Supporting Information for

Asymmetric Syntheses of (–)-1-Deoxymannojirimycin and (+)-1-Deoxyallonojirimycin via a Ring-Expansion Approach

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Table of Contents

1. Experimental

1.1. General Experimental

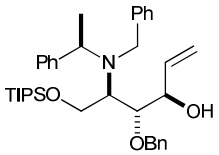
All reactions involving organometallic or other moisture sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[1] Water was purified by an Elix® UV–10 system. BuLi was purchased as a solution in hexanes and titrated against diphenylacetic acid before use. All other reagents were used as supplied without prior purification. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Melting points are uncorrected. Optical rotations were recorded in a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded using an ATR module. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded in the deuterated solvent stated. Spectra were recorded at rt. The field was locked by external referencing to the relevant deuteron resonance. $^1H–^1H$ COSY, $^1H–^{13}C$ HMQC, and $^1H–^{13}C$ HMBC analyses were used to establish atom connectivity. Accurate mass measurements were run on a TOF spectrometer internally calibrated with polyalanine.

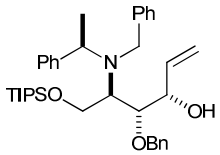
[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

1.2. Experimental Data

(*R*,*R*,*R*,*R*)- and (3*S*,4*R*,5*R*,α*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-6-(triisopropylsilyloxy)hex-1-en-3-ol 11 and 12



11



12

Step 1: DMSO (1.11 mL, 15.7 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (0.55 mL, 6.41 mmol) in CH_2Cl_2 (50 mL) at −78 °C. After 20 min, a solution of **10**[2] (2.00 g, 3.56 mmol, >99:1 dr) in CH_2Cl_2 (50 mL) at −78 °C was added dropwise via cannula. After a further 30 min, Et_3N (2.98 mL, 21.4 mmol) was added and the resultant mixture was stirred at −78 °C for 30 min before being allowed to warm to rt over a period of 30 min. The reaction mixture was then concentrated *in vacuo* and the residue was partitioned between H_2O (100 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (2 × 50 mL) and the combined organic extracts were then dried and concentrated *in vacuo* to give (*R*,*R*,*R*)-2-benzyloxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(triisopropylsilyloxy)butanal as a yellow oil (1.85 g, >99:1 dr);[3] δ_H (400 MHz, $CDCl_3$) 1.01–1.12 (21H, m, Si(C*HMe*$_2$)$_3$), 1.38 (3H, d, *J* 7.1, C(α)*Me*), 3.45–3.51 (1H, m, C(3)*H*), 3.56 (1H, dd, *J* 4.0, 2.7, C(2)*H*), 3.78 (1H, d, *J* 14.8, NCH_AH$_B$Ph), 3.81–3.92 (2H, m, C(4)H_A, C(α)*H*), 4.06 (1H, dd, *J* 9.6, 7.6, C(4)H_B), 4.12 (1H, d, *J* 14.8, NCH$_A$$H_B$Ph), 4.34 (1H, d, *J* 11.4, OCH_AH$_B$Ph), 4.48 (1H, d, *J* 11.4, OCH$_A$$H_B$Ph), 7.16–7.40 (15H, m, *Ph*), 9.19 (1H, d, *J* 2.7, C(1)*H*).

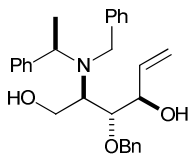
Step 2: Vinylmagnesium bromide (1.0 M in THF, 9.90 mL, 9.90 mmol) was added dropwise to a stirred solution of the residue (1.85 g, >99:1 dr) in THF (100 mL) at 0 °C. The reaction mixture was allowed to warm to rt and was stirred at rt for 16 h. The reaction mixture was then cooled to 0 °C and H_2O (2.5 mL) was added dropwise. The resultant mixture was concentrated *in vacuo* and the residue was partitioned between H_2O (100 mL) and EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2 × 50 mL) and the combined organic extracts were washed with brine (100 mL), then dried and concentrated *in vacuo* to give a 65:35 mixture of **11** and **12**. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 25:1) gave **11** as a colourless oil (1.06 g, 55% from **10**, >99:1 dr); $[\alpha]_D^{20}$ +36.5 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3370 (O−H), 2942, 2866 (C−H); δ_H (400 MHz, $CDCl_3$) 1.05–1.14 (21H, m, Si(C*HMe*$_2$)$_3$), 1.45 (3H, d, *J* 6.8,

[2] For the preparation of the antipode (*S*,*S*,*S*)-**10**, see: Abraham, E.; Brock, E. A.; Candela-Lena, J. I.; Davies, S. G.; Georgiou, M.; Nicholson, R. L.; Perkins, J. H.; Roberts, P. M.; Russell, A. J.; Sánchez-Fernández, E. M.; Scott, P. M.; Smith, A. D.; Thomson, J. E. *Org. Biomol. Chem.* **2008**, *6*, 1665.

[3] Abraham, E.; Davies, Brock, E. A.; Candela-Lena, J. I., Davies, S. G.; Georgiou, M.; Nicholson, R. L.; Perkins, J. H.; Roberts, P. M.; Russell, A. J.; Sanchez-Fernandez, E. M.; Scott, P. M.; Smith, A. D.; Thomson, J. E. *Org. Biomol. Chem.* **2008**, *6*, 1665.

