SUPPORTING INFORMATION

2-Nitropyrrole Cross-Coupling Enables a Second Generation Synthesis of the Heronapyrrole Antibiotic Natural Product Family

Xiao-Bo Ding,[†] Daniel P. Furkert[*†] and Margaret A. Brimble[*†]

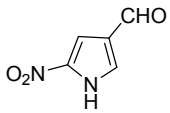
[†] *School of Chemical Sciences, The University of Auckland, 23 Symonds St, Auckland, New Zealand; Maurice Wilkins Centre for molecular Biodiscover, The University of Auckland, 3 Symonds St, Auckland, New Zealand*

CONTENTS

General Procedures

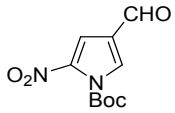
Unless otherwise noted, all reactions were performed under an oxygen-free atmosphere of nitrogen using standard techniques. Tetrahydrofuran (THF) and diethyl ether were freshly distilled over sodium/benzophenone ketyl. CH_2Cl_2 was freshly distilled from calcium hydride. All other reagents were used as received unless otherwise noted. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on silica gel plates using UV light as the visualizing agent and an ethanolic solution of vanillin and ammonium molybdate and heat as developing agents. Silica gel (60, 230−400 mesh) was used for flash column chromatography. NMR spectra were recorded at room temperature in $CDCl_3$ solution on either a spectrometer operating at 300 MHz for 1 H nuclei and 75 MHz for 13C nuclei or a spectrometer operating at 400 MHz for 1 H nuclei and 100 MHz for 13C nuclei. Chemical shifts are reported in parts per million on the δ scale, and coupling constants, J, are in hertz. Multiplicities are reported as “s” (singlet), “br s” (broad singlet), “d” (doublet), “dd” (doublet of doublets), “ddd” (doublet of doublets of doublets), “t” (triplet), and “m” (multiplet). Where distinct from those due to the major diastereomer, resonances due to minor diastereomers are denoted by an asterisk. ^{1}H and ^{13}C NMR resonances were assigned using a combination of DEPT 135, COSY, HSQC, HMBC, and NOESY spectra. Infrared (IR) spectra were recorded using a thin film on a composite of zinc selenide and diamond crystal on an FT-IR system transform spectrometer. Melting points are uncorrected. Highresolution mass spectrometry (HRMS) was performed using a spectrometer operating at a nominal accelerating voltage of 70 eV or a TOF-Q mass spectrometer.

5-Nitro-1*H*-pyrrole-3-carbaldehyde (18)



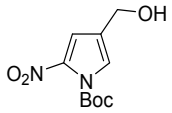
A solution of $AlCl_3$ (1.33 g, 10 mmol) in nitromethane (10 mL) was added dropwise to a solution of 2-nitropyrrole **16** (1.12 g, 10 mmol) in nitromethane (20 mL) at –35 °C. After stirring for 10 min, dichloromethylmethyl ether (3.45 g, 30 mmol) was added. The mixture was stirred overnight at –35 °C. The reaction mixture was poured to an ice/water (80 mL) mixture and extracted with EtOAc (3 × 80 mL). The combined organic extracts were washed with water and brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. Purification by flash chromatography (hexane/ EtOAc 1:1) afforded **18** (0.98 g, 70%) as a light brown solid; m.p. 160-162 °C; ν_{max} (neat)/cm^{-1}: 3133, 2849, 1660, 1446, 1295, 1235, 856; ^{1}H NMR (DMSO, 400 MHz) δ 13.86 (brs, 1H), 9.80 (s, 1H), 7.96 (d, J = 2.0 Hz, 1H), 7.48 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz,DMSO): δ 186.0, 138.9 (weak, *C*NO_2), 130.2, 125.9, 108.9; m/z (ESI) calcd for $[C_5H_4N_2NaO_3]^+$: 163.0120, found: 163.0124.

***tert*-Butyl 4-formyl-2-nitro-1*H*-pyrrole-1-carboxylate (S1)**



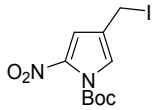
A mixture of aldehyde **18** (0.58 g, 4.2 mmol), Boc_2O (3.62 g, 16.6 mmol) and K_2CO_3 (2.31 g, 16.8 mmol) in DMF (8 mL) was stirred overnight at room temperature. The mixture was diluted with 50% brine (30 mL) and extracted with Et_2O (3 × 30 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. Purification by flash chromatography (hexane/ EtOAc 5:1) afforded **S1** (0.8 g, 80%) as a light yellow oil; mp 56.8-58.0 °C; ν_{max} (neat)/cm^{-1}: 3135, 1764, 1690, 1551, 1471, 1305, 1252, 1112, 809; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.84 (s, 1H), 7.82 (d, J = 2.0 Hz, 1H,), 7.38 (d, J = 2.0 Hz, 1H), 1.60 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 184.0, 145.8, 138.5 (weak, *C*NO_2), 130.5, 124.4, 112.5, 88.9, 27.4 (3C); *m/z* (ESI) calcd. for $[C_{10}H_{12}N_2NaO_5]^+$: 263.0368, found: 263.0639.

***tert*-Butyl 4-(hydroxymethyl)-2-nitro-1*H*-pyrrole-1-carboxylate (19)**



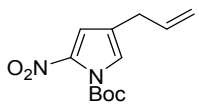
$NaBH_4$ (91 mg, 2.4 mmol) was added portionwise to a solution of aldehyde **S1** (383 mg, 1.6 mmol) in THF (5 mL) and methanol (0.1 mL) at 0 °C. After 1 h, the reaction was quenched by saturate aqueous NH_4Cl (1 mL) and diluted with water (20 mL). The resulting mixture was extracted with EtOAc (3 × 20 mL), the combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. Purification by flash chromatography (hexane/ EtOAc 1:1) afforded **19** (370 mg, 96%) as a light yellow oil; ν_{max} (neat)/cm^{-1}: 3383, 2982, 1761, 1521, 1472, 1371, 1325, 1292, 1252, 1147, 1087, 1022, 838, 809,768; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.24-7.23 (m, 1H), 7.07 (d, J = 2.0 Hz, 1H), 4.54 (s, 2H), 1.78 (brs, 1H), 1.57 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 146.8, 138.4 (weak, *C*NO_2), 124.5, 124.0, 115.7, 87.1, 57.6, 27.4 (3C); m/z (ESI) calcd. for $[C_{10}H_{14}N_2NaO_5]^+$: 265.0795, found: 265.0796.

tert-Butyl 4-(iodomethyl)-2-nitro-1*H*-pyrrole-1-carboxylate (20)



Iodine (1.62 g, 6.4 mmol) was added to a solution of PPh_3 (1.68 g, 6.4 mmol) in acetonitrile (4 mL) and dichloromethane (2 mL) portionwise at 0 °C. After 10 min, imidazole (326 mg, 4.8 mmol) was added, followed by dropwise addition of a solution of alcohol **19** (370 mg, 1.6 mmol) in dichloromethane (0.5 mL) at 0 °C. The resulting mixture was warmed to room temperature and stirred for 3 h. The reaction was quenched by saturated $Na_2S_2O_3$, diluted with water (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. Purification by flash chromatography (hexane/ EtOAc 10:1) afforded **20** (0.80 g, 80%) as a light yellow oil; ν_{max} (neat)/cm^{-1}: 3141, 2983, 1753, 1522, 1473, 1386, 1368, 1302, 1254, 1124, 1149, 1089, 843, 810, 762; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27-7.26 (m, 1H), 7.05 (d, J = 2.0 Hz, 1H), 4.22 (s, 2H), 1.57 (s, 9H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 146.4, 134.3 (weak, *C*NO_2), 124.2, 122.8, 116.7, 87.4, 27.4 (3C), -6.5; m/z (ESI) calcd. for $[C_{10}H_{13}IN_2NaO_4]^+$: 374.9812 , found: 374.9813.

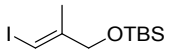
tert-Butyl 4-allyl-2-nitro-1*H*-pyrrole-1-carboxylate (21)



To a degassed solution of iodide **20** (70 mg, 0.2 mmol) and vinyltributylstannane (76 mg, 0.24 mmol) in DMF (1 mL) was added $Pd_2(dba)_3$ (10 mg, 5 mol%). The mixture was heated to 80 °C and stirred for 2 h. Then the mixture was diluted with diethyl ether (15 mL), washed with 50% brine, dried over sodium sulfate and concentrated *in vacuo*. The crude product was purified with flash chromatography (hexane/

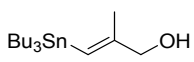
EtOAc 10:1) to afford **21** (45 mg, 90%) as a light yellow oil; ν_{max} (neat)/cm^{-1}: 3341, 2965, 1723, 1564, 1453, 1334, 1302, 1254, 1129, 810, 762, 643; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.05-7.04 (m, 1H), 6.93 (d, J = 2.3 Hz, 1H), 5.95-5.82 (m, 1H), 5.16-5.12 (m, 1H), 5.10-5.085 (m, 1H), 3.18 (d, J = 6.5 Hz, 2H), 1.60 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 146.6, 135.2, 124.2, 123.2, 117.3, 116.8, 86.6, 30.7, 27.4 (3C), *C*NO_2 was not observed; *m/z* (ESI) calcd. for $[C_{12}H_{16}N_2NaO_4]^+$ 275.2562, found: 275.2557.

(*E*)-1-(*tert*-Butyldimethylsiloxy)-3-iodo-2-methyl-2-propene (S2)



A solution of Me_3Al (25 mL, 2M in toluene, 40 mmol) were added dropwise to a mixture of Cp_2ZrCl_2 (1.17 g, 4 mmol) in dry CH_2Cl_2 (30 mL). The solution was then cooled to 0 °C before a solution of propargylic alcohol (1.12 g, 22 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise over 30min. After stirred overnight, the mixture was cooled to -30 °C and a solution of iodine (7.60 g, 30 mmol) in anhydrous THF (25 mL) was added slowly. Stirring was continued for additional 20 min at -30°C before a saturated $NaHCO_3$ solution (5 mL) were carefully added (caution: heavy gas and heat development). Then the cooling bath was removed. After the gas development had ceased, another 40 mL of saturated $NaHCO_3$ solution were added and the layers separated. The aqueous layer was extracted with ether (3×50 mL) and the combined organic layers were washed with saturated $Na_2S_2O_3$ solution (3×50 mL), dried with sodium sulfate and concentrated *in vacuo* to afford the crude vinyl iodide, which was dissolved in CH_2Cl_2 (50 mL), cooled to 0 °C and treated with TBSCl (3.61 g, 24 mmol) and imidazole (3.40 g, 50 mmol). The solution was warmed to room temperature and stirred until the starting material had been completely consumed. The resulting solution was transferred to a separation funnel and washed with 5% aqueous HCl (2×50 mL), saturated $NaHCO_3$ and brine, then dried over sodium sulfate and concentrated *in vacuo*. The crude product was purified by flash column chromatography (hexane/ Et_2O 15:1) to afford **S2** (6.7 g, 54%) as a clear yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.20 (s, 1H), 4.14 (br s, 2H), 1.78 (s, 3H), δ 0.95 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 76.3, 67.1, 29.9, 26.1, 21.4, −5.2; Spectroscopic data was consistent with that reported in the literature. [1]

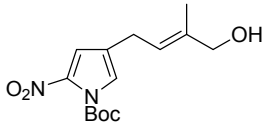
(*E*)-3-(Tributylstannyl)-2-methylpropen-1-ol (22)



A solution of **S2** (3.5 g, 11 mmol) in diethyl ether (50 mL) was cooled to −78 °C. To the cooled solution, 2.5 M ^{n}BuLi in hexanes (7.18 mL, 17.9 mmol) was added, followed immediately by addition of tributyltin chloride (4.87 mL, 17.9 mmol). After 3 h of stirring at low temperature, the solution was gradually warmed to room temperature over 1 h. The solution was quenched with H_2O (8.00 mL). The

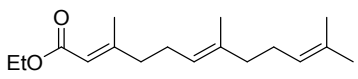
organic layer was partitioned, washed with saturated aqueous $NaHCO_3$, and brine, then dried over sodium sulfate and concentrated *in vacuo*. The crude product was disolved in dried THF (40 mL) before treated with TBAF (12 mL, 12 mmol, 1M in THF) at 0 °C. After 10 min at 0 °C, the reaction mixture was warmed to rt, stirred for an additional 40 min, and quenched with a saturated aqueous NH_4Cl solution (3 mL). The resulting mixture was concentrated *in vacuo* and dissolved in ether (40 mL). The organic phase was washed with water dried over sodium sulfate, and concentrated. Purification by column chromatography on silica gel (hexane/ EtOAc 6:1) **22** (2.4 g, 60%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (s, 1H), 4.07 (d, J = 4.2 Hz, 2H), 1.77 (s, 3H), 1.46-1.50 (6H, m), 1.27-1.33 (m, 6H), 0.85-0.95 (m, 15H); ^{13}C NMR (75 MHz, CDCl3) δ 152.3, 120.7, 68.8, 29.2, 27.3, 21.3, 13.7, 10.0; Spectroscopic data was consistent with that reported in the literature.[2]

(*E*)-2-Methyl-4-(1-Boc-5-nitro-1H-pyrrol-3-yl)but-2-en-1-ol (23)



To a degassed solution of iodide **20** (70 mg, 0.2 mmol), vinyl tributyltin **S3** (76 mg, 0.24 mmol) in DMF (1 mL) was added $Pd_2(dba)_3$ (10 mg, 5 mol%). The mixture was heated to 80 °C and stirred for 2 h. The mixture was diluted with diethyl ether (15 mL), washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The crude product was purified with flash chromatography (hexane/ EtOAc 10:1) to afford **23** (50 mg, 85%) as a light yellow oil; ν_{max} (neat)/cm^{-1}: 3346, 2919, 1760, 1519, 1470, 1386, 1252, 1147, 1086, 840, 809, 768; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05-7.01 (m, 1 H), 6.92 (d, J = 2.3 Hz, 1H), 5.58-5.51 (m, 1H), 4.06 (s, 2H), 3.19 (d, J = 7.45 Hz, 2H), 1.73 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 137.1, 123.9, 121.8, 117.3 (2C), 86.7, 68.2, 27.5 (3C), 24.7, 13.7, *C*NO_2 was not observed; *m/z* (ESI) calcd. for $[C_{14}H_{20}N_2NaO_5]^+$: 319.1264, found: 319.1267.

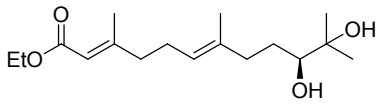
(2*E*,6*E*)-Ethyl 3,7,11-Trimethyldodeca-trienoate (24)



A solution of triethyl phosphonoacetate (2.91 g, 13.0 mmol) was added dropwise to a suspension of sodium hydride (60% in oil, 560 mg, 14.0 mmol) in dry THF (50 mL) at 0 °C under nitrogen. After 2 h, geranyl acetone (1.94 g, 10.0 mmol) in THF (10 mL) was added dropwise and the solution was stirred for another 3 h as the mixture warmed to room temperature. The reaction mixture was cooled to 0 °C and excess of hydride was quenched with water (10 mL). THF was removed *in vacuo*. The residue was diluted with water (90 mL) and extracted with hexane (3 × 80 mL). The combined organic layers were

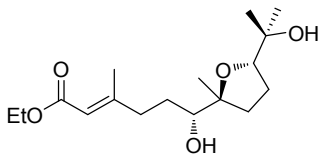
washed with water and brine, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was carefully purified by column chromatography (hexane/EtOAc 97:3) to remove small amount of *E* isomer. **24** (1.91 g, 72%) was obtained as a colourless oil; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.66 (s, lH), 5.15-5.06 (m, 2H), 4.14 (q, J = 6.57 Hz, 2H), 2.16 (s, 7H), 2.10-1.94 (m, 4H), 1.68 (s, 3H), 1.60 (s, 6H), 1.27 (t, J = 7.12 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 166.9, 159.8, 136.1, 131.4, 124.2, 122.9, 115.6, 59.4, 40.9, 39.6, 26.6, 25.9, 25.6, 18.8, 17.7, 16.0, 14.3. The spectroscopic data were in agreement with those reported in the literature.[3]

(*S*,2*E*,6*E*)-ethyl 10,11-dihydroxy-3,7,11-trimethyldodeca-2,6-dienoate (25)



To a suspension of $K_3Fe(CN)_6$ (3.73 g, 11.3 mmol), K_2CO_3 (1.56 g, 11.3 mmol) and (DHQ)PHAL (29.4 mg, 0.38 mmol) in *tert*-butanol (20 mL) and water (20 mL) was added OsO_4 (0.2 mL, 40 mg/mL in *tert*-butanol, 0.015 mmol) at 0 °C. After 10 min methanesulfonamide (359 mg, 3.78 mmol) was added followed by dropwise addition of olefin **24** (1.00 g, 3.78 mmol). After 24 h at 0 ^{0}C, the reaction mixture was quenched by addition of sodium sulfite (5 g), warmed to room temperature and stirred for another 1 h. Then the mixture was extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The crude product was purified by column chromatography (hexane/EtOAc 2:1) to afford **25** (367 mg, 32%) as a colourless oil together with some 6,7-diol and teraol byproduct; $[\alpha]_D^{20}$= −7.79 (*c* 2.60, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 3436.4, 2976.9, 1714.5, 1646.6, 1382.4, 1220.6, 1141.5, 1063.0, 755.1; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.65 (s, lH), 5.20-5.10 (m, lH), 4.14 (q, J = 7.11 Hz, 2H), 3.32 (d, J = 10.31 Hz, lH), 2.31 (brs, lH), 2.28-2.16 (m, 5H), 2.13 (d, J = 1.38 Hz, 3H), 2.14-2.04 (m, 1H), 1.77 (brs, 1H), 1.62 (d, J = 0.79 Hz, 3H), 1.60-1.53 (m, 1H), 1.46-1.34 (m, 1H), 1.27 (t, J = 7.25 Hz, 3H), 1.19 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDC1_3$): δ 167.0, 159.8, 116.0, 88.0, 86.2, 76.0, 70.6, 59.7, 37.9, 31.4, 29.5, 27.9, 26.7, 24.1, 24.0, 19.0, 14.5; m/z (ESI) calcd for $[C_{17}H_{30}NaO_4]^+$: 321.2040, found: 321.2045.

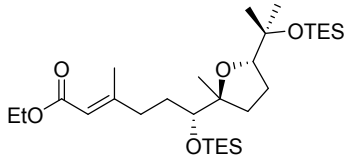
(*R*,*E*)-ethyl 6-hydroxy-6-((2*S*,5*S*)-5-(2-hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)-3-methylhex-2-enoate (26)



To a solution of alkene **25** (150 mg, 0.5 mmol) in acetonitrile-dimethoxymethane (7.5 mL, 1:2, v/v) was added buffer (0.05 M solution of $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} M aqueous Na_2(EDTA), 5.0 mL),

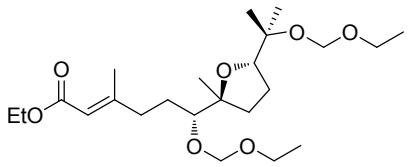
tetrabutylammonium hydrogen sulfate (6.8 mg, 0.02 mmol) and (-)-Shi diketal catalyst (129 mg, 0.5 mmol). The mixture was cooled to 0 °C with an ice bath. A solution of Oxone® (492 mg, 0.8 mmol) in aqueous Na_2(EDTA) (4×10^{-4} M, 3.5 mL) and a solution of K_2CO_3 (469 mg, 3.4 mmol) in water (3.5 mL) were added dropwise simultaneously but separately over 1.5 h. The reaction mixture was stirred for 0.5 h and then extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated *in vacuo*. The residue was disloved in toluene (10 mL) and treated with CSA (23 mg, 0.1 mmol) at 0 °C for 1 h. Then the mixture was filtered and concentrated *in vacuo*. The crude product was purified by chromatography (hexanes/*i*-propanol 4:1) to afford **26** (118 mg, 75%) as a colourless oil; $[\alpha]_D^{20}$ = -4.84 (*c* 1.40, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 3435.1, 2973.2, 1713.3, 1646.1, 1452.9, 1371.8, 1221.4, 1143.1, 1069.9, 1039.3,888.4; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.68-5.72 (m, lH), 4.14 (q, *J* = 7.11 Hz, 2H), 3.76 (dd, *J* = 5.87, 10.23 Hz, lH), 3.49 (dd, *J* = 2.05, 10.58 Hz, lH), 2.51-2.40 (m, lH), 2.27-2.18 (m, 1H), 2.16 (d, *J* = 1.43, 3H), 2.14-2.04 (m, 1H), 1.90-1.80 (m, 2H), 1.66-1.52 (m, 2H), 1.49-1.37 (m, 1H), 1.27 (t, *J* = 7.09 Hz, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 166.9, 159.7, 115.9, 87.9, 86.2, 76.0, 70.6, 59.6, 37.9, 31.4, 29.5, 27.8, 26.7, 24.1, 24.0, 19.0, 14.5; m/z (ESI) calcd for $[C_{17}H_{30}NaO_5]^+$: 337.1990, found 337.1995.

(*R*,*E*)-ethyl 3-methyl-6-((2*S*,5*S*)-2-methyl-5-(2-((triethylsilyl)oxy)propan-2-yl)tetrahydrofuran-2-yl)-6-((triethylsilyl)oxy)hex-2-enoate (27a)



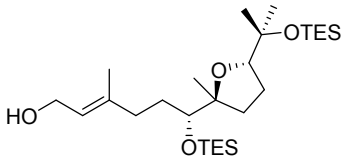
To a solution of diol **26** (314 mg, 1.0 mmol), imidazole (340 mg, 5.0 mmol) and DMAP (20 mg, 0.2 mmol) in DMF (3 mL) was added triethylsilyl chloride (360 mg, 2.4 mmol) dropwise at 0 °C under nitrogen. The mixture was stirred overnight and then subjected to flash chromatography (hexanes/EtOAc 50:1) to afford an inseparable mixture of **27a** and triethylsilane impurity, which was subjected to next step without further purification; $[\alpha]_D^{18}$ = -0.90 (*c* 1.60, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2985, 1719, 1644, 1124, 1029 1067, 1011, 720; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.69-5.66 (m, 1H), 4.15 (q, *J* = 7.10 Hz, 2H), 3.62 (dd, *J* = 8.94, 6.11 Hz, 1H), 3.50 (dd, *J* = 7.66, 3.42 Hz, 1H), 2.32-2.22 (m, 1H), 2.20-2.10 (m, 4H), 1.97-1.73 (m, 4H), 1.52-1.39 (m, 1H), 1.36-1.25 (m, 4H), 1.18 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H), 0.91-0.99 (m, 18H), 0.53-0.66 (m, 12 H); ^{13}C NMR (100 MHz, $CDC1_3$): δ 167.1, 160.7, 115.4, 87.3, 85.9, 77.7, 74.2, 59.6, 38.3, 34.9, 31.9, 27.9, 26.5, 25.7, 22.8, 22.5, 14.5, 7.2 (6C), 6.9 (3C), 5.7 (3C); m/z (ESI) calcd for $[C_{29}H_{58}NaO_5Si_2]^+$: 565.3710, found 565.3717.

(*R*,*E*)-ethyl 6-(ethoxymethoxy)-6-((2*S*,5*S*)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran-2-yl)-3-methylhex-2-enoate (27b)



To a solution of diol **26** (63 mg, 0.2 mmol) and N,N-diisopropylethylamine (0.52 mL, 3.0 mmol) in dichloromethane (2 mL) was added chloromethyl ethyl ether (0.15 mL, 2.0 mmol) dropwise at 0 °C. The mixture was stirred at room temperature overnight. Water (20 mL) was added to the solution, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/ethyl acetate 5:1) to afford **27b** (81 mg, 95% yield) as a colourless oil; $[\alpha]_D^{20}$ = + 27.33 (*c* 1.20, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2975, 1716, 1648, 1144, 1095, 1029; ^1H NMR (400 MHz, $CDC1_3$): δ 5.71-5.67 (m, lH), 4.84 (dd, *J* = 3.05, 7.24 Hz, 2H), 4.76 (dd, *J* = 7.24, 21.46 Hz, 2H), 4.14 (q, *J* = 7.21 Hz, 2H), 3.79-3.66 (m, 2H), 3.64-3.52 (m, 3H), 3,41(dd, *J* = 2.82, 9.25 Hz, lH), 2.43-2.33 (m, lH), 2.26-2.17 (m, 1H), 2.16 (d, *J* = 1.42, 3H), 2.12-2.00 (m, 1H), 1.88-1.44 (m, 5H), 1.27 (t, *J* = 7.09 Hz, 3H), 1.23-1.17 (m, 12H), 1.11 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 166.89, 159.96, 115.56, 111.00, 96.59, 89.96, 86.39, 85.78, 83.34, 63.81, 62.87, 59.49, 37.74, 33.03, 29.55, 26.94, 23.93, 23.27, 22.50, 18.98, 15.22, 15.07, 14.34; m/z (ESI) calcd for $[C_{23}H_{42}NaO_7]^+$: 453.2820, found 453.2864.

