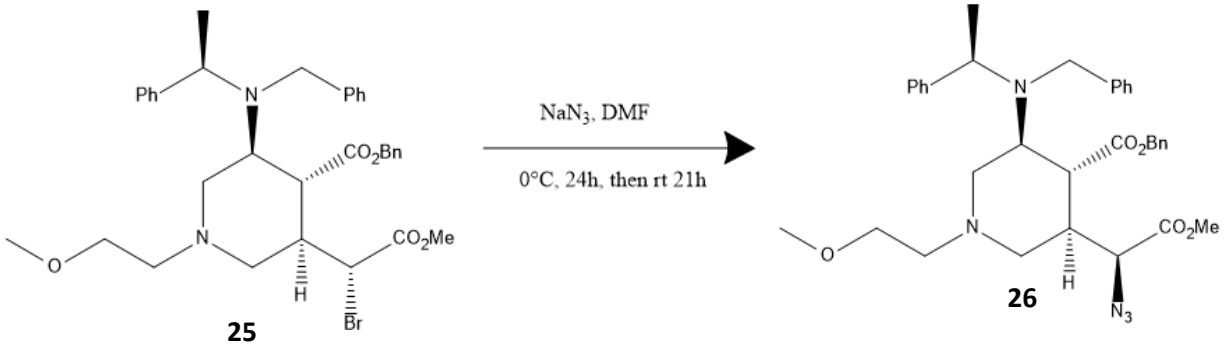


24 (3.644 g, 5.104 mmol) was dissolved in MeOH (61.2 mL) in a round bottom flask, and the solution was stirred and cooled in an ice bath. Sodium carbonate solid (0.2042 g) was added once solution was cooled. After stirring for 2 hours, ethyl ether was added to the solution and the solid

was filtered out via vacuum filtration. The product (2.73 g, 4.28 mmol, 84%) was isolated via column chromatography, using a gradient of 10% to 15% acetone in hexanes.

δ_H 1.35 (d, 3H, $CHCH_3$, J= 6.80 Hz), 2.01 (dd, 1H, $C^6H_{ax}H_{eq}$, J= 10.8 Hz), 2.07 (t, 1H, $C^2H_{ax}H_{eq,}$ J= 10.8 Hz), 2.42 (tt, 1H, C^5H, J= 10.8 Hz), 2.57 (dt, 2H, $N\mathbf{CH_2}CH_2$, J= 21.9 Hz, J= 5.70 Hz), 2.72 (t, 1H, C^4H, J= 11.0 Hz), 2.89 (dd, 1H, $C^6H_{ax}H_{eq}$, J= 11.0 Hz, J= 2.60 Hz), 3.17 (dd, 1H, $C^2H_{ax}H_{eq}$, J=11.0 Hz), 3.35-3.4 (m, 1H, C^3H; 3.37 s, 3H, OCH_3), 3.47 (t, 2H, OCH_2, J= 5.70 Hz), 3.64 (s, 3H, $COOCH_3$), 3.95 (m, 2H, C^7H_2), 3.91-3.99 (q, 1H, $CH_3\mathbf{CH}$, J= 6.89 Hz), 3.97 (d, 1H, BrCH, J= 2.60 Hz), 5.06 (d, 2H, C^8H_2, J=11.0 Hz), 7.11-7.44 (m, 15H, PhH)

Compound 26

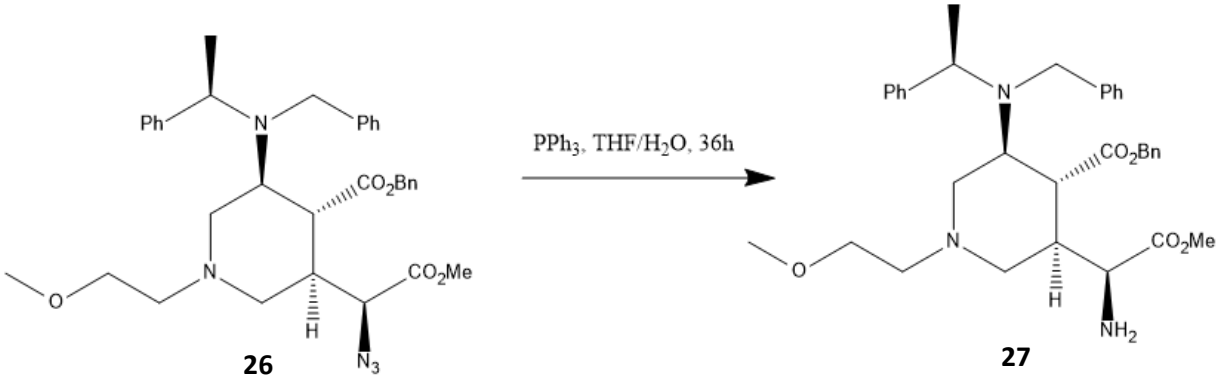


25 (2.731 g, 4.281 mmol) was dissolved in 4.281 mL of anhydrous DMF in a rbf, and the rbf flask was cooled in an ice bath. Sodium azide solid (0.6956 g, 10.70 mmol) was added to the rbf, and the reaction was stirred for 24 hours in ice bath. The ice bath was then removed, and the reaction further stirred for 21 hours at room temperature. Ethyl ether was added into the reaction, and the solid filtered out via gravity filtration. The DMF was removed by washing with water, and the aqueous phase was extracted once with ethyl ether. The combined organic phases were dried over magnesium sulfate. The product was purified with column chromatography, using a gradient of 10% to 20% acetone in hexanes, which came out at 20% acetone. Isolated 0.775 g (1.29 mmol) product.

δ_H 1.32 (d, 3H, $CHCH_3$, J= 6.90 Hz), 1.73 (dd, 1H, $C^6H_{ax}H_{eq}$, J= 11.4 Hz), 2.03 (t, 1H, $C^2H_{ax}H_{eq}$, J=11.4 Hz), 2.40-2.63 (m, 1H, C^4H, 1H, C^5H, 2H, $N\mathbf{CH_2}CH_2$), 2.85 (dd, 1H, $C^6H_{ax}H_{eq}$, J= 10.9 Hz, J= 3.00 Hz), 3.10 (dd, 1H, $C^2H_{ax}H_{eq}$, J= 10.9 Hz, J= 3.00 Hz), 3.32-3.38 (m, 1H, C^3H), 3.36 (s, 3H, OCH_3), 3.46 (t, 2H, OCH_2, J= 5.50 Hz), 3.64 (d, 1H, N_3CH, J= 4.30 Hz), 3.67(s, 3H,

$COOCH_3$), 3.87 (m, 2H, C^7H_2), 3.95 (q, 1H, CH_3**CH**, J = 6.90 Hz), 5.00 (m, 2H, C^8H_2), 7.14-7.42 (m, 15H, PhH)

Compound 27

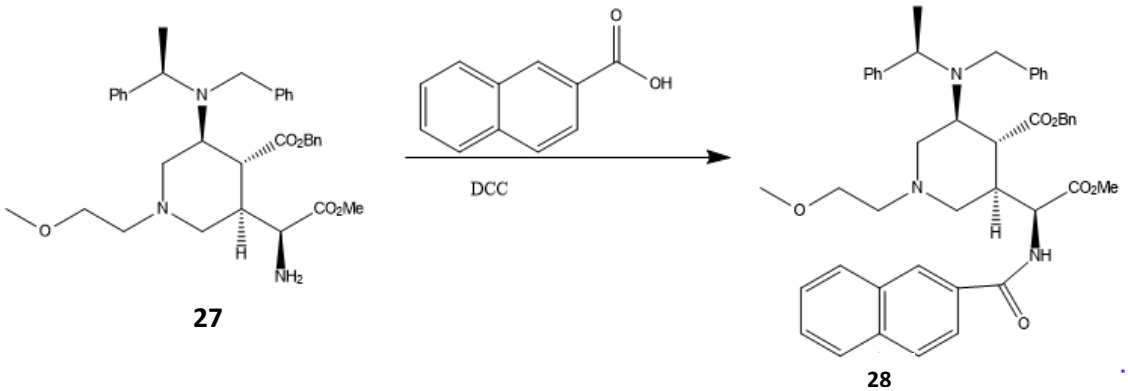


26 **27**

26 (0.472, 0.788 mmol) was dissolved in 12 mL of a 9:1 THF/H_2O mixture and then triphenylphosphine (0.206 g, 0.788 mmol) was added. The reaction was stirred for 36 hours. The solvent was removed directly via rotovap without any workup. The residue was loaded onto a manual column, and eluted with a gradient of 1:1 hexanes/ethyl acetate to pure ethyl acetate. Obtained 0.388 g, 0.676 mmol of product, 86% yield.

δ_H 1.32 (d, 3H, $CHCH_3$, J= 6.90 Hz), 1.77 (t, 1H, $C^6H_{ax}H_{eq}$, J= 11.4 Hz), 2.00 (t, 1H, $C^2H_{ax}H_{eq}$, J= 11.4 Hz), 2.28-2.42 (m, 1H, C^5H), 2.45-2.65 (m, 1H, C^4H; m, 2H, N**CH₂**CH_2), 2.81 (dd, 1H, $C^6H_{ax}H_{eq}$, J= 10.9 Hz, J= 3.00 Hz), 3.09 (dd, 1H, $C^2H_{ax}H_{eq}$, J= 10.9 Hz, J= 3.00 Hz), 3.15 (d, 1H, NCH, J= 4.30 Hz), 3.32-3.39 (m, 1H, C^3H), 3.36 (s, 3H, OCH_3), 3.47 (t, 2H, OCH_2, J= 5.50 Hz), 3.58 (s, 3H, $COOCH_3$), 3.87 (m, 2H, C^7H_2), 3.97 (q, 1H, CH_3**CH**, J= 6.90 Hz), 4.98 (m, 2H, C^8H_2), 7.10-7.42 (m, 15H, PhH)

Compound 28



27 **28**

27 (0.126 g, 0.220 mmol) was dissolved in chloroform (3 mL) in a round bottom flask. 2-Napthanoic acid (38 mg, 0.22 mmol) and DMAP (2.7 mg, 0.022 mmol) in 3 mL chloroform was added to the rbf. DCC (45 mg, 0.22 mmol) in 3 mL chloroform was added last. The reaction was stirred overnight. DCM was added, followed by a gravity filtration. The solvent was removed for HNMR analysis. Crude HNMR confirms **28** was synthesized.