C(α)*Me*), 3.18 (1H, d, *J* 7.0, O*H*), 3.23 (1H, dd, *J* 7.8, 2.3, C(4)*H*), 3.38–3.49 (1H, m, C(5)*H*), 3.96 (2H, app s, NCH_2Ph), 3.97–4.04 (1H, m, C(6)H_A), 4.05–4.19 (2H, m, C(6)H_B, C(α)*H*), 4.29 (1H, d, *J* 11.3, OCH_AH$_B$Ph), 4.46 (1H, br s, C(3)*H*), 4.51 (1H, d, *J* 11.3, OCH$_A$$H_B$Ph), 5.04 (1H, dd, *J* 10.5, 1.6, C(1)H_A), 5.24 (1H, dd, *J* 17.2, 1.6, C(1)H_B), 5.58 (1H, ddd, *J* 17.2, 10.6, 4.6, C(2)*H*), 7.14–7.44 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.1 (Si(*C*HMe$_2$)$_3$), 18.2 (Si(CH*Me*$_2$)$_3$), 19.5 (C(α)*Me*), 52.0 (N*C*H$_2$Ph), 59.2 (*C*(5)), 60.5 (*C*(α)), 62.7 (*C*(6)), 71.9 (*C*(3)), 74.0 (O*C*H$_2$Ph), 80.7 (*C*(4)), 114.6 (*C*(1)), 126.8, 126.9, 127.6, 127.8, 127.9, 128.2, 128.3, 128.9 (*o*,*m*,*p*-*Ph*), 138.2 (*i*-*Ph*), 139.6 (*C*(2)), 141.4, 145.6 (*i*-*Ph*); *m/z* (ESI$^+$) 588 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{37}H_{54}NO_3Si^+$ ([M+H]$^+$) requires 588.3867; found 588.3857. Further elution gave **12** as a colourless oil (490 mg, 26% from **10**, >99:1 dr); $[\alpha]_D^{20}$ +2.4 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3376 (O–H), 2942, 2866 (C–H); δ_H (400 MHz, $CDCl_3$) 1.03–1.18 (21H, m, Si(C*HMe*$_2$)$_3$), 1.34 (3H, d, *J* 6.7, C(α)*Me*), 3.20–3.26 (1H, m, C(5)*H*), 3.52 (1H, app t, *J* 4.4, C(4)*H*), 3.88–4.01 (3H, m, NCH_2Ph, C(6)H_A), 4.06 (1H, q, *J* 6.7, C(α)*H*), 4.12–4.20 (1H, m, C(6)H_B), 4.24 (1H, br s, C(3)*H*), 4.38 (1H, d, *J* 11.1, OCH_AH$_B$Ph), 4.67 (1H, d, *J* 11.1, OCH$_A$$H_B$Ph), 4.95 (1H, app d, *J* 10.4, C(1)H_A), 5.02 (1H, br s, O*H*), 5.18 (1H, app d, *J* 17.1, C(1)H_B), 5.43–5.54 (1H, m, C(2)*H*), 7.15–7.36 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.0 (Si(*C*HMe$_2$)$_3$), 18.0 (Si(CH*Me*$_2$)$_3$), 18.7 (C(α)*Me*), 51.7 (N*C*H$_2$Ph), 59.1 (*C*(α)), 59.3 (*C*(5)), 61.8 (*C*(6)), 71.7 (O*C*H$_2$Ph), 72.4 (*C*(3)), 82.1 (*C*(4)), 115.6 (*C*(1)), 126.7, 126.8, 127.5, 127.8, 128.2, 128.7 (*o*,*m*,*p*-*Ph*), 138.1 (*C*(2)), 138.3, 141.3, 144.8 (*i*-*Ph*); *m/z* (ESI$^+$) 588 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{37}H_{54}NO_3Si^+$ ([M+H]$^+$) requires 588.3867; found 588.3847.

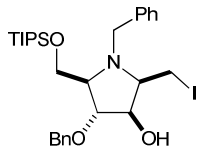
(*R*,*R*,*R*,*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]hex-1-en-3,6-diol 13



TBAF (1.0 M in THF, 2.49 mL, 2.49 mmol) was added dropwise to a stirred solution of **11** (978 mg, 1.66 mmol, >99:1 dr) in THF (80 mL) at 0 °C. The resultant mixture was allowed to warm to rt and was stirred at rt for 16 h. The reaction mixture was then concentrated *in vacuo* and the residue was partitioned between H_2O (100 mL) and CH_2Cl_2 (100 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL) and the combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/ EtOAc, 6:1) gave **13** as a white solid (555 mg, 77%, >99:1 dr); $[\alpha]_D^{20}$ +105.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3409 (O–H), 2931 (C–H); δ_H (400 MHz, $CDCl_3$) 1.46 (3H, d, *J* 6.8, C(α)*Me*), 2.61 (1H, br s, O*H*), 2.91 (1H, br s, O*H*), 3.20–3.27 (1H, m, C(5)*H*), 3.45–3.50 (1H, m, C(4)*H*), 3.72–3.85 (3H, m, C(6)H_2, NCH_AH$_B$Ph), 3.89 (1H, d, *J* 14.1, NCH$_A$$H_B$Ph), 4.01 (1H, q, *J* 6.8, C(α)*H*), 4.26 (1H, br s, C(3)*H*), 4.39 (1H, d, *J* 11.4, OCH_AH$_B$Ph), 4.60 (1H, d, *J* 11.4, OCH$_A$$H_B$Ph), 5.06 (1H, app dt, *J* 10.6, 1.5, C(1)H_A),

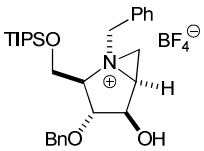
5.20 (1H, app d, *J* 17.1, C(1)H_B), 5.52 (1H, ddd, *J* 17.1, 10.6, 4.7, C(2)*H*), 7.20–7.37 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.9 (C(α)*Me*), 50.6 (N*C*H_2Ph), 58.3 (*C*(α)), 59.3 (*C*(5)), 61.9 (*C*(6)), 71.9 (*C*(3)), 74.0 (O*C*H_2Ph), 81.5 (*C*(4)), 115.2 (*C*(1)), 127.3, 127.5, 128.1, 128.2, 128.2, 128.2, 128.5, 128.6, 129.0 (*o*,*m*,*p*-*Ph*), 137.3, 140.1, 142.8 (*i*-*Ph*), 138.6 (*C*(2)); *m/z* (ESI^+) 432 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{28}H_{34}NO_3^+$ ($[M+H]^+$) requires 432.2533; found 432.2522.