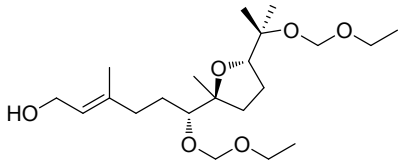
(*R*,*E*)-3-methyl-6-((2*S*,5*S*)-2-methyl-5-(2-((triethylsilyl)oxy)propan-2-yl)tetrahydrofuran-2-yl)-6-((triethylsilyl)oxy)hex-2-en-1-ol (28a)



To a stirred solution of **27a** in anhydrous toluene (10 mL) at 0 °C, was added DIBAL-H (l M in THF, 1.2 mL, 1.2 mmol,) slowly under argon. The reaction mixture was stirred at 0 °C for 30 minutes. When the reaction was complete (monitored by TLC), the mixture was quenched by aqueous NH_4Cl. Solid formed during the process was removed by filtration through celite®. Then, the solid was washed with hexane and the filtrate was extracted with hexane (3 × 30 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/ethyl acetate 5:1) to afford **28a** (410 mg,

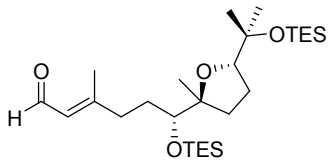
82%, over two steps) as a colourless oil; $[\alpha]_D^{18}$ = -1.90 (*c* 1.60, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 3306, 2954, 2876, 1458, 1237, 1097, 1004, 721; ^1H NMR (400 MHz, $CDC1_3$): δ 5.46-5.39 (m, 1H), 4.15 (d, *J* = 5.71 Hz, 2H), 3.63 (dd, *J* = 8.94, 6.11 Hz, 1H), 3.50 (dd, *J* = 7.66, 3.42 Hz, 1H), 2.12-2.22 (m, 1H), 1.70-2.07 (m, 5H), 1.69 (s, 3H), 1.50-1.54 (m, 1H), 1.34-1.45 (m, 1H), 1.17 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H), 0.91-0.99 (m, 18H), 0.53-0.66 (m, 12 H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 140.5, 123.0, 87.1, 85.8, 77.8, 74.1, 59.4, 36.8, 34.5, 32.1, 27.8, 26.4, 25.5, 22.5, 16.4, 7.1 (6C), 6.8 (3C), 5.5 (3C); m/z (ESI) calcd for $[C_{27}H_{56}NaO_4Si_2]^+$: 523.3609, found 523.3605.

(*R*,*E*)-6-(ethoxymethoxy)-6-((2*S*,5*S*)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran-2-yl)-3-methylhex-2-en-1-ol (28b)



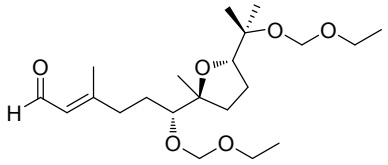
To a solution of ester **27b** (81 mg, 0.19 mmol) in anhydrous toluene (5 mL) at 0 °C, was added DIBAL-H (l M in THF, 0.22 mL, 0.22 mmol,) slowly under argon. The reaction mixture was stirred at 0 °C for 30 minutes. When the reaction was complete (monitored by TLC), the mixture was quenched by aqueous NH_4Cl. The solid formed during the process was simply removed by filtration through celite®. Then, the solid was washed with ethyl acetate and the filtrate was extracted twice with ethyl acetate (2 × 20 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/ethyl acetate 5:1) to afford **28b** (65 mg, 90% yield) as a colourless oil; $[\alpha]_D^{20}$ = +7.20 (*c* 2.40, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2974, 1382, 1094, 1027, 1011; ^1H NMR (400 MHz, $CDC1_3$): δ 5.40-5.34 (m, lH), 4.84 (dd, *J* = 3.05, 7.24 Hz, 2H), 4.76 (dd, *J* = 7.24, 21.46 Hz, 2H), 4.59 (d, *J* = 7.30 Hz, 2H), 3.79-3.66 (m, 2H), 3.64-3.52 (m, 3H), 3,41(dd, *J* = 2.82, 9.25 Hz, lH), 2.33-2.23 (m, lH), 2.14-2.04 (m, 5H), 1.89-1.74 (m, 2H), 1.68-1.41 (m, 3H), 1.23-1.17 (m, 12H), 1.12 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 142.41, 118.26, 96.55, 89.96, 86.32, 85.85, 83.38, 63.74, 62.84, 61.37, 36.33, 32.93, 29.79, 26.96, 24.00, 23.24, 22.50, 21.04, 16.55, 15.21, 15.06; m/z (ESI) calcd for $[C_{21}H_{40}NaO_6]^+$: 411.2720, found 411.2726.

(*R*,*E*)-3-methyl-6-((2*S*,5*S*)-2-methyl-5-(2-((triethylsilyl)oxy)propan-2-yl)tetrahydrofuran-2-yl)-6-((triethylsilyl)oxy)hex-2-enal (S3a)



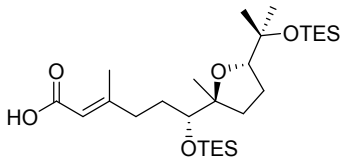
To a stirred solution of **28a** (410 g, 0.82 mmol) in hexane (10 mL) was added manganese dioxide (1.4 g, 16.4 mmol) at rt. After stirring overnight, the reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc, 10:1) to afford **S3a** (352 mg, 86%) as a colourless oil; $[\alpha]_D^{18}$ = -1.76 (*c* 2.23, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2954.6, 2875.7, 1677.2, 1458.1, 1173.1, 1098.4, 1037.4, 1005.2, 721.7; ^1H NMR (400 MHz, $CDC1_3$): δ 10.00 (d, *J* = 7.88 Hz, 1H), 5.87-5.92 (m, 1H), 3.63 (dd, *J* = 8.69, 5.92 Hz, 1H), 3.51 (dd, *J* = 7.79, 3.98 Hz, 1H), 2.31-2.41 (m, 1H), 2.19-2.29 (m, 1H), 2.17 (d, *J* = 1.49 Hz, 3H), 1.74-1.96 (m, 4H), 1.54-1.61 (m, 1H), 1.42-1.52 (m, 1H), 1.18 (s, 3H), 1.16 (s, 3H), 1.08 (s, 3H), 0.90-0.99 (m, 18H), 0.53-0.66 (m, 12 H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 191.3, 164.6, 127.1, 87.2, 85.6, 77.5, 74.0, 37.8, 35.0, 31.5, 27.7, 26.3, 25.6, 22.2, 17.7, 7.1 (6C), 6.8 (3C), 5.5 (3C); m/z (ESI) calcd for $[C_{26}H_{53}NaO_3Si_2]^+$: 521.3453, found 521.3447.

(*R*, *E*)-6-(ethoxymethoxy)-6-((2*S*, 5*S*)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran-2-yl)-3-methylhex-2-enal (S3b)



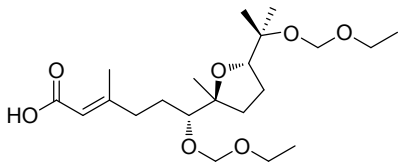
To a stirred solution of **28b** (65 g, 0.17 mmol) in hexane (5 mL) was added manganese dioxide (290 mg, 3.34 mmol) at rt. After stirring overnight, the reaction mixture was directly subjected to column chromatography (hexane/EtOAc, 1:1) to afford **S3b** (58 mg, 90%) as a colourless oil; $[\alpha]_D^{18}$ = 0.30 (*c* 0.98, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2974.2, 1673.8, 1282.8, 1094.9, 1028.1, 1011.8, 846.9; ^1H NMR (400 MHz, $CDC1_3$): δ 8.18 (d, *J* = 8.18, 7.24 Hz, 1H), 5.88-5.92 (m, lH), 4.82 (dd, *J* = 4.85, 6.43 Hz, 2H), 4.76 (dd, *J* = 7.50, 19.81 Hz, 2H), 3.64-3.79 (m, 2H), 3.64-3.50 (m, 3H), 3,41(dd, *J* = 3.54, 9.25 Hz, lH), 2.40-2.50 (m, lH), 2.24-2.34 (m, 1H), 2.17 (d, *J* = 1.02, 3H), 1.98-2.09 (m, 1H), 1.67-1.88 (m, 3H), 1.61-1.47 (m, 2H), 1.23-1.17 (m, 12H), 1.11 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 191.29, 164.14, 127.18, 96.63, 89.96, 86.45, 85.70, 83.37, 76.71, 63.85, 62.88, 37.43, 33.19, 29.21, 26.92, 23.80, 23.24, 22.51, 17.78, 15.23, 15.10; m/z (ESI) calcd for $[C_{21}H_{38}NaO_6]^+$: 409.2561, found 409.2559.

(*R*,*E*)-3-methyl-6-((2*S*,5*S*)-2-methyl-5-(2-((triethylsilyl)oxy)propan-2-yl)tetrahydrofuran-2-yl)-6-((triethylsilyl)oxy)hex-2-enoic acid (29a)



To a stirred mixture of **S3a** (176 mg, 0.35 mmol), 2-methyl-2-butene (123 mg, 1.75 mmol) and sodium dihydrogenphosphate dihydrate (242 mg, 1.75 mmol) in ^{t}BuOH (3.5 mL) and water (1.4 mL) was added sodium chlorite (126 mg, 1.4 mmol) at rt. After stirring for 1 h, the reaction was quenched by addition of aqueous sodium hydrogensulfite. The mixture was diluted with additional aqueous sodium hydrogensulfite and ethyl acetate. The phases were separated and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/ethyl acetate 5:1) to afford **29a** (162 mg, 95% yield) as a colourless oil; $[\alpha]_D^{18}$ = 0.27 (*c* 1.60, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2956.1, 2876.1, 1691.4, 1639.2, 1239.0, 1171.5, 1099.4, 1006.0, 756.1, 722.1; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.71 (s, 1H), 3.63 (dd, *J* = 8.64, 6.02 Hz, 1H), 3.51 (dd, *J* = 7.73, 3.70 Hz, 1H), 2.26-2.37 (m, 1H), 2.14-2.25 (m, 4H), 1.73-1.98 (m, 4H), 1.52-1.61 (m, 1H), 1.42-1.52 (m, 1H), 1.18 (s, 3H), 1.16 (s, 3H), 1.08 (s, 3H), 0.91-0.99 (m, 18H), 0.53-0.66 (m, 12 H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 171.8, 163.8, 114.7, 87.2, 85.7, 77.5, 74.0, 38.4, 34.8, 31.7, 27.8, 26.4, 25.6, 22.3, 19.3, 7.1 (6C), 6.8 (3C), 5.5 (3C); m/z (ESI) calcd for $[C_{27}H_{54}NaO_5Si_2]^+$: 537.3400, found 537.3407.

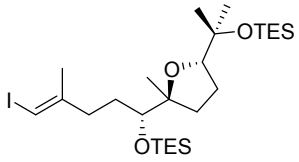
(*R*,*E*)-6-(ethoxymethoxy)-6-((2*S*,5*S*)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran-2-yl)-3-methylhex-2-enoic acid (29b)



To a stirred mixture of **S3b** (38 mg, 0.1 mmol), 2-methyl-2-butene (35 mg, 0.5 mmol) and sodium dihydrogenphosphate dihydrate (69 mg, 0.5 mmol) in ^{t}BuOH (1.0 mL) and water (0.4 mL) was added sodium chlorite (36 mg, 0.4 mmol) at rt. After stirring for 1 h, the reaction was quenched by addition of aqueous sodium hydrogensulfite. The mixture was diluted with additional aqueous sodium hydrogensulfite and ethyl acetate. The phases were separated and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/ethyl

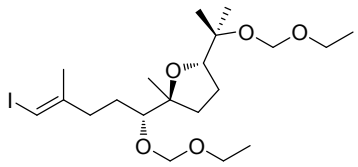
acetate 2:1) to afford **29b** (38 mg, 95% yield) as a colourless oil; $[\alpha]_D^{21}$ = 30.26 (*c* 1.80, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2974.9, 1690.3, 1639.6, 1095.7, 1029.7, 846.9, 762.4; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.72 (d, *J* = 1.13 Hz, lH), 4.84 (dd, *J* = 3.54, 7.09 Hz, 2H), 4.76 (dd, *J* = 7.53, 20.85 Hz, 2H), 3.76 (dd, *J* = 5.93, 9.65 Hz, 1H), 3.70 (dd, *J* = 7.11, 9.14 Hz, 1H), 3.64-3.52 (m, 3H), 3.41 (dd, *J* = 3.22, 8.97 Hz, 1H), 2.46-2.36 (m, lH), 2.29-2.19 (m, 1H), 2.17 (d, *J* = 0.97, 3H), 2.10-2.00 (m, 1H), 1.89-1.76 (m, 2H), 1.76-1.65 (m, 1H), 1.60-1.45 (m, 2H), 1.24-1.15 (m, 12H), 1.12 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 171.7, 163.1, 115.2, 96.7, 90.0, 86.5, 85.9, 83.4, 76.8, 63.9, 63.0, 38.1, 33.2, 29.6, 27.0, 24.0, 23.3, 22.6, 19.4, 15.3, 15.2; m/z (ESI) calcd for $[C_{21}H_{38}NaO_7]^+$: 425.2510, found 425.2515.

(((*R*,*E*)-5-Iodo-4-methyl-1-((2*S*,5*S*)-2-methyl-5-(2-((triethylsilyl)oxy)propan-2-yl)tetrahydrofuran-2-yl)pent-4-en-1-yl)oxy)silane (30a)



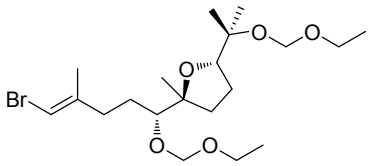
To a solution of cetrimonium bromide in acetonitrile (0.05 M, 3 mL) was added acid **29a** (82 mg, 0.16 mmol) and NIS (72 mg, 0.32 mmol). The mixture was heated to reflux until the starting material had been completely consumed (TLC). The mixture was filtered through a silica plug and the solid was washed with ethyl acetate. The combined filtrate was washed with saturated sodium bisulfite and brine, dried over sodium sulfate and concentrated *in vacuo*. The residue obtained was purified by column chromatography (hexane/ethyl acetate 10:1) to afford **30a** (66 mg, 70%) as a colourless oil; $[\alpha]_D^{18}$ = 0.90 (*c* 1.60, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2954, 2875, 1458, 1237, 1098, 1037, 1004, 721; ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.89 (q, *J* = 0.97, 1H), 3.62 (dd, *J* = 8.64, 6.11 Hz, 1H), 3.47 (dd, *J* = 8.02, 3.60 Hz, 1H), 2.30-2.39 (m, 1H), 2.18-2.27 (m, 1H), 1.85-1.96 (m, 1H), 1.84 (d, *J* = 0.97, 3H), 1.52-1.59 (m, 1H), 1.36-1.47 (m, 1H), 1.17 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H), 0.91-0.99 (m, 18H), 0.53-0.66 (m, 12 H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 148.6, 87.3, 85.8, 77.6, 74.6, 74.2, 36.9, 35.0, 32.2, 27.9, 26.5, 25.7, 24.2, 22.4, 7.3 (3C), 7.2 (3C), 6.9 (3C), 5.7 (3C); m/z(ESI) calcd for $[C_{26}H_{53}NaO_3Si_2]^+$: 619.2470, found 619.2477.

(2*S*,5*S*)-2-((*R*,*E*)-1-(ethoxymethoxy)-5-iodo-4-methylpent-4-en-1-yl)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran (29b)



To a solution of cetrimonium bromide in acetonitrile (0.05 M, 2 mL) was added acid **27b** (46 mg, 0.11 mmol) and NIS (38 mg, 0.17 mmol). The mixture was heated to reflux until the starting material had been completely consumed (TLC). The mixture was filtered through a silica plug and the solid was washed with ethyl acetate. The combined filtrate was washed with saturated sodium bisulfite and brine, dried over sodium sulfate and concentrated *in vacuo*. The residue obtained was purified by column chromatography (hexane/ethyl acetate 10:1) to afford **30b** (40 mg, 75%) as a colourless oil; $[\alpha]_D^{18}$ = 23.71 (*c* 1.53, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2964, 2856, 1438, 1237, 1118, 1037, 1024, 725; ^1H NMR (400 MHz, $CDC1_3$): δ 6.96-5.91 (m, lH), 4.88-4.67 (m, 4H), 3.75 (dd, *J* = 5.80, 9.48 Hz, 1H), 3.70 (dd, *J* = 7.19, 9.28 Hz, 1H), 3.64-3.51 (m, 3H), 3.39 (dd, *J* = 2.78, 9.21 Hz, 1H), 2.46-2.36 (m, lH), 2.36-2.25 (m, 1H), 2.10-2.00 (m, 1H), 1.91-1.75 (m, 5H), 1.66-1.52 (m, 2H), 1.52-1.41(m, 1H), 1.24-1.15 (m, 12H), 1.11 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 148.0, 96.6, 90.0, 86.3, 85.7, 83.1, 76.7, 75.0, 63.8, 62.9, 36.4, 33.0, 29.9, 26.9, 24.0, 23.9, 23.2, 22.5, 15.2, 15.1; m/z (ESI) calcd for $[C_{20}H_{37}INaO_5]^+$: 507.1580, found 507.1583.

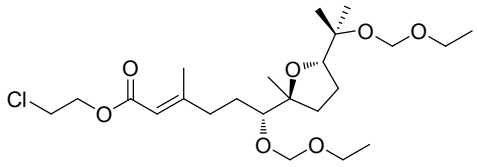
(2*S*,5*S*)-2-((*R*,*E*)-5-bromo-1-(ethoxymethoxy)-4-methylpent-4-en-1-yl)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran (30c)



To a stirred suspension of $PhI(OAc)_2$ (38.6 mg, 0.12 mmol) in dichloromethane (1.0 mL) was added TBAB (41.8 mg, 0.13 mmol) in one portion at room temperature. After being stirred for 5 min, acid **29b** (40 mg, 0.1 mmol) was added and stirring was continued at rt until the starting material had been completely consumed. The reaction mixture was diluted with dichloromethane (20 mL) and washed successively with 10% aq sodium bisulfite solution (20 mL), 10% $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The residue obtained was purified by column chromatography (hexane/ethyl acetate 10:1) to afford **30c** (3.4 mg, 8%) as a colourless oil; $[\alpha]_D^{21}$ = 16.93 (*c* 1.60, $CHCl_3$); ν_{max} (neat)/cm^{-1}: 2975.2, 1455.5, 1381.9, 1287.5, 1096.4, 1033.8, 761.9; ^1H NMR (400 MHz, $CDC1_3$): δ 6.00-5.94 (m, lH), 4.88-4.71 (m, 4H), 3.76 (dd, *J* = 5.88, 9.28 Hz, 1H), 3.70 (dd, *J* = 7.12, 9.28 Hz, 1H), 3.64-3.51 (m, 3H), 3.39 (dd, *J* = 2.72, 9.11 Hz, 1H), 2.37-2.26 (m, lH), 2.27-2.16 (m, 1H), 2.10-2.00 (m, 1H), 1.91-1.73 (m, 5H), 1.71-1.52 (m, 2H),

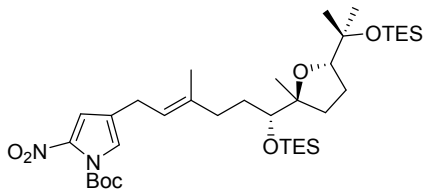
1.52-1.41(m, 1H), 1.24-1.15 (m, 12H), 1.12 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 141.9, 101.6, 96.7, 90.1, 86.5, 85.9, 83.3, 76.8, 63.9, 63.0, 35.3, 33.2, 29.8, 27.1, 24.0, 23.4, 22.6, 19.3, 15.4, 15.2; m/z (ESI) calcd for $[C_{20}H_{37}BrNaO_5]^+$: 459.1717, found 459.1718.

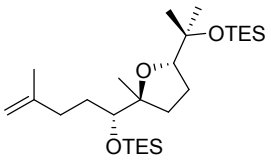
(*R*,*E*)-2-chloroethyl 6-(ethoxymethoxy)-6-((2*S*,5*S*)-5-(2-(ethoxymethoxy)propan-2-yl)-2-methyltetrahydrofuran-2-yl)-3-methylhex-2-enoate (31)



To a solution of cetrimonium bromide in 1,2-dichloroethane (0.05 M, 1 mL) was added acid **29b** (10 mg, 0.025 mmol) and NIS (8.5 mg, 0.038 mmol). The mixture was heated to reflux until the starting material had been completely consumed. The mixture was filtered through a silica plug. The filtrate was washed with saturated sodium bisulfite and brine, dried over sodium sulfate and concentrated *in vacuo*. The residue obtained was purified by column chromatography (hexane/ethyl acetate 10:1) to afford **31** (5.5 mg, 46%) as a colourless oil; ν_{max} (neat)/cm^{-1}: 2976, 1717, 1652, 1142, 1098, 1024; $[\alpha]_D^{18}$ = + 23.71 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDC1_3$): δ 5.75-5.70 (m, lH), 4.85-4.70 (m, 4H), 4.33 (t, *J* = 5.67 Hz, 2H), 3.75 (dd, *J* = 5.60, 9.58 Hz, 1H), 3.71-3.65 (m, 3H), 3.63-3.51 (m, 3H), 3.40 (dd, *J* = 2.78, 9.11 Hz, 1H), 2.45-2.36 (m, lH), 2.36-2.18 (m, 1H), 2.16 (d, *J* = 1.01 Hz, 3H), 2.10-2.00 (m, 1H), 1.88-1.75 (m, 2H), 1.73-1.64 (m, 1H), 1.60-1.44 (m, 2H), 1.24-1.15 (m, 12H), 1.11 (s, 3H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ166.3, 161.9, 114.9, 96.7, 90.1, 86.5, 85.9, 83.4, 76.8, 63.9, 63.4, 63.0, 41.9, 38.0, 33.2, 29.6, 27.1, 24.0, 23.4, 22.6, 19.3, 15.3, 15.2; m/z (ESI) calcd for $[C_{23}H_{41}ClNaO_7]^+$: 487.2433, found 487.2434;

***tert*-Butyl 4-((*R*,*E*)-3-methyl-6-((2*S*,5*S*)-2-methyl-5-(2-(((triethylsilyl)oxy)propan-2-yl)tetrahydrofuran-2-yl)-6-((triethylsilyl)oxy)hex-2-en-1-yl)-2-nitro-1*H*-pyrrole-1-carboxylate (14)**





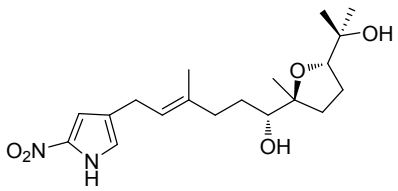
deiodinated byproduct **S7**

To a solution of vinyl iodide **30a** (60 mg, 0.1 mmol) in anhydrous Et_2O (2 mL) was added ^{t}BuLi (1.5 M in hexane, 0.2 mL, 0.3 mmol) dropwise at -78 °C. Then tributyltin chloride (97 mg, 0.3 mmol) was

added dropwise and the mixture was warmed slowly to rt and stirred overnight. The reaction was quenched with NH_4Cl and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The residue obtained was purified by column chromatography (hexane/ethyl acetate 20:1) to afford an inseparable mixture of vinyl stannane **13a** and deiodination byproduct **S7** (**13a**:**S7**, 6:1; 60 mg), which was used for next step without further purification;

To a solution of iodide **20** (14 mg, 0.04 mol) and the crude vinyl stannane **13a** (60 mg) obtained above in degassed DMF was added $Pd_2(dba)_3$ (2 mg, 0.002 mmol). The mixture was heated to 80°C and stirred for 2 h. The reaction mixture was subjected to column chromatography (hexane/ethyl acetate 10:1) to afford **14** (20 mg, 74%) as a yellow oil; $[\alpha]_D^{18}$ = -0.43 (*c* 0.580, $CHCl_3$); ν_{max} (neat)/cm^{-1}:2972, 2923, 2862, 1452, 1353, 1284, 1263, 1108, 933, 886, 734; ^1H NMR (400 MHz, $CDC1_3$): δ 7.00-7.02 (m, 1H), 6.92 (d, *J* = 2.02, 1H), 5.22-5.29 (m, 1H), 3.62 (dd, *J* = 8.62, 6.21 Hz, 1H), 3.48 (dd, *J* = 8.12, 3.43 Hz, 1H), 3.12 (d, *J* = 7.31, 2H), 2.22-2.12 (m, 1H), 2.08-1.68 (m, 5H), 1.66 (s, 3H), 1.56 (s, 9H), 1.51-1.54 (m, 1H), 1.42-1.33 (m, 1H), 1.17 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H), 0.91-0.99 (m, 18H), 0.53-0.66 (m, 12 H); ^{13}C NMR (75.4 MHz, $CDC1_3$): δ 147.1, 138.3, 124.8, 123.9, 120.3, 117.5, 87.1, 86.5, 85.8, 77.8, 74.1, 36.7, 34.6, 32.3, 27.7, 27.5, 26.4 (3×*C*H_3), 25.6, 25.0, 22.5, 16.2, 7.1 (6C), 6.8 (3C), 5.6 (3C); m/z (ESI) calcd for $[C_{36}H_{66}N_2NaO_7Si_2]^+$: 717.4301, found: 717.4294;

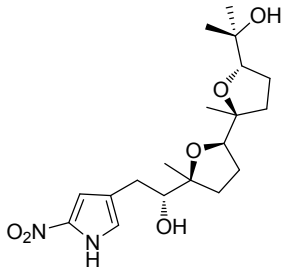
(-)-Heronapyrrole D (-)-**4**



To a solution of alkene **14** (20 mg, 0.029 mmol) in THF (0.5 mL) was added TBAF (0.07 mL, 1 M solution in THF, 0.07 mmol) at 0 °C. The mixture was stirred overnight at rt and then diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were dried over sodium sulfate and concentrated *in vacuo*. The crude material was dissolved in MeOH (0.5 mL) and HCl (1 M, 0.01 mL) was added at 0 °C. After 3 h, the mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were dried over sodium sulfate and concentrated *in vacuo*. The crude product was purified by preparative TLC (EtOAc) to afford (-)-heronapyrrole D **4** (8 mg, 75%) as a light yellow oil; $[\alpha]_D^{18}$= −3.9 (c 0.1, MeOH), lit. *Stark* (+)-**4**, $[\alpha]_D^{18}$= +3.9 (c 0.1, MeOH);[4] ν_{max} (neat)/cm^{-1}:3362, 2972, 2927, 2872, 1503, 1452, 1356, 1294, 1266, 1119, 963, 886, 743; ^1H NMR (500 MHz, CD_3OD) δ6.88 (d, *J* = 1.5 Hz, 1 H, H-5), 6.82 (d, *J* = 1.5 Hz, 1 H), 5.38 (t, *J* = 7.0 Hz, 1 H), 3.71 (dd, *J* = 9.5 Hz, *J* = 6.1 Hz, 1 H), 3.40 (dd, *J* = 10.3 Hz, 1.4 Hz), 3.19 (d, *J* = 7.0 Hz), 2.31-2.26 (m, 1H), 2.15–2.09 (m, 1H), 2.06–1.98 (m, 1H), 1.86–1.75 (m, 3H), 1.70

(s, 3H), 1.64-1.59 (m, 1H), 1.42-1.34 (m, 1H), 1.15 (s, 3H), 1.12 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ138.7, 137.4, 127.6, 123.9, 123.4, 111.3, 88.0, 86.7, 76.9, 72.2, 37.3, 35.1, 30.8, 27.7, 26.4, 26.1, 25.1, 22.7, 16.1; m/z (ESI) calcd for $[C_{19}H_{30}N_2NaO_5]^+$:389.2047; found: 389.2067.

