Supporting information for:

Studies Directed Toward the Construction of the Polypropionate Fragment of Superstolide A

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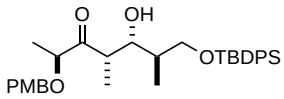
Experimental procedures and characterization data for compounds 2, 4, 5, and 8–17.

Melting points were taken on an Electrothermal apparatus and have not been corrected. Specific rotations were determined at 20 °C on a Perkin-Elmer 241 MC polarimeter. IR spectra were recorded on either a Perkin-Elmer 681 or a Nicolet 510 FT spectrometer and only the more representative frequencies (cm^{-1}) are reported. ^1H NMR (300 MHz) and ^{13}C NMR (75.4 MHz) spectra were recorded on a Varian Unity Plus 300 spectrometer; ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on a Varian Mercury-400 spectrometer; ^1H NMR (500 MHz) spectra were recorded in a Varian Inova-500 spectrometer. Chemical shifts (δ) are quoted in ppm and referenced to internal TMS for ^1H NMR and $CDCl_3$ (δ 77.0) or CD_3OD (δ 49.0) for ^{13}C NMR; coupling constants (*J*) are quoted in Hz; data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; where appropriate, 2D techniques were also used to assist in structure elucidation. High resolution mass spectra (HRMS) were obtained from the Centro de Apoio Cientifico Tecnoloxico a Investigacion (C.A.C.T.I.), Universidad de Vigo. HPLC analyses were performed on a Shimadzu Liquid Chromatograph (Tracer Spehrisorb S3W column, 4.6 mm × 25 cm, 3 μm silica gel, 0.9 mL min^{-1}). Flash chromatography was performed on SDS silica gel 60 (35–70 μm). Analytical thin-layer chromatography was carried out on Merck Kieselgel 60 F_{254} plates.

All reactions were conducted in oven-dried glassware under inert atmosphere of dry argon or nitrogen with anhydrous solvents. The solvents and reagents were purified and dried according to standard procedures.

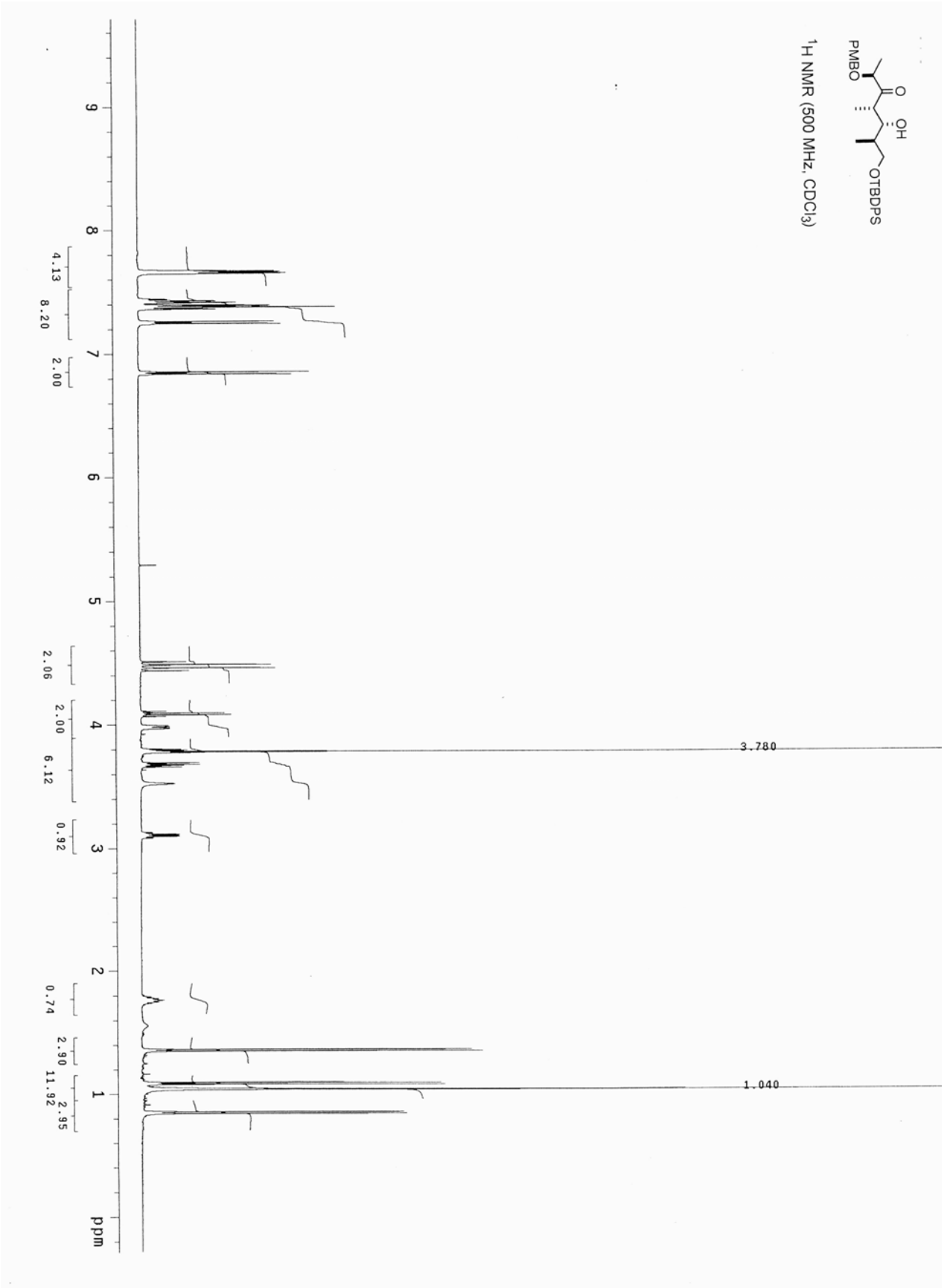
1. (2*S*,4*S*,5*R*,6*R*)-7-*tert*-Butyldiphenylsilyloxy-5-hydroxy-2-(*p*-methoxybenzyloxy)-4,6-dimethyl-3-heptanone (5).



Freshly distilled Ti(*i*-PrO)$_4$ (196 µL, 0.66 mmol) was added dropwise to a solution of $TiCl_4$ (218 µL, 1.98 mmol) in CH_2Cl_2 (2.3 mL) at 0 °C under N_2 and the yellow solution was stirred for 10 min at 0 °C and 10 min at rt. It was then diluted with CH_2Cl_2 (2.3 mL) and the resulting colorless solution was added dropwise (it was rinsed with 2 × 1.0 mL) for 10–15 min to a solution of **6** (535 mg, 2.4 mmol) in CH_2Cl_2 (4.3 mL) at –90 °C under N_2, followed by *i*-Pr_2EtN (0.46 mL, 2.6 mmol). The resulting red solution was stirred for 1.5 h at –78 °C and a solution of **7** (943 mg, 2.9 mmol) in CH_2Cl_2 (1.0 mL) was added slowly (it was rinsed with 2 × 0.5 mL).

After 2 h at –78 °C, the reaction mixture was quenched by the addition of saturated NH_4Cl (12 mL) and was vigorously stirred at rt. The mixture was partitioned with Et_2O (450 mL) and H_2O (120 mL) and the organic layer was washed with saturated $NaHCO_3$ (120 mL), and brine (120 mL). The aqueous layers were further extracted with Et_2O (200 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. The resulting oil was analyzed by HPLC and purified by flash column chromatography (hexanes/EtOAc 90:10), affording 1.079 g (82%) of **5**.

