Electronic Supplementary Information

Synthesis, structure and reactivity of [15]-macrodilactones

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Contents

1. Experimental procedure for all new compounds:

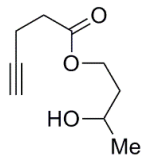
General Methods

Unless and otherwise noted, all reactions were performed at room temperature (rt) under nitrogen (N_2) atmosphere. All commercial available reagents and solvents were used as it is. All reactions were monitored by TLC (silica gel HL, w/UV254, 250μm) and visualized either under UV lamp or by charring with 2.5% *p*-anisaldehyde in H_2SO_4, AcOH and EtOH solutions or by staining with alkaline $KMnO_4$ solutions. Flash chromatography was performed on silica gel (230-400 Å). Melting points were recorded on Electrothermal melting point apparatus, and are uncorrected. Optical rotations were measured on Jasco P-2000 polarimeter using the sodium D line. ^{1}H NMR spectra were collected at 300 MHz and 400 MHz with chemical shift referenced the residual peak in $CDCl_3$ (δ_H 7.26 ppm). ^{13}C NMR spectra were collected at 75 MHz and 100 MHz and referenced to residual peak in $CDCl_3$ (δ_C 77.16 ppm). Mass spectra were obtained from Accu TOF high resolution mass spectrometer with DART source. HPLC data were recorded on LC-6AD Shimadzu liquid chromatograph with UV/Vis detector.

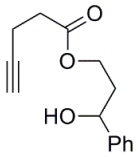
General procedure for chemoselective acylation of 1, 3-diols:

A cooled solution of DCC (1.1 mmol) and DMAP (0.1 mmol) in anhydrous CH_2Cl_2 (5 mL) at 0 ^oC was treated with 4-pentynoic acid **8** (1 mmol). The resulting mixture was stirred at same temp for 30 min before a solution of 1, 3-diol (1 mmol) in anhydrous CH_2Cl_2 (10 mL) was introduced and the mixture was stirred further at 0 ^oC for 4 h. The reaction mixture was filtered through a pad of Celite and washed with CH_2Cl_2. The filtrate was evaporated to give the crude product which on silica gel column chromatography (Hex: EtOAc) afforded the esteralkyne.

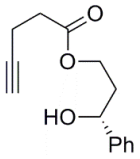
3-hydroxybutyl pent-4-ynoate (9): Isolated as colorless oil (0.60 g, 70%). R_f 0.28 (3:1 Hex: EtOAc); IR (neat): 3435, 3294, 2967, 2928, 1728, 1244, 1168, 1137 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 4.36 (ddd, *J* = 11.2, 8.2, 5.3 Hz, 1H), 4.16 (ddd, *J* = 11.3, 5.6, 5.6 Hz, 1H), 3.94-3.84 (m, 1H), 2.58-2.47 (m, 4H), 1.97 (t, *J* = 2.4 Hz, 1H), 1.85-1.64 (m, 2H), 1.22 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 172.2, 82.5, 69.2, 64.9, 62.1, 38.1, 33.5, 23.6, 14.5; TOF HRMS (DART): *m/z* for $C_9H_{15}O_3$ $[M+H]^+$ calcd. 171.1021, found 171.1010.



3-hydroxy-3-phenylpropyl pent-4-ynoate (10): Isolated as colorless oil (2.54 g, 62%). R_f 0.32 (3:1 Hex: EtOAc); IR (neat): 3463, 3290, 2959, 2922, 1728, 1243, 1165, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.34 (m, 4H), 7.31-7.27 (m, 1H), 4.80 (t, *J* = 6.3 Hz, 1H), 4.36 (ddd, *J* = 11.2, 7.6, 5.7 Hz, 1H), 4.16 (dt, *J* = 11.3, 5.7 Hz, 1H), 2.57-2.48 (m, 4H), 2.24 (bs, 1H), 2.10-2.01 (m, 2H), 1.98 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 172.0, 144.0, 128.7, 127.9, 125.8, 82.6, 71.3, 69.2, 61.9, 38.1, 33.4, 14.5; TOF HRMS (DART): *m/z* for $C_{14}H_{20}NO_3$ $[M+NH_4]^+$ calcd. 250.1443, found 250.1440.



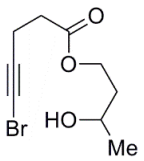
(*R*)-3-hydroxy-3-phenylpropyl pent-4-ynoate (11): Isolated as colorless oil (2.63 g, 65%). R_f 0.32 (3:1 Hex: EtOAc); $[\alpha]_D^{20}$: +8.30 (*c* 1.1, $CHCl_3$); IR (neat): 3471, 3291, 2959, 2923, 1728, 1243, 1165, 1022 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.32 (m, 4H), 7.30-7.25 (m, 1H), 4.78 (ddd, *J* = 8.3, 5.1, 3.6 Hz, 1H), 4.33 (ddd, *J* = 11.2, 7.6, 5.6 Hz, 1H), 4.15 (dt, *J* = 11.3, 5.8 Hz, 1H), 2.55-2.45 (m, 4H), 2.41 (d, *J* = 3.4 Hz, 1H), 2.12-2.01 (m, 2H), 1.98 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 172.0, 144.0, 128.6, 127.8, 125.8, 82.5, 71.3, 69.2, 61.9, 38.0, 33.4, 14.4; TOF HRMS (DART): *m/z* for $C_{14}H_{20}NO_3$ $[M+NH_4]^+$ calcd. 250.1443, found 250.1436.



General procedure for bromination of alkynes:

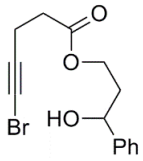
A solution of alkyne (1 mmol) in dry acetone (3.5 mL) was treated with *N*-bromosuccinimide (1.1 mmol) and $AgNO_3$ (0.1 mmol) at room temperature. The reaction mixture was stirred for 4 h in dark. It was then quenched with saturated aqueous $NaHCO_3$ (5 mL) and concentrated in *vacuo*. The residue was extracted with ethyl acetate (3 x 10 mL). The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Silica gel column chromatography (Hex: EtOAc) of the crude residue provided the bromoalkyne.

3-hydroxybutyl 5-bromopent-4-ynoate (12): Isolated as colorless liquid (0.61 g, 82%). R_f 0.28 (3:1 Hex: EtOAc); ^1H NMR (300 MHz, $CDCl_3$): δ ppm 4.36 (ddd, *J* = 11.2, 8.3, 5.3 Hz, 1H), 4.16 (ddd, *J* = 11.3, 5.6, 5.6 Hz, 1H), 3.93-3.82 (m, 1H), 2.55-2.49 (m, 4H), 2.03 (bs, 1H), 1.84-1.64 (m, 2H), 1.22 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 172.1, 78.3, 64.8, 62.1, 39.3, 38.1, 33.2, 23.6, 15.7;

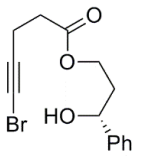


TOF HRMS (DART): *m/z* for $C_9H_{14}BrO_3$ $[M+H]^+$ calcd. 249.0126, found 249.0125.

3-hydroxy-3-phenylpropyl 5-bromopent-4-ynoate (13): Isolated as colorless thick liquid (2.60 g, 76%). R_f 0.32 (3:1 Hex: EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.35 (m, 4H), 7.32-7.27 (m, 1H), 4.81-4.77 (m, 1H), 4.35 (ddd, *J* = 11.2, 7.7, 5.6 Hz, 1H), 4.16 (dt, *J* = 11.2, 5.6 Hz, 1H), 2.52 (s, 4H), 2.26 (d, *J* = 2.5 Hz, 1H), 2.13-1.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 171.9, 143.9, 128.7, 127.9, 125.8, 71.3, 61.9, 38.0, 33.2, 15.7; TOF HRMS (DART): *m/z* for $C_{14}H_{19}BrNO_3$ $[M+NH_4]^+$ calcd. 328.0548, found 328.0517.



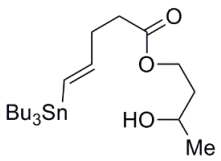
(*R*)-3-hydroxy-3-phenylpropyl 5-bromopent-4-ynoate (14): Isolated as colorless thick liquid (2.30 g, 74%). R_f 0.32 (3:1 Hex: EtOAc); $[\alpha]_D^{20}$: +4.29 (*c* 0.6, $CHCl_3$); IR (neat): 3448, 2958, 2921, 1726, 1166, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.33 (m, 4H), 7.31-7.27 (m, 1H), 4.80 (ddd, *J* = 8.4, 5.1, 3.6 Hz, 1H), 4.35 (ddd, *J* = 11.2, 7.7, 5.5 Hz, 1H), 4.16 (dt, *J* = 11.4, 5.8 Hz, 1H), 2.52 (s, 4H), 2.20 (d, *J* = 2.5 Hz, 1H), 2.14-2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 171.9, 144.0, 128.7, 127.9, 125.8, 71.4, 62.0, 38.0, 33.2, 15.7; TOF HRMS (DART): *m/z* for $C_{14}H_{19}BrNO_3$ $[M+NH_4]^+$ calcd. 328.0548, found 328.0539.



General procedure for the synthesis of vinylstannanes:

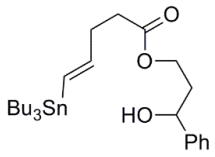
To a solution bromoalkyne (1.0 mmol) in anhydrous THF (10 mL) were added $Pd_2(dba)_3$ (0.05 mmol) and PPh_3 (0.23 mmol) at room temperature. The resulting solution was stirred for 15 min before *n*Bu_3SnH (2.2 mmol) was added drop wise over a period of 30 min and the mixture was stirred further for 12 h. The reaction mixture was concentrated in *vacuo* and purified by silica gel column chromatography (Hex: EtOAc) to afford vinylstannane.

(*E*)-3-hydroxybutyl 5-(tributylstannyl)pent-4-enoate (15): Isolated as colorless oil (0.59 g, 54%). R_f 0.35 (3:1 Hex: EtOAc); IR (neat): 3507, 2955, 2923, 2871, 2851, 1736, 1461, 1375, 1179, 1137, 988 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 5.94 (s, 2H, $J(^1_{H\text{-}}{}^{119}_{Sn})$ = 69.8 Hz, $J(^1_{H\text{-}}{}^{117}_{Sn})$ = 67.8 Hz), 4.35 (ddd, *J* = 11.2, 8.2, 5.3 Hz, 1H), 4.11 (ddd, *J* = 11.2, 5.6, 3.6 Hz, 1H), 3.92-3.80 (m, 1H), 2.43 (s, 4H), 1.96 (bs, 1H), 1.83-1.68 (m, 2H), 1.52-1.42 (m, 6H), 1.39-1.25 (m, 6H),



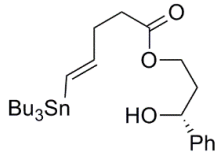
1.22 (d, J = 6.2 Hz, 1H), 0.94-.82 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.7, 146.7, 129.0, 65.0, 61.7, 38.2, 33.7, 32.7, 29.2, 27.4, 23.6, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{21}H_{43}O_3Sn$ $[M+H]^+$ calcd. 463.2238, found 463.2259.

(*E*)-3-hydroxy-3-phenylpropyl 5-(tributylstannyl)pent-4-enoate (16): Isolated as yellow oil



(2.40 g, 57%). R_f 0.42 (3:1 Hex: EtOAc); IR (neat): 3508, 2954, 2922, 2870, 2852, 1735, 1177 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.35 (m, 4H), 7.30-7.28 (m, 1H), 5.95 (s, 2H, $J(^1H\text{-}^{119}Sn)$ = 69.9 Hz, $J(^1H\text{-}^{117}Sn)$ = 67.9 Hz), 4.79 (ddd, J = 8.3, 5.0, 3.5 Hz, 1H), 4.33 (ddd, J = 11.2, 7.5, 5.7 Hz, 1H), 4.13 (dt, J = 11.4, 5.6 Hz, 1H), 2.47-2.39 (m, 4H), 2.22 (d, J = 3.5 Hz, 1H), 2.11-2.00 (m, 2H), 1.54-1.41 (m, 6H), 1.38-1.24 (m, 6H), 0.94-0.83 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.5, 146.7, 144.0, 129.0, 128.7, 127.9, 125.8, 71.5, 61.6, 38.2, 33.7, 32.7, 29.2, 27.4, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{26}H_{45}O_3Sn$ $[M+H]^+$ calcd. 525.2396, found 525.2384.

(*R*,*E*)-3-hydroxy-3-phenylpropyl 5-(tributylstannyl)pent-4-enoate (17): Isolated as yellow oil



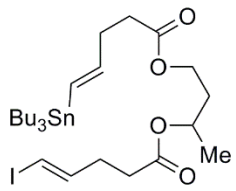
(2.30 g, 60%). R_f 0.42 (3:1 Hex: EtOAc); $[\alpha]_D^{20}$: +10.6 (*c* 0.7, $CHCl_3$); IR (neat): 3507, 2955, 2922, 2870, 2850, 1736, 1454, 1177 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.35 (m, 4H), 7.31-7.26 (m, 1H), 5.96 (s, 2H, $J(^1H\text{-}^{119}Sn)$ = 70.0 Hz, $J(^1H\text{-}^{117}Sn)$ = 67.9 Hz), 4.79 (ddd, J = 8.3, 5.0, 3.6 Hz, 1H), 4.33 (ddd, J = 11.2, 7.5, 5.7 Hz, 1H), 4.13 (dt, J = 11.5, 5.8 Hz, 1H), 2.47-2.40 (m, 4H), 2.22 (d, J = 3.5 Hz, 1H), 2.12-1.99 (m, 2H), 1.54-1.39 (m, 6H), 1.34-1.24 (m, 6H), 0.92-0.84 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.5, 146.7, 144.0, 129.0, 128.7, 127.8, 125.8, 71.5, 61.6, 38.2, 33.7, 32.7, 29.2, 27.4, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{26}H_{45}O_3Sn$ $[M+H]^+$ calcd. 525.2396, found 525.2401.

General procedure for the synthesis of iodostannanes:

To a cooled solution of DCC (1.1 mmol) and DMAP (0.1 mmol) in anhydrous CH_2Cl_2 (10 mL) at 0 ^{o}C was added 4*E*-5-iodo-pentenoic acid **18** (1 mmol). The resulting solution was stirred at same temp for 30 min before a solution of vinylstannane (1 mmol) in anhydrous CH_2Cl_2 (6 mL) was introduced. The mixture was allowed to raise to room temperature slowly and stirred overnight. The reaction mixture was then filtered through a pad of Celite, washed with CH_2Cl_2

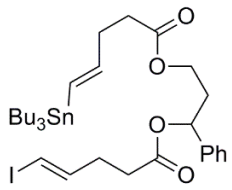
and the filtrate was evaporated to give the crude product which on silica gel column chromatography (Hex: EtOAc) provided iodostannane.

(*E*)-3-((*E*)-5-iodopent-4-enoyloxy)butyl 5-(tributylstannyl)pent-4-enoate (19): Isolated as



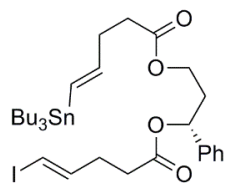
colorless oil (0.40 g, 73%). R_f 0.35 (9:1 Hex: EtOAc); IR (neat): 2955, 2922, 2870, 2852, 1732, 1340, 1177, 1142 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ ppm 6.55-6.46 (m, 1H), 6.09 (d, J = 14.2 Hz, 1H), 5.90 (s, 2H, $J(^1_{H\text{-}Sn})$ = 70.5 Hz), 5.06-4.96 (m, 1H), 4.13-4.08 (m, 2H), 2.42 (s, 4H), 2.37-2.35 (m, 4H), 1.96-1.78 (m, 2H), 1.52-1.42 (m, 6H), 1.35-1.24 (m, 6H), 0.96-0.74 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 173.2, 171.8, 146.7, 144.2, 128.9, 76.3, 68.2, 60.0, 34.9, 33.6, 33.2, 32.7, 31.3, 29.2, 27.3, 20.2, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{26}H_{48}IO_4Sn$ $[M+H]^+$ calcd. 671.1640, found 671.1622.

(*E*)-3-((*E*)-5-iodopent-4-enoyloxy)-3-phenylpropyl 5-(tributylstannyl)pent-4-enoate (20):



Isolated as colorless oil (1.7 g, 71%). R_f 0.40 (9:1 Hex: EtOAc); IR (neat): 2954, 2922, 2849, 1735, 1374, 1243, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.37-7.27 (m, 5H), 6.48 (dt, J = 14.2, 6.9 Hz, 1H), 6.06 (d, J = 14.4 Hz, 1H), 5.95 (s, 2H), 5.85 (dd, J = 7.4, 6.1 Hz, 1H), 4.17-4.11 (m, 1H), 4.04-3.98 (m, 1H), 2.47-2.38 (m, 5H), 2.37-2.34 (m, 3H), 2.29-2.20 (m, 1H), 2.14-2.06 (m, 1H), 1.56-1.39 (m, 6H), 1.34-1.25 (m, 6H), 0.92-0.84 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.2, 171.5, 146.7, 144.0, 139.8, 128.9, 128.8, 128.4, 126.5, 73.3, 60.5, 35.4, 33.6, 33.1, 32.7, 31.2, 29.2, 27.3, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{31}H_{50}IO_4Sn$ $[M+H]^+$ calcd. 733.1782, found 733.1773.

(*E*)-((*R*)-3-((*E*)-5-iodopent-4-enoyloxy)-3-phenylpropyl) 5-(tributylstannyl)pent-4-enoate



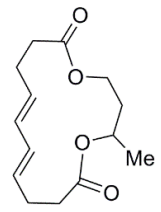
(21): Isolated as colorless oil (1.3 g, 82%). R_f 0.40 (9:1 Hex: EtOAc); $[\alpha]_D^{20}$: +11.8 (*c* 1.6, $CHCl_3$); IR (neat): 2954, 2922, 2870, 2849, 1735, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.37-7.27 (m, 5H), 6.48 (dt, J = 14.1, 6.8 Hz, 1H), 6.06 (d, J = 14.4 Hz, 1H), 5.94 (s, 2H), 5.85 (dd, J = 7.9, 5.7 Hz, 1H), 4.17-4.11 (m, 1H), 4.04-3.98 (m, 1H), 2.47-2.39 (m, 5H), 2.37-2.32 (m, 3H), 2.29-2.20 (m, 1H), 2.14-2.08 (m, 1H), 1.51-1.43 (m, 6H), 1.34-1.25 (m, 6H), 0.92-0.83 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.2, 171.5, 146.7, 144.0, 139.8, 128.9, 128.8, 128.4, 126.5,

73.3, 60.5, 35.4, 33.6, 33.1, 32.7, 31.2, 29.3, 27.3, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{31}H_{50}IO_4Sn$ $[M+H]^+$ calcd. 733.1782, found 733.1780.

General procedure for intramolecular Stille coupling:

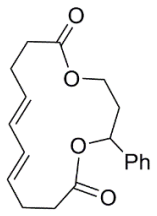
To a degassed solution of iodostannane (1.0 mmol) in anhydrous DMF (1.5 L, c ≈ 7 x 10^{-4}) were added $Pd_2(dba)_3.CHCl_3$ (0.32 mmol), Ph_3As (1.3 mmol) and DIPEA (20.8 mmol) successively at room temperature and the resulting mixture was stirred at same temperature for 24 h. The reaction mixture was diluted with CH_2Cl_2 (200 mL), washed with water (3 x 500 mL). The aqueous parts were separated and extracted with CH_2Cl_2 (4 x 200 mL). The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. Silica gel column chromatography (Hex: EtOAc) of the crude residue resulted macrodilactone.

(9*E*,11*E*)-2-methyl-1,5-dioxacyclopentadeca-9,11-diene-6,15-dione (3): Isolated as colorless



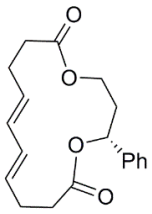
sticky liquid (47 mg, 65%). R_f 0.35 (3:1 Hex: EtOAc); IR (neat): 2977, 2933, 1725, 1264, 1176 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 5.97 (dd, *J* = 14.2, 10.5 Hz, 1H), 5.91 (dd, *J* = 14.3, 10.5 Hz, 1H), 5.57-5.44 (m, 2H), 4.77 (sex, *J* = 6.3 Hz, 1H), 4.00 (dt, *J* = 11.4, 6.7 Hz, 1H), 3.92 (dt, *J* = 11.2, 5.7 Hz, 1H), 2.42-2.27 (m, 6H), 2.26-2.19 (m, 2H), 1.79 (q, *J* = 6.1 Hz, 2H), 1.26 (d, *J* = 6.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.9, 173.1, 133.0, 132.2, 130.1, 129.4, 68.3, 60.4, 35.5, 35.4, 35.1, 29.8, 29.4, 19.7; TOF HRMS (DART): *m/z* for $C_{14}H_{21}O_4$ $[M+H]^+$ calcd. 253.1440, found 253.1456.

(9*E*,11*E*)-2-phenyl-1,5-dioxacyclopentadeca-9,11-diene-6,15-dione (4): Isolated as white solid



(50 mg, 59%). R_f 0.40 (3:1 Hex: EtOAc); mp 110 ^oC; IR (neat): 2927, 1735, 1721, 1435, 1365, 1348, 1172, 1131, 985 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.31 (m, 4H), 7.29-7.27 (m, 1H), 6.06-5.94 (m, 2H), 5.64-5.52 (m, 3H), 4.10 (ddd, *J* = 11.3, 7.7, 4.9 Hz, 1H), 3.76-3.70 (m, 1H), 2.48-2.23 (m, 8H), 2.14-2.06 (m, 1H), 2.05-1.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.9, 172.6, 140.2, 133.1, 132.1, 130.4, 129.3, 128.7, 128.1, 126.4, 73.4, 60.2, 36.1, 35.3, 29.8, 29.6; TOF HRMS (DART): *m/z* for $C_{19}H_{23}O_4$ $[M+H]^+$ calcd. 315.1596, found 315.1570.

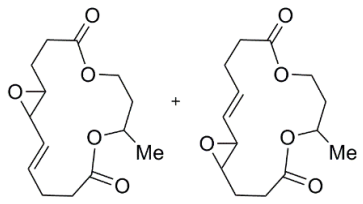
(*R*,9*E*,11*E*)-2-phenyl-1,5-dioxacyclopentadeca-9,11-diene-6,15-dione ((–)-4): Isolated as white solid (51 mg, 60%). R_f 0.40 (3:1 Hex: EtOAc); mp 111 ^oC; $[\alpha]_D^{20}$: –9.4 (*c* 0.8, $CHCl_3$); IR (neat): 2963, 2926, 2852, 1723, 1433, 1342, 1226, 1170, 1129, 956 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.31 (m, 4H), 7.29-7.27 (m, 1H), 6.06-5.94 (m, 2H), 5.64-5.25 (m, 3H), 4.10 (ddd, *J* = 11.3, 7.7, 4.9 Hz, 1H), 3.76-3.70 (m, 1H), 2.48-2.25 (m, 8H), 2.14-2.06 (m, 1H), 2.05-1.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.9, 172.6, 140.2, 133.1, 132.1, 130.4, 129.3, 128.7, 128.1, 126.4, 73.4, 60.2, 36.1, 35.3, 29.8, 29.6; TOF HRMS (DART): *m/z* for $C_{19}H_{23}O_4$ $[M+H]^+$ calcd. 315.1596, found 315.1609.

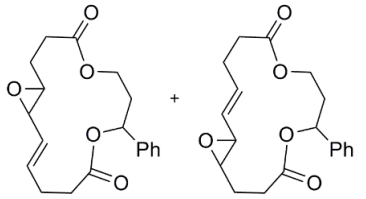


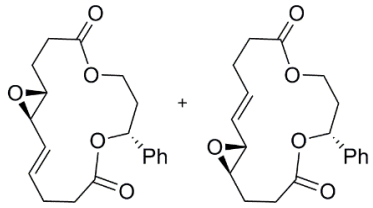
General procedure for DMDO-mediated epoxidation:

To a solution of macrodilactone (1 mmol) in acetone-H_2O-CH_2Cl_2 (1:1:1, 60 mL) was added excess amount of $NaHCO_3$ (13.3 mmol) and Oxone (2.8 mmol) at 0 ^oC. The resultant mixture was slowly raised to room temperature and stirred until complete consumption of starting material. The reaction mixture was diluted with water (50 mL), and extracted with CH_2Cl_2 (3 x 40 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The flash column chromatography (Hexane: EtOAc) of the crude residue provided macrocyclic monoepoxide as an inseparable mixture of regioisomers.

Epoxides (22a and 22b) as a mixture of regioisomers: Isolated as white solid (24 mg, 67%). R_f 0.25 (3:1 Hex: EtOAc); IR (neat): 2974, 2934, 1722, 1311, 1220, 1179, 1167, 1131, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 5.86-5.75 (m, 2H), 5.11 (dd, *J* = 15.4, 9.1 Hz, 1H), 5.06 (dd, *J* = 15.4, 9.1 Hz, 1H), 5.01-4.95 (m, 1H), 4.93-4.85 (m, 1H), 4.11-4.02 (m, 1H), 3.99 (d, *J* = 3.8 Hz, 1H), 3.95 (d, *J* = 3.4 Hz, 1H), 3.13 (dd, *J* = 9.1, 1.5 Hz, 1H), 3.01 (dd, *J* = 9.1, 1.5 Hz, 1H), 2.71 (dt, *J* = 10.1, 2.2 Hz, 1H), 2.61 (dt, *J* = 10.0, 2.2 Hz, 1H), 2.52-2.17 (m, 12H), 1.93-1.75 (m, 4H), 1.65-1.47 (m, 2H), 1.27 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.5, 173.3, 172.4, 133.6, 133.1, 131.2, 130.5, 67.5, 67.2, 60.8, 60.1, 60.0, 59.1, 58.8, 58.5, 34.6, 34.4, 34.3, 34.2, 30.6, 30.4, 29.4, 28.6, 28.3, 27.3, 20.3; TOF HRMS (DART): *m/z* for $C_{14}H_{21}O_5$ $[M+H]^+$ calcd. 269.1389, found 269.1381.



Epoxides ((±)-23a and (±)-23b) as a mixture of regioisomers: Isolated as white solid (107 g, 62%).  R_f 0.30 (3:1 Hex: EtOAc); IR (neat): 2968, 2929, 1725, 1433, 1344, 1220, 1173, 1130, 955 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.35-7.27 (m, 10H), 5.94-5.83 (m, 2H), 5.79 (dd, *J* = 10.5, 3.8 Hz, 1H), 5.72 (dd, *J* = 10.5, 3.2 Hz, 1H), 5.14 (td, *J* = 15.0, 9.1 Hz, 1H), 4.22-4.08 (m, 3H), 4.02-3.97 (m, 1H), 3.16 (dd, *J* = 9.1, 1.9 Hz, 1H), 3.06 (dd, *J* = 9.1, 1.9 Hz, 1H), 2.78 (dt, *J* = 10.0, 2.8 Hz, 1H), 2.67 (dt, *J* = 10.0, 2.3 Hz, 1H), 2.54-2.28 (m, 14H), 2.23-2.02 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.5, 173.4, 172.0, 171.9, 140.6, 140.5, 133.8, 133.0, 131.4, 130.6, 128.8, 128.7, 128.3, 128.1, 126.3, 126.1, 72.5, 72.1, 60.9, 60.1, 59.0, 58.9, 58.5, 35.4, 35.3, 34.4, 34.0, 30.6, 30.3, 29.4, 28.7, 28.3, 27.3; TOF HRMS (DART): *m/z* for $C_{19}H_{23}O_5$ $[M+H]^+$ calcd. 331.1546, found 331.1546.

Epoxides (23a and 23b) as a mixture of regioisomers: Isolated as white solid (112 mg, 64%).  R_f 0.30 (3:1 Hex: EtOAc); IR (neat): 2967, 2929, 1726, 1494, 1434, 1221, 1174, 1159, 1130, 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.26 (m, 10H), 5.94-5.85 (m, 2H), 5.79 (dd, *J* = 10.5, 3.8 Hz, 1H), 5.72 (dd, *J* = 10.5, 3.2 Hz, 1H), 5.14 (td, *J* = 15.0, 9.1 Hz, 1H), 4.22-4.08 (m, 3H), 4.02-3.97 (m, 1H), 3.16 (dd, *J* = 9.1, 1.9 Hz, 1H), 3.06 (dd, *J* = 9.1, 1.9 Hz, 1H), 2.78 (dt, *J* = 10.0, 2.8 Hz, 1H), 2.67 (dt, *J* = 10.0, 2.3 Hz, 1H), 2.54-2.28 (m, 14H), 2.23-2.02 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.5, 173.4, 172.0, 171.9, 140.6, 140.5, 133.8, 133.0, 131.4, 130.6, 128.8, 128.7, 128.3, 128.1, 126.3, 126.1, 72.5, 72.1, 60.9, 60.1, 59.0, 58.9, 58.5, 35.4, 35.3, 34.4, 34.0, 30.6, 30.3, 29.4, 28.7, 28.3, 27.3; TOF HRMS (DART): *m/z* for $C_{19}H_{23}O_5$ $[M+H]^+$ calcd. 331.1546, found 331.1546.

General procedure for transesterification:

The regioisomeric mixture of macrocyclic vinylepoxides (1.0 mmol) was dissolved in a solution of NaOMe in MeOH (36 mL, 0.5 mg/mL) and the mixture was stirred for 72h at room temperature. The reaction mixture was concentrated under reduced pressure, the residue was diluted with EtOAc and then with water. The water part was separated and extracted with EtOAc (3 x 20 mL). The combined organic parts were dried over anhydrous Na_2SO_4, filtered, and

concentrated in *vacuo*. The flash column chromatography (Hexane: EtOAc) of the crude residue afforded diester.

(*E*)-methyl 5-(3-(3-methoxy-3-oxopropyl)oxiran-2-yl)pent-4-enoate (24): Isolated as colorless sticky liquid (26 mg, 73%). R_f 0.30 (4:1 Hex: EtOAc); IR (neat): 2953, 1730, 1436, 1348, 1196, 1167, 966 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 5.93-5.86 (m, 1H), 5.22 (dd, *J* = 15.4, 7.7 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H), 3.09 (dd, *J* = 7.9, 2.0 Hz, 1H), 2.87 (ddd, *J* = 6.5, 4.6, 2.0 Hz, 1H), 2.45 (t, *J* = 7.9 Hz, 2H), 2.41-2.37 (m, 4H), 2.04-1.96 (m, 1H), 1.81-1.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.3, 134.4, 128.5, 59.2, 58.5, 51.8, 51.7, 33.4, 30.2, 27.6, 27.3; TOF HRMS (DART): *m/z* for $C_{12}H_{19}O_5$ $[M+H]^+$ calcd. 243.1232, found 243.1213.

