Supporting information for

Structure-inspired design of a sphingolipid mimic sphingosine-1-phosphate receptor agonist from a naturally occurring sphingomyelin synthase inhibitor

Mahadeva M. M. Swamy, [‡a,] Yuta Murai, [‡a,b] Yusuke Ohno,[c] Keisuke Jojima,[c] Akio Kihara,[c] Susumu Mitsutake,[a] Yasuyuki Igarashi,[a] Jian Yu,[d] Min Yao,[d] Yoshiko Suga,[a] Masaki Anetai,[a] and Kenji Monde [*a,b]

[a]Graduate School of Life Science, Kita 21 Nishi 11, Sapporo 001-0021, Japan

[b]Frontier Research Center for Advanced Material and Life Science, Faculty of Advanced Life Science, Hokkaido University, Kita 21 Nishi 11, Sapporo 001-0021, Japan

[c]Faculty of Pharmaceutical Sciences, Hokkaido University, Kita 12 Nishi 6, Sapporo 060-0812, Japan

[d]Faculty of Advanced Life Science, Hokkaido University, Kita 10 Nishi 8, Sapporo 060-0810, Japan

Email: kmonde@sci.hokudai.ac.jp

1. General experimental method

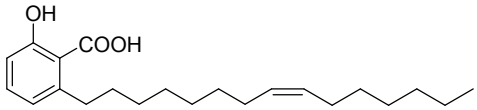
^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Varian Inova instrument at 25 °C in $CDCl_3$ or CD_3OD purchased from Cambridge Isotope Laboratories, Inc. (Tewksbury, USA). Chemical shifts (δ) are reported in ppm and coupling constant values (*J*) are in Hertz (Hz) relative to $CDCl_3$ (^{1}H, δ 7.26; ^{13}C, δ 77.00) or CD3OD (^{1}H, δ 3.4, 4.8; ^{13}C, δ 49.3) and tetramethylsilane. The following abbreviations were used for signal multiplicities: *s* = singlet; *d* = doublet; *t* = triplet; *q* = quartet; *m* = multiplet. High Resolution Mass spectra (HRMS (ESI)) were obtained on a AB sciex Triple TOF® 5600+ at Platform for Research on Biofunctional Molecules, Hokkaido University. Low-resolution mass spectra (ESI-MS) were obtained by a JEOL JMS-T100LP spectrometer. Analytical TLC was performed on 0.2 mm silica gel plates (Merck 60 F-254). SiO_2 gel column chromatography was carried out using silica gel (Wakogel® N60, spherical, 38-100 μm) with air flashing.

2. Construction of plant extracts library

To construct plants extracts library, approximately 650 plants grown wildly or cultivated in Hokkaido area were collected. Each plant was dried by hot air at 50°C for 24 hours. Dried plants were cut into small pieces/powdered by grinder. Each dried plants (20 g) were extracted with 200 ml of MeOH at room temperature for 1 day. The MeOH solutions were filtered, and concentrated *in vacuo* to dryness. Each of residues and the solutions dissolved in DMSO at the concentrations of 100 mg/ml were stocked at -20°C respectively.

3. Isolation of ginkgolic acid (15:1) from *Ginkgo biloba*

Ginkgo biloba stem collected from campus of Hokkaido University, Sapporo on 16th October, 2014 dried for 6 months. Dried *G. biloba* was grinded/powdered well. Five hundred g of powder extracted with MeOH (2 L) at room temperature three times after 24 h each. The combined MeOH extract was concentrated under reduced pressure to give a dark brown residue (15.9 g), which was dissolved in 20% MeOH in water (500 mL) and partitioned with hexane (250 mL × 3), Et_2O (250 mL × 3) and EtOAc (250 mL × 3). After removal of solvent, each of residues was used for SMS assay. We found that hexane fraction was more activity than Et_2O fraction but, EtOAc and water fractions turned out to be inactive. The active hexane fraction (3.8 g) was further purified by silica gel column chromatography. The active component was identified as ginkgolic acid (15:1) confirmed by NMR spectroscopy and HRMS. Yield: 0.006% (27.5 mg). Ginkgolic acid (15:1) is one of the major components of *G. biloba* leaves.



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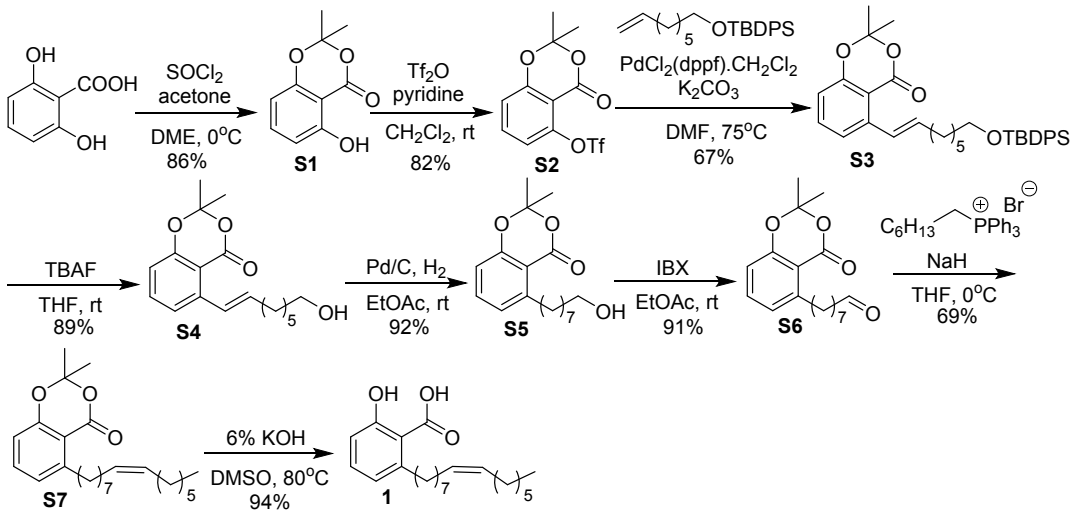
Ginkgolic acid (15:1); light yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 10.99 (1H, s), 7.37 (1H, t, 7.9 Hz), 6.88 (1H, d, J=8.3 Hz), 6.78 (1H, d, J=7.5 Hz), 5.32-5.38 (2H, m), 2.97-3.00 (2H, t, J=7.5 Hz), 2.02-2.06 (4H, m), 1.60-1.62 (2H, m), 1.26-1.33 (18H, m), 0.88 (3H, t, J=6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.2, 163.6, 147.8, 135.4, 129.9, 129.8, 122.7, 115.8, 110.4, 36.4, 32.0, 31.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 27.2, 26.9, 22.3, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{22}H_{34}O_3$: 347.2580; found 347.2555.

4. Total Synthesis of ginkgolic acid (15:1) and derivatives

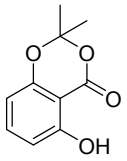
Ginkgolic acid (15:1) (1):

Compounds S**1** and S**2** were synthesized as reported method.[1] Compound **S3** was synthesized by palladium catalyzed reaction (heck reaction) of **S2** with hydroxyl group protected *7*-octene-*1*-ol in the presence of K_2CO_3[2] followed by deprotection of hydroxyl group with TBAF (tetra-*N*-butyl ammonium fluoride) to get **S4**. The hydrogenation of double bond was carried out using Pd/C, H_2 to obtain **S5**. Compound **S6** which was synthesized by oxidation of **S5** using IBX (2-iodoxybenzoic acid) followed by Wittig reaction of **S6** and heptyltriphenylphosphonium ion in the presence of NaH to get **S7**.[3] Finally, ginkgolic acid (15:1) was obtained by hydrolysis of **S7**. The natural and synthetic ginkgolic acid (15:1) is equally potent SMS inhibitor.



Scheme S1: Synthesis of ginkgolic acid (15:1)

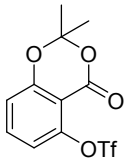
5-hydroxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (S1)



To the stirred solution of 2,6-dihydroxybenzoic acid (8 g, 51.9 mmol) in 1,2-dimethoxyethane (50 mL) at 0 °C was added acetone (4.9 mL, 67.5 mmol), $SOCl_2$ (4.8 mL, 67.5 mmol) and DMAP (316 mg, 2.6 mmol). The reaction mixture was stirred under Ar atmosphere for 1 h at 0 °C and stirred at room temperature overnight. After completion of the reaction saturated $NaHCO_3$ solution was added and extracted with Et_2O (100 mL × 2). The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$ and the solution was concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (8:2) to give **S1** (9.3 g, Yield 93%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 10.31 (1H, s), 7.38 (1H, t, 8.3 Hz), 6.59 (1H, d, 8.35 Hz), 6.41 (1H, d, 8.0 Hz), 1.72 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.4, 161.3, 155.5, 137.9, 110.7, 107.2, 107.1, 99.3, 25.5. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{10}H_{10}O_4$: 195.0651; found 195.0648

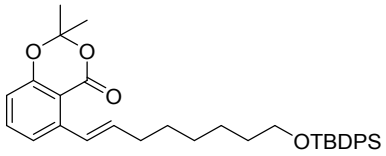
2,2-dimethyl-4-oxo-4*H*-benzo[d][1,3]dioxin-5-yl trifluoromethanesulfonate (S2)



To a stirred solution of **S1** (5 g, 25.8 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added anhydrous pyridine (7.4 mL, 92.7 mmol) and trifluoromethanesulfonic anhydride (4.4 mL, 30.9 mmol). The reaction mixture was stirred for additional 1 h at same temperature. After completion of the reaction the reaction mixture was extracted with Et_2O (100 mL × 2) and the combined organic layer was dried over $MgSO_4$ and concentrated under vacuum. The residue obtained was purified by silica gel column chromatography using hexane/EtOAc (7:3) to give **S2** (7.6 g, Yield 90%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.62 (1H, t, 8.3 Hz), 7.0 (1H, d, 8.5 Hz), 7.01 (1H, d, 8.3 Hz), 1.76 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.4, 157.0, 148.6, 136.2, 120.0, 117.9, 116.5, 108.2, 106.8, 25.4. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{11}H_9O_6F_3S$: 327.0144; found 327.0133.

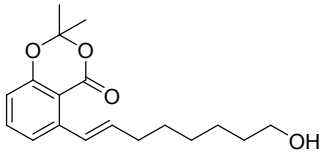
(*E*)-5-(8-((*tert*-butyldiphenylsilyl)oxy)oct-1-en-1-yl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (S3)



To a stirred solution of *tert*-butyl(oct-7-en-1-yloxy)diphenylsilane (240 mg, 0.68 mmol) in DMF (3 mL) at room temperature was added K_2CO_3 (94 mg, 0.68 mmol) and stirred for 0.5 h. Compound **S2** (202 mg, 0.62 mmol) and palladium catalyst $PdCl_2$(dppf) (15 mg, 0.02 mmol) were added to the reaction mixture. Then the reaction mixture was stirred overnight at 75 °C. The reaction mixture was acidified with 2M HCl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The residue obtained was purified by silica gel column chromatography using hexane/EtOAc (9:1) to give **S3** (227 mg, Yield 67%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.76 (4H, d, 7.8 Hz), 7.55 (1H, d, J=9.7 Hz), 7.42-7.45 (7H, m), 7.28 (1H, d, 7.8 Hz), 6.87(1H, d, J=8.0 Hz), 6.27-6.33 (1H, m), 3.76 (2H, t, 6.4 Hz), 2.34 (2H, q, 13.9, 7.0, 6.8 Hz), 1.75 (7H, s), 1.69-1.66 (2H, m), 1.43-1.65 (6H, m), 1.14 (9H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.3, 158.8, 142.7, 136.6, 135.1, 134.2, 129.5, 128.2, 127.7, 121.3, 115.5, 110.6, 105.1, 64.0, 33.2, 32.6, 31.7, 31.6, 29.2, 29.1, 27.0, 25.7, 22.7, 19.3, 19.3, 14.2. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{34}H_{42}O_4Si$: 543.2925; found 543.2929.

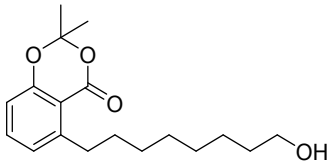
(*E*)-5-(8-hydroxyoct-1-en-1-yl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (S4)



To a stirred solution of **S3** (50 mg, 0.1 mmol) in THF (4 mL) at room temperature was added TBAF (36 mg, 0.14 mmol) and stirred for 2 h. After completion of the reaction the THF was evaporated and the residue was extracted with EtOAc. The organic layer was dried over $MgSO_4$ and concentrated under reduced vacuum. The residue obtained was purified by silica gel column chromatography using hexane/EtOAc (6:4) to give **S4** (24 mg, Yield 86%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.36-7.41 (2H, m), 7.19 (1H, d, J=7.8 Hz), 6.77 (1H, d, J=8.0 Hz), 6.15-6.21(1H, m), 3.59 (2H, t, J=6.6 Hz), 2.24 (2H, q, 13.9, 7.1, 6.8 Hz), 1.66 (6H, s), 1.49-1.51(4H, m), 1.34-1.37 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.4, 156.7, 142.5, 135.4, 135.0, 128.0, 121.2, 115.2, 110.4, 105.0, 62.6, 32.9, 32.6, 28.9, 28.8, 25.5, 25.5. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{18}H_{24}O_4$: 305.1747; found 305.1772.

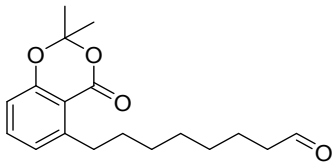
5-(8-hydroxyoctyl)-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (S5)



To a stirred solution of **S4** (94 mg, 0.31 mmol) in EtOAc (10 ml) was added 10% Pd/C (50 mg, 0.05 mmol). The reaction mixture was stirred overnight at room temperature under H_2 atmosphere. Pd/C was filtered off and the filtrate was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (6:4) to give **S5** (89 mg, 95%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.74 (1H, t, 8.0 Hz), 6.94(1H, d, J=7.5 Hz), 6.81(1H, d, 8.1 Hz), 3.64 (2H, t, 6.5 Hz), 3.09 (2H, t, 7.8 Hz), 1.71 (6H, s), 1.56-1.62 (4H, m), 1.32-1.41 (6H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.2, 157.0, 148.4, 135.0, 125.0, 115.0, 112.0, 104.9, 62.8, 34.3, 32.7, 31.1, 29.5, 29.3, 29.2, 25.6, 25.6. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{18}H_{26}O_4$: 307.1903; found 307.1921.

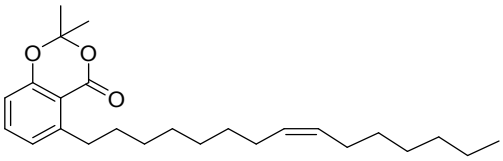
8-(2,2-dimethyl-4-oxo-4*H*-benzo[*d*][1,3]dioxin-5-yl)octanal (S6)



To a stirred solution of **S5** (150 mg, 0.49 mmol) in EtOAc (10 ml) was added IBX (412 mg, 1.47 mmol). The reaction mixture was stirred overnight at 40 °C. The white solid was filtered off and the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (9:1) to give **S6** (91 mg, 92%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.06(1H, s), 7.33 (1H, t, 8.1), 6.86 (1H, d, J=7.5 Hz), 6.73 (1H, d, 8.3 Hz), 3.01 (2H, t, 7.5 Hz), 2.35 (2H, t, 6.1 Hz), 1.63 (6H, s), 1.49-1.56 (4H, m), 1.27-1.31 (6H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 202.7, 160.1, 157.0, 148.2, 135.6, 125.0, 115.0, 111.9, 111.9, 104.8, 43.7, 34.2, 31.0, 28.9, 28.9, 25.5, 21.9. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{18}H_{24}O_4$: 305.1747; found 305.1776.

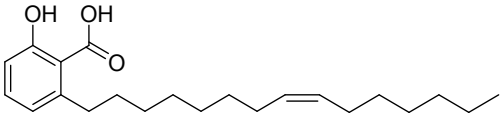
(*Z*)-2,2-dimethyl-5-(pentadec-8-en-1-yl)-4*H*-benzo[*d*][1,3]dioxin-4-one (S7)



To a stirred solution of bromo(heptyl)triphenylphosphonium ion (50 mg, 0.11 mmol) in THF (5 mL) and DMSO (1 mL) was added NaH (5 mg, 0.23 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 1 h. Compound **S6** (17 mg, 0.06 mmol) was added in THF (1 mL) at 0 °C and continued stirring for 1 h at the same temperature. After completion of the reaction, saturated NH_4Cl was added to the reaction mixture and extracted with hexane. The organic layer was dried under $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (9.75:0.25) to give **S7** (42 mg, 66%) as yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.38 (1H, t, 7.8 Hz), 6.92 (1H, d, J=7.8 Hz), 6.79 (1H, d, 8.3 Hz), 5.31-5.35 (2H, m), 3.08 (2H, t, 7.8 Hz), 1.98-2.02 (4H, m), 1.69 (6H, s), 1.55-1.61 (2H, m), 1.27-1.38 (18H, m), 0.87 (3H, t, 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.2, 157.1, 148.5, 135.0, 129.8, 125.0, 115.0, 112.2, 104.9, 34.3, 31.9, 31.1, 27.2, 27.2, 27.3, 27.4, 27.6, 27.6 28.9, 28.9, 27.2, 25.6, 22.6, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{25}H_{38}O_3$: 387.2893; found 387.2911.

Ginkgolic acid (15:1) (1)

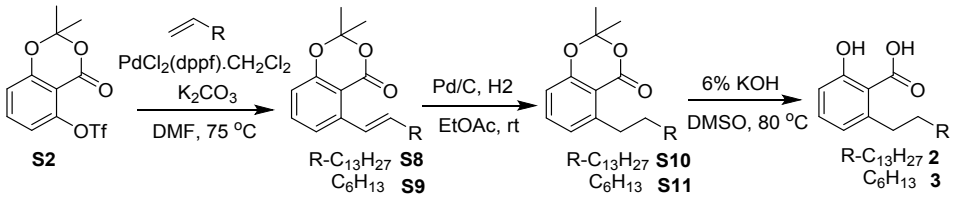


The solution of **S7** (37 mg, 0.1 mmol) in 50% KOH (0.5 mL) and DMSO (1.5 mL) stirred at 80°C for 1 h. The reaction was cooled to room temperature and acidified with 2M HCl, then extracted with EtOAc. The organic layer was dried under $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (9:1) as an eluent to give **1** (30 mg, 91%) as yellow oil.

^{1}H NMR ($CDCl_3$, 500MHz): δ = 10.99 (1H, s), 7.37 (1H, t, 7.9 Hz), 6.88 (1H, d, J=8.3 Hz), 6.78 (1H, d, J=7.5 Hz), 5.32-5.38 (2H, m), 2.97-3.00 (2H, t, J=7.5 Hz), 2.02-2.06 (4H, m), 1.60-1.62 (2H, m), 1.26-1.33 (18H, m), 0.88 (3H, t, J=6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.2, 163.6, 147.8, 135.42, 129.9, 129.9, 129.8, 122.8, 115.9, 110.5, 36.48, 32.1, 31.9, 31.8, 29.8, 29.7, 29.6, 29.3, 26.9, 26.9, 22.6, 22.3, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{22}H_{34}O_3$: 347.2580; found 347.2555

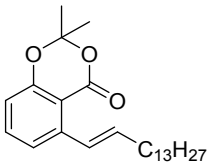
Synthesis of ginkgolic acid (15:0) (2) and its derivative (3)

Synthesis of ginkgolic acid (15:0) **2** and its derivative **3** were achieved in three steps starting from **S2**. It involves heck coupling of **S2** with 1-octene and 1-pentadecene using $PdCl_2(dppf).CH_2Cl_2$ to get compounds **S8** and **S9**, which were subjected to hydrogenation using Pd/C, H_2 to get compounds **S10** and **S11** followed by basic hydrolysis to obtain desired compounds ginkgolic acid (15:0) **2** and **3**.



Scheme S2: Synthesis of ginkgolic acid (15:0) **2** and compound **3**

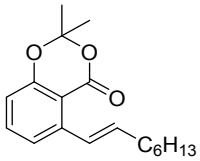
(*E*)-2,2-dimethyl-5-(pentadec-1-en-1-yl)-4H-benzo[d][1,3]dioxin-4-one (S8)



To a stirred solution of 1-pentadecene (354 mg, 1.68 mmol) in DMF (15 mL) at room temperature was added K_2CO_3 (231 mg, 1.68 mmol) and stirred for 0.5 h. Compound **S2** (500 mg, 1.53 mmol) and palladium catalyst $PdCl_2(dppf).CH_2Cl_2$ (37 mg, 0.05 mmol) was added to the reaction mixture. Then the reaction mixture was stirred overnight at 75 °C. After completion of the reaction, the reaction mixture was acidified with 2M HCl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The residue obtained was purified by silica gel column chromatography using hexane/EtOAc (9:1) to give **S8** (410 mg, Yield 69%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.38-7.46 (2H, m), 7.22 (1H, d, J=7.8 Hz), 6.80 (1H, d, 7.0 Hz), 6.19-6.25 (1H, m), 2.24-2.29 (2H, m), 1.69 (6H, s), 1.46-1.52 (2H, m), 1.22-1.30 (20H, m), 0.87 (3H, t, 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.2, 156.6, 142.6, 135.6, 134.8, 127.8, 121.1, 115.3, 110.4, 104.9, 33.1, 31.8, 29.6, 29.6, 29.6, 29.5, 29.4, 29.2, 29.2, 29.1, 25.5, 22.6, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{25}H_{38}O_3$: 387.2893; found 387.2869.

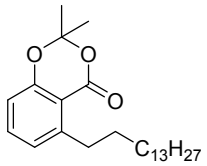
(*E*)-2,2-dimethyl-5-(oct-1-en-1-yl)-4H-benzo[d][1,3]dioxin-4-one (S9)



To a stirred solution of 1-octene (189 mg, 1.68 mmol) in DMF (15 mL) at room temperature was added K_2CO_3 (231 mg, 1.68 mmol) and stirred for 0.5 h. Compound **S2** (500 mg, 1.53 mmol) and palladium catalyst $PdCl_2(dppf).CH_2Cl_2$ (37 mg, 0.05 mmol) was added to the reaction mixture. Then the reaction mixture was stirred overnight at 75 °C. After completion of the reaction, the reaction mixture was acidified with 2M HCl and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The residue obtained was purified by silica gel column chromatography using hexane/EtOAc (9:1) to give **S9** (295 mg, Yield 67%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.39-7.46 (2H, m), 7.23 (1H, d, J=8.0 Hz), 6.81(1H, d, 8.0 Hz), 6.20-6.26 (1H, m), 2.25-2.29 (2H, m), 1.69 (6H, s), 1.46-1.52 (2H, m), 1.28-1.39 (6H, m), 0.88 (3H, t, 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.3, 156.6, 142.6, 135.6, 134.9, 127.8, 121.1, 115.3, 110.4, 104.9, 33.1, 31.6, 29.0, 28.8, 25.5, 22.5, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{18}H_{24}O_3$: 289.1752; found 289.1747.

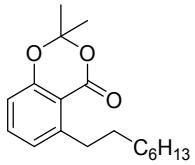
2,2-dimethyl-5-pentadecyl-4H-benzo[d][1,3]dioxin-4-one (S10)



To a stirred solution of **S8** (100 mg, 0.26 mmol) in EtOAc (10 ml) was added 10% Pd/C (30 mg, 0.026 mmol). The reaction mixture was stirred overnight at room temperature under H_2 atmosphere. Pd/C was filtered off and the filtrate was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (9:1) as an eluent to give **S10** (92 mg, 91%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.39 (1H, t, 8.0 Hz), 6.93 (1H, d, J=7.5 Hz), 6.80 (1H, d, 8.0 Hz), 3.09 (2H, t, 7.6 Hz), 1.70 (6H, s), 1.54-1.62 (2H, m), 1.19-1.31 (24H, m), 0.88 (3H, t, 6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.8, 156.9, 148.2, 134.8, 124.8, 114.8, 111.8, 104.6, 34.2, 31.7, 31.0, 29.5, 29.5, 29.5, 29.5, 29.4, 29.4, 29.4, 29.3, 29.2, 22.5, 13.9. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{25}H_{40}O_3$: 389.3050; found 387.3046.

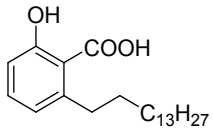
2,2-dimethyl-5-octyl-4H-benzo[d][1,3]dioxin-4-one (S11)



To a stirred solution of **S9** (100 mg, 0.35 mmol) in EtOAc (10 ml) was added 10% Pd/C (40 mg, 0.035 mmol). The reaction mixture was stirred overnight at room temperature under H_2 atmosphere. The solid was filtered off and the filtrate was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (9:1) to give **S11** (95 mg, 94%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.38 (1H, t, 8.3 Hz), 6.92 (1H, d, J=8.8 Hz), 6.79 (1H, d, 8.0 Hz), 3.08 (2H, t, 7.8 Hz), 1.68 (6H, s), 1.55-1.61 (2H, m), 1.21-1.32 (10H, m), 0.86 (3H, t, 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 157.0, 148.4, 134.9, 125.0, 115.0, 112.0, 104.8, 34.3, 31.8, 31.1, 29.4, 29.2, 25.6, 22.6, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{18}H_{24}O_3$: 291.1954; found 291.1949.

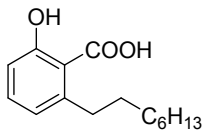
Ginkgolic acid (15:0) (2)



The solution of **S10** (50 mg, 0.13 mmol) in 50% KOH (0.75 mL) and DMSO (2 mL) stirred at 80 °C for 1 h. The reaction was cooled to temperature to room temperature and acidified with 2M HCl then extracted with EtOAc. The organic layer was dried under $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (7:3) as an eluent to give **2** (41 mg, 91%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 11.13 (1H, s), 7.37 (1H, t, 8.0 Hz), 6.88 (1H, d, J=8.3 Hz), 6.73 (1H, d, J=7.3 Hz), 3.00 (2H, t, J=7.8 Hz), 1.59-1.65 (2H, m), 1.29-1.34 (24H, m), 0.89 (3H, t, J=6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.3, 163.6, 147.8, 135.4, 122.7, 115.8, 110.4, 36.4, 32.0, 31.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.3, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{22}H_{36}O_3$: 349.2737; found 349.2712.

2-hydroxy-6-octylbenzoic acid (3)

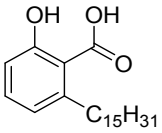


The solution of **S11** (30 mg, 0.10 mmol) in 50% KOH (0.5 mL) and DMSO (1.5 mL) stirred at 80 °C for 1 h. The reaction was cooled to temperature to room temperature and acidified with 2M HCl then extracted with EtOAc. The organic layer was dried under $MgSO_4$ and concentrated under vacuum. The

residue was purified by silica gel column chromatography using hexane/EtOAc (7:3) as an eluent to give **3** (25 mg, 96%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 10.99 (1H, s), 7.37 (1H, t, 8.0 Hz), 6.88 (1H, d, J=8.3 Hz), 6.79 (1H, d, J=7.1 Hz), 2.98 (2H, t, J=8.0 Hz), 1.58-1.64 (2H, m), 1.28-1.38 (10H, m), 0.88 (3H, t, J=6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.3, 163.6, 147.8, 135.4, 122.8, 115.8, 110.3, 36.4, 31.9, 31.8, 29.7, 29.4, 29.2, 22.6, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{15}H_{22}O_3$: 251.1641; found 251.1636.

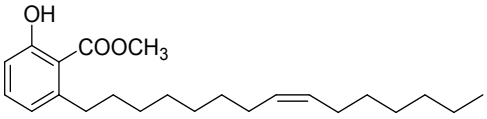
Ginkgolic acid (15:0) (2) from Ginkgolic acid (15:1) (1)



To a stirred solution of ginkgolic acid (15:1) **1** (50 mg, 0.14 mmol) in EtOAc (10 ml) was added 10% Pd/C (30 mg, 0.028 mmol). The reaction mixture was stirred overnight at room temperature under H_2 atmosphere. The solid was filtered off and the filtrate was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (9.0:1.0) to give **2** (48 mg, 96%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 11.13 (1H, s), 7.37 (1H, t, 8.0 Hz), 6.88 (1H, d, J=8.3 Hz), 6.73 (1H, d, J=7.3 Hz), 3.00 (2H, t, J=7.8 Hz), 1.59-1.65 (2H, m), 1.29-1.34 (24H, m), 0.89 (3H, t, J=6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.3, 163.6, 147.8, 135.4, 122.7, 115.8, 110.4, 36.4, 32.0, 31.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.3, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{22}H_{36}O_3$: 349.2737; found 349.2712

Methyl ester of Ginkgolic ester (4)

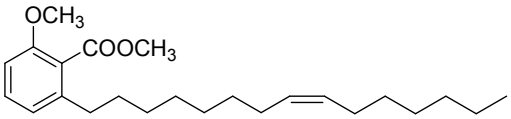


To a stirred solution of ginkgolic acid (15:1) **1** (25 mg, 0.1 mmol) in methanol (2 mL) and diethyl ether (2 mL) was added a solution of TMS-CH_2N_2 in hexane until the color of the solution became yellow at 0 °C. The reaction mixture was stirred at same temperature for 0.5 h. The reaction was quenched with acetic acid and extracted with EtOAc, dried over $MgSO_4$. The organic layer was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (9.75:0.25) as an eluent to give the ester **4** (25 mg, 96%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 11.13 (1H, s), 7.29 (1H, t, 7.8 Hz), 6.85 (1H, d, J=8.3 Hz), 6.73 (1H, d, J=7.3 Hz), 5.39-5.33 (2H, m), 3.90 (3H s), 2.89 (2H, t, J=7.8 Hz), 2.03-2.08 (4H, m), 1.51-1.56 (2H, m), 1.29-1.34 (18H, m), 0.91 (3H, t, J=7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.9, 162.5, 146.1, 134.1, 129.8, 129.8, 122.8, 122.4, 115.5, 111.8, 52.0, 36.6, 32.1, 31.9, 29.9, 29.7, 29.6, 29.6, 29.6, 29.5, 29.5,

29.5, 29.5, 29.3, 29.3, 27.2, 26.9, 22.3, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{23}H_{36}O_3$: 361.2737; found 361.2717.

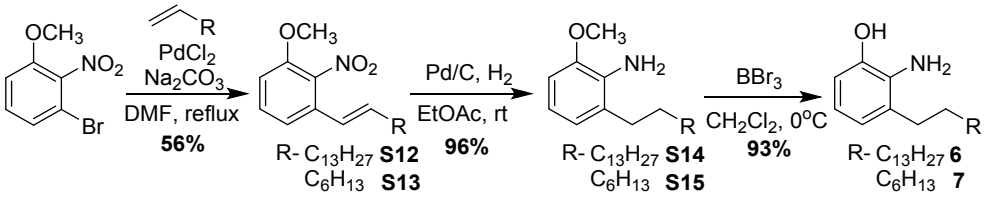
Methyl (*Z*)-2-methoxy-6-(pentadec-8-en-1-yl)benzoate (5)



To a stirred solution of Ginkgolic acid (15:1) **1** (100 mg, 0.29 mmol) in DMF (2mL) was added K_2CO_3 (0.73 mmol, 2.5 eq) and iodomethane (0.58 mmol, 2 eq) at room temperature. Then the reaction mixture was stirred at 90 °C under Ar atmosphere overnight. After completion of the reaction the reaction mixture was cooled to room temperature and acidified with 2M HCl and extracted with EtOAc, and dried over $MgSO_4$. The organic layer was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (9.5:0.5) to give the ester **5** (103 mg, 95%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.28 (1H, t, 8.3 Hz), 6.83 (1H, d, J=7.8 Hz), 6.77 (1H, d, J=8.3 Hz), 5.33-5.37 (2H, m), 3.92 (3H, s), 3.83 (3H, s), 2.55 (2H, t, J=8.0 Hz), 2.01-2.04 (4H, m), 1.56-1.61 (2H, m), 1.29-1.34 (18H, m), 0.90 (3H, t, J=7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.9, 156.2, 141.3, 130.2, 129.9, 129.8, 123.4, 121.4, 108.3, 33.4, 31.7, 31.1, 29.7, 29.7, 29.4, 29.3, 29.1, 28.9, 27.2, 27.1, 22.6, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{24}H_{38}O_3$: 375.2893; found 375.2867.

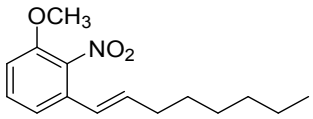
Synthesis of compound 6 and 7



Scheme S3: synthesis of compound **6** and **7**

Compound **6** and **7** synthesis was achieved in three steps from the commercially available compound, 3-bromo-2-nitro-anisole. Compounds **S12** and **S13** were synthesized by coupling of 3-bromo-2-nitro-anisole with 1-pentadecene and 1-octene under palladium catalyst through heck reaction. Reduction of nitro group and an unsaturation in hydrocarbon chain of **S12** and **S13** were achieved in single step by using H_2 and Pd/C at ambient temperature to get **S14** and **S15**, followed by O-demethylation was done by Lewis acid BBr_3 at 0 °C to get desired compounds **6** and **7**.

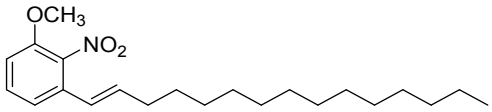
(*E*)-1-methoxy-2-nitro-3-(oct-1-en-1-yl)benzene (S13)



To a stirred solution of 3-bromo-2-nitro-anisole (750 mg, 3.23 mmol) in DMF (10 mL) was added 1-octene (725 mg, 6.46 mmol), Na_2CO_3 (536 mg, 3.87 mmol) and $PdCl_2$ (28 mg, 0.16 mmol). The reaction mixture was refluxed overnight. The reaction mixture was cooled to room temperature, neutralized with 2M HCl and extracted with Et_2O. The organic layer was dried under $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (9.5:0.5) to give **S13** (410 mg, 48%) as yellow oil.

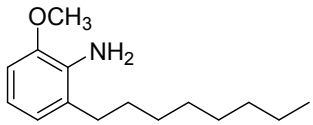
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.23 (1H, t, 8.3 Hz), 6.04(1H, d, J=7.85 Hz), 6.78(1H, d, 8.3 Hz), 6.20-6.26 (1H, m), 5.28- 3.53 (1H, m), 3.78 (3H, s), 2.45 (1H, t, 8.0 Hz), 2.13 (1H, q, 14.4, 7.1, 7.3) 1.65-1.84 (1H, m), 1.37-1.57 (1H, m), 1.20-1.35 (6H, m), 0.80 (3H, t, 6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.6, 137.5, 131.1, 130.4, 121.8, 121.6, 117.8, 110.3, 56.3, 56.2, 33.1, 31.6, 29.1, 28.8, 22.5, 14.0. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{15}H_{21}NO_3$: 264.1594; found 264.1575.

(*E*)-1-methoxy-2-nitro-3-(pentadec-1-en-1-yl)benzene (S12)



^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.31 (1H, t, 8.0 Hz), 6.86 (2H, d, 8.2 Hz), 6.21-6.34 (1H, m), 5.34-5.42 (1H, m), 3.87 (3H, s), 2.53(2H, t, 7.8 Hz), 2.15-2.18 (1H, m), 1.96-1.99 (2H, m), 1.57-1.60 (4H, m), 1.25-1.32 (16H, m), 0.87 (3H, t, 6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.6, 150.5, 137.5, 130.5, 130.4, 121.8, 121.6, 117.8, 110.3, 109.8, 56.3, 56.2, 43.8, 33.8, 33.2, 31.9, 30.8, 32.9, 30.5, 29.8, 28.7, 29.6, 29.3, 29.1, 28.2, 23.8, 22.6, 14.1. HRMS (*m/z*): $[M+Na]^+$ calculated for $C_{22}H_{35}NO_3Na$: 384.2509; found 384.2518.

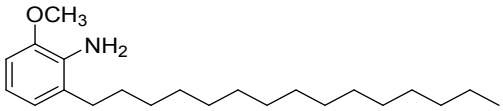
2-methoxy-6-octylaniline (S15)



To a stirred solution of **S13** (275 mg, 1.04 mmol) in EtOAc (10 ml) was added 10% Pd/C (220 mg, 0.21 mmol). The reaction mixture was stirred overnight under H_2 atmosphere at room temperature. Pd/C was filtered off and the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (9:1) to give **S15** (235 mg, 96%) as yellow oil.

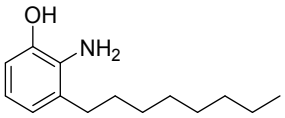
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.67-6.70 (3H, m), 3.84 (3H, s), 3.78(2H, s), 2.49 (2H, t, 7.6 Hz), 1.54-1.64 (2H, m), 1.21-1.37 (24H, m), 0.87 (3H, t, 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.2, 133.5, 127.4, 121.6, 117.7, 108.1, 55.5, 55.5, 55.4, 31.9, 31.2, 29.7, 29.7, 29.9, 29.6, 29.4, 28.8, 27.8, 27.6, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{15}H_{25}NO$: 236.2008; found 236.1998,

2-methoxy-6-pentadecylaniline (S14)



^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.67-6.70 (3H, m), 3.84 (3H, s), 3.78(2H, s), 2.49 (2H, t, 7.6 Hz), 1.54-1.64 (2H, m), 1.21-1.37 (24H, m), 0.87 (3H, t, 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.2, 133.5, 127.4, 121.6, 117.7, 108.1, 55.5, 55.5, 55.4, 31.9, 31.2, 29.7, 29.7, 29.9, 29.6, 29.4, 28.8, 27.8, 27.6, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{22}H_{39}NO$: 334.3104; found 334.3122.

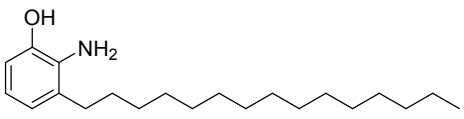
2-amino-3-octylphenol (7)



To a stirred solution of **s7b** (100 mg, 0.426 mmol) in CH_2Cl_2 (5 ml) under Ar atmosphere was added BBr_3 (320 mg, 1.28 mmol) at 0°C. The reaction mixture was stirred at 0 °C for additional 2h. After completion of the reaction, reaction mixture was quenched with EtOAc/H_2O (1:1) and extracted with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc (8:2) to give **7** (410 mg, 96%) as yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.57-6.70 (3H, m), 4.61 (3H, s), 2.50-2.53 (2H, t, 7.6 Hz), 1.60-1.64 (2H, m), 1.22-1.40 (10H, m), 0.91 (3H, t, 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.3, 131.7, 129.6, 121.5, 119.1, 112.9, 31.9, 31.6, 29.7, 29.7 29.3, 29.0, 22.8, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{14}H_{23}NO$: 222.1852; found 222.1831.