(+)-Heronapyrrole C (+)-**3**



To a solution of (-)-heronapyrrole D **4** (7 mg, 0.019 mmol) in acetonitrile-DMM (0.6 mL, 1:2, v/v) was added buffer (0.4.mL, 0.05 M solution of $Na_2B_4O_7{\cdot}10H_2O$ in 4 × 10^{-4} M aqueous Na_2(EDTA)), tetrabutylammonium hydrogen sulfate (0.7 mg, 0.002 mmol), and (−)-Shi catalyst (4.2 mg, 0.022 mmol). The mixture was cooled to 0 °C with an ice bath. A solution of Oxone® (16.8 mg, 0.027 mmol) in aqueous Na_2(EDTA) (4 × 10^{-4} M, 0.2 mL) and a solution of K_2CO_3 (16.1 mg, 5.8 mmol) in water (0.2 mL) were added dropwise separately *via* syringe pumps over a period of 1 h. The reaction mixture was stirred for a further 1 h at 0 °C, diluted with water (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The crude material was dissolved in toluene (0.5 mL) and CSA (1.0 mg, 0.004 mmol) added at 0 °C. After stirring for 1 h, the solvent was removed *in vacuo* and the crude product was purified by by preparative TLC (EtOAc) to afford (+)-heronapyrrole C **3** (5.4 mg, 75 %) as a light yellow oil; $[\alpha_D]^{20}$ = +7.8 (*c* 0.32, MeOH); lit. *isolated* (+)-heronapyrrole C (**4**): $[\alpha_D]^{20}$ = +6.7, (*c* = 0.05, MeOH);[5] *Stark* (-)-heronapyrrole C: $[\alpha_D]^{20}$ = -7.6, (*c* = 2.3, MeOH);[6] ^{1}H NMR (400 MHz, MeOD-d_6): δ 7.00 (d, *J* = 1.8 Hz, 1H, H-3), 6.93 (d, *J* = 1.8 Hz, 1H, H-5), 4.02 (dd, *J* = 8.4, 6.6 Hz, 1H, H-11), 3.81 (dd, *J* = 8.1, 7.1 Hz, 1H, H-15), 3.60 (dd, *J* = 10.2, 1.8 Hz, 1H, H-7), 2.82 (dd, *J* = 14.6, 1.4 Hz, 1H, H- 6a), 2.44 (dd, *J* = 14.8, 10.3 Hz, 1H, H-6b), 2.17-2.11 (m, 1H, H-9a), 2.00-1.79 (m, 5H, H-10, 13a and 14), 1.69-1.60 (m, 1H, H-13b), 1.220 (s, 3H, H-18), 1.215 (s, 3H, H-19), 1.16 (s, 3H, H-17), 1.13 (s, 3H, H-20); ^{13}C NMR (100 MHz, MeOD-d_6) δ 138.6, 126.0, 124.5, 112.2, 88.9, 87.0, 86.2, 86.1, 78.9, 72.1, 35.1, 34.8, 30.1, 28.3, 27.5, 26.1, 25.8, 25.1, 22.2; *m*/*z* (ESI+) calcd for $[C_{19}H_{30}N_2NaO_6]^+$: 405.1996, found: 405.1987.

References

[1] Brandt, D. R.; Pannone, K. M.; Romano, J. J.; Gasillas, E. G. *Tetrahedron* **2013**, *69*, 9994–10002

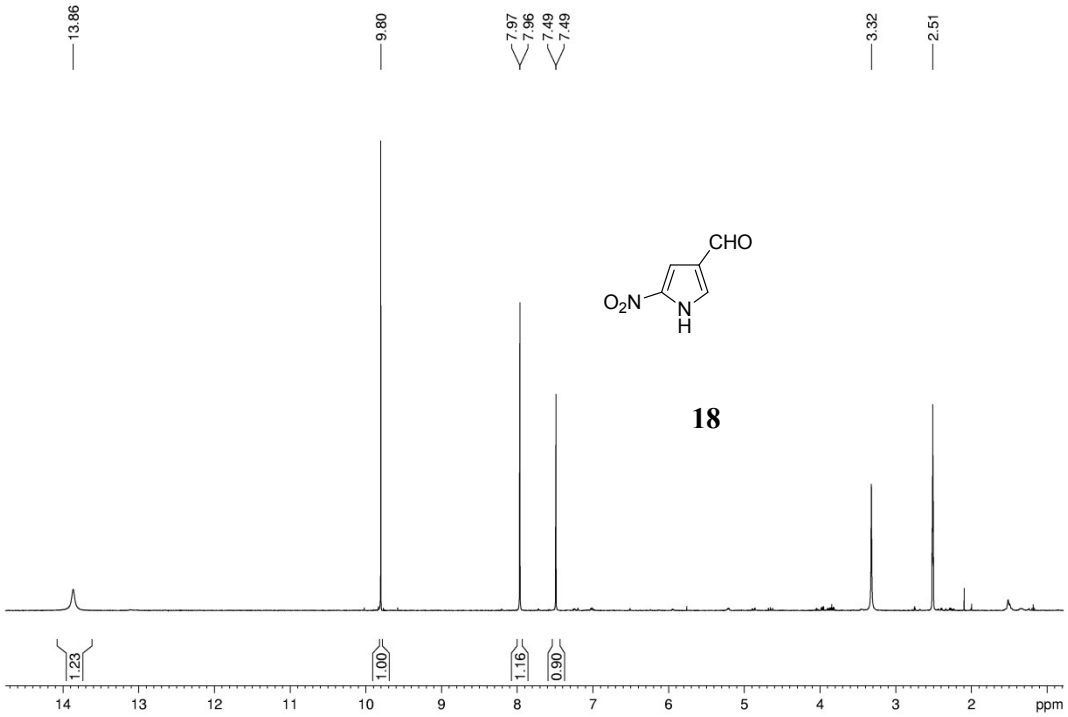
[2] Scarlato, G. R.; DeMattei, J. A.; Chong, L. S.; Ogawa, A. K.; Lin, M. R.; Armstrong, R. W. *J. Org. Chem.* **1996**, *61*, 6139-6152.

[3] Gibbs, R. A.; Krishnan, U.; Dolence, J. M.; Poulter, C. D. *J. Org. Chem.* **1995**, *60*, 7821-7829.

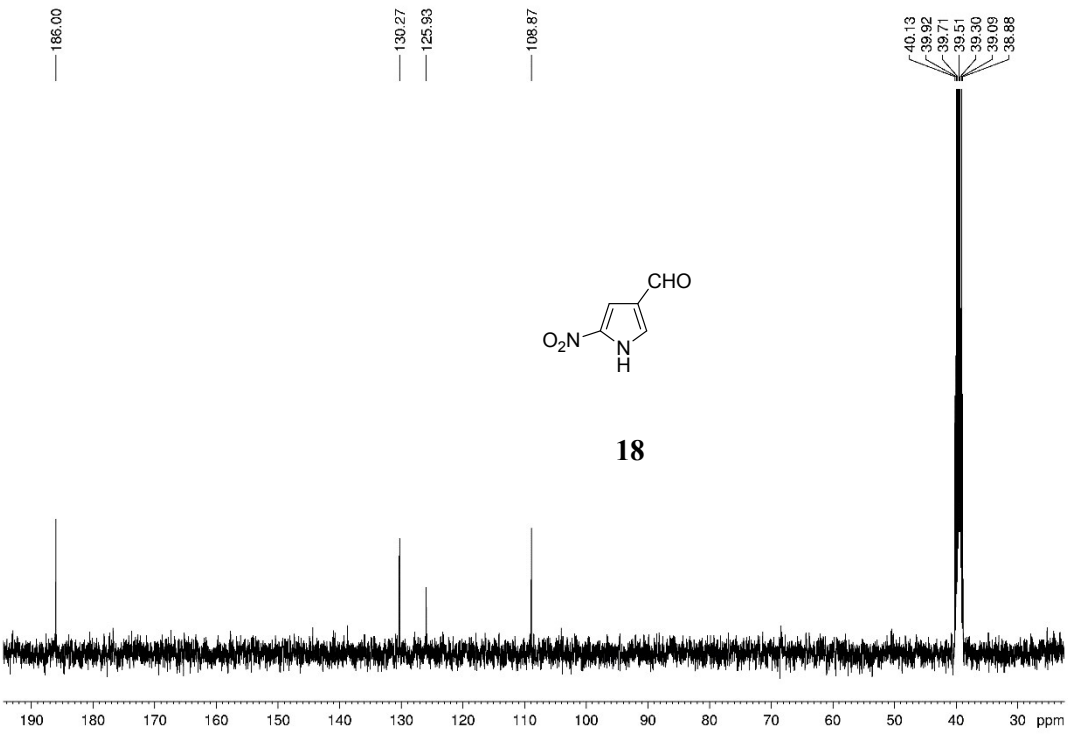
[4] Schmidt, J.; Khalil, Z.; Capon, R. J.; Stark, C. B. *Beilstein J. Org. Chem.* **2014,** *10*, 1228-32.

[5] Raju, R.; Piggott, A. M.; Barrientos Diaz, L. X.; Khalil, Z.; Capon, R. J. *Org. Lett.* **2010,** *12*, 5158-61.

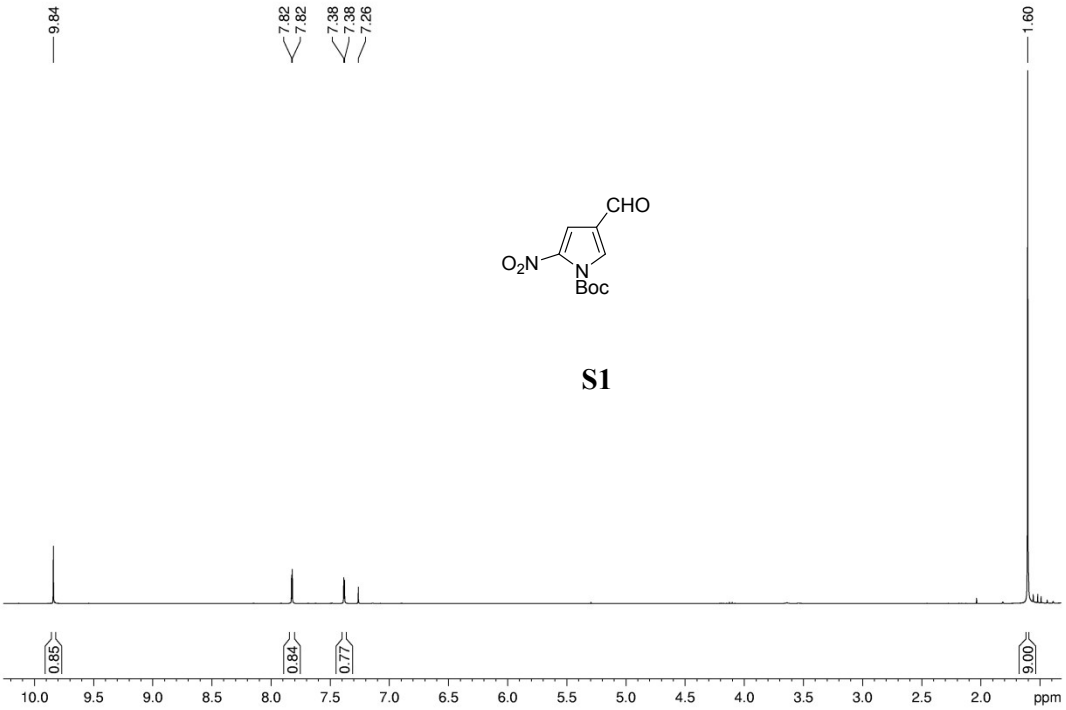
[6] Schmidt, J.; Stark, C. B. *Org. Lett.* **2012,** *14*, 4042-5.


13.86
9.80
7.97
7.96
7.49
7.49
3.32
2.51
CHO
O2N
N
H
1.23
1.00
1.16
0.90
14
13
12
11
10
9
8
7
6
5
4
3
2
ppm

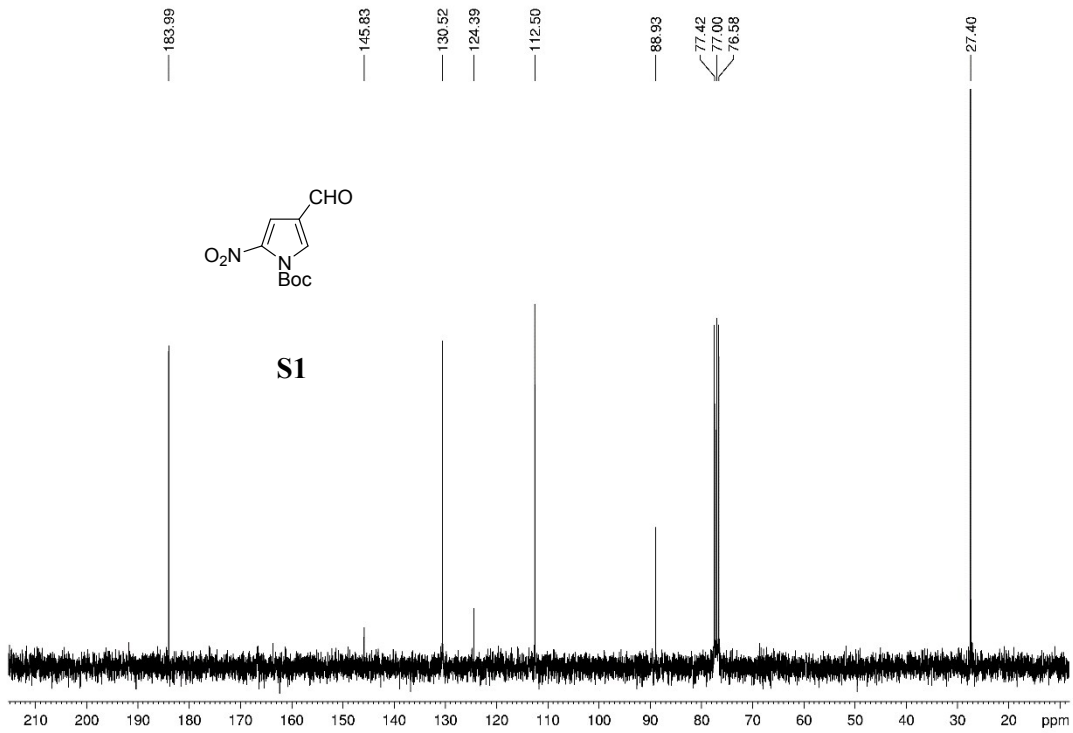
18


186.00
130.27
125.93
108.87
40.13
39.92
39.71
39.51
39.30
39.09
38.88
CHO
O2N
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

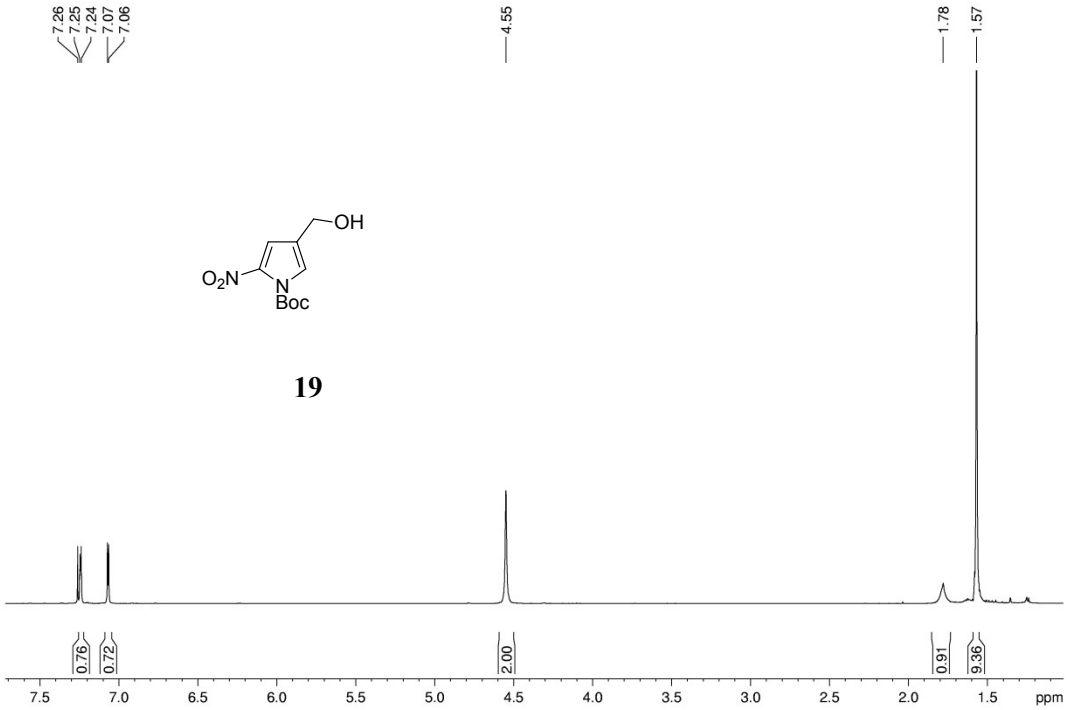
18


9.84
7.82
7.82
7.38
7.38
7.26
1.60
CHO
O2N
N
Boc
0.85
0.84
0.77
9.00
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
ppm

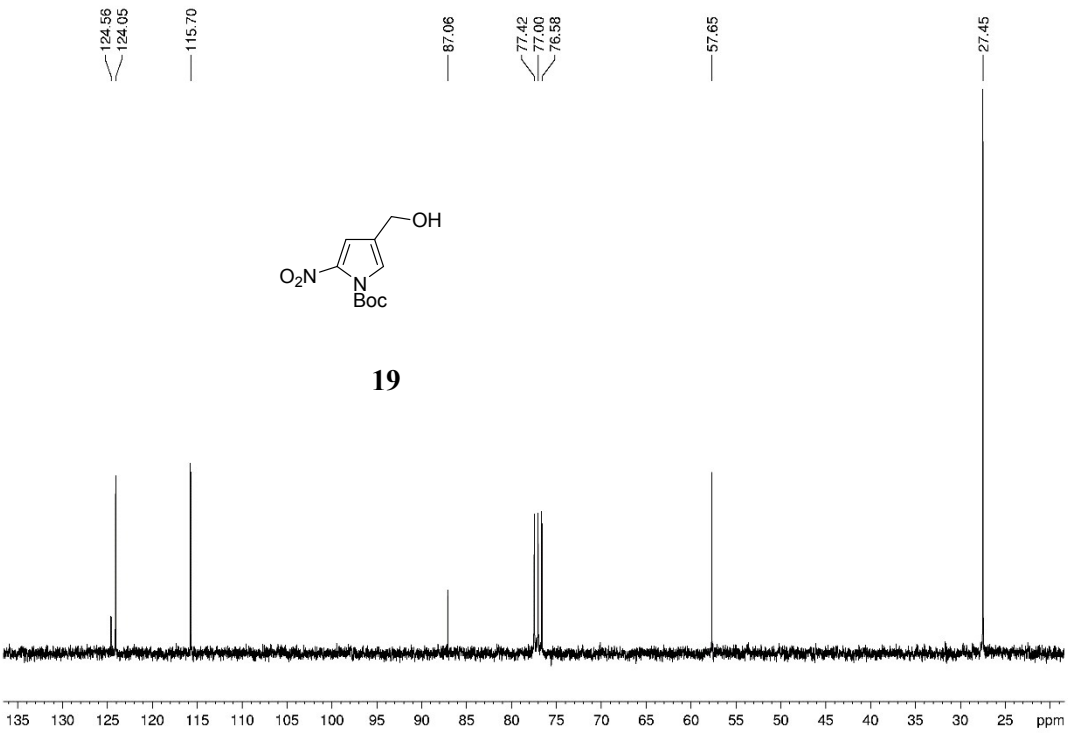
S1


183.99
145.83
130.52
124.39
112.50
88.93
77.42
77.00
76.58
27.40
CHO
O2N
N
Boc
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

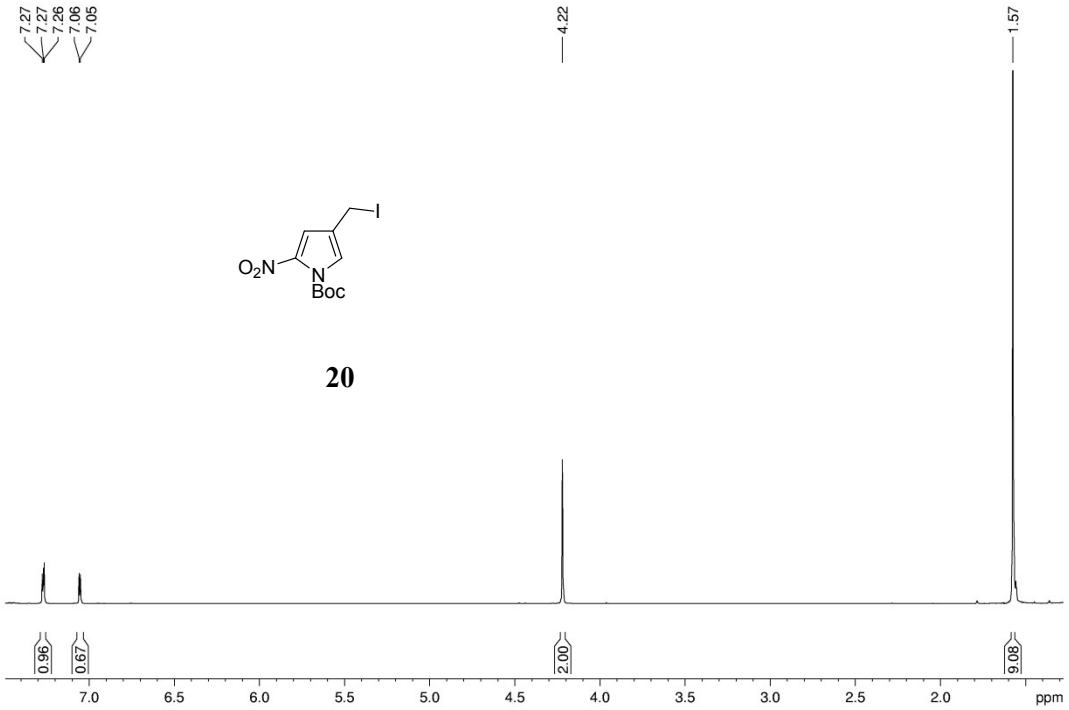
S1


7.26
7.25
7.24
7.07
7.06
4.55
1.78
1.57
OH
O2N
N
Boc
0.76
0.72
2.00
0.91
9.36
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
ppm

