A Stereoselective Synthesis of Digitoxin And Digitoxigen Mono- and Bisdigitoxoside from Digitoxigenin via a Palladium Catalyzed Glycosylation

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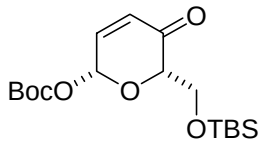
Supporting Information

Section A: General methods

Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon/nitrogen using oven-dried glassware and standard syringe/septa techniques. Ether, tetrahydrofuran, methylenechloride and methanol were dried by passing through activated alumina column with argon gas pressure. Hexanes refer to the petroleum fraction bp 40-60 ^{o}C. Commercial reagents were used without purification unless otherwise noted. Flash chromatography was performed using the indicated solvent system on Sorbent Technologies silica gel standard grade 60 (230-400 mesh). R_f values are reported for analytical TLCusing the specified solvents and 0.25 mm EMD silica gel 60 F_{254} plates that were visualized by UV irradiation (254 nm) or by staining (465 mL of 95% EtOH, 17 mL conc. H_2SO_4, 5 mL acetic acid, and 13 mL anisaldehyde). Optical rotations were obtained using a JASCO, DIP-370 digital polarimeter at sodium D line (589 nm) and were reported in concentration of g / 100 mL at 21 ^{o}C. ^{1}H and ^{13}C spectra were recorded on Varian Inova 600 MHz spectrometer, Chemical shifts are reported relative to $CDCl_3$ (δ 7.26 ppm) for ^{1}H and $CDCl_3$ (δ 77.0 ppm) for ^{13}C. IR was recorded on PerkinElmer Spectrum One FT-IR Spectrometer; thin film was formed in $CHCl_3$ solution. Melting points are uncorrected. High resolution mass spectrometric analyses were performed on a LTQ-FT Mass Spectrometer.

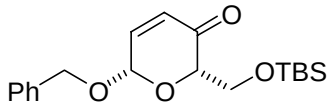
Section B: Experimental Procedures

(2R,6*S*)-Carbonic acid *tert*-butyl ester 6-(*tert*-butyl-dimethyl-silanyloxymethyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl ester (*ent*-8b):



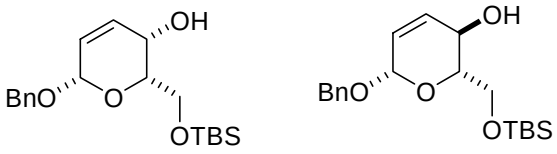
(5*S*)-1-Hydroxy-5-*tert*-butyldimethylsilanyloxymethyl-5*H*-pyran-4-(1*H*)-one (5.15 g, 20 mmol) was dissolved in CH_2Cl_2 (20 mL) and the solution was cooled to 0 ^oC. A CH_2Cl_2 (5 mL) solution of $(Boc)_2O$ (5.22 g, 24 mmol) and a catalytic amount of DMAP (122 mg, 1 μmol) was added to the reaction mixture. The reaction was stirred for 1 h at 0 ^oC. The reaction was quenched with 100 mL of satd. aq $NaHCO_3$, extracted (3 x 100 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 6% EtOAc/hexanes to give two diastereomers of carbonic acid *tert*-butyl ester 6-(*tert*-butyl-dimethyl-silanyloxymethyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl ester ***ent*-10b** and ***ent*-8b** in 1:1 ratio (5.87 g, 16.4 mmol, 82%). ***ent*-8b:** white crystals; R_f (20% Et_2O/hexanes) = 0.22; mp: 62-62.5 ^oC; $[\alpha]_D^{21}$ = -47.3 (*c* = 0.3, $CHCl_3$); IR (thin film, cm^{-1}) 2926, 1742, 1680, 1283, 1252, 1162, 1066; ^1H NMR (600 MHz, $CDCl_3$) δ 6.86 (dd, *J* = 10.2, 3.0 Hz, 1H), 6.40 (dd, *J* = 3.0, 1.2 Hz, 1H), 6.23 (dd, *J* = 10.2, 1.2 Hz, 1H), 4.33 (dd, *J* = 6.0, 3.6 Hz, 1H), 4.02 (dd, *J* = 11.4, 6.0 Hz, 1H), 3.96 (dd, *J* =11.4, 3.0 Hz, 1H), 1.51 (s, 9H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 193.5, 151.9, 142.5, 129.1, 89.4, 83.4, 80.7, 64.4, 27.7 (3C), 25.8 (3C), 18.3, -5.47, -5.51; CIHRMS Calcd for $[C_{17}H_{30}O_6SiNa]^+$: 381.1716. Found 381.1714.

(2R,6S)-(6-Benzyloxy-2-(*tert*-butyl-dimethyl-silanyloxymethyl)-6*H*-pyran-3-one (13)



A CH_2Cl_2 (2 mL) solution of Boc compound ***ent*-8b** (556 mg, 1.55 mmol) and benzyl alcohol (335 mg, 3.11 mmol) was cooled to 0 °C. A CH_2Cl_2 (1 mL) solution of $Pd_2(DBA)_3$•$CHCl_3$ (40 mg, 2.5 mol%) and PPh_3 (41 mg, 10 mol%) was added to the reaction mixture at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. The reaction mixture was quenched with 5 mL of satd aq $NaHCO_3$, extracted (3 x 5 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 4% EtOAc/hexanes to give product **13** (453 mg, 1.30 mmol, 84%) as a viscous oil: R_f (20% EtOAc/hexanes) = 0.43; $[\alpha]_D^{21}$ = +5.8 (*c* = 1.2, CH_2Cl_2); IR (thin film, cm^{-1}) 2929, 2856, 1696, 1255, 1124, 1054, 837; ^1H NMR (600 MHz, $CDCl_3$) δ 7.38 (m, 5H), 6.90 (dd, *J* = 10.2, 1.8 Hz, 1H), 6.13 (dd, *J* = 10.2, 1.8 Hz, 1H), 5.40 (d, *J* = 1.8 Hz, 1H), 4.99 (d, *J* = 11.4 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.24 (dd, *J* = 6.0, 4.2 Hz, 1H), 4.07 (m, 2H), 0.91 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 194.4, 146.3, 136.8, 128.5 (3C), 128.3 (2C), 128.0, 93.5, 80.4, 70.0, 63.6, 25.8 (3C), 18.3, -5.1 (2C); CIHRMS Calcd for $[C_{19}H_{28}O_4Si+H]^+$: 349.1835. Found 349.1834.

(2R,6S)-6-Benzyloxy-2-(*tert*-butyl-dimethyl-silanyloxymethyl)-6*H*-pyran-3-ol (14a/b)

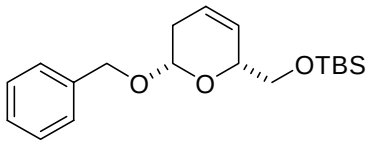


14a **14b**

A CH_2Cl_2 (0.8 mL) solution of enone **13** (270 mg, 0.78 mmol) and MeOH (0.8 mL) was cooled to -78 ^oC. $NaBH_4$ (32 mg, 0.85 mmol) was added and the reaction mixture was stirred at -78^oC for 3 h. The reaction mixture was diluted with ether (5 mL) and was quenched with 5 mL of satd aq $NaHCO_3$, extracted (3 x 5 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 18% EtOAc/hexanes to give product **14** (240 mg, 0.69 mmol, 88%) as a viscous oil (a:b = 1.5:1). **14a**: R_f (30% EtOAc/hexanes) = 0.36; $[\alpha]_D^{21}$ = + 96.8 (c = 1.60, $CHCl_3$); IR (thin film, cm^{-1}) 3443, 2929, 1463, 1254, 1043, 838, 796; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35 (m, 5H), 6.15 (ddd, J = 10.2, 4.8, 1.2 Hz, 1H), 5.87 (ddd, J = 10.2, 1.2, 1.2 Hz, 1H), 5.14 (ddd, J = 1.8 , 1.2, 1.2 Hz, 1H), 4.90 (d, J = 11.4 Hz, 1H), 4.66 (d, J = 11.4 Hz, 1H), 4.00 (m, 1H), 3.97 (dd, J = 10.2, 6.0 Hz, 1H), 3.85 (dd, J = 10.2, 5.4 Hz, 1H), 3.71 (ddd, J = 6.6, 6.0, 2.4 Hz, 1H), 2.15 (d, J = 9.0 Hz, 1H), 0.92 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.4, 131.1, 130.5, 128.4 (2C), 128.1 (2C), 127.8, 96.7, 75.5, 69.9, 62.75, 62.73, 25.8 (3C), 18.3, -5.3, -5.4; CIHRMS Calcd for [$C_{19}H_{30}O_4SiNa^+$]: 373.1806, Found 373.1820.

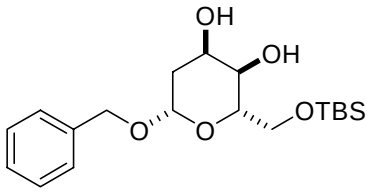
14b: R_f (30% EtOAc/hexanes) = 0.30; $[\alpha]_D^{21}$ = + 22.3 (c = 1.90, $CHCl_3$); IR (thin film, cm^{-1}) 3442, 2929, 1462, 1255, 1043, 838; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.99 (ddd, J = 10.2, 2.4, 1.8 Hz, 1H), 5.79 (ddd, J = 10.2, 1.8, 1.2 Hz, 1H), 5.23 (ddd, J = 1.8 , 1.8, 1.8 Hz, 1H), 4.83 (d, J = 12.0 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.28 (d, J = 5.4 Hz, 1H), 3.96 (dd, J = 10.2, 5.4 Hz, 1H), 3.83 (dd, J = 10.2, 8.4 Hz, 1H), 3.68 (ddd, J = 8.4, 6.0, 4.8 Hz, 1H), 2.88 (s, 1H), 0.92 (s, 9H), 0.120 (s, 3H), 0.117 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.6, 132.0, 128.4 (2C), 128.0, 127.9 (2C), 127.7, 95.8, 76.7, 69.3, 66.4, 65.3, 25.8 (3C), 18.2, -5.48, -5.55; CIHRMS Calcd for [$C_{19}H_{30}O_4SiNa^+$]: 373.1806, Found 373.1820.

(((2R,6S)-6-(Benzyloxy)-5,6-dihydro-2H-pyran-2-yl)methoxy)(*t*-butyl) dimethylsilane (15)



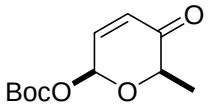
A flask was charged with dry N-methyl morpholine (NMM) 2.5 ml, triphenyl phosphine (674 mg, 2.57 mmol) and was cooled to -30 ^{o}C under Ar atmosphere. Diethylazodicarboxylate (448 µl, 2.57 mmol) was added and the reaction was stirred for 5 min, Allylic alcohols **14** (300 mg, 0.86 mmol) was added in a 1M solution of NMM and the reaction mixture was stirred for 10 min, followed by addition of o-nitrobenzenesulfonyl hydrazide (NBSH) (522 mg, 2.57 mmol). The reaction was stirred at -30 ^{o}C for 2h and was monitored by TLC, upon consumption of starting material, warm up to room temperature and stirred for another 4h. The reaction mixture was diluted with ether (10 mL) and was quenched with 5 mL of satd aq $NaHCO_3$, extracted (3 x 5 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 4% EtOAc/hexanes to afford product **15** (204 mg, 0.61 mmol, 71%) as a viscous oil: R_f (15% EtOAc/hexanes) = 0.62; $[\alpha]_D^{21}$ = +79.5 (*c* = 1.0, CH_2Cl_2); IR (thin film, cm^{-1}) 2927, 1472, 1256, 1074, 837; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (m, 5H), 5.76 (m, 2H), 4.92 (d, *J* = 11.4 Hz, 1H), 4.77 (dd, *J* = 7.2, 3.6 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.27 (dddd, *J* = 6.6, 6.0, 6.0, 3.0 Hz, 1H), 3.81 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.62 (dd, *J* = 9.6, 6.6 Hz, 1H), 2.27 (dddd, *J* = 17.4, 7.2, 3.6, 1.8 Hz, 1H), 2.22 (ddd, *J* = 17.4, 6.6, 3.6 Hz, 1H), 0.92 (s, 9H), 0.094 (s, 3H), 0.090 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.8, 128.4 (2C), 128.0 (2C), 127.6, 127.1, 123.6, 97.3, 75.2, 69.7, 65.9, 31.2, 25.9 (3C), 18.3, -5.2, -5.3; CIHRMS Calcd for [$C_{19}H_{30}O_3SiNa^+$]: 357.1856, Found 357.1869.

Benzyl 2-deoxy-6-*O*-(tert-butyl) dimethylsilyl-*β*-L-allose (16)



To a CH_2CH_2 (1.0 ml) solution of olefin **15** (187 mg, 0.56 mmol) at 0 ^oC was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide / water (0.5 mL). Crystalline OsO_4 (1.42 mg, 1 mol %) was added and the reaction was stirred for 3 h. The reaction was quenched with adding EtOAc and satd. $NaHCO_3$. The organic layer was separated and concentrated. It was purified by a silica gel column using 25% EtOAc/hexanes. Pure fractions were combined and concentrated to afford **16** (188 mg, 0.51 mmol, 91%) as a viscous oil: R_f (40% EtOAc/hexanes) = 0.46; $[\alpha]_D^{21}$ = +61.8 (*c* = 1.35, CH_2Cl_2); IR (thin film, cm-1) 3496, 1087, 1050, 830; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.97 (dd, *J* = 9.6, 2.4 Hz, 1H), 4.86 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.12 (ddd, *J* = 3.6, 3.0, 2.4 Hz , 1H), 4.03 (s, 1H), 3.99 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.80 (dd, *J* = 9.0, 9.0 Hz, 1H), 3.76 (ddd, *J* = 9.0, 9.0, 4.2 Hz, 1H), 3.66 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.38 (s, 1H), 2.17 (ddd, *J* = 14.4, 3.6, 2.4 Hz, 1H), 1.73 (ddd, *J* = 14.4, 9.6, 3.0 Hz, 1H), 0.93 (s, 9H), 0.140 (s, 3H), 0.136 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.6, 128.4 (2C) , 127.9 (2C), 127.7, 97.3, 72.8, 70.7, 70.2, 67.4, 66.4, 36.2, 25.8 (3C), 18.1, -5.6, -5.7 ; CIHRMS Calcd for $[C_{19}H_{32}O_5SiNa^+]$: 391.1911, Found 391.1924.

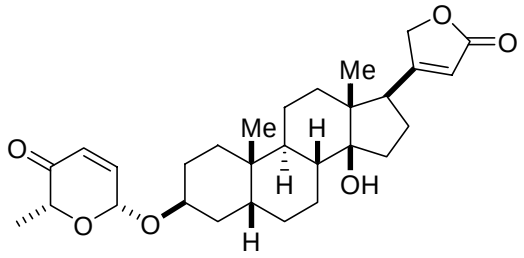
***Tert*-butyl (2S,6R)-5,6-dihydro-6-methyl-5-oxo-2H-pyran-2-yl carbonate (8a):**



To a benzene solution (300 mL) of (5*R*)-1-Hydroxy-5-*tert*-butyl dimethylsilanyloxymethyl-5*H*-pyran-4-(1*H*)-one (18.5g, 0.144 mol) and $(Boc)_2O$ (47.3 g, 0.22 mol) was added sodium acetate (13.2 g, 0.16 mol). After stirring at 80 ^oC for 2 h, the mixture was cooled down to room temperature. The mixture was quenched by adding of 300 mL of satd. aq $NaHCO_3$, extracted (3 x 300 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 7% EtOAc/hexanes to give two diastereomers of *tert*-butyl (2S,6R)-5,6-dihydro-6-methyl-5-oxo-2H-pyran-2-yl carbonate (29.0 g, 0.127 mol, 88%) of **10a** and **8a**(**10a**:**8a** = 1:1.3). **10a**: R_f(20% Et_2O/hexanes) = 0.43; $[\alpha]_D^{21}$= -97.1 (c = 1.0, CH_2Cl_2); IR (thin film, cm^{-1}) 2986, 1752, 1703, 1633, 1278, 1258, 1159, 1090, 1058, 1029, 944 ; ^1H NMR (270 MHz, $CDCl_3$) δ 6.86 (dd, *J* = 10.3, 3.8 Hz, 1H), 6.31 (d, *J* = 3.8 Hz, 1H), 6.17 (d, *J* = 10.3 Hz, 1H), 4.63 (q, *J* = 6.7 Hz, 1H), 1.50 (s, 9H), 1.39 (d, *J* = 6.7 Hz, 3H) ; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 195.7, 151.8, 140.9, 128.4, 89.1, 83.5, 72.1, 27.6(3C), 15.2; CIHRMS Calcd for $[C_{11}H_{16}0_5Na]^+$: 251.0890, Found 251.0884.

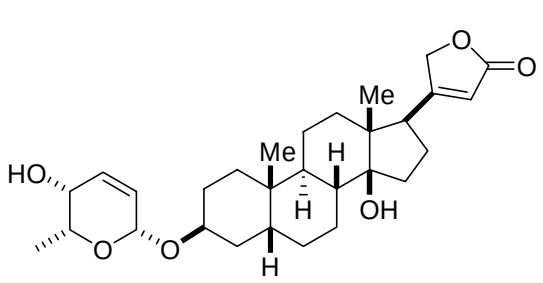
8a: R_f (20% EtOAc/hexanes) = 0.50; mp: 43-43.5 ^oC; $[\alpha]_D^{21}$ = +42.3 (*c* = 1.3, $CHCl_3$); IR (thin film, cm^{-1}) 2986, 1752, 1703, 1633, 1278, 1258, 1159, 1090, 1058, 1029, 944; ^1H NMR (270 MHz, $CDCl_3$) δ 6.88 (dd, *J* = 10.3, 2.6 Hz, 1H), 6.40 (dd, *J* = 2.6, 1.4 Hz, 1H), 6.20 (dd, *J* = 10.3, 1.2 Hz, 1H), 4.37 (q, *J* = 6.9 Hz, 1H), 1.51 (s, 9H), 1.49 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) *δ* 195.9, 151.7, 142.8, 128.3, 89.8, 83.7, 75.7, 27.6 (3C), 18.6 ; CIHRMS Calcd for $[C_{11}H_{16}0_5Na]^+$: 251.0890, Found 251.0883.

(2R,6R)-2-Digitoxigenoxy-6-methyl-2H-pyran-3(6H)-one (17)

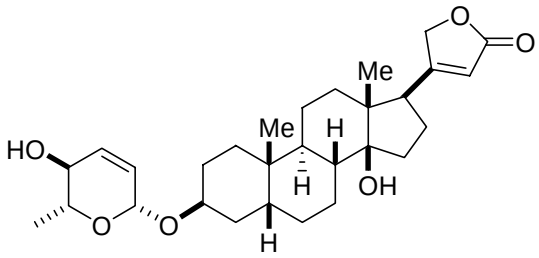


A CH_2Cl_2 /THF solution (8 mL, 4:1 V/V) of Boc pyranone **8a** (544 mg, 2.39 mmol) and digitoxigenin **2** (1.34 g, 3.58 mmol) was cooled to 0 ^oC. A CH_2Cl_2 (1 mL) solution of $Pd_2(DBA)_3$•$CHCl_3$ (72 mg, 2.5 mol%) and PPh_3 (73 mg, 10 mol%) was added to the reaction mixture at 0 ^oC. The reaction mixture was stirred at 0 ^oC for 8 hours and was quenched with 20 mL of satd aq $NaHCO_3$, extracted (3 x 20 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 40% EtOAc/hexanes to give **17** (993 mg, 2.05 mmol, 86%) as a white solid: R_f (40% EtOAc/hexanes) = 0.17; mp: 211-212 ^oC; $[\alpha]_D^{21}$ = + 17.6 (c = 3.60, $CHCl_3$); IR (thin film, cm^{-1}) 3498, 2937, 2875, 1780, 1741, 1698, 1620, 1448, 1374, 1164, 1144, 1053, 1025, 958, 754; ^1H NMR (600 MHz, $CDCl_3$) δ 6.86 (dd, J = 10.2, 1.8 Hz, 1H), 6.09 (dd, J = 10.2, 1.8 Hz, 1H), 5.86 (m, 1H), 5.38 (dd, J = 2.4, 1.8 Hz, 1H), 4.98 (dd, J = 18.0, 1.8 Hz, 1H), 4.79 (dd, J = 18.0, 1.8 Hz, 1H), 4.16 (q, J = 6.6 Hz, 1H), 4.15 (m, 1H), 2.76 (dd, J = 9.6, 6.0 Hz, 1H), 2.20-2.08 (m, 3H), 1.44 (d, J = 7.2 Hz, 3H), 1.92-1.16 (m, 18H), 0.93 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.0, 174.6, 174.5, 147.8, 128.0, 117.6, 93.9, 85.5, 75.1, 73.5, 73.4, 50.9, 49.6, 41.8, 40.0, 36.4, 35.7, 35.2, 33.1, 30.1, 29.9, 26.9, 26.56, 26.53, 23.6, 21.3, 21.1, 16.9, 15.7; ESIHRMS Calcd for [$C_{29}H_{40}O_6Na^+$]: 507.2717, Found 507.2717.

(2R,6R)-2-(Digitoxigenoxy)-2,5-dihydro-6-methyl-2H-pyran-5-ol (18a/b)



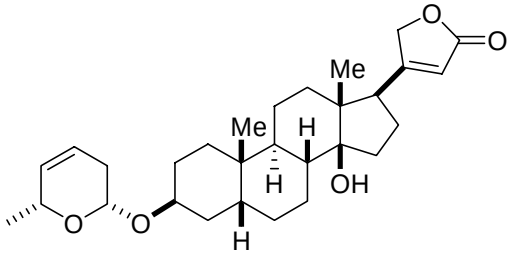
18a



18b

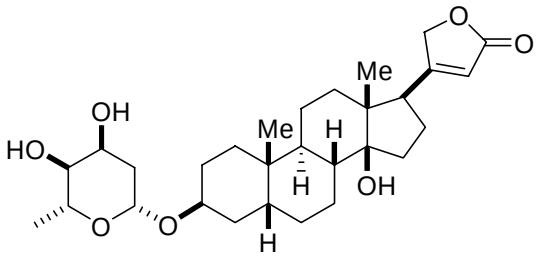
A CH_2Cl_2 (4 mL) solution of enone **17** (990 mg, 2.04 mmol) and $CeCl_3$ in MeOH solution (0.4 M, 4 mL) was cooled to -78 ^oC. $NaBH_4$ (77 mg, 2.04 mmol) was added and the reaction mixture was stirred at -78^oC for 3 h. The reaction mixture was diluted with ether (30 mL) and was quenched with 30 mL of satd aq $NaHCO_3$, extracted (3 x 30 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 55% EtOAc/hexanes to give allylic alcohols **18a/b** (893 mg, 1.84 mmol, 90%) as a white solid (diastereometric ratio 18a:18b = 1.5:1, inseparable by silica gel chromatography): R_f (60% EtOAc/hexanes) = 0.22; IR (thin film, cm^{-1}) 3448, 2933, 2871, 1780, 1741, 1618, 1446, 1378, 1320, 1180, 1135, 1049, 1024, 1004, 958, 751; ^1H NMR (600 MHz, $CDCl_3$):**18a**: δ 6.12 (ddd, *J* = 10.2, 4.8, 1.2 Hz, 1H), 5.86 (m, 1H), 5.80 (d, *J* = 10.2 Hz, 1H), 5.07 (m, 1H), 4.98 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.12 (dd, *J* = 4.2, 1.8 Hz, 1H), 4.114(s, 1H), 3.70 (qd, *J* = 6.6, 2.4Hz, 1H), 3.64 (br, 1H), 2.77 (dd, *J* = 9.6, 6.0 Hz, 1H), 2.25-2.05 (m, 3H), 1.29 (d, *J* = 6.0 Hz, 3H), 1.80-1.05 (m, 18H), 0.94 (s, 3H), 0.87 (s, 3H); **18b**: δ 5.93 (ddd, *J* = 10.2, 2.4, 2.4 Hz, 1H), 5.86 (m, 1H), 5.74 (ddd, *J* = 10.2, 1.2, 1.2 Hz, 1H), 5.14 (ddd, *J* = 1.8, 1.8, 1.8 Hz, 1H), 4.98 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.09 (m, 1H), 4.109 (s, 1H), 3.93 (br, 1H), 3.59(dq, *J* = 6.6, 6.6 Hz, 1H), 2.77 (dd, *J* = 9.6, 6.0 Hz, 1H), 2.25-2.05 (m, 3H), 1.35 (d, *J* = 6.0 Hz, 3H), 1.80-1.05 (m, 18H), 0.94 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) **18a**: δ 174.50, 174.46, 131.8, 130.9, 117.67, 96.1, 85.591, 73.43, 72.9, 71.4, 64.9, 50.90, 49.6, 41.9, 40.045, 36.4, 35.77, 35.19, 33.12, 30.20, 30.04, 26.9 (2C), 26.62, 23.64, 21.384, 21.151, 16.7, 15.8; **18b**: δ 174.52, 174.46, 131.7, 129.9, 117.66, 94.8, 85.598, 73.38, 73.4, 72.4, 68.7, 50.91, 49.6, 41.9, 40.052, 36.3, 35.76, 35.18, 33.13, 30.18, 30.06, 26.7 (2C), 26.66, 23.62, 21.380, 21.147, 18.4, 15.8; ESIHRMS Calcd for [$C_{29}H_{42}O_6Na^+$]: 509.2879, Found 509.2880.

