

Supporting Information for

Screening Libraries to Discover Molecular Design Principles for the Targeted Delivery of mRNA with One-Component Ionizable Amphiphilic Janus Dendrimers Derived from Plant Phenolic Acids †

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† Dedicated to the 85th Anniversary of Donald A. Tomalia.

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Table of Contents

1. Materials	S3
2. Methods and Techniques.....	S3
2.1 ¹H and ¹³C NMR	S3
2.2 Thin-Layer Chromatography (TLC)	S4
2.3 High-Pressure Liquid Chromatography (HPLC).....	S4
2.4 Matrix Assisted Laser Desorption Ionization-Time of Flight (MALDI-TOF) Mass Spectrometry	S4
2.5 Dynamic Light Scattering (DLS).....	S5
2.6 pK_a Measurements of Individual IAJDs.....	S5
2.7 Formulation of DNPs Co-assembled from IAJDs and Luc-mRNA	S5
2.8 Luminescence Characterization for <i>In Vivo</i> Transfection Experiments	S5
2.9 <i>In Vivo</i> mRNA Delivery in Mice with DNPs.....	S6
2.10 Molecular Modelling.....	S6
3. Synthesis	S7
3.1 Synthesis of Nonane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S7
3.2 Synthesis of Dodecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains.....	S26
3.3 Synthesis of Tetradecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S42
3.4 Synthesis of Hexadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains.....	S52
3.5 Synthesis of Heptadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S67
3.6 Synthesis of Octadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S78
3.7 Synthesis of Undecane and Pentadecane Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S88
3.8 Synthesis of Tridecane Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S93
3.9 Synthesis of IAJD131	S107
3.10 Synthesis of Decane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains	S109
3.11 Synthesis of IAJDs with 3,5-symmetric Alkyl Chains	S116
4. DLS Data of DNPs Co-Assembled from IAJDs and Luc-mRNA	S143
5. pK_a Measurements of Individual IAJD Molecules	S153
6. Supporting References.....	S166

1. Materials

3,5-Dihydroxybenzoic acid (Acros, 97%), 1-bromononane (Lancaster, 99%), 1-bromododecane (Alfa Aesar, 99%), 1-bromotetradecane (Acros, 98%), 1-bromohexadecane (TCI, 96%), 1-heptadecanol (TCI, 97%) (*rac*)-3-(bromomethyl)heptane, 1-bromooctadecane (Acros, 96%), 2-ethylhexyl bromide, (Aldrich, 95%), 1-bromooctane (Aldrich, 99%), 1-bromodecane (Acros, 98%), 1-bromoundecane (Aldrich, 99%), 1-bromopentadecane (Aldrich, 98%), benzyl chloride (Alfa Aesar, 99%), 4-toluenesulfonyl chloride (Alfa Aesar, 98%), palladium on activated carbon catalyst (Spectrum, 10 wt% loading), lithium aluminium hydride (LiAlH_4 , TCI, 95%), 4-bromobutyric acid (Acros, 98%), thionyl chloride (Alfa Aesar, 99+%), potassium phthalimide (Chem Impex, 99.8%), 1-methylpiperazine (Alfa Aesar, 98%), 1-(2-hydroxyethyl)piperazine (Acros, 99%), triethylamine (TCI, 99%) were used as received. All other reagents and solvents were obtained from commercial sources and were used as received. CH_2Cl_2 (DCM) was dried over CaH_2 and distilled before use. 4-(Dimethylamino)pyridinium 4-toluenesulfonate (DPTS) was prepared according to a literature method.^[1] Acetate buffer (10 mM) was prepared by dissolving sodium acetate (2.3 mM) and acetic acid (7.7 mM) in ultra-pure water. Final pH of the buffer was adjusted with 0.1 M HCl or 0.1 M NaOH solution. Nucleoside-modified messenger RNA encoding firefly luciferase (Luc-mRNA) was produced as reported.^[2] Human embryonic kidney (HEK) 293T cells (American Type Culture Collection) were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% inactivated fetal bovine serum (FBS) (Gemini Bio-Products), 2 mM L-glutamine and 100 U/mL penicillin/streptomycin (Life Technologies). DPBS (Corning), OptiMEM (Gibco), UltraPure DNase/RNase-Free Distilled Water (Invitrogen), Trypsin-EDTA (0.25%, Gibco), Trypan Blue (Sigma-Aldrich), Cell Culture Lysis 5X Reagent (Promega), Luciferase Assay System (Promega) and D-luciferin sodium salt (Regis Technologies) were used as received.

2. Methods and Techniques

The purity and structure of intermediate compounds and final products were determined by a combination of techniques including thin-layer chromatography (TLC), ^1H and ^{13}C NMR, high-pressure liquid chromatography (HPLC), and matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry.

2.1 ^1H and ^{13}C NMR. ^[3,4,5] ^1H and ^{13}C NMR spectra were recorded at 400 MHz and 101 MHz respectively, on a Bruker NEO (400 MHz) NMR spectrometer equipped with an autosampler, or 500 MHz

and 126 MHz respectively, on a Bruker DRX (500 MHz) NMR spectrometer. All NMR were measured at 23 °C in CDCl₃. Chemical shifts (δ) are reported in ppm. The resonance multiplicities in the ¹H NMR spectra are indicated as “s” (singlet), “d” (doublet), “t” (triplet), “m” (multiplet) and “br” (broad resonance). Residual protic solvent of CDCl₃ (¹H, δ 7.26 ppm; ¹³C, δ 77.16 ppm) and tetramethylsilane (TMS, δ 0 ppm) are used as the internal reference in the ¹H and ¹³C NMR spectra. NMR spectra were analyzed by MNova 14 or TopSpin 4.07 (Bruker).

2.2 Thin-Layer Chromatography (TLC).^[3,4,5] TLC was used to monitor the evolution of the extent of reaction by using silica gel 60 F₂₅₄ precoated plates (E. Merck). Individual compounds with aromatic groups were visualized by UV light (λ = 254 nm). For compounds without aromatic groups, the TLC plate was stained with iodine vapor to help visualization. Purification by flash column chromatography (SiO₂) was performed using silica gel from Silicycle (60 Å, 40–63 μ m) with the eluent mentioned in the experimental part for each compound in part.

2.3 High-Pressure Liquid Chromatography (HPLC).^[3,4,5] The determination of the purity of individual compounds by HPLC was performed by using a Shimadzu LC-20AD high-performance liquid chromatograph pump, a PE Nelson Analytical 900 Series integration data station, a Shimadzu SPD-10A VP (UV-vis, λ = 254 nm) and three AM gel columns (a guard column, two 500 Å, 10 μ m columns). THF with 5% of NEt₃ was used as the solvent and the characterization was carried out at 23 °C. Detection of compounds was determined by UV absorbance (λ = 254 nm) or RI (refractive index) detector.

2.4 Matrix Assisted Laser Desorption Ionization-Time of Flight (MALDI-TOF) Mass Spectrometry.

^[3,4,5] The molar mass of all molecules was determined by MALDI-TOF mass spectrometry employing a PerSeptive Biosystem-Voyager-DE (Framingham, MA) mass spectrometer equipped with nitrogen laser (337 nm) and operating in linear mode. Angiotensin II and Bombesin were used as standards for calibration. For the preparation of sample solution, the corresponding compound was first dissolved in THF (5–10 mg/mL). Subsequently, the matrix (2,5-dihydroxybenzoic acid) was dissolved in THF 10 mg/mL and the two solutions were mixed with a 1/5 (v/v, compound solution/matrix solution) ratio. Then one drop of solution was placed on the MALDI plate and dried at 23 °C. Afterwards, the plate was inserted into the vacuum chamber of the instrument for analysis. The laser intensity and voltages applied for the analysis were adjusted based on the molar mass and nature of each compound.

2.5 Dynamic Light Scattering (DLS).^[3,4,5] DLS for the dimensions (sizes and polydispersities) of DNPs was performed on a Malvern Instruments particle sizer (Zetasizer Nano S, Malvern Instruments, UK) equipped with 4 mW He–Ne laser 633 nm and avalanche photodiode positioned at 175° to the beam and temperature-controlled cuvette holder. Instrument parameters were set up automatically along with measurement times. Sample solution (c.a. 0.4 mL) was placed in a semi-micro cuvette (1.6 mL, polystyrene, 10 × 10 × 45 mm, Greiner Bio-One) and the experiments were performed at 23 °C.

2.6 pKa Measurements of Individual IAJDs.^[3,4,5] IAJDs were dissolved in ethanol (sat. with NaCl) at a concentration of 1.5 mg/mL and in a volume of 3 mL. Then 0.1 M HCl solution was added to the ethanol solution with an increment of 7.5 µL. The resulting pH, after each addition of HCl solution, was measured by an Thermo Scientific Orion Star A121 meter with Thermo Scientific Orion 8220BNWP pH probe. pK_a was determined using the half equivalence point titration.

2.7 Formulation of DNPs Co-assembled from IAJDs and Luc-mRNA.^[3,4,5] Nucleoside-modified mRNA encoding firefly luciferase (Luc-mRNA) was dissolved in UltraPure DNase/RNase-free distilled water with an initial concentration of 4.0 mg/mL. IAJDs were dissolved in ethanol at an initial concentration of 80 mg/mL. Luc-mRNA solution (12.5 µL) was placed into a clean RNAs free eppendorf (1.5 mL and 463 µL of acetate buffer (10 mM, pH 4.0) was added. IAJD stock solution in ethanol was taken (25 µL) and rapidly injected into the above Luc-mRNA solution in acetate buffer followed by vortex for 5 seconds.

2.8 Luminescence Characterization for *In Vivo* Transfection Experiments.^[3,4,5] Bioluminescence imaging was performed with an IVIS Spectrum imaging system (PerkinElmer, Waltham, MA). Mice were anesthetized with 3% of isoflurane (Piramal Healthcare Limited) and intraperitoneally (i.p.) administered with D-luciferin (Regis Technologies) at a dose of 150 mg/kg of body weight. Ten min post administration of D-luciferin, mice were placed on the imaging platform while being maintained on isoflurane *via* a nose cone and imaged using a certain exposure time (60, 30, or 15 seconds). Bioluminescence values were quantified by measuring photon flux (photons/second, p/s) in the region of interest (ROI) on mice where bioluminescence signal emanated using the Living Image Software (PerkinElmer). To quantify luminescent flux, an oval ROI was placed over each organ of interest and analyzed.

2.8 Production of nucleoside-modified Luc-mRNA mRNA was produced as previously described^[2] using T7 RNA polymerase on linearized DNA encoding codon-optimized Firefly Luciferase and a 101nt poly(A) tail. 1-methylpseudouridine-5'-triphosphate was used instead of UTP. A trinucleotide cap1 analog was added cotranscriptionally. Purification was performed as previously described.^[6] mRNA was analyzed for RNase, dsRNA, endotoxin, and other forms of contamination and stored frozen at -20°C.

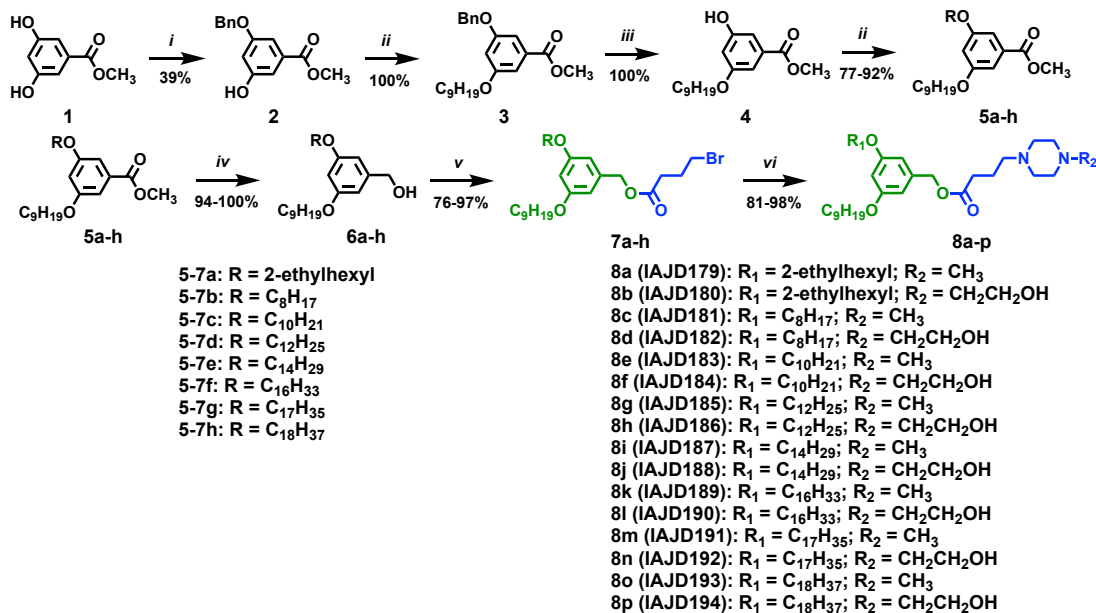
2.9 *In Vivo* mRNA Delivery in Mice with DNPs. ^[3,4,5] All mice used were in accordance with the guidelines and approval from the Pennsylvania University Institution of Animal Care and Use Committee. Female or male BALB/c mice (6-8 weeks old, from Charles River Laboratories) were anesthetized with isoflurane (Piramal Healthcare Limited) and injected *via* retro-orbital sinus with 100 µL of DNP solution containing 10 µg of Luc-mRNA. After 4 to 6 hours post injection, mice were i.p. injected with D-Luciferin (150 mg/kg of body weight, Regis Technologies) and imaged on a PerkinElmer IVIS Spectrum CT system (PerkinElmer, Waltham, MA). Tissue luminescence signal was measured on the IVIS imaging system using a certain exposure time (60, 30 or 15 seconds) and medium binning (binning = 8) to ensure that the signal obtained was within operative detection range. For IVIS imaging of the organs, mice were sacrificed, and heart, lungs, liver, and spleen were immediately collected, and bioluminescence imaging was performed as described above. Image analysis was conducted with the Living Image software (PerkinElmer). Bioluminescence values were quantified by measuring photon flux (photons/second) in the region of interest (ROI) using Living Image software.

2.10 Molecular Modelling. Molecular models of the IAJD bilayers were drawn using DS ViewerPro (version 5.0) software. Material Studio Modeling (version 3.1) software from Accelrys was used to perform the energy minimizations of the built models on the supramolecular structures. BIOVIA Discovery Studio Visualizer (version 2019) was used for display style and coloring. Color codes were used as in the ChemDraw structure (hydrophilic part in blue; hydrophobic part in light and dark green; oxygen and OH in pink; carbons in aromatic ring in gray; H groups on aromatic in white).

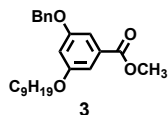
3. Synthesis

3.1 Synthesis of Nonane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

Scheme S1. Synthesis of Nonane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

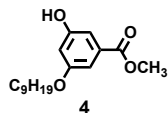


Reagents and conditions: (i) K₂CO₃, KI, DMF, 80 °C, 5 h; (ii) RBr/ROTs, K₂CO₃, DMF, 120 °C, 2 h; (iii) H₂, Pd/C, DCM, MeOH, 12 h; (iv) LiAlH₄, THF, 0–23 °C, 1 h; (v) DCC, DPTS, DCM, 12 h; (vi) K₂CO₃, MeCN, 95 °C, 3 h.

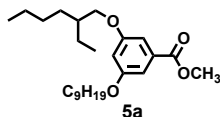


Methyl 3-(benzyloxy)-5-(nonyloxy)benzoate (3). The synthesis of methyl 3-(benzyloxy)-5-hydroxybenzoate (**2**) was adapted from literature procedures reported by our laboratory.^[3] A mixture of compound **2** (6.50 g, 25.17 mmol, 1 equiv), 1-bromononane (5.74 g, 27.68 mmol, 1.1 equiv), K₂CO₃ (6.96 g, 50.34 mmol, 2 equiv) and DMF (35 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (7.53 g, 78%). ¹H NMR (400 MHz, CDCl₃) δ 7.48–7.31 (m, 5 H, PhH), 7.28 (br, 1 H, PhH), 7.22 (br, 1 H, PhH), 6.74 (t, 1 H, PhH), 5.08 (s, 2 H, PhCH₂O-), 3.97 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.78 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃), 1.45 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃), 1.27 (m, 10 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.89 (t, 3 H, PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 161.3, 160.3, 159.9, 136.7, 132.1, 128.7, 128.2,

127.7, 108.3, 107.9, 107.0, 77.4, 70.3, 68.5, 64.2, 52.3, 32.0, 29.6, 29.5, 29.4, 29.3, 28.6, 26.1, 25.9, 22.8, 14.2. Mp = 31 °C.

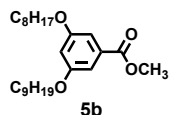


Methyl 3-hydroxy-5-(nonyloxy)benzoate (4). Compound **3** (7.53 g, 19.58 mmol) was dissolved in a mixture of DCM (40 mL) and methanol (20 mL). Then Pd/C (0.38 g, 5 wt%) was added to the solution and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at 23 °C under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (5.46 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 7.12 (d, 2 H, PhH), 6.64 (t, 1 H, PhH), 5.99 (s, 1 H, PhOH), 3.93 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.74 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃), 1.41 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃), 1.27 (m, 10 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 3 H, PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 161.9, 160.5, 157.2, 131.7, 109.3, 107.8, 107.4, 68.5, 52.5, 32.6, 32.0, 31.9, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 28.9, 26.1, 22.8, 14.2. Mp = 85 °C.

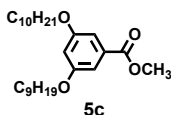


Methyl 3-((2-ethylhexyl)oxy)-5-(nonyloxy)benzoate (5a). A mixture of compound **4** (0.70 g, 2.38 mmol, 1 equiv), 2-ethylhexyl bromide (0.51 g, 2.66 mmol, 1.1 equiv), K₂CO₃ (0.66 g, 4.76 mmol, 2 equiv) and DMF (15 mL) was heated to 80 °C and stirred under N₂ atmosphere for 12 h. The reaction mixture was cooled to 23 °C and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/EtOAc = 20/1 as the eluent to give the title compound as a light-yellow oil (0.61 g, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.97 (t, 2 H, PhOCH₂(CH₂)₁₃CH₃), 3.89 (s, 3 H, PhCOOCH₃), 3.85 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 1.86–1.65 (m, 3 H, PhOCH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.57–1.18 (m, 20 H, PhOCH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.00–0.82 (m, 9 H, PhO(CH₂)₈CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.6, 160.3, 131.9, 107.9,

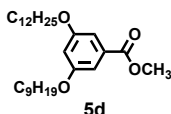
107.6, 106.7, 70.9, 68.4, 52.3, 39.5, 32.0, 30.7, 29.7, 29.5, 29.4, 29.3, 29.2, 26.2, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.



Methyl 3-(octyloxy)-5-(nonyloxy)benzoate (5b). A mixture of compound **4** (0.70 g, 2.38 mmol, 1 equiv), 1-bromooctane (0.51 g, 2.66 mmol, 1.1 equiv), K₂CO₃ (0.66 g, 4.76 mmol, 2 equiv) and DMF (10 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.64 g, 66%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 18 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.0, 29.7, 29.5, 29.5, 29.4, 29.4, 29.3, 26.2, 22.8, 14.2. Mp = 36 °C.

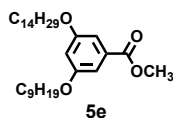


Methyl 3-(dectyloxy)-5-(nonyloxy)benzoate (5c). Compound **5c** was synthesized from compound **4** (0.70 g, 2.38 mmol, 1 equiv), 1-bromodecane (0.58 g, 2.66 mmol, 1.1 equiv) and K₂CO₃ (0.66 g, 4.76 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **5b**. The title compound was obtained as a white solid (0.68 g, 66%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 22 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 131.9, 107.8, 106.7, 68.4, 52.3, 32.0, 32.0, 29.7, 29.7, 29.7, 29.5, 29.4, 29.4, 29.3, 26.1, 22.8, 14.2. Mp = 41 °C.

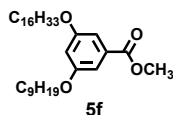


Methyl 3-(dodecylloxy)-5-(nonyloxy)benzoate (5d). Compound **5d** was synthesized from compound **4** (0.70 g, 2.38 mmol, 1 equiv), 1-bromododecane (0.63 g, 2.66 mmol, 1.1 equiv) and K₂CO₃ (0.66 g, 4.76 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **5b**. The title

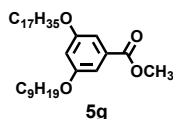
compound was obtained as a white solid (0.74 g, 67%). ^1H NMR (400 MHz, CDCl_3) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.45 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 26 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.4, 29.3, 26.2, 22.8, 14.2. Mp = 48 °C.



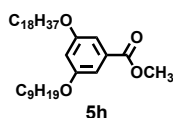
Methyl 3-(nonyloxy)-5-(tetradecyloxy)benzoate (5e). Compound **5e** was synthesized from compound **4** (0.70 g, 2.38 mmol, 1 equiv), 1-bromotetradecane (727 mg, 2.62 mmol, 1.1 equiv) and K_2CO_3 (0.66 g, 4.76 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **5b**. The title compound was obtained as a white solid (1.05 g, 90%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 30 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.0, 160.2, 131.8, 107.7, 106.6, 77.4, 68.3, 52.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 26.2, 25.9, 22.7, 22.7, 14.2. Mp = 53 °C.



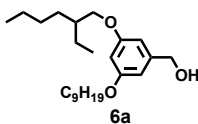
Methyl 3-(hexadecyloxy)-5-(nonyloxy)benzoate (5f). Compound **5f** was synthesized from compound **4** (0.70 g, 2.38 mmol, 1 equiv), 1-bromohexadecane (0.80 g, 2.66 mmol, 1.1 equiv) and K_2CO_3 (0.66 g, 4.76 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **5b**. The title compound was obtained as a white solid (1.24 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 34 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 26.2, 25.9, 22.8, 22.8, 14.3. Mp = 55 °C.



Methyl 3-(heptadecyloxy)-5-(nonyloxy)benzoate (5g). Heptadecyl 4-methylbenzenesulfonate ($C_{17}H_{35}OTs$) was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **5g** was synthesized from compound **4** (0.70 g, 2.38 mmol, 1 equiv), $C_{17}H_{35}OTs$ (1.08 g, 2.66 mmol, 1.1 equiv) and K_2CO_3 (0.66 g, 4.76 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **5b**. The title compound was obtained as a white solid (1.05 g, 83%). 1H NMR (400 MHz, $CDCl_3$) δ 7.15 (br, 2 H, *PhH*), 6.63 (t, 1 H, *PhH*), 3.96 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.77 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (m, 36 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.88 (t, 6 H, $PhO(CH_2)_{16}CH_3$ and $PhO(CH_2)_8CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 63.1, 52.3, 32.9, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 26.2, 22.8, 22.8, 14.3. M_p = 58 °C.

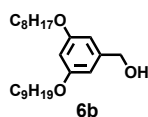


Methyl 3-(octadecyloxy)-5-(nonyloxy)benzoate (5h). Compound **5h** was synthesized from compound **4** (0.63 g, 1.50 mmol, 1 equiv), 1-bromooctadecanene (0.34 g, 1.65 mmol, 1.1 equiv) and K_2CO_3 (0.42 g, 3.00 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **5b**. The title compound was obtained as a white solid (0.76 g, 94%). 1H NMR (400 MHz, $CDCl_3$) δ 7.16 (br, 2 H, *PhH*), 6.63 (t, 1 H, *PhH*), 3.97 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.77 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.45 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (m, 38 H, $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.89 (t, 6 H, $PhO(CH_2)_{17}CH_3$ and $PhO(CH_2)_8CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 32.0, 29.8, 29.7, 29.7, 29.5, 29.4, 29.3, 26.2, 22.8, 22.8, 14.2. M_p = 60 °C.

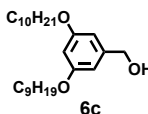


(3-(2-Ethylhexyloxy)-5-(nonyloxy)phenyl)methanol (6a). Compound **5a** (0.61 g, 1.50 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of $LiAlH_4$ (57 mg, 1.50 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N_2 atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered

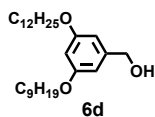
out. The filtrate was dried over anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.52 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (d, 2 H, PhH), 6.38 (t, 1H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.95 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_7\text{CH}_3$), 3.82 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)-$), 1.83–1.62 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.60–1.20 (m, 20 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 0.91 (m, 9 H, $\text{PhO}(\text{CH}_2)_8\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.9, 160.7, 143.3, 107.9, 105.3, 105.2, 105.1, 100.7, 70.7, 68.5, 68.2, 65.6, 39.5, 32.9, 32.0, 30.7, 30.5, 29.7, 29.6, 29.5, 29.5, 29.4, 29.4, 29.2, 26.2, 25.9, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.



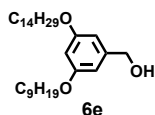
(3-(Octyloxy)-5-(nonyloxy)phenyl)methanol (6b). Compound **6b** was synthesized from compound **5b** (0.68 g, 1.48 mmol, 1 equiv) and LiAlH_4 (56 mg, 1.48 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a colorless oil (0.53 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 18 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 160.7, 143.3, 105.2, 100.7, 68.2, 65.6, 32.0, 32.0, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 14.2.



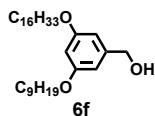
(3-(Decyloxy)-5-(nonyloxy)phenyl)methanol (6c). Compound **6c** was synthesized from compound **5c** (0.68 g, 1.56 mmol, 1 equiv) and LiAlH_4 (60 mg, 1.56 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a colorless oil (0.54 g, 85%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 22 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 143.4, 105.2, 100.7, 77.4, 68.2, 65.5, 65.5, 32.0, 32.0, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 14.2.



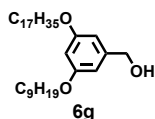
(3-(Decyloxy)-5-(nonyloxy)phenyl)methanol (6d). Compound **6d** was synthesized from compound **5d** (0.71 g, 1.53 mmol, 1 equiv) and LiAlH₄ (59 mg, 1.53 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a colorless oil (0.58 g, 87%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 26 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₁CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 143.3, 105.2, 100.7, 77.5, 77.4, 77.2, 76.8, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 14.2.



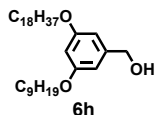
(3-(Nonyloxy)-5-(tetradecyloxy)phenyl)methanol (6e). Compound **6e** was synthesized from compound **5e** (0.60 g, 0.22 mmol, 1 equiv) and LiAlH₄ (46 mg, 1.22 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a colorless oil (0.55 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 30 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₃CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.6, 143.2, 105.1, 100.6, 77.4, 77.4, 77.0, 76.7, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.4, 29.3, 26.1, 22.7, 22.7, 14.2.



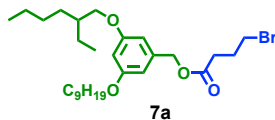
(3-(hexadecyloxy)-5-(nonyloxy)phenyl)methanol (6f). Compound **6f** was synthesized from compound **5f** (1.7 g, 2.25 mmol, 1 equiv) and LiAlH₄ (85 mg, 2.25 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a colorless oil (1.10 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.51 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 34 H, PhOCH₂CH₂CH₂(CH₂)₁₂CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₅CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.6, 143.2, 105.1, 100.6, 77.4, 77.4, 77.0, 76.7, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.4, 29.3, 26.1, 22.7, 22.7, 14.2.



(3-(Heptadecyloxy)-5-(nonyloxy)phenyl)methanol (6g). Compound **6g** was synthesized from compound **5g** (1.01 g, 1.90 mmol, 1 equiv) and LiAlH_4 (44 mg, 1.90 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a white solid (0.91 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 22 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.5, 63.2, 32.9, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 25.9, 22.8, 22.8, 14.2. Mp = 40 °C.

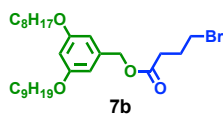


(3-(Octadecyloxy)-5-(nonyloxy)phenyl)methanol (6h). Compound **6h** was synthesized from compound **5h** (0.75 g, 1.14 mmol, 1 equiv) and LiAlH_4 (44 mg, 1.14 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **6a**. The title compound was obtained as a white solid (0.51 g, 97%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 22 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.3, 105.2, 100.7, 68.2, 65.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 14.2. Mp = 41 °C.

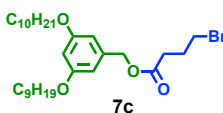


(3-(2-Ethylhexyl)oxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7a). Compound **6a** (0.50 g, 1.33 mmol, 1 equiv), 4-bromobutyric acid (0.33 g, 1.98 mmol, 1.5 equiv) and DPTS (0.58 g, 1.98 mmol, 1.5 equiv) were dissolved in 10 mL DCM. *N,N'*-Dicyclohexylcarbodiimide (DCC, 0.82 g, 3.96 mmol, 3 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/DCM = 1/1 as the mobile phase to give

the title compound as a colorless oil (0.52 g, 75%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (d, 2 H, PhH), 6.41 (t, 1H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_7\text{CH}_3$), 3.82 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.87–1.67 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.57–1.21 (m, 20 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 0.91 (m, 9 H, $\text{PhO}(\text{CH}_2)_8\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.9, 160.6, 137.9, 106.6, 106.4, 101.2, 70.7, 68.2, 66.6, 39.5, 32.8, 32.6, 32.0, 30.7, 29.7, 29.5, 29.5, 29.4, 29.2, 27.9, 26.2, 24.0, 23.2, 22.8, 14.2, 14.2, 11.3.

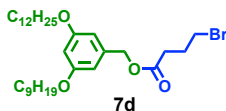


3-(Octyloxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7b). Compound **7b** was synthesized from compound **6b** (0.51 g, 1.35 mmol, 1 equiv), 4-bromobutyric acid (0.34 g, 2.02 mmol, 1.5 equiv), DPTS (0.60 g, 2.02 mmol, 1.5 equiv) and DCC (0.84 g, 4.05 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.70 g, 98%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 18 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 32.7, 32.6, 32.0, 32.0, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.2.

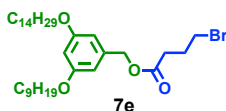


3-(Dectyloxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7c). Compound **7c** was synthesized from compound **6c** (0.52 g, 1.27 mmol, 1 equiv), 4-bromobutyric acid (0.30 g, 1.90 mmol, 1.5 equiv), DPTS (0.53 g, 1.90 mmol, 1.5 equiv) and DCC (0.75 g, 3.80 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.61 g, 92%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 22 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H,

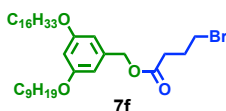
PhO(CH₂)₉CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.5, 32.8, 32.6, 32.0, 32.0, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.2.



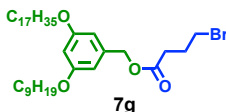
3-(Dodecetoxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7d). Compound **7d** was synthesized from compound **6d** (0.60 g, 1.30 mmol, 1 equiv), 4-bromobutyric acid (0.54 g, 1.86 mmol, 1.5 equiv), DPTS (0.55 g, 1.86 mmol, 1.5 equiv) and DCC (0.71 g, 3.42 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.74 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 26 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₁CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.5, 64.9, 32.7, 32.6, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 28.7, 27.9, 26.2, 26.0, 22.8, 22.8, 14.2.



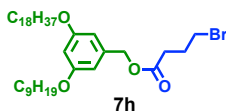
3-(Nonyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (7e). Compound **7e** was synthesized from compound **6e** (0.55 g, 1.19 mmol, 1 equiv), 4-bromobutyric acid (297 g, 1.78 mmol, 1.5 equiv), DPTS (382 mg, 1.78 mmol, 1.5 equiv) and DCC (737 mg, 3.57 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.43 g, 59%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.44 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.55 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 30 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₃CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.5, 137.8, 106.4, 101.2, 68.1, 66.4, 32.6, 32.5, 31.9, 31.8, 29.6, 29.6, 29.4, 29.4, 29.4, 29.3, 29.3, 27.8, 26.1, 22.7, 22.7, 14.1.



3-(Hexadecyloxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7f). Compound **7f** was synthesized from compound **6f** (0.55 g, 1.02 mmol, 1 equiv), 4-bromobutyric acid (256 g, 1.53 mmol, 1.5 equiv), DPTS (450 mg, 1.53 mmol, 1.5 equiv) and DCC (631 mg, 3.06 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.53 g, 83%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂OCO), 3.92 (t, 4 H, PhOCH₂CH₂CH₂-), 3.44 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.55 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.24 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.37 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 34 H, PhOCH₂CH₂CH₂(CH₂)₁₂CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₃CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.5, 137.8, 106.4, 101.2, 68.1, 66.4, 32.6, 32.5, 31.9, 31.8, 29.6, 29.6, 29.4, 29.4, 29.4, 29.3, 29.3, 27.8, 26.1, 22.7, 22.7, 14.1.

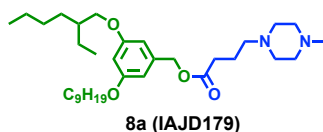


3-(Heptectyloxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7g). Compound **7g** was synthesized from compound **6g** (0.45 g, 0.89 mmol, 1 equiv), 4-bromobutyric acid (0.23 g, 1.34 mmol, 1.5 equiv), DPTS (0.38 g, 1.34 mmol, 1.5 equiv) and DCC (0.55 g, 2.67 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.60 g, 75%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 36 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₆CH₃ and PhO(CH₂)₈CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.6, 64.9, 32.9, 32.8, 32.7, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 28.8, 28.0, 27.9, 26.2, 26.1, 22.8, 22.8, 14.3.

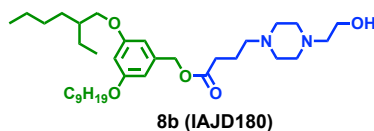


3-(Octadecyloxy)-5-(nonyloxy)benzyl 4-bromobutanoate (7h). Compound **7h** was synthesized from compound **6h** (0.36 g, 0.68 mmol, 1 equiv), 4-bromobutyric acid (0.17 g, 1.04 mmol, 1.5 equiv), DPTS (0.31 g, 1.04 mmol, 1.5 equiv) and DCC (0.43 g, 2.08 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **7a**. The title compound was obtained as a colorless oil (0.46 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH₂OCO),

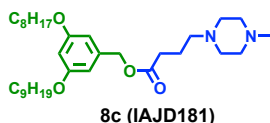
3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.46 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 38 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.6, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 22.8, 14.3.



3-((2-Ethylhexyl)oxy)-5-(nonyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8a, IAJD179). A mixture of compound **7a** (0.26 g, 0.50 mmol, 1.0 equiv), 1-methylpiperazine (60 mg, 0.60 mmol, 1.2 equiv), K_2CO_3 (83 mg, 0.60 mmol, 1.2 equiv) and MeCN (15 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO_4 . After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO_3 solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO_4 . Filtration and evaporation of the solvent yielded the title compound as a light-yellow oil (0.25 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.03 (s, 2 H, PhCH_2-), 3.92 (t, 4 H, PhOCH_2-), 3.81 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)-$), 2.70–2.16 (m, 15 H, $-\text{N}(\text{CH}_2\text{CH}_2)_2\text{N}-$, $-\text{NCH}_2\text{CH}_2\text{CH}_2\text{COO}-$ and $-\text{NCH}_3$), 1.82 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2-$), 1.79–1.64 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.55–1.14 (m, 20 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 0.88 (m, 9 H, $\text{PhO}(\text{CH}_2)_8\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 173.5, 160.7, 160.6, 138.2, 106.6, 106.4, 101.0, 70.7, 68.2, 66.3, 57.7, 55.3, 53.3, 46.2, 39.5, 32.4, 32.0, 30.7, 29.8, 29.7, 29.5, 29.4, 29.2, 26.2, 24.0, 23.4, 22.8, 22.4, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{33}\text{H}_{59}\text{N}_2\text{O}_4$: 547.4; Found: 547.6.



3-((2-Ethylhexyl)oxy)-5-(nonyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8b, IAJD180). Compound **8b** was synthesized from compound **7a** (0.26 g, 0.50 mmol), 1-(2-hydroxyethyl)piperazine (78 mg, 0.60 mmol) and K_2CO_3 (83 mg, 0.60 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.21 g, 72%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.40 (t, 1 H, *PhH*), 5.03 (s, 2 H, *PhCH*₂-), 3.92 (t, 4 H, *PhOCH*₂-), 3.81 (m, 2 H, *PhOCH*₂*CH*(*CH*₂*CH*₃)-), 3.60 (t, 2 H, -*CH*₂*CH*₂*OH*), 2.82–2.16 (m, 14 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₂-), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 3 H, *PhOCH*₂*CH*₂(*CH*₂)₆*CH*₃ and *PhOCH*₂*CH*(*CH*₂*CH*₃)(*CH*₂)₃*CH*₃), 1.56–1.17 (m, 20 H, *PhOCH*₂*CH*₂(*CH*₂)₆*CH*₃ and *PhOCH*₂*CH*(*CH*₂*CH*₃)(*CH*₂)₃*CH*₃), 0.88 (m, 9 H, *PhO*(*CH*₂)₈*CH*₃ and *PhOCH*₂*CH*(*CH*₂*CH*₃)(*CH*₂)₃*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 160.7, 160.6, 138.2, 106.6, 106.5, 101.0, 70.7, 68.2, 66.3, 59.3, 57.8, 57.7, 53.3, 53.0, 39.5, 32.4, 32.0, 30.7, 29.8, 29.7, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 22.3, 14.2, 14.2, 11.3. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [*M* + *H*]⁺ calculated for $C_{34}H_{61}N_2O_5$: 577.5; Found: 577.2.

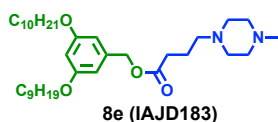


3-(Nonyloxy)-5-(octyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8c, IAJD181). Compound **8c** was synthesized from compound **7b** (0.30 g, 0.57 mmol), 1-methylpiperazine (85 mg, 0.61 mmol) and K_2CO_3 (95 mg, 0.68 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.28 g, 90%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.67–2.21 (m, 15 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.84 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.42 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.28 (br, 18 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₄*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₅*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.1, 57.5, 55.0, 52.8, 45.8, 32.2, 31.9, 31.8, 29.5, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [*M* + *H*]⁺ calculated for $C_{33}H_{59}N_2O_4$: 547.4; Found: 548.5.

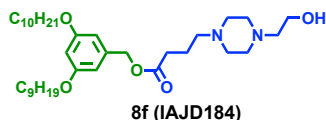


3-(Nonyloxy)-5-(octyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8d, IAJD182). Compound **8d** was synthesized from compound **7b** (0.38 g, 0.72 mmol), 1-(2-hydroxyethyl)piperazine

(141 mg, 1.08 mmol) and K_2CO_3 (119 mg, 0.86 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.30 g, 72%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.61 (t, 2 H, $-CH_2CH_2OH$), 2.62–2.31 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.75 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 18 H, $PhOCH_2CH_2CH_2(CH_2)_4CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.89 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.8, 32.2, 31.9, 31.8, 29.5, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{34}H_{61}N_2O_5$: 577.5; Found: 578.3.

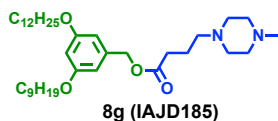


3-(Decyloxy)-5-(nonyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8e, IAJD183). Compound **8e** was synthesized from compound **7c** (0.30 g, 0.54 mmol), 1-methylpiperazine (81 mg, 0.81 mmol) and K_2CO_3 (90 mg, 0.68 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless (0.30 g, 97%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 2.67–2.21 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.82 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.74 (m, 4 H, $PhOCH_2CH_2-$), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 22 H, $PhOCH_2CH_2CH_2(CH_2)_6CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 160.4, 138.0, 106.4, 100.9, 77.4, 77.1, 76.8, 68.0, 66.1, 59.5, 57.7, 57.5, 52.9, 32.1, 31.9, 31.9, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 26.0, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{35}H_{63}N_2O_4$: 575.5; Found: 576.2.

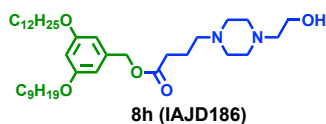


3-(Decyloxy)-5-(nonyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8f, IAJD184). Compound **8f** was synthesized from compound **7c** (0.30 g, 0.54 mmol), 1-(2-hydroxyethyl)piperazine (105 mg, 0.81 mmol) and K_2CO_3 (90 mg, 0.65 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.30 g, 95%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.61 (t, 2 H, $-CH_2CH_2OH$), 2.65–2.25 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$),

1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 22 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.4, 138.1, 106.3, 100.8, 68.0, 66.1, 57.4, 54.9, 52.7, 45.7, 32.1, 31.9, 31.8, 29.5, 29.5, 29.5, 29.4, 29.3, 29.2, 26.0, 22.6, 22.0, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₆H₆₅N₂O₅: 605.5; Found: 606.2.

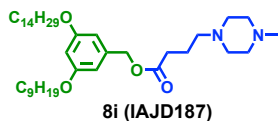


3-(Dodecyloxy)-5-(nonyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8g, IAJD185). Compound **8g** was synthesized from compound **7d** (0.37 g, 0.63 mmol), 1-methylpiperazine (68 mg, 0.68 mmol) and K₂CO₃ (128 mg, 0.92 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless (0.35 g, 92%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.63–2.25 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.74 (m, 4 H, PhOCH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 26 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 57.5, 55.0, 52.8, 45.8, 32.2, 31.9, 31.9, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₇H₆₇N₂O₄: 603.5; Found: 604.4.



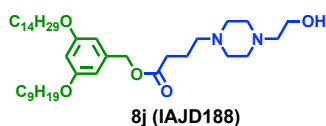
3-(Dodecyloxy)-5-(nonyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8h, IAJD186). Compound **8h** was synthesized from compound **7d** (0.30 g, 0.51 mmol), 1-(2-hydroxyethyl)piperazine (73 mg, 0.56 mmol) and K₂CO₃ (90 mg, 0.65 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.29 g, 91%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.61 (t, 2 H, -CH₂CH₂OH), 2.68–2.21 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 26 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.4, 138.1, 106.3, 100.9, 68.0, 66.1, 57.4, 54.9, 52.8, 45.7, 32.1, 31.9,

31.7, 29.6, 29.5, 29.4, 29.4, 29.4, 29.2, 26.0, 22.6, 22.0, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{38}H_{69}N_2O_5$: 633.5; Found: 634.1.



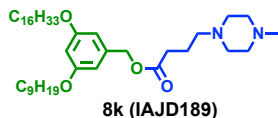
3-(Nonyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8i, IAJD187).

Compound **8i** was synthesized from compound **7e** (0.22 g, 0.35 mmol), 1-methylpiperazine (53 mg, 0.53 mmol) and K_2CO_3 (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless (0.10 g, 46%). 1H NMR (400 MHz, $CDCl_3$) δ 6.48 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, $PhCH_2-$), 3.93 (t, 4 H, $PhOCH_2-$), 2.90–2.18 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.85 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.76 (m, 4 H, $PhOCH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.29 (br, 30 H, $PhOCH_2CH_2CH_2(CH_2)_{10}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 57.4, 54.9, 52.6, 45.7, 32.2, 31.9, 31.9, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 29.2, 26.1, 22.7, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{39}H_{71}N_2O_4$: 631.5; Found: 632.0.



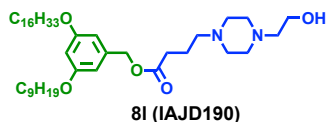
3-(Nonyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8j, IAJD188).

Compound **8j** was synthesized from compound **7e** (0.18 g, 0.30 mmol), 1-(2-hydroxyethyl)piperazine (58 mg, 0.44 mmol) and K_2CO_3 (49 mg, 0.36 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.15 g, 80%). 1H NMR (400 MHz, $CDCl_3$) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.04 (s, 2 H, $PhCH_2-$), 3.93 (t, 4 H, $PhOCH_2-$), 3.64 (t, 2 H, $-CH_2CH_2OH$), 2.59–2.37 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.76 (m, 4 H, $PhOCH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 30 H, $PhOCH_2CH_2CH_2(CH_2)_{10}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.4, 138.1, 106.3, 100.9, 68.0, 66.1, 57.4, 54.9, 52.8, 45.7, 32.1, 31.9, 31.7, 29.6, 29.5, 29.4, 29.4, 29.4, 29.2, 26.0, 22.6, 22.0, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{40}H_{73}N_2O_5$: 661.5; Found: 662.4.



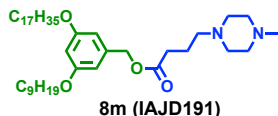
3-(Hexadecyloxy)-5-(nonyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8k, IAJD189).

Compound **8k** was synthesized from compound **7f** (0.27 g, 0.41 mmol), 1-methylpiperazine (46 mg, 0.46 mmol) and K_2CO_3 (86 mg, 0.62 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless (0.26 g, 95%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.62–2.26 (m, 15 H, -N(*CH*₂*CH*₂)₂N-, -N*CH*₂*CH*₂*CH*₂COO- and -N*CH*₃), 1.84 (m, 2 H, -OCO*CH*₂*CH*₂*CH*₂-), 1.75 (m, 4 H, *PhOCH*₂*CH*₂-), 1.44 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.28 (br, 34 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₅*CH*₃), 0.87 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.1, 64.6, 57.5, 57.4, 54.9, 54.9, 52.7, 52.6, 45.7, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 28.7, 26.1, 26.0, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₄₁H₇₅N₂O₄: 659.6; Found: 660.0.



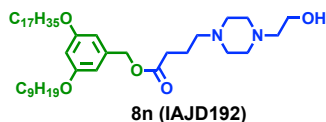
3-(Hexadecyloxy)-5-(nonyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8l, IAJD190).

Compound **8l** was synthesized from compound **7f** (0.25 g, 0.39 mmol), 1-(2-hydroxyethyl)piperazine (77 mg, 0.59 mmol) and K_2CO_3 (65 mg, 0.47 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.24 g, 89%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.01 (s, 2 H, *PhCH*₂-), 3.90 (t, 4 H, *PhOCH*₂-), 3.60 (t, 2H, -*CH*₂*CH*₂OH), 2.63–2.26 (m, 14 H, -N(*CH*₂*CH*₂)₂N-, -N*CH*₂*CH*₂*CH*₂COO- and -*CH*₂*CH*₂OH), 1.83 (m, 2 H, -OCO*CH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.43 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.25 (br, 34 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₅*CH*₃), 0.87 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.4, 138.1, 106.3, 100.8, 68.0, 66.1, 57.4, 54.9, 52.7, 45.7, 32.1, 31.9, 31.8, 29.5, 29.5, 29.5, 29.4, 29.3, 29.2, 26.0, 22.7, 22.1, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₄₂H₇₇N₂O₅: 689.6; Found: 689.9.



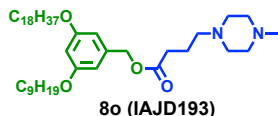
3-(Heptadecyloxy)-5-(nonyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8m, IAJD191).

Compound **8m** was synthesized from compound **7g** (0.26 g, 0.40 mmol), 1-methylpiperazine (42 mg, 0.42 mmol) and K_2CO_3 (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless (0.22 g, 82%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, *PhH*), 6.37 (t, 1 H, *PhH*), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 2.54–2.20 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.82 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.73 (m, 4 H, $PhOCH_2CH_2-$), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (br, 36 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 173.3, 160.4, 138.1, 106.4, 100.9, 68.0, 66.1, 57.6, 55.2, 53.1, 46.1, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{42}H_{77}N_2O_4$: 673.6; Found: 674.1.



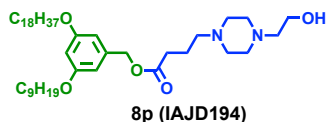
3-(Heptadecyloxy)-5-(nonyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8n, IAJD192).

Compound **8n** was synthesized from compound **7g** (0.26 g, 0.40 mmol), 1-(2-hydroxyethyl)piperazine (55 mg, 0.42 mmol) and K_2CO_3 (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.24 g, 86%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.59 (t, 2H, $-CH_2CH_2OH$), 2.60–2.28 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.74 (m, 4 H, $PhOCH_2CH_2-$), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 36 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.1, 59.2, 57.7, 57.6, 53.2, 52.9, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{43}H_{79}N_2O_5$: 703.6; Found: 703.7.



3-(Nonyloxy)-5-(octadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (8o, IAJD193).

Compound **8o** was synthesized from compound **7h** (0.23 g, 0.35 mmol), 1-methylpiperazine (42 mg, 0.42 mmol) and K₂CO₃ (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless (0.20 g, 84%). ¹H NMR (400 MHz, CDCl₃) δ 6.41 (br, 2 H, PhH), 6.33 (t, 1 H, PhH), 4.97 (s, 2 H, PhCH₂-), 3.85 (t, 4 H, PhOCH₂-), 2.77–2.14 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.77 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.69 (m, 4 H, PhOCH₂CH₂-), 1.39 (m, 4 H, PhOCH₂CH₂CH₂-), 1.21 (br, 38 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.83 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.1, 166.1, 160.4, 138.1, 106.3, 100.8, 77.5, 77.2, 76.9, 68.0, 66.0, 57.4, 55.0, 52.7, 45.8, 32.1, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.0, 22.7, 22.6, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₃H₇₉N₂O₄: 687.6; Found: 688.3.

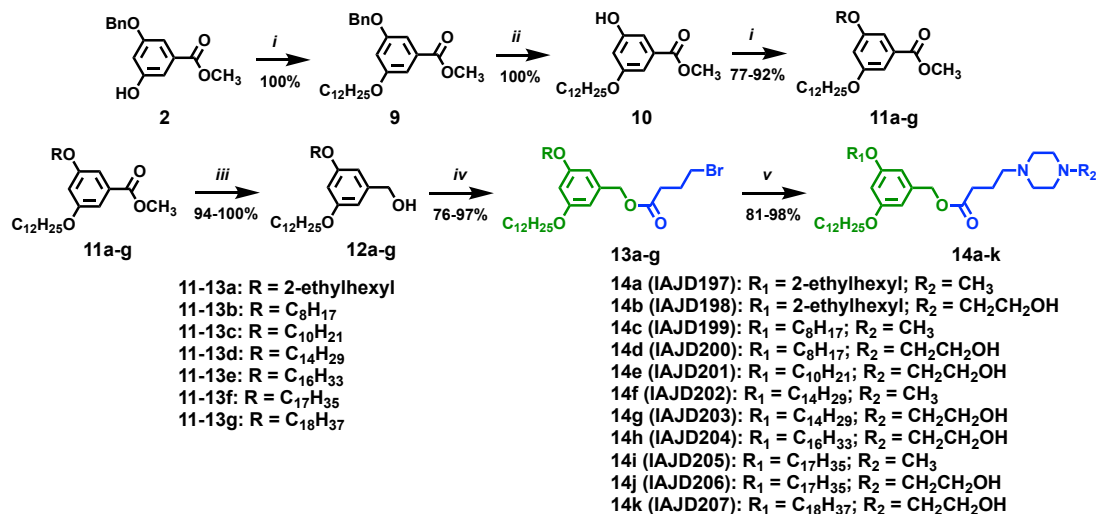


3-(Nonyloxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (8p, IAJD194).