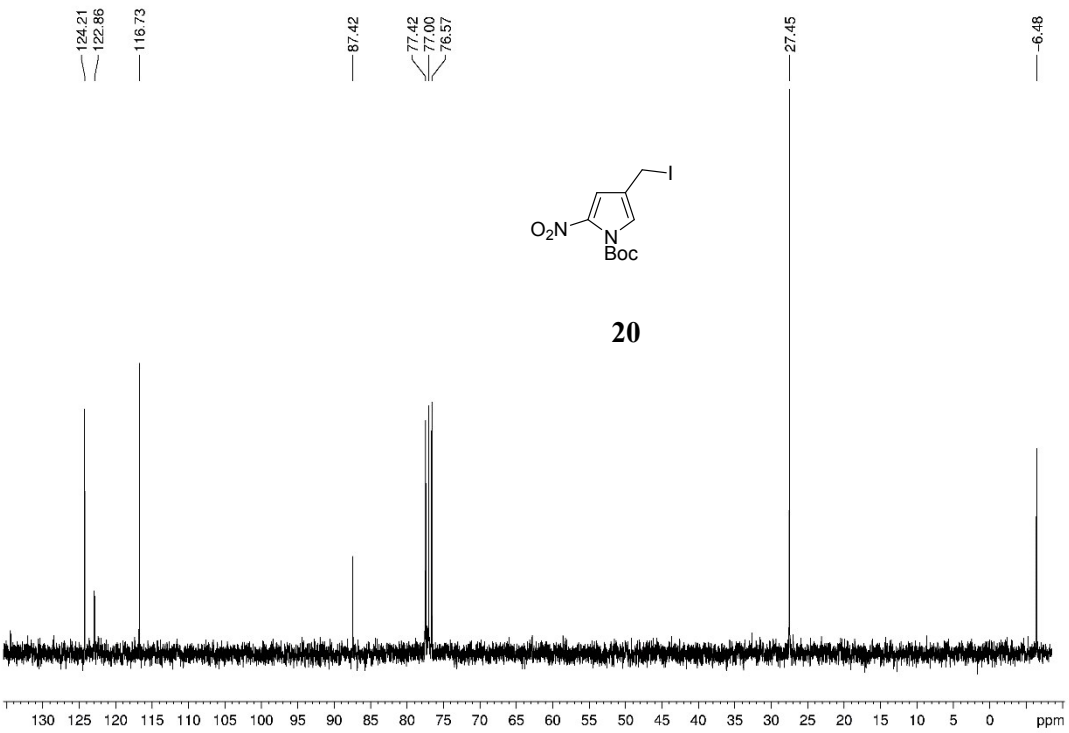
19


124.56
124.05
115.70
87.06
77.42
77.00
76.58
57.65
27.45
OH
O2N
N
Boc
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
ppm

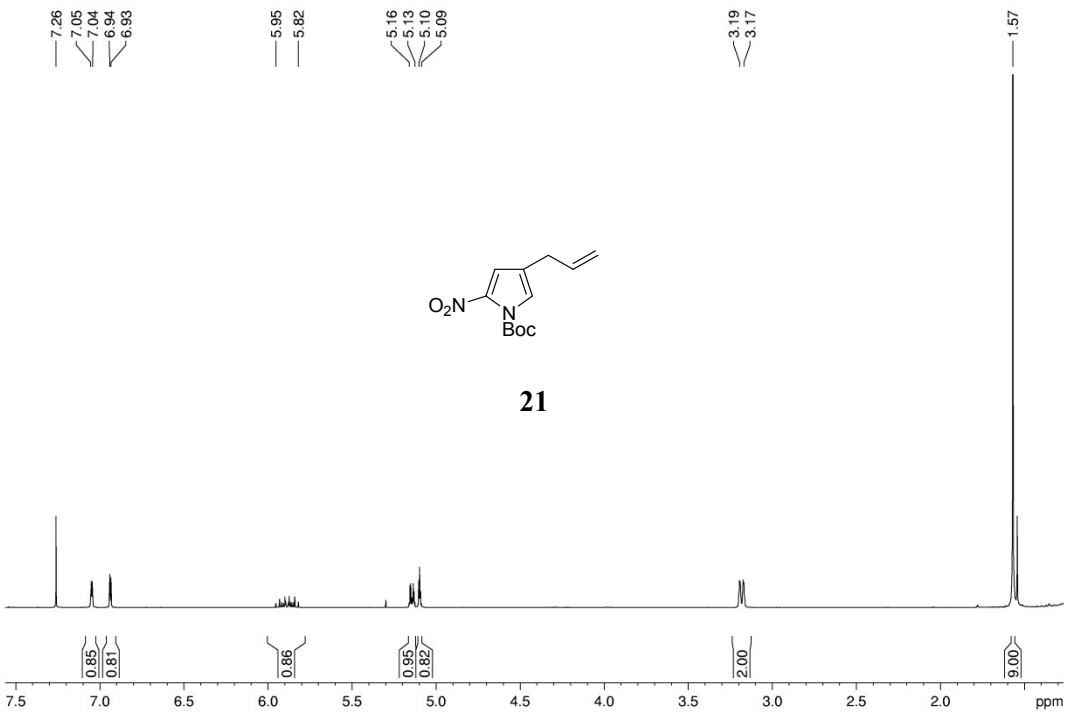
19


7.27
7.27
7.26
7.06
7.05
4.22
1.57
I
O2N
N
Boc
0.96
0.67
2.00
9.08
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

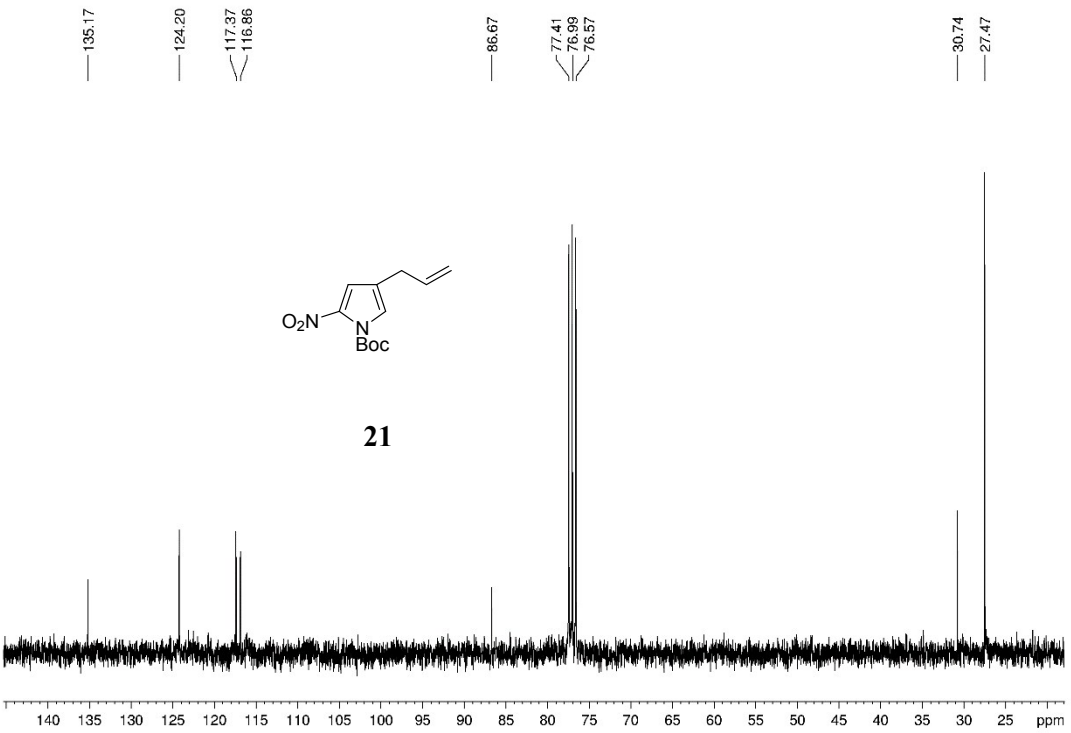
20


124.21
122.86
116.73
87.42
77.42
77.00
76.57
27.45
6.48
I
O2N
N
Boc
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
ppm

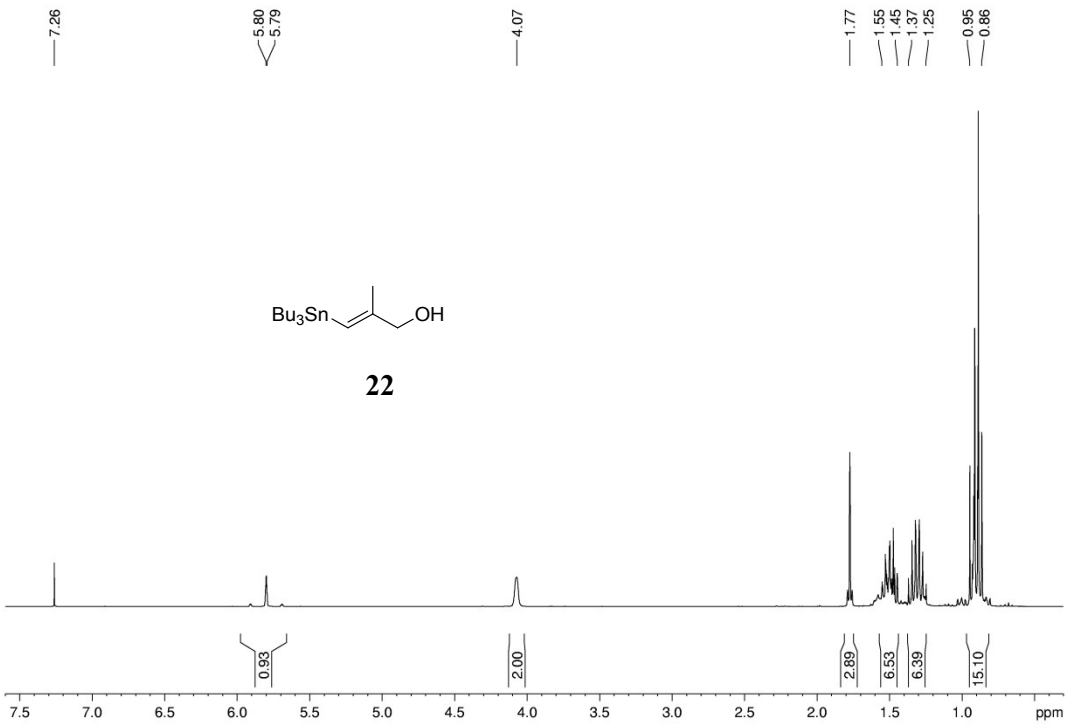
20


7.26
7.05
7.04
6.94
6.93
5.95
5.82
5.16
5.13
5.10
5.09
3.19
3.17
1.57
O2N
N
Boc
0.85
0.81
0.86
0.95
0.82
2.00
9.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

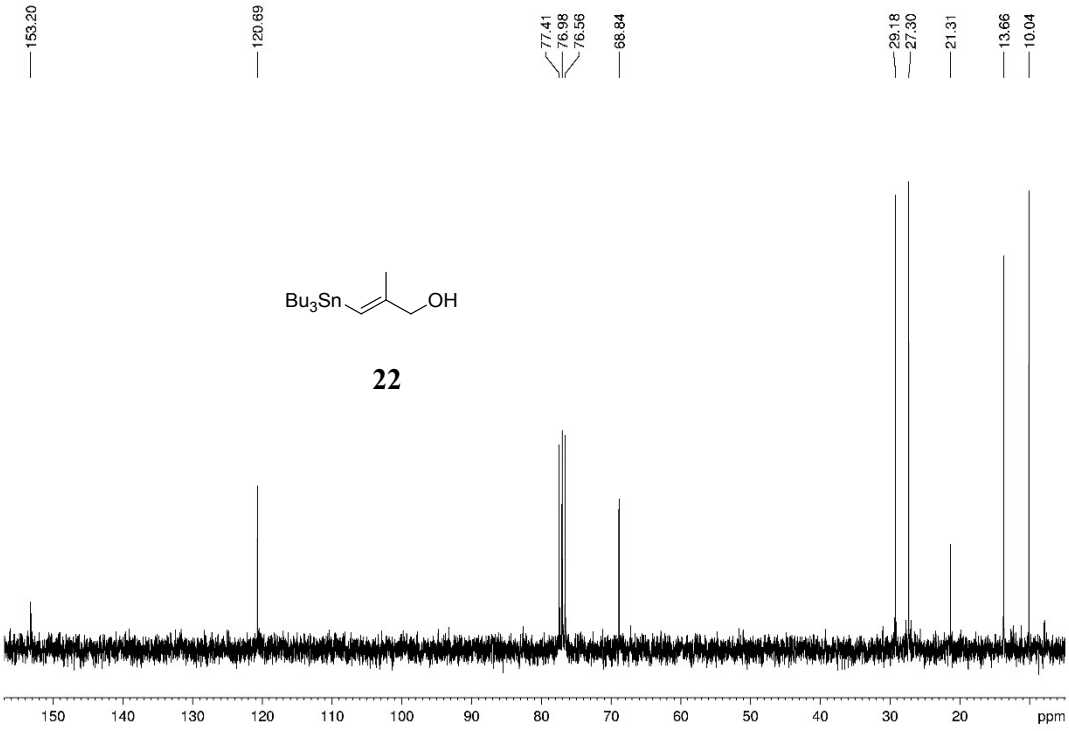
21


135.17
124.20
117.37
116.86
86.67
77.41
76.99
76.57
30.74
27.47
O2N
N
Boc
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
ppm

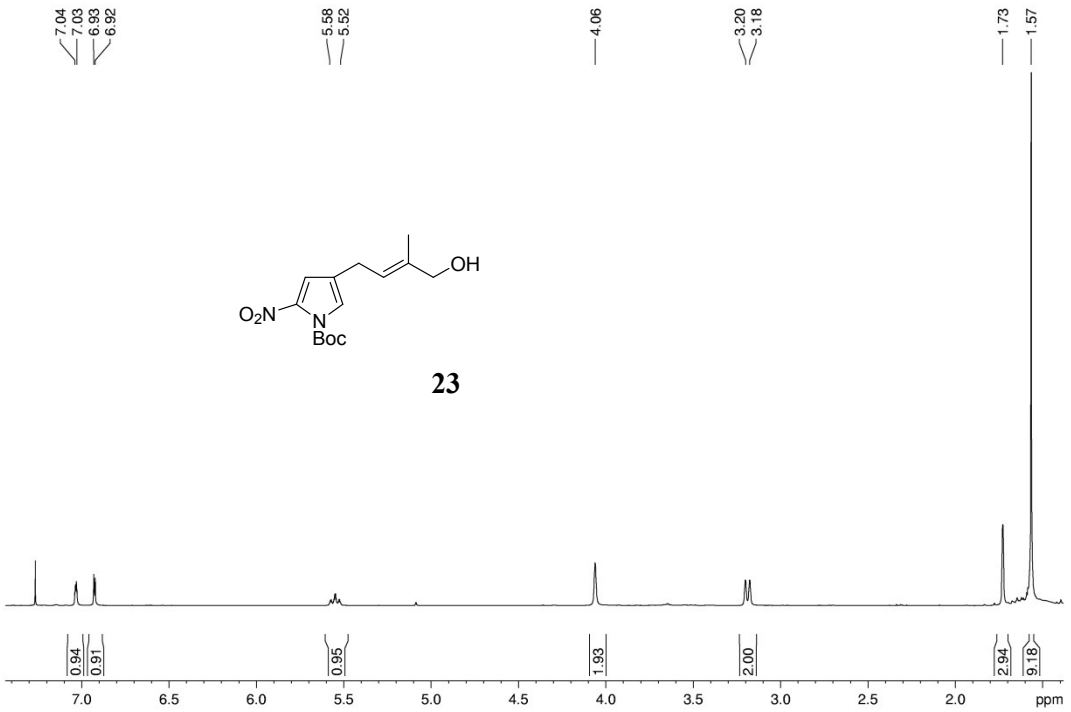
21


7.26
5.80
5.79
4.07
1.77
1.55
1.45
1.37
1.25
0.95
0.86
Bu3Sn
OH
0.93
2.00
2.89
6.53
6.39
15.10
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
ppm

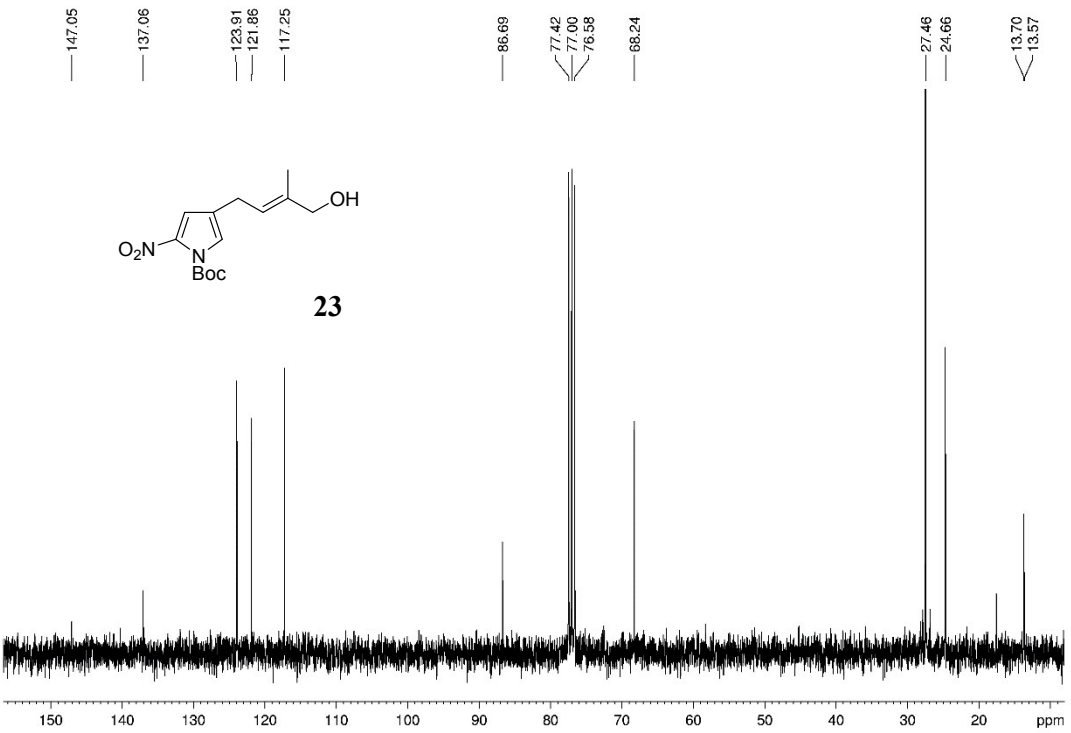
22


153.20
120.69
77.41
76.98
76.56
68.84
29.18
27.30
21.31
13.66
10.04
Bu3Sn
OH
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

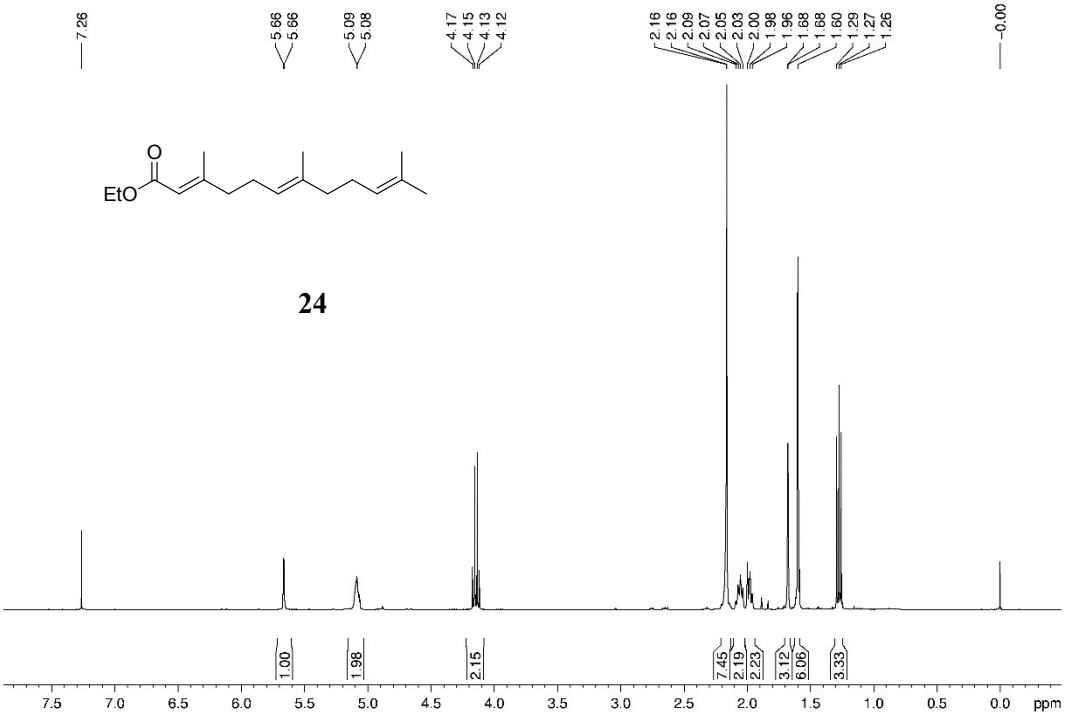
22


7.04
7.03
6.93
6.92
5.58
5.52
4.06
3.20
3.18
1.73
1.57
OH
O2N
N
Boc
0.94
0.91
0.95
1.93
2.00
2.94
9.18
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

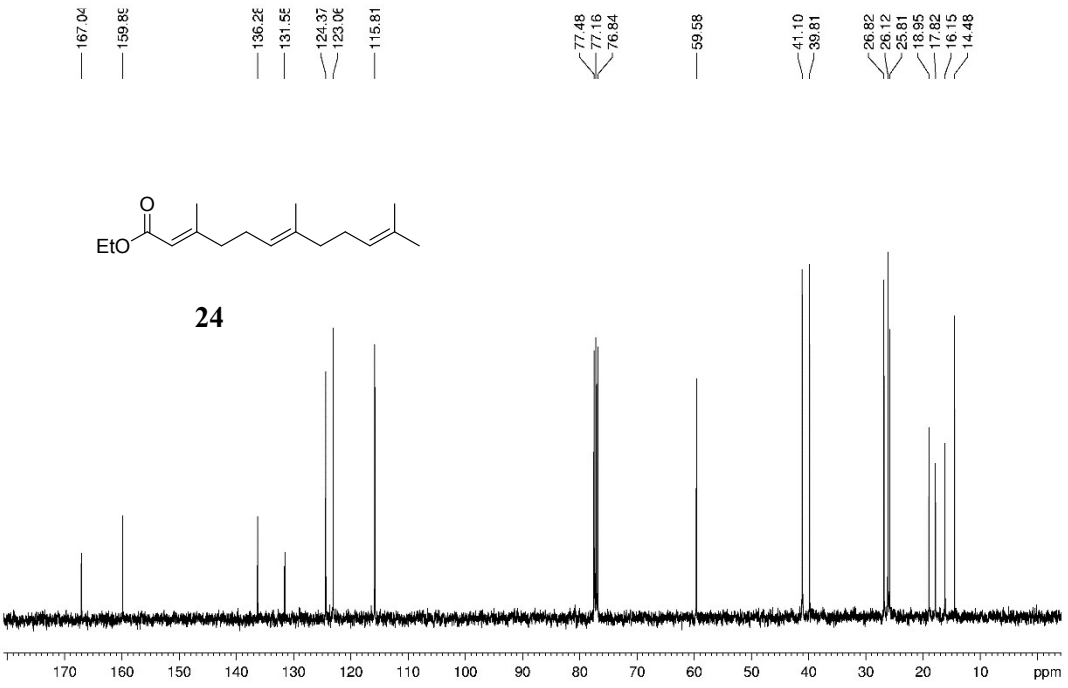
23


147.05
137.06
123.91
121.86
117.25
86.69
77.42
77.00
76.58
68.24
27.46
24.66
13.70
13.57
OH
O2N
N
Boc
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

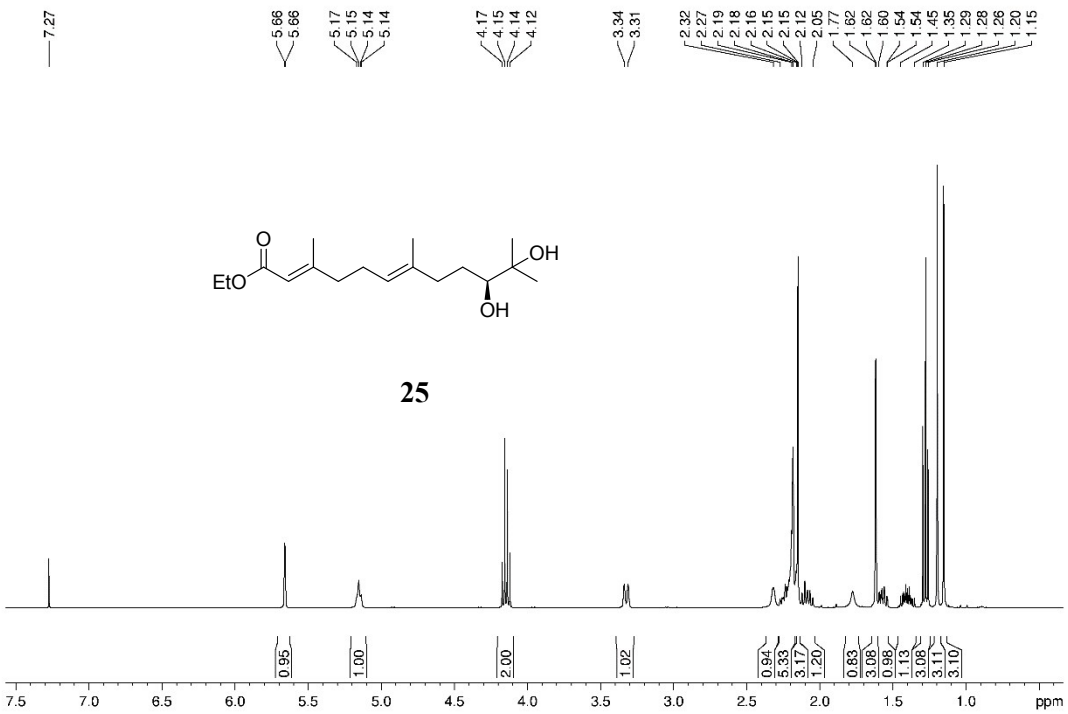
23


7.26
5.66
5.66
5.09
5.08
4.17
4.15
4.13
4.12
2.16
2.16
2.09
2.07
2.05
2.03
2.00
1.98
1.96
1.88
1.68
1.60
1.29
1.27
1.26
0.00
O
EtO
1.00
1.98
2.15
7.45
2.19
2.23
3.12
6.06
3.33
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
ppm

