Supporting Information

Synthesis of hydroxymethyl analogues of mannostatin A and their evaluation as inhibitors of GH38 α-mannosidases

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1. General experimental information

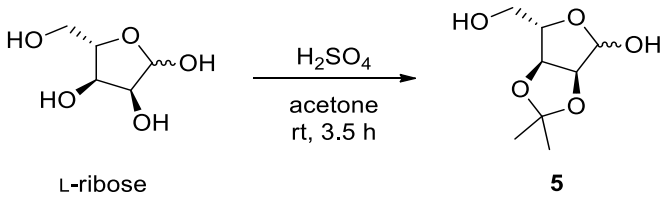
All reagents and anhydrous solvents were commercially sourced and were used as received. All solvents were of technical grade and were distilled before use. Dichloromethane (Slavus, Slovakia) was heated at reflux with P_2O_5 for 1 h and distilled immediately before use.

Melting points were determined with a Boetius PHMK 05 microscope. Specific optical rotations were determined with a Jasco P-2000 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AVANCE III HD 400 spectrometer operating at 400 and 100 MHz working frequencies, respectively. Chemical shifts are given in (δ) and were calibrated using the residual signal of deuterated solvent ($CDCl_3$, CD_3OD). Coupling constants are given in Hz. All given ^{13}C spectra are proton decoupled. High-resolution mass spectra were recorded with an Orbitrap Elite (Thermo Scientific) mass spectrometer with ESI ionization in positive mode. IR spectra (ATR) were measured with a Nicolet 6700 FTIR spectrometer.

Thin-layer chromatography (TLC) was carried out on glass plates and aluminium sheets pre-coated with TLC Silica gel 60 F_{254} (E. Merck). Plates were visualised by immersing into phospho-molybdenic acid (PMA; 10% solution in ethanol) or $KMnO_4$ (4.5 g of $KMnO_4$, 40 g of K_2CO_3, 0.5 g of NaOH, and 600 mL of water) and heating at ca 200 °C with a heat gun. Column chromatography was carried out as flash chromatography on Silica gel 60 (E. Merck, 0.040-0.063 mm). Solvents used for flash chromatography were of technical grade and were distilled before use.

2. Experimental procedures

(3a*S*,6*S*,6a*S*)-6-(Hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol (5)[1]

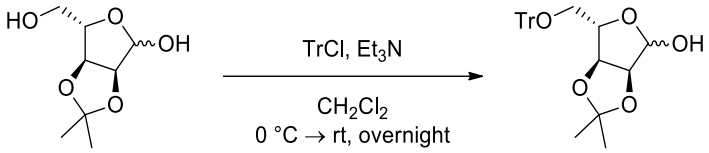


L-ribose **5**

Conc. H_2SO_4 (0.60 mL, 10.64 mmol) was added to a stirred suspension of L-ribose (20.00 g, 133.00 mmol) in anhydrous acetone (250 mL) and the reaction mixture was stirred at r.t. for 3.5 h. Then, the reaction mixture was alkalized with solid $NaHCO_3$ (20.00 g) and the resulting suspension was stirred at r.t. for 1 h. The reaction mixture was filtered, the filtration cake was washed with acetone (100 mL) and the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 1:1, v/v) to afford acetonide **5** (20.73 g, 81%, colorless oil) as a mixture of two anomers in ratio 1:6. R_f = 0.16 (hexanes/EtOAc = 1:1); $[\alpha]_D^{20}$ = +24.3 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$) minor anomer: δ = 5.42 (s, 2H, H-4), 4.74 (dt, *J* = 8.7, 4.4 Hz, 1H, H-6a), 4.66 (dd, *J* = 6.7, 4.2 Hz, 1H, H-3a), 4.02 (d, *J* = 9.6 Hz, 1H, H-6), 3.77 (dd, *J* = 11.8, 2.1 Hz, 4H, C*H*$_2$OH), 2.09 (bs, 1H, OH), 1.59 and 1.40 [2s, each 3H, C(C*H*$_3$)$_2$]; major anomer: δ = 5.42 (s, 2H, H-4), 4.85 (d, *J* = 5.9 Hz, 1H, H-6a), 4.59 (d, *J* = 5.9 Hz, 1H, H-3a), 4.52 (bs, 1H, OH), 4.42 (t, *J* = 5.9 Hz, 1H, H-6), 3.77 (dd, *J* = 11.8, 2.1 Hz, 4H, C*H*$_2$OH), 3.45 (bs, 1H, OH), 1.49 and 1.33 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$) minor anomer: δ = 114.4 (*C*H$_2$OH), 97.0 [*C*(CH$_3$)], 81.7 (C-6), 81.4 (C-6a), 79.6 (C-3a), 63.3 (C-4), 26.7 and 26.2 [C(*C*H$_3$)$_2$]; major anomer: δ = 112.2

(*C*H_2OH), 103.1 [*C*(CH_3)], 87.9 (C-6), 87.0 (C-6a), 81.2 (C-3a), 63.7 (C-4), 26.4 and 24.8 [C(*C*H_3)$_2$]. IR (ATR) υ_{max}: 3372, 2941, 1375, 1209, 1063, 1034, 867 cm^{-1}; HRMS *m/z* calcd for $C_8H_{14}O_5$: 229.0473 [*M*+K]$^+$, found: 229.0472.

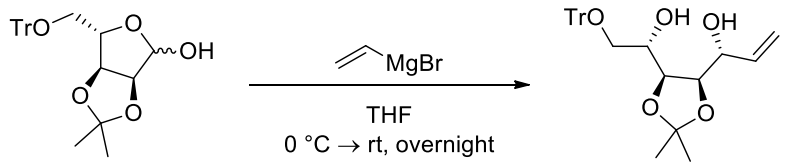
(3a*S*,6*S*,6a*S*)-2,2-Dimethyl-6-((trityloxy)methyl)tetrahydrofuro[3,4-*d*][1,3]dioxol-4-ol (6)[2]



5 **6**

TrCl (29.90, 100.90 mmol) was added to a stirred solution of acetonide **5** (16.00 g, 84.10 mmol) and Et_3N (17.50 mL, 117.78 mmol) in CH_2Cl_2 (300 mL) at 0 °C and the reaction mixture was stirred at r.t. overnight. Next, the reaction mixture was washed with water (3×300 mL) and the organic layer was dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (hexanes/EtOAc = 5:1, v/v) to afford trityl ether **6** (30.73 g, 84%, colorless oil) as a mixture of two anomers in ratio 1:6. R_f = 0.18 (hexanes/EtOAc = 5:1); $[\alpha]_D^{20}$ = +13.8 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$) minor anomer: δ = 7.47–7.36 (m, 6H, Ph), 7.36–7.19 (m, 9H, Ph), 5.73 (dd, *J* = 11.3, 4.0 Hz, 1H, H-4), 4.73 (dd, *J* = 6.2, 4.0 Hz, 1H, H-3a), 4.58 (dd, *J* = 6.3, 0.9 Hz, 1H, H-6a), 4.19 (t, *J* = 2.6 Hz, 1H, H-6), 3.97 (d, *J* = 11.3 Hz, 1H, OH), 3.33–3.46 (m, 1H, C*H*$_2$OTr), 3.02 (dd, *J* = 10.2, 2.8 Hz, 1H, C*H*$_2$OTr), 1.54 and 1.35 [2s, each 3H, C(C*H*$_3$)$_2$]; major anomer: δ = 7.47–7.36 (m, 6H, Ph), 7.36–7.19 (m, 9H, Ph), 5.33 (d, *J* = 9.2 Hz, 1H, H-4), 4.78 (dd, *J* = 5.9, 0.7 Hz, 1H, H-3a), 4.64 (d, *J* = 5.9 Hz, 1H, H-6a), 4.35 (t, *J* = 3.3 Hz, 1H, H-6), 3.85 (d, *J* = 9.2 Hz, 1H, O*H*), 3.33–3.46 (m, 2H, C*H*$_2$OTr), 1.47 and 1.33 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$) minor anomer: δ = 143.5 (Ph), 128.6 (Ph), 128.0 (Ph), 127.3 (Ph), 113.2 [*C*(CH_3)$_2$], 98.0, 87.5, 82.2, 80.2, 79.5, 65.5, 26.2 and 24.8 [C(*C*H_3)$_2$]; major anomer: δ = 142.9 (Ph), 128.7 (Ph), 128.1 (Ph), 127.5 (Ph), 112.3 [*C*(CH_3)$_2$], 103.5, 88.2, 87.0, 86.1, 82.0, 65.0, 26.6 and 25.2 [C(*C*H_3)$_2$]. IR (ATR) υ_{max}: 3432, 2938, 1448, 1210, 1066, 698, 632 cm^{-1}; HRMS *m/z* calcd for $C_{27}H_{28}O_5$: 433.2010 [*M*+H]$^+$, found: 433.2009.

(*R*)-1-((4*R*,5*S*)-5-((*S*)-1-Hydroxy-2-((trityloxy)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-en-1-ol (7)

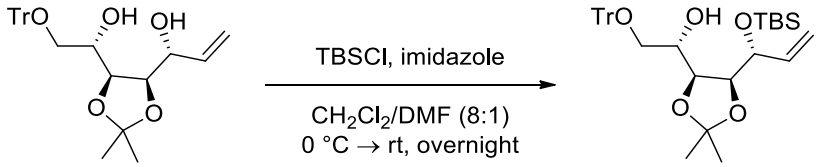


6 **7**

A solution of vinylmagnesium bromide (1 M in THF, 335 mL, 335.00 mmol) was added dropwise to a stirred solution of lactol **6** (29.00 g, 67.00 mmol) in anhydrous THF (420 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. overnight. The reaction progress was monitored by TLC (hexanes/Et_2O = 2:1). Next, the reaction mixture was cooled to 0 °C and it was carefully quenched with satd. aq. NH_4Cl (300 mL). THF was evaporated under reduced pressure and the residue was partitioned between EtOAc (400 mL) and water (340 mL). Layers were separated and the aqueous layer was extracted with additional

EtOAc (400 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 3:1, v/v) to afford diol **7** (28.30 g, 91%) as a white solid. M.p. 146–148 °C; R_f = 0.36 (hexanes/EtOAc = 3:1); $[\alpha]_D^{20}$ = −14.3 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.48–7.42 (m, 6H, Ph), 7.36–7.20 (m, 9H, Ph), 6.03 (ddd, *J* = 17.1, 10.6, 5.3 Hz, 1H, –C*H*=CH_2), 5.42 (dt, *J* = 17.1, 1.5 Hz, 1H, –CH=C$H_{2\text{-trans}}$), 5.25 (dt, *J* = 15.3, 3.7 Hz, 1H, –CH=C$H_{2\text{-cis}}$), 4.36–4.28 (m, 1H), 4.10 (dt, *J* = 8.0, 3.1 Hz, 1H), 4.02 (dd, *J* = 9.2, 5.3 Hz, 1H), 3.93 (dd, *J* = 9.5, 7.3 Hz, 1H), 3.52 (dd, *J* = 9.8, 2.8 Hz, 1H), 3.30 (dd, *J* = 9.8, 7.3 Hz, 1H), 3.21 (d, *J* = 2.2 Hz, 1H, OH), 1.28 and 1.26 [2s, each 3H, C(CH_3)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 143.7 (Ph), 137.5 (–*C*H=CH_2), 128.6 (Ph), 127.9 (Ph), 127.2 (Ph), 116.1 (–CH=*C*H_2), 108.8 [*C*(CH_3)$_2$], 87.2 (*C*Ph$_3$), 80.8, 77.3, 69.7, 69.0, 65.0, 27.9 and 25.5 [C(*C*H_3)$_2$]; IR (ATR) υ_{max}: 3215, 1449, 1219, 1070, 765, 700, 633 cm^{-1}; HRMS *m/z* calcd for $C_{29}H_{32}O_5$: 483.2142 [*M*+Na]$^+$, found: 483.2154.

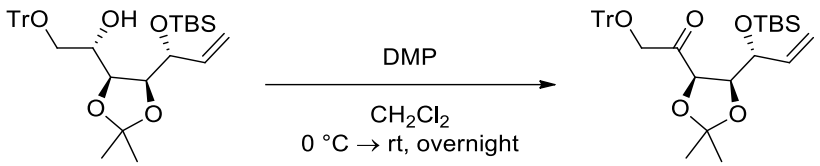
(*S*)-1-((4*S*,5*S*)-5-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)allyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-(trityloxy) ethanol (8)



7 **8**

TBSCl (5.78 g, 38.40 mmol) was added to a stirred solution of diol **7** (14.80 g, 32.00 mmol) and imidazole (6.53 g, 96.00 mmol) in mixture of CH_2Cl_2 (107 mL) and DMF (13 mL) at 0 °C and the reaction mixture was stirred at r.t. overnight. Next, the reaction mixture was washed with water (2×200 mL). Organic layer was separated, dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 15:1, v/v) to afford silyl ether **8** (17.10 g, 93%) as a colorless oil. R_f = 0.23 (hexanes/EtOAc = 15:1); $[\alpha]_D^{20}$ = +11.1 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.42 (m, 6H, Ph), 7.22–7.17 (m, 9H, Ph), 5.94–5.84 (m, 1H, –C*H*=CH_2), 5.26 (m, 2H, –CH=C$H_{2\text{-cis,trans}}$), 4.51–4.45 (m, 1H), 4.26–4.20 (m, 1H), 4.12 (dd, *J* = 9.4, 5.2 Hz, 1H), 4.04 (t, *J* = 5.3 Hz, 1H), 3.67 (d, *J* = 4.0 Hz, 1H, OH), 3.46–3.30 (m, 2H), 3.22 (dd, *J* = 9.5, 6.3 Hz, 1H), 1.28 and 1.27 [2s, each 3H, C(CH_3)$_2$], 0.95 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.17 and 0.12 [2s, each 3H, Si(CH_3)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1 (Ph), 137.5 (–*C*H=CH_2), 128.7 (Ph), 127.6 (Ph), 126.8 (Ph), 117.5 (–CH=*C*H_2), 107.9 [*C*(CH$_3$)$_2$], 86.6 (*C*Ph$_3$), 79.3, 76.3, 73.3, 68.1, 64.6, 26.4 and 24.9 [C(*C*H_3)$_2$], 25.8 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 18.2 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −3.8 and −4.7 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 3474, 2984, 1449, 1251, 835, 703, 632 cm^{-1}; HRMS *m/z* calcd for $C_{35}H_{46}O_5Si$: 597.3007 [*M*+Na]$^+$, found: 597.3012.

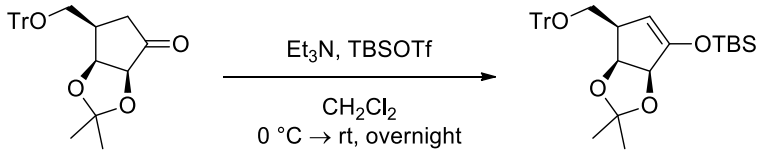
1-((4*R*,5*S*)-5-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)allyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-(trityloxy) ethenone (9)[2]



8 **9**

DMP (32.60 g, 76.88 mmol) was added to a stirred solution of alcohol **8** (17.00 g, 29.57 mmol) in CH_2Cl_2 (300 mL) at 0 °C under a nitrogen atmosphere, and the reaction mixture was stirred at r.t. overnight. Next, the reaction mixture was cooled to 0 °C, satd. aq. $NaHCO_3$ (150 mL) and 10% aq. $Na_2S_2O_3$ (150 mL) were added and the resulting mixture was stirred for 45 min. The organic layer was separated, washed 2× with mixture of satd. aq. $NaHCO_3$ (150 mL) and 10% aq. $Na_2S_2O_3$ (150 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 15:1, v/v) to afford ketone **9** (12.70 g, 75%) as a thick colorless oil. R_f = 0.21 (hexanes/EtOAc = 15:1); $[\alpha]_D^{20}$ = +20.6 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.43 (m, 6H, Ph), 7.34–7.20 (m, 9H, Ph), 5.78 (ddd, *J* = 17.5, 10.5, 7.3 Hz, 1H, –C*H*=CH_2), 5.09–5.06 (m, 2H, –CH=C*H*$_2$), 4.54 (d, *J* = 7.0 Hz, 1H), 4.35–4.26 (m, 2H), 4.12 (d, *J* = 17.7 Hz, 1H), 3.88 (d, *J* = 17.7 Hz, 1H), 1.34 and 1.27 [2s, each 3H, C(C*H*$_3$)$_2$], 0.79 [s, 9H, Si(CH$_3$)$_2$C(C*H*$_3$)$_3$], −0.03 and −0.06 [2s, each 3H, Si(C*H*$_3$)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.6 (C=O), 143.5 (Ph), 137.2 (–*C*H=CH_2), 128.6 (Ph), 127.8 (Ph), 127.1 (Ph), 117.9 (–CH=*C*H$_2$), 109.4 [*C*(CH$_3$)$_2$], 87.1 (*C*Ph$_3$), 82.4, 79.4, 73.0, 69.4, 26.2 and 24.7 [C(*C*H$_3$)$_2$], 26.0 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 18.3 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.3 and −4.5 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 2952, 1735, 1213, 1042, 836, 702 cm^{-1}; HRMS *m/z* calcd for $C_{35}H_{44}O_5Si$: 573.3031 [*M*+H]$^+$, found: 573.3023.

***tert*-Butyl(((3a*S*,6*R*,6a*S*)-2,2-dimethyl-6-((trityloxy)methyl)-6,6a-dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)oxy)dimethylsilane (12)**

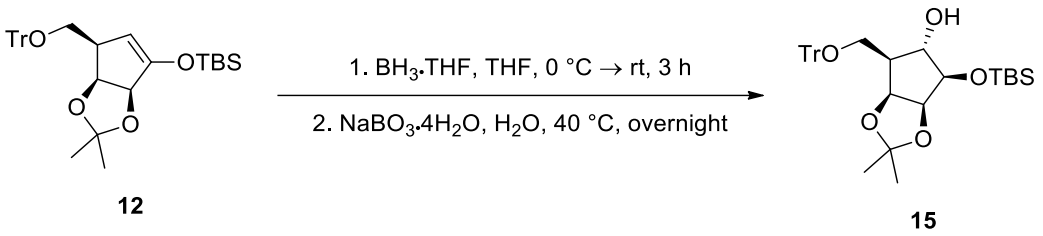


10 **12**

TBSOTf (5.4 mL, 23.35 mmol) was added to a stirred solution of ketone **10** (4.51 g, 9.34 mmol) and Et_3N (4.6 mL, 32.69 mmol) in anhydrous CH_2Cl_2 (160 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. overnight. Then, the reaction was diluted with $CHCl_3$ (100 mL) and washed with satd. aq. $NaHCO_3$ (100 mL). Aqueous layer was washed with additional $CHCl_3$ (2×50 mL) and the combined organic extracts were dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 30:1, v/v) to afford silylenolether **12** (5.07 g, quant.) as a white solid. M.p. 119–121 °C; R_f = 0.21 (hexanes/EtOAc = 30:1); $[\alpha]_D^{20}$ = +56.2 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.51–7.44 (m, 6H, Ph), 7.33–7.16 (m, 9H, Ph), 4.76 (d, *J* = 5.9 Hz, 1H, H-3a), 4.69 (td, *J* = 5.9, 0.9 Hz, 1H, H-6a), 4.67–4.63 (m, 1H, H-5), 3.40 (dd, *J* = 8.5, 6.9 Hz,

1H, CH_2OTr), 3.03 (dd, *J* = 8.5, 7.6 Hz, 1H, CH_2OTr), 2.93–2.84 (m, 1H, H-6), 1.30 and 1.23 [2s, each 3H, C(CH_3)$_2$], 0.96 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.16 [s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 153.7 (C-4), 144.3 (Ph), 128.8 (Ph), 127.6 (Ph), 126.7 (Ph), 110.6 [*C*(CH$_3$)$_2$], 104.9 (C-5), 86.4 (*C*Ph$_3$), 83.2 (C-3a), 76.8 (C-6a), 63.2 (*C*H$_2$OTr), 43.4 (C-6), 27.2 and 26.2 [C(*C*H$_3$)$_2$], 25.6 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 18.2 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.5 and −4.7 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 2926, 1645, 1256, 1073, 840, 702, 632 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{42}O_4Si$: 581.2484 [*M*+K]$^+$, found: 581.2509.

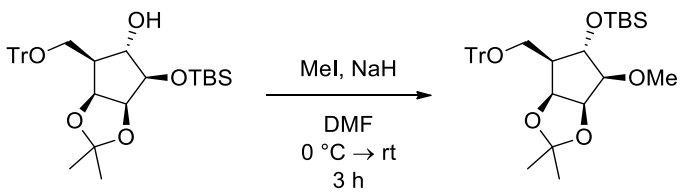
(3a*S*,4*R*,5*S*,6*S*,6a*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-ol (15)



12 **15**

A solution of BH_3 (1M in THF, 46.70 mL, 46.70 mmol) was added dropwise to a stirred solution of silyl enol ether **12** (5.07 g, 9.34 mmol) in anhydrous THF (50 mL) at 0 °C under a nitrogen atmosphere, and the reaction mixture was stirred at r.t. for 3 h. Next, the reaction mixture was carefully quenched with water (50 mL) at 0 °C, $NaBO_3{\cdot}4H_2O$ (21.56 g, 140.1 mmol) was added in one portion and the reaction mixture was stirred at 40 °C overnight. Then, layers were separated and the aqueous layer was extracted with Et_2O (2×50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 15:1, v/v) to afford alcohol **15** (5.20 g, 99%) as a white solid. M.p. = 92–94 °C; R_f = 0.23 (hexanes/EtOAc = 15:1); $[\alpha]_D^{20}$ = +26.1 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.41 (m, 5H, Ph), 7.32–7.19 (m, 10H, Ph), 4.49 (t, *J* = 5.7 Hz, 1H), 4.34 (t, *J* = 5.6 Hz, 1H), 3.80 (dd, *J* = 9.9, 8.5 Hz, 1H, H-5), 3.68 (dd, *J* = 8.4, 5.4 Hz, 1H, H-4), 3.58 (dd, *J* = 9.0, 6.4 Hz, 1H, CH_2OTr), 3.34 (t, *J* = 8.7 Hz, 1H, CH_2OTr), 2.53 (d, *J* = 2.1 Hz, 1H, OH), 1.87 (dtd, *J* = 10.1, 8.4, 6.1 Hz, 1H, H-6), 1.24 and 1.21 [2s, each 3H, C(CH_3)$_2$], 0.92 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.12 [s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9 (Ph), 128.7 (Ph), 127.8 (Ph), 127.0 (Ph), 110.2 [*C*(CH$_3$)$_2$], 87.2 (*C*Ph$_3$), 78.6 (C-4), 77.9 (C-5), 77.6, 76.5, 63.0 (*C*H$_2$OTr), 44.4 (C-6), 25.9 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 25.7 and 24.3 [C(*C*H$_3$)$_2$], 18.4 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.5 and −4.6 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 3557, 2928, 2856, 1491, 1448, 1380, 1249, 1067, 877, 699 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{44}O_5Si$: 583.2855 [*M*+H]$^+$, found: 583.2855.

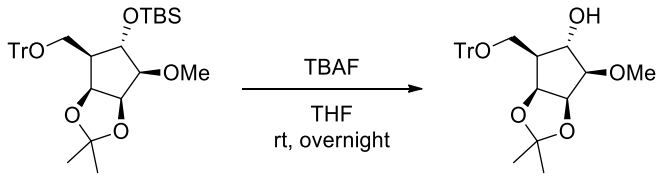
***tert*-Butyl((3a*S*,4*S*,5*S*,6*R*,6a*S*)-4-methoxy-2,2-dimethyl-6-(trityloxymethyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-yloxy)dimethylsilane (16)**



15 **16**

NaH (16 mg, 60%, 0.40 mmol) was added to a stirred solution of alcohol **15** (113 mg, 0.20 mmol) in anhydrous DMF (2 mL) at 0 °C followed by MeI (38 μL, 0.60 mmol) and the reaction mixture was stirred at r.t. for 3 h. Then, the reaction mixture was quenched at 0 °C with satd. aq. NH_4Cl (0.5 mL) and the resulting mixture was partitioned between EtOAc (25 mL) and water (25 mL). The organic layer was washed with water (2×25 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 15:1, v/v) to afford derivative **16** (81 mg, 70%) as a thick colorless oil. R_f = 0.21 (hexanes/EtOAc = 15:1); $[\alpha]_D^{20}$ = +9.5 (*c* 0.59; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.54–7.45 (m, 6H, Ph), 7.30–7.16 (m, 9H, Ph), 4.83 (t, *J* = 5.7 Hz, 1H), 4.62 (t, *J* = 5.6 Hz, 1H), 3.60 (dd, *J* = 10.6, 8.3 Hz, 1H), 3.43 (s, 3H, OC*H*$_3$), 3.41 (dd, *J* = 10.6, 8.3 Hz, 1H), 3.18 (dd, *J* = 8.3, 5.1 Hz, 1H), 3.05 (dd, *J* = 8.1, 3.9 Hz, 1H), 1.91 (tdd, *J* = 10.6, 5.3, 3.9 Hz, 1H, H-6), 1.41 and 1.38 [2s, each 3H, C(C*H*$_3$)$_2$], 0.66 [s, 9H, Si(CH$_3$)$_2$C(C*H*$_3$)$_3$], −0.07 and −0.28 [2s, each 3H, Si(C*H*$_3$)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 144.3 (Ph), 128.8 (Ph), 127.5 (Ph), 126.7 (Ph), 109.8 [*C*(CH$_3$)$_2$], 87.1, 86.5 (*C*Ph$_3$), 75.7, 74.3, 74.2, 60.4, 58.2 (O*C*H$_3$), 46.3, 25.9 and 24.2 [C(*C*H$_3$)$_2$], 25.7 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 17.8 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.4 and −5.3 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 1449, 1154, 1072, 835, 774, 706 cm^{-1}; HRMS *m/z* calcd for $C_{35}H_{46}O_5Si$: 597.3007 [*M*+Na]$^+$, found: 597.3016.

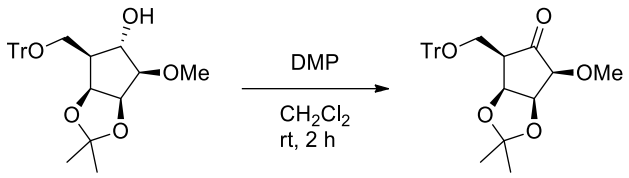
(3a*S*,4*R*,5*S*,6*S*,6a*S*)-4-Methoxy-2,2-dimethyl-6-(trityloxymethyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-ol (19)



16 **19**

A solution of TBAF (1M in THF, 0.19 mL, 0.19 mmol) was added to a stirred solution of silyl ether **16** (74 mg, 0.13 mmol) in anhydrous THF (1.8 mL) and the reaction mixture was stirred at r.t. overnight. Next, THF was evaporated under reduced pressure and a residue was partitioned between EtOAc (15 mL) and water (15 mL). The organic layer was washed with water (15 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 1:1, v/v) to afford alcohol **19** (53 mg, 90%) as a thick colorless oil. R_f = 0.29 (hexanes/EtOAc = 1:1); $[\alpha]_D^{20}$ = +18.5 (*c* 0.78; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.47–7.40 (m, 6H, Ph), 7.34–7.20 (m, 9H, Ph), 4.57 (t, *J* = 5.4 Hz, 1H), 4.51 (t, *J* = 5.9 Hz, 1H), 3.93 (ddd, *J* = 10.2, 8.7, 1.6 Hz, 1H), 3.63 (dd, *J* = 9.1, 6.0 Hz, 1H), 3.54 (s, 3H, OC*H*$_3$), 3.41 (d, *J* = 9.0 Hz, 1H), 3.39 (t, *J* = 9.0 Hz, 1H), 3.36 (dd, *J* = 8.7, 5.0 Hz, 1H), 2.86 (d, *J* = 1.8 Hz, 1H, O*H*), 1.98–1.88 (m, 1H), 1.26 and 1.22 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 143.6 (Ph), 128.6 (Ph), 127.8 (Ph), 127.1 (Ph), 110.3 [*C*(CH$_3$)$_2$], 87.3 (*C*Ph$_3$), 85.8, 77.2, 76.0, 75.4, 62.9, 58.5 (O*C*H$_3$), 44.9, 25.6 and 23.8 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3445, 1448, 1209, 1067, 746, 698 cm^{-1}; HRMS *m/z* calcd for $C_{29}H_{32}O_5$: 483.2142 [*M*+Na]$^+$, found: 483.2152.

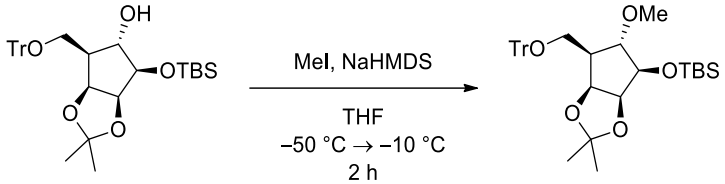
(3a*S*,4*S*,6*R*,6a*S*)-4-Methoxy-2,2-dimethyl-6-(trityloxymethyl)dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5(4*H*)-one (21)



19 **21**

DMP (62 mg, 0.15 mmol) was added to a stirred solution of alcohol **19** (45 mg, 0.1 mmol) in CH_2Cl_2 (1.5 mL) at r.t. and the reaction mixture was stirred for 2 h. Next, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and it was washed 3× with a mixture of satd. aq. $NaHCO_3$ (5 mL) and 10% aq. $Na_2S_2O_3$ (5 mL). The organic layer was separated, dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure to afford ketone **21** (41 mg, 91%) as a white solid, which was characterized only by NMR spectroscopy without purification. R_f = 0.44 (hexanes/EtOAc = 1:1); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.50–7.43 (m, 6H, Ph), 7.33–7.17 (m, 9H, Ph), 5.01 (t, *J* = 6.0 Hz, 1H, H-3a), 4.85 (t, *J* = 5.9 Hz, 1H, H-6a), 3.87 (dd, *J* = 6.0, 2.0 Hz, 1H, H-4), 3.57 (s, 3H, OC*H*$_3$), 3.53 (dd, *J* = 9.5, 4.9 Hz, 1H, C*H*$_2$OTr), 3.45 (dd, *J* = 9.5, 8.6 Hz, 1H, C*H*$_2$OTr), 2.66 (dddd, *J* = 8.6, 6.2, 4.9, 2.0 Hz, 1H, H-6), 1.37 and 1.26 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 208.3 (C=O), 143.9 (Ph), 128.8 (Ph), 127.6 (Ph), 126.9 (Ph), 111.0 [*C*(CH$_3$)$_2$], 86.8 (*C*Ph$_3$), 81.8 (C-4), 74.5 (C-3a), 73.2 (C-6a), 58.9 (O*C*H$_3$), 57.6 (*C*H$_2$OTr), 47.9 (C-6), 26.2 and 24.9 [C(*C*H$_3$)$_2$].

***tert*-Butyl((3a*S*,4*R*,5*S*,6*S*,6a*S*)-5-methoxy-2,2-dimethyl-6-(trityloxymethyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yloxy)dimethylsilane (17)**

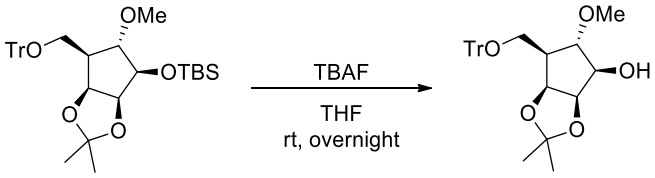


15 **17**

A solution of NaHMDS (2 M in THF, 0.69 mL, 1.39 mmol) was added to a stirred solution of alcohol **15** (390 mg, 0.69 mmol) in anhydrous THF (11 mL) at −50 °C under nitrogen a atmosphere followed by MeI (0.43 mL, 6.95 mmol) and the reaction mixture was allowed to warm to −10 °C within ~2 h. Then, the reaction mixture was quenched with satd. aq. NH_4Cl (1 mL) and THF was evaporated under reduced pressure. A residue was partitioned between EtOAc (35 mL) and water (35 mL). The organic layer was separated, dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 20:1, v/v) to afford derivative **17** (316 mg, 79%) as a white solid. M.p. 123–125 °C; R_f = 0.32 (hexanes/EtOAc = 20:1); $[\alpha]_D^{20}$ = +10.7 (*c* 0.67; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.52–7.45 (m, 6H, Ph), 7.32–7.17 (m, 9H, Ph), 4.66 (t, *J* = 5.5 Hz, 1H, H-6a), 4.32 (t, *J* = 5.7 Hz, 1H, H-3a), 3.71 (dd, *J* = 8.0, 5.7 Hz, 1H, H-4), 3.43 (t, *J* = 8.8 Hz, 1H, C*H*$_2$OTr), 3.31 (s, 3H, OC*H*$_3$), 3.28 (dd, *J* = 10.6, 8.0 Hz, 1H, H-5), 3.18 (dd, *J* = 8.5, 4.9 Hz, 1H, C*H*$_2$OTr), 1.90 (ddd, *J* = 10.5, 5.3, 3.9 Hz, 1H, H-6), 1.32 and 1.29 [2s, each 3H, C(C*H*$_3$)$_2$], 0.90 [s, 9H, Si(CH$_3$)$_2$C(C*H*$_3$)$_3$], 0.10 and 0.09 [2s, each 3H,

Si(C*H*$_3$)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz; CDCl$_3$): δ = 144.3 (Ph), 128.8 (Ph), 127.5 (Ph), 126.7 (Ph), 109.7 [*C*(CH$_3$)$_2$], 86.4 (*C*Ph$_3$), 85.5 (C-5), 78.6 (C-4), 76.9 (C-6a), 76.4 (C-3a), 60.9 (*C*H$_2$OTr), 59.2 (O*C*H$_3$), 44.0 (C-6), 25.9 and 24.5 [C(*C*H$_3$)$_2$], 25.8 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 18.2 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.4 and −4.8 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 1448, 1148, 1094, 879, 776, 708 cm^{-1}; HRMS *m/z* calcd for $C_{35}H_{46}O_5Si$: 597.3007 [*M*+Na]$^+$, found: 597.3017.

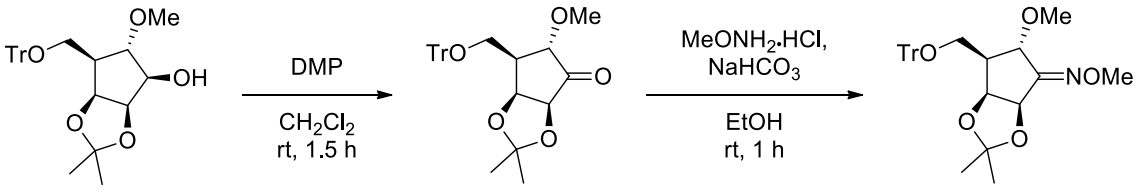
(3a*R*,4*R*,5*S*,6*S*,6a*S*)-5-Methoxy-2,2-dimethyl-6-(trityloxymethyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-ol (23)



17 **23**

A solution of TBAF (1M in THF, 0.69 mL, 0.69 mmol) was added to a stirred solution of silyl ether **17** (305 mg, 0.53 mmol) in anhydrous THF (6 mL) and the reaction mixture was stirred at r.t. overnight. Next, THF was evaporated under reduced pressure and a residue was partitioned between EtOAc (25 mL) and water (25 mL). The organic layer was washed with water (25 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 3:1, v/v) to afford alcohol **23** (228 mg, 93%) as a thick colorless oil. R_f = 0.18 (hexanes/EtOAc = 3:1); $[\alpha]_D^{20}$ = −20.3 (*c* 0.62; CHCl$_3$). ^{1}H NMR (400 MHz; CDCl$_3$): δ = 7.50–7.43 (m, 6H, Ph), 7.31–7.18 (m, 9H, Ph), 4.78 (dd, *J* = 5.8, 4.7 Hz, 1H), 4.47 (t, *J* = 6.2 Hz, 1H), 3.72 (ddd, *J* = 9.4, 7.6, 6.5 Hz, 1H, H-4), 3.42 (dd, *J* = 9.5, 8.6 Hz, 1H, C*H*$_2$OTr), 3.35 (s, 3H, OC*H*$_3$), 3.25 (dd, *J* = 8.6, 4.6 Hz, 1H, C*H*$_2$OTr), 3.18 (dd, *J* = 10.7, 7.6 Hz, 1H, H-5), 2.63 (d, *J* = 9.4 Hz, 1H, OH), 2.00–1.90 (m, 1H, H-6), 1.38 and 1.36 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; CDCl$_3$): δ = 144.2 (Ph), 128.8 (Ph), 127.5 (Ph), 126.7 (Ph), 110.2 [*C*(CH$_3$)$_2$], 86.5 (*C*Ph$_3$), 85.9, 77.1, 77.0, 75.6, 60.6 (*C*H$_2$OTr), 58.4 (O*C*H$_3$), 44.1 (C-6), 25.8 and 24.2 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3449, 1209, 1127, 1071, 746, 698 cm^{-1}; HRMS *m/z* calcd for $C_{29}H_{32}O_5$: 483.2142 [*M*+Na]$^+$, found: 483.2151.

(3a*R*,5*S*,6*S*,6a*S*)-5-Methoxy-2,2-dimethyl-6-(trityloxymethyl)dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4(5*H*)-one *O*-methyl oxime (25)



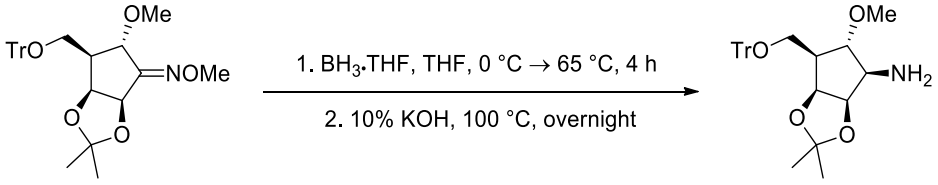
23 **24** **25**

DMP (284 mg, 0.67 mmol) was added to a stirred solution of alcohol **23** (220 mg, 0.48 mmol) in CH_2Cl_2 (6.5 mL) at r.t. and the mixture was stirred for 1.5 h. Then, the reaction mixture was diluted with CH_2Cl_2 (24 mL) and it was washed 3× with a mixture of satd. aq. $NaHCO_3$ (15 mL) and 10% aq. $Na_2S_2O_3$ (15 mL). The organic layer was separated, dried with Na_2SO_4 and filtered. Evaporation of the solvent under reduced pressure

afforded ketone **24** (218 mg, 99%) as a thick colorless oil, which was used in the next reaction without any other purification or characterization.