2-amino-3-pentadecylphenol (6)



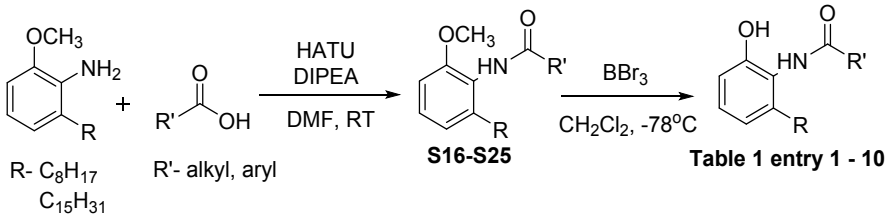
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.59-6.70 (3H, m), 4.36 (2H, s), 2.55 (2H, t, 7.8 Hz), 1.56-1.64 (4H, m), 1.22-1.39 (25H, m), 0.90 (3H, t, 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.2, 131.9, 129.6, 121.6,

118.9, 112.8, 31.9, 31.2, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.0, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{21}H_{37}NO$: 320.2947; found 320.2967.

7. Synthesis of ginkgolic acid ceramides

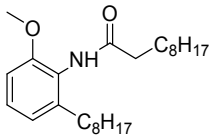
General procedure for amidation reaction:

To a stirred solution of acid (0.315 mmol) in DMF under Ar atmosphere was added *N,N*-diisopropylethylamine (1.1 mmol) at room temperature. To the reaction mixture amine (0.21 mmol) and HATU (0.42 mmol) was added. The reaction mixture was stirred under Ar atmosphere at room temperature for additional 2h. After completion of the reaction, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc to give desired compound.



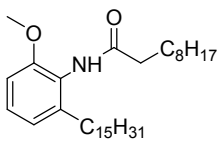
Scheme S4: Coupling reaction and *O*-demethylation reaction

***N*-(2-methoxy-6-octylphenyl)decanamide (S16)**



(As a white solid, 92%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.17 (1H, t, 7.8 Hz), 6.87 (1H, d, 7.8 Hz), 6.76 (1H, d, 7.8 Hz), 6.68 (1H, s), 3.80(3H, s), 2.56 (2H, t, 7.8), 2.41 (2H, t, 7.3 Hz), 1.73-1.78 (2H, m), 1.54-1.60 (2H, m), 1.41-1.43 (2H, m), 1.21-1.29 (20H, m), 0.84-0.89 (6H, m). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{25}H_{43}NO_2$: 390.3366; found 390.3363.

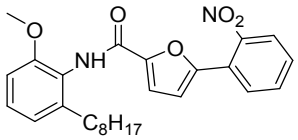
***N*-(2-methoxy-6-pentadecylphenyl)decanamide (S21)**



(As white solid, 93%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.15 (1H, t, 7.8 Hz), 6.85 (1H, d, 7.8 Hz), 6.74 (1H, d, 7.8 Hz), 6.67 (1H, s), 3.79 (3H, s), 2.55 (2H, t, 7.6), 2.40 (2H, t, 7.3 Hz), 1.73-1.77 (2H, m), 1.55-

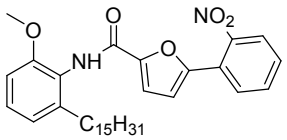
1.51 (2H, m), 1.42-1.44 (1H, m), 1.19-1.26 (36H, m), 0.87 (6H, t, 7.1 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{32}H_{57}NO_2$: 488.4462; found 488.4442.

_N_-(2-methoxy-6-octylphenyl)-5-(2-nitrophenyl)furan-2-carboxamide (S17)



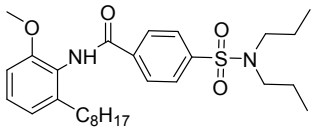
(As yellow oil, 87%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.01 (1H, s), 7.76 (2H, t, 8.1 Hz), 6.64 (1H, t, 8.0 Hz), 7.50-754 (2H, m), 7.28 (1H, d, 7.8 Hz), 6.89 (1H, d, 7.3), 6.78-6.82 (2H, m), 3.84(3H, s), 2.64 (2H, t, 7.8 Hz), 1.20-1.33 (10H, m), 0.83(3H, t, 6.8 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{26}H_{30}N_2O_5$: 451.2267; found 451.2247.

_N_-(2-methoxy-6-pentadecylphenyl)-5-(2-nitrophenyl)furan-2-carboxamide (S22)



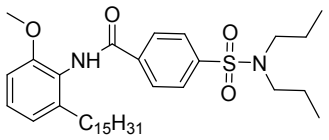
(As a yellow solid, 94%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.75-7.79 (2H, m), 7.65 (1H, t, 8.1 Hz), 7.58 (1H, s), 7.52 (1H, t, 8.0 Hz), 7.21-7.3 (2H, m), 6.91 (1H, d, 7.8), 6.79-6.84 (2H, m), 3.85 (3H, s), 2.66 (2H, t, 7.8 Hz), 1.60-1.64 (2H, m), 1.33-1.22 (24H, m), 0.89 (3H, t, 6.8 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{33}H_{44}N_2O_5$: 549.3323; found 549.3316.

4-(_N_,_N_-dipropylsulfamoyl)-_N_-(2-methoxy-6-octylphenyl)benzamide (S18)



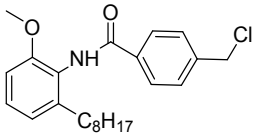
(As a white solid, 88%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.02 (1H, d, 7.8 Hz), 7.90 (2H, d, 7.3 Hz), 7.55 (1H, s), 7.23 (1H, t, 8.0 Hz), 6.92 (1H, d, 7.8 Hz), 6.80 (1H, d, 7.5 Hz), 3.80 (3H, s), 3.10 (4H, t, 7.8 Hz), 2.62 (2H, t, 7.8 Hz), 1.55-1.61 (6H, m), 1.55-1.61(10H, m), 0.83-0.90 (9H, m). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{28}H_{42}N_2O_4S$: 503.2938; found 503.2929.

4-(*N*,*N*-dipropylsulfamoyl)-*N*-(2-methoxy-6-pentadecylphenyl)benzamide (S23)



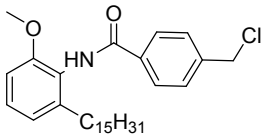
(As a yellow solid, 86%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.01 (1H, d, 5.4 Hz), 7.89 (2H, d, 7.1 Hz), 7.53 (1H, s), 7.22 (1H, t, 8.0 Hz), 6.91 (1H, d, 7.8 Hz), 6.79 (1H, d, 7.5 Hz), 3.79 (3H, s), 3.10 (4H, t, 7.6 Hz), 2.62 (2H, t, 7.8 Hz), 1.53-1.62 (6H, m), 1.22-1.30 (25H, m), 0.86-0.90 (9H, m). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{35}H_{56}N_2O_4S$: 601.4033; found 601.4031.

4-(chloromethyl)-*N*-(2-methoxy-6-octylphenyl)benzamide (S19)



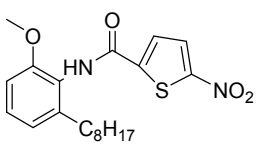
(As a yellow solid, 90%) ^{1}HNMR ($CDCl_3$, 500 MHz): δ = 8.69 (1H, d, 4.3 Hz), 8.33 (1H, d, 8.3 Hz), 7.9 (1H, s), 7.92 (1H, d, 8.3 Hz), 7.61 (2H, d, 7.1 Hz), 7.38 (1H, t, 4.0 Hz), 6.89 (1H, d, 7.8 Hz), 6.76 (1H, d, 8.0 Hz), 5.69 (2H, s), 3.76 (3H, s) 2.60 (2H, t, 7.8 Hz) 1.56-1.60 (2H, m), 1.20-1.24 (10H, m), 0.83 (3H, t, 6.8Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{23}H_{30}ClNO_2$: 388.2037; found 388.2033.

4-(chloromethyl)-*N*-(2-methoxy-6-pentadecylphenyl)benzamide (S24)



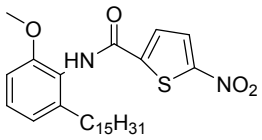
(As a yellow solid, 93%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.93 (2H, s), 7.48-7.53 (3H, m), 7.23 (1H, t, 8.0 Hz), 6.93 (1H, d, 7.8 Hz), 6.80 (1H, d, 7.8 Hz), 4.65 (2H, s), 3.81 (3H, s), 2.65 (2H, t, 7.5 Hz), 1.59-1.65 (2H, m), 1.24-1.27 (24H, m), 0.90 (3H, t, 6.8Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{30}H_{44}ClNO_2$: 48603133; found 486.3133.

***N*-(2-methoxy-6-octylphenyl)-5-nitrothiophene-2-carboxamide (S20)**



(As a light yellow solid, 87%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.90 (1H, s), 7.53 (1H, s), 7.25-7.37 (2H, m), 6.93 (1H, d, 7.8 Hz), 6.81 (1H, d, 8.0 Hz), 3.81 (3H, s), 2.61 (2H, t, 7.8 Hz), 1.55-1.60 (2H, m), 1.23-1.28 (10H, m), 0.86 (3H, t, 6.8 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{20}H_{26}N_2O_4S$: 391.1686; found 391.1675.

_N_-(2-methoxy-6-pentadecylphenyl)-5-nitrothiophene-2-carboxamide (S25)

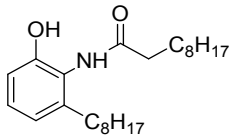


(As a yellow solid, 88%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.89 (1H, s), 7.53 (1H, s), 7.26-7.39 (2H, m), 6.92 (1H, d, 7.5 Hz), 6.81 (1H, d, 7.3 Hz), 3.81 (3H, s), 2.60 (2H, t, 8.1 Hz), 1.56-1.61 (2H, m), 1.23-1.31 (25H, m), 0.88 (3H, t, 6.8Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{27}H_{40}N_2O_4S$: 489.2781; found 489.2754.

General procedure for _O_-demethylation of compounds S16-S25:

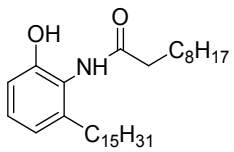
To a stirred solution of methyl phenyl ethers (0.06 mmol) in CH_2Cl_2 under Ar atmosphere was added BBr_3 (320 mg, 1.28 mmol) at 78°C. The reaction mixture was stirred for 1h at 0°C. After completion of the reaction, the reaction mixture was cooled to room temperature and quenched with EtOAc/H_2O (1:1) and extracted with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel column chromatography using hexane/EtOAc

_N_-(2-hydroxy-6-octylphenyl)decanamide (Table 1 entry 1)



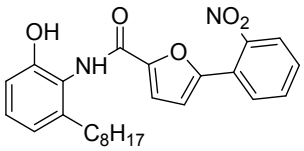
(As yellow oil, 90%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.31 (1H, d, 8.3 Hz), 7.20 (1H, t, 7.8 Hz), 7.11 (1H, d, 7.3 Hz), 2.91-2.98 (4H, m), 1.83-1.89 (2H, m), 1.71-1.77 (2H, m), 1.27-1.43 (22H, m), 0.87-0.89 (6H, m). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{24}H_{41}NO_2$: 376.3210; found 376.3198.

_N_-(2-hydroxy-6-pentadecylphenyl)decanamide (Table 1 entry 6)



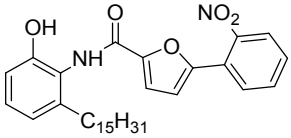
(As a white solid, 87%) ^{1}H NMR ($CDCl_3$, 500.MHz): δ = 7.08 (1H, t, 7.7 Hz), 6.91 (1H, d, 7.0 Hz), 6.75 (1H, d, 8.5 Hz), 2.54 (2H, t, 7.8), 2.47 (2H, t, 7.6 Hz), 1.74-1.78 (2H, m), 1.52-1.58 (2H, m), 1.23-1.41 (40H, m), 0.86-0.89 (6H, m). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{31}H_{55}NO_2$: 474.4305; found 474.4286.

_N_-(2-hydroxy-6-octylphenyl)-5-(2-nitrophenyl)furan-2-carboxamide (Table 1 entry 2)



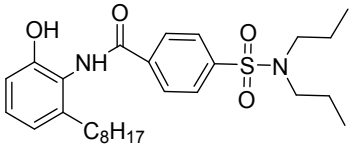
(As a red solid, 95%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.34 (1H, s), 8.10 (1H, d, 3.9 Hz), 7.79 (1H, d, 8.0 Hz), 7.72 (1H, d, 7.8 Hz), 7.67 (1H, t, 7.3 Hz), 7.57 (1H, t, 7.6 Hz), 7.14 (1H, t, 7.8 Hz), 6.97 (1H, s), 6.88 (1H, d, 3.6 Hz), 6.82 (1H, d, 7.6 Hz), 2.69 (2H, t, 7.5 Hz), 6.61-6.66 (2H, m), 1.04-1.40 (2H, m), 1.16-1.30 (10H, m), 0.83 (3H, t, 6.8 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{25}H_{28}N_2O_5$: 437.2071; found 437.2056.

_N_-(2-hydroxy-6-pentadecylphenyl)-5-(2-nitrophenyl)furan-2-carboxamide (Table 1 entry 7)



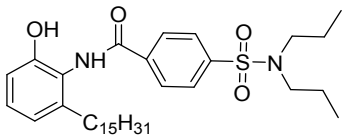
(As an orange solid, 97%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.35 (1H, s), 8.1 (1H, s), 7.81 (1H, d, 6.8 Hz), 7.73 (1H, d, 6.8 Hz), 7.68 (1H, t, 7.3), 7.57 (1H, t, 7.6 Hz), 7.40 (1H, d, 3.6), 7.15 (1H, t, 7.8 Hz), 6.98 (1H, t, 7.3) (2H, m), 6.90 (1H, d, 3.6 Hz), 6.83 (1H, d, 8.3 Hz), 2.70 (2H, t, 7.6 Hz), 1.62-1.67 (2H, m), 1.38-1.41 (2H, s), 1.19-1.31 (24H, m), 0.88 (3H, t, 6.6 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{32}H_{42}N_2O_5$: 535.3166; found 535.3162.

4-(_N_,_N_-dipropylsulfamoyl)-_N_-(2-hydroxy-6-octylphenyl)benzamide (Table 1 entry 3)



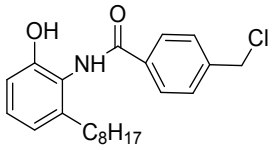
(As a yellow solid, 90%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.0 (2H, d, 8.5 Hz), 7.97 (3H, t, 8.3 Hz), 6.99 (1H, d, 8.3 Hz), 6.84 (1H, d, 8.5 Hz), 3.13 (4H, t, 7.8 Hz), 2.67 (2H, t, 7.6 Hz), 1.55-1.61 (6H, m), 1.21-1.30 (10H, m), 0.85-0.90 (9H, m). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{27}H_{40}N_2O_4S$: 489.2781; found 489.2785.

4-(*N*,*N*-dipropylsulfamoyl)-*N*-(2-hydroxy-6-pentadecylphenyl)benzamide (Table 1 entry 8)



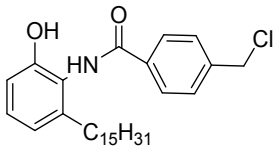
(As yellow oil, 92%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.96-8.03 (4H, m), 7.18 (1H, t, 7.8 Hz), 7.00 (1H, d, 5.6 Hz), 6.85 (1H, d, 7.3 Hz), 3.14 (4H, t, 7.8 Hz), 2.68 (2H, t, 7.3 Hz), 1.55-1.65 (6H, m), 1.25-1.35 (24H, m), 0.89 (9H, t, 7.3 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{34}H_{54}N_2O_4S$: 587.3877; found 587.3855.

4-(chloromethyl)-*N*-(2-hydroxy-6-octylphenyl)benzamide (Table 1 entry 4)



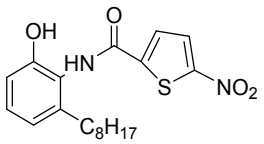
(As yellow oil, 90%) ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.30 (1H, s), 7.94 (1H, s), 7.88 (2H, d, 8.3 Hz), 7.56 (2H, d, 8.3 Hz), 7.14 (1H, t, 7.8 Hz), 6.8 (1H, d, 8.3 Hz), 6.81 (1H, d, 8.5 Hz), 4.53 (2H, s), 2.66 (2H, t, 7.6 Hz), 1.59-1.65 (2H, m), 1.21-1.39 (12H, m), 0.86 (3H, t, 7.0 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{22}H_{28}ClNO_2$: 374.1881; found 374.1873.

4-(chloromethyl)-*N*-(2-hydroxy-6-pentadecylphenyl)benzamide (Table 1 entry 9)



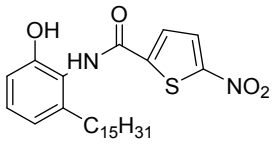
(As a white solid, 95%) ^{1}H NMR (CDCl3, 500 MHz): δ = 8.33 (1H, s), 7.91-8.00 (3H, m), 7.58 (2H, d, 7.5 Hz) 7.16 (1H, t, 8.0 Hz), 6.99 (1H, d, 7.8 Hz), 6.82 (1H, d, 7.5 Hz), 4.66 (2H, s), 2.67 (2H, t, 7.0 Hz), 1.56-1.68 (2H, m), 1.26-1.42 (25H, m), 0.88 (3H, t, 6.8Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{29}H_{42}ClNO_2$: 472.2976; found 472.2973.

***N*-(2-hydroxy-6-octylphenyl)-5-nitrothiophene-2-carboxamide (Table 1 entry 5)**



(As a yellow solid, 92%) ^{1}H NMR (CDCl3, 500 MHz): δ = 8.41 (1H, s), 7.4 (1H, s), 7.28 (1H, d, 7.3), 7.12 (1H, t, 7.8 Hz), 6.96 (1H, d, 8.0 Hz), 6.79 (1H, d, 7.3 Hz), 4.55 (1H, s), 2.63 (2H, t, 7.5 Hz), 1.50-1.64 (2H, m), 1.26-1.41 (10H, m), 0.88 (3H, t, 6.5 Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{19}H_{24}N_2O_4S$: 377.1529; found 377.1528.

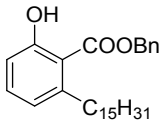
***N*-(2-hydroxy-6-pentadecylphenyl)-5-nitrothiophene-2-carboxamide (Table 1 entry 10)**



(As a yellow solid, 92%) ^{1}H NMR ($CDCl_3$, 500 MHz) δ = 8.41 (1H, s), 7.45 (1H, s), 7.28 (1H, s), 7.11 (1H, d, 7.8 Hz), 6.96 (1H, d, 7.6 Hz), 6.79 (1H, d, 7.5 Hz), 4.56 (1H, s), 2.63 (2H, t, 7.3 Hz), 1.58-1.63 (2H, m), 1.26-1.40 (24H, m), 0.88 (3H, t, 6.8Hz). HRMS (*m/z*): $[M+H]^+$ calculated for $C_{26}H_{38}N_2O_4S$: 475.0562; found 475.0548.

6. Synthesis of ginkgolic acid 2-phosphate

Benzyl 2-hydroxy-6-pentadecylbenzoate (S26)

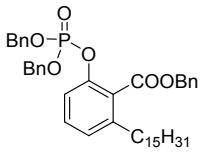


To a stirred solution of ginkgolic acid (15:0) **2** (100 mg, 0.29 mmol) in triethylamine (1:1 v/v) was stirred at 90 °C for few minutes. Then benzyl chloride (36 mg, 0.29 mmol) was added to the reaction mixture at 90 °C and stirred for additional 1.5 hours at 90 °C. After completion of the reaction, the reaction mixture was cooled to room temperature and acidified with 2M HCl, extracted with EtOAc and dried over $MgSO_4$. The organic layer was concentrated under vacuum to afford a residue that was purified by silica gel column chromatography using hexane/EtOAc (9.25:0.75) to give desired compound **S26** (118 mg, 94%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 11.21 (1H, s), 7.47 (2H, d, 6.11 Hz), 7.40-7.44 (3H, m), 7.30 (1H, t, 8.0 Hz), 6.86 (1H, d, J=8.3 Hz), 6.72 (1H, d, J=7.3 Hz), 5.41 (2H, s), 2.83 (2H, t, 9.8 Hz), 1.40-1.47 (2H, m), 1.30-1.37 (18H, m), 1.09-1.20 (6H, m), 0.92 (3H, t, J=6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.3,

162.7, 146.3, 134.8, 134.2, 129.0, 128.7, 122.4, 115.5, 111.8, 67.7, 29.8, 29.7, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{29}H_{42}O_3$: 439.3206; found 439.3215.

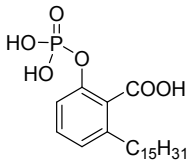
Benzyl 2-((bis(benzyloxy)phosphoryl)oxy)-6-pentadecylbenzoate (S27)



To a stirred solution of **S26** (60 mg, 0.18 mmol) in CH_3CN (5 mL) was stirred at 0 °C for few minutes under Ar atmosphere. DIPEA (57 mg, 0.44 mmol), DMAP (catalytic amount 0.05 eq), CCl_4 (270 mg, 1.75 mmol) and dibenzylphosphite (55 mg 0.21 mmol) were added to the reaction mixture at 0 °C and stirred at room temperature for 2 h.[4] After completion of the reaction, the reaction mixture was cooled to room temperature and acidified with 2M HCl, extracted with EtOAc and dried over $MgSO_4$. The organic layer was concentrated under vacuum. The residue was purified by silica gel column chromatography using chloroform (100%) as an eluent to get **S27** (86 mg, 91%) as colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.40 (2H, t, 6.8 Hz), 7.25-7.31 (15H, m), 7.03 (1H, d, 7.5 Hz), 5.29 (2H, s), 5.01-5-10 (4H, m), 2.57 (2H, t, 7.8 Hz), 1.51-1.56 (2H, m), 1.17-1.32 (24H, m), 0.90 (3H, t, J=6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 147.4, 142.5, 135.5, 135.4, 135.3, 130.5, 128.7, 128.5, 128.5, 128.5, 128.5, 128.4, 127.9, 127.9, 125.9, 117.2, 70.0, 67.2, 33.6, 31.9, 31.3, 29.7, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 22.7, 14.1. HRMS (*m/z*): $[M+H]^+$ calculated for $C_{43}H_{55}O_6P$: 699.3809; found 699.3816.

Ginkgolic acid 2-phosphate (GA2P)



To a stirred solution of **S27** (40 mg, 57 µmol) in MeOH (5 ml) was added 10% Pd/C (45 mg, 52 µmol). The reaction mixture was stirred overnight at rt under H_2 atmosphere. The solid was filtered off and the filtrate was concentrated under vacuum to afford a residue that was washed with non-polar solvents to get pure ginkgolic acid 2-phosphate (23 mg, 96%) as white solid.

^{1}H NMR (CD_3OD, 500 MHz): δ = 7.26-7.32 (2H, t, m), 7.01 (1H, d, 7.0 Hz), 2.66 (2H, t, 8.0 Hz), 1.57-1.61 (2H, m), 1.28-1.32 (24H, m), 0.89 (3H, t, J=7.1 Hz). HRMS (*m/z*): $[M+Na]^+$ calculated for $C_{22}H_{37}O_6PNa$: 451.2220; found 451.2214.

7. SMS assay

Cell lysates were prepared as follows: ZS/SMS1 and ZS/SMS2 cells (protein concentration 0.1 µg/µL) were diluted by Tris-buffer (pH 7.5) 20 mM and sonicated. Aiquots of the cell lysates 100 µL were added 1 µL of inhibitor of desired concentration and incubated at 37°C. After 30 min, the solutions were added 1 µL of C6-NBD-ceramide and incubated for 3 h at 37°C. The reaction was stopped by addition of 400 µL of MeOH/CHCl3 [1/2 (v/v)]; the mixture was shaken and centrifuged (1500 rpm x 5 min). The formation of C6-NBD-sphingomyelin was quantified by determination of the peak area of C6-NBD-sphingomyelin using HPLC. A reverse phase HPLC assay using a JACSO HPLC system was developed for the quantitative analysis of the inhibitory activity. The system was equipped with a PU-2089 Plus and FP-2020 Plus set at λex = 470 nm and λem = 530 nm. A 50 x 4.6 YMC-Pack Diol-120-NP column (5-µm particle size) was used with mobile phase (IPA/hexane/water) at a flow rate of 1.0 mL/min

SMS inhibition assay of ginkgolic acid (15:1)

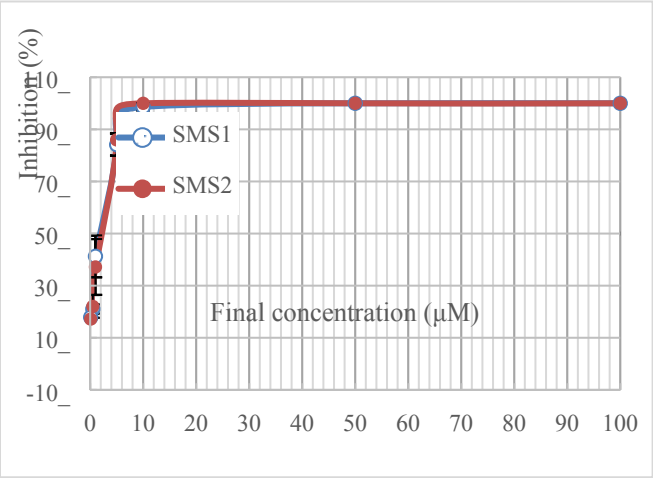


Figure S1: Inhibition activity of ginkgolic acid (15:1) with IC_{50} of 1.5 µM on both SMS1 and SMS2. IC_{50} values were measured by cell based assay system: SMS expressing cell lysates (20 mM tris-buffer, 100 mL) and compounds were incubated for 3 hours at 37°C, then fluorescent lipids were extracted from lysates by the Bligh-Dyer method, and directly applied to HPLC.

SMS2 inhibition activity of ginkgolic acid derivatives

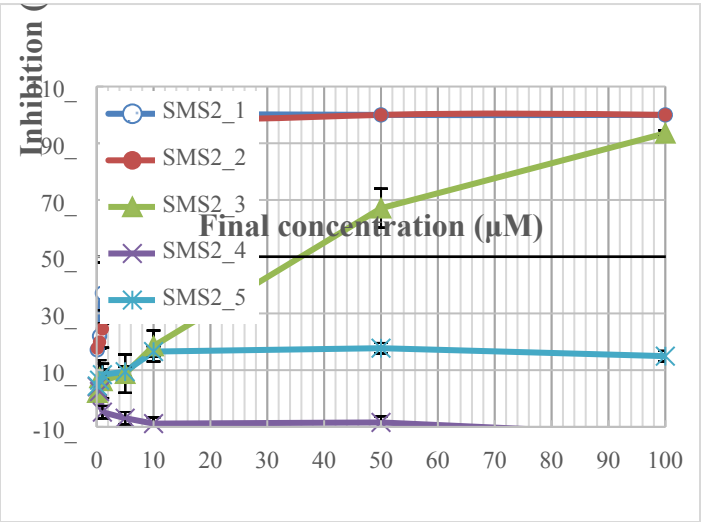
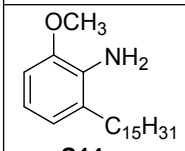
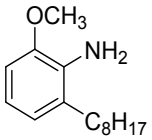
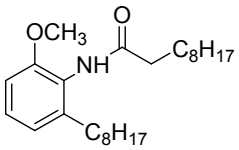
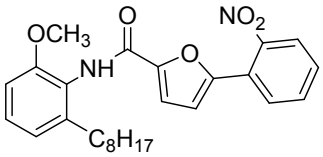
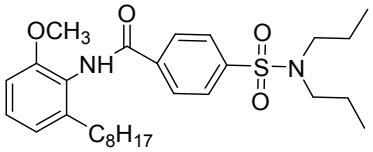
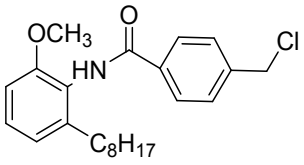
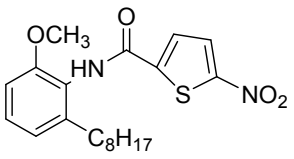
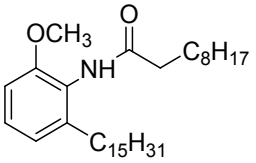
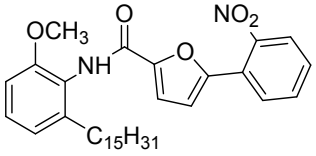
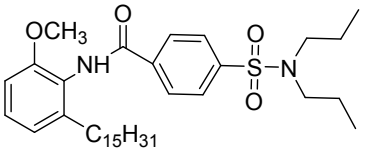
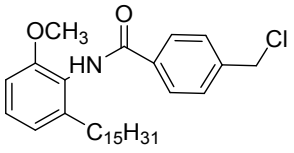
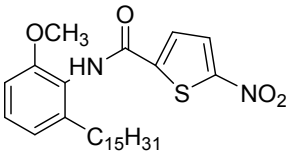


Figure S2: Inhibition activities of ginkgolic acid (15:1) and its derivatives **2-5** on SMS2. IC_{50} values were measured by cell based assay system: SMS expressing cell lysates (20 mM tris-buffer, 100 mL) and compounds were incubated for 3 hours at 37°C, then fluorescent lipids were extracted from lysates by the Bligh-Dyer method, and directly applied to HPLC.

Table S1: SMS1 and SMS2 Inhibition activities of intermediates with IC_{50} values. IC_{50} values were measured by cell based assay system: SMS expressing cell lysates (20 mM tris-buffer, 100 mL) and compounds were incubated for 3 hours at 37°C, then fluorescent lipids were extracted from lysates by the Bligh-Dyer method, and directly applied to HPLC.

Compounds	IC_{50} in µM	Compounds	IC_{50} in µM
 **S14**	SMS1- >100 µM SMS2- >100 µM	 **S15**	SMS1- >100 µM SMS2- >100 µM
 **S16**	SMS1- 15 µM SMS2- >100 µM	 **S17**	SMS1- 5 µM SMS2- 20 µM
 **S18**	SMS1- >100 µM SMS2- >100 µM	 **S19**	SMS1- 9 µM SMS2- 70 µM

 **S20**	SMS1- >100 µM SMS2- >100 µM	 **S21**	SMS1- >100 µM SMS2- >100 µM
 **S22**	SMS1- 80 µM SMS2- >100 µM	 **S23**	SMS1- >100 µM SMS2- >100 µM
 **S24**	SMS1- >100 µM SMS2- >100 µM	 **S25**	SMS1- >100 µM SMS2- 20 µM

8. [^{32}P] S1P binding assay

[^{32}P]S1P was synthesized enzymatically using [√-^{32}P]ATP, sphingosine and purified sphingosine kinase SPHK1 as described previously (reference 5). $S1P_1$-CHO cells (5.0 x 104 cells) were seeded in 24-well plate and incubated for 24 h. The cells were incubated for 12 h with F-12 medium containing charcoal-treated FBS, and for another 12 h with F-12 medium. Cells were washed twice with ice cold PBS, and incubated for 30 min at 4 °C in 200 µL of binding buffer [20 mM Tris-HCl (pH 7.4), 100 mM NaCl, 15 mM NaF, 2 mM deoxypyridoxine, 0.2 mM phenylmethylsulfonyl fluoride, protease inhibitor cocktail (cOmplete™, EDTA-free, Sigma), fatty acid–free BSA (4 mg/ml), and 1 nM [^{32}P]S1P, in the absence or presence of the indicated concentration of S1P or GA2P. Cells were then washed twice with wash buffer [20 mM Tris-HCl (pH 7.4), 100 mM NaCl, and fatty acid–free BSA (0.4 mg/ml)], and lysed with RIPA buffer [50 mM Tris–HCl (pH 7.4), 150 mM NaCl, 1 mM EDTA, 1% Triton X-100, 0.1% SDS and 0.1% sodium deoxycholate]. Bound [^{32}P]S1P was quantitated by scintillation counter Microbeta (PerkinElmer).

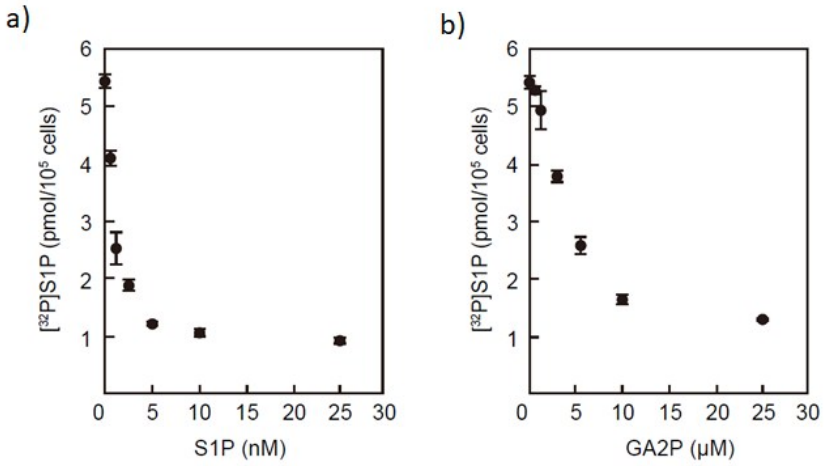
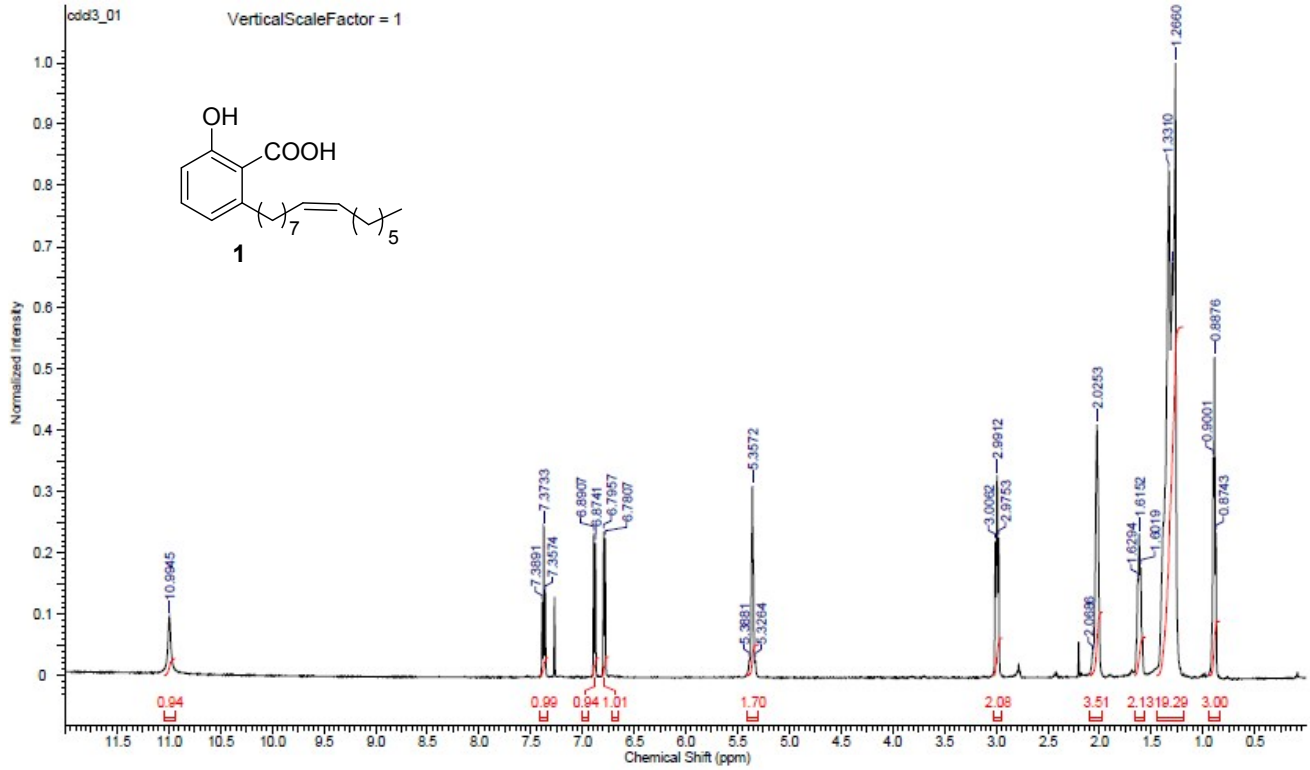


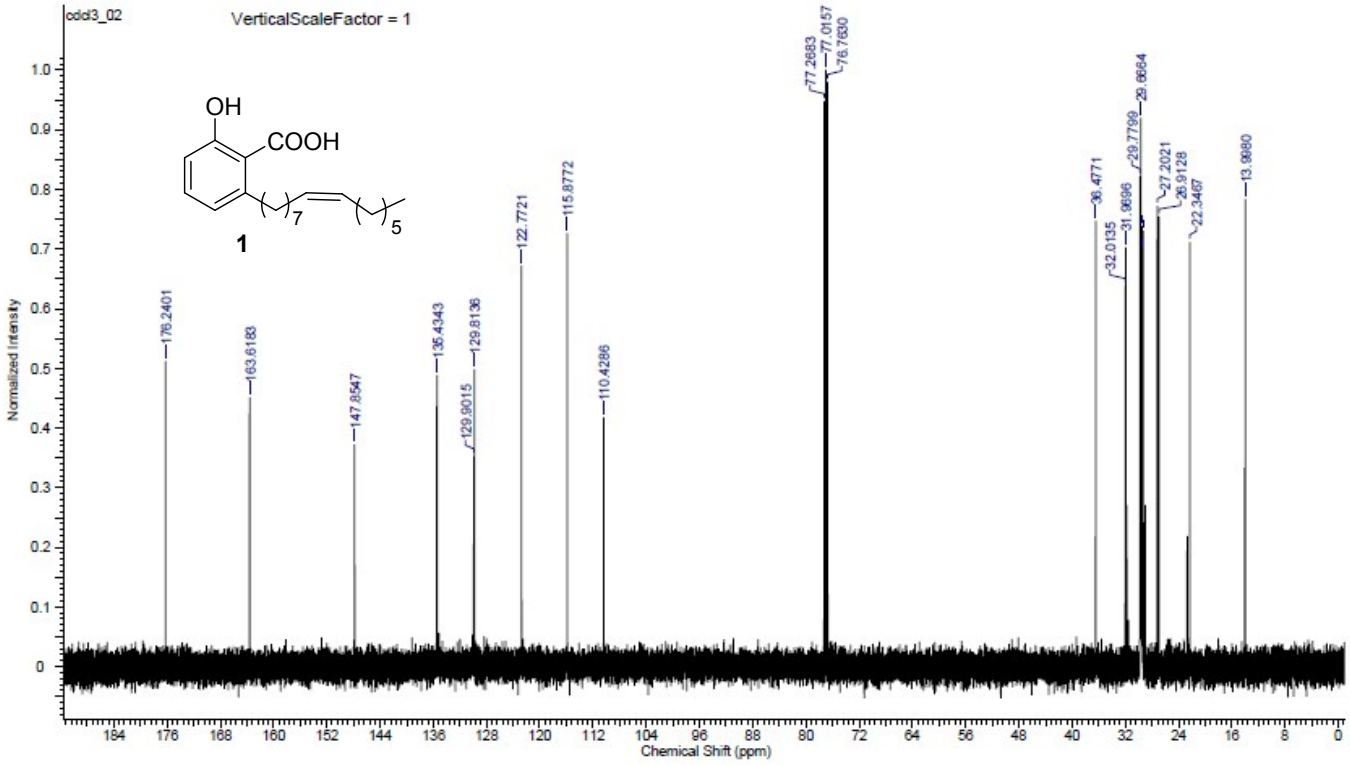
Figure S3: Competitive binding assay of GA2P with $S1P_1$. a) Competition of S1P and [^{32}P]S1P with $S1P_1$ is carried out by addition of S1P at different concentrations (0-25 nM) in the presence of 1 nM [^{32}P]S1P. b) Similarly, competitive assay of GA2P with $S1P_1$ has been carried out at different concentration of GA2P (0-25 μM) in the presence of 1 nM [^{32}P]S1P. Bound S1P was quantitated by scintillation counter Microbeta (PerkinElmer).

