Supporting Information

Biosynthesis of the Unusual Epoxy Isonitrile-Containing Antibiotics Aerocyanidin and Amycomicin

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Experimental Procedures

S1. General notes

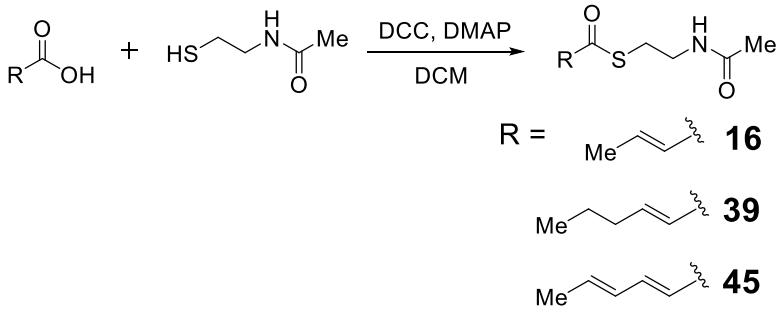
Materials: Oligonucleotide primers were prepared by Integrated DNA Technologies (Coralville, IA). Kits for DNA gel extraction and spin minipreps are products of Qiagen (Valencia, CA). Enzymes and molecular weight standards used in the cloning experiments were obtained from New England Biolabs (Ipswich, MA). Q5® High-Fidelity DNA polymerase and restriction enzymes were acquired from New England Biolabs (Ipswich, MA). Reagents for sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) were purchased from Bio-Rad (Hercules, CA). Amicon YM-10 ultrafiltration membranes are products of Millipore (Billerica, MA). Silica gel column chromatography was carried out using SiliaFlash P60 (230–400 mesh, Silicycle). All chemicals and reagents were purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO) or Fisher Scientific (Pittsburgh, PA) and were used without further purification unless otherwise specified.

Bacterial Strains and Plasmids: *Chromobacterium violaceum* ATCC 53434 was obtained from the American Type Culture Collection (ATCC). *Amycolatopsis* sp. AA4 was provided by Prof. Jon Clardy at Harvard Medical School. *E. coli* DH5α from Bethesda Research Laboratories (Gaithersburg, MD) was used for routine cloning procedures. The protein overexpression host *E. coli* BL21 star (DE3) was obtained from Invitrogen (Waltham, MA). The heterologous expression host *E. coli* K207 was generously provided by Prof. Adrian Keatinge-Clay at the University of Texas at Austin. Vector pET28b(+) for protein overexpression was purchased from Novagen (Madison, WI). Vectors pETDuet-1, pCDFDuet-1 and pACYCDuet-1 for heterologous expression experiments were purchased from Millipore (Burlington, MA). Vectors pNPTS138 Cm and pBBR1MCS-2[1] for gene deletion and complementation were purchased from Addgene (Watertown, MA). The plasmids *camA*/pET28b(+) and *camB*/pET28b(+) for expressing CamA and CamB proteins used in P450 enzymes assays were kindly provided by Prof. Ikuro Abe at the University of Tokyo.

Instrumentation: DNA and protein concentrations were measured using a NanoDrop ND-1000 UV−vis instrument from Thermo Fisher Scientific. LC-ESI-TOFMS analysis was performed using an Agilent Technologies HPLC system equipped with a pump (G1311C), an auto sampler (G1329B), and a ToF mass spectrometer (G6230B) with an electrospray ionization (ESI) source. LCMS separations were performed using Poroshell 120 EC-C18 column (2.7 μm, 4.6 × 100 mm) with Eclipse plus C18 guard column (1.8 μm, 2.1 × 5 mm) at a flow rate of 0.4 mL/min using 0.1% formic acid in H_2O (solvent A) and acetonitrile (solvent B) with the following gradient program unless otherwise specified: 0–8 min 5–95% B, 8–16 min 95% B, 16–18 min 95–5% B, 18–20 min 5% B. The obtained LCMS data were analyzed using MassHunter software (Agilent Technologies). NMR spectra were recorded using a Bruker Avance III HD 500 MHz NMR equipped with CryoProbeTM Prodigy, or a Varian DirectDrive 400 MHz NMR spectrometer at the Nuclear Magnetic Resonance Facility at the University of Texas at Austin. Deuterated solvents were used as internal standards in the NMR spectra unless stated otherwise. Used abbreviations in NMR assignments: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet/quintet, m = multiplet, brs = broad singlet.

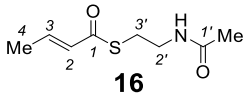
S2. Chemical synthesis

S2.1 Synthesis of SNAc analogs



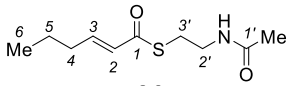
Scheme S1. Chemical synthesis of **16**, **39** and **45**.

To a stirred solution of the carboxylic acid (2 mmol) in dry dichloromethane (DCM) (8 mL) was added *N*-acetylcysteamine (238 mg, 10 mmol). The mixture was cooled to 0 °C. *N*,*N*′-Dicyclohexylcarbodiimide (DCC) (453 mg, 2.2 mmol) and 4-dimethylaminopyridine (DMAP) (48.8 mg, 0.4 mmol) were added. The reaction mixture was then stirred at room temperature overnight. The mixture was cooled to -20 °C for 1 h before filtered through Celite to obtain the filtrate. The filtrate was concentrated under reduced pressure. The resulting crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 8/2) to yield the corresponding SNAc analog.



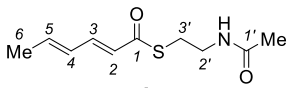
16

***S*-(2-Acetamidoethyl) (*E*)-but-2-enethioate (16)**. Yield: 49% as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 – 6.87 (m, 1H, H-3), 6.20 – 6.10 (m, 1H, H-2), 5.97 (brs, 1H, N*H*Ac), 3.45 (td, *J* = 5.9, 5.9 Hz, 2H, H-2′), 3.08 (dd, *J* = 6.8, 5.9 Hz, 2H, H-3′), 1.95 (s, 3H, NH*Ac*), 1.89 (d, *J* = 6.9 Hz, 3H, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.40, 170.42, 142.00, 129.99, 39.96, 28.32, 23.37, 18.17; ESI-HRMS calcd for $C_8H_{14}NO_2S^+$ $[M+H]^+$ 188.0740, found 188.0767.



39

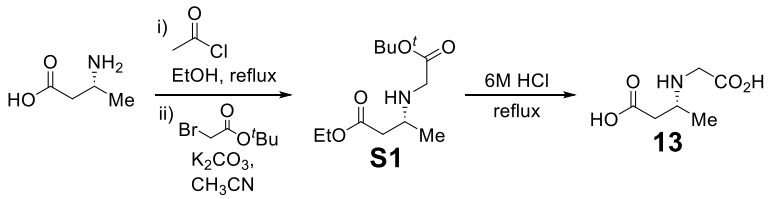
***S*-(2-Acetamidoethyl) (*E*)-hex-2-enethioate (39)**. Yield: 30% as a pale green oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (dt, *J* = 15.6, 6.9 Hz, 1H, H-3), 6.13 (dt, *J* = 15.6, 1.6 Hz, 1H, H-2), 5.88 (brs, 1H, N*H*Ac), 3.46 (td, *J* = 6.0, 6.0 Hz, 2H, H-2′), 3.09 (t, *J* = 6.4 Hz, 2H, H-3′), 2.24 – 2.14 (m, 2H, H-4), 1.96 (s, 3H, NH*Ac*), 1.51 (tq, *J* = 7.4, 7.4 Hz, 2H, H-5), 0.95 (t, *J* = 7.4 Hz, 3H, H-6). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.60, 170.40, 146.71, 128.60, 40.01, 34.37, 28.41, 23.39, 21.35, 13.81. ESI-HRMS calcd for $C_{10}H_{18}NO_2S^+$ $[M + H]^+$ 216.1053, found 216.1085.



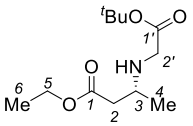
45

***S*-(2-Acetamidoethyl) (2*E*,4*E*)-hexa-2,4-dienethioate (45)**. Yield: 7.5% as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 15.2, 10.4 Hz, 1H, H-3), 6.33 – 6.12 (m, 2H, H-4 and H-5), 6.09 (d, *J* = 15.2 Hz, 1H, H-2), 5.88 (s, 1H, N*H*Ac), 3.47 (td, *J* = 6.0, 6.0 Hz, 2H, H-2′), 3.11 (t, *J* = 6.3 Hz, 2H, H-3′), 1.96 (s, 3H, NH*Ac*), 1.88 (d, *J* = 6.5 Hz, 3H, H-6). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.61, 170.42, 142.06, 141.98, 129.71, 125.81, 40.09, 28.49, 23.39, 19.05. ESI-HRMS calcd for $C_{10}H_{16}NO_2S^+$ $[M + H]^+$ 214.0896, found 214.0901.

S2.2 Synthesis of 13 and its enantiomer (13-*enantio*)

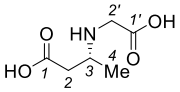


Scheme S2. Chemical synthesis of **13**.



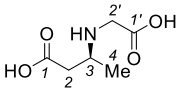
S1

Ethyl (*R*)-3-((2-(*tert*-butoxy)-2-oxoethyl)amino)butanoate (S1).[2] To EtOH (20 mL) was added acetyl chloride (2 mL) dropwise at 0 °C. The mixture was stirred at room temperature for 1 h followed by the addition of (*R*)-3-aminobutanoic acid (616 mg, 6 mmol). The reaction mixture was refluxed at 100 °C for 5 h. After cooled to room temperature, the mixture was concentrated under reduced pressure. The residue was redissolved in acetonitrile (15 mL), followed by the addition of K_2CO_3 (2.03 g, 15 mmol) at 0 °C. The mixture was stirred at 0 °C for 20 min. *Tert*-butyl bromoacetate (1.05 mL, 7.2 mmol) was added. The reaction mixture was then stirred at room temperature overnight. The reaction was quenched by adding H_2O (20 mL). The solution was extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 4/6 then 5/5) to yield **S1** (1.1 g, 75%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (q, *J* = 7.1 Hz, 2H, H-5), 3.34 (d, *J* = 17.1 Hz, 1H, H_a-2′), 3.29 (d, *J* = 17.1 Hz, 1H, H_b-2′), 3.10 (tq, *J* = 6.4 Hz, 6.4 Hz, 1H, H-3), 2.45 (dd, *J* = 15.1, 6.5 Hz, 1H, H_a-2), 2.31 (dd, *J* = 15.2, 6.5 Hz, 1H, H_b-2), 1.81 (brs, 1H, N*H*), 1.46 (s, 9H, ^{t}Bu), 1.26 (t, *J* = 7.1 Hz, 3H, H-6), 1.11 (d, *J* = 6.4 Hz, 3H, H-4).



13

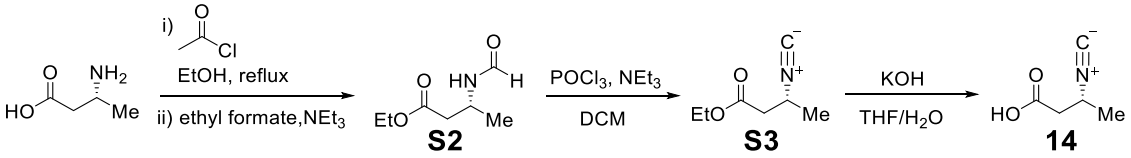
(*R*)-3-((Carboxymethyl)amino)butanoic acid (13). To **S1** (245 mg, 1 mmol) was added 6 M HCl (10 mL). The reaction mixture was refluxed at 120 °C for 4 h. The solvent was removed under reduced pressure to yield **13** (80 mg, 40%) as a yellow solid in its hydrochloride salt form. ^{1}H NMR (400 MHz, CD_3OD) δ 4.01 (d, *J* = 16.9 Hz, 1H, H_a-2′), 3.96 (d, *J* = 16.9 Hz, 1H, H_b-2′), 3.70 (tq, *J* = 6.6 Hz, 6.6 Hz, 1H, H-3), 2.82 (dd, *J* = 17.2, 5.6 Hz, 1H, H_a-2), 2.72 (dd, *J* = 17.2, 6.8 Hz, 1H H_b-2), 1.40 (d, *J* = 6.6 Hz, 3H, H-4). ^{13}C NMR (101 MHz, CD_3OD) δ 173.35, 168.98, 52.58, 46.05, 37.50, 16.69. ESI-HRMS calcd for $C_6H_{10}NO_4^-$ $[M-H]^-$ 160.0615, found 160.0616.



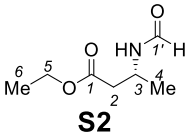
13-*enantio*

(*S*)-3-((Carboxymethyl)amino)butanoic acid (13-*enantio*). Compound **13**-*enantio* was synthesized from (*S*)-3-aminobutanoic acid based on the same method as described for **13**. ^{1}H NMR (500 MHz, CD_3OD) δ 4.01 (d, *J* = 17.0 Hz, 1H, H_a-2′), 3.96 (d, *J* = 16.9 Hz, 1H, H_b-2′), 3.70 (tq, *J* = 6.6 Hz, 6.6 Hz, 1H, H-3), 2.81 (dd, *J* = 17.1, 5.6 Hz, 1H, H_a-2), 2.72 (dd, *J* = 17.2, 6.8 Hz, 1H, H_b-2), 1.40 (d, *J* = 6.6 Hz, 3H, H-4). ^{13}C NMR (126 MHz, CD_3OD) δ 173.35, 168.98, 52.59, 46.05, 37.49, 16.69. ESI-HRMS calcd for $C_6H_{10}NO_4^-$ $[M-H]^-$ 160.0615, found 160.0621.

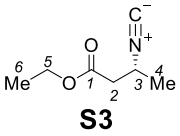
S2.3 Synthesis of 14



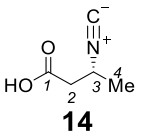
Scheme S3. Chemical synthesis of **14**.



Ethyl (*R*)-3-formamidobutanoate (S2). To EtOH (20 mL) was added acetyl chloride (2 mL) dropwise at 0 °C. The mixture was stirred at room temperature for 1 h. (*R*)-3-Aminobutanoic acid (616 mg, 6 mmol) was then added. The reaction mixture was refluxed at 100 °C for 5 h. After cooled to room temperature, the mixture was concentrated under reduced pressure. The residue was redissolved in ethyl formate (30 mL), followed by the addition of NEt_3 (3 mL, 21.5 mmol). The mixture was refluxed at 80 °C for 5 h. The reaction was quenched by adding saturated aqueous $NaHCO_3$ (20 mL). The solution was extracted with ethyl acetate (3 × 50 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 5/5) to yield **S2** (670 mg, 70%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H, H-1′), 6.23 (brs, 1H, N*H*), 4.51 – 4.39 (m, 1H, H-3), 4.16 (q, *J* = 7.1 Hz, 1H, H-5), 2.61 – 2.52 (m, 1H, H_a-2), 2.56 – 2.45 (m, 1H, H_b-2), 1.34 – 1.22 (m, 6H, H-4, H-6).



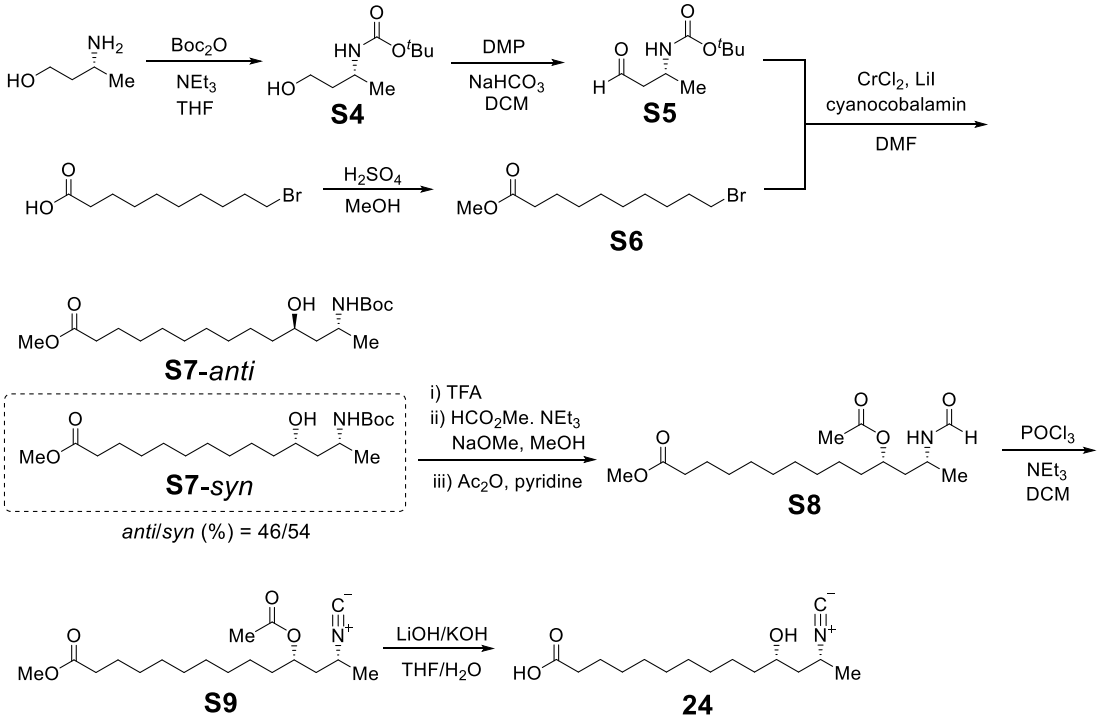
Ethyl (*R*)-3-isocyanobutanoate (S3). To a stirred solution of **S2** (500 mg, 3.1 mmol) in DCM (8 mL) was added NEt_3 (1 mL, 7.17 mmol) at −40 °C. $POCl_3$ (0.35 mL, 3.75 mmol) was then added dropwise. The reaction mixture was stirred at −40 °C for 1 h. The reaction was quenched by adding saturated aqueous $NaHCO_3$ (10 mL), extracted with DCM (3 × 20 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 2/8) to yield **S3** (250 mg, 57%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (q, *J* = 7.1 Hz, 2H, H-5), 4.15 – 4.06 (m, 1H, H-3), 2.75 (dd, *J* = 16.1, 7.5 Hz, 1H, H_a-2), 2.55 (ddt, *J* = 16.1, 6.4, 2.4 Hz, 1H, H_b-2), 1.45 (dt, *J* = 6.7, 2.1 Hz, 3H, H-4), 1.29 (t, *J* = 7.1 Hz, 3H, H-6). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.35, 156.06 (t, *J* = 4.9 Hz), 61.35, 46.61 (t, *J* = 6.3 Hz), 41.76, 21.55, 14.28.



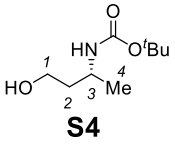
(*R*)-3-isocyanobutanoic acid (14). To a stirred solution of **S3** (70 mg, 0.5 mmol) in THF (3 mL) was added 0.83 M KOH aqueous solution (0.6 mL). The reaction was stirred at room temperature for 6 h. THF was removed under reduced pressure and the residue was diluted with H_2O (10 mL). The aqueous solution was washed with DCM (2 × 10 mL) and then lyophilized to yield **14** as a yellow solid in its potassium salt form. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.92 (tq, *J* = 6.8 Hz, 6.8 Hz, 1H, H-3), 2.22 (dd, *J* = 14.8, 6.2 Hz, 1H, H_a-2), 2.03 (dd, *J* = 14.8, 7.7 Hz, 1H, H_b-2), 1.25 (d, *J* = 6.7 Hz, 3H, H-4). ^{13}C NMR

(126 MHz, DMSO-d_6) δ 170.65, 153.37 (t, J = 4.2 Hz), 48.43 (t, J = 4.6 Hz), 46.40, 21.60. ESI-HRMS calcd for $C_5H_8NO_2^+$ $[M+H]^+$ 114.0550, found 114.0553.

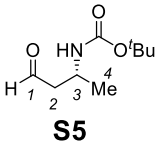
S2.4 Synthesis of 24 and its C11 epimer (11-*epi*-24)



Scheme S4. Chemical synthesis of **24**.

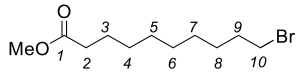


***tert*-Butyl (*R*)-(1-hydroxybutan-3-yl)carbamate (S4)**. To a stirred solution of (*R*)-3-amino-1-butanol (356 mg, 4 mmol) in THF (6 mL) was added NEt_3 (0.669 mL, 4.8 mmol) and Boc anhydride (873 mg, 4 mmol) in THF (2 mL). The reaction was stirred at room temperature overnight. The reaction was quenched with 10 mL H_2O. The aqueous phase was extracted with ethyl acetate (4 × 20 mL). The combined organic phase was washed with brine before dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 5/5) to yield **S4** (630 mg, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.95 – 3.85 (m, 1H, H-3), 3.63 (dd, J = 7.6, 3.2 Hz, 2H, H-1), 1.86 – 1.76 (m, 1H, H_a-2), 1.45 (s, 9H, *t*-Bu), 1.36 – 1.27 (m, 1H, H_b-2), 1.19 (d, J = 6.7 Hz, 3H, H-4).



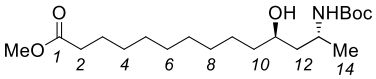
***tert*-Butyl (*R*)-(1-oxobutan-3-yl)carbamate (S5)**. To a stirred solution of **S4** (630 mg, 3.3 mmol) in dry DCM (18 mL) was added $NaHCO_3$ (2.8 g, 33 mmol) and Dess–Martin periodinane (DMP) (1.4 g, 3.3 mmol). The reaction was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (20 mL). The aqueous phase was extracted with DCM (3 × 20 mL). The combined

organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 4/6) to yield **S5** (568 mg, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 2.2, 1.7 Hz, 1H, H-1), 4.65 (s, 1H, N*H*), 4.20 – 4.08 (m, 1H, H-3), 2.68 – 2.61 (m, 1H, H_a-2), 2.60 – 2.54 (m, 1H, H_b-2), 2.04 (s, 9H, *t*-Bu), 1.23 (d, *J* = 6.8 Hz, 3H, H-4).

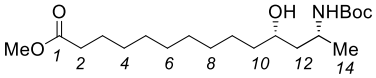


S6

Methyl 10-bromodecanoate (S6). To a stirred solution of 10-bromodecanoic acid (2.51 g, 10 mmol) in MeOH (20 mL) was added sulfuric acid (0.4 mL) dropwise. The mixture was refluxed at 100 °C for 4 h. The solvent was then removed under reduced pressure. The residue was redissolved in 50 mL H_2O and 50 mL ethyl acetate. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 1/9) to yield **S6** (2.53 g, 95%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67 (s, 3H, OMe), 3.40 (t, *J* = 6.9 Hz, 2H, H-10), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.85 (p, *J* = 7.0 Hz, 2H, H-9), 1.62 (p, *J* = 7.2 Hz, 2H, H-3), 1.41 (p, *J* = 7.1 Hz, 2H, H-8), 1.34 – 1.26 (m, 8H, H-4, H-5, H-6, H-7). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.45, 51.60, 34.24, 34.14, 32.95, 29.36, 29.27, 29.23, 28.83, 28.28, 25.07.



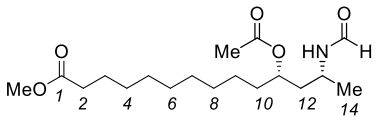
S7-*anti*



S7-*syn*

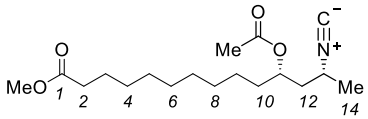
Methyl (11*R*,13*R*)-13-((*tert*-butoxycarbonyl)amino)-11-hydroxytetradecanoate (S7-*anti*) and **methyl (11*S*,13*R*)-13-((*tert*-butoxycarbonyl)amino)-11-hydroxytetradecanoate (S7-*syn*)**.[3] To a 50-mL flame-dried flask were added $CrCl_2$ (615 mg, 5 mmol), cyanocobalamin (101.5 mg, 0.75 mmol), LiI (10 mg, 0.75 mmol) and dry DMF (10 mL) under an Ar atmosphere. Ester **S6** (662.5 mg, 2.5 mmol) and aldehyde **S5** (234 mg, 1.25 mmol) together in dry DMF (5 mL) were then added. The reaction mixture was stirred at room temperature overnight. The reaction was quenched with 5 mL H_2O. The aqueous phase was extracted with ethyl acetate (4 × 5 mL). The combined organic phase was washed with H_2O and then brine before dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (**S7-*anti***, R_f 0.69; **S7-*syn***, R_f 0.45; ethyl acetate/hexanes = 3/7) to yield **S7-*anti*** (162 mg, 35%) as a white solid and **S7-*syn*** (190 mg, 41%) as a colorless oil. The assignment of the absolute configuration of the two products is based on the reported literature.[4] Spectroscopic data of **S7-*anti***: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 – 3.88 (m, 1H, H-13), 3.66 (s, 3H, OMe), 3.60 – 3.54 (m, 1H, H-11), 2.30 (t, *J* = 7.6 Hz, 2H, H-2), 1.61 (p, *J* = 7.4 Hz, 2H, H-3), 1.50 (ddd, *J* = 13.8, 10.8, 2.9 Hz, 1H, H_a-12), 1.48 (m, 1H, H_a-10), 1.45 (s, 9H, *t*-Bu), 1.42 (m, 1H, H_a-9), 1.35 (m, 1H, H_b-10), 1.30 (m, 1H, H_b-12), 1.28 (m, 1H, H_b-9), 1.28 – 1.22 (m, 10H, H-4, H-5, H-6, H-7, H-8), 1.17 (d, *J* = 6.7 Hz, 3H, H-14). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.50, 157.02, 80.00, 67.72, 51.59, 46.57, 43.50, 37.01, 34.27, 29.75, 29.68, 29.53, 29.38, 29.29, 28.51, 26.09, 25.11, 21.84. ESI-HRMS calcd for $C_{20}H_{40}NO_5^+$ $[M + H]^+$ 374.2901, found 374.2930. Spectroscopic data of **S7-*syn***: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (tq, *J* = 7.1, 7.1 Hz, 1H, H-13), 3.71 – 3.65 (m, 1H, H-11), 3.66 (s, 3H, OMe), 2.30 (t, *J* = 7.6 Hz, 2H, H-2), 1.61 (p, *J* = 7.2 Hz, 2H, H-3), 1.56 – 1.52 (m, 2H, H-12), 1.46 (m, 2H, H-10), 1.44 (s, 9H, *t*-Bu), 1.42 (m, 1H, H_a-9), 1.31 (m, 1H, H_b-9), 1.29 – 1.25 (m, 10H, H-4, H-5, H-6, H-7, H-8), 1.17 (d, *J* = 6.6 Hz, 3H, H-14). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.50, 155.97, 79.72, 70.49,

51.60, 45.51, 45.18, 38.06, 34.26, 29.70, 29.66, 29.50, 29.36, 29.27, 28.57, 25.72, 25.09, 22.07. ESI-HRMS calcd for $C_{20}H_{40}NO_5^+$ $[M + H]^+$ 374.2901, found 374.2908.



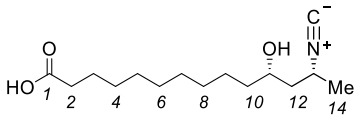
S8

Methyl (11*S*,13*R*)-11-acetoxy-13-formamidotetradecanoate (S8). To a stirred solution of **S7**-*syn* (75 mg, 0.2 mmol) in DCM (2 mL) was added TFA (1 mL) dropwise at 0 °C. The resulting mixture was allowed to warm to room temperature and stir for 1.5 h. DCM and TFA were then removed under reduced pressure to afford the crude. The crude product was redissolved in MeOH (0.45 mL), then Et_3N (0.071 mL), methyl formate (0.2 mL), and sodium methoxide (5.4 M in MeOH, 0.28 mmol, 0.052 mL) were added. The mixture was stirred at room temperature overnight. The reaction mixture was then concentrated under reduced pressure. The residue was redissolved in pyridine (1 mL), then acetic anhydride (0.057 mL, 0.6 mmol) was added. The mixture was stirred at room temperature overnight. The reaction was quenched by MeOH (0.024 mL). After stirring for 10 min, solvents were removed under reduced pressure. The residue was redissolved in H_2O and extracted with DCM (3 × 5 mL). The combined organic phase was washed with 1 M HCl and then saturated aqueous $NaHCO_3$ before dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 9/1) to yield **S8** (29 mg, 42% 3 steps) as a yellow oil. Compound **S8** exists as two rotamers as shown in the ^{1}H NMR spectrum. The spectroscopic data of the major rotamer is shown. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H, C*H*O), 5.67 (d, *J* = 7.8 Hz, 1H, N*H*), 4.85 – 4.76 (m, 1H, H-11), 4.13 – 4.06 (m, 1H, H-13), 1.18 (d, *J* = 6.6 Hz, 3H), 3.66 (s, 3H, OMe), 2.30 (t, *J* = 7.6 Hz, 2H, H-2), 2.05 (s, 3H, OAc), 1.81 – 1.73 (m, 1H, H_a-12), 1.63 (m, 1H, H_b-12), 1.61 (m, 2H, H-3), 1.57 (m, 2H, H-10), 1.31 – 1.23 (m, 12H, H-4, H-5, H-6, H-7, H-8, H-9), 1.18 (d, *J* = 6.6 Hz, 3H, H-14). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.49, 171.46, 160.73, 72.12, 51.60, 41.87, 41.28, 34.30, 34.26, 29.54, 29.49, 29.45, 29.34, 29.25, 25.42, 25.09, 21.49, 21.36. ESI-HRMS calcd for $C_{18}H_{34}NO_5^+$ $[M + H]^+$ 344.2431, found 344.2438.



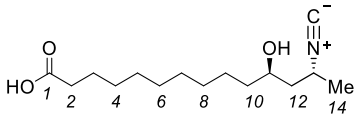
S9

Methyl (11*S*,13*R*)-11-acetoxy-13-isocyanotetradecanoate (S9). To a stirred solution of **S8** (29 mg, 0.085 mmol) in DCM (1 mL) were added Et_3N (0.071 mL, 0.9 mmol) and $POCl_3$ (0.028 mL, 0.3 mmol) dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 10 min, then allowed to warm to room temperature and stir for 1 h. The reaction was quenched by 2 mL saturated aqueous $NaHCO_3$, extracted with DCM (3 × 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S9** (24 mg, 87%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 – 4.94 (m, 1H, H-11), 3.67 (s, 3H, OMe), 3.66 (m, 1H, H-13), 2.30 (t, *J* = 7.6 Hz, 2H, H-2), 2.07 (s, 3H, OAc), 2.05 (m, 1H, H_a-12), 1.77 – 1.70 (m, 1H, H_b-12), 1.61 (m, 2H, H-3), 1.56 (m, 2H, H-10), 1.39 (dt, *J* = 6.6, 2.2 Hz, 1H, H-14), 1.32 – 1.24 (m, 12H, H-4, H-5, H-6, H-7, H-8 and H-9). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.46, 170.92, 155.34 (t, *J* = 5.4 Hz), 71.18, 51.60, 47.43, 47.38 (t, *J* = 5.6 Hz), 47.34, 41.38, 34.50, 34.25, 29.52, 29.47, 29.44, 29.34, 29.25, 25.19, 25.08, 21.85, 21.31. ESI-HRMS calcd for $C_{18}H_{32}NO_4^+$ $[M + H]^+$ 326.2326, found 326.2349.



24

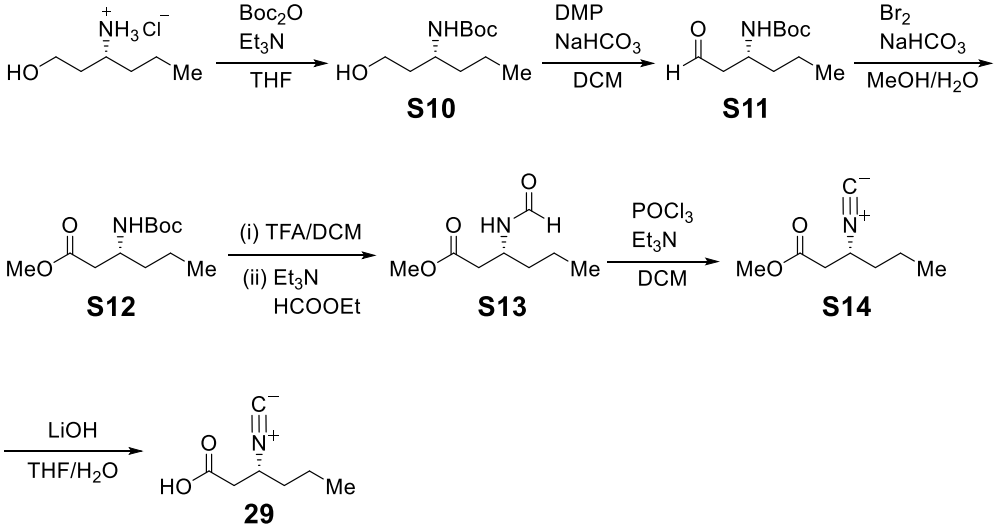
(11*S*,13*R*)-11-Hydroxy-13-isocyanotetradecanoic acid (24). To a stirred solution of **S9** (9 mg, 0.028 mmol) in THF/H_2O (1/1, 1 mL) were added 1 M LiOH aqueous solution (0.03 mL, 0.03 mmol) and 0.24 M KOH aqueous solution (0.138 mL, 0.033 mmol). The resulting mixture was stirred at room temperature overnight. The next day, LC-MS analysis showed that large amounts of acetylated substrate remained. Additional 0.24 M KOH aqueous solution (0.276 mL, 0.066 mmol) was then added and the reaction was stirred at room temperature overnight. The following day, LC-MS analysis suggested that the reaction was complete. The reaction mixture was then diluted with 10 mL H_2O and lyophilized to yield **24** as a yellow solid. ^{1}H NMR (400 MHz, CD_3OD) δ 3.93 – 3.84 (m, 1H, H-13), 3.62 (tt, *J* = 8.6, 4.3 Hz, 1H, H-11), 2.17 (t, *J* = 7.6 Hz, 2H, H-2), 1.84 (dt, *J* = 14.5, 7.5 Hz, 1H, H_a-12), 1.73 – 1.64 (m, 1H, H_b-12), 1.59 (p, *J* = 5.7 Hz, 2H, H-3), 1.45 – 1.48 (m, 2H, H-10), 1.39 (dt, *J* = 6.6, 2.2 Hz, 3H, H-14), 1.35 – 1.30 (m, 12H, H-4, H-5, H-6, H-7, H-8, H-9). ^{13}C NMR (126 MHz, CD_3OD) δ 182.09, 154.15 (t, *J* = 5.6 Hz), 68.94, 48.60 (buried in the solvent peak), 45.41, 38.47, 38.33, 30.74, 30.72, 30.71, 30.67, 30.60, 27.48, 26.63, 21.55. ESI-HRMS calcd for $C_{15}H_{28}NO_3^+$ $[M + H]^+$ 270.2064, found 270.2077.



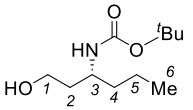
11-*epi*-**24**

(11*R*,13*R*)-11-Hydroxy-13-isocyanotetradecanoic acid (11-*epi*-24). Compound 11-epi-**24** was synthesized from **S7**-*anti* based on the same method as described for **24**. ^{1}H NMR (500 MHz, CD_3OD) δ 3.97 (tq, *J* = 8.9, 5.7 Hz, 1H, H-13), 3.74 (dddd, *J* = 9.6, 6.9, 5.8, 3.2 Hz, 1H, H-11), 2.14 (t, *J* = 7.6 Hz, 2H, H-2), 1.68 (ddd, *J* = 13.5, 10.7, 2.2 Hz, 1H, H_a-12), 1.59 (p, *J* = 7.3 Hz, 2H, H-3), 1.54 – 1.48 (m, 1H, H_b-12), 1.47 – 1.43 (m, 2H, H-10), 1.38 (dt, *J* = 6.5, 1.9 Hz, 3H, H-14), 1.36 – 1.30 (m, 12H, H-4, H-5, H-6, H-7, H-8, H-9). ^{13}C NMR (126 MHz, CD_3OD) δ 183.20, 153.99 (t, *J* = 5.9 Hz), 68.83, 48.71 (buried in the solvent peak), 45.38, 39.31, 38.75, 30.82, 30.71, 30.68, 30.66, 30.61, 27.79, 26.65, 22.49. ESI-HRMS calcd for $C_{15}H_{26}NO_3^-$ $[M-H]^-$ 268.1918, found 268.1925.

S2.5 Synthesis of 29

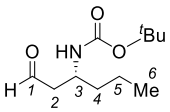


Scheme S5. Chemical synthesis of **29**.



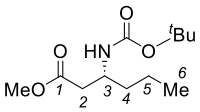
S10

***tert*-Butyl (*R*)-(1-hydroxyhexan-3-yl)carbamate (S10)**. To a stirred solution of (*R*)-3-aminohexan-1-ol hydrochloride (from Angene) (307.3 mg, 2 mmol) in THF (3 mL) was added NEt_3 (0.669 mL, 4.8 mmol) and Boc anhydride (480 mg, 2.2 mmol) in THF (1 mL). The reaction was stirred at room temperature for two days. The reaction was quenched with 10 mL H_2O. The aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic phase was washed with brine before dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 5/5) to yield **S10** (433 mg, 100%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.33 (brs, 1H, N*H*), 3.81 – 3.71 (m, 1H, H-3), 3.66 – 3.59 (m, 2H, H-1), 1.88 – 1.78 (m, 1H, H_a-2), 1.45 (s, 9H, *t*-Bu), 1.43 – 1.32 (m, 4H, H-4 and H-5), 1.30 – 1.21 (m, 1H, H_b-2), 0.92 (t, *J* = 6.3 Hz, 3H, H-6). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.36, 79.99, 58.93, 47.07, 39.26, 38.01, 28.48, 19.50, 14.02. ESI-HRMS calcd for $C_{11}H_{24}NO_3^+$ $[M + H]^+$ 218.1751, found 218.1769.



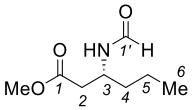
S11

***tert*-Butyl (*R*)-(1-oxohexan-3-yl)carbamate (S11)**. To a stirred solution of **S10** (433 mg, 2 mmol) in dry DCM (10 mL) was added $NaHCO_3$ (1.68 g, 20 mmol) and DMP (933 mg, 2.2 mmol). The reaction was stirred at room temperature for 1.5 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL). The aqueous phase was extracted with DCM (3 × 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S5** (316 mg, 73%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 2.0, 1.7 Hz, 1H, H-1), 4.61 (s, 1H, N*H*), 4.08 – 3.95 (m, 1H, H-3), 2.67 – 2.59 (m, 1H, H_a-2), 2.55 (ddd, *J* = 16.5, 6.9, 2.5 Hz, 1H, H_b-2), 1.54 – 1.44 (m, 2H, H-4), 1.44 (s, 9H, *t*-Bu), 1.41 – 1.27 (m, 2H, H-5), 0.92 (t, *J* = 7.2 Hz, 3H, H-6). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.48, 155.52, 79.66, 49.36, 46.41, 37.36, 28.48, 19.44, 13.92. ESI-HRMS calcd for $C_{11}H_{22}NO_3^+$ $[M + H]^+$ 216.1594, found 216.1618.



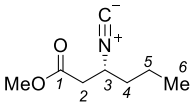
S12

Methyl (*R*)-3-((*tert*-butoxycarbonyl)amino)hexanoate (S12). To a stirred solution of **S11** (138 mg, 0.64 mmol) in MeOH/H_2O = 9/1 (1.4 mL) was added $NaHCO_3$ (2.15 g, 25.6 mmol) and bromine (0.291 mL, 6.4 mmol) in MeOH/H_2O = 9/1 (3 mL) at 0 ℃. The reaction was stirred at room temperature overnight. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ dropwise at 0 ℃. The aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 2/8) to yield **S12** (149 mg, 95%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.90 (d, *J* = 9.3 Hz, 1H, N*H*), 3.98 – 3.86 (m, 1H, H-3), 3.68 (s, 1H, OMe), 2.57 – 2.44 (m, 2H, H-2), 1.53 – 1.45 (m, 2H, H-4), 1.43 (s, 9H, *t*-Bu), 1.42 – 1.28 (m, 2H, H-5), 0.91 (t, *J* = 7.2 Hz, 3H, H-6). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.39, 155.52, 79.34, 51.79, 47.49, 39.32, 36.91, 28.52, 19.53, 13.97. ESI-HRMS calcd for $C_{12}H_{24}NO_4^+$ $[M + H]^+$ 246.1700, found 246.1706.



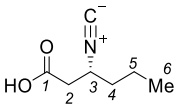
S13

Methyl (*R*)-3-formamidohexanoate (S13). To a stirred solution of **S12** (149 mg, 0.61 mmol) in DCM (6 mL) was added TFA (3 mL) dropwise at 0 °C. The resulting mixture was allowed to warm to room temperature and stir for 2 h. DCM and TFA were then removed under reduced pressure to afford the crude. The crude product was redissolved in ethyl formate (10 mL), then Et_3N (0.373 mL) was added. The mixture was refluxed at 65 °C for 15 h. The solvent was then removed under reduced pressure and the residue was redissolved in DCM and washed with H_2O. The organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 9/1) to yield **S13** (72 mg, 69%) as a pale yellow oil. Compound **S13** exists as two rotamers as shown in the ^{1}H NMR spectrum. The spectroscopic data of the major rotamer is shown. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H, H-1′), 6.18 (s, 1H, N*H*), 4.39 – 4.29 (m, 1H, H-3), 3.69 (s, 3H, OMe), 2.62 – 2.51 (m, 2H, H-2), 1.59 – 1.46 (m, 2H, H-4), 1.41 – 1.29 (m, 2H, H-5), 0.92 (t, *J* = 7.2 Hz, 3H, H-6). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.38, 160.75, 51.93, 44.60, 38.27, 36.20, 19.54, 13.88. ESI-HRMS calcd for $C_8H_{16}NO_3^+$ $[M + H]^+$ 174.1125, found 174.1141.



S14

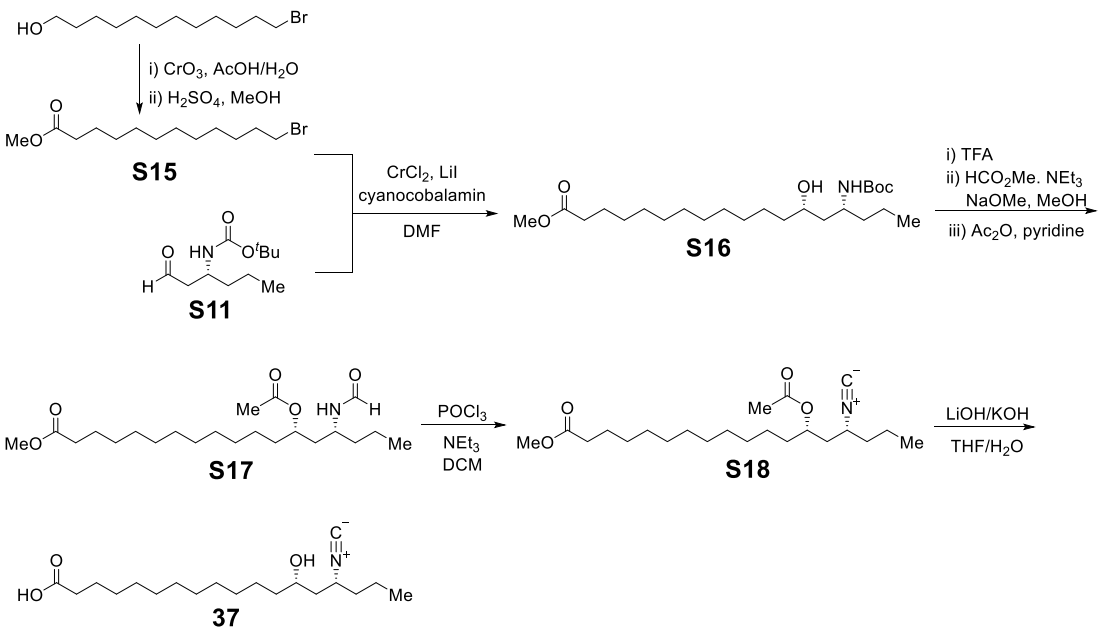
Methyl (*R*)-3-isocyanohexanoate (S14). To a stirred solution of **S13** (72 mg, 0.42 mmol) in DCM (4 mL) were added Et_3N (0.527 mL, 3.78 mmol) and $POCl_3$ (0.118 mL, 1.26 mmol) dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 10 min, then allowed to warm to room temperature and stir for 1 h. The reaction was quenched by saturated aqueous $NaHCO_3$, extracted with DCM (3 × 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S14** (58.4 mg, 90%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 – 3.94 (m, 1H, H-3), 2.73 (ddt, *J* = 16.2, 8.0, 1.5 Hz, 1H, H_a-2), 2.57 (ddt, *J* = 16.2, 5.6, 2.6 Hz, 1H, H_b-2), 1.69 – 1.59 (m, 3H, H-4 and H_a-5), 1.54 – 1.43 (m, 1H, H_b-5), 0.97 (t, *J* = 6.8 Hz, 1H, H-6). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.04, 156.50 (t, *J* = 4.5 Hz), 52.35, 51.10 (t, *J* = 6.1 Hz), 40.18, 36.71, 18.98, 13.43. ESI-HRMS calcd for $C_8H_{14}NO_2^+$ $[M + H]^+$ 156.1019, found 156.1035.



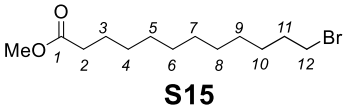
29

(*R*)-3-Isocyanohexanoic acid (29). To a stirred solution of **S14** (3.8 mg, 0.0245 mmol) in THF/H_2O (1/1, 0.5 mL) were added 1 M LiOH aqueous solution (0.0265 mL, 0.0265 mmol). The reaction was stirred at room temperature overnight. The mixture was then diluted with 10 mL H_2O, and lyophilized to yield **29** as a yellow solid. ^{1}H NMR (400 MHz, D_2O) δ 4.02 – 3.93 (m, 1H, H-3), 2.56 – 2.43 (m, 2H, H-2), 1.69 – 1.53 (m, 2H, H-4), 1.52 – 1.34 (m, 1H, H-5), 0.91 (t, *J* = 7.2 Hz, 3H, H-6). ^{13}C NMR (126 MHz, D_2O) δ 178.33, 150.18 (t, *J* = 6.4 Hz), 52.73 (t, *J* = 5.3 Hz), 43.15, 35.86, 18.28, 12.51. ESI-HRMS calcd for $C_7H_{10}NO_2^-$ $[M - H]^-$ 140.0717, found 140.0720.

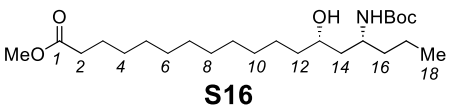
S2.6 Synthesis of 37



Scheme S6. Chemical synthesis of **37**.

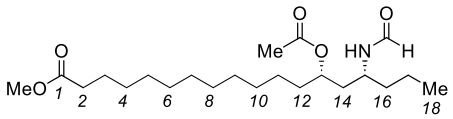


Methyl 12-bromododecanoate (S15).[5] To a stirred solution of CrO_3 (5.85 g, 58.5 mmol) in AcOH (52 mL) and H_2O (6 mL) was added 12-bromododecan-1-ol (4.0 g, 15.1 mmol) in acetone (15 mL) dropwise at 0 °C. The resulting mixture was then slowly allowed to warm to room temperature and stir overnight. The reaction was quenched by H_2O (200 mL), extracted with ethyl acetate (3 × 200 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude carboxylic acid was redissolved in MeOH (50 mL). Sulfuric acid (0.6 mL) was added dropwise. The mixture was refluxed at 100 °C for 4 h. The solvent was then removed under reduced pressure. The residue was redissolved in 50 mL H_2O and 50 mL ethyl acetate. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 1/9) to yield **S15** (3.59 g, 82%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 3H, OMe), 3.41 (t, *J* = 6.9 Hz, 2H, H-12), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.85 (p, *J* = 7.0 Hz, 2H, H-11), 1.67 – 1.57 (m, 2H, H-3), 1.46 – 1.36 (m, 2H, H-10), 1.36 – 1.22 (m, 12H, H-4, H-5, H-6, H-7, H-8 and H-9). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.52, 51.62, 34.25, 32.97, 29.59, 29.54, 29.52, 29.37, 29.27, 28.89, 28.31, 25.09.



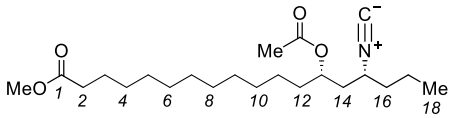
Methyl (13*S*,15*R*)-15-((*tert*-butoxycarbonyl)amino)-13-hydroxyoctadecanoate (S16). Compound **S16** was synthesized from **S11** and **S15** based on the same method as described for **S7**-*syn*. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 – 3.67 (m, 1H, H-15), 3.66 (s, 3H, OMe), 3.66 – 3.62 (m, 1H, H-13), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.65 – 1.56 (m, 3H, H-14 and H_a-16), 1.52 – 1.45 (m, 3H, H-12 and H_b-16), 1.43 (s, 9H, *t*-Bu), 1.42 – 1.32 (m, 4H, H-11 and H-17), 1.32 – 1.19 (m, 16H, H-3, H-4, H-5, H-6, H-7, H-8, H-9, and H-10), 0.91 (t, *J* = 6.9 Hz, 3H, H-18). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.55, 156.28, 79.65, 70.59, 51.61,

49.41, 43.86, 38.56, 37.86, 34.26, 29.75, 29.69, 29.57, 29.39, 29.29, 28.55, 25.78, 25.10, 19.17, 14.10. ESI-HRMS calcd for $C_{24}H_{48}NO_5^+$ $[M + H]^+$ 430.3527, found 430.3539.



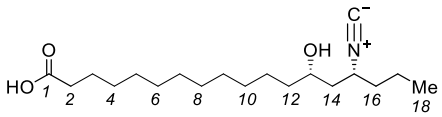
S17

Methyl (13*S*,15*R*)-13-acetoxy-15-formamidooctadecanoate (S17). Compound **S17** was synthesized from **S16** based on the same method as described for **S8**. Compound **S17** exists as two rotamers as shown in the ^{1}H NMR spectrum. The spectroscopic data of the major rotamer is shown. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H, NHC*H*O), 5.62 (s, 1H, N*H*CHO), 4.85 – 4.76 (m, 1H, H-13), 4.09 – 4.00 (m, 1H, H-15), 3.66 (s, 3H, OMe), 2.30 (t, *J* = 7.5 Hz, 3H, H-2), 2.04 (s, 3H, OAc), 1.71 – 1.67 (m, 2H, H-14), 1.64 – 1.56 (m, 3H, H-3 and H_a-12), 1.55 – 1.44 (m, 2H, H_b-12 and H_a-16), 1.41 – 1.33 (m, 3H, H_b-16 and H-17), 1.29 – 1.23 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11), 0.90 (t, *J* = 7.1 Hz, 3H, H-18). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.55, 171.46, 160.99, 72.23, 51.62, 45.42, 39.42, 37.58, 34.26, 34.05, 29.66, 29.64, 29.60, 29.55, 29.53, 29.38, 29.28, 25.41, 25.09, 21.52, 19.01, 14.00. ESI-HRMS calcd for $C_{22}H_{42}NO_5^+$ $[M + H]^+$ 400.3057, found 400.3053.



S18

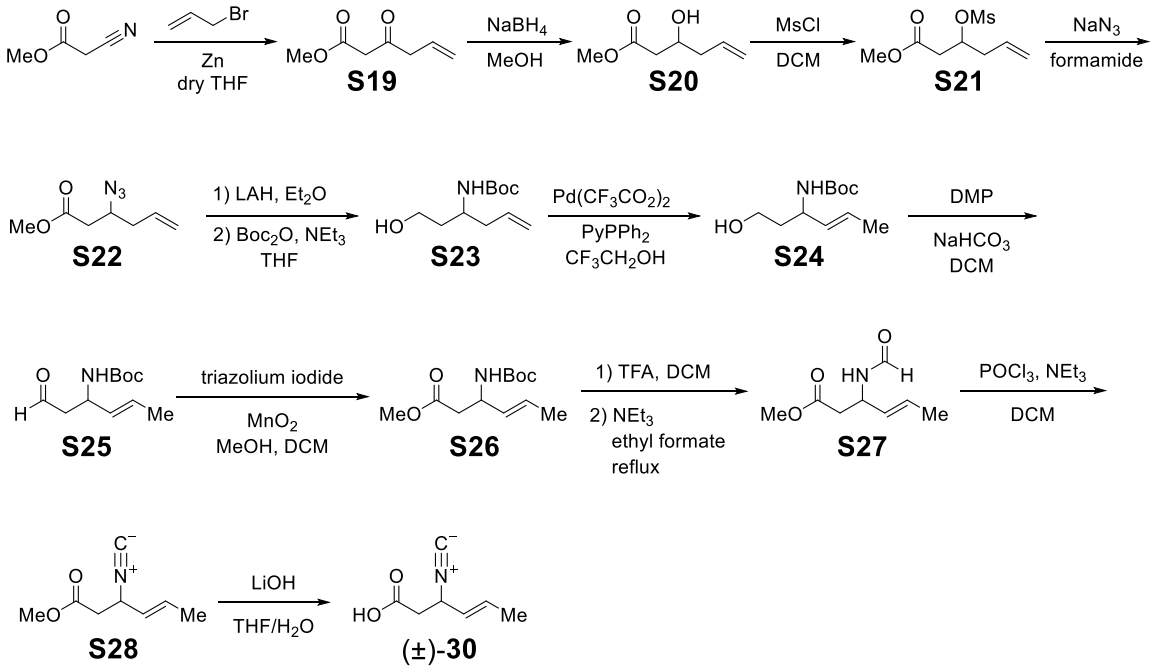
Methyl (13*S*,15*R*)-13-acetoxy-15-isocyanooctadecanoate (S18). Compound **S18** was synthesized from **S17** based on the same method as described for **S9**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.03 – 4.97 (m, 1H, H-13), 3.66 (s, 3H, OMe), 3.60 – 3.51 (m, 1H, H-15), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 2.07 (s, 3H, OAc), 2.05 – 1.98 (m, 1H, H_a-14), 1.79 – 1.73 (m, 1H, H_b-14), 1.63 – 1.55 (m, 7H, H-3, H-12, H-16, H_a-17), 1.48 – 1.39 (m, 1H, H_b-17), 1.29 – 1.23 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11), 0.94 (t, *J* = 6.9 Hz, 3H, H-18). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.53, 170.96, 155.75 (t, *J* = 4.9 Hz), 71.40, 52.00 (t, *J* = 5.7 Hz), 51.61, 39.72, 36.94, 34.44, 34.25, 29.66, 29.63, 29.59, 29.55, 29.51, 29.39, 29.28, 25.21, 25.08, 21.35, 18.85, 13.48. ESI-HRMS calcd for $C_{22}H_{40}NO_4^+$ $[M + H]^+$ 382.2952, found 382.2904.



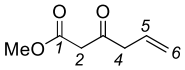
37

(13*S*,15*R*)-13-Hydroxy-15-isocyanooctadecanoic acid (37). Compound **37** was synthesized from **S18** based on the same method as described for **24**. ^{1}H NMR (500 MHz, CD_3OD) δ 3.83 – 3.74 (m, 1H, H-15), 3.69 – 3.60 (m, 1H, H-13), 2.14 (t, *J* = 7.6 Hz, 2H, H-2), 1.87 – 1.77 (m, 1H, H_a-14), 1.77 – 1.68 (m, 1H, H_b-14), 1.66 – 1.54 (m, 5H, H-3, H-16, H_a-17), 1.51 – 1.42 (m, 3H, H-12, H_b-17), 1.41 – 1.25 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11), 0.98 (t, *J* = 7.1 Hz, 3H, H-18). ^{13}C NMR (126 MHz, CD_3OD) δ 183.14, 154.84 (t, *J* = 5.4 Hz), 69.04, 53.35 (t, *J* = 4.9 Hz), 43.82, 39.34, 38.21, 37.42, 30.88, 30.68, 27.84, 26.64, 19.97, 13.75. ESI-HRMS calcd for $C_{19}H_{34}NO_3^-$ $[M - H]^-$ 324.2544, found 324.2566.

S2.7 Synthesis of (±)-30

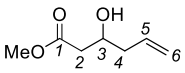


Scheme S7. Chemical synthesis of (±)-**30**.



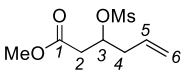
S19

Methyl 3-oxohex-5-enoate (S19). Compound **S19** was synthesized according to the reported method.[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (ddt, *J* = 17.1, 10.3, 7.0 Hz, 1H, H-5), 5.24 (dq, *J* = 10.2, 1.3 Hz, 1H, H_a-6), 5.18 (dq, *J* = 17.1, 1.5 Hz, 1H, H_b-6), 3.74 (s, 3H, OMe), 3.49 (s, 2H, H-2), 3.31 (dd, *J* = 1.4, 1.4 Hz, 1H, H_a-4), 3.30 (dd, *J* = 1.3, 1.3 Hz, 1H, H_b-4).



S20

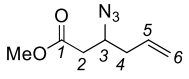
Methyl 3-hydroxyhex-5-enoate (S20). To a stirred solution of **S19** (1.9 g, 13.4 mmol) in MeOH (33 mL) was added $NaBH_4$ (253 mg, 6.7 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 1.5 h. MeOH was then removed under reduced pressure. The residue was redissolved in saturated NH_4Cl solution and extracted with ethyl acetate (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S20** (1.79 g, 93%) as a pale yellow oil. ^{1}H NMR (400 MHz, $cdcl_3$) δ 5.90 – 5.75 (m, 1H, H-5), 5.20 – 5.13 (m, 1H, H_a-6), 5.14 – 5.09 (m, 1H, H_b-6), 4.13 – 4.06 (m, 1H, H-3), 3.71 (s, 3H, OMe), 2.53 (dd, *J* = 16.4, 3.5 Hz, 1H, H_a-2), 2.44 (dd, *J* = 16.4, 8.8 Hz, 1H, H_b-2), 2.36 – 2.22 (m, 2H, H-4).



S21

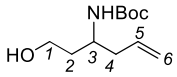
Methyl 3-((methylsulfonyl)oxy)hex-5-enoate (S21). To a stirred solution of **S20** (1.79 g, 12.4 mmol) in DCM (24 mL) was added Et_3N (2.08 mL, 14.88 mmol) and MsCl (1.05 mL, 13.64 mmol) dropwise at 0 ℃. The resulting mixture was stirred at 0 ℃ for 1.5 h. The reaction was quenched with H_2O (20 mL), and extracted with DCM (3 × 30 mL). The combined organic phase was dried over anhydrous Na_2SO_4,

filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S21** (2.48 g, 90%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.73 (m, 1H, H-5), 5.22 – 5.20 (m, 1H, H_a-6), 5.19 – 5.15 (m, 1H, H_b-6), 5.12 – 5.04 (m, 1H, H-3), 3.71 (s, 3H, OMe), 3.03 (s, 3H, OMs), 2.76 (dd, *J* = 16.7, 8.1 Hz, 1H, H_a-2), 2.66 (dd, *J* = 16.7, 4.6 Hz, 1H, H_b-2), 2.61 – 2.54 (m, 2H, H-4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.51, 131.62, 120.10, 78.21, 52.18, 39.50, 38.67, 38.53. ESI-HRMS calcd for $C_8H_{15}O_5S^+$ $[M + H]^+$ 223.0635, found 223.0597.



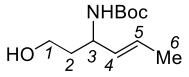
S22

Methyl 3-azidohex-5-enoate (S22). To a stirred solution of **S21** (2.48 g, 11.2 mmol) in formamide (11.2 mL) was added NaN_3 (2.91 g, 44.8 mmol). The resulting mixture was stirred at 55 ℃ for 2 h. The reaction was quenched with H_2O (20 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure to yield **S22** (1.9 g, 100%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 – 5.73 (m, 1H, H-5), 5.21 – 5.17 (m, 1H, H_a-6), 5.17 – 5.14 (m, 1H, H_b-6), 3.94 – 3.86 (m, 1H, H-3), 3.72 (s, 3H, OMe), 2.54 (dd, *J* = 16.1, 5.0 Hz, 1H, H_a-2), 2.46 (dd, *J* = 16.2, 8.5 Hz, 1H, H_b-2), 2.39 – 2.30 (m, 2H, H-4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 133.07, 119.24, 58.44, 52.12, 38.84, 38.73.



S23

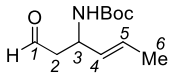
***tert*-Butyl (1-hydroxyhex-5-en-3-yl)carbamate (S23)**. To a stirred solution of **S22** (1.69 g, 10 mmol) in Et_2O (40 mL) was added $LiAlH_4$ (1.14 g, 30 mmol) at 0 ℃. The resulting mixture was stirred at room temperature for 5 h. The reaction was quenched by 3.75 mL 1M NaOH at 0 ℃. The white slurry mixture was filtered through Celite. The filtrate was concentrated under reduced pressure and the residue was redissolved in THF (15 mL) and cooled to 0 ℃. Et_3N (1.67 mL, 12 mmol) and Boc_2O (2.4 g, 11 mmol) in THF (5 mL) were added dropwise. The resulting mixture was stirred at room temperature overnight. The reaction was quenched with H_2O (30 mL), extracted with ethyl acetate (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 5/5) to yield **S23** (1.18 g, 55%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 – 5.70 (m, 1H, H-5), 5.17 – 5.10 (m, 1H, H_a-6), 5.11 – 5.07 (m, 1H, H_b-6), 3.93 – 3.79 (m, 1H, H-3), 3.69 – 3.57 (m, 2H, H-1), 2.33 – 2.18 (m, 2H, H-4), 1.89 – 1.77 (m, 1H, H_a-2), 1.44 (s, 9H, *t*-Bu), 1.40 – 1.30 (m, 1H, H_b-2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.09, 134.20, 118.31, 80.05, 59.00, 46.71, 39.84, 38.44, 28.48. ESI-HRMS calcd for $C_{11}H_{22}NO_3^+$ $[M + H]^+$ 216.1594, found 216.1559.



S24

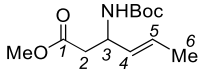
***tert*-Butyl (*E*)-(1-hydroxyhex-4-en-3-yl)carbamate (S24)**.[7] To a stirred solution of **S23** (1.18 g, 5.5 mmol) in F_3CCH_2OH (6 mL) was added $Pd(CF_3CO_2)_2$ (273 mg, 0.85 mmol) and diphenyl-2-pyridylphosphine (289.6 mg, 1.1 mmol). The reaction flask was purged with argon and the resulting mixture was stirred at room temperature for 14 days. ^{1}H NMR analysis showed the substrate had been fully consumed. The reaction was concentrated under reduced pressure and the residue was redissolved in H_2O (10 mL), extracted with ethyl acetate (3 × 20 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 4/6) to yield **S24** (817 mg, 69%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 – 5.60 (m, 1H, H-5), 5.43 (dd, *J* = 15.3, 5.7

Hz, 1H, H-4), 4.32 – 4.24 (m, 1H, H-3), 3.72 – 3.60 (m, 2H, H-1), 1.90 – 1.81 (m, 1H, H_a-2), 1.69 (d, *J* = 6.4 Hz, 3H, H-6), 1.45 (s, 9H, *t*-Bu), 1.51 – 1.39 (m, 1H, H_b-2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.76, 131.28, 126.51, 80.17, 59.01, 48.95, 38.78, 28.50, 17.89. ESI-HRMS calcd for $C_{11}H_{22}NO_3^+$ $[M + H]^+$ 216.1594, found 216.1594.



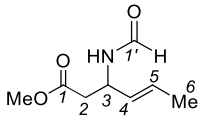
S25

***tert*-Butyl (*E*)-(1-oxohex-4-en-3-yl)carbamate (S25)**. To a stirred solution of **S24** (105 mg, 0.49 mmol) in dry DCM (4 mL) was added $NaHCO_3$ (411.6 mg, 4.9 mmol) and DMP (229 mg, 0.54 mmol). The reaction was stirred at room temperature for 2 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (5 mL). The aqueous phase was extracted with DCM (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S25** (90 mg, 86%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (t, *J* = 2.0 Hz, 1H, H-1), 5.70 – 5.60 (m, 1H, H-5), 5.46 (ddd, *J* = 15.3, 6.2, 1.7 Hz, 1H, H-4), 4.59 – 4.51 (m, 1H, H-3), 2.68 (dd, *J* = 6.2, 2.0 Hz, 2H, H-2), 1.68 (ddd, *J* = 6.4, 1.4, 1.4 Hz, 3H, H-6), 1.43 (s, 9H, *t*-Bu). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.94, 155.17, 130.07, 127.51, 79.87, 49.12, 48.11, 28.49, 17.81.



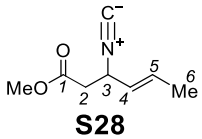
S26

Methyl (*E*)-3-((*tert*-butoxycarbonyl)amino)hex-4-enoate (S26).[8] To a 25-mL flame-dried round bottom flask were added 1,4-dimethyl-1,2,4-triazolium iodide (9.5 mg, 0.042 mmol), **S25** (90 mg, 0.42 mmol) in 2 mL DCM, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.069 mL, 0.46 mmol) and MnO_2 (183 mg, 2.1 mmol) and MeOH (0.084 mL) under an Ar atmosphere. The reaction mixture was stirred at room temperature overnight. The reaction was filtered through Celite and the filtrate was concentrated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 2/8) to yield **S26** (75 mg, 74%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 – 5.59 (m, 1H, H-5), 5.45 (ddd, *J* = 15.4, 6.2, 1.7 Hz, 1H, H-4), 4.47 – 4.40 (m, 1H, H-3), 3.67 (s, 3H, OMe), 2.58 (d, *J* = 5.7 Hz, 2H, H-2), 1.67 (ddd, *J* = 6.5, 1.3, 1.3 Hz, 3H, H-6), 1.44 (s, 9H, *t*-Bu). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.92, 155.23, 130.14, 127.11, 79.63, 51.81, 49.25, 39.83, 28.54, 17.81. ESI-HRMS calcd for $C_{12}H_{22}NO_4^+$ $[M + H]^+$ 244.1543, found 244.1492.



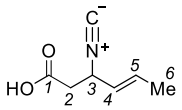
S27

Methyl (*E*)-3-formamidohex-4-enoate (S27). Compound **S27** was synthesized from **S26** based on the same method as described for **S13**. The spectroscopic data of the major rotamer is shown. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H, H-1′), 5.74 – 5.64 (m, 1H, H-5), 5.48 (ddd, *J* = 15.4, 6.3, 1.7 Hz, 1H, H-4), 4.90 – 4.82 (m, 1H, H-3), 3.69 (s, 3H, OMe), 2.64 (d, *J* = 5.1 Hz, 1H, H-2), 1.68 (ddd, *J* = 6.5, 1.4, 1.4 Hz, 3H, H-6). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.01, 160.41, 128.86, 128.27, 51.95, 46.35, 38.84, 17.80. ESI-HRMS calcd for $C_8H_{14}NO_3^+$ $[M + H]^+$ 172.0968, found 172.0971.



S28

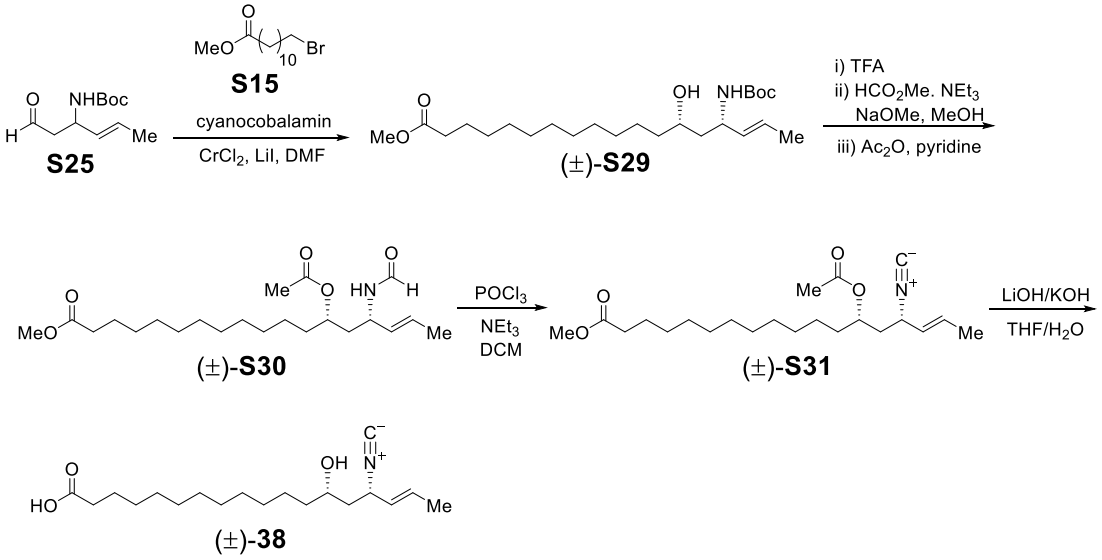
Methyl (*E*)-3-isocyanohex-4-enoate (S28). Compound **S28** was synthesized from **S27** based on the same method as described for **S14**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 – 5.83 (m, 1H, H-5), 5.42 (dd, *J* = 14.8, 5.1 Hz, 1H, H-4), 4.59 – 4.51 (m, 1H, H-3), 3.74 (s, 3H, OMe), 2.77 (dd, *J* = 16.1, 8.0 Hz, 1H, H_a-2), 2.65 – 2.58 (m, 1H, H_b-2), 1.74 (ddd, *J* = 6.6, 1.4, 1.4 Hz, 3H, H-6). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.56, 157.60 (t, *J* = 5.0 Hz), 129.87, 125.29, 52.51 (t, *J* = 6.5 Hz), 52.33, 41.14, 17.50. ESI-HRMS calcd for $C_8H_{12}NO_2^+$ $[M + H]^+$ 154.0863, found 154.0864.



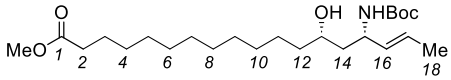
(±)-**30**

(*E*)-3-Isocyanohex-4-enoic acid ((±)-30). Compound **(±)-30** was synthesized from **S28** based on the same method as described for **29**. ^{1}H NMR (400 MHz, D_2O) δ 5.90 – 5.79 (m, 1H, H-5), 5.55 – 5.44 (m, 1H, H-4), 4.54 – 4.45 (m, 1H, H-3), 2.57 – 2.47 (m, 2H, H-2), 1.67 (d, *J* = 6.5 Hz, 3H, H-6). ^{13}C NMR (126 MHz, D_2O) δ 177.62, 151.44 (t, *J* = 6.4 Hz), 129.41, 125.74, 54.17 (t, *J* = 5.7 Hz), 44.07, 16.67. ESI-HRMS calcd for $C_7H_8NO_2^-$ $[M - H]^-$ 138.0561, found 138.0567.

S2.8 Synthesis of (±)-38

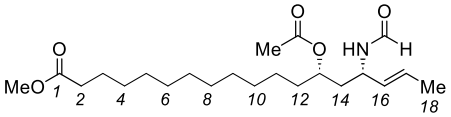


Scheme S8. Chemical synthesis of (±)-**38**.



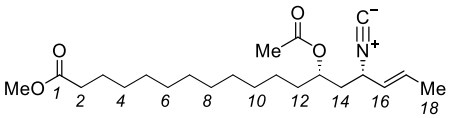
(±)-**S29**

(±)-**Methyl (13*S*,15*S*,*E*)-15-((tert-butoxycarbonyl)amino)-13-hydroxyoctadec-16-enoate ((±)-S29)**. Compound (±)-**S29** was synthesized from **S15** and **S25** based on the same method as described for **S7**-*syn*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 – 5.57 (m, 1H, H-17), 5.34 (ddd, *J* = 15.3, 6.9, 1.7 Hz, 1H, H-16), 4.15 (ddd, *J* = 7.0, 7.0, 7.0 Hz, 1H, H-15), 3.67 – 3.60 (m, 1H, H-13), 3.65 (s, 3H, OMe), 2.28 (t, *J* = 7.6 Hz, 2H, H-2), 1.66 (d, *J* = 6.5 Hz, 3H, H-18), 1.63 – 1.55 (m, 4H, H-3 and H-14), 1.43 – 1.40 (m, 2H, H-12), 1.42 (s, 9H, *t*-Bu), 1.32 – 1.20 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.49, 155.69, 131.79, 126.56, 79.64, 69.88, 51.56, 51.13, 43.28, 37.98, 34.22, 29.72, 29.70, 29.65, 29.52, 29.35, 29.24, 28.52, 25.69, 25.05, 17.82.



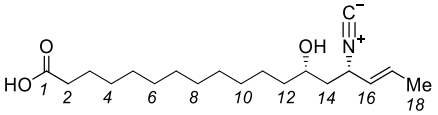
(±)-**S30**

(±)-**Methyl (13*S*,15*S*,*E*)-13-acetoxy-15-formamidooctadec-16-enoate ((**±)-**S30)**. Compound (±)-**S30** was synthesized from (±)-**S29** based on the same method as described for **S8**. Compound (±)-**S30** exists as two rotamers as shown in the ^{1}H NMR spectrum. The spectroscopic data of the major rotamer is shown. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H, N*H*CHO), 5.99 (d, *J* = 8.6 Hz, 1H, NHC*H*O), 5.64 – 5.51 (m, 1H, H-17), 5.33 (ddd, *J* = 15.4, 6.0, 1.7 Hz, 1H, H-16), 4.82 (dddd, *J* = 7.7, 6.0, 6.0, 6.0 Hz, 1H, H-13), 4.56 (dddd, *J* = 7.3, 7.3, 7.2, 7.2 Hz, 1H, H-15), 3.66 (s, 3H, OMe), 2.29 (t, *J* = 7.6 Hz, 2H, H-2), 2.01 (s, 3H, OAc), 1.81 (ddd, *J* = 14.4, 7.3, 7.3 Hz, 1H, H_a-14), 1.76 – 1.71 (m, 1H, H_b-14), 1.66 (ddd, *J* = 6.5, 1.5, 1.5 Hz, 3H, H-18), 1.63 – 1.58 (m, 2H, H-3), 1.57 – 1.51 (m, 2H, H-12), 1.28 – 1.21 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.53, 171.55, 160.78, 130.07, 126.91, 71.57, 51.59, 47.07, 39.43, 34.46, 34.24, 29.64, 29.61, 29.59, 29.53, 29.51, 29.36, 29.26, 25.35, 25.07, 21.46, 17.88.