Colorless oil. $\boldsymbol{R_f}$ (hexanes/EtOAc 85:15) = 0.25. **HPLC** (hexanes/*i*-PrOH 99.5:0.5) $\boldsymbol{t_R}$ = 13.4 min. $\boldsymbol{[\alpha]_D}$ = –11.5 (*c* = 1.10, $CHCl_3$). **IR** (film): υ 3504 (br), 3072, 2962, 2935, 1713, 1613, 1515, 1250, 1113, 1036 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70–7.60 (4H, m, ArH), 7.45–7.35 (6H, m, ArH), 7.28–7.22 (2H, m, ArH), 6.88–6.82 (2H, m, ArH), 4.49 (1H, d, *J* = 11.5, OC$\underline{H}_x$H$_y$Ar), 4.45 (1H, d, *J* = 11.5, OCH$_x\underline{H}_y$Ar), 4.08 (1H, q, *J* = 6.9, C$\underline{H}$OPMB), 4.00–3.95 (1H, m, C$\underline{H}$OH), 3.80–3.60 (1H, m, C$\underline{H}_x$H$_y$OSi), 3.78 (3H, s, OCH_3), 3.67 (1H, dd, *J* = 10.1, *J* = 6.1, CH$_x\underline{H}_y$OSi), 3.10 (1H, qd, *J* = 7.0, *J* = 3.2, COC$\underline{H}$CH$_3$), 1.80–1.70 (1H, m, C$\underline{H}$CH$_2$OSi), 1.36 (3H, d, *J* = 6.9, C$\underline{H}_3$CHOPMB), 1.09 (3H, d, *J* = 7.0, COCHC$\underline{H}_3$), 1.04 (9H, s, C(CH$_3$)$_3$), 0.85 (3H, d, *J* = 6.9, C$\underline{H}_3$CHCH$_2$OSi). **^{13}C NMR** (75.4 MHz, $CDCl_3$) δ 215.4 (C), 159.3 (C), 135.6 (CH), 133.1 (C), 133.0 (C), 129.8 (CH), 129.4 (CH), 127.7 (CH), 113.8 (CH), 79.0 (CH), 74.3 (CH), 71.4 (CH_2), 68.0 (CH_2), 55.3 (CH_3), 44.1 (CH), 37.6 (CH), 26.8 (CH_3), 19.2 (C), 17.4 (CH_3), 13.6 (CH_3), 8.7 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{33}H_{45}O_5Si$ $[M+H]^+$: 549.3036. Found: 549.3029.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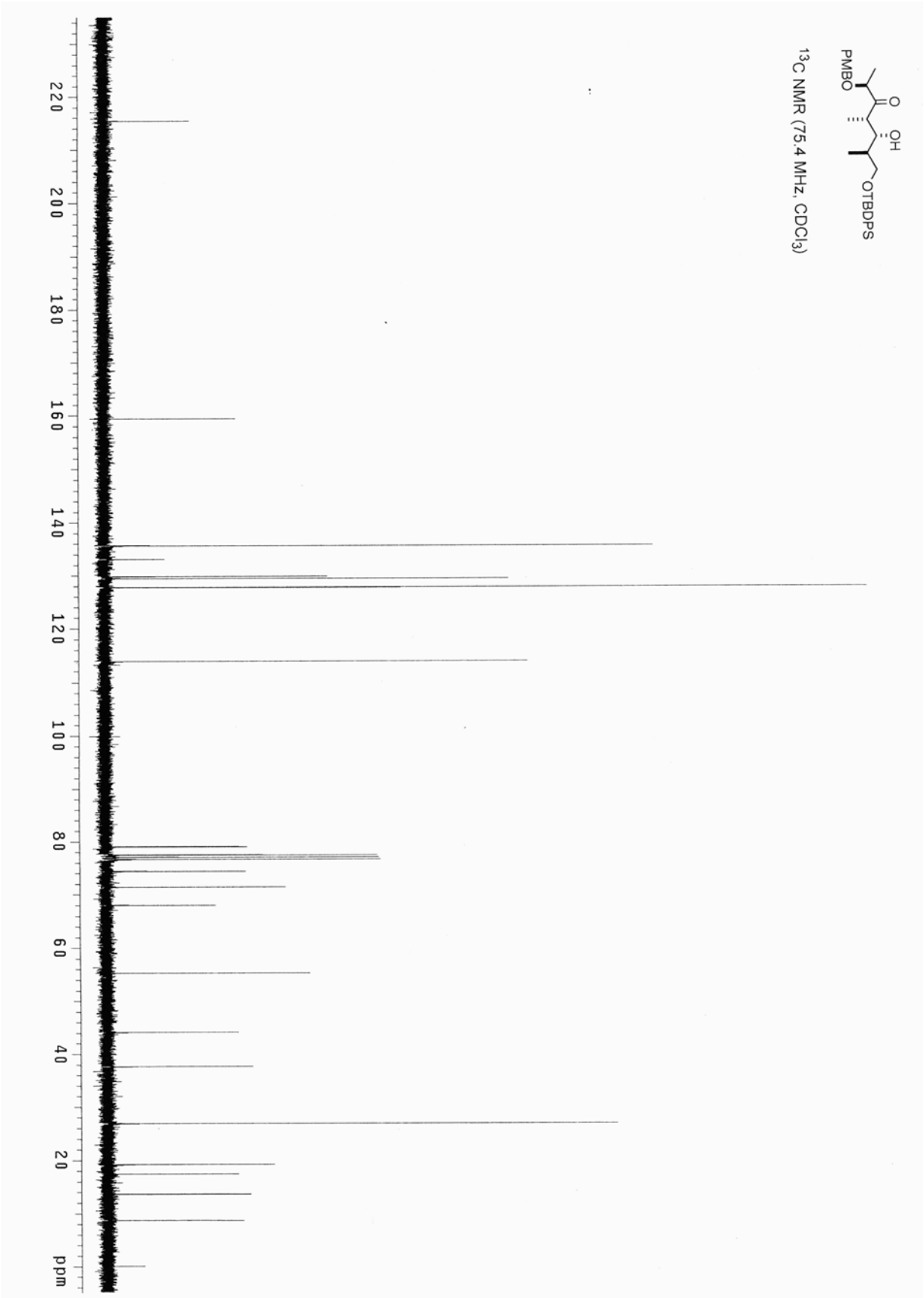
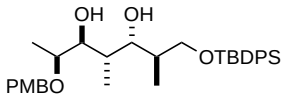
OH
OTBDPS
3.780
1.040
4.13
8.20
2.00
2.06
2.00
6.12
0.92
0.74
2.90
11.92
2.95
ppm


PMBO
O
OH
OTBDPS
^{13}C NMR (75.4 MHz, $CDCl_3$)
220
200
180
160
140
120
100
80
60
40
20
ppm

2. (2*R*,3*R*,4*S*,5*S*,6*S*)-1-*tert*-Butyldiphenylsilyloxy-6-(4-methoxybenzyloxy)-2,4-dimethyl-3,5-heptandiol (8).

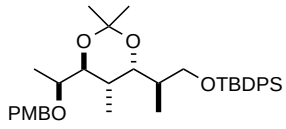


Glacial AcOH (8.1 mL) was added to a solution of $(Me_4N)HB(OAc)_3$ (3.795 g, 13.9 mmol) in CH_3CN (8.1 mL) and the resulting mixture was stirred at rt for 1 h. It was cooled to –40 °C and a solution of **5** (873 mg, 1.6 mmol) in CH_3CN (3.2 mL) was added dropwise (it was rinsed with 2 × 1.5 mL of CH_3CN). The reaction mixture was stirred at –40 °C for 5 h, kept overnight in the fridge (–25 °C) and stirred for 1 h at 0 °C.

The reaction was carefully quenched by addition of a 0.5 M aqueous solution of sodium potassium tartrate (27 mL) and stirred for 1 h at rt. The mixture was diluted with CH_2Cl_2 (40 mL) and washed with saturated $NaHCO_3$ (40 mL). The aqueous layer was extracted with CH_2Cl_2 (6 × 40 mL) and the combined organic extracts were washed with saturated $NaHCO_3$ (3 × 40 mL), dried ($MgSO_4$), filtered, and concentrated. The resulting oil was analyzed by HPLC (hexanes/*i*-PrOH 99:1), which showed the presence of two diols in a 94:6 dr. Purification through a flash column chromatography (from hexanes/EtOAc 95:5 to hexanes/EtOAc 80:20) afforded 806 mg (92%) of diastereomerically pure **8**.

Colorless wax. R_f (hexanes/EtOAc 85:15) = 0.10. **HPLC** (hexanes/*i*-PrOH 99:1) t_R = 12.4 min. $[\alpha]_D$ = +8.4 (*c* = 1.36, $CHCl_3$). **IR** (film): υ 3490 (br), 3072, 2964, 2933, 1613, 1515, 1250, 1113, 1038 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72–7.64 (4H, m, ArH), 7.46–7.34 (6H, m, ArH), 7.28–7.22 (2H, m, ArH), 6.90–6.84 (2H, m, ArH), 4.63 (1H, d, *J* = 11.3, $OC\underline{H}_xH_yAr$), 4.38 (1H, d, *J* = 11.3, $OCH_x\underline{H}_yAr$), 3.91 (1H, d, *J* = 9.6, $C\underline{H}OHCHCH_2OSi$), 3.82 (1H, s, OH), 3.79 (3H, s, OCH_3), 3.75 (2H, d, *J* = 5.4, CH_2OSi), 3.67 (1H, quintet, *J* = 6.1, $C\underline{H}OPMB$), 3.50–3.44 (1H, m, $CH(OPMB)C\underline{H}OH$), 2.84 (1H, d, *J* = 5.2, OH), 1.90–1.75 (2H, m, 2 × $C\underline{H}CH_3$), 1.22 (3H, d, *J* = 6.1, $C\underline{H}_3CHOPMB$), 1.06 (9H, s, $C(CH_3)_3$), 0.94 (3H, d, *J* = 7.0, $CHC\underline{H}_3$), 0.78 (3H, d, *J* = 6.9, $CHC\underline{H}_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.3 (C), 135.6 (CH), 135.5 (CH), 133.4 (C), 133.3 (C), 130.5 (C), 129.6 (CH), 129.4 (CH), 127.7 (CH), 113.8 (CH), 79.1 (CH), 75.4 (CH), 73.6 (CH), 70.7 (CH_2), 68.2 (CH_2), 55.2 (CH_3), 38.0 (CH), 35.3 (CH), 26.8 (CH_3), 19.2 (C), 15.9 (CH_3), 13.2 (CH_3), 10.1 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{33}H_{47}O_5Si$ $[M+H]^+$: 551.3193. Found: 551.3169.

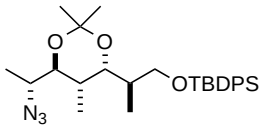
3. (2*R*,3*R*,4*S*,5*S*,6*S*)-1-*tert*-Butyldiphenylsilyloxy-3,5-isopropylidenedioxy-6-(4-methoxybenzyloxy)-2,4-dimethylheptane (9).



A solution of **8** (742 mg, 1.35 mmol) and a catalytic amount of PPTS in 1:1 CH_2Cl_2/2,2-dimethoxypropane (30 mL) was stirred for one day at rt under N_2. It was concentrated *in vacuo* and the residue was purified by flash column chromatography (hexanes/EtOAc 97:3), which afforded 732 mg (92%) of **9**.

Colorless wax. R_f (hexanes/EtOAc 95:5) = 0.20. $[\alpha]_D$ = –31.9 (*c* = 1.18, $CHCl_3$). **IR** (film): υ 3072, 2966, 2935, 1613, 1515, 1248, 1225, 1113 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70–7.62 (4H, m, ArH), 7.44–7.32 (6H, m, ArH), 7.28–7.24 (2H, m, ArH), 6.88–6.84 (2H, m, ArH), 4.61 (1H, d, *J* = 11.8, $OC\underline{H}_xH_yAr$), 4.46 (1H, d, *J* = 11.8, $OCH_x\underline{H}_yAr$), 3.79 (3H, s, OCH_3), 3.73–3.64 (3H, m, $OC\underline{H}CHC\underline{H}_2OSi$), 3.56 (1H, qd, *J* = 6.4, *J* = 4.1, $C\underline{H}OPMB$), 3.29 (1H, dd, *J* = 7.0, *J* = 4.1, $CH(OPMB)C\underline{H}O$), 1.98 (1H, quintetd, *J* = 7.0, *J* = 4.1, $OCHC\underline{H}CHO$), 1.73–1.64 (1H, m, $C\underline{H}CH_2OSi$), 1.28 (3H, s, CH_3CO_2), 1.24 (3H, s, CH_3CO_2), 1.20 (3H, d, *J* = 6.4, $C\underline{H}_3CHOPMB$), 1.06 (9H, s, $C(CH_3)_3$), 0.91 (3H, d, *J* = 7.0, $OCHCH(C\underline{H}_3)CHO$), 0.80 (3H, d, *J* = 6.7, $CH(C\underline{H}_3)CH_2OSi$). **^{13}C NMR** (75.4 MHz, $CDCl_3$) δ 159.1 (C), 135.8 (CH), 135.7 (CH), 134.1 (C), 134.0 (C), 131.0 (C), 129.4 (CH), 129.4 (CH), 129.3 (CH), 127.5 (CH), 127.4 (CH), 113.7 (CH), 100.6 (C), 77.5 (CH), 74.6 (CH), 71.0 (CH_2), 69.8 (CH), 65.2 (CH_2), 55.3 (CH_3), 35.5 (CH), 33.0 (CH), 27.0 (CH_3), 25.5 (CH_3), 23.5 (CH_3), 19.4 (C), 15.3 (CH_3), 13.1 (CH_3), 12.3 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{36}H_{51}O_5Si$ $[M+H]^+$: 591.3506. Found: 591.3503.

