Electronic Supplementary Material (ESI) for ChemComm.

1,4-Dimethoxynaphthalene-2-methyl ('DIMON'), an Oxidatively Labile Protecting Group for Synthesis of Polyunsaturated Lipids - Supporting Information

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Contents

Experimental

Materials and Methods

All the materials used were purchased from reputable commercial suppliers and used without further purification. All air sensitive reactions were performed under nitrogen by Schlenk technique unless stated otherwise. All reactions were performed using anhydrous solvents purchased from reputable commercial suppliers and without further drying unless stated otherwise. Petrol refers to the fraction with boiling point 40 – 60 °C. All reactions were monitored by thin layer chromatography on 0.25 mm silica gel plates (60GF-254) and visualized with UV light or permanganate stain. Melting points (mp) were measured using a Stuart SMP3 Melting Point Apparatus. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker Avance300 spectrometer operating at 300.13, 75.48 and 121.49 MHz, respectively, or a Bruker Avance400 spectrometer operating at 399.78 MHz (^{1}H NMR) using TMS as an internal standard in DMSO-d_6 or $CDCl_3$ solutions. Chemical shifts were reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane. Infrared (IR) spectra were obtained on a Varian 800 FT-IR Scimitar Series spectrometer. High resolution mass spectrometry (HRMS) was provided by SAgE Mass Spectrometry Facility at Newcastle University, performed by Dr Alex Charlton. The HRMS spectra were obtained on a Waters Acquity UPLC + Xevo TQ-S using either Electrospray Ionisation (ESI) or Atmospheric Pressure Chemical Ionisation (APCI) in the positive mode. HRMS was also provided by NMSF at Swansea University. The HRMS spectra were obtained on a Waters Xevo G2-S Quadripole Time of Flight (QTOF) mass spectrometer using Atmospheric Solids Analysis Probe (ASAP+) or Fourier Transform Ion Cyclotron Resonance Mass Spectrometer (FTMS) Nanoelectron Spray Ionisation (+p NSI). Optical rotations were measured using an Optical Activity polAAR 2001 polarimeter with a 50 mm length polarimeter tube.

General Procedure A

To a flask, purged with nitrogen via Schlenk technique, was added a solution of nucleophile (1 equiv.), 2-(chloromethyl)-1,4-dimethoxynaphthalene (1.2 equiv.) and tetrabutylammonium iodide (10 mol%) in tetrahydrofuran (~10 mL/mmol). To the reaction mixture was added sodium hydride (60% dispersion in mineral oil, 1.2 equiv.) portion-wise. Upon addition, the reaction was stirred at rt until consumption of the nucleophile was observed by TLC analysis. The reaction was quenched by addition of saturated aqueous ammonium chloride solution, diluted with water (~30 mL/mmol) and extracted with ethyl acetate (3 × ~30 mL/mmol). The combined organics were dried over $MgSO_4$, filtered, and the solvent was evaporated *in vacuo*. Purification by silica chromatography afforded the desired product.

General Procedure B

To a flask, purged with nitrogen via Schlenk technique, was added a solution of nucleophile (1 equiv.) in acetonitrile (~5 mL/mmol). To the solution was added caesium carbonate (1.1 equiv.) and the reaction was stirred at rt for 0.5 h. A solution of 2-(chloromethyl)-1,4-dimethoxynaphthalene (1.2 equiv.) in acetonitrile (~5 mL/mmol) was added and the reaction was refluxed until consumption of the nucleophile was observed by TLC analysis. The reaction was cooled to rt and vacuum filtered through a pad of Celite®, and the filtrate was evaporated *in vacuo*. Purification by silica chromatography afforded the desired product.

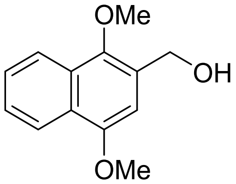
General Procedure C

To a flask, purged with nitrogen, was added a solution of nucleophile (1 equiv.) and 2-(chloromethyl)-1,4-dimethoxynaphthalene (1.2 equiv.) in tetrahydrofuran (~5 mL/mmol). To the solution was added triethylamine (1.2 equiv.) and the reaction was stirred at rt until consumption of the nucleophile was observed by TLC analysis. The solvent was evaporated *in vacuo*. Purification by silica chromatography afforded the desired product.

General Procedure D

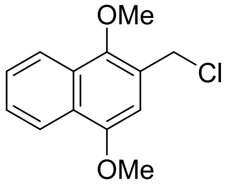
To a solution of starting material (1 equiv.) in 19:1 dichloromethane:H_2O (10 mL/mmol) was added 2,3-dichloro-5,6-dicyanobenzoquinone (1.1 equiv.) portion-wise. Upon addition the reaction was stirred at rt until consumption of the starting material was observed by TLC analysis. The reaction was quenched by addition of L-ascorbic acid (1.2 equiv.) and diluted with H_2O (50 mL/mmol). The mixture was extracted with dichloromethane (3 × 50 mL/mmol) and the combined organics were dried over $MgSO_4$, filtered, and evaporated *in vacuo*. Purification by silica chromatography afforded the desired product.

(1,4-Dimethoxynaphthalen-2-yl)methanol [2]



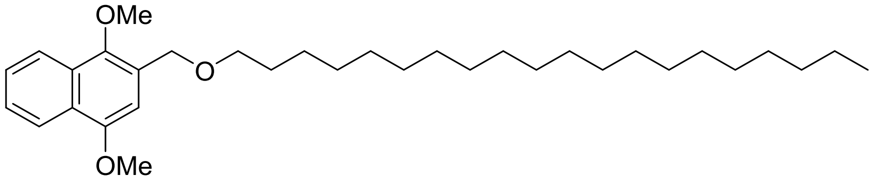
An oven-dried 3-necked reaction flask was charged with 2-bromo-1,4-dimethoxynaphthalene (2.00 g, 7.49 mmol), sealed, and purged with argon. Anhydrous diethyl ether (10 mL) was added and the solution was cooled to -78 °C before addition of *n*-butyllithium (2.5 M in hexanes, 4.49 mL, 11.2 mmol) dropwise over 0.5 h. The reaction mixture was stirred at -78 °C for 1 h, then slowly warmed to rt over 1 h. Following this time, paraformaldehyde (337 mg, 11.2 mmol) was added and the mixture was stirred at rt for 2 h. The reaction was quenched by addition of water (20 mL) and stirred for 0.5 h. The mixture was extracted with diethyl ether (3 × 30 mL) and the combined organic extracts were dried over $MgSO_4$, filtered, and evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (0:100 to 30:70 gradient), afforded (1,4-dimethoxynaphthalen-2-yl)methanol (1.01 g, 4.63 mmol, 62%) as off-white crystals: **R_f** 0.16 (3:1 40-60 petrol:ethyl acetate, UV active); **mp** 73-74 °C; **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.29 – 8.19 (1 H, m, Ar*H*), 8.09 – 8.00 (1 H, m, Ar*H*), 7.60 – 7.43 (2 H, m, 2 × Ar*H*), 6.82 (1 H, s, Ar*H*), 4.90 (2 H, d, *J* = 5.9 Hz, CH_2OH), 4.00 (3 H, s, OCH_3), 3.93 (3 H, s, OCH_3), 2.09 (1 H, t, *J* = 6.0 Hz, CH_2OH); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.1 (1 × Ar), 146.8 (1 × Ar), 128.6 (1 × Ar), 128.4 (1 × Ar),126.7 (1 × Ar), 126.2 (1 × Ar), 125.5 (1 × Ar), 122.4 (1 × Ar), 121.8 (1 × Ar), 103.8 (1 × Ar), 62.6 (1 × OMe), 60.8 (1 × CH_2OH), 55.7 (1 × OMe); **IR** ν_{max} / cm^{-1} 3341, 3067, 3000, 2942, 2887, 2833, 1597, 1452, 1366, 1266, 1225, 1211, 1155, 1119, 1092, 1032, 1021, 844, 765; **HRMS** (TOF MS ES+) calcd $C_{13}H_{14}O_3$ $[M+Na]^+$: 241.0836, found 241.0852.

2-(Chloromethyl)-1,4-dimethoxynaphthalene [1]



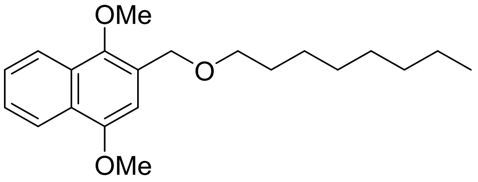
To (1,4-dimethoxynaphthalen-2-yl)methanol (670 mg, 3.07 mmol) in diethyl ether (1.5 mL) was added aqueous hydrochloric acid solution (12 M, 1.5 mL). The reaction mixture was stirred at rt for 1 h. Following this time, the mixture was diluted with water (20 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and solvent removed *in vacuo* to give 2-(chloromethyl)-1,4-dimethoxynaphthalene (727 mg, 3.07 mmol, 100%) as an off-white solid: **R_f** 0.77 (9:1 40-60 petrol:ethyl acetate, UV active); **mp** 62 – 63 °C; **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.33 – 8.18 (1 H, m, Ar*H*), 8.13 – 8.01 (1 H, m, Ar*H*), 7.62 – 7.45 (2 H, m, 2 × Ar*H*), 6.76 (1 H, s, Ar*H*), 4.85 (2 H, s, CH_2Cl), 4.01 (3 H, s, OCH_3), 3.99 (3 H, s, OCH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.3 (1 × Ar), 147.9 (1 × Ar), 128.4 (1 × Ar), 127.0 (2 × Ar), 126.2 (1 × Ar), 125.4 (1 × Ar), 122.5 (1 × Ar), 122.3 (1 × Ar), 104.5 (1 × Ar), 63.0 (1 × OMe), 55.7 (1 × OMe), 41.5 (1 × CH_2Cl); **IR** ν_{max} / cm^{-1} 3070, 3013, 2937, 2839, 1595, 1459, 1370, 1261, 1222, 1091, 999, 768, 726; **HRMS** (TOF MS ES+) calcd $C_{13}H_{13}ClO_2$ $[M+H+NH_4]^{2+}$ 255.1015, found 255.0986.

2-((Icosyloxy)methyl)-1,4-dimethoxynaphthalene [5a]



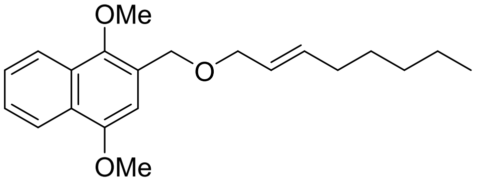
Prepared according to General Procedure A with the following reagents: 1-eicosanol (107 mg, 358 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (170 mg, 718 µmol), tetrabutylammonium iodide (26 mg, 72 µmol) and sodium hydride (60% dispersion in mineral oil, 22 mg, 528 µmol) in tetrahydrofuran (4 mL). The reaction was refluxed for 48 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (2:98 with 1% triethylamine), afforded 2-((icosyloxy)methyl)-1,4-dimethoxynaphthalene (167 mg, 335 µmol, 93%) as a white solid: **R_f** 0.65 (9:1 40-60 petrol:ethyl acetate, UV active); **mp** 50 – 51 °C; **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.27 – 8.18 (1 H, m, Ar*H*), 8.10 – 8.00 (1 H, m, Ar*H*), 7.59 – 7.41 (2 H, m, 2 × Ar*H*), 6.86 (1 H, s, Ar*H*), 4.73 (2 H, s, CH_2OCH_2), 4.00 (3 H, s, OCH_3), 3.90 (3 H, s, OCH_3), 3.53 (2 H, t, *J* = 6.6 Hz, CH_2OCH_2), 1.64 (2 H, p, *J* = 6.7 Hz CH_2), 1.45 – 1.18 (34 H, br m, 17 × CH_2), 0.87 (3 H, t, *J* = 6.6 Hz, CH_2CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.0 (1 × Ar), 147.4 (1 × Ar), 128.5 (1 × Ar), 126.5 (2 × Ar), 126.3 (1 × Ar), 125.4 (1 × Ar), 122.4 (1 × Ar), 121.9 (1 × Ar), 104.1 (1 × Ar), 70.7 (1 × OCH_2CH_2), 67.4 (1 × CH_2OCH_2), 62.7 (1 × OMe), 55.7 (1 × OMe), 32.0 (1 × CH_2), 29.9 (1 × CH_2), 29.7 (12 × CH_2), 29.5 (1 × CH_2), 29.4 (1 × CH_2), 26.3 (1 × CH_2), 22.7 (1 × CH_2), 14.1 (1 × CH_3); **IR** ν_{max} / cm^{-1} 2914, 2849, 1597, 1472, 1366, 1211, 1125, 1087, 762, 716; **HRMS** (TOF MS ES+) calcd $C_{33}H_{54}O_3$ $[M+H]^+$ 499.4107, found 499.4059.

1,4-Dimethoxy-2-((octyloxy)methyl)naphthalene [5b]



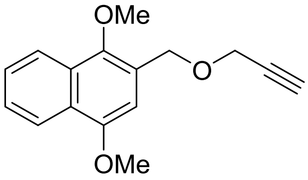
Prepared according to General Procedure A with the following reagents: octanol (46 mg, 352 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (100 mg, 422 µmol), tetrabutylammonium iodide (16 mg, 42 µmol) and sodium hydride (60% dispersion in mineral oil, 17 mg, 422 µmol) in tetrahydrofuran (3 mL). The reaction was stirred at rt for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (10:90 with 1% triethylamine), afforded 1,4-dimethoxy-2-((octyloxy)methyl)naphthalene (88 mg, 265 µmol, 75%) as a clear, colourless oil: **R_f** 0.56 (19:1 40-60 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.28 – 8.19 (m, 1H, Ar*H*), 8.11 – 8.01 (m, 1H, Ar*H*), 7.62 – 7.42 (m, 2H, 2 × Ar*H*), 6.88 (s, 1H, Ar*H*) 4.74 (s, 2H, CH_2OCH_2), 4.01 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.54 (t, *J* = 6.6 Hz, 2H, CH_2OCH_2), 1.66 (q, *J* = 6.4 Hz, 2H, OCH_2CH_2), 1.45 – 1.19 (m, 10H, 5 × CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_2CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.0 (1 × Ar), 147.4 (1 × Ar), 128.5 (1 × Ar), 126.5 (2 × Ar), 126.3 (1 × Ar), 125.4 (1 × Ar), 122.4 (1 × Ar), 121.9 (1 × Ar), 104.1 (1 × Ar), 70.7 (1 × OCH_2CH_2), 67.4 (1 × CH_2OCH_2), 62.8 (1 × OMe), 55.7 (1 × OMe), 31.8 (1 × CH_2), 29.9 (1 × CH_2), 29.5 (1 × CH_2), 29.3 (1 × CH_2), 26.3 (1 × CH_2), 22.7 (1 × CH_2), 14.1 (1 × CH_3);); **IR** ν_{max} / cm^{-1} 2927, 2854, 1597, 1460, 1369, 1212, 1123, 1089, 1000, 767; **HRMS** (TOF MS ES+) calcd $C_{21}H_{30}O_3$ $[M+H]^+$ 331.2268, found 331.2272.

(*E*)-1,4-Dimethoxy-2-((oct-2-en-1-yloxy)methyl)naphthalene [5c]



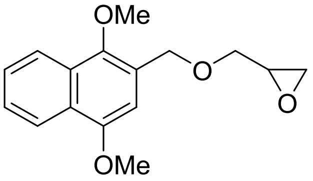
Prepared according to General Procedure A with the following reagents: (*E*)-oct-2-en-1-ol (46 mg, 54 µL, 352 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (100 mg, 422 µmol), tetrabutylammonium iodide (16 mg, 42 µmol) and sodium hydride (60% dispersion in mineral oil, 17 mg, 422 µmol) in tetrahydrofuran (3 mL). The reaction was stirred at rt for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (0:100 to 5:95 gradient with 1% triethylamine), afforded (*E*)-1,4-dimethoxy-2-((oct-2-en-1-yloxy)methyl)naphthalene (91 mg, 277 µmol, 79%) as a clear, yellow oil: **R_f** 0.72 (9:1 40-60 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.3 Hz, 1H, Ar*H*), 8.05 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.57 – 7.43 (m, 2H, 2 × Ar*H*), 6.87 (s, 1H, Ar*H*), 5.80 – 5.58 (m, 2H, C*H*=C*H*), 4.72 (s, 2H, CH_2OCH_2), 4.07 – 3.97 (m, 5H, OCH_2CH, OCH_3), 3.90 (s, 3H, OCH_3), 2.06 (q, *J* = 7.1 Hz, 2H, $CH{=}CHCH_2$), 1.40 (p, *J* = 7.2 Hz, 2H, $CHCH_2CH_2$), 1.29 (m, 4H, 2 × CH_2), 0.88 (t, *J* = 6.7 Hz, 3H, CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.1 (1 × Ar), 147.5 (1 × Ar), 135.3 (1 × *C*H=CH), 128.5 (1 × Ar), 127.0 (1 × Ar), 126.6 (1 × Ar), 126.4 (1 × Ar), 126.3 (1 × Ar), 125.5 (1 × CH=*C*H), 122.4 (1 × Ar), 121.9 (1 × Ar), 104.3 (1 × Ar), 71.3 (OCH_2CH), 66.6 (1 × CH_2O), 62.8 (OCH_3), 55.7 (OCH_3), 32.4 (CH_2), 31.5 (CH_2), 28.9 (CH_2), 22.6 (CH_2), 14.1 (CH_3); **IR** ν_{max} / cm^{-1} 2927, 2853, 1596, 1460, 1369, 1267, 1213, 1123, 1093, 1001, 975, 767; **HRMS** (TOF MS ES+) calcd $C_{21}H_{29}O_3$ $[M+H]^+$ 329.2111, found 329.2117.

1,4-Dimethoxy-2-((prop-2-yn-1-yloxy)methyl)naphthalene [5d]



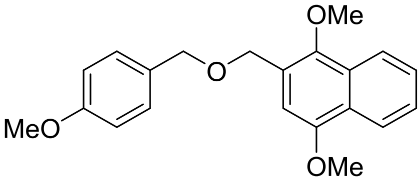
Prepared according to General Procedure A with the following reagents: propargyl alcohol (20 mg, 20 μL, 352 μmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (100 mg, 422 μmol), tetrabutylammonium iodide (16 mg, 42 μmol) and sodium hydride (60% dispersion in mineral oil, 17 mg, 442 μmol) in tetrahydrofuran (3 mL). The reaction was stirred at rt for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (10:90 with 1% triethylamine), afforded 1,4-dimethoxy-2-((prop-2-yn-1-yloxy)methyl)naphthalene (74 mg, 289 μmol, 82%) as a clear, neon yellow oil: **R_f** 0.57 (9:1 40-60 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.30 – 8.21 (m, 1H, Ar*H*), 8.13 – 8.04 (m, 1H, Ar*H*), 7.61 – 7.44 (m, 2H, 2 × Ar*H*), 6.86 (s, 1H, Ar*H*), 4.85 (s, 2H, CH_2OCH_2), 4.28 (d, *J* = 2.4 Hz, 2H, CH_2OCH_2), 4.01 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 2.53 (t, *J* = 2.4 Hz, 1H, C≡C*H*); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.1 (1 × Ar), 147.9 (1 × Ar), 128.5 (1 × Ar), 126.7 (2 × Ar), 126.6 (1 × Ar), 125.7 (1 × Ar), 122.4 (1 × Ar), 122.0 (1 × Ar), 104.2 (1 × Ar), 79.9 (*C*≡CH), 74.7 (C≡*C*H), 66.5 (CH_2OCH_2), 63.0 (OCH_3), 57.5 (CH_2OCH_2), 55.7 (OCH_3) **IR** ν_{max} / cm^{-1} 3288, 3071, 2937, 2840, 1597, 1460, 1368, 1267, 1213, 1122, 1096, 1073, 999, 769, 629; **HRMS** (TOF MS ESI+) calcd $C_{16}H_{16}O_3$ $[M+Na]^+$ 279.0992, found 279.0967.

2-(((1,4-Dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane [5e]



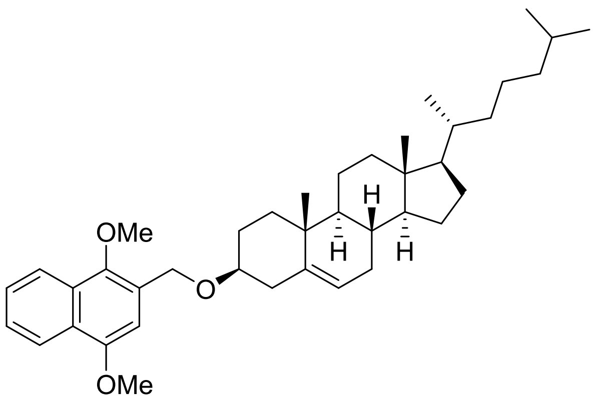
To a flask, purged with nitrogen via Schlenk technique, was added a solution of glycidol (104 mg, 1.41 mmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (400 mg, 1.69 mmol) and tetrabutylammonium iodide (62 mg, 169 µmol) in *N,N'*-dimethylformamide (6 mL). The reaction was cooled to 0 °C and sodium hydride (60% dispersion in mineral oil, 68 mg, 1.69 mmol) portionwise. Upon addition, the reaction was warmed to rt and stirred for 16 h. The reaction was quenched by addition of saturated aqueous ammonium chloride solution (3 mL), diluted with water (100 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organics were dried over $MgSO_4$, filtered, and the solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (10:90 to 20:80 gradient with 1% triethylamine), afforded 2-(((1,4-dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane (327 mg, 1.19 mmol, 85%) as a clear, colourless oil: **R_f** 0.72 (1:1 40-60 petrol:ethyl acetate, permanganate stain); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.27 – 8.20 (m, 1H, Ar*H*), 8.08 – 8.03 (m, 1H, Ar*H*), 7.57 – 7.45 (m, 2H, 2 × Ar*H*), 6.86 (s, 1H, Ar*H*), 4.87 – 4.75 (m, 2H, C*H*$_2$OCH$_2$), 4.01 (s, 3H, OC*H*$_3$), 3.91 (s, 3H, OC*H*$_3$), 3.84 (dd, *J* = 11.4, 3.0 Hz, 1H, OC*H*HCH(O)), 3.50 (dd, *J* = 11.4, 6.0 Hz, 1H, OCH*H*CH(O)), 3.23 (ddt, *J* = 5.8, 4.1, 2.9 Hz, 1H, OCH$_2$C*H*(O)), 2.82 (dd, *J* = 5.1, 4.1 Hz, 1H, CH(O)C*H*H), 2.64 (dd, *J* = 5.1, 2.7 Hz, 1H, CH(O)CH*H*); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.2 (1 × Ar), 147.7 (1 × Ar), 128.6 (1 × Ar), 126.8 (1 × Ar), 126.6 (1 × Ar), 125.8 (1 × Ar), 125.7 (1 × Ar), 122.5 (1 × Ar), 122.1 (1 × Ar), 104.2 (1 × Ar), 71.2 (O*C*H$_2$CH(O)), 68.1 (*C*H$_2$O), 63.0 (O*C*H$_3$), 55.8 (O*C*H$_3$), 51.0 (*C*H(O)), 44.5 (CH(O)*C*H$_2$(O)); **IR** ν_{max} / cm^{-1} 2936, 2839, 1629, 1596, 1460, 1369, 1267, 1214, 1123, 1097, 998, 844, 769; **HRMS** (TOF MS ESI+) calcd $C_{16}H_{18}O_4$ $[M+Na]^+$ 297.1097, found 297.1093.

1,4-Dimethoxy-2-(((4-methoxybenzyl)oxy)methyl)naphthalene [5f]



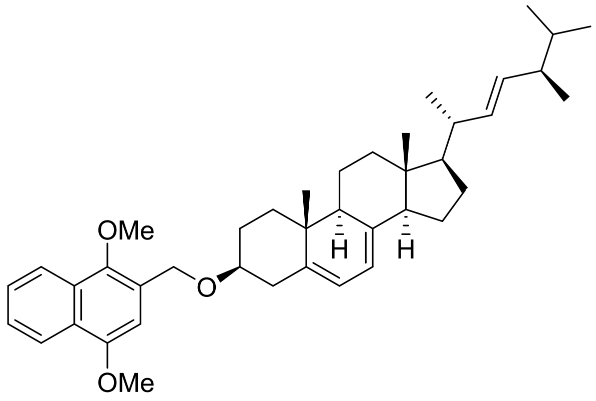
Prepared according to General Procedure A with the following reagents: (4-methoxyphenyl)methanol (51 mg, 370 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (105 mg, 444 µmol), tetrabutylammonium iodide (16 mg, 44 µmol) and sodium hydride (60% dispersion in mineral oil, 18 mg, 444 µmol) in tetrahydrofuran (3 mL). The reaction was stirred at rt for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (10:90 with 1% triethylamine), afforded 1,4-dimethoxy-2-(((4-methoxybenzyl)oxy)methyl)naphthalene (116 mg, 343 µmol, 93%) as a clear, colourless oil: **R$_f$** 0.34 (9:1 40-60 petrol:ethyl acetate, permanganate stain); **^{1}H NMR** δ $_H$ (300 MHz, $CDCl_3$) δ 8.29 – 8.20 (1 H, m, Ar*H*), 8.11 – 8.02 (1 H, m, Ar*H*), 7.60 – 7.43 (2 H, m, 2 × Ar*H*), 7.39 – 7.28 (2 H, m, 2 × Ar*H*), 6.98 – 6.85 (2 H, m, 2 × Ar*H*), 4.77 (2 H, s, CH_2OCH_2), 4.56 (2 H, s, CH_2OCH_2), 4.00 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3); **^{13}C NMR** δ $_C$ (75 MHz, $CDCl_3$) 159.4 (1 × Ar), 152.2 (1 × Ar), 147.7 (1 × Ar), 130.6 (1 × Ar), 129.7 (1 × Ar), 128.6 (1 × Ar), 126.7 (1 × Ar), 126.5 (1 × Ar), 126.3 (1 × Ar), 125.6 (1 × Ar), 122.5 (1 × Ar), 122.1 (1 × Ar), 114.0 (1 × Ar), 104.4 (1 × Ar), 72.2 (CH_2OCH_2), 66.7 (CH_2OCH_2), 62.9 (OCH_3), 55.8 (OCH_3), 55.4 (OCH_3); **IR** ν_{max} / cm^{-1} 2930, 2851, 1640, 1596, 1458, 1369, 1091, 998, 768; **HRMS** (FTMS +p NSI) calcd $C_{21}H_{22}O_4$ $[M+Na]^+$ 361.1410, found 361.1411.

(3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-3-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene [5g]



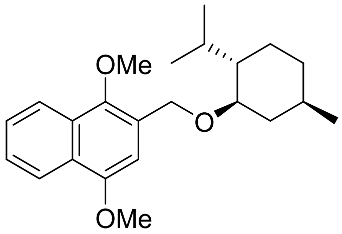
Prepared according to General Procedure A with the following reagents: cholesterol (85 mg, 220 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (104 mg, 440 µmol), tetrabutylammonium iodide (16 mg, 44 µmol) and sodium hydride (60% dispersion in mineral oil, 11 mg, 264 µmol) in tetrahydrofuran (3 mL). The reaction was refluxed for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (3:97 with 1% triethylamine), afforded (3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-3-((1,4-dimethoxynaphthalen-2-yl)methoxy)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene (117 mg, 199 µmol, 91%) as an off-white solid: : **R$_f$** 0.54 (19:1 petrol:ethyl acetate, UV active); **mp** 118 – 119 °C; **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.25 – 8.18 (1 H, m, Ar*H*), 8.07 – 8.01 (1 H, m, Ar*H*), 7.49 (2 H, dddd, *J* = 23.7, 8.2, 6.8, 1.4 Hz, 2 × Ar*H*), 6.87 (1 H, s, Ar*H*), 5.36 (1 H, d, *J* = 5.0 Hz, C=C*H*), 4.78 (2 H, s, ArCH_2O), 4.00 (3 H, s, OCH_3), 3.91 (3 H, s, OCH_3), 3.33 (1 H, td, *J* = 11.2, 5.6 Hz, OC*H*), 2.53 – 2.43 (1 H, m, OCHC*H*H), 2.38 – 2.27 (1 H, m, OCHCH*H*), 2.07 – 1.74 (4 H, m, C=CHCH_2, OCHCH_2), 1.63 – 1.04 (21 H, m, 8 × CH_2, 5 × C*H*), 1.02 (3 H, s, CCH_3), 0.91 (3 H, d, *J* = 6.5 Hz, CHCH_3), 0.86 (6 H, dd, *J* = 6.6, 1.8 Hz, CH(CH_3)$_2$), 0.68 (3 H, s, CCH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.1 (1 × Ar), 147.4 (1 × Ar), 141.1 (1 × *C*=CH), 128.6 (1 × Ar), 126.9 (1 × Ar), 126.6 (1 × Ar), 126.4 (1 × C=*C*H), 125.5 (1 × Ar), 122.5 (1 × Ar), 122.0 (1 × Ar), 121.8 (1 × Ar), 104.4 (1 × Ar), 78.9 (O*C*H), 64.8 (Ar*C*H$_2$), 62.9 (O*C*H$_3$), 56.9 (*C*H), 56.3 (*C*H), 55.8 (O*C*H$_3$), 50.3 (*C*H), 42.5 (*C*CH$_3$), 39.9 (*C*CH$_3$), 39.7 (C*H*), 39.4 (*C*CH$_3$), 37.4 (*C*H$_2$), 37.1 (*C*H$_2$), 36.3 (*C*H$_2$), 35.9 (*C*H$_2$), 32.1 (*C*H$_2$), 32.0 (*C*H$_2$), 28.7 (*C*H$_2$), 28.4 (*C*H$_2$), 28.2 (*C*H$_2$), 24.4 (*C*H$_2$), 24.0 (*C*H$_2$), 23.0 (*C*H$_3$), 22.7 (CH_3), 21.2 (CH_2), 19.6 (CH_3), 18.9 (CH_3), 12.0 (CH_3); **IR** ν_{max} / cm^{-1} 2933, 2866, 1597, 1460, 1369, 1266, 1213, 1097, 1084, 767; **HRMS** (TOF MS ESI+) calcd $C_{40}H_{58}O_3$ $[M+H]^+$ 587.4459, found 587.4471.