δ_H 1.28 (d, 3H, $CHCH_3$, J= 6.90 Hz), 1.77 (t, 1H, $C^6H_{ax}H_{eq}$, J= 11.4 Hz), 2.00 (t, 1H, $C^2H_{ax}H_{eq}$, J= 11.4 Hz), 2.28-2.42 (m, 1H, C^5H), 2.45-2.65 (m, 1H, C^4H; m, 2H, N**CH_2**CH_2), 2.81 (dd, 1H, $C^6H_{ax}H_{eq}$, J= 10.9 Hz, J= 3.00 Hz), 3.09 (dd, 1H, $C^2H_{ax}H_{eq}$, J= 10.9 Hz, J= 3.00 Hz), 3.15 (d, 1H, NCH, J= 4.30 Hz), 3.32-3.39 (m, 1H, C^3H), 3.36 (s, 3H, OCH_3), 3.47 (t, 2H, OCH_2, J= 5.50 Hz), 3.58 (s, 3H, $COOCH_3$), 3.87 (m, 2H, C^7H_2), 3.97 (q, 1H, CH_3**CH**, J= 6.90 Hz), 4.98 (m, 2H, C^8H_2), 7.10-7.42 (m, 15H, PhH), 7.80-8.07 (m, 3H, ArH), 8.19 (d, 1H, ArH, J = 8.67 Hz), 8.81 (s, 1H, NH, 1H, ArH)

References

ATSDR Case Studies in Environmental Medicine: Arsenic Toxicity, **2009**, pp. 11-13
www.atsdr.cdc.gov/csem/arsenic/docs/arsenic.pdf

"US EPA." Chemical Contaminant Rules. *US EPA*, **2016**. http://www.EPA.gov/dwreginfo/chemical-contaminant-rules

Hughes, M. et al. *Toxicological Sciences*, **2011**, *123*, (2), 305–332

Nordstrom, *D. K. Science*, **2002**, *296*, 2143-2144

World Health Organization, Water Sanitation Health: Arsenicosis,
www.WHO.int/water_sanitation_health/diseases/arsenicosis/en/

Center for Public Integrity, "What to Do If Your Drinking Water Contains Arsenic", **2014**.
https://www.publicintegrity.org/2014/06/28/15004/what-do-if-your-drinking-water-contains-arsenic

Oregon.gov,"Drinking Water Program Fact Sheet: Recommendations for Arsenic Removal from Private Drinking Water Wells in Oregon", www.public.health.oregon.gov/HealthyEnvironments/DrinkingWater/SourceWater/Documents/gw/arsenicremoval.pdf

Manufactures Water Quality Testing and Analytical Instruments & Reagents, "Arsenic Low Range Test Kit",
http://www.hach.com/arsenic-low-range-test-kit/product-details?id=7640217303

Water & Wastes Digest, "Arsenic Testing the Easy Way", http://www.wwdmag.com/arsenic/arsenic-testing-easy-way.

a) Das, J. et al., *Journal of Environmental Science and Health*, Part A: Toxic/Hazardous Substances and Environmental Engineering, **2014**, *49*, (1), p108-115 b) Baghel, A. et al. *Analytical Sciences*, **2007**, *23*

Grosser, Z., *Water Technology* "The Challenge: Measure Arsenic in Drinking Water":
http://crustal.usgs.gov/laboratories/icpms/intro.html.

Perkin Elmer, The 30-Minute Guide to ICP-MS, p. 1.
http://www.perkinelmer.com/pdfs/downloads/tch_icpmsthirtyminuteguide.pdf

The National Academies Press, "Chemistry and Analysis of Arsenic Species in Water and Biological Materials." Arsenic in Drinking Water: **1999,** 31-32. http://www.nap.edu/openbook.php?record_id=6444&page=31

Zahler, W. L., et. al.; *J. Biol. Chem.*, "A Specific And Sensitive Assay For Disulfides**." 1968,** 243, (4), 716-&.

Selvin, Paul. *Nature America*, "The renaissance of fluorescence resonance energy transfer", **2000,** *7(9)*, 730.
http://people.physics.illinois.edu/selvin/PRS/PSCV/PTP/2000/Nature2000.pdf

Olympus Microscopy Resource Center, "Fluorescence Resonance Energy Transfer (FRET) Microscopy." **2012,**
http://olympusmicro.com/primer/techniques/fluorescence/fret/fretintro.html

Veysoglu, T.; Mitscher, L.; Swayze, J.; *Communications*, "A Convenient Method for the Control of Selective Ozonizations of Olefins". **1980,** 87. *https*://www.thieme-connect.de/products/ejournals/pdf/10.1055/s-1980-29214.pdf

Cain, N. et al; *J. Org. Chem.*, **2012,** *77*, 3808-3819.

Research Group, ADT, et al; *J. Appl. Chem.*, **2015,** *4(5)*, 1308-1312. http://www.joac.info/ContentPaper/2015/4-2.pdf

Benjamin, N.; Martin, S.; *Org. Lett.*,**2011,** *13(3)*, 450-453.

Chemical Land 21, Sudan III MSDS, *http*://www.chemicalland21.com/specialtychem/finechem/SUDAN%20III.htm

Finnegan, D.; Seigal, B.; Snapper, M.; *Org. Lett.*, **2006**, *8(12)*, 2603-2606.

Yu, W.; Mei. Y.; Kang, Y.; Hua, Z., Jin, Z.; *Org. Lett.*, **2004**, *6(19)*, 3217-3219.

Ray, R.; Matteson, D.; *Tet. Lett.*, **1980**, *21*, 449-450.

Zhong, Y.; Shing, T.; *J. Org. Chem.*, **1997**, *62*, 2622-2624.

Blanchette, M. et al; *Tet. Lett.*, **1984**, *25(21)*, 2183-2186.

Nielsen, P.; Egholm, M.; *Current Issues Molec. Bio.*, **1999**, *1(2)*, 89-104

Hamilton, S. E.; Simmons, C. G.; Kathiriya, I. S.; Corey, D. R., *Chemistry & Biology*, "Cellular delivery of peptide nucleic acids and inhibition of human telomerase", **1999**, *6*, 343-351.

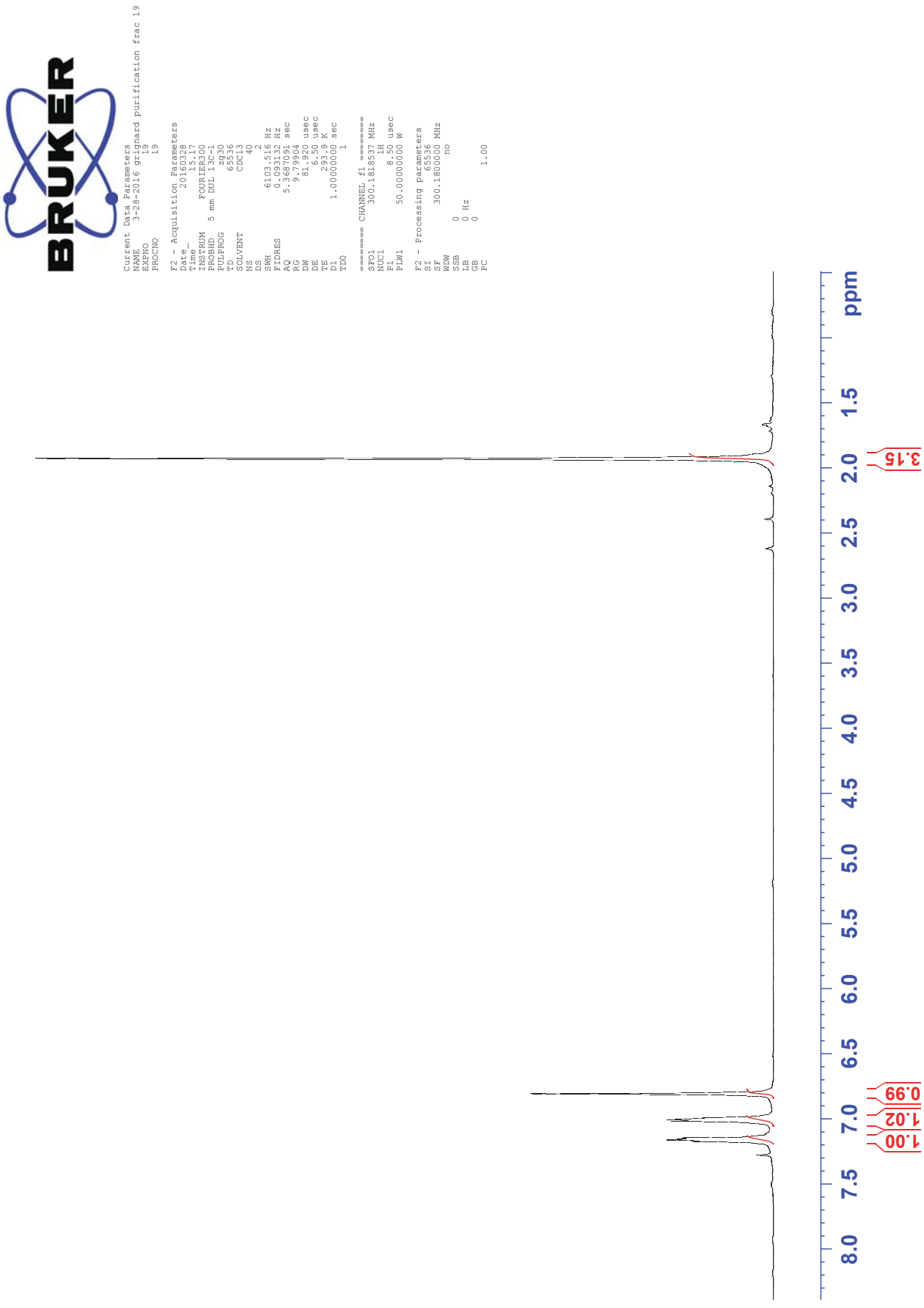
Babine, R.E.; Bender, S.L.; *Chem. Rev.* " Molecular Recognition of Protein−Ligand Complexes: Applications to Drug Design". **1997,** *97 (5)*, 1359–1472.

Nastruzzi, C.; Cortesi, R.; Esposito, E.; Gambari, R.; Borgatti, M.; Bianchi, N.; Feriotto, G.; Mischiati, C.; *J. Control Release*, "Liposomes as carriers for DNA–PNA hybrids", **2000**, *68*, 237-249.

Saido, T.; Leissring, M.; *Cold Spring Harb. Perspect. Med.*, **2012**, *2:a006379.* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3810020/

Reinert, Z.; Lengyel, G.; Horne, S.; *J. Am. Chem. Soc.*, **2013**, *135*, 12528-12531.