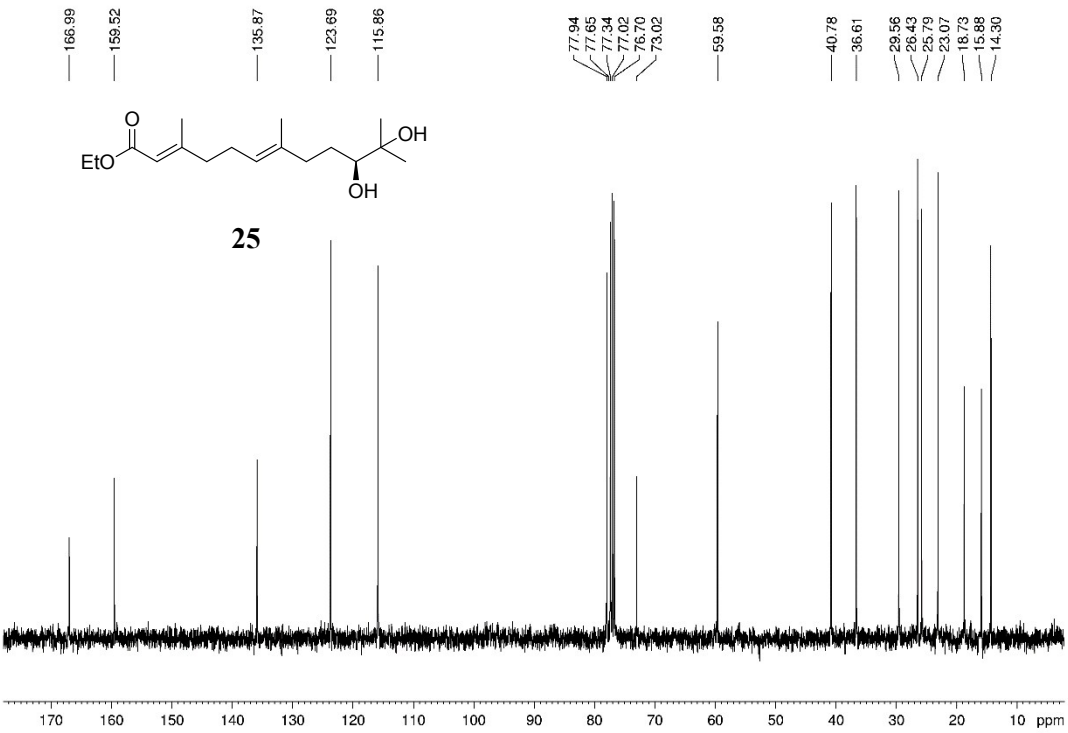
24


167.04
159.85
136.28
131.55
124.37
123.06
115.81
77.48
77.16
76.84
59.58
41.10
39.81
26.82
26.12
25.81
18.95
17.82
16.15
14.48
O
EtO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

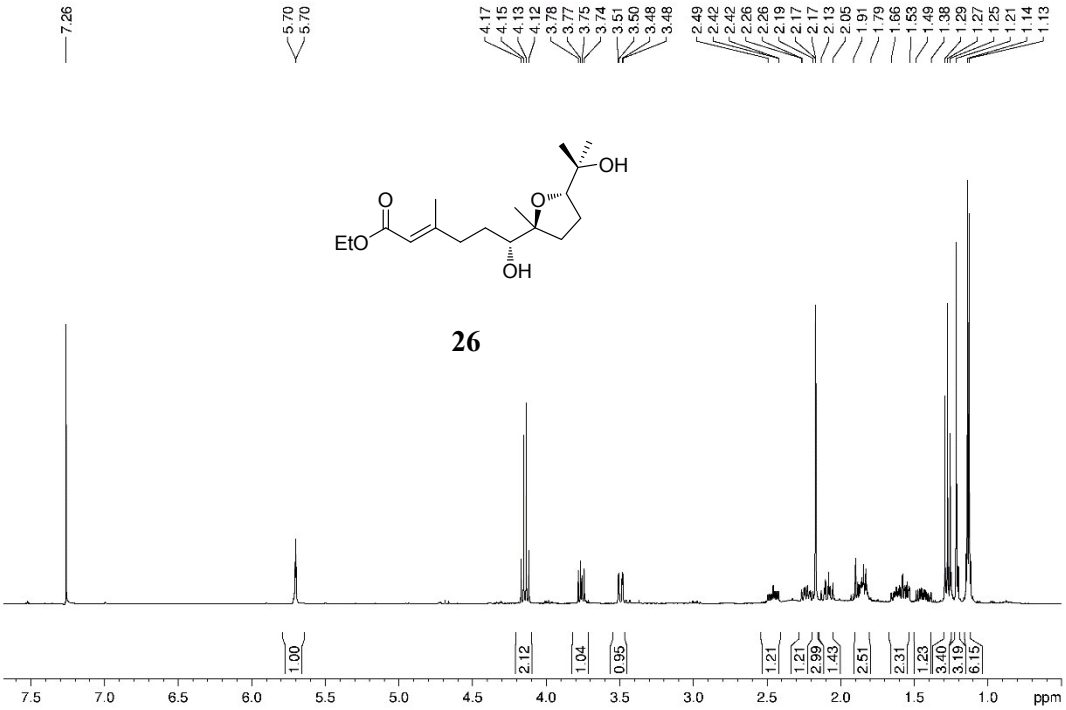
24


7.27
5.66
5.66
5.17
5.15
5.14
5.14
4.17
4.15
4.14
4.12
3.34
3.31
2.32
2.27
2.19
2.18
2.16
2.15
2.15
2.12
2.05
1.77
1.62
1.62
1.60
1.54
1.54
1.45
1.35
1.29
1.28
1.26
1.20
1.15
O
EtO
OH
OH
0.95
1.00
2.00
1.02
0.94
5.33
3.17
1.20
0.83
3.08
0.98
1.13
3.08
3.11
3.10
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
ppm

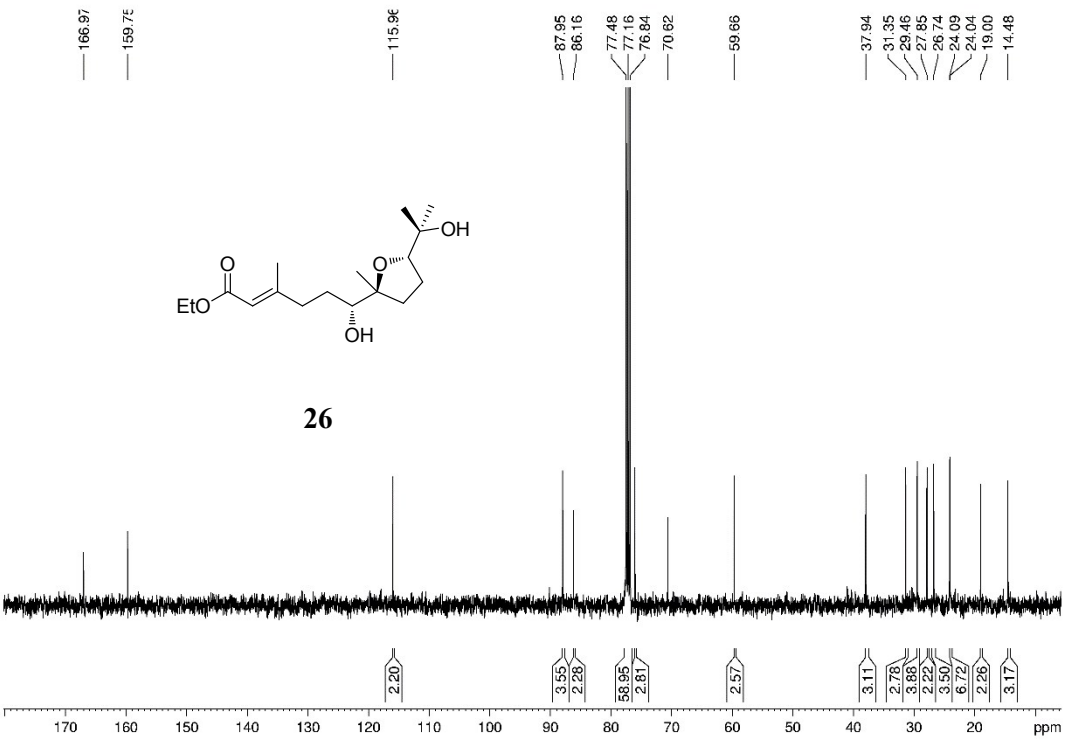
25


166.99
159.52
135.87
123.69
115.86
77.94
77.65
77.34
77.02
76.70
73.02
59.58
40.78
36.61
29.56
26.43
25.79
23.07
18.73
15.88
14.30
O
EtO
OH
OH
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

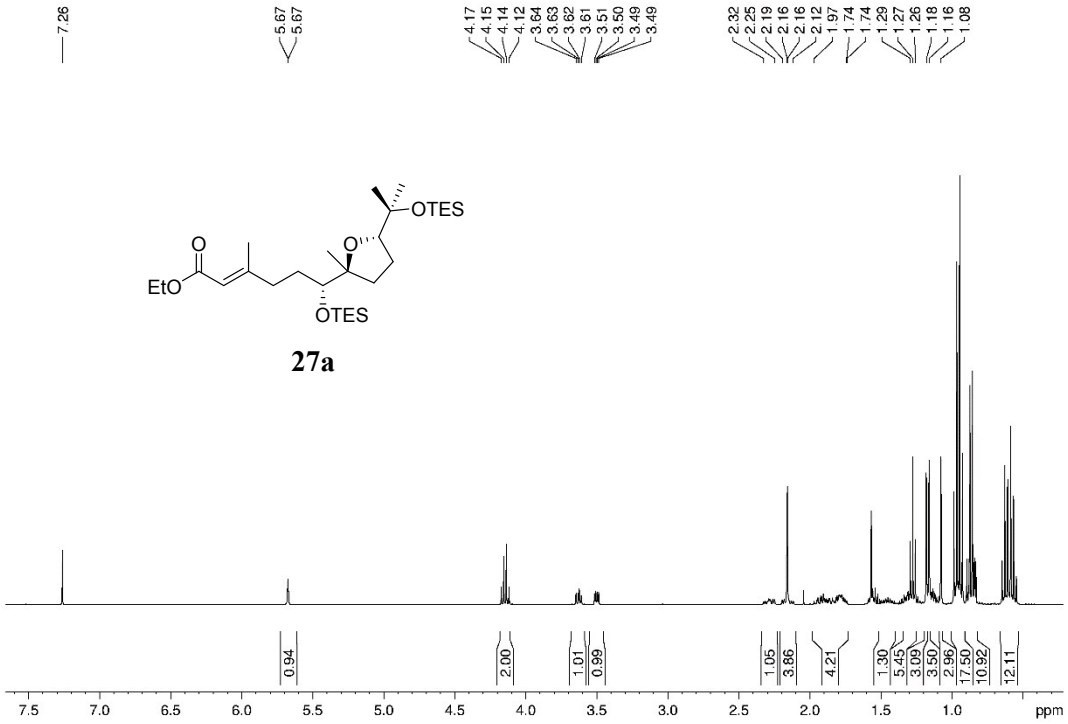
25


7.26
5.70
5.70
4.17
4.15
4.13
4.12
3.78
3.77
3.75
3.74
3.51
3.50
3.48
3.48
2.49
2.42
2.42
2.26
2.26
2.19
2.17
2.17
2.13
2.05
1.91
1.79
1.66
1.53
1.49
1.38
1.29
1.27
1.25
1.21
1.14
1.13
OH
O
O
EtO
OH
1.00
2.12
1.04
0.95
1.21
1.21
2.99
1.43
2.51
2.31
1.23
3.40
3.19
6.15
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
ppm

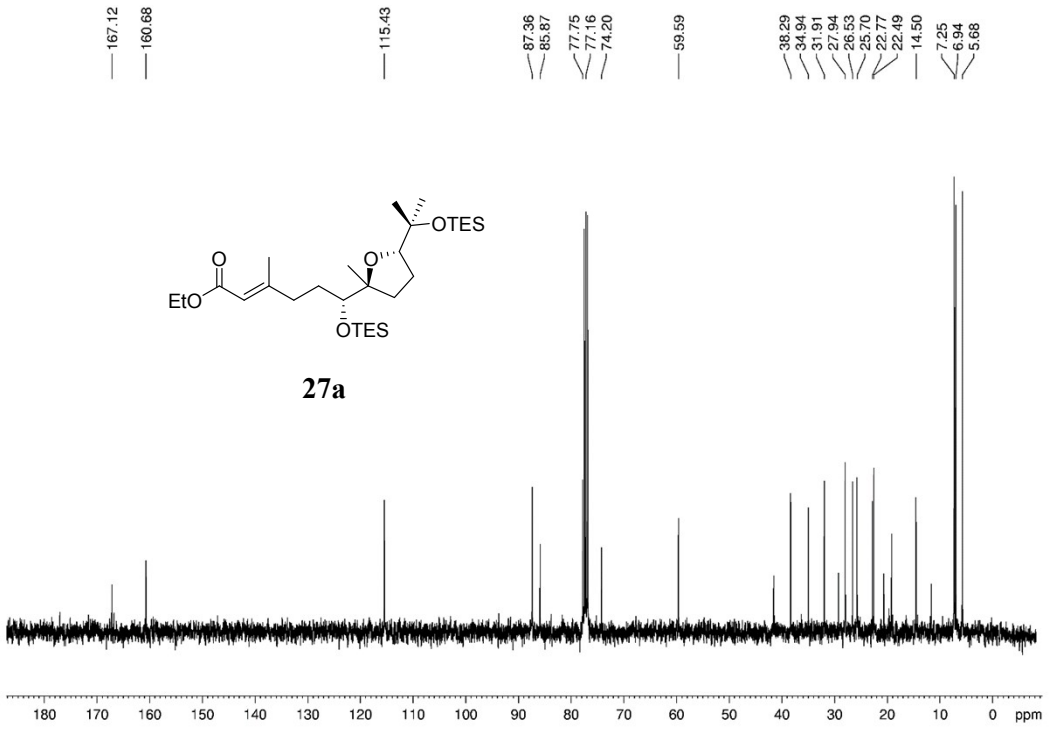
26


166.97
159.75
115.96
87.95
86.16
77.48
77.16
76.84
70.62
59.66
37.94
31.35
29.46
27.85
26.74
24.09
24.04
19.00
14.48
OH
O
O
EtO
OH
2.20
3.55
2.28
58.95
2.81
2.57
3.11
2.78
3.88
2.22
3.50
6.72
2.26
3.17
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

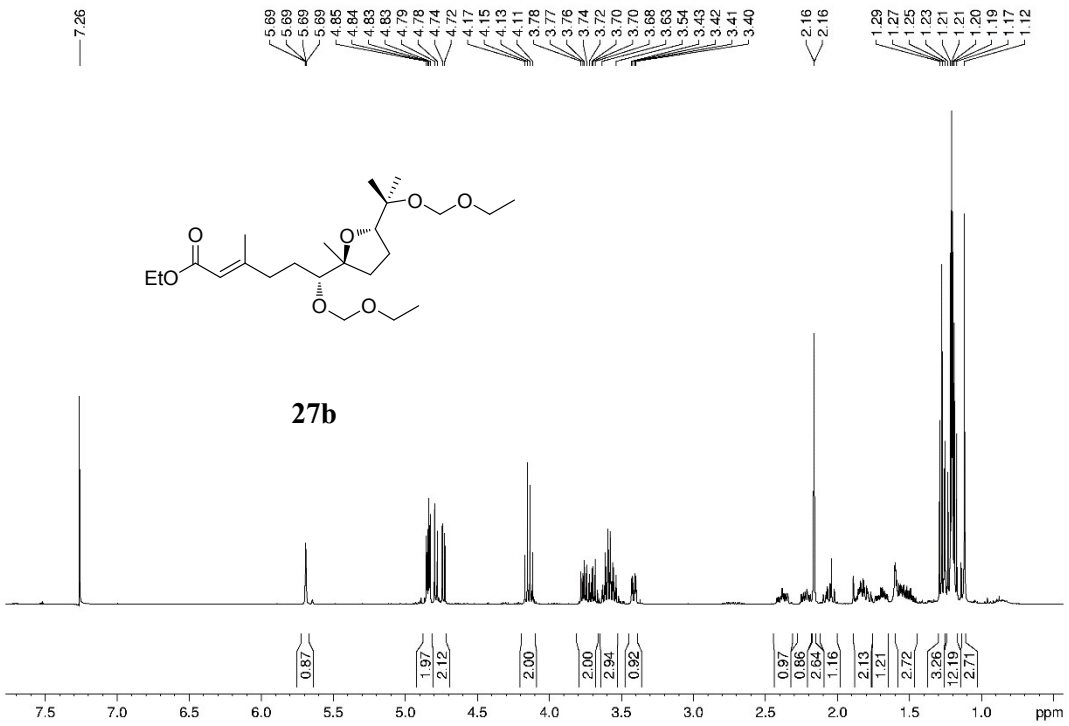
26


7.26
5.67
5.67
4.17
4.15
4.14
4.12
3.64
3.63
3.62
3.61
3.51
3.50
3.49
3.49
2.32
2.25
2.19
2.16
2.16
2.12
1.97
1.74
1.74
1.29
1.27
1.26
1.18
1.16
1.08
OTES
O
O
EtO
OTES
0.94
2.00
1.01
0.99
1.05
3.86
4.21
1.30
5.45
3.09
3.50
2.96
17.50
10.92
12.11
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
ppm

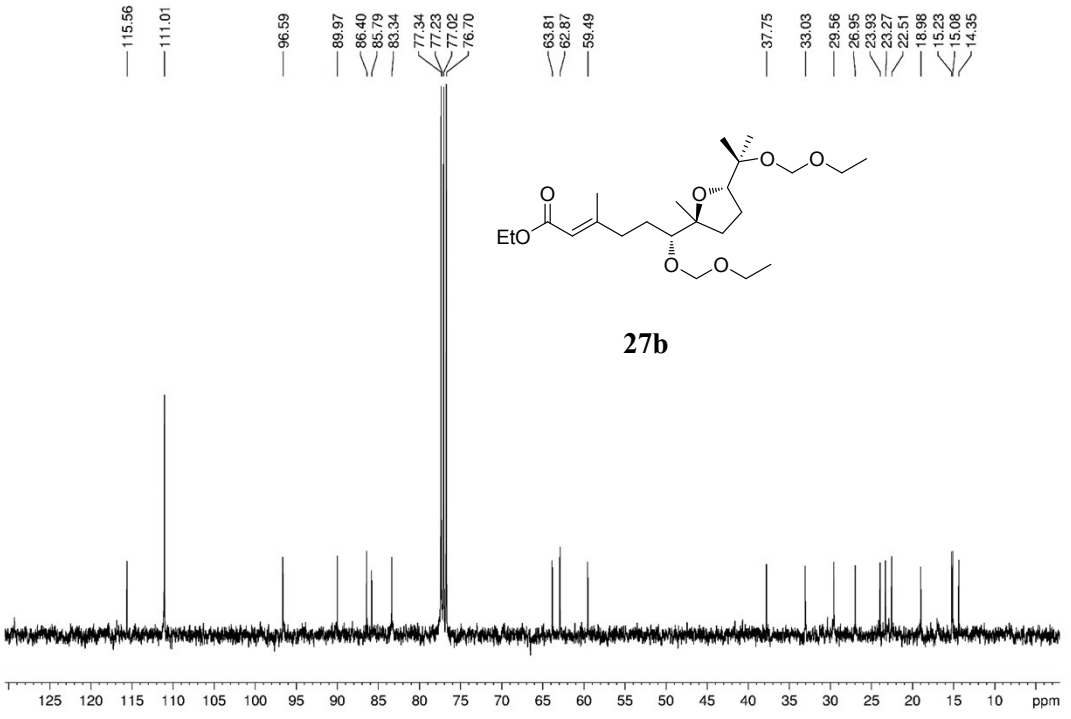
27a


167.12
160.68
115.43
87.36
85.87
77.75
77.16
74.20
59.59
38.29
34.94
31.91
27.94
26.53
25.70
22.77
22.49
14.50
7.25
6.94
5.68
OTES
O
O
EtO
OTES
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

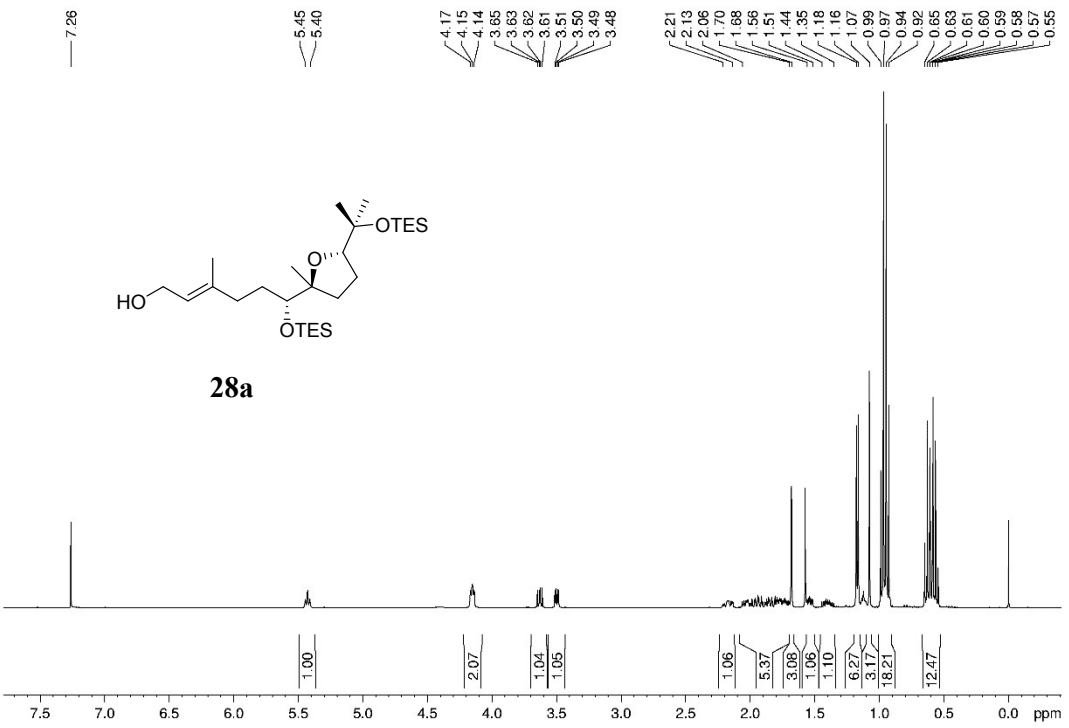
27a


7.26
5.69
5.69
5.69
4.85
4.84
4.83
4.83
4.79
4.78
4.74
4.72
4.17
4.15
4.13
4.11
3.78
3.77
3.76
3.74
3.72
3.70
3.70
3.68
3.63
3.54
3.43
3.42
3.41
3.40
2.16
2.16
1.29
1.27
1.25
1.23
1.21
1.21
1.20
1.19
1.17
1.12
EtO
0.87
1.97
2.12
2.00
2.00
2.94
0.92
0.97
0.86
2.64
1.16
2.13
1.21
2.72
3.26
12.19
2.71
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
ppm