(3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-3-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene [4h]



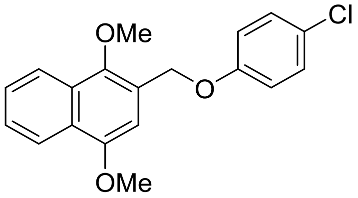
Prepared according to General Procedure A with the following reagents: ergosterol (84 mg, 212 μmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (100 mg, 424 μmol), tetrabutylammonium iodide (16 mg, 42 μmol) and sodium hydride (60% dispersion in mineral oil, 10 mg, 254 μmol) in *N*,*N'*-dimethylformamide (3 mL). The reaction was stirred at rt for 16 h. Purification by silica chromatography, eluting with ethyl acetate and petrol (3:97 with 1% triethylamine), afforded (3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-3-((1,4-dimethoxynaphthalen-2-yl)methoxy)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene (113 mg, 189 μmol, 89%) as a white solid: **R$_\mathrm{f}$** 0.49 (19:1 petrol:ethyl acetate, UV active); **mp** 122 – 123 °C; **^{1}H NMR** δ$_\mathrm{H}$ (400 MHz, CDCl$_3$) δ 8.22 (1 H, d, *J* = 8.2 Hz, Ar*H*), 8.04 (1 H, d, *J* = 8.2 Hz, Ar*H*), 7.56 – 7.43 (2 H, m, 2 × Ar*H*), 6.88 (1 H, s, Ar*H*), 5.58 (1 H, d, *J* = 5.3 Hz, C=C*H*-CH=C), 5.41 – 5.35 (1 H, m, C=CH-C*H*=C), 5.28 – 5.12 (2 H, m, C*H*=C*H*), 4.80 (2 H, s, ArCH_2O), 4.00 (3 H, s, OCH_3), 3.91 (3 H, s, OCH_3), 3.45 (1 H, td, *J* = 11.1, 5.6 Hz, OC*H*), 2.66 (1 H, d, *J* = 14.4 Hz, OCHC*H*H), 2.38 (1 H, t, *J* = 13.0 Hz, CH=CHC*H*), 2.12 – 1.82 (6 H, m, 4 × C*H*, OCHCH*H*, C*H*H), 1.80 – 1.57 (6 H, m, C*H*, CH*H*, 2 × CH_2), 1.53 – 1.18 (7 H, m, C*H*, 3 × CH_2), 1.04 (3 H, d, *J* = 6.6 Hz, CHCH_3), 0.96 (3 H, s, CCH_3), 0.92 (3 H, d, *J* = 6.8 Hz, CHCH_3), 0.88 – 0.79 (6 H, m, CH(CH_3)$_2$), 0.63 (3 H, s, CCH_3); **^{13}C NMR** δ$_\mathrm{C}$ (75 MHz, CDCl$_3$) δ 152.2 (1 × Ar), 147.4 (1 × Ar), 141.4 (*C*=CH-CH=C), 140.1 (C=CH-CH=*C*), 135.7 (*C*H=CH), 132.1 (CH=*C*H), 128.6 (1 × Ar), 126.8 (1 × Ar), 126.6 (1 × Ar), 126.5 (1 × Ar), 125.5 (1 × Ar), 122.5 (1 × Ar), 122.0 (1 × Ar), 119.7 (C=*C*H-CH=C), 116.4 (C=CH-*C*H=C), 104.4 (1 × Ar), 77.7 (O*C*H), 64.9 (ArCH_2O), 62.9 (OCH_3), 55.8 (OCH_3, *C*H), 54.7 (*C*H), 53.6 (*C*H), 46.4 (*C*H), 43.0 (*C*H), 40.6 (*C*H), 39.2 (*C*H), 38.5 (CH_2), 38.0 (CH_2), 37.6 (CH_2), 33.2 (CH_2), 28.9 (CH_2), 28.4 (CH_2), 23.1 (CH_2), 21.3 (CH_3), 20.1 (CH_3), 19.8 (CH_3), 17.8 (CH_3), 16.5 (CH_3), 12.2 (CH_3); **IR** ν_{max} / cm^{-1} 2958, 2930, 2870, 1598, 1459, 1369, 1211, 1097, 1084, 981, 769; **HRMS** (TOF MS ESI+) calcd $C_{41}H_{56}O_3$ $[M+H]^+$ 597.4302, found 597.4307.

2-((((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)methyl)-1,4-dimethoxynaphthalene [5i]



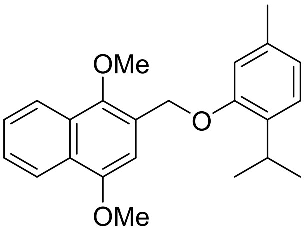
Prepared according to General Procedure A with the following reagents: L-menthol (36 mg, 230 μmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (109 mg, 460 μmol), tetrabutylammonium iodide (17 mg, 46 μmol) and sodium hydride (60% dispersion in mineral oil, 11 mg, 276 μmol) in tetrahydrofuran (3 mL). The reaction was refluxed for 64 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (3:97 with 1% triethylamine), afforded 2-((((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)-1,4-dimethoxynaphthalene (59 mg, 164 μmol, 71%) as a clear, colourless oil: **R_f** 0.49 (19:1 40-60 petrol:ethyl acetate, permanganate stain); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.28 – 8.20 (1 H, m, Ar*H*), 8.09 – 8.03 (1 H, m, Ar*H*), 7.50 (2 H, dddd, *J* = 23.7, 8.2, 6.8, 1.4 Hz, 2 × Ar*H*), 6.90 (1 H, s, Ar*H*), 4.89 (1 H, d, *J* = 11.4 Hz, C*H*HO), 4.64 (1 H, d, *J* = 11.4 Hz, CH*H*O), 4.00 (3 H, s, OCH_3), 3.91 (3 H, s, OCH_3), 3.26 (1 H, td, *J* = 10.5, 4.1 Hz, OC*H*), 2.43 – 2.27 (2 H, m, CH_2), 1.73 – 1.61 (2 H, m, CH_2), 1.48 – 1.25 (2 H, m, CH_2), 1.09 – 0.81 (9 H, m, 3 × C*H*, 2 × CH_3), 0.76 (3 H, d, *J* = 6.9 Hz, CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) 152.1 (1 × Ar), 147.2 (1 × Ar), 128.5 (1 × Ar), 127.1 (1 × Ar), 126.6 (1 × Ar), 126.4 (1 × Ar), 125.5 (1 × Ar), 122.5 (1 × Ar), 122.1 (1 × Ar), 104.6 (1 × Ar), 79.2 (O*C*H), 64.9 (CH_2O), 62.9 (OCH_3), 55.7 (OCH_3), 48.6 (*C*H), 40.6 (CH_2), 34.7 (CH_2), 31.7 (*C*H), 25.8 (*C*H), 23.4 (CH_2), 22.6 (CH_3), 21.2 (CH_3), 16.4 (CH_3); **IR** v_{max} / cm^{-1} 2951, 2923, 2867, 1597, 1459, 1368, 1211, 1096, 767; **HRMS** (TOF MS ESI+) calcd $C_{23}H_{32}O_3$ $[M+Na]^+$ 379.2244, found 379.2247.

2-((4-Chlorophenoxy)methyl)-1,4-dimethoxynaphthalene [5j]



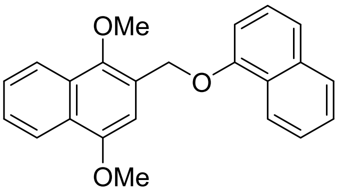
Prepared according to General Procedure B with the following reagents: 4-chlorophenol (45 mg, 370 μmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (105 mg, 444 μmol), and caesium carbonate (132 mg, 407 μmol) in acetonitrile (3 mL). The reaction was refluxed for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (3:97 with 1% triethylamine), afforded 2-((4-chlorophenoxy)methyl)-1,4-dimethoxynaphthalene (111 mg, 337 μmol, 91%) as a clear, colourless oil: **R$_f$** 0.73 (9:1 40-60 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.29 – 8.20 (1 H, m, Ar*H*), 8.14 – 8.03 (1 H, m, Ar*H*), 7.54 (2 H, dddd, *J* = 17.6, 8.2, 6.8, 1.4 Hz, 2 × Ar*H*), 7.31 – 7.19 (2 H, m, 2 × Ar*H*), 7.06 – 6.92 (2 H, m, 2 × Ar*H*), 6.85 (1 H, s, Ar*H*), 5.25 (2 H, s, CH_2O), 3.98 (3 H, s, OCH_3), 3.93 (3 H, s, OCH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.4 (1 × Ar), 147.8 (1 × Ar), 129.5 (2 × Ar), 128.5 (1 × Ar), 126.9 (1 × Ar), 126.8 (1 × Ar), 126.0 (1 × Ar), 124.5 (1 × Ar), 122.6 (1 × Ar), 122.1 (1 × Ar), 116.3 (2 × Ar), 103.9 (1 × Ar), 65.6 (CH_2O), 63.2 (OCH_3), 55.8 (OCH_3); **IR** ν_{max} / cm^{-1} 2995, 2958, 2841, 1596, 1490, 1386, 1234, 1092, 981, 819, 725; **HRMS** (FTMS +p NSI) calcd $C_{19}H_{17}O_3Cl$ $[M+NH_4]^+$ 346.1204, found 326.1206.

2-((2-Isopropyl-5-methylphenoxy)methyl)-1,4-dimethoxynaphthalene [5k]



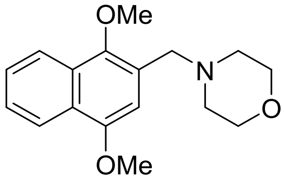
Prepared according to General Procedure B with the following reagents: thymol (56 mg, 370 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (105 mg, 444 µmol), and caesium carbonate (132 mg, 407 µmol) in acetonitrile (3 mL). The reaction was refluxed for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (2:98 with 1% triethylamine), afforded 2-((2-isopropyl-5-methylphenoxy)methyl)-1,4-dimethoxynaphthalene (105 mg, 298 µmol, 80%) as a clear, colourless oil: **R$_f$** 0.81 (9:1 40-60 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.28 (1 H, ddd, *J* = 8.0, 1.6, 0.7 Hz, Ar*H*), 8.12 (1 H, ddd, *J* = 8.3, 1.6, 0.7 Hz, Ar*H*), 7.55 (2 H, dddd, *J* = 18.0, 8.2, 6.8, 1.4 Hz, 2 × Ar*H*), 7.16 (1 H, d, *J* = 7.7 Hz, Ar*H*), 7.00 (1 H, s, Ar*H*), 6.95 – 6.88 (1 H, m, Ar*H*), 6.86 – 6.75 (1 H, m, Ar*H*), 5.30 (2 H, s, CH_2O), 4.00 (3 H, s, OCH_3), 3.97 (3 H, s, OCH_3), 3.39 (1 H, p, *J* = 6.9 Hz, $CH(CH_3)_2$), 2.38 (3 H, s, CH_3), 1.27 (3 H, s, CH_3), 1.25 (3 H, s, CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 156.1 (1 × Ar), 152.2 (1 × Ar), 147.3 (1 × Ar), 136.6 (1 × Ar), 134.3 (1 × Ar), 128.5 (1 × Ar), 126.8 (1 × Ar), 126.5 (1 × Ar), 126.1 (1 × Ar), 125.8 (1 × Ar), 125.6 (1 × Ar), 122.5 (1 × Ar), 122.1 (1 × Ar), 121.6 (1 × Ar), 112.8 (1 × Ar), 104.0 (1 × Ar), 65.1 (CH_2O), 63.0 (OCH_3), 55.7 (OCH_3), 26.9 ($CH(CH_3)_2$), 22.9 ($CH(CH_3)_2$), 21.5 (CH_3); **IR** ν_{max} / cm^{-1} 2957, 2868, 1598, 1460, 1369, 1092, 999, 768; **HRMS** (TOF MS ESI+) calcd $C_{23}H_{26}O_3$ [M+H]$^+$ 351.1955, found 351.1953.

1,4-Dimethoxy-2-((naphthalen-1-yloxy)methyl)naphthalene [5l]



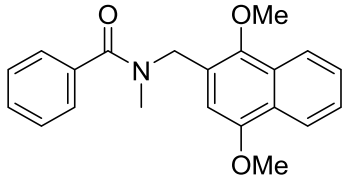
Prepared according to General Procedure B with the following reagents: 1-naphthol (53 mg, 370 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (105 mg, 444 µmol), and caesium carbonate (180 mg, 551 µmol) in acetonitrile (3 mL). The reaction was refluxed for 16 h. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (3:97 with 1% triethylamine), afforded 1,4-dimethoxy-2-((naphthalen-1-yloxy)methyl)naphthalene (113 mg, 329 µmol, 89%) as a white solid: **R$_f$** 0.65 (9:1 40-60 petrol:ethyl acetate, UV active); **mp** 143 – 144 °C; **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.46 – 8.29 (2 H, m, 2 × Ar*H*), 8.22 – 8.14 (1 H, m, Ar*H*), 7.93 – 7.80 (1 H, m, Ar*H*), 7.69 – 7.37 (6 H, m, 6 × Ar*H*), 7.13 – 7.00 (2 H, m, 2 × Ar*H*), 5.51 (2 H, s, CH_2O), 3.98 (3 H, OCH_3), 3.97 (3 H, OCH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 154.8 (1 × Ar), 152.3 (1 × Ar), 147.8 (1 × Ar), 134.7 (1 × Ar), 128.6 (1 × Ar), 127.6 (1 × Ar), 126.9 (1 × Ar), 126.8 (1 × Ar), 126.5 (1 × Ar), 126.1 (1 × Ar), 125.9 (2 × Ar), 125.3 (1 × Ar), 125.1 (1 × Ar), 122.6 (1 × Ar), 122.2 (1 × Ar), 122.1 (1 × Ar), 120.6 (1 × Ar), 105.4 (1 × Ar), 104.3 (1 × Ar), 65.6 (*C*H_2O), 63.3 (O*C*H_3), 55.8 (O*C*H_3); **IR** ν_{max} / cm^{-1} 3003, 2941, 1577, 1460, 1385, 1267, 1093, 975, 766; **HRMS** (TOF MS ESI+) calcd $C_{23}H_{20}O_3$ $[M+H]^+$ 345.1485, found 345.1495.

4-((1,4-Dimethoxynaphthalen-2-yl)methyl)morpholine [5m]



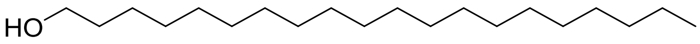
Prepared according to General Procedure C with the following reagents: morpholine (31 mg, 352 µmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (100 mg, 422 µmol) and triethylamine (43 mg, 59 µL, 422 µmol) in tetrahydrofuran (1.5 mL). The reaction was stirred at rt for 24 h. Purification by silica chromatography, eluting with methanol and dichloromethane (5:95), afforded 4-((1,4-dimethoxynaphthalen-2-yl)methyl)morpholine (70 mg, 244 µmol, 68%) as a pale yellow oil: **R_f** 0.28 (95:5 dichloromethane:methanol, UV active); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 8.29 – 8.19 (1 H, m, Ar*H*), 8.10 – 8.01 (1 H, m, Ar*H*), 7.59 – 7.42 (2 H, m, 2 × Ar*H*), 6.93 (1 H, s, Ar*H*), 4.00 (3 H, s, OC*H*$_3$), 3.91 (3 H, s, OC*H*$_3$), 3.80 – 3.68 (6 H, m, ArC*H*$_2$N, C*H*$_2$OC*H*$_2$), 2.58 – 2.49 (4 H, m, C*H*$_2$NC*H*$_2$); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) 151.9 (1 × Ar), 148.1 (1 × Ar), 128.6 (1 × Ar), 126.6 (1 × Ar), 126.2 (1 × Ar), 125.9 (1 × Ar), 125.4 (1 × Ar), 122.4 (1 × Ar), 122.0 (1 × Ar), 105.3 (1 × Ar), 67.2 (*C*H$_2$O*C*H$_2$), 62.5 (O*C*H$_3$), 57.0 (Ar*C*H$_2$N), 55.8 (O*C*H$_3$), 53.9 (*C*H$_2$N*C*H$_2$); **IR** ν_{max} / cm^{-1} 2935, 2837, 2805, 1595, 1455, 1366, 1116, 1090, 1002, 864, 768; **HRMS** (TOF MS ESI+) calcd $C_{17}H_{21}NO_3$ $[M+K]^+$ 326.1153, found 326.1177.

N-((1,4-Dimethoxynaphthalen-2-yl)methyl)-*N*-methylbenzamide [5n]



Prepared according to General Procedure A with the following reagents: *N*-methylbenzamide (48 mg, 352 μmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (100 mg, 422 μmol), tetrabutylammonium iodide (16 mg, 42 μmol) and sodium hydride (60% dispersion in mineral oil, 17 mg, 422 μmol) in tetrahydrofuran (3 mL). The reaction was stirred at rt for 16 h. Purification by silica chromatography, eluting with ethyl acetate and petrol (40:60), afforded *N*-((1,4-dimethoxynaphthalen-2-yl)methyl)-*N*-methylbenzamide (102 mg, 304 μmol, 86%) as a pale yellow oil: **R$_f$** 0.29 (7:3 petrol:ethyl acetate, UV active); **^{1}H NMR** (two rotamers present, the *cis*- and *trans*-amide) δ_H (300 MHz, $CDCl_3$) δ 8.30 – 8.21 (1 H, m, Ar*H*), 8.11 – 7.95 (1 H, m, Ar*H*), 7.61 – 7.36 (7 H, m, 7 × Ar*H*), 6.85 (major rotamer, s, Ar*H*), 6.57 (minor rotamer, s, Ar*H*), 5.03 (major rotamer, s, ArCH_2), 4.74 (minor rotamer, s, ArCH_2), 3.99 (3 H, s, OCH_3), 3.92 (major rotamer, s, OCH_3), 3.73 (minor rotamer, s, OCH_3), 3.07 (major rotamer, s, NCH_3), 2.86 (minor rotamer, s, NCH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 172.0 (*C*=O), 152.5 (1 × Ar), 148.2 (1 × Ar), 136.4 (1 × Ar), 129.7 (2 × Ar), 128.5 (2 × Ar), 126.9 (3 × Ar), 125.7 (2 × Ar), 122.5 (2 × Ar), 121.8 (1 × Ar), 103.8 (major rotamer Ar), 102.0 (minor rotamer Ar), 62.7 (major rotamer OCH_3), 62.1 (minor rotamer OCH_3), 55.8 (OCH_3), 50.0 (major rotamer ArCH_2N), 44.8 (minor rotamer ArCH_2N), 37.0 (major rotamer NCH_3), 33.3 (minor rotamer NCH_3); **IR** ν_{max} / cm^{-1} 2935, 2838, 1627, 1597, 1458, 1368, 1265, 1216, 1091, 1001, 769, 760; **HRMS** (TOF MS ESI+) calcd $C_{21}H_{21}NO_3$ $[M+Na]^+$ 358.1414, found 358.1394.

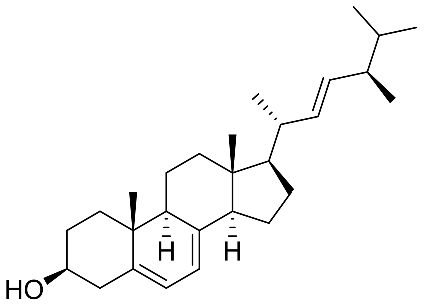
Oxidative cleavage of 2-((icosyloxy)methyl)-1,4-dimethoxynaphthalene to give icosan-1-ol [4a]



Prepared according to General Procedure D with the following reagents: 2-((icosyloxy)methyl)-1,4-dimethoxynaphthalene (130 mg, 261 µmol), 2,3-dichloro-5,6-dicyanobenzoquinone (65 mg, 287 µmol) in 19:1 dichloromethane:H_2O (3 mL). The reaction was quenched by L-ascorbic acid (55 mg, 313 µmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (5:95 to 15:85), afforded icosan-1-ol (71 mg, 237 µmol, 91%) as a white solid: **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 3.64 (2 H, td, *J* = 6.6, 5.4 Hz, CH_2OH), 1.51 – 1.62 (2 H, m, CH_2CH_2OH), 1.26 (32 H, s, br, 16 × CH_2), 1.18 (1 H, t, *J* = 5.5 Hz, OH), 0.88 (3 H, t, *J* = 6.6 Hz, CH_3).

The spectroscopic data agreed with published data.[1]

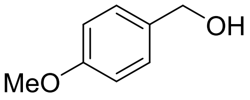
Oxidative cleavage of (3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-3-((1,4-dimethoxynaphthalen-2-yl)methoxy)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene to give (3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-ol [4h]



Prepared according to General Procedure D with the following reagents: (3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-3-((1,4-dimethoxynaphthalen-2-yl)methoxy)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene (100 mg, 168 μmol), 2,3-dichloro-5,6-dicyanobenzoquinone (42 mg, 184 μmol) in 19:1 dichloromethane:H_2O (2 mL). The reaction was quenched by L-ascorbic acid (37 mg, 213 μmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (5:95 to 15:85), afforded (3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-ol (53 mg, 134 μmol, 80%) as a white powder: **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 5.58 (1 H, dd, *J* = 5.6, 2.5 Hz, C=C*H*-CH=C), 5.39 (1 H, dd, *J* = 5.7, 2.8 Hz, C=CH-C*H*=C), 5.32 – 5.09 (2 H, m, C*H*=C*H*), 3.74 – 3.58 (1 H, m, C*H*OH), 2.53 – 2.39 (1 H, m, C*H*HCHOH), 2.34 – 2.20 (1 H, m, CH=CHC*H*), 2.11 – 1.90 (2 H, m, CH_2), 1.89 – 1.82 (3 H, m, C*H*, CH_2), 1.81 – 1.54 (5 H, m, C*H*H, 2 × C*H*, CH_2), 1.52 – 1.38 (4 H, m, 2 × CH_2), 1.37 – 1.17 (4 H, m, CH_2, 2 × C*H*), 1.04 (3 H, d, *J* = 6.6 Hz, CHCH_3), 0.95 (3 H, s, CCH_3), 0.92 (3 H, d, *J* = 6.8 Hz, CHCH_3), 0.84 (3 H, d, *J* = 4.5 Hz, CHCH_3), 0.82 (3 H, d, *J* = 4.6 Hz, CHCH_3), 0.63 (3 H, s, CCH_3).

The spectroscopic data agreed with published data.[2]

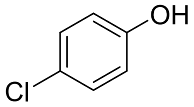
Oxidative cleavage of 1,4-dimethoxy-2-(((4-methoxybenzyl)oxy)methyl)naphthalene to give (4-methoxyphenyl)methanol [4f]



Prepared according to General Procedure D with the following reagents: 1,4-dimethoxy-2-(((4-methoxybenzyl)oxy)methyl)naphthalene (60 mg, 177 μmol), 2,3-dichloro-5,6-dicyanobenzoquinone (44 mg, 195 μmol) in 19:1 dichloromethane:H_2O (2 mL). The reaction was quenched by L-ascorbic acid (37 mg, 213 μmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (5:95 to 40:60), afforded (4-methoxyphenyl)methanol (21 mg, 152 μmol, 86%) as a clear, colourless oil: **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (2 H, m, 2 × Ar*H*), 6.97 – 6.83 (2 H, m, 2 × Ar*H*), 4.62 (2 H, d, *J* = 5.9 Hz, CH_2OH), 3.81 (3 H, s, OCH_3), 1.53 (1 H, t, *J* = 5.9 Hz, O*H*).

The spectroscopic data agreed with published data.[3]

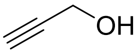
Oxidative cleavage of 2-((4-chlorophenoxy)methyl)-1,4-dimethoxynaphthalene to give 4-chlorophenol [4j]



Prepared according to General Procedure D with the following reagents: 2-((4-chlorophenoxy)methyl)-1,4-dimethoxynaphthalene (80 mg, 243 µmol), 2,3-dichloro-5,6-dicyanobenzoquinone (61 mg, 268 µmol) in 19:1 dichloromethane:H_2O (2 mL). The reaction was quenched by L-ascorbic acid (51 mg, 292 µmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (5:95 to 15:85), afforded 4-chlorophenol (28 mg, 214 µmol, 88%) as a clear, crystalline solid: **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 7.23 – 7.16 (2 H, m, 2 × Ar*H*), 6.80 – 6.73 (2 H, m, 2 × Ar*H*), 4.67 (1 H, s, O*H*).

The spectroscopic data agreed with published data.[4]

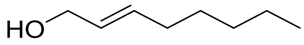
Oxidative cleavage of 1,4-dimethoxy-2-((prop-2-yn-1-yloxy)methyl)naphthalene to give prop-2-yn-1-ol [4d]



Prepared according to General Procedure D with the following reagents: 1,4-dimethoxy-2-((prop-2-yn-1-yloxy)methyl)naphthalene (66 mg, 258 μmol), 2,3-dichloro-5,6-dicyanobenzoquinone (64 mg, 283 μmol) in 19:1 dichloromethane:H_2O (2.5 mL). The reaction was quenched by L-ascorbic acid (51 mg, 292 μmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (5:95 to 25:75), afforded prop-2-yn-1-ol (14 mg, 247 μmol, 99%) as a light brown oil: **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 4.27 (2 H, d, *J* = 2.4 Hz, CH_2OH), 2.47 (1 H, t, *J* = 2.4 Hz, O*H*), 1.91 (1 H, s, C≡C*H*).

The spectroscopic data agreed with published data.[5]

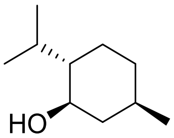
Oxidative cleavage of (*E*)-1,4-dimethoxy-2-((oct-2-en-1-yloxy)methyl)naphthalene to give (*E*)-oct-2-en-1-ol [4c]



Prepared according to General Procedure D with the following reagents: (*E*)-1,4-dimethoxy-2-((oct-2-en-1-yloxy)methyl)naphthalene (90 mg, 274 µmol), 2,3-dichloro-5,6-dicyanobenzoquinone (68 mg, 301 µmol) in 19:1 dichloromethane:H_2O (2.7 mL). The reaction was quenched by L-ascorbic acid (58 mg, 329 µmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (5:95 to 25:75), afforded (*E*)-oct-2-en-1-ol (30 mg, 233 µmol, 85%) as a pale yellow oil: **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 5.76 – 5.55 (2 H, m, C*H*=C*H*), 4.11 – 4.05 (2 H, m, CHCH_2OH), 2.10 – 1.98 (2 H, m, CHCH_2CH_2), 1.42 – 1.22 (6 H, m, 3 × CH_2), 0.90 (3 H, t, *J* = 7.0 Hz, CH_3).

The spectroscopic data agreed with published data.[6]

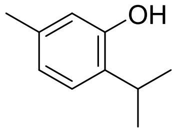
Acidic cleavage of 2-((((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)methyl)-1,4-dimethoxynaphthalene to give (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexan-1-ol [4i]



To a solution of 2-((((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)methyl)-1,4-dimethoxynaphthalene (110 mg, 309 μmol) in anhydrous methanol (3 mL) was added hydrochloric acid (12 M, 39 μL, 463 μmol). The reaction was refluxed for 16 h. The solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (0:100 to 30:70 gradient) afforded (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexan-1-ol (34 mg, 216 μmol, 70%) as a cloudy solid: **^{1}H NM** δ_H (400 MHz, $CDCl_3$) δ 3.47 – 3.35 (1 H, m, C*H*O), 2.23 – 2.09 (1 H, m, C*H*H), 2.02 – 1.92 (1 H, m, C*H*H), 1.72 – 1.56 (2 H, m, C*H*, CH*H*), 1.52 – 1.34 (1 H, m, CH*H*), 1.26 (1 H, d, *J* = 5.3 Hz, O*H*), 1.17 – 1.05 (1 H, m, C*H*), 1.03 – 0.85 (9 H, m, C*H*, CH_2, $CH(CH_3)_2$), 0.81 (3 H, d, *J* = 7.0 Hz, $CHCH_3$).

The spectroscopic data agreed with published data.[7]

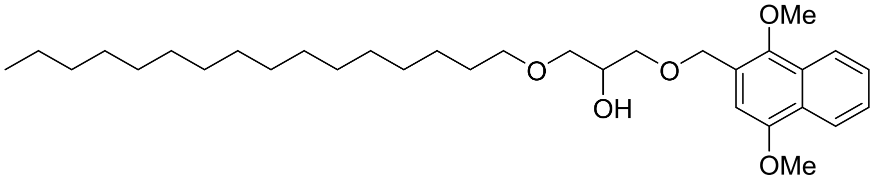
Reductive cleavage of 2-((2-isopropyl-5-methylphenoxy)methyl)-1,4-dimethoxynaphthalene to give 2-isopropyl-5-methylphenol [4k]



To a flask, purged with nitrogen, was added palladium on carbon (10%, 10 mg) and a solution of 2-((2-isopropyl-5-methylphenoxy)methyl)-1,4-dimethoxynaphthalene (100 mg, 285 µmol) in anhydrous 1:1 tetrahydrofuran:methanol (3 mL). The solution was bubbled with H_2 *via* a balloon for 10 mins, then the balloon was replaced by a fresh H_2 balloon and the reaction was stirred under an atmosphere of hydrogen for 4 h. The reaction mixture was vacuum filtered through a pad of Celite®, eluting with ethyl acetate, and the filtrate was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (0:100 to 10:90 gradient) afforded 2-isopropyl-5-methylphenol (37 mg, 245 µmol, 86%) as a white solid: **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 7.08 (1 H, d, *J* = 7.8 Hz, Ar*H*), 6.73 (1 H, dd, *J* = 7.8, 1.7 Hz, Ar*H*), 6.61 – 6.54 (1 H, m, Ar*H*), 4.56 (1 H, s, O*H*), 3.16 (1 H, hept, *J* = 6.9 Hz, C*H*(CH_3)$_2$), 2.27 (3 H, s, ArC*H*$_3$), 1.24 (6 H, d, *J* = 6.9 Hz, CH(C*H*$_3$)$_2$).

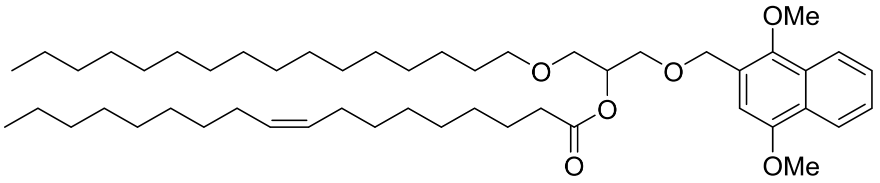
The spectroscopic data agreed with published data.[8]

1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol [10]



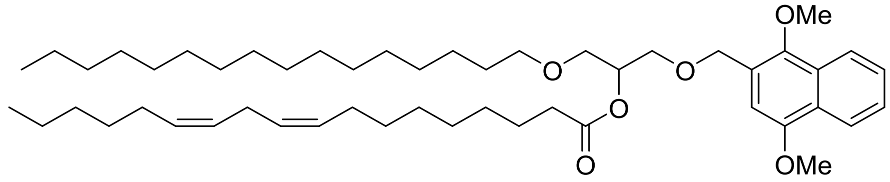
To a flask, purged with nitrogen *via* Schlenk technique, was added a solution of hexadecanol (795 mg, 3.28 mmol) in toluene (5 mL) and boron trifluoride diethyl etherate (78 mg, 67 µL, 55 µmol). To the mixture was added a solution of 2-(((1,4-dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane (300 mg, 1.09 mmol) in toluene (5 mL) dropwise. Upon addition, the reaction was stirred at rt for 16 h. The reaction was quenched by addition of saturated aqueous sodium bicarbonate solution (1 mL), diluted with H_2O (25 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organics were dried over $MgSO_4$, filtered, and evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (15:85), afforded 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol (424 mg, 821 µmol, 75%) as a clear, colourless oil: **R_f** 0.28 (85:15 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.27 – 8.20 (1 H, m, Ar*H*), 8.00 – 8.01 (1 H, m, Ar*H*), 7.51 (2 H, dddd, *J* = 22.4, 8.2, 6.8, 1.4 Hz, 2 × Ar*H*), 6.83 (1 H, s, Ar*H*), 4.78 (2 H, s, ArC*H*$_2$O), 4.06 – 3.96 (4 H, m, C*H*, OC*H*$_3$), 3.90 (3 H, s, OC*H*$_3$), 3.67 – 3.40 (6 H, m, 3 × OC*H*$_2$), 2.53 (1 H, d, *J* = 4.1 Hz, O*H*), 1.55 (2 H, m, C*H*$_2$CH$_2$O), 1.25 (26 H, s, br, 13 × C*H*$_2$), 0.88 (3 H, t, *J* = 6.7 Hz, C*H*$_3$); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 152.2 (1 × Ar), 147.8 (1 × Ar), 128.6 (1 × Ar), 126.8 (1 × Ar), 126.6 (1 × Ar), 125.9 (1 × Ar), 125.7 (1 × Ar), 122.5 (1 × Ar), 122.1 (1 × Ar), 104.2 (1 × Ar), 72.0 (O*C*H$_2$), 71.9 (O*C*H$_2$), 71.7 (O*C*H$_2$), 69.7 (*C*HOH), 68.2 (Ar*C*H$_2$O), 63.0 (O*C*H$_3$), 55.8 (O*C*H$_3$), 32.1 (*C*H$_2$), 29.9 – 29.7 (9 × *C*H$_2$), 29.6 (*C*H$_2$), 29.5 (*C*H$_2$), 26.2 (*C*H$_2$), 22.8 (*C*H$_2$), 14.3 (*C*H$_3$); **IR** ν_{max} / cm^{-1} 3400 br, 2917, 2850, 1599, 1464, 1370, 1122, 1091, 762; **HRMS** (TOF MS AP+) calcd $C_{32}H_{52}O_5$ $[M]^+$ 516.3809, found 516.3811.

