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Design and Synthesis of Lipids for the Fabrication of Functional Lipidic Cubic-Phase Biomaterials

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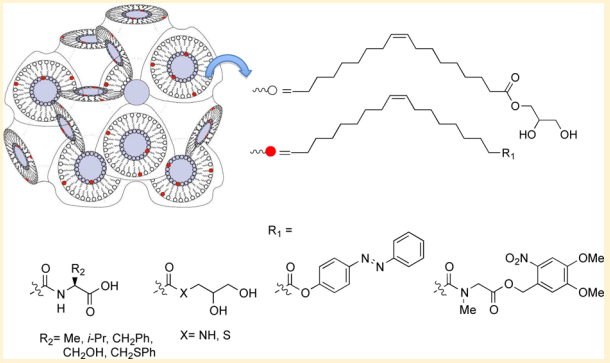
Supporting Information

ABSTRACT: A series of novel lipids with designed functionalities were synthesized. These lipids are based on conjugation of α-amino acids and their esters, cationic, anionic, neutral, and photochromic moieties to the lipophilic 9-*cis* octadecenyl chains by amide, ester, thioester, or amine bonds. Because of the plasticity of lipidic cubic phases, it is envisaged that when mixed with monooleoyl-*rac*-glycerol (monoolein, MO) and water at appropriate proportions, they would assemble to form bicontinuous lipidic cubic phases (LCPs) that exhibit the well-known material properties of LCPs such as phase stability, optical transparency, and chemical permeability. Moreover, due to the nature and position of the functionality at the headgroup region, we envision them to perform as functional materials by design.



INTRODUCTION

Lipidic cubic phases exhibit a unique combination of material properties: They are stable, structured, and transparent hydrogels with a flexible, curved lipid bilayer that spans the 3D space and can coexist stably with any amount of excess water.[1−4] LCPs utilized to date are almost exclusively restricted to the monoacylglycerol/water binary system at room temperature, with 1-monoolein (**1**) (1-(*cis*-9-octadecenoyl)-*rac*-glycerol, MO) being the most widely used lipid.[5] Crystallization of membrane proteins in LCPs[6] has contributed greatly to membrane biology, culminating with the recent high-resolution X-ray structures of several G-protein-coupled receptors.[7−9] With the notion that the material properties of host−guest LCPs can be controlled and tuned by molecular design of the constituent lipids, we have initiated a synthetic approach to map possible lipid modifications as additives to MO LCPs. Lipid molecules are composed of three regions: The hydrophobic tail, the hydrophilic headgroup, and the linkage region. In this investigation, all target lipids retain the 9-*cis*-octadecenyl hydrophobic tail, while the nature, size, and charge of the hydrophilic group, as well as the identity of the linkage, have been systematically modified (Figure 1). Modifications in the headgroup region include various α-amino acids and their esters, anionic, cationic, and neutral moieties, as well as photochromic units such as azobenzene[10,11] and *o*-nitrobenzyl groups.[12] The latter are of special interest because of the optical transparency of the host LCPs, which can therefore be envisioned as light-responsive biomaterials that undergo chemical or structural changes upon photoactivation. Moreover, such materials may provide biocompatible surfaces with photocleavable or photoswitchable groups.

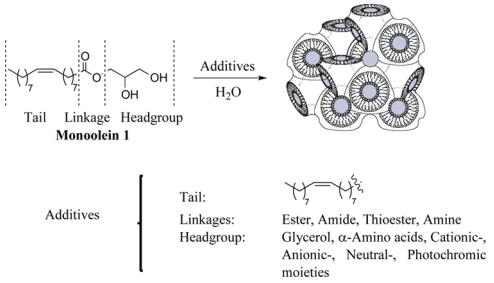


Figure 1. Upper panel: structure of monoolein (MO) and of the Pn3m lipidic cubic phase that forms at maximum hydration of MO. Lower panel: summary of the modifications of the target lipids (additives).

Previously reported syntheses of similar lipidic compounds were mostly motivated by their biological activity. Examples include the synthesis of saturated and unsaturated fatty acid L-serines, which form gels in water and in organic solvent, and whose low cytotoxicity was established;[13] preparation of a large synthetic library of endogenous fatty acid amides and their analogues, in order to assess their inhibitory effects on pro-inflammatory mediators;[14] investigation of the metabolic and biosynthetic pathways of fatty acyl glycines;[15] synthesis of a series of conjugates of a fatty acids and redox-active amino acids, which were used to coat colloidal noble-metal nanoparticles;[16] synthesis and formation of organogels of fatty *N*-acylamino acids and *N*-acylamino esters;[17] and the application

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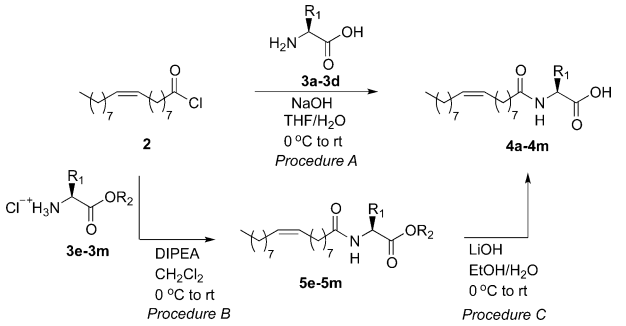
of novel fatty acid amides as anticancer drugs by inducing apoptosis in tumor cells.[18]

This paper presents the synthetic pathways of the various lipidic analogues that are of potential use in functional biomaterials. Their incorporation into MO-host LCPs, and the material properties of the resulting biomaterials will be presented in a following paper.

RESULTS AND DISCUSSION

I. Synthesis of α-Amino Acids Linked to the Oleoyl Chain. Initial work focused on the syntheses of lipid derivatives of the commercially available oleoyl chloride **2** covalently linked to α-amino acids **3a−d** and their esters **3e−m** (Scheme 1). The

Scheme 1. Synthesis of *N*-Oleoyl-α-amino Acids 4a−m Tagged to Oleoyl Chloride



lipidic derivatives of general structure **4** vary in their amino acid residue (hydrophobic, anionic or cationic), thereby modifying fundamental properties such as size, charge, binding, and diffusivity of the resulting LCPs. The initial approach to prepare *N*-oleoyl-α-amino acids **4** was direct acylation between commercially available L-amino acids and oleoyl chloride **2** (procedure A), using a THF/water mixture under basic conditions (Scheme 1, Table 1).[19] As test substrate, H-Gly-OH **3a** (1.5 equiv, 2.6 mmol scale) was coupled to oleoyl chloride (1.0 equiv) in a mixture of THF/water (1:2) using NaOH as a base, followed by neutralization with 1 M HCl to afford *N*-oleoyl-Gly-OH **4a** in excellent yield (87%, Table 1, entry 1). On the basis of this result, *N*-oleoyl-L-Ala-OH **4b** (entry 2), *N*-oleoyl-L-Val-OH **4c** (entry 3), and *N*-oleoyl-L-Phe-OH **4d** (entry 4) were prepared analogously, resulting in moderate to good yields. However, when the reaction was carried out on a 6−8 mmol scale, the reaction yields were typically less than 30% (entry 3 and 4), possibly due to the difficulty in handling those compounds during the isolation process and/or due to the physical state of the final products being foamy or waxy.

In order to improve the yields, a two-step synthesis was devised for the preparation *N*-oleoyl-α-amino acids containing aromatic, polar, anionic, and cationic side chains (Scheme 1, procedures B and C). Aromatic amino acids tagged to oleoyl chloride **2**, such as *N*-oleoyl-L-Phe-OH **4d** (Table 1, entry 5), *N*-oleoyl-L-Trp-OH **4f** (entry 6) and *N*-oleoyl-L-Tyr **4g** (entry 7) were obtained by direct coupling of the corresponding L-amino acid methyl or ethyl ester hydrochloride **3e**, **3f**, and **3g**, respectively, with oleoyl chloride **2** using DIPEA as a base in CH_2Cl_2, followed by hydrolysis of the ester under basic conditions (LiOH in a mixture of EtOH/H_2O). The acylation reaction (procedure B), and the hydrolysis reaction (procedure C) of all these compounds proceeded smoothly, with good to

Table 1. Preparation of α-Amino Acids and Their Esters Linked to Oleoyl Chain

entry	precursor **3**	product **4**[a,b] or **5**[c]	yield[d] (%) of **5**	yield[d] (%) of **4**
1	H-Gly-OH, **3a**	oleoyl-Gly-OH, **4a**		87
2	H-L-Ala-OH, **3b**	oleoyl-L-Ala-OH, **4b**		76
3	H-L-Val-OH, **3c**	oleoyl-L-Val-OH, **4c**		45 (19)[e]
4	H-L-Phe-OH, **3d**	oleoyl-L-Phe-OH, **4d**		40 (25)[e]
5	H-L-Phe-OMe, **3e**	oleoyl-L-Phe-OH, **4d**	91	71
6	H-L-Trp-OEt, **3f**	oleoyl-L-Trp-OH, **4f**	92	78
7	H-L-Tyr-OMe, **3g**	oleoyl-L-Tyr-OH, **4g**	88	93
8	H-L-Ser-OMe, **3h**	oleoyl-L-Ser-OH, **4h**	82	81
9	H-L-Cys(Bzl)-OEt, **3i**	oleoyl-L-Cys(Bzl)-OH, **4i**	90	91
10	H-L-Glu(OMe)-OMe, **3j**	oleoyl-L-Glu(OH)-OH, **4j**	87	85
11	H-L-His-OMe, **3k**	oleoyl-L-His-OMe, **5k**	46	
12	$(H\text{-L-Cys(OMe)})_2$, **3l**	$(oleoyl\text{-L-Cys(OMe)})_2$, **5l**	73	
13	H-Sar-OMe, **3m**	oleoyl-Sar-OH, **4m**	88[f]	98[f]

[a]General conditions for procedure A: amino acid **3a−d** (1.0−1.5 equiv), oleoyl chloride (1.0 equiv), 2N NaOH (2.0 mL/mmol), THF (1.5 mL/mmol), 0 °C to rt, 12 h. [b]General conditions for procedure C: *N*-oleoyl-α-amino acid **5e−m** (1 equiv), LiOH (3 equiv), EtOH/H_2O, 0 °C to rt, 12h. [c]General conditions for intermediates **5e−m** (Procedure B): amino acid ester hydrochloride **3e−3m** (1.0 equiv), DIPEA, oleoyl chloride (1.0−1.4 equiv), CH_2Cl_2 or CH_2Cl_2/MeOH (5 mL/mmol), 0 °C to rt, 2−5 h. [d]Isolated yield. [e]Yield based on a 6−8 mmol scale reaction in parentheses. [f]Rotamers.

excellent yields (71−93%). As shown in Table 1, amino acids with markedly different steric and electronic properties, including those with polar (serine **3h** and cysteine **3i**, entries 8 and 9), anionic (glutamic acid **3j**, entry 10), and cationic side chains (histidine **3k**, entry 11), as well as dimeric amino acid (cystine **3l**, entry 12) were acylated in good yields, except for *N*-oleoyl-L-His-OMe **5k**. In the latter case, in which the imidazole moiety is not protected, the monoacylated product is formed in 46% yield along with traces of the bis-acylated product. The hydrolysis reaction of intermediates **5e−m** proceeded smoothly to afford compounds **4d−m** in high yield.

Finally, the oleoyl moiety was also linked to sarcosine (H-Sar-OMe) **3m** (entry 13) to afford compound **5m** and **4m** in excellent yield. ^{1}H NMR spectra of these products show clearly a *cis*−*trans* population ratio of 4:1, caused by restricted rotation about the amide bond.[20−22] The correct assignment was established by NOESY experiment.

II. Synthesis of Oleoyl Derivatives Containing Amide, Thioester, and Ester Bonds to the Headgroup. With the aim of modifying the mode of binding between the hydrophobic chain and the headgroup, the ester bond of monoolein **1** was replaced with an amide or thioester bond. Initially, *N* and *S* heteroatoms were introduced into the 1-, 3-, or 1,3-position of the glycerol moiety. In this way, molecules **7**, **9**, **11** (Scheme 2), and **13**, **14**, **15** (Scheme 3) were targeted. Compound **7** was synthesized from 3-amino-1,2-propanediol **6** in 89% yield using standard acylation conditions (procedure B).

The rac-3-*S*-oleoyl-thioglycerol **9** was obtained with some modifications to a method previously described in the literature.[23,24] Racemic 1,2-*O*-isopropylidene-3-thio-*sn*-glycerol **8**[25] was treated with oleoyl chloride in the presence of dry

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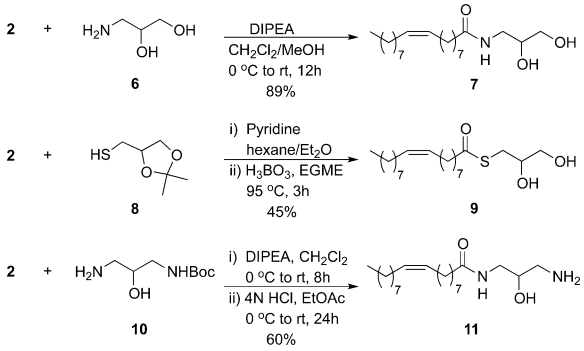
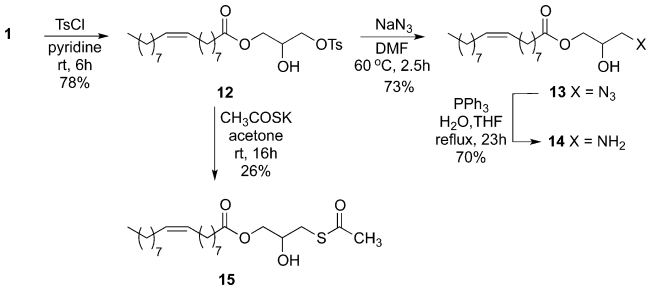
Scheme 2. Introduction of Heteroatoms into the 3- and 1,3-Positions of the Glycerol Headgroup



Scheme 3. Introduction of Heteroatoms into the 1-Position of the Glycerol Headgroup

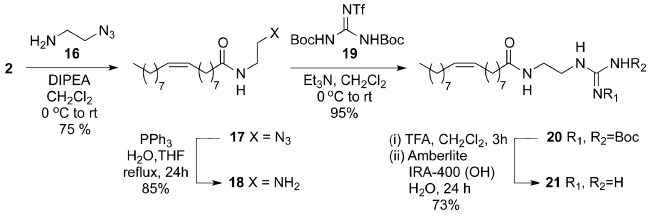


pyridine in a mixture of hexane/diethyl ether to produce *in situ* the *rac*-1,2-*O*-isopropylidene-3-*S*-oleoylthioglycerol, which was subjected to cleavage conditions using boric acid in 2-methoxymethanol to afford compound **9**. Spectroscopic data for this compound were identical to those reported, with no rearrangement of *S*- to *O*-acylated compounds observed.[23] Preparation of *N*-(3-amino-2-hydroxypropyl)oleamide **11** was synthesized in two steps starting from *N*-monoprotected diamine **10**.[26] Upon treatment with oleoyl chloride, the *N*-monoprotected diamine **10** underwent smooth acylation. Removal of the Boc protecting group with 4N HCl in EtOAc, followed by basification to pH 8 furnished compound **11** in 60% yield (over two steps).