Reinert, Z.; Horne, S.; *Chem. Sci.*, **2014**, *5*, 3325.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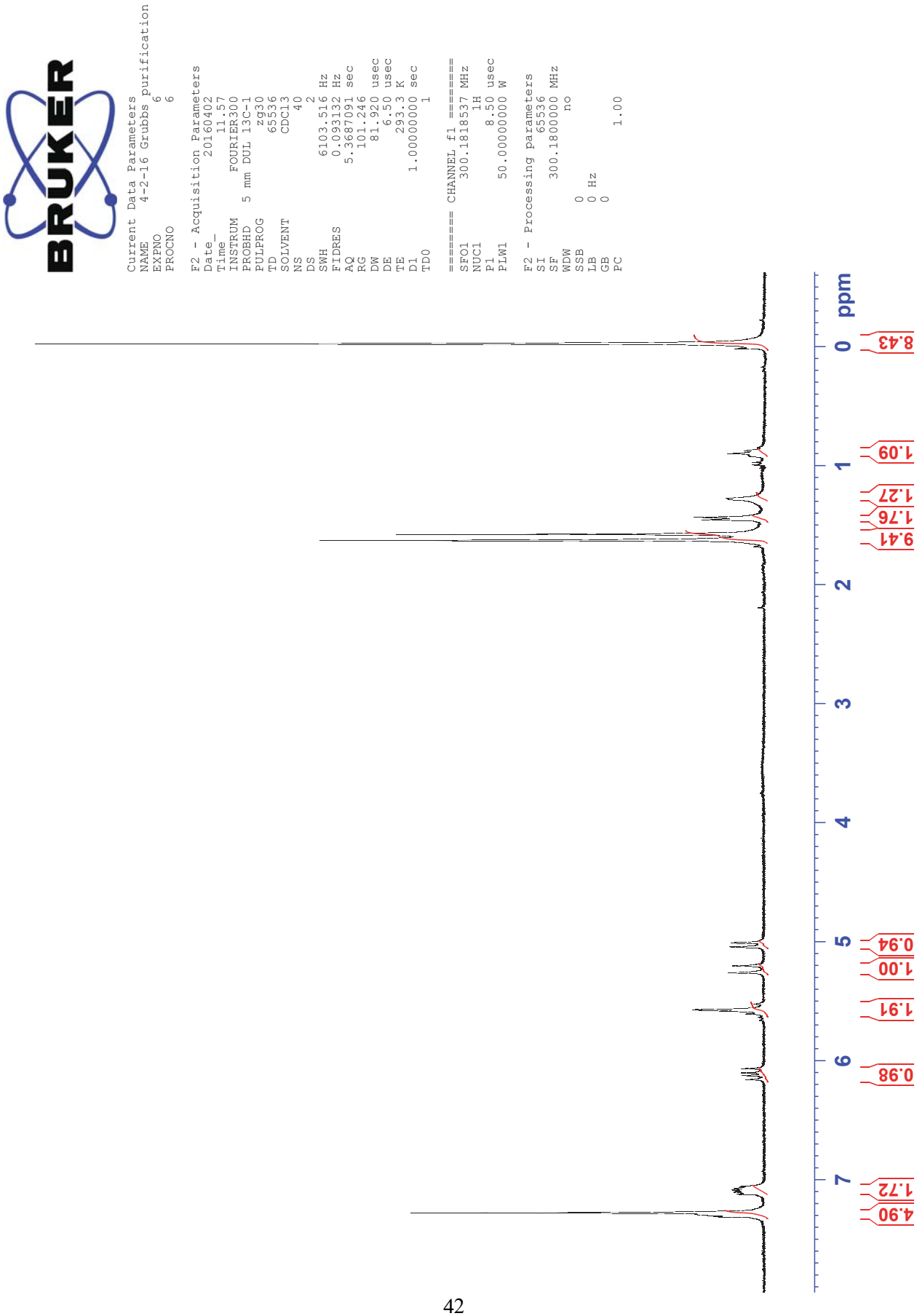
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ppm
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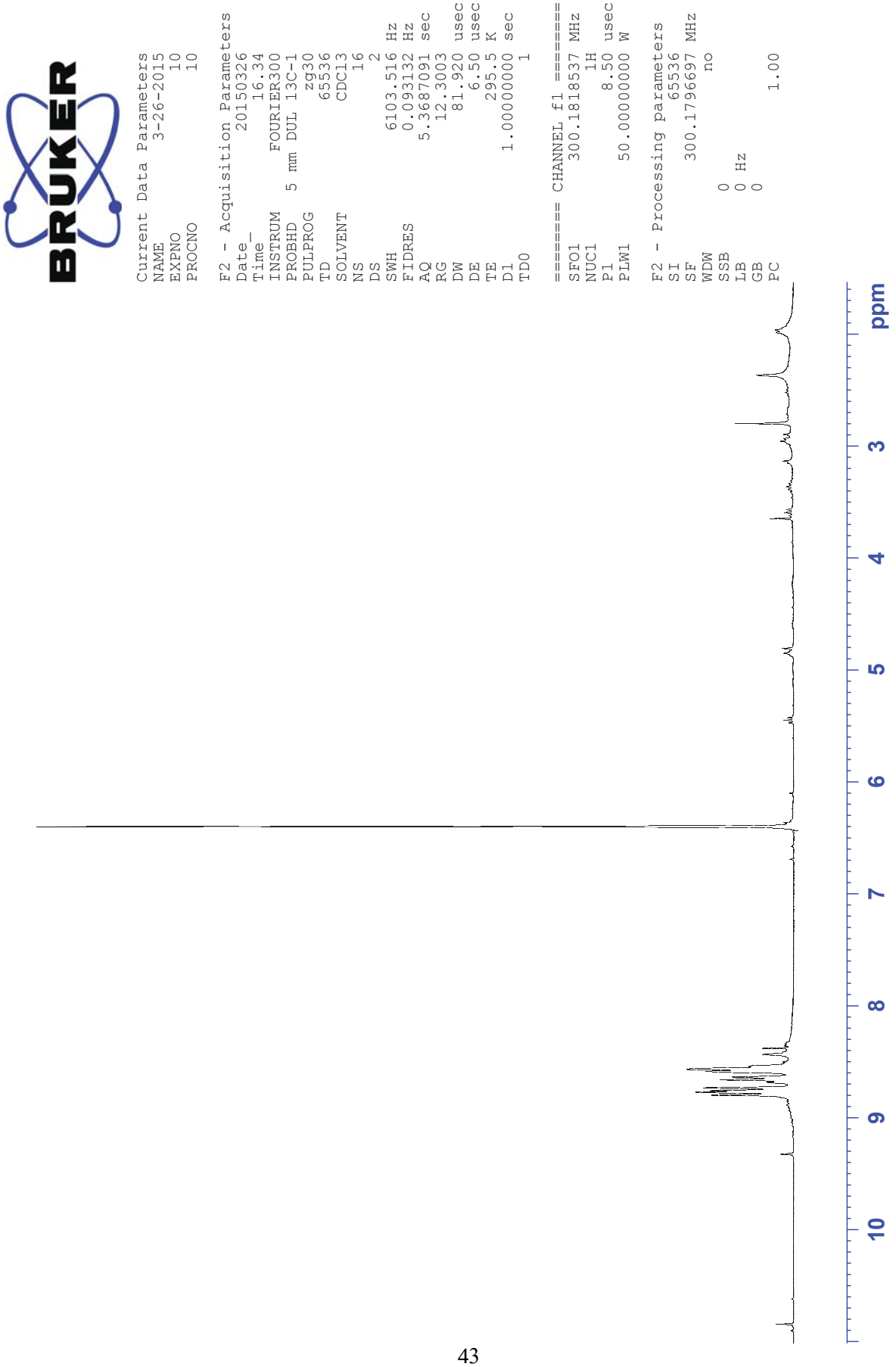
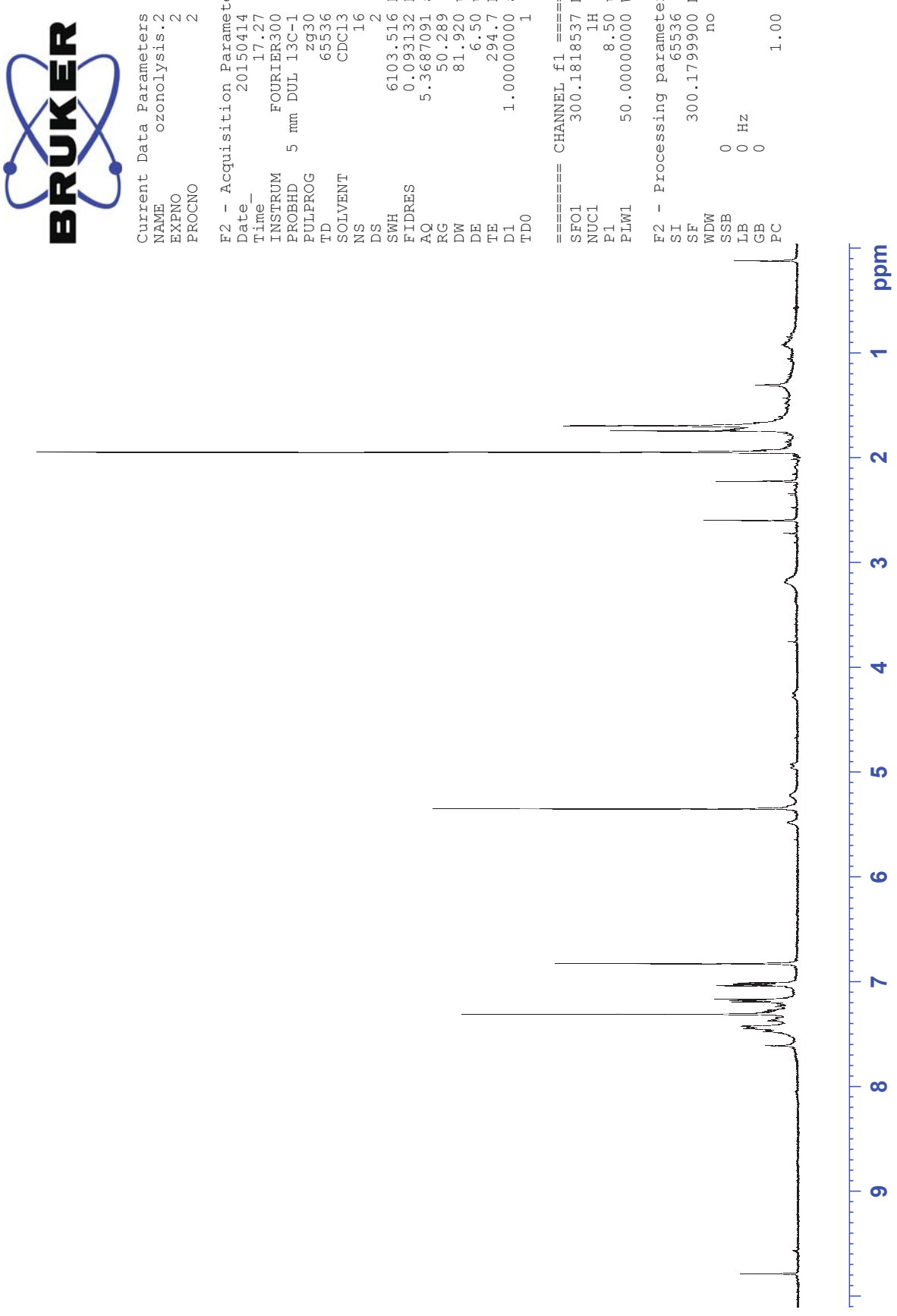
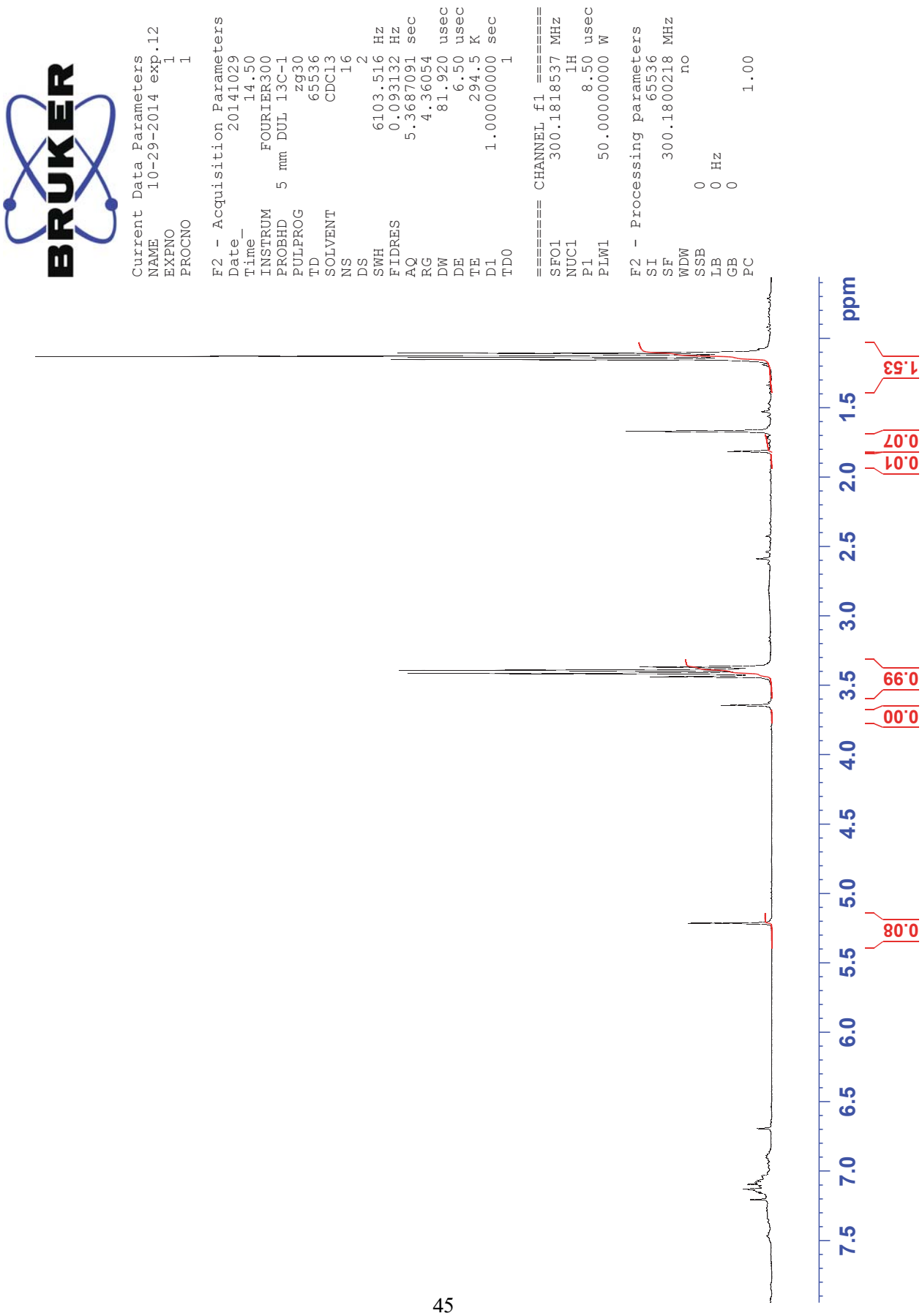
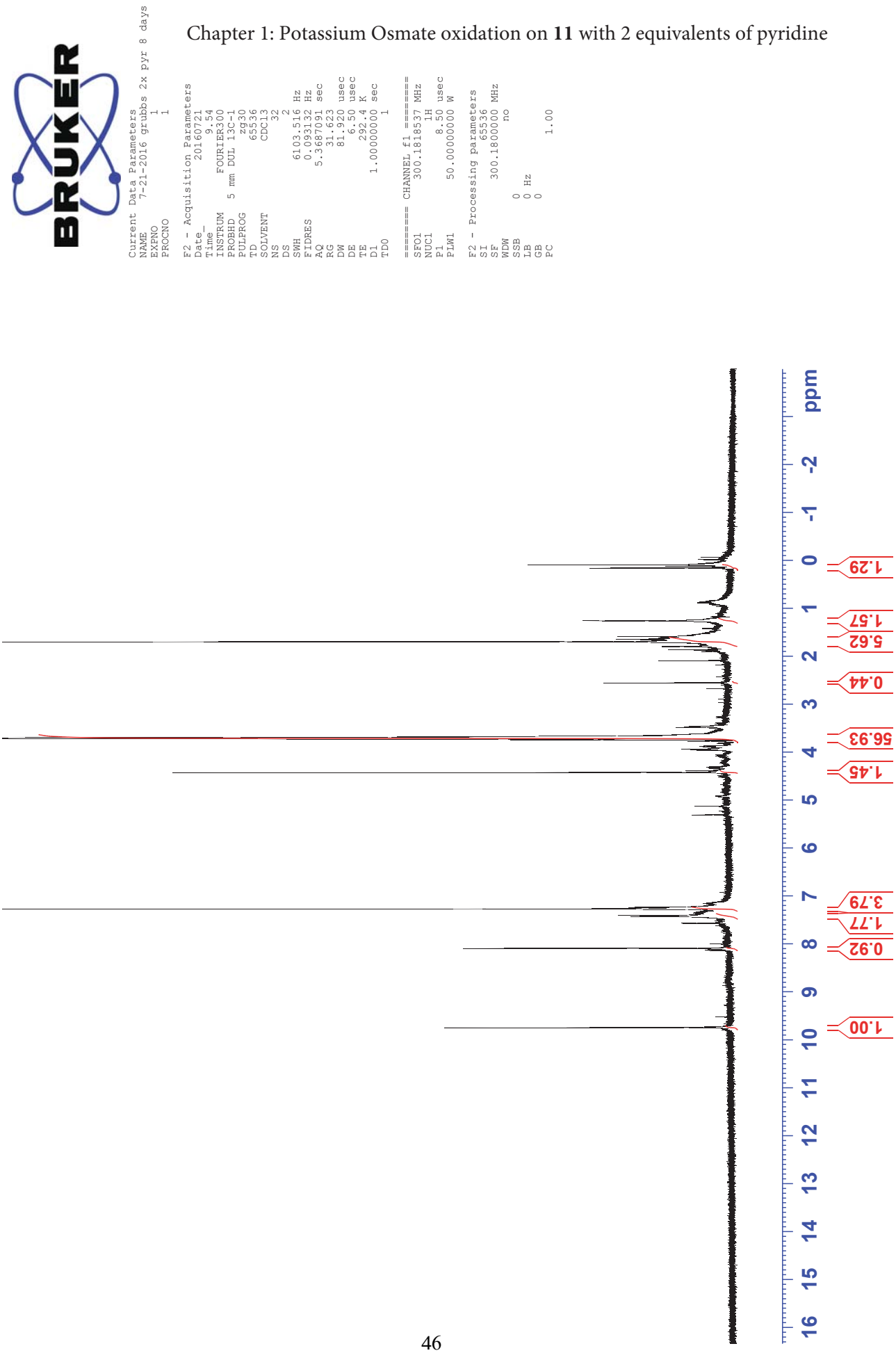
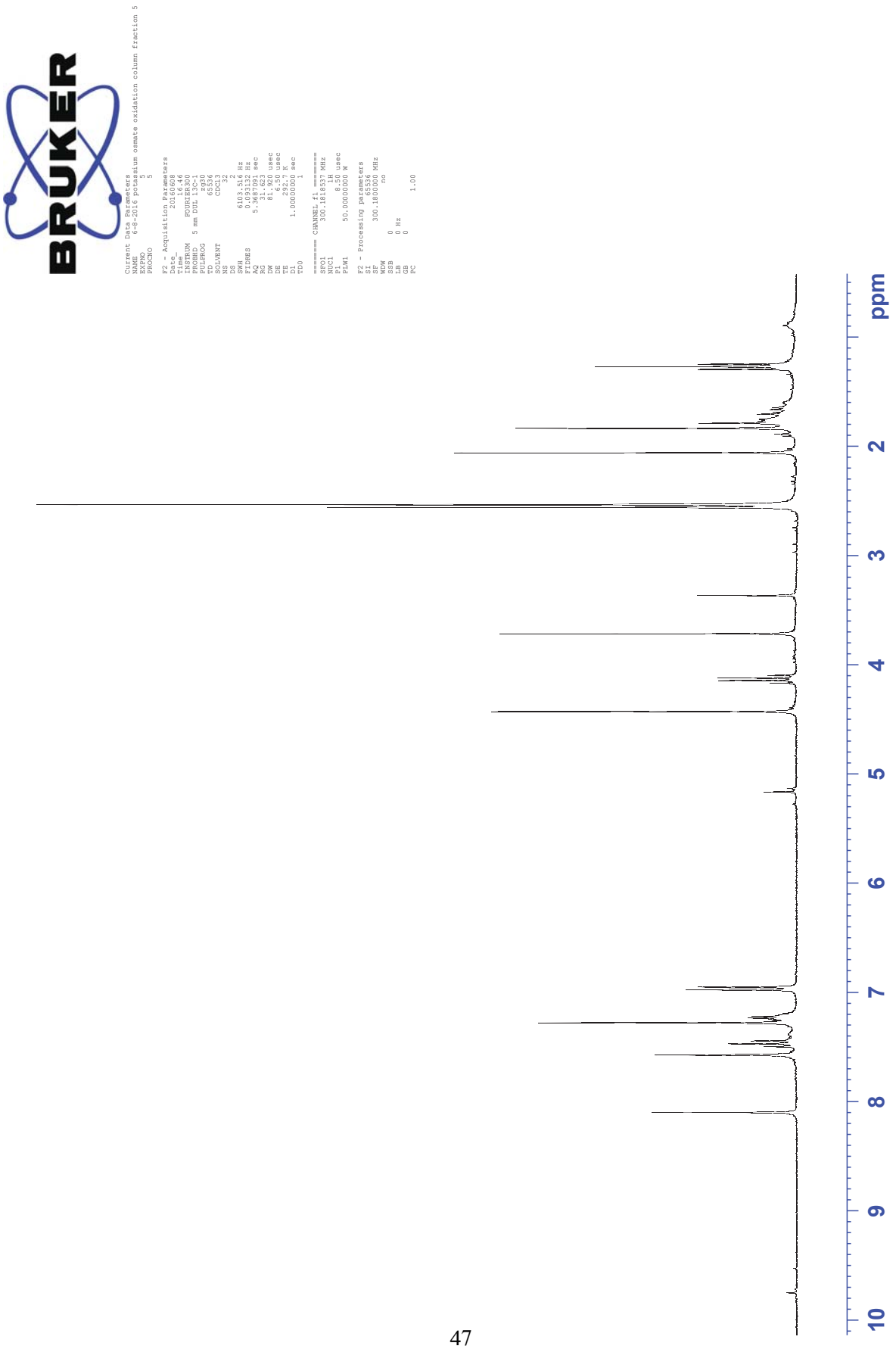
1
2
3
4
5
6
7
8.43
1.09
1.27
1.76
9.41
0.94
1.00
1.91
0.98
1.72
4.90