(2R,6R)-2-(Digitoxigenoxy)-3,6-dihydro-6-methyl-2H-pyran (19)



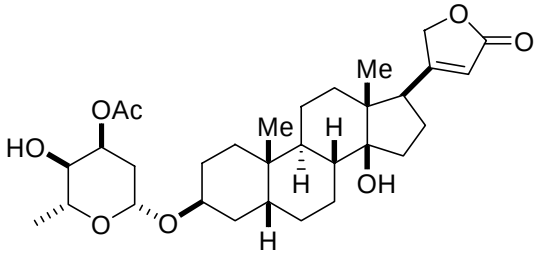
A flask was charged with dry *N*-methyl morpholine (NMM) 3.0 ml, triphenyl phosphine (1.75 g, 6.67 mmol) and was cooled to -30^{o}C under Ar atmosphere. Diethylazodicarboxylate (0.95 ml, 6.06 mmol) was added and the reaction was stirred for 5 min, allylic alcohol **18a/b** (985 mg, 2.02 mmol) was added in a 1M solution of NMM and the reaction mixture was stirred for 10 min, followed by addition of *o*-nitrobenzenesulfonyl hydrazide (NBSH) (1.23 g, 6.06 mmol). The reaction was stirred at -30 ^{o}C for 6h and was monitored by TLC, upon consumption of starting material, warm up to room temperature and stirred for another 1h. The reaction mixture was diluted with ether (30 mL) and was quenched with 30 mL of satd aq $NaHCO_3$, extracted (3 x 30 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 25% EtOAc/hexanes to give product **19** (760 mg, 1.61 mmol, 80%) as a white solid: R_f (30% EtOAc/hexanes) = 0.20; mp: 157-158 ^{o}C; $[\alpha]_D^{21}$ = -30.0 (*c* = 0.10, $CHCl_3$); IR (thin film, cm^{-1}) 3494, 2936, 2871, 1778, 1742, 1621, 1447, 1368, 1264, 1158, 1133, 1102, 1072, 1026, 974, 888, 781. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.86 (m, 1H), 5.66 (dddd, *J* = 10.2, 4.8, 2.4, 2.4 Hz, 1H), 5.55 (dddd, *J* = 10.2, 2.4, 1.2, 1.2 Hz, 1H), 4.99 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.70 (dd, *J* = 8.4, 3.0 Hz, 1H), 4.06 (m, 1H), 4.29 (m, 1H), 2.76 (m, 1H), 2.24-2.04 (m, 4H), 1.90-1.08 (m, 19H), 1.24 (d, *J* = 6.0 Hz, 3H), 0.92 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6, 174.5, 131.1, 123.0, 117.6, 96.7, 85.6, 73.4, 72.1, 70.7, 50.9, 49.6, 41.9, 40.1, 36.3, 35.7, 35.2, 33.1, 31.6, 30.2, 29.8, 26.9, 26.73, 26.65, 23.6, 21.4, 21.1, 21.03, 15.8; ESIHRMS Calcd for $[C_{29}H_{42}O_5Na^+]$: 493.2929, Found 493.2924.

Digitoxigen 2,6-dideoxy-β-D-ribo-hexopyranoside(20)



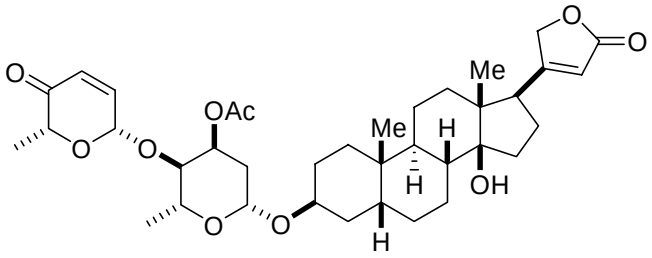
To a *t*-BuOH/acetone (4 mL) solution of olefin **19** (753 mg, 1.60 mmol) at 0 ^{o}C was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide / water (1.0 mL). Crystalline OsO_4 (4 mg, 1 mol %) was added and the reaction was stirred for 4 h. The reaction was quenched with adding EtOAc and satd. $NaHCO_3$. The organic layer was separated and concentrated. It was purified by a silica gel column using 90% EtOAc/hexanes. Pure fractions were combined, concentrated, and crystallized from acetone/hexanes to afford alcohol **20** as a white solid (868 mg, 1.72 mmol, 93%): R_f(EtOAc) = 0.25; $[\alpha]_D^{21}$ = - 6.8 (*c* = 0.65, MeOH); mp: 202-203 ^{o}C; IR (thin film, cm^{-1}) 3453, 2925, 2856, 1775, 1736, 1623, 1449, 1454, 1378, 1160, 1076, 1024, 951, 822; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.87 (m, 1H), 4.98 (d, *J* = 18.0 Hz, 1H), 4.87 (dd, *J* = 9.0, 1.8 Hz, 1H), 4.80 (d, *J* = 18.0 Hz, 1H), 4.13 (ddd, *J* = 3.0, 3.0, 3.0 Hz, 1H), 4.03 (m, 1H), 3.71 (dq, *J* = 9.0, 6.0 Hz, 1H), 3.34 (m, 1H), 2.77 (m, 1H), 2.33 (s, 1H), 2.20-2.00 (m, 4H), 1.29 (d, *J* = 6.0 Hz, 3H), 1.90-1.10 (m, 19H), 0.92 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.56, 174.52, 117.7, 95.4, 85.6, 73.5, 73.1, 72.7, 69.2, 68.3, 50.9, 49.6, 41.9, 40.1, 38.3, 36.3, 35.8, 35.2, 33.2, 30.2, 29.9, 26.9, 26.7, 26.6, 23.6, 21.4, 21.2, 18.1, 15.8; ESIHRMS Calcd for [$C_{29}H_{44}O_7Na^+$]: 527.2979, Found 527.2979.

Digitoxigen 3-*O*-acetyl-2,6-dideoxy-β-D-ribo-hexopyranoside (21)



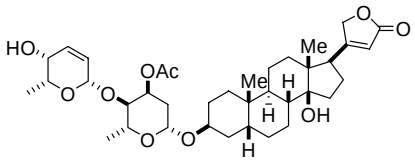
A round bottom flask containing a 0.5 M solution of diol **20** (620 mg, 1.23 mmol) in CH_2Cl_2 (3 ml) was stirring at room temperature. To this solution were added trimethylorthoacetate (0.47 mL, 3.69 mmol) and a catalytic amount of *p*-toluenesulfonic acid (12 mg, 61.5 μmol). The reaction was allowed to stir until starting material is gone. The solvent was removed under reduced pressure and the residue was dissolved in 6 ml THF/H_2O (1:1,v/v) solution. Then *p*-toluenesulfonic acid (120 mg, 0.62 mmol) was added. Stirring was continued until hydrolysis was complete as seen by TLC. The reaction mixture was quenched with 10 mL of satd aq $NaHCO_3$, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. It was purified by a silica gel column using 60% EtOAc/hexanes. Pure fractions were combined and concentrated to afford compound **21** (675 mg, 1.20 mmol, 98%) as a white solid: R_f (60% EtOAc/hexanes) = 0.14; $[\alpha]_D^{21}$ = + 1.7 (*c* = 1.15, $CHCl_3$); mp: 111-112 ^oC; IR (thin film, cm^{-1}) 3499, 2934, 2876, 1780, 1740, 1618, 1449, 1377, 1243, 1169, 1080, 1065, 1026, 1002, 948, 753, 666; ^1H NMR (600 MHz, $CDCl_3$) δ 5.86 (m, 1H), 5.28 (ddd, *J* = 3.6, 3.0, 3.0 Hz , 1H), 4.97 (d, *J* = 18.0 Hz ,1H), 4.80 (d, *J* = 18.0 Hz , 1H), 4.75 (dd, *J* = 9.0, 2.4 Hz, 1H), 4.01 (m, 1H), 3.67 (dq, *J* = 9.0, 6.0 Hz , 1H), 3.43 (dd, *J* = 9.6, 2.4 Hz , 1H), 2.76 (m, 1H), 2.20-2.00 (m, 4H), 2.13 (s, 3H), 1.90-1.10 (m, 19H), 1.29 (d, *J* = 6.0 Hz, 3H), 0.92 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.59, 174.51, 171.3, 117.6, 95.8, 85.6, 73.4, 73.1, 72.3, 71.4, 70.2, 50.9, 49.6, 41.8, 40.0, 36.3 (2C), 35.7, 35.2, 33.1, 30.1 (2C), 26.9, 26.64, 26.61, 23.6, 21.36, 21.2, 21.1, 18.1, 15.7; ESIHRMS Calcd for [$C_{31}H_{46}O_8Na^+$]: 569.3085, Found 569.3085.

Digitoxigen 3-*O*-acetyl-2,6-dideoxy-4-*O*-((2'R,6'R)-5',6'-dihydro-6'-methyl-5'-oxo-2H-pyran-2'-yl)-*β*-D-ribo-hexopyranoside (22)

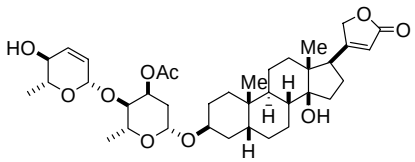


A CH_2Cl_2 (2 mL) solution of Boc pyranone **8a** (560 mg, 2.45 mmol) and alcohol **21** (670 mg, 1.23 mmol) was cooled to 0 °C. A CH_2Cl_2 (0.5 mL) solution of $Pd_2(DBA)_3$•$CHCl_3$ (63 mg, 2.5 mol%) and PPh_3 (64 mg, 10 mol%) was added to the reaction mixture at 0 °C. The reaction mixture was stirred at 0 °C for 8 hour. The reaction mixture was quenched with 10 mL of satd aq $NaHCO_3$, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 50% EtOAc/hexanes to give enone **22** (643 mg, 0.98 mmol, 80%) as a white solid: R_f (60% EtOAc/hexanes) = 0.24; mp: 119-120 °C; $[\alpha]_D^{21}$ = + 37.8 (*c* = 1.40, $CHCl_3$); IR (thin film, cm^{-1}) 3495, 2937, 2876, 1780, 1743, 1700, 1621, 1448, 1374, 1244, 1154, 1096, 1068, 1051, 1027, 1004, 755, 695; ^1H NMR (600 MHz, $CDCl_3$) δ 6.88 (dd, *J* = 10.2, 1.2 Hz, 1H), 6.11 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.86 (m, 1H), 5.41 (ddd, *J* = 3.6, 2.4, 2.4 Hz, 1H), 5.40 (dd, *J* = 1.2, 1.2 Hz, 1H), 4.97 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.79 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.76 (dd, *J* = 9.0, 1.8 Hz, 1H), 4.15 (q, *J* = 6.6 Hz, 1H), 4.01 (m, 1H), 3.90 (dq, *J* = 9.0, 6.0 Hz, 1H), 3.51 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.77 (m, 1H), 2.20-2.02 (m, 4H), 2.09 (s, 3H), 1.90-1.18 (m, 19H), 1.39 (d, *J* = 6.6 Hz, 3H), 1.31 (d, *J* = 6.0 Hz, 3H), 0.92 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.2, 174.5, 174.4, 170.2, 146.4, 128.8, 117.7, 97.0, 96.0, 85.6, 79.5, 75.2, 73.4, 73.1, 69.8, 69.0, 50.9, 49.6, 41.9, 40.1, 36.30, 36.26, 35.8, 35.2, 33.1, 30.15, 30.13, 26.9, 26.63, 26.60, 23.6, 21.4, 21.3, 21.1, 18.3, 16.3, 15.8; ESIHRMS Calcd for $[C_{37}H_{52}O_{10}Na^+]$: 679.3458, Found 679.3453.

Digitoxigen 3-*O*-acetyl -2,6-dideoxy-4-*O*-((2'R,6'R)-5',6'-dihydro-5'-hydroxyl-6'-methyl -2H-pyran-2'-yl)-β-D-ribo-hexopyranoside (23a/b)



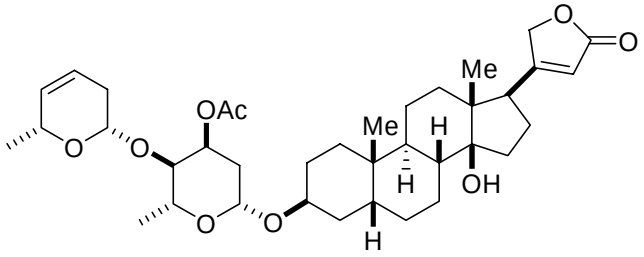
23a



23b

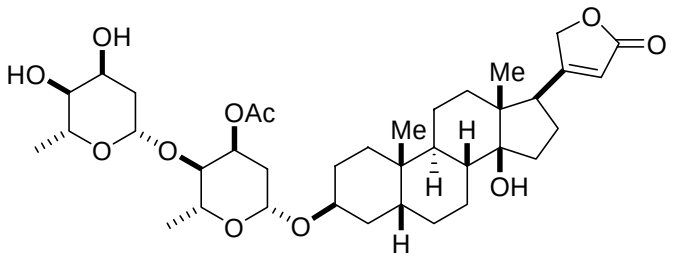
A CH_2Cl_2 (0.6 mL) solution of enone **22** (764 mg, 1.16 mmol) and $CeCl_3$ in MeOH solution (0.4 M, 1.2 mL) was cooled to -78 ^oC. $NaBH_4$ (44 mg, 1.16 mmol) was added and the reaction mixture was stirred at -78^oC for 3 h. The reaction mixture was diluted with ether (10 mL) and was quenched with 10 mL of H_2O, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 70% EtOAc/hexanes to give allylic alcohols **23a/b** (730 mg, 1.11 mmol, 95%) as a white solid (diastereometric ration **23a**:**23b** = 1.5:1, inseparable by silica gel chromatography): R_f (80% EtOAc/hexanes) = 0.33; IR (thin film, cm^{-1}) 3483, 2935, 2878, 1781, 1739, 1620, 1448, 1378, 1245, 1170, 1153, 1058, 1026, 1004, 914, 863, 732; ^1H NMR (600 MHz, $CDCl_3$): **23a**: δ 6.14 (ddd, *J* = 9.6, 5.4, 1.2 Hz, 1H), 5.84 (m, 1H), 5.72 (dd, *J* = 9.6, 1.2 Hz, 1H), 5.52 (ddd, *J* = 3.6, 3.0, 3.0 Hz, 1H), 5.11 (ddd, *J* = 1.8, 1.2, 1.2 Hz, 1H), 4.96 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.78 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.74 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.99 (m, 1H), 3.78 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.67 (qd, *J* = 6.6, 1.8 Hz, 1H), 3.57 (m, 1H), 3.42 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.75 (dd, *J* = 9.0, 6.0 Hz, 1H), 2.20-1.94 (m, 4H), 2.05 (s, 3H), 1.89-1.10 (m, 19H), 1.24 (d, *J* = 6.0 Hz, 3H), 1.23 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 3H), 0.84 (s, 3H); **23b**: δ 5.93 (ddd, *J* = 9.6, 1.8, 1.8 Hz, 1H), 5.84 (m, 1H), 5.75 (ddd, *J* = 9.6, 1.8, 1.8 Hz, 1H), 5.37 (ddd, *J* = 3.6, 3.0, 3.0 Hz, 1H), 5.14 (ddd, *J* = 1.8, 1.2, 1.2 Hz, 1H), 4.96 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.78 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.71 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.99 (m, 1H), 3.84 (m, 1H), 3.83 (qd, *J* = 9.6, 6.0 Hz, 1H), 3.53 (dq, *J* = 6.0, 6.0 Hz, 1H), 3.40 (dd, *J* = 9.6, 3.0 Hz, 1H), 2.75 (dd, *J* = 9.0, 6.0 Hz, 1H), 2.20-1.94 (m, 4H), 2.07 (s, 3H), 1.89-1.10 (m, 19H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) **23a** : δ 174.6, 174.5, 170.3(2C), 131.7, 129.4, 117.6, 98.2, 95.89, 85.5, 78.1, 73.4, 73.0, 71.4, 70.4, 69.2, 69.0, 50.9, 49.6, 41.8, 40.0, 36.42, 36.2, 35.7, 35.1, 33.1, 30.1, 26.9, 26.63, 26.59, 23.6, 21.34, 21.33, 21.1, 18.1, 16.7, 15.7; **23b**: δ 174.6, 174.5, 170.3(2C), 133.1, 128.1, 117.6, 97.4, 95.85, 85.5, 78.0, 74.5, 73.4, 70.1, 69.2, 68.4, 64.4, 50.9, 49.6, 41.8, 40.0, 36.37, 36.2, 35.7, 35.1, 33.1, 30.1, 26.9, 26.63, 26.59, 23.6, 21.34, 21.30, 21.1, 18.3, 18.2, 15.7; ESIHRMS Calcd for [$C_{37}H_{54}O_{10}Na^+$]: 681.3615, Found 681.3607.

Digitoxigen 3-*O*-acetyl-2,6-dideoxy-4-*O*-((2'R,6'R)-3',6'-dihydro-6'-methyl-2H-pyran-2'-yl)-β-D-ribo-hexopyranoside (24)



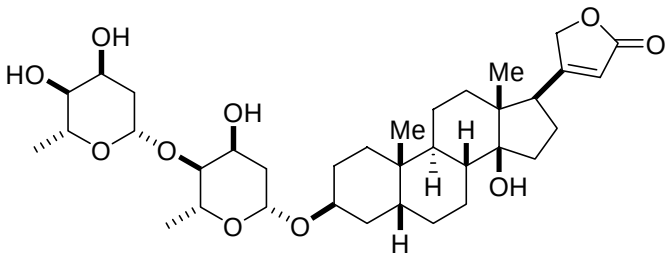
A flask was charged with dry *N*-methyl morpholine (NMM) 3.5 ml, triphenyl phosphine (951 mg, 3.63 mmol) and was cooled to -30 ^{o}C under Ar atmosphere. Diethylazodicarboxylate (0.52 ml, 3.30 mmol) was added and the reaction was stirred for 5 min, allylic alcohols **23a/b** (725 mg, 1.10 mmol) was added in a 1M solution of NMM and the reaction mixture was stirred for 10 min, followed by addition of *o*-nitrobenzenesulfonyl hydrazide (NBSH) (670 mg, 3.30 mmol). The reaction was stirred at -30 ^{o}C for 4 h and was monitored by TLC, upon consumption of starting material, warm up to room temperature and stirred for another 2 h. The reaction mixture was diluted with ether (20 mL) and was quenched with 10 mL of H_2O, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 85% Et_2O/hexanes to give product **24** (580 mg, 0.90 mmol, 82%) as a white solid: R_f (Et_2O) = 0.35; $[\alpha]_D^{21}$ = +28.3 (*c* = 1.20, $CHCl_3$); mp: 119-120 ^{o}C; IR (thin film, cm^{-1}) 3488, 2933, 2874, 1778, 1740, 1620, 1448, 1368, 1313, 1244, 1153, 1064, 1026, 1002, 973, 884, 784, 752, 684, 666. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.87 (m, 1H), 5.62 (dddd, *J* = 10.2, 5.4, 2.4, 2.4 Hz, 1H), 5.54 (dddd, *J* = 10.2, 4.8, 1.2 , 1.2 Hz, 1H), 5.39 (ddd, *J* = 3.6, 3.0, 3.0 Hz, 1H), 4.98 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.74 (dd, *J* = 9.0, 1.8 Hz, 1H), 4.66 (dd, *J* = 8.4, 3.6 Hz, 1H), 4.26 (m, 1H), 4.01 (m, 1H), 3.87 (dq, *J* = 9.0, 6.6 Hz, 1H), 3.35 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.77 (m, 1H), 2.21-2.03 (m, 5H), 2.11 (s, 3H), 1.90-1.19 (m, 20H), 1.27 (d, *J* = 6.6 Hz, 3H), 1.20 (d, *J* = 6.6 Hz, 3H), 0.92 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4, 173.4, 170.4, 131.2, 122.2, 117.7, 100.2, 96.0, 85.6, 79.3, 73.4, 73.0, 70.9, 70.2, 69.2, 50.9, 49.6, 41.9, 40.1, 36.4, 36.3, 35.8, 35.2, 33.1, 30.9, 30.173, 30.170, 26.9, 26.7, 26.6, 23.6, 22.6, 21.4, 21.2, 20.8, 18.2, 15.8; ESIHRMS Calcd for [$C_{37}H_{54}O_9Na^+$]: 665.3666, Found 665.3658.

Digitoxigen *O*-[2',6'-dideoxy-*β*-D-ribo-hexopyranosyl]-(1→4)-(3-*O*-acetyl-2,6-dideoxy-*β*-D-ribo-hexopyranoside) (25)



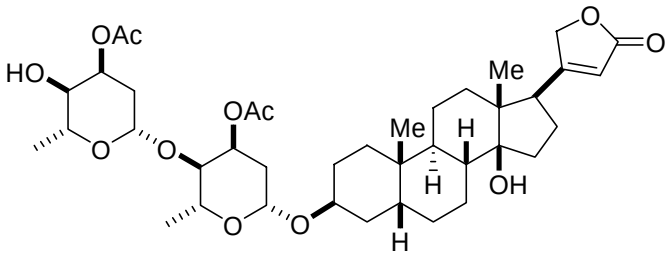
To a *t*-BuOH/acetone (1:1, 2 mL) solution of olefin **24** (530 mg, 0.824 mmol) at 0 ^{o}C was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide / water (0.8 mL). Crystalline OsO_4 (2.2 mg, 1 mol %) was added and the reaction was stirred for 8 h. The reaction was quenched with adding EtOAc and satd. $NaHCO_3$. The organic layer was separated and concentrated. It was purified by a silica gel column using EtOAc. Pure fractions were combined and concentrated to afford alcohol **25** (507 mg, 0.75 mmol, 91%) as a white solid: R_f(EtOAc) = 0.33; $[\alpha]_D^{21}$ = +23.5 (*c* = 2.25, $CHCl_3$); IR (thin film, cm^{-1}) 3467, 2936, 1780, 1741, 1618, 1449, 1370, 1246, 1164, 1023, 752, 666; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.86 (m, 1H), 5.36 (ddd, *J* = 3.6, 3.0, 3.0 Hz, 1H), 4.98 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.83 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.80 (d, *J* = 18.0, 1.2 Hz , 1H), 4.72 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.07 (ddd, *J* = 3.6, 3.0, 3.0 Hz, 1H), 3.99 (m, 1H), 3.82 (dq, *J* = 9.0, 6.0 Hz, 1H), 3.67 (dq, *J* = 9.0, 6.0 Hz, 1H), 3.32 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.25 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.76 (m, 1H), 2.08 (s, 3H), 2.20-2.02(m, 5H), 1.90-1.20 (m, 20H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H), 0.91 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.7, 174.6, 170.4, 117.6, 98.6, 95.9, 85.6, 79.5, 73.5, 73.0, 72.8, 70.0, 69.3, 69.1, 68.1, 50.9, 49.6, 41.8, 40.0, 37.6, 36.228, 36.223, 35.7, 35.1, 33.1, 30.1(2C), 26.9, 26.6, 26.6, 23.6, 21.4(2C), 21.1, 18.2, 18.0, 15.7; ESIHRMS Calcd for $[C_{37}H_{56}O_{11}Na^+]$: 699.3720, Found 699.3712.