$MeONH_2$·HCl (152 mg, 1.81 mmol) and $NaHCO_3$ (152 mg, 1.81 mmol) were added to a stirred solution of prepared ketone (208 mg, 0.45 mmol) in EtOH (5.5 mL) at r.t. and the reaction mixture was stirred for 1 h. Next, the ethanol was evaporated under reduced pressure, the residue was partitioned between EtOAc (25 mL) and water (25 mL) and the layers were separated. The organic layer was washed with water (25 mL), separated, dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 6:1, v/v) to afford oxime ether **25** (175 mg, 79%) as a thick colorless oil. R_f = 0.20 (hexanes/EtOAc = 6:1); $[\alpha]_D^{20}$ = +88.0 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.51–7.44 (m, 6H, Ph), 7.33–7.20 (m, 9H, Ph), 5.08 (dd, *J* = 5.7, 1.6 Hz, 1H, H-3a), 4.80 (dd, *J* = 5.6, 4.4 Hz, 1H, H-6a), 4.09 (dd, *J* = 10.2, 1.6 Hz, 1H, H-5), 3.96 (s, 3H, NOC*H*$_3$), 3.51 (t, *J* = 8.8 Hz, 1H, C*H*$_2$OTr), 3.41 (s, 3H, OC*H*$_3$), 3.36 (dd, *J* = 8.9, 5.2 Hz, 1H, C*H*$_2$OTr), 2.24–2.15 (m, 1H, H-6), 1.35 and 1.36 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 159.7 (C=N), 144.1 (Ph), 128.8 (Ph), 127.6 (Ph), 126.9 (Ph), 111.5 [*C*(CH$_3$)$_2$], 86.7 (*C*Ph$_3$), 79.7 (C-5), 76.4 (C-6a), 72.4 (C-3a), 62.6 (NO*C*H$_3$), 61.1 (*C*H$_2$OTr), 58.7 (O*C*H$_3$), 45.4 (C-6), 26.6 and 24.7 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 1448, 1211, 1066, 1031, 746, 698 cm^{-1}; HRMS *m/z* calcd for $C_{30}H_{33}NO_5$: 510.2251 [*M*+Na]$^+$, found: 510.2262.

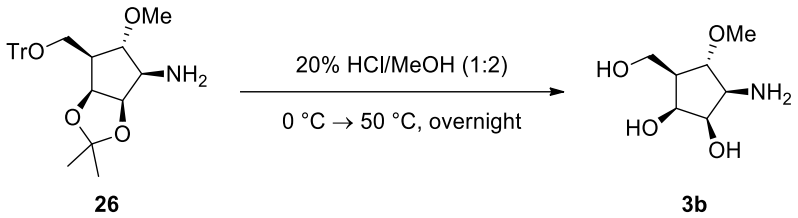
(3a*R*,4*R*,5*S*,6*S*,6a*S*)-5-Methoxy-2,2-dimethyl-6-(trityloxymethyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-amine (26)



25 **26**

A solution of BH_3 (1M in THF, 0.92 mL, 0.92 mmol) was added to a stirred solution of *O*-methyl oxime **25** (150 mg, 0.31 mmol) in anhydrous THF (2.5 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at 65 °C for 4 h. Next, the solvent was evaporated under reduced pressure and the residue was heated in a 10% aq. KOH (6 mL) at 100 °C overnight. The mixture was diluted with water (15 mL) and it was extracted with CH_2Cl_2 (2×15 mL). The combined organic extracts were dried with Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc containing 0.5% (v/v) of concd. aq. NH_3) to afford amine **26** (86 mg, 61%) as a thick colorless oil. R_f = 0.28 (EtOAc containing 0.5% (v/v) of concd. aq. NH_3); $[\alpha]_D^{20}$ = +17.6 (*c* 0.60; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.52–7.45 (m, 6H, Ph), 7.32–7.18 (m, 9H, Ph), 4.73 (t, *J* = 5.6 Hz, 1H, H-3a), 4.40 (t, *J* = 5.8 Hz, 1H, H-6a), 3.48 (t, *J* = 8.9 Hz, 1H, C*H*$_2$OTr), 3.27 (s, 3H, OC*H*$_3$), 3.22 (dd, *J* = 8.6, 4.9 Hz, 1H, C*H*$_2$OTr), 3.00 (dd, *J* = 10.3, 9.1 Hz, 1H, H-5), 2.82 (dd, *J* = 9.1, 5.7 Hz, 1H, H-4), 1.93 (ddt, *J* = 10.3, 9.0, 5.1 Hz, 1H, H-6), 1.35 and 1.33 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 144.2 (Ph), 128.8 (Ph), 127.6 (Ph), 126.8 (Ph), 109.1 [*C*(CH$_3$)$_2$], 86.8 (C-5), 86.6 (*C*Ph$_3$), 77.4 (C-6a), 76.5 (C-3a), 60.8 (*C*H$_2$OTr), 59.4 (O*C*H$_3$), 59.0 (C-4), 46.4 (C-6), 25.8 and 24.0 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3383, 1448, 1208, 1066, 746, 698 cm^{-1}; HRMS *m/z* calcd for $C_{29}H_{33}NO_4$: 482.2302 [*M*+Na]$^+$, found: 482.2308.

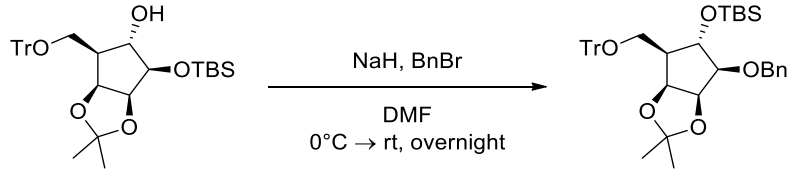
(1*S*,2*R*,3*S*,4*S*,5*R*)-3-Amino-5-(hydroxymethyl)-4-methoxycyclopentane-1,2-diol (3b)



26 **3b**

20% aq. HCl (1 mL) was added to a stirred solution of amine **26** (86 mg, 0.19 mmol) in MeOH (2 mL) at 0 °C and the reaction mixture was heated at 50 °C overnight. Next, the reaction mixture was cooled to r.t. and the volatiles were evaporated under reduced pressure. The residue was partitioned between $CHCl_3$ (15 mL) and distilled water (7 mL), layers were separated and the organic layer was extracted with additional distilled water (7 mL). Amberlite® IRA 400 (OH^-) (1.1 g) was added to the combined aqueous layers and the resulting suspension was stirred at r.t. overnight. The suspension was filtered and the filtrate was lyophilized to afford aminotriol **3b** (30 mg, 91%) as a colorless oil. R_f = 0.16 (MeOH/$CHCl_3$ = 1:1, containing 0.5% (v/v) of concd. aq. NH_3); $[\alpha]_D^{20}$ = −27.4 (*c* 1.00; MeOH). ^{1}H NMR (400 MHz; CD_3OD): δ = 4.21 (dd, *J* = 6.2, 3.7 Hz, 1H), 3.97 (dd, *J* = 6.0, 3.7 Hz, 1H), 3.84 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.77 (dd, *J* = 10.8, 5.1 Hz, 1H), 3.52 (dd, *J* = 6.5, 4.3 Hz, 1H), 3.40 (s, 3H, OC*H*$_3$), 3.14 (t, *J* = 5.1 Hz, 1H), 2.09–1.98 (m, 1H); ^{13}C NMR (100 MHz; CD_3OD): δ = 89.4, 74.2, 73.6, 61.2, 58.8, 58.2 (O*C*H$_3$), 50.3; IR (ATR) υ_{max}: 3345, 3284, 2932, 2892, 2834, 1571, 1465, 1381, 1088 cm^{-1}; HRMS *m/z* calcd for $C_7H_{15}NO_4$: 178.1074 [*M*+H]$^+$, found: 178.1077.

(((3a*S*,4*S*,5*S*,6*R*,6a*S*)-4-(Benzyloxy)-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-yl)oxy)(*tert*-butyl)dimethylsilane (18)

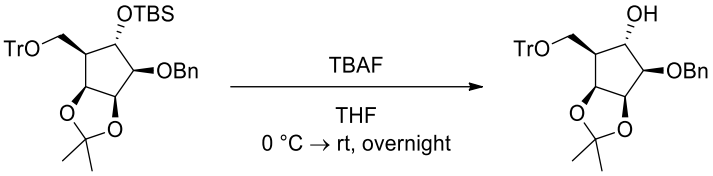


15 **18**

NaH (60% in mineral oil, 9 mg, 0.18 mmol) was added to a solution of alcohol **15** (50 mg, 0.089 mmol) in anhydrous DMF (1 mL) at 0 °C under a nitrogen atmosphere followed by BnBr (14 µL, 0.27 mmol) and the reaction mixture was stirred at r.t. overnight. Next, the reaction mixture was carefully quenched with water (10 mL) at 0 °C and the resulting mixture was extracted with EtOAc (2×5 mL). The combined organic extracts were washed with water (4×5 mL) and brine (2 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 50:1→40:1→30:1, v/v) to afford benzyl ether **18** (55 mg, 95%) as thick colorless oil. R_f = 0.19 (hexanes/EtOAc = 30:1); $[\alpha]_D^{20}$ = +14.3 (*c* 0.25; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.52–7.44 (m, 5H, Ph), 7.40–7.16 (m, 15H, Ph), 4.81 (t, *J* = 5.5 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H, OC*H*$_2$Ph), 4.55 (d, *J* = 12.0 Hz, 1H, OC*H*$_2$Ph), 4.49 (t, *J* = 5.6 Hz, 1H), 3.70 (dd, *J* = 10.5, 8.2 Hz, 1H, H-5), 3.44–3.35 (m, 2H, C*H*$_2$OTr, H-4), 3.03 (dd, *J* = 8.0, 3.9 Hz, 1H, C*H*$_2$OTr), 1.89 (qd, *J* = 10.6, 4.1 Hz, 1H, H-6), 1.42 and 1.38 [2s, each 3H, C(C*H*$_3$)$_2$], 0.66 [s, 9H, Si(CH$_3$)$_2$C(C*H*$_3$)$_3$], −0.06 and −0.32 [2s, each 3H, Si(C*H*$_3$)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100

MHz; $CDCl_3$): δ = 144.4 (Ph), 138.4 (Ph), 128.9 (Ph), 128.2 (Ph), 128.0 (Ph), 127.6 (Ph), 127.5 (Ph), 126.8 (Ph), 109.9 [*C*$(CH_3)_2$], 86.5 (*C*Ph_3), 84.0 (C-4), 76.1, 74.8, 74.6 (C-5), 71.8 (O*C*H_2Ph), 60.6 (*C*H_2OTr), 46.2 (C-6), 26.1 and 24.5 [C(*C*$H_3)_2$], 25.7 [Si$(CH_3)_2$C(*C*$H_3)_3$], 17.8 [Si$(CH_3)_2$*C*$(CH_3)_3$], −4.3 and −5.2 [Si(*C*$H_3)_2$C$(CH_3)_3$]; IR (ATR) υ_{max}: 3087, 2928, 2855, 1449, 1380, 1073, 874, 745, 696 cm^{-1}; HRMS *m/z* calcd for $C_{41}H_{50}O_5Si$: 673.3320 [*M*+Na]$^+$, found: 673.3329.

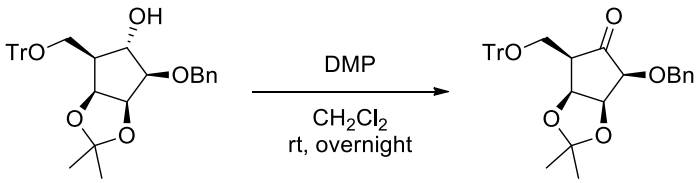
(3a*S*,5*S*,6*S*,6a*S*)-4-(Benzyloxy)-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-ol (20)



18 **20**

A solution of TBAF (1M in THF, 0.61 mL, 0.61 mmol) was added to a stirred solution of silyl ether **18** (200 mg, 0.31 mmol) in anhydrous THF (3 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. overnight. Then, water (10 mL) was carefully added and the reaction mixture was extracted with Et_2O (2×10 mL). The combined organic extracts were dried over Na_2SO_4, filtered and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 5:1, v/v) to afford alcohol **20** (149 mg, 90%) as a thick colorless oil. R_f = 0.17 (hexanes/EtOAc = 5:1); $[\alpha]_D^{20}$ = +18.2 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.40–7.44 (m, 8H, Ph), 7.38–7.19 (m, 12H, Ph), 4.83 (d, *J* = 12.2 Hz, 1H, OC*H*$_2$Ph), 4.69 (d, *J* = 12.2 Hz, 1H, OC*H*$_2$Ph), 4.51–4.44 (m, 1H), 4.05–3.96 (m, 1H), 3.60 (dd, *J* = 9.1, 6.2 Hz, 1H, C*H*$_2$OTr), 3.54–3.48 (m, 1H), 3.38 (t, *J* = 8.9 Hz, 1H, C*H*$_2$OTr), 2.76 (d, *J* = 1.9 Hz, 1H, OH), 1.99–1.79 (m, 1H, H-6), 1.28 and 1.22 [2s, each 3H, C(C*H*$_3)_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 143.8 (Ph), 138.3 (Ph), 128.7 (Ph), 128.4 (Ph), 128.0 (Ph), 127.9 (Ph), 127.7 (Ph), 127.1 (Ph), 110.4 [*C*$(CH_3)_2$], 87.4 (*C*Ph_3), 82.9, 77.2, 76.3, 76.0, 71.9 (O*C*H_2Ph), 63.0 (*C*H_2OTr), 44.9 (C-6), 25.8 and 24.0 [C(*C*$H_3)_3$]; IR (ATR) υ_{max}: 3447, 2932, 1448, 1208, 1092, 745, 696, 632 cm^{-1}; HRMS *m/z* calcd for $C_{35}H_{36}O_5$: 575.2194 [*M*+K]$^+$, found: 575.2198.

(3a*S*,4*S*,6*R*,6a*S*)-4-(Benzyloxy)-2,2-dimethyl-6-((trityloxy)methyl)dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5(4*H*)-one (22)

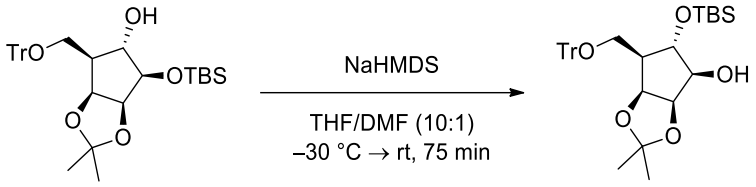


20 **22**

DMP (102 mg, 0.24 mmol) was added to a solution of alcohol **20** (45 mg, 0.082 mmol) in CH_2Cl_2 (1 mL) and the reaction mixture was stirred at r.t. overnight. Then, water (5 mL) was added and the layers were separated. The organic layer was washed 2× with a mixture of satd. aq. $NaHCO_3$ (4 mL) and 10% aq. $Na_2S_2O_3$ (4 mL). The organic layer was dried over Na_2SO_4 and filtered. Evaporation of the solvent under reduced

pressure afforded ketone **22** (48 mg, quant.) as a colorless oil, which was characterized only by NMR without purification. R_f = 0.15 (hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.50–7.43 (m, 6H, Ph), 7.40–7.14 (m, 19H, Ph), 4.96 (t, *J* = 6.0 Hz, 1H, H-3a), 4.82 (d, *J* = 1.1 Hz, 2H, C*H*$_2$Ph), 4.75 (t, *J* = 5.9 Hz, 1H, H-6a), 3.96 (dd, *J* = 6.1, 2.1 Hz, 1H, H-4), 3.51 (dd, *J* = 9.4, 4.9 Hz, 1H, C*H*$_2$OTr), 3.43 (t, *J* = 9.0 Hz, 1H, C*H*$_2$OTr), 2.67–2.56 (m, 1H, H-6), 1.37 and 1.28 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 208.7 (CO), 144.0 (Ph), 137.1 (Ph), 128.8 (Ph), 128.5 (Ph), 128.2 (Ph), 128.1 (Ph), 127.9 (Ph), 127.0 (Ph), 111.1 [*C*(CH$_3$)$_2$], 86.8 (*C*Ph$_3$), 78.2, 74.6, 73.8, 72.0, 57.7 (*C*H$_2$OTr), 48.0 (C-6), 26.3 and 25.0 [C(*C*H$_3$)$_3$].

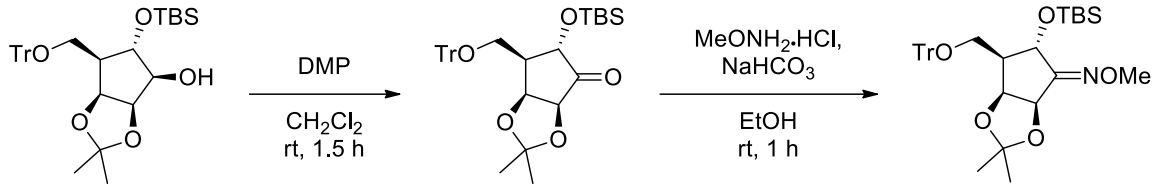
(3a*R*,4*S*,5*S*,6*R*,6a*S*)-5-((*tert*-Butyldimethylsilyl)oxy)-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-ol (27)



15 **27**

A solution of NaHMDS (2 M in THF, 9.27 ml, 18.54 mmol) was added dropwise to a stirred solution of silyl ether **15** (5.20, 9.27 mmol) in anhydrous THF (100 mL) at −30 °C under a nitrogen atmosphere. After 30 min of stirring, the cooling bath was removed and the reaction mixture was stirred at r.t. for 30 min. Then, anhydrous DMF (10 mL) was added and the reaction mixture was stirred at r.t. for 15 min. Water (100 mL) was carefully added and the reaction mixture was extracted with EtOAc (2×50 mL). The combined organic extracts were washed with water (4×50 mL), brine (50 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 15:1, v/v) to afford silyl ether **27** (5.00 g, 96%) as a colorless oil. R_f = 0.16 (hexanes/EtOAc = 15:1); $[\alpha]_D^{20}$ = +45.1 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ =7.52–7.41 (m, 5H, Ph), 7.32–7.17 (m, 10H, Ph), 4.89 (dd, *J* = 5.7, 4.8 Hz, 1H), 4.50 (t, *J* = 6.1 Hz, 1H), 3.56 (ddd, *J* = 9.7, 7.7, 6.4, 1H, H-4), 3.44–3.36 (m, 2H, C*H*$_2$OTr, C-5), 3.05 (dd, *J* = 8.2, 3.9 Hz, 1H, C*H*$_2$OTr), 2.36 (d, *J* = 9.8 Hz, 1H, OH), 1.92 (tt, *J* = 10.6, 4.2 Hz, 1H, H-6), 1.41 and 1.40 [2s, each 3H, C(C*H*$_3$)$_2$], 0.68 [s, 9H, Si(CH$_3$)$_2$C(C*H*$_3$)$_3$], −0.03 and −0.25 [2s, each 3H, Si(C*H*$_3$)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 144.3 (Ph), 128.8 (Ph), 127.6 (Ph), 126.8 (Ph), 110.1 [*C*(CH$_3$)$_2$], 86.5 (*C*Ph$_3$), 77.8 (C-4), 77.4 (C-5) 76.4, 75.7, 60.5 (*C*H$_2$OTr), 45.9 (C-6), 26.0 and 24.3 [C(*C*H$_3$)$_2$], 25.7 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 17.8 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.3 and −5.3 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 3549, 2959, 2855, 1490, 1382, 1139, 1071, 836, 698, 632 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{44}O_5Si$: 583.2850 [*M*+Na]$^+$, found: 583.2853.

(3a*R*,5*S*,6*R*,6a*S*)-5-((*tert*-Butyldimethylsilyl)oxy)-2,2-dimethyl-6-((trityloxy)methyl)dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4(5*H*)-one *O*-methyl oxime (29)

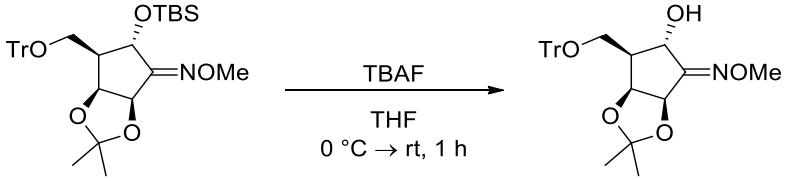


27 **28** **29**

DMP (5.67 g, 13.38 mmol) was added to a stirred solution of alcohol **27** (5.00 g, 8.92 mmol) in CH_2Cl_2 (100 mL) at r.t. and the mixture was stirred for 2 h. Then, satd. aq. $NaHCO_3$ (100 mL) and 10% aq. $Na_2S_2O_3$ (100 mL) were added and the resulting mixture was stirred at r.t. for 45 min. The layers were separated and the organic layer was washed 2× with mixture of satd. aq. $NaHCO_3$ solution (100 mL) and 10% aq. $Na_2S_2O_3$ (100 mL), dried over Na_2SO_4 and filtered. Evaporation of the solvent under reduced pressure afforded ketone **28** (4.99 g, quant.), which was used in the next reaction without any other characterization and purification.

$MeONH_2$·HCl (2.98 g, 35.68 mmol) and $NaHCO_3$ (300 g, 35.68 mmol) were added to a stirred solution of prepared ketone (4.99 g, 8.92 mmol) in EtOH (100 mL) at r.t. and the reaction mixture was stirred for 2 h. Next, the ethanol was evaporated under reduced pressure and the residue was partitioned between EtOAc (100 mL) and water (100 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2×50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 20:1, v/v) to afford oxime ether **29** (4.51 g, 86%) as a thick colorless oil. R_f = 0.14 (hexanes/EtOAc = 20:1); $[\alpha]_D^{20}$ = +43.2 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.52–7.45 (m, 5H, Ph), 7.32–7.19 (m, 10H, Ph), 5.10 (dd, *J* = 5.6, 1.5 Hz, 1H, H-3a), 4.95 (dd, *J* = 5.5, 4.3 Hz, 1H, H-6a), 4.30 (dd, *J* = 10.6, 1.5 Hz, 1H, H-5), 3.92 (s, 3H, NOCH_3), 3.48 (dd, *J* = 10.3, 8.4 Hz, 1H, CH_2OTr), 3.21 (dd, *J* = 8.3, 4.1 Hz, 1H, CH_2OTr), 2.16 (tt, *J* = 10.4, 4.1 Hz, 1H, H-6), 1.43 and 1.38 [2s, each 3H, C(CH_3)$_2$], 0.70 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.00 and −0.17 [2s, each 3H, Si(CH_3)$_2$C(CH$_3$)$_3$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 159.9 (*C*NOCH$_3$), 144.2 (Ph), 128.8 (Ph), 127.7 (Ph), 126.9 (CH-Ph), 111.5 [*C*(CH$_3$)$_2$], 86.7 (*C*Ph$_3$), 76.0 (C-6a), 72.1 (C-3a), 71.4 (C-5), 62.4 (CNO*C*H$_3$), 61.1 (*C*H$_2$OTr), 47.6 (C-6), 26.8 and 24.9 [C(*C*H$_3$)$_2$], 25.7 [Si(CH$_3$)$_2$C(*C*H$_3$)$_3$], 18.2 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$], −4.3 and −5.6 [Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; IR (ATR) υ_{max}: 3086, 2962, 2855, 1449, 1211, 1032, 836, 698, 632 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{44}O_5Si$: 626.2699 [*M*+K]$^+$, found: 626.2693.

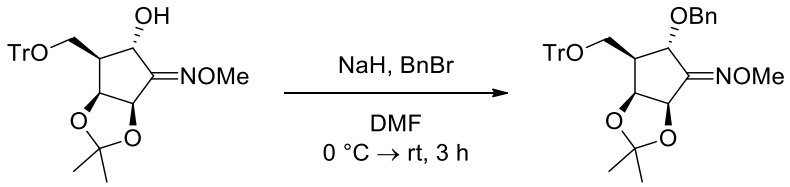
(3a*R*,5*S*,6*S*,6a*S*)-5-Hydroxy-2,2-dimethyl-6-((trityloxy)methyl)dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4(5*H*)-one *O*-methyl oxime (30)



29 **30**

TBAF·3H_2O (2.87 g, 9.11 mmol) was added to a stirred solution of silyl ether **29** (4.46 g, 7.59 mmol) in anhydrous THF (75 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. for 2 h. Then, water (70 mL) was carefully added and the resulting mixture was extracted with Et_2O (2×20mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 3:1, v/v) to afford alcohol **30** (3.60 g, quant.) as a white foam. R_f = 0.15 (hexanes/EtOAc = 3:1); $[\alpha]_D^{20}$ = +73.0 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.50–7.40 (m, 5H, Ph), 7.35–7.21 (m, 10H, Ph), 5.10 (dd, *J* = 5.6, 1.5 Hz, 1H), 4.69 (dd, *J* = 5.5, 4.5 Hz, 1H), 4.50 (ddd, *J* = 10.5, 3.1, 1.5 Hz, 1H, H-5), 3.96 (s, 3H, NOC*H*$_3$), 3.65 (dd, *J* = 9.0, 7.4 Hz, 1H, C*H*$_2$OTr), 3.52 (dd, *J* = 9.0, 7.2 Hz, 1H, C*H*$_2$OTr), 2.67 (d, *J* = 3.2 Hz, 1H, OH), 2.12–2.03 (m, 1H, H-6), 1.32 and 1.31 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 159.8 (*C*NOCH$_3$), 143.8 (Ph), 128.7 (Ph), 127.9 (Ph), 127.1 (Ph), 112.0 [*C*(CH$_3$)$_2$], 87.3 (*C*Ph$_3$), 76.6, 72.2 (2×, H-5), 62.7 (CNO*C*H$_3$), 62.4 (*C*H$_2$OTr), 46.9 (C-6), 26.7 and 24.6 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3433, 3058, 2935, 1448, 1211, 1029, 747, 698, 632 cm^{-1}; HRMS *m/z* calcd for $C_{29}H_{31}NO_5$: 512.1834 [*M*+K]$^+$, found: 512.1838.

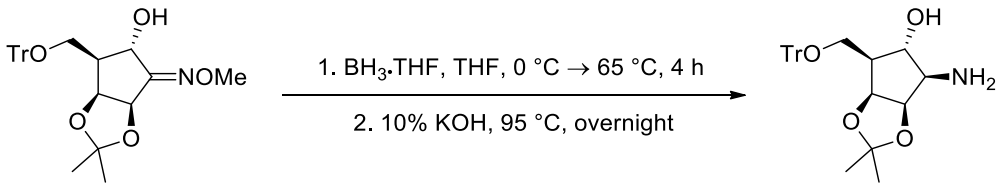
(3a*R*,5*S*,6*S*,6a*S*)-5-(Benzyloxy)-2,2-dimethyl-6-((trityloxy)methyl)dihydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4(5*H*)-one *O*-methyl oxime (31)



30 **31**

NaH (60% in mineral oil, 23 mg, 0.60 mmol) was added to a stirred solution of alcohol **30** (141 mg, 0.30 mmol) in anhydrous DMF (5 mL) at 0 °C under a nitrogen atmosphere followed by BnBr (42 µL, 0.36 mmol) and the reaction mixture was stirred at r.t. for 3 h. Then, water (20 mL) was carefully added and the resulting mixture was extracted with EtOAc (2×20 mL). The combined organic extracts were washed with water (4×20 mL) and brine (10 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 10:1, v/v) to afford benzyl ether **31** (163 mg, 97%) as a colorless oil. R_f = 0.18 (hexanes/EtOAc = 10:1); $[\alpha]_D^{20}$ = +43.4 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.50–7.42 (m, 6H, Ph), 7.33–7.20 (m, 12H, Ph), 7.18–7.11 (m, 2H, Ph), 5.12 (dd, *J* = 5.6, 1.5 Hz, 1H), 4.88 (d, *J* = 11.6 Hz, 1H, OC*H*$_2$Ph), 4.83 (dd, *J* = 5.4, 4.6 Hz, 1H), 4.48 (d, *J* = 11.6 Hz, 1H, OC*H*$_2$Ph), 4.22 (dd, *J* = 10.3, 1.5 Hz, 1H), 3.98 (s, 3H, NOC*H*$_3$), 3.45 (t, *J* = 8.9 Hz, 1H, C*H*$_2$OTr), 3.31 (dd, *J* = 8.8, 4.9 Hz, 1H, C*H*$_2$OTr), 2.29 (ddd, *J* = 14.7, 9.1, 4.7 Hz, 1H, H-6), 1.37 and 1.34 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 160.1 (*C*NOCH$_3$), 144.1 (Ph), 138.0 (Ph), 128.8 (Ph), 128.3 (Ph), 127.8 (Ph), 127.7 (Ph), 127.6 (Ph), 126.9 (Ph), 111.6 [*C*(CH$_3$)$_2$], 86.8 (*C*Ph$_3$), 77.3, 76.4, 72.8 (O*C*H$_2$Ph), 72.7, 62.7 (CNO*C*H$_3$), 61.0 (*C*H$_2$OTr), 45.8 (C-6), 26.7 and 24.9 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3086, 2987, 1652, 1449, 1210, 1032, 869, 746, 697 cm^{-1}; HRMS *m/z* calcd for $C_{36}H_{37}NO_5$: 602.2303 [*M*+K]$^+$, found: 602.2317.

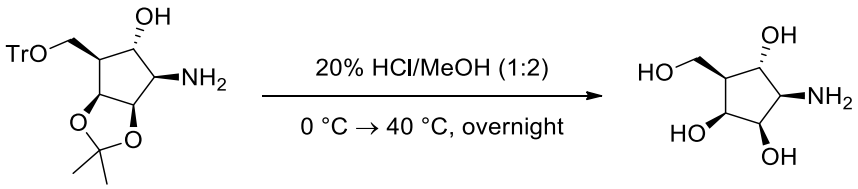
(3a*R*,4*R*,5*S*,6*S*,6a*S*)-4-Amino-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-ol (32)



30 **32**

A solution of BH_3 (1M in THF, 30.36 mL, 30.36 mmol) was added to a stirred solution of oxime ether **30** (3.60 g, 7.59 mmol) in anhydrous THF (30 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at 65 °C for 4 h. The reaction mixture was cooled to 0 °C, 10% aq. KOH (100 mL) was added and the reaction mixture was stirred at 95 °C overnight. Next, the reaction mixture was allowed to cool to r.t., the layers were separated and the aqueous layer was extracted with Et_2O (2×40 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 30:1, containing 0.5% (v/v) of concd aq. NH_3) to afford amine **32** (2.23 g, 66%) as a white foam. R_f = 0.21 ($CHCl_3$/MeOH = 30:1, containing (v/v) 0.5% concd aq. NH_3); $[\alpha]_D^{20}$ = +2.2 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.47–7.41 (m, 5H, Ph), 7.34–7.19 (m, 10H, Ph), 4.53 (t, *J* = 5.8 Hz, 1H), 4.41 (t, *J* = 5.7 Hz, 1H), 3.62 (dd, *J* = 9.1, 6.3 Hz, 1H, C*H*$_2$OTr), 3.48 (t, *J* = 9.6 Hz, 1H, H-5), 3.38 (t, *J* = 8.9 Hz, 1H, C*H*$_2$OTr), 2.76 (dd, *J* = 9.2, 5.5 Hz, H-4), 2.23–1.48 (m, 4H, OH, NH_2, H-6), 1.24 and 1.22 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 143.8 (Ph), 128.7 (Ph), 127.9 (Ph), 127.1 (Ph), 109.6 [*C*(CH$_3$)$_2$], 87.3 (*C*Ph$_3$), 79.1 (C-5), 78.3, 76.6, 62.9 (*C*H$_2$OTr), 60.6 (C-4), 46.6 (C-6), 25.7 and 23.8 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3361, 3296, 2931, 1448, 1208, 1064, 762, 697, 632 cm^{-1}; HRMS *m/z* calcd for $C_{30}H_{33}NO_5$: 446.2326 [*M*+H]$^+$, found: 446.2333.

(1*S*,2*R*,3*R*,4*S*,5*S*)-3-Amino-5-(hydroxymethyl)cyclopentane-1,2,4-triol (3a)

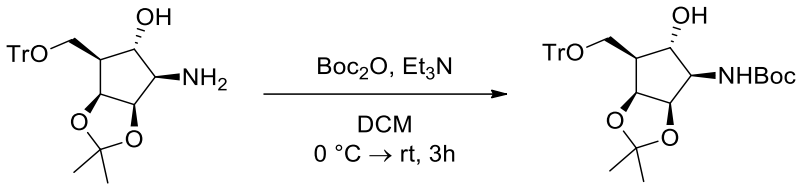


32 **3a**

20% HCl (1 mL) was added to a stirred solution of trityl ether **32** (100 mg, 224 µmol) in MeOH (2 mL) at 0 °C and the reaction mixture was stirred at 40 °C overnight. The reaction mixture was cooled to r.t. and the volatiles were evaporated under reduced pressure. The residue was partitioned between distilled water (7 mL) and $CHCl_3$ (15 mL), layers were separated and the organic layer was washed with additional distilled water (7 mL). Amberlite® IRA 400 (OH^-) (1 g) was added to the combined aqueous layers and the resulting suspension was stirred at r.t. overnight. The suspension was filtered and the filtrate was lyophilized. The residue was dissolved in MeOH (4 mL) and filtered through a PTFE syringe filter (0.45 µm). The solvent was evaporated under reduced pressure, the residue was dissolved in distilled water (4 mL) and lyophilized to afford

aminotetraol **3a** (38 mg, quant.) as a thick yellowish oil. R_f = 0.00 ($CHCl_3$/MeOH = 1:1); $[\alpha]_D^{20}$ = +20.7 (*c* 0.50; MeOH). ^{1}H NMR (400 MHz; CD_3OD): δ = 4.28 (dd, *J* = 6.5, 4.2 Hz, 1H, H-1), 4.06 (dd, *J* = 6.0, 4.3 Hz, 1H, H-2), 3.91–3.78 (m, 3H, C*H*$_2$OH, H-4), 3.04 (t, *J* = 6.1 Hz, 1H, H-3), 2.03–1.94 (m, 1H, H-5); ^{13}C NMR (100 MHz; CD_3OD): δ = 79.8 (C-4), 74.0 (C-1), 73.7 (C-2), 62.0 (C-3), 61.5 (C*H*$_2$OH), 52.5 (C-5); IR (ATR) υ_{max}: 3280, 2927, 1574, 1470, 1386, 1324, 1054, 697, 564 cm^{-1}; HRMS *m/z* calcd for $C_6H_{13}NO_4$: 164.0917 [*M*+H]$^+$, found: 164.0918.

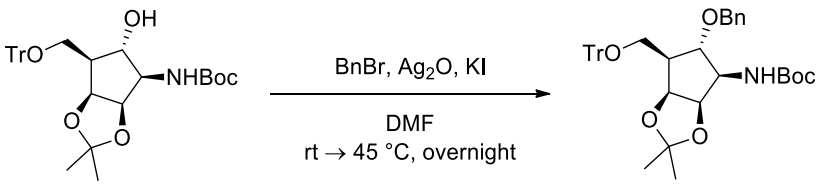
***tert*-Butyl ((3a*R*,4*R*,5*S*,6*S*,6a*S*)-5-hydroxy-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)carbamate (33)**



32 **33**

Boc_2O (1.09 g, 4.98 mmol) was added to a stirred solution of amine **32** (2.22 g, 4.98 mmol) and Et_3N (1.04 mL, 7.47 mmol) in anhydrous DCM (50 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. for 3 h. Next, the reaction mixture was washed with water (2×20 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 5:1, v/v) to afford carbamate **33** (2.57 g, 94%) as a white foam. R_f = 0.19 (hexanes/EtOAc = 5:1); $[\alpha]_D^{20}$ = −45.5 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.50–7.41 (m, 5H, Ph), 7.32–7.18 (m, 10H, Ph), 5.16 [d, *J* = 7.0 Hz, 1H, N*H*$CO_2C(CH_3)_3$], 4.67 (t, *J* = 5.4 Hz, 1H), 4.50 (t, *J* = 5.8 Hz, 1H), 3.75–3.57 (m, 2H, H-4, H-5), 3.54 (t, *J* = 8.4, 1H, C*H*$_2$OTr), 3.37 (dd, *J* = 8.9, 6.9 Hz, 1H, C*H*$_2$OTr), 2.01–1.91 (m, 1H, H-6), 1.44 [s, 9H, $NHCO_2C(CH_3)_3$], 1.28 and 1.26 [2s, each 3H, $C(CH_3)_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 156.8 [$NHCO_2C(CH_3)_3$], 144.0 (Ph), 128.8 (Ph), 127.7 (Ph), 127.0 (Ph), 110.1 [$C(CH_3)_2$], 87.0 (*C*Ph$_3$), 80.0 [$NHCO_2C(CH_3)_3$], 77.7 (C-5), 77.3, 76.4, 61.9 (*C*H$_2$OTr), 59.1 (C-4), 46.8 (C-6), 28.4 [$NHCO_2C(CH_3)_3$], 25.8 and 24.0 [$C(CH_3)_2$]; IR (ATR) υ_{max}: 3440, 2979, 2932 1690, 1491, 1367, 1163, 1091, 1070, 747, 699, 633 cm^{-1}; HRMS *m/z* calcd for $C_{33}H_{39}NO_6$: 584.2410 [*M*+K]$^+$, found: 584.2421.