(±)-**S31**

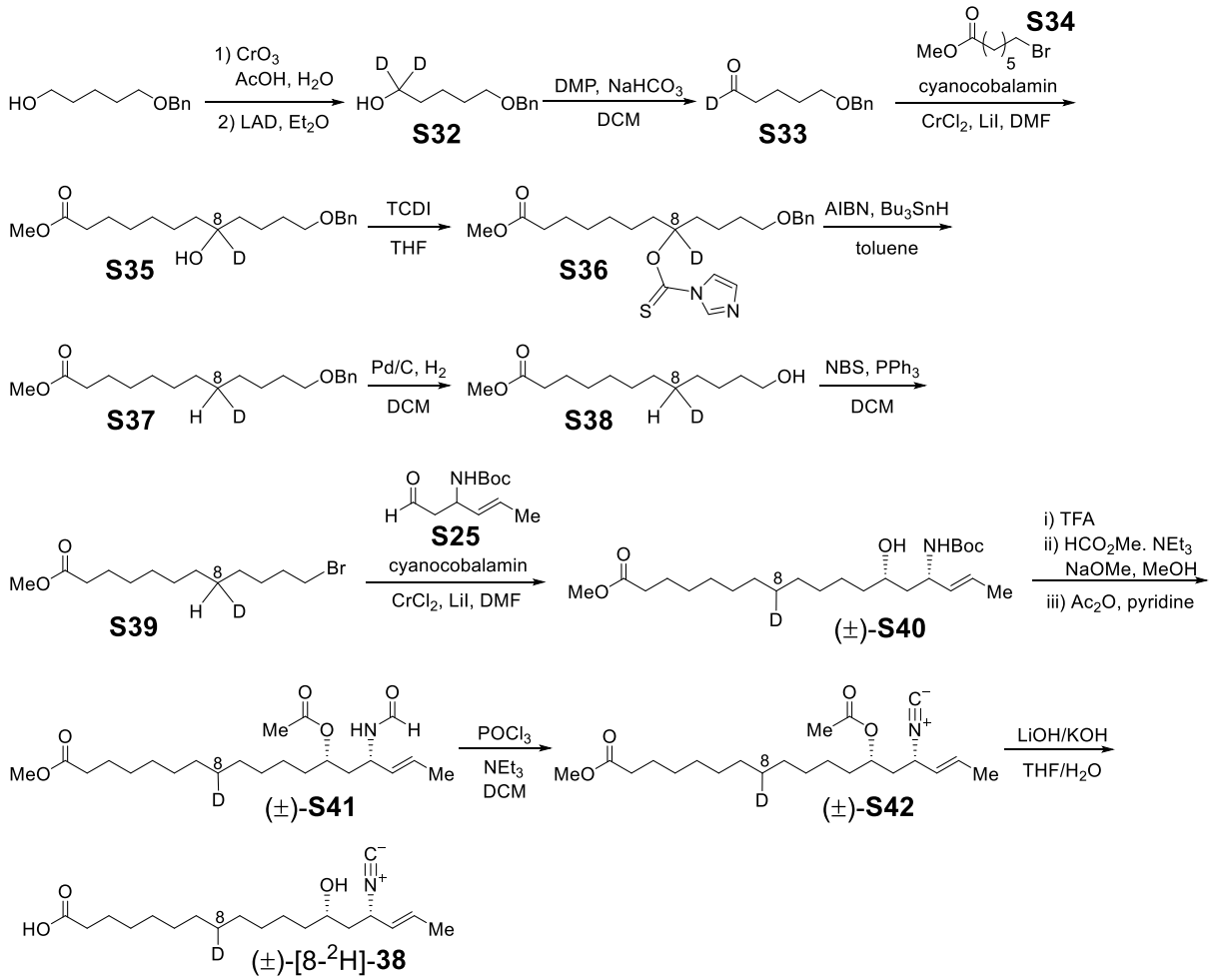
(±)-**Methyl (13*S*,15*S*,*E*)-13-acetoxy-15-isocyanooctadec-16-enoate ((**±)-**S31)**. Compound (±)-**S31** was synthesized from (±)-**S30** based on the same method as described for **S9**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 – 5.73 (m, 1H, H-17), 5.37 (dd, *J* = 15.6, 6.3 Hz, 1H, H-16), 4.92 (dddd, *J* = 9.5, 9.5, 5.9, 3.4 Hz, 1H, H-13), 4.07 (ddd, *J* = 6.9, 6.9, 6.9 Hz, 1H, H-15), 3.66 (s, 3H, OMe), 2.29 (t, *J* = 7.5 Hz, 2H, H-2), 2.09 – 2.03 (m, 1H, H_a-14), 2.06 (s, 3H, OAc), 1.86 – 1.78 (m, 1H, H_b-14), 1.73 (d, *J* = 6.5 Hz, 3H, H-18), 1.64 – 1.58 (m, 2H, H-3), 1.57 – 1.48 (m, 2H, H-12), 1.31 – 1.21 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.47, 170.70, 156.65, 129.64, 126.14, 70.95, 53.63 (t, *J* = 5.9 Hz), 51.57, 40.77, 34.53, 34.25, 29.65, 29.61, 29.57, 29.54, 29.52, 29.37, 29.27, 25.10, 25.08, 21.29, 17.55. ESI-HRMS calcd for $C_{22}H_{38}NO_4^+$ $[M + H]^+$ 380.2795, found 380.2801.



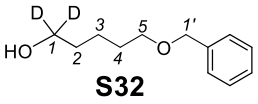
(±)-**38**

(±)-**(13*S*,15*S*,*E*)-13-Hydroxy-15-isocyanooctadec-16-enoic acid ((**±)-**38)**. Compound (±)-**38** was synthesized from (±)-**S31** based on the same method as described for **24**. ^{1}H NMR (400 MHz, CD_3OD) δ 5.90 – 5.77 (m, 1H, H-17), 5.47 (dd, *J* = 15.1, 7.1 Hz, 1H, H-16), 4.31 (ddd, *J* = 7.5, 7.4, 7.4 Hz, 1H, H-15), 3.57 – 3.50 (m, 1H, H-13), 2.14 (t, *J* = 7.6 Hz, 2H, H-2), 1.86 – 1.80 (m, 1H, H_a-14), 1.78 – 1.72 (m, 1H, H_b-14), 1.75 (d, *J* = 6.5 Hz, 3H, H-18), 1.59 (p, *J* = 7.2 Hz, 2H, H-3), 1.47 – 1.42 (m, 2H, H-12), 1.38 – 1.25 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (101 MHz, CD_3OD) δ 183.12, 155.48, 130.48, 128.20, 68.62, 54.91 (t, *J* = 5.6 Hz), 44.95, 39.35, 38.39, 30.88, 30.74, 30.72, 30.71, 30.66, 27.83, 26.60, 17.55. ESI-HRMS calcd for $C_{19}H_{32}NO_3^-$ $[M - H]^-$ 322.2388, found 322.2401.

S2.9 Synthesis of (±)-[8-^{2}H]-38



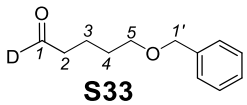
Scheme S9. Chemical synthesis of (±)-[8-^{2}H]-**38**.



S32

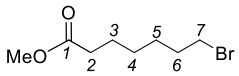
5-(Benzyloxy)pentan-1,1-*d*$_2$-1-ol (S32). To a stirred solution of CrO_3 (3.85 g, 38.5 mmol) in AcOH (34.5 mL) and H_2O (4 mL) was added 5-benzyloxy-1-pentanol (1.94 g, 10 mmol) in acetone (10 mL) dropwise at 0 ℃. The resulting mixture was then slowly allowed to warm to room temperature and stir overnight. The reaction was quenched by H_2O (100 mL), extracted with ethyl acetate (3 × 100 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude carboxylic acid was redissolved in Et_2O (40 mL) and cool to 0 ℃. $LiAlD_4$ (697 mg, 16.6 mmol) was then added portionwise. The resulting mixture was stirred at room temperature overnight. The reaction was quenched by 3 mL 1 M NaOH at 0 ℃. The resulting white slurry mixture was filtered through Celite. The filtrate was washed with H_2O (30 mL). The aqueous phase was extracted with ethyl acetate (2 × 50 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 4/6) to yield **S32** (746 mg, 38%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H, Ar-H), 4.50 (s, 2H, H-1′), 3.48 (t, *J* = 6.5 Hz, 2H, H-5), 1.71 – 1.60 (m, 2H, H-4), 1.58 (t, *J* = 7.4 Hz, 2H, H-2), 1.51 – 1.39 (m, 2H, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.71, 128.51, 127.79, 127.67, 73.08, 70.43, 62.15 (p, *J* = 21.8 Hz), 32.44, 29.61, 22.53. ESI-HRMS calcd for $C_{12}H_{17}D_2O_2^+$ [M + H]$^+$ 197.1505, found 197.1506.



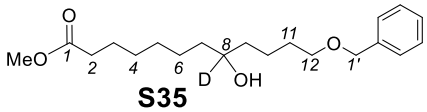
S33

5-(Benzyloxy)pentanal-1-*d* (S33). To a stirred solution of **S33** (882 mg, 4.5 mmol) in dry DCM (22.5 mL) was added $NaHCO_3$ (3.78 g, 45 mmol) and DMP (2.1 g, 4.95 mmol). The reaction was stirred at room temperature for 3 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (20 mL). The aqueous phase was extracted with DCM (3 × 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 2/8) to yield **S33** (777 mg, 89%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H, Ar-H), 4.50 (s, 2H. H-1′), 3.49 (t, *J* = 6.2 Hz, 2H, H-5), 2.45 (t, *J* = 7.2 Hz, 2H, H-2), 1.79 – 1.71 (m, 2H, H-3), 1.69 – 1.62 (m, 2H, H-4). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.33 (t, *J* = 26.5 Hz), 138.61, 128.53, 127.78, 127.72, 73.11, 69.91, 43.56 (t, *J* = 3.6 Hz), 29.30, 19.09. ESI-HRMS calcd for $C_{12}H_{16}DO_2^+$ [M + H]$^+$ 194.1286, found 194.1278.



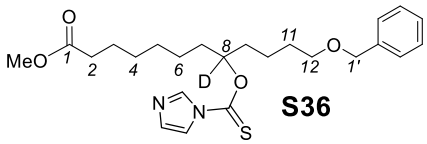
S34

Methyl 7-bromoheptanoate (S34). Compound **S34** was synthesized from 7-bromoheptanoic acid based on the same method as described for **S6**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 3H, OMe), 3.40 (t, *J* = 6.8 Hz, 2H, H-7), 2.32 (t, *J* = 7.5 Hz, 2H, H-2), 1.86 (p, *J* = 7.0 Hz, 2H, H-6), 1.64 (p, *J* = 7.5 Hz, 2H, H-3), 1.51 – 1.41 (m, 2H, H-5), 1.39 – 1.29 (m, 2H, H-4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.25, 51.66, 34.06, 33.94, 32.66, 28.37, 27.92, 24.84.



S35

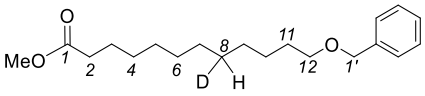
Methyl 12-(benzyloxy)-8-hydroxydodecanoate-8-*d* (S35). To a flame-dried 50-mL flask were added $CrCl_2$ (1.97 g, 16 mmol), cyanocobalamin (326 mg, 0.24 mmol), LiI (32 mg, 0.24 mmol) and dry DMF (20 mL) under an Ar atmosphere. Ester **S34** (1.78 g, 8 mmol) and aldehyde **S33** (772 mg, 4 mmol) together in dry DMF (10 mL) were then added. The reaction mixture was stirred at room temperature overnight. The reaction was quenched with 40 mL H_2O. The aqueous phase was extracted with ethyl acetate (4 × 40 mL). The combined organic phase was washed with H_2O and then brine before dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S35** (1.11 g, 83%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H, Ar-H), 4.50 (s, 2H,H-1′), 3.66 (s, 3H,OMe), 3.48 (t, *J* = 6.5 Hz, 2H, H-12), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.71 – 1.59 (m, 4H, H-3 and H-11), 1.55 – 1.27 (m, 12H, H-4, H-5, H-6, H-7, H-9, and H-10). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.41, 138.75, 128.50, 127.80, 127.66, 73.07, 71.47 (t, *J* = 21.5 Hz), 70.45, 51.59, 37.41, 37.25, 34.21, 29.87, 29.43, 29.24, 25.55, 25.02, 22.46. ESI-HRMS calcd for $C_{20}H_{32}DO_4^+$ [M + H]$^+$ 338.2436, found 338.2504.



S36

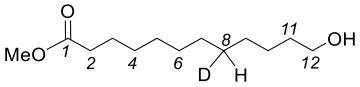
Methyl 8-((1*H*-imidazole-1-carbonothioyl)oxy)-12-(benzyloxy)dodecanoate-8-*d* (S36). To compound **S35** (1.11 g, 3.3 mmol) and 1,1′-thiocarbonyldiimidazole (TCDI) (1.77 g, 9.9 mmol) was added THF

(20 mL) under argon. The reaction was refluxed at 65 °C overnight. The reaction mixture was concentrated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 3/7) to yield **S36** (1.21 g, 82%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 – 8.59 (m, 1H, imidazole), 7.74 – 7.68 (m, 1H, imidazole), 7.39 – 7.27 (m, 5H, phenyl), 7.16 (s, 1H, imidazole), 4.48 (s, 2H, H-1′), 3.66 (s, 3H, OMe), 3.47 (t, *J* = 6.2 Hz, 2H, H-12), 2.29 (t, *J* = 7.4 Hz, 2H, H-2), 1.90 – 1.27 (m, 16H, H-3, H-4, H-5, H-6, H-7, H-9, H-10, and H-11). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.33, 174.26, 138.55, 135.63, 128.53, 127.79, 127.76, 127.35, 118.51, 73.12, 69.91, 51.64, 34.07, 33.20, 33.09, 29.60, 29.16, 29.01, 25.01, 24.87, 22.03.



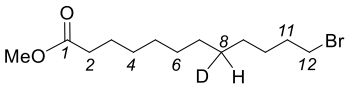
S37

Methyl 12-(benzyloxy)dodecanoate-8-*d* (S37). To compound **S36** (1.21 g, 2.7 mmol), azobisisobutyronitrile (AIBN) (26.6 mg, 0.16 mmol) and Bu_3SnH (0.948 mL, 3.51 mmol) was added dry toluene (20 mL) under argon. The reaction was refluxed at 110 °C for 20 min. The reaction mixture was concentrated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 5/95) to yield **S37** (638 mg, 74%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H, Ar-H), 4.50 (s, 2H, H-1′), 3.66 (s, 3H, OMe), 3.46 (t, *J* = 6.6 Hz, 2H, H-12), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.69 – 1.57 (m, 4H, H-3 and H-11), 1.40 – 1.22 (m, 13H, H-4, H-5, H-6, H-7, H-8, H-9, and H-10). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.50, 138.88, 128.48, 127.76, 127.60, 73.00, 70.68, 51.58, 34.27, 29.92, 29.55, 29.54, 29.51, 29.47, 29.39, 29.30, 26.31, 25.11.



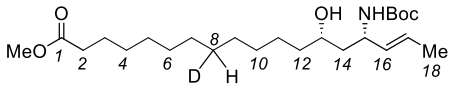
S38

Methyl 12-hydroxydodecanoate-8-*d* (S38). To a stirred solution of **S37** (638 mg, 1.99 mmol) in DCM (10 mL) was added 5% Pd/C (844 mg, 0.40 mmol). The reaction mixture was purged with H_2 and stirred under H_2 (1 atm) at room temperature overnight. The reaction was filtered through Celite and the filtrate was concentrated under reduce pressure to yield **S38** (445 mg, 97%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H, OMe), 3.64 (t, *J* = 6.7 Hz, 2H, H-12), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.66 – 1.52 (m, 4H, H-3 and H-11), 1.38 – 1.22 (m, 13H, H-4, H-5, H-6, H-7, H-8, H-9, and H-10). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.51, 63.23, 51.59, 34.26, 32.95, 29.51, 29.44, 29.37, 29.27, 25.84, 25.09. ESI-HRMS calcd for $C_{13}H_{26}DO_3^+$ $[M + H]^+$ 232.2017, found 232.2009.



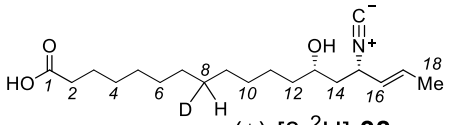
S39

Methyl 12-bromododecanoate-8-*d* (S39). To a stirred solution of **S38** (445 mg, 1.93 mmol) in DCM (5 mL) was added PPh_3 (506 mg, 1.93 mmol) and *N*-bromosuccinimide (NBS) (343 mg, 1.93 mmol) at 0 °C. The resulting mixture was stirred at room temperature overnight. The reaction was filter though a pad of silica gel, washed with ethyl acetate/hexanes = 5/95. The filtrate was concentrated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 5/95) to yield **S39** (508 mg, 90%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H, OMe), 3.40 (t, *J* = 6.8 Hz, 2H, H-12), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.85 (p, *J* = 7.0 Hz, 2H, H-11), 1.66 – 1.59 (m, 2H, H-3), 1.41 (p, *J* = 7.0 Hz, 2H, H-10), 1.36 – 1.21 (m, 11H, H-4, H-5, H-6, H-7, H-8 and H-9). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.48, 51.58, 34.25, 34.18, 32.98, 29.49, 29.37, 29.27, 29.12 (t, *J* = 19.0 Hz), 28.79, 28.29, 25.09.



(±)-**S40**

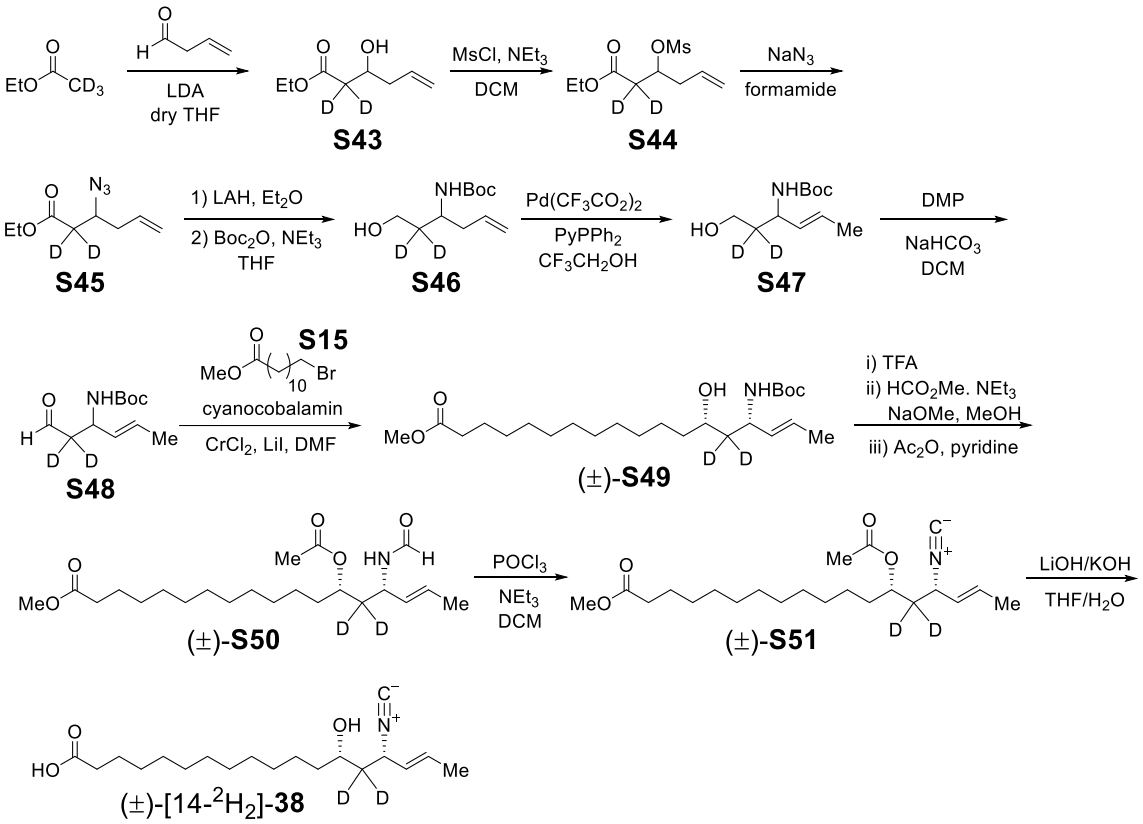
(±)-Methyl (13*S*,15*S*,*E*)-15-((*tert*-butoxycarbonyl)amino)-13-hydroxyoctadec-16-enoate-8-*d* ((±)-S40). Compound (±)-**S40** was synthesized from **S25** and **S39** based on the same method as described for **S7**-*syn*. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 – 5.60 (m, 1H, H-17), 5.36 (dd, *J* = 15.3, 6.4 Hz, 1H, H-16), 4.17 (ddd, *J* = 6.9, 6.9, 6.9 Hz, 1H, H-15), 3.69 – 3.64 (m, 1H, H-13), 3.66 (s, 3H, OMe), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.68 (d, *J* = 6.5 Hz, 3H, H-18), 1.65 – 1.58 (m, 4H, H-3 and H-14) , 1.46 – 1.42 (m, 2H, H-12), 1.44 (s, 9H, *t*-Bu), 1.33 – 1.21 (m, 15H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.53, 155.77, 131.80, 126.69, 79.84, 70.02, 51.60, 51.23, 43.33, 38.03, 34.27, 29.72, 29.62, 29.58, 29.54, 29.39, 29.29, 28.56, 25.72, 25.10, 17.86. ESI-HRMS calcd for $C_{24}H_{45}DNO_5^+$ $[M + H]^+$ 429.3433, found 429.3407.



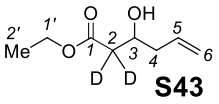
(±)-[8-^{2}H]-**38**

(±)-(13*S*,15*S*,*E*)-13-Hydroxy-15-isocyanooctadec-16-enoic-8-*d* acid ((±)-[8-^{2}H]-38). Compound (±)-[8-^{2}H]-**38** was synthesized from (±)-**S40** based on the same method as described for (±)-**38**. ^{1}H NMR (500 MHz, CD_3OD) δ 5.89 – 5.78 (m, 1H, H-17), 5.47 (ddd, *J* = 15.1, 7.1, 1.7 Hz, 1H, H-16), 4.31 (ddd, *J* = 7.4, 7.4, 7.2 Hz, 1H, H-15), 3.54 (dddd, *J* = 8.6, 8.6, 4.0, 4.0 Hz, 1H, H-13), 2.14 (t, *J* = 7.4 Hz, 2H, H-2), 1.88 – 1.81 (m, 1H, H_a-14), 1.78 – 1.72 (m, 1H, H_b-14), 1.75 (dd, *J* = 6.6, 1.2 Hz, 3H, H-18), 1.59 (p, *J* = 7.3 Hz, 2H, H-3), 1.47 – 1.42 (m, 2H, H-12), 1.37 – 1.26 (m, 15H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, CD_3OD) δ 183.11, 155.48 (t, *J* = 5.4 Hz), 130.52, 128.17, 68.60, 54.91 (t, *J* = 6.0 Hz), 44.93, 39.32, 38.39, 30.87, 30.71, 30.69, 30.67, 30.66, 30.62, 30.32 (t, *J* = 18.7 Hz), 27.82, 26.62, 17.58. ESI-HRMS calcd for $C_{19}H_{31}DNO_3^-$ $[M - H]^-$ 323.2450, found 323.2457.

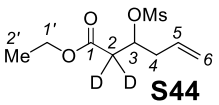
S2.10 Synthesis of (±)-[14-$^{2}H_2$]-38



Scheme S10. Chemical synthesis of (±)-[14-$^2H_2$]-**38**.

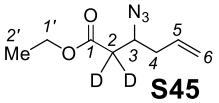


Ethyl 3-hydroxyhex-5-enoate-2,2-*d*$_2$ (S43). To a flame-dried 100-mL flask was added dry THF (2 mL) and 2 M lithium diisopropylamide (LDA) (10 mL). The mixture was cooled to −78 ℃. Ethyl acetate-d_3[9] (1.95 mL, 20 mmol) was added dropwise. The mixture was stirred at −78 ℃ for 1.5 h. Freshly prepared but-3-enal[10] (ca. 10 mmol) in DCM was added dropwise at −78 ℃. The resulting mixture was stirred at −78 ℃ for 2.5 h. The reaction was quenched by adding saturated NH_4Cl solution (10 mL) at −78 ℃. The aqueous phase was extracted with DCM (3 × 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified using flash chromatography on silica gel (ethyl acetate/hexanes = 2/8 then 3/7) to yield **S43** (1.06 g, 66%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 – 5.75 (m, 1H, H-5), 5.18 – 5.09 (m, 2H, H-6), 4.17 (q, *J* = 7.2 Hz, 2H, H-1′), 4.08 (t, *J* = 6.4 Hz, 1H, H-3), 2.36 – 2.22 (m, 2H, H-4), 1.27 (t, *J* = 7.1 Hz, 3H, H-2′). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.96, 134.11, 118.34, 67.42, 60.85, 41.05, 40.18 (p, *J* = 19.3 Hz), 14.31. ESI-HRMS calcd for $C_8H_{13}D_2O_3^+$ $[M + H]^+$ 161.1141, found 161.1147.



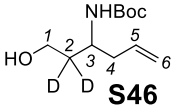
Ethyl 3-((methylsulfonyl)oxy)hex-5-enoate-2,2-*d*$_2$ (S44). Compound **S44** was synthesized from **S43** based on the same method as described for **S21**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 – 5.71 (m, 1H, H-5), 5.25 – 5.14 (m, 2H, H-6), 5.07 (t, *J* = 6.0 Hz, 1H, H-3), 4.16 (q, *J* = 7.1 Hz, 2H, H-1′), 3.03 (s, 3H, OMs), 2.61 – 2.54 (m, 2H, H-4), 1.27 (t, *J* = 7.2 Hz, 3H, H-2′). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.09, 131.66,

120.06, 78.24, 61.22, 39.46, 38.52, 14.28. ESI-HRMS calcd for $C_9H_{15}D_2O_5S^+$ $[M + H]^+$ 239.0917, found 239.0963.



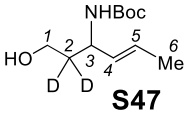
S45

Ethyl 3-azidohex-5-enoate-2,2-d_2 (S45). Compound **S45** was synthesized from **S44** based on the same method as described for **S22**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 – 5.75 (m, 1H. H-5), 5.22 – 5.13 (m, 2H, H-6), 4.18 (q, *J* = 7.1 Hz, 2H, H-1′), 3.89 (t, *J* = 6.6 Hz, 1H, H-3), 2.41 – 2.28 (m, 2H, H-4), 1.28 (t, *J* = 7.1 Hz, 3H, H-2′). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.80, 133.13, 119.17, 61.05, 58.41, 38.72, 38.58 (p, *J* = 19.2 Hz), 14.30.



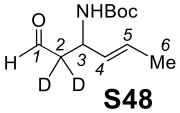
S46

***tert*-Butyl (1-hydroxyhex-5-en-3-yl-2,2-d_2)carbamate (S46)**. Compound **S46** was synthesized from **S45** based on the same method as described for **S23**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dddd, *J* = 14.2, 9.9, 7.1, 7.1 Hz, 1H, H-5), 5.15 – 5.08 (m, 2H, H-6), 3.85 (t, *J* = 6.5 Hz, 1H, H-3), 3.65 (d, *J* = 11.9 Hz, 1H, H_a-1), 3.61 (d, *J* = 12.2 Hz, 1H, H_b-1), 2.33 – 2.18 (m, 2H, H-4), 1.44 (s, 9H, *t*-Bu). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.11, 134.18, 118.34, 80.14, 58.91, 46.68, 39.79, 37.64 (p, *J* = 19.3 Hz), 28.48. ESI-HRMS calcd for $C_{11}H_{20}D_2NO_3^+$ $[M + H]^+$ 218.1720, found 218.1742.



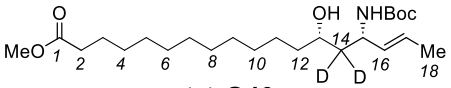
S47

***tert*-Butyl (*E*)-(1-hydroxyhex-4-en-3-yl-2,2-d_2)carbamate (S47)**. Compound **S47** was synthesized from **S46** based on the same method as described for **S24**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (dqd, *J* = 14.4, 6.5, 1.4 Hz, 1H, H-5), 5.42 (ddd, *J* = 15.5, 5.7, 2.1 Hz, 1H, H-4), 4.27 (d, *J* = 3.2 Hz, 1H, H-3), 3.65 (d, *J* = 11.8 Hz, 1H, H_a-1), 3.62 (d, *J* = 12.3 Hz, 1H, H_b-1), 1.69 (ddd, *J* = 6.3, 1.5, 1.5 Hz, 3H, H-6), 1.44 (s, 9H, *t*-Bu). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.70, 131.28, 126.44, 80.01, 58.87, 48.67, 37.94 (p, *J* = 19.3 Hz), 28.48, 17.90.



S48

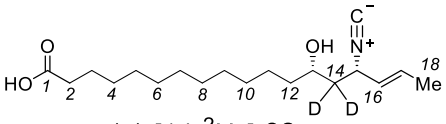
***tert*-Butyl (*E*)-(1-oxohex-4-en-3-yl-2,2-d_2)carbamate (S48)**. Compound **S48** was synthesized from **S47** based on the same method as described for **S25**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74 (s, 1H, H-1), 5.70 – 5.61 (m, 1H, H-5), 5.46 (dd, *J* = 15.5, 5.3 Hz, 1H, H-4), 4.54 (d, *J* = 3.0 Hz, 1H, H-3), 1.68 (d, *J* = 6.5 Hz, 3H, H-6), 1.43 (s, 9H, *t*-Bu).



(±)-**S49**

(±)-Methyl (13*S*,15*S*,*E*)-15-((*tert*-butoxycarbonyl)amino)-13-hydroxyoctadec-16-enoate-14,14-d_2 ((±)-S49). Compound (±)-**S49** was synthesized from **S48** and **S15** based on the same method as described for **S7**-*syn*. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.67 – 5.60 (m, 1H, H-17), 5.36 (ddd, *J* = 15.3, 6.9, 1.7 Hz, 1H, H-16), 4.16 (d, *J* = 6.9 Hz, 1H, H-15), 3.68 – 3.64 (m, 1H, H-13), 3.66 (s, 3H, OMe), 2.30 (t, *J* = 7.6 Hz, 2H, H-2), 1.68 (d, *J* = 6.5 Hz, 3H, H-18), 1.64 – 1.58 (m, 2H, H-3), 1.46 – 1.41 (m, 11H, H-12 and *t*-Bu),

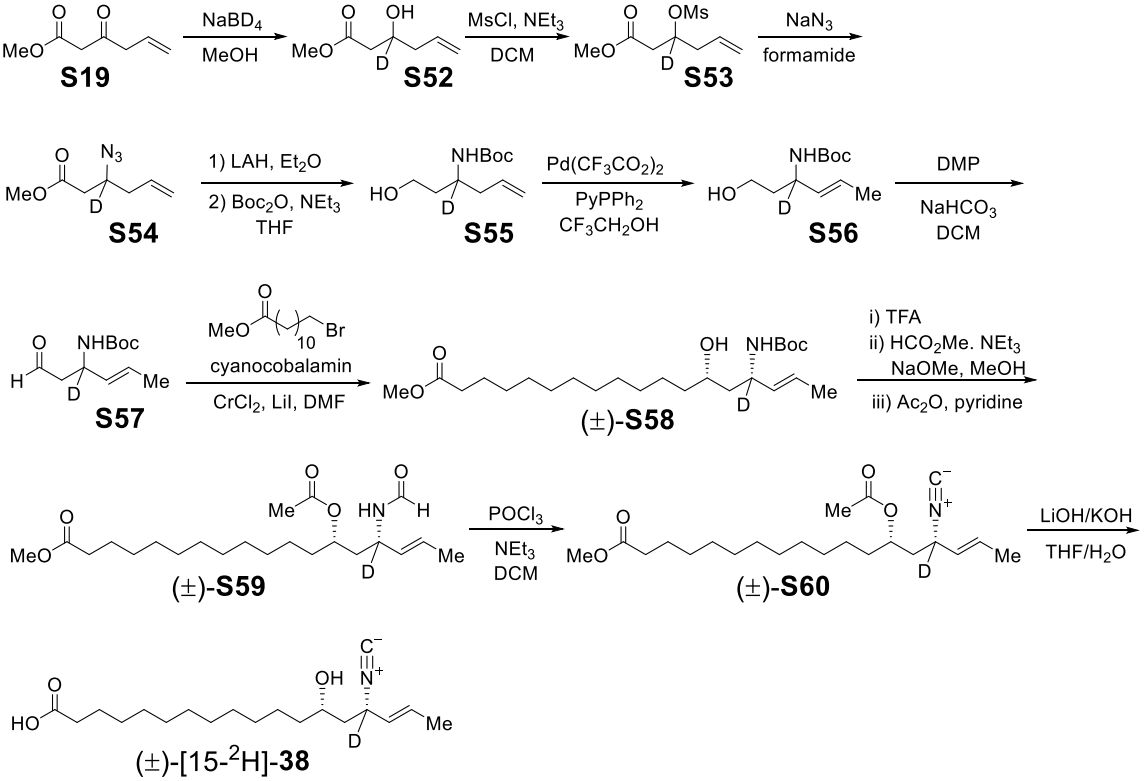
1.32 – 1.23 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.53, 155.77, 131.79, 126.67, 79.77, 69.91, 51.60, 51.09, 42.53, 37.99, 34.27, 29.75, 29.73, 29.68, 29.56, 29.38, 29.29, 28.56, 25.71, 25.10, 17.86. ESI-HRMS calcd for $C_{24}H_{44}D_2NO_5^+$ $[M + H]^+$ 430.3496, found 430.3530.



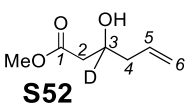
(±)-[14-^{2}H$_2$]-**38**

(±)-(13*S*,15*S*,*E*)-13-Hydroxy-15-isocyanooctadec-16-enoic-14,14-*d*$_2$ acid ((±)-[14-^{2}H$_2$]-38). Compound (±)-[14-^{2}H$_2$]-**38** was synthesized from (±)-**S49** based on the same method as described for (±)-**38**. ^{1}H NMR (400 MHz, CD_3OD) δ 5.83 (dq, *J* = 15.4, 6.6 Hz, 1H, H-17), 5.47 (ddd, *J* = 15.0, 7.0, 1.6 Hz, 1H, H-16), 4.30 (d, *J* = 7.1 Hz, 1H, H-15), 3.53 (t, *J* = 5.6 Hz, 1H, H-12), 2.14 (t, *J* = 7.6 Hz, 3H, H-2), 1.75 (d, *J* = 6.7 Hz, 3H, H-18), 1.59 (p, *J* = 7.1 Hz, 2H, H-3), 1.49 – 1.40 (m, 2H, H-12), 1.38 – 1.24 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.09, 155.48 (t, *J* = 5.8 Hz), 130.49, 128.15, 68.51, 54.79 (t, *J* = 5.9 Hz), 44.18 (p, *J* = 20.1 Hz), 39.31, 38.34, 30.87, 30.76, 30.74, 30.72, 30.66, 27.82, 26.60, 17.57. ESI-HRMS calcd for $C_{19}H_{30}D_2NO_3^-$ $[M - H]^-$ 324.2513, found 324.2523.

S2.11 Synthesis of (±)-[15-^{2}H]-38

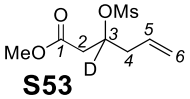


Scheme S11. Chemical synthesis of (±)-[15-^{2}H]-**38**.



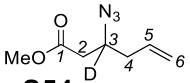
S52

Methyl 3-hydroxyhex-5-enoate-3-*d* (S52). Compound **S52** was synthesized from **S19** based on the same method as described for **S20** except that $NaBD_4$ was used as the reductant. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 – 5.76 (m, 1H, H-5), 5.19 – 5.09 (m, 2H, H-6), 3.71 (s, 3H, OMe), 2.53 (d, *J* = 16.4 Hz, 1H, H_a-2), 2.44 (d, *J* = 16.4 Hz, 1H, H_b-2), 2.30 (dd, *J* = 10.9, 4.0 Hz, 1H, H_a-4), 2.26 (dd, *J* = 11.2, 4.1 Hz, 1H, H_b-4). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.30, 134.05, 118.40, 67.09 (t, *J* = 22.5 Hz), 51.91, 40.99, 40.50. ESI-HRMS calcd for $C_7H_{12}DO_3^+$ $[M + H]^+$ 146.0922, found 146.0914.



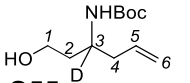
S53

Methyl 3-((methylsulfonyl)oxy)hex-5-enoate-3-*d* (S53). Compound **S53** was synthesized from **S52** based on the same method as described for **S21**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 – 5.72 (m, 1H, H-5), 5.23 – 5.14 (m, 2H, H-6), 3.71 (s, 3H, OMe), 3.03 (s, 3H, Ms), 2.75 (d, *J* = 16.7 Hz, 1H, H_a-2), 2.66 (d, *J* = 16.7 Hz, 1H, H_b-2), 2.57 (d, *J* = 7.1 Hz, 2H, H-4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.50, 131.61, 120.10, 77.88 (t, *J* = 23.3 Hz), 52.18, 39.39, 38.58, 38.55. ESI-HRMS calcd for $C_8H_{14}DO_5S^+$ $[M + H]^+$ 224.0697, found 224.0701.



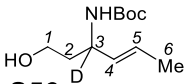
S54

Methyl 3-azidohex-5-enoate-3-*d* (S54). Compound **S54** was synthesized from **S53** based on the same method as described for **S22**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 – 5.73 (m, 1H, H-5), 5.22 – 5.14 (m, 2H, H-6), 3.72 (s, 3H, OMe), 2.53 (d, *J* = 16.1 Hz, 1H, H_a-2), 2.46 (d, *J* = 16.2 Hz, 1H, H_b-2), 2.38 (dd, *J* = 14.0, 6.7 Hz, 1H, H_a-4), 2.32 (dd, *J* = 14.3, 4.9 Hz, H_b-4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.26, 133.05, 119.22, 58.05 (t, *J* = 22.5 Hz), 52.11, 38.73, 38.61.



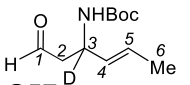
S55

***tert*-Butyl (1-hydroxyhex-5-en-3-yl-3-*d*)carbamate (S55)**. Compound **S55** was synthesized from **S54** based on the same method as described for **S23**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.71 (m, 1H, H-5), 5.16 – 5.07 (m, 2H, H-6), 3.70 – 3.57 (m, 2H, H-1), 2.28 (dd, *J* = 14.3, 7.4 Hz, 1H, H_a-4), 2.22 (dd, *J* = 14.3, 7.0 Hz, 1H, H_b-4), 1.89 – 1.78 (m, 1H, H_a-2), 1.39 – 1.30 (m, 1H, H_b-2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.13, 134.16, 118.34, 80.13, 58.99, 46.22, 39.74, 38.30, 28.48. ESI-HRMS calcd for $C_{11}H_{21}DNO_3^+$ $[M + H]^+$ 217.1657, found 217.1650.



S56

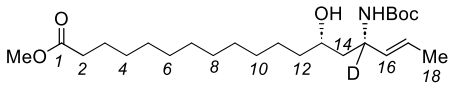
***tert*-Butyl (*E*)-(1-hydroxyhex-4-en-3-yl-3-*d*)carbamate (S56)**. Compound **S56** was synthesized from **S55** based on the same method as described for **S24**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (dq, *J* = 15.5, 6.5 Hz, 1H, H-5), 5.42 (dd, *J* = 15.6, 2.1 Hz, 1H, H-4), 3.68 – 3.60 (m, 3H, H-1), 1.87 – 1.82 (m, 1H, H_a-2), 1.69 (dd, *J* = 6.4, 1.7 Hz, 3H, H-6), 1.44 (t, *J* = 1.1 Hz, 10H, *t*-Bu and H_b-2).



S57

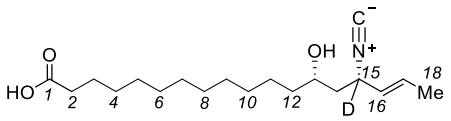
***tert*-Butyl (*E*)-(1-oxohex-4-en-3-yl-3-*d*)carbamate (S57)**. Compound **S57** was synthesized from **S56** based on the same method as described for **S25**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (t, *J* = 2.0 Hz, 1H, H-

1), 5.65 (dq, *J* = 15.3, 6.4 Hz, 1H, H-5), 5.46 (dd, *J* = 15.3, 1.9 Hz, 1H, H-4), 2.67 (d, *J* = 1.9 Hz, 2H, H-2), 1.68 (dd, *J* = 6.4, 1.6 Hz, 3H, H-6), 1.43 (s, 9H, *t*-Bu).



(±)-**S58**

(±)-Methyl (13*S*,15*S*,*E*)-15-((*tert*-butoxycarbonyl)amino)-13-hydroxyoctadec-16-enoate-15-*d* ((±)-S58). Compound (±)-**S58** was synthesized from **S57** and **S15** based on the same method as described for **S7**-*syn*. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 – 5.61 (m, 1H, H-17), 5.36 (dd, *J* = 15.4, 1.9 Hz, 1H, H-16), 3.68 – 3.64 (m, 1H, H-13), 3.66 (s, 3H, OMe), 2.30 (t, *J* = 7.5 Hz, 2H, H-2), 1.68 (dd, *J* = 6.5, 1.7 Hz, 3H, H-18), 1.62 – 1.58 (m, 4H, H-3 and H-14), 1.45 – 1.42 (m, 11H, H-12 and *t*-Bu), 1.30 – 1.23 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.53, 155.70, 131.77, 126.67, 79.70, 69.99, 51.60, 43.25, 38.04, 34.27, 29.75, 29.73, 29.68, 29.56, 29.38, 29.29, 28.56, 25.72, 25.10, 17.87. ESI-HRMS calcd for $C_{24}H_{45}DNO_5^+$ $[M + H]^+$ 429.3433, found 429.3459.



(±)-[15-^{2}H]-**38**

(±)-**(13*S*,15*S*,*E*)-13-hydroxy-15-isocyanooctadec-16-enoic-15-*d* acid ((**±)-[15-^{2}H]-**38)**. Compound (±)-[15-^{2}H]-**38** was synthesized from (±)-**S58** based on the same method as described for (±)-**38**. ^{1}H NMR (500 MHz, CD_3OD) δ 5.83 (dq, *J* = 15.2, 6.6 Hz, 1H, H-17), 5.47 (dd, *J* = 14.9, 2.0 Hz, 1H, H-16), 3.54 (dddd, *J* = 8.6, 8.6, 3.9, 3.9 Hz, 1H, H-13), 2.14 (t, *J* = 7.4 Hz, 2H, H-2), 1.84 (dd, *J* = 13.5, 8.9 Hz, 1H, H_a-14), 1.75 (dd, *J* = 6.6, 1.7 Hz, 3H, H-18), 1.73 – 1.70 (m, 1H, H_b-14), 1.59 (p, *J* = 7.1 Hz, 2H, H-3), 1.47 – 1.43 (m, 2H, H-12), 1.34 – 1.28 (m, 16H, H-4, H-5, H-6, H-7, H-8, H-9, H-10, and H-11). ^{13}C NMR (126 MHz, CD_3OD) δ 183.13, 155.50 (t, *J* = 5.3 Hz), 130.53, 128.13, 68.60, 54.65 (tt, *J* = 21.6, 6.6 Hz), 44.84, 39.34, 38.39, 30.88, 30.76, 30.74, 30.72, 30.67, 27.83, 26.61, 17.58. ESI-HRMS calcd for $C_{19}H_{31}DNO_3^-$ $[M - H]^-$ 323.2450, found 323.2456.

S3. Gene deletion and complementation of *aecF*

The deletion and complementation of *aecF* in *Chromobacterium violaceum* ATCC 53434 was conducted based on the reported method for the deletion and complementation of *aecE*.[11] The native *aec* promoter was used in the plasmid for the complementation experiment. The primers are listed in Table S1.

Chromobacterium violaceum ATCC 53434 strains were inoculated into 25 mL media containing 0.5% tryptone, 0.3% yeast extract, 0.3% malt extract, 1% *N*-acetyl-glucosamine in 3-(*N*-morpholino)propanesulfonic acid (MOPS) buffer (100 mM, pH 7.0). For the *aecF* complemented strain which harbors a pBBR1MCS-2 derived plasmid, the medium was supplemented with 50 μg/mL kanamycin. The cultures were incubated at 25 ℃ with shaking (140 rpm) for 3 or 4 days. The culture supernatants were obtained by centrifugation (4000 × *g* for 10 min) with the pH subsequently adjusted to 6.0 prior to extraction with ethyl acetate (3 × 25 mL). The ethyl acetate was then removed under reduced pressure at room temperature, and the residue was redissolved in acetonitrile (200 μL) for LCMS analysis using the method as described in Section S1. Production of aerocyanidin (ESI-HRMS calcd for $C_{15}H_{24}NO_4^-$ $[M-H]^-$: 282.1711, found: 282.1711) from the wildtype strain was confirmed by LCMS and MS analysis as shown in Figure S20.

S4. Heterologous expression experiments

To construct plasmids for heterologous expression, the five *aec* genes of the cluster were PCR-amplified from the genomic DNA of *Chromobacterium violaceum* ATCC 53434 using primers shown in

Table S1. The PCR-amplified gene fragments were digested with the corresponding restriction enzymes and cloned into pETDuet-1, pCDFDuet-1, pACYCDuet-1, respectively (see Figure S21).

The plasmids were used to transform the *E. coli* K207 strain for heterologous expression. An overnight culture grown in the LB medium (1 mL) containing 25 μg/mL ampicillin, 25 μg/mL streptomycin and 12.5 μg/mL chloramphenicol was used to inoculate 100 mL of the same growth medium. The culture was incubated at 37 °C with shaking (200 rpm) until the OD_{600} reached ~0.6. Heterologous expression was then induced by the addition of isopropyl *β*-D-1-thiogalactopyranoside (IPTG), glycine and crotonic acid to final concentrations of 0.5 mM, 1 mM and 1 mM, respectively. The cells were then allowed to grow at 20 °C and 160 rpm for additional 3 days.

The culture supernatant was obtained by centrifugation (3500 × *g* for 10 min) with the pH subsequently adjusted to 6.0 prior to extraction with ethyl acetate (3 × 50 mL). The ethyl acetate was then removed under reduced pressure at room temperature, and the residue was redissolved in acetonitrile (200 μL) for LCMS analysis using the method as described in Section S1.

S5. Protein overexpression and purification

The *aecA*, *aecB*, *aecC*, *aecD* and *aecE* genes were individually amplified by polymerase chain reaction (PCR) from the genomic DNA of *Chromobacterium violaceum* ATCC 53434, while the *amcA*, *amcB*, *amcC*, *amcD*, *amcE*, *amcF*, *amcG*, *amcH*, and *amcQ* were respectively amplified from the genomic DNA of *Amycolatopsis* sp. AA4. The DNA fragments were digested with the corresponding restriction enzymes and ligated into the pET28b(+) vector. The primers used in the cloning are shown in Table S1.

The resulting plasmids were used to transform *E. coli* BL21 Star (DE3) cells. The overnight culture of each recombinant strain grown at 37 ℃ in Luria broth (LB) medium containing 50 μg/mL kanamycin was used to inoculate 1 L of the same medium in a 100-fold dilution. These cultures were incubated at 37 ℃ with shaking (200 rpm) until the OD 600 reached ~0.6. Protein expression was then induced by the addition of isopropyl β-D-1-thiogalactopyranoside (IPTG) to a final concentration of 0.1 mM. After overnight incubation at 18 ℃ (120 rpm), the cells were harvested by centrifugation at 4000 × g for 10 min and stored at –80 °C until lysis. For expressing the three P450 enzymes (i.e., AmcB, AmcC and AmcQ), 1 mM 5-aminolevulinic acid (5-ALA) and 1 mM $Fe(NH_4)_2(SO_4)_2$ were added during induction apart from IPTG.

All purification steps were carried out at 4 °C. The thawed cells were resuspended in 50 mM 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) buffer (pH 7.5) containing 10% (v/v) glycerol, 10 mM imidazole, and 300 mM NaCl. The cells were disrupted by sonication using 10 × 10 s pulses with a 20 s cooling pause between each pulse. The resulting lysate was centrifuged at 18,000 × *g* for 35 min, and the supernatant was subjected to Ni-nitrilotriacetic acid (NTA) resin. Bound protein was eluted using 50 mM HEPES buffer (pH 7.5) buffer containing 10% (v/v) glycerol, 250 mM imidazole, and 300 mM NaCl. The collected protein solution was dialyzed against 3 × 1 L of 50 mM HEPES buffer (pH 7.5) containing 300 mM NaCl and 10% (v/v) glycerol. The protein solution was then flash-frozen in liquid nitrogen and stored at –80 °C until use. All the proteins were obtained as *N*-His_6-tagged proteins. The SDS-PAGE of purified enzymes are shown in Figure S1.

The heme contents ([heme]/[protein]) in AmcB, AmcC and AmcQ were measured by UV-vis spectrometry using the following extinction coefficients predicted by Benchling: ε_{280} = 50420 $M^{-1}\cdot cm^{-1}$ (for AmcB), ε_{280} = 44920 $M^{-1}\cdot cm^{-1}$ (for AmcC), and ε_{280} = 43430 $M^{-1}\cdot cm^{-1}$ (for AmcQ). The extinction coefficient for heme is ε_{416} = 110000 $M^{-1}\cdot cm^{-1}$ according to the literature.[12] The UV-vis spectra of the three P450 enzymes are shown in Figure S22. The heme contents in AmcB, AmcC and AmcQ were thus respectively determined to be 40%, 9%, 39%.

S6. *In vitro* enzymatic assays

S6.1 AecB assay conditions

A solution of 2 mM compound **16** was incubated with 10 μM AecB and 5 mM glycine in 50 mM HEPES buffer (pH 7.5) at room temperature in a volume of 50 μL for 3 h. The reaction was quenched by

adding 50 µL methanol and centrifuged at 21130 × *g* for 10 min. The supernatant was diluted 10-fold with water before subjected to LCMS analysis using the method as described in Section S1.

For the Marfey's analysis of the AecB product, the AecB reaction was conducted in potassium phosphate buffer (50 mM, pH 7.4). The reaction supernatant was mixed with 200 µL Marfey's reagent (10 mg/mL in acetone), 50 µL 1 M $NaHCO_3$ aqueous solution and 50 µL DMSO. The mixture was incubated at 40 °C for 1 h. The reaction was quenched by adding 25 µL 2 M HCl. The resultant solution was diluted 10-fold with water before subjected to LCMS analysis using InfinityLab Poroshell 120 Chiral-CF column (2.7 µm, 4.6 × 100 mm) at a flow rate of 0.4 mL/min using 0.1% formic acid in H_2O (solvent A) and acetonitrile (solvent B) with the following gradient program: 0–5 min 5–95% B, 5–11 min 95% B, 11–13 min 95–5% B, 13–15 min 5% B.

S6.2 AecA assay conditions

A solution of 1 mM compound **13** was incubated with 20 µM AecA, 4 mM ascorbic acid, 5 mM α-KG, and 0.2 mM $Fe(NH_4)_2(SO_4)_2$ in 50 mM HEPES buffer (pH 7.5) at room temperature under aerobic atmosphere in a volume of 50 µL for 30 min. The reaction was quenched by adding 50 µL methanol and centrifuged at 21130 × *g* for 10 min. The supernatant was diluted 10-fold with water before subjected to LCMS analysis using the method as described in Section S1.

For the Marfey's analysis of the AecA product, the AecA reaction was quenched by first adding 50 µL methanol and 5 µL concentrated HCl and then stirred at room temperature for 5 h. The remainder of the workup was the same as described in Section S6.1. The LCMS analysis method was the same as mentioned in Section S1.

S6.3 AecC and AecE assay conditions

A solution of 1 mM crotonic acid or 1 mM compound **14** was incubated with 5 µM AecE, 20 µM *apo* AecC, 0.6 µM 4′-phosphopantetheinyl transferase (Sfp) from *Bacillus subtilis*, 60 µM coenzyme A (CoA), 10 mM $MgCl_2$, 5 mM tris-(2-carboxyethyl)phosphine (TCEP), 2.5 mM ATP in 50 mM HEPES buffer (pH 7.5) at room temperature in a volume of 50 µL for 2 h. The reaction mixture was quenched by adding 50 µL acetonitrile and centrifuged at 21130 × *g* for 10 min. The supernatant was analyzed by LCMS using an AdvanceBio Peptide Mapping column (Agilent, 2.7 µm, 2.1 × 150 mm) at a flow rate of 0.25 mL/min using 0.1% trifluoroacetic acid (TFA) in H_2O (solvent A) and 0.08% trifluoroacetic acid (TFA) in acetonitrile (solvent B) with the following gradient program: 0–2 min 40% B, 2–15 min 40–60% B, 15–16 min 60–70% B, 16–23 min 70% B, 23–27 min 70–40% B, 27–35 min 40% B. The temperature was set to 40 ℃.

S6.4 AecD assay conditions

A solution of 1 mM compound **14** was incubated with 5 µM AecE, 20 µM *apo*-AecC, 1 µM Sfp, 5 mM CoA, 10 mM $MgCl_2$, 10 mM TCEP, 10 mM ATP, 5 mM malonic acid, 0.5 µM malonyl CoA synthetase (MatB) from *Streptomyces coelicolor*, 10 mM NADPH and 36 µM AecD in 50 mM HEPES buffer (pH 7.5) at room temperature in a volume of 50 µL for 4 h or overnight. The reaction mixture was adjusted to pH 9.5 with 1 M KOH and incubated at room temperature. After 2 h, the proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

S6.5 AmcD assay conditions

A solution of 2 mM compound **39** or 1 mM compound **45** was incubated with 10 µM AmcD and 5 mM glycine in 50 mM HEPES buffer (pH 7.5) at room temperature in a volume of 50 µL for 4 h. The protein was removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

S6.6 AmcD-AmcA coupled assay conditions

An aliquot of 25 µL of AmcD reaction filtrate from Section S6.5 was incubated with 20 µM AmcA, 4 mM ascorbic acid, 5 mM α-KG, and 0.2 mM $Fe(NH_4)_2(SO_4)_2$ in 50 mM HEPES buffer (pH 7.5) at room temperature under aerobic atmosphere in a volume of 50 µL for 1 h. The protein was removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

S6.7 AmcE and AmcH assay conditions

A solution of 1 mM compound **29** or 1 mM compound **30** was incubated with 5 µM AmcH, 20 µM *apo* AmcE, 0.6 µM Sfp, 120 µM CoA, 10 mM $MgCl_2$, 5 mM TCEP, 2.5 mM ATP in 50 mM HEPES buffer (pH 7.5) at room temperature in a volume of 50 µL for 2 h. The reaction mixture was worked up and analyzed using the same method as described in Section S6.3.

S6.8 AmcF and AmcG assay conditions

A solution of 1 mM compound **29** or 1 mM compound **30** was incubated with 5 µM AmcH, 20 µM *apo*-AmcE, 1 µM Sfp, 5 mM CoA, 10 mM $MgCl_2$, 10 mM TCEP, 10 mM ATP, 5 mM malonic acid, 0.5 µM MatB, 10 mM NADPH, 30 µM AmcF, and 10 µM AmcG in 50 mM HEPES buffer (pH 7.5) at room temperature in a volume of 50 µL overnight. The reaction mixture was adjusted to pH 9.5 with 1 M KOH and incubated at room temperature. After 2 h, the proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

S6.9 AmcQ assay conditions

A solution of 0.4 mM compound (±)-**38** was incubated with 20 µM AmcQ (7.8 µM heme), 10 µM CamA, 30 µM CamB, 2.2 units/µL catalase, 10 mM NADH in 50 mM HEPES buffer (pH 7.5) at room temperature under an aerobic atmosphere in a volume of 50 µL for 1 h. The proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

For the $^{18}O_2$ incorporation experiment, a reaction mixture of AmcQ with (±)-**38** was prepared anaerobically as described above. The reaction was initiated by introducing $^{18}O_2$ (97 atom %) using a balloon. After 0.5 h, the protein was removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

For the $H_2{}^{18}O$ incorporation experiment, a same reaction mixture of AmcQ with (±)-**38** as described in above was prepared aerobically in an ^{18}O-containing buffer solution with a volumetric ratio of $H_2{}^{18}O$ (98 atom %) and $H_2{}^{16}O$ of 39.31 to 10.69. After 1 h, the protein was removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

S6.10 AmcB and AmcC assay conditions

A solution of 0.4 mM compound (±)-**38** was incubated with 20 µM AmcB (8.0 µM heme) or 80 µM AmcC (7.2 µM heme), 10 µM CamA, 30 µM CamB, 2.2 units/µL catalase, 10 mM NADH in 50 mM HEPES buffer (pH 7.5) at room temperature under an aerobic atmosphere in a volume of 50 µL for 1 h. The proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

S6.10 AmcB, AmcC and AmcQ coupled assay conditions

A solution of 0.4 mM compound (±)-**38** was incubated with 20 µM AmcB (8.0 µM heme) and 80 µM AmcC (7.2 µM heme), 10 µM CamA, 30 µM CamB, 2.2 units/µL catalase, 10 mM NADH in 50 mM HEPES buffer (pH 7.5) at room temperature under an aerobic atmosphere in a volume of 47.46 µL for 10 min. An aliquot of 2.54 µL of AmcQ stock solution was added to the preceding mixture to a final concentration of 20 µM. After 20 min, the proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

For the $^{18}O_2$ incorporation experiment, a reaction mixture of AmcB and AmcC with (±)-**38** was prepared anaerobically as described above. The reaction was initiated by introducing $^{18}O_2$ (97 atom %) using a balloon. After 10 min, the reaction vial was opened anaerobically. The deaerated AmcQ stock solution was quickly added. The reaction vial was sealed and stirred under the balloon of $^{18}O_2$ for 20 min. The proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

For the $H_2{}^{18}O$ incorporation experiment, a same reaction mixture of AmcB and AmcC with (±)-**38** as described in above was prepared aerobically in an ^{18}O-containing buffer solution with a volumetric ratio of $H_2{}^{18}O$ (98 atom %) and $H_2{}^{16}O$ of 33.05 to 14.41. After 10 min, an aliquot of 2.54 µL of AmcQ stock solution in $H_2{}^{16}O$ buffer was added to the preceding mixture. The proteins were removed using YM-10 centrifugal filtration. The resulting filtrate was analyzed by LCMS using the method described in Section S1.

Supplementary Tables

Table S1. Primers used in this study.

Primer	Sequence (5′ → 3′)	Target	Restriction site
pNP-aecF-left-fwd	GGCCGAAGCTAGCGAATTTGGACTGGCATCCGGAGG	*aecF* deletion	–
pNP-aecF-left-rev	CCAGCCGGGCCTGCTGCCGGTATCAACCTCTCGCAG	*aecF* deletion	–
pNP-aecF-right-fwd	GGCAGCAGGCCCGGCTGG	*aecF* deletion	–
pNP-aecF-right-rev	AAGCCGGCTGGCGCCAAGCTCCTGCTTCAAGTTTACCG	*aecF* deletion	–
pBB-fra1-fwd	GCCTGGGGTGCCTAATGAG	*aecF* complementation	–
pBB-fra1-rev	GTGGGCGAAAAGCTGCTG	*aecF* complementation	–
pBB-fra2-fwd	CAGCAGCTTTTCGCCCAC	*aecF* complementation	–
pBB-fra2-rev-1	CTCCAATTCGCCCTATAGTGAGTC	*aecF* complementation	–
pBB-aecF-fwd	CTCATTAGGCACCCCAGGCATGTACCATCCGCCATTC	*aecF* complementation	–
pBB-aecF-rev	CTATAGGGCGAATTGGAGTCAATCGGCCGCCTGCCG	*aecF* complementation	–
pBB-fra2-rev-2	GACTCCAGGGAGCATGGAATGTACCATCCGCCATTC	*aecF* complementation	–
aec_prom-fwd	TCCATGCTCCCTGGAGTCGCTACAAATC	*aecF* complementation	–
aec_prom-rev	ACTCATTAGGCACCCCAGGCGGGGCGGGCGTCAAGCCG	*aecF* complementation	–
aecA-pETD-fwd	CATG**CCATGG**CA ATGAAGAACCTTGTGATC	*aecA*/*aecB*/pETDuet-1	*NcoI*
aecA-pETD-rev	CCC**AAGCTT**TCAAGCAAGGCTCAGTCC	*aecA*/*aecB*/pETDuet-1	*HindIII*
aecB-pETD-fwd	CGC**CATATG**CTGACGCGACAGCCGGCG	*aecA*/*aecB*/pETDuet-1	*NdeI*
aecB-pETD-rev	CCG**CTCGAG**TCAGGGGTTGAGAATGGCCAG	*aecA*/*aecB*/pETDuet-1	*XhoI*
aecC-pCDF-fwd	CATG**CCATGG**CACTGATAGGGCGGACCCGC	*aecC*/*aecD*/pCDFDuet-1	*NcoI*
aecC-pCDF-rev	CCC**AAGCTT**TTAGACTCCAAATTCCTTTTTCAGGATTTC	*aecC*/*aecD*/pCDFDuet-1	*HindIII*
aecD-pCDF-fwd	GA**AGATCT**TATGGATCACCCGGATTCTCAGCTGGCG	*aecC*/*aecD*/pCDFDuet-1	*BglII*
aecD-pCDF-rev	CCG**CTCGAG**TCATGCCAACTCCTCCACATTGG	*aecC*/*aecD*/pCDFDuet-1	*XhoI*
aecE-pACYC-fwd	CGC**CATATG**AGCGTGGCCGAGACGGTCGTAC	*aecE*/pACYCDuet-1	*NdeI*

aecE-pACYC-rev	CCG**CTCGAG**TCAGACCCGACGCGCCCTGTC	*aecE*/pACYCDuet-1	*XhoI*
aecA-28b-fwd	CGC**CATATG**AAGAACCTTGTGATCAGC	*aecA*/pET28b(+)	*NdeI*
aecA-28b-rev	CCC**AAGCTT**TCAAGCAAGGCTCAGTCC	*aecA*/pET28b(+)	*HindIII*
aecB-28b-fwd	CGC**CATATG**CTGACGCGACAGCCGGCG	*aecB*/pET28b(+)	*NdeI*
aecB-28b-rev	CCC**AAGCTT**TCAGGGGTTGAGAATGGCCAGGTCG	*aecB*/pET28b(+)	*HindIII*
aecC-28b-fwd	CGC**CATATG**CTGATAGGGCGGACCCG	*aecC*/pET28b(+)	*NdeI*
aecC-28b-rev	CCC**AAGCTT**TTAGACTCCAAATTCCTTTTTCAGGATTTC	*aecC*/pET28b(+)	*HindIII*
aecD-28b-fwd	CTA**GCTAGC**ATGGATCACCCGGATTCTCAGCTG	*aecD*/pET28b(+)	*BmtI*
aecD-28b-rev	CCG**CTCGAG**TCATGCCAACTCCTCCACATTGG	*aecD*/pET28b(+)	*XhoI*
aecE-28b-fwd	CGC**CATATG**AGCGTGGCCGAGACGGTC	*aecE*/pET28b(+)	*NdeI*
aecE-28b-rev	CCG**CTCGAG**TCAGACCCGACGCGCCCT	*aecE*/pET28b(+)	*XhoI*
amcA-28b-fwd	CGC**CATATG**GTCGTCAGCAAGCAGGCTG	*amcA*/pET28b(+)	*NdeI*
amcA-28b-rev	CCC**AAGCTT**TCAGGCTCCGGCGTCGAA	*amcA*/pET28b(+)	*HindIII*
amcB-28b-fwd	CGC**CATATG**ACGAGCAAATGCCCGTTC	*amcB*/pET28b(+)	*NdeI*
amcB-28b-rev	CCC**AAGCTT**TCACGGGCGGAGCGACAC	*amcB*/pET28b(+)	*HindIII*
amcC-28b-fwd	CGC**CATATG**CCGAGCAAATGCCCAGTC	*amcC*/pET28b(+)	*NdeI*
amcC-28b-rev	CCC**AAGCTT**TCATCGGACGGTCACCGG	*amcC*/pET28b(+)	*HindIII*
amcD-28b-fwd	CGC**CATATG**AGGACGGACGAACACCCG	*amcD*/pET28b(+)	*NdeI*
amcD-28b-rev	CCC**AAGCTT**TCAGACGGGATTGGAGAT	*amcD*/pET28b(+)	*HindIII*
amcE-28b-fwd	CGC**CATATG**CTGCTGGCGCTGCCG	*amcE*/pET28b(+)	*NdeI*
amcE-28b-rev	CCC**AAGCTT**TCAGTGTTCGTAGAGGTCTTCGAGCAGGGA	*amcE*/pET28b(+)	*HindIII*
amcF-28b-fwd	CGC**CATATG**GTGTCCGAGACCCGCGCC	*amcF*/pET28b(+)	*NdeI*
amcF-28b-rev	CCC**AAGCTT**TCACATCCCCCGCAGCGC	*amcF*/pET28b(+)	*HindIII*
amcG-28b-fwd	CGC**CATATG**CCGGGACCGGCGCG	*amcG*/pET28b(+)	*NdeI*
amcG-	CCC**AAGCTT**TCATGACCAGCGATGCGTTTC	*amcG*/pET28b(+)	*HindIII*

28b-rev	AGGCCA		
amcH-28b-fwd	CGC**CATATG**TACTACGGCGAGCTG	*amcH*/pET28b(+)	*NdeI*
amcH-28b-rev	CCC**AAGCTT**TCAATTCACCTTACGAGC	*amcH*/pET28b(+)	*HindIII*
amcQ-28b-fwd	CGC**CATATG**CAGAACACCTCTGAGCTG	*amcQ*/pET28b(+)	*NdeI*
amcQ-28b-rev	CCC**AAGCTT**TCACGACACCGTTTCGGG	*amcQ*/pET28b(+)	*HindIII*

Supplementary Figures

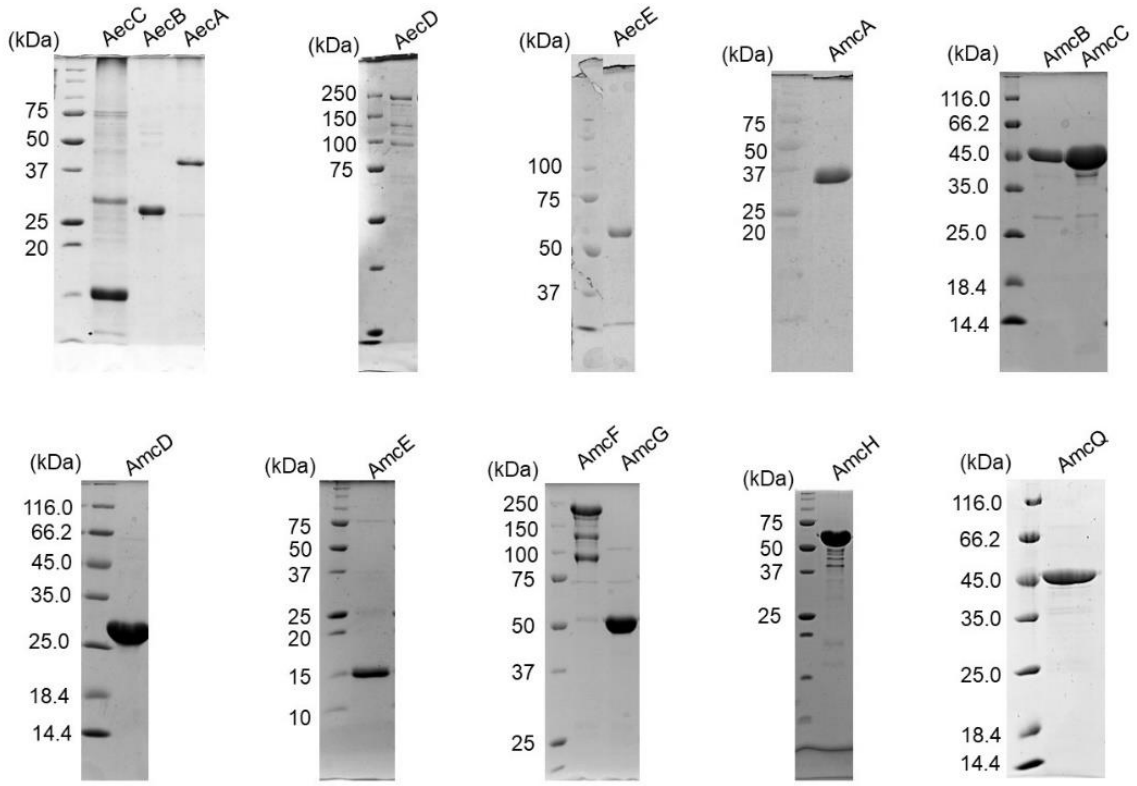


Figure S1. SDS-PAGE analysis of purified *N*-His_6 tagged proteins, including AecA (36.3 kDa), AecB (22.0 kDa), AecC (16.5 kDa), AecD (227.7 kDa), AecE (59.5 kDa), AmcA (35.2 kDa), AmcB (47.7 kDa), AmcC (47.9 kDa), AmcD (23.6 kDa), AmcE (15.1 kDa), AmcF (228.6 kDa), AmcG (56.0 kDa), AmcH (59.0 kDa), and AmcQ (48.2 kDa).

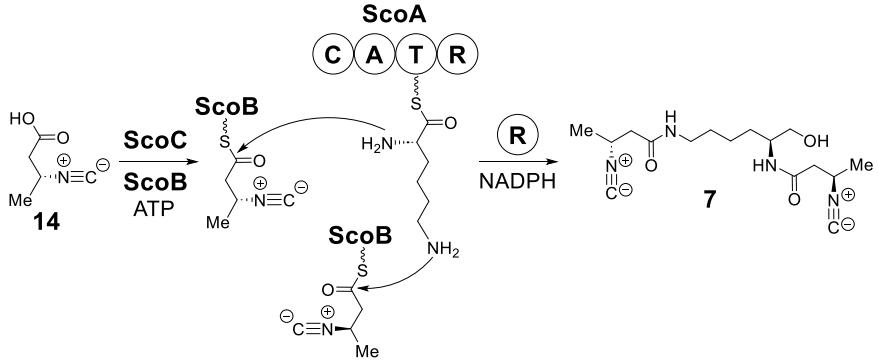


Figure S2. Late stages of the biosynthesis of INLP-1 (**7**).

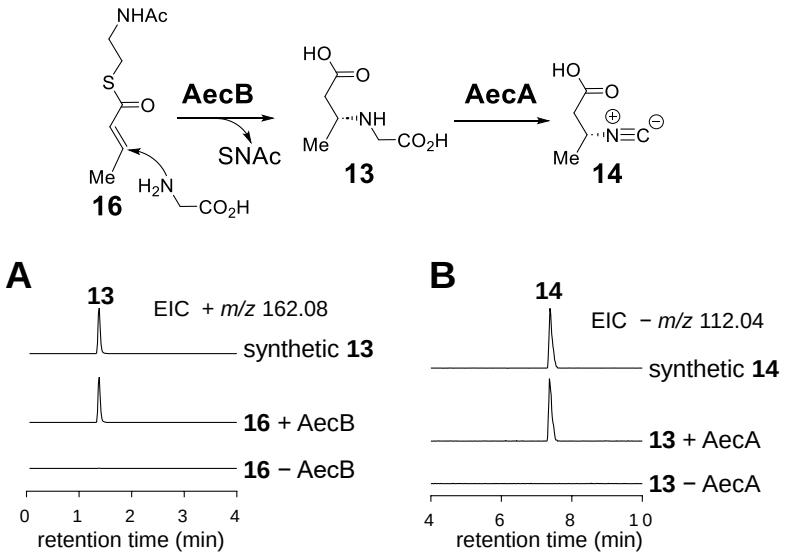


Figure S3. LCMS analysis of (A) the AecB reaction and (B) the AecA reaction.

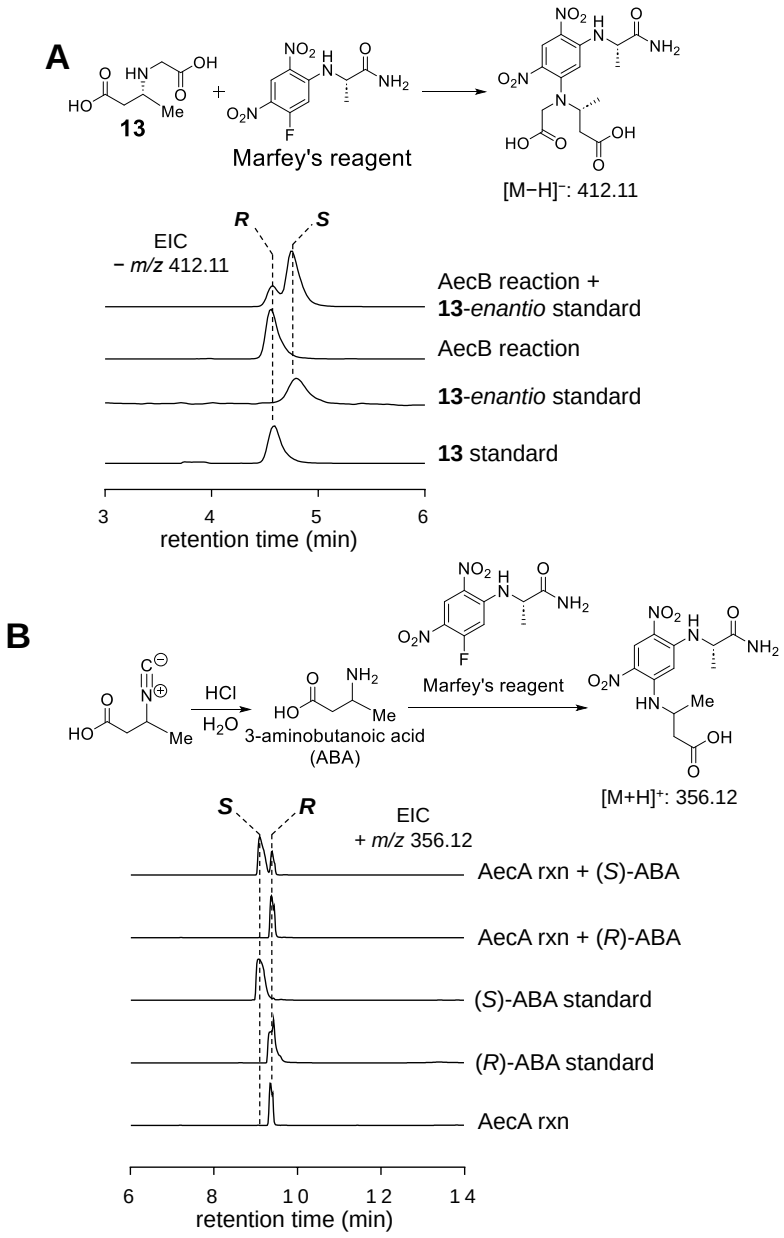


Figure S4. Marfey's analysis of (A) the AecB reaction and (B) the AecA reaction.

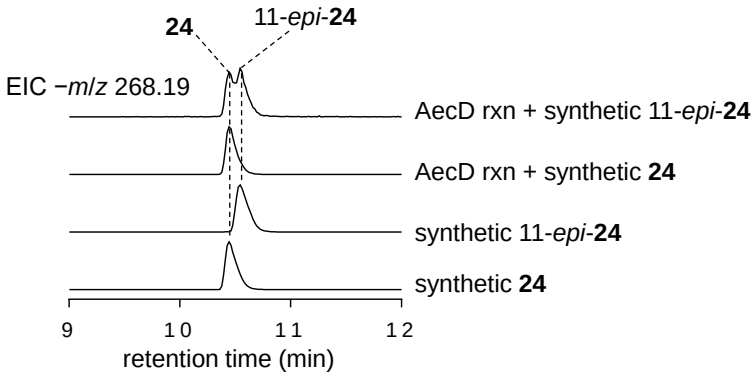


Figure S5. Comparison of **24** produced in the *in vitro* AecD reaction with synthetic **24** and its C11 epimer 11-*epi*-**24**.