Digitoxigen *O*-[2',6'-dideoxy-β-D-ribo-hexopyranosyl]-(1→4)- (2,6-dideoxy-β-D-ribo-hexopyranoside) (26)



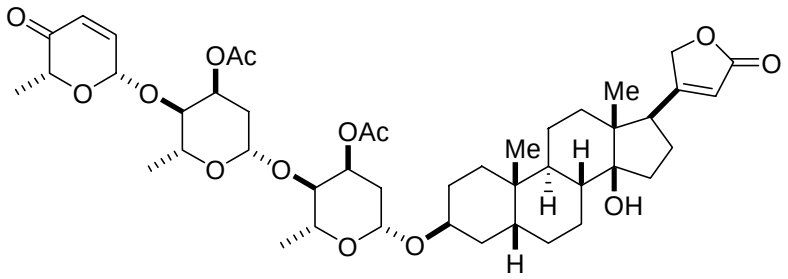
To a MeOH/H_2O (0.3 mL, 4:1, 1M) solution of alcohol **25** (17 mg, 25 μmol) at room temperature was added LiOH·H_2O (1.6 mg, 38 μmol) and the reaction was stirred for 3 h. The reaction was quenched with adding 5 mL pH = 6.0 buffering solution. The mixture was extracted with CH_2Cl_2 (3×5 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. It was purified by a silica gel column using EtOAc. Pure fractions were combined and concentrated, and further crystallized from acetone/hexanes to afford **26** (13 mg, 20.5 μmol, 82%) as a white solid: R_f(EtOAc) = 0.27; mp: 230-231 ^oC; $[\alpha]_D^{21}$ = + 6.0 (*c* = 0.40, $CHCl_3$); IR (thin film, cm^{-1}) 3450, 2933, 2876, 1778, 1740, 1621, 1449, 1380, 1165, 1132, 1067, 1013, 867, 754, 667; ^1H NMR (600 MHz, $CDCl_3$) δ 5.87 (m, 1H), 4.98 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.91 (dd, *J* = 9.6, 2.4 Hz, 1H), 4.86 (dd, *J* = 9.6, 2.4 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.24 (ddd, *J* = 3.6, 3.0, 3.0Hz, 1H), 4.13 (ddd, *J* = 3.6, 3.0, 3.0Hz, 1H), 4.02 (m, 1H), 3.77 (dq, *J* = 9.0, 6.0 Hz, 1H), 3.66 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.31 (m, 1H), 3.24 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.02 (s, 1H), 2.77 (m, 1H), 2.33 (s, 1H), 2.20-2.00 (m, 5H), 1.90-1.20 (m, 20H), 1.29 (d, *J* = 6.0 Hz, 3H), 1.23 (d, *J* = 6.0 Hz, 3H), 0,92 (s, 3H), 0,87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.52, 174.48, 117.7, 98.2, 95.4, 85.6, 82.7, 73.4, 72.8, 72.6, 69.5, 68.2, 68.1, 66.5, 51.0, 49.6, 41.9, 40.1, 37.9, 37.2, 36.2, 35.8, 35.2, 33.2, 30.2, 29.8, 26.9, 26.7, 26.6, 23.6, 21.4, 21.2, 18.2, 18.1, 15.8; ESIHRMS Calcd for [$C_{35}H_{54}O_{10}Na^+$]: 657.3615, Found 657.3608.

Digitoxigen *O*-[3'-*O*-acetyl-2',6'-dideoxy-*β*-D-ribo-hexopyranosyl]-(1→4)- (3-*O*-acetyl-2,6-dideoxy-*β*-D-ribo-hexopyranoside) (27)



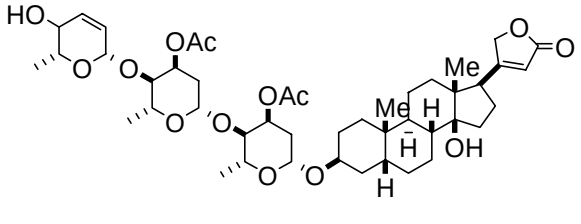
A round bottom flask containing a 0.5 M solution of alcohol **25** (391 mg, 0.578 mmol) in CH_2Cl_2 (2.5 ml) was stirring at room temperature. To this solution were added trimethylorthoacetate (0.22 mL, 1.73 mmol) and a catalytic amount of *p*-toluenesulfonic acid (5 mg, 29 μmol). The reaction was allowed to stir until starting material was gone. The solvent was removed under reduced pressure and the residue was dissolved in 3 ml THF/H_2O (1:1, v/v) solution. Then *p*-toluenesulfonic acid (55 mg, 0.29 mmol) was added. Stirring was continued until hydrolysis was complete as seen by TLC. The reaction was quenched with adding EtOAc and satd. $NaHCO_3$. The organic layer was separated and concentrated. It was purified by a silica gel column using 90% EtOAc/hexanes. Pure fractions were combined and concentrated to afford compound **27** (413 mg, 0.574 mmol, 99%) as a white solid: R_f (EtOAc) = 0.44; mp: 139-140 ^oC; $[\alpha]_D^{21}$ = + 32.5 (*c* = 1.10, $CHCl_3$); IR (thin film, cm^{-1}) 3460, 2972, 2937, 2876, 1780, 1740, 1619, 1449, 1371, 1318, 1244, 1167, 1066, 1024, 1004, 949, 868, 752; ^1H NMR (600 MHz, $CDCl_3$) δ 5.86 (m, 1H), 5.37 (ddd, *J* = 3.0, 3.0, 3.0 Hz , 1H), 5.25 (ddd, *J* = 3.0, 3.0, 3.0 Hz , 1H), 4.97 (dd, *J* = 18.0, 1.2 Hz ,1H), 4.79 (dd, *J* = 18.0, 1.2 Hz ,1H), 4.725 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.718 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.00 (m, 1H), 3.82 (dq, *J* = 9.0, 6.0 Hz , 1H), 3.64 (dq, *J* = 9.6, 6.0 Hz , 1H), 3.36 (ddd, *J* = 9.0, 6.0, 3.0 Hz , 1H), 3.32 (dd, *J* = 9.0, 3.0 Hz , 1H), 2.76 (m, 1H), 2.20-1.96 (m, 5H), 2.13 (s, 3H), 2.09 (s, 3H), 1.90-1.15 (m , 20H), 1.241 (d, *J* = 6.0 Hz, 3H), 1.240 (d, *J* = 6.0 Hz, 3H), 0.915 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.5, 174.4, 171.2, 170.2, 117.7, 98.5, 95.9, 85.6, 79.5, 73.4, 73.0, 72.1, 71.1, 70.2, 69.8, 69.0, 50.9, 49.6, 41.8, 40.0, 36.2 (2C), 35.8, 35.7, 35.2, 33.1, 30.14, 30.12, 26.9, 26.63, 26.59, 23.6, 21.4, 21.3, 21.1 (2C), 18.2, 17.9, 15.7; ESIHRMS Calcd for [$C_{39}H_{58}O_{12}Na^+$]:741.3826, Found 741.3819.

Digitoxigen *O*-[3'-*O*-acetyl -2',6'-dideoxy-4'-*O*-((2''R,6''R)-5'',6''-dihydro-6''-methyl-5''-oxo-2H-pyran-2''-yl)-β-D-ribo-hexopyranosyl]-(1→4)- (3-*O*-acetyl-2,6-dideoxy-β-D-ribo-hexopyranoside) (28)

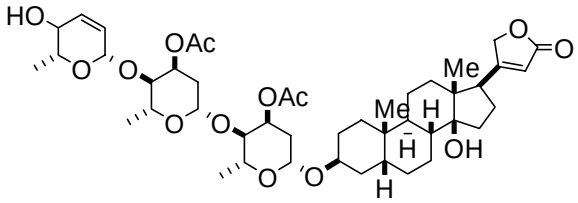


A CH_2Cl_2 (1.0 mL) solution of Boc pyranone **8a** (418 mg, 1.83 mmol) and alcohol **27** (410 mg, 0.57 mmol) was cooled to 0 °C. A CH_2Cl_2 (0.3 mL) solution of $Pd_2(DBA)_3$•$CHCl_3$ (15 mg, 2.5 mol%) and PPh_3 (15 mg, 10 mol%) was added to the reaction mixture at 0 °C. The reaction mixture was stirred at 0 °C for 8 hour. The reaction mixture was quenched with 10 mL of saturated aqeous $NaHCO_3$, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 58% EtOAc/hexanes to give enone **28** (425 mg, 0.513 mmol, 90%) as a white solid: R_f (60% EtOAc/hexanes) = 0.27; mp: 174-175 °C; $[\alpha]_D^{21}$ = + 58.3 (*c* = 1.40, $CHCl_3$); IR (thin film, cm^{-1}) 3524, 2980, 2938, 2876, 1780, 1744, 1702, 1622, 1449, 1372, 1243, 1156, 1094, 1056, 1026, 1004, 950, 756; ^1H NMR (600 MHz, $CDCl_3$) δ 6.87 (dd, *J* = 10.2, 1.8 Hz, 1H), 6.10 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.86 (m, 1H), 5.40-5.36 (m, 3H), 4.97 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.79 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.73 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.71 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.14 (q, *J* = 6.6 Hz, 1H), 3.99 (m, 1H), 3.86 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.81 (dq, *J* = 9.6, 6.0 Hz, 1H), 3. 44 (dd, *J* = 9.0, 3.0 Hz, 1H), 3. 31 (dd, *J* = 9.6, 3.0 Hz, 1H), 2.76 (m, 1H), 2.20-2.00 (m, 5H), 2.09 (s, 3H), 2.08 (s, 3H), 1.90-1.15 (m, 20H), 1.38 (d, *J* = 6.6 Hz, 3H), 1.25 (d, *J* = 6.6 Hz, 3H), 1.23 (d, *J* = 6.0 Hz, 3H), 0.91 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 174.5, 174.4, 170.2, 170.1, 146.2, 128.7, 117.6, 98.7, 97.1, 95.9, 85.5, 79.6, 79.2, 75.1, 73.4, 73.0, 70.0, 69.7, 68.99, 68.97, 50.9, 49.6, 41.8, 40.0, 36.3, 36.2, 35.9, 35.7, 35.1, 33.1, 30.1(2C), 26.9, 26.62 26.59, 23.6, 21.4, 21.3, 21.2, 21.1, 18.2, 18.0, 16.3, 15.7; ESIHRMS Calcd for $[C_{45}H_{64}O_{14}Na^+]$: 851.4194, Found 851.4183.

Digitoxigen *O*-[3'-*O*-acetyl-2',6'-dideoxy- 4'-*O*-((2''R,6''R)-5'',6''-dihydro-6''-methyl-5''-hydroxyl-2H-pyran-2''-yl)-*β*-D-ribo-hexopyranosyl]-(1→4)- (3-*O*-acetyl-2,6-dideoxy-*β*-D-ribo-hexopyranoside) (29a/b)



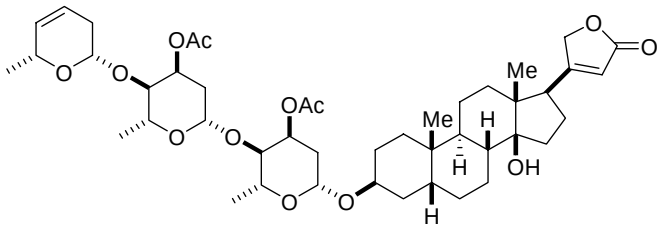
29a



29b

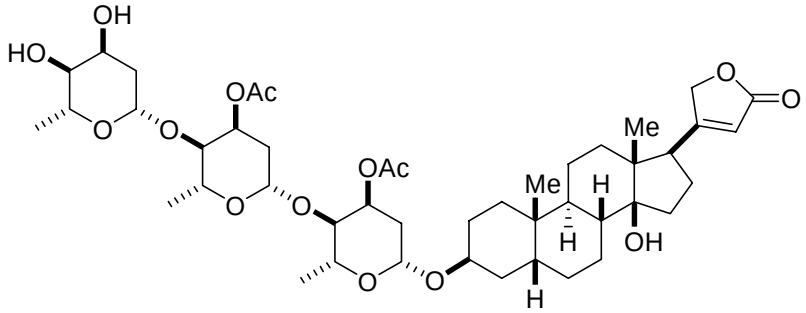
A CH_2Cl_2 (1.2 mL) solution of enone **40** (405 mg, 0.488 mmol) and $CeCl_3$ in MeOH solution (0.4 M, 1.2 mL) was cooled to -78 ^oC. $NaBH_4$ (18.5 mg, 0.49 mmol) was added and the reaction mixture was stirred at -78^oC for 3 h. The reaction mixture was diluted with ether (20 mL) and was quenched with 10 mL of satd aq $NaHCO_3$, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 85% EtOAc/hexanes to give allylic alcohols **29a/b** (397 mg, 0.478 mmol, 98%) as a white solid (diastereomeric ratio **29a**:**29b** = 1.7:1, inseparable in chromatography): R_f (90% EtOAc/hexanes) = 0.33; IR (thin film, cm^{-1}) 3480, 2972, 2934, 2876, 1780, 1742, 1621, 1449, 1372, 1316, 1244, 1155, 1060, 1025, 1008, 755, 668; ^1H NMR (600 MHz, $CDCl_3$): **29a**: δ 6.14 (ddd, *J* = 9.6, 5.4, 1.2 Hz, 1H), 5.84 (m, 1H), 5.70 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.51 (ddd, *J* = 3.6, 3.0, 3.0Hz, 1H), 5.36 (ddd, *J* = 3.6, 3.0, 3.0 Hz, 1H), 5.10 (ddd, *J* = 1.2, 1.2, 1.2 Hz, 1H), 4.96 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.78 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.710 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.706 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.98 (m, 1H), 3.80 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.74 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.66 (qd, *J* = 6.0, 1.8 Hz, 1H), 3.57 (m, 1H), 3.37 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.30 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.75 (dd, *J* = 9.6, 6.0 Hz, 1H), 2.20-1.96 (m, 5H), 2.073 (s, 3H), 2.05 (s, 3H), 1.90-1.12 (m, 20H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.19 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 3H), 0.85 (s, 3H); **29b**: δ 5.92 (ddd, *J* = 10.2, 2.4, 1.8 Hz, 1H), 5.84 (m, 1H), 5.74 (ddd, *J* = 10.2, 2.4, 1.8 Hz, 1H), 5.35 (m, 2H), 5.12 (ddd, *J* = 1.8, 1.8, 1.2 Hz, 1H), 4.96 (dd, *J* = 18.0, 1.2 Hz, 1H), 4.78 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.70 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.67 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.98 (m, 1H), 3.84 (m, 1H), 3.79 (m, 2H), 3.52 (dq, *J* = 6.0, 6.0 Hz, 1H), 3.33 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.28 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.75 (dd, *J* = 9.6, 6.0 Hz, 1H), 2.20-1.96 (m, 5H), 2.071 (s, 3H), 2.066 (s, 3H), 1.90-1.12 (m, 20H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.21 (d, *J* = 6.0 Hz, 3H), 1.20 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) **29a** : δ 174.5, 174.4, 170.3 (2C), 131.7, 129.2, 117.6, 98.72, 98.2, 95.9, 85.6, 79.46, 77.8, 73.4, 73.0, 70.2, 69.06(2C), 69.04, 68.4, 50.9, 49.6, 41.8, 40.0, 36.28, 36.24, 36.0, 35.7, 35.1, 33.1, 30.1(2C), 26.9, 26.63, 26.59, 23.6, 21.35, 21.34, 21.30, 21.1, 18.21, 17.9, 16.7, 15.7; **29b**: δ 174.5, 174.4, 170.2 (2C), 132.9, 128.1, 98.70, 97.6, 95.9, 85.6, 79.53, 78.0, 74.5, 73.4, 71.4, 69.98, 69.94, 69.2, 68.4, 64.4, 50.9, 49.6, 41.8, 40.0, 36.25, 36.24, 35.9, 35.7, 35.1, 33.1, 30.1(2C), 26.9, 26.63, 26.59, 23.6, 21.35, 21.34, 21.27, 21.1, 18.19, 18.16, 18.0, 15.7; ESIHRMS Calcd for [$C_{45}H_{66}O_{14}Na^+$]: 853.4350, Found 853.4339.

Digitoxigen *O*-[3'-*O*-acetyl-2',6'-dideoxy- 4'-*O*-((2''R,6''R)-3'',6''-dihydro-6''-methyl-2H-pyran-2''-yl)-β-D-ribo-hexopyranosyl]-(1→4)- (3-*O*-acetyl-2,6-dideoxy-β-D-ribo-hexopyranoside) (30)



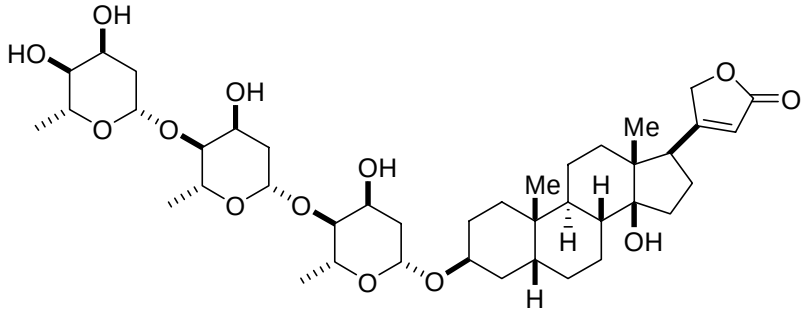
A flask was charged with dry *N*-methyl morpholine (NMM) 2.0 ml, triphenyl phosphine (411 mg, 1.57 mmol) and was cooled to -30 ^{o}C under Ar atmosphere. Diethylazodicarboxylate (0.22 ml, 1.42 mmol) was added and the reaction was stirred for 5 min, allylic alcohols **29a/b** (395 mg, 0.475 mmol) was added in a 1 M solution of NMM and the reaction mixture was stirred for 10 min, followed by addition of o-nitrobenzenesulfonyl hydrazide (NBSH) (289 mg, 1.42 mmol). The reaction was stirred at -30 ^{o}C for 4 h and was monitored by TLC, upon consumption of starting material, warm up to room temperature and stirred for another 1 h. The reaction mixture was diluted with ether (20 mL) and was quenched with 10 mL of H_2O, extracted (3 x 10 mL) with Et_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 88% Et_2O/hexanes to give product **30** (345 mg, 0.42 mmol, 89%) as a white solid: R_f (Et_2O) = 0.33; mp: 144-145 ^{o}C; $[\alpha]_D^{21}$ = +48.2 (c = 1.50, $CHCl_3$); IR (thin film, cm^{-1}) 3516, 2967, 2935, 2871, 1782, 1742, 1621, 1449, 1369, 1316, 1243, 1155, 1091, 1064, 1047, 1026, 1005, 950, 882, 753; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.86 (m, 1H), 5.61 (dddd, J = 9.6, 4.8, 2.4, 2.4 Hz, 1H), 5.53 (dddd, J = 10.2, 2.4, 1.2, 1.2 Hz, 1H), 5.38 (ddd, J = 3.6, 3.0, 3.0 Hz, 1H), 5.36 (ddd, J = 3.6, 3.0, 3.0 Hz, 1H), 4.97 (dd, J = 18.0, 1.2 Hz, 1H), 4.79 (dd, J = 18.0, 1.2 Hz, 1H), 4.72 (dd, J = 9.6, 1.8 Hz, 1H), 4.69 (dd, J = 9.6, 1.8 Hz, 1H), 4.65 (dd, J = 8.4, 3.6 Hz, 1H), 4.25 (m, 1H), 3.99 (m, 1H), 3.84 (dq, J = 9.0, 6.0 Hz, 1H), 3.82 (dq, J = 9.6, 6.0 Hz, 1H), 3.31 (dd, J = 9.6, 3.0 Hz, 1H), 3.28 (dd, J = 9.6, 3.0 Hz, 1H), 2.76 (m, 1H), 2.20-2.02 (m, 6H), 2.10 (s, 3H), 2.09 (s, 3H), 1.90-1.15 (m, 21H), 1.23 (d, J = 6.6 Hz, 3H), 1.22 (d, J = 6.6 Hz, 3H), 1.20 (d, J = 6.6 Hz, 3H), 0.92 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.45, 174.41, 170.3, 170.2, 131.1, 122.2, 117.7, 100.3, 98.8, 95.9, 85.6, 79.5, 79.0, 73.4, 73.0, 70.9, 70.10, 70.06, 69.2, 69.1, 50.9, 49.6, 41.9, 40.1, 36.30, 36.25, 35.9, 35.8, 35.2, 33.1, 30.9, 30.2 (2C), 26.9, 26.65, 26.61, 23.6, 21.37, 21.35, 21.34, 21.1, 20.8, 18.2, 18.0, 15.8; ESIHRMS Calcd for [$C_{45}H_{66}O_{13}Na^{+}$]: 837.4401, Found 837.4390.

Digitoxigen *O*-[2'',6''-dideoxy-β-D-ribo-hexopyranosyl]– (1→4)-*O*-[3'-*O*-acetyl-2',6'-dideoxy-β-D-ribo-hexopyranosyl]–(1→4)-(3-*O*-acetyl-2,6-dideoxy-β-D-ribo-hexopyranoside) (31)



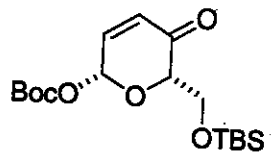
To a CH_2Cl_2 (0.8 mL) solution of olefin **30** (115 mg, 0.14 mmol) at 0 ^oC was added a solution of (50% w/v) of *N*-methyl morpholine *N*-oxide / water (100 μL). Crystalline OsO_4 (0.4 mg, 1 mol %) was added and the reaction was stirred for 4 h. The reaction was concentrated and was purified by a silica gel column using EtOAc. Pure fractions were combined and concentrated to afford alcohol **31** (110 mg, 0.13 mmol, 91%) as a white solid: R_f(EtOAc) = 0.31; mp: 162-163 ^oC; $[\alpha]_D^{21}$= +47.2 (*c* = 1.0, $CHCl_3$); IR (thin film, cm^{-1}) 3494, 2962, 2934, 2881, 1780, 1741, 1624, 1449, 1370, 1246, 1164, 1064, 1024, 948, 870, 753; ^1H NMR (600 MHz, $CDCl_3$) δ 5.86 (m, 1H), 5.37 (ddd, *J* = 3.0, 3.0, 3.0 Hz, 1H), 5.33 (ddd, *J* = 3.0, 3.0, 3.0 Hz, 1H), 4.98 (dd, *J* = 18.0, 1.8 Hz , 1H), 4.82 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.2 Hz , 1H), 4.71 (dd, *J* = 9.0, 1.8 Hz, 1H), 4.67 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.08 (ddd, *J* = 3.0, 3.0, 3.0 Hz , 1H), 3.99 (m, 1H), 3.82 (dq, *J* = 9.0, 6.0 Hz, 1H), 3.79 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.66 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.29 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.26 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.25 (ddd, *J* = 9.6, 6.0, 3.0 Hz, 1H), 2.76 (m, 1H), 2.20-2.01 (m, 6H), 2.09 (s, 6H), 1.90-1.18 (m, 21H), 1.22 (d, *J* = 6.0 Hz, 6H), 1.19 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.7, 174.6, 170.33, 170.27, 117.6, 98.76, 98.71, 95.8, 85.6, 79.6, 79.2, 73.5, 73.0, 72.8, 70.02, 69.95, 69.3, 69.08, 69.05, 68.0, 50.9, 49.6, 41.8, 40.0, 37.7, 36.250, 36.245, 35.9, 35.7, 35.2, 33.1, 30.14, 30.12, 26.9, 26.63, 26.60, 23.6, 21.37, 21.34, 21.32, 21.1, 18.2, 17.97, 17.95, 15.8; ESIHRMS Calcd for $[C_{45}H_{68}O_{15}Na^+]$: 871.4456, Found 871.4448.