(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4-hydroxy-5-(iodomethyl)pyrrolidine 14



I_2 (518 mg, 2.04 mmol) and $NaHCO_3$ (171 mg, 2.04 mmol) were added to a stirred solution of **11** (400 mg, 0.68 mmol, >99:1 dr) in MeCN (20 mL) at rt and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (50 mL), washed with satd aq $Na_2S_2O_3$ (50 mL) and the organic layer was dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 50:1) gave **14** as a yellow oil (83 mg, 20%, >99:1 dr); $[\alpha]_D^{20}$ +50.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3384 (O–H), 2942, 2866 (C–H); δ_H (400 MHz, $CDCl_3$) 0.95–1.04 (21H, m, Si(C*HMe*$_2$)$_3$), 3.11 (1H, dd, *J* 8.9, 3.1, CH_AH_BI), 3.19 (1H, m, C(2)*H*), 3.22–3.28 (1H, m, C(2)CH_AH_B), 3.30 (1H, d, *J* 8.9, CH$_A$$H_B$I), 3.40 (1H, app dt, *J* 11.1, 3.1, C(5)*H*), 3.48 (1H, d, *J* 10.4, C(2)CH$_A$$H_B$), 3.68 (1H, d, *J* 14.0, NCH_AH_BPh), 3.86 (1H, app s, C(3)*H*), 3.95–4.02 (2H, m, NCH$_A$$H_B$Ph, O*H*), 4.23 (1H, dd, *J* 11.1, 3.2, C(4)*H*), 4.53 (1H, d, *J* 12.0, OCH_AH_BPh), 4.66 (1H, d, *J* 12.0, OCH$_A$$H_B$Ph), 7.22–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 3.4 (*C*H_2I), 11.8 (Si(*C*HMe$_2$)$_3$), 17.8 (Si(CH*Me*$_2$)$_3$), 58.8 (N*C*H_2Ph), 64.5 (C(2)*C*H_2), 70.0 (*C*(5)), 71.2 (O*C*H_2Ph), 74.0 (*C*(4)), 74.3 (*C*(2)), 84.7 (*C*(3)), 127.2, 127.6, 127.7, 128.3, 128.4, 128.6 (*o*,*m*,*p*-*Ph*), 138.0, 139.7 (*i*-*Ph*); *m/z* (ESI^+) 610 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{29}H_{45}INO_3Si^+$ ($[M+H]^+$) requires 610.2208; found 610.2198.

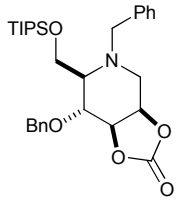
(1*S*,2*R*,3*R*,4*R*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4-hydroxy-1-azabicyclo[3.1.0]hexanium tetrafluoroborate 15



$AgBF_4$ (23 mg, 0.118 mmol) was added to a stirred solution of **14** (60 mg, 0.10 mmol, >99:1 dr) in CH_2Cl_2 at rt and the resultant mixture was allowed to stir at rt for 1 h. The reaction mixture was then filtrated through

Celite® (eluent CH_2Cl_2) and concentrated *in vacuo* to give **15** as an orange oil (65 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ +0.6 (*c* 0.4 in $CHCl_3$); ν_{max} (ATR) 3510 (O–H), 2945, 2867 (C–H); δ_H (400 MHz, CD_2Cl_2) 0.94–1.24 (21H, m, Si(C*H*Me_2)$_3$), 3.09 (1H, dd, *J* 8.0, 4.5, C(6)H_A), 3.56 (1H, dd, *J* 6.3, 4.5, C(6)H_B), 3.76–3.86 (2H, m, C(2)*H*, C(3)*H*), 3.98–4.04 (2H, m, C(2)CH_AH$_B$, O*H*), 4.07–4.20 (2H, m, C(2)CH$_A$$H_B$, C(5)*H*), 4.42 (1H, d, *J* 13.1, NCH_AH$_B$Ph), 4.54 (1H, d, *J* 11.6, OCH_AH$_B$Ph), 4.77 (1H, d, *J* 13.1, NCH$_A$$H_B$Ph), 4.82 (1H, d, *J* 11.6, OCH$_A$$H_B$Ph), 4.83–4.88 (1H, m, C(4)*H*), 7.28–7.58 (10H, m, *Ph*); δ_C (100 MHz, CD_2Cl_2) 11.7 (Si(*C*HMe$_2$)$_3$), 17.8 (Si(CH*Me*$_2$)$_3$), 37.4 (*C*(6)), 49.2 (*C*(5)), 59.5 (C(2)*C*H$_2$), 61.3 (N*C*H$_2$Ph), 68.3 (*C*(2)), 72.6 (*C*(4)), 72.7 (O*C*H$_2$Ph), 79.0 (*C*(3)), 128.1, 128.3, 128.5, 129.9, 131.0, 131.2 (*o*,*m*,*p*-*Ph*), 136.9 (2 × *i*-*Ph*); *m/z* (ESI$^+$) 514 ([M+MeOH]$^+$, 40%), 482 ([M]$^+$, 100%); HRMS (ESI$^+$) $C_{30}H_{48}NO_4Si^+$ ([M+MeOH]$^+$) requires 514.3347; found 514.3345.

(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxy-4,5-*O*-carbonylpiperidine 16



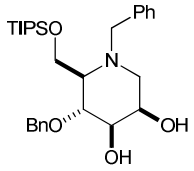
*Method A (from **11**) – Step 1*: I_2 (129 mg, 0.51 mmol) and $NaHCO_3$ (43 mg, 0.51 mmol) were added to a stirred solution of **11** (100 mg, 0.17 mmol, >99:1 dr) in dioxane/H_2O (3:1, 4 mL) at rt and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (15 mL) and washed with satd aq $Na_2S_2O_3$ (15 mL), then dried and concentrated *in vacuo* to give a 50:50 mixture of **16** and 1-phenylethanol (100 mg).