Next, desired compounds **14** and **15** were synthesized from monoolein **1** as shown in Scheme 3. The primary alcohol of diol **1** was selectively monoprotected as tosylate by reaction with 1.2 equiv of *p*-TsCl in pyridine to afford compound **12** in 78% yield, which was easily separated from the starting material and the disubstituted side product using silica gel column chromatography. The resulting monotosylate **12** was converted into its azide derivative **13** in 73% yield by nucleophilic displacement with sodium azide in dry DMF, which, in turn, was reduced into the amine **14** upon refluxing with triphenylphosphine in a mixture of THF/water. Under these conditions no isomerization or degradation of the oleoyl moiety were observed. Nucleophilic displacement of the tosyl group with the potassium salt of thioacetic acid in dry acetone proceeded with high conversion (one spot on the TLC plate), but isolation of thioacetate **15** was not quantitative. Purification by column chromatography afforded **15** in 26% yield. Low yield is attributed to the lability of the primary thioacetate group.

In order to expand the library of lipids containing oleoyl chain covalently bound to various cationic or anionic moieties in the headgroup region, a series of compounds, which include azide, amine, guanidine, amine having hydroxyethyl, cyanoethyl, proline, or iminodiacetic groups, were synthesized according to Schemes 4 and 5.

Scheme 4. Synthesis of Cationic Lipids 17, 18, 20, and 21



Scheme 5. Synthesis of the Amide Derivatives 23a–e

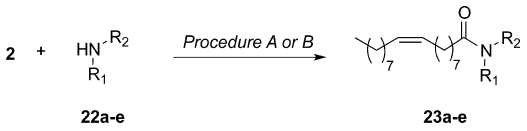
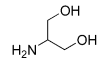
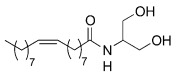
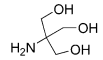
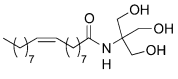
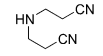
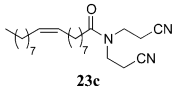
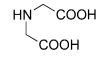
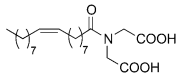
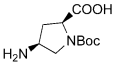
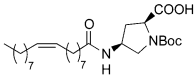


Table 2. Preparation of the Amide Derivatives 23a–e

entry	amine **22**	procedure[a]	time (h) temp (°C)	yield[b] of **23** (%)	product **23**
1	 **22a**	B	12, rt	83	 **23a**
2	 **22b**	B	12, rt	62	 **23b**
3	 **22c**	B	1, 0	96	 **23c**
4	 **22d**	A	1, 0	50	 **23d**
5	 **22e**	A	7, 0	82	 **23e**

[a]General conditions for procedures A and B: as described in Table 1. [b]Isolated yield.

The guanidinylated lipid derivative **21** (Scheme 4) was prepared from the primary azide **17**,[27] (readily available from 2-azidoethylamine **16** and oleoyl chloride **2**), which was reduced to the amine derivative **18** under neutral conditions with PPh_3 in THF/water in 85% yield. Subsequently, the guanidinylation reaction of oleamide **18** was performed under mild conditions using *N*,*N*′-di-Boc-*N*″-triflylguanidine **19**[28,29] (1.0 equiv) and Et_3N (1 equiv) in CH_2Cl_2 (0.1 M) to afford the corresponding *N*,*N*′-di-Boc-protected intermediate **20** in high yield (95%). Removal of the Boc groups using trifluoroacetic acid followed by ion exchange with the Amberlite IRA-400 (OH) resin, resulting in the desired guanidine compound **21** in good yield.

Next, various amines having hydroxyethyl groups **22a**, **22b**, 3,3-iminodipropionitrile **22c**, and iminodiacetic acid **22d** moieties were linked to the oleoyl group in good yields

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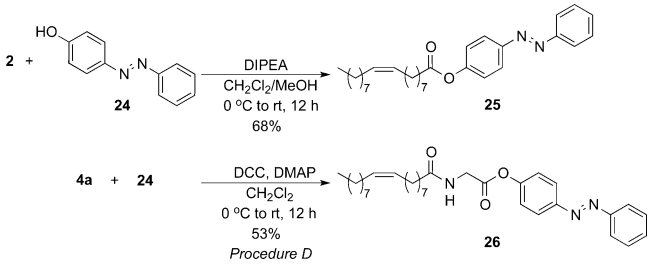
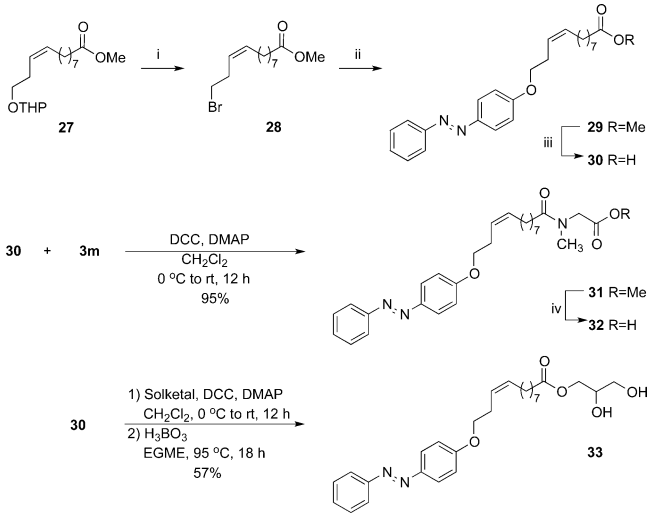
(Scheme 5, Table 2, entries 1−4) using standard acylation conditions as described above (either procedure A or B). The free primary amine at C4 of the pyrrolidine ring in **22e**[30] allows diverse array of functionalization, such as the tagging of the oleoyl moiety to *N*-Boc-*cis*-4-amine-L-proline amino acid **23e** in 82% yield (entry 5).

III. Synthesis of Lipids Containing an Azobenzene Moiety. In order to incorporate photochromic units into the LCPs, lipids bearing azobenzene photoactive units in two positions were designed, either by linking the azobenzene in the headgroup region (compounds **25**, **26**, Scheme 6), or by its incorporation into the alkyl tail (compounds **31**−**33**, Scheme 7).

Scheme 6. Synthesis of the Azobenzene Derivatives 25 and 26



Scheme 7. [a] **Synthesis of the Azobenzene Derivatives 31−33**



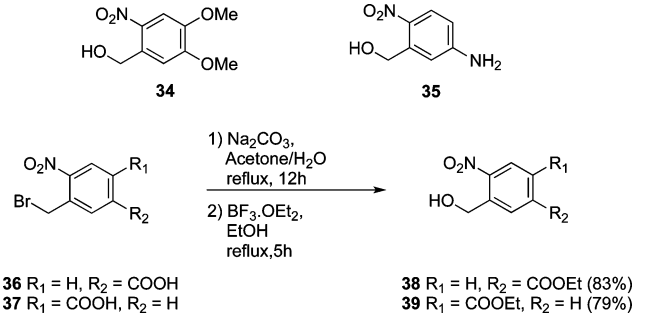
[a]Reagents and conditions: (i) PPh_3, CBr_4, CH_2Cl_2, rt, 20 h, 76%; (ii) 4-phenylazophenol **24**, K_2CO_3, acetone, reflux, 16 h, 76%; (iii) KOH, MeOH, 40 °C, rt, 87%; (iv) LiOH, EtOH/H_2O, 0 °C to rt, 12 h, 92%.

Compound **25** was obtained by direct displacement of chloride **2** with 4-phenylazophenol **24** in presence of DIPEA in a mixture of CH_2Cl_2/MeOH. Compound **26**, which has an additional glycine spacer (linked by an amide bond to the oleoyl chain and by an ester bond to the azobenzene), was synthesized in one step starting from compound **4a** via amide condensation using DCC and DMAP in CH_2Cl_2 (procedure D).

Target molecules **32** and **33** are based on a C12-alkyl chain attached at the C1-position to a sarcosine or glycerol residue, respectively, exhibiting one *cis* double bond at the C9-position, and an azobenzene moiety at the C12-position. The syntheses of compounds **32** and **33** commenced with the preparation of the common intermediate alkene **27** with the required (*Z*)-stereochemistry. Methyl (9*Z*)-12-(tetrahydro-2′*H*-pyran-2′-yloxy)-1-dodec-9-enoate **27** was synthesized in two steps starting from the commercially available methyl oleate via ozonolysis[31] and Wittig olefination[32] as previously described. A tetrahydropyranyl (THP) group was converted in one-pot into its corresponding bromide **28** by treatment with PPh_3/CBr_4,[33] which was subsequently alkylated according to similar procedure[34] with 4-phenylazophenol using K_2CO_3 as a base in dry acetone to afford compound **29** in 76% yield. Hydrolysis of the ester group with KOH in MeOH produced acid **30**, which was then coupled with sarcosine methyl ester hydrochloride in the presence of DCC and DMAP to yield **31** (procedure D). Methyl ester **31** was converted to corresponding acid **32** by alkaline hydrolysis. The *sn*-glycerol derivative **33** was obtained by standard DCC-coupling of **30** with solketal followed by deprotection of acetonide group using boric acid in 2-methoxyethanol.[23]

IV. Synthesis of Lipids Containing an *o*-Nitrobenzyl Moiety. In order to control the headgroup charge and identity by photochemical means, a series of lipids containing *o*-nitrobenzyl moieties were synthesized. 4,5-dimethoxy-2-nitrobenzyl alcohol (NVOC) **34** is commercially available. The 5-amino-2-nitrobenzyl alcohol **35** was obtained by reduction of the commercially available 5-amino-2-nitrobenzoic acid with borane in THF according to a literature procedure,[12,35] while the *o*-nitrobenzyl alcohol building block **38** was conveniently obtained from 4-nitro-3-bromomethylbenzoic acid **36** in two steps (Scheme 8). Hydrolysis of the bromide **36**[36,37] using

Scheme 8. Syntheses of the *o*-Nitrobenzyl Derivatives 35, 38, and 39



Na_2CO_3 in a mixture of water/acetone, followed by esterification of the free acid with 1 equiv of boron trifluoride diethyl etherate (BFEE)[38] provided compound **38** in 50% yield (over two steps). An excess of BFEE (3 equiv) resulted in a significant increase of the yield of **38** to 83%. The photocleavable linker **39** was prepared along similar lines from 3-nitro-4-bromomethylbenzoic acid **37** (79% over two steps).

2-Nitrobenzyl alcohol **34** was acylated with oleoyl chloride **2** using general procedure B (DIPEA in CH_2Cl_2) to furnish the ester **40** in 86% yield (Scheme 9). The synthesis of compound **41** relied on the condensation between *N*-oleoyl-sarcosine **4m** and the photocleavable linker **34** in a classical DCC-mediated esterification (procedure D). Compounds **42** and **43** were prepared in a similar way to compound **41** by coupling oleic acid or 2,2′-(oleoylimino)diacetic acid **23d** to compound **35**, respectively.

The *o*-nitrobenzyl protecting groups **38** and **39** were linked to the lipidic chain through a carbamate bond, according to

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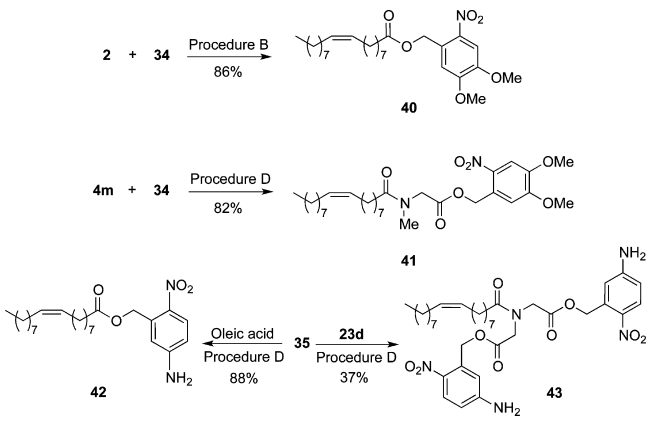
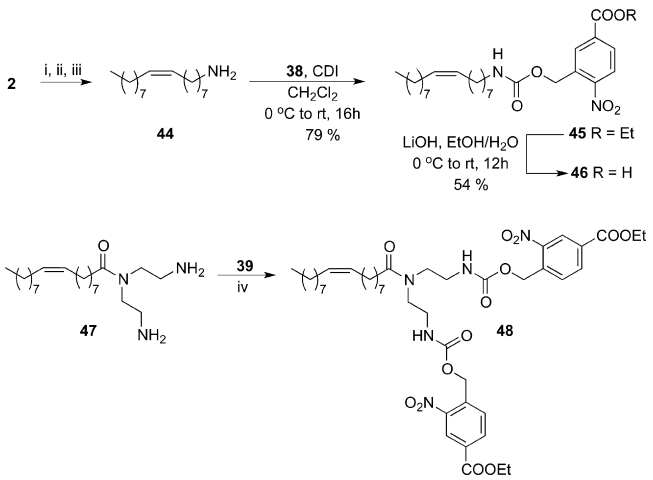
Scheme 9. Syntheses of the Lipidic *o*-Nitrobenzyl Derivatives 40−43



Scheme 10. The carbamate **45** was prepared analogous to literature procedure[39] by the successive mixing of alcohol **38**

Scheme 10. Syntheses of the Carbamates 45, 46 and 48[a]



[a]Reagents and conditions: (i) NaN_3, TBAB, CH_2Cl_2/H_2O, 0 °C, 2.5 h; (ii) TFA, CH_2Cl_2, reflux, 5h, 86% (two steps); (iii) 2 N NaOH, EtOH, rt, 40 h, 88%; (iv) **39**, CDI, CH_2Cl_2, 0 °C to rt, 12 h, 64%.

with CDI and amine **44**. The latter was prepared by nucleophilic substitution of the oleoyl chloride **2** with sodium azide, followed by in situ formation of the trifluoroacetamide (using a modification of the Curtius reaction)[40] and subsequent cleavage with NaOH. Compound **45** was subjected to basic hydrolysis to produce the corresponding acid **46** in 54% yield. Following a procedure similar to that described for the preparation of **45**, target molecule **48** was obtained in 64% yield starting from oleic acid bis(2-aminoethyl)amide **47** and *o*-nitrobenzyl alcohol **39**. Compound **47** was synthesized in three steps starting from diethylenetriamine according to known procedures.[41,42]

CONCLUSIONS

In order to expand the scope of lipidic cubic phase biomaterials, an array of novel lipids with designed functionalities were synthesized. These are based on the structure of MO, which is the most widely used lipid that forms LCPs. The target lipids' hydrophobic tail, responsible for scaffolding of the resulting LCPs, was retained as MO's 9-*cis* octadecenyl. The nature, size, and charge of the hydrophilic group, as well as the identity of the linkage have been systematically modified. Modifications in the headgroup region include various α-amino acids and their esters, anionic, cationic, and neutral moieties, as well as photochromic units such as and *o*-nitrobenzyl groups. Linkages include amide, ester, thioester, or amine bonds. Such designed lipids, when incorporated as additives to MO-water LCPs, modify the LCP's physical and chemical properties. Having access to this broad array of derivatives opens the door to controlled structure−activity studies of LCPs as well as to formation of novel biomaterials with designed functionalities.