4. Protected azido poliol 4.

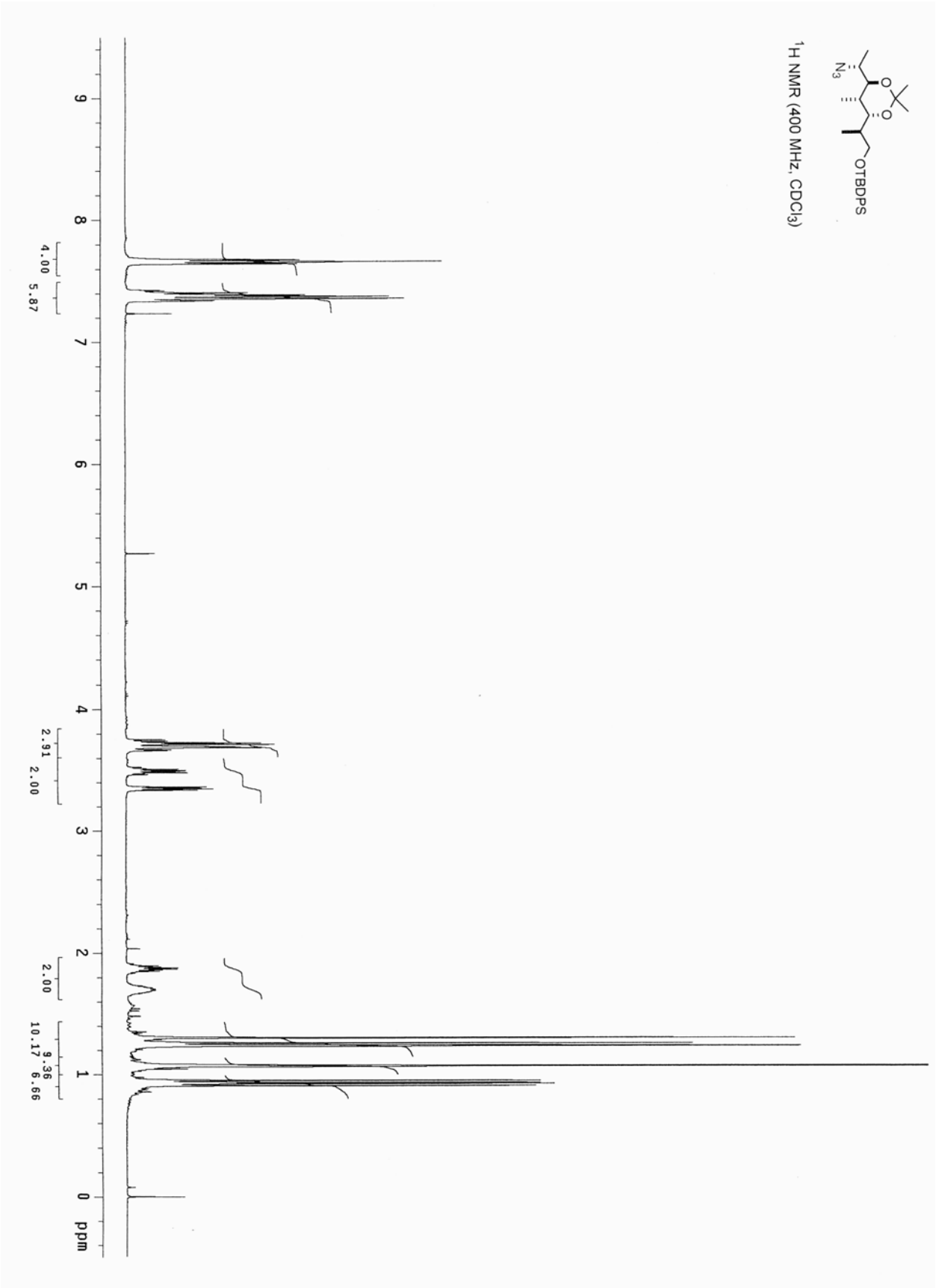


DDQ (186 mg, 0.82 mmol) was added to a mixture of **9** (373 mg, 0.63 mmol) in 10:1 CH_2Cl_2/phosphate pH 7 buffer (16.5 mL) at 0 °C. The reaction mixture was vigorously stirred for 2 h at 0 °C and partitioned between CH_2Cl_2 (200 mL) and saturated $NaHCO_3$ (120 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL) and the combined organic extracts were washed with saturated $NaHCO_3$ (120 mL), dried ($MgSO_4$), filtered, and concentrated. The resulting oil was eluted through a pad of silica gel (hexanes/EtOAc 85:15) and the colorless oil (396 mg) remaining after evaporation of the volatiles was taken on to the next reaction without further purification.

It was dissolved in CH_2Cl_2 (8.8 mL), cooled to 0 °C under N_2, and Et_3N (132 µL, 0.95 mmol) and MsCl (59 µL, 0.76 mmol) were added dropwise. The reaction was stirred for 4 h at 0 °C, diluted with CH_2Cl_2 (40 mL), and washed with H_2O (50 mL), saturated $NaHCO_3$ (50 mL), and H_2O (50 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated. The resulting oil was taken on to the next reaction without further purification.

It was diluted with DMF (2.5 mL) and NaN_3 (305 mg, 4.69 mmol) was added. The resulting suspension was stirred for 22 h at 70 °C. The mixture was diluted with Et_2O (50 mL) and washed with H_2O (3 × 15 mL), and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting oil was purified by flash column chromatography (hexanes/EtOAc 97:3), affording 250 mg (80%) of **4**.

Colorless oil. R_f (hexanes/EtOAc 97:3) = 0.40. $[\alpha]_D$ = –24.9 (*c* = 1.11, $CHCl_3$). **IR** (film): υ 3074, 2935, 2101, 1474, 1428, 1380, 1225, 1113, 1026 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.63 (4H, m, ArH), 7.45–7.33 (6H, m, ArH), 3.77–3.65 (3H, m, OC<u>H</u>CHC<u>H</u>$_2$OSi), 3.50 (1H, qd, *J* = 6.7, *J* = 4.2, CHN_3), 3.35 (1H, dd, *J* = 6.6, *J* = 4.2, $CH(N_3)C\underline{H}O$), 1.87 (1H, quintetd, *J* = 6.6, *J* = 3.9, OCHC<u>H</u>CHO), 1.76–1.62 (1H, m, C<u>H</u>CH_2OSi), 1.30 (3H, s, CH_3CO_2), 1.25 (3H, d, *J* = 6.7, C<u>H</u>$_3$CHN$_3$), 1.24 (3H, s, CH_3CO_2), 1.07 (9H, s, $C(CH_3)_3$), 0.94 (3H, d, *J* = 6.7, CH(C<u>H</u>$_3$)CH_2OSi), 0.92 (3H, d, *J* = 6.6, OCHCH(C<u>H</u>$_3$)CHO). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 135.8 (CH), 135.7 (CH), 134.0 (C), 133.9 (C), 129.5 (CH), 129.4 (CH), 127.5 (CH), 100.7 (C), 78.1 (CH), 69.5 (CH), 65.0 (CH_2), 59.6 (CH), 35.4 (CH), 34.0 (CH), 27.0 (CH_3), 25.3 (CH_3), 23.6 (CH_3), 19.4 (C), 14.6 (CH_3), 13.0 (CH_3), 12.7 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{28}H_{42}NO_3Si$ $[M+H]^+$: 496.2995. Found: 496.2995.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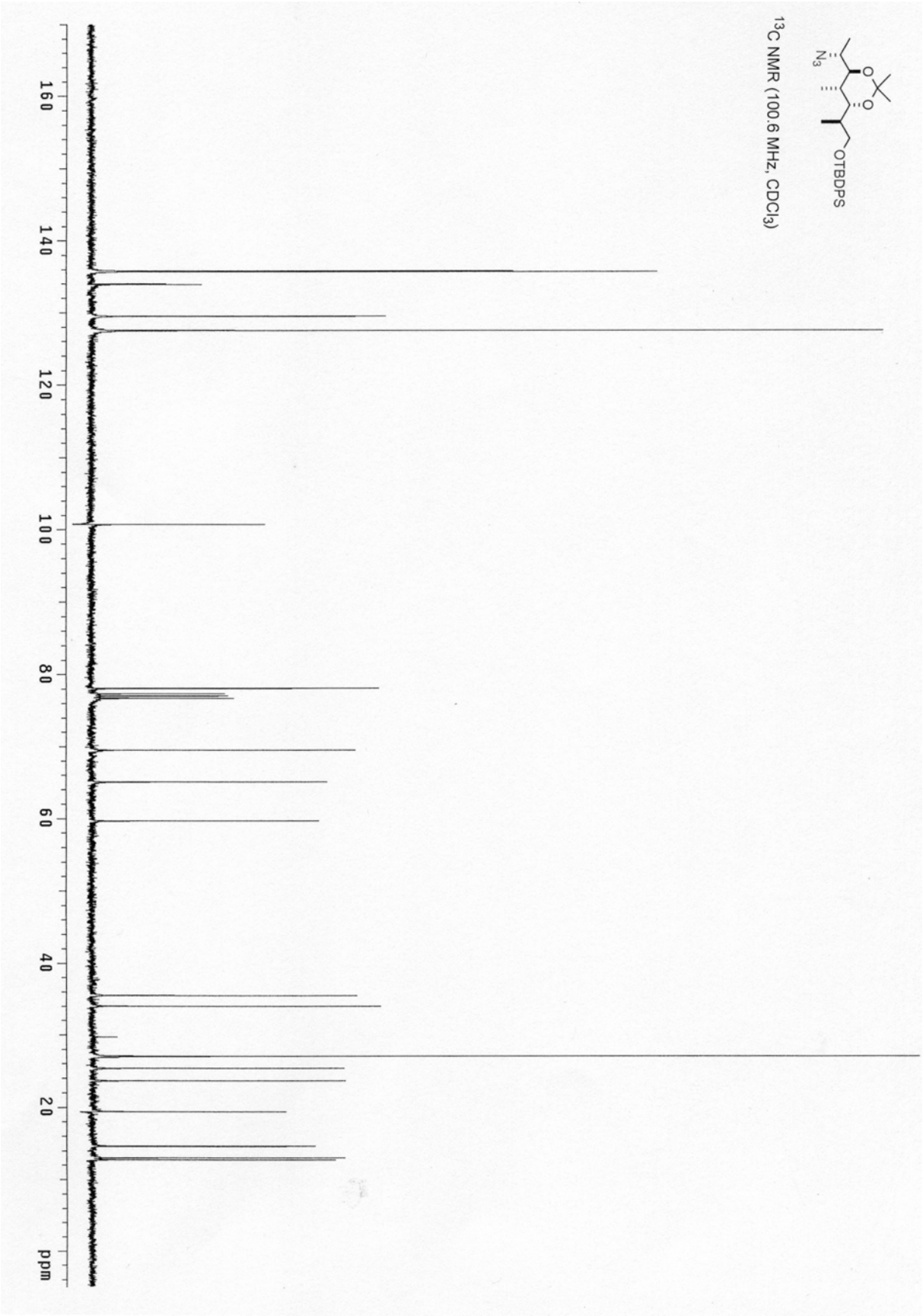
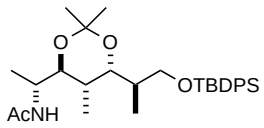
N$_3$
OTBDPS
9
8
7
6
5
4
3
2
1
0
ppm
4.00
5.87
2.91
2.00
2.00
10.17
9.36
6.66