Step 2: Ac_2O (0.18 mL, 1.9 mmol) and DMAP (4 mg, 0.04 mmol) were added to a stirred solution of the residue of **16** and 1-phenylethanol (100 mg) in pyridine (8 mL) at 0 °C. The resultant mixture was allowed to warm to rt and was stirred at rt for 16 h. The reaction mixture was then diluted with H_2O (20 mL) and EtOAc (20 mL), and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine, then dried and concentrated *in vacuo* to give a 50:50 mixture of **16** and α-methylbenzylacetate. Purification via flash column chromatography (eluent 30–40 °C petrol/ EtOAc, 12:1) gave **16** as a colourless oil (23 mg, 26%, >99:1 dr); $[\alpha]_D^{20}$ –32.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2943, 2866 (C–H), 1810 (C=O); δ_H (400 MHz, $CDCl_3$) 1.02–1.15 (21H, m, Si(C*H*Me_2)$_3$), 2.83 (1H, dd, *J* 13.7, 1.0, C(6)H_A), 2.90 (1H, dd, *J* 13.7, 2.0, C(6)H_B), 2.98 (1H, app dd, *J* 9.2, 4.5, C(2)*H*), 3.43 (1H, d, *J* 14.2, NCH_AH$_B$Ph), 3.71 (1H, app t, *J* 9.2, C(2)CH_AH$_B$), 3.91 (1H, dd, *J* 10.1, 4.5, C(2)CH$_A$$H_B$), 4.06 (1H, d, *J* 14.2,

NCH_AH_BPh), 4.30 (1H, app d, *J* 3.6, C(3)*H*), 4.52 (1H, d, *J* 11.6, OCH_AH_BPh), 4.70–4.78 (2H, m, C(5)*H*, OCH_AH_BPh), 4.79–4.84 (1H, dd, *J* 8.3, 3.6, C(4)*H*), 7.23–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 11.9 ($Si(CHMe_2)_3$), 18.0 ($Si(CHMe_2)_3$), 49.1 (*C*(6)), 59.6 (NCH_2Ph), 62.8 (C(2)CH_2), 65.0 (*C*(2)), 71.8 (OCH_2Ph), 72.4 (*C*(3)), 73.4 (*C*(4)), 74.4 (*C*(5)), 127.3, 127.6, 128.0, 128.3, 128.5, 128.5 (*o*,*m*,*p*-*Ph*), 137.5, 137.9 (*i*-*Ph*), 154.6 (*C*O); *m/z* (ESI^+) 526 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{30}H_{44}NO_5Si^+$ ($[M+H]^+$) requires 526.2983; found 526.2968.

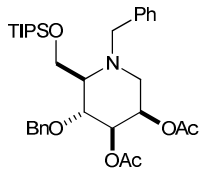
*Method B (from **14**)*: $AgBF_4$ (23 mg, 0.118 mmol) was added to a stirred solution of **14** (60 mg, 0.10 mmol, >99:1 dr) in CH_2Cl_2 at rt and the resultant mixture was allowed to stir at rt for 1 h. The reaction mixture was then filtered through Celite® (eluent CH_2Cl_2) and concentrated *in vacuo* to give **15** as an orange oil (65 mg, quant, >99:1 dr). $NaHCO_3$ (25 mg, 0.29 mmol) was added to a stirred solution of the residue of **15** (65 mg, >99:1 dr) in dioxane/H_2O (3:1, 4 mL) at rt and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (15 mL) and washed with satd aq $Na_2S_2O_3$ (15 mL), then dried and concentrated *in vacuo* to give **16** as a yellow oil (52 mg, quant, >99:1 dr).

(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxypiperidine 17



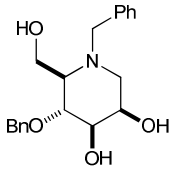
K_2CO_3 (32 mg, 0.23 mmol) was added to a stirred solution of **16** (40 mg, 0.08 mmol, >99:1 dr) in MeOH (2 mL) at rt and the resulting mixture was allowed to stir at rt for 16 h. The reaction mixture was then concentrated *in vacuo* and the residue was partitioned between H_2O (15 mL) and EtOAc (15 mL). The aqueous layer was extracted with EtOAc (2 × 5 mL) and the combined organic extracts were then dried and concentrated *in vacuo* to give **17** as a yellow oil (40 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ −19.8 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3395 (O–H), 2942, 2866 (C–H); δ_H (400 MHz, $CDCl_3$) 1.02–1.14 (21H, m, $Si(CHMe_2)_3$), 2.24 (1H, d, *J* 12.4, C(6)H_A), 2.38–2.47 (1H, m, C(2)*H*), 2.92 (1H, dd, *J* 12.4, 4.6, C(6)H_B), 3.36 (1H, d, *J* 13.3, NCH_AH_BPh), 3.57 (1H, app t, *J* 8.1, C(3)*H*), 3.65 (1H, dd, *J* 8.1, 3.3, C(4)*H*), 3.72–3.80 (1H, m, C(5)*H*), 4.03 (1H, dd, *J* 11.1, 4.0, C(2)CH_AH_B), 4.22 (1H, dd, *J* 11.1, 1.8, C(2)CH_AH_B), 4.43 (1H, d, *J* 13.3, NCH_AH_BPh), 4.65 (1H, d, *J* 11.4, OCH_AH_BPh), 5.03 (1H, d, *J* 11.4, OCH_AH_BPh), 7.26–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.0 ($Si(CHMe_2)_3$), 18.1 ($Si(CHMe_2)_3$), 54.1 (*C*(6)), 57.2 (NCH_2Ph), 61.9 (C(2)CH_2), 66.6 (*C*(2)), 67.9 (*C*(5)), 74.3 (OCH_2Ph), 75.8 (*C*(4)), 78.6 (*C*(3)), 127.2, 127.6, 127.9, 128.4, 128.5, 129.0 (*o*,*m*,*p*-*Ph*), 138.5 (*i*-*Ph*); *m/z* (ESI^+) 500 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{29}H_{46}NO_4Si^+$ ($[M+H]^+$) requires 500.3191; found 500.3190.