EXPERIMENTAL SECTION

General Remarks. Melting points are uncorrected. IR spectra were recorded on an FT-IR spectrophotometer as films, KBr pills, or via an ATR sample unit. Nuclear magnetic resonance (NMR) spectra were recorded under conditions as indicated. Chemical shifts are given in ppm. Coupling constants J are expressed in Hz. Column chromatography was performed on silica gel 60 (0.04−0.063 mm, 230−440 mesh or 0.063−0.200 mm, 70−230 mesh). Unless otherwise stated, starting materials were obtained from commercial suppliers and used without further purification.

General Procedure for the Preparation of Amides 4a−c, 23d,e (Procedure A). A solution of oleoyl chloride (1.0 equiv) in THF (1.5 mL/mmol) was added dropwise over a period of 15 min to a stirred solution of the α-amino acid or amine derivative (1.0−1.5 equiv) in 2 N aqueous NaOH (2.0 mL/mmol) at 0 °C under argon. The resulting mixture was stirred for 30 min at 0 °C and then warmed to room temperature and stirred until the reaction was judged complete by TLC analysis. The reaction mixture was diluted with H_2O (10 mL), cooled to 0 °C, and acidified to pH 2 using aqueous HCl (3 N). Subsequently, the mixture was diluted with 100 mL of H_2O and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by recrystallization or column chromatography.

*N-Oleoylglycine (**4a**).* Prepared according to general procedure A from glycine (200 mg, 2.66 mmol) and oleoyl chloride (585 μL, 1.77 mmol). Recrystallization of the crude product in EtOH afforded the title compound (522 mg, 87%) as colorless crystals: mp 92−93 °C; R_f 0.36 (EtOAc/CH_2Cl_2/MeOH 80:15:5 with 1% AcOH); IR (ATR) ν (cm^{-1}) 3305, 3001, 2917, 2849, 1698, 1643, 1550, 1407, 1226, 1027, 759, 672; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (br s, 1H), 6.25 (t, J = 5.2 Hz, 1H), 5.30−5.38 (m, 2H), 4.07 (d, J = 5.2 Hz, 2H), 2.27 (t, J = 7.6 Hz, 2H), 1.98−2.03 (m, 4H), 1.60−1.67 (m, 2H), 1.26−1.34 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 173.0, 130.2, 129.9, 41.7, 36.5, 32.1, 30.0, 29.9, 29.7, 29.54, 29.53, 29.43, 29.39, 29.3, 27.44, 27.39, 25.8, 22.9, 14.3; HRMS (ESI, [M + H]$^+$) calcd for $C_{20}H_{38}N_1O_3$ 340.2846, found 340.2847.

*N-Oleoyl-L-alanine (**4b**).* Prepared according to general procedure A from L-alanine (200 mg, 2.22 mmol) and oleoyl chloride (496 μL, 1.50 mmol). Purification by column chromatography (CH_2Cl_2/MeOH 95:5 with 0.5% AcOH) afforded the title compound (403 mg, 76%) as a white solid: mp 58−60 °C; R_f 0.5 (EtOAc/CH_2Cl_2/MeOH 80:15:5 with 1% AcOH); IR (ATR) ν (cm^{-1}) 3334, 2926, 2856, 1718, 1649, 1541, 1456, 1210, 1161; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (d, J = 6.8 Hz, 1H), 5.29−5.38 (m, 2H), 4.58 (appears as quin, J = 7.2 Hz, 1H), 2.23 (t, J = 7.6 Hz, 2H), 1.98−2.03 (m, 4H), 1.59−1.67 (m, 2H), 1.46 (d, J = 7.2 Hz, 3H), 1.26−1.30 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 174.2, 130.2, 129.9, 48.5, 36.6, 32.1, 30.0, 29.9, 29.7, 29.54, 29.53, 29.43, 29.38, 29.3, 27.44, 27.39, 25.8, 22.9, 18.2, 14.3; HRMS (ESI, [M − H]$^+$) calcd for $C_{21}H_{38}N_1O_3$ 352.2857, found 352.2860.

*N-Oleoyl-L-valine (**4c**).* Prepared according general procedure A from L-valine (300 mg, 2.56 mmol) and oleoyl chloride (562 μL, 1.70 mmol). Purification by column chromatography (Et_2O/MeOH/AcOH 96:3:1) afforded the title compound (292 mg, 45%) as a white waxy solid: mp 71.2−73.9 °C; R_f 0.38 (EtOAc/MeOH/AcOH

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94:5:1); IR (ATR) ν (cm^{-1}) 3325, 2924, 2854, 1719, 1632, 1540, 1463, 1210, 968, 725; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (br s, 1H), 6.01 (d, J = 8.8 Hz, 1H), 5.29−5.38 (m, 2H), 4.59 (dd, J = 8.8 Hz, 4.8 Hz, 1H), 2.19−2.32 (m, 3H), 1.98−2.02 (m, 4H), 1.60−1.67 (m, 2H), 1.26−1.30 (m, 20H), 0.98 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 174.1, 130.2, 129.9, 57.2, 36.9, 32.1, 31.2, 30.0, 29.9, 29.7, 29.54, 29.53, 29.44, 29.42, 29.3, 27.44, 27.39, 25.9, 22.9, 19.2, 17.9, 14.3; HRMS (ESI, $[M - H]^+$) calcd for $C_{23}H_{42}N_1O_3$ 380.3170, found 380.3169.

*3-(Oleamido)diacetic Acid (**23d**).* Prepared according the general procedure A from iminodiacetic acid **22d** (316 mg, 2.37 mmol) and oleoyl chloride (529 μL, 1.60 mmol). Purification by column chromatography (Et_2O/MeOH 80:20 with 1% AcOH) afforded the title compound (317 mg, 50%) as colorless foam: R_f 0.41 (Et_2O/MeOH 60:40 with 1% AcOH); IR (neat, cm^{-1}) 3005, 2935, 2854, 1732, 1616, 1466, 1407, 1193, 970, 722; ^1H NMR (300 MHz, $CDCl_3$) δ 9.68 (br s, 2H), 5.32−5.36 (m, 2H), 4.20 (br s, 4H), 2.33 (t, J = 7.5 Hz, 2H), 1.98−2.02 (m, 4H), 1.60−1.62 (m, 2H), 1.27−1.30 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 173.6, 172.2, 130.0, 129.7, 50.9, 49.3, 32.8, 31.9, 29.78, 29.75, 29.6, 29.3 (2C), 29.2, 27.2, 24.8, 22.7, 14.1; HRMS (ESI, $[M - H]^+$) calcd for $C_{22}H_{38}NO_5$ 396.2755, found 396.2752.

*(4S)-4-(Oleamido)-N-(tert-butoxycarbonyl)-L-proline (**23e**).* Prepared according general procedure A from *N*-Boc-*cis*-4-amine-L-proline **22e**[30] (317 mg, 1.38 mmol) and oleoyl chloride (456 μL, 1.38 mmol). Purification by column chromatography (Et_2O/MeOH 90:10) afforded the title compound (558 mg, 82%) as a colorless oil: R_f 0.18 (Et_2O/MeOH 90:10); IR (neat, cm^{-1}) 3303, 2922, 2854, 1751, 1650, 1539, 1415, 1254, 1163. ^1H NMR (300 MHz, MeOD) δ 5.40−5.28 (m, 2H), 4.35 (appears as quin, J = 6.5 Hz, 1H), 4.21 (dd, J = 6.0 Hz, 1H,), 3.72−3.81 (m, 1H), 3.22−3.30 (m, 1H), 2.50−2.62 (m, 1H), 2.16 (t, J = 7.5 Hz, 2H), 1.97−2.08 (m, 4H), 1.86−1.97 (m, 1H), 1.51−1.64 (m, 2H), 1.45 (appears as d, 9H), 1.25−1.37 (m, 20H), 0.90 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, MeOD) δ 176.1, 155.7, 130.9, 130.8, 81.8, 59.7, 52.9, 52.1, 37.2, 37.1, 33.1, 30.9 (2C), 30.7, 30.5, 30.4 (2C), 30.3 (2C), 28.7, 28.6, 28.2 (2C), 26.9, 23.8, 14.5; HRMS (ESI, $[M - H]^+$) calcd for $C_{28}H_{49}N_2O_5$ 493.3647, found 493.3647.

General Procedure for the Preparation of Amides 5e−m, 7, 11, 17, and 23a−c and the Esters 25 and 40 (Procedure B). A stirred solution of the α-amino acid ester hydrochloride salt, amine, or alcohol derivative (1.0 equiv), DIPEA in anhydrous CH_2Cl_2 (5 mL/mmol), or in a mixture of anhydrous CH_2Cl_2/MeOH (5 mL/mmol 2:1) was cooled to 0 °C and treated dropwise with a solution of oleoyl chloride (1.0−1.4 equiv) in CH_2Cl_2 (1.0 mL/mmol). The reaction mixture was allowed to warm to room temperature and stirred until no more starting material was observed by TLC. The reaction mixture was poured into brine and extracted three times with CH_2Cl_2. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

*N-Oleoyl-L-phenylalanine Methyl Ester (**5e**).* Prepared according general procedure B from L-phenylalanine methyl ester hydrochloride (1.1 g, 5.10 mmol), oleoyl chloride (2.19 mL, 6.63 mmol), DIPEA (2.22 mL, 12.74 mmol) in CH_2Cl_2. Purification by column chromatography (hexane/EtOAc 85:15) afforded the title compound (2.05 g, 91%) as a white waxy solid: mp 30−32 °C; R_f 0.44 (hexane/EtOAc 70:30); IR (ATR) ν (cm^{-1}) 3297, 2923, 2853, 1746, 1647, 1538, 1437, 1211, 1176, 1030, 741, 699; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21−7.30 (m, 3H), 7.07−7.10 (m, 2H), 5.91 (d, J = 7.6 Hz, 1H), 5.30−5.38 (m, 2H), 4.90 (ddd appears as dt, J = 7.6 Hz, 6.0 Hz, 1H), 3.72 (s, 3H), 3.15 (dd, J = 14.0 Hz, 6.0 Hz, 1H), 3.07 (dd J = 14.0 Hz, 5.6 Hz, 1H), 2.16 (t, J = 7.2 Hz, 2H), 1.98−2.03 (m, 4H), 1.54−1.61 (m, 2H), 1.27−1.31 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 172.4, 136.1, 130.2, 129.9, 129.4 (2C), 128.7 (2C), 127.3, 53.1, 52.5, 38.1, 36.7, 32.1, 30.0, 29.9, 29.7, 29.5, 29.42, 29.36, 29.3, 27.41, 27.37, 25.7, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{28}H_{46}N_1O_3$ 444.3472, found 444.3476.

*N-Oleoyl-L-tryptophan Ethyl Ester (**5f**).* Prepared according general procedure B from L-tryptophan methyl ester hydrochloride (377 mg, 1.48 mmol), oleoyl chloride (638 μL, 1.93 mmol), DIPEA (650 μL, 3.72 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (EtOAc/hexane 20:80) afforded the title compound (680 mg, 92%) as a pale yellow oil: R_f 0.54 (EtOAc/hexane 40:60); IR (neat, cm^{-1}) 3299, 2926, 2854, 1737, 1652, 1530, 1459, 1377, 1203, 1097, 741; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.18 (td, J = 7.2 Hz, 1.2 Hz, 1H), 7.11 (td, J = 7.2 Hz, 1.2 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 5.96 (d, J = 7.6 Hz, 1H), 5.30−5.39 (m, 2H), 4.95 (ddd appears as dt, J = 7.6 Hz, 5.4 Hz, 1H), 4.07−4.20 (m, 2H), 3.34 (dd, J = 14.8 Hz, 5.4 Hz, 1H), 3.29 (dd J = 14.8 Hz, 5.0 Hz, 1H), 2.13 (t, J = 7.6 Hz, 2H), 1.97−2.03 (m, 4H), 1.53−1.60 (m, 2H), 1.25−1.30 (m, 20H), 1.22 (t, J = 7.2 Hz, 3H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 172.3, 136.3, 130.2, 130.0, 128.0, 122.9, 122.4, 119.8, 118.9, 111.4, 110.5, 61.6, 53.1, 36.8, 32.1, 30.0, 29.9, 29.7, 29.53, 29.52, 29.44, 29.41, 29.3, 27.9, 27.44, 27.40, 25.7, 22.9, 14.31, 14.29; HRMS (ESI, $[M + H]^+$) calcd for $C_{31}H_{49}N_2O_3$ 497.3738, found 497.3739.

*N-Oleoyl-L-tyrosine Methyl Ester (**5g**).* Prepared according general procedure B from L-tyrosine methyl ester hydrochloride (1.0 g, 4.32 mmol), oleoyl chloride (1.57 mL, 4.74 mmol), and DIPEA (1.66 mL, 9.50 mmol) in CH_2Cl_2. Purification by column chromatography (EtOAc/hexane 30:70) gave the title compound (1.75 g, 88%) as a white solid: mp 73−74 °C. R_f 0.44 (EtOAc/hexane 40:60); IR (ATR) ν (cm^{-1}) 3305, 3006, 2923, 2853, 1740, 1648, 1514, 1443, 1366, 1217, 829, 721; ^1H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, J = 8.4, 2H), 6.72 (d, J = 8.4, 2H), 6.01 (d, J = 7.6 Hz, 1H), 5.29−5.35 (m, 2H), 4.85−4.89 (m, 1H), 3.72 (s, 3H), 3.07 (dd, J = 14 Hz, 5.6 Hz, 1H), 2.97 (dd J = 14.0 Hz, 6.0 Hz, 1H), 2.17 (t, J = 7.6 Hz, 2H), 1.97−2.02 (m, 4H), 1.54−1.61 (m, 2H), 1.26−1.29 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 172.6, 155.8, 130.4, 130.2, 129.9, 127.1, 115.8, 53.4, 52.3, 37.5, 36.8, 32.1, 30.0, 29.9, 29.7, 29.52, 29.50, 29.40, 29.35, 29.32, 27.43, 27.38, 25.8, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{28}H_{46}N_1O_4$ 460.3421, found 460.3421.