^{13}C NMR (100.6 MHz, $CDCl_3$)
N_3
OTBDPS
160
140
120
100
80
60
40
20
ppm

5. Acetamide derivative 10.

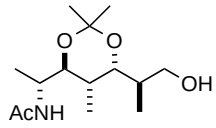


A 1 M solution of Me_3P in toluene (0.18 mL, 0.18 mmol) was added dropwise to a solution of **4** (69.6 mg, 0.14 mmol) and water (10 μL) in THF (1.5 mL) under N_2. The reaction mixture was stirred overnight at rt and concentrated. Water was removed by adding toluene (3 × 4 mL) and concentrating *in vacuo*.

The residue was dissolved in CH_2Cl_2 (1.5 mL) and Et_3N (215 μL, 1.54 mmol) and Ac_2O (23 μL, 0.24 mmol) were successively added. The reaction mixture was stirred for 1 h at rt. The solvent was removed and the resulting oil was purified by flash column chromatography (hexanes/EtOAc 50:50), which provided 63.2 mg (88%) of **10**.

Viscous oil. R_f (hexanes/EtOAc 50:50) = 0.40. $[\alpha]_D$ = –2.1 (*c* = 1.03, $CHCl_3$). **IR** (film): υ 3284 (br), 2966, 2935, 1654, 1559, 1542, 1459, 1225, 1113, 1023 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.60 (4H, m, ArH), 7.45–7.30 (6H, m, ArH), 5.74 (1H, d, *J* = 8.8, NH), 4.14–4.00 (1H, m, C<u>H</u>NH), 3.71 (1H, dd, *J* = 9.7, *J* = 5.1, C<u>H</u>$_x$H$_y$OTBDPS), 3.67 (1H, dd, *J* = 9.7, *J* = 3.1, CH$_x$<u>H</u>$_y$OTBDPS), 3.62 (1H, dd, *J* = 10.8, *J* = 4.2, C<u>H</u>OCHCH$_2$OSi), 3.28 (1H, dd, *J* = 7.4, *J* = 2.8, CH(NH)C<u>H</u>O), 1.96 (3H, s, C<u>H</u>$_3$CONH), 1.82–1.65 (2H, m, 2 × C<u>H</u>CH$_3$), 1.27 (3H, s, CH$_3$CO$_2$), 1.22 (3H, s, CH$_3$CO$_2$), 1.15 (3H, d, *J* = 6.7, C<u>H</u>$_3$CHNH), 1.07 (9H, s, C(CH$_3$)$_3$), 0.93 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$), 0.90 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 169.0 (C), 135.8 (CH), 135.7 (CH), 134.0 (C), 133.8 (C), 129.5 (CH), 129.4 (CH), 127.5 (CH), 127.4 (CH), 100.6 (C), 77.4 (CH), 69.5 (CH), 65.1 (CH$_2$), 46.6 (CH), 35.4 (CH), 34.2 (CH), 27.0 (CH$_3$), 25.1 (CH$_3$), 23.7 (CH$_3$), 23.5 (CH$_3$), 19.3 (C), 14.1 (CH$_3$), 13.1 (CH$_3$), 12.0 (CH$_3$). **HRMS** (+FAB): *m/z* calcd. for $C_{30}H_{46}NO_4Si$ $[M+H]^+$: 512.3196. Found: 512.3178.

6. Hydroxy amide 11.



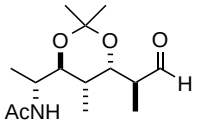
A 1 M solution of TBAF·3H_2O in THF (1.4 mL, 1.4 mmol) was added to a solution of **10** (61.2 mg, 0.12 mmol) in THF (0.8 mL) at 0 °C under N_2. The reaction mixture was stirred for 1 h at 0 °C and 30 h at rt.

The solvent was removed and the resulting oil was purified by flash column chromatography (hexanes/EtOAc 90:10), which provided 32.4 mg (99%) of **11**.

White solid. R_f (EtOAc) = 0.30. $[\alpha]_D$ = –3.5 (*c* = 1.46, $CHCl_3$). **IR** (film): υ 3301 (br), 2983, 2937, 1654, 1559, 1459, 1380, 1225, 1022 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.76 (1H, d, *J* = 8.4, NH), 4.17–4.02 (1H, m, C<u>H</u>NH), 3.66–3.50 (3H, m, C<u>H</u>OCHC<u>H</u>$_2$OH), 3.23 (1H, dd, *J* = 7.7, *J* = 2.9, CH(NH)C<u>H</u>O), 3.18 (1H, br s, O<u>H</u>), 1.97 (3H, s, C<u>H</u>$_3$CONH),

1.95–1.75 (2H, m, 2 × C<u>H</u>CH$_3$), 1.39 (3H, s, CH$_3$CO$_2$), 1.33 (3H, s, CH$_3$CO$_2$), 1.14 (3H, d, *J* = 6.7, C<u>H</u>$_3$CHNH), 0.95 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$), 0.79 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$). **^{13}C NMR** (100.6 MHz, CDCl$_3$) δ 169.0 (C), 100.8 (C), 77.2 (CH), 75.6 (CH), 68.6 (CH$_2$), 46.3 (CH), 34.9 (CH), 34.4 (CH), 25.0 (CH$_3$), 23.6 (CH$_3$), 23.4 (CH$_3$), 14.1 (CH$_3$), 12.7 (CH$_3$), 11.9 (CH$_3$). **HRMS** (+FAB): *m/z* calcd. for $C_{14}H_{28}NO_4$ $[M+H]^+$: 274.2018. Found: 274.2024.

7. Formyl amide 12.

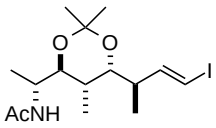


DMSO (24 μL, 0.34 mmol) was added dropwise to a solution of (COCl)$_2$ (15 μL, 0.17 mmol) in CH$_2$Cl$_2$ (0.35 mL) at –78 °C under N$_2$. The resulting mixture was stirred for 1 h at –78 °C and a solution of **11** (31.3 mg, 0.11 mmol) in CH$_2$Cl$_2$ (0.60 mL) was added dropwise. The reaction mixture was stirred for 1 h at –78 °C, followed by the addition of Et$_3$N (72 μL, 0.51 mmol).

The resulting white suspension was allowed to warm to rt and stirred for 2 h. It was partitioned between CH$_2$Cl$_2$ (20 mL) and H$_2$O (20 mL). The aqueous layer was further extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic extracts were washed with H$_2$O (2 × 10 mL) and brine (10 mL), dried (Na$_2$SO$_4$), filtered, and concentrated. The residue was filtered through a pad of silica gel (EtOAc) and concentrated to give a colorless oil (35.7 mg) that was taken on to the next step without further purification.

***R**$_f$* (EtOAc) = 0.40. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 9.68 (1H, d, *J* = 2.7, CH=O), 5.78 (1H, d, *J* = 8.6, NH), 4.20–4.00 (1H, m, NCH), 3.91 (1H, dd, *J* = 10.8, *J* = 4.3, CHO), 3.35 (1H, dd, *J* = 7.6, *J* = 3.1, CHO), 2.57–2.42 (1H, m, C<u>H</u>CH=O), 1.98 (3H, s, C<u>H</u>$_3$CONH), 1.90–1.75 (1H, m, C<u>H</u>CH$_3$), 1.32 (3H, s, CH$_3$CO$_2$), 1.31 (3H, s, CH$_3$CO$_2$), 1.16 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$), 0.99 (3H, d, *J* = 7.0, CHC<u>H</u>$_3$), 0.96 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$). **^{13}C NMR** (75.4 MHz, CDCl$_3$) δ 204.2, 169.0, 100.9, 77.2, 70.1, 46.4, 45.8, 33.9, 24.8, 23.4, 23.4, 14.2, 10.0, 8.6.