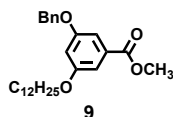
Compound **8p** was synthesized from compound **7h** (0.23 g, 0.35 mmol), 1-(2-hydroxyethyl)piperazine (55 mg, 0.42 mmol) and K₂CO₃ (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **8a**. The title compound was obtained as a colorless oil (0.19 g, 76%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 3.61 (t, 2H, -CH₂CH₂OH), 2.74–2.12 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.82 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.25 (br, 38 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.86 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.5, 101.0, 68.2, 66.2, 59.5, 57.7, 57.6, 53.0, 53.0, 32.3, 32.0, 32.0, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 26.1, 22.8, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₄H₈₁N₂O₅: 717.6; Found: 718.7.

3.2 Synthesis of Dodecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

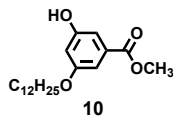
Scheme S2. Synthesis of Dodecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains



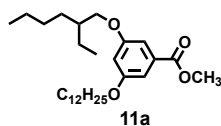
Reagents and conditions: (i) RBr/ROTs, K₂CO₃, DMF, 120 °C, 2 h; (ii) H₂, Pd/C, DCM, MeOH, 12 h; (iii) LiAlH₄, THF, 0–23 °C, 1 h; (iv) DCC, DPTS, DCM, 12 h; (v) K₂CO₃, MeCN, 95 °C, 3 h.



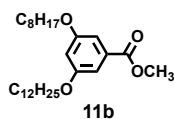
Methyl 3-(benzyloxy)-5-(dodecyloxy)benzoate (9). A mixture of compound **2** (5.50 g, 21.30 mmol, 1 equiv), 1-bromododecane (5.84 g, 23.43 mmol, 1.1 equiv), K₂CO₃ (5.89 g, 42.60 mmol, 2 equiv) and DMF (20 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (6.53 g, 74%). ¹H NMR (400 MHz, CDCl₃) δ 7.49–7.31 (m, 5 H, PhH), 7.27 (br, 1 H, PhH), 7.20 (br, 1 H, PhH), 6.73 (t, 1 H, PhH), 5.08 (s, 2 H, PhCH₂O-), 3.97 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.78 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃), 1.44 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃), 1.29 (m, 16 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.89 (t, 3 H, PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.4, 159.9, 136.7, 132.1, 128.8, 128.2, 127.7, 108.3, 108.0, 107.1, 77.4, 70.4, 68.5, 52.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.3, 26.1, 22.8, 14.3. Mp = 36 °C.



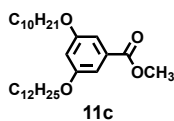
Methyl 3-hydroxy-5-(dodecyloxy)benzoate (10). Compound **9** (6.53 g, 15.8 mmol) was dissolved in a mixture of DCM (40 mL) and methanol (20 mL). Then Pd/C (0.34 g, 5 wt%) was added to the solution and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at 23 °C under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (5.04 g, 95%). ¹H NMR (400 MHz, CDCl₃) δ 7.15 (d, 2 H, PhH), 6.62 (t, 1 H, PhH), 5.99 (s, 1 H, PhOH), 3.95 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.74 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃), 1.43 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃), 1.27 (m, 16 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 3 H, PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.4, 160.6, 157.0, 157.0, 132.0, 109.2, 107.9, 107.3, 68.5, 52.5, 34.2, 33.0, 32.1, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.3, 28.9, 28.3, 26.1, 22.8, 14.2. Mp = 89 °C.



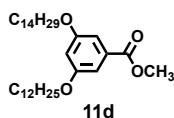
Methyl 3-((2-ethylhexyl)oxy)-5-(dodecyloxy)benzoate (11a). A mixture of compound **10** (0.60 g, 1.78 mmol, 1 equiv), 2-ethylhexyl bromide (0.38 g, 1.96 mmol, 1.1 equiv), K₂CO₃ (0.49 g, 3.56 mmol, 2 equiv) and DMF (15 mL) was heated to 80 °C and stirred under N₂ atmosphere for 12 h. The reaction mixture was cooled to 23 °C and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/EtOAc = 20/1 as the eluent to give the title compound as a light-yellow oil (0.55 g, 69%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.62 (t, 1 H, PhH), 3.97 (t, 2 H, PhOCH₂(CH₂)₁₃CH₃), 3.89 (s, 3 H, PhCOOCH₃), 3.85 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 1.86–1.65 (m, 3 H, PhOCH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.57–1.18 (m, 26 H, PhOCH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.00–0.82 (m, 9 H, PhO(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.3, 160.6, 160.3, 132.2, 131.9, 107.9, 107.8, 107.6, 106.7, 70.9, 68.5, 52.4, 52.3, 30.7, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 29.2, 26.2, 22.8, 14.2, 14.2, 11.2.



Methyl 3-(octyloxy)-5-(dodecyloxy)benzoate (11b). A mixture of compound **10** (0.60 g, 1.78 mmol, 1 equiv), 1-bromooctane (0.38 g, 1.96 mmol, 1.1 equiv), K₂CO₃ (0.49 g, 3.56 mmol, 2 equiv) and DMF (10 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.43 g, 54%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 24 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 29.3, 26.2, 22.8, 22.8, 14.2. Mp = 39 °C.

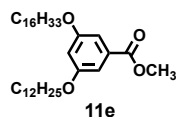


Methyl 3-(decyloxy)-5-(dodecyloxy)benzoate (11c). Compound **11c** was synthesized from compound **10** (0.60 g, 1.78 mmol, 1 equiv), 1-bromodecane (0.43 g, 1.96 mmol, 1.1 equiv) and K₂CO₃ (0.49 g, 3.56 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **11b**. The title compound was obtained as a white solid (0.69 g, 81%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 50 °C.

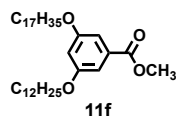


Methyl 3-(dodecyloxy)-5-(tetradecyloxy)benzoate (11d). Compound **11d** was synthesized from Compound **10** (0.60 g, 1.78 mmol, 1 equiv), 1-bromotetradecane (0.54 g, 1.96 mmol, 1.1 equiv) and K₂CO₃ (0.49 g, 3.56 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **11b**. The title compound was obtained as a white solid (0.81 g, 85%). ¹H NMR (400 MHz,

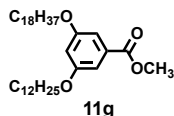
CDCl₃) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 36 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₃CH₃ and PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.3, 26.2, 22.8, 14.2. Mp = 57 °C.



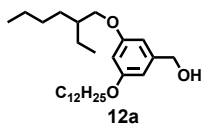
Methyl 3-(dodecyloxy)-5-(hexadecyloxy)benzoate (11e). Compound **11e** was synthesized from compound **10** (0.60 g, 1.78 mmol, 1 equiv), 1-bromohexadecane (0.60 g, 1.96 mmol, 1.1 equiv) and K₂CO₃ (0.49 g, 3.56 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **11b**. The title compound was obtained as a white solid (730 g, 73%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.88 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.25 (m, 40 H, PhOCH₂CH₂CH₂(CH₂)₁₂CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.87 (t, 6 H, PhO(CH₂)₁₅CH₃ and PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.2, 131.8, 107.6, 106.6, 77.3, 77.0, 76.7, 68.3, 52.2, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.3, 29.2, 26.0, 22.7, 14.1. Mp = 45 °C.



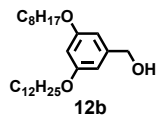
Methyl 3-(dodecyloxy)-5-(heptadecyloxy)benzoate (11f). Compound **11f** was synthesized from compound **10** (0.60 g, 1.78 mmol, 1 equiv), C₁₇H₃₅OTs (0.81 g, 1.96 mmol, 1.1 equiv) and K₂CO₃ (0.49 g, 3.56 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **11b**. The title compound was obtained as a white solid (0.72 g, 70%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 42 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₆CH₃ and PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 68.2, 52.3, 51.9, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 60 °C.



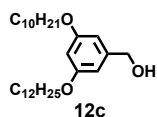
Methyl 3-(dodecyloxy)-5-(octadecyloxy)benzoate (11g). Compound **11g** was synthesized from compound **10** (0.60 g, 1.78 mmol, 1 equiv), 1-bromooctadecane (0.63 g, 1.96 mmol, 1.1 equiv) and K_2CO_3 (0.49 g, 3.56 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **11b**. The title compound was obtained as a white solid (0.78 g, 76%). 1H NMR (400 MHz, $CDCl_3$) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.97 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.77 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.45 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (m, 44 H, $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_8CH_3$), 0.88 (t, 6 H, $PhO(CH_2)_{17}CH_3$ and $PhO(CH_2)_{11}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 68.2, 52.3, 51.9, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 22.7, 14.2. Mp = 62 °C.



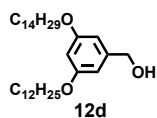
(3-(2-Ethylhexyloxy)-5-(dodecyloxy)phenyl)methanol (12a). Compound **11a** (0.55 g, 1.23 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of $LiAlH_4$ (47 mg, 1.23 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N_2 atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.36 g, 70%). 1H NMR (400 MHz, $CDCl_3$) δ 6.50 (d, 2 H, PhH), 6.38 (t, 1H, PhH), 4.61 (s, 2 H, $PhCH_2OH$), 3.93 (t, 2 H, $PhOCH_2(CH_2)_{10}CH_3$), 3.82 (m, 2 H, $PhOCH_2CH(CH_2CH_3)-$), 1.86–1.65 (m, 3 H, $PhOCH_2CH_2(CH_2)_9CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 1.55–1.18 (m, 26 H, $PhOCH_2CH_2(CH_2)_9CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 0.90 (m, 9 H, $PhO(CH_2)_{11}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 160.7, 143.3, 105.3, 105.2, 105.1, 100.7, 77.4, 70.7, 68.2, 65.6, 65.6, 39.5, 32.1, 30.7, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.2.



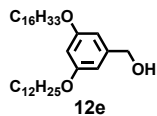
(3-(Dodecyloxy)-5-(octyloxy)phenyl)methanol (12b). Compound **12b** was synthesized from compound **11b** (0.46 g, 1.03 mmol, 1 equiv) and LiAlH_4 (39 mg, 1.03 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **12a**. The title compound was obtained as a colorless oil (0.43 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 18 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_8\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.3, 105.2, 100.7, 77.4, 68.2, 65.6, 65.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.8, 14.3, 14.2.



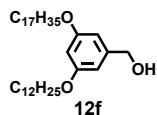
(3-(Decyloxy)-5-(dodecyloxy)phenyl)methanol (12c). Compound **12c** was synthesized from compound **11c** (0.69 g, 1.45 mmol, 1 equiv) and LiAlH_4 (55 mg, 1.45 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **12a**. The title compound was obtained as a colorless oil (0.52 g, 83%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 28 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 26.2, 22.8, 14.2.



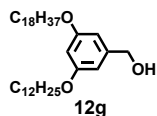
(3-(Tetradecyloxy)-5-(dodecyloxy)phenyl)methanol (12d). Compound **12d** was synthesized from compound **11d** (0.78 g, 1.46 mmol, 1 equiv) and LiAlH_4 (56 mg, 1.46 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **12a**. The title compound was obtained as a colorless oil (0.63 g, 86%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.5, 32.9, 32.1, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 25.9, 22.8, 14.3.



(3-(Dodecyloxy)-5-(hexadecyloxy)phenyl)methanol (12e). Compound **12d** was synthesized from **12f** (580 mg, 1.21 mmol, 1 equiv) and LiAlH_4 (46 mg, 1.21 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **12a**. The title compound was obtained as a white solid (630 mg, 98%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.62 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.75 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.30 (m, 40 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 160.6, 143.2, 105.1, 100.6, 77.3, 77.0, 76.7, 68.1, 65.5, 31.9, 30.3, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.4, 29.3, 26.1, 22.7, 14.1. Mp = 40 °C.

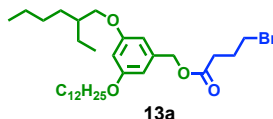


(3-(Heptadecyloxy)-5-(decyloxy)phenyl)methanol (12f). Compound **12f** was synthesized from compound **11f** (0.72 g, 1.25 mmol, 1 equiv) and LiAlH_4 (48 mg, 1.25 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **12a**. The title compound was obtained as a white solid (0.61 g, 89%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 42 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 68.2, 65.6, 63.2, 33.0, 32.1, 29.8, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 25.9, 22.8, 14.2. Mp = 45 °C.

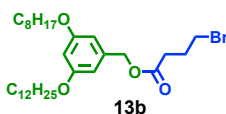


(3-(Dodecyloxy)-5-(octadecyloxy)phenyl)methanol (12g). Compound **12g** was synthesized from compound **11g** (770 mg, 1.31 mmol, 1 equiv) and LiAlH_4 (50 mg, 1.31 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **12a**. The title compound was obtained as a colorless oil (729 mg, 99%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.75 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 44 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89

(t, 6 H, $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 143.2, 105.1, 100.6, 68.1, 65.5, 31.9, 31.8, 30.3, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 29.3, 26.1, 22.7, 14.1. $\text{Mp} = 48\text{ }^\circ\text{C}$.

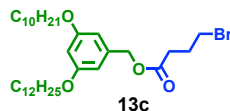


(3-(2-Ethylhexyloxy)-5-(dodecyloxy)benzyl 4-bromobutanoate (13a). Compound **12a** (0.36 g, 0.80 mmol, 1 equiv), 4-bromobutyric acid (0.15 g, 0.88 mmol, 1.1 equiv) and DPTS (0.26 g, 0.88 mmol, 1.1 equiv) were dissolved in 10 mL DCM. DCC (0.33 g, 1.60 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at $23\text{ }^\circ\text{C}$ for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.38 g, 83%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (d, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_7\text{CH}_3$), 3.82 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.83–1.67 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.57–1.21 (m, 26 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 0.91 (m, 9 H, $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.5, 172.4, 160.9, 160.6, 137.9, 106.6, 106.5, 106.4, 101.2, 77.5, 77.2, 76.9, 70.7, 68.2, 66.6, 39.5, 32.8, 32.7, 32.6, 32.1, 30.7, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 29.2, 28.0, 27.9, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.3.

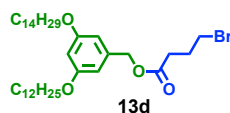


3-(Octyloxy)-5-(dodecyloxy)benzyl 4-bromobutanoate (13b). Compound **13b** was synthesized from compound **12b** (0.43 g, 0.96 mmol, 1 equiv), 4-bromobutyric acid (0.18 g, 1.05 mmol, 1.1 equiv), DPTS (0.31 g, 1.05 mmol, 1.1 equiv) and DCC (0.40 g, 1.92 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **13a**. The title compound was obtained as a colorless oil (0.43 g, 79%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.46 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 24 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 138.0, 106.5, 101.2,

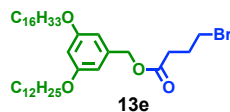
77.5, 77.2, 76.9, 68.3, 68.2, 66.5, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.6, 29.5, 29.4, 27.9, 26.2, 22.8, 22.8, 14.3, 14.2.



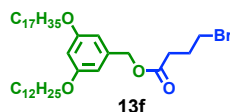
3-(Decyloxy)-5-(dodecyloxy)benzyl 4-bromobutanoate (13c). Compound **13c** was synthesized from compound **12c** (0.20 g, 0.45 mmol, 1 equiv), 4-bromobutyric acid (0.08 g, 0.49 mmol, 1.1 equiv), DPTS (0.14 g, 0.49 mmol, 1.1 equiv) and DCC (0.18 g, 0.89 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **13a**. The title compound was obtained as a colorless oil (0.24 g, 90%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 28 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



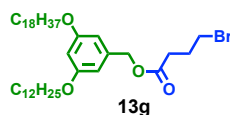
3-(Dodecyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (13d). Compound **13d** was synthesized from compound **12d** (0.63 g, 1.24 mmol, 1 equiv), 4-bromobutyric acid (0.22 g, 1.36 mmol, 1.1 equiv), DPTS (0.40 g, 1.36 mmol, 1.1 equiv) and DCC (0.57 g, 2.48 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **13a**. The title compound was obtained as a colorless oil (0.75 g, 97%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.45 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 64.9, 32.7, 32.6, 32.1, 29.8, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



3-(Dodecyloxy)-5-(hexadecyloxy)benzyl 4-bromobutanoate (13e). Compound **13e** was synthesized from compound **12e** (0.20 g, 0.38 mmol, 1 equiv), 4-bromobutyric acid (0.07 g, 0.41 mmol, 1.1 equiv), DPTS (0.12 g, 0.41 mmol, 1.1 equiv) and DCC (0.16 mg, 0.75 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **13a**. The title compound was obtained as a colorless oil (0.25 g, 97%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (br, 2 H, *PhH*), 6.40 (t, 1 H, *PhH*), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.46 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.21 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 40 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_7\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 160.5, 137.8, 106.4, 101.1, 77.4, 77.03, 76.7, 76.7, 68.1, 66.4, 32.6, 32.5, 31.22, 29.7, 29.7, 29.7, 29.7, 29.64, 29.61, 29.4, 29.4, 29.3, 27.7, 26.1, 22.7, 14.1.

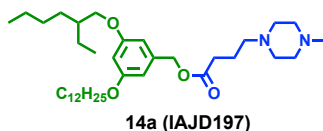


3-(Dodecyloxy)-5-(heptadecyloxy)benzyl 4-bromobutanoate (13f). Compound **13f** was synthesized from compound **12f** (0.58 g, 1.06 mmol, 1 equiv), 4-bromobutyric acid (0.20 g, 1.17 mmol, 1.1 equiv), DPTS (0.34 g, 1.17 mmol, 1.1 equiv) and DCC (0.45 g, 2.12 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **13a**. The title compound was obtained as a colorless oil (0.71 g, 96%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, *PhH*), 6.40 (t, 1 H, *PhH*), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.46 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.21 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 42 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{11}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 64.9, 32.8, 32.7, 32.6, 32.6, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 28.7, 27.9, 27.9, 26.2, 26.0, 22.8, 14.2.



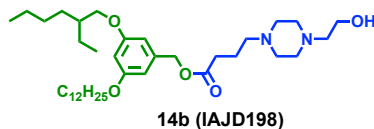
3-(Dodecyloxy)-5-(octadecyloxy)benzyl 4-bromobutanoate (13g). Compound **13g** was synthesized from compound **12g** (0.20 g, 0.34 mmol, 1 equiv), 4-bromobutyric acid (0.06 g, 0.37 mmol, 1.1 equiv),

DPTS (0.11 g, 0.37 mmol, 1 equiv) and DCC (0.14 g, 0.68 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound 30a. The title compound was obtained as a colorless oil (0.24 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₇CH₃ and PhO(CH₂)₁₁CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.5, 137.8, 106.4, 101.2, 68.1, 66.4, 32.6, 32.5, 31.9, 31.8, 29.6, 29.6, 29.4, 29.4, 29.4, 29.3, 29.3, 27.8, 26.1, 22.7, 22.7, 14.1.

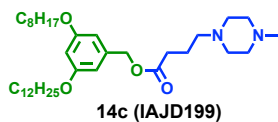


3-((2-Ethylhexyl)oxy)-5-(dodecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (14a, IAJD197).

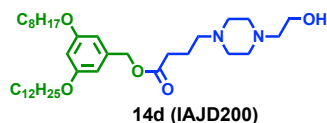
A mixture of compound **13a** (0.19 g, 0.33 mmol, 1.0 equiv), 1-methylpiperazine (36 mg, 0.36 mmol, 1.1 equiv), K₂CO₃ (56 mg, 0.40 mmol, 1.2 equiv) and MeCN (15 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.16 g, 81%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.79 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 2.64–2.26 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.45–1.16 (m, 26 H, PhOCH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.91 (m, 9 H, PhO(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 160.8, 160.5, 138.1, 106.6, 106.5, 106.4, 101.0, 70.6, 68.2, 66.3, 66.2, 57.6, 55.1, 52.8, 45.9, 39.5, 32.3, 32.0, 30.6, 29.8, 29.7, 29.7, 29.7, 29.5, 29.4, 29.4, 29.2, 26.2, 24.0, 23.1, 22.8, 22.2, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₆H₆₅N₂O₄: 589.5; Found: 590.2.



3-((2-Ethylhexyl)oxy)-5-(dodecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14b, IAJD198). Compound **14b** was synthesized from compound **13a** (0.19 g, 0.33 mmol), 1-(2-hydroxyethyl)piperazine (66 mg, 0.50 mmol) and K_2CO_3 (56 mg, 0.40 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.16 g, 77%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.80 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 3.61 (t, 2 H, -CH₂CH₂OH), 2.70–2.29 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₂-), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.73 (m, 3 H, PhOCH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.52–1.15 (m, 26 H, PhOCH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.89 (m, 9 H, PhO(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.8, 160.6, 138.2, 138.1, 106.6, 106.5, 106.4, 101.0, 70.6, 68.2, 66.3, 59.4, 57.8, 57.6, 53.1, 53.0, 39.5, 32.3, 32.0, 30.6, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.1, 22.8, 22.2, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for C₃₇H₆₇N₂O₅: 619.5; Found: 620.5.

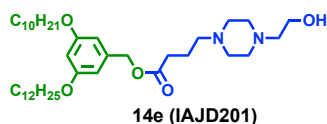


3-(Dodecyloxy)-5-(octyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (14c, IAJD199). Compound **14c** was synthesized from compound **13b** (0.22 g, 0.38 mmol), 1-methylpiperazine (46 mg, 0.46 mmol) and K_2CO_3 (64 mg, 0.46 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.19 g, 84%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 2.77–2.14 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 24 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 160.6, 138.2, 106.5, 101.1, 68.2, 66.3, 57.7, 55.3, 53.2, 46.1, 32.4, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.8, 22.3, 14.3, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for C₃₆H₆₅N₂O₄: 589.5; Found: 590.0.



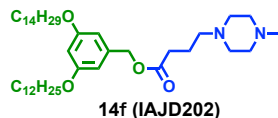
3-(Dodecyloxy)-5-(octyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14d, IAJD200).

Compound **14d** was synthesized from compound **13b** (0.22 g, 0.38 mmol), 1-(2-hydroxyethyl)piperazine (60 mg, 0.46 mmol) and K_2CO_3 (64 mg, 0.46 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.18 g, 75%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.92 (t, 4 H, $PhOCH_2-$), 3.60 (t, 2 H, $-CH_2CH_2OH$), 2.74–2.12 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.81 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.76 (m, 4 H, $PhOCH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (br, 24 H, $PhOCH_2CH_2CH_2(CH_2)_4CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_8CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 160.6, 138.2, 106.6, 101.0, 68.2, 66.3, 59.3, 57.8, 57.7, 53.3, 53.0, 32.4, 32.1, 32.0, 29.9, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.8, 22.3, 14.3, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{37}H_{67}N_2O_5$: 619.5; Found: 620.3.



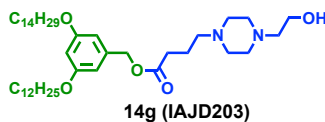
3-(Decyloxy)-5-(dodecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14e, IAJD201).

Compound **14e** was synthesized from compound **13c** (0.24 g, 0.40 mmol), 1-(2-hydroxyethyl)piperazine (78 mg, 0.60 mmol) and K_2CO_3 (67 mg, 0.48 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.24 g, 92%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.60 (t, 2 H, $-CH_2CH_2OH$), 2.65–2.29 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.74 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.27 (br, 28 H, $PhOCH_2CH_2CH_2(CH_2)_6CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_8CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.5, 138.2, 106.5, 101.0, 77.4, 68.2, 66.2, 59.4, 57.8, 57.6, 53.1, 53.0, 32.3, 32.0, 32.0, 29.8, 29.7, 29.7, 29.7, 29.7, 29.5, 29.4, 29.4, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{39}H_{71}N_2O_5$: 647.5; Found: 647.4.



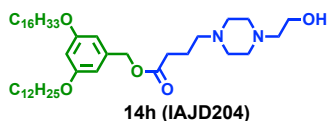
3-(Dodecyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (14f, IAJD202).

Compound **14f** was synthesized from compound **13d** (0.35 g, 0.54 mmol), 1-methylpiperazine (81 mg, 0.80 mmol) and K_2CO_3 (89 mg, 0.64 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.30 g, 86%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.90 (t, 4 H, *PhOCH*₂-), 2.63–2.21 (m, 15 H, -N(*CH*₂*CH*₂)₂N-, -N*CH*₂*CH*₂*CH*₂COO- and -N*CH*₃), 1.83 (m, 2 H, -OCO*CH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.42 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.27 (br, 36 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₀*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₈*CH*₃), 0.86 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 160.4, 138.0, 106.4, 100.9, 77.4, 77.1, 76.8, 68.0, 66.1, 59.5, 57.7, 57.5, 52.9, 32.1, 31.9, 31.9, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 26.0, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₄₂H₇₇N₂O₄: 673.6; Found: 673.7.

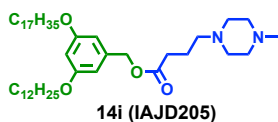


3-(Dodecyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14g, IAJD203).

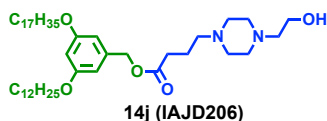
Compound **14g** was synthesized from compound **13d** (0.35 g, 0.54 mmol), 1-(2-hydroxyethyl)piperazine (105 mg, 0.80 mmol) and K_2CO_3 (90 mg, 0.64 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.32 g, 84%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 3.60 (t, 2 H, -*CH*₂*CH*₂OH), 2.64–2.25 (m, 14 H, -N(*CH*₂*CH*₂)₂N-, -N*CH*₂*CH*₂*CH*₂COO- and -*CH*₂*CH*₂OH), 1.83 (m, 2 H, -OCO*CH*₂*CH*₂*CH*₂-), 1.75 (m, 4 H, *PhOCH*₂*CH*₂-), 1.43 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.27 (br, 40 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₀*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₈*CH*₃), 0.87 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 59.4, 57.8, 57.6, 53.1, 53.0, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₄₃H₇₉N₂O₅: 703.6; Found: 703.3.



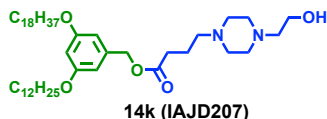
3-(Dodecyloxy)-5-(hexadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14h, IAJD204). Compound **14h** was synthesized from compound **13e** (250 mg, 0.38 mmol), 1-(2-hydroxyethyl)piperazine (74 mg, 0.57 mmol) and K_2CO_3 (64 mg, 0.46 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (200 mg, 74%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (s, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2$ -), 3.90 (t, 4 H, $PhOCH_2$ -), 3.61 (t, 2H, $-CH_2CH_2OH$), 2.57–2.32 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.75 (m, 4 H, $PhOCH_2CH_2$ -), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.26 (br, 40 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_8CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.19, 173.16, 160.43, 138.05, 106.37, 100.85, 77.45, 77.13, 76.82, 68.02, 66.11, 66.10, 59.47, 57.72, 57.48, 52.94, 52.92, 52.91, 32.16, 31.92, 31.91, 29.70, 29.68, 29.66, 29.63, 29.60, 29.58, 29.40, 29.36, 29.34, 29.25, 26.05, 22.68, 22.07, 14.11. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{45}H_{83}N_2O_5$: 731.6; Found: 732.5.



3-(Dodecyloxy)-5-(heptadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (14i, IAJD205). Compound **14i** was synthesized from compound **13f** (0.35 g, 0.50 mmol), 1-methylpiperazine (55 mg, 0.55 mmol) and K_2CO_3 (0.10 g, 0.72 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.31 g, 86%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2$ -), 3.91 (t, 4 H, $PhOCH_2$ -), 2.58–2.25 (m, 15 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-NCH_3$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.77 (m, 4 H, $PhOCH_2CH_2$ -), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.25 (br, 42 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_8CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.1, 59.3, 57.7, 57.5, 53.4, 53.0, 52.9, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{45}H_{83}N_2O_4$: 715.6; Found: 716.2.



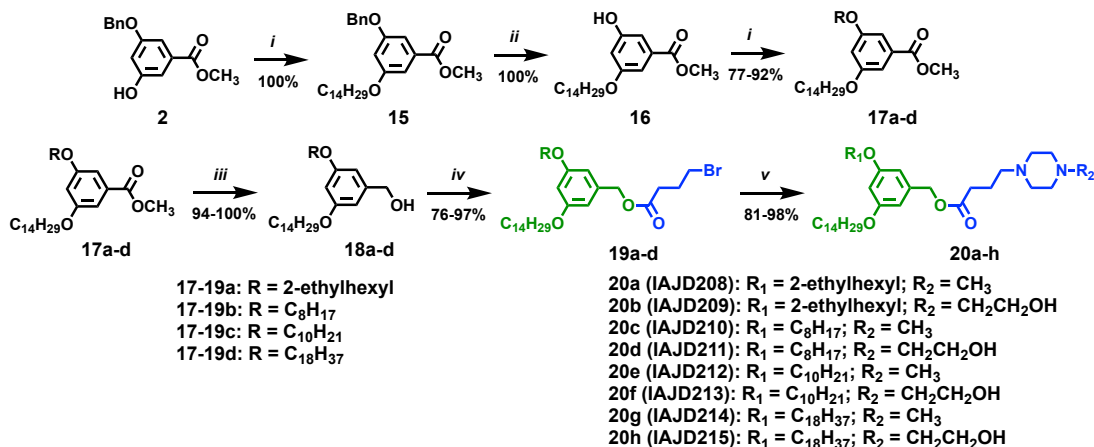
3-(Dodecyloxy)-5-(heptadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14j, IAJD206). Compound **14j** was synthesized from compound **13g** (0.35 g, 0.50 mmol), 1-(2-hydroxyethyl)piperazine (72 mg, 0.55 mmol) and K_2CO_3 (0.10 g, 0.72 mmol) following a procedure similar to that used for the synthesis of compound **14a**. The title compound was obtained as a colorless oil (0.33 g, 89%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2$ -), 3.91 (t, 4 H, $PhOCH_2$ -), 3.61 (t, 2 H, $-CH_2CH_2OH$), 2.58–2.31 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.82 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.73 (m, 4 H, $PhOCH_2CH_2$ -), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.27 (br, 42 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_8CH_3$), 0.89 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 64.6, 57.5, 57.5, 55.0, 52.8, 52.7, 45.8, 45.8, 32.3, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 26.1, 26.0, 22.7, 22.1, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{46}H_{85}N_2O_5$: 745.6; Found: 746.7.



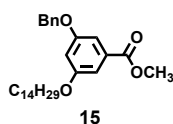
3-(Dodecyloxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (14k, IAJD207). Compound **14k** was synthesized from compound **13g** (240 mg, 0.34 mmol), 1-(2-hydroxyethyl)piperazine (66 mg, 0.51 mmol) and K_2CO_3 (57 mg, 0.41 mmol) following a procedure similar to that used for the synthesis of compound **31a**. The title compound was obtained as a colorless oil (100 mg, 40%). 1H NMR (400 MHz, $CDCl_3$) δ 6.48 (s, 2 H, PhH), 6.42 (t, 1 H, PhH), 5.05 (s, 2 H, $PhCH_2$ -), 3.94 (t, 4 H, $PhOCH_2$ -), 3.64 (t, 2 H, $-CH_2CH_2OH$), 2.63–2.36 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.86 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.78 (m, 4 H, $PhOCH_2CH_2$ -), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.29 (br, 44 H, $PhOCH_2CH_2CH_2(CH_2)_8CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$), 0.90 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.28, 160.46, 138.06, 106.43, 100.89, 77.35, 77.03, 76.72, 68.10, 66.16, 59.29, 57.62, 57.50, 52.95, 52.83, 32.21, 31.93, 29.71, 29.67, 29.64, 29.63, 29.61, 29.59, 29.41, 29.37, 29.36, 29.27, 26.07, 22.69, 22.09, 14.12. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{47}H_{87}N_2O_5$: 759.7; Found: 760.1.

3.3 Synthesis of Tetradecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

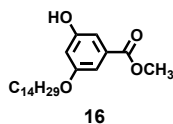
Scheme S3. Synthesis of Tetradecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains



Reagents and conditions: (i) RBr, K₂CO₃, DMF, 120 °C, 2 h; (ii) H₂, Pd/C, DCM, MeOH, 12 h; (iii) LiAlH₄, THF, 0–23 °C, 1 h; (iv) DCC, DPTS, DCM, 12 h; (v) K₂CO₃, MeCN, 95 °C, 3 h.

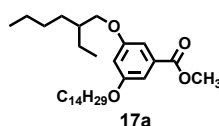


Methyl 3-(benzyloxy)-5-(tetradecyloxy)benzoate (15). A mixture of compound **2** (4.00 g, 15.49 mmol, 1 equiv), 1-bromotetradecane (4.72 g, 17.04 mmol, 1.1 equiv), K₂CO₃ (4.28 g, 30.98 mmol, 2 equiv) and DMF (20 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (5.77 g, 82%). ¹H NMR (400 MHz, CDCl₃) δ 7.49–7.31 (m, 5 H, PhH), 7.27 (br, 1 H, PhH), 7.20 (br, 1 H, PhH), 6.73 (t, 1 H, PhH), 5.08 (s, 2 H, PhCH₂O-), 3.97 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.77 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 1.45 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 1.29 (m, 20 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.89 (t, 3 H, PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.4, 159.9, 136.7, 132.1, 128.7, 128.2, 127.7, 108.3, 108.0, 107.1, 70.4, 68.5, 52.3, 33.0, 32.1, 29.8, 29.7, 29.6, 29.5, 29.3, 28.9, 28.3, 26.1, 22.8, 14.2. Mp = 55 °C.

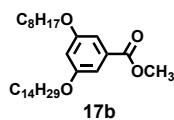


Methyl 3-hydroxy-5-(tetradecyloxy)benzoate (16). Compound **15** (5.77 g, 12.70 mmol) was dissolved in a mixture of DCM (30 mL) and methanol (15 mL). Then Pd/C (0.30 g, 5 wt%) was added to the solution

and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at 23 °C under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (4.56 g, 98%). ¹H NMR (400 MHz, CDCl₃) δ 7.14 (d, 2 H, PhH), 6.61 (t, 1 H, PhH), 5.59 (s, 1 H, PhOH), 3.95 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.75 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 1.45 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 1.27 (m, 20 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 3 H, PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 160.6, 156.9, 132.1, 109.1, 108.0, 107.2, 77.4, 68.5, 52.5, 34.2, 33.0, 32.1, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.3, 28.9, 28.3, 26.1, 22.8, 14.3. Mp = 94 °C.

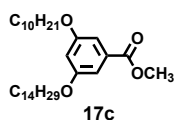


Methyl 3-((2-ethylhexyl)oxy)-5-(tetradecyloxy)benzoate (17a). A mixture of compound **16** (0.70 g, 1.92 mmol, 1 equiv), 2-ethylhexyl bromide (0.41 g, 2.11 mmol, 1.1 equiv), K₂CO₃ (0.53 g, 3.84 mmol, 2 equiv) and DMF (15 mL) was heated to 80 °C and stirred under N₂ atmosphere for 12 h. The reaction mixture was cooled to 23 °C and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/EtOAc = 20/1 as the eluent to give the title compound as a light-yellow oil (0.58 g, 64%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.97 (t, 2 H, PhOCH₂(CH₂)₁₂CH₃), 3.90 (s, 3 H, PhCOOCH₃), 3.85 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 1.84–1.68 (m, 3 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.55–1.22 (m, 30 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.00–0.76 (m, 9 H, PhO(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.3, 167.1, 160.6, 160.3, 157.0, 132.1, 131.9, 109.1, 107.9, 107.8, 107.6, 107.2, 106.8, 70.9, 68.5, 52.4, 52.3, 30.7, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.3, 29.3, 29.3, 29.2, 26.2, 26.1, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.

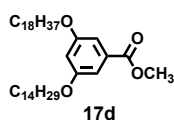


Methyl 3-(octyloxy)-5-(tetradecyloxy)benzoate (17b). A mixture of compound **16** (0.70 g, 1.92 mmol, 1 equiv), 1-bromooctane (0.41 g, 2.11 mmol, 1.1 equiv), K₂CO₃ (0.53 g, 3.84 mmol, 2 equiv) and DMF

(10 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.58 g, 64%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 29.3, 26.2, 22.8, 22.8, 14.3, 14.2. Mp = 42 °C.

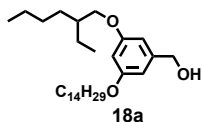


Methyl 3-(decyloxy)-5-(tetradecyloxy)benzoate (17c). Compound **17c** was synthesized from compound **16** (0.70 g, 1.92 mmol, 1 equiv), 1-bromodecane (0.47 g, 2.11 mmol, 1.1 equiv) and K₂CO₃ (0.53 g, 3.84 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **17b**. The title compound was obtained as a white solid (0.58 g, 60%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 32 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.3, 26.2, 22.8, 14.2. Mp = 52 °C.

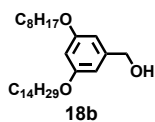


Methyl 3-(octadecyloxy)-5-(tetradecyloxy)benzoate (17d). Compound **17d** was synthesized from compound **16** (0.70 g, 1.92 mmol, 1 equiv), 1-bromooctadecanene (0.70 g, 2.11 mmol, 1.1 equiv) and K₂CO₃ (0.53 g, 3.84 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **17b**. The title compound was obtained as a white solid (0.73 g, 62%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 48 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₇CH₃ and

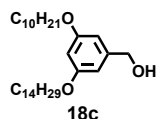
PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 34.1, 33.0, 32.1, 29.9, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.3, 28.9, 28.3, 26.2, 22.8, 14.3. Mp = 66 °C.



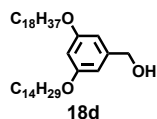
(3-((2-Ethylhexyl)oxy)-5-(tetradecyloxy)phenyl)methanol (18a). Compound **17a** (0.55 g, 1.15 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of LiAlH₄ (44 mg, 1.23 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N₂ atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous MgSO₄ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.38 g, 74%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (d, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 2 H, PhOCH₂(CH₂)₁₂CH₃), 3.82 (m, 2 H, PhOCH₂CH(CH₂CH₃)₂), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.53–1.24 (m, 30 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.90 (m, 9 H, PhO(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 160.7, 143.3, 105.3, 105.2, 105.1, 100.7, 77.4, 70.7, 68.2, 65.5, 62.9, 39.5, 32.1, 30.7, 30.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.



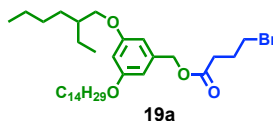
(3-(Octyloxy)-5-(tetradecyloxy)phenyl)methanol (18b). Compound **17b** was synthesized from compound **17b** (0.51 g, 1.07 mmol, 1 equiv) and LiAlH₄ (41 mg, 1.07 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **18a**. The title compound was obtained as a colorless oil (0.46 g, 96%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 160.7, 143.3, 143.3, 105.2, 100.7, 68.2, 65.6, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 26.2, 22.8, 14.2.



(3-(Decyloxy)-5-(tetradecyloxy)phenyl)methanol (18c). Compound **18c** was synthesized from compound **17c** (0.69 g, 1.45 mmol, 1 equiv) and LiAlH_4 (55 mg, 1.45 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **18a**. The title compound was obtained as a colorless oil (0.52 g, 83%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 32 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 160.6, 143.4, 105.2, 100.7, 77.5, 77.2, 76.8, 68.2, 65.5, 65.4, 32.1, 31.9, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 14.2, 14.2.

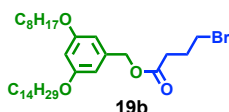


(3-(Octadecyloxy)-5-(tetradecyloxy)phenyl)methanol (18d). Compound **18d** was synthesized from compound **17d** (0.83 g, 1.35 mmol, 1 equiv) and LiAlH_4 (51 mg, 1.35 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **18a**. The title compound was obtained as a white solid (0.76 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.34 (m, 48 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 68.2, 65.6, 32.1, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 22.8, 14.3. Mp = 52 °C.

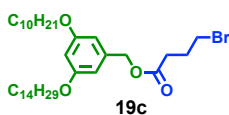


3-((2-Ethylhexyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (19a). Compound **18a** (0.52 g, 1.16 mmol, 1 equiv), 4-bromobutyric acid (0.21 g, 1.27 mmol, 1.1 equiv) and DPTS (0.38 g, 1.27 mmol, 1.1 equiv) were dissolved in 10 mL DCM. DCC (0.48 g, 2.32 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.66 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (d, 2 H, PhH), 6.42 (t, 1 H, PhH),

5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 2 H, PhOCH₂(CH₂)₁₂CH₃), 3.82 (m, 2 H, PhOCH₂CH(CH₂CH₃)₂), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.21 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.83–1.67 (m, 3 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.57–1.21 (m, 30 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.91 (m, 9 H, PhO(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.9, 160.6, 137.9, 106.6, 106.5, 106.4, 101.2, 70.7, 68.2, 66.6, 39.5, 32.7, 32.6, 32.1, 30.7, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.2, 27.9, 26.2, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.

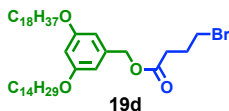


3-(Octyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (19b). Compound **19b** was synthesized from compound **18b** (0.35 g, 0.78 mmol, 1 equiv), 4-bromobutyric acid (0.14 g, 0.86 mmol, 1.1 equiv), DPTS (0.25 g, 0.86 mmol, 1.1 equiv) and DCC (0.32 g, 1.56 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **19a**. The title compound was obtained as a colorless oil (0.35 g, 79%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.6, 32.8, 32.6, 32.1, 32.0, 30.5, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

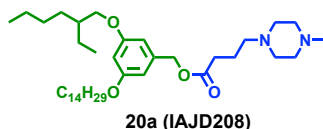


3-(Decyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (19c). Compound **19c** was synthesized from compound **18c** (0.35 g, 0.74 mmol, 1 equiv), 4-bromobutyric acid (0.135 g, 0.81 mmol, 1.1 equiv), DPTS (0.24 g, 0.81 mmol, 1.1 equiv) and DCC (0.30 g, 1.47 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **19a**. The title compound was obtained as a colorless oil (0.35 g, 80%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 32 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 6 H,

PhO(CH₂)₉CH₃ and PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

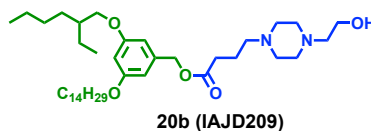


3-((Octadecyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (19d). Compound **19d** was synthesized from compound **18d** (0.35 g, 0.59 mmol, 1 equiv), 4-bromobutyric acid (0.11 g, 0.65 mmol, 1.1 equiv), DPTS (0.19 g, 0.65 mmol, 1.1 equiv) and DCC (0.25 g, 1.19 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **19a**. The title compound was obtained as a colorless oil (0.42 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 48 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₇CH₃ and PhO(CH₂)₁₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.6, 32.8, 32.6, 32.1, 32.0, 30.5, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

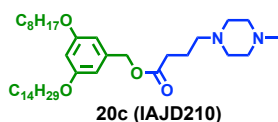


3-((2-Ethylhexyl)oxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (20a, IAJD208). A mixture of compound **19a** (0.33 g, 0.55 mmol, 1.0 equiv), 1-methylpiperazine (61 mg, 0.61 mmol, 1.1 equiv), K₂CO₃ (92 mg, 0.66 mmol, 1.2 equiv) and MeCN (20 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.28 g, 82%). ¹H NMR (400 MHz, CDCl₃) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.00 (s, 2 H, PhCH₂-), 3.89 (t, 4 H, PhOCH₂-), 3.77 (m, 2 H,

PhOCH₂CH(CH₂CH₃)-, 2.61–2.22 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.81 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.49–1.19 (m, 30 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.87 (m, 9 H, PhO(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 173.2, 160.7, 160.5, 138.1, 106.5, 106.4, 106.3, 100.9, 70.5, 68.1, 66.2, 57.5, 55.0, 52.7, 45.8, 39.4, 32.2, 31.9, 30.6, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 26.1, 23.9, 23.1, 22.7, 22.1, 14.1, 14.1, 11.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₈H₆₉N₂O₄: 617.5; Found: 617.8.

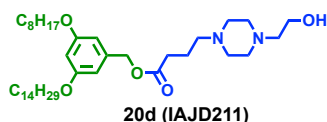


3-((2-Ethylhexyl)oxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (20b, IAJD209). Compound **20b** was synthesized from compound **19a** (0.19 g, 0.32 mmol), 1-(2-hydroxyethyl)piperazine (46 mg, 0.35 mmol) and K₂CO₃ (53 mg, 0.38 mmol) following a procedure similar to that used for the synthesis of compound **20a**. The title compound was obtained as a colorless oil (0.20 g, 95%). ¹H NMR (400 MHz, CDCl₃) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.00 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 3.78 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 3.61 (t, 2 H, -CH₂CH₂OH), 2.84–2.22 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₂-), 1.81 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.52–1.10 (m, 30 H, PhOCH₂CH₂(CH₂)₁₁CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.87 (m, 9 H, PhO(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 173.2, 160.7, 160.5, 138.1, 106.5, 106.4, 106.3, 100.9, 70.5, 68.1, 66.2, 57.5, 55.0, 52.7, 45.8, 39.4, 32.2, 31.9, 30.6, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 26.1, 23.9, 23.1, 22.7, 22.1, 14.1, 14.1, 11.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₉H₇₁N₂O₅: 647.5; Found: 647.9.

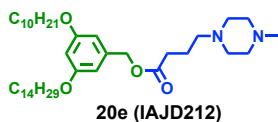


3-(Octyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (20c, IAJD210). Compound **20c** was synthesized from compound **19b** (0.22 g, 0.35 mmol), 1-methylpiperazine (0.05g, 0.53 mmol) and K₂CO₃ (0.06 g, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **31a**. The title compound was obtained as a colorless oil (200 mg, 92%). ¹H NMR (400 MHz,

CDCl₃) δ 6.46 (p, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.03 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 2.73–2.24 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.42 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 28 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.4, 138.1, 106.4, 100.9, 77.4, 77.1, 76.6, 68.1, 66.1, 57.4, 54.9, 52.6, 45.7, 45.7, 32.2, 32.2, 31.9, 31.8, 29.7, 29.7, 29.67, 29.6, 29.6, 29.6, 29.4, 29.3, 29.2, 29.2, 26.1, 22.7, 22.6, 22.0, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₈H₆₉N₂O₄: 617.5; Found: 618.5.

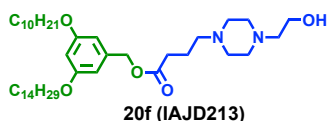


3-(Octyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (20d, IAJD211). Compound **20d** was synthesized from compound **19b** (0.18 g, 0.29 mmol), 1-(2-hydroxyethyl)piperazine (0.06 g, 0.53 mmol) and K₂CO₃ (0.05 g, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **31a**. The title compound was obtained as a colorless oil (180 mg, 94%). ¹H NMR (400 MHz, CDCl₃) δ 6.48 (s, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂-), 3.94 (t, 4 H, PhOCH₂-), 3.68 (t, 2H, -CH₂CH₂OH), 2.72–2.35 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.87 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.78 (m, 4 H, PhOCH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 28 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.90 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.5, 138.1, 106.5, 100.9, 77.4, 77.0, 76.7, 68.1, 68.0, 66.2, 59.4, 57.4, 57.4, 52.8, 52.5, 32.1, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 21.9, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₉H₇₁N₂O₅: 648.0; Found: 648.3.

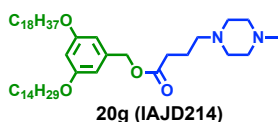


3-(Decyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (20e, IAJD212). Compound **20e** was synthesized from compound **19c** (0.18 g, 0.28 mmol), 1-methylpiperazine (31 mg, 0.31 mmol) and K₂CO₃ (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **20a**. The title compound was obtained as a colorless oil (0.20 g, 99%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.63–2.30 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.86 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.77 (m, 4 H, PhOCH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 32 H,

PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 57.4, 54.9, 52.4, 45.7, 32.2, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₀H₇₃N₂O₄: 645.6; Found: 646.3.

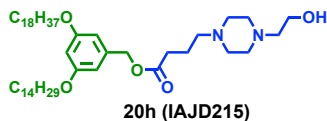


3-(Decyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (20f, IAJD213). Compound **20f** was synthesized from compound **19c** (0.18 g, 0.28 mmol), 1-(2-hydroxyethyl)piperazine (41 mg, 0.31 mmol) and K₂CO₃ (58 mg, 0.42 mmol) following a procedure similar to that used for the synthesis of compound **20a**. The title compound was obtained as a colorless oil (0.17 g, 89%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.62 (t, 2 H, -CH₂CH₂OH), 2.61–2.30 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₂-), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.73 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 32 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.89 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.5, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₁H₇₅N₂O₅: 675.6; Found: 676.5.



3-(Octadecyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (20g, IAJD214). Compound **20g** was synthesized from compound **19d** (0.22 g, 0.31 mmol), 1-methylpiperazine (34 mg, 0.34 mmol) and K₂CO₃ (52 mg, 0.37 mmol) following a procedure similar to that used for the synthesis of compound **20a**. The title compound was obtained as a colorless oil (0.23 g, 98%). ¹H NMR (400 MHz, CDCl₃) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 2.59–2.26 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.82 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.73 (m, 4 H, PhOCH₂CH₂-), 1.42 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 48 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₀CH₃), 0.86 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.4, 138.1, 106.4, 100.9, 68.1, 66.1, 57.4, 54.9, 52.7, 45.7, 32.2, 31.9, 29.7,

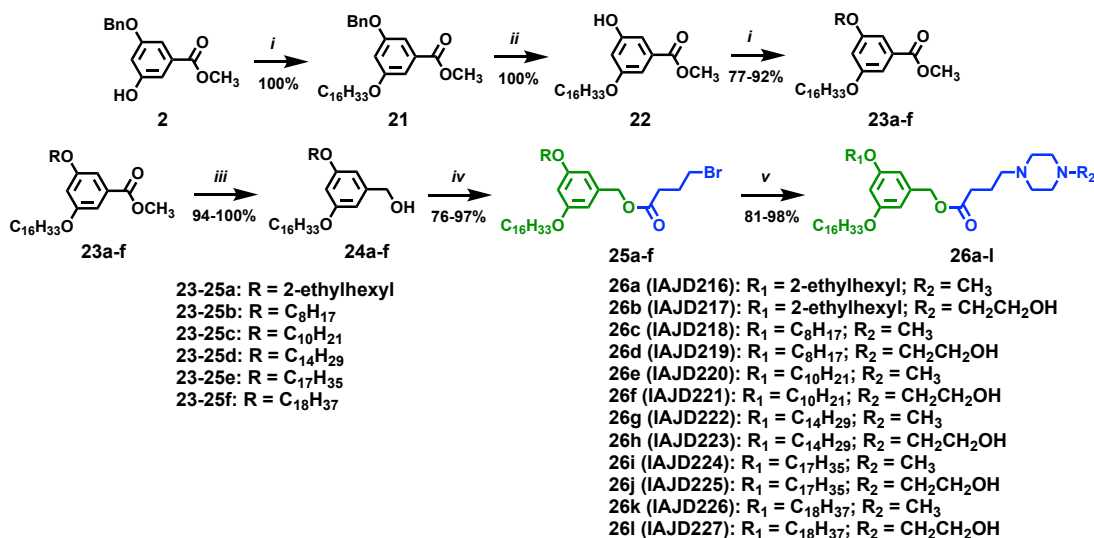
29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{48}H_{89}N_2O_4$: 757.7; Found: 757.5.