(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-diacetoxypiperidine 18



Ac_2O (0.08 mL, 0.80 mmol) and DMAP (2 mg, 0.02 mmol) were added to a stirred solution of **17** (40 mg, 80 μmol, >99:1 dr) in pyridine (4 mL) at 0 °C. The resultant mixture was allowed to warm to rt and was stirred at rt for 16 h. The reaction mixture was then diluted with H_2O (15 mL) and EtOAc (15 mL), and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic extracts were washed with brine, then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 9:1) gave **18** as a yellow oil (47 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ −14.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2942, 2866 (C–H), 1748 (C=O); δ_H (400 MHz, $CDCl_3$) 0.90–1.07 (21H, m, Si(C*H*Me_2)$_3$), 2.00 (3H, s, CO*Me*), 2.07 (3H, s, CO*Me*), 2.41 (1H, dd, *J* 13.2, 2.6, C(6)H_A), 2.66–2.72 (1H, m, C(2)*H*), 2.94 (1H, dd, *J* 13.2, 6.2, C(6)H_B), 3.53 (1H, d, *J* 14.0, NC$H_A$$H_B$Ph), 3.88 (1H, app t, *J* 7.3, C(3)*H*), 3.98 (1H, dd, *J* 10.6, 5.3, C(2)C$H_A$$H_B$), 4.12 (1H, dd, *J* 10.6, 3.5, C(2)C$H_A$$H_B$), 4.33 (1H, d, *J* 14.0, NC$H_A$$H_B$Ph), 4.62 (1H, d, *J* 11.4, OC$H_A$$H_B$Ph), 4.74 (1H, d, *J* 11.4, OC$H_A$$H_B$Ph), 5.15 (1H, dd, *J* 7.3, 3.2, C(4)*H*), 5.26 (1H, app dt, *J* 6.2, 3.2, C(5)*H*), 7.20–7.37 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 11.9 (Si(*C*HMe_2)$_3$), 18.0 (Si(CH*Me*$_2$)$_3$), 21.0 (2 × CO*Me*), 49.9 (*C*(6)), 57.7 (N*C*H_2Ph), 60.4 (C(2)*C*H_2), 61.3 (*C*(2)), 65.2 (*C*(5)), 67.1 (*C*(4)), 73.8 (O*C*H_2Ph), 75.0 (*C*(3)), 126.9, 127.4, 127.6, 128.1, 128.3, 128.5 (*o*,*m*,*p*-*Ph*), 138.3, 139.3 (*i*-*Ph*), 170.1, 170.3 (*C*OMe); *m/z* (ESI^+) 584 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{33}H_{50}NO_6Si^+$ ($[M+H]^+$) requires 584.3402; found 584.3401.

(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-(hydroxymethyl)-3-benzyloxy-4,5-dihydroxypiperidine 19



*Method A (from **18**) – Step 1*: HF·pyridine (70%, 0.15 mL, 5.70 mmol) was added dropwise to a stirred solution of **18** (111 mg, 0.19 mmol, >99:1 dr) in THF (5 mL) at 0 °C. The resultant mixture was allowed to warm to rt and was stirred at rt for 16 h. The reaction mixture was cooled to 0 °C and satd aq $NaHCO_3$ (0.5 mL) was then carefully added. The resultant mixture was concentrated *in vacuo* and the residue was partitioned between H_2O (10 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (2 × 5 mL) and the combined organic extracts were then dried and concentrated *in vacuo* (89 mg).

Step 2: K_2CO_3 (73 mg, 0.57 mmol) was added to a stirred solution of the residue (89 mg) in MeOH (5 mL) at rt and the resultant mixture was allowed to stir at rt for 6 h before being concentrated *in vacuo*. The residue was

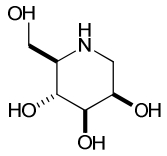
dissolved in H_2O (10 mL) and extracted with $CHCl_3$/^{i}PrOH (3:1, 3 × 5 mL). The combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 50:1) gave **19** as a white solid (46 mg, 70% from **18**, >99:1 dr); mp 70–72 °C; $[\alpha]_D^{20}$ −36.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3384 (O−H), 2921 (C−H); δ_H (400 MHz, $CDCl_3$) 2.29–2.34 (2H, m, C(2)*H*, C(6)H_A), 3.04 (1H, dd, *J* 12.6, 3.8, C(6)H_B), 3.39 (1H, d, *J* 13.2, NCH_AH$_B$Ph), 3.60 (1H, dd, *J* 8.7, 3.3, C(4)*H*), 3.77 (1H, app t, *J* 8.7, C(3)*H*), 3.85 (1H, br s, C(5)*H*), 3.93 (1H, dd, *J* 12.0, 1.6, C(2)CH_AH$_B$), 4.03 (1H, dd, *J* 12.0, 2.7, C(2)CH$_A$$H_B$), 4.14 (1H, d, *J* 13.2, NCH$_A$$H_B$Ph), 4.78 (1H, d, *J* 11.3, OCH_AH$_B$Ph), 4.93 (1H, d, *J* 11.3, OCH$_A$$H_B$Ph), 7.26–7.42 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 54.8 (*C*(6)), 57.0 (N*C*H$_2$Ph), 58.3 (C(2)*C*H$_2$), 65.7 (*C*(2)), 67.8 (*C*(5)), 75.0 (O*C*H$_2$Ph), 75.2 (*C*(4)), 77.2 (*C*(3)), 127.5, 128.0, 128.1, 128.6, 128.7, 128.8 (*o*,*m*,*p*-*Ph*), 137.7, 138.3 (*i*-*Ph*); *m/z* (ESI$^+$) 344 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_4^+$ ([M+H]$^+$) requires 344.1856; found 344.1855.

*Method B (from **11**) – Step 1*: I_2 (411 mg, 1.62 mmol) and $NaHCO_3$ (136 mg, 1.62 mmol) were added to a stirred solution of **11** (319 mg, 0.54 mmol, >99:1 dr) in dioxane/H_2O (3:1, 20 mL) at rt and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (20 mL) and washed with satd aq $Na_2S_2O_3$ (20 mL), then dried and concentrated *in vacuo* to give a 50:50 mixture of **16** and 1-phenylethanol (319 mg).

Step 2: HF·pyridine (70%, 0.46 mL, 17.7 mmol) was added dropwise to a solution of the residue of **16** and 1-phenylethanol (319 mg) in THF (5 mL) at 0 °C. The resultant mixture was allowed to warm to rt and was stirred at rt for 16 h. The reaction mixture was then cooled to 0 °C and satd aq $NaHCO_3$ (1 mL) was carefully added. The resultant mixture was concentrated *in vacuo* and the residue was partitioned between H_2O (10 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (2 × 5 mL) and the combined organic extracts were then dried and concentrated *in vacuo* to give **20** (230 mg).