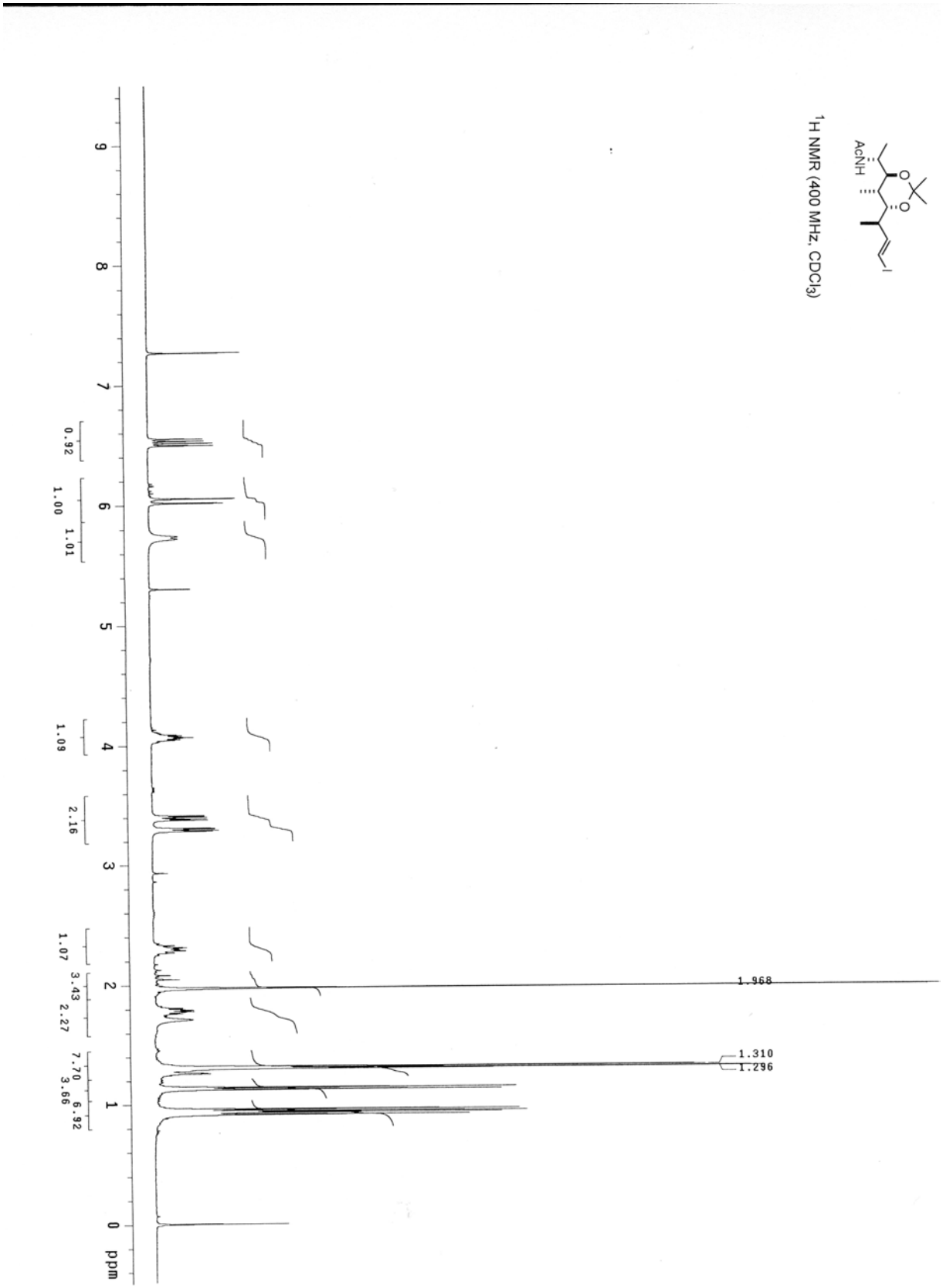
8. Vinyl iodide 2.

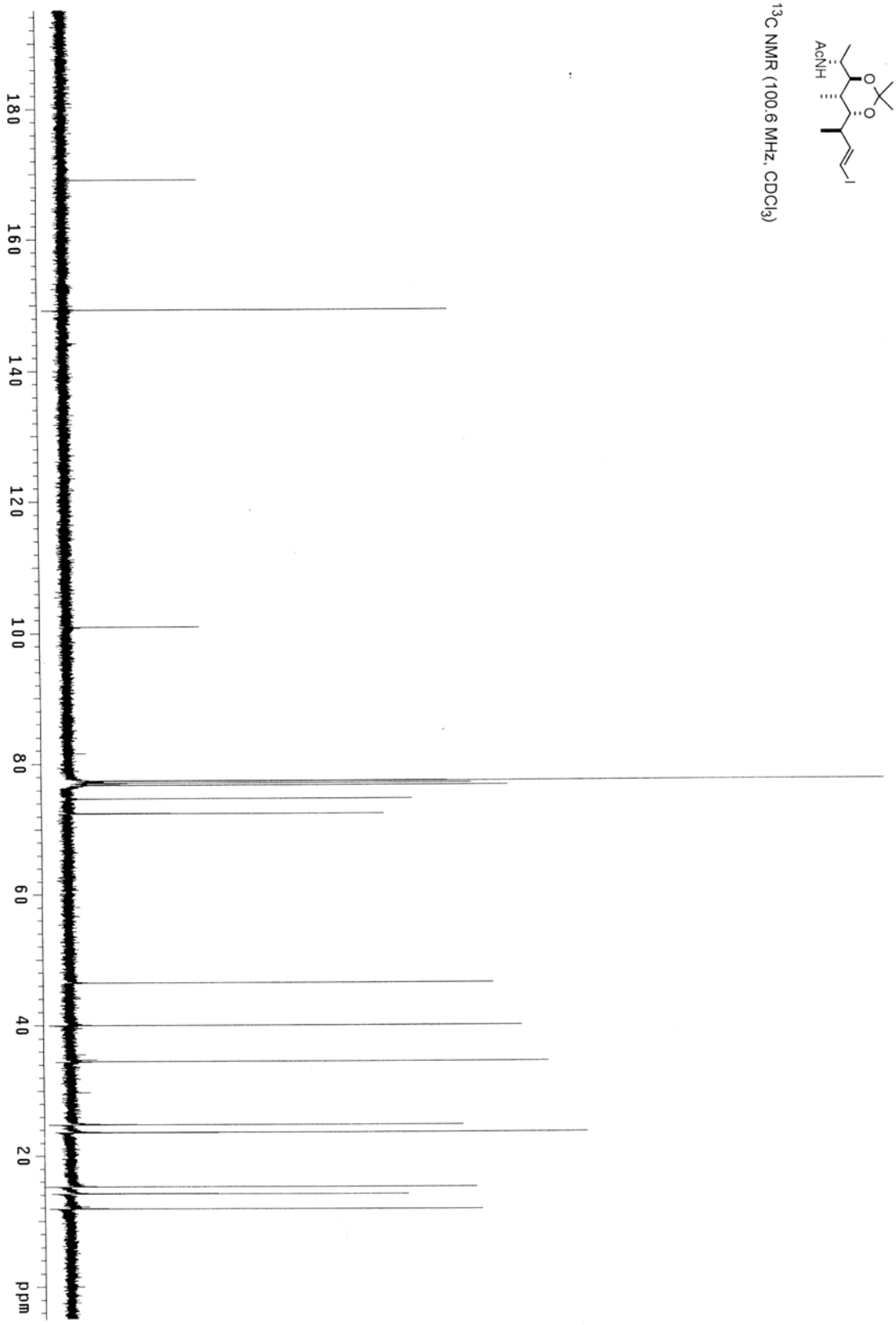


$CrCl_2$ (105 mg, 0.81 mmol) was added to a 10 mL round bottom flask and gently flame dried under high vacuum. Upon cooling, the flask was released under argon, charged with THF (0.9 mL) and the resulting slurry stirred for 10 min at 0 °C. Then, a solution of **2** (31.0 mg, 0.11 mmol) and CHI_3 (91 mg, 0.23 mmol) in THF (1.5 mL) was added dropwise via syringe (it was rinsed with 3 × 0.2 mL). The reaction mixture, which turned to a brown-red color, was stirred for 2 h at 0 °C and overnight at rt in the dark.

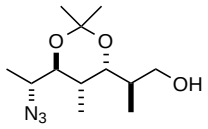
The mixture was diluted with Et_2O (65 mL) and washed with saturated $NaHCO_3$ (2 × 30 mL). The aqueous layers were extracted with Et_2O (3 × 45 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. Purification by flash column chromatography (hexanes/EtOAc 50:50) afforded 27.0 mg (61% over two steps from **11**) of a 95:5 mixture of *E*/*Z* olefins **2**.

Pale orange oil. R_f (hexanes/EtOAc 50:50) = 0.25. $[\alpha]_D$ = +23.2 (*c* = 0.75, $CHCl_3$). **IR** (film): υ 3282 (br), 2925, 2854, 1654, 1559, 1542, 1459, 1378, 1225, 1023 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.52 (1H, dd, *J* = 14.5, *J* = 7.4, C<u>H</u>=CHI), 6.04 (1H, dd, *J* = 14.5, *J* = 1.0, CH=C<u>H</u>I), 5.73 (1H, br d, *J* = 8.4, NH), 4.10–4.00 (1H, m, C<u>H</u>NH), 3.40 (1H, dd, *J* = 10.4, *J* = 4.2, C<u>H</u>OCHCH=CHI), 3.30 (1H, dd, *J* = 7.5, *J* = 2.9, CH(NH)C<u>H</u>O), 2.35–2.25 (1H, m, C<u>H</u>CH=CHI), 1.97 (3H, s, C<u>H</u>$_3$CONH), 1.85–1.75 (1H, m, OCHC<u>H</u>CHO), 1.31 (3H, s, CH_3CO_2), 1.30 (3H, s, CH_3CO_2), 1.13 (3H, d, *J* = 6.7, C<u>H</u>$_3$CHNH), 0.95 (3H, d, *J* = 6.7, CH(C<u>H</u>$_3$)CH=CHI), 0.92 (3H, d, *J* = 6.7, OCHCH(C<u>H</u>$_3$)CHO). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 169.0 (C), 149.2 (CH), 100.9 (C), 77.3 (CH), 74.6 (CH), 72.4 (CH), 46.4 (CH), 39.9 (CH), 34.4 (CH), 24.7 (CH_3), 23.6 (CH_3), 23.5 (CH_3), 15.2 (CH_3), 14.1 (CH_3), 11.8 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{15}H_{27}NO_3I$ $[M+H]^+$: 396.1036. Found: 396.1022.