(*E*)-methyl 5-((2*R*,3*R*)-3-(3-methoxy-3-oxopropyl)oxiran-2-yl)pent-4-enoate ((+)-24) *via* transesterification of macrodilactone: Isolated as colorless sticky liquid (19 mg, 76%). R_f 0.30 (4:1 Hex: EtOAc); $[\alpha]_D^{20}$: +24.0 (*c* 0.6, $CHCl_3$); IR (neat): 2953, 1730, 1436, 1359, 1196, 1166, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 5.93-5.86 (m, 1H), 5.22 (dd, *J* = 15.2, 7.9 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H), 3.09 (dd, *J* = 7.8, 1.8 Hz, 1H), 2.87 (ddd, *J* = 6.5, 4.6, 2.0 Hz, 1H), 2.45 (t, *J* = 7.9 Hz, 2H), 2.41-2.37 (m, 4H), 2.04-1.96 (m, 1H), 1.81-1.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.3, 134.4, 128.5, 59.2, 58.5, 51.8, 51.7, 33.4, 30.2, 27.6, 27.3; TOF HRMS (DART): *m/z* for $C_{12}H_{19}O_5$ $[M+H]^+$ calcd. 243.1232, found 243.1230.

Ethyl 5-bromopent-4-ynoate (26): To a solution of ethyl 4-pentynoate **25** (150 mg, 1.19 mmol) in dry acetone (5 mL) was added with *N*-bromosuccinimide (2.1 g, 1.30 mmol) and $AgNO_3$ (20 mg, 0.12 mmol) at room temperature. The reaction mixture was stirred for 1 h in dark. It was then quenched with saturated aqueous $NaHCO_3$ (5 mL) and concentrated in *vacuo*. The residue was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Silica gel column chromatography (19:1 Hex: EtOAc) of the crude residue provided the bromoalkyne **26** (165 mg, 68%) as a colorless liquid. R_f 0.40 (9:1 Hex: EtOAc); ^1H NMR (400 MHz, $CDCl_3$): δ ppm 4.16 (q, *J* = 7.1 Hz, 2H), 2.52 (s, 4H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 171.7, 78.4, 60.8, 39.1, 33.2, 15.7, 14.3; TOF HRMS (DART): *m/z* for $C_7H_{10}BrO_2$ $[M+H]^+$ calcd. 204.9869, found 204.9878.

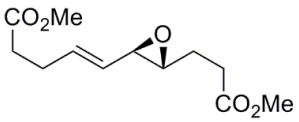
(*E*)-Ethyl 5-(tributylstannyl)pent-4-enoate (27): To a solution bromoalkyne **26** (120 mg, 0.58 mmol) in anhydrous THF (3.2 mL) were added $Pd_2(dba)_3$ (27 mg, 0.03 mmol) and PPh_3 (35 mg, 0.13 mmol) at room temperature. The resulting solution was stirred for 15 min before nBu$_3$SnH (0.34 mL, 1.27 mmol) was added over a period of 30 min and the mixture was stirred further for 1h. The reaction mixture was concentrated in *vacuo* and purified by silica gel column chromatography (30:1 Hex: EtOAc) to afford vinylstannane **27** (182 mg, 75%) as colorless oil. R_f 0.65 (9:1 Hex: EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 5.95 (s, 2H, $J(^1_{H}\text{-}^{119}_{Sn})$ = 71.0 Hz, $J(^1_{H}\text{-}^{117}_{Sn})$ = 68.5 Hz), 4.12 (q, J = 7.1 Hz, 2H), 2.46-2.35 (m, 4H), 1.51-1.43 (m, 6H), 1.33-1.23 (m, 6H), 0.94-0.83 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.4, 146.9, 128.8, 60.3, 33.8, 32.8, 29.3, 29.2, 27.4, 14.4, 13.8, 9.5; TOF HRMS (DART): *m/z* for $C_{19}H_{38}O_2Sn$ $[M+H]^+$ calcd. 419.2018, found 419.2023.

(4*E*,6*E*)-1-ethyl 10-methyl deca-4,6-dienedioate (29): A solution of vinyl stannane **27** (51 mg, 0.12 mmol) and vinyl iodide **28** (18 mg, 0.072 mmol) in degassed NMP (3 mL) was treated with $Pd_2(dba)_3$ (14 mg, 0.015 mmol), Ph_3As (185 mg, 0.60 mmol) and LiCl (26 mg, 0.60 mmol) at room temperature. The reaction mixture was stirred for 12h and was quenched with water. The resulting mixture was extracted with EtOAc (3 x 10 mL), combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtred and concentrated. Silical gel column chromatography (15:1 Hex: EtOAc) of the crude residue afforded mixed ester **29** (18 mg, 62%) as a yellow oil. R_f 0.35 (9:1 Hex: EtOAc); IR (neat): 2981, 2953, 1727, 1372, 1160, 1022 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 6.07-5.97 (m, 2H), 5.62-5.54 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.67 (s, 3H), 2.38 (t, J = 2.9 Hz, 8H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.6, 173.1, 131.2, 131.1, 130.8, 130.6, 60.5, 51.7, 34.1, 33.9, 28.0, 27.9, 14.4; TOF HRMS (DART): *m/z* for $C_{13}H_{21}O_4$ $[M+H]^+$ calcd. 241.1440, found 241.1453.

(4*E*,6*E*)-dimethyl deca-4,6-dienedioate (30): Mixed ester **29** (45 mg, 0.18 mmol) was dissolved in a solution of NaOMe in MeOH (12 mL, 0.5 mg/mL) and the mixture was stirred for 6h at room temperature. The reaction mixture was concentrated under reduced pressure and the residue was diluted with EtOAc and then with water. The water part was separated and extracted with EtOAc (3 x 20 mL). The combined organic parts were dried over anhydrous Na_2SO_4, filtered,

and concentrated in *vacuo*. The flash column chromatography (15:1 Hex: EtOAc) of the crude residue afforded diene ester **30** (34 mg, 84%) as a colorless liquid. R_f 0.38 (9:1 Hex: EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 6.06-5.98 (m, 2H), 5.59-5.55 (m, 2H), 3.67 (s, 6H), 2.39 (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.5, 131.2, 130.7, 51.7, 33.9, 27.9; TOF HRMS (DART): *m/z* for $C_{12}H_{19}O_4$ $[M+H]^+$ calcd. 227.1283, found 227.1264.

(*E*)-methyl 5-((2*R*,3*R*)-3-(3-methoxy-3-oxopropyl)oxiran-2-yl)pent-4-enoate ((+)-24) *via* Shi epoxidation: To a solution of diene ester **30** (30 mg, 0.13 mmol) in dimethoxymethane/acetonitrile (2:1, 2.7 mL), were added buffer (0.05 M $Na_2B_2O_4.10H_2O$ in 4 x 10^{-4} M EDTA, 1.3 mL), tetrabutylammonium hydrogen sulfate (2 mg, 0.006 mmol) and catalyst **31** (10.3 mg, 0.04 mmol), and the reaction mixture was cooled to 0 ^oC. A solution of Oxone (46 mg, 0.15 mmol) in aqueous EDTA (4 x 10^{-4} M, 1.3 mL) and a solution of K_2CO_3 (91 mg, 0.65 mmol) in water (1.3 mL) were added separately via syringe pump over a period of 1.5h. After complete addition the reaction was quenched with hexane (1 mL). The aqueous layer was separated and was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (6:1 Hex: EtOAc) of the crude residue afforded epoxyester **24** (20 mg, 65%) as a colorless sticky liquid. R_f 0.30 (4:1 Hex: EtOAc); $[\alpha]_D^{20}$: +25.5 (*c* 0.6, $CHCl_3$); IR (neat): 2953, 1730, 1437, 1365, 1253, 1197, 1165, 970 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 5.94-5.87 (m, 1H), 5.22 (dd, *J* = 15.4, 7.8 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H), 3.09 (dd, *J* = 8.0, 2.0 Hz, 1H), 2.88 (ddd, *J* = 6.6, 4.6, 2.1 Hz, 1H), 2.45 (t, *J* = 8.0 Hz, 2H), 2.42-2.37 (m, 4H), 2.05-1.96 (m, 1H), 1.82-1.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 173.3, 134.4, 128.5, 59.2, 58.5, 51.8, 51.7, 33.4, 30.2, 27.6, 27.3; TOF HRMS (DART): *m/z* for $C_{12}H_{19}O_5$ $[M+H]^+$ calcd. 243.1232, found 243.1240.



2. X-ray crystallographic structure of [15]-macrodilactone ((–)-4):

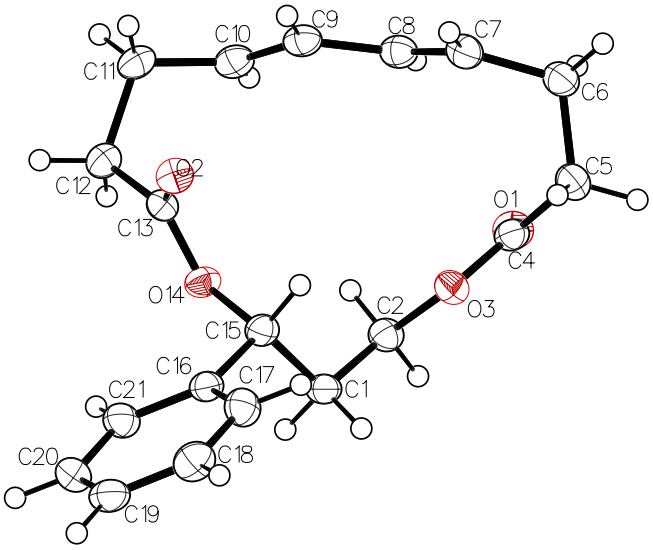


Figure S1. The full numbering scheme of (–)-**4**. All atoms shown are depicted with 50% thermal contours. The hydrogen atoms are shown as sphears. Atom C1 has a chirality of *R*.

Table S1. Crystal data and structure refinement for (–)-**4** (CCDC 1055302).

Identification code	007-14195	
Empirical formula	$C_{19}H_{22}O_4$	
Formula weight	314.36	
Temperature	93(2) K	
Wavelength	1.54187 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 8.8516(3) Å	α = 90°
	b = 9.0800(4) Å	β = 108.971(8)°
	c = 11.1409(8) Å	γ = 90°
Volume	846.79(9) $Å^3$	
Z	2	
Density (calculated)	1.233 Mg/m^3	
Absorption coefficient	0.694 mm^{-1}	
F(000)	336	

Crystal size	0.300 x 0.200 x 0.080 mm^3
Theta range for data collection	4.196 to 68.089°.
Index ranges	$-10 \leq h \leq 10$, $-10 \leq k \leq 10$, $-13 \leq l \leq 13$
Reflections collected	27457
Independent reflections	3044 [R(int) = 0.0484]
Completeness to theta = 67.687°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.947 and 0.836
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3044 / 1 / 208
Goodness-of-fit on F^2	1.066
Final R indices [I>2sigma(I)]	R1 = 0.0251, wR2 = 0.0597
R indices (all data)	R1 = 0.0296, wR2 = 0.0623
Absolute structure parameter	0.12(8)
Largest diff. peak and hole	0.139 and -0.154 e.$Å^{-3}$

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (–)-**4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

__	x	y	z	U(eq)
O(1)	2806(2)	745(2)	8464(1)	32(1)
C(1)	5172(2)	4602(2)	8294(2)	27(1)
O(2)	1144(1)	7133(2)	6860(1)	28(1)
C(2)	4382(2)	3222(2)	8565(2)	27(1)
O(3)	3557(2)	2511(1)	7367(1)	26(1)
C(4)	2775(2)	1264(2)	7460(2)	26(1)
C(5)	1839(2)	641(2)	6188(2)	29(1)
C(6)	62(2)	554(2)	6083(2)	30(1)
C(7)	-557(2)	2063(2)	6200(2)	29(1)

C(8)	-544(2)	2676(2)	7286(2)	28(1)
C(9)	-881(2)	4217(2)	7434(2)	28(1)
C(10)	-518(2)	4935(2)	8529(2)	29(1)
C(11)	-656(2)	6561(2)	8648(2)	30(1)
C(12)	996(2)	7297(2)	8969(2)	28(1)
C(13)	1747(2)	6906(2)	7982(2)	24(1)
O(14)	3172(1)	6230(2)	8490(1)	26(1)
C(15)	3996(2)	5791(2)	7607(2)	25(1)
C(16)	4820(2)	7099(2)	7253(2)	25(1)
C(17)	5116(2)	7101(2)	6100(2)	32(1)
C(18)	5918(2)	8264(3)	5775(2)	35(1)
C(19)	6445(2)	9438(2)	6598(2)	34(1)
C(20)	6151(2)	9444(2)	7741(2)	33(1)
C(21)	5344(2)	8283(2)	8064(2)	30(1)

Table S3. Bond lengths [Å] and angles [°] for (–)-**4**.

O(1)-C(4)	1.206(2)	C(5)-H(5A)	0.9900
C(1)-C(2)	1.512(3)	C(5)-H(5B)	0.9900
C(1)-C(15)	1.522(3)	C(6)-C(7)	1.496(3)
C(1)-H(1A)	0.9900	C(6)-H(6A)	0.9900
C(1)-H(1B)	0.9900	C(6)-H(6B)	0.9900
O(2)-C(13)	1.206(2)	C(7)-C(8)	1.329(3)
C(2)-O(3)	1.448(2)	C(7)-H(7)	0.9500
C(2)-H(2A)	0.9900	C(8)-C(9)	1.452(3)
C(2)-H(2B)	0.9900	C(8)-H(8)	0.9500
O(3)-C(4)	1.349(2)	C(9)-C(10)	1.327(3)
C(4)-C(5)	1.501(3)	C(9)-H(9)	0.9500
C(5)-C(6)	1.541(2)	C(10)-C(11)	1.491(3)

C(10)-H(10)	0.9500	O(3)-C(2)-H(2B)	110.1
C(11)-C(12)	1.540(3)	C(1)-C(2)-H(2B)	110.1
C(11)-H(11A)	0.9900	H(2A)-C(2)-H(2B)	108.4
C(11)-H(11B)	0.9900	C(4)-O(3)-C(2)	114.91(14)
C(12)-C(13)	1.500(3)	O(1)-C(4)-O(3)	122.82(17)
C(12)-H(12A)	0.9900	O(1)-C(4)-C(5)	124.60(18)
C(12)-H(12B)	0.9900	O(3)-C(4)-C(5)	112.55(16)
C(13)-O(14)	1.350(2)	C(4)-C(5)-C(6)	109.12(15)
O(14)-C(15)	1.458(2)	C(4)-C(5)-H(5A)	109.9
C(15)-C(16)	1.512(3)	C(6)-C(5)-H(5A)	109.9
C(15)-H(15)	1.0000	C(4)-C(5)-H(5B)	109.9
C(16)-C(21)	1.384(3)	C(6)-C(5)-H(5B)	109.9
C(16)-C(17)	1.392(2)	H(5A)-C(5)-H(5B)	108.3
C(17)-C(18)	1.385(3)	C(7)-C(6)-C(5)	109.87(16)
C(17)-H(17)	0.9500	C(7)-C(6)-H(6A)	109.7
C(18)-C(19)	1.385(3)	C(5)-C(6)-H(6A)	109.7
C(18)-H(18)	0.9500	C(7)-C(6)-H(6B)	109.7
C(19)-C(20)	1.379(3)	C(5)-C(6)-H(6B)	109.7
C(19)-H(19)	0.9500	H(6A)-C(6)-H(6B)	108.2
C(20)-C(21)	1.386(3)	C(8)-C(7)-C(6)	124.62(18)
C(20)-H(20)	0.9500	C(8)-C(7)-H(7)	117.7
C(21)-H(21)	0.9500	C(6)-C(7)-H(7)	117.7
C(2)-C(1)-C(15)	113.74(15)	C(7)-C(8)-C(9)	124.50(19)
C(2)-C(1)-H(1A)	108.8	C(7)-C(8)-H(8)	117.7
C(15)-C(1)-H(1A)	108.8	C(9)-C(8)-H(8)	117.7
C(2)-C(1)-H(1B)	108.8	C(10)-C(9)-C(8)	125.49(19)
C(15)-C(1)-H(1B)	108.8	C(10)-C(9)-H(9)	117.3
H(1A)-C(1)-H(1B)	107.7	C(8)-C(9)-H(9)	117.3
O(3)-C(2)-C(1)	108.23(15)	C(9)-C(10)-C(11)	124.42(19)
O(3)-C(2)-H(2A)	110.1	C(9)-C(10)-H(10)	117.8
C(1)-C(2)-H(2A)	110.1	C(11)-C(10)-H(10)	117.8

C(10)-C(11)-C(12)	110.59(16)	C(16)-C(15)-H(15)	109.5
C(10)-C(11)-H(11A)	109.5	C(1)-C(15)-H(15)	109.5
C(12)-C(11)-H(11A)	109.5	C(21)-C(16)-C(17)	118.58(18)
C(10)-C(11)-H(11B)	109.5	C(21)-C(16)-C(15)	121.80(16)
C(12)-C(11)-H(11B)	109.5	C(17)-C(16)-C(15)	119.58(17)
H(11A)-C(11)-H(11B)	108.1	C(18)-C(17)-C(16)	120.56(19)
C(13)-C(12)-C(11)	109.92(15)	C(18)-C(17)-H(17)	119.7
C(13)-C(12)-H(12A)	109.7	C(16)-C(17)-H(17)	119.7
C(11)-C(12)-H(12A)	109.7	C(19)-C(18)-C(17)	120.33(19)
C(13)-C(12)-H(12B)	109.7	C(19)-C(18)-H(18)	119.8
C(11)-C(12)-H(12B)	109.7	C(17)-C(18)-H(18)	119.8
H(12A)-C(12)-H(12B)	108.2	C(20)-C(19)-C(18)	119.37(19)
O(2)-C(13)-O(14)	123.39(16)	C(20)-C(19)-H(19)	120.3
O(2)-C(13)-C(12)	124.52(16)	C(18)-C(19)-H(19)	120.3
O(14)-C(13)-C(12)	112.08(14)	C(19)-C(20)-C(21)	120.31(19)
C(13)-O(14)-C(15)	116.45(13)	C(19)-C(20)-H(20)	119.8
O(14)-C(15)-C(16)	110.56(15)	C(21)-C(20)-H(20)	119.8
O(14)-C(15)-C(1)	105.40(14)	C(16)-C(21)-C(20)	120.84(18)
C(16)-C(15)-C(1)	112.28(14)	C(16)-C(21)-H(21)	119.6
O(14)-C(15)-H(15)	109.5	C(20)-C(21)-H(21)	119.6

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (–)-**4**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	33(1)	34(1)	29(1)	5(1)	11(1)	-1(1)
C(1)	20(1)	33(1)	29(1)	-5(1)	7(1)	-1(1)
O(2)	28(1)	31(1)	26(1)	3(1)	9(1)	2(1)
C(2)	24(1)	32(1)	23(1)	-3(1)	5(1)	0(1)

O(3)	27(1)	27(1)	25(1)	-2(1)	8(1)	-3(1)
C(4)	22(1)	27(1)	30(1)	1(1)	10(1)	1(1)
C(5)	31(1)	28(1)	29(1)	-3(1)	11(1)	-4(1)
C(6)	27(1)	27(1)	32(1)	1(1)	7(1)	-3(1)
C(7)	27(1)	28(1)	30(1)	2(1)	6(1)	-2(1)
C(8)	24(1)	29(1)	31(1)	4(1)	9(1)	-2(1)
C(9)	23(1)	31(1)	32(1)	4(1)	11(1)	-1(1)
C(10)	26(1)	34(1)	31(1)	4(1)	16(1)	-1(1)
C(11)	25(1)	35(1)	32(1)	0(1)	13(1)	4(1)
C(12)	27(1)	30(1)	28(1)	0(1)	11(1)	2(1)
C(13)	22(1)	21(1)	29(1)	-1(1)	9(1)	-3(1)
O(14)	21(1)	33(1)	24(1)	-2(1)	9(1)	1(1)
C(15)	23(1)	32(1)	24(1)	-5(1)	10(1)	-1(1)
C(16)	20(1)	29(1)	25(1)	-2(1)	6(1)	1(1)
C(17)	34(1)	34(1)	29(1)	-5(1)	11(1)	-2(1)
C(18)	36(1)	39(1)	34(1)	4(1)	17(1)	2(1)
C(19)	24(1)	32(1)	45(1)	7(1)	12(1)	0(1)
C(20)	27(1)	31(1)	38(1)	-7(1)	6(1)	-4(1)
C(21)	27(1)	35(1)	27(1)	-5(1)	10(1)	-3(1)

Table S5. Hydrogen coordinates (Å x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for (–)-**4**.

	x	y	z	U(eq)
H(1A)	5848	4336	7772	33
H(1B)	5881	5007	9107	33
H(2A)	5196	2550	9115	32
H(2B)	3614	3478	9009	32
H(5A)	2241	-354	6091	35
H(5B)	1966	1277	5505	35

H(6A)	-561	120	5254	35
H(6B)	-63	-88	6763	35
H(7)	-988	2621	5444	35
H(8)	-298	2063	8015	33
H(9)	-1404	4758	6684	34
H(10)	-146	4374	9289	34
H(11A)	-1121	6782	9324	36
H(11B)	-1379	6966	7840	36
H(12A)	880	8379	9000	33
H(12B)	1692	6961	9813	33
H(15)	3208	5366	6825	31
H(17)	4765	6297	5531	38
H(18)	6108	8256	4983	42
H(19)	7004	10232	6378	40
H(20)	6504	10249	8308	40
H(21)	5147	8300	8853	36

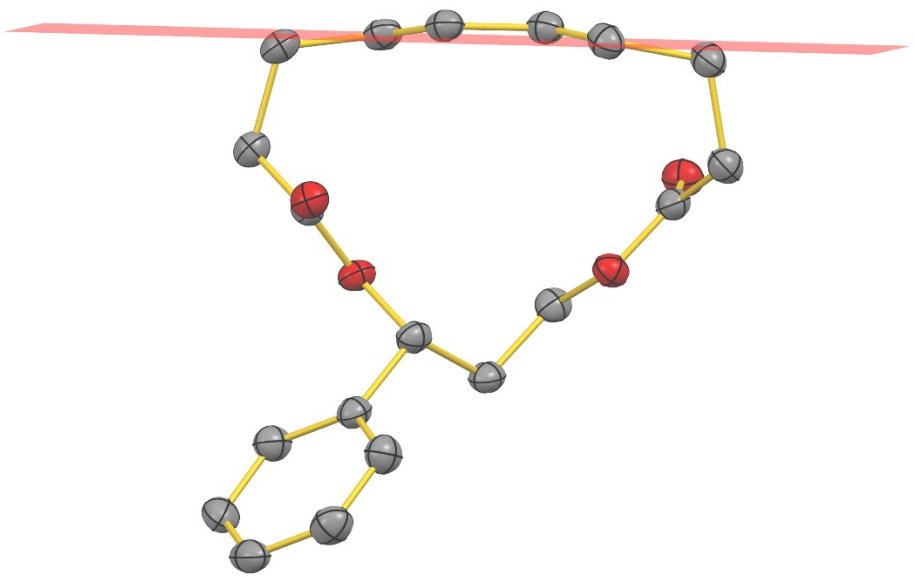
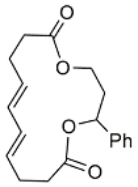


Figure S2. Crystal structure of (–)-**4** depicting a plane made by C6-C7-C8-C9-C10-C11. The average RMSD between the atoms and the plane is 0.1328.

3. HPLC data for [15]-macrodilactones 4 and (–)-4:

==== Shimadzu LCsolution Analysis Report ====

Sample name: DS-i-124
Column: Chiralcel AY
Solvent system: 15% *iso*-propanol in hexane
Flow rate: 1.5 mL/min
Detector A Ch1 254 nm
Detector B Ch2 209 nm



4

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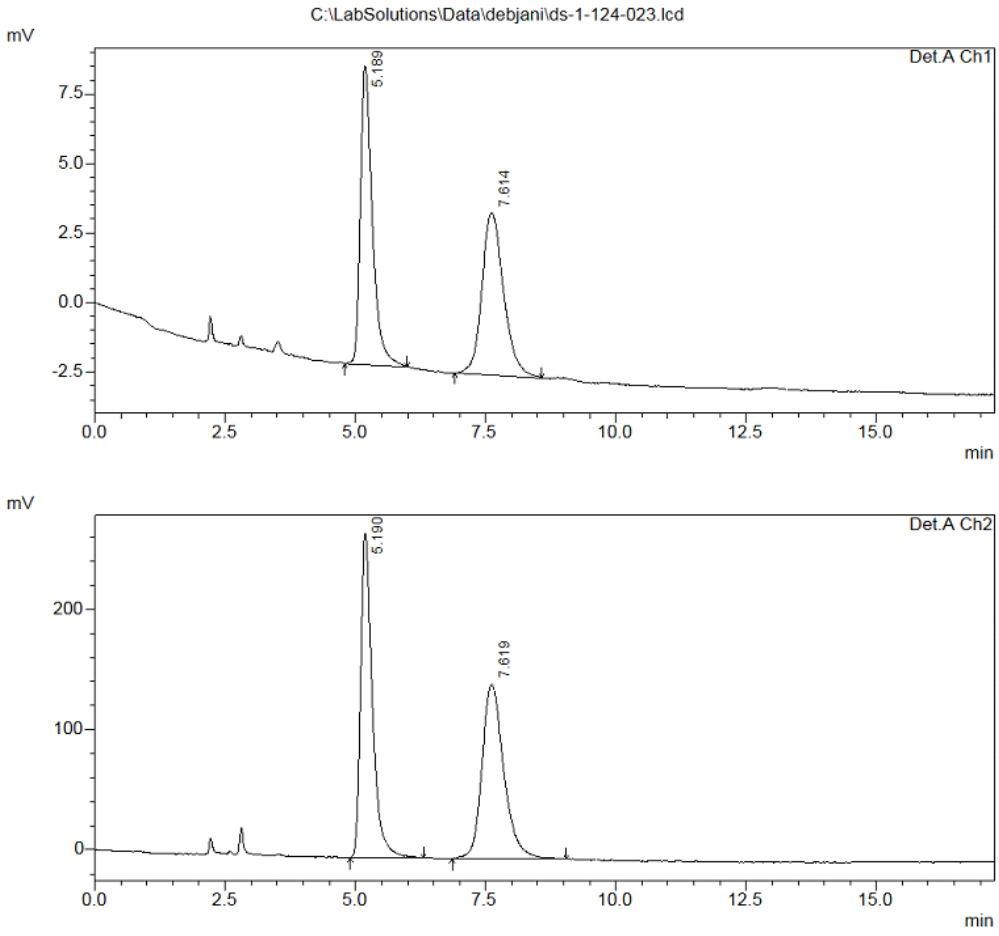


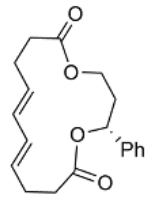
Peak table

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.189	172917	10737	50.454	64.744
2	7.614	169804	5847	49.546	35.256
Total		342721	16584	100.000	100.000

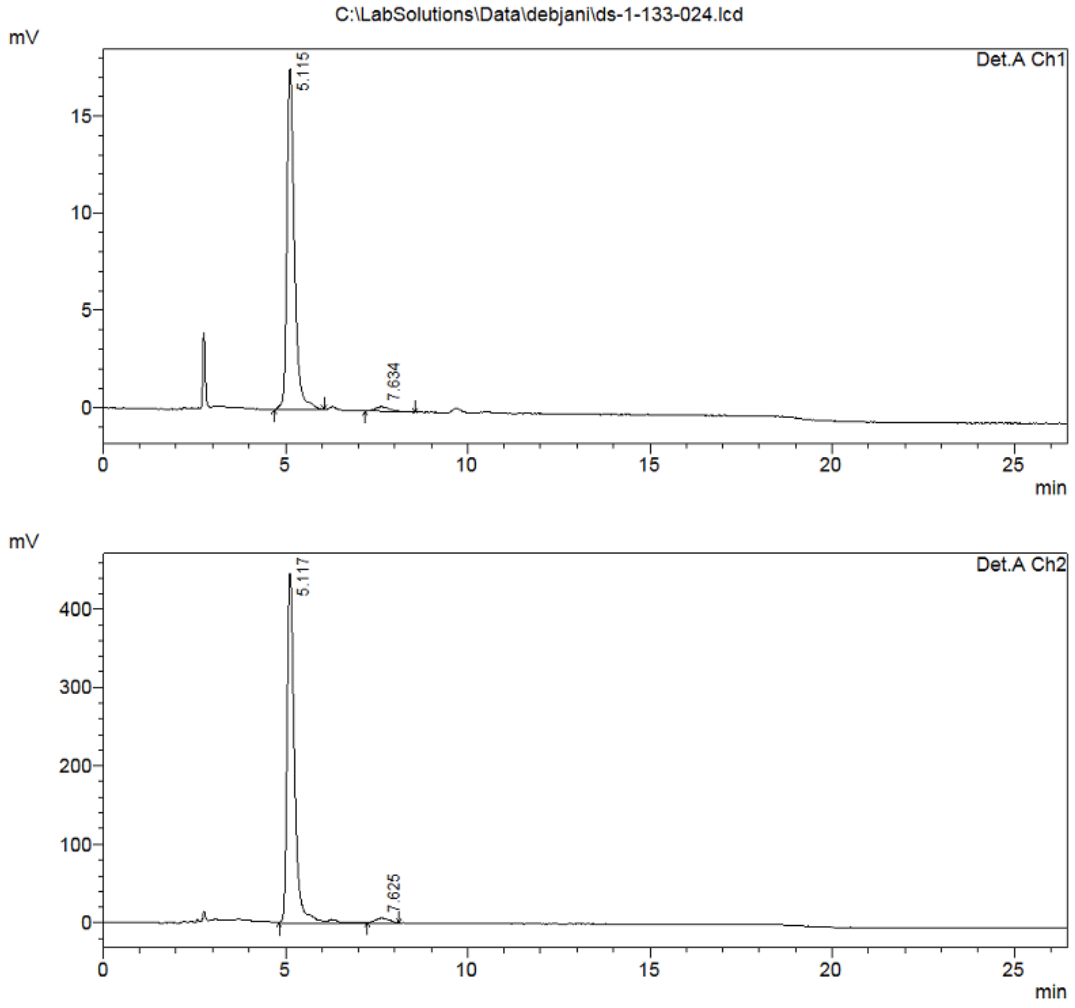
==== Shimadzu LCsolution Analysis Report ====

Sample name: DS-i-133
Column: Chiralcel AY
Solvent system: 15% *iso*-propanol in hexane
Flow rate: 1.5 mL/min
Detector A Ch1 254 nm
Detector B Ch2 209 nm



(–)-4

<Chromatogram>



Peak table
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.115	251416	17491	97.442	98.627
2	7.634	6601	243	2.558	1.373
Total		258017	17735	100.000	100.000

4. Determination of epoxide stereochemistry in macrodilactone 23a and 23b:

The determination of epoxide stereochemistry in macrodilactone **23a** and **23b** were carried out by comparing ^{1}H and ^{13}C NMR data, polarimetry data and chiral HPLC data of **24**, **(+)-24** (synthesized via transesterification of **23a** and **23b**) and **(+)-24** (synthesized via Shi epoxidation of **30**). For ^{1}H and ^{13}C NMR data see the spectra of respective compounds.