Digitoxin (1)

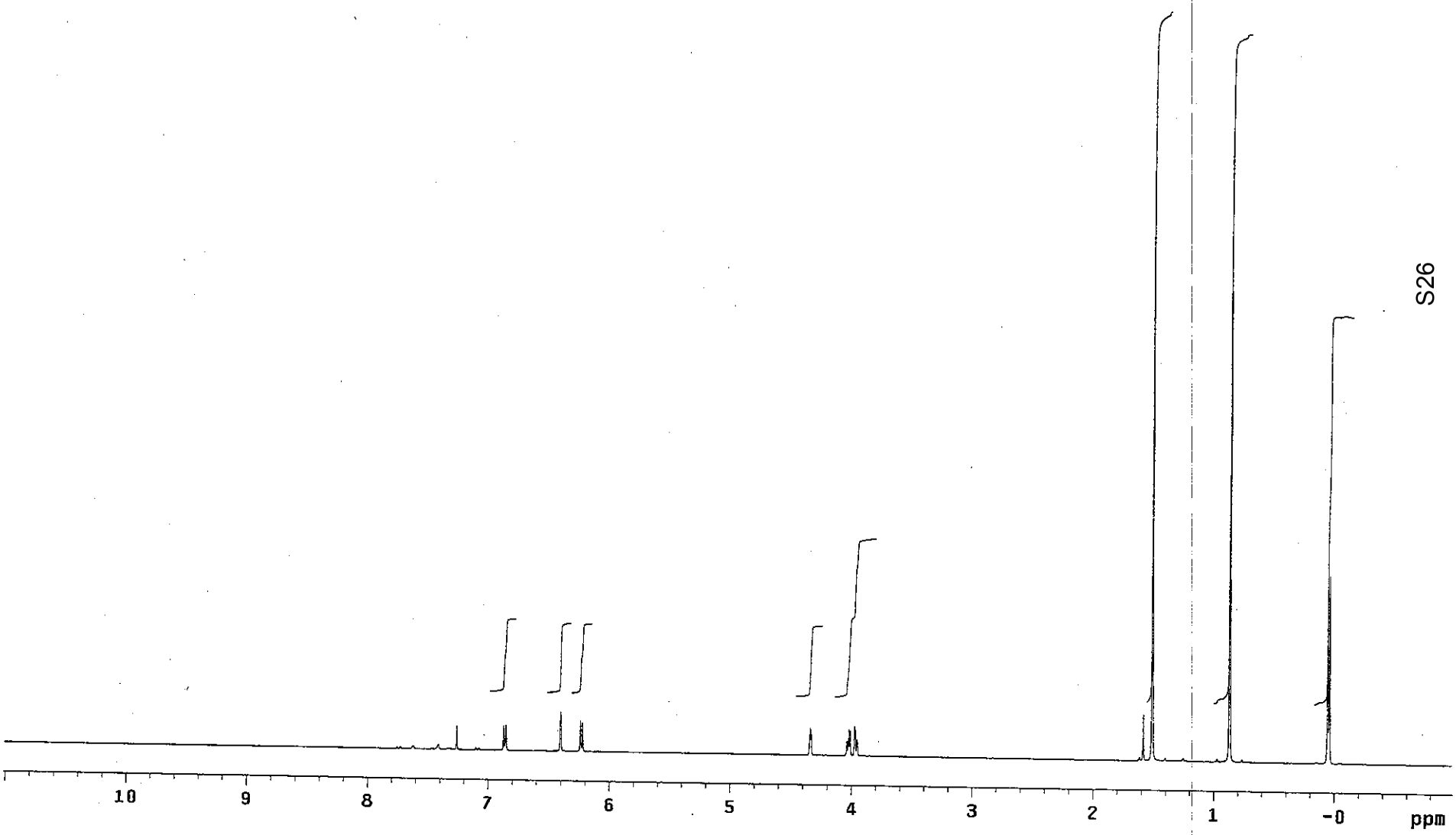


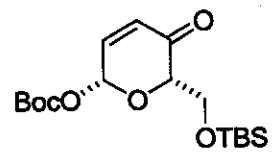
To a MeOH/H_2O (2 mL, 4:1) solution of diacetate **31** (20 mg, 23.5 μmol) at room temperature was added LiOH·H_2O (3 mg, 70 μmol) and the reaction was stirred for 2 h. The reaction was quenched with adding 5 mL pH = 6.0 buffering solution. The mixture was extracted with CH_2Cl_2 (3×5 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. It was purified by a silica gel column using 5% MeOH/EtOAc. Pure fractions were combined and concentrated, and the product was crystallized by acetone/hexanes to afford digitoxin **1** (15 mg, 19.6 μmol, 83%) as a white crystal: R_f (EtOAc) = 0.20; mp: 253-254 °C; $[\alpha]_D^{21}$ = +18.0 (*c* = 0.20, $CHCl_3$); IR (thin film, cm^{-1}) 3466, 2926, 2856, 1777, 1736, 1449, 1378, 1368, 1163, 1128, 1068, 1013, 991, 869, 732; ^1H NMR (600 MHz, $CDCl_3$) δ 5.87 (m, 1H), 4.98 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.91 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.89 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.86 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.80 (dd, *J* = 18.0, 1.8 Hz, 1H), 4.25 (ddd, *J* = 3.0, 3.0, 3.0 Hz, 1H), 4.24 (ddd, *J* = 3.0, 3.0, 3.0 Hz, 1H), 4.13 (m, 1H), 4.02 (m, 1H), 3.83 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.78 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.76 (dq, *J* = 9.6, 6.0 Hz, 1H), 3.31 (ddd, *J* = 9.6, 6.0, 3.0 Hz, 1H), 3.24 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.20 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.03 (s, 1H), 2.96 (s, 1H), 2.39 (s, 1H), 2.77 (m, 1H), 2.19-1.99 (m, 6H), 2.02 (s, 1H), 2.01 (s, 1H), 1.90-1.18 (m, 21H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.223 (d, *J* = 6.0 Hz, 3H), 1.221 (d, *J* = 6.0 Hz, 3H), 0.92 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.51, 174.48, 117.7, 98.3, 98.2, 95.4, 85.6, 82.6, 82.2, 73.4, 72.7 (2C) 72.5, 69.5, 68.3, 68.11, 68.08, 66.5, 66.4, 51.0, 49.6, 41.9, 40.1, 37.8, 37.2, 36.7, 36.2, 35.8, 35.2, 33.2, 30.2, 29.8, 26.9, 26.7, 26.5, 23.6, 21.4, 21.2, 18.16, 18.13, 15.8; ESIHRMS Calcd for $[C_{41}H_{64}O_{13}Na^+]$: 787.4245, Found 787.4237.

Section C: ^{1}H NMR and ^{13}C NMR Spectra

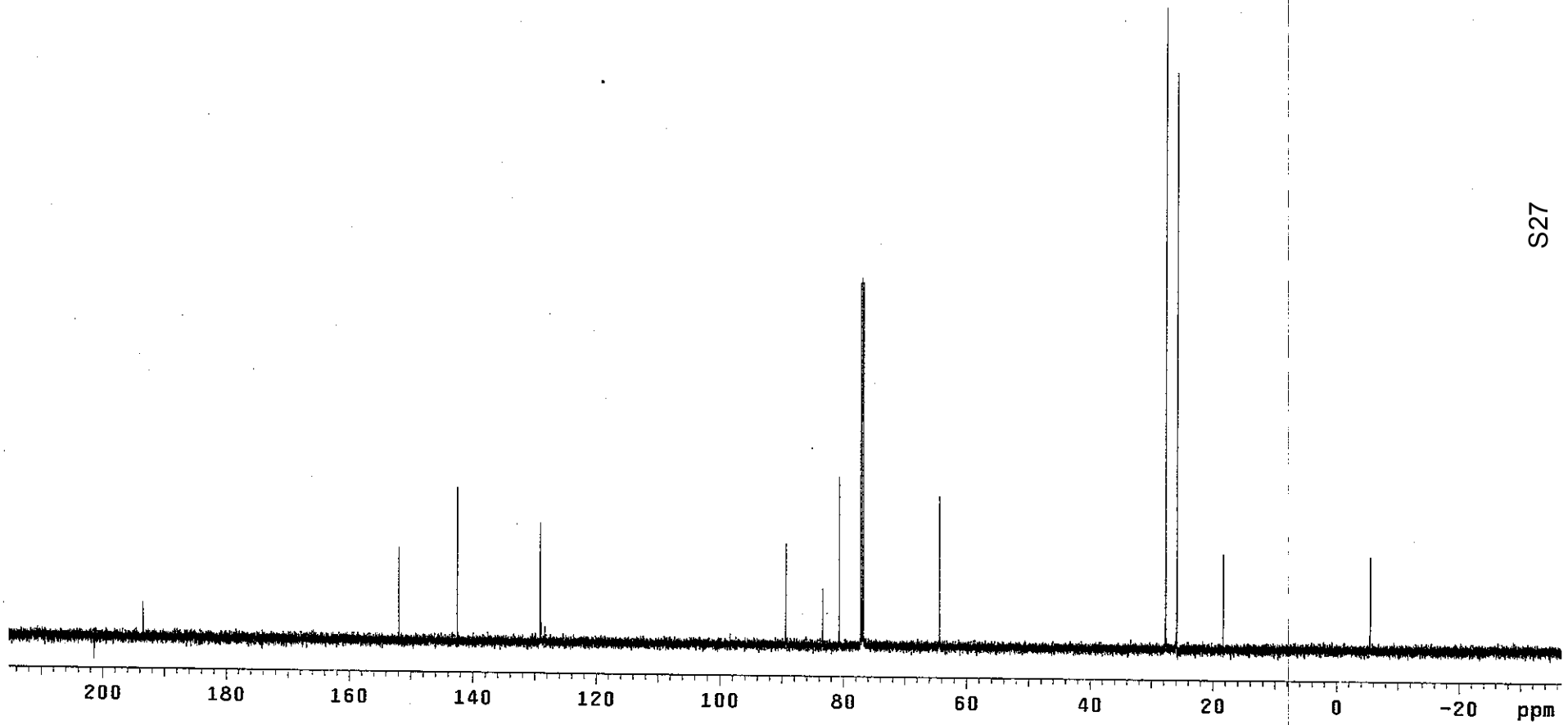


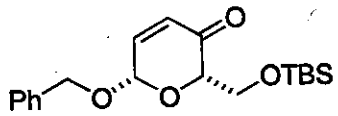
^{1}H NMR (600 MHz, $CDCl_3$)



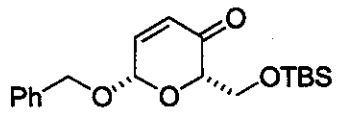


^{13}C NMR (67.5 MHz, $CDCl_3$)





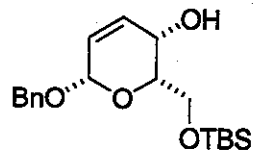
^{1}H NMR (600 MHz, $CDCl_3$)



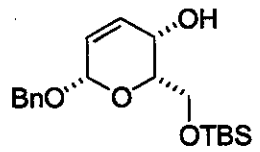
^{13}C NMR (67.5 MHz, $CDCl_3$)

220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0

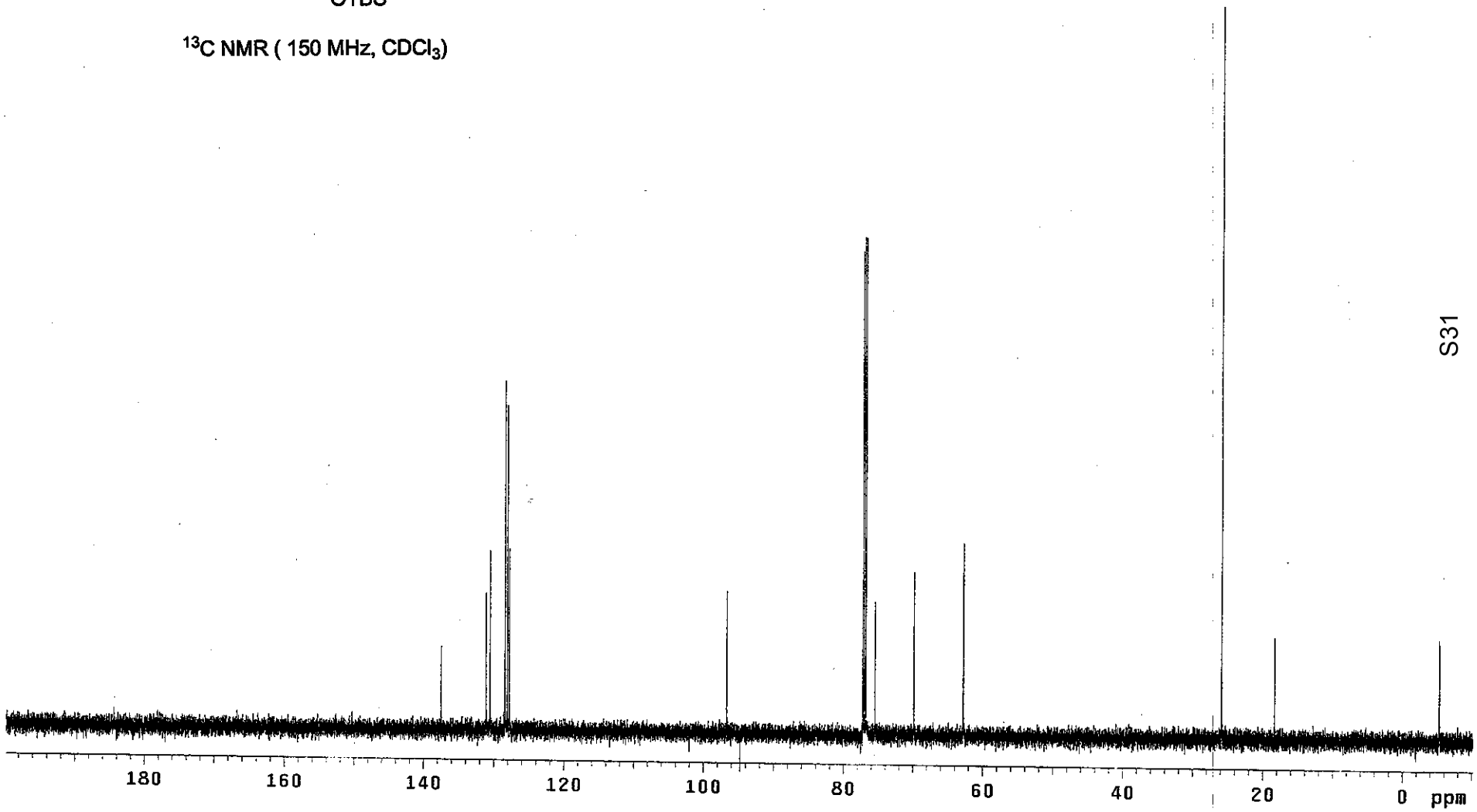
X : parts per Million : 13C

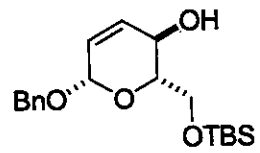


^{1}H NMR (600 MHz, $CDCl_3$)

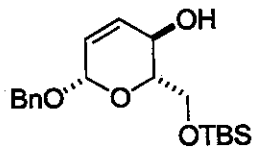


^{13}C NMR (150 MHz, $CDCl_3$)

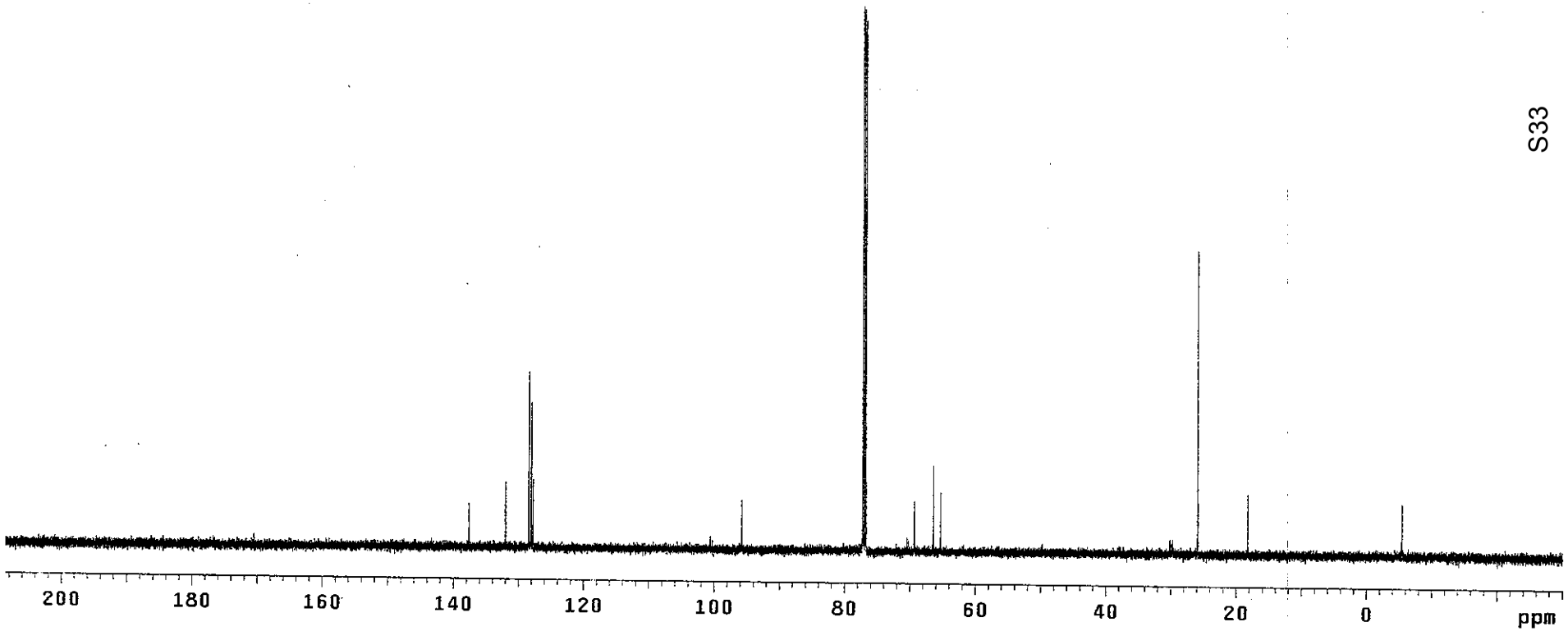


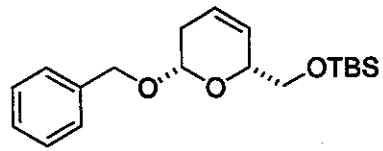


^{1}H NMR (600 MHz, $CDCl_3$)

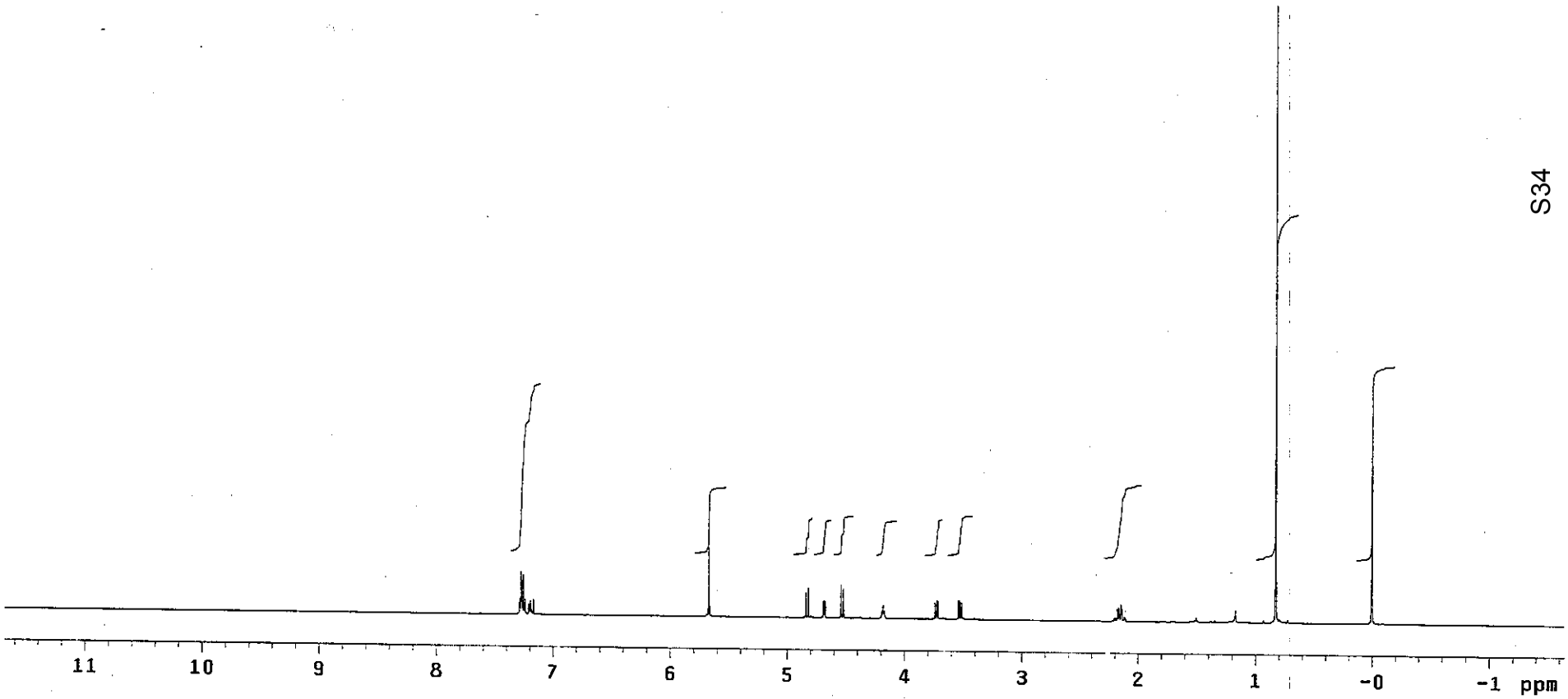


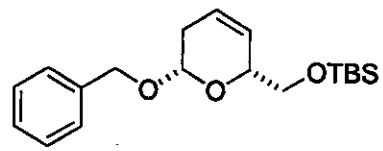
^{13}C NMR (150 MHz, $CDCl_3$)



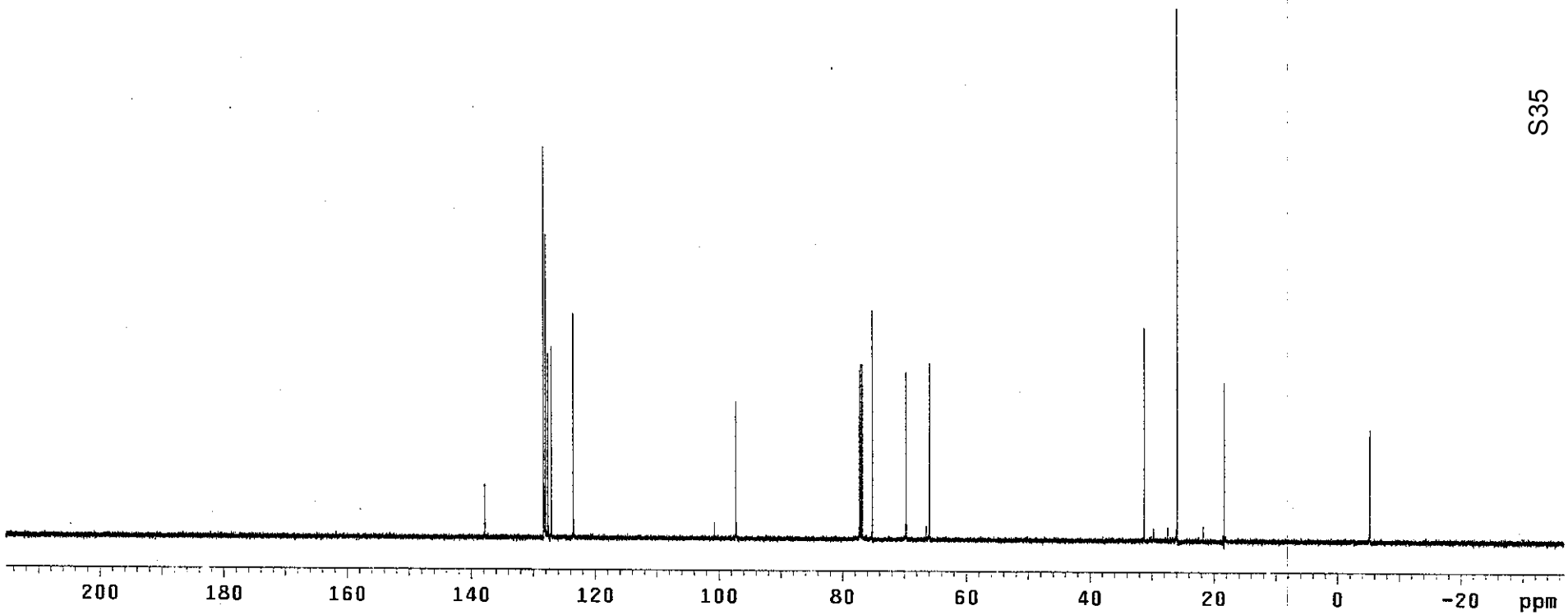


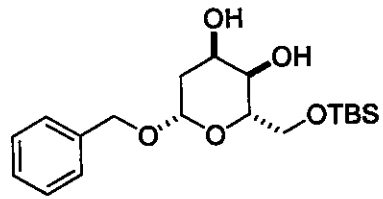
^{1}H NMR (600 MHz, $CDCl_3$)



