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Heterolithic branched liquid crystalline materials prepared via the Passerini three-component reaction

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Abstract of the Dissertation

Heterolithic branched liquid crystalline materials prepared via the Passerini three-component reaction

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Precisely defined and multifunctional molecular architectures that can form liquid crystalline mesophases are part of a new generation of functional supramolecular materials. Liquid crystalline compounds (mesogens) form phases of matter intermediate between crystalline solids and isotropic liquids (mesophases). The presence of molecular order in a fluid phase has led to the widespread use of conventional liquid crystal mesogens in displays and optoelectronic devices. Combining different types of mesogens or mesogens with other functional components to create heterolithic star-branched or dendritic architectures is of interest as a strategy to engineer liquid crystalline materials with new structural and functional properties. Heterolithic branched molecular architectures are difficult to synthesize, and so very little is known about the properties of heterolithic star-branched or dendritic mesogens. This thesis demonstrates that highly convergent synthesis strategies based on multicomponent reactions can accelerate the synthesis of heterolithic branched compounds. We employed the Passerini three-component reaction in the most convergent synthesis of a star-branched mesogen in which each arm is composed of a different calamitic mesogen and flexible linker (i.e., an ABC star-branched mesogen). The ABC star-branched mesogen forms a mesophase that is more ordered than the mesophases observed in more symmetric star-branched mesogens. The

modularity of the Passerini reaction was exploited to prepare focused libraries of mesogens. Differential scanning calorimetry (DSC), polarized optical microscopy (POM), and X-ray diffraction (XRD) experiments with materials from these focused libraries established how each arm contributes to the phase behavior of the ABC star-branched mesogens. Analysis of the DSC data confirmed the limited stability of the mesophases formed by the ABC star-branched mesogens. Higher molecular weight analogs of the ABC star-branched mesogens (i.e., triblock dendrimers) are expected to improve the stability of the mesophase. Kinetic studies of model Passerini reactions identified an electronic effect that accelerates the reaction, and this enhanced reactivity has enabled the synthesis of three generations of dendrimers via the Passerini three-component reaction. This work has demonstrated a rapid approach to synthesize heterolithic star-branched mesogens and the feasibility to prepare multifunctional dendritic mesogens via the Passerini reaction.

Table of Contents

Chapter 3

Three-Arm Star-branched Mesogens Based on an α-Acyloxyamide Core

Chapter 4

Enhanced Reactivity of Dendrons in the Passerini Three-Component Reaction

List of Figures

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Schemes

Chapter 2

List of Tables

Chapter 2

Chapter 3

Chapter 4

List of Abbreviations

δ	chemical shift
Ac	acetyl
Ar	aryl
Bu	Butyl
CB	cyanobiphenyl
DCE	1,2-dichloroethane
DSC	differential scanning calorimetry
DMF	*N*,*N*-dimethylformamide
d	doublet (NMR)
dd	doublet of doublets (NMR)
dt	doublet of triplets (NMR)
e.g.	exempli gratia (Latin meaning "for example")
ESI	electrospray ionization
Et	ethyl
et al.	et alii (Latin meaning "and others")
etc	et cetera
EtOAc	ethyl acetate
FTIR	Fourier transform infrared spectroscopy
g	glassy phase; or the unit of mass grams when preceded by a number
g/mol	grams per mole
GPC	gel permeation chromatography
h	hours
HRMS	high-resolution mass spectrometry
Hz	Hertz
i	isotropic
i.e.	id est (Latin meaning "it is" or "that is")
iPr	isopropyl

IR	infrared
J	coupling constant
k	kilo- (scale); crystalline
L	liter
LC	liquid crystal or liquid crystalline
M	mega- (scale); molar
m	milli- (scale); multiplet (NMR)
MB	methoxybiphenyl
MCR	multicomponent reaction
Me	methyl
M_n	number-average molecular weight
Ms	mesyl (methanesulfonyl)
MS	mass spectrometry
M_w	weight-average molecular weight
n	nano- (scale)
N	nematic
NMR	nuclear magnetic resonance
p	para
PAMAM	poly(amidoamine)
PCC	pyridinium chlorochromate
Ph	phenyl
POM	polarized optical microscopy
ppm	parts per million
Pr	propyl
q	quartet
rt	room temperature
R_f	retention factor
s	second (time); singlet (NMR)
S	sinister (Latin meaning “Left”)
Sm	smectic
(*S*)MB	(*S*)-2-methylbutoxybiphenyl

t	time; triplet (NMR)
t	tert
td	triplet of doublets (NMR)
THF	tetrahydrofuran
TLC	thin layer chromatography

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Chapter 1

1. General Introduction

1.1 Star-branched and dendritic liquid crystal mesogens

Liquid crystalline materials are widely used in optoelectronic devises[1-2] because the anisotropic molecular order present in the mesomorphic state is responsive to field parameters (e.g., temperature, magnetic fields, and applied voltages). Molecules that form liquid crystalline phases are called mesogens. Conventional liquid crystal mesogens are low-molecular weight compounds having either a rod-like (i.e., calamitic mesogens) or a disk-like shape (i.e., discotic mesogens) (Figure 1.1a).[3-8] Liquid crystalline phases are fluid states of matter, so the molecules are highly mobile yet not completely disordered. Nematic phases of rod-like and disk-like mesogens are examples of liquid crystalline mesophases that possess orientational order but not positional order of the mesogens (Figure 1.1b). The mesogens are organized such that their long axes are pointing in the same direction, but there is no positional registry between the mesogens. Switching the orientation of nematic mesogens so that the long axes are pointing in the direction of or orthogonal to the direction of propagating light serves as the operating principle for liquid crystal displays.[5, 9] The presence of positional and orientational order in liquid crystal phases of calamitic mesogens leads to smetic phases where the mesogens are arranged in layers (Figure 1.1b). Discotic mesogens can stack into columns that organize into various two-dimensional lattices (e.g., columnar hexagonal phase) (Figure 1.1b). Expanding the range of anisotropic molecular shapes and molecular topologies that are compatible with liquid crystal phase formation is of interest to broaden the diversity of mesophases and for potential new applications of liquid crystals.[3, 10-12]

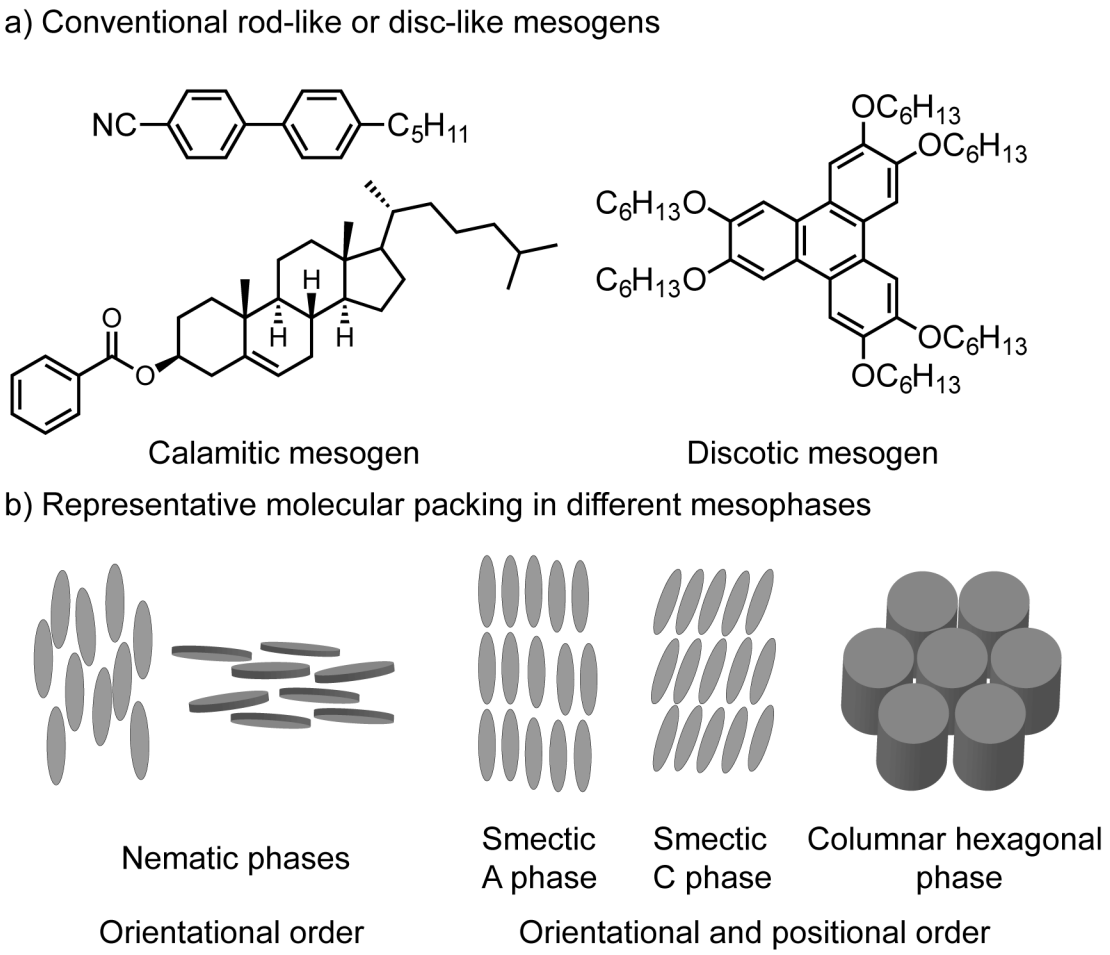


Figure 1.1. Conventional liquid crystalline molecules and their mesophases.

The branched topology of dendritic macromolecules is an intriguing scaffold for the design of novel liquid crystalline materials.[13] Dendrimers are perfectly branched polymers composed of branched monomers arranged in layers around a branched core. Figure 1.2a presents a schematic illustration of a series of dendrimers ranging from the branched core (i.e., G0) to a third-generation (G3) dendrimer. The generation number of a dendrimer refers to the number of layers branched repeat units. Each layer is color coded in Figure 1.2a. The molecular weight, physical size (e.g., diameter), and number of peripheral end groups increase with increasing generation. The nanometer-sized dimensions, limited molecular entanglement, and

well-defined structure of dendrimers are attractive features for tailoring the physical properties and nanoscale structure of liquid crystals.

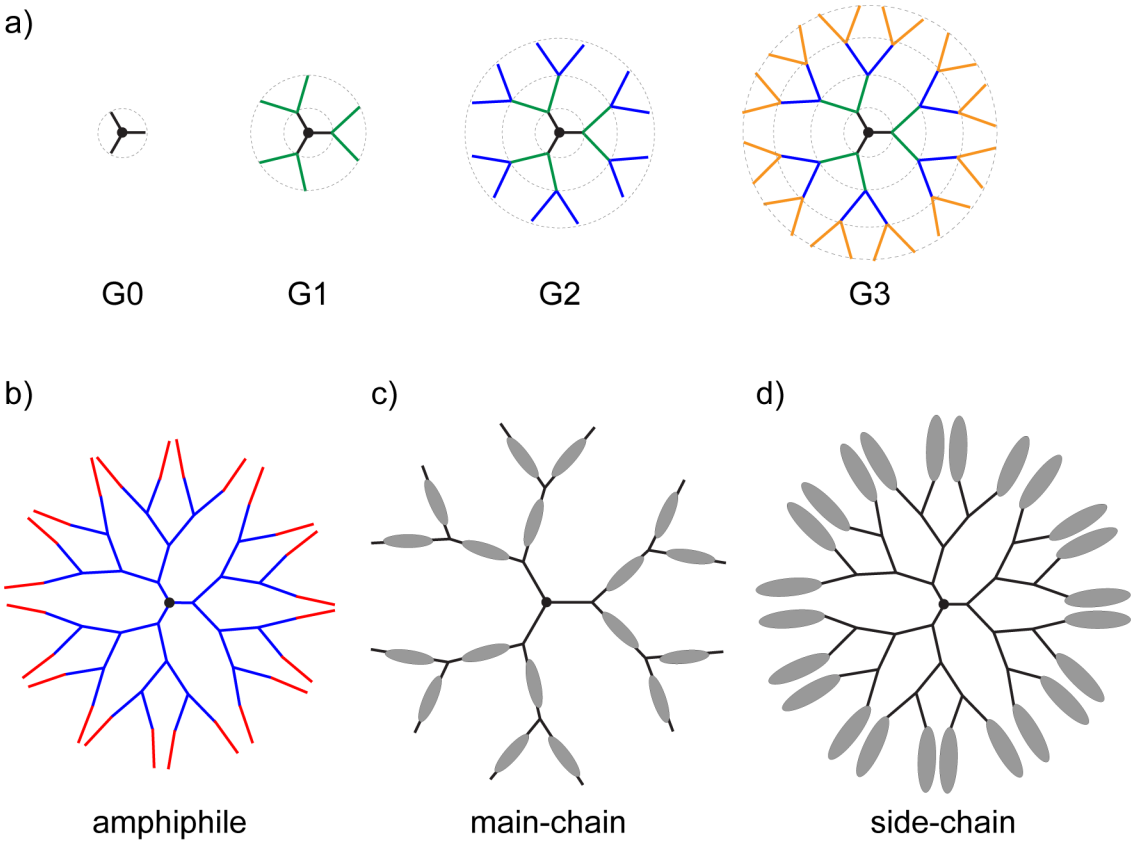


Figure 1.2. Dendrimers of different generations and strategies to introduce liquid crystalline dendrimers.

Three strategies for designing liquid crystalline dendrimers have emerged, and these molecular architectures are illustrated in Figure 1.2b-d. Amphiphilic dendrimers that have immiscible periphery and branched segments (Figure 1.2b) form liquid crystal mesophases due to segregation between the incompatible segments.[14-15] Main-chain liquid crystalline dendrimers have conventional mesogens within the branched repeat units (Figure 1.2c). By far, the most common and successful approach to design liquid crystal dendrimers is to attach mesogens to the periphery of a dendrimer.[16-17] Liquid crystal dendrimers of this last type are referred to as side-chain liquid crystalline dendrimers (Figure 1.2d).

The lowest generation (G0) side-chain liquid crystal dendrimers (Figure 1.2a) belong to another class of non-conventional mesogens, star-branched mesogens.[17-18] Star-branched mesogens are composed of a branched core through which linear mesogenic arms are attached.[19-20] Star-branched mesogens wherein each of the arms is identical to the others are referred to as either homolithic or symmetric stars. The number of arms emanating from the core can vary depending on the structure of the core moiety, but three- and four-arm star-branched mesogens are among the most common examples. Compared to higher generation dendrimers, star-branched mesogens are more convenient to synthesize.

Star-branched mesogens are useful models for exploring the phase behavior of side-chain liquid crystalline dendrimers. The mesophases of star-branched mesogens and side-chain liquid crystalline dendrimers persist over a wider range of temperatures (i.e., are more stable) than the corresponding conventional, monomeric mesogen.[8, 13] The phase behavior of star-branched mesogens and side-chain liquid crystalline dendrimers is determined almost exclusively by the structure of the terminal mesogens. Star-branched mesogens[21-23] and side-chain liquid dendrimers[24-25] with terminal calamitic mesogens exhibit nematic and/or smectic phases. Star-branched mesogens[26-28] and side-chain liquid dendrimers[29-30] with terminal discotic mesogens exhibit columnar mesophases. Only in one case has it been observed that, upon increasing the generation of a side-chain liquid crystalline dendrimer, the branched topology of a high-generation dendrimer induced a columnar mesophase from a dendrimer bearing calamitic mesogens.[13] This lone example helps to emphasize that the primary effects of increasing generation compared to star-branched mesogens are to further stabilize the mesophase and to increase the characteristic dimensions of the mesophase.

Introducing more than one type of mesogen in a side-chain liquid crystalline dendrimer has the potential to enrich the phase behavior of these liquid crystalline materials. Star-branched

mesogens and side-chain liquid crystalline dendrimers usually exhibit only one type of mesophase or two closely related mesophases (e.g., smectic A and smectic C phases). Liquid crystal polymorphism has been engineered into dendrimers bearing two different types of mesogens.[31-35] Novel mesophases have also been observed in star-branched mesogens with three structurally different arms[31] and in amphiphilic diblock dendrimers with two mutually incompatible peripheral groups.[36] Increasing the diversity of terminal mesogen groups in star-branched mesogens and side-chain liquid crystalline dendrimers is expected to further expand the diversity of liquid crystalline properties.

1.2 Diblock liquid crystalline dendrimers

Diblock dendrimers are dendrimers in which two different types of end group are arranged in clusters at the periphery of a dendrimer. Most commonly, diblock dendrimers are made by directly coupling two dendrons. The first examples of diblock dendrimers were reported by Wooley, Hawker, and Fréchet.[37-39] However, interest in diblock dendrimers remained low until Saez and Goodby reported the first example of a liquid crystalline diblock dendrimer, which they referred to as a Janus liquid crystalline dendrimer (Figure 1.3a).[31]

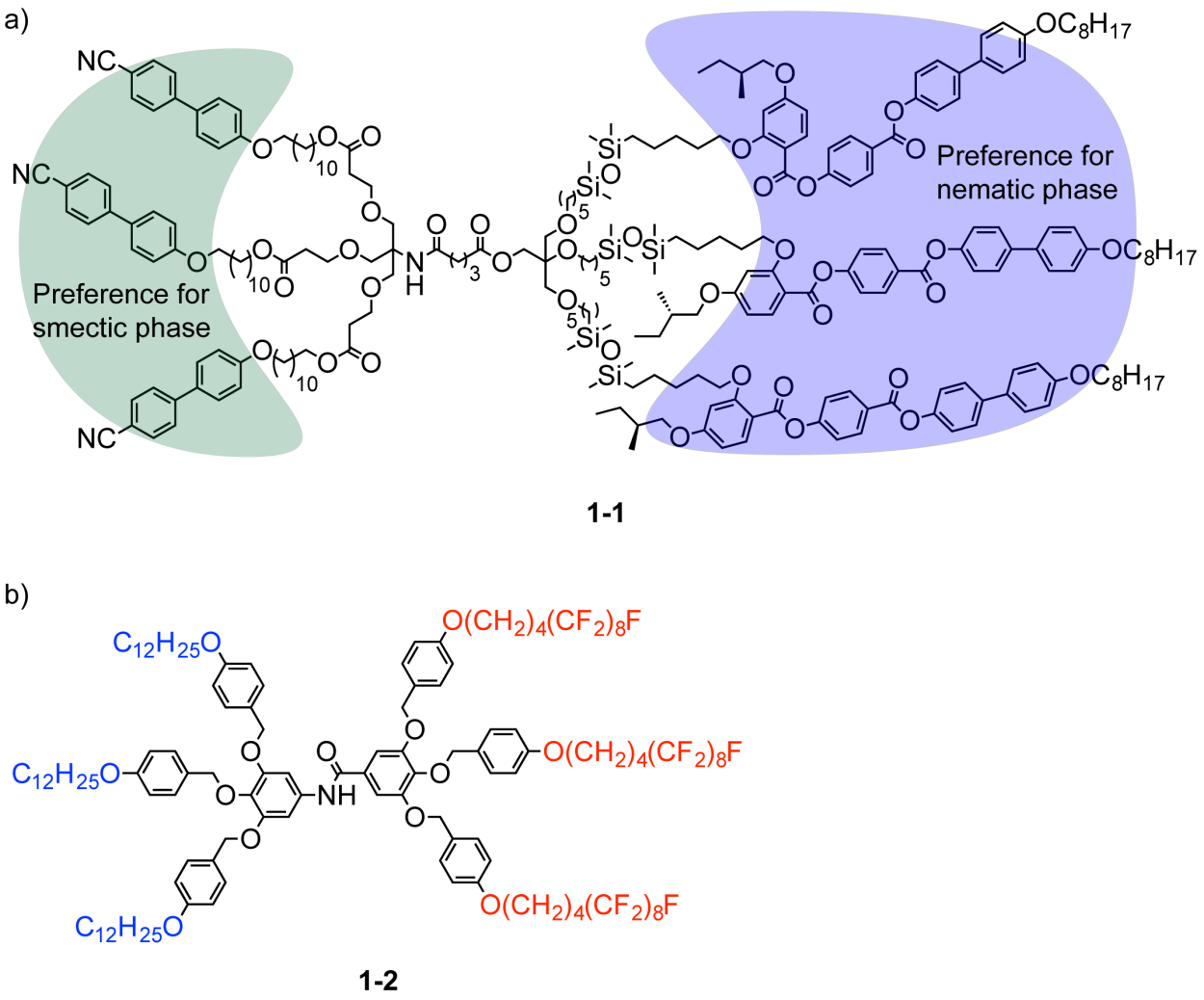


Figure 1.3. Janus liquid crystalline dendrimers by Saez and Goodby [31] and Percec et al.[36]

Combining two dendrons that prefer to form different types of mesophases (e.g., nematic and smectic phases) due to types of peripheral mesogens on the dendrons leads to dendrimers that can exhibit both phases. In their seminal work,[31] Saez and Goodby combined an achiral mesogen that prefers to form a smectic phase with a chiral mesogen that forms a chiral nematic (a.k.a., cholesteric) phase (Figure 1.3a). The resulting dendrimer (**1-1**) reversibly interconverts between a chiral nematic phase at higher temperature and a chiral smectic C phase at lower temperature.[31] The individual mesogens are immiscible and cannot be blended. Covalently

tethering the mesogens to the dendrimer in a diblock arrangement may provide a mechanism to rationally engineer liquid crystal polymorphism.

Segregation between different end groups on diblock dendrimers offers an additional mechanism for generating materials with unusual liquid crystalline properties. As described above, segregation between the peripheral groups and branched repeat units of a dendrimer can lead to liquid crystal mesomorphism in amphiphilic dendrimers.[14-15] Combining end groups that are mutually immiscible on a dendrimer that is also incompatible with the end groups leads to complex self-organization in the liquid crystalline phase. Percec and coworkers used hydrocarbon and semiperfluorinated hydrocarbon peripheral groups on a benzyl ether dendrimer. The resulting diblock dendrimer (**1-2**) (Figure 1.3b) formed an unusual multilayered cylindrical structure organized on a hexagonal lattice.[36] The multilayered structure arises from nanoscale segregation of the hydrocarbon and fluorocarbon peripheral groups. Donnio and coworkers showed that diblock dendrimers with hydrocarbon and polyhydroxylated peripheral groups form liquid crystalline mesophases due to segregation of the hydrophilic and hydrophobic groups.[40] Choi and coworkers pursued a similar design strategy with polyether and hydrocarbon peripheral groups.[41] Addition of an ionic dopant was required to induce strong enough segregation between the hydrocarbon and polyether groups. Nierengarten and coworkers observed segregation of cyanobiphenyl periperal groups from hydrocarbon peripheral groups in a diblock liquid crystalline dendrimer.[32] Similar to the example reported by Percec and coworkers,[36] more recent examples have shown that segregation of the end groups on liquid crystalline diblock dendrimers leads to unusual morphologies of the liquid crystalline phases.[32, 40] Furthermore, these segregated liquid crystalline diblock dendrimers exhibit liquid crystalline polymorphism.[32, 40]

1.3 Heterolithic star-branched liquid crystal mesogens

Similar to diblock liquid crystalline dendrimers, the liquid crystalline properties of star-branched mesogens (i.e., G0 dendrimers) can be tailored by combining different mesogens. Star-branched liquid crystal mesogens in which the arms are not equivalent are referred to as heterolithic stars, nonsymmetrical star-branched mesogens, or heterolithic multipedes. Various heterolithic star-branched architectures can be envisioned, and Figure 1.4 illustrates the possibilities for three- and four-arm star-branched mesogens. Replacing with a different group one arm of a three- or four-arm star-branched mesogen produces AB_2[20, 33, 41-60] and AB_3 stars,[61] respectively. A_2B_2 Four-arm star-branched mesogens are the lowest generation diblock dendrimers, but there are no examples of this architecture. ABC Three-arm star-branched mesogens[20, 33, 48-49, 60, 62-63] have three different arms.

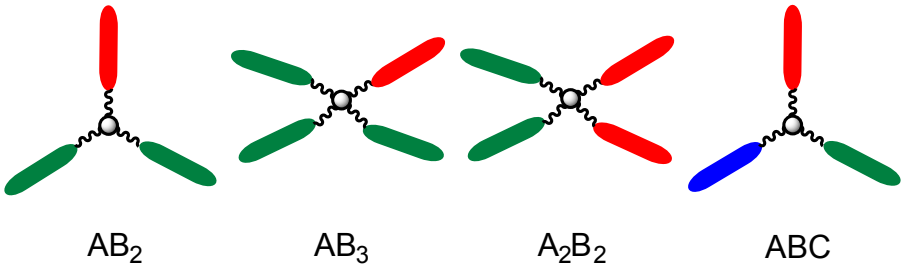


Figure 1.4. Representative architectures of common hetereolithic star-branched mesogens.

Heterolithic star-branched mesogens provide a platform from which liquid crystal properties can be engineered through molecular design. By replacing one arm of a non-mesogenic three-arm star-branched compound with a strongly mesogenic group, mesogenic AB_2 star-branched compounds have been obtained.[46, 50-51] Chiral groups in AB_2 three-arm star-branched mesogens have been used to induce chiral mesophases into star-branched mesogens that form achiral mesophases.[42, 45-46, 53] Systematic changes in molecular structure that are only available to heterolithic star mesogens allow for more careful tuning of liquid crystal mesophase stability.[50, 52, 55, 58] The versatility for molecular engineering of heterolithic star-branched

mesogens also presents opportunities for discovering phase behavior that is not readily predicted from the structures of the components.[20, 47, 50, 59]

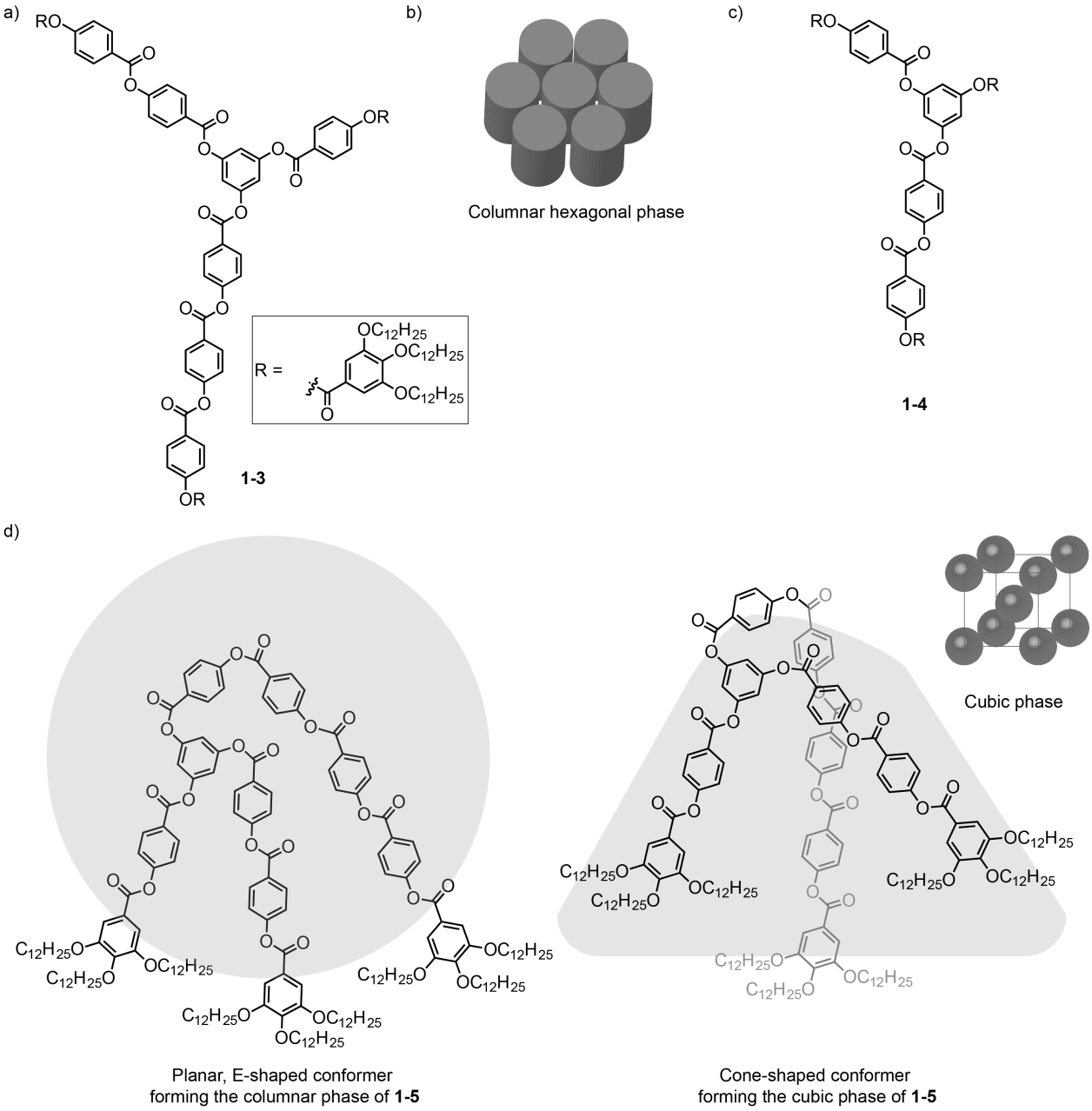


Figure 1.5. ABC star-branched mesogens that exhibit cubic phases and columnar-cubic transitions by Lehmann and Jahr. [33, 49] Adapted with permission from Lehmann, M.; Jahr, M., *Chem. Mater.* **2008**, *20*, 5453-5456. Copyright 2016 American Chemical Society.

The reduced symmetry of heterolithic star-branched mesogens promotes the formation of novel phase behaviors such as the formation of unusual mesophases and liquid crystal polymorphism. Lehmann's pioneering work on ABC three-arm star-branched mesogens best exemplifies these behaviors.[20, 33, 48] The three-arm star mesogens are based on a symmetric core (i.e., phloroglucinol) to which polycatenar mesgens are attached. Polycatenar mesogens usually form columnar mesophases.[49, 64] Symmetric star-branched mesogens from this series, in fact, do form columnar mesophases.[33] ABC Three-arm star-branched mesogens wherein the lengths of the polycatenar oligobenzoate arms are all different exhibit more diverse mesomorphism. Mesogen **1-3** (Figure 1.5a) forms a colunmar hexagonal mesophase (Figure 1.5b) despite its highly asymmetric disk-like structure. Mesogen **1-4** forms a highly unusual micellar body-centered cubic mesophase (Figure 1.5c). Mesogen **1-5** exhibits thermoreversible polymorphism that allows for the interconversion between the columnar and cubic mesophases. To rationalize the formation of the columnar and cubic mesophases by the ABC star mesogens, Lehmann and coworkers have proposed two collapsed conformations of the star-branched mesogens (Figure 1.5d).

Segregation of different arms can alter the morphology of mesophases formed by heterolithic star-branched mesogens compared to symmetrical star mesogens.[20, 50] Donnio and coworkers have thoroughly investigated the phase behavior of a series of homolithic and AB_2 heterolithic star-branched mesogens.[50] The star-branched mesogens were based on a symmetric core (i.e., phloroglucinol) to which calamitic mesogens are attached. The symmetric star-branched mesogens were characterized to determine the liquid crystal mesophase preferred by each terminal mesogen. All of the AB_2 heterolithic star mesogens form smectic phases (i.e., smectic A or smectic C) even when the major component of the star preferred to form a different phase. Characterization of the smectic phase structure (i.e., layer spacing or *d*-spacing) by

powder X-ray diffraction experiments revealed very different packing of the mesogens in the liquid crystalline phase. AB_2 stars based on azobenzene and alkoxy-biphenyl mesogenic groups form smectic C bilayer organization due to segregation between the two different mesogens (Figure 1.6a).[50] However, the AB_2 mesogen with azobenzene and cyanobiphenyl groups forms a smectic A phase with the mesogens in monolayers that result from mixing of the cyanobiphenyl and azobenzene groups (Figure 1.6b).[50]

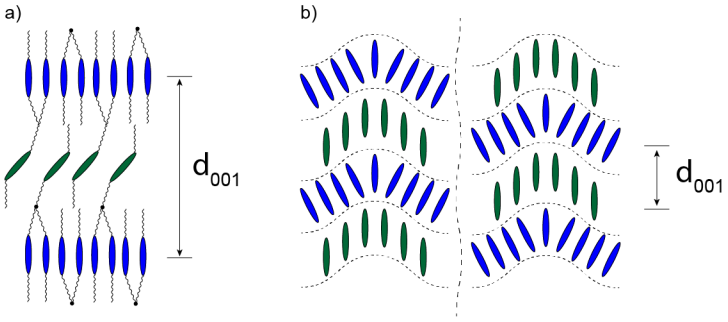


Figure 1.6. Different packing of the mesogens in the smectic phases of heterolithic star mesogens by Donnio and coworkers.[50] Reproduced from Ref. 50 with permission from The Royal Society of Chemistry.

1.4 Characterizations of liquid crystalline materials

Thermotropic liquid crystalline materials form, in response to changes in temperature, mesophases that possess the mobility of a liquid and ordering of a solid.[3-5] Differential scanning calorimetry (DSC) measures heat capacities and therefore provides information of phase transitions of a material.[65] For liquid crystalline materials, more than one transition (liquid-solid) is observed, and the phase(s) between solid and isotropic are mesophases (Figure 1.10). Endothermic transitions occur when a material melts from solid to mesophases or mesophases to liquid, while reverse processes (disorder to order) release heat being exothermic.[5] First order transitions cause no baseline shift, while second order transitions such as glass transition happen

due to change in heat capacity of the material and result in shift in the baseline (Figure 1.10).[66] The magnitude of enthalpy change reflects the difference in the structural ordering of two phases, which also provide information for phase assignment.[5]

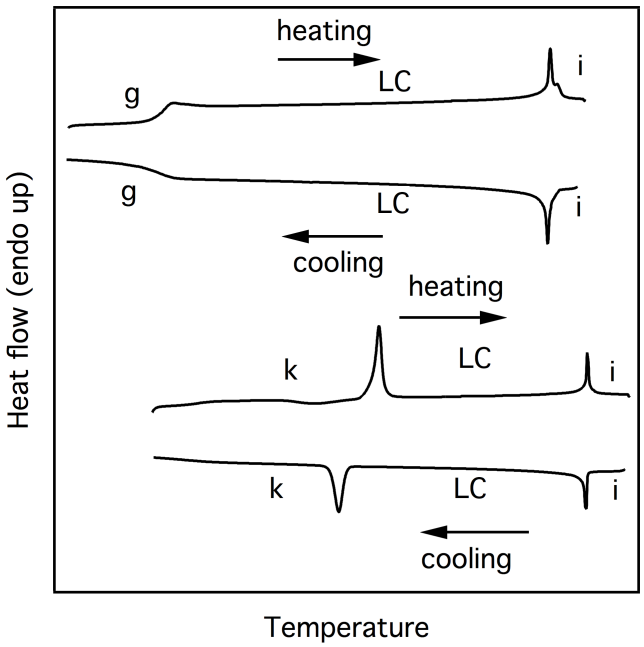


Figure 1.7. Generic differential scanning calorimetry thermograms showing the typical patterns of a LC exhibiting a glass or crystal to mesophase and mesophase to isotropic liquid.

Polarized optical microscopy (POM) experiments detect the existence of mesophases by the appearance of birefringence, which indicates anisotropy, while the material is in fluid form. Different mesophases can be identified by the different textures they exhibit. For example, nematic phase usually exhibit defects with curved brushes converging to the point defect, which are characteristics of Schlieren textures (Figure 1.8a).[5, 67-68] Smectic A phase usually exhibits focal conic or fan-shaped textures (Figure 1.8b).[69] These will be the major types of texture discussed in this thesis. When the molecules align perpendicular to the glass plates (homeotropic alignment), birefringence disappears.[5]

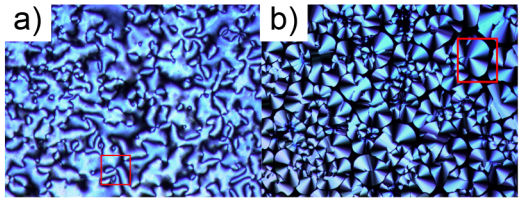


Figure 1.8. Typical Schlieren and fan-shaped textures.

X-Ray diffraction (XRD) technique provides more structural information of the mesophases. X-Ray diffraction of nematic phase where molecules pack only with orientation order only gives single diffuse peak unless the molecules are aligned.[70] Mesogens at smectic phase form layers, and the X-ray diffraction pattern usually shows sharp first-order reflection peak and higher order peaks in integer ratio for smectic (q_1 = 1, q_2 = 2, q_3 = 3…).[70-71] The analysis of liquid crystalline materials can be achieved base on the combination of DSC, POM, and XRD as well as other techniques. These methods provide precise information of the thermal properties and structural characteristic of mesogens.

1.5 Synthesis of ABC star-branched mesogens and triblock dendrimers

ABC Three-arm stars and triblock dendrimers can both be prepared by a linear, iterative strategy (Figure 1.9). The strategy outlined in Figure 1.9 employs orthogonal protecting groups on a desymmetrized core to ensure that each arm is incorporated correctly. However, the use of protecting groups increases the total number of steps in the synthesis. Lehmann and coworkers have used this strategy for the synthesis of ABC three-arm star branched mesogens,[19-20, 33, 62] and Morin and coworkers used this strategy for the only synthesis of a triblock dendrimer.[72] In both cases, the use of orthogonal protecting groups allows for well-controlled, successive modification of the core and avoids byproducts that are difficult to remove, which increases the overall yields.[62, 72] In principle, a trifunctional core with orthogonal reactive groups would avoid

the use of protecting groups and shorten the synthesis of ABC stars and triblock dendrimers. To date, no such asymmetric core has been reported.

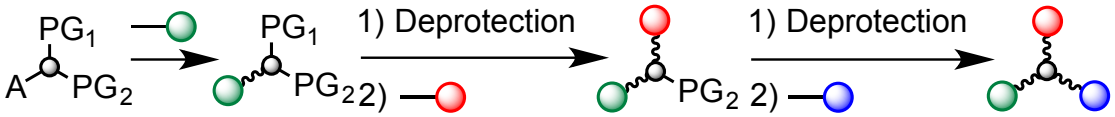


Figure 1.9. Five-step synthesis towards an ABC star-branched or triblock compound.

Lehmann and coworkers have shown that the linear, iterative strategy outlined in Figure 1.9 is superior to another more concise synthesis strategy that combines limited use of protecting groups with controlled reaction stoichiometry.[48] The synthesis started from the dibenzyl ether of phloroglucinol. Following acylation of the unprotected phenol, the benzyl ether protecting groups were removed. Subsequent attempts to monoacylate the diphenol were contaminated with diacylated products, which required careful separation by chromatography. The desired intermediate was only obtained in low yield. The disappointing results from this strategy led Lehmann and Jahr to develop the linear, iterative strategy outlined in Figure 1.9.[62]

The desymmetrized cores employed by Lehmann[62] and Morin[72] are not available from commercial sources, so Figure 1.10 underestimates the number of synthesis operations required to prepare ABC star-branched mesogens and triblock dendrimers. The desymmetrized core developed by Lehmann and Jahr required four steps to make and was obtained in less 40% overall yield from phloroglucinol ($0.82/g or $103/mol from Aldrich) (Figure 1.10).[62] Morin and coworkers reported a four-step synthesis of a desymmetrize trifunctional core in 20% overall yield from 3,5-diiodobromobenzene (Figure 1.11),[72] which was prepared in two steps from 4-bromoaniline ($0.45/g or $78/mol from Aldrich).[73] Therefore, the minimum number of steps to prepare ABC star-branched mesogens or triblock dendrimers is 9-10 steps.

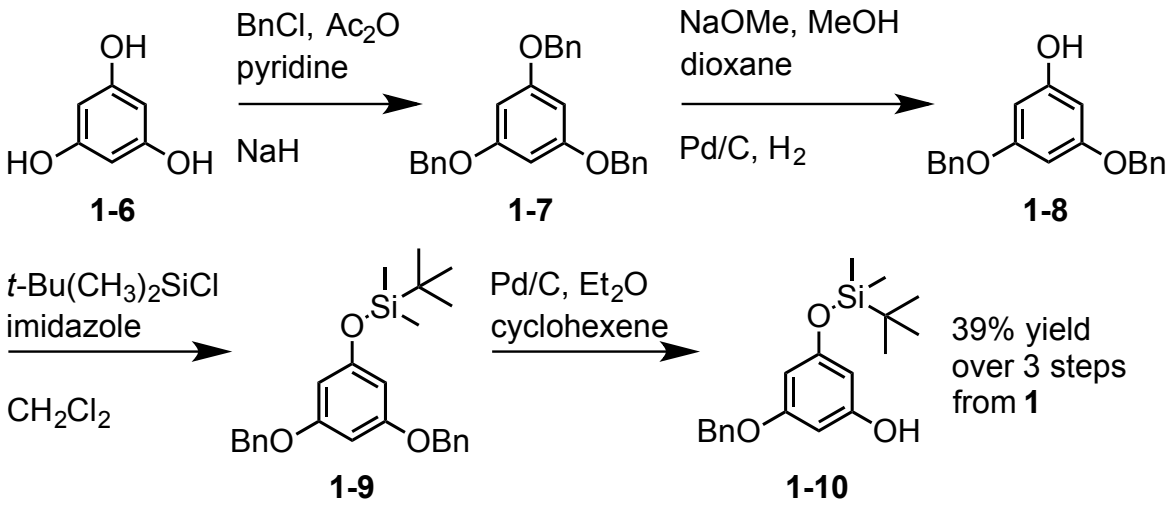


Figure 1.10. Synthesis of an asymmetrical core by Lehmann and Jahr.[62]

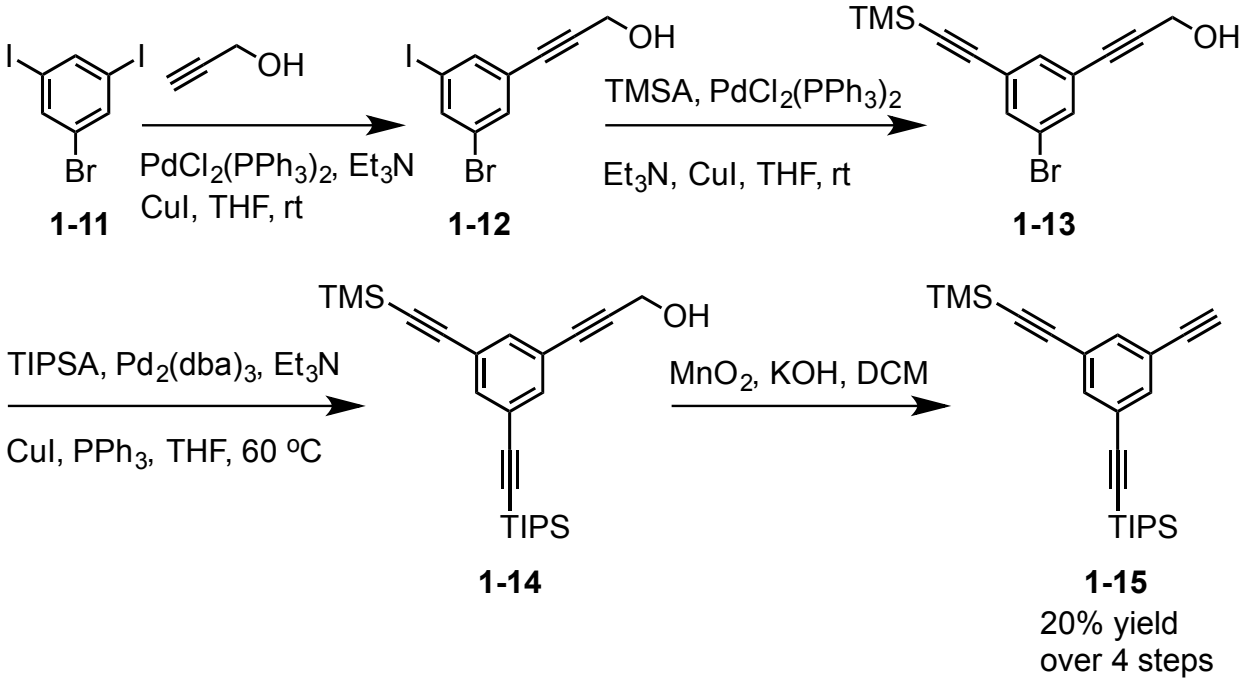


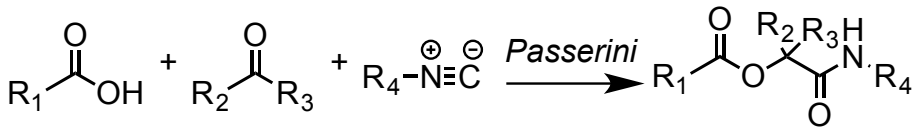
Figure 1.11. Synthesis of an asymmetrical core by Morin and coworkers.[72]

A more convergent synthesis of triblock dendrimers has been proposed by Rudick and coworkers.[74] The different dendrons can be brought together in a multicomponent reaction. This convergent, non-iterative strategy does not require a core group. Rather, the asymmetric core is generated by the multicomponent reaction. As proof-of-concept for this strategy, Rudick and

coworkers prepared one example of a second-generation dendrimer via the Passerini three-component reaction.[74] The resulting dendrimer, however, was a diblock dendrimer since two of the component dendrons had the same peripheral groups.