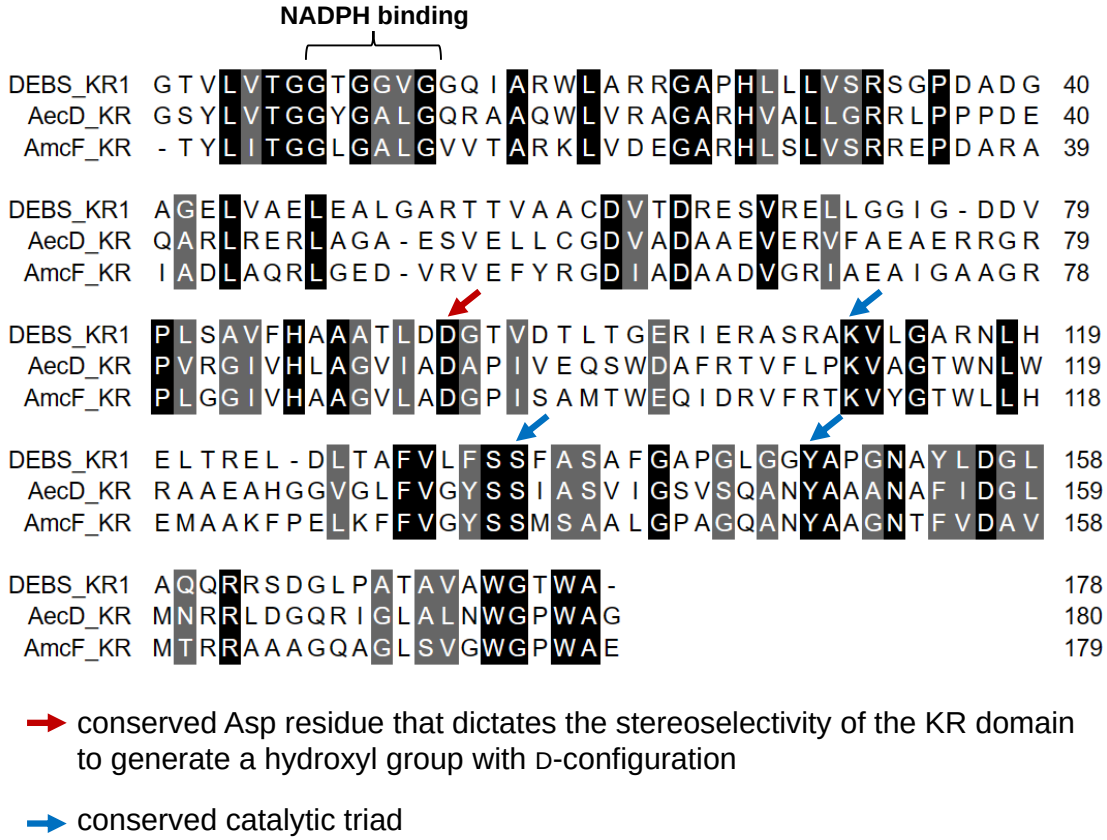


Figure S6. Sequence alignment of the first KR domain of 6-deoxyerythronolide B synthase (DEBS) with the respective KR domains of AecD and AmcF by Clustal Omega.[13]

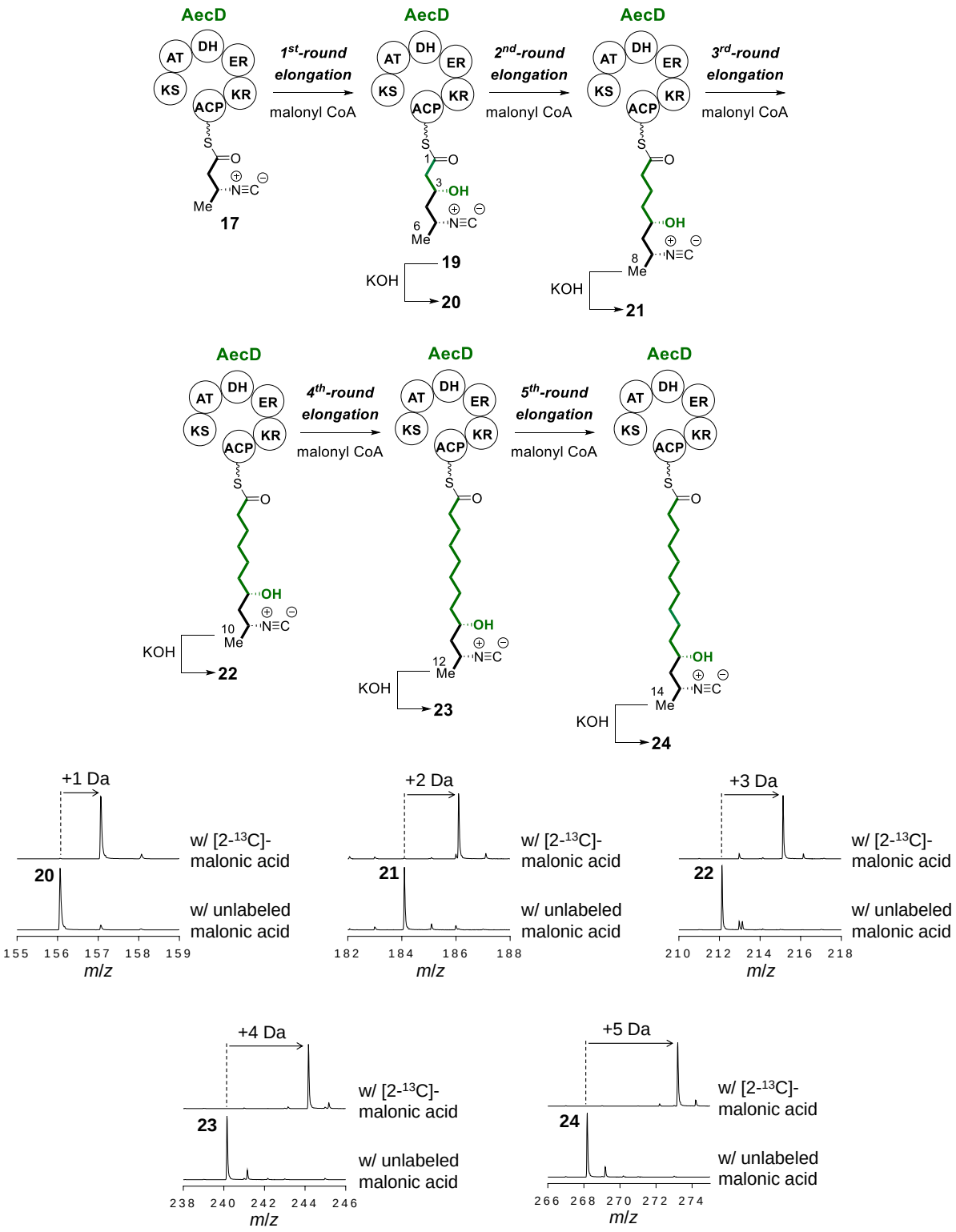


Figure S7. Mass analysis of the chain elongated products in the AecD reaction with unlabeled malonic acid or [2-^{13}C] malonic acid.

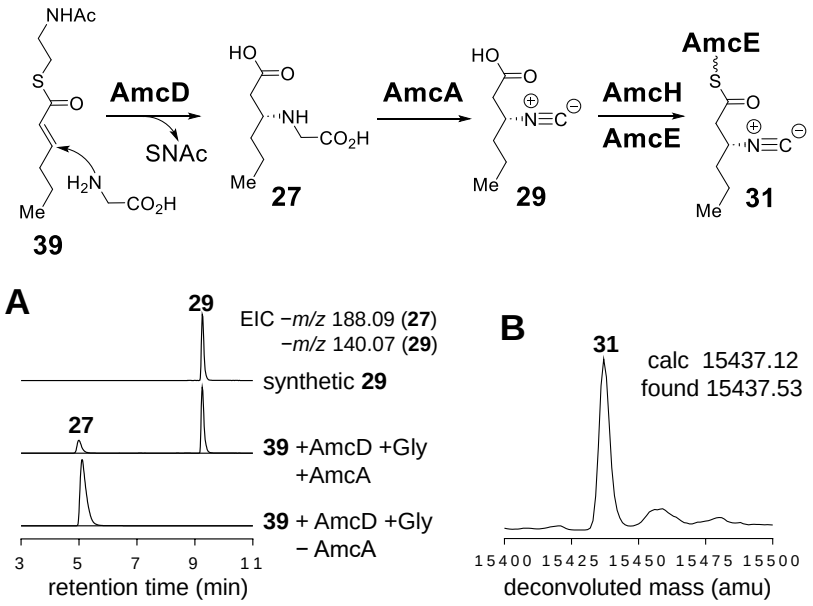


Figure S8. (A) LCMS analysis of the AmcD reaction and the AmcD-AmcA coupled reaction with **39**. (B) Mass analysis of **31**.

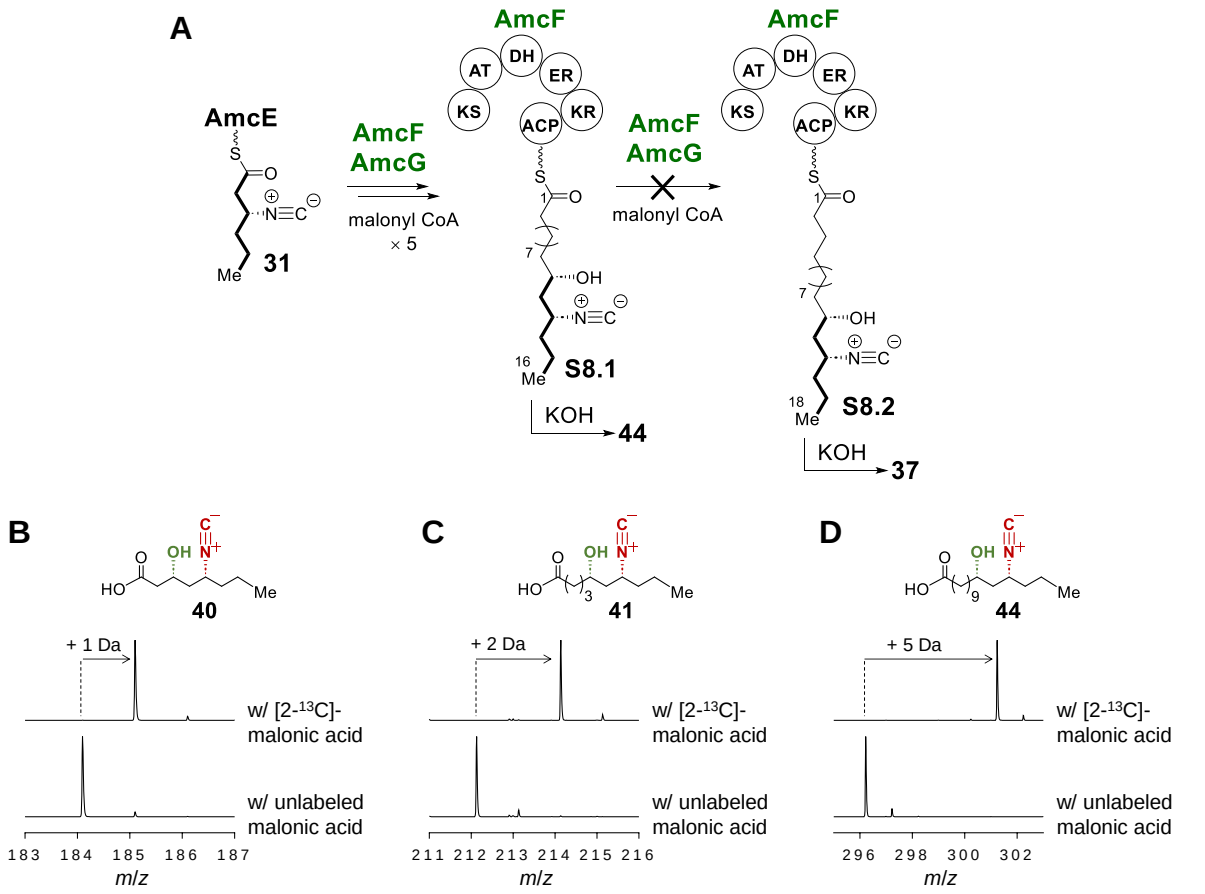


Figure S9. (A) Scheme of the AmcF-AmcG reaction with **31**. The acyl chain of **S8.1** cannot be accepted by AmcF or AmcG to be further elongated to **S8.2** which has the correct carbon chain length as amycomicin. (B) Mass analysis of **40**, (C) **41**, and (D) **44** generated in the AmcF-AmcG reaction with **31** using unlabeled malonic acid or [2-^{13}C]-malonic acid.

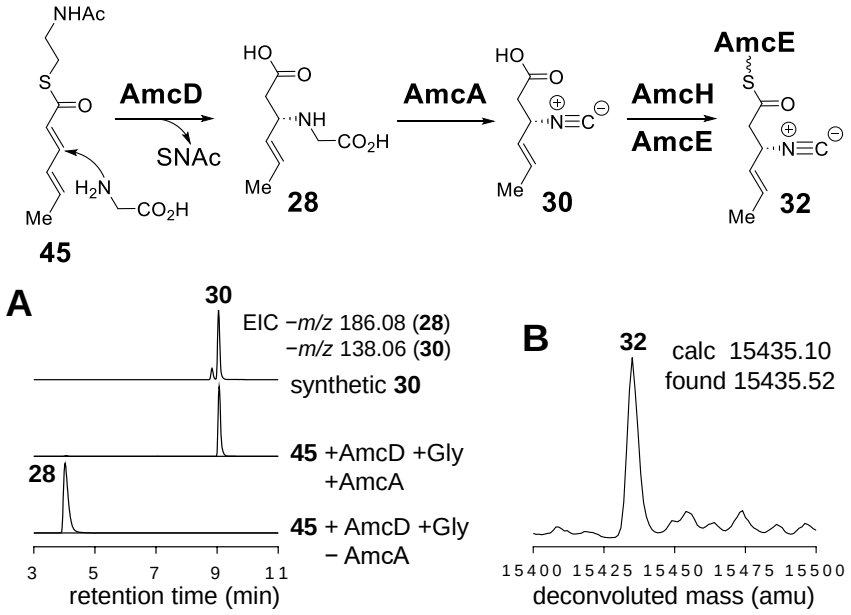


Figure S10. (A) LCMS analysis of the AmcD reaction and the AmcD-AmcA coupled reaction with **45**. (B) Mass analysis of **32**.

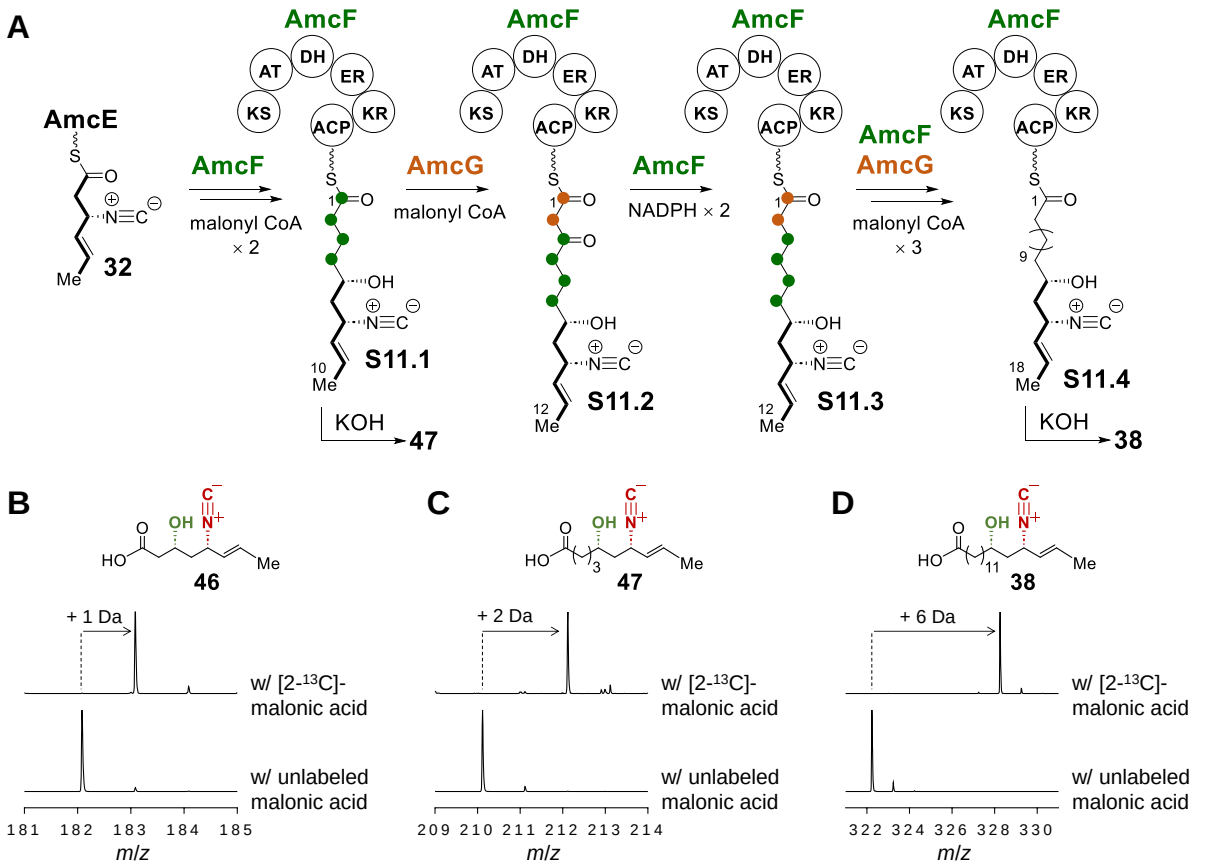


Figure S11. (A) Scheme of the AmcF-AmcG reaction with **32**. The acyl chain of **S11.1** cannot be accepted by AmcF but instead requires AmcG to be further elongated to afford **S11.2**. (B) Mass analysis of **46**, (C) **47**, and (D) **38** generated in the AmcF-AmcG reaction with **32** using unlabeled malonic acid or [2-^{13}C]-malonic acid.

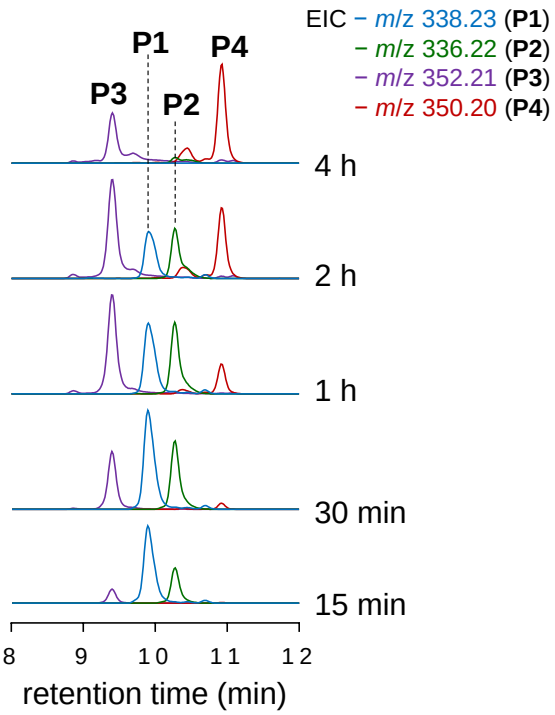


Figure S12. Time course analysis of the AmcQ reaction with **38**.

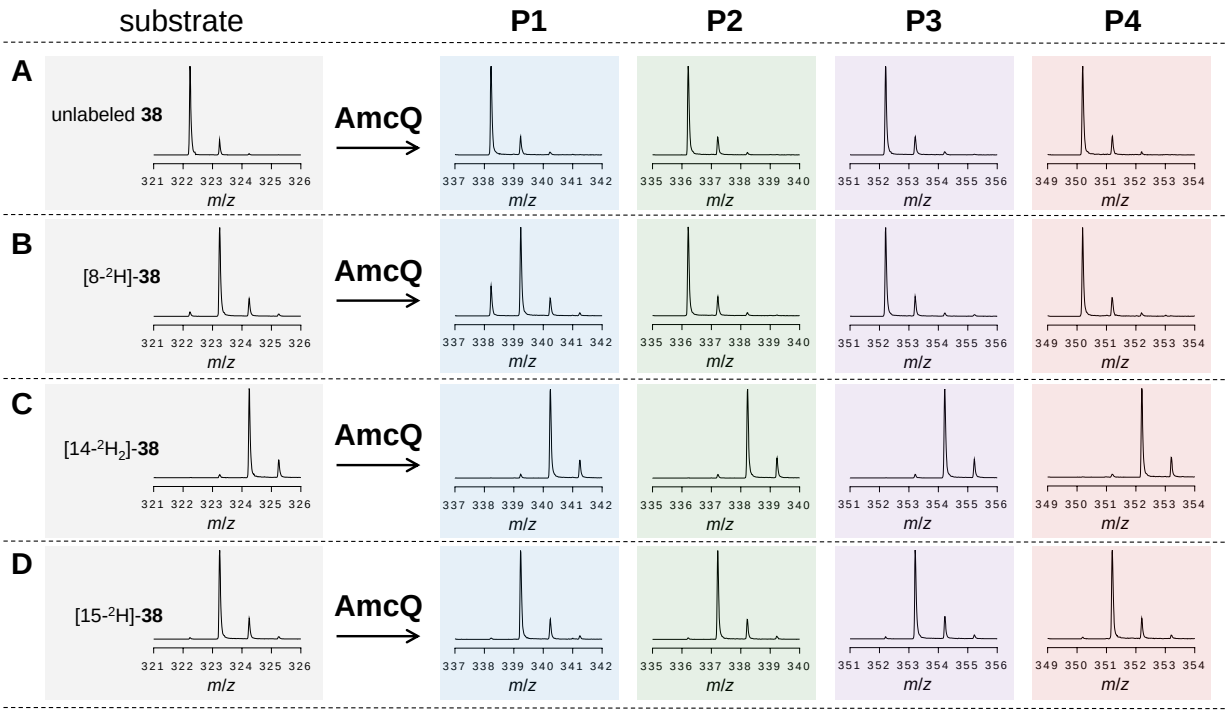


Figure S13. Mass analysis of **P1**, **P2**, **P3** and **P4** generated in the AmcQ reaction with (A) unlabeled **38**, (B) [8-^{2}H]-**38**, (C) [14-^{2}H$_{2}$]-**38** or (D) [15-^{2}H]-**38**.

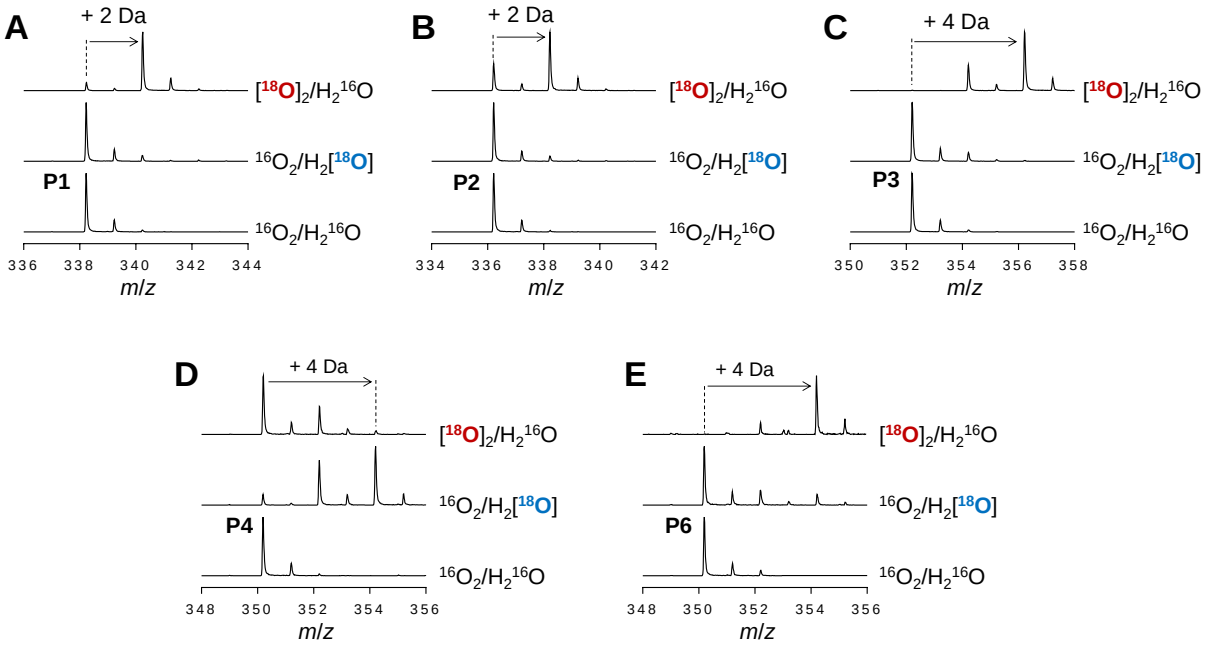


Figure S14. Mass analysis of (A) **P1**, (B) **P2**, (C) **P3** and (D) **P4** generated in the AmcQ reaction with **38** under $^{16}O_2/H_2{}^{16}O$, $^{16}O_2/H_2[^{18}O]$ (77 atom %), or $[^{18}O]_2$ (97 atom %)/$H_2{}^{16}O$. (E) Mass analysis of **P6** generated in the AmcB-AmcC-AmcQ coupled reaction with **38** under $^{16}O_2/H_2{}^{16}O$, $^{16}O_2/H_2[^{18}O]$ (65 atom %), or $[^{18}O]_2$ (97 atom %)/$H_2{}^{16}O$.

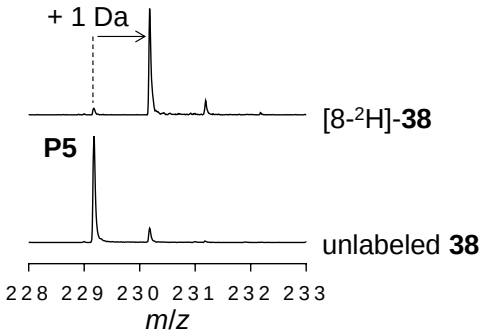


Figure S15. Mass analysis of **P5** generated in the AmcB-AmcC coupled reaction with unlabeled **38** or [8-^{2}H]-**38**.

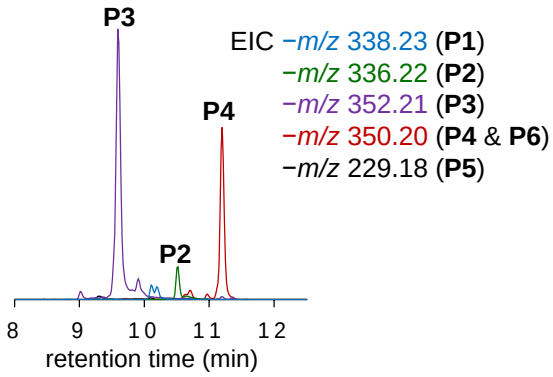


Figure S16. LCMS analysis of the AmcBCQ one-pot reaction with **38** showing EIC traces for **P1**, **P2**, **P3**, **P4**, **P5**, and **P6**.

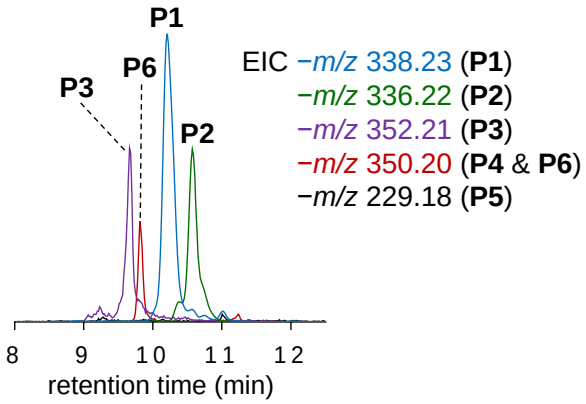


Figure S17. LCMS analysis of the AmcBC-AmcQ sequential reaction showing EIC traces for **P1**, **P2**, **P3**, **P4**, **P5**, and **P6**.

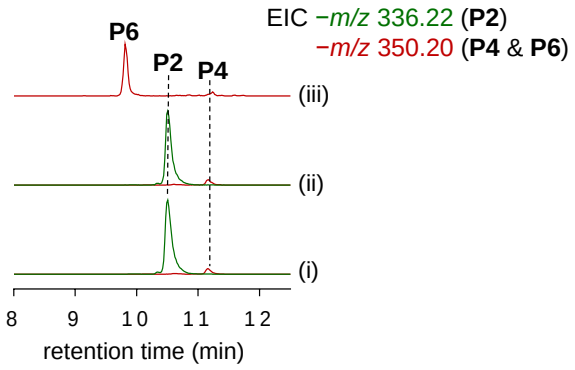


Figure S18. LCMS analysis of the reactions of the P450 enzymes with **38**: (i) incubation of **38** with AmcQ for 20 min; (ii) incubation of **38** with AmcQ for 20 min followed by ultrafiltration to remove AmcQ and then addition of AmcB and AmcC, and incubation for another 10 min; (iii) incubation of **38** with AmcB and AmcC for 10 min followed by addition of AmcQ and incubation for another 20 min.

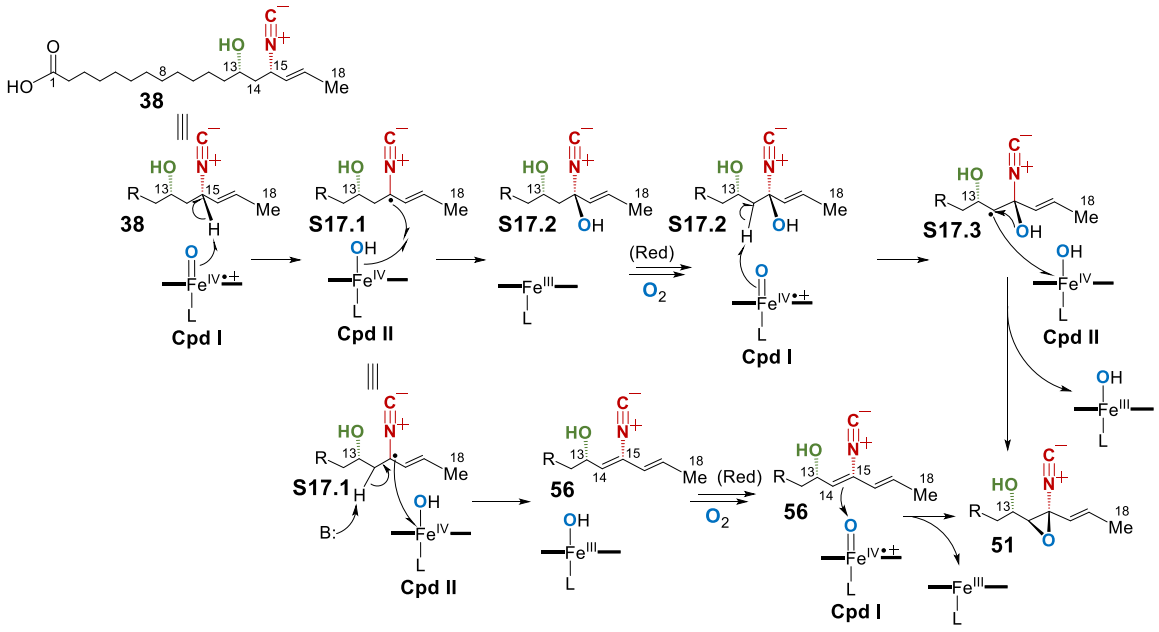


Figure S19. Proposed mechanisms for the AmcB/C catalyzed epoxidation involving the first hydrogen atom abstraction at C15 of **38**. Red stands for the reduction that is required for the resting Fe(III) complex to react with O_2 to form Cpd I.

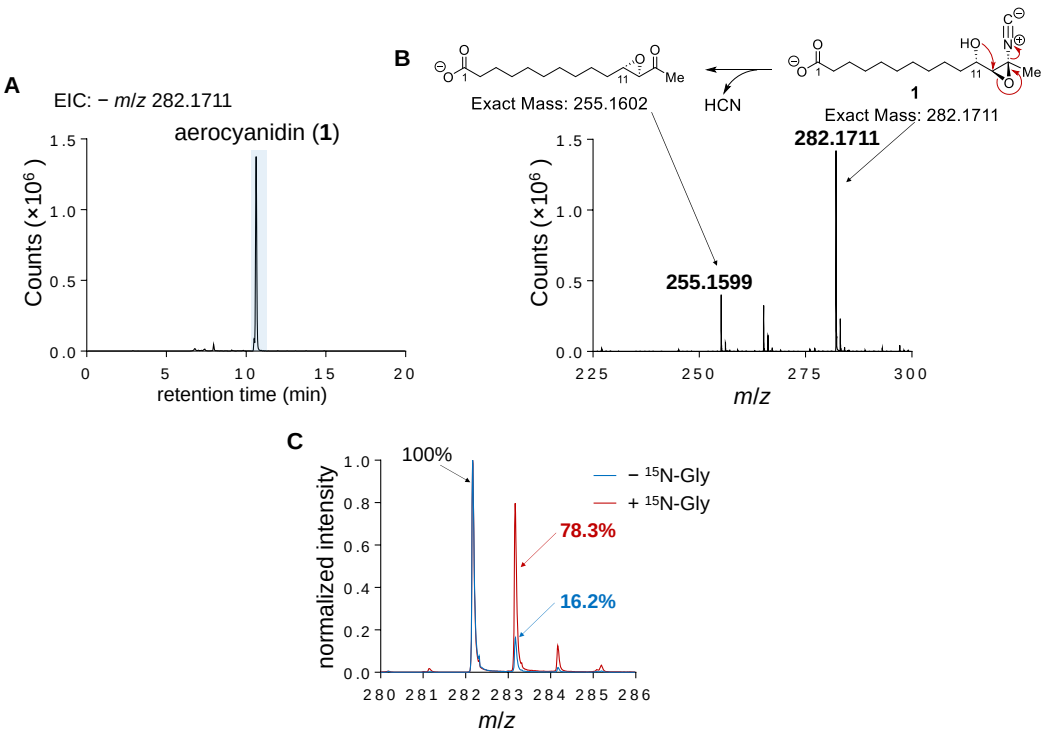


Figure S20. (A) and (B) Production of aerocyanidin (ESI-HRMS calcd for $C_{15}H_{24}NO_4^-$ [M−H]$^-$: 282.1711, found: 282.1711) from the wildtype strain was confirmed by LCMS and MS analysis. (B) The Payne rearrangement product (ESI-HRMS calcd for $C_{14}H_{23}O_4^-$ [M−H]$^-$: 255.1602, found: 255.1599) of aerocyanidin was detected in source in the mass spectrometry. (C) Supplementation of 10 mM [^{15}N]-glycine into the culture medium resulted in the incorporation of ^{15}N into aerocyanidin as revealed by MS analysis.

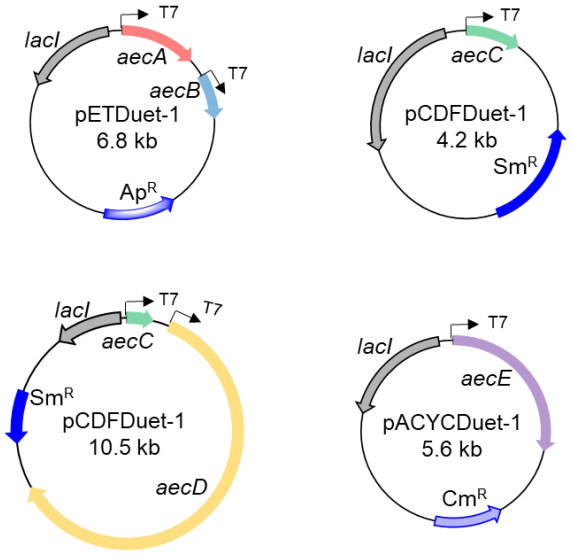


Figure S21. Plasmids constructed for the heterologous expression experiments of *aec* genes.

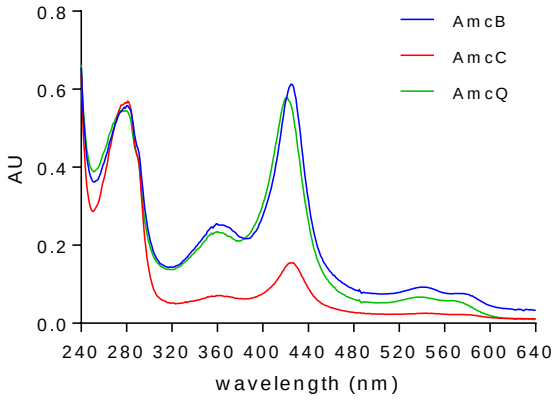
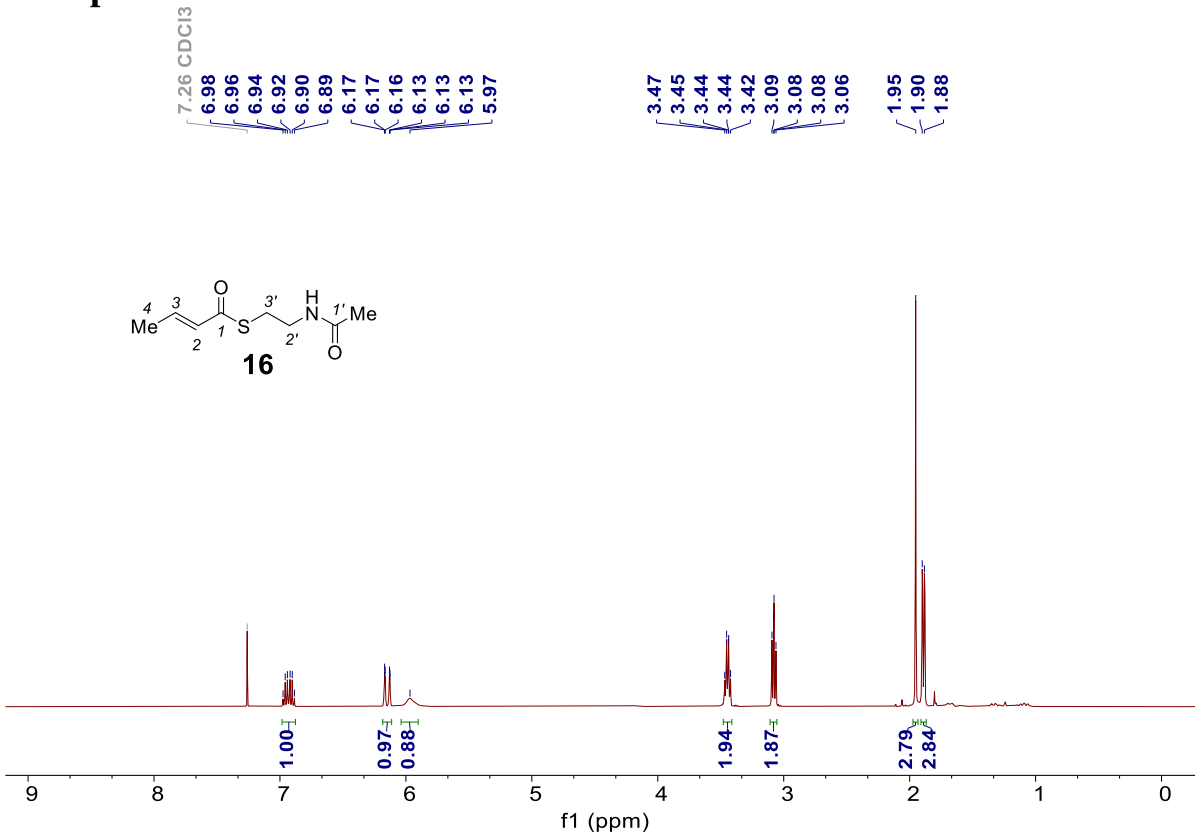


Figure S22. UV-vis spectra of the three P450 enzymes, i.e., AmcB, AmcC and AmcQ.

References

(1) Kovach, M. E.; Elzer, P. H.; Hill, D. S.; Robertson, G. T.; Farris, M. A.; Roop, R. M.; Peterson, K. M. *Gene* **1995**, *166* (1), 175−176.
(2) Chisuga, T.; Miyanaga, A.; Kudo, F.; Eguchi, T. *J. Biol. Chem.* **2017**, *292* (26), 10926−10937.
(3) Takai, K.; Nitta, K.; Fujimura, O.; Utimoto, K. *J. Org. Chem.* **1989**, *54* (20), 4732−4734.
(4) Toujas, J. L.; Toupet, L.; Vaultier, M. *Tetrahedron* **2000**, *56* (17), 2665−2672.
(5) Novotny, J.; Pospechová, K.; Hrabálek, A.; Cáp, R.; Vávrová, K. *Bioorg. Med. Chem. Lett.* **2009**, *19* (24), 6975−6977.
(6) Tyrikos-Ergas, T.; Giannopoulos, V.; Smonou, I. *Molecules* **2018**, *23* (3), 640.
(7) Ren, W. L.; Sun, F.; Chu, J. X.; Shi, Y. *Org. Lett.* **2020**, *22* (5), 1868−1873.
(8) Maki, B. E.; Scheidt, K. A. *Org. Lett.* **2008**, *10* (19), 4331−4334.
(9) Hawkins, D. R.; Calvin, M. *J. Label. Compd. Radiopharm.* **1987**, *24* (10), 1229−1233.
(10) Airiau, E.; Spangenberg, T.; Girard, N.; Breit, B.; Mann, A. *Org. Lett.* **2010**, *12* (3), 528−531.
(11) Pishchany, G.; Mevers, E.; Ndousse-Fetter, S.; Horvath, D. J.; Paludo, C. R.; Silva, E. A.; Koren, S.; Skaar, E. P.; Clardy, J.; Kolter, R. *Proc. Natl. Acad. Sci. U.S.A.* **2018**, *115* (40), 10124−10129.
(12) Nguyen, R. C.; Yang, Y.; Wang, Y.; Davis, I.; Liu, A. *ACS Catal.* **2020**, *10* (2), 1628−1639.
(13) Madeira, F.; Pearce, M.; Tivey, A. R. N.; Basutkar, P.; Lee, J.; Edbali, O.; Madhusoodanan, N.; Kolesnikov, A.; Lopez, R. *Nucleic. Acids. Res.* **2022**, *50* (W1), W276−W279.

NMR spectra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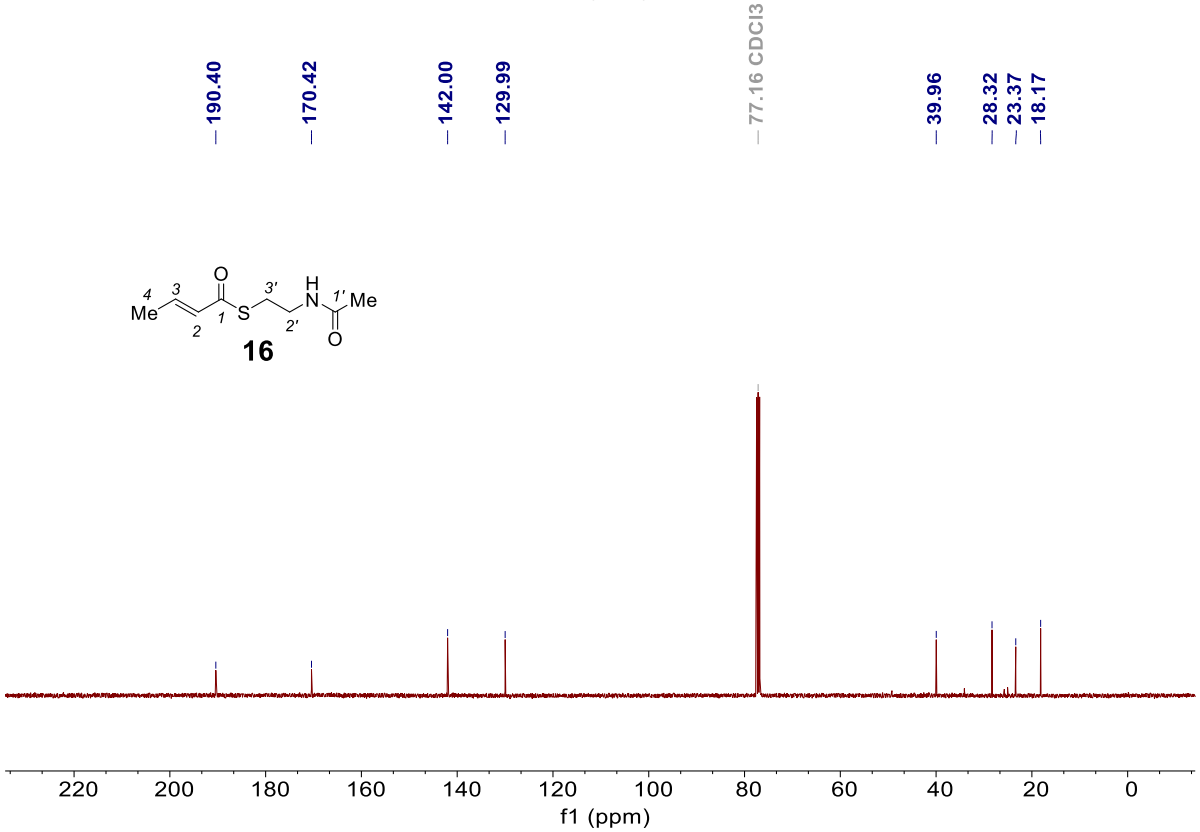
6.96
6.94
6.92
6.90
6.89
6.17
6.17
6.16
6.13
6.13
6.13
5.97
3.47
3.45
3.44
3.44
3.42
3.09
3.08
3.08
3.06
1.95
1.90
1.88
16
1.00
0.97
0.88
1.94
1.87
2.79
2.84
f1 (ppm)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129.99
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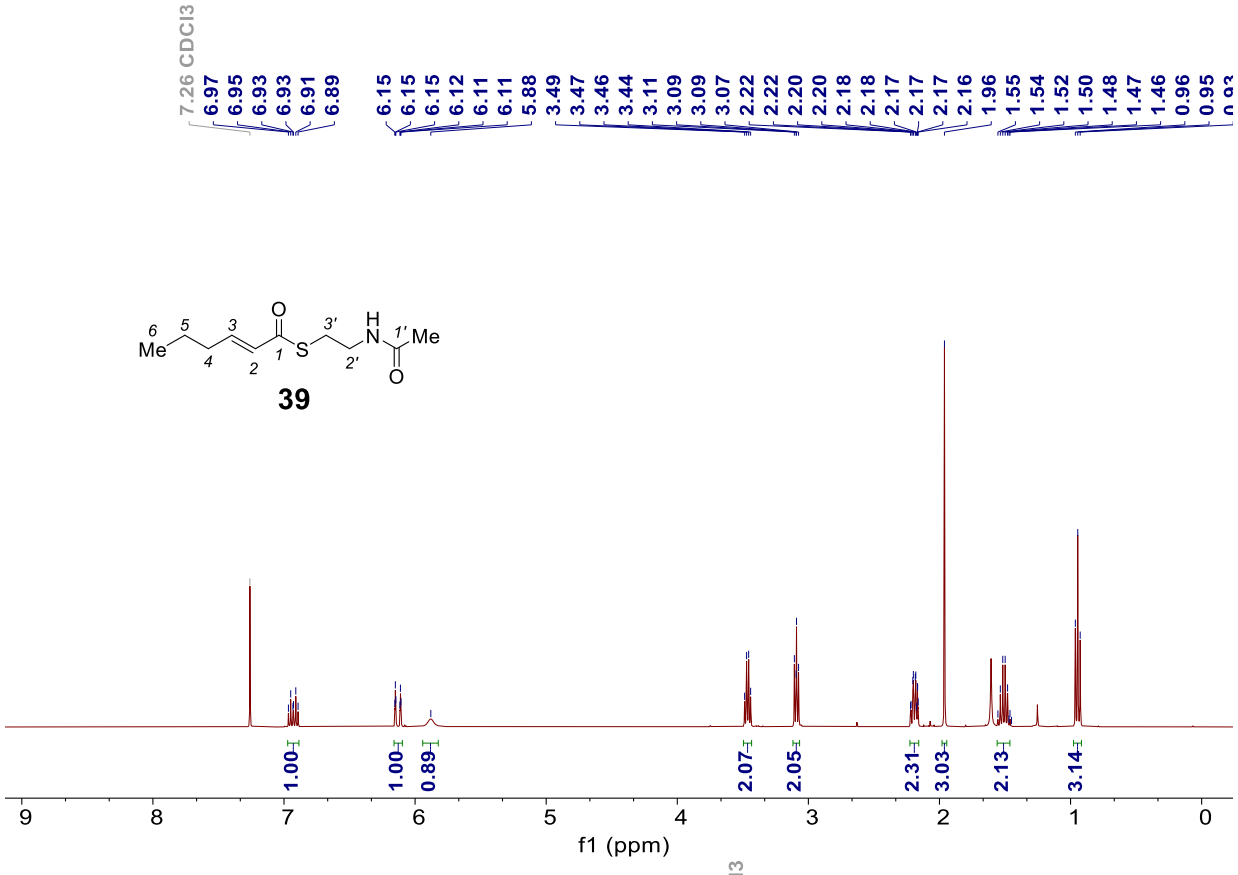
28.32
23.37
18.17
16
f1 (ppm)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6.12
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6.11
5.88
3.49
3.47
3.46
3.44
3.11
3.09
3.09
3.07
2.22
2.22
2.20
2.20
2.18
2.18
2.17
2.17
2.17
2.16
1.96
1.55
1.54
1.52
1.50
1.48
1.47
1.46
0.96
0.95
Me
1
2
3
4
5
6
S
N
H
O
1'
2'
3'
Me
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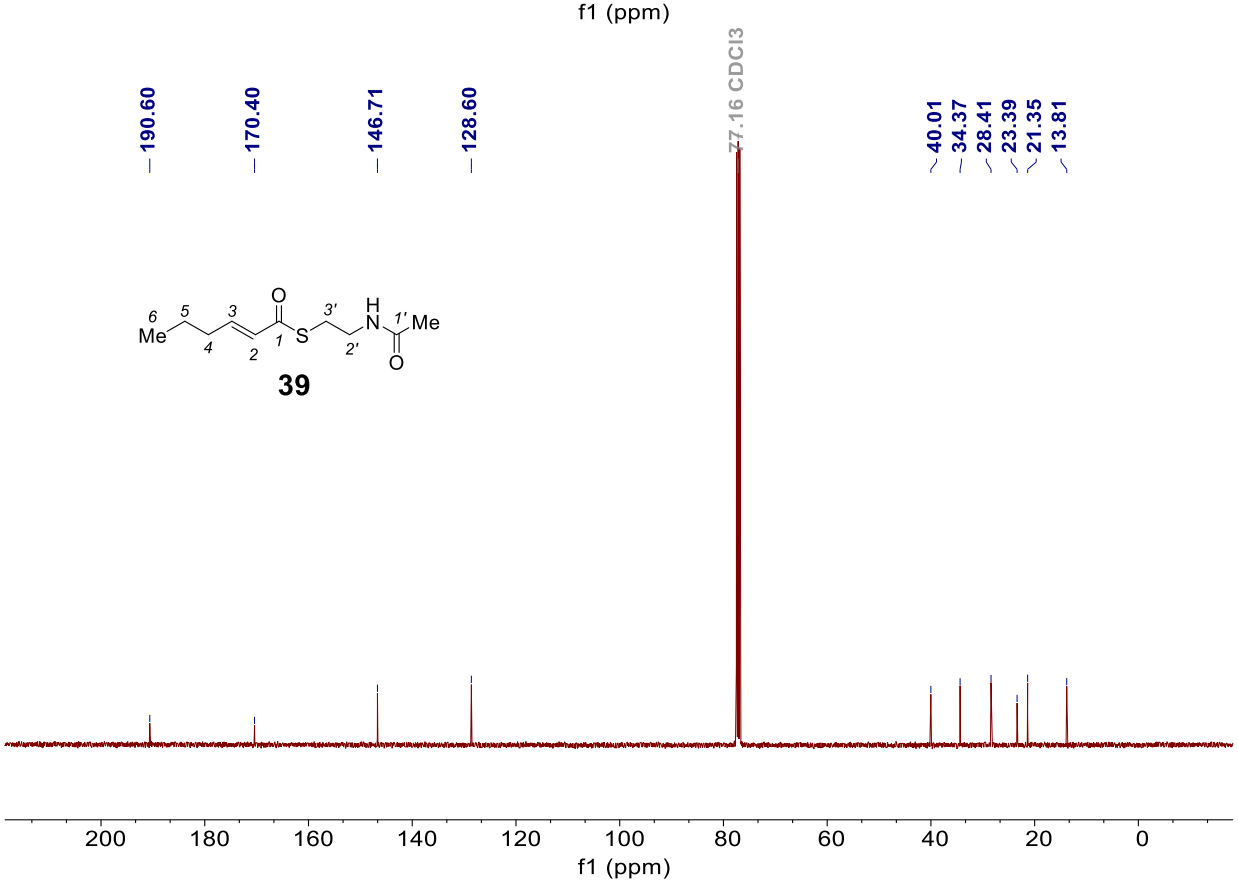
1.00
0.89
2.07
2.05
2.31
3.03
2.13
3.14
f1 (ppm)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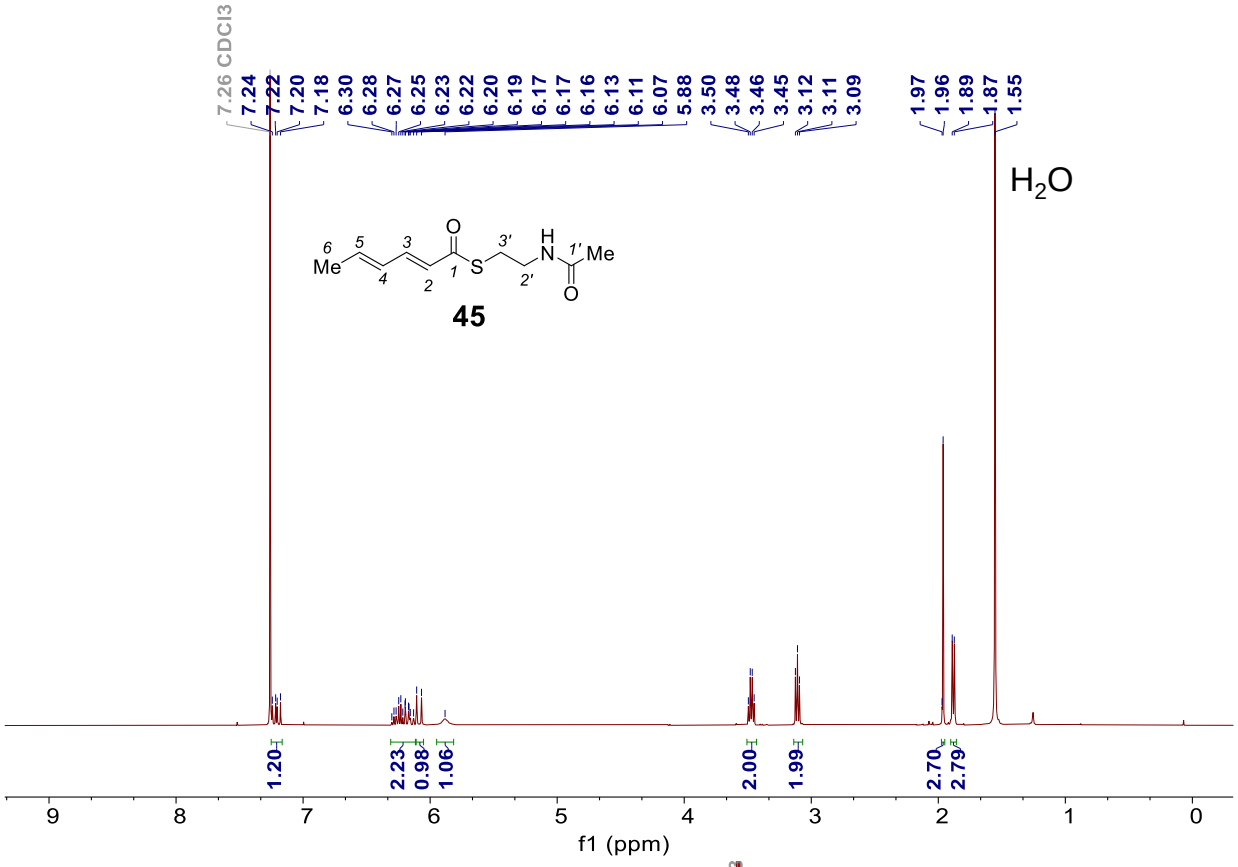
13.81
Me
1
2
3
4
5
6
S
N
H
O
1'
2'
3'
Me
39
f1 (ppm)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6.20
6.19
6.17
6.17
6.16
6.13
6.11
6.07
5.88
3.50
3.48
3.46
3.45
3.12
3.11
3.09
1.97
1.96
1.89
1.87
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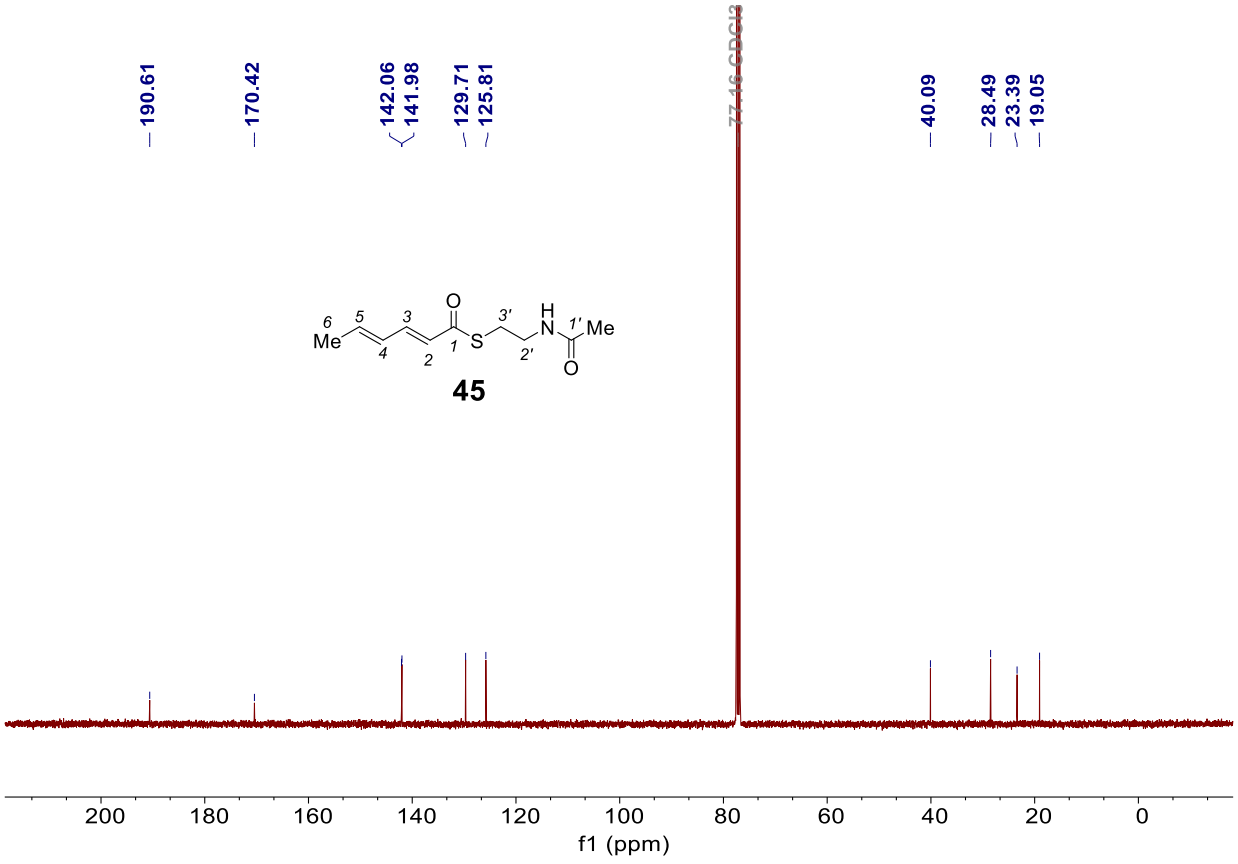
f1 (ppm)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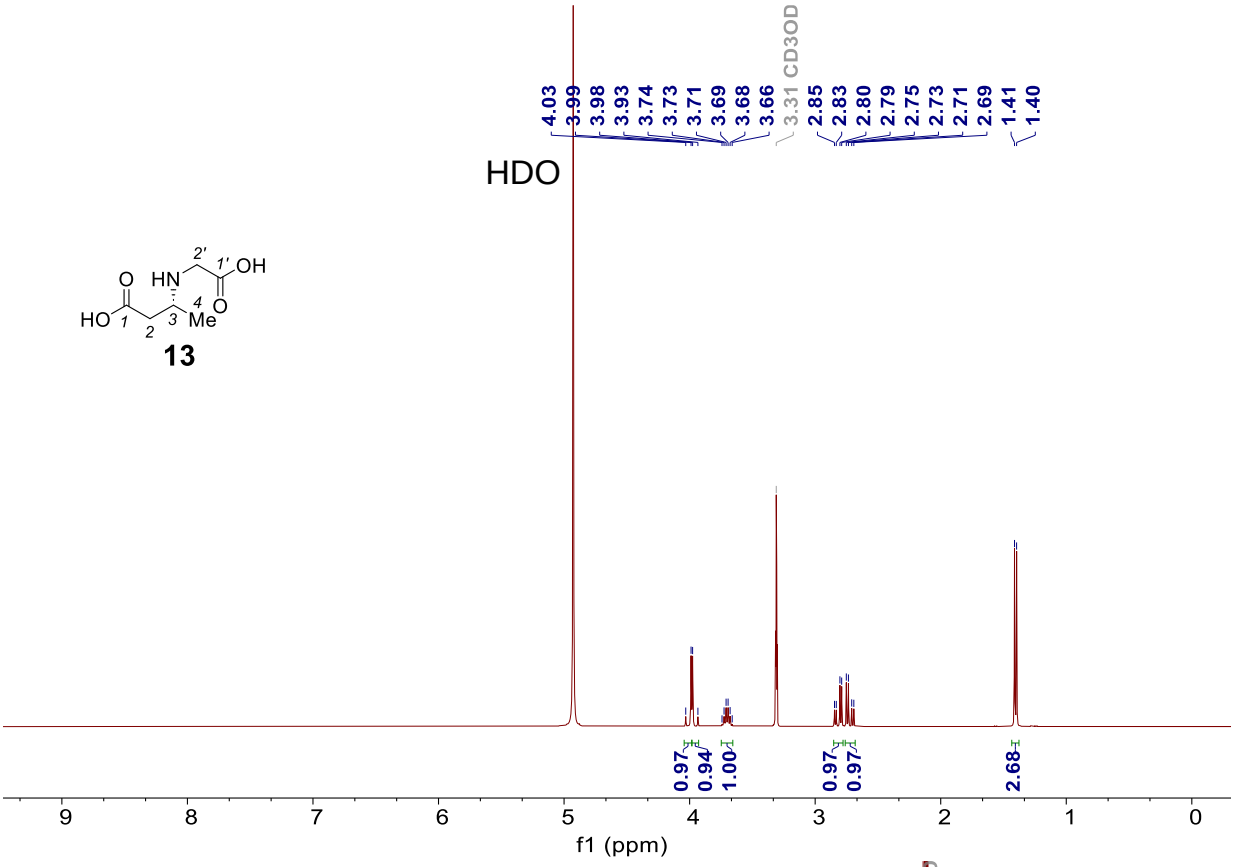
19.05
45
f1 (ppm)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2.80
2.79
2.75
2.73
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1.40
HDO
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0.97
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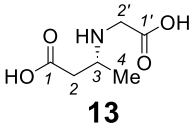
2.68
f1 (ppm)


O
HN
2'
1'
OH
HO
1
2
3
4
Me
O

13

173.35
168.98
52.58
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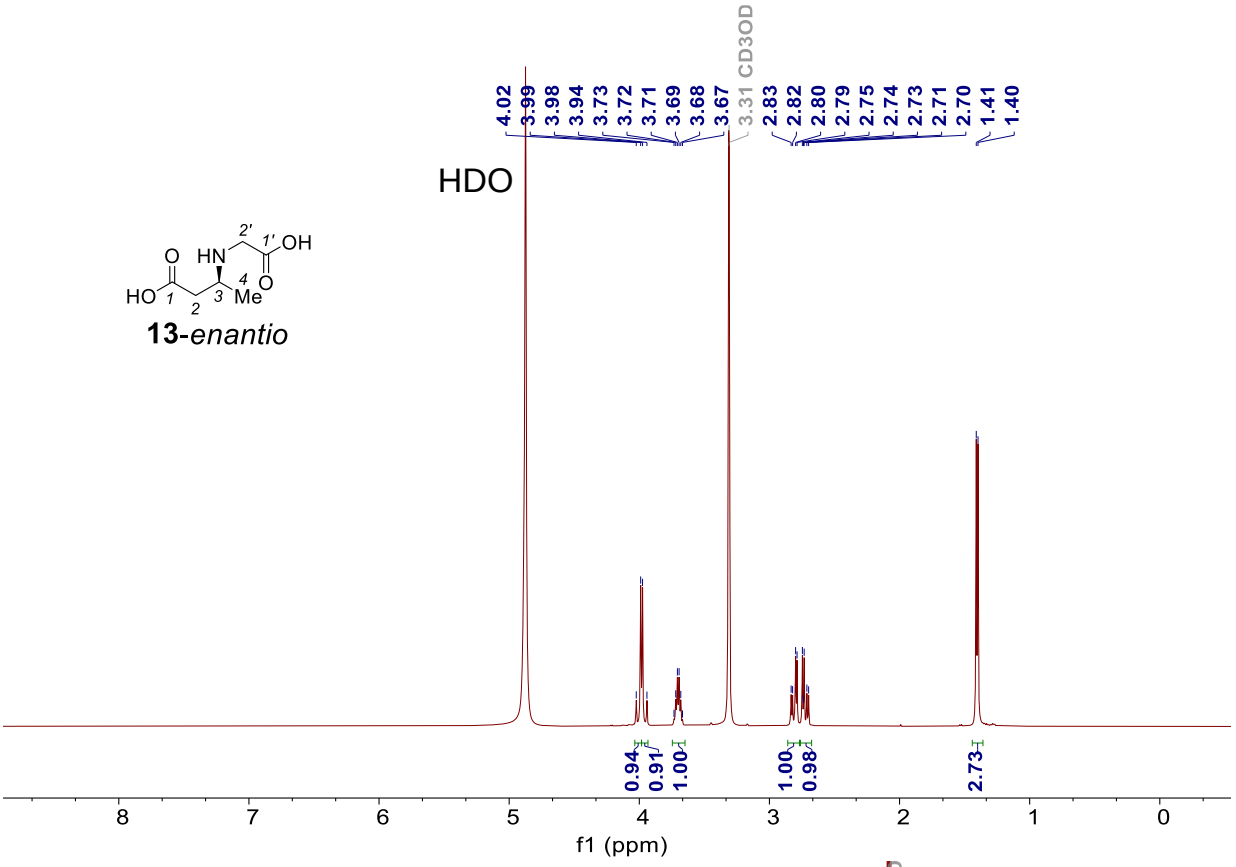
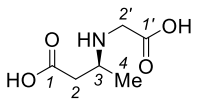
46.05
37.50
16.69
f1 (ppm)

O
HN
2'
1'
OH
HO
1
2
3
4
Me
O

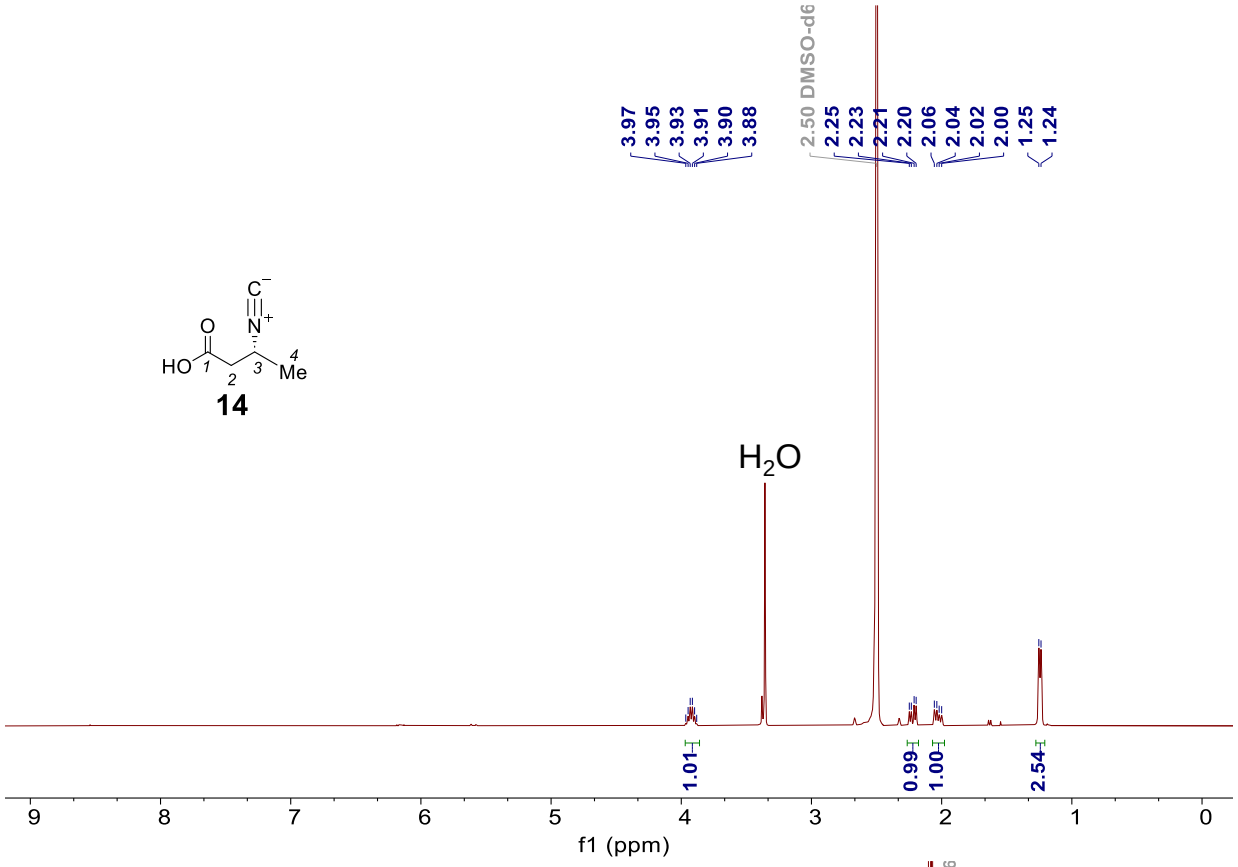
13





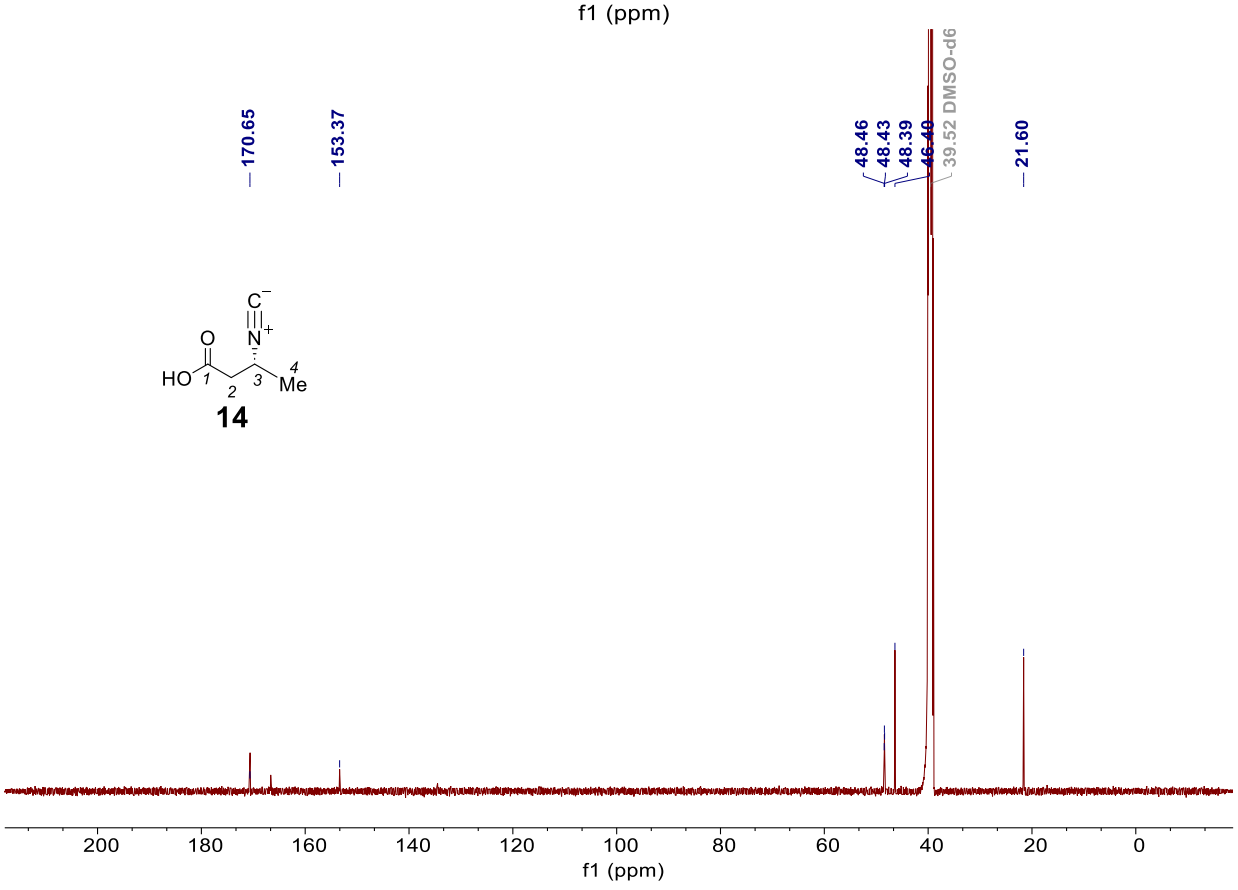
13-*enantio*

13-*enantio*


3.97
3.95
3.93
3.91
3.90
3.88
2.50 DMSO-d6
2.25
2.23
2.21
2.20
2.06
2.04
2.02
2.00
1.25
1.24
H2O
1.01
0.99
1.00
2.54
f1 (ppm)