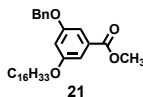
3-(Octadecyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (20h, IAJD215). Compound **20h** was synthesized from compound **19d** (0.22 g, 0.31 mmol), 1-(2-hydroxyethyl)piperazine (44 mg, 0.34 mmol) and K_2CO_3 (52 mg, 0.37 mmol) following a procedure similar to that used for the synthesis of compound **20a**. The title compound was obtained as a colorless oil (0.24 g, 100%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2$ -), 3.91 (t, 4 H, $PhOCH_2$ -), 3.62 (t, 2 H, $-CH_2CH_2OH$), 2.61–2.28 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_2$ -), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.74 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 48 H, $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{10}CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{49}H_{91}N_2O_5$: 787.7; Found: 788.5.

3.4 Synthesis of Hexadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

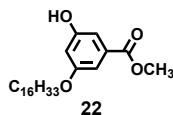
Scheme S4. Synthesis of Hexadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains



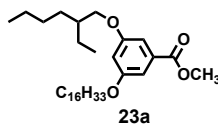
Reagents and conditions: (i) $RBr/ROTs$, K_2CO_3 , DMF, 120 °C, 2 h; (ii) H_2 , Pd/C, DCM, MeOH, 12 h; (iii) $LiAlH_4$, THF, 0–23 °C, 1 h; (iv) DCC, DPTS, DCM, 12 h; (v) K_2CO_3 , MeCN, 95 °C, 3 h.



Methyl 3-(benzyloxy)-5-(hexadecyloxy)benzoate (21). A mixture of compound **2** (2.40 g, 9.29 mmol, 1 equiv), 1-bromohexadecane (3.10 g, 10.22 mmol, 1.1 equiv), K_2CO_3 (2.57 g, 18.58 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N_2 atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (4.36 g, 97%). 1H NMR (400 MHz, $CDCl_3$) δ 7.39 (m, 5 H, PhH), 7.27 (br, 1 H, PhH), 7.20 (br, 1 H, PhH), 6.73 (t, 1 H, PhH), 5.08 (s, 2 H, $PhCH_2O-$), 3.97 (t, 2 H, $PhOCH_2-$), 3.91 (s, 3 H, $PhCOOCH_3$), 1.78 (m, 2 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 1.44 (m, 2 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 1.29 (m, 24 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 0.89 (t, 3 H, $PhO(CH_2)_{15}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.3, 159.9, 136.7, 132.1, 128.7, 128.2, 127.7, 108.3, 108.0, 107.1, 77.4, 70.4, 68.5, 52.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 26.4, 26.1, 22.8, 14.2. $Mp = 61$ °C.

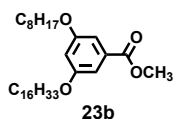


Methyl 3-(hexadecyloxy)-5-hydroxybenzoate (22). Compound **21** (3.28 g, 6.42 mmol) was dissolved in a mixture of DCM (20 mL) and methanol (10 mL). Then Pd/C (0.16 g, 5 wt%) was added to the solution and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at 23 °C under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (2.70 g, 100%). 1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.95 (t, 2 H, $PhOCH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.76 (m, 2 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 1.46 (m, 2 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 1.28 (m, 24 H, $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 0.88 (t, 3 H, $PhO(CH_2)_{15}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.4, 157.0, 131.9, 109.0, 107.7, 107.1, 68.4, 52.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.2, 26.0, 22.7, 14.2. $Mp = 97$ °C.

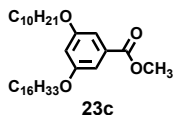


Methyl 3-((2-ethylhexyl)oxy)-5-(hexadecyloxy)benzoate (23a). A mixture of compound **22** (0.50 g, 1.27 mmol, 1 equiv), 2-ethylhexyl bromide (0.27 g, 1.40 mmol, 1.1 equiv), K_2CO_3 (0.35 g, 2.54 mmol, 2

equiv) and DMF (15 mL) was heated to 80 °C and stirred under N₂ atmosphere for 12 h. The reaction mixture was cooled to 23 °C and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/EtOAc = 20/1 as the eluent to give the title compound as a light-yellow oil (0.30 g, 47%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.97 (t, 2 H, PhOCH₂(CH₂)₁₄CH₃), 3.90 (s, 3 H, PhCOOCH₃), 3.85 (m, 2 H, PhOCH₂CH(CH₂CH₃)₂), 1.86–1.68 (m, 3 H, PhOCH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.55–1.18 (m, 34 H, PhOCH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.90 (m, 9 H, PhO(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 160.6, 160.3, 131.9, 107.9, 107.6, 106.7, 70.9, 68.5, 52.3, 52.3, 39.5, 32.1, 30.7, 29.9, 29.8, 29.8, 29.7, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.2.

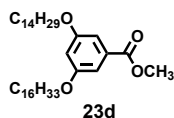


Methyl 3-(hexadecyloxy)-5-(octyloxy)benzoate (23b). A mixture of compound **22** (0.50 g, 1.27 mmol, 1 equiv), 1-bromooctane (0.31 g, 1.40 mmol, 1.1 equiv), K₂CO₃ (0.35 g, 2.54 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.45 g, 66%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 32 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₂CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₅CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 111.0, 107.8, 106.7, 77.4, 68.5, 68.1, 52.3, 32.1, 31.9, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.3, 26.3, 26.2, 22.8, 14.2. Mp = 52 °C.

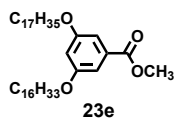


Methyl 3-(decyloxy)-5-(hexadecyloxy)benzoate (23c). Compound **23c** was synthesized from compound **22** (0.50 g, 1.27 mmol, 1 equiv), 1-bromodecane (0.31 g, 1.40 mmol, 1.1 equiv) and K₂CO₃ (0.35 g, 2.54 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **23b**. The title

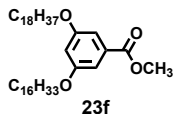
compound was obtained as a white solid (0.55 g, 81%). ^1H NMR (400 MHz, CDCl_3) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 131.9, 107.8, 106.7, 77.4, 68.4, 68.1, 52.3, 32.1, 32.0, 29.9, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.3, 26.1, 22.8, 14.2. Mp = 60 °C.



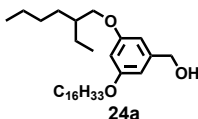
Methyl 3-(hexadecyloxy)-5-(tetradecyloxy)benzoate (23d). Compound **23d** was synthesized from compound **22** (0.50 g, 1.27 mmol, 1 equiv), 1-bromotetradecanene (0.39 g, 1.40 mmol, 1.1 equiv) and K_2CO_3 (0.35 g, 2.54 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **23b**. The title compound was obtained as a white solid (0.68 g, 91%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.46 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 44 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 64 °C.



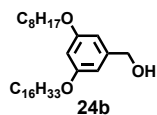
Methyl 3-(heptadecyloxy)-5-(hexadecyloxy)benzoate (23e). Compound **23e** was synthesized from compound **22** (0.50 g, 1.27 mmol, 1 equiv), $\text{C}_{17}\text{H}_{35}\text{OTs}$ (0.58 g, 1.40 mmol, 1.1 equiv) and K_2CO_3 (0.35 g, 2.54 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **23b**. The title compound was obtained as a white solid (0.75 g, 94%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.46 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 50 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.2, 32.1, 29.9, 29.8, 29.7, 29.7, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 69 °C.



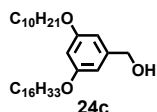
Methyl 3-(hexadecyloxy)-5-(octadecyloxy)benzoate (23f). Compound **23f** was synthesized from compound **22** (0.50 g, 1.27 mmol, 1 equiv), 1-bromooctadecanene (0.47 g, 1.40 mmol, 1.1 equiv) and K_2CO_3 (0.35 g, 2.54 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **23b**. The title compound was obtained as a white solid (0.71 g, 87%). 1H NMR (400 MHz, $CDCl_3$) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.77 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (m, 52 H, $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 0.89 (t, 6 H, $PhO(CH_2)_{17}CH_3$ and $PhO(CH_2)_{15}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 131.9, 107.8, 106.7, 77.4, 68.5, 68.1, 52.3, 32.1, 29.9, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 26.2, 25.7, 22.8, 14.2. Mp = 70 °C.



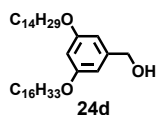
(3-((2-Ethylhexyl)oxy)-5-(hexadecyloxy)phenyl)methanol (24a). Compound **23a** (0.30 g, 0.59 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of $LiAlH_4$ (23 mg, 0.59 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N_2 atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.22 g, 78%). 1H NMR (400 MHz, $CDCl_3$) δ 6.50 (d, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, $PhCH_2OH$), 3.94 (t, 2 H, $PhOCH_2(CH_2)_{14}CH_3$), 3.83 (m, 2 H, $PhOCH_2CH(CH_2CH_3)-$), 1.72 (m, 3 H, $PhOCH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 1.51–1.17 (m, 34 H, $PhOCH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 0.91 (m, 9 H, $PhO(CH_2)_{15}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9, 160.7, 143.3, 105.3, 105.1, 100.7, 70.7, 68.2, 65.6, 62.9, 39.5, 32.1, 30.7, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.



(3-(Hexadecyloxy)-5-(octyloxy)phenyl)methanol (24b). Compound **24b** was synthesized from compound **23b** (0.45 g, 0.89 mmol, 1 equiv) and LiAlH₄ (34 mg, 0.89 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **24a**. The title compound was obtained as a colorless oil (0.39 g, 92%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 32 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₂CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₅CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.8, 14.2, 14.2.

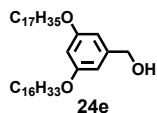


(3-(Decyloxy)-5-(hexadecyloxy)phenyl)methanol (24c). Compound **24c** was synthesized from compound **23c** (0.45 g, 0.85 mmol, 1 equiv) and LiAlH₄ (32 mg, 0.85 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **24a**. The title compound was obtained as a white solid (0.41 g, 96%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 36 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₂CH₃), 0.89 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₁₅CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 26.2, 22.8, 14.2. Mp = 40 °C.

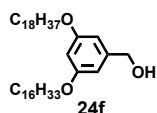


(3-(Hexadecyloxy)-5-(tetradecyloxy)phenyl)methanol (24d). Compound **24d** was synthesized from compound **23d** (0.55 g, 0.93 mmol, 1 equiv) and LiAlH₄ (35 mg, 0.93 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **24a**. The title compound was obtained as a white solid (0.50 g, 95%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₀CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₂CH₃), 0.88

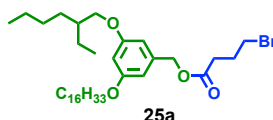
(t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 143.4, 105.2, 100.7, 77.4, 68.2, 65.4, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 14.2. $\text{Mp} = 47\text{ }^\circ\text{C}$.



(3-(Heptadecyloxy)-5-(hexadecyloxy)phenyl)methanol (24e). Compound **24e** was synthesized from compound **23e** (0.72 g, 1.14 mmol, 1 equiv) and LiAlH_4 (43 mg, 1.14 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **24a**. The title compound was obtained as a white solid (0.67 g, 97%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.59 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 50 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.4, 32.1, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 22.8, 14.3. $\text{Mp} = 56\text{ }^\circ\text{C}$.

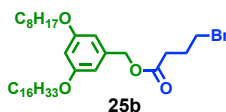


(3-(Hexadecyloxy)-5-(octadecyloxy)phenyl)methanol (24f). Compound **24f** was synthesized from compound **23f** (0.70 g, 1.09 mmol, 1 equiv) and LiAlH_4 (41 mg, 1.09 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **24a**. The title compound was obtained as a white solid (0.56 g, 83%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 52 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 125.6, 105.2, 100.7, 68.2, 65.5, 32.1, 30.5, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 22.8, 14.3. $\text{Mp} = 58\text{ }^\circ\text{C}$.

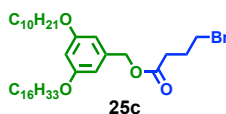


3-((2-Ethylhexyl)oxy)-5-(hexadecyloxy)benzyl 4-bromobutanoate (25a). Compound **24a** (0.22 g, 0.46 mmol, 1 equiv), 4-bromobutyric acid (0.09 g, 0.51 mmol, 1.1 equiv) and DPTS (0.15 g, 0.51 mmol, 1.1 equiv) were dissolved in 8 mL DCM. DCC (0.19 g, 0.92 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at $23\text{ }^\circ\text{C}$ for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a

colorless oil (0.30 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (d, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_{14}\text{CH}_3$), 3.82 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.21 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.81–1.71 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.55–1.20 (m, 34 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 0.91 (m, 9 H, $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.9, 160.6, 137.9, 106.6, 106.4, 101.2, 70.7, 68.2, 66.6, 39.5, 32.7, 32.6, 32.1, 30.7, 30.5, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 29.2, 27.9, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.3.

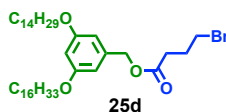


3-(Hexadecyloxy)-5-(octyloxy)benzyl 4-bromobutanoate (25b). Compound **25b** was synthesized from compound **24b** (0.39 g, 0.82 mmol, 1 equiv), 4-bromobutyric acid (0.15 g, 0.90 mmol, 1.1 equiv), DPTS (0.27 g, 0.90 mmol, 1.1 equiv) and DCC (0.34 g, 1.64 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **25a**. The title compound was obtained as a colorless oil (0.42 g, 80%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 32 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.5, 160.6, 137.9, 106.5, 101.2, 77.4, 68.3, 66.6, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 22.8, 14.3, 14.2.

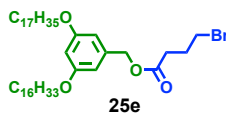


3-(Decyloxy)-5-(hexadecyloxy)benzyl 4-bromobutanoate (25c). Compound **25c** was synthesized from compound **24c** (0.44 g, 0.87 mmol, 1 equiv), 4-bromobutyric acid (0.16 g, 0.96 mmol, 1.1 equiv), DPTS (0.28 g, 0.96 mmol, 1.1 equiv) and DCC (0.36 g, 1.74 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **25a**. The title compound was obtained as a colorless oil (0.46 g, 81%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$),

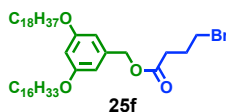
1.27 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 138.0, 106.5, 101.2, 77.4, 68.3, 66.6, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



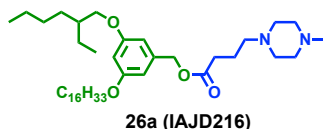
3-(Hexadecyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (25d). Compound **25d** was synthesized from compound **24d** (0.50 g, 0.89 mmol, 1 equiv), 4-bromobutyric acid (0.16 g, 0.98 mmol, 1.1 equiv), DPTS (0.29 g, 0.98 mmol, 1.1 equiv) and DCC (0.37 g, 1.78 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **25a**. The title compound was obtained as a colorless oil (0.38 g, 60%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 44 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.6, 32.8, 32.6, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



3-(Heptadecyloxy)-5-(hexadecyloxy)benzyl 4-bromobutanoate (25e). Compound **25e** was synthesized from compound **24e** (0.67 g, 1.11 mmol, 1 equiv), 4-bromobutyric acid (0.20 g, 1.22 mmol, 1.1 equiv), DPTS (0.36 g, 1.22 mmol, 1.1 equiv) and DCC (0.46 g, 2.22 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **25a**. The title compound was obtained as a colorless oil (0.72 g, 86%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.45 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 50 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{15}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 138.0, 106.5, 101.2, 68.2, 66.6, 32.8, 32.6, 32.1, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



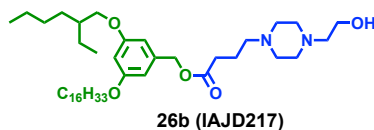
3-(Hexadecyloxy)-5-(octadecyloxy)benzyl 4-bromobutanoate (25f). Compound **25f** was synthesized from compound **24f** (0.56 g, 0.91 mmol, 1 equiv), 4-bromobutyric acid (0.17 g, 1.00 mmol, 1.1 equiv), DPTS (0.29 g, 1.00 mmol, 1.1 equiv) and DCC (0.38 g, 1.82 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **25a**. The title compound was obtained as a colorless oil (0.64 g, 92%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 52 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₂CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₇CH₃ and PhO(CH₂)₁₅CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 125.6, 106.5, 101.2, 68.2, 66.5, 32.7, 32.6, 32.1, 30.5, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



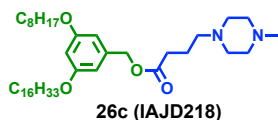
3-((2-Ethylhexyl)oxy)-5-(hexadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (26a, IAJD216).

A mixture of compound **25a** (0.12 g, 0.19 mmol, 1.0 equiv), 1-methylpiperazine (21 mg, 0.21 mmol, 1.1 equiv), K₂CO₃ (33 mg, 0.23 mmol, 1.2 equiv) and MeCN (15 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.12 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.79 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 2.62–2.23 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.45–1.16 (m, 34 H, PhOCH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.90 (m, 9 H, PhO(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 160.8, 160.6, 138.1, 106.6, 106.4, 101.0, 77.4, 70.6, 68.2, 66.3, 57.6, 55.0, 52.8, 50.7, 45.9, 39.5, 32.3, 32.0, 30.6, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2,

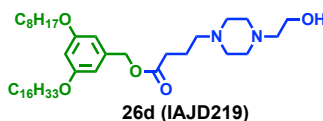
24.0, 23.1, 22.8, 22.2, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{40}H_{73}N_2O_4$: 645.6; Found: 645.6.



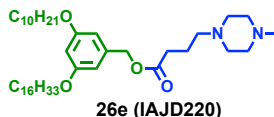
3-((2-Ethylhexyl)oxy)-5-(hexadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (26b, IAJD217). Compound **26b** was synthesized from compound **25a** (0.12 g, 0.19 mmol), 1-(2-hydroxyethyl)piperazine (27 mg, 0.21 mmol) and K_2CO_3 (33 mg, 0.23 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.11 g, 85%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.80 (m, 2 H, $PhOCH_2CH(CH_2CH_3)-$), 3.62 (t, 2 H, $-CH_2CH_2OH$), 2.68–2.28 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_2-$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.72 (m, 3 H, $PhOCH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 1.53–1.15 (m, 34 H, $PhOCH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 0.89 (m, 9 H, $PhO(CH_2)_{15}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.8, 160.5, 138.1, 106.6, 106.4, 101.0, 70.6, 68.2, 66.3, 59.5, 57.7, 57.5, 52.9, 52.9, 39.5, 32.3, 32.0, 30.6, 29.8, 29.8, 29.7, 29.7, 29.5, 29.4, 29.4, 29.2, 26.2, 24.0, 23.1, 22.8, 22.1, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{41}H_{75}N_2O_5$: 675.6; Found: 675.4.



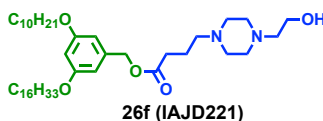
3-(Hexadecyloxy)-5-(octyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (26c, IAJD218). Compound **26c** was synthesized from compound **25b** (0.20 g, 0.37 mmol), 1-methylpiperazine (41 mg, 0.41 mmol) and K_2CO_3 (77 mg, 0.55 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.22 g, 92%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, $PhCH_2-$), 3.92 (t, 4 H, $PhOCH_2-$), 2.63–2.28 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.85 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.75 (m, 4 H, $PhOCH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.25 (br, 32 H, $PhOCH_2CH_2CH_2(CH_2)_4CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 57.4, 54.9, 52.7, 45.7, 32.2, 31.9, 31.8, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{40}H_{73}N_2O_4$: 645.6; Found: 646.3.



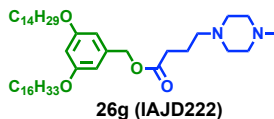
3-(Hexadecyloxy)-5-(octyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (26d, IAJD219). Compound **26d** was synthesized from compound **25b** (0.20 g, 0.37 mmol), 1-(2-hydroxyethyl)piperazine (53 mg, 0.41 mmol) and K_2CO_3 (77 mg, 0.55 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.24 g, 96%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.92 (t, 4 H, *PhOCH*₂-), 3.61 (t, 2 H, -*CH*₂*CH*₂*OH*), 2.64–2.32 (m, 14 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*CH*₂*CH*₂*OH*), 1.84 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.75 (m, 4 H, *PhOCH*₂*CH*₂-), 1.44 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.27 (br, 32 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₄*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.8, 32.2, 31.9, 31.8, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{41}H_{75}N_2O_5$: 675.6; Found: 676.7.



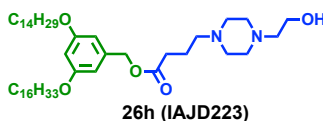
3-(Decyloxy)-5-(hexadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (26e, IAJD220). Compound **26e** was synthesized from compound **25c** (0.20 g, 0.31 mmol), 1-methylpiperazine (34 mg, 0.34 mmol) and K_2CO_3 (51 mg, 0.37 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.21 g, 100%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.01 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.54–2.22 (m, 15 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.44 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.25 (br, 36 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₆*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 57.5, 55.0, 52.8, 50.7, 45.8, 32.3, 32.0, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.1, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{42}H_{77}N_2O_4$: 673.6; Found: 674.1.



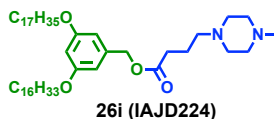
3-(Decyloxy)-5-(hexadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (26f, IAJD221). Compound **26f** was synthesized from compound **25c** (0.15 g, 0.23 mmol), 1-(2-hydroxyethyl)piperazine (32 mg, 0.25 mmol) and K_2CO_3 (37 mg, 0.27 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.13 g, 81%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 3.62 (t, 2 H, -*CH*₂*CH*₂*OH*), 2.64–2.31 (m, 14 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*CH*₂*CH*₂*OH*), 1.84 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.75 (m, 4 H, *PhOCH*₂*CH*₂-), 1.42 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.26 (br, 36 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₆*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.6, 138.2, 106.5, 101.0, 77.4, 68.2, 66.3, 59.5, 57.7, 57.6, 53.0, 52.9, 50.8, 32.3, 32.0, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{43}H_{79}N_2O_5$: 703.6; Found: 703.8.



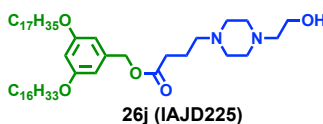
3-(Hexadecyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (26g, IAJD222). Compound **26g** was synthesized from compound **25d** (0.18 g, 0.25 mmol), 1-methylpiperazine (28 mg, 0.28 mmol) and K_2CO_3 (38 mg, 0.28 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a light-yellow oil (0.18 g, 98%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.77–2.14 (m, 15 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.76 (m, 4 H, *PhOCH*₂*CH*₂-), 1.44 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.25 (br, 44 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₀*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 160.6, 138.2, 106.5, 101.1, 68.2, 66.3, 57.7, 55.3, 53.2, 46.2, 32.4, 32.1, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 22.8, 22.3, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{46}H_{85}N_2O_4$: 729.6; Found: 730.7.



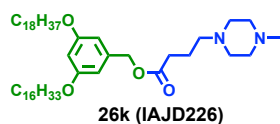
3-(Hexadecyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (26h, IAJD223). Compound **26h** was synthesized from compound **25d** (0.18 g, 0.25 mmol), 1-(2-hydroxyethyl)piperazine (35 mg, 0.28 mmol) and K_2CO_3 (38 mg, 0.28 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a light-yellow oil (0.14 g, 76%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.03 (s, 2 H, *PhCH*₂-), 3.92 (t, 4 H, *PhOCH*₂-), 3.60 (t, 2 H, -*CH*₂*CH*₂*OH*), 2.74–2.12 (m, 14 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*CH*₂*CH*₂*OH*), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.76 (m, 4 H, *PhOCH*₂*CH*₂-), 1.43 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.26 (br, 44 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₀*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 59.3, 57.8, 57.7, 53.3, 53.0, 32.4, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 22.8, 22.3, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{47}H_{87}N_2O_5$: 759.7; Found: 760.8.



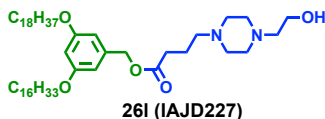
3-(Heptadecyloxy)-5-(hexadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (26i, IAJD224). Compound **26i** was synthesized from compound **25e** (0.30 g, 0.40 mmol), 1-methylpiperazine (44 mg, 0.44 mmol) and K_2CO_3 (66 mg, 0.48 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.30 g, 97%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.60–2.22 (m, 15 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.84 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.42 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.25 (br, 50 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₃*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₂*CH*₃), 0.87 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 57.6, 55.1, 52.9, 45.9, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{49}H_{91}N_2O_4$: 771.7; Found: 772.7.



3-(Heptadecyloxy)-5-(hexadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (26j, IAJD225). Compound **26j** was synthesized from compound **25e** (0.15 g, 0.20 mmol), 1-(2-hydroxyethyl)piperazine (29 mg, 0.22 mmol) and K_2CO_3 (33 mg, 0.24 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.15 g, 94%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2$ -), 3.90 (t, 4 H, $PhOCH_2$ -), 3.60 (t, 2 H, $-CH_2CH_2OH$), 2.64–2.25 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.73 (m, 4 H, $PhOCH_2CH_2$ -), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.27 (br, 50 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.5, 101.0, 68.1, 66.2, 59.4, 57.8, 57.6, 53.1, 53.0, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.3, 26.1, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{50}H_{93}N_2O_5$: 801.7; Found: 802.1.



3-(Hexadecyloxy)-5-(octadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (26k, IAJD226). Compound **26k** was synthesized from compound **25f** (0.25 g, 0.33 mmol), 1-methylpiperazine (36 mg, 0.36 mmol) and K_2CO_3 (55 mg, 0.40 mmol) following a procedure similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.21 g, 81%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2$ -), 3.90 (t, 4 H, $PhOCH_2$ -), 2.56–2.24 (m, 15 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-NCH_3$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.74 (m, 4 H, $PhOCH_2CH_2$ -), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.24 (br, 52 H, $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{12}CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.2, 106.5, 101.0, 68.2, 66.2, 57.6, 55.1, 52.9, 45.9, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{50}H_{93}N_2O_4$: 785.7; Found: 785.9.

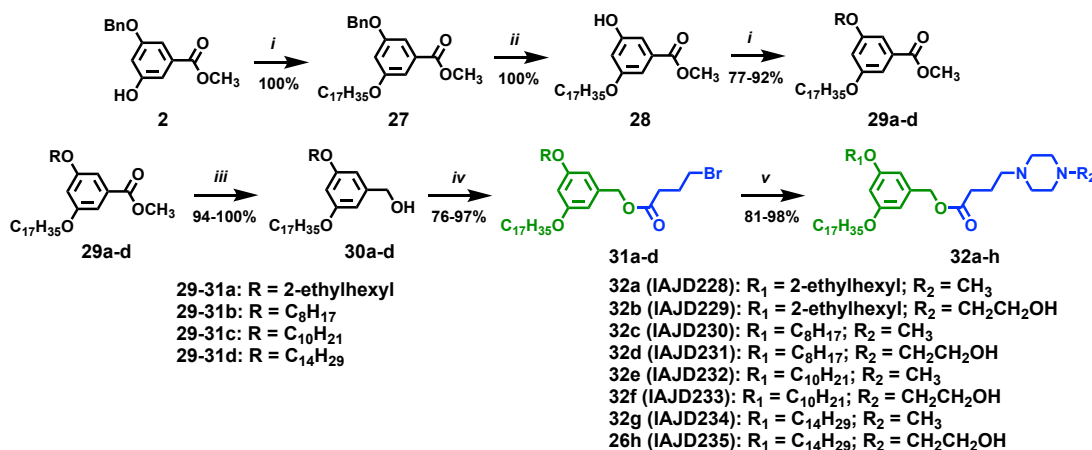


3-(Hexadecyloxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (26l, IAJD227). Compound **26l** was synthesized from compound **25f** (0.30 g, 0.39 mmol), 1-(2-hydroxyethyl)piperazine (56 mg, 0.43 mmol) and K_2CO_3 (65 mg, 0.47 mmol) following a procedure

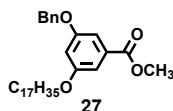
similar to that used for the synthesis of compound **26a**. The title compound was obtained as a colorless oil (0.32 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH_2 -), 3.91 (t, 4 H, PhOCH_2 -), 3.61 (t, 2 H, $-\text{CH}_2\text{CH}_2\text{OH}$), 2.64–2.28 (m, 14 H, $-\text{N}(\text{CH}_2\text{CH}_2)_2\text{N}-$, $-\text{NCH}_2\text{CH}_2\text{CH}_2\text{COO}-$ and $-\text{CH}_2\text{CH}_2\text{OH}$), 1.84 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2-$), 1.75 (m, 4 H, $\text{PhOCH}_2\text{CH}_2-$), 1.42 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.25 (br, 52 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.87 (t, 6 H, $-\text{CH}_2\text{CH}_2\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 59.4, 57.8, 57.6, 53.5, 53.1, 53.0, 32.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{51}\text{H}_{95}\text{N}_2\text{O}_5$: 815.7; Found: 815.6.

3.5 Synthesis of Heptadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

Scheme S5. Synthesis of Heptadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

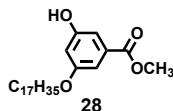


Reagents and conditions: (i) RBr/ROT s, K_2CO_3 , DMF, 120 $^\circ\text{C}$, 2 h; (ii) H_2 , Pd/C, DCM, MeOH, 12 h; (iii) LiAlH_4 , THF, 0–23 $^\circ\text{C}$, 1 h; (iv) DCC, DPTS, DCM, 12 h; (v) K_2CO_3 , MeCN, 95 $^\circ\text{C}$, 3 h.

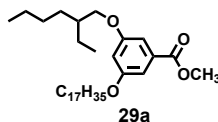


Methyl 3-(benzyloxy)-5-(heptadecyloxy)benzoate (27). A mixture of compound **2** (1.20 g, 4.64 mmol, 1 equiv), $\text{C}_{17}\text{H}_{35}\text{OTs}$ (2.11 g, 5.11 mmol, 1.1 equiv), K_2CO_3 (1.28 g, 9.28 mmol, 2 equiv) and DMF (15 mL) was heated to 120 $^\circ\text{C}$ and stirred under N_2 atmosphere for 2 h. The reaction mixture was cooled to 23 $^\circ\text{C}$ and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (2.25 g, 97%). ^1H NMR (400 MHz, CDCl_3) δ 7.47–7.29 (m, 5 H, PhH), 7.27 (br, 1 H, PhH), 7.20 (br, 1 H, PhH), 6.73 (t, 1 H, PhH), 5.08 (s, 2 H, $\text{PhCH}_2\text{O}-$), 3.96 (t, 2 H, PhOCH_2-),

3.90 (s, 3 H, PhCOOCH_3), 1.77 (m, 2 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 1.45 (m, 2 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 1.27 (m, 26 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.89 (t, 3 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.0, 160.3, 159.9, 136.7, 132.1, 128.7, 128.2, 127.7, 108.3, 108.0, 107.1, 77.4, 70.4, 68.5, 63.0, 52.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 26.4, 26.1, 25.9, 22.8, 14.2. $\text{Mp} = 63\text{ }^\circ\text{C}$.

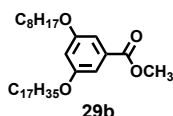


Methyl 3-hydroxy-5-(heptadecyloxy)benzoate (28). Compound **27** (2.25 g, 4.49 mmol) was dissolved in a mixture of DCM (20 mL) and methanol (10 mL). Then Pd/C (0.11 g, 5 wt%) was added to the solution and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at $23\text{ }^\circ\text{C}$ under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (1.92 g, 99%). ^1H NMR (400 MHz, CDCl_3) δ 7.14 (d, 2 H, PhH), 6.62 (t, 1 H, PhH), 3.95 (t, 2 H, PhOCH_2 -), 3.90 (s, 3 H, PhCOOCH_3), 1.73 (m, 2 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 1.41 (m, 2 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 1.26 (m, 26 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.88 (t, 3 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.0, 160.4, 157.0, 132.0, 108.2, 107.8, 107.1, 68.4, 52.2, 32.8, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.2, 26.2, 26.0, 25.8, 22.7, 14.1. $\text{Mp} = 98\text{ }^\circ\text{C}$.

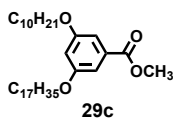


Methyl 3-((2-ethylhexyl)oxy)-5-(heptadecyloxy)benzoate (29a). A mixture of compound **28** (0.60 g, 1.47 mmol, 1 equiv), 2-ethylhexyl bromide (0.31 g, 1.62 mmol, 1.1 equiv), K_2CO_3 (0.41 g, 2.94 mmol, 2 equiv) and DMF (15 mL) was heated to $80\text{ }^\circ\text{C}$ and stirred under N_2 atmosphere for 12 h. The reaction mixture was cooled to $23\text{ }^\circ\text{C}$ and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO_4 . After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/ $\text{EtOAc} = 20/1$ as the eluent to give the title compound as a light-yellow oil (0.47 g, 61%). ^1H NMR (400 MHz, CDCl_3) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.97 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_{15}\text{CH}_3$), 3.90 (s, 3 H, PhCOOCH_3), 3.85 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)$ -), 1.83–1.69 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.55–1.18 (m, 36 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$ and

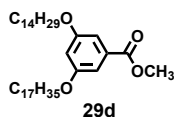
PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.01–0.85 (m, 9 H, PhO(CH₂)₁₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 160.6, 160.3, 131.9, 107.9, 107.6, 106.7, 70.9, 68.5, 52.3, 39.5, 32.1, 30.7, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.2, 14.2, 11.2.



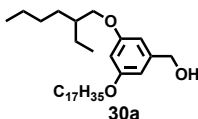
Methyl 3-(heptadecyloxy)-5-(octyloxy)benzoate (29b). A mixture of compound **28** (0.40 g, 0.98 mmol, 1 equiv), 1-bromooctane (0.21 g, 1.08 mmol, 1.1 equiv), K₂CO₃ (0.27 g, 1.97 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.33 g, 66%). ¹H NMR (400 MHz, CDCl₃) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 34 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₆CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 131.9, 107.8, 106.7, 77.4, 68.5, 52.3, 32.9, 32.1, 31.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.3, 26.1, 25.9, 22.8, 22.8, 14.2, 14.2. Mp = 56 °C.



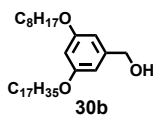
Methyl 3-(decyloxy)-5-(heptadecyloxy)benzoate (29c). Compound **29c** was synthesized from compound **28** (0.40 g, 0.98 mmol, 1 equiv), 1-bromodecane (0.24 g, 1.08 mmol, 1.1 equiv) and K₂CO₃ (0.27 g, 1.97 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **29b**. The title compound was obtained as a white solid (0.34 g, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.62 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 38 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₁₆CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 131.9, 107.8, 106.7, 77.4, 68.5, 63.0, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.3, 26.1, 25.9, 22.8, 14.2. Mp = 58 °C.



Methyl 3-(heptadecyloxy)-5-(tetradecyloxy)benzoate (29d). Compound **29d** was synthesized from compound **28** (0.40 g, 0.98 mmol, 1 equiv), 1-bromotetradecane (0.30 g, 1.08 mmol, 1.1 equiv) and K_2CO_3 (0.27 g, 1.97 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **29b**. The title compound was obtained as a white solid (0.48 g, 81%). 1H NMR (400 MHz, $CDCl_3$) δ 7.15 (br, 2 H, PhH), 6.62 (t, 1 H, PhH), 3.96 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.88 (s, 3 H, $PhCOOCH_3$), 1.76 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.25 (m, 46 H, $PhOCH_2CH_2CH_2(CH_2)_{10}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$), 0.86 (t, 6 H, $PhO(CH_2)_{13}CH_3$ and $PhO(CH_2)_{16}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 131.9, 107.8, 106.7, 77.4, 68.4, 63.0, 52.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.3, 26.4, 26.1, 25.9, 22.8, 14.2. Mp = 65 °C.

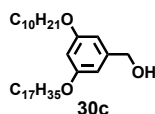


(3-((2-Ethylhexyl)oxy)-5-(heptadecyloxy)phenyl)methanol (30a). Compound **29a** (0.48 g, 0.93 mmol, 1 equiv) was dissolved in 6 mL dry THF, which was added dropwise to a slurry of $LiAlH_4$ (35 mg, 0.93 mmol, 1 equiv) in dry THF (6 mL) at 0 °C under N_2 atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.3 mL), 15% NaOH aqueous solution (0.3 mL) and water (1.5 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.40 g, 83%). 1H NMR (400 MHz, $CDCl_3$) δ 6.50 (d, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.62 (s, 2 H, $PhCH_2OH$), 3.94 (t, 2 H, $PhOCH_2(CH_2)_{15}CH_3$), 3.82 (m, 2 H, $PhOCH_2CH(CH_2CH_3)-$), 1.72 (m, 3 H, $PhOCH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 1.56–1.17 (m, 36 H, $PhOCH_2CH_2(CH_2)_{14}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$), 0.89 (m, 9 H, $PhO(CH_2)_{16}CH_3$ and $PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 160.7, 143.3, 105.3, 105.1, 100.7, 70.7, 68.2, 65.6, 39.5, 32.1, 30.7, 30.5, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.2.

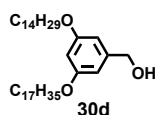


(3-(Heptadecyloxy)-5-(octyloxy)phenyl)methanol (30b). Compound **30b** was synthesized from compound **29b** (0.33 g, 0.64 mmol, 1 equiv) and $LiAlH_4$ (24 mg, 0.64 mmol, 1 equiv) following a

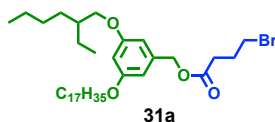
procedure similar to that used for the synthesis of compound **30a**. The title compound was obtained as a colorless oil (0.22 g, 70%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 34 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.4, 63.1, 32.9, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 29.4, 26.2, 25.9, 22.8, 22.8, 14.3, 14.2.



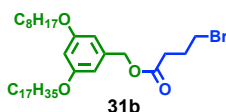
(3-(Decyloxy)-5-(heptadecyloxy)phenyl)methanol (30c). Compound **30c** was synthesized from compound **29c** (0.34 g, 0.62 mmol, 1 equiv) and LiAlH_4 (23 mg, 0.62 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **30a**. The title compound was obtained as a white solid (0.21 g, 65%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 38 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 143.5, 105.2, 100.7, 77.4, 68.2, 65.3, 64.0, 63.0, 32.9, 32.1, 29.8, 29.8, 29.8, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.3, 26.4, 26.2, 25.9, 22.9, 22.8, 14.2. Mp = 42 °C.



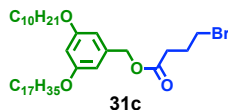
(3-(Heptadecyloxy)-5-(tetradecyloxy)phenyl)methanol (30d). Compound **30d** was synthesized from compound **29d** (0.47 g, 0.78 mmol, 1 equiv) and LiAlH_4 (30 mg, 0.78 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **30a**. The title compound was obtained as a white solid (0.52 g, 83%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.36 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.92 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 46 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 160.6, 143.4, 105.2, 100.7, 77.5, 77.2, 76.8, 68.2, 65.5, 65.4, 32.1, 31.9, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 14.2, 14.2. Mp = 48 °C.



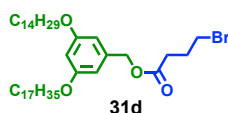
3-((2-Ethylhexyl)oxy)-5-(heptadecyloxy)benzyl 4-bromobutanoate (31a). Compound **30a** (0.40 g, 0.82 mmol, 1 equiv), 4-bromobutyric acid (0.15 g, 0.90 mmol, 1.1 equiv) and DPTS (0.26 g, 0.90 mmol, 1.1 equiv) were dissolved in 8 mL DCM. DCC (0.34 g, 1.64 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.41 g, 79%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (d, 2 H, PhH), 6.42 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.92 (t, 2 H, PhOCH₂(CH₂)₁₅CH₃), 3.82 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.82–1.65 (m, 3 H, PhOCH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.56–1.25 (m, 36 H, PhOCH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.90 (m, 9 H, PhO(CH₂)₁₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.5, 160.9, 160.6, 137.9, 106.6, 106.4, 101.2, 77.4, 70.7, 68.2, 66.6, 39.5, 32.8, 32.6, 32.1, 30.7, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.2, 27.9, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.3.



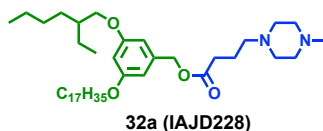
3-(Heptadecyloxy)-5-(octyloxy)benzyl 4-bromobutanoate (31b). Compound **31b** was synthesized from compound **30b** (0.22 g, 0.45 mmol, 1 equiv), 4-bromobutyric acid (0.08 g, 0.49 mmol, 1.1 equiv), DPTS (0.15 g, 0.49 mmol, 1.1 equiv) and DCC (0.19 g, 0.90 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **31a**. The title compound was obtained as a colorless oil (0.26 g, 91%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 34 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₆CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.5, 64.9, 32.8, 32.7, 32.7, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 28.7, 28.0, 27.9, 26.2, 26.1, 22.8, 22.8, 14.3, 14.2.



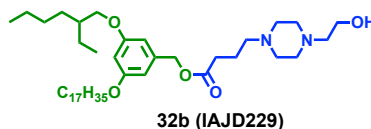
3-(Decyloxy)-5-(heptadecyloxy)benzyl 4-bromobutanoate (31c). Compound **31c** was synthesized from compound **30c** (0.22 g, 0.42 mmol, 1 equiv), 4-bromobutyric acid (0.08 g, 0.47 mmol, 1.1 equiv), DPTS (0.14 g, 0.47 mmol, 1.1 equiv) and DCC (0.18 g, 0.85 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **31a**. The title compound was obtained as a colorless oil (0.28 g, 99%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.53 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 38 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 64.9, 32.8, 32.7, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 28.8, 28.0, 27.9, 26.2, 26.1, 22.8, 14.3.



3-(Heptadecyloxy)-5-(tetradecyloxy)benzyl 4-bromobutanoate (31d). Compound **31d** was synthesized from compound **30d** (0.40 g, 0.70 mmol, 1 equiv), 4-bromobutyric acid (0.13 g, 0.77 mmol, 1.1 equiv), DPTS (0.24 g, 0.77 mmol, 1.1 equiv) and DCC (0.29 g, 1.40 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **31a**. The title compound was obtained as a colorless oil (0.41 g, 81%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.53 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 46 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.7, 172.4, 160.6, 137.9, 106.5, 101.2, 77.5, 77.2, 76.9, 68.2, 66.5, 64.9, 32.8, 32.8, 32.7, 32.7, 32.6, 32.1, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 28.8, 28.0, 27.9, 26.2, 26.1, 22.8, 14.3.

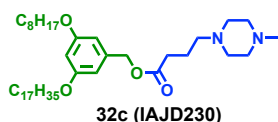


3-((2-Ethylhexyl)oxy)-5-(heptadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (32a, IAJD228). A mixture of compound **31a** (0.21 g, 0.32 mmol, 1.0 equiv), 1-methylpiperazine (98 mg, 0.98 mmol), K_2CO_3 (89 mg, 0.64 mmol) and MeCN (15 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous $MgSO_4$. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by $NaHCO_3$ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.18 g, 85%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH_2*-), 3.91 (t, 4 H, *PhOCH_2*-), 3.80 (m, 2 H, *PhOCH_2CH(CH_2CH_3)*-), 2.59–2.23 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.73 (m, 3 H, *PhOCH_2CH_2(CH_2)_{14}CH_3* and *PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3*), 1.34–1.16 (m, 36 H, *PhOCH_2CH_2(CH_2)_{14}CH_3* and *PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3*), 0.89 (m, 9 H, *PhO(CH_2)_{16}CH_3* and *PhOCH_2CH(CH_2CH_3)(CH_2)_3CH_3*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.7, 160.5, 138.0, 106.5, 106.3, 100.9, 70.5, 68.1, 66.2, 57.5, 55.0, 52.9, 45.9, 39.4, 32.2, 31.9, 30.5, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 26.1, 23.9, 23.0, 22.7, 22.1, 14.1, 14.1, 11.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{41}H_{75}N_2O_4$: 659.6; Found: 660.1.



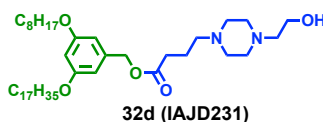
3-((2-Ethylhexyl)oxy)-5-(heptadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (32b, IAJD229). Compound **32b** was synthesized from compound **31a** (0.21 g, 0.32 mmol), 11-(2-hydroxyethyl)piperazine (98 mg, 0.98 mmol), K_2CO_3 (89 mg, 0.64 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a colorless oil (0.18 g, 80%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH_2*-), 3.91 (t, 4 H, *PhOCH_2*-), 3.80 (m, 2 H, *PhOCH_2CH(CH_2CH_3)*-), 3.62 (t, 2 H, $-CH_2CH_2OH$), 2.71–2.27 (m,

14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₂-), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.53–1.15 (m, 36 H, PhOCH₂CH₂(CH₂)₁₄CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.89 (m, 9 H, PhO(CH₂)₁₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.7, 160.5, 138.1, 106.5, 106.4, 101.0, 70.6, 68.2, 66.3, 59.5, 57.7, 57.4, 52.9, 52.9, 39.5, 32.3, 32.0, 30.5, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.4, 29.2, 26.2, 24.0, 23.1, 22.8, 22.1, 14.2, 14.1, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₂H₇₇N₂O₅: 689.6; Found: 690.3.



3-(Heptadecyloxy)-5-(octyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (32c, IAJD230).

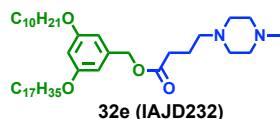
Compound **32c** was synthesized from compound **31b** (0.12 g, 0.18 mmol), 1-methylpiperazine (20 mg, 0.20 mmol) and K₂CO₃ (38 mg, 0.27 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a colorless oil (0.12 g, 98%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 2.61–2.22 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.74 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 34 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 57.5, 54.9, 52.7, 45.8, 32.2, 31.9, 31.8, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 26.0, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₁H₇₅N₂O₄: 659.6; Found: 660.1.



3-(Heptadecyloxy)-5-(octyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (32d, IAJD231).

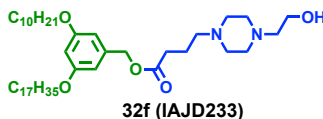
Compound **32d** was synthesized from compound **31b** (0.12 g, 0.18 mmol), 1-(2-hydroxyethyl)piperazine (26 mg, 0.20 mmol) and K₂CO₃ (38 mg, 0.27 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a colorless oil (0.10 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 3.65 (t, 2 H, -CH₂CH₂OH), 2.70–2.36 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 34 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and

PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₂H₇₇N₂O₅: 689.6; Found: 690.4.



3-(Decyloxy)-5-(heptadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (32e, IAJD232).

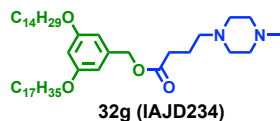
Compound **32e** was synthesized from compound **31c** (0.19 g, 0.21 mmol), 1-methylpiperazine (32 mg, 0.32 mmol) and K₂CO₃ (35 mg, 0.25 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a light-yellow oil (0.17 g, 80%). ¹H NMR (400 MHz, CDCl₃) δ 6.43 (br, 2 H, PhH), 6.36 (t, 1 H, PhH), 5.00 (s, 2 H, PhCH₂-), 3.89 (t, 4 H, PhOCH₂-), 2.59–2.24 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.81 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.73 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.24 (br, 38 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.4, 138.1, 106.3, 100.9, 68.0, 66.1, 57.5, 55.0, 52.8, 45.8, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₃H₇₉N₂O₄: 687.6; Found: 688.3.



3-(Decyloxy)-5-(heptadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (32f, IAJD233).

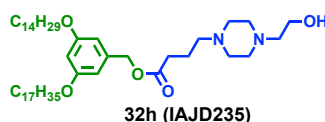
Compound **32f** was synthesized from compound **31c** (0.19 g, 0.21 mmol), 1-(2-hydroxyethyl)piperazine (42 mg, 0.32 mmol) and K₂CO₃ (35 mg, 0.25 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a colorless oil (0.10 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.64 (t, 2 H, -CH₂CH₂OH), 2.62–2.30 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.25 (br, 38 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 52.9, 52.8, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6,

29.6, 29.4, 29.4, 29.3, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{44}H_{81}N_2O_5$: 717.6; Found: 717.6.



3-(Heptadecyloxy)-5-(tetradecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (32g, IAJD234).

Compound **32g** was synthesized from compound **31d** (0.20 g, 0.28 mmol), 1-methylpiperazine (30 mg, 0.30 mmol) and K_2CO_3 (42 mg, 0.30 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a light-yellow oil (0.17 g, 80%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.92 (t, 4 H, $PhOCH_2-$), 2.77–2.14 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.75 (m, 4 H, $PhOCH_2CH_2-$), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.25 (br, 46 H, $PhOCH_2CH_2CH_2(CH_2)_{10}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 160.6, 138.2, 106.5, 101.1, 68.2, 66.3, 57.7, 55.3, 53.2, 46.2, 32.4, 32.1, 29.8, 29.8, 29.8, 29.8, 29.5, 29.5, 29.4, 26.2, 22.8, 22.3, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{47}H_{87}N_2O_4$: 743.7; Found: 745.5.

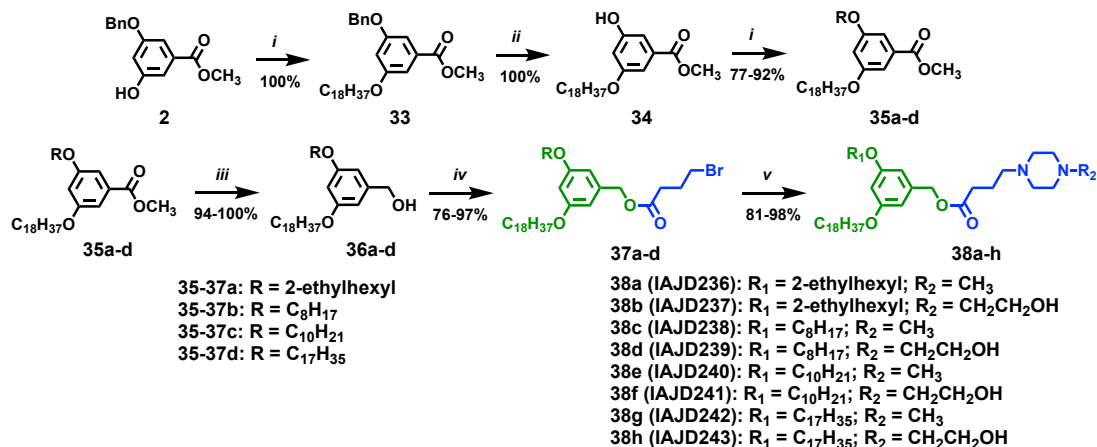


3-(Heptadecyloxy)-5-(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (32h, IAJD235).

Compound **32h** was synthesized from compound **31d** (0.20 g, 0.28 mmol), 1-(2-hydroxyethyl)piperazine (39 mg, 0.30 mmol) and K_2CO_3 (42 mg, 0.30 mmol) following a procedure similar to that used for the synthesis of compound **32a**. The title compound was obtained as a light-yellow oil (0.16 g, 73%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.61 (t, 2 H, $-CH_2CH_2OH$), 2.74–2.12 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.75 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.25 (br, 46 H, $PhOCH_2CH_2CH_2(CH_2)_{10}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.2, 59.4, 57.8, 57.6, 53.0, 53.0, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{48}H_{89}N_2O_5$: 773.7; Found: 774.3.