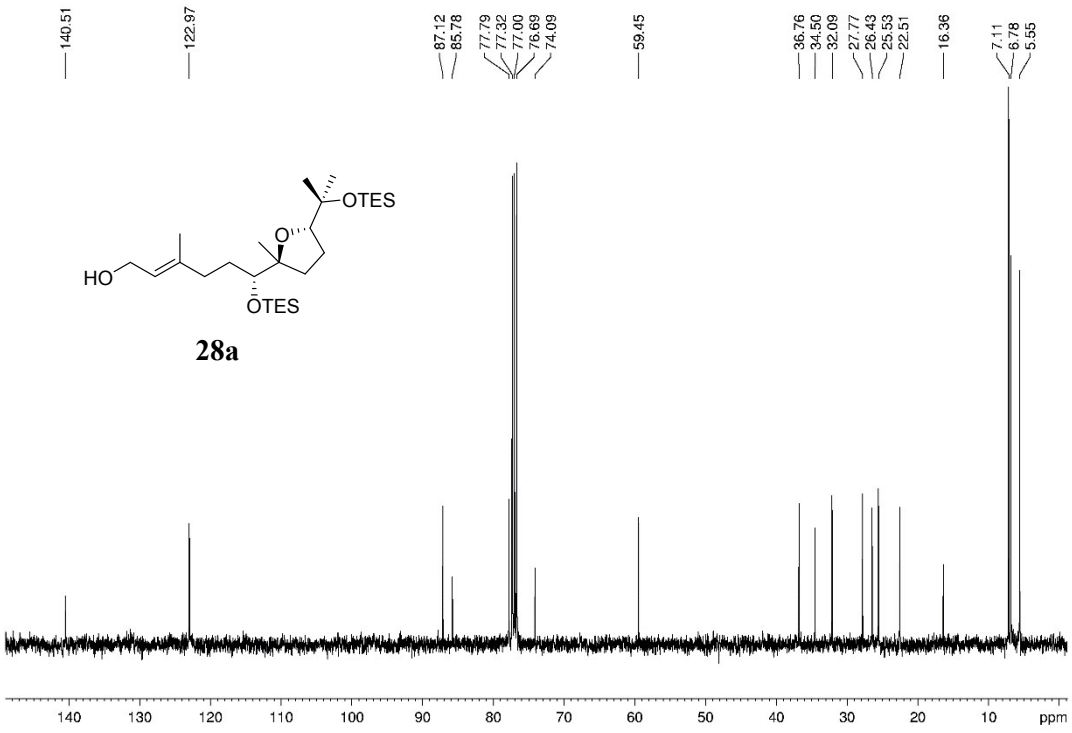
27b


115.56
111.01
96.59
89.97
86.40
85.79
83.34
77.34
77.23
77.02
76.70
63.81
62.87
59.49
37.75
33.03
29.56
26.95
23.93
23.27
22.51
18.98
15.23
15.08
14.35
EtO
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
ppm

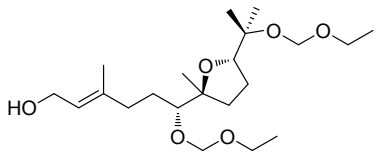
27b


7.26
5.45
5.40
4.17
4.15
4.14
3.65
3.63
3.62
3.61
3.51
3.50
3.49
3.48
2.21
2.13
2.06
1.70
1.68
1.56
1.51
1.44
1.35
1.18
1.16
1.07
0.99
0.97
0.94
0.92
0.65
0.63
0.61
0.60
0.59
0.58
0.57
0.55
OTES
O
HO
OTES
1.00
2.07
1.04
1.05
1.06
5.37
3.08
1.06
1.10
6.27
3.17
18.21
12.47
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
ppm

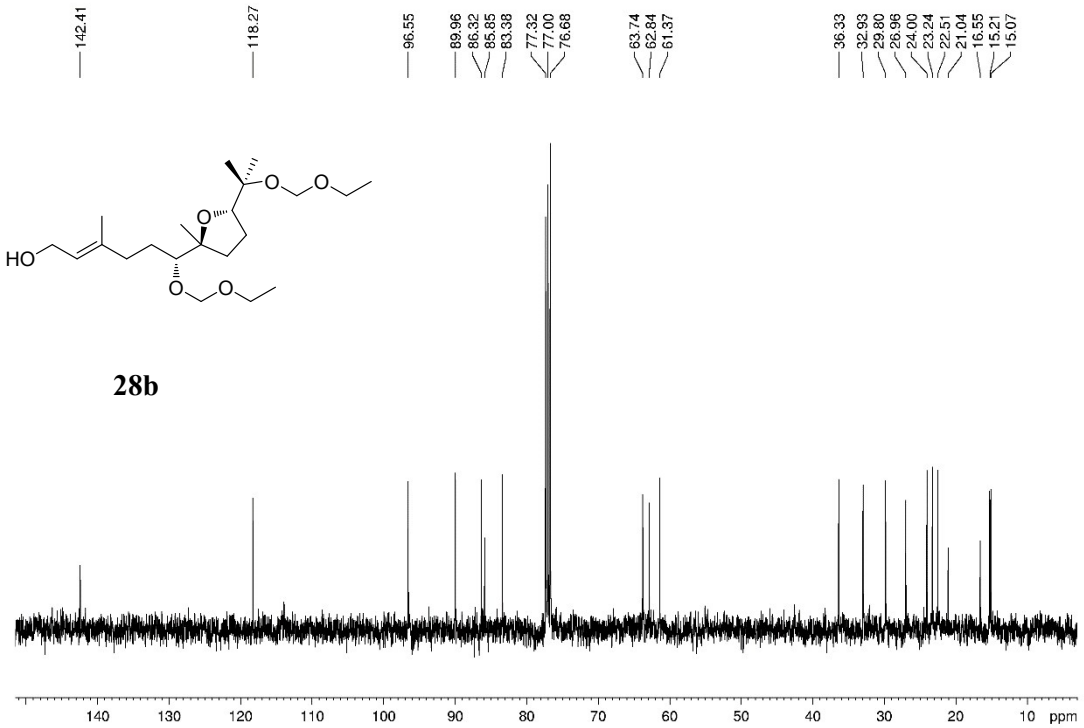
28a


140.51
122.97
87.12
85.78
77.79
77.32
77.00
76.69
74.09
59.45
36.76
34.50
32.09
27.77
26.43
25.53
22.51
16.36
7.11
6.78
5.55
OTES
O
HO
OTES
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

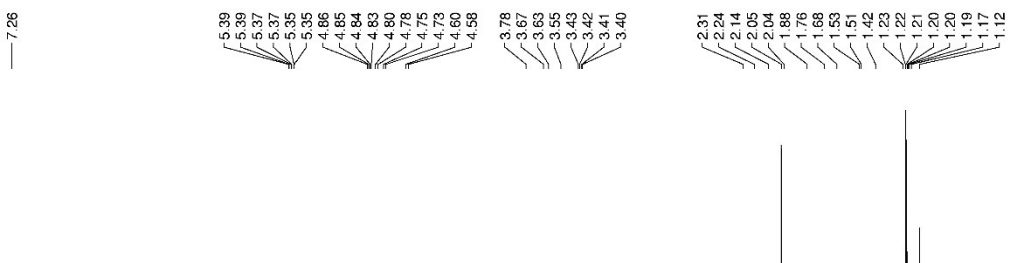
28a

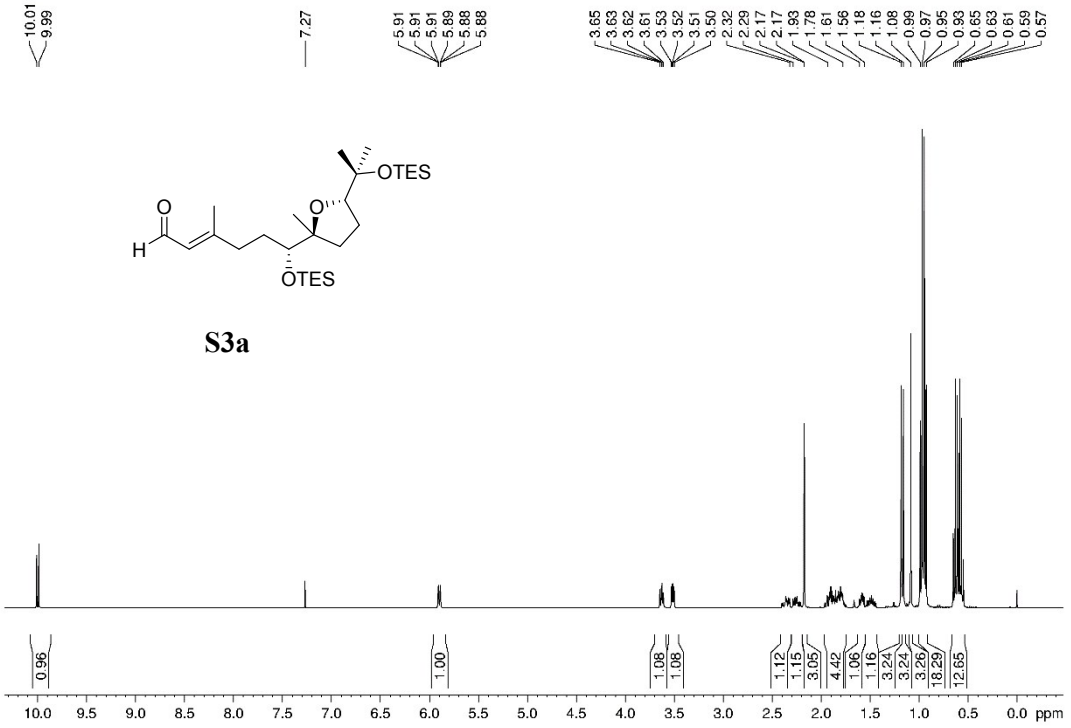

HO
O
O
O
O
O
O

28b

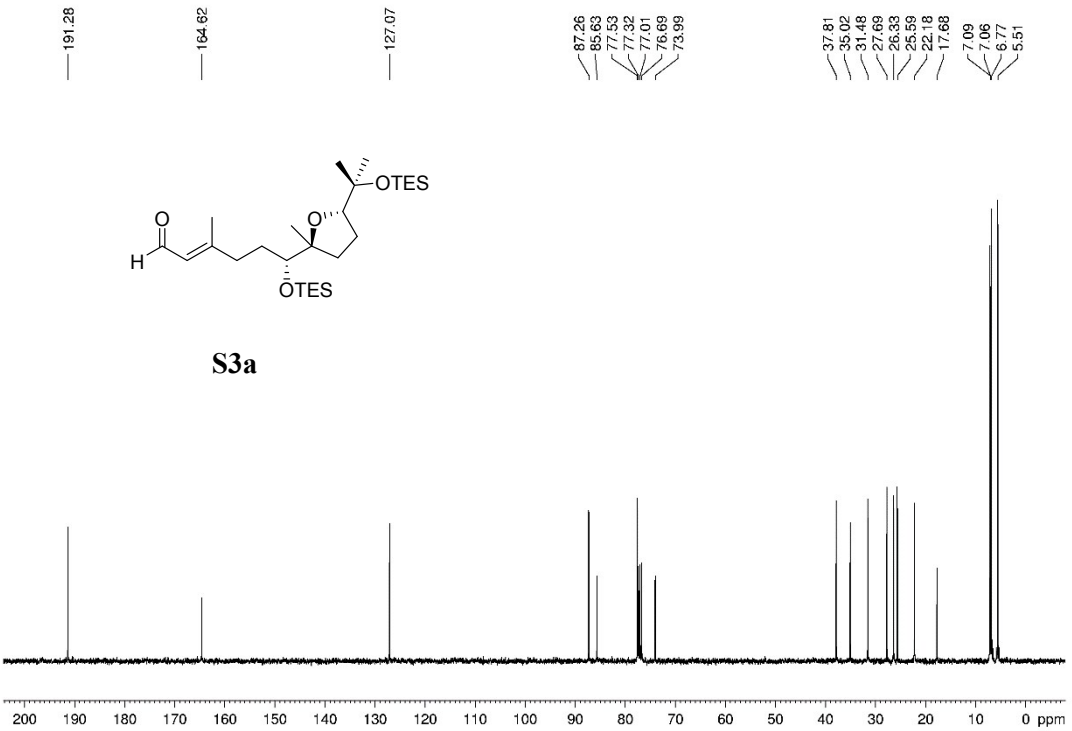

142.41
118.27
96.55
89.96
86.32
85.85
83.38
77.32
77.00
76.68
63.74
62.84
61.37
36.33
32.93
29.80
26.96
24.00
23.24
22.51
21.04
16.55
15.21
15.07
HO
O
O
O
O
O
O
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

28b

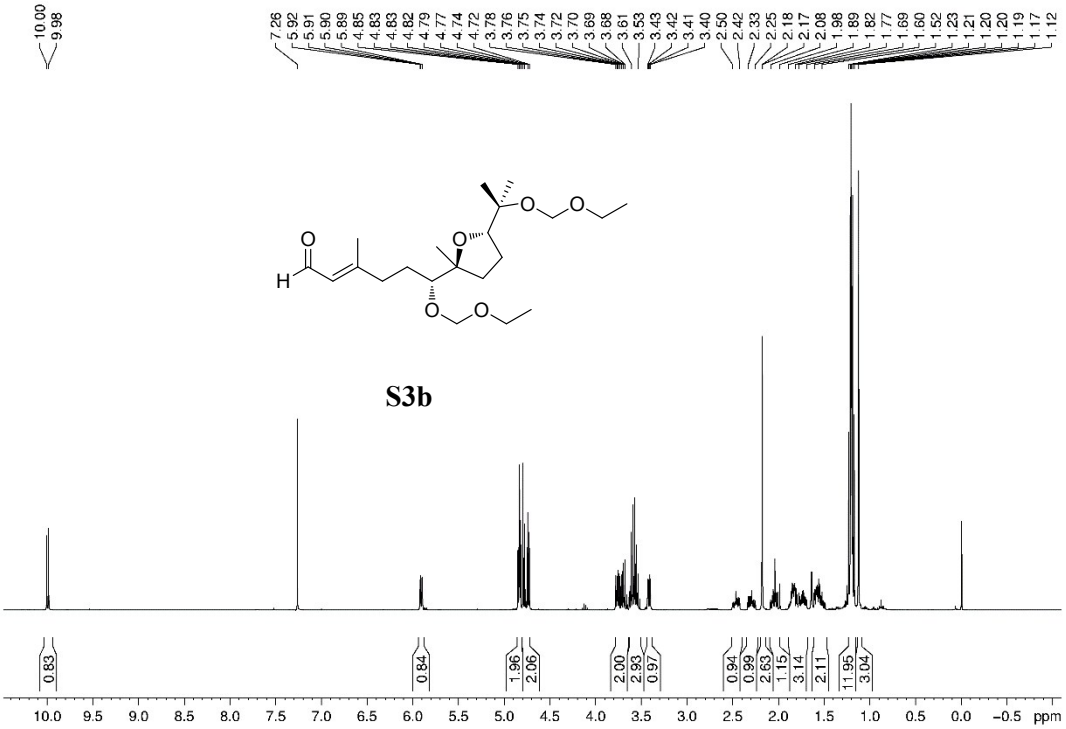

7.26
5.39
5.39
5.37
5.37
5.35
5.35
4.86
4.85
4.84
4.83
4.80
4.78
4.75
4.73
4.60
4.58
3.78
3.67
3.63
3.55
3.43
3.42
3.41
3.40
2.31
2.24
2.14
2.05
2.04
1.88
1.76
1.68
1.53
1.51
1.42
1.23
1.22
1.21
1.20
1.19
1.17
1.12


10.01
9.99
7.27
5.91
5.91
5.91
5.89
5.88
5.88
3.65
3.63
3.62
3.61
3.53
3.52
3.51
3.50
2.32
2.29
2.17
2.17
1.93
1.78
1.61
1.56
1.18
1.16
1.08
0.99
0.97
0.95
0.93
0.65
0.63
0.61
0.59
0.57
OTES
O
O
H
OTES
0.96
1.00
1.08
1.08
1.12
1.15
3.05
4.42
1.06
1.16
3.24
3.24
3.26
18.29
12.65
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 ppm

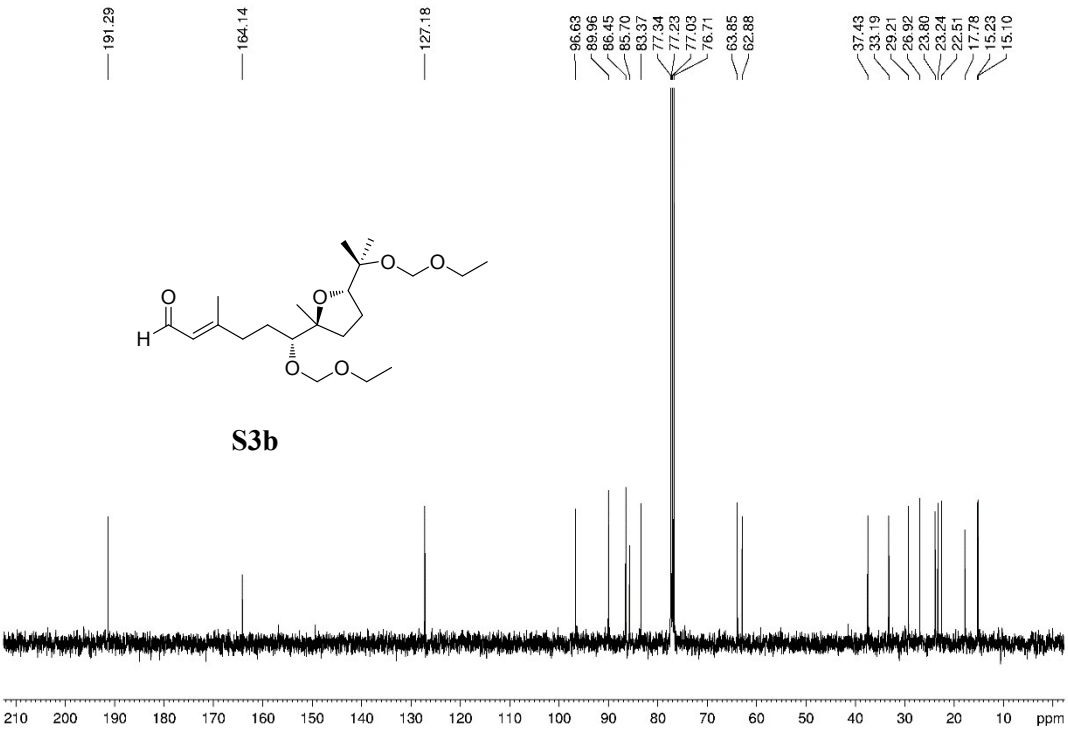
S3a


191.28
164.62
127.07
87.26
85.63
77.53
77.32
77.01
76.69
73.99
37.81
35.02
31.48
27.69
26.33
25.59
22.18
17.68
7.09
7.06
6.77
5.51
OTES
O
O
H
OTES
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

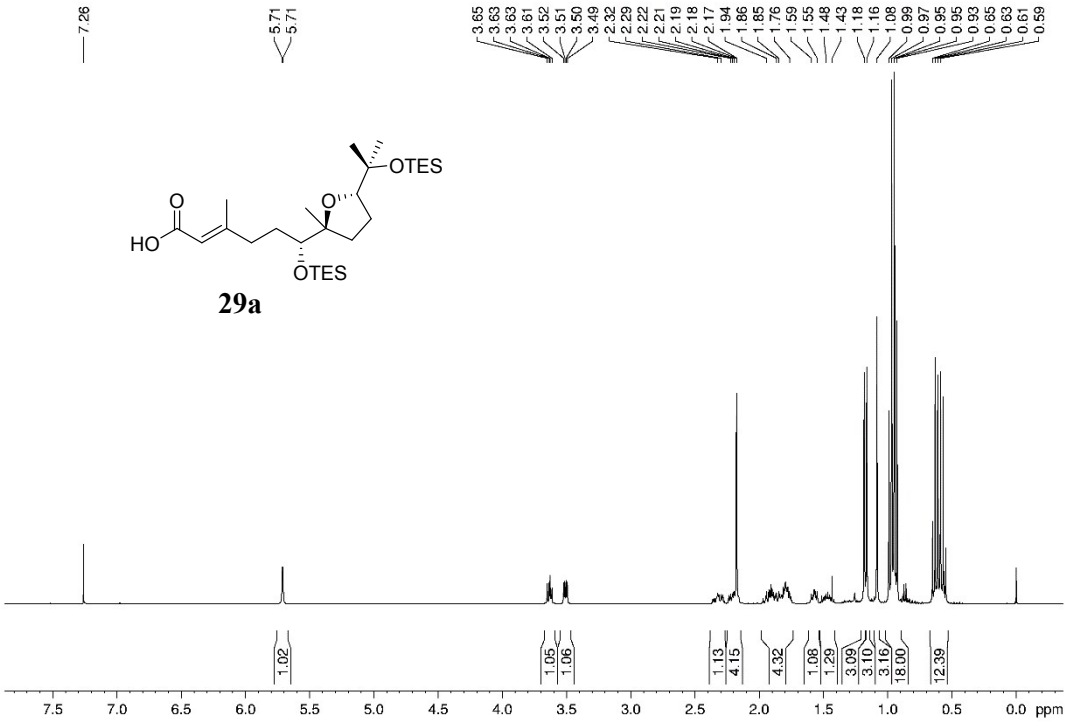
S3a


10.00
9.98
7.26
5.92
5.91
5.90
5.89
4.85
4.83
4.83
4.82
4.79
4.77
4.74
4.72
3.78
3.76
3.75
3.74
3.72
3.70
3.69
3.68
3.61
3.53
3.43
3.42
3.41
3.40
2.50
2.42
2.33
2.25
2.18
2.17
2.08
1.98
1.89
1.82
1.77
1.69
1.60
1.52
1.23
1.21
1.20
1.20
1.19
1.17
1.12
0.83
0.84
1.96
2.06
2.00
2.98
0.97
0.94
0.99
2.63
1.15
3.14
2.11
11.95
3.04
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 −0.5 ppm

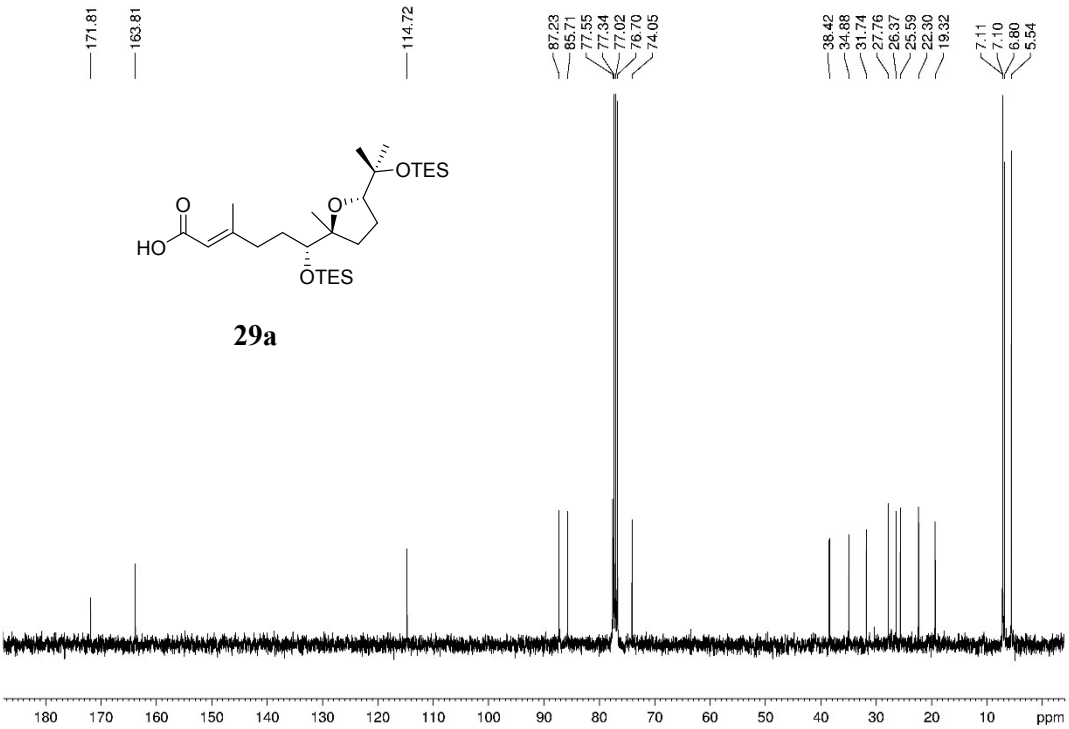
S3b


191.29
164.14
127.18
96.63
89.96
86.45
85.70
83.37
77.34
77.23
77.03
76.71
63.85
62.88
37.43
33.19
29.21
26.92
23.80
23.24
22.51
17.78
15.23
15.10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