1.6 The Passerini three-component reaction:

The Passerini reaction is a three-component reaction involving an aldehyde or ketone, a carboxylic acid, and an isocyanide to form an α-acyloxyamide product (Figure 1.12).[75] The Passerini reaction is a one-pot reaction that has robust reactivity and can be performed under mild conditions, which makes it an efficient approach to assemble molecules with sensitive functional groups.[74, 76-80] However, attempts to apply the Passerini reaction in assembling macromolecules such as dendrimers have seen difficulty due to the large steric hindrance that comes from the increasing generations of dendritic structures, and this has prevented the synthesis of high-generation multiblock dendrimers via this approach.[74] Therefore optimized conditions to perform the Passerni reaction is needed to expand the application of this reaction.



1-16 **1-17** **1-18** **1-19**

Figure 1.12. The Passerini reaction affords an α-acyloxyamide product.

The mechanism of the Passerini reaction proposed by Ugi (Figure 1.13)[81] starts with the α-addition of the isocyanide (**1-18**) to the hydrogen-bonded ketone and acid component (**1-20**). Subsequent addition of the carboxylate (**1-22**) to form carboximidate intermediate (**1-23**) is believed to be the rate-determining step.[82] The product (**1-19**) is obtained after a Mumm rearrangement of the carboximidate intermediate (**1-23**). This mechanism has been widely accepted to agree with the observed third-order kinetics,[82] and the favor for nonpolar and aprotic

solvents.[81] Maeda et al. proposed mechanism of the Passerini reaction going through a four-component transition state involving an extra carboxylic acid as a fourth component based on quantum chemical calculations.[83]

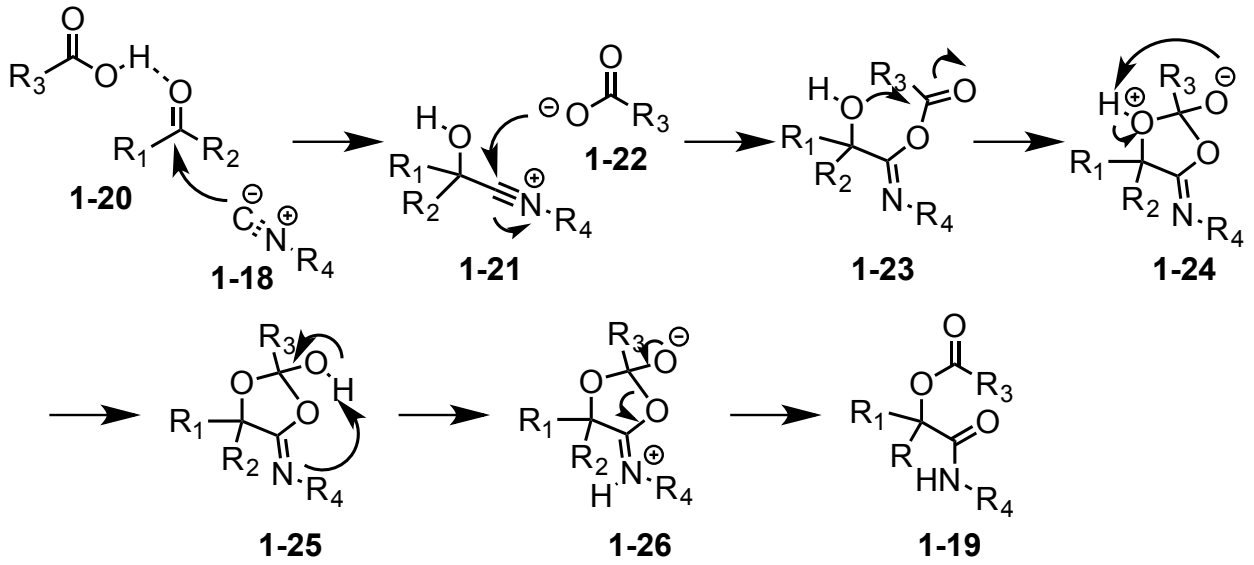
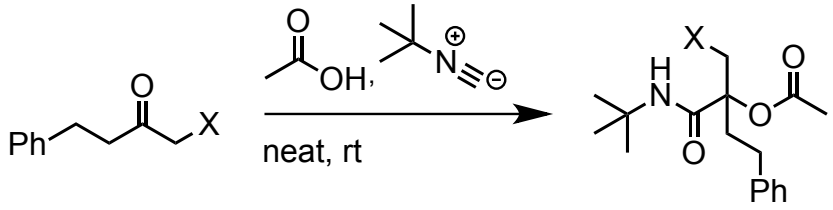


Figure 1.13. Mechanism of the Passerini Reaction proposed by Ugi.

Even though Ugi claimed that the Passerini reaction favors nonpolar and aprotic solvents, no experimental support was listed.[81] Radha Krishna and Lopinti found that CH_2Cl_2 gave optimum yields compared to THF, DMSO and MeOH.[84] Okandeji and Sello screened several different solvents and found that chlorinated solvents such as $CHCl_3$ and CH_2Cl_2 gave Passerini products in higher yields, while protic solvents such as methanol tend to give lower yields and side products.[85] Ramozzi and Morokuma reported computational calculations indicating the existence of nitrilium species, which better explained the fact that the Passerini reaction is accelerated in nonpolar and aprotic solvents.[86] Nevertheless, the Passerini reactions are reported to have higher yields under solvent-free conditions.[87-88] Achieving high yields will be critical in assembling multifunctionalities in macromolecules such as dendrons and dendrimers via the Passerini reaction, since any residual starting materials will cause difficulty in purification.

Even though many experiments have screened various reaction conditions and substrates to achieve high reaction conversions or high isolated yields,[85, 87, 89] not much study has been done on tracking the reaction kinetics under these optimized conditions. Pirrung et al. studied conversions of Passerini reactions in aqueous and organic solvents to evaluate the effect of water as solvent.[90] Ganem and coworkers performed a qualitative kinetics study on a series of Passerini reactions with various α-substituted ketone substrates, where they monitored the reactions by the disappearance of starting ketone using NMR spectroscopy and observed that ketones with electronegative substituents tend to have higher reactivity (Figure 1.14).[91] These insights helped to validate the effect of various conditions and substrates on reaction kinetics. However besides the limited number of examples discussed above on the Passerini reaction, the reaction kinetics need to be further explored in order to achieve optimized reaction conditions and higher yield, especially in preparing macromolecules generated by the Passerini reaction.



Reaction rate using different α-substituted ketones:

$X = OMs > Cl \approx N_3 > OCOCH_3 > SO_2Ar > H$

Figure 1.14. Reactivity of various ketones in the Passerini reaction by Ganem and coworkers.[91]

1.7 Overview of the thesis

Star-branched mesogens have been studied because of their well-defined chemical composition and hierarchical supramolecular arrays they could form. The significance of heterolithic systems of star-branched mesogens lies in the feasibility of manipulating their thermal properties by tailoring their chemical structures, which are of increased complexity and

variations. However compared to homolithic star-branched mesogens, the difficulty to synthesize heterolithic systems has been an obstacle to further exploring how combined multifunctionalities in star-branched scaffolds will affect their corresponding mesophases. An efficient approach is therefore needed to create libraries of heterolithic structures, upon which their structure-property relationships can be viewed. Multicomponent reactions have been applied as an effective way to assembly multifunctional ties, which is ideal to create heterolithic star-branched liquid crystals.

In chapter 2 we will discuss the efficiency of the Passerini three-component reaction in assembling different mesogenic arms to create such molecules. The first example of an ABC three-arm star-branched mesogen with calamitic mesogenic arms was prepared. Each mesogenic arm was individually prepared prior to undergoing the Passerini reaction, and a series of symmetrical, AB_2 and ABC stars containing calamitic mesogens and flexible linkers was synthesized in a convergent manner. We identified solution-based and solvent-free conditions that overcame the solubility issue of carboxylic acid component in common solvents and provided the star mesogens in good yields. The ABC mesogen exhibited higher ordered smectic phase based on DSC and POM experiments, compared to the nematic phase observed in the symmetrical and AB_2 mesogens. We presumed that the longer flexible linkers in the ABC star-branched mesogens might be the determinant for such an ordered phase.

Therefore we continued to expand the library of such asymmetric mesogens with varied linker lengths to validate their effect in the phase types, which will be discussed in chapter 3. However the mesogenic ABC stars only exhibited smectic phase with limited stability regardless of linker lengths, which was confirmed by DSC, POM and XRD experiments. A series of symmetrical and AB_2 star-branched mesogens was also prepared via the Passerini three-component reaction and their liquid crystalline properties were investigated. The 4'-(*S*)-2-methylbutoxy mesogenic group induced smectic phase in all the asymmetrical star mesogens.

Considering the limited stability of mesophases we observed from the ABC star-branched mesogens above, we reason that incorporating dendritic branches instead on linear arms to create multiblock liquid crystalline dendrimes may improve the stabilize the mesophases of these molecules.

In chapter 4 we will discuss an electronic effect that were prove to enhance reactivity of the Passerini reaction. Kinetics study of model Passerini reactions were performed to validate an electronic effect that had been observed to accelerate the dendrimer synthesis using the Passerini approach. Small molecules were chosen in the model reactions and NMR spectroscopy was used to quantify the progress of model Passerini reactions using different aldehydes and in different solvents. Ether-substituted aldehydes were proved to accelerate the Passerini reaction. Triblock dendrimers up to third generation were successfully synthesized benefitting from this effect in Passerini reactions. This work proves the feasibility to synthesize high generations of surface block dendrimers more effectively.

Triblock dendrimers have been successfully synthesized up to third generation, based on which triblock dendrimers consisting of different mesogens on each block can be synthesized via the Passerini reaction in future plans. Triblock liquid crystalline dendrimers are considered as ABC star-branched mesogens of higher generations, where the dendritic topology is expected to induce more stabilized mesophases (Figure 1.15).

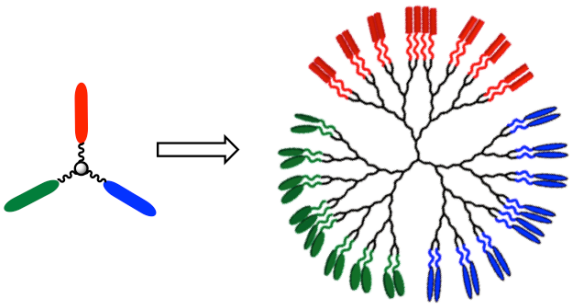


Figure 1.15. Triblock dendrimers containing up to three different peripheral mesogens.

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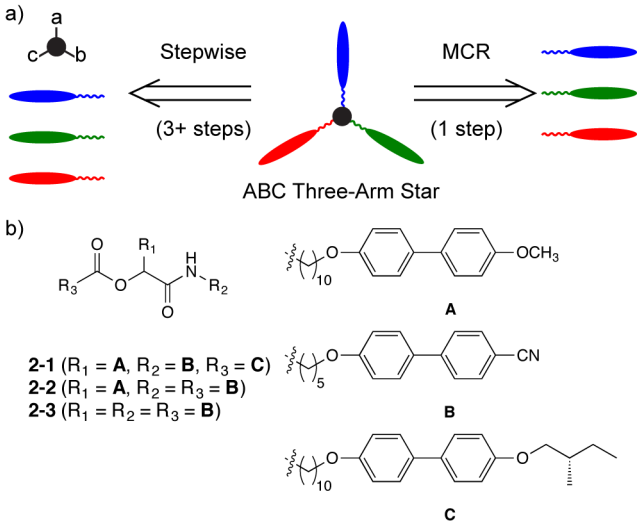
Chapter 2

2. Efficient Syntheses of Star-Branched, Multifunctional Mesogens

Adapted with permission from Song, S.; Rudick, J. G. *Org. Lett.* **2015**, *17*, 3244–3247.

2.1 Introduction

Multicomponent reactions (MCRs) enable rapid access to enormous structural diversity by assembling three or more different reactants in a single chemical transformation.[1-3] Convergent synthesis strategies that culminate in a MCR minimize the number of chemical operations that are performed on valuable, functional moieties (Scheme 2.1a). Such strategies also help to mitigate functional group incompatibilities during a synthesis campaign. A hallmark of MCRs that has been exploited to produce combinatorial libraries of compounds with potential biological activities is their modularity.[1-3] Each component in these reactions offers a degree of freedom for introducing structural and functional variability. The combination of efficiency and modularity of MCRs is well suited for the synthesis of multifunctional materials (Scheme 2.1a), where the properties of different functional subunits are combined into a single molecule.[4-6]



Scheme 2.1. Multifunctional ABC three-arm star-branched compounds.

Identifying a suitable core through which the arms of the star-branched molecule are joined is a critical challenge when different functional modalities are to be combined.[7-8] Star-branched molecules with identical arms have been synthesized for multivalent display of carbohydrates,[9] peptides and peptidomimetics,[10] supramolecular host-guest systems,[11] and liquid crystal mesogens.[12-13] Successful syntheses of non-symmetric star-branched materials have relied heavily on strategies to desymmetrize core molecules with equivalent reactive functional groups.[7-8] An ABC three-arm star in which all three arms are different from each other has C_1-symmetry that matches the symmetry of a Passerini reaction[14] product (e.g., **2-1** in Scheme 2.1b).[15] The Passerini reaction can also be applied to the synthesis of star compounds in which two arms (AB_2) or all three arms are identical such as **2-2** and **2-3** (Scheme 2.1b), respectively. Herein the Passerini reaction[14] serves as a representative MCR for synthesizing star-branched mesogens of varied composition. Other MCRs in which three or more different components are combined would yield similarly novel and complex star-branched, multifunctional materials.

Thermotropic mesogens exist, over a certain temperature range, in a liquid phase that retains some of the positional or orientational order that is found in crystalline solids.[16-17] Liquid crystalline mesophases comprised of thermotropic mesogens have made a profound impact with respect to display technologies.[18-19] The increased molecular weight of the star-branched mesogen compared to the monomeric precursor helps to stabilize the liquid crystalline mesophase,[20-21,22-25] and, upon cooling, symmetric star-branched mesogens tend to form stable glassy phases that retain the molecular organization of the liquid crystal phase.[21,26-28] The presence of anisotropic molecular organization in the fluid and glassy states of these materials is promising for bottom-up fabrication of nanostructured materials.[12-13,29-34] Interest in non-symmetric star-branched mesogens, wherein one or more arms is different from the others, has focused on the prospect that combinations of different mesogenic subunits will lead to unique polymorphism or novel mesophases.[35-40,41-43-44]

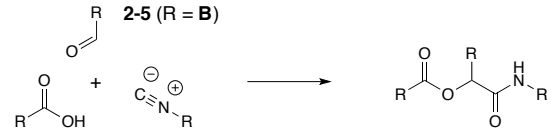
A direct synthesis of ABC three-arm star-branched mesogens from mesogen precursors has yet to be reported. Lehmann and Jahr developed a four-step synthesis of a desymmetrized and orthogonally protected derivative of phloroglucinol[45] that has been

used in the synthesis of the largest series of ABC three-arm star-branched mesogens.[41-43] Assembling star-branched mesogens directly from mesogen components circumvents the challenges of synthesizing and/or functionalizing a non-symmetric core. Lai and co-workers reported the one-pot synthesis of 2,4,6-trisubstituted pyrimidine-based AB_2 star-branched liquid crystals directly from promesogen presursors.[46-47] The syntheses of **2-1**–**2-3** via the Passerini reaction highlight the efficiency and versatility of the MCR strategy compared to these previous reports. Because compounds **2-1**–**2-3** are the first examples of thermotropic liquid crystals based on the flexible and non-symmetric a-acyloxyamide core, it is of interest to determine whether this motif supports mesomorphism. We were also intrigued as to whether mesomorphism would be present in the ABC star with calamitic mesogens (**2-1**).

2.2 Results and discussion

To explore a convergent synthesis of three-arm star-branched mesogens from monomeric precursors via a MCR, we focused on the Passerini reaction of **2-4**–**2-6** (Table 2.1). Carboxylic acid **2-4** has been used in syntheses of star-branched[48-49] and dendritic liquid crystals,[50] and aldehyde **2-5** has been used as a mesogen for side-chain liquid crystalline polymers.[51] Each was prepared in two steps from commercially available materials. We designed isocyanide **2-6** to have the same mesogen and flexible linker as **2-4** and **2-5**, and **2-6** was prepared in five steps. Because compound **2-4** has limited solubility in a range of organic solvents,[52] we were pleased to find that Passerini reactions of **2-4** were successful under a range of heterogeneous and solvent-free conditions.[53-56] Good yields of **2-3** were obtained from heterogeneous reactions at reflux in THF or 1,2-dichloroethane (DCE). Our best results were obtained when the reaction was performed without any solvent and at a temperature where compounds **2-3** to **2-6** were in their isotropic liquid phases. Unlike the reactions in THF and DCE, the solvent-free Passerini reaction remained homogenous throughout the experiment. The convenience of performing reactions in the melt motivated us to apply these conditions to the synthesis of three-arm star-branched compounds **2-1** and **2-2**.

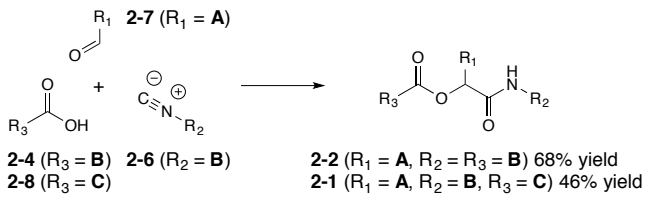
Table 2.1. Evaluation of Reaction Conditions



entry	conditions	yield
1	THF, rt, 7 d [a]	54%
2	THF, reflux, 7 h [a]	67%
3	DCE, reflux, 7 h [a]	67%
4	neat, 110 ºC , 7 h [b]	75%

[a]The heterogeneous reaction was performed with a nominal $[\mathbf{2\text{-}6}]_0$ = 0.53 M and $[\mathbf{2\text{-}4}]_0$:$[\mathbf{2\text{-}5}]_0$:$[\mathbf{2\text{-}6}]_0$ = 1:1:1. [b]$[\mathbf{2\text{-}6}]_0$ = 1.12 M and $[\mathbf{2\text{-}4}]_0$:$[\mathbf{2\text{-}5}]_0$:$[\mathbf{2\text{-}6}]_0$ = 1:1:1.

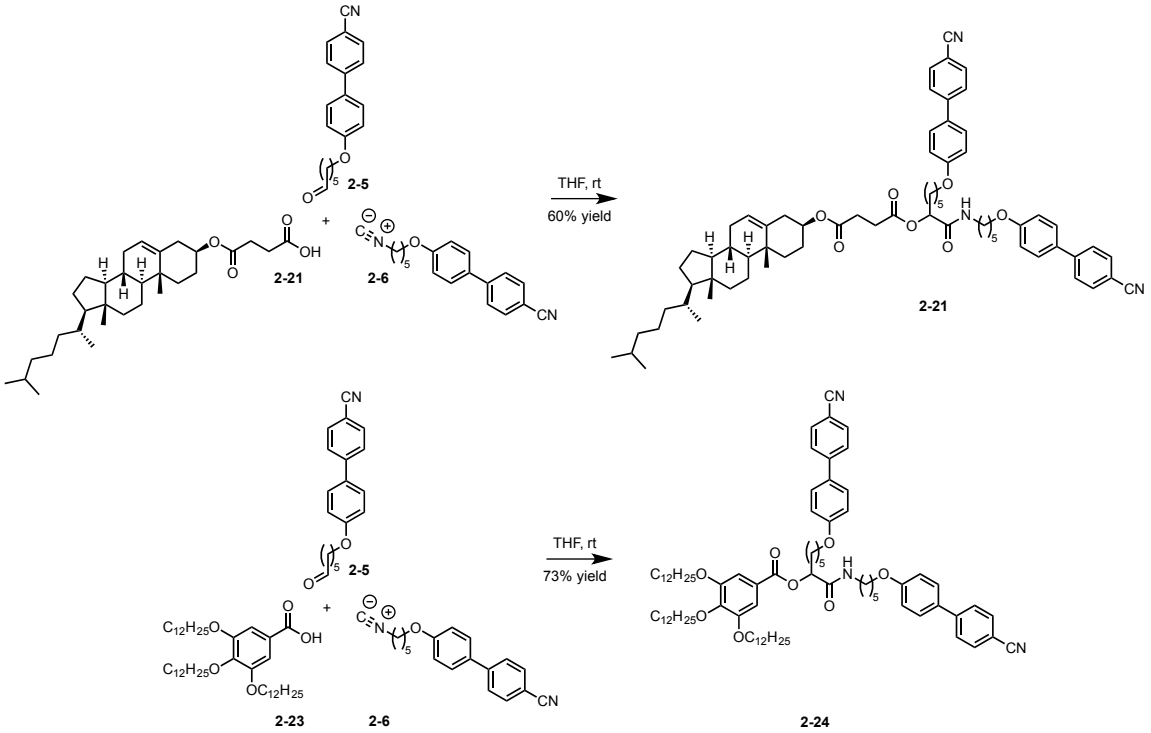
The Passerini reaction offers tremendous flexibility with respect to the diversity of mesogens that can be incorporated in the star-branched compounds. Isocyanide and aldehyde functional groups are rare among mesogens,[16-19] and carboxylic acid-containing mesogens are generally used in cases where specialized supramolecular interactions are desired.[57] Thus, the functional groups required for the Passerini reaction are largely orthogonal to those found in thermotropic mesogens. Furthermore, the Passerini reaction has been shown to be compatible with a wide range of functional groups found in mesogens, including azo compounds,[14] electron-rich and -poor aromatics and heteroaromatics (esp. nitroaromatics),[53-54, 58,59] halogens,[53-54, 58-60] and sulfones. Imines (and their precursors) are notable exceptions, as these participate in the Ugi reaction[61] with carboxylic acids and isocyanides. The mesogenic groups **A**, **B**, and **C** (Scheme 2.1b) were, therefore, chosen for convenience rather than concern for the substrate scope of the Passerini reaction.



Scheme 2.2: Synthesis of AB_2 and ABC three-arm star-branched mesogens.

We exploited the modularity of the Passerini reaction to prepare the AB_2 (**2-2**) and ABC (**2-1**) three-arm star-branched mesogens directly from mesogen precursors.

Aldehyde **2-7** was prepared in three steps. Substituting **2-7** for **2-5** in a Passerini reaction with **2-4** and **2-6** provided **2-2** in 68% yield after heating the neat reaction mixture for 2 h at 110 ºC (Scheme 2.3), a temperature that is below the isotropization temperature of the product (vide infra). When the reaction was heated above the isotropization temperature of **2-2**, we isolated the product in lower overall yield (e.g., 58% yield after 7 h at 130 ºC) due to side-reaction products that were difficult to separate by flash column chromatography. Carboxylic acid **2-8** was prepared in 5 steps from (*S*)-amyl alcohol. We then replaced carboxylic acid **2-4** with **2-8** in a Passerini reaction with **2-6** and **2-7**. The reaction was performed for 7 h at 150 ºC, because the product (**2-1**) has such a high melting temperature (vide infra). The ABC three-arm star-branched compound **2-1** was obtained in 46% yield (Scheme 2.2). By incorporating a cholesterol mesogenic carboxylic acid (**2-21**) or benzyl ether dendritic carboxylic acid (**2-23**) component in the Passerini reaction with **2-5** and **2-6** afford AB_2 star-branched meosgens **2-22** and **2-24** in similar fashion (Scheme 2.3).



Scheme 2.3: Synthesis of two additional AB_2 three-arm star-branched mesogens.

Each of the star-branched mesogens (**2-1**, **2-2**, and **2-3**) was characterized to assess the mesomorphic properties of these new compounds. Polarizing optical

microscopy (POM) experiments were performed on samples of each star-branched mesogen in a temperature-controlled microscopy stage to identify liquid crystalline mesophases by the appearance of a birefringent liquid phase. Indeed, each of the three star-branched mesogens exhibited a mesophase, which demonstrates that the flexibility of the α-acyloxyamide core is tolerated in the mesophase. A fan-shaped focal conic texture was observed from ABC star **2-1** (Figure 1a), which suggests that this material forms a smectic liquid crystalline phase.[62] Star-branched mesogens **2-2** (Figure 2.1b) and **2-3** (Figure 2.1c) both exhibit a Schlieren texture that is typical of nematic mesophases.[62] While the low symmetry of the ABC mesogen **2-1** might be expected to promote the emergence of a nematic phase,[44] which is less ordered than the smectic phase, we believe that the difference in phase behavior between compound **2-1** and compounds **2-2** and **2-3** is related to the number of long versus short aliphatic chains in the arms. Short spacers restrict ordering of the calamitic mesogens and promote the formation of the nematic phase,[63-64] whereas longer spacers promote smectic ordering by allowing greater conformational freedom to the mesogens.[20, 49] Two of the arms in **2-1** have long alkyl spacers that can promote smectic ordering of the calamitic mesogens, whereas compounds **2-2** and **2-3** lack sufficiently flexible arms to allow for such a high degree of order.

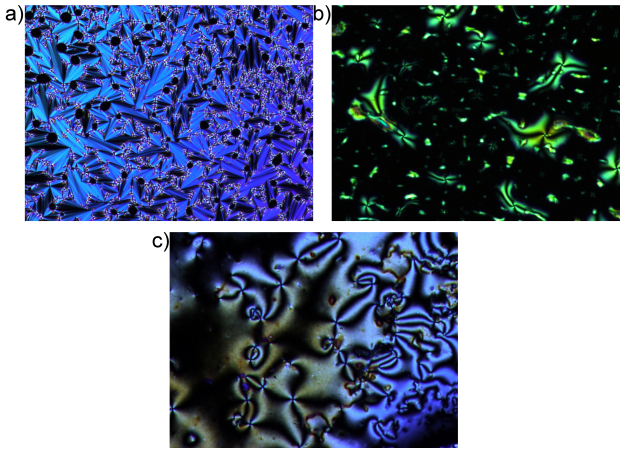


Figure 2.1. Polarized optical micrographs of samples that were slowly cooled from the isotropic liquid phase: (a) **2-1** (10×) at 143 ºC, (b) **2-2** (10×) at 120 ºC, and (c) **2-3** (20×) at 109 ºC.

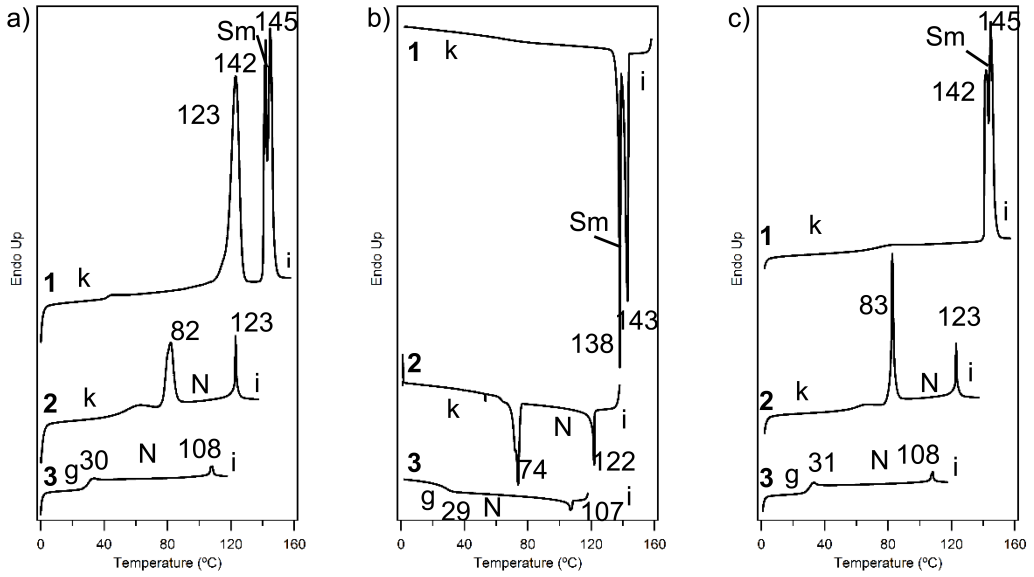


Figure 2.2. Differential scanning calorimetry thermograms of star mesogens **2-1**, **2-2** and **2-3** (top to bottom). From left to right are (a) first heating, (b) first cooling, and (c) second heating. Heating and cooling scans were performed at 10 ^{o}C/min.

Differential scanning calorimetry (DSC) experiments provided temperatures for the corresponding phase transitions and confirmed that the phase behavior is reversible. Representative heating and cooling curves are shown in Figure 2.2. Thermal transition temperatures (ºC) and corresponding enthalpy changes (kcal/mol) are summarized in Table 2.2. The temperature range over which the mesophase is present increases in the series of mesogens from the ABC star (**2-1**) to the AB_2 star (**2-2**) to the pseudosymmetric star with identical arms (**2-3**). As the number of arms with long linkers increases both the melting transition temperature and the isotropization temperature increase, but the former increases more rapidly than the latter. While the ABC (**2-1**) and AB_2 (**2-2**) star mesogens form crystalline solids upon cooling, star-branched mesogen **2-3** exhibits characteristics of a symmetric star-branched mesogen[20-21,26-28] such as vitrification upon cooling (Figure 2.2b). The observed variations in the thermal properties and phase behavior of these star mesogens illustrate the potential to uncover diverse functional properties from libraries of materials prepared via MCRs.[65]

Table 2.2 Thermal Transition Temperatures (ºC) and Corresponding Enthalpy Changes (kcal/mol) [a]

Compound	
2-1	i 143 (6.29) Sm 138 (5.20) k [b]
	k 142 (5.02) Sm 145 (6.56) i [c]
2-2	i 122 (0.91) N 74 (2.00) k [b]
	k 83 (2.79) N 123 (0.80) i [c]
2-3	i 107 (0.27) N 29 g [b]
	g 31 N 108 (0.19) i [c]

[a] Notation: i, isotropic liquid; N, nematic mesophase; g, glassy solid; k, crystalline solid; Sm, smectic mesophase. [b] First cooling cycle. [c] Second heating cycle.

2.3 Conclusion

Multicomponent reactions are a powerful class of transformations with which to explore structural complexity and structural diversity in organic chemistry. The modularity and high degree of convergence achieved through MCRs has fueled combinatorial campaigns aimed at discovering novel compounds with biological activity.[1-3] Interest in creating innovative organic materials via MCRs has undergone a recent resurgence (e.g., polymers[66]).[4-6] Of particular concern is how MCRs can accelerate studies of multifunctional materials that have been stymied by lengthy and/or low yielding syntheses. ABC Three-arm star-branched liquid crystals are an example of such materials. We have shown that a three-component reaction, the Passerini reaction, makes it feasible to prepare each permutation of three-arm star-branched mesogens directly from mesogen precursors. Looking forward, we envision that detailed structure-activity relationships will be established from libraries of star mesogens prepared via MCRs.

2.4 Experimental procedures

2.4.1 Material

Celite 545 powder, hydrochloric acid (HCl), hexanes (hex), ethyl acetate (EtOAc), chloroform, acetone, dichloromethane, anhydrous *N*,*N*-dimethylformamide (DMF), and anhydrous tetrahydrofuran (THF) were used as received from EMD. Toluene, ammonium

hydroxide (28-30%), and methanol (MeOH) were used as received from BDH. 6-Bromohexanoic acid, 11-bromoundecanoic acid, 1,5-dibromopentane, dimethylsulfate, phthalimide, isovaleric acid (99%), 1,2-dichloroethane (DCE) and *tert*-butyl isocyanide (98%) and (*S*)-(−)-2-methylbutanol were used as received from Aldrich. Pyridinium chlorochromate (PCC) (98%), triethylamine (NEt_3), *p*-toluenesulfonyl chloride (TsCl), hydrazine monohydrate (98+%), anhydrous dichloromethane, isovaleraldehyde (98%), and triphenylphosphine (PPh_3, 99+%) were used as received from Alfa Aesar. Propyl formate (96%) was used as received from Acros Organics. Anhydrous $MgSO_4$, sand (pure), KOH pellets, 6-bromohexanol, and 11-bromoundecanol were used as received from Fisher. 4'-Cyano-4-hydroxybiphenyl was used as received from Ark Pharm. 4,4'-Biphenol and ethyl 6-bromohexanoate were used as received from TCI. Sodium hydroxide was used as received from Amresco. Carbon tetrachloride was used as received from MP. Absolute ethanol (EtOH) was used as received from Pharmco-AAPER. Potassium carbonate was used as received from J. T. Baker. Silica gel 60 (40-63 microns) was used as received from Mallinckrodt Chemicals. Chloroform-*d* (+ 0.03% v/v TMS), methylenechloride-d_2, and dimethyl sulfoxide-d_6 (DMSO-d_6) were used as received from Cambridge Isotope Laboratories. Ammoniacal $CHCl_3$ was prepared by washing $CHCl_3$ with NH_4OH. 3,4,5-Tris(n-dodecan-1-yloxy)benzoic acid (**2-23**) was prepared according to a literature procedure[67] by Deborah A. Barkley and Rachelle David.

2.4.2 Techniques

^1H NMR (400MHz, 500 MHz), ^{13}C NMR (100 MHz, 125 MHz), COSY, HSQC, and HMBC spectra were recorded on a Bruker Avance III NMR spectrometer. Peak multiplicities are denoted as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Thin layer chromatography (TLC) was performed using Whatman silica gel 60 Å plates (250 μm) with fluorescent indicator and visualized using a UV lamp (254 nm). Flash column chromatography was performed on a Teledyne Isco CombiFlash Rf with RediSep Rf Normal Phase disposable silica columns. Gel permeation chromatography (GPC) in THF (1 mL/min) was performed using a Shimadzu LC-20AD liquid chromatography pump equipped with a DGU-20A5 degasser, CBM-20A

controller, RID-10A RI detector, CTO-20A column oven (all from Shimadzu), and three American Polymer Standards AM GPC gel columns of 100 Å (5 μm), 500 Å (5 μm), and 10,000 Å (5 μm). Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 FT-IR spectrophotometer. High-resolution electrospray ionization mass spectra (HRMS–ESI) were acquired by the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign on a Micromass Q-Tof Ultima. M-H-W Laboratories (Phoenix, AZ) performed elemental analysis. Differential scanning calorimetry (DSC) data were acquired using DSC TA Q2000 at the Thermomechanical & Imaging Nanoscale Characterization (ThINC) core facility of the Advanced Energy Research and Technology Center at Stony Brook University. Polarized optical microscopy was performed on an Olympus BX43 optical microscope with a FP82HT hot stage and FP900 controller (both from Mettler Toledo). Melting point determinations were performed on a Thomas-Hoover Unimelt capillary melting point apparatus.

2.4.3 Experimentals

Ethyl 6-(4'-cyanobiphenyl-4-oxy)hexanoate (2-9).[68] A solution of ethyl 6-bromohexanoate (2.2 mL, 0.12 mmol) in anhydrous DMF (20.0 mL) was added dropwise to an ice-water bath-cooled mixture of 4'-cyano-4-hydroxybiphenyl (2.00 g, 0.102 mol) and K_2CO_3 (4.25 g, 3.08 mmol) in anhydrous DMF (35.0 mL). Under a N_2 atmosphere, the reaction mixture was stirred at 80 ^oC for 15 h. The reaction was cooled to room temperature and the residual solids were removed by filtration. The crude product was obtained by rotary evaporation of volatiles from the filtrate. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 9:1 to 7:3) and recrystallized from EtOH to give **2-9** as colorless crystals (2.79 g, 81%). TLC (SiO_2, 3:2 hex/EtOAc): $R_f = 0.61$. ^1H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.70 (m, 2H; *H*3'), 7.64 (m, 2H; *H*2'), 7.53 (m, 2H; *H*2), 6.98 (m, 2H; *H*3), 4.14 (q, J = 7.2 Hz, 2H; $CO_2CH_2CH_3$), 4.01 (t, J = 6.4 Hz, 2H; $PhOCH_2$), 2.35 (t, J = 7.4 Hz, 2H; $CH_2CO_2C_2H_5$), 1.84 (m, 2H; $PhOCH_2CH_2$), 1.62 (m, 2H; $CH_2CH_2CO_2C_2H_5$), 1.54 (m, 2H; $PhOCH_2CH_2CH_2$), 1.26 (t, J = 7.2 Hz, 1H; $CO_2CH_2CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 173.8 (CH_2CO_2), 159.9 (*C*1), 145.5 (*C*4), 132.8 (*C*3'), 131.6 (*C*4'), 128.6 (*C*2), 127.3 (C2'), 119.3 (*C*1'), 115.3 (*C*3), 110.3 (*C*N), 68.0 (OCH_2CH_2), 60.5 ($CO_2CH_2CH_3$), 34.5 (CH_2CO_2), 29.1 (OCH_2CH_2), 25.9

($OCH_2CH_2CH_2CH_2$), 24.9 ($OCH_2CH_2CH_2$), 14.5 (CH_3). Spectral data agree with those previously reported.[69]

6-(4'-Cyanobiphenyl-4-oxy)hexanoic acid (2-4).[70] A solution of KOH (0.1177 g, 2.098 mmol) in absolute EtOH (4.8 mL) was added to a solution of **2-9** (0.3298 g, 0.9774 mmol) in EtOH (5.0 mL). The reaction mixture was stirred at reflux under a N_2 atmosphere for 3.5 h. The reaction mixture was cooled in an ice-water bath and acidified to pH 2 with 1 M HCl (aq). A precipitate formed and was collected by filtration. Compound **2-4** (0.17 g, 55%) was obtained as a colorless solid after recrystallization from EtOH. ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 12.01 (s, 1H; CO_2H), 7.85 (m, 4H; *H*3', *H*2'), 7.70 (m, 2H; *H*2), 7.05 (m, 2H; *H*3), 4.02 (t, J = 6.5 Hz, 2H; $PhOCH_2$), 2.24 (t, J = 7.3 Hz, 2H; CH_2CO_2H), 1.73 (m, 2H; $PhOCH_2CH_2$), 1.57 (m, 2H; $CH_2CH_2CO_2H$), 1.43 (m, 2H; $PhOCH_2CH_2CH_2$). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 174.4 (CH_2CO_2), 1159.3 (*C*1), 144.3 (*C*4), 132.8 (*C*3'), 130.3 (*C*4'), 128.3 (*C*2), 126.8 (C2'), 119.0 (*C*1'), 115.1 (*C*3), 109.1 (CN), 67.5 (OCH_2CH_2), 33.6 (CH_2CO_2H), 28.4 (OCH_2CH_2), 25.1 ($CH_2CH_2CO_2H$), 24.3 ($OCH_2CH_2CH_2$). IR (solid): 2948 cm^{-1} (CO_2H), 2227 cm^{-1} (CN), 1698 cm^{-1} (C=O). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19, N, 4.53. Found: C, 73.77; H, 6.10, N, 4.29. HRMS-ESI (*m/z*): $[M-H]^-$ calcd for $C_{19}H_{18}NO_3$, 308.1287, found 308.1286. Spectral data agree with those previously reported.[50]

6-(4'-Cyanobiphenyl-4-oxy)hexanol (2-10).[71] A solution of 6-bromo-1-hexanol (1.4 mL, 0.010 mol) in anhydrous DMF (13.5 mL) was added dropwise to an ice-water bath-cooled mixture of 4'-cyano-4-hydroxybiphenyl (1.6655 g, 8.5314 mmol) and K_2CO_3 (3.53 g, 0.0255 mol) in anhydrous DMF (21.0 mL). Under a N_2 atmosphere, the reaction mixture was stirred at 80 ^{o}C for 3.5 h. The reaction was cooled to room temperature and the residual solids were removed by filtration. The crude product was obtained by rotary evaporation of volatiles from the filtrate. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 7:3 to 1:1) and recrystallized from toluene to give **2-10** as colorless crystals (1.88 g, 75%). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.17. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.70 (m, 2H; *H*3'), 7.64 (m, 2H; *H*2'), 7.53 (m, 2H; *H*2), 6.99 (m, 2H; *H*3), 4.02 (t, J = 6.5 Hz, 2H; $PhOCH_2$), 3.68 (dt, J_1 = 8.0 Hz, J_2 = 5.8 Hz, 2H; CH_2OH), 1.83 (m, 2H; $PhOCH_2CH_2$), 1.62 (m, 2H; CH_2CH_2OH), 1.53 (m, 2H; $PhOCH_2CH_2CH_2$), 1.47 (m, 2H; $CH_2CH_2CH_2OH$), 1.24 (t, J = 5.2 Hz, 1H; O*H*). ^{13}C

NMR (125 MHz, $CDCl_3$, δ, ppm): 159.9 (*C*1), 145.4 (*C*4), 132.7 (*C*3'), 131.4 (*C*4'), 128.4 (*C*2), 127.2 (*C*2'), 119.3 (*C*1'), 115.2 (*C*3), 110.1 (*C*N), 68.1 (O*C*$H_2$$CH_2$), 62.9 (*C*$H_2$OH), 32.8 (OC$H_2$*C*$H_2$), 29.3 ($CH_2$*C*$H_2$OH), 26.0 (OC$H_2CH_2$*C*$H_2$), 25.7 (OC$H_2CH_2CH_2$*C*$H_2$). Spectral data agree with those previously reported.[48]

6-(4'-Cyanobiphenyl-4-oxy)hexanal (2-5).[51] A solution of **2-10** (0.2402 g, 0.8132 mmol) in anhydrous CH_2Cl_2 (8.2 mL) was sparged with N_2 for 15 min. To the solution, PCC (0.2161 g, 1.003 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 18 h under a N_2 atmosphere. The crude product was obtained by filtering the reaction mixture though Celite and sand. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) to give **2-5** as a colorless solid (0.15 g, 62%). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 9.80 (t, *J* = 1.7 Hz,1H, C*H*O), 7.69 (m, 2H; *H*3'), 7.64 (m, 2H; *H2*'), 7.53 (m, 2H; *H*2), 6.98 (m, 2H; *H*3), 4.02 (t, *J* = 6.4 Hz, 2H; PhOCH_2), 2.50 (td, J_1 = 7.3 Hz, J_2 = 1.7 Hz, 2H; CH_2CHO), 1.85 (m, 2H; PhOCH_2CH_2), 1.73 (m, 2H; C$H_2$$CH_2$CHO), 1.54 (m, 2H; PhOC$H_2$$CH_2CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 202.6 (*C*HO), 159.9 (*C*1), 145.5 (*C*4), 132.8 (*C*3'), 131.6 (*C*4'), 128.6 (*C*2), 127.3 (*C*2'), 119.3 (*C*1'), 115.3 (*C*3), 110.3 (*C*N), 67.9 (O*C*$H_2$$CH_2$), 44.0 (*C*$H_2$CHO), 29.2 (OC$H_2$*C*$H_2$), 26.0 (OC$H_2CH_2$*C*$H_2$), 22.0 (*C*$H_2$$CH_2$CHO). Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.91; H, 6.56; N, 4.56. HRMS-EI (*m/z*): calcd for $C_{19}H_{19}NO_2$, 293.1416, found 293.1416. ^{1}H NMR spectral data agree with those previously reported.[51]

***N*-(5-Bromopentyl)phthalimide (2-11).**[72] A solution of 1,5-dibromopentane (4.2 mL, 0.030 mol) in anhydrous DMF (10 mL) was added dropwise to an ice-water bath-cooled suspension of phthalimide (3.00 g, 0.0204 mol) and K_2CO_3 (5.63 g, 0.407 mol) in anhydrous DMF (10.0 mL). The reaction mixture was stirred under a N_2 atmosphere for 50 h at room temperature. Residual solids were removed from the reaction mixture by filtration. The crude product was obtained by rotary evaporation of the volatiles from the filtrate. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2) to give **2-11** as colorless solid (2.66 g, 44%). TLC (SiO_2, CH_2Cl_2): R_f = 0.44. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.85 (m, 2H; *H*2), 7.72 (m, 2H; *H*3), 3.70 (t, *J* = 7.2 Hz, 2H; NCH_2), 3.40 (t, *J* = 6.8 Hz, 2H; CH_2Br), 1.91 (m, 2H; C$H_2$$CH_2$Br), 1.72 (m, 2H; NC$H_2CH_2$), 1.51 (m, 2H; NC$H_2CH_2CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.4

(*C*O), 134.0 (*C*3), 132.1 (*C*1), 123.2 (*C*2), 37.7 (N*C*H_2), 33.4 (*C*H_2Br), 32.2 (CH_2*C*H_2Br), 27.8 (NCH_2*C*H_2), 25.4 (NCH_2CH_2*C*H_2). Spectral data agree with those previously reported.[72]

***N*-(5-(4'-Cyanobiphenyl-4-oxy)pentyl)phthalimide (2-12).** A solution of **2-11** (5.53 g, 0.0186 mol) in anhydrous DMF (37.0 mL) was added dropwise to a mixture of 4'-cyano-4-hydroxybiphenyl (3.03 g, 0.0155 mol) and K_2CO_3 (6.43 g, 0.0465 mol) in anhydrous DMF (40.0 mL). The reaction mixture was stirred under a N_2 atmosphere for 6 h at 80 ^oC. The reaction mixture was cooled to room temperature. The residual solids were removed by filtration. The filtrate was diluted with EtOAc and CH_2Cl_2, and the resulting precipitate was removed by filtration. The crude product was obtained by rotary evaporation of the volatiles from the filtrate. The product **2-12** was obtained as colorless crystals (5.04 g, 79%) after recrystallization from toluene. TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.84 (m, 2H; (Phth)*H*2), 7.72 (m, 2H; (Phth)*H*3), 7.69 (m, 2H; (CB)*H*3'), 7.74 (m, 2H; (CB)*H*2'), 7.52 (m, 2H; (CB)*H*2), 6.97 (m, 2H; (CB)*H*3'), 4.01 (t, *J* = 6.4 Hz, 2H; PhOCH_2), 3.73 (t, *J* = 7.2 Hz, 2H; NCH_2), 1.87 (m, 2H; OCH_2CH_2), 1.78 (m, 2H; NCH_2CH_2), 1.55(m, 2H; NCH_2CH_2CH_2). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 159.9 (*C*1), 145.5 (*C*4), 134.1 ((Phth)*C*3), 132.8 (*C*3'), 132.3 (Phth)*C*1), 131.6 (*C*4'), 128.5 (*C*2), 127.3 (*C*2'), 123.4 (Phth)*C*2), 119.4 (*C*1'), 115.2 (*C*3), 110.1 (CN), 68.0 (O*C*H_2), 38.1 (N*C*H_2), 29.0 (NCH_2*C*H_2), 28.6 (OCH_2*C*H_2), 23.6 (OCH_2CH_2*C*H_2).