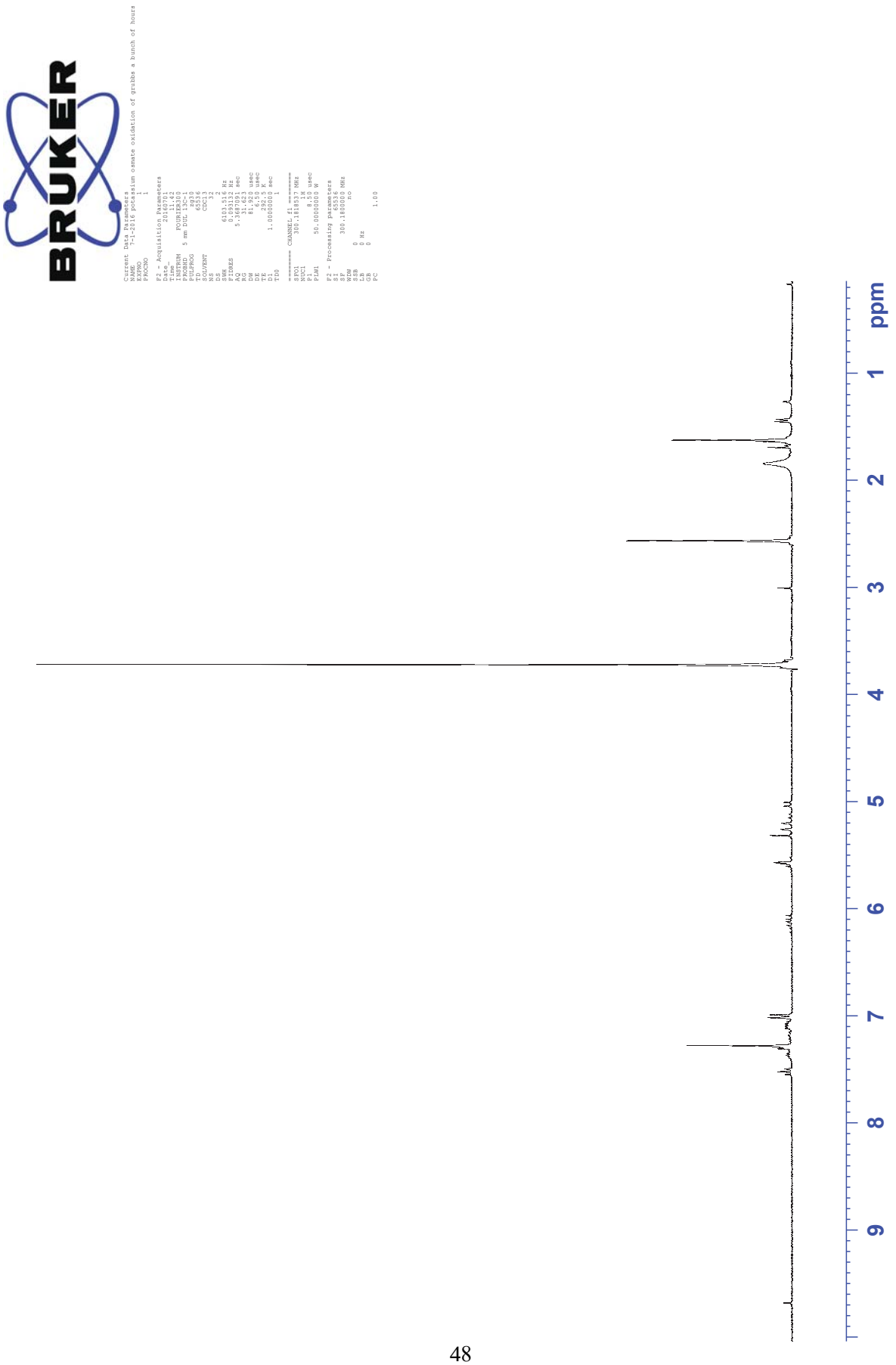

Current Data Parameters
NAME 3-26-2015
EXPNO 10
PROCNO 10
F2 - Acquisition Parameters
Date_ 20150326
Time 16.34
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 12.3003
DW 81.920 usec
DE 6.50 usec
TE 295.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1796697 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
ppm

