Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information for:

Synthesis of the (−)-TAN-2483B ring system via a D-mannose-derived cyclopropane

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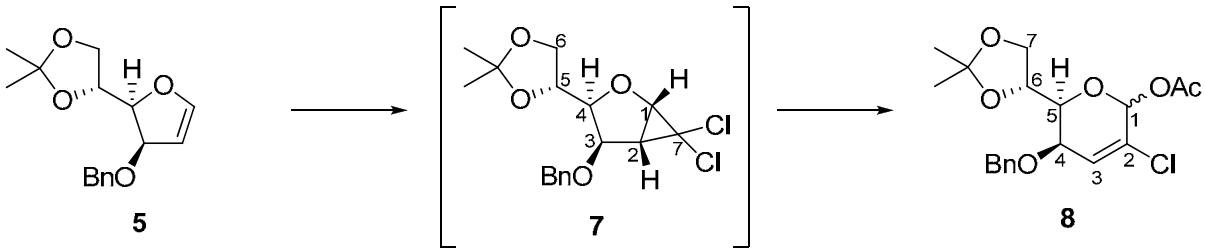
General experimental methods

Unless otherwise stated, the following conditions apply. All reactions were performed under argon in flame–dried or vacuum–dried glassware using dry solvents and standard syringe techniques. Methanol was distilled from sodium. Tetrahydrofuran (THF) was distilled from the sodium salt of the benzophenone ketyl radical anion. KHMDS was purchased as a 0.5 $molL^{-1}$ solution in toluene. Sodium hydride was obtained as a 60% (w/w) dispersion in paraffin oil and used as received. *m*-CPBA was obtained as an approximately 70% dispersion in water and *m*-chlorobenzoic acid. All other reagents were of commercial quality and used as received. After workup, partitioned organic layers were dried over magnesium sulfate ($MgSO_4$).

Reaction progress was monitored using aluminium–backed thin layer chromatography (TLC) plates pre–coated with silica UV254, which were visualised by UV radiation (254 nm) and developed with anisaldehyde dip. Purification of products by flash chromatography was conducted using a column filled with silica gel 60 (220–240 mesh) using eluting solvent systems as indicated. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Inova 500 spectrometer, operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C. All chemical shifts (δ) were referenced to the solvent peaks of $CDCl_3$ (7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C). NOe measurements were made on a Varian DirectDrive 600 spectrometer, operating at 600 MHz for ^{1}H, using NOESY experiments. Infrared spectra were obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Optical rotation was measured on a polarimeter operating at the sodium D-line. High–resolution mass spectrometry was performed on a Waters Q-TOF Premier™ Tandem mass spectrometer.

Acetyl 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-α-D-*arabino*-hept-2-enopyranoside and acetyl 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-β-D-*arabino*-hept-2-enopyranoside (8)



Glycal **5**[1] (462 mg, 1.67 mmol) was dissolved in chloroform (3 mL), treated with TEBAC (8 mg, 0.04 mmol), followed by a solution of sodium hydroxide (3.01 g, 75.3 mmol) in water (3.0 mL) and allowed to stir in air at room temperature for 2.5 hours. The reaction mixture was dissolved in water (20 mL), then extracted with diethyl ether (3 x 20 mL). The ethereal fractions were combined, dried, filtered and concentrated to afford a brown oil. This oil was purified by column chromatography (5:1 hexanes:ethyl acetate) to afford crude cyclopropane **7** as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.31 (complex m, 5H, Bn), 4.67 (d, *J* = 11.8 Hz, 1H, one of $PhCH_2$), 4.61 (d, *J* = 11.5 Hz, 1H, one of $PhCH_2$), 4.48 (apparent t, *J* = 5.9 Hz, 1H, H-4), 4.35–4.31 (complex m, H-3 and H-5), 4.27 (dd, *J* = 5.9, 0.8 Hz, 1H, H-1), 4.05 (dd, *J* = 8.3, 6.9 Hz, 1H, H-6), 3.93 (dd, *J* = 7.9, 6.5 Hz, 1H, H-6), 2.47 (d, *J* = 5.9 Hz, 1H, H-2), 1.44 (s, 3H, one of CH_3), 1.36 (s, 3H, one of CH_3).

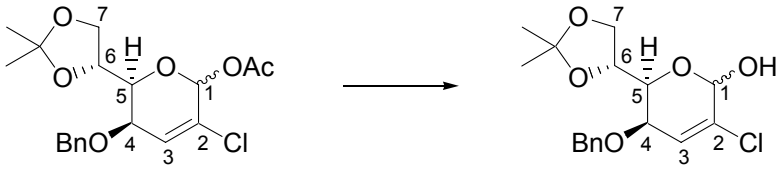
This sample was dissolved in acetic acid (17 mL), treated with silver acetate (435 mg, 2.61 mmol), and then stirred at 80 °C for two hours. The solution was filtered through Celite® and eluted with diethyl ether (20 mL). The reaction mixture was concentrated to provide a yellow oil, which was purified by column chromatography (1:5 EtOAc/hexanes), affording an inseparable mixture of acetyl pyranoside anomers **8** (495 mg, 77% over two steps, 3:1 ratio **8a**:**8b**) as a pale–yellow oil.

R_f = 0.4 (1:5 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.30 (complex m, 5H, Bn), 6.28–6.24 (complex m, 2H, H-1 and H-3), 4.70 (s, 0.5H, $PhCH_{2\ 8b}$), 4.68 (s, 1.5H, $PhCH_{2\ 8a}$), 4.39 (m, 1H, H-6), 4.12 (dd, *J* = 8.8, 6.3 Hz, 0.75H, one of H-7_{8a}), 4.10 (m, 0.25H, one of H-7_{8b}), 4.04 (dd, *J* = 8.8, 4.7 Hz, 0.25H, one of H-7_{8b}), 4.00 (m, 0.25H, H-4_{8b}), 3.98 (dd, *J* = 5.9, 2.5 Hz, 0.75H, H-4_{8a}), 3.88 (dd, *J* = 8.8, 4.7 Hz, 0.75H, one of H-7_{8a}), 3.84 (dd, *J* = 8.5, 2.4 Hz, 0.75H, H-5_{8a}), 3.67 (dd, *J* = 8.6, 1.9 Hz, 0.25H, H-5_{8b}), 2.16 (s, 0.75H, CH_3CO_{8b}), 2.13 (s, 2.25H, CH_3CO_{8a}), 1.41 (s, 2.25H, one of $(CH_3)_2C_{8a}$), 1.40 (s, 0.75H, one of $(CH_3)_2C_{8b}$), 1.38 (s, 2.25H, one of $(CH_3)_2C_{8a}$), 1.37 (s, 0.75H, one of $(CH_3)_2C_{8b}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5 (C, CH_3CO_{8a}), 169.2 (C, CH_3CO_{8b}), 138.0 (C, $C_{Ph\ 8b}$), 137.8 (C, $C_{Ph\ 8a}$), 133.7 (C, C-2_{8b}), 132.4 (C, C-2_{8a}), 128.42 (CH, CH_{Ph}

[1] C. Kim, R. Hoang and E. A. Theodorakis, *Org. Lett.*, 1999, **1**, 1295–1297.

$_{8a}$), 128.35 (CH, $CH_{Ph\ 8b}$), 128.02 (CH, $CH_{Ph\ 8b}$), 127.96 (CH, $CH_{Ph\ 8a}$), 127.93 (CH, $CH_{Ph\ 8a}$), 127.85 (CH, $CH_{Ph\ 8b}$), 127.2 (CH, C-3_{8b}), 125.9 (CH, C-3_{8a}), 109.4 (C, $(CH_3)_2C$), 90.0 (CH, C-1_{8b}), 89.0 (CH, C-1_{8a}), 76.8 (CH, C-5_{8b}), 73.1 (CH, C-5_{8a}), 73.0 (CH, C-6_{8b}), 72.9 (CH, C-6_{8a}), 72.0 (CH_2, $PhCH_{2\ 8a}$), 71.9 (CH_2, $PhCH_{2\ 8b}$), 68.5 (CH, C-4_{8b}), 68.3 (CH, C-4_{8a}), 67.1 (CH_2, C-7_{8a}), 67.0 (CH_2, C-7_{8b}), 27.0 (CH_3, one of $(CH_3)_2C_{8b}$), 26.9 (CH_3, one of $(CH_3)_2C_{8a}$), 25.3 (CH_3, one of $(CH_3)_2C_{8b}$), 25.2 (CH_3, one of $(CH_3)_2C_{8a}$), 20.90 (CH_3, CH_3CO_{8a}), 20.86 (CH_3, CH_3CO_{8b}), IR (KBr): 2986, 2935, 2874, 1754, 1372, 1213, 1074, 1004, 930, 768 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{23}O_6{}^{35}ClNa^+$ $[M + Na]^+$ 405.1081, found 405.1078.

4-*O*-Benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-D-*arabino*-hept-2-enopyranose (4)

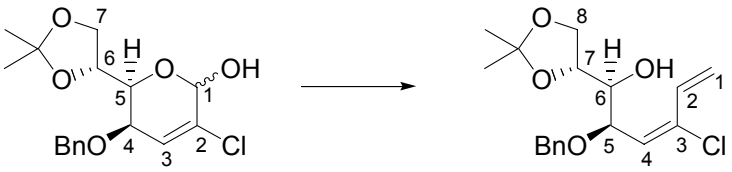


8 **4**

A solution of acetates **8a** and **8b** (306 mg, 0.799 mmol) in methanol (8 mL) was treated with a small piece of sodium (4 mg, 0.17 mmol), then stirred at room temperature for 30 minutes. The mixture was concentrated to afford a yellow oil, which was dissolved in dichloromethane, passed through a silica plug, eluting with further dichloromethane. The organic solution was concentrated to provide hemiacetal **4** (272 mg, 100%, *ca.* 13:1 anomeric ratio) as a viscous yellow oil, which was used without further purification.

R_f = 0.2 (1:5 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) major isomer: δ 7.36–7.30 (complex m, 5H, Bn), 6.17 (d, *J* = 5.7 Hz, 1H, H-3), 5.34 (d, *J* = 4.6 Hz, 1H, H-1), 4.68 (s, 2H, $PhCH_2$), 4.40 (m, 1H, H-6), 4.14 (dd, *J* = 8.4, 6.6 Hz, 1H, H-7), 4.02 (m, 1H, H-5), 3.99 (m, 1H, H-7), 3.92 (d, *J* = 5.9 Hz, 1H, H-4), 2.82 (br m, 1H, OH), 1.42 (s, 3H, one of $(CH_3)_2C$), 1.40 (s, 3H, one of $(CH_3)_2C$); ^{13}C NMR (125 MHz, $CDCl_3$) major isomer: δ 137.9 (C, C_{Ph}), 134.6 (C, C-2), 128.4 (CH, CH_{Ph}), 128.0 (CH, CH_{Ph}), 127.9 (CH, CH_{Ph}), 124.6 (CH, C-3), 109.3 (C, $(CH_3)_2C$), 90.9 (CH, C-1), 73.2 (CH, C-6), 72.1 (CH_2, $PhCH_2$), 71.2 (CH, C-5), 68.8 (CH, C-4), 67.2 (CH_2, C-7), 26.9 (CH_3, one of $(CH_3)_2C$), 25.4 (CH_3, one of $(CH_3)_2C$); IR (KBr): 3400, 2986, 2933, 2874, 1455, 1372, 1213, 1043, 738, 698 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{21}O_5{}^{35}ClNa^+$ $[M + Na]^+$ 363.0975, found 363.0971.