*N-Oleoyl-L-serine Methyl Ester (**5h**).* Prepared according general procedure B from L-serine methyl ester hydrochloride (1.0 g, 6.43 mmol), oleoyl chloride (2.76 mL, 8.36 mmol), and DIPEA (2.80 mL, 16.07 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (EtOAc/hexane 60:40) gave the title compound (2.0 g, 82%) as a white waxy solid: mp 37−39 °C; R_f 0.53 (EtOAc/hexane 85:15); IR (neat, cm^{-1}) 3296, 2925, 2853, 1738, 1639, 1551, 1468, 1239, 1081, 723; ^1H NMR (400 MHz, $CDCl_3$) δ 6.45 (d, J = 6.8 Hz, 1H), 5.29−5.37 (m, 2H), 4.65−4.68 (m, 1H), 3.96 (dd, J = 11.2 Hz, 4.0 Hz, 1H), 3.90 (dd J = 11.2 Hz, 3.2 Hz, 1H), 3.78 (s, 3H), 2.55 (br s, 1H), 2.25 (t, J = 7.6 Hz, 2H), 1.97−2.02 (m, 4H), 1.60−1.67 (m, 2H), 1.26−1.30 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 171.3, 130.2, 129.9, 63.8, 54.9, 52.9, 36.7, 32.1, 30.0, 29.9, 29.7, 29.52, 29.51, 29.45, 29.41, 29.3, 27.43, 27.38, 25.7, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{22}H_{42}N_1O_4$ 384.3108, found 384.3110.

*N-Oleoyl-S-benzyl-L-cysteine Ethyl Ester (**5i**).* Prepared according general procedure B from *S*-benzyl-L-cysteine ethyl ester hydrochloride (500 mg, 1.81 mmol), oleoyl chloride (780 μL, 2.36 mmol), and DIPEA (695 μL, 3.98 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (EtOAc/hexane 15:85) afforded the title compound (821 mg, 90%) as a colorless oil: R_f 0.38 (EtOAc/hexane 20:80); IR (ATR) ν (cm^{-1}) 3294, 2922, 2853, 1740, 1649, 1533, 1455, 1372, 1199, 1028, 700; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23−7.34 (m, 5H), 6.11 (d, J = 8.0 Hz, 1H), 5.32−5.37 (m, 2H), 4.79 (ddd appears as dt, J = 8.0 Hz, 5.4 Hz, 1H), 4.20 (qd, J = 7.8 Hz, 2.8 Hz, 2H), 3.71 (s, 2H), 2.93 (dd, J = 13.6 Hz, 5.0 Hz, 1H), 2.86 (dd J = 13.6 Hz, 5.4 Hz, 1H), 2.19 (t, J = 7.6 Hz, 2H), 1.98−2.03 (m, 4H), 1.60−1.65 (m, 2H), 1.25−1.30 (m, 23H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 171.2, 137.9, 130.2, 130.0, 128.8, 127.5, 62.0, 51.7, 36.9, 36.7, 33.9, 32.1, 30.0, 29.9, 29.7, 29.53, 29.52, 29.46, 29.42, 29.35, 27.43, 27.39, 25.7, 22.9, 14.3 (2C); HRMS (ESI, $[M + H]^+$) calcd for $C_{30}H_{50}N_1O_3S_1$ 504.3506, found 504.3509.

*N-Oleoyl-L-glutamic Acid Dimethyl Ester (**5j**).* Prepared according general procedure B from L-glutamic acid dimethyl ester hydrochloride (1.0 g, 4.72 mmol), oleoyl chloride (1.72 mL, 5.19 mmol), and DIPEA (1.81 mL, 10.38 mmol) in CH_2Cl_2. Purification by column

chromatography (EtOAc/hexane 45:55) afforded the title compound (1.80 g, 87%) as white waxy solid mp: 33−35 °C. R_f 0.50 (EtOAc/hexane 70:30); IR (ATR) ν (cm^{-1}) 3295, 2923, 2853, 1740, 1649, 1536, 1436, 1374, 1255, 1203, 1171, 986, 722; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (d, J = 7.6 Hz, 1H), 5.29−5.38 (m, 2H), 4.60−4.66 (m, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 2.31−2.47 (m, 2H), 2.16−2.25 (m, 3H), 1.95−2.04 (m, 5H), 1.58−1.66 (m, 2H), 1.26−1.29 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 173.3, 172.7, 130.2, 129.9, 52.7, 52.0, 51.7, 36.7, 32.1, 30.3, 30.0, 29.9, 29.7, 29.49 (2C), 29.42, 29.40, 29.3, 27.6, 27.39, 27.36, 25.7, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{25}H_{46}N_1O_5$ 440.3370, found 440.3372.

*N-Oleoyl-L-histidine Methyl Ester (**5k**).* Prepared according general procedure B from L-histidine methyl ester hydrochloride (1.0 g, 4.13 mmol), oleoyl chloride (1.37 mL, 4.13 mmol), and DIPEA (1.59 mL, 9.08 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (CH_2Cl_2/MeOH 98:2) gave the title compound (823 mg, 46%) as a white solid: mp 87−89 °C. R_f 0.55 (CH_2Cl_2/MeOH 96:4); IR (KBr, cm^{-1}) 3419, 3184, 3008, 2923, 2853, 1735, 1645, 1572, 1241, 1155, 1042, 1003; ^{1}H NMR (500 MHz, MeOD) δ 7.58 (s, 1H), 6.86 (s, 1H), 5.31−5.38 (m, 2H), 4.86−4.94 (m, 1H), 4.67 (dd, J = 8.9 Hz, 5.3 Hz, 1H), 4.63 (br s, 1H), 3.70 (s, 3H), 3.10 (dd, J = 14.8 Hz, 5.3 Hz, 1H), 2.97 (dd, J = 14.8 Hz, 8.9 Hz, 1H), 2.19 (t, J = 7.6 Hz, 2H), 1.97−2.02 (m, 4H), 1.52−1.1.59 (m, 2H), 1.22−1.37 (m, 20H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, MeOD) δ 176.4, 173.7, 136.5, 131.02, 130.97, 54.1, 52.9, 36.8, 33.2, 31.0 (2C), 30.8, 30.6, 30.5 (2C), 30.4, 30.3, 28.30, 28.28, 27.0, 23.9, 14.6; HRMS (ESI, $[M + H]^+$) calcd for $C_{25}H_{44}N_3O_3$ 434.3377, found 434.3369.

*N,N′-Bis(oleoyl)-L-cystine (**5l**).* Prepared according general procedure B from L-cystine dimethyl ester dihydrochloride (505 mg, 1.48 mmol), oleoyl chloride (1.26 mL, 3.80 mmol), and DIPEA (1.27 mL, 7.3 mmol) in CH_2Cl_2. Purification by column chromatography (EtOAc/hexane 35:65) afforded the title compound (860 mg, 73%) as a white solid: mp 74−77 °C; R_f 0.38 (EtOAc/hexane 60:40); IR (ATR) ν (cm^{-1}) 3311, 3005, 2922, 2852, 1747, 1647, 1525, 1435, 1209, 1165, 977, 720; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (d, J = 7.2 Hz, 2H), 5.30−5.38 (m, 4H), 4.87 (ddd appears as dt, J = 7.2 Hz, 5.2 Hz, 2H), 3.76 (s, 6H), 3.23 (dd, J = 14.4 Hz, 5.2 Hz, 2H), 3.18 (dd J = 14.4 Hz, 5.2 Hz, 2H), 2.25 (t, J = 7.6 Hz, 4H), 1.98−2.03 (m, 8H), 1.60−1.68 (m, 4H), 1.26−1.30 (m, 40H), 0.87 (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 171.2, 130.2, 129.9, 52.9, 51.7, 41.0, 36.7, 32.1, 30.0, 29.9, 29.7, 29.53, 29.52, 29.47, 29.45, 29.37, 27.43, 27.40, 25.7, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{44}H_{81}N_2O_6S_2$ 797.5531, found 797.5522.

*N-Oleoylsarcosine Methyl Ester (**5m**).* Prepared according general procedure B from sarcosine methyl ester hydrochloride (420 mg, 3.0 mmol), oleoyl chloride (1.09 mL, 3.3 mmol), and DIPEA (1.40 mL, 8.0 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (Et_2O/MeOH 98:2) afforded the title compound (966 mg, 88%) as a colorless oil: R_f 0.49 (Et_2O/MeOH 98:2); IR (neat, cm^{-1}) 3003, 2925, 2854, 1753, 1658, 1464, 1401, 1206, 722. *This compound appears in the ^{1}H NMR spectrum as a distinct pair of cis/trans rotamers in a ratio 4:1*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.29−5.39 (m, 2H, *cis/trans*), 4.12 (s, 2H, *cis*), 4.04 (s, 2H, *trans*), 3.77 (s, 3H, *trans*), 3.73 (s, 3H, *cis*), 3.07 (s, 3H, *cis*), 2.97 (s, 3H, *trans*), 2.37 (t, J = 7.6 Hz, 2H, *cis*), 2.22 (t, J = 7.5 Hz, 2H, *trans*), 1.98−2.02 (m, 4H, *cis/trans*), 1.60−1.67 (m, 2H, *cis/trans*), 1.27−1.32 (m, 20H, *cis/trans*), 0.88 (t, J = 6.8 Hz, 3H, *cis/trans*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 173.5, 170.0, 169.6, 130.0, 129.8, 52.4, 52.1, 51.5, 49.3, 36.6, 34.9, 33.2, 33.0, 31.9, 29.8, 29.5, 29.4 (2C), 29.3 (3C), 29.2, 27.22, 27.20, 25.1, 24.9, 22.7, 14.1; HRMS (ESI, $[M + H]^+$) calcd for $C_{22}H_{42}NO_3$ 368.3159, found 368.3164.

*N-(2,3-Dihydroxypropyl)oleamide (**7**).* Prepared according general procedure B from 3-amino-1,2-propanediol (218 mg, 2.39 mmol), oleoyl chloride (861 μL, 2.6 mmol), DIPEA (437 μL, 2.50 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (Et_2O/MeOH 90:10) afforded the title compound (756 mg, 89%) as a white waxy solid: mp 70−71.5 °C; R_f 0.29 (Et_2O/MeOH 90:10); IR (neat, cm^{-1}) 3305, 3003, 2920, 2850, 1639, 1550, 1467, 1418, 1114, 1055; ^{1}H NMR (600 MHz, d_5-pyridine) δ 8.79 (br s, 1H), 6.32 (br s, 2H), 5.46−5.49 (m, 2H), 4.37 (appears as quin, J = 5.6 Hz, 1H), 3.85−4.13 (m, 4H), 2.43 (t, J = 7.5 Hz, 2H), 2.02−2.11 (m, 4H), 1.81 (quin, J = 7.7 Hz, 2H), 1.24−1.39 (m, 20H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (150.9 MHz, d_5-pyridine) δ 174.3, 130.2 (2C), 72.2, 65.0, 43.6, 36.7, 32.1, 30.07, 30.04, 29.8, 29.70, 29.65, 29.58, 29.56, 29.45, 27.5 (2C), 26.3, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{21}H_{42}NO_3$ 356.3159, found 356.3158.

*N-(3-Amino-2-hydroxypropyl)oleamide (**11**).* Prepared according general procedure B from 1-*N*-Boc-3-aminopropan-2-ol **10** (159 mg, 0.84 mmol), oleoyl chloride (285 μL, 0.86 mmol), and DIPEA (147 μL, 0.84 mmol) in CH_2Cl_2. Purification by column chromatography (Et_2O/MeOH 50:1) afforded the protected compound NHBoc (307 mg) as a white waxy solid which was dissolved in EtOAc (10 mL) and treated with a 4N solution of HCl (1 mL) at 0 °C under argon for 10 min. Subsequently, the reaction mixture was stirred overnight at room temperature and poured into water. The aqueous solution was basified with 1 M aqueous NaOH until pH ∼8 and extracted three times with CH_2Cl_2. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and the filtrate was evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH/concd NH_4OH 10:5:1) to yield **11** (179 mg, 60%) as a colorless solid: mp 84.5−85.4 °C; R_f 0.42 (CH_2Cl_2/MeOH 4:1 with 5% concd NH_4OH); IR (KBr, cm^{-1}) 3350, 3317, 3003, 2920, 2850, 1647, 1555, 1464, 1437, 1384, 1229, 1119, 994, 718; ^{1}H NMR (300 MHz, d_5-pyridine) δ 8.42 (br s, 1H), 5.23−5.34 (m, 2H), 4.35 (br s, 2H), 3.95−4.03 (m, 1H), 3.55−3.71 (m, 2H), 2.85−2.99 (m, 2H), 2.23 (t, J = 7.6 Hz, 2H), 1.84−1.94 (m, 4H), 1.57−1.67 (m, 2H), 1.02−1.22 (m, 20H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 130.0, 129.7, 70.5, 44.5, 43.1, 36.7, 31.9, 29.8, 29.7, 29.5, 29.3, 29.23, 29.16, 27.22, 27.18, 25.6, 22.7, 14.1; HRMS (ESI, $[M + H]^+$) calcd for $C_{21}H_{43}N_2O_2$ 355.3319, found 355.3316.

*N-(2-Azidoethyl)oleamide (**17**).* Prepared according general procedure B, from 2-azidoethylamine **16** (1.20 g, 13.9 mmol), oleoyl chloride (5.3 mL, 16 mmol), and DIPEA (5.33 mL, 30.5 mmol) in CH_2Cl_2. Purification by column chromatography (hexane/EtOAc 50:50) afforded **17** (3.75 g, 75%) as a white waxy solid: mp 33−35 °C; R_f 0.28 (hexane/EtOAc 50:50); IR (neat) ν (cm^{-1}) 3297, 2921, 2852, 2098, 1644, 1547, 1459, 1347, 1260, 1228, 720; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (br s, 1H, NHCO), 5.30−5.39 (m, 2H), 3.41−3.47 (m, 4H), 2.19 (t, J = 7.6 Hz, 2H), 1.98−2.02 (m, 4H), 1.59−1.65 (m, 2H), 1.27−1.31 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 130.0, 129.8, 51.1, 38.9, 36.7, 31.9, 29.8, 29.7, 29.5, 29.34 (2C), 29.26 (2C), 29.1, 27.24, 27.19, 25.6, 22.7, 14.1; HRMS (ESI, $[M + Na]^+$) calcd for $C_{20}H_{38}N_4NaO$ 373.2932, found 373.2933.