***tert*-Butyl ((3a*R*,4*R*,5*S*,6*S*,6a*S*)-5-(benzyloxy)-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)carbamate (34)**

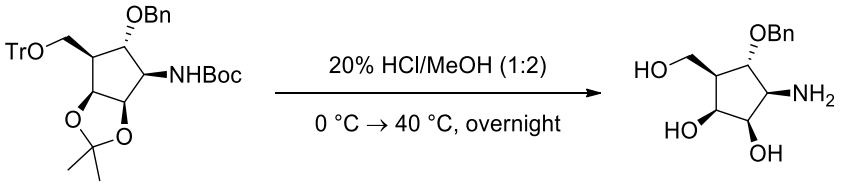


33 **34**

BnBr (26 µL, 0.54 mmol) was added to a suspension of alcohol **33** (73 mg, 0.13 mmol), Ag_2O (124 mg, 0.54 mmol) and KI (5 mg, 3 µmol) in anhydrous DMF (2 mL) at r.t. under a nitrogen atmosphere and the reaction mixture was stirred at 45 °C overnight. Then, the reaction mixture was filtered and the filtrate was partitioned

between EtOAc (15 mL) and water (15 mL). Layers were separated and the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic extracts were washed with water (4×10 mL) and brine (10 mL), dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 10:1, v/v) to afford benzyl ether **34** (45 mg, 53%) as thick colorless oil. R_f = 0.14 (hexanes/EtOAc = 10:1); $[\alpha]_D^{20}$ = −40.7 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.53–7.44 (m, 5H, Ph), 7.32–7.18 (m, 13H, Ph), 7.04 (dt, *J* = 5.7, 3.2 Hz, 2H, Ph), 4.99 [d, *J* = 9.5 Hz, 1H, N*H*CO$_2$C(CH$_3$)$_3$], 4.77 (t, *J* = 5.6 Hz, 1H, H-6a), 4.49 (m, 2H, OC*H*$_2$Ph, H-3a), 4.33 (d, *J* = 11.2 Hz, 1H, OC*H*$_2$Ph), 3.98 (q, *J* = 9.2 Hz, 1H, H-4), 3.45 (t, *J* = 9.0 Hz, 1H, C*H*$_2$OTr), 3.35 (t, *J* = 10.0 Hz, 1H, H-5), 3.24 (dd, *J* = 8.6, 4.4 Hz, 1H, C*H*$_2$OTr), 2.11 (tt, *J* = 9.6, 4.8 Hz, 1H, H-6), 1.46 [s, 9H, NHCO$_2$C(C*H*$_3$)$_3$], 1.33 [s, 6H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 155.2 [NH*C*O$_2$C(CH$_3$)$_3$], 144.2 (Ph), 138.4 (Ph), 128.9 (Ph), 128.1 (Ph), 127.6 (Ph), 127.4 (Ph), 126.8 (Ph), 109.5 [*C*(CH$_3$)$_2$], 86.7 (*C*Ph$_3$), 82.4 (C-5), 79.5 [NHCO$_2$*C*(CH$_3$)$_3$], 76.3 (C-3a), 76.1 (C-6a), 71.8 (O*C*H$_2$Ph), 60.6 (*C*H$_2$OTr), 57.0 (C-4), 45.6 (C-6), 28.4 [NHCO$_2$C(*C*H$_3$)$_3$], 25.9 and 24.0 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3445, 2931, 1714, 1496, 1164, 1075, 746, 697, 632 cm^{-1}; HRMS *m/z* calcd for $C_{40}H_{45}NO_6$: 674.2879 [*M*+K]$^+$, found: 674.2881.

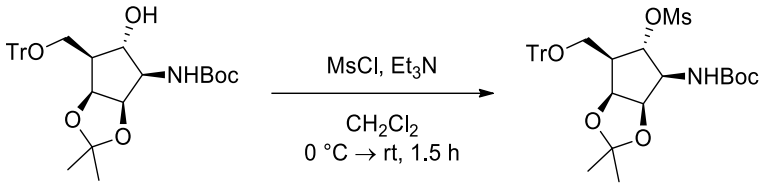
(1*S*,2*R*,3*S*,4*S*,5*R*)-3-Amino-4-(benzyloxy)-5-(hydroxymethyl)cyclopentane-1,2-diol (3c)



34 **3c**

20% HCl (1 mL) was added to a stirred solution of trityl ether **34** (90 mg, 142 μmol) in MeOH (2 mL) at 0 °C and the reaction mixture was stirred at 40 °C overnight. The reaction mixture was cooled to r.t. and the volatiles were evaporated under reduced pressure. The residue was partitioned between distilled water (7 mL) and $CHCl_3$ (15 mL), layers were separated and the organic layer was washed with additional distilled water (7 mL). Amberlite® IRA 400 (OH^-) (1 g) was added to the combined aqueous layers and the resulting suspension was stirred at r.t. overnight. The suspension was filtered and the filtrate was lyophilized. The residue was dissolved in MeOH (10 mL) and filtered through a PTFE syringe filter (0.45 μm). The solvent was evaporated under reduced pressure, the residue was dissolved in distilled water (5 mL) and lyophilized to afford aminotetraol **3c** (20 mg, 56%) as a thick yellowish oil. R_f = 0.00 (hexanes/EtOAc = 1:1); $[\alpha]_D^{20}$ = −11.6 (*c* 1.00; MeOH). ^{1}H NMR (400 MHz; CD_3OD): δ = 7.41–7.23 (m, 5H, Ph), 4.64 (d, *J* = 11.5 Hz, 1H, OC*H*$_2$Ph), 4.59 (d, *J* = 11.5 Hz, 1H, OC*H*$_2$Ph), 4.25 (dd, *J* = 5.8, 3.9 Hz, 1H, H-2), 4.04 (dd, *J* = 6.0, 3.8 Hz, 1H, H-1), 3.86–3.73 (m, 3H, C*H*$_2$OH, H-4), 3.27 (dd, *J* = 5.4, 4.6 Hz, 1H, H-3), 2.14 (p, *J* = 6.5 Hz, 1H, H-5); ^{13}C NMR (100 MHz; CD_3OD): δ = 139.7 (Ph), 129.4 (Ph), 128.9 (Ph), 128.7 (Ph), 87.5 (H-4), 74.2 (C-2), 73.6 (C-1), 73.3 (O*C*H$_2$Ph), 61.1 (*C*H$_2$OH), 59.3 (C-3), 50.6 (C-5); IR (ATR) υ_{max}: 3342, 3287, 2925, 1586, 1454, 1352, 1071, 737, 697 cm^{-1}; HRMS *m/z* calcd for $C_{13}H_{19}NO_4$: 254.1387 [*M*+H]$^+$, found: 254.1385.

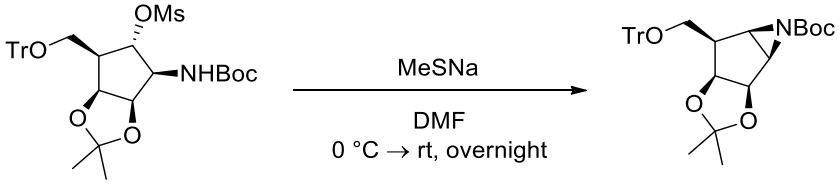
(3a*R*,4*S*,5*S*,6*R*,6a*S*)-4-((tert-Butoxycarbonyl)amino)-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-yl methanesulfonate (36)



33 **36**

MsCl (0.3 mL, 3.86 mmol) was added to a stirred solution of alcohol **33** (1.40 g, 2.57 mmol) and Et_3N (0.72 mL, 5.14 mmol) in anhydrous CH_2Cl_2 (25 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. for 1.5 h. Then, the reaction mixture was washed with water (2×25 mL), organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 5:1) to afford mesylate **36** (1.59 g, quant.) as a white foam. R_f = 0.14 (hexanes/EtOAc = 5:1); $[\alpha]_D^{20}$ = −11.1 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.52–7.46 (m, 6H, Ph), 7.34–7.22 (m, 9H, Ph), 5.17–5.06 [m, 1H, N*H*$CO_2C(CH_3)_3$], 4.83 (t, *J* = 5.6 Hz, 1H, H-6a), 4.55 (t, *J* = 5.9 Hz, 1H, H-3a), 4.39 (d, *J* = 10.7 Hz, 1H, H-5), 4.05 (td, *J* = 9.4, 5.8 Hz, 1H, H-4), 3.59 (t, *J* = 9.4 Hz, C*H*$_2$OTr), 3.27 (dd, *J* = 9.1, 4.3 Hz, 1H, C*H*$_2$OTr), 2.81 (s, 3H, SO_2CH_3), 2.11 (ddt, *J* = 15.1, 9.9, 5.1 Hz, 1H, H-6), 1.45 [s, 9H, $NHCO_2C(CH_3)_3$], 1.41 and 1.37 [2s, each 3H, $C(CH_3)_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 153.3 [$NHCO_2C(CH_3)_3$], 143.9 (Ph), 128.8 (Ph), 127.7 (Ph), 127.0 (Ph), 110.1 [$C(CH_3)_2$], 87.0 (*C*Ph_3), 83.1 (C-5), 80.0 [$NHCO_2C(CH_3)_3$], 75.5 (C-3a), 75.4 (C-6a), 59.4 (*C*H_2OTr), 56.4 (H-4), 45.2 (C-6), 38.4 (SO_2CH_3), 28.3 [$NHCO_2C(CH_3)_3$], 25.8 and 23.8 [$C(CH_3)_2$]; IR (ATR) υ_{max}: 3347, 3342, 2932, 1712, 1505, 1364, 1171, 954, 862, 761, 699, 516 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{41}NO_8S$: 646.2445 [*M*+Na]$^+$, found: 646.2449.

(1a*R*,1b*R*,4a*S*,5*R*,5a*R*)-*tert*-Butyl 3,3-dimethyl-5-((trityloxy)methyl)tetrahydro-[1,3]dioxolo[4',5':3,4] cyclopenta[1,2-b]azirine-1(1a*H*)-carboxylate (37)

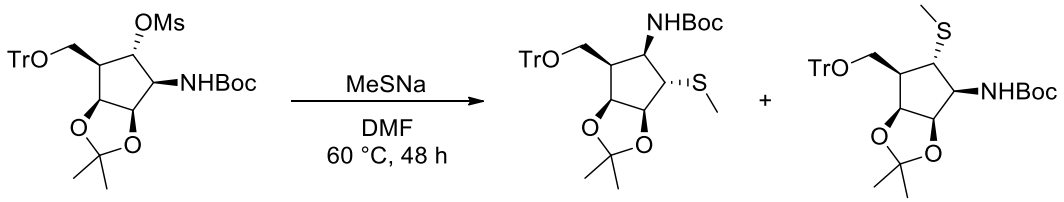


36 **37**

MeSNa (5 mg, 65 µmol) was added to a stirred solution of mesylate **36** (27 mg, 43 µmol) in anhydrous DMF (1 mL) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred at r.t. overnight. Then, the reaction mixture was partitioned between water (5 mL) and EtOAc (5 mL) and the layers were separated. Aqueous layer was extracted with additional EtOAc (2×5 mL). The combined organic extracts were washed with water (3×5 mL), brine (5 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by preparative TLC on silica gel (hexanes/EtOAc = 5:1) to afford aziridine **37** (11 mg, 48%) as a thick yellowish oil. R_f = 0.23 (hexanes/EtOAc = 5:1); $[\alpha]_D^{20}$ = +15.4 (*c* 0.50; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.61–7.39 (m, 5H, Ph), 7.35–7.17 (m, 10H, Ph), 4.64 (dd, *J* = 6.5, 3.1 Hz, 1H, H-4a), 4.47 (t, *J* = 6.4 Hz, 1H, H-1b), 3.55 (dd, *J* = 9.1, 8.1 Hz, 1H, C*H*$_2$OTr), 3.45 (dd, *J* = 9.1, 6.3 Hz,

1H, C*H*$_2$OTr), 3.24 (ddd, *J* = 4.4, 3.1, 1.0 Hz, 1H, H-5a), 3.04–2.97 (t, *J* = 3.7 Hz, 1H, H-1a), 2.26 (dtd, *J* = 8.1, 6.4, 2.9 Hz, 1H, H-5), 1.46 and 1.22 [2s, each 3H, C(C*H*$_3$)$_2$], 1.41 [s, 9H, NCO$_2$C(C*H*$_3$)$_3$]; ^{13}C NMR (100 MHz; CDCl$_3$): δ = 161.3 [N*C*O$_2$C(CH$_3$)$_3$], 144.3 (Ph), 128.9 (Ph), 127.6 (Ph), 126.8 (Ph), 113.3 [*C*(CH$_3$)$_2$], 86.7 (*C*Ph$_3$), 80.8 [NCO$_2$*C*(CH$_3$)$_3$], 80.4 (C-4a), 79.6 (C-1b), 60.1 (*C*H$_2$OTr), 46.5 (C-5a), 44.6 (C-1a), 43.3 (C-5), 28.0 [NCO$_2$C(*C*H$_3$)$_3$], 26.6 and 25.9 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 2979, 2931, 1714, 1369, 1152, 1067, 747, 705, 633 cm^{-1}; HRMS *m/z* calcd for $C_{33}H_{37}NO_5$: 550.2564 [*M*+Na]$^+$, found: 550.2568.

***tert*-Butyl ((3a*S*,4*S*,5*R*,6*R*,6a*S*)-2,2-dimethyl-4-(methylthio)-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-5-yl)carbamate (38a) and *tert*-butyl ((3a*R*,4*S*,5*S*,6*R*,6a*S*)-2,2-dimethyl-5-(methylthio)-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)carbamate (38b)**

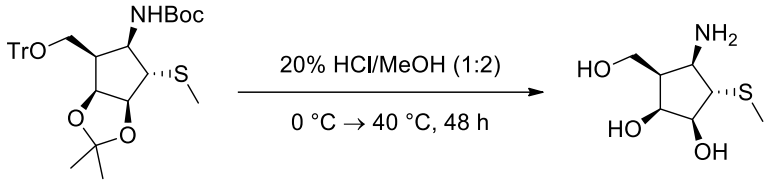


36 **38a** **38b**

MeSNa (509 mg, 7.26 mmol) was added to a stirred solution of mesylate **36** (1.51 g, 2.42 mmol) in anhydrous DMF (24 mL) at r.t. under a nitrogen atmosphere and the reaction mixture was stirred at 60 °C for 48 h. Then, the reaction mixture was partitioned between water (30 mL) and EtOAc (30 mL), the layers were separated and the aqueous layer was extracted with additional EtOAc (2×30 mL). The combined organic extracts were washed with water (3×30 mL), brine (30 mL), dried over Na_2SO_4, filtered a and the solvent was evaporated under reduced pressure. The products of the reaction were two regioisomers **38a** and **38b**, which were separated by column chromatography (hexanes/EtOAc = 10:1) to afford pure products **38a** (854 mg, 61%) and **38b** (300 mg, 22%) as colorless oils. Analytical data for thioether **38a**: R_f = 0.21 (hexanes/EtOAc = 10:1); $[\alpha]_D^{20}$ = +8.1 (*c* 1.00; CHCl$_3$). ^{1}H NMR (400 MHz; CDCl$_3$): δ = 7.50–7.43 (m, 5H, Ph), 7.33–7.20 (m, 10H, Ph), 5.34 [d, *J* = 9.3 Hz, 1H, N*H*CO$_2$C(CH$_3$)$_3$], 4.79 (t, *J* = 5.1 Hz, 1H, H-6a), 4.44 (d, *J* = 5.6 Hz, 1H, H-3a), 4.00 (dd, *J* = 9.3, 5.7 Hz, 1H, H-5), 3.44 (dd, *J* = 9.2, 7.7 Hz, 1H, C*H*$_2$OTr), 3.28 (dd, *J* = 9.2, 6.5 Hz, 1H, C*H*$_2$OTr), 3.09 (s, 1H, H-4), 2.64 (dtd, *J* = 7.8, 6.3, 4.6 Hz, 1H, H-6), 2.25 (s, 3H, SC*H*$_3$), 1.44 and 1.30 [2s, each 3H, C(C*H*$_3$)$_2$], 1.39 [s, 9H, NHCO$_2$C(C*H*$_3$)$_3$]; ^{13}C NMR (100 MHz; CDCl$_3$): δ = 155.1 [NH*C*O$_2$C(CH$_3$)$_3$], 144.1 (Ph), 128.8 (Ph), 127.7 (Ph), 126.9 (Ph), 110.5 [*C*(CH$_3$)$_2$], 86.6 (*C*Ph$_3$), 85.2 (C-3a), 81.2 (C-6a), 79.2 [NHCO$_2$*C*(CH$_3$)$_3$], 59.0 (*C*H$_2$OTr), 57.8 (C-5), 57.0 (C-4), 44.1 (C-6), 28.4 [NHCO$_2$C(*C*H$_3$)$_3$], 26.1 and 23.5 [C(*C*H$_3$)$_2$], 15.6 (S*C*H$_3$); IR (ATR) υ_{max}: 3438, 2979, 2930, 1712, 1489, 1375, 1160, 1063, 1036, 752, 703, 633 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{41}NO_5S$: 598.2604 [*M*+Na]$^+$, found: 598.2598. Analytical data for thioether **38b**: R_f = 0.12 (hexanes/EtOAc = 10:1); $[\alpha]_D^{20}$ = −19.9 (*c* 1.00; CHCl$_3$). ^{1}H NMR (400 MHz; CDCl$_3$): δ = 7.53–7.45 (m, 5H, Ph), 7.33–7.18 (m, 10H, Ph), 4.86 [d, *J* = 9.9 Hz, 1H, N*H*CO$_2$C(CH$_3$)$_3$], 4.77 (t, *J* = 5.4 Hz, 1H, H-6a), 4.49 (t, *J* = 5.6 Hz, 1H, H-3a), 3.76 (td, *J* = 10.5, 5.4 Hz, 1H, H-4), 3.40 (d, *J* = 7.1 Hz, 2H, C*H*$_2$OTr), 2.32–2.20 (m, 1H, H-5), 1.83 (s, 3H, SC*H*$_3$), 1.81–1.72 (m, 1H, H-6), 1.44 [s, 9H, NHCO$_2$C(C*H*$_3$)$_3$], 1.35 and 1.34 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; CDCl$_3$): δ = 155.5 [NH*C*O$_2$C(CH$_3$)$_3$], 144.3 (Ph), 128.8 (Ph), 127.6 (Ph), 126.9 (Ph), 109.7 [*C*(CH$_3$)$_2$], 86.8 (*C*Ph$_3$), 79.5 [NHCO$_2$*C*(CH$_3$)$_3$], 77.5 (C-6a), 77.2 (C-3a), 61.8 (*C*H$_2$OTr), 55.5 (C-4), 47.6 (C-5), 44.0 (C-6), 28.4 [NHCO$_2$C(*C*H$_3$)$_3$], 25.8 and 24.1 [C(*C*H$_3$)$_2$], 10.5 (S*C*H$_3$); IR

(ATR) υ_{max}: 3340, 2978, 1717, 1493, 1209, 1163, 1067, 763, 699 cm^{-1}; HRMS *m/z* calcd for $C_{34}H_{41}NO_5S$: 598.2598 $[M+Na]^+$, found: 598.2607.

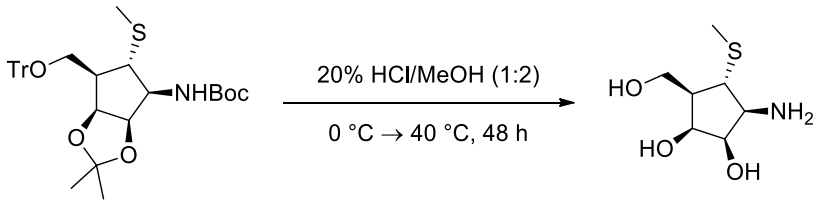
(1*S*,2*S*,3*R*,4*R*,5*S*)-4-Amino-3-(hydroxymethyl)-5-(methylthio)cyclopentane-1,2-diol (42)



38a **42**

20% HCl (1 mL) was added to a solution of carbamate **38a** (39 mg, 0.068 mmol) in MeOH (2 mL) at 0 °C and the reaction mixture was stirred at 40 °C for 48 h. Then, the volatiles were evaporated under reduced pressure and the residue was partitioned between $CHCl_3$ (15 mL) and distilled water (7 mL). The layers were separated and the organic extract was washed with additional distilled water (7 mL). Amberlite® IRA 400 (OH^-) (1 g) was added to the combined aqueous layers and the resulting suspension was stirred at r.t. overnight. The suspension was filtered and the filtrate was lyophilized. The residue was dissolved in MeOH (10 mL) and the resulting solution was filtered through a PTFE syringe filter (0.45 µm). The solvent was evaporated under reduced pressure, the residue was dissolved in distilled water (5 mL) and lyophilized to afford methylthiocyclopentane **42** (10 mg, 77%) as a thick colorless oil. R_f = 0.05 ($CHCl_3$/MeOH = 30:1, containing (v/v) 0.5% concd aq. NH_3); $[\alpha]_D^{20}$ = +7.6 (*c* 1.00; MeOH). ^{1}H NMR (400 MHz; CD_3OD): δ = 4.07 (td, *J* = 4.0, 0.9 Hz, 1H, H-2), 3.92 (d, *J* = 0.8 Hz, 1H, C*H*$_2$OH), 3.90 (d, *J* = 1.2 Hz, 1H, C*H*$_2$OH), 3.85 (dd, *J* = 7.3, 4.1 Hz, 1H, H-1), 3.33–3.30 (m, 1H, H-4), 2.88 (dd, *J* = 7.3, 4.3 Hz, H-5), 2.23 (s, 3H, SC*H*$_3$), 2.21 (dd, *J* = 7.4, 3.6 Hz, 1H, H-3); ^{13}C NMR (100 MHz; $CDCl_3$): δ = 80.3 (C-1), 75.02 (C-2), 58.9 (C-4), 58.6 (*C*H$_2$OH), 58.5 (C-5), 46.6 (C-3), 14.2 (S*C*H$_3$); IR (ATR) υ_{max}: 3336, 3277, 2916, 1579, 1383, 1110, 1013, 642, 557 cm^{-1}; HRMS *m/z* calcd for $C_7H_{15}NO_3S$: 216.0665 $[M+Na]^+$, found: 216.0664.

(1*S*,2*R*,3*S*,4*S*,5*R*)-3-Amino-5-(hydroxymethyl)-4-(methylthio)cyclopentane-1,2-diol (4)

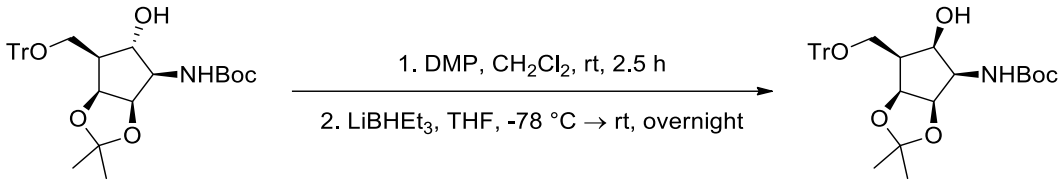


38b **4**

20% HCl (4 mL) was added to a solution of carbamate **38b** (278 mg, 0.48 mmol) in MeOH (8 mL) at 0 °C and the reaction mixture was stirred at 40 °C for 48 h. Then, the volatiles were evaporated under reduced pressure and the residue was partitioned between $CHCl_3$ (15 mL) and distilled water (10 mL). The layers were separated and the organic extract was washed with additional distilled water (10 mL). Amberlite® IRA 400 (OH^-) (1 g) was added to the combined aqueous layers and the resulting suspension was stirred at r.t. overnight. The suspension was filtered and the filtrate was lyophilized. The residue was dissolved in MeOH (15 mL) and the resulting solution was filtered through a PTFE syringe filter (0.45 µm). The solvent was evaporated under

reduced pressure, the residue was dissolved in distilled water (10 mL) and lyophilized to afford methylthiocyclopentane **4** (67 mg, 72%) as a thick colorless oil. R_f = 0.07 ($CHCl_3$/MeOH = 10:1, containing (v/v) 0.5% concd aq. NH_3); $[\alpha]_D^{20}$ = −11.8 (*c* 1.00; MeOH). ^{1}H NMR (400 MHz; CD_3OD): δ = 4.24 (dd, *J* = 6.3, 3.9 Hz, 1H, H-1), 4.00 (dd, *J* = 5.7, 3.9 Hz, 1H, H-2), 3.81 (d, *J* = 5.6 Hz, 2H, C*H*$_2$OH), 3.17 (t, *J* = 6.2 Hz, 1H, H-3), 2.82–2.72 (m, 1H, H-4), 2.14 (s, 3H, SC*H*$_3$), 2.04 (dq, *J* = 9.3, 5.8 Hz, 1H, H-5); ^{13}C NMR (100 MHz; CD_3OD): δ = 72.6 (C-1), 72.3 (C-2), 59.3 (*C*H$_2$OH), 58.1 (C-3), 50.2 (C-4), 48.8 (C-5), 11.8 (S*C*H$_3$); IR (ATR) υ_{max}: 3273, 2917, 1575, 1470, 1124, 1022, 993, 579 cm^{-1}; HRMS *m/z* calcd for $C_7H_{15}NO_3S$: 216.0665 [*M*+Na]$^+$, found: 216.0665.

***tert*-Butyl ((3a*R*,4*R*,5*R*,6*S*,6a*S*)-5-hydroxy-2,2-dimethyl-6-((trityloxy)methyl)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)carbamate (35)**

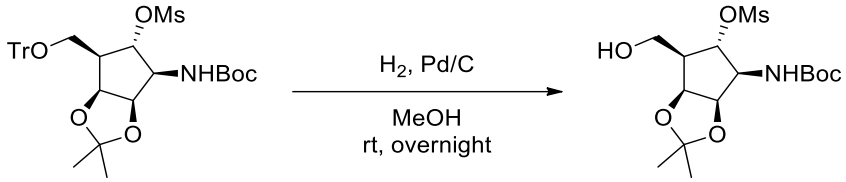


33 **35**

DMP (285 mg, 0.67 mmol) was added to a stirred solution of alcohol **33** (244 mg, 0.45 mmol) in CH_2Cl_2 (10 mL) and the reaction mixture was stirred at r.t. for 2.5 h. Then, the reaction mixture was diluted with $CHCl_3$ (10 mL), satd. aq. $NaHCO_3$ (10 mL) and 10% aq. $Na_2S_2O_3$ (10 mL) were added and the resulting mixture was stirred at r.t. for 1 h. The layers were separated and the aqueous layers was extracted with $CHCl_3$ (10 mL). The combined organic extracts were washed 2× with mixture of satd aq. $NaHCO_3$ (20 mL) and 10% aq. $Na_2S_2O_3$ solution (10 mL), dried over Na_2SO_4 and filtered**.** Evaporation of the solvent under reduced pressure afforded corresponding ketone (257 mg, quant.), which was used in the next reaction without any purification or characterization**.**

A solution of $LiBHEt_3$ (1.7 M in THF, 136 µL, 0.23 mmol) was added dropwise to a stirred solution of ketone (126 mg, 0.23 mmol) in anhydrous THF (5 mL) at −78 °C under a nitrogen atmosphere and the reaction mixture was stirred with gradual warming to r.t. overnight. Then, the reaction mixture was quenched with satd aq. NH_4Cl solution (5 mL), the layers were separated and the aqueous layer was extracted EtOAc (2×5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexnes/EtOAc = 8:1) to afford alcohol **35** (102 mg, 80%) as a colorless oil. R_f = 0.10 (hexanes/EtOAc = 8:1); $[\alpha]_D^{20}$ = +4.0 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 7.51–7.44 (m, 5H, Ph), 7.33–7.19 (m, 10H, Ph), 5.34 [d, *J* = 9.3 Hz, 1H, N*H*CO$_2$C(CH$_3$)$_3$], 4.68 (t, *J* = 5.2 Hz, 1H, H-6a), 4.59 (t, *J* = 5.8 Hz, 1H, H-3a), 4.11 (dt, *J* = 9.2, 4.4 Hz, 1H, H-4), 3.83 (ddd, *J* = 9.8, 6.1, 4.3 Hz, 1H, H-5), 3.58–3.43 (m, 2H, C*H*$_2$OTr), 2.07–1.90 (m, 2H, OH, H-6), 1.46 [s, 9H, NHCO$_2$C(C*H*$_3$)$_3$], 1.39 and 1.28 [2s, each 3H, C(C*H*$_3$)$_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 155.5 [NH*C*O$_2$C(CH$_3$)$_3$], 144.1 (Ph), 128.8 (Ph), 127.7 (Ph), 126.9 (Ph), 110.4 [*C*(CH$_3$)$_2$], 86.7 (*C*Ph$_3$), 80.2 (C-6a), 79.6 [NHCO$_2$*C*(CH$_3$)$_3$], 78.8 (C-3a), 74.5 (C-4), 58.6 (*C*H$_2$OTr), 55.5 (C-4), 45.4 (C-6), 28.4 [NHCO$_2$C(*C*H$_3$)$_3$], 26.5 and 23.0 [C(*C*H$_3$)$_2$]; IR (ATR) υ_{max}: 3451, 2978, 2932, 1710, 1491, 1163, 1070, 747, 705, 632 cm^{-1}; HRMS *m/z* calcd for $C_{33}H_{39}NO_6$: 568.2670 [*M*+Na]$^+$, found: 568.2678.

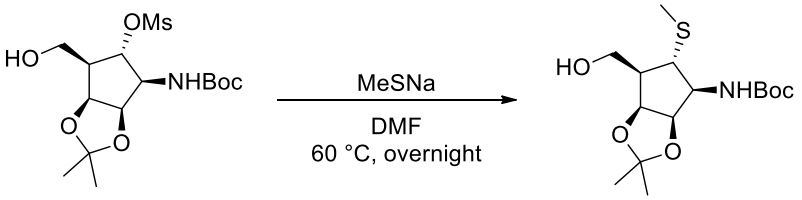
(3aR,4S,5S,6R,6aS)-4-((tert-Butoxycarbonyl)amino)-6-(hydroxymethyl)-2,2-dimethyltetrahydro-3aH-cyclopenta[d][1,3]dioxol-5-yl methanesulfonate (39)



36 **39**

Pd/C (10%, 61 mg) was added to a stirred solution of trityl ether **36** (610 mg, 0.978 mmol) in MeOH (15 mL) and the suspension was stirred at rt under a H_2 atmosphere (baloon) overnight. Then, the catalyst was filtered of and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 1:1→1:3, v/v) to afford alcohol **39** (308 mg, 83%) as a white solid. M.p. 140–142 °C; R_f = 0.11 (hexanes/EtOAc = 1:1); $[\alpha]_D^{20}$ = −10.8 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 5.19 [d, *J* = 9.4 Hz, 1H, N*H*$CO_2C(CH_3)_3$], 4.79 (t, *J* = 10.1 Hz, 1H, H-5), 4.72 (t, *J* = 5.9 Hz, 1H, H-6a), 4.56 (t, *J* = 5.9 Hz, 1H, H-3a), 4.12 (ddt, *J* = 10.3, 6.7, 3.6 Hz, 1H, H-4), 4.02 (dt, *J* = 11.9, 3.8 Hz, 1H, C*H*$_2$OH), 3.85 (ddd, *J* = 11.9, 8.5, 6.3 Hz, 1H, C*H*$_2$OH), 3.08 (s, 3H, SO_2CH_3), 2.35 (dd, *J* = 8.6, 4.1 Hz, 1H, CH_2OH), 2.11 (dtd, *J* = 10.0, 6.0, 3.6 Hz, 1H, H-6), 1.49 and 1.31 [2s, each 3H, $C(CH_3)_2$], 1.46 [s, 9H, $NHCO_2C(CH_3)_3$]; ^{13}C NMR (100 MHz; $CDCl_3$): 155.4 [$NHCO_2C(CH_3)_3$], 110.6 [$C(CH_3)_2$], 82.1 (C-5), 80.1 [$NHCO_2C(CH_3)_3$], 76.9 (C-6a), 75.8 (C-3a), 58.9 (CH_2OH), 56.3 (C-4), 45.7 (C-6), 38.3 (SO_2CH_3), 28.3 [$NHCO_2C(CH_3)_3$], 25.7 and 23.4 [$C(CH_3)_2$]; IR (ATR) υ_{max}: 3578, 3311, 2934, 1678, 1543, 1344m 1163, 956, 866, 524 cm^{-1}; HRMS *m/z* calcd for $C_{15}H_{27}NO_8S$: 382.1530 $[M+H]^+$, found: 382.1534.

***tert*-Butyl ((3a*R*,4*S*,5*S*,6*R*,6a*S*)-6-(hydroxymethyl)-2,2-dimethyl-5-(methylthio)tetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl)carbamate (41)**

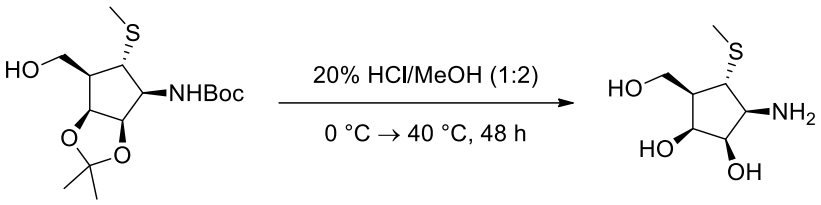


39 **41**

MeSNa (170 mg, 2.42 mmol) was added to a stirred solution of alcohol **39** (308 mg, 0.807 mmol) in anhydrous DMF (10 mL) and the reaction mixture was stirred at 60 °C under a nitrogen atmosphere overnight. Then, the reaction mixture was cooled to rt and partitioned between water (10 mL) and EtOAc (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2×15 mL). The combined organic extracts were washed with water (3×10 mL), brine (10 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 2:1, v/v) to afford thioeter **41** (127 mg, 47%) as a white solid. M.p. 143–145 °C; R_f = 0.14 (hexanes/EtOAc = 2:1); $[\alpha]_D^{20}$ = −8.4 (*c* 1.00; $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ = 4.93 [d, *J* = 9.9 Hz, 1H,

N*H*$CO_2C(CH_3)_3$], 4.69 (t, *J* = 5.7 Hz, 1H, H-6a), 4.54 (t, *J* = 5.6 Hz, 1H, H-3a), 4.00 (ddd, *J* = 11.9, 3.7, 1.8 Hz, 1H, C*H*$_2$OH), 3.88 (m, 3H, H-4, C*H*$_2$OH), 2.72 (t, *J* = 11.7 Hz, 1H, H-5), 2.52 (dd, *J* = 9.1, 3.7 Hz, 1H, CH_2O*H*), 2.09 (s, 3H, SC*H*$_3$), 1.81 (dtd, *J* = 11.9, 6.0, 4.3 Hz, 1H, H-6), 1.47 [s, 9H, $NHCO_2C(CH_3)_3$], 1.46 and 1.32 [2s, each 3H, $C(CH_3)_2$]; ^{13}C NMR (100 MHz; $CDCl_3$): δ = 155.5 [$NHCO_2C(CH_3)_3$], 110.3 [$C(CH_3)_2$], 79.7 [$NHCO_2C(CH_3)_3$], 79.1 (C-6a), 77.8 (C-3a), 60.66 (*C*H_2OH), 55.5 (C-4), 47.2 (C-5), 44.8 (C-6), 28.4 [$NHCO_2C(CH_3)_3$], 25.7 a 23.7 [$C(CH_3)_2$], 11.1 (SCH_3); IR (ATR) υ_{max}: 3405, 3273, 2980, 2875, 1688, 1516, 1246, 1165, 1081, 995, 545 cm^{-1}; HRMS *m/z* calcd for $C_{15}H_{27}NO_5S$: 356.1502 [*M*+Na]$^+$, found: 356.1506.

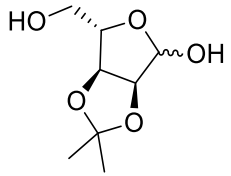
(1*S*,2*R*,3*S*,4*S*,5*R*)-3-Amino-5-(hydroxymethyl)-4-(methylthio)cyclopentane-1,2-diol (4)



41 **4**

20% HCl (1 mL) was added to a solution of carbamate **41** (50 mg, 0.15 mmol) in MeOH (2 mL) at 0 °C and the reaction mixture was stirred at 40 °C for 48 h. Then, the volatiles were evaporated under reduced pressure, the residue was dissolved in distilled water (6 ml), Amberlite® IRA 400 (OH^-) (0.5 g) was added and the resulting suspension was stirred at r.t. overnight. The suspension was filtered and the filtrate was lyophilized. The residue was dissolved in MeOH (5 mL) and the resulting solution was filtered through a PTFE syringe filter (0.45 μm). The solvent was evaporated under reduced pressure, the residue was dissolved in distilled water (5 mL) and lyophilized to afford methylthiocyclopentane **4** (28 mg, 97%) as a thick colorless oil. The NMR spectra and analytical data were consistent with data from preparation of **4** from **38b**.