(3*E*,5*R*,6*S*,7*R*)-5-Benzyloxy-3-chloro-6-hydroxy-7,8-*O*-isopropylidene-octa-1,3-diene (9)

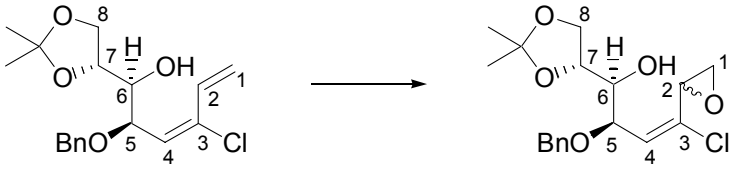


4 **9**

A solution of methyl triphenylphosphonium bromide (1.06 g, 2.97 mmol) in THF (10 mL) was cooled to −78 °C, treated with KHMDS (6.0 mL, 3.0 mmol) and stirred at −78 °C for one hour. The mixture was then treated with a solution of hemiacetal **4** (478 mg, 1.40 mmol) in THF (10 mL) and immediately allowed to warm to room temperature. The reaction was stirred at room temperature for two hours, then diluted with saturated ammonium chloride solution (50 mL) and extracted with diethyl ether (2 x 50 mL). The organic fractions were combined, dried, filtered and concentrated to provide a crude brown oil. Upon purification by column chromatography (1:5 EtOAc/hexanes), diene **9** (326 mg, 69%) was obtained as a colourless oil.

R_f = 0.3 (1:5 EtOAc/hexanes); $[\alpha]_D^{19}$ –34 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.30 (complex m, 5H, Bn), 6.61 (dd, *J* = 16.1, 10.5 Hz, 1H, H-2), 5.99 (d, *J* = 9.7 Hz, 1H, H-4), 5.82 (d, *J* = 16.1 Hz, 1H, one of H-1), 5.40 (d, *J* = 10.7 Hz, 1H, one of H-1), 4.64 (d, *J* = 11.7 Hz, 1H, one of $PhCH_2$), 4.49 (dd, *J* = 9.9, 2.8 Hz, 1H, H-5), 4.41 (d, *J* = 11.7 Hz, 1H, one of $PhCH_2$), 4.12 (app. dt, *J* = 7.5, 5.9 Hz, 1H, H-7), 4.05 (dd, *J* = 8.3, 6.4 Hz, 1H, one of H-8), 3.98 (dd, *J* = 8.5, 5.6 Hz, 1H, one of H-8), 3.51 (app. td, *J* = 7.9, 2.8 Hz, 1H, H-6), 2.45 (d, *J* = 8.3 Hz, 1H, OH), 1.39 (s, 3H, one of $(CH_3)_2C$), 1.34 (s, 3H, one of $(CH_3)_2C$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4 (C, C_{Ph}), 134.9 (C, C-3), 128.5 (CH, CH_{Ph}), 128.4 (CH, C-2), 128.2 (CH, C-4), 127.9 (2 x CH, CH_{Ph}), 120.7 (CH_2, C-1), 109.2 (C, $(CH_3)_2C$), 75.4 (CH, C-7), 75.0 (CH, C-6), 73.3 (CH, C-5), 70.6 (CH_2, $PhCH_2$), 66.7 (CH_2, C-8), 26.8 (CH_3, one of $(CH_3)_2C$), 25.3 (CH_3, one of $(CH_3)_2C$); IR (KBr): 3454, 2987, 2934, 2879, 1371, 1253, 1216, 1059, 847, 698 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{23}O_4{}^{35}ClNa^+$ $[M + Na]^+$ 361.1183, found 361.1180.

(2*R*,3*E*,5*R*,6S,7*R*)-5-Benzyloxy-3-chloro-1,2-epoxy-6-hydroxy-7,8-*O*-isopropylidene-octa-3-ene (10a) and (2*S*,3*E*,5*R*,6S,7*R*)-5-benzyloxy-3-chloro-1,2-epoxy-6-hydroxy-7,8-*O*-isopropylidene-octa-3-ene (10b)



9 **10**

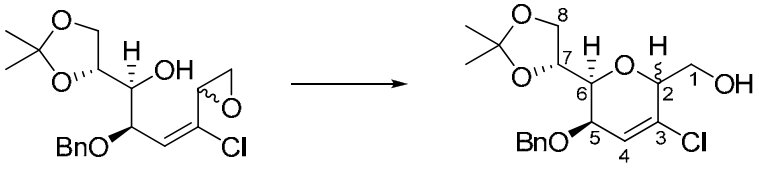
A A solution of diene **9** (112 mg, 0.33 mmol) in dichloromethane (5 mL) was treated with *m*-CPBA (163 mg, 0.66 mmol). The mixture was stirred at room temperature for two days, then diluted sequentially with saturated sodium bicarbonate solution (20 mL), water (10 mL) and diethyl ether (30 mL). The biphasic mixture was stirred rapidly for ten minutes, then the phases were separated. The ethereal fraction was washed with brine (10 mL), dried, filtered and concentrated to provide a colourless oil. Upon purification by column chromatography (1:3 EtOAc/hexanes), an inseparable mixture of epimeric epoxides **10a** and **10b** was obtained as a colourless oil (57 mg, 49%, 1.5:1), in addition to complicated mixtures of unidentified products.

R_f = 0.3 (1:3 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.29 (complex m, 5H, Bn), 6.17 (d, *J* = 9.8 Hz, 0.6H, H-4_{10a}), 6.14 (d, *J* = 9.8 Hz, 0.4H, H-4_{10b}), 4.68 (d, *J* = 11.4 Hz, 1H, one of $PhCH_2$), 4.59 (dd, *J* = 9.8, 2.7 Hz, 1H, H-5), 4.48 (d, *J* = 11.5 Hz, 1H, one of $PhCH_2$), 4.14–3.97 (complex m, 3H, H-7 and H-8), 3.72 (m, 0.6H, H-2_{10a}), 3.66 (m, 0.4H, H-2_{10b}), 3.50 (m, 1H, H-6), 3.05 (dd, *J* = 5.5, 2.3 Hz, 0.6H, one of H-1_{10a}), 2.99 (dd, *J* = 5.5, 2.4 Hz, 0.4H, one of H-1_{10b}), 2.92 (dd, *J* = 5.4, 4.2 Hz, 0.6H, one of H-1_{10a}), 2.86 (dd, *J* = 5.4, 4.1 Hz, 0.4H, one of H-1_{10b}), 2.41 (d, *J* = 8.5 Hz, 0.6H, OH_{10a}), 2.35 (d, *J* = 8.1 Hz, 0.4H, OH_{10b}), 1.39 (s, 1.2H, one of $(CH_3)_2C_{10b}$), 1.37 (s, 1.8H, one of $(CH_3)_2C_{10a}$), 1.35 (s, 1.2H, one of $(CH_3)_2C_{10b}$), 1.33 (s, 1.8H, one of $(CH_3)_2C_{10a}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2 (C, C_{Ph}), 133.7 (C, C-3_{10b}), 133.5 (C, C-3_{10a}), 132.0 (CH, C-4_{10a}), 131.3 (CH, C-4_{10b}), 128.5 (CH, CH_{Ph}), 128.03 (CH, CH_{Ph}), 128.00 (CH, CH_{Ph}), 127.96 (CH, CH_{Ph}), 127.92 (CH, CH_{Ph}), 109.3 (C, $(CH_3)_2C_{10b}$), 109.2 (C, $(CH_3)_2C_{10a}$), 75.5 (CH, C-7), 75.2 (CH, C-6_{10a}), 75.0 (CH, C-6_{10b}), 73.3 (CH, C-5_{10b}), 73.1 (CH, C-5_{10a}), 70.9 (CH_2, $PhCH_2$), 66.8 (CH_2, C-8_{10a}), 66.7 (CH_2, C-8_{10b}), 49.4 (CH, C-2_{10b}), 48.7 (CH, C-2_{10a}), 46.6 (CH_2, C-1_{10a}), 46.5 (CH_2, C-1_{10b}), 26.8 (CH_3, one of $(CH_3)_2C_{10a}$), 26.7 (CH_3, one of $(CH_3)_2C_{10b}$), 25.3 (CH_3, one of $(CH_3)_2C_{10b}$), 25.2 (CH_3, one of $(CH_3)_2C_{10a}$); HRMS (ESI) calcd for $C_{18}H_{23}O_5{}^{35}ClNa^+$ $[M + Na]^+$ 377.1132, found 377.1128.

B A solution of diene **9** (27 mg, 80 μmol) in dichloromethane (1 mL) was treated with (*R*,*R*)-Jacobsen's catalyst (2 mg, 3 μmol), followed by bleach (0.55 $molL^{-1}$, pH 11.3, 1 mL). The mixture was stirred at room temperature for two days, then separated between water (20 mL) and diethyl

ether (20 mL). The ethereal fraction was washed with brine (10 mL), dried, filtered and concentrated to provide a brown oil. Upon purification by column chromatography (1:3 EtOAc/hexanes), a mixture of epoxides **10a** and **10b** was obtained (5 mg, 18%, 1.2:1 ratio).

[(2*S*,3*R*,6*S*,4′*R*)-2,3-Dihydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5-chloro-6*H*-pyran-6-yl]methanol (11a) and [(2*S*,3*R*,6*R*,4′*R*)-2,3-dihydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5-chloro-6*H*-pyran-6-yl]methanol (11b)



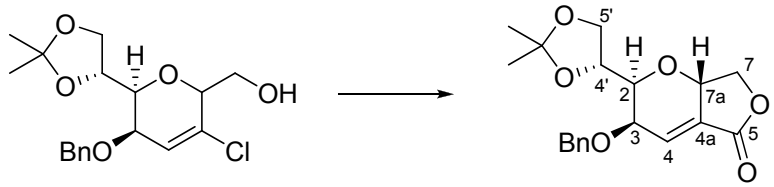
10 **11**

Method A A solution of epoxides **10a** and **10b** (73 mg, 0.21 mmol) in methanol (2 mL) was treated with sodium (12 mg, 0.52 mmol) and then stirred at room temperature for two days. The mixture was concentrated, then passed through a silica plug, which was eluted with dichloromethane (10 mL). The solution was dried and concentrated to provide a yellow oil. Upon purification by column chromatography (1:3 EtOAc/hexanes), an inseparable mixture of epimeric alcohols **11a** and **11b** was obtained as a pale–yellow oil (31 mg, 42%, *ca.* 3:1 ratio).