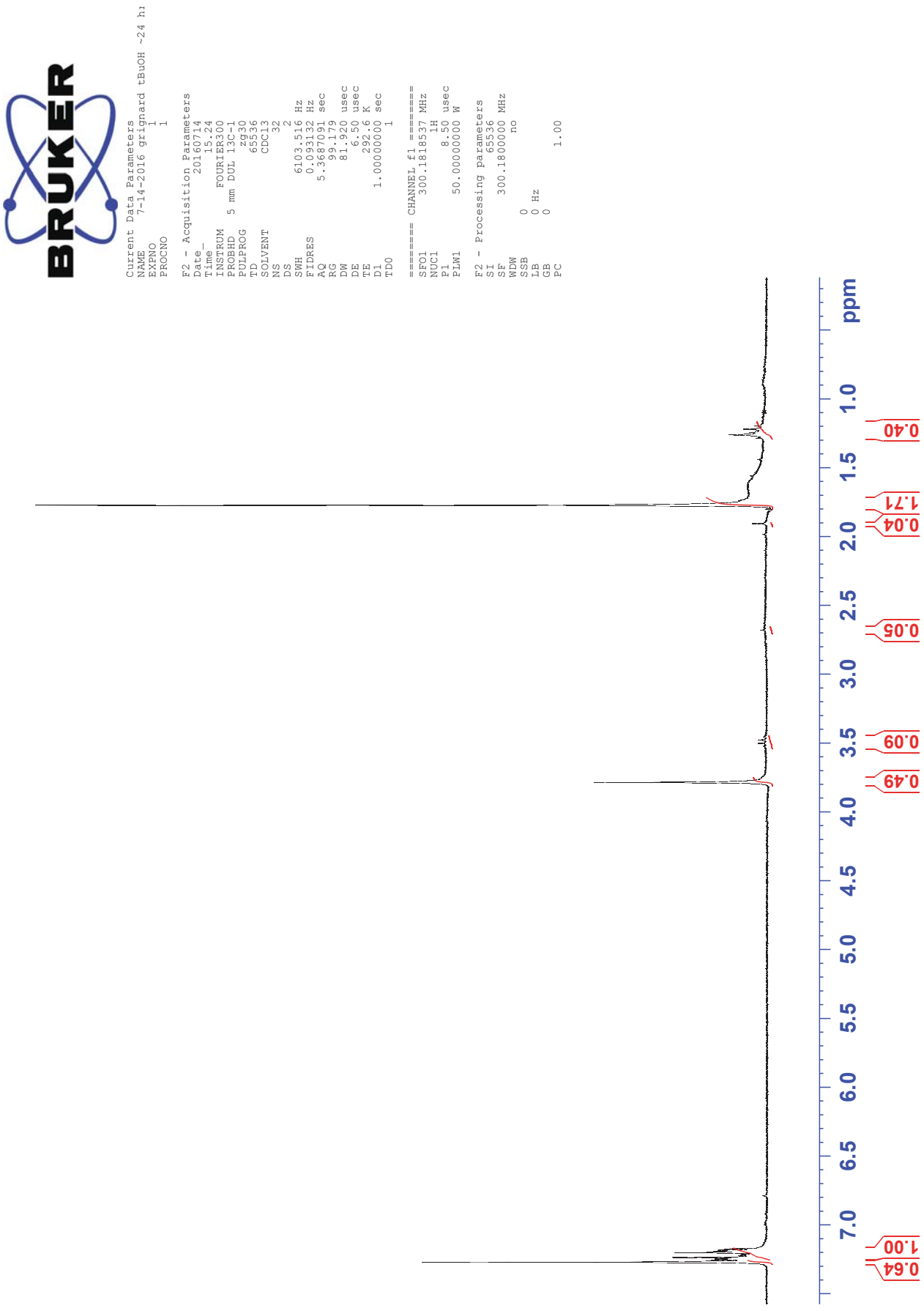

Current Data Parameters
NAME ozonolysis.2
EXPNO 2
PROCNO 2
F2 - Acquisition Parameters
Date_ 20150414
Time 17.27
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.36870912 sec
RG 50.289
DW 81.920 usec
DE 6.50 usec
TE 294.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1799900 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
ppm

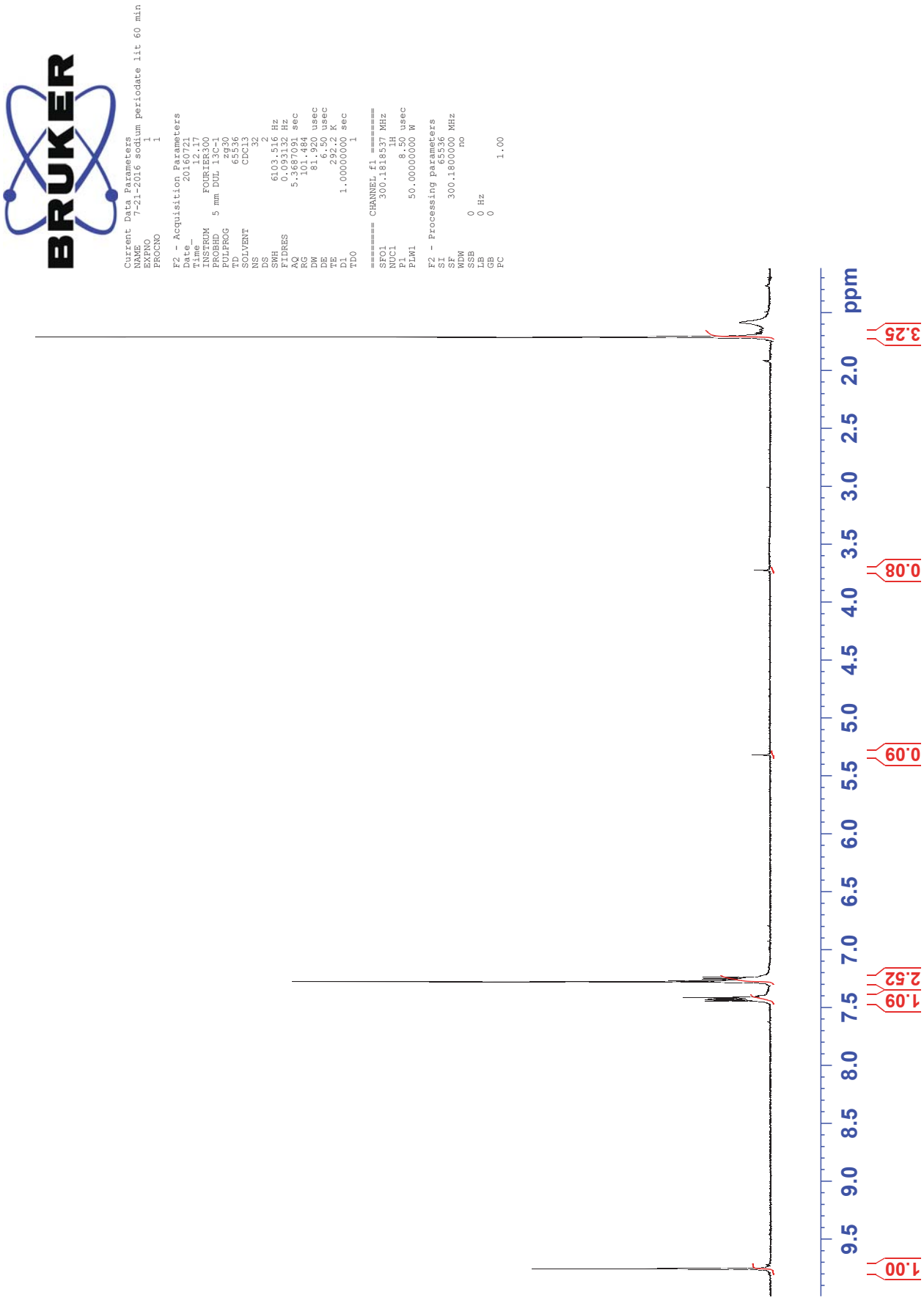

Current Data Parameters
NAME 10-29-2014 exp.12
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141029
Time 14.50
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.36870910 sec
RG 4.36054
DW 81.920 usec
DE 6.50 usec
TE 294.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800218 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.53
0.07
0.01
0.99
0.00
0.08

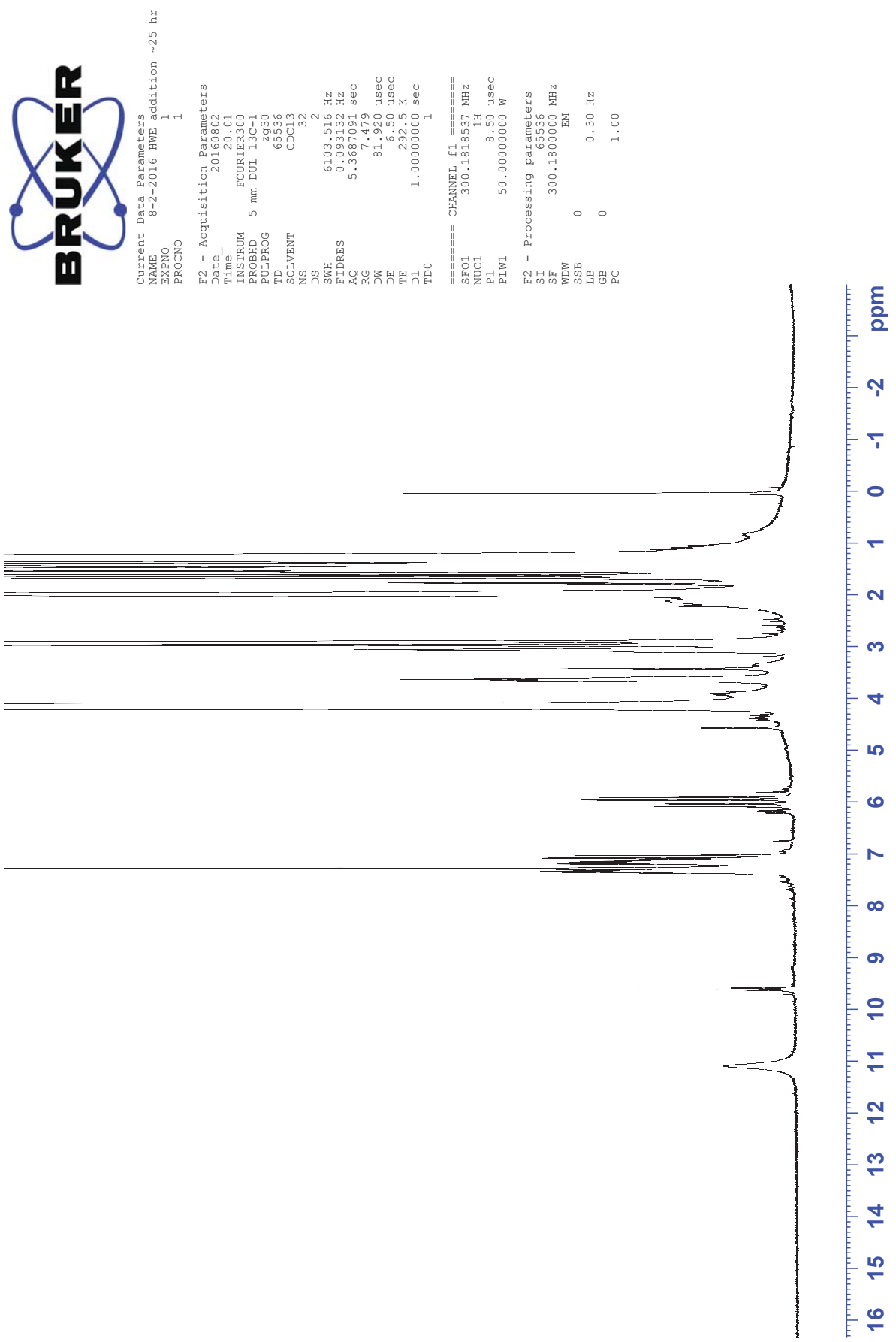

Current Data Parameters
NAME 7-21-2016 grubbs 2x pyr 8 days
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160721
Time 9.54
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 31.623
DW 81.920 usec
DE 6.50 usec
TE 292.4 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
1.29
1.57
5.62
0.44
56.93
1.45
3.79
1.77
0.92
1.00