3. Copies of ^{1}H and ^{13}C NMR spectra of synthesised compounds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O

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3.38
2.05
1.58
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1.40
1.33
1.10
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0.14
0.16
0.98
0.87
0.99
0.14
0.14
1.85
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0.13
0.47
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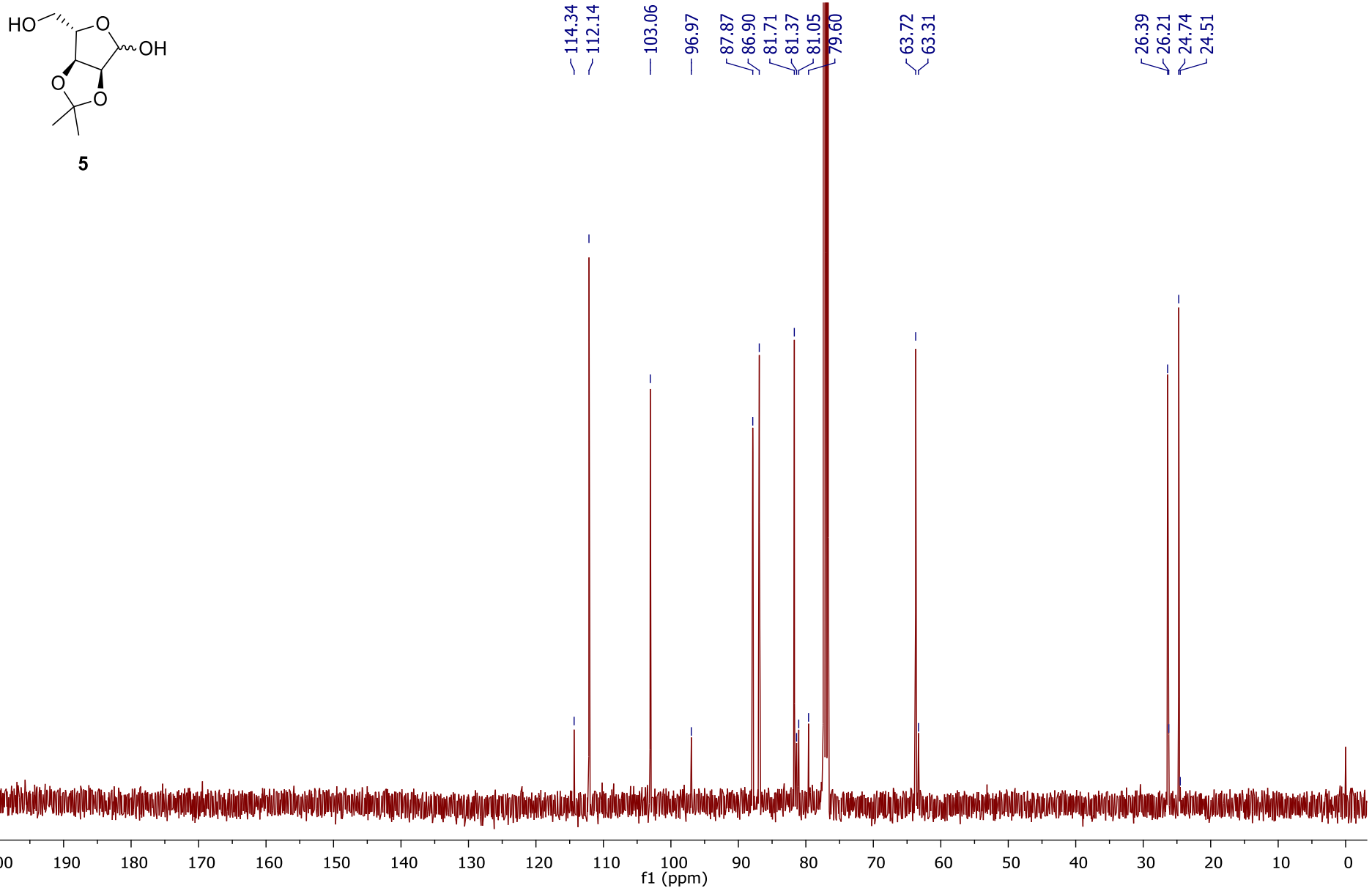
f1 (ppm)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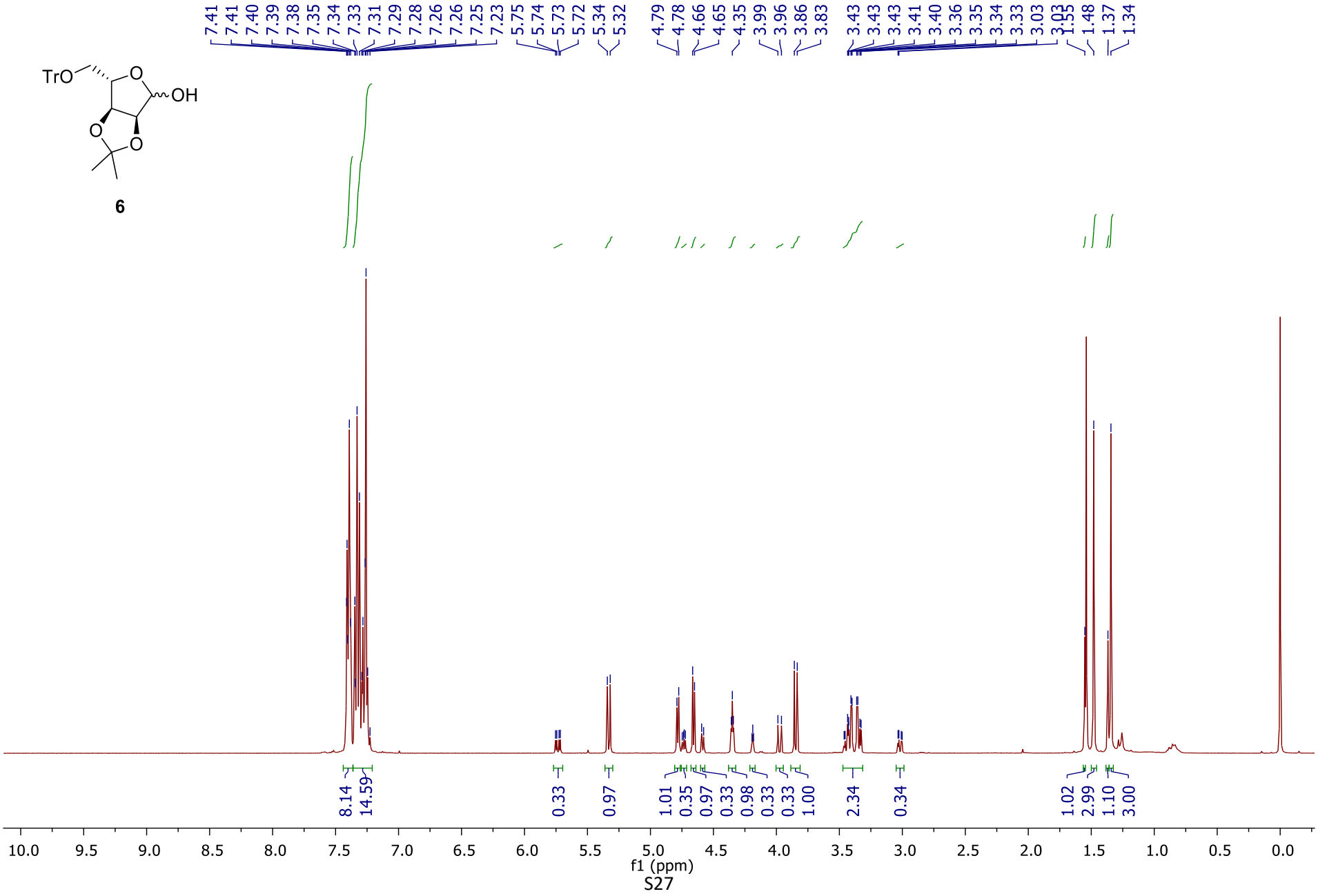
f1 (ppm)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3.33
3.03
1.55
1.48
1.37
1.34
TrO
O
OH
O
O
6
8.14
14.59
0.33
0.97
1.01
0.35
0.97
0.33
0.98
0.33
0.33
1.00
2.34
0.34
1.02
2.99
1.10
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
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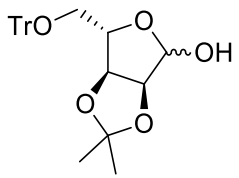
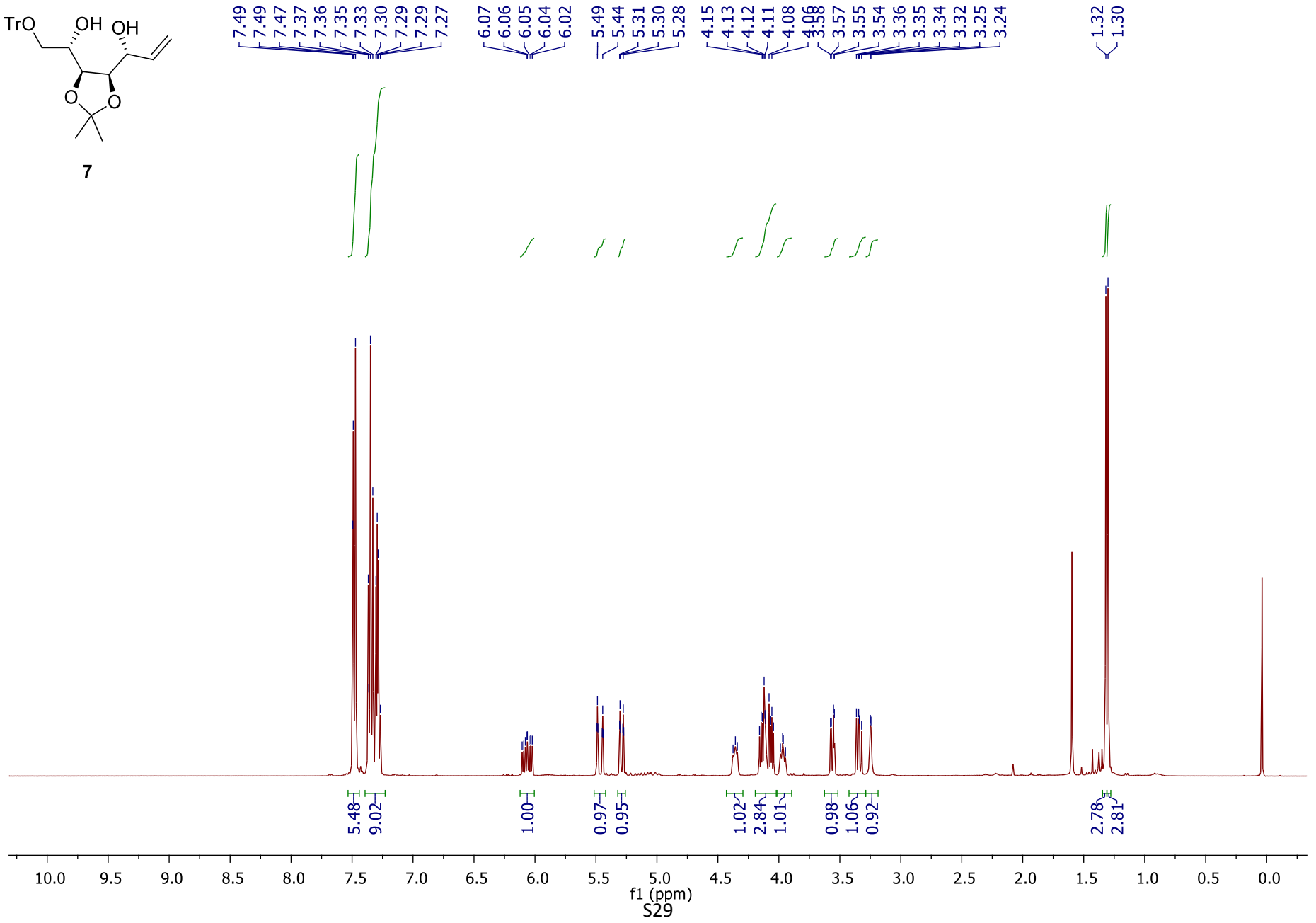
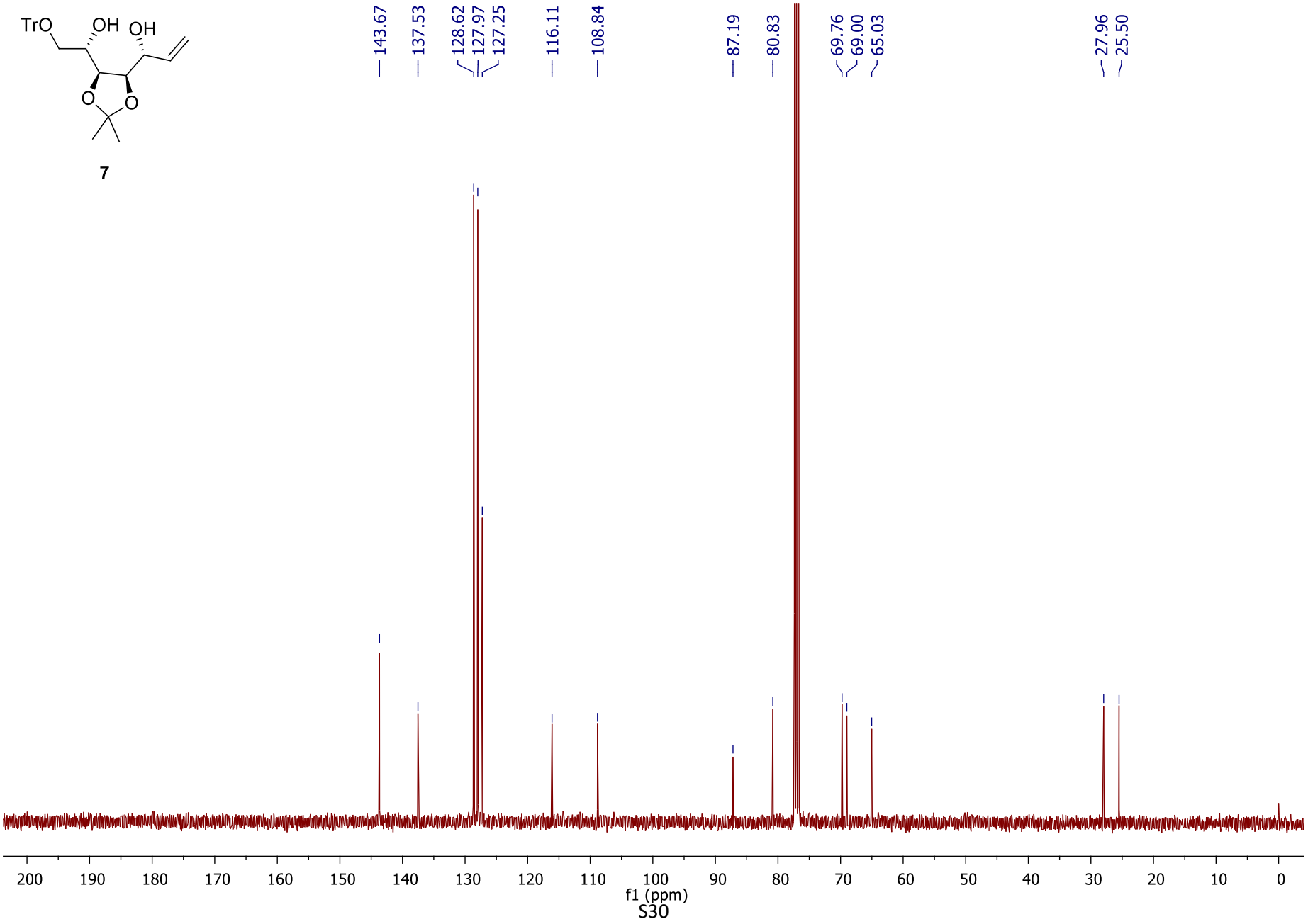
f1 (ppm)

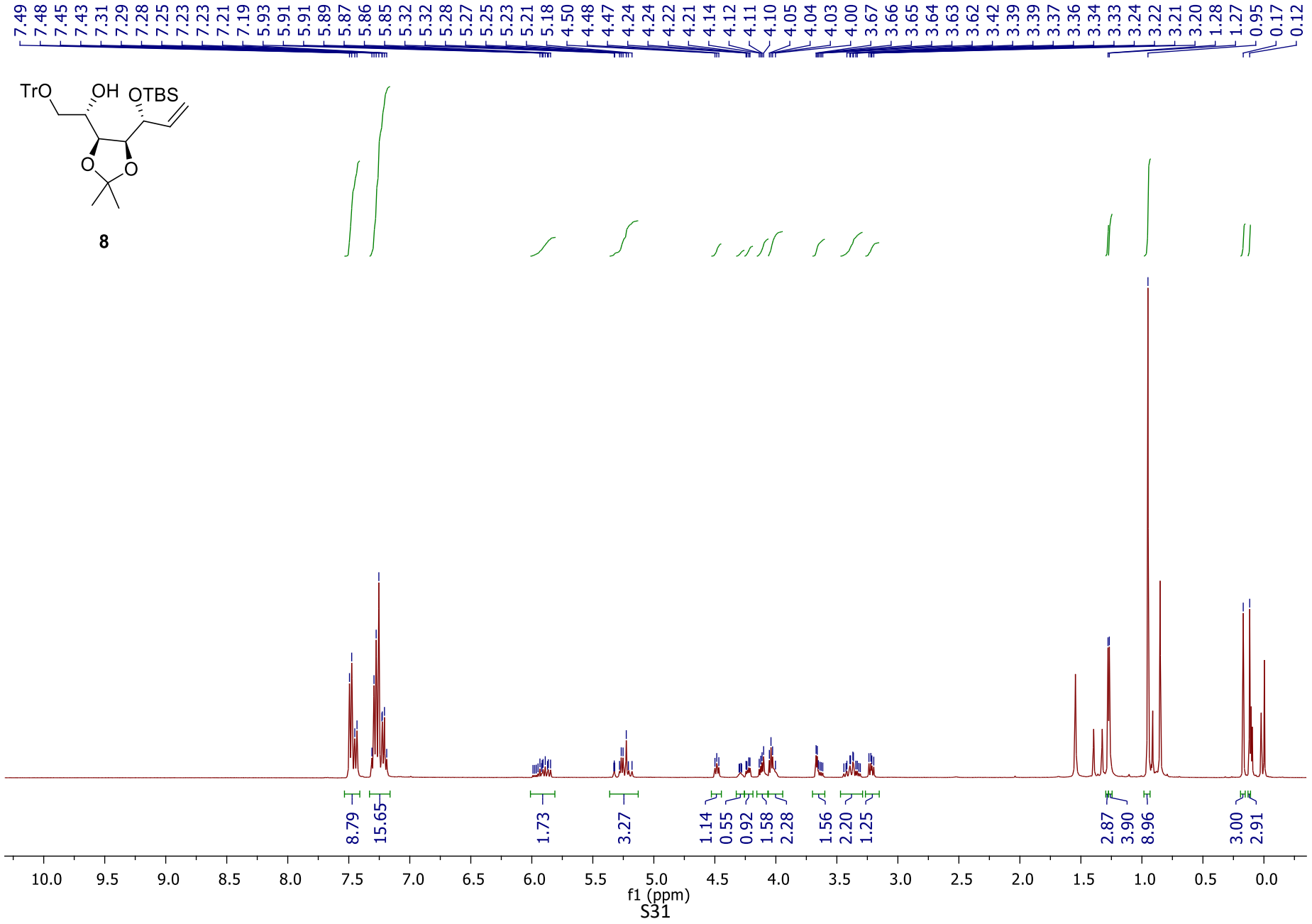

TrO
O
OH
O
O

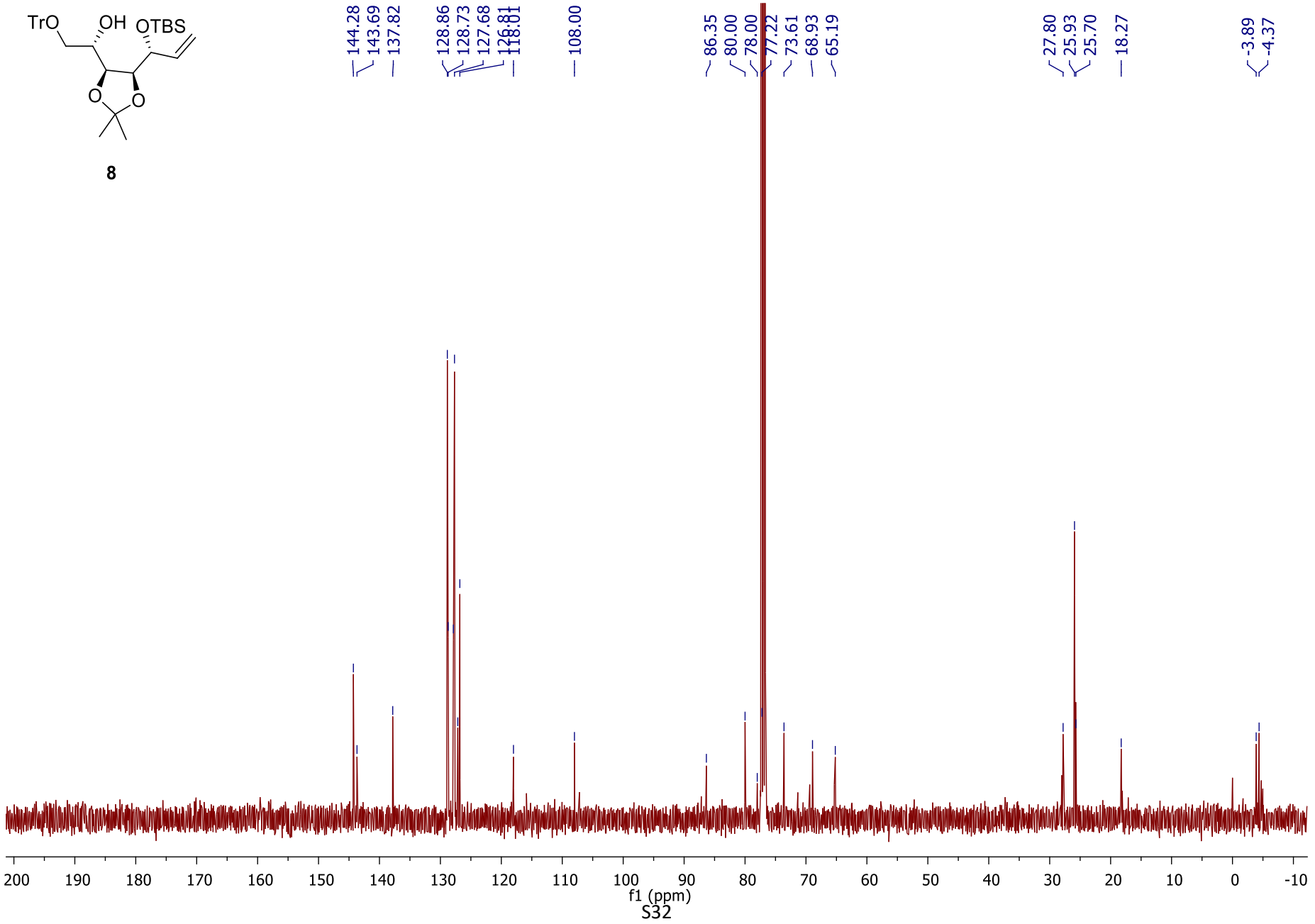
6

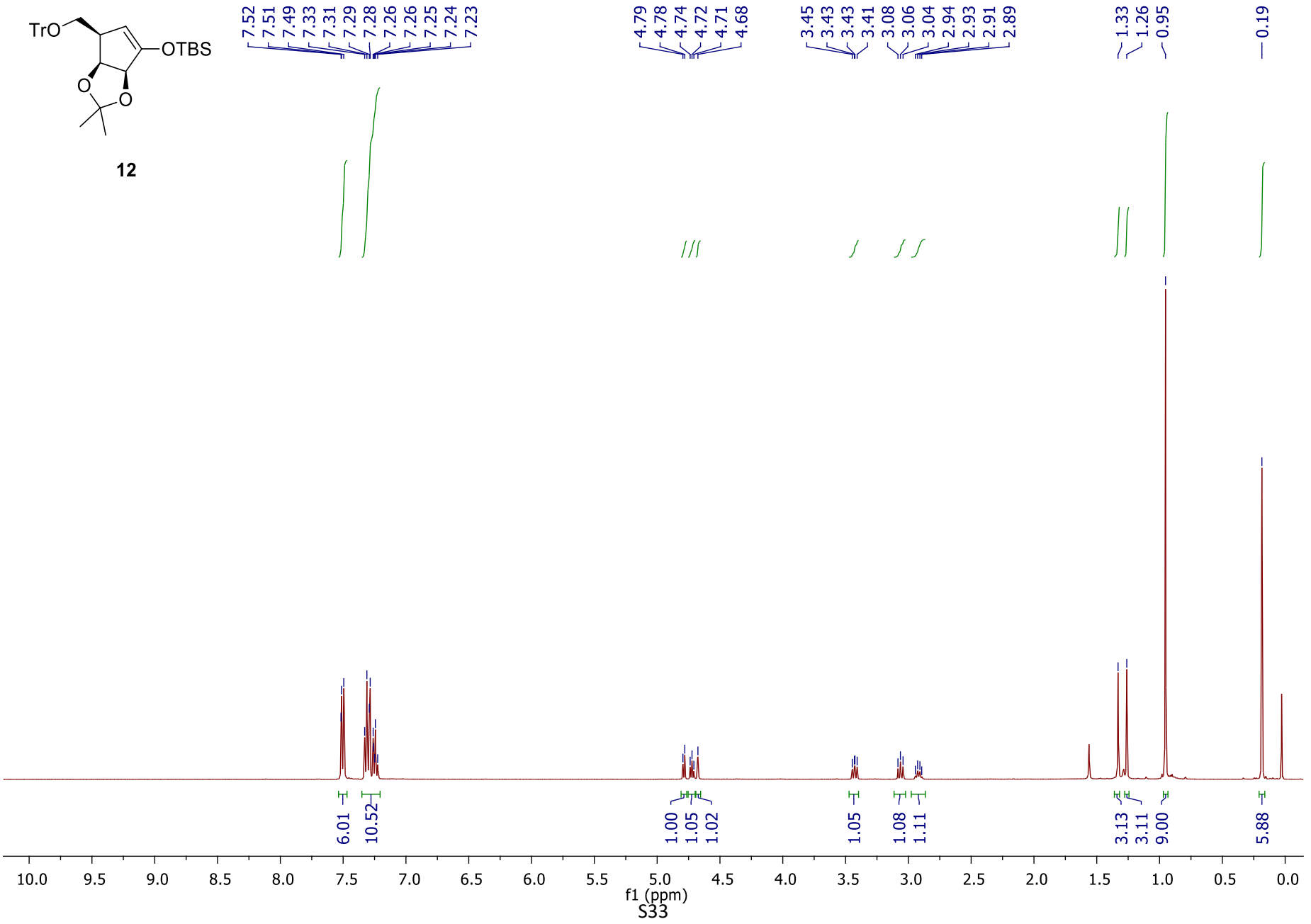
143.50
142.81
128.69
128.60
128.11
127.99
127.52
127.22
113.15
112.28
103.57
98.03
88.26
87.54
87.11
86.11
82.21
81.93
80.14
79.46
65.46
65.10
26.54
26.19
25.13
24.78
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

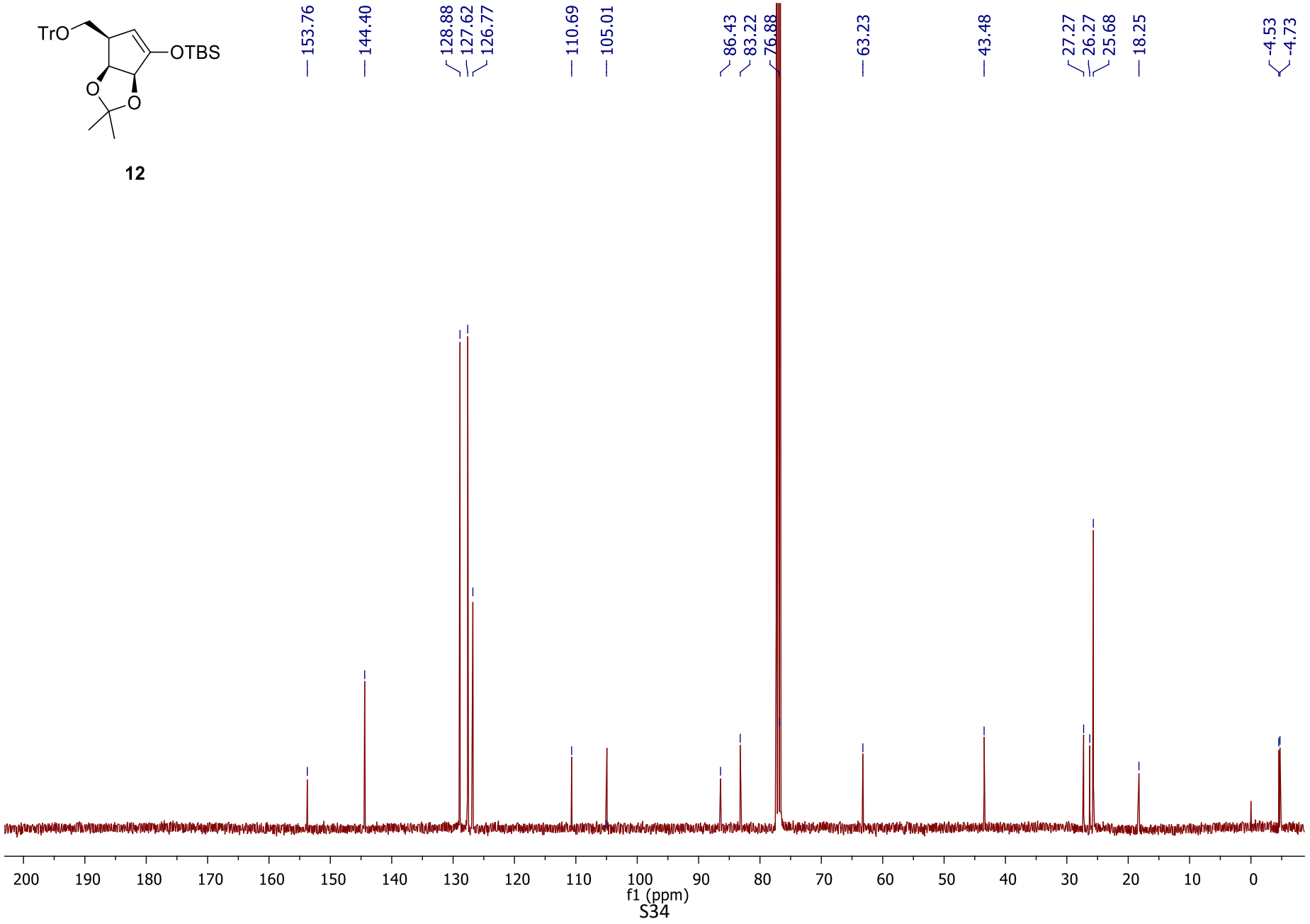

TrO
OH
OH
O
O
7
7.49
7.49
7.47
7.37
7.36
7.35
7.33
7.30
7.29
7.29
7.27
6.07
6.06
6.05
6.04
6.02
5.49
5.44
5.31
5.30
5.28
4.15
4.13
4.12
4.11
4.08
4.06
3.58
3.57
3.55
3.54
3.36
3.35
3.34
3.32
3.25
3.24
1.32
1.30
5.48
9.02
1.00
0.97
0.95
1.02
2.84
1.01
0.98
1.06
0.92
2.78
2.81
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

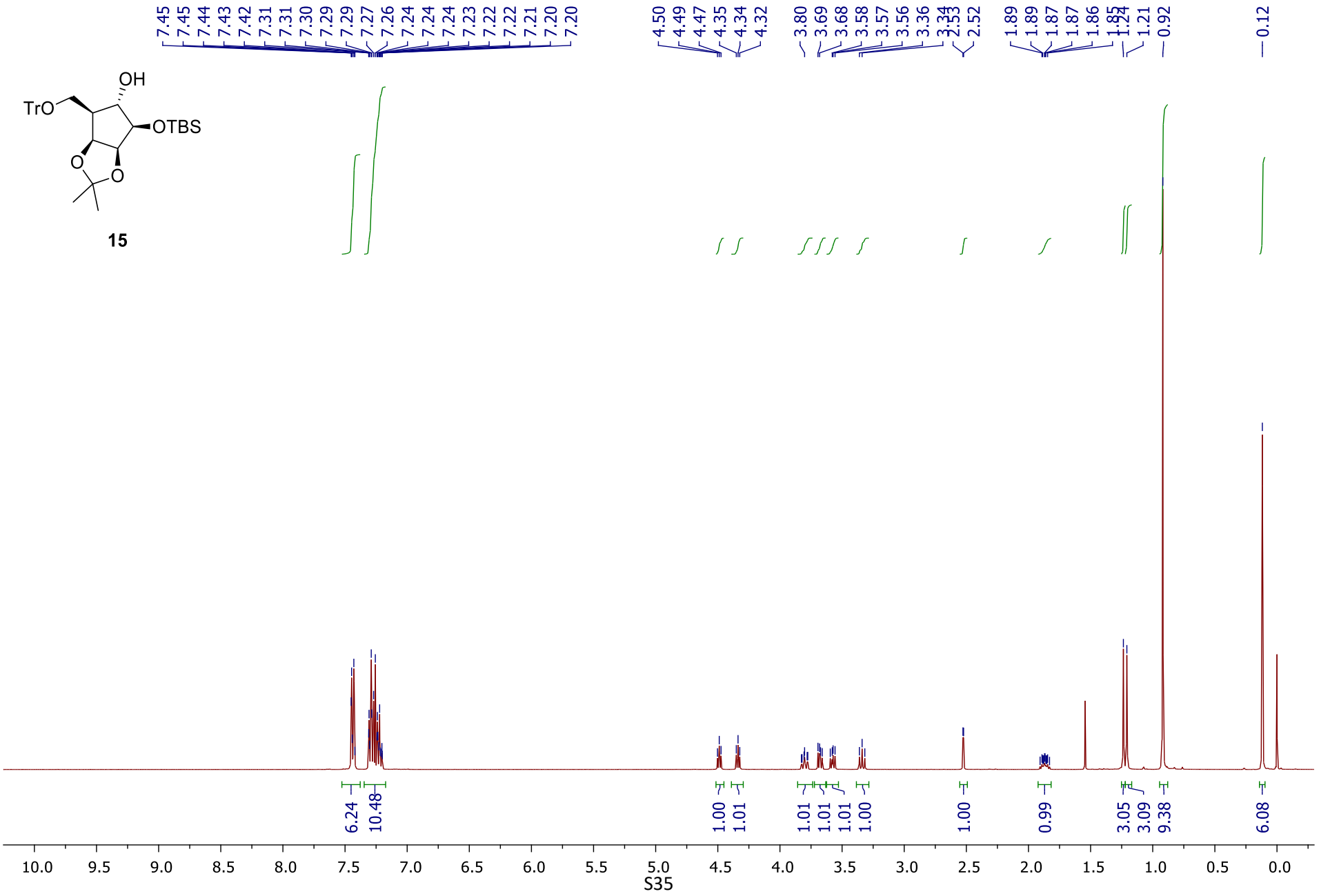

TrO
OH
OH
O
O
7
143.67
137.53
128.62
127.97
127.25
116.11
108.84
87.19
80.83
69.76
69.00
65.03
27.96
25.50
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

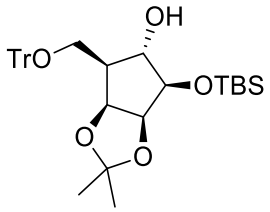

7.49 7.48 7.45 7.43 7.31 7.29 7.28 7.25 7.23 7.23 7.21 7.19 5.93 5.91 5.91 5.89 5.87 5.86 5.85 5.32 5.32 5.28 5.27 5.25 5.23 5.21 5.18 4.50 4.48 4.47 4.24 4.24 4.22 4.21 4.14 4.12 4.11 4.10 4.05 4.04 4.03 4.00 3.67 3.66 3.65 3.64 3.63 3.62 3.42 3.39 3.39 3.37 3.36 3.34 3.33 3.24 3.22 3.21 3.20 1.28 1.27 0.95 0.17 0.12
TrO
OH
OTBS
O
O
8
8.79 15.65 1.73 3.27 1.14 0.55 0.92 1.58 2.28 1.56 2.20 1.25 2.87 3.90 8.96 3.00 2.91
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


TrO
OH
OTBS
O
O
8
144.28
143.69
137.82
128.86
128.73
127.68
126.81
118.01
108.00
86.35
80.00
78.00
77.22
73.61
68.93
65.19
27.80
25.93
25.70
18.27
-3.89
-4.37
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


TrO
OTBS
O
O
12
7.52
7.51
7.49
7.33
7.31
7.29
7.28
7.26
7.26
7.25
7.24
7.23
4.79
4.78
4.74
4.72
4.71
4.68
3.45
3.43
3.43
3.41
3.08
3.06
3.04
2.94
2.93
2.91
2.89
1.33
1.26
0.95
0.19
6.01
10.52
1.00
1.05
1.02
1.05
1.08
1.11
3.13
3.11
9.00
5.88
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

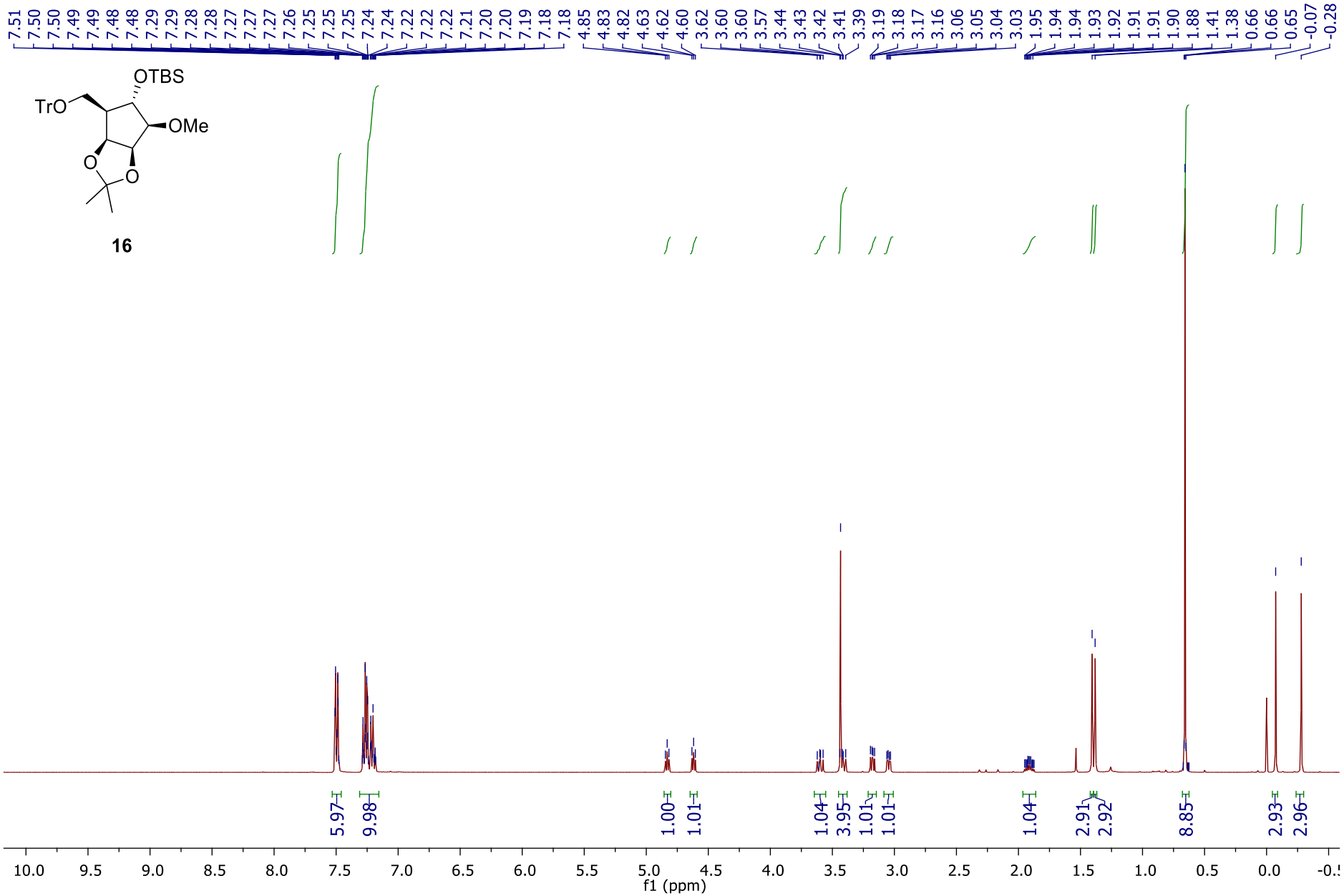

TrO
OTBS
O
O
12
153.76
144.40
128.88
127.62
126.77
110.69
105.01
86.43
83.22
76.88
63.23
43.48
27.27
26.27
25.68
18.25
-4.53
-4.73
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