R_f = 0.3 (1:2 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.29 (complex m, 5H, Bn), 6.29 (d, *J* = 6.3 Hz, 0.25H, H-4_{11b}), 6.19 (d, *J* = 5.9 Hz, 0.75H, H-4_{11a}), 4.694 (d, *J* = 11.7 Hz, 0.25H, one of $PhCH_{2\ 11b}$), 4.688 (d, *J* = 11.7 Hz, 0.75H, one of $PhCH_{2\ 11a}$), 4.61 (d, *J* = 11.7 Hz, 1H, one of $PhCH_2$), 4.38–4.33 (complex m, 1.75H, H-2_{11a} and H-6), 4.25 (m, 0.25H, H-2_{11b}), 4.16–4.10 (complex m, 1H, one of H-8), 4.06–3.98 (complex m, 1.25H, H-5_{11b} and one of H-8), 3.91 (m, 0.75H, H-5_{11a}), 3.89–3.86 (complex m, 2.75H, H-1 and H-7_{11a}), 3.54 (d, *J* = 8.0 Hz, 0.25H, H-7_{11b}), 1.89 (br s, 1H, OH), 1.41 (s, 2.25H, one of $(CH_3)_2C_{11a}$), 1.40 (s, 0.75H, one of $(CH_3)_2C_{11b}$), 1.39 (s, 2.25H, one of $(CH_3)_2C_{11a}$), 1.38 (s, 0.75H, one of $(CH_3)_2C_{11b}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0 and 137.9 (C, C_{Ph}), 136.0 (C, C-3_{11b}), 134.8 (C, C-3_{11a}), 128.42 and 128.37 and 128.0 and 127.9 and 127.8 (CH, CH_{Ph}), 125.0 (CH, C-4_{11b}), 123.6 (CH, C-4_{11a}), 109.2 (C, $(CH_3)_2C_{11b}$), 108.9 (C, $(CH_3)_2C_{11a}$), 78.1 (CH, C-2_{11b}), 77.6 (CH, C-7_{11b}), 77.0 (CH, C-2_{11a}), 74.2 (CH, C-6_{11a}), 73.5 (CH, C-6_{11b}), 72.4 (CH, C-7_{11a}), 71.6 (CH_2, $PhCH_{2\ 11a}$), 71.4 (CH_2, $PhCH_{2\ 11b}$), 69.29 and 69.26 (CH, C-5), 67.0 (CH_2, C-8_{11b}), 66.7 (CH_2, C-8_{11a}), 62.6 (CH_2, C-1_{11b}), 60.6 (CH_2, C-1_{11a}), 26.9 (CH_3, one of $(CH_3)_2C_{11b}$), 26.6 (CH_3, one of $(CH_3)_2C_{11a}$), 25.4 (CH_3, one of $(CH_3)_2C_{11a}$), 25.3 (CH_3, one of $(CH_3)_2C_{11b}$); IR (KBr): 3463, 2988, 2933, 2874, 1455, 1372, 1219, 1072, 771, 698 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{23}O_5{}^{35}ClNa^+$ $[M + Na]^+$ 377.1132, found 377.1137.

Method B A solution of epoxides **10a** and **10b** (69 mg, 0.19 mmol) in DMF (2 mL) was treated with sodium hydride (11 mg, 0.28 mmol). The mixture was stirred at room temperature for one day, then diluted with saturated copper sulfate solution (10 mL) and water (10 mL), then extracted with dichloromethane (2 x 20 mL). The organic fractions were combined, dried, filtered and concentrated to provide a yellow oil. Upon purification by column chromatography (1:3 EtOAc/hexanes), an inseparable mixture of epimeric alcohols **11a** and **11b** were obtained as a pale–yellow oil (1.5:1 ratio, 16 mg, 23%), in addition to recovered starting material (24 mg, 35%).

(2*S*,3*R*,7a*S*,4′*R*)-2,3,7,7a-Tetrahydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5*H*-furo[3,4-*b*]pyran-5-one (6)

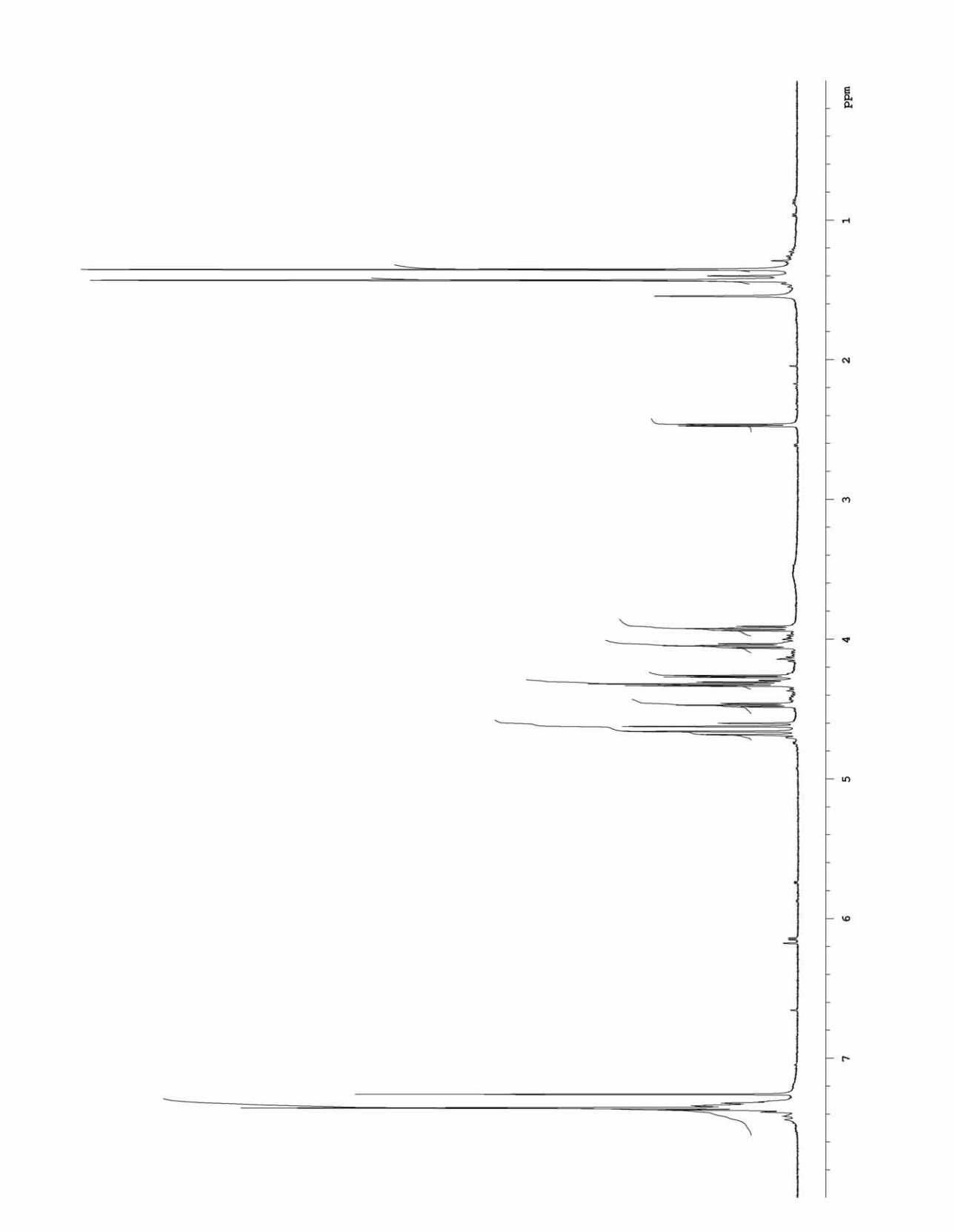


11 **6**

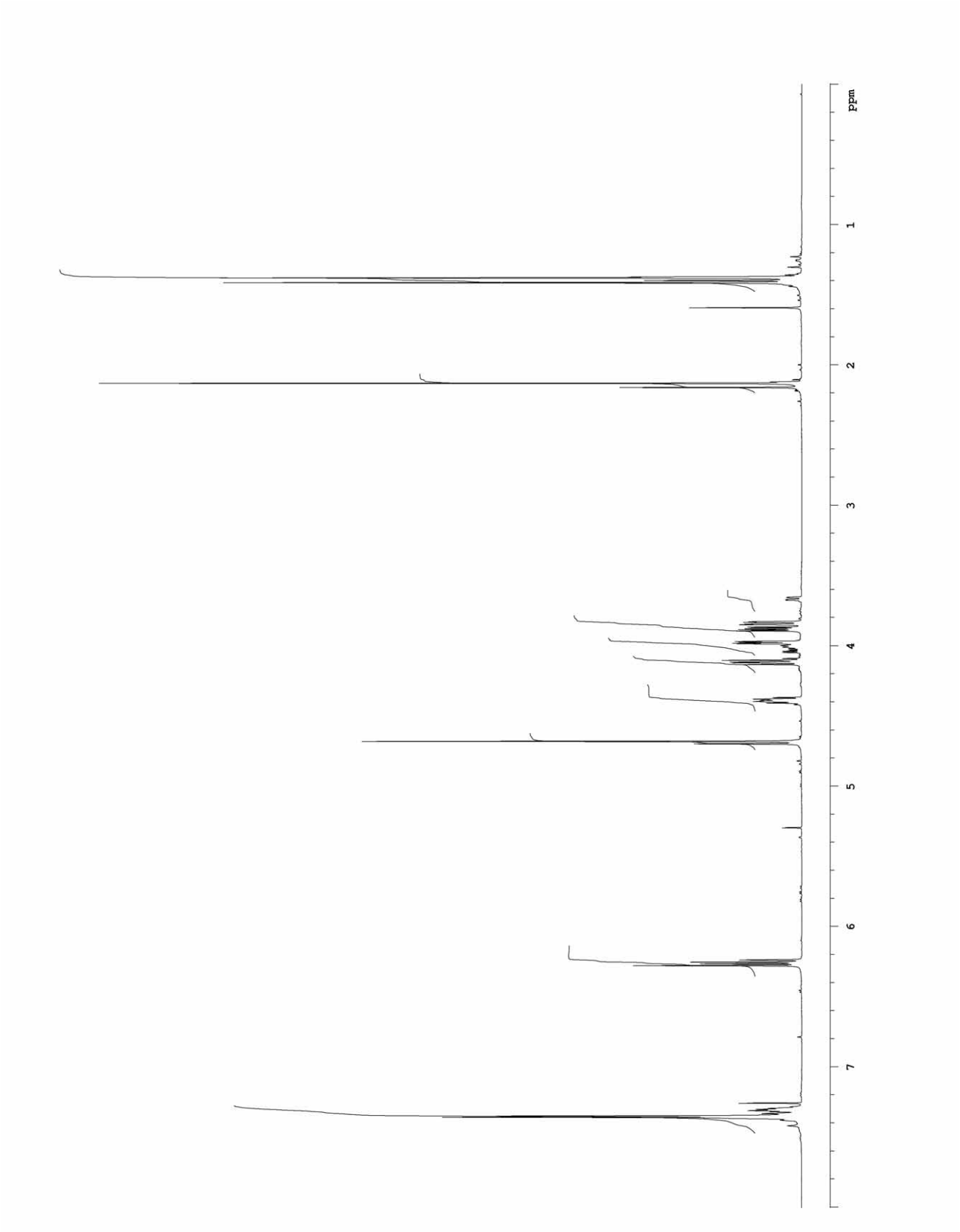
A solution of alcohols **11a** and **11b** (40 mg, 0.11 mmol, 2.8:1 ratio) in 1,4-dioxane (3.0 mL) was treated with palladium(II) acetate (10 mg, 0.044 mmol), triphenylphosphine (60 mg, 0.23 mmol) and *N*,*N*-diisopropylethylamine (30 μL, 0.17 mmol), then stirred at reflux under an atmosphere of carbon monoxide for one day. The solution was filtered through a pad of silica, then washed with diethyl ether (20 mL). The ethereal solution was dried, filtered and concentrated to provide a brown oil. Upon column chromatography (1:3 EtOAc/hexanes), starting material **11** was recovered (3.7:1 ratio, 25 mg, 63%) and bicycle **6** (7 mg, 18%) was obtained as a pale–yellow solid.