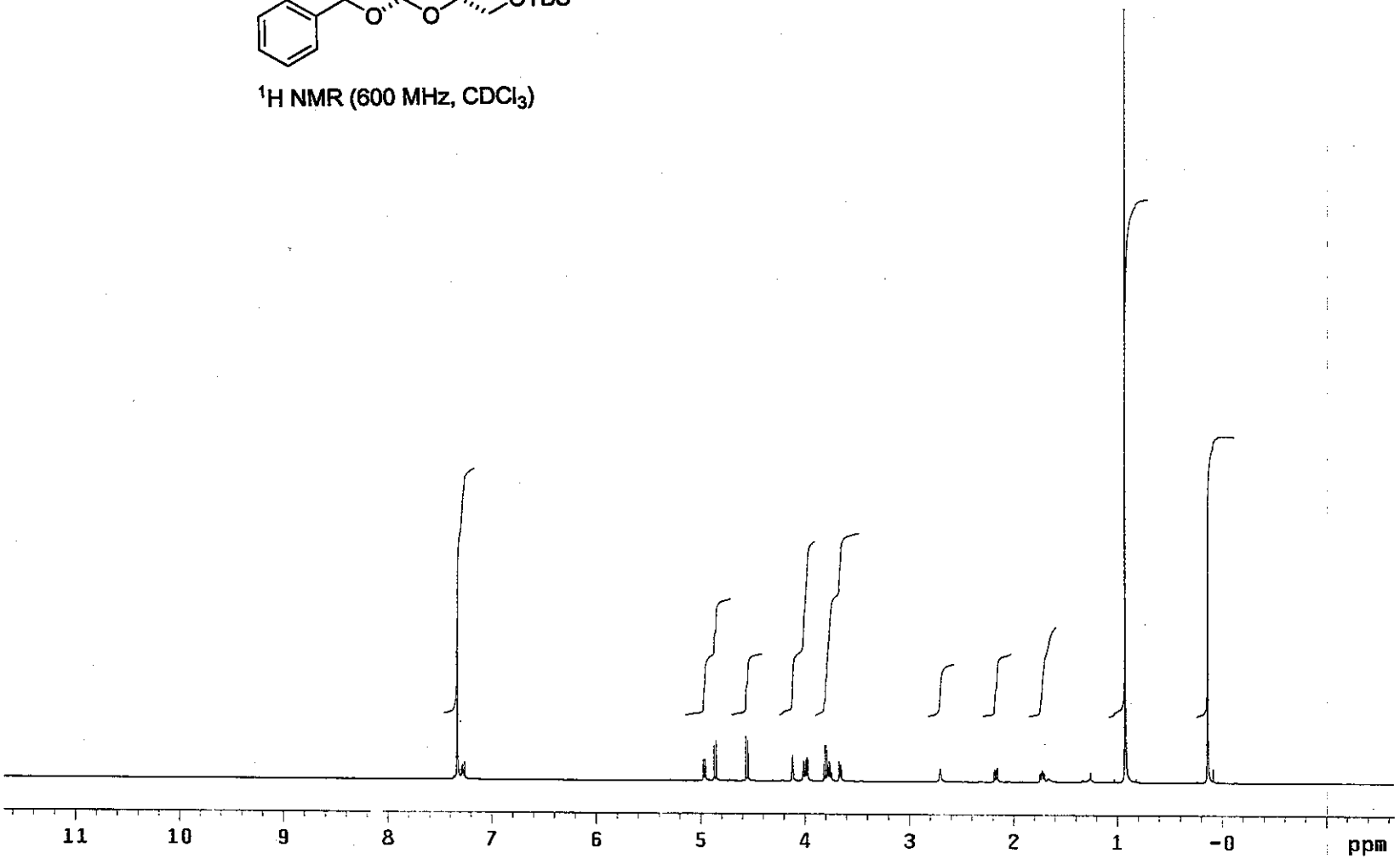


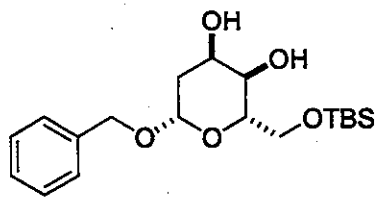
^{13}C NMR (150 MHz, $CDCl_3$)



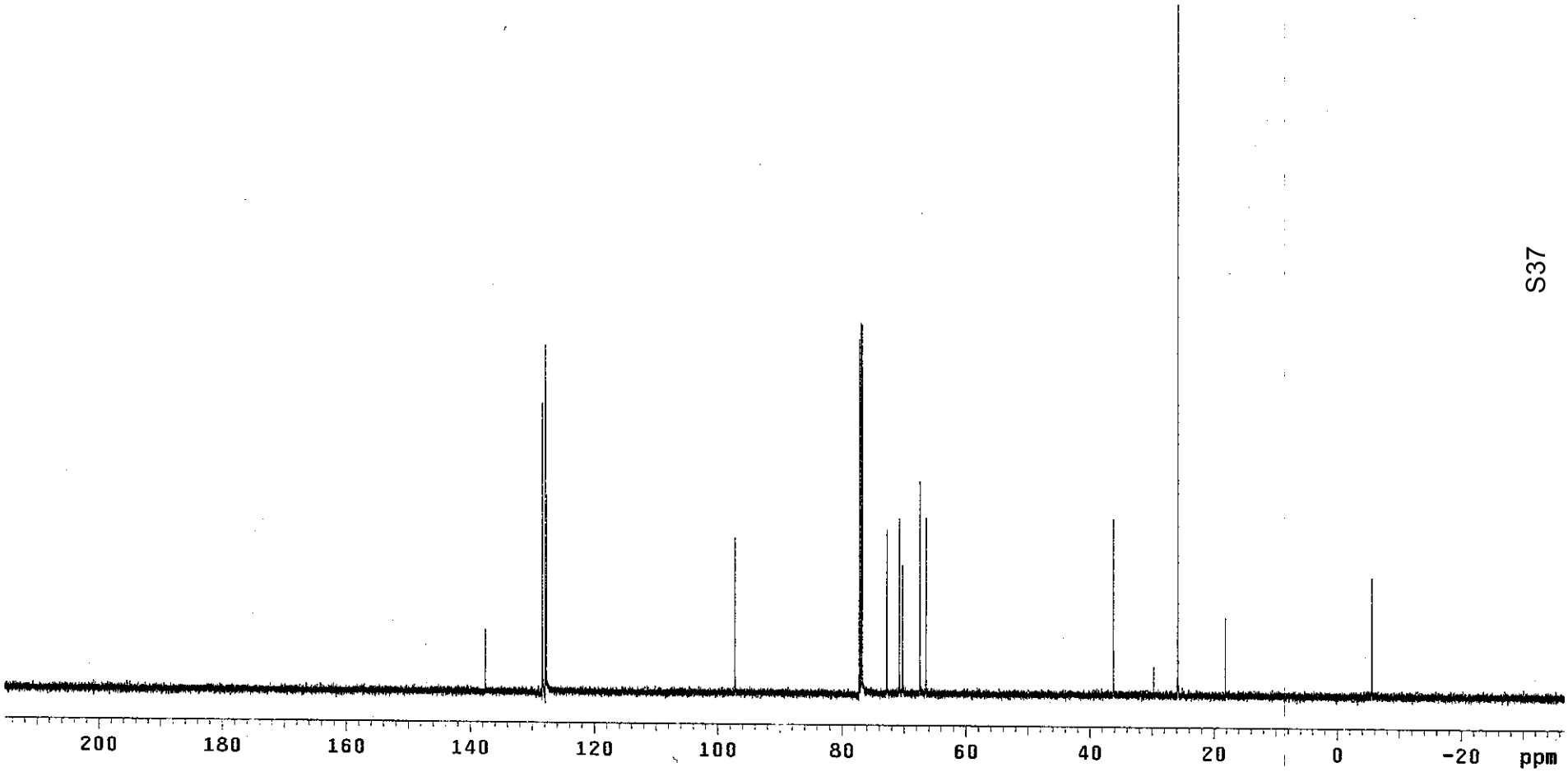


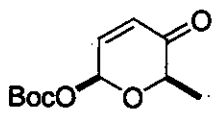
^{1}H NMR (600 MHz, $CDCl_3$)





^{13}C NMR (150 MHz, $CDCl_3$)

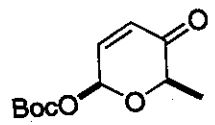




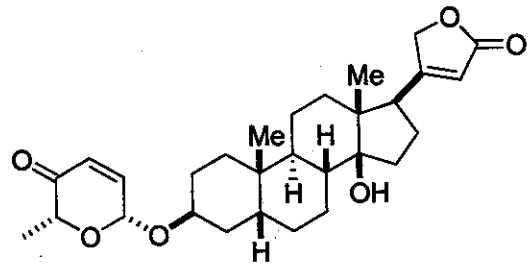
^{1}H NMR (270 MHz, $CDCl_3$)

11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

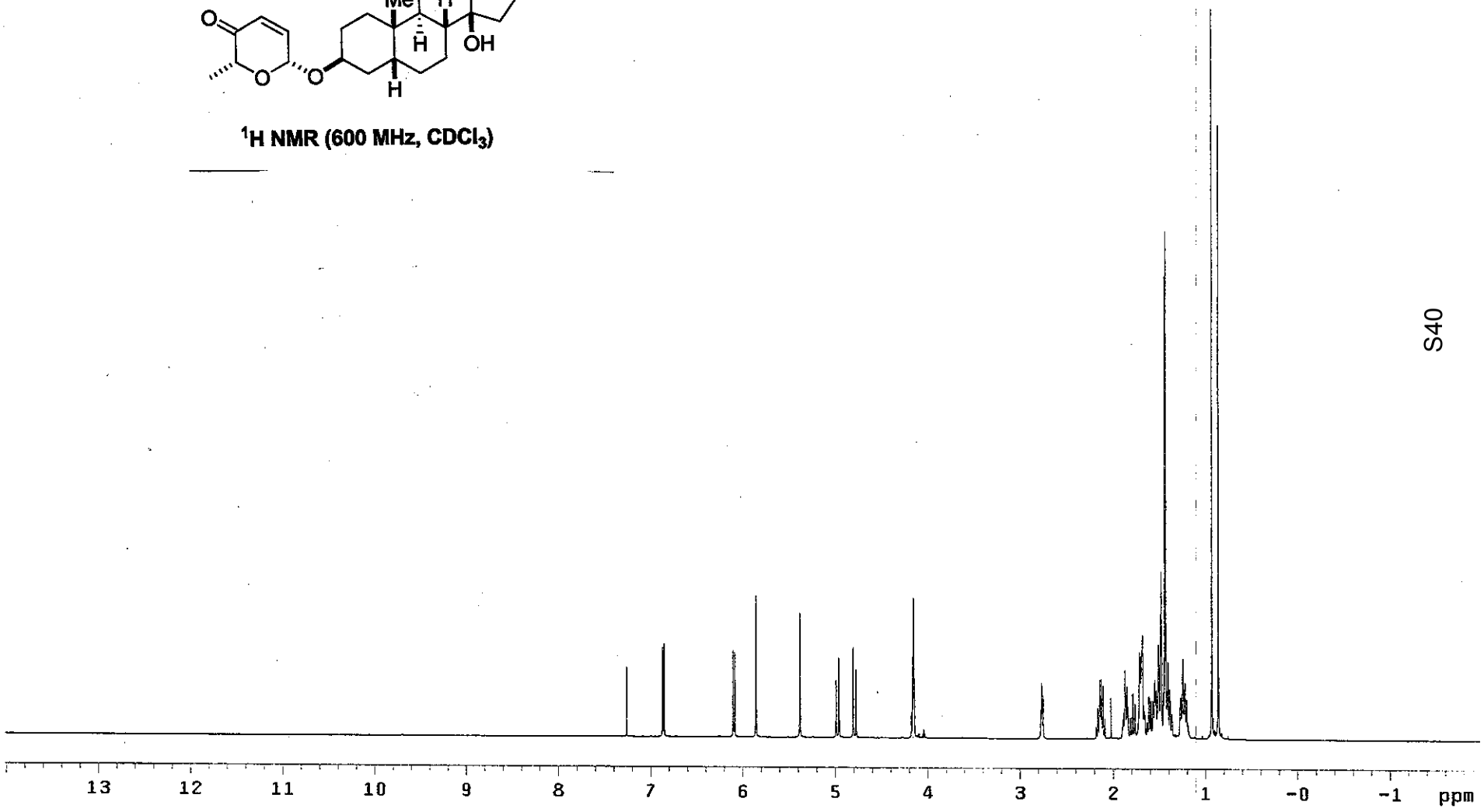
X : parts per Million : 1H

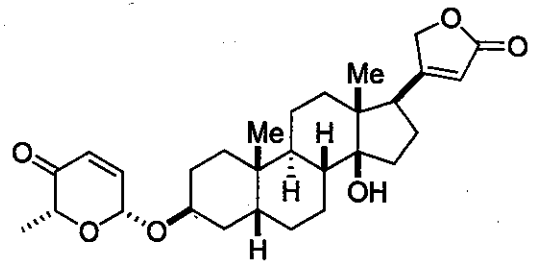


^{13}C NMR (67.5 MHz, $CDCl_3$)

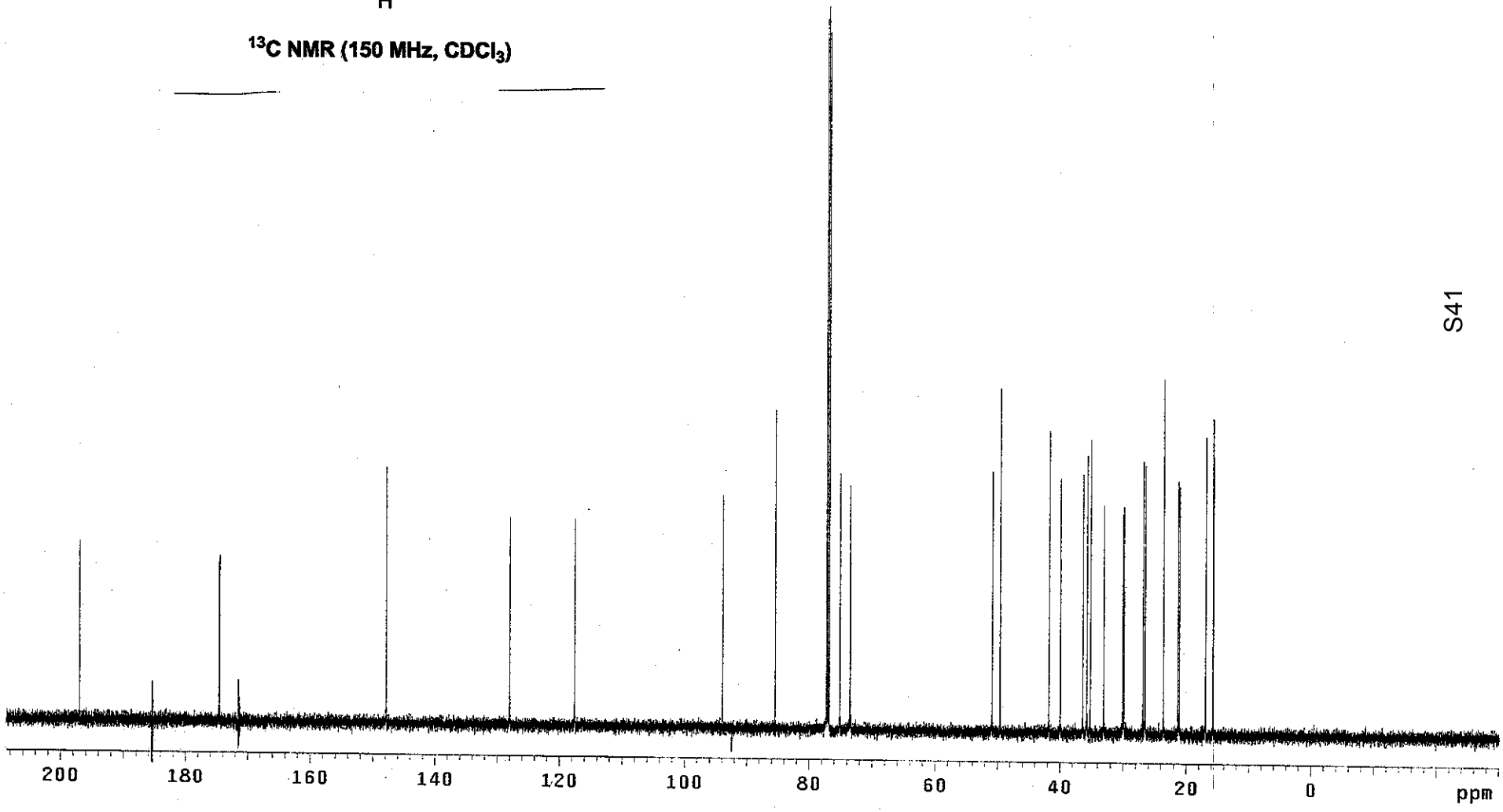


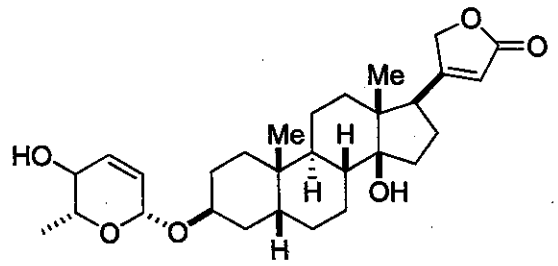
^{1}H NMR (600 MHz, $CDCl_3$)



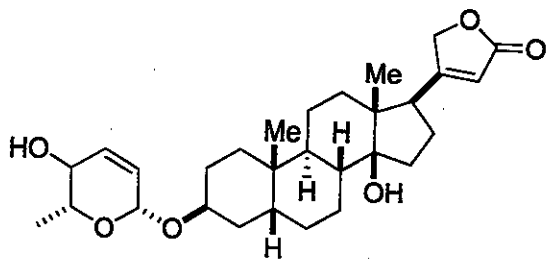


^{13}C NMR (150 MHz, $CDCl_3$)

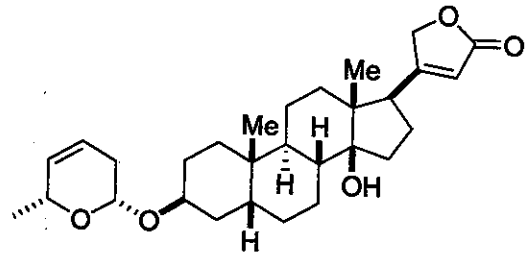




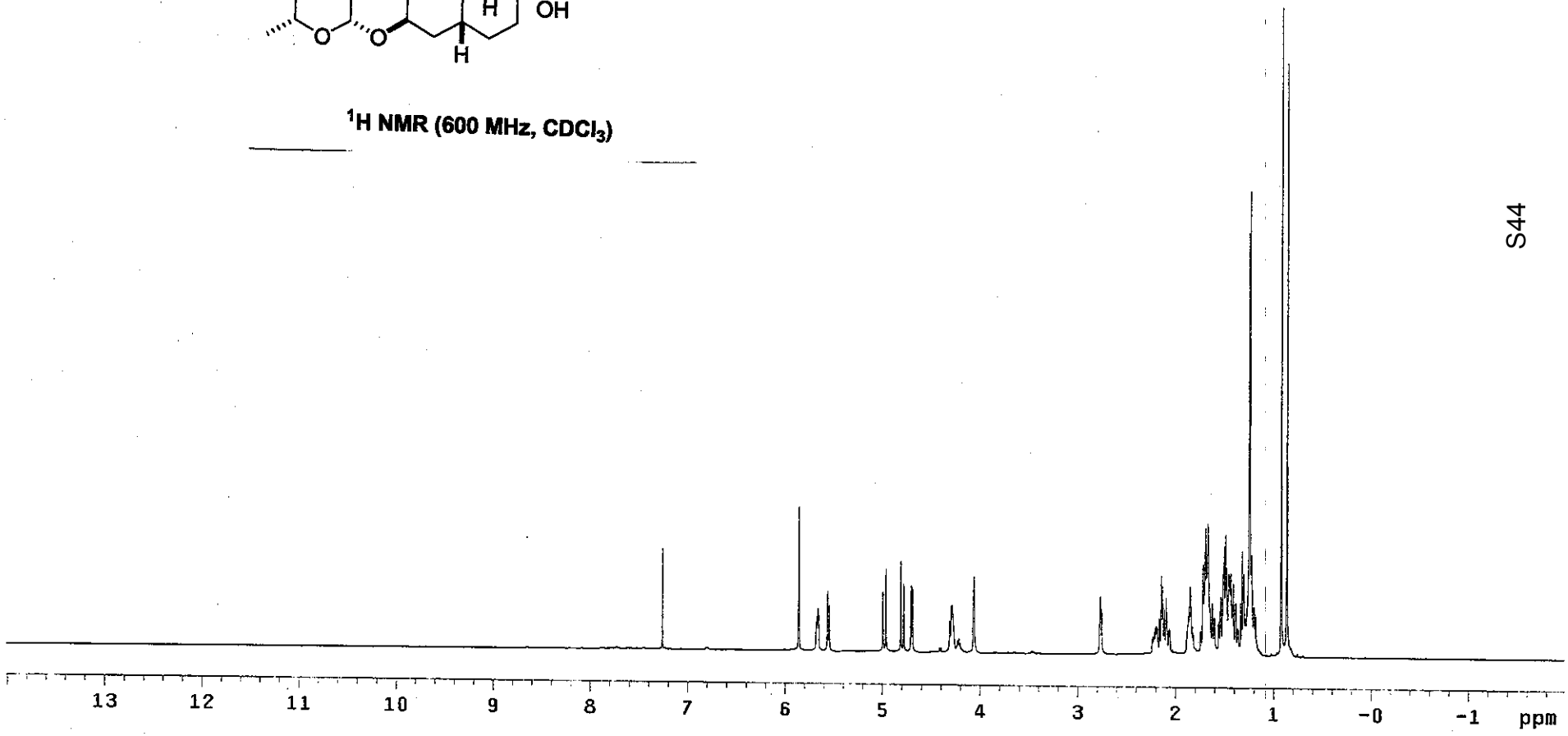
^{1}H NMR (600 MHz, $CDCl_3$)

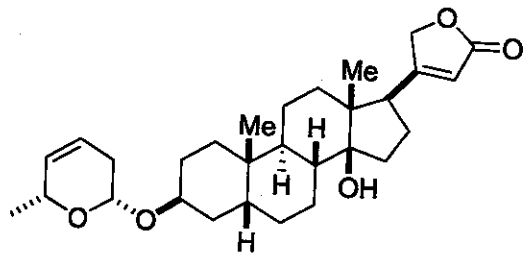


^{13}C NMR (150 MHz, $CDCl_3$)

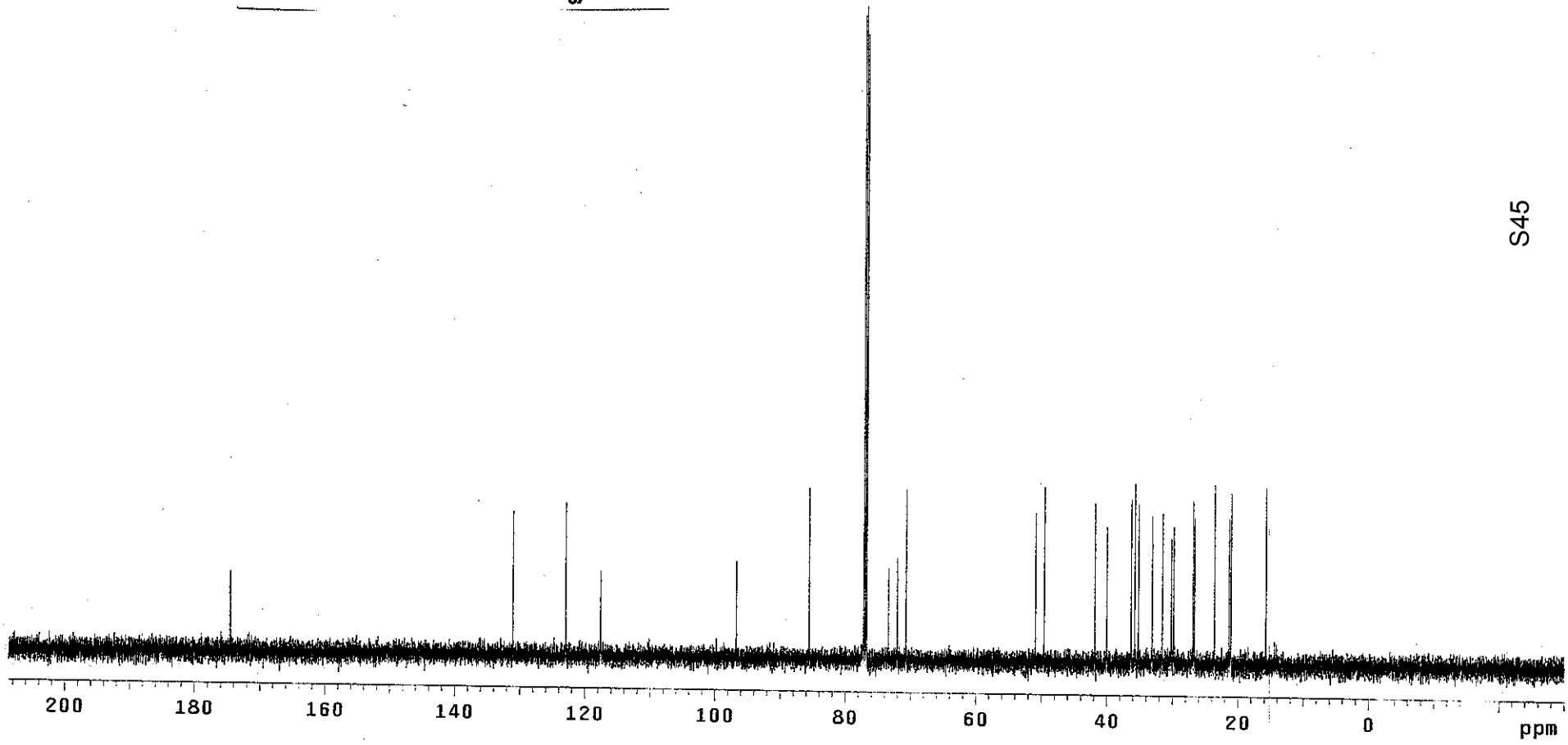


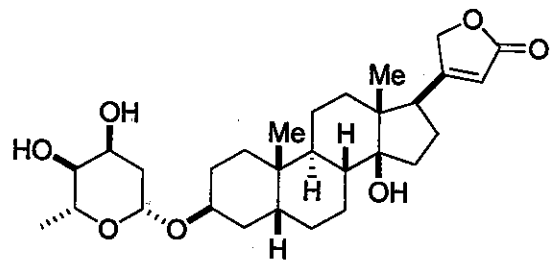
^{1}H NMR (600 MHz, $CDCl_3$)