(i) Polarimetry data:

24: $[\alpha]_D^{20}$: –0.38 (*c* 1.0, $CHCl_3$)

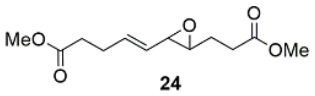
(+)-24 (via transesterification of **23a** and **23b**): $[\alpha]_D^{20}$: +24.0 (*c* 0.6, $CHCl_3$)

(+)-24 (via Shi epoxidation of **30**): $[\alpha]_D^{20}$: +25.5 (*c* 0.6, $CHCl_3$)

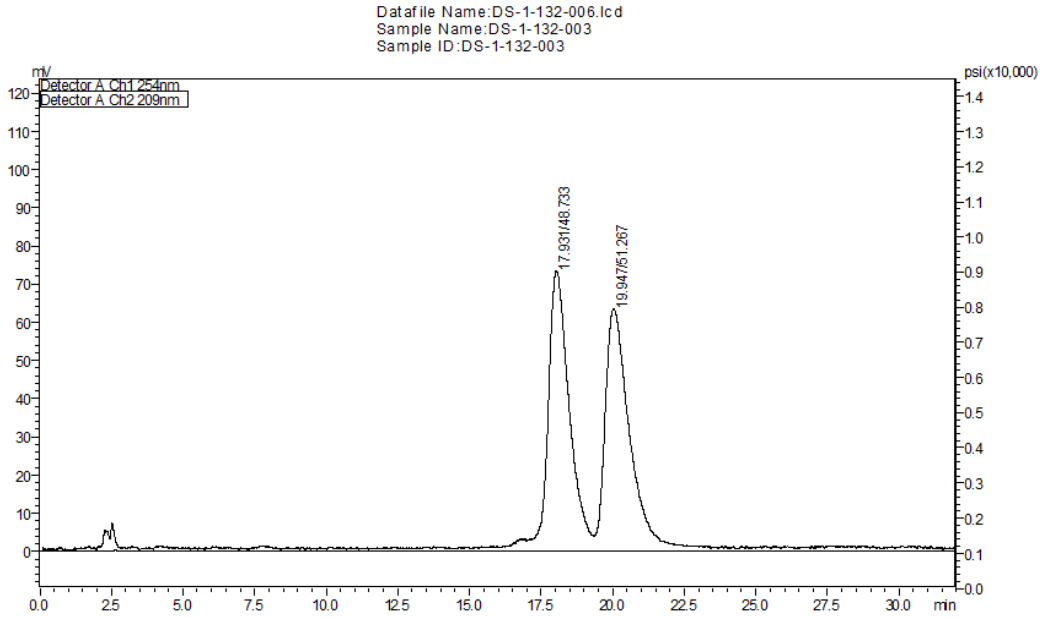
(ii) Chiral HPLC data:

==== Shimadzu LCsolution Analysis Report ====

Sample name: DS-i-132
Column: Chiralcel OD
Solvent system: 2% *iso*-propanol in hexane
Flow rate: 1.5 mL/min
Detector A Ch2 209 nm



24

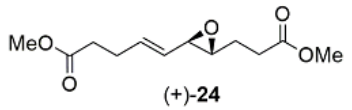


Peak table

Peak#	Ret. time	Area	Height	Area%
1	17.931	3690171	73222	48.733
2	19.947	3882113	63255	51.267
Total		7572284	136477	100

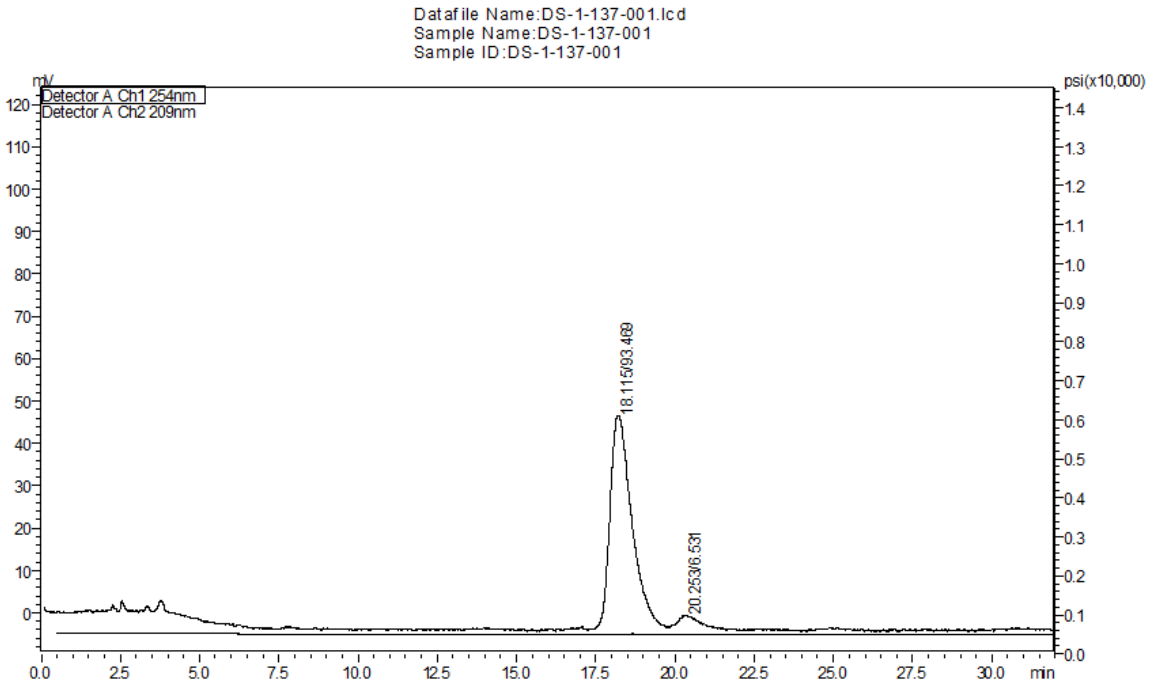
==== Shimadzu LCsolution Analysis Report ====

Sample name: DS-i-137
Column: Chiralcel OD
Solvent system: 2% *iso*-propanol in hexane
Flow rate: 1.5 mL/min
Detector A Ch2 209 nm



(+)-**24**

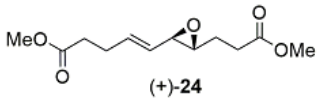
(via transesterification of **23a** and **23b**)



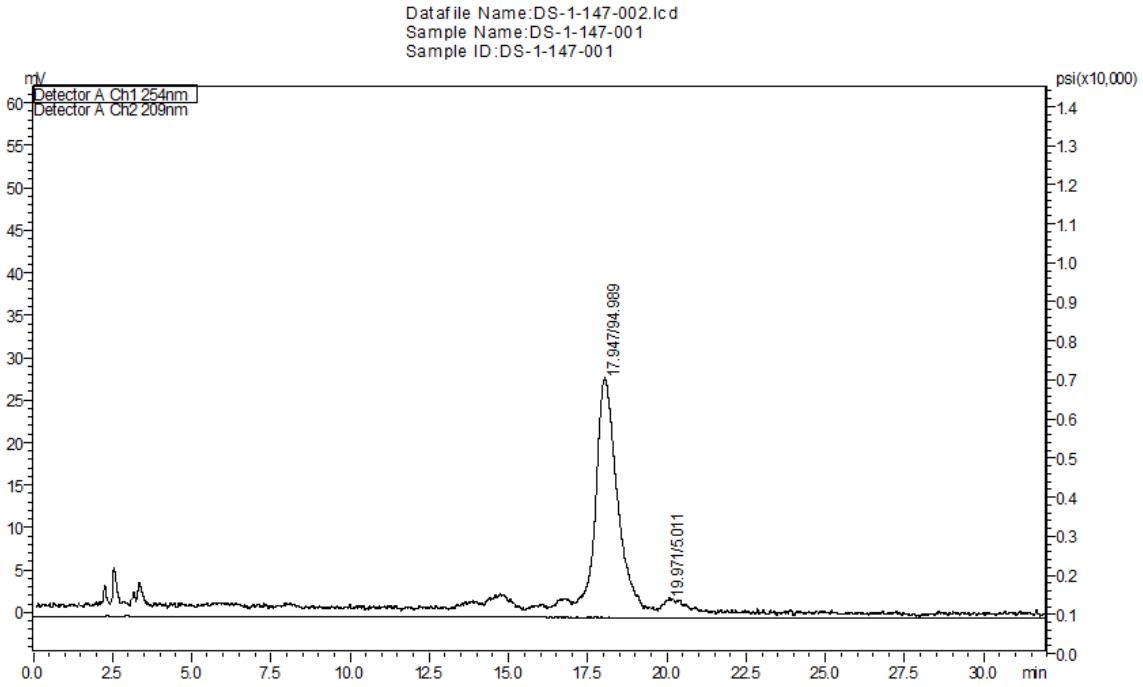
Peak table

Peak#	Ret. time	Area	Height	Area%
1	18.115	2416310	50506	93.469
2	20.253	168840	3222	6.531
Total		2585151	53728	100

Sample name: DS-i-147
Column: Chiralcel OD
Solvent system: 2% *iso*-propanol in hexane
Flow rate: 1.5 mL/min
Detector A Ch2 209 nm



(+)-**24**
(via Shi epoxidation of **30**)



Peak table

Peak#	Ret. time	Area	Height	Area%
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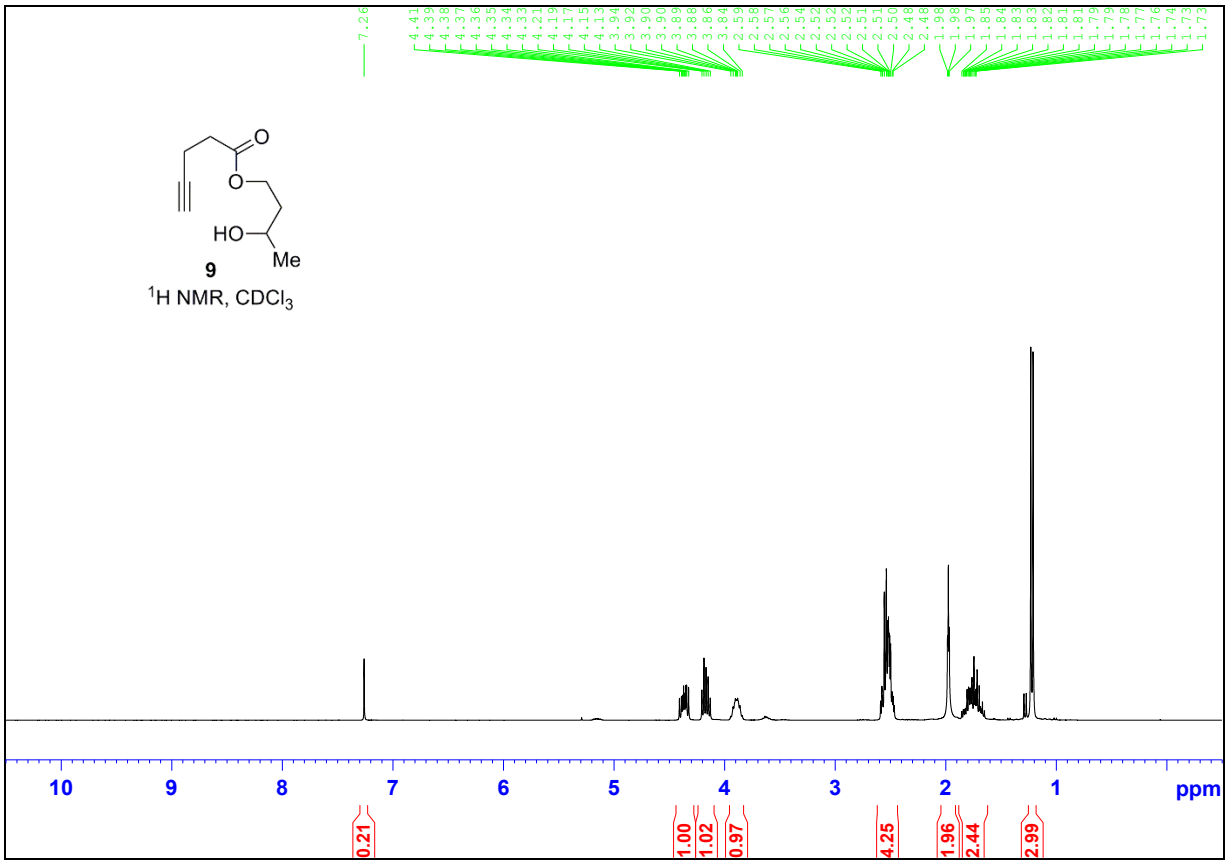
2	19.971	66648	1623	5.011
Total		1330111	29077	100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4.34
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4.13
3.94
3.92
3.90
3.90
3.89
3.88
3.86
3.84
2.59
2.58
2.57
2.56
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1.81
1.81
1.79
1.79
1.78
1.77
1.76
1.74
1.74
1.73
1.73
O
O
HO
Me
9
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
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1.02
0.97
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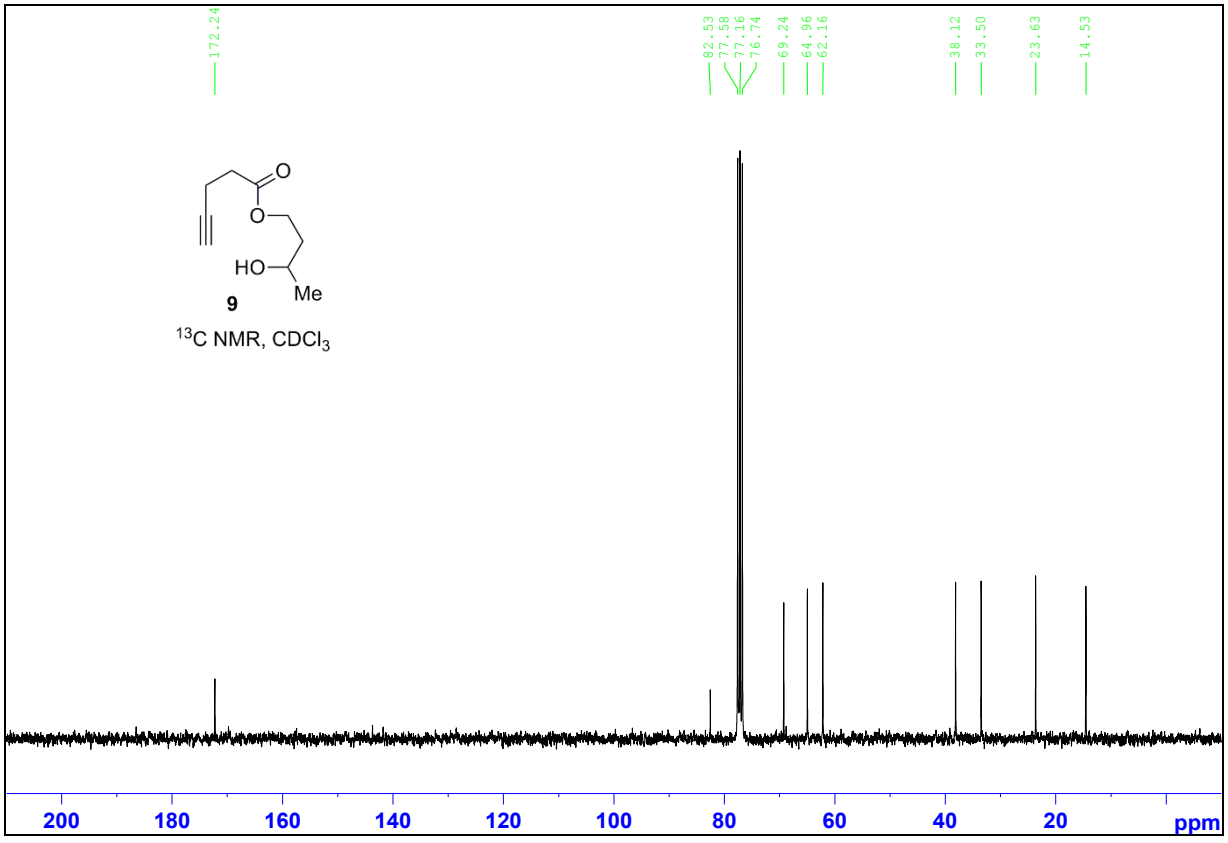
1.96
2.44
2.99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77.16
76.74
69.24
64.96
62.16
38.12
33.50
23.63
14.53
O
O
HO
Me
9
13C NMR, CDCl3
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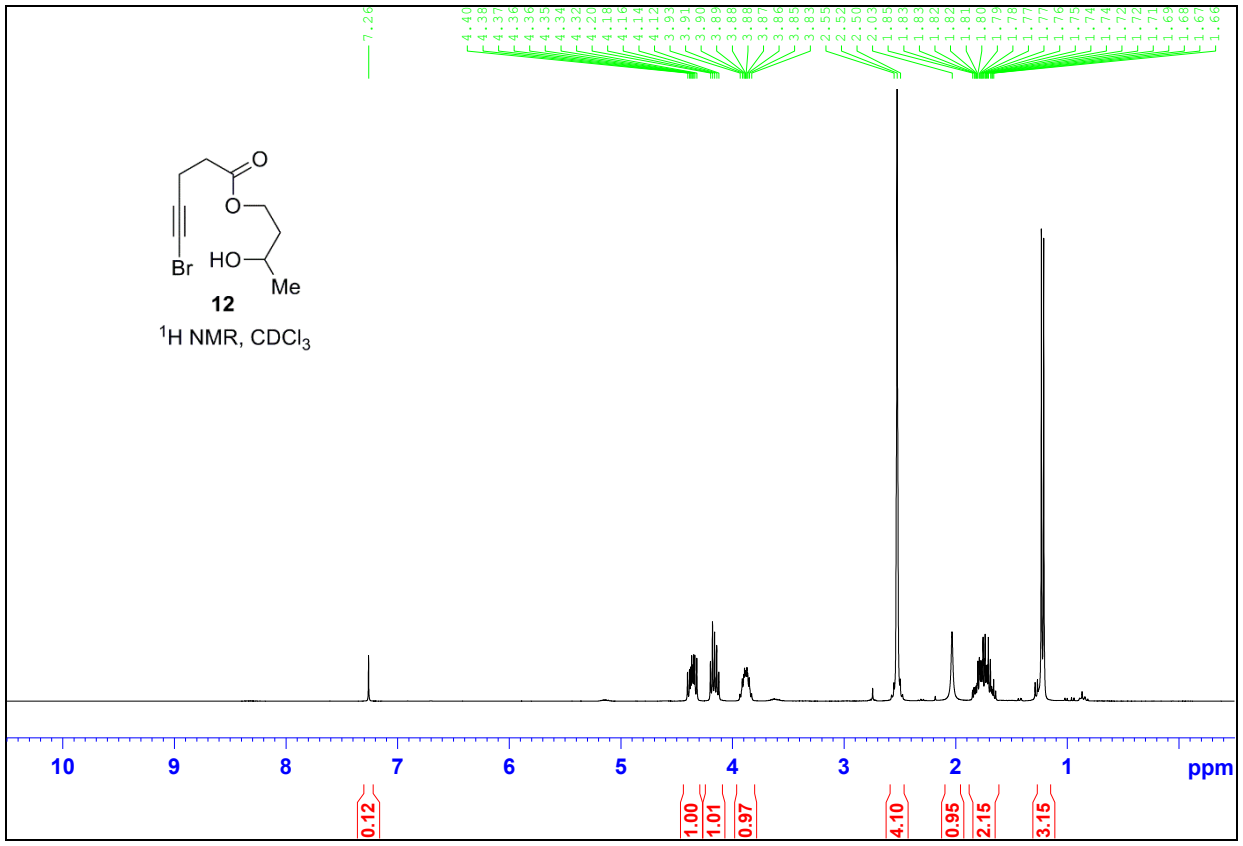
160
140
120
100
80
60
40
20
ppm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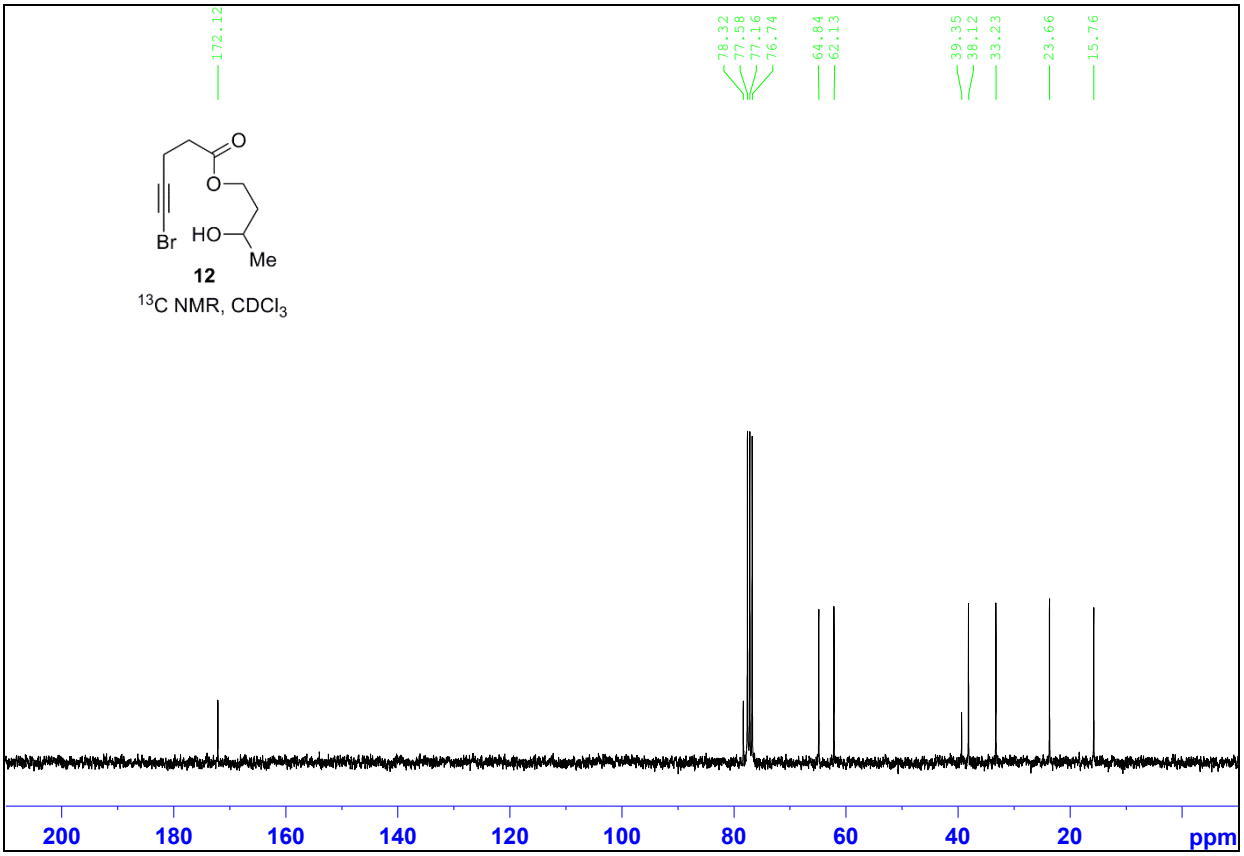
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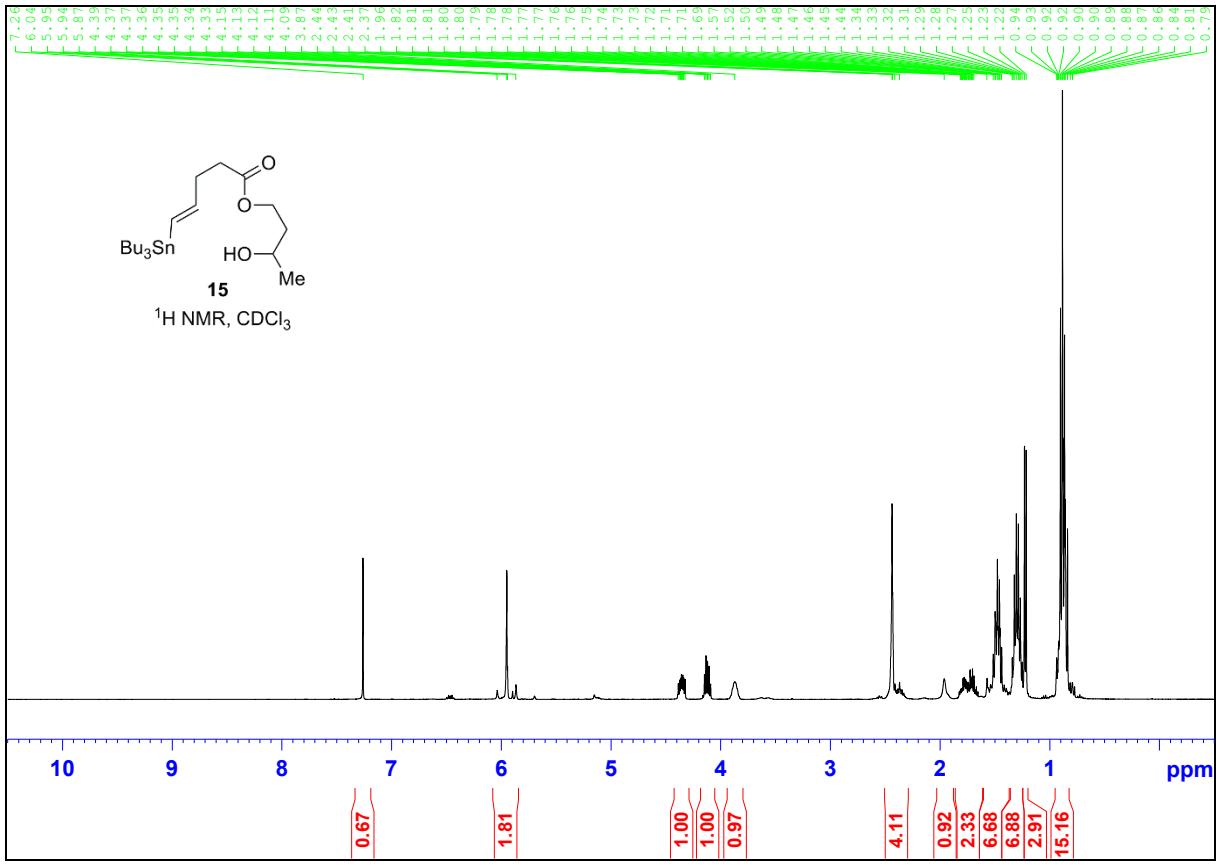
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O
HO
Me
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1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
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1.81
1.00
1.00
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4.11
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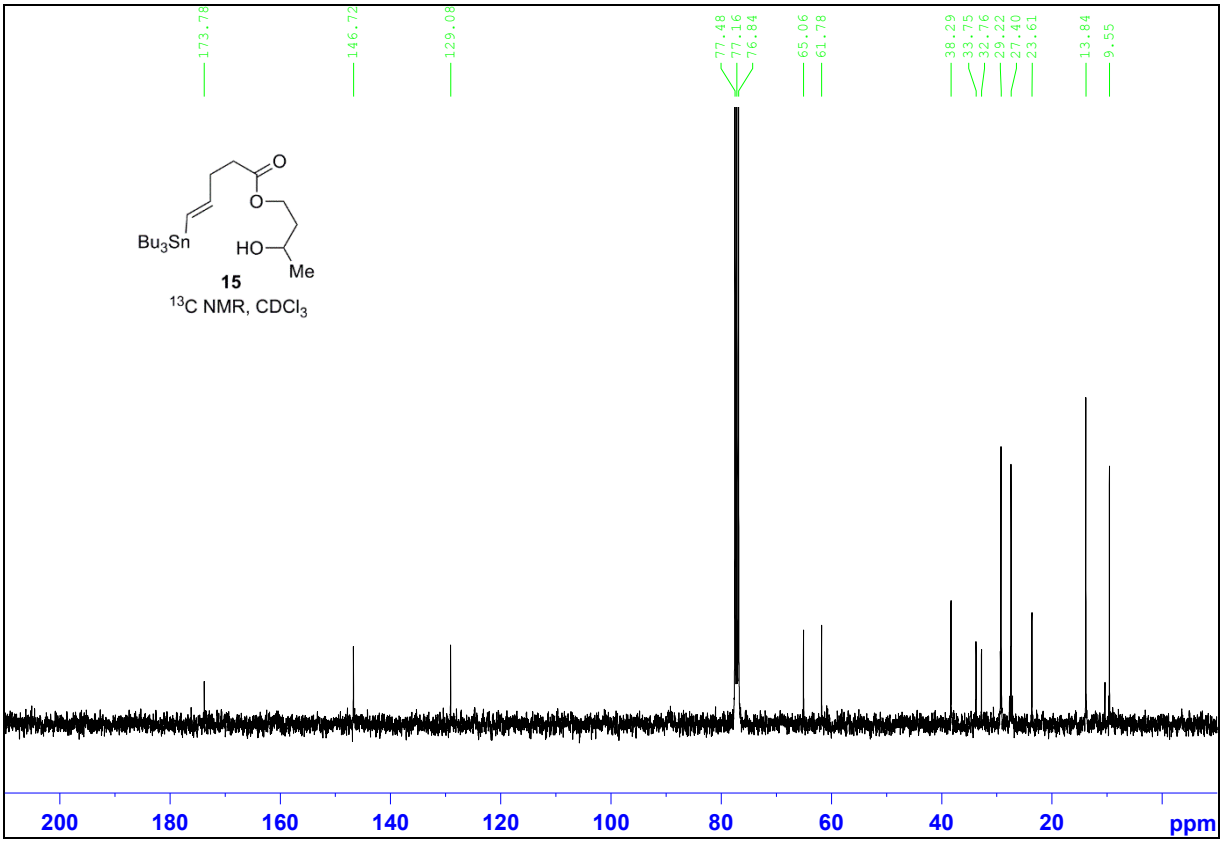
6.88
2.91
15.16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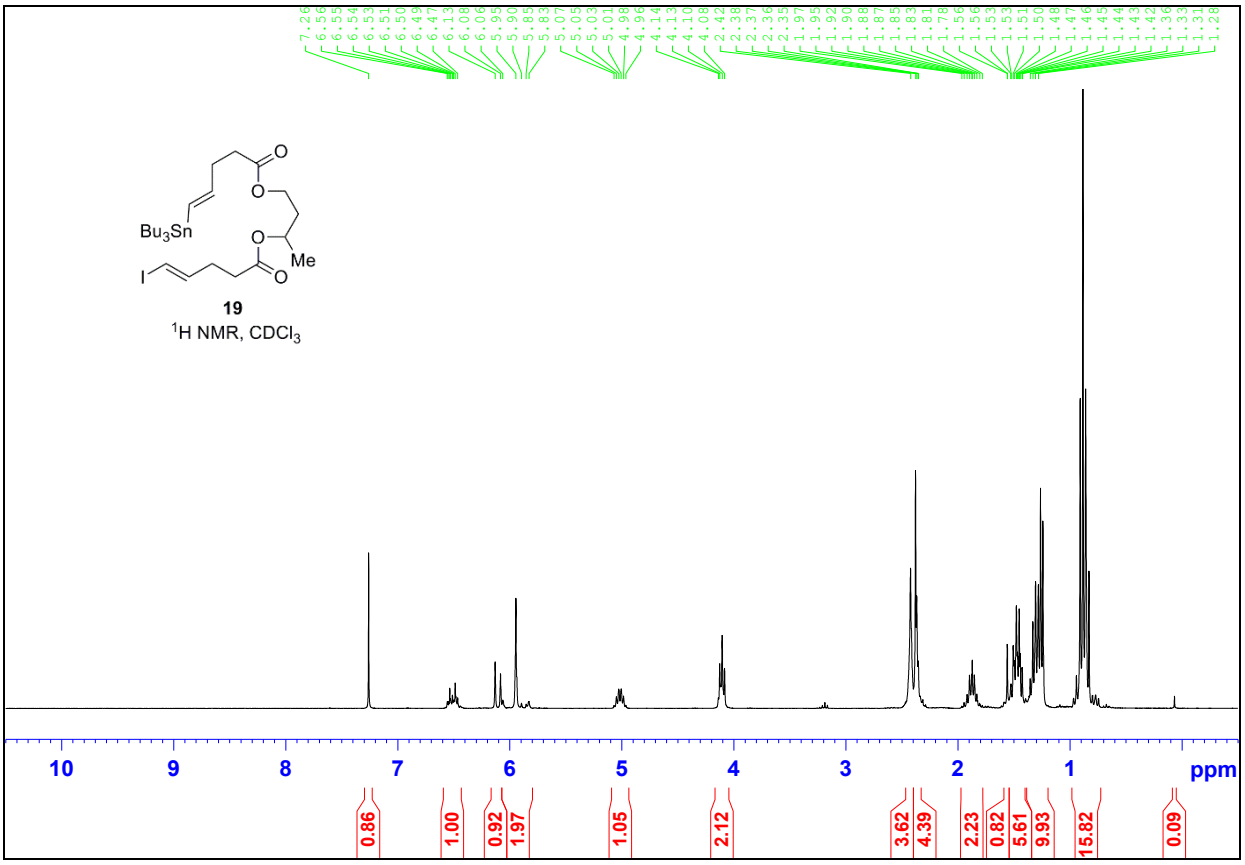
61.78
38.29
33.75
32.76
29.22
27.40
23.61
13.84
9.55
Bu3Sn
O
O
HO
Me
15
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm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O
O
Me
I
O
19
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
0.86
1.00
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1.05
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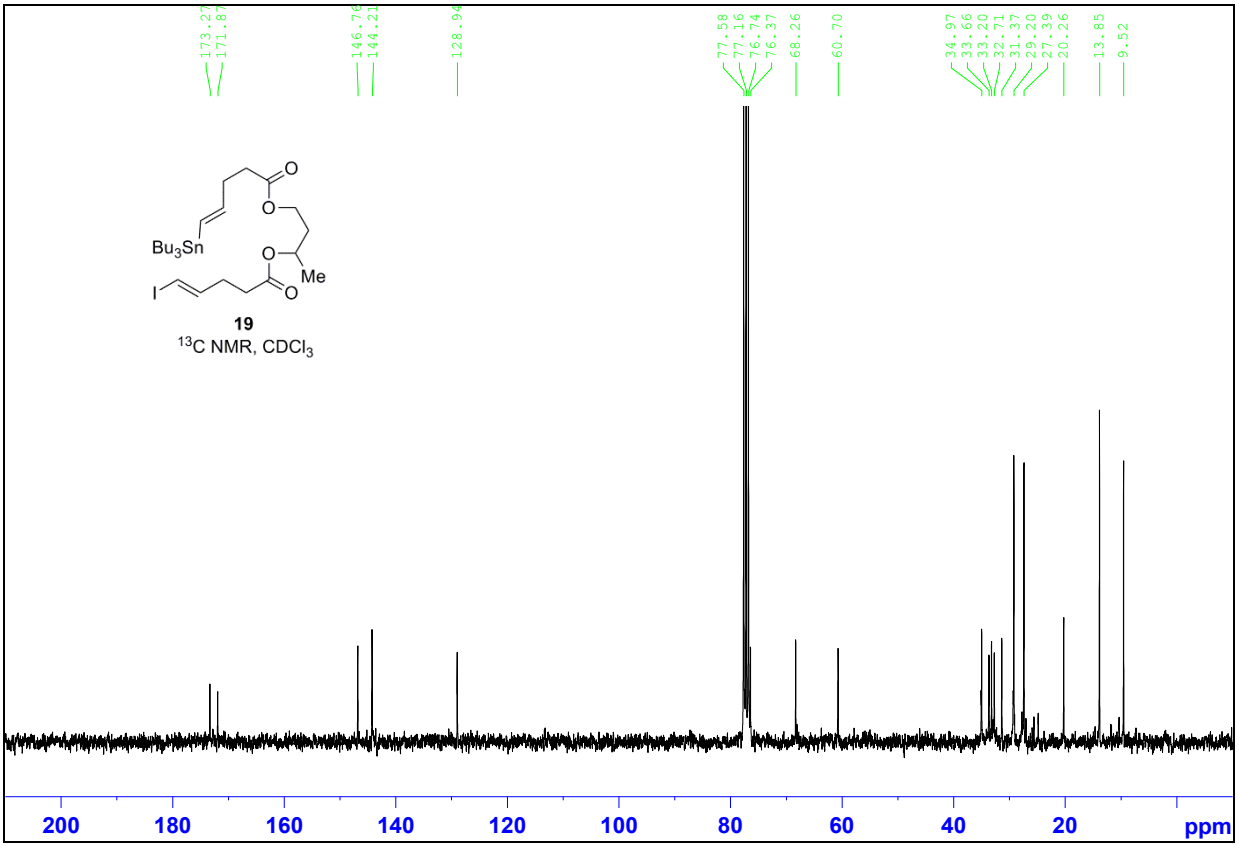
3.62
4.39
2.23
0.82
5.61
9.93
15.82
0.09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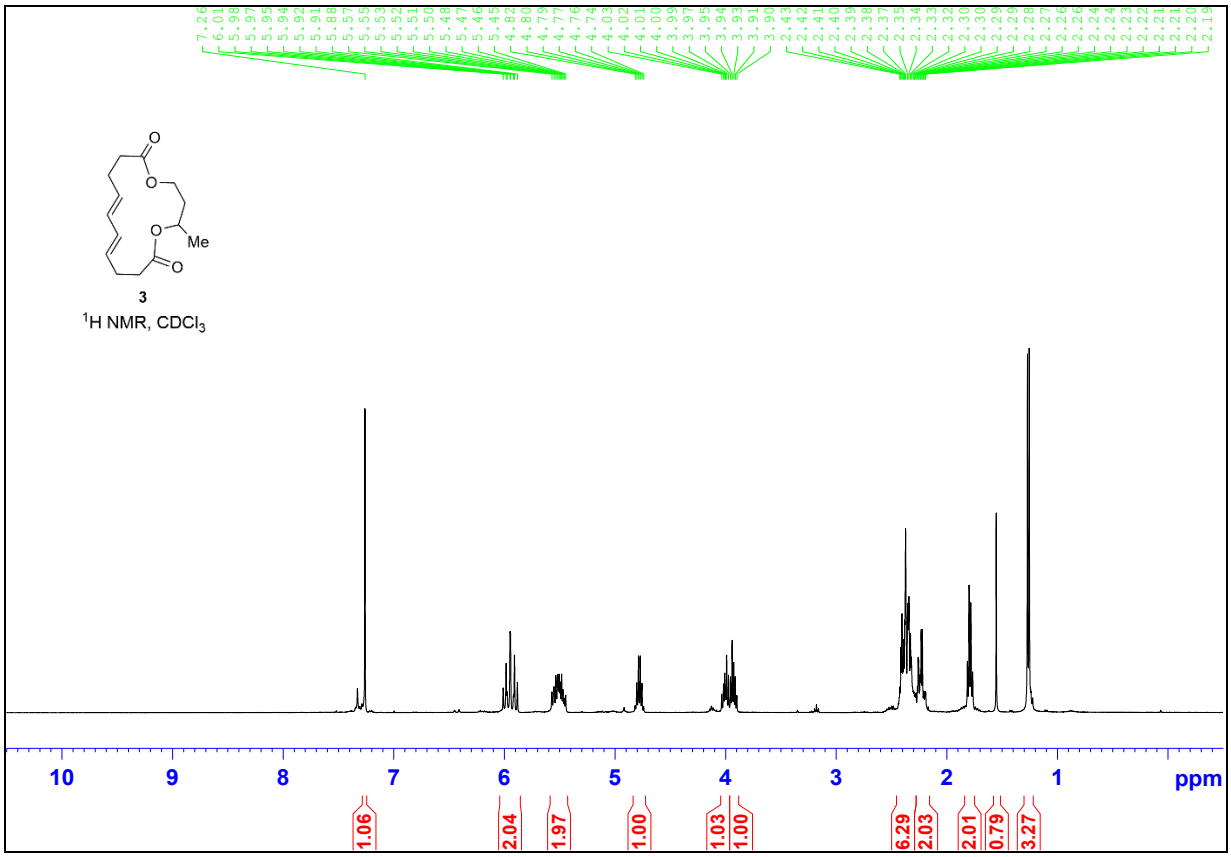
O
O
O
Me
I
O
19
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm


3
^{1}H NMR, $CDCl_3$
10
9
8
7
6
5
4
3
2
1
ppm
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6.29
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2.01
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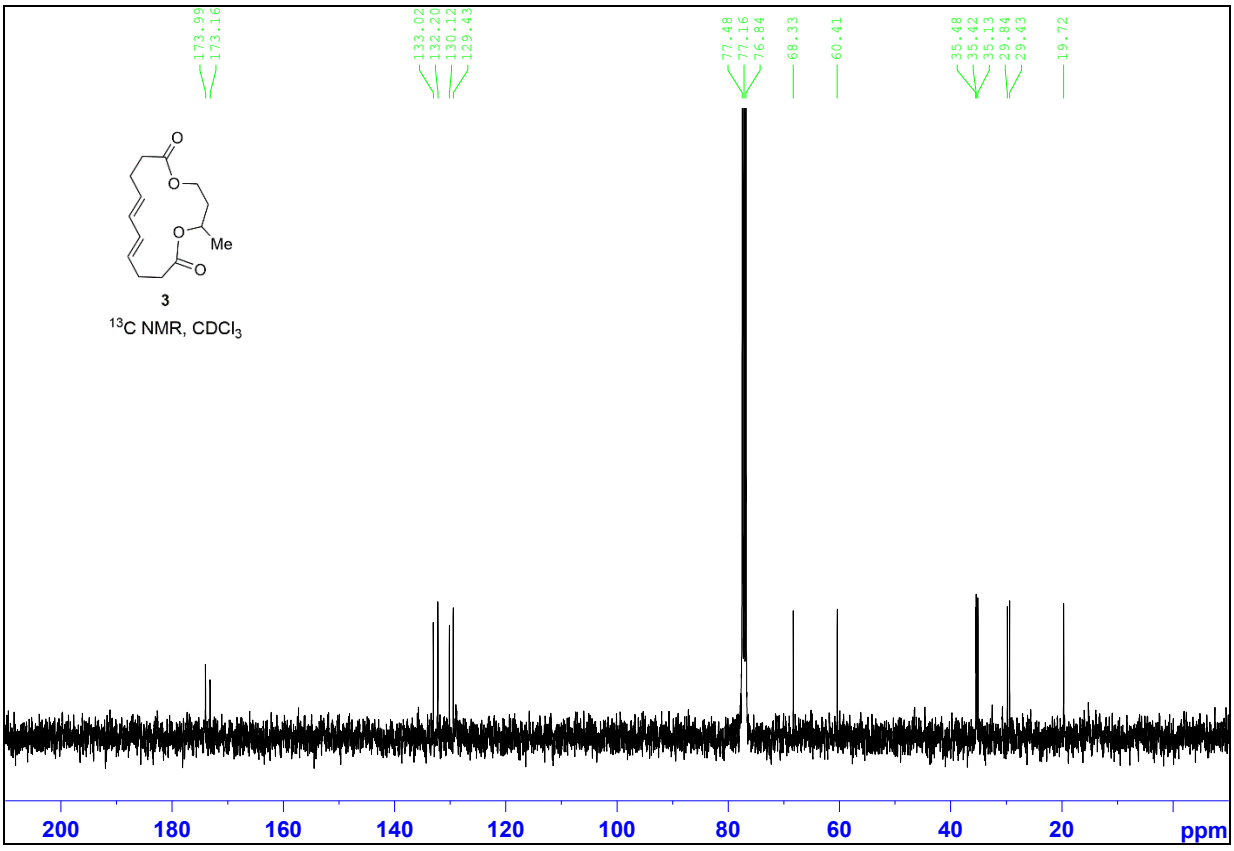
3.27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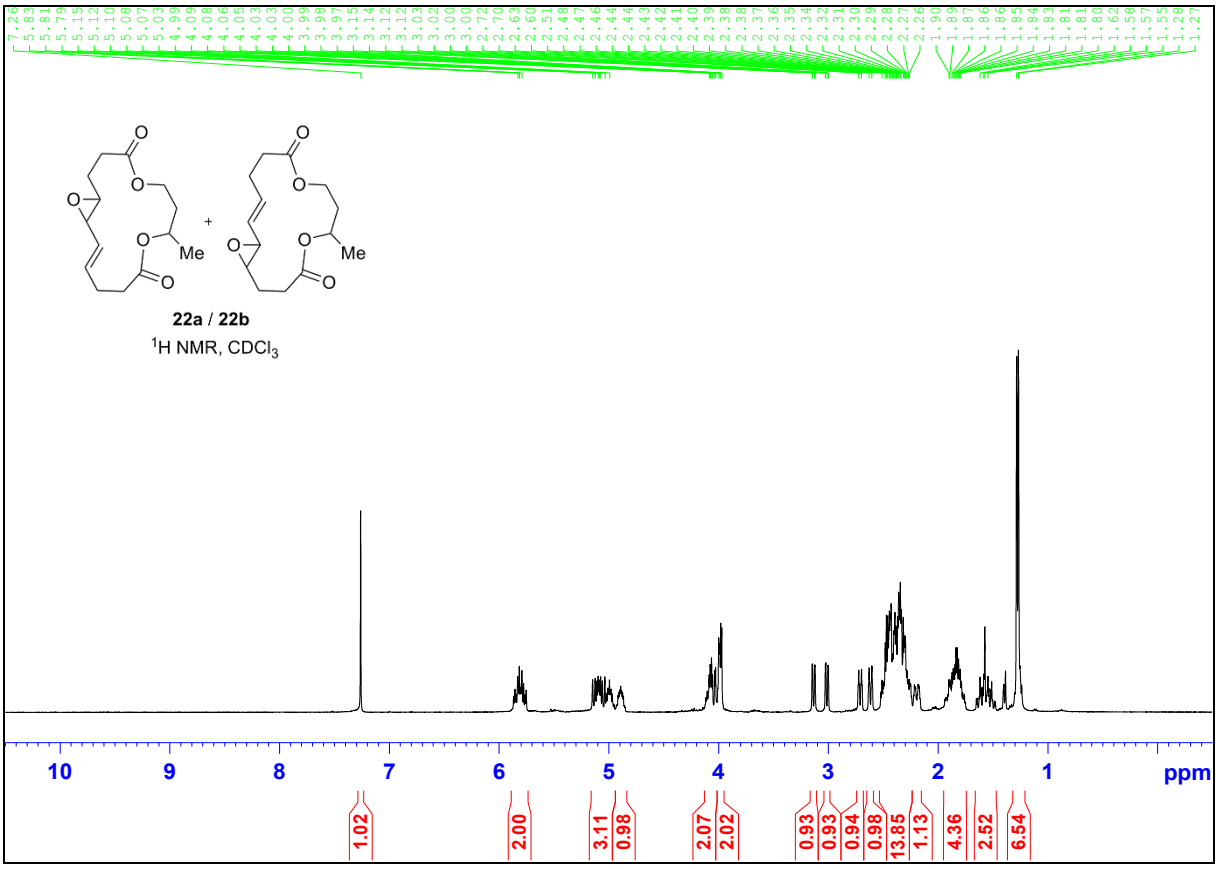
^{13}C NMR, $CDCl_3$
200
180
160
140
120
100
80
60
40
20
ppm


Me
Me
22a / 22b
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
1.02
2.00
3.11
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2.02
0.93
0.93
0.94
0.98
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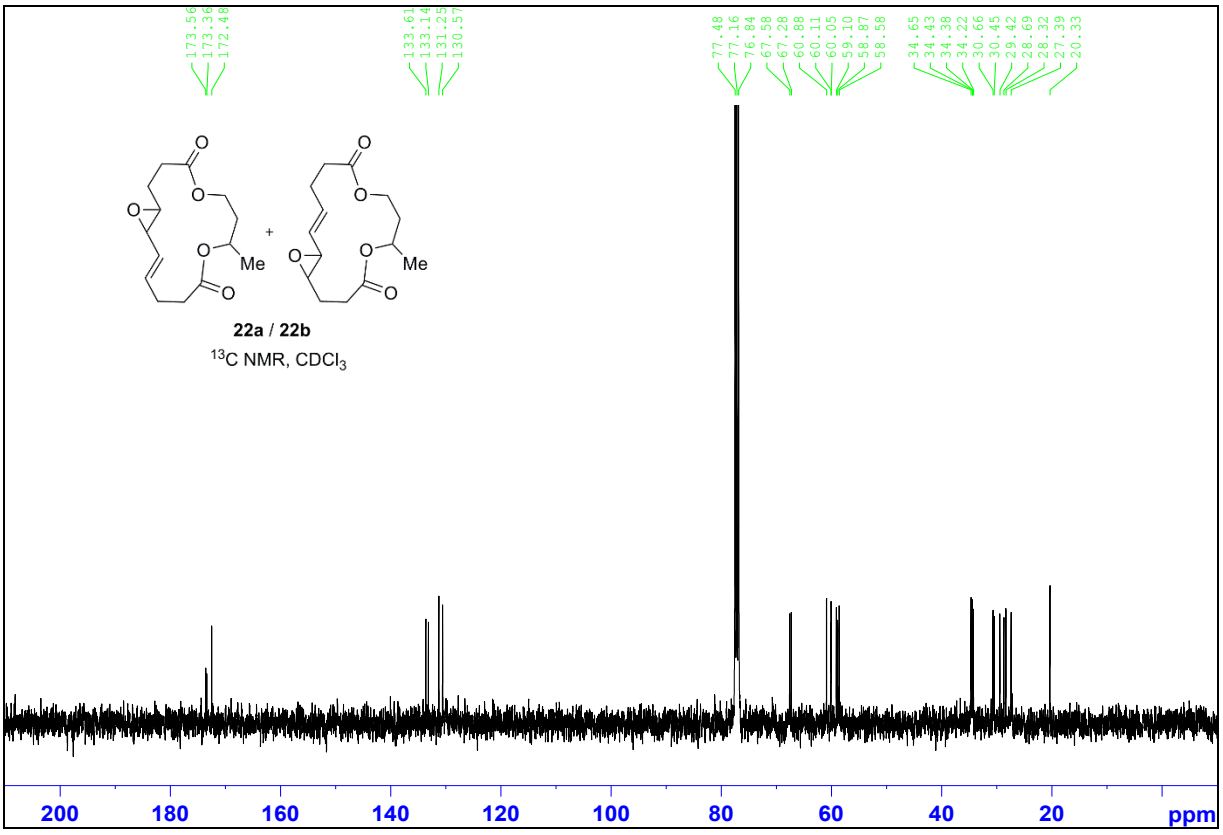
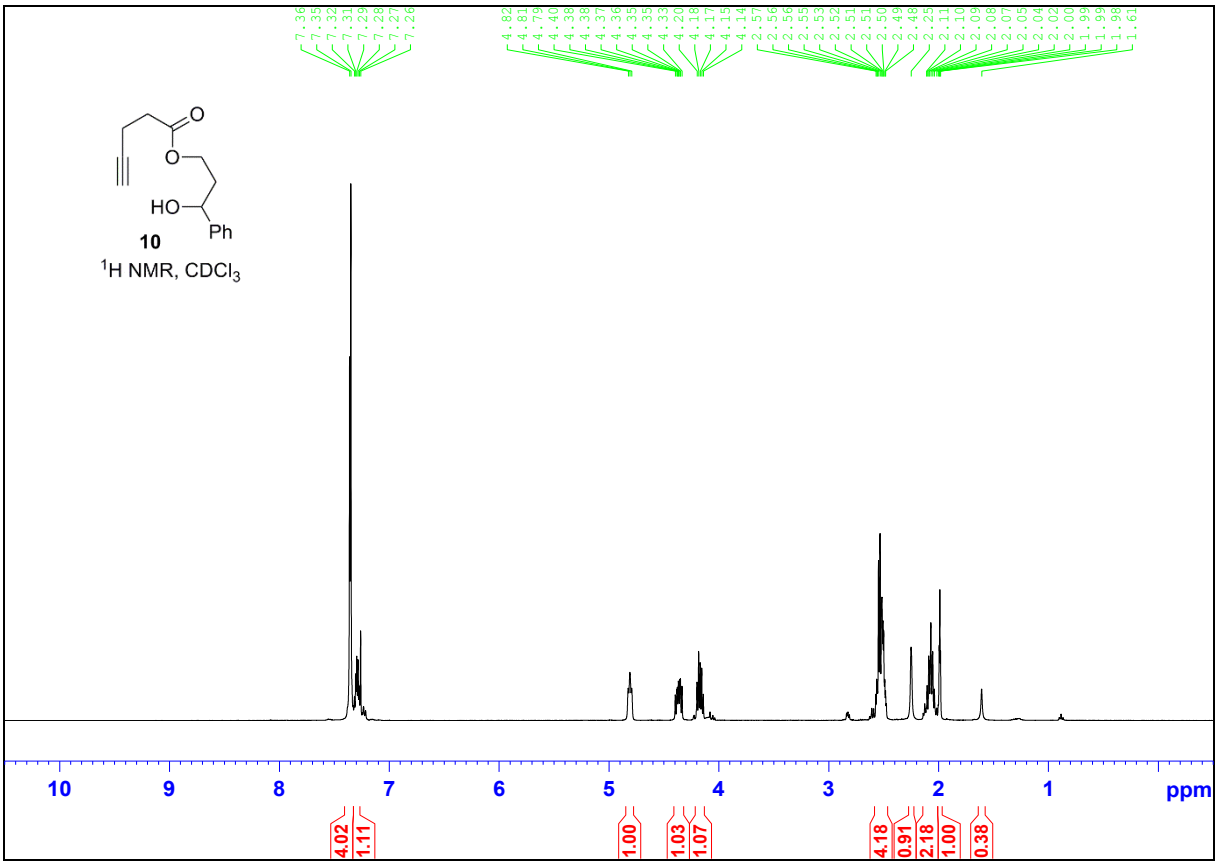
2.52
6.54


Me
Me
22a / 22b
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm


10
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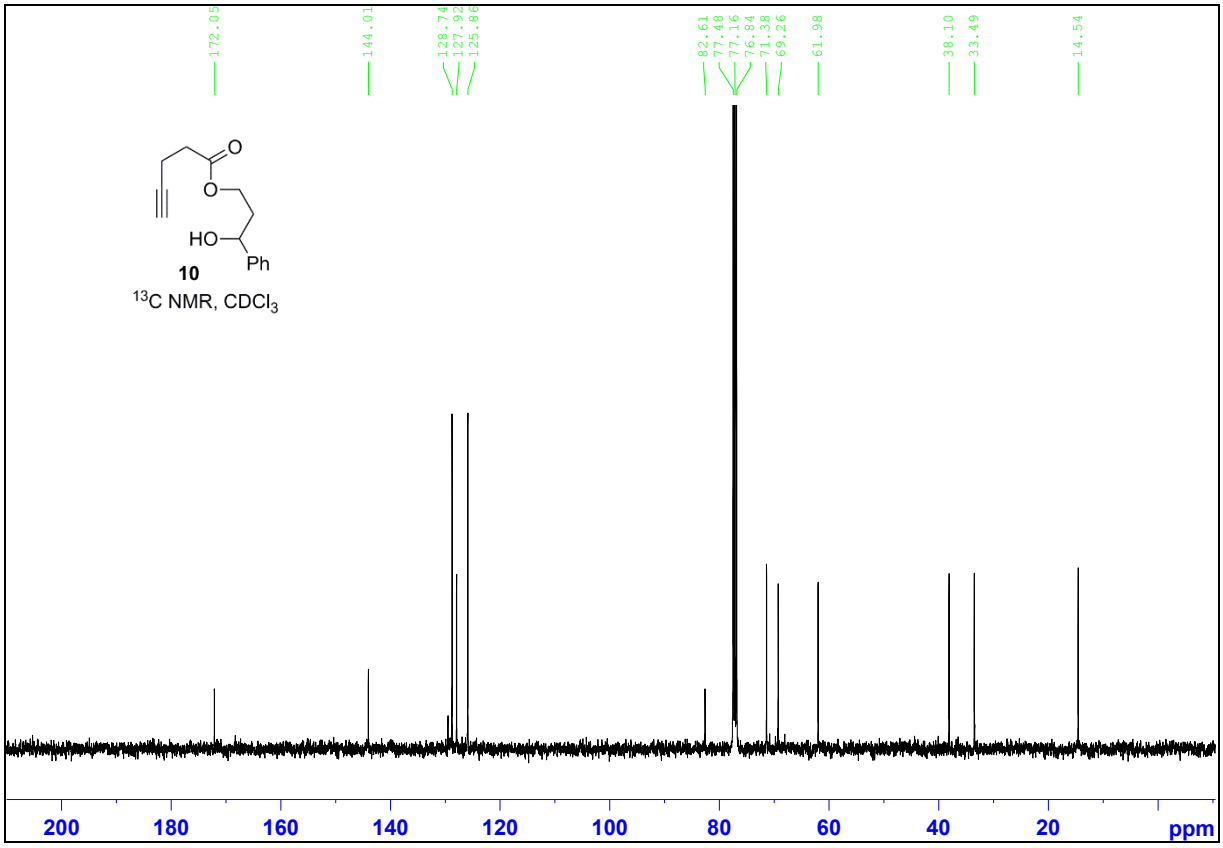
ppm