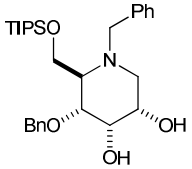
Step 3: K_2CO_3 (245 mg, 1.77 mmol) was added to a stirred solution of the residue of **20** (230 mg) in MeOH (5 mL) at rt and the resultant mixture was allowed to stir at rt for 6 h before being concentrated *in vacuo*. The residue was then dissolved in H_2O (10 mL) and extracted with $CHCl_3$/^{i}PrOH (3:1, 3 × 5 mL). The combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 50:1) gave **19** as a white solid (75 mg, 40% from **11**, >99:1 dr).

(*R*,*R*,*R*,*R*)-1,5-Dideoxy-1,5-imino-D-mannose [(–)-1-deoxymannojirimycin] 21



$Pd(OH)_2/C$ (35 mg) was added to a stirred solution of **19** (70 mg, 0.20 mmol, >99:1 dr) in degassed MeOH (4 mL) and the resultant suspension was stirred at rt for 48 h under an atmosphere of H_2 (5 atm). HCl (1.0 M in Et_2O, 1 mL) was then added and the resultant suspension was stirred for a further 5 min before being filtered through Celite® (eluent MeOH). The filtrate was concentrated *in vacuo*. Purification via ion exchange chromatography on Dowex-50WX8 resin (hydrogen form, 100–200 mesh, eluent H_2O) gave **21** as a white solid (29 mg, 87%, >99:1 dr); mp 180–182 °C; {lit.[4] mp 185 °C}; $[\alpha]_D^{20}$ –38.6 (*c* 1.0 in H_2O); {lit.[5] for sample isolated from a natural source $[\alpha]_D$ –41.4 (*c* 0.74 in H_2O); lit.[6] $[\alpha]_D^{20}$ –40 (*c* 1.35 in H_2O); lit.[7] $[\alpha]_D^{22}$ –36.1 (*c* 0.33 in H_2O); lit.[8] $[\alpha]_D$ –39.0 (*c* 0.1 in H_2O); lit.[9] for enantiomer $[\alpha]_D$ +40.2 (*c* 0.65 in H_2O); lit.[10] for enantiomer $[\alpha]_D$ +40.42 (*c* 0.728 in H_2O)}; ν_{max} (ATR) 3300 (O–H), 2921 (C–H); δ_H (400 MHz, D_2O) 2.44 (1H, dt, *J* 9.8, 4.1, C(5)*H*), 2.72 (1H, dd, *J* 14.3, 1.4, C(1)H_A), 2.96 (1H, dd, *J* 14.3, 2.7, C(1)H_B), 3.52 (1H, dd, *J* 9.8, 2.9, C(3)*H*), 3.56 (1H, app t, *J* 9.8, C(4)*H*), 3.73 (2H, d, *J* 4.1, C(6)H_2), 3.94–3.97 (1H, m, C(2)*H*); δ_C (100 MHz, D_2O) 48.1 (*C*(1)), 60.4 (*C*(5)), 60.5 (*C*(6)), 68.2 (*C*(4)), 69.0 (*C*(2)), 74.4 (*C*(3)); *m/z* (FI^+) 163 ($[M]^+$, 100%); HRMS (FI^+) $C_6H_{13}NO_4^+$ ($[M]^+$) requires 163.0839; found 163.0851.

(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxypiperidine 22



K_2CO_3 (32 mg, 0.23 mmol) was added to a stirred solution of **24** (45 mg, 0.08 mmol, >99:1 dr) in MeOH (4 mL) at rt and the resultant mixture was allowed to stir at rt for 16 h. The resultant mixture was concentrated *in vacuo* and the residue was partitioned between H_2O (10 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (2 × 5 mL) and the combined organic extracts were then dried

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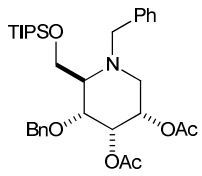
and concentrated *in vacuo* to give **22** as a yellow oil (40 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ −1.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3425 (O–H), 2942, 2866 (C–H); δ_H (400 MHz, $CDCl_3$) 1.01–1.12 (21H, m, Si(C*H*Me_2)$_3$), 2.80 (1H, dd, *J* 12.4, 4.0, C(6)H_A), 2.94 (1H, dd, *J* 12.4, 2.0, C(6)H_B), 3.10–3.18 (1H, m, C(2)*H*), 3.70–3.75 (1H, m, C(5)*H*), 3.80–3.98 (6H, m, C(3)*H*, C(4)*H*, C(2)CH_2, NCH_2Ph), 4.44 (1H, d, *J* 11.5, OCH_AH$_B$Ph), 4.52 (1H, d, *J* 11.5, OCH$_A$$H_B$Ph), 7.25–7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 11.8 (Si(*C*HMe$_2$)$_3$), 18.0 (Si(CH*Me*$_2$)$_3$), 52.6 (*C*(6)), 58.1, 58.3 (C(2)*C*H$_2$, N*C*H$_2$Ph), 59.9 (*C*(2)), 67.4 (*C*(4)), 69.7 (*C*(5)), 72.1 (O*C*H$_2$Ph), 78.6 (*C*(3)), 127.2, 127.8, 127.9, 128.3, 128.5, 128.6 (*o*,*m*,*p*-*Ph*), 137.8 (*i*-*Ph*); *m/z* (ESI^+) 500 ([M+H]$^+$, 100%); HRMS (ESI^+) $C_{29}H_{46}NO_4Si^+$ ([M+H]$^+$) requires 500.3191; found 500.3185.