5-(4'-Cyanobiphenyl-4-oxy)pentylamine (2-13).[73] A solution of hydrazine monohydrate (24.0 mL, 0.488 mol) in EtOH (48.0 mL) was added dropwise to an ice-water bath-cooled suspension of **2-12** (4.01 g, 9.77 mmol) in EtOH (50 mL). The reaction mixture was heated at reflux for 2.5 h under a N_2 atmosphere. The reaction mixture was cooled in an ice-water bath as H_2O was added. The reaction mixture was extracted with CH_2Cl_2 (15 mL) three times. The combined organic extracts were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was obtained by flash column chromatography (SiO_2, ammoniacal $CHCl_3$ to 10% MeOH/ammoniacal $CHCl_3$) to give **S5** as a slightly yellow solid (2.22 g, 81%). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 7.87 (m, 2H, *H*3'), 7.83 (m, 2H, *H*2'), 7.70 (m, 2H; *H*2), 7.05 (m, 2H; *H*3), 4.02 (t, *J* = 6.5 Hz, 2H; PhOCH_2), 2.59

(m, 2H; C*H*$_2$NH$_2$), 1.73 (m, 2H; OCH$_2$C*H*$_2$), 1.44 (m, 4H; C$_2$*H*$_4$CH$_2$NH$_2$). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 159.4 (*C*1), 144.3 (*C*4), 132.8 (*C*3'), 130.3 (*C*4'), 128.3 (*C*2), 126.8 (C2'), 119.0 (*C*1'), 115.1 (*C*3), 109.1 (CN), 67.6 (O*C*H$_2$CH$_2$), 41.2 (*C*H$_2$NH$_2$), 32.1 (*C*H$_2$CH$_2$NH$_2$), 28.5 (OCH$_2$*C*H$_2$), 22.9 (OCH$_2$CH$_2$*C*H$_2$). IR (dry film): 3331 cm^{-1} (N-H), 2234 cm^{-1} (CN).

1-Formamido-5-(4'-cyanobiphenyl-4-oxy)pentane (2-14). Propyl formate (1.11 mL, 0.0114 mol) and **2-13** (0.16 g, 0.57 mmol) were stirred at reflux for 24 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. Compound **2-14** was obtained as a colorless solid (0.13 g, 73%) after purification by flash column chromatography (SiO_2, CH_2Cl_2 to 95:5 CH_2Cl_2/MeOH). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.39. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 8.19 (s, 1H; C*H*O), 7.69 (d, 1H; *H*3'), 7.64 (m, 2H; *H*2'), 7.52 (m, 2H; *H*2), 6.98 (m, 2H; *H*3), 5.53 (s, 1H; N*H*), 4.02 (m, 2H; PhOC*H*$_2$), 3.35 (m, 2H; NHC*H*$_2$), 1.85 (m, 2H; C*H*$_2$CH$_2$O), 1.64 (m, 2H; NHCH$_2$C*H*$_2$), 1.55 (m, 2H; NHCH$_2$CH$_2$C*H*$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 164.7 (NH*C*HO), 161.3 (NH*C*HO), 159.8 (*C*1), 145.4 (*C*4), 132.8 (*C*3'), 131.7 (*C*4'), 128.6 (*C*2), 127.3 (C2'), 119.3 (*C*1'), 115.3 (*C*3), 110.3 (*C*N), 68.0 (O*C*H$_2$), 41.8 (*C*H$_2$NHCHO), 38.3 (*C*H$_2$NHCHO), 31.3 (*C*H$_2$CH$_2$NH), 29.6 (*C*H$_2$CH$_2$NH), 29.0 (OCH$_2$*C*H$_2$), 23.6 (OCH$_2$CH$_2$*C*H$_2$), 23.3 (OCH$_2$CH$_2$*C*H$_2$).

1-Isocyano-5-(4'-cyanobiphenyl-4-oxy)pentane (2-6). A solution of **2-14** (2.32g, 7.52 mmol) and PPh_3 (2.36 g, 9.00 mmol) in CCl_4 (0.90 mL, 9.0 mmol), Et_3N (1.30 mL, 9.00 mmol), and anhydrous CH_2Cl_2 (15.0 mL) was heated at reflux for 22 h under a N_2 atmosphere. The volatiles were removed by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) followed by recrystallization from ethanol and yielded **2-6** as colorless crystals (1.39 g, 64%). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.56. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.69 (m, 2H; *H*3'), 7.74 (m, 2H; *H*2'), 7.54 (m, 2H; *H*2), 6.99 (m, 2H; *H*3), 4.04 (t, J = 6.2 Hz, 2H; PhOC*H*$_2$), 3.45 (m, 2H; C*H*$_2$NC), 1.87 (m, 2H; OCH$_2$C*H*$_2$), 1.79 (m, 2H; C*H*$_2$CH$_2$NC), 1.69 (m, 2H; OCH$_2$CH$_2$C*H*$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 159.8 (*C*1), 156.3 (CH$_2$N*C*), 145.4 (*C*4), 132.8 (*C*3'), 131.8 (*C*4'), 128.6 (*C*2), 127.3 (C2'), 119.3 (*C*1'), 115.3 (*C*3), 110.4 (CN), 67.8 (O*C*H$_2$), 41.7 (*C*H$_2$NC), 29.1 (*C*H$_2$CH$_2$NC), 28.6 (OCH$_2$*C*H$_2$), 23.4 (OCH$_2$CH$_2$*C*H$_2$). Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25;

N, 9.65. Found: C, 78.50; H, 6.15; N, 9.49. HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{19}N_2O$, 291.1497, found 291.1419.

4-Hydroxy-4'-methoxybiphenyl (2-15).[74] Dimethyl sulfate (5 mL, 0.05 mol) was added to a suspension of 4,4'-dihydroxybiphenyl (10.00 g, 0.05370 mol) and NaOH (4.30 g, 0.108 mol) in H_2O (40 mL). The reaction mixture was stirred in a 250-mL Erlenmeyer flask and a precipitate formed. The precipitate was collected by filtration and washed with 10 wt% aqueous NaOH. The dry solid was dissolved in boiling water and traces of insoluble material were removed by hot filtration. The filtrate was acidified with dilute HCl. The resulting precipitate was collected by filtration and washed with H_2O. Compound **2-15** was recrystallized from EtOH and obtained as colorless crystals (3.55 g, 33%). mp 180-182 ^oC (lit.[74] mp 179-181 ^oC). ^1H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.47 (m, 2H; *H*2), 7.43 (m, 2H; *H*2'), 6.96 (m, 2H; *H*3), 6.89 (m, 2H; *H*3'), 4.74 (s, 1H; O*H*), 3.85 (s, 3H; C*H*$_3$O). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 158.9 (*C*1), 154.8 (*C*1'), 134.0 (*C*4), 133.6 (*C*4'), 128.2 (*C*2), 127.9 (*C*2'), 115.8 (*C*3), 114.4 (*C*4'), 55.6 (*C*H$_3$O).

11-(4'-Methoxybiphenyl-4-oxy)undecanol (2-16).[75] 11-Bromo-1-undecanol (1.5089 g, 6.0068 mmol) was added slowly to a mixture of **2-15** (1.00 g, 4.99 mmol) in anhydrous DMF (25.0 mL) and K_2CO_3 (1.41 g, 0.0102 mol). The reaction mixture was stirred for 21 h at 80 ^oC under a N_2 atmosphere. The reaction mixture was cooled to room temperature and volatiles were removed by rotary evaporation. Residual K_2CO_3 was removed by rinsing the crude product with chilled H_2O (50 mL). The product was collected by filtration followed by recrystallization from toluene to yield **2-16** as colorless crystals (0.87 g, 47%). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.44. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.47 (overlapping m, 4H; *H*2, *H*2'), 6.95 (overlapping m, 4H; *H*3, *H*3'), 3.99 (t, *J* = 6.6 Hz, 2H; OC*H*$_2$C$_{10}$H$_{20}$OH), 3.84 (s, 3H; C*H*$_3$O), 3.64 (t, *J* = 6.6 Hz, 2H; C*H*$_2$OH), 1.80 (m, 2H; OCH$_2$C*H*$_2$C$_9$H$_{18}$OH), 1.57 (m, 2H; C*H*$_2$CH$_2$OH), 1.47 (m, 2H; OCH$_2$CH$_2$C*H*$_2$C$_8$H$_{16}$OH), 1.30 (overlapping, 12H; OC$_3$H$_6$C$_6$*H*$_{12}$C$_2$H$_4$OH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.9 (*C*1), 158.5 (*C*1'), 133.8 (*C*4), 133.5 (*C*4'), 127.92 (*C*2), 127.90 (*C*2'), 115.0 (*C*3), 114.4 (*C*3'), 68.3 (O*C*H$_2$C$_{10}$H$_{20}$OH), 63.3 (*C*H$_2$OH), 55.6 (*C*H$_3$O), 33.0 (*C*H$_2$CH$_2$OH), 29.80 (OCH$_2$*C*H$_2$C$_9$H$_{18}$OH), 29.77 (OCH$_2$CH$_2$(*C*H$_2$)$_7$C$_2$H$_4$OH), 29.73 (OCH$_2$CH$_2$(*C*H$_2$)$_7$C$_2$H$_4$OH), 29.64

($OCH_2CH_2(CH_2)_7C_2H_4OH$), 29.61 ($OCH_2CH_2(CH_2)_7C_2H_4OH$), 29.53 ($OC_8H_{16}CH_2C_2H_4OH$), 26.3 ($OC_7H_{14}CH_2C_3H_6OH$), 26.0 ($OC_2H_4CH_2$).

11-(4'-Methoxybiphenyl-4-oxy)undecanal (2-7). A suspension of **2-16** (0.41 g, 1.1 mmol) in anhydrous CH_2Cl_2 (110.0 mL) was sparged with N_2 for 15 min. To the solution, PCC (0.3124 g, 1.449 mmol) was added as a solid. The reaction mixture was stirred for 14.5 h at room temperature under a N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to a total volume of ~ 20 mL. The crude product was obtained by filtering the remaining reaction mixture through Celite and sand. The product was purified by flash column chromatography (SiO_2, hex/CH_2Cl_2 1:3) to give **2-7** as a colorless solid (0.25 g, 62%). TLC (SiO_2, 1:3 hex/CH_2Cl_2): R_f = 0.26. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 9.77 (t, J = 1.9 Hz, 1H; C*H*O), 7.47 (overlapping m, 4H; *H*2, *H*2'), 6.95 (overlapping m, 4H; *H*3, *H*3'), 3.99 (t, J = 6.5 Hz, 2H; MeOBp-OC*H*$_2C_9H_{18}$CHO), 3.84 (s, 3H; C*H*$_3$O), 2.42 (td, J_1 = 7.9 Hz, J_2 = 1.9 Hz, 2H; C*H*$_2$CHO), 1.80 (m, 2H; MeOBp-$OCH_2CH_2C_8H_{16}$CHO), 1.63 (m, 2H; C*H*$_2CH_2$CHO), 1.47 (m, 2H; MeOBp-$OCH_2CH_2CH_2C_7H_{14}$CHO), 1.34 (overlapping, 12H; MeOBp-$OC_3H_6C_5H_{10}C_2H_4$CHO).). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 203.2 (*C*HO), 158.9 (*C*1), 158.5 (*C*1'), 133.8 (*C*4), 133.5 (*C*4'), 127.91 (*C*2), 127.89 (C2'), 115.0 (*C*3), 114.4 (*C*3'), 68.3 (MeOBp-O*C*$H_2C_9H_{18}$CHO), 55.6 (*C*H_3O), 44.1 (*C*H_2CHO), 29.7 (MeOBp-$OCH_2CH_2C_8H_{16}$CHO), 29.6 (MeOBp-$OC_3H_6C_5H_{10}C_2H_4$CHO) 29.55 (MeOBp-$OC_3H_6C_5H_{10}C_2H_4$CHO), 29.52 (MeOBp-$OC_3H_6C_5H_{10}C_2H_4$CHO) 29.4 (MeOBp-$OC_3H_6C_5H_{10}C_2H_4$CHO), 26.3 (MeOBp-$OC_2H_4CH_2C_7H_{14}$CHO), 22.30 (MeOBp-OC_8H_{16} *C*H_2CH_2CHO). Anal. Calcd for $C_{24}H_{32}O_3$: C, 78.22; H, 8.75. Found: C, 77.98; H, 8.51. HRMS-EI (*m/z*): calcd for $C_{24}H_{32}O_3$, 368.2351, found 368.2361.

(*S*)-2-Methylbutyl tosylate (2-17).[76] To an ice-water bath-cooled solution of (*S*)-(−)-2-methylbutanol (0.65 mL, 6.0 mmol) in anhydrous CH_2Cl_2 (5.8 mL), NEt_3 (1.0 mL, 7.2 mmol) and TsCl (0.8985 g, 4.713 mmol) were added. The reaction mixture was stirred under a N_2 atmosphere at room temperature for 21 h. The reaction mixture was washed with saturated solution of $NaHCO_3$ (10 mL) and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL) twice. The organic portions were combined and dried over $MgSO_4$. The solid was removed by filtration and the volatiles were removed from the filtrate by rotary evaporation. The product was purified by flash

column chromatography (SiO_2, hex/EtOAc 95:5) to give **2-17** as a colorless oil (0.93 g, 68%). TLC (SiO_2, 9:1 hex/EtOAc): R_f = 0.29. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.79 (m, 2H; *H*2), 7.34 (m, 2H; *H*3), 3.88 (dd, J_1= 5.8 Hz, J_2 = 9.3 Hz, 1H; TsOC*H*$_2$), 3.82 (dd, J_1 = 6.4 Hz, J_2 = 9.3 Hz, 1H; TsOC*H*$_2$), 2.45 (s, 3H; PhC*H*$_3$), 1.71 (m, 1H; TsOCH$_2$C*H*CH$_3$), 1.38 (m, 1H; C*H*$_2$CH$_3$), 1.16 (m, 1H; C*H*$_2$CH$_3$), 0.88 (d, *J* = 6.8 Hz, 3H; TsOCH$_2$CHC*H*$_3$), 0.83 (t, *J* = 7.5 Hz, 3H; CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 144.8 (*C*1), 133.4 (*C*2), 130.0 (*C*3), 128.1 (*C*4), 75.04 (TsO*C*H$_2$), 34.6 (TsOCH$_2$C*H*CH$_3$), 25.6 (C*H*$_2$CH$_3$), 21.9 (Ph*C*H$_3$), 16.2 (TsOCH$_2$CHC*H*$_3$), 11.2 (CH$_2$C*H*$_3$). ^{1}H NMR spectral data agree with those previously reported.[77]

4-Hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (2-18).[78] A solution of **2-17** (4.6927 g, 19.360 mmol) in anhydrous DMF (25.0 mL) was added to an ice-water bath-cooled mixture of 4,4'-biphenol (3.01 g, 0.0162 mol) and K_2CO_3 (6.65 g, 0.0481 mol) in anhydrous DMF (40.0 mL). The reaction mixture was heated for 5 h at 90 ^{o}C under a N_2 atmosphere. The reaction mixture was cooled to room temperature. The volatiles were removed by rotary evaporation. To the resulting solid, H_2O and EtOAc were added and two layers were separated. The aqueous layer was extracted with EtOAc (25 mL) three times. The organic portions were combined, washed with saturated NaCl solution (20 mL) and dried over $MgSO_4$. The salt was removed by filtration and the volatiles were removed from the filtrate by rotary evaporation. The product **2-18** was obtained as a colorless solid (1.60 g, 39%) by flash column chromatography (SiO_2, hex/EtOAc 9:1). TLC (SiO_2, 9:1 hex/EtOAc): R_f = 0.29. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.44 (overlapping, 4H; *H*2, *H*2'), 6.96 (m, 2H; *H*3), 6.88 (m, 2H; *H*3'), 4,71 (s, 1H; O*H*), 3.86 (m 1H; OC*H*$_2$), 3.77 (m, 1H; OC*H*$_2$), 1.89 (m, 1H; OCH$_2$C*H*CH$_3$), 1.60 (m, 1H;C*H*$_2$CH$_3$), 1.29 (m, 1H; C*H*$_2$CH$_3$), 1.04 (d, *J* = 6.8 Hz, 3H; OCH$_2$CHC*H*$_3$), 0.97 (t, *J* = 7.5 Hz, 3H; CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 158.7 (*C*1'), 154.7 (*C*1), 134.1 (*C*4'), 133.4 (*C*4), 128.2 (*C*2'), 127.9 (*C*2) 115.8 (*C*3'), 115.0 (*C*3), 73.2 (O*C*H$_2$), 35.0 (OCH$_2$*C*HCH$_3$), 26.4 (*C*H$_2$CH$_3$), 16.8 (OCH$_2$CHC*H*$_3$), 11.6 (CH$_2$*C*H$_3$). ^{1}H NMR spectral data agree with those previously reported.[78]

11-Bromoundecanoic acid ethyl ester (2-19).[79] A solution of 11-bromoundecanoic acid (5.00 g, 0.0189 mol) and H_2SO_4 (5.0 mL) in absolute EtOH (250 mL) was heated at reflux for 17.5 h under a N_2 atmosphere. The solvent was removed by rotary evaporation.

The crude oil was dissolved in a mixture of hex/EtOAc (1:1 v/v) and washed with saturated $NaHCO_3$ (aq), and water. The organic layer was dried over $MgSO_4$. The solids were removed by filtration and volatiles were removed from the filtrate by rotary evaporation to give a crude oil. The product was obtained by flash column chromatography (SiO_2, hex to hex/EtOAc 19:1) to give a colorless oil (4.71 g, 85%). TLC (SiO_2, 9:1 hex/EtOAc): $R_f = 0.33$. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 4.12 (q, J = 8.3 Hz, 2H; $CO_2CH_2CH_3$), 3.40 (t, J = 6.9 Hz, 2H; $BrCH_2$), 2.28 (t, J = 7.6 Hz, 2H; $CH_2CO_2CH_2CH_3$), 1.85 (m, 2H; $BrCH_2CH_2$), 1.61 (m, 2H; $CH_2CH_2CO_2CH_2CH_3$), 1.41 (m, 2H; $BrCH_2CH_2CH_2$), 1.29 (overlapping, 10H; $O(CH_2)_3(CH_2)_5$), 1.25 (t, J = 7.1 Hz, 3H; $CO_2CH_2CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 174.1 (CO_2), 60.4 ($CO_2CH_2CH_3$), 34.6 ($CH_2CO_2CH_2CH_3$), 34.3 (CH_2Br), 33.0 (CH_2CH_2Br), 29.6 ($O_2C(CH_2)_2CH_2$), 29.5 ($O_2C(CH_2)_3CH_2$), 29.4 ($O_2C(CH_2)_5CH_2$), 29.3 ($O_2C(CH_2)_4CH_2$), 29.0 ($O_2C(CH_2)_6CH_2$), 28.4 ($O_2C(CH_2)_7CH_2$), 25.2 ($O_2CCH_2CH_2$), 14.5 ($CO_2CH_2CH_3$). Spectral data agree with those previously reported.[79]

Ethyl 11-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)undecanoate (2-20). A solution of 11-bromoundecanoic acid ethyl ester (1.0708 g, 3.6641 mmol) in DMF (5.2 mL) was added to a mixture of **2-18** (0.78 g, 3.0 mmol) and K_2CO_3 (0.8504 g, 6.153 mmol) in anhydrous DMF (10.0 mL). The reaction mixture was heated at 80 ^{o}C for 24 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and H_2O (20 mL) and CH_2Cl_2 (15 mL) were added. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL) two times. The organic portions were combined and dried over $MgSO_4$. The solids were removed by filtration and the volatiles were removed from the filtrate by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 9:1) and recrystallized from EtOH to give **2-20** as a colorless solid (0.93 g, 65%). TLC (SiO_2, 9:1 hex/EtOAc): $R_f = 0.44$. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.46 (overlapping m, 4H; *H*2, *H*2'), 6.95 (overlapping m, 4H; *H*3, *H*3'), 4.13 (m, 2H; $CO_2CH_2CH_3$), 3.99 (t, J = 6.5 Hz, 2H; $PhOCH_2(CH_2)_9$), 3.86 (m, 1H; OCH_2CHCH_3), 3.77 (m, 1H; OCH_2CHCH_3), 2.29 (t, J = 7.5 Hz, 2H; $CH_2CO_2CH_2CH_3$), 1.88 (m, 1H; OCH_2CHCH_3), 1.79 (m, 2H; $OCH_2CH_2(CH_2)_8$), 1.62 (overlapping, 1H, $CHCH_2CH_3$; 2H; $CH_2CH_2CO_2CH_2CH_3$), 1.47 (m, 2H; $O(CH_2)_2CH_2(CH_2)_7$), 1.31 (overlapping, 10H; $O(CH_2)_3(CH_2)_5$; 1H, $CHCH_2CH_3$; 3H,

$CO_2CH_2CH_3$), 1.04 (d, *J* = 6.7 Hz; OCH_2CHCH_3), 0.97 (t, *J* = 7.5 Hz, 3H; CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 174.1 (CO_2), 158.6 (*C*1'), 158.4 (*C*1), 134.6 (*C*4'), 133.5 (*C*4), 127.86 (*C*2'), 127.85 (*C*2), 114.96 (*C*3'), 114.94 (*C*3), 73.2 (OCH_2CHCH_3), 68.3 ($PhOCH_2(CH_2)_9$), 60.4 ($CO_2CH_2CH_3$), 35.0 (OCH_2CHCH_3), 34.6 ($CH_2CO_2CH_2CH_3$), 29.7 ($OCH_2CH_2(CH_2)_8$), 29.6 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.53 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.47 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.4 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 26.4 ($OCHCH_2CH_3$),), 26.3 ($OCH_2CH_2CH_2(CH_2)_7$), 25.2 ($CH_2CH_2CO_2CH_2CH_3$), 16.8 ($OCH_2CHCH_3$), 14.5 ($CO_2CH_2CH_3$), 11.6 ($CH_2CH_3$).

11-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)undecanoic acid (2-8). A solution of KOH (0.2026 g, 3.611 mmol) in EtOH (5.6 mL) was added to a solution of **2-20** (0.7289 g, 1.557 mmol) in EtOH (10.0 mL). The reaction mixture was heated at reflux for 3.5 h under a N_2 atmosphere. The reaction mixture was then cooled in an ice-water bath and acidified to pH 2 with 1 M HCl (aq). The precipitate was collected by filtration, washed three times with cold H_2O, and washed once with cold acetone (5 mL). The product was recrystallizated from EtOH to give **2-8** as a colorless solid (0.51 g, 75%). ^1H NMR (500 MHz, $CDCl_3$, δ, ppm): 10.18 (s, 1H, CO_2H), 7.45 (overlapping m, 4H; *H*2, *H*2'), 6.94 (overlapping m, 4H; *H*3, *H*3'), 3.98 (t, *J* = 6.6 Hz, 2H; $PhOCH_2(CH_2)_9$), 3.85 (m, 1H; OCH_2CHCH_3), 3.77 (m, 1H; OCH_2CHCH_3), 2.35 (t, *J* = 7.5 Hz, 2H; CH_2CO_2H), 1.89 (m, 1H; OCH_2CHCH_3), 1.79 (m, 2H; $OCH_2CH_2(CH_2)_8$), 1.63 (overlapping, 1H, $CHCH_2CH_3$; 2H; $CH_2CH_2CO_2H$), 1.46 (m, 2H; $O(CH_2)_2CH_2(CH_2)_7$), 1.31 (overlapping, 10H; $O(CH_2)_3(CH_2)_5$; 1H, $CHCH_2CH_3$), 1.04 (d, *J* = 6.8 Hz, 3H; OCH_2CHCH_3), 0.97 (t, *J* = 7.5 Hz, 3H; CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 178.6 (CO_2H), 158.6 (*C*1'), 158.4 (*C*1), 133.6 (*C*4'), 133.5 (*C*4),' 127.87 (*C*2'), 127.86 (*C*2), 114.98 (*C*3'), 114.95 (*C*3), 73.2 (OCH_2CHCH_3), 68.3 ($OCH_2(CH_2)_9$), 35.0 (OCH_2CHCH_3), 34.0 (OCH_2CO_2H), 29.7 (OCH_2CH_2), 29.6 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.5 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.4 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.3 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 26.4 ($OCHCH_2CH_3$), 26.3 ($OCH_2CH_2CH_2(CH_2)_7$), 24.9 ($CH_2CH_2CO_2H$), 16.8 ($OCH_2CHCH_3$), 11.6 ($CH_2CH_3$). Anal. Calcd for $C_{28}H_{40}O_4$: C, 76.33; H, 9.15. Found: C, 76.40; H, 9.02. HRMS-ESI (*m/z*): $[M-H]^-$ calcd for $C_{28}H_{39}O_4$, 439.2848, found 439.2847.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 6-(4'-cyanobiphenyl-4-oxy)hexanoate (2-3) (neat). A N_2-filled, sealed 10-

mL Schlenk tube containing **2-5** (0.1409 g, 0.4803 mmol), **2-6** (0.1395 g, 0.4805 mmol), and **4** (0.1486 g, 0.4822 mmol) was immersed in an oil bath that was preset to 110 ^{o}C. The reaction mixture was stirred for 7 h. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 1:1 to 2:3) to give **2-3** as a colorless waxy solid (0.33 g, 75%). TLC (SiO_2, 1:1 hex/EtOAc): R_f = 0.11. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 6H; *H*3'), 7.61 (m, 6H; *H*2'), 7.51(m, 6H; *H*2), 6.96 (m, 6H; *H*3), 6.04 (t, J = 5.9 Hz, 1H; N*H*), 5.19 (m, 1H; NCOC*H*O), 3.98 (m, 6H; PhOCH_2), 3.32 (m, 2H; CH_2NH), 2.45 (t, J = 6.8 Hz, 2H; O_2CCH_2), 1.81 (overlapping, 10H; OCH$_2$CH_2, O_2CCH$_2$CH_2, NHCOCHCH_2), 1.54 (overlapping, 10H; NHCH$_2$CH_2CH$_2$, NHCH$_2$CH$_2$CH_2, NHCOCHCH$_2$CH_2, NHCOCHCH$_2$CH$_2$CH_2, O_2CCH$_2$CH$_2$CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.3 (O_2*C*), 169.9 (NH*C*O), 159.9 (*C*1), 159.8 (*C*1), 159.8 (*C*1), 145.4 (*C*4), 145.3 (*C*4), 145.3 (*C*4), 132.8 (*C*3'), 131.7 (*C*4'), 131.6 (*C*4'), 131.6 (*C*4'), 128.6 (*C*2), 128.5 (*C*2), 127.3(*C*2'), 119.3 (*C*1'), 119.3 (*C*1'), 115.2 (*C*3), 115.2 (*C*3), 110.4 (*C*N), 110.3 (*C*N), 74.1 (CO*C*HO$_2$C), 68.0 (O*C*H$_2$CH$_2$), 68.0 (O*C*H$_2$CH$_2$), 67.9 (O*C*H$_2$CH$_2$), 39.3 (*C*H$_2$NHCO), 34.4 (O_2C*C*H$_2$), 32.0 (O_2CCH$_2$*C*H$_2$), 29.6 (OCH$_2$*C*H$_2$), 29.2 (OCH$_2$*C*H$_2$), 29.1 (OCH$_2$*C*H$_2$), 29.0 (NHCH$_2$*C*H$_2$), 26.0 (O_2CCH$_2$CH$_2$*C*H$_2$), 25.9 (NHCOCHCH$_2$CH$_2$*C*H$_2$), 24.9 (OCH$_2$CH$_2$*C*H$_2$), 24.8 (NHCOCHCH$_2$*C*H$_2$), 23.6 (NHCOCH*C*H$_2$). Anal. Calcd for $C_{57}H_{56}N_4O_6$: C, 76.66; H, 6.32; N, 6.27. Found: C, 76.60; H, 6.33; N, 6.09. HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{57}H_{57}N_4O_6$, 893.4278, found 893.4252. GPC: M_n = 1,160, M_w/M_n = 1.09.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 6-(4'-cyanobiphenyl-4-oxy)hexanoate (2-3) (solution). A mixture of **2-5** (0.2534 g, 0.8638 mmol), **2-6** (0.2510 g, 0.8645 mmol), and **2-4** (0.2681 g, 0.8666 mmol) in anhydrous THF (0.90 mL) was refluxed for 7 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. Compound **2-3** was obtained as a colorless waxy solid (0.52 g, 67%) after purification by flash column chromatography (SiO_2, hex/EtOAc 1:1 to 2:3).

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 6-(4'-cyanobiphenyl-4-oxy)hexanoate (2-2). A N_2-filled, sealed 10-mL Schlenk tube containing **2-7** (0.1689 g, 0.4583 mmol), **2-6** (0.1329 g, 0.4577 mmol), and **2-4** (0.1419 g, 0.4587 mmol) and was heated to 110 ^{o}C and stirred for 2 h. The product

was purified by flash column chromatography (SiO_2, hex/EtOAc 3:7 to 7:3) to give **2-2** as colorless solid (0.30 g, 68%). TLC (SiO_2, 1:1 hex/EtOAc): R_f = 0.28. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 4H; (CB)*H*3'), 7.62 (m, 4H; (CB)*H*2'), 7.51 (m, 4H; (CB)*H*2), 7.46 (m, 4H; (MB) *H*2, *H*2'), 6.96 (overlapping m, 4H, (CB)*H*3; m, 4H, (MB)*H*3, *H*3'), 6.01 (t, 1H, *J* = 6.0 Hz; N*H*), 5.16 (m, 1H; NCOC*H*O), 3.98 (m, 6H; PhOCH_2), 3.84 (s, 3H; CH_3O), 3.31 (m, 2H; CH_2NH), 2.45 (t, 2H, *J* = 7.5 Hz; O_2CCH_2), 1.80 (overlapping, 10H; PhOCH$_2$CH_2, O_2CCH$_2$CH_2, NHCOCHCH_2), 1.57 (overlapping m, 10H; (CB)O(CH$_2$)$_2$(CH_2)$_2$CH$_2$NH, O_2CCH$_2$CH$_2$CH_2, NHCOCHCH$_2$CH_2). 1.30 (overlapping m, 10H; (MB)O(CH$_2$)$_3$(CH_2)$_5$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.5 (O_2C), 170.1 (NH*C*O), 159.83 ((CB)*C*1), 159.80 ((CB)*C*1), 158.9 ((MB)*C*1), 158.4 ((MB)*C*1'), 145.38 ((CB)*C*4), 145.36 ((CB)*C*4), 133.5 ((MB)*C*4), 132.8 ((MB)*C*4'), 131.68 ((CB)*C*3'), 131.64 ((CB)*C*4'), 128.6 ((CB)*C*2), 127.9 ((MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.2 ((CB)*C*3), 114.9 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.4 (*C*N), 110.3 (*C*N), 74.3 (CO*C*HO$_2$C), 68.3 ((MB)O*C*H$_2$CH$_2$), 68.0 ((CB)O*C*H$_2$CH$_2$), 67.9 ((CB)O*C*H$_2$CH$_2$), 55.6 (*C*H$_3$O), 39.3 (*C*H$_2$NHCO), 34.4 (O_2C*C*H$_2$), 32.1 (O_2CCH$_2$*C*H$_2$), 29.73 ((MB)OCH$_2$*C*H$_2$), 29.67 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.63 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.60 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.57 ((CB)O(CH$_2$)$_2$*C*H$_2$), 29.53 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.45 ((CB)OCH$_2$*C*H$_2$), 29.1 ((CB)OCH$_2$*C*H$_2$), 29.0 (NHCH$_2$*C*H$_2$), 26.3 ((MB)O(CH$_2$)$_2$*C*H$_2$), 25.9 (O_2CCH$_2$CH$_2$*C*H$_2$), 25.0 ((CB)O(CH$_2$)$_2$*C*H$_2$), 24.9 (NHCOCHCH$_2$*C*H$_2$), 23.6 (NHCOCH*C*H$_2$). Anal. Calcd for $C_{62}H_{69}N_3O_7$: C, 76.91; H, 7.18; N, 4.34. Found: C, 76.69; H, 7.00; N, 4.20. HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{62}H_{70}N_3O_7$, 968.5214, found 968.5189. GPC: M_n = 1,220, M_w/M_n = 1.09.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 11-(4'-((S)-2-methylbutoxy)biphenyl-4-oxy)undecanoate (2-1). A N_2-filled, sealed 10-mL Schlenk tube containing **2-7** (0.1362 g, 0.3696 mmol), **2-6** (0.1074 g, 0.3699 mmol), and **2-8** (0.1629 g, 0.3697 mmol) was immersed in an oil bath that was preset to 150 °C. The reaction mixture was stirred for 7 h. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to EtOAc/CH_2Cl_2 5:95) to give **2-1** as colorless solid (0.19 g, 46%). TLC (SiO_2, EtOAc/ CH_2Cl_2 5:95): R_f = 0.31. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 4H; (CB)*H*3'), 7.51 (m, 2H; (CB)*H*2'), 7.46 (overlapping m, 2H, (CB)*H*2; 8H, (MeO)*H*2 and *H*2', (2MB)*H*2 and *H*2'), 6.95

(overlapping m, 2H, (CB)*H*3; 4H, (MeO)*H*3 and *H*3'; 4H, (2MB)*H*3 and *H*3'), 6.02 (t, *J* = 6.0 Hz, 1H; N*H*), 5.18 (m, 1H; m, 1H, NCOC*H*O), 4.00 (m, 6H, PhOCH_2), 3.84 (overlapping, 3H, CH_3O; 1H, PhOCH_2CHCH$_3$), 3.77 (m, 1H; PhOCH_2CHCH$_3$), 3.31 (m, 2H; CH_2NH), 2.39 (t, *J* = 7.5 Hz, 2H; O_2CCH_2), 1.82 (overlapping, 9H; BPOCH$_2$CH_2, PhOCH$_2$C*H*CH$_3$, NHCOCHCH_2), 1.57 (overlapping m, 13H; OCH$_2$CH$_2$CH_2, (CB)OC$_3$H$_6$CH_2, NHCOCHCH$_2$CH_2, O_2CCH$_2$CH_2; 1H, PhOCH$_2$CHCH_2), 1.28 (overlapping m, 21H; NHCOCHC$_2$H$_4$C$_5$$H_{10}$, O_2CC$_2H_4C_5$$H_{10}$; 1H, PhOCH$_2CHCH_2$), 1.03 (d, *J* = 6.8 Hz, 3H; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2*C*), 170.2 (NH*C*O), 159.8 ((CB)*C*1), 158.9 ((MB)*C*1), 158.6 ((2MB)*C*1), 158.5 ((MB)*C*1'), 158.4 ((2MB)*C*1'), 145.4 ((CB)*C*4), 133.7 ((MB)*C*4), 133.6 ((2MB)*C*4), 133.44 ((MB)*C*4'), 133.41 ((2MB)*C*4'), 132.8 ((CB)*C*4'), 128.5 ((CB)*C*3'), 127.88 ((CB)*C*2), 127.87 ((MB)*C*2'), 127.84 ((2MB)*C*2), 127.82 ((2MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.2 ((CB)*C*3), 115.0 ((2MB)*C*3), 114.94 ((2MB)*C*3'), 114.91 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.1 (CO*C*HO$_2$C), 73.2 ((2MB)O*C*H$_2$CHCH$_3$), 68.3 (O*C*H$_2$CH$_2$), 68.2 (O*C*H$_2$CH$_2$), 68.0 (O*C*H$_2$CH$_2$), 55.5 (*C*H$_3$O), 39.2 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.5 (O_2C*C*H$_2$), 32.1 (O_2CCH$_2$*C*H$_2$), 29.73 ((MB)OCH$_2$*C*H$_2$), 29.67 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.62 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.60 ((CB)O(CH$_2$)$_2$*C*H$_2$), 29.53 ((MB)OC$_3$H$_6$*C*$_5$H$_{10}$), 29.47 ((2MB)O(CH$_2$)$_3$(*C*H$_2$)$_5$(CH$_2$)$_2$), 29.45 ((CB)OCH$_2$*C*H$_2$), 29.33 ((2MB)O(CH$_2$)$_3$(*C*H$_2$)$_5$(CH$_2$)$_2$), 29.02 (NHCH$_2$*C*H$_2$), 26.4 ((2MB)OCH*C*H$_2$CH$_3$), 26.3 ((MB)O(CH$_2$)$_2$*C*H$_2$), 25.2 (NHCOCHCH$_2$*C*H$_2$), 25.0 ((CB)O(CH$_2$)$_2$*C*H$_2$), 23.6 (NHCOCH*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.5 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{71}H_{90}N_2O_8$: C, 77.56; H, 8.25; N, 2.55. Found: C, 77.77; H, 8.09; N, 2.80. HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{71}H_{91}N_2O_8$, 1099.6775, found 1099.6754. GPC: M_n = 1,600, M_w/M_n = 1.08.

Butanedioic acid monocholesterol ester (2-21). This compound was prepared according to previous reported procedures.[80] To a mixture of cholesterol (3.86 g, 9.98 mmol) in anhydrous THF (20.0 mL) in ice-water bath, succinic acid (1.00 g, 9.99 mmol) and Et3N (2.1 mL, 15 mmol) were added and the reaction mixture was stirred at reflux under an N2 atmosphere for 20.5 h. The reaction mixture was cooled down to room temperature and was slowly poured into cold H_2O and the mixture was acidified to pH 3 with 1 M HCl (aq). The precipitate was collected by filtration and washed with cold H_2O and cold

EtOH. The product was recrystallized from EtOH to give **2-21** as a colorless solid (1.91 g, 39%). ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 5.38 (m, 1H, C6), 4.62 (m, 1H, C3), 2.68 (m, 2H, C29), 2.61 (m, 2H, C30), 2.32 (m, 2H, C4), 2.00 (m, 2H, C2), 1.87 (overlapping, 3H, C7(e), C12(e), C16(pro*S*)), 1.52-0.92 (overlapping, 32H, C11, C15, C23, C25, C16(pro*R*), C2(a), C22, C8, C7(a), C20, C1, C24, C12(a), C14, C17), 0.91 (d, 3H, J = 6.5 Hz, C21), 0.87 (d, 2H, J = 2.3 Hz, C26 or C27), 0.86 (d, 2H, J = 2.3 Hz, C27 or C26), 0.68 (s, 3H, C18). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 176.8 (C28), 171.8 (C31), 139.8 (C5), 123.0 (C6), 74.8 (C3), 56.9 (C14 or C17), 56.4 (C17 or C14), 50.2 (C9), 42.5 (C13), 40.0 (C4), 39.7 (C12), 38.2 (C24), 37.2 (C1), 36.8 (C20), 36.4 (C22), 36.0 (C10), 32.1 (C7), 32.1 (C8), 29.5 (C2), 29.0 (C16), 28.5 (C25), 28.2 (C23), 27.9 (C15), 24.1 (C27 or C26), 23.1 (C26 or C27), 22.8 (C11), 19.5 (C19), 19.0 (C21), 12.1 (C18). The assignments for cholesterol was based on previous literature.[81]

1-(5-(4'-cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl cholesteryl succinate (2-22). A mixture of **2-5** (0.3065 g, 1.045 mmol), **2-6** (0.3033 g, 1.045 mmol), and **2-21**[82] (0.5085 g, 1.045 mmol) in anhydrous THF (1.0 mL) was stirred for 40 h. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. Compound **2-22** was obtained as a colorless waxy solid (0.67 g, 60%) after purification by flash column chromatography (SiO_2, hex/EtOAc 3:2 to 2:3). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.17. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.69 (m, 4H, *H*3), 7.64 (m, 4H, *H*3'), 7.52 (m, 4H, *H*2), 6.98 (m, 4H, *H*2'), 6.77 (m, 1H, N*H*), 5.35 (m, 1H, C6), 5.20 (m, 1H, NCOC*H*O), 4.61 (m, 1H, C3), 3.99 (m, 6H, PhOCH_2), 3.29 (m, 2H, CH_2NH), 2.67 (overlapping, 4H, C29 and C30), 2.31 (m, 2H, C4), 1.97 (m, 2H, C2), 1.84 (overlapping, 7H, C7(e), C12(e), C16(pro*S*), $PhOCH_2CH_2$), 1.68-1.09 (overlapping, 44H, C11, C15, C23, C25, C16(pro*R*), C2(a), C22, C8, C7(a), C20, C1, C24, C12(a), C14, C17), OCH_2CH_2, $CH_2CH_2NHOCOCH_2CH_2$, $OCHCH_2$, $PhOCH_2CH_2CH_2$, $OCHCH_2CH_2$), 1.11-0.85 (overlapping, 9H, C21, C26, C27), 0.68 (s, 3H, C18). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.9 (C28), 171.7 (NH*C*O), 170.0 (C31), 159.9 (*C*4'), 145.4 (*C*1), 145.4 (*C*1), 139.7 (*C*5), 139.6 (*C*5'), 132.8 (*C*3), 131.5 (*C*1'), 131.5 (*C*1'), 128.5 (*C*2'), 128.5 (*C*2'), 127.2 (*C*2), 123.1 (*C*6), 119.3 (*C*N), 119.3 (*C*N), 115.3 (*C*3'), 110.3 (*C*4), 75.4 (CO*C*HOCO), 75.4 (C3), 68.1 (OCH_2CH_2), 68.1 (OCH_2CH_2), 56.8 (C14 or C17), 56.4 (C14 or C17), 50.2 (C9), 42.5 (C13), 39.9 (C4),

39.7 (C12), 39.4 (*C*H_2NHCO), 38.3 (C24), 37.2 (C1), 36.8 (C20), 36.8 (C22), 36.4 (C10), 36.0 (OCO*C*H_2), 32.1 (CH_2*C*H_2NHCO), 32.0 (C7), 31.9 (C8), 29.9 (OCH_2*C*H_2), 29.6 (CH_2*C*H_2NHCO), 29.3 (C2), 29.2 (COCHCH$_2$*C*H_2), 29.2 (C16), 28.4 (C23), 28.3 (C20), 28.0 (C15), 27.9 (C25), 25.0 (PhOCH$_2$CH$_2$*C*H_2), 24.4 (PhOCH$_2$CH$_2$*C*H_2), 24.1 (C27 or C26), 23.6 (PhOCH$_2$CH$_2$*C*H_2).23.0 (C27 or C26), 22.8 (C11), 19.5 (C19), 18.9 (C21), 12.0 (C18). The assignments for cholesterol was based on compound **2-22** and previous literature.[81] Anal. Calcd for $C_{69}H_{87}N_3O_7$: C, 77.42; H, 8.19; N, 3.93. Found: C, 77.69; H, 7.96; N, 3.66.

1-(5-(4'-cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 3,4,5-tridodecyloxybenzoate (2-24). A mixture of **5** (0.2493 g, 0.8498 mmol), **6** (0.2466 g, 0.8498 mmol) and **2-23** (0.5741 g, 0.8498 mmol) in anhydrous THF (0.86 mL) was stirred for 42 h. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. Compound **2-24** was obtained as a colorless solid (0.78 g, 73%) after purification by flash column chromatography (SiO_2, hex/EtOAc 1:4 to 3:2). The product was further purified by recrystallization from EtOH (0.58 g, 54%). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.46. . ^{1}H NMR (500 MHz, CD_2Cl_2, δ, ppm): 7.66 (overlapping m, 8H; *H*3, *H*3'), 7.51 (m, 4H; *H*2), 7.26 (s, 2H;(OCO)*H*2), 6.93 (m, 4H; *H*2'), 6.06 (t, 1H, *J* = 6.0 Hz; N*H*), 5.28 (m, 1H, NCOC*H*O), 3.96 (overlapping m, 10H; PhOCH_2), 3.26 (m, 2H; CH_2NH), 1.98 (m, 2H; OCHCH_2), 1.79 (overlapping, 8H; OCH$_2$CH_2), 1.69 (m, 2H; OCH$_2$CH_2), 1.52 (overlapping, 6H, OCOPhO(CH$_2$)$_3$CH_2; 2H, (CB)O(CH$_2$)$_3$CH_2), 1.44 (overlapping, 6H, OCOPhO(CH$_2$)$_3$CH_2; 2H, (CB)O(CH$_2$)$_3$CH_2), 1.25 (overlapping, 44H; OCOPhO(CH$_2$)$_3$(CH_2)$_7$, (CB)O(CH$_2$)$_4$CH_2), 0.86 (overlapping, 9H; CH_3). ^{13}C NMR (125 MHz, CD_2Cl_2, δ, ppm): 170.2 (NH*C*O), 165.8 (O*C*O), 160.31 (*C*4'), 160.27 (*C*4'), 153.6 (*C*2'), 145.62 (*C*1), 145.55 (*C*1), 133.1 (*C*3), 131.78 (*C*3), 131.76 (*C*1'), 128.84 (*C*2'), 128.82 (*C*2'), 127.5 (C2), 119.6 (*C*N), 115.5 (*C*3'), 110.6 (C4), 108.6 (C4), 75.2 (CO*C*HOCO), 74.1 (), 69.9 (O*C*H$_2$CH$_2$), 68.5 (O*C*H$_2$CH$_2$), 68.4 (O*C*H$_2$CH$_2$), 39.5 (*C*H$_2$NHCO), 32.52 (*C*H$_2$CH$_2$NHCO), 32.51 (OCH*C*H$_2$), 32.4 (OCH*C*H$_2$), 30.9 (OC$_3$H$_6$(*C*H$_2$)$_6$C$_3$H$_7$), 30.3 (OC$_3$H$_6$(*C*H$_2$)$_6$C$_3$H$_7$), 30.0 (OC$_3$H$_6$(*C*H$_2$)$_6$C$_3$H$_7$), 29.9 (OC$_3$H$_6$(*C*H$_2$)$_6$C$_3$H$_7$), 29.6 ((CB)O(CH$_2$)$_2$*C*H$_2$), 29.4 ((CB)O(CH$_2$)$_2$*C*H$_2$), 26.7 (OC$_3$H$_6$(*C*H$_2$)$_6$C$_3$H$_7$), 26.6 (OC$_3$H$_6$(*C*H$_2$)$_6$C$_3$H$_7$), 26.3

((CB)O(CH_2)$_3$*C*H_2), 25.5 (OC_9H_{18}*C*$H_2C_2H_5$), 23.9 ((CB)O(CH_2)$_3$*C*H_2), 23.3 ($OC_{10}H_{20}CH_2$*C*H_3), 14.5 (CH_3).