10
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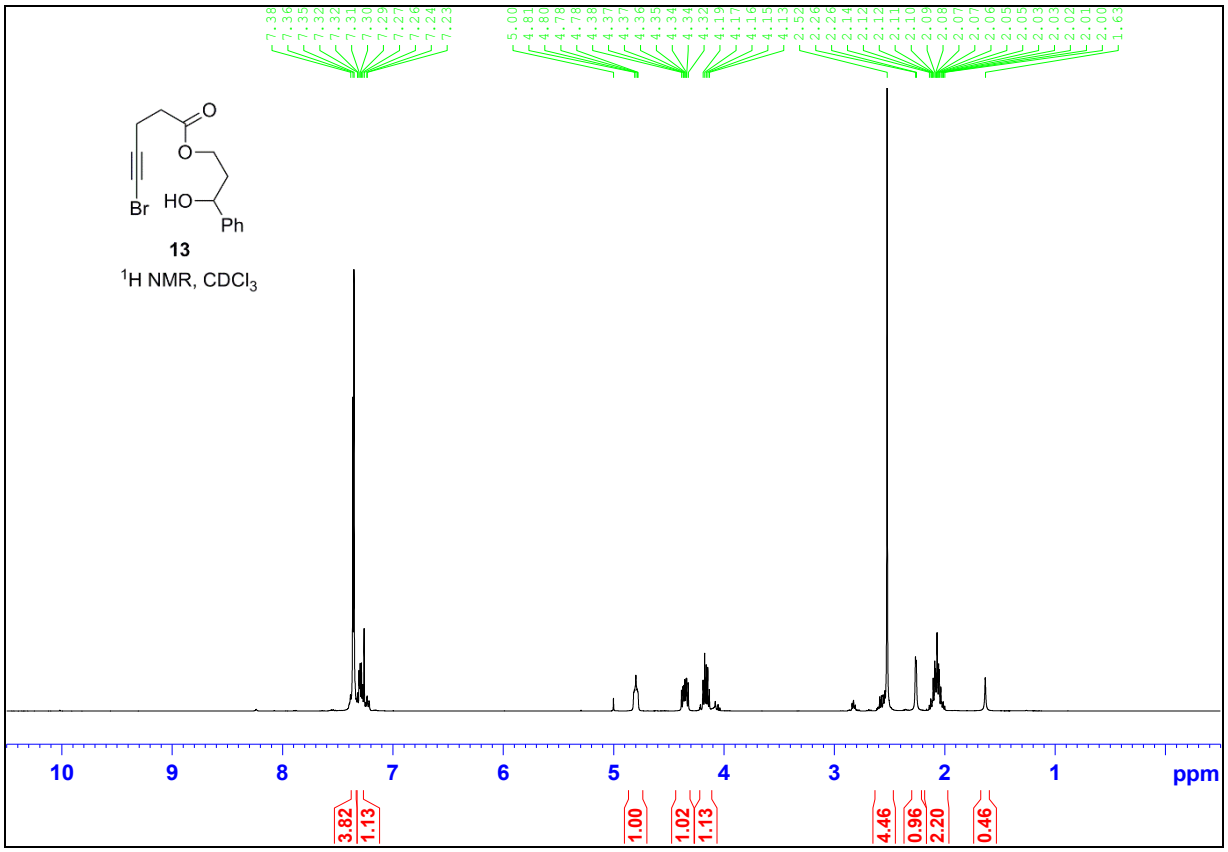
ppm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7.31
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7.29
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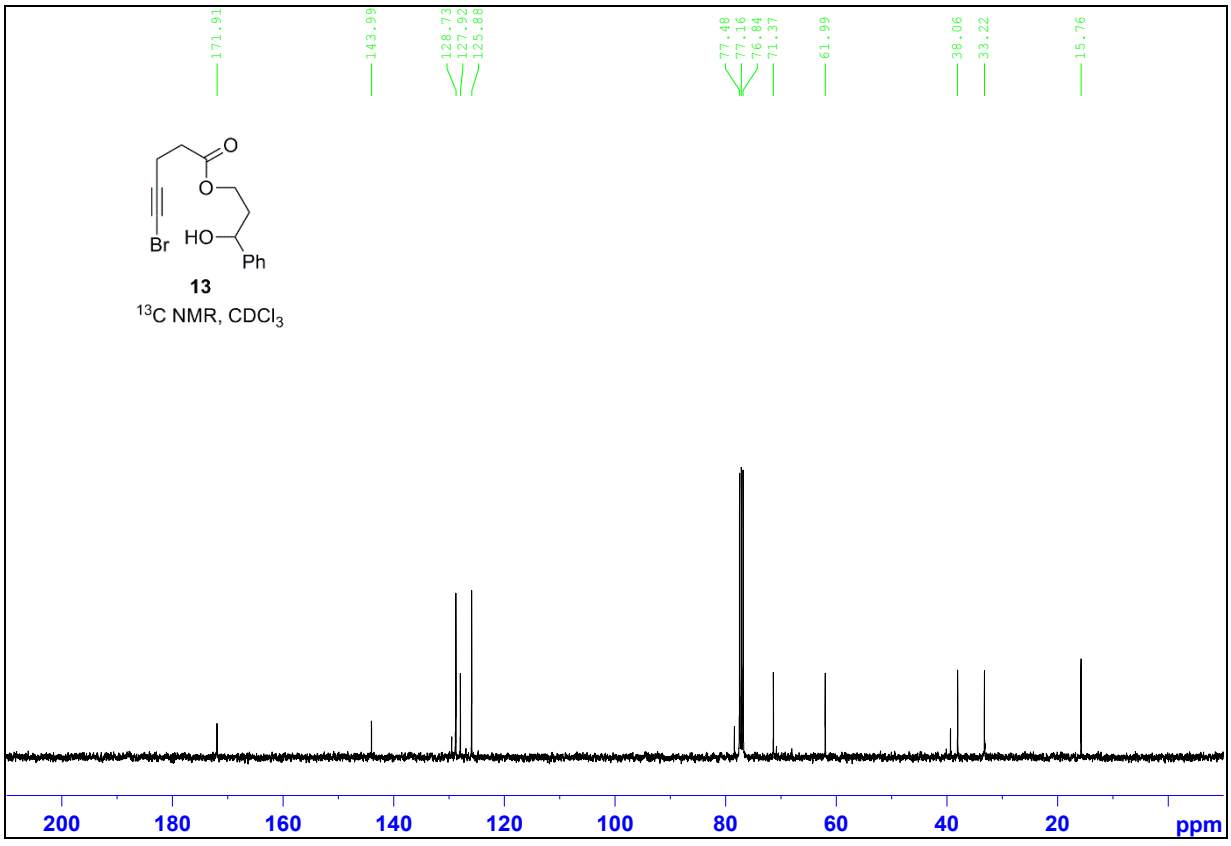
7.23
5.00
4.81
4.80
4.78
4.78
4.38
4.37
4.37
4.36
4.35
4.34
4.34
4.32
4.19
4.17
4.16
4.15
4.13
2.52
2.26
2.26
2.14
2.12
2.11
2.10
2.09
2.08
2.07
2.07
2.06
2.05
2.05
2.03
2.03
2.02
2.01
2.00
1.63
O
O
Br
HO
Ph
13
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
3.82
1.13
1.00
1.02
1.13
4.46
0.96
2.20
0.46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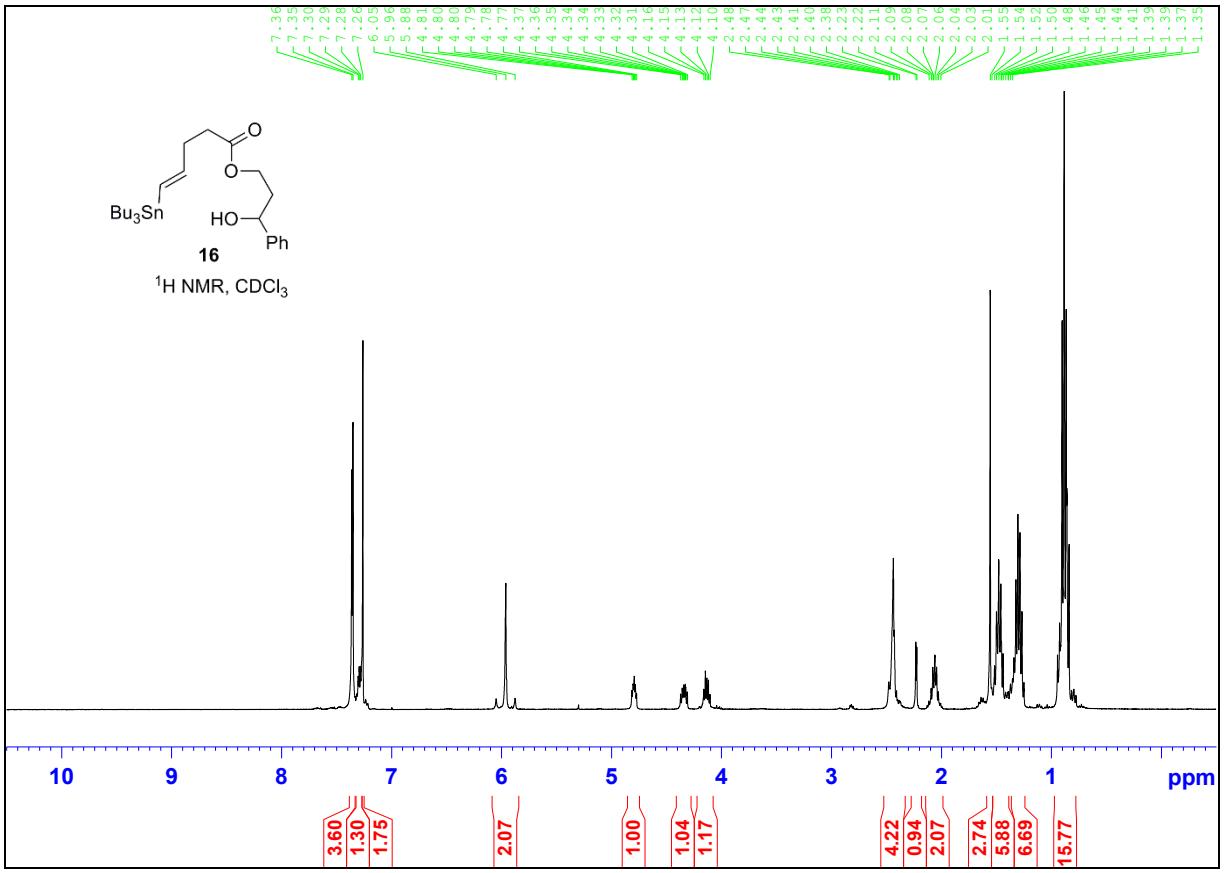
127.92
125.88
77.48
77.16
76.84
71.37
61.99
38.06
33.22
15.76
O
O
Br
HO
Ph
13
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm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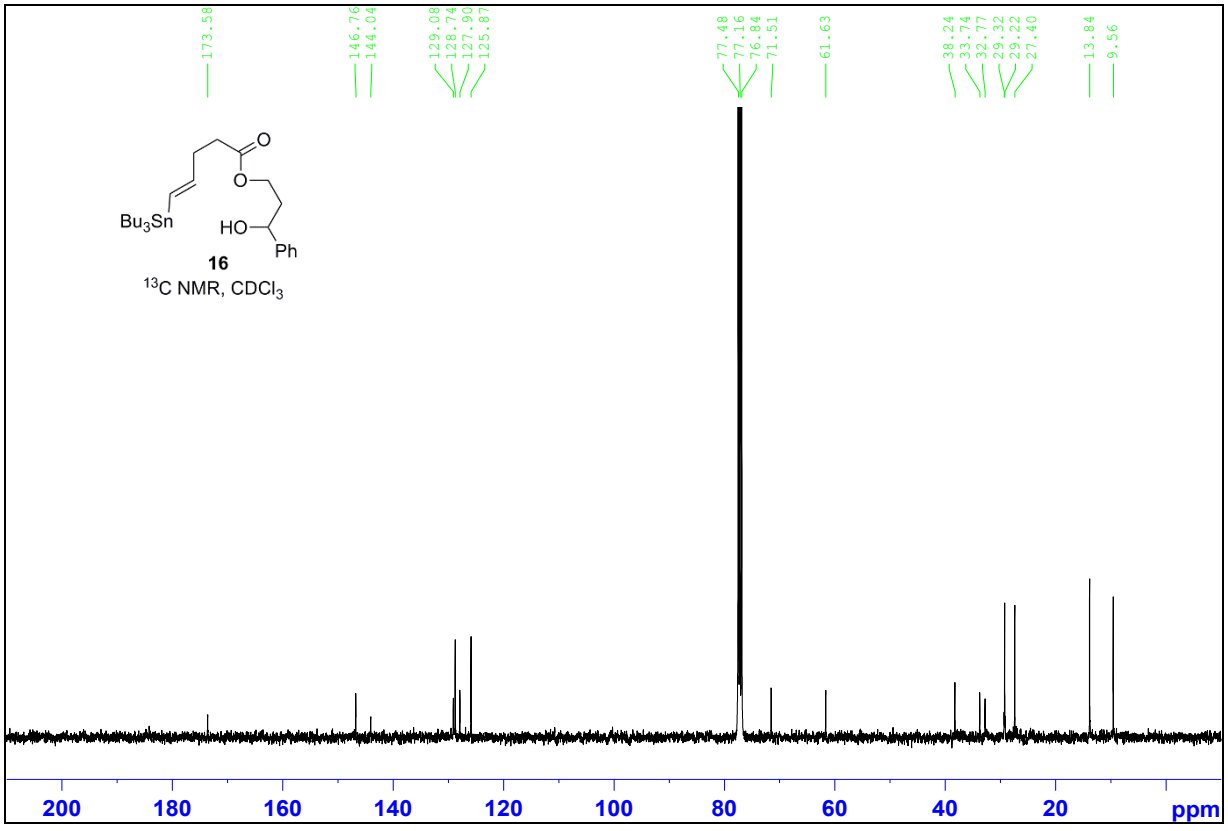
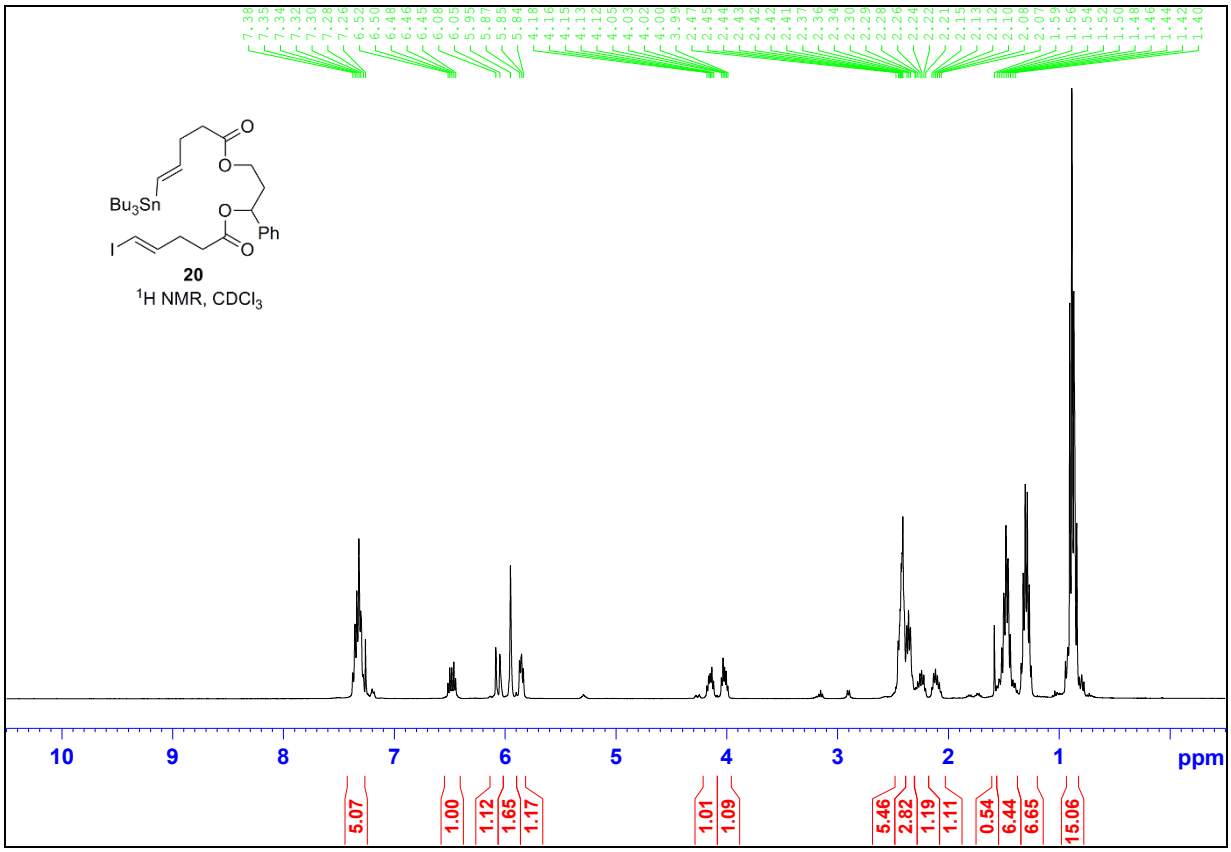
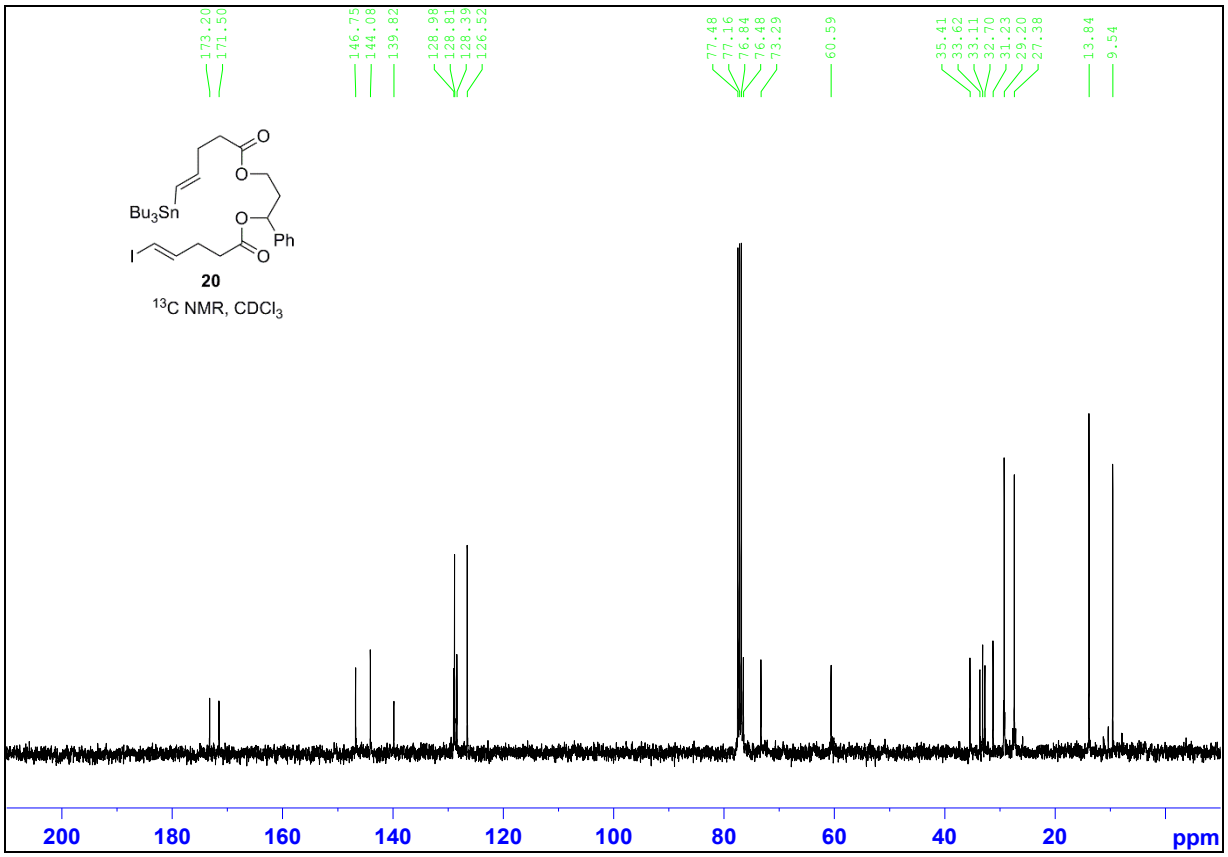
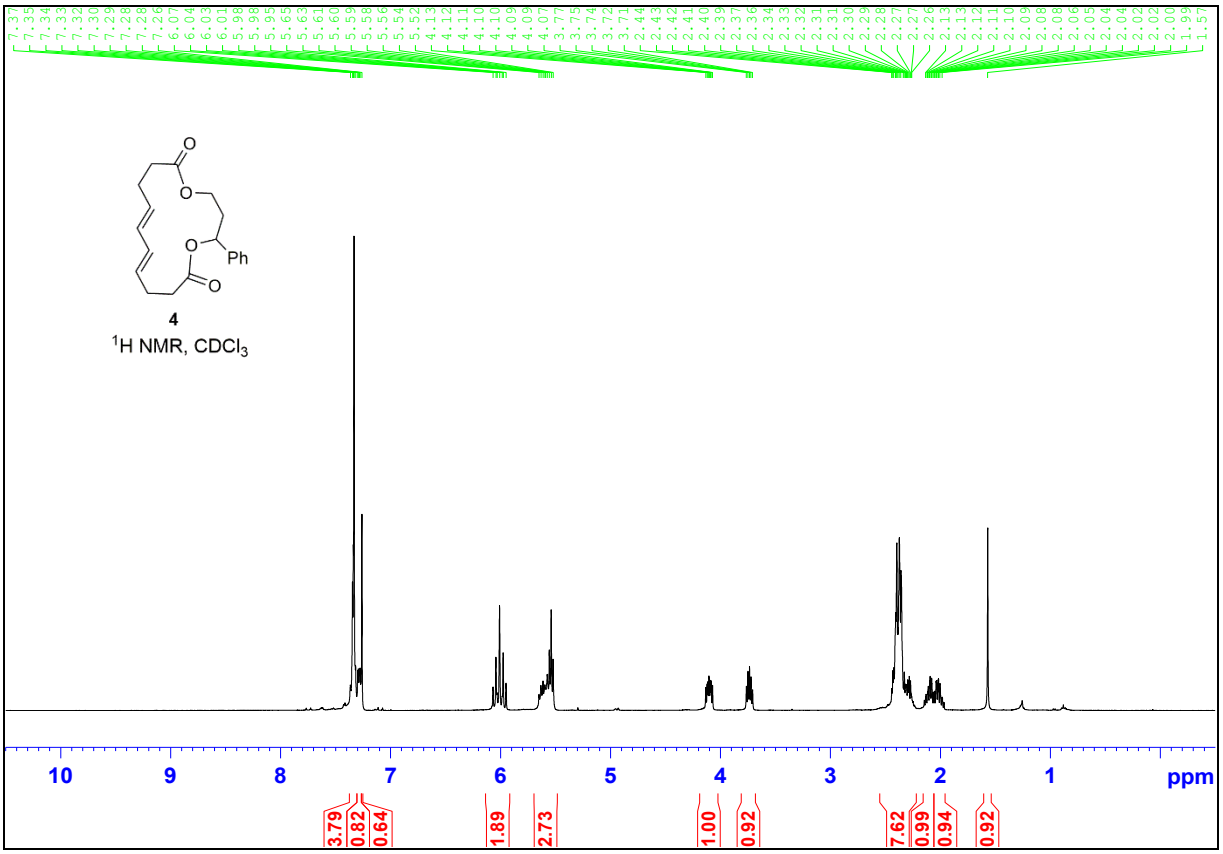
O
O
HO
Ph
16
1H NMR, CDCl3
ppm


Bu3Sn
O
O
HO
Ph
16
13C NMR, CDCl3
ppm


Bu3Sn
O
O
O
Ph
I
O
20
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
5.07
1.00
1.12
1.65
1.17
1.01
1.09
5.46
2.82
1.19
1.11
0.54
6.44
6.65
15.06


Bu3Sn
O
O
O
Ph
I
O
20
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm


4
^{1}H NMR, $CDCl_3$
10
9
8
7
6
5
4
3
2
1
ppm
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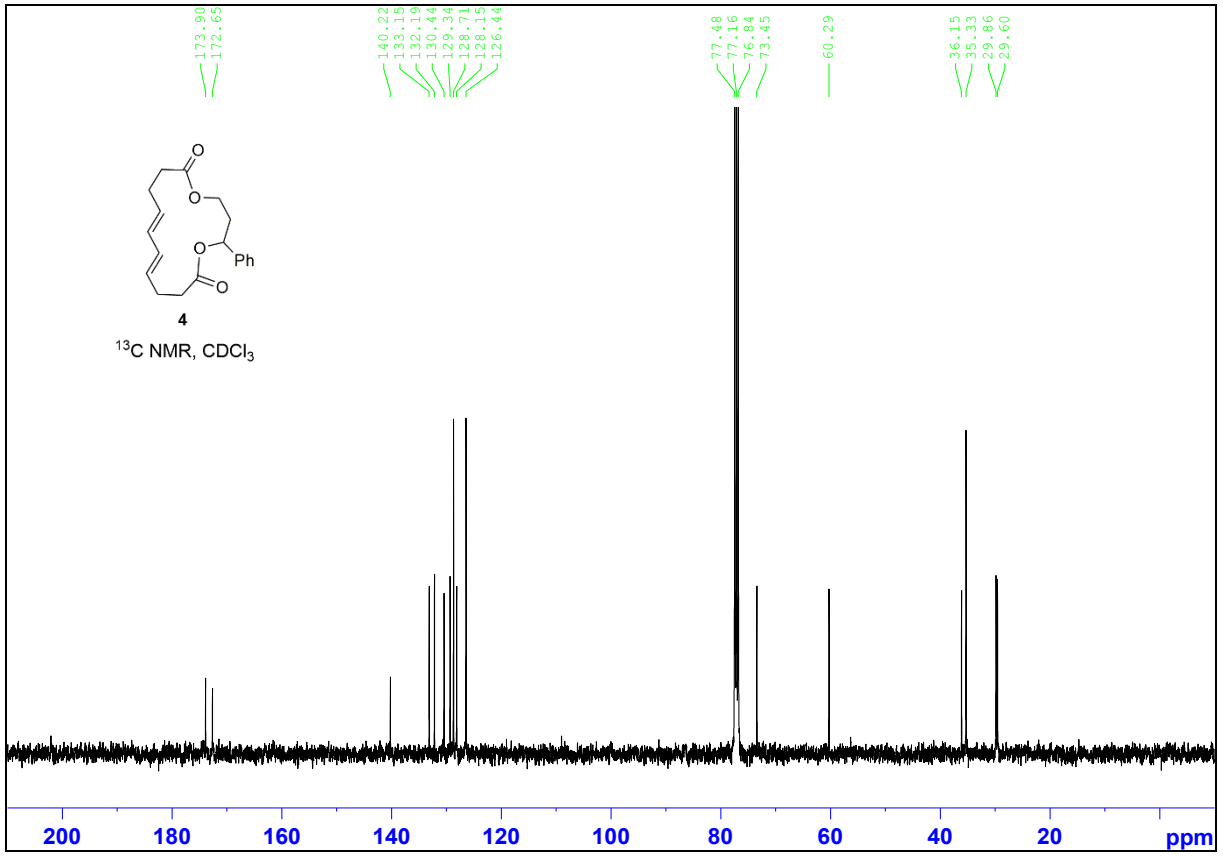
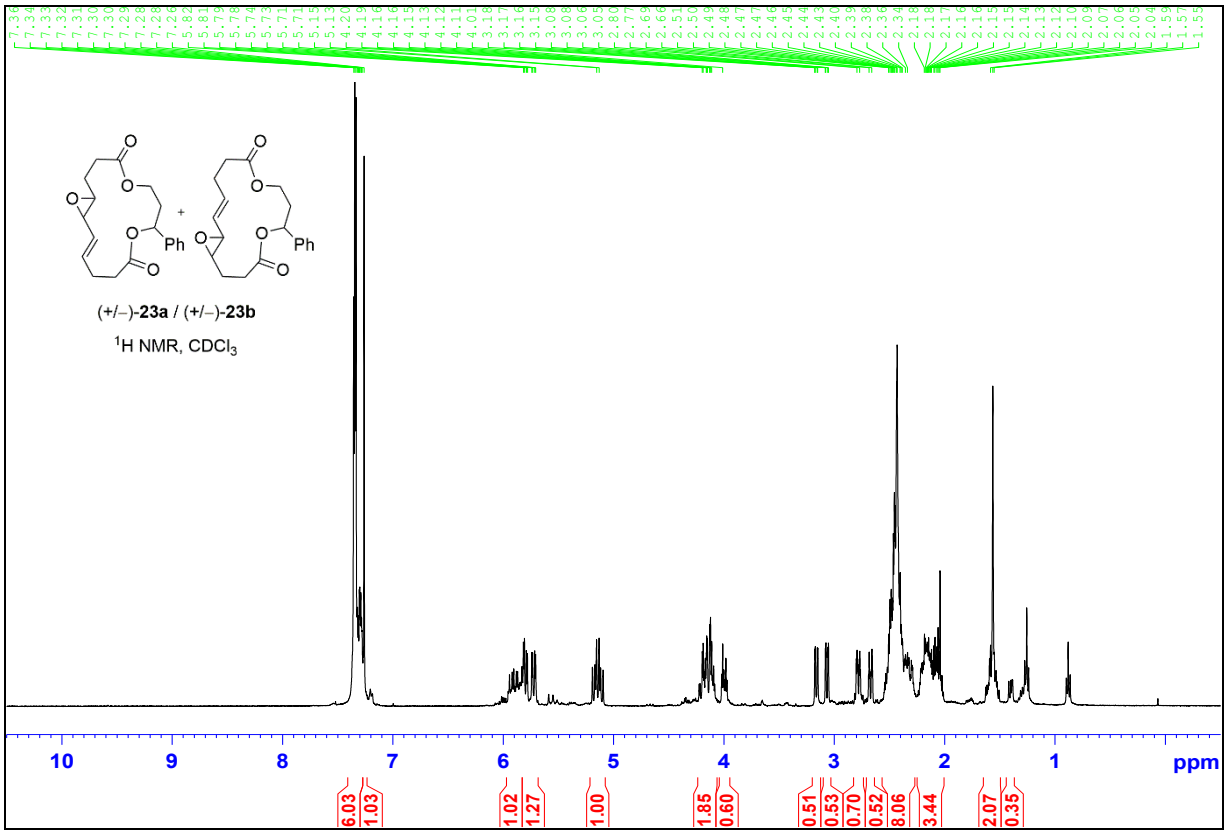
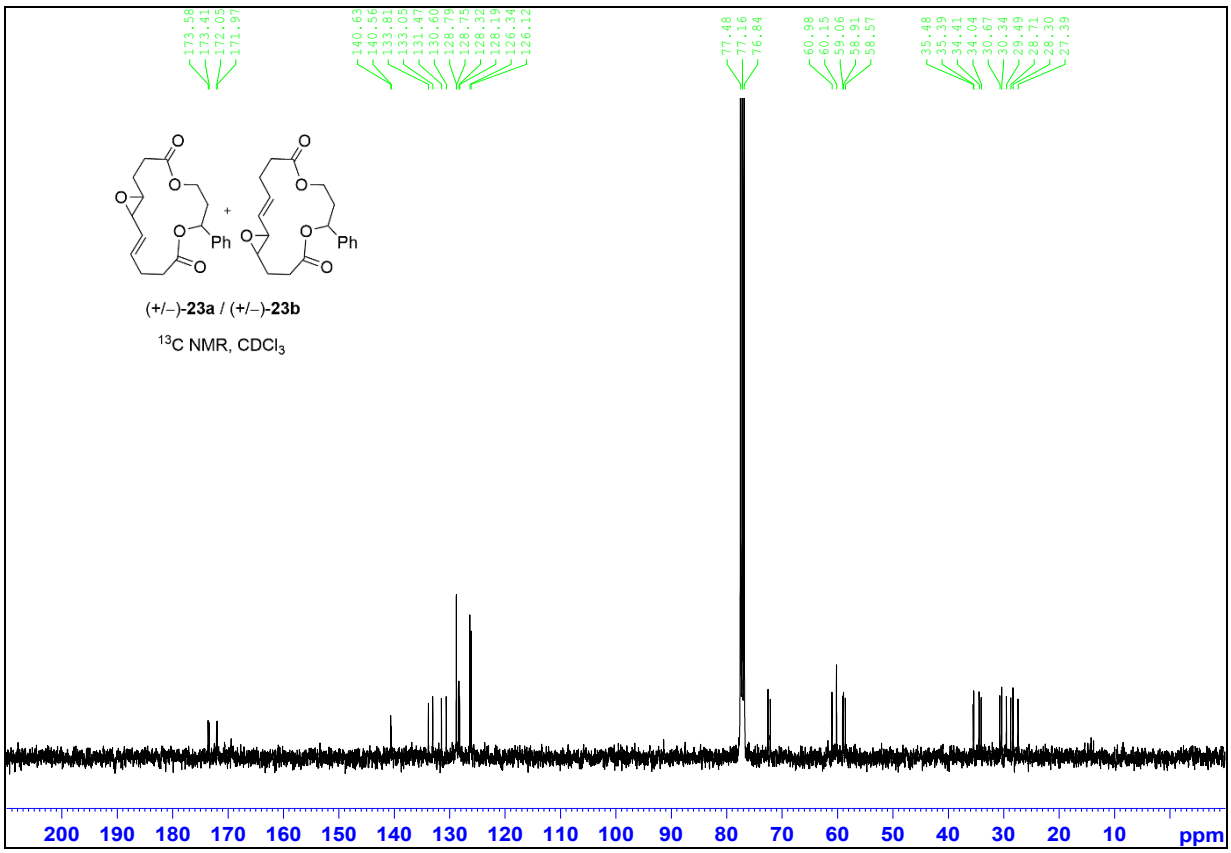
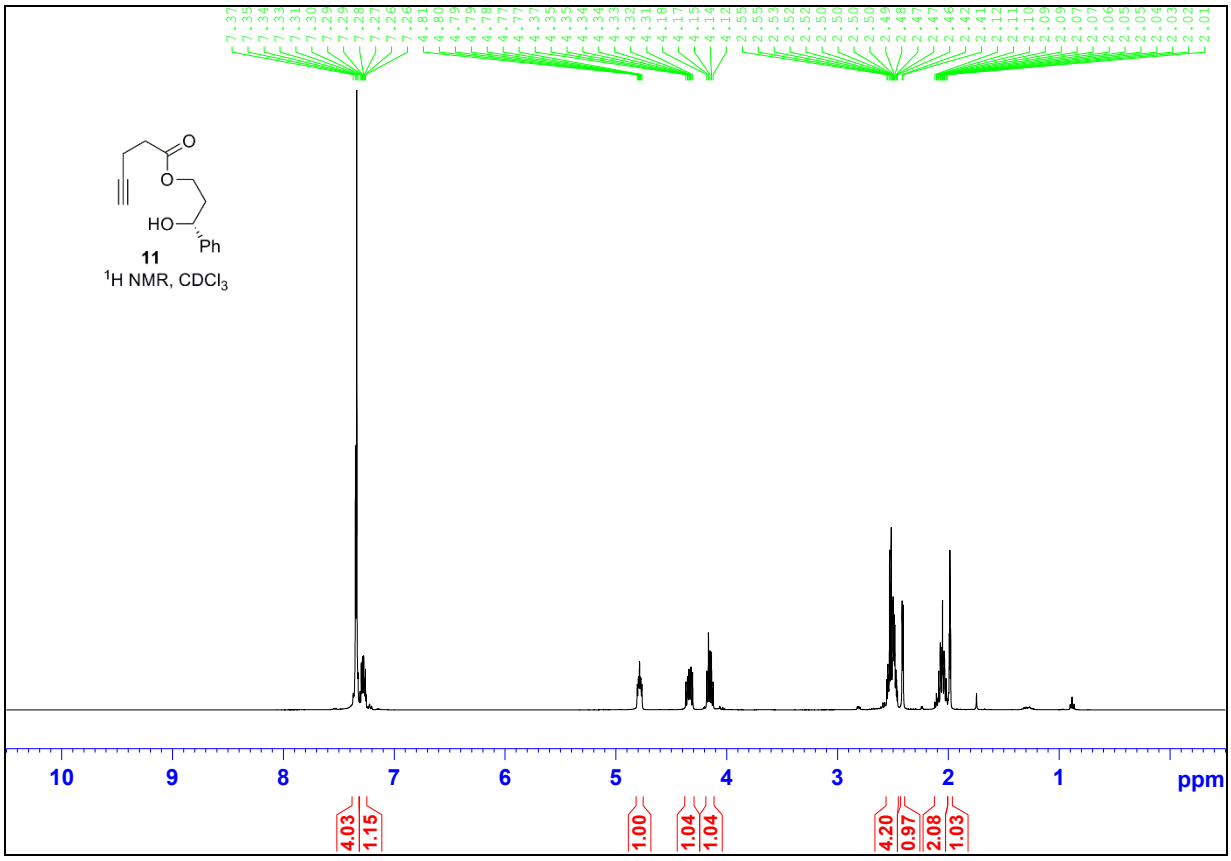
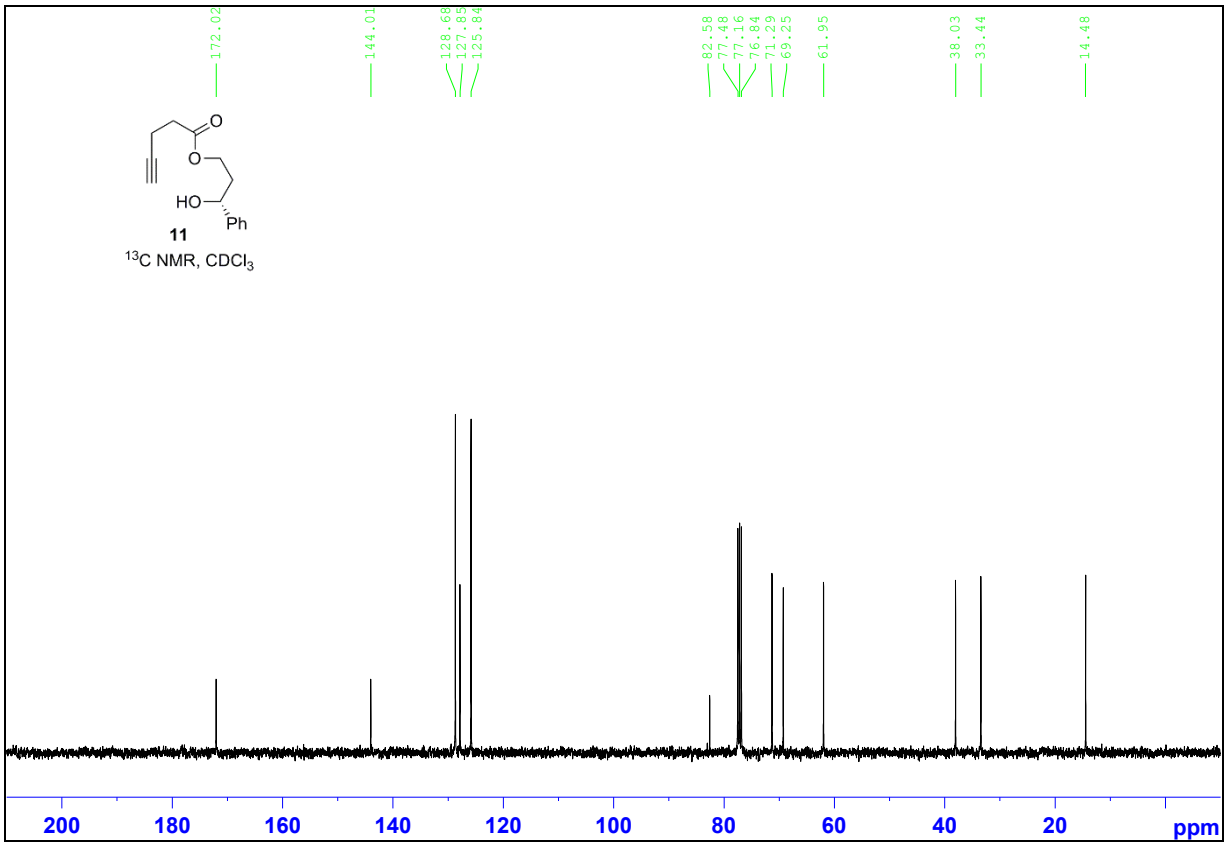
0.82
0.64
1.89
2.73
1.00
0.92
7.62
0.99
0.94
0.92