*2-(Oleamido)propane-1,3-diol (**23a**).* Prepared according general procedure B from 2-amino-1,3-propanediol **22a** (500 mg, 5.48 mmol), oleoyl chloride (2.17 mL, 6.57 mmol), and Et_3N (1.68 mL, 12.06 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (CH_2Cl_2/MeOH 90:10) afforded the title compound (1.62 g, 83%) as a white solid: mp 99−100 °C;[18] R_f 0.50 (CH_2Cl_2/MeOH 90:10); IR (ATR) ν (cm^{-1}) 3396, 2958, 2921, 2851, 1638, 1545, 1466, 1422, 1384, 1246, 1071, 972, 682, 636; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (d, J = 7.2 Hz, 1H), 5.32−5.38 (m, 2H), 3.91−3.97 (m, 1H), 3.83 (dd, J = 11.2 Hz, 4.4 Hz, 1H), 3.74 (dd, J = 11.2 Hz, 4.4 Hz, 2H), 2.72 (br s, 2H), 2.20 (t, J = 7.8 Hz, 2H), 1.97−2.02 (m, 4H), 1.56−1.63 (m, 2H), 1.25−1.29 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 130.2, 129.9, 62.5 (2C), 52.7, 36.9, 32.1, 30.0, 29.9, 29.7, 29.52, 29.50, 29.49, 29.47, 29.38, 27.42, 27.38, 26.0, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{21}H_{42}N_1O_3$ 356.3159, found 356.3157.

*2-(Oleamido)-2-(hydroxymethyl)propane-1,3-diol (**23b**).* Prepared according general procedure B from tris(hydroxymethyl) aminomethane **22b** (500 mg, 4.12 mmol), oleoyl chloride (1.63 mL, 4.94 mmol), and Et_3N (1.26 mL, 9.08 mmol) in CH_2Cl_2. Purification by column chromatography (CH_2Cl_2/MeOH 90:10) afforded the title compound (985 mg, 62%) as a white solid: mp 86−88 °C;[18] R_f 0.47 (CH_2Cl_2/MeOH 90:10); IR (ATR) ν (cm^{-1}) 3354, 3286, 3006, 2922, 2853, 1620, 1530, 1464, 1289, 1131, 1024, 721; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (s, 1H), 5.30−5.38 (m, 2H), 5.25 (br s, 3H), 3.56 (s, 2H), 2.22 (t, J = 7.8 Hz, 2H), 1.98−2.04 (m, 4H), 1.58−1.62 (m, 2H),

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1.26−1.30 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 130.2, 129.9, 62.2, 61.2 (2C), 37.2, 32.1, 30.0, 29.9, 29.7, 29.5 (2C), 29.4, 29.33, 29.31, 27.43, 27.38, 26.0, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{22}H_{44}N_1O_4$ 386.3265, found 386.3264.

*3-(Oleamido)pentanedinitrile (**23c**).* Prepared according general procedure B from 3,3-iminodipropionitrile **22c** (369 mg, 362 μL, 3.0 mmol), oleoyl chloride (1.09 mL, 3.30 mmol), and DIPEA (1.43 mL, 8.18 mmol) in CH_2Cl_2. Purification by column chromatography (Et_2O/MeOH 90:10) afforded the title compound (1.12 g, 96%) as a white solid: mp 40.5−41.2 °C; R_f 0.33 (Et_2O/MeOH 90:10); IR (neat, cm^{-1}) 3004, 2925, 2854, 2249, 1652, 1465, 1455, 1418, 1377, 1196, 1071, 723; ^{1}H NMR (300 MHz, $CDCl_3$) 5.33−5.37 (m, 2H), 3.78 (t, J = 6.7 Hz, 2H), 3.62 (t, J = 6.2 Hz, 2H), 2.73 (t, J = 6.2 Hz, 2H), 2.65 (t, J = 6.7 Hz, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.00−2.02 (m, 4H), 1.65−1.69 (m, 2H), 1.26−1.28 (m, 20H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 173.5, 130.0, 129.7, 118.4, 116.8, 44.9, 43.4, 33.1, 31.9, 29.8, 29.7, 29.5, 29.33, 29.28, 29.1, 27.23, 27.19, 25.0, 22.7, 18.2, 16.4, 14.1; HRMS (ESI, $[M + H]^+$) calcd for $C_{24}H_{42}N_3O$ 388.3322, found 388.3323.

*4-[(E)-Phenyldiazenyl]phenyl Oleoate (**25**).*[43] Prepared according to general procedure B from 4-phenylazophenol **24** (299 mg, 1.51 mmol), oleoyl chloride (648 μL, 1.96 mmol), DIPEA (791 μL, 4.53 mmol) in CH_2Cl_2/MeOH. Purification by column chromatography (hexane/EtOAc 97:3) afforded the title compound (475 mg, 68%) as an orange solid: mp 39−41 °C; R_f 0.25 (hexane/EtOAc 98:2); IR (ATR) ν (cm^{-1}) 3005, 2922, 2852, 1760, 1749, 1592, 1493, 1466, 1200, 1149, 923, 854, 722, 688; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 6.8 Hz, 2H), 7.45−7.54 (m, 3H), 7.24 (d, J = 8.8 Hz, 2H), 5.32−5.40 (m, 2H), 2.59 (t, J = 7.2 Hz, 2H), 2.00−2.04 (m, 4H), 1.74−1.82 (m, 2H), 1.27−1.36 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 153.0, 152.8, 150.4, 131.3, 130.3, 129.9, 129.3, 124.3, 123.1, 122.4, 34.7, 32.1, 30.0, 29.9, 29.8, 29.6 (2C), 29.4, 29.3 (2C), 27.46, 27.39, 25.1, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{30}H_{43}N_2O_2$ 463.3319, found 463.3319.

*4,5-Dimethoxy-2-nitrobenzyl Oleate (**40**).* Prepared according general procedure B from 4,5-dimethoxy-2-nitrobenzyl alcohol **34** (300 mg, 1.41 mmol), oleoyl chloride (651 μL, 1.97 mmol), DIPEA (613 μL, 3.51 mmol), and DMAP (17 mg, 0.14 mmol) in CH_2Cl_2. Purification by column chromatography (hexane/EtOAc 80:20) afforded the title compound (580 mg, 86%) as a yellow solid: mp 36−38 °C; R_f 0.44 (hexane/EtOAc 85:15); IR (KBr, cm^{-1}) 3003, 2922, 2855, 1729, 1616, 1582, 1507, 1470, 1390, 1273, 1069, 974, 796; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 6.99 (s, 1H), 5.50 (s, 2H), 5.30−5.36 (m, 2H), 3.97 (s, 3H), 3.95 (s, 3H), 2.41 (t, J = 7.6 Hz, 2H), 1.98−2.02 (m, 4H), 1.63−1.71 (m, 2H), 1.26−1.31 (m, 20H), 0.87 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 153.7, 148.5, 140.3, 130.3, 129.9, 127.4, 110.7, 108.5, 63.3, 56.6, 56.6, 34.5, 32.1, 30.0, 29.9, 29.7, 29.54, 29.53, 29.40, 29.37, 29.3, 27.44, 27.37, 25.2, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{27}H_{44}N_1O_6$ 478.3163, found 478.3163.

General Procedure for the Preparation of the Acids 4d,f−j,m, 32, and 46 Using LiOH (Procedure C). A mixture of the ester derivative (1 equiv) in ethanol (15 mL/mmol) and lithium hydroxide (3 equiv) in H_2O (5 mL/mmol) was stirred at room temperature overnight. The EtOH was evaporated in vacuo at room temperature. The residue was diluted with H_2O (25 mL), acidified to pH 2 using aqueous HCl (1 N), and extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and evaporated. The crude products were purified by recrystallization or column chromatography.

*N-Oleoyl-L-phenylalanine (**4d**).* Prepared following general procedure C from **5e** (500 mg, 1.13 mmol). The crude product was precipitated from cold hexane and recrystallized from EtOH to afford the title compound (345 mg, 71%) as a white waxy solid: mp 68.5−71 °C; R_f 0.32 (EtOAc/MeOH/AcOH 94:5:1); IR (ATR) ν (cm^{-1}) 3309, 3005, 2922, 2853, 1727, 1626, 1536, 1455, 1214, 754, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (br s, 1H), 7.25−7.31 (m, 3H), 7.15−7.17 (m, 2H), 6.01 (d, J = 7.6 Hz, 1H), 5.33−5.37 (m, 2H), 4.90 (ddd appears as dt, J = 7.6 Hz, 6.0 Hz, 1H), 3.24 (dd, J = 14 Hz, 5.6 Hz, 1H), 3.13 (dd J = 14.0 Hz, 6.0 Hz, 1H), 2.18 (app td, J = 7.6 Hz, 2.8 Hz, 2H), 1.98−2.03 (m, 4H), 1.54−1.57 (m, 2H), 1.25−1.29 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 174.1, 135.9, 130.2, 129.9, 129.6, 128.8, 127.4, 53.3, 37.5, 36.7, 32.1, 30.0, 29.9, 29.7, 29.53, 29.52, 29.4, 29.3 (2C), 27.4, 27.4, 25.7, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{27}H_{44}N_1O_3$ 430.3316, found 430.3315.

*N-Oleoyl-L-tryptophane (**4f**).* Prepared according to general procedure C from **5f** (1.0 g, 2.01 mmol). Column chromatography of the crude product (CH_2Cl_2/MeOH 95:5 with 1% AcOH) gave **4f** (736 mg, 78%) as a pale yellow waxy solid: mp 68 °C dec; R_f 0.32 (EtOAc/MeOH/AcOH 94:5:1); IR (KBr, cm^{-1}) 3410, 3309, 3006, 2925, 2853, 1723, 1650, 1527, 1457, 1342, 1230, 740; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (br s, 1H), 8.35 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.18 (td, J = 7.2 Hz, 0.8 Hz, 1H), 7.10 (td, J = 7.2 Hz, 0.8 Hz, 1H), 6.97 (d, J = 2.0 Hz, 1H), 6.13 (d, J = 7.6 Hz, 1H), 5.30−5.39 (m, 2H), 4.95 (ddd appears as dt, J = 7.6 Hz, 5.6 Hz, 1H), 3.36 (dd, J = 15.0 Hz, 5.2 Hz, 1H), 3.31 (dd J = 15.0 Hz, 5.6 Hz, 1H), 2.09 (t, J = 7.6 Hz, 2H), 1.97−2.03 (m, 4H), 1.48−1.52 (m, 2H), 1.20−1.27 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 174.5, 136.3, 130.2, 130.0, 128.0, 123.4, 122.4, 119.9, 118.6, 111.6, 109.7, 53.6, 36.6, 32.1, 30.0, 29.9, 29.7, 29.54, 29.52, 29.4, 29.3 (2C), 27.5, 27.4, 27.3, 25.6, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{29}H_{45}N_2O_3$ 469.3425, found 469.3421.

*N-Oleoyl-L-tyrosine (**4g**).* Prepared according general procedure C from **5g** (1.0 g, 2.17 mmol). The crude product was precipitated from cold hexane to afford the title compound (899 mg, 93%) as a white solid: mp 76−78 °C: R_f 0.28 (EtOAc/MeOH/AcOH 94:5:1); IR (ATR) ν (cm^{-1}) 3310, 2923, 2853, 1722, 1647, 1614, 1514, 1449, 1365, 1217, 833, 724; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (br s, 1H), 6.94 (d, J = 8.4, 2H), 6.69 (d, J = 8.4, 2H), 6.26 (d, J = 7.6 Hz, 1H), 5.28−5.37 (m, 2H), 4.83−4.88 (m, 1H), 2.99−3.09 (m, 2H), 2.18 (t, J = 7.6 Hz, 2H), 1.97−2.02 (m, 4H), 1.54−1.57 (m, 2H), 1.25−1.32 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 174.8, 155.5, 130.6, 130.3, 129.9, 127.1, 115.9, 53.5, 37.0, 36.6, 32.1, 29.98, 29.95, 29.8, 29.6, 29.5, 29.44, 29.37 (2C), 27.5, 27.4, 25.8, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{27}H_{44}N_1O_4$ 446.3265, found 446.3262.

*N-Oleoyl-L-serine (**4h**).* Prepared according general procedure C from **5h** (1.0 g, 2.60 mmol). The crude product was precipitated from cold hexane and recrystallized from EtOH to afford the title compound (780 mg, 81%) as a white solid: mp 80−82 °C (lit.[13] mp 50−60 °C); R_f 0.34 (EtOAc/MeOH 85:15 with 1% AcOH); IR (ATR) ν (cm^{-1}) 3374, 3337, 3001, 2921, 2852, 1727, 1587, 1537, 1465, 1213, 1033, 788, 648; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO) δ 6.75 (d, J = 6.8 Hz, 1H), 5.18−5.46 (m, 3H), 4.49−4.51 (m, 1H), 3.90 (dd, J = 11.6 Hz, 3.8 Hz, 1H), 3.77 (dd J = 11.6 Hz, 3.4 Hz, 1H), 2.17 (t, J = 7.6 Hz, 2H), 1.90−1.93 (m, 4H), 1.49−1.59 (m, 2H), 1.18−1.22 (m, 20H), 0.80 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO) δ 173.9, 172.6, 130.0, 129.8, 63.1, 54.8, 36.5, 31.9, 29.8, 29.7, 29.5, 29.30 (2C), 29.27 (2C), 29.17, 27.22, 27.20, 25.6, 22.7, 14.1; HRMS (ESI, $[M + H]^+$) calcd for $C_{21}H_{40}N_1O_4$ 370.2952, found 370.2953.

*N-Oleoyl-L-cysteine (**4i**).* Prepared according general procedure C from **5i** (500 mg, 0.99 mmol). Column chromatography of the crude product (CH_2Cl_2/MeOH 95:5 with 1% AcOH) gave **4i** (430 mg, 91%) as a white solid: mp 59−62 °C; R_f 0.34 (EtOAc/MeOH 95:5 + 1% AcOH); IR (ATR) ν (cm^{-1}) 3308, 3004, 2922, 2853, 1728, 1625, 1524, 1454, 1210, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (br s, 1H), 7.22−7.32 (m, 5H), 6.31 (d, J = 7.2 Hz, 1H), 5.30−5.38 (m, 2H), 4.74−4.78 (m, 1H), 3.71 (s, 2H), 2.95 (dd, J = 14.0 Hz, 5.0 Hz, 1H), 2.91 (dd J = 14.0 Hz, 5.8 Hz, 1H), 2.21 (t, J = 7.2 Hz, 2H), 1.98−2.01 (m, 4H), 1.59−1.62 (m, 2H), 1.27−1.29 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 174.0, 137.9, 130.2, 129.9, 129.1, 128.9, 127.5, 51.8, 36.9, 36.6, 33.3, 32.1, 30.0, 29.9, 29.7, 29.52, 29.51, 29.43, 29.37, 29.35, 27.43, 27.39, 25.7, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{28}H_{46}N_1O_3S$ 476.3193, found 476.3191.