2.5 References

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Chapter 3

3. Three-Arm Star-Branched Mesogens Based on an α-Acyloxyamide Core

3.1 Introduction:

Supramolecular assemblies made up of structurally defined components are of special interest for understanding relationships between molecular structure and hierarchical organization that are critical to material function in a variety of applications.[1-9] Particular attention has been paid to the supramolecular assemblies that are present in thermotropic liquid crystals. Liquid crystalline mesophases are fluid states of matter in which molecular order is present. The combination of molecular order and fluidity has led to applications of liquid crystalline materials in displays and other technologies.[10-11] The supramolecular assemblies present in liquid crystalline mesophases depend strongly on molecular shape. Conventional liquid crystalline mesogens are either rod-like (calamitic) or disc-like (discotic).[12] Unconventional mesogens whose shapes are not strictly rod-like or disc-like are of interest for their potential to form novel mesophases or give rise to unique properties.[6-8]

Three-arm star-branched mesogens are examples of unconventional mesogens.[7, 13] Most of the previous work focused on three-arm star-branched liquid crystals wherein the arms are identical to each other, which are called homolithic or symmetrical stars.[14-20] Homolithic star-branched mesogens usually form the same liquid crystalline mesophases as the anisotropic unit in the arms.[16, 21] Introducing structural complexity in star-branched mesogens by making one or more arms different from the others can lead to more complex mesomorphism.[22-25] Lehmann and coworkers discovered unusual cubic phases in ABC three arm star mesogens as well as reversible liquid crystal polymorphism between cubic and columnar phases.[22] Liquid crystal polymorphism has also been observed in heterolithic AB_2 three-arm star-branched mesogens.[23-24]

We recently reported a series of three-arm star-branched mesogens based on an asymmetric core generated through the Passerini three-component reaction.[26] The series included a homolithic (symmetrical) three-arm star, an AB_2 three-arm star, and an ABC three-arm star. We found that the ABC three-arm star formed the most ordered liquid crystalline mesophase (i.e., smectic) in the series, albeit over the smallest range of temperatures. We rationalized that the ABC three-arm star-branched mesogen formed the smectic phase because the arms contained

longer, more flexible linkers than the other two mesogens. Since there are no other examples of ABC stars with calamitic mesogens we decided to explore this further.

We took advantage of the Passerini reaction to elaborate libraries of three-arm star-branched mesogens (Figure 3.1) in a combinatorial manner. The first series of ABC three-arm star-branched mesogens (**3-1** to **3-6**) with flexible linkers of different lengths between the core and the calamitic mesogens was characterized to understand how the length of the flexible linkers contributes to the smectic ordering. A complete set of homolithic stars (**3-7** to **3-12**) in which the linker length and terminal calamitic group were varied was characterized to understand the phase preferences of each arm in the ABC three-arm star-branched mesogens. The studies suggested that the phase behavior of the three-arm stars is dictated by one of the terminal calamitic groups (i.e., a (*S*)-2-methylbutyloxybiphenyl) moiety) rather than the length of the flexible linker. To confirm that a minority component in the system can dictate phase behavior, we also examined a series of AB_2 mesogens (**3-13** to **3-15**). The results of these studies provide structure-property relationships to help guide the rational design of heterolithic three-arm star-branched mesogens.

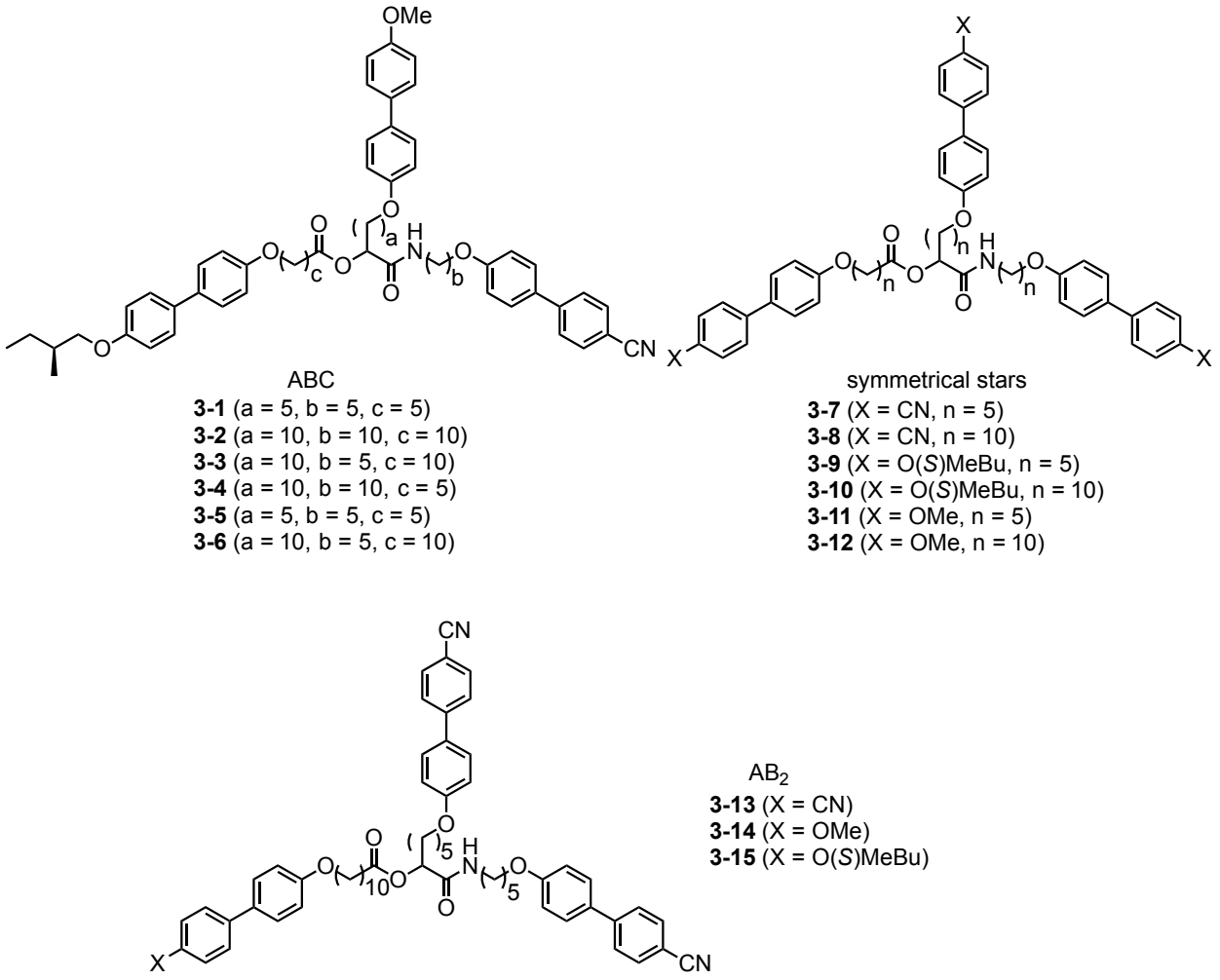

Figure 3.1: Structures of star-branched compounds: ABC stars (**3-1** to **3-6**), symmetric stars (**3-7** to **3-12**), and AB_2 stars (**3-13** to **3-15**).

3.2 Results and discussion:

3.2.1 Synthesis of ABC stars with varied spacer lengths

Heterolithic star-branched mesogens are conveniently prepared through multicomponent reactions. We have demonstrated the synthesis of ABC and AB_2 heterolithic three-arm star-branched mesogens via the Passerini three-component reaction.[26] Each arm of the star-branched mesogen comes from a different component in the Passerini reaction (i.e., aldehyde, carboxylic acid, and isocyanide), so the approach is highly modular. Our original approach to synthesize ABC three-arm star-branched mesogens involved the Passerini reaction as the final step of the synthesis whereby the Passerini reaction components had the calamitic groups and flexible linkers.[26] While the previously described strategy is highly convergent, we recognized that we

could further reduce the total number of steps to make each ABC three-arm star from nine to eight by using commercially available ω-bromocarboxylic acids in the Passerini reaction in place of the mesogen-containing carboxylic acids. In this alternative approach, the final calamitic group is introduced after the Passerini reaction, which increases the longest linear sequence by one extra synthesis operation. We thought that this alternate route to the ABC star-branched mesogens could address two related problems in our original approach. High temperatures were required to circumvent the poor solubility of the mesogen-containing carboxylic acid component by performing the reaction in the melt phase. However, the high temperatures also promote decomposition of the aldehyde component, which lowers the yield of the Passerini reaction. The ω-bromocarboxylic acids are soluble in solvents that are good for the Passerini reaction (e.g., 1,2-dichloroethane (DCE)).

Each of the ABC three-arm star-branched compounds **3-1** to **3-6** was obtained in good overall yield following the two-step sequence (Figure 3.2). The identity and purity of compounds **3-1** to **3-6** were analyzed and confirmed by ^{1}H and ^{13}C NMR spectroscopy, thin layer chromatography (TLC), mass spectrometry (HRMS-ESI or MALDI-TOF), and elemental analysis. Compounds **3-22** to **3-26** were prepared in a solution-phase Passerini reaction of either 6-bromohexanoic acid (**3-16**) or 11-bromoundecanoic acid (**3-17**) with a 4'-methoxybiphenyl-containing aldehyde (**3-18** or **3-19**) and a 4'-cyanobiphenyl-containing isocyanide (**3-20** or **3-21**). Nucleophilic substitution of the terminal bromide in **3-22** to **3-26** with 4'-((*S*)-2-methylbutyloxybiphenol) (**3-27**) proceeded smoothly under Williamson ether synthesis conditions at 80 ^{o}C in DMF. Similar overall yields were obtained for **3-3** by the direct synthesis strategy (46%)[26] and the two-step sequence (39%). ABC Star-branched compound **3-6** was prepared through a similar two-step sequence (Figure 3.2b). In the Passerini reaction stage, 6-bromohexanal (**3-28**) was reacted with carboxylic acid **3-29** and isocyanide **3-21**. Williamson etherification of 4'-methoxybiphenol (**3-31**) with **3-30** yielded **3-6**.

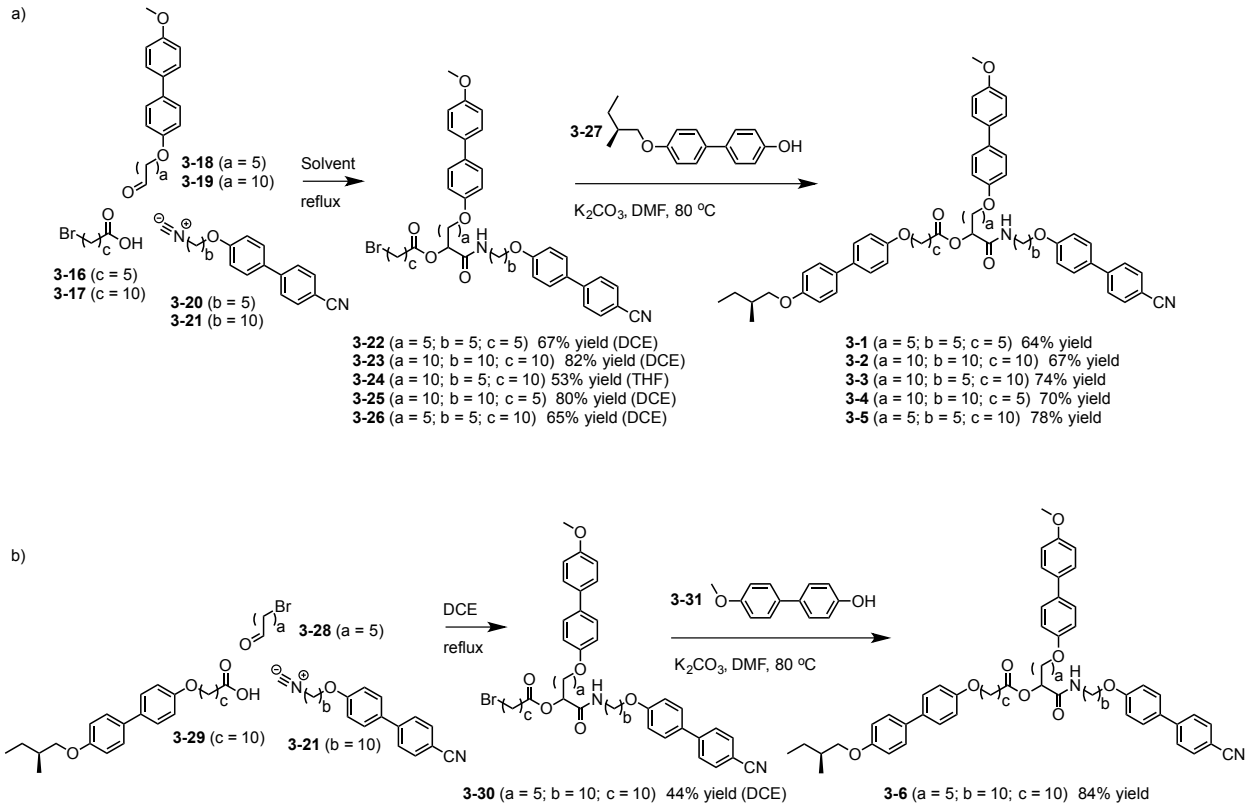

Figure 3.2: Synthesis of star-branched compounds **3-1** to **3-6**.

3.2.2 Thermal analysis of ABC stars

The thermal properties of the series of ABC stars were studied by differential scanning calorimetry (DSC) and polarized optical microscopy (POM). Phase transition temperatures and the enthalpies of first-order transitions were determined from the DSC experiments. Liquid crystalline mesophases can be thermodynamically stable (i.e., enantiotropic) or thermodynamically metastable (i.e., monotropic). Enantiotropic liquid crystalline mesophases are observed on both heating and cooling cycles, whereas monotropic liquid crystalline mesophases are observed only in the cooling cycle.[27] The reversibility of the phase transitions was confirmed by subjecting the samples to three cycles of heating and cooling at a constant rate (10 ^{o}C/min). Liquid crystalline phases can be identified if more than one transition is present in a scan. Mesogens **3-1**, **3-3**, and **3-4** form enantiotropic mesophases, while mesogen **3-2** forms a monotropic liquid crystal phase. Figure 3.3 shows the first heating, the first cooling, and the second heating cycles from the DSC experiments. In the POM experiments, the materials were observed under polarized optical microscopy while being heated on a hot stage. The appearance

of birefringence and fluidity of mesophases was confirmed in POM experiments. Slow cooling of the samples from the isotropic liquid phase to the mesophase produced focal conic textures in POM experiments (Figure 3.4). From the observed textures we conclude that all four ABC mesogens (**3-1** to **3-4**) form smectic phases. The enthalpy of the isotropic-to-liquid crystal phase transition for each ABC star mesogen was calculated from the DSC thermograms to be ~5 kcal/mol (Table 3.1), which is in the range expected for smectic liquid crystals (4-10 kcal/mol).[11] In contrast to our earlier report,[26] these data show that the length of the flexible linkers is not a critical determinant of the phase.

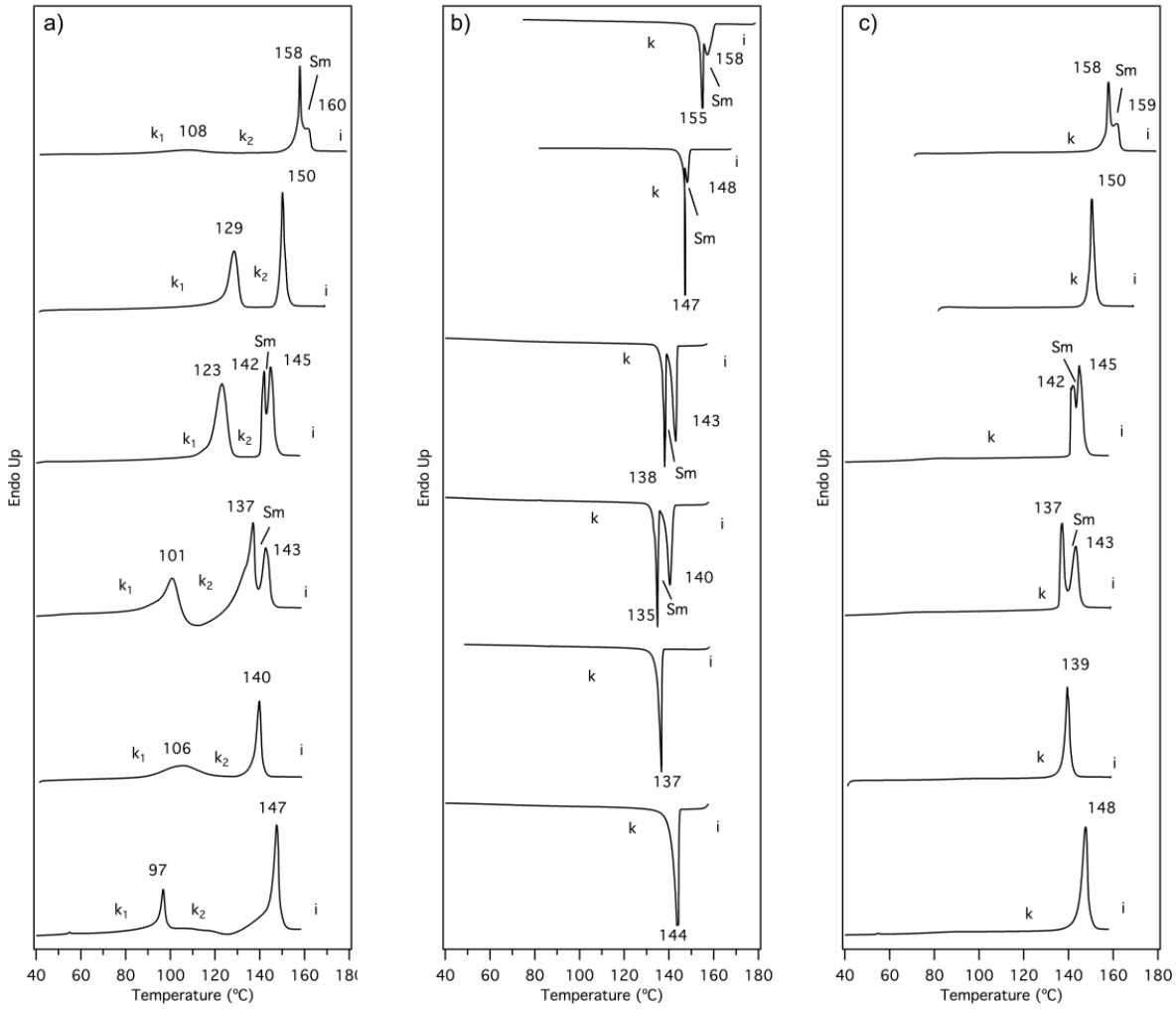

Figure 3.3: Differential scanning calorimetry thermograms of ABC stars **3-1** to **3-6** (top to bottom). From left to right are a) first heating, b) first cooling and c) second heating. Heating and cooling scans were performed at (10 °C/min)

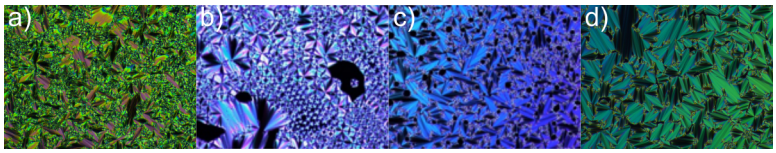

Figure 3.4: Polarized optical micrographs of corresponding samples that were slowly cooled from the isotropic liquid phase: (a) **3-1** (10×) at 159 ºC, (b) **3-2** (10×) at 149 ºC, (c) **3-3** (10×) at 143 ºC and (d) **3-4** (10×) at 139 °C.

Table 3.1: Structure of ABC star-branched compounds and their phase transition temperatures as determined by DSC; scanning rate 10 °C/min.

Compound	a/OMe	b/CN	c/O(*S*)MeBu	M_w g/mol	thermal transitions (°C) and corresponding enthalpy changes (kcal/mol)[a]	
					heating	cooling
3-1	5	5	5	959.24	k_1 107.67 (2.04) k_2 158.15 (6.34) Sm 160.00 (4.57) i [b] k 158.22 (6.32) Sm 159.42 (4.24) i [d]	i 157.81 (4.92) Sm 154.55 (5.24) k [c]
3-2	10	10	10	1169.64	k_1 129 (10.58) k_2 150 (12.28) i k 150 (11.95) i	i 148 (4.96) Sm 147 (6.99) k
3-3	10	5	10	1099.51	k_1 123.08 (12.19) k_2 141.95 (4.73) Sm 144.80 (6.83) i [b] k 141.87 (5.02) Sm 144.78 (6.56) i [d]	i 143.00 (6.29) Sm 138.06 (5.20) k [c]
3-4	10	10	5	1099.51	k_1 101.06 (9.20) k_2 136.95 (12.53) Sm 142.62 (5.92) i [b] k 137.09 (5.22) Sm 143.21 (5.65) i [d]	i 140.48 (4.79) Sm 134.88 (4.57) k[c]
3-5	5	5	10	1029.37	k_1 106 (7.26) k_2 140 (9.21) i k 139 (9.37) i	i 137 (9.29) k
3-6	5	10	10	1099.51	k_1 97 (3.53) k_2 147 (13.50) i k 144 (10.52) i	i 148 (10.46) k

[a] Notation: i, isotropic liquid; N, nmatic mesophase; g, glassy solid; k, crystalline solid; Sm, smectic mesophase. [b] first heating cycle. [c] First cooling cycle. [d] Second heating cycle.

3.2.3 XRD analysis of ABC stars **3-1** to **3-4**

The mesomorphic behaviors of liquid crystalline ABC stars **3-1** to **3-4** were characterized by X-ray diffraction (XRD).* Each of the four compounds showed two reflections in an integer ratio of 1 : 2 (q_1 : q_2) and no higher-order reflections. The XRD experiments confirmed the phase assignments made on the basis of the textures observed in the POM experiments. The layer spacing (d) of the smectic phase can be calculated from the peak positions in the XRD experiments ($d = 2\pi/q$). The layer spacing for each ABC star mesogen is reported in Table 3.2.

Table 3.2. Indexed d-spacing of the four ABC star mesogens.

Compound	Spacer length (a, b, c)	d/Å	Mesophase
3-1	5, 5, 5	20.7	Sm
3-2	10, 10, 10	29.5	Sm
3-3	10, 5, 5	26.0	Sm
3-4	10, 10, 5	26.0	Sm

3.2.4 Synthesis and thermal characterizations of symmetrical stars

In order to better understand how the terminal mesogen and flexible linker in each arm contributes to the properties of the ABC stars, we wanted to compare compounds **3-1** to **3-6** with symmetrical star-branched compounds **3-7** to **3-12** (Figure 3.1). We had previously reported the symmetrical star-branched mesogen **3-7**[26] and knew that its properties were similar to other cyanobiphenyl-containing star-branched mesogens.[17, 23, 28-29] However, there are no examples of symmetric three-arm star-branched mesogens with the same linkers and terminal mesogens as **3-7** to **3-12**. We therefore synthesized and characterized compounds **3-8** to **3-12**.

A two-step sequence for the synthesis of symmetrical three-arm stars was investigated to complete the series of compounds **3-8** to **3-12**. We envisioned introducing the terminal mesogens on all three arms in the final step of the sequence. That approach required ω-bromoalkyl isocyanides. Unfortunately, the reported approaches to making ω-bromoalkyl isocyanides[30-31] led to polar intermediates that were tedious to purify. We therefore settled on using mesogen-containing isocyanides in the Passerini reaction.

* XRD data was acquired by Prof. Heiney at University of Pennsylvania.

The syntheses of compounds **3-8** to **3-12** are shown in Figure 3.5. Passerini reactions involving the 6-bromohexanal (**3-28**) were relatively low yield, while those with 11-bromoundecanal (**3-32**) were high yield. Having UV-active chromophores in the Passerini reaction product is convenient for purification of intermediates **3-37** to **3-41**. Nucleophilic substitution of the two terminal bromides was especially low yield in all cases. The situation was especially bad when we tried to prepare compound **3-10** from **3-39**. Because of the poor solubility of **3-10** we could not isolate it from the reaction mixture. Compound **3-10** was successfully prepared via the one-step Passerini route (Figure 3.5b).

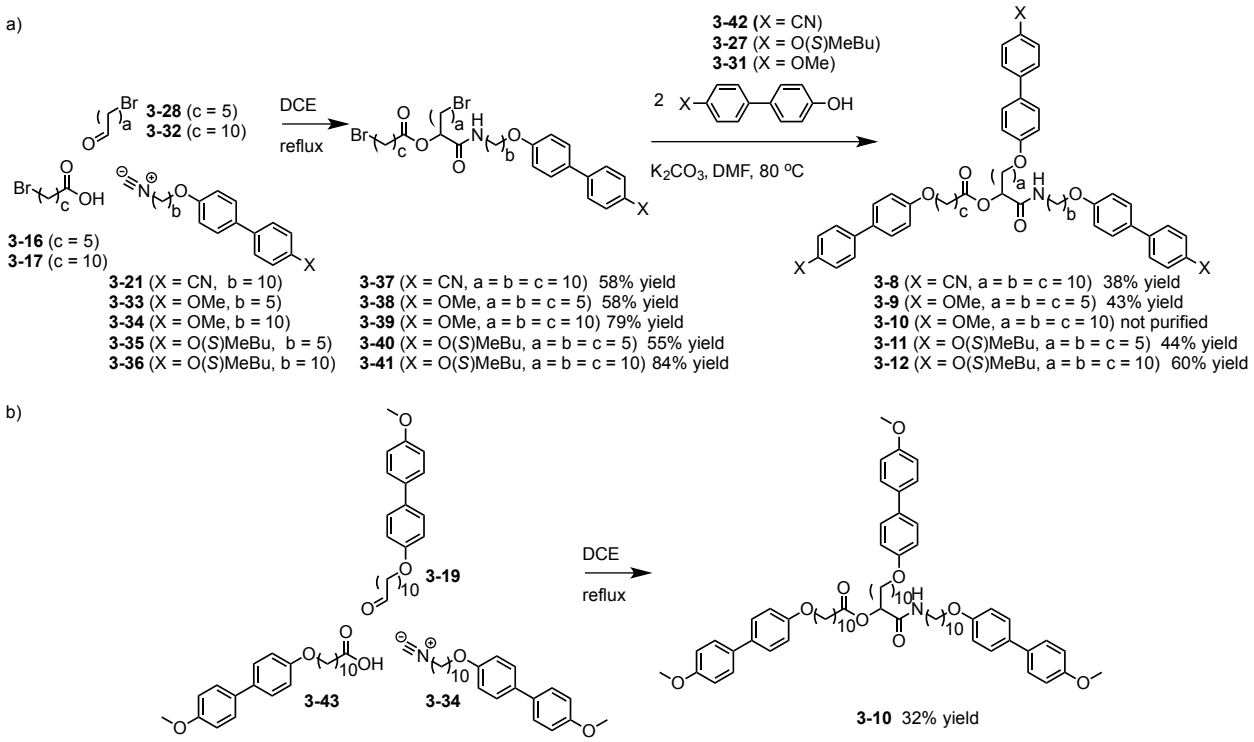

Figure 3.5: Synthesis of symmetrical star-branched compounds **3-8** to **3-12**.

Characterization of compounds **3-7** to **3-12** revealed that three of the star-branched compounds are liquid crystal mesogens. Figure 3.6 shows the DSC thermograms, and Table 3.3 summarizes the phase transition temperatures and corresponding enthalpies for all of the compounds. The isotropic-to-liquid crystal phase transition enthalpies for compounds **3-7** and **3-8** are small (<1 kcal/mol). A Schlieren texture was observed in POM of **3-7** and **3-8** upon cooling slowly from the isotropic liquid (Figure 3.7a and 3.7b). The texture and enthalpy data indicate that both compounds form nematic mesophases. Additional low-enthalpy transitions are observed as mesogen **3-8** was cooled in the DSC. In the POM experiment with **3-8** we observed

the Schlieren texture transform to a focal conic texture (Figure 3.7c) indicating a smectic A phase, followed by the appearance of a broken fan texture (Figure 3.7d) of a smectic C phase. Compound **3-11** exhibits a liquid crystal mesophase over a narrow range of temperatures. In contrast to **3-7** and **3-8**, the isotropic-liquid crystal phase transition enthalpy is large (>9 kcal/mol) (Table 3.3). From the texture observed in POM (Figure 3.7e), we determined that **3-11** forms a smectic liquid crystalline mesophase. The other star-branched compounds **3-9**, **3-10**, and **3-12** did not exhibit any mesomorphism. The three mesogens at the termini of the star-branched compounds **3-1** to **3-12** were chosen because each one tends to induce a different type of mesophase. 4'-Cyanobiphenol ethers induce either nematic or smectic mesophases depending on the linker separating the mesogen and the core.[28] The same trend is observed in side-chain liquid crystalline polymers with cyanbiphenol mesogens. Star-branched mesogens with 4'-methoxybiphenol ether or 4'-(*S*)-2-methylbutoxybiphenol ether terminal groups have not been reported. However, monomers[32] and polymers[33-35] containing 4'-methoxybiphenol ether mesogens form smectic mesophases. Surprisingly, compounds **3-9** and **3-10** do not exhibit any mesomorphism. Side-chain liquid crystalline polymers with 4'-(*S*)-2-methylbutoxybiphenol ether mesogens form chiral smectic phases,[36] and mesogen **3-11** seems to do the same. Interestingly, some of the ABC three-arm star-branched mesogens (i.e., **3-2** and **3-3**) have only one arm that forms a stable liquid crystalline mesophase.

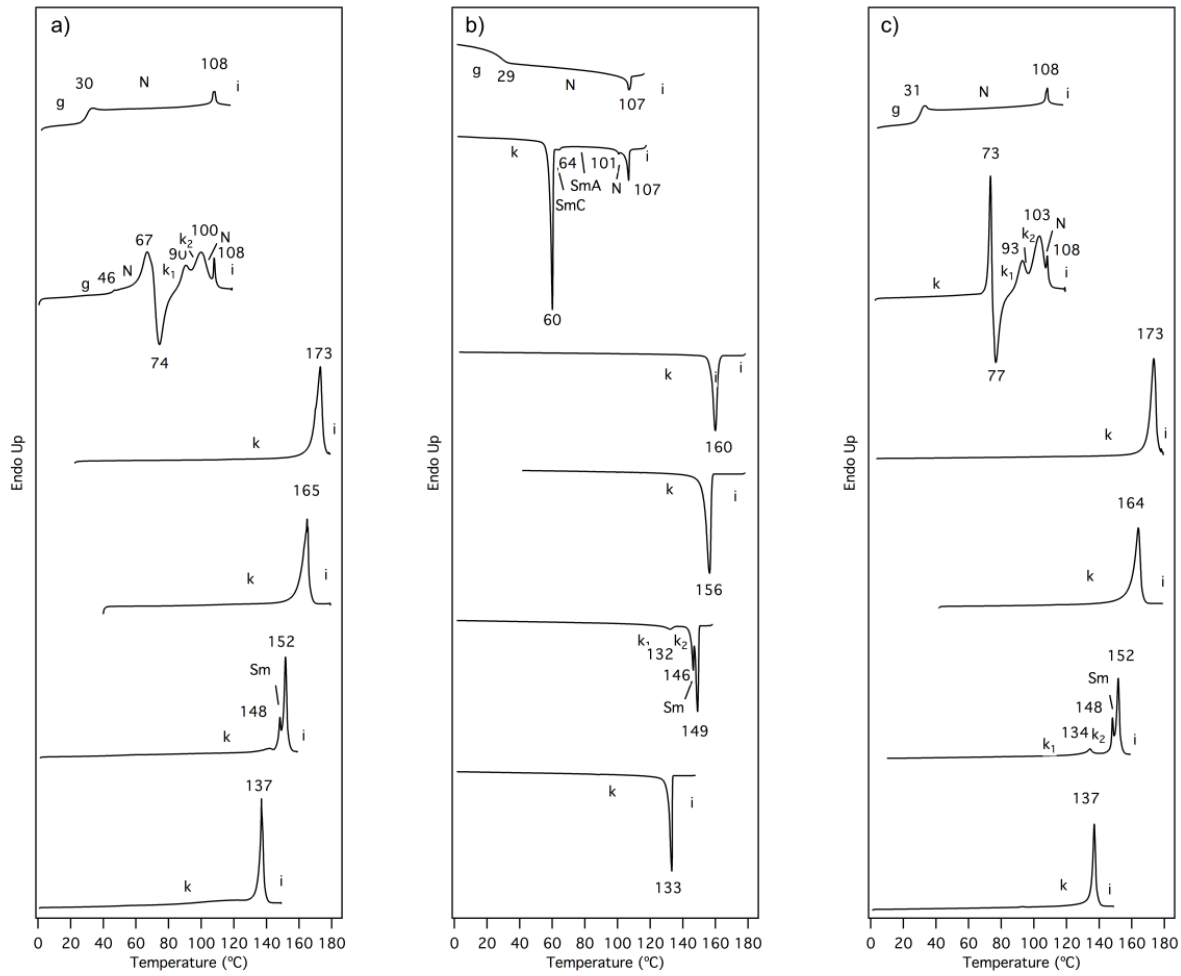

Figure 3.6: Differential scanning calorimetry thermograms of symmetrical star compounds **3-7** to **3-12** (top to bottom). From left to right are (a) first heating, (b) first cooling, and (c) second heating. Heating and cooling scans were performed at (10 °C/min).

Table 3.3: Structure of symmetrical star-branched compounds **3-7** to **3-12** and their phase transition temperatures as determined by DSC; scanning rate 10 ^{o}C/min.

Compound	X	n	M_w g/mol	thermal transitions (°C) and corresponding enthalpy changes (kcal/mol)[a]	
				heating	cooling
3-7	CN	5	893.10	g 30 N 108 (0.21) i [b] g 31 N 108 (0.19) i [d]	i 107 (0.27) N 29 g[c]
3-8	CN	10	1103.50	g 46 N 67 (8.83) 74 (-3.94) k1 90 (1.10) k2 100 (2.46) N 108 (0.55) i k 73 (4.92) 77 (-4.14) k_1 93 (1.74) k_2 103 (3.53) N 108 (0.32) i	i 107 (0.88) N 101 (0.04) SmA 64 (0.03) SmC 60 (6.67) k
3-9	OMe	5	908.15	k 173 (18.12) i k 173 (17.47) i	i 160 (18.63) k
3-10	OMe	10	1118.55	k 165 (25.15) i k 164 (23.47) i	i 156 (24.69) k
3-11	O(*S*)MeBu	5	1076.47	k 148 (2.46) Sm 152 (9.26) i k_1 134 (0.58) k_2 148 (3.34) Sm 152 (9.58) i	i 149 (9.52) Sm 146 (3.49) k_2 132 (0.54) k_1
3-12	O(*S*)MeBu	10	1286.87	k 137 (18.08) i k 137 (20.11) i	i 133 (20.88) k

[a] Notation: i, isotropic liquid; N, nmatic mesophase; g, glassy solid; k, crystalline solid; Sm, smectic mesophase. [b] first heating cycle. [c] First cooling cycle. [d] Second heating cycle.

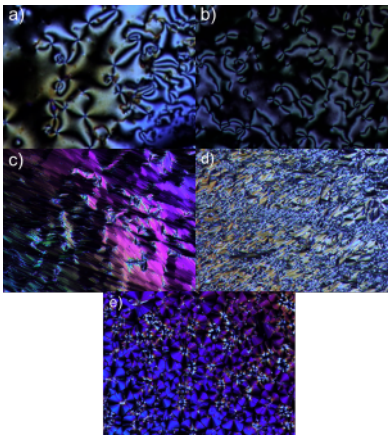

Figure 3.7: Polarized optical micrographs of corresponding samples that were slowly cooled from the isotropic liquid phase: (a) **3-7** (20×) at 109 ºC, (b) **3-8** (10×) at 109 ºC, (c) **3-8** (10×) at 110 ºC, (d) **3-8** (20×) at 61 ºC, (e) **3-11** (10×) at 148 ºC.

3.2.5 Heterolithic AB_2 three-arm star-branched mesogens

From the experiments described above, it appeared that the observed smectic phase in ABC three-arm star mesogens **3-1** to **3-4** was due to one of the terminal groups. To determine whether the terminal group in a single arm could dictate the phase behavior of a three-arm star-branched mesogen, we designed AB_2 stars with two arms that favor a nematic phase and one arm that might favor a smectic phase. We thought we might observe a disproportionate response when we introduced a smectic-phase promoting arm in a three-arm star mesogen. The AB_2 stars **3-13** to **3-15** were designed to test this idea. The long flexible linker was intended to help promote smectic mesomorphism for each of the three possible terminal groups.

The syntheses of compounds **3-13** to **3-15** are shown in Figure 3.8. The Passerini reaction involving 11-bromoundecanoic acid (**3-17**) along with cyanobiphenyl-containing isocyanide (**3-20**) and aldehyde (**3-44**) gave intermediate compound (**3-45**) in high yield. Nucleophilic substitution of the bromide with different mesogens (**3-42**, **3-27** or **3-31**) yielded heterolithic AB_2 star-branched mesogens **3-13** to **3-15**.

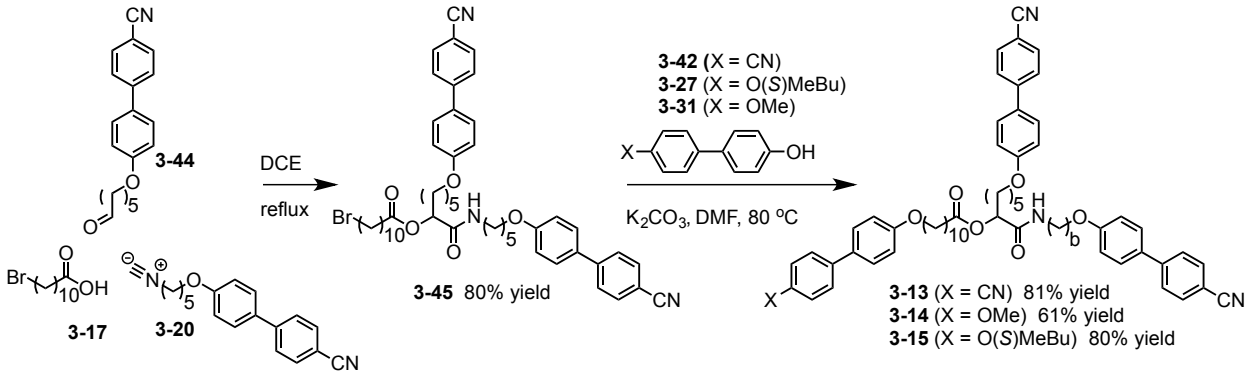

Figure 3.8: Synthesis of AB_2 star-branched mesogens **3-13** to **3-15**.

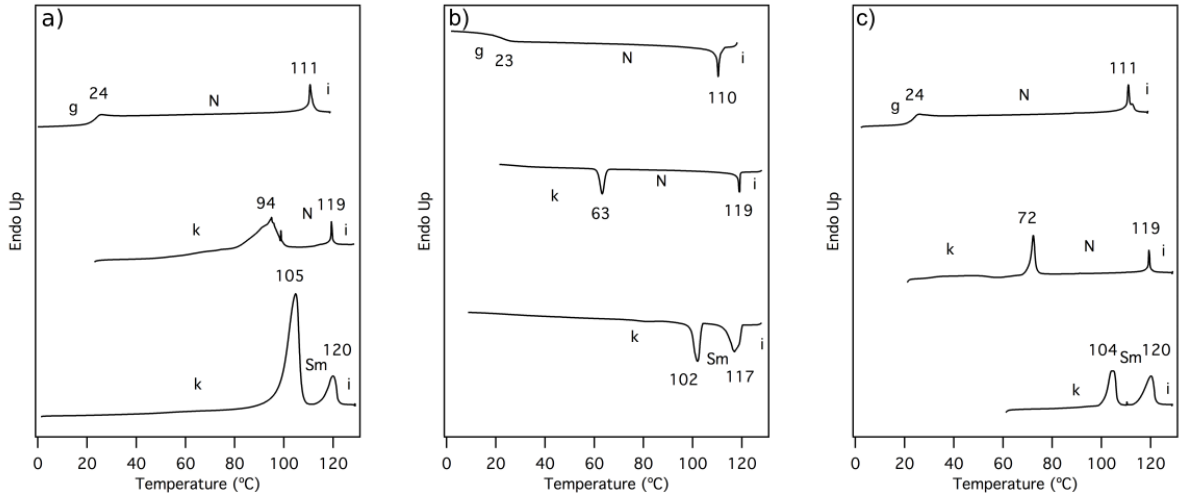

Figure 3.9: Differential scanning calorimetry thermograms of AB_2 three-arm star mesogens **3-13** to **3-15** (top to bottom). From left to right are (a) first heating, (b) first cooling, and (c) second heating. Heating and cooling scans were performed at (10 °C/min).

Figure 3.9 presents the DSC traces for AB_2 three-arm star mesogens **3-13** to **3-15**. The textures we observed from these compounds are shown in Figure 3.10. The transition temperatures and corresponding enthalpies as well as the phase assignment are presented in Table 3.4. A nematic liquid crystal phase is the only mesophase we observe for mesogens **3-13** and **3-14**. Heterolithic AB_2 star-branched mesogen **3-15** forms a smectic mesophase. These results clearly show that the 4'-(*S*)-2-methylbutoxy terminal group dominates the phase behavior of the three-arm star mesogens.

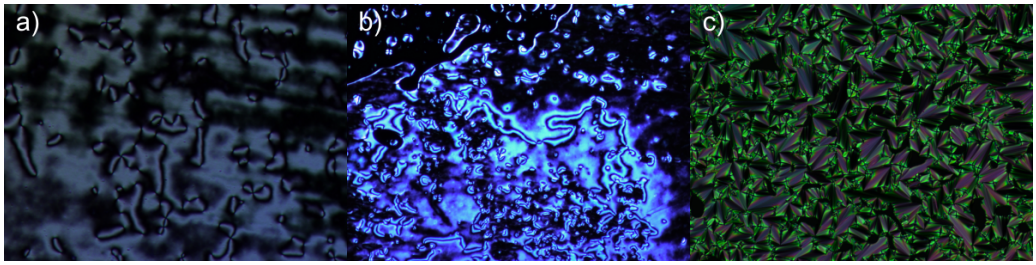

Figure 3.10: Polarized optical micrographs of corresponding samples that were slowly cooled from the isotropic liquid phase: (a) **3-13** (10×) at 112 ºC, (b) **3-14** (10×) at 118 ºC and (c) **3-15** (10×) at 118 ºC.

Table 3.4: Structure of AB_2 star-branched compounds **3-13** to **3-15** and their phase transition temperatures as determined by DSC; scanning rate 10 ^{o}C/min.

Compound	X	a, b, c	M_w g/mol	thermal transitions (°C) and corresponding enthalpy changes (kcal/mol)[a]	
				heating	cooling
3-13	CN	5, 5, 10	963.23	g 23.62 N 111 (0.63) i [b] g 24.39 N 111 (0.64) i [d]	i 110 (0.27) N 23 g [c]
3-14	OMe	5, 5, 10	968.25	k 95 (4.68) N 119 (0.41) i [b] k 72 (1.60) N 119 (0.42) i [d]	i 119 (0.47) N 63 (1.02) k
3-15	O(*S*)MeBu	5, 5, 10	1024.36	k 105 (13.05) Sm 120 (2.28) i k 104 (2.58) Sm 120 (2.39) i	i 117 (2.46) Sm 102 (2.28) k

[a] Notation: i, isotropic liquid; N, nmatic mesophase; g, glassy solid; k, crystalline solid; Sm, smectic mesophase. [b] first heating cycle. [c] First cooling cycle. [d] Second heating cycle.

3.3 Conclusions

A series of three-arm star-branched molecules containing different types of calamitic mesogens and flexible spacers of differing lengths were synthesized via the Passerini three-component reaction. A combination of DSC, POM, and XRD experiments has led to detailed structure-property relationships with respect to liquid crystal mesomorphism of heterolithic ABC three-arm star-branched compounds. It is notable that star-branched compounds having a small, asymmetric and conformationally flexible core can form liquid crystalline mesophases. The structure of the terminal mesogens in the arms of the star-branched compounds and the length of

the flexible linkers that connect the terminal groups to the core play important roles in determining the properties of these materials (e.g., mesogenic or not, the structure of the liquid crystalline phase, and the transition temperatures). With regard to the unexpected phase behavior of ABC star-branched mesogens **3-1** to **3-4**, we have shown that the preferred smectic ordering of the 4'-(*S*)-2-methylbutoxybiphenyl ether moiety causes these low-symmetry compounds to form smectic rather than nematic phases. This work demonstrates the feasibility of designing and preparing liquid crystalline star mesogens through multicomponent reactions.