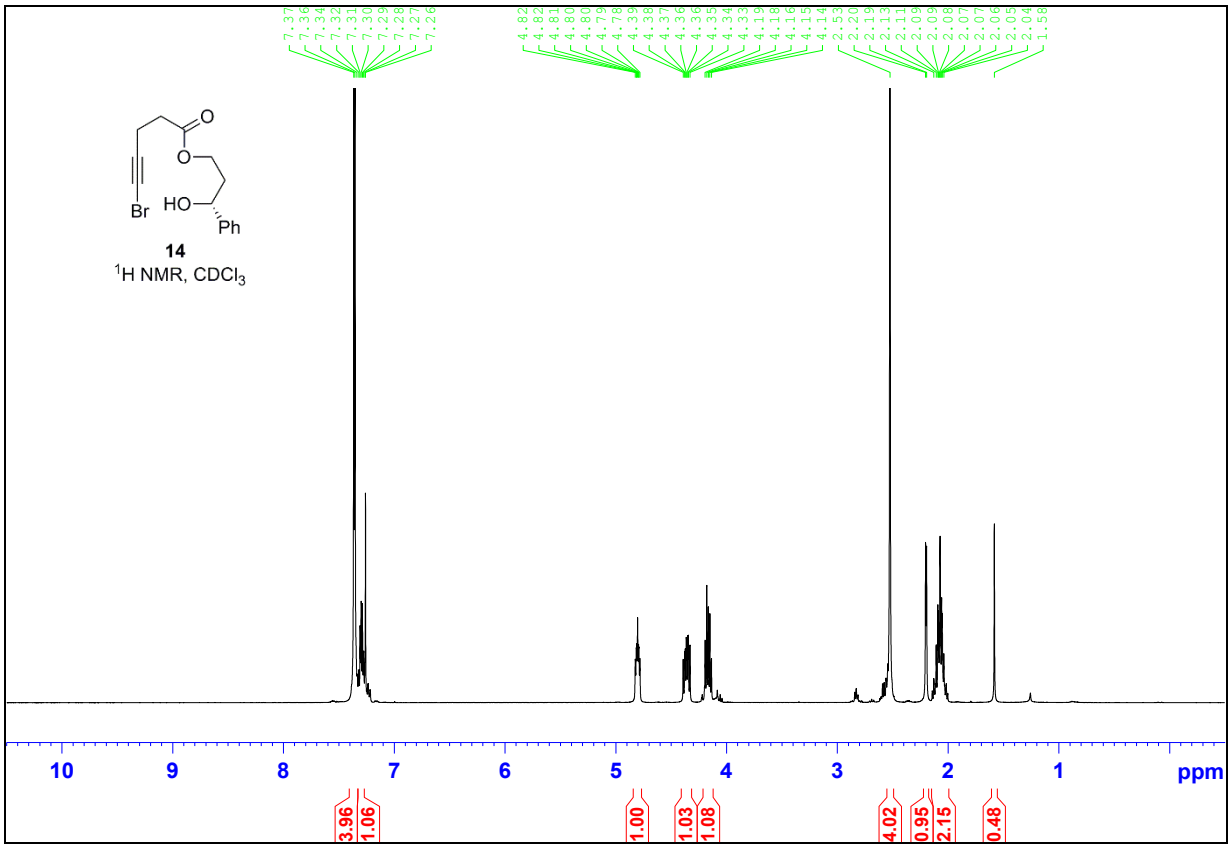

4
^{13}C NMR, $CDCl_3$
200
180
160
140
120
100
80
60
40
20
ppm


(+/–)-23a / (+/–)-23b
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
6.03
1.03
1.02
1.27
1.00
1.85
0.60
0.51
0.53
0.70
0.52
8.06
3.44
2.07
0.35


(+/–)-23a / (+/–)-23b
13C NMR, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


11
^{1}H NMR, CDCl$_3$
10
9
8
7
6
5
4
3
2
1
ppm
4.03
1.15
1.00
1.04
1.04
4.20
0.97
2.08
1.03


11
^{13}C NMR, CDCl$_3$
172.02
144.01
128.68
127.85
125.84
82.58
77.48
77.16
76.84
71.29
69.25
61.95
38.03
33.44
14.48
200
180
160
140
120
100
80
60
40
20
ppm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7.26
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4.82
4.81
4.80
4.80
4.79
4.78
4.39
4.38
4.37
4.36
4.36
4.35
4.34
4.33
4.19
4.18
4.16
4.15
4.14
2.53
2.20
2.19
2.13
2.11
2.09
2.09
2.08
2.07
2.07
2.06
2.05
2.04
1.58
O
O
Br
HO
Ph
14
1H NMR, CDCl3
10
9
8
7
6
5
4
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ppm
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1.06
1.00
1.03
1.08
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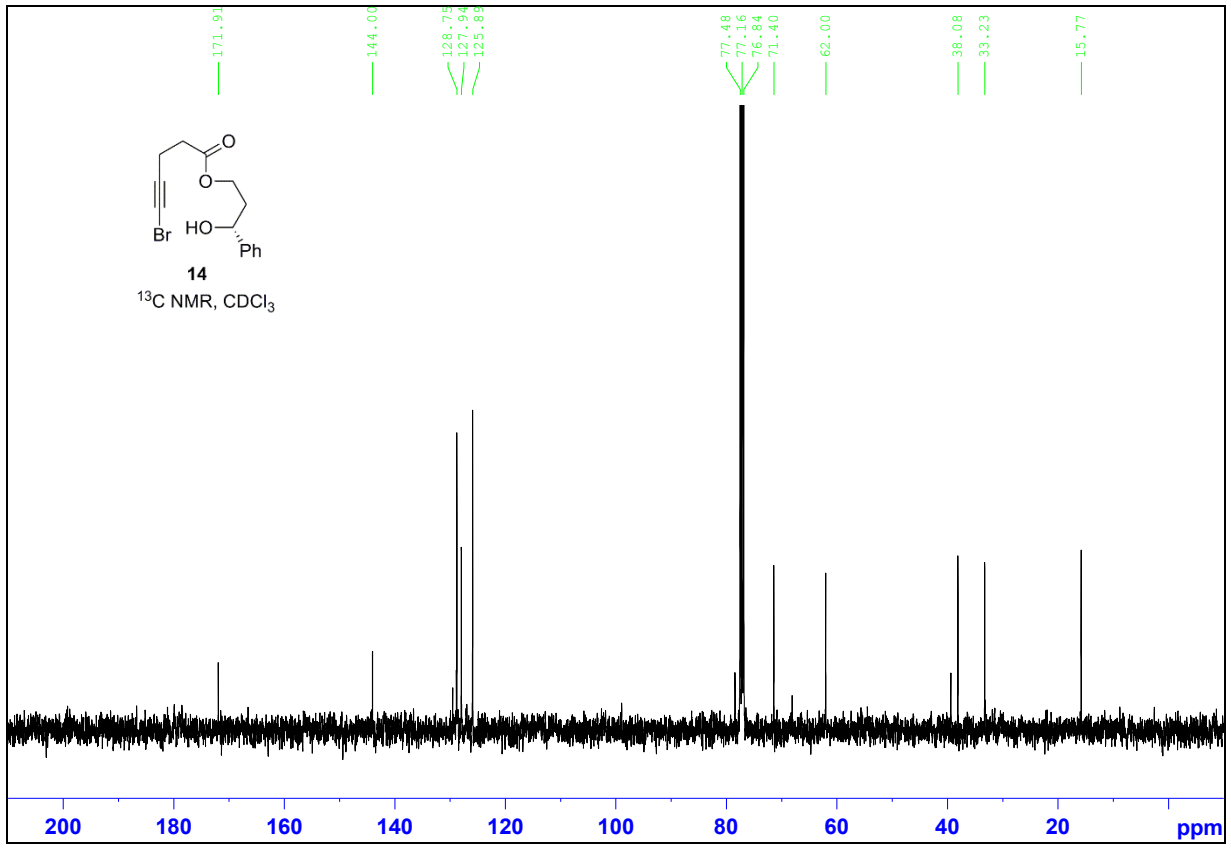
0.48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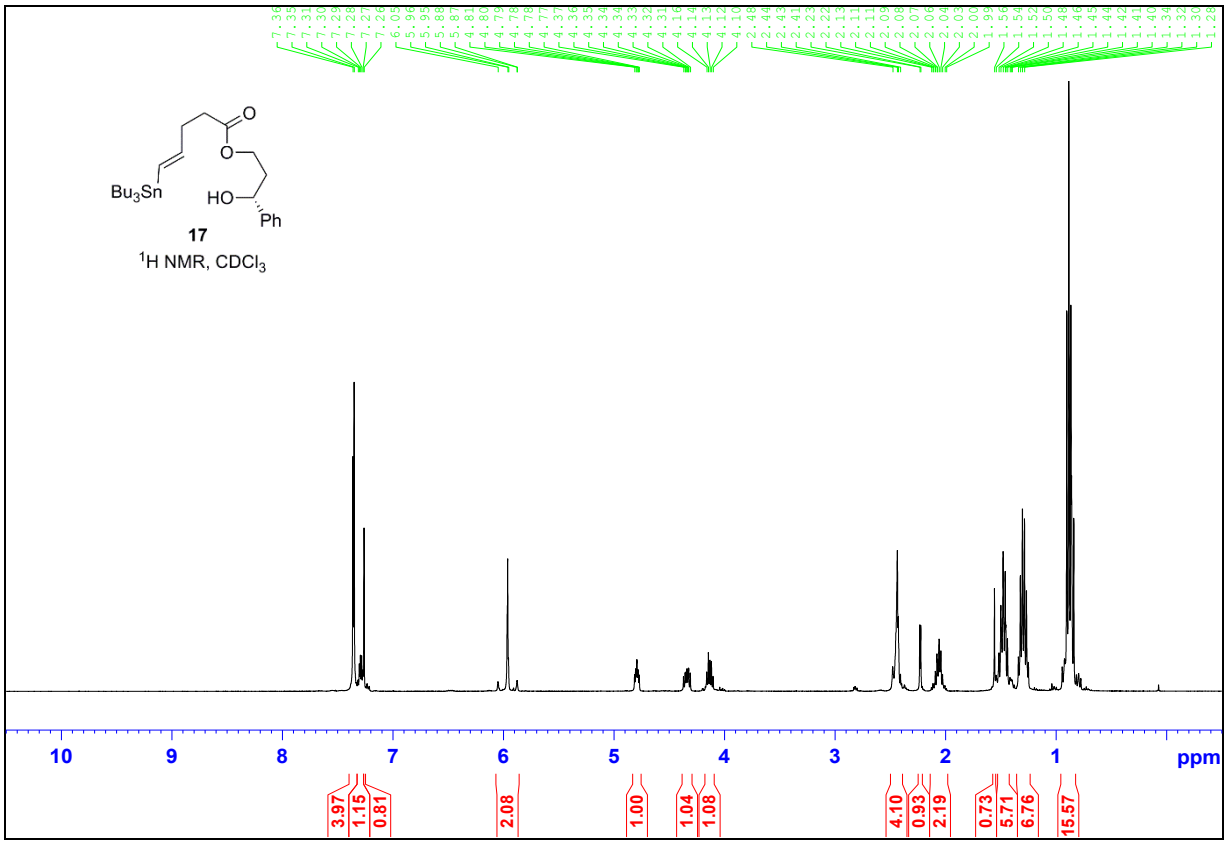
76.84
71.40
62.00
38.08
33.23
15.77
O
O
Br
HO
Ph
14
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm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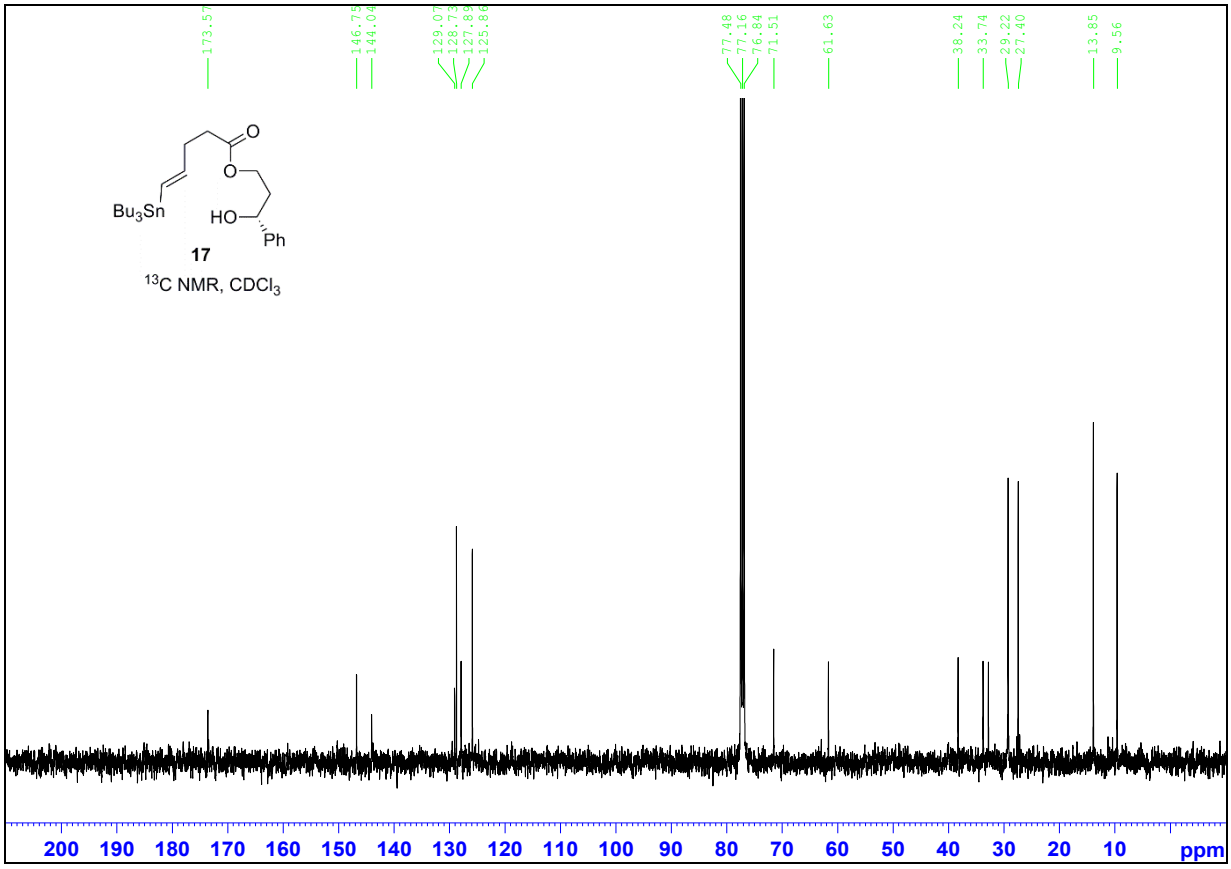
HO
Ph
17
1H NMR, CDCl3
ppm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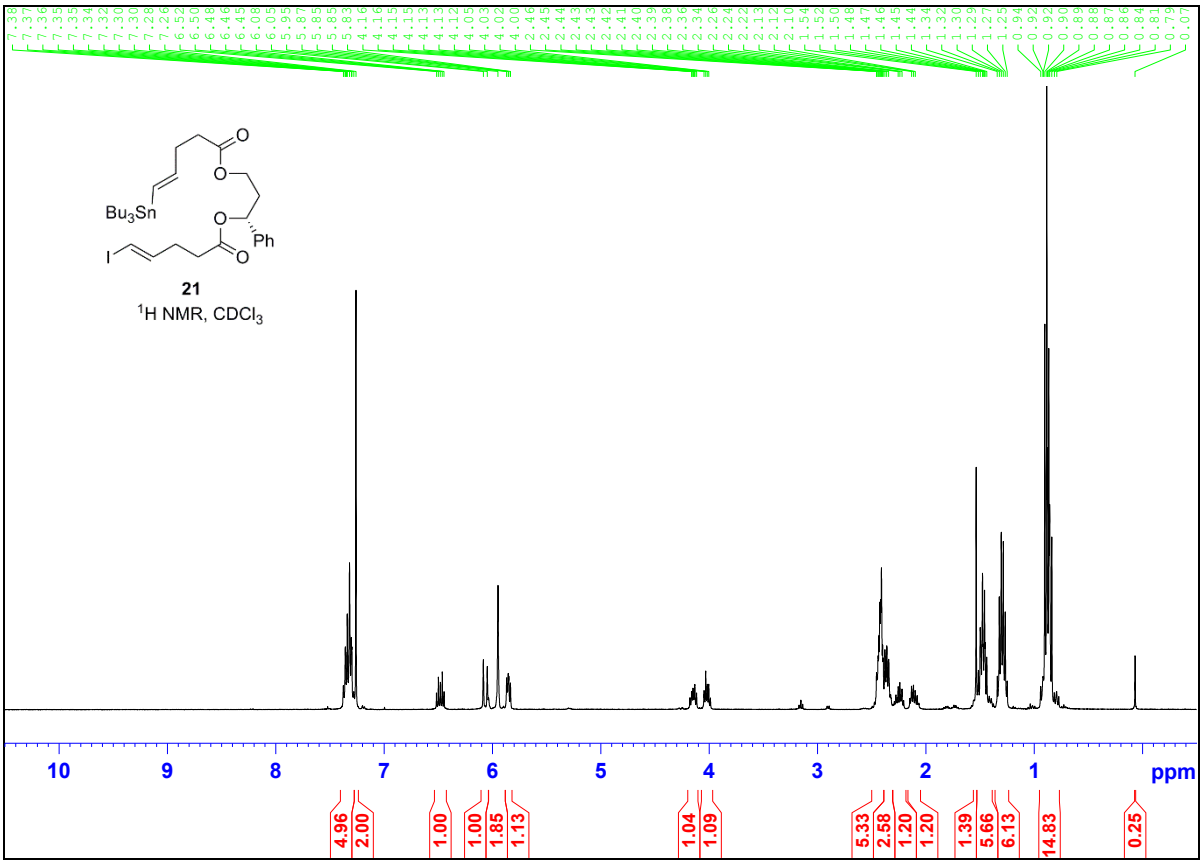
HO
Ph
17
13C NMR, CDCl3
ppm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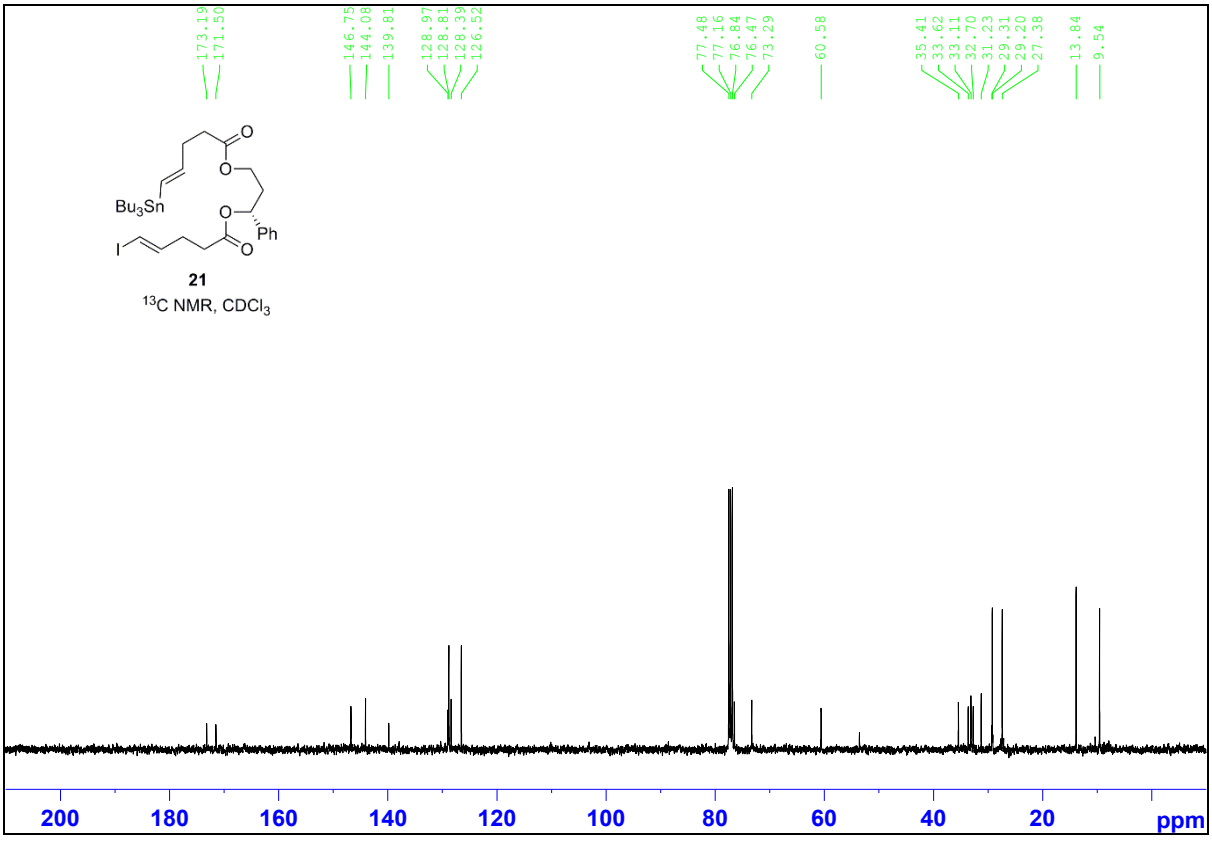
Ph
I
21
1H NMR, CDCl3
ppm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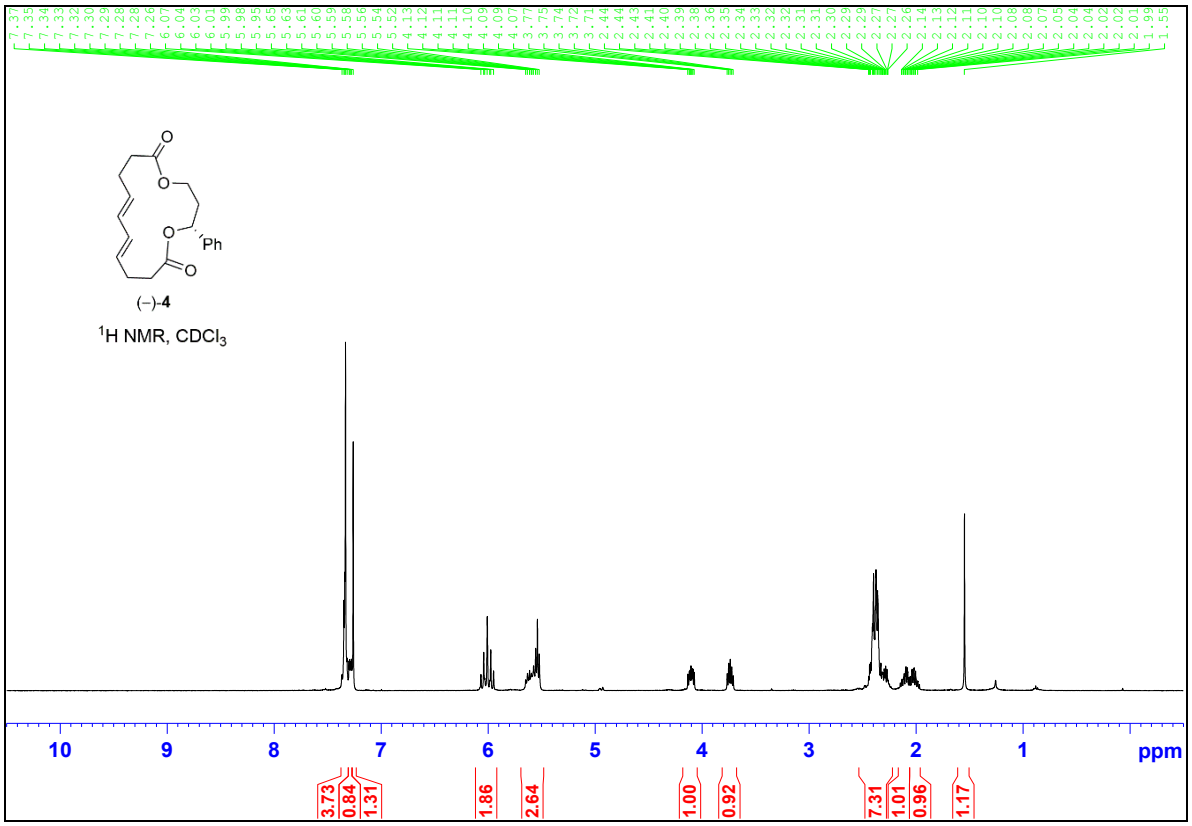
Ph
I
21
13C NMR, CDCl3
ppm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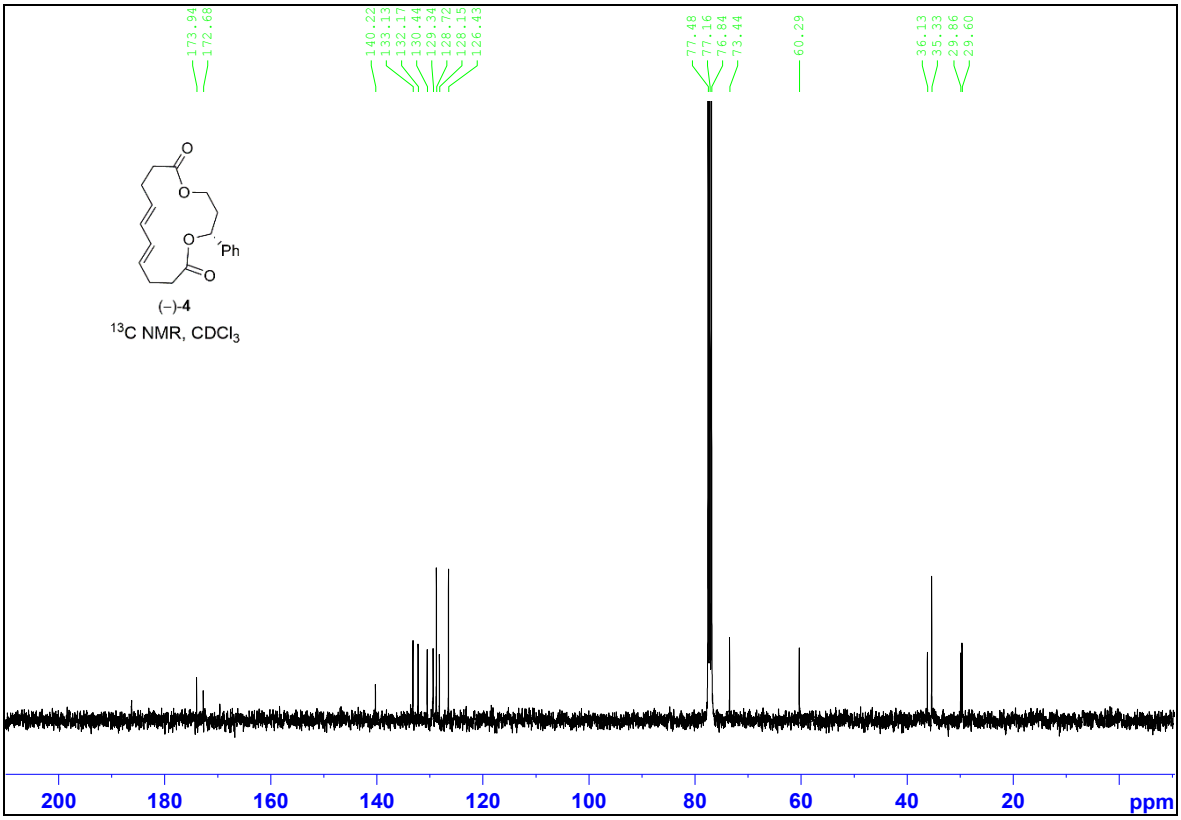
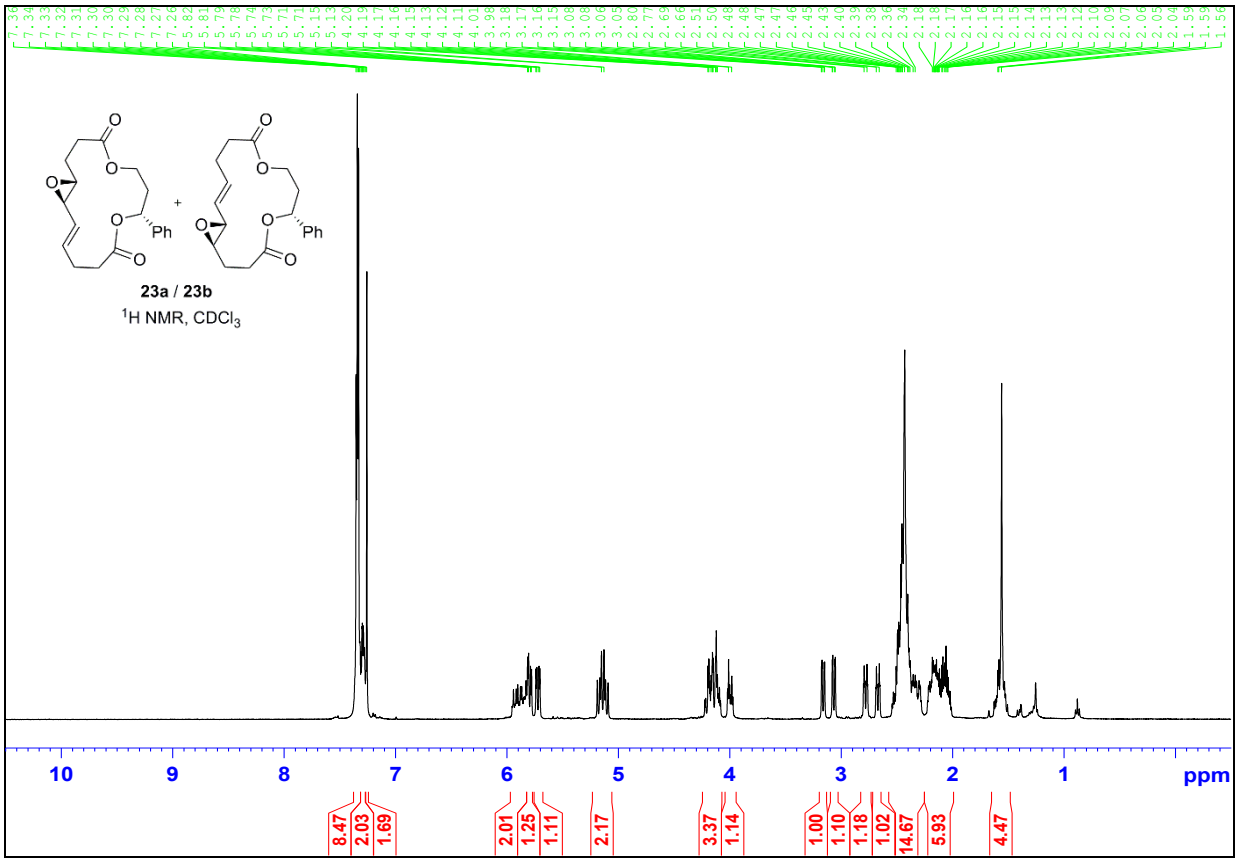
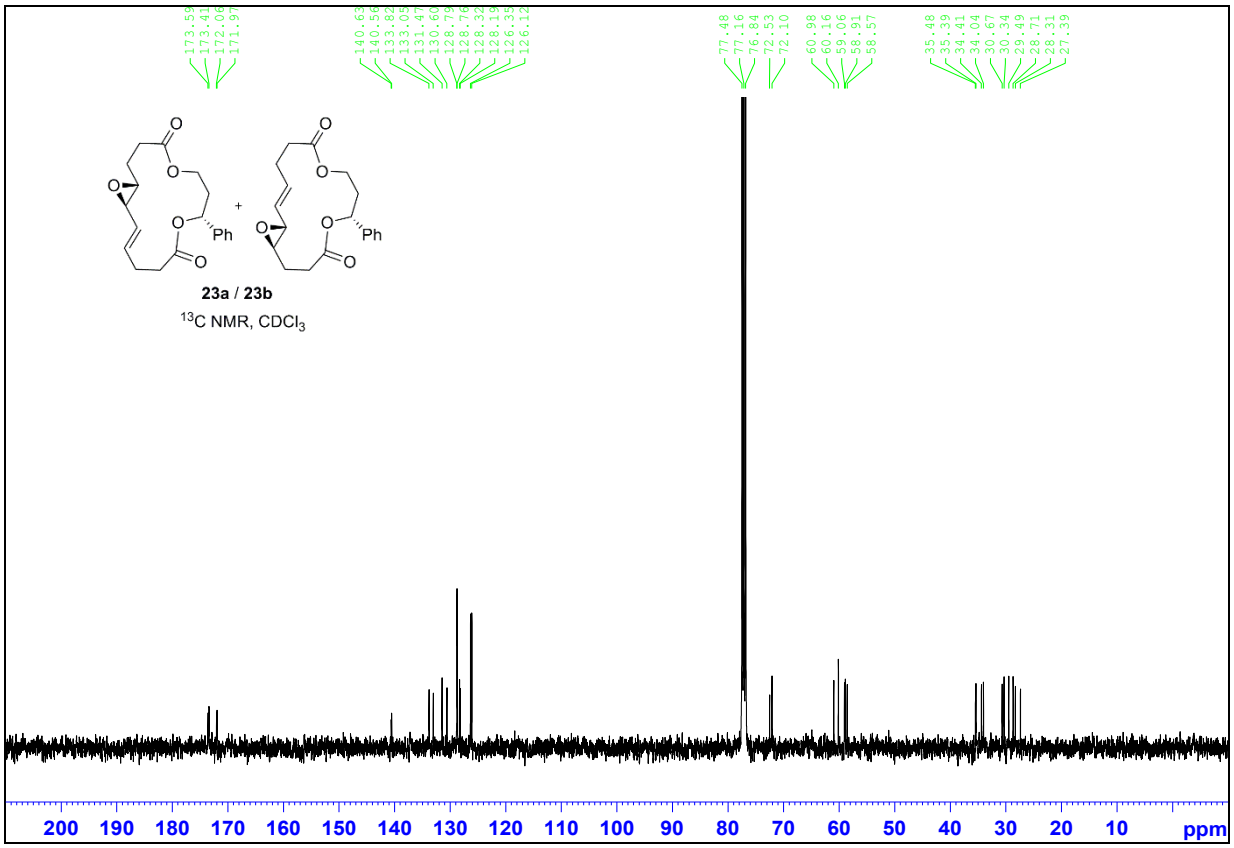
ppm