^{1}H NMR (400 MHz, CDCl$_3$)
AcNH
I
1.968
1.310
1.296
0.92
1.00
1.01
1.09
2.16
1.07
3.43
2.27
7.70
3.66
6.92
ppm


^{13}C NMR (100.6 MHz, CDCl$_3$)
AcNH
180
160
140
120
100
80
60
40
20
ppm

9. (2*R*,3*R*,4*S*,5*S*,6*R*)-6-Azido-3,5-isopropylidenedioxy-2,4-dimethyl-1-heptanol (14).

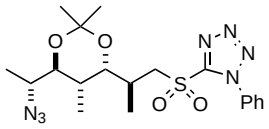


A 1 M solution of TBAF·3H_2O in THF (3 mL, 3 mmol) was added to a solution of **4** (123 mg, 0.25 mmol) in THF (1.7 mL) at 0 °C under N_2. The reaction mixture was stirred for 1 h at 0 °C and overnight at rt.

It was diluted with Et_2O (100 mL) and washed with a 10% aqueous solution of $KHSO_4$ 10% (40 mL), saturated $NaHCO_3$ (40 mL) and H_2O (40 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Purification by flash column chromatography (hexanes/EtOAc 90:10) afforded 58 mg (91%) of **14**.

Colorless oil. R_f (hexanes/EtOAc 85:15) = 0.17. $[\alpha]_D$ = –58.1 (*c* = 1.13, $CHCl_3$). **IR** (film): υ 3350 (br), 2980, 2940, 2120, 1380, 1240, 1030 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.67 (1H, dd, *J* = 10.7, *J* = 4.0, C$\underline{H}_x$H$_y$OH), 3.63 (1H, dd, *J* = 10.7, *J* = 7.9, CH$_x\underline{H}_y$OH), 3.57–3.52 (1H, m, CH(N_3)C$\underline{H}$O), 3.50 (1H, qd, *J* = 6.7, *J* = 4.0, CHN_3), 3.40 (1H, dd, *J* = 6.8, *J* = 4.0, OC$\underline{H}$CHCH_2OH), 3.10 (1H, br s, OH), 1.96–1.82 (2H, m, 2 × C$\underline{H}$CH_3), 1.40 (3H, s, CH_3CO_2), 1.37 (3H, s, CH_3CO_2), 1.26 (3H, d, *J* = 6.7, C$\underline{H}_3$CHN_3), 0.96 (3H, d, *J* = 6.7, CHC$\underline{H}_3$), 0.80 (3H, d, *J* = 6.8, CHC$\underline{H}_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 100.9 (C), 77.7 (CH), 75.6 (CH), 68.6 (CH_2), 59.4 (CH), 34.9 (CH), 34.2 (CH), 25.3 (CH_3), 23.5 (CH_3), 14.5 (CH_3), 12.6 (CH_3), 12.5 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{12}H_{24}N_3O_3$ $[M+H]^+$: 258.1818. Found: 258.1828.

10. Azido sulfone 15.



DEAD (51 μL, 033 mmol) was added to a solution of Ph_3P (75 mg, 0.29 mmol) and 1-phenyl-1*H*-tetrazole-5-thiol (60 mg, 0.33 mmol) in THF (1.5 mL) at 0 °C under N_2. It was stirred for 10 min and a solution of **14** (56 mg, 0.22 mmol) in THF (0.55 mL) was added dropwise (it was rinsed with 3 × 0.25 mL of THF). The resulting bright yellow solution was stirred for 15 min at 0 °C and 4 h at rt. It was finally diluted with EtOH (4.6 mL) and cooled to 0 °C.

In a separate flask, 30% aq H_2O_2 (0.9 mL, 8.7 mmol) and $(NH_4)_2MoO_4$ (136 mg, 0.11 mmol) were mixed, producing a bright yellow solution that was added dropwise to the reaction mixture.

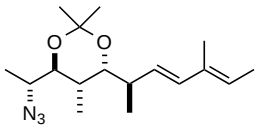
The resulting yellow suspension was stirred for 10 min at 0 °C and one day at rt and partitioned between CH_2Cl_2 (35 mL) and H_2O (15 mL). The layers were separated and the aqueous one was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with H_2O (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated.

Purification by flash chromatography (hexanes/EtOAc 85:15) provided 82 mg (84%) of **15**.

Colorless wax. R_f (hexanes/EtOAc 75:25) = 0.52. $[\alpha]_D$ = –22.7 (*c* = 1.11, $CHCl_3$). **IR** (film): υ 2985, 2939, 2105, 1499,

1383, 1343, 1225, 1154, 1026 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.50 (5H, m, ArH), 4.18 (1H, dd, *J* = 14.5, *J* = 2.5, C$\underline{H}_x$H$_y$SO$_2$), 3.56–3.44 (3H, m, CH$_x\underline{H}_y$SO$_2$, CHN$_3$ and C$\underline{H}$OCHCH$_2$SO$_2$), 3.36 (1H, dd, *J* = 6.6, *J* = 4.1, CH(N$_3$)C$\underline{H}$O), 2.48–2.32 (1H, m, C$\underline{H}$CHSO$_2$), 2.02–1.92 (1H, m, CHOC$\underline{H}$CHO), 1.33 (3H, s, CH$_3$CO$_2$), 1.32 (3H, s, CH$_3$CO$_2$), 1.24 (3H, d, *J* = 6.7, C$\underline{H}_3$CHN$_3$), 1.13 (3H, d, *J* = 6.7, CH(C$\underline{H}_3$)CH$_2$SO$_2$), 0.93 (3H, d, *J* = 6.8, OHCCH(C$\underline{H}_3$)CHO). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 154.2 (C), 133.1 (C), 131.4 (CH), 129.6 (CH), 125.3 (CH), 101.2 (C), 77.7 (CH), 71.6 (CH), 59.5 (CH), 58.8 (CH_2), 33.6 (CH), 29.0 (CH), 25.1 (CH_3), 23.3 (CH_3), 15.2 (CH_3), 14.6 (CH_3), 12.3 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{19}H_{28}N_7O_4S$ $[M+H]^+$: 450.1923. Found: 450.1921.

11. Azido diene 16.

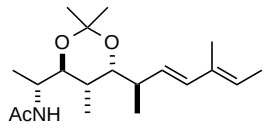


A 1 M solution of LiHMDS in THF (0.36 mL, 0.36 mmol) was added dropwise to a solution of **15** (81 mg, 0.18 mmol) and (*E*)-2-methyl-2-butenal (0.22 mL, 0.22 mmol) in 1,2-dimethoxyethane (4.2 mL) at –65 °C under N_2. The resulting yellow solution was stirred at –65 °C for 6 h, allowed to warm very slowly, and stirred for an additional hour at rt.

The reaction was quenched by addition of saturated NH_4Cl (5 mL) and partitioned between Et_2O (120 mL) and saturated NH_4Cl (60 mL). The aqueous layer was extracted with Et_2O (3 × 80 mL) and the combined organic extracts were washed with brine (80 mL), dried ($MgSO_4$), filtered, and concentrated. Purification by flash column chromatography (hexanes/EtOAc 97:3) afforded 40 mg (72%) of >94:6 mixture of *E*,*E*- and *Z*,*E*-**16** dienes according to the ^{1}H NMR (400 MHz).

Colorless oil. R_f (hexanes/EtOAc 95:5) = 0.43. $[\alpha]_D$ = –44.5 (*c* = 1.72, CH_2Cl_2). **IR** (film): υ 2985, 2937, 2101, 1457, 1380, 1263, 1225, 1183, 1027 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.09 (1H, d, *J* = 15.8, CHCH=C$\underline{H}$), 5.57 (1H, dd, *J* = 15.8, *J* = 7.0, CHC$\underline{H}$=CH), 5.50–5.40 (1H, m, C=C$\underline{H}$CH$_3$), 3.55–3.40 (2H, m, C$\underline{H}$OCHCH=CH and CHN$_3$), 3.37 (1H, dd, *J* = 6.8, *J* = 4.0, CH(N$_3$)C$\underline{H}$O), 2.35–2.25 (1H, m, CHOC$\underline{H}$CH=CH), 1.91 (1H, quintetd, *J* = 6.7, *J* = 4.0, OCHC$\underline{H}$CHO), 1.71 (3H, s, (C$\underline{H}_3$)C=CHCH$_3$), 1.70 (3H, d, *J* ≈ 6.0, (CH$_3$)C=CHC$\underline{H}_3$), 1.35 (3H, s, CH$_3$CO$_2$), 1.29 (3H, s, CH$_3$CO$_2$), 1.25 (3H, d, *J* = 6.8, C$\underline{H}_3$CHN$_3$), 0.96 (3H, d, *J* = 6.7, CHC$\underline{H}_3$), 0.95 (3H, d, J = 6.7, CHCH3). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 134.5 (C), 133.8 (CH), 130.2 (CH), 124.6 (CH), 100.9 (C), 77.9 (CH), 73.6 (CH), 59.6 (CH), 35.9 (CH), 34.4 (CH), 24.9 (CH_3), 23.6 (CH_3), 16.1 (CH_3), 14.5 (CH_3), 13.7 (CH_3), 12.7 (CH_3), 12.0 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{17}H_{30}N_3O_2$ $[M+H]^+$: 308.2338. Found: 308.2343.