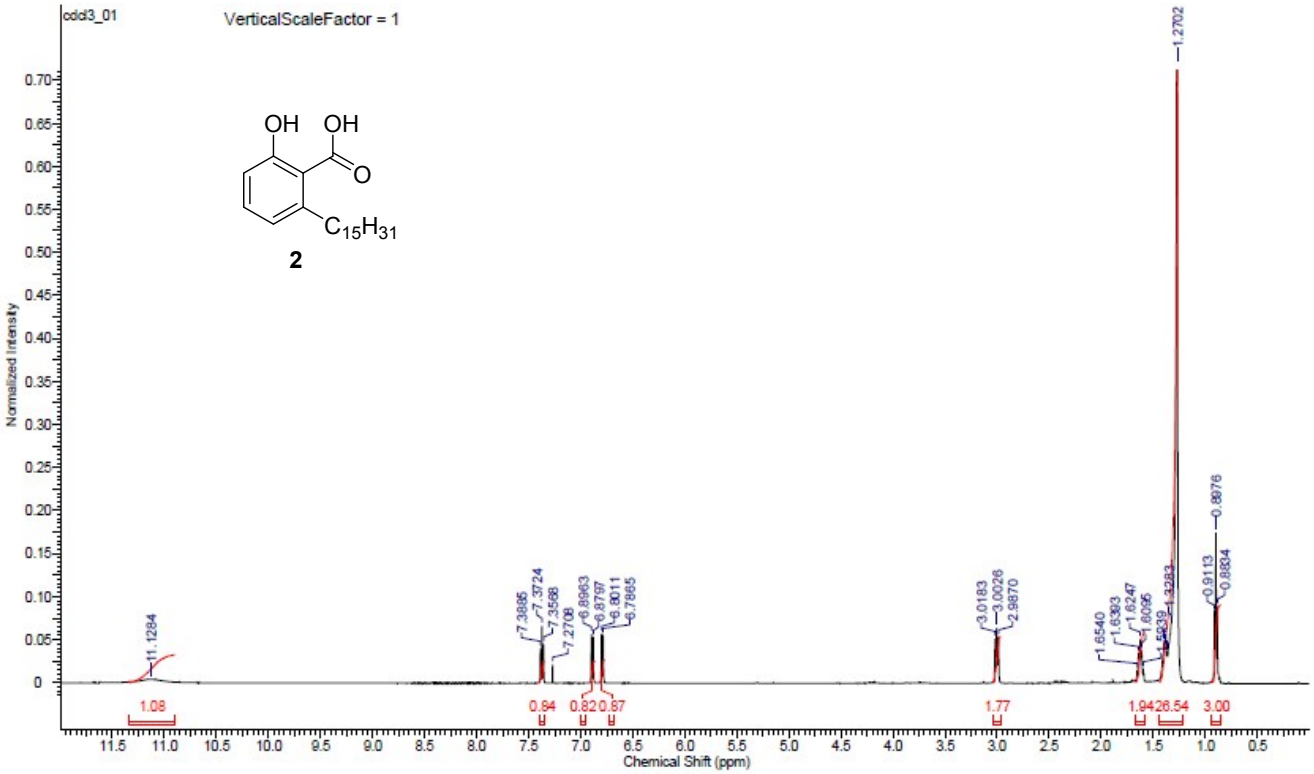
9. References:

1. Yadav, J. S.; Mishra, A. K.; Dachavaram, S. S.; Kumar, S. G.; Das, S. *Tet. Lett.* **2014**, *55*, 2921.
2. Fu, Y.; Hong, S.; Li, D.; Liu, S. *J. Agri. Food Chem*. **2013**, *61*, 5347.
3. Maegawa, T.; Koutani, Y.; Otake, K; Fujioka, H. *J, Org. Chem*. **2013**, *78*, 3384.
4. Sanchini, S.; Perruccio, F.; Piizzi, G. *ChemBioChem*. **2014**, *15*, 961.
5. Kihara, A.; Anada, Y.; Igarashi, Y. *J. Biol. Chem.*, **2006**, *281*, 4532.

9. NMR spectra of compounds 1-7 and S1-S27



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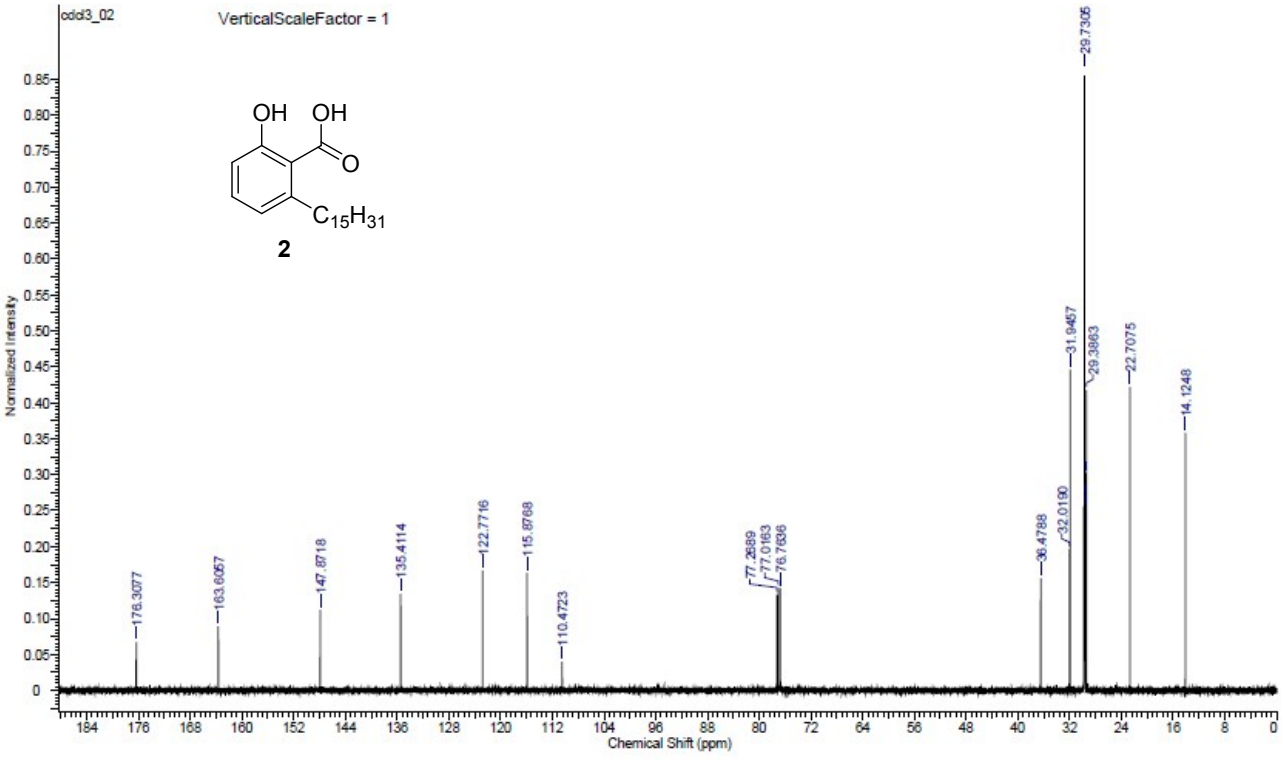
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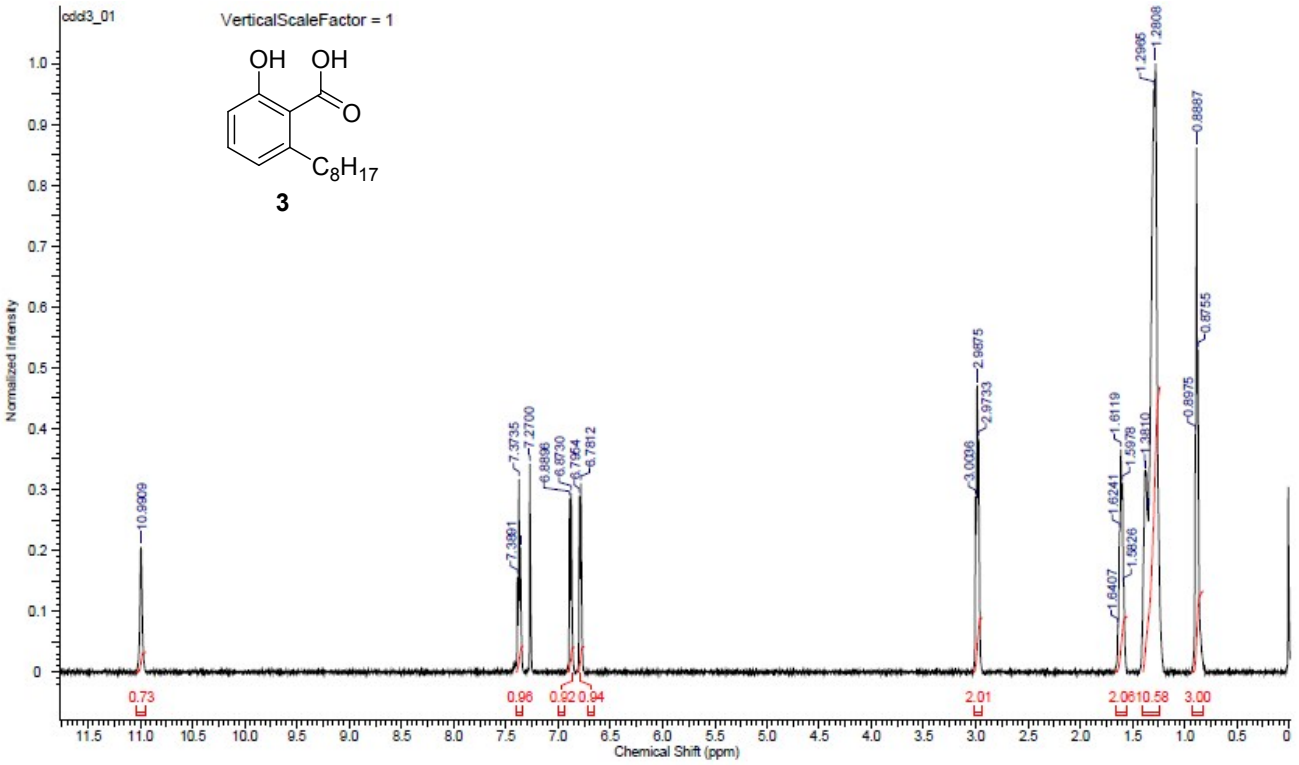
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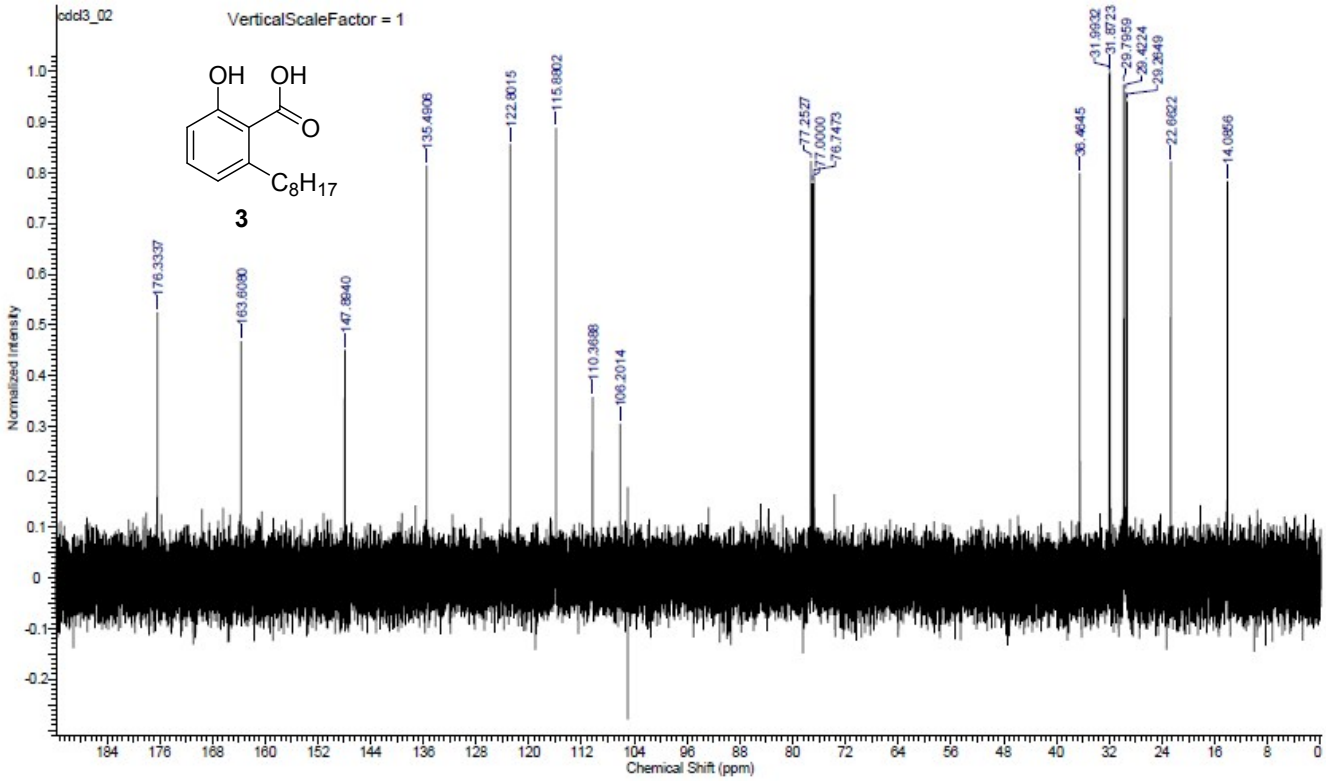
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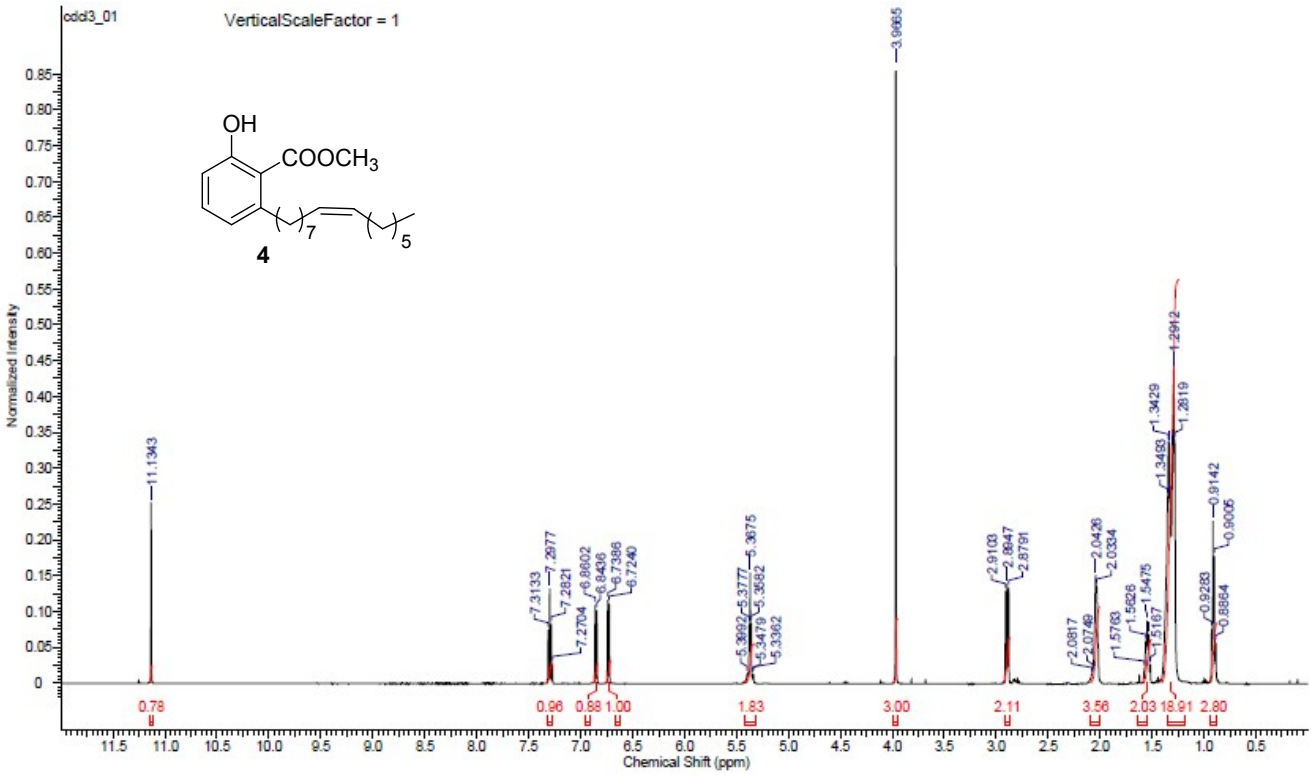
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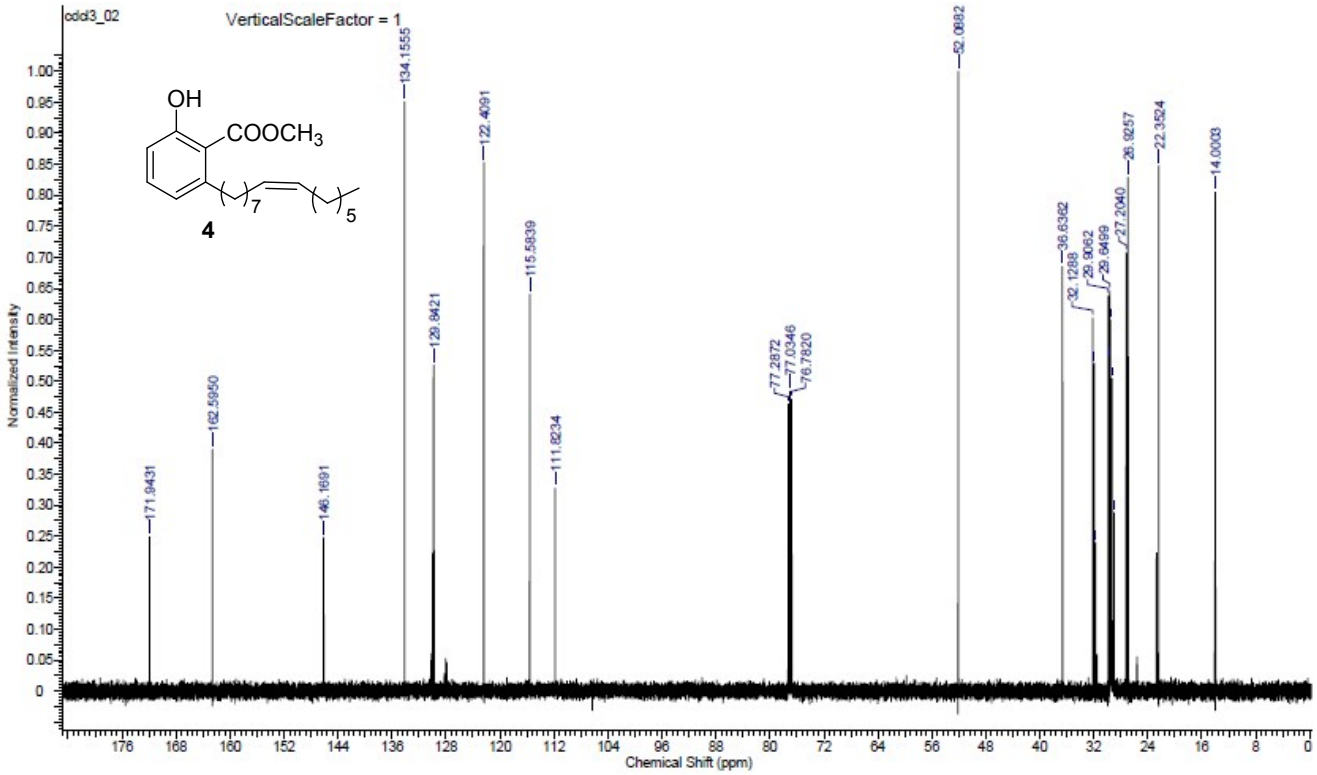
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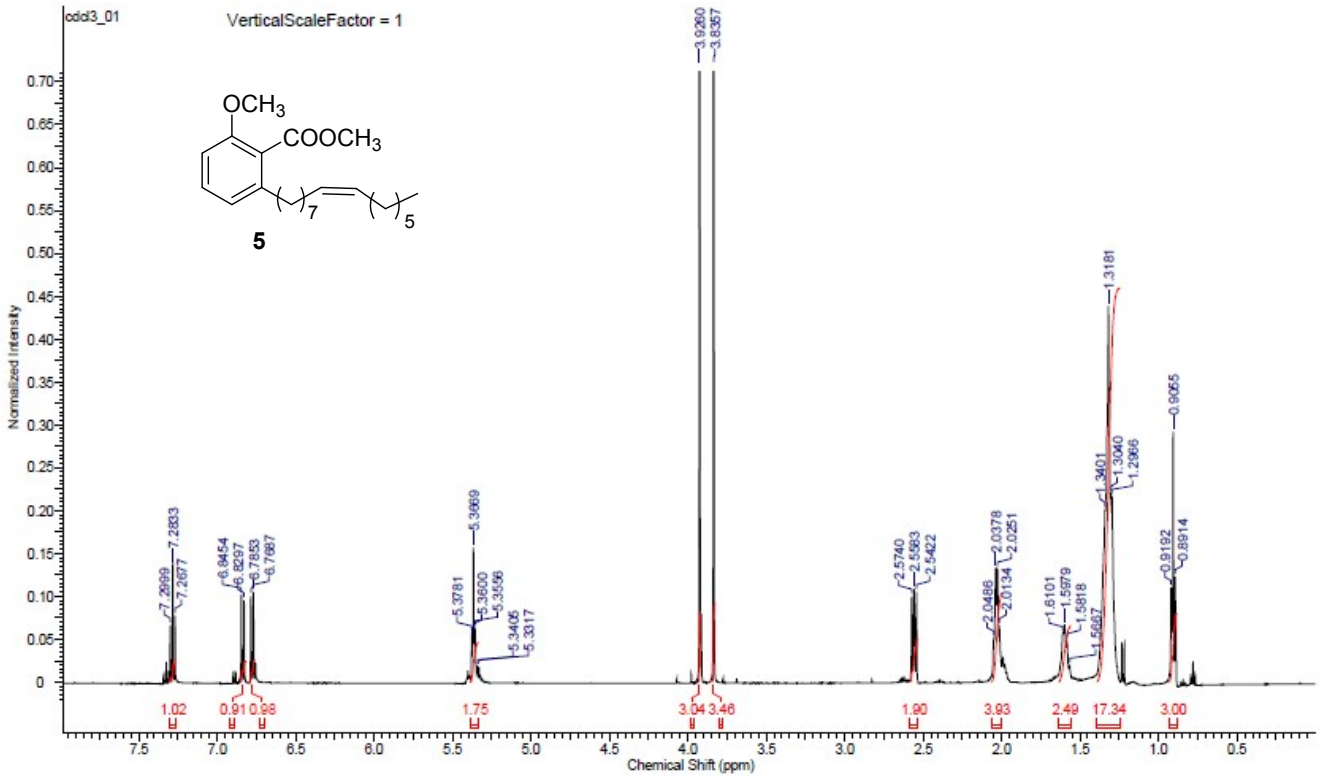
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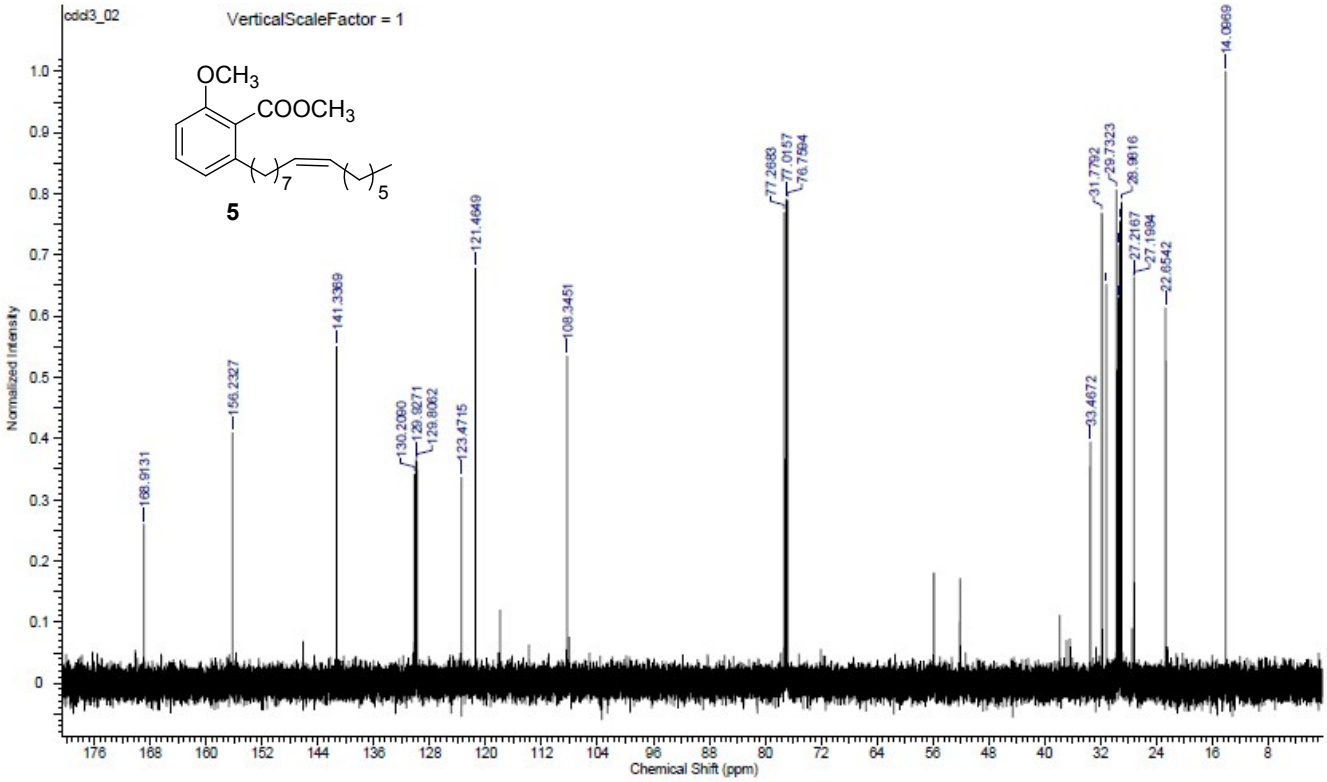
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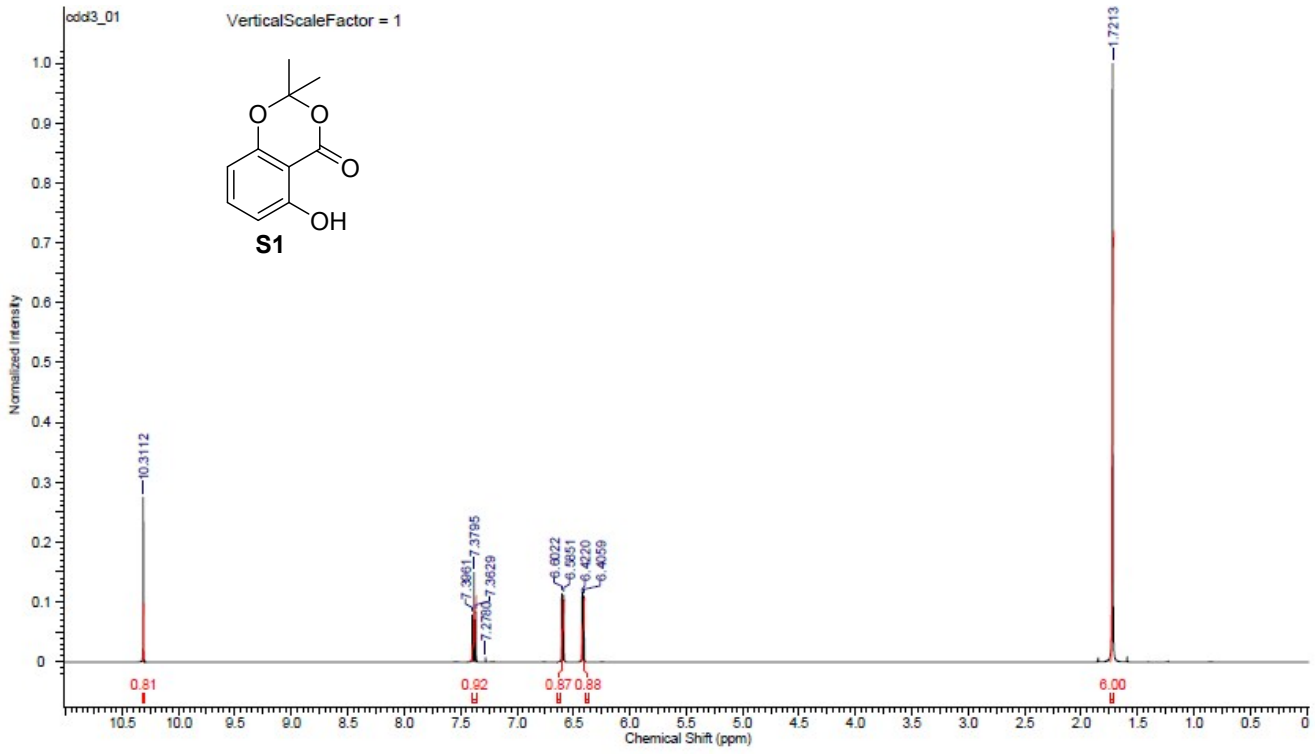
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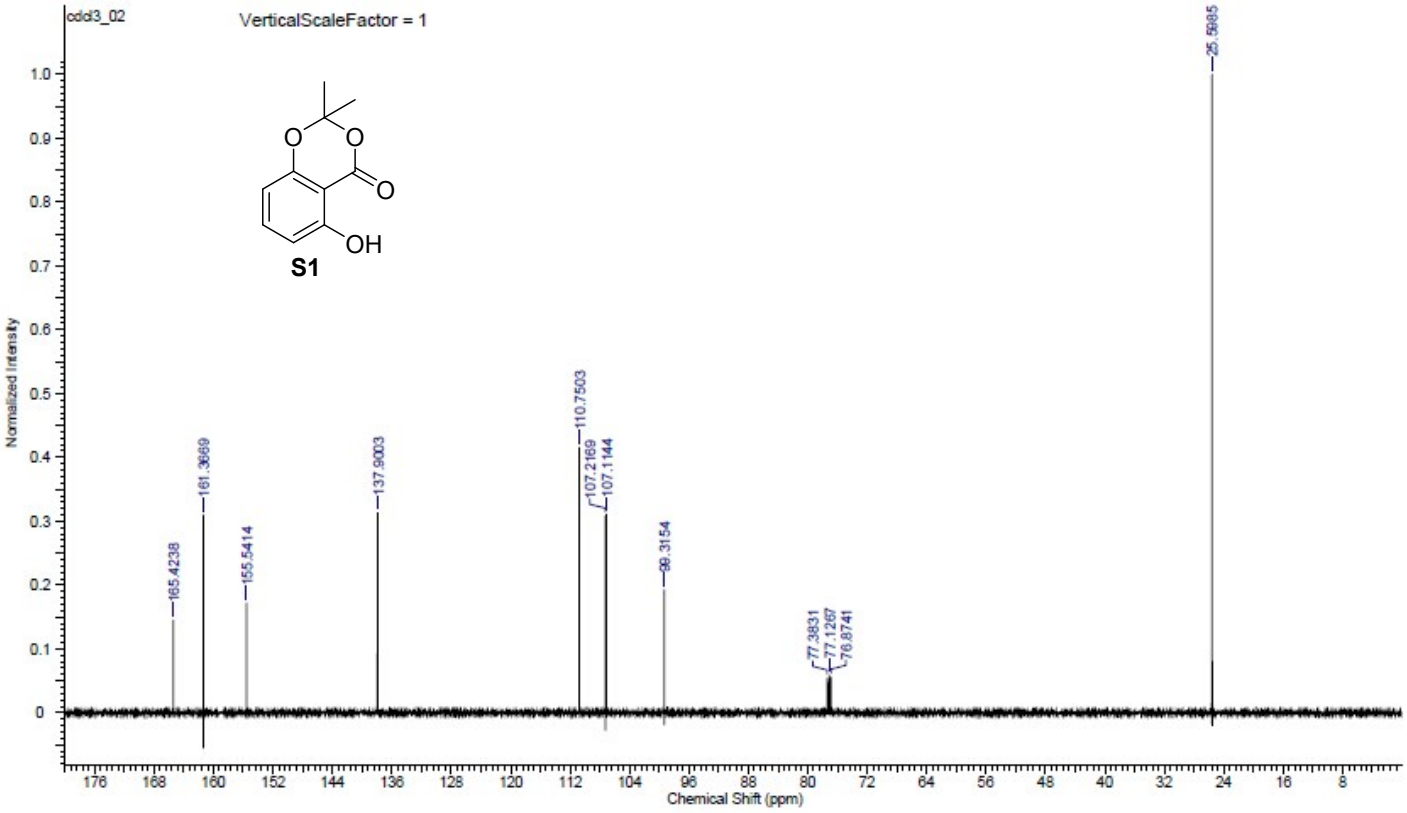
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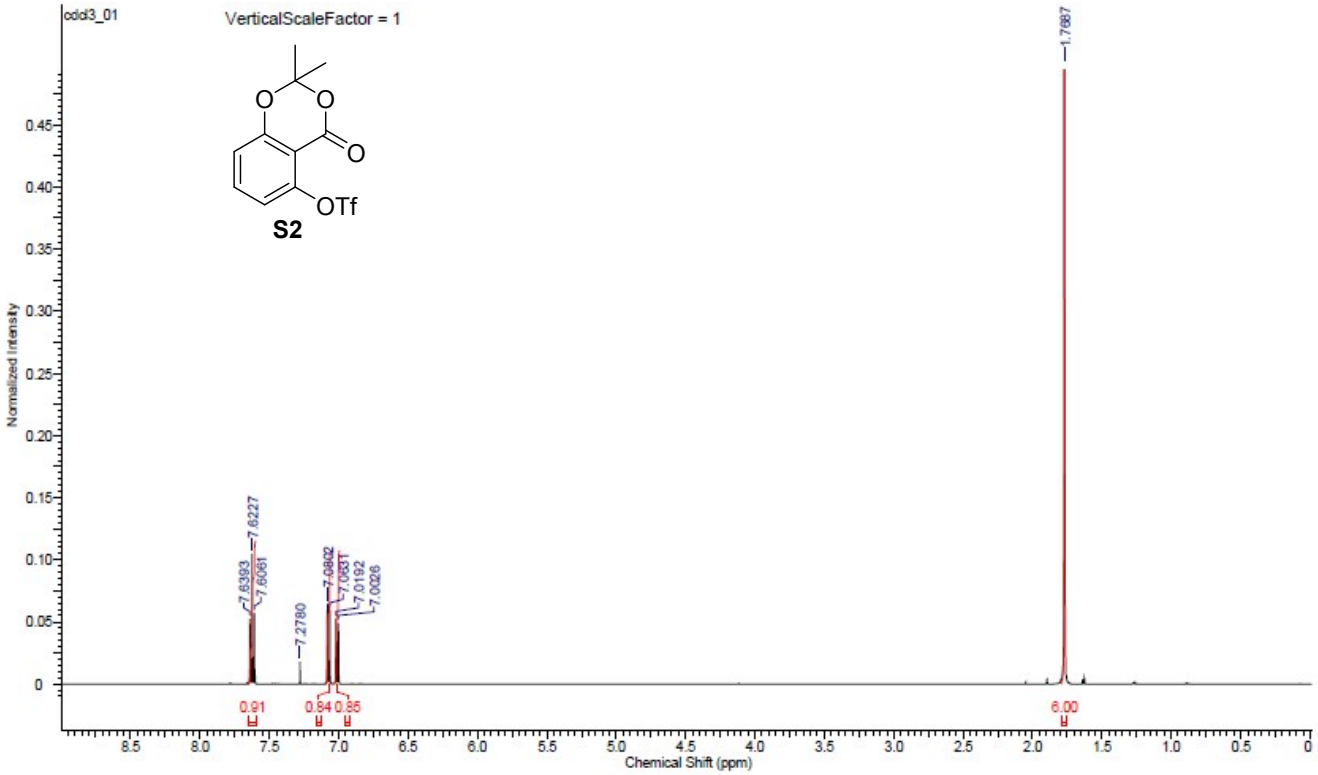
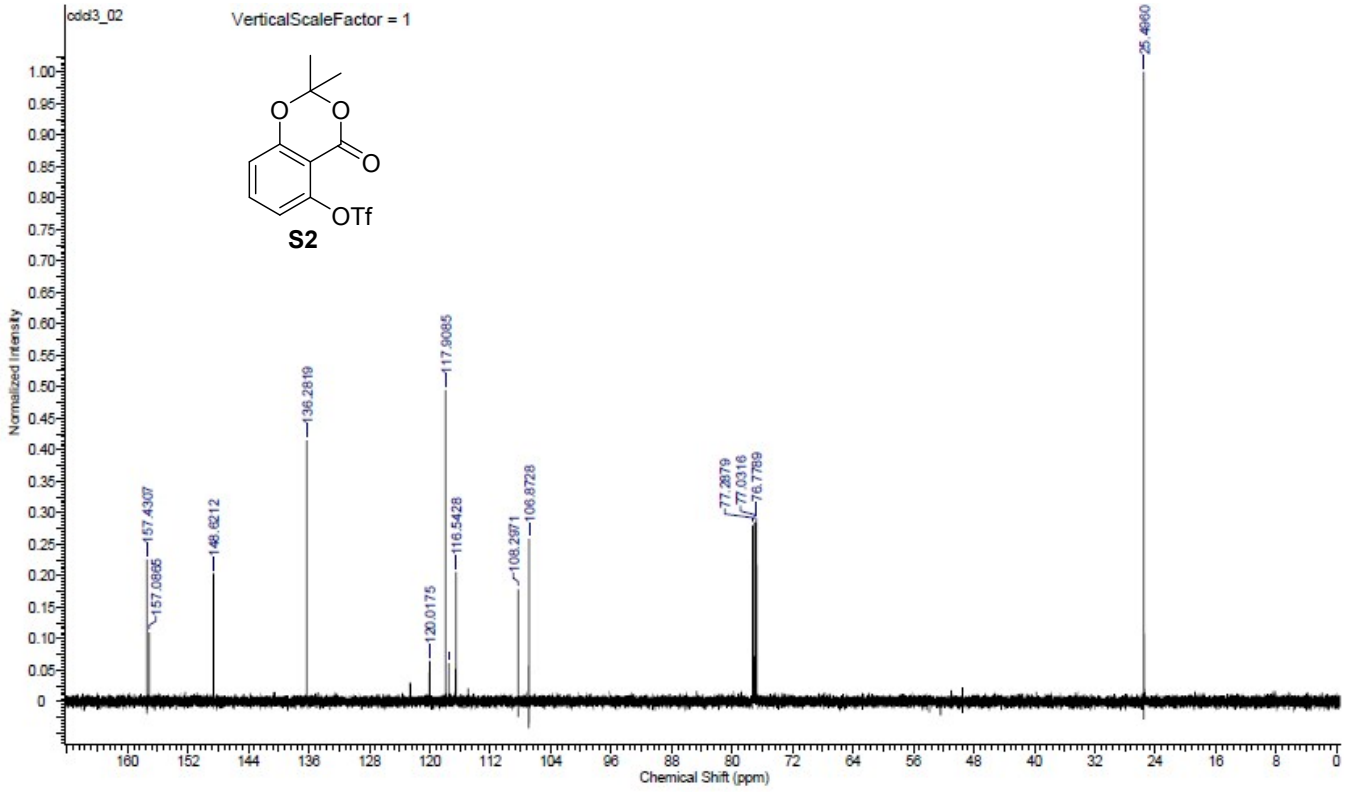
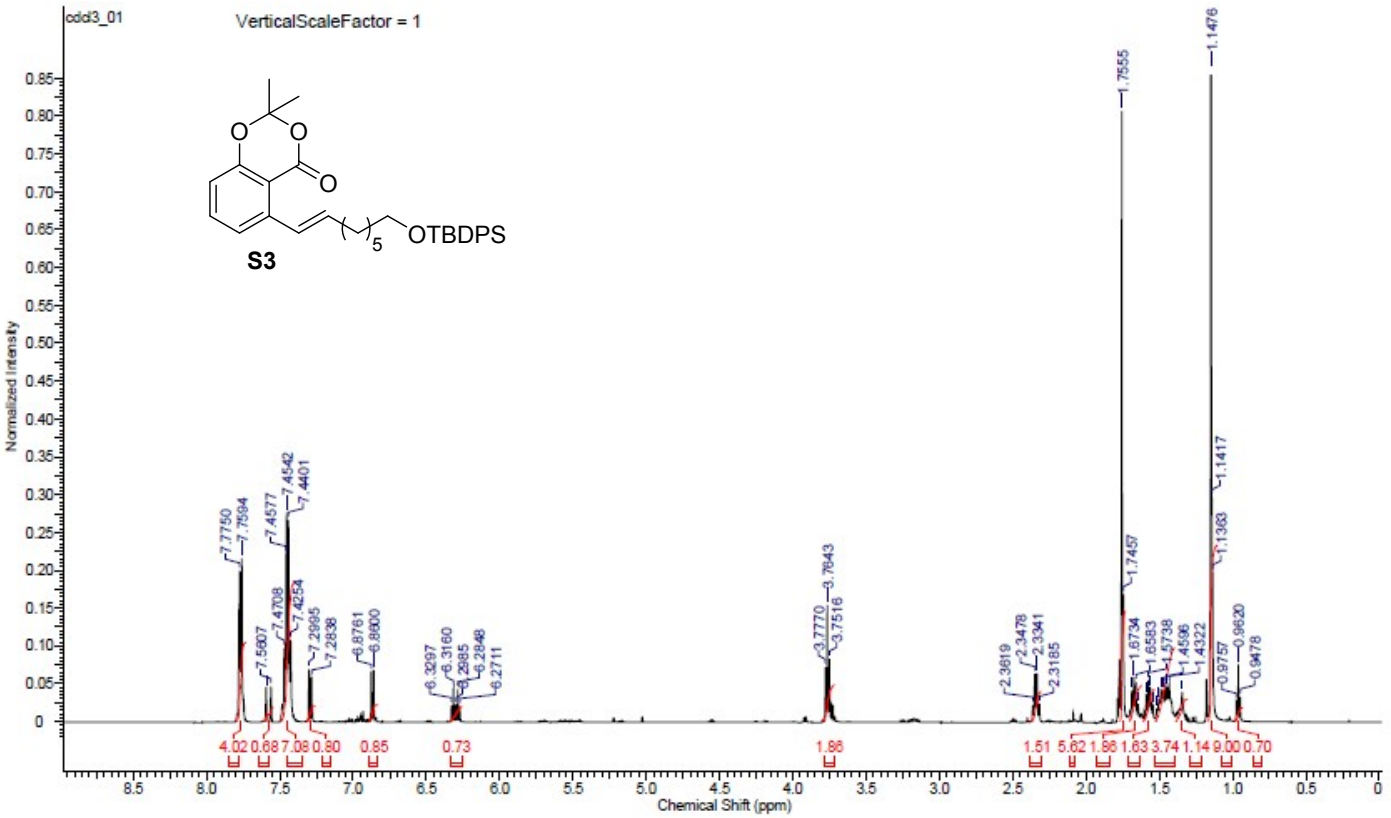
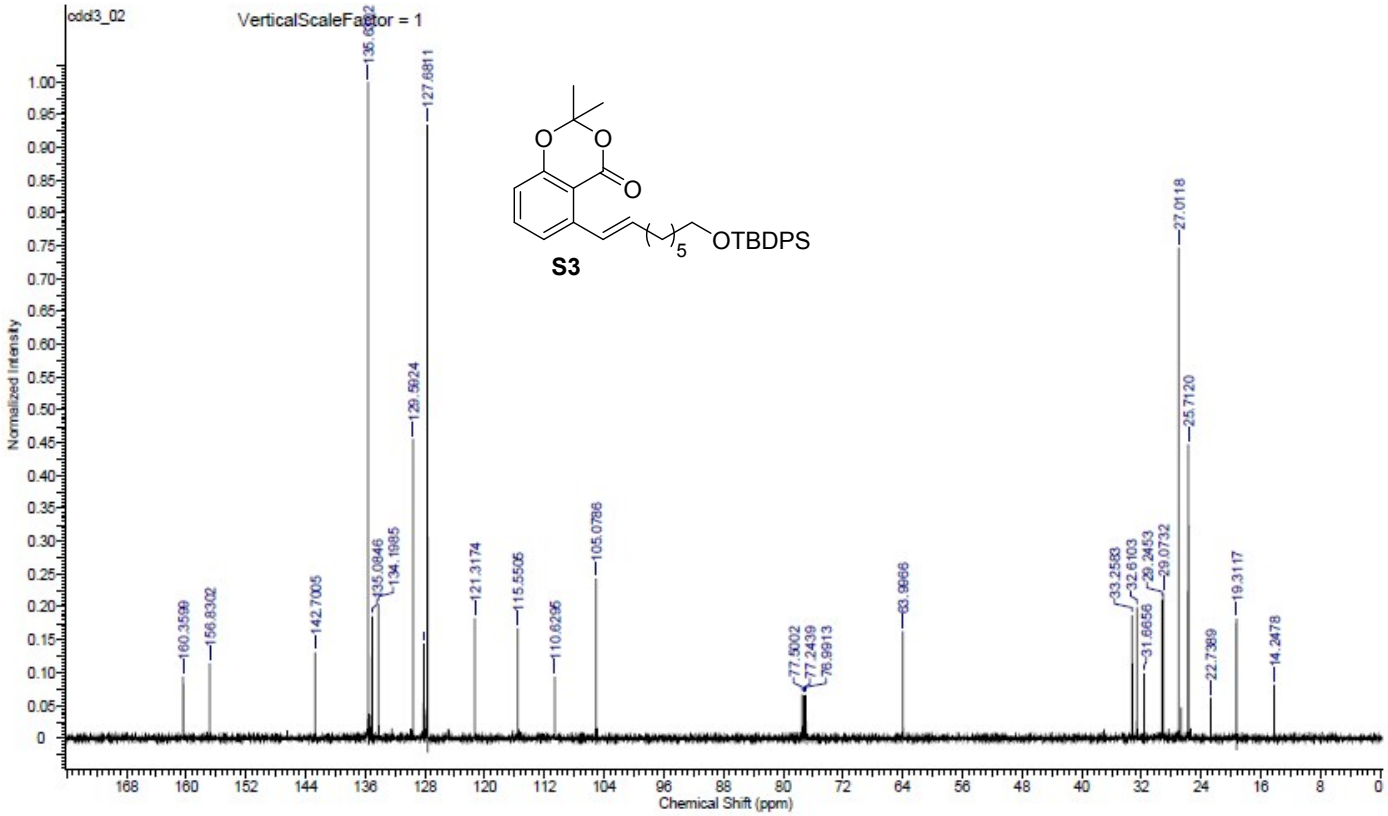
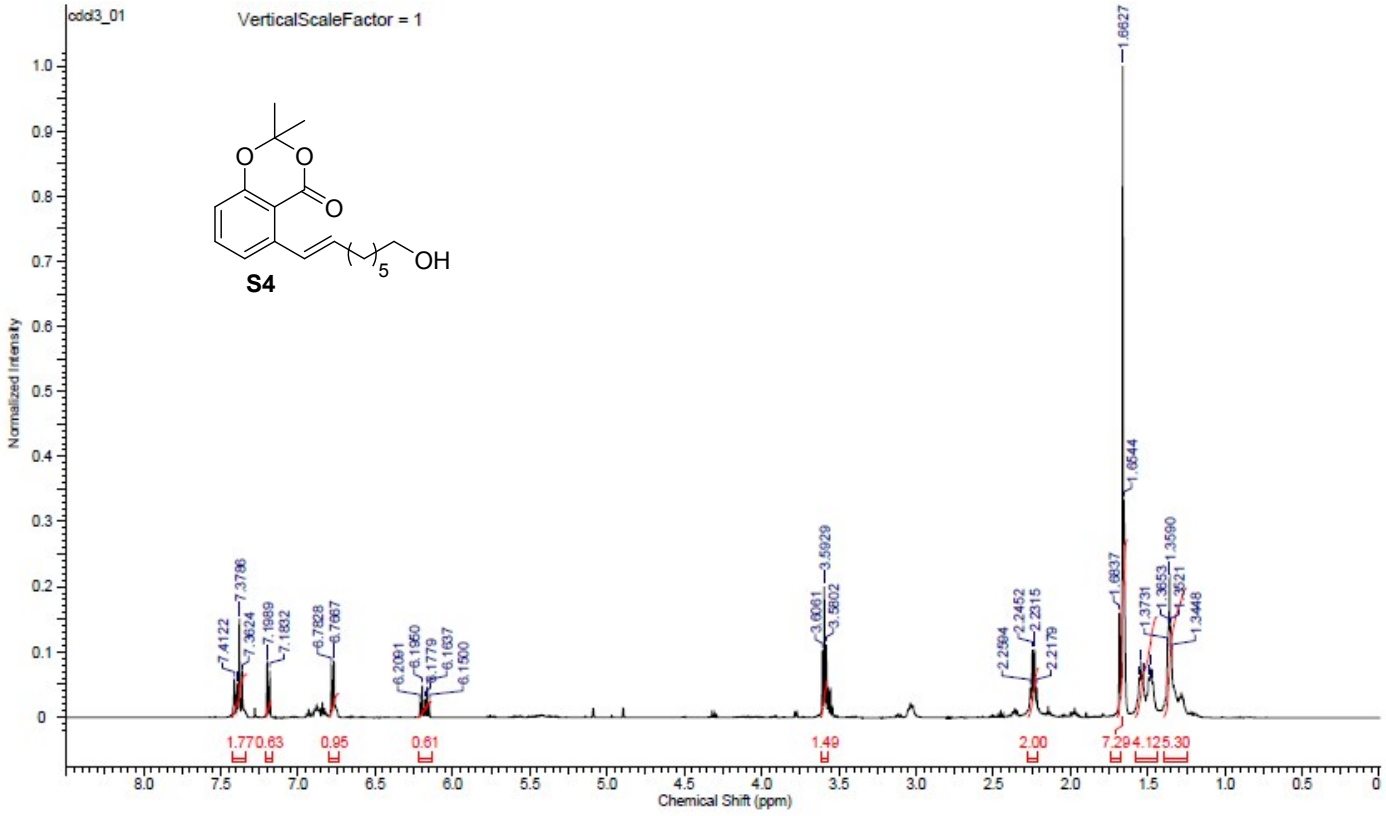
110.7503
107.2169
107.1144
98.3154
77.3831
77.1267
76.8741
25.5985