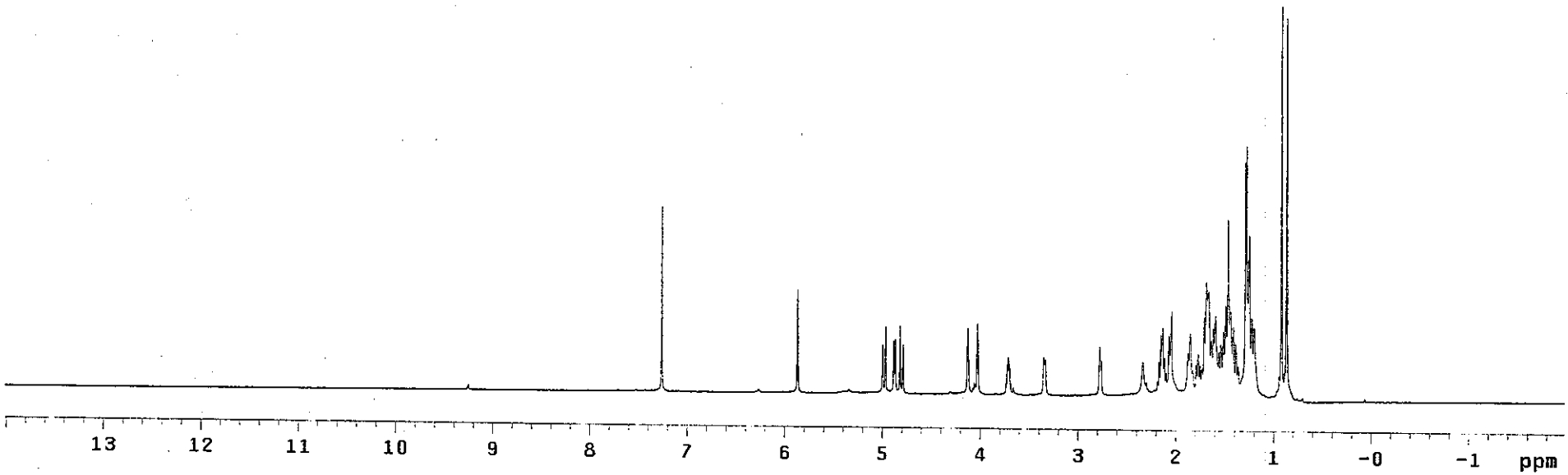


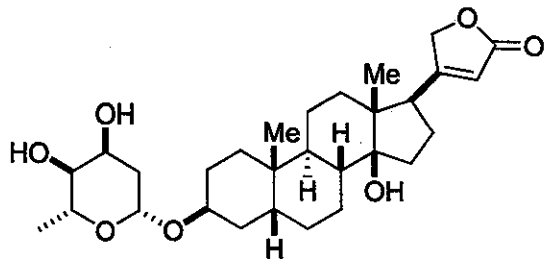
^{13}C NMR (150 MHz, $CDCl_3$)



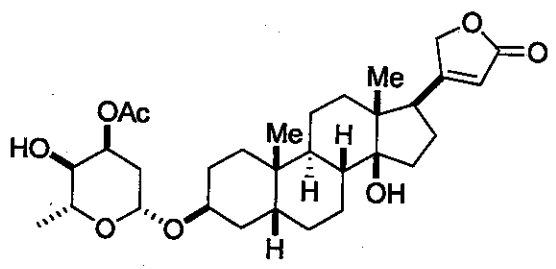


^{1}H NMR (600 MHz, $CDCl_3$)

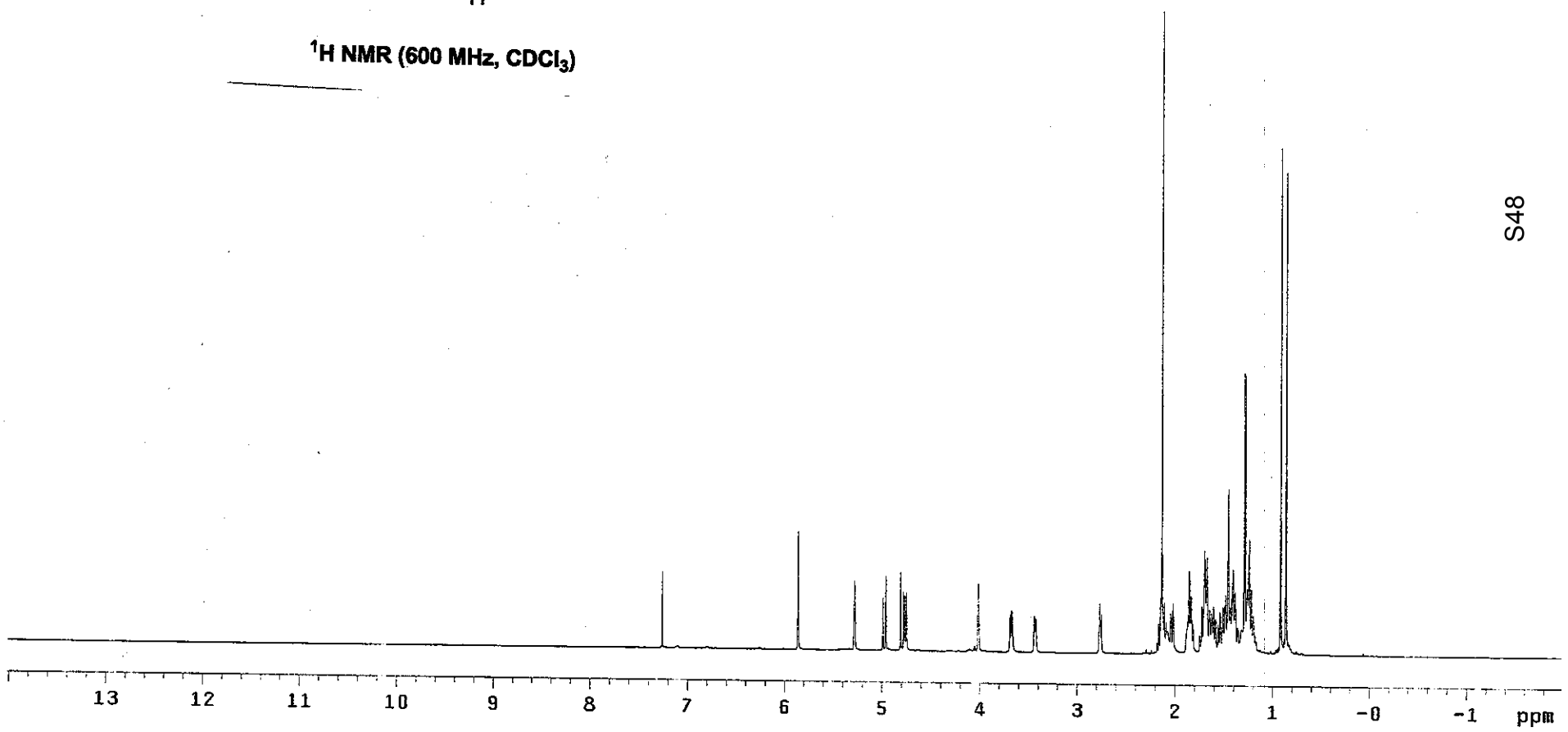


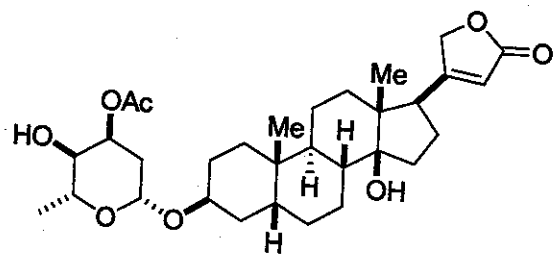


^{13}C NMR (150 MHz, $CDCl_3$)

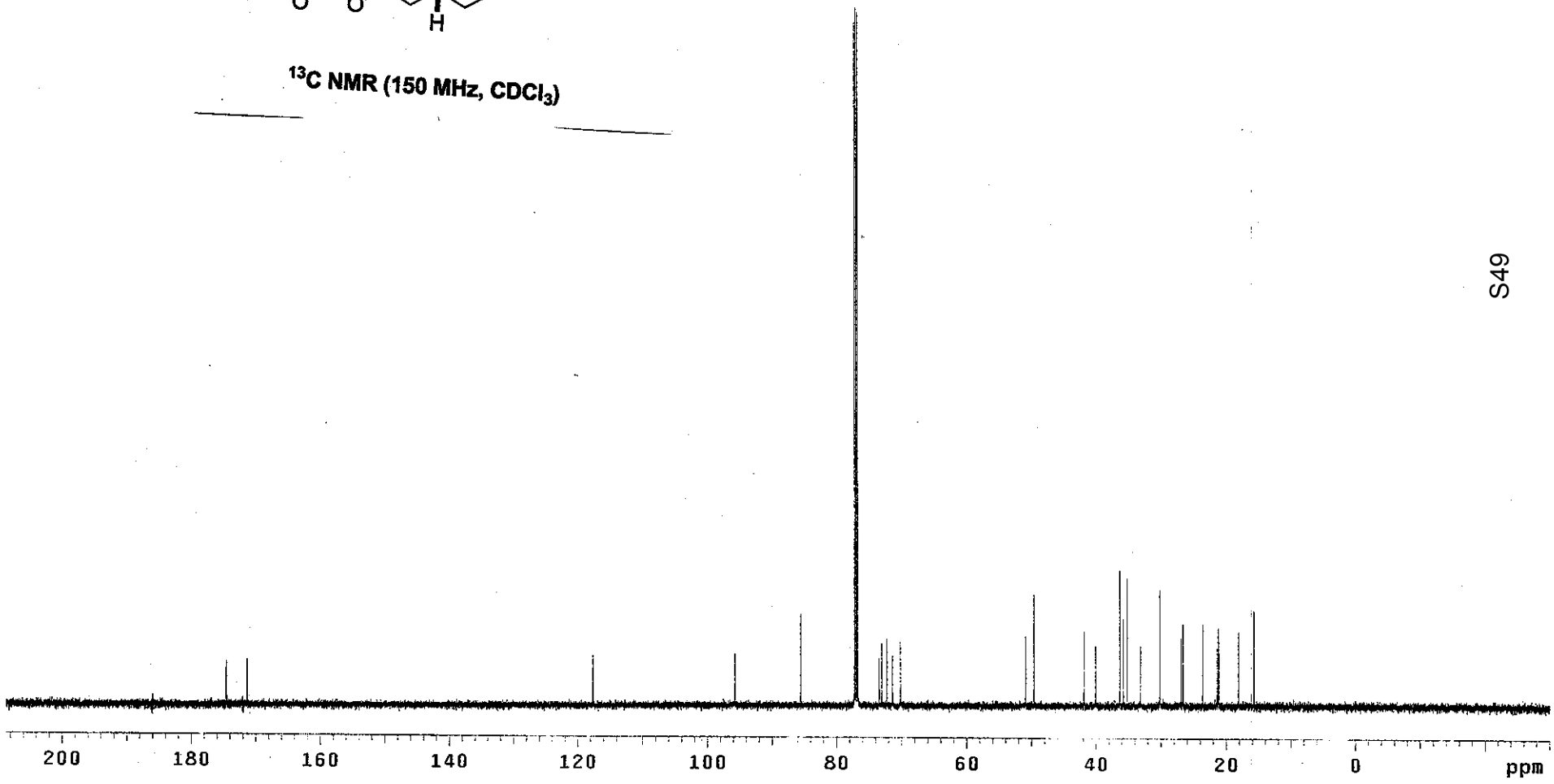


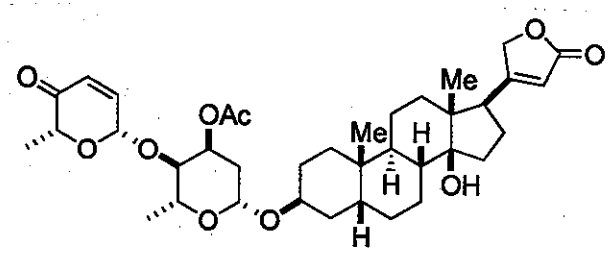
^{1}H NMR (600 MHz, $CDCl_3$)





^{13}C NMR (150 MHz, $CDCl_3$)





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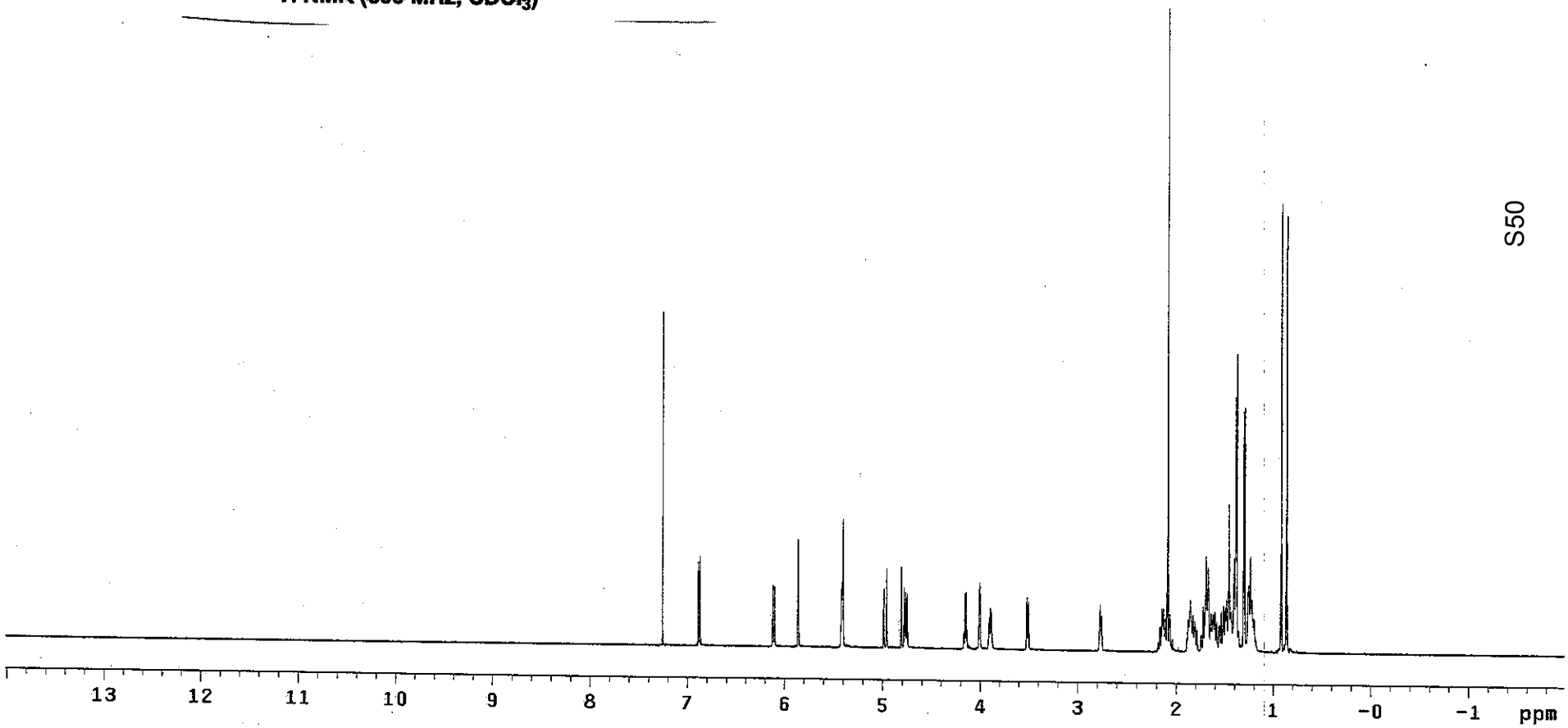
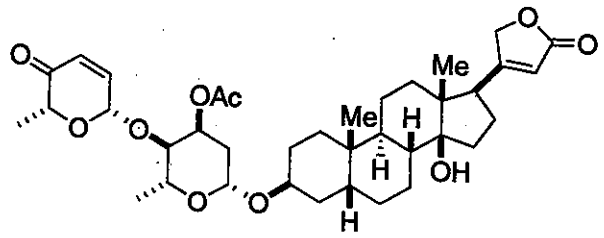
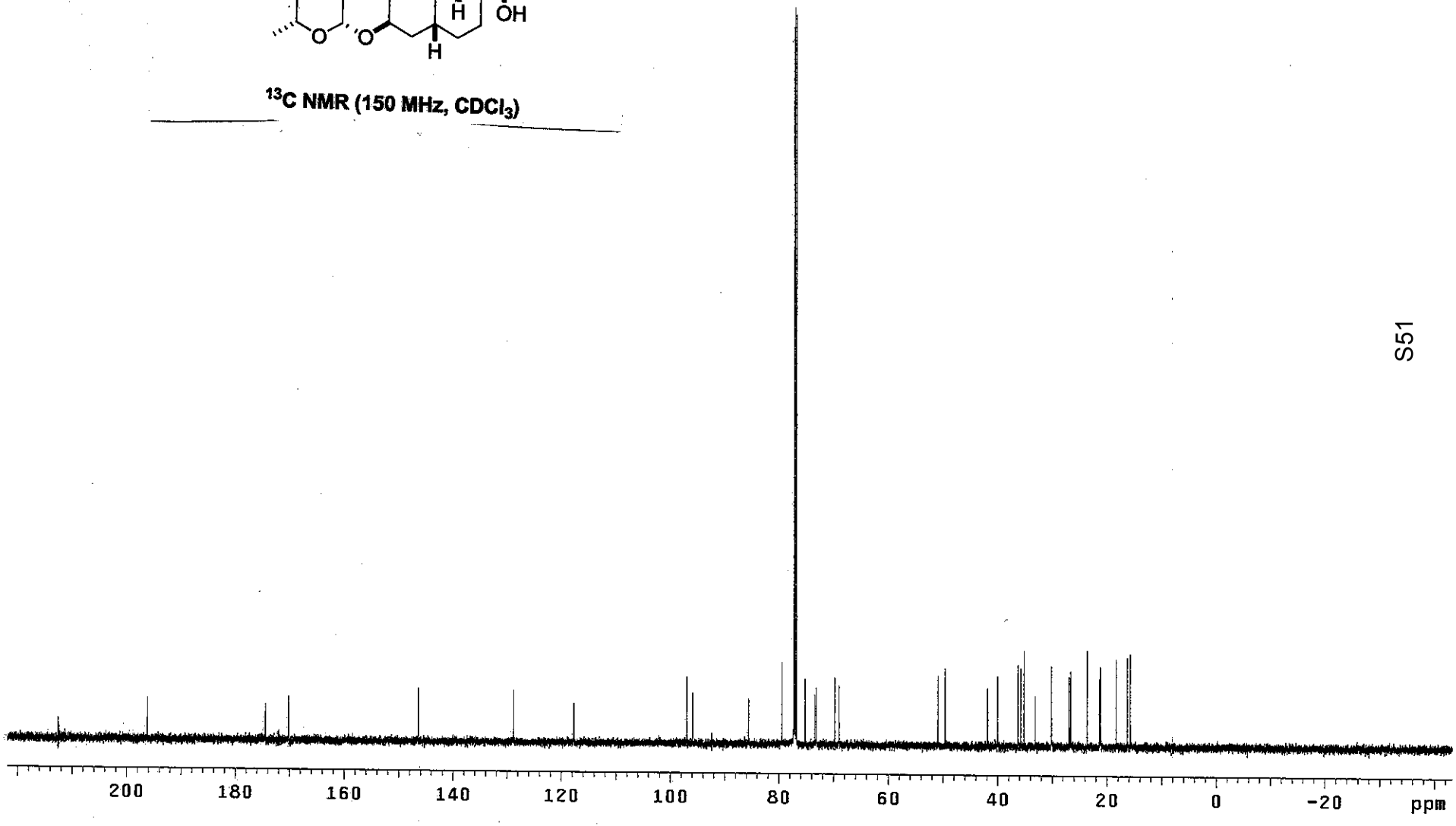
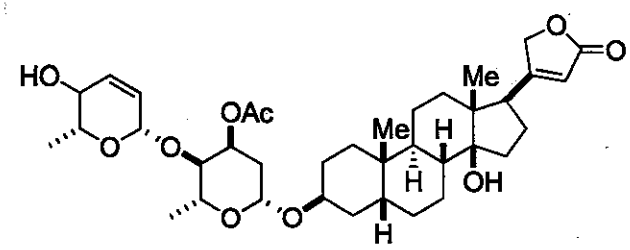