3.4 Experimental procedures

3.4.1 Material

Celite 545 powder, hydrochloric acid (HCl), hexanes (hex), ethyl acetate (EtOAc), chloroform, acetone, dichloromethane, anhydrous *N*,*N*-dimethylformamide (DMF), and anhydrous tetrahydrofuran (THF) were used as received from EMD. Toluene, ammonium hydroxide (28-30%), and methanol (MeOH) were used as received from BDH. 6-Bromohexanoic acid, 11-bromoundecanoic acid, 1,5-dibromopentane, dimethylsulfate, phthalimide, isovaleric acid (99%), tert-butyl isocyanide (98%) and (*S*)-(−)-2-methylbutanol were used as received from Aldrich. Pyridinium chlorochromate (PCC) (98%), triethylamine (NEt_3), *p*-toluenesulfonyl chloride (TsCl), hydrazine monohydrate (98+%), anhydrous dichloromethane, isovaleraldehyde (98%), and triphenylphosphine (PPh_3, 99+%) were used as received from Alfa Aesar. Propyl formate (96%), and 1,2-dichloroethane (DCE) were used as received from Acros Organics. Anhydrous $MgSO_4$, sand (pure), KOH pellets, 6-bromohexanol, and 11-bromoundecanol were used as received from Fisher. 4'-Cyano-4-hydroxybiphenyl was used as received from Ark Pharm. 4,4'-Biphenol and ethyl 6-bromohexanoate were used as received from TCI. Sodium hydroxide was used as received from Amresco. Carbon tetrachloride was used as received from MP. Absolute ethanol (EtOH) was used as received from Pharmco-AAPER. Potassium carbonate was used as received from J. T. Baker. Silica gel 60 (40-63 microns) was used as received from Mallinckrodt Chemicals. Chloroform-*d* (+ 0.03% v/v TMS) was used as received from Cambridge Isotope Laboratories. 11-Bromoundecanoic acid ethyl ester, **3-19**, **3-20**, **3-27**, **3-29**, and **3-31** were prepared as described in the prior publication.[26]

3.4.2 Techniques

^{1}H NMR (400MHz, 500 MHz, 700 MHz), ^{13}C NMR (100 MHz, 125 MHz, 175 MHz), COSY, HSQC, and HMBC spectra were recorded on a Bruker Avance III NMR spectrometer. Peak multiplicities are denoted as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Thin layer chromatography (TLC) was performed using Whatman silica gel 60 Å plates (250 μm) with fluorescent indicator and visualized using a UV lamp (254 nm). Flash column chromatography was performed on a Teledyne Isco CombiFlash Rf with RediSep Rf Normal Phase disposable silica columns. Gel permeation chromatography (GPC) in THF (1 mL/min) was performed using a Shimadzu LC-20AD liquid chromatography pump equipped with a DGU-20A5 degasser, CBM-20A controller, RID-10A RI detector, CTO-20A column oven (all from Shimadzu), and three American Polymer Standards AM GPC gel columns of 100 Å (5 μm), 500 Å (5 μm), and 10,000 Å (5 μm). High-resolution electrospray ionization mass spectra (HRMS–ESI) were acquired by the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign on a Micromass Q-Tof Ultima. Elemental analysis was performed by the Microanalysis Laboratory at the University of Illinois at Urbana-Champaign. Differential scanning calorimetry (DSC) data were acquired using a DSC TA Q2000 at the Thermomechanical & Imaging Nanoscale Characterization (ThINC) core facility of the Advanced Energy Research and Technology Center at Stony Brook University. Polarized optical microscopy was performed on an Olympus BX43 optical microscope with a FP82HT hot stage and FP900 controller (both from Mettler Toledo). Melting point determinations were performed on a Thomas-Hoover Unimelt capillary melting point apparatus.

3.4.3 Experimental

6-(4'-Methoxybiphenyl-4-oxy)hexanol (3-46). 6-Bromo-1-hexanol (0.80 mL, 6.1 mmol) was added to an ice-water bath-cooled mixture of 4-hydroxy-4'-methoxybiphenyl (1.03 g, 5.14 mmol) and K_2CO_3 (1.4612 g, 10.57 mmol) in anhydrous DMF (20.0 mL). The reaction mixture was stirred at 80 ^{o}C for 6.5 h under a N_2 atmosphere. Additional 6-bromo-1-hexanol (0.33 mL, 2.5 mmol) and K2CO3 (0.7040 g, 5.094 mmol) were added and the reaction mixture was stirred at 80 ^{o}C for another 16 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and volatiles were removed by rotary evaporation. Residual K_2CO_3 was removed by rinsing the crude product with chilled H2O three times (30 mL total) and the crude product was

rinsed with cold acetone (5 mL) twice. The product was collected by filtration followed by recrystallization from toluene to give **3-46** as colorless crystals (0.97 g, 63%). TLC (SiO_2, CH_2Cl_2): R_f = 0.11. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.47 (overlapping m, 4H; *H*2, *H*2'), 6.95 (overlapping m, 4H; *H*3, *H*3'), 4.00 (t, *J* = 6.5 Hz, 2H; PhOC*H*$_2$C$_4$H$_8$OH), 3.84 (s, 3H; C*H*$_3$O), 3.68 (dt, J_1 = 8.4 Hz, J_2 = 5.8 Hz, 2H; CH$_2$O*H*), 1.82 (m, 2H; OCH$_2$C*H*$_2$), 1.62 (m, 2H; C*H*$_2$CH$_2$OH), 1.51 (overlapping m, 4H; OC$_2$H$_4$C$_2$*H*$_4$), 1.23 (t, *J* = 5.4 Hz, 1H; OH). ^{13}C NMR (125 MHz, CDCl3, δ, ppm): 158.9 (C1), 158.4 (C1'), 133.8 (C4), 133.5 (C4'), 127.9 (C2 or C2'), 115.0 (C3), 114.4 (C3'), 68.1 (O*C*H$_2$), 63.2 (*C*H$_2$OH), 55.6 (*C*H$_3$O), 32.9 (*C*H$_2$CH$_2$OH), 29.5 (OCH$_2$*C*H$_2$), 26.1 (OC$_2$H$_4$*C*H$_2$), 25.8 (OC$_3$H$_6$*C*H$_2$).

6-(4'-Methoxybiphenyl-4-oxy)hexanal (3-18). A mixture of **3-46** (0.40 g, 1.3 mmol) in anhydrous CH_2Cl_2 (26.7 mL) was sparged with N_2 for 15 min. To the solution, PCC (0.3756 g, 1.742 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 19 h under a N_2 atmosphere. The crude product was obtained by filtering the reaction mixture though Celite and sand. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2/hex 3:1) to give **3-18** as a colorless solid (0.33 g, 84%). TLC (SiO_2, CH_2Cl_2/hex 3:1): R_f = 0.14. ^{1}H NMR (700 MHz, $CDCl_3$, δ, ppm): 9.79 (t, *J* = 1.7 Hz, 1H; C*H*O), 7.47 (overlapping m, 4H; *H*2, *H*2'), 6.94 (overlapping m, 4H; *H*3, *H*3'), 4.00 (t, *J* = 6.3 Hz, 2H; PhOC*H*$_2$), 3.84 (s, 3H; CH$_3$O), 3.68 (td, J_1 = 7.3 Hz, J_2 = 1.7 Hz, 2H; C*H*$_2$CHO), 1.83 (m, 2H; OCH$_2$C*H*$_2$), 1.62 (m, 2H; C*H*$_2$CH$_2$CHO), 1.54 (overlapping m, 4H; OC$_2$H$_4$C*H*$_2$). ^{13}C NMR (175 MHz, $CDCl_3$, δ, ppm): 202.8 (*C*HO), 158.9 (*C*1), 158.3 (*C*1'), 133.7 (*C*4), 133.6 (*C*4'), 127.9 (*C*2 or *C*2'), 114.9 (*C*3), 114.4 (*C*3'), 67.8 (O*C*H$_2$), 55.6 (*C*H$_3$O), 44.1(*C*H$_2$CHO), 29.3 (OCH$_2$*C*H$_2$), 26.0 (OC$_2$H$_4$*C*H$_2$), 22.0 (*C*H$_2$CH$_2$CHO). Anal. Calcd for $C_{28}H_{39}NO_2$: C, 76.48; H, 7.43. Found: C, 76.23; H, 7.31. HRMS-EI (*m*/*z*): calcd for $C_{19}H_{22}O_3$, 298.1569, found 298.1569.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-methoxybiphenyl-4-oxy)hexyl 6-bromohexanoate (3-22). A mixture of **3-18** (0.1282 g, 0.4297 mmol), **3-20** (0.1248 g, 0.4298 mmol), and 6-bromohexanoic acid (**3-16**) (0.0837 g, 0.429 mmol) in anhydrous DCE (0.43 mL) was refluxed for 17 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2/EtOAc 95:5) to give **3-22** as slightly yellow solid (0.22 g, 67%). TLC (SiO_2, 95:5 CH_2Cl_2/EtOAc): R_f = 0.19. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.66 (m, 4H; (CB)*H*3' and *H*2'), 7.52 (m, 2H, (CB)*H*2), 7.46 (m, 4H; (MB)*H*2 and *H*2'), 6.94 (overlapping m,

2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'), 6.03 (t, J = 6.0 Hz, 1H; N*H*), 5.18 (dd, J_1 = 6.9 Hz, J_2 = 6.9 Hz, 1H; NHCOC*H*), 3.98 (m, 4H; PhOCH_2), 3.84 (s, 3H, CH_3O), 3.39 (t, J = 6.7 Hz, 2H; CH_2Br), 3.32 (m, 2H; CH_2NH), 2.42 (t, J = 7.4 Hz, 2H; O_2CCH_2), 1.85 (overlapping, 8H; PhOCH$_2$CH_2, BrCH$_2$CH_2, NHCOCHCH_2), 1.66 (overlapping m, 4H; NHCOCHCH$_2$CH_2, O_2CCH$_2$CH_2), 1.48 (overlapping m, 8H; OCH$_2$CH$_2$CH_2, NHCH$_2$CH_2, BrC$_2$H$_4$CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.3 (O_2C), 169.9 (NH*C*O), 159.8 ((CB)*C*1), 158.9 ((MB)*C*1), 158.3 ((MB)*C*1'), 145.4 ((CB)*C*4), 133.7 ((MB)*C*4), 133.6 ((MB)*C*4'), 132.8 ((CB)*C*3'), 131.6 ((CB)*C*4'), 128.6 ((CB)*C*3'), 127.9 ((CB)*C*2), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 114.9 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.2 (CO*C*HO$_2$C), 68.0 (O*C*H$_2$CH$_2$), 67.9 (OCH$_2$*C*H$_2$), 55.6 (*C*H$_3$O), 39.3 (*C*H$_2$NHCO), 34.3 (O_2C*C*H$_2$), 33.6 (*C*H$_2$CH$_2$Br), 32.5 (*C*H$_2$Br), 32.0 (NHCOCH*C*H$_2$), 29.6 (OCH$_2$*C*H$_2$), 29.3 (OCH$_2$*C*H$_2$), 29.0 (*C*H$_2$), 27.8 (*C*H$_2$), 26.0 (*C*H$_2$), 25.0 (*C*H$_2$), 24.8 (*C*H$_2$), 24.3 (*C*H$_2$), 23.6 (*C*H$_2$). HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{44}H_{52}BrN_2O_6$, 783.3009, found 783.2997.

***N*-(10-Bromodecyl)phthalimide (3-47).**[37] A solution of 1,10-dibromopentane (9.2 mL, 0.041 mol) in anhydrous DMF (17.2 mL) was added dropwise to an ice-water bath-cooled suspension of phthalimide (4.02 g, 0.0273 mol) and K_2CO_3 (7.58 g, 0.0527 mol) in anhydrous DMF (10.0 mL). The reaction mixture was stirred under a N_2 atmosphere for 70 h at room temperature. Residual solids were removed from the reaction mixture by filtration. The crude product was obtained by rotary evaporation of the volatiles from the filtrate. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) to give **3-47** as a colorless solid (5.64 g, 57%). TLC (SiO_2, 4:1 hex/EtOAc): R_f = 0.58. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.84 (m, 2H; *H*2), 7.71 (m, 2H; *H*3), 3.67 (t, J = 7.3 Hz, 2H; NCH_2), 3.40 (t, J = 6.8 Hz, 2H; CH_2Br), 1.84 (m, 2H; CH_2CH$_2$Br), 1.67 (m, 2H; NCH$_2$CH_2), 1.39 (m, 2H; NCH$_2$CH$_2$CH_2), 1.31 (overlapping, 10H; NCH$_2$CH$_2$C$_5$$H_{10}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 134.1 (*C*3), 132.4 (*C*1), 123.4 (*C*2), 38.3 (NCH_2), 34.3 (*C*H$_2$Br), 33.0 (CH$_2$*C*H$_2$Br), 29.6 (*C*H$_2$), 29.5 (*C*H$_2$), 29.3 (*C*H$_2$), 28.9 (*C*H$_2$), 28.8 (*C*H$_2$), 28.4 (*C*H$_2$), 27.0 (*C*H$_2$). ^{1}H Spectral data agree with those previously reported.[37]

***N*-(10-(4'-Cyanobiphenyl-4-oxy)decyl)phthalimide (3-48).** A solution of *N*-(10-bromodecyl)phthalimide (**3-47**) (4.76 g, 13.0 mmol) in anhydrous DMF (25.0 mL) was added dropwise to a ice-water bath-cooled mixture of 4'-cyano-4-hydroxybiphenyl (2.10 g, 10.8 mmol) and K_2CO_3 (2.98 g, 21.6 mmol) in anhydrous DMF (11.0 mL). The reaction mixture was stirred

under a N_2 atmosphere for 6 h at 80 ^oC. The reaction was cooled to room temperature before H_2O (20 mL) was added. Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL) three times. The combined organic extracts were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was purified by flash column chromatography (SiO2, hex/EtOAc 4:1 to 3:2) and recrystallized from EtOH to give **3-48** as a colorless solid (3.77 g, 73%). TLC (SiO_2, CH_2Cl_2): R_f = 0.26. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.84 (m, 2H; (Phth)*H*2), 7.70 (m, 2H; (Phth)*H*3), 7.69 (m, 2H; (CB)*H*3'), 7.74 (m, 2H; (CB)*H*2'), 7.52 (m,2H; (CB)*H*2), 6.99 (m, 2H; (CB)*H*3'), 4.00 (t, *J* = 7.0 Hz, 2H; PhOCH_2), 3.67 (t, *J* = 7.3 Hz, 2H; NCH_2), 1.79 (m, 2H; OCH_2CH_2), 1.67 (m, 2H; NCH_2CH_2), 1.46 (m, 2H; $NC_2H_4CH_2$), 1.32 (overlapping m, 10H; $OC_2H_4C_5H_{10}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 160.0 (*C*1), 145.5 (*C*4), 134.1 ((Phth)*C*3), 132.8 (*C*3'), 132.4 (Phth)*C*1), 131.5 (*C*4'), 128.5 (*C*2), 127.3 (*C*2'), 123.4 (Phth)*C*2), 119.4 (*C*1'), 115.3 (*C*3), 110.2 (*C*N), 68.4 (OCH_2), 38.3 (NCH_2), 29.7 (OCH_2CH_2), 29.6 ($OC_2H_4C_6H_{12}$), 29.5 ($OC_2H_4C_6H_{12}$), 29.4 ($OC_2H_4C_6H_{12}$), 29.4 ($OC_2H_4C_6H_{12}$), 28.8 ($OC_2H_4C_6H_{12}$), 27.1 ($OC_2H_4C_6H_{12}$), 26.2 ($NC_2H_4CH_2$).

10-(4'-Cyanobiphenyl-4-oxy)decylamine (3-49). Hydrazine monohydrate (3.6 mL, 74 mmol) was added slowly to an ice-water bath-cooled suspension of **3-48** (3.51 g, 7.30 mmol) in EtOH (29.0 mL). The reaction mixture was heated at reflux for 1 h under a N_2 atmosphere. The reaction mixture was cooled in an ice-water bath and H_2O (30 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (20 mL) three times. The combined organic extracts were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give **3-49** as crude solid (2.46 g).

1-Formamido-10-(4'-cyanobiphenyl-4-oxy)decane (3-50). Propyl formate (6.0 mL, 0.062 mol) and **3-49** (crude product 2.15 g) were stirred at reflux for 17 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to 95:5 CH_2Cl_2/MeOH) to give **3-50** as a slightly yellow solid (2.22 g, 80 % over two steps). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.34. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.17 (br s, 0.8H; *cis*-amide C*H*O), 8.05 (d, *J* = 12.0 Hz, 0.2H; *trans*-amide CHO), 7.70 (m, 2H; H3'), 7.63 (m, 2H; H2'), 7.53 (m, 2H; *H*2), 6.99 (m, 2H; *H*3), 5.46 (br s, 1H; N*H*), 4.00 (t, J = 6.5 Hz, 2H; $PhOCH_2$), 3.30 (dt, *J* = 7.5 Hz, *J* = 6.6 Hz, 1.6H; *cis*-isomer NCH_2), 3.21 (dt, *J* = 6.8 Hz, *J* = 4.9

Hz, 0.4H; *trans*-isomer NCH_2), 1.80 (m, 2H; $OCH_2CH_2C_9H_{18}NH$), 1.47 (overlapping m, 4H; $OCH_2CH_2CH_2C_8H_{16}NH$, CH_2CH_2NH), 1.35 (overlapping m, 10H; $OC_3H_6C_5H_{10}C_2H_4NH$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 164.7 (*trans*-isomer CHO), 161.3 (*cis*-isomer *C*HO), 160.0 (*C*1), 145.5 (*C*4), 132.8 (*C*3'), 131.5 (*C*4'), 128.5 (*C*2), 127.3 (*C*2'), 119.3 (*C*1'), 115.3 (*C*3), 110.3 (*C*N), 68.4 (O*C*H_2), 41.9 (*trans*-isomer N*C*H_2), 38.4 (*cis*-isomer NCH_2), 31.5 (*trans*-isomer CH_2), 29.8 (*cis*-isomer CH_2), 29.7 (CH_2), 29.64 (CH_2), 29.61 (*trans*-isomer CH_2), 29.5 (CH_2), 29.42 (CH_2), 29.40 (*cis*-isomer CH_2), 29.3 (*trans*-isomer CH_2), 27.0 ($OCH_2CH_2CH_2$), 26.6 (*trans*-isomer *C*H_2), 26.2 (*cis*-isomer CH_2).

1-Isocyano-10-(4'-cyanobiphenyl-4-oxy)decane (3-21). A suspension of **3-50** (2.19 g, 5.79 mmol) and PPh_3 (1.8220 g, 6.9465 mmol) in CCl_4 (0.68 mL, 7.0 mmol), Et_3N (0.98 mL, 7.0 mmol), and anhydrous CH_2Cl_2 (12.0 mL) was heated at reflux for 15 h under a N_2 atmosphere. The volatiles were removed by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) followed by recrystallization from ethanol and yielded **3-21** as colorless crystals (1.41 g, 68%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.34. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.70 (m, 2H; H3'), 7.64 (m, 2H; H2'), 7.53 (m, 2H; H2), 7.00 (m, 2H; H3), 4.01 (t, J = 6.5 Hz, 2H; $PhOCH_2$), 3.38 (tt, ^3J= 6.7 Hz, ^2J= 1.9 Hz, 2H; CH_2NC), 1.81 (m, 2H; $OCH_2CH_2C_9H_{18}NH$), 1.68 (m, 2H; CH_2CH_2NC), 1.47 (overlapping m, 4H; $OCH_2CH_2CH_2C_8H_{16}NC$, CH_2CH_2NC), 1.35 (overlapping m, 8H; $OC_3H_6C_5H_{10}C_2H_4NC$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 160.0 (*C*1), 155.7 (t, J = 5.8 Hz, N*C*), 145.5 (*C*4), 132.8 (*C*3'), 131.5 (*C*4'), 128.5 (*C*2), 127.3 (*C*2'), 119.3 (*C*1'), 115.3 (*C*3), 110.2 (*C*N), 68.3 (O*C*H_2), 41.8 (t, J = 6.4 Hz; N*C*), 29.6 (CH_2CH_2NC), 29.51 (OCH_2CH_2), 29.49 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 26.5 (CH_2), 26.2 (CH_2). Anal. Calcd for $C_{24}H_{28}N_2O$: C, 79.96; H, 7.83; N, 7.77. Found: C, 80.10; H, 7.71; N, 7.85. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{24}H_{28}N_2ONa$, 383.2099, found 383.2097.

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 11-bromoundecanoate (3-23). A mixture of **3-19** (0.1009 g, 0.2738 mmol), **3-21** (0.0987 g, 0.274 mmol), and 11-bromoundecanoic acid (**3-17**) (0.0726 g, 0.274 mmol) in anhydrous DCE (0.55 mL) was refluxed for 18 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO2, $CHCl_3$ to $CHCl_3$/EtOAc 95:5) to give **15a** as colorless solid (0.23 g, 82%). TLC (SiO_2, 95:5 CH_2Cl_2/EtOAc): R_f = 0.61. ^{1}H NMR (500 MHz,

$CDCl_3$, δ, ppm): 7.66 (m, 4H; (CB)*H*3' and *H*2'), 7.52 (m, 2H; (CB)*H*2), 7.46 (m, 4H; (MB)*H*2 and *H*2'), 6.97 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'), 5.97 (t, J = 6.0 Hz, 1H; N*H*), 5.17 (dd, J_1 = 7.2 Hz, J_2 = 7.2 Hz, 1H; NHCOC*H*), 3.98 (m, 6H; PhOCH_2), 3.84 (s, 3H, CH_3O), 3.39 (t, J = 6.8 Hz, 2H; BrCH_2), 3.26 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz, 2H; O_2CCH_2), 1.83 (overlapping m, 8H; NHCOCHCH_2, BrCH$_2$CH_2, PhOCH$_2$CH_2), 1.65 (m, 2H; O_2CCH$_2$CH_2), 1.46 (overlapping m, 8H; CH_2CH$_2$NH, OC$_2$H$_4$CH_2, BrC$_2$H$_4$CH_2), 1.31 (overlapping m, 30H; (CB)OC$_3$H$_6$C$_5$$H_{10}$, (MB)OC$_3H_6C_6$$H_{12}$, ((*S*)MB)OC$_3H_6C_4$$H_8$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2*C*), 170.0 (NH*C*O), 160.0 ((CB)*C*1), 158.9 ((MB)*C*1), 158.5 ((MB)*C*1'), 145.5((CB)*C*4), 133.8 ((MB)*C*4), 133.5 ((MB)*C*4'), 132.8 ((CB)*C*3'), 131.5 ((CB)*C*4'), 128.5 ((CB)C3'), 127.91 ((CB)*C*2), 127.89 ((MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.0 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.2 (CO*C*HO$_2$C), 68.4 (OCH$_2$*C*H$_2$), 68.3 (OCH$_2$*C*H$_2$), 55.5 (*C*H$_3$O), 39.4 (*C*H$_2$NHCO), 34.6 (O_2C*C*H$_2$), 34.2 (*C*H$_2$CH$_2$Br), 33.0 (*C*H$_2$Br), 32.1 (NHCOCH*C*H$_2$), 29.80 (OCH$_2$*C*H$_2$), 29.76 (OCH$_2$*C*H$_2$), 29.72 (OCH$_2$*C*H$_2$), 27.70 (*C*H$_2$), 26.65 (*C*H$_2$), 29.62 (*C*H$_2$), 29.60 (*C*H$_2$), 29.56 (*C*H$_2$), 29.48 (*C*H$_2$), 29.46 (*C*H$_2$), 29.3 (*C*H$_2$), 29.0 (*C*H$_2$), 28.4 (*C*H$_2$), 27.1 (*C*H$_2$), 26.30 (*C*H$_2$), 26.27 (*C*H$_2$), 25.2 (*C*H$_2$), 25.0 (*C*H$_2$).

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 11-bromoundecanoate (3-24). A mixture of **3-19** (0.1420 g, 0.3853 mmol), **3-20** (0.1118 g, 0.3851 mmol), and 11-bromoundecanoic acid (**3-17**) (0.1020 g, 0.3846 mmol) in anhydrous THF (0.40 mL) was refluxed for 7 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) to give **3-24** as colorless solid (0.19 g, 53%). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.22. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 2H; (CB)*H*3'), 7.64 (m, 2H; (CB)*H*2'), 7.52 (m, 2H; (CB)*H*2), 7.46 (m, 4H; (MB)*H*2 and *H*2'), 6.97 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'), 6.03 (t, J = 5.9 Hz, 1H; N*H*), 5.17 (dd, J_1 = 7.3 Hz, J_2 = 7.2 Hz, 1H; NHCOC*H*), 4.00 (t, J = 6.6 Hz , 2H; PhOCH_2), 3.99 (m, 2H; PhOCH_2), 3.84 (s, 3H, CH_3O), 3.39 (t, J = 6.8 Hz, 2H; BrCH_2), 3.32 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz, 2H; O_2CCH_2), 1.83 (overlapping m, 8H; NHCOCHCH_2, BrCH$_2$CH_2, PhOCH$_2$CH_2), 1.64 (m, 4H; O_2CCH$_2$CH_2, CH_2CH$_2$NH), 1.51 (m, 2H; OC$_2$H$_4$CH_2) 1.46 (overlapping m, 4H; OC$_2$H$_4$CH_2, BrC$_2$H$_4$CH_2), 1.31 (overlapping m, 22H; BrC$_5$$H_{10}$, (MB)OC$_3H_6C_6$$H_{12}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2*C*), 170.2 (NH*C*O), 159.8

((CB)*C*1), 158.9 ((MB)*C*1), 158.5 ((MB)*C*1'), 145.4((CB)*C*4), 133.8 ((MB)*C*4), 133.5 ((MB)*C*4'), 132.8 ((CB)*C*3'), 131.6 ((CB)*C*4'), 128.6 ((CB)*C*3'), 127.91 ((CB)*C*2), 127.90 ((MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.0 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.2 (CO*C*HO$_2$C), 68.3 (OCH$_2$*C*H$_2$), 68.0 (OCH$_2$*C*H$_2$), 55.6 (*C*H$_3$O), 39.3 (*C*H$_2$NHCO), 34.6 (O$_2$C*C*H$_2$), 34.3 (*C*H$_2$CH$_2$Br), 33.0 (*C*H$_2$Br), 32.1 (NHCOCH*C*H$_2$), 29.8 (OCH$_2$*C*H$_2$), 29.7 (OCH$_2$*C*H$_2$), 29.64 (OCH$_2$*C*H$_2$), 29.61 (*C*H$_2$), 26.60 (*C*H$_2$), 29.58 (*C*H$_2$), 29.56 (*C*H$_2$), 29.54 (*C*H$_2$), 29.46 (*C*H$_2$), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 29.0 (*C*H$_2$), 28.9 (*C*H$_2$), 28.4 (*C*H$_2$), 26.3 (*C*H$_2$), 25.2 (*C*H$_2$), 25.0 (*C*H$_2$), 23.6 (*C*H$_2$).

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-6-(4'-methoxybiphenyl-4-oxy)hexyl 11-bromoundecanoate (3-25). A mixture of **3-19** (0.1491 g, 0.4046 mmol), **3-21** (0.1458 g, 0.4044 mmol), and 6-bromohexanoic acid (**3-16**) (0.0789 g, 0.405 mmol) in anhydrous DCE (0.40 mL) was refluxed for 15 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) to give **3-25** as colorless solid (0.30 g, 80%). TLC (SiO_2, 95:5 CH_2Cl/EtOAc): R_f = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 2H; (CB)*H*3'), 7.64 (m, 2H; (CB)*H*2'), 7.52 (m, 2H; (CB)*H*2), 7.46 (m, 4H; (MB)*H*2 and *H*2'), 6.97 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'), 5.96 (t, *J* = 5.9 Hz, 1H; N*H*), 5.16 (dd, J_1 = 7.2 Hz, J_2 = 7.1 Hz, 1H; NHCOC*H*), 4.00 (t, *J* = 6.6 Hz , 2H; PhOCH_2), 3.98 (t, *J* = 6.5 Hz , 2H; PhOCH_2), 3.86 (s, 3H, CH_3O), 3.41 (t, *J* = 6.7 Hz, 2H; BrCH_2), 3.26 (m, 2H; CH_2NH), 2.42 (t, *J* = 7.4 Hz, 2H; O$_2$CCH_2), 1.83 (overlapping m, 8H; NHCOCHCH_2, BrCH$_2$CH_2, PhOCH$_2$CH_2), 1.69 (m, 2H; O$_2$CCH$_2$CH_2), 1.46 (overlapping m, 8H; CH_2CH$_2$NH, OC$_2$H$_4$CH_2, BrC$_2$H$_4$CH_2), 1.31 (overlapping m, 30H; (CB)OC$_3$H$_6$C$_5$$H_{10}$, (MB)OC$_3H_6C_6$$H_{12}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.3 (O$_2$*C*), 169.9 (NH*C*O), 160.0 ((CB)*C*1), 158.9 ((MB)*C*1), 158.5 ((MB)*C*1'), 145.5((CB)*C*4), 133.7 ((MB)*C*4), 133.5 ((MB)*C*4'), 132.8 ((CB)*C*3'), 131.5 ((CB)*C*4'), 128.5 ((CB)C3'), 127.90 ((CB)*C*2), 127.89 ((MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.0 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.3 (CO*C*HO$_2$C), 68.4 (OCH$_2$*C*H$_2$), 68.3 (OCH$_2$*C*H$_2$), 55.6 (*C*H$_3$O), 39.4 (*C*H$_2$NHCO), 34.3 (O$_2$C*C*H$_2$), 33.6 (*C*H$_2$CH$_2$Br), 32.5 (*C*H$_2$Br), 32.1 (NHCOCH*C*H$_2$), 29.80 (OCH$_2$*C*H$_2$), 29.75 (OCH$_2$*C*H$_2$), 29.71 (OCH$_2$*C*H$_2$), 27.69 (*C*H$_2$), 26.64 (*C*H$_2$), 29.61 (*C*H$_2$), 29.59 (*C*H$_2$), 29.54 (*C*H$_2$), 29.47 (*C*H$_2$), 29.45 (*C*H$_2$), 27.8 (*C*H$_2$), 27.1 (*C*H$_2$), 26.30 (*C*H$_2$), 26.29 (*C*H$_2$), 25.26 (*C*H$_2$), 25.0 (*C*H$_2$), 24.3 (*C*H$_2$).

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-methoxybiphenyl-4-oxy)hexyl 11-bromoundecanoate (3-26). A mixture of **3-18** (0.3066 g, 1.028 mmol), **3-20** (0.2983 g, 1.027 mmol), and 11-bromoundecanoic acid (**3-17**) (0.2724 g, 1.027 mmol) in anhydrous DCE (1.0 mL) was refluxed for 18 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-26** as colorless solid (0.57 g, 65%). TLC (SiO_2, 3:2 hex/EtOAc): $R_f = 0.14$. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.66 (m, 4H; (CB)*H*3' and *H*2'), 7.52 (m, 2H; (CB)*H*2), 7.46 (overlapping m, 4H; (MB)*H*2 and *H*2'), 6.94 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'), 6.04 (t, $J = 5.9$ Hz, 1H; N*H*), 5.19 (dd, $J_1 = 6.9$ Hz, $J_1 = 6.9$ Hz, 1H; NHCOC*H*), 3.98 (m, 4H; PhOCH_2), 3.84 (s, 1H; CH_3O), 3.39 (t, $J = 6.8$ Hz, 2H; CH_2Br), 3.32 (m, 2H; CH_2NH), 2.39 (t, $J = 7.5$ Hz, 2H; O_2CCH_2), 1.85 (overlapping, 8H; PhOCH$_2$CH_2, BrCH$_2$CH_2, NHCOCHCH_2), 1.64 (overlapping 4H, NHCOCHCH$_2$CH_2, O_2CCH$_2$CH_2), 1.46 (overlapping m, 8H; OCH$_2$CH$_2$CH_2, BrC_2H_4CH_2, NHCH$_2$CH_2), 1.27 (overlapping m, 10H, $O_2C_2H_4C_5H_{10}$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2C), 170.0 (NH*C*O), 159.8 ((CB)*C*1), 158.9 ((MB)*C*1), 158.3 ((MB)*C*1'), 145.4 ((CB)*C*4), 133.7 ((MB)*C*4 or ((MB)*C*4'), 132.8 ((CB)*C*3'), 131.6 ((CB)*C*4'), 128.6 ((CB)C3'), 127.9 ((CB)C2), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 114.9 ((MB)*C*3), 114.4 ((MB)C3'), 110.3 (*C*N), 74.0 (CO*C*HO$_2$C), 67.98 (O*C*H$_2$CH$_2$), 67.95 (O*C*H$_2$CH$_2$), 55.6 (*C*H$_3$O), 39.3 (*C*H$_2$NHCO), 34.5 (O_2C*C*H$_2$), 34.3 (*C*H$_2$CH$_2$Br), 33.0 (*C*H$_2$Br), 32.0 (NHCOCH*C*H$_2$), 29.58 (OCH$_2$*C*H$_2$), 29.55 (OCH$_2$*C*H$_2$), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 29.0 (*C*H$_2$), 28.9 (*C*H$_2$), 28.3 (*C*H$_2$), 26.0 (*C*H$_2$), 25.2 (*C*H$_2$), 24.8 (*C*H$_2$), 23.6 (*C*H$_2$). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{49}H_{62}BrN_2O_6$, 853.3791, found 853.3768.

6-Bromohexanal (3-28).[38-39] A mixture of 6-bromohexanol (1.0061 g, 5.5555 mmol) in anhydrous CH_2Cl_2 (11.0 mL) was sparged with N_2 for 15 min. To the solution, PCC (1.5590 g, 7.2323 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 3 h under a N_2 atmosphere. The crude product was obtained by filtering the reaction mixture though Celite and sand. The product was purified by flash column chromatography (SiO_2, hex to EtOAc/hex 1:4) to give **3-28** as colorless oil (0.45 g, 45%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.38. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 9.77 (t, $J = 1.7$ Hz, 1H; C*H*O), 3.40 (t, $J = 6.7$ Hz, 2H; BrCH$_2$), 2.46 (td, $J_1 = 7.3$ Hz, $J_2 = 1.6$ Hz, 2H; CH_2CHO), 1.88 (m, 2H; BrCH$_2$CH_2), 1.66 (m, 2H; CH_2CH$_2$CHO), 1.48 (m, 2H; BrC_2H_4CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 202.4

(*C*HO), 43.9 (*C*H_2CHO), 33.6 (Br*C*H_2*C*H_2), 32.6 (Br*C*H_2), 27.9 (*C*H_2*C*H_2CHO), 21.4 (*C*H_2*C*$_2$H$_4$CHO). ^{1}H NMR spectral data agree with those previously reported.[40]

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-6-bromohexyl 6-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)hexanoate (3-30). A mixture of 6-bromohexanal (**3-28**) (0.0524 g, 0.263 mmol), **3-21** (0.1050 g, 0.2913 mmol), and **3-29** (0.1282 g, 0.2910 mmol) in anhydrous DCE (0.58 mL) was refluxed for 19.5 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-30** as colorless solid (0.12 g, 44%). TLC (SiO_2, 95:5 CH_2Cl_2/EtOAc): R_f = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 2H; (CB)*H*3'), 7.64 (m, 2H; (CB)*H*2'), 7.52 (m, 2H; (CB)*H*2), 7.46 (m, 4H; ((*S*)MB)*H*2 and *H*2'), 6.97 (overlapping m, 2H, (CB)*H*3; 4H, ((*S*)MB)*H*3 and *H*3'), 5.99 (t, *J* = 5.9 Hz, 1H; N*H*), 5.18 (dd, J_1 = 7.1 Hz, J_2 = 7.0 Hz, 1H; NHCOC*H*), 4.00 (t, *J* = 6.5 Hz , 2H; PhOCH_2), 3.98 (t, *J* = 6.5 Hz, 2H; PhOCH_2), 3.84 (m, 1H; PhOCH_2CHCH$_3$), 3.75 (m, 1H; PhOCH_2CHCH$_3$), 3.38 (t, *J* = 6.8 Hz, 2H; BrCH_2), 3.26 (m, 2H; CH_2NH), 2.40 (t, *J* = 7.5 Hz, 2H; O_2CCH_2), 1.83 (overlapping m, 8H; NHCOCHCH_2, BrCH$_2$CH_2, PhOCH$_2$CH_2; 1H, PhOCH$_2$C*H*CH$_3$), 1.64 (overlapping m, 4H; O_2CCH$_2$CH_2, CH_2CH$_2$NH; 1H, PhOCH$_2$CHCH_2), 1.51 (m, 2H; OC$_2$H$_4$CH_2) 1.46 (overlapping m, 4H; OC$_2$H$_4$CH_2, BrC$_2$H$_4$CH_2), 1.31 (overlapping m, 22H; BrC$_5$*H*$_{10}$, (MB)OC$_3$H$_6$C$_6$*H*$_{12}$; 1H, PhOCH$_2$CHCH_2), 1.03 (d, *J* = 6.8 Hz, 3H; OCH$_2$CHC*H*$_3$), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH$_3$).. ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.6 (O_2*C*), 169.8 (NH*C*O), 160.0 ((CB)*C*1), 158.7 (((*S*)MB)*C*1), 158.4 (((*S*)MB)*C*1'), 145.5 ((CB)*C*4), 133.6 (((*S*)MB)*C*4), 133.4 (((*S*)MB)*C*4'), 132.8 ((CB)*C*3'), 131.5 ((CB)*C*4'), 128.5 ((CB)C3'), 127.9 ((CB)*C*2), 127.8 (((*S*)MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.0 (((*S*)MB)*C*3), 114.9 (((*S*)MB)*C*3'), 110.3 (*C*N), 73.9 (CO*C*HO$_2$C), 73.2 (((*S*)MB)OCH$_2$*C*HCH$_3$), 68.4 (OCH$_2$*C*H$_2$), 68.3 (OCH$_2$*C*H$_2$), 39.4 (*C*H$_2$NHCO), 35.0 (O_2C*C*H$_2$), 34.6 (*C*H$_2$CH$_2$Br), 33.8 (*C*H$_2$Br), 32.7 (NHCOCH*C*H$_2$), 31.9 (OCH$_2$*C*H$_2$), 29.8 (OCH$_2$*C*H$_2$), 29.75 (OCH$_2$*C*H$_2$), 29.72 (OCH$_2$*C*H$_2$), 29.71 (OCH$_2$*C*H$_2$), 29.63 (OCH$_2$*C*H$_2$), 29.61 (*C*H$_2$), 26.60 (*C*H$_2$), 29.54 (*C*H$_2$), 29.49 (*C*H$_2$), 29.45 (*C*H$_2$), 29.4 (*C*H$_2$), 28.0 (*C*H$_2$), 27.1 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 26.3 (*C*H$_2$), 25.2 (*C*H$_2$), 24.2 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$).

11-Bromoundecanal (3-32).[41] A mixture of 11-bromoundecanol (0.80 g, 3.2 mmol) in anhydrous CH_2Cl_2 (6.4 mL) was sparged with N_2 for 15 min. To the solution, PCC (0.8929 g, 4.142 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 16 h

under a N_2 atmosphere. The crude product was obtained by filtering the reaction mixture though Celite and sand. The product was purified by flash column chromatography (SiO_2, hex to EtOAc/hex 1:4) to give **3-32** as colorless oil (0.47 g, 59%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.49. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 9.76 (t, J = 1.8 Hz, 1H; C*H*O), 3.40 (t, J = 6.8 Hz, 2H; BrCH_2), 2.42 (td, J_1 = 7.4 Hz, J_2 = 1.9 Hz, 2H; CH_2CHO), 1.85 (m, 2H; $BrCH_2CH_2$), 1.62 (m, 2H; CH_2CH_2CHO), 1.42 (m, 2H; $BrC_2H_4CH_2$), 1.31 (overlapping m, 10H; $BrC_3H_6C_5H_{10}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 203.1 (*C*HO), 44.1 (*C*H_2CHO), 34.3 ($BrCH_2CH_2$), 33.0 (Br*C*H_2), 29.6 (*C*H_2), 29.5 (*C*H_2), 29.3 (*C*H_2), 28.9 (*C*H_2), 28.4 (*C*H_2), 22.3 (*C*H_2). Spectral data agree with those previously reported.[42]

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-11-bromoundecyl 11-bromoundecanoate (3-37). A mixture of 11-bromoundecanal (**3-32**) (0.1096 g, 0.4398 mmol), **3-21** (0.1585 g, 0.4397 mmol), and 11-bromoundecanoic acid (**3-17**) (0.1159 g, 0.4371 mmol) in anhydrous DCE (0.45 mL) was refluxed for 21 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, hex to 4:1 hex/EtOAc) and recrystallized from EtOH to give **3-37** as colorless solid (0.22 g, 58%). TLC (SiO_2, 3:2 hex/EtOAc): R_f = 0.52. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.70 (m, 2H; H3'), 7.64 (m, 2H; H2'), 7.53 (m, 2H; H2), 6.99 (m, 2H; H3), 5.97 (t, J = 5.8 Hz, 1H; NH), 5.17 (dd, J_1 = 7.2 Hz, J_2 = 7.2 Hz, 1H; NCOC*H*O), 4.00 (t, J = 6.5, 2H; PhOCH_2), 3.40 (t, J = 6.8 Hz, 4H; BrCH_2), 3.26 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz, 2H; OCOCH_2), 1.84 (overlapping, 8H; OCH_2CH_2, $BrCH_2CH_2$, $NHCOCHCH_2$), 1.66 (m, 2H; $O_2CCH_2CH_2$), 1.29 (overlapping, 40H; $NHCH_2C_7H_{14}$, $NHCOCHCH_2C_7H_{14}$, $O2CC_2H_4C_6H_{12}$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.6 (O_2C), 170.0 (NH*C*O), 160.0 (*C*1), 145.5 (*C*4), 132.8 (*C*3'), 131.5 (*C*4'), 128.5 (*C*2), 127.3 (*C*2'), 119.3 (*C*1'), 115.3 (*C*3), 110.3 (*C*N), 74.1 (CO*C*HO_2C), 68.4 (OCH_2CH_2), 39.4 (*C*H_2NHCO), 34.6 (O_2CCH_2), 34.3 ($BrCH_2CH_2$), 34.2 ($BrCH_2CH_2$), 33.04 ($BrCH_2CH_2$), 33.01 ($BrCH_2CH_2$), 32.1 (*C*H_2), 29.8 (*C*H_2), 29.7 (*C*H_2), 29.61 (*C*H_2), 29,59 (*C*H_2), 29.56 (*C*H_2), 29.5 (*C*H_2), 29.3 (*C*H_2), 29.0 (*C*H_2), 28.38 (*C*H_2), 29.36 (*C*H_2), 27.1 (*C*H_2), 26.3 (*C*H_2), 25.2 (*C*H_2), 25.0 (*C*H_2). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{46}H_{71}Br_2N_2O_4$, 873.3781, found 873.3755.

***N*-(5-(4'-Methoxybiphenyl-4-oxy)pentyl)phthalimide (3-51).** To an ice-water bath-cooled suspension of 4-hydroxy-4'-methoxybiphenyl (0.10 g, 0.50 mmol) in anhydrous DMF (2.5 mL), K_2CO_3 (0.1452 g, 1.051 mmol) and *N*-(5-bromopentyl)phthalimide (0.2303 g, 0.7776 mol) were

added. The reaction mixture was stirred under a N_2 atmosphere for 27 h at 80 ^oC. The reaction was cooled to room temperature before H_2O (10 mL) was added and the reaction mixture was extracted with EtOAc (8 mL) three times. The combined organic extracts were washed with saturated solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was purified by flash column chromatography (SiO2, hex/EtOAc 9:1 to 3:2) and recrystallized from toluene/EtOH (v/v 1:1) to give **3-51** as colorless solid (0.10 g, 50%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.17. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.84 (m, 2H; (Phth)H_2), 7.71 (m, 2H; (Phth)H_3), 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (m, 2H; *H*3), 3.98 (t, *J* = 6.4 Hz, 2H; PhOCH_{2d}), 3.84 (s, 3H; CH_3O), 3.73 (t, *J* = 7.3 Hz, 2H; NCH_2), 1.85 (m, 2H; OCH_2CH_2), 1.78 (m, 2H; NCH_2CH_2), 1.55 (m, 2H; $NC_2H_4CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 158.9 (*C*1'), 158.4 (*C*1), 134.1 ((Phth)*C*3), 133.8 (*C*4'), 133.6 (*C*4), 132.4 (Phth)*C*1), 128.0 (*C*2'), 127.9 (*C*2), 123.5 ((Phth)*C*2), 115.0 (*C*3'), 114.4 (*C*3), 67.9 (OCH_2), 55.6 (CH_3O), 38.1 (NCH_2), 29.1 (OCH_2CH_2), 28.6 (NCH_2CH_2), 23.7 ($NC_2H_4CH_2$).

5-(4'-Methoxybiphenyl-4-oxy)pentylamine (3-52). Hydrazine monohydrate (1.20 mL, 24.6 mmol) was added slowly to an ice-water bath-cooled suspension of **3-51** (0.98 g, 2.4 mmol) in EtOH (9.5 mL). The reaction mixture was heated at reflux for 3 h under a N_2 atmosphere. The reaction mixture was cooled in an ice-water bath and H_2O (30 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (20 mL) five times. The combined organic extracts were dried over MgSO4. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give **3-52** as crude solid (0.56 g).