(–)-4
^{13}C NMR, CDCl$_3$
ppm


23a / 23b
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
8.47
2.03
1.69
2.01
1.25
1.11
2.17
3.37
1.14
1.00
1.10
1.18
1.02
14.67
5.93
4.47


23a / 23b
13C NMR, CDCl3
200
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140
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120
110
100
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70
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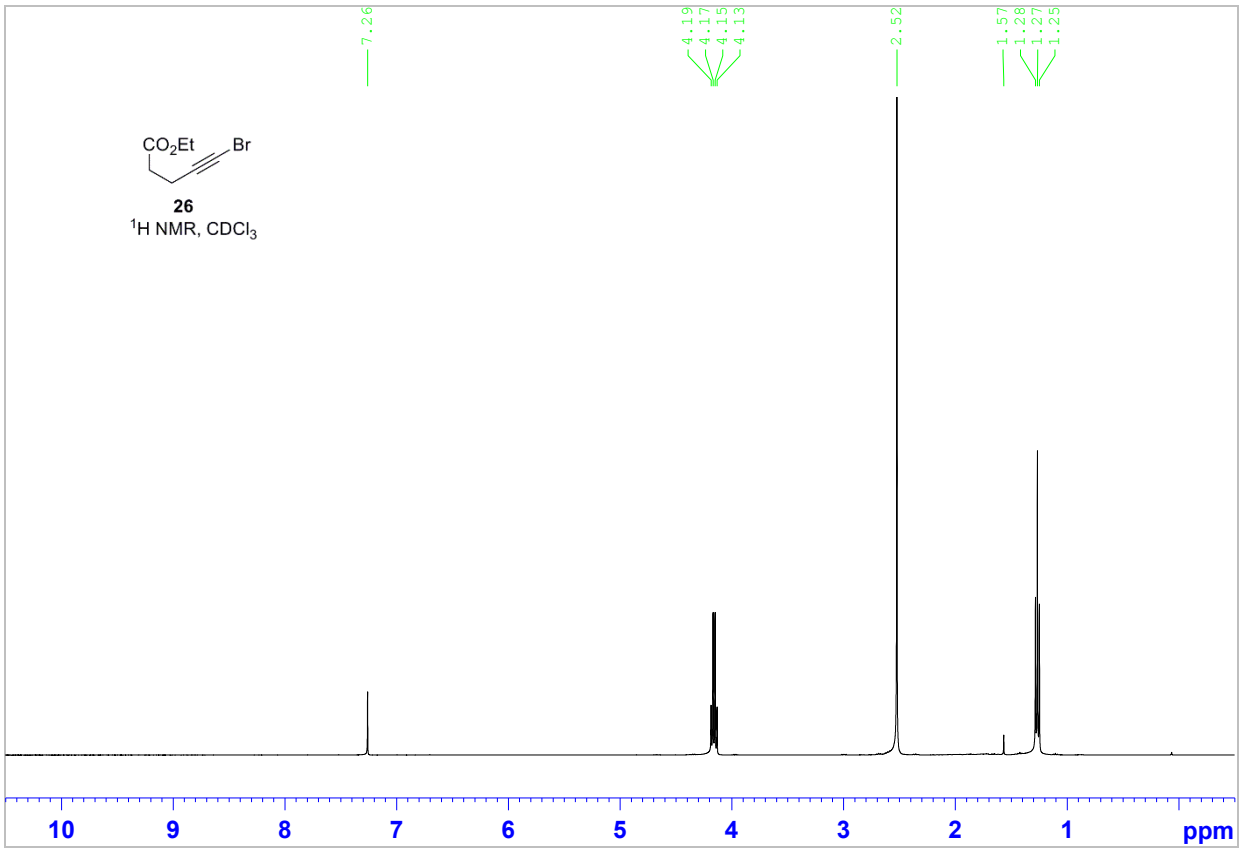
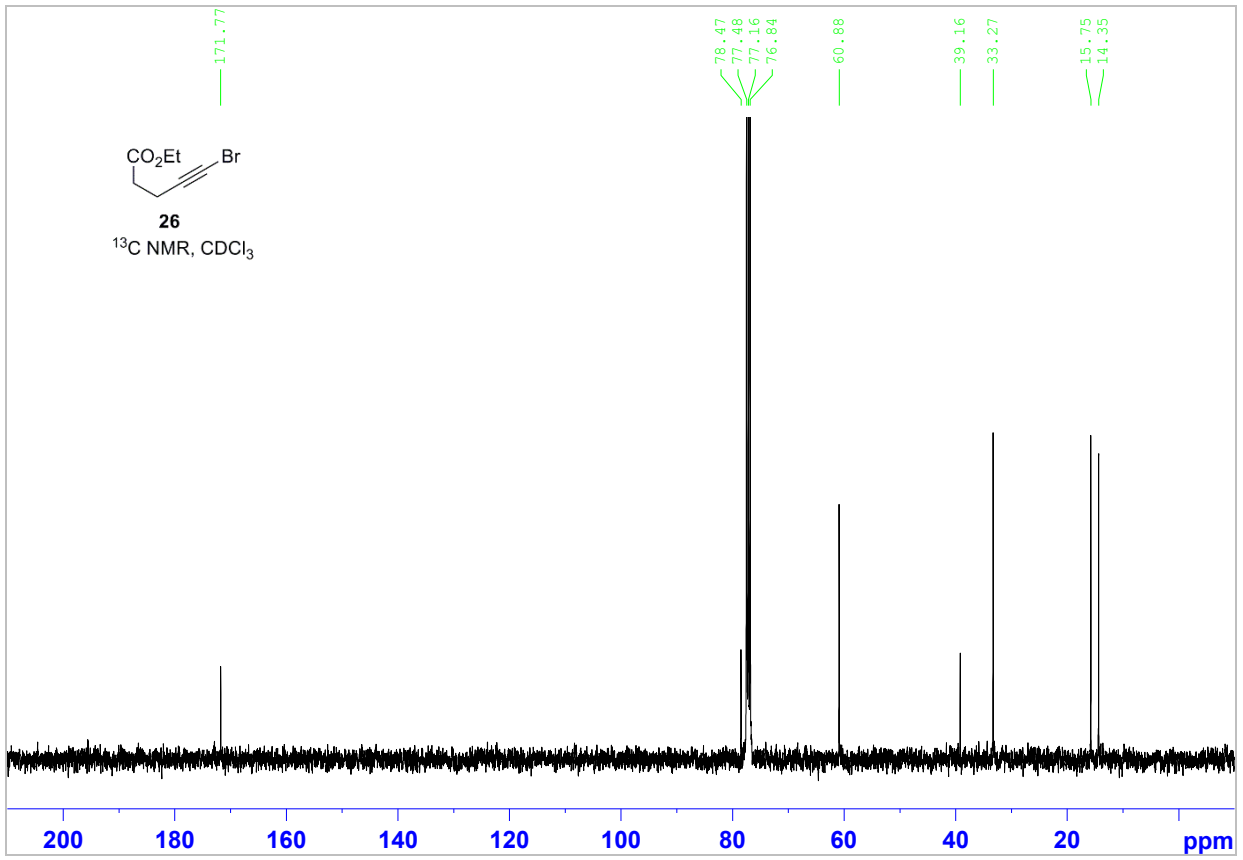
50
40
30
20
10
ppm


7.26
4.19
4.17
4.15
4.13
2.52
1.57
1.28
1.27
1.25
CO2Et
Br
26
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm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77.16
76.84
60.88
39.16
33.27
15.75
14.35
CO2Et
Br
26
13C NMR, CDCl3
200
180
160
140
120
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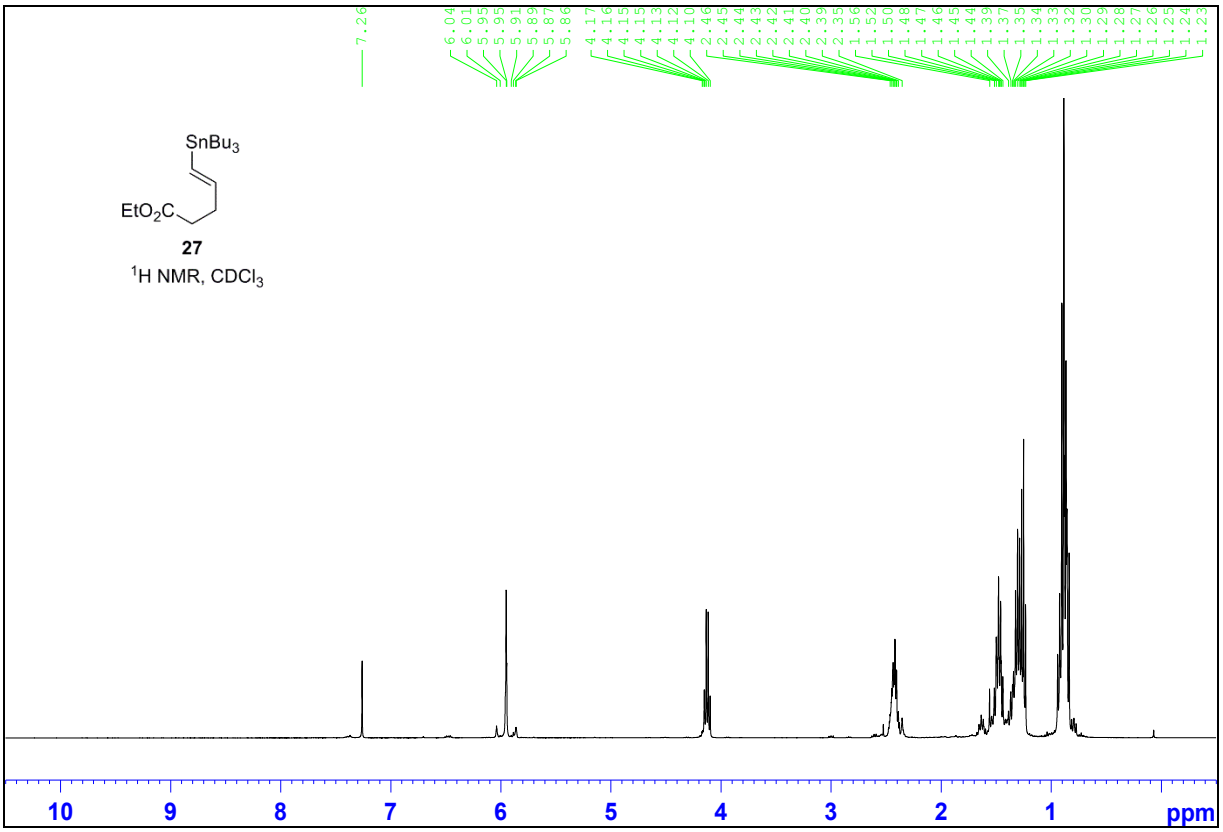
20
ppm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6.04
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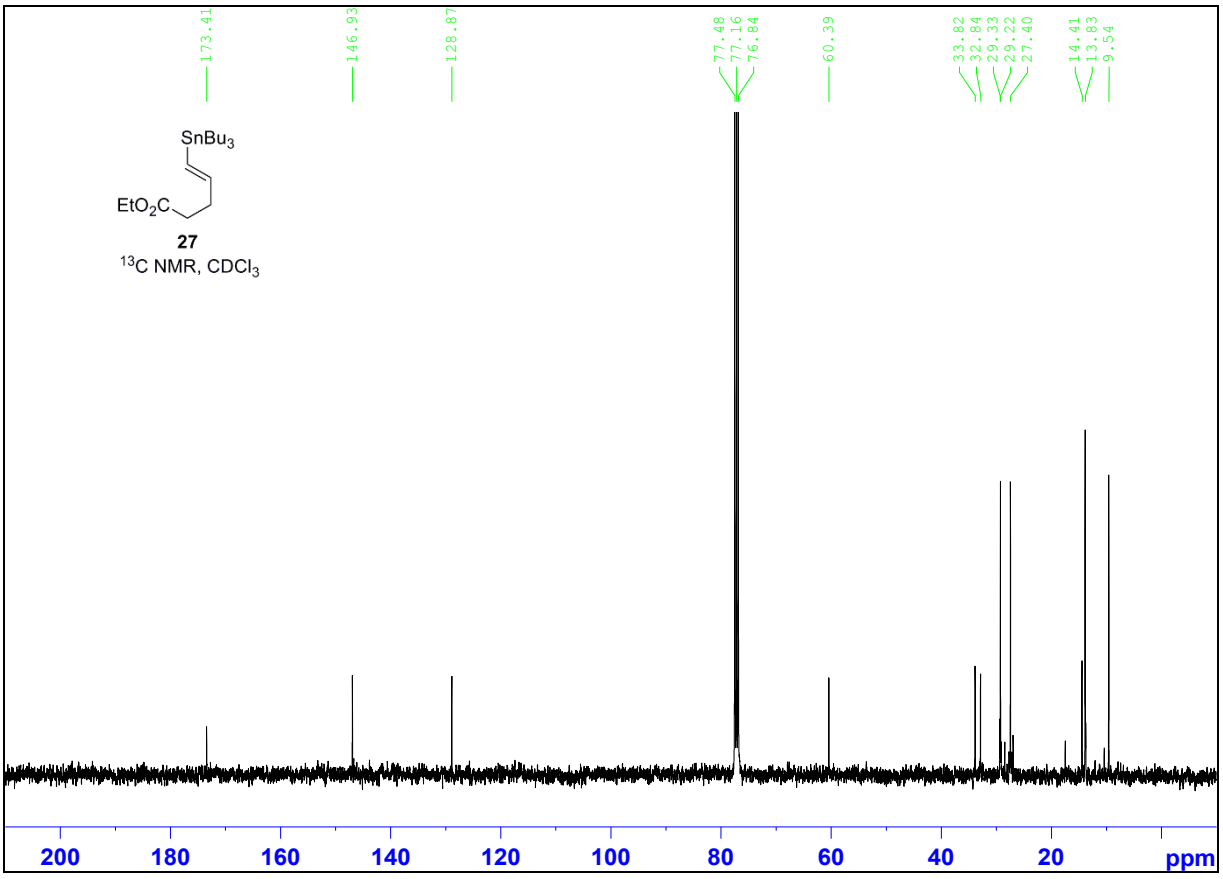
4.15
4.13
4.12
4.10
2.46
2.45
2.44
2.43
2.42
2.41
2.40
2.39
2.35
1.56
1.52
1.50
1.48
1.47
1.46
1.45
1.44
1.39
1.37
1.35
1.34
1.33
1.32
1.30
1.29
1.28
1.27
1.26
1.25
1.24
1.23
SnBu3
EtO2C
27
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm


173.41
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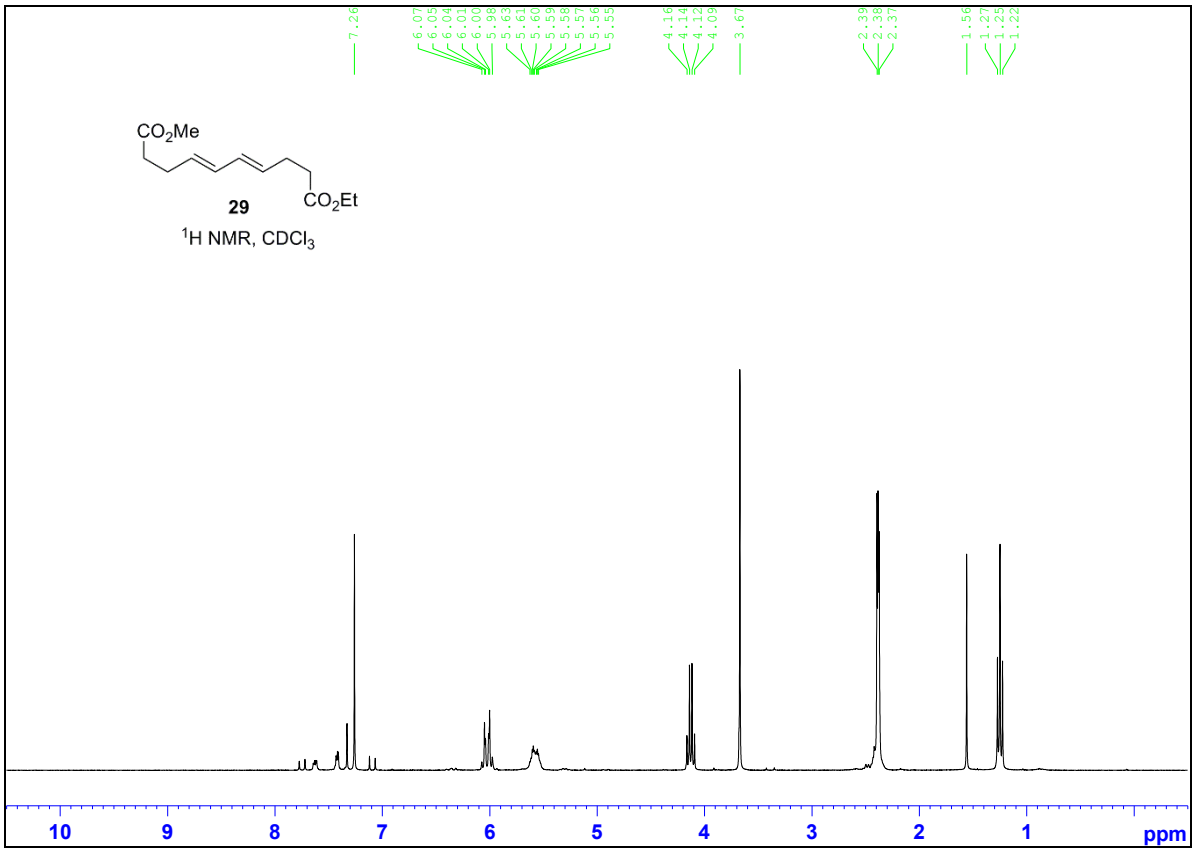
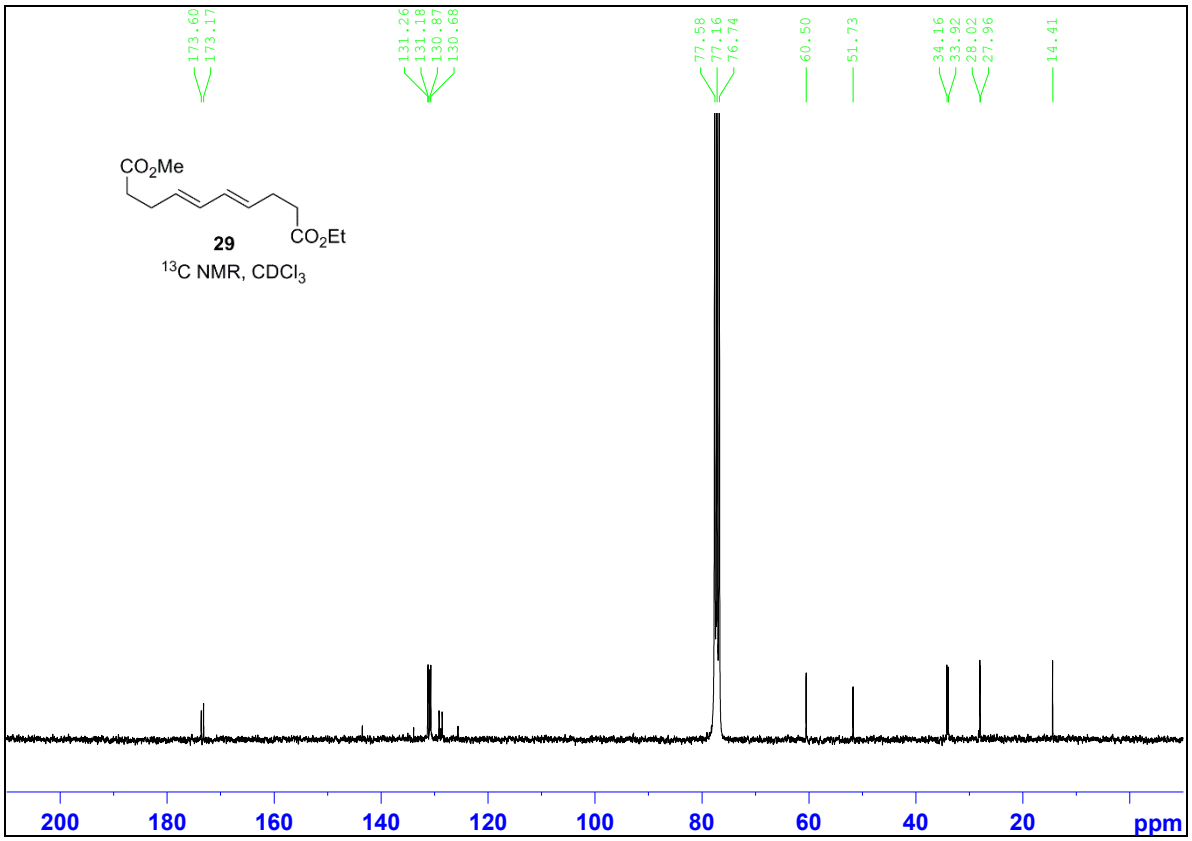
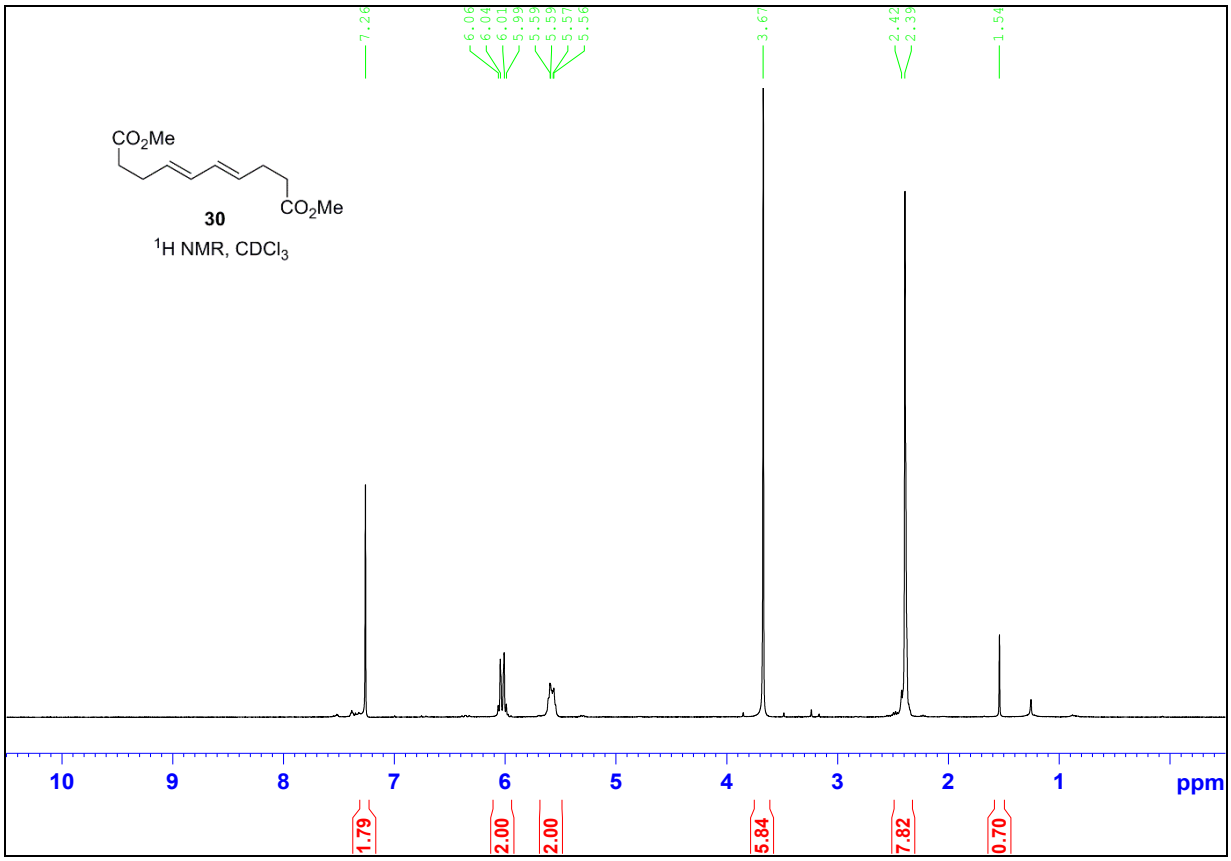
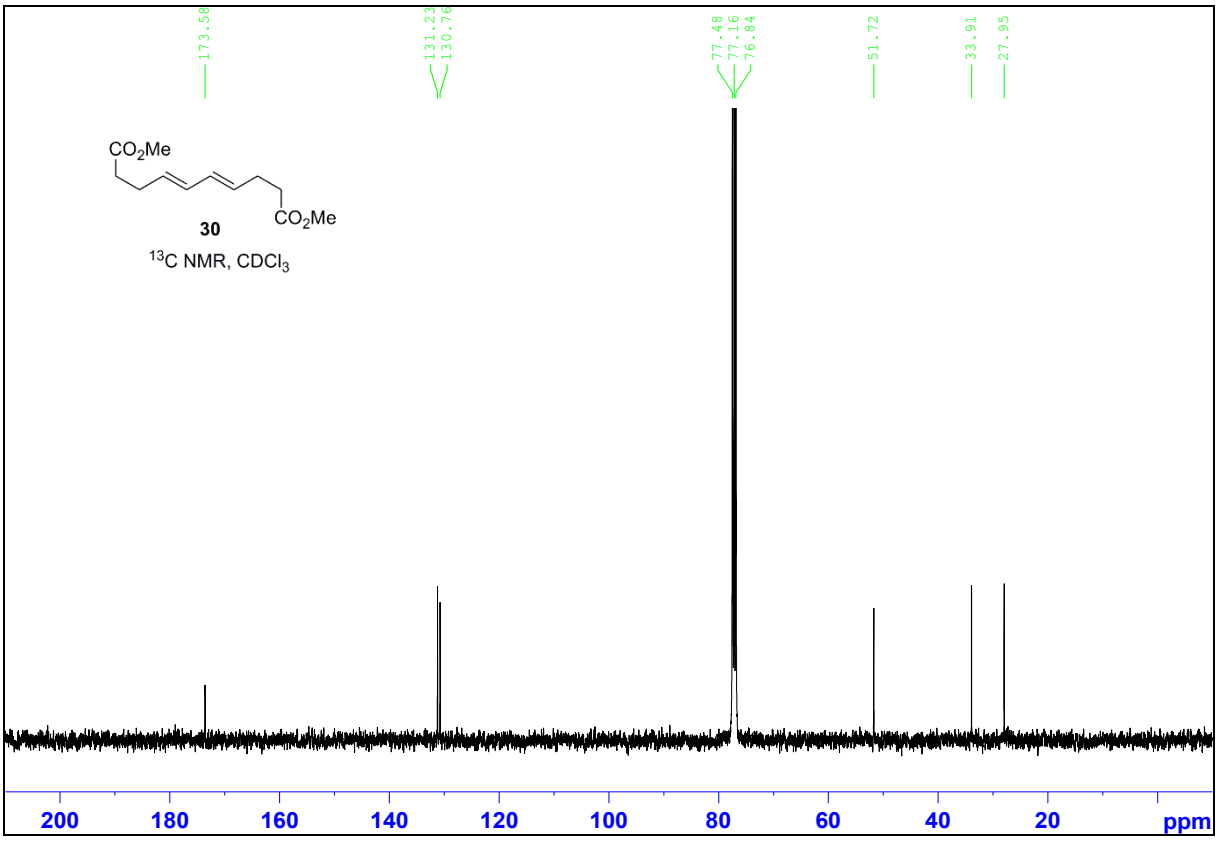
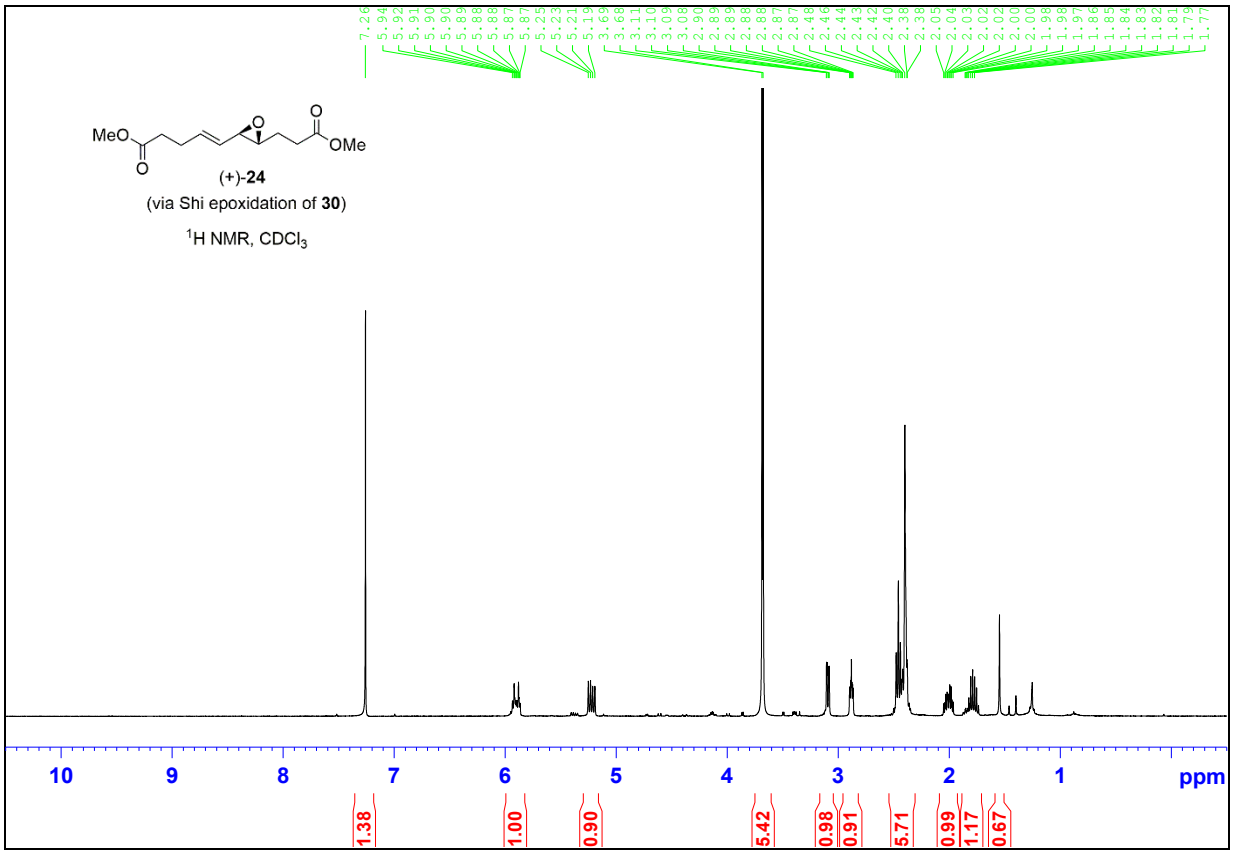
128.87
77.48
77.16
76.84
60.39
33.82
32.84
29.33
29.22
27.40
14.41
13.83
9.54
SnBu3
EtO2C
27
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm

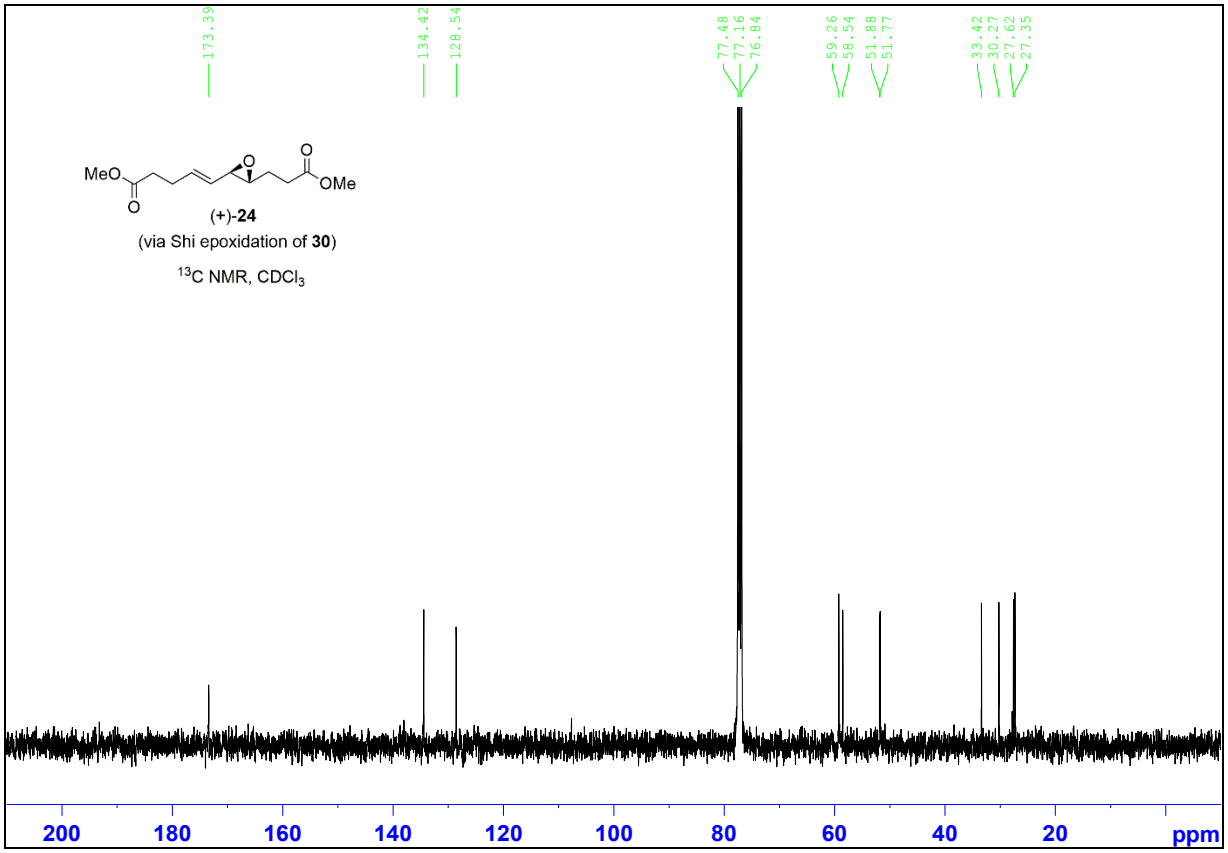

7.26
6.07
6.05
6.04
6.01
6.00
5.98
5.63
5.61
5.60
5.59
5.58
5.57
5.56
5.55
4.16
4.14
4.12
4.09
3.67
2.39
2.38
2.37
1.56
1.27
1.25
1.22
CO2Me
CO2Et
29
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm

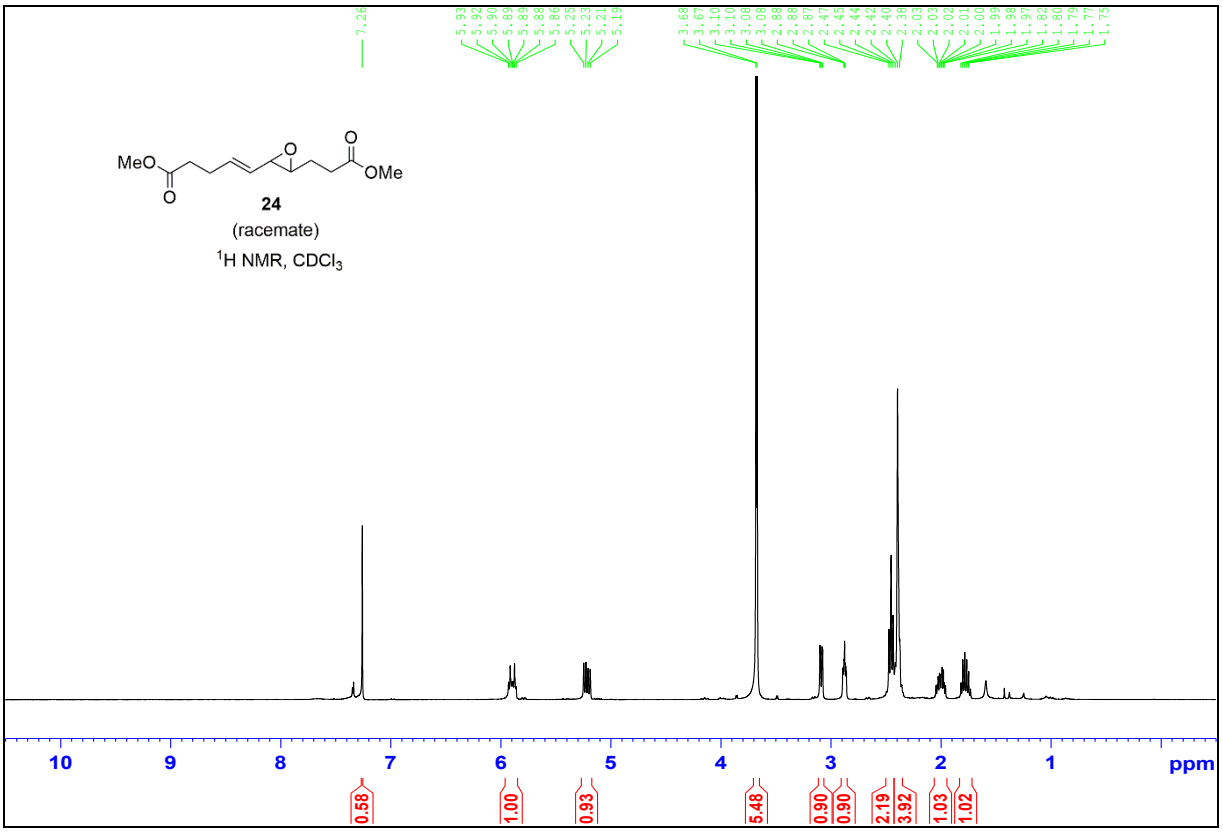

173.60
173.17
131.26
131.18
130.87
130.68
77.58
77.16
76.74
60.50
51.73
34.16
33.92
28.02
27.96
14.41
CO2Me
CO2Et
29
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm

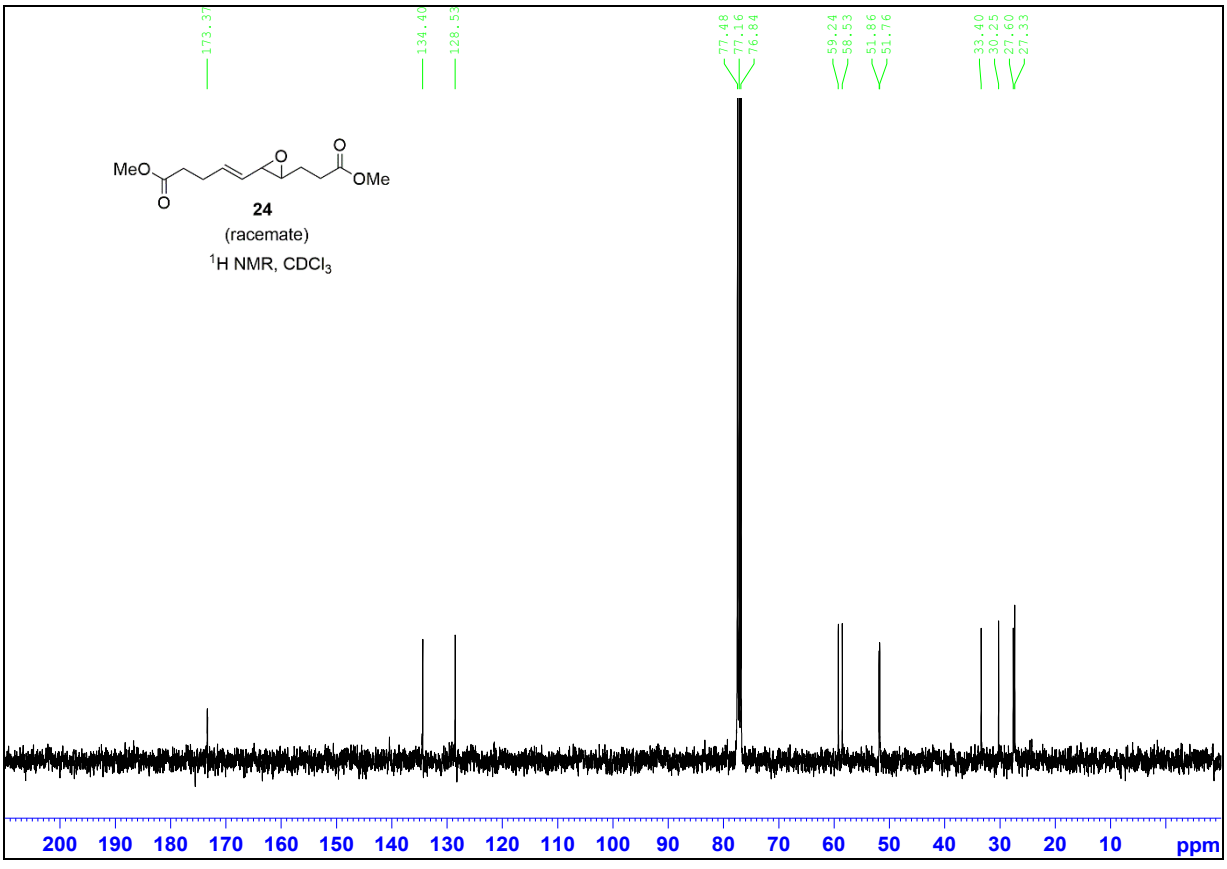

7.26
6.06
6.04
6.01
5.99
5.59
5.59
5.57
5.56
3.67
2.42
2.39
1.54
CO2Me
CO2Me
30
1H NMR, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
1.79
2.00
2.00
5.84
7.82
0.70

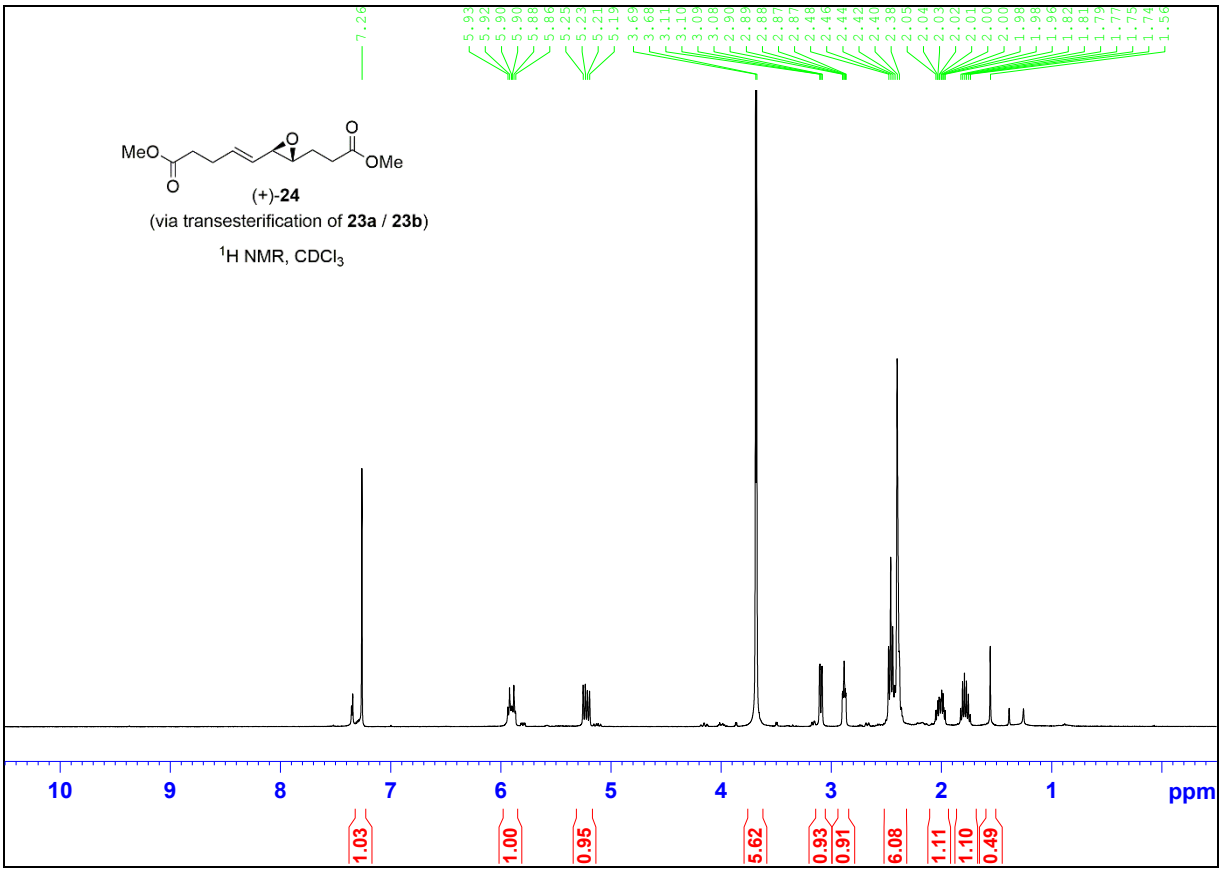

173.58
131.23
130.76
77.48
77.16
76.84
51.72
33.91
27.95
CO2Me
CO2Me
30
13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm

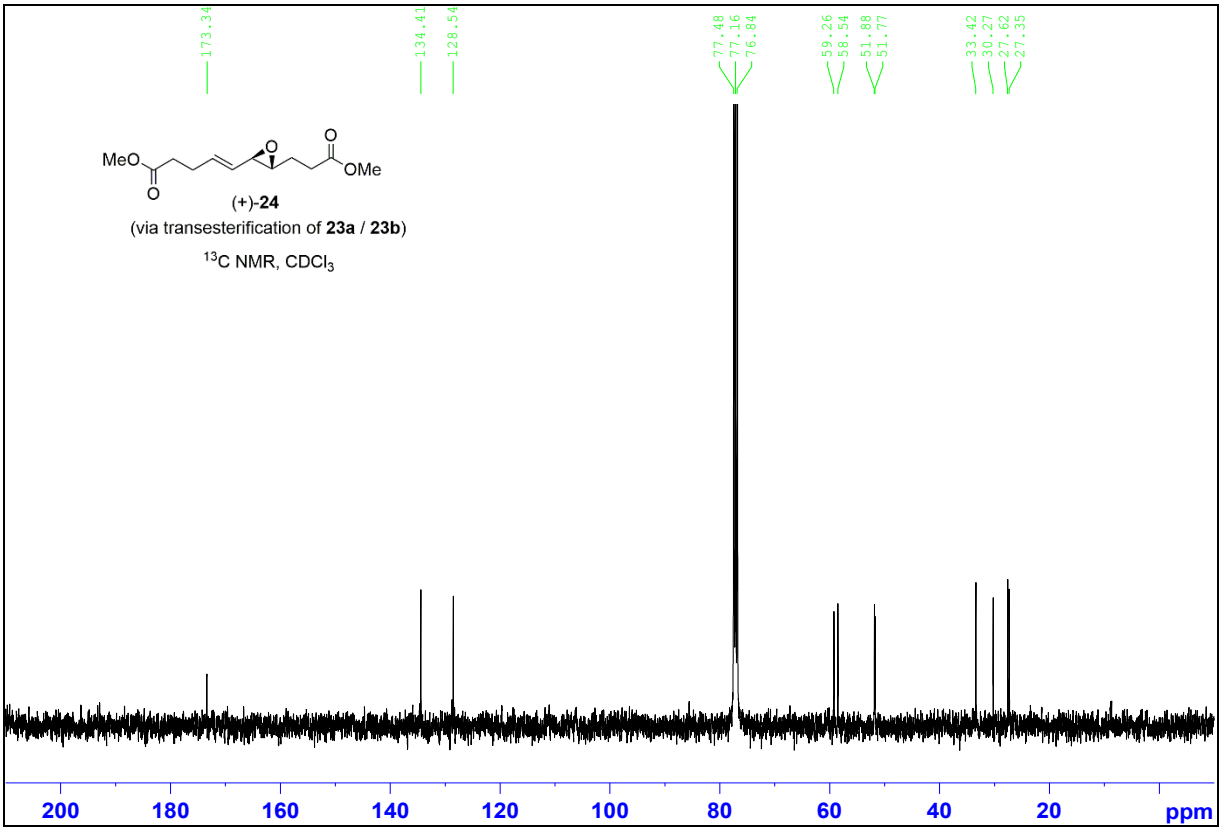

MeO
O
O
O
OMe
(+)-24
(via Shi epoxidation of 30)
1H NMR, CDCl3
ppm
1.38
1.00
0.90
5.42
0.98
0.91
5.71
0.99
1.17
0.67


MeO
O
O
O
OMe
(+)-24
(via Shi epoxidation of 30)
13C NMR, CDCl3
ppm


MeO
O
O
OMe
24
(racemate)
^{1}H NMR, CDCl$_3$
ppm


MeO
O
O
OMe
24
(racemate)
^{1}H NMR, CDCl$_3$
ppm


MeO
O
O
O
OMe
(+)-24
(via transesterification of 23a / 23b)
1H NMR, CDCl3
ppm


MeO
O
O
O
OMe
(+)-24
(via transesterification of 23a / 23b)
13C NMR, CDCl3
ppm