R_f = 0.3 (1:3 EtOAc/hexanes); $[\alpha]_D^{18}$ –142 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.31 (complex m, 5H, Bn), 7.25 (dd, *J* = 6.1, 3.4 Hz, 1H, H-4), 5.18 (app. td, *J* = 7.9, 3.0 Hz, 1H, H-7a), 4.64 (d, *J* = 11.5 Hz, 1H, one of $PhCH_2$), 4.60 (partially obscured dd, *J* = 8.7, 8.3 Hz, 1H, one of H-7), 4.59 (d, *J* = 11.5 Hz, 1H, one of $PhCH_2$), 4.42–4.38 (complex m, 2H, H-3 and H-4′), 4.13 (dd, *J* = 8.6, 6.2 Hz, 1H, one of H-5′), 4.00 (dd, *J* = 8.8, 7.6 Hz, 1H, one of H-7), 3.96 (dd, *J* = 8.8, 5.1 Hz, 1H, one of H-5′), 3.38 (dd, *J* = 8.3, 0.9 Hz, 1H, H-2), 1.38 (s, 6H, $(CH_3)_2C$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0 (C, C-5), 137.6 (C, Ph), 135.4 (CH, C-4), 133.8 (CH, C-4a), 128.5 (CH, Ph), 128.0 (CH, Ph), 127.8 (CH, Ph), 109.2 (C, $(CH_3)_2C$), 75.7 (CH, C-2), 73.5 (CH, C-4′), 72.0 (CH_2, $PhCH_2$), 71.1 (CH_2, C-7), 70.3 (CH, C-7a), 67.5 (CH_2, C-5′), 67.3 (CH, C-3), 26.9 (CH_3, one of $(CH_3)_2C$), 25.3 (CH_3, one of $(CH_3)_2C$); IR (KBr): 2984, 2923, 2874, 1772, 1377, 1369, 1204, 1108, 1067, 768 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}O_6Na^+$ $[M + Na]^+$ 369.1314, found 369.1308. For nOe results, see page 22.

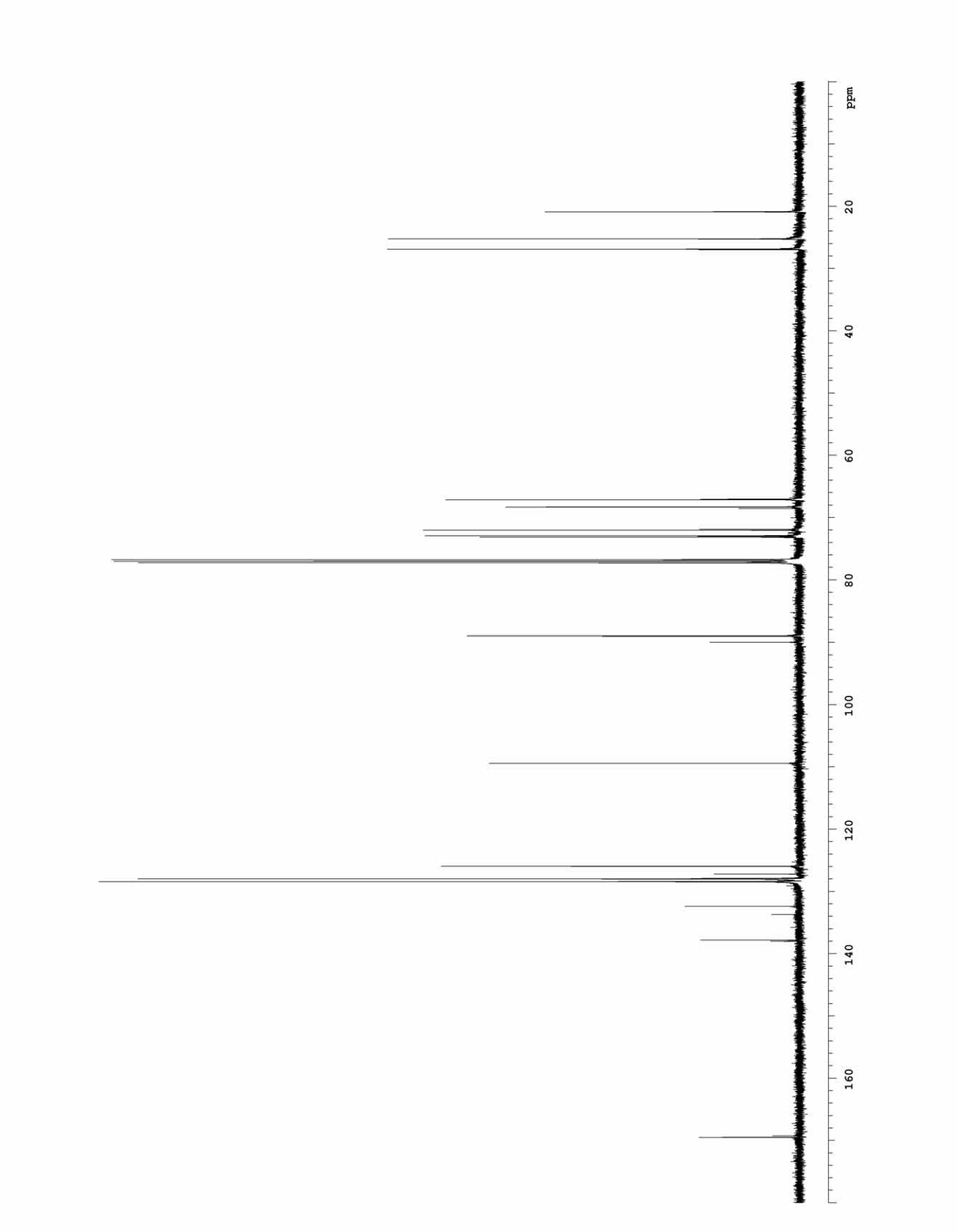
^{1}H NMR spectrum of 1,4-anhydro-3-*O*-benzyl-2-deoxy-1,2-*C*-(dichloromethylene)-5,6-*O*-isopropylidene-D-*glycero*-D-*gulo*-hexitol (**7**) (500 MHz, $CDCl_3$)



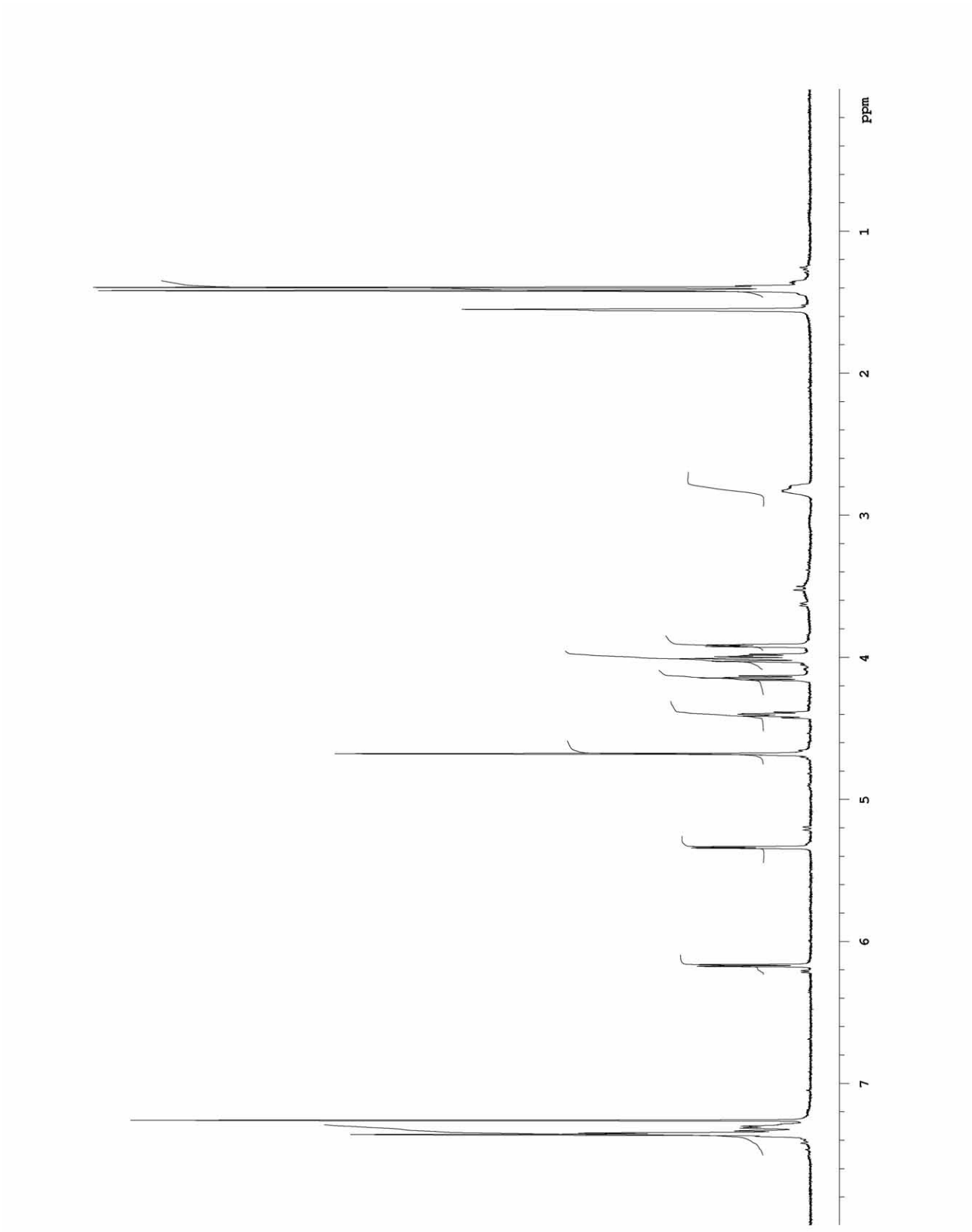
^{1}H NMR spectrum of acetyl 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-α-D-*arabino*-hept-2-enopyranoside and acetyl 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-β-D-*arabino*-hept-2-enopyranoside (**8**) (500 MHz, $CDCl_3$)