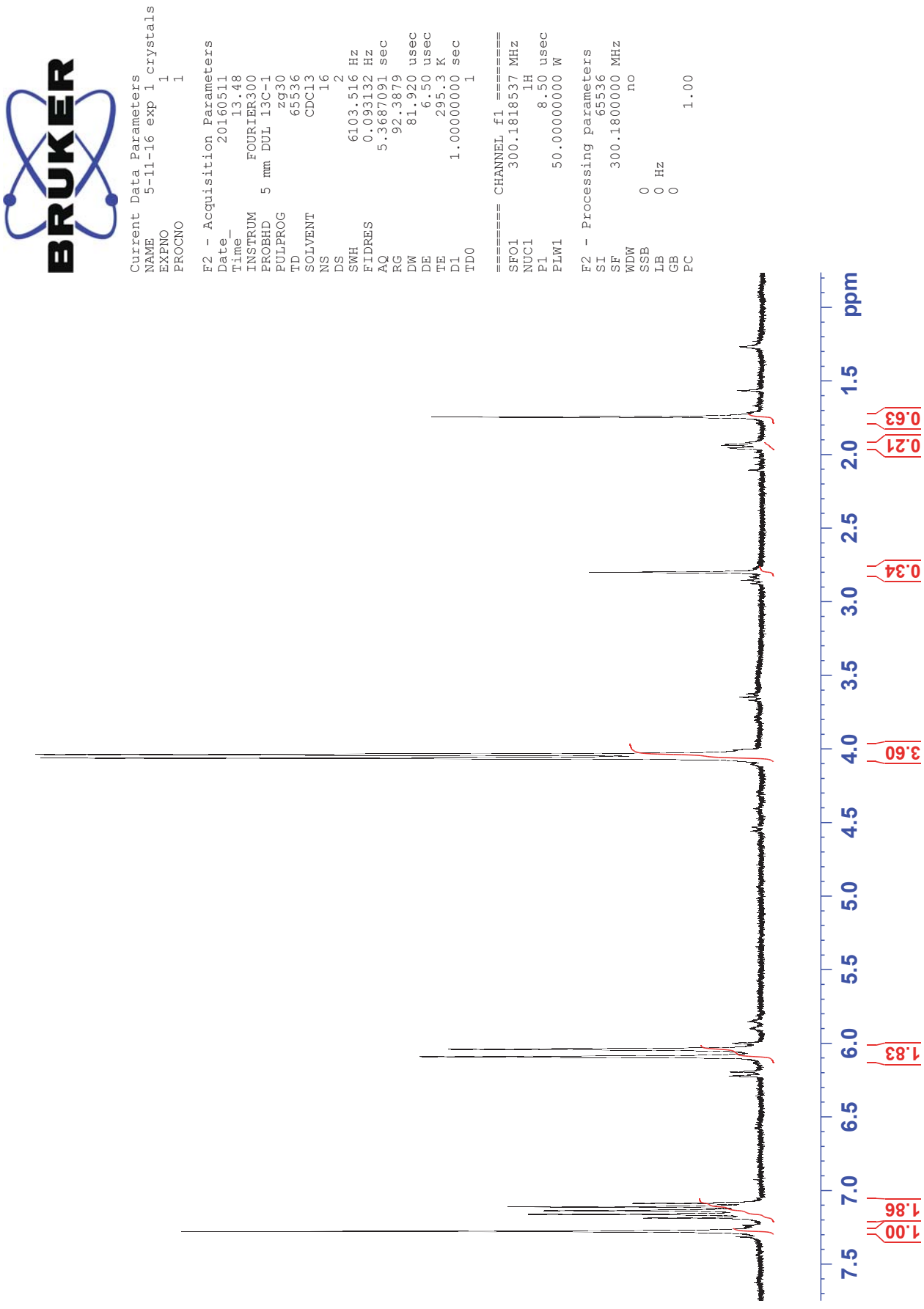

Current Data Parameters
NAME 6-8-2016 potassium osmate oxidation column fraction 5
EXPNO 5
PROCNO 5
F2 - Acquisition Parameters
Date_ 20160608
Time 16.40
INSTRUM POURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3673472 sec
RG 31.623
DW 81.920 usec
DE 6.50 usec
TE 292.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
10
9
8
7
6
5
4
3
2

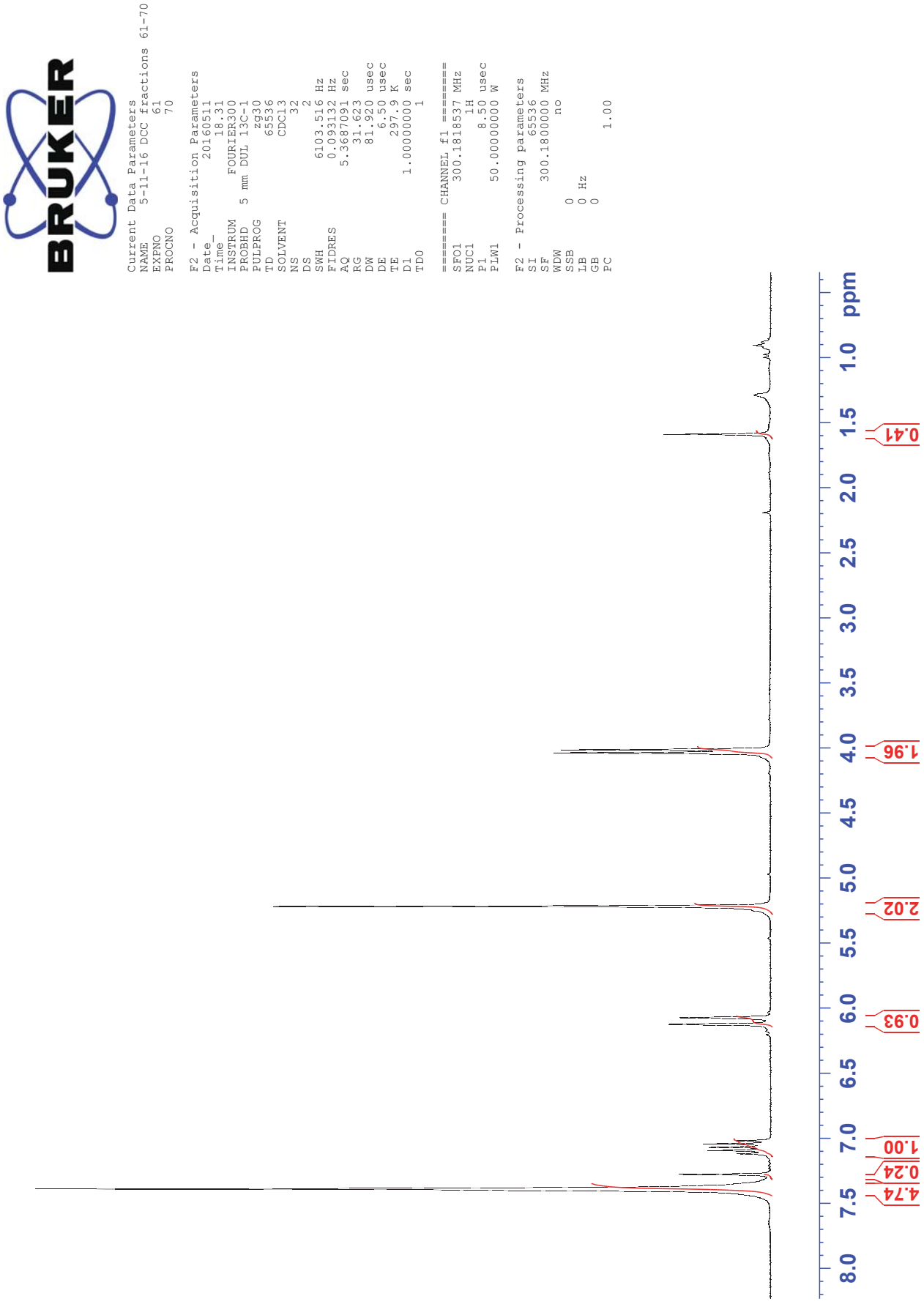

Current Data Parameters
NAME 7-i-2016 potassium osmate oxidation of grubbs a bunch of hours
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160701
Time 14.12
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6103.516 Hz
FIDRES 0.093113 Hz
AQ 5.3687091 sec
RG 161.6
DW 81.920 usec
DE 6.50 usec
TE 293.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SF01 300.1816537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
ppm

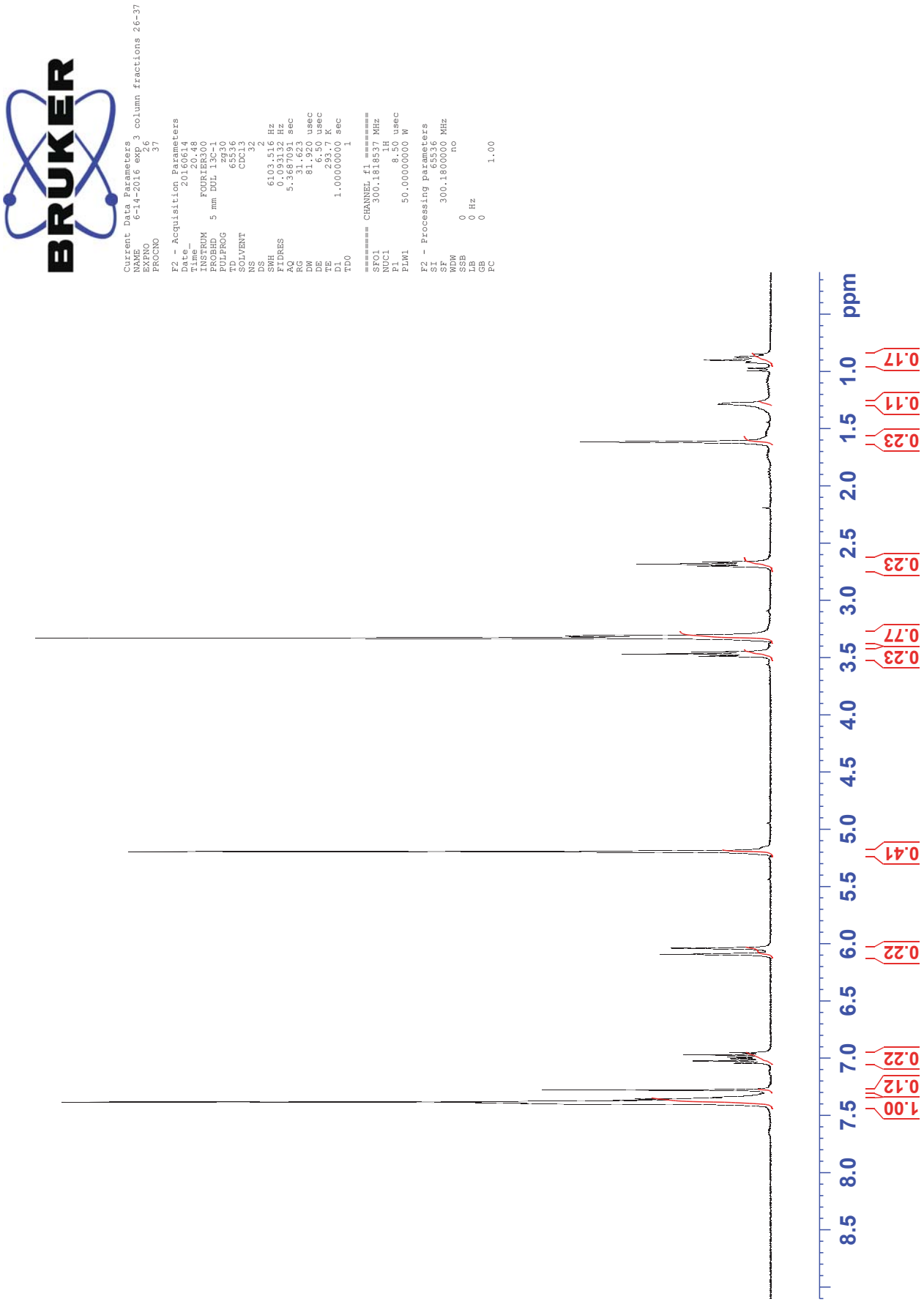

Current Data Parameters
NAME 7-14-2016 grignard tBuOH ~24 h
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160714
Time 15.24
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 99.179
DW 81.920 usec
DE 6.50 usec
TE 292.6 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
0.40
1.71
0.04
0.05
0.09
0.49
0.64
1.00