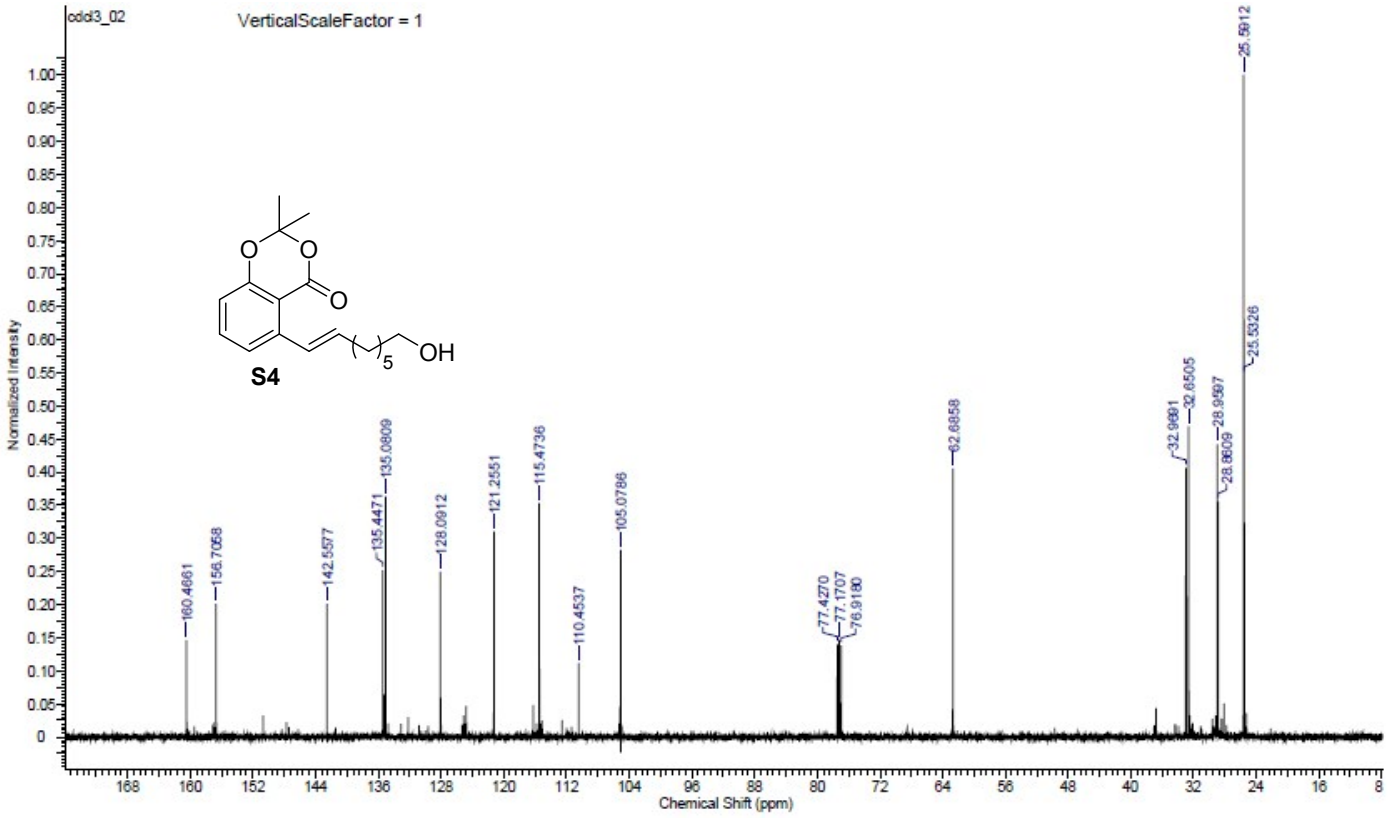

cdcl3_01
VerticalScaleFactor = 1
S2
Normalized Intensity
Chemical Shift (ppm)
7.8393
7.8227
7.8061
7.2780
7.0862
7.0631
7.0192
7.0026
1.7687
0.91
0.84
0.85
6.00

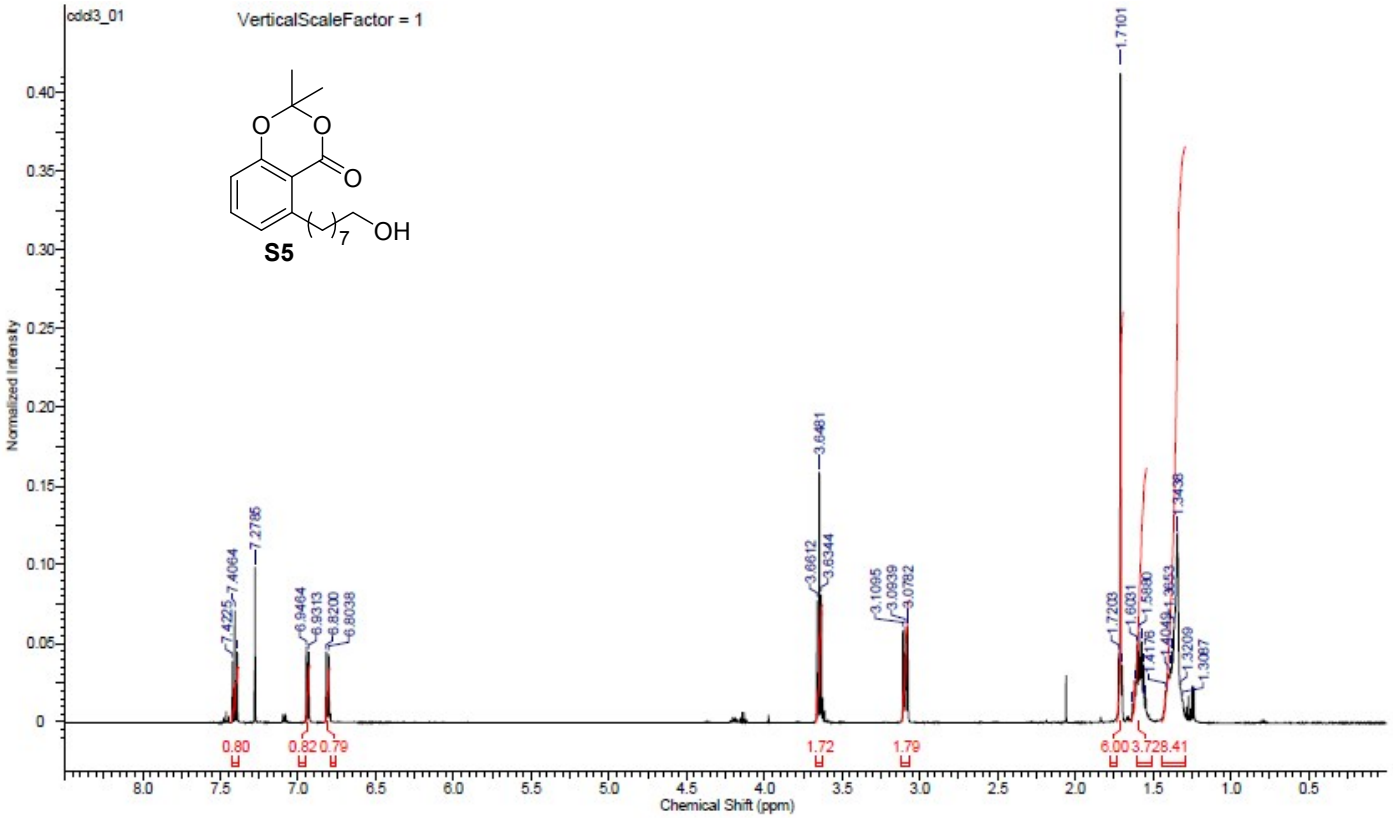

cdcl3_02
VerticalScaleFactor = 1
S2
Normalized Intensity
Chemical Shift (ppm)
157.4307
157.0865
149.6212
136.2819
120.0175
117.9085
116.5428
108.2971
106.8728
77.2879
77.0316
76.7789
25.4660

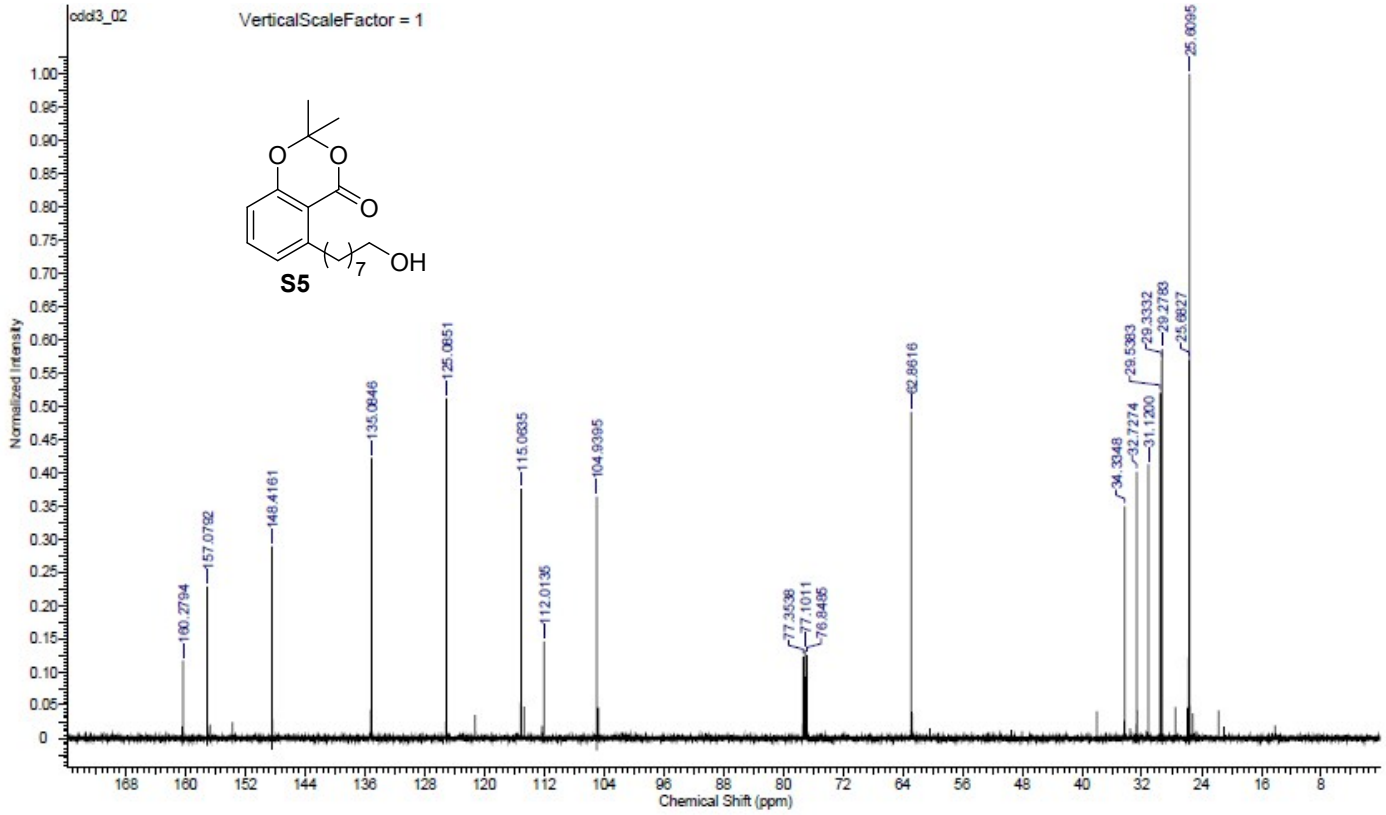

cdd3_01
VerticalScaleFactor = 1
OTBDPS
S3
Normalized Intensity
Chemical Shift (ppm)

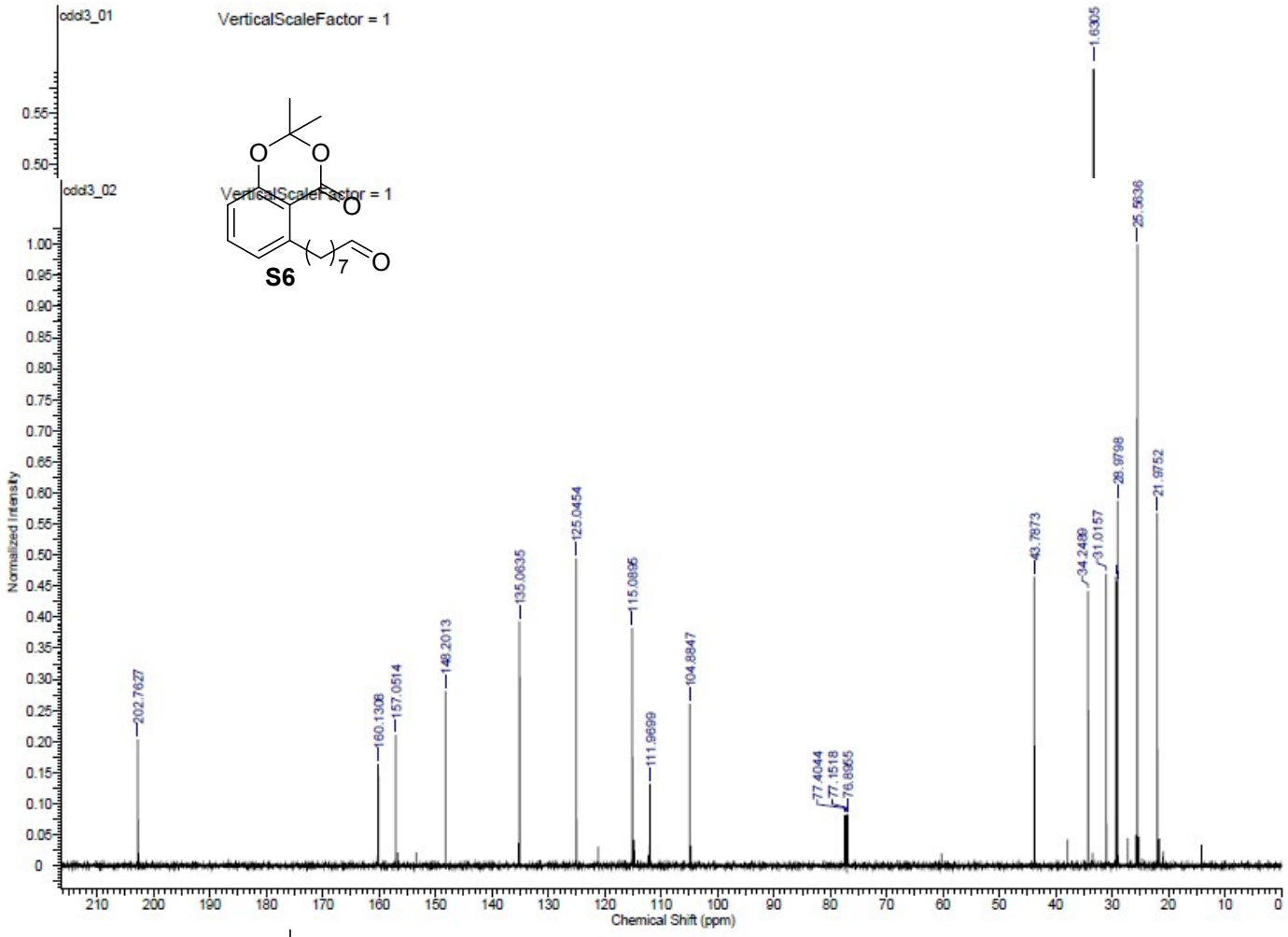

cdd3_02
VerticalScaleFactor = 1
OTBDPS
S3
Normalized Intensity
Chemical Shift (ppm)

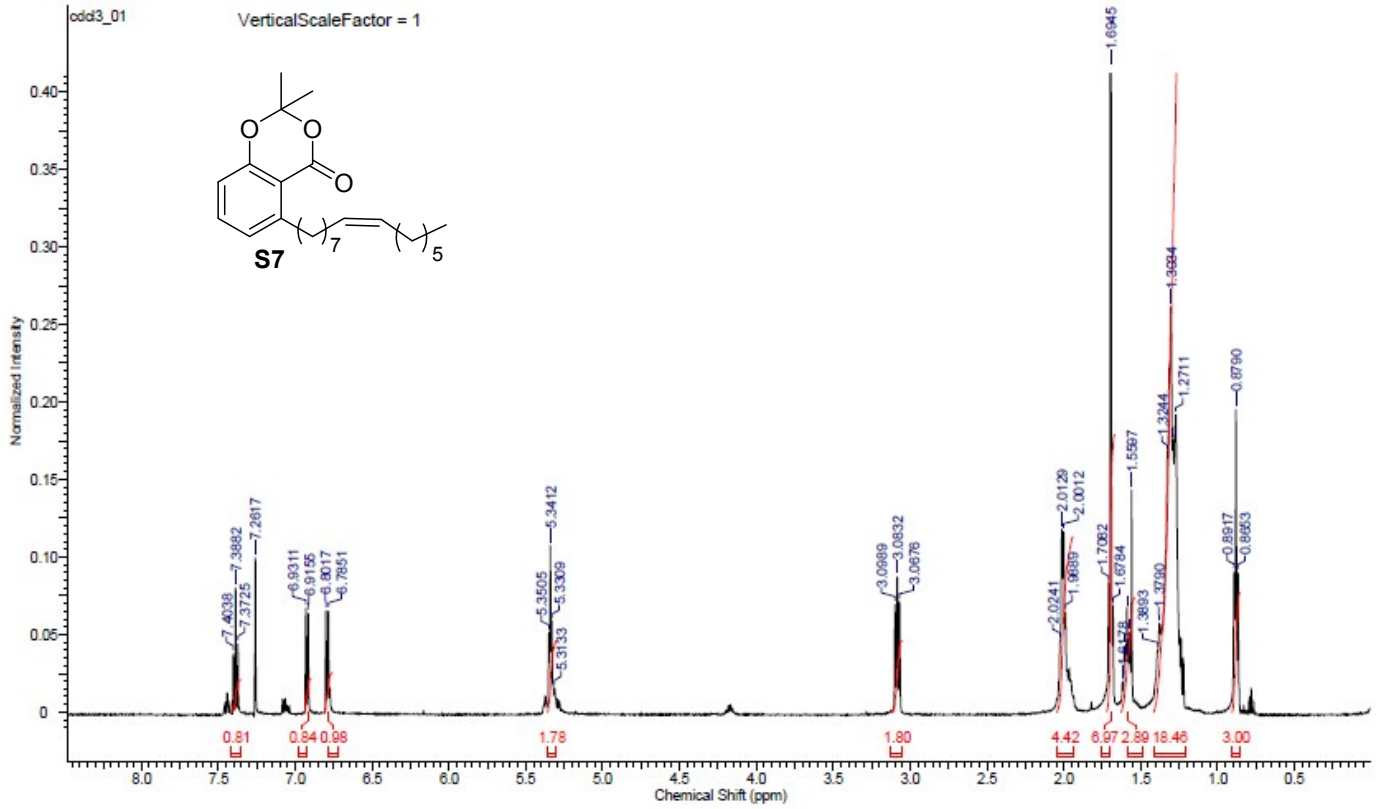

odd3_01
VerticalScaleFactor = 1
S4
Normalized Intensity
Chemical Shift (ppm)
1.6627
1.6544
7.4122
7.3786
7.3624
7.1989
7.1832
6.7828
6.7667
6.2091
6.1950
6.1779
6.1637
6.1500
3.6061
3.5929
3.5802
2.2594
2.2452
2.2315
2.2179
1.6837
1.3731
1.3653
1.3590
1.3521
1.3448
1.77
0.63
0.95
0.61
1.49
2.00
7.29
4.12
5.30

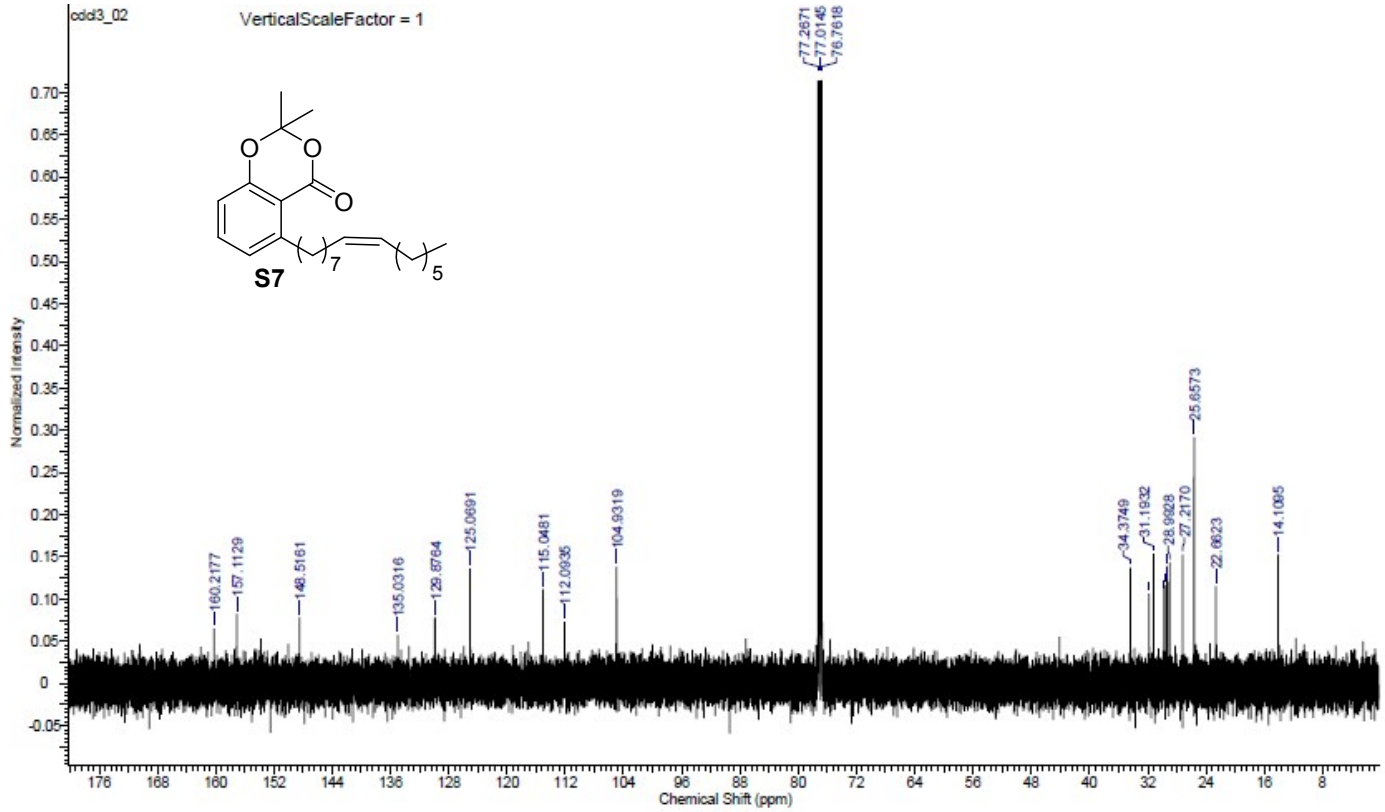

odd3_02
VerticalScaleFactor = 1
S4
Normalized Intensity
Chemical Shift (ppm)
25.5912
25.5326
32.6505
32.9991
28.9597
28.8609
62.6858
160.4661
156.7058
142.5577
135.4471
135.0809
128.0912
121.2551
115.4736
110.4537
105.0786
77.4270
77.1707
76.9180

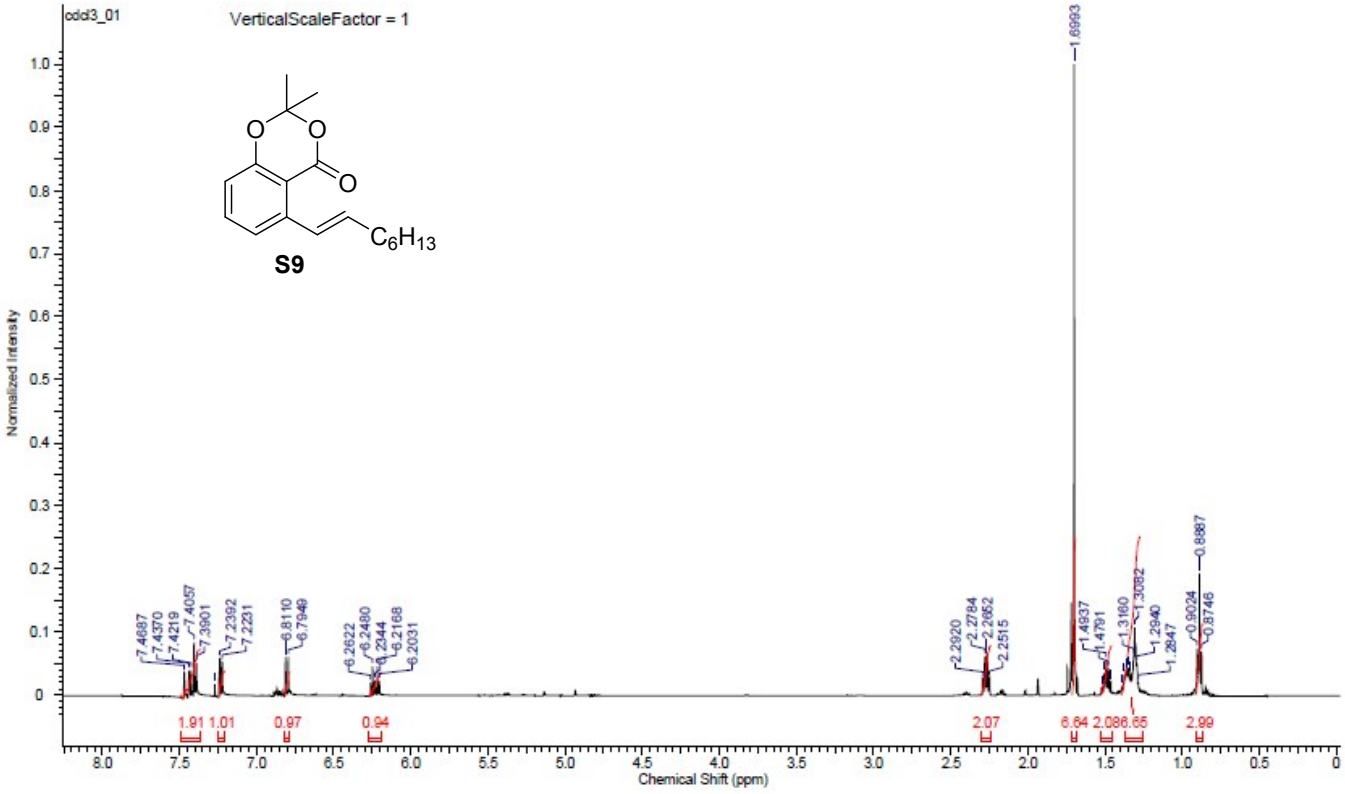

oddl3_01
VerticalScaleFactor = 1
S5
Normalized Intensity
Chemical Shift (ppm)
7.4225
7.4064
7.2786
6.9464
6.9313
6.8200
6.8038
3.6481
3.6612
3.6344
3.1095
3.0939
3.0782
1.7101
1.7203
1.6031
1.5880
1.4176
1.4049
1.3653
1.3438
1.3209
1.3067
0.80
0.82
0.79
1.72
1.79
6.00
3.72
8.41