1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl oleate [11a]



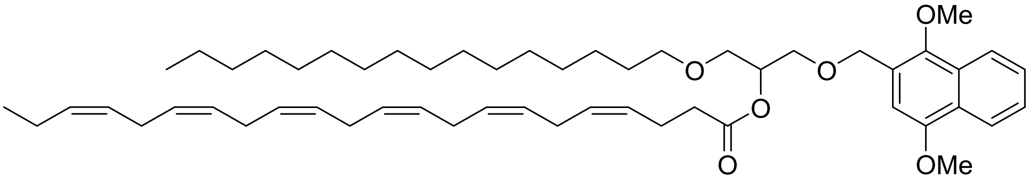
A solution of 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol (140 mg, 271 μmol), *N*,*N′*-dicyclohexylcarbodiimide (84 mg, 406 μmol) and 4-dimethylaminopyridine (17 mg, 135 μmol) in dichloromethane (5 mL) was stirred at rt for 1 h. To the reaction was added oleic acid (92 mg, 103 μL, 325 μmol) dropwise. Upon addition, the mixture was stirred at rt for a further 24 h. The solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (4:96 with 1% triethylamine) afforded 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl oleate (197 mg, 252 μmol, 93%) as a clear, colourless oil*:* **$\mathbf{R_f}$** 0.33 (19:1 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (300 MHz, $\mathrm{CDCl_3}$) δ 8.28 – 8.17 (1 H, m, $\mathrm{Ar}H$), 8.09 – 8.00 (1 H, m, $\mathrm{Ar}H$), 7.59 – 7.42 (2 H, m, 2 × $\mathrm{Ar}H$), 6.83 (1 H, s, $\mathrm{Ar}H$), 5.41 – 5.27 (2 H, m, $\mathrm{C}H\mathrm{=C}H$), 5.23 (1 H, p, *J* = 5.1 Hz, $\mathrm{C}H\mathrm{OC{=}O}$), 4.76 (2 H, d, *J* = 1.7 Hz, $\mathrm{ArC}H_2\mathrm{O}$), 3.99 (3 H, s, $\mathrm{OC}H_3$), 3.89 (3 H, s, $\mathrm{OC}H_3$), 3.69 (2 H, d, *J* = 5.1 Hz, $\mathrm{OC}H_2\mathrm{CH}$), 3.58 (2 H, d, *J* = 5.2 Hz, $\mathrm{CHC}H_2\mathrm{O}$), 3.50 – 3.33 (2 H, m, $\mathrm{CH_2C}H_2\mathrm{O}$), 2.32 (2 H, t, *J* = 7.5 Hz, $\mathrm{C}H_2\mathrm{C{=}O}$), 2.00 (4 H, m, $\mathrm{C}H_2\mathrm{CH{=}CHC}H_2$), 1.68 – 1.46 (4 H, m, 2 × $\mathrm{C}H_2$), 1.41 – 1.20 (46 H, m, 23 × $\mathrm{C}H_2$), 0.94 – 0.83 (6 H, m, 2 × $\mathrm{C}H_3$); **^{13}C NMR** δ_C (75 MHz, $\mathrm{CDCl_3}$) δ 173.5 ($C\mathrm{=O}$), 152.2 (1 × Ar), 147.6 (1 × Ar), 130.1 ($C\mathrm{H{=}CH}$), 129.9 ($\mathrm{CH{=}}C\mathrm{H}$), 128.6 (1 × Ar), 126.7 (1 × Ar), 126.5 (1 × Ar), 126.0 (1 × Ar), 125.7 (1 × Ar), 122.5 (1 × Ar), 122.0 (1 × Ar), 104.1 (1 × Ar), 71.8 ($\mathrm{O}C\mathrm{H_2}$), 71.5 ($\mathrm{O}C\mathrm{H_2}$), 69.5 ($\mathrm{O}C\mathrm{H_2}$), 69.2 ($C\mathrm{HOC{=}O}$), 68.1 ($\mathrm{Ar}C\mathrm{H_2O}$), 62.9 ($\mathrm{O}C\mathrm{H_3}$), 55.8 ($\mathrm{O}C\mathrm{H_3}$), 34.6 ($C\mathrm{H_2C{=}O}$), 32.1 (2 × $C\mathrm{H_2}$), 30.5 – 28.5 (20 × $C\mathrm{H_2}$), 27.3 ($C\mathrm{H_2CH{=}CH}C\mathrm{H_2}$), 26.2 ($C\mathrm{H_2}$), 25.1 ($C\mathrm{H_2}$), 22.8 ($C\mathrm{H_2}$), 14.3 (2 × $C\mathrm{H_3}$); **IR** ν_max / $\mathrm{cm^{-1}}$ 2922, 2853, 1738, 1598, 1461, 1370, 1124, 1091, 768; **HRMS** (TOF MS AP+) calcd $\mathrm{C_{50}H_{85}O_6}$ $[\mathrm{M+H}]^+$ 781.6341, found 781.6324.

1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate [11b]



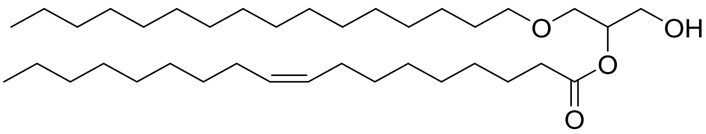
A solution of 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol (140 mg, 271 μmol), *N*,*N'*-dicyclohexylcarbodiimide (84 mg, 406 μmol) and 4-dimethylaminopyridine (17 mg, 135 μmol) in dichloromethane (5 mL) was stirred at rt for 1 h. To the reaction was added linoleic acid (91 mg, 101 μL, 325 μmol) dropwise. Upon addition, the mixture was stirred at rt for a further 24 h. The solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (4:96 with 1% triethylamine) afforded 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate (167 mg, 214 μmol, 79%) as a clear, colourless oil: **R_f** 0.30 (19:1 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (400 MHz, CDCl$_3$) δ 8.20 – 8.11 (1 H, m, Ar*H*), 7.97 (1 H, ddd, *J* = 8.4, 1.4, 0.7 Hz, Ar*H*), 7.43 (2 H, dddd, *J* = 22.3, 8.2, 6.8, 1.4 Hz, Ar*H*), 6.75 (1 H, s, Ar*H*), 5.34 – 5.20 (4 H, m, 2 × C*H*=C*H*), 5.16 (1 H, p, *J* = 5.2 Hz, C*H*OC=O), 4.73 – 4.64 (2 H, m, ArC*H*$_2$O), 3.92 (3 H, s, OC*H*$_3$), 3.82 (3 H, s, OC*H*$_3$), 3.68 – 3.58 (2 H, m, OC*H*$_2$CH), 3.51 (2 H, d, *J* = 5.2 Hz, CHC*H*$_2$O), 3.42 – 3.26 (2 H, CH$_2$C*H*$_2$O), 2.69 (2 H, dd, *J* = 7.1, 5.6 Hz, CHC*H*$_2$CH), 2.31 – 2.18 (2 H, m, C*H*$_2$C=O), 2.05 – 1.91 (4 H, m, 2 × C*H*$_2$CH=CH), 1.59 – 1.50 (2 H, m, C*H*$_2$), 1.47 – 1.39 (2 H, m, C*H*$_2$), 1.35 – 1.09 (40 H, m, 20 × C*H*$_2$), 0.85 – 0.77 (6 H, m, 2 × C*H*$_2$); **^{13}C NMR** δ_C (75 MHz, CDCl$_3$) δ 173.5 (*C*=O), 152.2 (1 × Ar), 147.6 (1 × Ar), 130.4 (*C*H=CH), 130.2 (CH=*C*H), 128.6 (*C*H=CH), 128.2 (CH=*C*H), 128.0 (1 × Ar), 126.7 (1 × Ar), 126.5 (1 × Ar), 126.0 (1 × Ar), 125.7 (1 × Ar), 122.5 (1 × Ar), 122.0 (1 × Ar), 104.1 (1 × Ar), 71.8 (O*C*H$_2$), 71.5 (O*C*H$_2$), 69.5 (O*C*H$_2$), 69.2 (*C*HOC=O), 68.1 (Ar*C*H$_2$O), 62.9 (O*C*H$_3$), 55.8 (O*C*H$_3$), 34.6 (*C*H$_2$C=O), 32.1 (*C*H$_2$), 31.7 (*C*H$_2$), 30.0 – 29.1 (18 × *C*H$_2$), 27.3 (*C*H$_2$CH=CH*C*H$_2$), 26.2 (*C*H$_2$), 25.8 (*C*H$_2$), 25.1 (*C*H$_2$), 14.3 (*C*H$_3$), 14.2 (*C*H$_3$); **IR** ν_{max} / cm^{-1} 2923, 2853, 1737, 1597, 1461, 1370, 1124, 1092, 768; **HRMS** (TOF MS AP+) calcd $C_{50}H_{82}O_6$ $[M+H]^+$ 779.6184, found 779.6169.

1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [11c]



A solution of 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol (140 mg, 271 µmol), *N*,*N′*-dicyclohexylcarbodiimide (84 mg, 406 µmol) and 4-dimethylaminopyridine (17 mg, 135 µmol) in dichloromethane (5 mL) was stirred at rt for 1 h. To the reaction was added docosahexaenoic acid (107 mg, 113 µL, 325 µmol) dropwise. Upon addition, the mixture was stirred at rt for a further 24 h. The solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (4:96 with 1% triethylamine) afforded 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (220 mg, 266 µmol, 98%) as a clear, colourless oil: **R$_f$** 0.29 (19:1 petrol:ethyl acetate, UV active); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.26 – 8.18 (1 H, m, Ar*H*), 8.04 (1 H, ddd, *J* = 8.3, 1.4, 0.7 Hz, Ar*H*), 7.50 (2 H, dddd, *J* = 22.3, 8.2, 6.8, 1.4 Hz, Ar*H*), 6.82 (1 H, s, Ar*H*), 5.45 – 5.28 (12 H, m, 6 × C*H*=C*H*), 5.23 (1 H, p, *J* = 5.2 Hz, C*H*OC=O), 4.76 (2 H, d, *J* = 2.5 Hz, ArCH_2O), 3.99 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 3.69 (2 H, d, *J* = 5.1 Hz, OCH_2CH), 3.58 (2 H, d, *J* = 5.2 Hz, CHCH_2O), 3.49 – 3.33 (2 H, m, CH$_2$CH_2O), 2.90 – 2.77 (10 H, m, 5 × CHCH_2CH), 2.43 – 2.35 (4 H, m, 2 × CH=CHCH_2), 2.13 – 2.01 (2 H, m, CH_2C=O), 1.54 – 1.46 (2 H, m, CH_2), 1.34 – 1.17 (26 H, m, 13 × CH_2), 0.97 (3 H, t, *J* = 7.5 Hz, CH_3), 0.88 (3 H, t, *J* = 6.6 Hz, CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) δ 172.7 (*C*=O), 152.2 (1 × Ar), 147.7 (1 × Ar), 132.2 (*C*H=CH), 129.4 (CH=*C*H), 128.7 (*C*H=CH), 128.5 (CH=*C*H), 128.4 (3 × *C*H=CH), 128.3 (*C*H=CH), 128.2 (2 × CH=*C*H), 128.0 (1 × Ar, *C*H=CH), 127.2 (CH=*C*H), 126.7 (1 × Ar), 126.5 (1 × Ar), 125.9 (1 × Ar), 125.7 (1 × Ar), 122.5 (1 × Ar), 122.0 (1 × Ar), 104.1 (1 × Ar), 71.8 (O*C*H$_2$), 71.7 (O*C*H$_2$), 69.4 (O*C*H$_2$), 69.1 (*C*HOC=O), 68.1 (Ar*C*H$_2$O), 62.9 (O*C*H$_3$), 55.8 (O*C*H$_3$), 34.4 (*C*H$_2$C=O), 32.1 (*C*H$_2$), 29.9 – 29.4 (11 × *C*H$_2$), 26.2 (*C*H$_2$), 25.7 (5 × CH*C*H$_2$CH), 22.9 (2 × CH=CH*C*H$_2$), 20.7 (*C*H$_2$), 14.4 (*C*H$_3$), 14.3 (*C*H$_3$); **IR** ν_{max} / cm^{-1} 3012, 2923, 2853, 1737, 1597, 1461, 1370, 1124, 1092, 769; **HRMS** (TOF MS AP+) calcd $C_{54}H_{82}O_6$ $[M+H]^+$ 827.6184, found 827.6134.

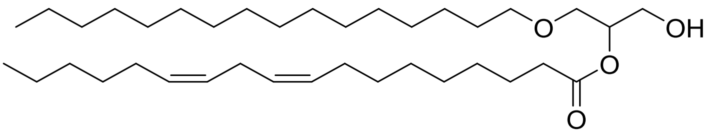
Oxidative cleavage of 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl oleate to afford 1-(hexadecyloxy)-3-hydroxypropan-2-yl oleate [12a]



Prepared according to General Procedure D with the following reagents: 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl oleate (170 mg, 218 µmol), 2,3-dichloro-5,6-dicyanobenzoquinone (54 mg, 195 µmol) in 19:1 dichloromethane:H_2O (2 mL). The reaction was quenched by *L*-ascorbic acid (46 mg, 261 µmol). Purification by silica chromatography, eluting with ethyl acetate and petrol (15:85), afforded 1-(hexadecyloxy)-3-hydroxypropan-2-yl oleate (108 mg, 186 µmol, 86%) as a clear, colourless oil: **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 5.41 – 5.26 (2 H, m, C*H*=C*H*), 4.99 (1 H, p, *J* = 4.8 Hz, C*H*OC=O), 3.86 – 3.74 (2 H, m, OCH_2CH), 3.69 – 3.53 (2 H, m, CH_2OH), 3.45 (2 H, tt, *J* = 6.6, 3.2 Hz, CH_2CH_2O), 2.35 (2 H, t, *J* = 7.5 Hz, CH_2C=O), 2.07 – 1.94 (4 H, m, 2 × CH_2CH=CH), 1.71 – 1.50 (4 H, m, 2 × CH_2), 1.41 – 1.18 (46 H, m, 23 × CH_3), 0.95 – 0.82 (6 H, m, 2 × CH_3).

The spectroscopic data agreed with published data.[9]

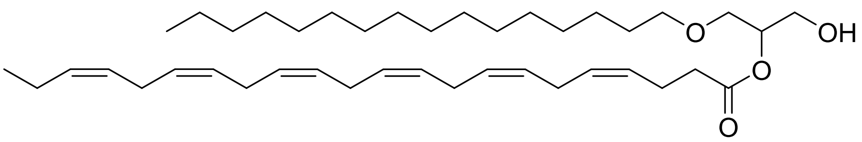
Oxidative cleavage of 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate to afford 1-(hexadecyloxy)-3-hydroxypropan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate [12b]



Prepared according to General Procedure D with the following reagents: 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate (91 mg, 117 µmol), 2,3-dichloro-5,6-dicyanobenzoquinone (29 mg, 129 µmol) in 19:1 dichloromethane:H_2O (2 mL). The reaction was quenched by *L*-ascorbic acid (25 mg, 140 µmol). Purification by silica chromatography, eluting with ethyl acetate and petrol (15:85), afforded 1-(hexadecyloxy)-3-hydroxypropan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate (55 mg, 95 µmol, 81%) as a clear, colourless oil: **^{1}H NMR** δ $_H$ (300 MHz, $CDCl_3$) δ 5.46 – 5.25 (4 H, m, 2 × C*H*=C*H*), 5.00 (1 H, p, *J* = 4.8 Hz, C*H*OC=O), 3.86 – 3.76 (2 H, m, CH_2OH), 3.70 – 3.54 (2 H, m, OCH_2CH), 3.45 (2 H, tt, *J* = 6.6, 3.2 Hz, CH_2CH_2O), 2.77 (2 H, t, *J* = 6.1 Hz, CHCH_2CH), 2.35 (2 H, t, *J* = 7.5 Hz, CH_2C=O), 2.18 (1 H, t, *J* = 6.2 Hz, O*H*), 2.09 – 1.99 (4 H, m, 2 × CH_2CH=CH), 1.70 – 1.58 (4 H, m, 2 × CH_2), 1.47 – 1.21 (40 H, m, 20 × CH_2), 0.98 – 0.82 (6 H, m, 2 × CH_3).

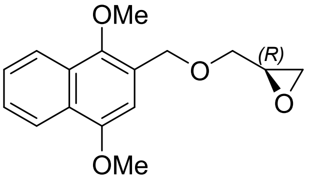
The spectroscopic data agreed with published data.[10]

Oxidative cleavage of 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate to afford 1-(hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [12c]



Prepared according to General Procedure D with the following reagents: 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (200 mg, 242 μmol), 2,3-dichloro-5,6-dicyanobenzoquinone (55 mg, 242 μmol) in 19:1 dichloromethane:H_2O (2.5 mL). The reaction was quenched by L-ascorbic acid (47 mg, 266 μmol). Purification by silica chromatography, eluting with ethyl acetate and petrol (15:85), afforded 1-(hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (94 mg, 150 μmol, 62%) as a clear, colourless oil: **R_f** 0.34 (9:1 petrol:ethyl acetate, permanganate stain); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 5.49 – 5.23 (12 H, m, 6 × C*H*=C*H*), 5.00 (1 H, p, *J* = 4.8 Hz, C*H*OC=O), 3.85 – 3.76 (2 H, m, CH_2OH), 3.69 – 3.53 (2 H, m, OCH_2CH), 3.51 – 3.38 (2 H, m, CH_2CH_2O), 2.93 – 2.75 (10 H, m, 5 × CHCH_2CH), 2.48 – 2.35 (4 H, m, 2 × CH_2CH=CH), 2.19 (1 H, t, *J* = 6.3 Hz, O*H*), 2.14 – 2.00 (2 H, m, CH_2C=O), 1.55 (2 H, q, *J* = 6.9 Hz, CH_2CH_2O), 1.25 (26 H, s, br, 13 × CH_2), 0.97 (3 H, t, *J* = 7.5 Hz, CH_3), 0.88 (3 H, t, *J* = 6.3 Hz, CH_3); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) 173.0 (*C*=O), 132.2 (*C*H=CH), 129.6 (*C*H=CH), 128.7 (*C*H=CH), 128.5 – 128.4 (3 × *C*H=CH), 128.2 (2 × *C*H=CH), 128.2 (*C*H=CH), 128.0 (2 × *C*H=CH), 127.2 (*C*H=CH), 73.2 (O*C*H_2), 72.1 (O*C*H_2), 70.1 (*C*HOC=O), 63.1 (O*C*H_2), 34.4 (*C*H_2C=O), 32.1 (*C*H_2), 30.0 – 29.4 (11 × *C*H_2), 26.2 (*C*H_2), 25.9 – 25.6 (5 × CH*C*H_2CH), 22.9 (*C*H_2), 22.8 (*C*H_2), 20.7 (*C*H_2), 14.4 (*C*H_3), 14.3 (*C*H_3); **IR** ν_{max} / cm^{-1} 3425 br, 3013, 2923, 2853, 1732, 1464, 1377, 1167, 1112, 1055, 979, 720; **HRMS** (TOF MS AP+) calcd $C_{41}H_{70}O_4$ $[M+H]^+$ 627.5347, found 627.5339.

(*R*)-2-(((1,4-Dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane [16]

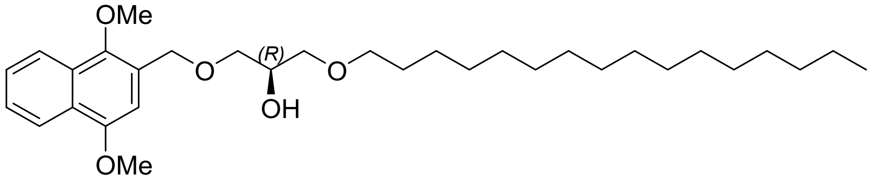


To a flask, purged with nitrogen *via* Schlenk technique, was added a solution of (*S*)-glycidol (34 mg, 458 μmol), 2-(chloromethyl)-1,4-dimethoxynaphthalene (130 mg, 549 μmol) and tetrabutylammonium iodide (20 mg, 55 μmol) in *N,N'*-dimethylformamide (3 mL). The reaction was cooled to 0 °C and sodium hydride (60% dispersion in mineral oil, 22 mg, 549 μmol) was added portion-wise. Upon addition, the reaction was warmed to rt and stirred for 16 h. The reaction was quenched by addition of saturated aqueous ammonium chloride solution (1 mL), diluted with water (50 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organics were dried over $MgSO_4$, filtered, and the solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and petrol (10:90 to 20:80 gradient with 1% triethylamine), afforded (*R*)-2-(((1,4-dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane (97 mg, 353 μmol, 77%) as a clear, colourless oil: **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.26 – 8.21 (1 H, m, Ar*H*), 8.09 – 8.03 (1 H, m, Ar*H*), 7.60 – 7.48 (2 H, m, 2 × Ar*H*), 6.91 (1 H, s, Ar*H*), 4.89 – 4.75 (2 H, m, $ArCH_2O$), 4.01 (3 H, s, OCH_3), 3.92 (3 H, s, OCH_3), 3.84 (1 H, dd, *J* = 11.5, 3.2 Hz, OC*H*HCH(O)), 3.52 (1 H, dd, *J* = 11.4, 6.0 Hz, OCH*H*CH(O)), 3.21 (1 H, ddt, *J* = 5.9, 4.1, 3.0 Hz, $OCH_2CH(O)$), 2.81 (1 H, dd, *J* = 5.1, 4.2 Hz, CH(O)C*H*H), 2.64 (1 H, dd, *J* = 5.1, 2.9 Hz, CH(O)CH*H*).

The spectroscopic data agreed with racemic 2-(((1,4-dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane.

$[\alpha]_D^{19}$ = +4.1 (c = 1.02, $CHCl_3$).

(*R*)-1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol [17]

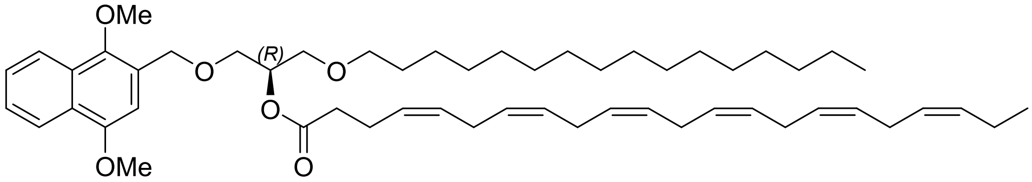


To a flask, purged with nitrogen via Schlenk technique, was added a solution of hexadecanol (3.71 g, 15.31 mmol) in toluene (25 mL) and boron trifluoride diethyl etherate (37 mg, 32 µL, 255 µmol). To the mixture was added a solution of (*R*)-2-(((1,4-dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane (1.40 g, 5.10 mmol) in toluene (25 mL) dropwise. Upon addition, the reaction was stirred at rt for 16 h. The reaction was quenched by addition of saturated aqueous sodium bicarbonate solution (1 mL), diluted with H_2O (100 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organics were dried over $MgSO_4$, filtered, and evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (15:85), afforded (*R*)-1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol (1.98 g, 3.83 mmol, 75%) as a clear, colourless oil: **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.26 – 8.21 (1 H, m, Ar*H*), 8.00 – 8.02 (1 H, m, Ar*H*), 7.50 (2 H, dddd, *J* = 22.4, 8.2, 6.8, 1.4 Hz, 2 × Ar*H*), 6.83 (1 H, s, Ar*H*), 4.79 (2 H, s, ArCH_2O), 4.08 – 3.96 (4 H, m, C*H*, OCH_3), 3.91 (3 H, s, OCH_3), 3.66 – 3.39 (6 H, m, 3 × OCH_2), 2.51 (1 H, d, *J* = 4.1 Hz, O*H*), 1.54 (2 H, m, CH_2CH_2O), 1.25 (26 H, s, br, 13 × CH_2), 0.88 (3 H, t, *J* = 6.7 Hz, CH_3).

The spectroscopic data agreed with racemic 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol.

$[\alpha]_D^{19}$ = +2.0 (c = 0.98, $CHCl_3$).

(*R*)-1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [18]

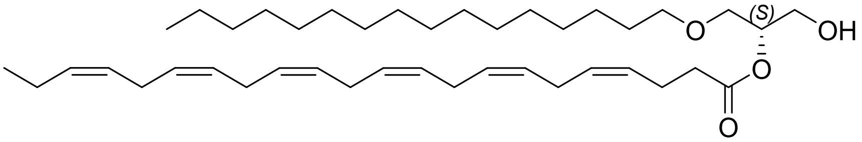


A solution of (*R*)-1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol (450 mg, 871 µmol), *N*,*N*′-dicyclohexylcarbodiimide (270 mg, 1.31 mmol) and 4-dimethylaminopyridine (53 mg, 435 µmol) in dichloromethane (36 mL) was stirred at rt for 1 h. To the reaction was added docosahexaenoic acid (315 mg, 334 µL, 958 µmol) dropwise. Upon addition, the mixture was stirred at rt for a further 24 h. The solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (4:96 with 1% triethylamine) afforded (*R*)-1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (706 mg, 853 µmol, 98%) as a clear, colourless oil: **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) δ 8.26 – 8.18 (1 H, m, Ar*H*), 8.05 (1 H, ddd, *J* = 8.3, 1.4, 0.7 Hz, Ar*H*), 7.50 (2 H, dddd, *J* = 22.3, 8.2, 6.8, 1.4 Hz, Ar*H*), 6.83 (1 H, s, Ar*H*), 5.46 – 5.29 (12 H, m, 6 × C*H*=C*H*), 5.23 (1 H, p, *J* = 5.2 Hz, C*H*OC=O), 4.77 (2 H, d, *J* = 2.5 Hz, ArCH_2O), 4.00 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 3.69 (2 H, d, *J* = 5.1 Hz, OCH_2CH), 3.56 (2 H, d, *J* = 5.2 Hz, CHCH_2O), 3.46 – 3.34 (2 H, m, CH_2CH_2O), 2.91 – 2.79 (10 H, m, 5 × CHCH_2CH), 2.43 – 2.36 (4 H, m, 2 × CH=CHCH_2), 2.13 – 2.02 (2 H, m, CH_2C=O), 1.54 – 1.46 (2 H, m, CH_2), 1.34 – 1.17 (26 H, m, 13 × CH_2), 0.97 (3 H, t, *J* = 7.5 Hz, CH_3), 0.88 (3 H, t, *J* = 6.6 Hz, CH_3).

The spectroscopic data agreed with racemic 1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate.

$[\alpha]_D^{19}$ = -5.0 (c = 1.00, $CHCl_3$).

Oxidative cleavage of (*R*)-1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate to afford (*S*)-1-(hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [14]

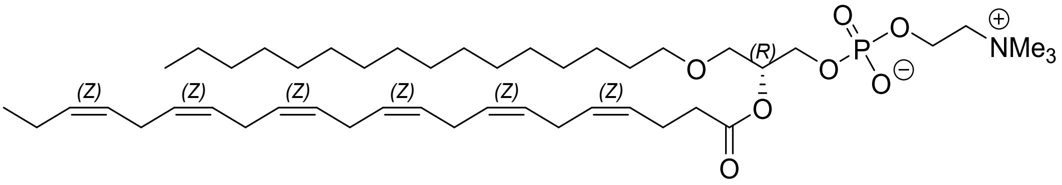


Prepared according to General Procedure D with the following reagents: (*R*)-1-((1,4-dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (640 mg, 774 µmol), 2,3-dichloro-5,6-dicyanobenzoquinone (193 mg, 851 µmol) in 19:1 dichloromethane:H_2O (8 mL). The reaction was quenched by L-ascorbic acid (164 mg, 928 µmol). Purification by silica chromatography, eluting with ethyl acetate and 40-60 petrol (15:85), afforded (*S*)-1-(hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (301 mg, 480 µmol, 62%) as a clear, colourless oil: **R_f** 0.34 (9:1 40-60 petrol:ethyl acetate, permanganate stain); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 5.49 – 5.24 (12 H, m, 6 × C*H*=C*H*), 5.01 (1 H, p, *J* = 4.8 Hz, C*H*OC=O), 3.86 – 3.76 (2 H, m, CH_2OH), 3.69 – 3.53 (2 H, m, OCH_2CH), 3.50 – 3.39 (2 H, m, CH_2CH_2O), 2.91 – 2.73 (10 H, m, 5 × CHCH_2CH), 2.48 – 2.36 (4 H, m, 2 × CH_2CH=CH), 2.20 (1 H, t, *J* = 6.3 Hz, O*H*), 2.15 – 2.00 (2 H, m, CH_2C=O), 1.55 (2 H, q, *J* = 6.9 Hz, C$H_2$$CH_2$O), 1.25 (26 H, s, br, 13 × CH_2), 0.97 (3 H, t, *J* = 7.5 Hz, CH_3), 0.88 (3 H, t, *J* = 6.3 Hz, CH_3).

The spectroscopic data agreed with racemic 1-(hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate.

$[\alpha]_D^{19}$ = -3.1 (c = 1.04, $CHCl_3$).