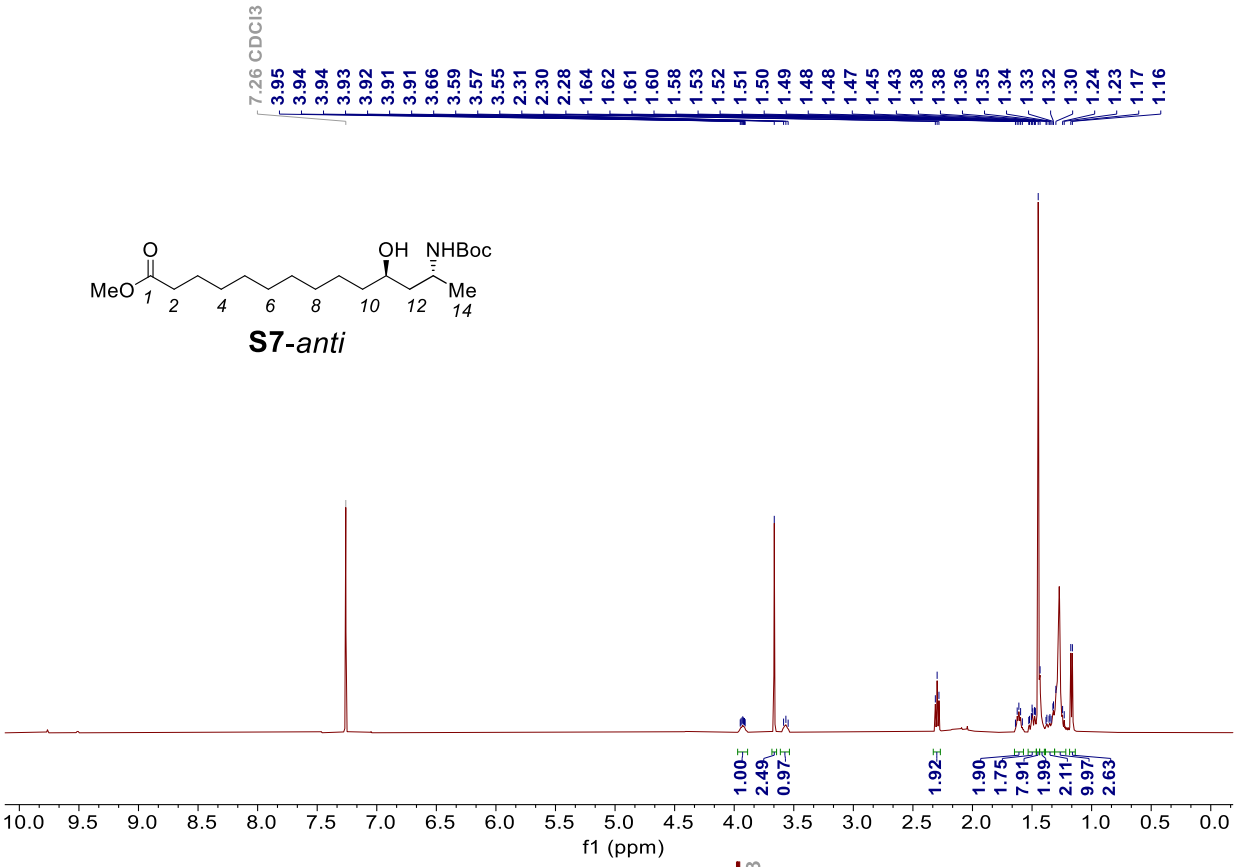
HO
O
N+
C−
1
2
3
4
Me

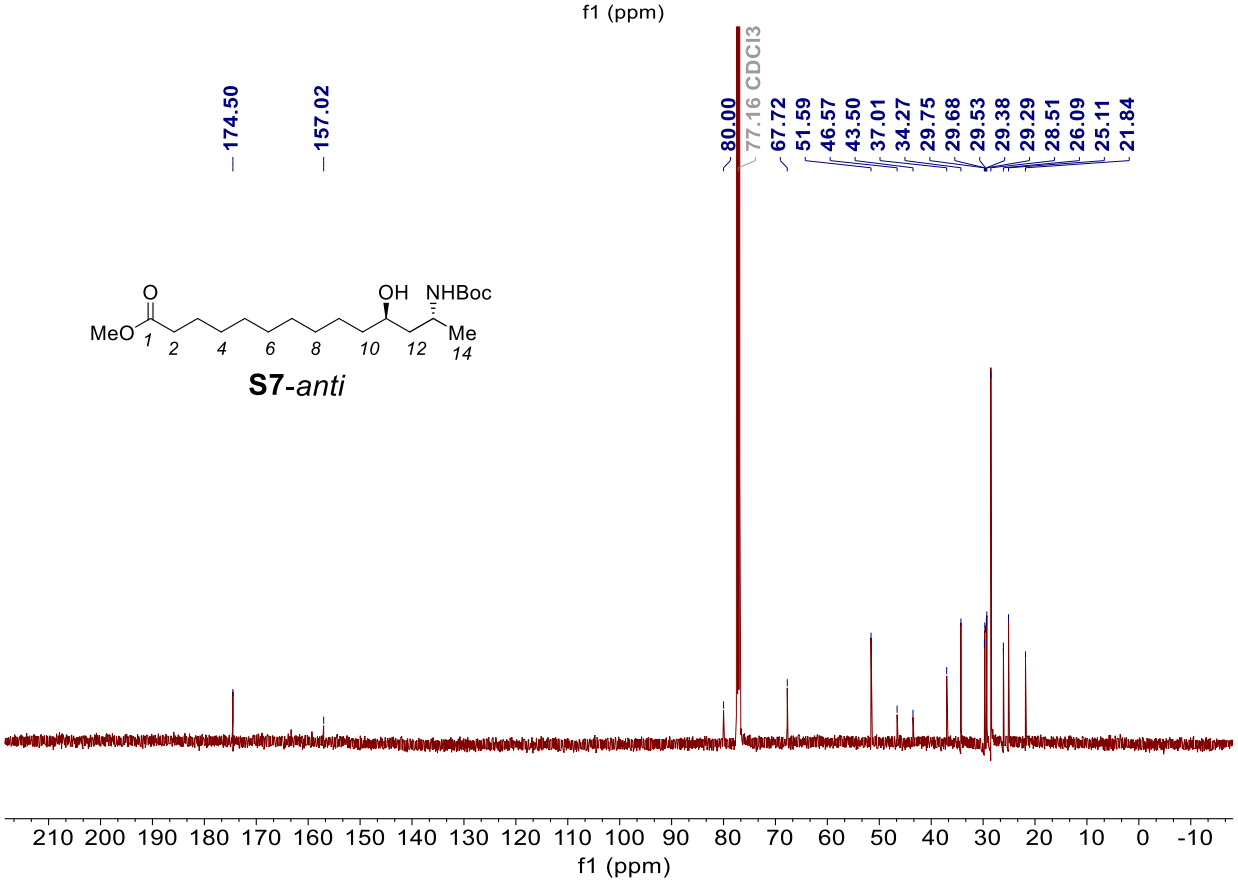
14

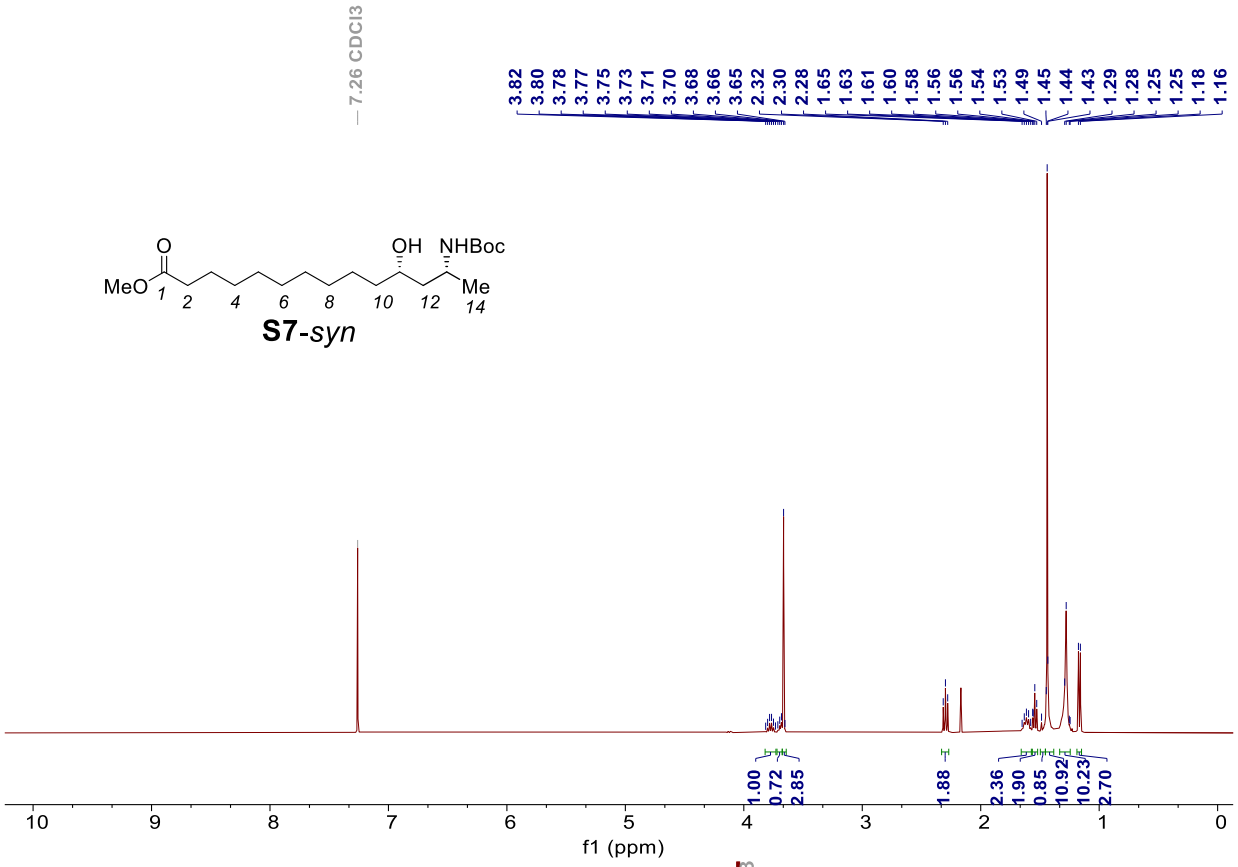

170.65
153.37
48.46
48.43
48.39
48.40
39.52 DMSO-d6
21.60
f1 (ppm)

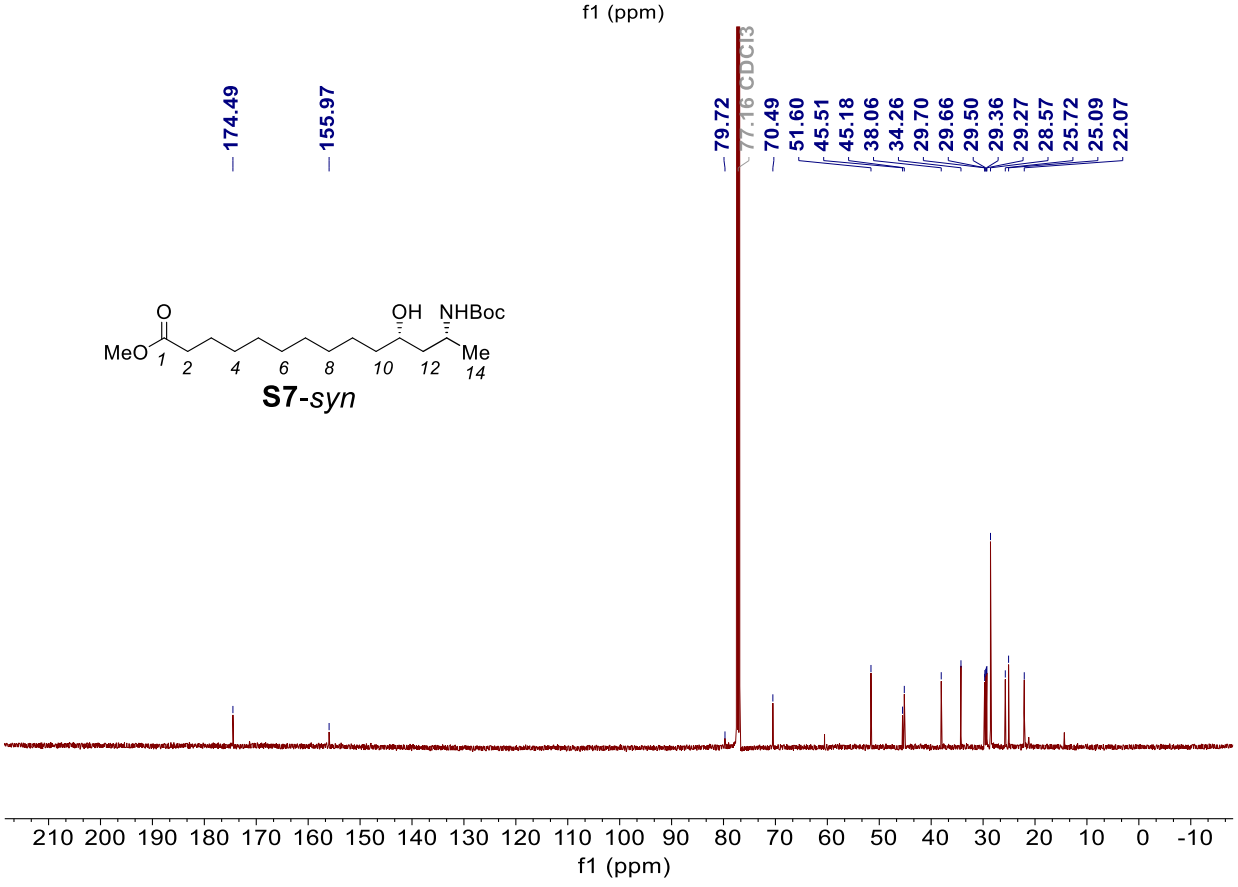
HO
O
N+
C−
1
2
3
4
Me

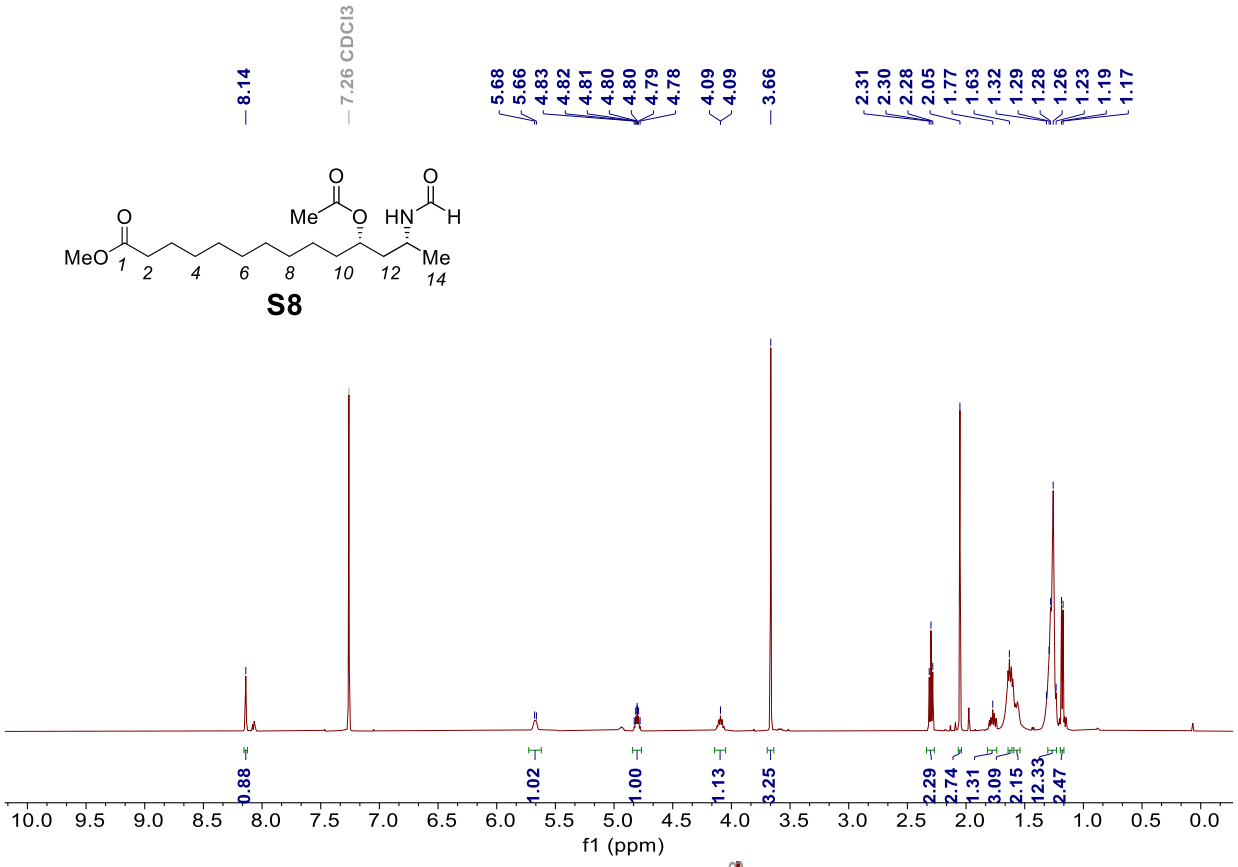
14

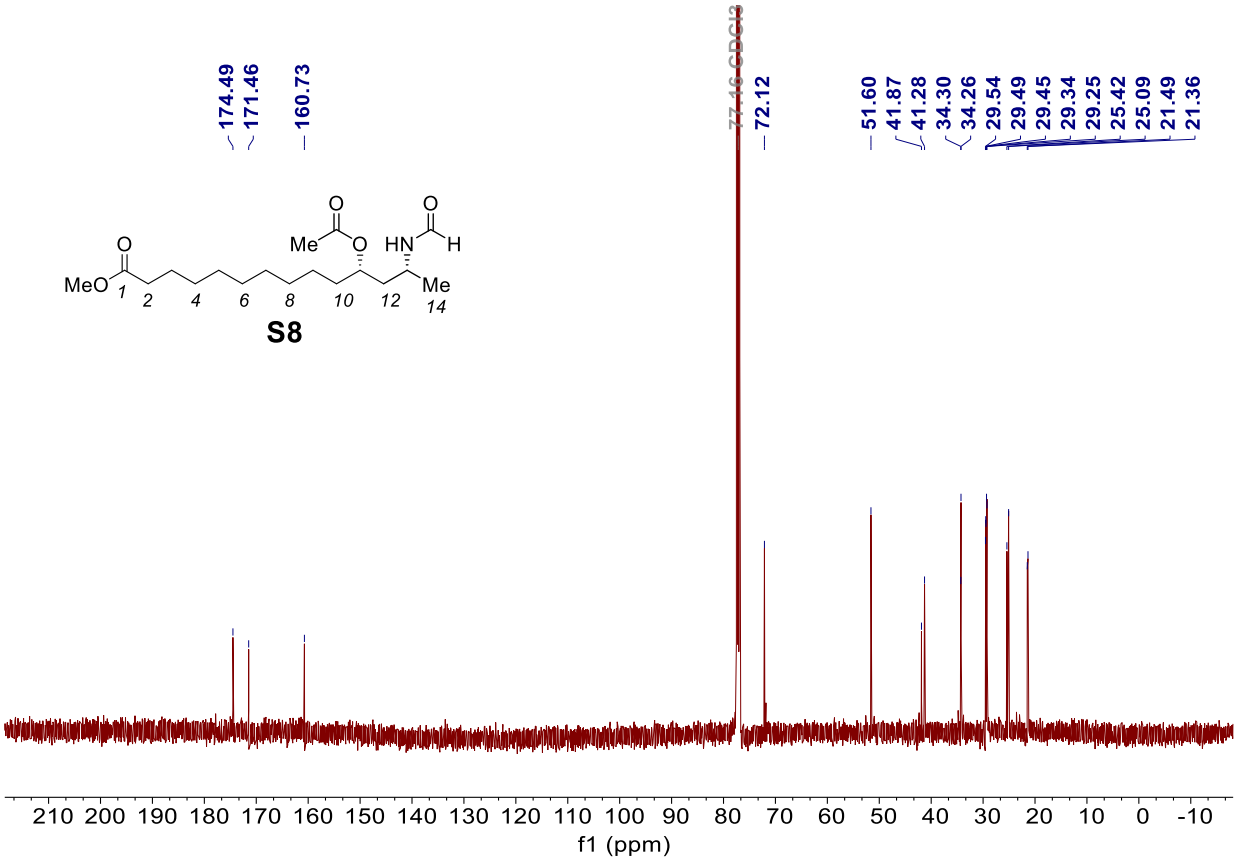

7.26 CDCl3
3.95 3.94 3.94 3.93 3.92 3.91 3.91 3.66 3.59 3.57 3.55 2.31 2.30 2.28 1.64 1.62 1.61 1.60 1.58 1.53 1.52 1.51 1.50 1.49 1.48 1.48 1.47 1.45 1.43 1.38 1.38 1.36 1.35 1.34 1.33 1.32 1.30 1.24 1.23 1.17 1.16
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14
S7-anti
1.00 2.49 0.97 1.92 1.90 1.75 7.91 1.99 2.11 9.97 2.63
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

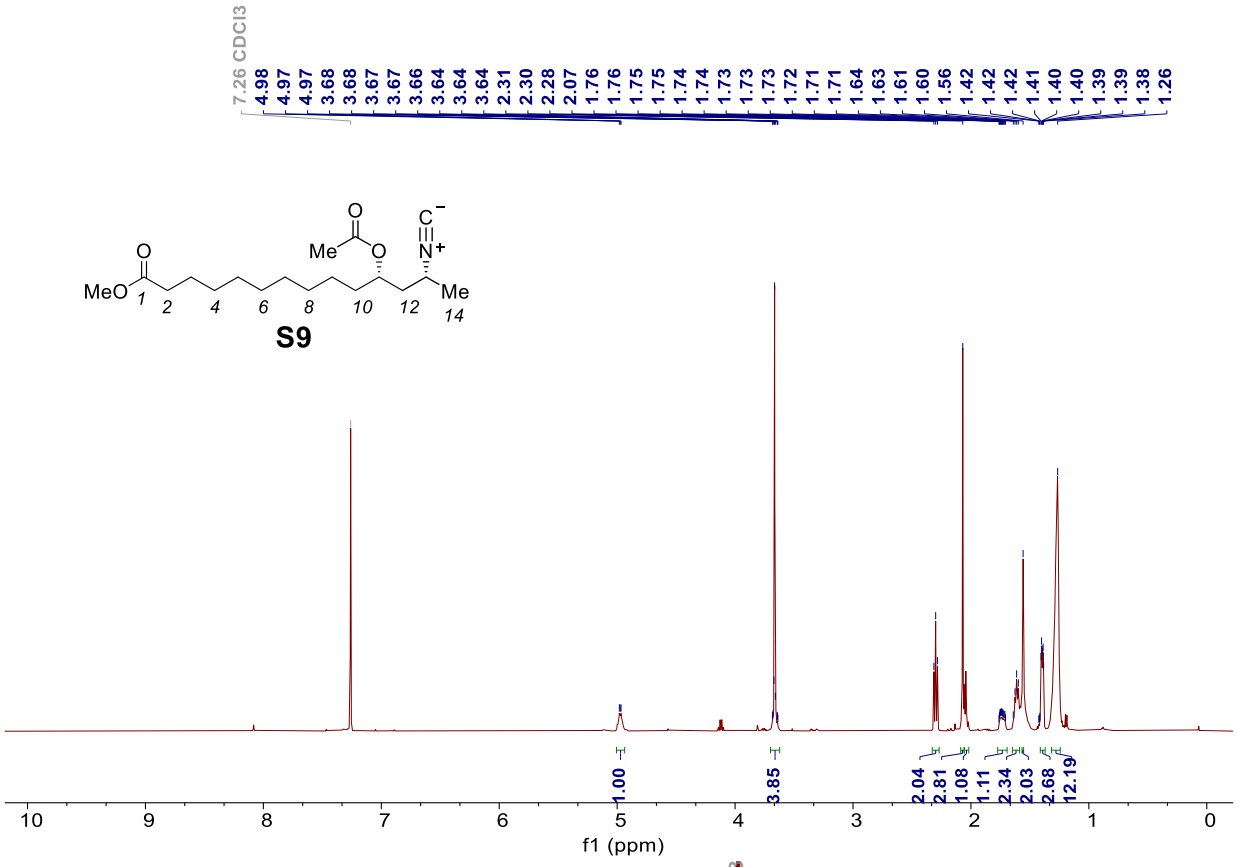

174.50
157.02
80.00
77.16 CDCl3
67.72
51.59
46.57
43.50
37.01
34.27
29.75
29.68
29.53
29.38
29.29
28.51
26.09
25.11
21.84
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14
S7-anti
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

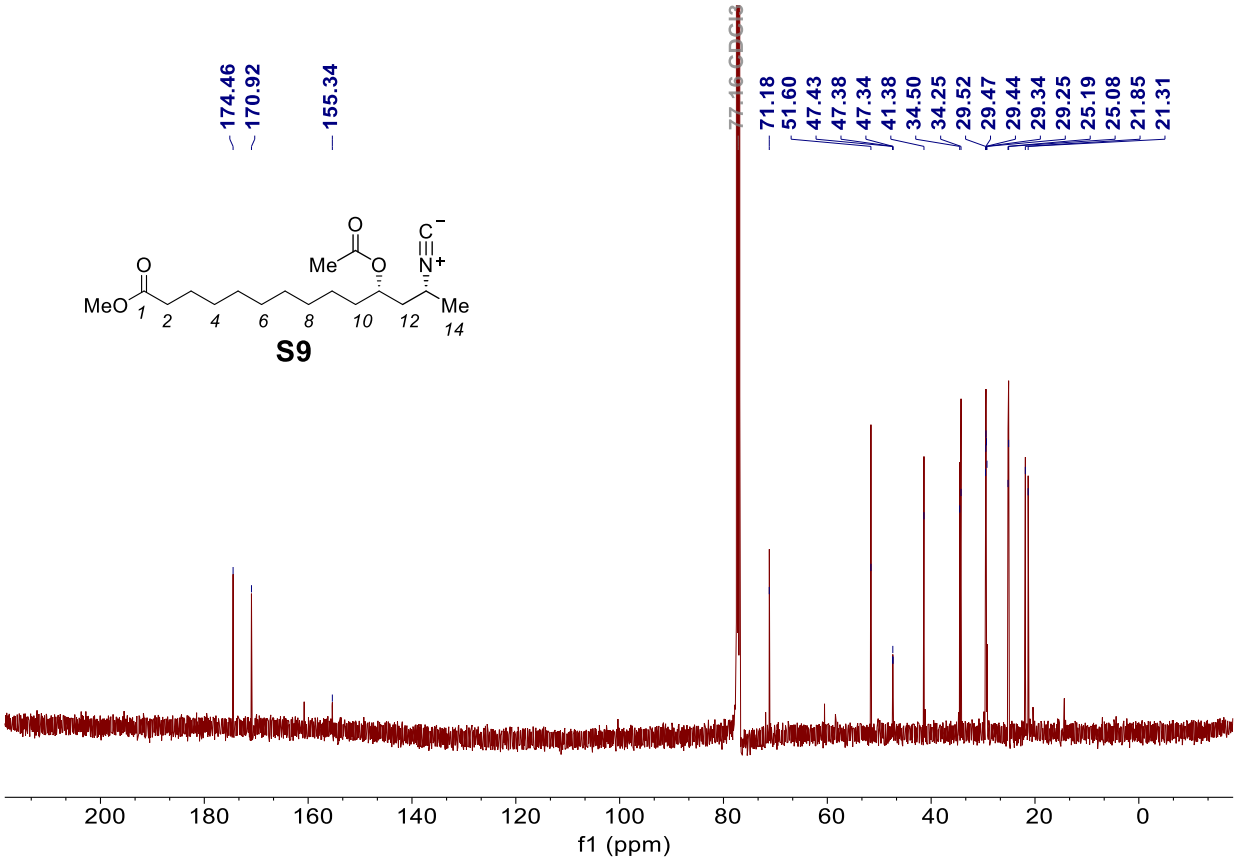

7.26 CDCl3
3.82
3.80
3.78
3.77
3.75
3.73
3.71
3.70
3.68
3.66
3.65
2.32
2.30
2.28
1.65
1.63
1.61
1.60
1.58
1.56
1.56
1.54
1.53
1.49
1.45
1.44
1.43
1.29
1.28
1.25
1.25
1.18
1.16
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14
S7-syn
1.00
0.72
2.85
1.88
2.36
1.90
0.85
10.92
10.23
2.70
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

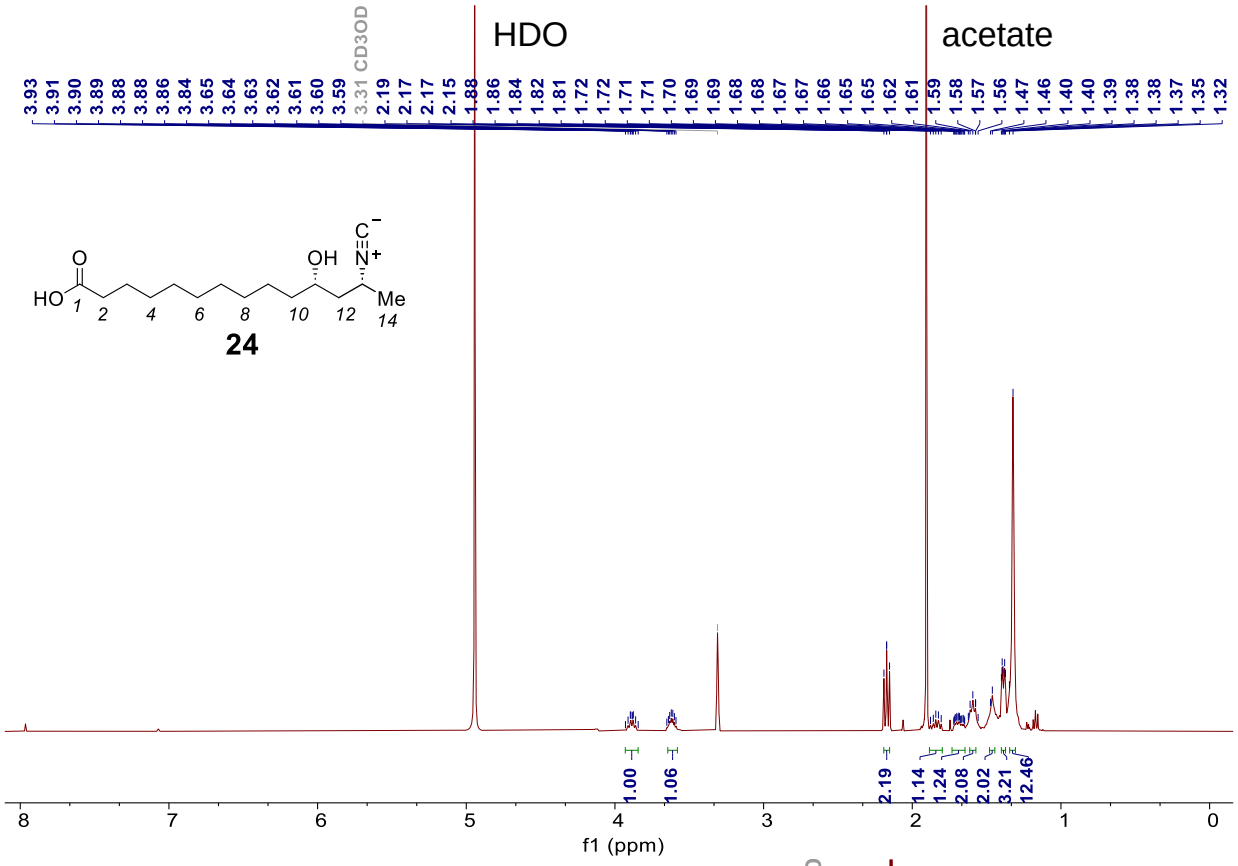

174.49
155.97
79.72
77.16 CDCl3
70.49
51.60
45.51
45.18
38.06
34.26
29.70
29.66
29.50
29.36
29.27
28.57
25.72
25.09
22.07
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14
S7-syn
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

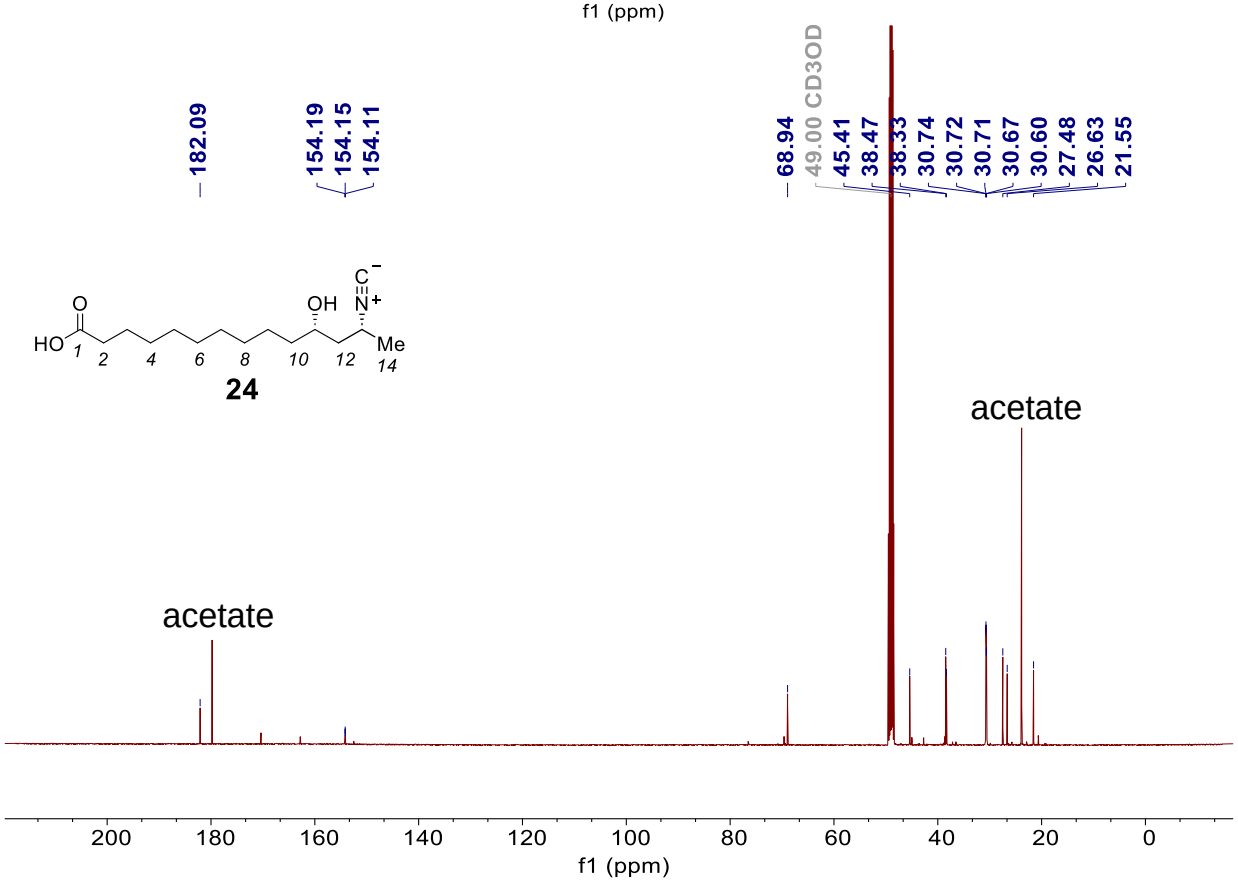

8.14
7.26 CDCl3
5.68
5.66
4.83
4.82
4.81
4.80
4.80
4.79
4.78
4.09
4.09
3.66
2.31
2.30
2.28
2.05
1.77
1.63
1.32
1.29
1.28
1.26
1.23
1.19
1.17
MeO
Me
HN
H
Me
1 2 4 6 8 10 12 14
S8
0.88
1.02
1.00
1.13
3.25
2.29
2.74
1.31
3.09
2.15
12.33
2.47
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

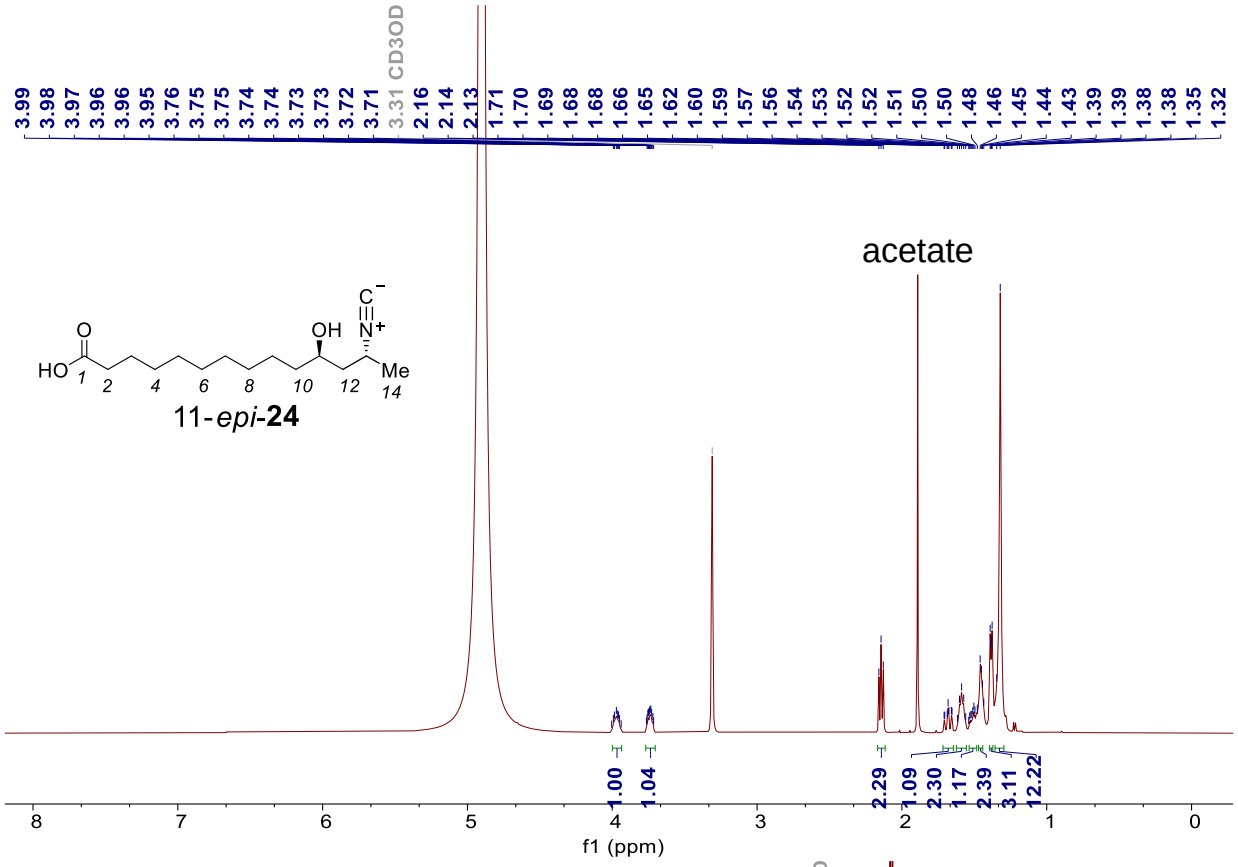

174.49
171.46
160.73
77.16 CDCl3
72.12
51.60
41.87
41.28
34.30
34.26
29.54
29.49
29.45
29.34
29.25
25.42
25.09
21.49
21.36
MeO
Me
HN
H
Me
1 2 4 6 8 10 12 14
S8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

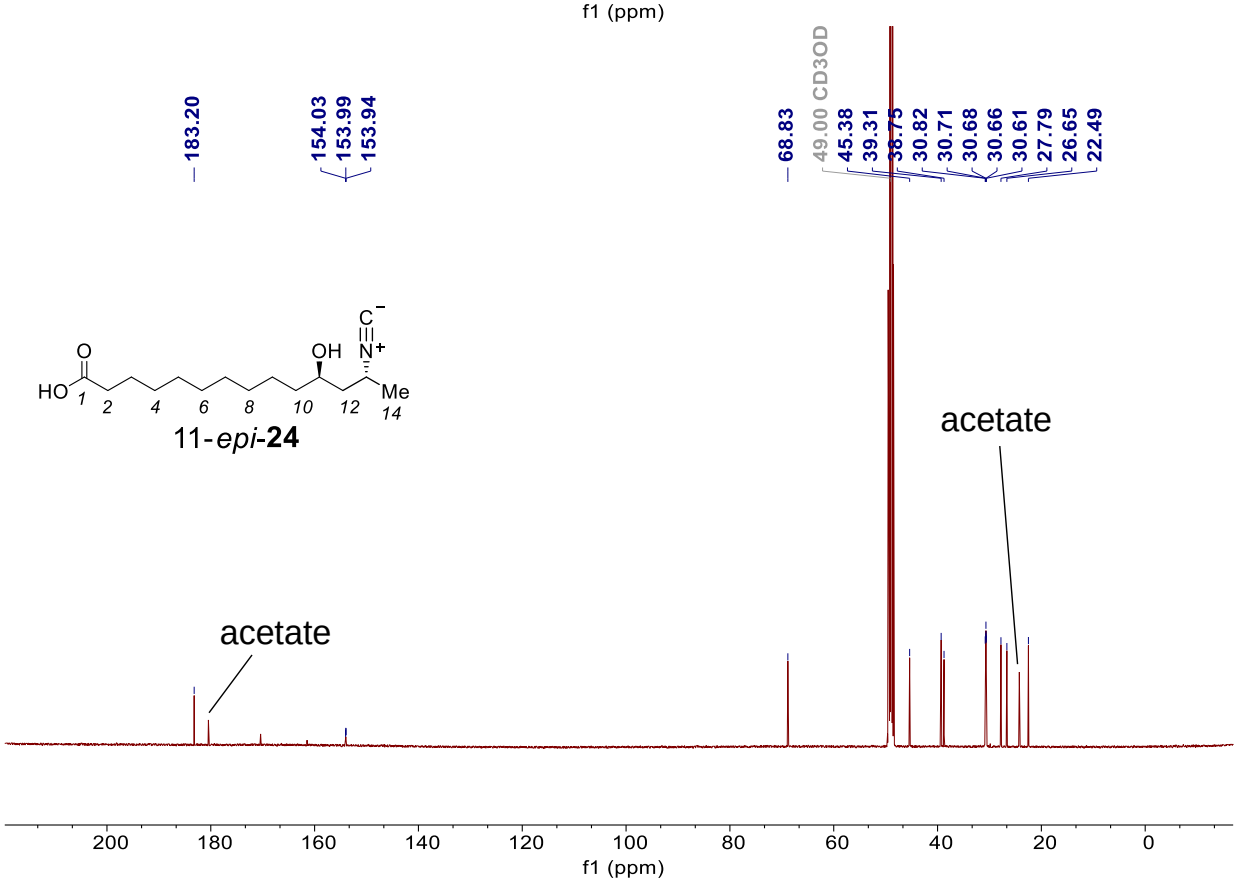

7.26 CDCl3
4.98
4.97
4.97
3.68
3.68
3.67
3.67
3.66
3.64
3.64
3.64
2.31
2.30
2.28
2.07
1.76
1.76
1.75
1.75
1.74
1.74
1.73
1.73
1.73
1.72
1.71
1.71
1.64
1.63
1.61
1.60
1.56
1.42
1.42
1.42
1.41
1.40
1.40
1.39
1.39
1.38
1.26
MeO
Me
Me
S9
1.00
3.85
2.04
2.81
1.08
1.11
2.34
2.03
2.68
12.19
f1 (ppm)

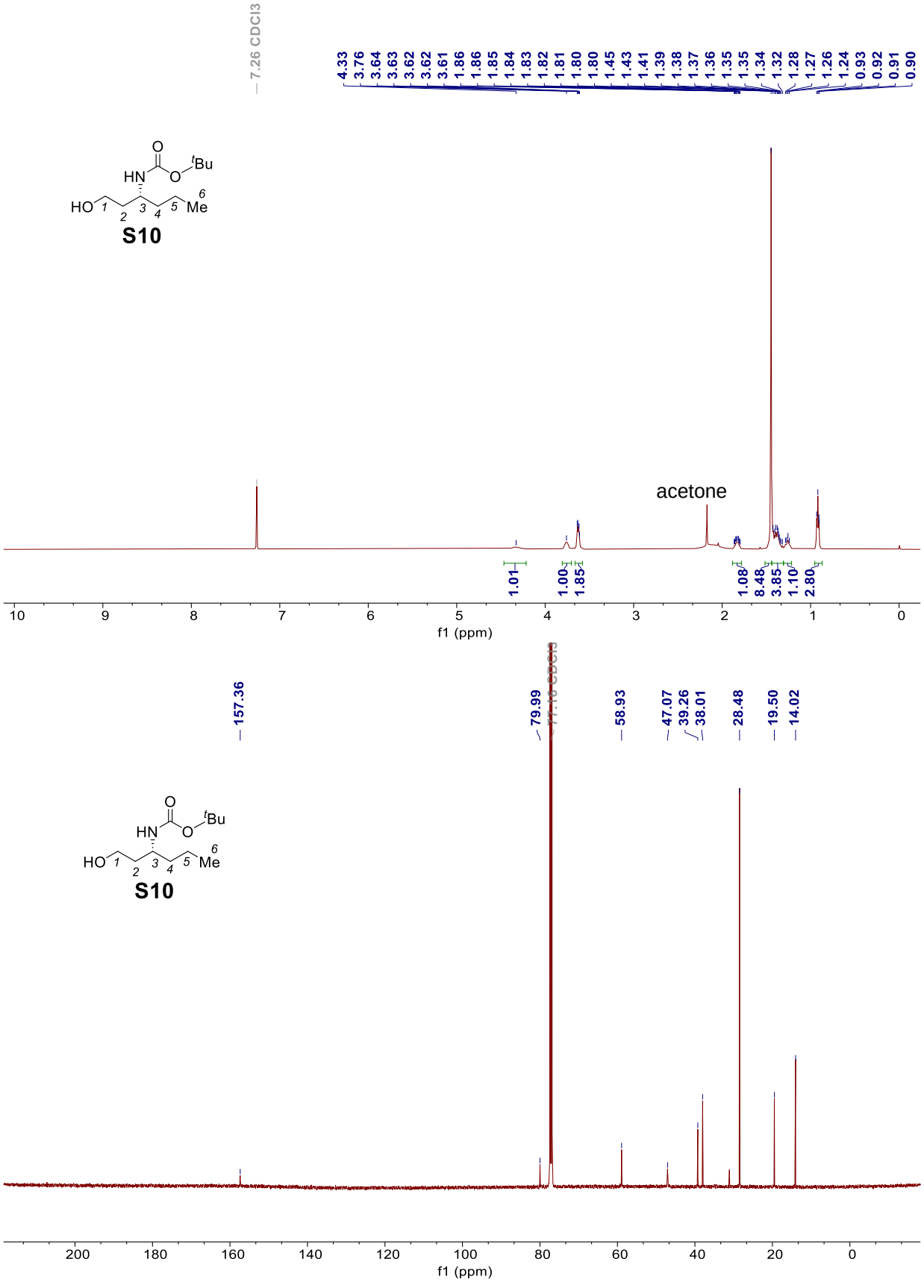

174.46
170.92
155.34
77.16 CDCl3
71.18
51.60
47.43
47.38
47.34
41.38
34.50
34.25
29.52
29.47
29.44
29.34
29.25
25.19
25.08
21.85
21.31
MeO
Me
Me
S9
f1 (ppm)

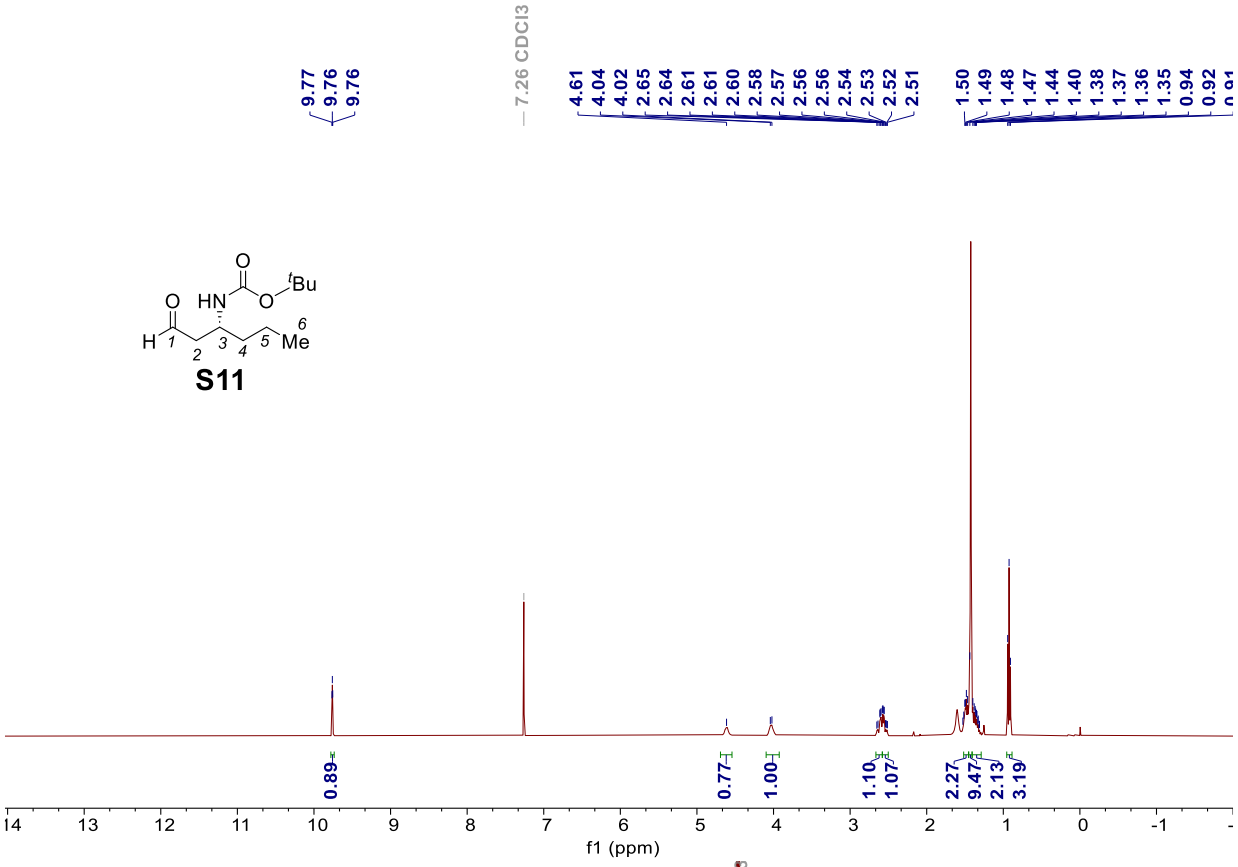

HDO
acetate
3.31 CD3OD
3.93 3.91 3.90 3.89 3.88 3.88 3.86 3.84 3.65 3.64 3.63 3.62 3.61 3.60 3.59 3.31 2.19 2.17 2.17 2.15 1.88 1.86 1.84 1.82 1.81 1.72 1.72 1.71 1.71 1.70 1.69 1.69 1.68 1.68 1.67 1.67 1.66 1.65 1.65 1.62 1.61 1.59 1.58 1.57 1.56 1.47 1.46 1.40 1.40 1.39 1.38 1.38 1.37 1.35 1.32
HO
O
OH
N
C
Me
1 2 4 6 8 10 12 14
24
1.00 1.06 2.19 1.14 1.24 2.08 2.02 3.21 12.46
8 7 6 5 4 3 2 1 0
f1 (ppm)

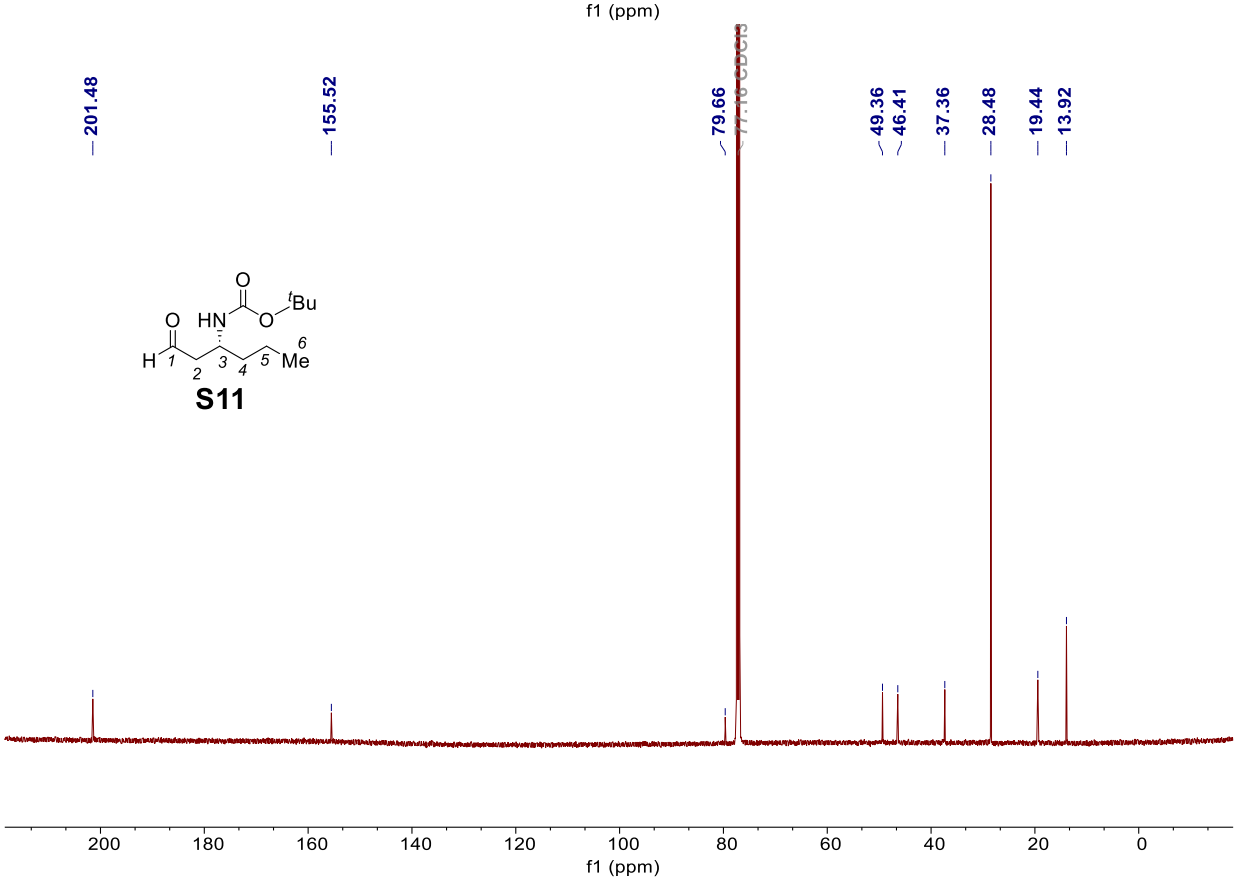

182.09
154.19 154.15 154.11
68.94 49.00 CD3OD 45.41 38.47 38.33 30.74 30.72 30.71 30.67 30.60 27.48 26.63 21.55
HO
O
OH
N
C
Me
1 2 4 6 8 10 12 14
24
acetate
acetate
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

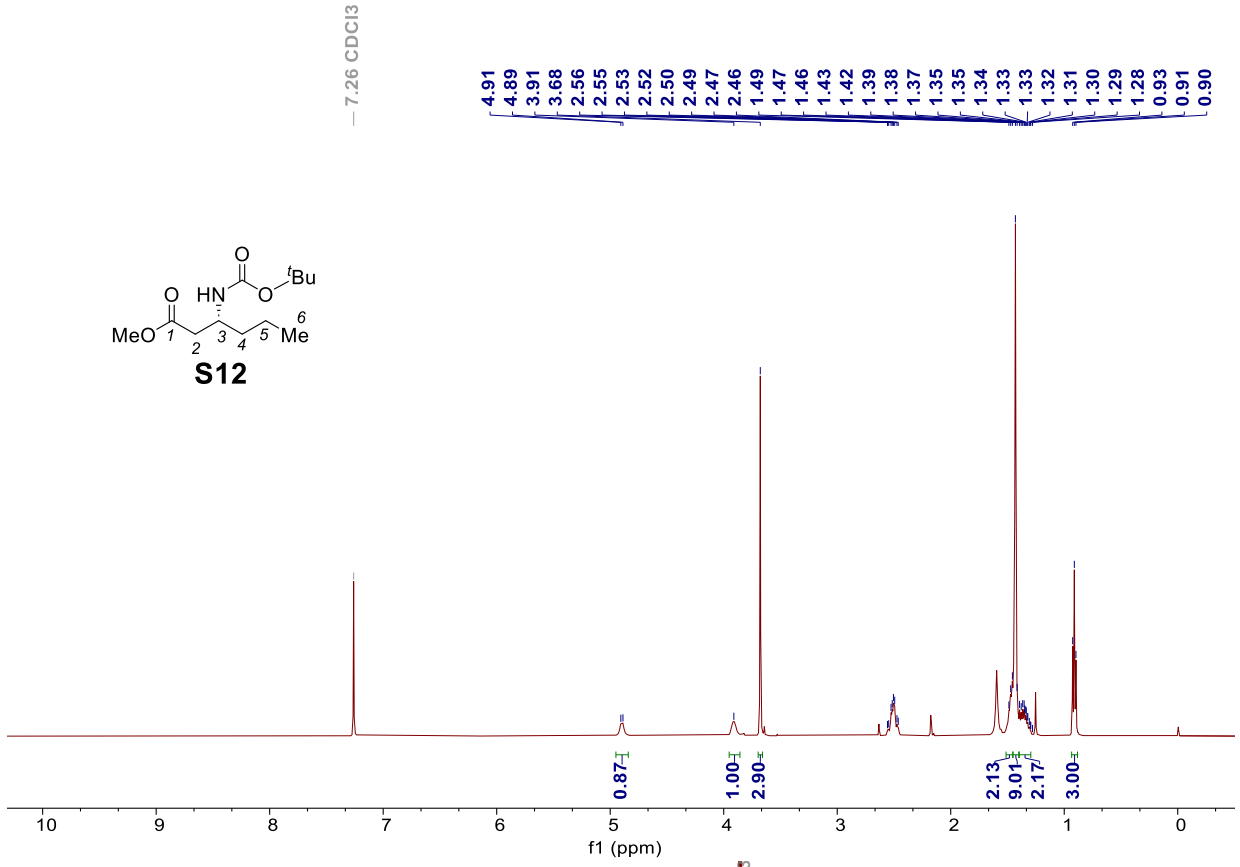

3.99 3.98 3.97 3.96 3.96 3.95 3.76 3.75 3.75 3.74 3.74 3.73 3.73 3.72 3.71 3.31 CD3OD 2.16 2.14 2.13 1.71 1.70 1.69 1.68 1.68 1.66 1.65 1.62 1.60 1.59 1.57 1.56 1.54 1.53 1.52 1.52 1.51 1.50 1.50 1.48 1.46 1.45 1.44 1.43 1.39 1.39 1.38 1.38 1.35 1.32
acetate
11-epi-24
1.00 1.04 2.29 1.09 2.30 1.17 2.39 3.11 12.22
f1 (ppm)

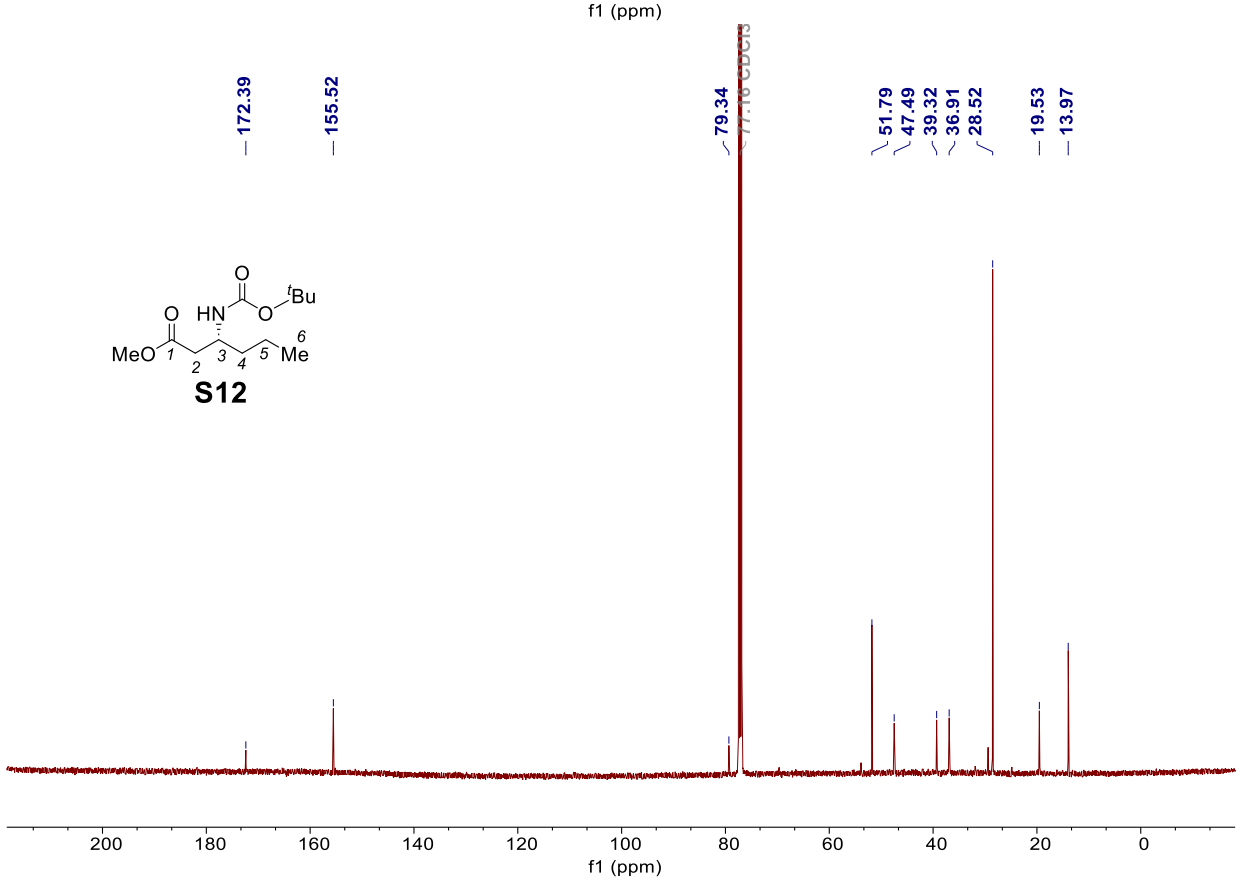

183.20 154.03 153.99 153.94 68.83 49.00 CD3OD 45.38 39.31 38.75 30.82 30.71 30.68 30.66 30.61 27.79 26.65 22.49
acetate
acetate
11-epi-24
f1 (ppm)

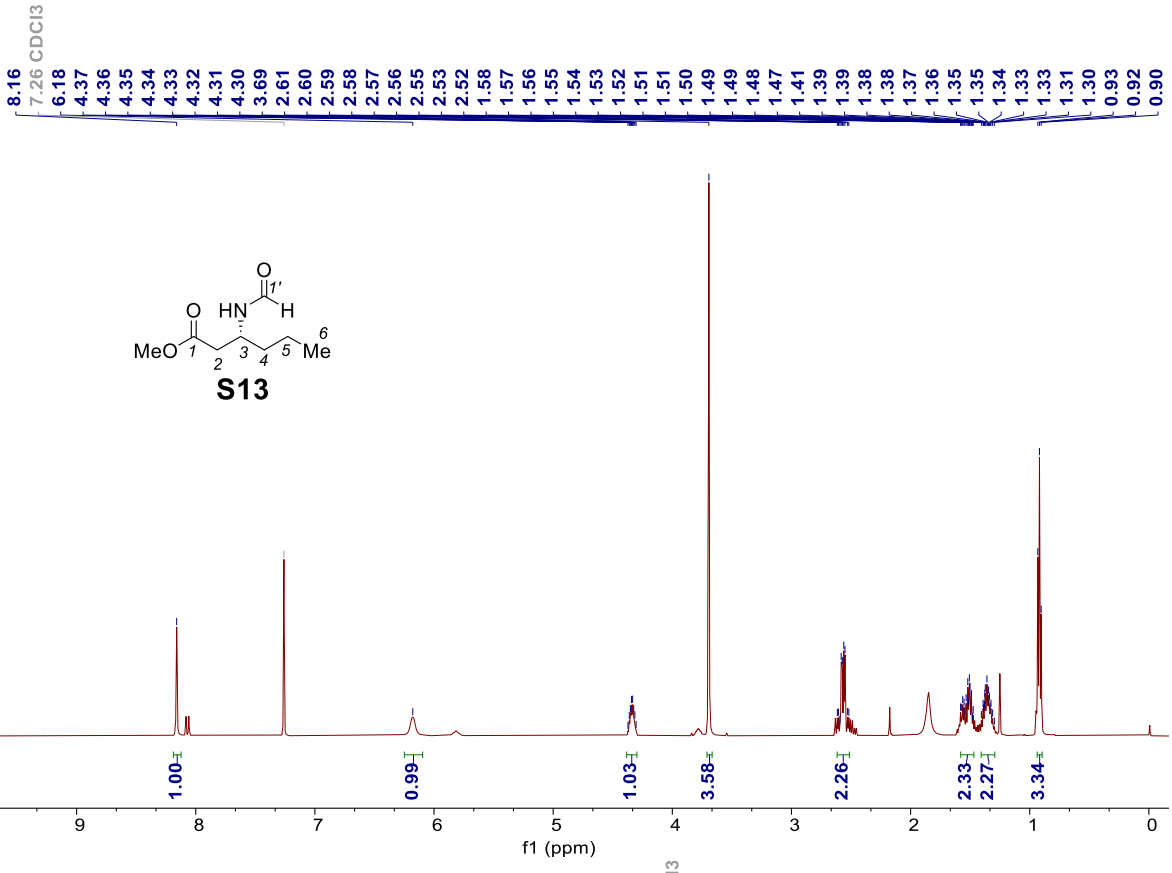

7.26 CDCl3
4.33
3.76
3.64
3.63
3.62
3.62
3.61
1.86
1.86
1.85
1.84
1.83
1.82
1.81
1.80
1.80
1.45
1.43
1.41
1.39
1.38
1.37
1.36
1.35
1.35
1.34
1.32
1.28
1.27
1.26
1.24
0.93
0.92
0.91
0.90
HO
HN
O
O
tBu
Me
1
2
3
4
5
6
S10
acetone
1.01
1.00
1.85
1.08
8.48
3.85
1.10
2.80
f1 (ppm)
157.36
79.99
77.16 CDCl3
58.93
47.07
39.26
38.01
28.48
19.50
14.02
S10
f1 (ppm)

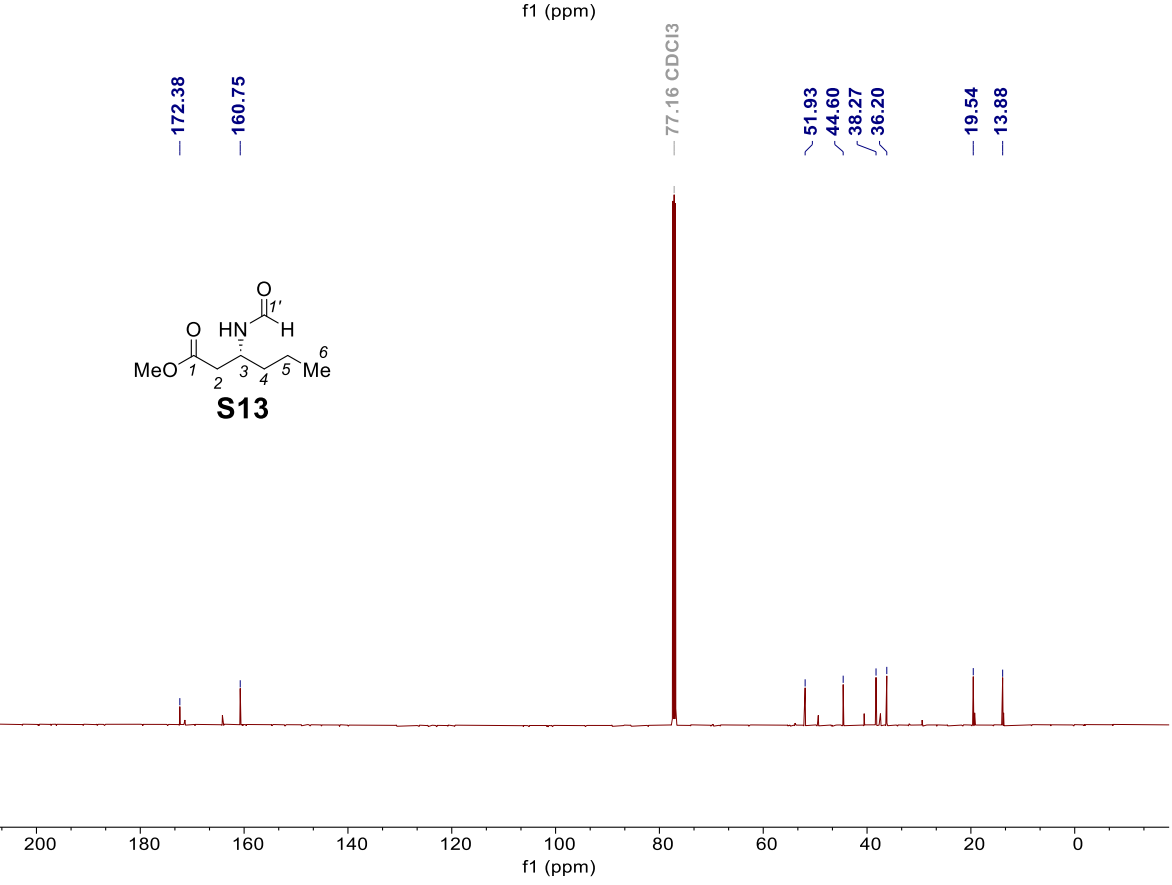

9.77
9.76
9.76
7.26 CDCl3
4.61
4.04
4.02
2.65
2.64
2.61
2.61
2.60
2.58
2.57
2.56
2.56
2.54
2.53
2.52
2.51
1.50
1.49
1.48
1.47
1.44
1.40
1.38
1.37
1.36
1.35
0.94
0.92
O
HN
O
tBu
O
H
1
2
3
4
5
Me
6
S11
0.89
0.77
1.00
1.10
1.07
2.27
9.47
2.13
3.19
f1 (ppm)

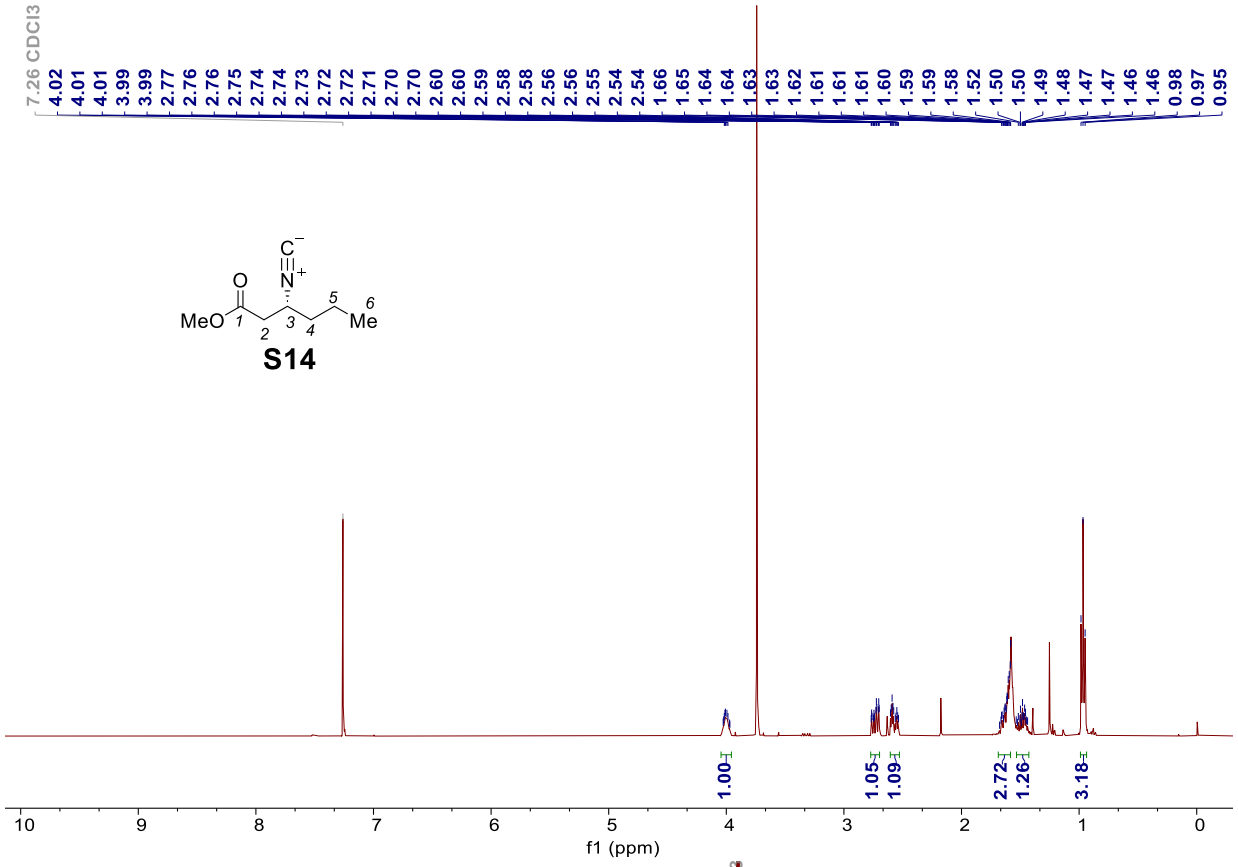

201.48
155.52
79.66
77.16 CDCl3
49.36
46.41
37.36
28.48
19.44
13.92
O
HN
O
tBu
O
H
1
2
3
4
5
Me
6
S11
f1 (ppm)

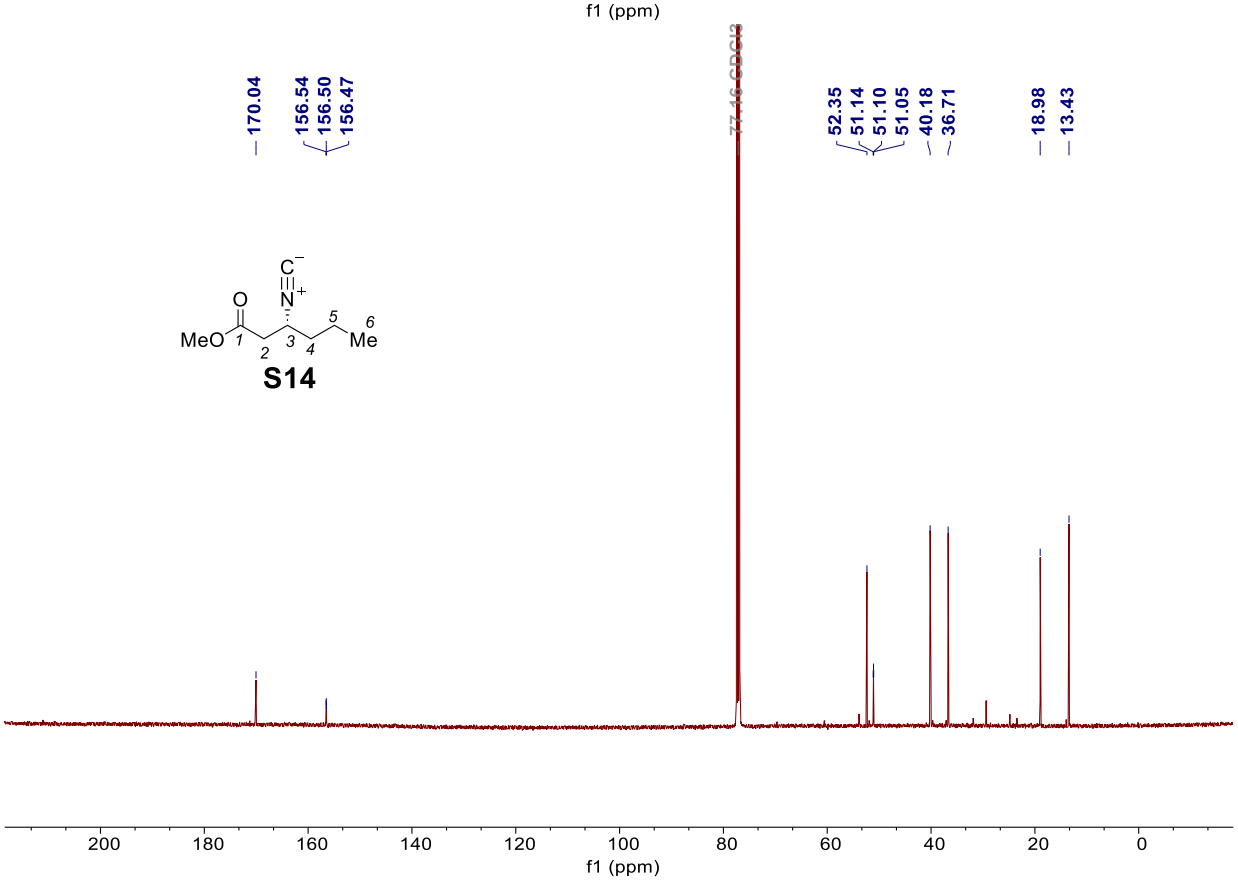

7.26 CDCl3
4.91
4.89
3.91
3.68
2.56
2.55
2.53
2.52
2.50
2.49
2.47
2.46
1.49
1.47
1.46
1.43
1.42
1.39
1.38
1.37
1.35
1.35
1.34
1.33
1.33
1.32
1.31
1.30
1.29
1.28
0.93
0.91
0.90
S12
0.87
1.00
2.90
2.13
9.01
2.17
3.00
f1 (ppm)