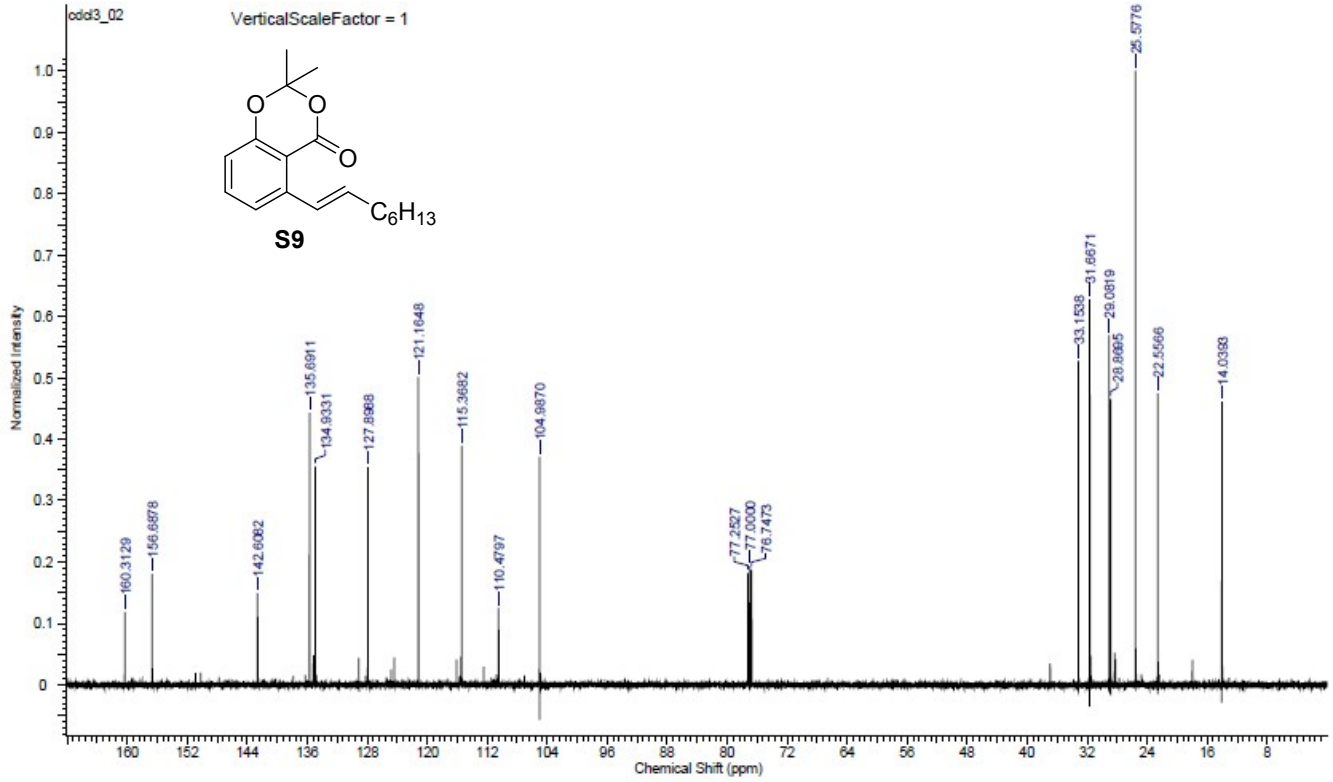

oddl3_02
VerticalScaleFactor = 1
S5
Normalized Intensity
Chemical Shift (ppm)
160.2794
157.0792
148.4161
135.0846
125.0851
115.0635
112.0135
104.9395
77.3538
77.1011
76.8486
62.8616
34.3348
32.7274
31.1200
29.5383
29.3332
29.2783
25.8827
25.6095

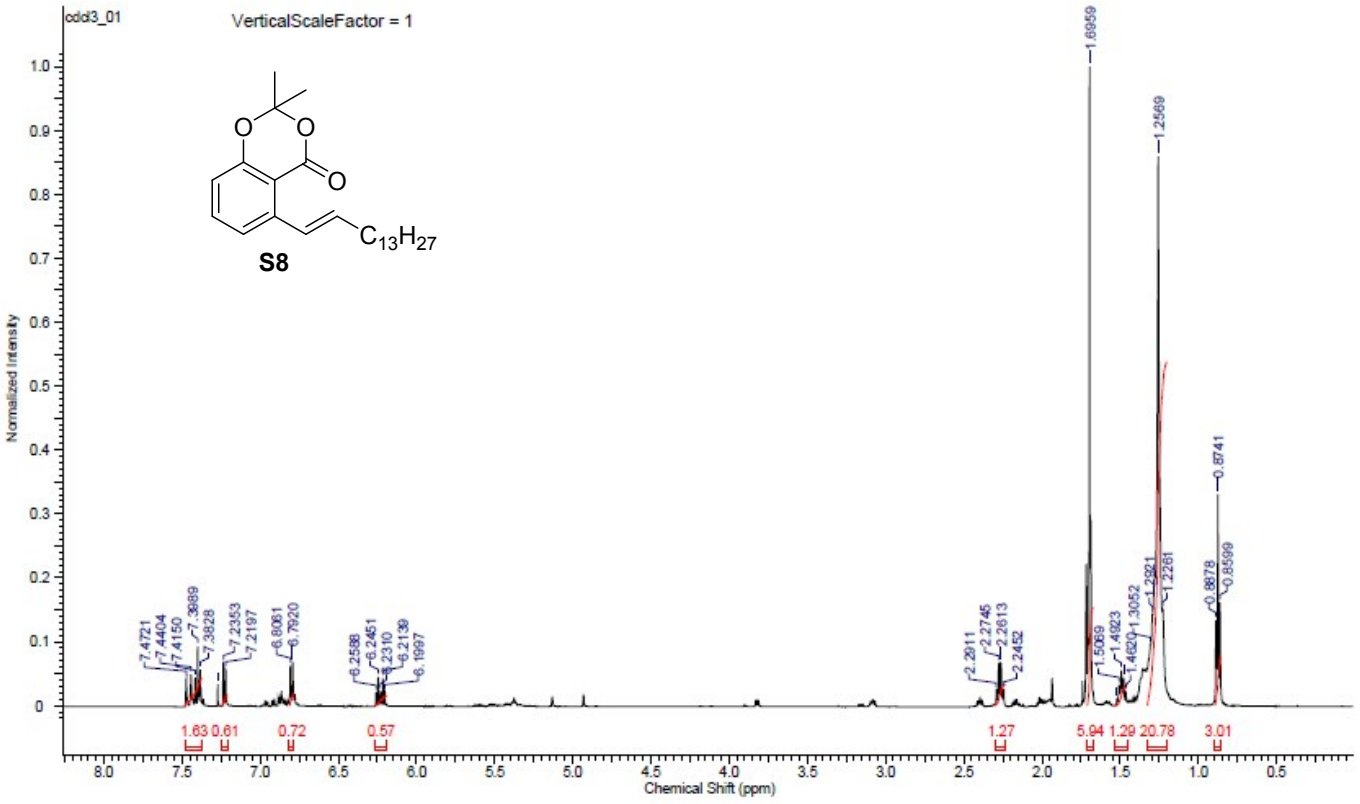

oddi3_01
VerticalScaleFactor = 1
oddi3_02
VerticalScaleFactor = 1
S6
S6
Normalized Intensity
Chemical Shift (ppm)
1.6305
25.5636
28.9798
21.9752
43.7873
34.2489
31.0157
125.0454
135.0635
115.0895
148.2013
104.8847
111.9899
157.0514
160.1308
202.7627
77.4044
77.1518
76.8865

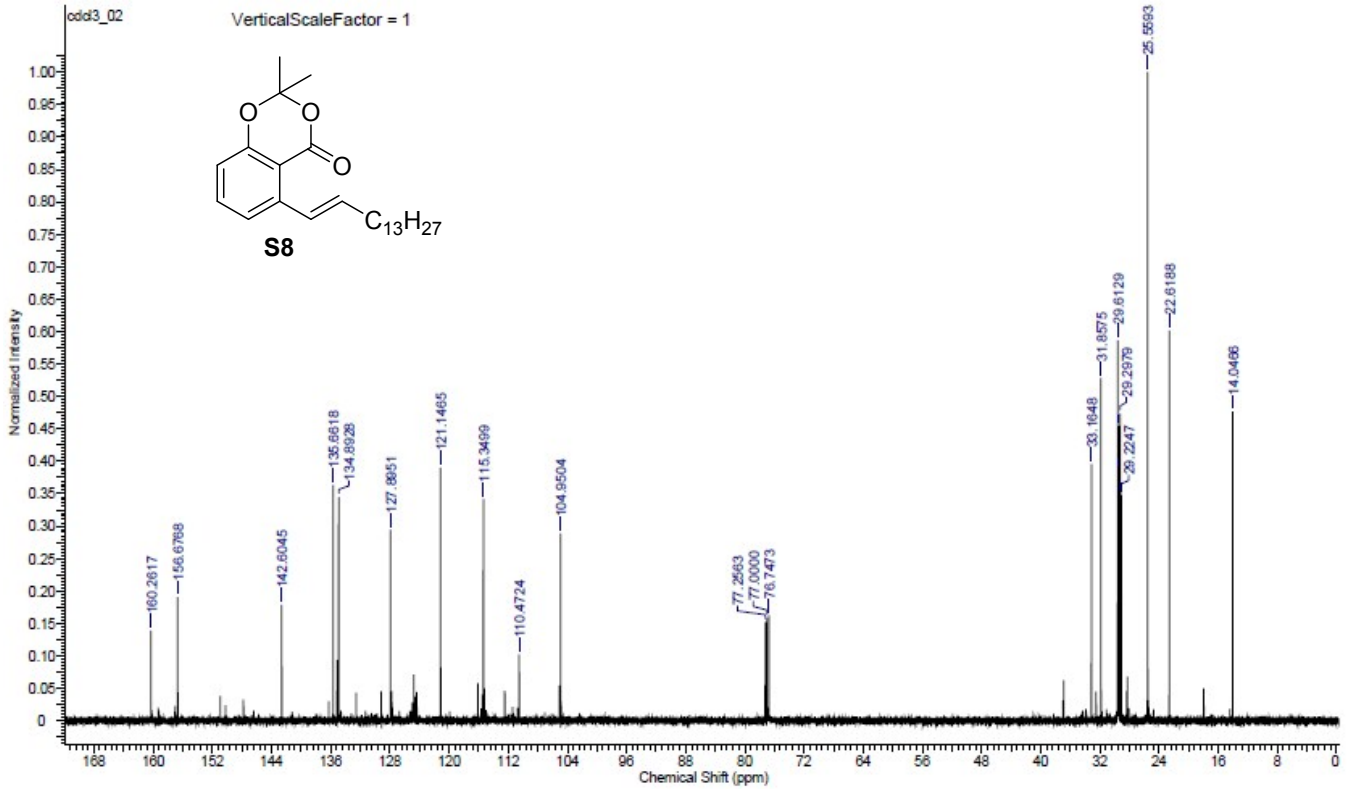

cdcl3_01
VerticalScaleFactor = 1
S7
Normalized Intensity
Chemical Shift (ppm)
1.6945
1.3984
1.2711
1.3244
0.8790
1.5597
2.0129
2.0012
1.7082
1.6784
1.3893
1.3790
0.8917
0.8683
3.0989
3.0832
3.0676
5.3412
5.3505
5.3309
5.3133
7.4038
7.3882
7.3725
7.2617
6.9311
6.9155
6.8017
6.7851
2.0241
1.9889
0.81
0.84
0.98
1.78
1.80
4.42
6.97
2.89
18.46
3.00

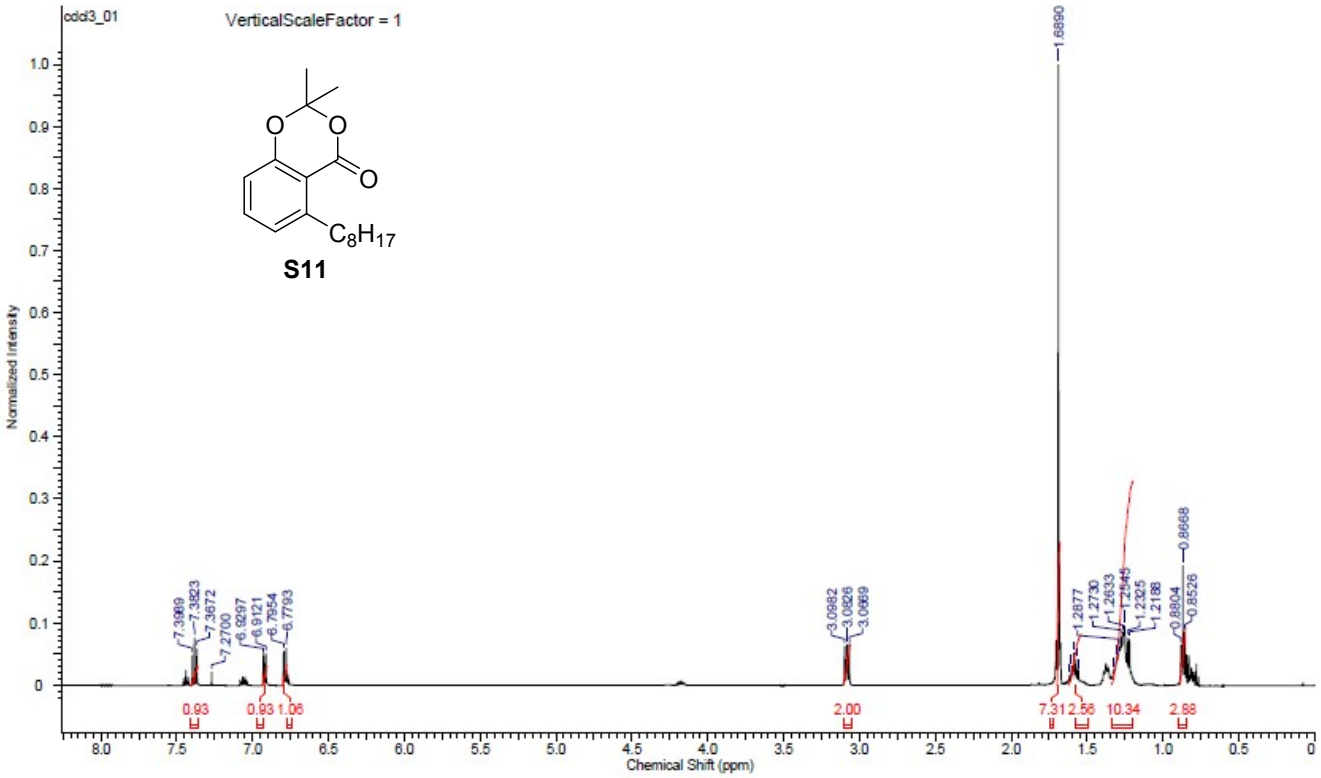

cdcl3_02
VerticalScaleFactor = 1
S7
Normalized Intensity
Chemical Shift (ppm)
77.2671
77.0145
76.7618
25.6573
34.3749
31.1932
28.9928
27.2170
22.6623
14.1065
160.2177
157.1129
148.5161
135.0316
129.6764
125.0691
115.0481
112.0936
104.9319

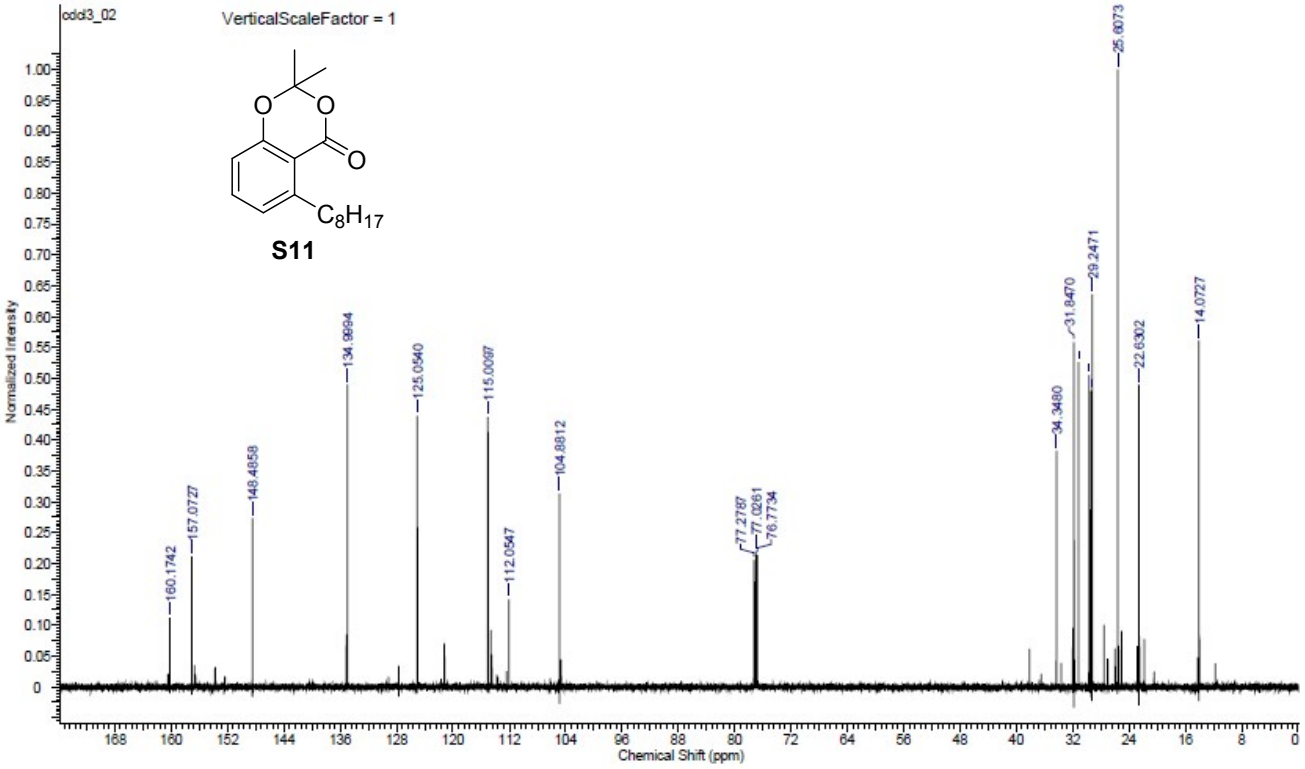

odd3_01
VerticalScaleFactor = 1
S9
Normalized Intensity
Chemical Shift (ppm)

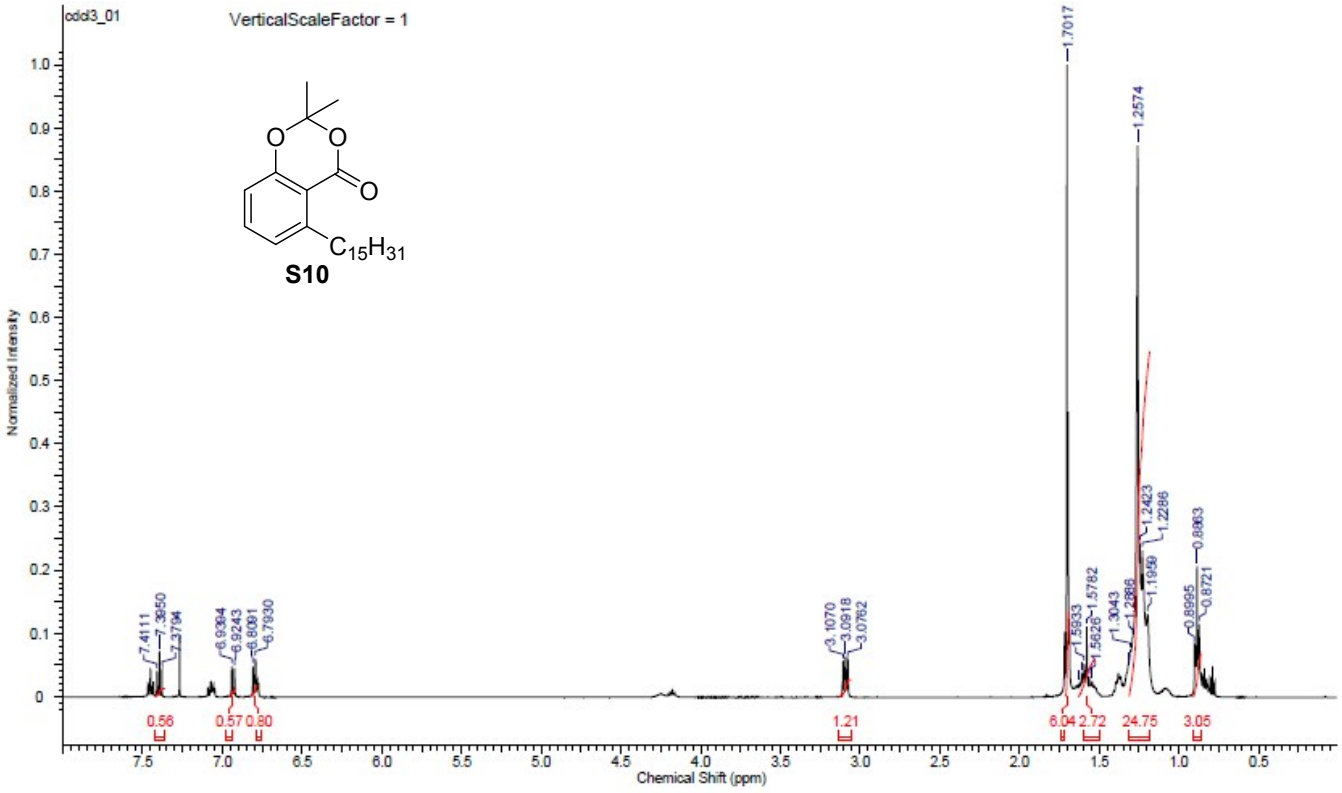

odd3_02
VerticalScaleFactor = 1
S9
Normalized Intensity
Chemical Shift (ppm)

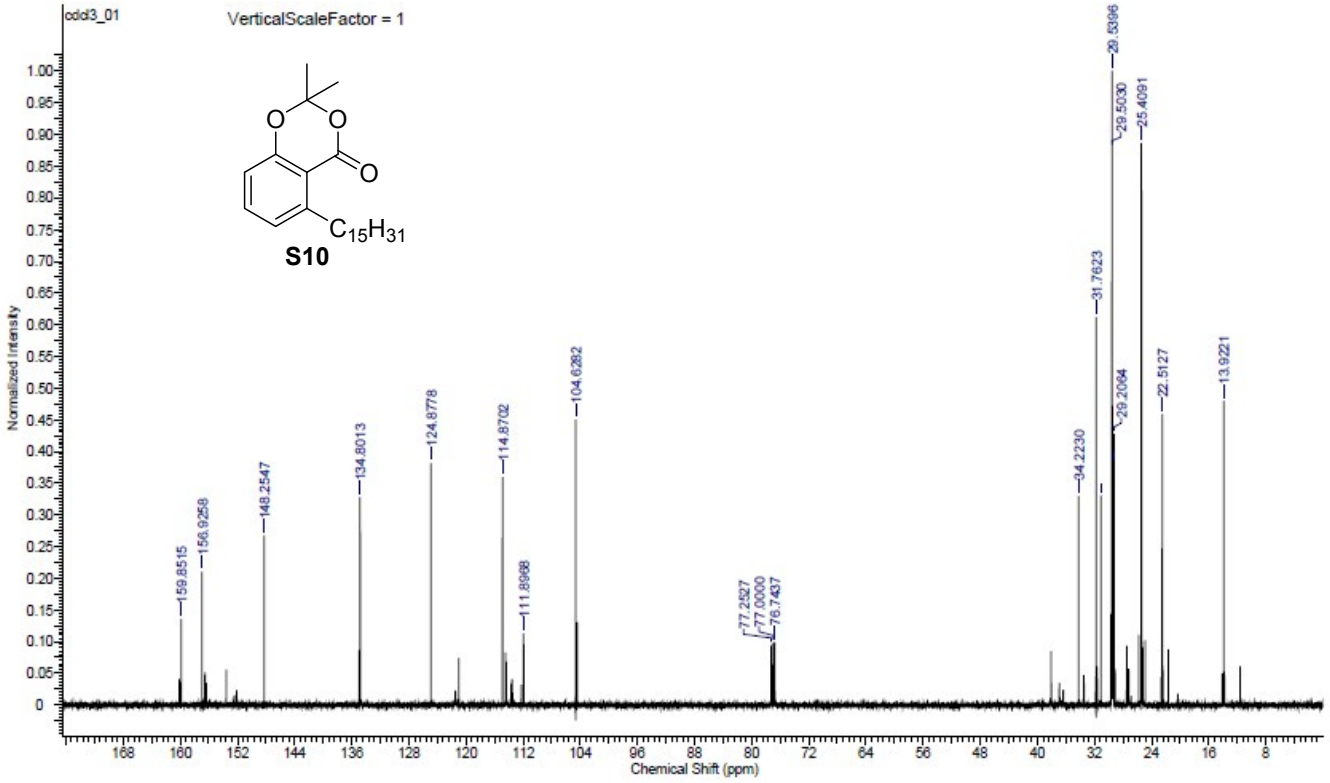

cdd3_01
VerticalScaleFactor = 1
S8
Normalized Intensity
Chemical Shift (ppm)
1.6959
1.2569
0.8741
0.8599
0.8878
1.2921
1.2261
1.3052
1.4923
1.5069
2.2911
2.2745
2.2613
2.2452
7.4721
7.4404
7.4150
7.3689
7.3828
7.2353
7.2197
6.8061
6.7920
6.2588
6.2451
6.2310
6.2139
6.1997
1.63 0.61 0.72 0.57 1.27 5.94 1.29 20.78 3.01

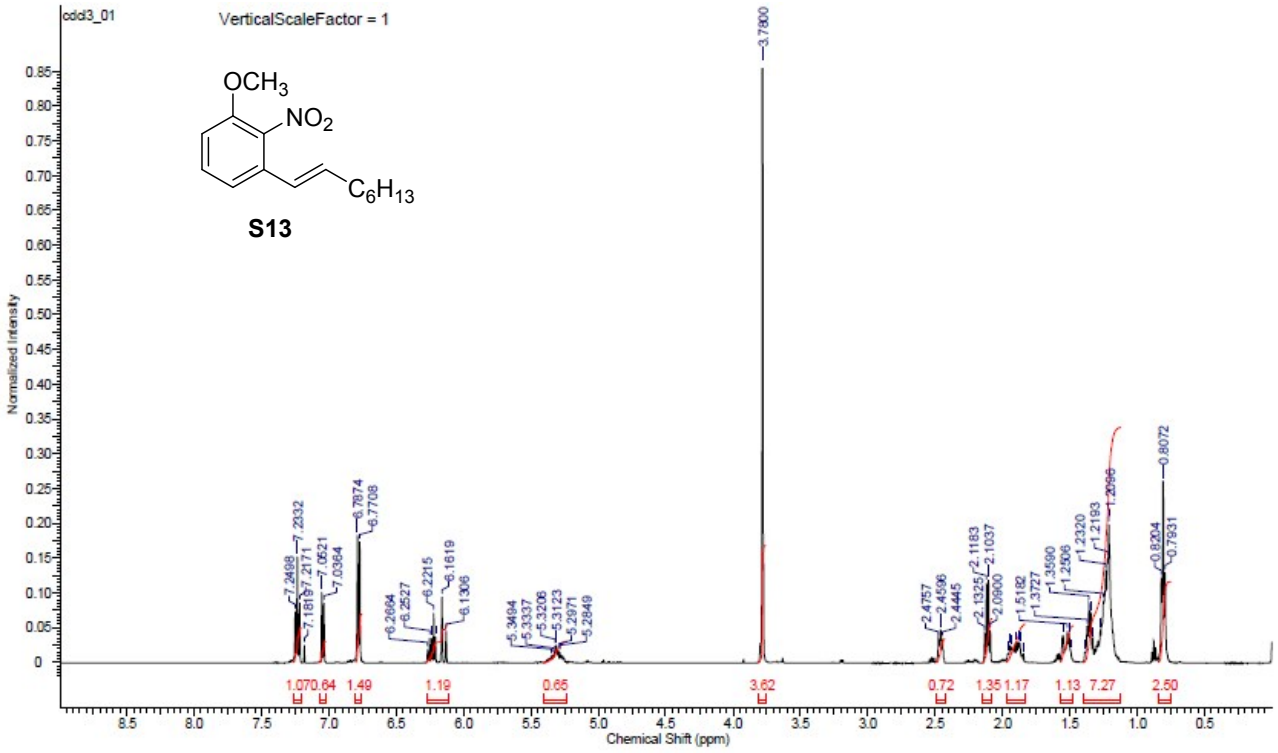

cdd3_02
VerticalScaleFactor = 1
S8
Normalized Intensity
Chemical Shift (ppm)
25.5693
22.6188
14.0466
31.8575
29.6129
29.2979
29.2247
33.1648
160.2617
156.6768
142.6045
135.8618
134.8928
127.8851
121.1465
115.3499
110.4724
104.9504
77.2563
77.0000
76.7473

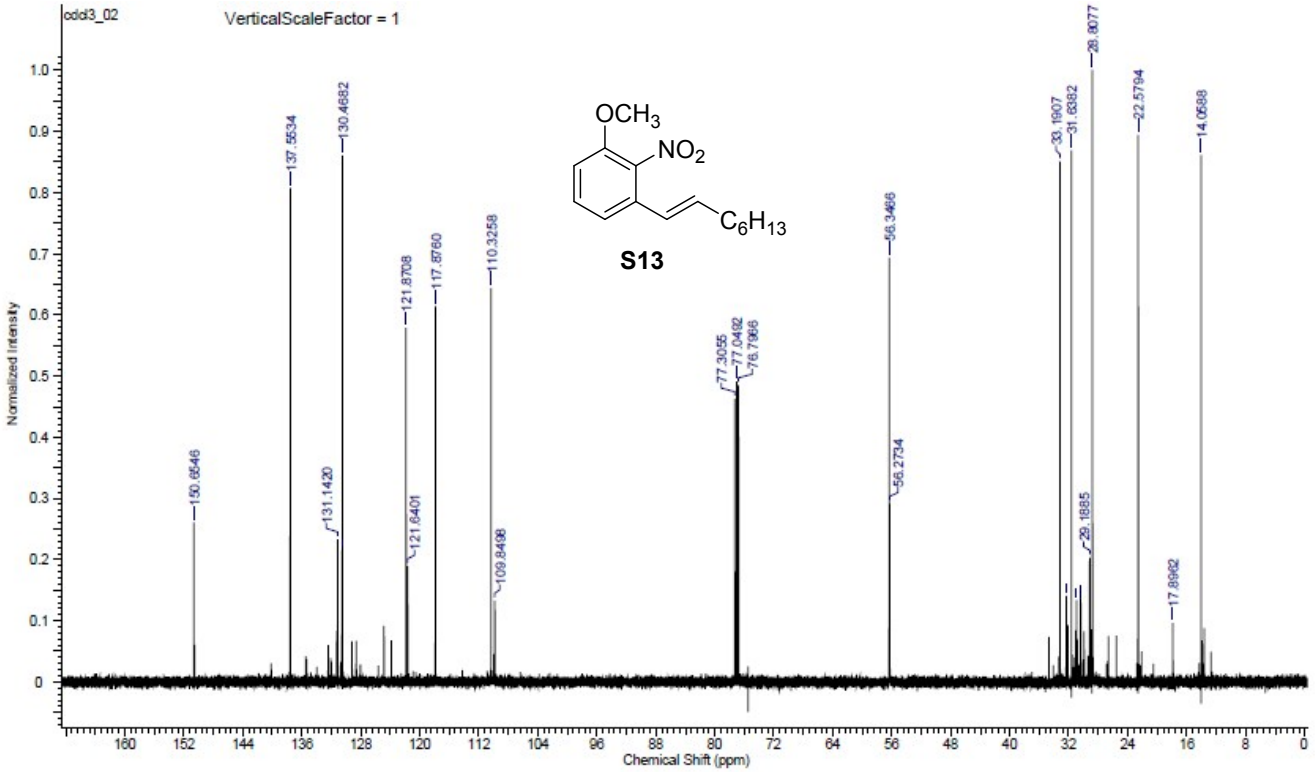

odd3_01
VerticalScaleFactor = 1
O
O
O
C_8H_{17}
S11
Normalized Intensity
Chemical Shift (ppm)
7.3989
7.3823
7.3672
7.2700
6.9297
6.9121
6.7954
6.7793
3.0982
3.0826
3.0669
1.6890
1.2877
1.2730
1.2633
1.2545
1.2325
1.2188
0.8904
0.8668
0.8526
0.93
0.93
1.06
2.00
7.31
2.56
10.34
2.88

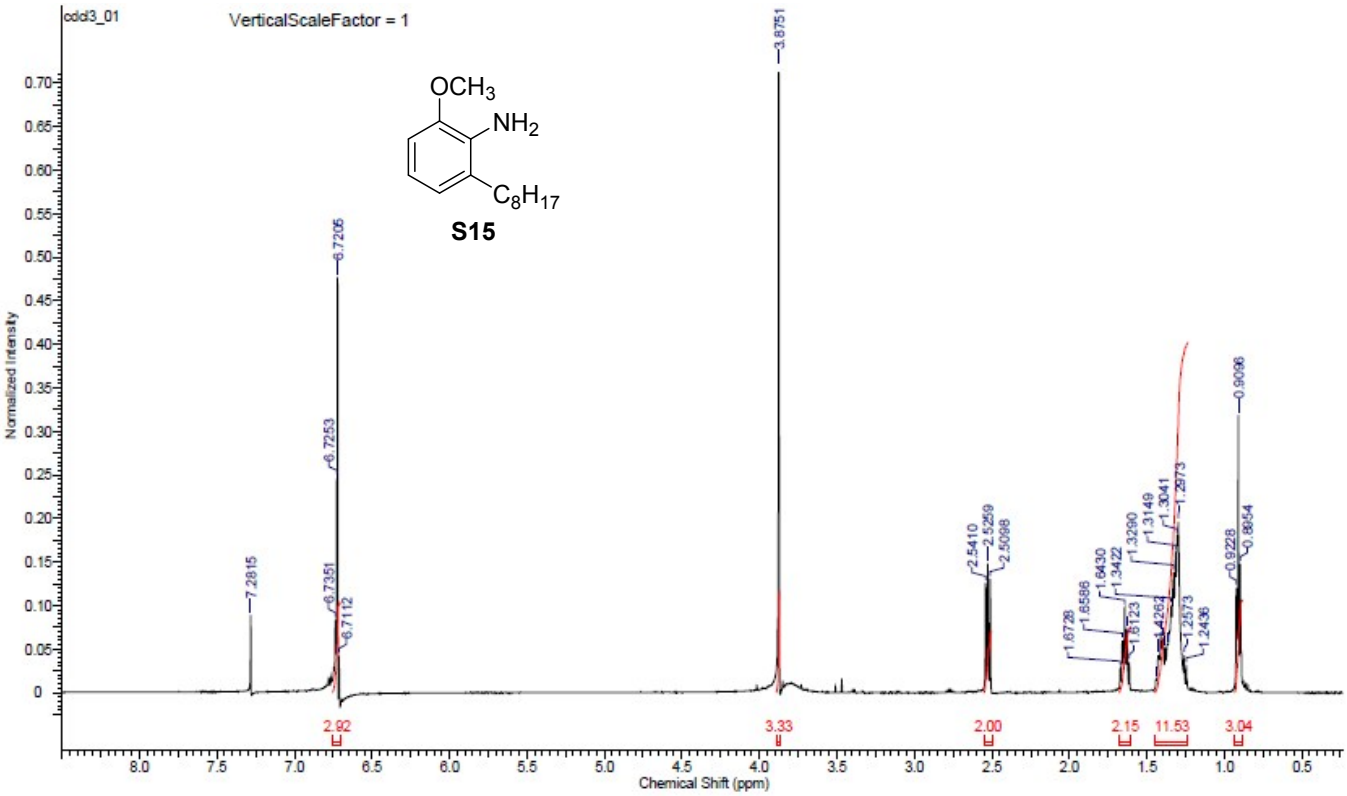

odd3_02
VerticalScaleFactor = 1
O
O
O
C_8H_{17}
S11
Normalized Intensity
Chemical Shift (ppm)
160.1742
157.0727
148.4858
134.9994
125.0540
115.0097
112.0547
104.8812
77.2787
77.0261
76.7734
34.3480
31.8470
29.2471
25.6073
22.6302
14.0727