*N-Oleoyl-L-glutamic Acid (**4j**).* Prepared according general procedure C from **5j** (1.0 g, 2.27 mmol). The crude product was precipitated from cold hexane and recrystallized from EtOH to afford the title compound (790 mg, 85%) as a white solid: mp 92−93.5 °C; R_f 0.40 (EtOAc/MeOH 85:15 with 1% AcOH); IR (ATR) ν (cm^{-1}) 3329, 3005, 2922, 2853, 1727, 1642, 1541, 1454, 1411, 1212, 720; ^1H NMR (400 MHz, $CDCl_3$) δ 10.97 (br s, 2H), 6.71 (d, J = 7.6 Hz, 1H), 5.29−5.37 (m, 2H), 4.62−4.67 (m, 1H), 2.43−2.53 (m, 2H), 2.21−2.27 (m, 3H), 1.97−2.09 (m, 5H), 1.59−1.61 (m, 2H), 1.26−1.29 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 175.7, 174.9, 130.2, 129.9, 51.8, 36.6, 32.1, 30.1, 29.98, 29.95, 29.8, 29.54, 29.52, 29.47, 29.43, 29.39, 27.44, 27.41, 27.0, 25.8, 22.9, 14.3; HRMS (ESI, $[M - H]^+$) calcd for $C_{23}H_{40}N_1O_5$ 410.2912, found 410.2917.

*N-Oleoylsarcosine (**4m**).* Prepared according general procedure C from **5m** (265 mg, 0.72 mmol). The crude product was purified by column chromatography (EtOAc/MeOH/AcOH 97:2:1) to afford **4m** (248 mg, 98%) as a colorless oil (lit.[44] mp 16.1−17 °C): R_f 0.25 (EtOAc/MeOH 90:10 + 0.5% AcOH); ^1H NMR (400 MHz, $CDCl_3$, appears as a 5:1 mixture of *cis/trans* isomers, assignments in analogy to **5m**) δ 8.02 (br s, 1H, *cis/trans*), 5.30−5.39 (m, 2H, *cis/trans*), 4.14 (s, 2H, *cis*), 4.07 (s, 2H, *trans*), 3.09 (s, 3H, *cis*), 2.98 (s, 3H, *trans*), 2.38 (t, J = 7.6 Hz, 2H, *cis*), 2.24 (t, J = 7.6 Hz, 2H, *trans*), 1.98−2.02 (m, 4H, *cis/trans*), 1.62−1.69 (m, 2H, *cis/trans*), 1.27−1.32 (m, 20H, *cis/trans*), 0.88 (t, J = 6.6 Hz, 3H, *cis/trans*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 173.5, 130.2, 130.0, 50.0, 37.0, 33.4, 32.1, 30.0, 29.9, 29.7, 29.5 (3C), 29.4 (2C), 27.44, 27.41, 25.1, 22.9, 14.3.

*[[(9Z)-12-[4-[(E)-Phenyldiazenyl]phenoxy]dodec-9-enoyl]-(methyl)amino]acetic Acid (**32**).* Prepared according general procedure C from **31** (24.0 mg, 0.05 mmol). The crude product was purified by column chromatography (EtOAc/MeOH 90:10 with 0.5% AcOH) to afford **32** (21.4 mg, 92%) as an orange solid: mp 90.2−92.3 °C; R_f 0.22 (EtOAc/MeOH 10:1); IR (neat, cm^{-1}) 3010, 2927, 2854, 1737, 1602, 1500, 1414, 1298, 1141, 839; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 7.2 Hz, 2H), 7.41−7.51 (m, 3H), 7.00 (d, J = 8.8 Hz, 2H), 5.43−5.58 (m, 2H), 4.10 (s, 2H), 4.04 (t, J = 7.2 Hz, 2H), 3.08 (s, 3H), 2.55−2.60 (m, 2H), 2.36 (t, J = 7.2 Hz, 2H), 2.06−2.11 (m, 2H), 1.62−1.66 (m, 3H), 1.25−1.33 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 173.0, 161.7, 153.0, 147.1, 133.2, 130.5, 129.2, 1245.0, 124.6, 122.8, 115.0, 68.1, 50.1, 37.0, 33.3, 29.8, 29.5 (2C), 29.3, 27.6 (2C), 25.0; HRMS (ESI, $[M - H]^+$) calcd for $C_{27}H_{34}N_3O_4$ 464.2555, found 464.2555.

*3-[[[(8Z)-Heptadec-8-en-1-ylcarbamoyl]oxy]methyl]-4-nitrobenzoic Acid (**46**).* Prepared according general procedure C from ethyl benzoate derivative **45** (160 mg, 0.32 mmol). Purification by preparative layer chromatography (silica gel, CH_2Cl_2/MeOH 98:2 with 0.5% AcOH) afforded title compound **46** (82 mg, 54%) as a yellow solid: mp 94−97 °C; R_f 0.37 (EtOAc/hexane 3:2 + 2% AcOH); IR (neat, cm^{-1}) 3352, 3004, 2921, 2852, 2531, 1703, 1625, 1590, 1538, 1480, 1418, 1339, 1306, 1256, 1127, 1046, 923; ^1H NMR (300 MHz, $CDCl_3$) δ 8.78 (br s, 1H), 8.32 (br d, J = 7.8 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 5.58 (s, 2H), 5.31−5.38 (m, 2H), 4.91 (br s, 1H), 3.18−3.25 (m, 2H), 2.00−2.02 (m, 4H), 1.42−1.51 (m, 1H), 1.26−1.32 (m, 20H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 155.9, 147.5, 139.0, 134.8, 130.4, 130.3, 129.9, 129.1, 126.8, 63.3, 41.5, 32.1, 30.1, 30.0, 29.89, 29.7, 29.5 (2C), 29.4 (2C), 27.42, 27.37, 26.9, 22.9, 14.3; HRMS (ESI, $[M - H]^+$) calcd for $C_{26}H_{39}N_2O_6$ 475.2814, found 475.2816.

General Procedure for the Preparation of 26, 31, 33, and 41−43 Using DCC (Procedure D). DCC (1 equiv) and DMAP (1 equiv) were added to a stirred suspension of the carboxylic acid derivative (1 equiv) in dry CH_2Cl_2 (20 mL/mmol) at 0 °C under argon. The reaction mixture was allowed to reach room temperature and stirred for 1 h. Subsequently, the amine or alcohol derivative (1 equiv) was added to the reaction mixture and stirred overnight. The dicyclohexylurea was filtered off over Celite, and the filtrate was diluted with CH_2Cl_2 (20 mL/mmol) and washed successively with 1 N HCl, saturated $NaHCO_3$ (aq), H_2O and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

*4-[(E)-Phenyldiazenyl]phenyl (Oleoylamino)acetate (**26**).* Prepared according general procedure D from **4a** (100 mg, 0.295 mmol), 4-phenylazophenol **24** (58 mg, 0.295 mmol). Purification by column chromatography (EtOAc/hexane 30:70) afforded the title compound (81 mg, 53%) as a yellow solid: mp 117−121 °C; R_f 0.43 (EtOAc/hexane 40:60); IR (ATR) ν (cm^{-1}) 3333, 3002, 2919, 2850, 1759, 1650, 1538, 1465, 1236, 1174, 855, 764, 685; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 7.6 Hz, 2H), 7.48−7.54 (m, 3H), 7.28 (d, J = 8.8 Hz, 2H), 5.96 (br s, 1H), 5.29−5.38 (m, 2H), 4.34 (d, J = 5.2 Hz, 2H), 2.29 (t, J = 7.2 Hz, 2H), 1.98−2.03 (m, 4H), 1.66−1.71 (m, 2H), 1.26−1.31 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 168.8, 152.7, 152.3, 150.7, 131.4, 130.2, 130.0, 129.3, 124.4, 123.1, 122.2, 41.7, 36.6, 32.1, 29.98, 29.92, 29.7, 29.54, 29.53, 29.46, 29.43, 29.3, 27.44, 27.39, 25.8, 22.9, 14.3; HRMS (ESI, $[M + Na]^+$) calcd for $C_{32}H_{45}N_3NaO_3$ 542.3353, found 542.3349.

*Methyl [[(9Z)-12-[4-[(E)-Phenyldiazenyl]phenoxy]dodec-9-enoyl]-methylamino]acetate (**31**).* Prepared according general procedure D from sarcosine methyl ester hydrochloride **3m** (21.7 mg, 0.156 mmol) and acid **30** (61.5 mg, 0.156 mmol). Flash column chromatography of the crude product (Et_2O/hexane 90:10) afforded **31** (71 mg, 95%) as an orange oil: R_f 0.22 (hexane/Et_2O 10:90); IR (neat, cm^{-1}) 3009, 2926, 2853, 1750, 1653, 1600, 1500, 1468, 1402, 1250, 1209, 1142, 1023, 840; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.8 Hz, 2H), 7.87 (d, J = 7.2 Hz, 2H), 7.42−7.51 (m, 3H), 7.01 (d, J = 8.8 Hz, 2H), 5.44−5.58 (m, 2H), 4.12 (s, 2H), 4.05 (t, J = 6.9 Hz, 2H), 3.73 (s, 3H), 3.06 (s, 3H), 2.55−2.60 (m, 2H), 2.36 (t, J = 6.9 Hz, 2H), 2.07−2.11 (m, 2H), 1.62−1.67 (m, 2H), 1.31−137 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 170.2, 161.7, 153.0, 147.2, 133.2, 130.5, 129.2, 125.0, 124.6, 122.8, 115.0, 68.1, 52.3, 49.5, 36.8, 33.3, 29.8, 29.6 (2C), 29.4, 27.6 (2C), 25.1; HRMS (ESI, $[M + Na]^+$) calcd for $C_{28}H_{37}N_3NaO_4$ 502.2676, found 502.2681.

*(9Z)-2,3-Dihydroxypropyl-12-[4-[(E)-phenyldiazenyl]phenoxy]-dodec-9-enoate (**33**).* Compound **33** was synthesized in two steps. The first step was prepared according general procedure D from solketal (13.8 mg, 0.104 mmol), **30** (41 mg, 0.104 mmol), DCC (21.46 mg, 0.104 mmol), and DMAP (12.70 mg, 0.104 mmol) in dry CH_2Cl_2. Purification by preparative layer chromatography (Et_2O/hexane 50:50) afforded the oxirane (46 mg, 86%) as a white solid, which was used in the next step. To a stirred solution of the oxirane (30 mg, 0.059 mmol) in 3 mL of 2-methoxyethanol was added boric acid (742 mg, 12 mmol), and the mixture was heated up to 95 °C and stirred at this temperature for 20 h. The reaction mixture was allowed to cool to room temperature and was diluted with water (3 mL) and CH_2Cl_2 (5 mL), and the resulting mixture was shaken for some minutes. The precipitated boric acid was filtered off and washed with CH_2Cl_2 and water. The filtrate was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic phases were washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the residue was purified by column chromatography (Et_2O/hexane 80:20) to afford **33** (18.5 mg, 67%) as an orange solid: mp 69.8−71.6 °C; R_f 0.22 (EtOAc/hexane 80:20); IR (neat, cm^{-1}) 3355, 3005, 2920, 2849, 1731, 1603, 1582, 1497, 1298, 1181, 842; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 7.2 Hz, 2H), 7.41−7.52 (m, 3H), 7.00 (d, J = 8.8 Hz, 2H), 5.43−5.59 (m, 2H), 4.13−4.23 (m, 2H), 4.06 (t, J = 6.8 Hz, 2H), 3.87−3.95 (m, 1H), 3.57−3.71 (m, 2H), 2.56−2.61 (m, 2H), 2.35 (t, J = 6.8 Hz, 2H), 2.07−2.12 (m, 2H), 1.58−1.66 (m, 2H), 1.26−1.38 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 161.5, 152.8, 147.0, 132.9, 130.3, 129.0, 124.74, 124.4, 122.5, 114.8, 70.3, 67.9, 65.2, 63.3, 34.1, 29.6, 29.13 (2C), 29.06, 27.40, 27.36, 24.9; HRMS (ESI, $[M + Na]^+$) calcd for $C_{27}H_{36}N_2NaO_5$ 491.2516, found 491.2523.

*4,5-Dimethoxy-2-nitrobenzyl [Methyl(oleoylamino)]acetate (**41**).* Prepared according general procedure D from 4,5-dimethoxy-2-nitrobenzyl alcohol **34** (102 mg, 0.48 mmol) and *N*-oleoylsarcosine **4m** (170 mg, 0.48 mmol). Purification by column chromatography (EtOAc/hexane 30:70 to 60:40) afforded the title compound (216 mg, 82%) as a pale yellow solid: mp 41.2−42.3 °C. R_f 0.20 (hexane/EtOAc 60:40); IR (neat, cm^{-1}) 2925, 2853, 1752, 1651, 1523, 1462, 1329, 1277, 1179, 873; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.05 (s,

1H), 5.59 (s, 2H), 5.31−5.36 (m, 2H), 4.19 (s, 2H), 4.05 (s, 3H), 3.96 (s, 3H), 3.13 (s, 3H), 2.37 (t, J = 7.5 Hz, 2H), 1.97−2.01 (m, 4H), 1.59−1.64 (m, 2H), 1.26−1.29 (m, 20H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0, 169.3, 154.0, 148.2, 139.6, 130.0, 129.7, 127.2, 110.1, 108.2, 63.8, 56.83, 56.4, 49.9, 36.9, 33.1, 31.9, 29.8, 29.7, 29.5, 29.34, 29.32 (2C), 29.2, 27.21, 27.18, 24.9, 22.7, 14.1; HRMS (ESI, $[M + Na]^+$) calcd for $C_{30}H_{48}N_2NaO_7$ 571.3354, found 571.3355.