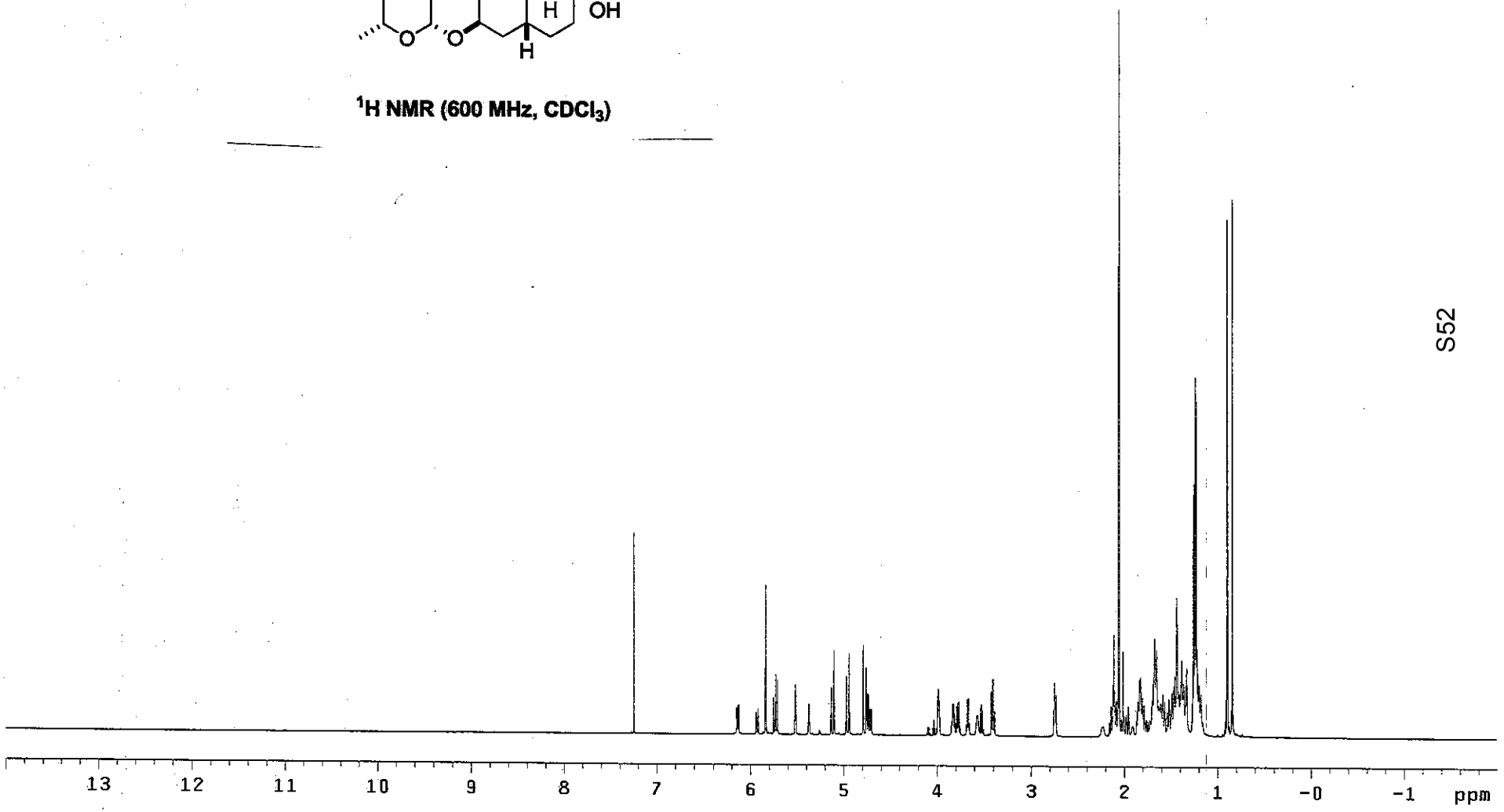


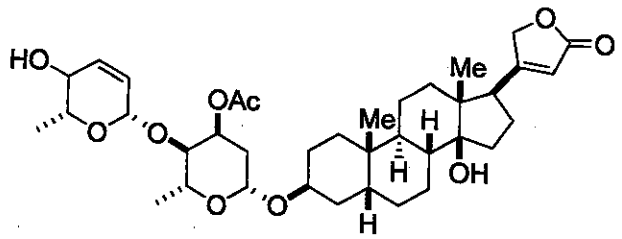
^{13}C NMR (150 MHz, $CDCl_3$)



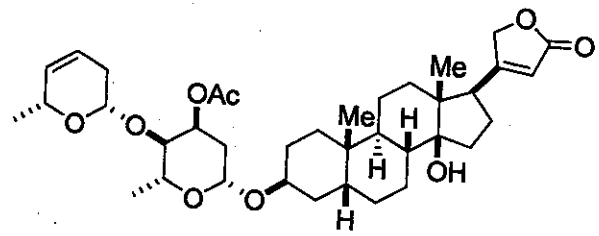


^{1}H NMR (600 MHz, $CDCl_3$)

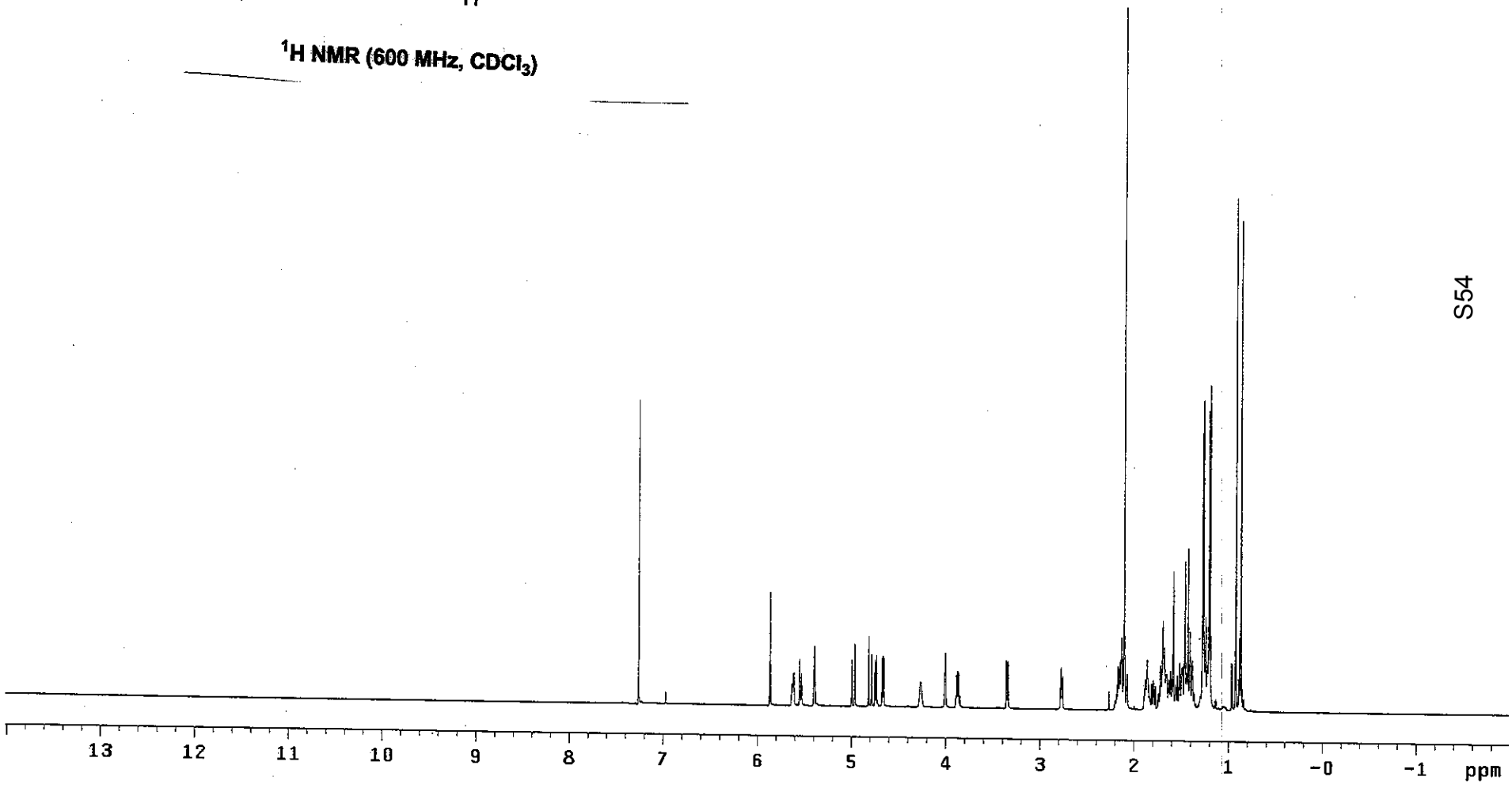


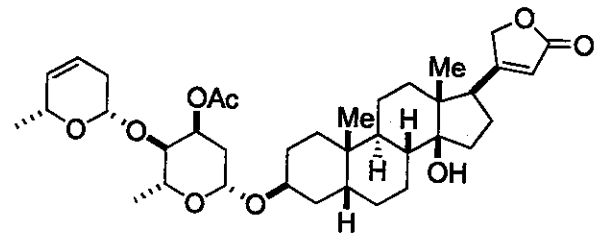


^{13}C NMR (150 MHz, $CDCl_3$)

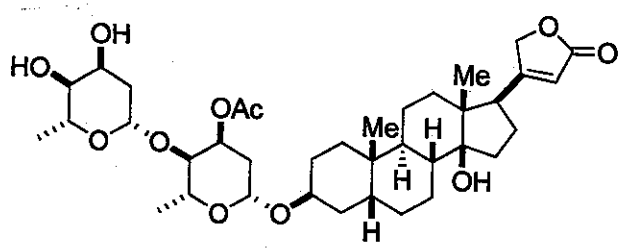


^{1}H NMR (600 MHz, $CDCl_3$)

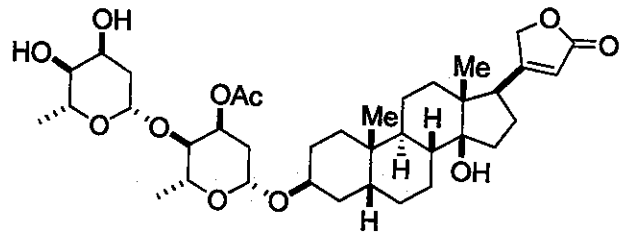




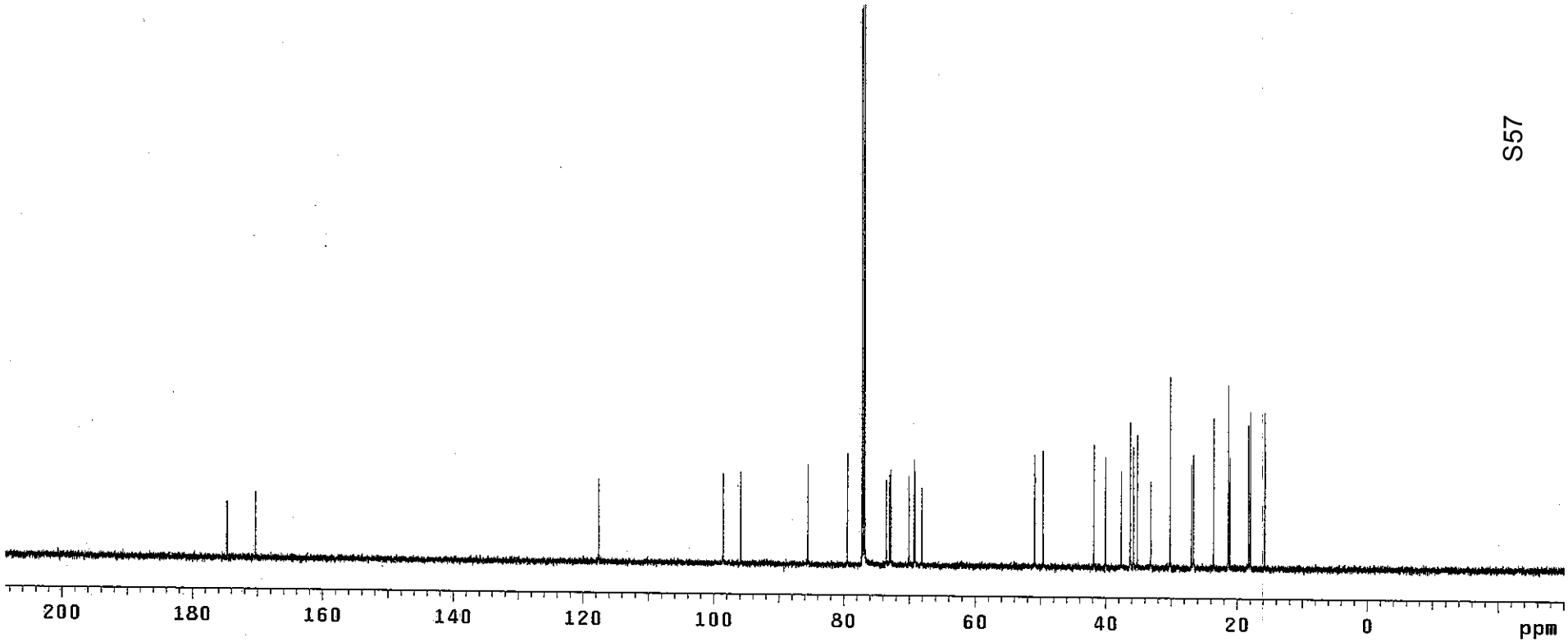
^{13}C NMR (150 MHz, $CDCl_3$)

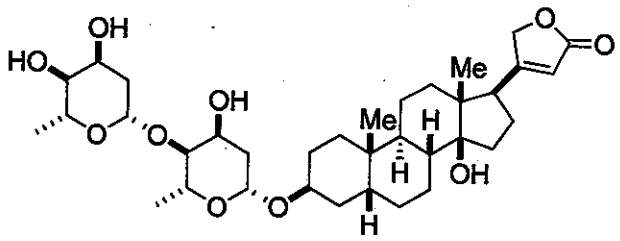


^{1}H NMR (600 MHz, $CDCl_3$)

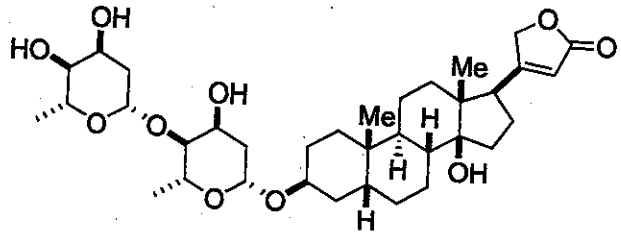


^{13}C NMR (150 MHz, $CDCl_3$)

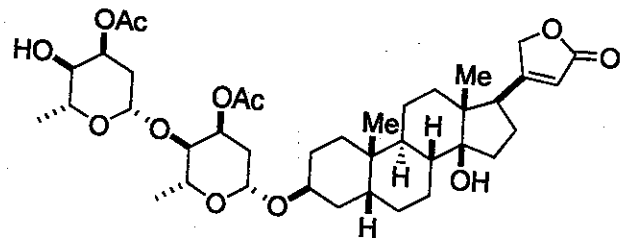




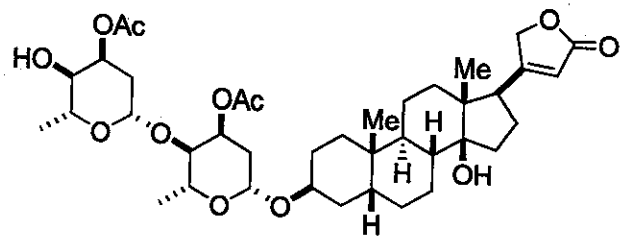
^{1}H NMR (600 MHz, $CDCl_3$)



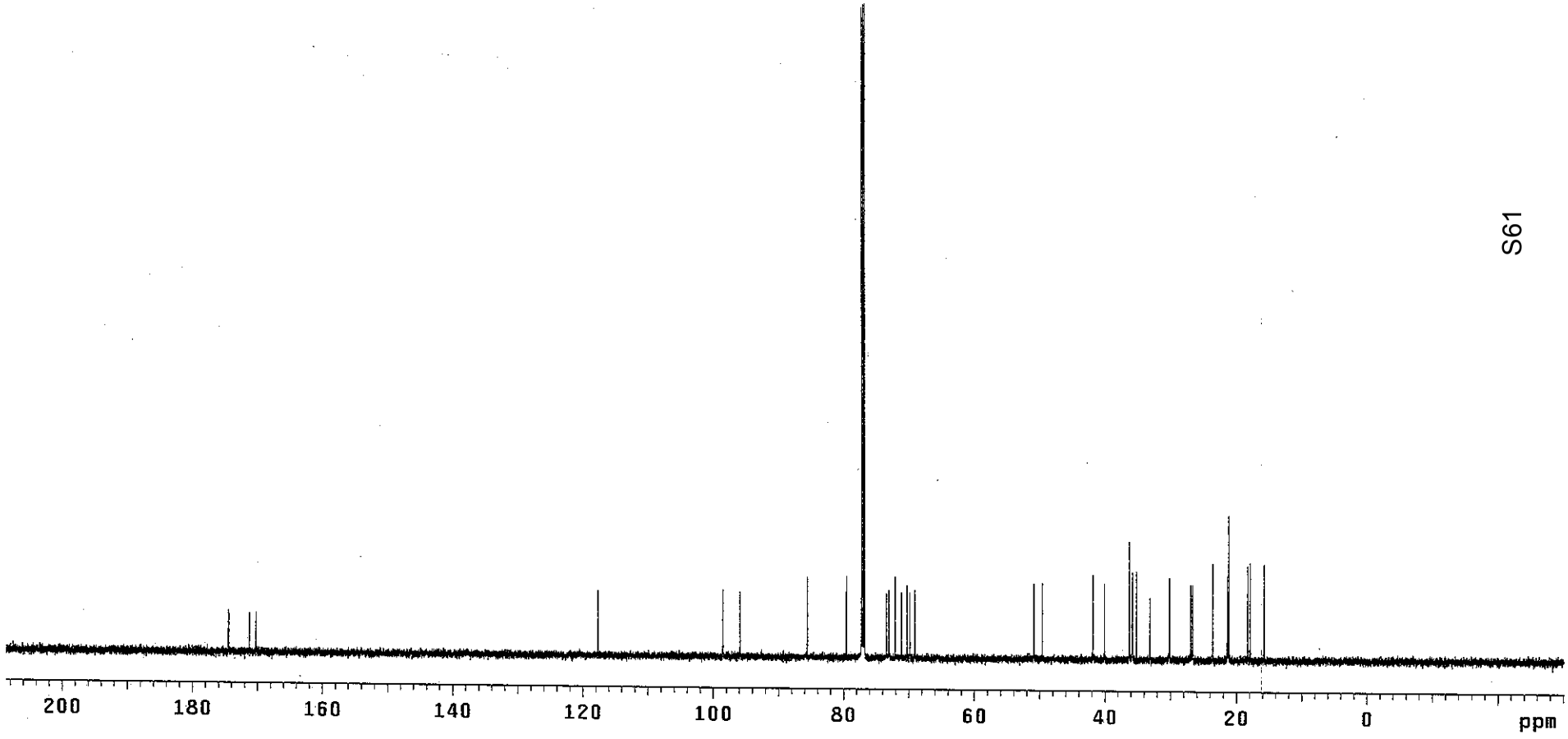
^{13}C NMR (150 MHz, $CDCl_3$)

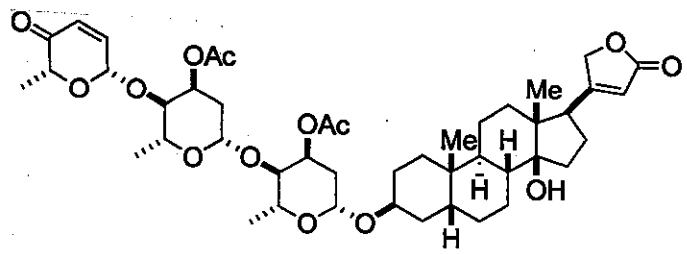


^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)





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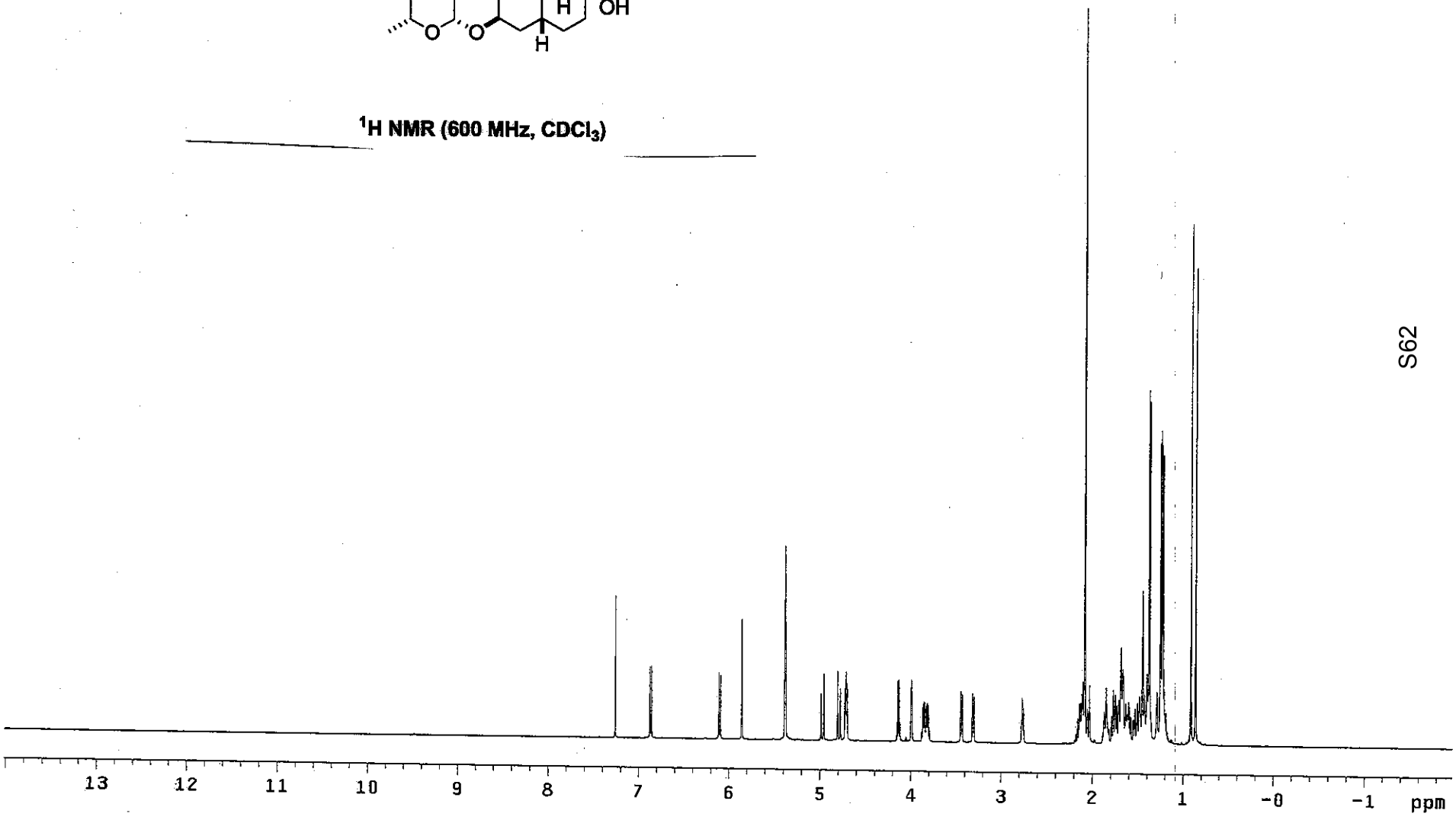
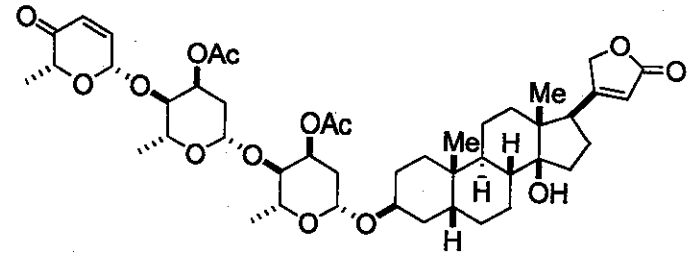
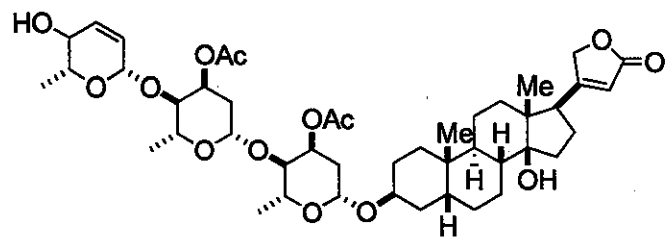
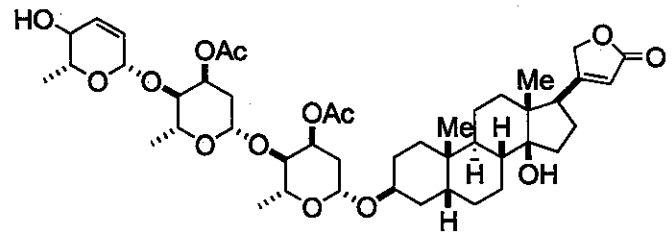




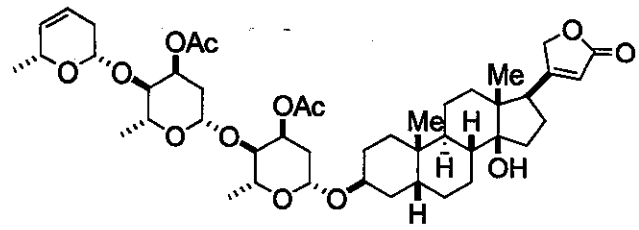
^{13}C NMR (150 MHz, $CDCl_3$)