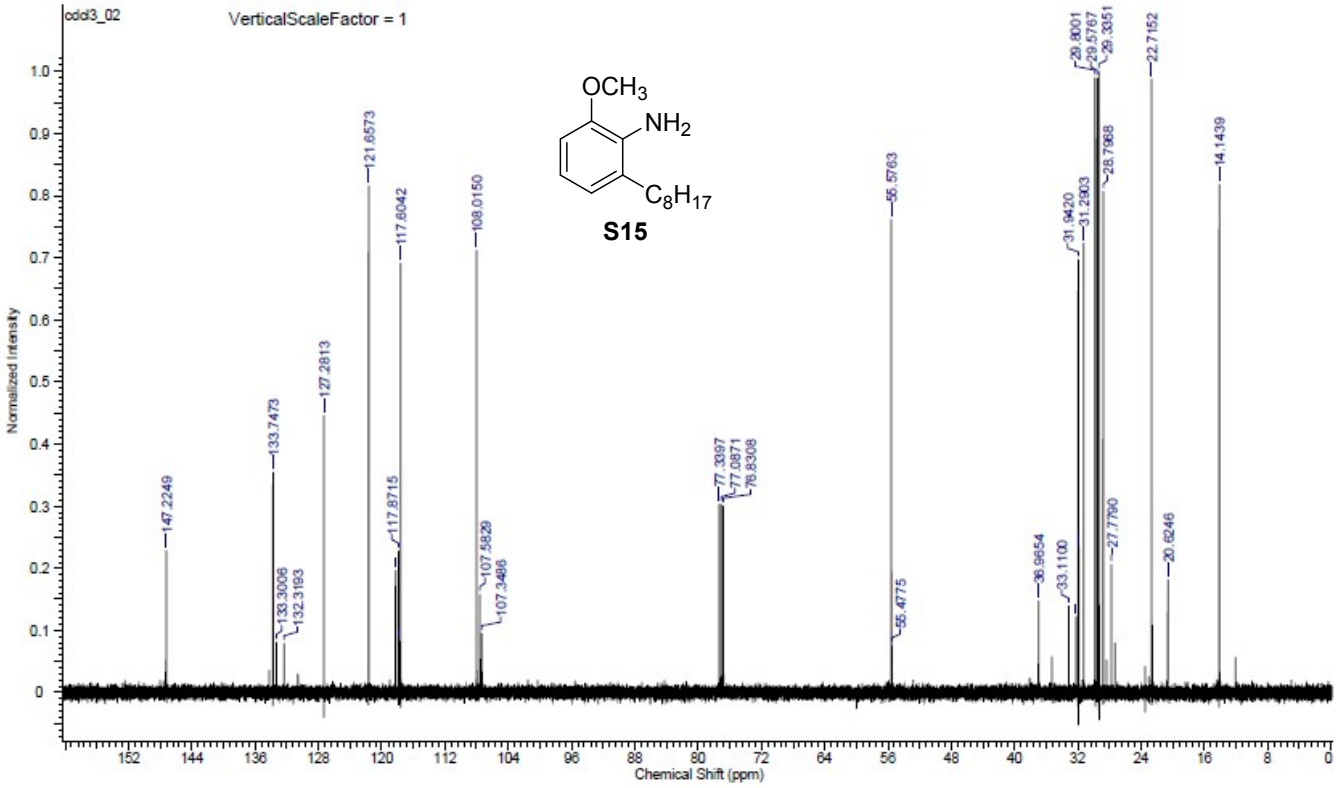

cdcl3_01
VerticalScaleFactor = 1
$C_{15}H_{31}$
S10
Normalized Intensity
Chemical Shift (ppm)
7.4111
7.3850
7.3794
6.9364
6.9243
6.8091
6.7930
3.1070
3.0918
3.0762
1.7017
1.5933
1.5782
1.5626
1.3043
1.2886
1.2574
1.2423
1.2286
1.1939
0.8995
0.8863
0.8721
0.56
0.57
0.80
1.21
6.04
2.72
24.75
3.05

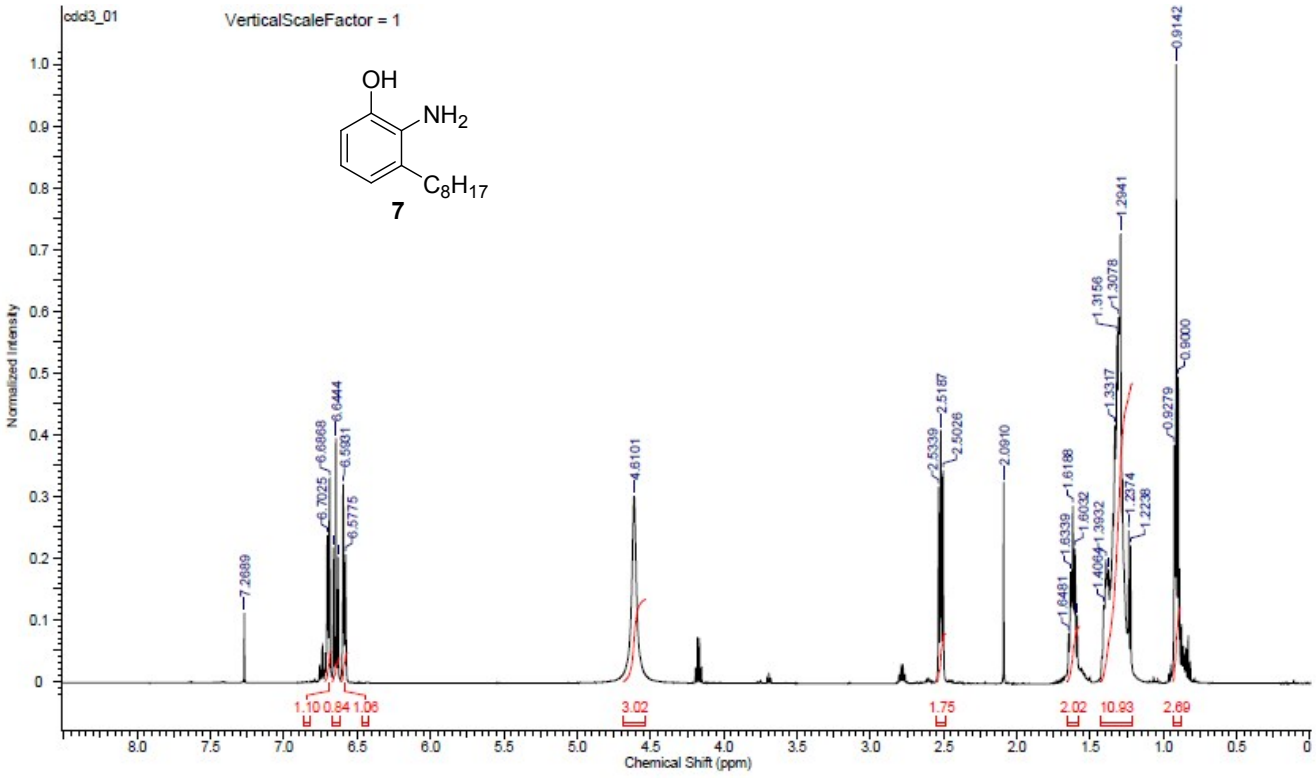

cdcl3_01
VerticalScaleFactor = 1
$C_{15}H_{31}$
S10
Normalized Intensity
Chemical Shift (ppm)
159.8515
156.9258
148.2547
134.8013
124.8778
114.8702
111.8968
104.6282
77.2527
77.0000
76.7437
34.2230
31.7623
29.5996
29.5030
29.2064
25.4091
22.5127
13.9221

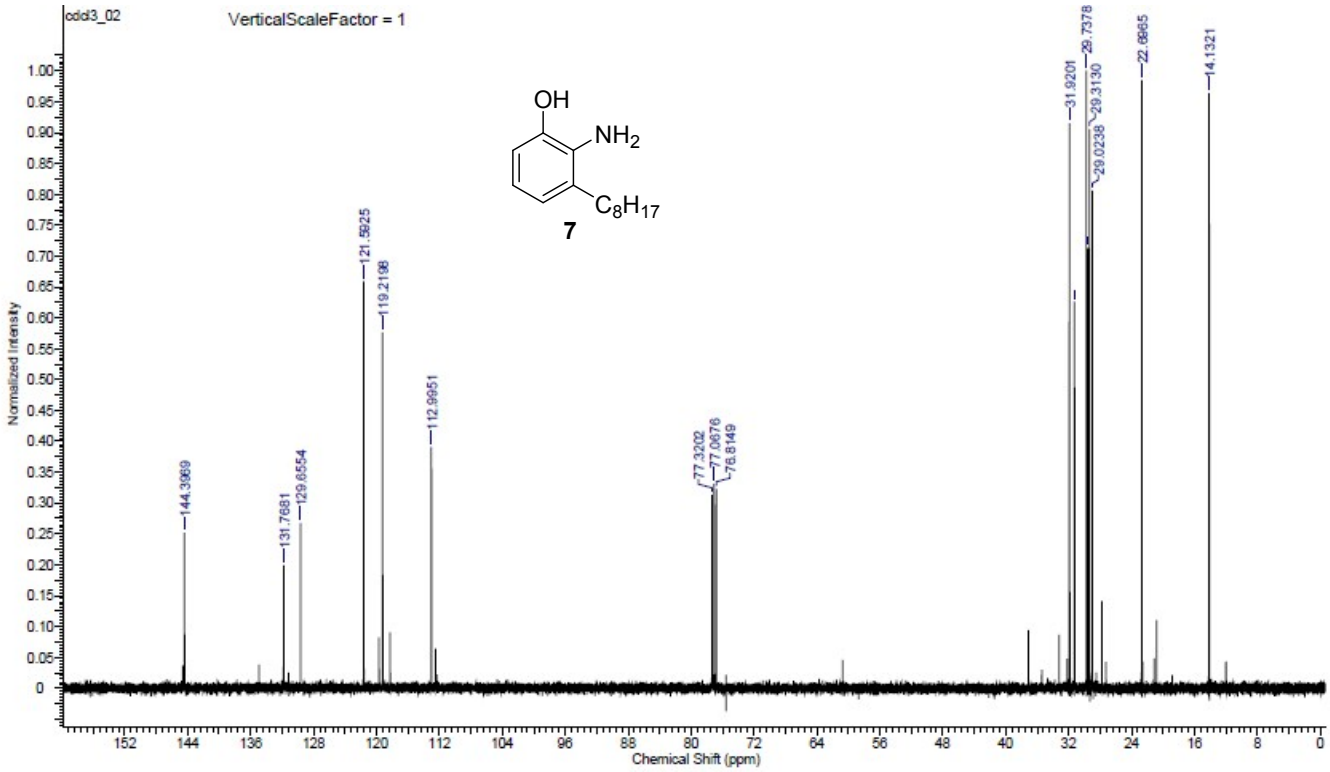

cdd3_01
VerticalScaleFactor = 1
OCH3
NO2
C6H13
S13
Normalized Intensity
Chemical Shift (ppm)

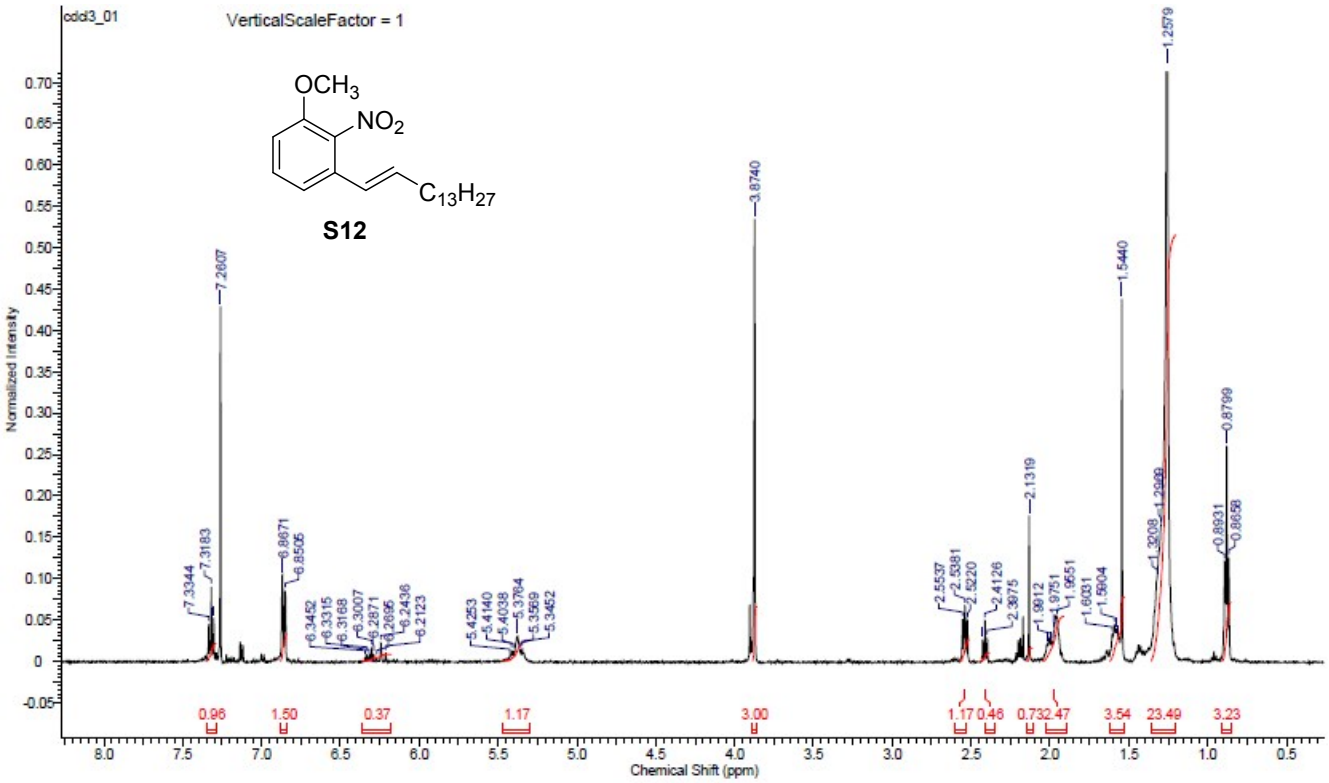

cdd3_02
VerticalScaleFactor = 1
OCH3
NO2
C6H13
S13
Normalized Intensity
Chemical Shift (ppm)

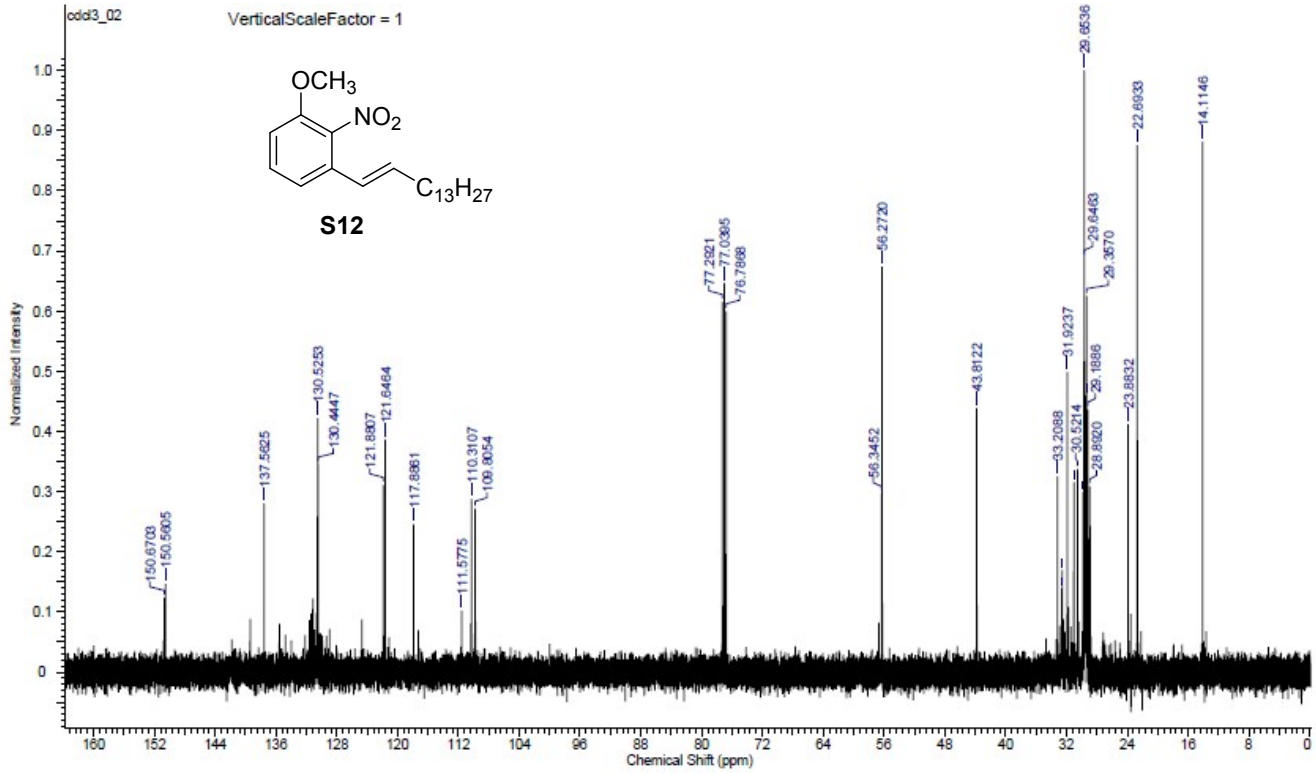

cdd3_01
VerticalScaleFactor = 1
OCH3
NH2
C8H17
S15
Normalized Intensity
Chemical Shift (ppm)

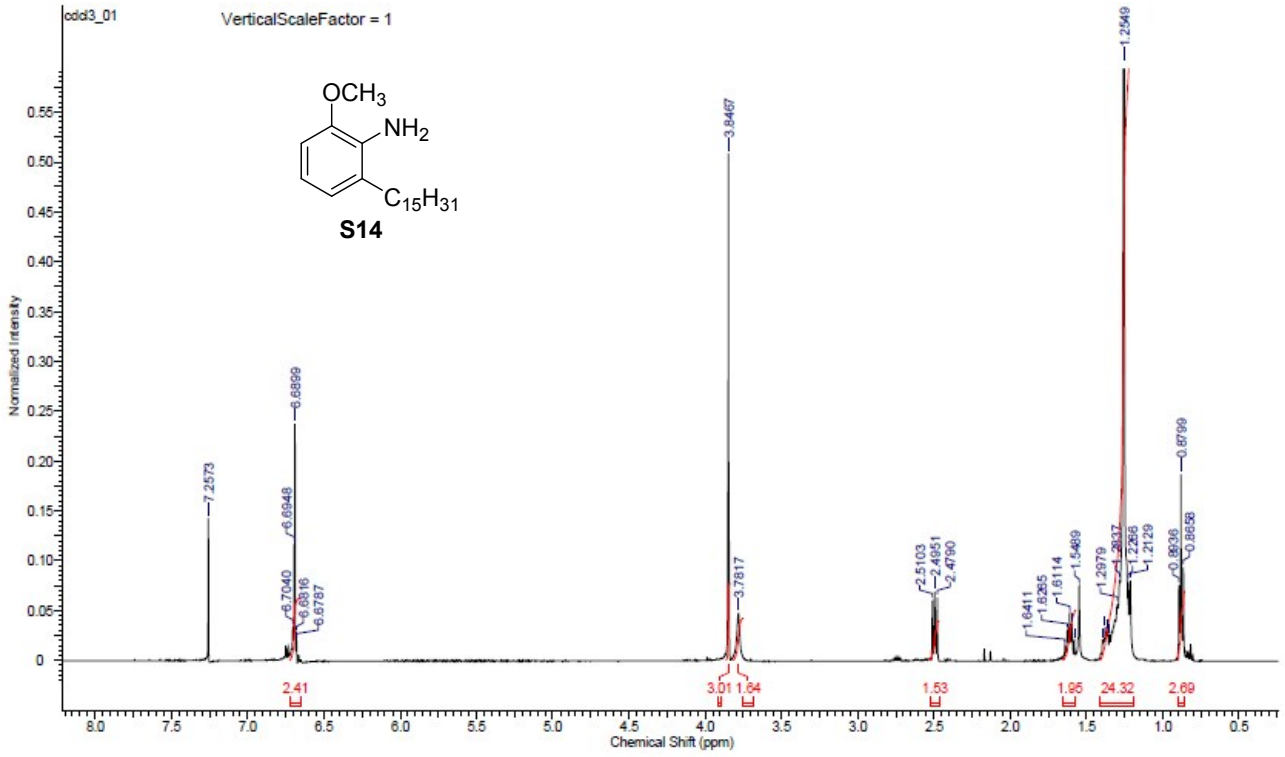

cdd3_02
VerticalScaleFactor = 1
OCH3
NH2
C8H17
S15
Normalized Intensity
Chemical Shift (ppm)

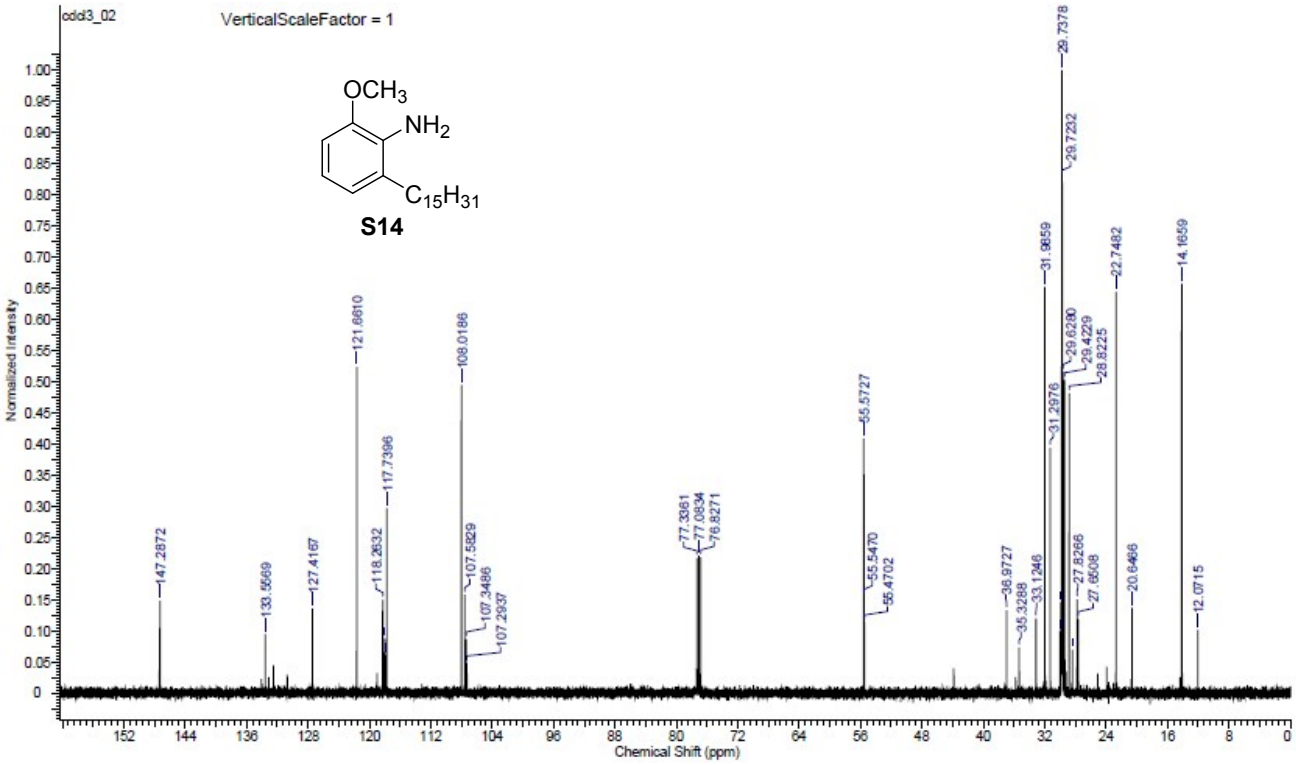

cdd3_01
VerticalScaleFactor = 1
OH
NH2
C8H17
7
Normalized Intensity
Chemical Shift (ppm)
7.2689
6.7025
6.6868
6.6444
6.5931
6.5775
4.6101
2.5339
2.5187
2.5026
2.0910
1.6481
1.6339
1.6188
1.6032
1.3932
1.3317
1.3156
1.3078
1.2941
1.2374
1.2238
0.9279
0.9142
0.9000
1.10
0.84
1.06
3.02
1.75
2.02
10.93
2.69

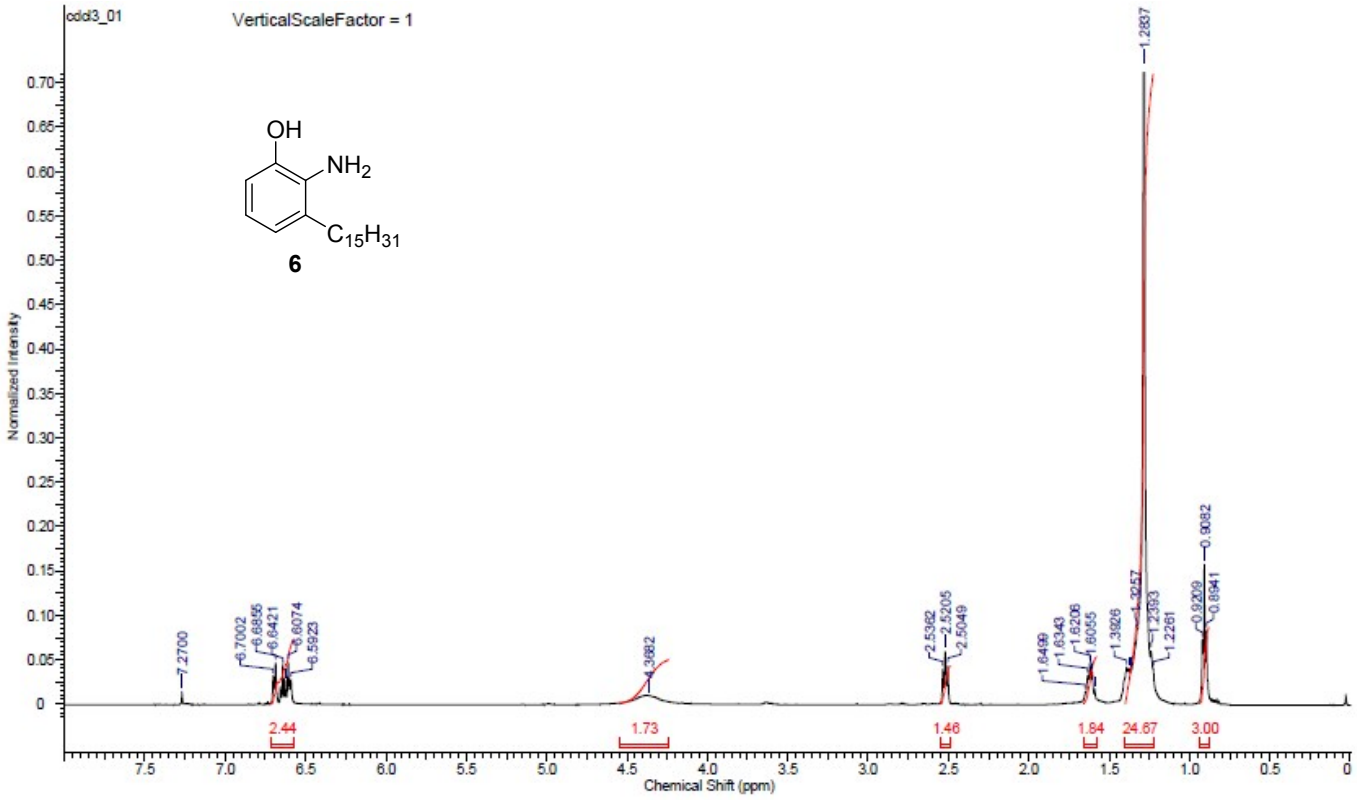

cdd3_02
VerticalScaleFactor = 1
OH
NH2
C8H17
7
Normalized Intensity
Chemical Shift (ppm)
144.3969
131.7681
129.6554
121.5925
119.2196
112.9951
77.3202
77.0676
76.8149
31.9201
29.7378
29.3130
29.0238
22.6865
14.1321

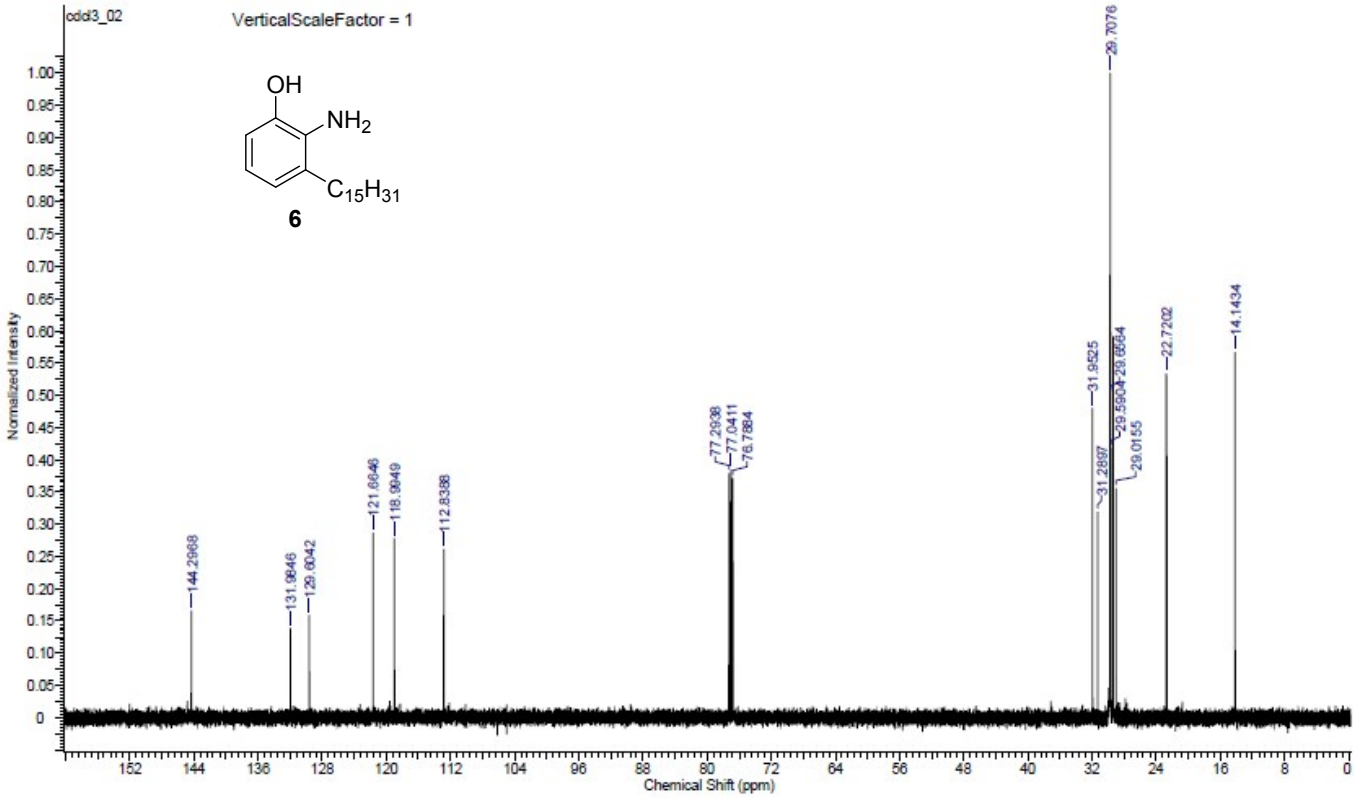

cdd3_01
VerticalScaleFactor = 1
OCH3
NO2
C13H27
S12
Normalized Intensity
Chemical Shift (ppm)

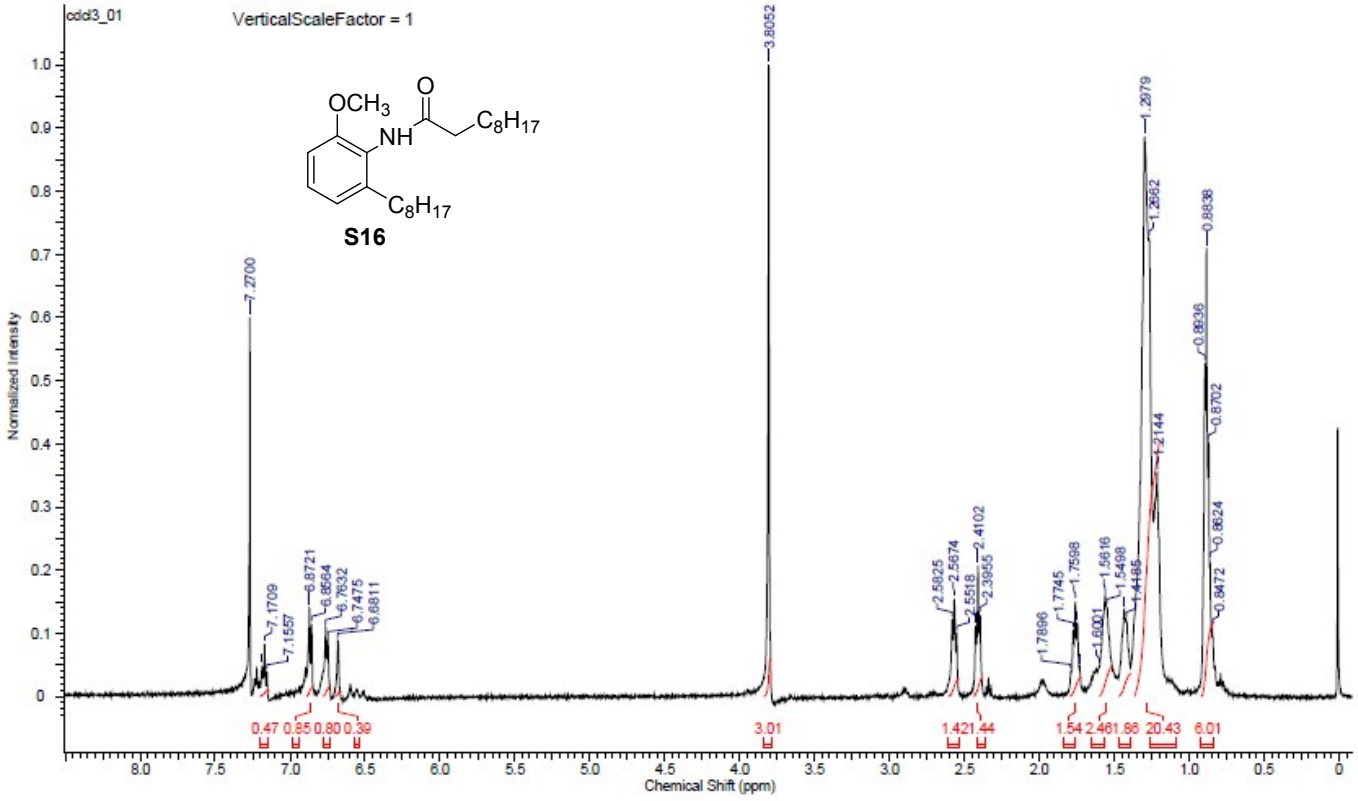

cdd3_02
VerticalScaleFactor = 1
OCH3
NO2
C13H27
S12
Normalized Intensity
Chemical Shift (ppm)

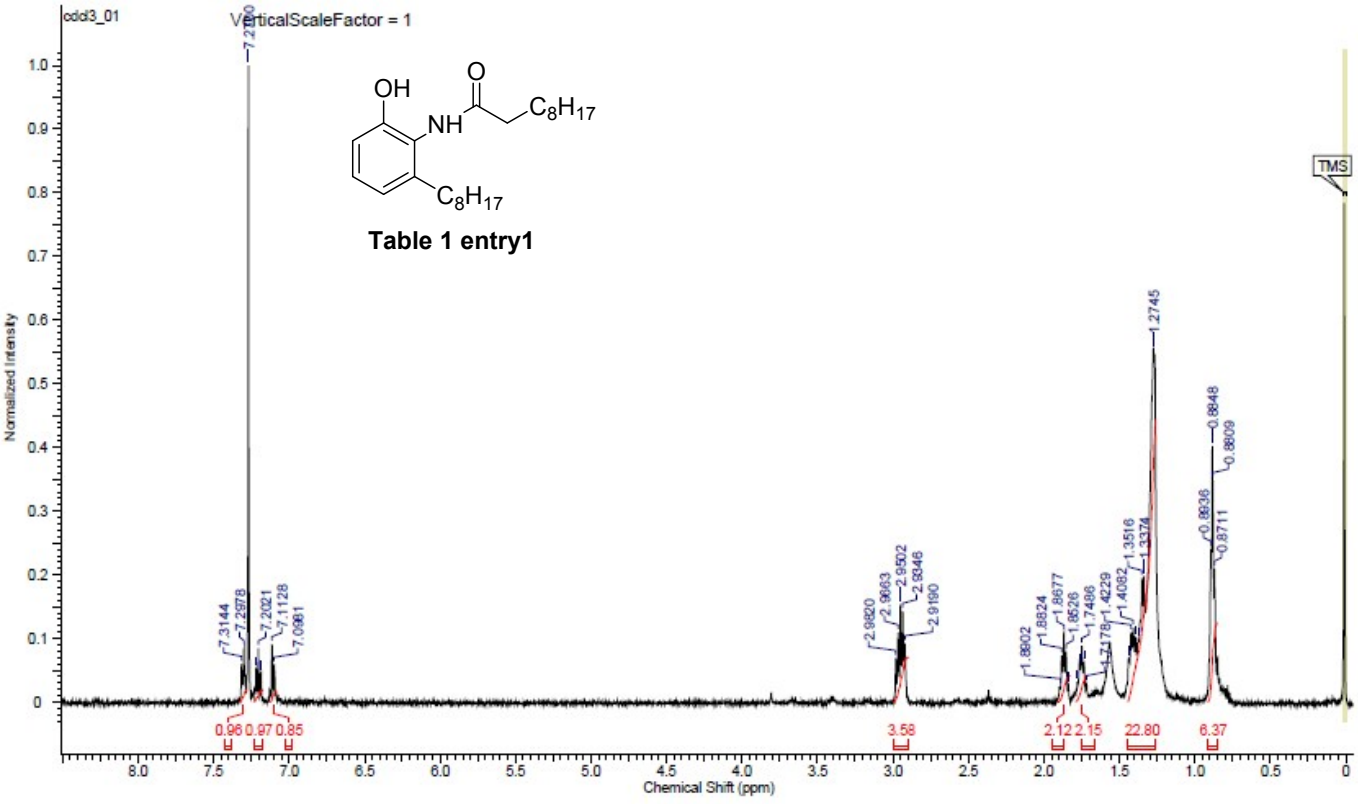

odd3_01
VerticalScaleFactor = 1
OCH3
NH2
C15H31
S14
Normalized Intensity
Chemical Shift (ppm)
7.2573
6.8899
6.6948
6.7040
6.6816
6.6787
3.8467
3.7817
2.5103
2.4951
2.4790
1.6411
1.6285
1.6114
1.5469
1.2979
1.2549
1.2286
1.2129
0.8799
0.8636
0.8558
2.41
3.01
1.64
1.53
1.95
24.32
2.69