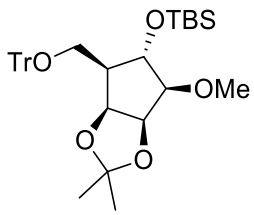

7.45 7.45 7.44 7.43 7.42 7.31 7.31 7.30 7.29 7.29 7.27 7.26 7.24 7.24 7.24 7.23 7.22 7.22 7.21 7.20 7.20
4.50 4.49 4.47 4.35 4.34 4.32
3.80 3.69 3.68 3.58 3.57 3.56 3.36 3.34 2.53 2.52
1.89 1.89 1.87 1.87 1.86 1.85 1.24 1.21 0.92
0.12
OH
TrO
OTBS
O
O
15
6.24 10.48 1.00 1.01 1.01 1.01 1.01 1.00 1.00 0.99 3.05 3.09 9.38 6.08
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


OH
TrO
OTBS
O
O

15

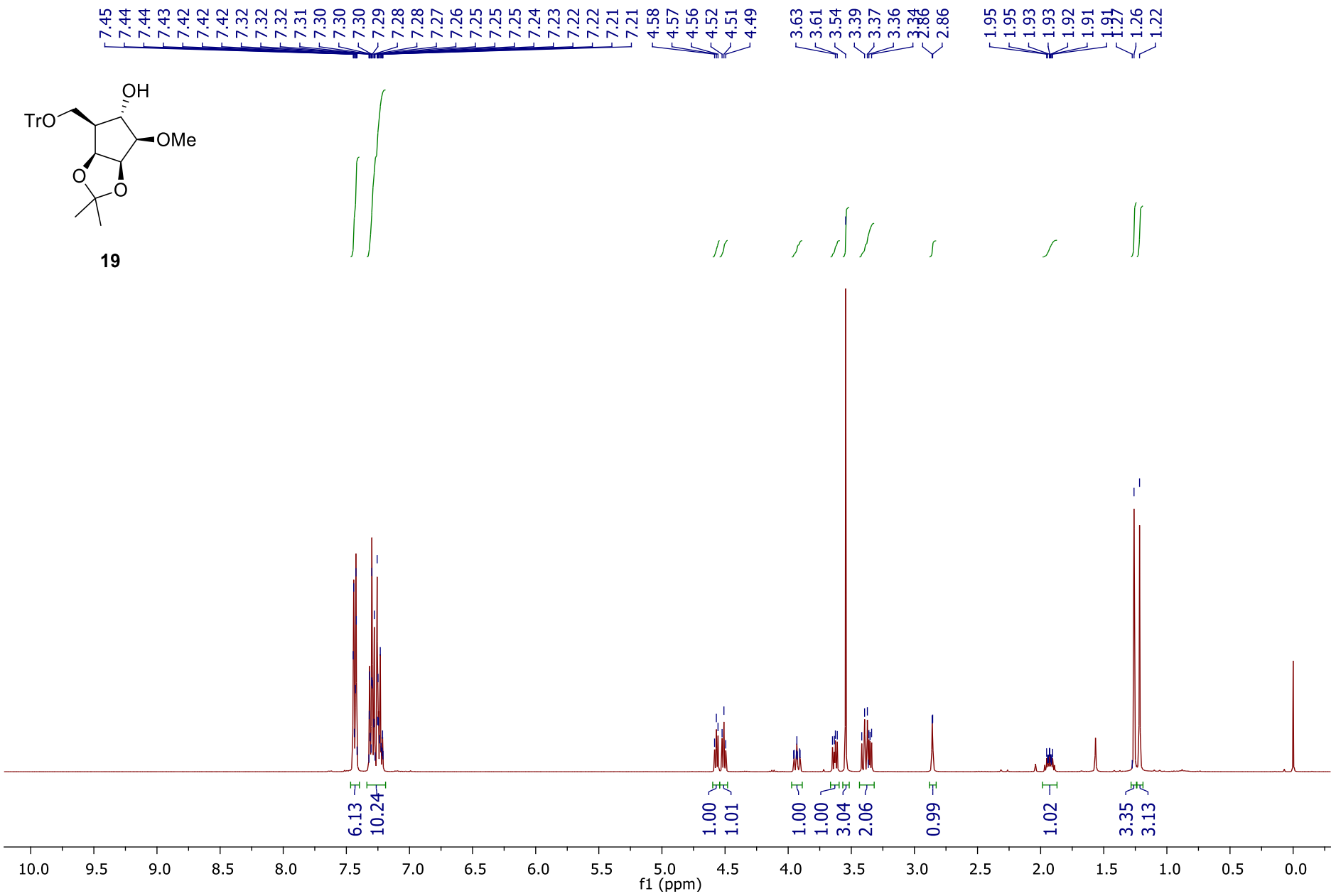
143.89
128.74
127.83
127.00
110.16
87.24
78.64
77.92
77.58
76.46
44.43
25.93
25.74
24.34
18.41
-4.49
-4.55
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

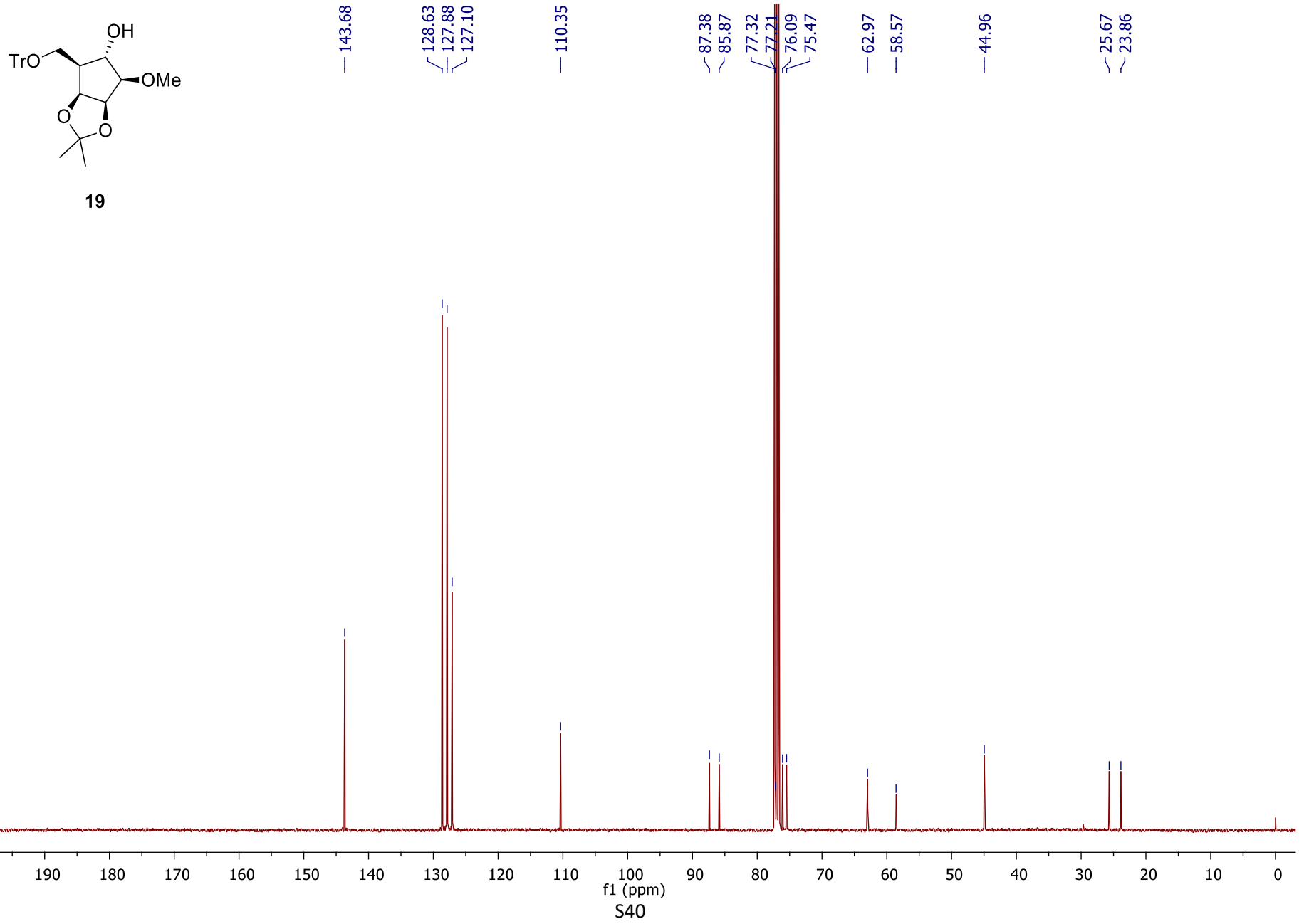

OTBS
TrO
OMe
O
O
16
7.51 7.50 7.50 7.49 7.49 7.48 7.48 7.29 7.29 7.28 7.28 7.27 7.27 7.27 7.26 7.25 7.25 7.25 7.24 7.24 7.22 7.22 7.22 7.21 7.20 7.20 7.19 7.18 7.18
4.85 4.83 4.82 4.63 4.62 4.60
3.62 3.60 3.60 3.57 3.44 3.43 3.42 3.41 3.39 3.19 3.18 3.17 3.16 3.06 3.05 3.04 3.03
1.95 1.94 1.94 1.93 1.92 1.91 1.91 1.90 1.88 1.41 1.38
0.66 0.66 0.65 -0.07 -0.28
5.97 9.98 1.00 1.01 1.04 3.95 1.01 1.01 1.04 2.91 2.92 8.85 2.93 2.96
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OTBS
TrO
OMe
O
O

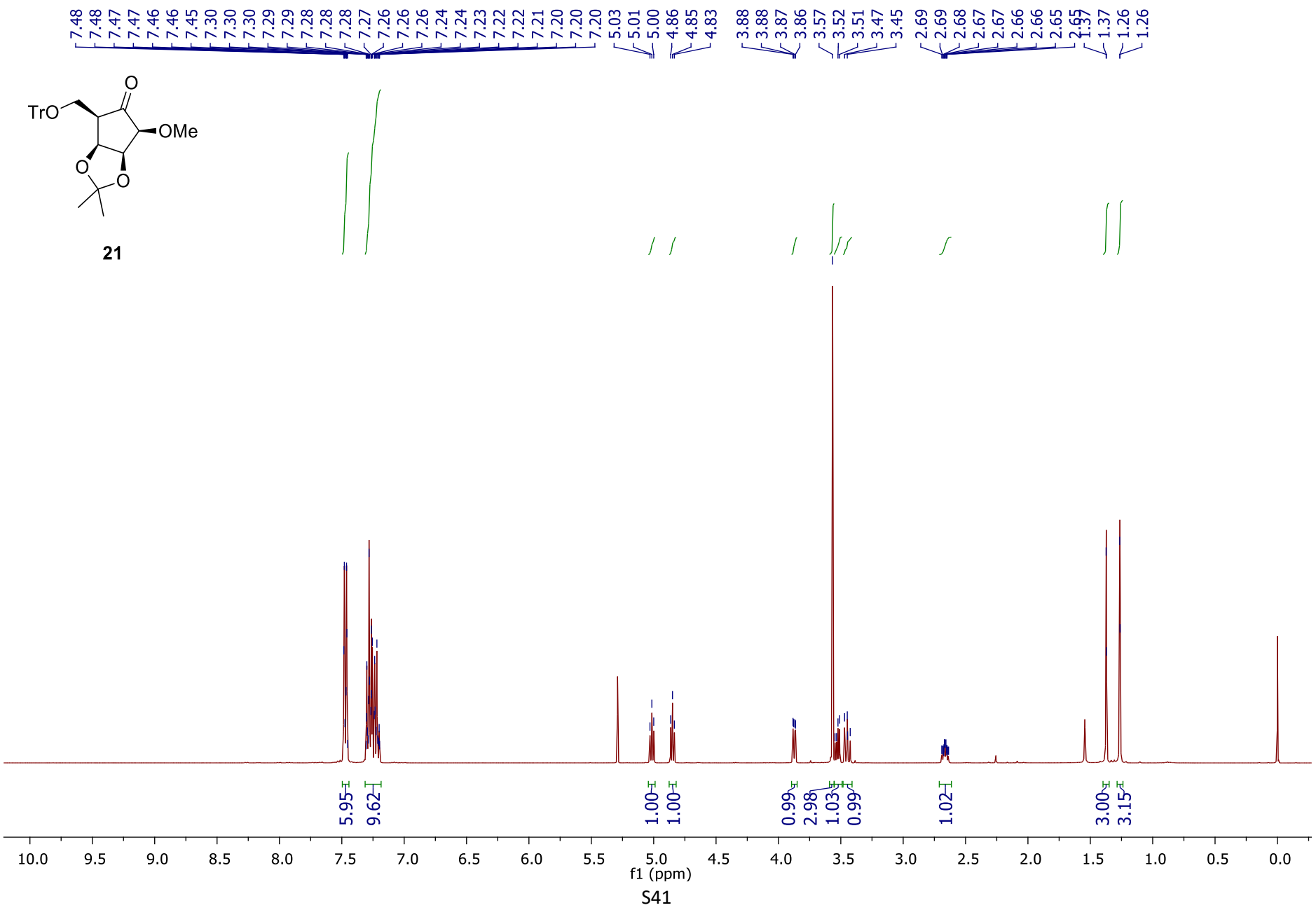
16

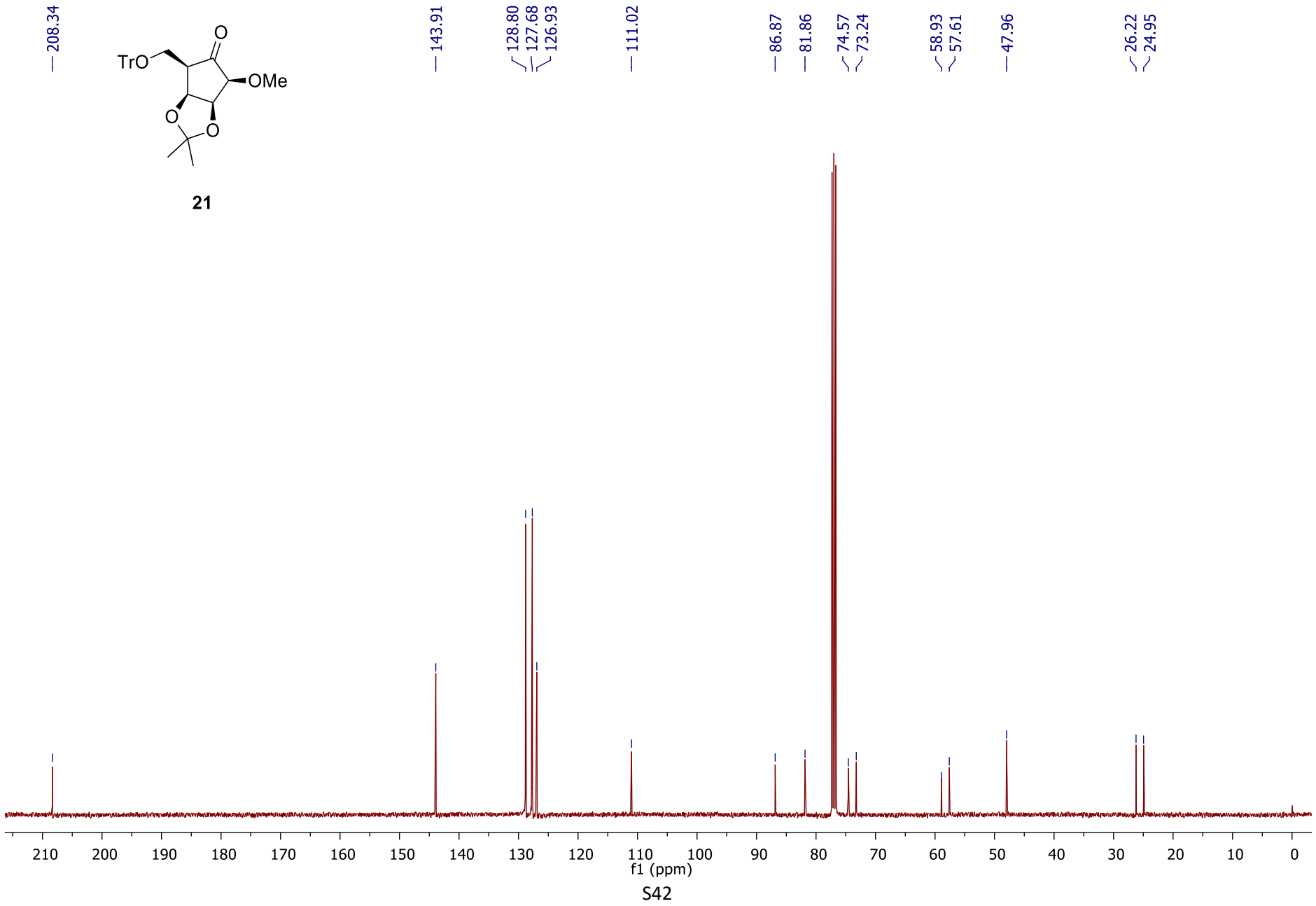
144.37
128.84
127.58
126.76
109.82
87.19
86.51
75.78
74.35
74.24
60.47
58.23
46.35
25.99
25.70
24.24
17.82
-4.44
-5.31
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

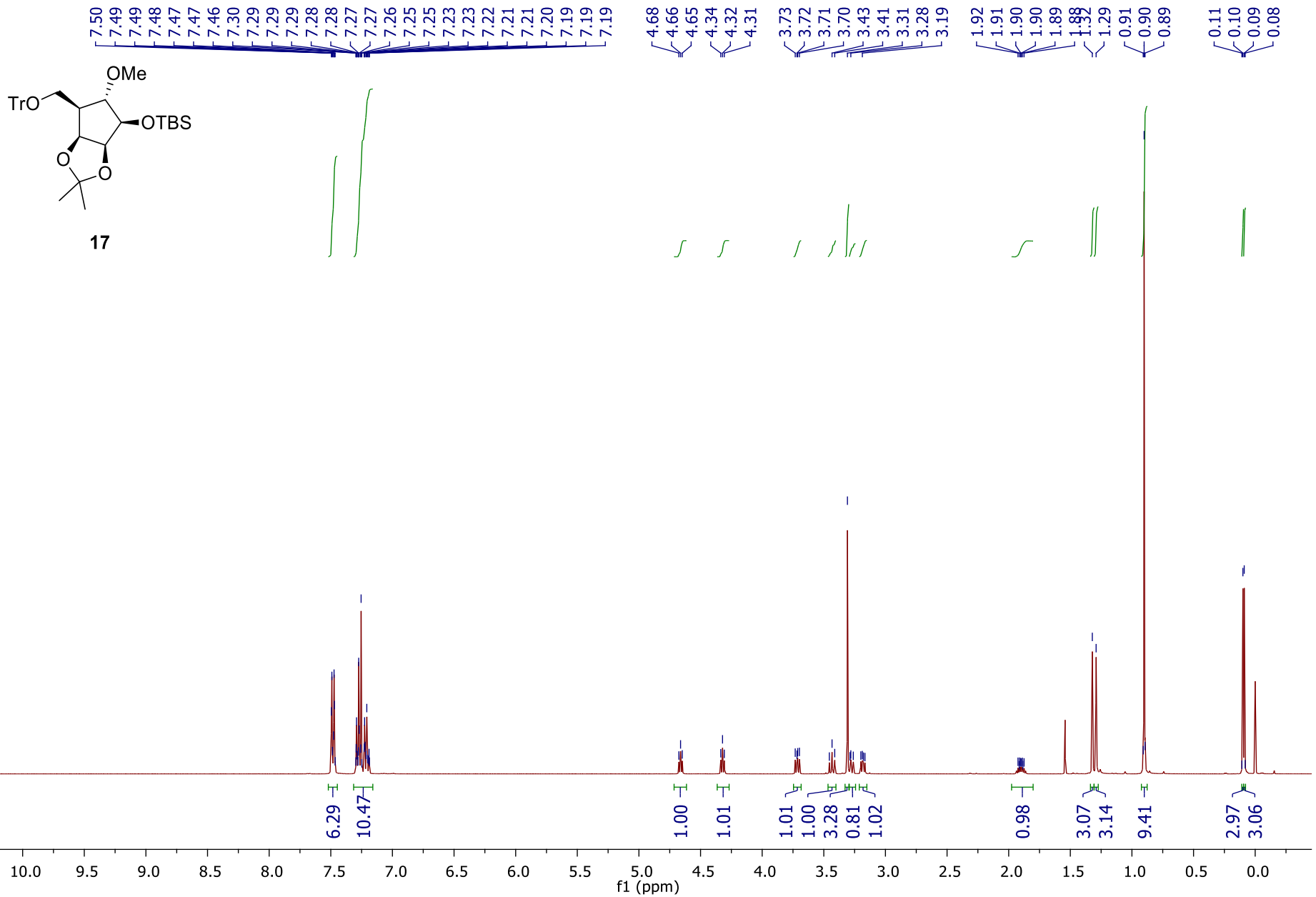

7.45 7.44 7.44 7.43 7.42 7.42 7.42 7.32 7.32 7.32 7.31 7.30 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.25 7.25 7.25 7.24 7.23 7.22 7.22 7.21 7.21
4.58 4.57 4.56 4.52 4.51 4.49
3.63 3.61 3.54 3.39 3.37 3.36 2.86
1.95 1.95 1.93 1.93 1.92 1.91 1.26 1.22
OH
TrO
OMe
O
O
19
6.13 10.24 1.00 1.01 1.00 1.00 3.04 2.06 0.99 1.02 3.35 3.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


TrO
OH
OMe
O
O
143.68
128.63
127.88
127.10
110.35
87.38
85.87
77.32
77.21
76.09
75.47
62.97
58.57
44.96
25.67
23.86
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

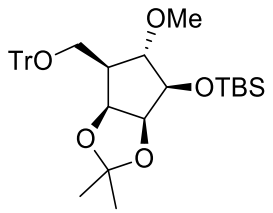
19


7.48 7.48 7.47 7.47 7.46 7.46 7.45 7.30 7.30 7.30 7.29 7.29 7.28 7.28 7.28 7.27 7.26 7.26 7.26 7.24 7.24 7.23 7.22 7.22 7.21 7.20 7.20 7.20
5.03 5.01 5.00 4.86 4.85 4.83
3.88 3.88 3.87 3.86 3.57 3.52 3.51 3.47 3.45
2.69 2.69 2.68 2.67 2.67 2.66 2.66 2.65 2.65
1.37 1.37 1.26 1.26
TrO
O
OMe
O
O
21
5.95 9.62 1.00 1.00 0.99 2.98 1.03 0.99 1.02 3.00 3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


208.34
143.91
128.80
127.68
126.93
111.02
86.87
81.86
74.57
73.24
58.93
57.61
47.96
26.22
24.95
TrO
OMe
O
O
O
21
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.50 7.49 7.49 7.48 7.47 7.47 7.46 7.30 7.29 7.29 7.29 7.28 7.28 7.27 7.27 7.26 7.25 7.25 7.23 7.23 7.22 7.21 7.21 7.20 7.19 7.19 7.19
4.68 4.66 4.65 4.34 4.32 4.31
3.73 3.72 3.71 3.70 3.43 3.41 3.31 3.28 3.19
1.92 1.91 1.90 1.90 1.89 1.32 1.29 0.91 0.90 0.89
0.11 0.10 0.09 0.08
OMe
TrO
OTBS
O
O
6.29 10.47 1.00 1.01 1.01 1.00 3.28 0.81 1.02 0.98 3.07 3.14 9.41 2.97 3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

17


OMe
TrO
OTBS
O
O

17

144.35
128.88
127.56
126.73
109.78
86.47
85.55
78.60
76.93
76.41
60.97
59.27
44.05
25.92
25.84
24.59
18.25
-4.43
-4.82
200
190
180
170
160
150
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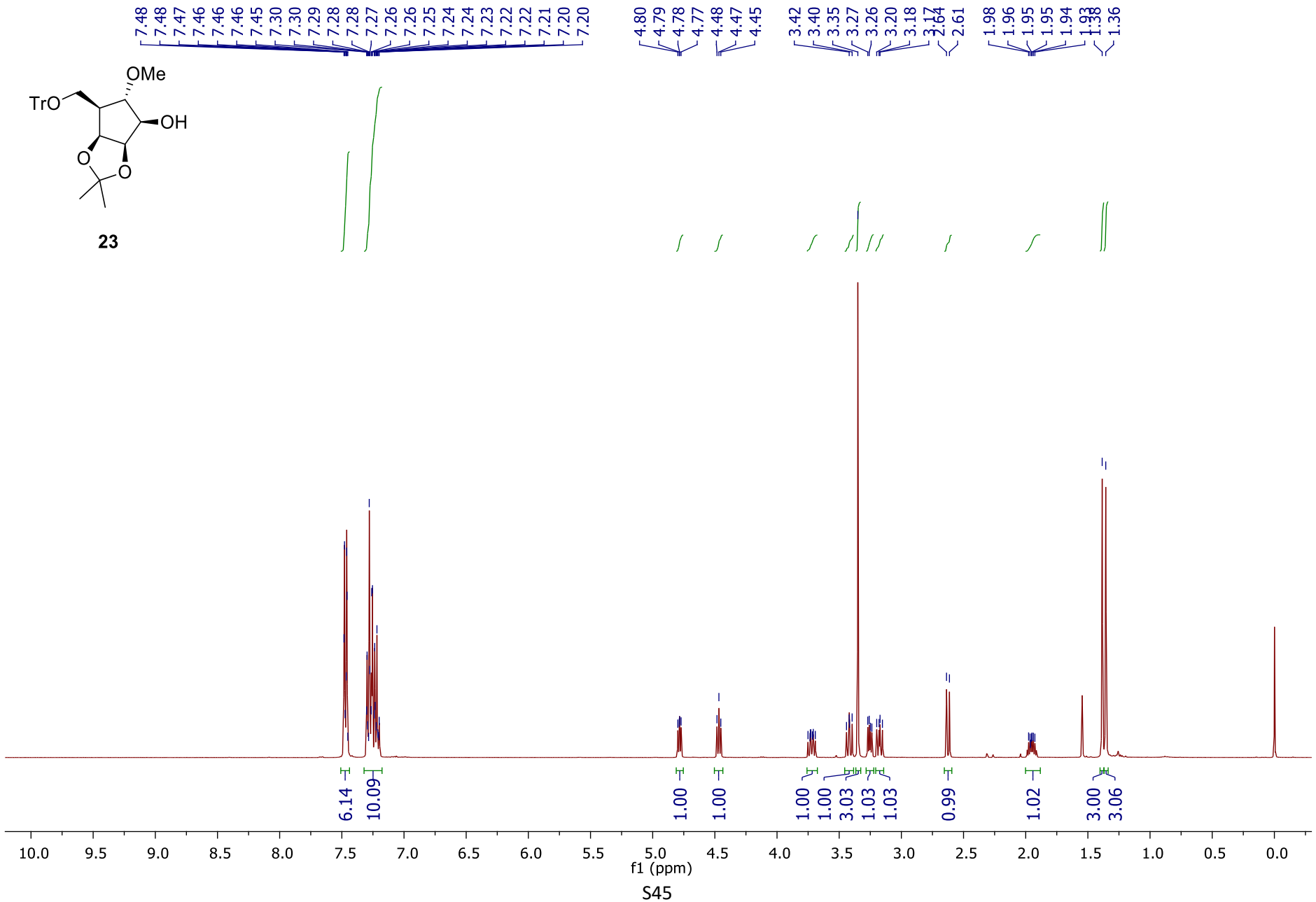
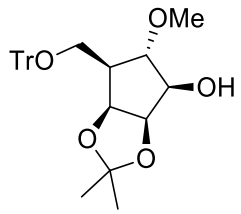
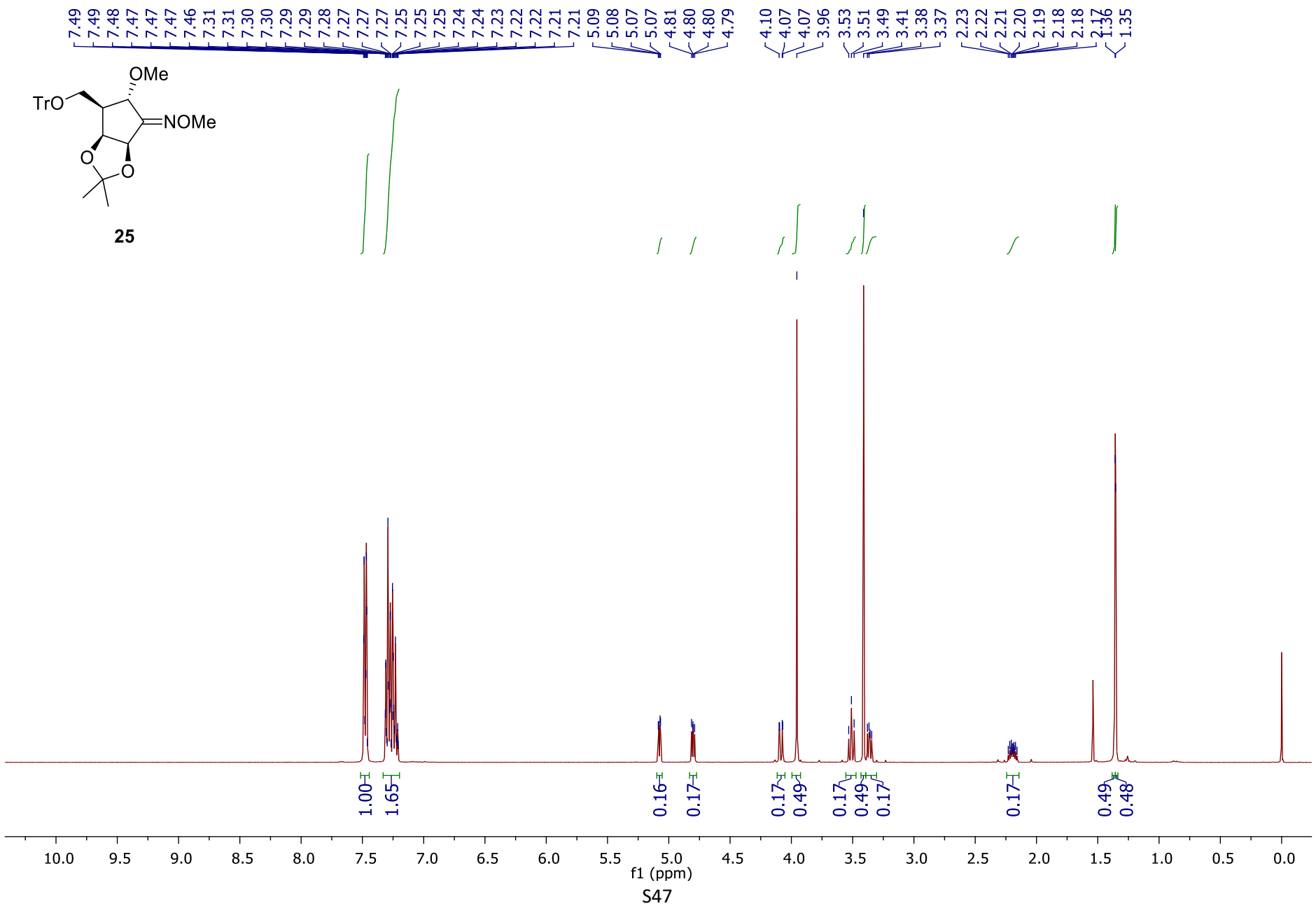
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

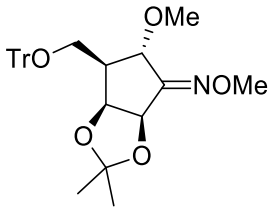

7.48 7.48 7.47 7.46 7.46 7.46 7.45 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.26 7.25 7.24 7.24 7.23 7.22 7.22 7.21 7.20 7.20
4.80 4.79 4.78 4.77 4.48 4.47 4.45
3.42 3.40 3.35 3.27 3.26 3.20 3.18 3.17 2.64 2.61
1.98 1.96 1.95 1.95 1.94 1.93 1.38 1.36
OMe
TrO
OH
O
O
23
6.14 10.09 1.00 1.00 1.00 1.00 3.03 1.03 1.03 0.99 1.02 3.00 3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OMe
TrO
OH
O
O

23

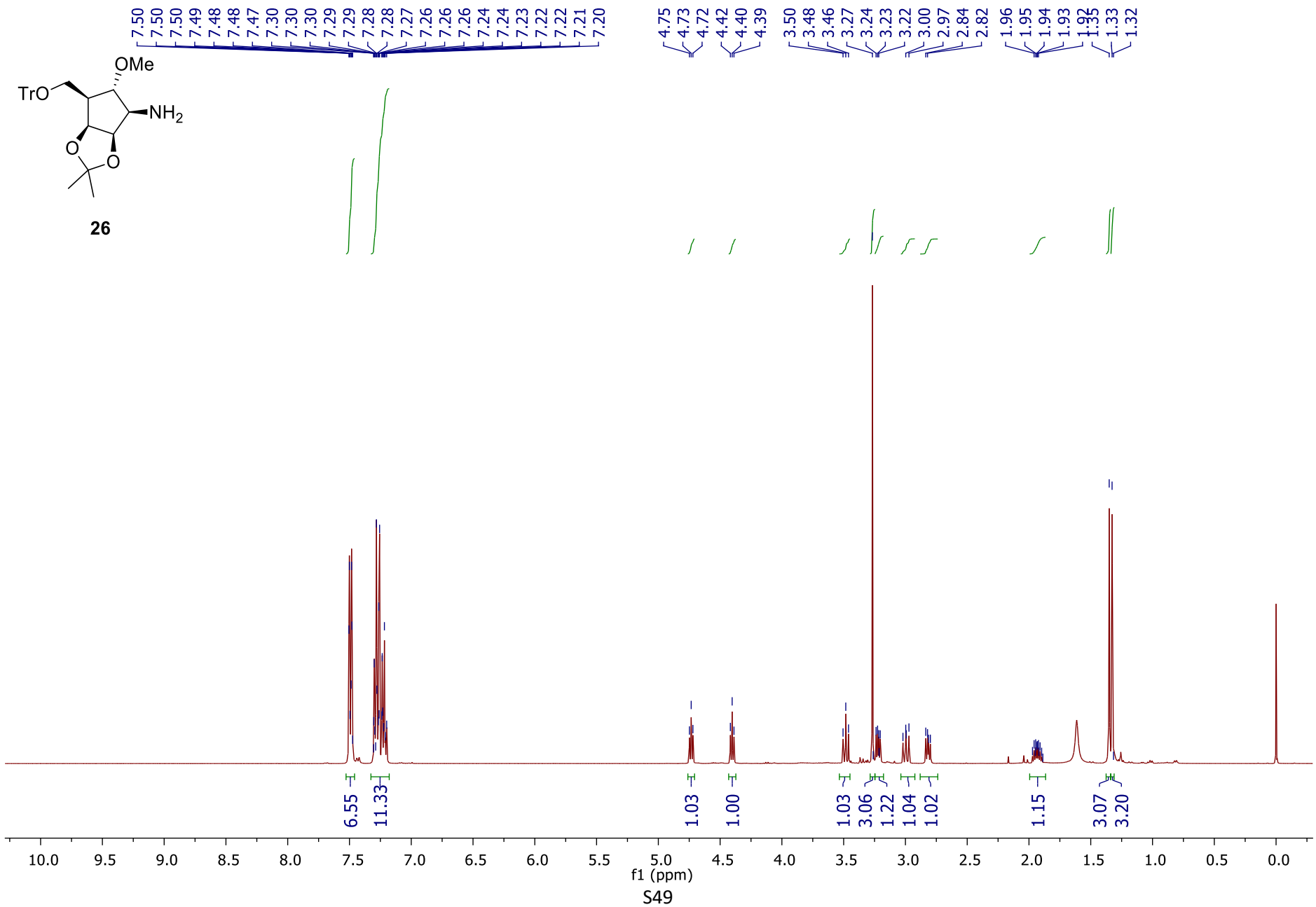
144.23
128.84
127.58
126.79
110.23
86.51
85.96
77.18
77.00
75.66
60.65
58.44
44.13
25.86
24.27
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

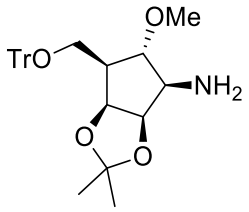

7.49 7.49 7.48 7.47 7.47 7.47 7.46 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.27 7.27 7.25 7.25 7.25 7.24 7.24 7.23 7.22 7.22 7.21 7.21
5.09 5.08 5.07 5.07
4.81 4.80 4.80 4.79
4.10 4.07 4.07 3.96
3.53 3.51 3.49 3.41 3.38 3.37
2.23 2.22 2.21 2.20 2.19 2.18 2.18 2.17
1.36 1.35
OMe
TrO
NOMe
O
O
25
1.00 1.65 0.16 0.17 0.17 0.49 0.17 0.49 0.17 0.17 0.49 0.48
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OMe
TrO
NOMe
O
O

25

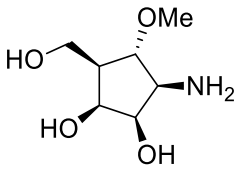
159.74
144.10
128.80
127.68
126.91
111.56
86.73
79.77
76.44
72.40
62.68
61.15
58.79
45.43
26.65
24.79
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.50 7.50 7.50 7.49 7.48 7.48 7.47 7.30 7.30 7.30 7.29 7.29 7.28 7.28 7.27 7.26 7.26 7.26 7.24 7.24 7.23 7.22 7.22 7.21 7.20
4.75 4.73 4.72 4.42 4.40 4.39 3.50 3.48 3.46 3.27 3.24 3.23 3.22 3.00 2.97 2.84 2.82 1.96 1.95 1.94 1.93 1.92 1.35 1.33 1.32
OMe
TrO
NH2
O
O
26
6.55 11.33 1.03 1.00 1.03 3.06 1.22 1.04 1.02 1.15 3.07 3.20
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OMe
TrO
NH2
O
O