1-Formamido-5-(4'-methoxybiphenyl-4-oxy)pentane (3-53). Propyl formate (4.0 mL, 0.041 mol) and **3-52** (crude product 0.56 g) were stirred at reflux for 19 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to 95:5 CH_2Cl_2/MeOH) and recrystallized from EtOH to give **3-53** as a colorless solid (0.50 g, 68% over two steps). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.30. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.18 (br s, 0.8H; *cis*-amide C*H*O), 8.06 (d, *J* = 12.0 Hz, 0.2H; *trans*-amide C*H*O), 7.47 (overlapping m, 4H; H2, H2'), 6.97 (overlapping m, 4H; H3, H3'), 5.50 (br s, 1H; N*H*), 4.00 (t, *J* = 6.3 Hz, 2H; OCH_2), 3.84 (s, 3H; CH_3O), 3.35 (dt, *J* = 6.6 Hz, 1.6H; *cis*-isomer NCH_2), 3.21 (dt, *J* = 6.6 Hz, 0.4H; *trans*-isomer NCH_2), 1.83 (m, 2H; OCH_2CH_2), 1.61 (overlapping m, 4H;

$OCH_2CH_2C_2H_4$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 161.3 (*cis*-isomer *C*HO), 158.9 (biphenyl C(4) or C(4')), 158.3 (biphenyl *C*(4) or *C*(4')), 133.7 (biphenyl *C*(1) or *C*(1')), 133.7 (biphenyl *C*(1) or *C*(1')), 127.96 (biphenyl *C*(2) or *C*(2')), 127.93 (biphenyl *C*(2) or *C*(2')), 114.9 (biphenyl *C*(3) or *C*(3')), 114.4 (biphenyl *C*(3) or *C*(3')), 67.9 ($PhOCH_2$), 55.6 ($PhOCH_3$), 41.8 (*trans*-isomer NCH_2), 38.3 (*cis*-isomer NCH_2), 31.3 (*trans*-isomer CH_2), 29.6 (*cis*-isomer CH_2), 29.1 (CH_2), 23.7 (*trans*-isomer CH_2), 23.3 (*cis*-isomer CH_2).

1-Isocyano-5-(4'-methoxybiphenyl-4-oxy)pentane (3-33). A suspension of **3-53** (0.3987 g, 1.273 mmol) and PPh_3 (0.5084 g, 1.938 mmol) in CCl_4 (0.19 mL, 2.0 mmol), Et_3N (0.27 mL, 1.9 mmol), and anhydrous CH_2Cl_2 (2.5 mL) was heated at reflux for 23 h under a N_2 atmosphere. The volatiles were removed by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) followed by recrystallization from ethanol and yielded **3-33** as colorless crystals (0.33 g, 88%). TLC (SiO_2, hex/EtOAc 3:2): R_f = 0.49. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.47 (overlapping m, 4H; H2, H2'), 6.95 (overlapping m, 4H; H3, H3'), 4.02 (t, *J* = 6.2 Hz, 2H; OCH_2), 3.84 (s, 3H; CH_3O), 3.44 (t, *J* = 6.2 Hz, 2H; CH_2NC), 1.83 (overlapping m, OCH_2CH_2, NCH_2CH_2), 1.67 ($OC_2H_4CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.9 (C1), 158.2 (C1'), 156.2 (t, *J* = 5.7 Hz, N*C*), 133.8 (C4), 133.7 (C4'), 128.0 (C2), 127.9 (C2'), 114.9 (C3), 114.4 (C3'), 67.7 (OCH_2), 55.6 (CH_3O), 41.7 (t, *J* = 6.4 Hz; CH_2NC), 29.1 (OCH_2CH_2), 28.7 (NCH_2CH_2), 23.4 ($OC_2H_4CH_2$). Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 76.88; H, 7.18; N, 4.84. HRMS-EI (*m*/*z*): calcd for $C_{19}H_{21}NO_2$, 295.1572, found 295.1566.

1-(5-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)pentylaminocarbonyl)-6-bromohexyl 6-bromohexanoate (3-38). A mixture of 6-bromohexanal (**3-28**) (0.1234 g, 0.6892 mmol), **3-33** (0.2036 g, 0.6893 mmol), and 6-bromohexanoic acid (**3-16**) (0.1342 g, 0.6880 mmol) in anhydrous DCE (0.69 mL) was refluxed for 17 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) and recrystallized from EtOH to give **3-38** as colorless solid (0.27 g, 58%). TLC (SiO_2, CH_2Cl_2/EtOAc 95:5): R_f = 0.46. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.47 (m, 4H; *H*2, *H*2'), 6.95 (m, 4H; *H*3, *H*3'), 6.05 (t, 1H, *J* = 5.9 Hz, N*H*), 5.17 (dd, J_1 = 6.9 Hz, J_2 = 6.9 Hz, 1H, NCOC*H*O), 3.99 (t, *J* = 6.2 Hz, 2H; $PhOCH_2$), 3.84 (s, 3H; CH_3O), 3.40 (t, *J* = 6.7 Hz, 2H; $BrCH_2$), 3.38 (t, J = 6.7 Hz, 2H; $BrCH_2$), 3.32 (m, 2H; CH_2NH), 2.42 (t, *J* = 7.3 Hz; 2H,

O_2CCH_2), 1.81 (overlapping m, 8H; $PhOCH_2CH_2$, $BrCH_2CH_2$, $NHCOCHCH_2$), 1.67 (m, 2H; $O_2CCH_2CH_2$), 1.58 (m, 2H; $NHCH_2CH_2$), 1.50 (overlapping m, 8H; $NHC_2H_4CH_2$, $NHCOCHCH_2CH_2$, $NHCOCHC_2H_4CH_2$, $O_2CC_2H_4CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.3 (O_2C), 169.8 (NH*C*O), 158.9 (C1), 158.3 (C1'), 133.7 (C4 or C4'), 127.94 (C2), 127.92 (C2'), 114.9 (C3), 114.4 (C3'), 74.1 (CO*C*HO$_2$C), 67.9 (O*C*H$_2$), 55.6 (*C*H$_3$O), 39.4 (*C*H$_2$NHCO), 33.8 (O_2CCH_2), 33.7 ($O_2CCH_2CH_2$), 32.7 (*C*H$_2$), 32.5 (*C*H$_2$), 29.5 (*C*H$_2$), 28.0 (*C*H$_2$), 27.8 (*C*H$_2$), 24.3 (*C*H$_2$), 24.2 (*C*H$_2$). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{31}H_{44}Br_2NO_5$, 668.1586, found 668.1581.

***N*-(10-(4'-Methoxybiphenyl-4-oxy)decyl)phthalimide (3-54).** A solution of *N*-(10-bromodecyl)phthalimide (1.7105 g, 4.6697 mol) in anhydrous DMF (15.0 mL) was added dropwise to a ice-water bath-cooled mixture of 4-hydroxy-4'-methoxybiphenyl (0.75 g, 3.7 mmol) and K_2CO_3 (1.0864 g, 7.8605 mol) in anhydrous DMF (4.0 mL). The reaction mixture was stirred under a N_2 atmosphere for 22 h at 80 °C. Additional *N*-(10-bromodecyl)phthalimide (0.2833 g, 0.7734 mmol) was added and the reaction mixture was stirred at 80 °C for another 19 h under a N_2 atmosphere. The reaction was cooled to room temperature and was diluted with CH_2Cl_2 (30 mL) before H_2O (20 mL) was added. Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL) three times. The combined organic extracts were washed with saturated solution of NaCl (20 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was purified by flash column chromatography (SiO2, hex/EtOAc 9:1 to 3:2) and recrystallized from EtOH to give **3-54** as a colorless solid (1.42 g, 78%). TLC (SiO_2, CH_2Cl_2): R_f = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.84 (m, 2H; (Phth)*H*$_2$), 7.70 (m, 2H; (Phth)*H*$_3$), 7.46 (overlapping, 4H; *H*2, *H*2'), 6.95 (m, 2H; *H*3), 3.98 (t, *J* = 6.6 Hz, 2H; $PhOCH_2$), 3.84 (s, 3H; CH_3O), 3.68 (t, *J* = 7.3 Hz, 2H; NCH_2), 1.79 (m, 2H; OCH_2CH_2), 1.67 (m, 2H; NCH_2CH_2), 1.55 (m, 2H; $NC_2H_4CH_2$), 1.33 (overlapping m, 10H; $OC_2H_4C_5H_{10}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 158.9 (*C*1'), 158.5 (*C*1), 134.1 ((Phth)*C*3), 133.8 (*C*4'), 133.4 (*C*4), 132.3 (Phth)*C*1), 127.9 (*C*2'), 127.9 (*C*2), 123.4 ((Phth)*C*2), 115.0 (*C*3'), 114.3 (*C*3), 68.3 (O*C*H$_2$), 55.6 (*C*H$_3$O), 38.3 (N*C*H$_2$), 29.7 (OCH_2CH_2), 29.6 ($OC_2H_4C_6H_{12}$), 29.6 ($OC_2H_4C_6H_{12}$), 29.5 ($OC_2H_4C_6H_{12}$), 29.4 ($OC_2H_4C_6H_{12}$), 28.8 ($OC_2H_4C_6H_{12}$), 27.1 ($OC_2H_4C_6H_{12}$), 26.3 ($NC_2H_4CH_2$).

10-(4'-Methoxybiphenyl-4-oxy)decylamine (3-55). Hydrazine monohydrate (1.31 mL, 26.9 mmol) was added slowly to an ice-water bath-cooled suspension of **3-54** (1.30 g, mmol) in EtOH (10.7 mL). The reaction mixture was heated at reflux for 3 h under a N_2 atmosphere. The reaction mixture was cooled in an ice-water bath and was diluted with CH_2Cl_2 (100 mL) before H_2O (30 mL) was added. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL) three times. The combined organic extracts were washed with saturated solution of NaCl (40 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give **3-55** as crude solid (0.87 g).

1-Formamido-10-(4'-methoxybiphenyl-4-oxy)decane (3-56). Propyl formate (7.2 mL, 0.074 mol) and **3-55** (crude product 0.87 g) were stirred at reflux for 17 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to 9:1 CH_2Cl_2/MeOH) and recrystallized from EtOH to give **3-56** as a colorless solid (0.78 g, 76% over two steps). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.33. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.16 (br s, 0.8H; *cis*-amide C*H*O), 8.05 (d, *J* = 12.0 Hz, 0.2H; *trans*-amide CHO), 7.47 (overlapping m, 4H; H2, H2'), 6.95 (overlapping m, 4H; *H*3, *H*3'), 5.45 (br s, 1H; N*H*), 3.99 (t, *J* = 6.5 Hz, 2H; OC*H*$_2$C$_{10}$H$_{20}$OH), 3.84 (s, 3H; C*H*$_3$O), 3.30 (dt, *J* = 7.3 Hz, *J* = 6.6 Hz, 1.6H; *cis*-isomer NC*H*$_2$), 3.21 (dt, *J* = 6.8 Hz, *J* = 4.9 Hz, 0.4H; *trans*-isomer NC*H*$_2$), 1.80 (m, 2H; OCH$_2$C*H*$_2$C$_9$H$_{18}$NH), 1.47 (overlapping m, 4H; OCH$_2$CH$_2$C*H*$_2$C$_8$H$_{16}$NH, C*H*$_2$CH$_2$NH), 1.35 (overlapping m, 10H; OC$_3$H$_6$C$_5$*H*$_{10}$C$_2$H$_4$NH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 164.7 (*trans*-isomer CHO), 161.3 (*cis*-isomer CHO), 158.9 (biphenyl C(4) or C(4')), 158.5 (biphenyl C(4) or C(4')), 133.8 (biphenyl C(1) or C(1')), 133.5 (biphenyl C(1) or C(1')), 127.91 (biphenyl C(2) or C(2')), 127.90 (biphenyl C(2) or C(2')), 115.0 (biphenyl C(3) or C(3')), 114.4 (biphenyl C(3) or C(3')), 68.3 (PhO*C*H$_2$), 55.6 (PhO*C*H$_3$), 41.9 (*trans*-isomer N*C*H$_2$), 38.4 (*cis*-isomer N*C*H$_2$), 31.5 (*trans*-isomer *C*H$_2$), 29.8 (*cis*-isomer *C*H$_2$), 29.7 (*C*H$_2$), 29.6 (*C*H$_2$), 29.55 (*C*H$_2$), 29.51 (*C*H$_2$), 29.4 (*cis*-isomer *C*H$_2$), 29.3 (*trans*-isomer *C*H$_2$), 27.0 (PhOCH$_2$CH$_2$*C*H$_2$), 26.6 (*trans*-isomer *C*H$_2$), 26.3 (*cis*-isomer *C*H$_2$).

1-Isocyano-10-(4'-methoxybiphenyl-4-oxy)decane (3-34). A suspension of **3-56** (0.3742 g, 0.9757 mmol) and PPh_3 (0.3872 g, 1.477 mmol) in CCl_4 (0.14 mL, 1.4 mmol), Et_3N (0.20 mL, 1.4 mmol), and anhydrous CH_2Cl_2 (2.0 mL) was heated at reflux for 22 h under a N_2

atmosphere. The volatiles were removed by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2) followed by recrystallization from EtOH and yielded **3-34** as slightly yellow crystals (0.25 g, 71%). TLC (SiO_2, CH_2Cl_2): R_f = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.47 (overlapping m, 4H; H2, H2'), 6.95 (overlapping m, 4H; H3, H3'), 3.99 (t, J = 6.5 Hz, 2H; $OCH_2C_{10}H_{20}OH$), 3.84 (s, 3H; CH_3O), 3.38 (tt, ^3J = 6.7 Hz, ^2J = 1.9 Hz, 2H; CH_2NC), 1.80 (m, 2H; $OCH_2CH_2C_9H_{18}NC$), 1.68 (m, 2H; CH_2CH_2NC), 1.47 (overlapping m, 4H; $OCH_2CH_2CH_2C_8H_{16}NC$), 1.35 (overlapping, 8H; $OC_3H_6C_5H_{10}C_2H_4NC$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.9 (C1), 158.5 (C1'), 133.8 (C4), 133.5 (C4'), 127.9 (C2), 115.0 (C3), 114.4 (C3'), 68.3 (OCH_2), 55.6 (CH_3O), 41.8 (t, J = 6.4 Hz, 2H; CH_2NC), 29.6 (CH_2CH_2NC), 29.54 (OCH_2CH_2), 29.51 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 26.5 (CH_2), 26.3 (CH_2). Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 78.52; H, 8.65; N, 4.00. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{24}H_{32}NO_2$, 366.2433, found 366.2420.

1-(10-(4'-Methoxybiphenyl-4-oxy)decylaminocarbonyl)-11-bromoundecyl 11-bromoundecanoate (3-39). A mixture of 11-bromoundecanal (**3-32**) (0.1238 g, 0.4968 mmol), **3-34** (0.1816 g, 0.4968 mmol), and 11-bromoundecanoic acid (**3-17**) (0.1318 g, 0.4970 mmol) in anhydrous DCE (0.50 mL) was refluxed for 15 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-38** as a colorless solid (0.34 g, 79%). TLC (SiO_2, CH_2Cl_2/EtOAc 95:5): R_f = 0.44. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.47 (m, 4H; *H*2, *H*2'), 6.95 (m, 4H; *H*3, *H*3'), 5.98 (t, 1H, J = 5.8 Hz, N*H*), 5.17 (dd, J_1 = 7.2 Hz, J_2 = 7.2 Hz, 1H, NCOC*H*O), 3.98 (t, J = 6.5 Hz, 2H; PhOCH_2), 3.84 (s, 3H; CH_3O), 3.40 (t, J = 6.8 Hz, 4H; BrCH_2), 3.26 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz; 2H, O_2CCH_2), 1.81 (overlapping m, 8H; $PhOCH_2CH_2$, $BrCH_2CH_2$, $NHCOCHCH_2$), 1.67 (m, 2H; $O_2CCH_2CH_2$), 1.65 (m, 2H; $NHCH_2CH_2$), 1.50 (overlapping m, 8H; $NHC_2H_4CH_2$, $NHCOCHCH_2CH_2$, $NHCOCHC_2H_4CH_2$, $O_2CC_2H_4CH_2$), 1.34 (overlapping m, 32H; $O_2CC_3H_6C_5H_{10}$, $NHC_2H_4C_5H_{10}$, $NHCOCHC_2H_4C_6H_{12}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.6 (O_2C), 170.0 (NH*C*O), 158.9 (C1), 158.5 (C1'), 133.7 (C4), 133.5 (C4'), 127.90 (C2), 127.88 (C2'), 114.9 (C3), 114.4 (C3'), 74.1 ($COCHO_2C$), 68.3 (OCH_2), 55.6 (CH_3O), 39.4 (CH_2NHCO), 34.5 ($BrCH_2$), 34.3 ($BrCH_2$), 34.2 (O_2CCH_2), 33.03 ($O_2CCH_2CH_2$), 33.01 (CH_2), 32.1 (CH_2), 29.8 (CH_2), 29.72 (CH_2), 29.96 (CH_2), 29.61 (CH_2), 29.59 (CH_2), 29.55 (CH_2), 29.54

(CH_2), 29.46 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.37 (CH_2), 28.36 (CH_2), 27.1 (CH_2), 26.3 (CH_2), 25.2 (CH_2), 25.0 (CH_2). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{46}H_{74}Br_2NO_5$, 878.3934, found 878.3902.

***N*-(5-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)pentyl)phthalimide (3-57).** A solution of *N*-(5-bromopentyl)phthalimide (1.26 g, 4.25 mmol) in anhydrous DMF (4.8 mL) was added to a mixture of 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.91 g, 3.5 mmol) and K_2CO_3 (0.9918 g, 7.176 mmol) in anhydrous DMF (13.0 mL). The reaction mixture was stirred under a N_2 atmosphere for 24 h at 80 ^oC. The reaction was cooled to room temperature before H_2O (25 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (100 mL) four times. The combined organic extracts were washed with saturated solution of NaCl (15 mL) and were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was recrystallized from EtOH to give **3-57** as a colorless solid (1.38 g, 82%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.17. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.85 (m, 2H; (Phth)*H*2), 7.71 (m, 2H; (Phth)*H*3), 7.45 (overlapping, 4H; *H*2, *H*2'), 6.93 (overlapping, 4H; *H*3, *H*3'), 3.98 (t, *J* = 6.4 Hz, 2H; PhOCH_2), 3.86 (m, 1H; OCH_2CHCH$_3$), 3.77 (m, 1H; OCH_2CHCH$_3$), 3.73 (t, *J* = 7.2 Hz, 2H; NCH_2), 1.85 (overlapping m, 4H, OCH$_2$CH_2, NCH$_2$CH_2; m, 1H, OCH$_2$C*H*CH$_3$), 1.57 (overlapping m, 2H, NC$_2$H$_4$CH_2; 1H, CHCH_2CH$_3$), 1.28 (m, 1H; CHCH_2CH$_3$), 1.03 (d, J = 6.7 Hz; OCH$_2$CHCH_3), 0.97 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 158.6 (C1'), 158.3 (C1), 134.1 ((Phth)*C*3), 133.7 (C4'), 133.5 (C4), 132.4 (Phth)*C*1), 127.9 (*C*2' or *C*2), 123.4 (Phth)*C*2), 115.0 (C3'), 114.9 (C3), 73.2 (OCH_2CHCH$_3$), 68.9 (OCH_2CH$_2$), 38.1 (NCH_2), 35.0 (OCH$_2$CHCH$_3$), 29.1 (OCH$_2$CH_2), 28.6 (NCH$_2$CH_2), 26.4 (CH_2CH$_3$), 23.7 (OCH$_2$CH$_2$CH_2), 16.8 (OCH$_2$CHCH_3), 11.6 (CH$_2$CH_3).

5-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)pentylamine (3-58). Hydrazine monohydrate (1.34 mL, 0.0275 mmol) was added slowly to an ice-water bath-cooled suspension of **3-57** (1.29 g, 2.74 mmol) in EtOH (11.0 mL). The reaction mixture was heated at reflux for 1.5 h under a N_2 atmosphere. The reaction mixture was cooled in an ice-water bath and diluted with CH_2Cl_2 (20 mL) before H_2O (30 mL) was added. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL) three times. The combined organic extracts were washed with saturated solution of NaCl (20 mL) and dried over $MgSO_4$. The solids were removed by filtration

and solvent was removed from the filtrate under reduced pressure to give **3-58** as crude solid (0.86 g).

1-Formamido-5-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)pentane (3-59). Propyl formate (2.50 mL, 0.0256mol) and **3-58** (crude product 0.86 g) were stirred at reflux for 18 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to 95:5 CH_2Cl_2/MeOH) and recrystallized from EtOH to give **3-59** as a colorless solid (0.78g, 77% over two steps). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.37. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 8.18 (br s, 0.8H; *cis*-amide C*H*O), 8.07 (d, *J* = 12.0 Hz, 0.2H; *trans*-amide CHO), 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (overlapping, 4H; *H*3, *H*3'), 5.50 (br s, 1H; N*H*), 4.00 (t, *J* = 6.5 Hz, 2H; PhOCH_2), 3.85 (m, 1H; OCH_2CHCH$_3$), 3.76 (m, 1H; OCH_2CHCH$_3$), 3.35 (dt, *J* = 7.5 Hz, *J* = 6.6 Hz, 1.6H; *cis*-isomer NCH_2), 3.27 (dt, *J* = 6.8 Hz, *J* = 4.9 Hz, 0.4H; *trans*-isomer NCH_2), 1.86 (overlapping m, 1H, OCH$_2$C*H*CH$_3$; 2H, OCH$_2$CH_2), 1.63 (overlapping m, 1H, CHCH_2CH$_3$; 4H, OCH$_2$CH$_2$C$_2H_4$), 1.28 (m, 1H; CHCH_2CH$_3$), 1.03 (d, *J* = 6.7 Hz; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 161.3 (*cis*-isomer CHO), 158.7 (*C*1'), 158.3 (*C*1), 133.8 (*C*4'), 133.4 (*C*4), 127.91s (*C*2'), 127.86 (*C*2), 115.0 (*C*3'), 114.9 (*C*3), 73.2 (O*C*H$_2$CHCH$_3$), 67.9 (O*C*H$_2$), 38.3 (*cis*-isomer NCH$_2$), 35.0 (OCH$_2$*C*HCH$_3$), 29.5 (*cis*-isomer CH$_2$), 29.1 (*cis*-isomer *C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 23.7 (*cis*-isomer CH$_2$), 23.3 (*trans*-isomer CH$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$).

1-Isocyano-5-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)pentane (3-35). A mixture of **3-59** (0.3654 g, 0.9889 mmol) and PPh_3 (0.3112 g, 1.186 mmol) in CCl_4 (0.12 mL, 1.2 mmol), Et_3N (0.17 mL, 1.2 mmol), and anhydrous CH_2Cl_2 (2.0 mL) was heated at reflux for 21 h under a N_2 atmosphere. The volatiles were removed by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 9:1 to 7:3) followed by recrystallization from EtOH and yielded **3-35** as colorless crystals (0.25 g, 72%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.30. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (overlapping, 4H; *H*3, *H*3'), 4.02 (t, *J* = 6.2 Hz, 2H; PhOCH_2), 3.86 (m, 1H; OCH_2CHCH$_3$), 3.77 (m, 1H; OCH_2CHCH$_3$), 3.73 (tt, ^3J= 6.6 Hz, ^2J= 1.9 Hz, 2H; NCH_2), 1.87 (overlapping m, 4H, OCH$_2$CH_2, CH_2CH$_2$NC; m, 1H, OCH$_2$C*H*CH$_3$), 1.67 (m, 2H, NC$_2$H$_4$CH_2), 1.60 (m, 1H, CHCH_2CH$_3$), 1.28 (m, 1H; CHCH_2CH$_3$), 1.03 (d, *J* = 6.7 Hz; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 158.7 (C1'), 158.2 (C1),

133.9 (C4'), 133.4 (C4), 127.94 (C2'), 127.88 (C2), 115.0 (C3'), 114.9 (C3), 73.2 (OCH_2CHCH_3), 67.7 (OCH_2CH_2), 35.0 (OCH_2CHCH_3), 29.1 (OCH_2CH_2), 28.7 (NCH_2CH_2), 26.4 (CH_2CH_3), 23.4 ($OCH_2CH_2CH_2$), 16.8 (OCH_2CHCH_3), 11.6 (CH_2CH_3). Anal. Calcd for $C_{23}H_{29}NO_2$: C, 78.59; H, 8.32; N, 3.99. Found: C, 78.76; H, 8.05; N, 3.85. HRMS-EI (*m*/*z*): calcd for $C_{23}H_{29}NO_2$, 351.2198, found 351.2191.

1-(5-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)pentylaminocarbonyl)-6-bromohexyl 6-bromohexanoate (3-40). A mixture of 6-bromohexanal (**3-28**) (0.1044 g, 0.5830 mmol), **3-35** (0.2048 g, 0.5835 mmol), and 6-bromohexanoic acid (**3-16**) (0.1137 g, 0.5830 mmol) in anhydrous DCE (0.58 mL) was refluxed for 16 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) and recrystallized from EtOH/CH_2Cl_2 to give **3-40** as colorless solid (0.23 g, 55%). TLC (SiO_2, CH_2Cl_2/EtOAc 95:5): R_f = 0.17. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (overlapping, 4H; *H*3, *H*3'), 6.04 (t, *J* = 5.9 Hz, 1H; N*H*), 5.17 (dd, J_1 = 6.9 Hz, J_2 = 6.9 Hz, 1H; NCOC*H*O), 3.99 (t, *J* = 6.2 Hz, 2H; PhOCH_2), 3.85 (m, 1H; OCH_2CHCH$_3$), 3.77 (m, 1H; O*C*H$_2$CHCH$_3$), 3.40 (t, *J* = 6.6 Hz, 2H; CH_2Br), 3.38 (t, *J* = 6.7 Hz, 2H; CH_2Br), 3.32 (m, 2H; CH$_2$N*H*), 2.42 (t, *J* = 7.4 Hz, 2H; OCOCH_2), 1.87 (overlapping m, 8H; PhOCH$_2$CH_2, BrCH$_2$CH_2, NHCOCHCH_2; 1H; OCH$_2$C*H*CH$_3$), 1.66 (m, 4H; NHCH$_2$CH_2, O_2CCH$_2$CH_2; 1H, CHCH_2CH$_3$), 1.51 (overlapping m, 6H; BrC$_2$H$_4$CH_2, NHCOCHCH$_2$CH_2), 1.31 (overlapping, 2H; NHCOCHC$_2$H$_4$CH_2; 1H, CHCH_2CH$_3$), 1.03 (d, *J* = 6.7 Hz; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.3 (O_2C), 169.8 (NH*C*O), 158.7 (C1'), 158.2 (C1), 133.8 (C4'), 133.4 (C4), 127.91 (C2'), 127.85 (C2), 115.0 (C3'), 114.9 (C3), 74.1 (CO*C*HO$_2$C), 73.2 (O*C*H$_2$CHCH$_3$), 67.9 (O*C*H$_2$), 39.4 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.3 (O_2C*C*H$_2$), 33.8 (*C*H$_2$Br), 33.7 (*C*H$_2$Br), 32.7 (BrCH$_2$*C*H$_2$), 32.5 (BrCH$_2$*C*H$_2$), 31.9 (O_2CCH$_2$*C*H$_2$), 29.5 (*C*H$_2$), 29.1 (*C*H$_2$), 28.0 (*C*H$_2$), 27.8 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 24.3 (*C*H$_2$), 24.2 (*C*H$_2$), 23.7 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{35}H_{52}Br_2NO_5$, 724.2212, found 724.2200.

***N*-(10-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)decyl)phthalimide (3-60).** A solution of *N*-(10-bromodecyl)phthalimide (1.9078 g, 5.2083 mmol) in anhydrous DMF (12.0 mL) was added slowly to a mixture of 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (1.11 g, 4.33 mmol) and K_2CO_3 (1.2001 g, 8.6832 mmol) in anhydrous DMF (10.0 mL). The reaction mixture was stirred

under a N_2 atmosphere for 21 h at 80 ^oC. The reaction was cooled to room temperature before H_2O (20 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (15 mL) three times. The combined organic extracts were washed with saturated solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was purified by flash column chromatography (SiO_2, hex to hex/EtOAc 7:3) and recrystallized from EtOH to give **3-60** as a colorless crystal (1.34 g, 57%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.19. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.84 (m, 2H; (Phth)*H*2), 7.70 (m, 2H; (Phth)*H*3), 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (overlapping, 4H; *H*3, *H*3'), 3.97 (t, *J* = 6.6 Hz, 2H; PhOCH_2), 3.85 (m, 1H; OCH_2CHCH$_3$), 3.77 (m, 1H; OCH_2CHCH$_3$), 3.68 (t, *J* = 7.3 Hz, 2H; NCH_2), 1.89 (m, 1H; OCH$_2$C*H*CH$_3$), 1.78 (m, 2H; OCH$_2$CH_2), 1.67 (m, 2H; NCH$_2$CH_2), 1.60 (m, 1H; CHCH_2CH$_3$), 1.46 (m, 2H; OC$_2$H$_4$CH_2), 1.32 (overlapping m, 10H, OC$_3$H$_4$C$_5H_{10}$; m, 1H, CHCH_2CH$_3$), 1.03 (d, J = 6.7 Hz; OCH$_2$CHCH_3), 0.97 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 168.7 (*C*O), 158.6 (C1'), 158.4 (C1), 134.0 ((Phth)*C*3), 133.6 (C4'), 133.5 (C4), 132.4 (Phth)*C*1), 127.9 (*C*2' or *C*2), 123.4 (Phth)*C*2), 115.0 (C3'), 115.0 (C3), 73.2 (O*C*H$_2$CHCH$_3$), 68.3 (O*C*H$_2$CH$_2$), 38.3 (N*C*H$_2$), 35.0 (OCH$_2$*C*HCH$_3$), 29.7 (OCH$_2$*C*H$_2$), 29.6 (OC$_2$H$_4$*C*$_6$H$_{12}$), 29.6 (OC$_2$H$_4$*C*$_6$H$_{12}$), 29.5 (OC$_2$H$_4$*C*$_6$H$_{12}$), 29.4 (OC$_2$H$_4$*C*$_6$H$_{12}$), 28.8 (OC$_2$H$_4$*C*$_6$H$_{12}$), 27.1 (OC$_2$H$_4$*C*$_6$H$_{12}$), 26.4 (*C*H$_2$CH$_3$), 26.2 (NC$_2$H$_4$*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$).

10-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)decylamine (3-61). Hydrazine monohydrate (1.1 mL, 23 mmol) was added slowly to an ice-water bath-cooled suspension of **3-60** (1.20 g, 2.21 mmol) in EtOH (9.0 mL). The reaction mixture was heated at reflux for 1.5 h under a N_2 atmosphere. The reaction mixture was cooled in an ice-water bath and diluted with CH_2Cl_2 (30 mL) before H_2O (50 mL) was added. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL) three times. The combined organic extracts were washed with saturated solution of NaCl (25 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give **3-61** as crude solid (0.84 g).

1-Formamido-10-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)decane (3-62). Propyl formate (2.0 mL, 0.021 mol) and **3-61** (crude product 0.84 g) were stirred at reflux for 16 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The product was purified by flash column chromatography

(SiO_2, CH_2Cl_2 to 95:5 CH_2Cl_2/MeOH) and recrystallized from EtOH to give **3-62** as a colorless solid (0.72 g, 74% over two steps). TLC (SiO_2, 95:5 CH_2Cl_2/MeOH): R_f = 0.31. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 8.17 (br s, 0.8H; *cis*-amide C*H*O), 8.05 (d, *J* = 12.0 Hz, 0.2H; *trans*-amide CHO), 7.46 (overlapping, 4H; *H*2, *H*2'), 6.95 (overlapping, 4H; *H*3, *H*3'), 5.44 (br s, 1H; N*H*), 3.98 (t, *J* = 6.5 Hz, 2H; $PhOCH_2$), 3.85 (m, 1H; OCH_2CHCH_3), 3.77 (m, 1H; OCH_2CHCH_3), 3.30 (dt, *J* = 7.5 Hz, *J* = 6.6 Hz, 1.6H; *cis*-isomer NCH_2), 3.21 (dt, J_1 = 6.8 Hz, J_2 = 4.9 Hz, 0.4H; *trans*-isomer NCH_2), 1.89 (m, 1H, OCH_2CHCH_3), 1.79 (m, 2H; $OCH_2CH_2C_9H_{18}NH$), 1.60 (m, 1H, $CHCH_2CH_3$), 1.50 (overlapping m, 4H; $OCH_2CH_2CH_2C_8H_{16}NH$, CH_2CH_2NH), 1.35 (overlapping m, 10H, $OC_3H_6C_5H_{10}C_2H_4NH$; m, 1H; $CHCH_2CH_3$), 1.03 (d, *J* = 6.7 Hz; OCH_2CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 164.7 (*trans*-isomer CHO), 161.3 (*cis*-isomer CHO), 158.6 (*C*1'), 158.4 (*C*1), 133.6 (*C*4'), 133.5 (*C*4), 127.88 (*C*2'), 127.86 (*C*2), 114.98 (*C*3'), 114.95 (*C*3), 73.2 (OCH_2CHCH_3), 68.3 (OCH_2), 41.9 (*trans*-isomer NCH_2), 38.4 (*cis*-isomer NCH_2), 35.0 (OCH_2CHCH_3), 31.5 (*trans*-isomer CH_2), 29.8 (*cis*-isomer CH_2), 29.67 (CH_2), 29.64 (CH_2), 29.63 (*trans*-isomer CH_2), 29.55 (CH_2), 29.52 (CH_2), 29.42 (*cis*-isomer CH_2), 29.35 (*trans*-isomer CH_2), 27.0 ($OCH_2CH_2CH_2$), 26.6 (*trans*-isomer CH_2), 26.4 (CH_2CH_3), 26.3 (*cis*-isomer CH_2), 16.8 (OCH_2CHCH_3), 11.6 (CH_2CH_3).

1-Isocyano-10-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)decane (3-36). A suspension of **3-62** (0.3804 g, 0.8653 mmol) and PPh_3 (0.2818 g, 1.074 mmol) in CCl_4 (0.10 mL, 1.0 mmol), Et_3N (0.15 mL, 1.1 mmol), and anhydrous CH_2Cl_2 (1.8 mL) was heated at reflux for 20 h under a N_2 atmosphere. The volatiles were removed by rotary evaporation to give the crude product. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 3:2) followed by recrystallization from EtOH and yielded **3-36** as colorless crystals (0.28 g, 76%). TLC (SiO_2, hex/EtOAc 4:1): R_f = 0.51. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (overlapping, 4H; *H*3, *H*3'), 3.99 (t, *J* = 6.5 Hz, 2H; $PhOCH_2$), 3.85 (m, 1H; OCH_2CHCH_3), 3.77 (m, 1H; OCH_2CHCH_3), 3.38 (tt, ^3J = 6.7 Hz, ^2J = 1.9 Hz, 2H; NCH_2), 1.89 (m, 1H, OCH_2CHCH_3), 1.80 (m, 2H; OCH_2CH_2,), 1.68 (m, 2H; CH_2CH_2NC), 1.60 (m, 1H, $CHCH_2CH_3$), 1.46 (overlapping m, 4H; $OCH_2CH_2CH_2C_8H_{16}NC$, CH_2CH_2NC), 1.35 (overlapping m, 8H; $OC_3H_6C_5H_{10}C_2H_4NC$), 1.28 (m, 1H; $CHCH_2CH_3$), 1.03 (d, J = 6.7 Hz; OCH_2CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 158.7 (C1'), 158.4 (C1), 155.8 (t, *J* = 5.7 Hz; N*C*), 133.6 (C4'), 133.5 (C4), 127.88 (C2'), 127.86 (C2), 114.98

(C3'), 114.95 (C3), 73.2 (O*C*H_2CHCH$_3$), 68.3 (O*C*H_2CH$_2$), 41.8 (t, *J* = 6.4 Hz; *C*H_2NC), 35.0 (OCH$_2$*C*HCH$_3$), 29.6 (*C*H_2CH$_2$NC), 29.55 (OCH$_2$*C*H$_2$), 29.52 (OC$_2$H$_4$*C*$_6$H$_{12}$C$_2$H$_4$NC), 29.3 (OC$_2$H$_4$*C*$_6$H$_{12}$C$_2$H$_4$NC), 28.9 (OC$_2$H$_4$*C*$_6$H$_{12}$C$_2$H$_4$NC), 26.5 (OC$_2$H$_4$*C*$_6$H$_{12}$C$_2$H$_4$NC), 26.4 (*C*H_2CH$_3$), 26.3 (OC$_2$H$_4$*C*$_6$H$_{12}$C$_2$H$_4$NC), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{28}H_{39}NO_2$: C, 79.76; H, 9.32; N, 3.32. Found: C, 79.93; H, 9.37; N, 3.26. HRMS-EI (*m*/*z*): calcd for $C_{28}H_{39}NO_2$, 421.2981, found 421.2972.

1-(10-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)decylaminocarbonyl)-11-bromoundecyl 11-bromoundecanoate (3-41). A mixture of 11-bromoundecanal (**3-32**) (0.1247 g, 0.5004 mmol), **3-36** (0.2110 g, 0.5004 mmol), and 11-bromoundecanoic acid (**3-17**) (0.1325 g, 0.4996 mmol) in anhydrous DCE (0.50 mL) was refluxed for 16 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-41** as colorless solid (0.39 g, 84%). TLC (SiO_2, CH_2Cl_2/EtOAc 95: 5): R_f = 0.77. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.46 (overlapping, 4H; *H*2, *H*2'), 6.94 (overlapping, 4H; *H*3, *H*3'), 5.97 (t, *J* = 5.8 Hz, 1H; N*H*), 5.17 (dd, J_1 = 7.1 Hz, J_2 = 7.2 Hz, 1H; NCOC*H*O), 3.98 (t, *J* = 6.5 Hz, 2H; PhOCH_2), 3.85 (m, 1H; OCH_2CHCH$_3$), 3.76 (m, 1H; O*C*H$_2$CHCH$_3$), 3.40 (t, *J* = 6.8 Hz, 4H; CH_2Br), 3.26 (m, 2H; CH$_2$N*H*), 2.40 (t, *J* = 7.5 Hz, 2H; OCOCH_2), 1.87 (overlapping m, 8H; PhOCH$_2$CH_2, BrCH$_2$CH_2, NHCOCHCH_2; 1H; OCH$_2$C*H*CH$_3$), 1.66 (m, 2H; O$_2$CCH$_2$CH$_2$; 1H, CHCH_2CH$_3$), 1.47 (overlapping m, 8H; NHCH$_2$CH_2, OC$_2$H$_4$CH_2), 1.31 (overlapping, 32H; NHC$_2$H$_4$C$_5$$H_{10}$, NHCOCHCH$_2C_6$$H_{12}$, O$_2CC_2H_4C_5$$H_{10}$; 1H, CHC$H_2CH_3$), 1.03 (d, *J* = 6.7 Hz; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.6 (O$_2$*C*), 170.0 (NH*C*O), 158.6 (C1'), 158.4 (C1), 133.6 (C4'), 133.5 (C4), 127.87 (C2'), 127.85 (C2), 115.0 (C3'), 114.9 (C3), 74.2 (CO*C*HO$_2$C), 73.1 (O*C*H$_2$CHCH$_3$), 68.3 (O*C*H$_2$), 39.4 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.6 (O$_2$C*C*H$_2$), 34.3 (*C*H$_2$Br), 34.2 (*C*H$_2$Br), 33.04 (BrCH$_2$*C*H$_2$), 33.02 (BrCH$_2$*C*H$_2$), 32.1 (O$_2$CCH$_2$*C*H$_2$), 29.8 (*C*H$_2$), 29.73 (*C*H$_2$), 29.70 (*C*H$_2$), 29.62 (*C*H$_2$), 29.60 (*C*H$_2$), 29.56 (*C*H$_2$), 29.5 (*C*H$_2$), 29.3 (*C*H$_2$), 29.0 (*C*H$_2$), 28.38 (*C*H$_2$), 28.36 (*C*H$_2$), 27.1 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 26.3 (*C*H$_2$), 25.2 (*C*H$_2$), 25.0 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{50}H_{82}Br_2NO_5$, 934.4560, found 934.4516.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 11-bromoundecanoate (3-45). A mixture of **3-44** (0.3008 g, 1.025 mmol), **3-20** (0.2977 g, 1.025 mmol), and 11-bromoundecanoic acid (**3-17**) (0.2719 g, 1.025 mmol) in anhydrous DCE (1.00

mL) was refluxed for 18 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 4:1 to 1:1) to give **3-45** as colorless solid (0.71 g, 80%). TLC (SiO_2, 1:1 hex/EtOAc): R_f = 0.42. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.69 (m, 4H; *H*3), 7.63 (m, 4H; *H*3'), 7.52 (m, 4H; *H*2), 6.97 (m, 4H; *H*2'), 6.07 (t, 1H; *J* = 6.0 Hz, N*H*), 5.20 (dd, J_1 = 7.2 Hz, J_2 = 7.2 Hz, 1H; NCOC*H*O), 3.99 (m, 4H; PhOCH_2), 3.38 (t, *J* = 6.8 Hz, 2H; CH_2Br), 3.32 (m, 2H; CH_2NH), 2.40 (t, *J* = 7.5 Hz, 2H; OCOCH_2), 1.83 (overlapping, 8H; $OCH_2C_2H_4$, CH_2CH_2NH), 1.61 (overlapping, 4H; CH_2CH_2Br, OCHCH_2), 1.52 (overlapping, 4H; $OCH_2CH_2CH_2$), 1.41 (overlapping, 4H; $OCHCH_2CH_2$, $CH_2CH_2CH_2$Br), 1.30 (overlapping, 10H; $CHOCOC_2H_4C_5H_{10}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2C), 170.0 (NH*C*O), 159.9 (*C*1), 159.8 (*C*1), 145.4 (*C*4), 145.4 (*C*4), 132.8 (*C*3'), 131.6 (*C*4'), 131.5 (*C*4'), 128.5 (*C*2), 128.5 (*C*2), 127.3 (C2'), 119.3 (*C*1'), 119.3 (*C*1'), 115.2 (*C*3), 110.3 (*C*N), 110.3 (*C*N), 73.9 (CO*C*HOCO), 68.0 (PhO*C*H_2), 68.0 (PhO*C*H_2), 39.3 (*C*H_2NHCO), 34.5 (OCO*C*H_2), 34.2 (*C*H_2CH_2Br), 33.0 (*C*H_2Br), 32.0 ($O_2CCH_2CH_2$), 29.6 (*C*$H_2C_2H_4$NHCO), 29.6 (OCH_2CH_2), 29.5 (OCH_2CH_2), 29.4 (*C*H_2CH_2NHCO), 29.3 (COCH*C*H_2), 29.2 ($COCHCH_2CH_2$), 29.0 ($O_2CC_2H_4CH_2$), 28.9 ($COCHC_2H_4CH_2$), 28.3 (*C*$H_2C_2H_4$Br), 26.0 ($O_2CC_3H_6CH_2$), 24.8 ($O_2CC_6H_{12}CH_2$), 24.3 ($O_2CC_4H_8CH_2$), 23.4 ($O_2CC_5H_{10}CH_2$). HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{49}H_{59}BrN_3O_5$, 848.3638, found 848.3625.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-methoxybiphenyl-4-oxy)hexyl 6-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)hexanoate (3-1). To a solution of compound **3-22** (0.1034 g, 0.1319 mmol) in anhydrous DMF (1.3 mL)) in a 25-mL one-neck flask, K_2CO_3 (0.0759 g, 0.549 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.0532 g, 0.208 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 22.5 h. The reaction was cooled to room temperature and diluted with CH_2Cl_2 (10 mL) and H_2O (8 mL). Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (5 mL) three times. The combined organic extracts were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) and recrystallized from EtOH/CH_2Cl_2 (v/v 3:1) to give **3-1** as colorless solid (0.08 g, 64%). TLC (SiO_2, 95:5 CH_2Cl_2/EtOAc): R_f = 0.51. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.67 (m, 2H; (CB)*H*3'), 7.66 (m, 2H; (CB)*H*2'), 7.50 (m, 2H; (CB)*H*2), 7.45 (overlapping m, 8H; (MB)*H*2

and *H*2', ((*S*)MB)*H*2 and *H*2'), 6.92 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'; 4H, ((*S*)MB)*H*3 and *H*3'), 6.05 (t, J = 5.9 Hz, 1H; N*H*), 5.21 (dd, J_1 = 7.0 Hz, J_2 = 7.0 Hz, 1H; NHCOC*H*), 3.96 (m, 6H; PhOCH_2), 3.84 (overlapping, 3H, CH_3O; 1H, PhOCH_2CHCH$_3$), 3.75 (m, 1H; PhOCH_2CHCH$_3$), 3.31 (m, 2H; CH_2NH), 2.45 (t, J = 7.5 Hz, 2H; O_2CCH_2), 1.83 (overlapping, 10H; PhOCH$_2$CH_2, NHCH$_2$CH_2, NHCOCHCH_2; 1H, PhOCH$_2$C*H*CH$_3$), 1.60 (overlapping m, 2H; O_2CCH$_2$CH_2; 1H, PhOCH$_2$CHCH_2), 1.50 (overlapping m, 8H; OCH$_2$CH$_2$CH_2, NHCOCHCH$_2$CH_2), 1.27 (m, 1H; PhOCH$_2$CHCH_2), 1.03 (d, J = 6.8 Hz, 3H; OCH$_2$CHCH_3), 0.96 (t, J = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.5 (O_2C), 170.0 (NH*C*O), 159.8 ((CB)*C*1), 158.9 ((MB)*C*1), 158.7 (((*S*)MB)*C*1), 158.3 ((MB)*C*1'), 158.2 (((*S*)MB)*C*1'), 145.4 ((CB)*C*4), 133.8 ((MB)*C*4, 133.6 ((*S*)MB)C4), 133.5 ((MB)C4'), 133.3 ((*S*)MB)C4'), 132.8 ((CB)*C*3'), 131.6 ((CB)*C*4'), 128.6 ((CB)C3'), 127.9 ((CB)C2), 127.8 (((*S*)MB)C2' or C2), 127.3 ((CB)C2'), 119.3 ((CB)C1'), 115.3 ((CB)C3), 115.0 (((*S*)MB)C3), 114.92 (((*S*)MB)C3'), 114.88 ((MB)C3), 114.4 ((MB)C3'), 110.2 (*C*N), 74.1 (CO*C*HO$_2$C), 73.2 (((*S*)MB)O*C*H$_2$CHCH$_3$), 68.0 (O*C*H$_2$CH$_2$), 67.9 (O*C*H$_2$CH$_2$), 67.8 (O*C*H$_2$CH$_2$), 55.6 (*C*H$_3$O), 39.3 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.4 (O_2C*C*H$_2$), 32.0 (NHCOCH*C*H$_2$), 29.6 (OCH$_2$CH$_2$), 29.3 (OCH$_2$*C*H$_2$), 29.2 (OCH$_2$*C*H$_2$), 29.0 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 25.99 (*C*H$_2$), 25.95 (*C*H$_2$), 25.0 (*C*H$_2$), 24.8 (*C*H$_2$), 23.6 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{61}H_{70}N_2O_8$: C, 76.38; H, 7.36; N, 2.92. Found: C, 76.58; H, 7.27; N, 2.83. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{61}H_{70}N_2O_8Na$, 981.5030, found 981.5005.