(*R*)-2-(((4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoyl)oxy)-3-(hexadecyloxy)propyl (2-(trimethylammonio)ethyl) phosphate [15]

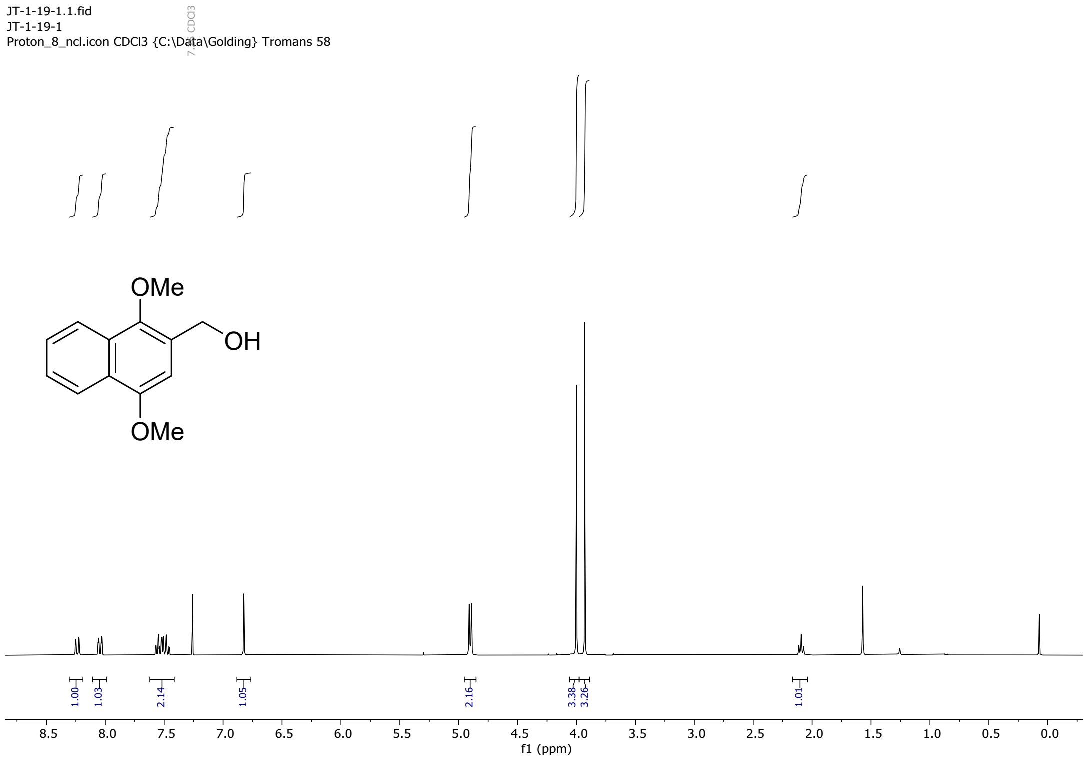


To an oven-dried flask, purged with nitrogen, was added a solution of (*S*)-1-(hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (150 mg, 240 µmol) in trifluorotoluene (4 mL). The solution was cooled to 0 °C and pyridine (58 µL, 720 µmol) and 2-chloro-1,3,2-dioxaphospholane 2-oxide (33 µL, 360 µmol) were added dropwise sequentially. Upon addition, the reaction was warmed to rt and stirred for 1 h. The solution was vacuum filtered through a pad of Celite® and the filtrate was evaporated *in vacuo* to afford the intermediate (*R*)-1-(hexadecyloxy)-3-((2-oxido-1,3,2-dioxaphospholan-2-yl)oxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (175 mg, 240 µmol, 100%) as a white solid. To a solution of (*R*)-1-(hexadecyloxy)-3-((2-oxido-1,3,2-dioxaphospholan-2-yl)oxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate (175 mg, 240 µmol) in trifluorotoluene (2 mL) under nitrogen was added trimethylamine (2 M in acetonitrile, 6 mL, 12.0 mmol). Upon addition, the reaction mixture was refluxed for 16 h. The mixture was cooled to rt and the solvent was evaporated *in vacuo*. Purification by silica chromatography, eluting with a 65:25:0 to 65:25:4 gradient of dichloromethane:methanol:water, afforded (*R*)-2-(((4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoyl)oxy)-3-(hexadecyloxy)propyl (2-(trimethylammonio)ethyl) phosphate (69 mg, 87 µmol, 35%) as a pale yellow oil: **R_f** 0.39 (70:30:4 dichloromethane:methanol:water, permanganate stain); **$[\alpha]_D^{19}$** = -2.5 (c = 1.02, $CHCl_3$); **^{1}H NMR** δ_H (300 MHz, $CDCl_3$) δ 5.45 – 5.24 (12 H, m, 6 × C*H*=C*H*), 5.16 – 5.07 (1 H, m, C*H*OC=O), 4.31 – 4.20 (2 H, m, POC*H*$_2$), 3.96 – 3.85 (2 H, m, CHC*H*$_2$OP), 3.75 (2 H, m, C*H*$_2$N), 3.59 – 3.47 (2 H, m, OC*H*$_2$CH), 3.46 – 3.22 (11 H, s, CH_2C*H*$_2$O, N(C*H*$_3$)$_3$), 2.90 – 2.74 (10 H, m, 5 × CHC*H*$_2$CH), 2.44 – 2.28 (4 H, m, CHC*H*$_2$C*H*$_2$C=O), 2.13 – 1.97 (2 H, m, CHC*H*$_2$$CH_3$), 1.48 (2 H, p, *J* = 6.9 Hz, C*H*$_2$$CH_2$O), 1.34 – 1.20 (26 H, m, 13 × C*H*$_2$), 0.95 (3 H, t, *J* = 7.5 Hz, C*H*$_3$), 0.86 (3 H, t, *J* = 6.5 Hz, C*H*$_3$); **^{13}C NMR** δ_C (75 MHz, $CDCl_3$) 172.9 (*C*=O), 132.1 (*C*H=CH), 129.4 (*C*H=CH), 128.7 (*C*H=CH), 128.4 (3 × *C*H=CH), 128.2 (3 × *C*H=CH), 128.1

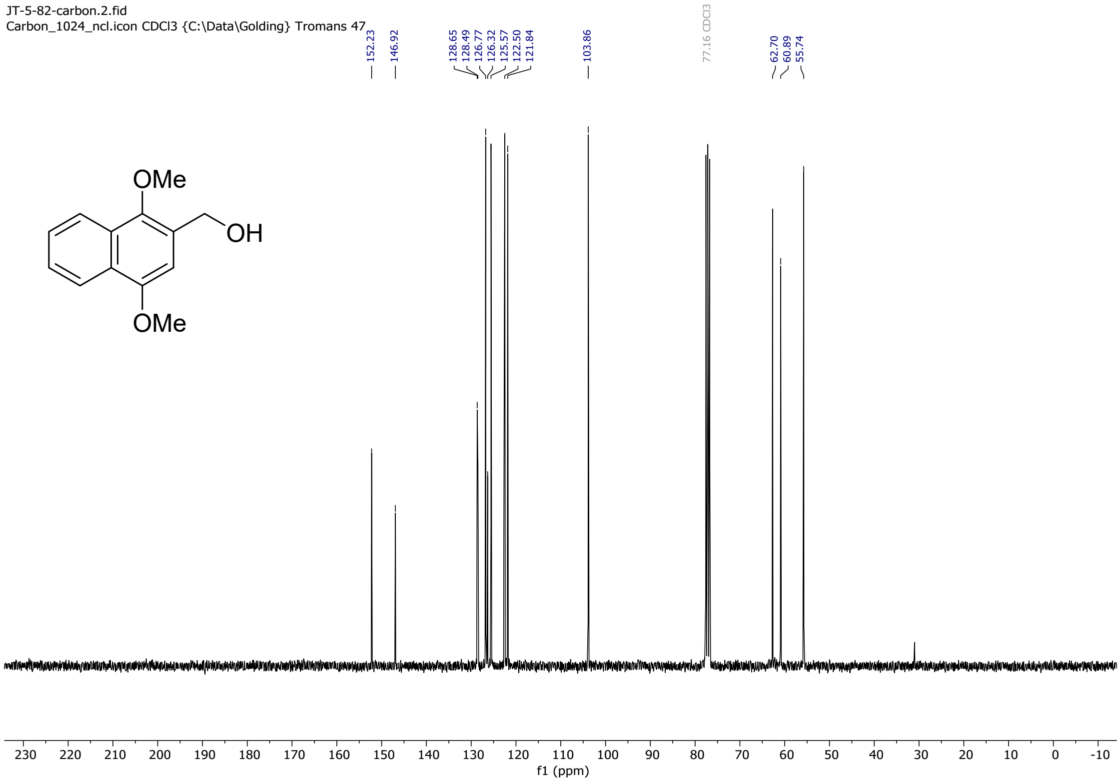
(*C*H=CH), 128.0 (*C*H=CH), 127.1 (*C*H=CH), 72.3 (*C*H_2O), 71.8 (O*C*H_2CH), 69.5 (*C*HOC=O), 66.5 (*C*H_2N), 64.0 (*C*H_2OP), 59.4 (PO*C*H_2), 54.5 (N(*C*H_3)$_3$), 34.4 (*C*H_2C=O), 32.0 (*C*H_2), 29.8 (11 × *C*H_2), 29.5 (*C*H_2), 26.2 (*C*H_2), 25.7 (5 × CH*C*H_2CH), 22.8 (*C*H_2CH_2C=O, *C*H_2), 20.7 (CH*C*H_2CH_3), 14.4 (*C*H_3), 14.2 (*C*H_3); ^{31}**P NMR** δ $_P$ (121 MHz, $CDCl_3$) δ -1.0; **IR** ν_{max} / cm^{-1} 3360 br, 3014, 2925, 2855, 1733, 1461, 1239, 1090, 1053, 969, 770, 719; **HRMS** (TOF MS ESI+) calcd $C_{46}H_{92}NO_7P$ [M+H]$^+$ 792.5902, found 792.5905.

^{1}H, ^{13}C and ^{31}P NMR spectra

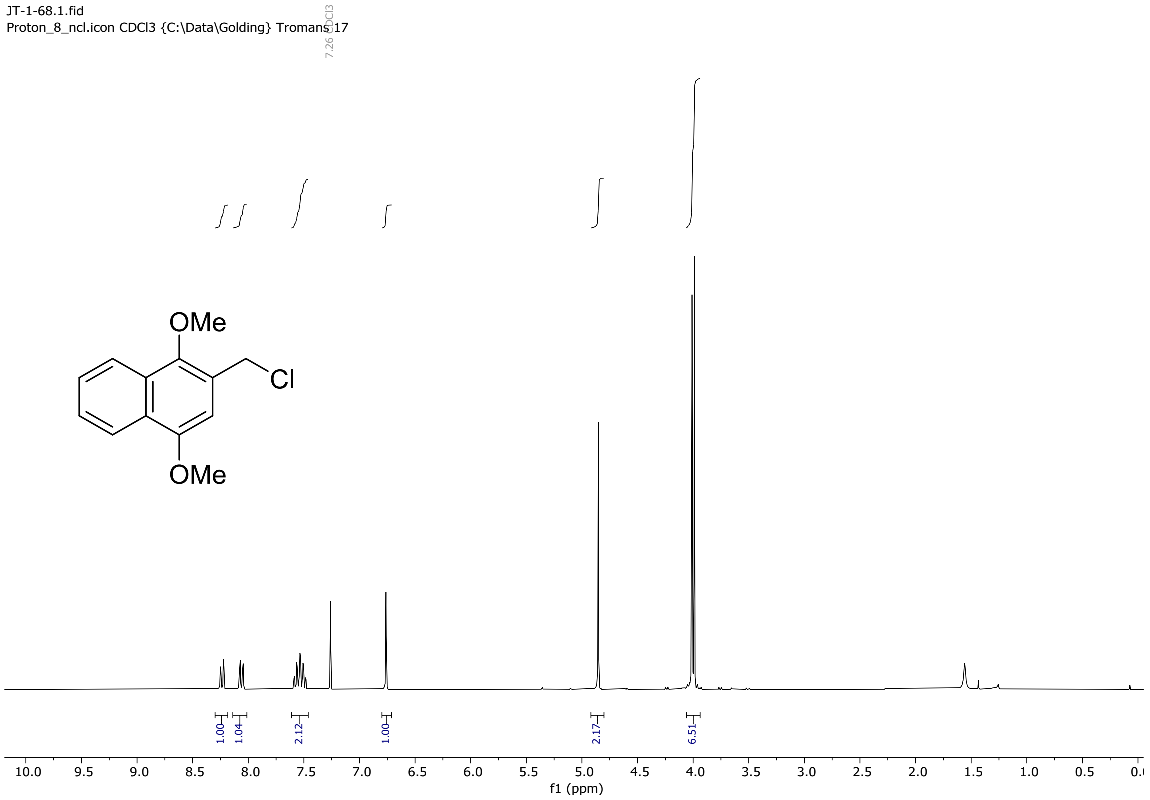
(1,4-Dimethoxynaphthalen-2-yl)methanol [2] ^{1}H NMR ($CDCl_3$)



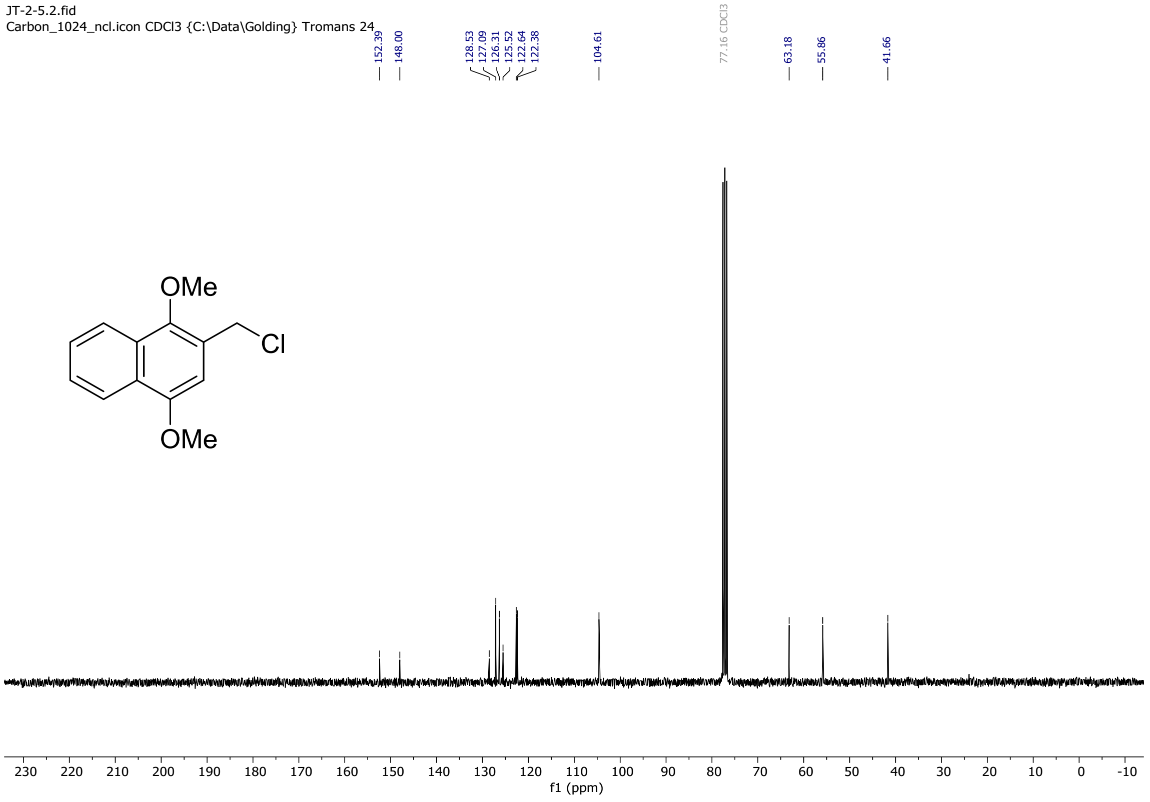
(1,4-Dimethoxynaphthalen-2-yl)methanol [2] ^{13}C NMR ($CDCl_3$)



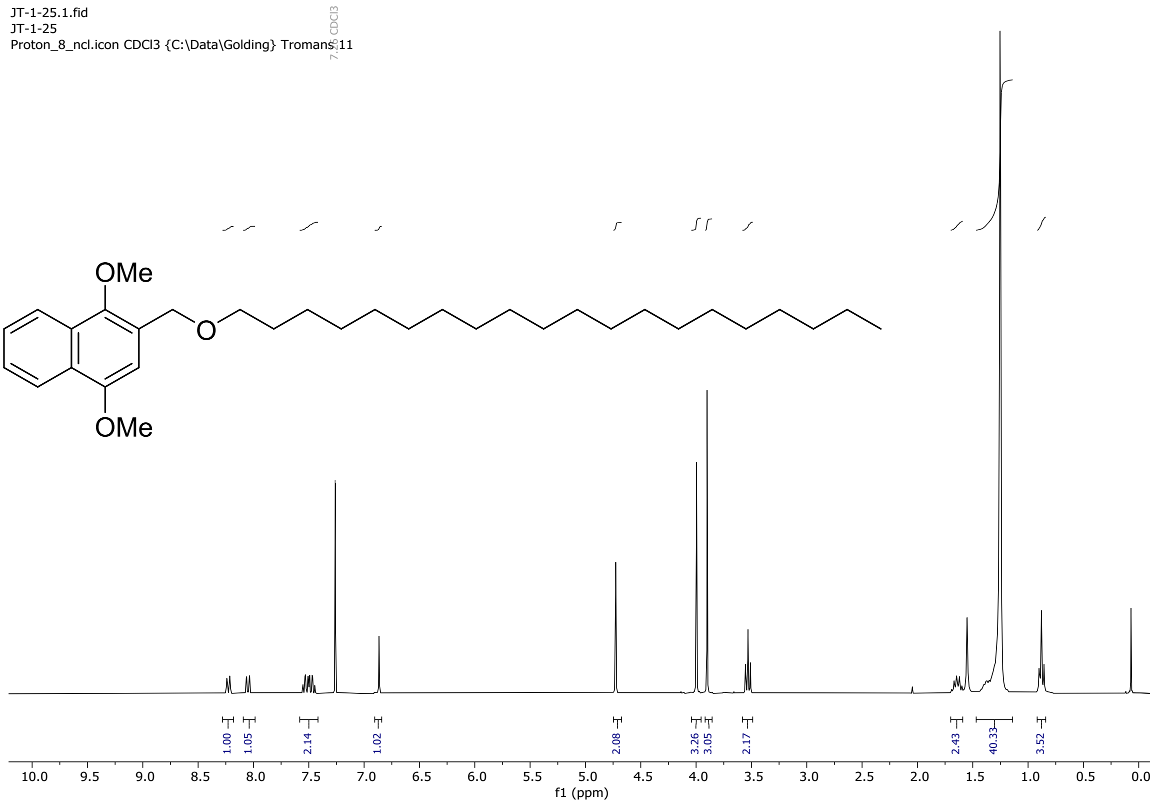
2-(Chloromethyl)-1,4-dimethoxynaphthalene [1] ^{1}H NMR (CDCl$_3$)



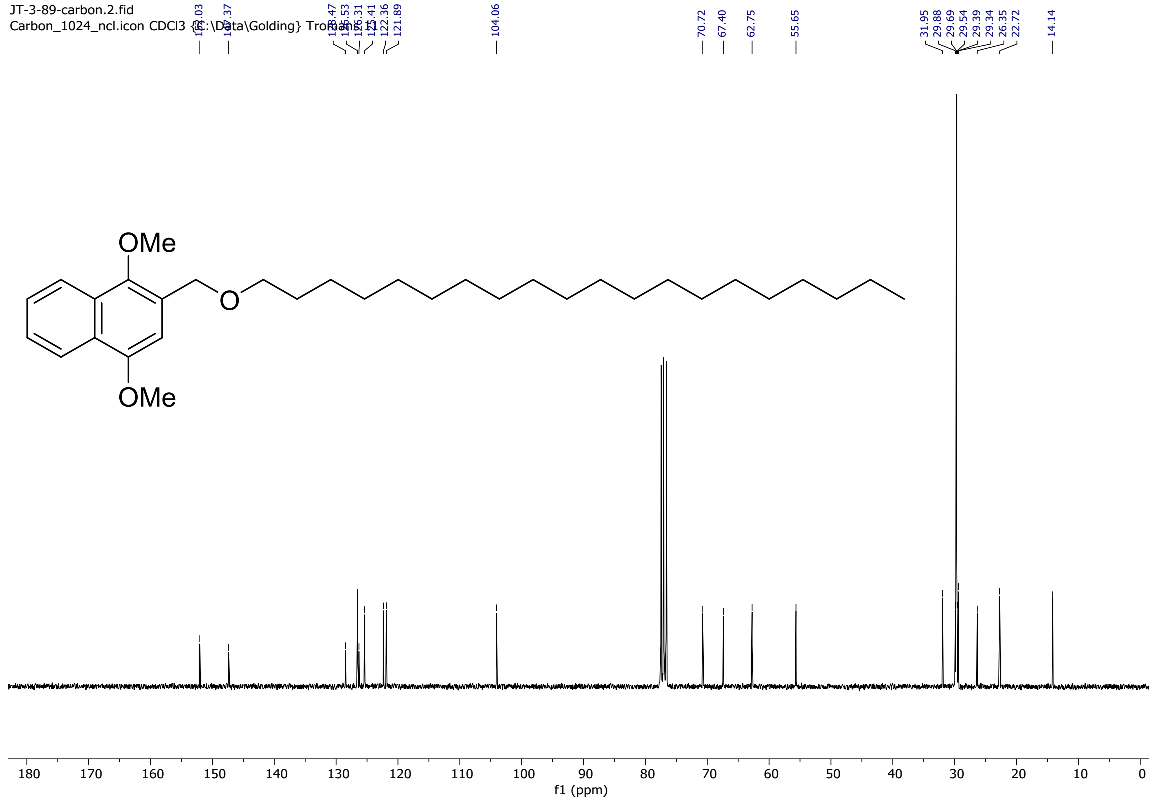
2-(Chloromethyl)-1,4-dimethoxynaphthalene [1] ^{13}C NMR (CDCl$_3$)



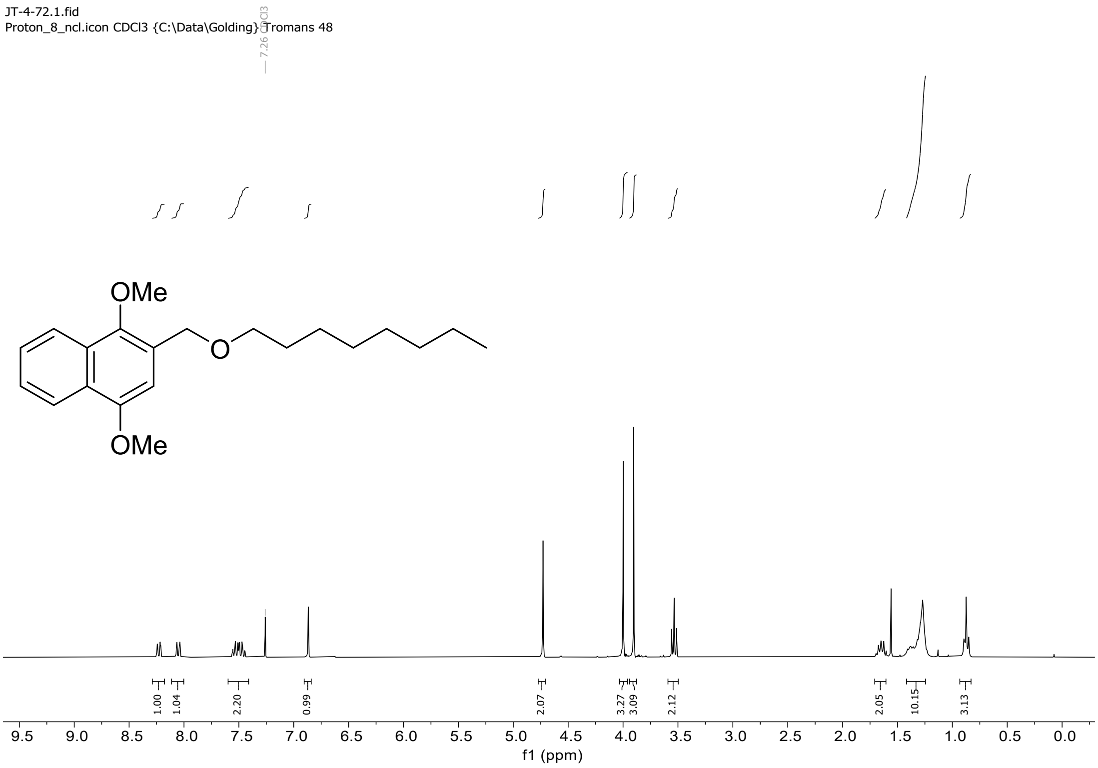
2-((Icosyloxy)methyl)-1,4-dimethoxynaphthalene [5a] ^{1}H NMR (CDCl$_3$)



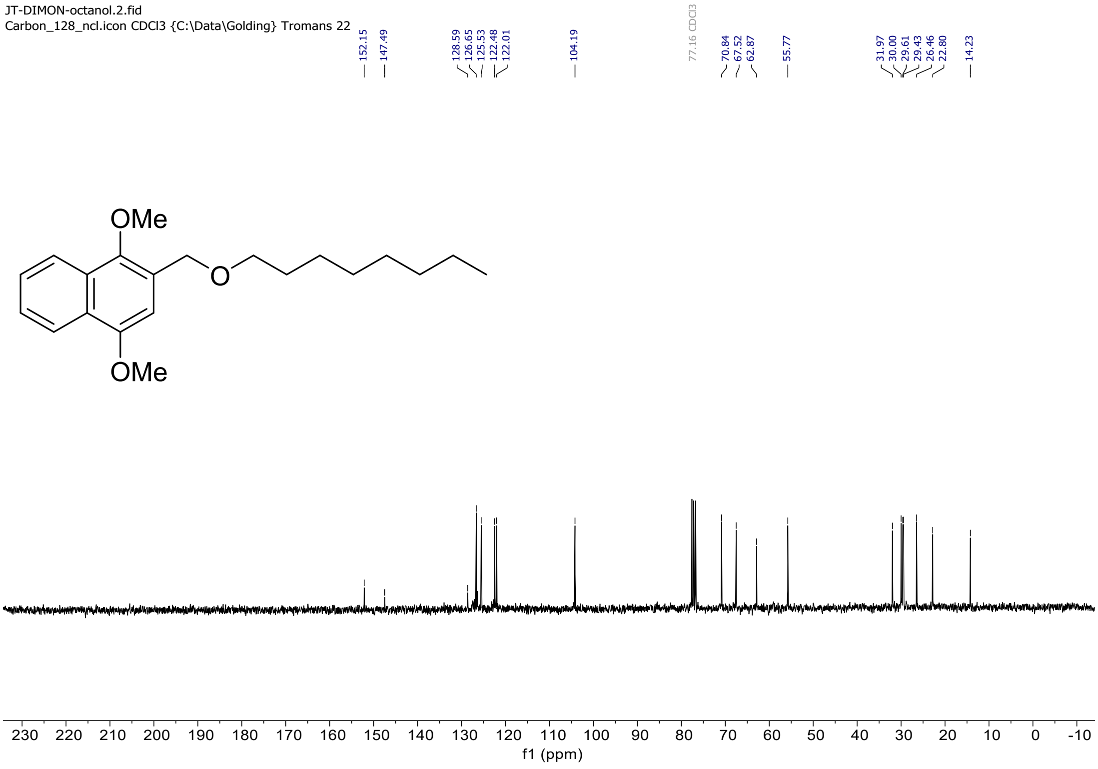
2-((Icosyloxy)methyl)-1,4-dimethoxynaphthalene [5a] ^{13}C NMR (CDCl$_3$)



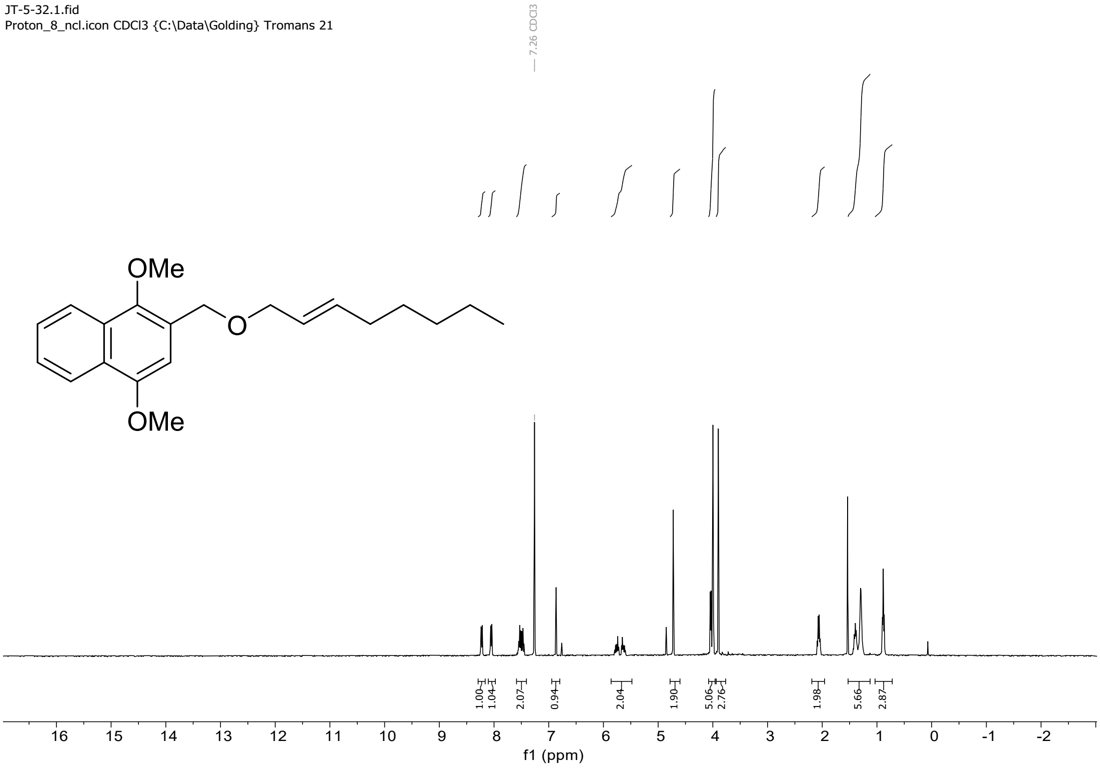
1,4-Dimethoxy-2-((octyloxy)methyl)naphthalene [5b] ^{1}H NMR ($CDCl_3$)



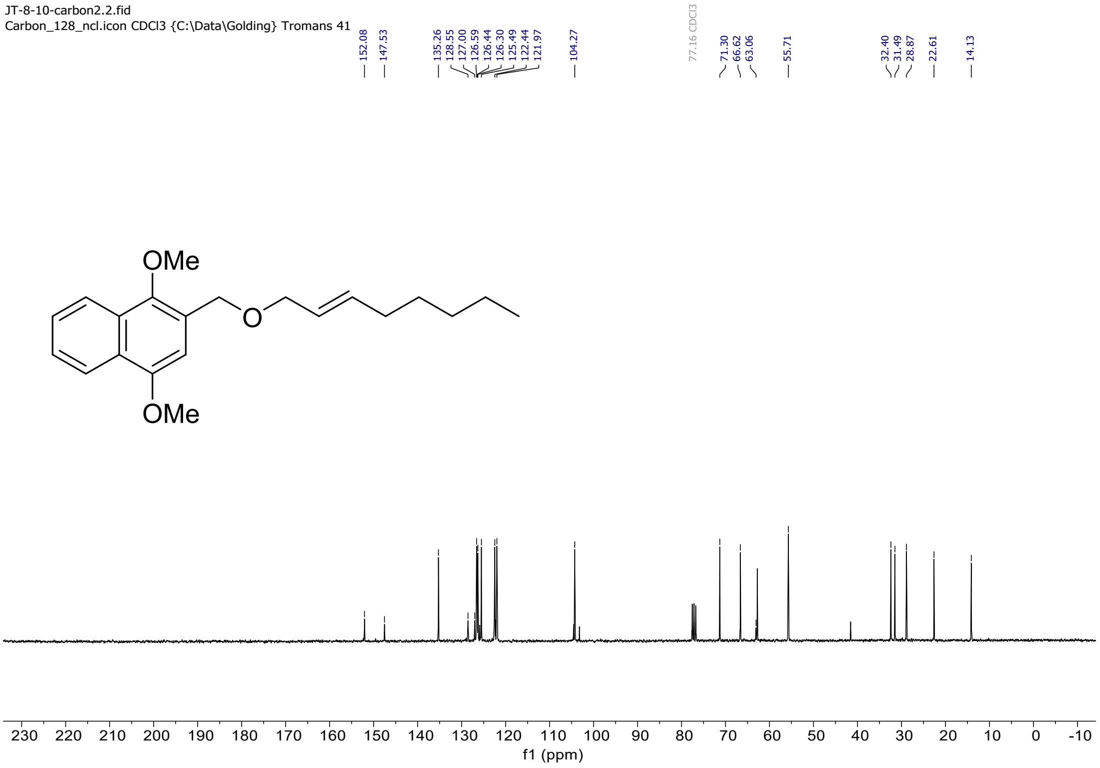
1,4-Dimethoxy-2-((octyloxy)methyl)naphthalene [5b] ^{13}C NMR ($CDCl_3$)