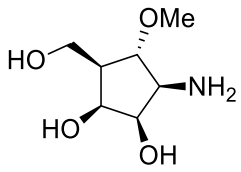
26

144.29
128.88
127.60
126.81
109.16
86.83
86.60
77.47
76.53
60.89
59.44
59.09
46.46
25.86
24.01
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OMe
HO
NH2
HO
OH

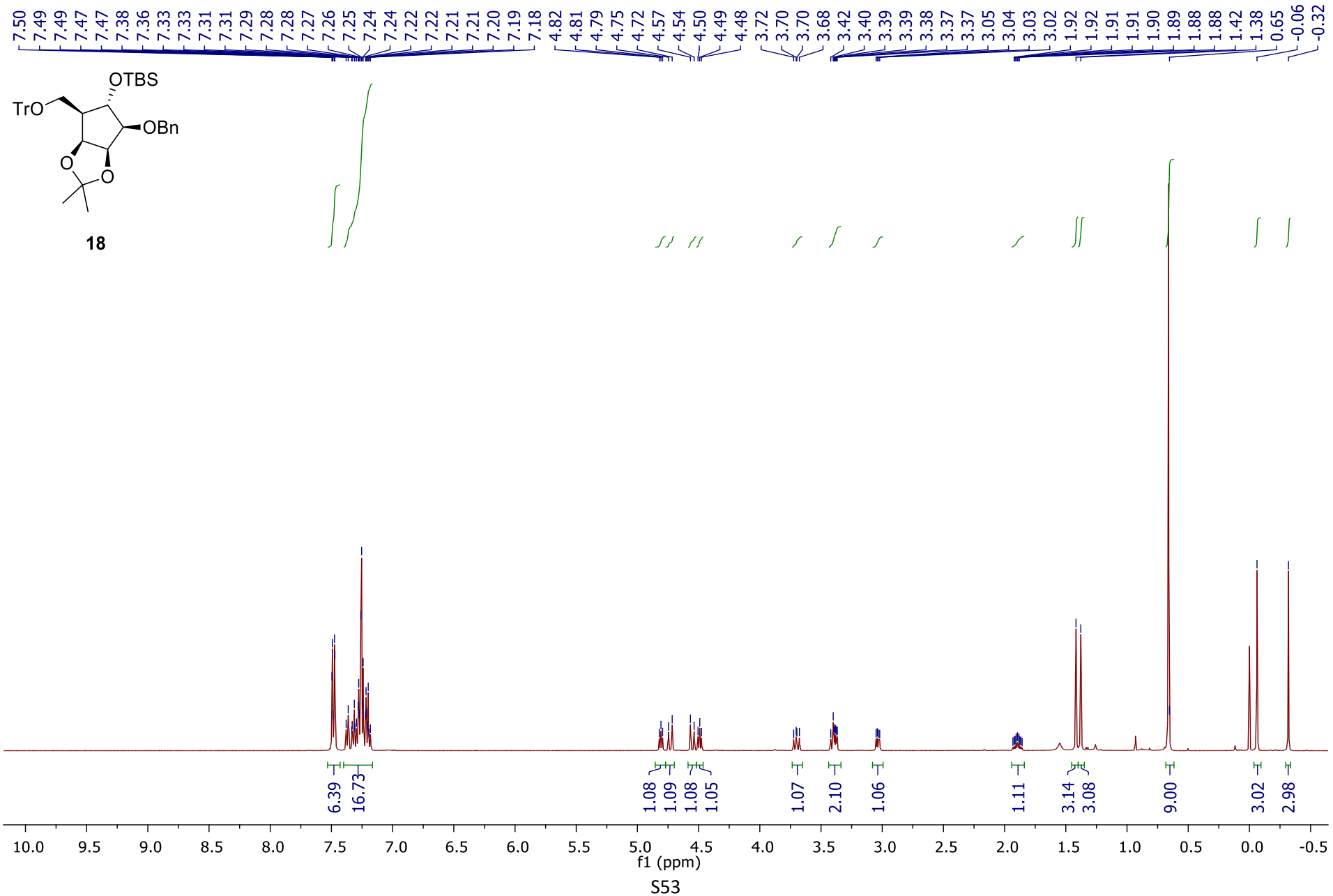
3b

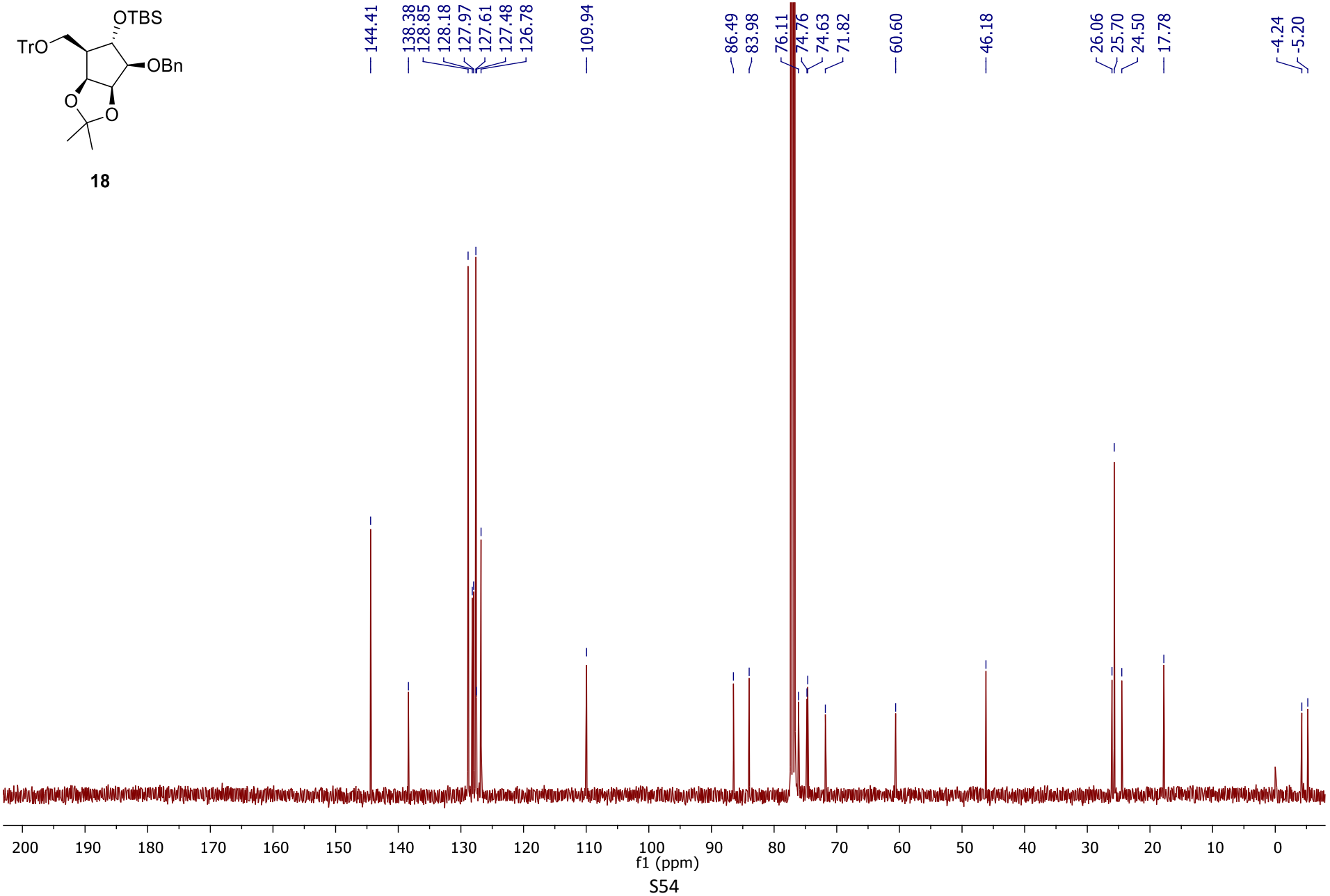
4.22
4.21
4.21
4.20
3.98
3.97
3.97
3.96
3.86
3.84
3.83
3.82
3.79
3.78
3.76
3.75
3.54
3.52
3.52
3.51
3.40
3.40
3.15
3.14
3.13
2.05
2.04
2.04
2.03
2.02
0.99
1.02
1.08
1.12
1.02
3.02
0.96
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

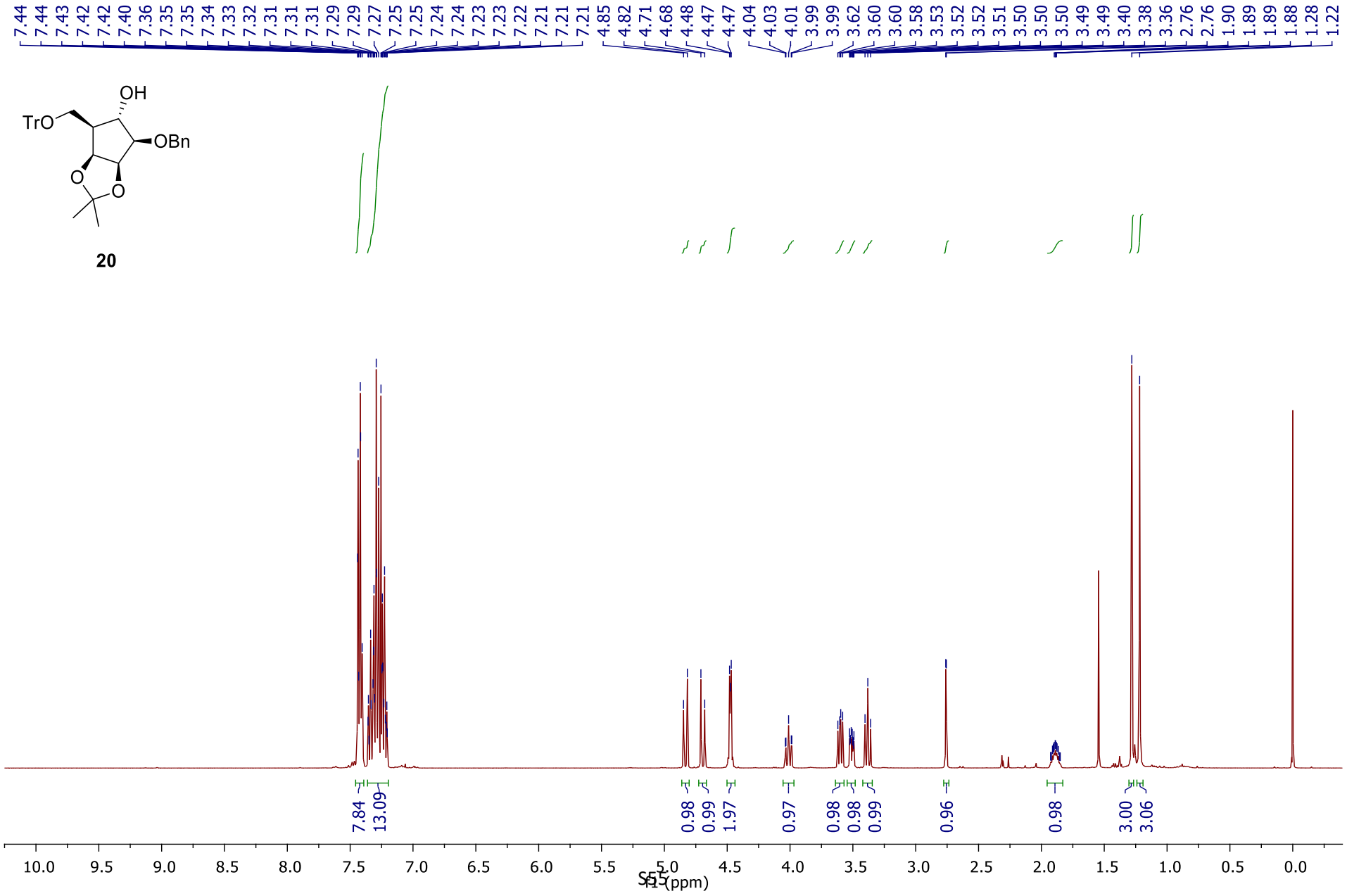

OMe
HO
NH2
HO
OH

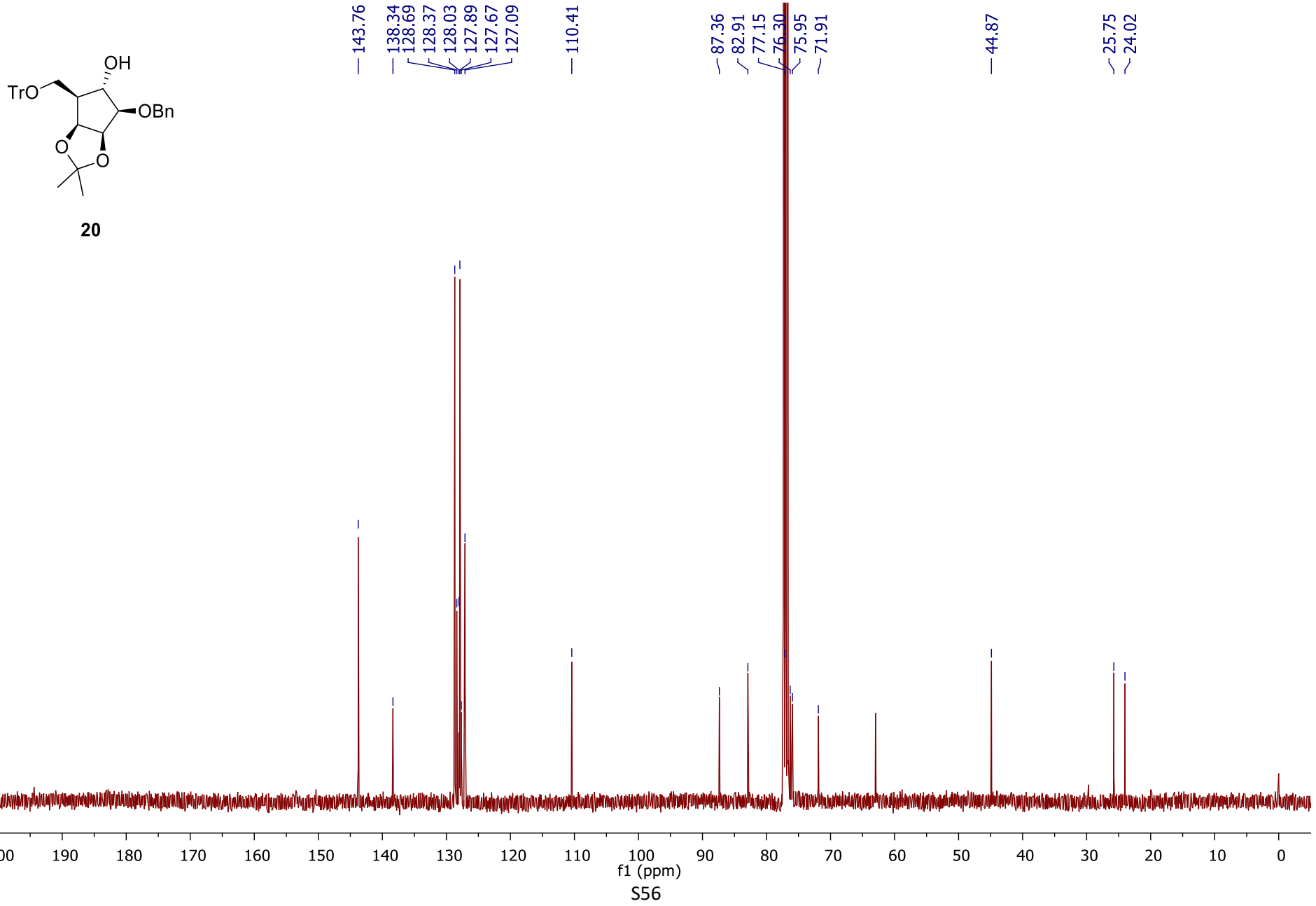
3b

89.47
74.21
73.65
61.25
58.85
58.26
50.30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

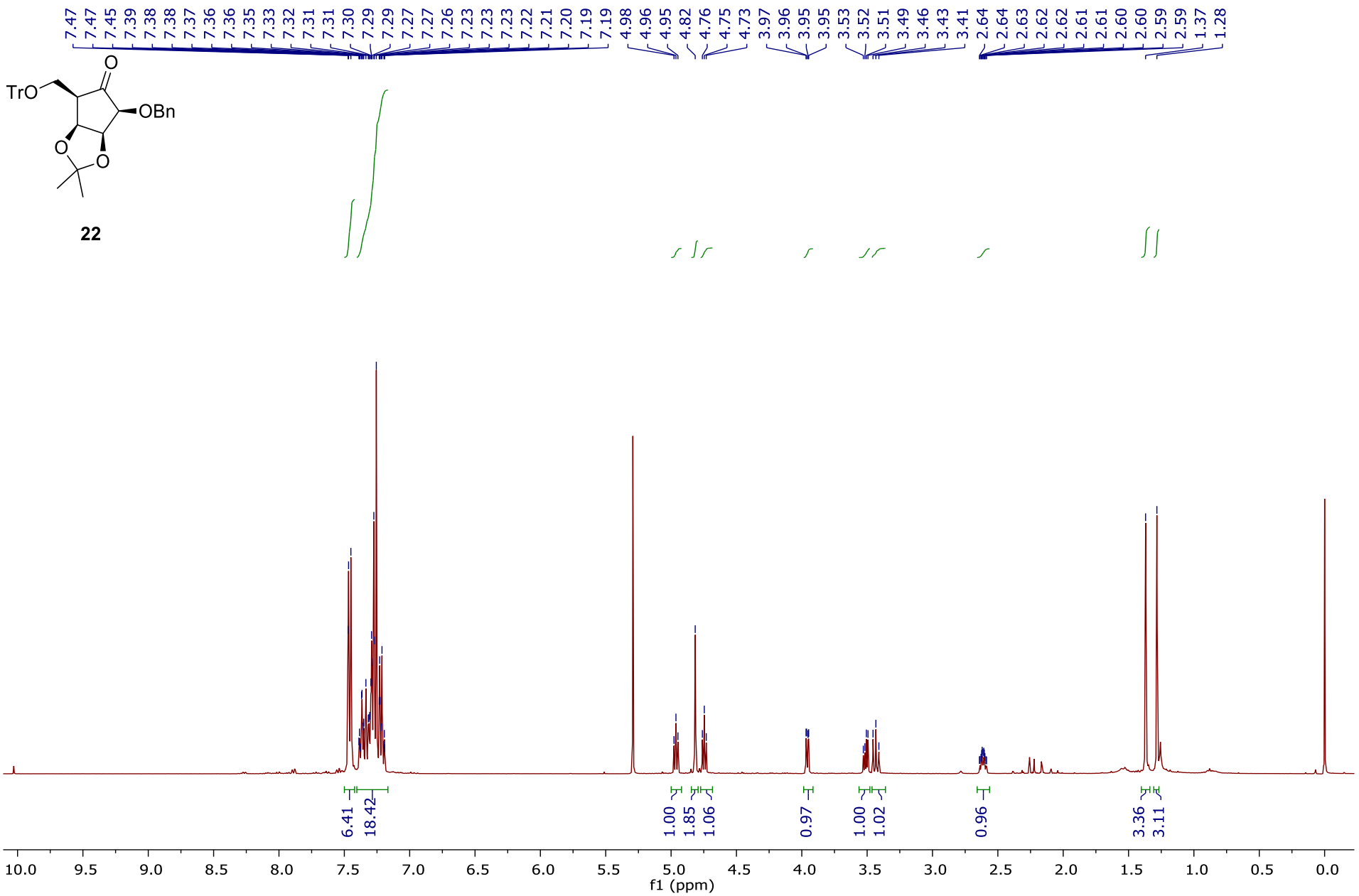

7.50 7.49 7.49 7.47 7.47 7.38 7.36 7.33 7.33 7.31 7.31 7.29 7.28 7.28 7.27 7.26 7.25 7.24 7.24 7.22 7.22 7.21 7.21 7.20 7.19 7.18
4.82 4.81 4.79 4.75 4.72 4.57 4.54 4.50 4.49 4.48
3.72 3.70 3.70 3.68 3.42 3.40 3.39 3.39 3.38 3.37 3.37 3.05 3.04 3.03 3.02
1.92 1.92 1.91 1.91 1.90 1.89 1.88 1.88 1.42 1.38 0.65 -0.06 -0.32
OTBS
TrO
OBn
O
O
18
6.39 16.73 1.08 1.09 1.08 1.05 1.07 2.10 1.06 1.11 3.14 3.08 9.00 3.02 2.98
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
f1 (ppm)

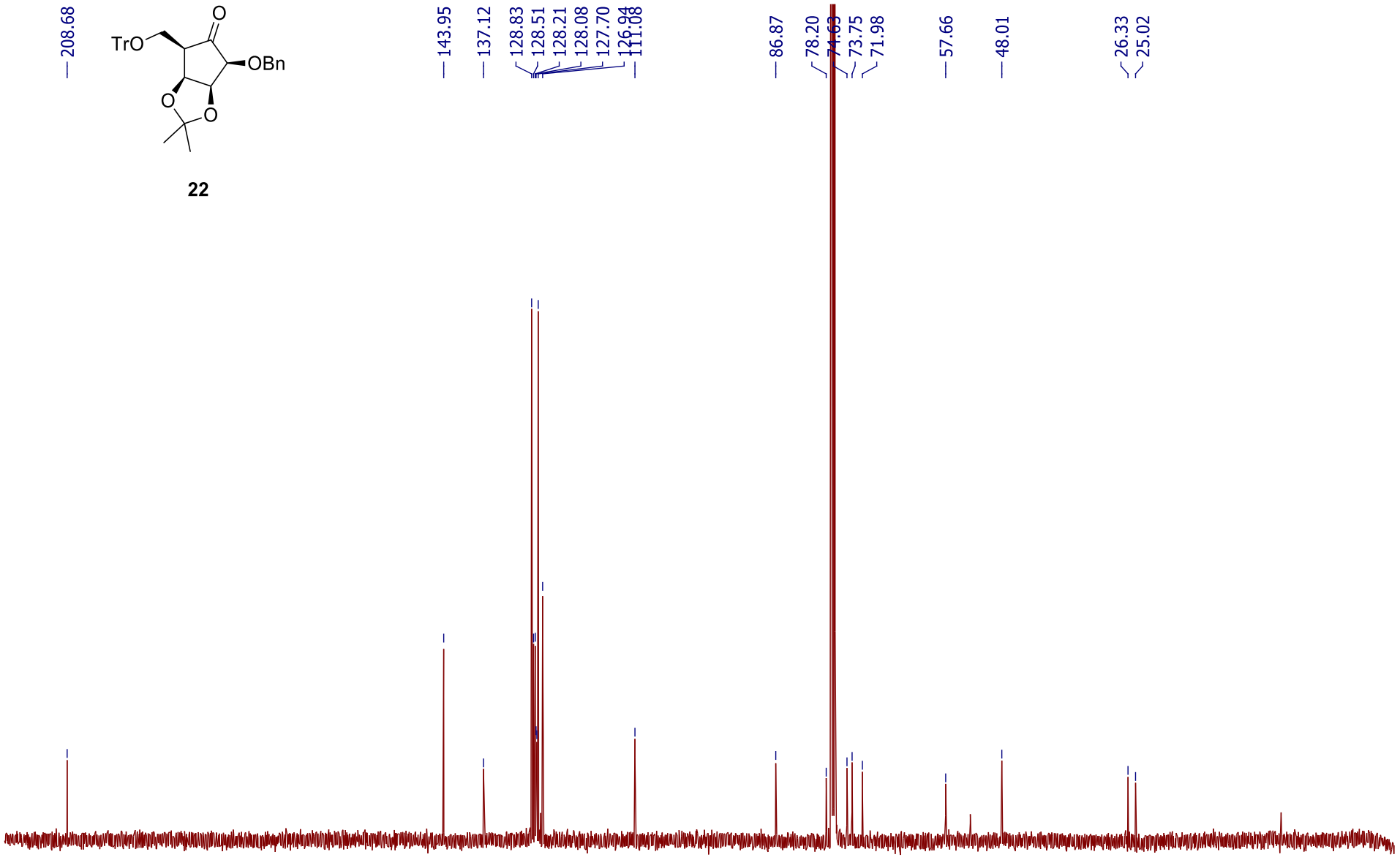

OTBS
TrO
OBn
O
O
18
144.41
138.38
128.85
128.18
127.97
127.61
127.48
126.78
109.94
86.49
83.98
76.11
74.76
74.63
71.82
60.60
46.18
26.06
25.70
24.50
17.78
-4.24
-5.20
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

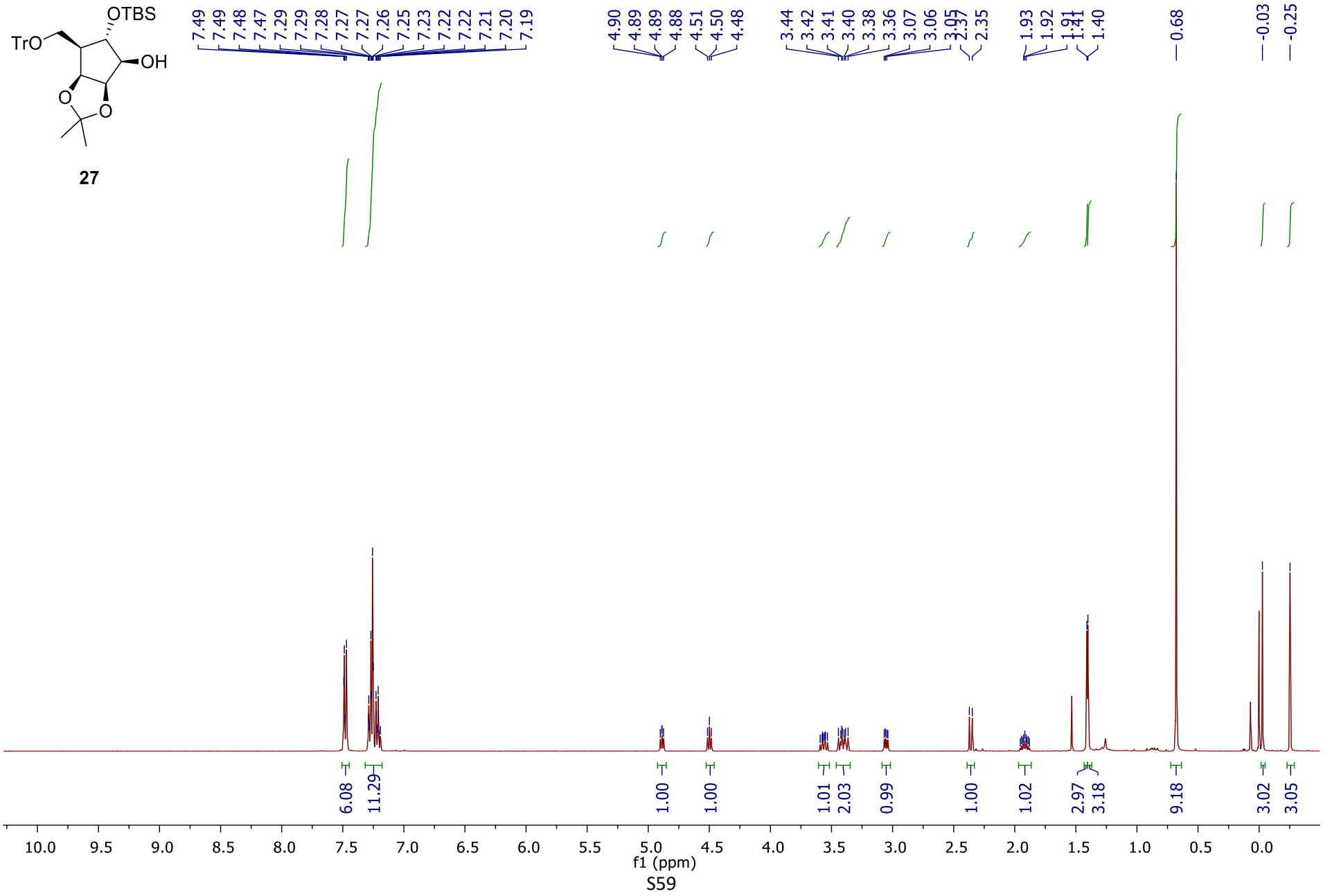

7.44 7.44 7.43 7.42 7.42 7.40 7.36 7.35 7.35 7.34 7.33 7.32 7.31 7.31 7.31 7.29 7.29 7.27 7.25 7.25 7.24 7.24 7.23 7.23 7.22 7.21 7.21 7.21
4.85 4.82 4.71 4.68 4.48 4.47 4.47 4.04 4.03 4.01 3.99 3.99 3.62 3.60 3.60 3.58 3.53 3.52 3.52 3.51 3.50 3.50 3.50 3.49 3.49 3.40 3.38 3.36 2.76 2.76 1.90 1.89 1.89 1.88 1.28 1.22
OH
TrO
OBn
O
O
20
7.84
13.09
0.98
0.99
1.97
0.97
0.98
0.98
0.99
0.96
0.98
3.00
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

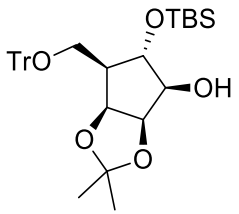

143.76
138.34
128.69
128.37
128.03
127.89
127.67
127.09
110.41
87.36
82.91
77.15
76.30
75.95
71.91
44.87
25.75
24.02
OH
TrO
OBn
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

20


7.47 7.47 7.45 7.39 7.38 7.38 7.37 7.36 7.36 7.35 7.33 7.32 7.31 7.31 7.30 7.29 7.29 7.27 7.27 7.26 7.23 7.23 7.23 7.22 7.21 7.20 7.19 7.19
4.98 4.96 4.95 4.82 4.76 4.75 4.73
3.97 3.96 3.95 3.95
3.53 3.52 3.51 3.49 3.46 3.43 3.41
2.64 2.64 2.63 2.62 2.62 2.61 2.61 2.60 2.60 2.59 2.59 1.37 1.28
TrO
O
OBn
O
O
22
6.41
18.42
1.00
1.85
1.06
0.97
1.00
1.02
0.96
3.36
3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

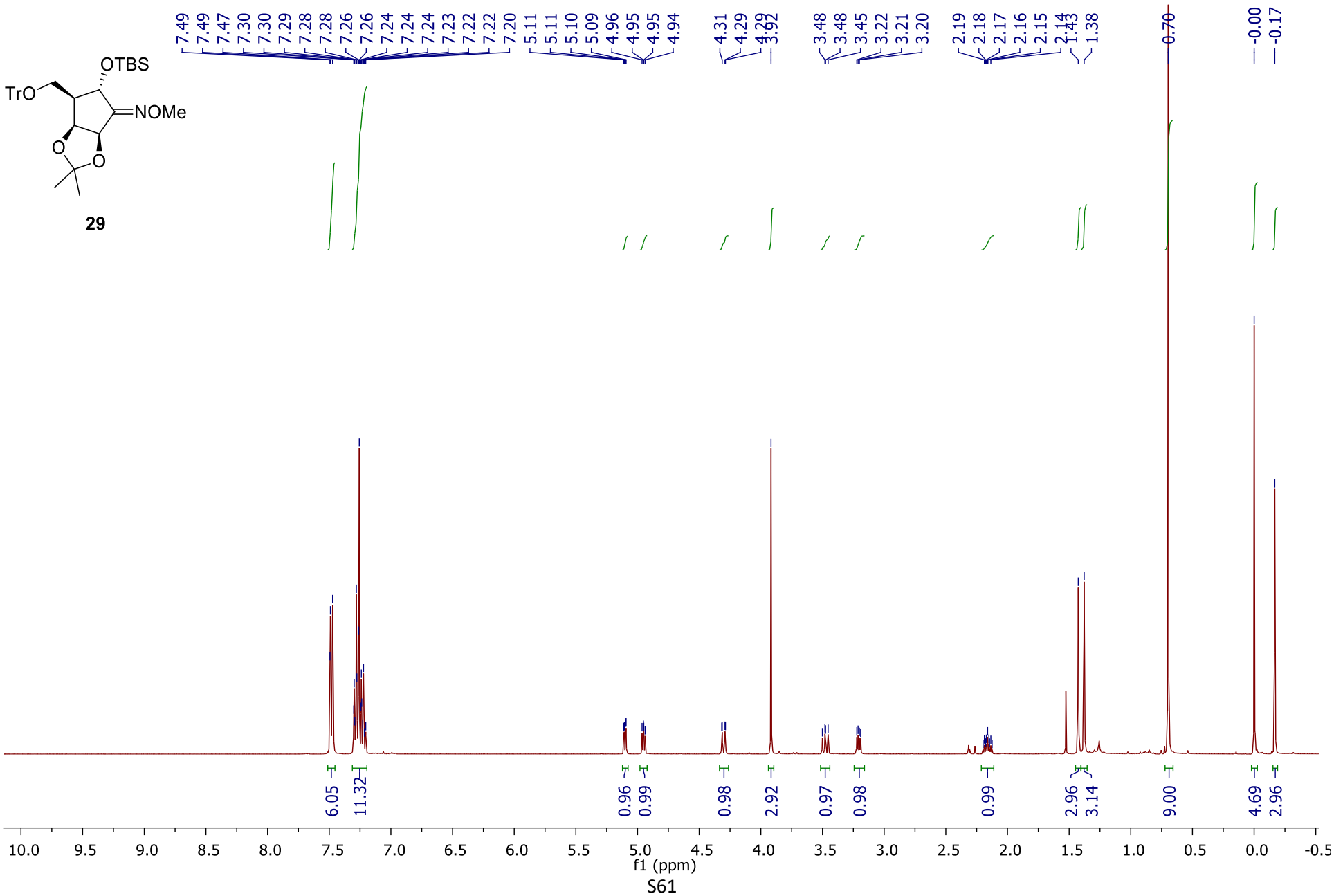

208.68
143.95
137.12
128.83
128.51
128.21
128.08
127.70
126.94
111.08
86.87
78.20
74.63
73.75
71.98
57.66
48.01
26.33
25.02
TrO
OBn
O
O
O
22
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

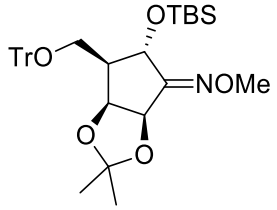

OTBS
TrO
OH
O
O
27
7.49
7.49
7.48
7.47
7.29
7.29
7.28
7.27
7.27
7.26
7.25
7.23
7.22
7.22
7.21
7.20
7.19
4.90
4.89
4.89
4.88
4.51
4.50
4.48
3.44
3.42
3.41
3.40
3.38
3.36
3.07
3.06
3.05
2.37
2.35
1.93
1.92
1.91
1.41
1.40
0.68
-0.03
-0.25
6.08
11.29
1.00
1.00
1.01
2.03
0.99
1.00
1.02
2.97
3.18
9.18
3.02
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OTBS
TrO
OH
O
O

27

144.33
128.82
127.63
126.83
110.09
86.52
77.79
76.39
75.72
60.52
45.88
25.97
25.69
24.32
17.84
-4.27
-5.26
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OTBS
TrO
NOMe
O
O
29
7.49
7.49
7.47
7.30
7.30
7.29
7.28
7.28
7.26
7.26
7.24
7.24
7.24
7.23
7.22
7.22
7.20
5.11
5.11
5.10
5.09
4.96
4.95
4.95
4.94
4.31
4.29
4.29
3.92
3.48
3.48
3.45
3.22
3.21
3.20
2.19
2.18
2.17
2.16
2.15
2.14
1.43
1.38
0.70
-0.00
-0.17
6.05
11.32
0.96
0.99
0.98
2.92
0.97
0.98
0.99
2.96
3.14
9.00
4.69
2.96
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
f1 (ppm)