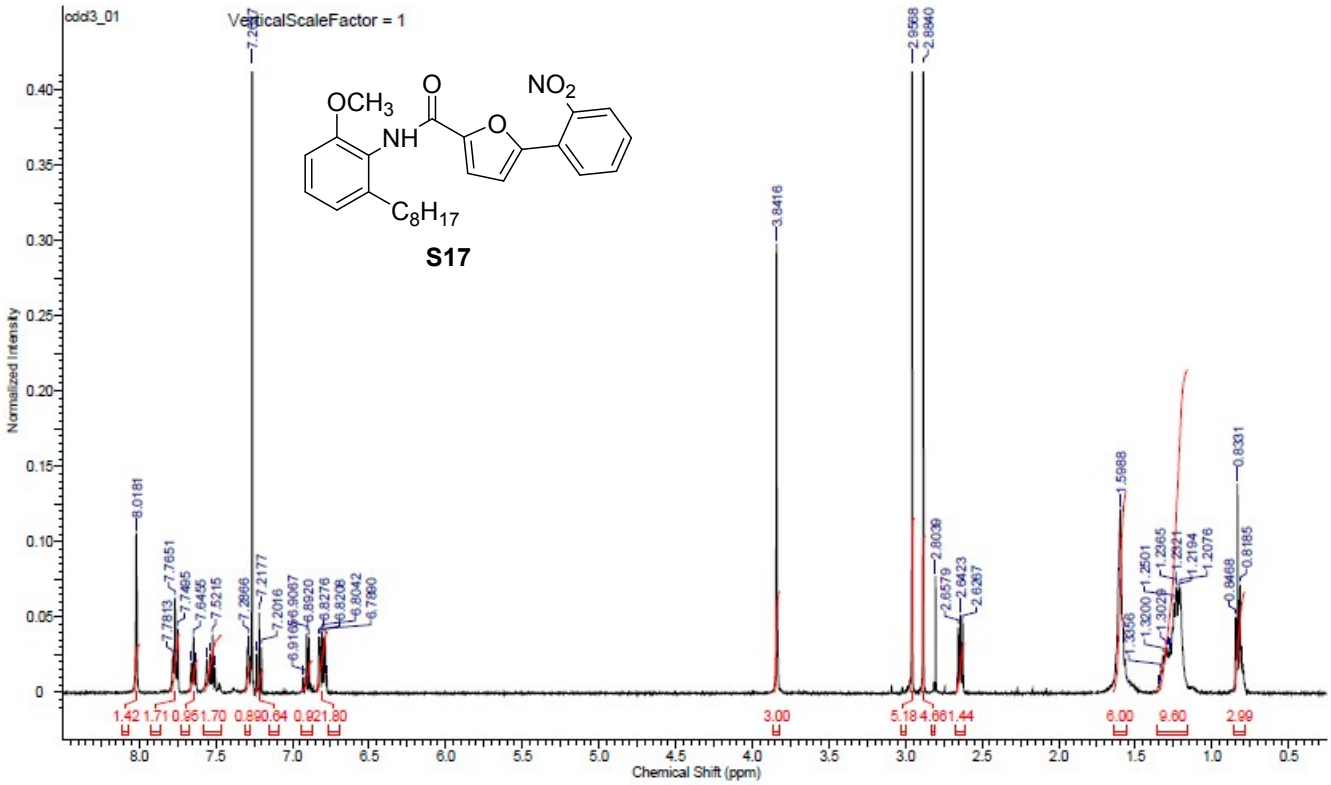

odd3_02
VerticalScaleFactor = 1
OCH3
NH2
C15H31
S14
Normalized Intensity
Chemical Shift (ppm)
147.2872
133.5669
127.4167
121.6610
118.2632
117.7396
108.0186
107.5829
107.3486
107.2937
77.3361
77.0834
76.8271
55.5727
55.5470
55.4702
36.9727
35.3288
33.1246
31.9659
31.2976
29.7378
29.7232
29.6280
29.4229
28.8225
27.8266
27.6608
22.7482
20.6466
14.1659
12.0715


cdd3_01
VerticalScaleFactor = 1
OH
NH2
C15H31
6
Normalized Intensity
Chemical Shift (ppm)
7.2700
6.7002
6.6855
6.6421
6.6074
6.5923
4.3682
2.5382
2.5205
2.5049
1.6499
1.6343
1.6206
1.6055
1.3926
1.2887
1.2393
1.2261
0.9209
0.9082
0.8941
2.44
1.73
1.46
1.84
24.67
3.00


cdd3_02
VerticalScaleFactor = 1
OH
NH2
C15H31
6
Normalized Intensity
Chemical Shift (ppm)
144.2968
131.9846
129.6042
121.6646
118.9949
112.8388
77.2938
77.0411
76.7884
31.9525
31.2897
29.7076
29.5904
29.6664
29.0155
22.7202
14.1434


cdcl3_01
VerticalScaleFactor = 1
OCH3
NH
O
C8H17
C8H17
S16
Normalized Intensity
Chemical Shift (ppm)
7.2700
3.8052
1.2979
1.2662
0.8838
0.8636
0.8702
1.2144
0.8624
0.8472
2.5825
2.5674
2.5518
2.4102
2.3945
1.7896
1.7745
1.7598
1.5616
1.5498
1.5001
1.4485
7.1709
7.1557
6.8721
6.8564
6.7832
6.7475
6.6811
0.47 0.85 0.80 0.39
3.01
1.42 1.44
1.54 2.46 1.86 20.43 6.01


cdcl3_01
VerticalScaleFactor = 1
OH
NH
O
C8H17
C8H17
Table 1 entry1
TMS
Normalized Intensity
Chemical Shift (ppm)
7.2700
1.2745
0.8848
0.8809
0.8636
0.8711
7.3144
7.2978
7.2021
7.1128
7.0981
2.9820
2.9663
2.9502
2.9346
2.9190
1.8802
1.8824
1.8677
1.8526
1.7486
1.4229
1.4082
1.3516
1.3374
0.96 0.97 0.85
3.58
2.12 2.15 22.80 6.37



S17

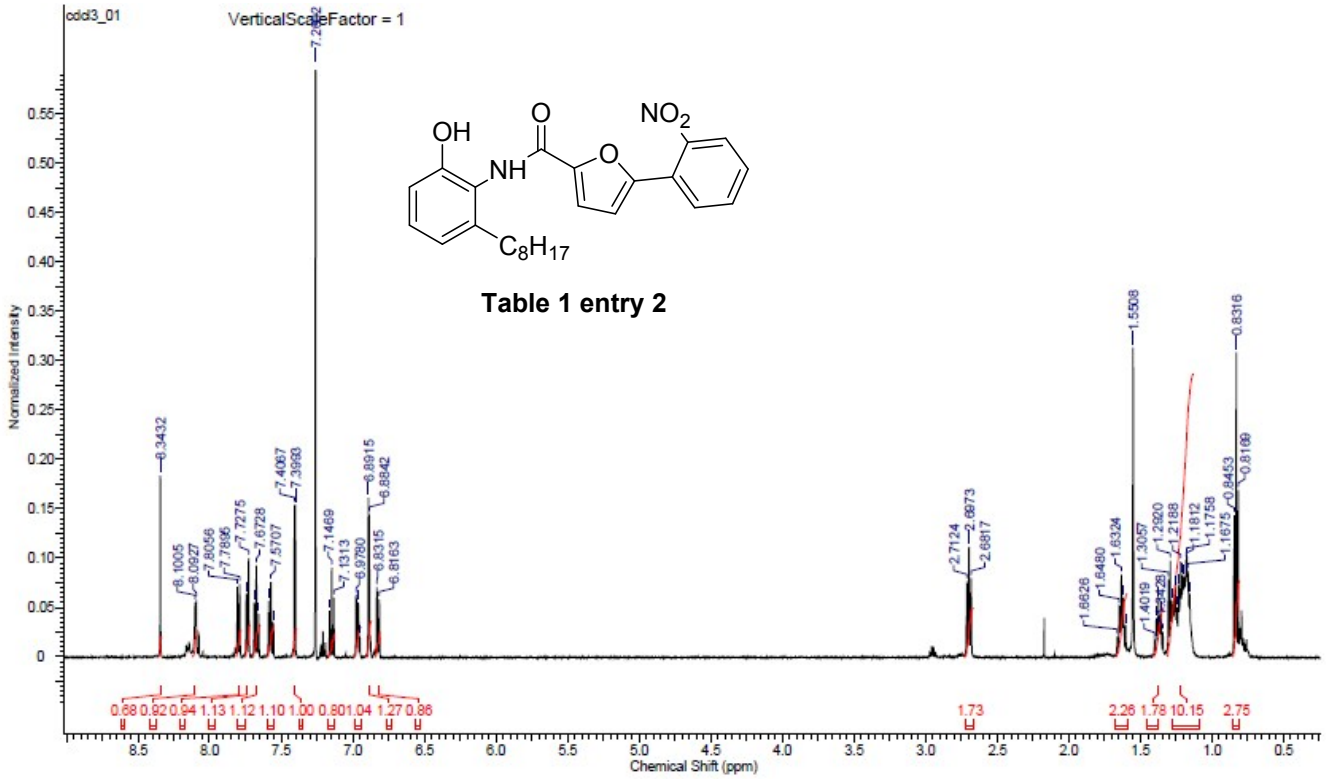
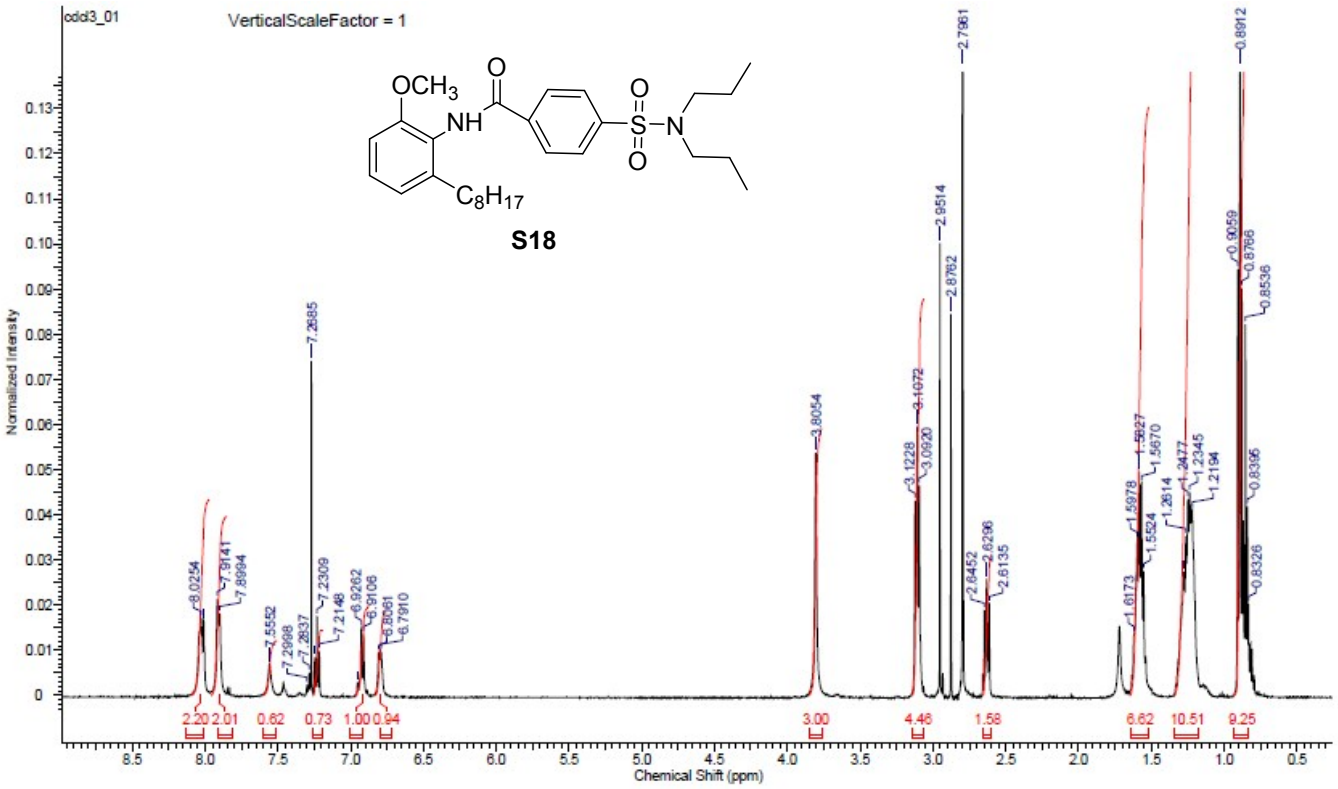
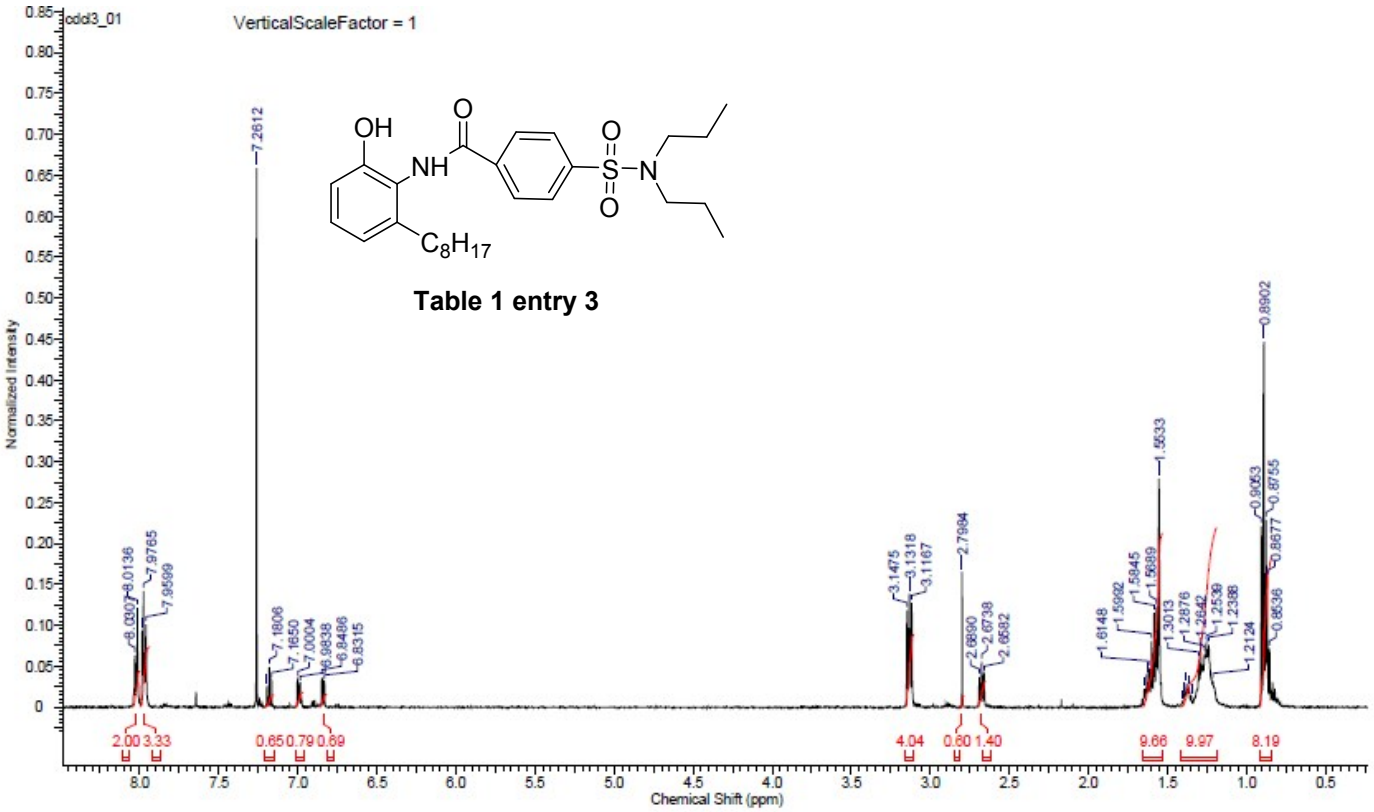


Table 1 entry 2



S18



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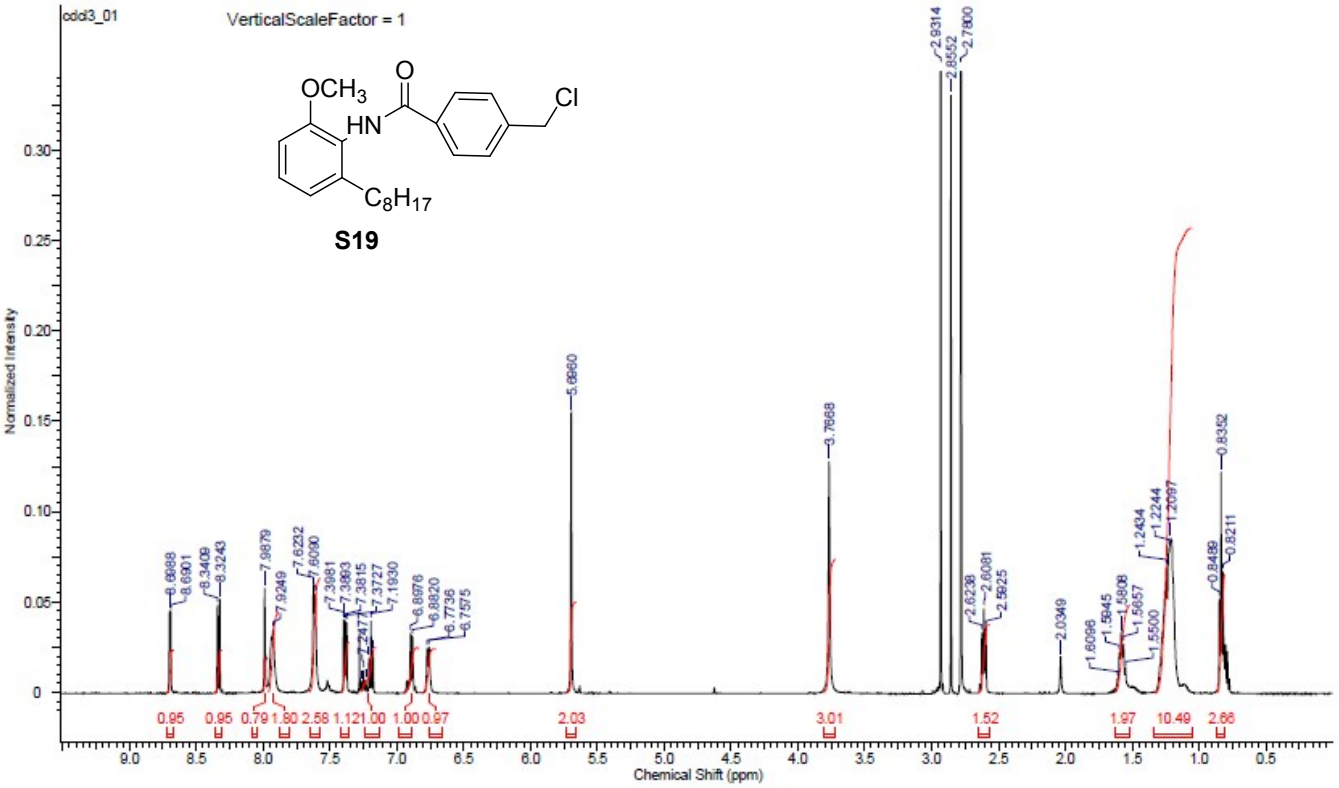
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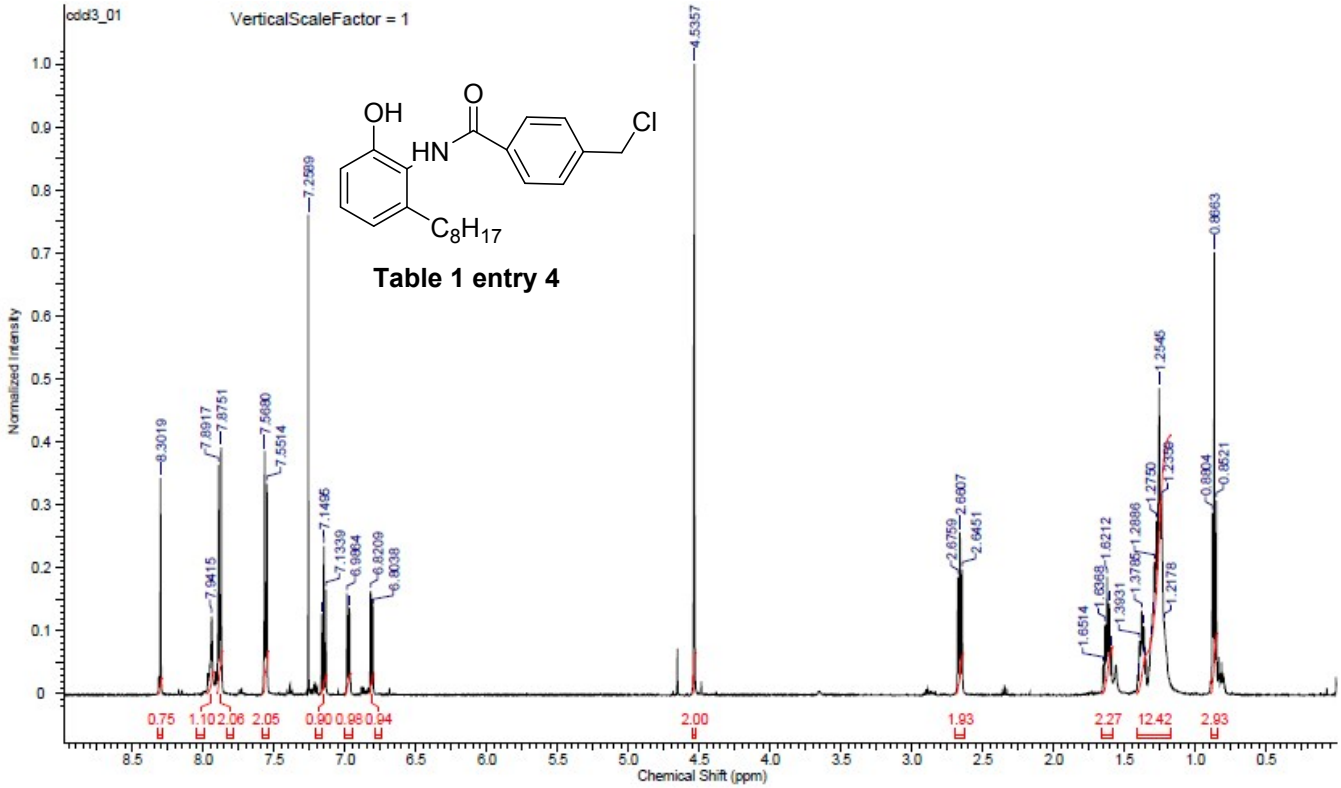
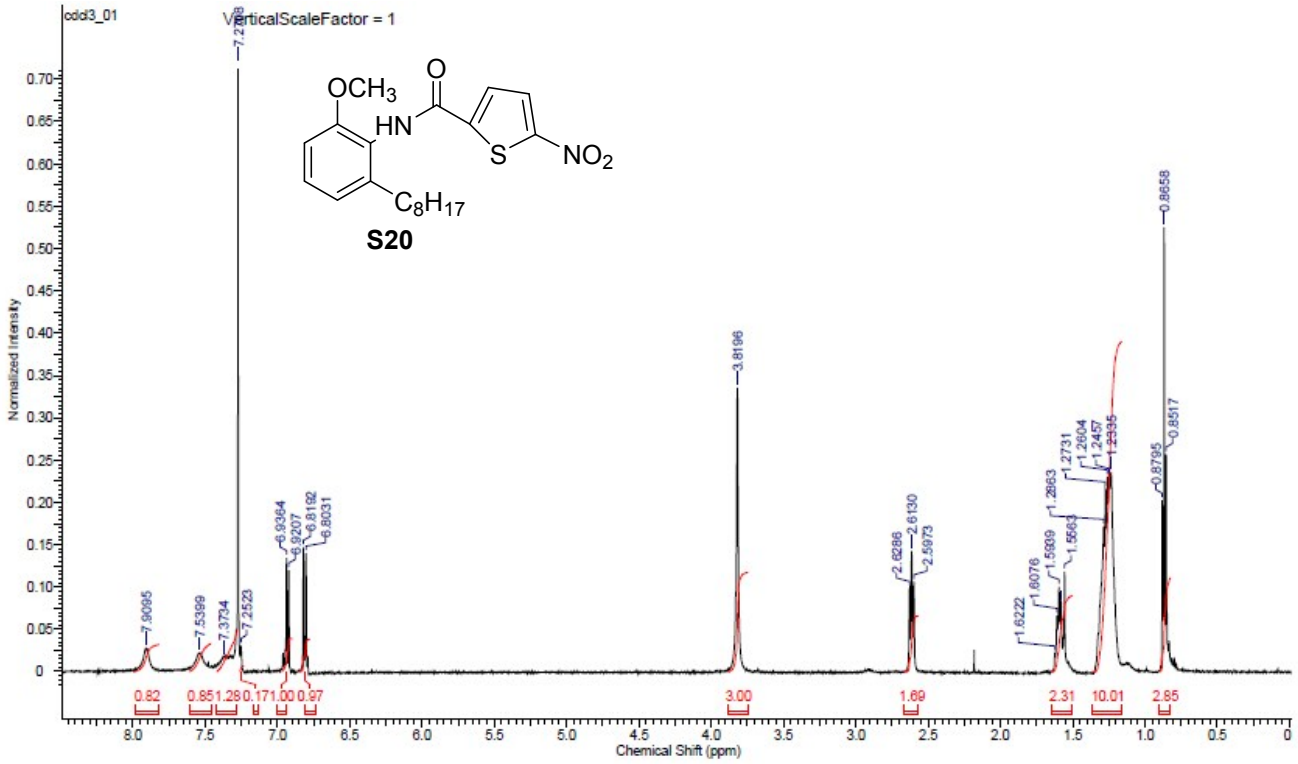
VerticalScaleFactor = 1
OCH3
O
HN
Cl
C8H17
S19
Normalized Intensity
Chemical Shift (ppm)


cdcl3_01
VerticalScaleFactor = 1
OH
O
HN
Cl
C8H17
Table 1 entry 4
Normalized Intensity
Chemical Shift (ppm)



S20

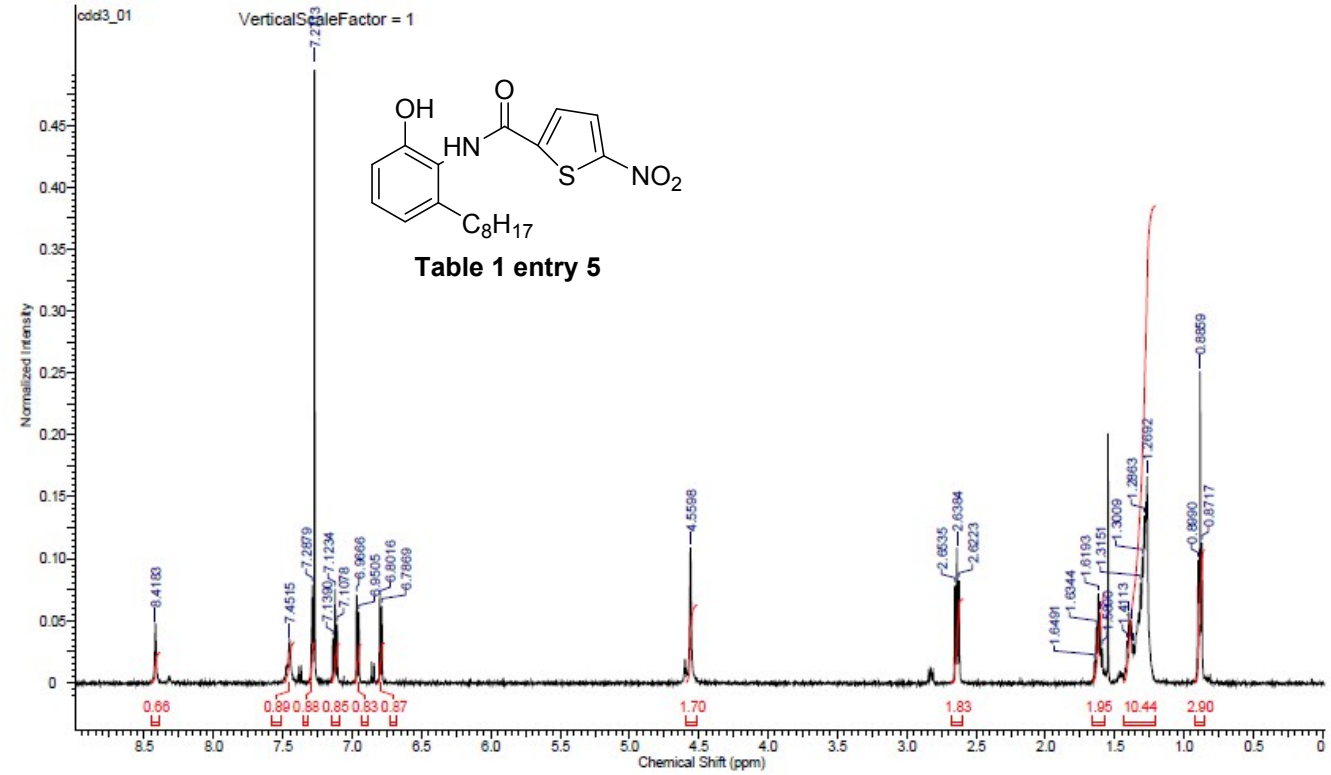
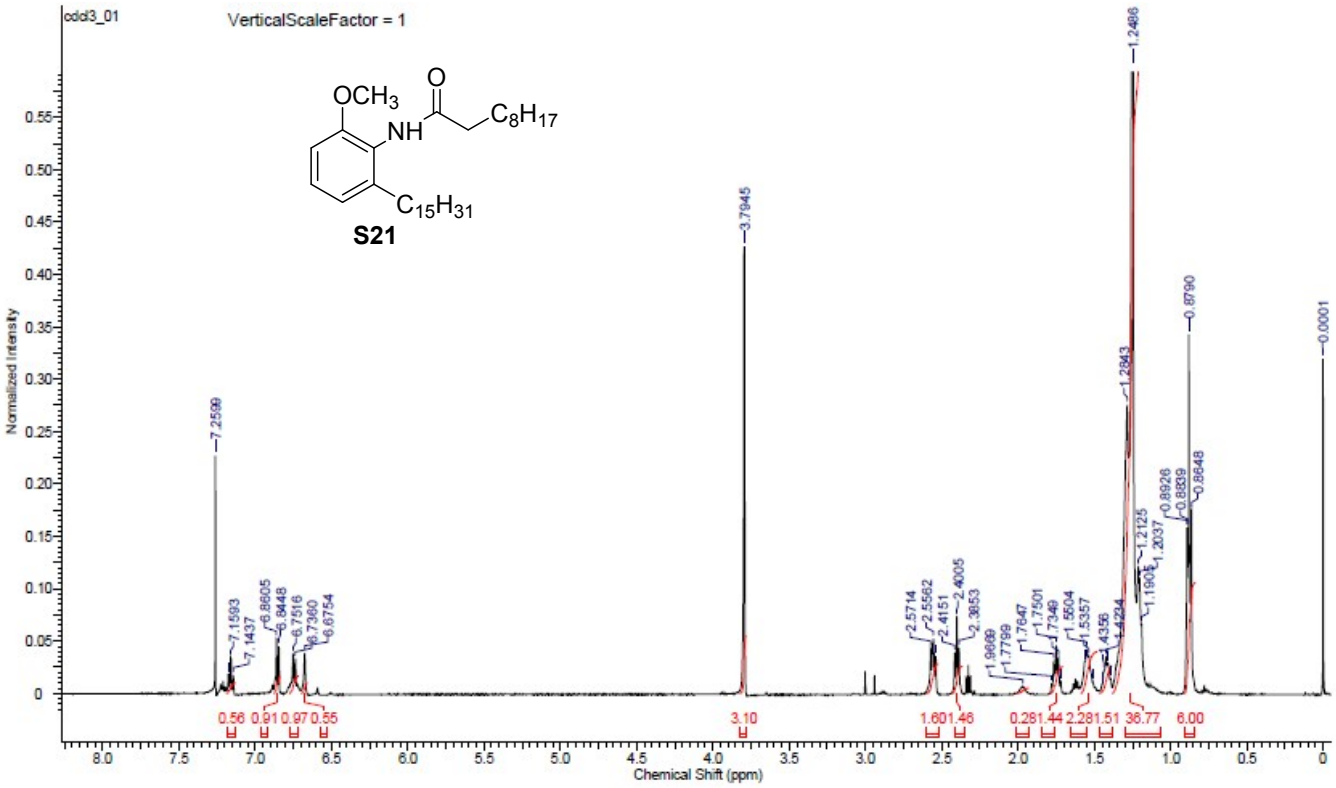


Table 1 entry 5



S21

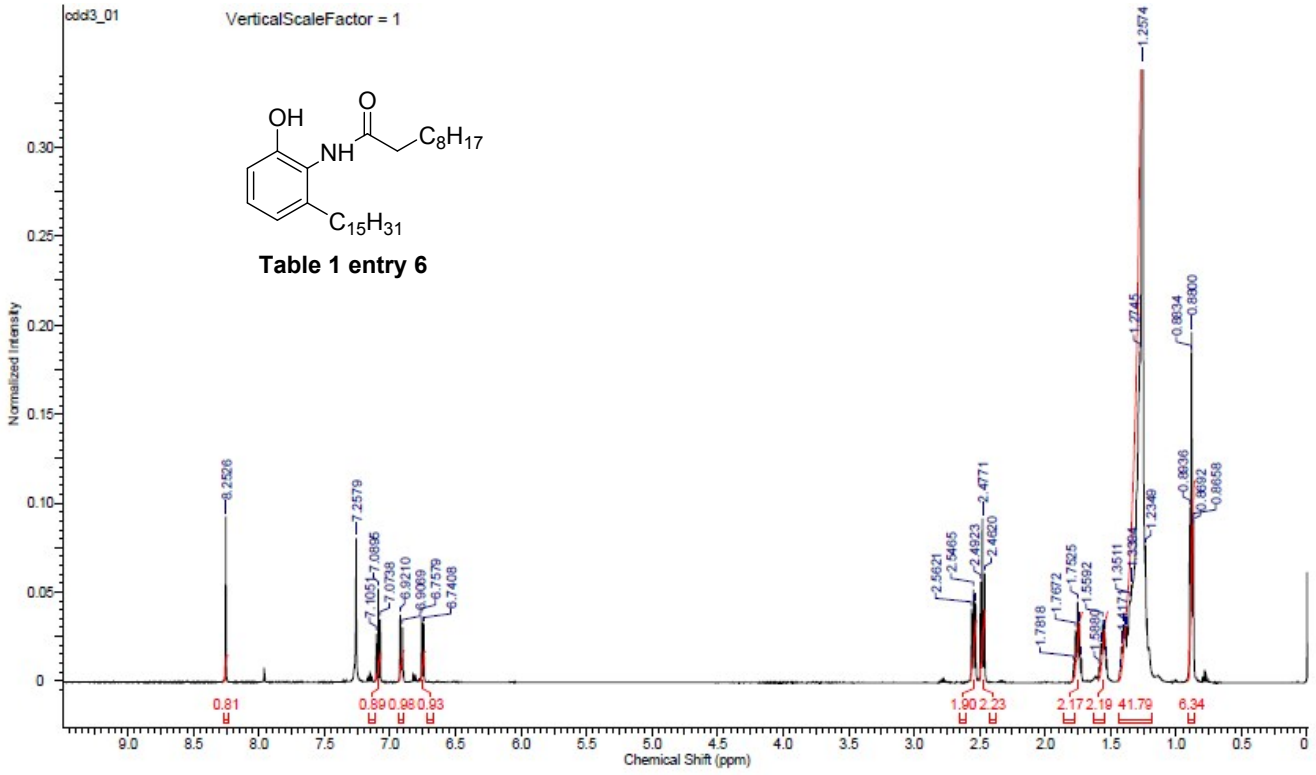
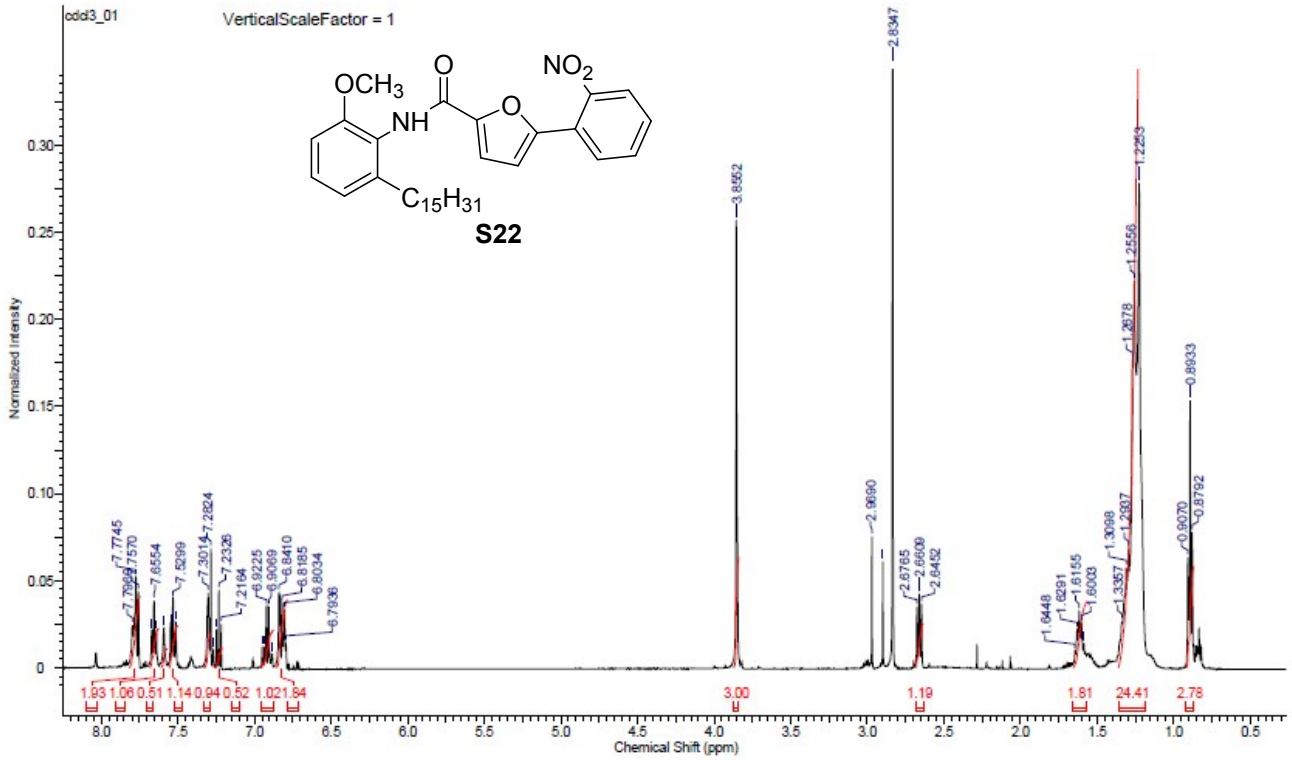