*5-Amino-2-nitrobenzyl Oleate (**42**).* Prepared according general procedure D from 5-amino-2-nitrobenzyl alcohol **35** (59 mg, 0.35 mmol) and oleic acid (99 mg, 0.35 mmol). Preparative layer chromatography of the crude product (Et_2O/pentane 70:30) afforded **42** (135 mg, 88%) as a pale yellow solid: mp 57.2−58.4 °C; R_f 0.23 (Et_2O/hexane 60:40); IR (neat, cm^{-1}) 3386, 2924, 2853, 1731, 1618, 1578, 1420, 1293, 1088; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.9 Hz, 1H), 6.70 (d, J = 2.8 Hz, 1H), 6.57 (dd, J = 8.9 Hz, 2.8 Hz, 1H), 5.52 (s, 2H), 5.30−5.38 (m, 2H), 4.39 (br s, 2H), 2.43 (t, J = 7.6 Hz, 2H), 2.00−2.03 (m, 4H), 1.65−1.72 (m, 2H), 1.26−1.32 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 152.0, 137.8, 136.2, 130.2, 129.9, 128.7, 112.8, 112.6, 63.6, 34.4, 32.0, 29.9, 29.8, 29.7, 29.46, 29.45, 29.33, 29.29, 29.26, 27.4, 27.3, 25.1, 22.8, 14.3; HRMS (ESI, $[M + Na]^+$) calcd for $C_{25}H_{40}N_2NaO_4$ 455.2880, found 455.2874.

*Bis(5-amino-2-nitrobenzyl)-2,2′-(oleoylimino)diacetate (**43**).* Prepared according general procedure D from 5-amino-2-nitrobenzyl alcohol **35** (30 mg, 0.18 mmol), 2,2′-(oleoylimino)diacetic acid **23d** (35 mg, 0.088 mmol), DCC (37 mg, 0.18 mmol), and DMAP (22 mg, 0.18 mmol). Purification by preparative layer chromatography (silica gel, Et_2O/MeOH 99:1) afforded the title compound (23 mg, 37%) as a light yellow oil: R_f 0.27 (Et_2O/MeOH 99:1); IR (neat, cm^{-1}) 3365, 3234, 2925, 2854, 1748, 1633, 1582, 1455, 1302, 1260, 1183, 996; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.8 Hz, 1H), 8.06 (d, J = 9.2 Hz, 1H), 6.79 (d, J = 2.4 Hz, 1H), 6.66 (d, J = 2.8 Hz, 1H), 6.57 (dd, J = 9.2 Hz, 2.4 Hz, 1H), 6.51 (dd, J = 8.8 Hz, 2.8 Hz, 1H), 5.58 (s, 2H), 5.56 (s, 2H), 5.31−5.35 (m, 2H), 4.60 (br s, 2H), 4.56 (br s, 2H), 4.33 (s, 2H), 4.32 (s, 2H), 2.37 (t, J = 7.6 Hz, 2H), 1.96−2.00 (m, 4H), 1.62−1.66 (m, 2H), 1.26−1.31 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 169.3, 168.5, 152.8, 152.4, 135.6, 134.7, 130.2, 129.9, 128.9, 128.8, 113.04, 112.95, 112.4 (2C), 65.2, 64.7, 50.9, 49.0, 33.0, 32.0, 29.91, 29.85, 29.7, 29.50, 29.47, 29.45, 29.4, 29.3, 27.4, 27.3, 25.1, 22.8, 14.3; HRMS (ESI, $[M + Na]^+$) calcd for $C_{36}H_{51}N_5NaO_9$ 720.3579, found 720.3575.

Synthesis of Compounds 12−15, 18, 20, 21, 28−30, 39, 44, 45, and 48. *2-Hydroxy-3(O-tosyl)propyl Oleate (**12**).* To a solution of monoolein **1** (1.0 g, 2.80 mmol) in absolute pyridine (7.5 mL) was added *p*-toluenesulfonyl chloride (642 mg, 3.37 mmol) in small portions over 30 min at 0 °C. After addition, stirring was continued at room temperature for 6 h. The reaction mixture was poured into water and extracted three times with MTBE. The combined organic phases were washed with half-saturated brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was subjected to column chromatography (Et_2O/hexane 60:40) to give **12** (1.11 g, 78%) as a colorless oil: R_f 0.33 (Et_2O/hexane 80:20); IR (neat, cm^{-1}) 3462, 2926, 2855, 1741, 1599, 1457, 1364, 1190, 1178, 988, 815; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 7.8 Hz, 2H), 5.29−5.38 (m, 2H), 4.03−4.13 (m, 5H), 2.83 (br s, 1H), 2.46 (s, 3H), 2.28 (t, J = 7.2 Hz, 2H), 1.96−2.02 (m, 4H), 1.56−1.61 (m, 2H), 1.25−1.31 (m, 20H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 145.4, 132.6, 130.2, 130.1, 129.9, 128.2, 70.4, 68.0, 64.5, 34.2, 32.1, 29.92, 29.86, 29.7, 29.5 (2C), 29.31, 29.25, 29.2, 27.4, 27.3, 25.0, 22.8, 21.8, 14.3; HRMS (ESI, $[M + Na]^+$) calcd for $C_{28}H_{46}NaO_6S$ 533.2907, found 533.2903.

*3-Azido-2-hydroxypropyl Oleate (**13**).* To a solution of monotosylate **12** (0.36 g, 0.7 mmol) in dry DMF (5 mL) was added NaN_3 (122 mg, 1.88 mmol) at room temperature under argon. The mixture was heated to 60 °C for 2.5 h. The reaction mixture was left to cool to room temperature, poured into water (30 mL) and extracted with ether (3 × 20 mL). The combined organic phases were washed with water and brine, dried over $MgSO_4$, and filtered, and the filtrate was evaporated in vacuo. The residue was purified by column chromatography (Et_2O/hexane 60:40) to give **13** (195 mg, 73%) as a colorless oil: R_f 0.34 (Et_2O/hexane 50:50); IR (neat, cm^{-1}) 3455, 3004, 2926, 2855, 2103, 1741, 1457, 1271, 1118; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.29−5.40 (m, 2H), 4.13−4.21 (m, 2H), 3.98−4.04 (m, 1H), 3.34−3.46 (m, 2H), 2.45 (br s, 1H), 2.35 (t, J = 7.5 Hz, 2H), 1.98−2.04 (m, 4H), 1.59−1.63 (m, 2H), 1.26−1.31 (m, 20H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0, 130.1, 129.7, 69.2, 65.5, 53.5, 34.1, 31.9, 29.8, 29.7, 29.5, 29.3 (2C), 29.2, 29.1 (2C), 27.23, 27.16, 24.9, 22.7, 14.1; HRMS (ESI, $[M + Na]^+$) calcd for $C_{21}H_{39}N_3NaO_3$ 404.2884, found 404.2880.

*3-Amino-2-hydroxypropyl Oleate (**14**).* To a solution of azide **13** (108 mg, 0.28 mmol) in THF/H_2O 3:2 (5 mL) was added Ph_3P (74 mg, 0.28 mmol) and the mixture was heated under reflux for 23 h. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo. The residue was purified by column chromatography (EtOAc/MeOH 95:5) to give **14** (70 mg, 70%) as a colorless waxy solid: mp 69.8−71.7 °C; R_f 0.27 (EtOAc/MeOH 95:5); IR (neat, cm^{-1}) 3304, 3001, 2919, 2850, 1642, 1556, 1462, 1115, 720; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (br s, 1H), 5.28−5.40 (m, 2H), 3.72−3.77 (m, 1H), 3.56 (br s, 2H), 3.36−3.47 (m, 2H), 2.99 (br s, 1H), 2.22 (t, J = 7.6 Hz, 2H), 1.99−2.03 (m, 4H), 1.58−1.65 (m, 2H), 1.27−1.31 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 130.1, 129.7, 71.3, 63.5, 42.2, 36.6, 31.9, 29.8, 29.7, 29.5, 29.34, 29.32, 29.25, 29.1, 27.23, 27.16, 25.7, 22.7, 14.1; HRMS (ESI, $[M + H]^+$) calcd for $C_{21}H_{42}NO_3$ 356.3159, found 356.3157.

*3-(Acetylsulfanyl)-2-hydroxypropyl Oleate (**15**).* A solution of monotosylate **12** (491 mg, 0.96 mmol) and potassium thioacetate (142 mg, 1.24 mmol) in dry acetone (7.5 mL) was stirred in a sealed Schlenk tube at room temperature under argon for 16 h. The mixture was poured into half saturated brine (70 mL) and extracted with MTBE (3 × 20). The organic phases were combined and washed with 1 M HCl (20 mL), followed by saturated $NaHCO_3$ (20 mL) and brine, and dried over $MgSO_4$, and the solvent was evaporated at reduced pressure. The residue was subjected to column chromatography (MTBE/hexane 50:50) to afford **15** (103 mg, 26%) as a colorless oil: R_f 0.36 (Et_2O/hexane 50:50); IR (neat, cm^{-1}) 3386, 2925, 2854, 1745, 1458, 1372, 1231, 1049; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.28−5.40 (m, 2H), 5.05−5.08 (m, 1H), 4.35 (dd, J = 12 Hz, 3.9 Hz, 1H), 4.23 (dd, J = 12 Hz, 5.7 Hz, 1H), 2.71−2.77 (m, 2H), 2.32 (t, J = 7.5 Hz, 2H), 2.09 (s, 3H), 1.98−2.04 (m, 4H), 1.54−1.61 (m, 2H), 1.27−1.31 (m, 20H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 173.8, 130.0, 129.7, 69.2, 66.6, 34.1, 32.6, 31.9, 30.6, 29.8, 29.7, 29.5, 29.3 (2C), 29.2, 29.1 (2C), 27.22, 27.17, 24.9, 22.7, 14.1; HRMS (ESI, $[M + Na]^+$) calcd for $C_{23}H_{42}NaO_4S$ 437.2696, found 437.2697.

*N-(2-Aminoethyl)oleamide (**18**).* To a solution of *N*-(2-Azidoethyl)oleamide **17** (1 g, 2.85 mmol) in THF/H_2O 3:2 (30 mL) was added triphenylphosphine (748 mg, 2.85 mmol) and the mixture was heated under reflux for 24 h. The reaction mixture was allowed to reach room temperature, poured into brine (30 mL) and extracted with EtOAc (3 × 25 mL). The organic layers were combined and dried over $MgSO_4$, concentrated under reduced pressure and the residue was purified by column chromatography (CH_2Cl_2/MeOH 95:5 with 1% Et_3N) to afford **18** (785 mg, 85%) as a colorless solid: mp 74−76 °C; R_f 0.26 (CH_2Cl_2/MeOH 95:5 with 1% Et_3N); IR (neat, cm^{-1}) 3293, 2922, 2852, 1643, 1552, 1451, 1252, 1053, 892; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.04 (br s, 1H, NHCO), 5.29−5.38 (m, 2H), 3.32 (q, J = 6.0 Hz, 2H), 2.85 (t, J = 6.0 Hz, 2H), 2.18 (t, J = 7.6 Hz, 2H), 1.98−2.01 (m, 4H), 1.93 (br s, 2H, NH_2), 1.59−1.64 (m, 2H), 1.26−1.30 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 130.2, 130.0, 41.8, 41.6, 37.1, 32.1, 30.0, 29.9, 29.7, 29.53 (2C), 29.50 (2C), 29.4, 27.44, 27.40, 26.0, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{20}H_{41}N_2O$ 325.3214, found 325.3214.

*N-2-[2,3-Di(tert-butoxycarbonyl)guanidino]oleamide (**20**).* *N*-(2-Aminoethyl)oleamide **18** (120 mg, 0.37 mmol) in CH_2Cl_2 (1 mL) was added in one portion to a solution of *N*,*N*′-di-Boc-*N*′-trifluoromethanesulfonylguanidine **19** (131 mg, 0.34 mmol) and Et_3N (51.5 μL, 0.37 mmol) in CH_2Cl_2 (2 mL, filtered over neutral alumina) at 0 °C. The

reaction was allowed to warm to room temperature and stirred for 3 h. Then the mixture was diluted with CH_2Cl_2 (5 mL) and washed with 2 M sodium bisulfate, saturated $NaHCO_3$ aq, and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure, and the residue was purified by column chromatography (hexane/EtOAc 80:20 to 50:50) to afford **20** (181 mg, 95%) as a white solid: mp 53−54 °C; R_f 0.25 (hexane/EtOAc 50:50); IR (neat, cm^{-1}) 3322, 2971, 2856, 1724, 1640, 1617, 1559, 1411, 1365, 1228, 1133, 1051, 880, 772; ^1H NMR (400 MHz, $CDCl_3$) δ 11.41 (s, 1H, NHBoc), 8.62 (br s, 1H, NH), 7.45 (br s, 1H, NHCO), 5.30−5.37 (m, 2H), 3.54−3.57 (m, 2H), 3.40−3.43 (m, 2H), 2.17 (t, J = 7.6 Hz, 2H), 1.98−2.02 (m, 4H), 1.60−1.65 (m, 2H), 1.50 (s, 18H), 1.26−1.29 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 163.1, 157.8, 153.3, 130.2, 130.0, 83.8, 79.7, 41.7, 40.5, 37.0, 32.1, 29.99, 29.96, 29.7, 29.56 (2C), 29.54, 29.53 (2C), 29.4, 28.5, 28.3, 27.44, 27.42, 26.0, 22.9, 14.3; HRMS (ESI, $[M + Na]^+$) calcd for $C_{31}H_{58}N_4NaO_5$ 589.4299, found 589.4297.

*N-[2-[(Aminoiminomethyl)amino]butyl]oleamide (**21**).* To a stirred solution of **20** (150 mg, 0.26 mmol) in CH_2Cl_2 (2 mL) cooled at 0 °C under argon was added TFA (2 mL). The mixture was stirred at 0 °C for 30 min and then at room temperature for 2 h. The solvent and excess of TFA were removed under reduced pressure and the residue coevaporated with toluene (3 × 5 mL) to afford the trifluoroacetate salt in quantitative yield. The salt was dissolved in H_2O, to which Amberlite IRA-402 resin in its OH form was added. The mixture was stirred for 36 h at room temperature after which the Amberlite resin was removed by vacuum filtration. The aqueous layer was washed with CH_2Cl_2 and concentrated under reduced pressure to yield **21** (70 mg, 73%) as a white waxy solid: mp 64−66 °C dec; IR (neat, cm^{-1}) 3275, 2969, 2922, 2853, 1738, 1651, 1540, 1435, 1366, 1228, 1091; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (br s, 1H, N*H*), 7.17 (br s, 3H, NH_2, N*H*CO), 5.24−5.44 (m, 2H), 3.14−3.50 (m, 4H), 2.10−2.33 (m, 2H), 1.89−2.08 (m, 4H), 1.48−1.69 (m, 2H), 1.18−1.38 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 158.1, 130.2, 129.9, 40.9, 39.0, 36.5, 32.1, 30.0, 29.9, 29.8, 29.54 (2C), 29.45, 29.42, 29.39, 27.44, 27.41, 25.8, 22.9, 14.3; HRMS (ESI, $[M + H]^+$) calcd for $C_{21}H_{43}N_4O$ 367.3432, found 367.3432.