(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-diacetoxypiperidine 24



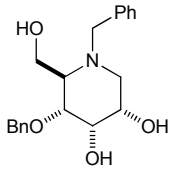
Step 1: I_2 (1.35 g, 5.31 mmol) and $NaHCO_3$ (446 mg, 5.31 mmol) were added to a stirred solution of **12** (1.04 g, 1.77 mmol, >99:1 dr) in dioxane/H_2O (3:1, 40 mL) at rt and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (50 mL) and washed with satd aq $Na_2S_2O_3$ (50 mL), then dried and concentrated *in vacuo* to give a 73:27 mixture of **22** and **23** (1.10 g). Data for mixture: ν_{max} (ATR) 2943, 2866 (C–H), 1804 (C=O); *m/z* (ESI^+) 526 ([M+H]$^+$, 100%); HRMS (ESI^+) $C_{30}H_{44}NO_5Si^+$ ([M+H]$^+$) requires 526.2983; found 526.2970. Data for **23**: δ_H (400 MHz, $CDCl_3$) 1.00–1.16 (21H, m, Si(C*H*Me_2)$_3$), 2.95 (1H, dd, *J* 12.3, 6.1, C(6)H_A), 3.01–3.06 (1H, m, C(2)*H*), 3.21 (1H, dd, *J* 12.3, 5.6, C(6)H_B), 3.67 (1H, d, *J* 13.7, NCH_AH$_B$Ph), 3.72–3.80 (2H, m, C(2)CH_2), 3.89 (1H, d, *J* 13.7, NCH$_A$$H_B$Ph), 4.13 (1H, dd, *J* 5.8, 3.2, C(3)*H*), 4.60 (1H, d, *J* 11.4, OCH_AH$_B$Ph), 4.68–4.76 (2H, m, C(5)*H*, OCH$_A$$H_B$Ph), 4.96 (1H, dd, *J* 8.4, 3.2, C(4)*H*), 7.24–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.0 (Si(*C*HMe$_2$)$_3$), 18.1 (Si(CH*Me*$_2$)$_3$), 48.7 (*C*(6)), 58.6 (N*C*H$_2$Ph), 61.7 (*C*(2)), 62.0 (C(2)*C*H$_2$), 72.6 (O*C*H$_2$Ph), 73.6 (*C*(4)), 73.8, 73.9 (*C*(3), *C*(5)), 126.9, 127.7, 127.8, 128.2, 128.4, 128.6 (*o*,*m*,*p*-*Ph*), 137.5, 138.0 (*i*-*Ph*), 155.2 (*C*O).

Step 2: K_2CO_3 (734 mg, 5.31 mmol) was added to a stirred solution of the residue of the 73:27 mixture of **22** and **23** (1.10 g) in MeOH (50 mL) at rt and the resultant mixture was allowed to stir at rt for 16 h. The reaction mixture was then concentrated *in vacuo* and the residue was partitioned between H_2O (50 mL) and EtOAc (50 mL). The aqueous layer was extracted with EtOAc (2 × 25 mL) and the combined organic extracts were then dried and concentrated *in vacuo* to give **22** (760 mg, >99:1 dr).

Step 3: Ac_2O (1.67 mL, 17.7 mmol) and DMAP (43 mg, 0.35 mmol) were added to a stirred solution of the residue of **22** (760 mg) in pyridine (40 mL) at 0 °C. The resultant mixture was allowed to warm to rt and was

stirred at rt for 16 h. The reaction mixture was then diluted with H_2O (50 mL) and EtOAc (50 mL), and the aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic extracts were washed with brine (25 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/ EtOAc, 12:1) gave **24** as a colourless oil (440 mg, 43% from **12**, >99:1 dr); $[\alpha]_D^{20}$ −1.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2944, 2866 (C–H), 1747 (C=O); δ_H (400 MHz, $CDCl_3$) 0.95–1.12 (21H, m, Si(C*H*Me_2)$_3$), 1.95 (3H, s, CO*Me*), 2.12 (3H, s, CO*Me*), 2.41 (1H, t, *J* 10.9, C(6)H_A), 2.64 (1H, dd, *J* 10.9, 4.7, C(6)H_B), 2.69 (1H, app dd, *J* 9.6, 3.2, C(2)*H*), 3.31 (1H, d, *J* 13.7, NC$H_A$$H_B$Ph), 3.58 (1H, dd, *J* 9.6, 2.2, C(3)*H*), 3.96 (1H, dd, *J* 11.1, 3.2, C(2)C$H_A$$H_B$), 4.22 (1H, app d, *J* 11.1, C(2)C$H_A$$H_B$), 4.36 (1H, d, *J* 10.8, OC$H_A$$H_B$Ph), 4.50 (1H, d, *J* 13.7, NC$H_A$$H_B$Ph), 4.69 (1H, d, *J* 10.8, OC$H_A$$H_B$Ph), 4.83–4.89 (1H, m, C(5)*H*), 5.83 (1H, br s, C(4)*H*), 7.22–7.36 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.0 (Si(*C*HMe_2)$_3$), 18.1 (Si(CH*Me*$_2$)$_3$), 20.8, 20.9 (CO*Me*), 48.8 (*C*(6)), 57.1 (N*C*H_2Ph), 61.9 (C(2)*C*H_2), 62.8 (*C*(2)), 66.6 (*C*(4)), 68.0 (*C*(5)), 71.1 (O*C*H_2Ph), 74.2 (*C*(3)), 126.9, 127.7, 128.2, 128.2, 128.3, 128.7 (*o,m,p-Ph*), 137.6, 139.4 (*i-Ph*), 170.0, 170.5 (*C*OMe); *m/z* (ESI^+) 584 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{33}H_{50}NO_6Si^+$ ($[M+H]^+$) requires 584.3402; found 584.3402.

(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-(hydroxymethyl)-3-benzyloxy-4,5-dihydroxypiperidine 25



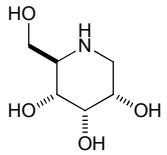
*Method A (from **24**)*: 6.0 M aq HCl (2 mL) was added to a stirred solution of **24** (110 mg, 0.19 mmol, >99:1 dr) in MeOH (5 mL) and the resultant mixture was heated at 50 °C for 16 h before being allowed to cool to rt and concentrated *in vacuo*. The residue was dissolved in MeOH (5 mL) and K_2CO_3 (520 mg, 3.76 mmol) was added to the resultant solution. The reaction mixture was then stirred at rt for 6 h, then concentrated *in vacuo*. The residue was then dissolved in H_2O (10 mL) and the resultant solution was extracted with $CHCl_3$/^{i}PrOH (3:1, 3 × 5 mL). The combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 50:1) gave **25** as a white solid (56 mg, 86%, >99:1 dr); mp 70–72 °C; $[\alpha]_D^{20}$ −5.4 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3500 (O–H); δ_H (400 MHz, $CDCl_3$) 2.53 (1H, dd, *J* 11.1, 9.3, C(6)H_A), 2.57 (1H, br s, O*H*), 2.68–2.74 (1H, m, C(2)*H*), 2.80 (1H, dd, *J* 11.1, 4.2, C(6)H_B), 3.45 (1H, d, *J* 13.6, NC$H_A$$H_B$Ph), 3.61–3.69 (1H, m, C(5)*H*), 3.71 (1H, dd, *J* 7.8, 3.0, C(3)*H*), 3.88 (1H, dd, *J* 11.6, 2.0, C(2)C$H_A$$H_B$), 3.95 (1H, dd, *J* 11.6, 3.8, C(2)C$H_A$$H_B$), 4.06 (1H, d, *J* 13.6, NC$H_A$$H_B$Ph), 4.10–4.14 (1H, m, C(4)*H*), 4.62 (2H, app s, OCH_2Ph), 7.25–7.43 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 51.8 (*C*(6)), 57.5 (N*C*H_2Ph), 57.8 (C(2)*C*H_2), 59.9 (*C*(2)), 67.6 (*C*(4)), 68.0 (*C*(5)), 72.2 (O*C*H_2Ph), 76.5 (*C*(3)), 127.4, 128.0,