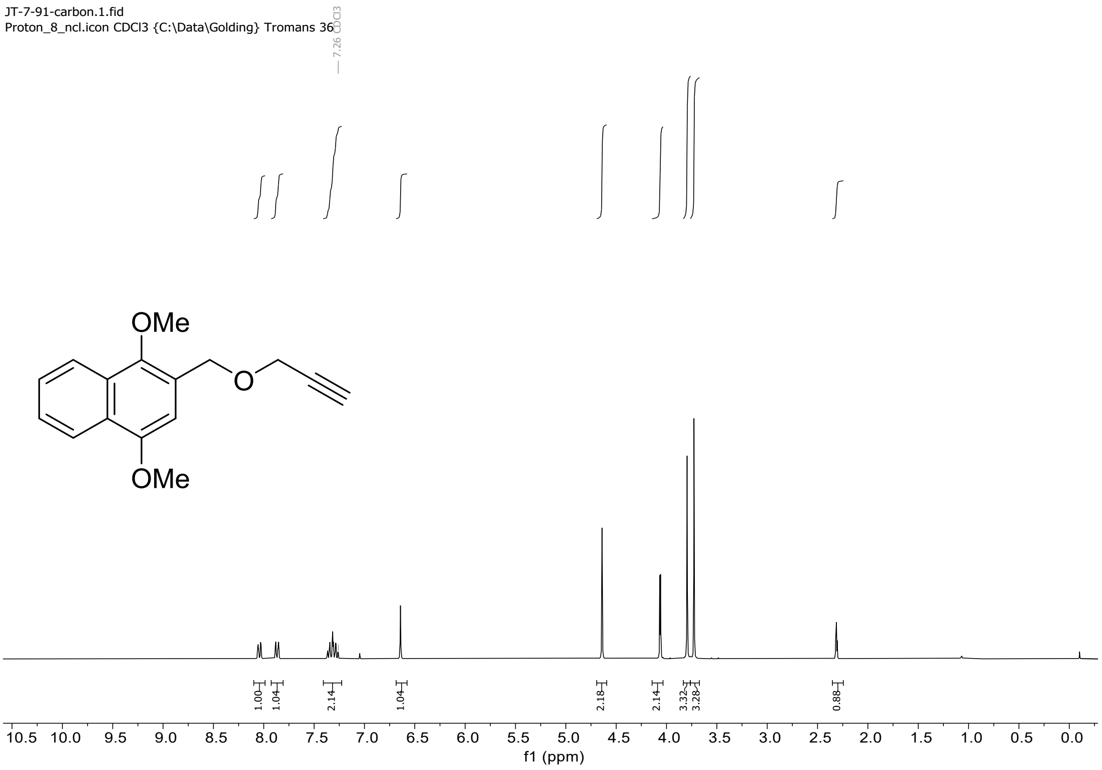
(*E*)-1,4-Dimethoxy-2-((oct-2-en-1-yloxy)methyl)naphthalene [5c] ^{1}H NMR (CDCl$_3$)



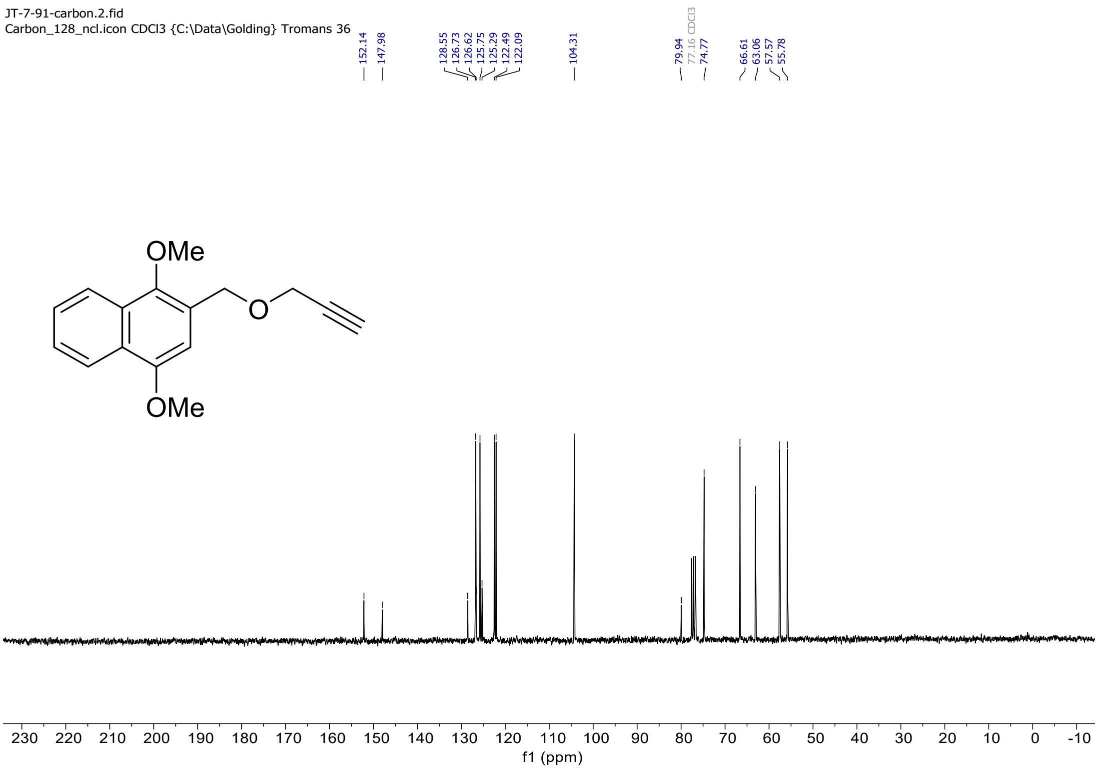
(*E*)-1,4-Dimethoxy-2-((oct-2-en-1-yloxy)methyl)naphthalene [5c] ^{13}C NMR (CDCl$_3$)



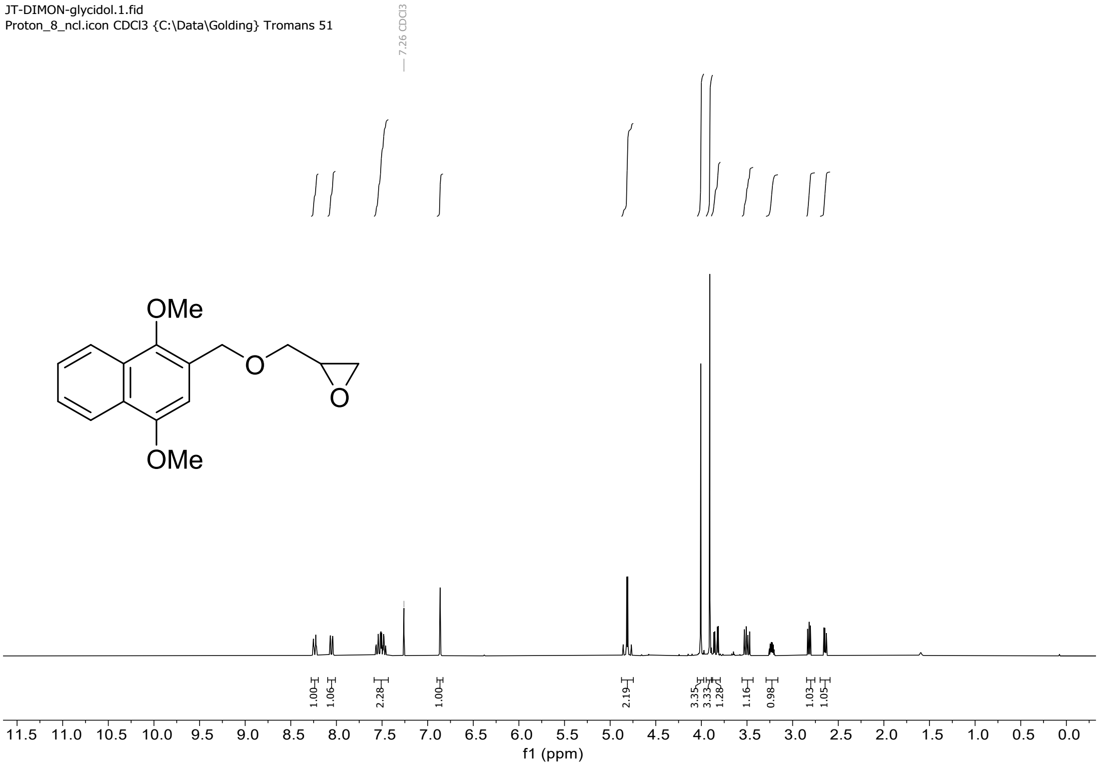
1,4-Dimethoxy-2-((prop-2-yn-1-yloxy)methyl)naphthalene [5d] ^{1}H NMR (CDCl$_3$)



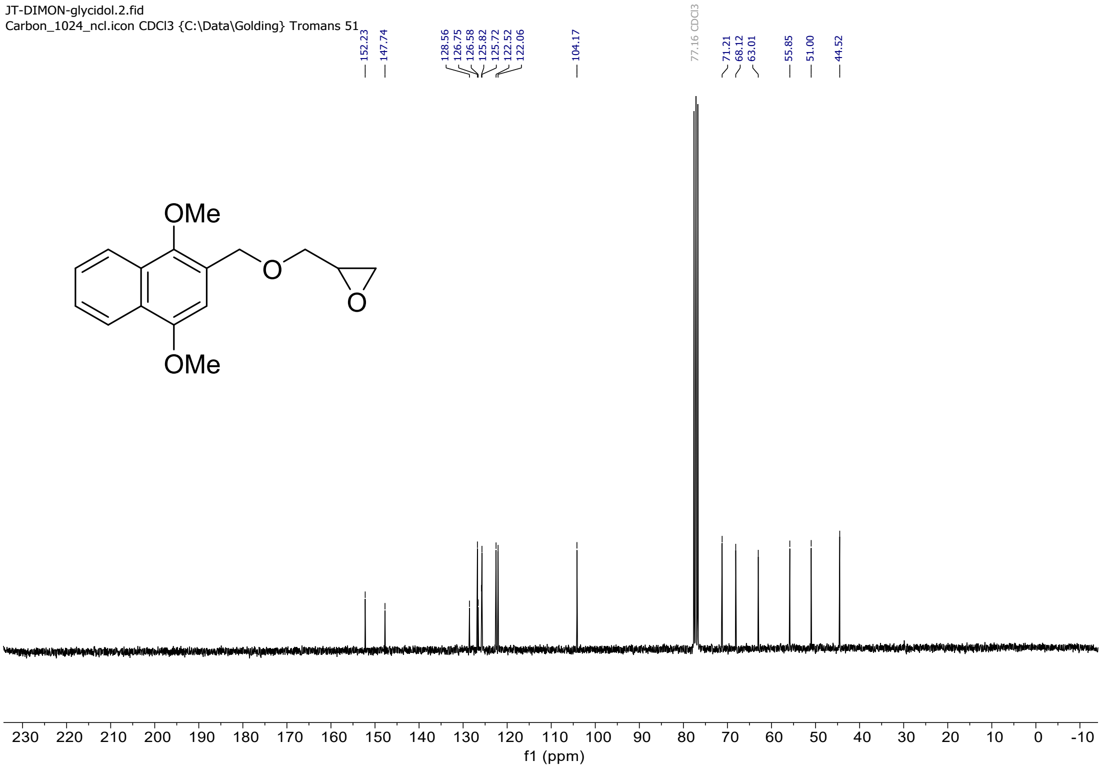
1,4-Dimethoxy-2-((prop-2-yn-1-yloxy)methyl)naphthalene [5d] ^{13}C NMR (CDCl$_3$)



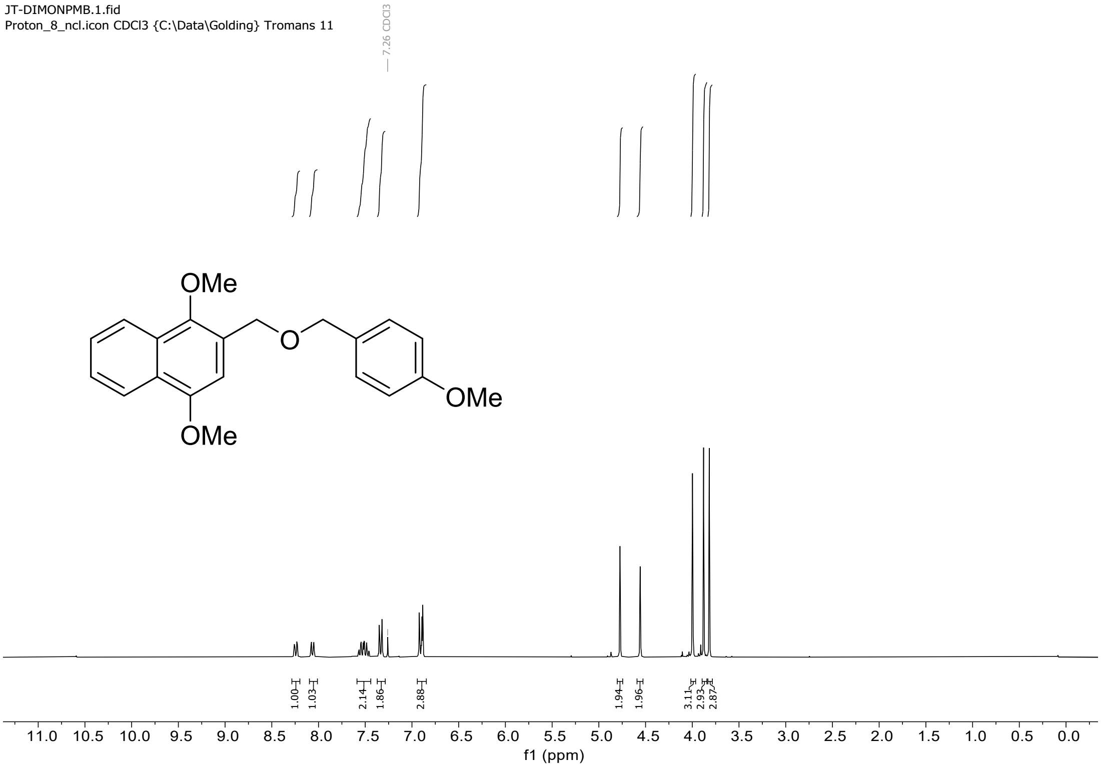
2-(((1,4-Dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane [5e] ^{1}H NMR (CDCl$_3$)



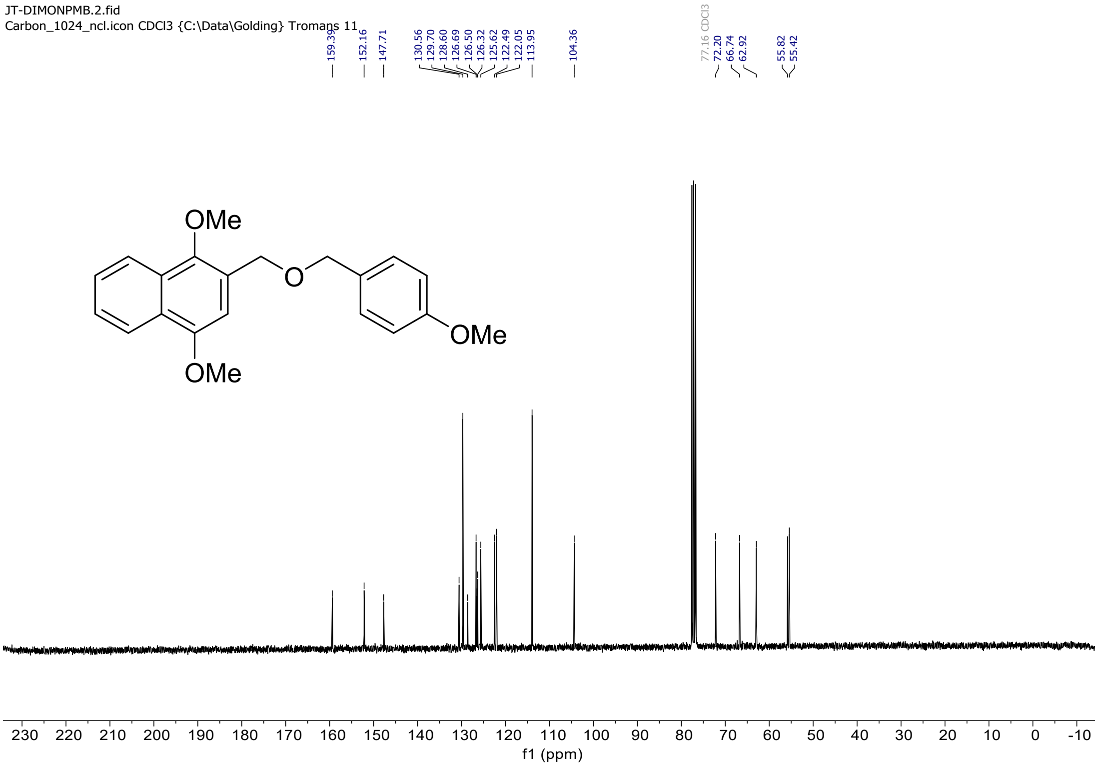
2-(((1,4-Dimethoxynaphthalen-2-yl)methoxy)methyl)oxirane [5e] ^{13}C NMR (CDCl$_3$)



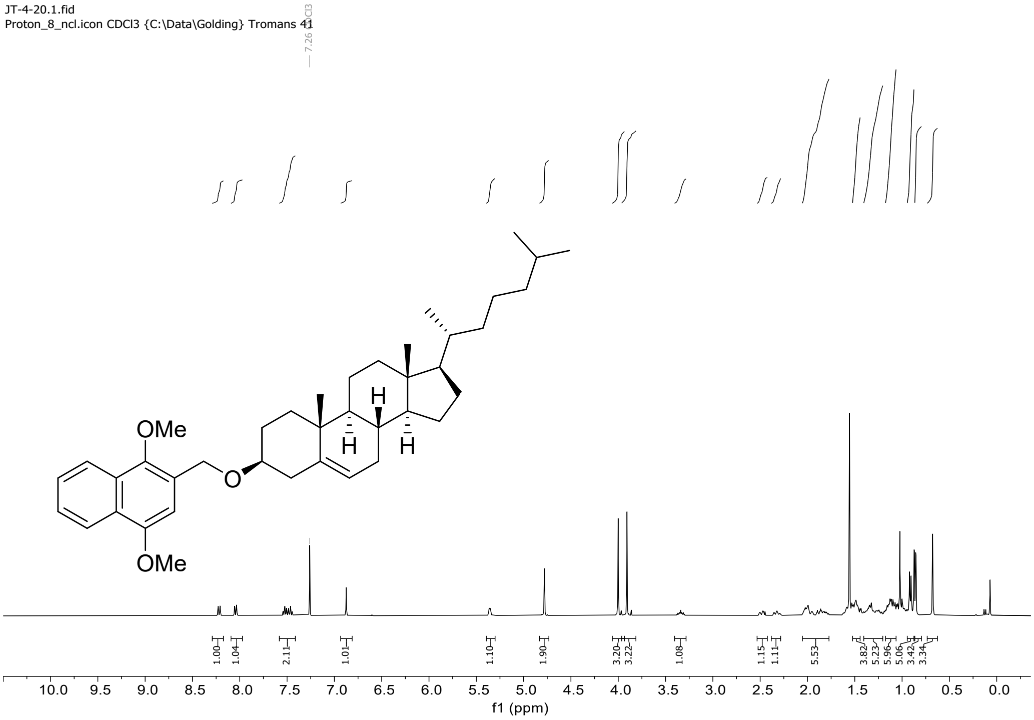
1,4-Dimethoxy-2-(((4-methoxybenzyl)oxy)methyl)naphthalene [5f] ^{1}H NMR (CDCl$_3$)



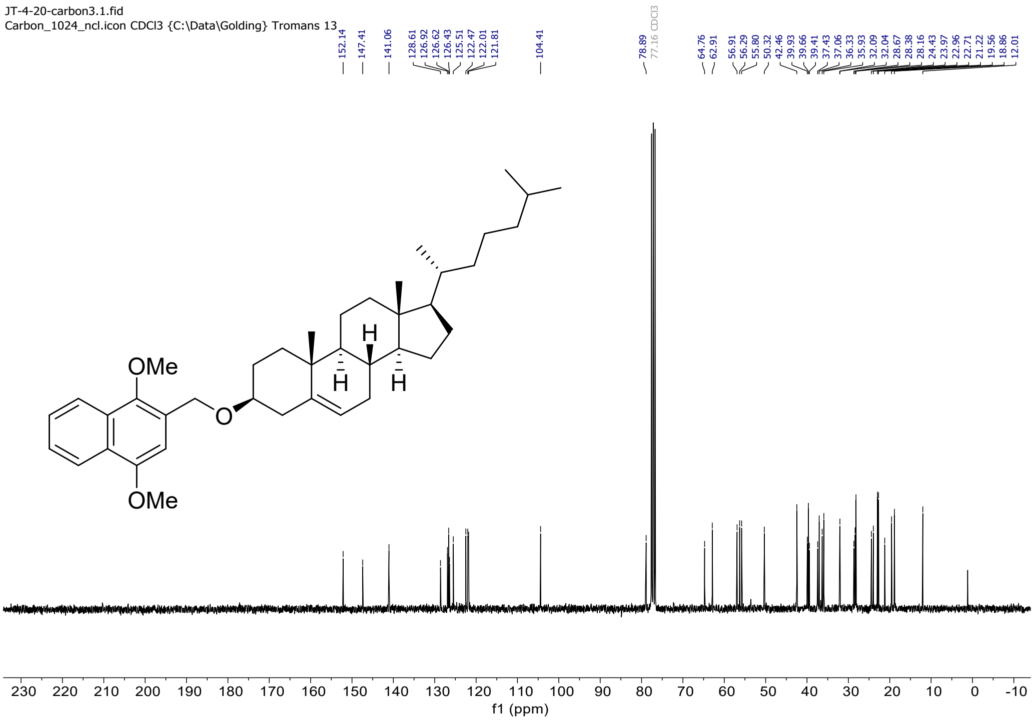
1,4-Dimethoxy-2-(((4-methoxybenzyl)oxy)methyl)naphthalene [5f] ^{13}C NMR (CDCl$_3$)



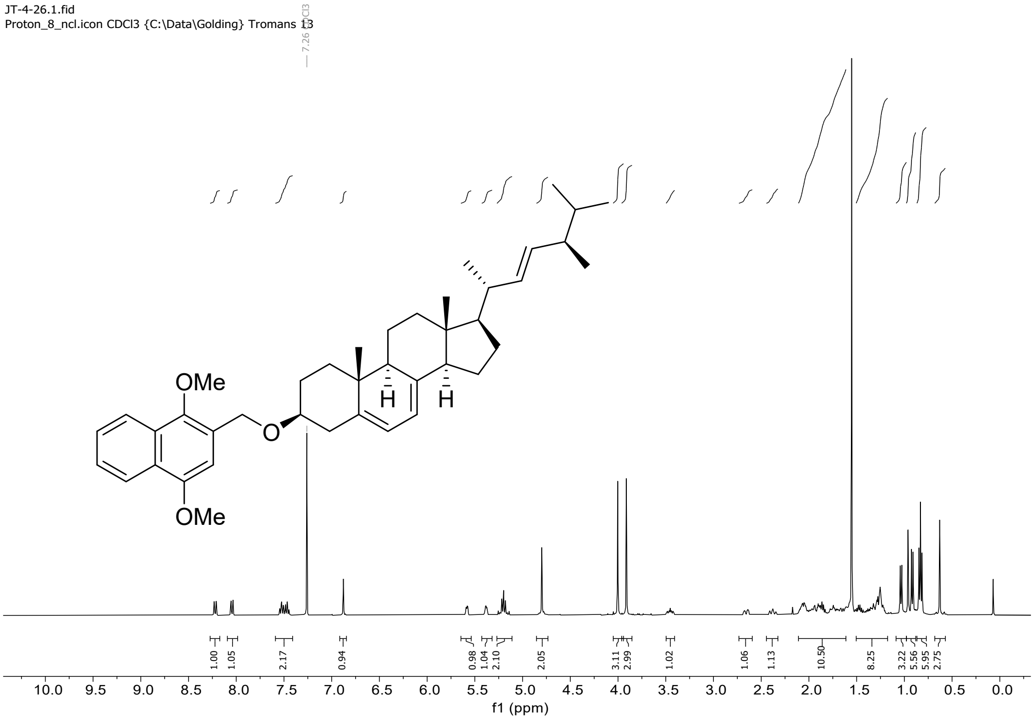
(3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-3-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene [5g] ^{1}H NMR (CDCl$_3$)



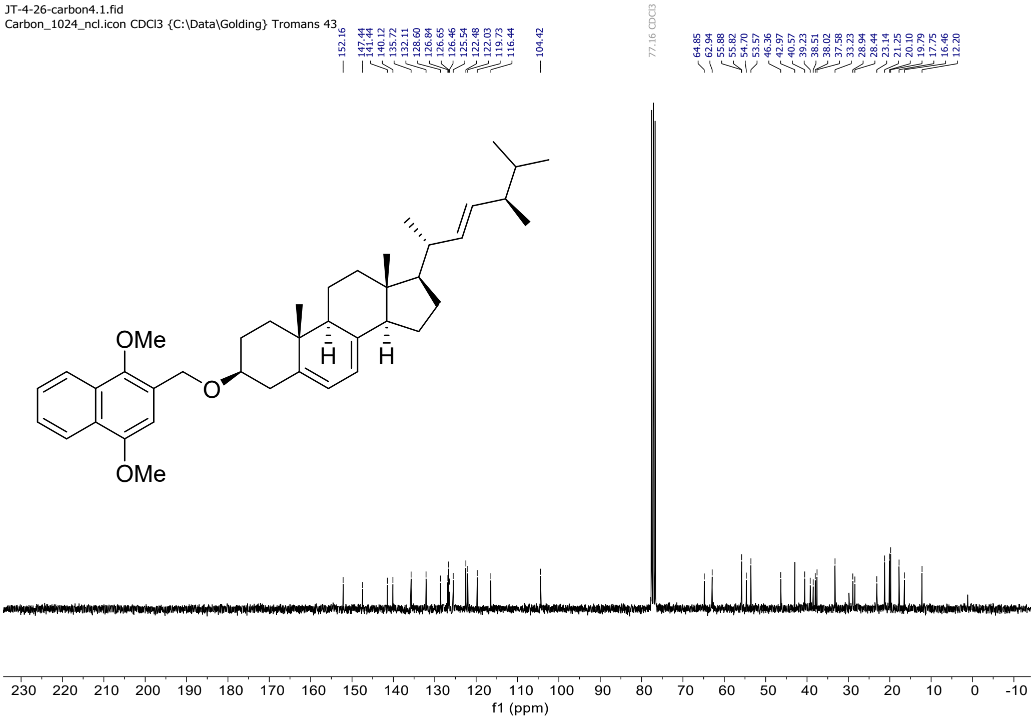
(3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-3-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene [5g] ^{13}C NMR (CDCl$_3$)



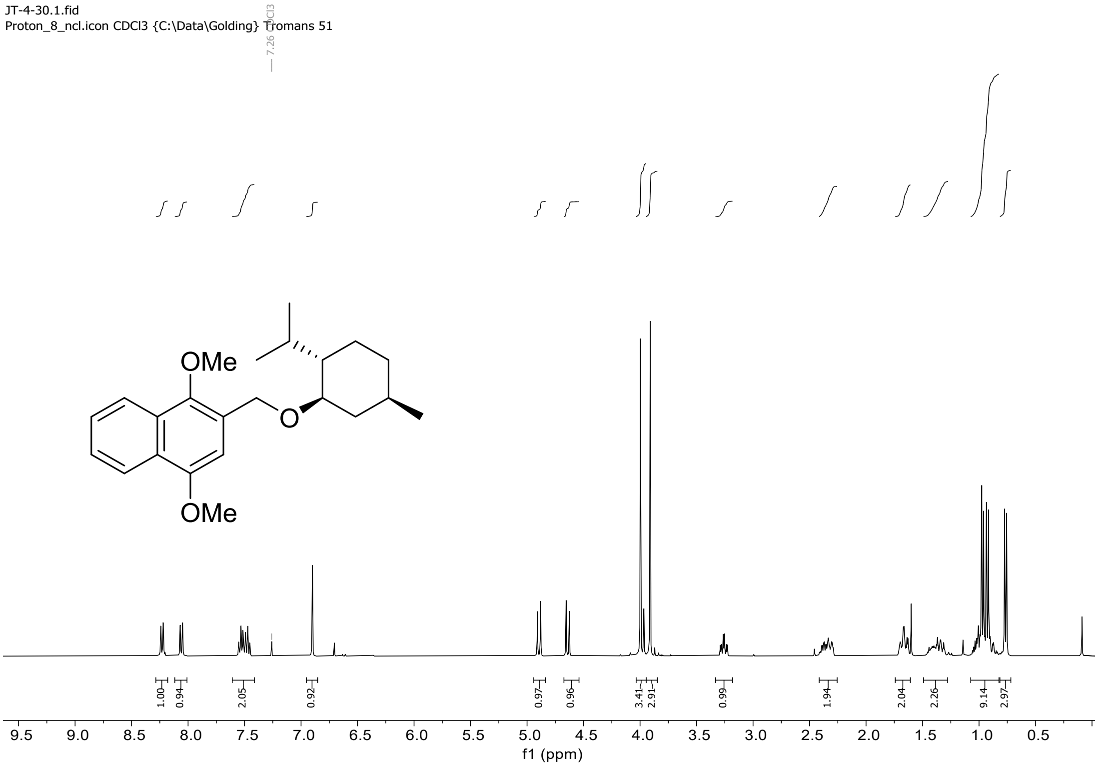
(3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-3-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene [5h] ^{1}H NMR ($CDCl_3$)



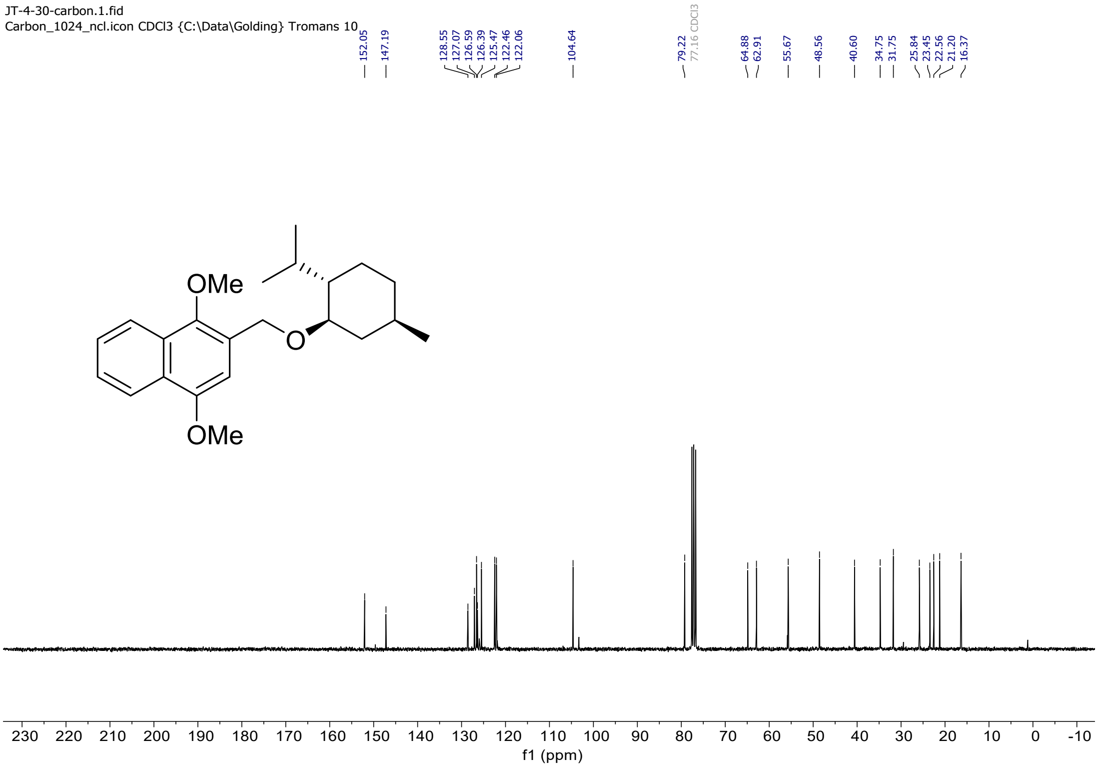
(3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-3-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-17-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene [5h] ^{13}C NMR ($CDCl_3$)