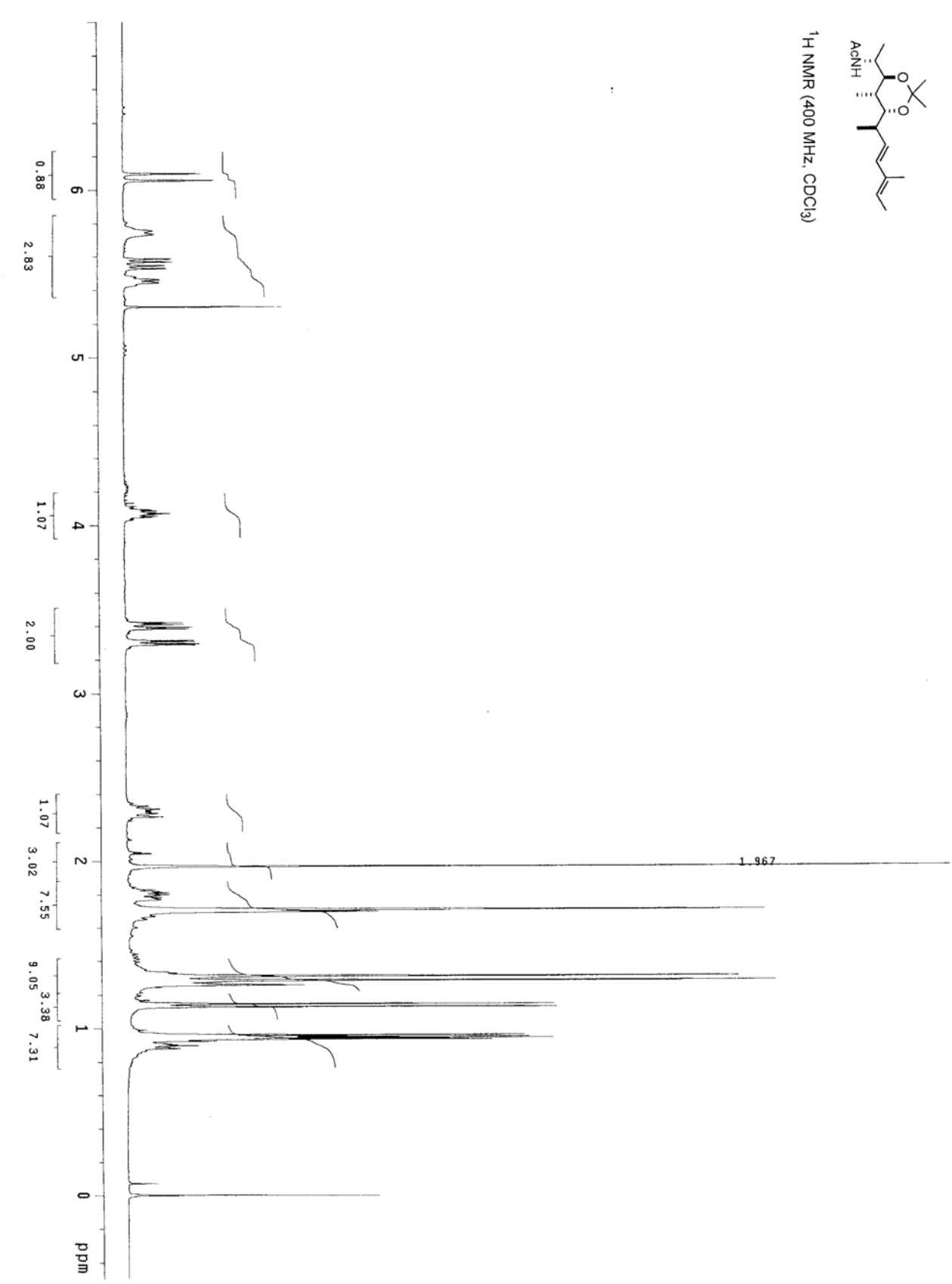
12. Amido diene 17.

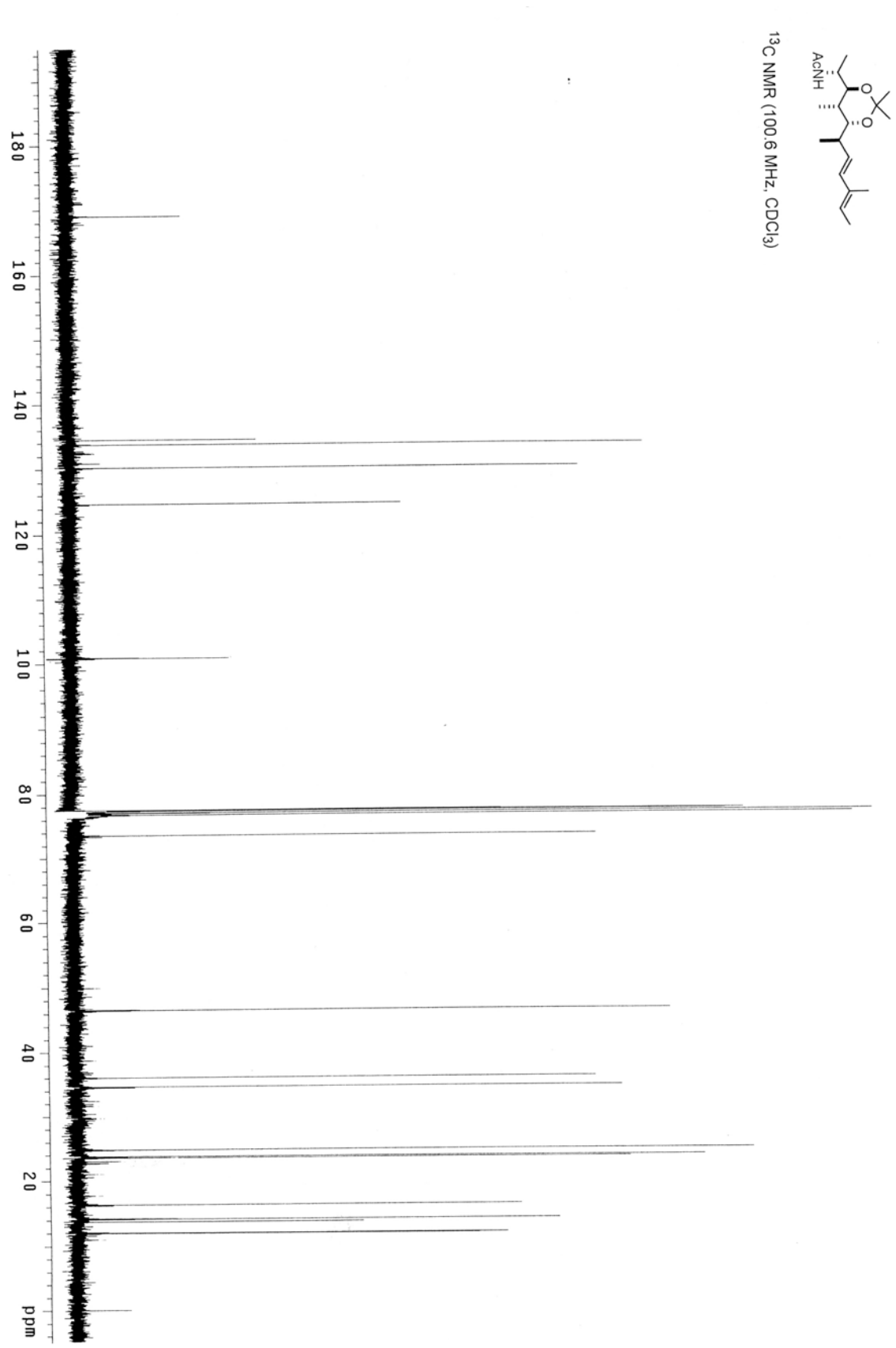


A 1 M solution of Me_3P in toluene (0.12 mL, 0.12 mmol) was added dropwise to a solution of **16** (30.8 mg, 0.10 mmol) in benzene (0.5 mL) under N_2. The reaction mixture was stirred for 2 h at rt and cooled at 0 °C. Then, a 1 M solution of AcCl in benzene (0.12 mL, 0.12 mmol) was added slowly and the resulting mixture was allowed to stir for 5 min at 0 °C and 5 h at rt.

The reaction was quenched by addition of H_2O (5 mL), stirred for 15 min and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. Purification by flash column chromatography (hexanes/EtOAc 35:65) afforded 20.7 mg (64%) of **17**.

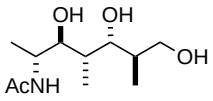
White solid. R_f (hexanes/EtOAc 35:65) = 0.32. $[\alpha]_D$ = +17.1 (*c* = 1.10, CH_2Cl_2). **IR** (film): υ 3286 (br), 2985, 2935, 2101, 1648, 1551, 1459, 1378, 1225, 1183, 1023 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.08 (1H, d, *J* = 15.8, CHCH=C<u>H</u>), 5.80–5.70 (1H, m, NH), 5.56 (1H, dd, *J* = 15.8, *J* = 7.0, CHC<u>H</u>=CH), 5.50–5.40 (1H, m, C=C<u>H</u>CH_3), 4.10–4.00 (1H, m, NHC<u>H</u>), 3.40 (1H, dd, *J* = 10.5, *J* = 4.2, C<u>H</u>OCHCH=CH), 3.30 (1H, dd, *J* = 7.5, *J* = 2.8, CH(NH)C<u>H</u>O), 2.35–2.25 (1H, m, CHOC<u>H</u>CH=CH), 1.97 (3H, s, C<u>H</u>$_3$CONH), 1.85–1.75 (1H, m, OCHC<u>H</u>CHO), 1.71 (3H, s, (C<u>H</u>$_3$)C=CHCH_3), 1.70 (3H, d, *J* ≈ 6.0, (CH_3)C=CHC<u>H</u>$_3$), 1.31 (3H, s, CH_3CO_2), 1.28 (3H, s, CH_3CO_2), 1.14 (3H, d, *J* = 6.7, C<u>H</u>$_3$CHNH), 0.95 (3H, d, *J* = 6.7, CHC<u>H</u>$_3$), 0.94 (3H, d, *J* = 6.6, CHC<u>H</u>$_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 169.0 (C), 134.5 (C), 133.7 (CH), 130.2 (CH), 124.6 (CH), 100.8 (C), 77.4 (CH), 73.5 (CH), 46.5 (CH), 36.0 (CH), 34.6 (CH), 24.7 (CH_3), 23.7 (CH_3), 23.5 (CH_3), 16.2 (CH_3), 14.1 (CH_3), 13.7 (CH_3), 12.0 (CH_3), 11.9 (CH_3). **HRMS** (+FAB): *m/z* calcd. for $C_{19}H_{34}NO_3$ $[M+H]^+$: 324.2539. Found: 324.2537.