3.6 Synthesis of Octadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

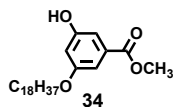
Scheme S6. Synthesis of Octadecane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains



Reagents and conditions: (i) RBr/ROTs, K₂CO₃, DMF, 120 °C, 2 h; (ii) H₂, Pd/C, DCM, MeOH, 12 h; (iii) LiAlH₄, THF, 0–23 °C, 1 h; (iv) DCC, DPTS, DCM, 12 h; (v) K₂CO₃, MeCN, 95 °C, 3 h.

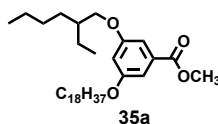


Methyl 3-(benzyloxy)-5-(octadecyloxy)benzoate (33). A mixture of compound **2** (2.00 g, 7.74 mmol, 1 equiv), 1-bromooctadecane (2.84 g, 8.52 mmol, 1.1 equiv), K₂CO₃ (2.14 g, 15.48 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (3.28 g, 84%). ¹H NMR (400 MHz, CDCl₃) δ 7.48–7.29 (m, 5 H, PhH), 7.27 (br, 1 H, PhH), 7.20 (br, 1 H, PhH), 6.73 (t, 1 H, PhH), 5.08 (s, 2 H, PhCH₂O-), 3.97 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.78 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 1.44 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 1.28 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.89 (t, 3 H, PhO(CH₂)₁₇CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.3, 159.9, 136.7, 132.1, 128.7, 128.2, 127.7, 108.3, 108.0, 107.1, 77.4, 70.4, 68.5, 52.3, 32.1, 29.8, 29.7, 29.7, 29.5, 29.3, 26.4, 26.1, 22.9, 22.8, 14.2. Mp = 65 °C.

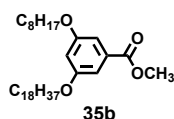


Methyl 3-hydroxy-5-(octadecyloxy)benzoate (34). Compound **33** (3.28 g, 6.42 mmol) was dissolved in a mixture of DCM (20 mL) and methanol (10 mL). Then Pd/C (0.16 g, 5 wt%) was added to the solution

and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at 23 °C under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (2.70 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, 2 H, *PhH*), 6.64 (t, 1 H, *PhH*), 3.95 (t, 2 H, *PhOCH*₂-), 3.89 (s, 3 H, *PhCOOCH*₃), 1.75 (m, 2 H, *PhOCH*₂*CH*₂*CH*₂(CH₂)₁₄CH₃), 1.44 (m, 2 H, *PhOCH*₂*CH*₂*CH*₂(CH₂)₁₄CH₃), 1.26 (m, 28 H, *PhOCH*₂*CH*₂*CH*₂(CH₂)₁₄CH₃), 0.88 (t, 3 H, *PhO*(CH₂)₁₇CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.4, 157.0, 131.9, 109.0, 107.7, 107.1, 68.4, 52.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.2, 26.0, 22.7, 14.2. Mp = 99 °C.

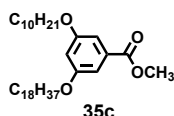


Methyl 3-((2-ethylhexyl)oxy)-5-(octadecyloxy)benzoate (35a). A mixture of compound **34** (0.60 g, 1.43 mmol, 1 equiv), 2-ethylhexyl bromide (0.30 g, 1.57 mmol, 1.1 equiv), K₂CO₃ (0.39 g, 2.86 mmol, 2 equiv) and DMF (15 mL) was heated to 80 °C and stirred under N₂ atmosphere for 12 h. The reaction mixture was cooled to 23 °C and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/EtOAc = 20/1 as the eluent to give the title compound as a light-yellow oil (0.63 g, 83%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, *PhH*), 6.64 (t, 1 H, *PhH*), 3.97 (t, 2 H, *PhOCH*₂(CH₂)₁₆CH₃), 3.90 (s, 3 H, *PhCOOCH*₃), 3.86 (m, 2 H, *PhOCH*₂CH(CH₂CH₃)-), 1.85–1.69 (m, 3 H, *PhOCH*₂*CH*₂(CH₂)₁₅CH₃ and *PhOCH*₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.52–1.17 (m, 38 H, *PhOCH*₂*CH*₂(CH₂)₁₅CH₃ and *PhOCH*₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.90 (m, 9 H, *PhO*(CH₂)₁₇CH₃ and *PhOCH*₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.4, 160.2, 131.8, 107.7, 107.5, 106.6, 70.8, 68.3, 52.1, 39.4, 31.9, 30.5, 29.7, 29.7, 29.6, 29.6, 29.4, 29.2, 29.1, 26.0, 23.9, 23.0, 22.7, 14.1, 14.1, 11.1.

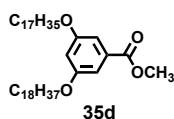


Methyl 3-(octadecyloxy)-5-(octyloxy)benzoate (35b). A mixture of compound **34** (0.50 g, 1.19 mmol, 1 equiv), 1-bromooctane (0.25 g, 1.31 mmol, 1.1 equiv), K₂CO₃ (0.33 g, 2.38 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered

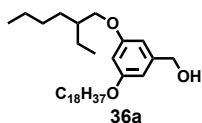
and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.48 g, 76%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 31.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.3, 26.2, 22.8, 22.8, 14.2, 14.2. Mp = 58 °C.



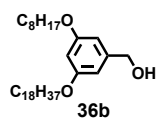
Methyl 3-(decyloxy)-5-(octadecyloxy)benzoate (35c). Compound **35c** was synthesized from compound **34** (0.50 g, 1.19 mmol, 1 equiv), 1-bromodecane (0.29 g, 1.31 mmol, 1.1 equiv) and K_2CO_3 (0.33 g, 2.38 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **35b**. The title compound was obtained as a white solid (0.48 g, 72%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 40 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 68.1, 52.3, 32.1, 32.0, 29.9, 29.8, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.3, 26.3, 26.2, 22.8, 14.2. Mp = 60 °C.



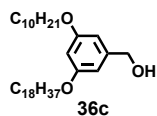
Methyl 3-(heptadecyloxy)-5-(octadecyloxy)benzoate (35d). Compound **35d** was synthesized from compound **34** (0.50 g, 1.19 mmol, 1 equiv), $\text{C}_{17}\text{H}_{35}\text{OTs}$ (0.54 g, 1.31 mmol, 1.1 equiv) and K_2CO_3 (0.33 g, 2.38 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **35b**. The title compound was obtained as a white solid (0.70 g, 89%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 54 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 34.1, 33.0, 32.1, 29.9, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.3, 28.9, 28.3, 26.2, 22.8, 14.3. Mp = 72 °C.



(3-((2-Ethylhexyl)oxy)-5-(octadecyloxy)phenyl)methanol (36a). Compound **35a** (0.30 g, 0.56 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of LiAlH₄ (22 mg, 0.56 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N₂ atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous MgSO₄ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.24 g, 84%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (d, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.94 (t, 2 H, PhOCH₂(CH₂)₁₆CH₃), 3.82 (m, 2 H, PhOCH₂CH(CH₂CH₃)₂), 1.72 (m, 3 H, PhOCH₂CH₂(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.52–1.17 (m, 38 H, PhOCH₂CH₂(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.91 (m, 9 H, PhO(CH₂)₁₇CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 161.0, 160.7, 143.3, 105.3, 105.1, 100.7, 70.7, 68.2, 65.6, 62.9, 39.5, 32.1, 30.7, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.2.

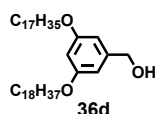


(3-(Octadecyloxy)-5-(octyloxy)phenyl)methanol (36b). Compound **35b** (0.50 g, 0.94 mmol, 1 equiv) and LiAlH₄ (36 mg, 0.94 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **36a**. The title compound was obtained as a white solid (0.46 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.59 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 36 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₇CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.6, 143.4, 105.2, 100.7, 77.4, 68.2, 65.4, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.8, 14.2, 14.2. Mp = 37 °C.

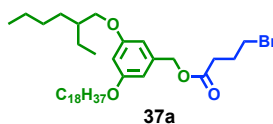


(3-(Decyloxy)-5-(octadecyloxy)phenyl)methanol (36c). Compound **35c** (0.44 g, 0.78 mmol, 1 equiv) and LiAlH₄ (30 mg, 0.78 mmol, 1 equiv) following a

procedure similar to that used for the synthesis of compound **36a**. The title compound was obtained as a white solid (0.40 g, 96%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 40 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 160.7, 143.4, 105.2, 100.7, 77.4, 68.2, 65.5, 32.1, 32.1, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.5, 29.4, 26.2, 22.8, 14.3. Mp = 42 °C.

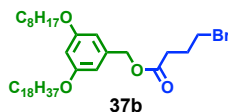


(3-(Heptadecyloxy)-5-(octadecyloxy)phenyl)methanol (36d). Compound **36d** was synthesized from compound **35d** (0.70 g, 1.06 mmol, 1 equiv) and LiAlH_4 (40 mg, 1.06 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **36a**. The title compound was obtained as a white solid (0.46 g, 69%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 54 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 160.6, 143.4, 125.7, 105.2, 100.7, 68.2, 65.6, 32.1, 30.5, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 25.9, 22.8, 14.3. Mp = 62 °C.

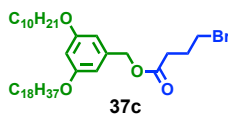


3-((2-Ethylhexyl)oxy)-5-(octadecyloxy)benzyl 4-bromobutanoate (37a). Compound **36a** (0.24 g, 0.48 mmol, 1 equiv), 4-bromobutyric acid (0.09 g, 0.52 mmol, 1.1 equiv) and DPTS (0.15 g, 0.52 mmol, 1.1 equiv) were dissolved in 8 mL DCM. DCC (0.20 g, 0.95 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.29 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (d, 2 H, PhH), 6.42 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_{16}\text{CH}_3$), 3.82 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.21 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.83–1.67 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_{15}\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.45–1.21 (m, 38 H,

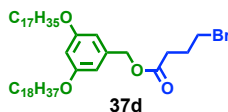
PhOCH₂CH₂(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.91 (m, 9 H, PhO(CH₂)₁₇CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.9, 160.6, 137.9, 106.6, 106.4, 101.2, 70.7, 68.2, 66.6, 39.5, 32.8, 32.6, 32.1, 30.7, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 27.9, 26.2, 24.0, 23.2, 22.8, 14.3, 14.2, 11.3.



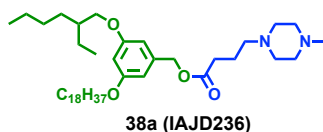
3-(Octadecyloxy)-5-(octyloxy)benzyl 4-bromobutanoate (37b). Compound **37b** was synthesized from compound **36b** (0.46 g, 0.91 mmol, 1 equiv), 4-bromobutyric acid (0.17 g, 1.00 mmol, 1.1 equiv), DPTS (0.30 g, 1.00 mmol, 1.1 equiv) and DCC (0.38 g, 1.82 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **37a**. The title compound was obtained as a colorless oil (0.37 g, 62%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 36 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₇CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 32.7, 32.6, 32.1, 32.0, 30.5, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 22.8, 14.3, 14.2.



3-(Decyloxy)-5-(octadecyloxy)benzyl 4-bromobutanoate (37c). Compound **37c** was synthesized from compound **36c** (0.40 g, 0.75 mmol, 1 equiv), 4-bromobutyric acid (0.14 g, 0.83 mmol, 1.1 equiv), DPTS (0.24 g, 0.83 mmol, 1.1 equiv) and DCC (0.31 g, 1.50 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **37a**. The title compound was obtained as a colorless oil (0.35 g, 68%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 40 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.89 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₁₇CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 32.7, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

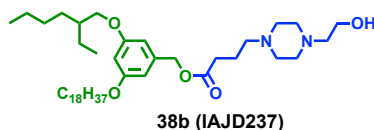


3-((2-Ethylhexyl)oxy)-5-(octadecyloxy)benzyl 4-bromobutanoate (37d). Compound **37d** was synthesized from compound **36d** (0.46 g, 0.73 mmol, 1 equiv), 4-bromobutyric acid (0.13 g, 0.80 mmol, 1.1 equiv), DPTS (0.24 g, 0.80 mmol, 1.1 equiv) and DCC (0.30 g, 1.46 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **37a**. The title compound was obtained as a white solid (0.45 g, 79%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.54 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 54 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₆CH₃ and PhO(CH₂)₁₇CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.5, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3. Mp = 45 °C.

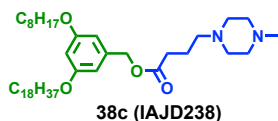


3-((2-Ethylhexyl)oxy)-5-(octadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (38a, IAJD236). A mixture of compound **37a** (0.14 g, 0.21 mmol, 1.0 equiv), 1-methylpiperazine (23 mg, 0.23 mmol, 1.1 equiv), K₂CO₃ (35 mg, 0.25 mmol, 1.2 equiv) and MeCN (10 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.14 g, 99%). ¹H NMR (400 MHz, CDCl₃) δ 6.44 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 3.79 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 2.63–2.25 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.82 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.71 (m, 3 H, PhOCH₂CH₂(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.48–1.17 (m, 38 H, PhOCH₂CH₂(CH₂)₁₅CH₃ and

PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.88 (m, 9 H, PhO(CH₂)₁₇CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.8, 160.5, 138.1, 106.5, 106.4, 101.0, 70.6, 68.1, 66.2, 57.5, 55.1, 52.8, 45.9, 39.5, 32.3, 32.0, 30.6, 29.8, 29.8, 29.7, 29.7, 29.5, 29.4, 29.4, 29.2, 26.2, 24.0, 23.1, 22.8, 22.2, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₂H₇₇N₂O₄: 673.6; Found: 674.1.

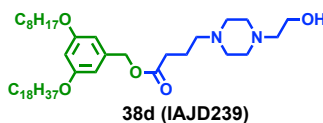


3-((2-Ethylhexyl)oxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (38b, IAJD237). Compound **38b** was synthesized from compound **37a** (0.14 g, 0.21 mmol), 1-(2-hydroxyethyl)piperazine (30 mg, 0.23 mmol) and K₂CO₃ (35 mg, 0.25 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.14 g, 98%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.80 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 3.61 (t, 2 H, -CH₂CH₂OH), 2.73–2.32 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₂-), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.73 (m, 3 H, PhOCH₂CH₂(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.62–1.17 (m, 38 H, PhOCH₂CH₂(CH₂)₁₅CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.88 (m, 9 H, PhO(CH₂)₁₇CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 160.8, 160.6, 138.1, 106.6, 106.6, 106.5, 101.0, 77.4, 70.7, 68.2, 66.3, 59.4, 57.7, 57.6, 53.0, 52.9, 39.5, 32.3, 32.1, 30.7, 29.8, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 22.2, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₃H₇₉N₂O₅: 703.6; Found: 703.8.

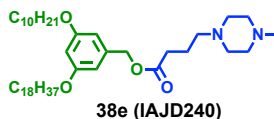


3-(Octadecyloxy)-5-(octyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (38c, IAJD238). Compound **38c** was synthesized from compound **37b** (0.17 g, 0.26 mmol), 1-methylpiperazine (29 mg, 0.29 mmol) and K₂CO₃ (43 mg, 0.31 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.18 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.65–2.29 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.74 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 36 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR

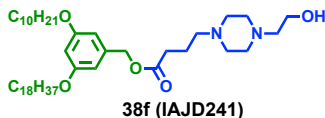
(101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 57.5, 54.9, 53.5, 52.7, 45.8, 32.2, 32.0, 31.9, 29.7, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.3, 26.1, 22.7, 22.7, 22.1, 14.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for C₄₂H₇₇N₂O₄: 673.6; Found: 674.1.



3-(Octadecyloxy)-5-(octyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (38d, IAJD239). Compound **38d** was synthesized from compound **37b** (0.17 g, 0.26 mmol), 1-(2-hydroxyethyl)piperazine (38 mg, 0.29 mmol) and K₂CO₃ (43 mg, 0.31 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.17 g, 98%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.60 (t, 2 H, -CH₂CH₂OH), 2.64–2.25 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 36 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 59.4, 57.8, 57.6, 53.1, 53.0, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for C₄₃H₇₉N₂O₅: 703.6; Found: 703.9.

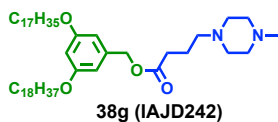


3-(Decyloxy)-5-(octadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (38e, IAJD240). Compound **38e** was synthesized from compound **37c** (0.17 g, 0.25 mmol), 1-methylpiperazine (28 mg, 0.28 mmol) and K₂CO₃ (42 mg, 0.30 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.18 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.59–2.26 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.42 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 40 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 160.6, 138.2, 106.5, 101.0, 77.4, 68.2, 66.3, 57.6, 55.2, 53.0, 46.0, 32.4, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.3, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for C₄₄H₈₁N₂O₄: 701.6; Found: 701.4.



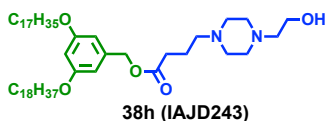
3-(Decyloxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (38f, IAJD241).

Compound **38f** was synthesized from compound **37c** (0.17 g, 0.25 mmol), 1-(2-hydroxyethyl)piperazine (36 mg, 0.28 mmol) and K_2CO_3 (42 mg, 0.30 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.18 g, 98%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 3.60 (t, 2 H, $-CH_2CH_2OH$), 2.62–2.30 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.74 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.27 (br, 40 H, $PhOCH_2CH_2CH_2(CH_2)_6CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.5, 100.9, 68.1, 66.2, 59.4, 57.8, 57.6, 53.0, 52.9, 32.3, 32.0, 32.0, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{45}H_{83}N_2O_5$: 731.6; Found: 731.6.



3-(Heptadecyloxy)-5-(octadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (38g, IAJD242).

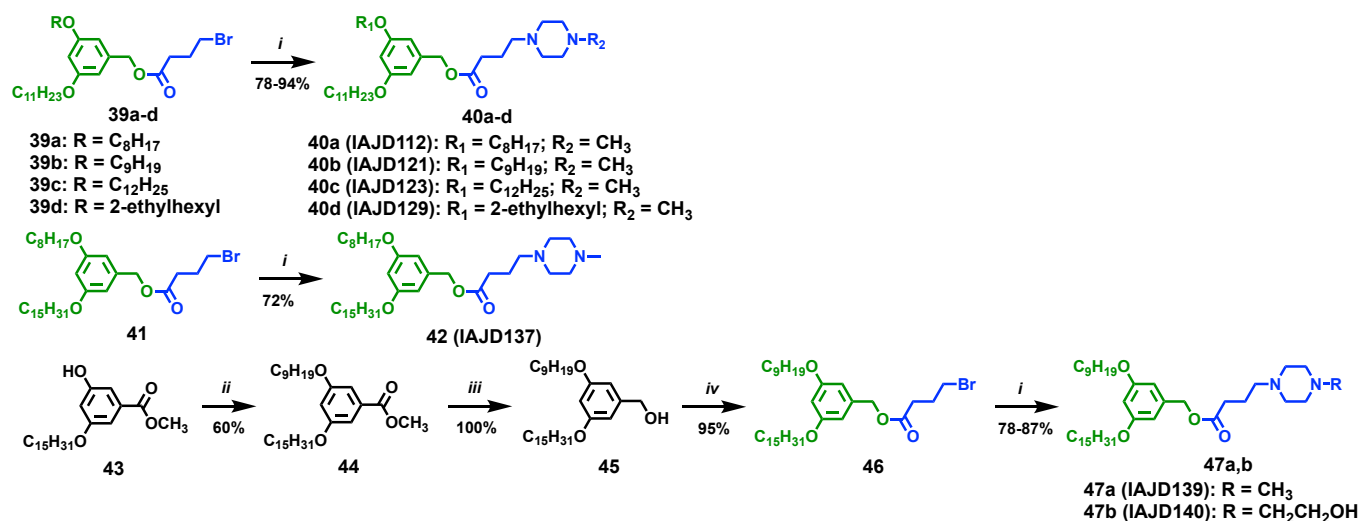
Compound **38g** was synthesized from compound **37d** (0.18 g, 0.23 mmol), 1-methylpiperazine (25 mg, 0.25 mmol) and K_2CO_3 (39 mg, 0.28 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.18 g, 99%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 2.59–2.25 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.77 (m, 4 H, $PhOCH_2CH_2-$), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.27 (br, 54 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.2, 106.5, 101.0, 68.2, 66.2, 57.6, 55.1, 52.9, 45.9, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{51}H_{95}N_2O_4$: 799.7; Found: 799.8.



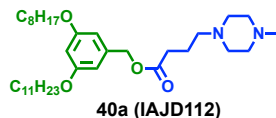
3-(Heptadecyloxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (38h, IAJD243). Compound **38h** was synthesized from compound **37d** (0.18 g, 0.23 mmol), 1-(2-hydroxyethyl)piperazine (33 mg, 0.25 mmol) and K_2CO_3 (39 mg, 0.28 mmol) following a procedure similar to that used for the synthesis of compound **38a**. The title compound was obtained as a colorless oil (0.18 g, 95%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2$ -), 3.91 (t, 4 H, $PhOCH_2$ -), 3.60 (t, 2 H, $-CH_2CH_2OH$), 2.63–2.31 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.74 (m, 4 H, $PhOCH_2CH_2$ -), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.25 (br, 54 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{14}CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 59.5, 57.8, 57.6, 53.0, 53.0, 32.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{52}H_{97}N_2O_5$: 829.7; Found: 829.9.

3.7 Synthesis of Undecane and Pentadecane Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

Scheme S7. Synthesis of Undecane and Pentadecane Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

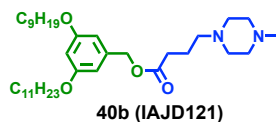


Reagents and conditions: (i) K_2CO_3 , MeCN, 95 °C, 3 h; (ii) $C_9H_{19}Br$, K_2CO_3 , DMF, 120 °C, 2 h; (iii) $LiAlH_4$, THF, 0–23 °C, 1 h; (iv) DCC, DPTS, DCM, 12 h.



3-(Octyloxy)-5-(undecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (40a, IAJD112).

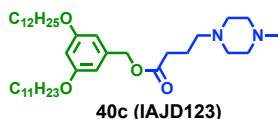
Compound **39a** was synthesized according to a literature procedure reported by our laboratory.^[5] A mixture of compound **39a** (0.20 g, 0.36 mmol, 1.0 equiv), 1-methylpiperazine (40 mg, 0.40 mmol, 1.1 equiv), K₂CO₃ (59 mg, 0.43 mmol, 1.2 equiv) and MeCN (10 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.18 g, 83%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 2.64–2.17 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 22 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₇CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.4, 138.1, 106.3, 100.8, 68.0, 66.1, 57.6, 55.2, 53.1, 46.0, 32.2, 31.9, 31.8, 29.6, 29.6, 29.4, 29.3, 29.3, 29.2, 26.0, 22.7, 22.6, 22.2, 14.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₅H₆₃N₂O₄: 575.5; Found: 576.9.



3-(Nonyloxy)-5-(undecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (40b, IAJD121).

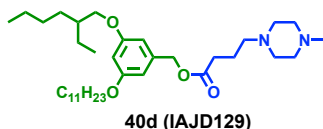
Compound **39b** was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **40b** was synthesized from compound **39b** (0.15 g, 0.26 mmol), 1-methylpiperazine (29 mg, 0.29 mmol) and K₂CO₃ (43 mg, 0.31 mmol) following a procedure similar to that used for the synthesis of compound **40a**. The title compound was obtained as a colorless oil (0.14 g, 93%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 2.68–2.18 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-),

1.74 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (br, 24 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃ and PhOCH₂CH₂CH₂(CH₂)₇CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.4, 138.1, 106.3, 100.8, 68.0, 66.1, 57.5, 55.2, 53.1, 46.0, 32.2, 31.9, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 29.2, 26.0, 22.7, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₆H₆₅N₂O₄: 589.5; Found: 591.2.



3-(Dodecyloxy)-5-(undecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (40c, IAJD123).

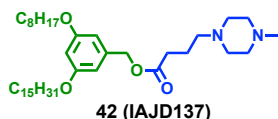
Compound **39c** was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **40c** was synthesized from compound **39c** (0.25 g, 0.41 mmol), 1-methylpiperazine (45 mg, 0.45 mmol) and K₂CO₃ (68 mg, 0.49 mmol) following a procedure similar to that used for the synthesis of compound **40a**. The title compound was obtained as a colorless oil (0.20 g, 78%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.63–2.20 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.42 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 30 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH₂CH₂(CH₂)₇CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 160.6, 138.2, 106.5, 101.0, 77.4, 68.2, 66.3, 60.5, 57.7, 55.3, 53.2, 46.2, 32.4, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.3, 21.2, 14.3, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₉H₇₁N₂O₄: 631.5; Found: 632.8.



3-((2-Ethylhexyl)oxy)-5-(undecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (40d, IAJD129).

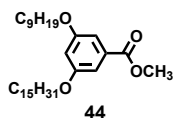
Compound **39d** was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **40d** was synthesized from compound **39d** (0.28 g, 0.49 mmol), 1-methylpiperazine (55 mg, 0.54 mmol) and K₂CO₃ (81 mg, 0.59 mmol) following a procedure similar to that used for the synthesis of compound **40a**. The title compound was obtained as a colorless oil (0.26 g, 94%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 3.80 (m, 2 H, PhOCH₂CH(CH₂CH₃)-), 2.62–2.18 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.71 (m, 3 H, PhOCH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.52–1.19 (m, 24 H, PhOCH₂CH₂(CH₂)₈CH₃ and

PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.89 (m, 9 H, PhO(CH₂)₁₀CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 160.8, 160.6, 138.1, 106.6, 106.4, 101.0, 77.4, 70.6, 68.2, 66.3, 57.7, 55.3, 53.2, 46.2, 39.5, 32.4, 32.0, 30.6, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 26.2, 24.0, 23.2, 22.8, 22.3, 14.2, 14.2, 11.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₅H₆₃N₂O₄: 575.5; Found: 576.6.



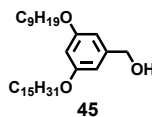
3-(Octyloxy)-5-(pentadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (42, IAJD137).

Compound **41** was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **42** was synthesized from compound **41** (0.25 g, 0.41 mmol), 1-methylpiperazine (45 mg, 0.45 mmol) and K₂CO₃ (68 mg, 0.49 mmol) following a procedure similar to that used for the synthesis of compound **40a**. The title compound was obtained as a colorless oil (0.18 g, 72%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.62–2.24 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 30 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 57.5, 55.0, 52.8, 45.8, 32.2, 31.9, 31.8, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₉H₇₁N₂O₄: 631.5; Found: 632.8.

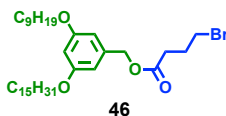


Methyl 3-(nonyloxy)-5-(pentadecyloxy)benzoate (44). Compound **43** was synthesized according to a literature procedure reported by our laboratory.^[5] A mixture of compound **43** (0.50 g, 1.32 mmol, 1 equiv), 1-bromononane (0.30 g, 1.45 mmol, 1.1 equiv), K₂CO₃ (0.36 g, 2.64 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.39 g, 60%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 32 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.88

(t, 6 H, $\text{PhO}(\text{CH}_2)_8\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{14}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.0, 160.2, 131.8, 107.6, 106.6, 68.3, 52.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.2, 26.0, 22.7, 22.7, 14.1. Mp = 52°C.

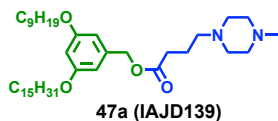


(3-(Nonyloxy)-5-(pentadecyloxy)phenyl)methanol (45). Compound **44** (0.35 g, 0.69 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of LiAlH_4 (26 mg, 0.69 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N_2 atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous MgSO_4 and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.25 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.29 (m, 32 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{11}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_8\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{14}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.5, 143.2, 105.1, 100.6, 68.1, 65.5, 31.9, 31.8, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 14.1, 14.1.



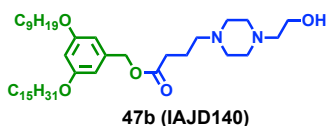
3-(Nonyloxy)-5-(pentadecyloxy)benzyl 4-bromobutanoate (46). Compound **45** (0.29 g, 0.61 mmol, 1 equiv), 4-bromobutyric acid (0.11 g, 0.67 mmol, 1.1 equiv) and DPTS (0.19 g, 0.67 mmol, 1.1 equiv) were dissolved in 8 mL DCM. DCC (0.26 g, 1.22 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.32 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 32 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{11}\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_8\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{14}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 160.5, 137.8,

106.4, 101.0, 77.2, 68.1, 66.4, 32.7, 32.5, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 29.3, 27.7, 26.1, 22.7, 14.1.



3-(Nonyloxy)-5-(pentadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (47a, IAJD139).

Compound **47a** was synthesized from compound **46** (0.20 g, 0.31 mmol), 1-methylpiperazine (34 mg, 0.34 mmol) and K_2CO_3 (51 mg, 0.37 mmol) following a procedure similar to that used for the synthesis of compound **40a**. The title compound was obtained as a colorless oil (0.15 g, 78%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.62–2.26 (m, 15 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.84 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.43 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.27 (br, 32 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₅*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₁*CH*₃), 0.87 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 57.5, 55.0, 52.8, 45.8, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{40}H_{73}N_2O_4$: 645.6; Found: 647.7.

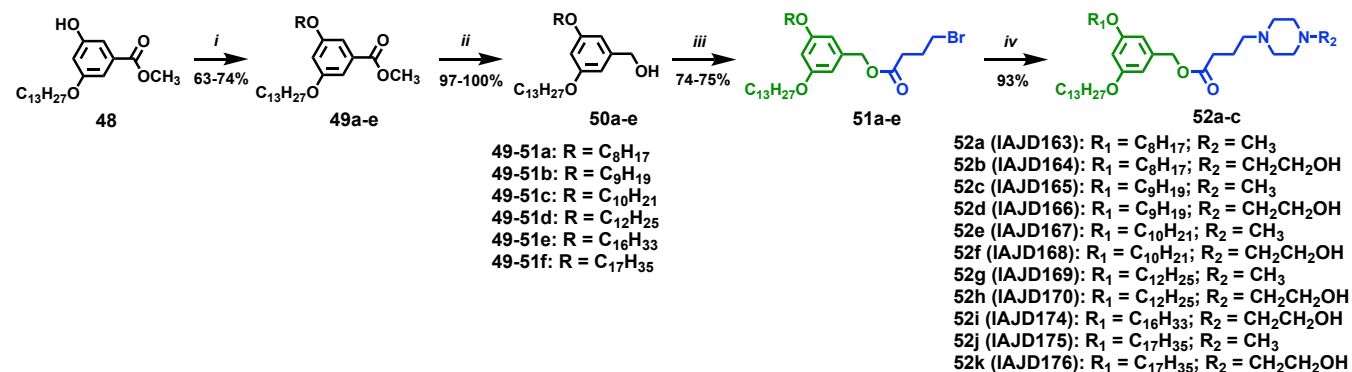


3-(Nonyloxy)-5-(pentadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (47b, IAJD140).

Compound **47b** was synthesized from compound **46** (0.20 g, 0.31 mmol), 1-(2-hydroxyethyl)piperazine (44 mg, 0.34 mmol) and K_2CO_3 (51 mg, 0.37 mmol) following a procedure similar to that used for the synthesis of compound **40a**. The title compound was obtained as a colorless oil (0.20 g, 87%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 3.61 (t, 2 H, -*CH*₂*CH*₂*OH*), 2.63–2.27 (m, 14 H, -*N*(*CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*CH*₂*CH*₂*OH*), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.43 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.25 (br, 32 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₅*CH*₃ and *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₁₁*CH*₃), 0.88 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 59.3, 59.3, 57.6, 57.5, 53.4, 53.0, 52.8, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of $[M + H]^+$ calculated for $C_{41}H_{75}N_2O_5$: 675.6; Found: 676.9.

3.8 Synthesis of Tridecane Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

Scheme S8. Synthesis of Tridecane Based IAJDs with 3,5-Nonsymmetric Alkyl Chains



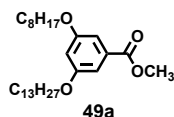
Reagents and conditions: (i) RBr, K₂CO₃, DMF, 120 °C, 2 h; (ii) LiAlH₄, THF, 0–23 °C, 1 h; (iii) DCC, DPTS, DCM, 12 h; (iv) K₂CO₃, MeCN, 95 °C, 3 h.

General Synthetic Procedure for Compounds 51e. Compounds **49e** were synthesized according to a procedure elaborated and optimized by our laboratory.³ Generally, compound **48** (1 equiv) and K₂CO₃ (2 equiv) were stirred in dry DMF. RBr (2.2 equiv) was added, and the mixture was stirred at 120 °C under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C. The reaction mixture was poured into ice/water and the white precipitates were filtered and collected. Then the precipitates were purified by recrystallization from acetone to give the title compound as a white solid. The synthesis and characterizations of compounds **50e** were reported in the literature.⁵

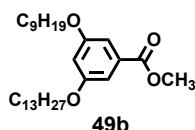
General Synthetic Procedure for Compounds 50e. Compounds **50e** were synthesized according to a procedure reported by our group.⁴ Generally, compounds **49e** (1 equiv) were dissolved in dry THF, which was added dropwise to a slurry of LiAlH₄ (1 equiv) in dry THF at 0 °C under N₂ atmosphere. The resulted mixture was stirred at 23 °C for 1 h. The reaction was quenched by the successive addition of water, 15% NaOH aqueous solution and water. Then the mixture was filtered and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a white solid or light-yellow oil. The synthesis and characterizations of compounds **50e** were reported in the literature.⁵

General Synthetic Procedure for Compounds 51e. Compounds **51e** were synthesized according to a procedure reported by our group.⁴ Generally, compounds **50e** (1 equiv), 4-bromobutyric acid (1.1 equiv) and DPTS (1.1 equiv) were dissolved in dry DCM. DCC (2 equiv) was added into the above mixture and stirred for 12h. Hexane was added to the reaction mixture, which was then vacuum filtered. The filtrate was concentrated and further purified by column chromatography on silica gel with a mobile phase of

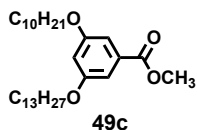
hexane/DCM = 1/1 (v/v) to afford the title compound as a transparent oil. The synthesis and characterizations of compounds **51e** were reported in the literature.⁵



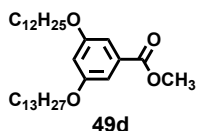
Methyl 3-(octyloxy)-5-(tridecyloxy)benzoate (49a). Compound **48** was synthesized according to a literature procedure reported by our laboratory.^[5] A mixture of compound **48** (0.60 g, 1.71 mmol, 1 equiv), 1-bromooctane (0.37 g, 1.88 mmol, 1.1 equiv), K₂CO₃ (0.47 g, 3.42 mmol, 2 equiv) and DMF (15 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.51 g, 64%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 26 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 29.8, 29.8, 29.7, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 47 °C.



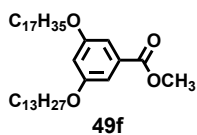
Methyl 3-(nonyloxy)-5-(tridecyloxy)benzoate (49b). Compound **49b** was synthesized from Compound **27** (0.60 g, 1.71 mmol, 1 equiv), 1-bromononane (0.39 g, 1.88 mmol, 1.1 equiv) and K₂CO₃ (0.47 g, 3.42 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **49a**. The title compound was obtained as a white solid (0.51 g, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.88 (t, 6 H, PhO(CH₂)₈CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 26.2, 22.8, 14.2. Mp = 48 °C.



Methyl 3-(decyloxy)-5-(tridecyloxy)benzoate (49c). Compound **49c** was synthesized from compound **48** (0.60 g, 1.71 mmol, 1 equiv), 1-bromodecane (0.39 g, 1.88 mmol, 1.1 equiv) and K_2CO_3 (0.47 g, 3.42 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **49a**. The title compound was obtained as a white solid (0.62 g, 74%). 1H NMR (400 MHz, $CDCl_3$) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.77 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (m, 30 H, $PhOCH_2CH_2CH_2(CH_2)_6CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_9CH_3$), 0.88 (t, 6 H, $PhO(CH_2)_9CH_3$ and $PhO(CH_2)_{12}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 50 °C.

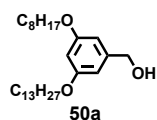


Methyl 3-(Dodecyloxy)-5-(tridecyloxy)benzoate (49d). Compound **49d** was synthesized from Compound **48** (0.60 g, 1.71 mmol, 1 equiv), 1-bromononane (0.39 g, 1.88 mmol, 1.1 equiv) and K_2CO_3 (0.47 g, 3.42 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **49a**. The title compound was obtained as a white solid (0.71 g, 80%). 1H NMR (400 MHz, $CDCl_3$) δ 7.16 (br, 2 H, PhH), 6.64 (t, 1 H, PhH), 3.96 (t, 4 H, $PhOCH_2CH_2CH_2-$), 3.89 (s, 3 H, $PhCOOCH_3$), 1.77 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.45 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (m, 34 H, $PhOCH_2CH_2CH_2(CH_2)_8CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_9CH_3$), 0.88 (t, 6 H, $PhO(CH_2)_{11}CH_3$ and $PhO(CH_2)_{12}CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 132.0, 107.8, 106.7, 77.4, 68.5, 52.3, 32.1, 29.8, 29.7, 29.7, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 51 °C.

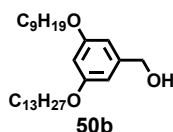


Methyl 3-(Heptadecyloxy)-5-(tridecyloxy)benzoate (49f). Compound **49f** was synthesized from Compound **48** (0.60 g, 1.71 mmol, 1 equiv), 1-bromononane (0.39 g, 1.88 mmol, 1.1 equiv) and K_2CO_3 (0.47 g, 3.42 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **49a**. The title compound was obtained as a white solid (0.75 g, 75%). 1H NMR (400 MHz, $CDCl_3$) δ 7.16

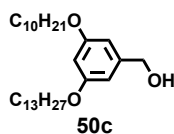
(br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₆CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.3, 132.0, 107.8, 106.7, 68.5, 52.3, 32.1, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.3, 26.2, 22.8, 14.3. Mp = 54 °C.



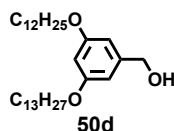
(3-(Octyloxy)-5-(tridecyloxy)phenyl)methanol (50a). Compound **49a** (0.47 g, 1.02 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of LiAlH₄ (39 mg, 1.02 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N₂ atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous MgSO₄ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.45 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 26 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 143.4, 143.3, 105.2, 100.7, 68.2, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.8, 14.2, 14.2.



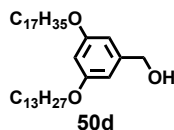
(3-(Nonyloxy)-5-(tridecyloxy)phenyl)methanol (50b). Compound **49b** (0.45 g, 0.94 mmol, 1 equiv) and LiAlH₄ (36 mg, 0.94 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound 23a. The title compound was obtained as a colorless oil (0.41 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, PhO(CH₂)₈CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 160.6, 143.4, 143.4, 105.2, 100.7, 77.5, 77.2, 76.9, 68.2, 65.6, 65.4, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 14.2.



(3-(Decyloxy)-5-(tridecyloxy)phenyl)methanol (50c). Compound **50c** was synthesized from compound **49b** (0.56 g, 1.14 mmol, 1 equiv) and LiAlH_4 (44 mg, 1.14 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **50a**. The title compound was obtained as a colorless oil (0.51 g, 97%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 30 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, PhO(CH₂)₉CH₃ and PhO(CH₂)₁₂CH₃). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 160.7, 143.4, 105.2, 100.7, 100.7, 68.2, 65.6, 65.5, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.5, 29.4, 26.2, 22.8, 14.3.

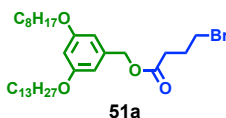


(3-(Dodecyloxy)-5-(tridecyloxy)phenyl)methanol (50d). Compound **49d** (0.68 g, 1.31 mmol, 1 equiv) and LiAlH_4 (50 mg, 1.31 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **23a**. The title compound was obtained as a colorless oil (0.60 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 34 H, PhOCH₂CH₂CH₂(CH₂)₈CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₁CH₃ and PhO(CH₂)₁₂CH₃). ^{13}C NMR (101 MHz, CDCl_3) δ 160.7, 160.7, 143.4, 143.3, 105.2, 100.7, 100.7, 68.2, 65.6, 65.5, 32.1, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 14.3.

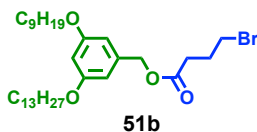


(3-(Heptadecyloxy)-5-(tridecyloxy)phenyl)methanol (50f). Compound **49f** (0.73 g, 1.24 mmol, 1 equiv) and LiAlH_4 (47 mg, 1.24 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **23a**. The title compound was obtained as a colorless oil (0.65 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 44 H,

PhOCH₂CH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₆CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 160.7, 143.4, 143.3, 105.2, 100.7, 100.7, 68.2, 65.6, 65.5, 32.1, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 14.3. Mp = 46 °C.

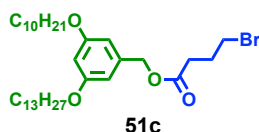


3-(Octyloxy)-5-(tridecyloxy)benzyl 4-bromobutanoate (51a). Compound **50a** (0.47 g, 1.08 mmol, 1 equiv), 4-bromobutyric acid (0.20 g, 1.19 mmol, 1.1 equiv) and DPTS (0.34 g, 1.19 mmol, 1.1 equiv) were dissolved in 8 mL DCM. DCC (0.45 g, 2.16 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.46 g, 74%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 26 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.5, 32.8, 32.6, 32.1, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 22.8, 14.3, 14.2.

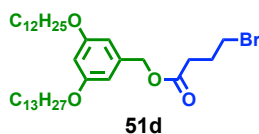


3-(Nonyloxy)-5-(tridecyloxy)benzyl 4-bromobutanoate (51b). Compound **51b** was synthesized from compound **50b** (0.45 g, 1.00 mmol, 1 equiv), 4-bromobutyric acid (0.25 g, 1.50 mmol, 1.5 equiv), DPTS (0.32 g, 1.50 mmol, 1.5 equiv) and DCC (0.62 g, 3.00 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **51b**. The title compound was obtained as a colorless oil (0.60 g, 75%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-),

1.28 (m, 28 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{12}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 172.4, 160.6, 138.0, 106.5, 101.2, 77.5, 77.2, 76.9, 68.3, 68.2, 66.6, 66.5, 32.8, 32.7, 32.6, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

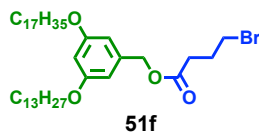


3-(Decyloxy)-5-(tridecyloxy)benzyl 4-bromobutanoate (51c). Compound **51c** was synthesized from compound **50c** (0.60 g, 1.30 mmol, 1 equiv), 4-bromobutyric acid (0.33 g, 1.94 mmol, 1.5 equiv), DPTS (0.46 g, 1.94 mmol, 1.5 equiv) and DCC (0.81 g, 3.90 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **51c**. The title compound was obtained as a colorless oil (0.60 g, 75%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.46 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.56 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 30 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{12}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 172.4, 160.6, 138.0, 106.5, 101.2, 77.5, 77.2, 76.9, 68.3, 68.2, 66.6, 66.5, 32.8, 32.7, 32.6, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

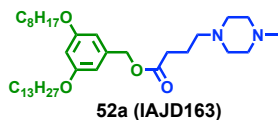


3-(Dodecyloxy)-5-(tridecyloxy)benzyl 4-bromobutanoate (51d). Compound **51d** was synthesized from compound **29c** (0.51 g, 1.04 mmol, 1 equiv), 4-bromobutyric acid (0.26 g, 1.56 mmol, 1.5 equiv), DPTS (0.46 g, 1.56 mmol, 1.5 equiv) and DCC (0.64 g, 3.12 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **51d**. The title compound was obtained as a colorless oil (0.58 g, 87%). ^1H NMR (400 MHz, CDCl_3) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.45 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.27 (m, 34 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_8\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_9\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_{12}\text{CH}_3$).

PhO(CH₂)₇CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 77.4, 68.2, 66.5, 32.7, 32.6, 32.1, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.

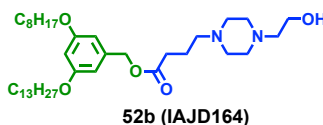


3-(Heptecyloxy)-5-(tridecyloxy)benzyl 4-bromobutanoate (51f). Compound **51f** was synthesized from compound **29c** (0.30 g, 0.54 mmol, 1 equiv), 4-bromobutyric acid (0.13 g, 0.80 mmol, 1.5 equiv), DPTS (0.24 g, 0.80 mmol, 1.5 equiv) and DCC (0.33 g, 0.60 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **51f**. The title compound was obtained as a colorless oil (0.28 g, 74%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.88 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 160.6, 137.9, 106.5, 101.2, 68.2, 66.6, 32.8, 32.6, 32.1, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 27.9, 26.2, 22.8, 14.3.



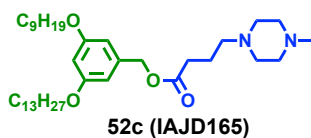
3-(Octyloxy)-5-(tridecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (52a, IAJD163). Compound **52a** was synthesized from compound **51a** (280 mg, 0.48 mmol, 1 equiv), 1-methylpiperazine (72 mg, 0.72 mmol, 1.5 equiv) and K₂CO₃ (80 mg, 0.58 mmol) in 10 mL MeCN was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.20 g, 87%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.62–2.26 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.74 (m, 4

H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 28 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.1, 160.4, 138.1, 106.3, 100.8, 77.5, 77.2, 76.9, 68.0, 66.0, 57.4, 55.0, 52.8, 45.8, 32.1, 31.9, 31.8, 29.7, 29.6, 29.6, 29.6, 29.4, 29.3, 29.2, 29.2, 26.0, 22.7, 22.6, 22.1, 14.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₇H₆₇N₂O₄: 603.6; Found: 604.3.



3-(Octyloxy)-5-(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (52b, IAJD164).

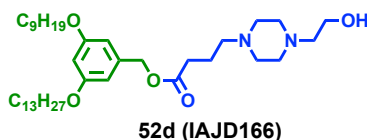
Compound 52b was synthesized from compound 51b (278 mg, 0.48 mmol, 1equiv), 1-(2-hydroxyethyl)piperazine (98 mg, 0.72 mmol, 1.5 equiv) and K₂CO₃ (80 mg, 0.58 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a colorless oil (230 mg, 76%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (s, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 3.62 (t, 2 H, -CH₂CH₂OH), 2.63–2.27 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.86 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.74 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 28 H, PhOCH₂CH₂CH₂(CH₂)₅CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.89 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.4, 138.1, 106.4, 100.9, 68.1, 66.2, 59.3, 59.3, 57.6, 57.5, 53.4, 53.0, 52.8, 32.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₈H₆₈N₂O₅: 634.3; Found: 634.0.



3-(nonyloxy)-5-(tridecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (52c, IAJD165).

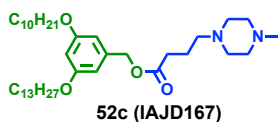
Compound **52c** was synthesized from compound **51b** (0.27 g, 0.44 mmol), 1-methylpiperazine (53 mg, 0.53 mmol) and K₂CO₃ (74 mg, 0.53 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a light-yellow oil (0.23 g, 85 %). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, -CH₂Ph), 3.92 (t, 4 H, 2×PhOCH₂-), 2.77–2.14 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.25 (br, 28 H, PhOCH₂CH₂CH₂(CH₂)₉CH₃ and

PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 160.6, 138.2, 106.5, 101.5, 68.2, 66.3, 57.7, 55.3, 53.2, 46.2, 32.4, 32.1, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 22.3, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₃₈H₆₉N₂O₄: 617.5; Found: 618.4.



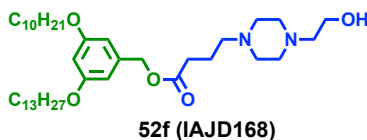
3-(nonyloxy)-5-(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (52d, IAJD166).

Compound **52d** was synthesized from compound **51b** (0.26 g, 0.44 mmol), 1-(2-hydroxyethyl)piperazine (69 mg, 0.53 mmol) and K₂CO₃ (74 mg, 0.53 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a light-yellow oil (0.18 g, 62 %). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, -CH₂Ph), 3.92 (t, 4 H, 2×PhOCH₂-), 3.60 (t, 2 H, -CH₂CH₂OH), 2.74–2.12 (m, 15 H, -CH₂CH₂OH, -N(CH₂CH₂)₂N-, -OCOCH₂CH₂CH₂- and -CH₂CH₂OH), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 28 H, PhOCH₂CH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 160.6, 138.2, 106.5, 101.0, 68.2, 66.3, 59.3, 57.8, 57.7, 53.3, 53.0, 32.4, 32.0, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.8, 22.3, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₃₉H₇₁N₂O₅: 647.5; Found: 647.2.

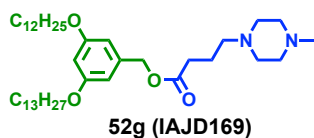


3-(Decyloxy)-5-(tridecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (52c, IAJD167). Compound **52c** was synthesized from compound **51b** (0.25 g, 0.41 mmol), 1-methylpiperazine (45 mg, 0.45 mmol) and K₂CO₃ (68 mg, 0.49 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a colorless oil (0.24 g, 93%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 2.73–2.19 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.81 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 30 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₅CH₃).

PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.5, 138.1, 106.4, 100.9, 68.1, 66.1, 57.5, 55.0, 52.8, 45.8, 32.2, 31.9, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₉H₇₁N₂O₄: 631.5; Found: 631.4.

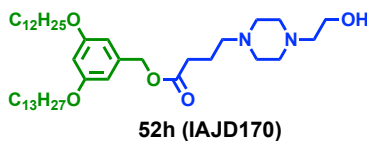


3-(Dectyloxy)-5-(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (52f, IAJD168). Compound **52f** was synthesized from compound **51c** (0.14 g, 0.21 mmol), 1-(2-hydroxyethyl)piperazine (29 mg, 0.22 mmol) and K₂CO₃ (31 mg, 0.22 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a colorless oil (0.24 g, 93%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.60 (t, 2H, -CH₂CH₂OH), 2.65–2.24 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.42 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 30 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 160.6, 138.2, 106.5, 101.0, 77.4, 68.2, 66.3, 59.4, 57.8, 57.6, 53.1, 53.0, 32.3, 32.0, 32.0, 29.8, 29.8, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.4, 29.4, 26.2, 22.8, 22.2, 14.2. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₀H₇₃N₂O₅: 661.55; Found: 662.6.

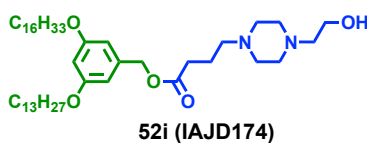


3-(dodecyloxy)-5-(tridecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (52g, IAJD169). Compound **52g** was synthesized from compound **51d** (0.3 g, 0.47 mmol), 1-methylpiperazine (56 mg, 0.56 mmol) and K₂CO₃ (78 mg, 0.56 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a light-yellow oil (0.26 g, 85 %). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, -CH₂Ph), 3.92 (t, 4 H, 2×PhOCH₂-), 2.77–2.14 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 34 H, PhOCH₂CH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR

(101 MHz, CDCl₃) δ 173.5, 160.6, 138.2, 106.5, 101.1, 68.2, 66.3, 57.7, 55.3, 53.3, 46.2, 32.4, 32.6, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 22.8, 22.4, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₁H₇₅N₂O₄: 659.6 ; Found: 659.0 .