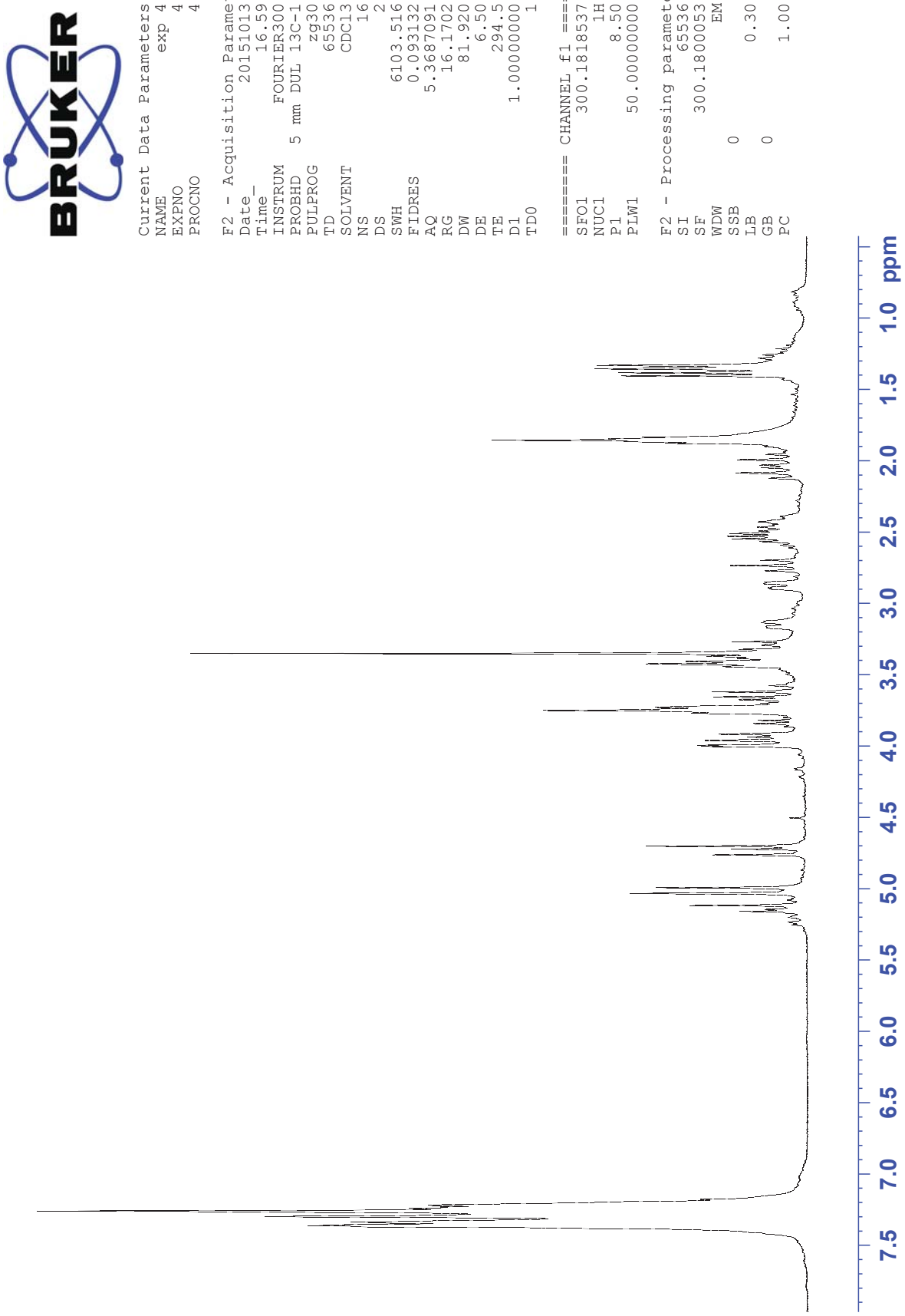

Current Data Parameters
NAME 7-21-2016 sodium periodate 1it 60 min
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160721
Time_ 12.17
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 101.484
DW 81.920 usec
DE 6.50 usec
TE 292.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
3.25
0.08
0.09
2.52
1.09
1.00

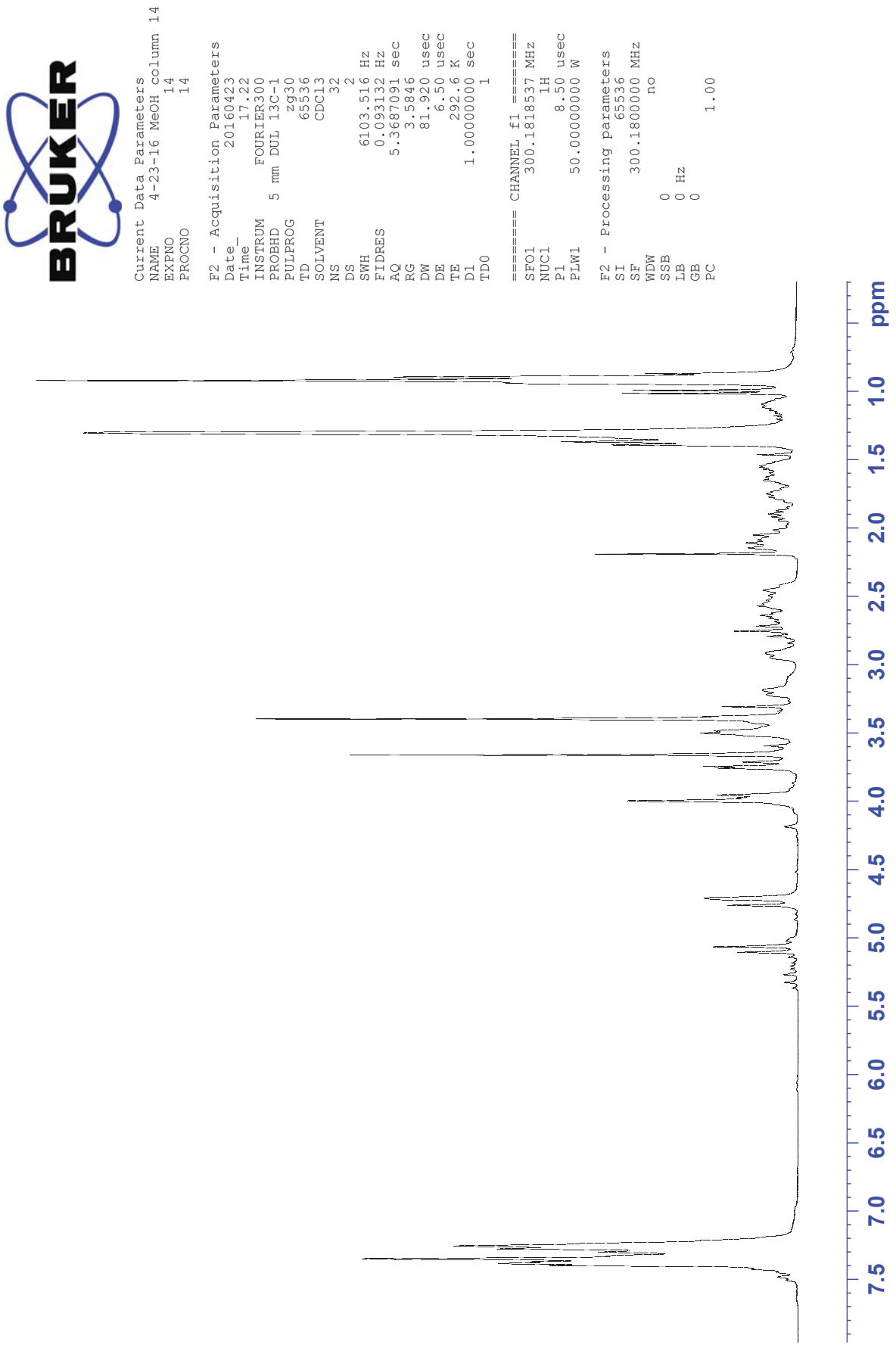

Current Data Parameters
NAME 8-2-2016 HWE addition ~25 hr
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160802
Time_ 20.01
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 7.479
DW 81.920 usec
DE 6.50 usec
TE 292.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 ppm

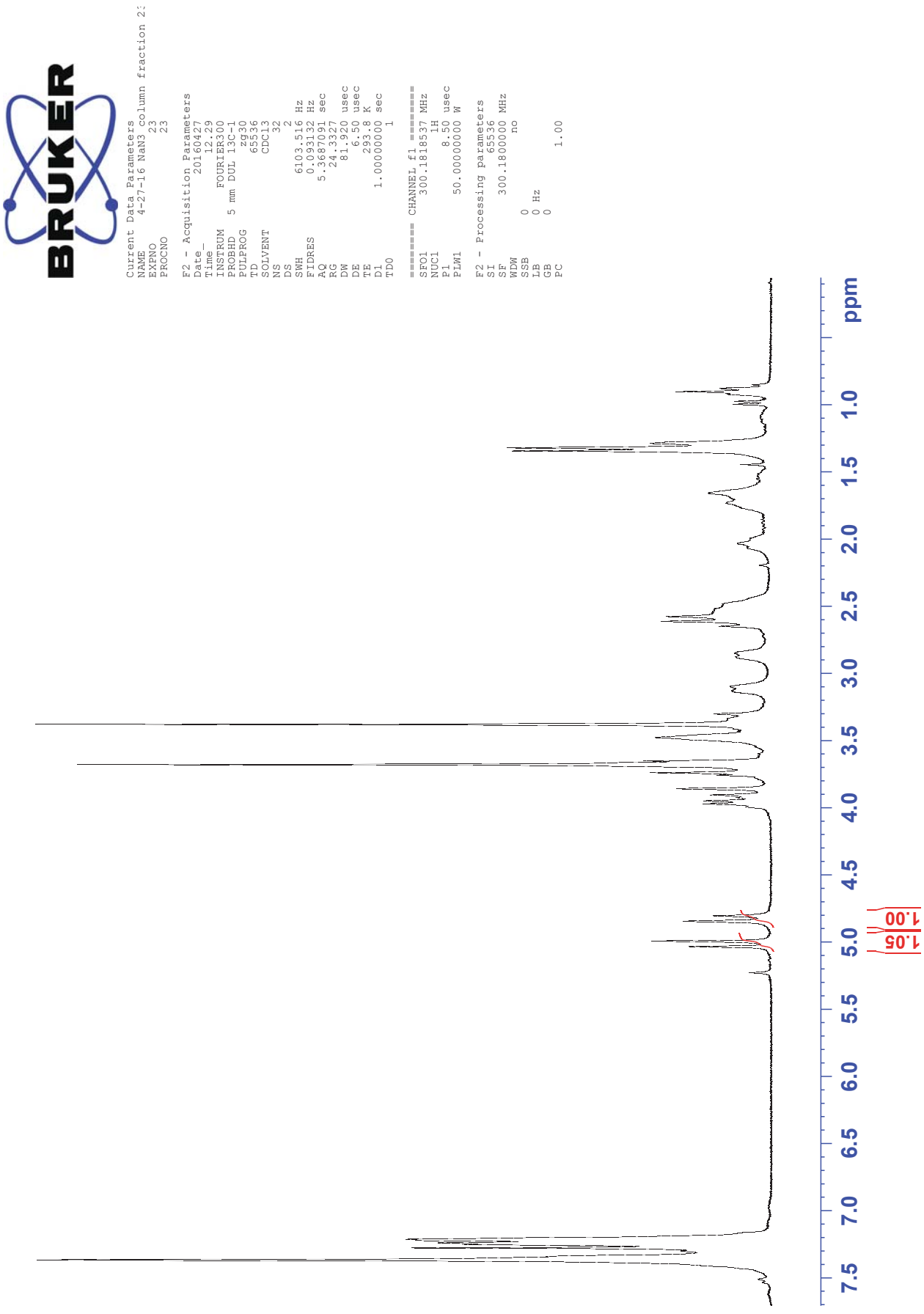

Current Data Parameters
NAME 5-11-16 exp 1 crystals
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160511
Time_ 13.48
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 92.3879
DW 81.920 usec
DE 6.50 usec
TE 295.3 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.86
1.00
1.83
3.60
0.34
0.21
0.63