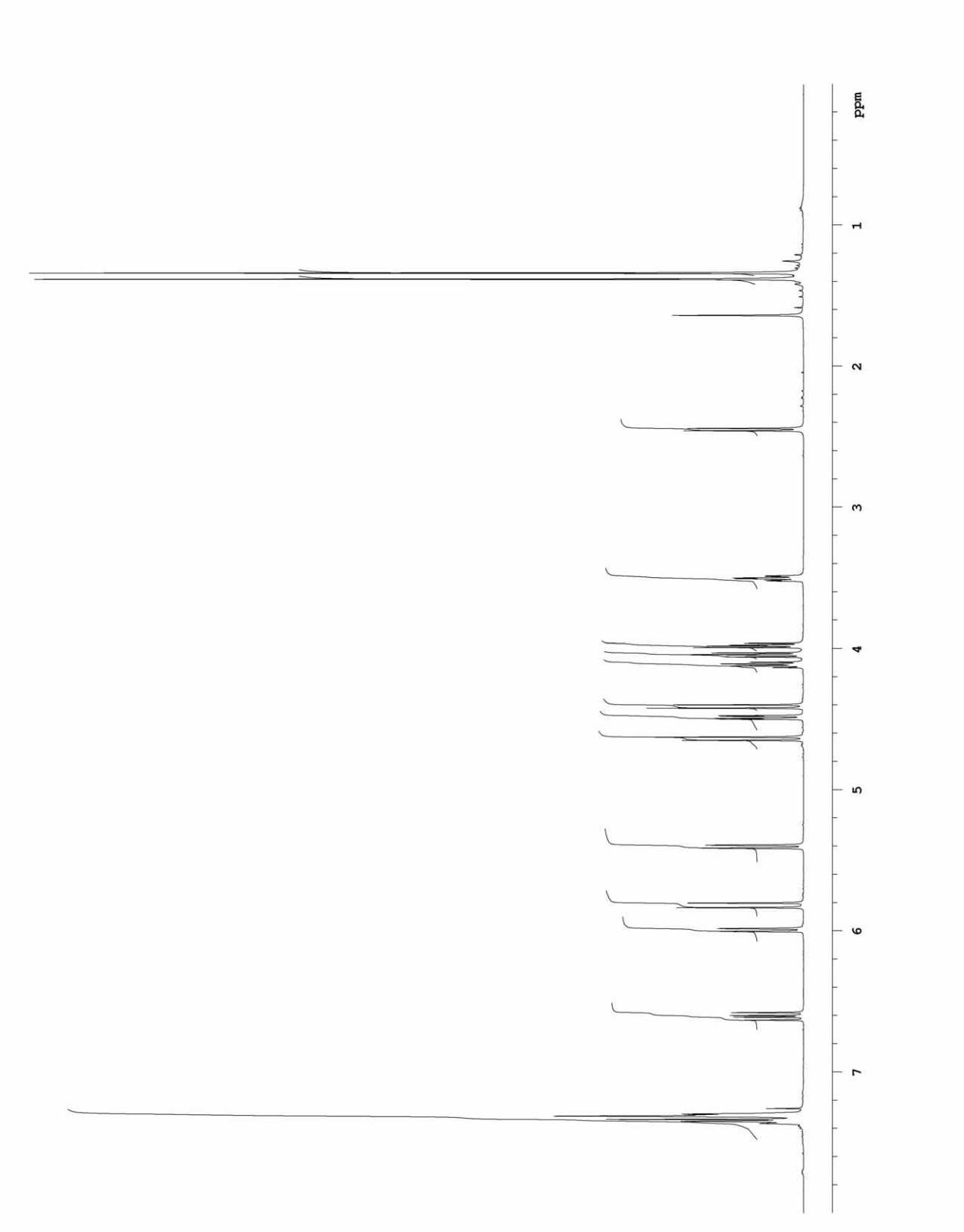
^{13}C NMR spectrum of acetyl 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-α-D-*arabino*-hept-2-enopyranoside and acetyl 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-β-D-*arabino*-hept-2-enopyranoside (**8**) (125 MHz, $CDCl_3$)



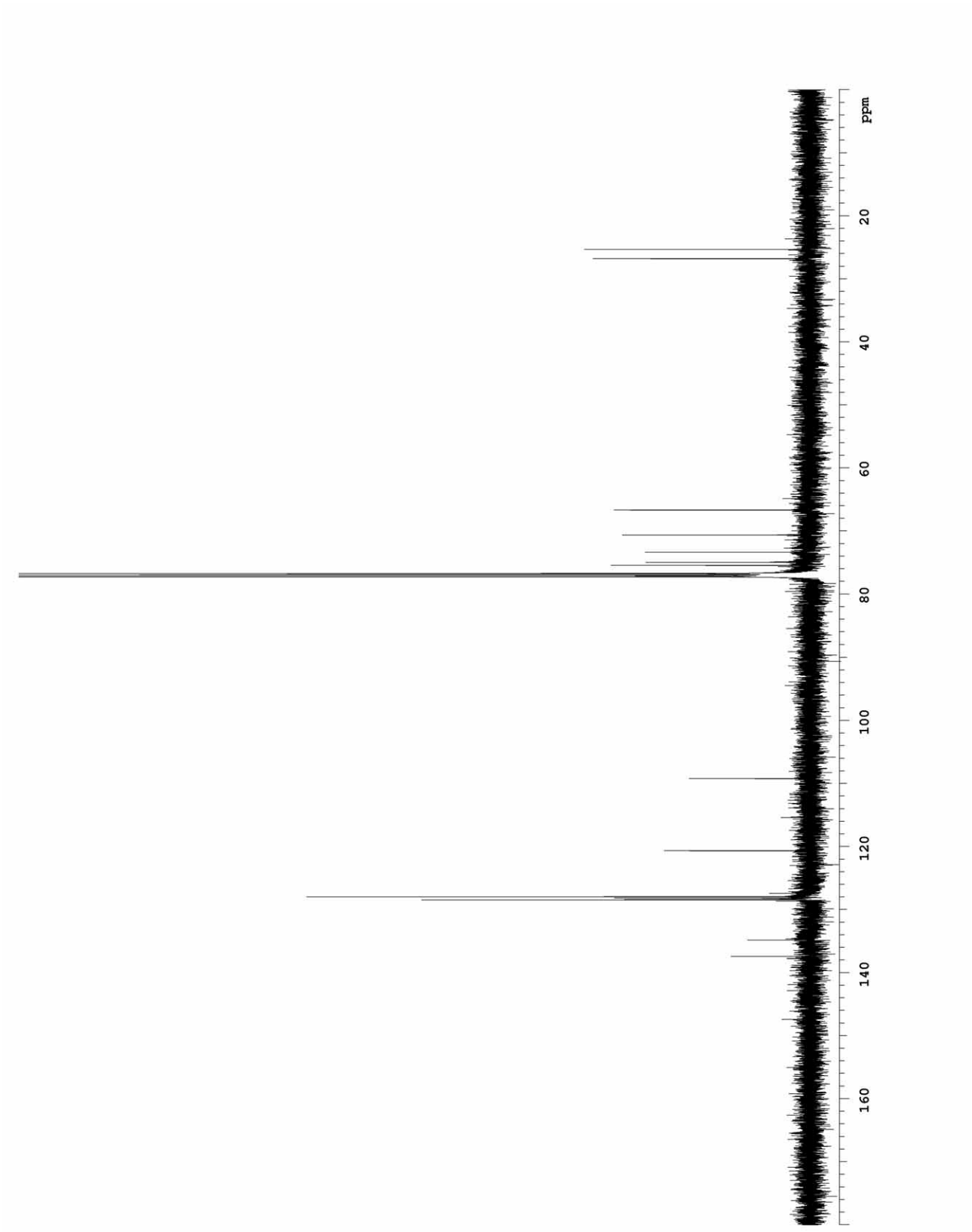
^{1}H NMR spectrum of 4-*O*-benzyl-2-chloro-2,3-dideoxy-6,7-*O*-isopropylidene-D-*arabino*-hept-2-enopyranose (**4**) (500 MHz, $CDCl_3$)



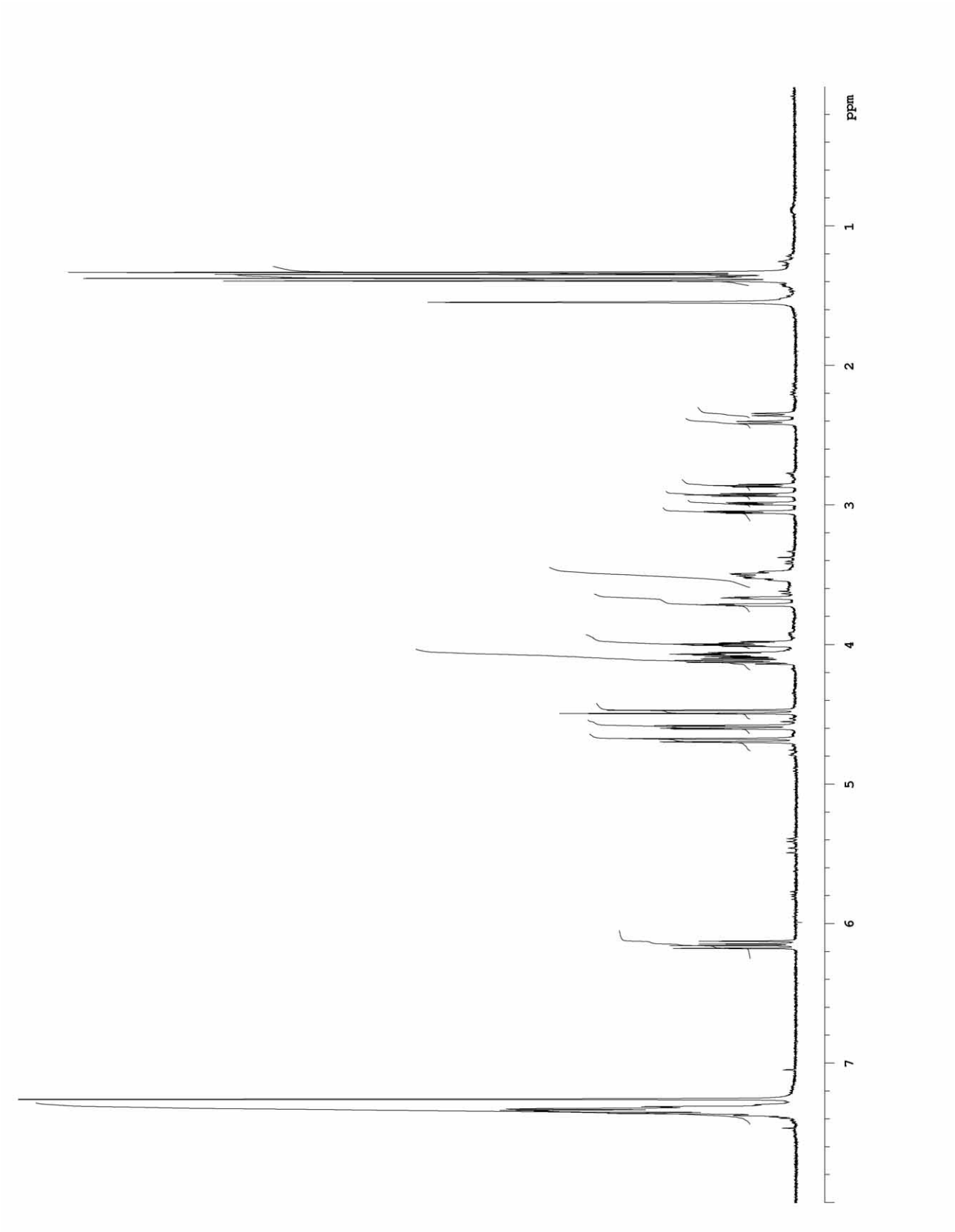
^{1}H NMR spectrum of (3*E*,5*R*,6*S*,7*R*)-5-benzyloxy-3-chloro-6-hydroxy-7,8-*O*-isopropylidene-octa-1,3-diene (**9**) (500 MHz, $CDCl_3$)