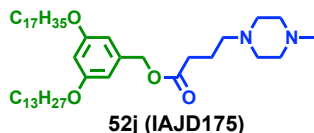


3-(dodecyloxy)-5-(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (52h, IAJD170). Compound **52h** was synthesized from compound **51d** (0.3 g, 0.47 mmol), 1-(2-hydroxyethyl)piperazine (73 mg, 0.56 mmol) and K₂CO₃ (77 mg, 0.56 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a light-yellow oil (0.28 g, 87 %). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, -CH₂Ph), 3.92 (t, 4 H, 2×PhOCH₂-), 3.59 (t, 2 H, -CH₂CH₂OH), 2.75–2.24 (m, 15 H, -CH₂CH₂OH, -N(CH₂CH₂)₂N-, -OCOCH₂CH₂CH₂- and -CH₂CH₂OH), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 34 H, PhOCH₂CH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH₂CH₂(CH₂)₈CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 160.6, 138.2, 106.6, 101.0, 68.2, 66.3, 59.3, 57.8, 57.7, 53.3, 53.0, 32.4, 32.6, 29.8, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 26.2, 22.8, 22.3, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₂H₇₇N₂O₅: 689.6; Found: 689.5.



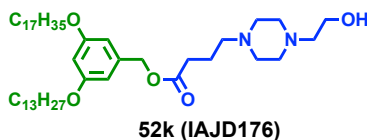
3-(Hexadecyloxy)-5-(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (52i, IAJD174). Compound **52i** was synthesized from compound **51e** (0.14 g, 0.20 mmol), 1-(2-hydroxyethyl)piperazine (34 mg, 0.24 mmol) and K₂CO₃ (40 mg, 0.30 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a colorless oil (0.14 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.61 (t, 2H, -CH₂CH₂OH), 2.64–2.31 (m, 14 H, -N(CH₂CH₂)₂N-,

-NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.84 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.75 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.25 (br, 42 H, PhOCH₂CH₂CH₂(CH₂)₁₂CH₃ and PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.5, 138.1, 106.4, 100.9, 77.3, 68.1, 66.1, 59.3, 57.6, 57.5, 52.9, 52.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₄₆H₈₅N₂O₅: 745.65; Found: 747.9.



3-(heptadecyloxy)-5-(tridecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (52j, IAJD175).

Compound **52j** was synthesized from compound **51f** (0.14 g, 0.20 mmol), 1-methylpiperazine (25 mg, 0.25 mmol) and K₂CO₃ (35 mg, 0.25 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a light-yellow oil (0.13 g, 90 %). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, -CH₂Ph), 3.92 (t, 4 H, 2×PhOCH₂-), 2.77–2.14 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 44 H, PhOCH₂CH₂CH₂(CH₂)₉CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 160.6, 138.2, 106.5, 101.1, 68.2, 66.3, 57.8, 55.3, 53.3, 46.2, 32.4, 32.1, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 22.8, 22.4, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₄₆H₈₅N₂O₄: 729.6; Found: 729.6.



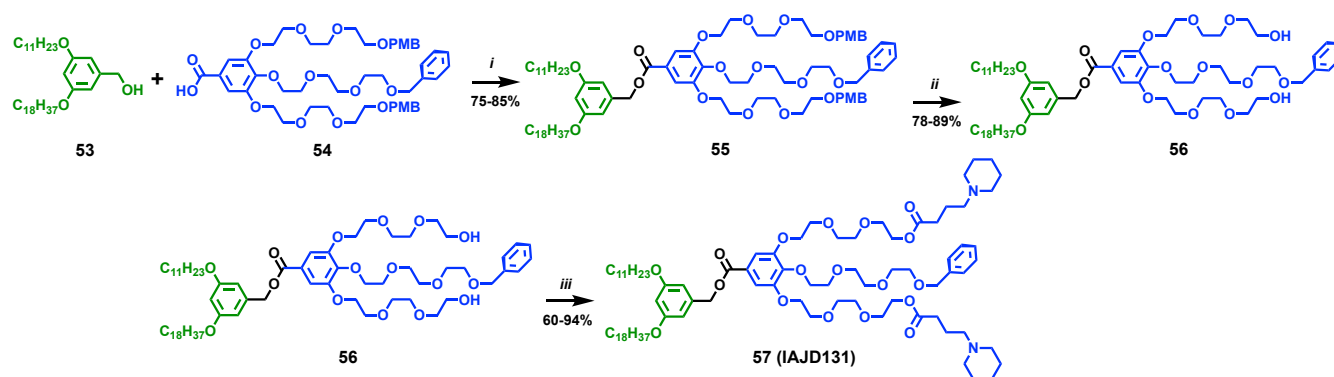
3-(heptadecyloxy)-5-(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (52k, IAJD176).

Compound **52k** was synthesized from compound **51f** (0.14 g, 0.20 mmol), 1-(2-hydroxyethyl)piperazine (33 mg, 0.25 mmol) and K₂CO₃ (35 mg, 0.25 mmol) following a procedure similar to that used for the synthesis of compound **52a**. The title compound was obtained as a light-yellow oil (0.10 g, 67 %). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, -CH₂Ph), 3.92 (t, 4 H, 2×PhOCH₂-), 3.60 (t, 2 H, -CH₂CH₂OH), 2.63–2.23 (m, 15 H, -CH₂CH₂OH, -

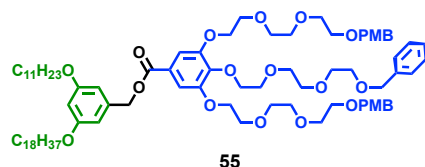
$N(CH_2CH_2)_2N$ -, $-OCOCH_2CH_2CH_2-$ and $-CH_2CH_2OH$), 1.82 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.76 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (br, 44 H, $PhOCH_2CH_2CH_2(CH_2)_9CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 160.6, 138.2, 106.6, 101.0, 68.3, 66.3, 59.3, 57.8, 57.7, 53.2, 53.0, 32.4, 32.0, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 26.2, 22.8, 22.3, 14.3. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{47}H_{86}N_2O_5$: 759.7; Found: 759.6 .

3.9 Synthesis of IAJD131

Scheme S9. Synthesis of IAJD131



Reagents and conditions: (i) EDC.HCl, DMAP, DCM, 23 °C, 12 h; (ii) DDQ, DCM/ H_2O , 23 °C, 1 h; (iii) 4-(piperidin-1-yl)butanoic acid hydrochloride, DCC, DCM, 23 °C, 12 h.

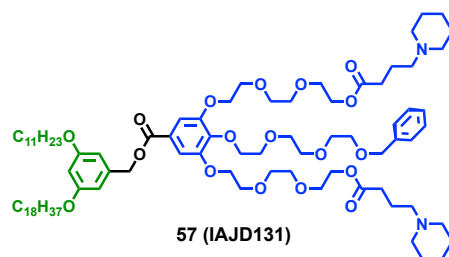


Compound 55. Compound **53** was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **54** was synthesized according to a literature procedure elaborated and optimized by our laboratory.^[4] Compound **53** (0.28 g, 0.51 mmol, 1.1 equiv), compound **54** (0.41 g, 0.46 mmol, 1.0 equiv), EDC.HCl (0.98 g, 0.51 mmol, 1.1 equiv) and DMAP (17 mg, 0.14 mmol, 0.3 equiv) were dissolved in dry DCM (6 mL). The reaction mixture was stirred at 23 °C for 12 h. Brine (20 mL) was then added, and the mixture was extracted by DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous $MgSO_4$. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with EtOAc/hexane = 1/1 as the mobile phase to give the title

compound as a colorless oil (0.53 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 7.25 (m, 11 H, PhH), 6.86–6.78 (m, 4 H, PhH), 6.51 (d, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.21 (s, 2 H, $-\text{OCH}_2\text{Ph}$), 4.51 (s, 2 H, $-\text{CH}_2\text{Ph}$), 4.44 (s, 4 H, $-\text{OCH}_2\text{Ph}$), 4.17 (m, 6 H, $\text{PhOCH}_2\text{CH}_2\text{O}-$), 3.89 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.78 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{O}-$), 3.74 (m, 8 H, $\text{PhOCH}_2\text{CH}_2\text{O}-$ and PhOCH_3), 3.68 (m, 6 H, $\text{PhOCH}_2\text{CH}_2\text{OCH}_2-$), 3.61–3.55 (m, 18 H, $\text{PhOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$), 1.73 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.41 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.23 (br, 42 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.85 (t, 6 H, $-\text{CH}_2\text{CH}_2\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 165.9, 160.5, 159.2, 152.3, 142.8, 138.3, 138.1, 130.4, 129.4, 128.3, 127.7, 127.6, 124.9, 113.7, 109.3, 106.6, 101.0, 73.2, 72.9, 72.5, 70.9, 70.7, 70.7, 70.7, 70.6, 70.6, 69.7, 69.5, 69.1, 69.0, 68.1, 66.8, 55.2, 31.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 14.2.



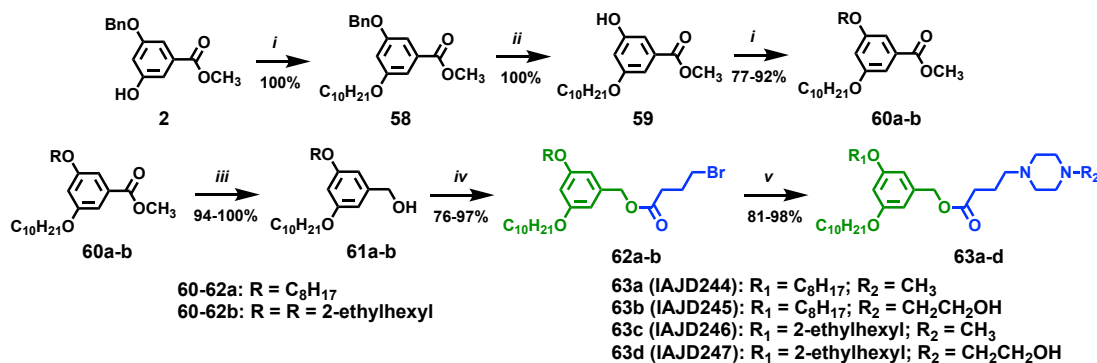
Compound 56. Compound **55** (0.45 g, 0.30 mmol, 1 equiv) was dissolved in 6 mL DCM and 0.42 mL water (7 v%) was added. To this solution was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 0.15 g, 0.66 mmol, 2.2 equiv). The reaction mixture was stirred at 23 °C for 1 h. Then the precipitates were filtered out and DCM (20 mL) was added. The mixture was washed by NaHCO_3 aqueous solution (saturated), NaHSO_3 aqueous solution (2%) and NaHCO_3 aqueous solution (saturated) successively. The organic phases were collected and dried over anhydrous MgSO_4 . After filtration, the obtained filtrate was concentrated and purified by column chromatography (SiO_2) with $\text{EtOAc}/\text{MeOH} = 20/1$ as the mobile phase to give the title compound as a light-yellow oil (0.45 g, 78%). ^1H NMR (400 MHz, CDCl_3) δ 7.36–7.16 (m, 7 H, PhH), 6.50 (d, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.20 (s, 2 H, $-\text{OCH}_2\text{Ph}$), 4.51 (s, 2 H, $-\text{OCH}_2\text{Ph}$), 4.18 (m, 6 H, $\text{PhOCH}_2\text{CH}_2\text{O}-$), 3.92 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.84 (t, 6 H, $\text{PhOCH}_2\text{CH}_2\text{O}-$), 3.77–3.47 (m, 24 H, $\text{PhOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$), 3.04 (br, 2H, $-\text{OCH}_2\text{CH}_2\text{OH}$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.40 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.24 (br, 42 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{14}\text{CH}_3$), 0.84 (t, 6 H, $-\text{CH}_2\text{CH}_2\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 165.9, 160.4, 152.2, 142.7, 138.2, 138.0, 128.3, 127.7, 127.6, 124.9, 109.2, 107.8, 106.6, 100.9, 73.2, 72.6, 72.4, 70.8, 70.6, 70.6, 70.5, 70.5, 70.4, 69.6, 69.4, 68.9, 68.1, 67.5, 66.8, 61.6, 60.4, 31.9, 31.9, 29.7, 29.6, 29.6, 29.6, 29.4, 29.3, 29.3, 29.2, 29.2, 26.0, 23.9, 22.7, 14.1.



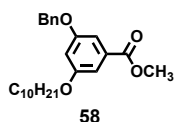
Compound 57 (IAJD131). Compound **56** (0.21 g, 0.18 mmol, 1 equiv) and 4-(piperidin-1-yl)butanoic acid hydrochloride (83 mg, 0.40 mmol, 2.2 equiv) were dissolved in 6 mL dry DCM. DCC (0.11 g, 0.54 mmol, 3 equiv) was added in one portion into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1, 10/1, 8/1 and 8/1 with 0.1% NEt₃ as the mobile phase. Then the product was dissolved in DCM (20 mL), which was washed by NaHCO₃ aqueous solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.23 g, 85%). ¹H NMR (400 MHz, CDCl₃) δ 7.29 (m, 7 H, PhH), 6.50 (d, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.20 (s, 2 H, -OCH₂Ph), 4.51 (s, 2 H, -OCH₂Ph), 4.16 (m, 10 H, PhOCH₂CH₂O- and -OCH₂CH₂OCO(CH₂)₃-), 3.89 (t, 4 H, PhOCH₂CH₂CH₂-), 3.80 (t, 6 H, PhOCH₂CH₂O-), 3.63 (m, 20 H, PhOCH₂CH₂OCH₂CH₂OCH₂CH₂-), 2.27 (m, 16 H, N(CH₂-)₂CH₂CH₂CH₂COO-), 1.84–1.73 (m, 4 H, PhOCH₂CH₂(CH₂)₈CH₃, PhOCH₂CH₂(CH₂)₁₅CH₃ and N(CH₂-)₂CH₂CH₂CH₂COO-), 1.58–1.53 (m, 8 H, N(CH₂CH₂)₂CH₂), 1.44 (m, 8 H, PhOCH₂CH₂CH₂(CH₂)₇CH₃, PhOCH₂CH₂CH₂(CH₂)₁₄CH₃ and N(CH₂CH₂)₂CH₂), 1.26 (br, 42 H, PhOCH₂CH₂CH₂(CH₂)₇CH₃ and PhOCH₂CH₂CH₂(CH₂)₁₄CH₃), 0.84 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 165.8, 160.4, 152.3, 142.8, 138.3, 138.0, 128.3, 127.7, 127.5, 124.9, 109.3, 106.5, 73.2, 72.4, 70.8, 70.7, 70.6, 70.6, 70.6, 69.7, 69.4, 69.2, 68.9, 68.0, 66.8, 63.4, 58.4, 54.5, 50.0, 32.2, 31.9, 31.9, 29.7, 29.6, 29.6, 29.6, 29.4, 29.3, 29.3, 29.2, 26.2, 26.0, 26.0, 24.5, 24.4, 22.7, 22.3, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₈₆H₁₄₃N₂O₁₈: 1492.0; Found: 1492.5.

3.10 Synthesis of Decane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains

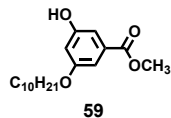
Scheme S10. Synthesis of Decane-Based IAJDs with 3,5-Nonsymmetric Alkyl Chains



Reagents and conditions: (i) RBr/ROTs, K₂CO₃, DMF, 120 °C, 2 h; (ii) H₂, Pd/C, DCM, MeOH, 12 h; (iii) LiAlH₄, THF, 0–23 °C, 1 h; (iv) DCC, DPTS, DCM, 12 h; (v) K₂CO₃, MeCN, 95 °C, 3 h.

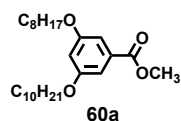


Methyl 3-(benzyloxy)-5-(decyloxy)benzoate (58). A mixture of compound **2** (4.00 g, 15.49 mmol, 1 equiv), 1-Bromodecane (1.41 g, 6.39 mmol, 1.1 equiv), K₂CO₃ (1.6 g, 11.6 mmol, 2 equiv) and DMF (10 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (1.26 g, 70%). ¹H NMR (400 MHz, CDCl₃) δ 7.49–7.33 (m, 5 H, PhH), 7.29 (br, 1 H, PhH), 7.21 (br, 1 H, PhH), 6.73 (t, 1 H, PhH), 5.08 (s, 2 H, PhCH₂O-), 3.97 (t, 2 H, PhOCH₂-), 3.90 (s, 3 H, PhCOOCH₃), 1.78 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃), 1.43 (m, 2 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃), 1.28 (m, 12 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃), 0.89 (t, 3 H, PhO(CH₂)₁₀CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.9, 160.2, 159.8, 136.6, 132.0, 128.6, 128.1, 127.6, 108.2, 107.8, 107.0, 70.3, 68.4, 52.2, 32.0, 29.6, 29.5, 29.4, 29.3, 29.2, 26.0, 22.7, 14.1. Mp = 51 °C.

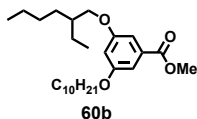


Methyl 3-(decyloxy)-5-hydroxybenzoate (59). Compound **59** (1.26 g, 3.16 mmol) was dissolved in a mixture of DCM (30 mL) and methanol (15 mL). Then Pd/C (0.06 g, 5 wt%) was added to the solution and the flask was evacuated and filled with hydrogen for three times. Afterwards, the mixture was stirred at 23 °C under hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, and the filter cake was washed with DCM. Evaporation of the solvent yielded the title compound as a white solid (2.70 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, 2 H, PhH), 6.64 (t, 1 H, PhH), 5.32 (s, 1 H, PhOH),

3.95 (t, 2 H, PhOCH_2 -), 3.89 (s, 3 H, PhCOOCH_3), 1.75 (m, 2 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$), 1.44 (m, 2 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$), 1.26 (m, 12 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$), 0.88 (t, 3 H, $\text{PhO}(\text{CH}_2)_{17}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.2, 160.4, 156.9, 131.9, 109.1, 107.8, 107.1, 68.4, 52.4, 31.9, 29.6, 29.6, 29.4, 29.3, 29.2, 26.0, 22.7, 14.1. $\text{Mp} = 99\text{ }^\circ\text{C}$.

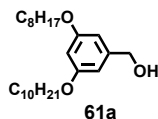


Methyl 3-(decyloxy)-5-(octyloxy)benzoate (60a). A mixture of compound **59** (0360 mg, 1.17 mmol, 1 equiv), 1-bromodecane (250 mg, 1.29 mmol, 1.1 equiv), K_2CO_3 (320 mg, 2.34 mmol, 2 equiv) and DMF (15 mL) was heated to $120\text{ }^\circ\text{C}$ and stirred under N_2 atmosphere for 2 h. The reaction mixture was cooled to $23\text{ }^\circ\text{C}$ and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.28 g, 57%). ^1H NMR (400 MHz, CDCl_3) δ 7.15 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.95 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2$ -), 3.89 (s, 3 H, PhCOOCH_3), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2$ -), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2$ -), 1.26 (m, 20 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3$ and $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_7\text{CH}_3$ and $\text{PhO}(\text{CH}_2)_9\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 167.0, 160.2, 131.8, 107.7, 106.6, 68.3, 52.2, 31.9, 31.8, 29.6, 29.6, 29.4, 29.3, 29.3, 29.2, 29.2, 26.0, 22.7, 22.7, 14.1, 14.1. $\text{Mp} = 33\text{ }^\circ\text{C}$.

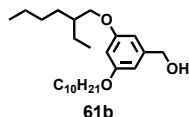


Methyl 3-(decyloxy)-5-((2-ethylhexyl)oxy)benzoate (60b). A mixture of compound **59** (0.36 g, .17 mmol, 1 equiv), 2-ethylhexyl bromide (250 mg, 1.29 mmol, 1.1 equiv), K_2CO_3 (320 mg, 2.34 mmol, 2 equiv) and DMF (15 mL) was heated to $80\text{ }^\circ\text{C}$ and stirred under N_2 atmosphere for 12 h. The reaction mixture was cooled to $23\text{ }^\circ\text{C}$ and DMF was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO_4 . After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with hexane/ $\text{EtOAc} = 20/1$ as the eluent to give the title compound as a light-yellow oil (0.34 g, 69%). ^1H NMR (400 MHz, CDCl_3) δ 7.17 (br, 2 H, PhH), 6.68 (t, 1 H, PhH), 3.97 (t, 2 H, $\text{PhOCH}_2(\text{CH}_2)_{16}\text{CH}_3$), 3.90 (s, 3 H, PhCOOCH_3), 3.86 (m, 2 H, $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)$ -), 1.85–1.69 (m, 3 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$ and $\text{PhOCH}_2\text{CH}(\text{CH}_2\text{CH}_3)(\text{CH}_2)_3\text{CH}_3$), 1.52–1.17 (m, 22 H, $\text{PhOCH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$ and

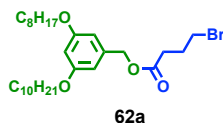
PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.90 (m, 9 H, PhO(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.4, 160.1, 131.8, 107.7, 107.5, 106.6, 70.8, 68.3, 52.1, 39.4, 31.9, 30.5, 29.6, 29.6, 29.4, 29.3, 29.2, 29.1, 26.0, 25.2, 23.9, 23.0, 22.7, 14.1, 14.1, 11.1.



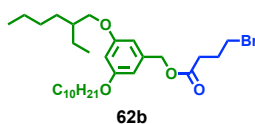
(3-(Decyloxy)-5-(octyloxy)phenyl)methanol (61a). Compound **61a** (0.28 g, 0.67 mmol, 1 equiv) was dissolved in 5 mL dry THF, which was added dropwise to a slurry of LiAlH₄ (25 mg, 0.67 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N₂ atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous MgSO₄ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.52 g, 81%). ¹H NMR (400 MHz, CDCl₃) δ 6.49 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.59 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.29 (m, 20 H, PhOCH₂CH₂CH₂(CH₂)₄CH₃ and PhOCH₂CH₂CH₂(CH₂)₆CH₃), 0.91 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₉CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.6, 143.2, 105.1, 100.6, 68.1, 65.5, 31.9, 31.8, 30.3, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 29.3, 26.1, 22.7, 22.7, 14.1, 14.1.



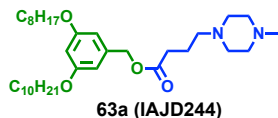
(3-(Decyloxy)-5-((2-ethylhexyl)oxy)phenyl)methanol (61b). Compound **61b** was synthesized from compound **60b** (0.34 g, 0.81 mmol, 1 equiv) and LiAlH₄ (31 mg, 0.81 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **61a**. The title compound was obtained as a colorless oil (240 mg, 73%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.60 (s, 2 H, PhCH₂OH), 3.93 (t, 2 H, PhOCH₂CH₂CH₂-), 3.81 (m, 2 H, PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.73 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 6 H, PhOCH₂CH₂CH₂- and PhOCH₂CH(CH₂CH₃)CH₂(CH₂)₂CH₃), 1.27 (m, 16 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH(CH₂CH₃)CH₂(CH₂)₂CH₃), 0.93 (m, 9 H, PhO(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)CH₂(CH₂)₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.8, 160.6, 143.2, 105.1, 105.0, 100.6, 70.6, 68.1, 65.5, 39.4, 31.9, 30.6, 30.3, 29.6, 29.6, 29.4, 29.3, 29.3, 29.1, 26.1, 23.9, 23.1, 22.7, 14.1, 14.1, 11.1.



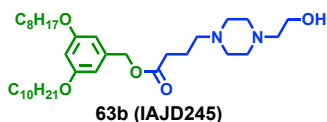
3-(Decyloxy)-5-(octyloxy)benzyl 4-bromobutanoate (62a). Compound **61a** (0.22 g, 0.54 mmol, 1 equiv), 4-bromobutyric acid (0.11 g, 0.60 mmol, 1.1 equiv), and DPTS (0.16 g, 0.54 mmol, 1 equiv) were dissolved in 8 mL DCM. DCC (0.23 g, 1.08 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at 23 °C for 12 h. Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.28 g, 63%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 20 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH₂CH₂(CH₂)₄CH₃), 0.89 (t, 6 H, PhO(CH₂)₇CH₃ and PhO(CH₂)₉CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.5, 137.8, 106.4, 101.2, 68.1, 66.4, 32.6, 32.5, 31.9, 31.8, 29.6, 29.6, 29.4, 29.4, 29.4, 29.3, 29.3, 27.8, 26.1, 22.7, 22.7, 14.1.



3-(Decyloxy)-5-(3-ethylheptyl)benzyl 4-bromobutanoate (62b). Compound **62b** was synthesized from compound **61b** (0.22 g, 0.54 mmol, 1 equiv), 4-bromobutyric acid (0.11 g, 0.60 mmol, 1.1 equiv), DPTS (0.16 g, 0.54 mmol, 1 equiv) and DCC (0.22 g, 1.08 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **62a**. The title compound was obtained as a colorless oil (200 mg, 82%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂OCO), 3.93 (t, 2 H, PhOCH₂CH₂CH₂-), 3.81 (m, 2 H, PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.58 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.19 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.73 (m, 3 H, PhOCH₂CH₂CH₂- and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 1.47 (m, 6 H, PhOCH₂CH₂CH₂- and PhOCH₂CH(CH₂CH₃)CH₂(CH₂)₂CH₃), 1.27 (m, 16 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH(CH₂CH₃)CH₂(CH₂)₂CH₃), 0.90 (m, 9 H, PhO(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.8, 160.5, 137.8, 106.5, 106.3, 101.1, 70.5, 68.1, 66.4, 39.4, 32.6, 31.9, 30.6, 29.6, 29.6, 29.4, 29.3, 29.3, 29.1, 27.8, 26.1, 23.9, 23.1, 22.7, 14.1, 14.1, 11.1.

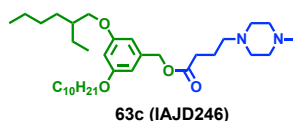


3-(Decyloxy)-5-(octyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (63a, IAJD244). A mixture of compound **62a** (0.14 g, 0.17 mmol, 1 equiv), 1-methylpiperazine (26 mg, 0.26 mmol, 1.5 equiv), K_2CO_3 (28 mg, 0.20 mmol, 1.2 equiv) and MeCN (10 mL) was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous $MgSO_4$. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO_2) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by $NaHCO_3$ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (60 mg, 63%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (p, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.89 (t, 4 H, $PhOCH_2-$), 2.78–2.24 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.81 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.73 (m, 4 H, $PhOCH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 20 H, $PhOCH_2CH_2CH_2(CH_2)_6CH_3$ and $PhOCH_2CH_2CH_2(CH_2)_4CH_3$), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 57.4, 54.9, 52.6, 45.7, 32.2, 31.9, 31.9, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 29.2, 26.1, 22.7, 22.7, 22.1, 14.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{34}H_{61}N_2O_4$: 561.5; Found: 562.5.



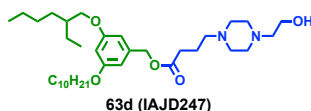
3-(Decyloxy)-5-(octyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (63b, IAJD245). Compound **63b** was synthesized from compound **62a** (90 mg, 0.17 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (34 mg, 0.26 mmol, 1.5 equiv) and K_2CO_3 (28 mg, 0.20 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **63a**. The title compound was obtained as a colorless oil (80 mg, 84%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (s, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 3.61 (t, 2H, $-CH_2CH_2OH$), 2.54–2.33 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.73 (m, 4 H, $PhOCH_2CH_2-$), 1.41 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (br, 20 H, $PhOCH_2CH_2CH_2(CH_2)_4CH_3$ and

PhOCH₂CH₂CH₂(CH₂)₆CH₃), 0.89 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.1, 68.1, 66.1, 66.2, 59.4, 57.6, 57.5, 52.8, 52.8, 32.2, 31.9, 31.8, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 29.3, 29.2, 26.1, 22.7, 22.7, 22.0, 14.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₅H₆₃N₂O₅: 591.5; Found: 591.9.



3-(Decyloxy)-5-((2-ethylhexyl)oxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (63c, IAJD246).

Compound **63c** was synthesized from compound **62b** (100 mg, 0.19 mmol, 1 equiv), 1-methylpiperazine (29 mg, 0.29 mmol, 1.5 equiv) and K₂CO₃ (32 mg, 0.23 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **63a**. The title compound was obtained as a colorless oil (60 mg, 56%). ¹H NMR (400 MHz, CDCl₃) δ 6.44 (p, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.00 (s, 2 H, PhCH₂-), 3.90 (t, 4 H, PhOCH₂-), 2.78–2.15 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.70 (m, 4 H, PhOCH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.42–1.27 (br, 18 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.89 (t, 9 H, PhO(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.7, 160.5, 138.0, 106.5, 106.3, 100.9, 77.5, 68.1, 66.2, 57.5, 55.0, 52.3, 45.8, 39.4, 32.0, 31.9, 29.6, 29.6, 29.4, 29.3, 29.3, 29.1, 26.1, 23.9, 23.0, 22.7, 22.1, 14.1, 14.1, 11.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₃₄H₆₁N₂O₄: 561.5; Found: 562.3.



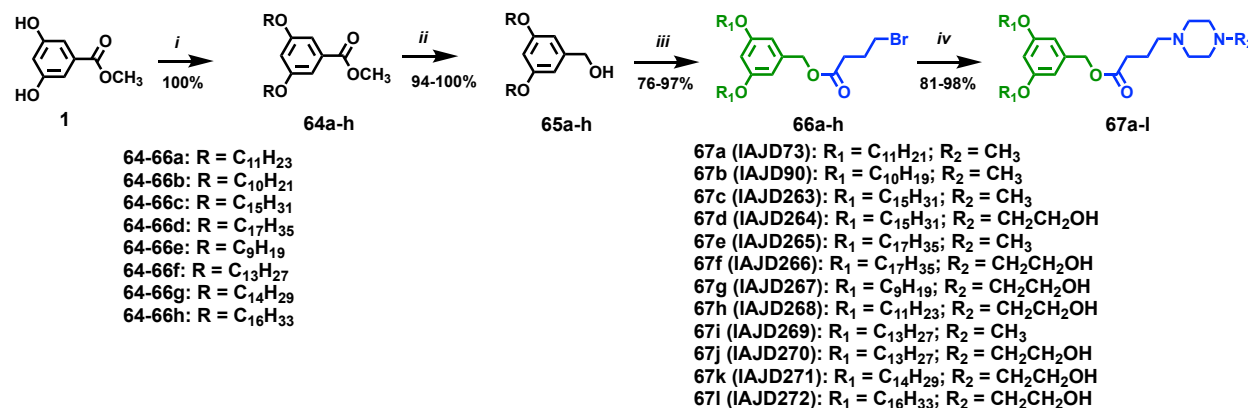
3-(Decyloxy)-5-((2-ethylhexyl)oxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (63d, IAJD247).

Compound **63d** was synthesized from compound **62b** (100 mg, 0.19 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (38 mg, 0.29 mmol, 1.5 equiv) and K₂CO₃ (32 mg, 0.23 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **63a**. The title compound was obtained as a colorless oil (80 mg, 75%). ¹H NMR (400 MHz, CDCl₃) δ 6.44 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.01 (s, 2 H, PhCH₂-), 3.88 (t, 4 H, PhOCH₂-), 3.60 (t, 2H, -CH₂CH₂OH), 2.65–2.29 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.81 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.71 (m, 4 H, PhOCH₂CH₂-), 1.47 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (br, 18 H, PhOCH₂CH₂CH₂(CH₂)₆CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃), 0.92 (t, 9 H, PhO(CH₂)₉CH₃ and PhOCH₂CH(CH₂CH₃)(CH₂)₃CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.7, 160.5, 138.0, 106.5, 106.3, 100.9, 70.5, 68.1, 66.2, 59.3,

57.6, 57.5, 52.9, 52.8, 39.4, 32.2, 31.9, 31.9, 30.5, 29.7, 29.6, 29.6, 29.4, 29.3, 29.3, 29.1, 26.1, 23.9, 23.0, 22.7, 22.0, 14.1, 14.1, 11.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{35}H_{63}N_2O_5$: 591.5; Found: 591.8.

3.11 Synthesis of IAJDs with 3,5-symmetric Alkyl Chains

Scheme S11. Synthesis of IAJDs with 3,5-symmetric Alkyl Chains



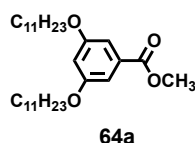
Reagents and conditions: (i) RBr/ROT_s, K₂CO₃, DMF, 120 °C, 2 h; (ii) LiAlH₄, THF, 0–23 °C, 1 h; (iii) DCC, DPTS, DCM, 12 h; (iv) K₂CO₃, MeCN, 95 °C, 3 h.

General Synthetic Procedure for Compounds 64b, 64e, and 64g-h. Compounds **64b**, **64e**, and **64g-h** were synthesized according to a procedure elaborated and optimized by our laboratory.⁴ Generally, compound **64b**, **64e**, and **64g-h** (1 equiv) and K₂CO₃ (2 equiv) were stirred in dry DMF. RBr (2.2 equiv) was added, and the mixture was stirred at 120 °C under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C. The reaction mixture was poured into ice/water and the white precipitates were filtered and collected. Then the precipitates were purified by recrystallization from acetone to give the title compound as a white solid. The synthesis and characterizations of compounds **64b**, **64e**, and **64g-h** were reported in the literature.⁴

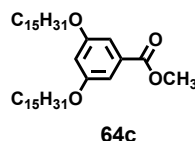
General Synthetic Procedure for Compounds 65b, 65e, and 65g-h. Compounds **65b**, **65e**, and **65g-h** were synthesized according to a procedure reported by our group.⁴ Generally, compounds **65b**, **65e**, and **65g-h** (1 equiv) were dissolved in dry THF, which was added dropwise to a slurry of LiAlH₄ (1 equiv) in dry THF at 0 °C under N₂ atmosphere. The resulted mixture was stirred at 23 °C for 1 h. The reaction was quenched by the successive addition of water, 15% NaOH aqueous solution and water. Then the mixture was filtered and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title

compound as a white solid or light-yellow oil. The synthesis and characterizations of compounds **65b**, **65e**, and **65g-h** were reported in the literature.⁴

General Synthetic Procedure for Compounds 66b and 66e. Compounds **66b** and **66e** were synthesized according to a procedure reported by our group.⁴ Generally, compounds **66b** and **66e** (1 equiv), 4-bromobutyric acid (1.2 equiv) and DPTS (1.2 equiv) were dissolved in dry DCM. DCC (2 equiv) was added into the above mixture and stirred for 12h. Hexane was added to the reaction mixture, which was then vacuum filtered. The filtrate was concentrated and further purified by column chromatography on silica gel with a mobile phase of hexane/DCM = 1/1 (v/v) to afford the title compound as a transparent oil. The synthesis and characterizations of compounds **66b** and **66e** were reported in the literature.⁴

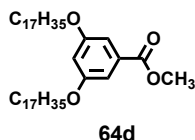


Methyl 3,5-bis(undecyloxy)benzoate) (64a). Compound **64a** was synthesized from compound **1** (0.40 g, 2.38 mmol, 1 equiv), 1-Bromoundecane (1.23 g, 5.23 mmol, 2.2 equiv), K₂CO₃ (0.82 g, 5.95 mmol, 2.5 equiv) and DMF (20 mL) was heated to 120 °C and stirred under N₂ atmosphere for 2 h. The reaction mixture was cooled to 23 °C and poured into ice/water (150 mL). The resulted white precipitates in the solution were filtered and collected. Then the precipitates were recrystallized from minimum acetone to afford the title compound as a white solid (0.89 g, 78%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.78 (m, 4 H, PhOCH₂CH₂CH₂-), 1.46 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₇CH₃), 0.87 (t, 6 H, PhO(CH₂)₁₀CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.2, 131.8, 107.6, 106.6, 77.2, 68.3, 64.1, 52.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.2, 26.0, 25.8, 22.7, 14.1. Mp = 45 °C.

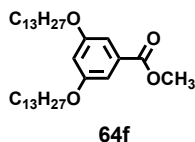


Methyl 3,5-bis(pentadecyloxy)benzoate) (64c). A mixture of compound **1** (0.40 g, 2.38 mmol, 1 equiv), 1-Bromopentadecane (1.52 g, 5.23 mmol, 2.2 equiv), K₂CO₃ (0.82 g, 5.95 mmol, 2.5 equiv) following a procedure similar to that used for the synthesis of compound **64a**. The title compound was obtained as a white solid (1.30 g, 95%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.78 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₄CH₃). ¹³C

NMR (101 MHz, CDCl₃) δ 167.0, 160.2, 131.8, 107.6, 106.6, 77.2, 68.3, 52.2, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.2, 26.0, 22.7, 14.1. Mp = 65 °C.

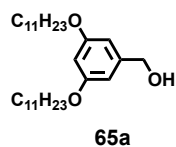


Methyl 3,5-bis(heptadecyloxy)benzoate) (64d). Heptadecyl 4-methylbenzenesulfonate (C₁₇H₃₅OTs) was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **64d** was synthesized from compound **1** (0.40 g, 2.38 mmol, 1 equiv), C₁₇H₃₅OTs (2.30 g, 5.23 mmol, 2.2 equiv), K₂CO₃ (0.82 g, 5.95 mmol, 2.5 equiv) following a procedure similar to that used for the synthesis of compound **64a**. The title compound was obtained as a white solid (1.33 g, 87%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 52 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₆CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 160.2, 131.8, 107.6, 106.6, 77.2, 68.3, 64.1, 52.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.2, 26.0, 25.8, 22.7, 14.1. Mp = 70 °C.

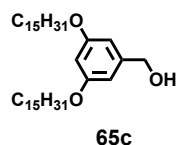


Methyl 3,5-bis(tridecyloxy)benzoate) (64f). Tridecyl 4-methylbenzenesulfonate (C₁₃H₂₇OTs) was synthesized according to a literature procedure reported by our laboratory.^[5] Compound **64f** was synthesized from compound **1** (1.28 g, 7.6 mmol, 1 equiv), C₁₃H₂₇OTs (6.01 g, 16.9 mmol, 2.2 equiv), K₂CO₃ (3.14 g, 22.8 mmol, 3 equiv) following a procedure similar to that used for the synthesis of compound **64a**. The title compound was obtained as a white solid (2.83 g, 88%). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (br, 2 H, PhH), 6.63 (t, 1 H, PhH), 3.96 (t, 4 H, PhOCH₂CH₂CH₂-), 3.89 (s, 3 H, PhCOOCH₃), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 36 H, PhOCH₂CH₂CH₂(CH₂)₉CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 160.2,

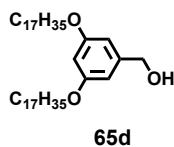
131.8, 107.6, 106.6, 77.2, 68.3, 64.1, 52.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.2, 26.1, 25.8, 22.7, 14.1.
Mp = ? °C.



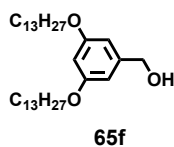
(3,5-Bis(undecyloxy)phenyl)methanol (65a). Compound **64a** (0.83 g, 1.41 mmol, 1 equiv) was dissolved in 10 mL dry THF, which was added dropwise to a slurry of LiAlH₄ (54 mg, 1.41 mmol, 1 equiv) in dry THF (5 mL) at 0 °C under N₂ atmosphere. Afterwards, the resulted mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched by the successive addition of water (0.2 mL), 15% NaOH aqueous solution (0.2 mL) and water (1.0 mL). White precipitates were formed in the mixture and filtered out. The filtrate was dried over anhydrous MgSO₄ and filtered. The solvent was removed under reduced pressure to afford the title compound as a colorless oil (0.83 g, 99%). ¹H NMR (400 MHz, CDCl₃) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₇CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₀CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.6, 143.2, 105.1, 100.6, 77.2, 68.1, 65.5, 31.9, 30.3, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 26.1, 22.7, 14.1.



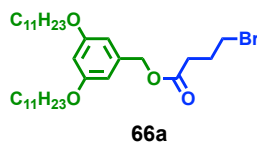
(3,5-Bis(pentadecyloxy)phenyl)methanol (65c). Compound **65c** was synthesized from compound **64c** (0.89 g, 1.87 mmol, 1 equiv) and LiAlH₄ (71 mg, 1.87 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **65a**. The title compound was obtained as a white solid (0.80 g, 100%). δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH₂OH), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₄CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.6, 143.2, 105.1, 100.6, 77.2, 68.1, 65.5, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 14.1. Mp = 55 °C.



(3,5-Bis(heptadecyloxy)phenyl)methanol (65d). Compound **65d** was synthesized from compound **64d** (0.66 g, 1.02 mmol, 1 equiv) and LiAlH_4 (38 mg, 1.02 mmol, 1 equiv) following a procedure similar to that used for the synthesis of compound **65a**. The title compound was obtained as a white solid (0.62 g, 100%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.45 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 52 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 143.2, 105.1, 100.6, 77.2, 68.1, 65.5, 34.0, 32.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 28.8, 28.2, 26.1, 22.7, 14.1. $\text{Mp} = 64\text{ }^\circ\text{C}$.

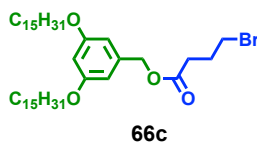


(3,5-Bis(tridecyloxy)phenyl)methanol (65f). Compound **65f** was synthesized from compound **64f** (2.8 g, 5.02 mmol, 1 equiv) and LiAlH_4 (239 mg, 6.30 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **65a**. The title compound was obtained as a colorless oil (2.46 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 6.50 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 4.61 (s, 2 H, PhCH_2OH), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.76 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.26 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 0.89 (t, 6 H, $\text{PhO}(\text{CH}_2)_{12}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 160.6, 143.2, 125.5, 105.1, 100.6, 77.2, 68.1, 65.5, 34.2, 31.9, 30.3, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 21.2, 14.1.

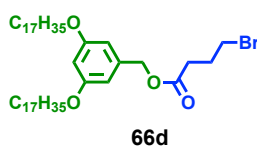


3,5-Bis(undecyloxy)benzyl 4-bromobutanoate (66a). Compound **66a** was synthesized from compound **65a** (0.20 g, 0.45 mmol, 1 equiv), 4-bromobutyric acid (0.09 g, 0.54 mmol, 1.2 equiv), DPTS (0.16 g, 0.54 mmol, 1.2 equiv) were dissolved in 10 mL DCM. *N,N'*-Dicyclohexylcarbodiimide (DCC 0.18 g, 0.89 mmol, 2 equiv) was added into the above mixture. The reaction mixture was stirred at $23\text{ }^\circ\text{C}$ for 12 h.

Afterwards, the resulted precipitates (urea) were filtered out from the reaction mixture. The filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with hexane/DCM = 1/1 as the mobile phase to give the title compound as a colorless oil (0.24 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.46 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.56 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 28 H, PhOCH₂CH₂CH₂(CH₂)₇CH₃), 0.89 (t, 6 H, PhO(CH₂)₁₀CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.5, 137.8, 106.4, 101.1, 77.2, 68.1, 66.4, 64.8, 32.7, 32.6, 32.5, 32.5, 31.9, 30.3, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 27.8, 27.8, 26.1, 25.9, 22.7, 14.1.

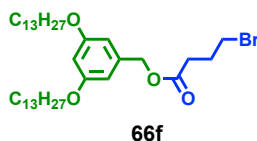


3,5-Bis(pentadecyloxy)benzyl 4-bromobutanoate (66c). Compound **65c** (0.80 g, 1.41 mmol, 1 equiv), 4-bromobutyric acid (0.28 g, 1.69 mmol, 1.2 equiv), DPTS (0.50 g, 1.69 mmol, 1.2 equiv), and DCC (0.58 g, 2.82 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **66a**. The title compound was obtained as a white solid (1.00 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.77 (m, 4 H, PhOCH₂CH₂CH₂-), 1.45 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (m, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₄CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 172.3, 160.5, 137.8, 106.4, 101.1, 68.1, 66.4, 32.6, 32.5, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 27.8, 26.1, 22.7, 14.1. Mp = 40 °C.

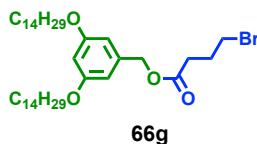


3,5-Bis(heptadecyloxy)benzyl 4-bromobutanoate (66d). Compound **66d** was synthesized from compound **65d** (0.62 g, 1.02 mmol, 1 equiv), 4-bromobutyric acid (0.20 g, 1.22 mmol, 1.2 equiv), DPTS (0.36 g, 1.22 mmol, 1.2 equiv) and DCC (0.42 g, 2.04 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **66a**. The title compound was obtained as a white solid (0.75 g, 96%). ¹H NMR (400 MHz, CDCl₃) δ 6.47 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO),

3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.77 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.45 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 52 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{16}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 160.5, 137.8, 106.4, 101.1, 77.2, 68.1, 66.4, 64.8, 32.7, 32.6, 32.5, 32.5, 31.9, 30.3, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 27.8, 27.8, 26.1, 25.9, 22.7, 14.1. Mp = 55 °C.

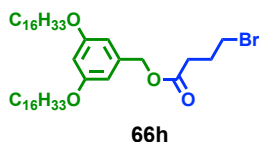


3,5-Bis(tridecyloxy)benzyl 4-bromobutanoate (66f). Compound **66f** was synthesized from compound **65f** (1.00 g, 1.98 mmol, 1 equiv), 4-bromobutyric acid (0.36 g, 2.18 mmol, 1.1 equiv), DPTS (0.64 g, 2.18 mmol, 1.1 equiv) and DCC (0.82 g, 3.96 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **66a**. The title compound was obtained as a colorless oil (1.2 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.47 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.75 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.44 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 36 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{12}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 153.5, 138.1, 130.6, 106.3, 75.9, 71.2, 66.9, 40.6, 39.7, 32.6, 32.5, 30.5, 29.4, 29.3, 29.3, 29.1, 27.8, 23.8, 23.8, 23.2, 23.1, 14.2, 14.1, 11.1.

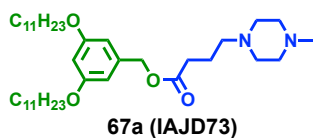


3,5-Bis(tetradecyloxy)benzyl 4-bromobutanoate (66g). Compound **66g** was synthesized from compound **65g** (0.20 g, 0.36 mmol, 1 equiv), 4-bromobutyric acid (0.07 g, 0.43 mmol, 1.2 equiv), DPTS (0.13 g, 0.43 mmol, 1.2 equiv) and DCC (0.15 g, 0.71 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **66a**. The title compound was obtained as a colorless oil (240 mg, 99%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.40 (t, 1 H, PhH), 5.04 (s, 2 H, PhCH_2OCO), 3.93 (t, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 3.48 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.57 (t, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 2.20 (m, 2 H, $-\text{OCOCH}_2\text{CH}_2\text{CH}_2\text{Br}$), 1.75 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.43 (m, 4 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2-$), 1.28 (m, 40 H, $\text{PhOCH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_{10}\text{CH}_3$), 0.88 (t, 6 H, $\text{PhO}(\text{CH}_2)_{13}\text{CH}_3$). ^{13}C NMR (101 MHz, CDCl_3) δ

δ 172.3, 160.5, 138.1, 130.6, 106.3, 75.9, 71.2, 66.9, 40.6, 39.7, 32.6, 32.5, 30.5, 29.4, 29.3, 29.3, 29.1, 27.8, 23.8, 23.8, 23.2, 23.1, 22.7, 14.2, 14.1.

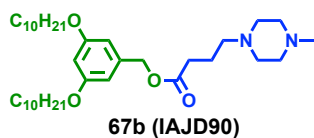


3,5-Bis(hexadecyloxy)benzyl 4-bromobutanoate (66h). Compound **66h** was synthesized from compound **65h** (0.20 g, 0.34 mmol, 1 equiv), 4-bromobutyric acid (0.07 g, 0.41 mmol, 1.2 equiv), DPTS (0.12 g, 0.41 mmol, 1.2 equiv) and DCC (0.15 g, 0.68 mmol, 2 equiv) following a procedure similar to that used for the synthesis of compound **66a**. The title compound was obtained as a white solid (240 mg, 96%). ^1H NMR (400 MHz, CDCl_3) δ 6.46 (br, 2 H, PhH), 6.41 (t, 1 H, PhH), 5.05 (s, 2 H, PhCH₂OCO), 3.93 (t, 4 H, PhOCH₂CH₂CH₂-), 3.47 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.57 (t, 2 H, -OCOCH₂CH₂CH₂Br), 2.20 (m, 2 H, -OCOCH₂CH₂CH₂Br), 1.76 (m, 4 H, PhOCH₂CH₂CH₂-), 1.44 (m, 4 H, PhOCH₂CH₂CH₂-), 1.27 (m, 48 H, PhOCH₂CH₂CH₂(CH₂)₁₂CH₃), 0.88 (t, 6 H, PhO(CH₂)₁₅CH₃). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 160.5, 137.8, 106.4, 101.1, 77.2, 68.1, 66.4, 32.6, 32.5, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 27.8, 26.1, 22.7, 14.1. Mp = 43 °C.

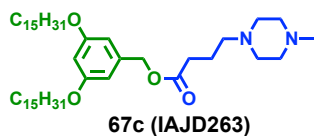


3,5-Bis(undecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (67a, IAJD73). Compound **67a** was synthesized from compound **66a** (390 mg, 0.65 mmol, 1 equiv), 1-methylpiperazine (68 mg, 0.68 mmol, 1.05 equiv) and K₂CO₃ (94 mg, 0.68 mmol, 1.05 equiv) in 20ml MeCN was heated to 95 °C and stirred for 3 h. The reaction mixture was cooled to 23 °C and MeCN was removed under reduced pressure. Then water (20 mL) was added, and the resulted mixture was extracted with DCM (20 mL) for three times. The organic phases were collected and dried over anhydrous MgSO₄. After filtration, the obtained filtrate was concentrated to around 3 mL and purified by column chromatography (SiO₂) with DCM/MeOH = 30/1 and 15/1 as the eluent. Then the obtained product was dissolved in DCM (20 mL), which was washed by NaHCO₃ solution (2%, 20 mL). The aqueous phase was extracted by DCM (20 mL) for another two times. The organic phases were combined and dried over anhydrous MgSO₄. Filtration and evaporation of the solvent yielded the title compound as a colorless oil (0.36 g, 90%). ^1H NMR (400 MHz, CDCl_3) δ 6.44

(br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.01 (s, 2 H, *PhCH*₂-), 3.90 (t, 4 H, *PhOCH*₂-), 2.58–2.21 (m, 14 H, -*N(CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*CH*₂*CH*₂*OH*), 1.82 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.43 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.27 (br, 28 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₇*CH*₃), 0.86 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 160.4, 138.1, 106.4, 100.9, 77.3, 68.0, 66.1, 57.6, 55.2, 53.1, 46.1, 32.2, 31.9, 29.6, 29.6, 29.4, 29.3, 29.3, 26.1, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₃₈H₆₉N₂O₄: 617.6; Found: 617.2.