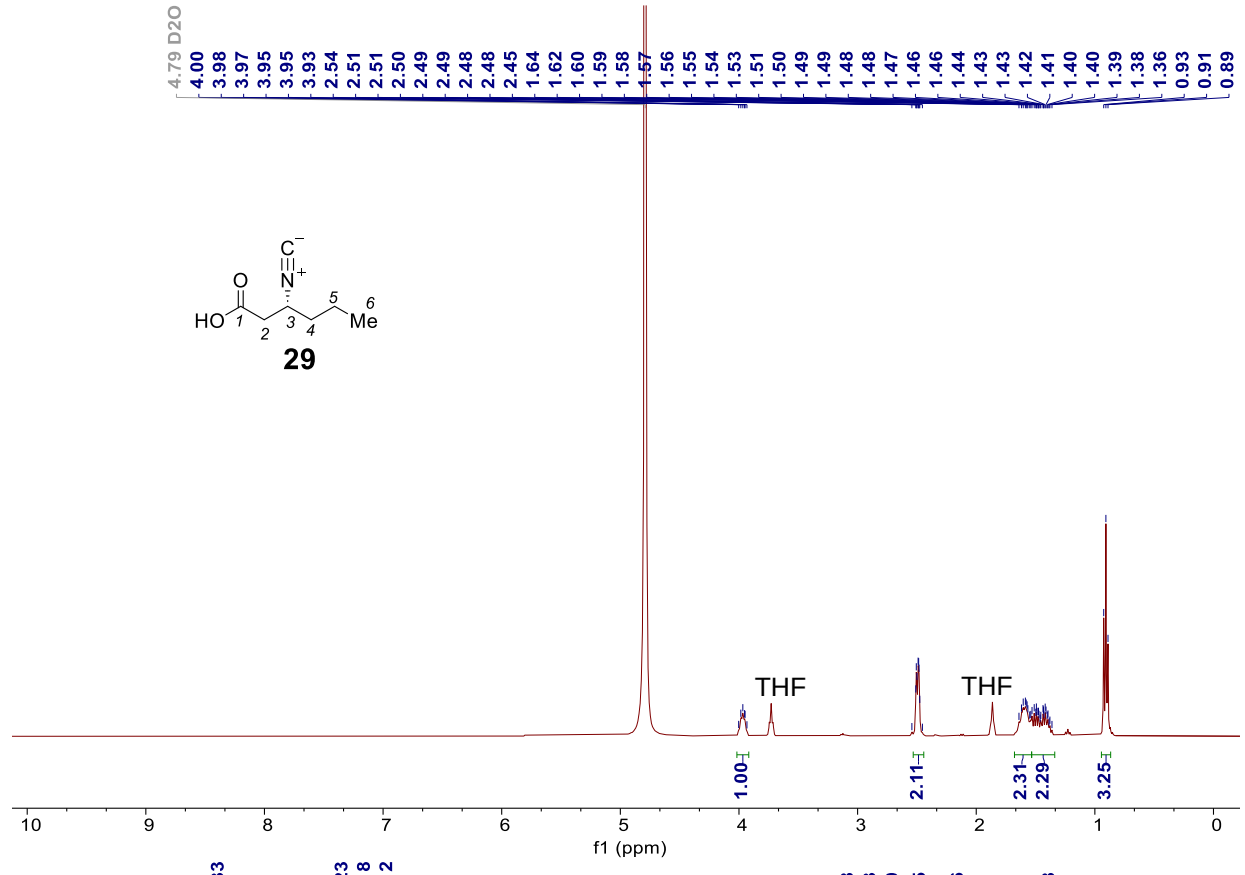

172.39
155.52
79.34
77.16 CDCl3
51.79
47.49
39.32
36.91
28.52
19.53
13.97
S12
f1 (ppm)


8.16
7.26 CDCl3
6.18
4.37
4.36
4.35
4.34
4.33
4.32
4.31
4.30
3.69
2.61
2.60
2.59
2.58
2.57
2.56
2.55
2.53
2.52
1.58
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.51
1.50
1.49
1.49
1.48
1.47
1.41
1.39
1.39
1.38
1.38
1.37
1.36
1.35
1.35
1.34
1.33
1.33
1.31
1.30
0.93
0.92
0.90
MeO
HN
H
Me
S13
1.00
0.99
1.03
3.58
2.26
2.33
2.27
3.34
f1 (ppm)


172.38
160.75
77.16 CDCl3
51.93
44.60
38.27
36.20
19.54
13.88
MeO
HN
H
Me
S13
f1 (ppm)

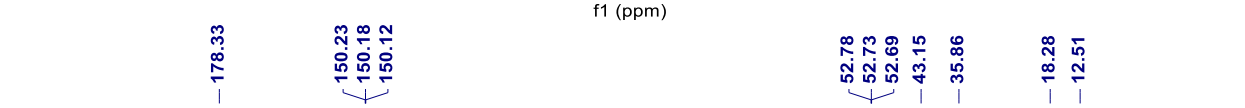

7.26 CDCl3
4.02 4.01 4.01 3.99 3.99 2.77 2.76 2.76 2.75 2.74 2.74 2.73 2.72 2.72 2.71 2.70 2.70 2.60 2.60 2.59 2.58 2.58 2.56 2.56 2.55 2.54 2.54 1.66 1.65 1.64 1.64 1.63 1.63 1.62 1.61 1.61 1.60 1.59 1.59 1.58 1.52 1.50 1.50 1.49 1.48 1.47 1.47 1.46 1.46 0.98 0.97 0.95
MeO
Me
S14
1.00 1.05 1.09 2.72 1.26 3.18
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

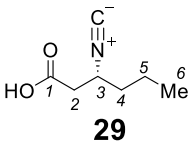

170.04
156.54 156.50 156.47
77.16 CDCl3
52.35 51.14 51.10 51.05 40.18 36.71
18.98 13.43
MeO
Me
S14
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


4.79 D2O
4.00 3.98 3.97 3.95 3.95 3.93 2.54 2.51 2.51 2.50 2.49 2.49 2.48 2.48 2.45 1.64 1.62 1.60 1.59 1.58 1.57 1.56 1.55 1.54 1.53 1.51 1.50 1.49 1.49 1.48 1.48 1.47 1.46 1.46 1.44 1.43 1.43 1.42 1.41 1.40 1.40 1.39 1.38 1.36 0.93 0.91 0.89
THF
THF
1.00
2.11
2.31
2.29
3.25
f1 (ppm)

HO
O
C
N
Me
1
2
3
4
5
6

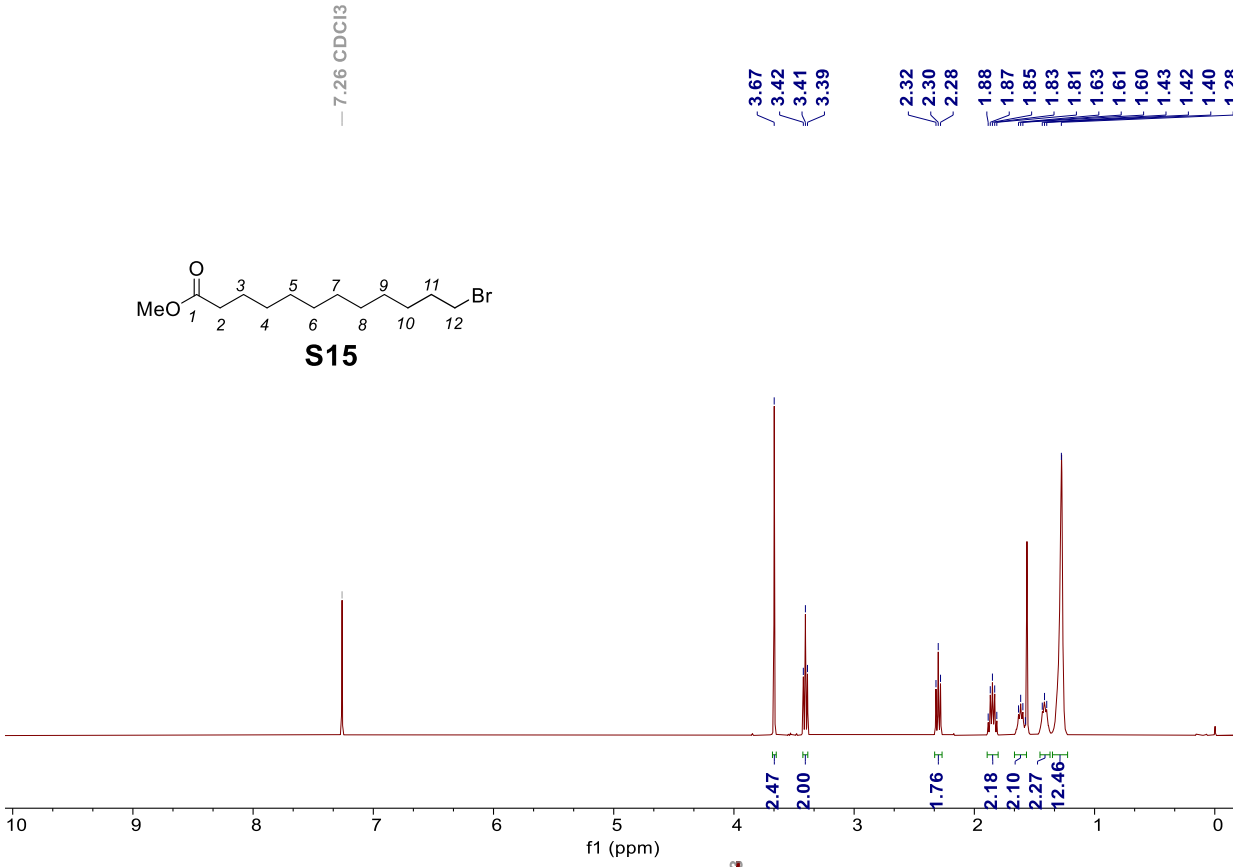
29

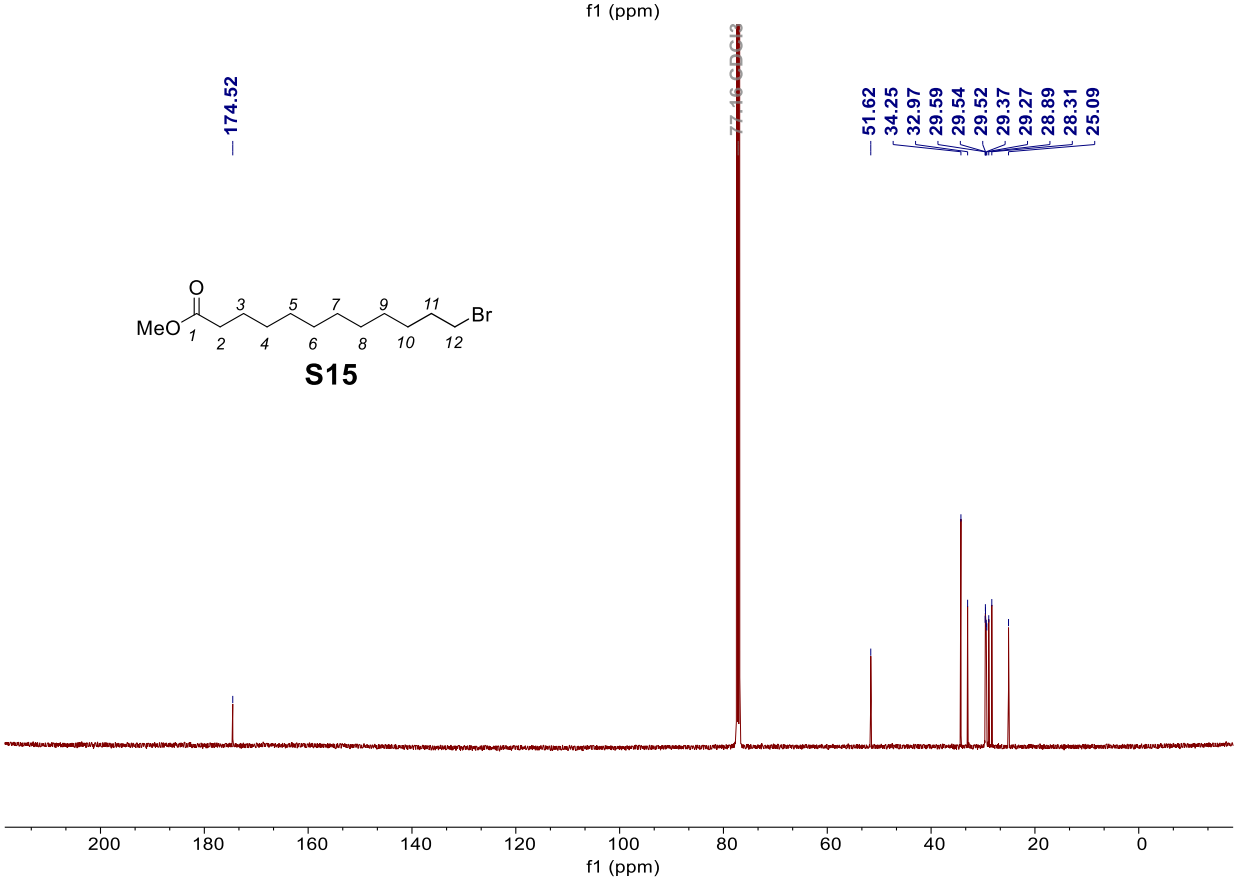

178.33
150.23
150.18
150.12
52.78
52.73
52.69
43.15
35.86
18.28
12.51

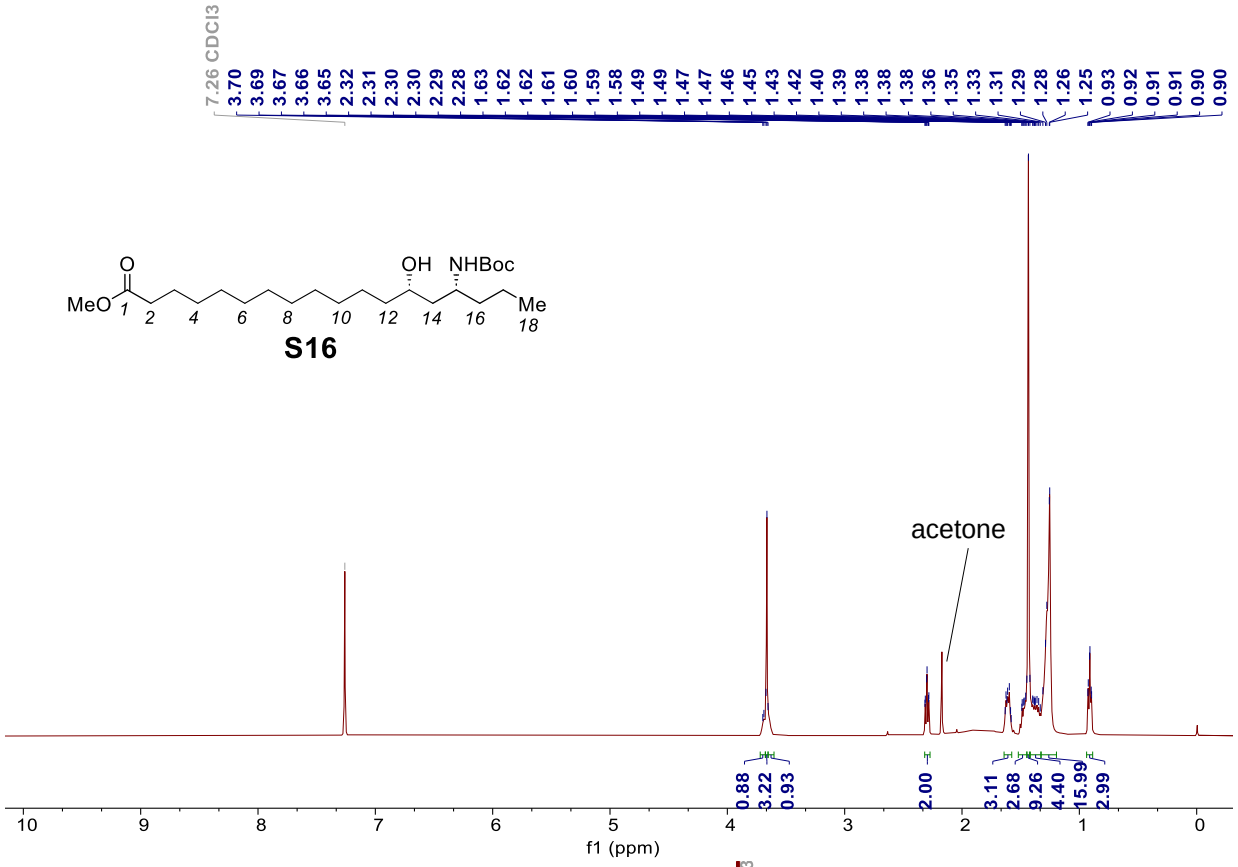

HO
O
C
N
Me
1
2
3
4
5
6

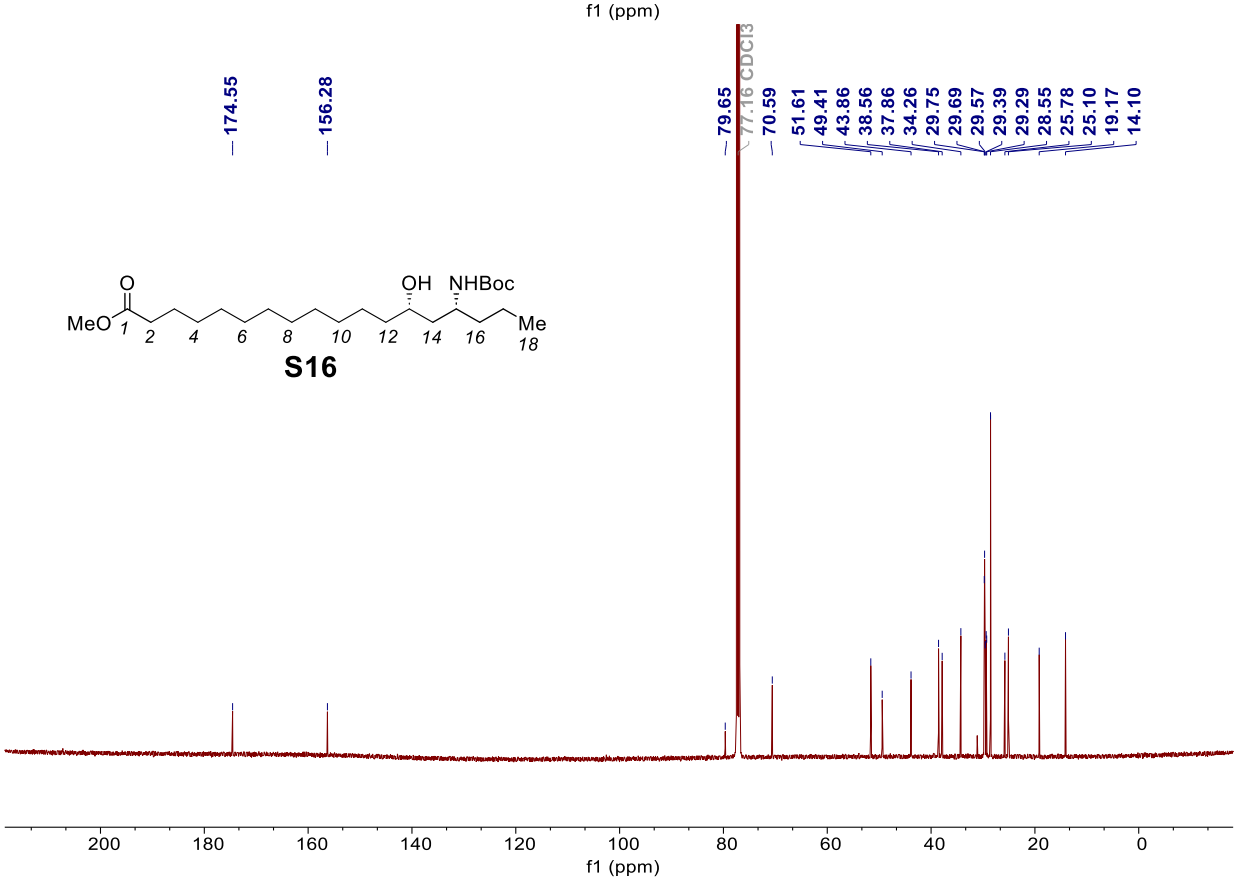
29

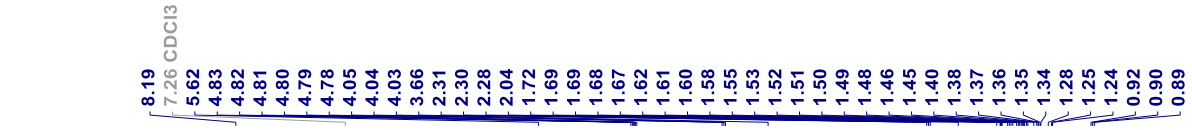
THF
THF
f1 (ppm)

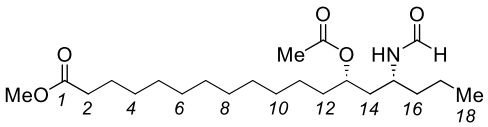

7.26 CDCl3
3.67
3.42
3.41
3.39
2.32
2.30
2.28
1.88
1.87
1.85
1.83
1.81
1.63
1.61
1.60
1.43
1.42
1.40
MeO
Br
1 2 3 4 5 6 7 8 9 10 11 12
S15
2.47
2.00
1.76
2.18
2.10
2.27
12.46
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)


174.52
77.16 CDCl3
51.62
34.25
32.97
29.59
29.54
29.52
29.37
29.27
28.89
28.31
25.09
MeO
Br
1 2 3 4 5 6 7 8 9 10 11 12
S15
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

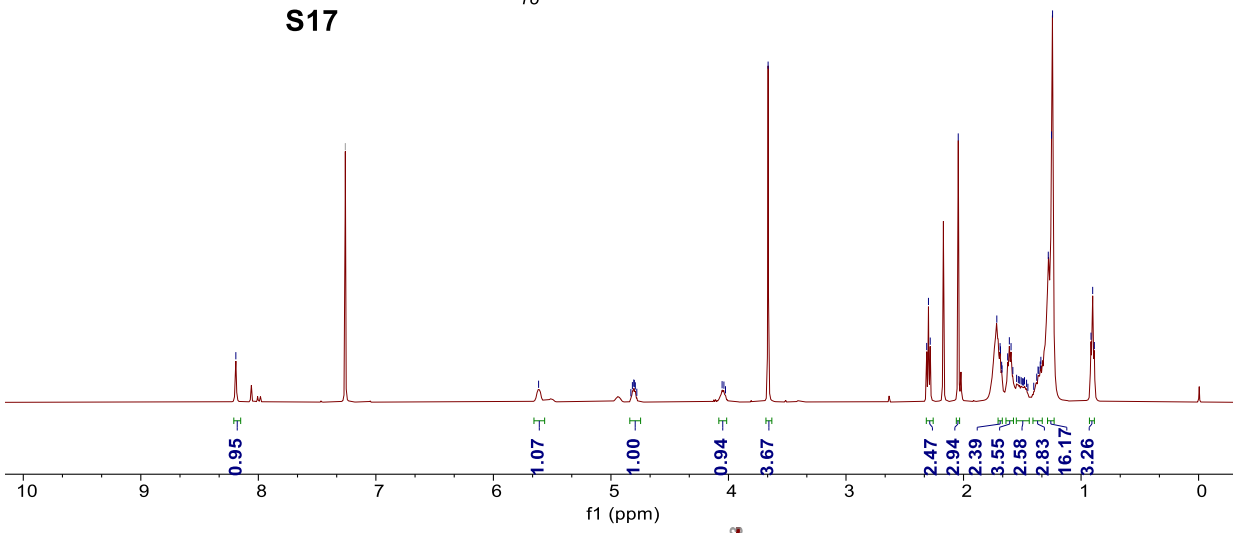

7.26 CDCl3
3.70 3.69 3.67 3.66 3.65 2.32 2.31 2.30 2.30 2.29 2.28 1.63 1.62 1.62 1.61 1.60 1.59 1.58 1.49 1.49 1.47 1.47 1.46 1.45 1.43 1.42 1.40 1.39 1.38 1.38 1.38 1.36 1.35 1.33 1.31 1.29 1.28 1.26 1.25 0.93 0.92 0.91 0.91 0.90 0.90
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14 16 18
S16
acetone
0.88 3.22 0.93 2.00 3.11 2.68 9.26 4.40 15.99 2.99
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

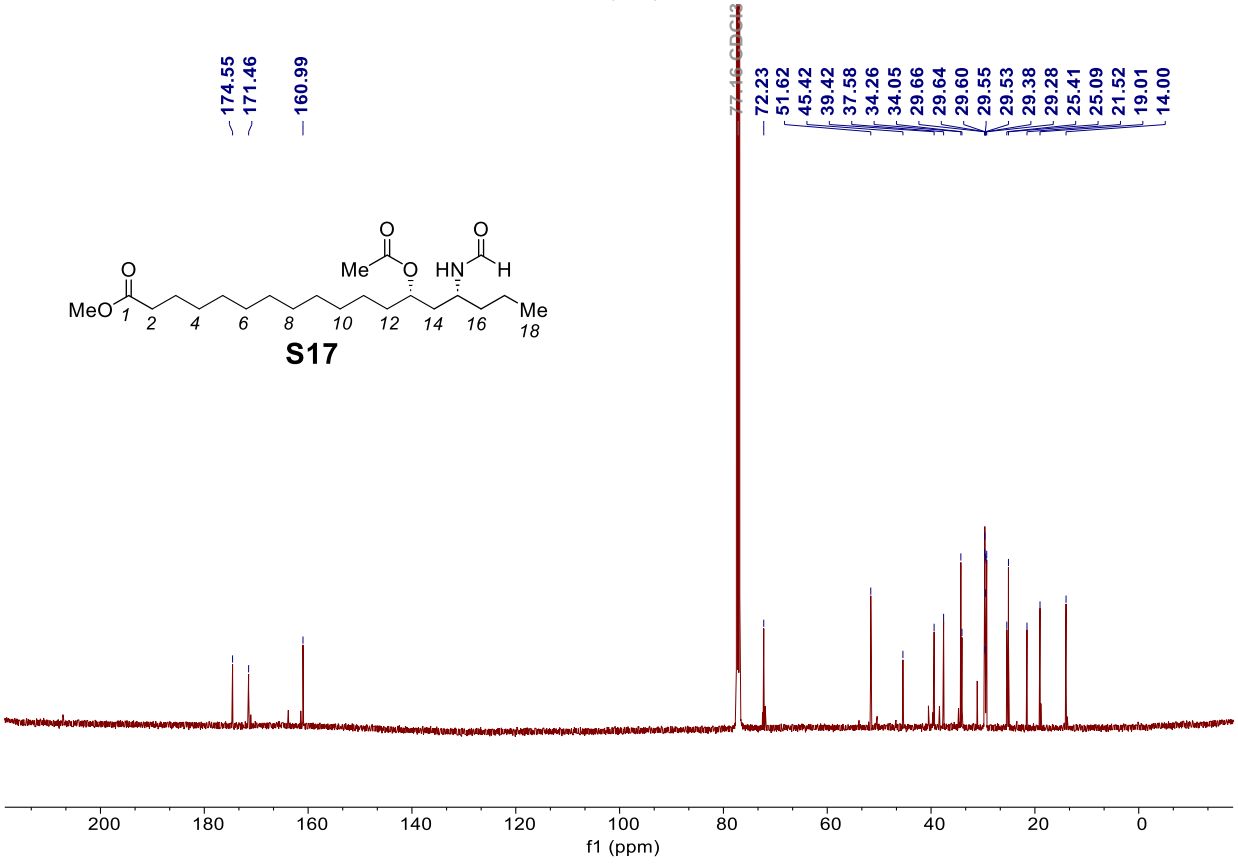

174.55
156.28
79.65
77.16 CDCl3
70.59
51.61 49.41 43.86 38.56 37.86 34.26 29.75 29.69 29.57 29.39 29.29 28.55 25.78 25.10 19.17 14.10
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14 16 18
S16
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


8.19
7.26 CDCl3
5.62
4.83
4.82
4.81
4.80
4.79
4.78
4.05
4.04
4.03
3.66
2.31
2.30
2.28
2.04
1.72
1.69
1.69
1.68
1.67
1.62
1.61
1.60
1.58
1.55
1.53
1.52
1.51
1.50
1.49
1.48
1.46
1.45
1.40
1.38
1.37
1.36
1.35
1.34
1.28
1.25
1.24
0.92
0.90
0.89


O
Me
O
HN
H
MeO
1
2
4
6
8
10
12
14
16
Me
18

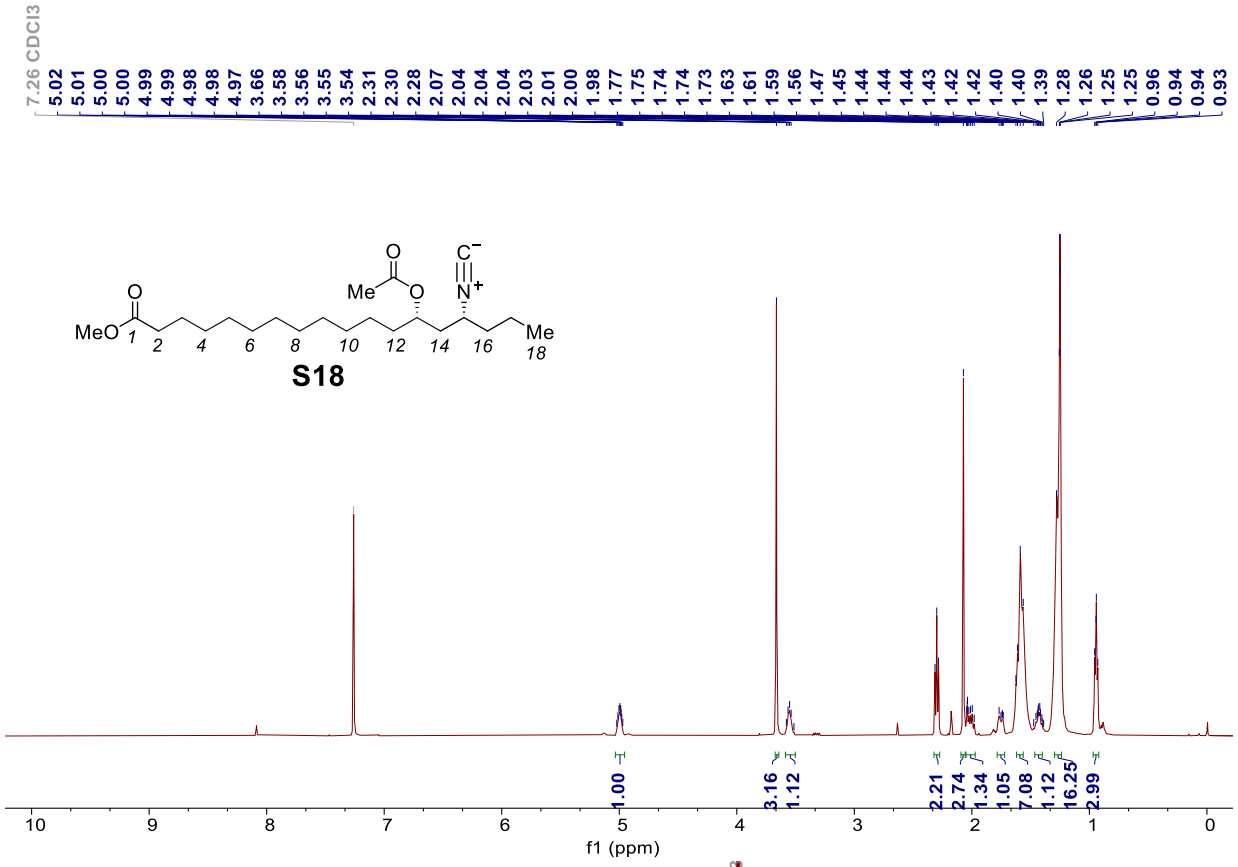
S17

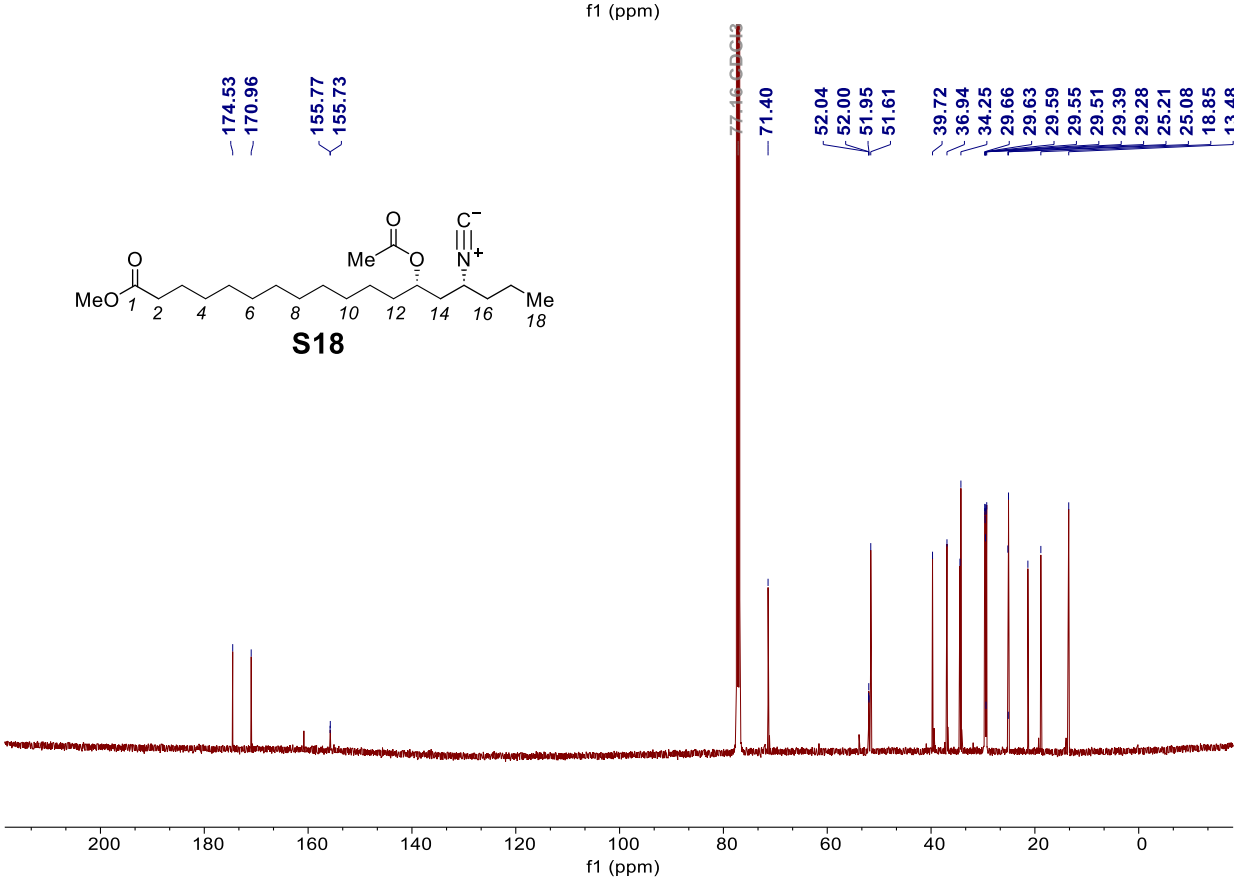

0.95
1.07
1.00
0.94
3.67
2.47
2.94
2.39
3.55
2.58
2.83
16.17
3.26
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

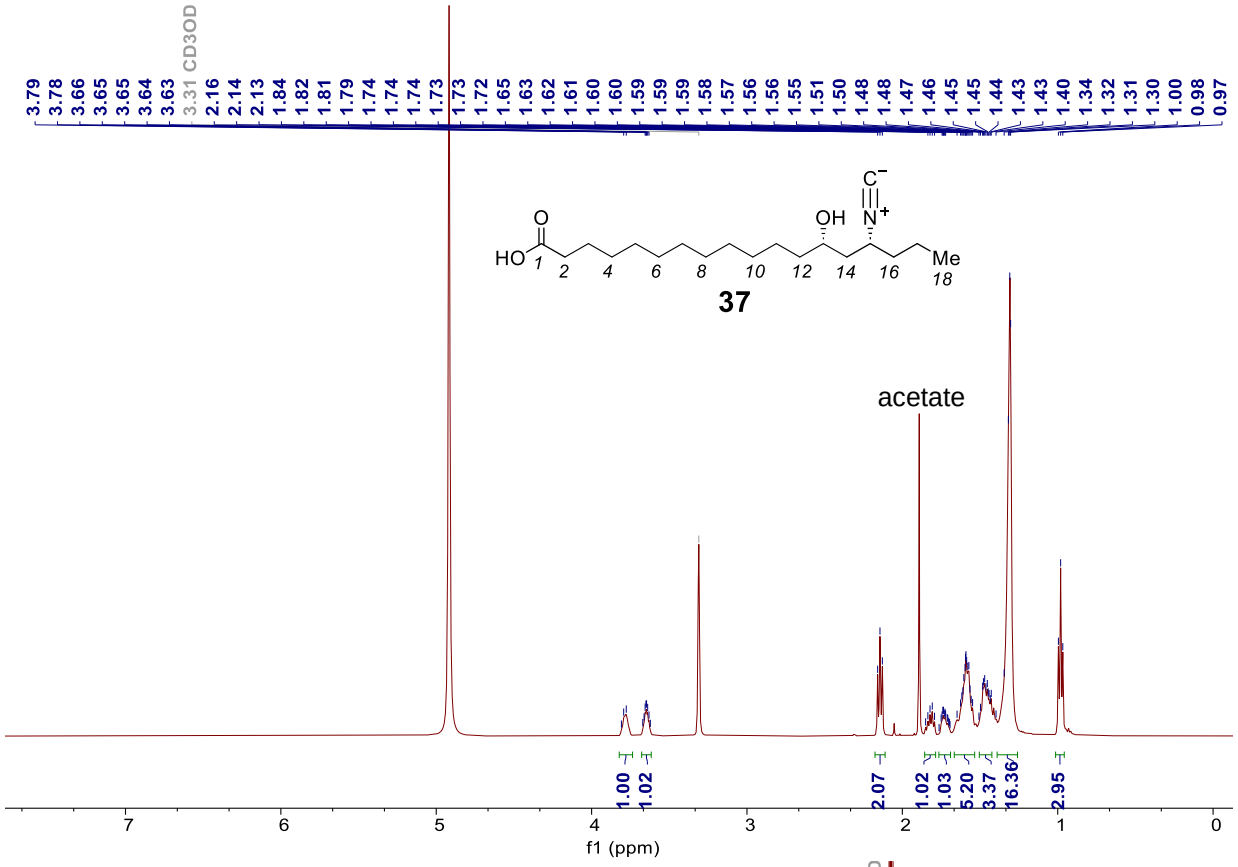

174.55
171.46
160.99
77.16 CDCl3
72.23
51.62
45.42
39.42
37.58
34.26
34.05
29.66
29.64
29.60
29.55
29.53
29.38
29.28
25.41
25.09
21.52
19.01
14.00
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

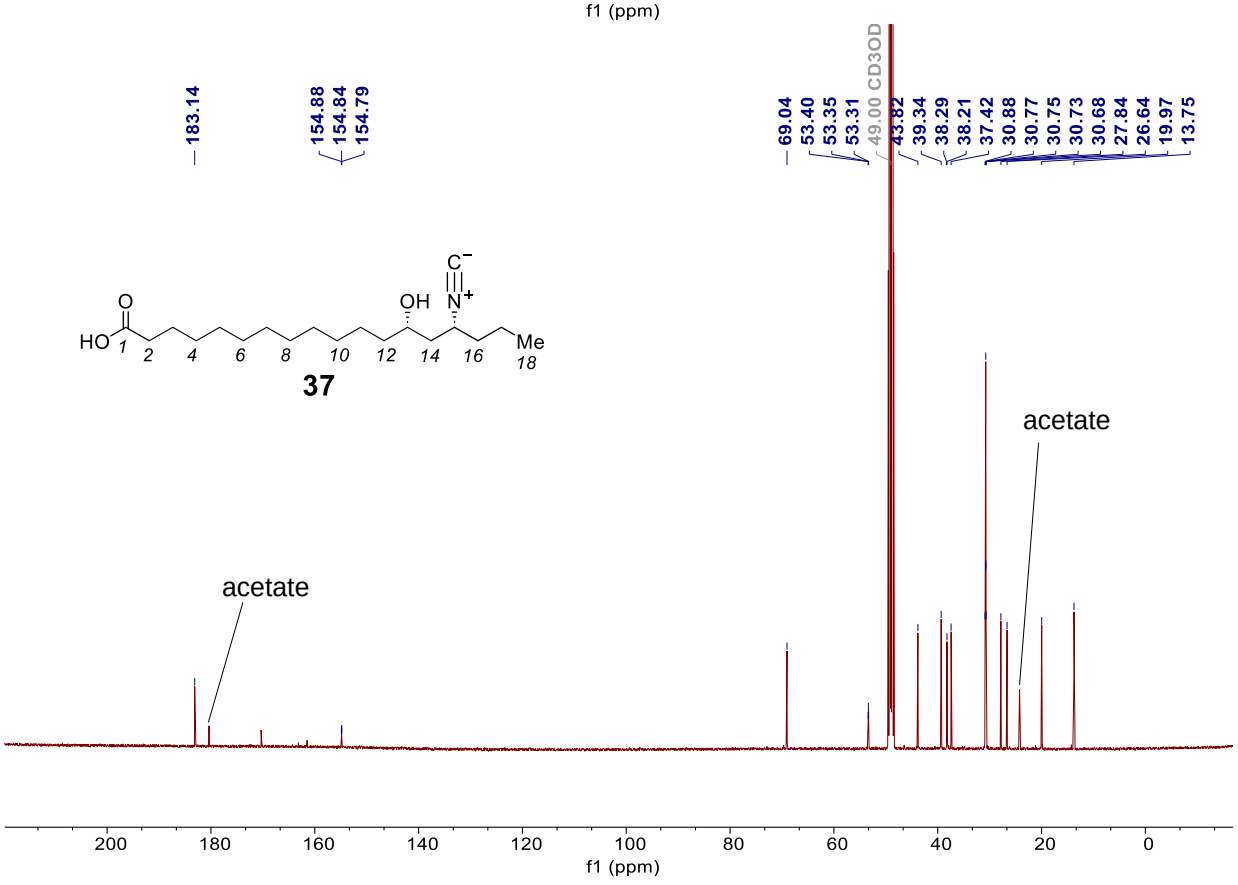
O
Me
O
HN
H
MeO
1
2
4
6
8
10
12
14
16
Me
18

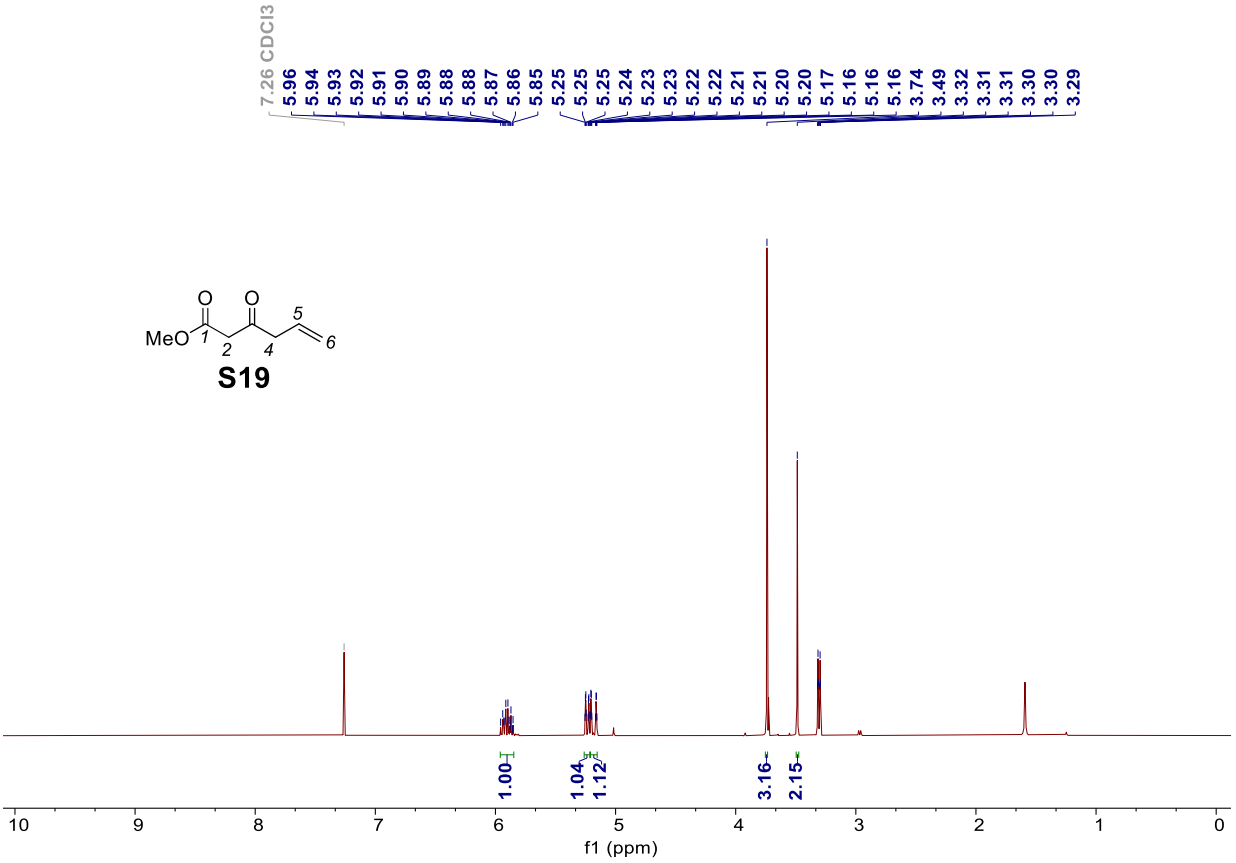
S17

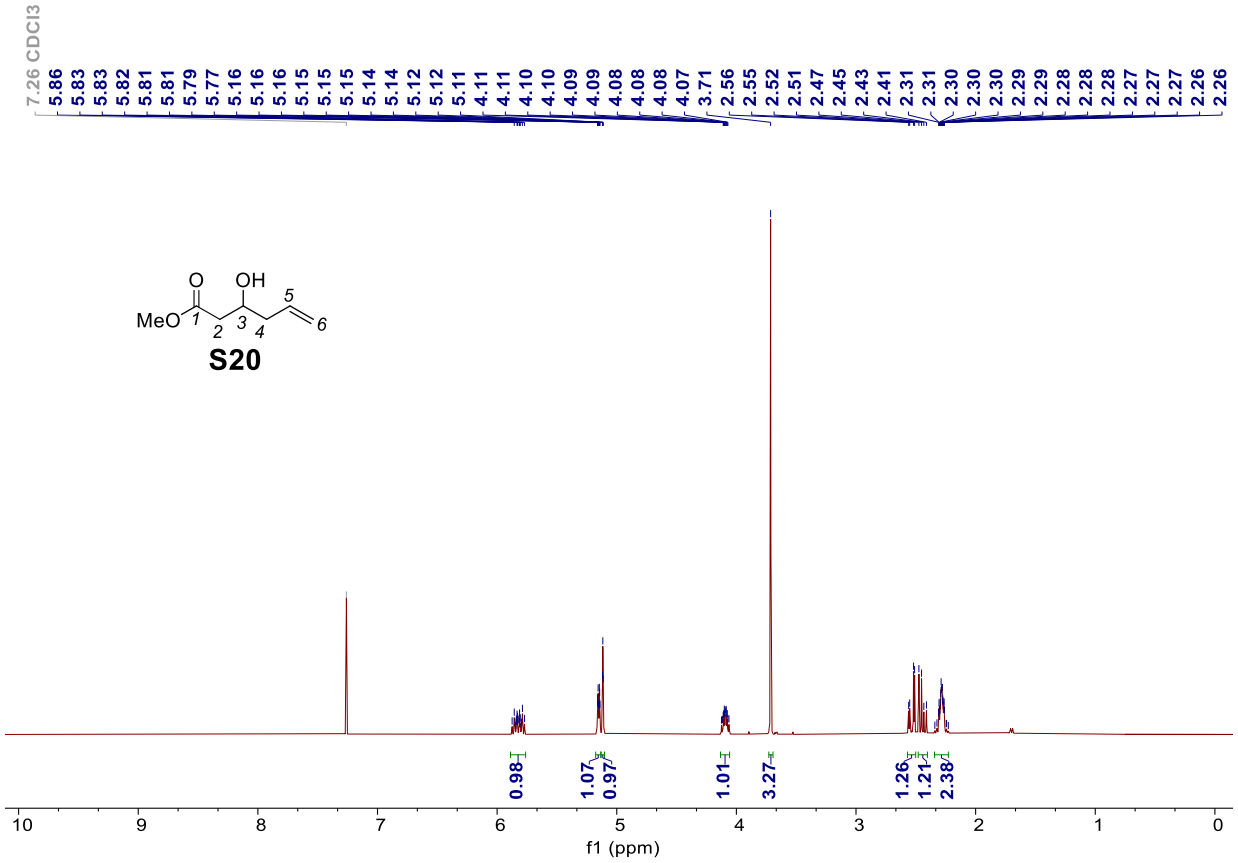

7.26 CDCl3
5.02 5.01 5.00 5.00 4.99 4.99 4.98 4.98 4.97 3.66 3.58 3.56 3.55 3.54 2.31 2.30 2.28 2.07 2.04 2.04 2.04 2.03 2.01 2.00 1.98 1.77 1.75 1.74 1.74 1.73 1.63 1.61 1.59 1.56 1.47 1.45 1.44 1.44 1.44 1.43 1.42 1.42 1.40 1.40 1.39 1.28 1.26 1.25 1.25 0.96 0.94 0.94 0.93
MeO
Me
S18
1.00 3.16 1.12 2.21 2.74 1.34 1.05 7.08 1.12 16.25 2.99
f1 (ppm)

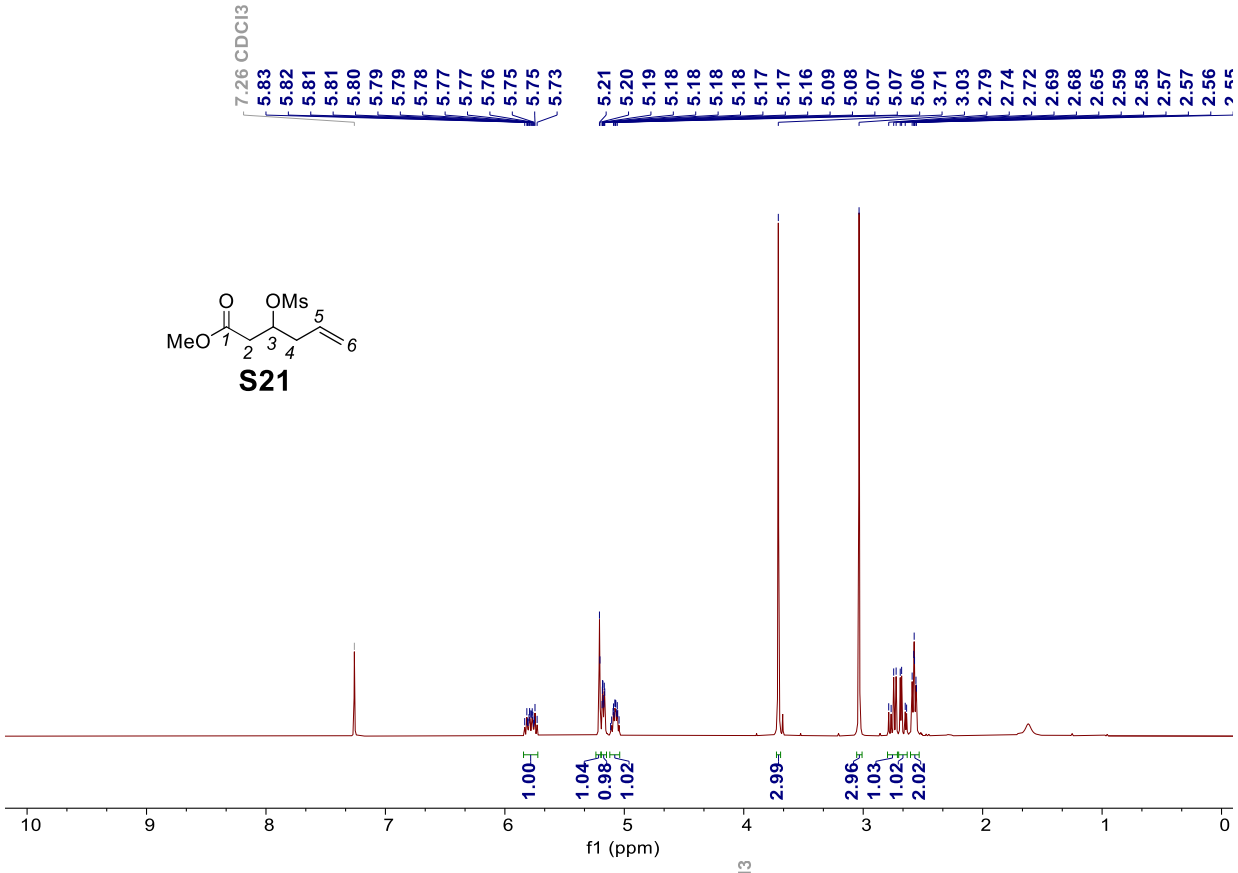

174.53 170.96 155.77 155.73
77.46 CDCl3
71.40
52.04 52.00 51.95 51.61 39.72 36.94 34.25 29.66 29.63 29.59 29.55 29.51 29.39 29.28 25.21 25.08 18.85
MeO
Me
S18
f1 (ppm)

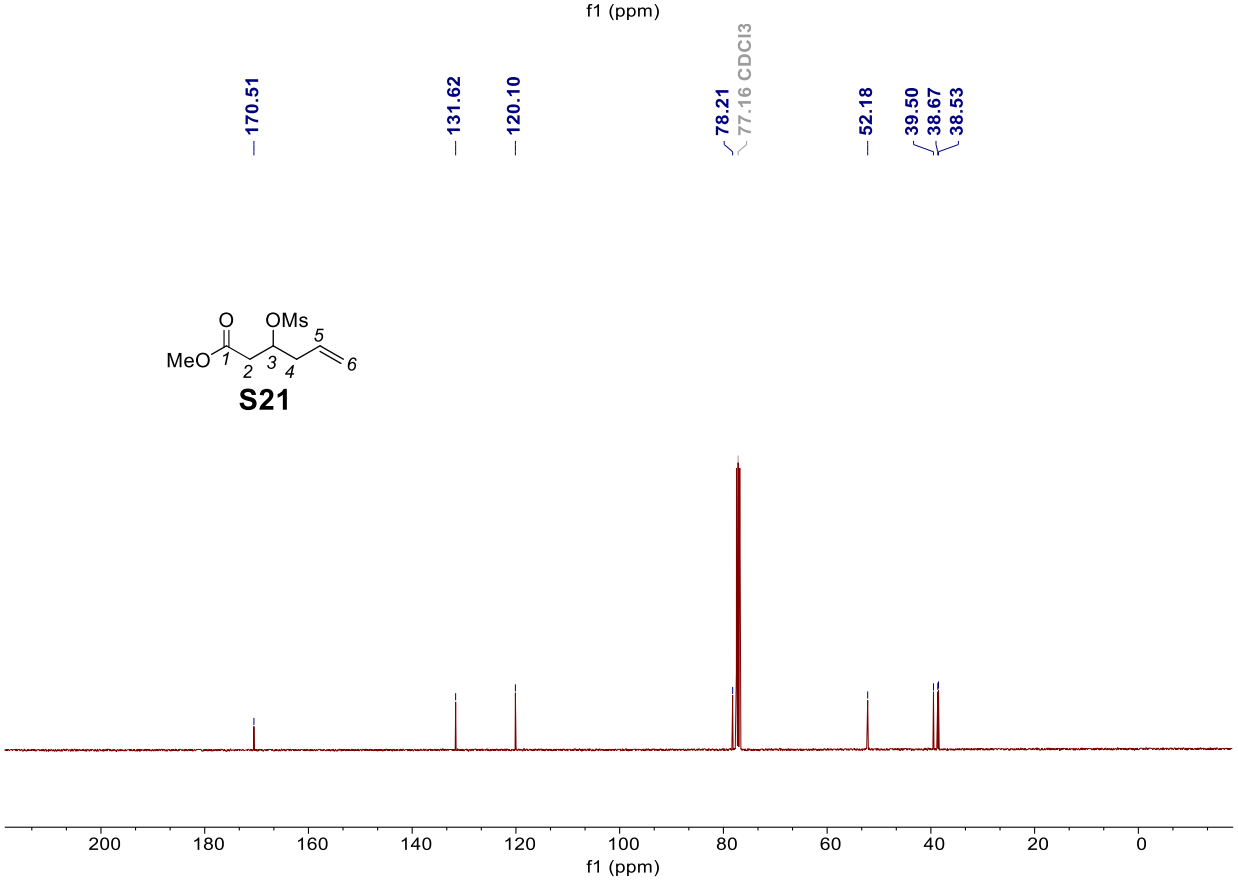

3.79 3.78 3.66 3.65 3.65 3.64 3.63 3.31 CD3OD 2.16 2.14 2.13 1.84 1.82 1.81 1.79 1.74 1.74 1.74 1.73 1.73 1.72 1.65 1.63 1.62 1.61 1.60 1.60 1.59 1.59 1.59 1.58 1.57 1.56 1.56 1.55 1.51 1.50 1.48 1.48 1.47 1.46 1.45 1.45 1.44 1.43 1.43 1.40 1.34 1.32 1.31 1.30 1.00 0.98 0.97
HO
O
OH
N+
C−
Me
1 2 4 6 8 10 12 14 16 18
37
acetate
1.00 1.02 2.07 1.02 1.03 5.20 3.37 16.36 2.95
7 6 5 4 3 2 1 0
f1 (ppm)


183.14
154.88 154.84 154.79
69.04 53.40 53.35 53.31 49.00 CD3OD 43.82 39.34 38.29 38.21 37.42 30.88 30.77 30.75 30.73 30.68 27.84 26.64 19.97 13.75
HO
O
OH
N+
C−
Me
1 2 4 6 8 10 12 14 16 18
37
acetate
acetate
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


7.26 CDCl3
5.96
5.94
5.93
5.92
5.91
5.90
5.89
5.88
5.88
5.87
5.86
5.85
5.25
5.25
5.25
5.24
5.23
5.23
5.22
5.22
5.21
5.21
5.20
5.20
5.17
5.16
5.16
5.16
3.74
3.49
3.32
3.31
3.31
3.30
3.30
3.29
MeO
1
2
4
5
6
S19
1.00
1.04
1.12
3.16
2.15
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


7.26 CDCl3
5.86 5.83 5.83 5.82 5.81 5.81 5.79 5.77 5.16 5.16 5.16 5.15 5.15 5.15 5.14 5.14 5.12 5.12 5.11 4.11 4.11 4.10 4.10 4.09 4.09 4.08 4.08 4.08 4.07 3.71 2.56 2.55 2.52 2.51 2.47 2.45 2.43 2.41 2.31 2.31 2.30 2.30 2.30 2.29 2.29 2.28 2.28 2.28 2.27 2.27 2.26 2.26
O
OH
MeO
1
2
3
4
5
6
S20
0.98
1.07
0.97
1.01
3.27
1.26
1.21
2.38
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


7.26 CDCl3
5.83 5.82 5.81 5.81 5.80 5.79 5.79 5.78 5.77 5.77 5.76 5.75 5.75 5.73
5.21 5.20 5.19 5.18 5.18 5.18 5.17 5.17 5.16 5.09 5.08 5.07 5.07 5.06 3.71 3.03 2.79 2.74 2.72 2.69 2.68 2.65 2.59 2.58 2.57 2.57 2.56
O
OMs
5
MeO
1
2
3
4
6
S21
1.00 1.04 0.98 1.02 2.99 2.96 1.03 1.02 2.02
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)


170.51
131.62
120.10
78.21
77.16 CDCl3
52.18
39.50
38.67
38.53
O
OMs
5
MeO
1
2
3
4
6
S21
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


7.26 CDCl3
5.85
5.83
5.83
5.82
5.81
5.81
5.80
5.79
5.79
5.78
5.77
5.76
5.75
5.21
5.20
5.20
5.19
5.19
5.18
5.18
5.18
5.18
5.16
5.16
5.15
3.94
3.92
3.91
3.91
3.90
3.90
3.89
3.88
3.87
3.72
2.56
2.55
2.52
2.51
2.50
2.47
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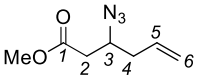
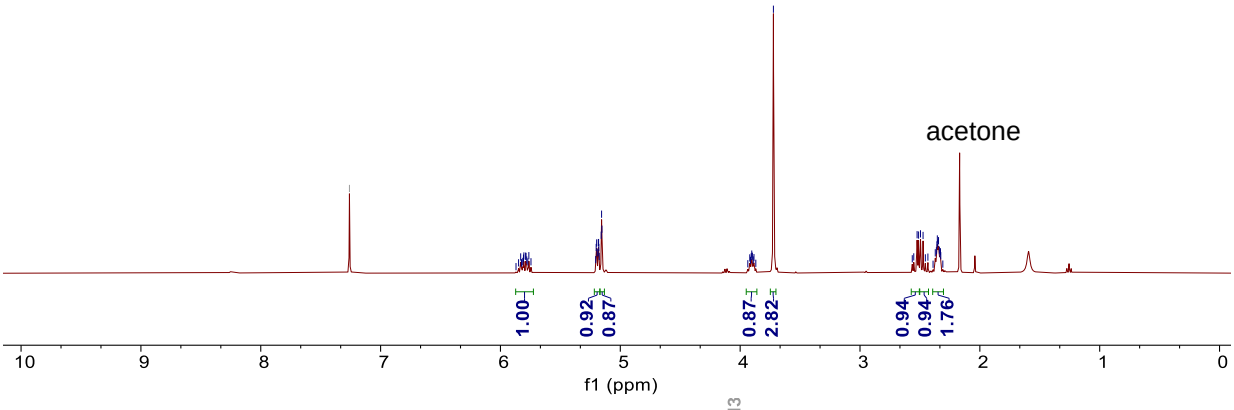
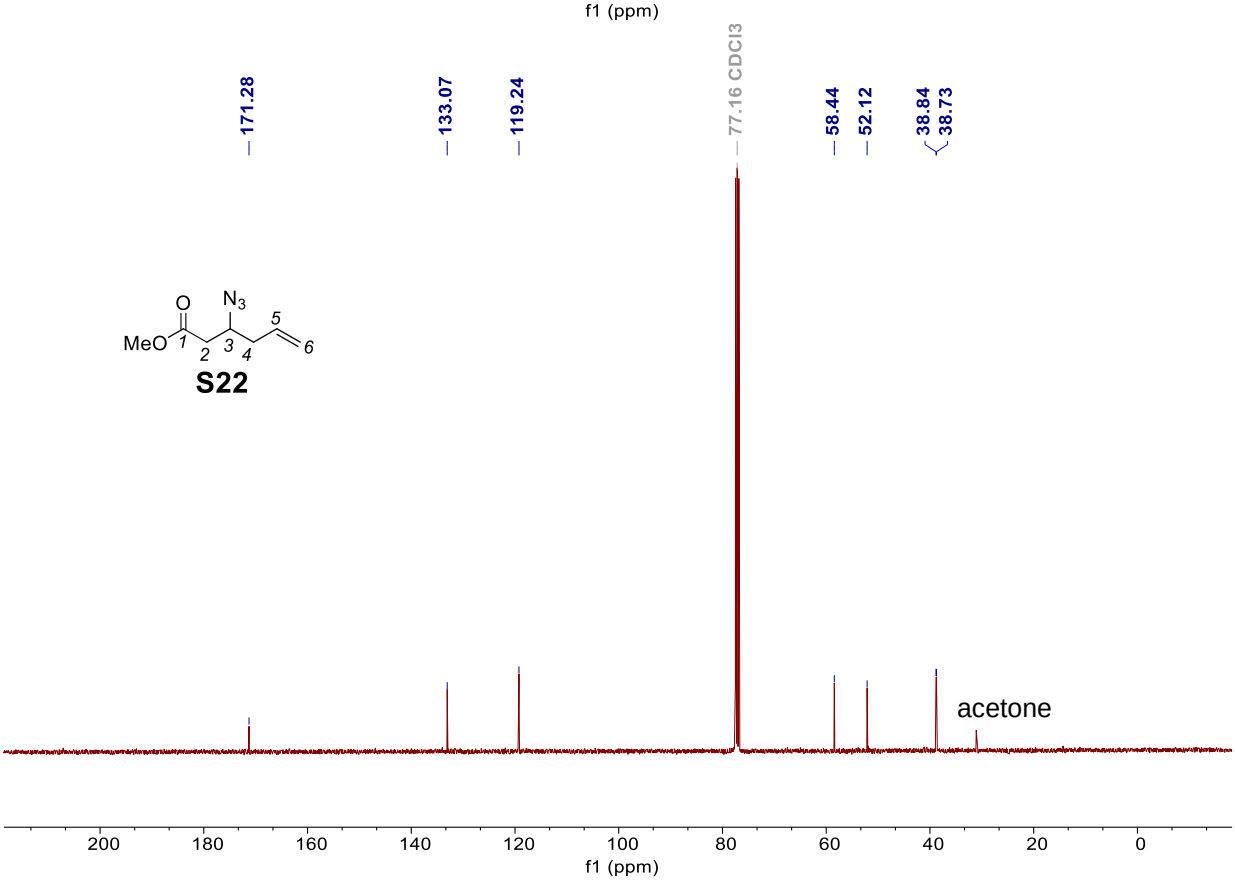
2.35
2.34
2.34
2.33
2.33
2.33


O
N3
MeO
1
2
3
4
5
6

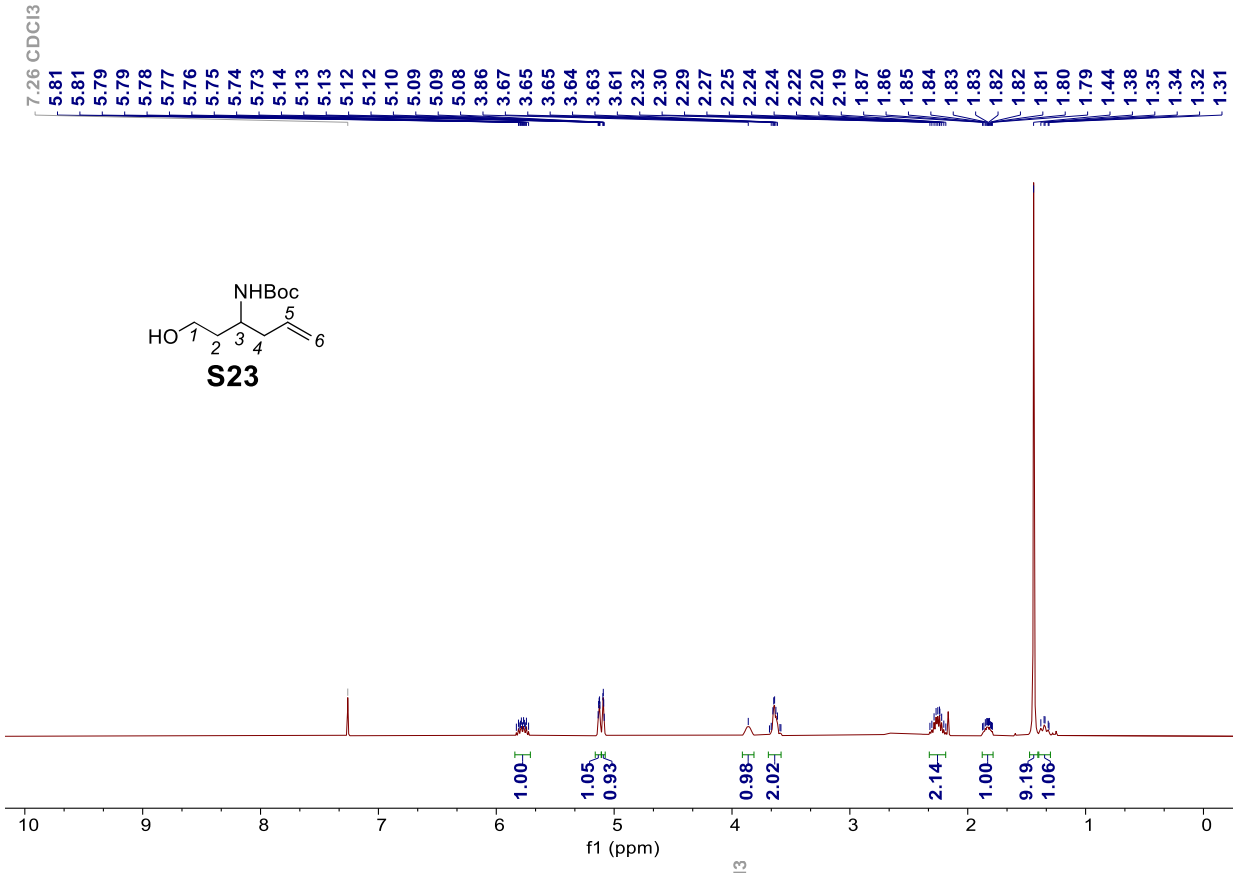
S22

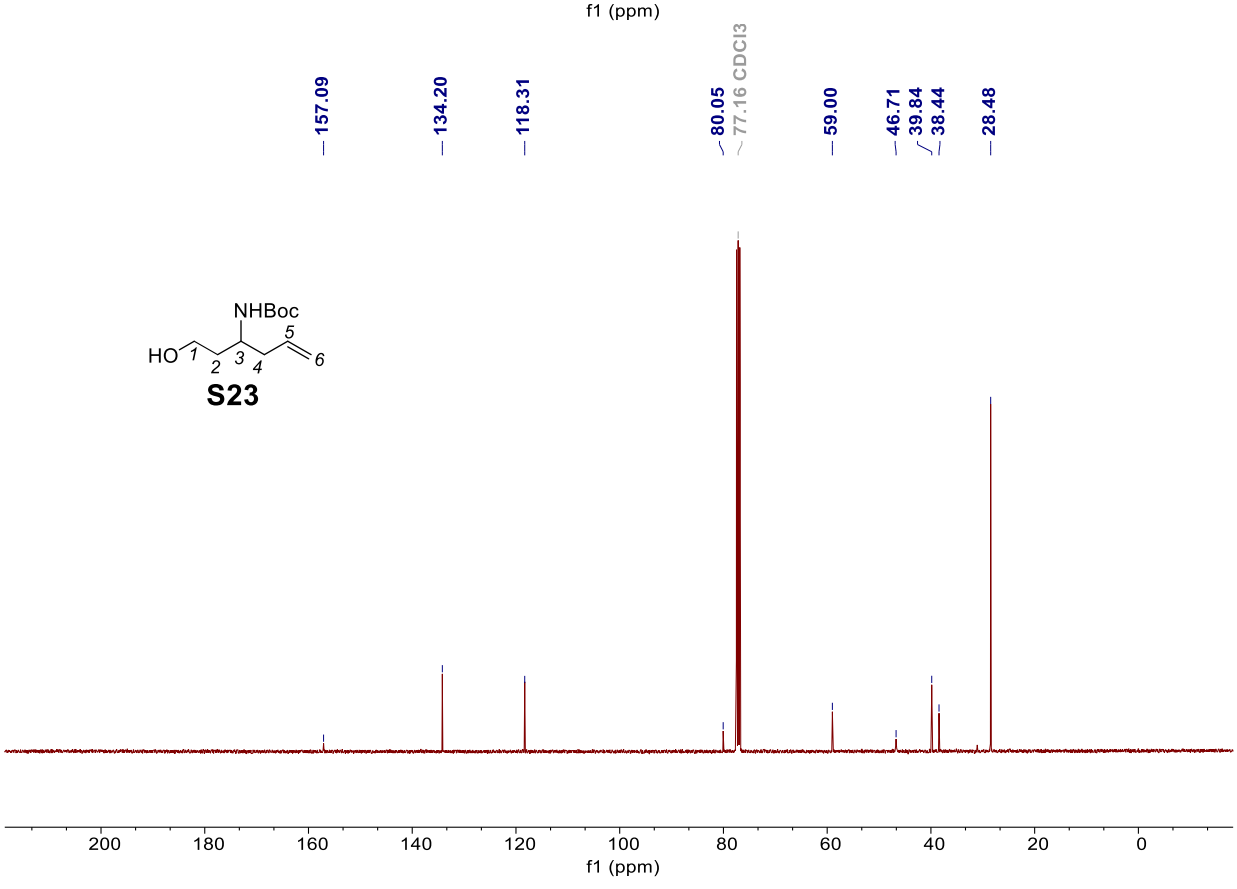

acetone
1.00
0.92
0.87
0.87
2.82
0.94
0.94
1.76
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

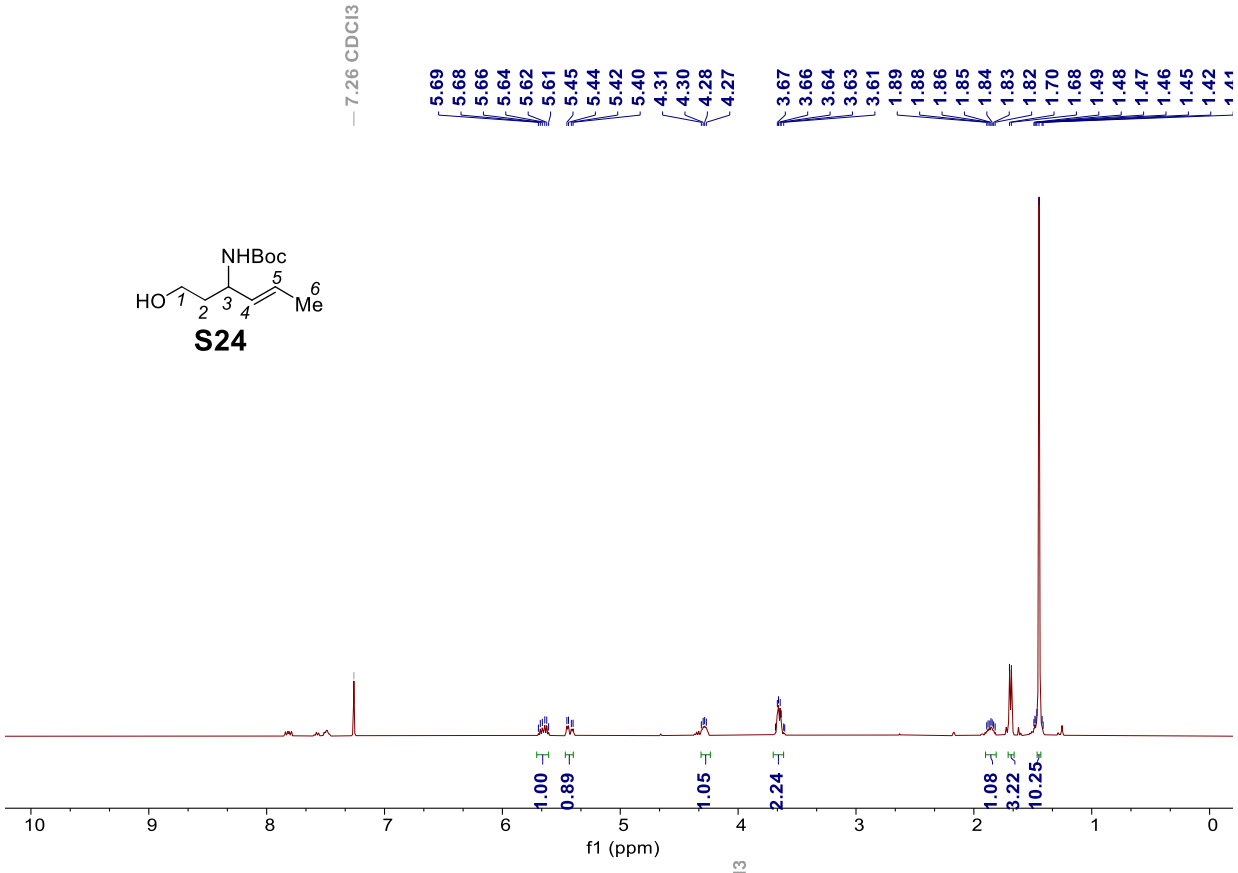

171.28
133.07
119.24
77.16 CDCl3
58.44
52.12
38.84
38.73
acetone
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