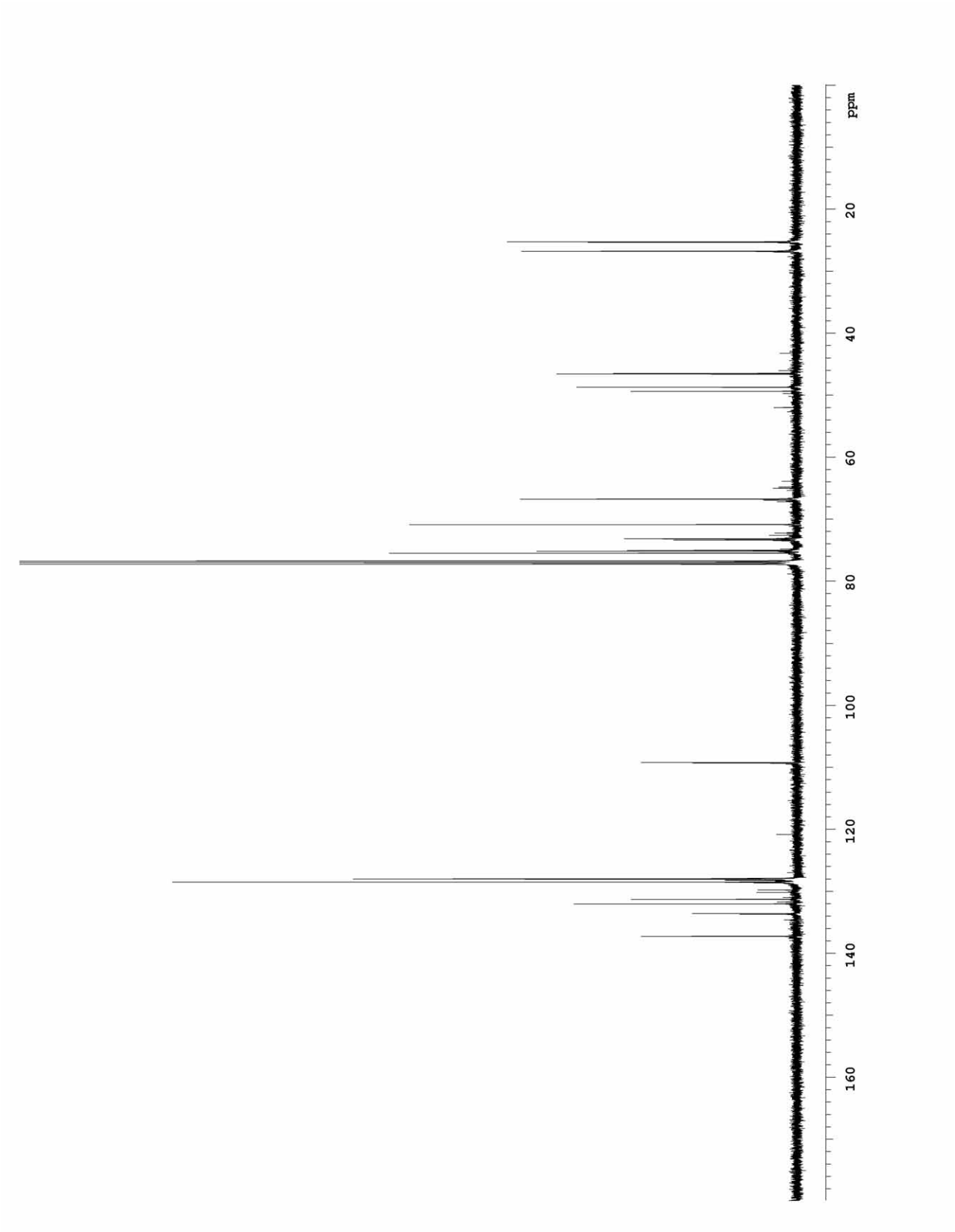
^{13}C NMR spectrum of (3*E*,5*R*,6*S*,7*R*)-5-benzyloxy-3-chloro-6-hydroxy-7,8-*O*-isopropylidene-octa-1,3-diene (**9**) (125 MHz, $CDCl_3$)



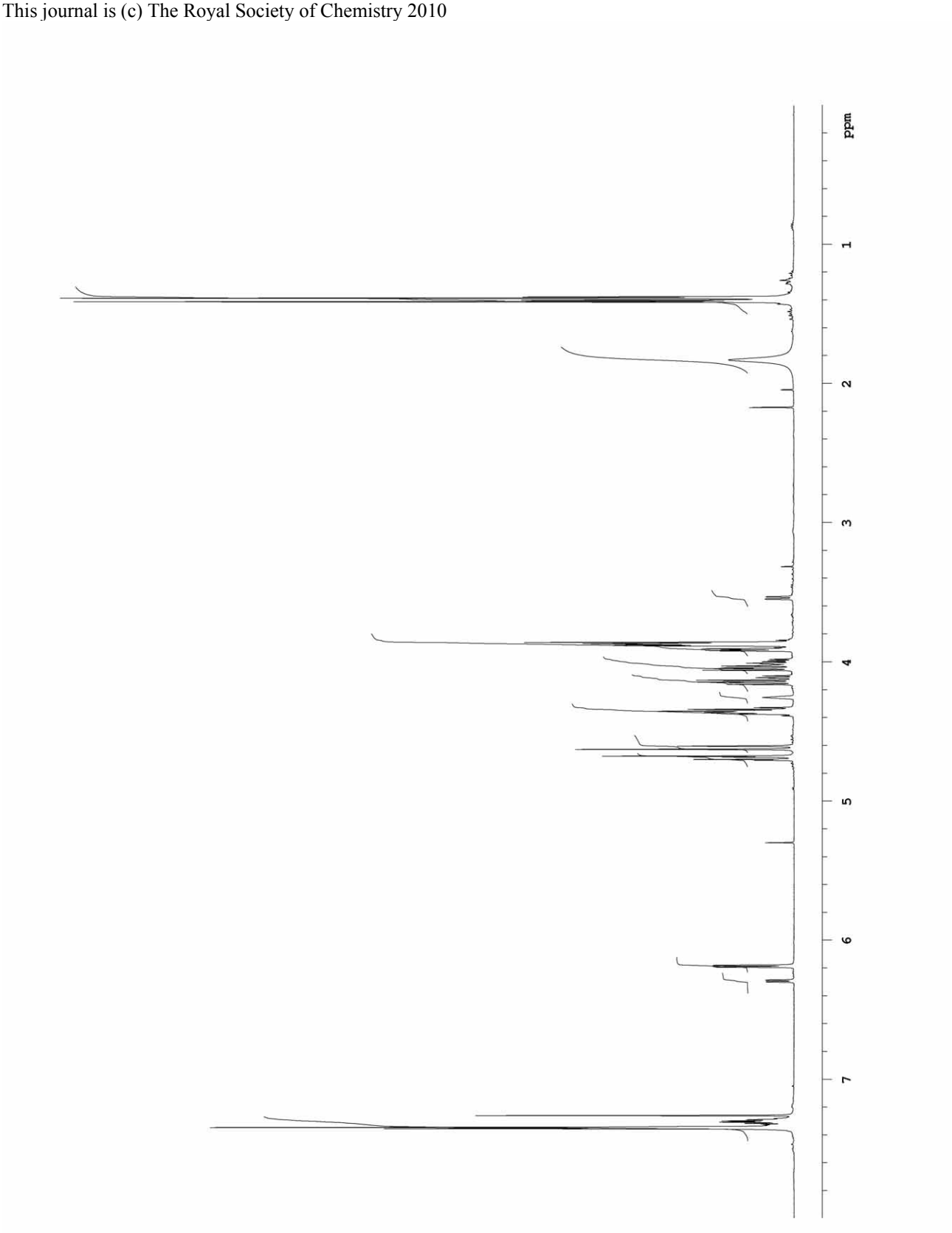
^{1}H NMR spectrum of (2*R*,3*E*,5*R*,6S,7*R*)-5-benzyloxy-3-chloro-1,2-epoxy-6-hydroxy-7,8-*O*-isopropylidene-octa-3-ene (**10a**) and (2*S*,3*E*,5*R*,6S,7*R*)-5-benzyloxy-3-chloro-1,2-epoxy-6-hydroxy-7,8-*O*-isopropylidene-octa-3-ene (**10b**) (500 MHz, $CDCl_3$)



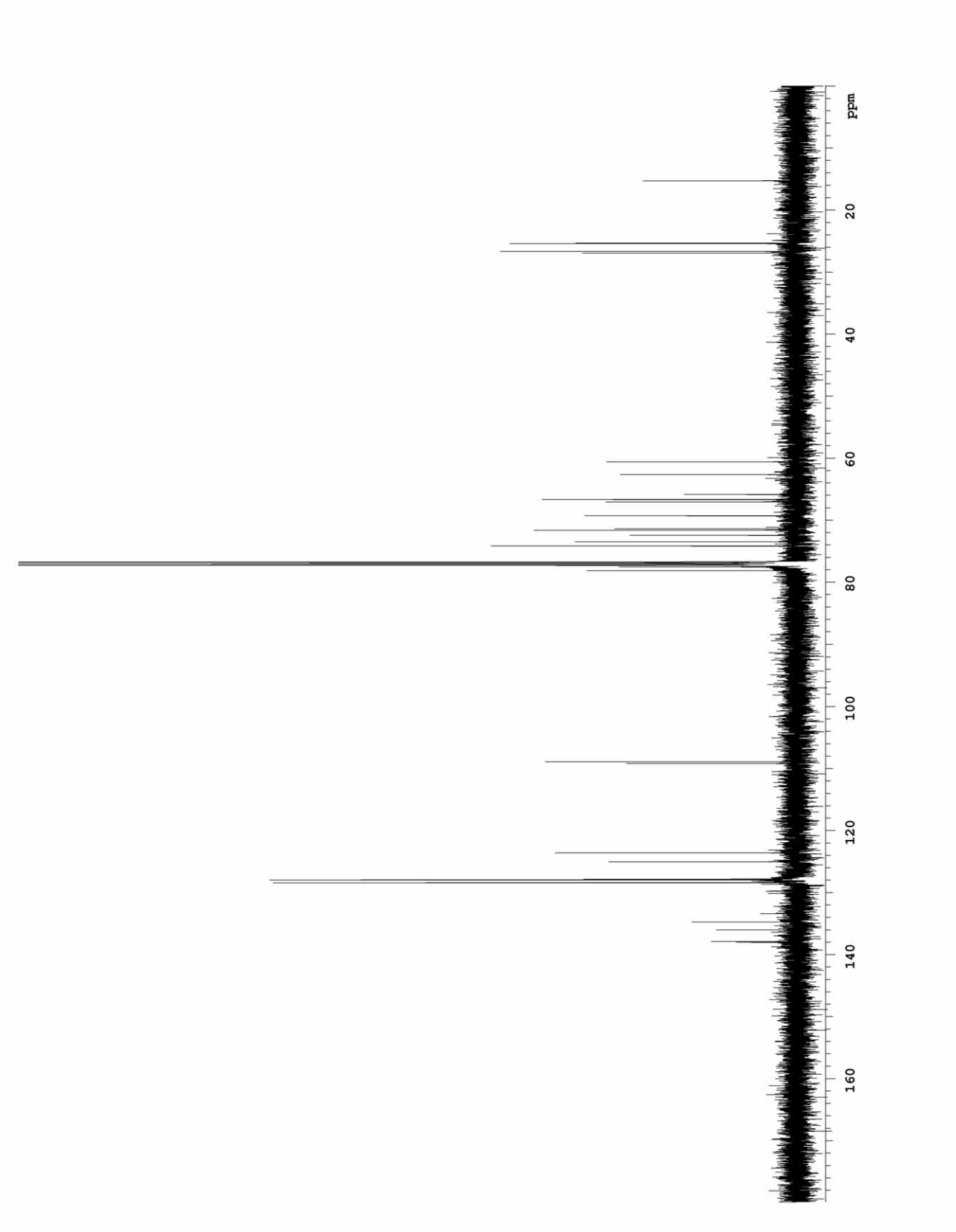
^{13}C NMR spectrum of (2*R*,3*E*,5*R*,6S,7*R*)-5-benzyloxy-3-chloro-1,2-epoxy-6-hydroxy-7,8-*O*-isopropylidene-octa-3-ene (**10a**) and (2*S*,3*E*,5*R*,6S,7*R*)-5-benzyloxy-3-chloro-1,2-epoxy-6-hydroxy-7,8-*O*-isopropylidene-octa-3-ene (**10b**) (125 MHz, $CDCl_3$)