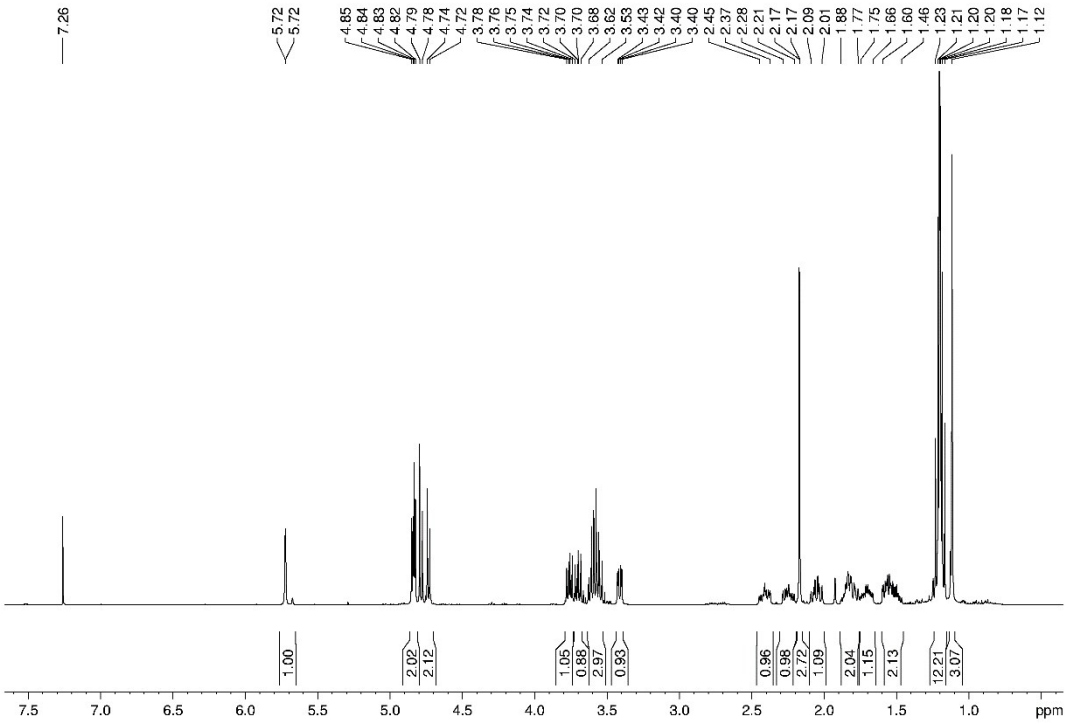
S3b

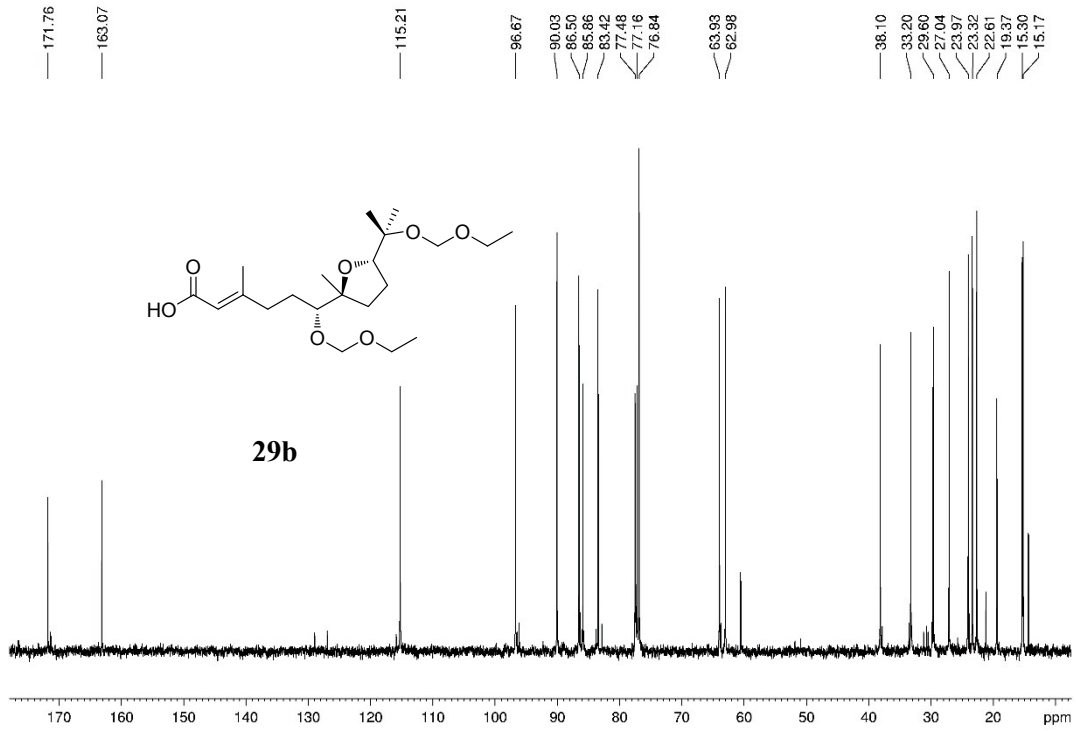

7.26
5.71
5.71
3.65
3.63
3.63
3.61
3.52
3.51
3.50
3.49
2.32
2.29
2.22
2.21
2.19
2.18
2.17
1.94
1.86
1.85
1.76
1.59
1.55
1.48
1.43
1.18
1.16
1.08
0.99
0.97
0.95
0.95
0.93
0.65
0.63
0.61
0.59
OTES
O
O
HO
OTES
1.02
1.05
1.06
1.13
4.15
4.32
1.08
1.29
3.09
3.10
3.16
18.00
12.39
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

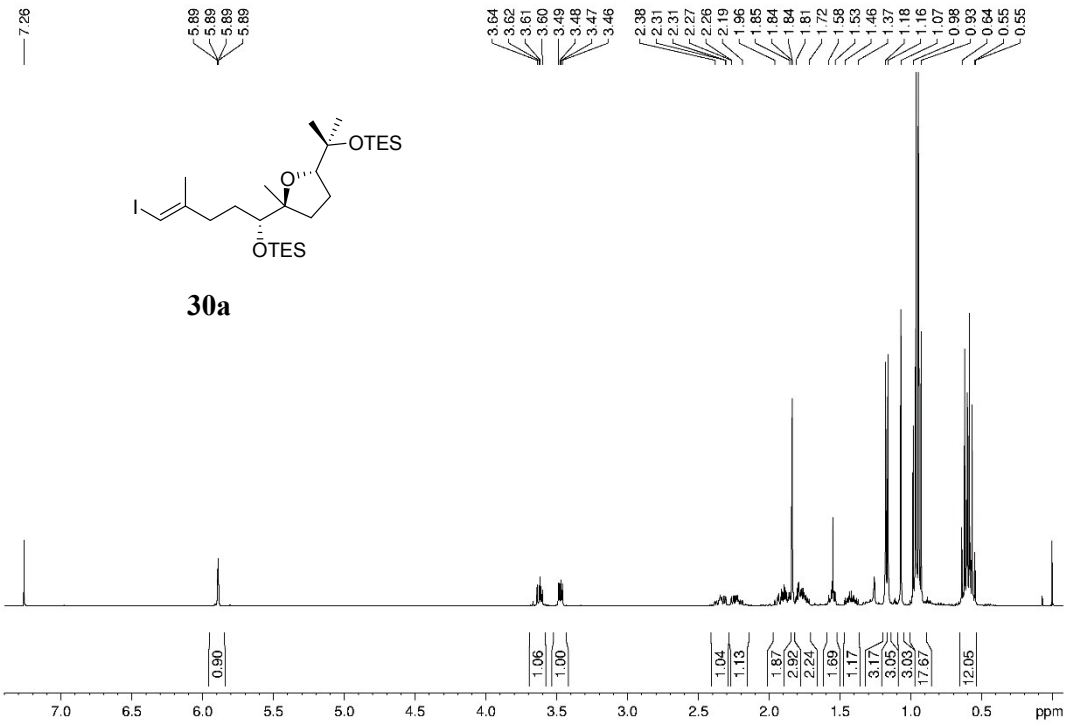
29a


171.81
163.81
114.72
87.23
85.71
77.55
77.34
77.02
76.70
74.05
38.42
34.88
31.74
27.76
26.37
25.59
22.30
19.32
7.11
7.10
6.80
5.54
OTES
O
O
HO
OTES
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

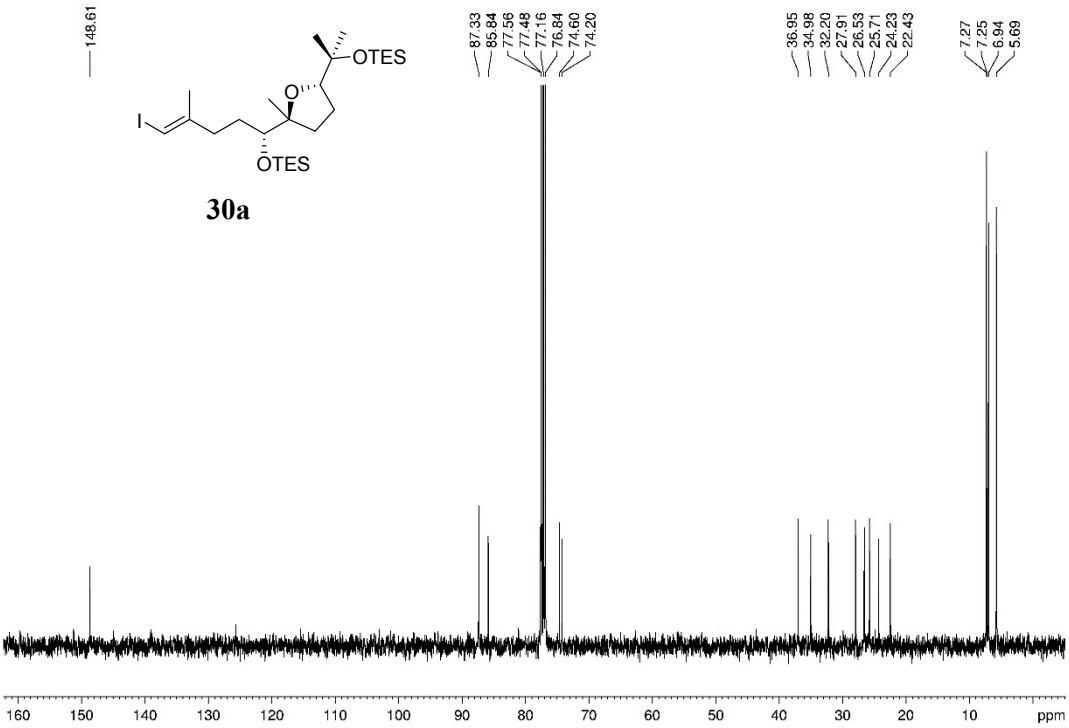
29a


7.26
5.72
5.72
4.85
4.84
4.83
4.82
4.79
4.78
4.74
4.72
3.78
3.76
3.75
3.74
3.72
3.70
3.70
3.68
3.62
3.53
3.43
3.42
3.40
3.40
2.45
2.37
2.28
2.21
2.17
2.17
2.09
2.01
1.88
1.77
1.75
1.66
1.60
1.46
1.23
1.21
1.20
1.20
1.18
1.17
1.12
1.00
2.02
2.12
1.05
0.88
2.97
0.93
0.96
0.98
2.72
1.09
2.04
1.15
2.13
12.21
3.07
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
ppm

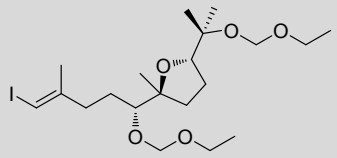

171.76
163.07
115.21
96.67
90.03
86.50
85.86
83.42
77.48
77.16
76.84
63.93
62.98
38.10
33.20
29.60
27.04
23.97
23.32
22.61
19.37
15.30
15.17
HO
O
O
O
O
O
O
29b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


7.26
5.89
5.89
5.89
5.89
3.64
3.62
3.61
3.60
3.49
3.48
3.47
3.46
2.38
2.31
2.31
2.27
2.26
2.19
1.96
1.85
1.84
1.84
1.81
1.72
1.58
1.53
1.46
1.37
1.18
1.16
1.07
0.98
0.93
0.64
0.55
0.55
OTES
O
I
OTES
0.90
1.06
1.00
1.04
1.13
1.87
2.92
2.24
1.69
1.17
3.17
3.05
3.03
17.67
12.05
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
ppm

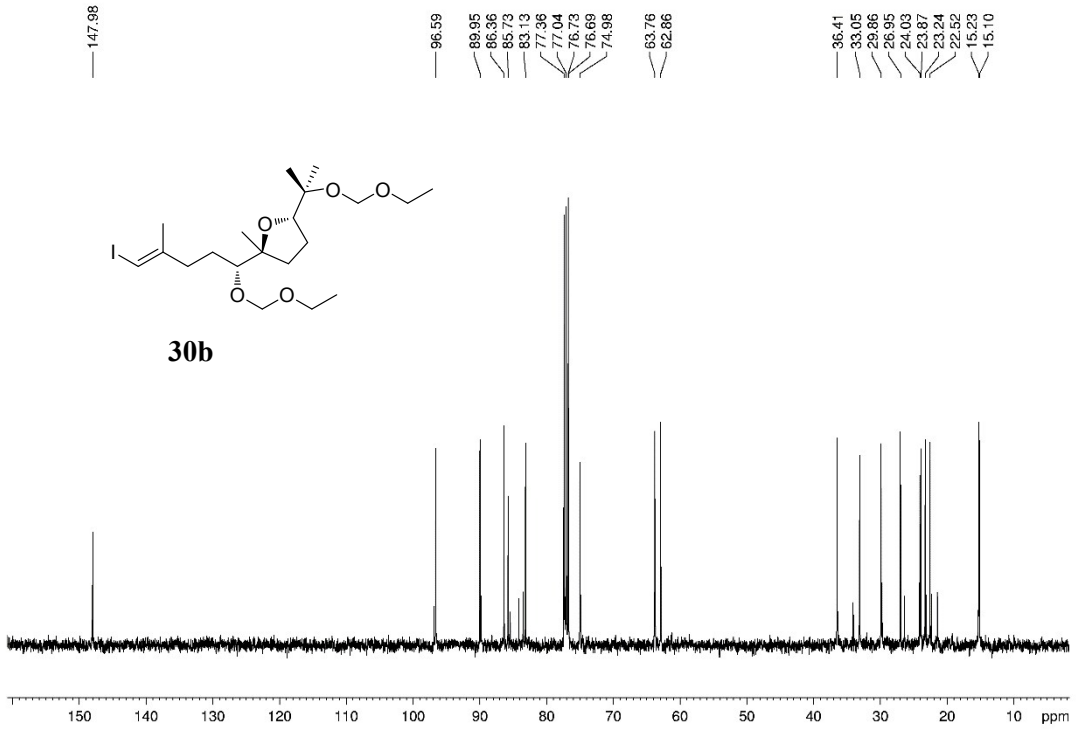
30a


148.61
87.33
85.84
77.56
77.48
77.16
76.84
74.60
74.20
36.95
34.98
32.20
27.91
26.53
25.71
24.23
22.43
7.27
7.25
6.94
5.69
OTES
O
I
OTES
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

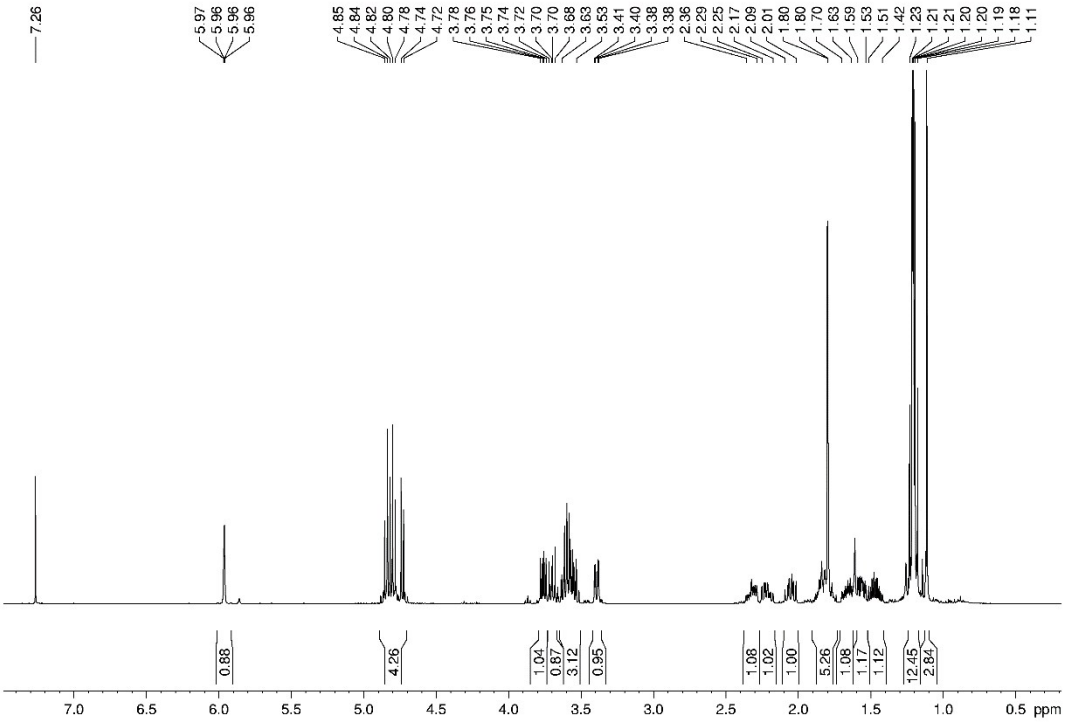
30a



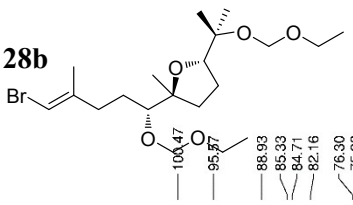
30b

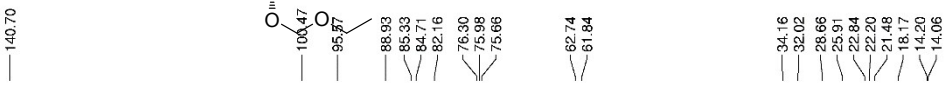

147.98
96.59
89.95
86.36
85.73
83.13
77.36
77.04
76.73
76.69
74.98
63.76
62.86
36.41
33.05
29.86
26.95
24.03
23.87
23.24
22.52
15.23
15.10
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

30b

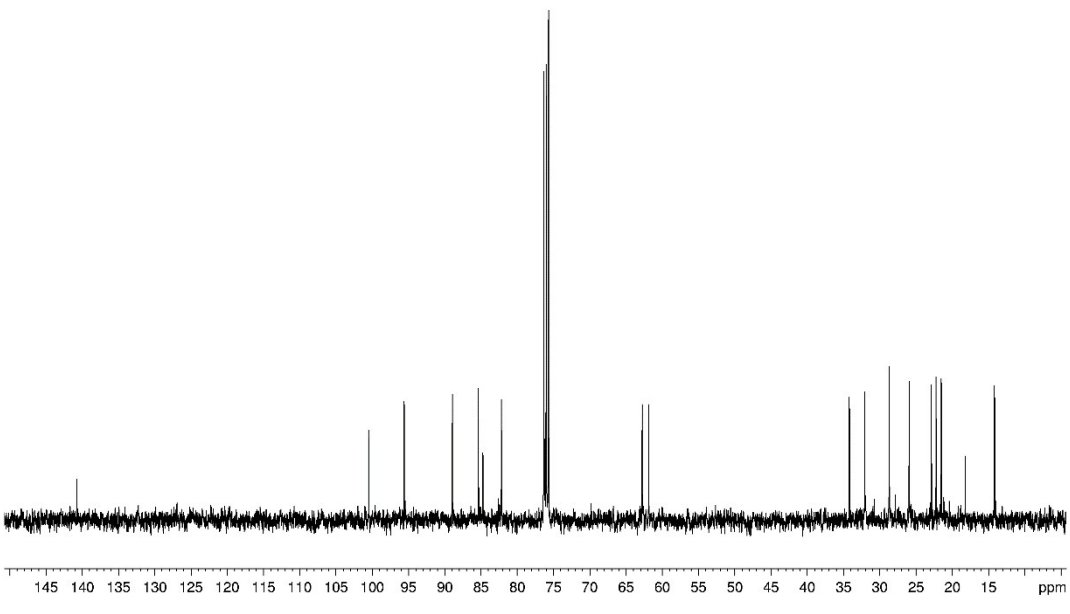

7.26
5.97
5.96
5.96
5.96
4.85
4.84
4.82
4.80
4.78
4.74
4.72
3.78
3.76
3.75
3.74
3.72
3.70
3.70
3.68
3.63
3.53
3.41
3.40
3.38
3.38
2.36
2.29
2.25
2.17
2.09
2.01
1.80
1.80
1.70
1.63
1.59
1.53
1.51
1.42
1.23
1.21
1.21
1.20
1.20
1.19
1.18
1.11
0.68
4.26
1.04
0.87
3.12
0.95
1.08
1.02
1.00
5.26
1.08
1.17
1.12
12.45
2.84
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 ppm

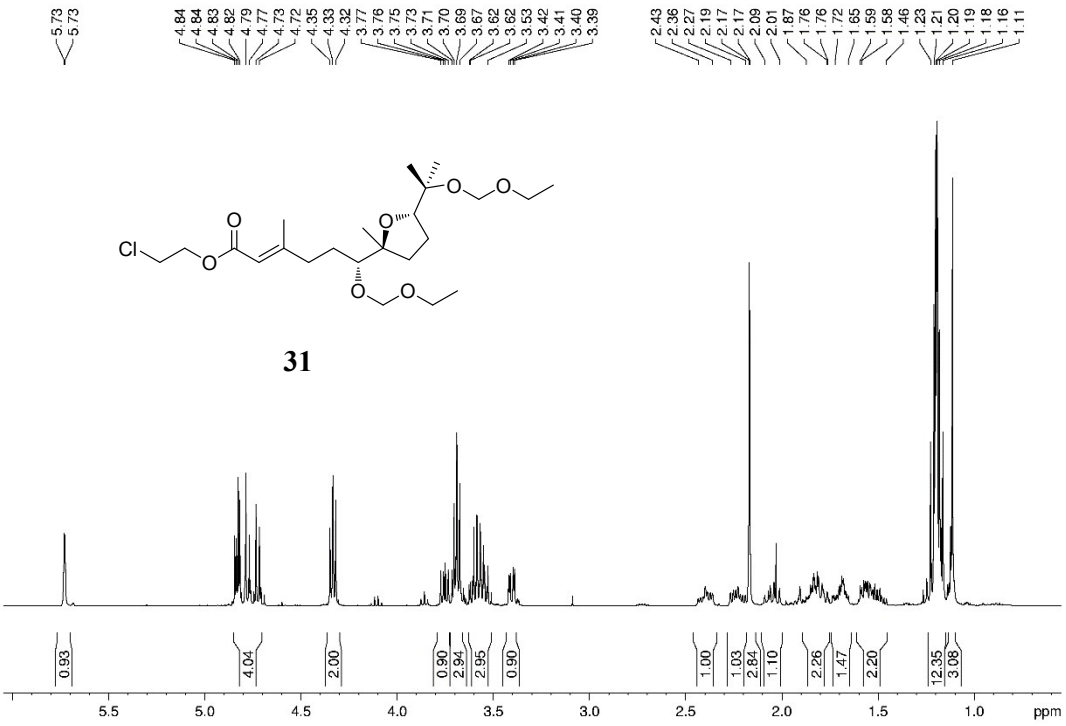
28b


Br
O
O
O
O

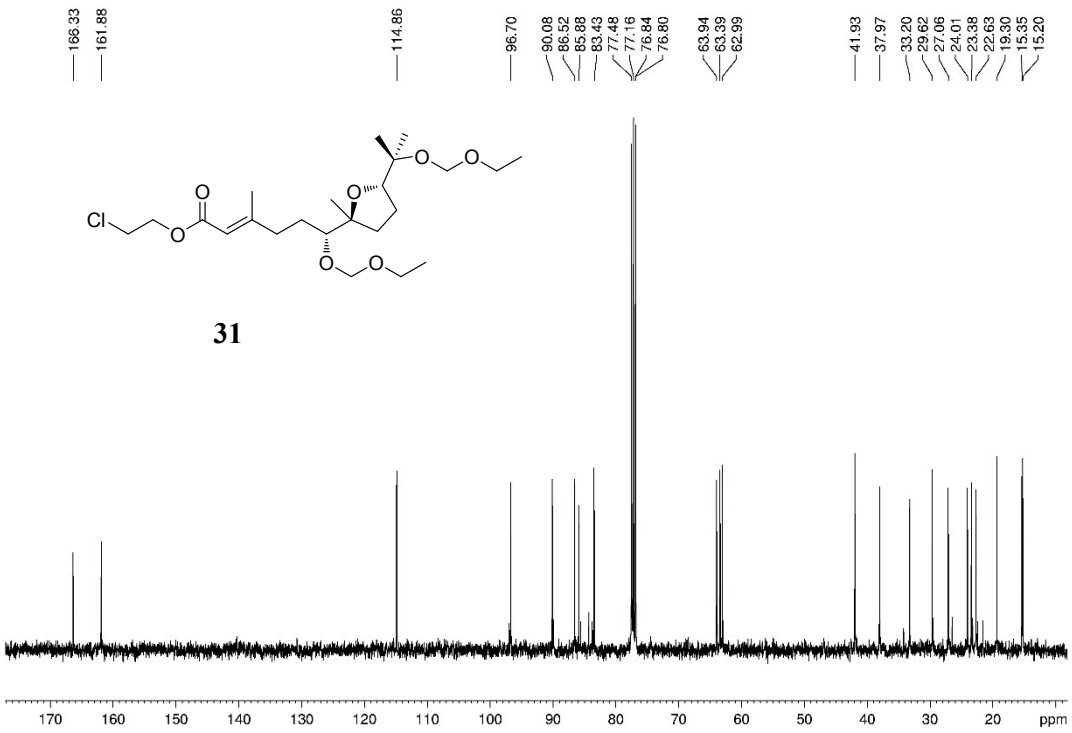

140.70
100.47
95.37
88.93
85.33
84.71
82.16
76.30
75.98
75.66
62.74
61.84
34.16
32.02
28.66
25.91
22.84
22.20
21.48
18.17
14.20
14.06