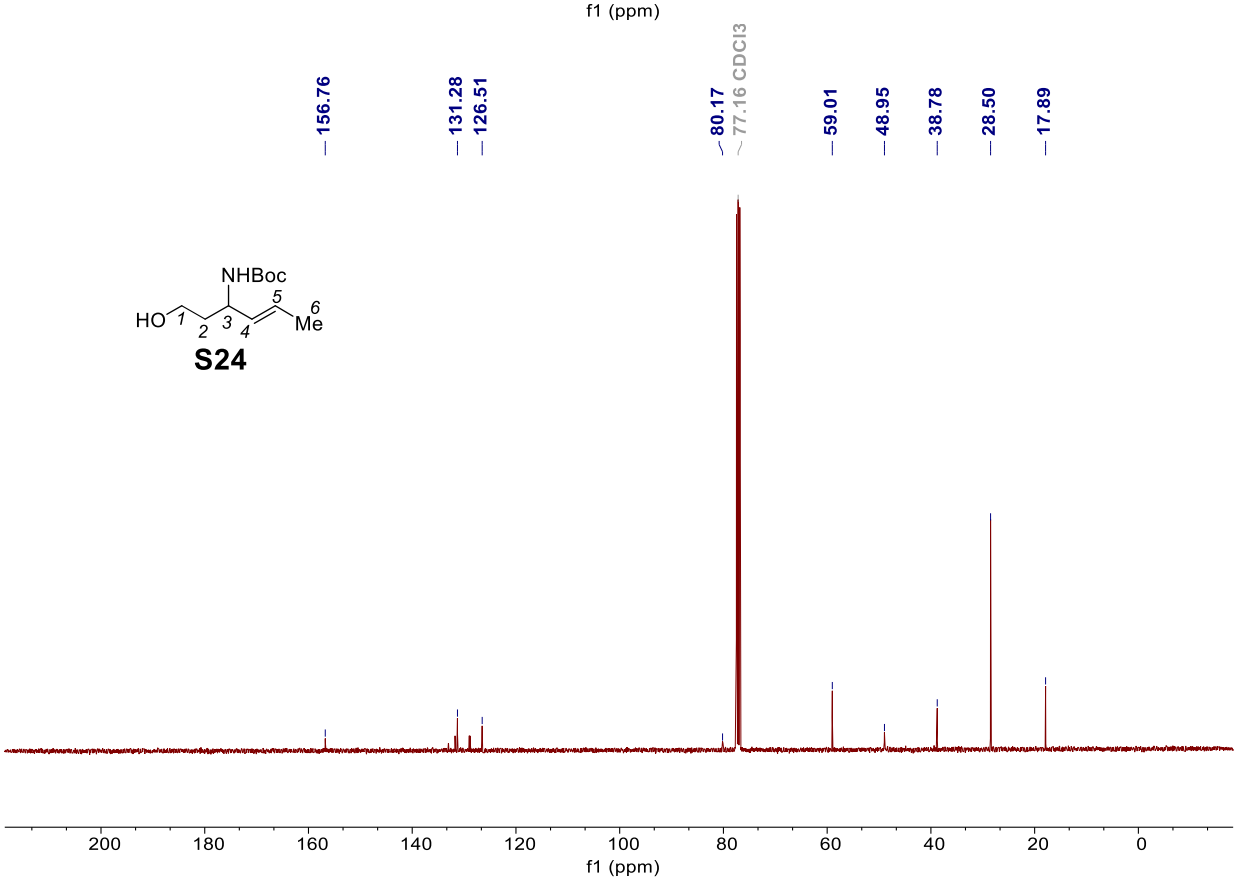
O
N3
MeO
1
2
3
4
5
6

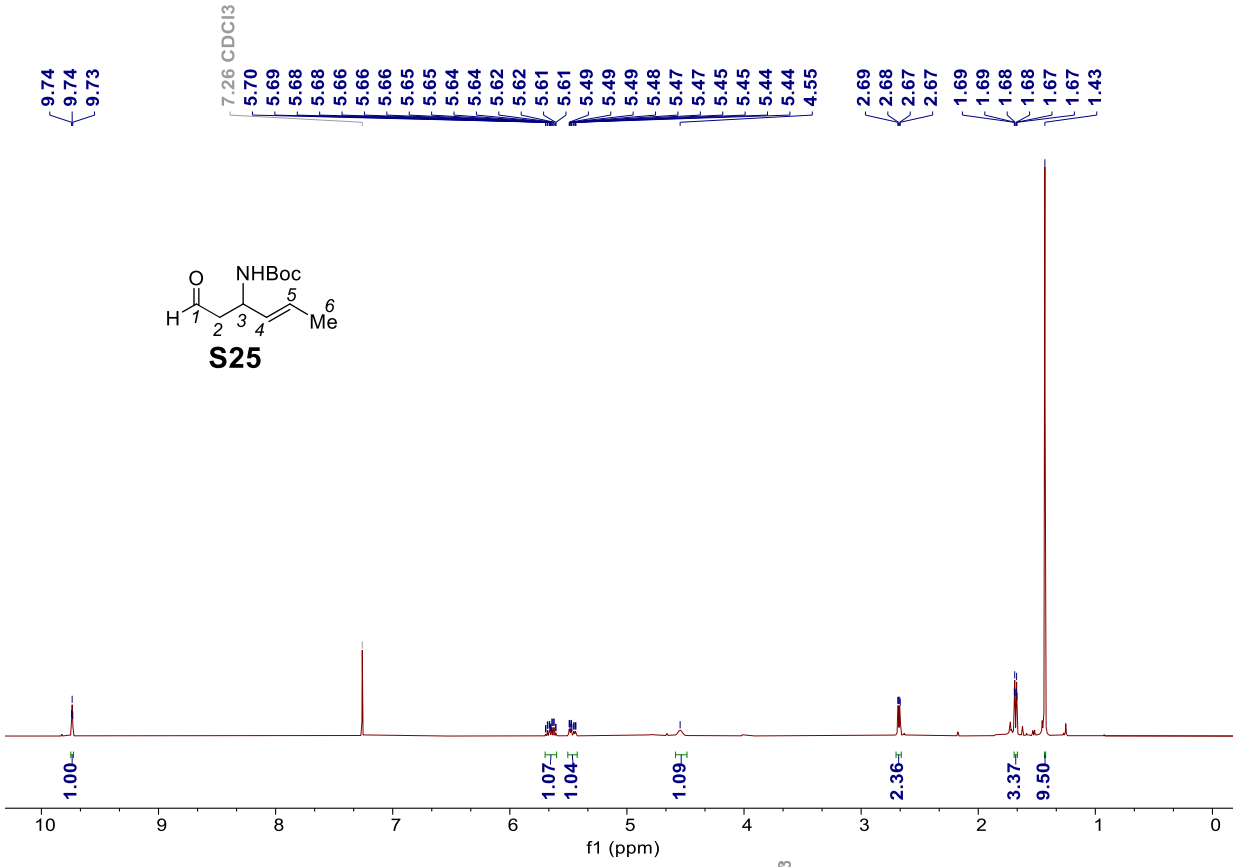
S22

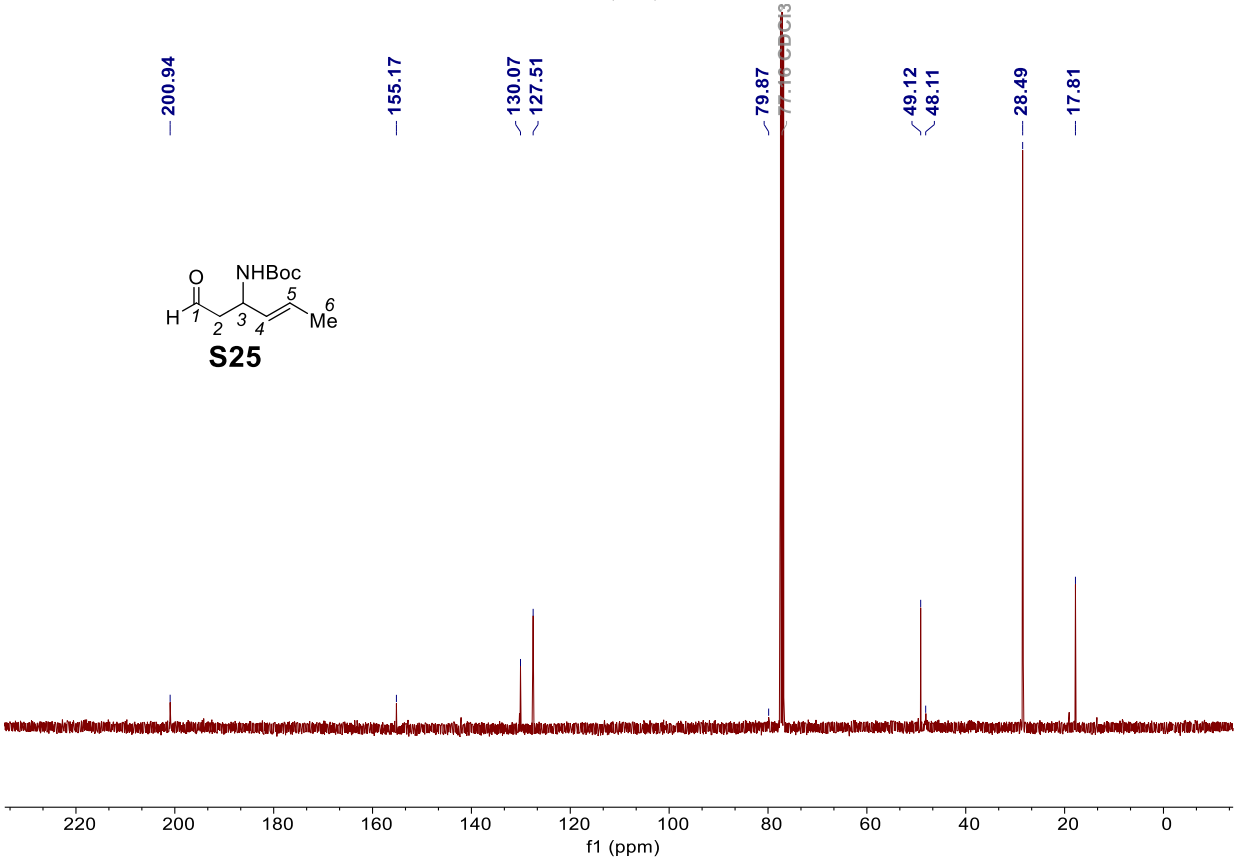

7.26 CDCl3
5.81 5.81 5.79 5.79 5.78 5.77 5.76 5.75 5.74 5.73 5.14 5.13 5.13 5.12 5.12 5.10 5.09 5.09 5.08 3.86 3.67 3.65 3.65 3.64 3.63 3.61 2.32 2.30 2.29 2.27 2.25 2.24 2.24 2.22 2.20 2.19 1.87 1.86 1.85 1.84 1.83 1.83 1.82 1.82 1.81 1.80 1.79 1.44 1.38 1.35 1.34 1.32 1.31
NHBoc
HO
1 2 3 4 5 6
S23
1.00 1.05 0.93 0.98 2.02 2.14 1.00 9.19 1.06
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

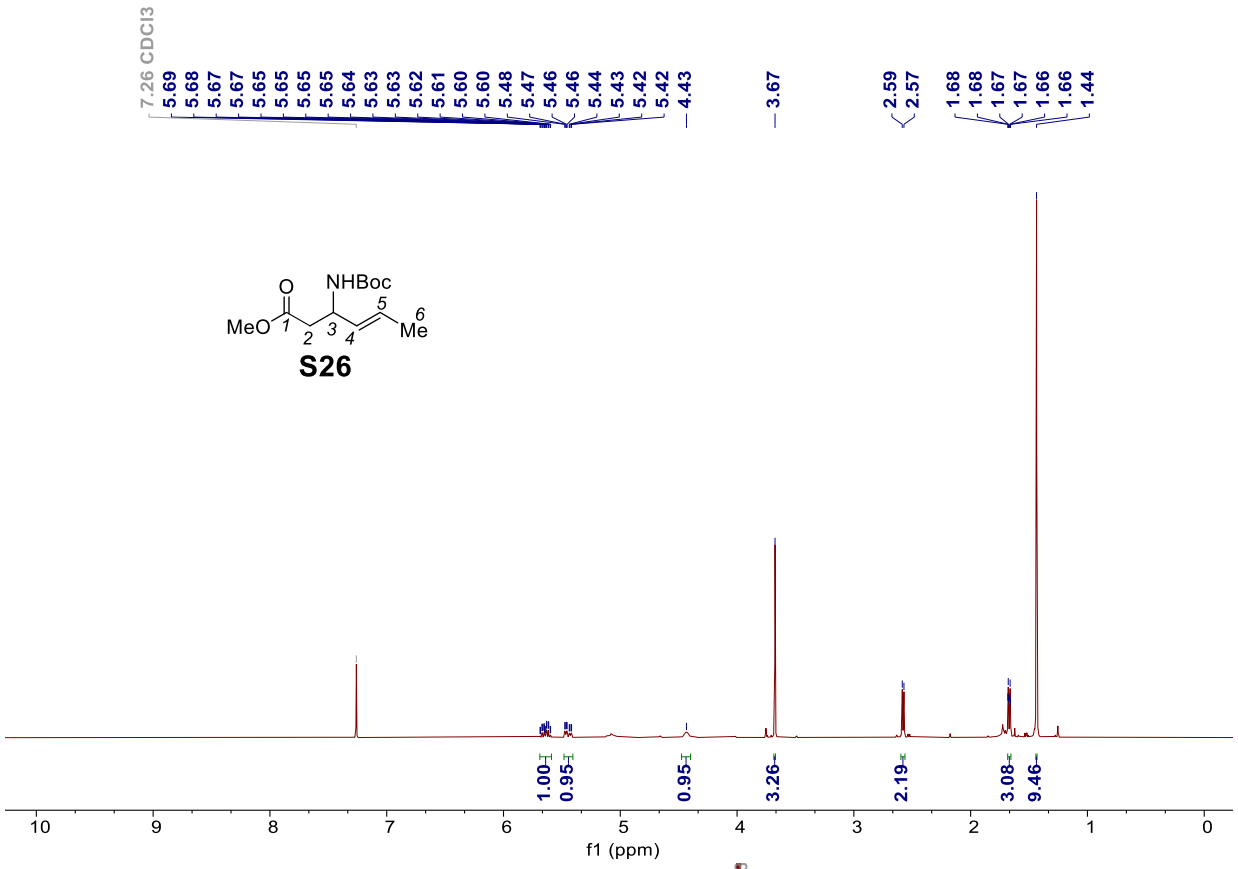

157.09 134.20 118.31 80.05 77.16 CDCl3 59.00 46.71 39.84 38.44 28.48
NHBoc
HO
1 2 3 4 5 6
S23
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


7.26 CDCl3
5.69
5.68
5.66
5.64
5.62
5.61
5.45
5.44
5.42
5.40
4.31
4.30
4.28
4.27
3.67
3.66
3.64
3.63
3.61
1.89
1.88
1.86
1.85
1.84
1.83
1.82
1.70
1.68
1.49
1.48
1.47
1.46
1.45
1.42
NHBoc
HO
Me
S24
1.00
0.89
1.05
2.24
1.08
3.22
10.25
f1 (ppm)

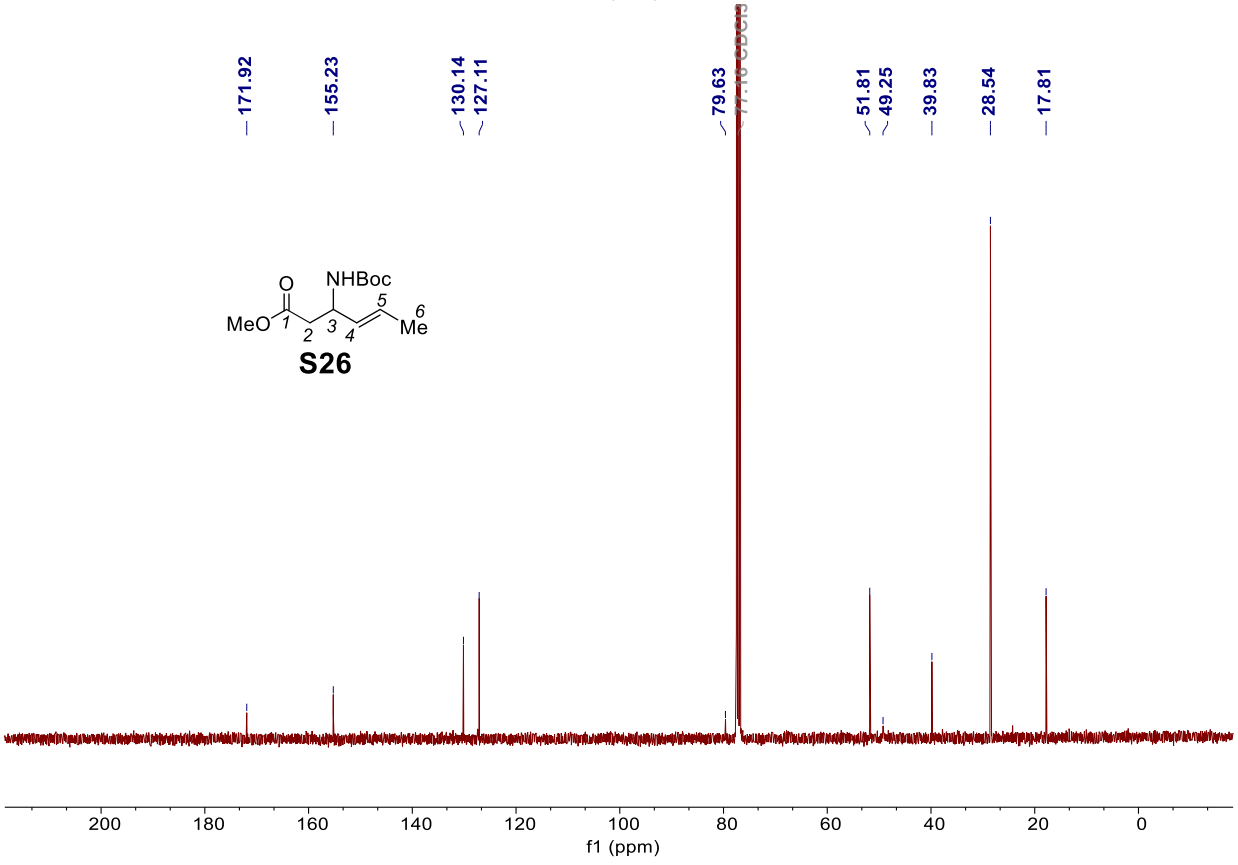

156.76
131.28
126.51
80.17
77.16 CDCl3
59.01
48.95
38.78
28.50
17.89
NHBoc
HO
Me
S24
f1 (ppm)


9.74
9.74
9.73
7.26 CDCl3
5.70
5.69
5.68
5.68
5.66
5.66
5.66
5.65
5.65
5.64
5.64
5.62
5.62
5.61
5.61
5.49
5.49
5.49
5.48
5.47
5.47
5.45
5.45
5.44
5.44
4.55
2.69
2.68
2.67
2.67
1.69
1.69
1.68
1.68
1.67
1.67
1.43
NHBoc
O
H
1
2
3
4
5
6
Me
S25
1.00
1.07
1.04
1.09
2.36
3.37
9.50
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

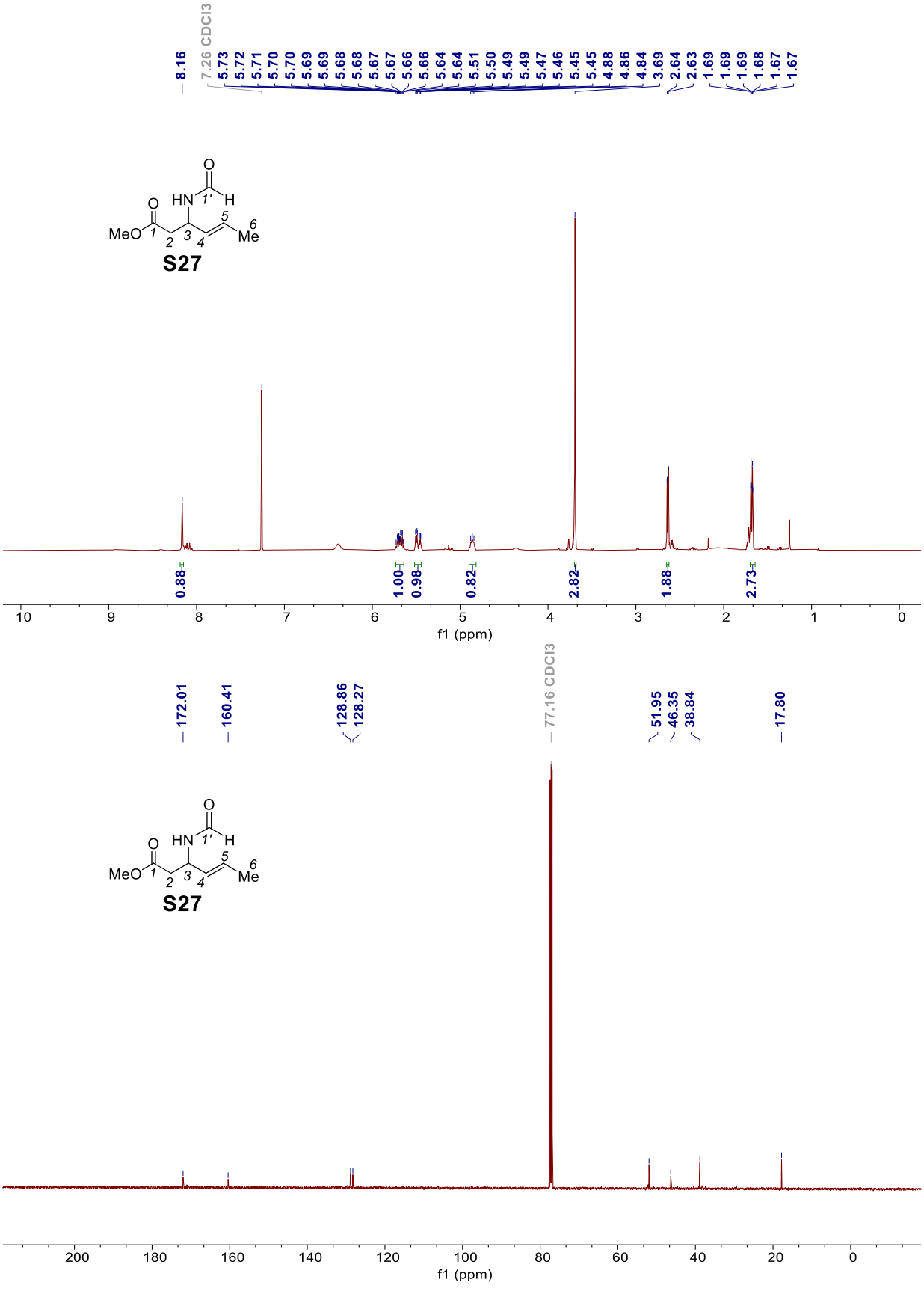

200.94
155.17
130.07
127.51
79.87
77.16 CDCl3
49.12
48.11
28.49
17.81
NHBoc
O
H
1
2
3
4
5
6
Me
S25
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

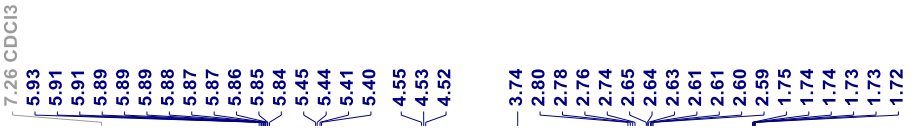

7.26 CDCl3
5.69
5.68
5.67
5.67
5.65
5.65
5.65
5.65
5.64
5.63
5.63
5.62
5.61
5.60
5.60
5.48
5.47
5.46
5.46
5.44
5.43
5.42
5.42
4.43
3.67
2.59
2.57
1.68
1.68
1.67
1.67
1.66
1.66
1.44
NHBoc
O
MeO
Me
1
2
3
4
5
6
1.00
0.95
0.95
3.26
2.19
3.08
9.46
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

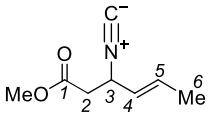
S26


171.92
155.23
130.14
127.11
79.63
77.16 CDCl3
51.81
49.25
39.83
28.54
17.81
NHBoc
O
MeO
Me
1
2
3
4
5
6
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

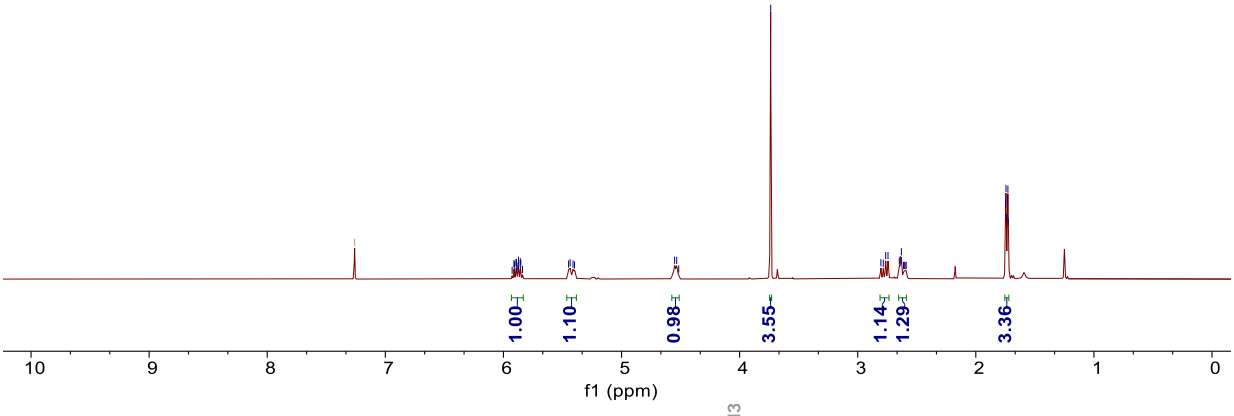
S26


8.16
7.26 CDCl3
5.73
5.72
5.71
5.70
5.70
5.69
5.69
5.68
5.68
5.67
5.67
5.66
5.66
5.64
5.64
5.51
5.50
5.49
5.49
5.47
5.46
5.45
5.45
4.88
4.86
4.84
3.69
2.64
2.63
1.69
1.69
1.69
1.68
1.67
1.67
MeO
HN
Me
S27
0.88
1.00
0.98
0.82
2.82
1.88
2.73
f1 (ppm)
172.01
160.41
128.86
128.27
77.16 CDCl3
51.95
46.35
38.84
17.80
MeO
HN
Me
S27
f1 (ppm)

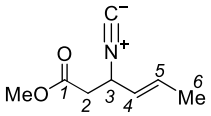

7.26 CDCl3
5.93
5.91
5.91
5.89
5.89
5.89
5.88
5.87
5.87
5.86
5.85
5.84
5.45
5.44
5.41
5.40
4.55
4.53
4.52
3.74
2.80
2.78
2.76
2.74
2.65
2.64
2.63
2.61
2.61
2.60
2.59
1.75
1.74
1.74
1.73
1.73
1.72


C
N
O
MeO
1
2
3
4
5
6
Me

S28

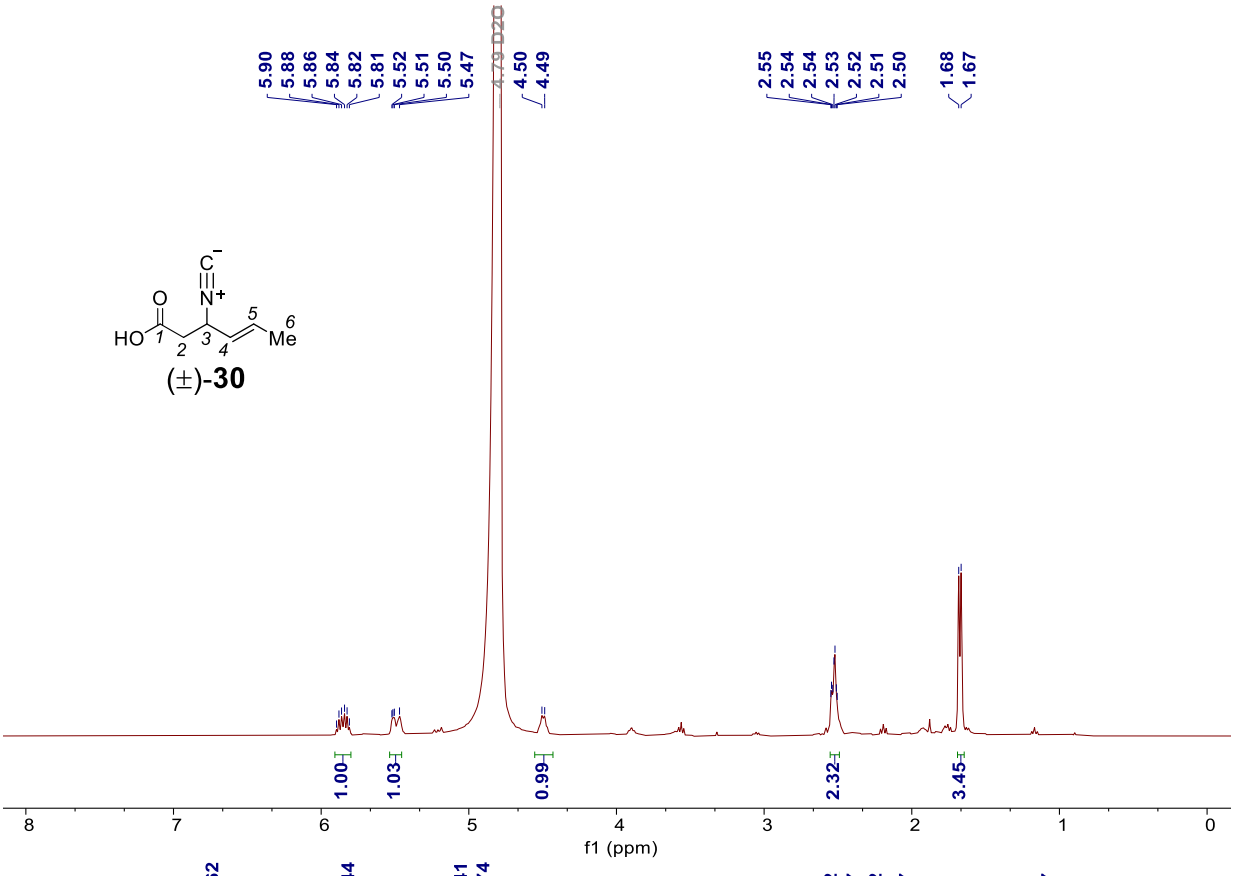

1.00
1.10
0.98
3.55
1.14
1.29
3.36
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


169.56
157.60
129.87
125.29
77.16 CDCl3
52.58
52.51
52.45
52.33
41.14
17.50


C
N
O
MeO
1
2
3
4
5
6
Me

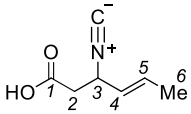
S28

200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

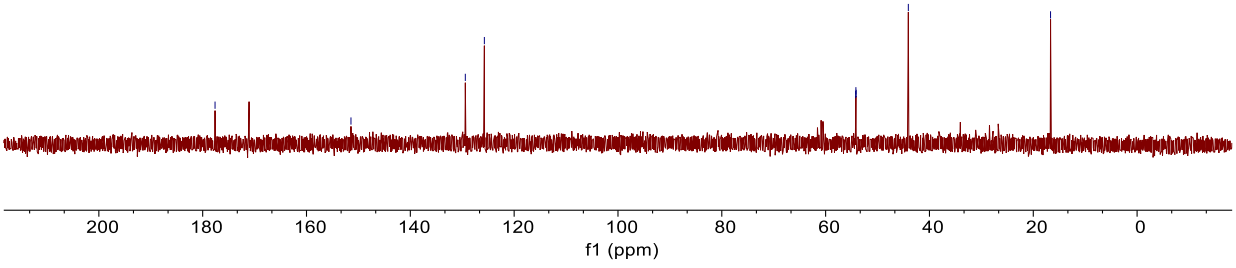

5.90
5.88
5.86
5.84
5.82
5.81
5.52
5.51
5.50
5.47
4.79 D2O
4.50
4.49
2.55
2.54
2.54
2.53
2.52
2.51
2.50
1.68
1.67
1.00
1.03
0.99
2.32
3.45
8
7
6
5
4
3
2
1
0
f1 (ppm)

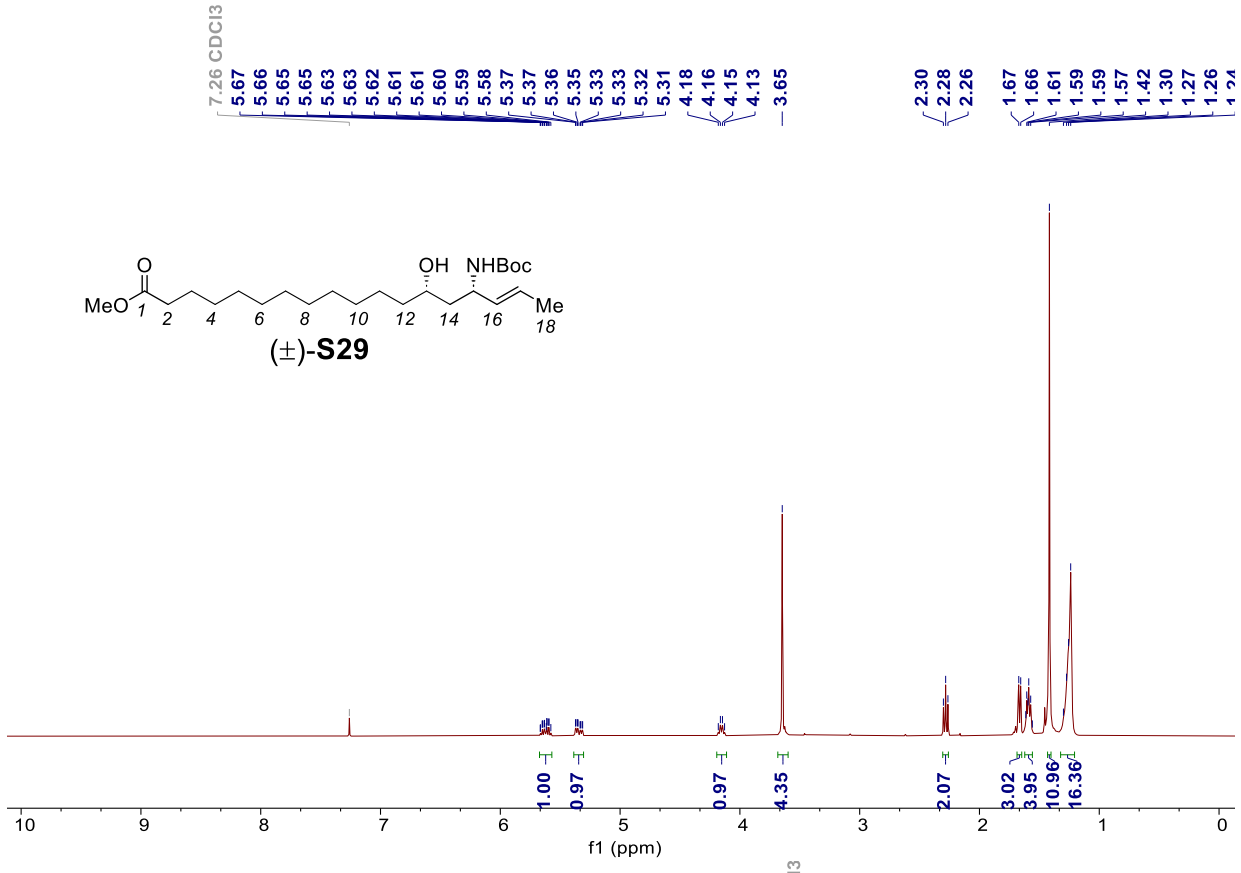
(±)-**30**

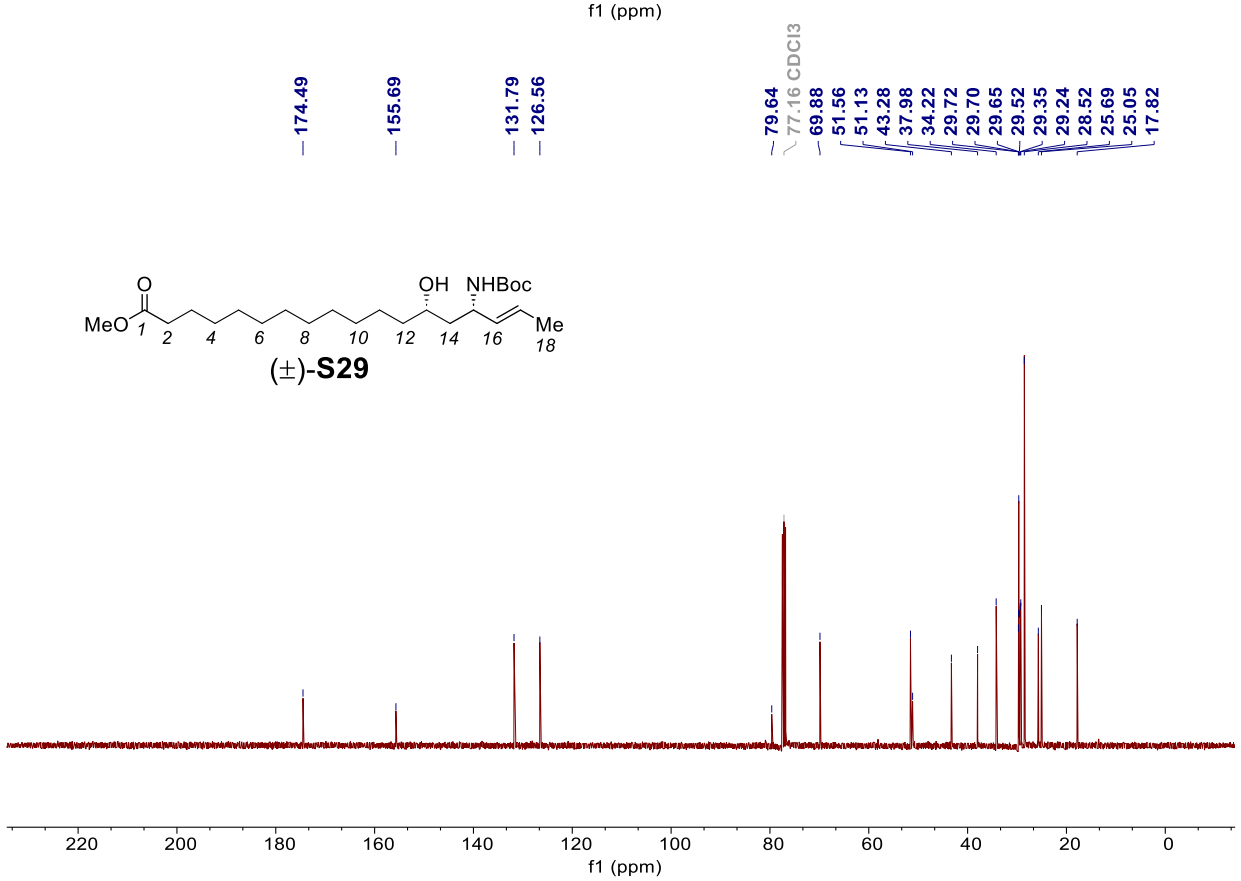
177.62
151.44
129.41
125.74
54.22
54.17
54.12
44.07
16.67

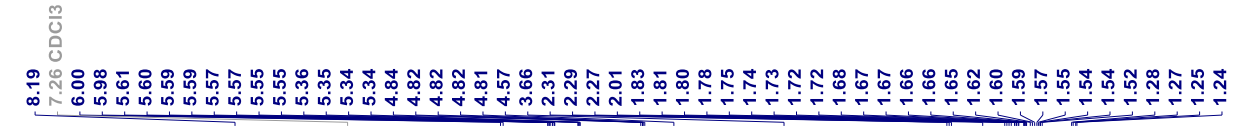


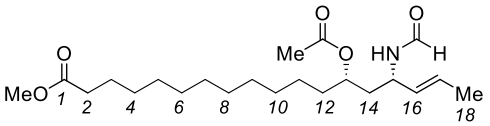
(±)-**30**


200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.26 CDCl3
5.67 5.66 5.65 5.65 5.63 5.63 5.62 5.61 5.61 5.60 5.59 5.58 5.37 5.37 5.36 5.35 5.33 5.33 5.32 5.31
4.18 4.16 4.15 4.13
3.65
2.30 2.28 2.26
1.67 1.66 1.61 1.59 1.59 1.57 1.42 1.30 1.27 1.26
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14 16 18
(±)-S29
1.00 0.97 0.97 4.35 2.07 3.02 3.95 10.96 16.36
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

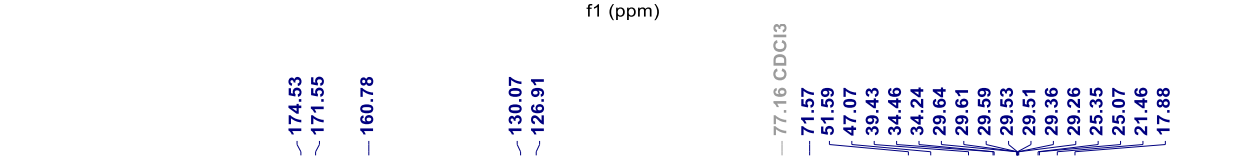

174.49
155.69
131.79
126.56
79.64
77.16 CDCl3
69.88
51.56 51.13 43.28 37.98 34.22 29.72 29.70 29.65 29.52 29.35 29.24 28.52 25.69 25.05 17.82
O
MeO
OH
NHBoc
Me
1 2 4 6 8 10 12 14 16 18
(±)-S29
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

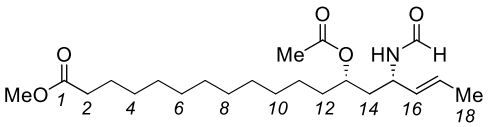

8.19
7.26 CDCl3
6.00
5.98
5.61
5.60
5.59
5.59
5.57
5.57
5.55
5.55
5.36
5.35
5.34
5.34
4.84
4.82
4.82
4.82
4.81
4.57
3.66
2.31
2.29
2.27
2.01
1.83
1.81
1.80
1.78
1.75
1.74
1.73
1.72
1.72
1.68
1.67
1.67
1.66
1.66
1.65
1.62
1.60
1.59
1.57
1.55
1.54
1.54
1.52
1.28
1.27
1.25
1.24


O
Me
O
HN
O
H
MeO
1
2
4
6
8
10
12
14
16
Me
18

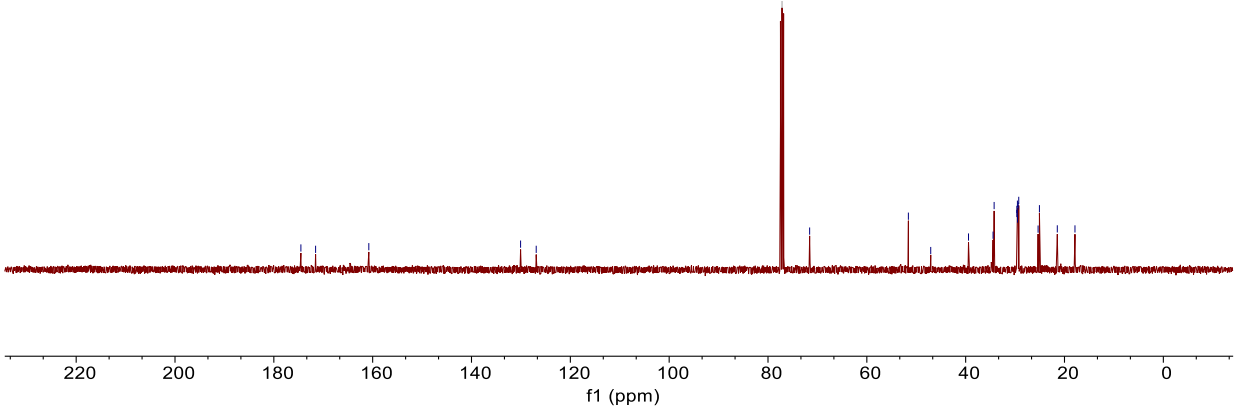
(±)-**S30**

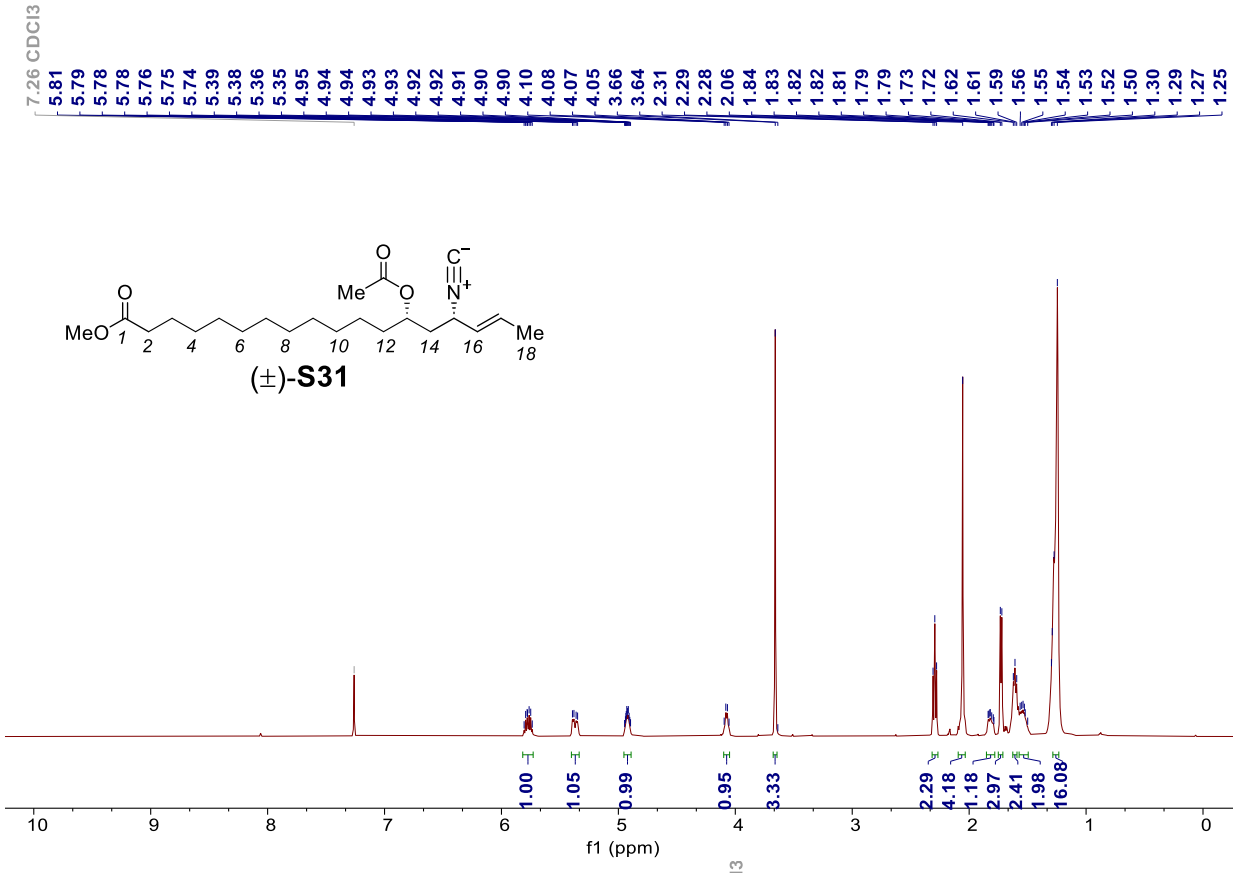
1.01
0.82
1.25
1.00
1.07
1.01
3.10
2.41
2.86
1.30
1.03
2.93
2.11
2.27
16.29
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

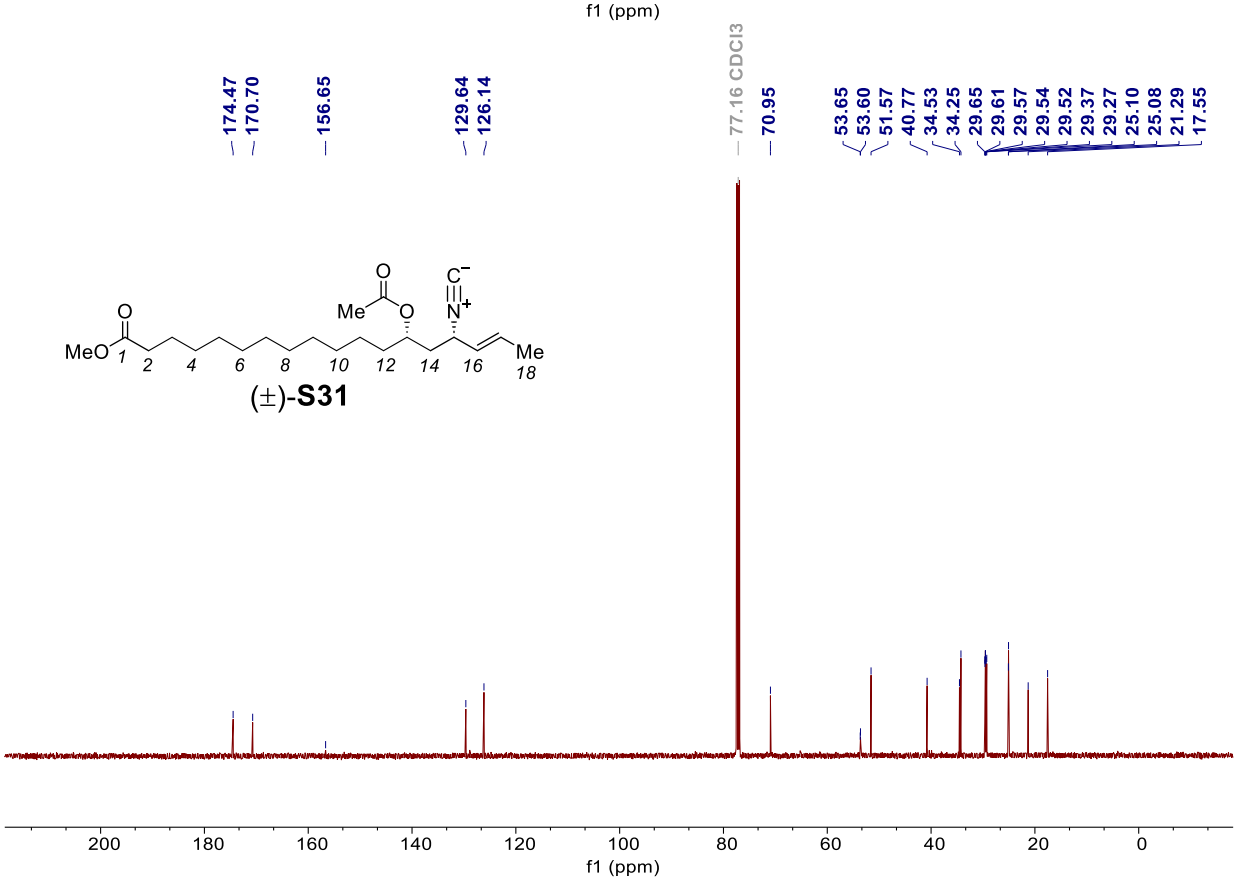

174.53
171.55
160.78
130.07
126.91
77.16 CDCl3
71.57
51.59
47.07
39.43
34.46
34.24
29.64
29.61
29.59
29.53
29.51
29.36
29.26
25.35
25.07
21.46
17.88

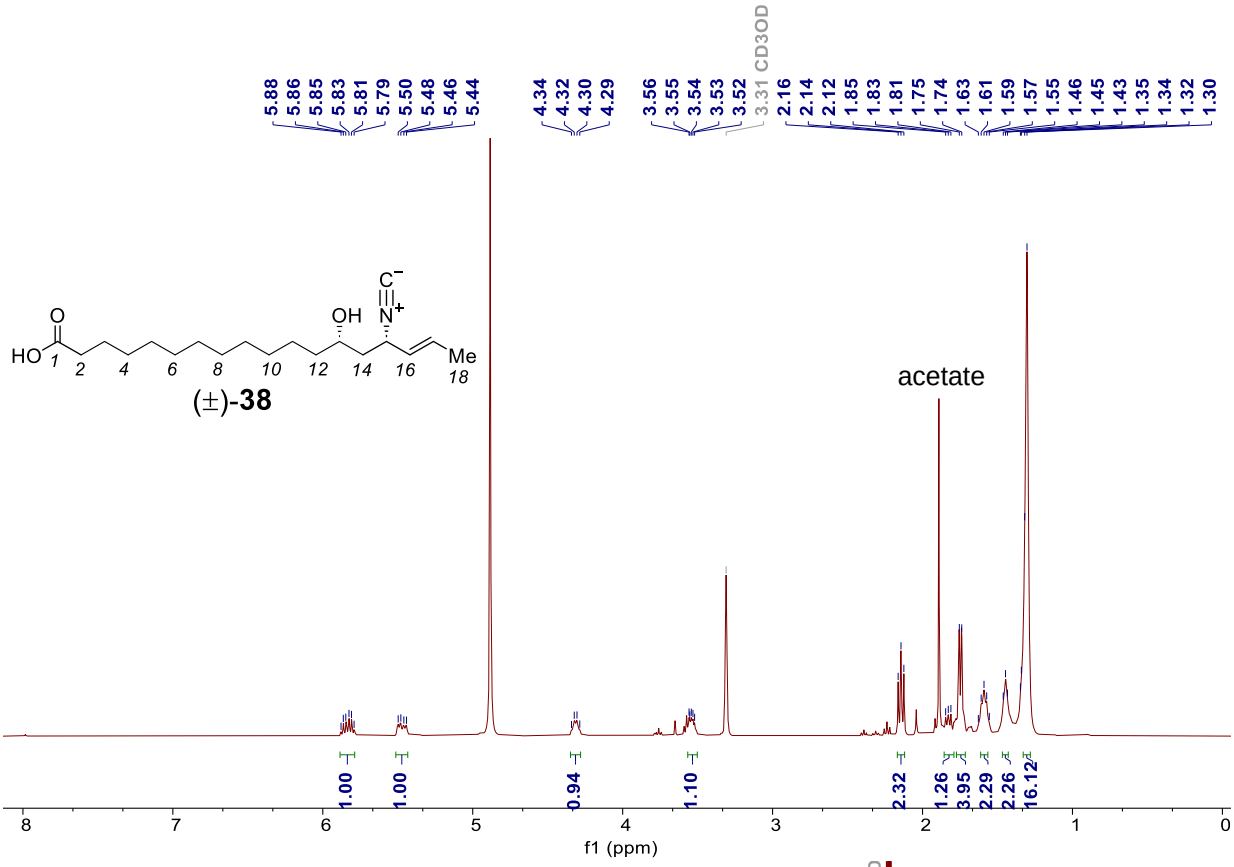

O
Me
O
HN
O
H
MeO
1
2
4
6
8
10
12
14
16
Me
18

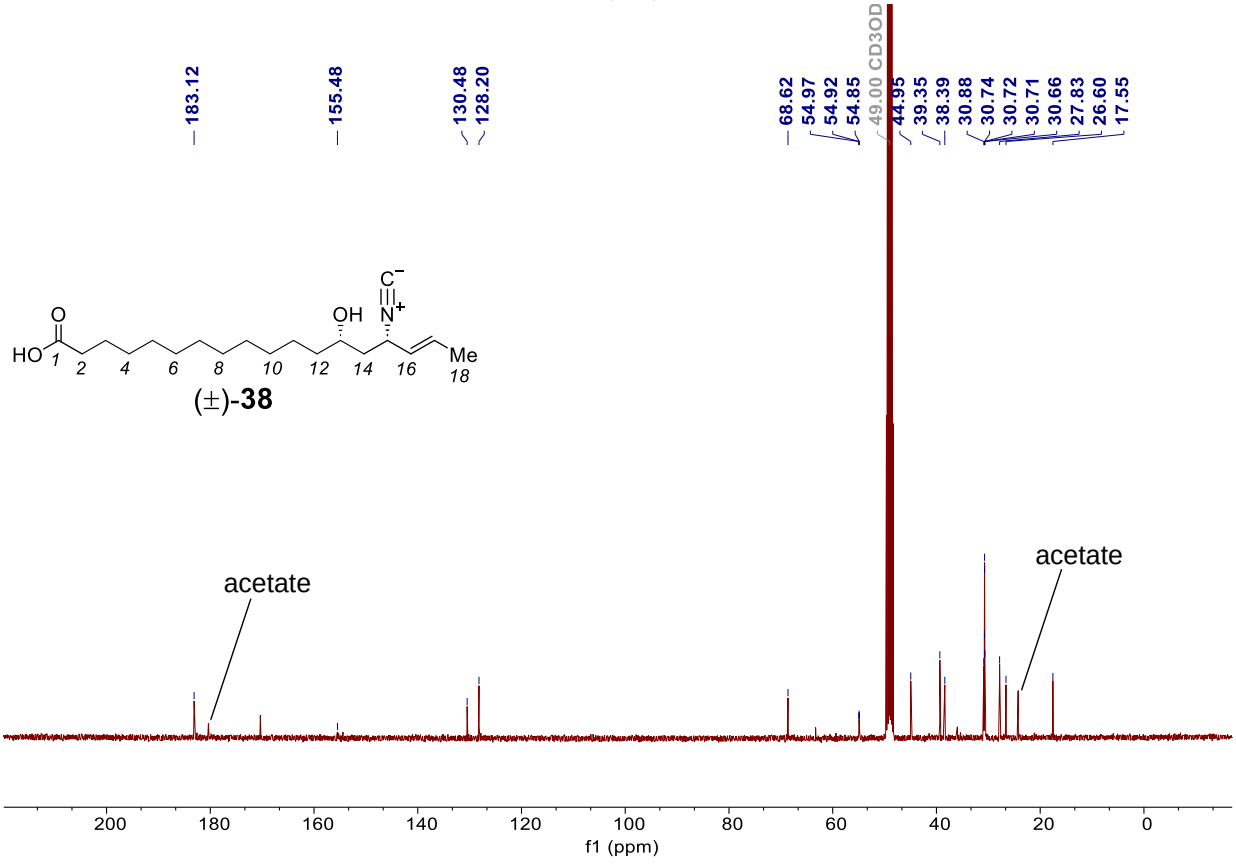
(±)-**S30**

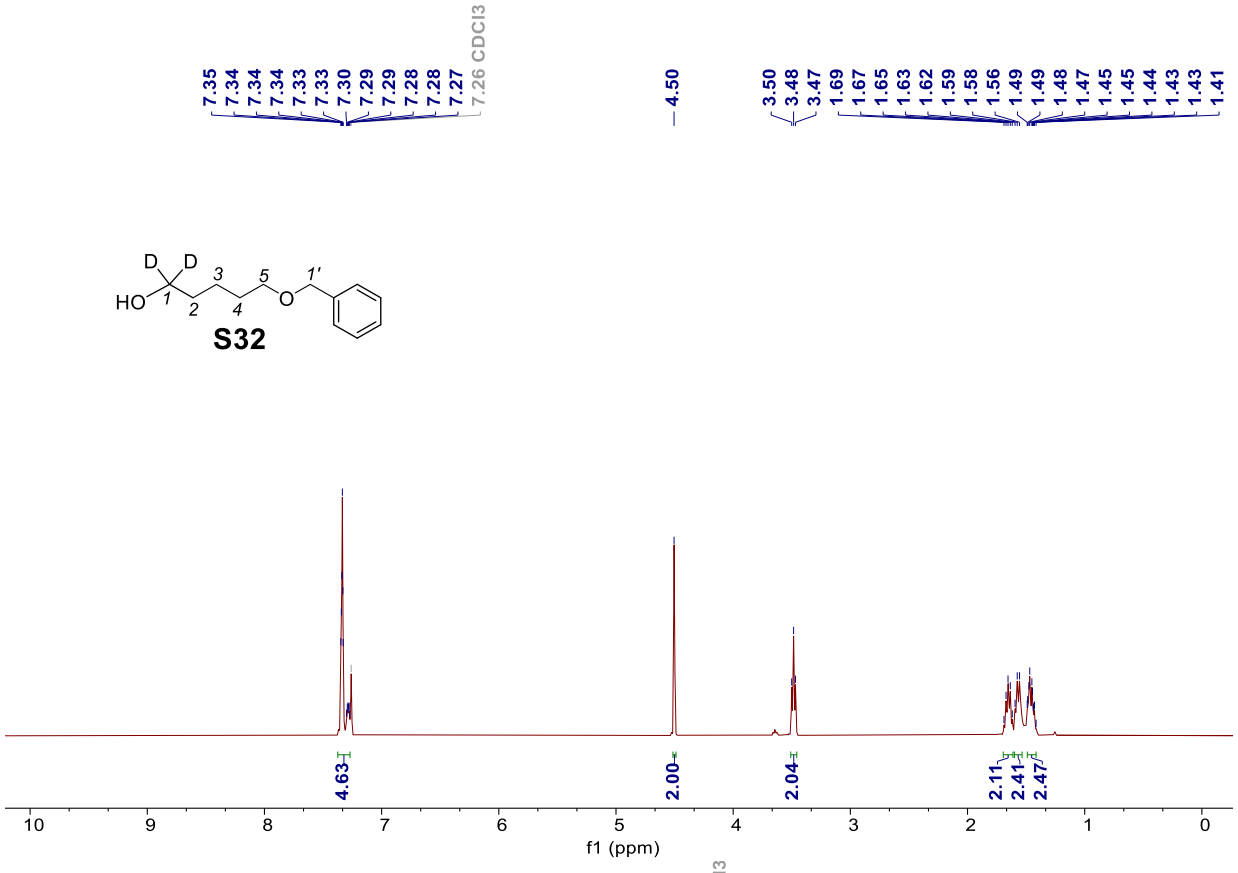

220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

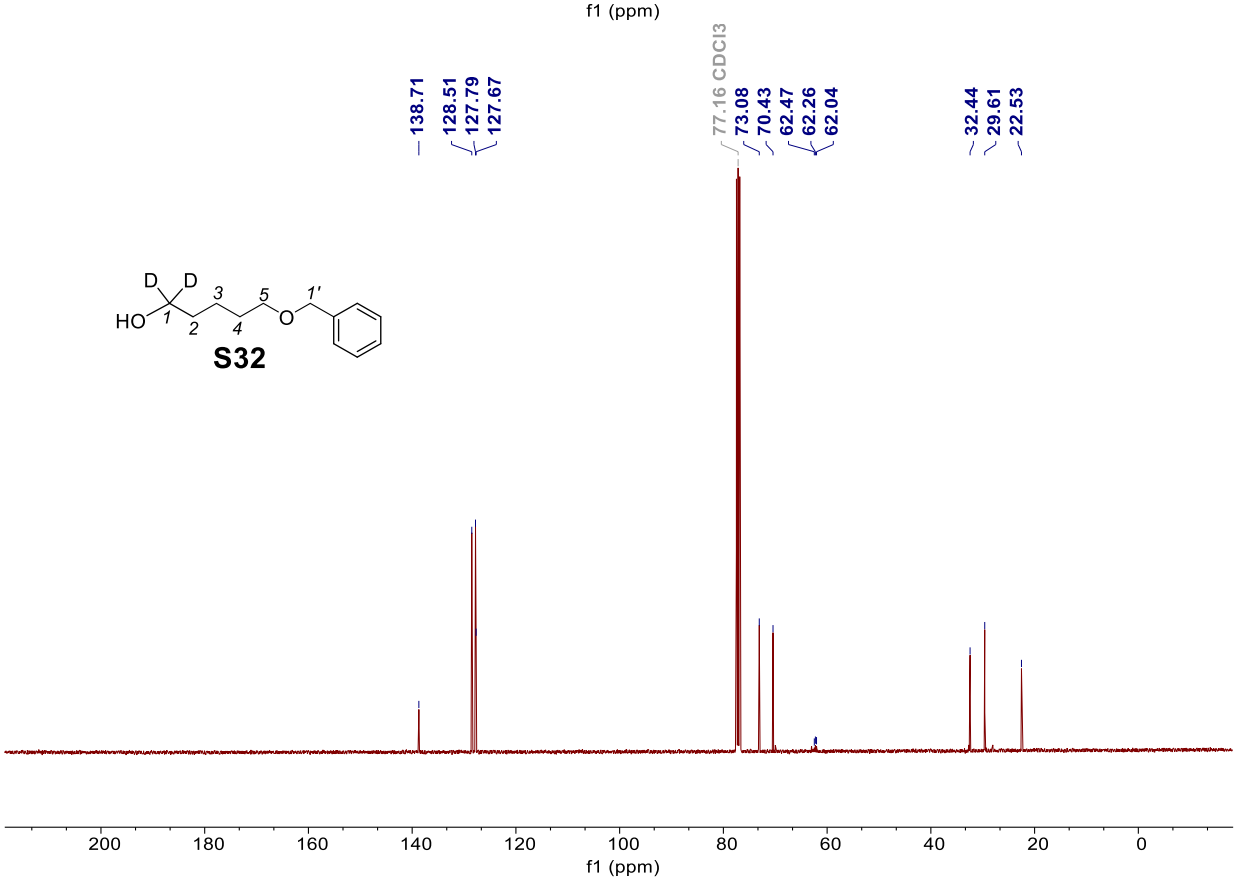

7.26 CDCl3
5.81 5.79 5.78 5.78 5.76 5.75 5.74 5.39 5.38 5.36 5.35 4.95 4.94 4.94 4.93 4.93 4.92 4.92 4.91 4.90 4.90 4.10 4.08 4.07 4.05 3.66 3.64 2.31 2.29 2.28 2.06 1.84 1.83 1.82 1.82 1.81 1.79 1.79 1.73 1.72 1.62 1.61 1.59 1.56 1.55 1.54 1.53 1.52 1.50 1.30 1.29 1.27 1.25
MeO
Me
Me
1 2 4 6 8 10 12 14 16 18
(±)-S31
1.00 1.05 0.99 0.95 3.33 2.29 4.18 1.18 2.97 2.41 1.98 16.08
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

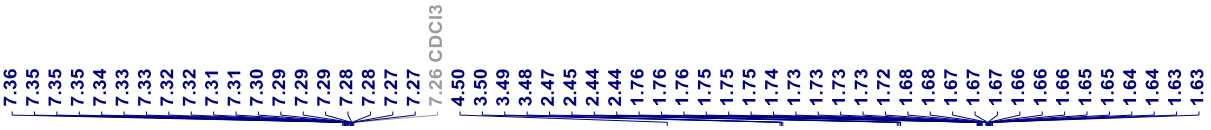

174.47 170.70 156.65 129.64 126.14
77.16 CDCl3
70.95
53.65 53.60 51.57 40.77 34.53 34.25 29.65 29.61 29.57 29.54 29.52 29.37 29.27 25.10 25.08 21.29 17.55
MeO
Me
Me
1 2 4 6 8 10 12 14 16 18
(±)-S31
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

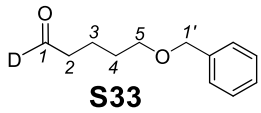

5.88 5.86 5.85 5.83 5.81 5.79 5.50 5.48 5.46 5.44
4.34 4.32 4.30 4.29
3.56 3.55 3.54 3.53 3.52 3.31 CD3OD
2.16 2.14 2.12 1.85 1.83 1.81 1.75 1.74 1.63 1.61 1.59 1.57 1.55 1.46 1.45 1.43 1.35 1.34 1.32 1.30
HO
OH
Me
(±)-38
acetate
1.00 1.00 0.94 1.10 2.32 1.26 3.95 2.29 2.26 16.12
f1 (ppm)


183.12 155.48 130.48 128.20
68.62 54.97 54.92 54.85 49.00 CD3OD 44.95 39.35 38.39 30.88 30.74 30.72 30.71 30.66 27.83 26.60 17.55
HO
OH
Me
(±)-38
acetate
acetate
f1 (ppm)

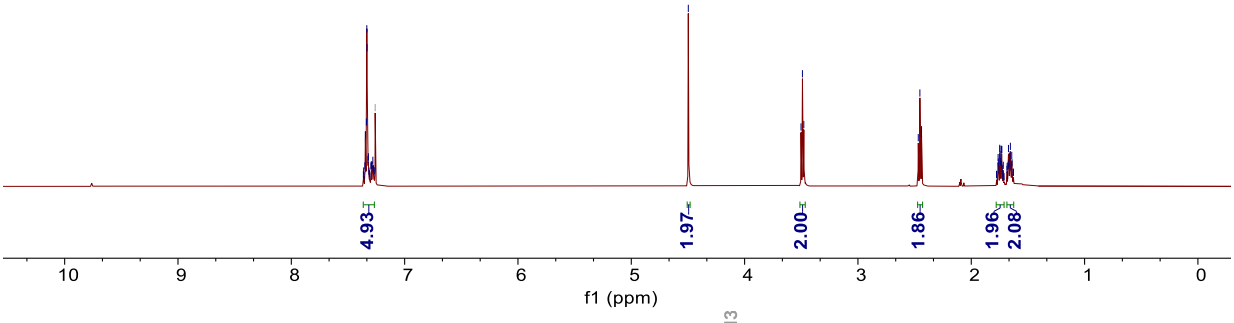

7.35
7.34
7.34
7.34
7.33
7.33
7.30
7.29
7.29
7.28
7.28
7.27
7.26 CDCl3
4.50
3.50
3.48
3.47
1.69
1.67
1.65
1.63
1.62
1.59
1.58
1.56
1.49
1.49
1.48
1.47
1.45
1.45
1.44
1.43
1.43
1.41
D
D
HO
1
2
3
4
5
O
1'
S32
4.63
2.00
2.04
2.11
2.41
2.47
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

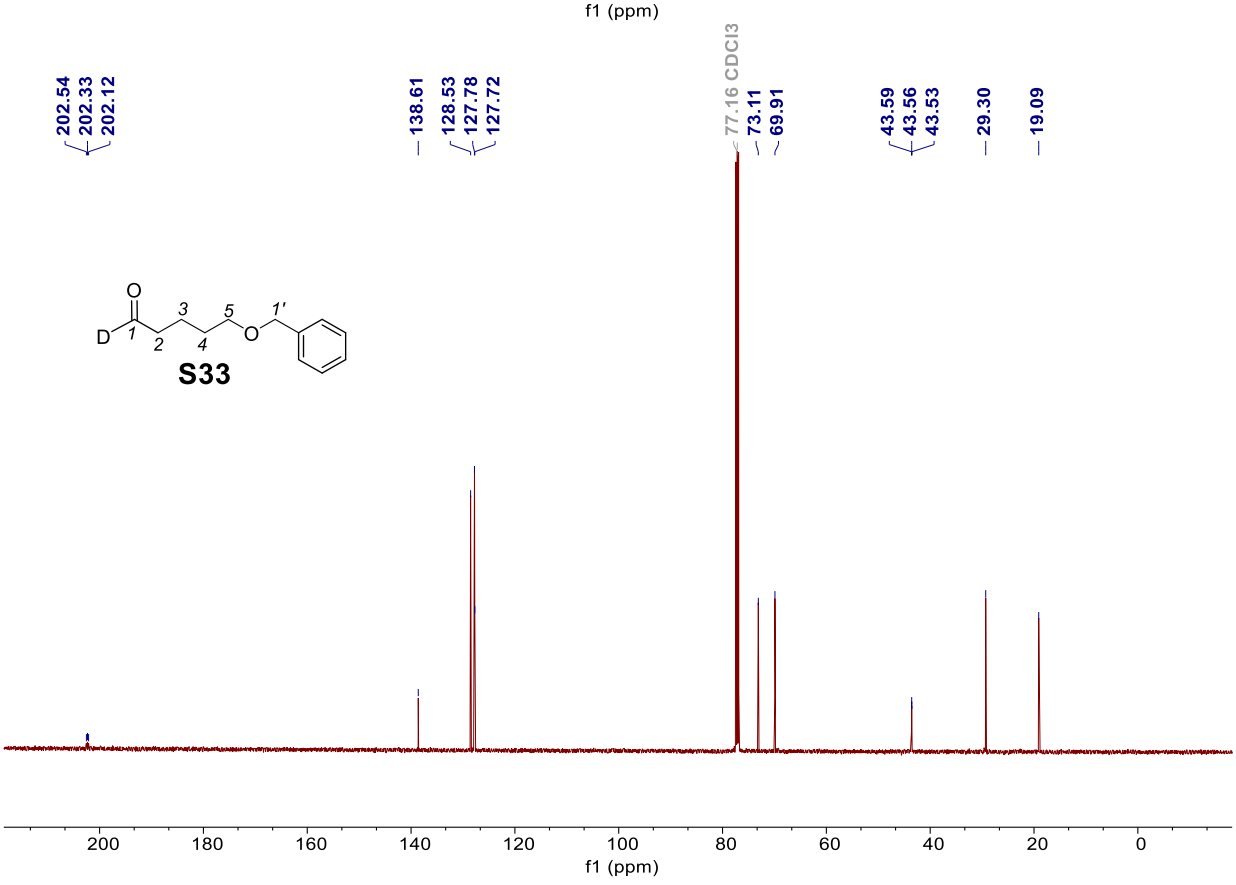

138.71
128.51
127.79
127.67
77.16 CDCl3
73.08
70.43
62.47
62.26
62.04
32.44
29.61
22.53
D
D
HO
1
2
3
4
5
O
1'
S32
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.36 7.35 7.35 7.35 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.29 7.29 7.29 7.28 7.28 7.27 7.27
7.26 CDCl3
4.50 3.50 3.49 3.48 2.47 2.45 2.44 2.44 1.76 1.76 1.76 1.75 1.75 1.75 1.74 1.73 1.73 1.73 1.73 1.72 1.68 1.68 1.67 1.67 1.67 1.66 1.66 1.66 1.65 1.65 1.64 1.64 1.63 1.63


O
D
1
2
3
4
5
O
1'