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 11-(4'-((S)-2-methylbutoxy)biphenyl-4-oxy)undecanoate (3-2). To a mixture of compound **3-23** (0.6615 g, 0.6654 mmol) in anhydrous DMF (6.6 mL) in a 25-mL one-neck flask, K_2CO_3 (0.2804 g, 2.029 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.3378 g, 1.318 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 16.5 h. The reaction was cooled to room temperature and diluted with $CHCl_3$ (30 mL) and H_2O (20 mL). Two layers were separated and the aqueous layer was extracted with $CHCl_3$ (20 mL) three times. The combined organic extracts were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 98:2) to give **3-2** as colorless solid (0.52 g, 67%). TLC (SiO_2, 98:2 CH_2Cl_2/EtOAc): R_f = 0.22. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.64 (m, 4H; (CB)*H*3' and

*H*2'), 7.46 (overlapping m, 2H, (CB)*H*2; 8H, (MB)*H*2 and *H*2', ((*S*)MB)*H*2 and *H*2'), 6.93 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'; 4H, ((*S*)MB)*H*3 and *H*3'), 5.98 (t, J = 6.0 Hz, 1H; N*H*), 5.17 (dd, J_1 = 7.1 Hz, J_2 = 7.2 Hz, 1H; NHCOC*H*), 3.98 (m, 6H; PhOCH_2), 3.84 (overlapping, 4H, CH_3O, PhOCH_2CHCH$_3$), 3.75 (m, 1H; PhOCH_2CHCH$_3$), 3.31 (m, 2H; CH_2NH), 2.45 (t, J = 7.5 Hz, 2H; O_2CCH_2), 1.82 (overlapping, 9H; NHCOCHCH_2, PhOCH$_2$CH_2, PhOCH$_2$C*H*CH$_3$), 1.66 (m, 2H; O_2CCH$_2$CH_2), 1.53 (overlapping m, 8H; CH_2CH$_2$NH, OCH$_2$CH$_2$CH$_2$; 1H, PhOCH$_2$CHCH_2), 1.30 (overlapping m, 33H,; (CB)OC$_3$H$_6$C$_5$H$_{10}$, (MB)OC$_3$H$_6$C$_6$H$_{12}$, ((*S*)MB)OC$_3$H$_6$C$_5$H$_{10}$, PhOCH$_2$CHCH_2), 1.03 (d, J = 6.8 Hz, 3H; OCH$_2$CHCH_3), 0.96 (t, J = 7.5 Hz, 3H; CH$_2$CH$_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2C), 170.0 (NH*C*O), 160.0 ((CB)*C*1), 158.9 ((MB)*C*1), 158.6 (((*S*)MB)*C*1), 158.5 ((MB)*C*1'), 158.4 (((*S*)MB)*C*1'), 145.5((CB)*C*4), 133.7 ((MB)*C*4), 133.6 (((*S*)MB)*C*4), 133.5 ((MB)*C*4'), 133.4 (((*S*)MB)*C*4'), 132.8 ((CB)*C*3'), 131.5 ((CB)*C*4'), 128.5 ((CB)C3'), 127.9 ((CB)*C*2), 127.9 ((MB)*C*2'), 127.9 (((*S*)MB)*C*2), 127.8 (((*S*)MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.0 (((*S*)MB)*C*3), 115.0 (((*S*)MB)*C*3'), 114.9 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.2 (CO*C*HO$_2$C), 73.2 (((*S*)MB)OCH$_2$*C*HCH$_3$), 68.4 (OCH$_2$*C*H$_2$), 68.3 (OCH$_2$*C*H$_2$), 68.3 (OCH$_2$*C*H$_2$), 55.5 (*C*H$_3$O), 39.4 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.6 (O_2C*C*H$_2$), 32.1 (NHCOCH*C*H$_2$), 29.79 (OCH$_2$*C*H$_2$), 29.75 (OCH$_2$*C*H$_2$), 29.7 (OCH$_2$*C*H$_2$), 26.64 (*C*H$_2$), 29.6 (*C*H$_2$), 29.62 (*C*H$_2$), 29.60 (*C*H$_2$), 29.55 (*C*H$_2$), 29.50 (*C*H$_2$), 29.46 (*C*H$_2$), 29.4 (*C*H$_2$), 27.1 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 26.30 (*C*H$_2$), 26.27 (*C*H$_2$), 25.2 (*C*H$_2$), 25.0 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.5 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{76}H_{100}N_2O_8$: C, 78.04; H, 8.62; N, 2.40. Found: C, 78.40; H, 8.57; N, 2.45. MALDI: $[M+H]^+$ calcd for $C_{76}H_{101}N_2O_8$, 1169.756, found 1169.396.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 11-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)undecanoate (3-3). To a mixture of compound **3-24** (0.17 g, 0.18 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.08 g, 0.31 mmol) in anhydrous DMF (0.95 mL) in a 25-mL one-neck flask, K_2CO_3 (0.0791 g, 0.572 mmol) was added. The reaction mixture was stirred at 80 ^oC under a N_2 atmosphere for 22 h. The reaction was cooled to room temperature and H_2O (15 mL) was added. Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL) three times. The combined organic extracts were dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give crude solid. The product was purified

by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-4** as colorless solid (0.15 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 4H; (CB)*H*3'), 7.51 (m, 2H; (CB)*H*2'), 7.46 (overlapping m, 10H; (CB)*H*2, (MB)*H*2 and *H*2', ((*S*)MB)*H*2 and *H*2'), 6.95 (overlapping m, 10H; (CB)*H*3, (MeO)*H*3 and *H*3', ((*S*)MB)*H*3 and *H*3'), 6.02 (t, *J* = 6.0 Hz, 1H; N*H*), 5.18 (m, 1H; m, 1H, NCOC*H*O), 4.00 (m, 6H, PhOCH_2), 3.84 (overlapping, 4H, CH_3O, PhOCH_2CHCH$_3$), 3.77 (m, 1H; PhOCH_2CHCH$_3$), 3.31 (m, 2H; CH_2NH), 2.39 (t, *J* = 7.5 Hz, 2H; O_2CCH_2), 1.82 (overlapping, 9H; BPOCH$_2$CH_2, PhOCH$_2$C*H*CH$_3$, NHCOCHCH_2), 1.57 (overlapping m, 13H; OCH$_2$CH$_2$CH_2, (CB)OC$_3$H$_6$CH_2, NHCOCHCH$_2$CH_2, O_2CCH$_2$CH_2, PhOCH$_2$CHCH_2), 1.28 (overlapping m, 21H; NHCOCHC$_2$H$_4$C$_5$$H_{10}$, O_2CC$_2H_4C_5$$H_{10}$, PhOCH$_2CHCH_2$), 1.03 (d, *J* = 6.8 Hz, 3H; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). Characterization agrees with previous work.[26]

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 6-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)hexanoate (3-4). To a mixture of compound **3-25** (0.2417 g, 0.2616 mmol) in anhydrous DMF (2.60 mL) in a 25-mL one-neck flask, K_2CO_3 (0.0741 g, 0.536 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.0882 g, 0.344 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 19 h. The reaction was cooled to room temperature and diluted with CH_2Cl_2 (20 mL) and H_2O (15 mL). Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (8 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (20 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) to give **3-4** as a colorless solid (0.20 g, 70%). TLC (SiO_2, 95:5 CH_2Cl_2/EtOAc): R_f = 0.43. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 2H; (CB)*H*3'), 7.63 (m, 2H; (CB)*H*2'), 7.51 (m, 2H, (CB)*H*2), 7.46 (overlapping 8H, (MB)*H*2 and *H*2', ((*S*)MB)*H*2 and *H*2'), 6.95 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'; 4H, ((*S*)MB)*H*3 and *H*3'), 5.97 (t, *J* = 5.8 Hz, 1H; N*H*), 5.17 (dd, J_1 = 7.2 Hz, J_2 = 7.2 Hz, 1H; NHCOC*H*), 3.98 (m, 6H; PhOCH_2), 3.84 (overlapping, 3H, CH_3O; 1H, PhOCH_2CHCH$_3$), 3.75 (m, 1H; PhOCH_2CHCH$_3$), 3.25 (m, 2H; CH_2NH), 2.45 (t, *J* = 7.5 Hz, 2H; O_2CCH_2), 1.82 (overlapping, 11H; NHCOCHCH_2, NHCOCHCH$_2$CH_2, PhOCH$_2$CH_2, PhOCH$_2$C*H*CH$_3$), 1.66 (m, 2H; O_2CCH$_2$CH_2), 1.53 (overlapping m, 9H; NHCH$_2$CH_2, OCH$_2$CH$_2$CH$_2$, PhOCH$_2$CHCH_2), 1.30 (overlapping m, 23H,; (CB)OC$_3$H$_6$C$_5$H$_{10}$,

(MB)$OC_3H_6C_6H_{12}$, $PhOCH_2CHCH_2$), 1.03 (d, J = 6.8 Hz, 3H;OCH_2CHCH_3), 0.96 (t, J = 7.5 Hz, 3H; CH_2CH_3). ^{13}C NMR (125 MHz, CDCl3, δ, ppm): 172.5 (O_2C), 170.0 (NH*C*O), 160.0 ((CB)*C*1), 158.9 ((MB)*C*1), 158.7 (((*S*)MB)*C*1), 158.5 ((MB)*C*1'), 158.2 (((*S*)MB)*C*1'), 145.5 ((CB)*C*4), 133.77 ((MB)*C*4), 133.75 (((*S*)MB)*C*4), 133.5 ((MB)*C*4'), 133.4 (((*S*)MB)*C*4'), 132.8 ((CB)*C*3'), 131.5 ((CB)*C*4'), 128.5 ((CB)C3'), 127.90 ((CB)*C*2), 127.89 ((MB)*C*2' or (*S*)MB)*C*2), 127.8 (((*S*)MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 114.99 (((*S*)MB)*C*3), 114.95 (((*S*)MB)*C*3'), 114.9 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (*C*N), 74.3 (CO*C*HO_2C), 73.2 (((*S*)MB)OCH_2CHCH_3), 68.4 (OCH_2CH_2), 68.3 (OCH_2CH_2), 67.8 (OCH_2CH_2), 55.6 (CH_3O), 39.4 (CH_2NHCO), 35.0 (OCH_2CHCH_3), 34.6 (O_2CCH_2), 32.1 (NHCOCHCH_2), 29.79 (OCH_2CH_2), 29.75 (OCH_2CH_2), 29.71 (OCH_2CH_2), 29.69 (CH_2), 29.65 (CH_2), 29.62 (CH_2), 29.60 (CH_2), 29.54 (CH_2), 29.47 (CH_2), 29.45 (CH_2), 29.2 (CH_2), 27.0 (CH_2), 26.4 (CH_2CH_3), 26.29 (CH_2), 26.26 (CH_2), 25.9 (CH_2), 25.00 (CH_2), 24.95 (CH_2), 16.8 (OCH_2CHCH_3), 11.6 (CH_2CH_3). Anal. Calcd for $C_{76}H_{100}N_2O_8$: C, 77.56; H, 8.25; N, 2.55. Found: C, 77.25; H, 8.13; N, 2.75. MALDI: $[M+Na]^+$ calcd for $C_{71}H_{90}N_2NaO_8$, 1121.662, found 1121.664.

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 6-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)hexanoate (3-5). To a mixture of compound **3-26** (0.4985 g, 0.5838 mmol) in anhydrous DMF (5.9 mL) in a 50-mL one-neck flask, K_2CO_3 (0.2507 g, 1.813 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.2249 g, 0.8774 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 18 h. The reaction was cooled to room temperature and diluted with CH_2Cl_2 (10 mL) and H_2O (15 mL). Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (8 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-5** as a colorless solid (0.47 g, 78%). TLC (SiO_2, 95:5 CH_2Cl/EtOAc): R_f = 0.47. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.64 (m, 4H; (CB)*H*3' and *H*2'), 7.51 (m, 2H; (CB)*H*2), 7.45 (overlapping m, 8H; (MB)*H*2 and *H*2', ((*S*)MB)*H*2 and *H*2'), 6.94 (overlapping m, 2H, (CB)*H*3; 4H, (MB)*H*3 and *H*3'; 4H, ((*S*)MB)*H*3 and *H*3'), 6.05 (t, J = 5.9 Hz, 1H; N*H*), 5.20 (dd, J_1 = 7.0 Hz, J_2 = 6.9 Hz, 1H; NHCOC*H*), 3.99 (m, 6H; $PhOCH_2$), 3.84 (overlapping, 4H; CH_3O, $PhOCH_2CHCH_3$),

3.76 (m, 1H; PhOCH_2CHCH$_3$), 3.32 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz, 2H; O_2CCH_2), 1.85 (overlapping, 9H; PhOCH$_2$CH_2, NHCOCHCH_2, PhOCH$_2$CHCH$_3$), 1.64 (overlapping 5H, NHCOCHCH$_2$CH_2, O_2CCH$_2$CH_2, PhOCH$_2$CHCH_2), 1.46 (overlapping m, 9H; OCH$_2$CH$_2$CH_2, NHCH$_2$CH_2, PhOCH$_2$CHCH_2), 1.27 (overlapping m, 11H, $O_2C_2H_4C_5H_{10}$, PhOCH$_2$CHCH_2), 1.03 (d, J = 6.8 Hz, 3H; OCH$_2$CHCH_3), 0.96 (t, J = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2C), 170.1 (NHCO), 159.8 ((CB)C1), 158.9 ((MB)C1), 158.6 (((*S*)MB)C1), 158.4 ((MB)C1'), 158.3 (((*S*)MB)C1'), 145.4 ((CB)C4), 133.7 ((MB)C4), 133.60 ((*S*)MB)C4), 133.55 ((MB)C4'), 133.4 ((*S*)MB)C4'), 132.8 ((CB)C3'), 131.6 ((CB)C4'), 128.6 ((CB)C3'), 127.88 ((CB)C2), 127.86 (((*S*)MB)C2'), 127.8 (((*S*)MB)C2), 127.3 ((CB)C2'), 119.3 ((CB)C1'), 115.3 ((CB)C3), 115.0 (((*S*)MB)C3), 114.9 (((*S*)MB)C3'), 114.4 ((MB)C3'), 110.3 (CN), 74.0 (COCHO$_2$C), 73.2 (((*S*)MB)OCH$_2$CHCH$_3$), 68.3 (OCH$_2$CH$_2$), 67.98 (OCH$_2$CH$_2$), 67.95 (OCH$_2$CH$_2$), 55.6 (CH$_3$O), 39.3 (CH$_2$NHCO), 35.0 (OCH$_2$$CHCH_3$), 34.5 ($O_2CCH_2$), 32.0 (NHCOCH$CH_2$), 29.7 (OCH$_2$$CH_2$), 29.62 (OCH$_2$$CH_2$), 29.59 (OCH$_2$$CH_2$), 29.53 ($CH_2$), 29.47 ($CH_2$), 29.34 ($CH_2$), 29.32 ($CH_2$), 29.0 ($CH_2$), 26.4 ($CH_2CH_3$), 26.3 ($CH_2$), 25.99 ($CH_2$), 25.2 ($CH_2$), 24.8 ($CH_2$), 23.6 ($CH_2$), 16.8 (OCH$_2CHCH_3$), 11.6 (CH$_2$$CH_3$). Anal. Calcd for $C_{66}H_{80}N_2O_8$: C, 77.01; H, 7.83; N, 2.72. Found: C, 77.25; H, 7.71; N, 2.74. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{66}H_{80}N_2O_8Na$, 1051.5812, found 1051.5789.

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-6-(4'-methoxybiphenyl-4-oxy)hexyl 11-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)undecanoate (3-6). To a mixture of compound **3-30** (0.1004 g, 0.1024 mmol) in anhydrous DMF (1.0 mL) in a 25-mL one-neck flask, K_2CO_3 (0.0581 g, 0.421 mmol) and **3-31** (0.0315 g, 0.157 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 16 h. The reaction was cooled to room temperature and diluted with CH_2Cl_2 (15 mL) and H_2O (5 mL). Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-6** as a colorless solid (0.0941 g, 84%). TLC (SiO_2, 95:5 CH_2Cl/EtOAc): R_f = 0.33. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.65 (m, 4H; (CB)H3' and H2'), 7.51 (m, 2H; (CB)H2), 7.47 (overlapping m, 8H; (MB)H2 and H2', ((*S*)MB)H2 and H2'), 6.94 (overlapping m, 2H, (CB)H3; 4H, (MB)H3 and H3'; 4H, ((*S*)MB)H3 and H3'), 5.99 (t, J = 6.0

Hz, 1H; N*H*), 5.20 (dd, J_1 = 7.1 Hz, J_2 = 7.0 Hz, 1H; NHCOC*H*), 3.97 (m, 6H; PhOCH_2), 3.84 (overlapping, 3H, CH_3O; 1H, PhOCH_2CHCH$_3$), 3.76 (m, 1H; PhOCH_2CHCH$_3$), 3.36 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz, 2H; O_2CCH_2), 1.80 (overlapping, 9H; PhOCH$_2$CH_2, NHCOCHCH_2, PhOCH$_2$C*H*CH$_3$), 1.64 (overlapping 5H; NHCOCHCH$_2$CH_2, O_2CCH$_2$CH_2, PhOCH$_2$CHCH_2), 1.43 (overlapping m, 31H; OCH$_2$CH$_2$CH_2, NHCH$_2$CH_2, (CB)OC$_3$H$_6$C$_5$H$_{10}$, (MB)OC$_3$H$_6$C$_6$H$_{12}$, PhOCH$_2$CHCH_2), 1.03 (d, J = 6.8 Hz, 3H; OCH$_2$CHCH_3), 0.96 (t, J = 7.5 Hz, 3H; CH$_2$CH$_3$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.6 (O_2C), 169.9 (NH*C*O), 160.0 ((CB)*C*1), 158.9 ((MB)*C*1), 158.6 (((*S*)MB)*C*1), 158.40 ((MB)*C*1'), 158.36 (((*S*)MB)*C*1'), 145.5 ((CB)*C*4), 133.7 ((MB)*C*4), 133.60 ((*S*)MB)*C*4), 133.55 ((MB)*C*4'), 133.4 ((*S*)MB)*C*4'), 132.8 ((CB)*C*3'), 131.5 ((CB)*C*4'), 128.5 ((CB)*C*3'), 127.90 ((CB)*C*2), 127.87 (((*S*)MB)*C*2'), 127.8 (((*S*)MB)*C*2), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 115.0 (((*S*)MB)*C*3), 114.9 (((*S*)MB)*C*3'), 114.4 ((MB)C3'), 110.3 (*C*N), 74.0 (CO*C*HO$_2$C), 73.2 (((*S*)MB)O*C*H$_2$CHCH$_3$), 68.4 (O*C*H$_2$CH$_2$), 68.3 (O*C*H$_2$CH$_2$), 68.0 (O*C*H$_2$CH$_2$), 55.6 (*C*H$_3$O), 39.4 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.6 (O_2C*C*H$_2$), 32.0 (NHCOCH*C*H$_2$), 29.79 (OCH$_2$*C*H$_2$), 29.75 (OCH$_2$*C*H$_2$), 29.7 (OCH$_2$*C*H$_2$), 29.64 (*C*H$_2$), 29.62 (*C*H$_2$), 29.60 (*C*H$_2$CH$_3$), 29.55 (*C*H$_2$), 29.49 (*C*H$_2$), 29.45 (*C*H$_2$), 29.4 (*C*H$_2$), 29.3 (*C*H$_2$), 27.1 (*C*H$_2$), 26.4 (*C*H$_2$), 26.30 (*C*H$_2$), 26.27 (*C*H$_2$), 26.0 (*C*H$_2$), 25.2 (*C*H$_2$), 24.8 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{66}H_{80}N_2O_8Na$

1-(10-(4'-Cyanobiphenyl-4-oxy)decylaminocarbonyl)-11-(4'-cyanobiphenyl-4-oxy)undecyl 11-(4'-cyanobiphenyl-4-oxy)undecanoate (3-8). To a solution of compound **3-37** (0.1874 g, 0.2142 mmol) in anhydrous DMF (2.2 mL) in a 25-mL one-neck flask, K_2CO_3 (0.1224 g, 0.8856 mmol) and 4'-cyano-4-hydroxybiphenyl (0.0956 g, 0.490 mmol) were added. The reaction mixture was stirred at 80 °C under a N_2 atmosphere for 15 h. The reaction was cooled to room temperature and H_2O (10 mL) was added. The reaction mixture was extracted with EtOAc (8 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (10 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) to give **3-8** as a colorless solid (0.0907 g, 38%). TLC (SiO_2, CH_2Cl_2/EtOAc 95:5): R_f = 0.19. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.69 (m, 6H; H3'), 7.63 (m, 6H; *H*2'), 7.52 (m, 6H; *H*2), 6.98 (m, 6H; *H*3), 5.97 (t, J = 5.8 Hz, 1H; NH), 5.17 (dd, J_1 = 7.4 Hz, J_2 = 7.3 Hz, 1H; NCOCHO), 3.99 (t, J = 6.5 Hz, 6H;

PhOCH_2), 3.26 (m, 2H; CH_2NH), 2.39 (t, J = 7.5 Hz, 2H; OCOCH_2), 1.81 (overlapping, 8H; OCH_2CH_2, $NHCOCHCH_2$), 1.66 (m, 2H; $O_2CCH_2CH_2$), 1.49 (overlapping m, 8H; $NHCH_2CH_2$, $OC_2H_4CH_2$), 1.31 (overlapping, 32H; $NHC_2H_4C_5H_{10}$, $NHCOCHCH_2C_6H_{12}$, $O_2CC_2H_4C_5H_{10}$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.7 (O_2C), 170.0 (NH*C*O), 160.0 (*C*1), 145.5 (*C*4), 145.5 (*C*4), 132.8(*C*3'), 131.5 (*C*4'), 128.5 (*C*2), 127.3(*C*2'), 119.3 (*C*1'), 115.3 (*C*3), 110.4 (*C*N), 74.1 (CO*C*HO_2C), 68.4 (O*C*H_2), 68.4 (OCH_2), 39.4 (CH_2NHCO), 34.6 (O_2CCH_2), 32.1 ($O_2CCH_2CH_2$), 29.8 (*C*H_2), 29.7 (*C*H_2), 29.7 (*C*H_2), 29.6 (*C*H_2), 29.6 (*C*H_2), 29.5 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 27.1 (*C*H_2), 26.3 (*C*H_2), 25.2 (*C*H_2), 25.0 (*C*H_2), 25.9 (*C*H_2), 24.9 (*C*H_2), 24.8 (*C*H_2), 23.6 (*C*H_2). Anal. Calcd for $C_{72}H_{86}N_4O_6$: C, 78.37; H, 7.86; N, 5.08. Found: C, 78.12; H, 7.86; N, 4.91. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{72}H_{86}N_4O_6Na$, 1125.6445, found 1125.6420.

1-(5-(4'-Methoxybiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-methoxybiphenyl-4-oxy)hexyl 6-(4'-methoxybiphenyl-4-oxy)hexanoate (3-9). To a solution of compound **3-38** (0.2035 g, 0.3040 mmol) in anhydrous DMF (3.0 mL) in a 25-mL one-neck flask, K_2CO_3 (0.1682 g, 1.217 mmol) and 4-hydroxy-4'-methoxybiphenyl (0.1348 g, 0.6732 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 19 h. The reaction was cooled to room temperature and H_2O (10 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (20 mL) four times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (20 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) and recrystallized from toluene to give **3-9** as a colorless solid (0.12 g, 43%). TLC (SiO_2, CH_2Cl_2/EtOAc 98:2): R_f = 0.40. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.45 (m, 12H; *H*2, *H*2'), 6.93 (m, 12H; H3, H3'), 6.06 (t, 1H, J = 5.9 Hz, N*H*), 5.21 (dd, J_1 = 7.0 Hz, J_2 = 7.0 Hz, 1H, NCOC*H*O), 3.96 (m, 6H, PhOCH_2), 3.83 (overlapping s, 9H; CH_3O), 3.31 (m, 2H; CH_2NH), 2.44 (t, J = 7.5 Hz; 2H, O_2CCH_2), 1.81 (overlapping m, 10H; $PhOCH_2CH_2$, $NHCOCHCH_2$, $O_2CCH_2CH_2$), 1.50 (overlapping m, 10H, $NHCH_2CH_2$, $NHC_2H_4CH_2$, $NHCOCHCH_2CH_2$, $NHCOCHC_2H_4CH_2$, $O_2CC_2H_4CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.5 (O_2C), 170.0 (NH*C*O), 158.88 (*C*1), 158.86 (*C*1), 158.4 (*C*1 or *C*1'), 158.30 (*C*1'), 158.28 (*C*1'), 133.64 (*C*4), 133.62 (*C*4 or *C*4'), 133.7 (*C*4'), 127.91 (*C*2 or *C*2'), 127.89 (*C*2 or *C*2'), 114.91 (*C*3), 114.89 (*C*3), 114.4 (C3'), 74.1 (CO*C*HO_2C), 67.93 (O*C*H_2), 67.88 (O*C*H_2), 67.8 (O*C*H_2), 55.6 (*C*H_3O),

39.3 (*C*H_2NHCO), 34.4 (O_2CCH_2), 32.0 ($O_2CCH_2CH_2$), 29.5 (*C*H_2), 29.3 (*C*H_2), 29.2 (*C*H_2), 29.1 (*C*H_2), 26.0 (*C*H_2), 25.9 (*C*H_2), 24.9 (*C*H_2), 24.8 (*C*H_2), 23.7 (*C*H_2). Anal. Calcd for $C_{57}H_{65}NO_9$: C, 75.39; H, 7.21; N, 1.54. Found: C, 75.59; H, 7.17; N, 1.39. HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{57}H_{66}NO_9$, 908.4738, found 908.4698.

Ethyl 11-(4'-methoxybiphenyl-4-oxy)undecanoate (3-63). To a mixture of **3-31** (0.70 g, 3.5 mmol) in anhydrous DMF (16.0 mL), 11-bromoundecanoic acid ethyl ester (1.0190 g, 3.8425 mmol) and K_2CO_3 (0.93 g, 6.7 mmol) were added. The reaction mixture was heated at 80 ^oC for 25 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature and solvents were removed by rotary evaporation. Cold H_2O (20 mL) was added to the crude solid and filtered. The filter cake was washed with cold H_2O (10 mL) three times and was purified by recrystallized from EtOH to give **3-63** as a colorless solid (0.95 g, 72%). TLC (SiO_2, 4:1 hex/EtOAc): R_f = 0.46. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.46 (overlapping m, 4H; *H*2, *H*2'), 6.95 (overlapping m, 4H; *H*3, *H*3'), 4.13 (q, *J* = 7.1 Hz, 2H; $CO_2CH_2CH_3$), 3.98 (t, *J* = 6.6 Hz, 2H; PhOCH_2), 3.84 (s, 3H; CH_3O), 2.29 (t, *J* = 7.5 Hz, 2H; $CH_2CO_2CH_2CH_3$), 1.79 (m, 2H; $OCH_2CH_2(CH_2)_8$), 1.62 (overlapping, 2H; $CH_2CH_2CO_2CH_2CH_3$), 1.47 (m, 2H; $O(CH_2)_2CH_2(CH_2)_7$), 1.37 (overlapping, 11H; $O(CH_2)_3(CH_2)_5$, $CHCH_2CH_3$; 3H, $CO_2CH_2CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 174.1 (*C*O_2), 158.9 (*C*1'), 158.5 (*C*1), 133.8 (*C*4'), 133.5 (*C*4), 127.92 (*C*2'), 127.89 (*C*2), 115.0 (*C*3'), 114.4 (*C*3), 68.3 (PhO*C*H_2), 60.4 ($CO_2CH_2CH_3$), 55.6 (CH_3O), 34.6 ($CH_2CO_2CH_2CH_3$), 29.7 (OCH_2CH_2), 29.6 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.53 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.47 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 29.4 ($O(CH_2)_3(CH_2)_5(CH_2)_2$), 26.3 ($OCH_2CH_2CH_2(CH_2)_7$), 25.2 ($CH_2CH_2CO_2CH_2CH_3$), 14.5 ($CO_2CH_2CH_3$).

11-(4'-Methoxybiphenyl-4-oxy)undecanoic acid (3-43). A solution of KOH (0.3440 g, 6.132 mmol) in H_2O (0.4 mL) was added to a solution of **3-63** (0.83 g, 2.0 mmol) in THF (20.0 mL). The reaction mixture was heated at reflux for 2.5 h under a N2 atmosphere. Additional solution of KOH (0.2256 g, 4.021 mmol) in H_2O (0.2 mL) and the reaction mixture was stirred at reflux for another 3 h. Additional solution of KOH (0.3325 g, 5.927 mmol) in EtOH (5.0 mL) and the reaction mixture was stirred at reflux for another 0.5 h. The reaction mixture was then cooled in an ice-water bath and acidified to pH 2 with 1 M HCl (aq). The precipitate was collected by filtration, washed three times with cold H_2O (8 mL). The product was collected by filtration (0.56 g, 73%) and used as crude. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.47 (m, 4H; *H*3', *H*2'), 6.95 (m, 2H; *H*2, *H*3), 3.98 (t, *J* = 6.4 Hz, 2H; PhOCH_2), 3.84 (s, 3H; CH_3O), 2.36 (t, *J* = 7.5 Hz,

2H; CH_2CO$_2$H), 1.78 (m, 2H; PhOCH$_2$CH_2), 1.64 (m, 2H; CH_2CH$_2$CO$_2$H), 1.43 (m, 2H; PhOCH$_2$CH$_2$CH_2), 1.31 (m, 10H; PhOC$_3$H$_6$C$_5$$H_{10}$).

1-(10-(4'-methoxybiphenyl-4-oxy)decylaminocarbonyl)-11-(4'-methoxybiphenyl-4-oxy)undecyl 11-(4'-methoxybiphenyl-4-oxy)undecanoate (3-10). A mixture of **3-19** (0.0482 g, 0.131 mmol), **3-43** (0.0479 g, 0.131 mmol), and **3-43** (0.0504 g, 0.131 mmol) in anhydrous DCE (0.52 mL) was refluxed for 17 h under a N_2 atmosphere. The crude product was obtained by rotary evaporation of the volatiles from the reaction mixture. The product was purified by flash column chromatography (SiO_2, $CHCl_3$ to $CHCl_3$/EtOAc 9:1) and recrystallized from toluene to give **3-10** as colorless solid (0.0471 g, 32%). TLC (SiO_2, CH_2Cl_2/EtOAc 95:5): R_f = 0.77. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.45 (m, 12H; *H*2, *H*2'), 6.93 (m, 12H; *H*3, *H*3'), 5.97 (t, J = 5.9 Hz, 1H; N*H*), 5.17 (dd, J_1 = 7.0 Hz, J_2 = 7.0 Hz, 1H; NCOC*H*O), 3.98 (m, 6H, PhOCH_2), 3.83 (overlapping s, 9H; CH_3O), 3.27 (m, 2H; CH_2NH), 2.38 (m, J = 7.5 Hz, 2H; O$_2$CCH_2), 1.81 (overlapping m, 10H; PhOCH$_2$CH_2, NHCOCHCH_2, O$_2$CCH$_2$CH_2), 1.50 (overlapping m, 10H, NHCH$_2$CH_2, NHC$_2$H$_4$CH_2, NHCOCHCH$_2$CH_2, NHCOCHC$_2$H$_4$CH_2, O$_2$CC$_2$H$_4$CH_2). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm): 172.7 (O$_2$*C*), 170.0 (NH*C*O), 158.9 (*C*1), 158.5 (*C*1'), 133.8 (*C*4 or *C*4'), 127.91 (*C*2 or *C*2'), 127.89 (*C*2 or *C*2'), 115.0 (*C*3), 114.4 (*C*3 or C3'), 74.2 (CO*C*HO$_2$C), 68.29 (O*C*H$_2$), 68.27 (O*C*H$_2$), 55.6 (*C*H$_3$O), 39.4 (*C*H$_2$NHCO), 34.6 (O$_2$C*C*H$_2$), 32.1 (O$_2$CCH$_2$*C*H$_2$), 29.79 (*C*H$_2$), 29.76 (*C*H$_2$), 29.73 (*C*H$_2$), 29.71 (*C*H$_2$), 29.65 (*C*H$_2$), 29.63 (*C*H$_2$), 29.55 (*C*H$_2$), 29.51 (*C*H$_2$), 29.48 (*C*H$_2$), 29.4 (*C*H$_2$), 27.1 (*C*H$_2$), 26.3 (*C*H$_2$), 25.2 (*C*H$_2$), 25.0 (*C*H$_2$). MALDI: $[M+H]^+$ calcd for $C_{72}H_{96}NO_9$, 1118.709, found 1118.213.

1-(5-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)hexyl 6-(4'-cyanobiphenyl-4-oxy)hexanoate (3-11). To a mixture of compound **3-40** (0.2093 g, 0.2884 mmol) in anhydrous DMF (2.90 mL) in a 25-mL one-neck flask, K_2CO_3 (0.1598 g, 1.156 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.1659 g, 0.6472 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 38 h. The reaction was cooled to room temperature and diluted with CH_2Cl_2 (10 mL) and H_2O (10 mL). Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (8 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) and

recrystallized from toluene to give **3-11** as a colorless solid (0.14 g, 44%). TLC (SiO_2, CH_2Cl_2/EtOAc 95:5): R_f = 0.28. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.44 (overlapping, 12H; *H*2, *H*2'), 6.91 (overlapping, 4H; *H*3, *H*3'), 6.05 (t, *J* = 5.9 Hz, 1H; N*H*), 5.21 (dd, J_1 = 6.9 Hz, J_2 = 6.9 Hz, 1H; NCOC*H*O), 3.96 (m, 6H; PhOCH_2), 3.84 (m, 1H; OCH_2CHCH$_3$), 3.75 (m, 1H; OCH_2CHCH$_3$), 3.40 (t, *J* = 6.8 Hz, 4H; CH_2Br), 3.31 (m, 2H; CH$_2$N*H*), 2.44 (t, *J* = 7.5 Hz, 2H; OCOCH_2), 1.84 (overlapping, 13H; OCH$_2$CH_2, NHCOCHCH_2, O$_2$CCH$_2$CH_2, OCH$_2$C*H*CH$_3$), 1.59 (overlapping m, 5H; NHCH$_2$CH_2, CHCH_2CH$_3$), 1.52 (overlapping m, 8H; NHC$_2$H$_4$CH_2, NHCOCHCH$_2$C$_2$*H*$_4$, O$_2$CC$_2$H$_4$CH_2), 1.28 (m, 3H; CHCH_2CH$_3$), 1.03 (d, *J* = 6.7 Hz; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 172.5 (O$_2$*C*), 169.9 (NH*C*O), 158.67 (C1'), 158.65 (C1'), 158.31 (C1), 158.25 (C1), 158.2 (C1), 133.74 (C4'), 133.72 (C4'), 133.6 (C4'), 133.42 (C4), 133.37 (C4), 127.88 (C2'), 127.86 (C2), 127.83 (C2), 115.0 (C3'), 114.9 (C3), 74.1 (CO*C*HO$_2$C), 73.2 (O*C*H$_2$CHCH$_3$), 67.93 (O*C*H$_2$), 67.89 (O*C*H$_2$), 67.8 (O*C*H$_2$), 39.3 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.4 (O$_2$C*C*H$_2$), 32.0 (O$_2$CCH$_2$*C*H$_2$), 29.5 (*C*H$_2$), 29.3 (*C*H$_2$), 29.2 (*C*H$_2$), 29.1 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 26.0 (*C*H$_2$), 25.95 (*C*H$_2$), 25.0 (*C*H$_2$), 24.8 (*C*H$_2$), 23.7 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{69}H_{89}NO_9$: C, 76.99; H, 8.33; N, 1.30. Found: C, 76.76; H, 8.13; N, 1.24. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{69}H_{89}NO_9Na$, 1098.6435, found 1098.6411.

1-(10-(4'-((*S*)-2-Methylbutoxy)biphenyl-4-oxy)decylaminocarbonyl)-11-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)undecyl 11-(4'-((*S*)-2-methylbutoxy)phenyl-4-oxy)undecanoate (3-12). To a solution of compound **3-41** (0.1948 g, 0.2081 mmol) in anhydrous DMF (2.1 mL) in a 25-mL one-neck flask, K_2CO_3 (0.1178 g, 0.8523 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.1659 g, 0.6472 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 15 h. The reaction was cooled to room temperature and diluted with CH_2Cl_2 (15 mL) and H_2O (10 mL). Two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate by rotary evaporation to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) and recrystallized from toluene to give **3-12** as a colorless solid (0.16 g, 60%). TLC (SiO_2, CH_2Cl_2/EtOAc 98:2): R_f = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.45 (overlapping, 12H; *H*2, *H*2'), 6.94 (overlapping, 12H; *H*3, *H*3'), 5.98 (t, *J* = 5.9 Hz,

1H; N*H*), 5.17 (dd, J_1 = 7.2 Hz, J_2 = 7.0 Hz, 1H; NCOC*H*O), 3.97 (t, *J* = 6.5 Hz, 6H; PhOCH_2), 3.85 (m, 3H; OCH_2CHCH$_3$), 3.76 (m, 3H; O*C*H$_2$CHCH$_3$), 3.27 (m, 2H; CH$_2$N*H*), 2.40 (t, *J* = 7.5 Hz, 2H; OCOCH_2), 1.81 (overlapping, 11H; OCH$_2$CH_2, NHCOCHCH$_2$, OCH$_2$C*H*CH$_3$), 1.66 (overlapping m, 5H; O$_2$CCH$_2$CH$_2$, CHCH_2CH$_3$), 1.49 (overlapping m, 8H; NHCH$_2$CH_2, OC$_2$H$_4$CH_2), 1.31 (overlapping, 35H; NHC$_2$H$_4$C$_5H_{10}$, NHCOCHCH$_2$C$_6H_{12}$, O$_2$CC$_2$H$_4$C$_5H_{10}$, CHCH_2CH$_3$), 1.03 (d, *J* = 6.7 Hz; OCH$_2$CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH$_2$CH_3). ^{13}C NMR (100 MHz, CDCl$_3$, δ, ppm): 172.6 (O$_2$*C*), 170.0 (NH*C*O), 158.6 (C1'), 158.3 (C1), 133.6 (C4'), 133.5 (C4), 127.86 (C2'), 127.84 (C2), 115.0 (C3'), 114.9 (C3), 74.2 (CO*C*HO$_2$C), 73.2 (O*C*H$_2$CHCH$_3$), 68.29 (O*C*H$_2$), 68.26 (O*C*H$_2$), 39.4 (*C*H$_2$NHCO), 35.0 (OCH$_2$*C*HCH$_3$), 34.6 (O$_2$C*C*H$_2$), 32.1 (O$_2$CCH$_2$*C*H$_2$), 29.78(*C*H$_2$), 29.76 (*C*H$_2$), 29.73 (*C*H$_2$), 29.70 (*C*H$_2$), 29.65 (*C*H$_2$), 29.62 (*C*H$_2$), 29.55 (*C*H$_2$), 29.50 (*C*H$_2$), 29.47 (*C*H$_2$), 29.4 (*C*H$_2$), 27.1 (*C*H$_2$), 26.4 (*C*H$_2$CH$_3$), 26.3 (*C*H$_2$), 25.2 (*C*H$_2$), 25.0 (*C*H$_2$), 16.8 (OCH$_2$CH*C*H$_3$), 11.6 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{84}H_{119}NO_9$: C, 78.40; H, 9.32; N, 1.09. Found: C, 78.47; H, 9.12; N, 1.01. HRMS-ESI (*m*/*z*): [M+Na]$^+$ calcd for $C_{84}H_{119}NO_9Na$, 1308.8783, found 1308.8743.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 11-(4'-cyanobiphenyl-4-oxy)decanoate (3-13). To a solution of compound **3-45** (0.61 g, 0.72 mmol) in anhydrous DMF (3.6 mL) in a 50-mL one-neck flask, K_2CO_3 (0.3017 g, 2.183 mmol) and 4'-cyano-4-hydroxybiphenyl (0.1544 g, 0.7909 mmol) were added. The reaction mixture was stirred at 80 ^{o}C under a N_2 atmosphere for 17 h. The reaction was cooled to room temperature and the residual solids were removed by filtration and the crude product was obtained by rotary evaporation of volatiles from the filtrate. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 3:2 to 1:1) to give **3-13** as a colorless waxy solid (0.56 g, 81%). TLC (SiO_2, 1:1 hex/EtOAc): R_f = 0.39. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 7.68 (m, 6H; *H*3), 7.62 (m, 6H; *H*3'), 7.52 (m, 6H; *H*2), 6.97 (m, 6H; *H*2'), 6.07 (t, *J* = 5.9 Hz, 1H; N*H*), 5.20 (dd, J_1 = 7.1 Hz, J_2 = 7.2 Hz, 1H; NCOC*H*O), 3.98 (m, 6H; PhOCH_2), 3.32 (m, 2H; CH_2NH), 2.40 (t, *J* = 7.5 Hz, 2H; OCOCH_2), 1.81 (overlapping, 8H; OCH$_2$CH_2, CH_2CH$_2$NH), 1.62 (overlapping, 4H; OCOCH$_2$CH_2, OCHCH_2), 1.49 (overlapping, 8H; PhOCH$_2$CH$_2$CH_2, OCHCH$_2$CH_2,), 1.32 (overlapping, 10H; O$_2$CCH$_2$CH$_2$CH_2, O$_2$C(CH$_2$)$_3$CH_2, O$_2$C(CH$_2$)$_4$CH_2, O$_2$C(CH$_2$)$_5$CH_2, O$_2$C (CH$_2$)$_6$CH_2). ^{13}C NMR (125 MHz, CDCl$_3$, δ, ppm): 172.7 (O*C*O), 170.0 (NH*C*O), 160.0 (*C*1), 159.9 (*C*1), 159.8 (*C*1), 145.42 (*C*4), 145.38 (*C*4), 145.36 (*C*4), 132.8 (*C*3'), 131.6 (*C*4'), 131.54 (*C*4'), 131.49 (*C*4'), 128.54 (*C*2), 128.52 (*C*2), 127.3 (C2'), 119.30

(*C*1'), 119.28 (*C*1'), 119.27 (*C*1'), 115.3 (*C*3), 115.2 (*C*3), 110.30 (*C*N), 110.28 (*C*N), 110.26 (*C*N), 73.9 (CO*C*HOCO), 68.3 (O*C*$H_2$$CH_2$), 68.04 (O*C*$H_2$$CH_2$), 67.96 (O*C*$H_2$$CH_2$), 39.3 (*C*$H_2$NHCO), 34.5 (OCO*C*$H_2$), 32.0 ($O_2CCH_2$*C*$H_2$), 29.7 (OCH*C*$H_2$), 29.62 (COCHC$H_2$*C*$H_2$), 29.59 (*C*$H_2$$CH_2$NHCO), 29.57 (*C*$H_2$), 29.5 (*C*$H_2$), 29.4 (*C*$H_2$), 29.3 (*C*$H_2$), 29.2 (*C*$H_2$), 29.0 (*C*$H_2$), 26.3 (*C*$H_2$), 25.9 (*C*$H_2$), 25.2 (*C*$H_2$), 24.8 (*C*$H_2$), 23.6 (*C*$H_2$). Anal. Calcd for $C_{62}H_{66}N_4O_6$: C, 77.31; H, 6.91; N, 5.82. Found: C, 77.52; H, 7.06; N, 5.59. HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{62}H_{67}N_4O_6$, 963.5061, found 963.5035.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 11-(4'-methoxybiphenyl-4-oxy)undecanoate (3-14). To a solution of compound **3-45** (0.2930 g, 0.3451 mmol) in anhydrous DMF (3.5 mL) in a 25-mL one-neck flask, K_2CO_3 (0.1017 g, 0.7358 mmol) and 4-hydroxy-4'-methoxybiphenyl (0.0921 g, 0.460 mmol) were added. The reaction mixture was stirred at 80 ^oC under a N_2 atmosphere for 17.5 h. The reaction was cooled to room temperature before H_2O (15 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (10 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (20 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 9:1) to give **3-14** as a colorless solid (0.20 g, 61%). TLC (SiO_2, 1:1 hex/EtOAc): R_f = 0.18. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 4H; (CB)*H*3'), 7.62 (m, 4H; (CB)*H*2'), 7.51 (m, 4H; (CB)*H*2), 7.45 (m, 4H; (MB) *H*2, *H*2'), 6.95 (overlapping m, 8H; (CB)*H*3, (MB) *H*3, *H*3'), 6.05 (t, *J* = 6.0 Hz, 1H; N*H*), 5.21 (dd, J_1 = 7.2 Hz, J_2 = 7.1 Hz, 1H; NCOCHO), 3.98 (m, 6H; PhOCH_2), 3.84 (s, 3H; OCH_3), 3.32 (m, 2H; CH_2NH), 2.40 (t, *J* = 7.5 Hz, 2H; O_2CCH_2), 1.80 (overlapping m, 8H; PhOCH_2CH_2, C$H_2$$CH_2$NH), 1.57 (overlapping m, 5H; O_2CCH_2CH_2, NHCOCHCH_2, PhOCH_2CHCH_2), 1.50 (overlapping m, 8H; PhOC_2H_4CH_2, O_2C$(CH_2)_2$CH_2, NHCOCHCH_2CH_2), 1.30 (overlapping m, 10H; (MB)O$(CH_2)_3(CH_2)_5$). ^{13}C NMR (125 MHz, CDCl3, δ, ppm): 172.7 (O*C*O), 170.0 (NH*C*O), 159.9 ((CB)*C*1), 159.8 ((CB)*C*1), 158.9 ((MB)*C*1), 158.4 ((MB)*C*1'), 145.4 ((CB)*C*4), 145.4 ((CB)*C*4), 133.7 ((MB)*C*4), 133.5 ((MB)*C*4'), 132.8 ((CB)*C*3'), 131.7 ((CB)*C*3'), 131.6 ((CB)*C*4'), 128.6 ((CB)*C*2), 128.5 ((CB)*C*2), 127.9 ((MB)*C*2'), 127.3 ((CB)*C*2'), 119.3 ((CB)*C*1'), 119.3 ((CB)*C*1'), 115.3 ((CB)*C*3), 114.9 ((MB)*C*3), 114.4 ((MB)*C*3'), 110.3 (CN), 110.3 (CN), 74.0 (CO*C*HO_2C), 68.2 ((MB)O*C*$H_2$$CH_2$), 68.1 ((CB)O*C*$H_2$$CH_2$), 68.0 ((CB)O*C*$H_2$$CH_2$), 55.6 ($CH_3$O), 39.3

(*C*H_2NHCO), 34.6 (O_2CCH_2), 32.0 ($O_2CCH_2CH_2$), 29.7 (*C*H_2), 29.6 (*C*H_2), 29.6 (*C*H_2), 29.5 (*C*H_2), 29.5 (*C*H_2), 29.4 (*C*H_2), 29.3 (*C*H_2), 29.0 (*C*H_2), 26.3 (*C*H_2), 26.0 (*C*H_2), 25.2 (*C*H_2), 24.8 (*C*H_2), 23.6 (*C*H_2). Anal. Calcd for $C_{62}H_{69}N_3O_7$: C, 76.91; H, 7.18; N, 4.34. Found: C, 77.06; H, 7.20; N, 4.26. HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{62}H_{70}N_3O_7$, 968.5214, found 968.5169.