30c

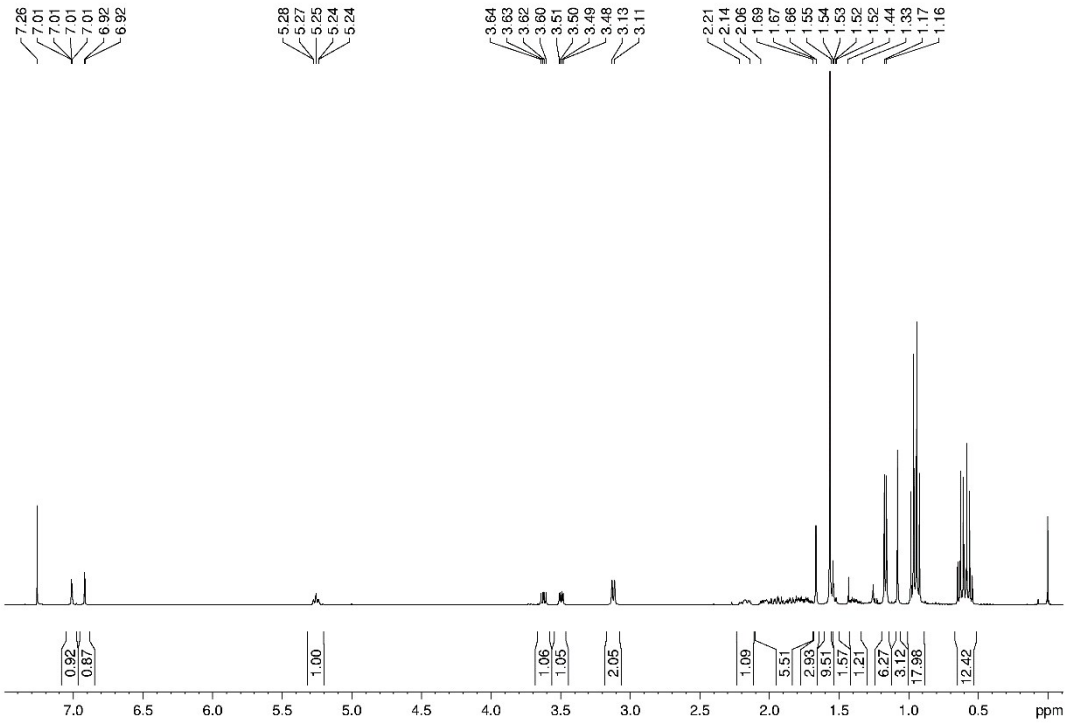

145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 ppm

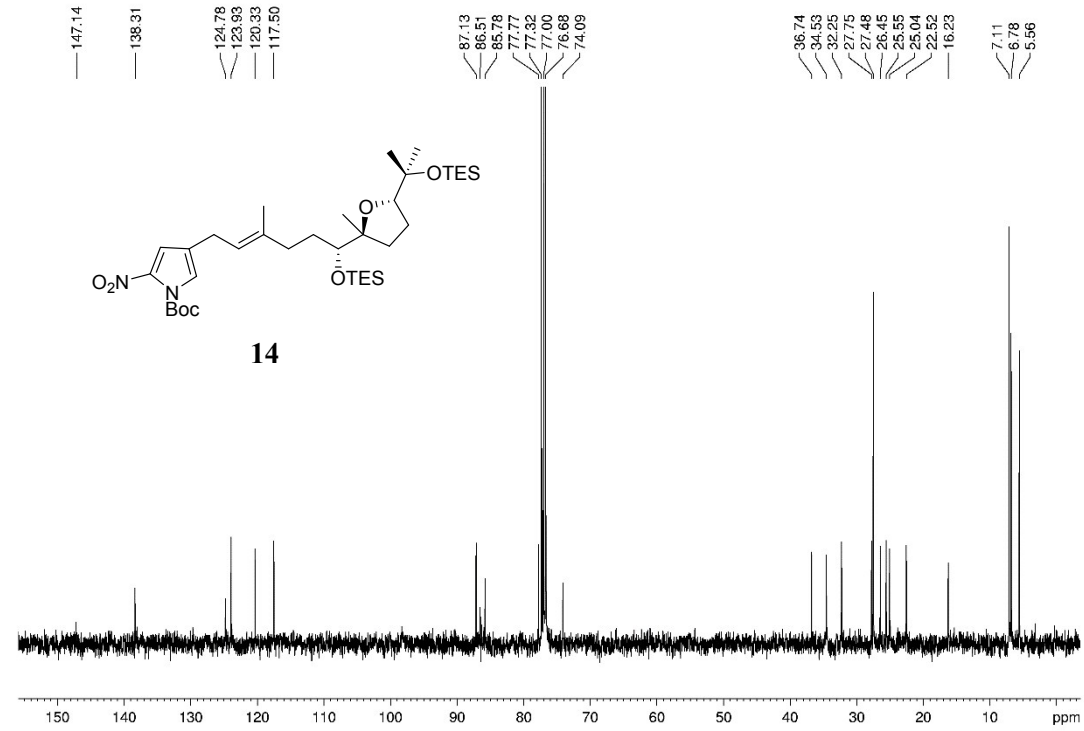

5.73
5.73
4.84
4.84
4.83
4.82
4.79
4.77
4.73
4.72
4.35
4.33
4.32
3.77
3.76
3.75
3.73
3.71
3.70
3.69
3.67
3.62
3.62
3.53
3.42
3.41
3.40
3.39
2.43
2.36
2.27
2.19
2.17
2.17
2.09
2.01
1.87
1.76
1.76
1.72
1.65
1.59
1.58
1.46
1.23
1.21
1.20
1.19
1.18
1.16
1.11
Cl
O
O
O
O
O
O
O
O
0.93
4.04
2.00
0.90
2.94
2.95
0.90
1.00
1.03
2.84
1.10
2.26
1.47
2.20
12.35
3.08
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

31

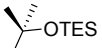

166.33
161.88
114.86
96.70
90.08
86.52
85.88
83.43
77.48
77.16
76.84
76.80
63.94
63.39
62.99
41.93
37.97
33.20
29.62
27.06
24.01
23.38
22.63
19.30
15.35
15.20
Cl
O
O
O
O
O
O
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

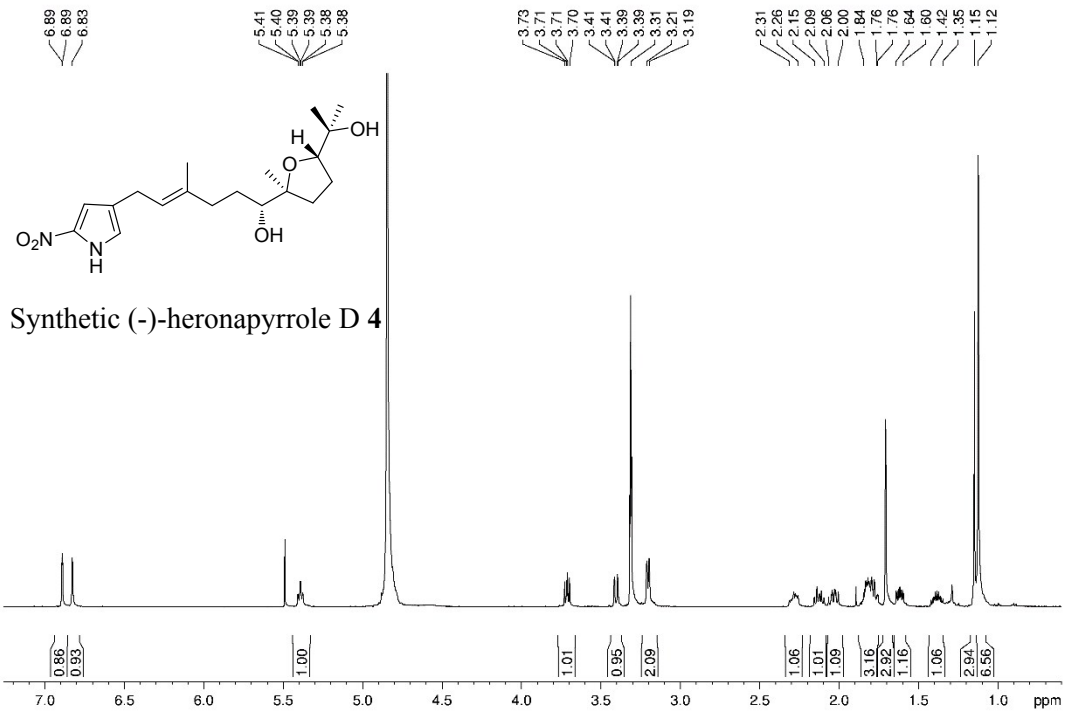
31


7.26
7.01
7.01
7.01
7.01
6.92
6.92
5.28
5.27
5.25
5.24
5.24
3.64
3.63
3.62
3.60
3.51
3.50
3.49
3.48
3.13
3.11
2.21
2.14
2.06
1.69
1.67
1.66
1.55
1.54
1.53
1.52
1.52
1.44
1.33
1.17
1.16
0.92
0.67
1.00
1.06
1.05
2.05
1.09
5.51
2.93
9.51
1.57
1.21
6.27
3.12
17.98
12.42
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
ppm

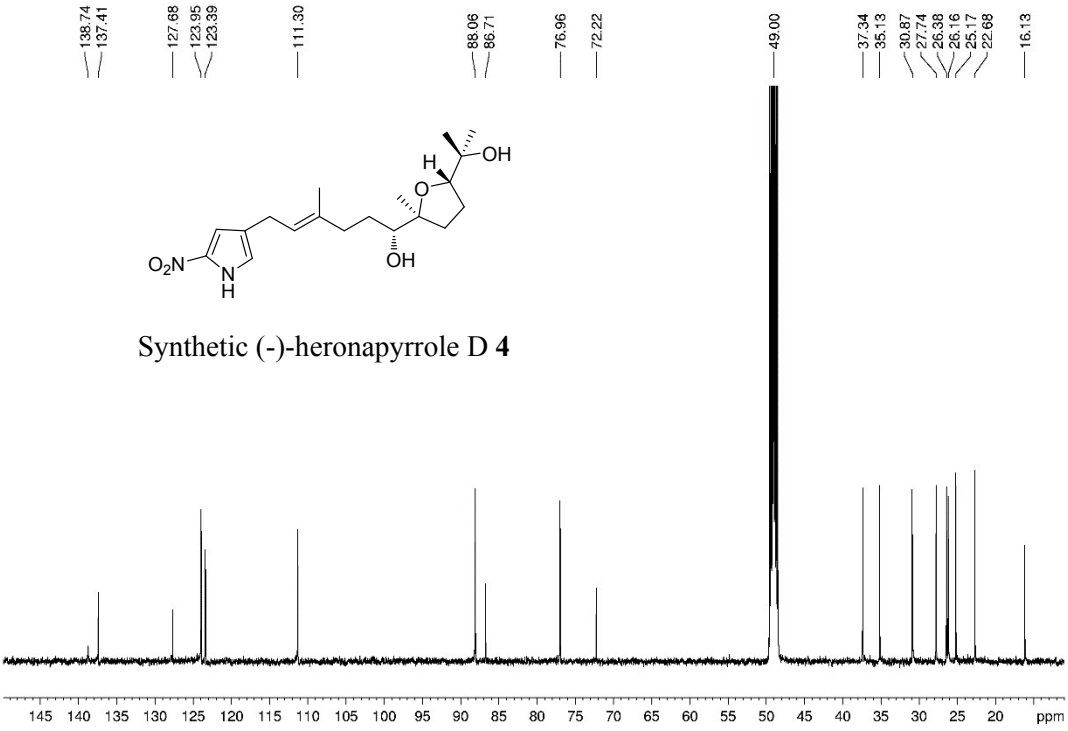

147.14
138.31
124.78
123.93
120.33
117.50
87.13
86.51
85.78
77.77
77.32
77.00
76.68
74.09
36.74
34.53
32.25
27.75
27.48
26.45
25.55
25.04
22.52
16.23
7.11
6.78
5.56
OTES
O
OTES
O2N
N
Boc
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

14

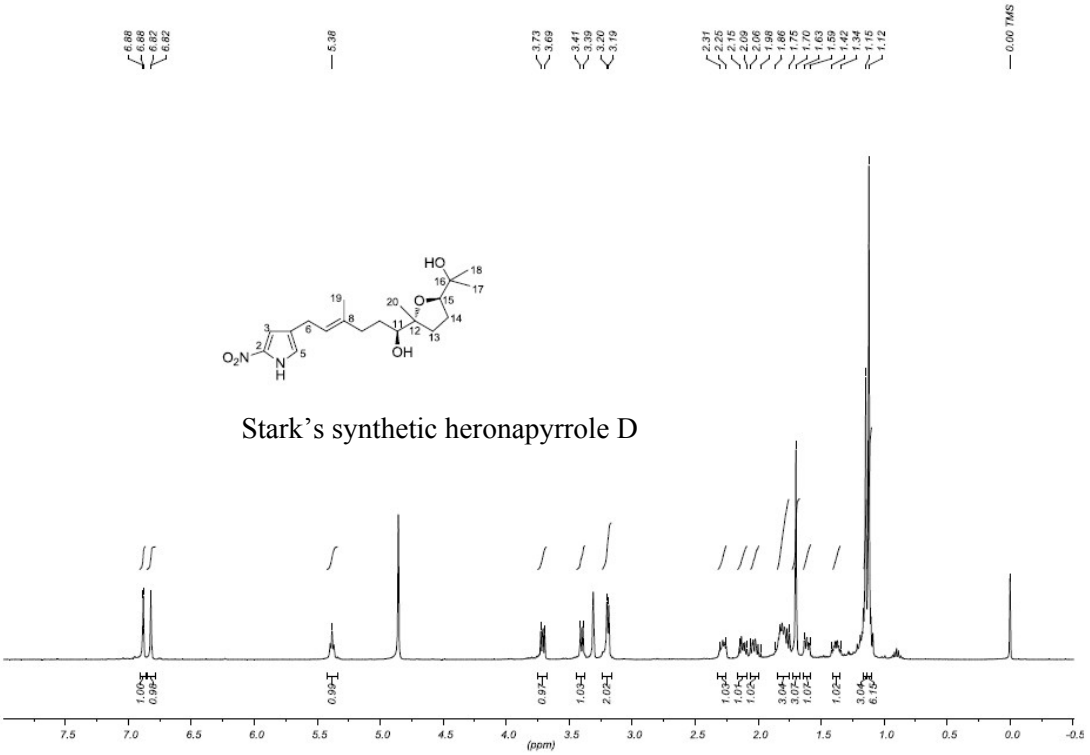

OTES



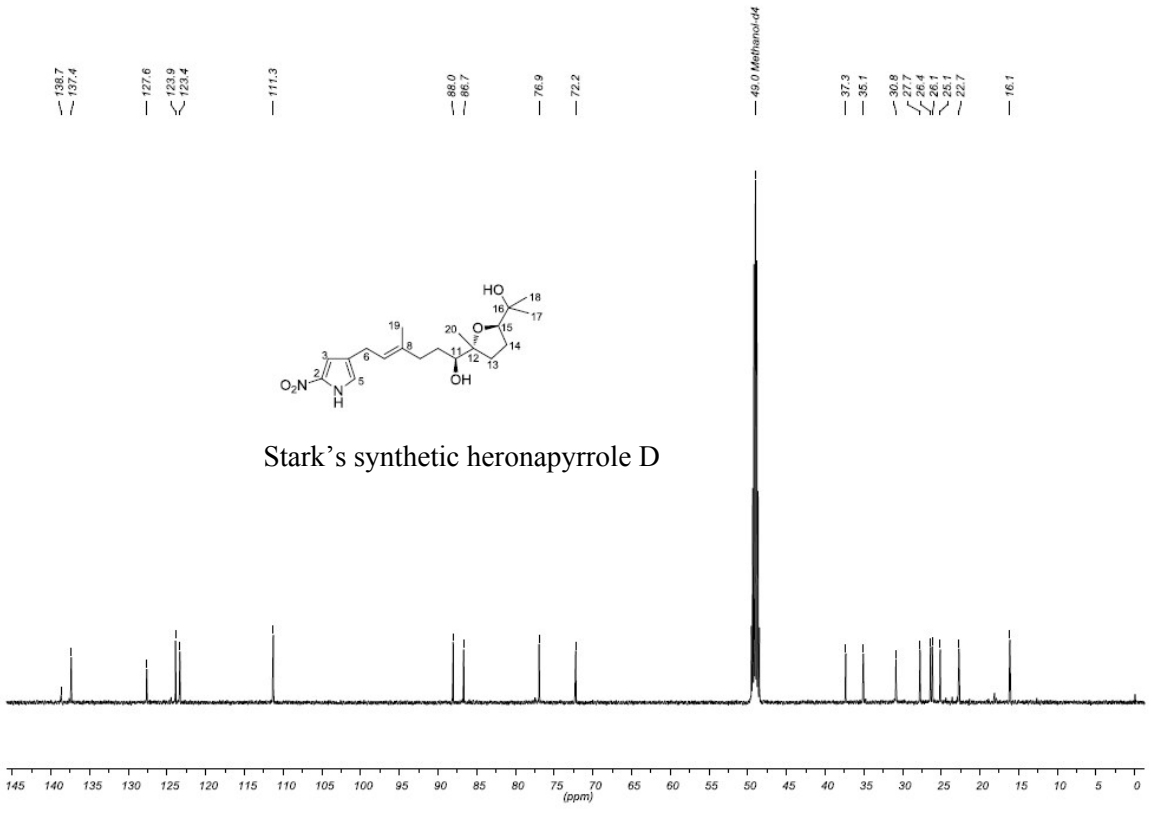
Synthetic (-)-heronapyrrole D **4**



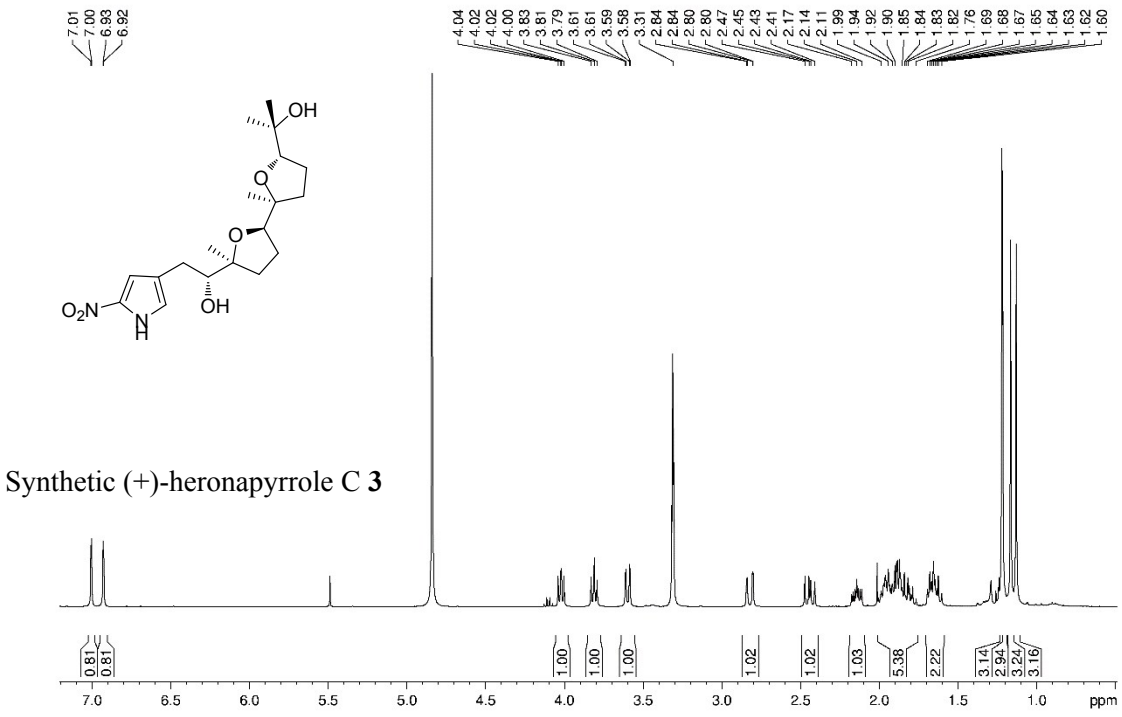
Synthetic (-)-heronapyrrole D **4**

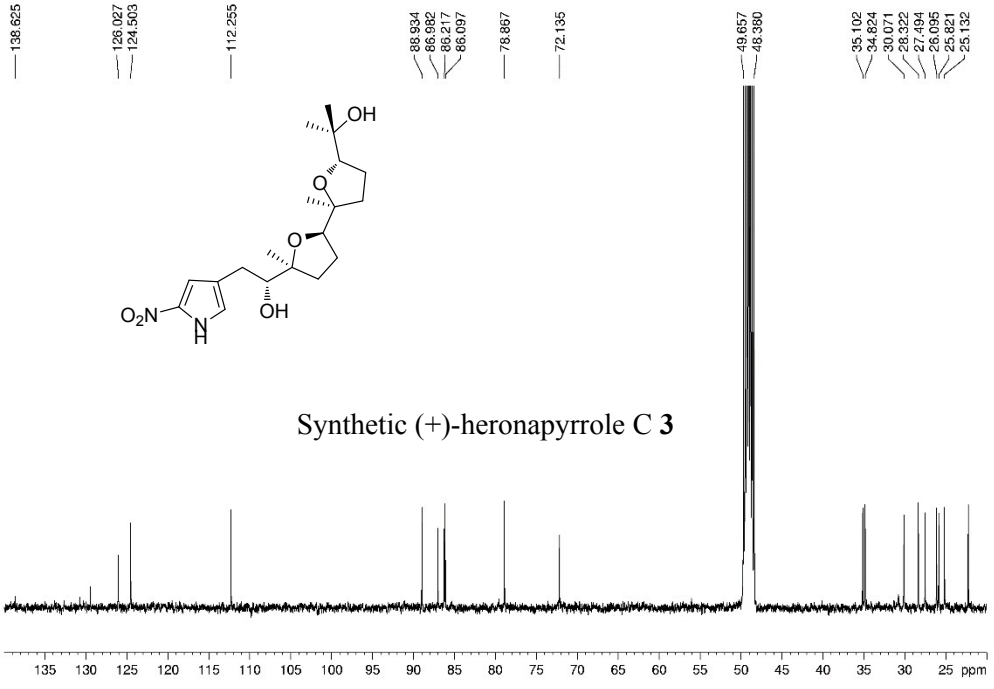


Stark's synthetic heronapyrrole D

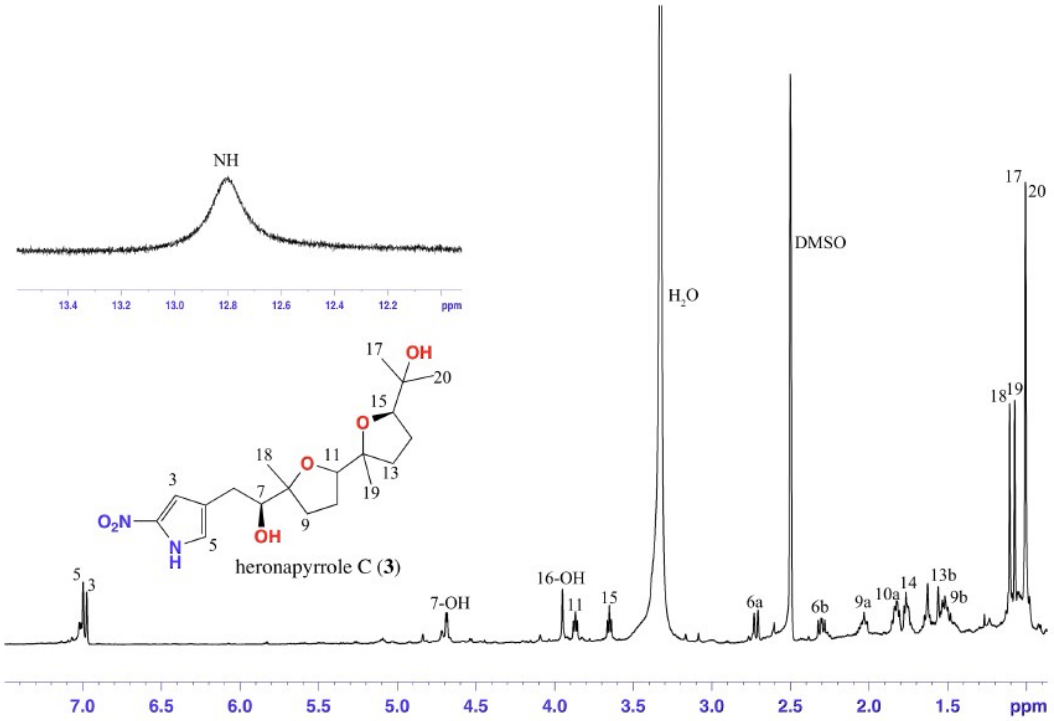


Stark's synthetic heronapyrrole D


Synthetic (+)-heronapyrrole C **3**
ppm


Synthetic (+)-heronapyrrole C **3**
ppm

Isolated (+)-heronapyrrole C



Stark's synthetic *ent*-heronapyrrole C