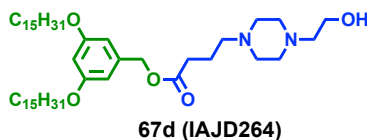


3,5-Bis(decyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (67b, IAJD90). Compound **67b** was synthesized from compound **66b** (300 mg, 0.53 mmol, 1 equiv), 1-methylpiperazine (73 mg, 0.56 mmol, 1.05 equiv) and K₂CO₃ (77 mg, 0.56 mmol, 1.05 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.28 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, *PhH*), 6.38 (t, 1 H, *PhH*), 5.01 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.65–2.21 (m, 15 H, -*N(CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.74 (m, 4 H, *PhOCH*₂*CH*₂-), 1.42 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.28 (br, 24 H, *PhOCH*₂*CH*₂*CH*₂(*CH*₂)₆*CH*₃), 0.87 (t, 6 H, -*CH*₂*CH*₂*CH*₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.4, 138.1, 106.4, 100.9, 77.3, 68.1, 66.1, 57.6, 55.2, 53.1, 46.1, 32.3, 31.9, 29.6, 29.6, 29.4, 29.3, 29.3, 26.1, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS *m/z* of [M + H]⁺ calculated for C₃₆H₆₅N₂O₄: 589.6; Found: 590.4.



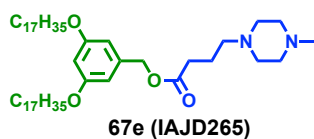
3,5-Bis(pentadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (67c, IAJD263). Compound **67c** was synthesized from compound **66c** (500 mg, 0.70 mmol, 1 equiv), 1-methylpiperazine (85 mg, 0.85 mmol, 1.2 equiv) and K₂CO₃ (146 mg, 1.06 mmol, 1.5 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.50 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ 6.45 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH*₂-), 3.91 (t, 4 H, *PhOCH*₂-), 2.59–2.25 (m, 15 H, -*N(CH*₂*CH*₂)₂*N*-, -*NCH*₂*CH*₂*CH*₂*COO*- and -*NCH*₃), 1.83 (m, 2 H, -*OCOCH*₂*CH*₂*CH*₂-), 1.75 (m, 4 H, *PhOCH*₂*CH*₂-), 1.42 (m, 4 H, *PhOCH*₂*CH*₂*CH*₂-), 1.28 (br, 44 H,

PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.1, 57.5, 54.9, 52.7, 45.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1.. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₆H₈₅N₂O₄: 729.7; Found: 730.3.



3,5-Bis(pentadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (67d, IAJD264).

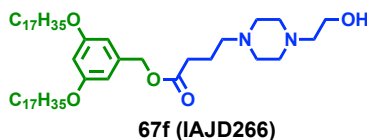
Compound **67d** was synthesized from compound **66c** (500 mg, 0.70 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (110 mg, 0.85 mmol, 1.2 equiv) and K₂CO₃ (146 mg, 1.06 mmol, 1.5 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.50 g, 94%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.91 (t, 4 H, PhOCH₂-), 3.61 (t, 2H, -CH₂CH₂OH), 2.60–2.30 (m, 14 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -CH₂CH₂OH), 1.85 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.74 (m, 4 H, PhOCH₂CH₂-), 1.43 (m, 4 H, PhOCH₂CH₂CH₂-), 1.28 (br, 44 H, PhOCH₂CH₂CH₂(CH₂)₁₁CH₃), 0.87 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 52.9, 52.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of [M + H]⁺ calculated for C₄₇H₈₇N₂O₅: 759.9; Found: 759.6.



3,5-Bis(pentadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (67e, IAJD265).

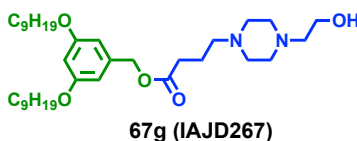
Compound **67e** was synthesized from compound **66d** (300 mg, 0.39 mmol, 1 equiv), 1-methylpiperazine (47 mg, 0.47 mmol, 1.2 equiv) and K₂CO₃ (81 mg, 0.59 mmol, 1.5 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.50 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.02 (s, 2 H, PhCH₂-), 3.92 (t, 4 H, PhOCH₂-), 2.63–2.25 (m, 15 H, -N(CH₂CH₂)₂N-, -NCH₂CH₂CH₂COO- and -NCH₃), 1.83 (m, 2 H, -OCOCH₂CH₂CH₂-), 1.73 (m, 4 H, PhOCH₂CH₂-), 1.42 (m, 4 H, PhOCH₂CH₂CH₂-), 1.26 (br, 52 H, PhOCH₂CH₂CH₂(CH₂)₁₃CH₃), 0.88 (t, 6 H, -CH₂CH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 160.5,

138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 57.6, 55.2, 53.1, 46.1, 32.3, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{50}H_{93}N_2O_4$: 785.8; Found: 786.0.



3,5-Bis(pentadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (67f, IAJD266).

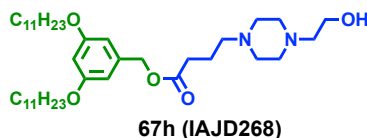
Compound **67f** was synthesized from compound **66d** (300 mg, 0.39 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (62 mg, 0.47 mmol, 1.2 equiv) and K_2CO_3 (81 mg, 0.59 mmol, 1.5 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.50 g, 94%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2$ -), 3.89 (t, 4 H, $PhOCH_2$ -), 3.61 (t, 2H, $-CH_2CH_2OH$), 2.62–2.31 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.82 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.72 (m, 4 H, $PhOCH_2CH_2$ -), 1.40 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.28 (br, 52 H, $PhOCH_2CH_2CH_2(CH_2)_{13}CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.8, 32.2, 31.9, 31.8, 29.5, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{51}H_{95}N_2O_5$: 815.8; Found: 815.7.



3,5-Bis(noncyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (67g, IAJD267).

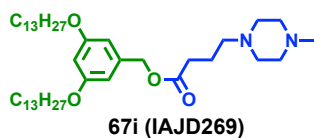
Compound **67g** was synthesized from compound **66e** (280 mg, 0.52 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (74 mg, 0.57 mmol, 1.1 equiv) and K_2CO_3 (84 mg, 0.57 mmol, 1.1 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.27 g, 88%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, PhH), 6.39 (t, 1 H, PhH), 5.03 (s, 2 H, $PhCH_2$ -), 3.92 (t, 4 H, $PhOCH_2$ -), 3.61 (t, 2H, $-CH_2CH_2OH$), 2.62–2.31 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.75 (m, 4 H, $PhOCH_2CH_2$ -), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2$ -), 1.28 (br, 20 H, $PhOCH_2CH_2CH_2(CH_2)_5CH_3$), 0.89 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 59.2,

57.7, 57.6, 53.2, 52.8, 32.3, 31.9, 29.5, 29.4, 29.3, 26.1, 22.7, 22.2, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{35}H_{63}N_2O_5$: 591.5; Found: 592.5.



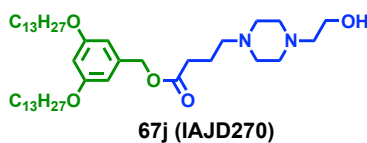
3,5-Bis(undecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (67h, IAJD268).

Compound **67h** was synthesized from compound **66a** (240 mg, 0.40 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (79 mg, 0.60 mmol, 1.5 equiv) and K_2CO_3 (67 mg, 0.48 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.25 g, 96%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 3.60 (t, 2H, $-CH_2CH_2OH$), 2.67 – 2.26 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.86 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.73 (m, 4 H, $PhOCH_2CH_2-$), 1.44 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.27 (br, 28 H, $PhOCH_2CH_2CH_2(CH_2)_7CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 100.9, 77.2, 68.1, 66.2, 59.3, 57.6, 57.5, 53.0, 52.8, 32.2, 31.9, 31.8, 29.5, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{39}H_{71}N_2O_5$: 647.6; Found: 648.1.



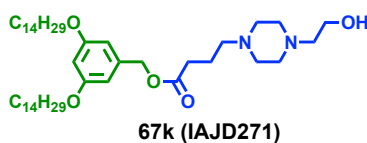
3,5-Bis(tridecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate (67i, IAJD269).

Compound **67i** was synthesized from compound **66f** (200 mg, 0.31 mmol, 1 equiv), 1-methylpiperazine (46 mg, 0.46 mmol, 1.5 equiv) and K_2CO_3 (51 mg, 0.37 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.50 g, 97%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, PhH), 6.37 (t, 1 H, PhH), 5.01 (s, 2 H, $PhCH_2-$), 3.90 (t, 4 H, $PhOCH_2-$), 2.61–2.24 (m, 15 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-NCH_3$), 1.82 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.78 (m, 4 H, $PhOCH_2CH_2-$), 1.42 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.28 (br, 36 H, $PhOCH_2CH_2CH_2(CH_2)_9CH_3$), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 160.4, 138.1, 106.4, 100.9, 68.1, 66.1, 57.4, 55.0, 53.4, 52.7, 45.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{42}H_{77}N_2O_4$: 673.7; Found: 672.8.



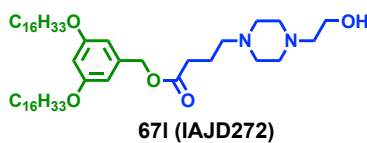
3,5-Bis(tridecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (67j, IAJD270).

Compound **67j** was synthesized from compound **66f** (200 mg, 0.31 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (60 mg, 0.46 mmol, 1.5 equiv) and K_2CO_3 (51 mg, 0.37 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.50 g, 94%). 1H NMR (400 MHz, $CDCl_3$) δ 6.46 (br, 2 H, *PhH*), 6.39 (t, 1 H, *PhH*), 5.02 (s, 2 H, *PhCH_2*-), 3.91 (t, 4 H, *PhOCH_2*-), 3.62 (t, 2H, $-CH_2CH_2OH$), 2.68–2.31 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.75 (m, 4 H, *PhOCH_2CH_2*-), 1.43 (m, 4 H, *PhOCH_2CH_2CH_2*-), 1.27 (br, 36 H, *PhOCH_2CH_2CH_2(CH_2)_9CH_3*), 0.88 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 160.5, 138.1, 106.4, 105.1, 100.9, 77.2, 68.1, 66.2, 59.3, 57.5, 57.4, 53.4, 52.7, 52.7, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.0, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{43}H_{79}N_2O_5$: 703.7; Found: 703.8.



3,5-Bis(tetradecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (67k, IAJD271).

Compound **67k** was synthesized from compound **66g** (280 mg, 0.52 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (69 mg, 0.53 mmol, 1.5 equiv) and K_2CO_3 (59 mg, 0.42 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.47 g, 93%). 1H NMR (400 MHz, $CDCl_3$) δ 6.44 (br, 2 H, *PhH*), 6.37 (t, 1 H, *PhH*), 5.01 (s, 2 H, *PhCH_2*-), 3.90 (t, 4 H, *PhOCH_2*-), 3.60 (t, 2H, $-CH_2CH_2OH$), 2.61–2.24 (m, 14 H, $-N(CH_2CH_2)_2N$ -, $-NCH_2CH_2CH_2COO$ - and $-CH_2CH_2OH$), 1.83 (m, 2 H, $-OCOCH_2CH_2CH_2$ -), 1.75 (m, 4 H, *PhOCH_2CH_2*-), 1.42 (m, 4 H, *PhOCH_2CH_2CH_2*-), 1.28 (br, 40 H, *PhOCH_2CH_2CH_2(CH_2)_5CH_3*), 0.86 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 160.4, 138.1, 106.4, 100.9, 68.1, 66.1, 57.5, 53.4, 52.9, 52.9, 32.2, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.1, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{45}H_{83}N_2O_5$: 731.7; Found: 732.1.



3,5-Bis(hexadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate (671, IAJD272).

Compound **671** was synthesized from compound **66h** (240 mg, 0.33 mmol, 1 equiv), 1-(2-hydroxyethyl)piperazine (64 mg, 0.49 mmol, 1.5 equiv) and K_2CO_3 (53 mg, 0.39 mmol, 1.2 equiv) following a procedure similar to that used for the synthesis of compound **67a**. The title compound was obtained as a colorless oil (0.24 g, 94%). 1H NMR (400 MHz, $CDCl_3$) δ 6.45 (br, 2 H, PhH), 6.38 (t, 1 H, PhH), 5.02 (s, 2 H, $PhCH_2-$), 3.91 (t, 4 H, $PhOCH_2-$), 3.61 (t, 2H, $-CH_2CH_2OH$), 2.67–2.29 (m, 14 H, $-N(CH_2CH_2)_2N-$, $-NCH_2CH_2CH_2COO-$ and $-CH_2CH_2OH$), 1.84 (m, 2 H, $-OCOCH_2CH_2CH_2-$), 1.75 (m, 4 H, $PhOCH_2CH_2-$), 1.43 (m, 4 H, $PhOCH_2CH_2CH_2-$), 1.26 (br, 44 H, $PhOCH_2CH_2CH_2(CH_2)_{11}CH_3$), 0.87 (t, 6 H, $-CH_2CH_2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 160.5, 138.1, 106.4, 100.9, 68.1, 66.2, 59.4, 57.6, 57.5, 52.8, 32.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 26.1, 22.7, 22.0, 14.1. Purity by HPLC: 99+%. MALDI-TOF MS m/z of $[M + H]^+$ calculated for $C_{49}H_{91}N_2O_5$: 787.8; Found: 787.2.

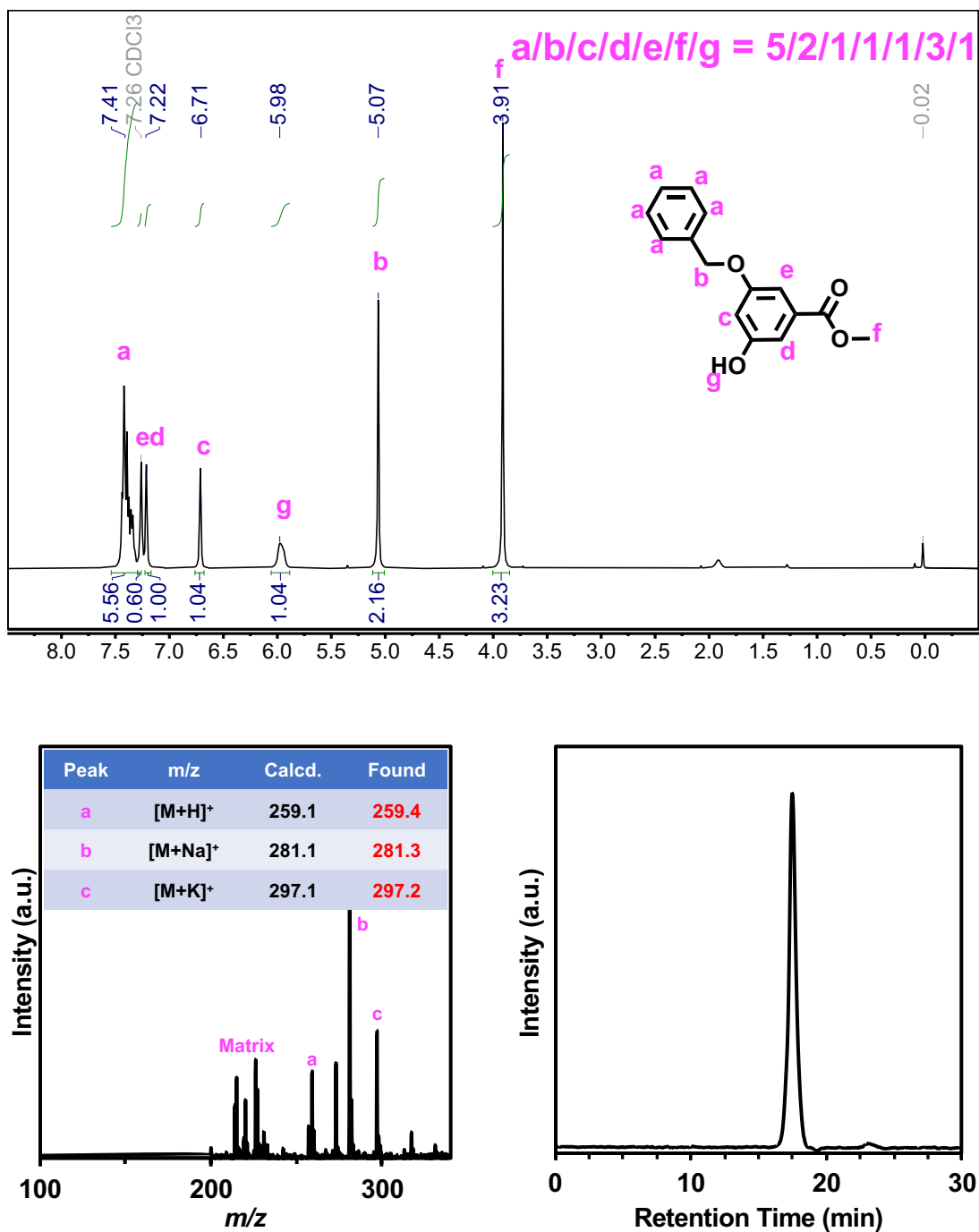


Figure S1. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of Monoprotected Benzyl Ether of Methyl 3,5-Dihydroxybenzoate **2**.

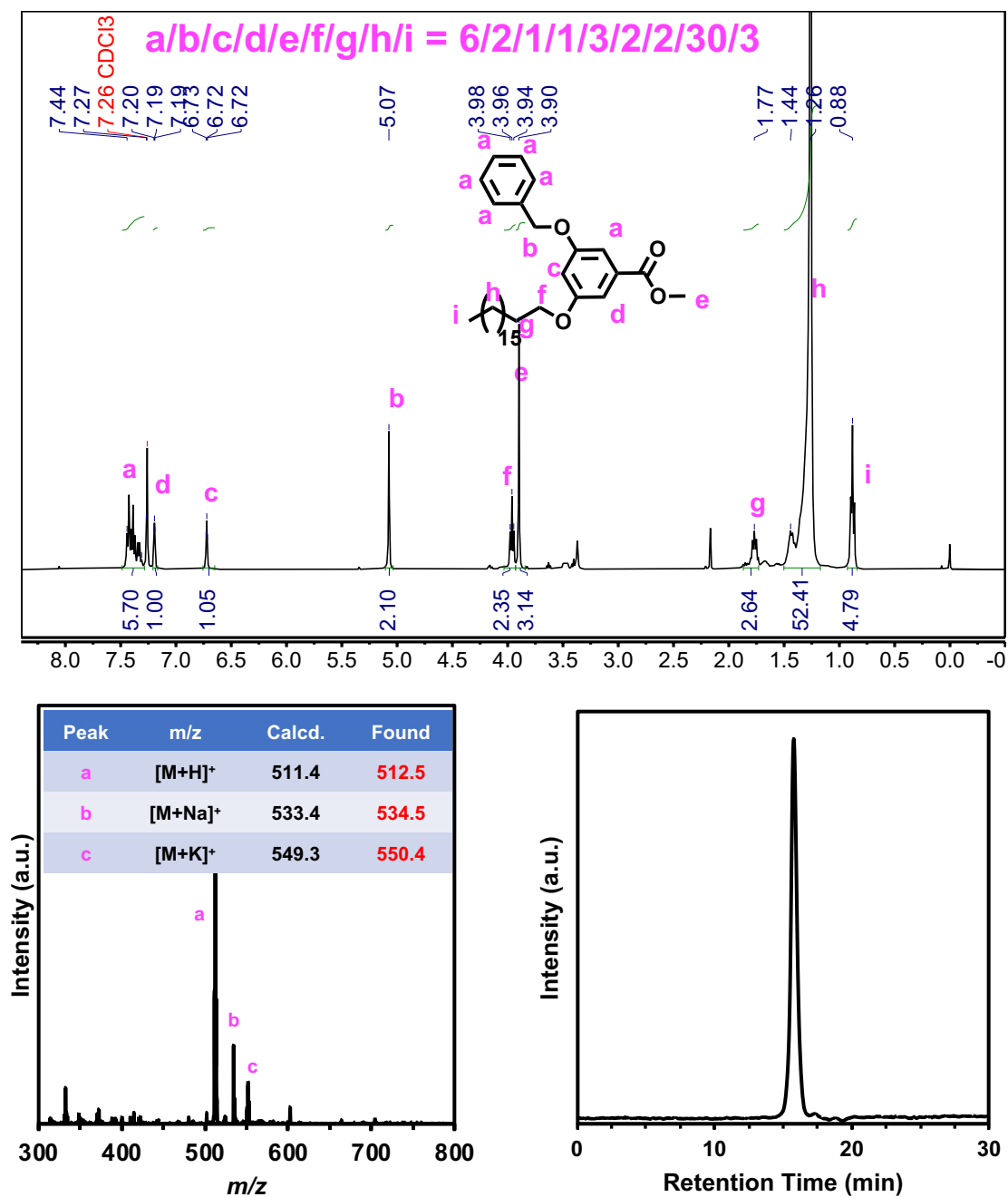


Figure S2. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of Methyl 3-(benzyloxy)-5-(octadecyloxy)benzoate, **33**.

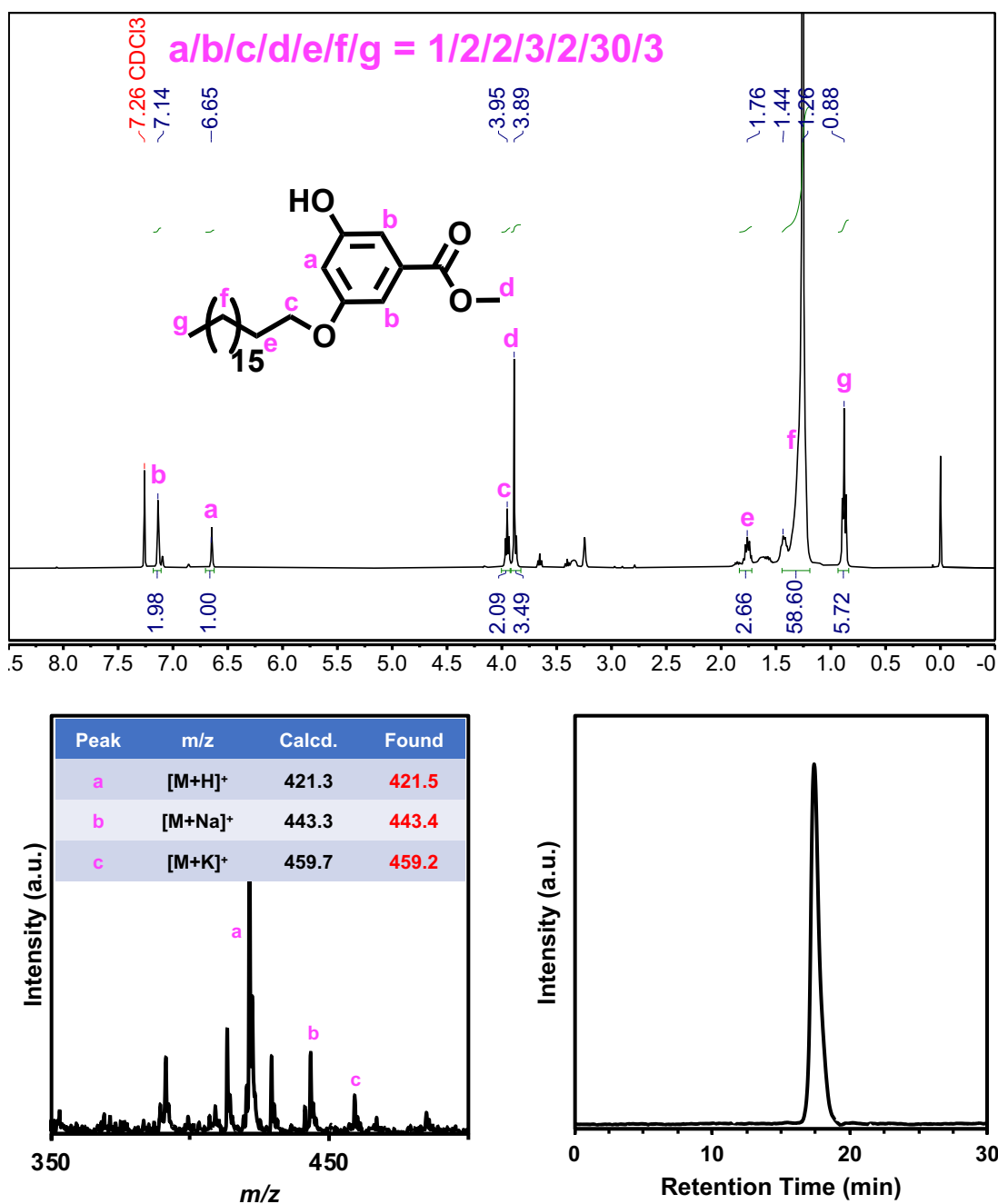


Figure S3. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of Methyl 3-hydroxy-5-(octadecyloxy)benzoate, **34**.

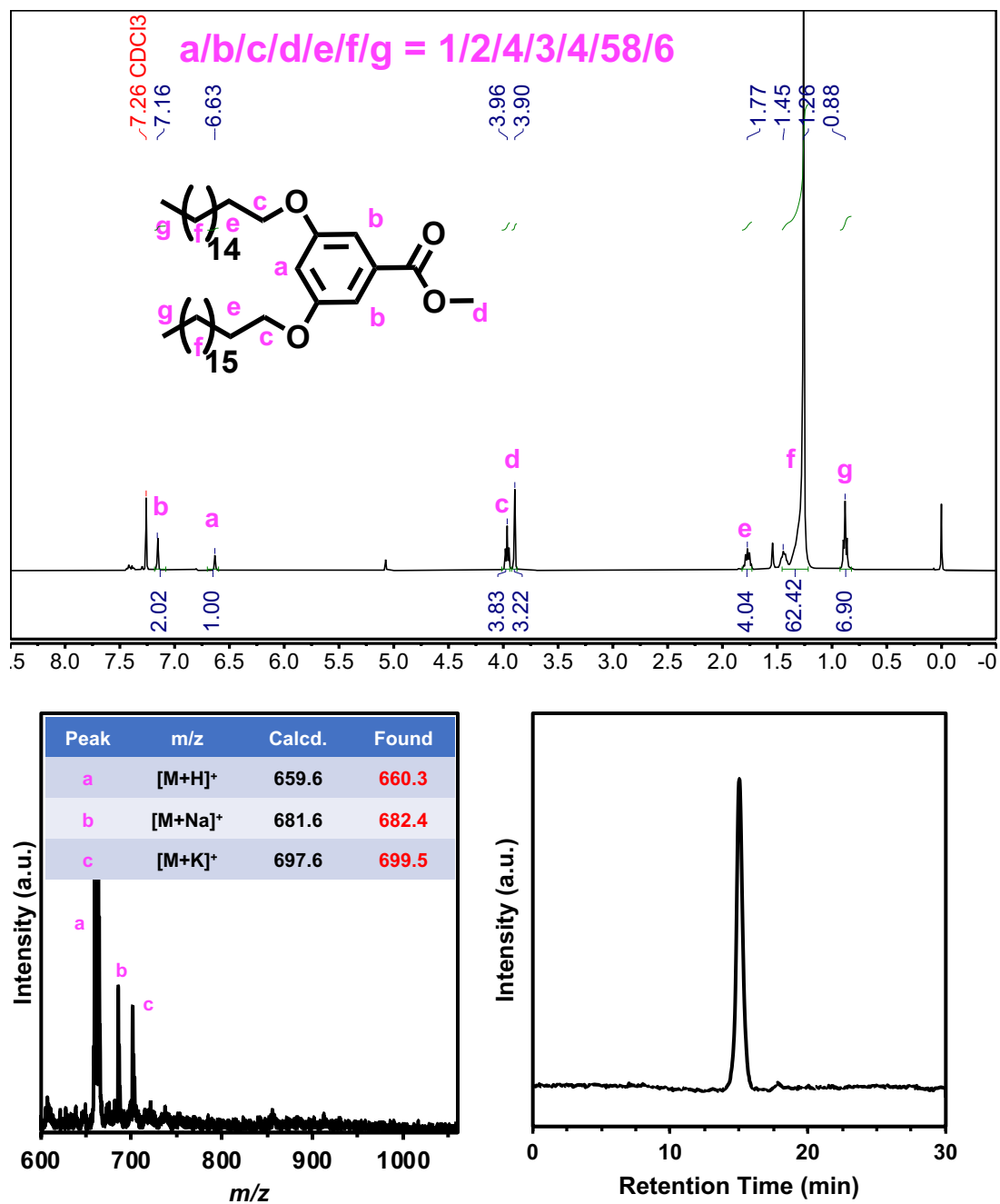


Figure S4. ¹H NMR spectra (top), MALDI-TOF MS spectra (bottom left) and HPLC trace (bottom right) of Methyl 3-(heptadecyloxy)-5-(octadecyloxy)benzoate, **35d**.

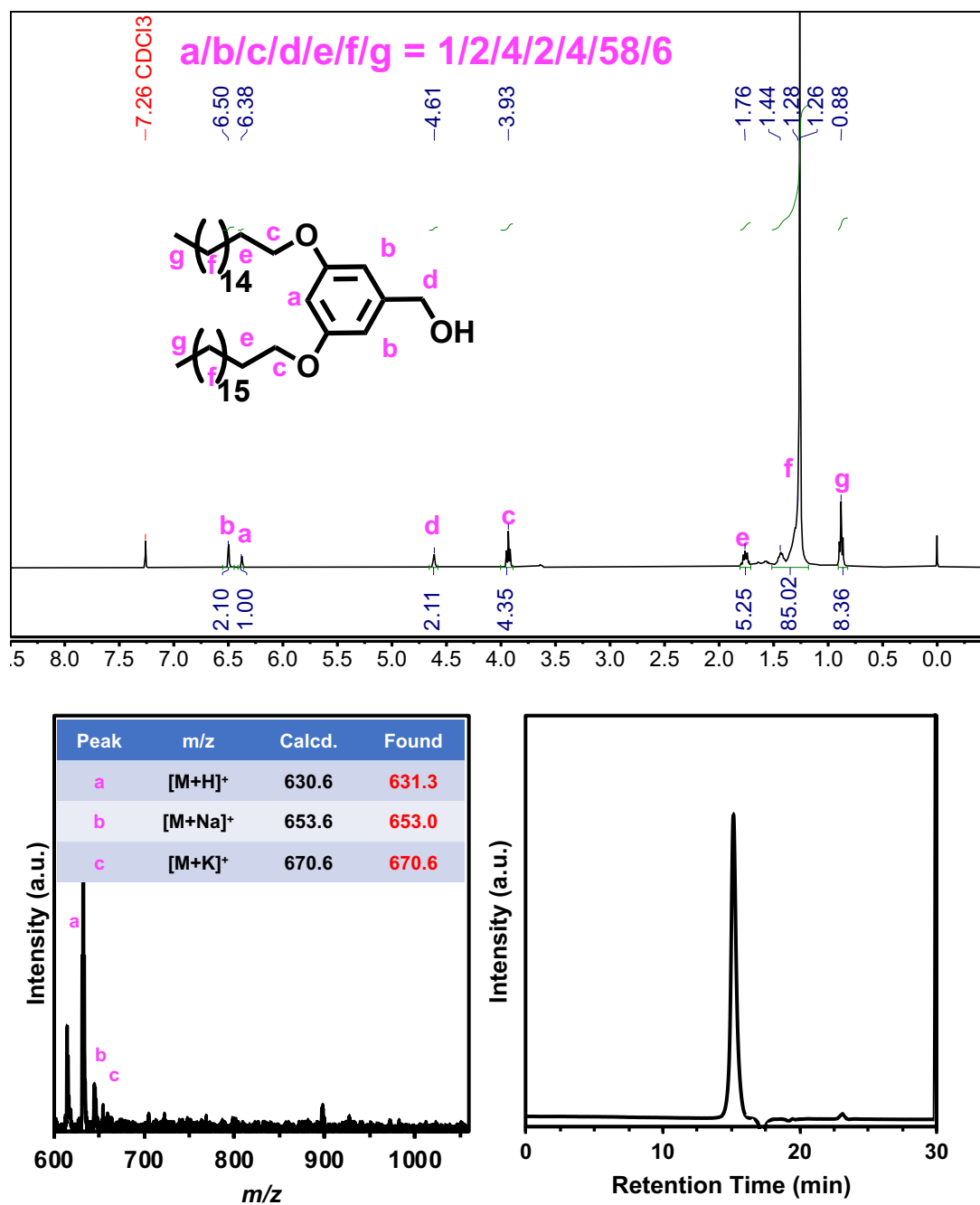


Figure S5. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of (3-(Heptadecyloxy)-5-(octadecyloxy)phenyl)methanol, **36d**.

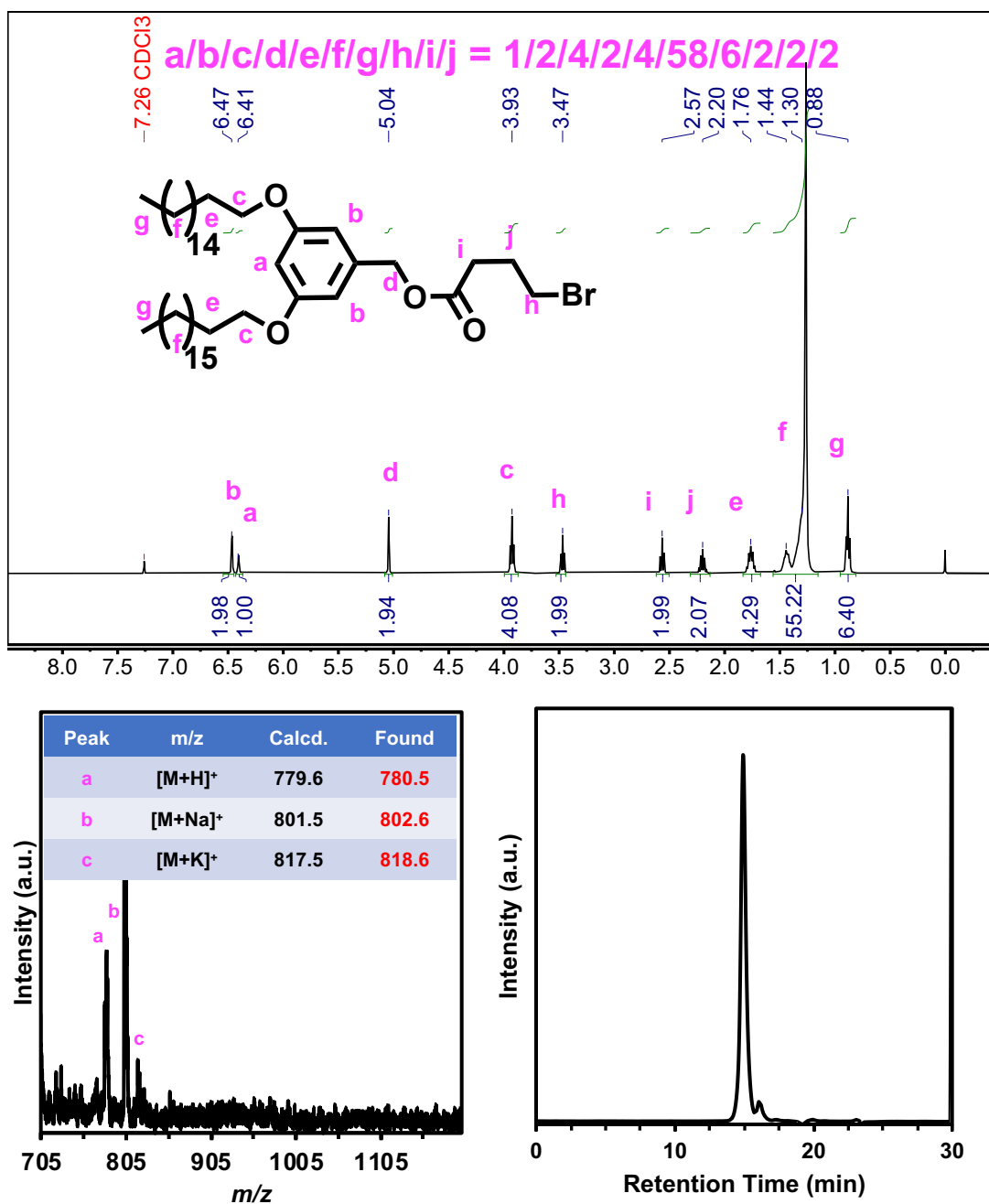


Figure S6. ^1H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of 3-(Heptadecyloxy)-5-(octadecyloxy)benzyl 4-bromobutanoate, **37d**.

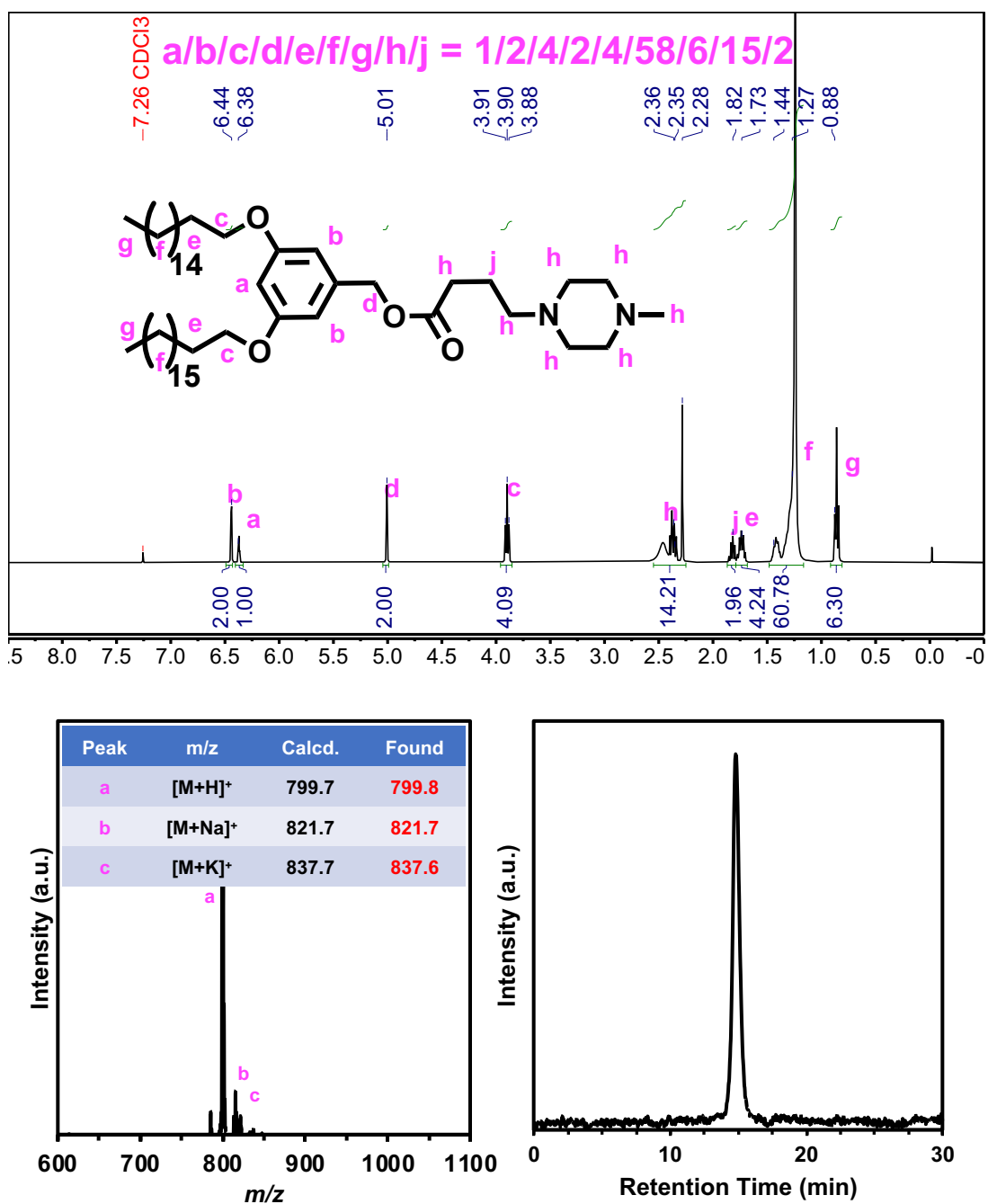


Figure S7. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of 3-(heptadecyloxy)-5-(octadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate, **38g**, IAJD242.

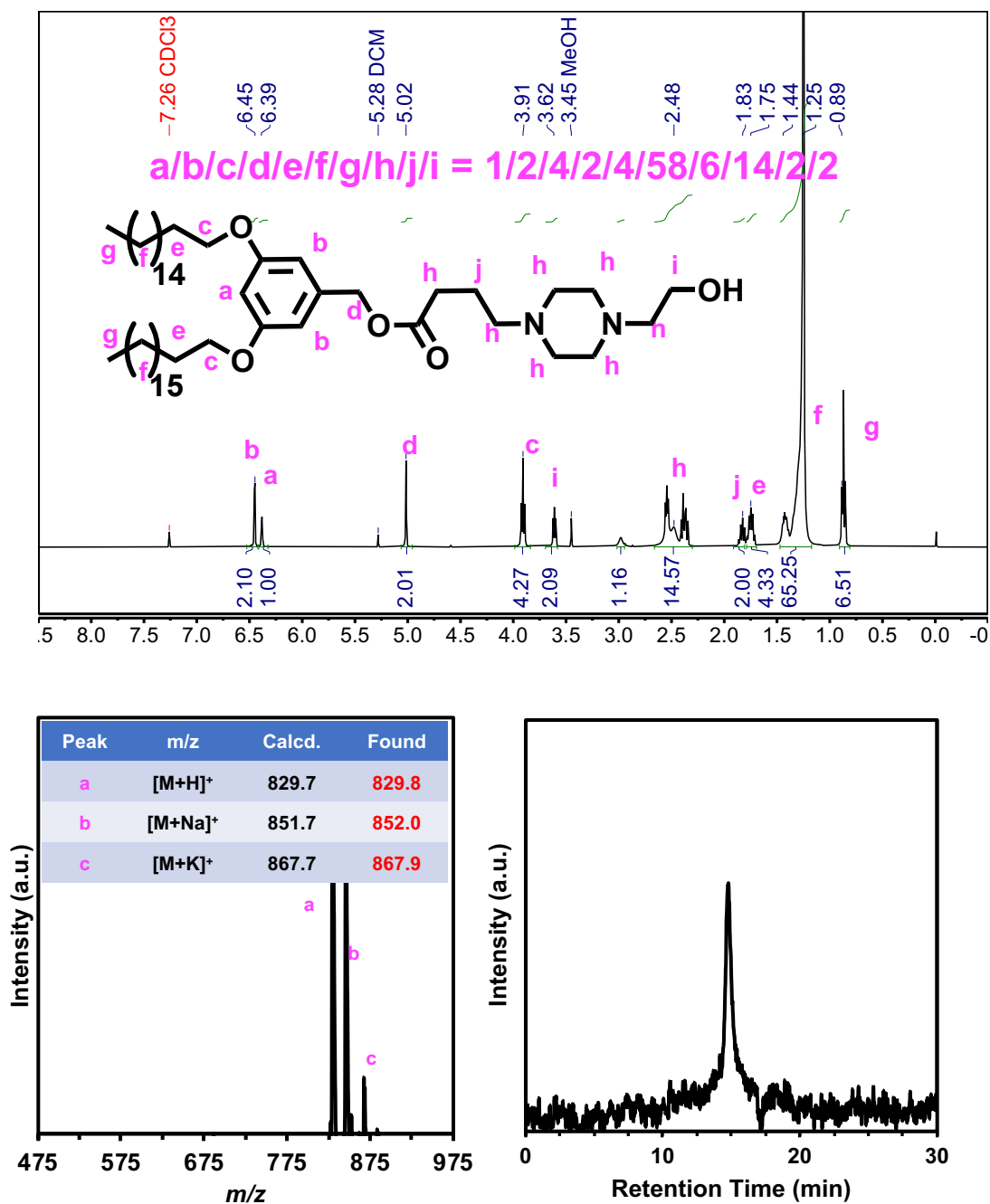


Figure S8. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of 3-(Heptadecyloxy)-5-(octadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate, **38h**, IAJD243.

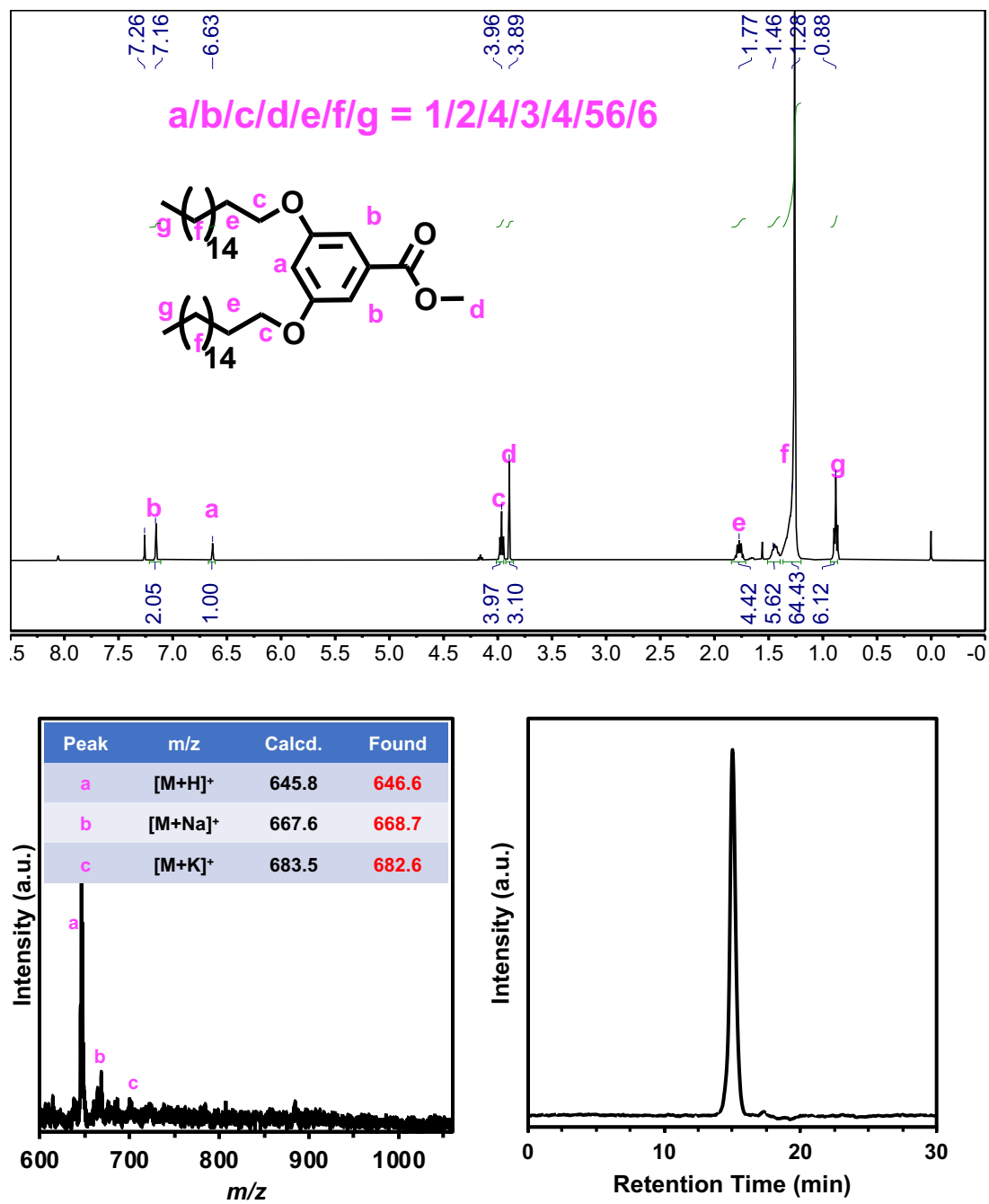


Figure S9. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of methyl 3,5-bis(heptadecyloxy)benzoate, **64d**.

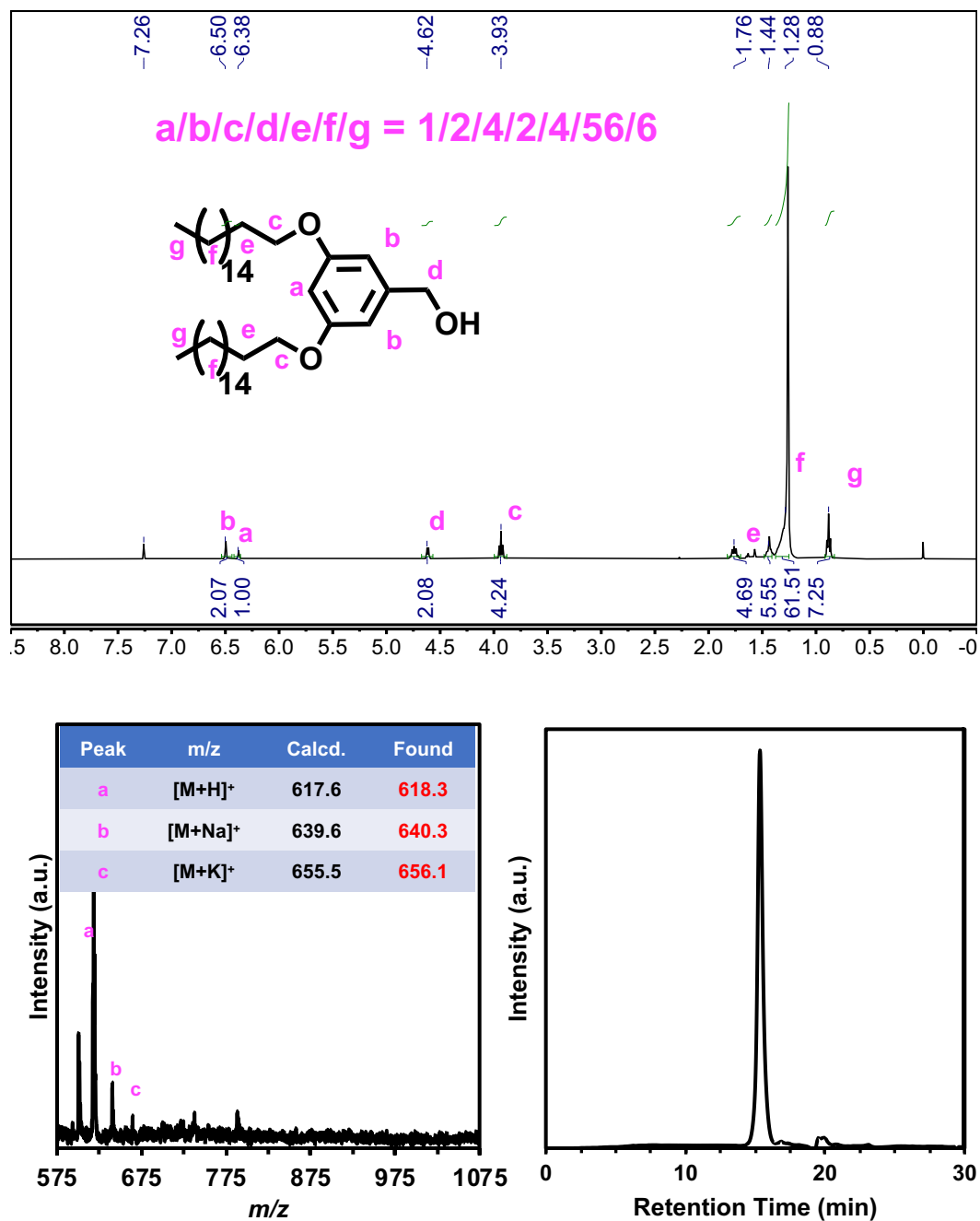


Figure S10. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of (3,5-bis(heptadecyloxy)phenyl)methanol, **65d**.