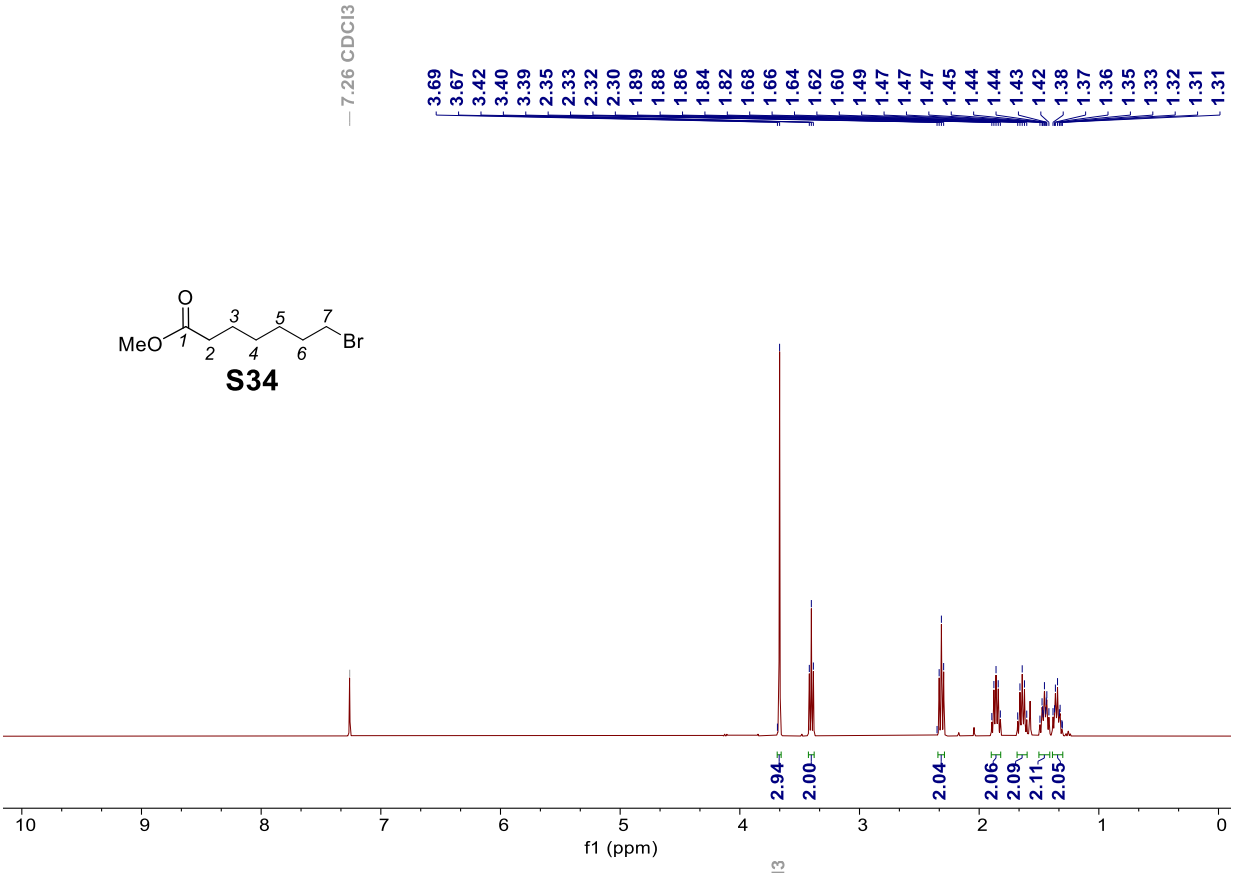
S33

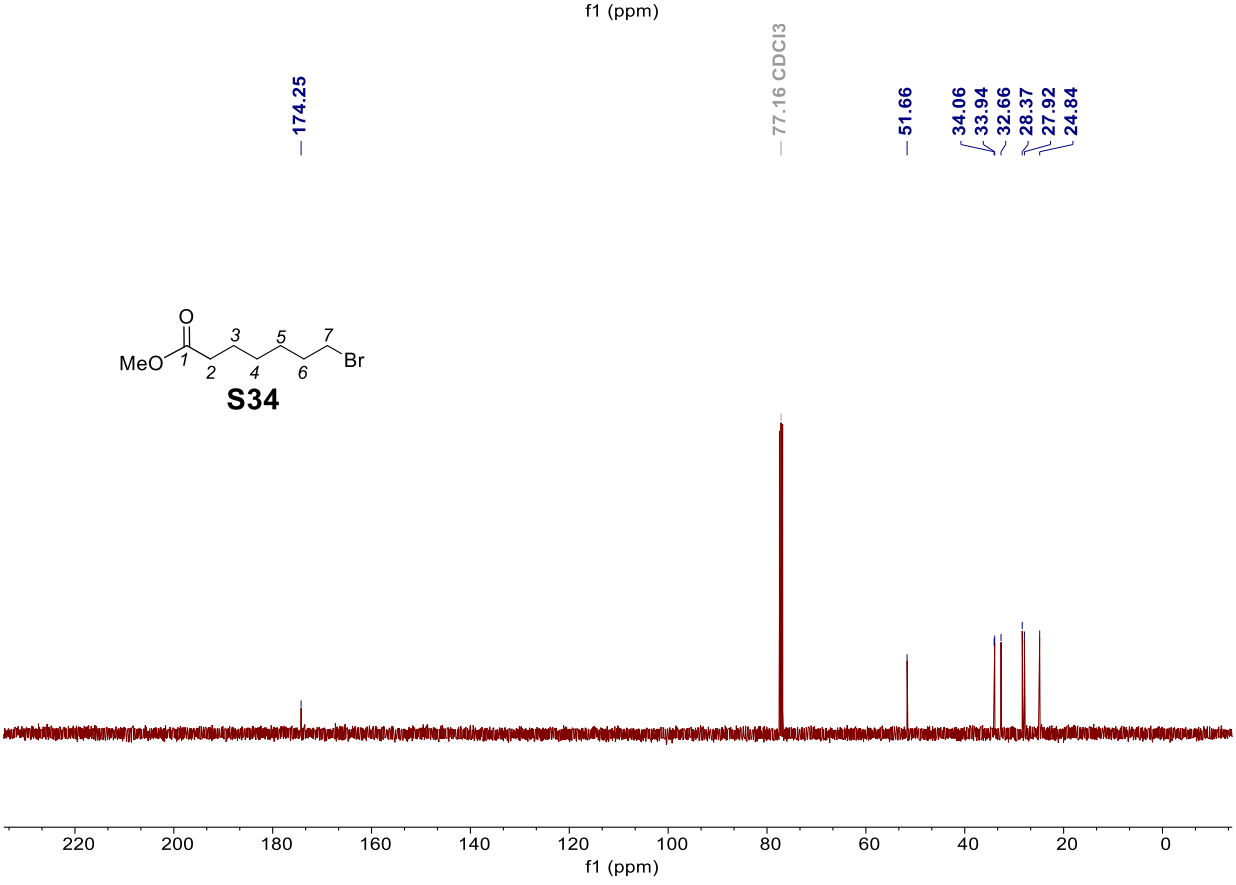

4.93
1.97
2.00
1.86
1.96
2.08
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

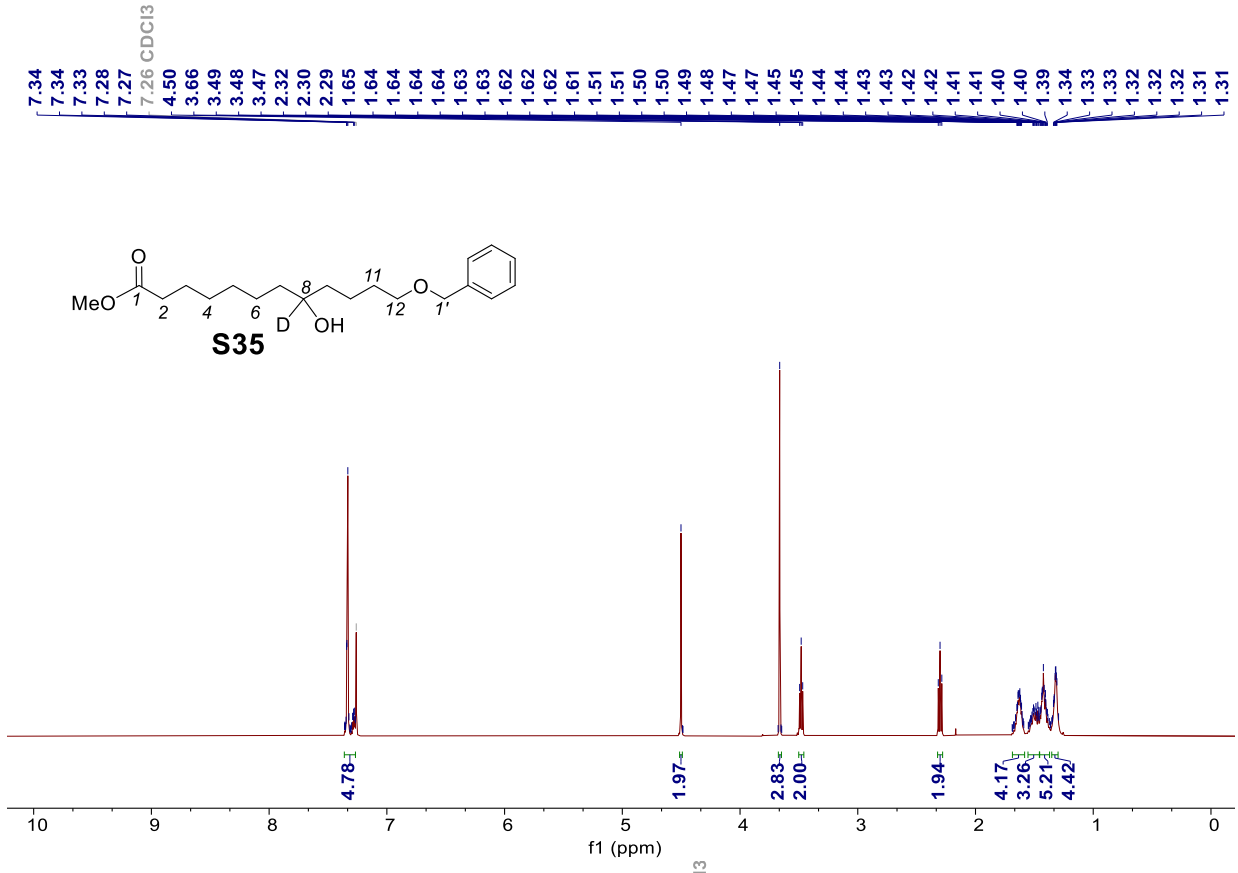

202.54
202.33
202.12
138.61
128.53
127.78
127.72
77.16 CDCl3
73.11
69.91
43.59
43.56
43.53
29.30
19.09
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

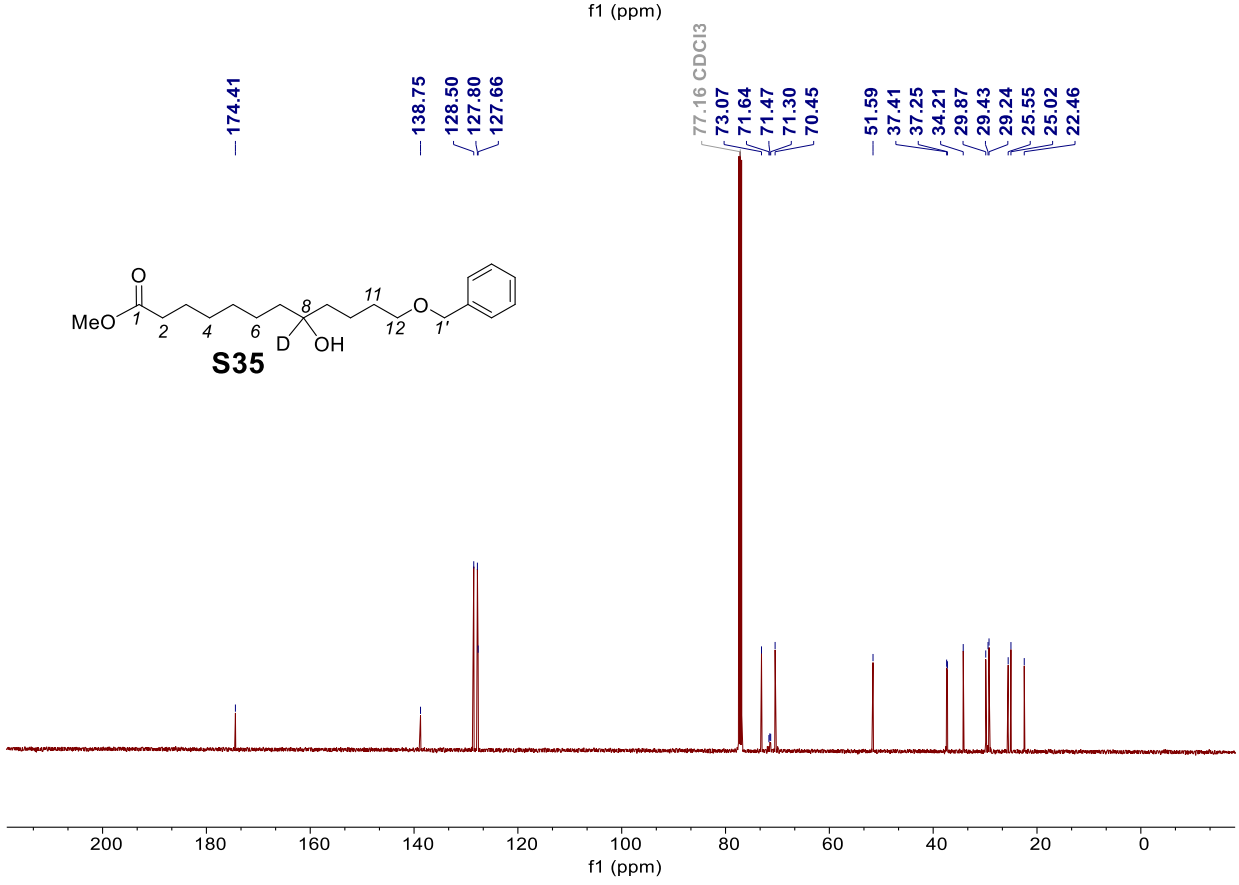
O
D
1
2
3
4
5
O
1'

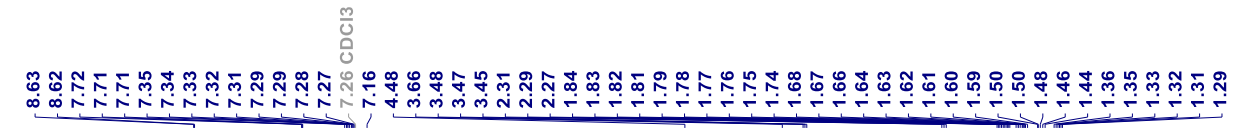
S33

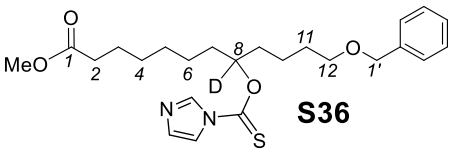

7.26 CDCl3
3.69
3.67
3.42
3.40
3.39
2.35
2.33
2.32
2.30
1.89
1.88
1.86
1.84
1.82
1.68
1.66
1.64
1.62
1.60
1.49
1.47
1.47
1.47
1.45
1.44
1.44
1.43
1.42
1.38
1.37
1.36
1.35
1.33
1.32
1.31
1.31
MeO
Br
S34
2.94
2.00
2.04
2.06
2.09
2.11
2.05
f1 (ppm)


174.25
77.16 CDCl3
51.66
34.06
33.94
32.66
28.37
27.92
24.84
MeO
Br
S34
f1 (ppm)

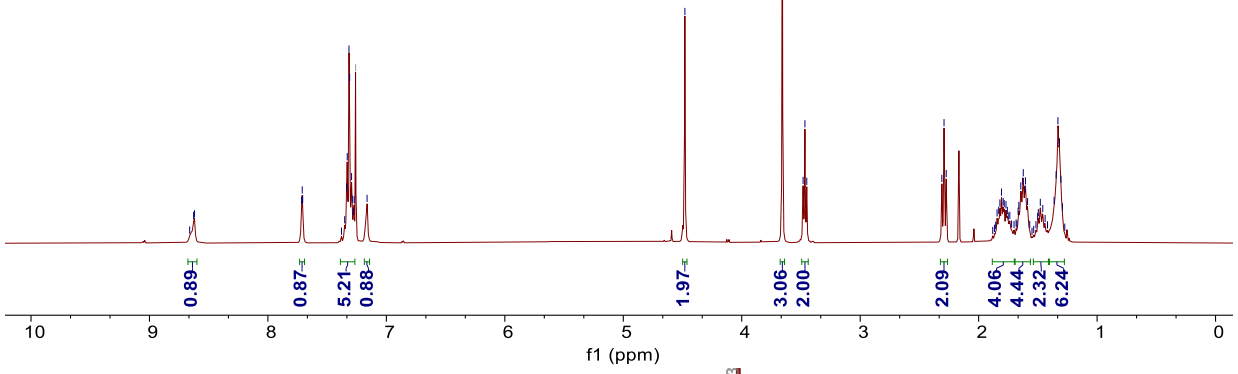

7.34 7.34 7.33 7.28 7.27 7.26 CDCl3 4.50 3.66 3.49 3.48 3.47 2.32 2.30 2.29 1.65 1.64 1.64 1.64 1.64 1.63 1.63 1.62 1.62 1.62 1.61 1.51 1.51 1.50 1.50 1.49 1.48 1.47 1.47 1.45 1.45 1.44 1.44 1.43 1.43 1.42 1.42 1.41 1.41 1.40 1.40 1.39 1.34 1.33 1.33 1.32 1.32 1.32 1.31 1.31
MeO
O
1
2
4
6
8
D
OH
11
12
O
1'
S35
4.78
1.97
2.83
2.00
1.94
4.17
3.26
5.21
4.42
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

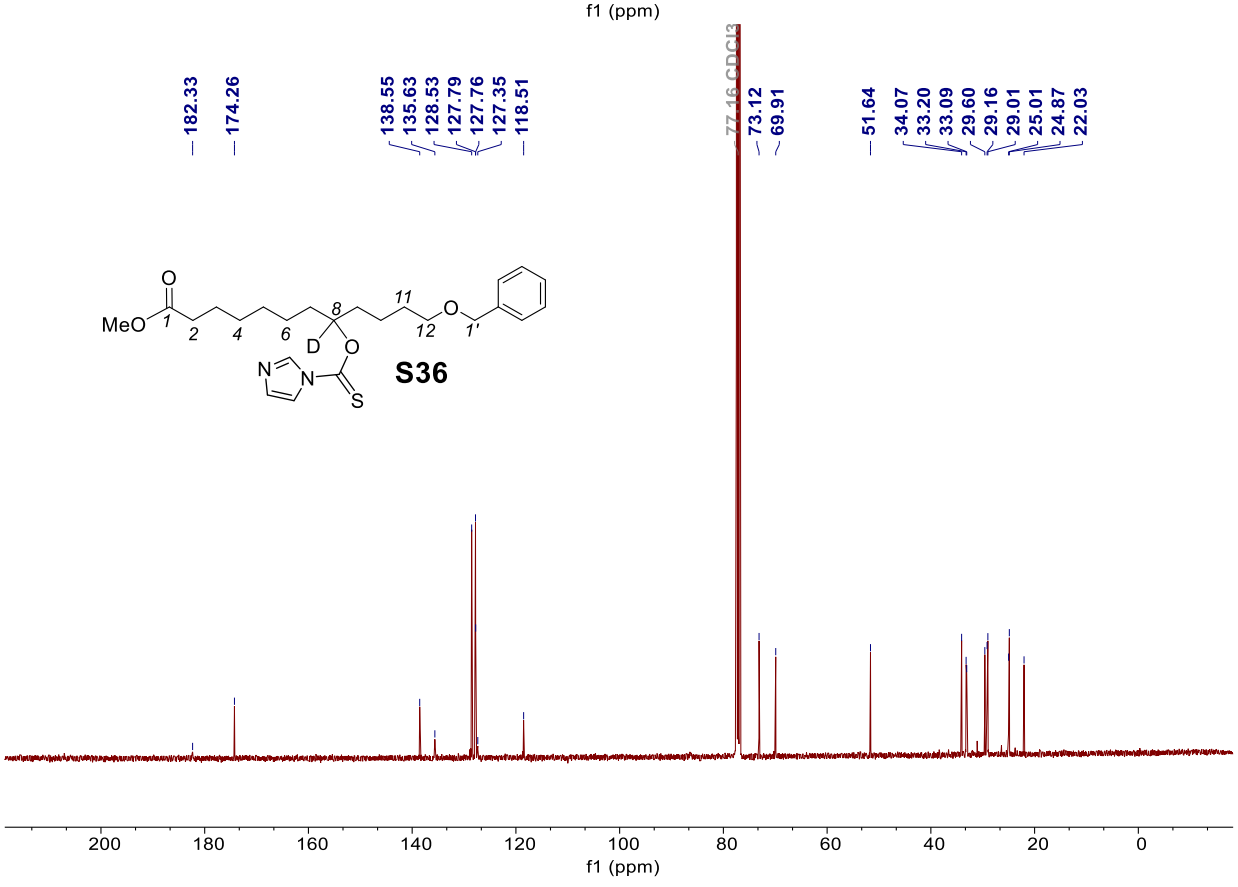

174.41
138.75
128.50
127.80
127.66
77.16 CDCl3
73.07
71.64
71.47
71.30
70.45
51.59
37.41
37.25
34.21
29.87
29.43
29.24
25.55
25.02
22.46
MeO
O
1
2
4
6
8
D
OH
11
12
O
1'
S35
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


8.63
8.62
7.72
7.71
7.71
7.35
7.34
7.33
7.32
7.31
7.29
7.29
7.28
7.27
7.26 CDCl3
7.16
4.48
3.66
3.48
3.47
3.45
2.31
2.29
2.27
1.84
1.83
1.82
1.81
1.79
1.78
1.77
1.76
1.75
1.74
1.68
1.67
1.66
1.64
1.63
1.62
1.61
1.60
1.59
1.50
1.50
1.48
1.46
1.44
1.36
1.35
1.33
1.32
1.31
1.29


MeO
O
1
2
4
6
8
D
O
N
N
S
11
O
12
1'

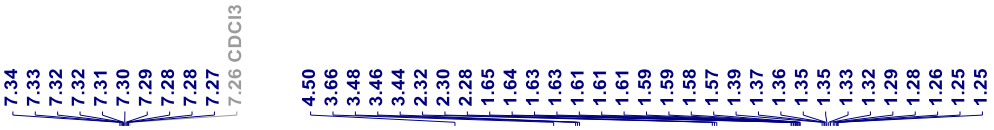
S36

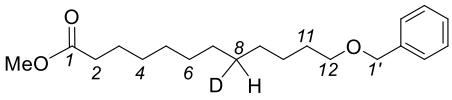

0.89
0.87
5.21
0.88
1.97
3.06
2.00
2.09
4.06
4.44
2.32
6.24
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


182.33
174.26
138.55
135.63
128.53
127.79
127.76
127.35
118.51
77.16 CDCl3
73.12
69.91
51.64
34.07
33.20
33.09
29.60
29.16
29.01
25.01
24.87
22.03
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

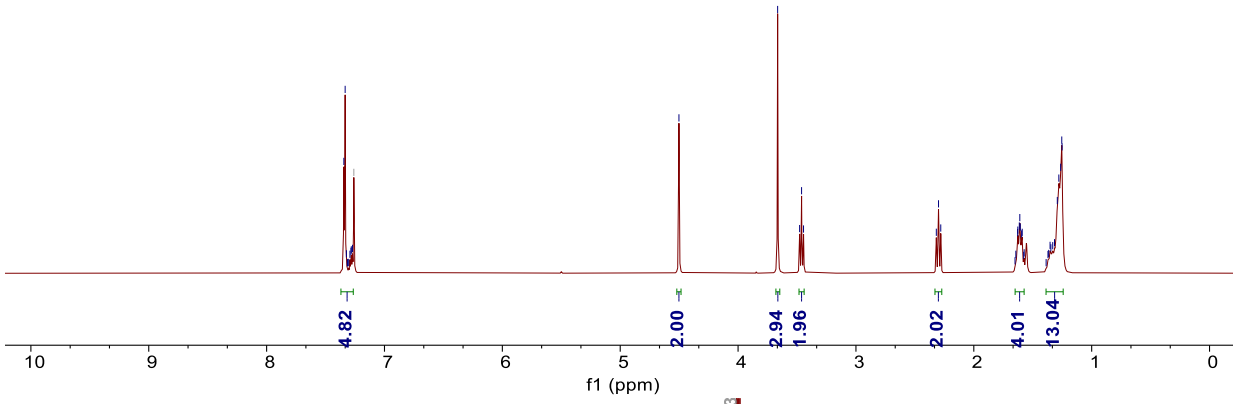
MeO
O
1
2
4
6
8
D
O
N
N
S
11
O
12
1'

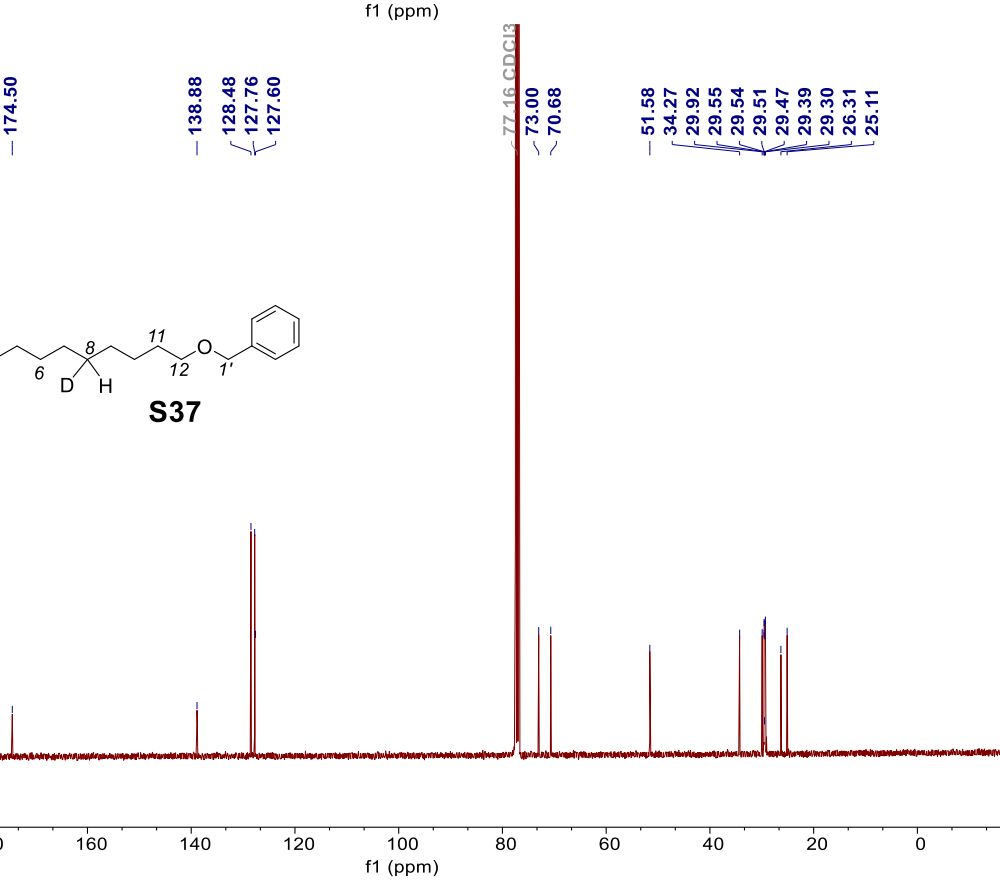
S36


7.34
7.33
7.32
7.32
7.31
7.30
7.29
7.28
7.28
7.27
7.26 CDCl3
4.50
3.66
3.48
3.46
3.44
2.32
2.30
2.28
1.65
1.64
1.63
1.63
1.61
1.61
1.61
1.59
1.59
1.58
1.57
1.39
1.37
1.36
1.35
1.35
1.33
1.32
1.29
1.28
1.26
1.25
1.25


MeO
O
1
2
4
6
8
D
H
11
12
O
1'

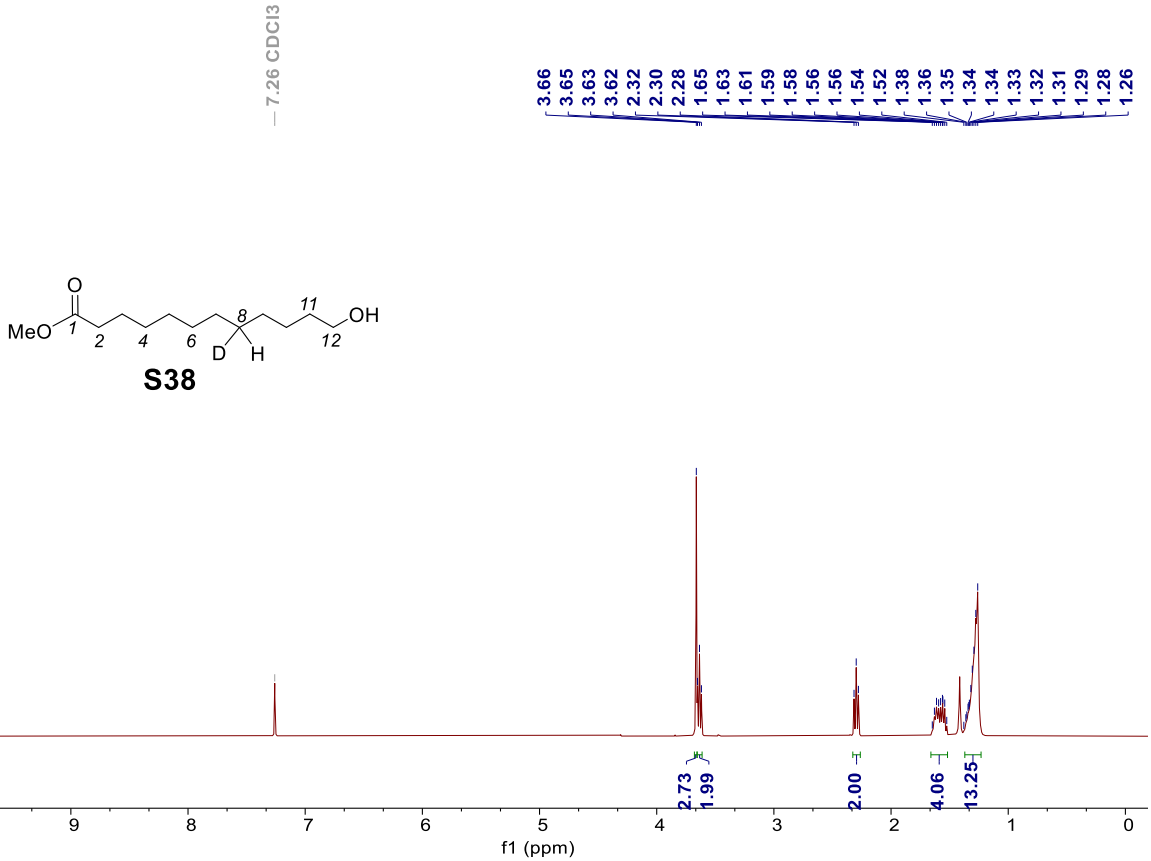
S37

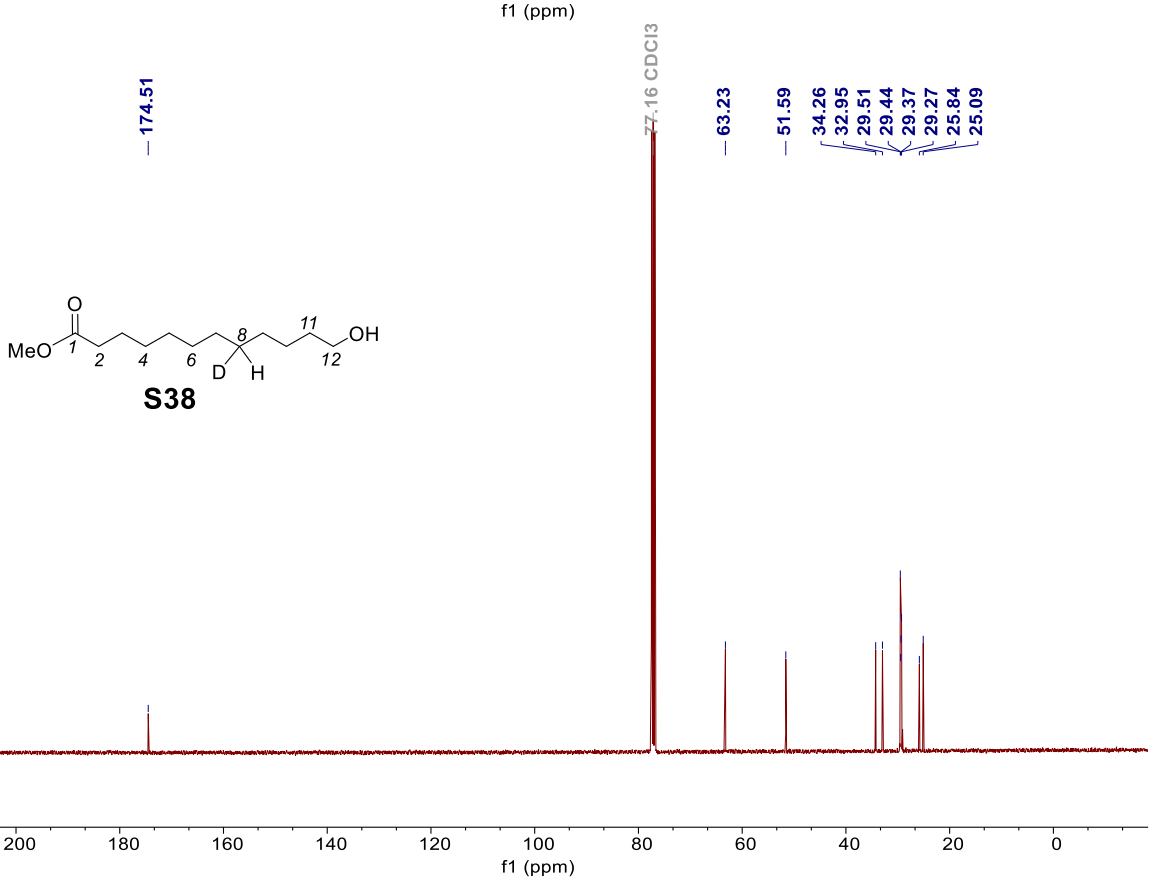

4.82
2.00
2.94
1.96
2.02
4.01
13.04
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

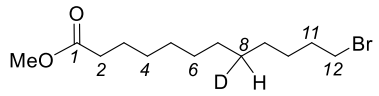

174.50
138.88
128.48
127.76
127.60
77.16 CDCl3
73.00
70.68
51.58
34.27
29.92
29.55
29.54
29.51
29.47
29.39
29.30
26.31
25.11
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

MeO
O
1
2
4
6
8
D
H
11
12
O
1'

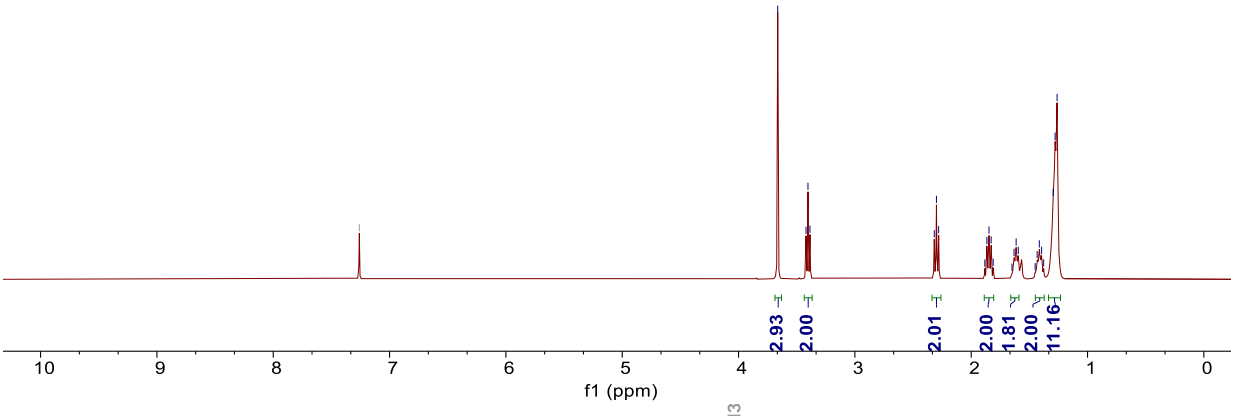
S37

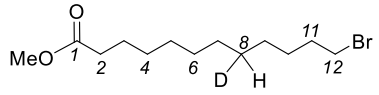

7.26 CDCl3
3.66
3.65
3.63
3.62
2.32
2.30
2.28
1.65
1.63
1.61
1.59
1.58
1.56
1.56
1.54
1.52
1.38
1.36
1.35
1.34
1.34
1.33
1.32
1.31
1.29
1.28
1.26
MeO
OH
D
H
S38
2.73
1.99
2.00
4.06
13.25
f1 (ppm)


174.51
77.16 CDCl3
63.23
51.59
34.26
32.95
29.51
29.44
29.37
29.27
25.84
25.09
MeO
OH
D
H
S38
f1 (ppm)


MeO
O
1
2
4
6
8
D
H
11
12
Br

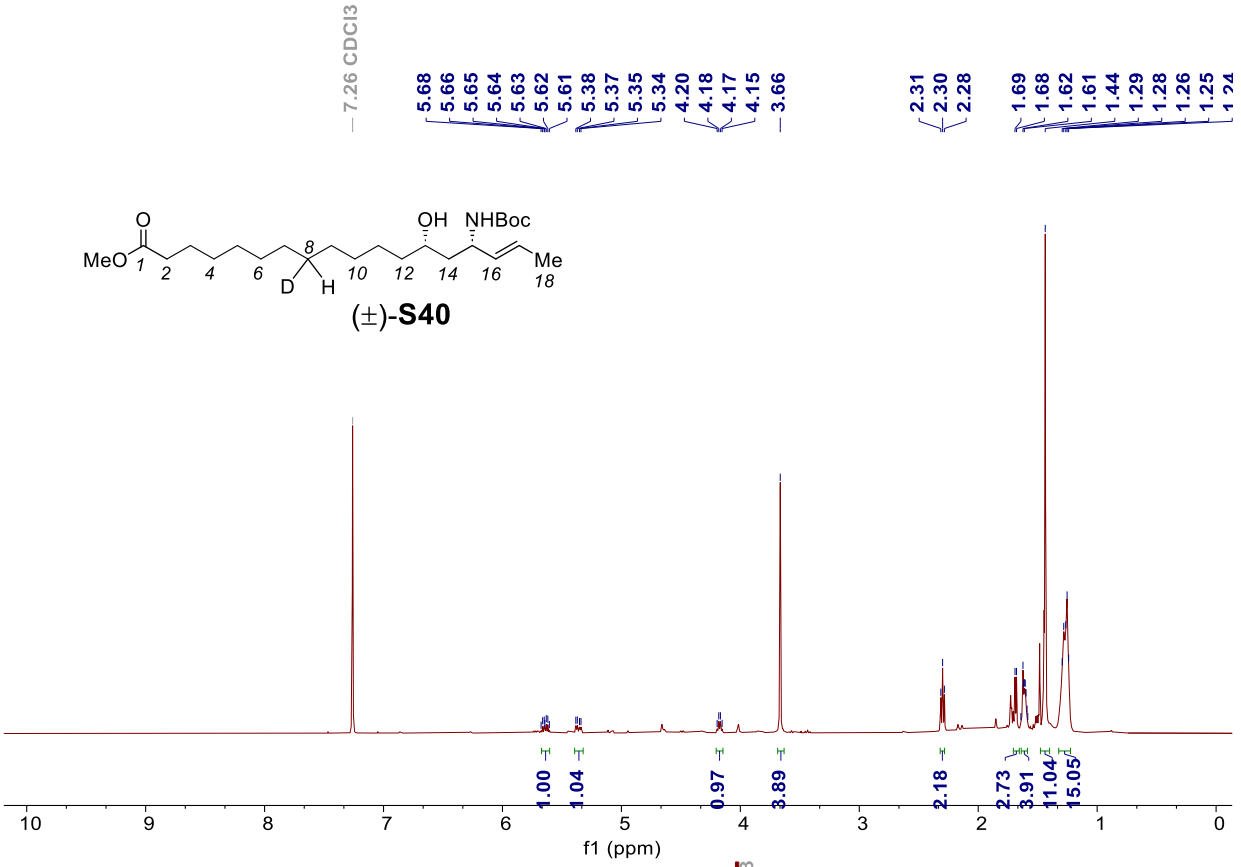
S39

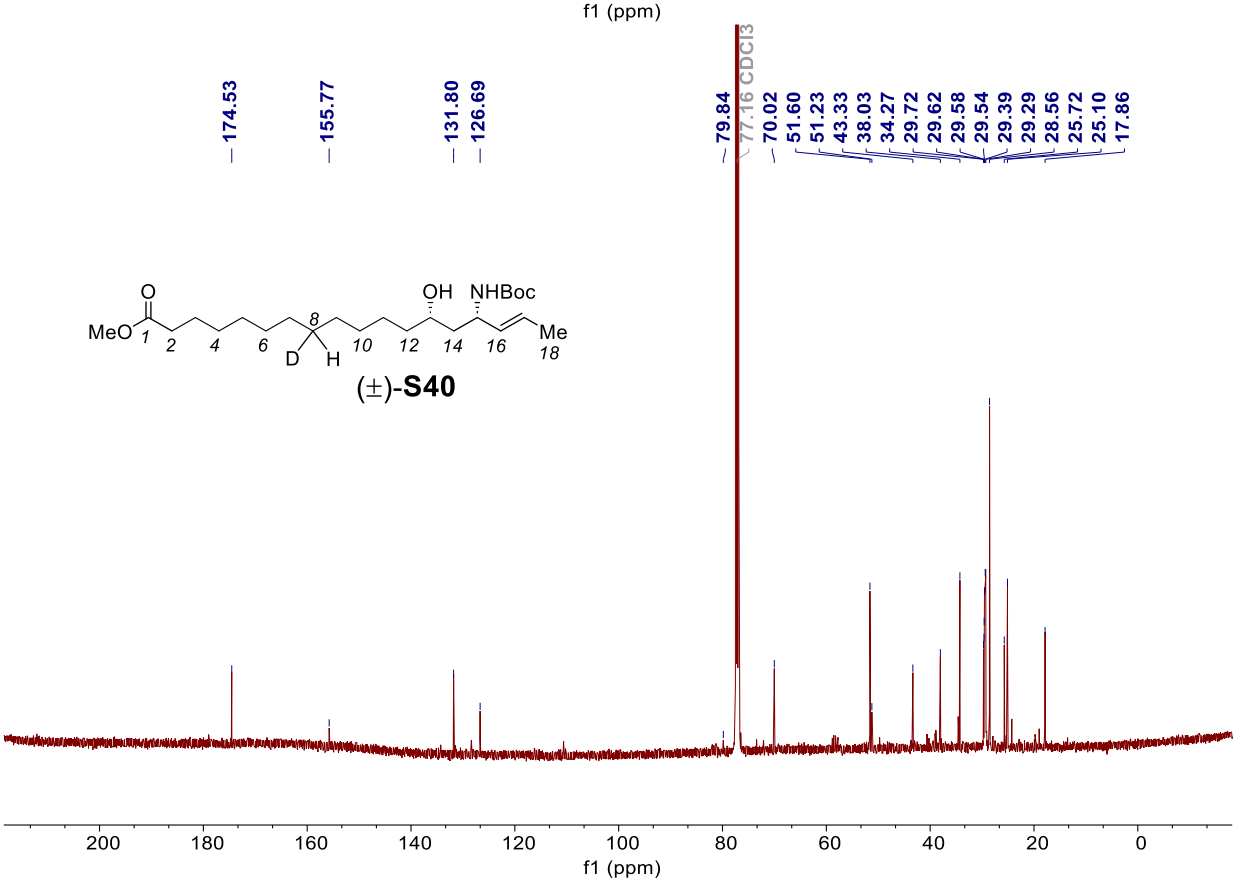

7.26 CDCl3
3.66
3.42
3.40
3.39
2.32
2.30
2.28
1.87
1.85
1.83
1.63
1.61
1.60
1.43
1.41
1.39
1.30
1.28
2.93
2.00
2.01
2.00
1.81
2.00
11.16
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

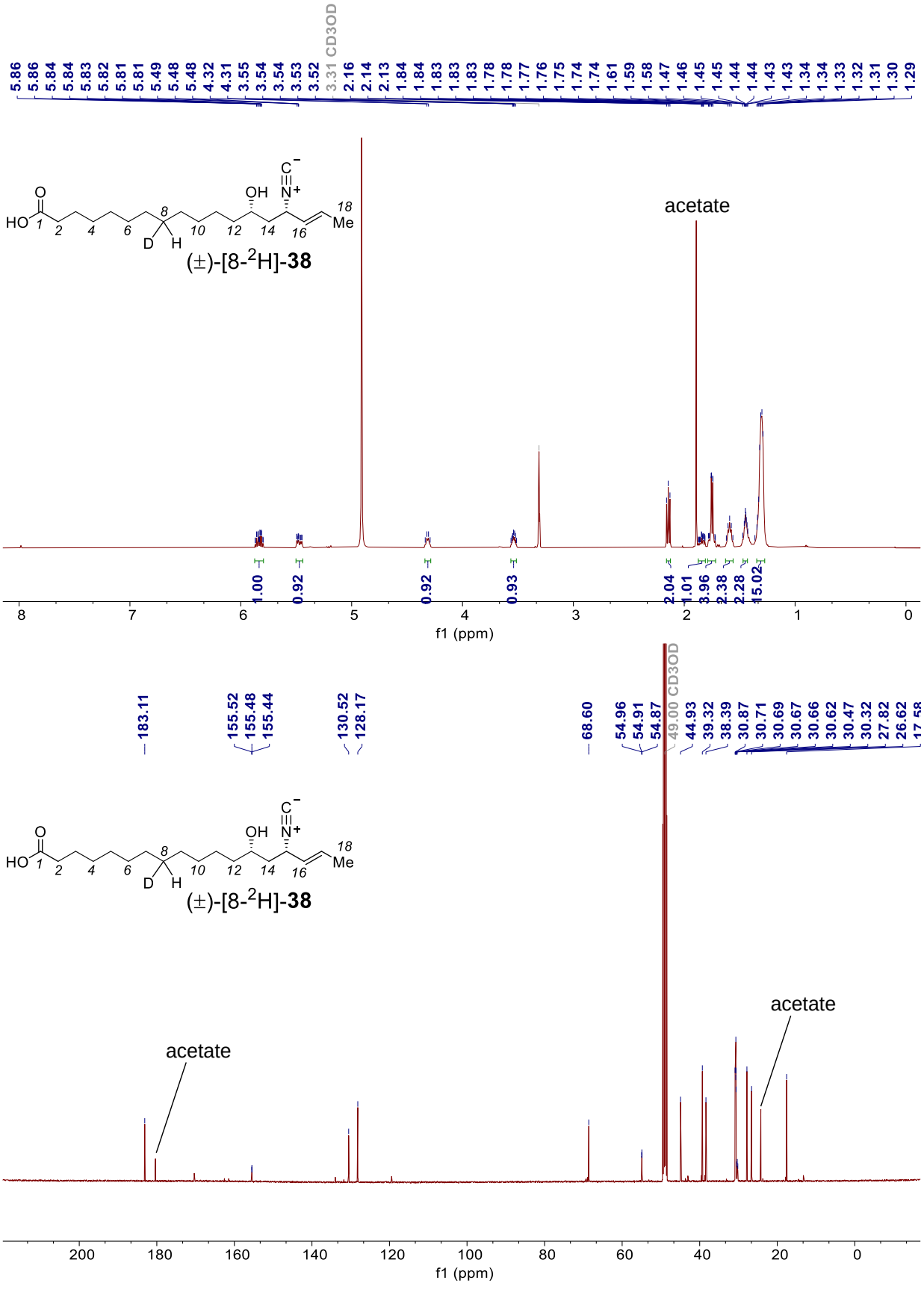

MeO
O
1
2
4
6
8
D
H
11
12
Br

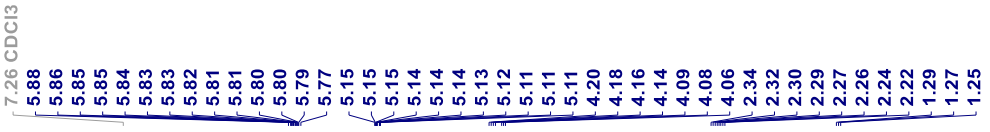
S39

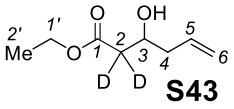
174.48
77.16 CDCl3
51.58
34.25
34.18
32.98
29.49
29.37
29.31
29.27
29.12
28.93
28.79
28.29
25.09
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.26 CDCl3
5.68
5.66
5.65
5.64
5.63
5.62
5.61
5.38
5.37
5.35
5.34
4.20
4.18
4.17
4.15
3.66
2.31
2.30
2.28
1.69
1.68
1.62
1.61
1.44
1.29
1.28
1.26
1.25
MeO
OH
NHBoc
Me
D
H
(±)-S40
1.00
1.04
0.97
3.89
2.18
2.73
3.91
11.04
15.05
f1 (ppm)

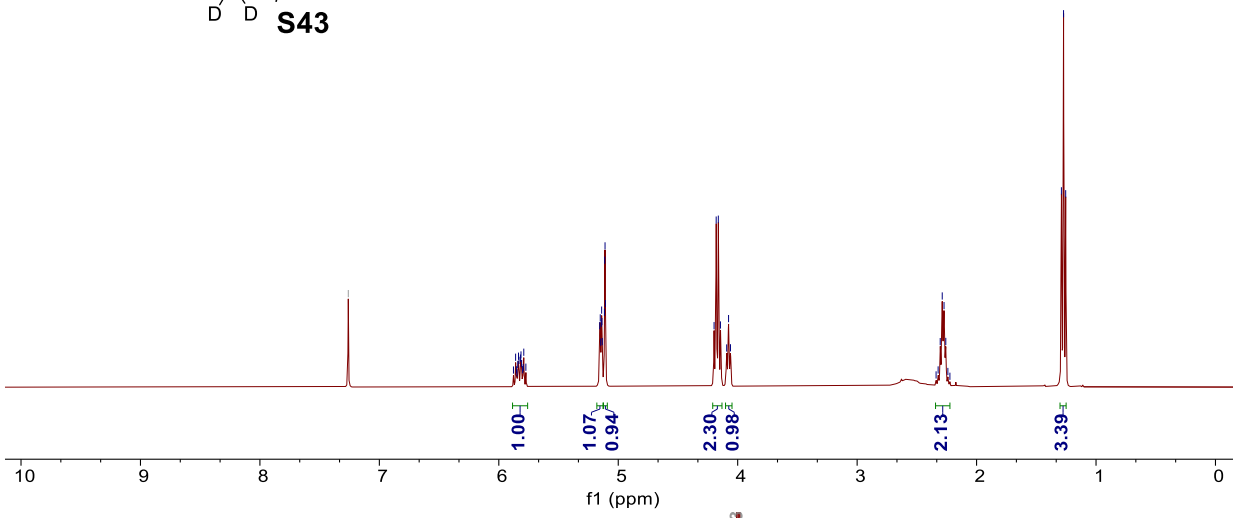

174.53
155.77
131.80
126.69
79.84
77.16 CDCl3
70.02
51.60
51.23
43.33
38.03
34.27
29.72
29.62
29.58
29.54
29.39
29.29
28.56
25.72
25.10
17.86
MeO
OH
NHBoc
Me
D
H
(±)-S40
f1 (ppm)


5.86 5.86 5.84 5.84 5.83 5.82 5.81 5.81 5.49 5.48 5.48 4.32 4.31 3.55 3.54 3.54 3.53 3.52 3.31 CD3OD 2.16 2.14 2.13 1.84 1.84 1.83 1.83 1.83 1.78 1.77 1.76 1.75 1.74 1.74 1.61 1.59 1.58 1.47 1.46 1.45 1.45 1.44 1.44 1.43 1.43 1.34 1.34 1.33 1.32 1.31 1.30 1.29
(±)-[8-2H]-38
acetate
1.00 0.92 0.92 0.93 2.04 1.01 3.96 2.38 2.28 15.02
f1 (ppm)
183.11 155.52 155.48 155.44 130.52 128.17 68.60 54.96 54.91 54.87 49.00 CD3OD 44.93 39.32 38.39 30.87 30.71 30.69 30.67 30.66 30.62 30.47 30.32 27.82 26.62
(±)-[8-2H]-38
acetate
acetate
f1 (ppm)

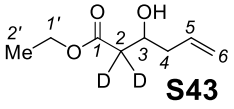

7.26 CDCl3
5.88
5.86
5.85
5.85
5.84
5.83
5.83
5.82
5.81
5.81
5.80
5.80
5.79
5.77
5.15
5.15
5.15
5.14
5.14
5.14
5.13
5.12
5.11
5.11
5.11
4.20
4.18
4.16
4.14
4.09
4.08
4.06
2.34
2.32
2.30
2.29
2.27
2.26
2.24
2.22
1.29
1.27
1.25


2'
1'
O
OH
Me
O
1
2
3
4
5
6
D
D

S43

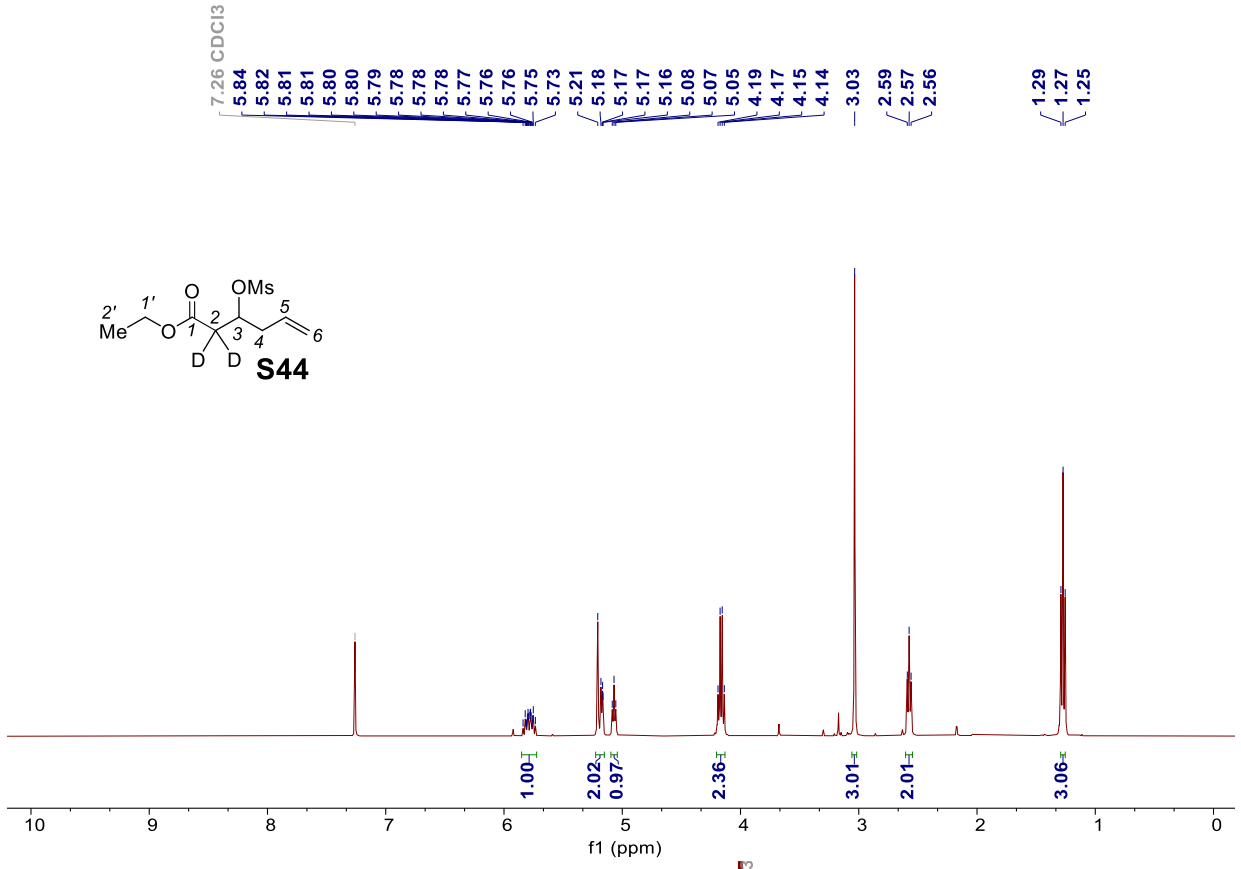

1.00
1.07
0.94
2.30
0.98
2.13
3.39
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

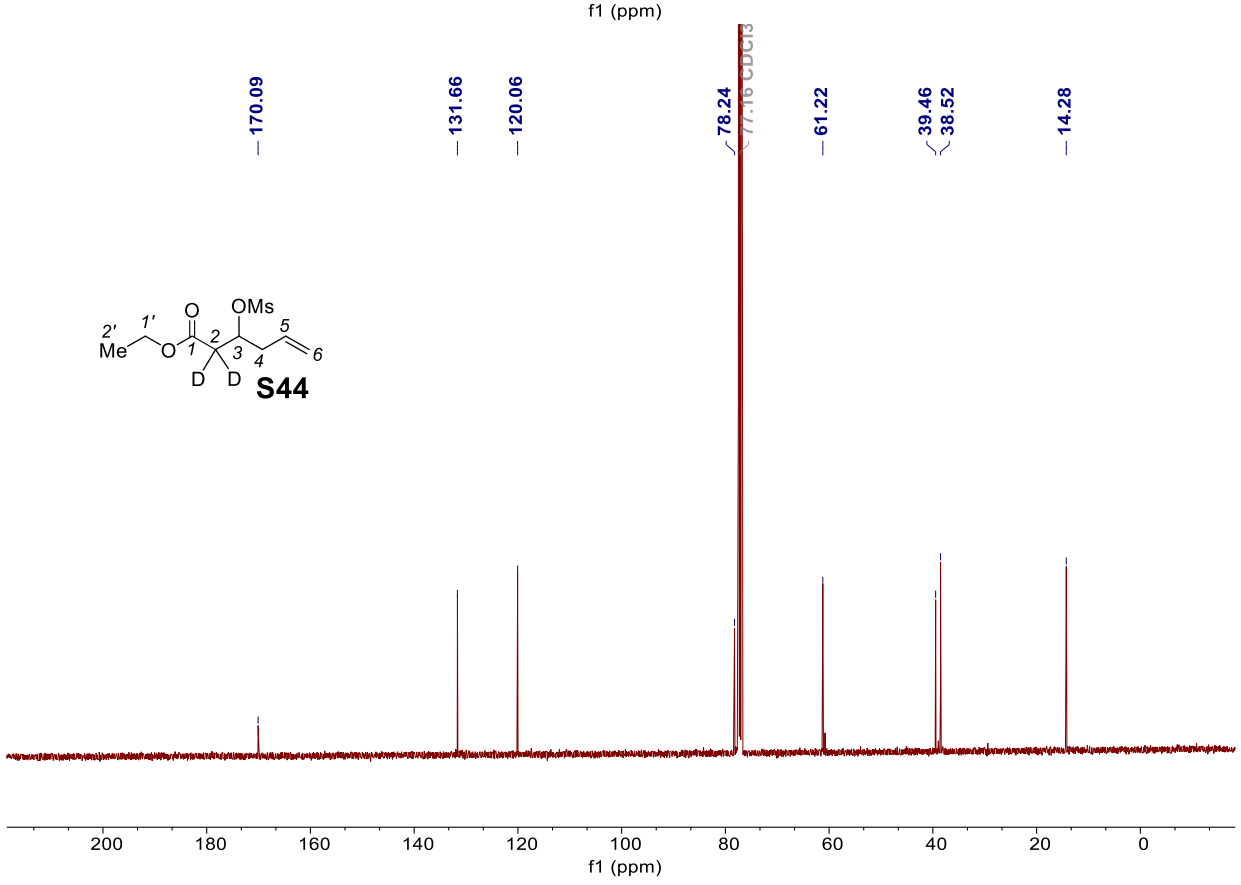

172.96
134.11
118.34
77.16 CDCl3
67.42
60.85
41.05
40.37
40.18
39.99
14.31

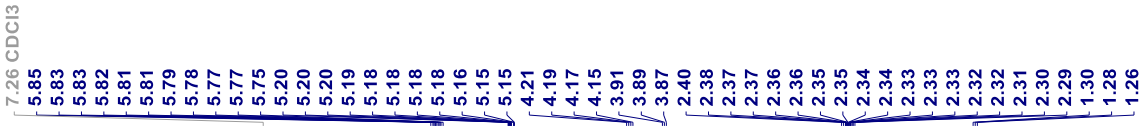

2'
1'
O
OH
Me
O
1
2
3
4
5
6
D
D

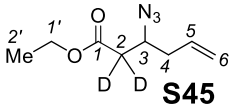
S43

200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

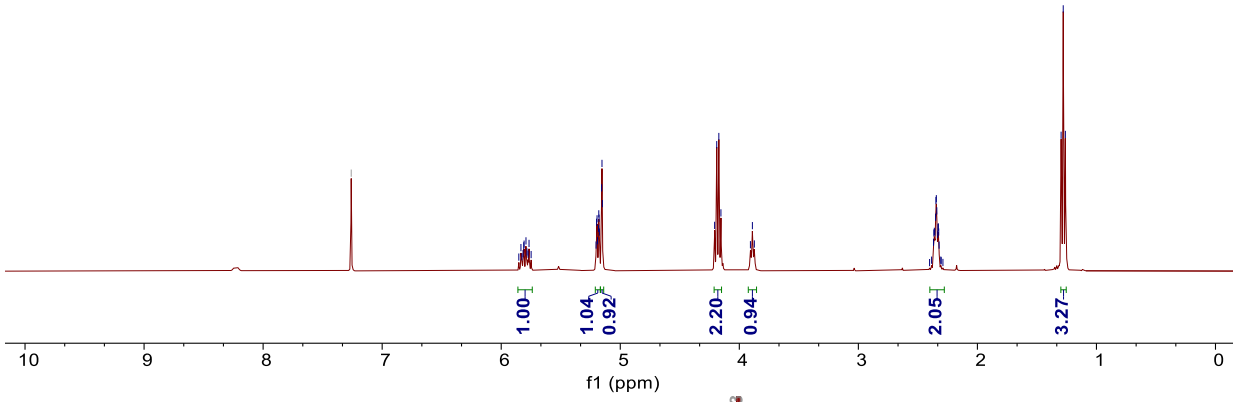

7.26 CDCl3
5.84
5.82
5.81
5.81
5.80
5.80
5.79
5.78
5.78
5.78
5.77
5.76
5.76
5.75
5.73
5.21
5.18
5.17
5.17
5.16
5.08
5.07
5.05
4.19
4.17
4.15
4.14
3.03
2.59
2.57
2.56
1.29
1.27
1.25
OMs
O
Me
D
D
S44
1.00
2.02
0.97
2.36
3.01
2.01
3.06
f1 (ppm)

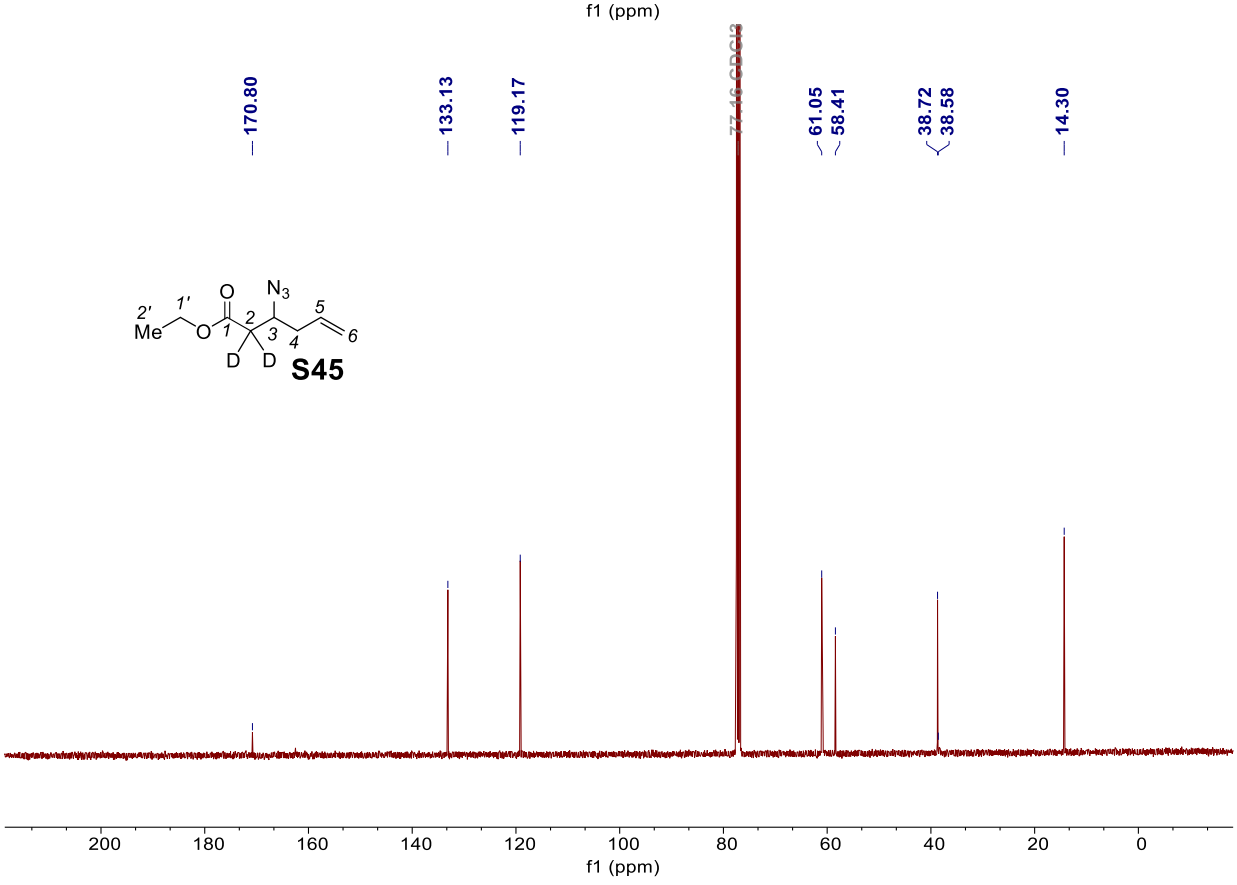

170.09
131.66
120.06
78.24
77.16 CDCl3
61.22
39.46
38.52
14.28
OMs
O
Me
D
D
S44
f1 (ppm)


7.26 CDCl3
5.85
5.83
5.83
5.82
5.81
5.81
5.79
5.78
5.77
5.77
5.75
5.20
5.20
5.19
5.18
5.18
5.18
5.16
5.15
5.15
4.21
4.19
4.17
4.15
3.91
3.89
3.87
2.40
2.38
2.37
2.37
2.36
2.36
2.35
2.35
2.34
2.34
2.33
2.33
2.33
2.32
2.32
2.31
2.30
2.29
1.30
1.28
1.26


2'
1'
Me
O
1
2
O
N3
3
4
5
6
D
D

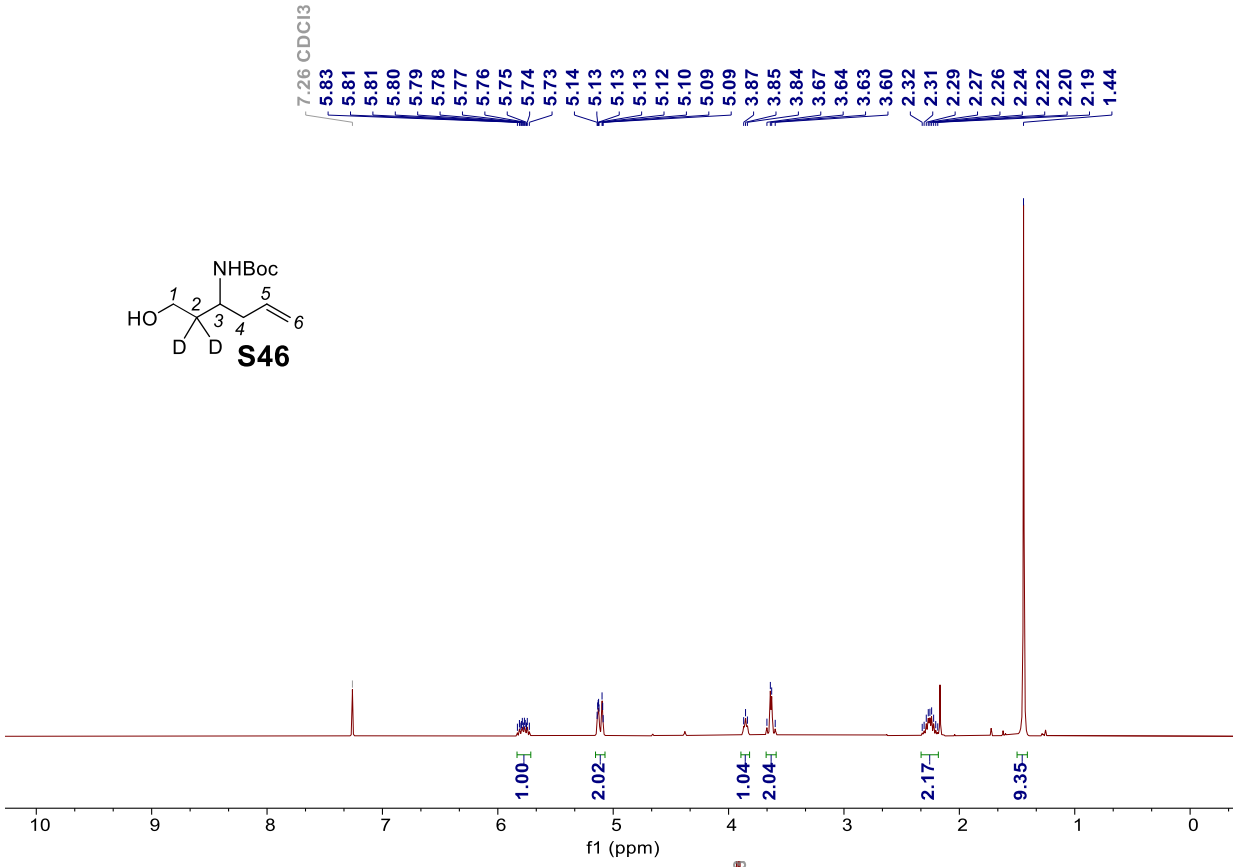
S45

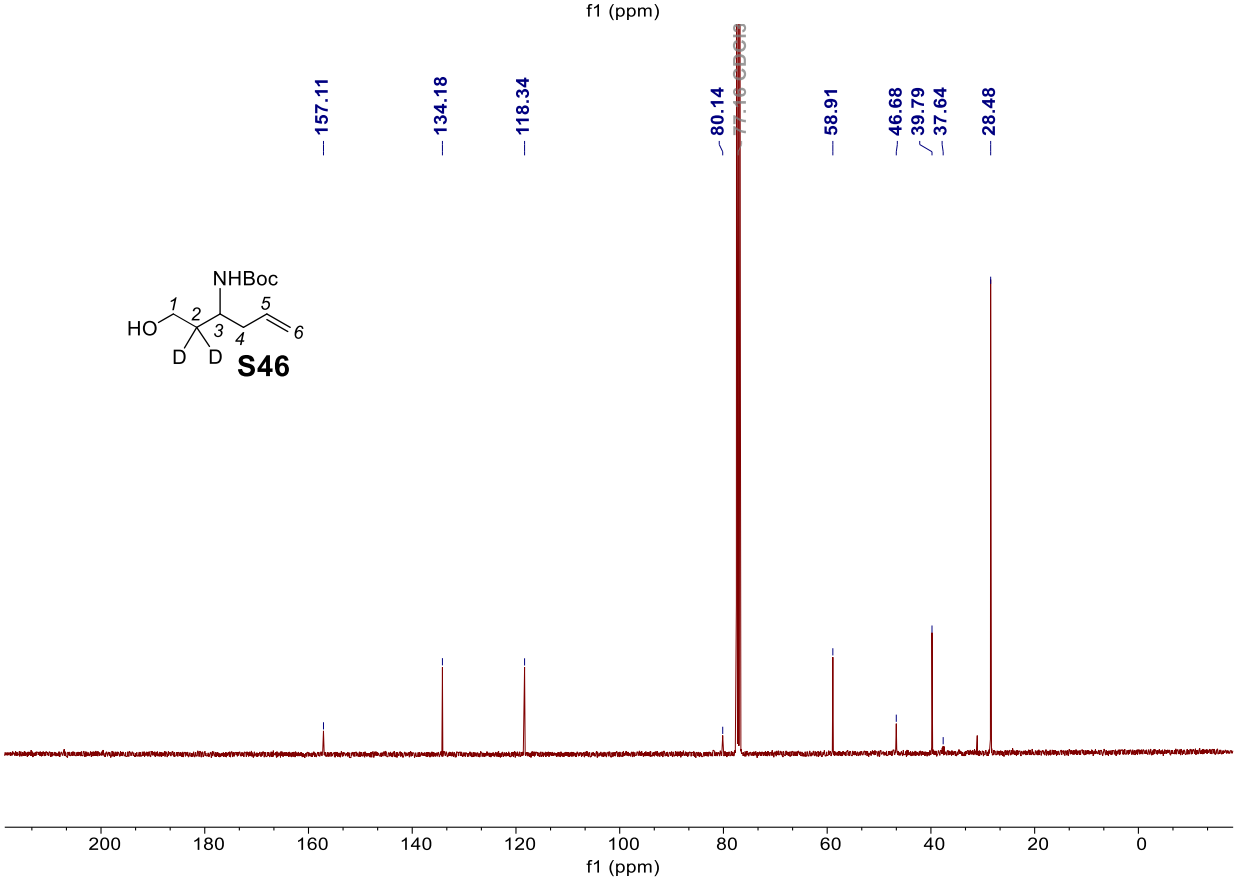

1.00
1.04
0.92
2.20
0.94
2.05
3.27
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