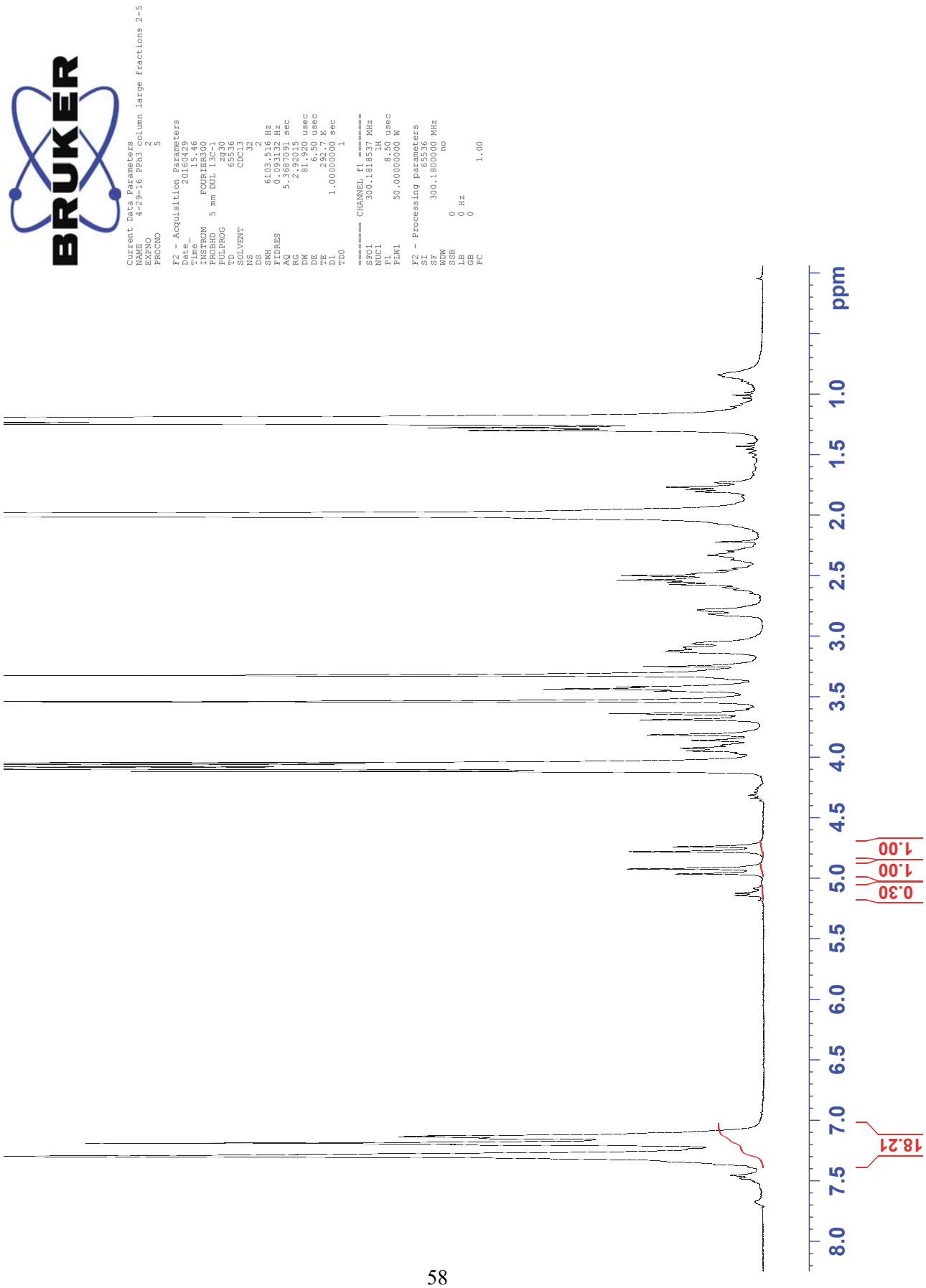

Current Data Parameters
NAME 5-11-16 DCC fractions 61-70
EXPNO 61
PROCNO 70
F2 - Acquisition Parameters
Date_ 20160511
Time 18.31
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 31.623
DW 81.920 usec
DE 6.50 usec
TE 297.9 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
0.41
1.96
2.02
0.93
1.00
0.24
4.74

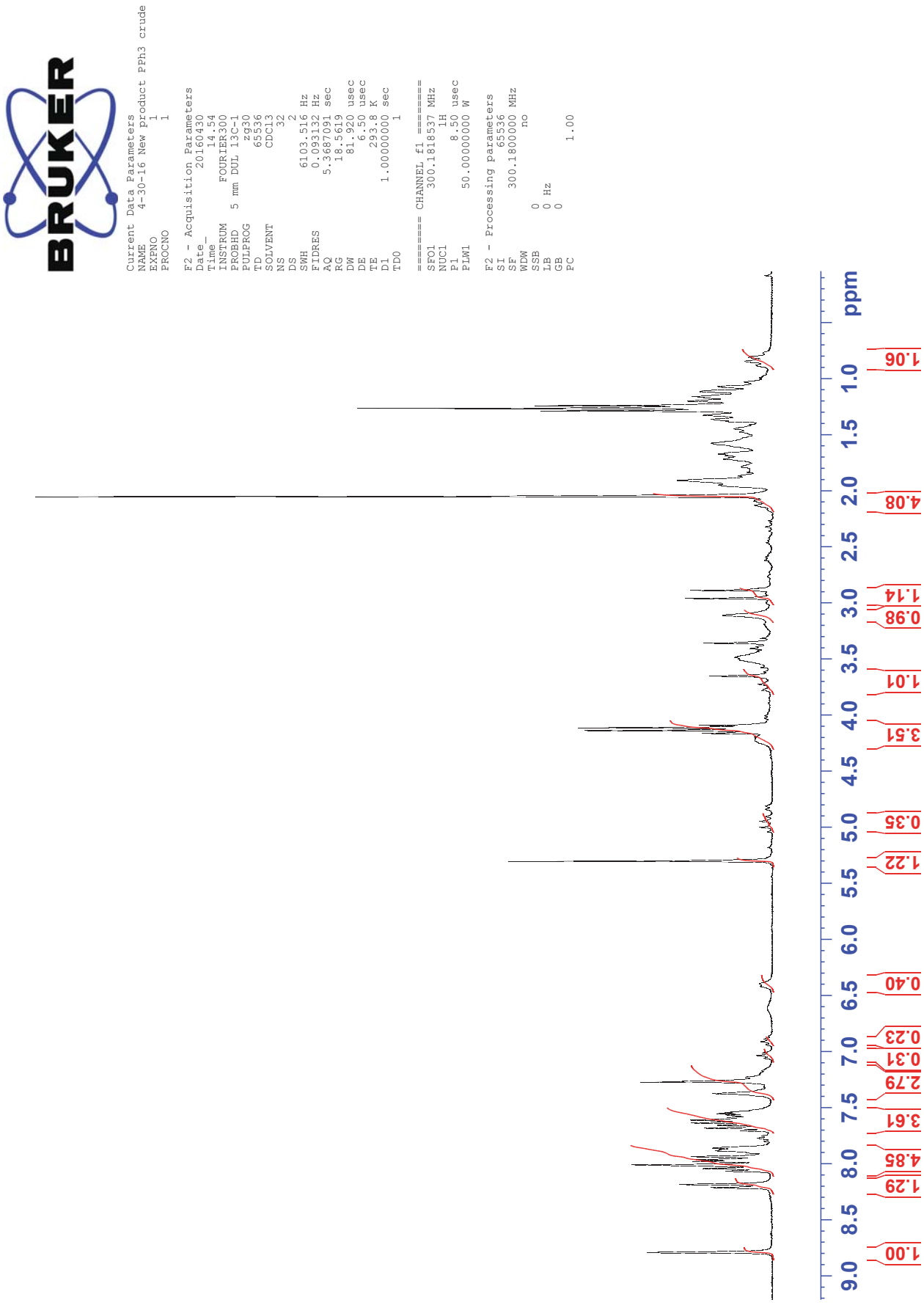

Current Data Parameters
NAME 6-14-2016 exp_3 column fractions 26-37
EXPNO 26
PROCNO 37
F2 - Acquisition Parameters
Date_ 20160614
Time_ 20.48
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 31.623
DW 81.920 usec
DE 6.50 usec
TE 293.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
1.00
0.12
0.22
0.41
0.23
0.77
0.23
0.23
0.11
0.17


Current Data Parameters
NAME exp 4
EXPNO 4
PROCNO 4
F2 - Acquisition Parameters
Date_ 20151013
Time 16.59
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 16.1702
DW 81.920 usec
DE 6.50 usec
TE 294.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


Current Data Parameters
NAME 4-23-16 MeOH column 14
EXPNO 14
PROCNO 14
F2 - Acquisition Parameters
Date_ 20160423
Time_ 17.22
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 3.5846
DW 81.920 usec
DE 6.50 usec
TE 292.6 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


Current Data Parameters
NAME 4-27-16 NaN3 column fraction 2
EXPNO 23
PROCNO 23
F2 - Acquisition Parameters
Date_ 20160427
Time 12.29
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 24.3327
DW 81.920 usec
DE 6.50 usec
TE 293.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
1.05
1.00
ppm


Current Data Parameters
NAME 4-29-16 PPh3 column large fractions 2-5
EXPNO 2
PROCNO 5
F2 - Acquisition Parameters
Date_ 20160429
Time_ 15.46
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 2.92015
DW 81.920 usec
DE 6.50 usec
TE 292.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
18.21
0.30
1.00
1.00


Current Data Parameters
NAME 4-30-16 New product PPh3 crude
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160430
Time 14.54
INSTRUM FOURIER300
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6103.516 Hz
FIDRES 0.093132 Hz
AQ 5.3687091 sec
RG 18.5619
DW 81.920 usec
DE 6.50 usec
TE 293.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 300.1818537 MHz
NUC1 1H
P1 8.50 usec
PLW1 50.00000000 W
F2 - Processing parameters
SI 65536
SF 300.1800000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1.00
1.29
4.85
3.61
2.79
0.31
0.23
0.40
1.22
0.35
3.51
1.01
0.98
1.14
4.08
1.06