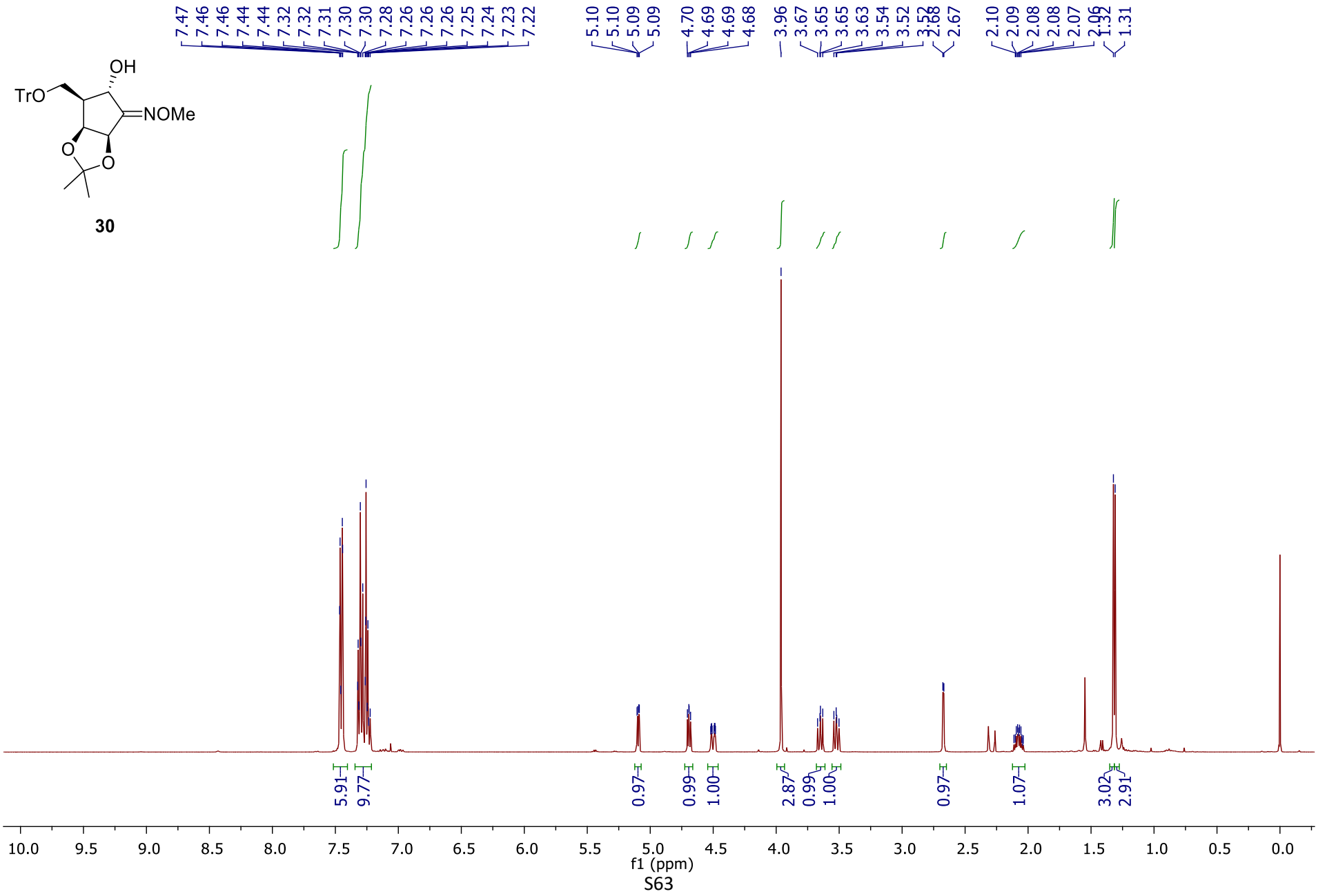


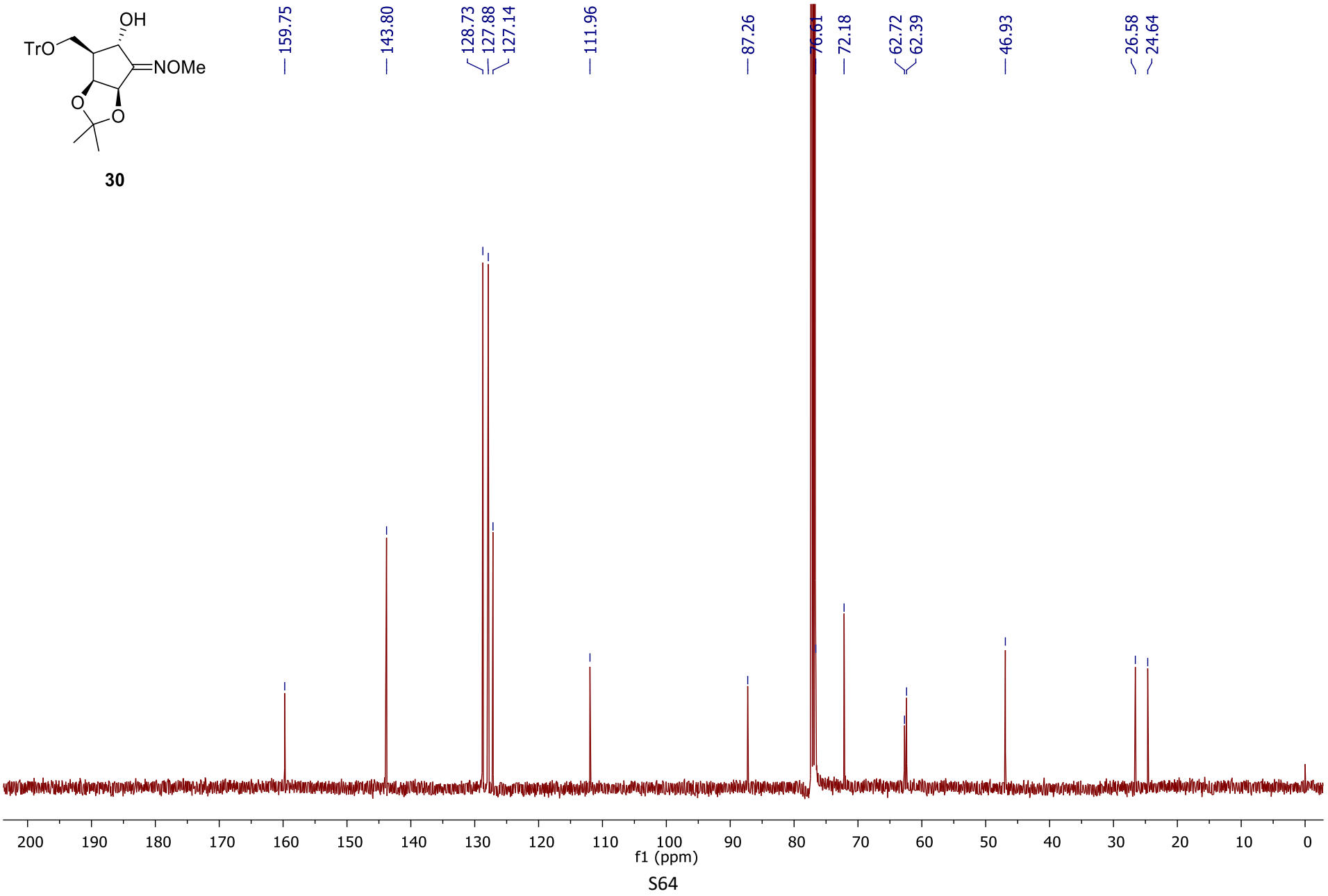
29

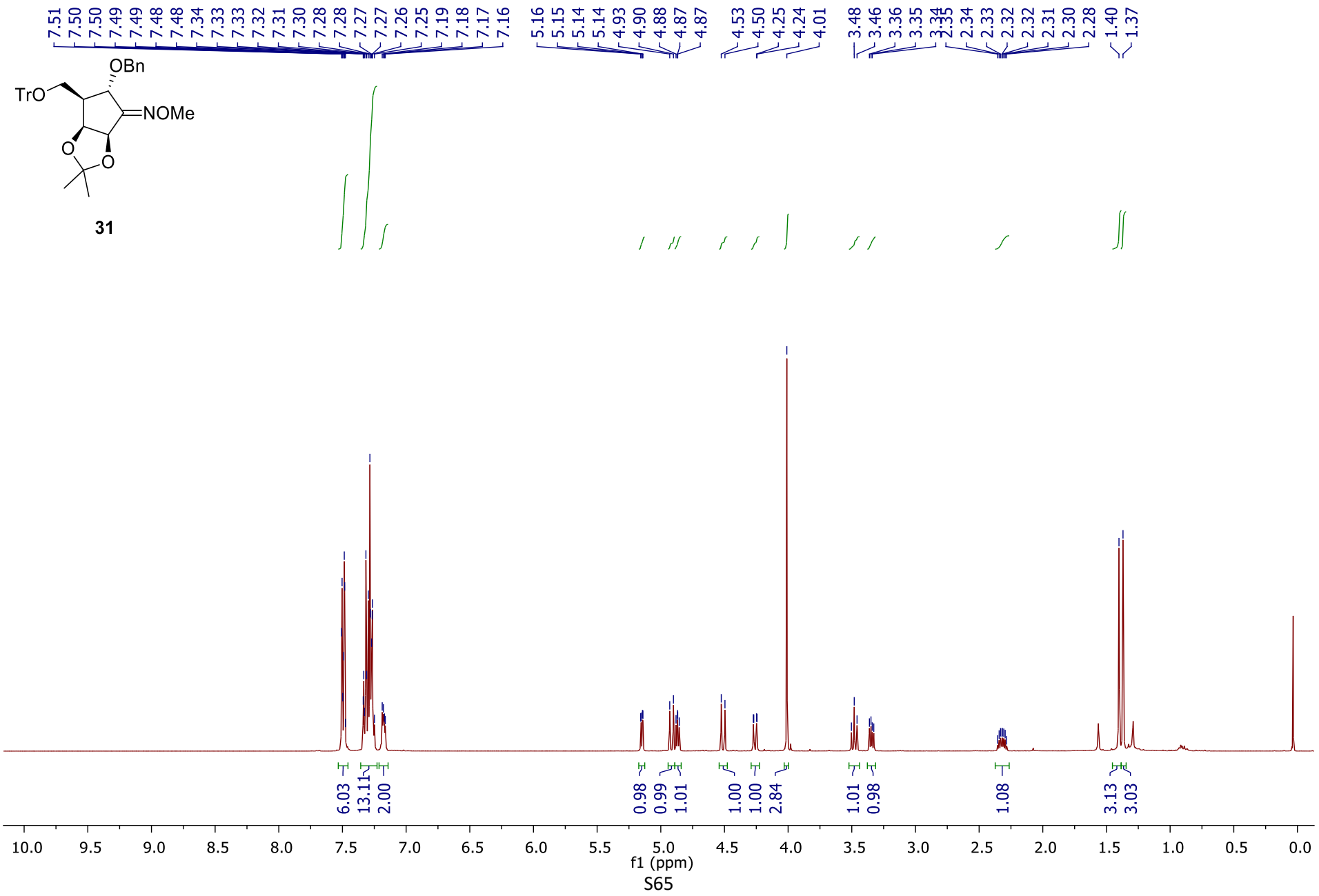
159.86
144.17
128.78
127.70
126.93
111.47
86.69
76.02
72.07
71.44
62.46
62.44
61.05
47.62
26.82
25.68
24.93
18.17
-4.25
-5.57

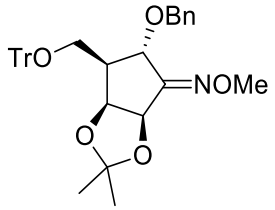
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)


7.47 7.46 7.46 7.44 7.44 7.32 7.32 7.31 7.30 7.30 7.28 7.26 7.26 7.26 7.25 7.24 7.23 7.22
5.10 5.10 5.09 5.09
4.70 4.69 4.69 4.68
3.96
3.67 3.65 3.65 3.63 3.54 3.52 3.52 2.68 2.67
2.10 2.09 2.08 2.08 2.07 2.06 1.32 1.31
OH
TrO
NOMe
O
O
30
5.91 9.77 0.97 0.99 1.00 2.87 0.99 1.00 0.97 1.07 3.02 2.91
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

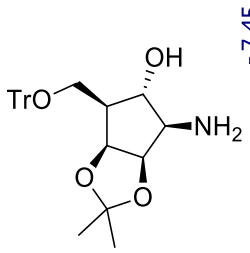

OH
TrO
NOMe
O
O
30
159.75
143.80
128.73
127.88
127.14
111.96
87.26
76.61
72.18
62.72
62.39
46.93
26.58
24.64
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.51 7.50 7.50 7.49 7.49 7.48 7.48 7.34 7.33 7.33 7.32 7.31 7.30 7.28 7.28 7.27 7.27 7.26 7.25 7.19 7.18 7.17 7.16
5.16 5.15 5.14 5.14 4.93 4.90 4.88 4.87 4.87
4.53 4.50 4.25 4.24 4.01
3.48 3.46 3.36 3.35 3.34 3.33 2.35 2.34 2.33 2.32 2.32 2.31 2.30 2.28
1.40 1.37
OBn
TrO
NOMe
O
O
31
6.03
13.11
2.00
0.98
0.99
1.01
1.00
1.00
2.84
1.01
0.98
1.08
3.13
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OBn
TrO
NOMe
O
O

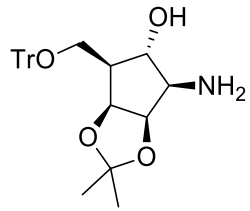
31

160.11
144.13
138.03
128.84
128.25
127.81
127.70
127.57
126.93
111.62
86.76
76.41
72.76
72.73
62.74
61.01
45.75
26.67
24.86
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
TrO
NH2
O
O

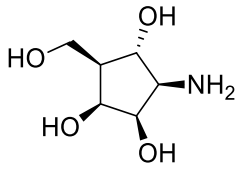
32

7.45 7.45 7.44 7.43 7.32 7.31 7.30 7.30 7.28 7.26 7.25 7.25 7.25 7.24 7.23 7.23 7.22 7.22 7.21
4.54 4.53 4.51 4.42 4.41 4.39
3.61 3.60 3.48 3.41 3.38 3.38 2.78 2.76 2.75 2.74
1.90 1.88 1.87 1.86 1.86 1.85 1.24 1.22
6.18 11.18 1.00 0.97 1.02 1.01 1.05 1.00 6.07 3.31 2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OH
TrO
NH2
O
O

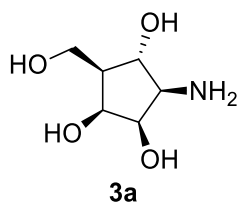
32

143.81
128.69
127.86
127.07
87.31
79.08
78.32
62.92
60.64
46.60
25.66
23.80
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
HO
NH2
HO
OH

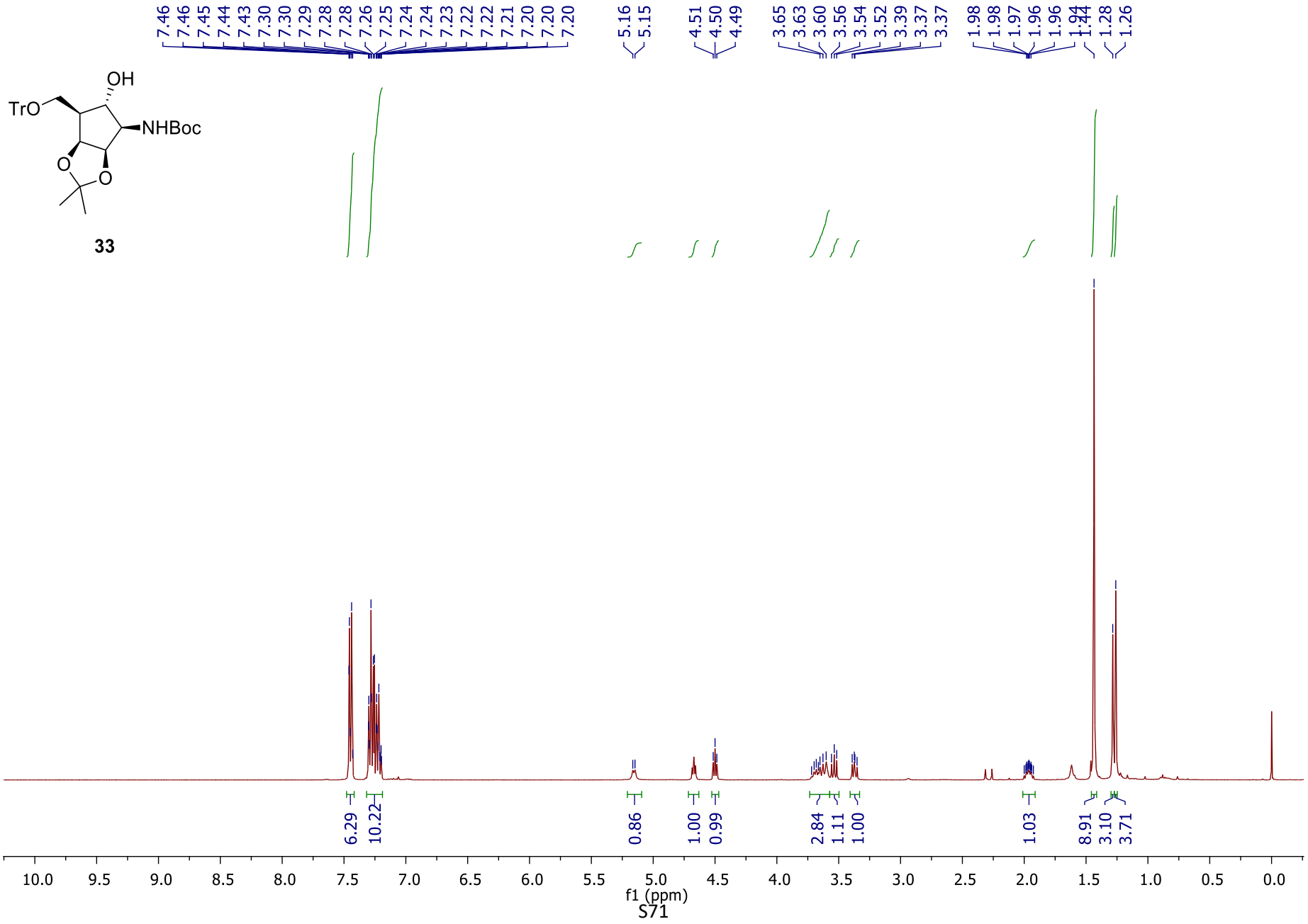
3a

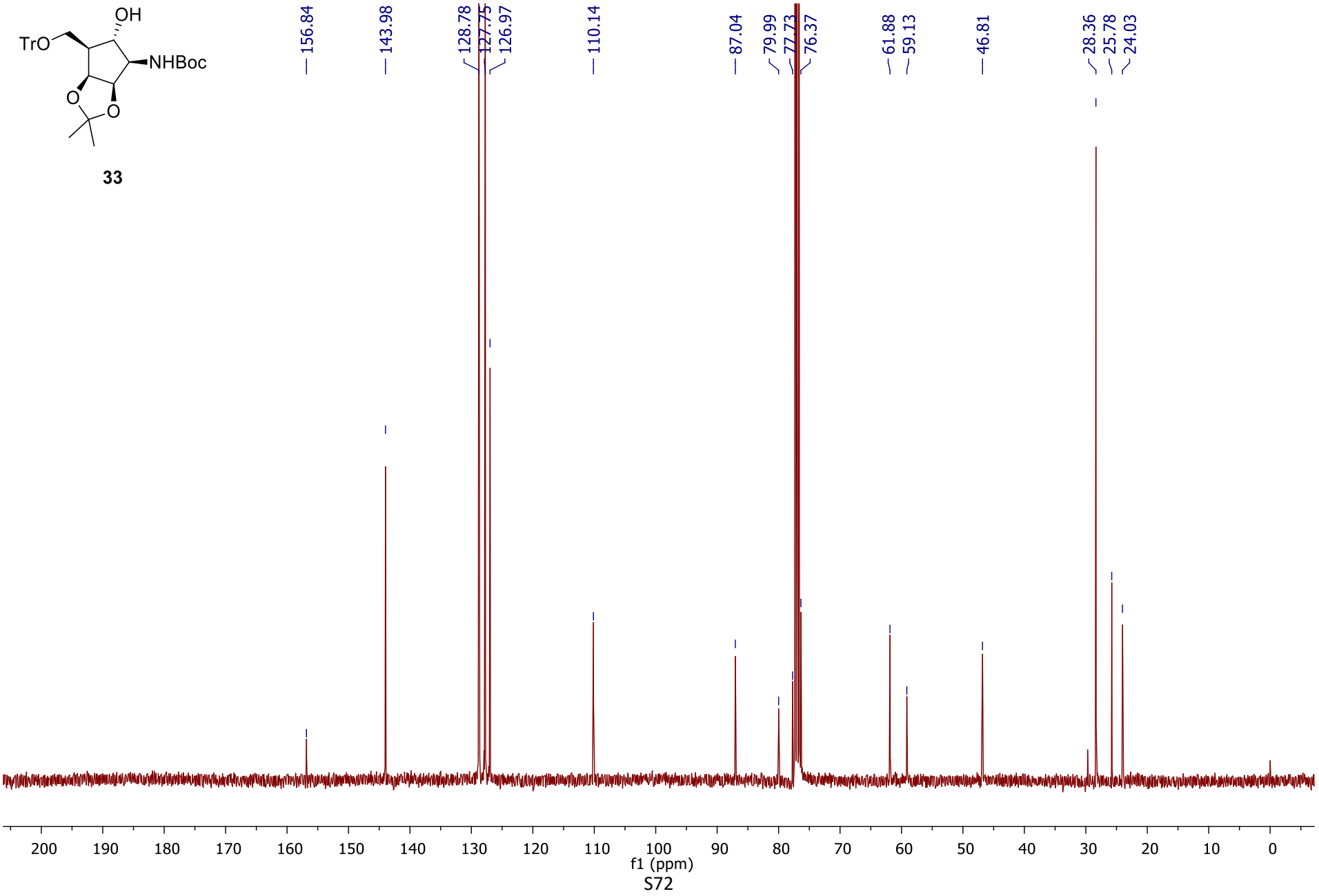
4.30
4.29
4.28
4.27
4.07
4.06
4.06
4.05
3.89
3.87
3.87
3.85
3.85
3.83
3.83
3.82
3.81
3.79
3.34
3.34
3.33
3.33
3.33
3.04
3.01
2.00
2.00
1.98
1.98
1.98
1.96
1.96
1.95
1.00
0.98
3.09
0.97
1.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OH
HO
NH2
HO
OH

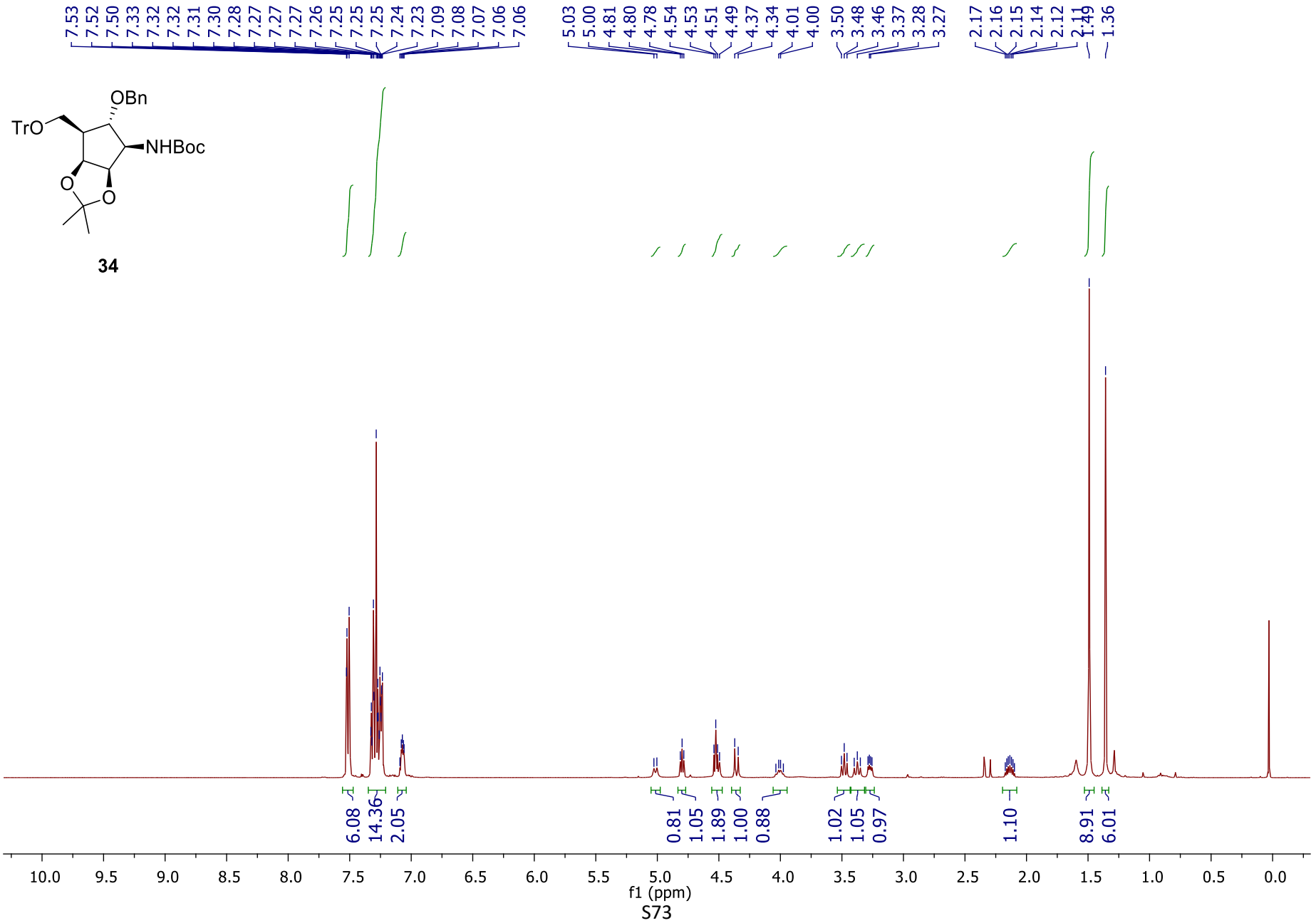
3a

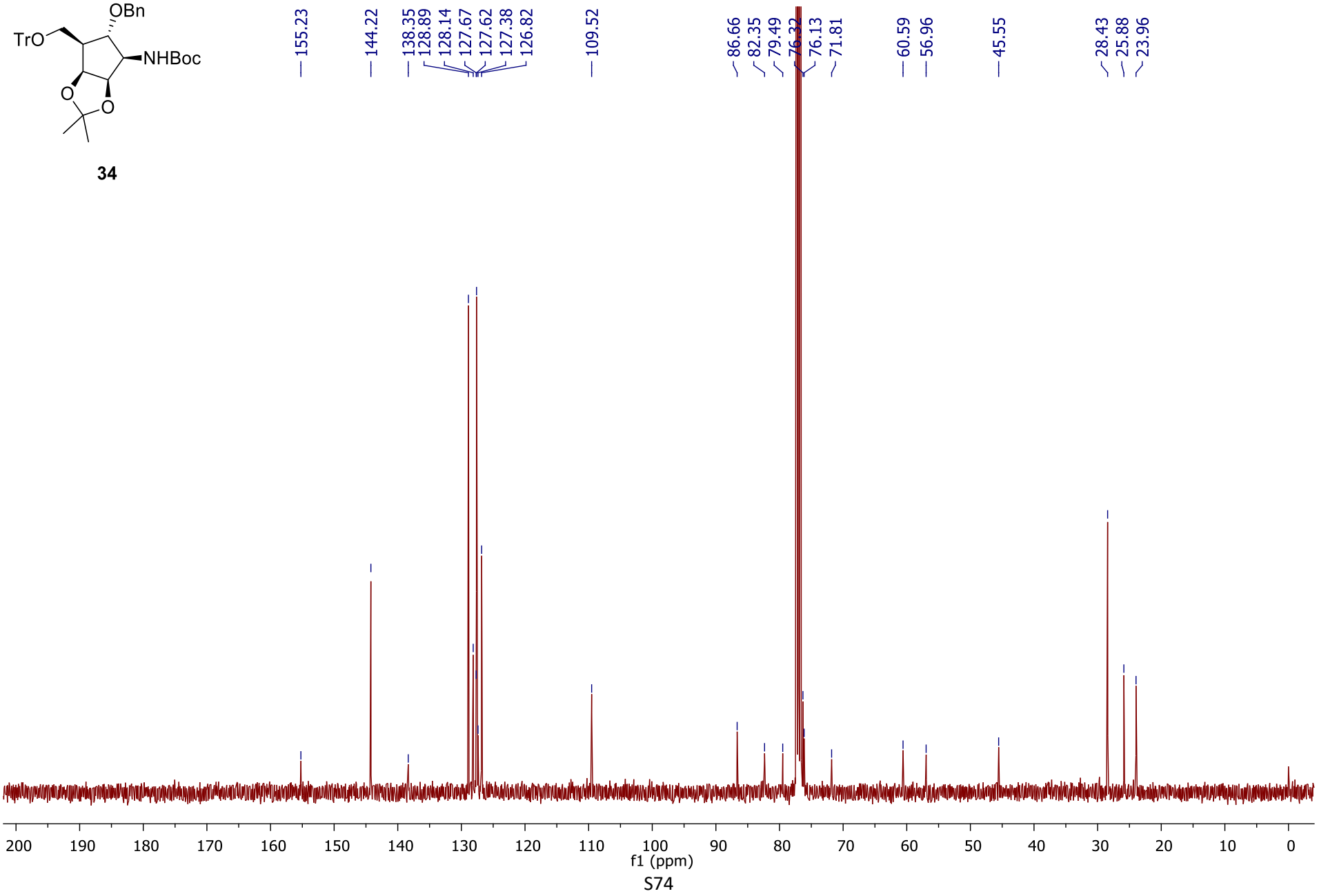
77.57
71.73
71.48
59.69
59.27
50.27
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.46 7.46 7.45 7.44 7.43 7.30 7.30 7.29 7.28 7.28 7.26 7.25 7.24 7.24 7.23 7.22 7.22 7.21 7.20 7.20 7.20
5.16 5.15
4.51 4.50 4.49
3.65 3.63 3.60 3.56 3.54 3.52 3.39 3.37 3.37
1.98 1.98 1.97 1.96 1.96 1.94 1.44 1.28 1.26
OH
TrO
NHBoc
O
O
O
33
6.29
10.22
0.86
1.00
0.99
2.84
1.11
1.00
1.03
8.91
3.10
3.71
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

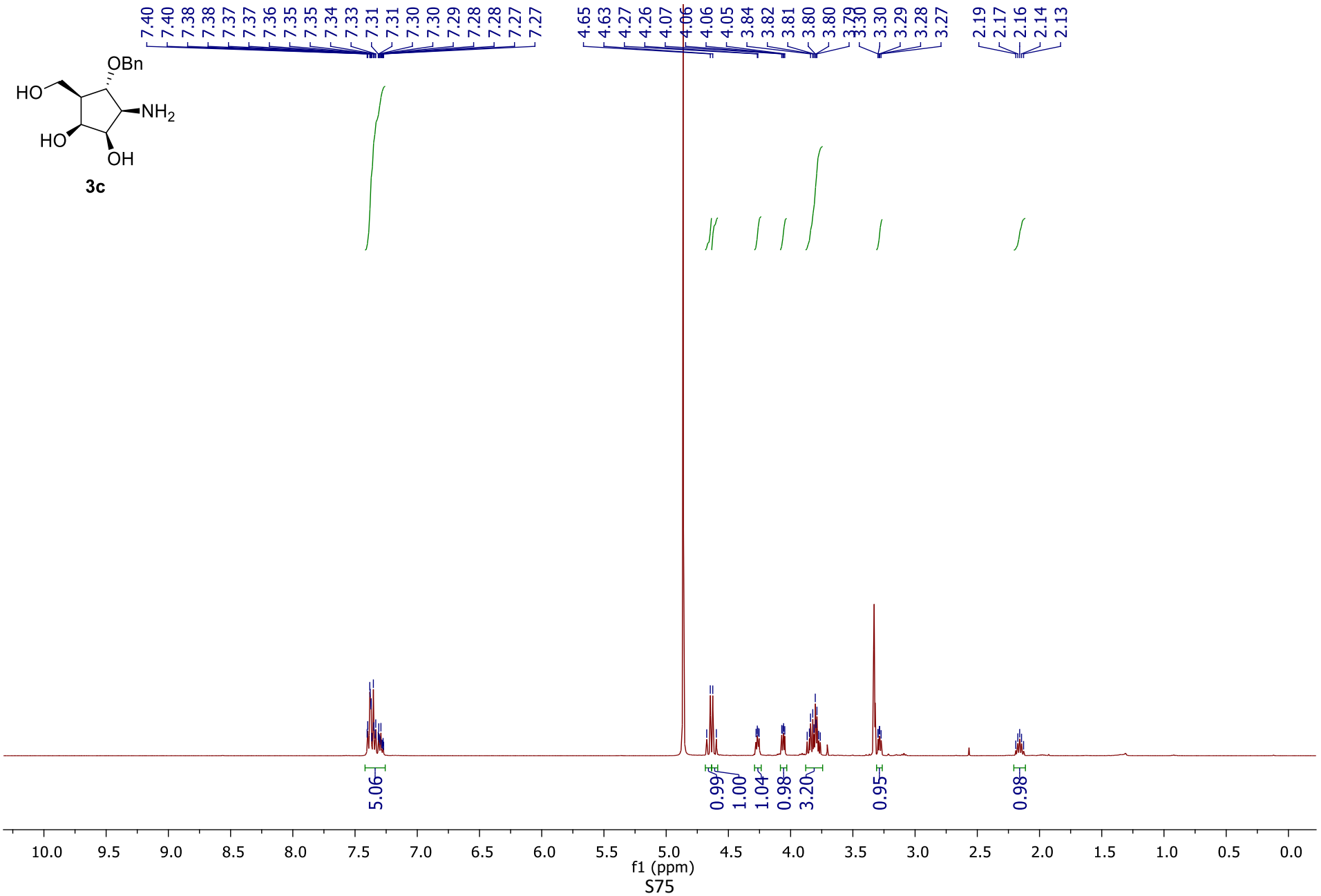

OH
TrO
NHBoc
O
O
O
156.84
143.98
128.78
127.75
126.97
110.14
87.04
79.99
77.73
76.37
61.88
59.13
46.81
28.36
25.78
24.03
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

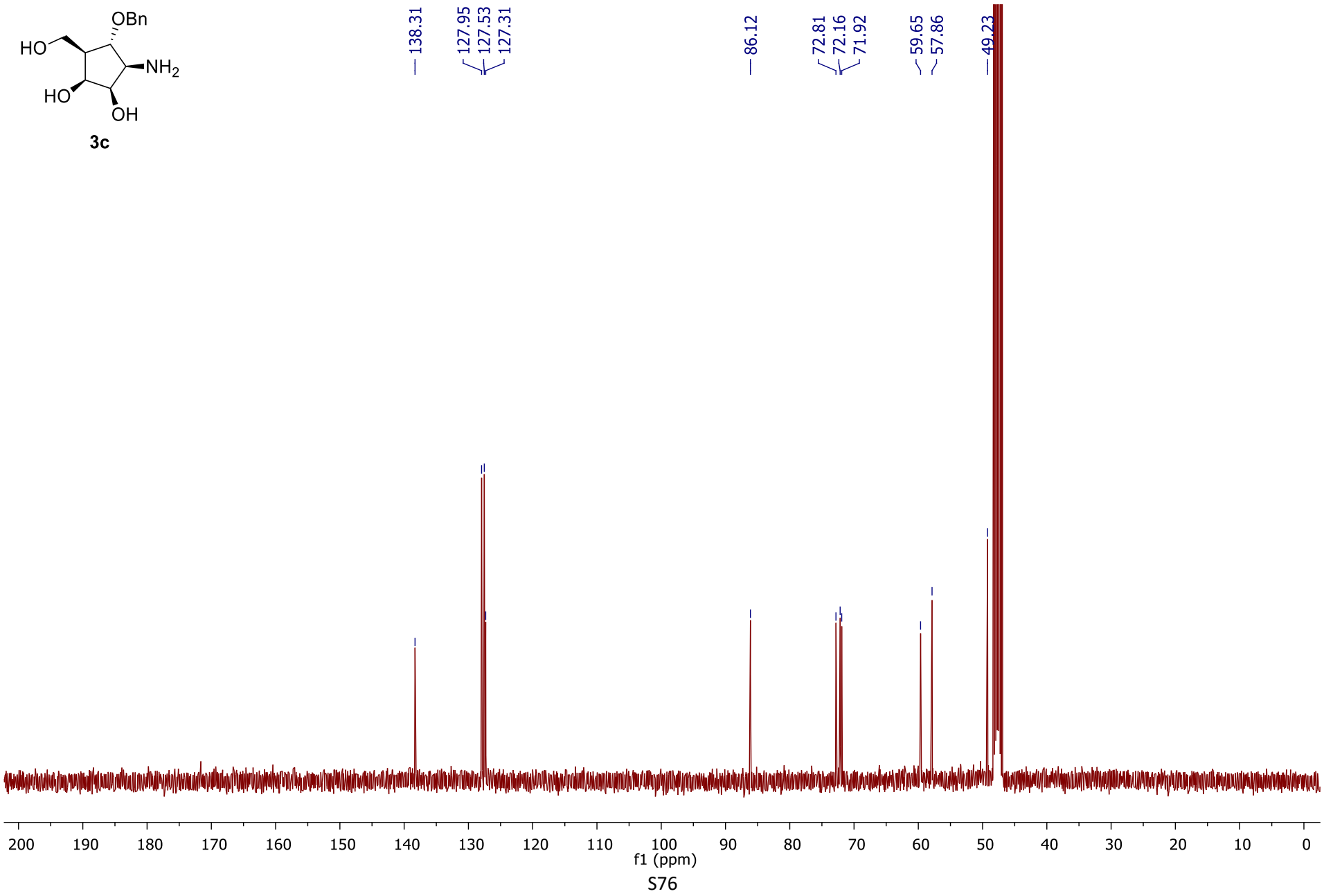
33

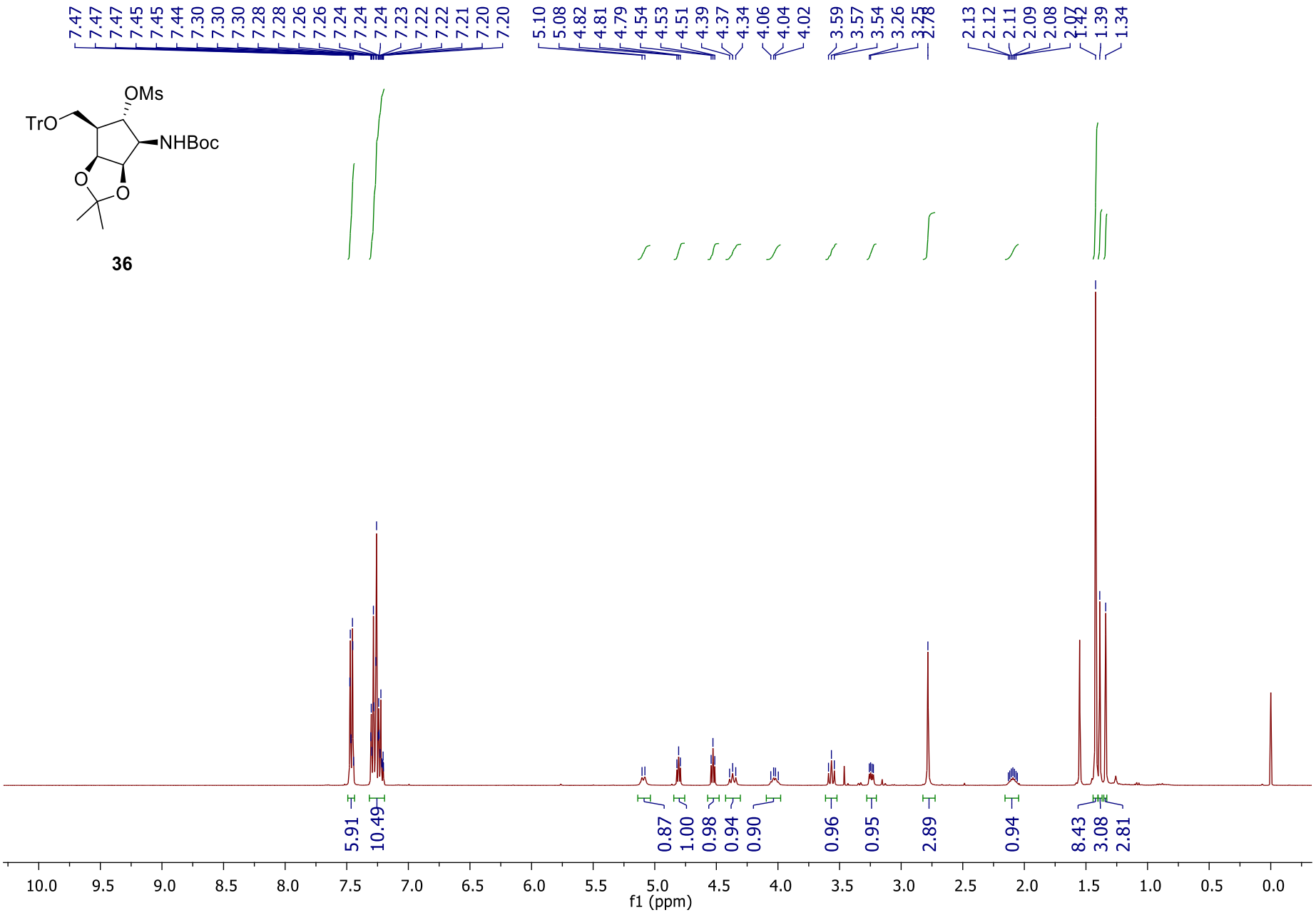

7.53 7.52 7.50 7.33 7.32 7.32 7.31 7.30 7.28 7.27 7.27 7.27 7.26 7.25 7.25 7.25 7.24 7.23 7.09 7.08 7.07 7.06 7.06
5.03 5.00 4.81 4.80 4.78 4.54 4.53 4.51 4.49 4.37 4.34 4.01 4.00 3.50 3.48 3.46 3.37 3.28 3.27
2.17 2.16 2.15 2.14 2.12 2.11 1.49 1.36
OBn
TrO
NHBoc
O
O
34
6.08 14.36 2.05 0.81 1.05 1.89 1.00 0.88 1.02 1.05 0.97 1.10 8.91 6.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