^{1}H NMR (400 MHz, CDCl$_3$)
AcNH
1.967
0.88
2.83
1.07
2.00
1.07
3.02
7.55
9.05
3.38
7.31
6
5
4
3
2
1
0
ppm


^{13}C NMR (100.6 MHz, CDCl$_3$)
AcNH
180
160
140
120
100
80
60
40
20
ppm

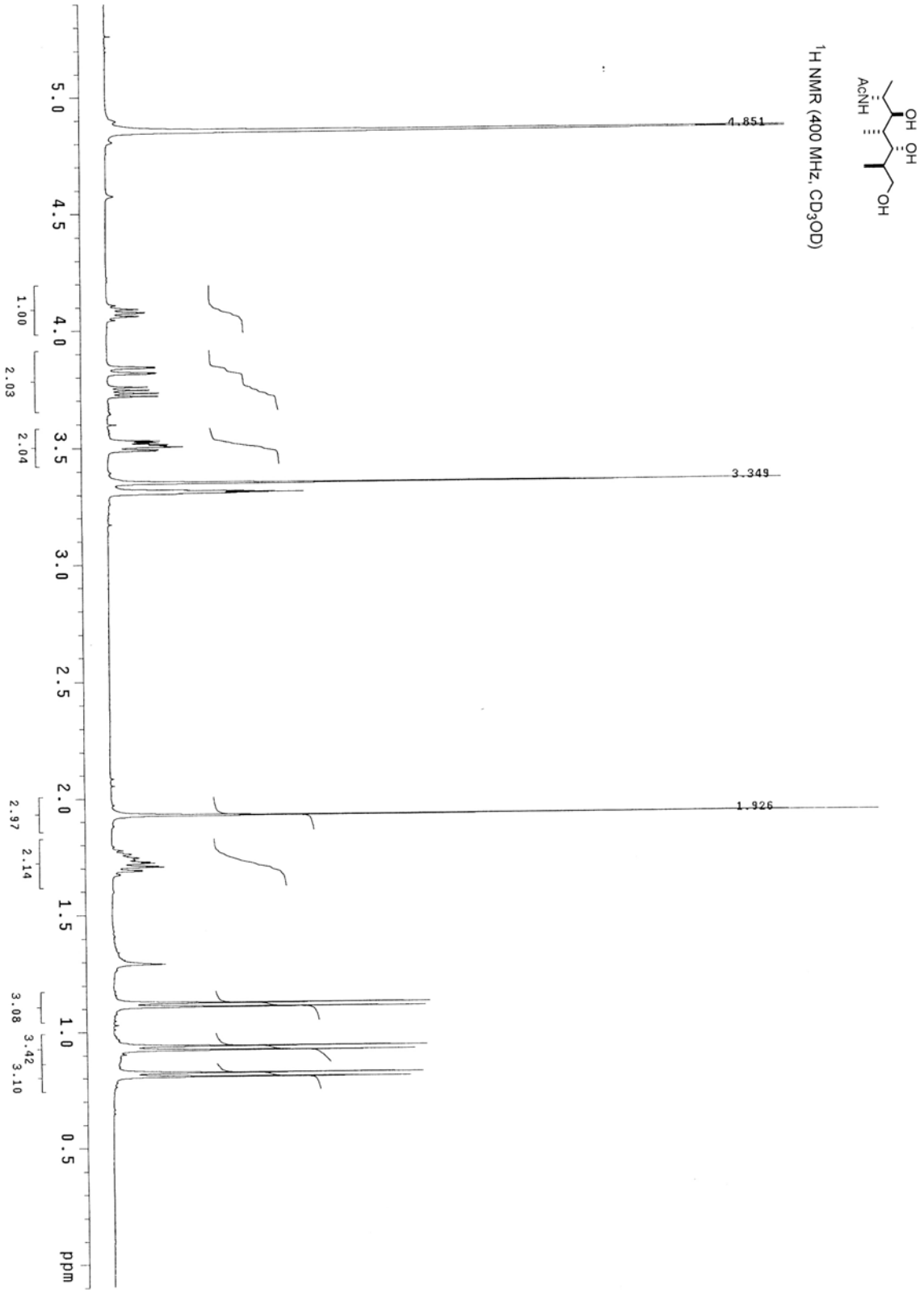
Correlation of Stereochemistry

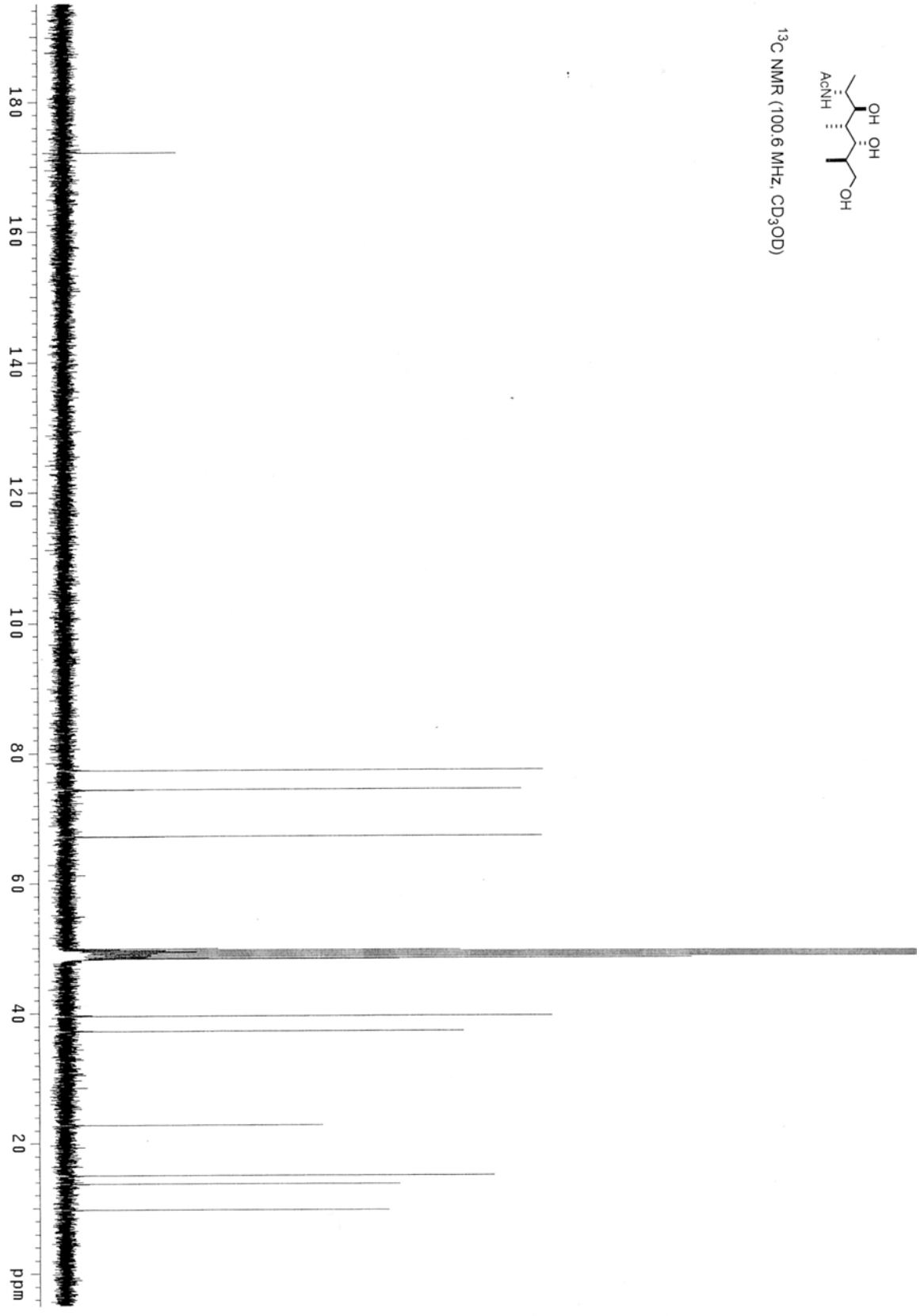
Trihydroxy amide 13.



A mixture of **11** (17.7 mg, 60 mmol) and Amberlyst 15 (35 mg, 200% w/w) in CH_3OH (1.8 mL) was shaken for three days at rt. It was filtered and concentrated. Purification of the residue by flash column chromatography (CH_2Cl_2/CH_3OH 90:10) afforded 12.1 mg (80%) of **13**.

White solid. R_f (CH_2Cl_2/CH_3OH 90:10) = 0.20. $[\alpha]_D$ = +32.4 (*c* = 0.85, CH_3OH). $[\alpha]_D$ = +25.4 (*c* = 0.13, CH_3OH). **IR** (KBr): υ 3311 (br), 2971, 2931, 1654, 1559, 1542, 1457, 1376, 972 cm^{-1}. **^{1}H NMR** (400 MHz, CD_3OD) δ 4.12–4.04 (1H, m, C<u>H</u>NH), 3.83 (1H, dd, *J* = 9.9, *J* = 1.7, C<u>H</u>OCHCH$_2$OH), 3.74 (1H, dd, *J* = 10.6, *J* = 5.3, C<u>H</u>$_x$H$_y$OH), 3.54–3.48 (2H, m, CH(NH)C<u>H</u>O and CH$_x$<u>H</u>$_y$OH), 1.93 (3H, s, C<u>H</u>$_3$CONH), 1.80–1.65 (2H, m, 2 × C<u>H</u>CH$_3$), 1.12 (3H, d, *J* = 6.7, C<u>H</u>$_3$CHNH), 0.93 (3H, d, *J* = 7.0, CHC<u>H</u>$_3$), 0.81 (3H, d, *J* = 6.8, CHC<u>H</u>$_3$). **^{13}C NMR** (100.6 MHz, CD_3OD) δ 172.1, 77.3, 74.3, 67.2, 48.2, 39.5, 37.2, 22.7, 14.9, 13.7, 9.7.


^{1}H NMR (400 MHz, CD_3OD)
AcNH
OH
OH
OH
4.851
3.349
1.926
1.00
2.03
2.04
2.97
2.14
3.08
3.42
3.10
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


^{13}C NMR (100.6 MHz, CD_3OD)
AcNH
OH
OH
OH
180
160
140
120
100
80
60
40
20
ppm