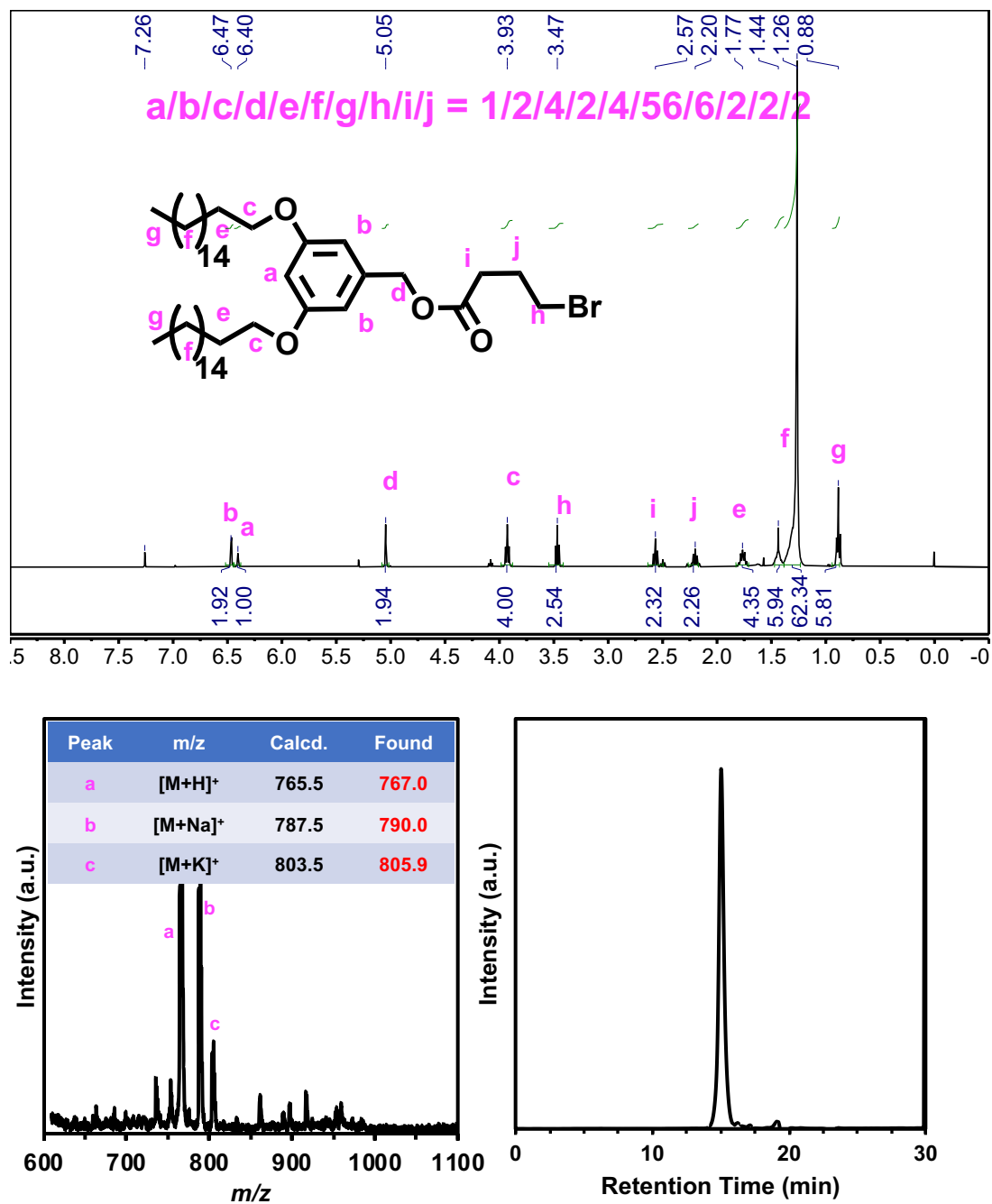


Figure S11. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of 3,5-bis(heptadecyloxy)benzyl 4-bromobutanoate, **66d**.

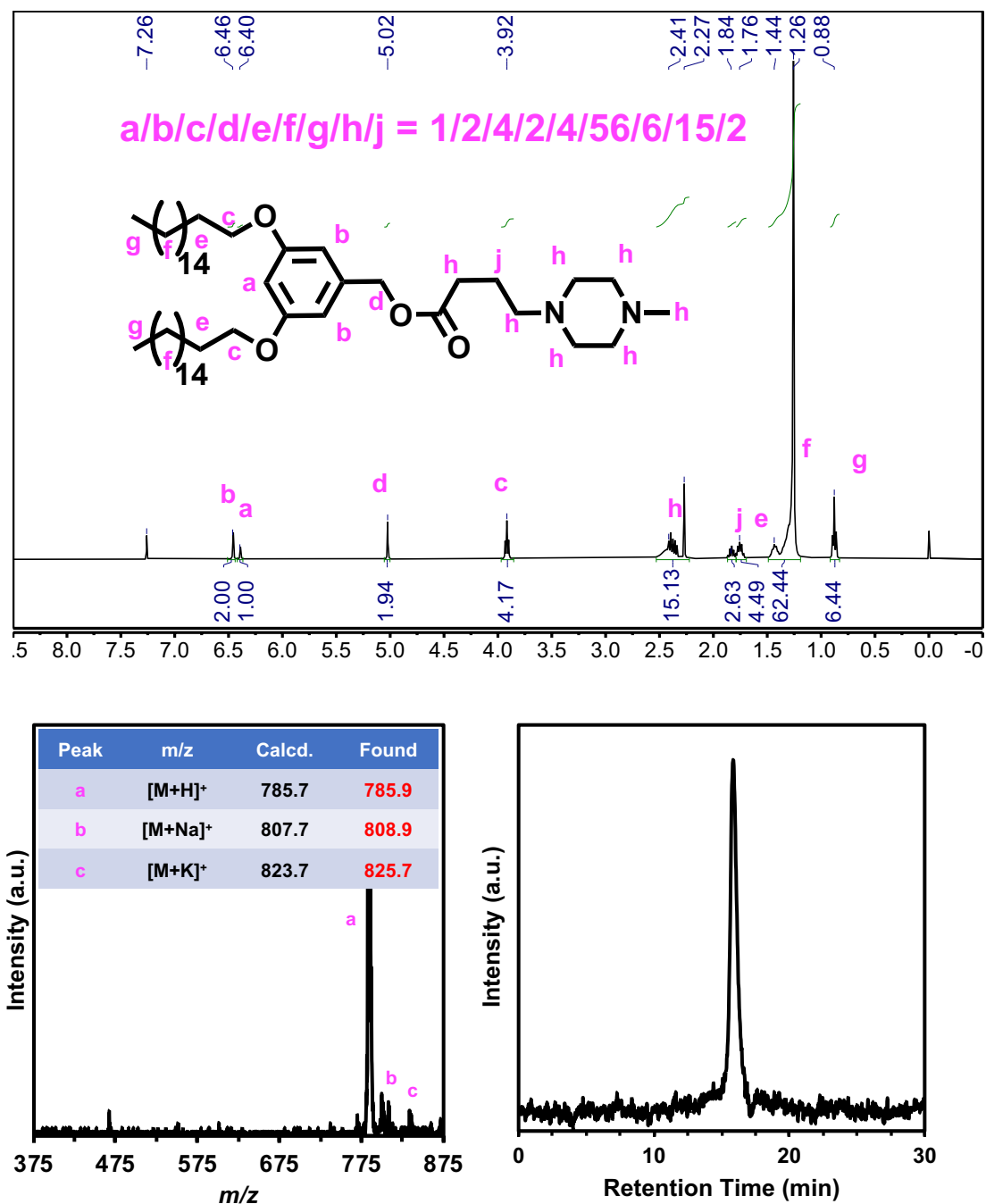


Figure S12. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of 3,5-bis(pentadecyloxy)benzyl 4-(4-methylpiperazin-1-yl)butanoate, **67e**, IAJD265.

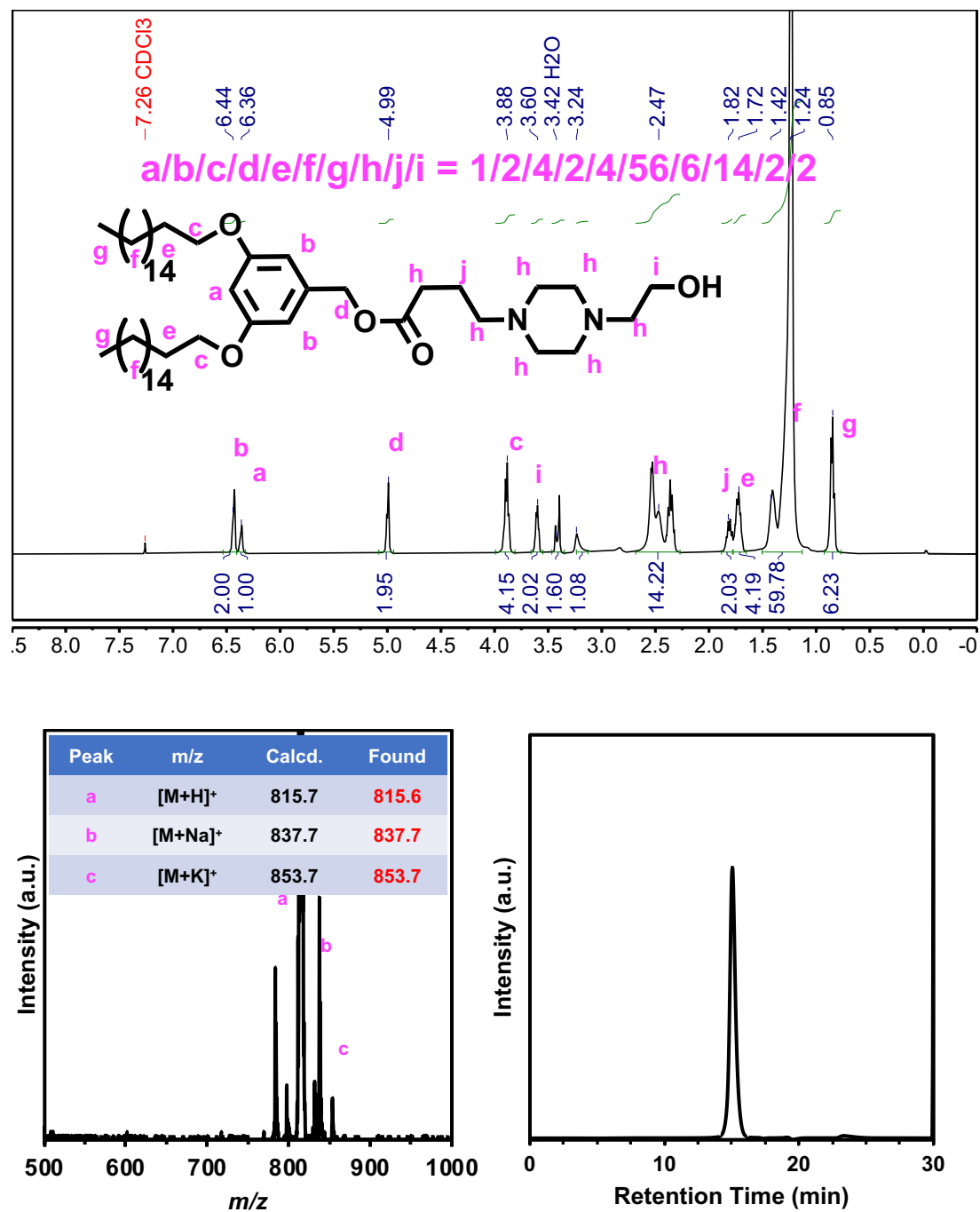


Figure S13. ¹H NMR spectrum (top), MALDI-TOF MS spectrum (bottom left) and HPLC trace (bottom right) of 3,5-Bis(pentadecyloxy)benzyl 4-(4-(2-hydroxyethyl)piperazin-1-yl)butanoate, **67f**, IAJD266.

4. DLS Data of DNPs Co-Assembled from IAJDs and Luc-mRNA

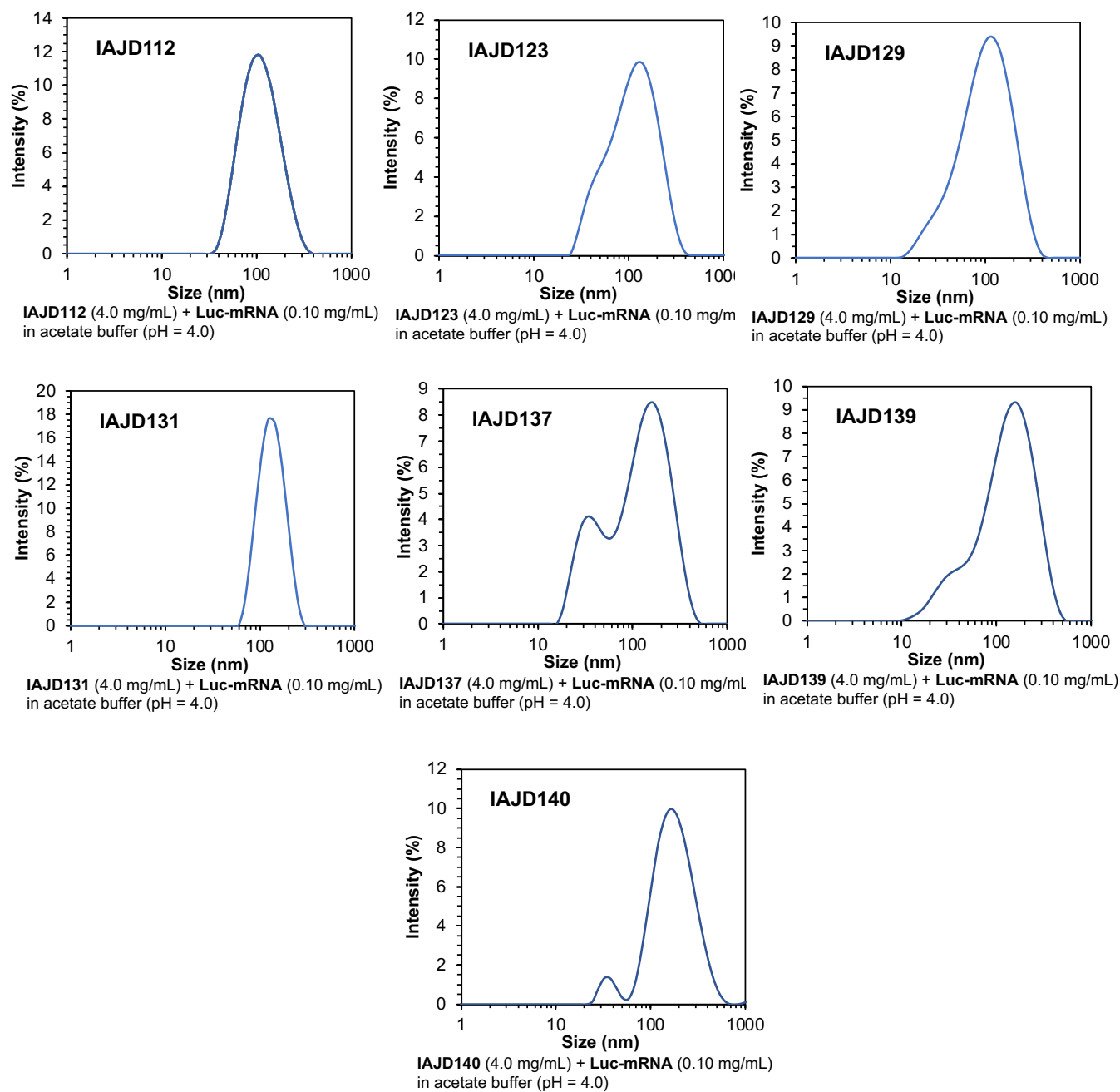


Figure S14. DLS data of DNPs assembled from IAJDs 112,123,129,131,137,139 and 140.

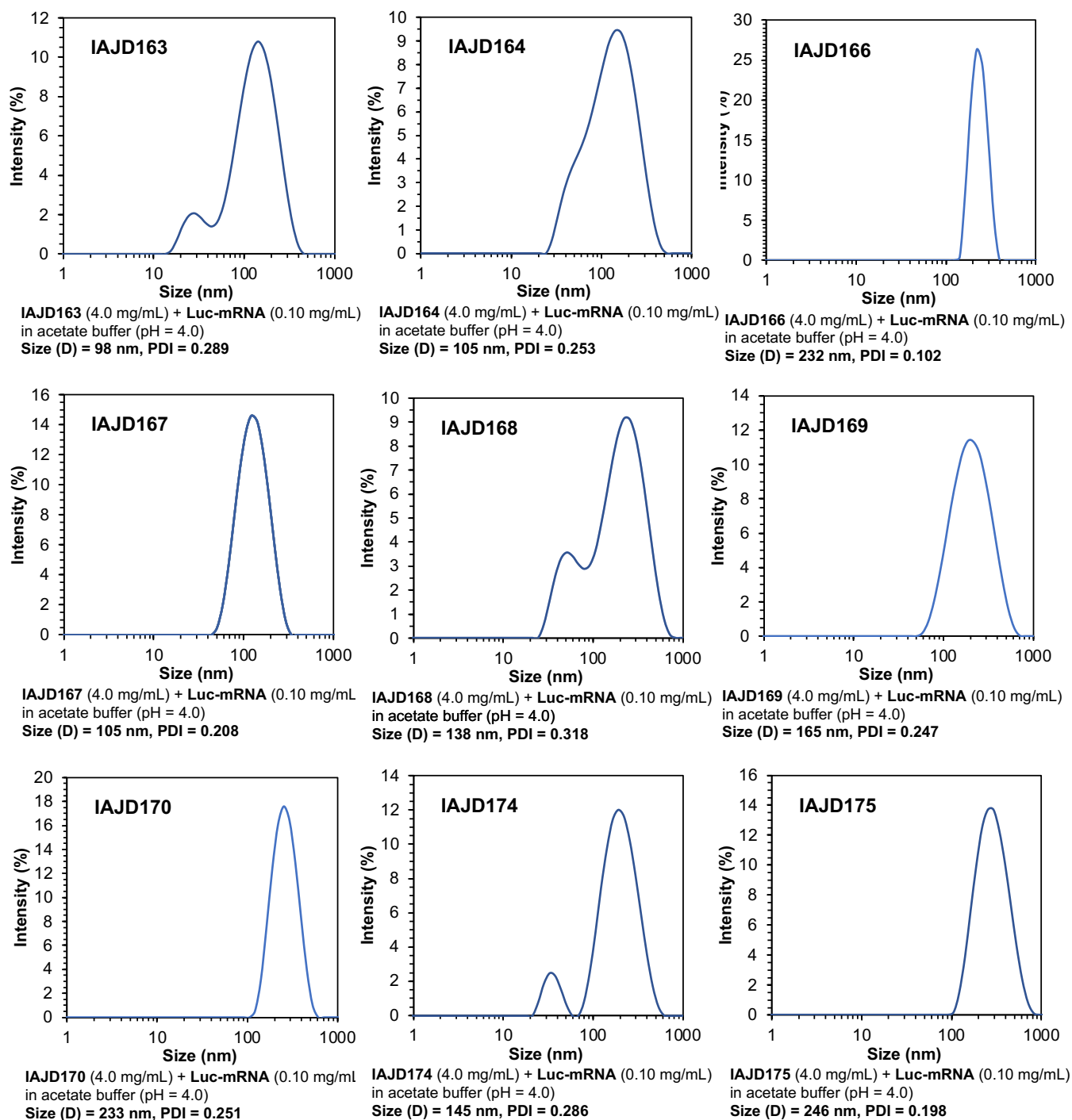


Figure S15. DLS data of DNPs assembled from IAJDs 163,164,166 – 170, 174, 175.

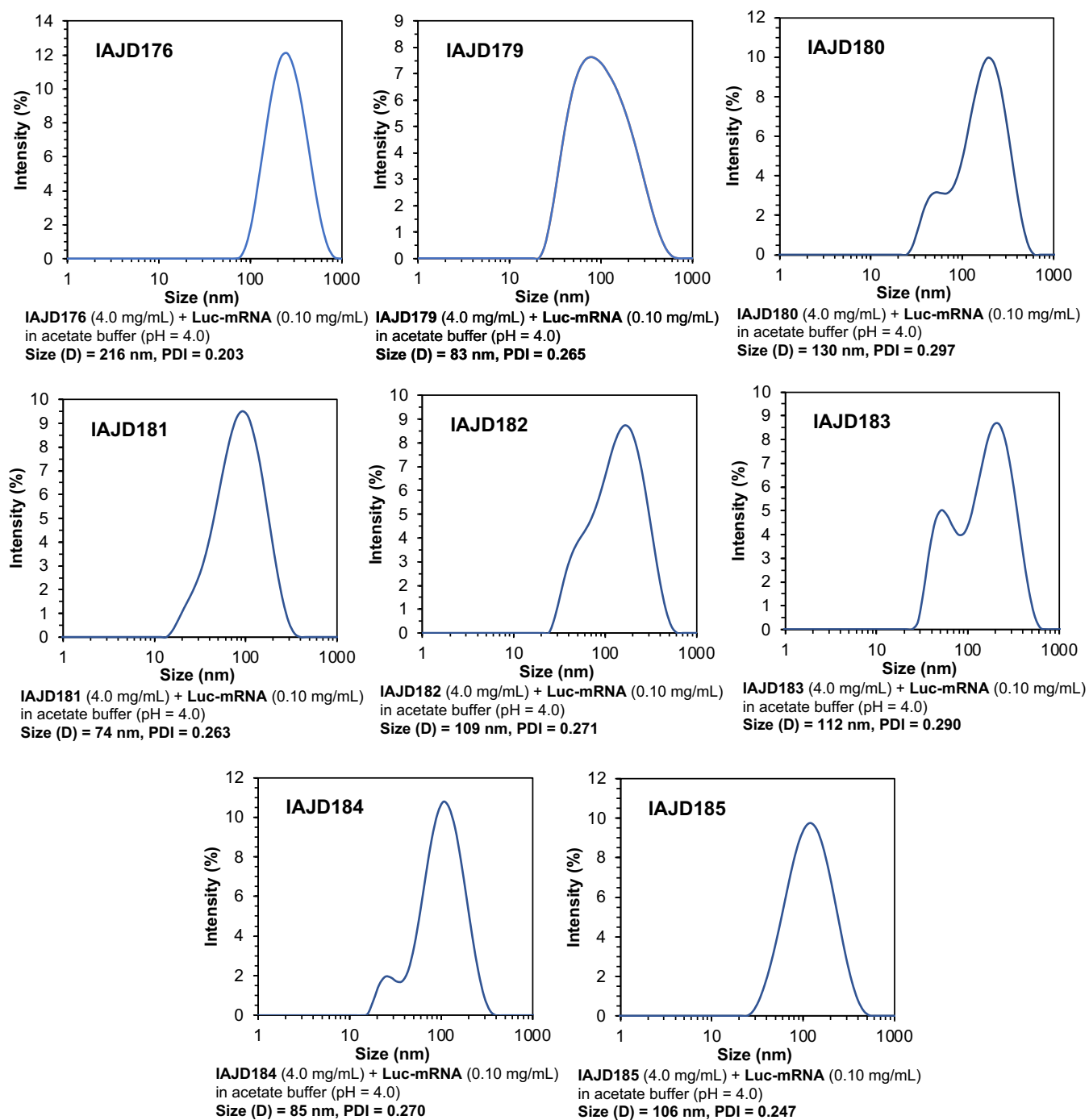


Figure S16. DLS data of DNPs assembled from IAJDs 176,179-185.

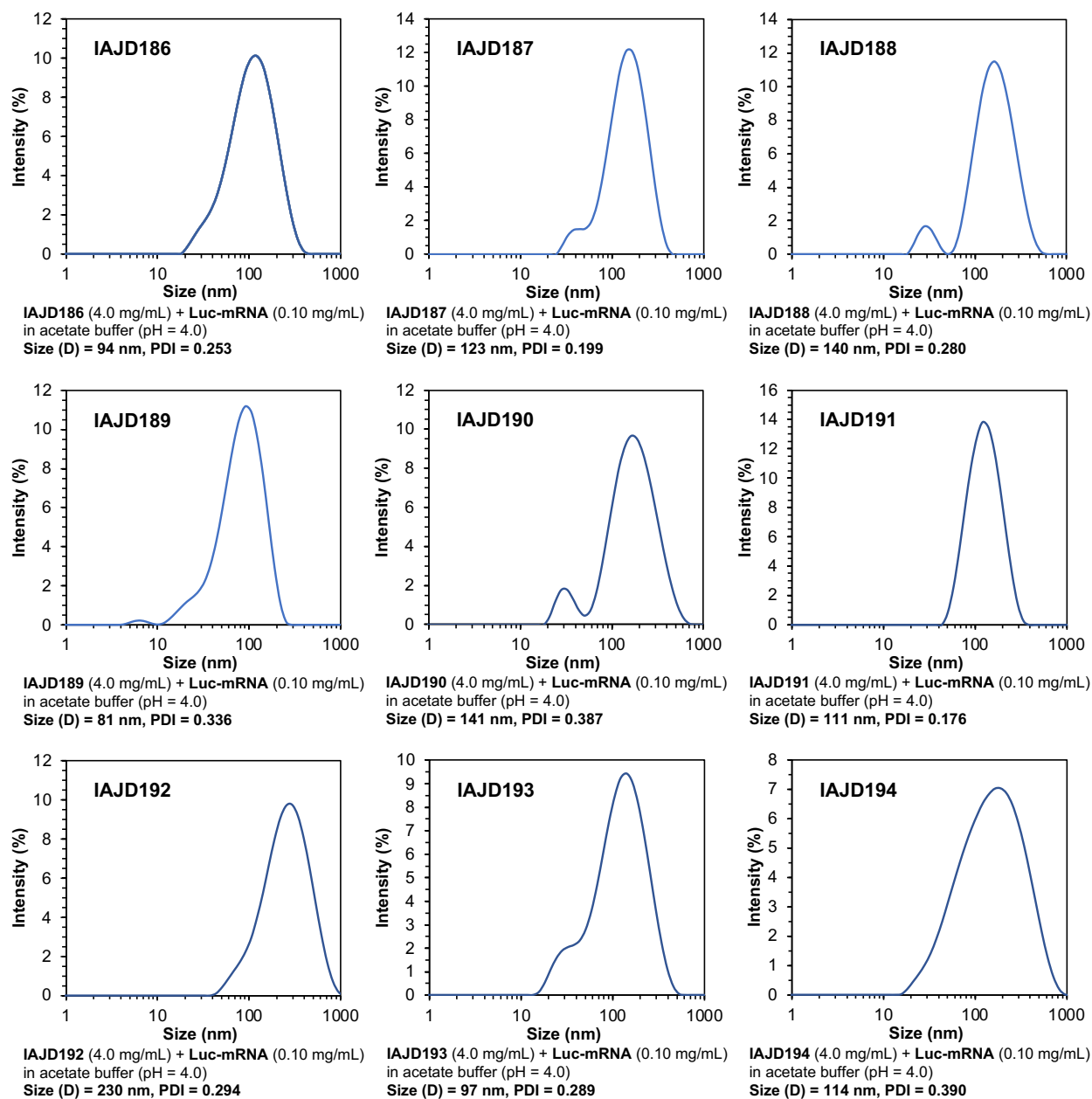


Figure S17. DLS data of DNPs assembled from IAJDs 186-194.

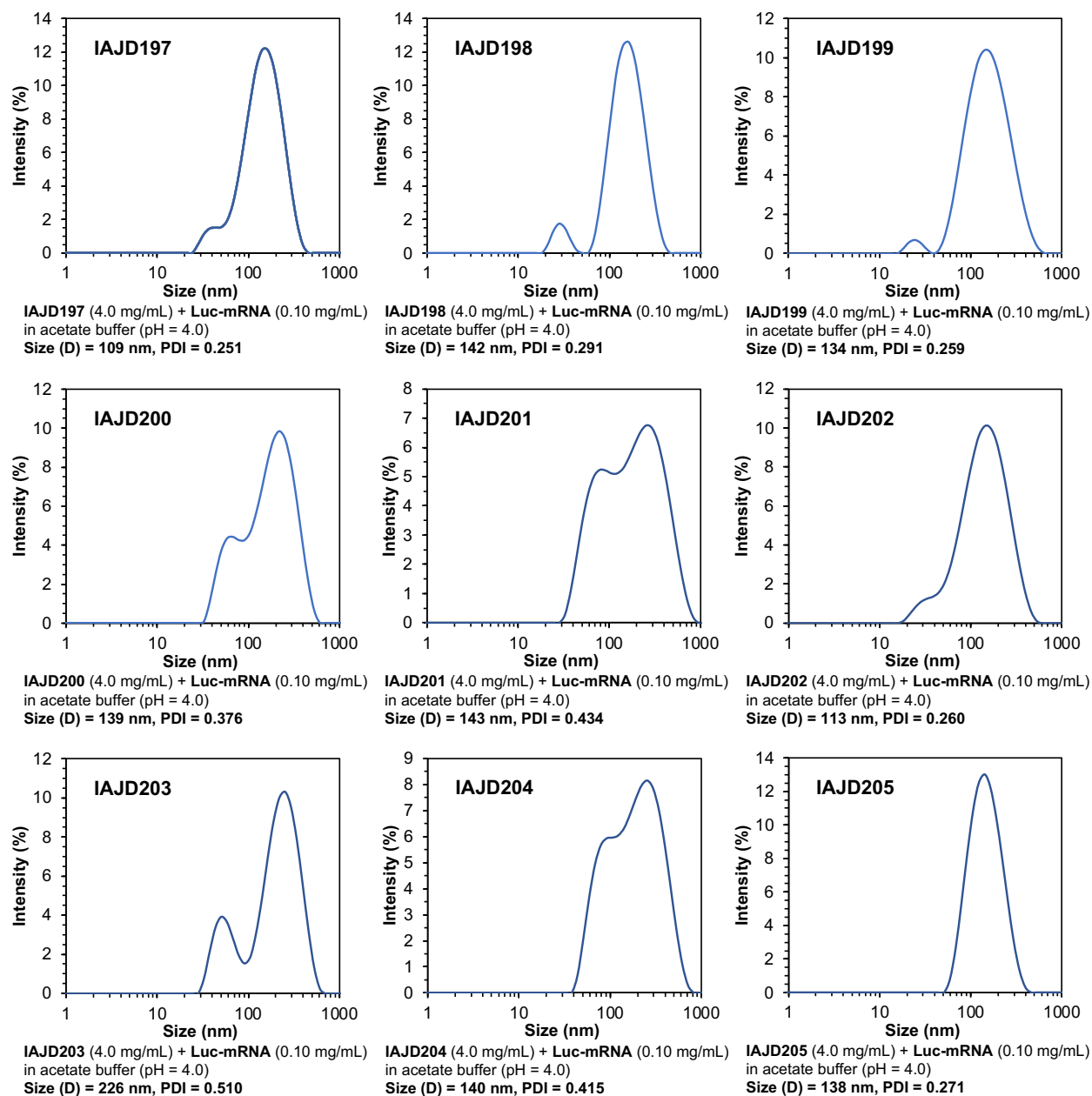


Figure S18. DLS data of DNPs assembled from IAJDs 197-205.

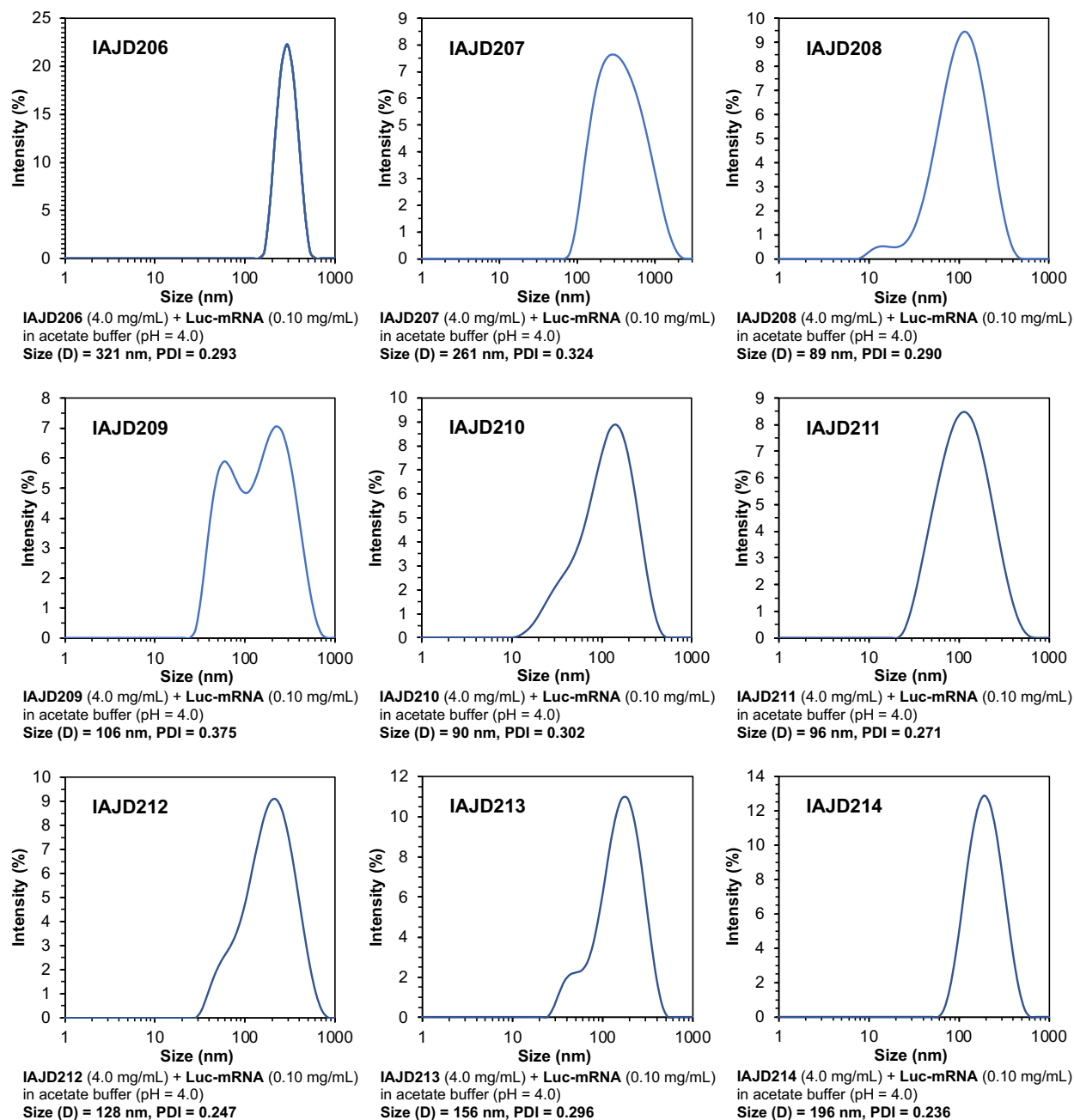


Figure S19. DLS data of DNPs assembled from IAJDs 206-214.

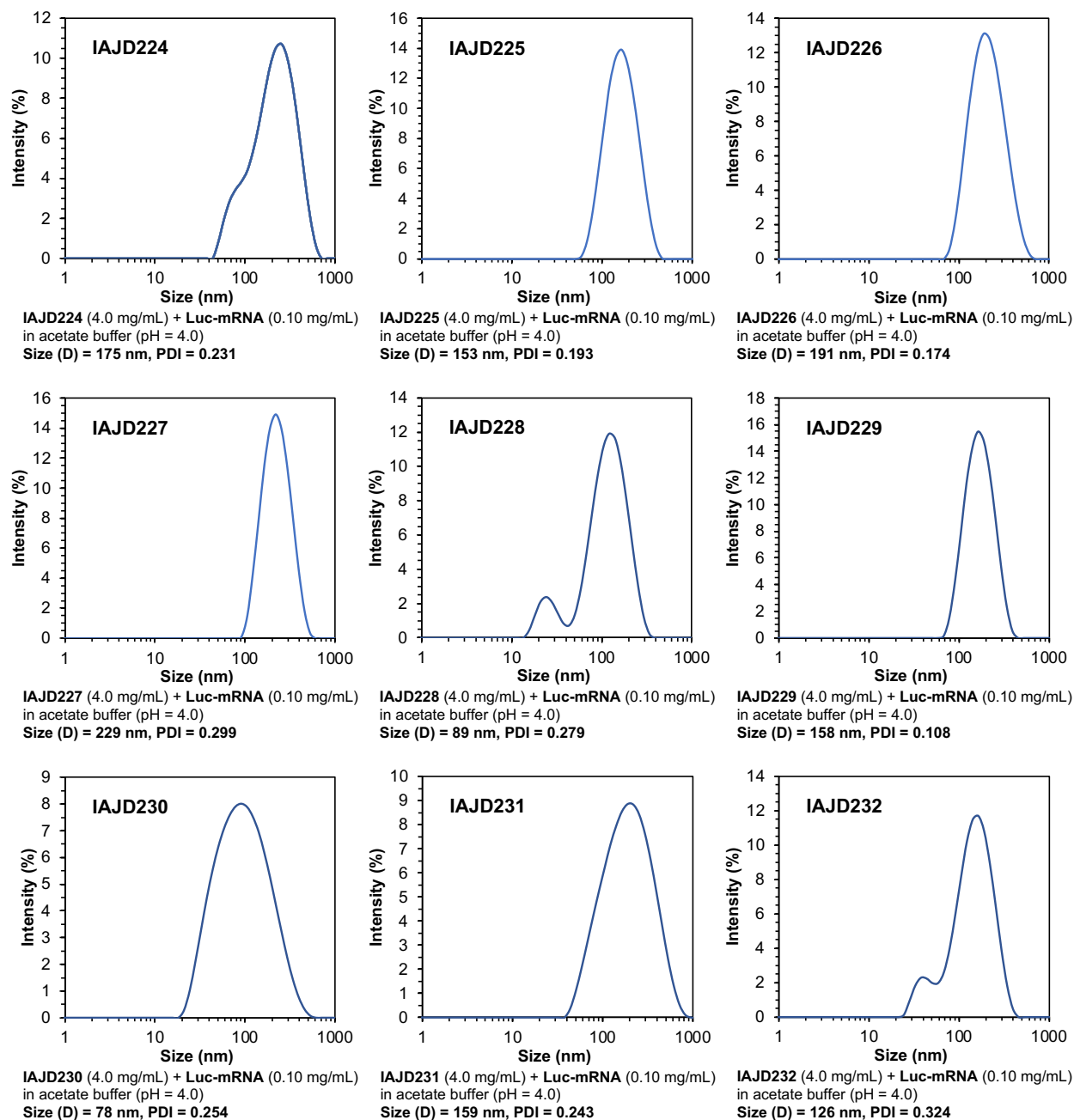


Figure S20. DLS data of DNPs assembled from IAJDs 224-232.

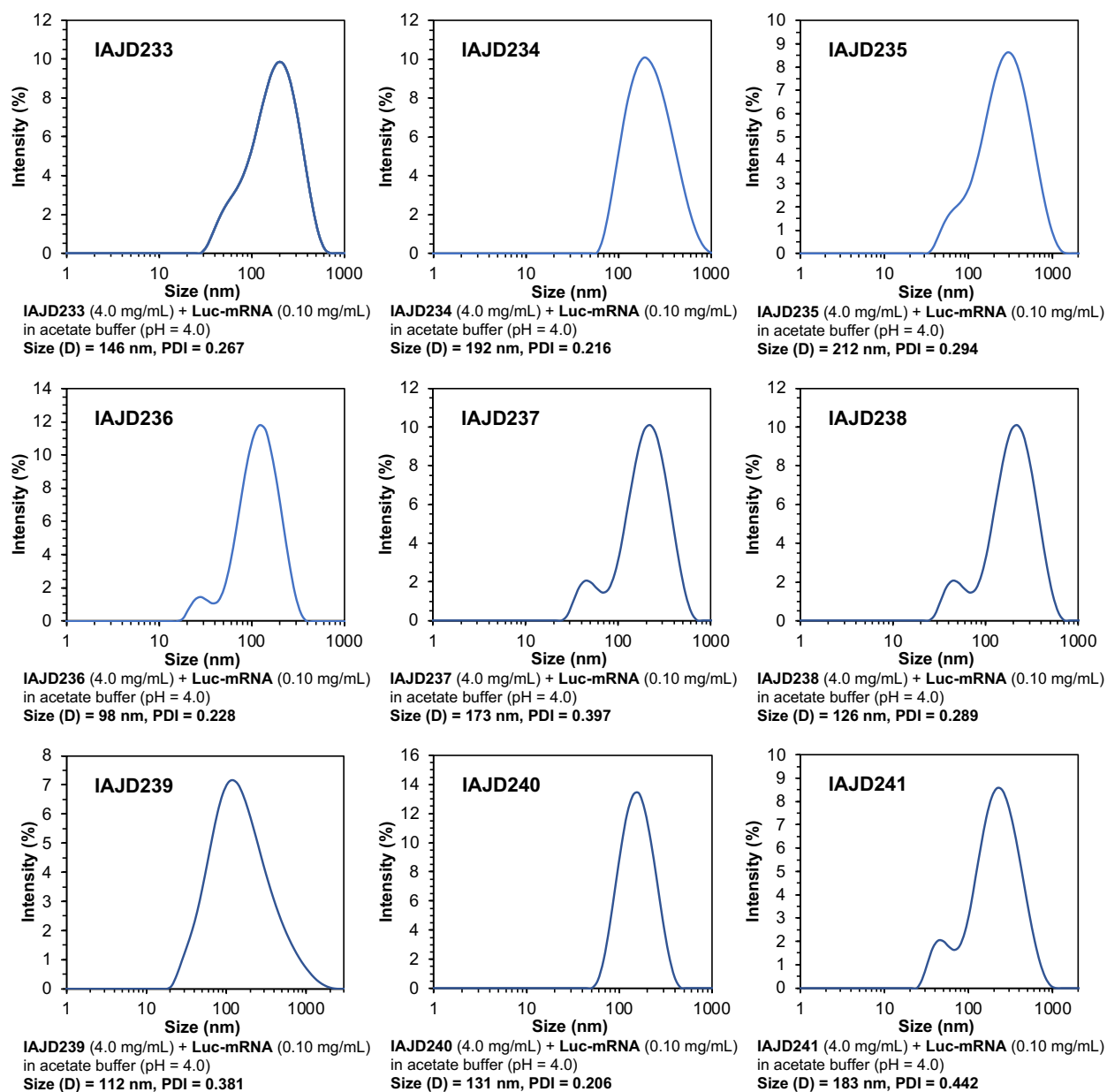


Figure S21. DLS data of DNPs assembled from IAJDs 233-241.

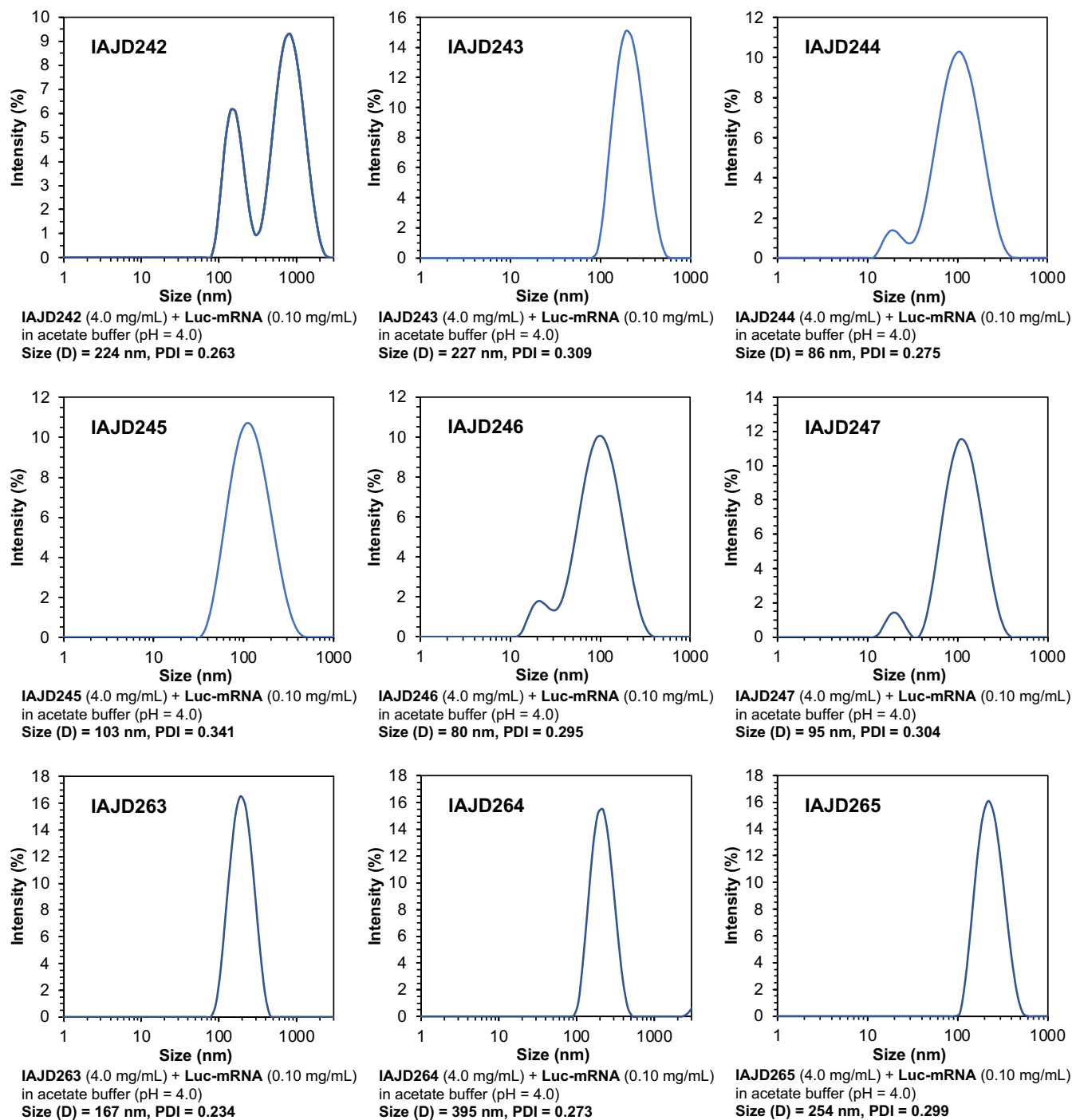


Figure S22. DLS data of DNPs assembled from IAJDs 242-247, 263-265.

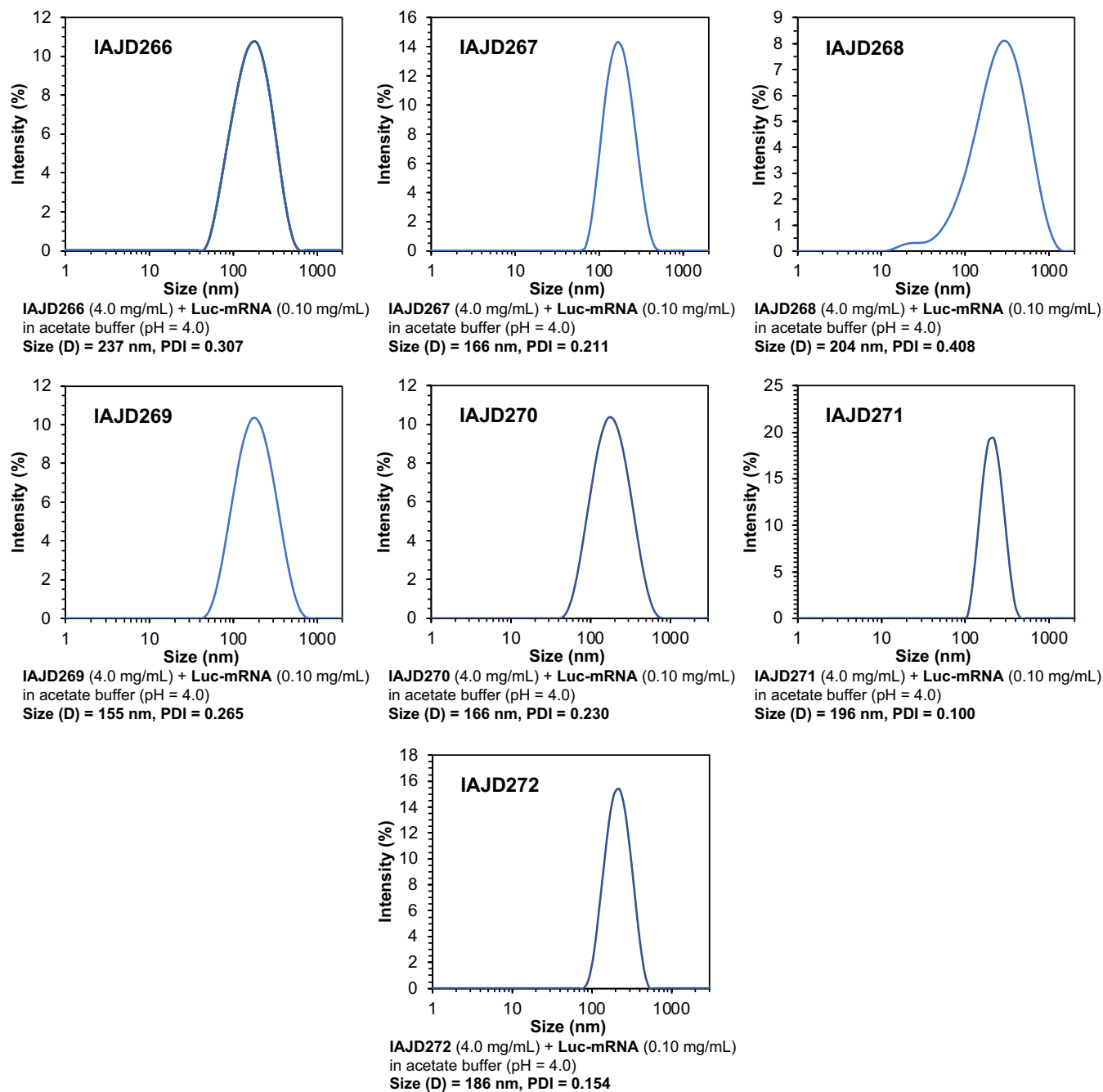


Figure S23. DLS data of DNPs assembled from IAJDs 266-272.