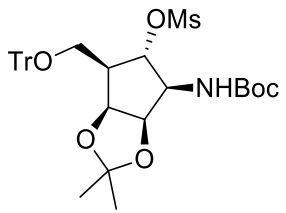

OBn
TrO
NHBoc
O
O
155.23
144.22
138.35
128.89
128.14
127.67
127.62
127.38
126.82
109.52
86.66
82.35
79.49
76.32
76.13
71.81
60.59
56.96
45.55
28.43
25.88
23.96
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

34


7.40 7.40 7.38 7.38 7.37 7.37 7.36 7.35 7.35 7.34 7.33 7.31 7.31 7.30 7.30 7.29 7.28 7.28 7.27 7.27
4.65 4.63 4.27 4.26 4.07 4.06 4.06 4.05 3.84 3.82 3.81 3.80 3.80 3.79 3.30 3.30 3.29 3.28 3.27
2.19 2.17 2.16 2.14 2.13
OBn
HO
NH2
HO
OH
3c
5.06
0.99
1.00
1.04
0.98
3.20
0.95
0.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

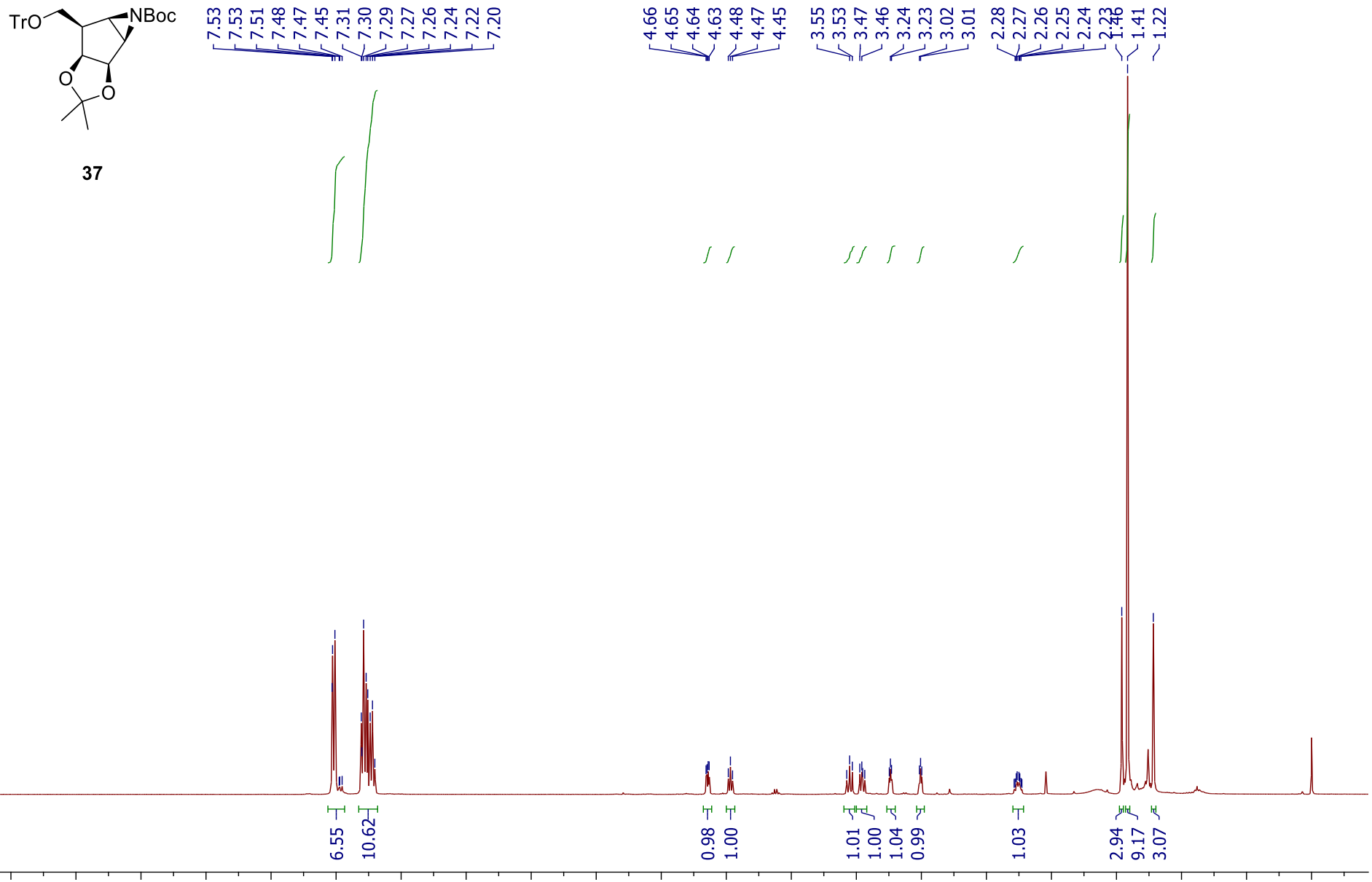

OBn
HO
NH2
HO
OH
3c
138.31
127.95
127.53
127.31
86.12
72.81
72.16
71.92
59.65
57.86
49.23
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

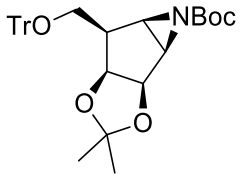

7.47 7.47 7.47 7.45 7.45 7.44 7.30 7.30 7.30 7.28 7.28 7.26 7.26 7.24 7.24 7.24 7.23 7.22 7.22 7.21 7.20 7.20
5.10 5.08 4.82 4.81 4.79 4.54 4.53 4.51 4.39 4.37 4.34 4.06 4.04 4.02
3.59 3.57 3.54 3.26 3.25 2.78
2.13 2.12 2.11 2.09 2.08 2.07 1.42 1.39 1.34
OMs
TrO
NHBoc
O
O
36
5.91
10.49
0.87
1.00
0.98
0.94
0.90
0.96
0.95
2.89
0.94
8.43
3.08
2.81
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OMs
TrO
NHBoc
O
O

36

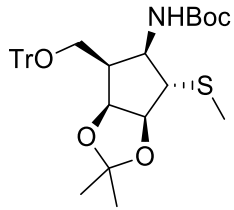
155.34
143.91
128.82
127.68
126.98
110.09
86.98
83.06
79.98
75.48
75.42
59.41
56.38
45.21
38.41
28.30
25.83
23.83
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


TrO
NBoc
O
O
37
7.53
7.53
7.51
7.48
7.47
7.45
7.31
7.30
7.29
7.27
7.26
7.24
7.22
7.20
4.66
4.65
4.64
4.63
4.48
4.47
4.45
3.55
3.53
3.47
3.46
3.24
3.23
3.02
3.01
2.28
2.27
2.26
2.25
2.24
2.23
1.46
1.41
1.22
6.55
10.62
0.98
1.00
1.01
1.00
1.04
0.99
1.03
2.94
9.17
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


TrO
NBoc
O
O

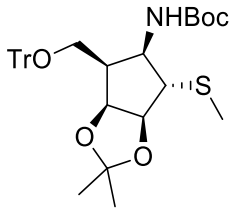
37

161.26
144.34
128.94
127.65
126.79
113.26
86.68
80.76
80.36
79.63
60.14
46.45
44.58
43.28
28.01
26.61
25.87
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NHBoc
TrO
S
O
O

38a

7.50
7.50
7.48
7.34
7.34
7.33
7.32
7.32
7.30
7.28
7.28
7.28
7.27
7.26
7.26
7.25
7.24
7.24
7.24
5.37
5.35
4.83
4.81
4.80
4.47
4.46
4.03
4.02
4.01
3.46
3.46
3.33
3.31
3.12
2.68
2.67
2.65
2.27
1.47
1.41
1.32
7.01
13.01
1.05
1.03
1.26
1.26
1.11
1.24
1.02
1.12
3.01
3.06
9.00
2.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

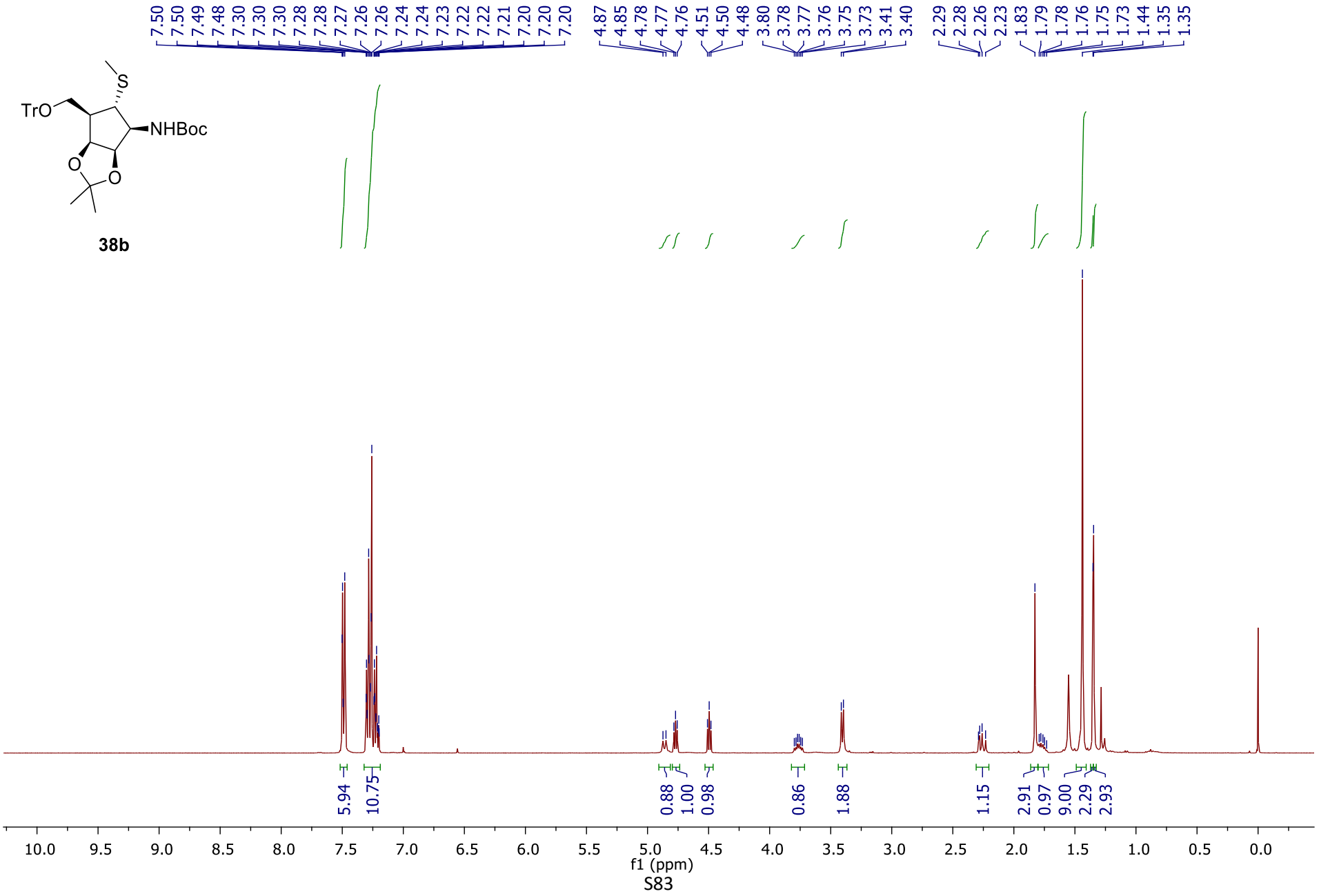


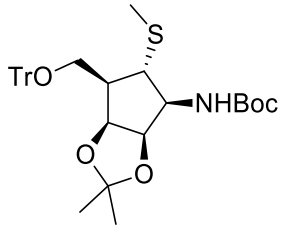
38a

155.05
144.05
128.80
127.72
126.92
110.53
86.64
85.13
81.19
79.16
59.04
57.77
57.00
44.11
28.42
26.10
23.50
15.56

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

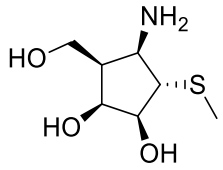
f1 (ppm)


7.50 7.50 7.49 7.48 7.30 7.30 7.30 7.28 7.28 7.27 7.26 7.26 7.24 7.24 7.23 7.22 7.22 7.21 7.20 7.20 7.20
4.87 4.85 4.78 4.77 4.76 4.51 4.50 4.48 3.80 3.78 3.77 3.76 3.75 3.73 3.41 3.40
2.29 2.28 2.26 2.23 1.83 1.79 1.78 1.76 1.75 1.73 1.44 1.35 1.35
TrO
NHBoc
S
O
O
38b
5.94 10.75 0.88 1.00 0.98 0.86 1.88 1.15 2.91 0.97 9.00 2.29 2.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


TrO
S
NHBoc
O
O

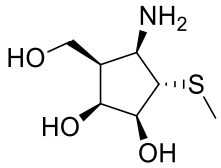
38b

155.50
144.34
128.84
127.63
126.85
109.67
86.78
79.51
77.53
77.22
60.81
55.45
47.60
43.98
28.36
25.76
24.11
10.48
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NH2
HO
S
HO
OH

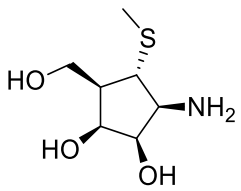
42

4.07
4.06
4.05
3.92
3.90
3.90
3.86
3.85
3.84
3.83
3.31
3.31
2.89
2.88
2.87
2.23
2.22
2.21
2.20
2.19
1.00
0.97
0.97
0.98
0.80
1.00
3.16
0.80
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


NH2
HO
S
HO
OH

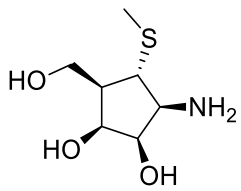
42

78.85
73.62
57.45
57.22
57.07
45.19
12.75
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HO
S
NH2
HO
OH

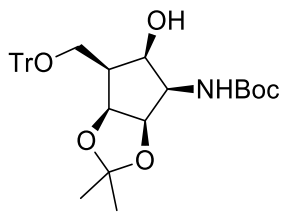
4

4.25
4.24
4.24
4.23
4.03
4.02
4.01
4.00
3.82
3.81
3.21
3.19
3.18
2.81
2.79
2.79
2.15
2.07
2.06
2.05
2.05
2.04
2.03
2.02
2.01
1.00
1.00
1.97
0.98
0.98
2.95
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


S
HO
NH2
HO
OH

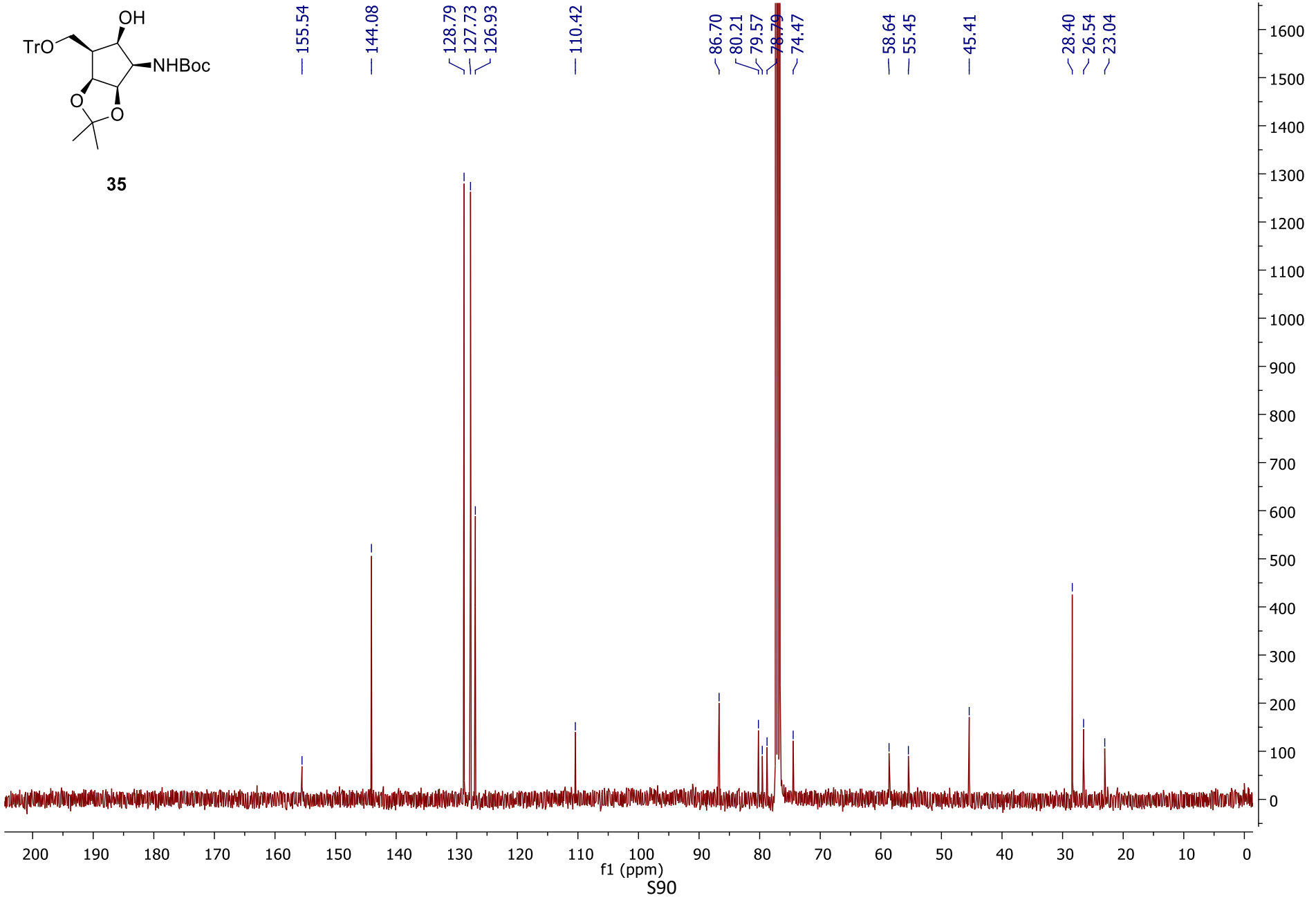
4

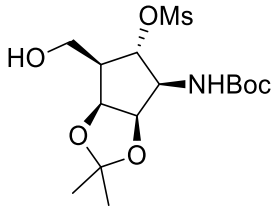
72.67
72.34
59.34
58.06
50.17
11.79
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
TrO
NHBoc
O
O

35

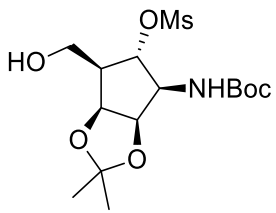
7.52
7.51
7.49
7.34
7.33
7.32
7.30
7.28
7.27
7.25
7.25
7.24
5.38
5.36
4.71
4.70
4.63
4.62
4.60
4.15
4.14
4.12
3.87
3.85
3.84
3.56
3.54
3.52
3.51
2.03
2.01
1.99
1.98
1.97
1.96
1.49
1.42
1.30
6.17
11.27
0.95
1.05
1.08
1.09
0.98
2.17
1.24
0.85
9.00
2.96
3.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OH
TrO
NHBoc
O
O
O
35
155.54
144.08
128.79
127.73
126.93
110.42
86.70
80.21
79.57
78.79
74.47
58.64
55.45
45.41
28.40
26.54
23.04
f1 (ppm)


OMs
HO
NHBoc
O
O

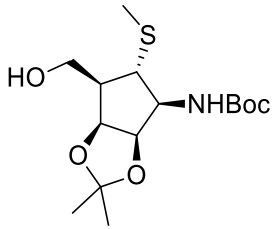
39

5.22
5.19
4.74
4.73
4.59
4.58
4.05
4.03
4.02
4.01
3.89
3.88
3.87
3.10
2.39
2.38
2.37
2.36
2.15
2.14
2.12
2.11
1.51
1.47
1.33
0.92
0.97
1.00
1.00
0.97
1.04
1.02
2.97
0.98
1.02
3.07
8.69
2.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OMs
HO
NHBoc
O
O

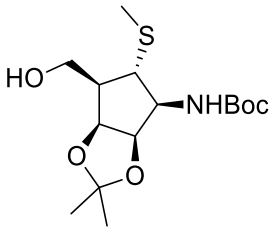
39

155.42
110.56
82.06
80.10
76.95
75.76
58.92
56.35
45.73
38.27
28.33
25.74
23.43
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HO
S
NHBoc
O
O

41

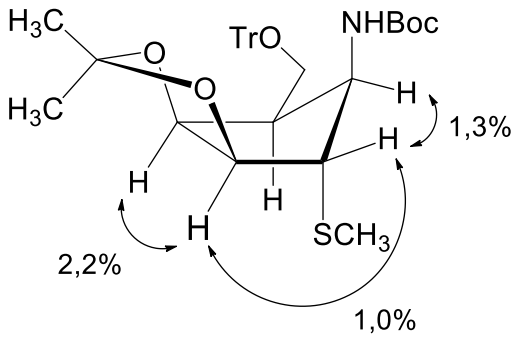
4.94
4.92
4.70
4.69
4.67
4.55
4.54
4.52
4.01
3.99
3.91
3.89
3.87
3.86
3.85
2.75
2.72
2.69
2.52
2.51
2.09
1.84
1.83
1.81
1.80
1.79
1.47
1.46
1.32
0.84
1.04
1.00
1.03
1.98
1.04
0.95
3.00
1.03
8.50
3.48
3.21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


HO
S
NHBoc
O
O

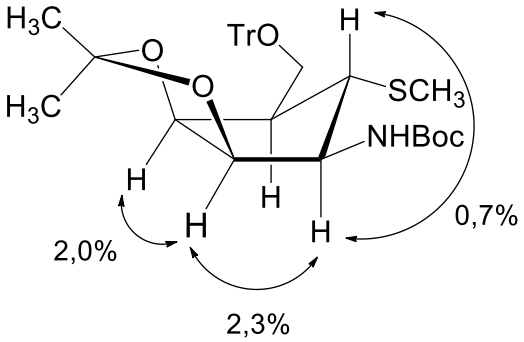
41

155.52
110.27
79.70
79.12
77.78
60.65
55.48
47.22
44.75
28.36
25.67
23.70
11.14
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4. NOE data of the compounds 38a and 38b



38a



38b

5. Crystal structure data and refinement details for compound 10

CCDC deposition number	2078997
Empirical formula	$C_{28}H_{28}O_4$
Formula weight	428.50
Temperature/K	100
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.7282(2)
b/Å	8.6664(1)
c/Å	14.9347(3)
α/°	90
β/°	96.234(1)
γ/°	90
Volume/Å^3	1123.01(4)
Z	2
ρ_{calc}g/cm^3	1.267
μ/mm^{-1}	0.668
F(000)	456.0
Crystal size/mm^3	0.45 × 0.26 × 0.15
Radiation	CuKα (λ = 1.54186)
2Θ range for data collection/°	5.954 to 146.27
Index ranges	$-10 \leq h \leq 10$, $-5 \leq k \leq 10$, $-18 \leq l \leq 17$
Reflections collected	61296
Independent reflections	3315 [R_{int} = 0.0180, R_{sigma} = 0.0077]
Data/restraints/parameters	3315/1/292
Goodness-of-fit on F^2	1.086
Final R indexes [I>=2σ (I)]	R_1 = 0.0250, wR_2 = 0.0627
Final R indexes [all data]	R_1 = 0.0253, wR_2 = 0.0629
Largest diff. peak/hole / e Å^{-3}	0.12/−0.19
Flack parameter	0.01(6)

Experimental

Single crystals of ketone **10** were obtained by crystallization from a mixture of EtOAc/hexanes, 1:5 (v/v). Data collection and cell refinement of **10** were made on a Stoe StadiVari diffractometer using HPC detector (Dectris Pilatus3R 300K) and microfocused X-ray source Xenocs Genix3D Cu HF. The structure was solved by the program SIR-2014 and refined by the full-matrix least-squares procedure with SHELXL (version 2018/3).[4,5] The structure was drawn using OLEX2 package.[6] The absolute structure and configuration was determined. The Flack parameter was calculated by the Parsons method.[7]

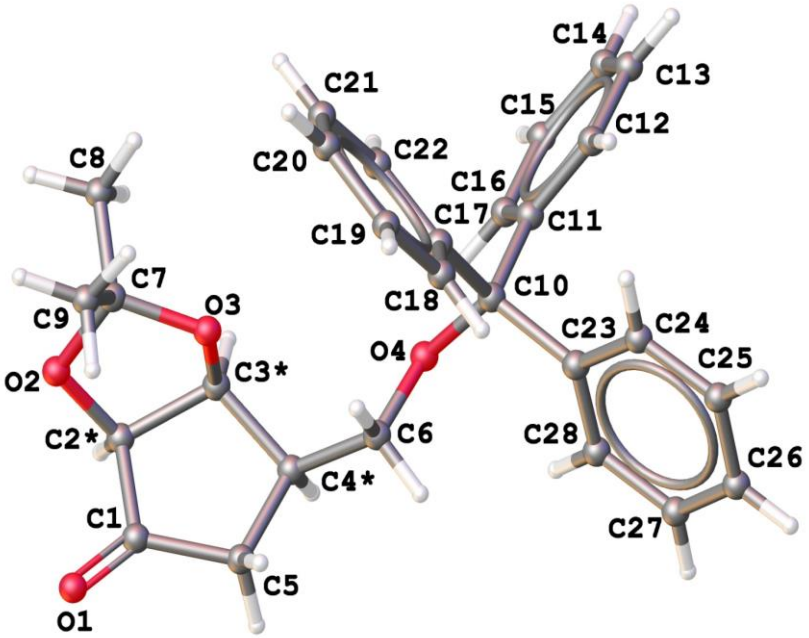


Figure S1 The crystal structure of compound **10** (OLEX2 drawing). Atomic displacement ellipsoids are drawn at 50% probability level.

6. Molecular modelling

6.1. QM calculations

A structural model depicted in Figure S2 was used to simulate ring-opening reactions of the aziridine intermediates **37** and **40** by sodium methanethiolate in DMF (*N*,*N*-dimethylformamide) solvent at 60°C. In this model only corresponding aziridine intermediate and methanetiolate anion (nucleophile) are included. A Na^+ ion from sodium methanethiolate reagent is not included into the reaction scheme. In this model the Na^+ ion is supposed to be fully solvated by aprotic polar DMF solvent and it does not directly participate in stabilization of a transition state or carbamate anions. To simulate DMF as a solvent a standard Poisson-Boltzmann continuum solvation model was employed using the Jaguar[8] program of the Schrödinger package. In the process of the formation of a product the Boc protecting group is partially rotated in order to carbamate anion be planarized. Thus, two possible conformations of the Boc protecting group in **37** had to be included in the calculations for reaction pathway A (**37A_conf1**, **37A_conf2**) and the reaction pathway B (**37B_conf1**, **37B_conf2**). A similar situation is with conformers for the reaction starting from aziridine **40**. There are also two conformations for the reaction pathway A (**40A_conf1** and **40A_conf2**) and two ones for the reaction pathway B (**40B_conf1** and **40B_conf2**). In the conformation **conf1** the carbonyl oxygen of carbamate is oriented toward the *exo*-face of the tricyclic skeleton, while in **conf2** it is oriented toward the *endo*-face of the tricyclic skeleton. Overall, four possible reactions were modeled for the ring-opening of aziridine **37** and other four for opening of aziridine **40** (Figure S2).

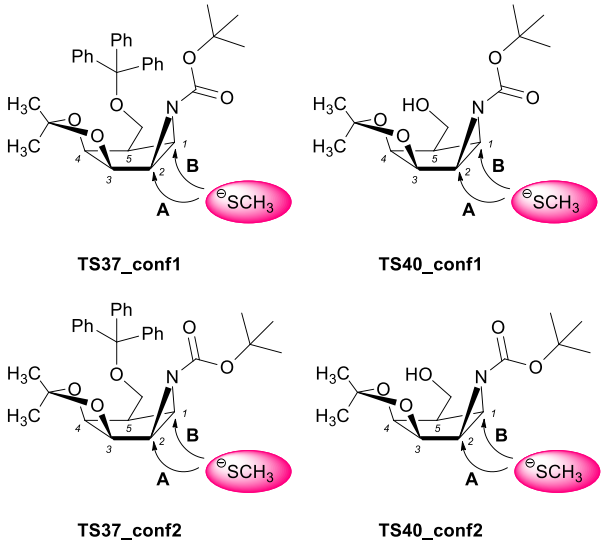


Figure S2 Schematic representation of a structural model used in QM calculations for the ring-opening of aziridines **37** and **40**.

To obtain reaction profiles for the calculated ring-opening reactions three DFT (Density Functional Theory) methods were used. The meta hybrid Minnesota functional with double the amount of nonlocal exchange (M06-2X),[9] meta hybrid PWB6K (modified MPW91 + modified B95)[10] and hybrid MPW1K[11] functionals, were used with the Pople's split valence double-ξ basis set [6-31G(d)] augmented by polarization functions on all heavy atoms for geometry optimization of all transition states and intermediates. Then, the Poisson-Boltzmann continuum solvation model (DMF solvent) was applied on optimized M06-2X structures using single point energy calculations.

In mapping the potential energy surface (PES) of the ring-opening reaction, one-dimensional scan procedures were performed along the C1-N and C2-N reaction coordinates (see the atom numbering in Figure S2) stepped by 0.1 Å or 0.05 Å with remaining coordinates optimized using the Jaguar[8] program of the Schrödinger package. Transition states were refined from maxima found on the scanned PES and optimized without any geometry constraints. Transition state searches (keywords IQST = 0, IGEOPT = 2) were performed by using a quasi-Newton method.[12] All stationary points were characterized as minima or transition states by vibrational frequency calculations calculated from Hessian from the end of the optimization (keyword IFREQ = −1). The ultrafine integration grid (the Mura-Knowles radial shell distribution scheme[13]), which has 125 radial shells and uses an angular offset of 30 (434 angular points per shell) with no pruning as defined in the Qsite program (keywords GDFTFINE = −14, GDFTGRAD = −14, GDFTMED = −14), was set for all calculations because of the systematic grid errors found for some DFT functionals (used in this work) with a standard integration grid.[14]

Further, for each transition state, intrinsic reaction coordinate (IRC) calculations were performed to prove that it connects the right reactant and product minima using the Gaussian package.[15]

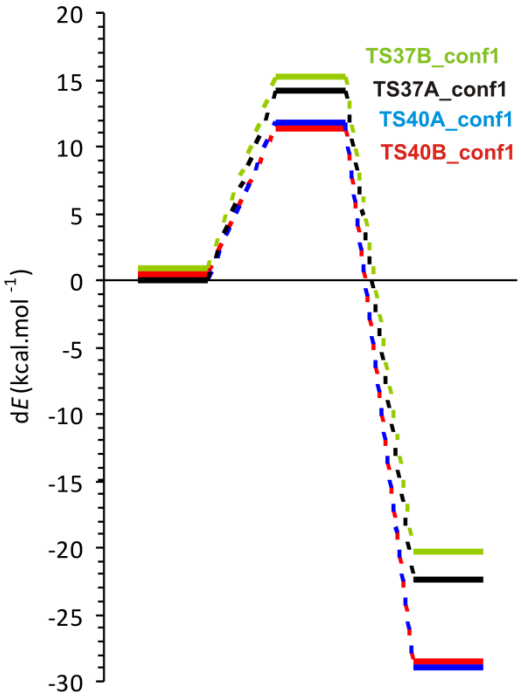


Figure S3 The M06-2X relative energies (ΔE, in kcal.mol^{-1}) for the reaction mechanisms A and B of ring-opening of aziridines **37** and **40**.

6.2. Molecular docking

An X-ray structure of recombinant *Drosophila melanogaster* Golgi α-mannosidase II with bound mannostatin A (PDB ID: 2F7O)[16] was used as a 3-D enzyme model of human GMII for docking of the synthesized compounds with the GLIDE program[17,18] of the Schrödinger package. Protonation states of amino acid residues of the enzyme were calculated with the bound mannostatin A for the pH = 6.0 using the Propka v.2 program.[19,20] In all docking calculations the catalytic acid (Asp341) was modelled in the ionized form in accordance with Propka calculations. The receptor box for the docking conformational search was centred at the Zn^{2+} ion co-factor at the bottom of the active site with a size of 25×25×25 Å using partial atomic charges for the receptor from the OPLS2005 force field. The grid maps were created with no Van der Waals radius and charge scaling for the atoms of the receptor. Flexible docking in standard (SP) precision was used. The partial charges of the ligands were calculated at the DFT level (M06-2X/LACVP**)[8] using the Jaguar program[9] of the Schrödinger package. All ligands were docked with the amino group attached at the cyclopentane ring in a protonated form. The potential for non-polar parts of the ligands was softened by scaling the Van der Waals radii by a factor of 0.8 for atoms of the ligands with partial atomic charges less than specified cut-off of 0.15. The 5000 poses were kept per ligand for the initial docking stage with scoring window of 100 kcal mol^{-1} for keeping initial poses; the best 400 poses were kept per ligand for energy minimization. The ligand poses with RMS deviations less than 0.5 Å and maximum atomic displacement less than 1.3 Å were discarded as duplicates. The post-docking minimization for 10 ligand poses with the best docking score was performed and optimized structures were saved for subsequent analyses using the MAESTRO viewer[21] of the Schrödinger package.

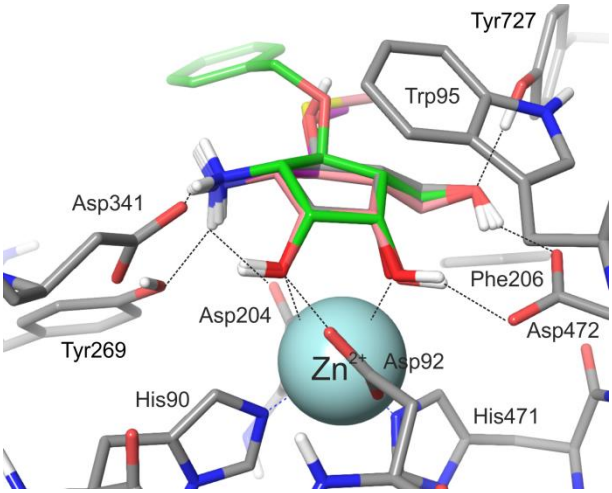


Figure S4 Superposition of the docked compounds **3a** (carbons in grey), **3b** (carbons in magenta), **3c** (carbons in green) and **4** (carbons in pink). The key interactions (hydrogen bonds and interactions with Zn^{2+} ion) of bound compounds with amino acid residues of GMII are visualized with dash lines.

7. Biochemical assay

The isolation and purification of recombinant *Drosophila melanogaster* Golgi (GMIIb) and lysosomal (LManII) α-mannosidases was carried out as described previously.[22] The α-mannosidase from *Canavalia ensiformis* (JBMan) was purchased from Sigma-Aldrich. Mannostatin A hydrochloride as a standard was purchased from Enzo Life Sciences Inc. The mannosidase activities of these enzyme preparations were measured using *p*-nitrophenyl-α-D-mannopyranoside (pNP-Man; Sigma-Aldrich; 100 mM stock in DMSO) as a substrate at 2 mM final concentration in acetate buffer (50 mM) at the optimal pH (GMIIb at pH 6.0, JBMan at pH 5.0, and LManII at pH 5.2) and using 0.5 µL of enzyme (0.05 µg of protein for JBMan), in a total volume of 50 µL for 1–2 h at 37 °C. GMIIb was assayed in the presence of $CoCl_2$ (0.5 mM). The inhibitor was pre-incubated with the enzyme in the buffer for 5 min at room temperature, and the reaction was started by addition of the substrate. The reactions were terminated with two volumes (0.1 mL) of sodium carbonate (0.5 M), and the production of *p*-nitrophenol was measured at 405 nm with a Mithras LB943 multimode reader (Berthold Technologies). The averages of representative result of three independent experiments performed in duplicate are presented. IC_{50} values were determined with *p*NP-Man (2 mM).

8. References

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