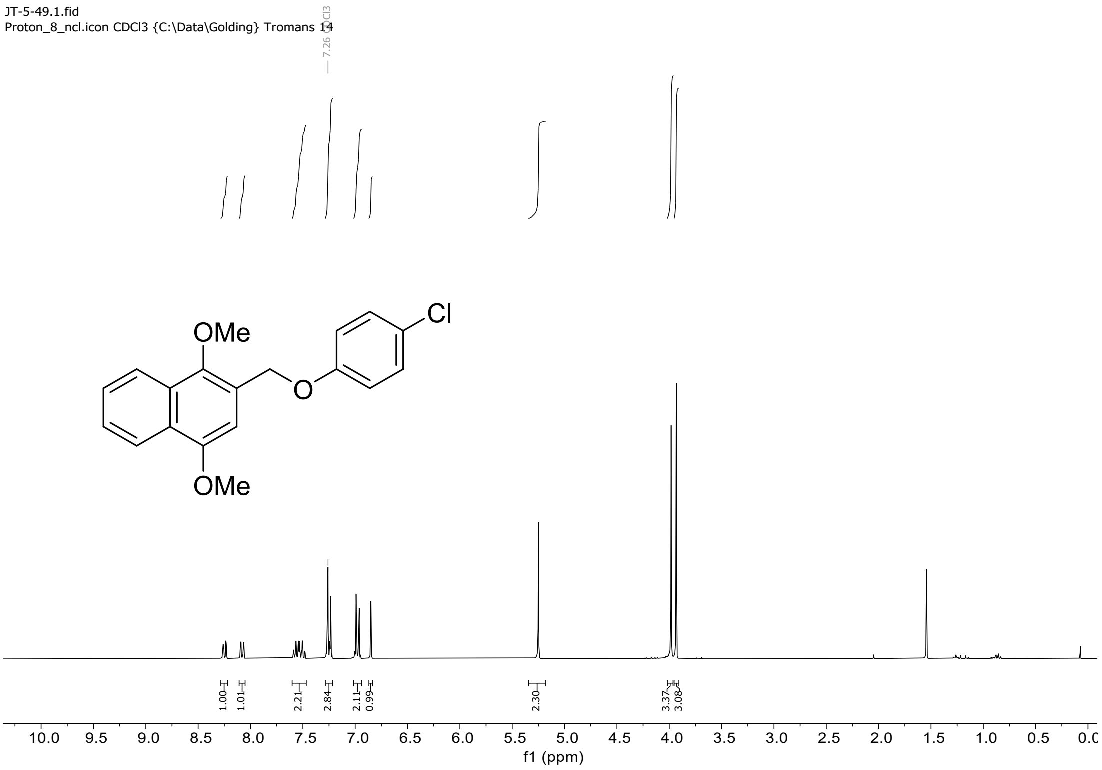
2-((((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)methyl)-1,4-dimethoxynaphthalene [5i] ^{1}H NMR (CDCl$_3$)



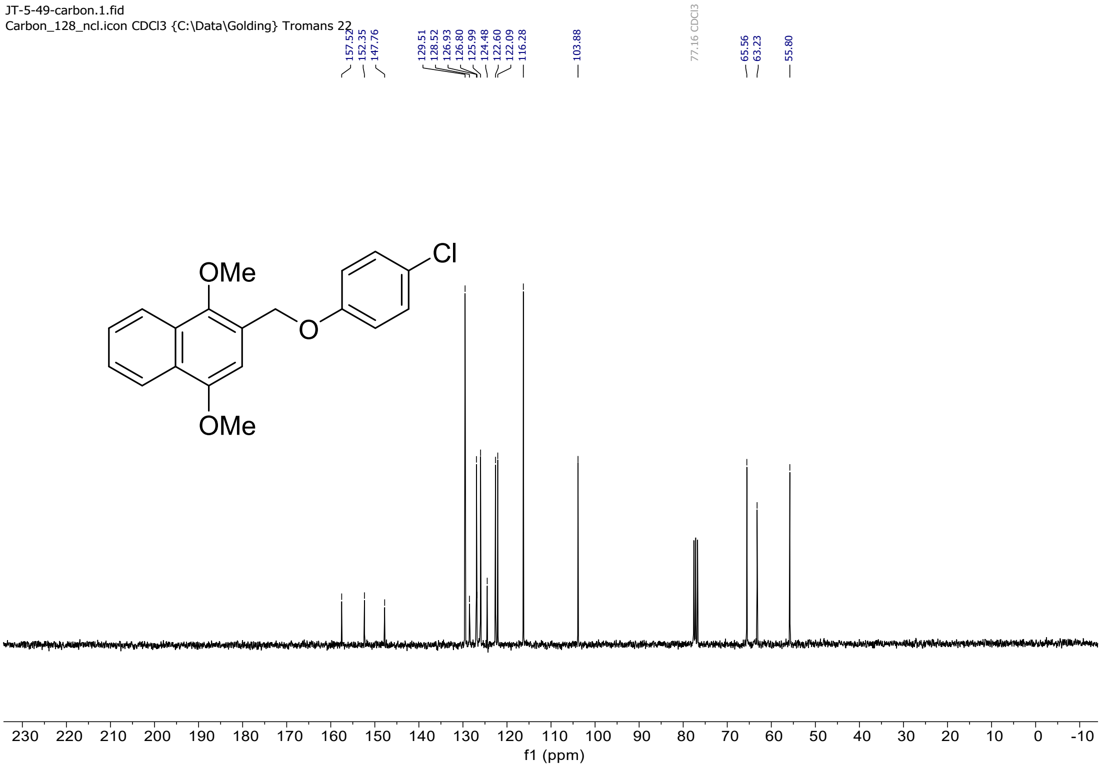
2-((((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)methyl)-1,4-dimethoxynaphthalene [5i] ^{13}C NMR (CDCl$_3$)



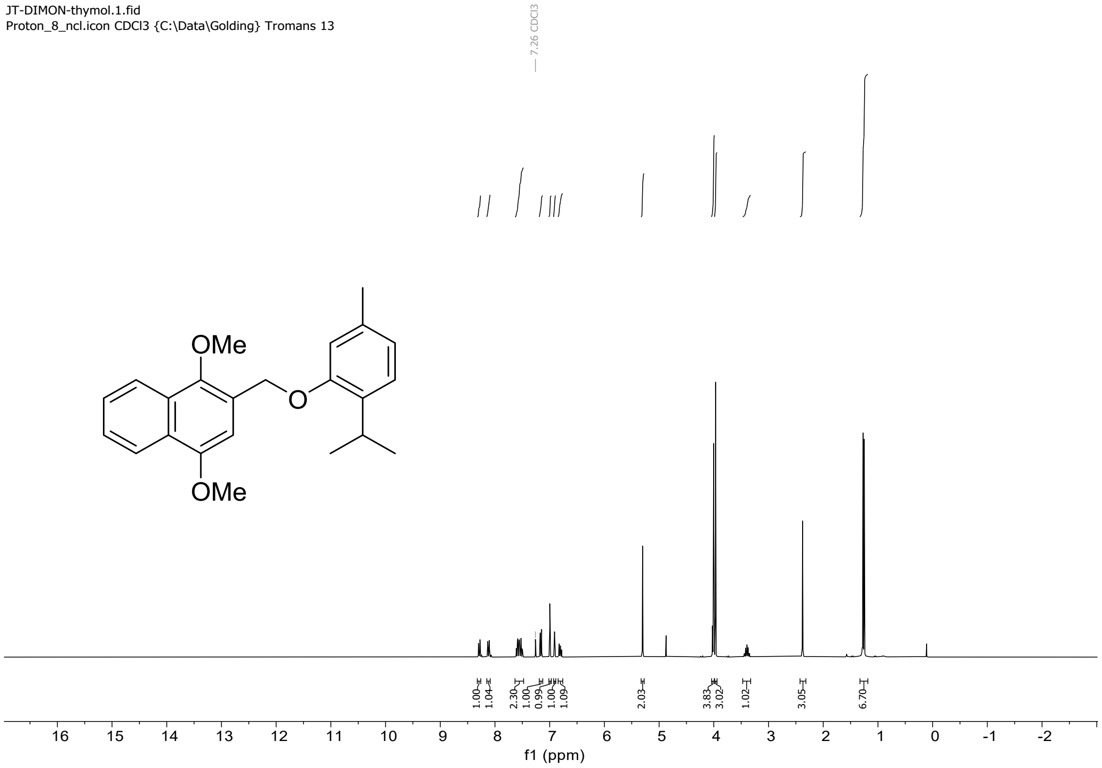
2-((4-Chlorophenoxy)methyl)-1,4-dimethoxynaphthalene [5j] ^{1}H NMR (CDCl$_3$)



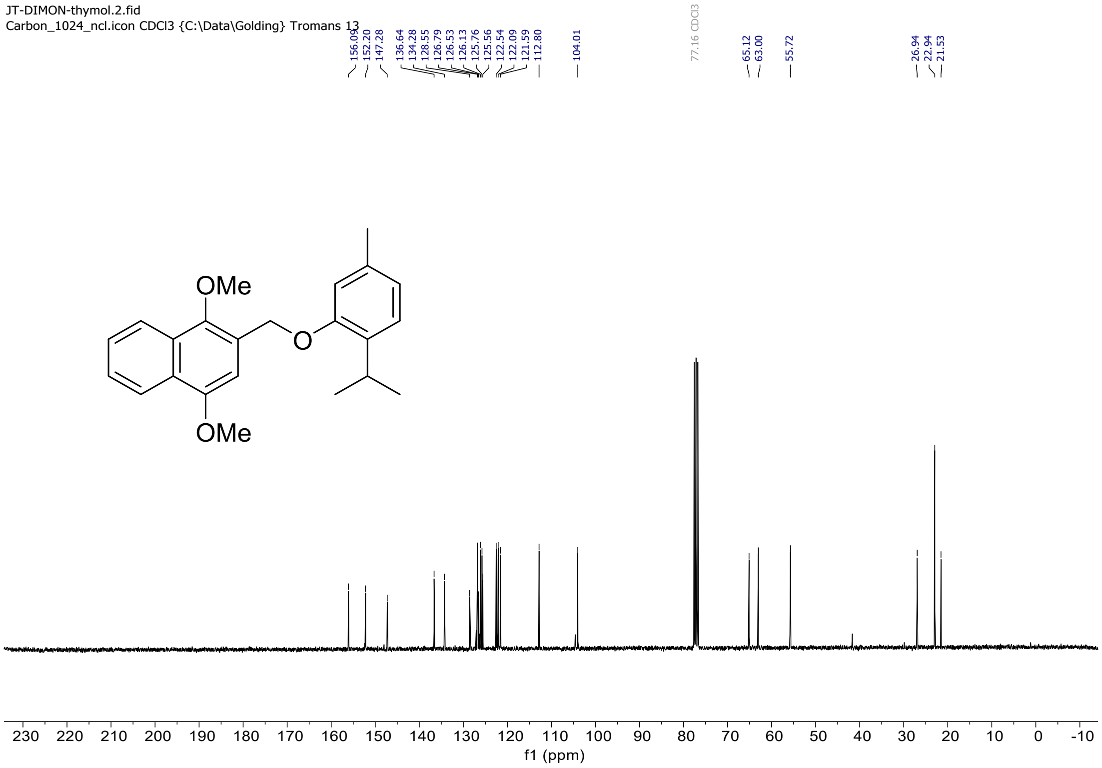
2-((4-Chlorophenoxy)methyl)-1,4-dimethoxynaphthalene [5j] ^{13}C NMR (CDCl$_3$)



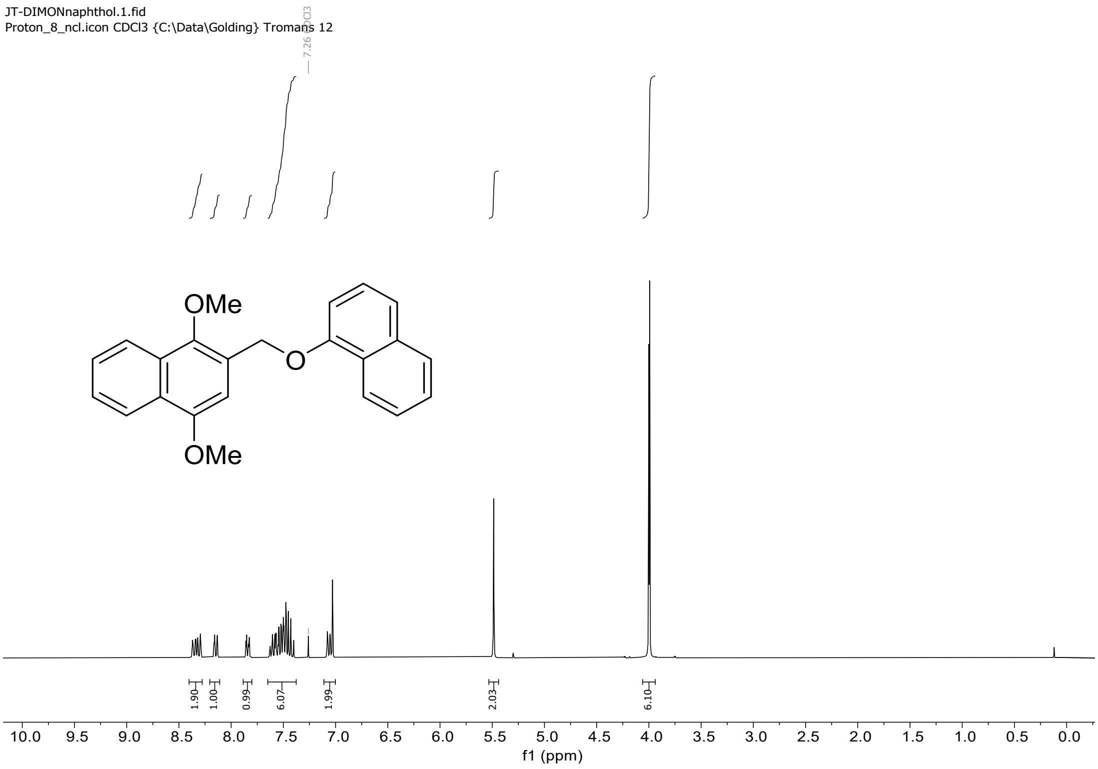
2-((2-Isopropyl-5-methylphenoxy)methyl)-1,4-dimethoxynaphthalene [5k] ^{1}H NMR (CDCl$_3$)



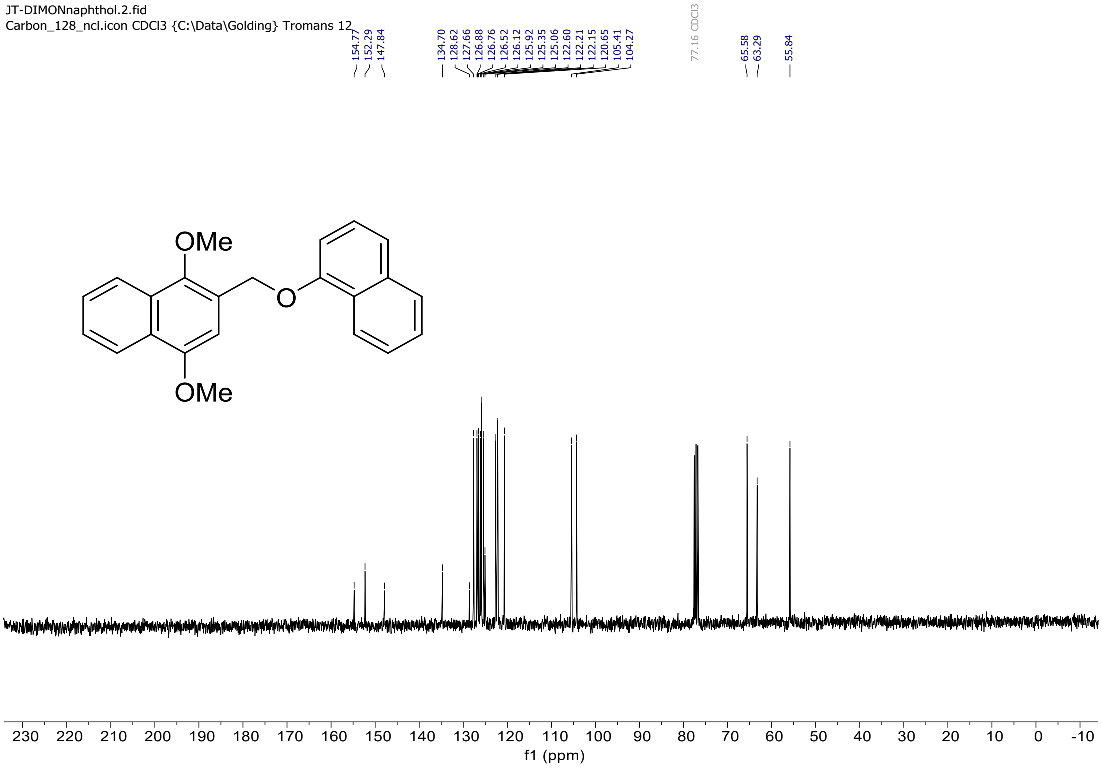
2-((2-Isopropyl-5-methylphenoxy)methyl)-1,4-dimethoxynaphthalene [5k] ^{13}C NMR (CDCl$_3$)



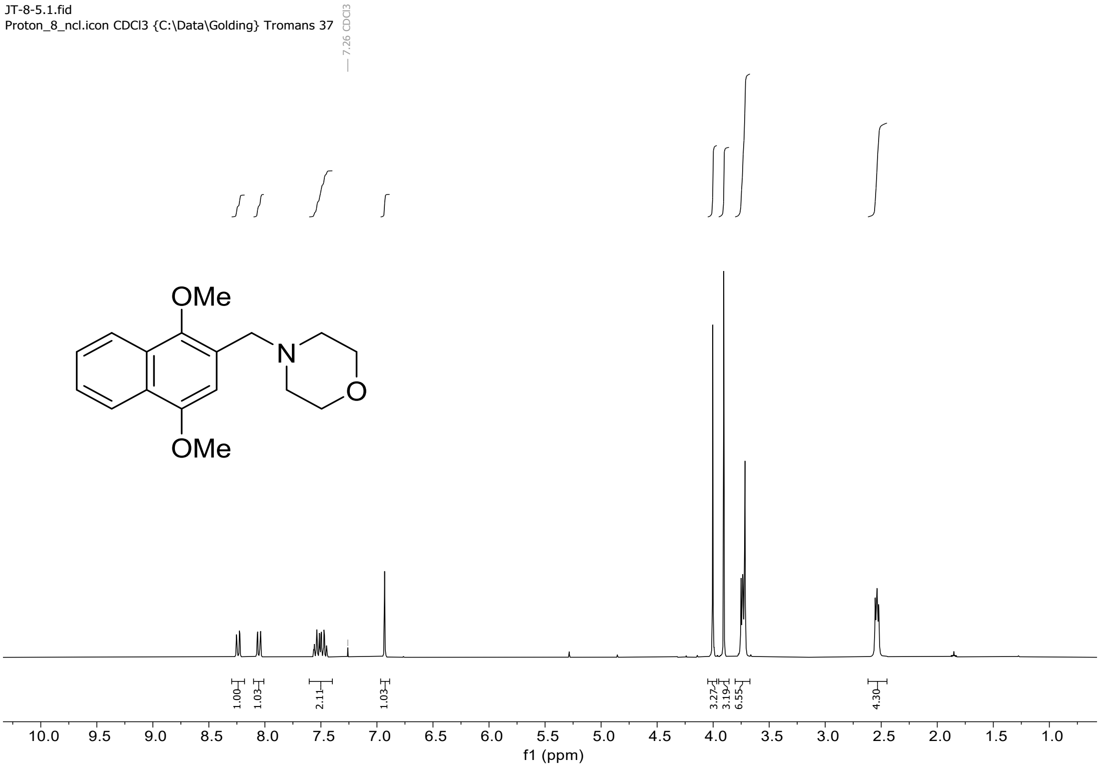
1,4-Dimethoxy-2-((naphthalen-1-yloxy)methyl)naphthalene [5l] ^{1}H NMR (CDCl$_3$)



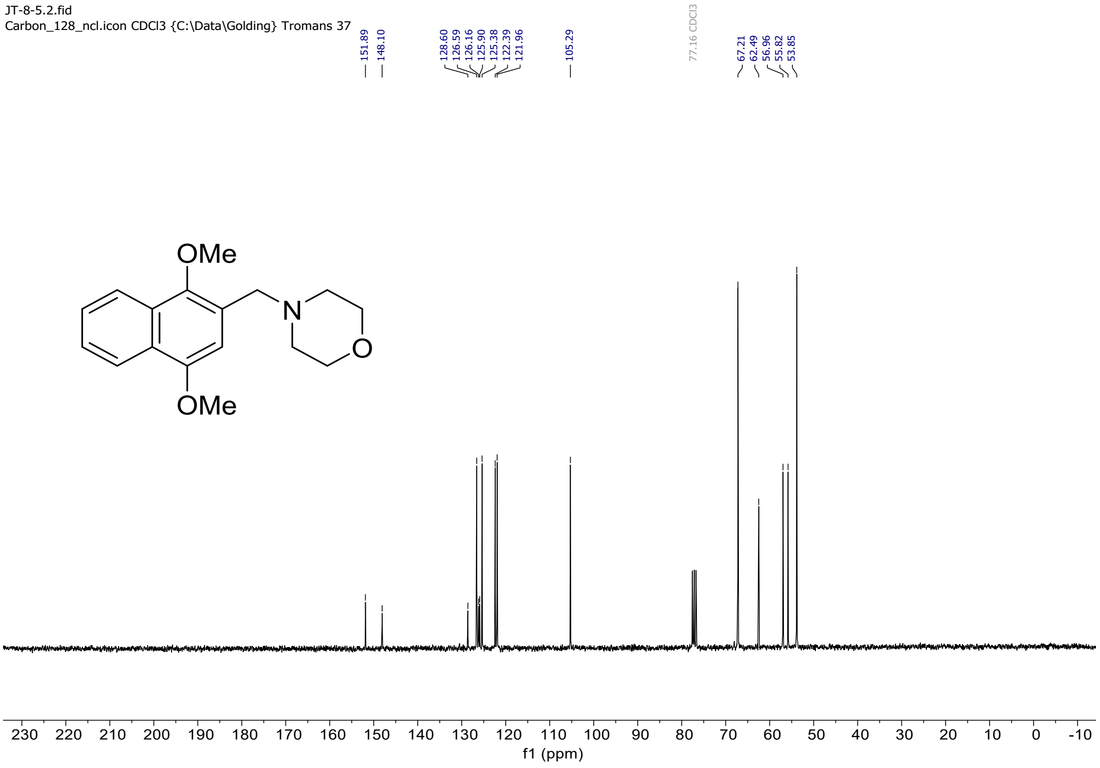
1,4-Dimethoxy-2-((naphthalen-1-yloxy)methyl)naphthalene [5l] ^{13}C NMR (CDCl$_3$)



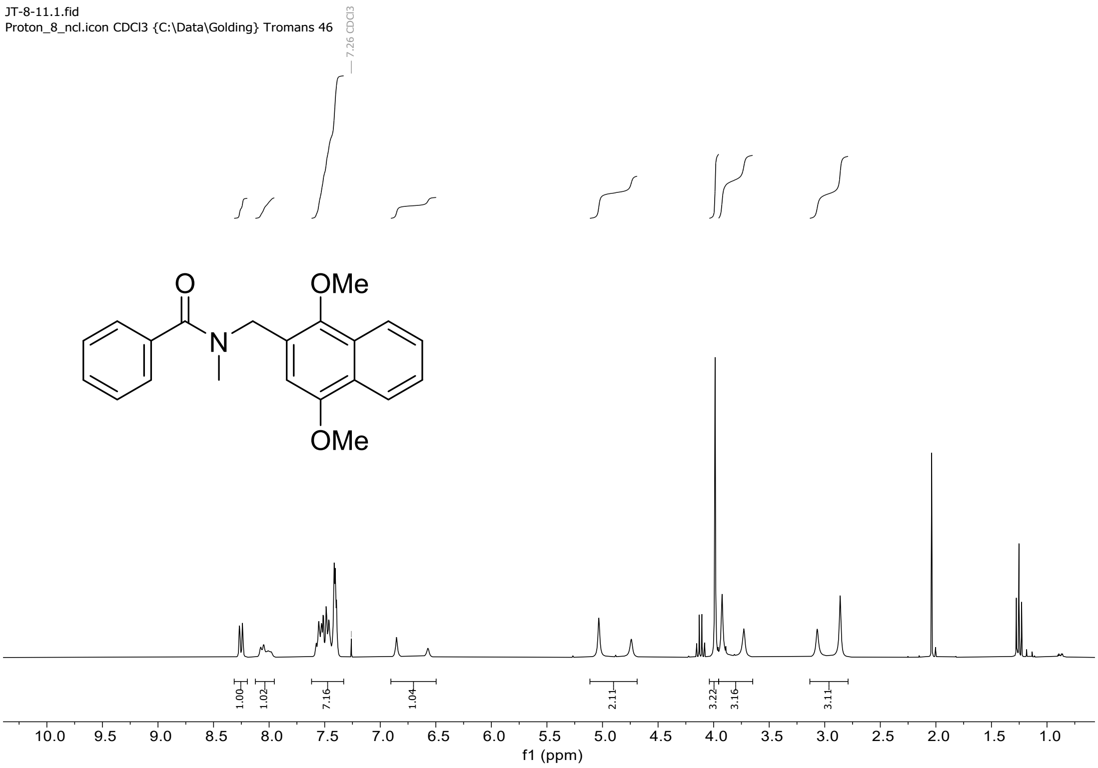
4-((1,4-Dimethoxynaphthalen-2-yl)methyl)morpholine [5m] ^{1}H NMR (CDCl$_3$)



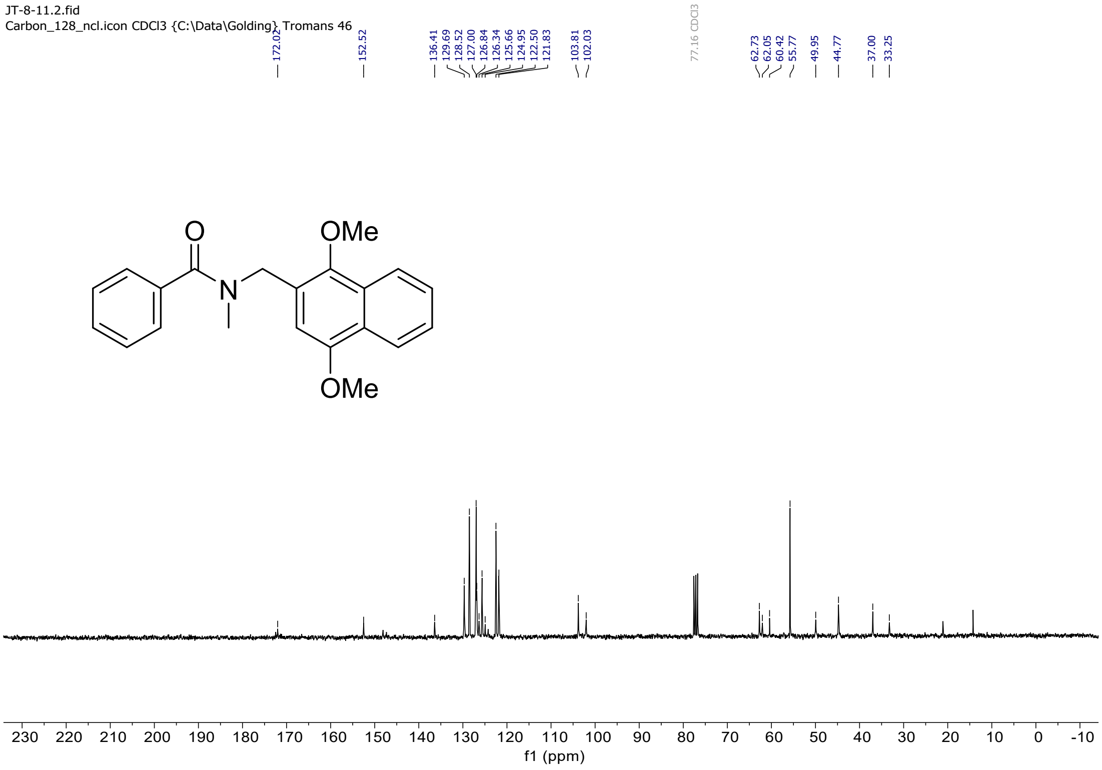
4-((1,4-Dimethoxynaphthalen-2-yl)methyl)morpholine [5m] ^{13}C NMR (CDCl$_3$)



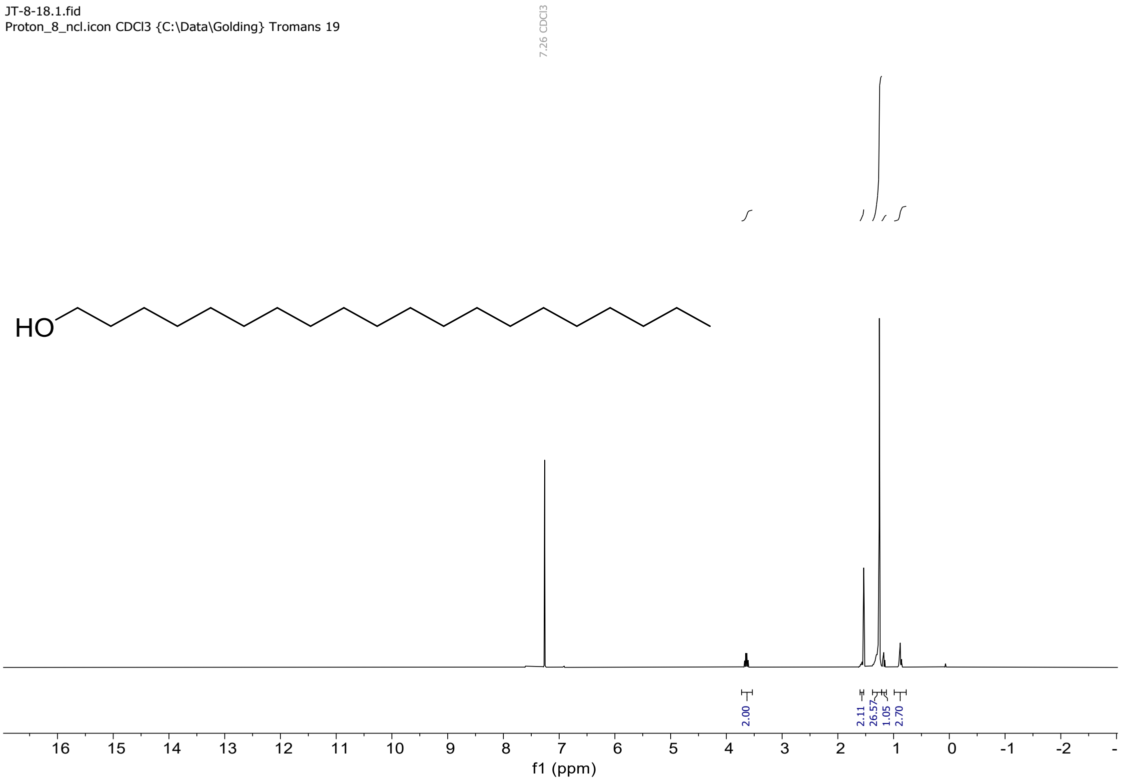
N-((1,4-Dimethoxynaphthalen-2-yl)methyl)-*N*-methylbenzamide [5n] ^{1}H NMR (CDCl$_3$)