*Methyl (9Z)-12-Bromododec-9-enoate (**28**).* To a solution of methyl (9*Z*)-12-(tetrahydro-2′*H*-pyran-2′-yl-oxy)-1-dodec-9-enoate **27** (1.15 g, 3.95 mmol) in dry CH_2Cl_2 (20 mL) was added triphenylphosphine (2.64 g, 10.06 mmol) followed by tetrabromomethane (1.58 g, 4.77 mmol) at 0 °C under argon. The reaction mixture was stirred overnight at room temperature, and then saturated aqueous $NaHCO_3$ (50 mL) was added to the solution. The mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to column chromatography (hexane/Et_2O 83:17) to give **28** as a colorless oil (874 mg, 76%): IR (neat, cm^{-1}) 2929, 2855, 1740, 1437, 1362, 1263, 1172, 1098, 970; ^1H NMR (300 MHz, $CDCl_3$) δ 5.51−5.57 (m, 1H), 5.31−5.40 (m, 1H), 3.67 (s, 3H), 3.36 (t, J = 6.9 Hz, 2H), 2.58−2.65 (m, 2H), 2.31 (t, J = 6.9 Hz, 2H), 2.00−2.07 (m, 2H), 1.57−1.64 (m, 2H), 1.31−1.37 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 132.0, 124.8, 50.4, 33.1, 31.6, 29.8, 28.4, 28.09, 28.06, 28.02, 26.4, 23.9; HRMS (ESI, $[M + Na]^+$) calcd for $C_{13}H_{23}BrNaO_2$ 313.0773, found 313.0770.

*Methyl (9Z)-12-[4-[(E)-Phenyldiazenyl]phenoxy]dodec-9-enoate (**29**).* To a solution of **28** (687 mg, 2.36 mmol) in dry acetone (45 mL) was added 4-phenylazophenol **24** (0.99 g, 5 mmol) followed by anhydrous potassium carbonate (3.46 g, 25.1 mmol). The reaction mixture was refluxed for 16 h, cooled to room temperature, poured into water (300 mL), and extracted with EtOAc (3 × 70 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography (Et_2O/hexane 10:90 to Et_2O 100) to afford **29** (732 mg, 76%) as an orange waxy solid: mp 34.1−34.6 °C; R_f 0.48 (hexane/Et_2O 2:1); IR (neat, cm^{-1}) 3010, 2927, 2854, 1738, 1600, 1582, 1501, 1468, 1436, 1250, 1209, 1141, 1024, 833, 689; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 9.0 Hz, 2H), 7.87 (d, J = 7.2 Hz, 2H), 7.41−7.53 (m, 3H), 7.00 (d, J = 9.0 Hz, 2H), 5.43−5.60 (m, 2H), 4.05 (t, J = 6.9 Hz, 2H), 3.66 (s, 3H), 2.54−2.61 (m, 2H), 2.30 (t, J = 6.9 Hz, 2H), 2.05−2.12 (m, 2H), 1.59−1.64 (m, 2H), 1.25−1.40 (m, 10H,); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 161.5, 152.8, 147.0, 132.9, 130.3, 129.0, 124.7, 124.4, 122.5, 114.7, 67.8, 51.4, 34.1, 29.5, 29.2, 29.11, 29.09, 27.4 (2C), 24.9; HRMS (ESI, $[M + Na]^+$) calcd for $C_{25}H_{32}N_2NaO_3$ 431.2305, found 431.2302.

*(9Z)-12-[4-[(E)-Phenyldiazenyl]phenoxy]dodec-9-enoic Acid (**30**).* A solution of KOH (0.79 g, 14.1 mmol) in MeOH (6.8 mL) was added dropwise to a stirred solution of **29** (0.70 g, 1.71 mmol) in MeOH (13 mL) at room temperature under argon. The reaction mixture was heated at 40 °C for 1 h and stirred overnight at room temperature. The reaction mixture was poured into water, acidified with 2 N HCl until pH ∼2, and extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by recrystallization in hexane to afford **30** (588 mg, 87%) as an orange solid: mp 93.5−94 °C; IR (neat, cm^{-1}) 3021, 2920, 2851, 1706, 1599, 1501, 1468, 1260, 1209, 1141, 1032, 844; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 9.0 Hz, 2H), 7.87 (d, J = 7.2 Hz, 2H), 7.40−7.52 (m, 3H), 7.00 (d, J = 9.0 Hz, 2H), 5.43−5.60 (m, 2H), 4.04 (t, J = 6.9 Hz, 2H), 2.54−2.61 (m, 2H), 2.34 (t, J = 6.9 Hz, 2H), 2.05−2.12 (m, 2H), 1.58−1.66 (m, 2H), 1.25−1.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.7, 161.5, 152.8, 146.9, 132.9, 130.3, 129.0, 124.7, 124.4, 122.5, 114.7, 67.8, 34.0, 29.5, 29.12, 29.06, 29.00, 27.4 (2C), 24.7; HRMS (ESI, $[M + Na]^+$) calcd for $C_{24}H_{30}N_2NaO_3$ 417.2149, found 417.2149.

*Ethyl 4-(Hydroxymethyl)-3-nitrobenzoate (**39**).* A 2.6 g (10 mmol) portion of 3-nitro-4-bromomethylbenzoic acid and 5.3 g (50 mmol) of Na_2CO_3 were dissolved in water (40 mL) and acetone (40 mL). The mixture was placed under reflux overnight, following by evaporation of the acetone in vacuo. The mixture was washed with diethyl ether (50 mL) and the aqueous phase was acidified until pH ∼2 with a 2 M solution of HCl. The product was extracted with ethyl acetate (3 × 60 mL) while the pH was kept at 2. The organic layers were combined and washed with water (100 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to afford 1.8 g of the corresponding 4-(hydroxymethyl)-3-nitrobenzoic acid as an orange solid. The above crude acid was dissolved in ethanol abs (30 mL), boron trifluoride diethyl etherate (3.7 mL, 30 mmol) was added at room temperature, and the reaction mixture was refluxed for 5 h. After the mixture was cooled to room temperature, the solvent was evaporated in vacuo. To the residue 50 mL of water was added, the mixture was extracted with EtOAc (3 × 40 mL), the combined organic layers were dried over $MgSO_4$, and the solvent was evaporated in vacuo. The residue was purified by column chromatography (hexane/EtOAc 70:30) to yield **39** (1.77 g, 79%) as a yellow solid: mp 112−114 °C. R_f 0.36 (hexane/EtOAc 70:30); ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 2.0 Hz, 1H), 8.30 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 7.90 (dd, J = 8.0 Hz, 0.4 Hz, 1H), 5.07 (s, 2H), 4.43 (q, J = 7.2 Hz, 2H), 2.50 (br s, 1H, OH), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 147.5, 141.6, 134.7, 131.2, 129.8, 126.2, 62.4, 62.1, 14.5; HRMS (ESI, $[M + Na]^+$) calcd for $C_{10}H_{11}N_1NaO_5$ 248.0529, found 248.0528.

*(8Z)-Heptadec-8-en-1-amine (**44**).* A solution of sodium azide (4.0 g, 61 mmol) in water (13 mL) was added dropwise to a stirred solution of oleoyl chloride **2** (15 g, 49.8 mmol) in CH_2Cl_2 (75 mL) containing TBAB (50 mg, 0.16 mmol) at 0 °C under argon, and the resulting two-phase mixture was stirred vigorously for 2 h. The organic phase was then separated, washed with water (2 × 20 mL), and dried over $MgSO_4$ for 60 h. Continued evolution of nitrogen as small bubbles was observed during this period. $MgSO_4$ was filtered off over Celite, and the resulting crude acid solution was transferred into a two-neck flask equipped with septum, condenser, and argon inlet and was used for the next step without further purification. TFA (7.7 g, 5.17 mL, 67 mmol) was added dropwise at room temperature to this solution, which was thereafter refluxed for 5 h. The reaction mixture was allowed to cool to room temperature, washed with saturated aqueous $NaHCO_3$ (2 × 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was subjected to column chromatography (EtOAc/hexane 30:70) to afford the oleic acid trifluoroacetamide (15.0 g, 86%) as a colorless oil (dried at 40 °C/

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2mbar). 6.3 g (18.03 mmol) thereof were cleaved to the amine by stirring with 15 mL of 2 N aq NaOH in 70 mL of EtOH for 40 h at room temperature. Subsequently, most of the solvent was evaporated in vacuo, and the residue was diluted with water (250 mL) and extracted with Et_2O (3 × 70 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, and evaporated. The crude product was purified by Kugelrohr distillation at 110 °C/0.05 mbar to afford **44** (4.2 g, 92%) as a colorless oil: R_f 0.20 (CH_2Cl_2/MeOH 90:10 with 2% Et_3N); IR (neat, cm^{-1}) 3375, 3296, 3005, 2924, 2853, 1619, 1464, 1378, 801; ^1H NMR (300 MHz, $CDCl_3$) δ. 5.29−5.40 (m, 2H), 2.67 (t, J = 7.7 Hz, 2H), 2.00−2.04 (m, 4H), 1.19−1.43 (m, 22H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.0, 129.8, 42.3, 33.9, 31.9, 29.8, 29.7, 29.5, 29.4, 29.33 (2C), 29.28, 27.20, 27.18, 26.9, 22.7, 14.1; MS (EI) m/z (relative intensity) 253 ($[M]^+$, 32), 154 (49), 140 (85); HRMS (EI, $[M + H]^+$) calcd for $C_{17}H_{36}N$ 254.2842, found 254.2841.

*Ethyl 3-[[[(8Z)-Heptadec-8-en-1-ylcarbamoyl]oxy]methyl]-4-nitrobenzoate (**45**).* To a stirred suspension of 1,1′-carbonyldiimidazole (50 mg, 0.31 mmol) in dry CH_2Cl_2 (1 mL) was added under argon dropwise a solution of ethyl 3-(hydroxymethyl)-4-nitrobenzoate **38** (70 mg, 0.31 mmol) in dry CH_2Cl_2 (1 mL) at 0 °C. After the mixture was stirred for 1 h at room temperature, the (8Z)-8-heptadecen-1-amine **44** (79 mg, 0.31 mmol) was added and stirring continued overnight. The reaction mixture was diluted with EtOAc (30 mL) and washed with aq HCl 10% (2 × 20 mL) and brine (1 × 20 mL). The organic layer was dried over $MgSO_4$ and filtered, and the solvent was evaporated in vacuo. Preparative layer chromatography of the crude product (silica gel, EtOAc/hexane 40:60) afforded **45** (123 mg, 79%) as a pale yellow waxy solid: mp 62.7−64.5 °C; R_f 0.43 (hexane/EtOAc 60:40); IR (neat, cm^{-1}) 3378, 3344, 3004, 2923, 2852, 1724, 1688, 1527, 1344, 1290, 1269, 1201, 1162, 1138, 1025; ^1H NMR (300 MHz, $CDCl_3$) δ 8.72 (d, J = 1.5 Hz, 1H), 8.28 (dd, J = 1.4 Hz, 8.1 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 5.55 (s, 2H), 5.32−5.37 (m, 2H), 4.86 (br s, 1H), 4.43 (q, J = 7.2 Hz, 2H), 3.17−3.24 (m, 2H), 2.00−2.02 (m, 4H), 1.50−1.54 (m, 1H), 1.42 (t, J = 7.2 Hz, 3H), 1.26−1.31 (m, 20H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 155.5, 147.3, 138.0, 134.1, 131.2, 130.1, 129.7, 128.7, 126.0, 62.9, 61.9, 41.3, 31.9, 29.9, 29.8, 29.7, 29.5, 29.3 (2C), 29.2 (2C), 27.23, 27.16, 26.7, 22.7, 14.3, 14.1; HRMS (ESI, $[M + Na]^+$) calcd for $C_{28}H_{44}N_2NaO_6$ 527.3092, found 527.3084.

*Bisethyl [[[[(Oleoylimino)ethyl]carbamoyl]oxy]methyl]-3-nitrobenzoate (**48**).* To a suspension of 1,1′-carbonyldiimidazole (353 mg, 2.17 mmol) in dry CH_2Cl_2 (15 mL) was added dropwise at 0 °C a solution of alcohol **39** (490 mg, 2.17 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred at room temperature for 1 h. The amine **47** (400 mg, 1.08 mmol) was added, and the mixture was stirred overnight. EtOAc (50 mL) was added, and the mixture was washed two times with aq HCl 10% (2 × 30 mL) and brine (1 × 30 mL). The organic layer was dried over $MgSO_4$ and filtered, and the solvent was evaporated in vacuo. The residue was purified by column chromatography (EtOAc/hexane 70:30) to yield 350 mg of **48**. Additional 250 mg of product was collected by eluting the CC with EtOAc/MeOH (95:5) to give a total of **48** (600 mg, 64%) as a white solid: mp 72.5−74.0 °C; R_f 0.40 (EtOAc/hexane 80:20); ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 1.6 Hz), 8.68 (d, J = 1.6 Hz, 1H), 8.26 (dd, J = 8.0 Hz, 1.6 Hz, 2H), 7.69 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 5.62−5.72 (m, 2H), 5.53 (s, 4H), 5.26−5.35 (m, 2H), 4.43 (q, J = 7.2 Hz, 4H), 3.36−3.55 (m, 8H), 2.32 (t, J = 7.6 Hz, 2H), 1.95−2.00 (m, 4H), 1.56−1.61 (m, 2H), 1.42 (t, J = 7.2 Hz, 6H, 2 CH_3), 1.25−1.29 (m, 20 H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 164.40, 164.36, 156.4, 156.0, 147.5, 147.3, 138.0, 137.5, 134.41, 134.38, 131.6, 131.4, 130.2 129.9, 128.9, 128.8, 126.22, 126.16, 63.5, 63.3, 62.2, 48.6, 46.2, 40.9, 40.2, 33.3, 32.1, 29.95, 29.93, 29.7, 29.6 (2C), 29.51, 29.49, 29.4, 27.41, 27.37, 25.7, 22.9 (2C), 14.5 (2C), 14.3; HRMS (ESI, $[M + Na]^+$) calcd for $C_{44}H_{63}N_5NaO_{13}$ 892.4315, found 892.4322.

■ ASSOCIATED CONTENT

Supporting Information

^1H NMR, ^{13}C NMR, and HRMS spectral data for compounds **4a−d,g−j,m**, **5e−m**, **7**, **11−15**, **17**, **18**, **20**, **21**, **23a−e**, **25**, **26**, **28−33**, **38−46**, and **48**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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