5. pK_a Measurements of Individual IAJDs

Table S1. pK_a of Individual IAJDs

IAJD No.	pK _a	IAJD No.	pK _a	IAJD No.	pK _a
IAJD 73	6.30	IAJD 191	6.54	IAJD 226	6.46
IAJD 90	6.36	IAJD 192	6.42	IAJD 227	6.49
IAJD 112	6.4	IAJD 193	6.34	IAJD 228	6.56
IAJD 121	6.64	IAJD 194	6.37	IAJD 229	6.3
IAJD 123	6.61	IAJD 197	6.33	IAJD 230	6.3
IAJD 129	6.49	IAJD 198	6.28	IAJD 231	5.95
IAJD 131	7.34	IAJD 199	6.41	IAJD 232	6.28
IAJD 137	6.44	IAJD 200	6.17	IAJD 233	6.31
IAJD 139	6.43	IAJD 201	6.27	IAJD 234	6.35
IAJD 140	6.43	IAJD 202	6.24	IAJD 235	6.24
IAJD 163	6.3	IAJD 203	6.35	IAJD 236	6.34
IAJD 164	6.29	IAJD 204	6.26	IAJD 237	6.26
IAJD 165	6.41	IAJD 205	6.27	IAJD 238	6.25
IAJD 166	6.34	IAJD 206	6.28	IAJD 239	6.22
IAJD 167	6.24	IAJD 207	6.14	IAJD 240	6.29
IAJD 168	6.56	IAJD 208	6.2	IAJD 241	6.33
IAJD 169	6.44	IAJD 209	6.26	IAJD 242	6.31
IAJD 170	6.27	IAJD 210	6.19	IAJD 243	6.34
IAJD 174	6.31	IAJD 211	6.1	IAJD 244	6.3
IAJD 175	6.44	IAJD 212	6.26	IAJD 245	6.4
IAJD 176	6.29	IAJD 213	6.05	IAJD 246	6.32
IAJD 179	6.51	IAJD 214	6.23	IAJD 247	6.39
IAJD 180	6.49	IAJD 215	6.3	IAJD 263	6.48
IAJD 181	6.42	IAJD 216	6.26	IAJD 264	6.54
IAJD 182	6.41	IAJD 217	6.2	IAJD 265	6.54
IAJD 183	6.32	IAJD 218	6.26	IAJD 266	6.54
IAJD 184	6.36	IAJD 219	6.35	IAJD 267	6.52
IAJD 185	6.3	IAJD 220	6.26	IAJD 268	6.45
IAJD 186	6.19	IAJD 221	6.22	IAJD 269	6.5
IAJD 187	6.43	IAJD 222	6.39	IAJD 270	6.5
IAJD 188	6.46	IAJD 223	6.46	IAJD 271	6.45
IAJD 189	6.3	IAJD 224	6.33	IAJD 272	6.48
IAJD 190	6.35	IAJD 225	6.36		

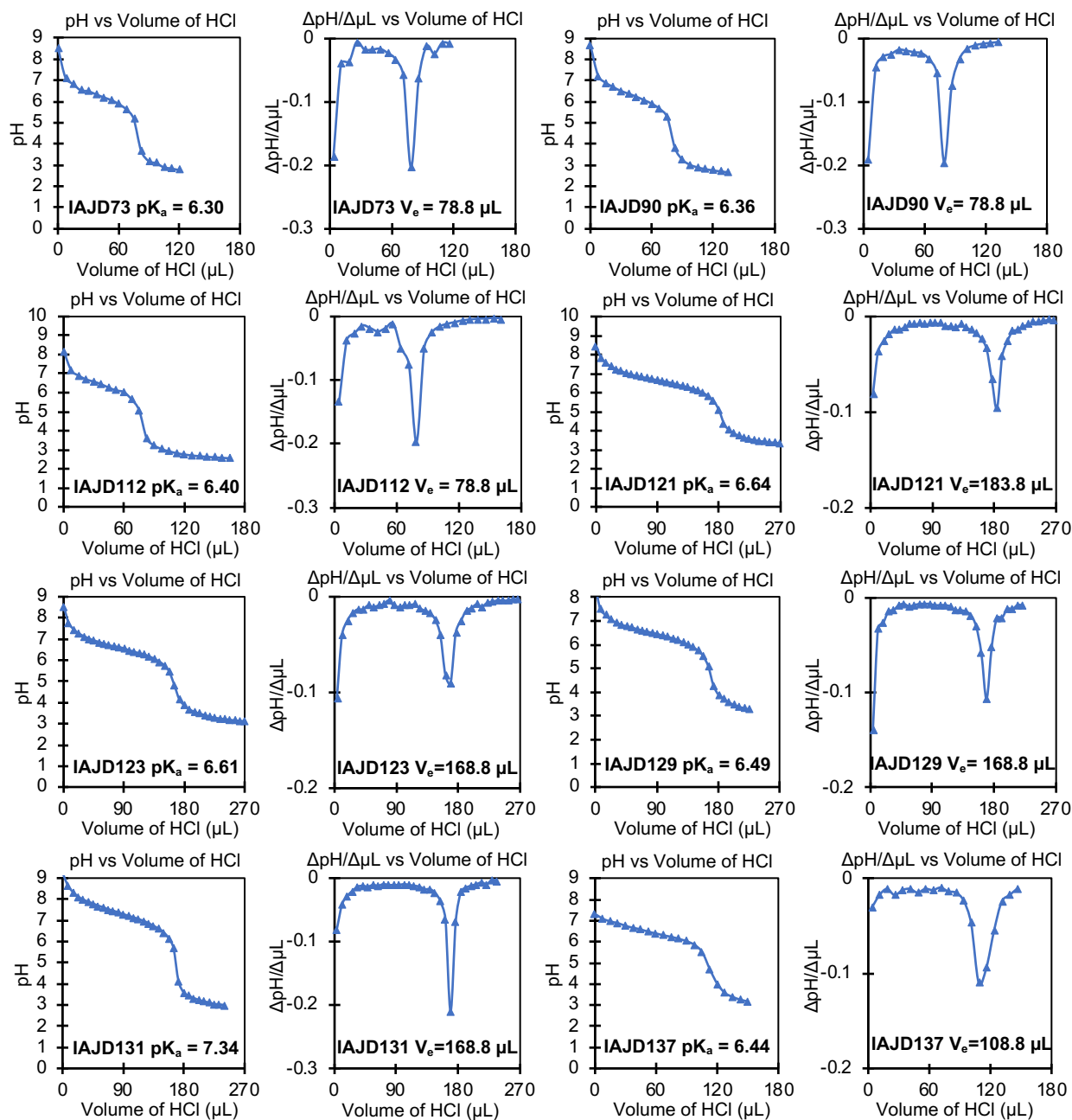


Figure S24. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pK_a for IAJDs 73,90,112,121,123,129,131,137.

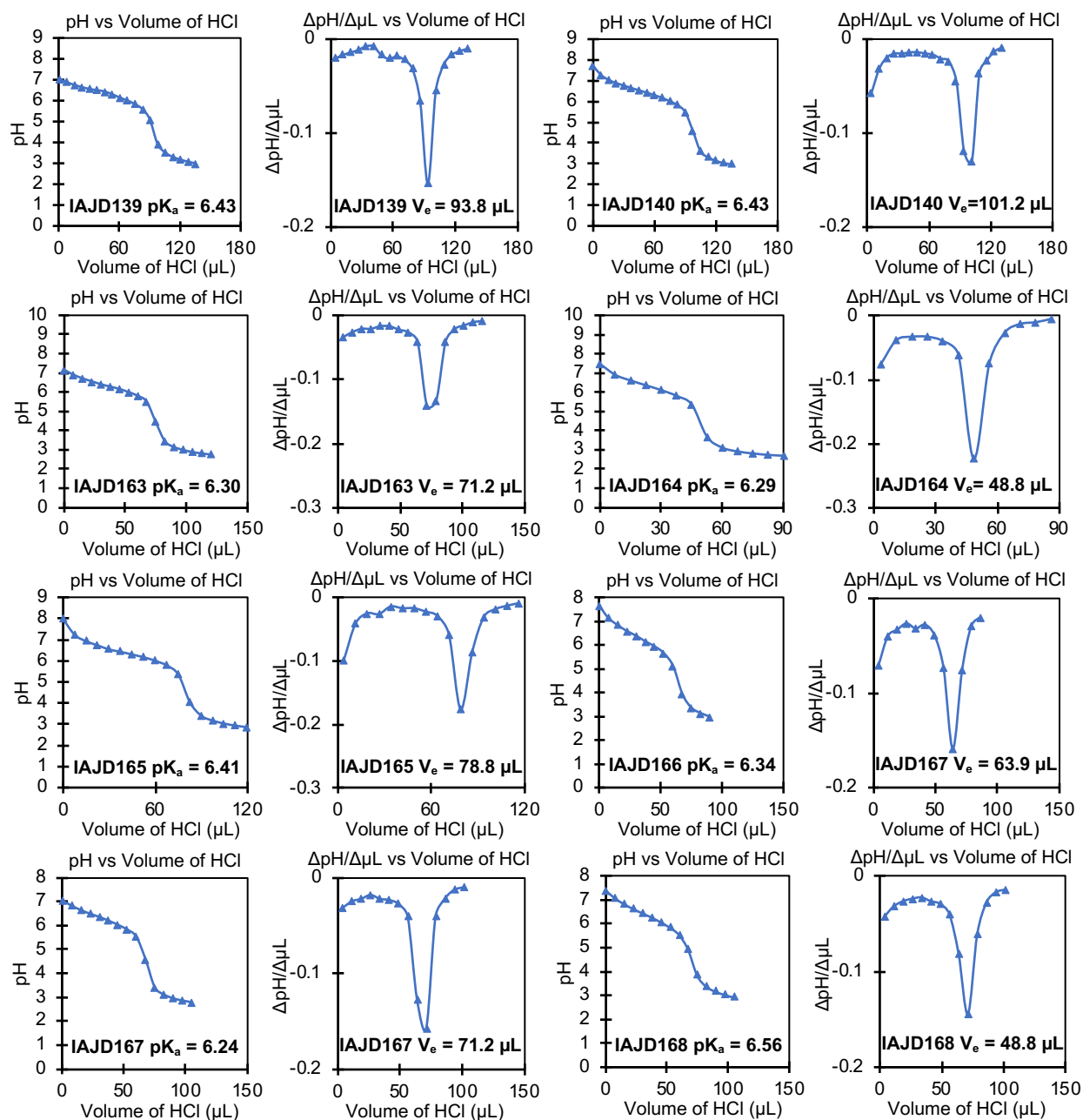


Figure S25. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pK_a for IAJDs 139, 140, 163-168.

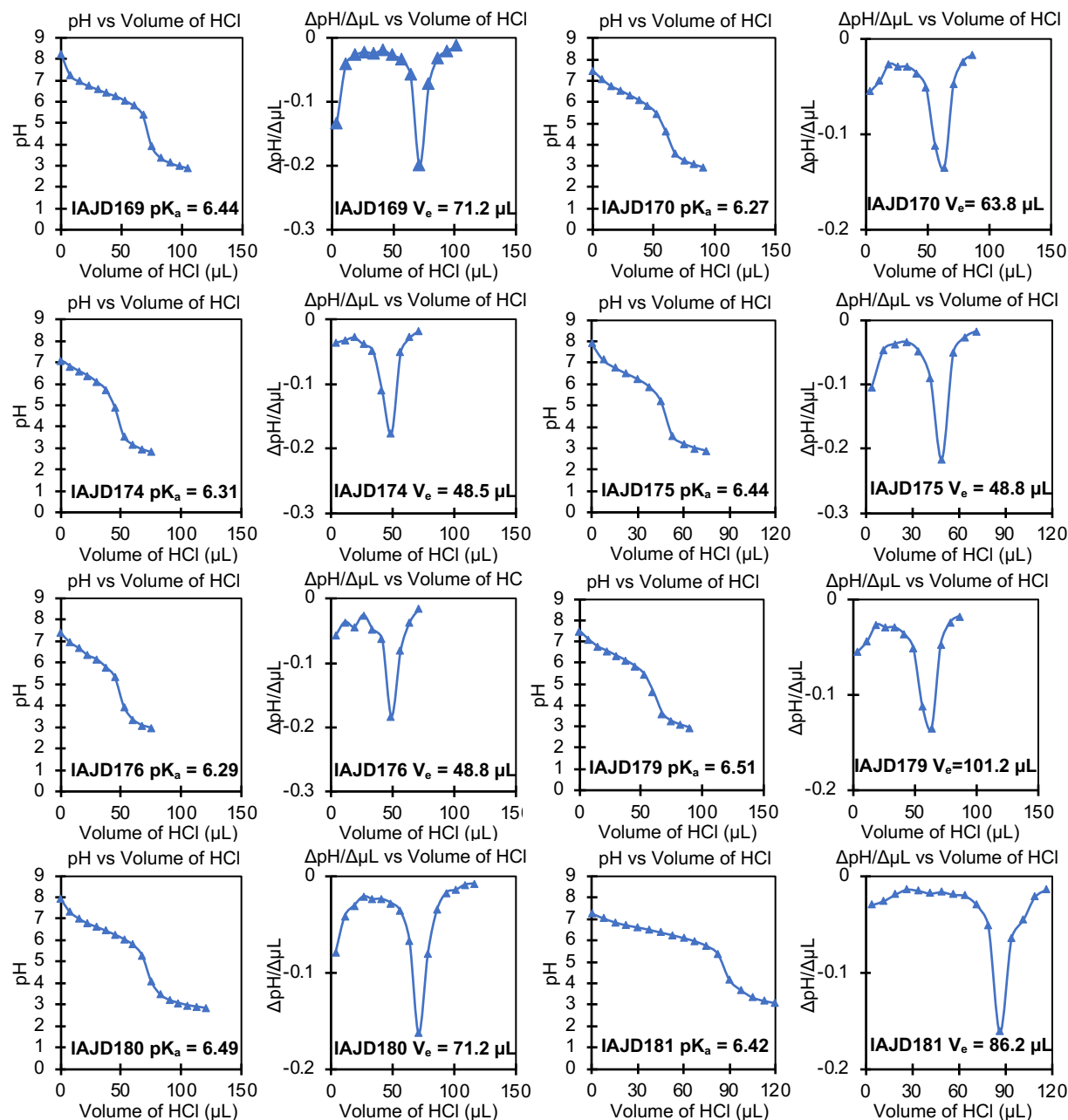


Figure S26. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pK_a for IAJDs 169,170,174-176, 179-181.

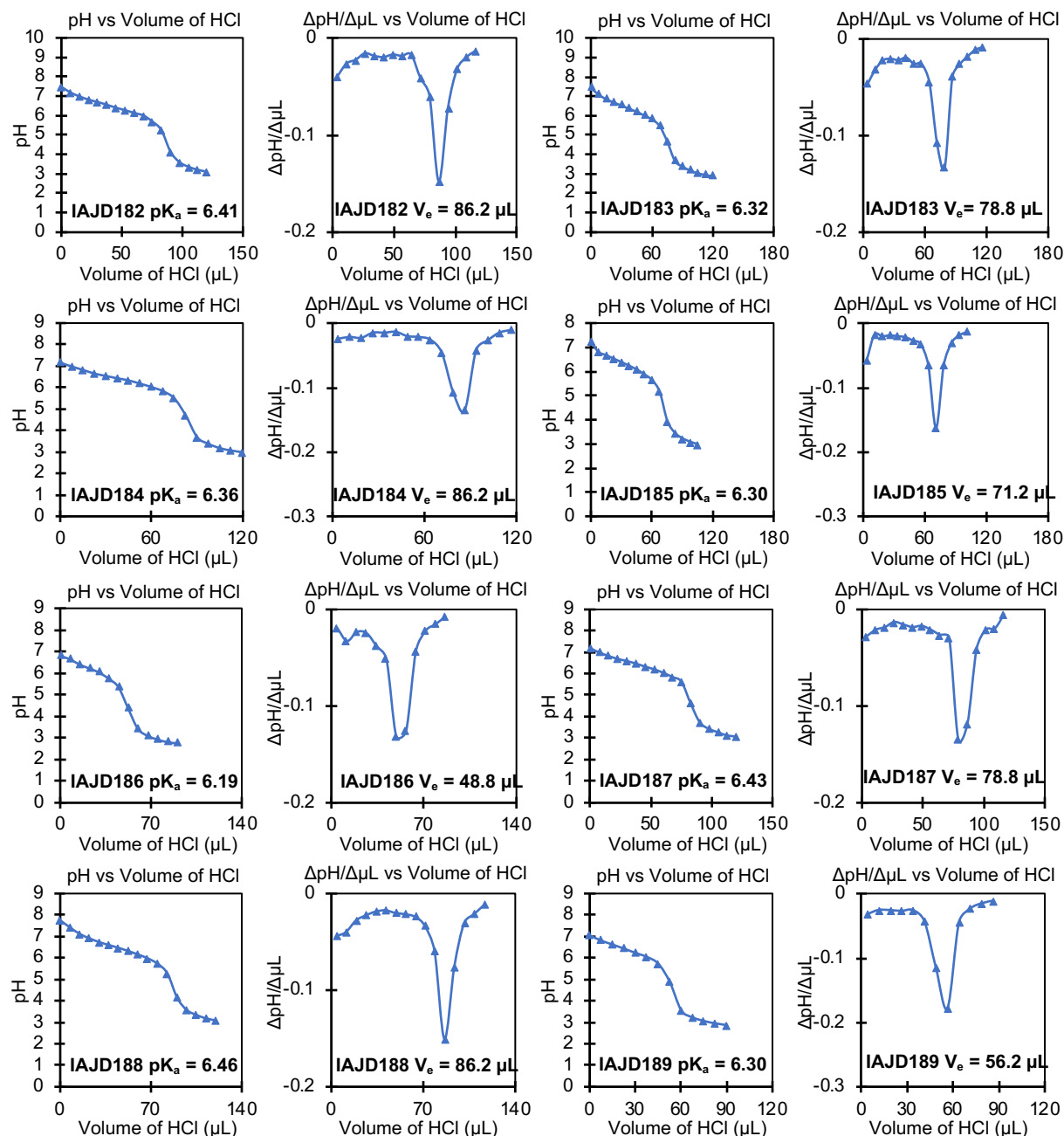


Figure S27. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pK_a for IAJDs 182-189.

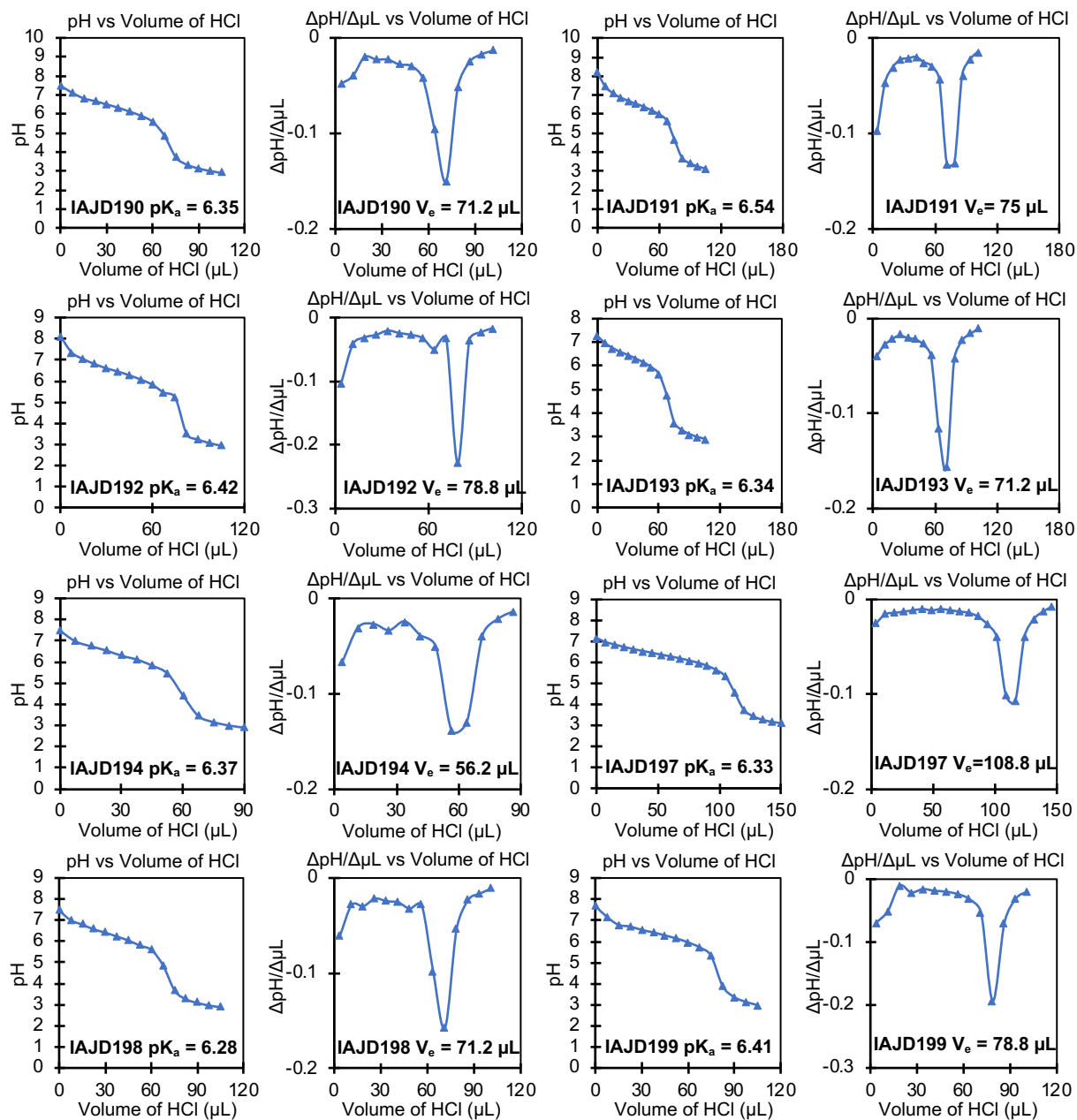


Figure S28. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pK_a for IAJDs 190-194,197-199.

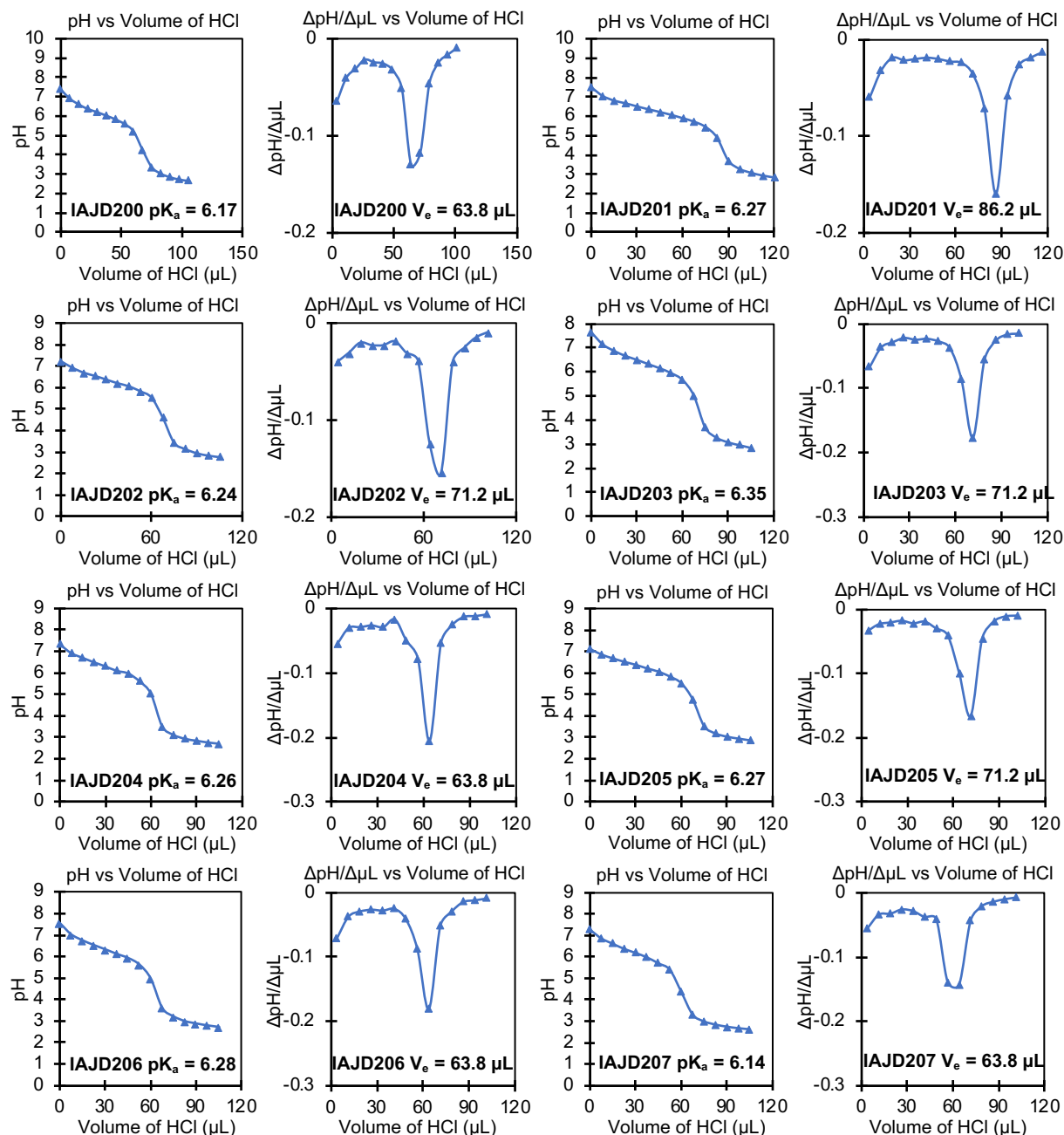


Figure S29. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 200-207.

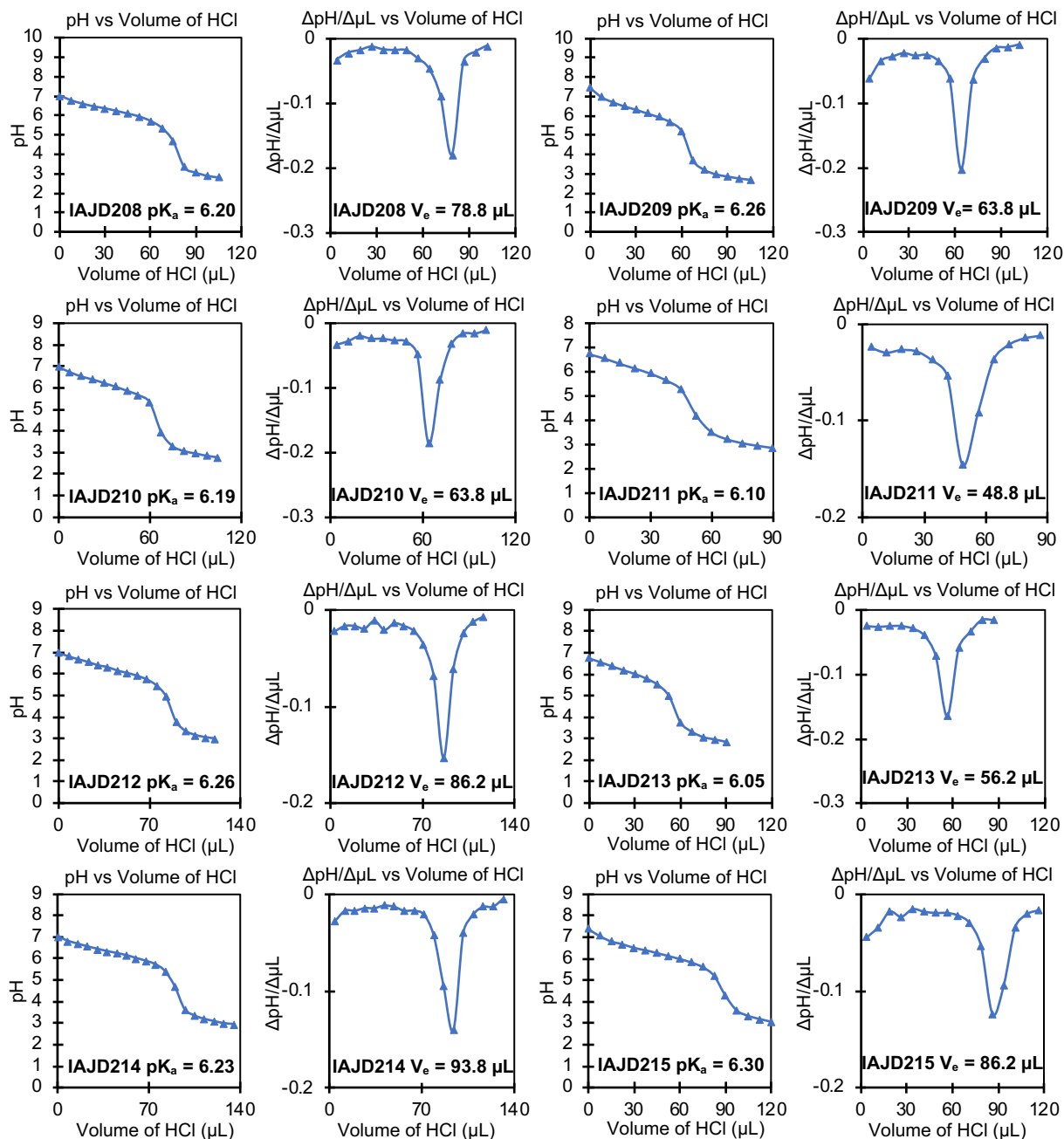


Figure S30. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 208-215.

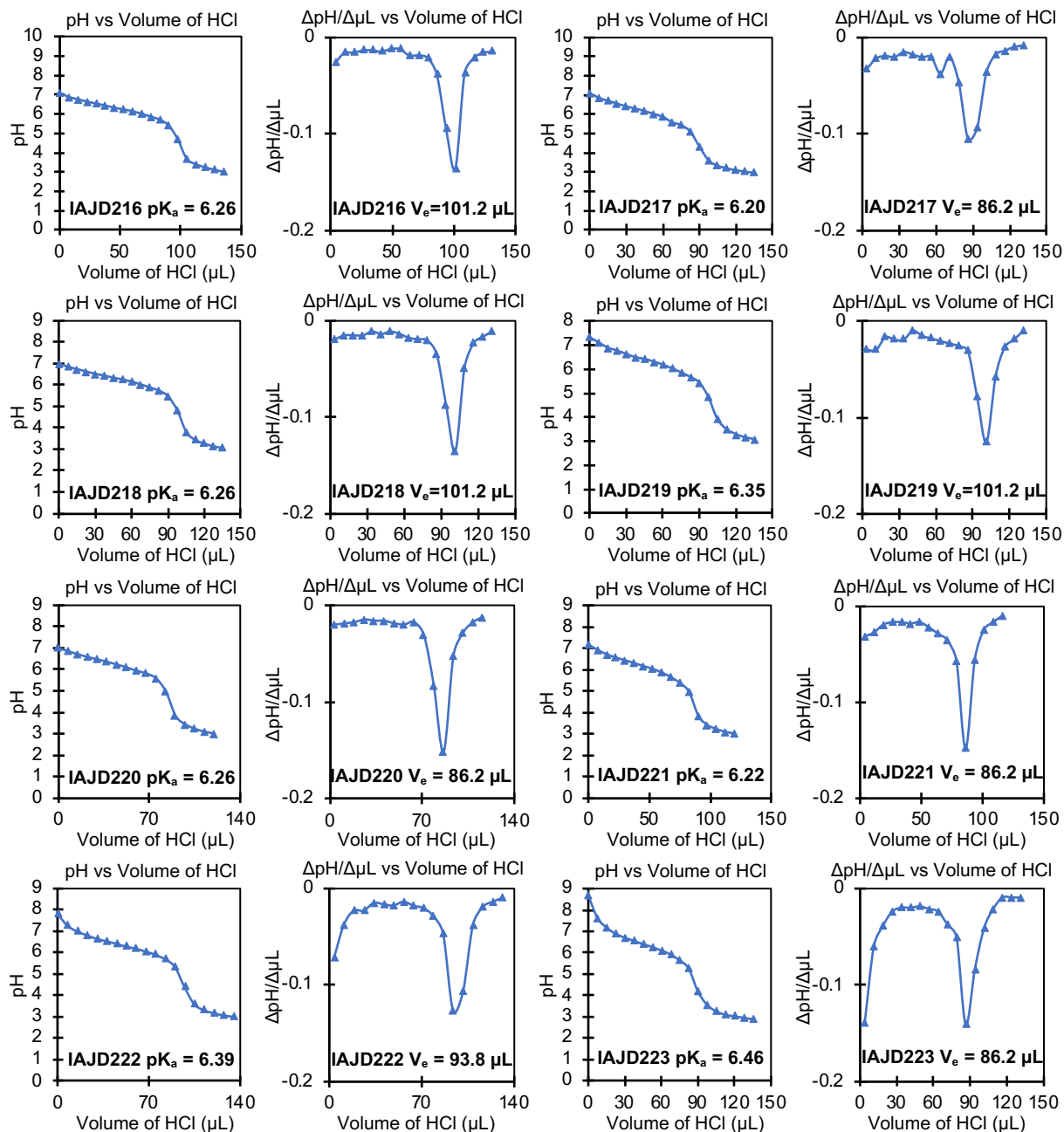


Figure S31. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 261-223.

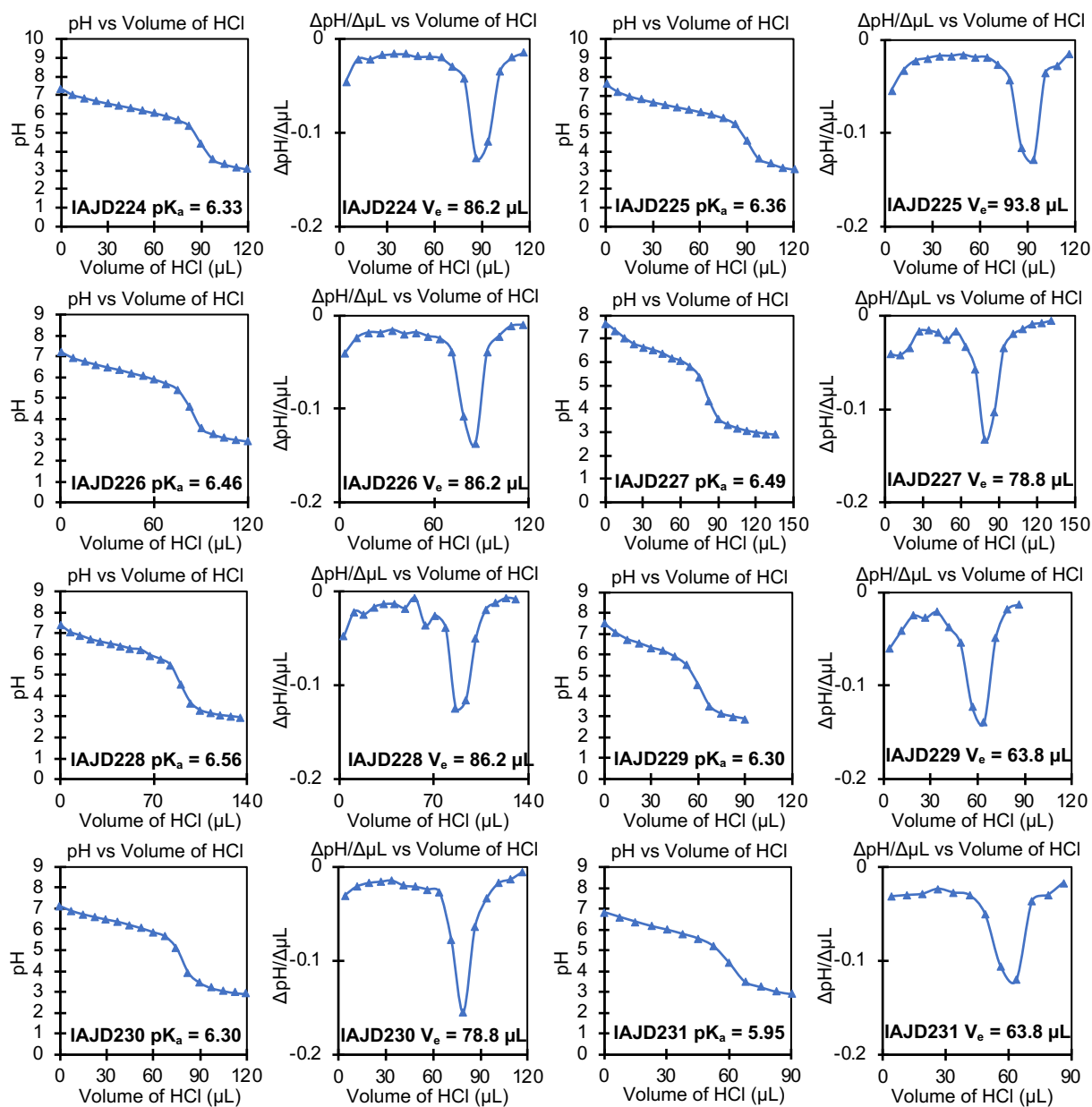


Figure S32. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 224-231.

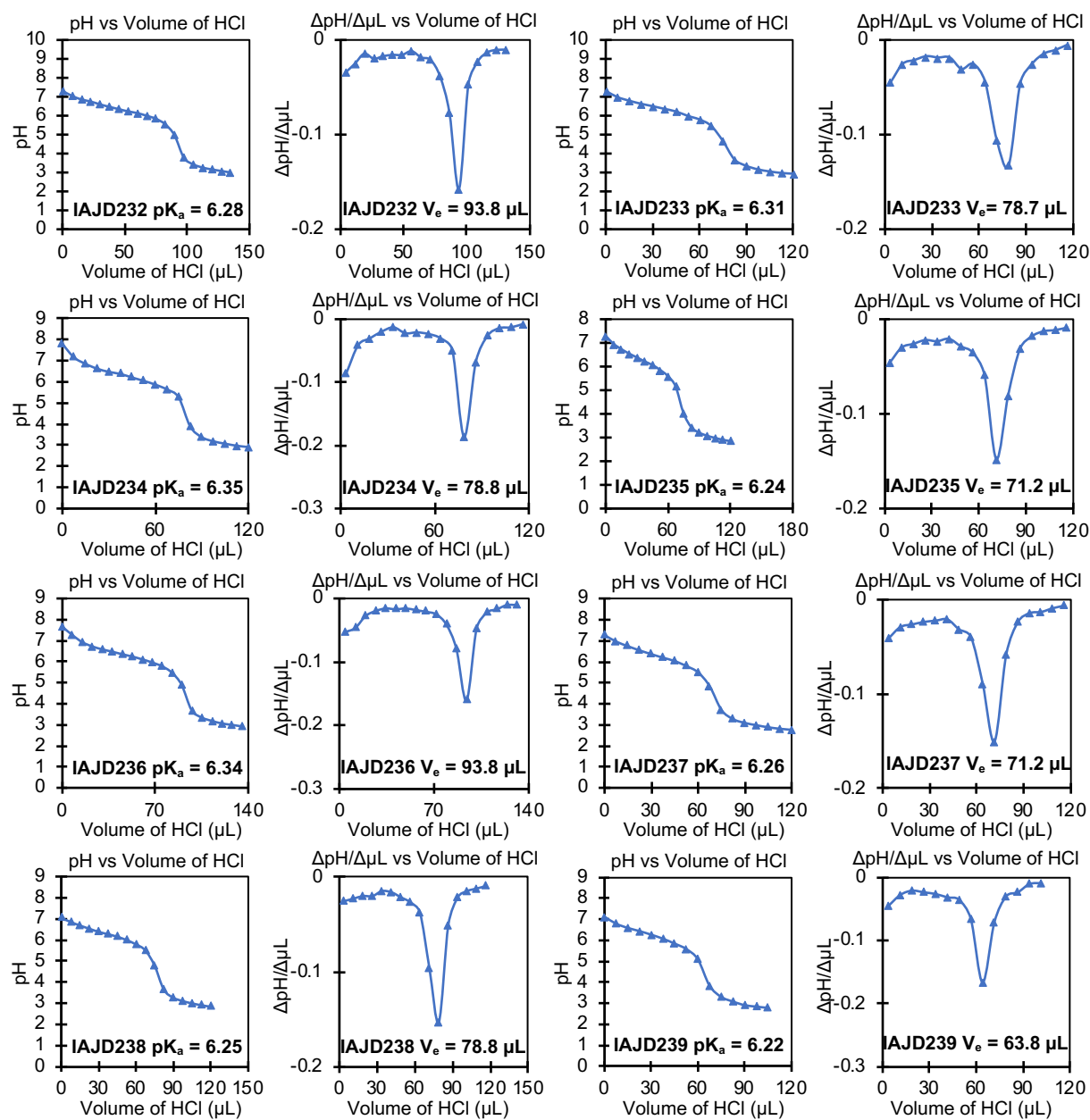


Figure S33. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 232-239.

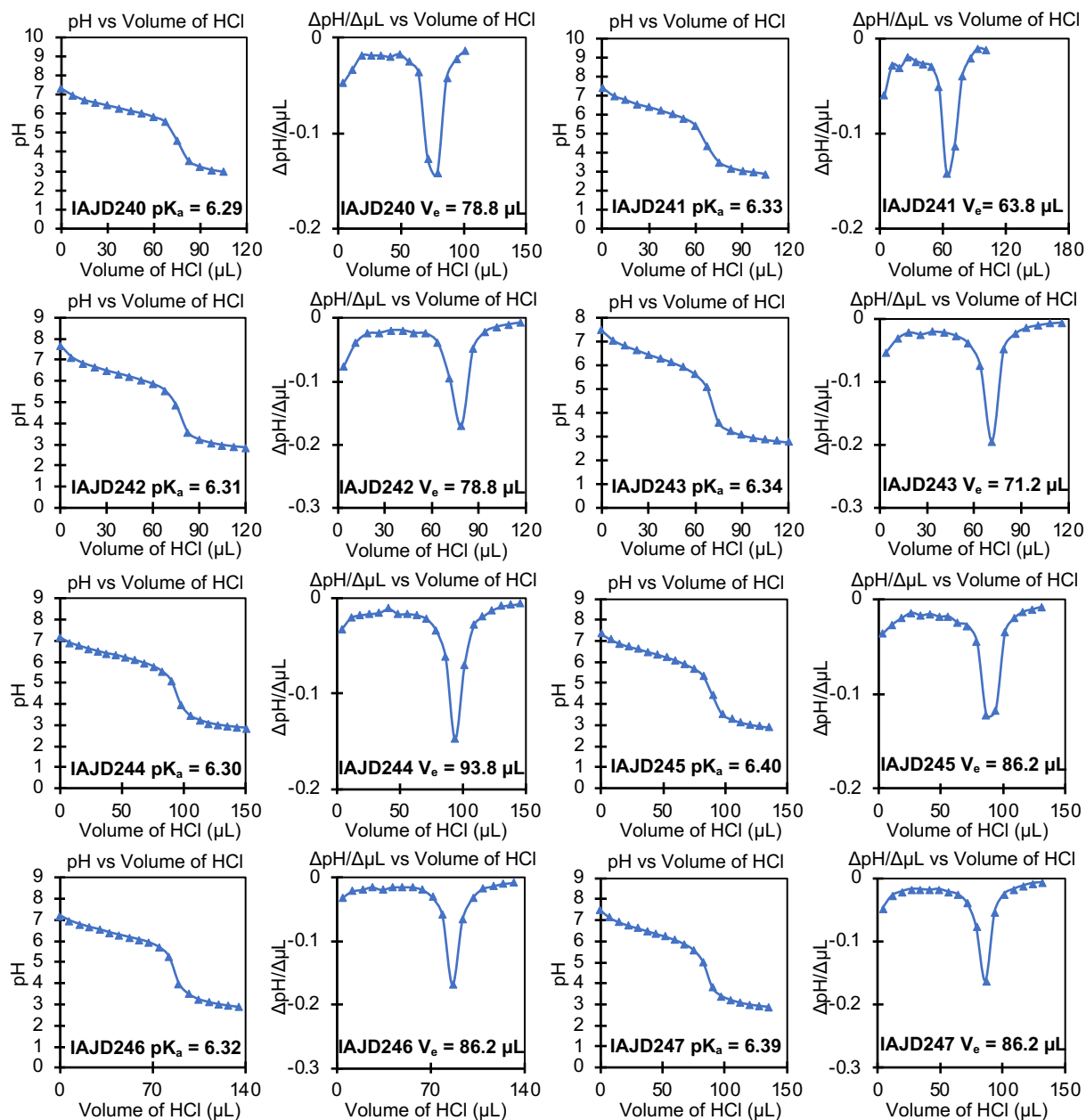


Figure S34. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pK_a for IAJDs 240-247.

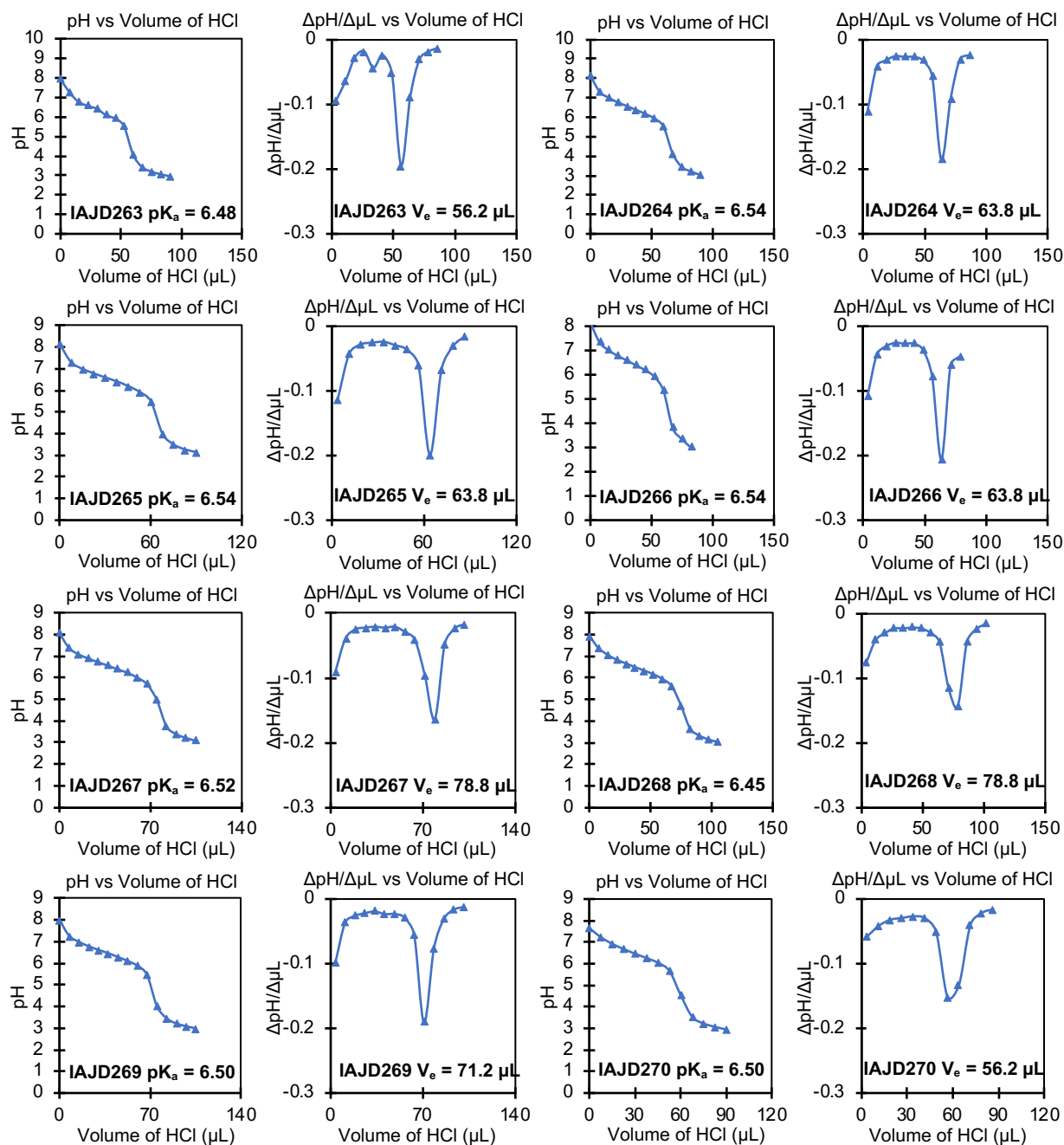


Figure S35. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 263-270.

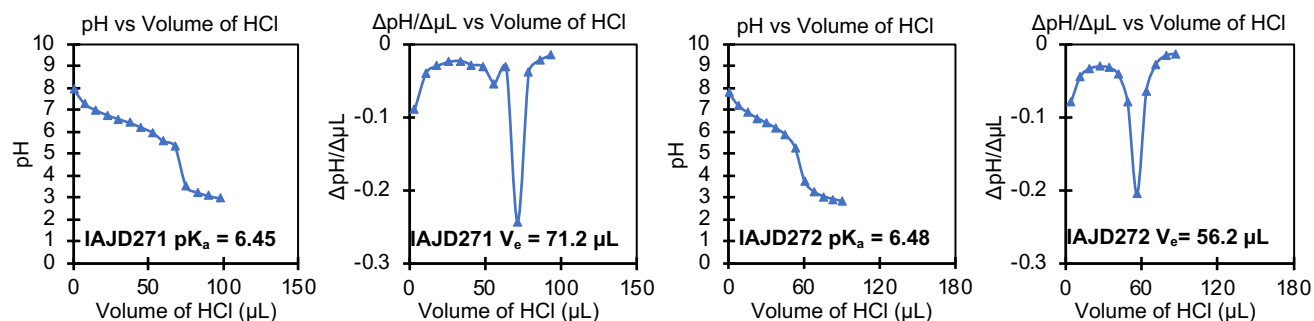


Figure S36. Titration curves showing changes in solution pH in response to addition of a strong acid and calculated pKa for IAJDs 271,272.

6. Supporting References

- (1) Moore, J. S.; Stupp, S. I. Room Temperature Polyesterification. *Macromolecules* **1990**, *23*, 65–70. 10.1021/ma00203a013
- (2) Pardi, N.; Muramatsu, H.; Weissman, D.; Kariko, K. In Vitro Transcription of Long RNA Containing Modified Nucleosides. *Methods Mol. Biol.* **2013**, *969*, 29–42. 10.1007/978-1-62703-260-5_2
- (3) Zhang, D.; Atochina-Vasserman, E. N.; Maurya, D. S.; Liu, M.; Xiao, Q.; Lu, J.; Lauri, G.; Ona, N.; Reagan, E. K.; Ni, H.; Weissman, D.; Percec, V. Targeted Delivery of mRNA with One-Component Ionizable Amphiphilic Janus Dendrimers. *J. Am. Chem. Soc.* **2021**, *143*, 17975–17982. 10.1021/jacs.1c09585
- (4) Zhang, D.; Atochina-Vasserman, E. N.; Maurya, D. S.; Huang, N.; Xiao, Q.; Ona, N.; Liu, M.; Shahnawaz, H.; Ni, H.; Kim, K.; Billingsley, M. M.; Pochan, D. J.; Mitchell, M. J.; Weissman, D.; Percec, V. One-Component Multifunctional Sequence-Defined Ionizable Amphiphilic Janus Dendrimer Delivery Systems for mRNA. *J. Am. Chem. Soc.* **2021**, *143*, 12315–12327. 10.1021/jacs.1c05813
- (5) Zhang, D.; Atochina-Vasserman, E. N.; Lu, J.; Maurya, D. S.; Xiao, Q.; Liu, M.; Adamson, J.; Ona, N.; Reagan, E. K.; Ni, H.; et al. The Unexpected Importance of the Primary Structure of the Hydrophobic Part of One-Component Ionizable Amphiphilic Janus Dendrimers in Targeted MRNA Delivery Activity. *J. Am. Chem. Soc.* **2022**, *144* (11), 4746–4753. 10.1021/jacs.2c00273
- (6) May, J. P.; Undzys, E.; Roy, A.; Li, S.-D. Synthesis of a Gemcitabine Prodrug for Remote Loading into Liposomes and Improved Therapeutic Effect. *Bioconjugate Chem.* **2016**, *27* (1), 226–237. 10.1021/acs.bioconjchem.5b00619