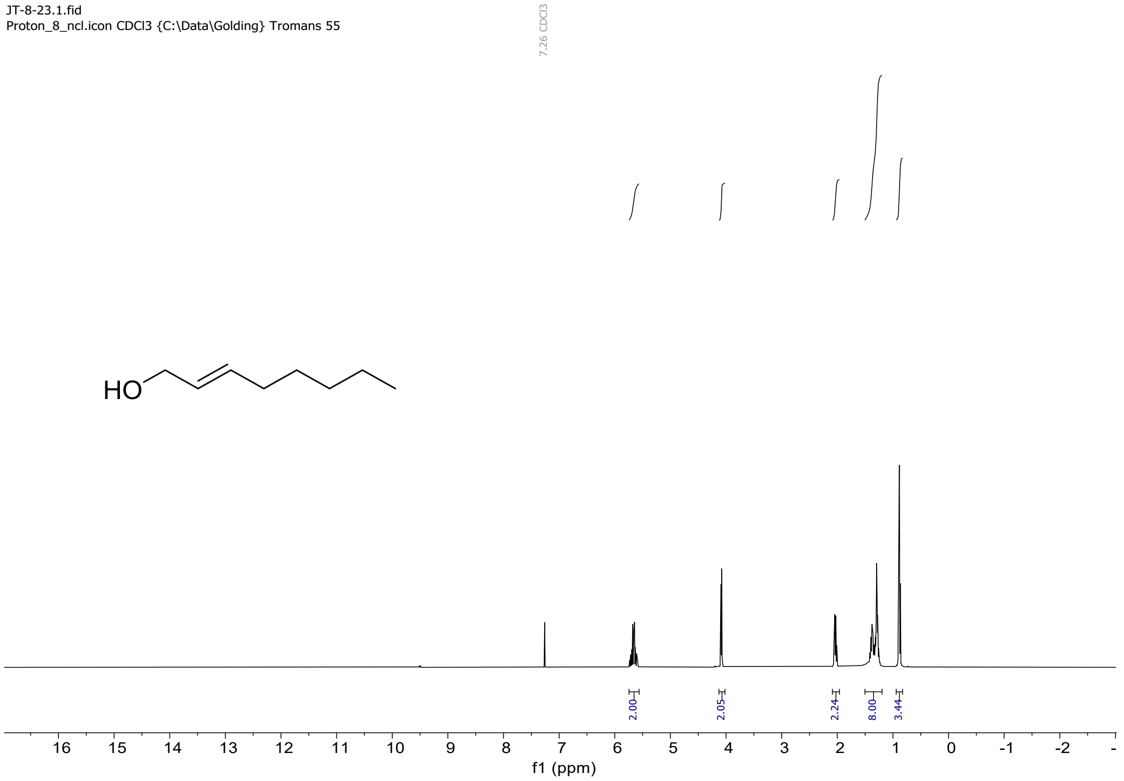
N-((1,4-Dimethoxynaphthalen-2-yl)methyl)-*N*-methylbenzamide [5n] ^{13}C NMR (CDCl$_3$)



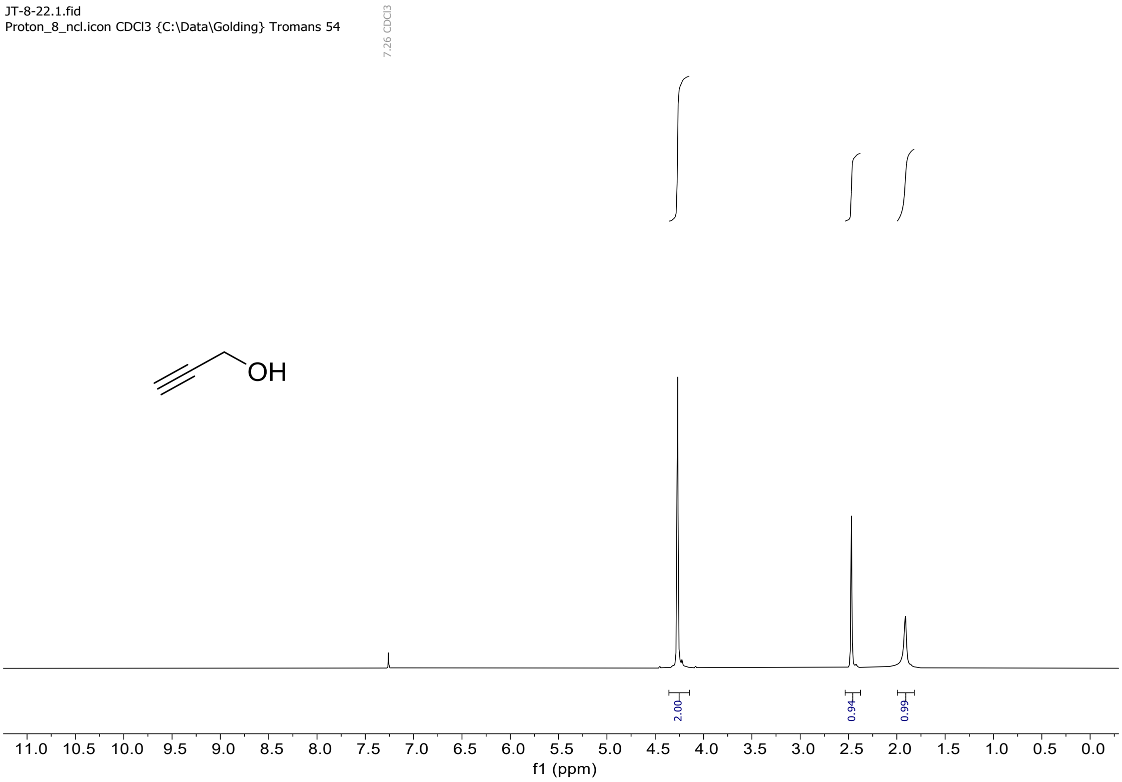
Icosan-1-ol [4a] ^{1}H NMR ($CDCl_3$)



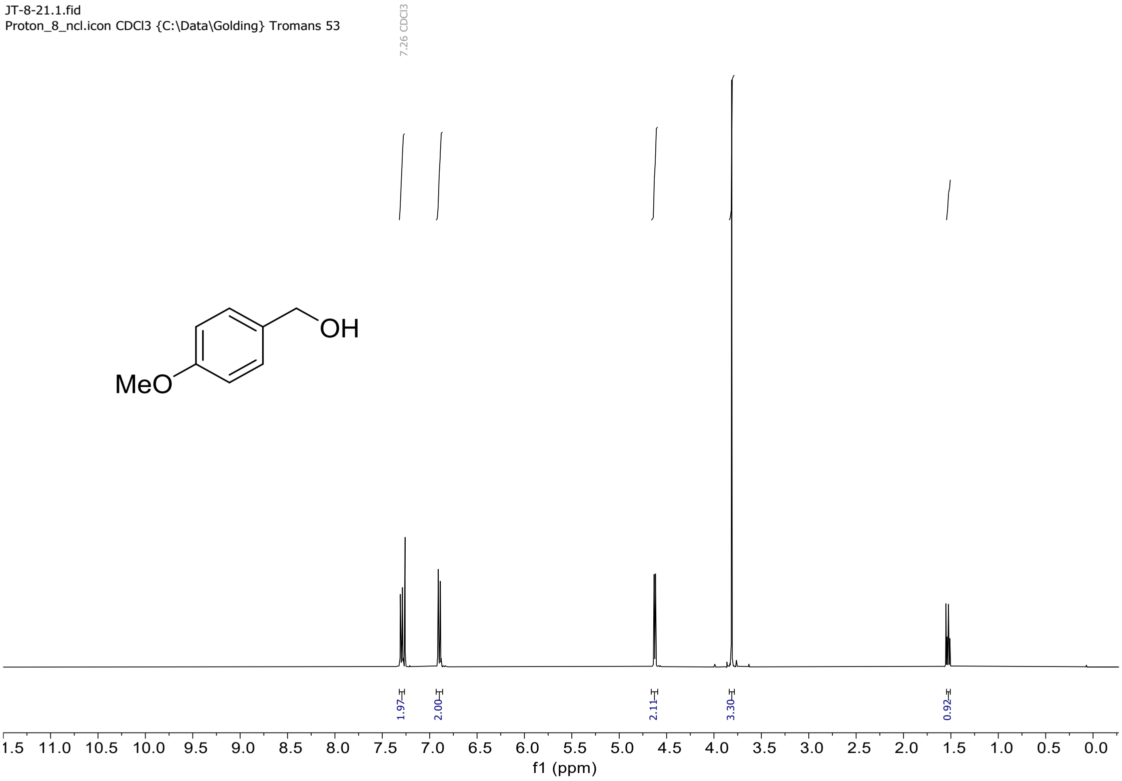
(*E*)-Oct-2-en-1-ol [4c] ^{1}H NMR ($CDCl_3$)



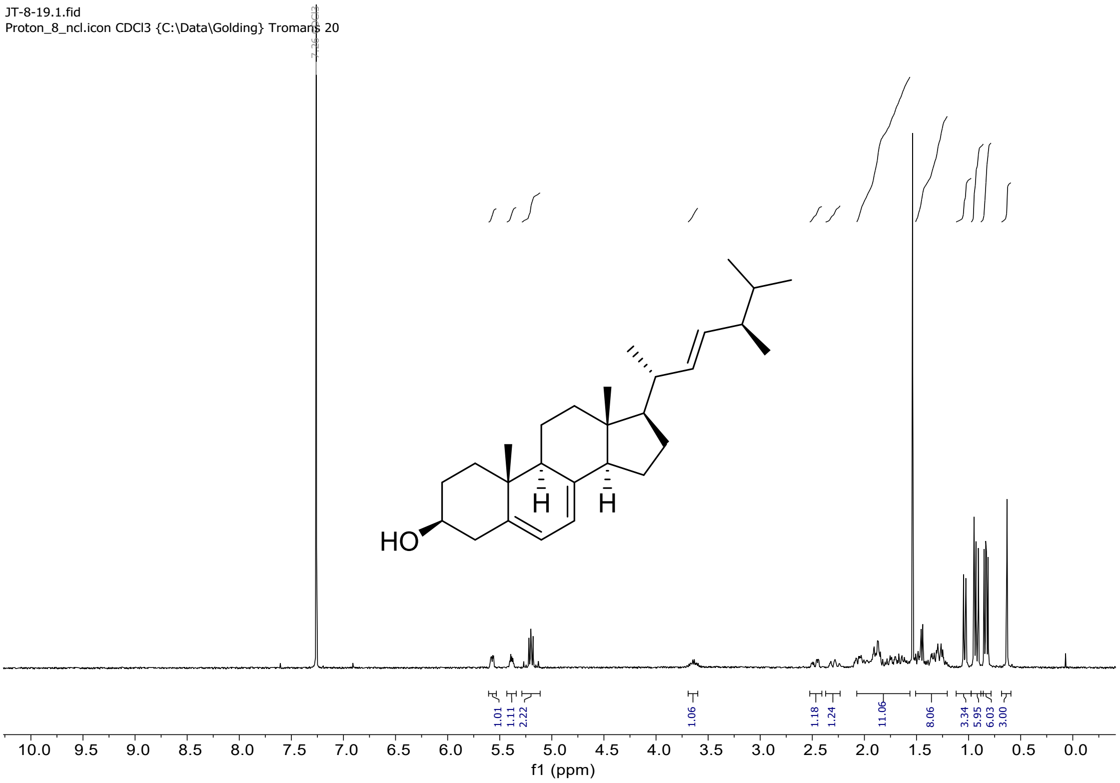
Prop-2-yn-1-ol [4d] ^{1}H NMR ($CDCl_3$)



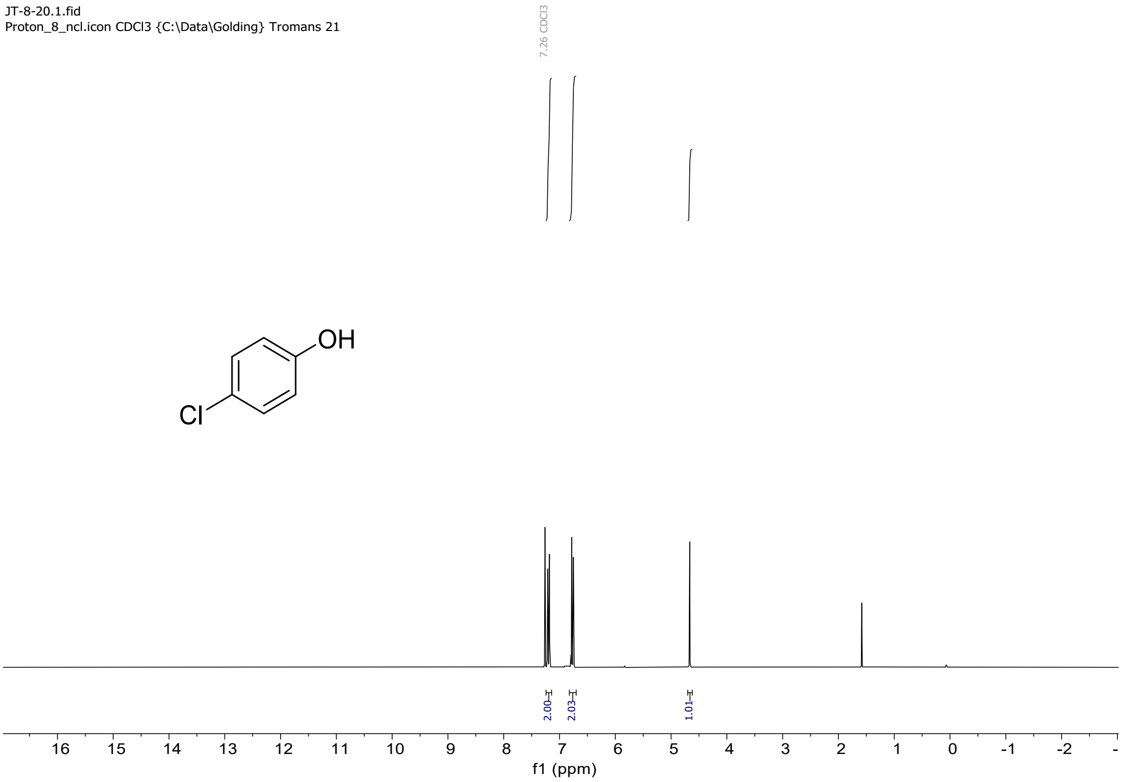
(4-Methoxyphenyl)methanol [4f] ^{1}H NMR ($CDCl_3$)



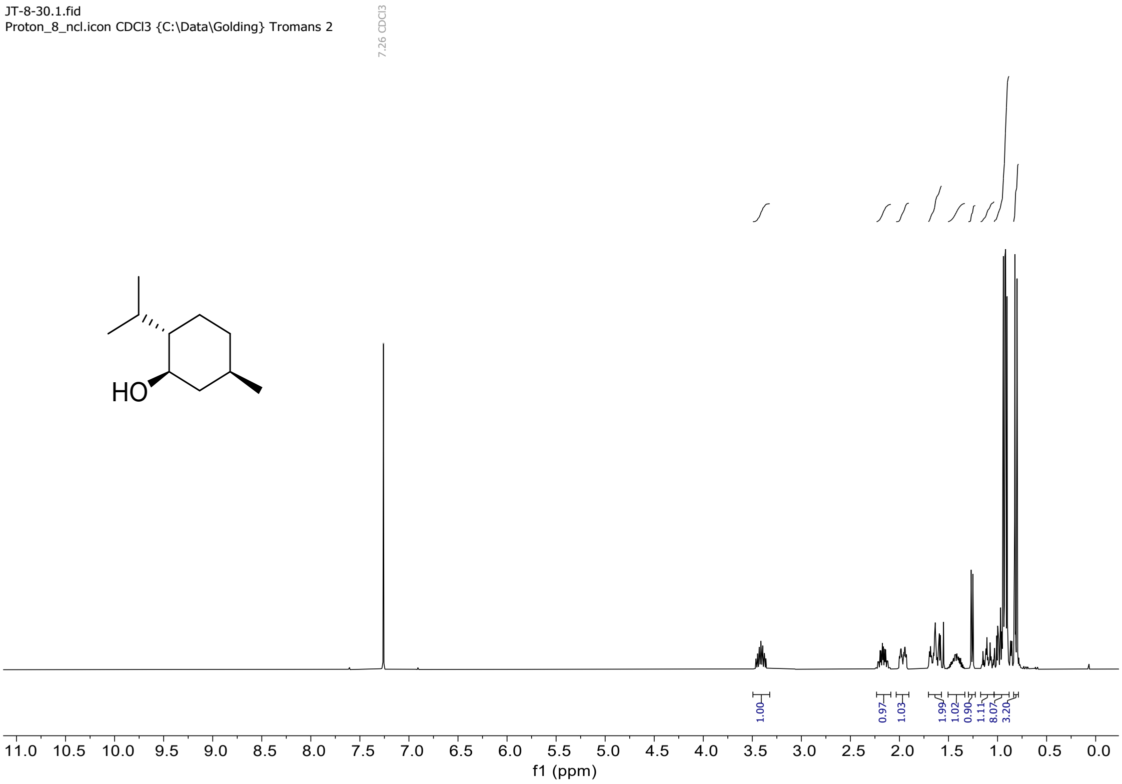
(3*S*,9*S*,10*R*,13*R*,14*R*,17*R*)-17-((2*R*,5*R*,*E*)-5,6-Dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-ol [4h] ^{1}H NMR ($CDCl_3$)



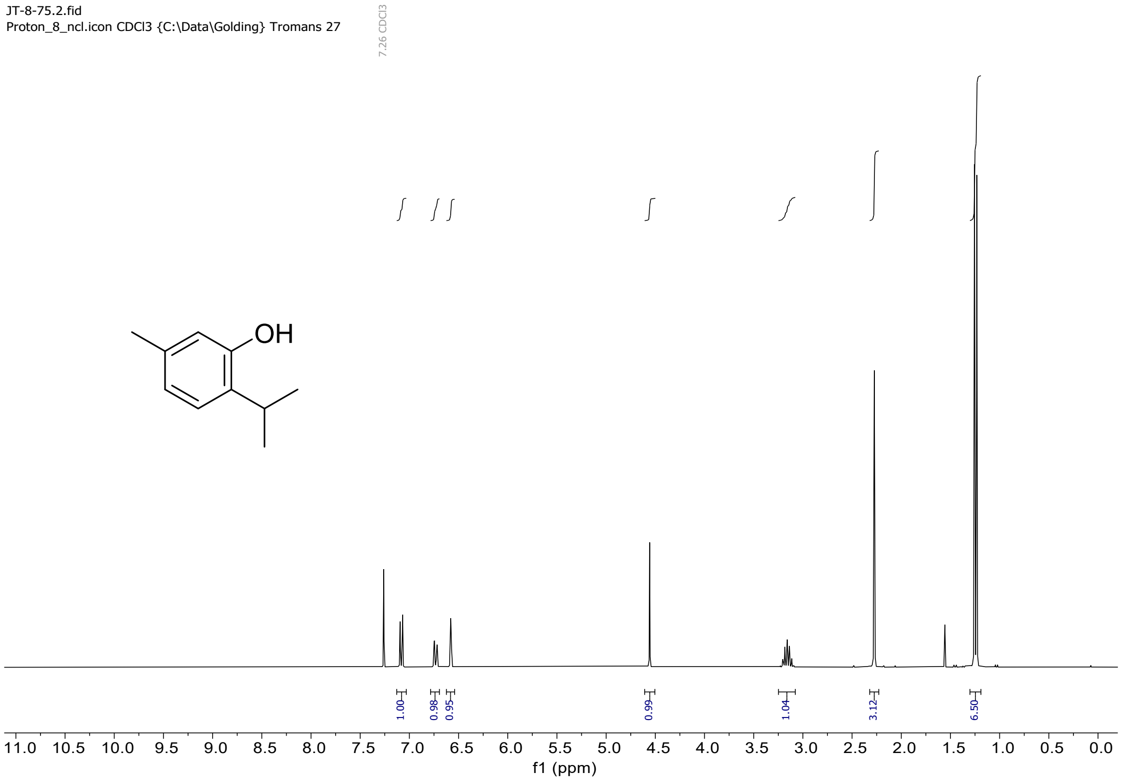
4-Chlorophenol [4j] ^{1}H NMR ($CDCl_3$)



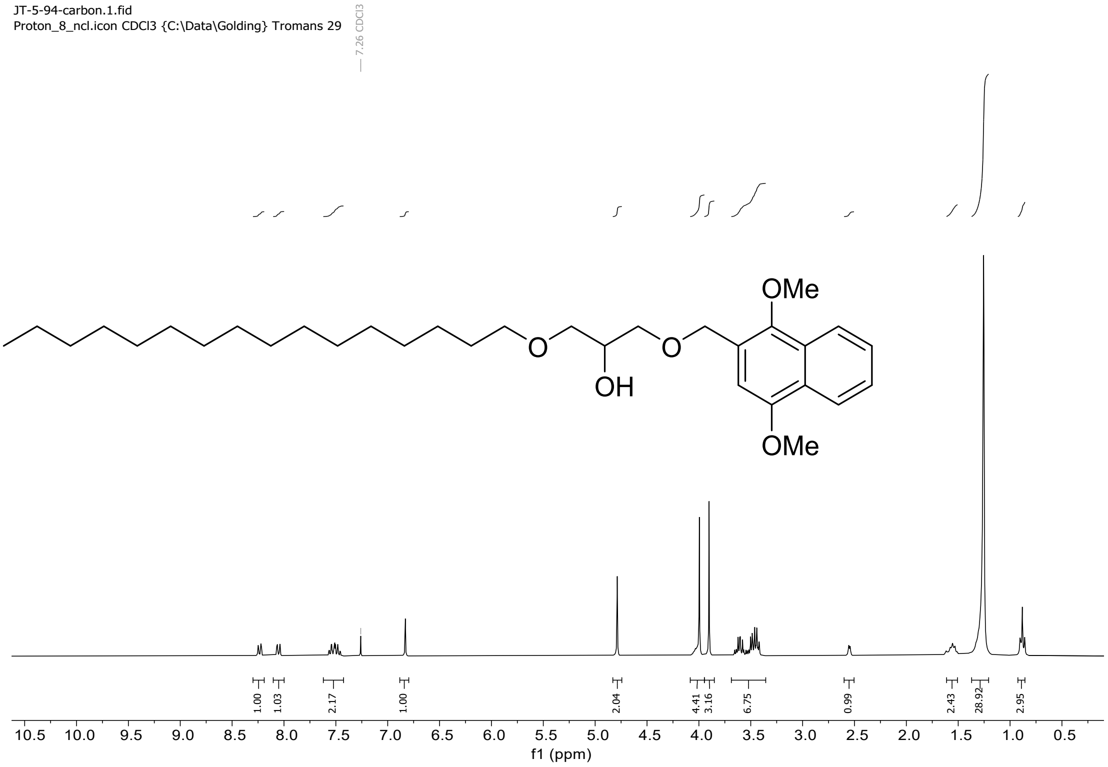
(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexan-1-ol [4i] ^{1}H NMR ($CDCl_3$)



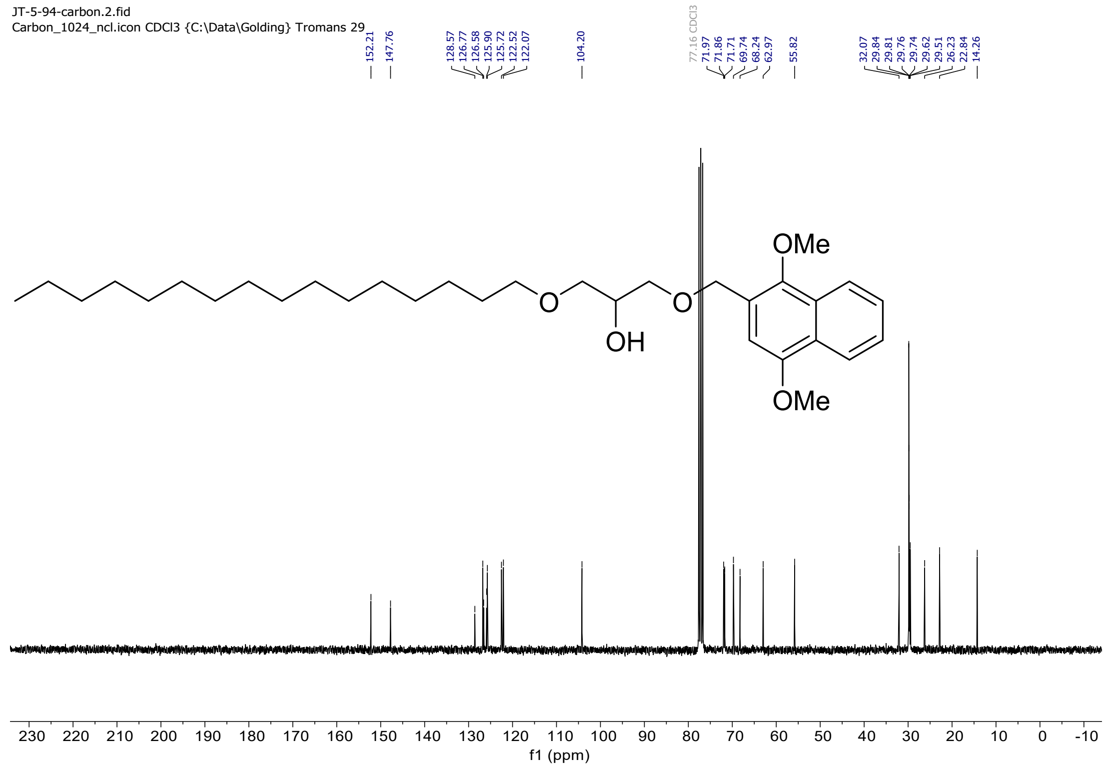
2-Isopropyl-5-methylphenol [4k] ^{1}H NMR ($CDCl_3$)



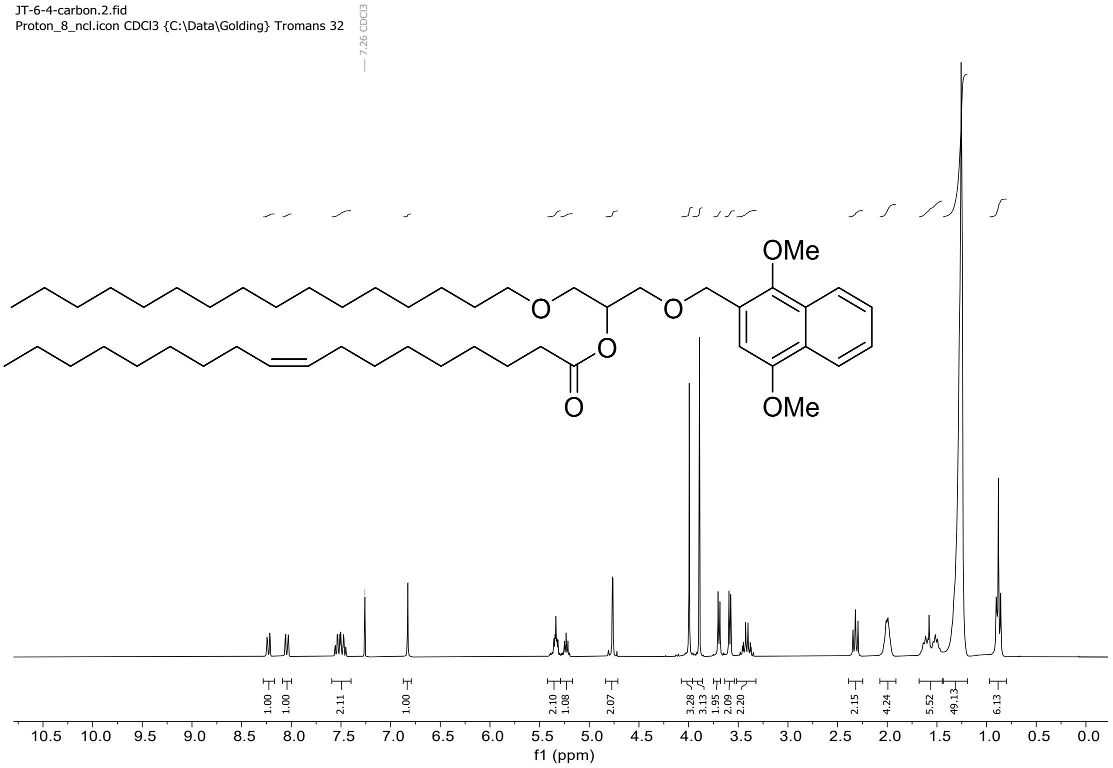
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol [10] ^{1}H NMR (CDCl$_3$)



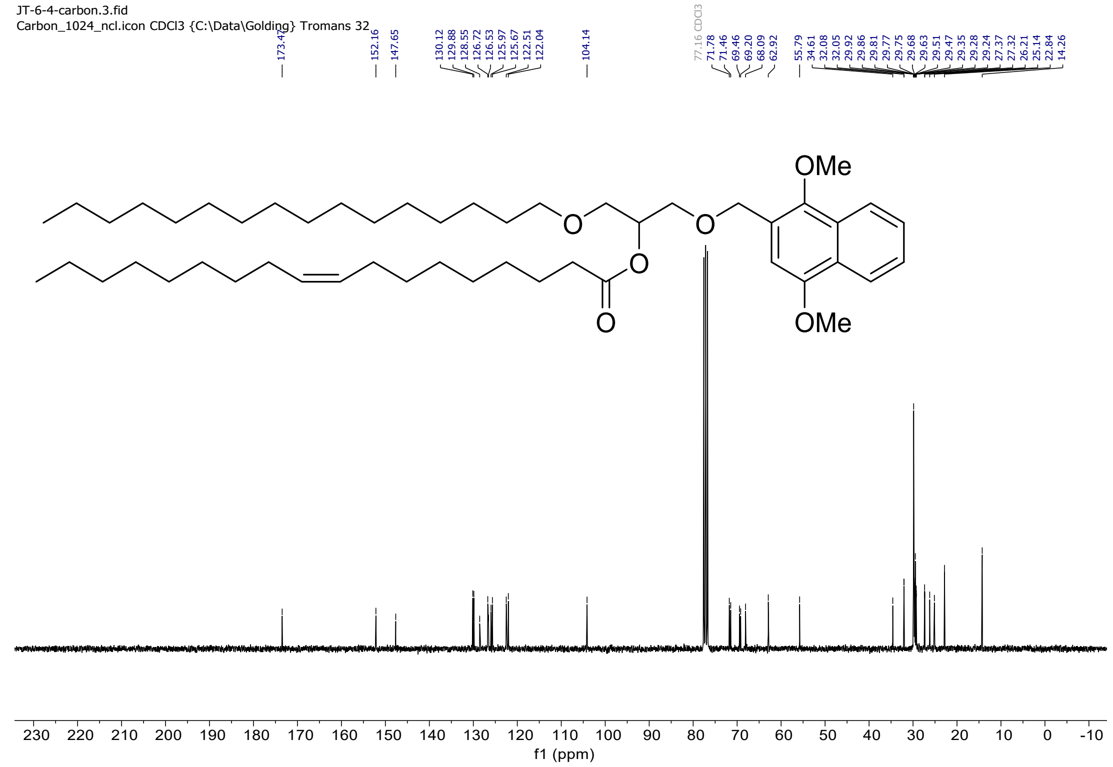
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-ol [10] ^{13}C NMR (CDCl$_3$)