Table 1 entry 6



S22

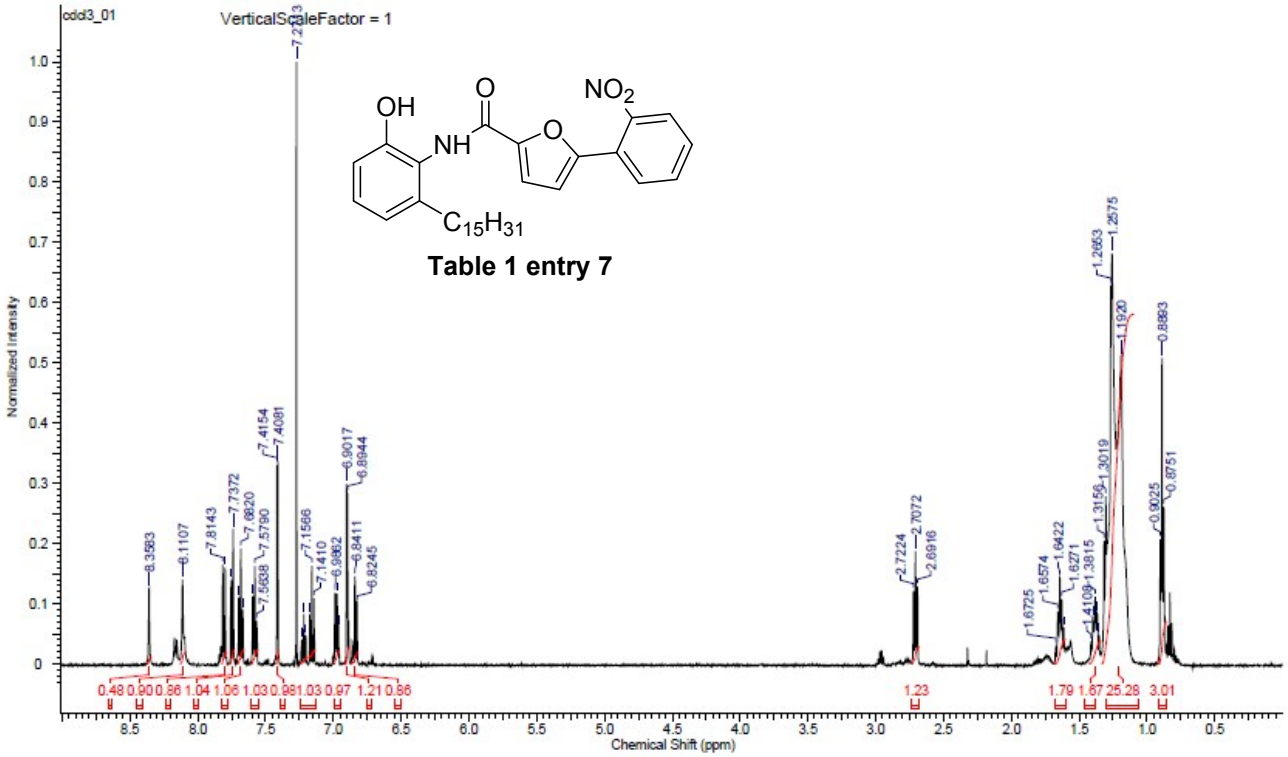
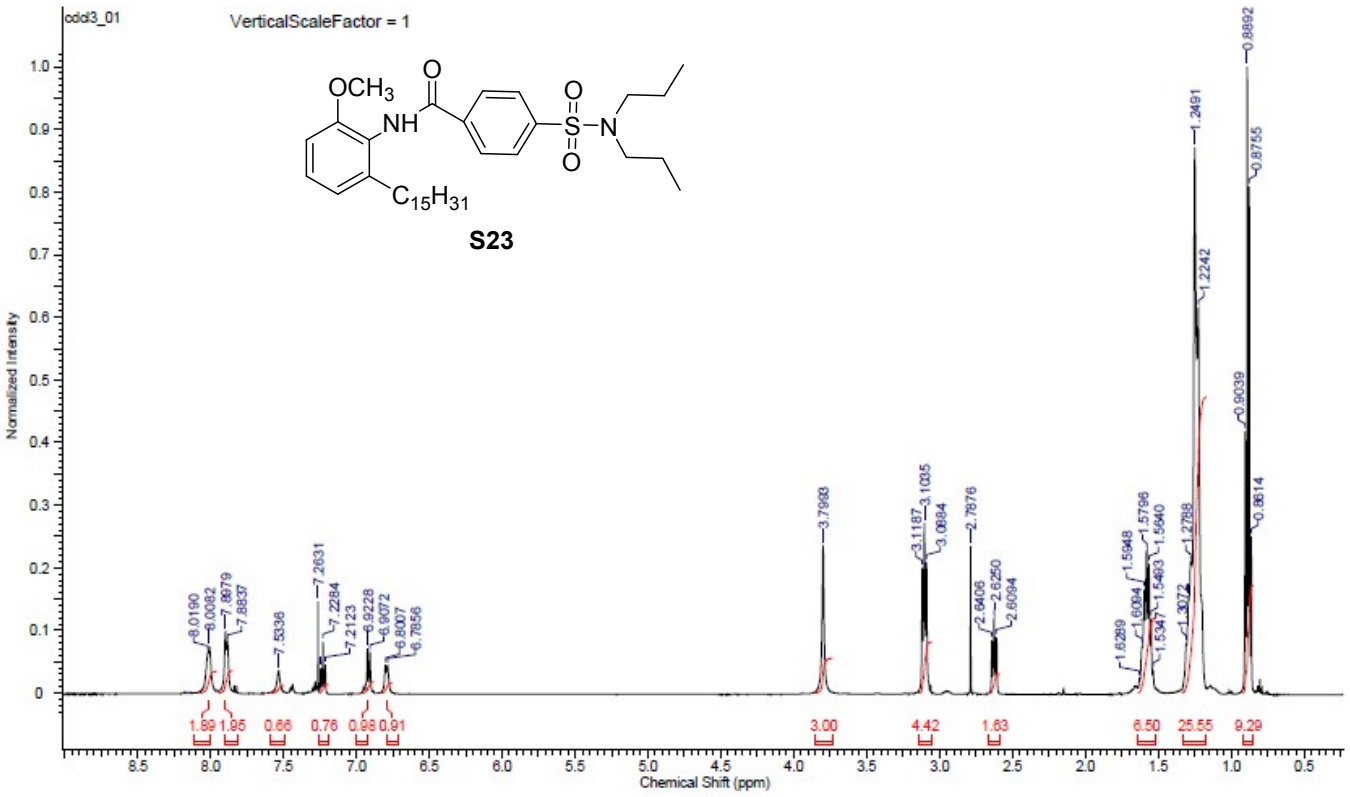


Table 1 entry 7



S23

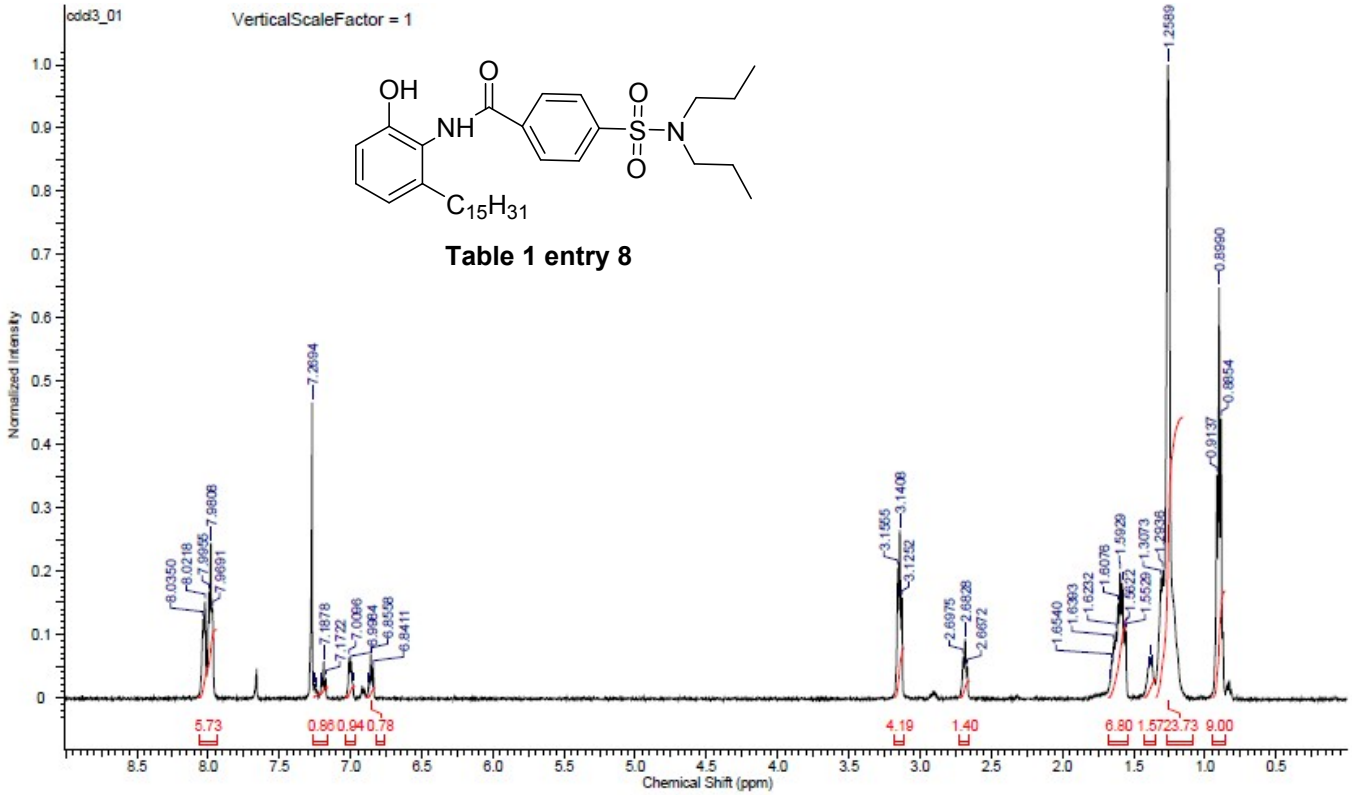
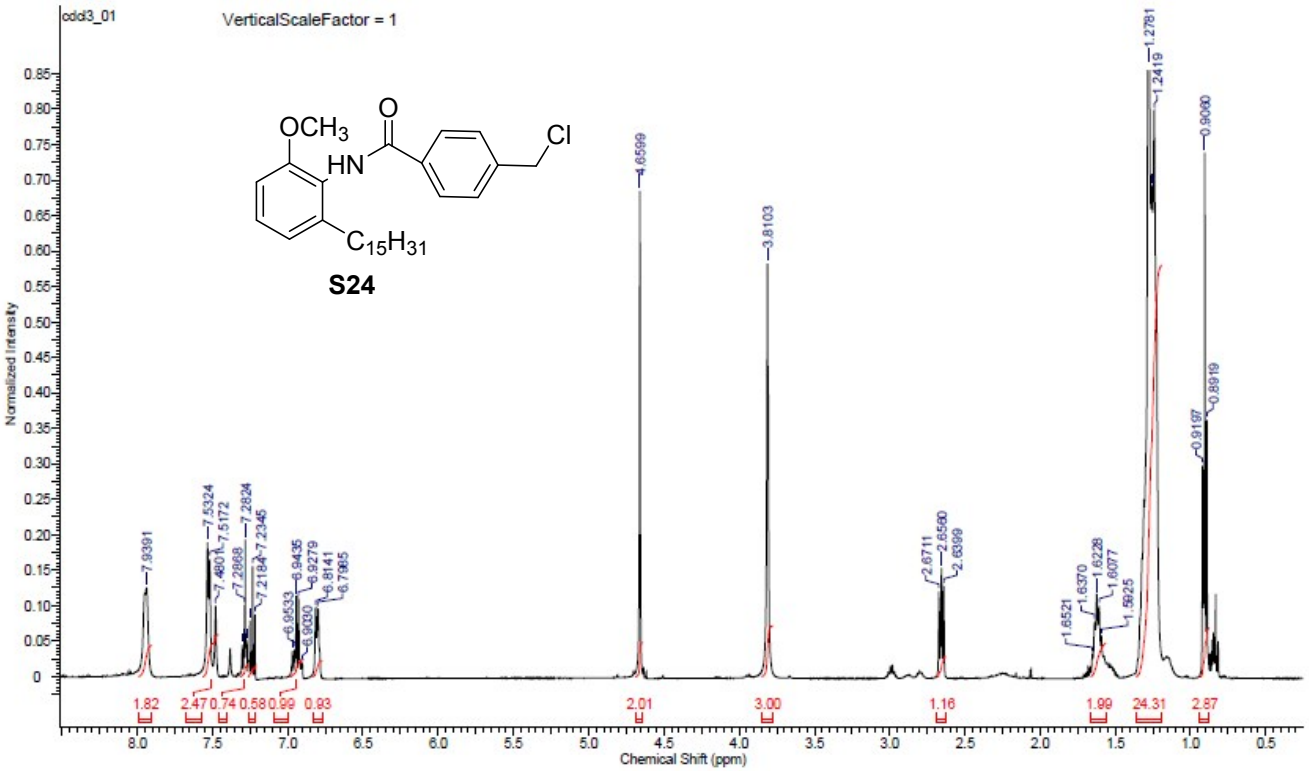


Table 1 entry 8



S24

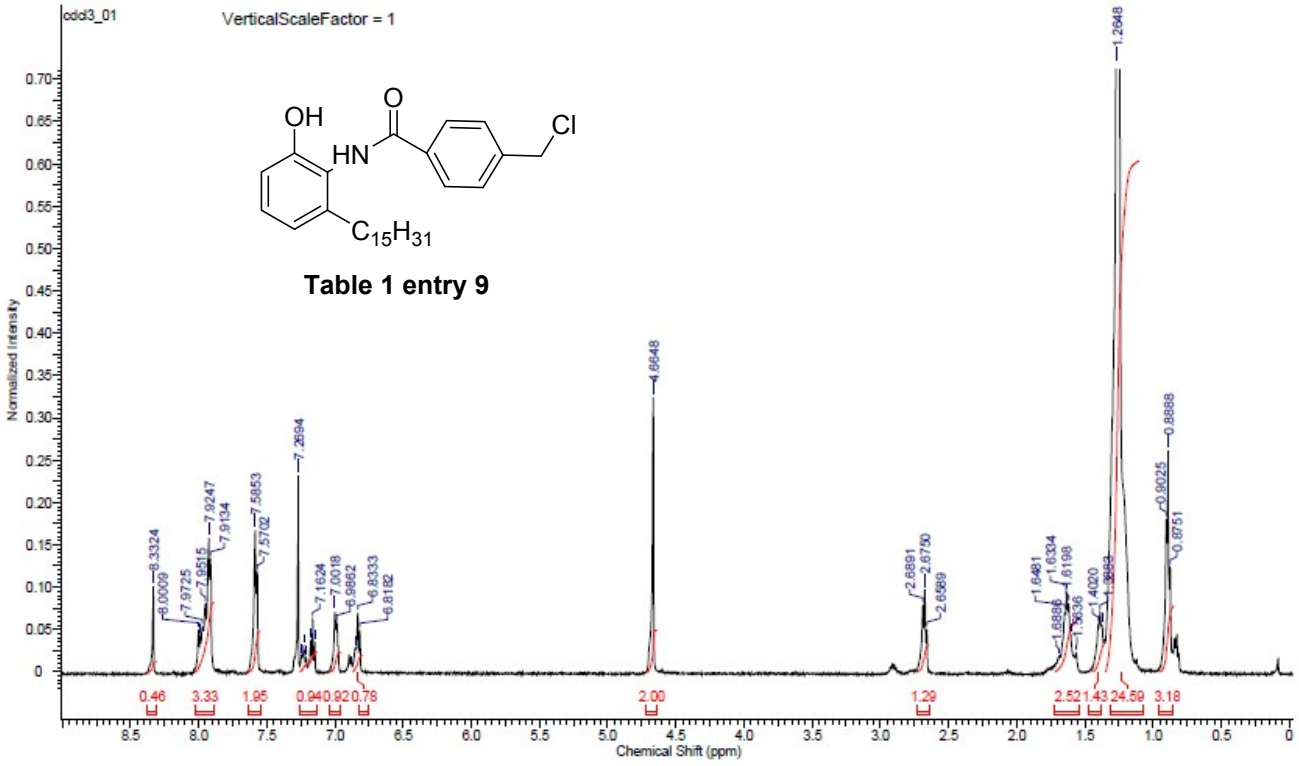
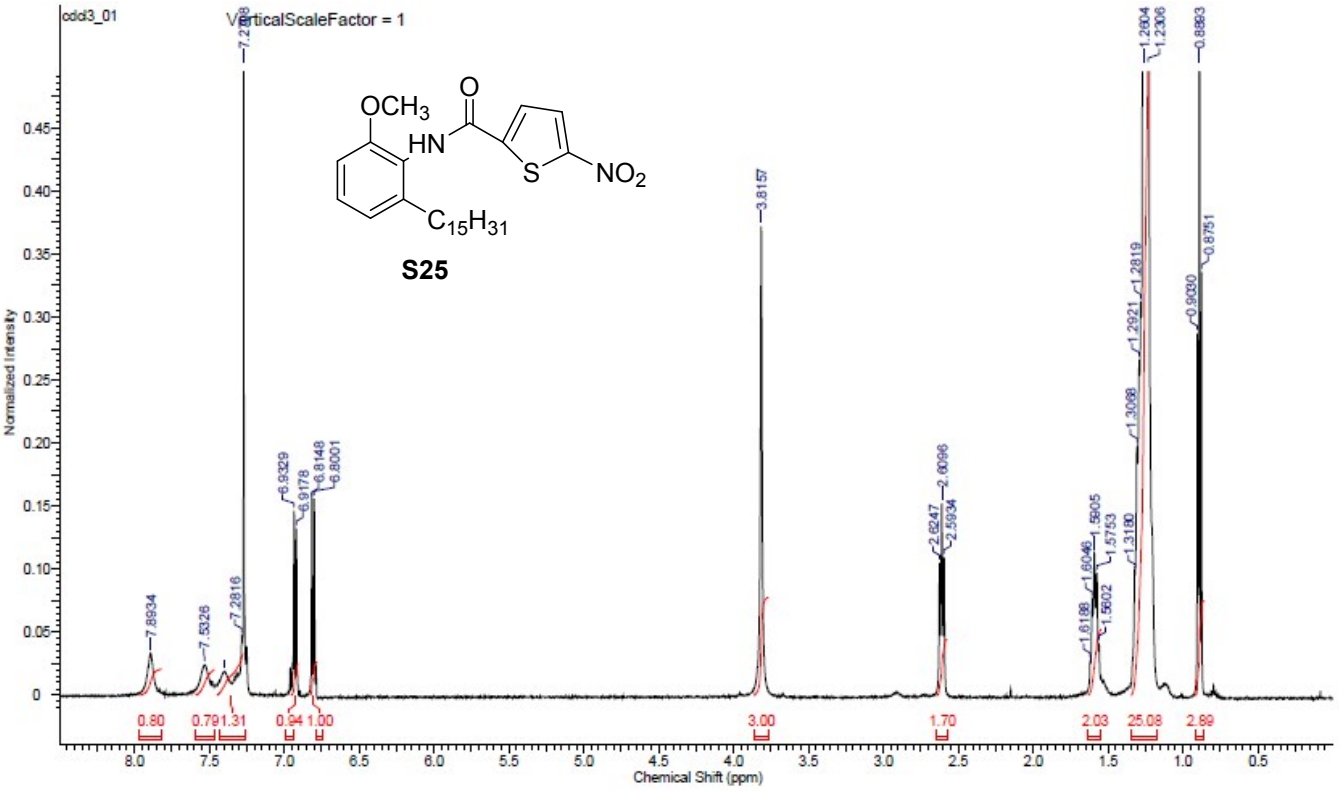


Table 1 entry 9



S25

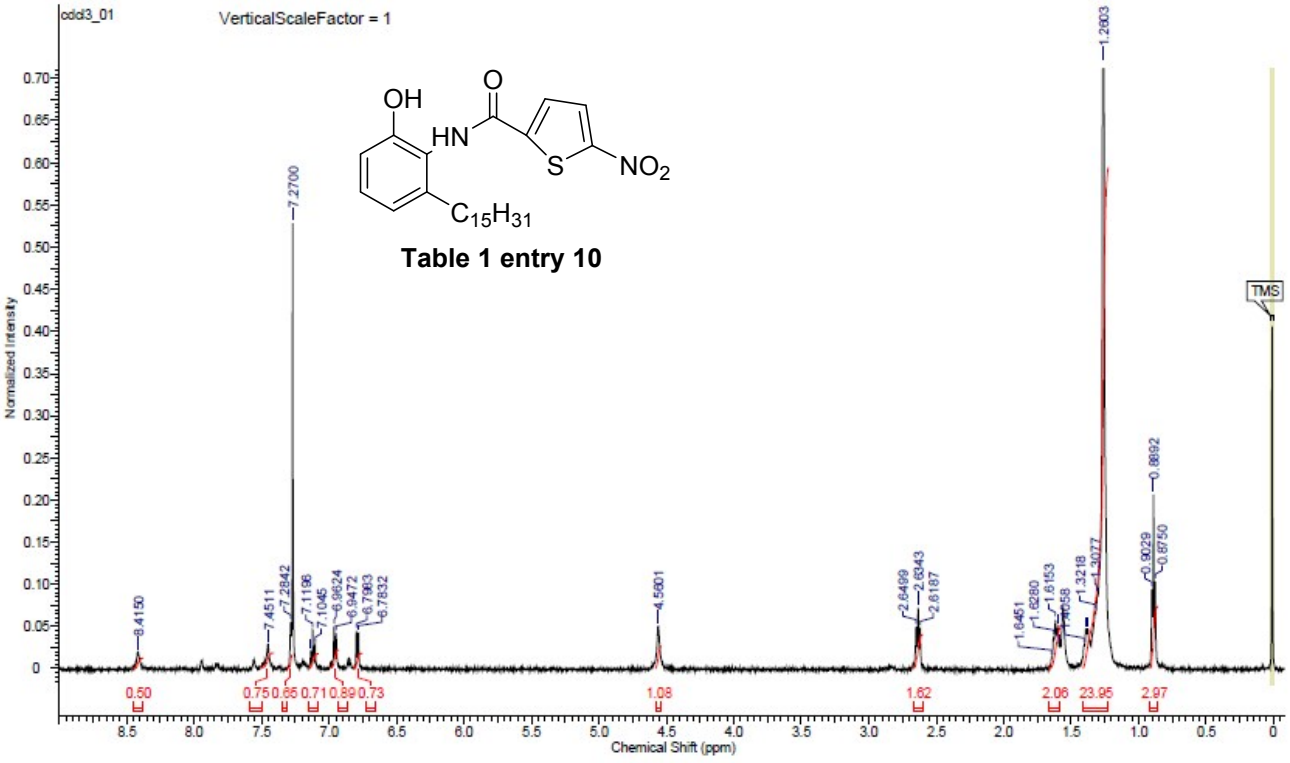
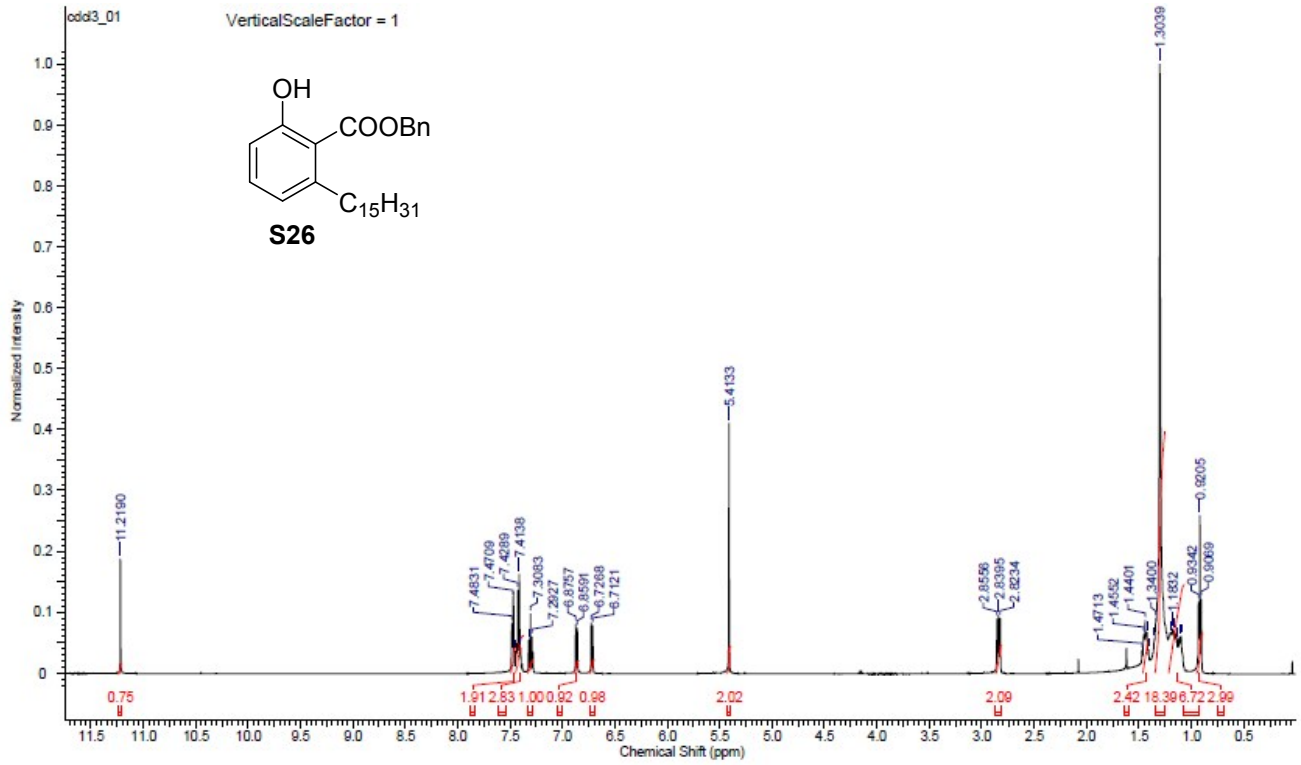


Table 1 entry 10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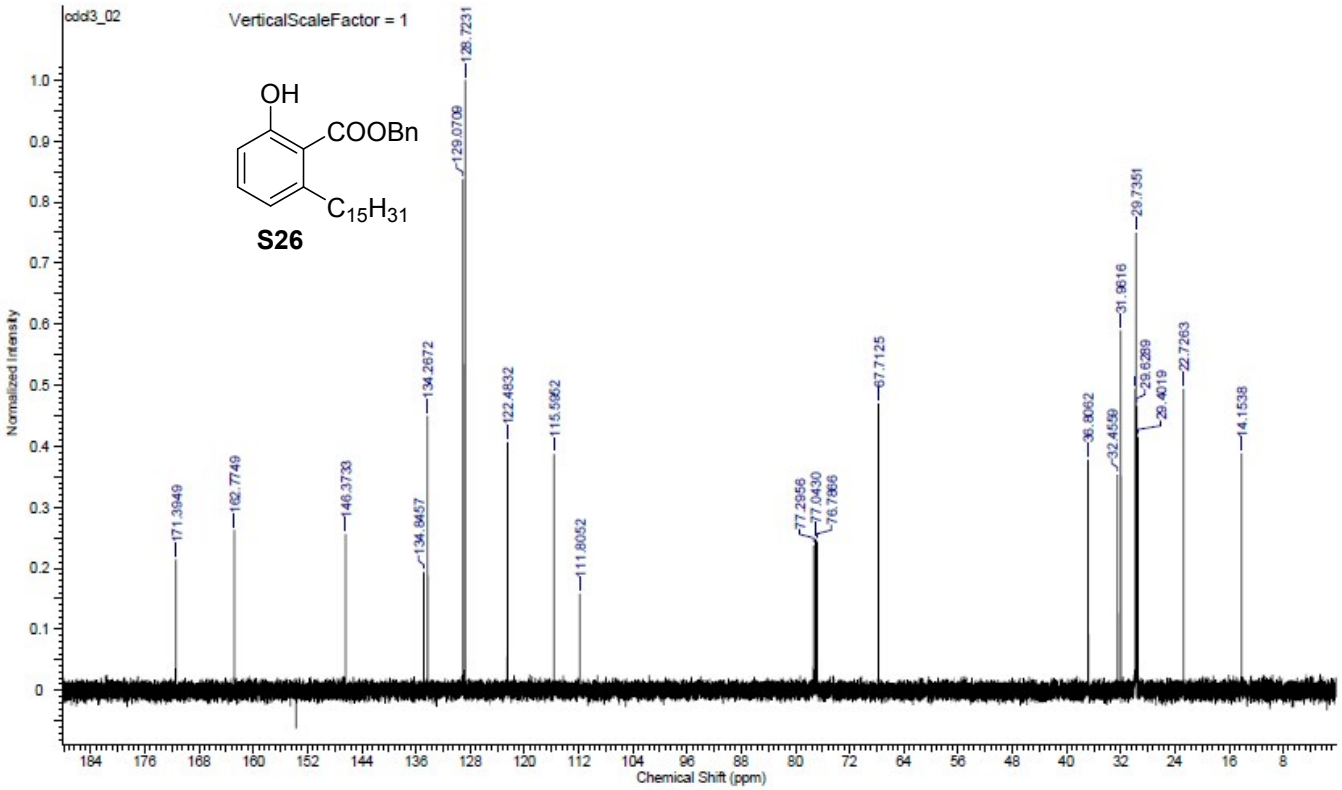
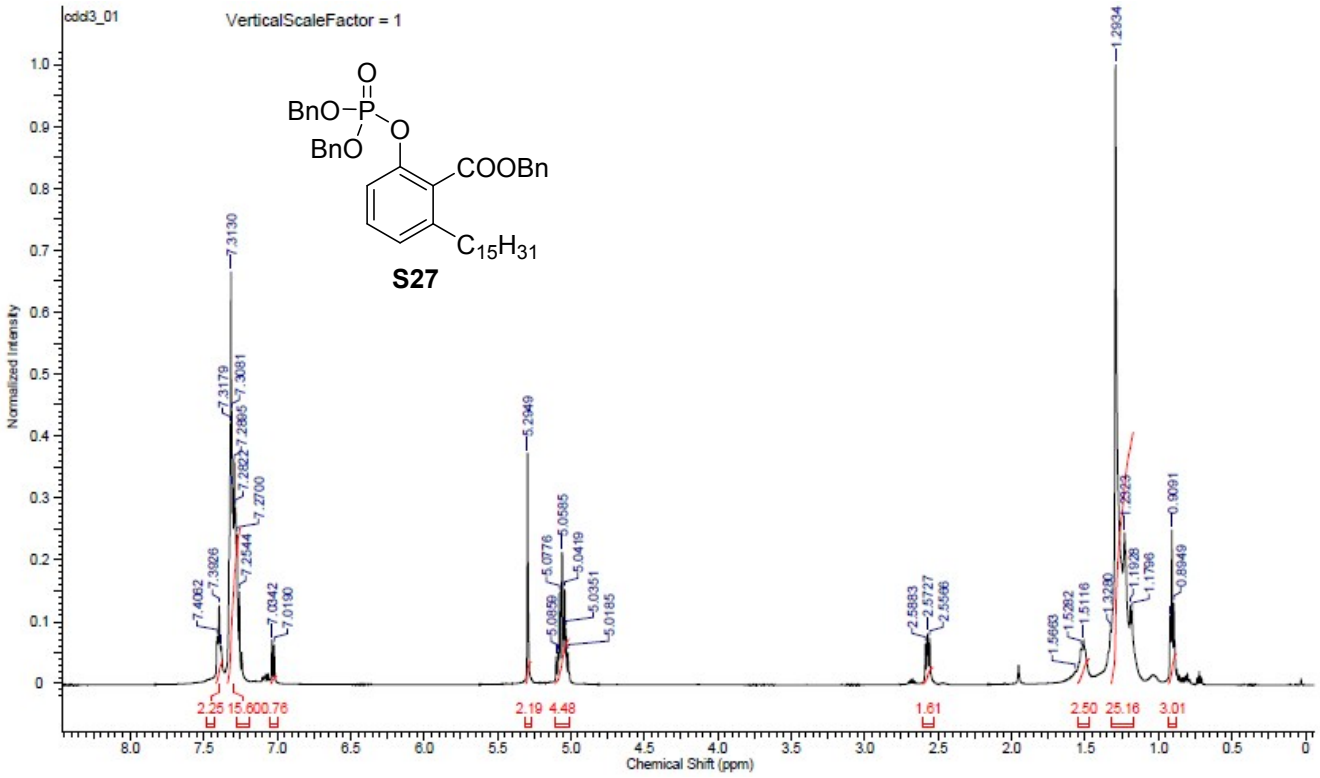
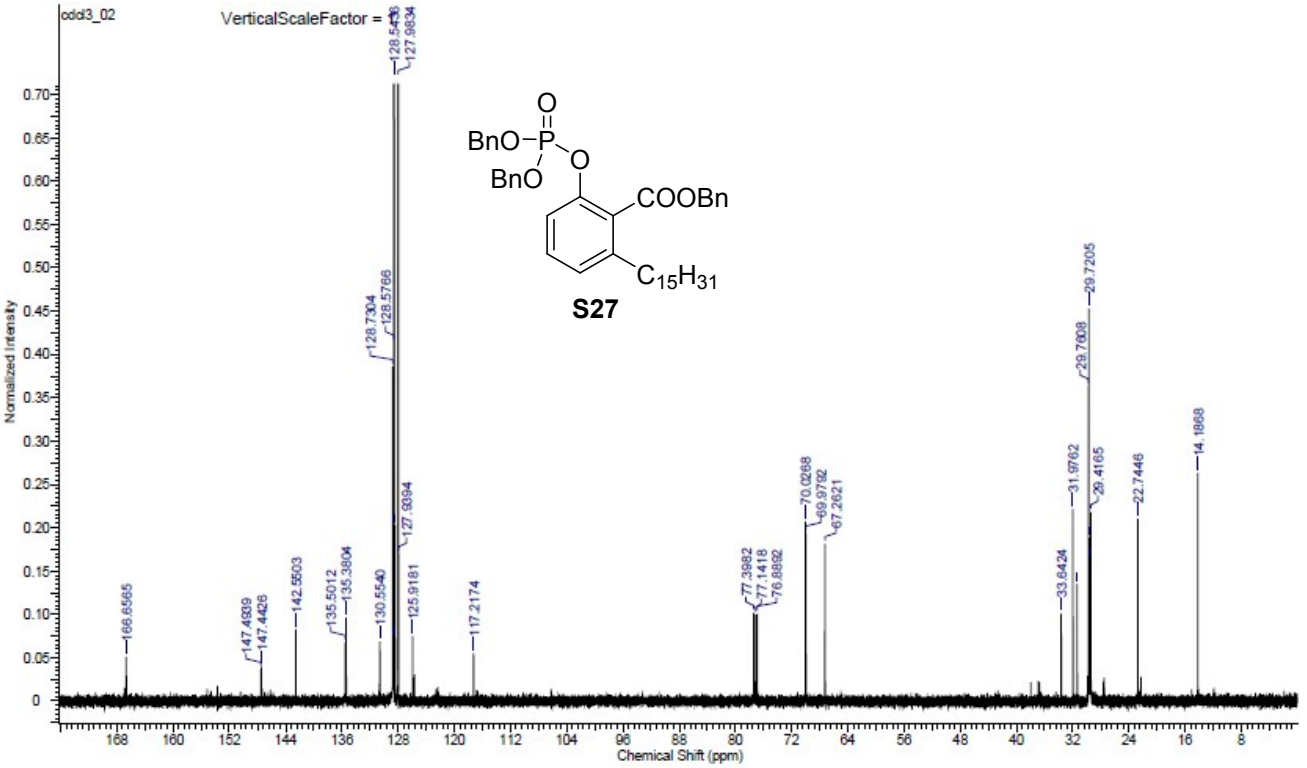
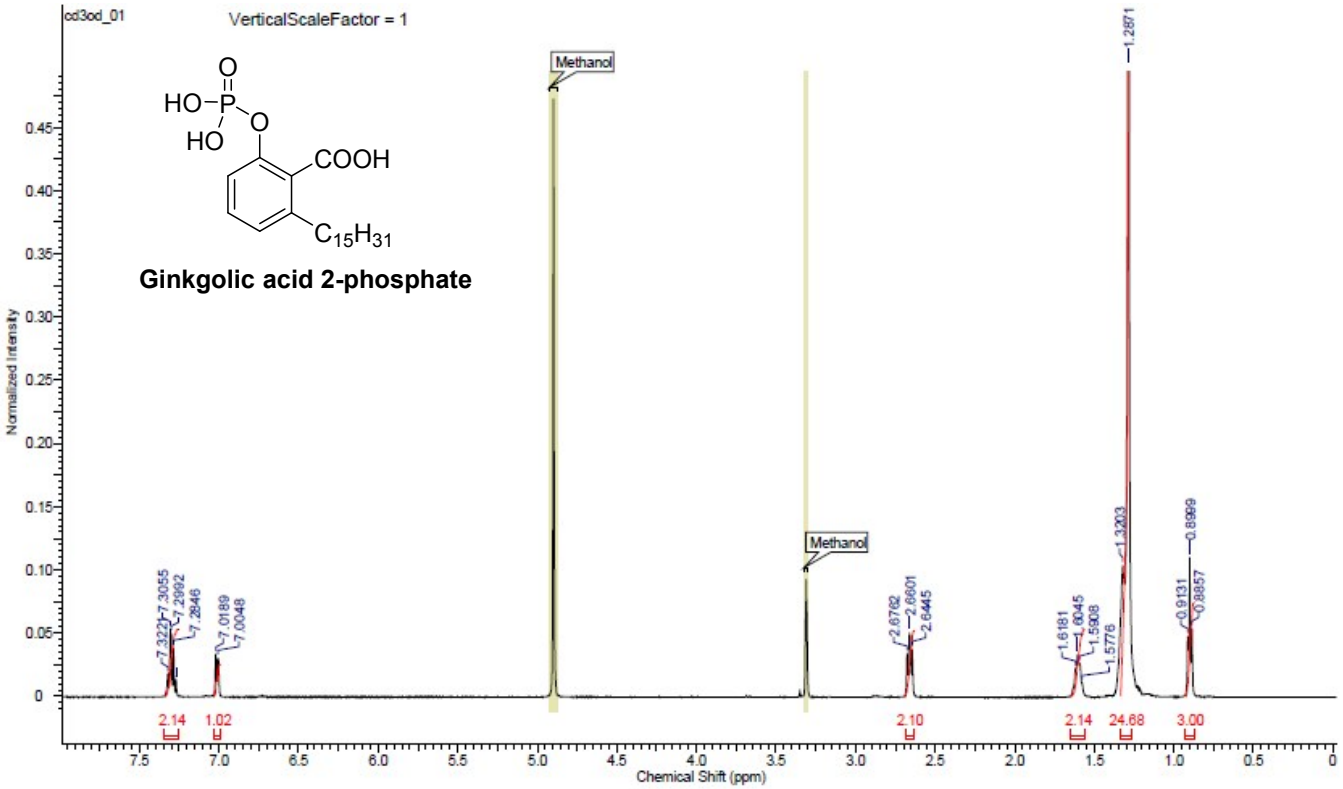
OH
COOBn
$C_{15}H_{31}$
S26
Normalized Intensity
Chemical Shift (ppm)


cdcl3_02
VerticalScaleFactor = 1
OH
COOBn
$C_{15}H_{31}$
S26
Normalized Intensity
Chemical Shift (ppm)


cdcl3_01
VerticalScaleFactor = 1
BnO
BnO
O
P
O
COOBn
C15H31
S27
Normalized Intensity
Chemical Shift (ppm)


cdcl3_02
VerticalScaleFactor =
BnO
BnO
O
P
O
COOBn
C15H31
S27
Normalized Intensity
Chemical Shift (ppm)



Ginkgolic acid 2-phosphate