1-(5-(4'-Cyanobiphenyl-4-oxy)pentylaminocarbonyl)-6-(4'-cyanobiphenyl-4-oxy)hexyl 11-(4'-((*S*)-2-methylbutoxy)biphenyl-4-oxy)undecanoate (3-15). To a solution of compound **3-45** (0.5680 g, 0.6691 mmol) in anhydrous DMF (6.7 mL) in a 50-mL one-neck flask, K_2CO_3 (0.2785 g, 2.015 mmol) and 4-hydroxy-4'-((*S*)-2-methylbutoxy)biphenyl (0.2584 g, 1.008 mmol) were added. The reaction mixture was stirred at 80 ^oC under a N_2 atmosphere for 20 h. The reaction was cooled to room temperature before H_2O (15 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (10 mL) three times. The combined organic extracts were washed with a saturated aqueous solution of NaCl (15 mL) and dried over $MgSO_4$. The solids were removed by filtration and solvent was removed from the filtrate under reduced pressure to give the crude solid. The product was purified by flash column chromatography (SiO_2, CH_2Cl_2 to CH_2Cl_2/EtOAc 95:5) to give **3-15** as a colorless solid (0.55 g, 80%). TLC (SiO_2, 95:5 CH_2Cl_2/EtOAc): R_f = 0.19. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.68 (m, 4H; (CB)*H*3'), 7.62 (m, 4H; (CB)*H*2'), 7.51 (m, 4H; (CB)*H*2), 7.45 (m, 4H; ((*S*)MB) *H*2, *H*2'), 6.96 (overlapping m, 8H; (CB)*H*3, ((*S*)MB) *H*3, *H*3'), 6.06 (t, *J* = 6.0 Hz, 1H; N*H*), 5.21 (dd, J_1 = 7.1 Hz, J_2 = 7.1 Hz, 1H; NCOCHO), 3.98 (m, 6H; $PhOCH_2$), 3.85 (m, 1H; $PhOCH_2CHCH_3$), 3.76 (m, 1H; $PhOCH_2CHCH_3$), 3.32 (3.31 (m, 2H; CH_2NH), 2.40 (t, *J* = 7.5 Hz, 2H; O_2CCH_2), 1.80 (overlapping m, 9H; $PhOCH_2CH_2$, $NHCOCHCH_2$, OCH_2CHCH_3), 1.57 (overlapping m, 5H, CH_2CH_2NH, $O_2CCH_2CH_2$, $PhOCH_2CHCH_2$), 1.50 (overlapping m, 8H; $PhOC_2H_4CH_2$, $O_2C(CH_2)_2CH_2$, $NHCOCHCH_2CH_2$), 1.30 (overlapping m, 11H; ((*S*)$MBO(CH_2)_3(CH_2)_5$, $PhOCH_2CHCH_2$), 1.03 (d, *J* = 6.8 Hz, 3H; OCH_2CHCH_3), 0.96 (t, *J* = 7.5 Hz, 3H; CH_2CH_3). ^{13}C NMR (100 MHz, CDCl3, δ, ppm): 172.7 (O*C*O), 170.0 (NH*C*O), 159.9 ((CB)*C*1), 159.8 ((CB)*C*1), 158.7 (((*S*)MB)*C*1), 158.4 ((*S*)MB)*C*1'), 145.4 ((CB)*C*4), 133.6 (((*S*)MB)*C*4), 133.4(((*S*)MB)*C*4'), 132.8 ((CB)*C*3'), 131.7 ((CB)*C*4'), 131.6 ((CB)*C*4'), 128.6 (*C*2), 128.5 (*C*2), 127.9 (((*S*)MB)*C*2), 127.8 ((((*S*)MB)*C*2'), 127.3((CB)C2'), 119.3 ((CB)*C*1'), 115.3 (*C*3), 115.3 ((CB)*C*3), 115.0 (((*S*)MB)*C*3), 114.9 (((*S*)MB)*C*3'), 110.3 (*C*N), 74.0 (CO*C*HOCO), 73.2 (((*S*)MB)O*C*H_2CHCH_3), 68.2 (O*C*H_2CH_2), 68.1 (O*C*H_2CH_2), 68.0 (O*C*H_2CH_2), 39.3 (*C*H_2NHCO), 35.0 (OCH_2CHCH_3), 34.6 (O_2CCH_2), 32.0 ($O_2CCH_2CH_2$), 29.7 ($COCHCH_2$),

29.6(COCHCH$_2$*C*H$_2$), 29.5 (*C*H$_2$CH$_2$NHCO), 29.5 (OCH$_2$*C*H$_2$), 29.3 (OCH$_2$*C*H$_2$), 29.2 (*C*H$_2$), 29.0 (*C*H$_2$), 26.4 (((*S*)MB)OCH*C*H$_2$CH$_3$)), 26.3 (*C*H$_2$), 26.0 (*C*H$_2$), 25.2 (*C*H$_2$), 24.8 (*C*H$_2$), 23.6 (*C*H$_2$), 16.8 (OCH$_2$*C*HCH$_3$), 11.5 (CH$_2$*C*H$_3$). Anal. Calcd for $C_{66}H_{77}N_3O_7$: C, 77.39; H, 7.58; N, 4.10. Found: C, 77.16; H, 7.67; N, 4.09. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{66}H_{77}N_3O_7Na$, 1046.5659, found 1046.5626.

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Chapter 4

4. Enhanced Reactivity of Dendrons in the Passerini Three-Component Reaction

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4.1 Introduction

Multicomponent reactions offer strategic advantages for the synthesis of structurally complex polymers.[1-2,3-10] Multifunctional materials can be prepared from simpler polymers by introducing two or more new functionalities at each side-chain[11-12] or chain-end[13-14,15] functional group. In this way, multicomponent reactions have begun to address the synthetic challenges[16] of synthesizing multifunctional dendrimers.[17-19] We have demonstrated an approach in which three different component dendrons are transformed into a dendrimer via the Passerini reaction,[20] however long reaction times are a disadvantage to our approach.

Poor reactivity of dendrons has also been observed in polymerization reactions. Separating the polymerizable group from the apex branch point of the dendron with an unbranched linker group has been shown to greatly improve the reactivity of dendritic macromonomers.[21-25] We reasoned that short linkers in the dendrons would result in faster reactions by reducing the steric interactions between the reactants. Gratifyingly, we observed very short reaction times for Passerini reactions with dendron **4-1b** (Figure 4.1). Contrary to our expectation, though, the distance between the apex branch point and the reactive functional groups added by the linkers is not the reason for the observed reactivity. Rather, an unexpected electronic effect greatly enhances the reactivity of the dendritic aldehyde **4-1b** in the Passerini reaction.

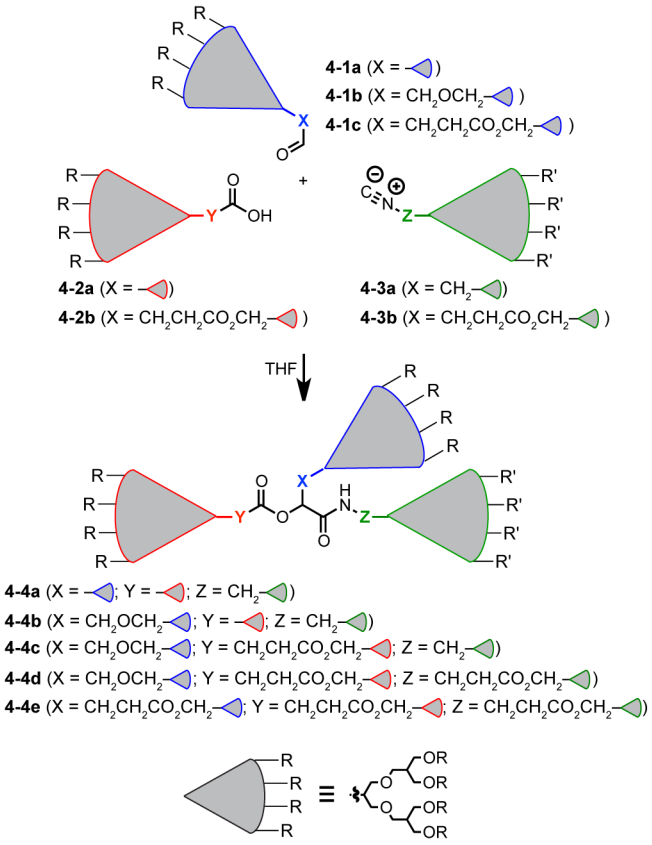

Figure 4.1. Passerini reactions of second-generation dendrons revealed an unexpected substituent in the aldehyde component **4-1**. For dendrons **4-1** and **4-2** and dendrimers **4-4**, R = $C_{10}H_{21}$. For dendron **4-3a** and dendrimers **4-4a**, **4-4b**, and **4-4c**, R' = Bn; and for dendron **4-3b** and dendrimers **4-4d** and **4-4e**, R' = $C_{10}H_{21}$.

4.2 Results and discussion

4.2.1 Discovery of accelerated Passerini reactions[†]

Passerini reactions of second-generation dendrons in THF were investigated to test our hypothesis (Figure 4.1 and Table 4.1). We have used poly(alkyl ether) dendrons as our model system, because the alkyl ether linkage is chemically robust and the dendrons are conveniently prepared in a convergent manner.[26-28] The multicomponent reactions were monitored by ^{1}H NMR spectroscopy and were judged to be complete when the aldehyde resonance at δ 9.7 ppm disappeared. We previously reported that the Passerini reaction of dendrons **4-1a**, **4-2a**, and **4-3a** was complete after 65 h and dendrimer **4-4a** was obtained in 43% yield.[20] This reaction served as

[†] These experiments were performed by Dr. Jo-Ann Jee.

our benchmark for the slow reaction of dendrons without linkers between the apical branch point and the functional groups involved in the Passerini reaction. When a short linker was introduced to only the aldehyde component we observed a significant improvement of the reaction time. Aldehyde **4-1b** was reacted with carboxylic acid **4-2a** and isocyanide **4-3a**. The reaction was judged to be complete after 24 h, and the product (**4-4b**) was isolated in 49% yield. This result supported our hypothesis that relieving steric interactions between the reactants would yield faster Passerini reactions of dendrons.

Table 4.1. Reaction times and yields for the Passerini three-component reaction of second-generation dendrons.

Aldehyde	Carboxylic Acid	Isocyanide	Time[a]	Dendrimer (yield)
4-1a	**4-2a**	**4-3a**	65 h	**4-4a** (43%)[b]
4-1b	**4-2a**	**4-3a**	24 h	**4-4b** (49%)
4-1b	**4-2b**	**4-3a**	24 h	**4-4c** (52%)
4-1b	**4-2b**	**4-3b**	24 h	**4-4d** (74%)
4-1c	**4-2b**	**4-3b**	72 h	**4-4e** (52%)

[a]Time required for the aldehyde resonance at δ 9.7 ppm to disappear. [b]Data from reference [20].

Following the logic of our hypothesis we expected that introducing linkers into the carboxylic acid and isocyanide components would further reduce the overall time of reaction. Dendrons **4-2b** and **4-3b** include short linkers derived from succinic anhydride and β-alanine, respectively. When dendron **4-1b** was subjected to the Passerini reaction with **4-2b** and **4-3a** or with **4-2b** and **4-3b**, however, we did not observe any additional rate enhancement compared to the reaction of **4-1b** with **4-2a** and **4-3a**. These results could be rationalized by speculating that relieving steric bulk in any one of the components was sufficient to promote the Passerini reaction of second-generation dendrons.

What caught us by surprise was the reaction of aldehyde **4-1c** with **4-2b** and **4-3b**. Aldehyde **4-1c** includes a linker that is derived from 4-pentenoic acid and is longer than the linker in **4-1b**. We expected that aldehyde **4-1c** would perform as well as or even better than aldehyde **4-1b** in the Passerini reaction with **4-2b** and **4-3b**. Even though the linker in **4-1c** is longer than the linker in **4-1b**, the Passerini reaction with **4-1c** reached completion only after 72

h. This is similar to the reaction time for second-generation dendrons without linkers (i.e., **4-1a**, **4-2a**, and **4-3a**).[20] The dramatic reactivity difference between the aldehydes **4-1b** and **4-1c** was corroborated in Passerini reactions of first-generation analogues of **4-1b**, **4-1c**, **4-2b**, and **4-3b**. Clearly, the enhanced reactivity we observed in Passerini reactions with aldehyde **4-1b** is due to something other than steric effects.

4.2.2 Validation of the accelerated Passerini reaction using a model reaction[‡]

Such a dramatic increase of the reaction rate as we see for aldehyde **4-1b** compared to **4-1a** or **4-1c** is likely the result of an electronic effect, however this has not been reported for Passerini reactions. Ganem and coworkers have reported that chloride, azide, and sulfonate ester substituents on the α-carbon of ketones accelerate the Passerini reaction under solvent-free conditions.[29] However, less strongly withdrawing groups (e.g., sulfonyl) showed no rate enhancement.[29] We, therefore, were surprised by the high reactivity of aldehyde **4-1b** in the Passerini reaction. The prevailing view of the Passerini reaction mechanism involves nucleophilic attack at the carbonyl by the isocyanide. Whether this is the rate-determining step is unclear,[30-32] but sufficiently strong electron-withdrawing substituents should increase the electrophilicity of the aldehyde by stabilizing the tetrahedral intermediate in a manner analogous to that observed for hydration of aldehydes.[33]

To validate our observation that ether substituents on the α-carbon of the carbonyl component enhance the rate of the Passerini reaction, we monitored the progress of reactions involving small-molecule reactants. We compared two aldehydes and two ketones in Passerini reactions with isovaleric acid and *t*-butylisocyanide (Figure 4.2). Isovaleraldehyde (**4-5a**) and acetone (**4-5c**) were used as the carbonyl components in control experiments lacking any activating substituents. α-Butoxyacetaldehyde (**4-5b**) and methoxyacetone (**4-5d**) served as reactants representative of the activated dendritic aldehyde component **4-1b**. The reactions were performed at room temperature in THF, and the reaction progress was determined from ^{1}H NMR spectra of aliquots taken at different times. From the data plotted in Figure 4.2 it is evident that aldehydes react significantly faster than ketones. Furthermore, the aldehyde (**4-5b**) and the ketone (**4-5d**) with ether substituents on the α-carbon undergo the Passerini reaction in THF much faster than the corresponding control compound.

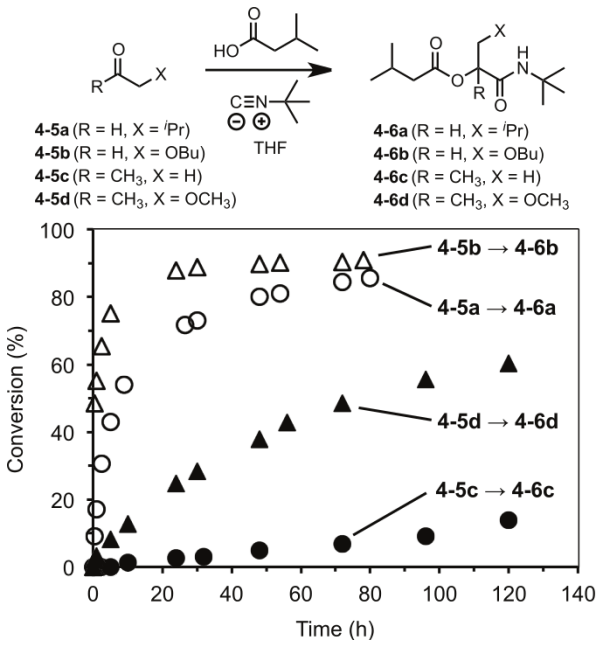

Figure 4.2. Plot of reaction conversion for Passerini reactions of isovaleric acid and *t*-butylisocyanide in THF with isovaleraldehyde (**4-5a**) (○), α-butoxyacetaldehyde (**4-5b**) (△), acetone (**4-5c**) (●), and methoxyacetone (**4-5d**) (▲) ([**4-5**]$_0$:[CO_2H]$_0$:[N≡C]$_0$ = 1:1.1:1.1, [**4-5**]$_0$ = 0.7 M).

To better understand the role that solvent plays in the enhanced rate of the Passerini reaction, we monitored the progress of reactions involving small-molecule reactants in both THF and CH_2Cl_2. Ugi reported anecdotally that the Passerini reaction is accelerated in less polar solvents.[31] Radha Krishna and Lopinti reported a study of reaction solvents for Passerini reactions with tosylmethylisocyanide (TosMIC) in which the isolated yield of product after a fixed reaction time increased with decreasing solvent polarity (i.e., CH_2Cl_2 > THF ~ DMSO > MeOH).[34] The Passerini reaction of isovaleric acid and *t*-butylisocyanide with isovaleraldehyde (**4-5a**) was performed in THF (ε = 7.52), CH_2Cl_2 (ε = 9.08), 1,2-dichloroethane (ε = 10.42), $CHCl_3$ (ε = 4.81), and CCl_4 (ε = 2.24).[35] The progress of each reaction was determined from ^{1}H NMR spectra of aliquots taken at different times. Plots of the percentage of isocyanide that is transformed to the Passerini reaction in the different solvents are shown in Figure 4.3. All reactions that were performed in chlorinated solvents reached almost full conversion within 10 min, and we could not distinguish a difference in reaction rate regardless of solvent polarity. The reaction in THF was dramatically slower than the reactions in chlorinated solvents.

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‡ These experiments were performed by Shuang Song.

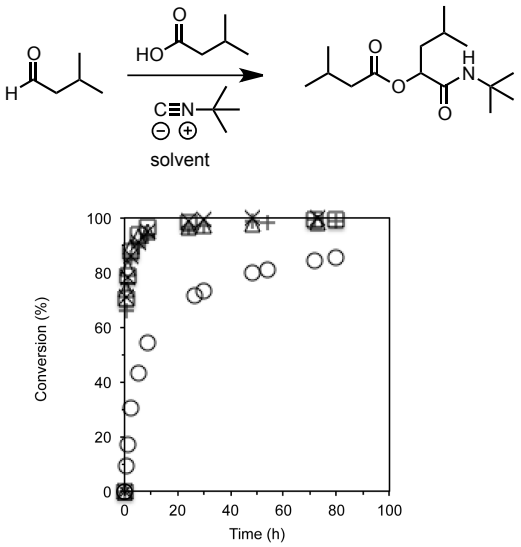

Figure 4.3. Plot of reaction conversion for Passerini reactions of isovaleric acid, *t*-butylisocyanide with isovaleraldehyde (**4-5a**) in THF (○), CH_2Cl_2 (+), $CHCl_3$ (△), CCl_4 (×) and 1,2-dichloroethane (□).The data for the reactions in THF (○) and CH_2Cl_2 (+) are from ref.[36] ($[CHO]_0$:$[CO_2H]_0$:$[N{\equiv}C]_0$ = 1.1:1.1:1, $[N{\equiv}C]_0$ = 0.7 M).

We compared Passerini reactions of isovaleraldehyde acid and *t*-butyl isocyanide with oxo-compounds **4-5a**-**4-5d** in THF and CH_2Cl_2 to assess whether the enhanced reactivity in THF is also observed in chlorinated solvents (Figure 4.4). While **4-5a**, **4-5b**, and **4-5d** reacted cleanly with isovaleric acid and *t*-butylisocyanide in CH_2Cl_2, we observed a significant amount of an undesired product in the reaction of acetone (**4-5c**) in CH_2Cl_2 that prevented us from quantifying the progress of this reaction. The Passerini reaction is accelerated in less polar solvents (e.g., CH_2Cl_2)[31, 34] or under solvent-free conditions.[37] We observed faster reaction kinetics in CH_2Cl_2 and could not distinguish the rate enhancement due to the ether substituent in this solvent. We conclude from these observations that the accelerating effect of weakly electron withdrawing groups is magnified in slow reactions.

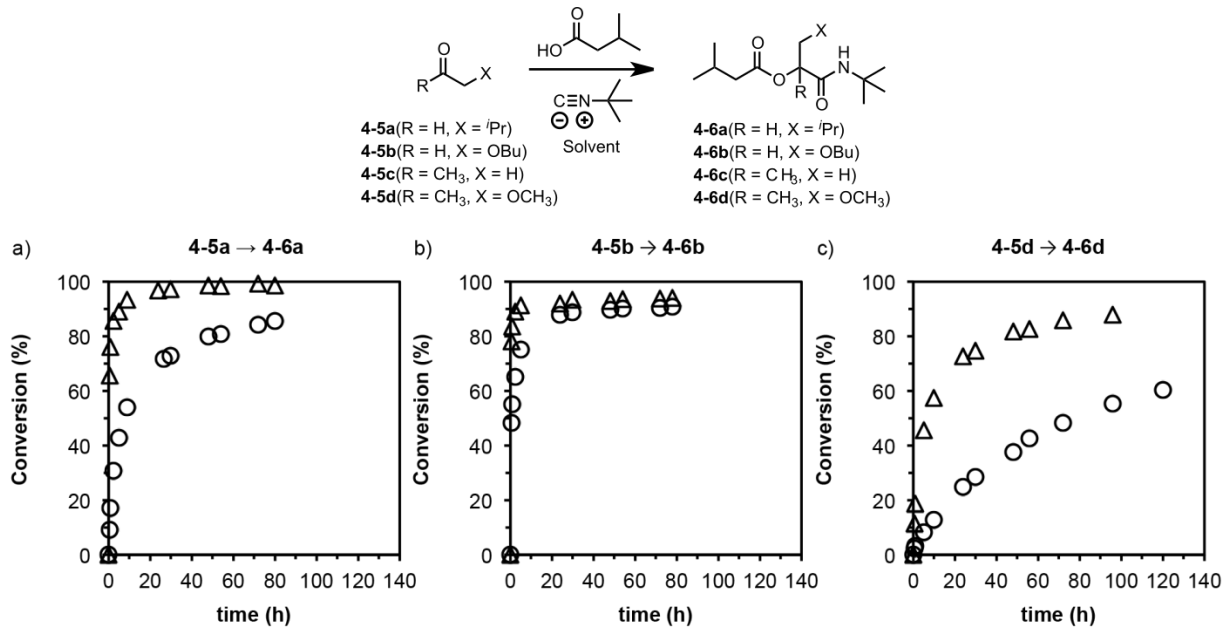

Figure 4.4. Plot of reaction conversion for Passerini reactions of isovaleric acid and *t*-butylisocyanide in with oxo-compounds **4-5a**–**4-5d** in THF (○) and CH_2Cl_2 (△). a) Isovaleraldehyde (**4-5a**); b) α-butoxyacetaldehyde (**4-5b**); and c) methoxyacetone (**4-5d**) ([**4-5**]$_0$:[CO_2H]$_0$:[N≡C]$_0$ = 1:1.1:1.1, [**4-5**]$_0$ = 0.7 M).

4.2.3 Application of the accelerated Passerini reaction to the synthesis of three generations of three-component dendrimers[§]

Three generations of three-component dendrimers were synthesized via the Passerini reaction and taking advantage of the enhanced reactivity of ether-substituted aldehydes (Figure 4.5a). The time required to reach completion of the Passerini reaction increased with increasing generation of the component dendrons. It is noteworthy, though, that the reaction of third-generation dendrons **4-8**, **4-10**, and **4-12** was complete after 44 h, which is less time than was required for Passerini reactions of dendrons, regardless of generation, when an unactivated aldehyde component was used. The dendrimers were purified by flash column chromatography. Gel permeation chromatography (GPC) traces of the dendrimers were monomodal and symmetric (Figure 4.5b), which confirms that there are no residual dendrons in the isolated products. The narrow molecular weight distribution (M_w/M_n) for each dendrimer is further evidence for the homogeneity of the products. MALDI-TOF Mass spectra of the dendrimers

[§] These experiments were performed by Dr. Jo-Ann Jee.

confirmed the identity of the products, and showed no evidence for residual starting materials or two-component reaction products.

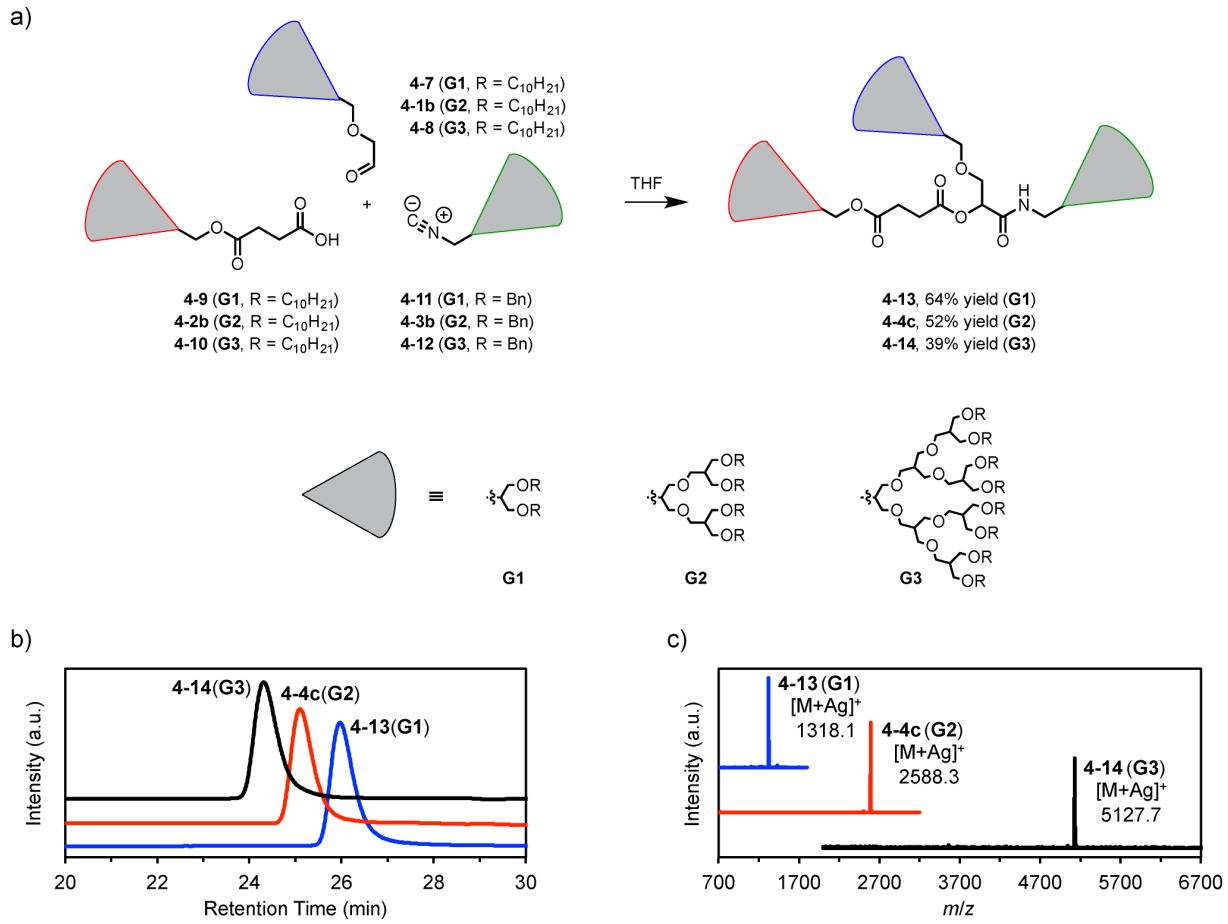

Figure 4.5. a) Three generations of three-component dendrimers synthesized via the Passerini reaction. b) Gel permeation chromatograms of the dendrimers **4-13** (blue), **4-4c** (red), and **4-14** (black). c) MALDI-TOF Mass spectra of the dendrimers **4-13** (blue), **4-4c** (red), and **4-14** (black).

4.3 Conclusion

Short linkers are commonly used to achieve better reactivity of dendrons by reducing crowding of the apex functional group, but we have found an electronic effect that accelerates the convergent synthesis of dendrimers via the Passerini reaction. A heteroatom substituent on the a-carbon of the carbonyl component dramatically reduced the reaction time of first- and second-generation dendrons compared to components with a longer linker or no linker at all. This unexpected reactivity provides a design principle for the convergent synthesis of higher generation dendrimers via the Passerini three-component reaction. Furthermore, this insight may

help to increase the achievable molecular weight for linear polymers[3-10] and the degree of functionalization that can be achieved in post-polymerization modification reactions.[11-15]

4.4 Experimental procedures

4.4.1 Materials

Ethyl acetate (EtOAc, A.C.S. grade), hexanes (hex, A.C.S. grade), acetone (A.C.S. grade) and anhydrous tetrahydrofuran (THF) were purchased from EMD. Methanol (MeOH, A.C.S. grade) and Chloroform ($CHCl_3$, A.C.S. grade) were purchased from BDH. Allyl butyl ether (98%), isovaleric acid (99%), 1,2-dichloroethane (99.0%) and tert-butyl isocyanide (98%) were purchased from Aldrich. Isovaleraldehyde (98%) and anhydrous dichloromethane (99.7+%, CH_2Cl_2) were purchased from Alfa Aesar. Carbon tetrachloride was purchased from Acros Organics. Anhydrous magnesium sulfate ($MgSO_4$), anhydrous potassium carbonate (K_2CO_3) and anhydrous sodium sulfate (Na_2SO_4) were purchased from J. T. Baker. Silica gel (60 Å) was purchased from Macron Fine Chemicals. Drierite (anhydrous calcium sulfate, 4-mesh) was purchased from VWR. Chloroform-*d* (+ 0.03% v/v TMS) was purchased from Cambridge Isotope Laboratories. All reagents and solvents were used as received. Anhydrous acetone was prepared by shaking with drierite (anhydrous $CaSO_4$) (25g/L) overnight and then decanted and distilled from fresh drierite and was used immediately. Anhydrous chloroform was prepared by washing with H_2O and drying over K_2CO_3 followed by refluxing with Na_2SO_4 for overnight and distillation prior to use. Anhydrous carbon tetrachloride was distilled prior to use.

4.4.2 Techniques

^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker Avance III (500) NMR spectrometer. Peak multiplicities are denoted as follows: s = singlet, d = doublet, t = triplet, and m = multiplet. Thin layer chromatography (TLC) was performed using Whatman silica gel 60 Å plates (250 μm) with fluorescent indicator and visualized using a UV lamp (254 nm) or $KMnO_4$ stain. Flash chromatography was performed on a Teledyne Isco CombiFlash Rf with RedSep Rf Normal Phase disposable silica columns. Ozone was produced using using an Ozone Services GE 60/FM 500 from Yanco Industries Ltd.

4.4.3 Experimental

α-Butoxyacetaldehyde (4-5b).[38-39] To a 100-mL one-neck flask, allyl butyl ether (7.67 mL, 52.6 mmol) was dissolved in anhydrous CH_2Cl_2 (26.0 mL) and the reaction mixture was treated with O_3 for 7 h at -78 ^oC. Then a solution of PPh_3 (13.86 g, 52.84 mmol) in anhydrous CH_2Cl_2 (26.0 mL) was added dropwise while the reaction was stirred under N_2 in ice-water bath. Then the reaction was stirred at room temperature under N_2 for 44 h. The product was distilled under reduced pressure to give **4-5b** as a colorless oil (1.75 g, 29%). ^1H NMR (500 MHz, $CDCl_3$, δ): 9.74 (t, J = 0.92 Hz, 1H; C*H*O), 4.06 (d, J = 0.96 Hz, 2H; CH_2CHO), 3.54 (t, J = 6.6 Hz, 2H; $C_3H_7CH_2OCH_2CHO$), 1.62 (m, 2H; $C_2H_5CH_2CH_2O$), 1.41 (m, 2H; $CH_3CH_2C_2H_4O$), 0.94 (t, J =7.4 Hz, 3H, $CH_3C_3H_6O$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 201.4 (*C*HO), 76.5 (*C*H_2CHO), 72.2 ($OCH_2C_3H_7$), 31.8 ($OCH_2CH_2C_2H_5$), 19.4 ($OC_2H_4CH_2CH_3$), 14.1 ($OC_2H_4CH_2CH_3$). ^1H NMR Spectral data agree with literature.[39]

General Procedure for Kinetics Study. Each experiment was performed under an N_2 atmosphere in a 25-mL one-neck flask equipped with a magnetic stir bar and capped with a rubber septum. The amounts of reagents and reaction solvent were measured by mass, and were added to the reaction vessel in the following order: solvent, oxo-component (**4-5a-d**), isovaleric acid, and *t*-butyl isocyanide. The reactions were stirred at ambient temperature, and aliquots (50 μL) were taken at the times indicated in the plots. The aliquots were diluted with $CDCl_3$ and the ^1H NMR spectrum of the diluted aliquot was recorded within 10 min. The conversion for each reaction was calculated from the integration of the resonances corresponding to the *t*-butyl group in *t*-butyl isocyanide and the product (**4-6a-d**). Exact quantities from a representative kinetic experiment are provided in the synthesis of **4-6b** reported below.

1-(*t*-Butylaminocarbonyl)-3-methylbutyl 3-methylbutanoate (4-6a). To a 25-mL one-neck flask, isovaleraldehyde (0.660 mL, 6.02 mmol), *t*-butyl isocyanide (0.680 mL, 6.01 mmol) isovaleric acid (0.670 mL, 6.07 mmol), anhydrous THF (6.1 mL) were added and stirred under N_2 at room temperature for 32 h. Excess reagents and solvent of the reaction mixture was removed by rotary evaporation. The product was purified by flash column chromatography (SiO_2, hex to hex/EtOAc 4:1) to give product **4-6a** as a colorless solid (1.31 g, 80%). TLC (SiO_2, 4:1 hex/EtOAc): R_f = 0.49. ^1H NMR (500 MHz, $CDCl_3$, δ): 5.77 (s, 1H; N*H*), 5.08 (dd, J_1 = 8.2 Hz, J_2 = 4.4 Hz, 1H; CO_2CHCO), 2.27 (d, J = 7.1 Hz, 2H; $O_2CCH_2CH(CH_3)_2$), 2.13 (m, 1H; $O_2CCH_2CH(CH_3)_2$), 1.68 (overlapped m, 3H; $CO_2CHCH_2CH(CH_3)_2$, $CO_2CHCH_2CH(CH_3)_2$),

1.34 (s, 9H; NHC(CH_3)$_3$), 0.99 (d, J = 6.6 Hz, 6H; $O_2CCH_2CH(CH_3)_2$), 0.93 (d, J = 6.3 Hz, 3H; $CO_2CHCH_2CH(CH_3)_2$), 0.91 (d, J = 6.1 Hz, 3H; $CO_2CHCH_2CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 172.1 (NH*C*O), 169.7 (O*C*O), 73.1 (NHCO*C*), 51.4 ($(CH_3)_3C$), 43.7 ($OCOCH_2$), 41.0 ($NHCOCHCH_2CH(CH_3)_2$), 28.9 ($(CH_3)_3C$), 26.1 ($OCOCH_2CH(CH_3)_2$), 24.8 ($NHCOCHCH_2CH(CH_3)_2$), 23.4 ($OCOCH_2CH(CH_3)_2$), 22.5 ($NHCOCHCH_2CH(CH_3)_2$), 22.0 ($NHCOCHCH_2CH(CH_3)_2$).

1-(*t*-Butylaminocarbonyl)-2-butoxyethyl 3-methylbutanoate (4-6b). Compound **4-6b** was isolated in low yield from a reaction mixture used for the kinetics experiments. To a 25-mL one-neck flask, anhydrous THF (3.8071 g), α-butoxyacetaldehyde **4-5b** (0.4722 g, 4.065 mmol), isovaleric acid (0.4568 g, 4.473 mmol), and *t*-butyl isocyanide (0.3555 g, 4.276 mmol) were added in the sequence of listed above and stirred under N_2 at room temperature. After 76 h, volatiles were removed by rotary evaporation. The product was purified by flash column chromatography (SiO_2, hex to hex/EtOAc 4:1). Slight isovaleric acid impurity was removed under reduced pressure. Product **4-6b** was obtained as colorless oil (0.55 g, 45%). TLC (SiO_2, 4:1 hex/EtOAc): R_f = 0.41. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 6.00 (s, 1H; N*H*), 5.08 (dd, J_1 = 4.8 Hz, J_2 = 3.7 Hz, 1H; CO_2CHCO), 3.78 (dd, ^3J = 4.9 Hz, ^2J = 10.8 Hz, 1H; $CHCH_2OC_4H_9$), 3.72 (dd, ^3J = 3.8 Hz, ^2J = 10.8 Hz, 1H; $CHCH_2OC_4H_9$), 3.48 (dt, ^3J = 6.5 Hz, ^2J = 9.5 Hz, 1H; $CH_2OCH_2C_3H_7$), 3.48 (dt, ^3J =6.6 Hz, ^2J = 9.5 Hz, 1H; $CH_2OCH_2C_3H_7$), 2.31 (d, J = 7.2 Hz, 2H; $OCOCH_2CH(CH_3)_2$), 2.13 (m, 1H; $OCOCH_2CH(CH_3)_2$), 1.52 (m, 2H; $CH_2OCH_2CH_2C_2H_5$), 1.35 (overlapping s, 9H; NHC(CH_3)$_3$; overlapped m, 2H; $CH_2OC_2H_4CH_2CH_3$), 0.994 (d, J = 6.7 Hz, 3H; $OCOCH_2CH(CH_3)_2$), 0.991 (d, J = 6.7 Hz, 3H; $OCOCH_2CH(CH_3)_2$), 0.90 (t, J = 7.4 Hz, 3H; $CH_2OC_3H_6CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$, δ): 171.7 (NH*C*O), 167.3 (O*C*O), 73.2 ($NHCOCHOCO$), 71.5 ($NHCOCHCH_2OCH_2C_3H_7$), 70.2 ($NHCOCHCH_2OC_4H_9$), 51.5 ($(CH_3)_3CNH$), 43.5 ($OCOCH_2$), 31.8 ($OCH_2CH_2C_2H_5$), 28.9 ($(CH_3)_3CNH$), 26.1 ($OCOCH_2CH(CH_3)_2$), 22.5 ($OC_2H_4CH_2CH_3$), 19.4 ($OCOCH_2CH(CH_3)_2$), 14.1 ($OC_3H_6CH_3$).

2-(*t*-Butylaminocarbonyl)-prop-2-yl 3-methylbutanoate (4-6c). To a 25-mL one-neck flask, acetone (0.3014 g, 5.189 mmol), isovaleric acid (0.3414 g, 3.343 mmol), and *t*-butyl isocyanide (0.2888 g, 3.474mmol) were added in the sequence of listed above and stirred under N_2 at room temperature for 68 h. Excess reagents were removed under reduced pressure. The product was purified by flash column chromatography (SiO_2, hex/EtOAc 95:5) to give product **4-6c** as colorless oil (0.32 g, 39 %). TLC (SiO_2, 9:1 hex/EtOAc): R_f = 0.19. ^{1}H NMR (500 MHz, $CDCl_3$,

δ): 5.83 (s, 1H; N*H*), 2.19 (d, *J* = 7.1 Hz, 2H; OCOC*H*$_2$CH(CH$_3$)$_2$), 2.10 (m, 1H; OCOCH$_2$C*H*(CH$_3$)$_2$), 1.59 (s, 6H; NHCOC(C*H*$_3$)$_2$O), 1.35 (s, 9H; NHC(C*H*$_3$)$_3$), 0.98 (d, *J* = 6.6 Hz, 6H; OCOCH$_2$CH(C*H*$_3$)$_2$); ^{13}C NMR (125 MHz, CDCl$_3$, δ): 172.4 (NH*C*O), 171.4 (O*C*O), 81.8 (NHCO*C*(CH$_3$)$_2$), 51.1 (NH*C*(CH$_3$)$_3$), 44.4 (OCO*C*H$_2$), 28.8 (C(*C*H$_3$)$_3$), 26.0 (OCOCH$_2$*C*H(CH$_3$)$_2$), 24.5 (NHCOC(*C*H$_3$)$_2$), 22.6 (OCOCH$_2$CH(*C*H$_3$)$_2$).

1-Methoxy-2-(*t*-butylaminocarbonyl)-prop-2-yl 3-methylbutanoate (4-6d). To a 25-mL one-neck flask, methoxyacetone (0.3877 g, 4.400 mmol), isovaleric acid (0.3616 g, 3.225 mmol), and *t*-butyl isocyanide (0.2972 g, 3.5751 mmol) were added in the sequence of listed above and stirred under N_2 at room temperature for 20 h. Excess reagents were removed under reduced pressure. The product was purified by flash column chromatography (SiO_2, hex to hex/EtOAc 4:1) to give product **6d** as colorless oil (0.43 g, 44%). TLC (SiO_2, 4:1 hex/EtOAc): R_f = 0.29. ^{1}H NMR (500 MHz, CDCl$_3$, δ): 6.21 (s, 1H; NH), 4.02 (d, ^2J = 9.9 Hz, 1H; NHCOCC*H*$_2$OCH$_3$), 3.61 (d, ^2J = 9.9 Hz, 1H; NHCOCC*H*$_2$OCH$_3$), 3.34 (s, 3H; OC*H*$_3$), 2.24 (d, *J* =3.8 Hz, 1H; OCOC*H*$_2$CH(CH$_3$)$_2$), 2.23 (d, *J* = 3.3 Hz, 1H; OCOC*H*$_2$CH(CH$_3$)$_2$), 2.11 (m, 1H; OCOCH$_2$C*H*(CH$_3$)$_2$), 1.55 (s, 3H; NHCOCC*H*$_3$), 1.35 (s, 1H; C(C*H*$_3$)$_3$), 0.99 (d, *J* = 6.6 Hz , 6H; OCOCH$_2$CH(C*H*$_3$)$_2$); ^{13}C NMR (125 MHz, CDCl$_3$, δ): 171.4 (NH*C*O), 170.5 (O*C*O), 82.9 (NHCO*C*), 74.5 (NHCOC*C*H$_2$OCH$_3$), 59.5 (O*C*H$_3$), 51.2 (NH*C*(CH$_3$)$_3$), 44.3 (OCO*C*H$_2$), 28.8 (C(*C*H$_3$)$_3$), 26.0 (OCOCH$_2$*C*H(CH$_3$)$_2$), 22.6 (OCOCH$_2$CH(*C*H$_3$)$_2$), 20.2 (NHCOC*C*H$_3$).

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