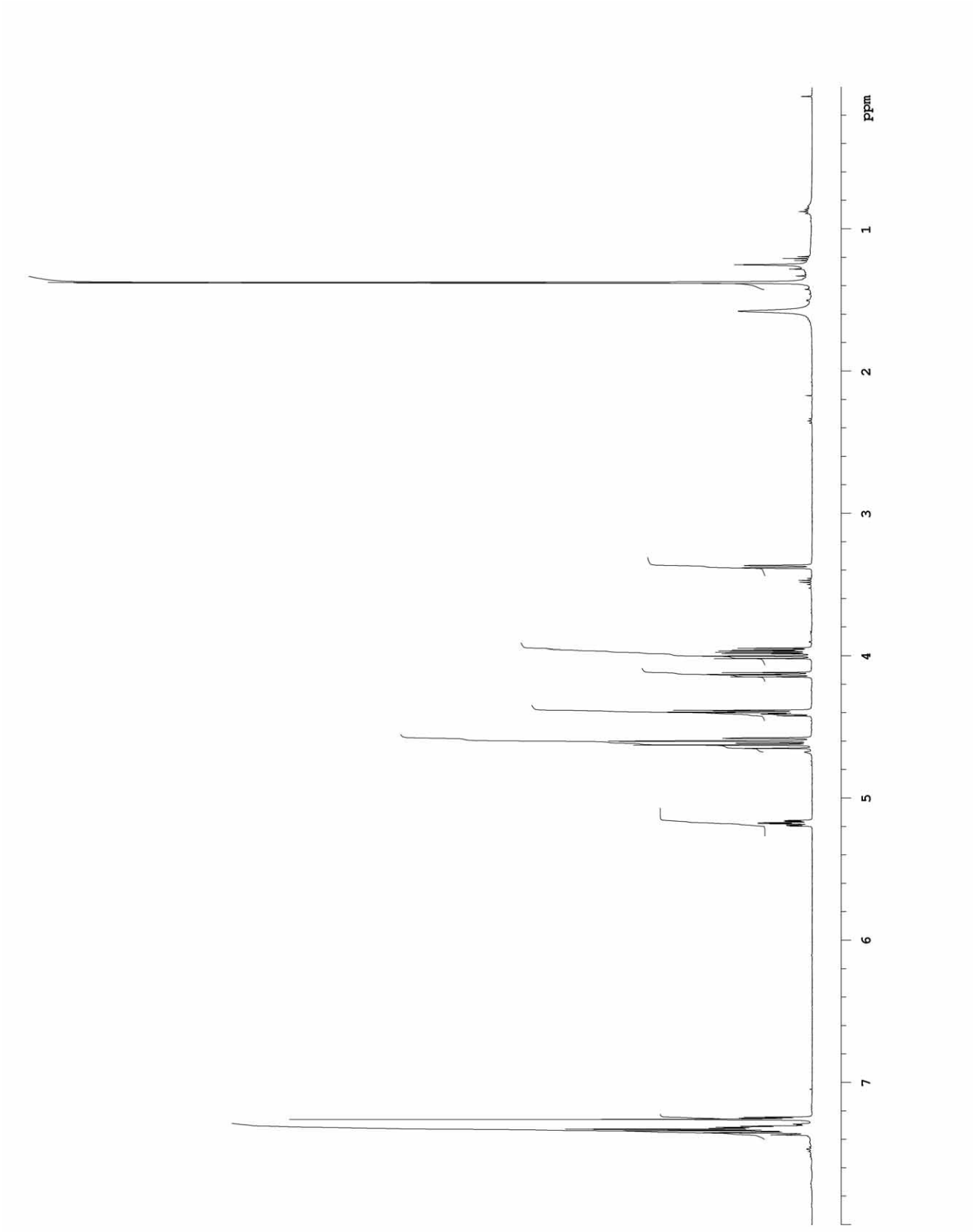
^{1}H NMR spectrum of [(2*S*,3*R*,6*S*,4′*R*)-2,3-dihydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5-chloro-6*H*-pyran-6-yl]methanol (**11a**) and [(2*S*,3*R*,6*R*,4′*R*)-2,3-dihydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5-chloro-6*H*-pyran-6-yl]methanol (**11b**) (500 MHz, $CDCl_3$)


ppm
1
2
3
4
5
6
7

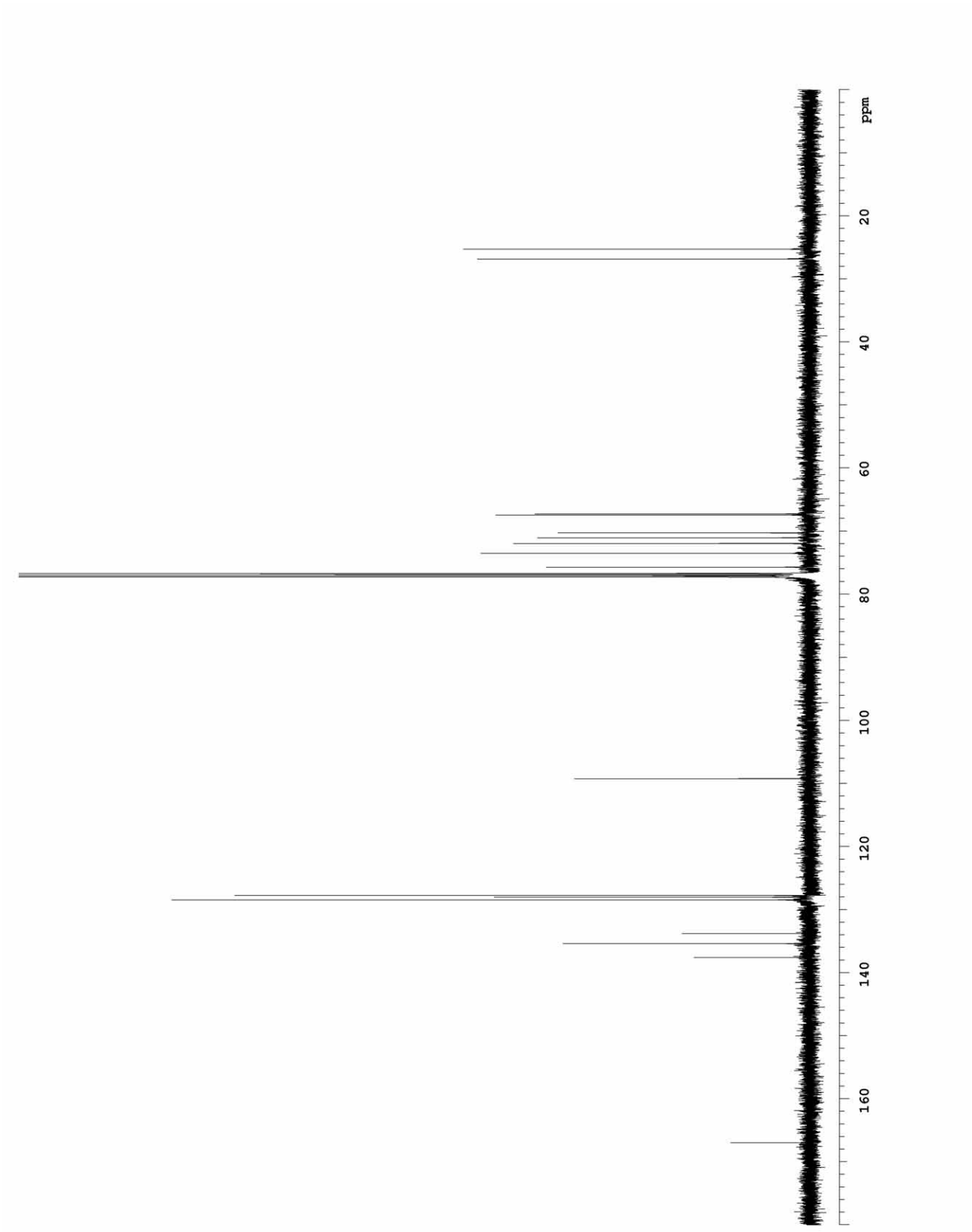
^{13}C NMR spectrum of [(2*S*,3*R*,6*S*,4′*R*)-2,3-dihydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5-chloro-6*H*-pyran-6-yl]methanol (**11a**) and [(2*S*,3*R*,6*R*,4′*R*)-2,3-dihydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5-chloro-6*H*-pyran-6-yl]methanol (**11b**) (125 MHz, $CDCl_3$)