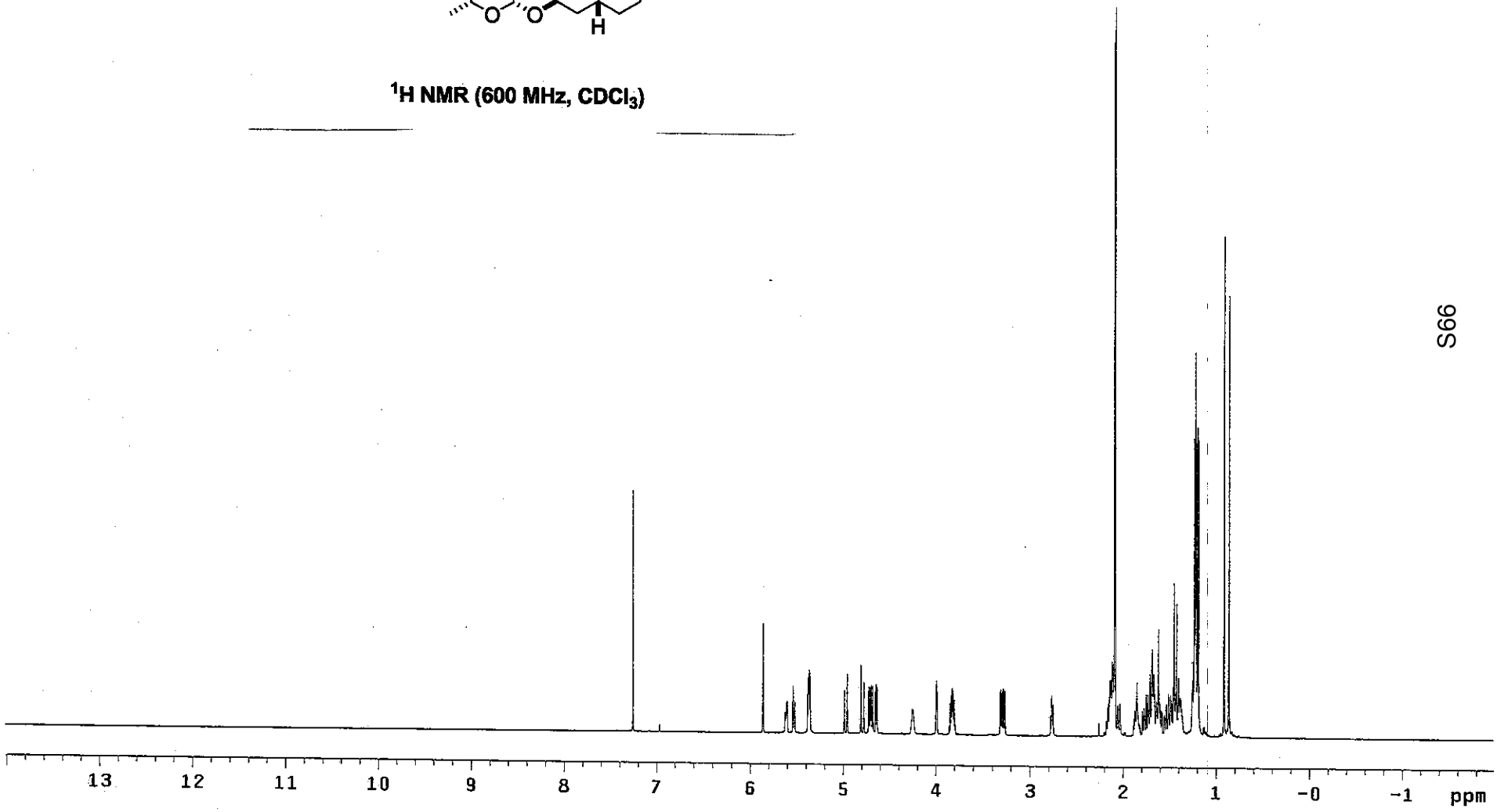
^{1}H NMR (600 MHz, $CDCl_3$)

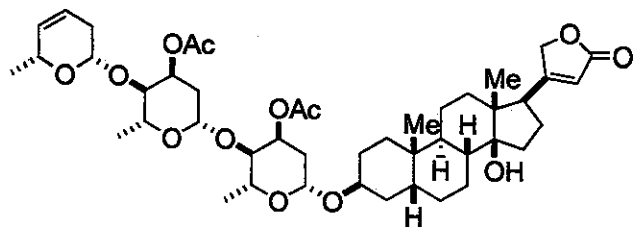


^{13}C NMR (150 MHz, $CDCl_3$)

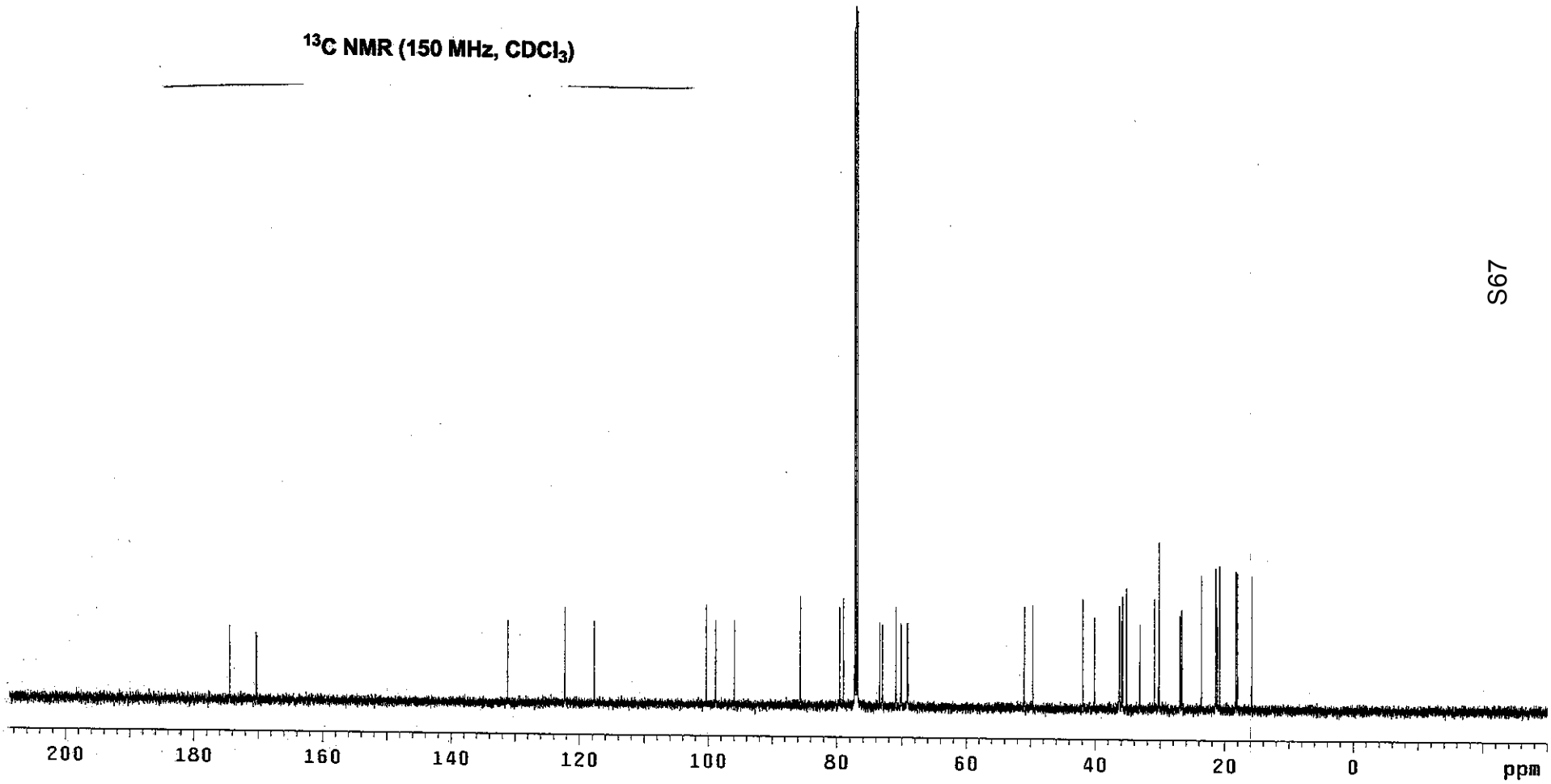


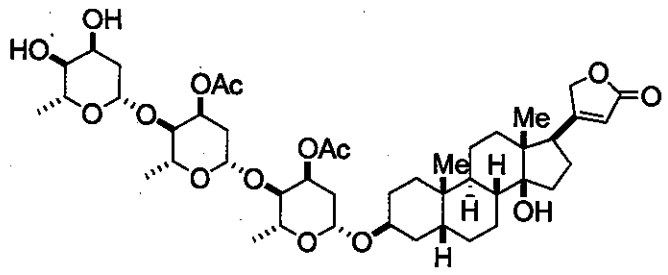
^{1}H NMR (600 MHz, $CDCl_3$)



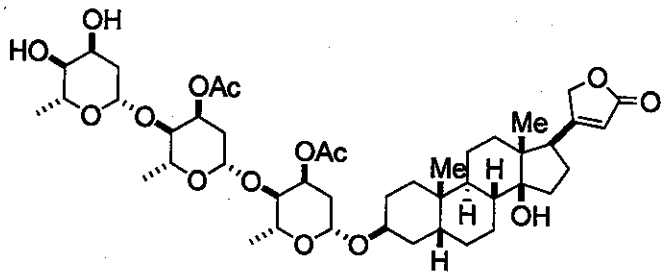


^{13}C NMR (150 MHz, $CDCl_3$)

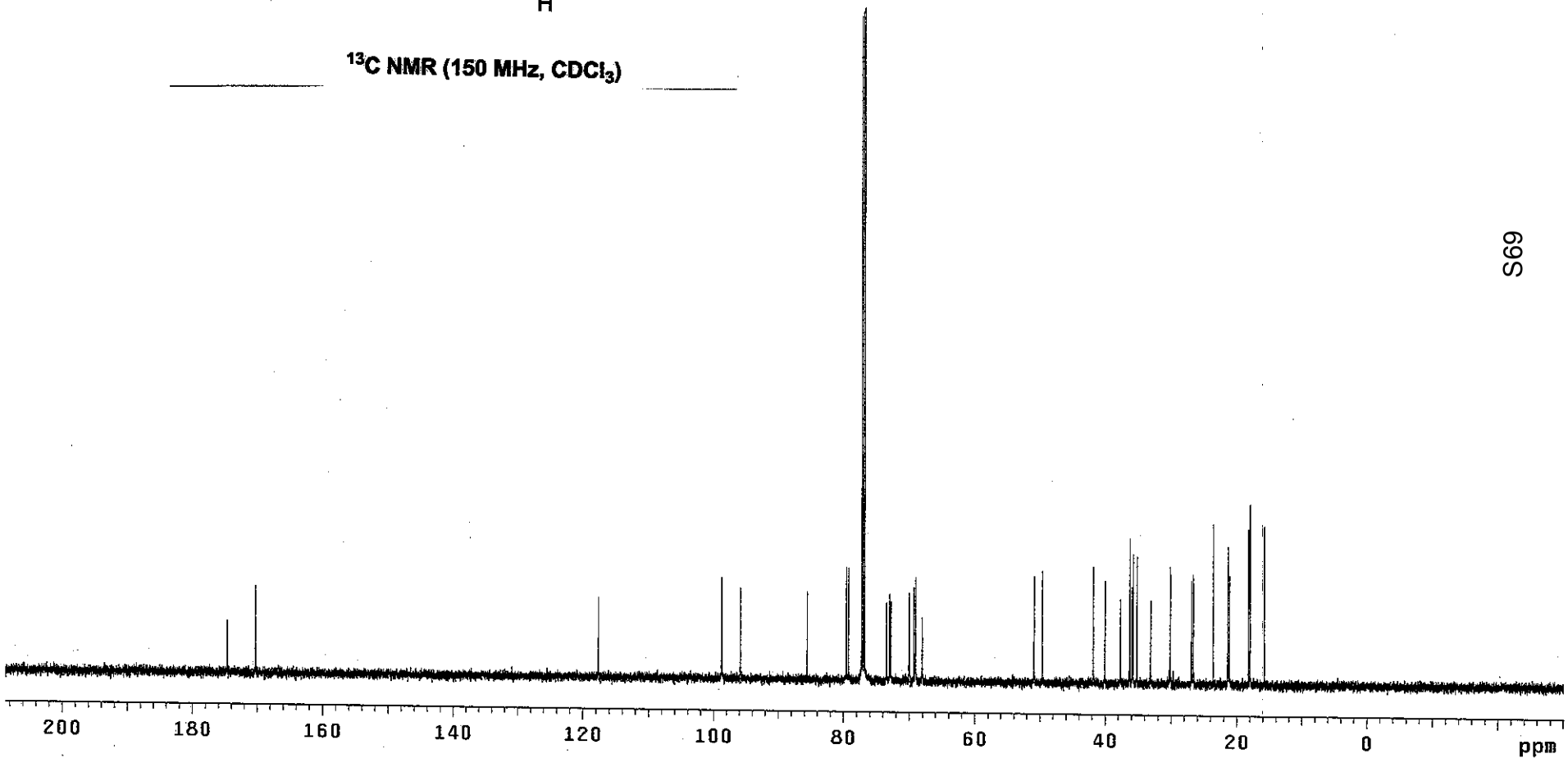


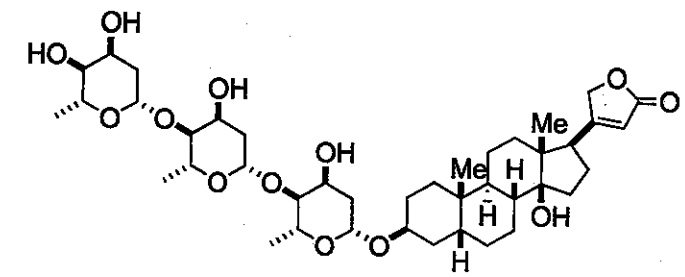


^{1}H NMR (600 MHz, $CDCl_3$)

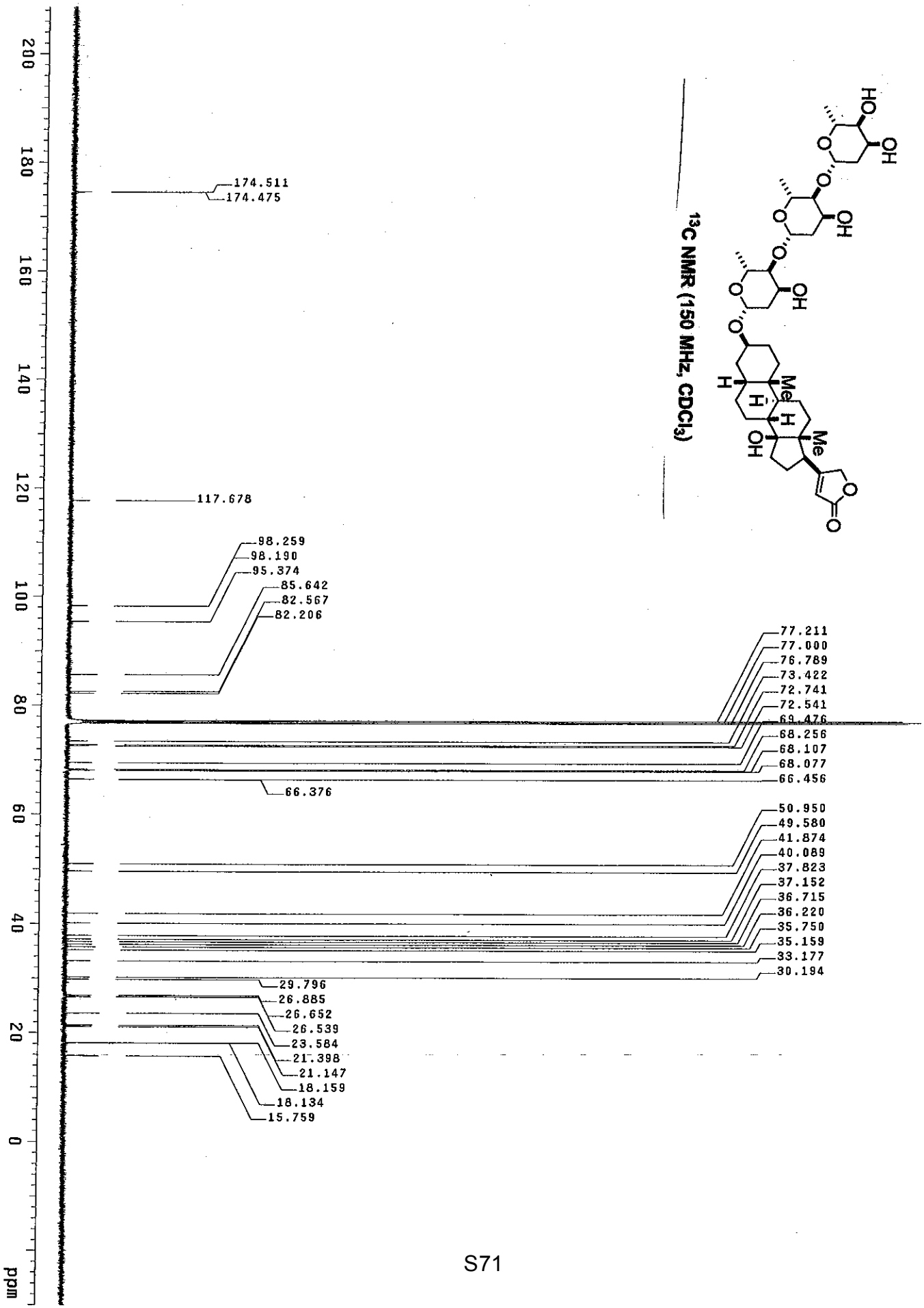


^{13}C NMR (150 MHz, $CDCl_3$)





^{1}H NMR (600 MHz, $CDCl_3$)


^{13}C NMR (150 MHz, CDCl$_3$)
174.511
174.475
117.678
98.259
98.190
95.374
85.642
82.567
82.206
77.211
77.000
76.789
73.422
72.741
72.541
69.476
68.256
68.107
68.077
66.456
66.376
50.950
49.580
41.874
40.089
37.823
37.152
36.715
36.220
35.750
35.159
33.177
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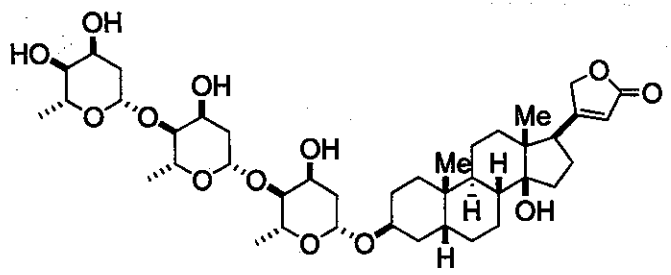
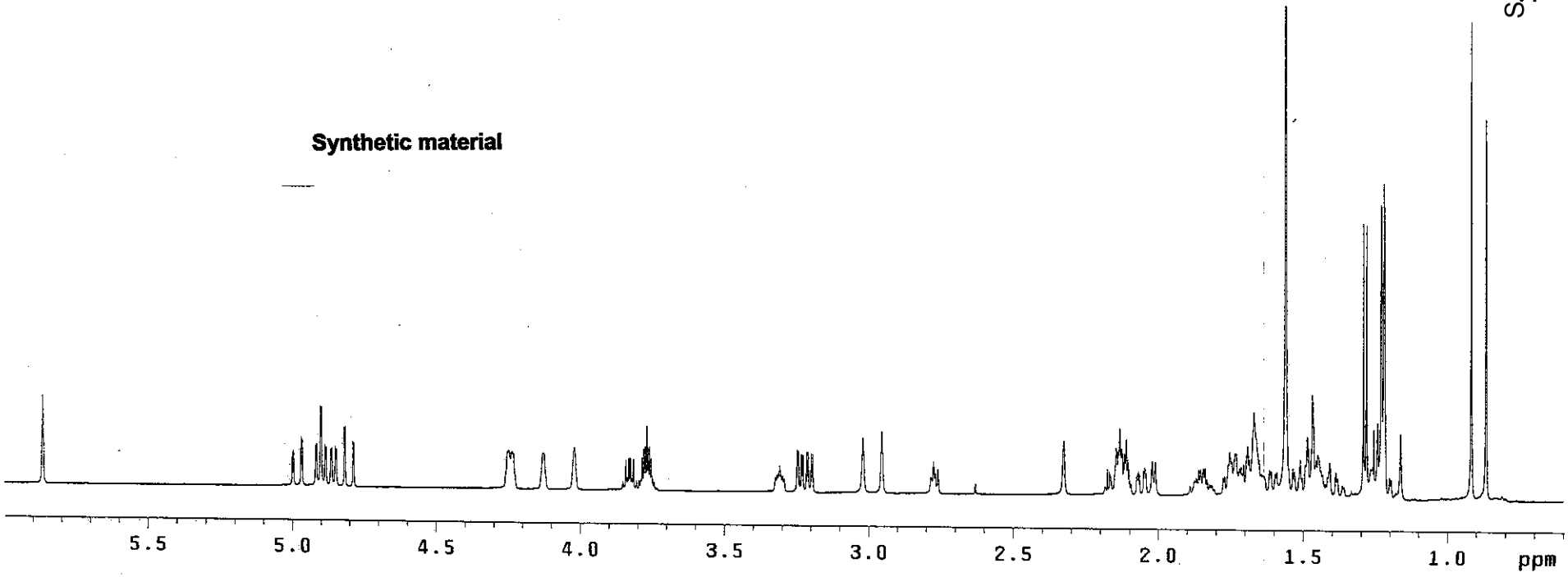
26.885
26.652
26.539
23.584
21.398
21.147
18.159
18.134
15.759
ppm

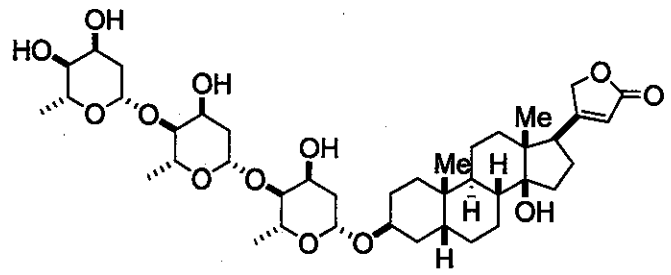


^{1}H NMR (600 MHz, $CDCl_3$)

natural product

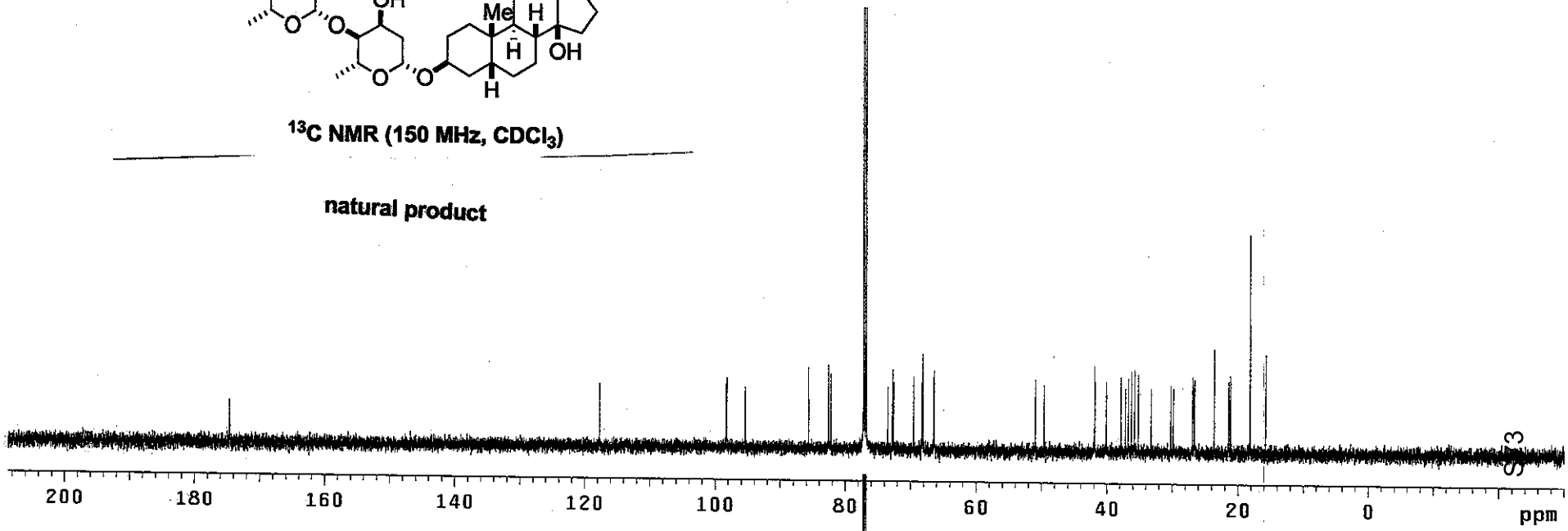
Synthetic material





^{13}C NMR (150 MHz, $CDCl_3$)

natural product



Synthetic material