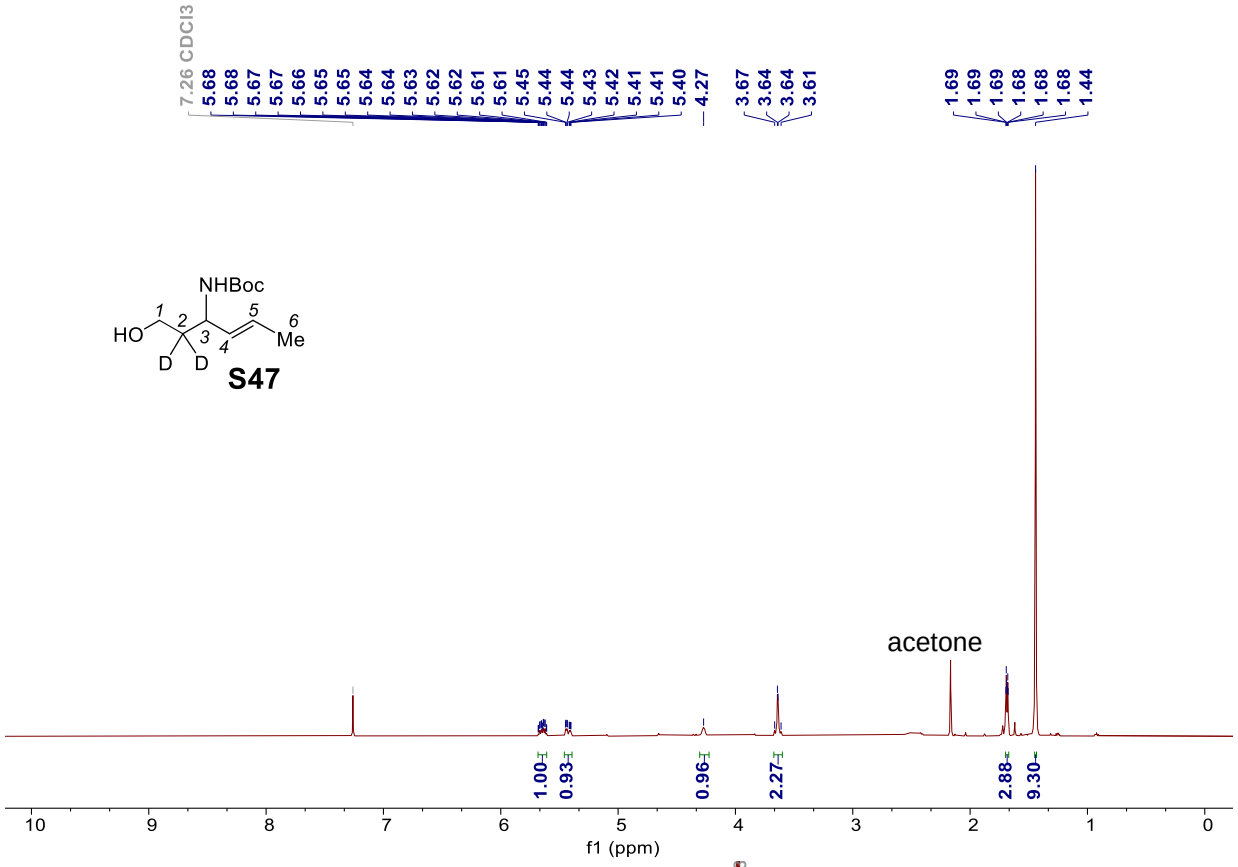

170.80
133.13
119.17
77.16 CDCl3
61.05
58.41
38.72
38.58
14.30
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

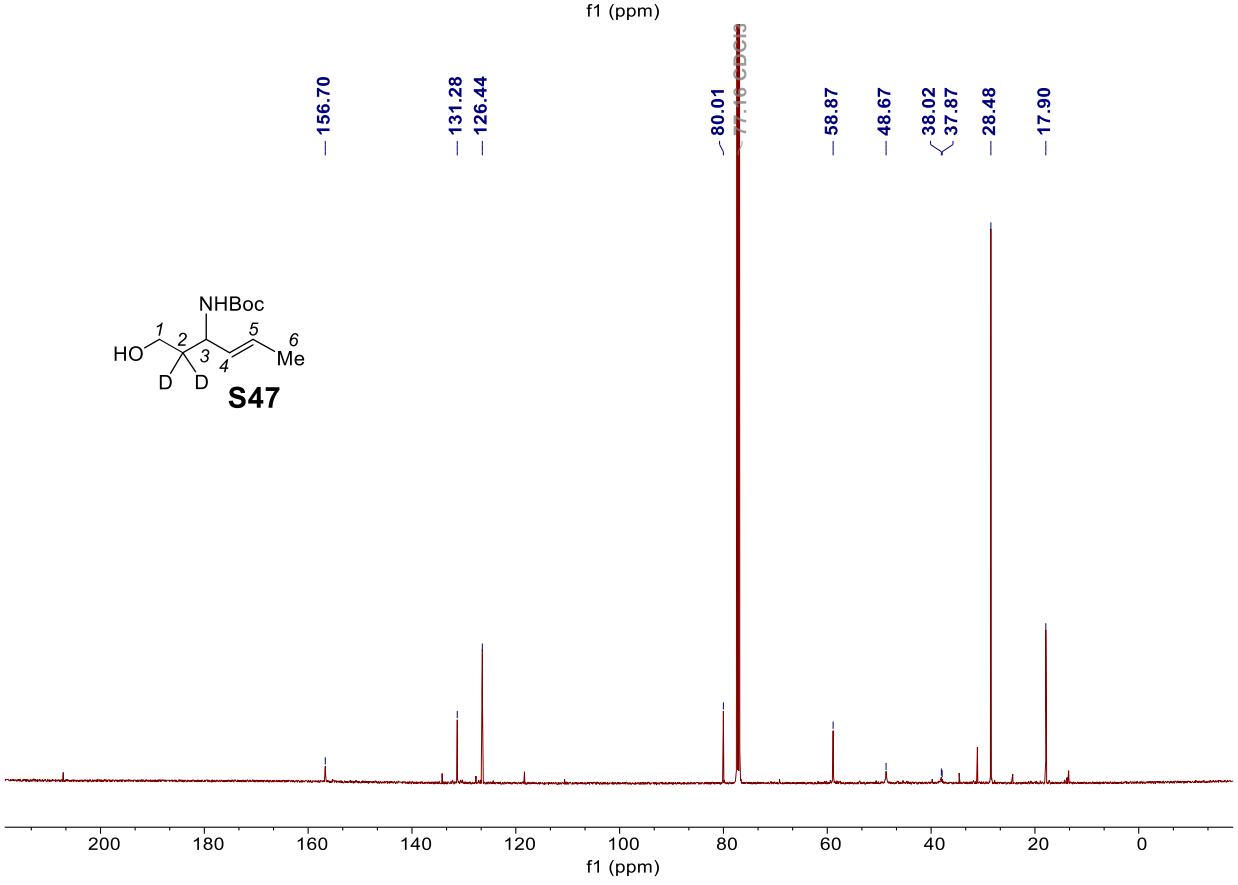
2'
1'
Me
O
1
2
O
N3
3
4
5
6
D
D

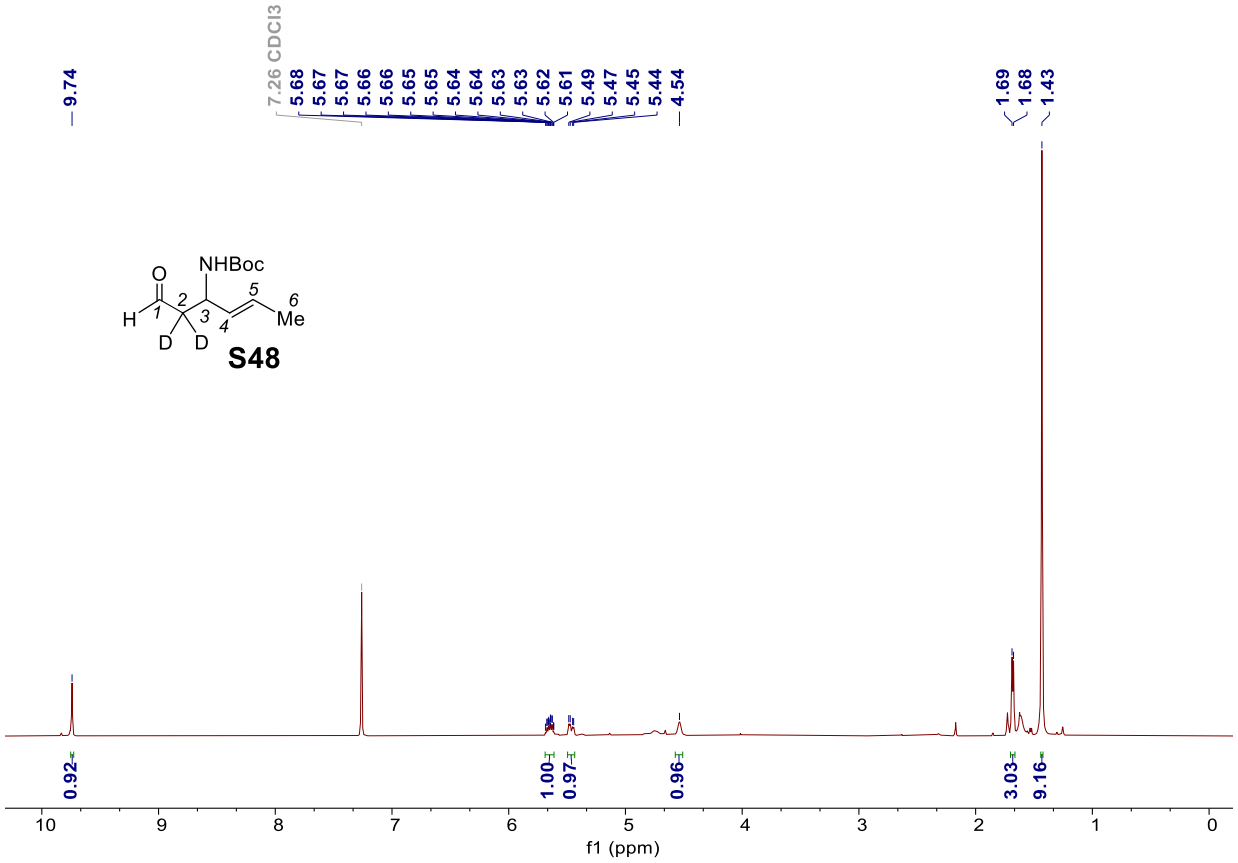
S45

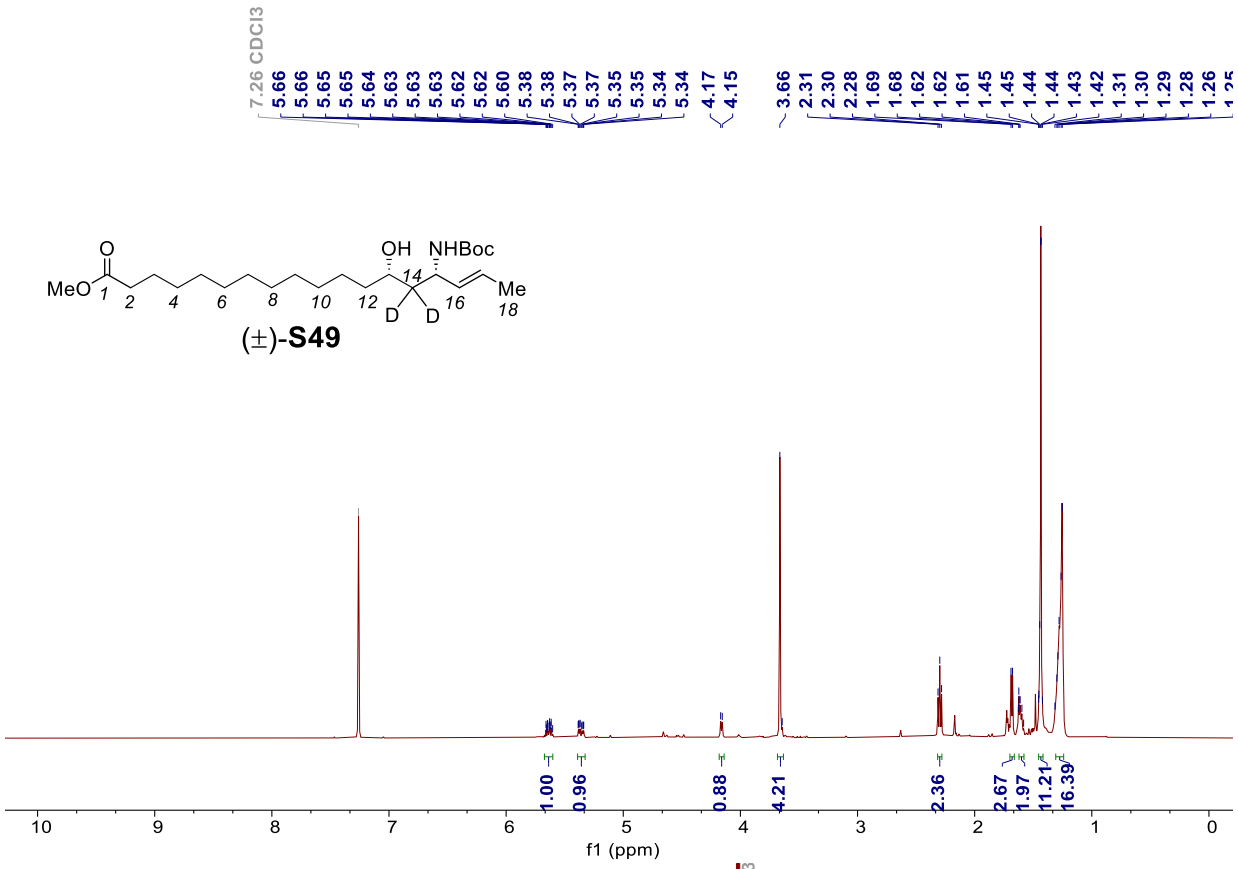

7.26 CDCl3
5.83
5.81
5.81
5.80
5.79
5.78
5.77
5.76
5.75
5.74
5.73
5.14
5.13
5.13
5.13
5.12
5.10
5.09
5.09
3.87
3.85
3.84
3.67
3.64
3.63
3.60
2.32
2.31
2.29
2.27
2.26
2.24
2.22
2.20
2.19
1.44
NHBoc
HO
D
D
S46
1.00
2.02
1.04
2.04
2.17
9.35
f1 (ppm)

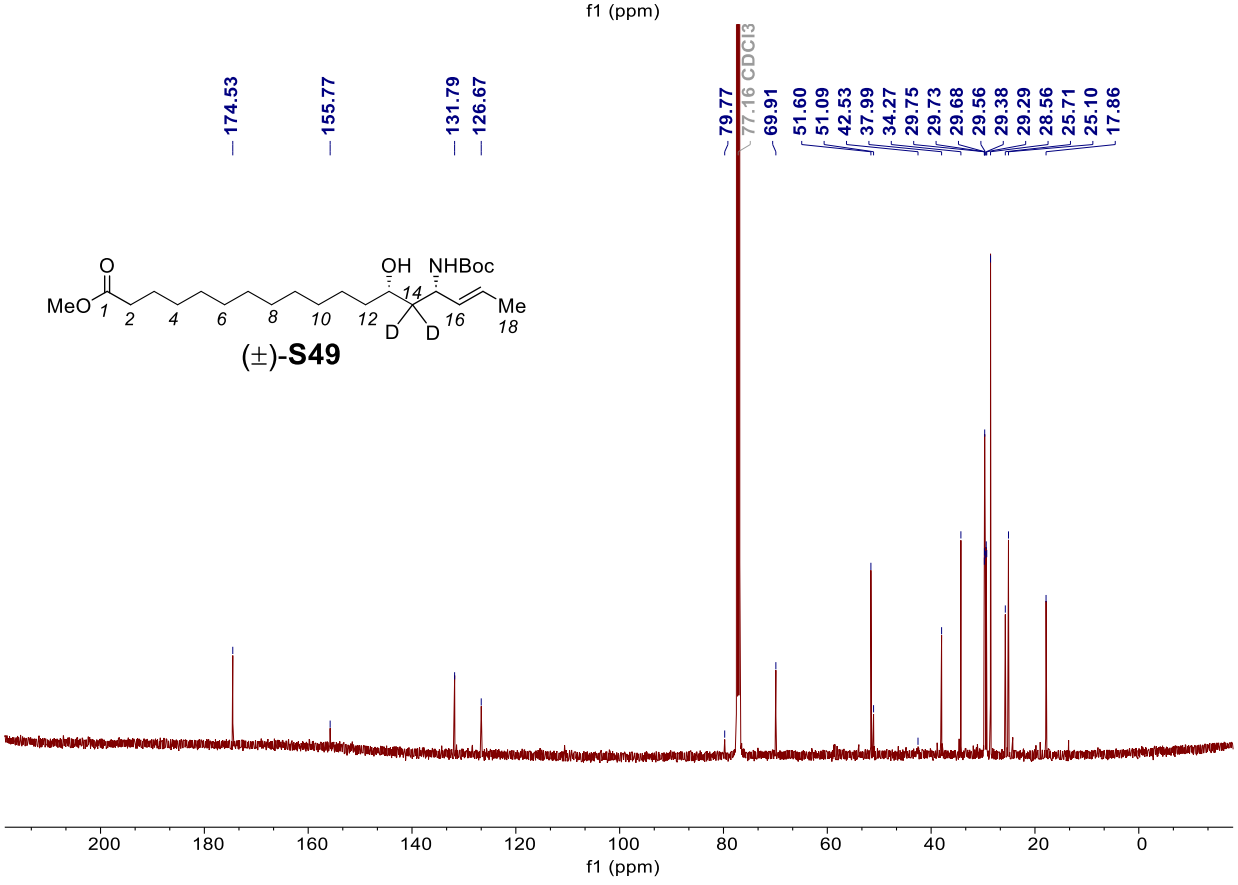

157.11
134.18
118.34
80.14
58.91
46.68
39.79
37.64
28.48
NHBoc
HO
D
D
S46
f1 (ppm)

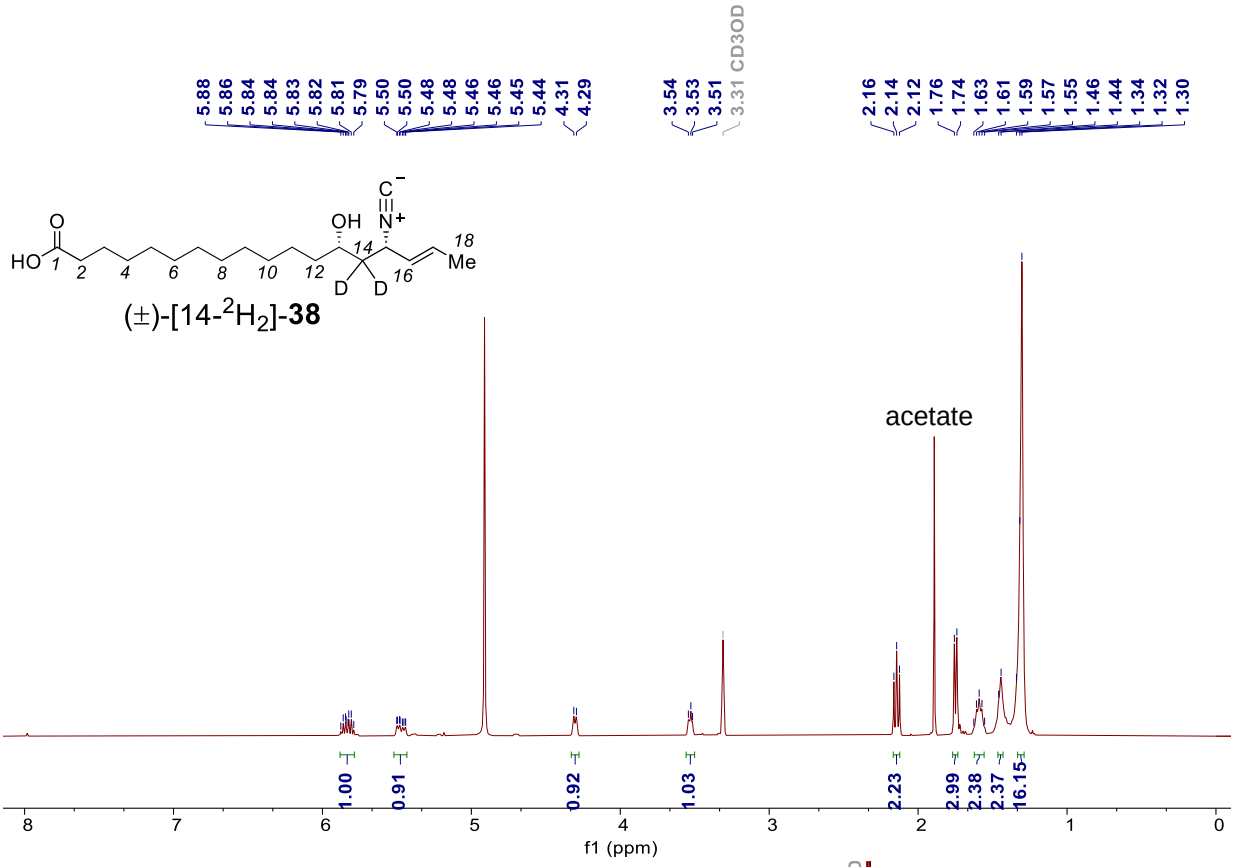

7.26 CDCl3
5.68
5.68
5.67
5.67
5.66
5.65
5.65
5.64
5.64
5.63
5.62
5.62
5.61
5.61
5.45
5.44
5.44
5.43
5.42
5.41
5.41
5.40
4.27
3.67
3.64
3.64
3.61
1.69
1.69
1.69
1.68
1.68
1.68
1.44
NHBoc
HO
D
D
Me
S47
acetone
1.00
0.93
0.96
2.27
2.88
9.30
f1 (ppm)

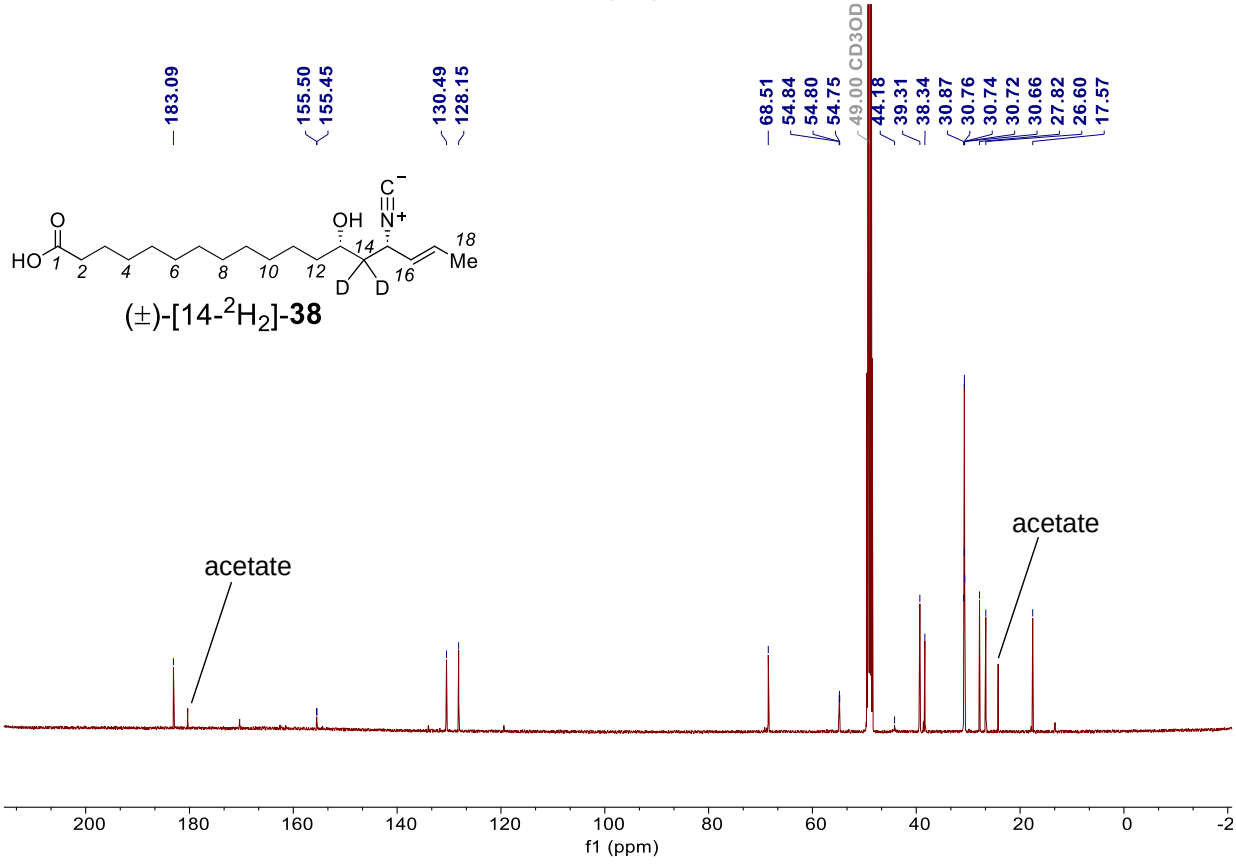

156.70
131.28
126.44
80.01
77.16 CDCl3
58.87
48.67
38.02
37.87
28.48
17.90
NHBoc
HO
D
D
Me
S47
f1 (ppm)

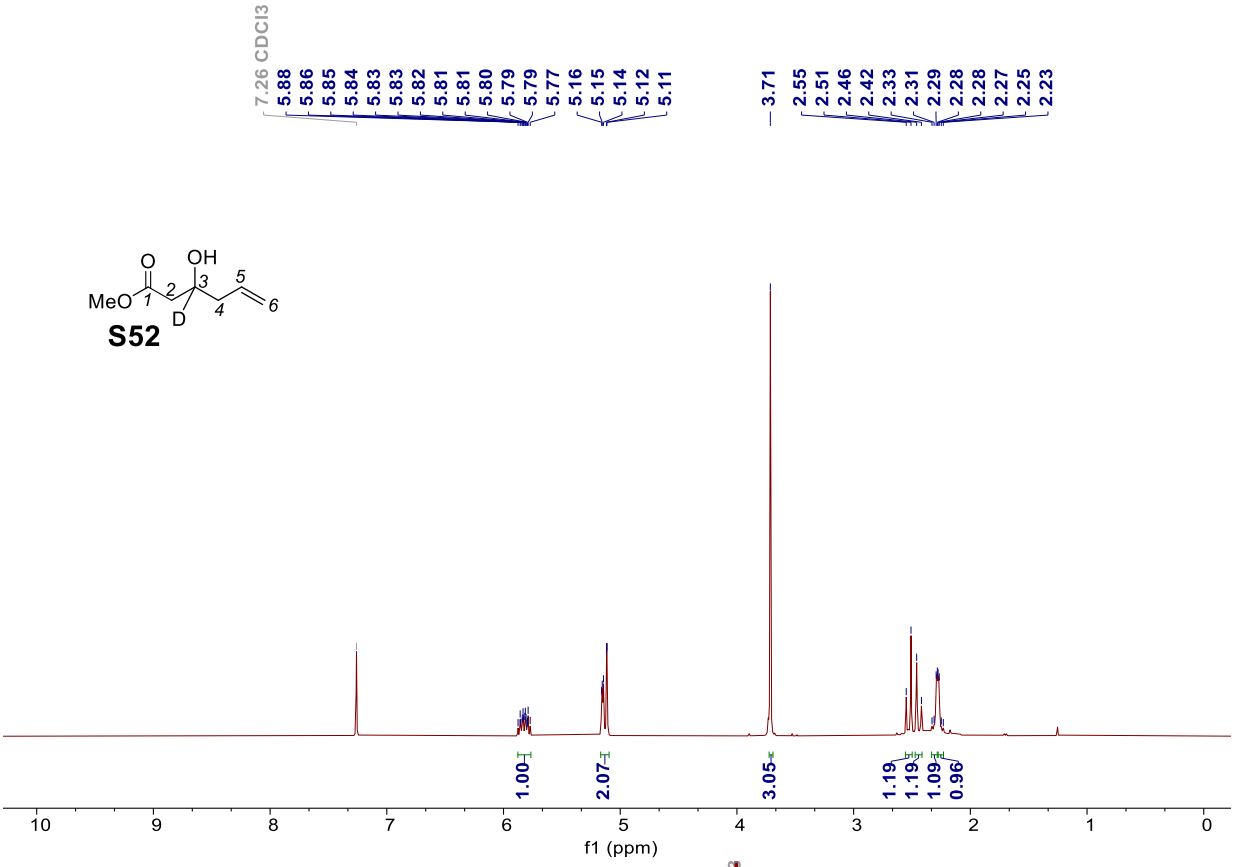

9.74
7.26 CDCl3
5.68
5.67
5.67
5.66
5.66
5.65
5.65
5.64
5.64
5.63
5.63
5.62
5.61
5.49
5.47
5.45
5.44
4.54
1.69
1.68
1.43
NHBoc
O
H
D
D
Me
1
2
3
4
5
6
S48
0.92
1.00
0.97
0.96
3.03
9.16
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

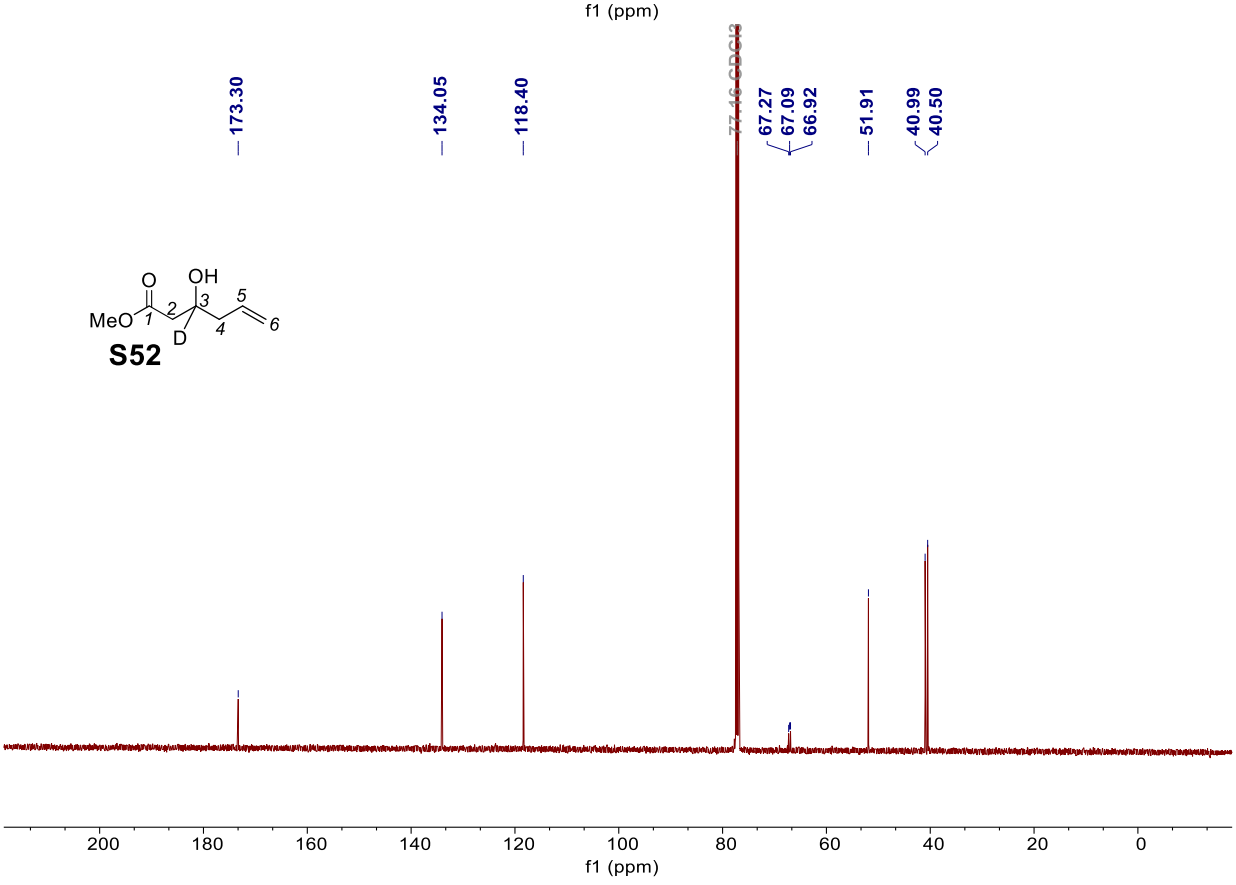

7.26 CDCl3
5.66 5.66 5.65 5.65 5.64 5.63 5.63 5.63 5.62 5.62 5.60 5.38 5.38 5.37 5.37 5.35 5.35 5.34 5.34
4.17 4.15
3.66 2.31 2.30 2.28 1.69 1.68 1.62 1.62 1.61 1.45 1.45 1.44 1.44 1.43 1.42 1.31 1.30 1.29 1.28
MeO
OH
NHBoc
Me
D
D
(±)-S49
1.00 0.96 0.88 4.21 2.36 2.67 1.97 11.21 16.39
f1 (ppm)

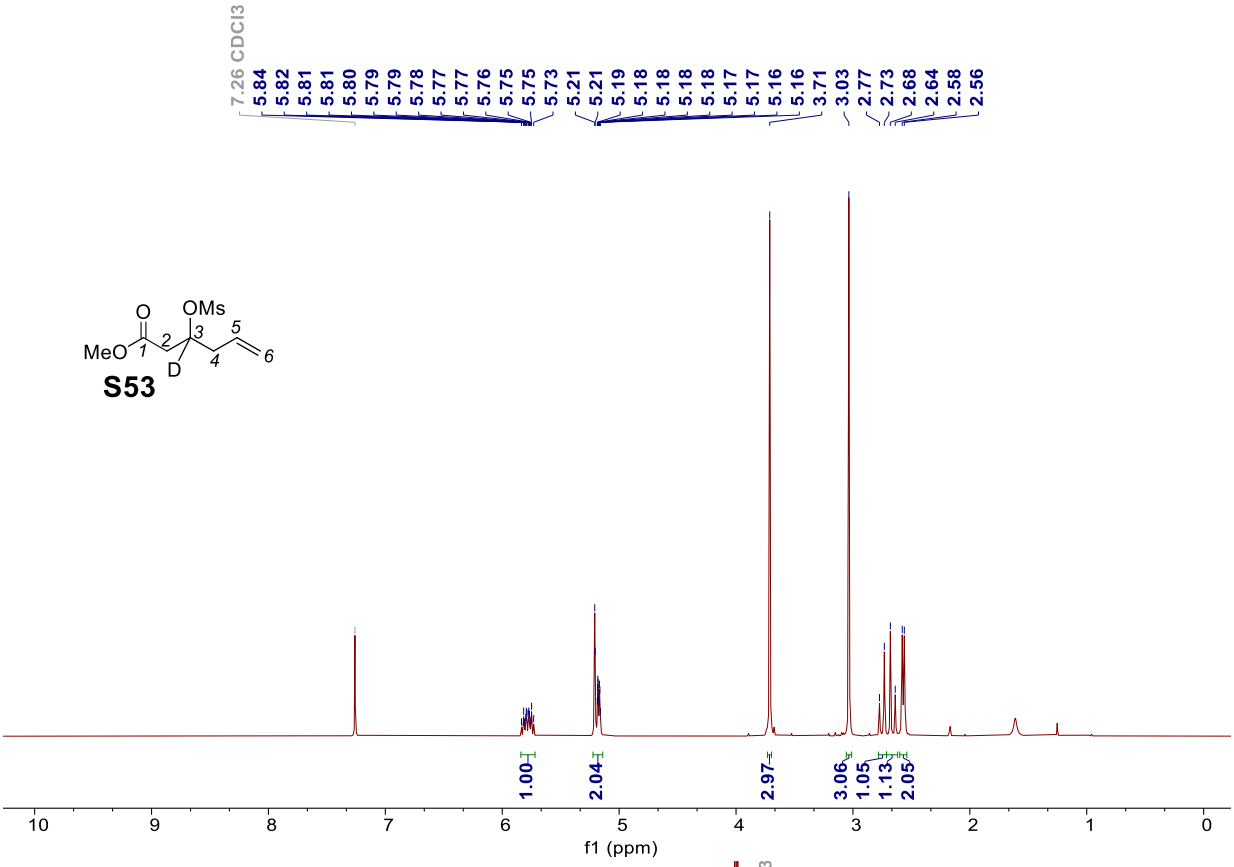

174.53 155.77 131.79 126.67
79.77 77.16 CDCl3 69.91 51.60 51.09 42.53 37.99 34.27 29.75 29.73 29.68 29.56 29.38 29.29 28.56 25.71 25.10 17.86
MeO
OH
NHBoc
Me
D
D
(±)-S49
f1 (ppm)

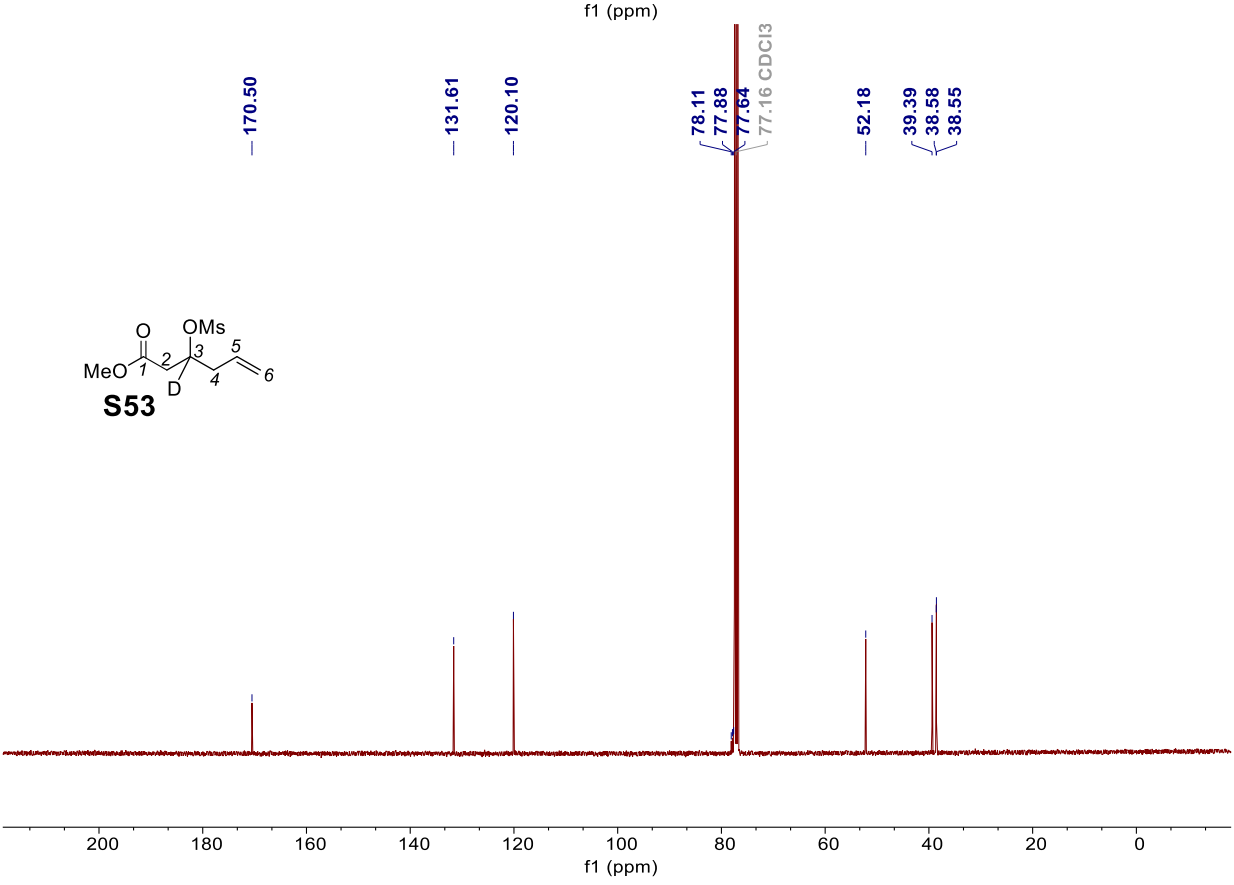

5.88 5.86 5.84 5.84 5.83 5.82 5.81 5.79 5.50 5.50 5.48 5.48 5.46 5.46 5.45 5.44 4.31 4.29
3.54 3.53 3.51 3.31 CD3OD
2.16 2.14 2.12 1.76 1.74 1.63 1.61 1.59 1.57 1.55 1.46 1.44 1.34 1.32 1.30
(±)-[14-2H2]-38
acetate
1.00 0.91 0.92 1.03 2.23 2.99 2.38 2.37 16.15
f1 (ppm)

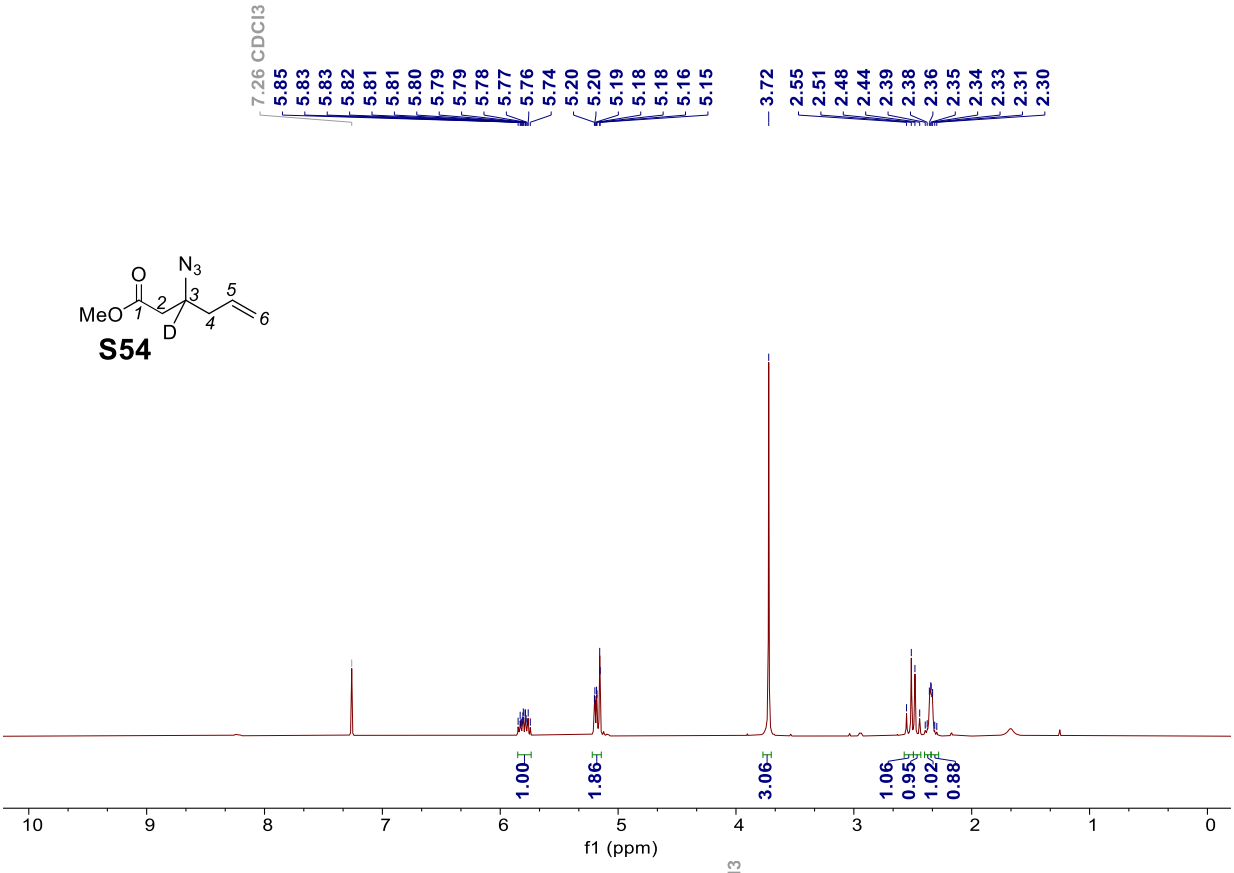

183.09
155.50 155.45
130.49 128.15
68.51 54.84 54.80 54.75 49.00 CD3OD 44.18 39.31 38.34 30.87 30.76 30.74 30.72 30.66 27.82 26.60 17.57
(±)-[14-2H2]-38
acetate
acetate
f1 (ppm)

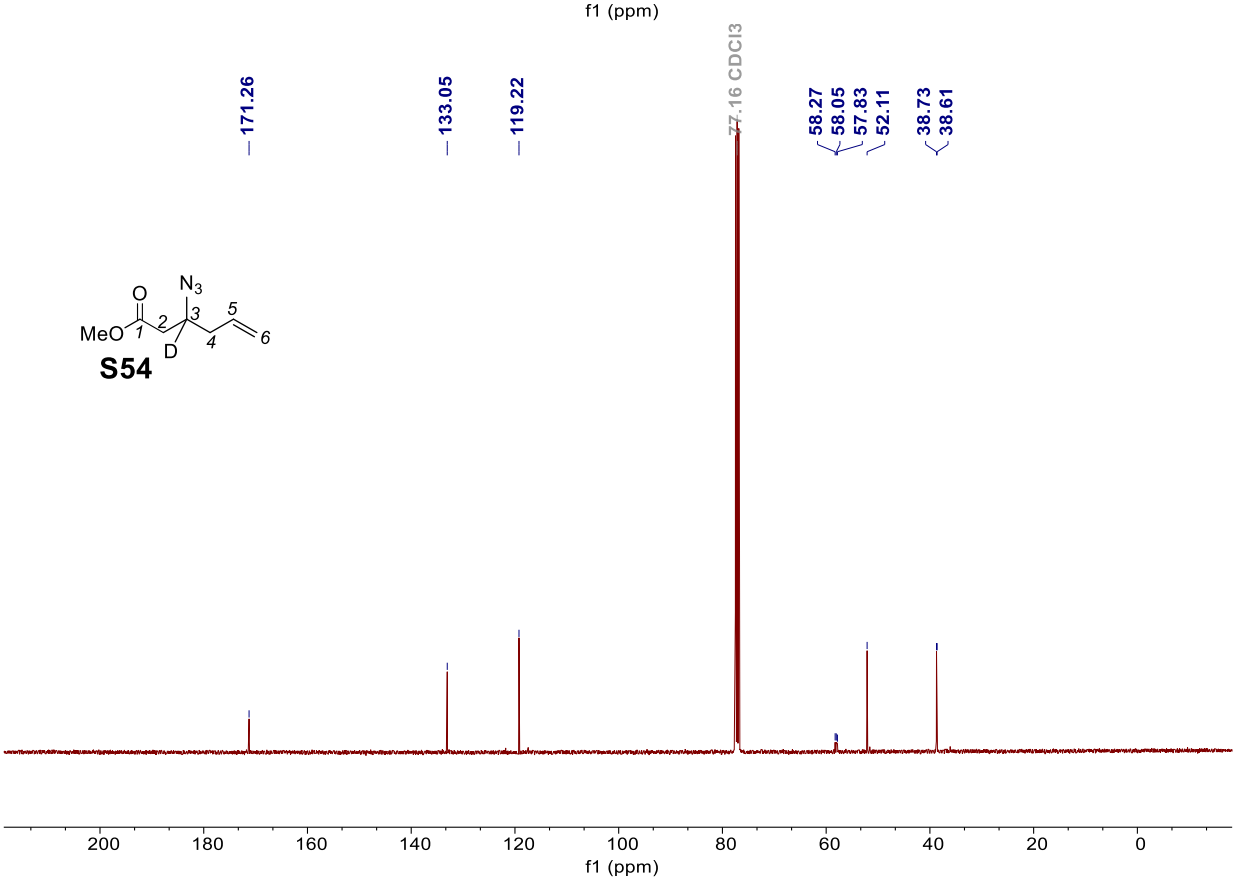

7.26 CDCl3
5.88
5.86
5.85
5.84
5.83
5.83
5.82
5.81
5.81
5.80
5.79
5.79
5.77
5.16
5.15
5.14
5.12
5.11
3.71
2.55
2.51
2.46
2.42
2.33
2.31
2.29
2.28
2.28
2.27
2.25
2.23
MeO
OH
D
S52
1.00
2.07
3.05
1.19
1.19
1.09
0.96
f1 (ppm)

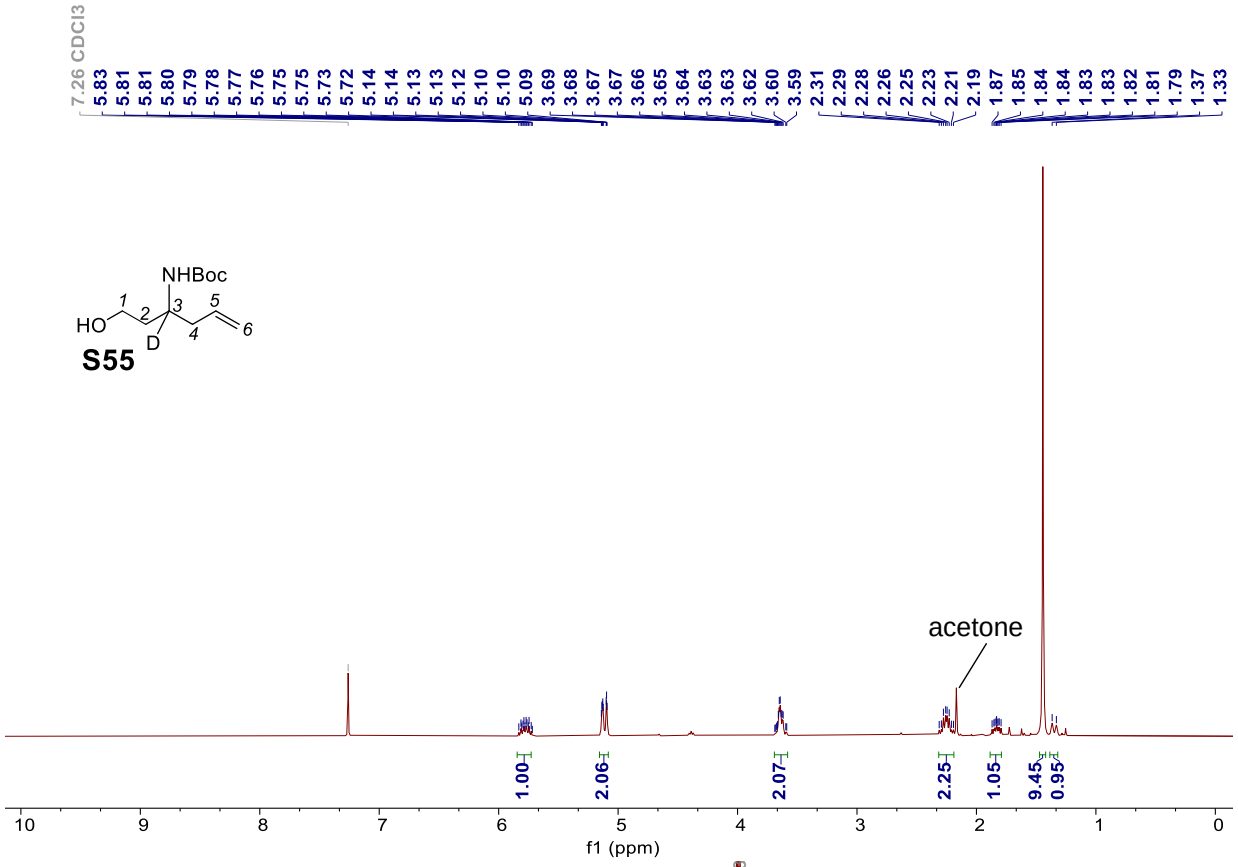

173.30
134.05
118.40
77.16 CDCl3
67.27
67.09
66.92
51.91
40.99
40.50
MeO
OH
D
S52
f1 (ppm)

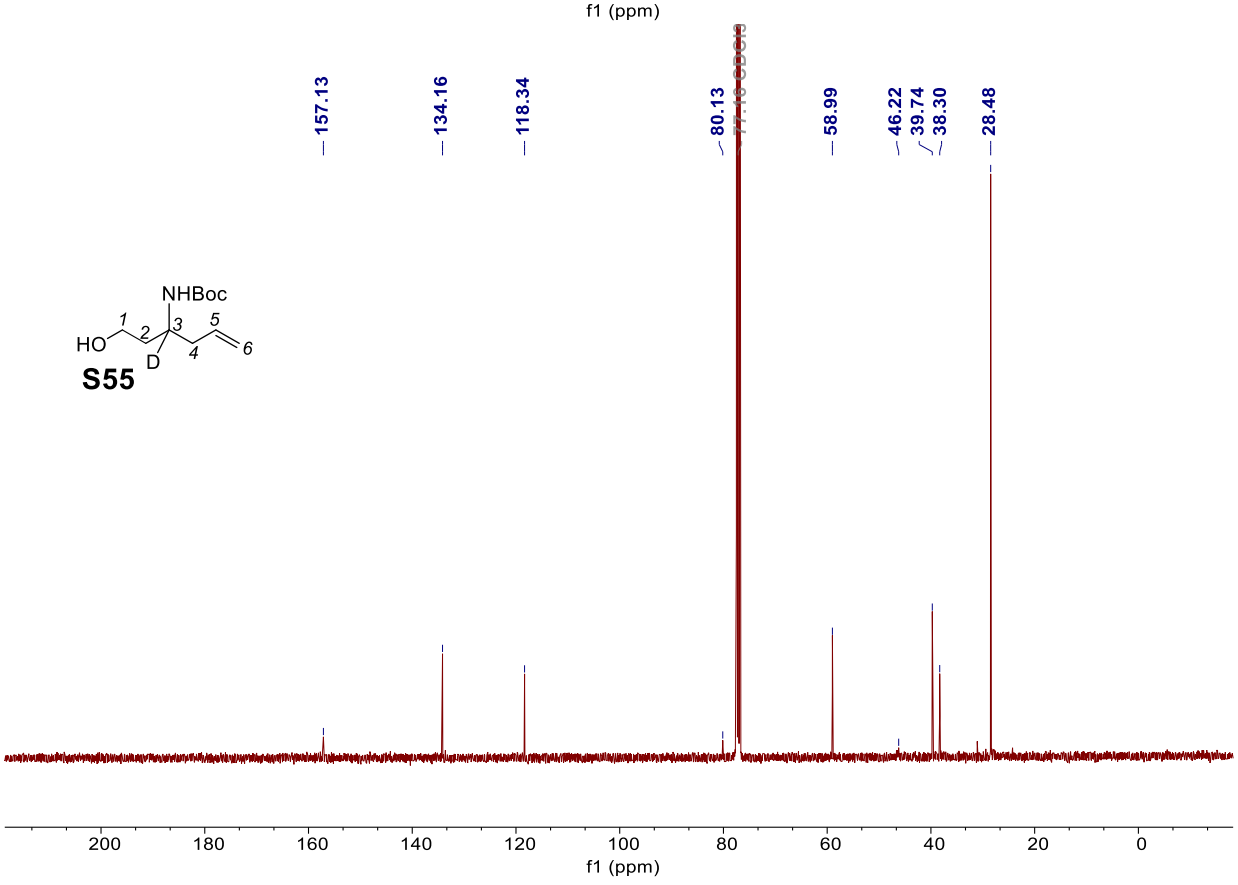

7.26 CDCl3
5.84
5.82
5.81
5.81
5.80
5.79
5.79
5.78
5.77
5.77
5.76
5.75
5.75
5.73
5.21
5.21
5.19
5.18
5.18
5.18
5.18
5.17
5.17
5.16
5.16
3.71
3.03
2.77
2.73
2.68
2.64
2.58
2.56
O
OMs
MeO
1
2
3
4
5
6
D
S53
1.00
2.04
2.97
3.06
1.05
1.13
2.05
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

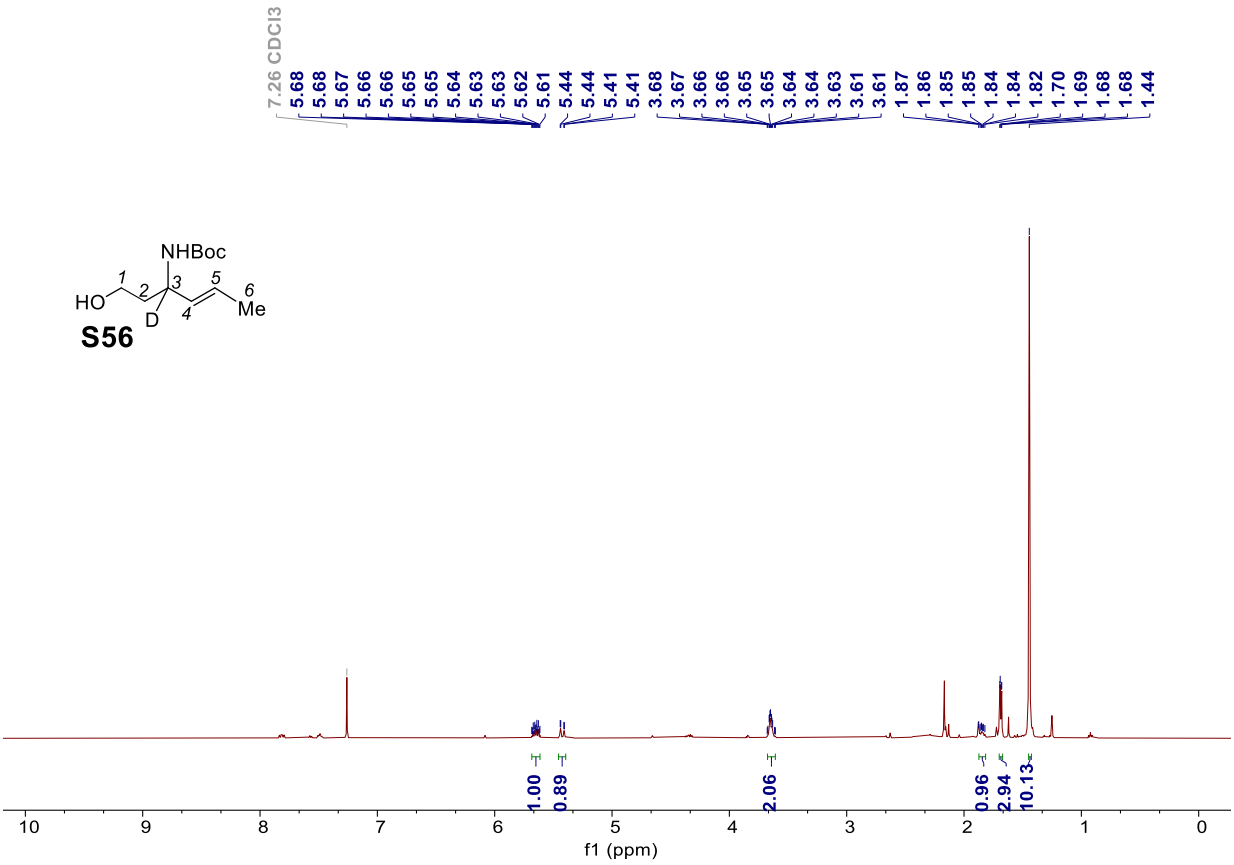

170.50
131.61
120.10
78.11
77.88
77.64
77.16 CDCl3
52.18
39.39
38.58
38.55
O
OMs
MeO
1
2
3
4
5
6
D
S53
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

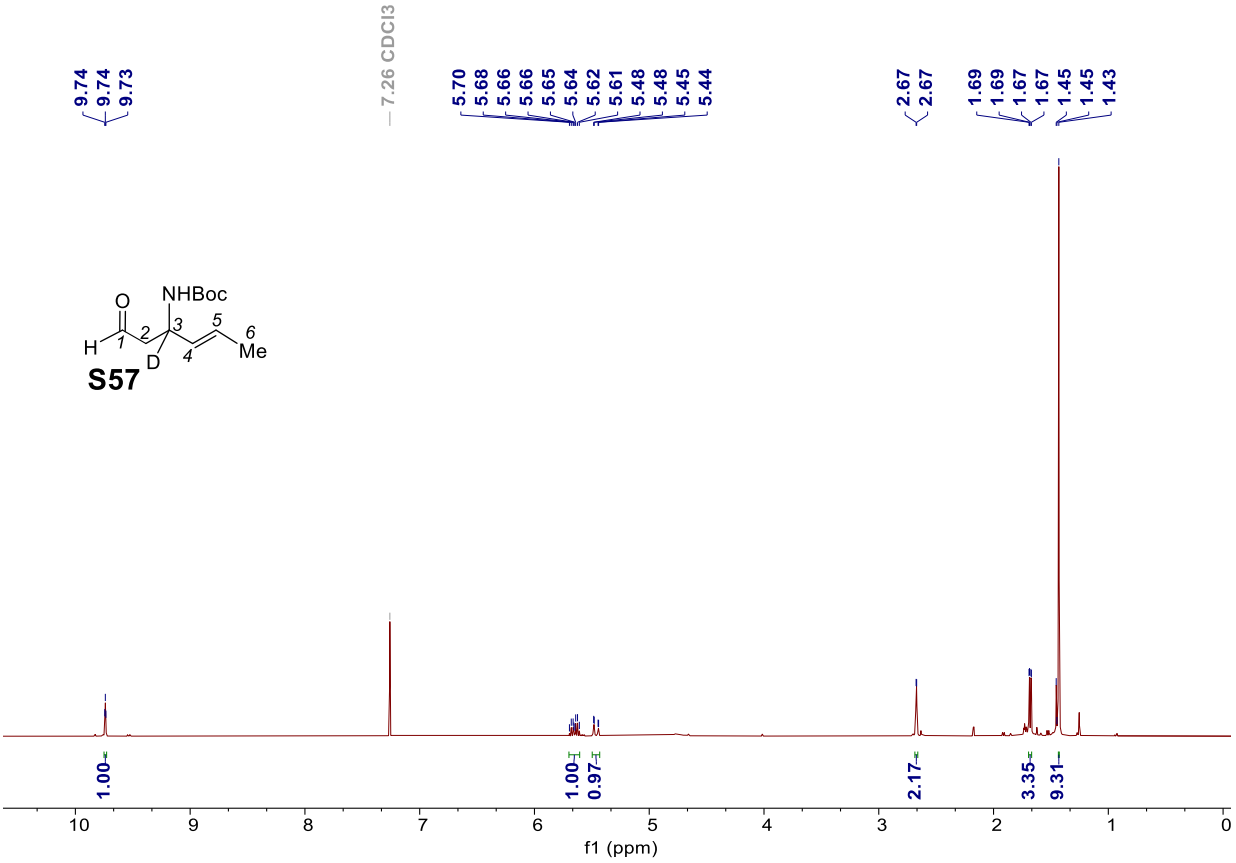

7.26 CDCl3
5.85
5.83
5.83
5.82
5.81
5.81
5.80
5.79
5.79
5.78
5.77
5.76
5.74
5.20
5.19
5.18
5.18
5.16
5.15
3.72
2.55
2.51
2.48
2.44
2.39
2.38
2.36
2.35
2.34
2.33
2.31
2.30
N3
O
MeO
D
1
2
3
4
5
6
S54
1.00
1.86
3.06
1.06
0.95
1.02
0.88
f1 (ppm)

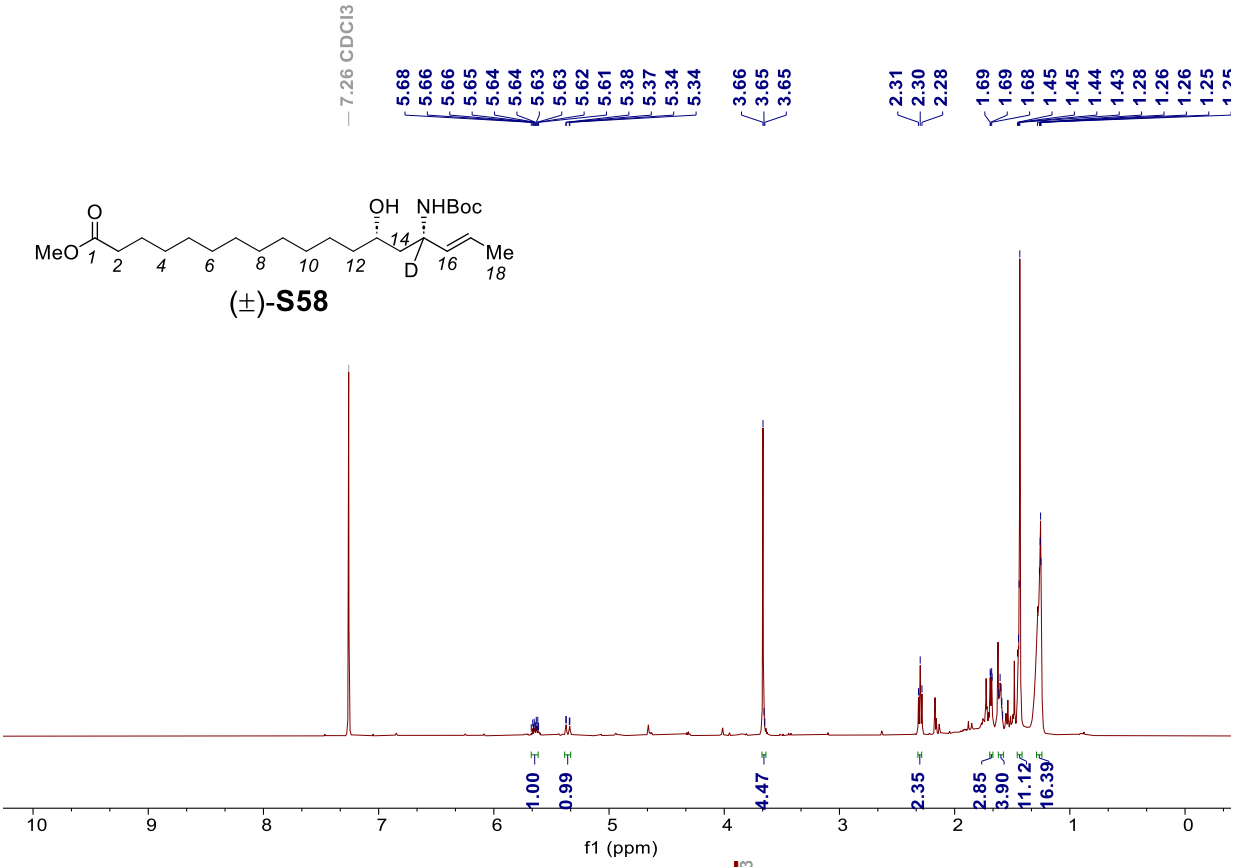

171.26
133.05
119.22
77.16 CDCl3
58.27
58.05
57.83
52.11
38.73
38.61
N3
O
MeO
D
1
2
3
4
5
6
S54
f1 (ppm)

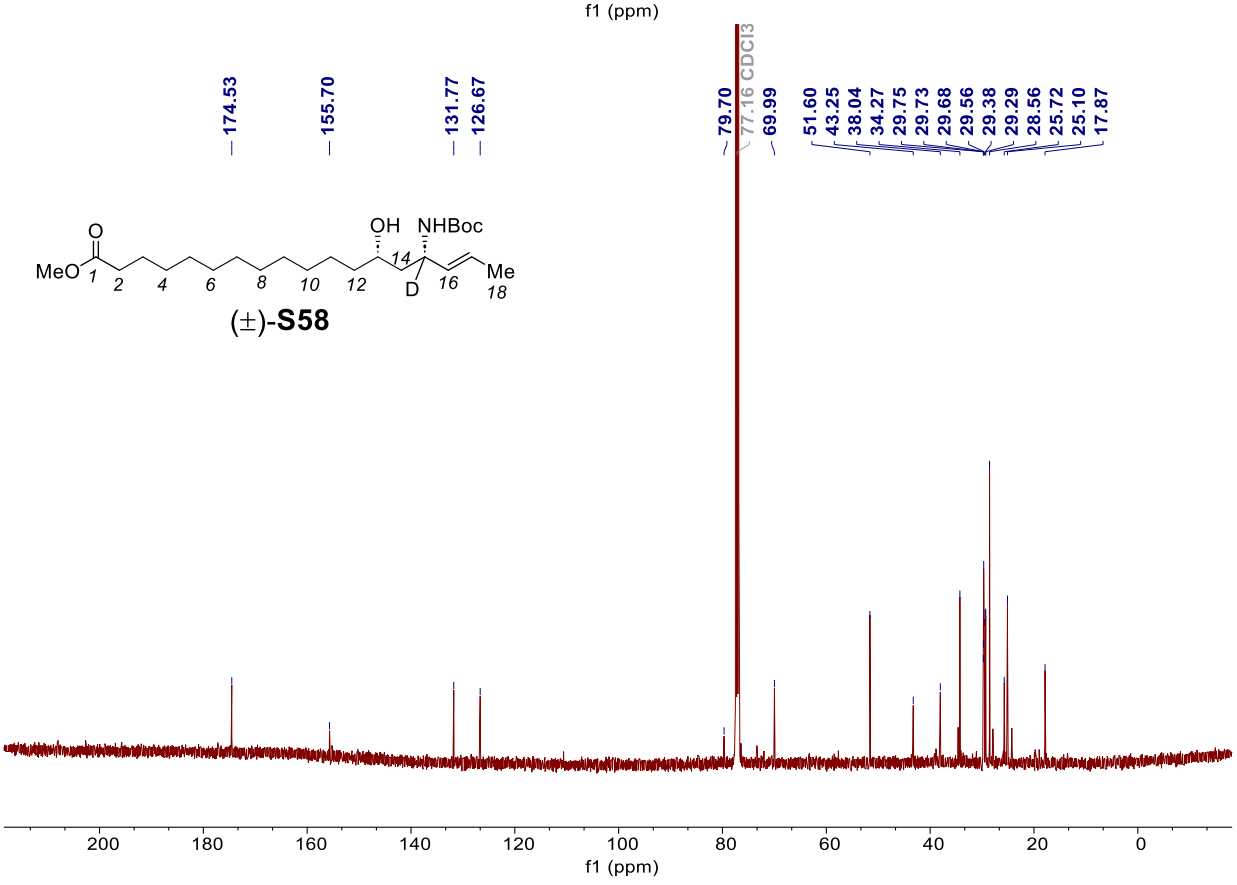

7.26 CDCl3
5.83 5.81 5.81 5.80 5.79 5.78 5.77 5.76 5.75 5.75 5.73 5.72 5.14 5.14 5.13 5.13 5.12 5.10 5.10 5.09 3.69 3.68 3.67 3.67 3.66 3.65 3.64 3.63 3.63 3.62 3.60 3.59 2.31 2.29 2.28 2.26 2.25 2.23 2.21 2.19 1.87 1.85 1.84 1.84 1.83 1.83 1.82 1.81 1.79 1.37 1.33
NHBoc
HO
D
1 2 3 4 5 6
S55
acetone
1.00 2.06 2.07 2.25 1.05 9.45 0.95
10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

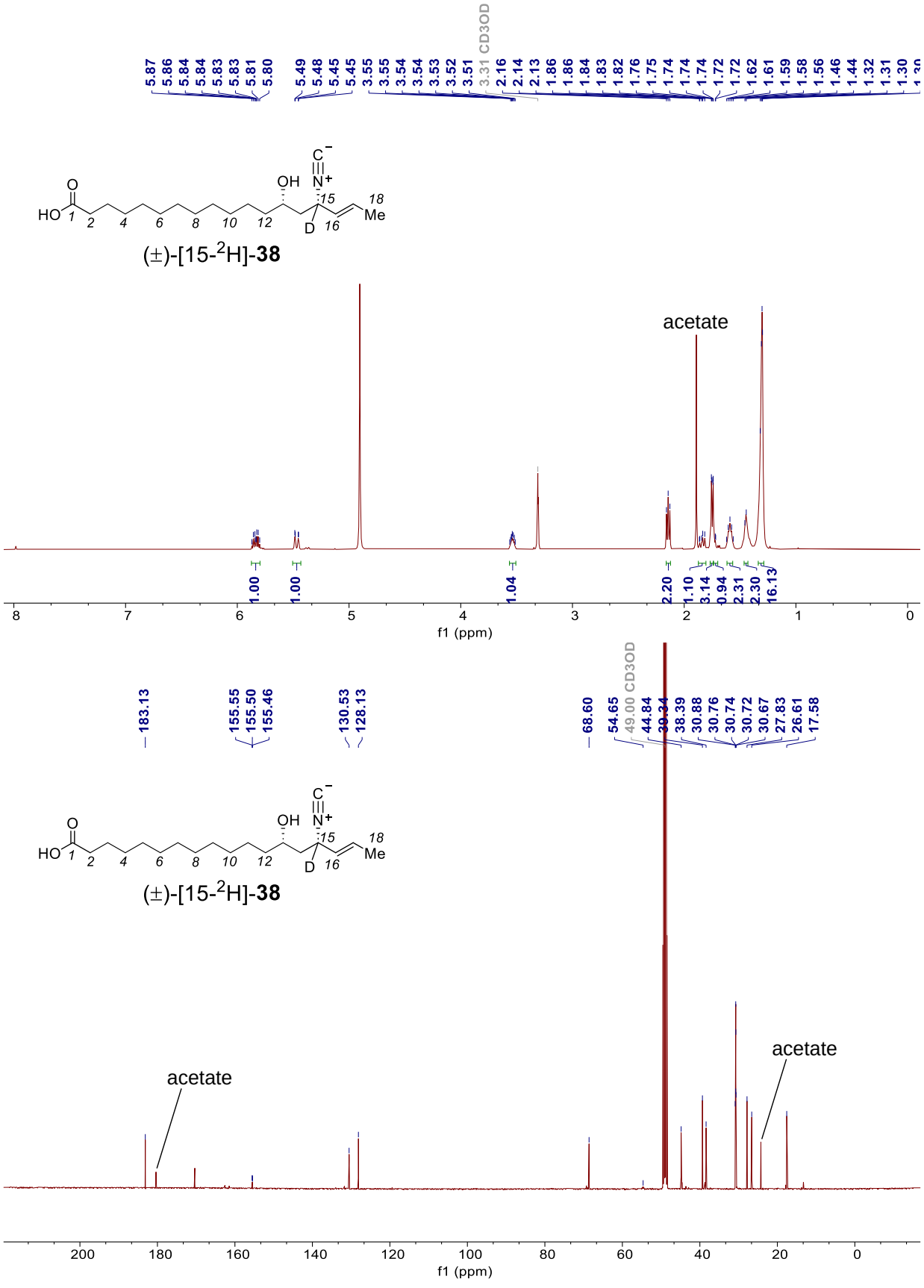

157.13
134.16
118.34
80.13
77.16 CDCl3
58.99
46.22
39.74
38.30
28.48
NHBoc
HO
D
1 2 3 4 5 6
S55
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


7.26 CDCl3
5.68
5.68
5.67
5.66
5.66
5.65
5.65
5.64
5.63
5.63
5.62
5.61
5.44
5.44
5.41
5.41
3.68
3.67
3.66
3.66
3.65
3.65
3.64
3.64
3.63
3.61
3.61
1.87
1.86
1.85
1.85
1.84
1.84
1.82
1.70
1.69
1.68
1.68
1.44
NHBoc
HO
D
Me
S56
1.00
0.89
2.06
0.96
2.94
10.13
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


9.74
9.74
9.73
7.26 CDCl3
5.70
5.68
5.66
5.66
5.65
5.64
5.62
5.61
5.48
5.48
5.45
5.44
2.67
2.67
1.69
1.69
1.67
1.67
1.45
1.45
1.43
O
NHBoc
H
1
2
3
4
5
6
D
Me
S57
1.00
1.00
0.97
2.17
3.35
9.31
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


7.26 CDCl3
5.68
5.66
5.66
5.65
5.64
5.64
5.63
5.63
5.62
5.61
5.38
5.37
5.34
5.34
3.66
3.65
3.65
2.31
2.30
2.28
1.69
1.69
1.68
1.45
1.45
1.44
1.43
1.28
1.26
1.26
1.25
OH
NHBoc
MeO
O
Me
D
1
2
4
6
8
10
12
14
16
18
(±)-S58
1.00
0.99
4.47
2.35
2.85
3.90
11.12
16.39
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


174.53
155.70
131.77
126.67
79.70
77.16 CDCl3
69.99
51.60
43.25
38.04
34.27
29.75
29.73
29.68
29.56
29.38
29.29
28.56
25.72
25.10
17.87
OH
NHBoc
MeO
O
Me
D
1
2
4
6
8
10
12
14
16
18
(±)-S58
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


5.87 5.86 5.84 5.84 5.83 5.83 5.81 5.80
5.49 5.48 5.45 5.45
3.55 3.55 3.54 3.54 3.53 3.52 3.51 3.31 CD3OD 2.16 2.14 2.13 1.86 1.86 1.84 1.83 1.82 1.76 1.75 1.74 1.74 1.74 1.72 1.72 1.62 1.61 1.59 1.58 1.56 1.46 1.44 1.32 1.31 1.30
(±)-[15-2H]-38
acetate
1.00 1.00 1.04 2.20 1.10 3.14 0.94 2.31 2.30 16.13
f1 (ppm)
183.13
155.55 155.50 155.46
130.53 128.13
68.60 54.65 49.00 CD3OD 44.84 38.39 38.88 30.76 30.74 30.72 30.67 27.83 26.61 17.58
(±)-[15-2H]-38
acetate
acetate
f1 (ppm)