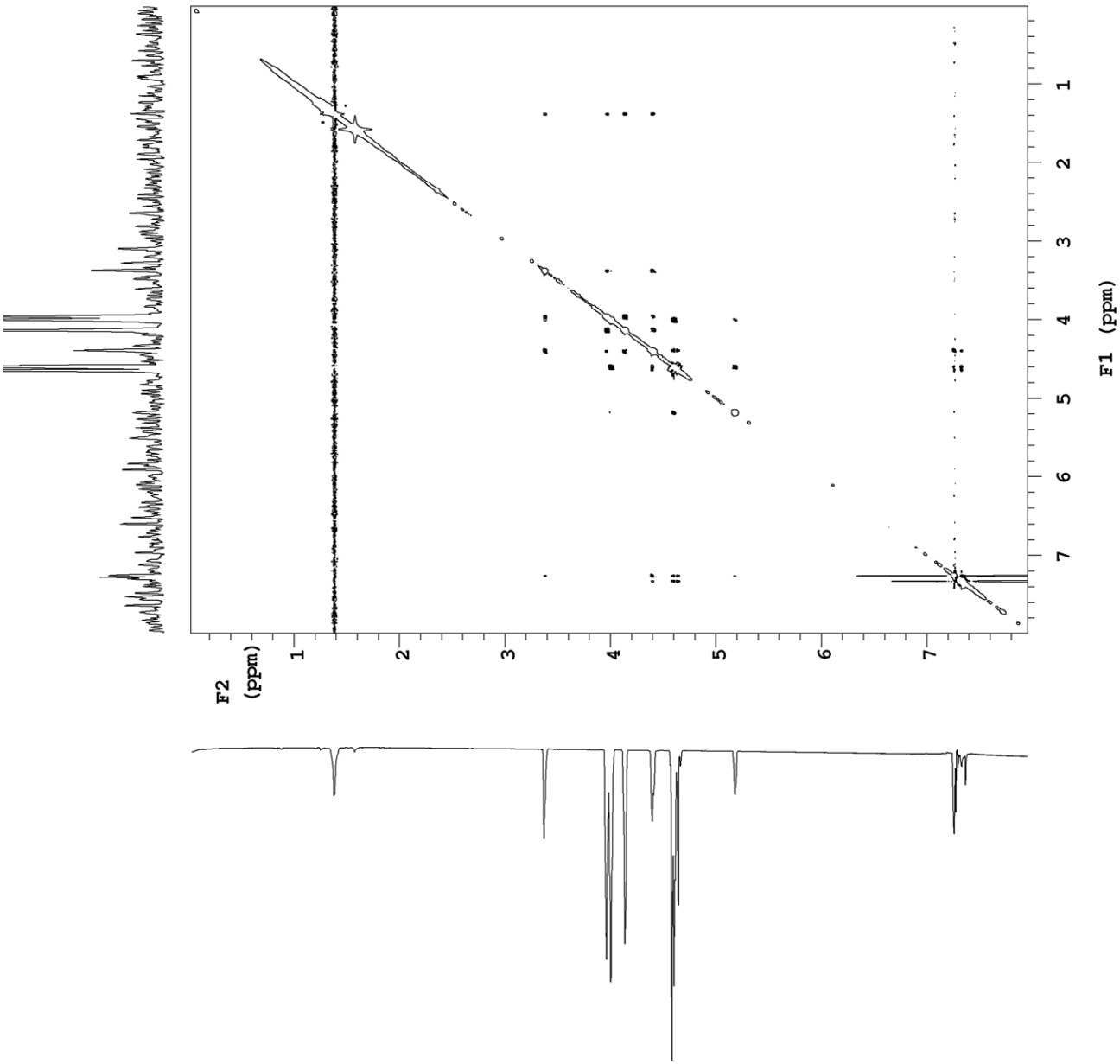
^{1}H NMR spectrum of (2*R*,3*R*,7a*S*,4′*R*)-2,3,7,7a-tetrahydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5*H*-furo[3,4-*b*]pyran-5-one (**6**) (500 MHz, $CDCl_3$)



^{13}C NMR spectrum of (2*R*,3*R*,7a*S*,4′*R*)-2,3,7,7a-tetrahydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5*H*-furo[3,4-*b*]pyran-5-one (**6**) (125 MHz, $CDCl_3$)



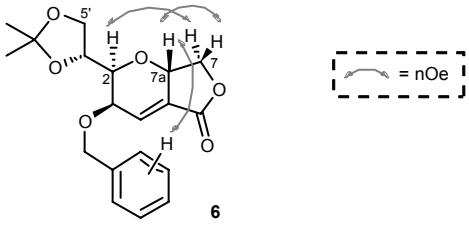
2D NOESY spectrum of (2*R*,3*R*,7a*S*,4′*R*)-2,3,7,7a-tetrahydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5*H*-furo[3,4-*b*]pyran-5-one (**6**) (600 MHz, $CDCl_3$)

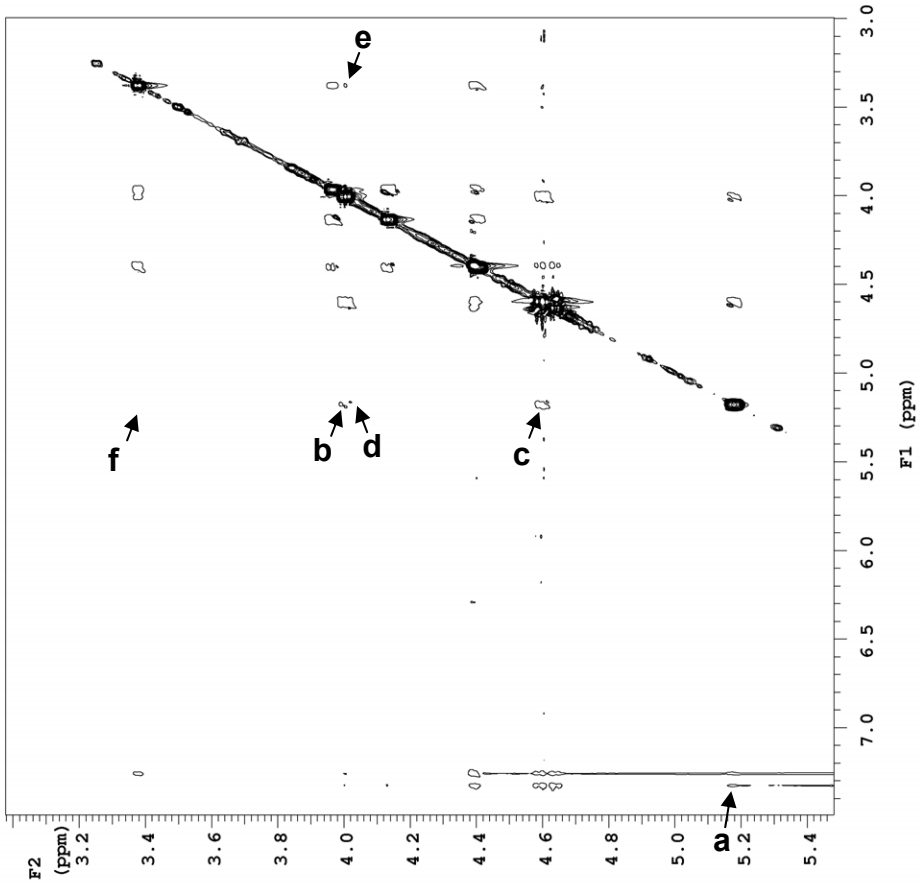


2D NOESY spectrum of (2*R*,3*R*,7a*S*,4′*R*)-2,3,7,7a-tetrahydro-2-(2′2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-benzyloxy-5*H*-furo[3,4-*b*]pyran-5-one (**6**) (600 MHz, $CDCl_3$) – expansion

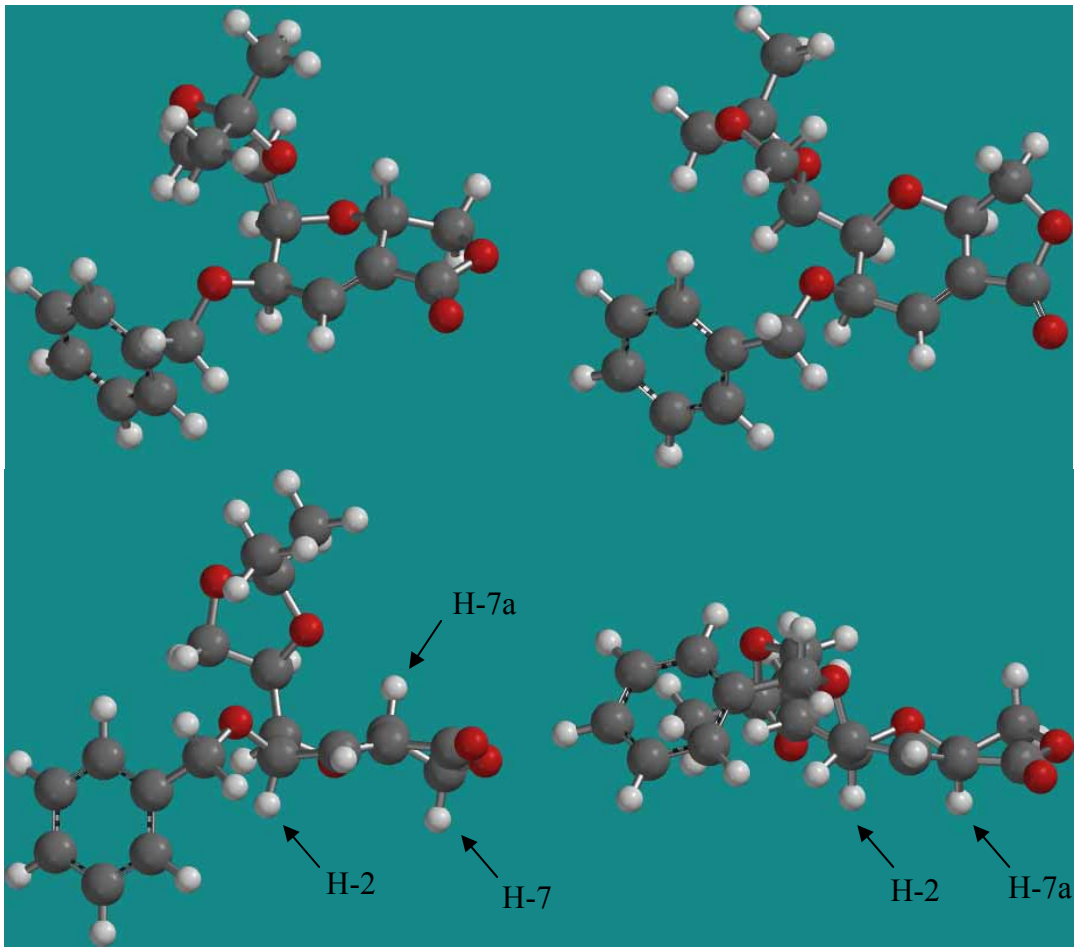
Arrows show key correlations helpful in determining the C-7a stereochemistry:

a. An nOe between H-7a and the aromatic protons on the top face
b. An nOe between H-7a and the H-5′ peak at δ 3.96 on the top face
c. A strong nOe between H-7a and the H-7 peak at δ 4.60
d. A weaker nOe between H-7a and the H-7 peak at δ 4.00
e. An nOe between the H-7 peak at δ 4.00 and H-2 on the bottom face
f. No observable nOe between H-2 and H-7a





Molecular Mechanics Calculations of Ground State Conformations of **6** and 7a-*epi*-**6**



Face-on (top) and side-on (bottom) views of **6** (left) and 7a-*epi*-**6** (right) based on MMFF calculations at ground state [2]

The coupling constants between H-7a and the two H-7 protons are similar in magnitude. This is consistent with interception of the Karplus graph at two points: once at a small dihedral angle and once at a large dihedral angle. Using a $^{3}J_{H,H}$ calculation that takes into account the electronegativities of the neighbouring substituents,[3] the observed coupling constants of *ca.* 8.3 and *ca.* 7.6 Hz between H-7a and the protons assigned as *cis*- and *trans*-H-7, respectively, give the following results:

1) $^{3}J_{H,H} = 8.3$ gives the following solutions to the Karplus equation: 5°, 134°, 199°, and 325°. The dihedral angle in the calculated structures between H-7a and the *cis*-H-7 is -35° ≡ 325°.
2) $^{3}J_{H,H} = 7.6$ gives the following solutions to the Karplus equation: 24°, 145°, 217°, and 339°. The dihedral angle in the calculated structures between H-7a and the *trans*-H-7 is -157° ≡ 203°. Presumably the less accurate fit seen here is due in part to the fact that the equations used in reference 3 are biased towards dihedral angles close to 60° and 180° because of their derivation from cyclohexane-type structures. The angle of -157° means that the most electronegative elements attached to each of the centres are not anti-periplanar, as in the calculation model used.

[2] Conformational searches were conducted with the Spartan© program using the Merck molecular force field (MMFF) to determine the equilibrium conformation of each structure at ground state.
[3] http://www.stenutz.eu/conf/haasnoot.php – sighted November 2010. Based on C. A. G. Haasnoot, F. A. A. M. de Leeuw, C. Altona, *Tetrahedron*, **1980**, *36*, 2783–2792.