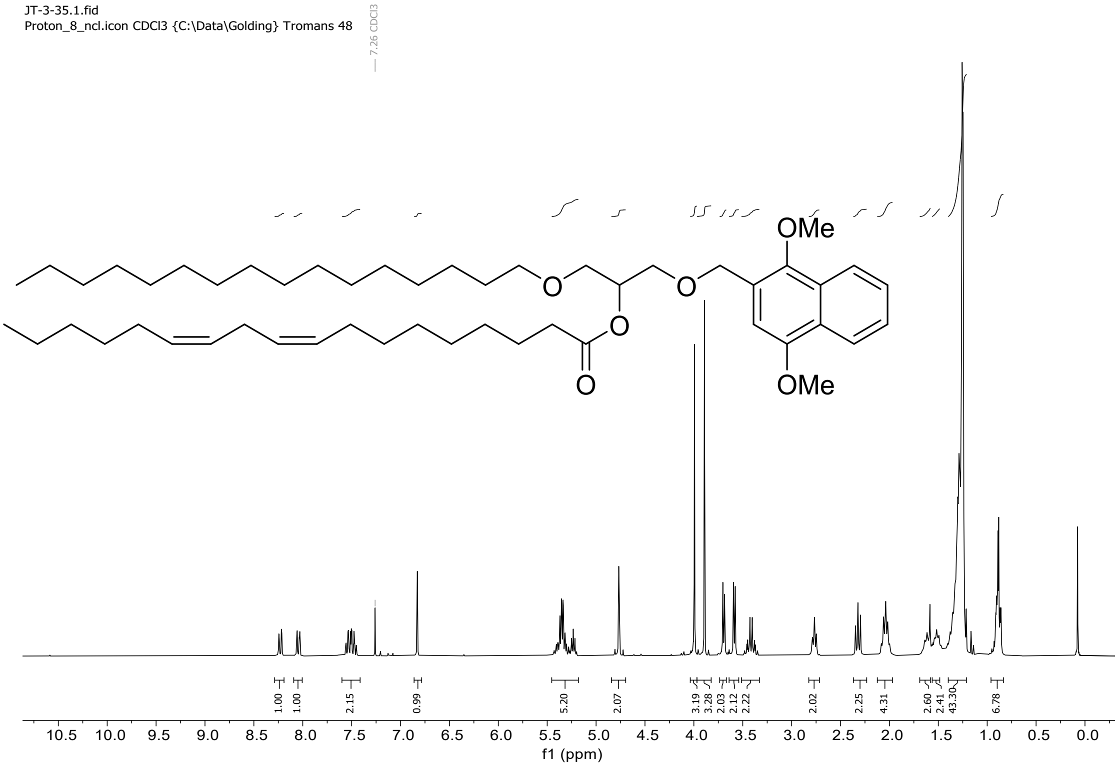
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl oleate [11a] ^{1}H NMR ($CDCl_3$)



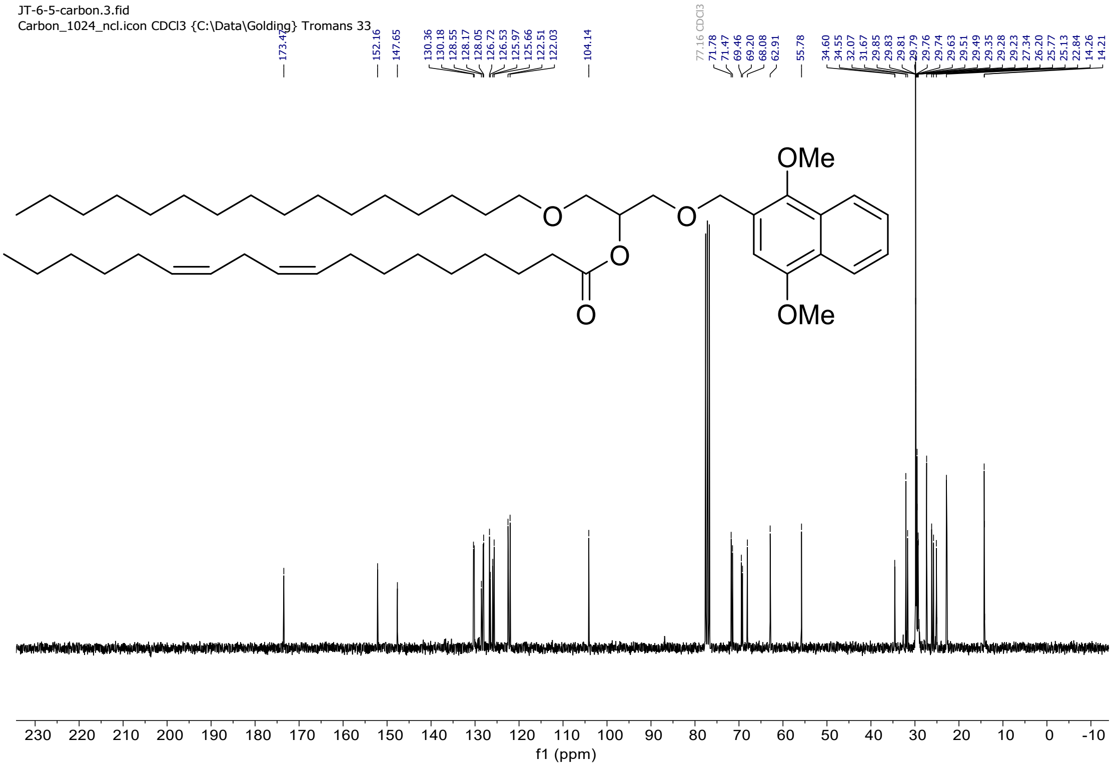
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl oleate [11a] ^{13}C NMR ($CDCl_3$)



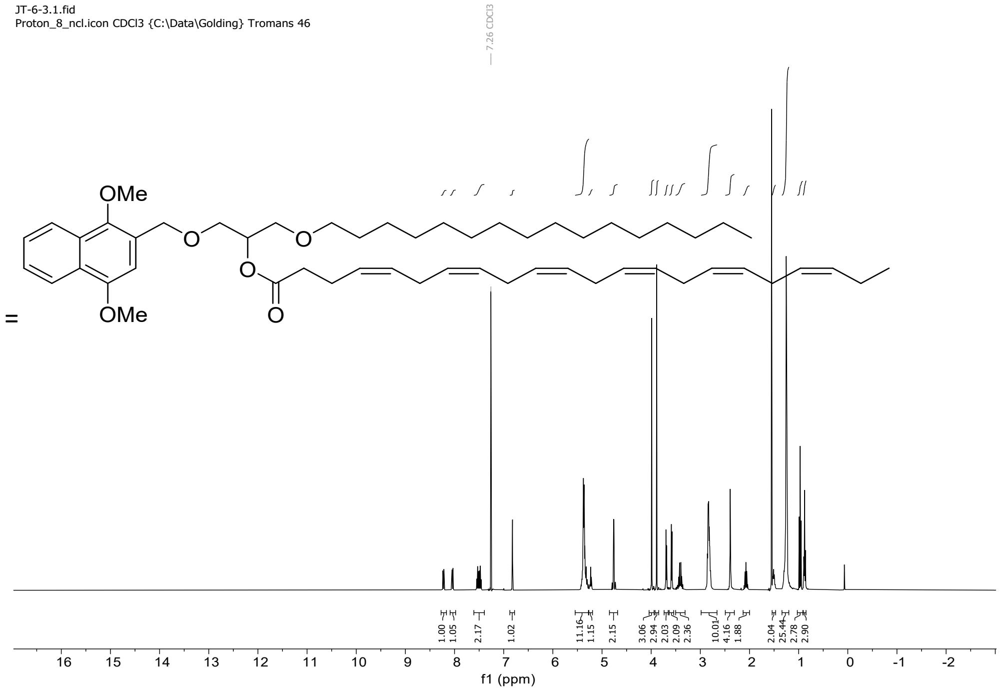
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate [11b] ^{1}H NMR (CDCl$_3$)



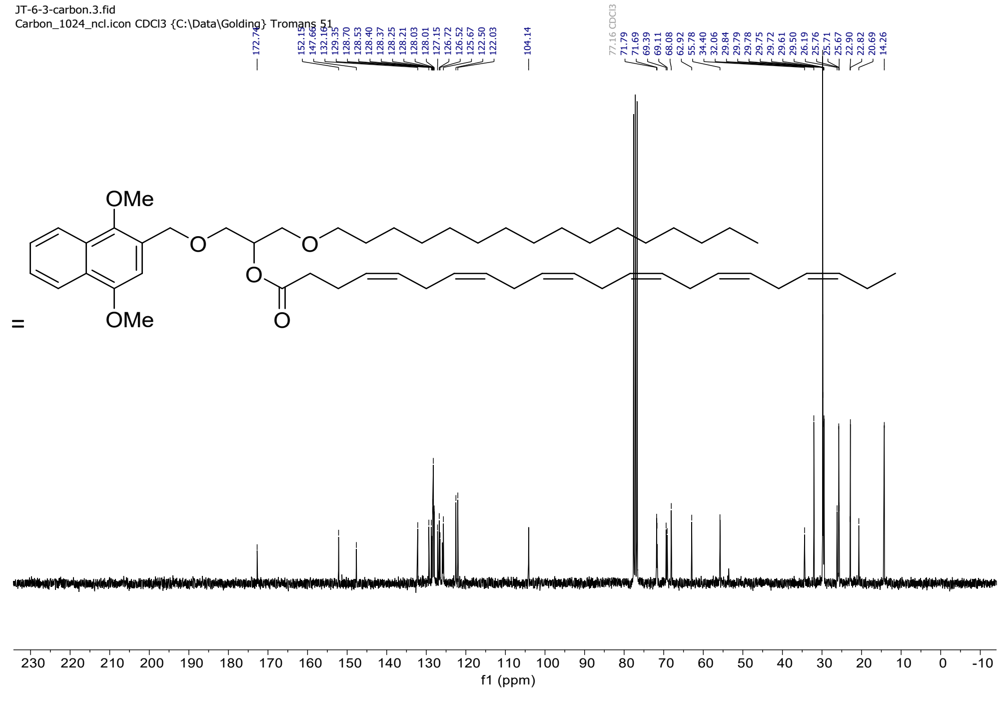
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate [11b] ^{13}C NMR (CDCl$_3$)



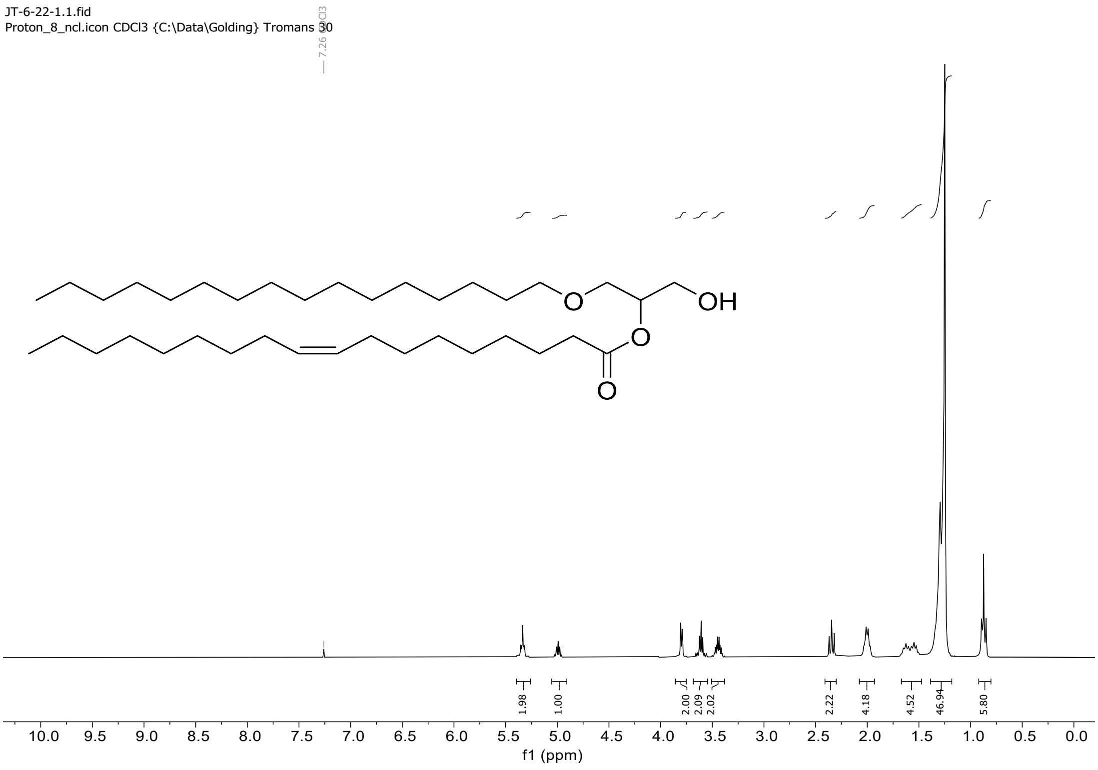
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [11c] ^{1}H NMR (CDCl$_3$)



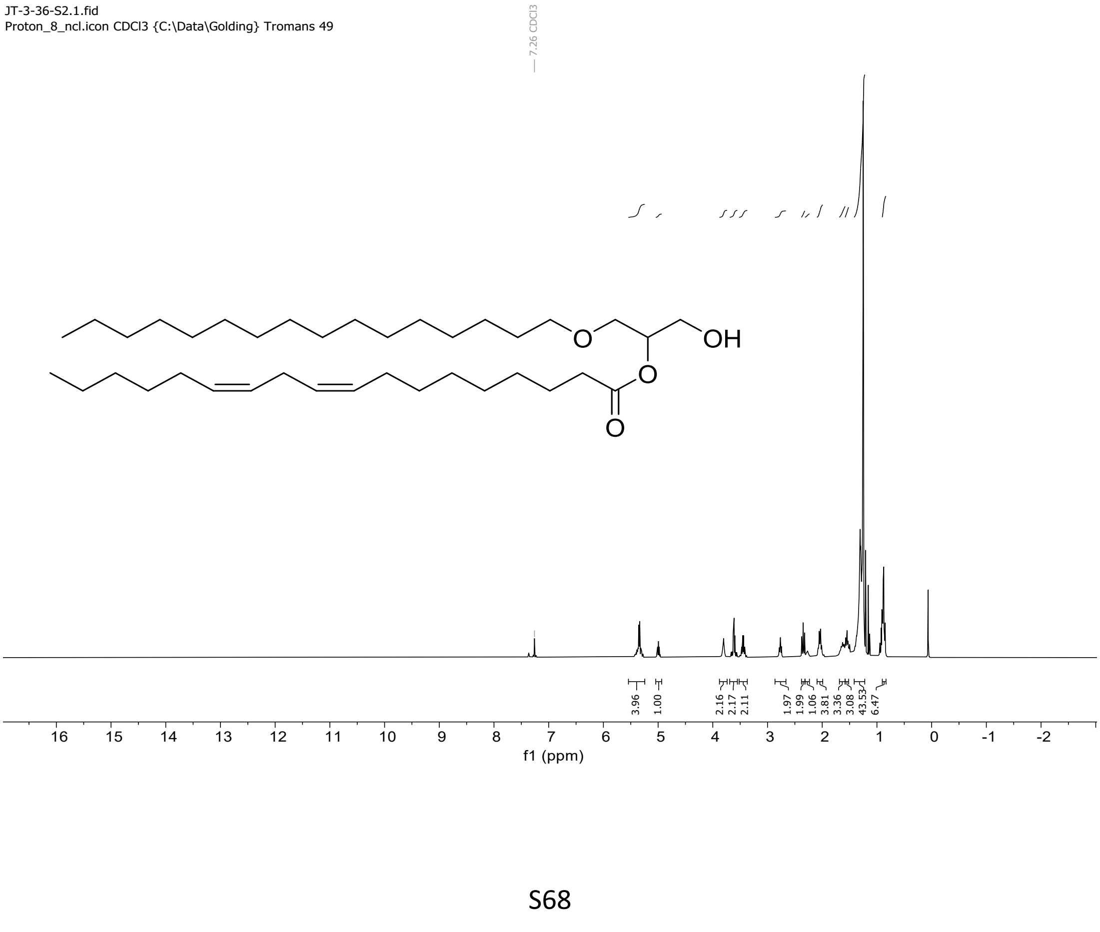
1-((1,4-Dimethoxynaphthalen-2-yl)methoxy)-3-(hexadecyloxy)propan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [11c] ^{13}C NMR (CDCl$_3$)



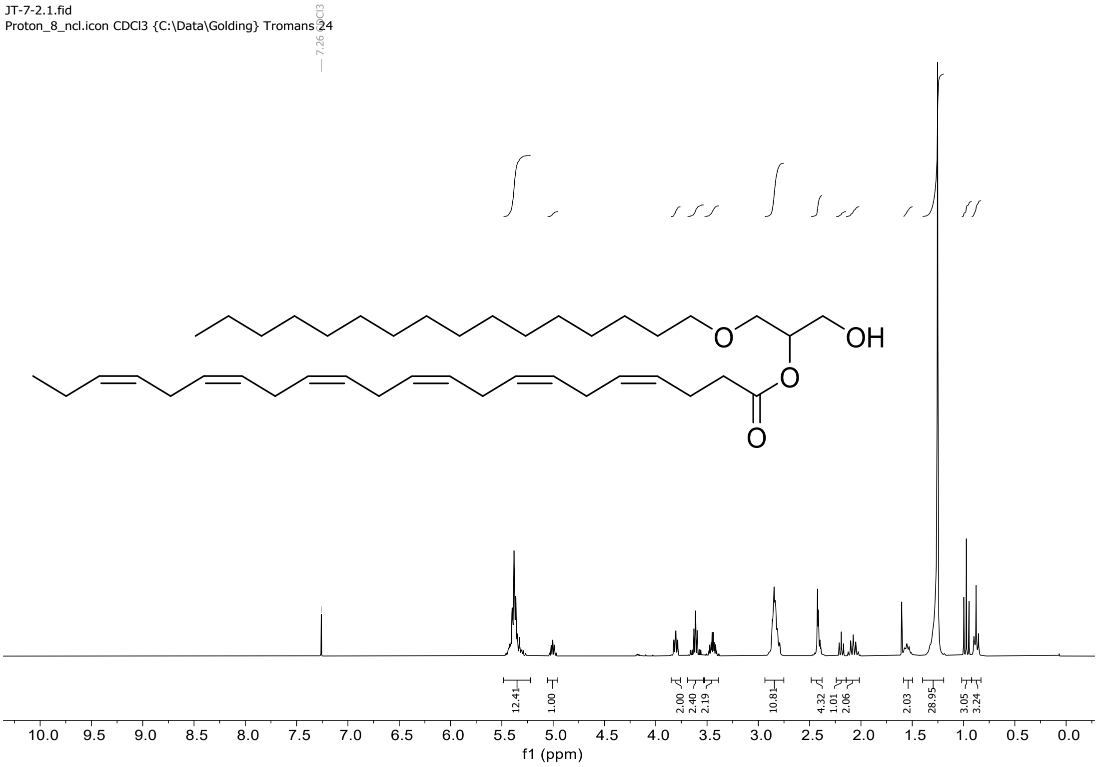
1-(Hexadecyloxy)-3-hydroxypropan-2-yl oleate [12a] ^{1}H NMR ($CDCl_3$)



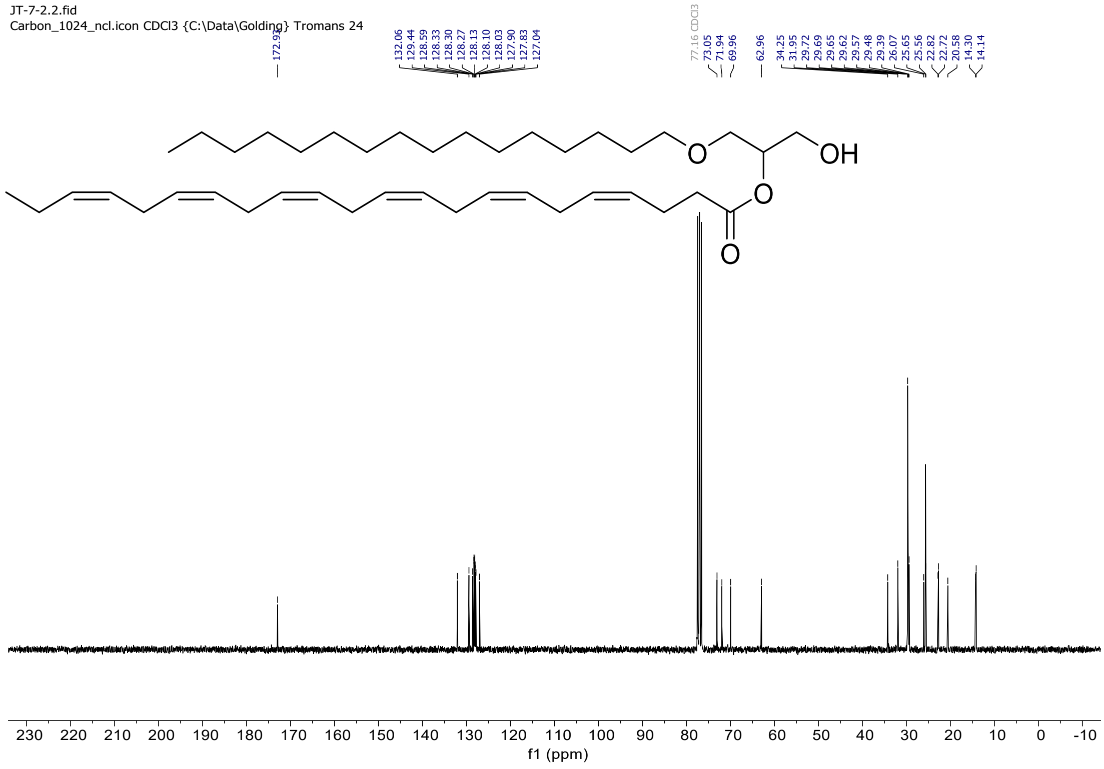
1-(Hexadecyloxy)-3-hydroxypropan-2-yl (9*Z*,12*Z*)-octadeca-9,12-dienoate [12b] ^{1}H NMR ($CDCl_3$)



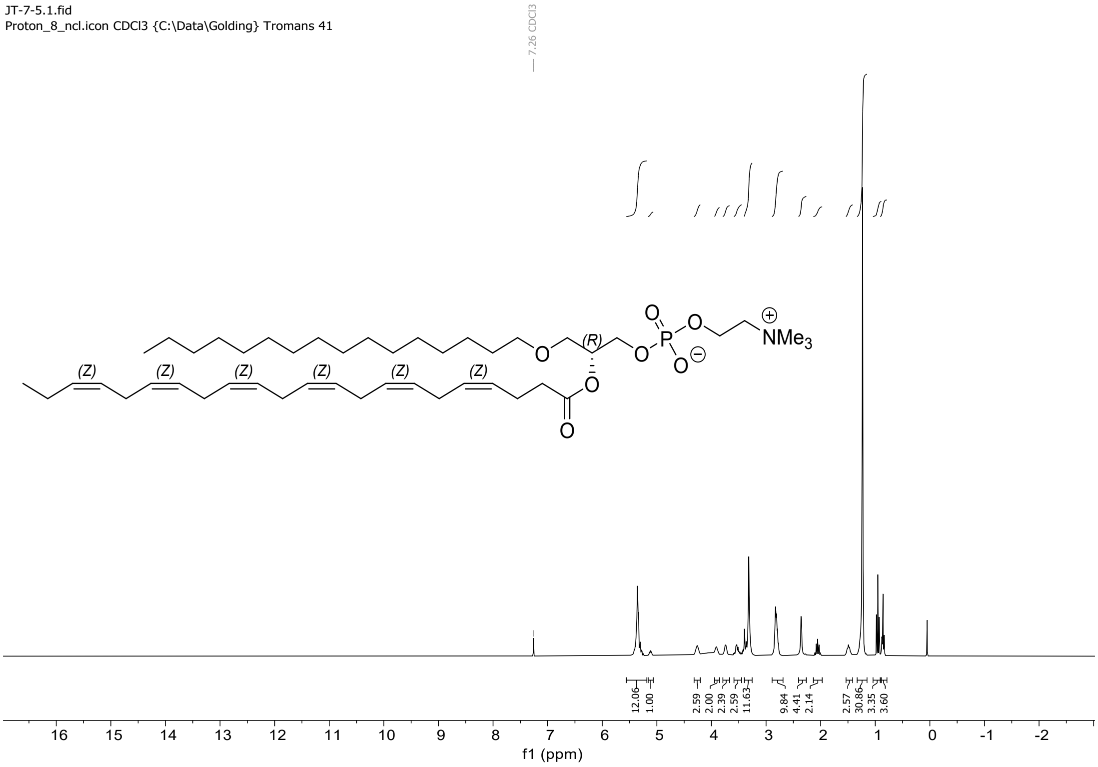
1-(Hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [12c] ^{1}H NMR (CDCl$_3$)



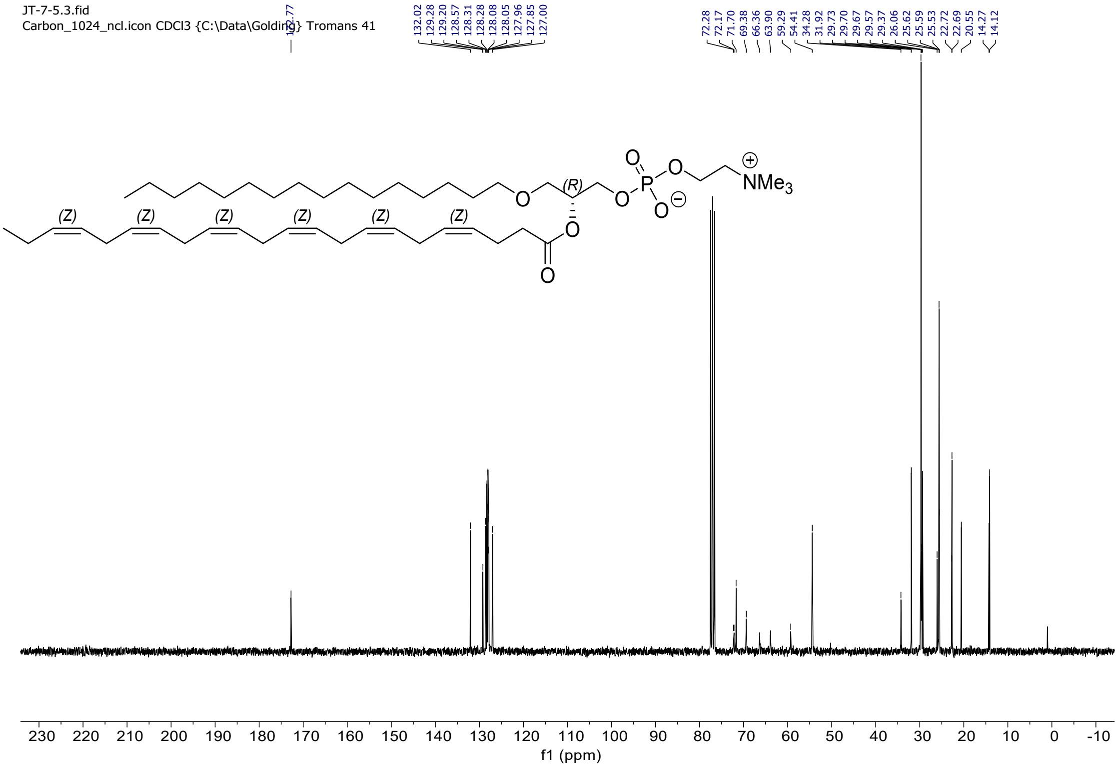
1-(Hexadecyloxy)-3-hydroxypropan-2-yl (4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa-4,7,10,13,16,19-hexaenoate [12c] ^{13}C NMR (CDCl$_3$)



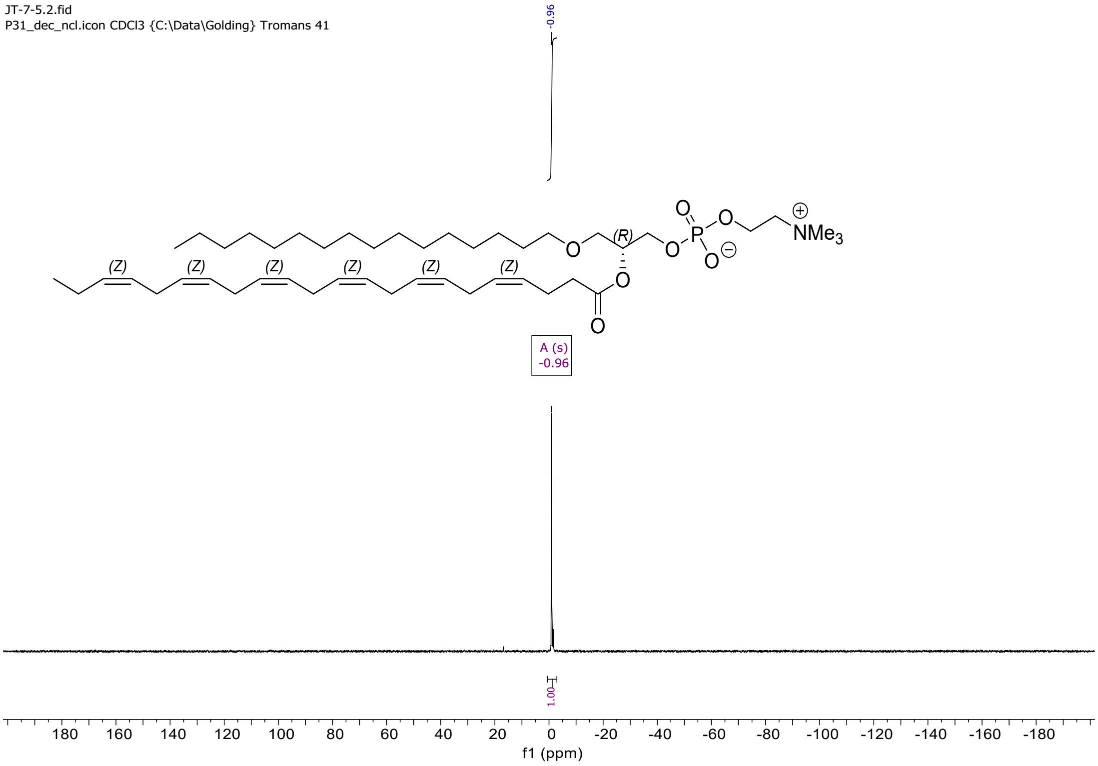
(*R*)-2-(((4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-Docosa-4,7,10,13,16,19-hexaenoyl)oxy)-3-(hexadecyloxy)propyl (2-(trimethylammonio)ethyl) phosphate [15] ^{1}H NMR ($CDCl_3$)



(*R*)-2-(((4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-Docosa-4,7,10,13,16,19-hexaenoyl)oxy)-3-(hexadecyloxy)propyl (2-(trimethylammonio)ethyl) phosphate [15] ^{13}C NMR ($CDCl_3$)



(*R*)-2-(((4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-Docosa-4,7,10,13,16,19-hexaenoyl)oxy)-3-(hexadecyloxy)propyl (2-(trimethylammonio)ethyl) phosphate [15] ^{31}P NMR (CDCl$_3$)



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