128.2, 128.5, 128.7, 128.8 (*o*,*m*,*p*-*Ph*), 137.5, 138.2 (*i*-*Ph*); *m/z* (ESI$^+$) 344 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{25}NNaO_4^+$ ([M+Na]$^+$) requires 366.1676; found 366.1682.

*Method B (from **12**) – Step 1*: I_2 (207 mg, 0.82 mmol) and $NaHCO_3$ (69.0 mg, 0.82 mmol) were added to a stirred solution of **12** (160 mg, 0.27 mmol, >99:1 dr) in dioxane/H_2O (3:1, 4 mL) at rt and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then diluted with Et_2O (10 mL) and washed with satd aq $Na_2S_2O_3$ (10 mL), then dried and concentrated *in vacuo* to give a 73:27 mixture of **22** and **23** and benzylalcohol (127 mg).

Step 2: 6.0 M aq HCl (3 mL) was added to a stirred solution of the residue (127 mg) in MeOH (5 mL) and the resultant mixture was heated at 50 °C for 16 h before being concentrated *in vacuo*. The residue was dissolved in MeOH (5 mL) and K_2CO_3 (752 mg, 5.44 mmol) was added to the resultant solution. The reaction mixture was then stirred at rt for 6 h, then concentrated *in vacuo*. The residue was then dissolved in H_2O (10 mL) and the resultant solution was extracted with $CHCl_3$/^{i}PrOH (3:1, 3 × 5 mL). The combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 50:1) gave **25** as a white solid (37 mg, 39% from **12**, >99:1 dr).

(2*S*,3*S*,4*R*,5*R*)-1,5-Dideoxy-1,5-imino-D-allose [(+)-1-deoxyallonojirimycin] 26



$Pd(OH)_2$/C (32 mg) was added to a stirred solution of **25** (64 mg, 0.19 mmol, >99:1 dr) in degassed MeOH (4 mL) and the resultant suspension was stirred at rt for 48 h under an atmosphere of H_2 (5 atm). HCl (1.0 M in Et_2O, 1 mL) was then added and the resultant suspension was stirred for a further 5 min before being filtered through Celite® (eluent MeOH) and concentrated *in vacuo*. Purification via ion exchange chromatography on Dowex-50WX8 resin (hydrogen form, 100–200 mesh, eluent H_2O) gave **26** as a white solid (25 mg, 83%, >99:1dr); mp 162–164 °C; {lit.[11] mp 163 °C}; $[\alpha]_D^{20}$ +28.3 (*c* 1.0 in H_2O); $[\alpha]_D^{20}$ +30.2 (*c* 1.0 in MeOH); {lit.[12] for sample isolated from a natural source $[\alpha]_D$ +25.7 (*c* 0.65 in H_2O); lit.[13] $[\alpha]_D^{25}$ +30.5 (*c* 0.15 in H_2O); lit.[14] $[\alpha]_D^{20}$ +28.1 (*c* 0.8 in H_2O); lit.[15] for enantiomer $[\alpha]_D$ −37.0 (*c* 1.04 in MeOH); lit.[16] $[\alpha]_D^{25}$ +35.1 (*c* 0.1 in

[11] Sridhar, R.; Srinivas, B.; Rao, K. *Tetrahedron* **2009**, *65*, 70701.
[12] Asano, N.; Oseki, K.; Kizu, H.; Matsui, K. *J. Med. Chem.* **1994**, *37*, 3701.
[13] Hong, B.-C.; Chen, Z.-Y.; Nagarajan, A.; Kottani, R.; Chavan, V.; Chen, W.-H.; Jiang, Y.-F.; Zhang, S.-C.; Liaoa, J.-H.; Sarsharb, S. *Carbohydr. Res.* **2005**, *340*, 2457.
[14] Ikota, N.; Hirano, J.-I.; Gamage, R.; Nakagawa, H.; Hama-Inaba, H. *Heterocycles* **1997**, 46, 637.
[15] Kato, A.; Kato, N.; Kano, E.; Adachi, I.; Ikeda, K.; Yu, L.; Okamoto, T.; Banba, Y.; Ouchi, H.; Takahata, H.; Asano, N. *J. Med. Chem.* **2005**, *48*, 2036.
[16] Sridhar, R.; Srinivas, B.; Rao, K. *Tetrahedron* **2009**, *65*, 70701.

MeOH); lit.[17] $[\alpha]_D$ +34.0 (*c* 0.1 in MeOH)}; ν_{max} (ATR) 3275 (O–H), 2873 (C–H); δ_H (400 MHz, D_2O) 2.65 (1H, app t, *J* 11.8, C(1)H_A), 2.70 (1H, ddd, *J* 10.2, 5.8, 2.8, C(5)*H*), 2.81 (1H, dd, *J* 11.8, 5.0, C(1)H_B), 3.43 (1H, dd, *J* 10.2, 2.8, C(4)*H*), 3.60 (1H, dd, *J* 11.8, 5.8, C(6)CH_A), 3.65 (1H, ddd, *J* 11.8, 5.0, 2.8, C(2)*H*), 3.75 (1H, dd, *J* 11.8, 2.8, C(6)H_B), 4.04 (1H, app t, *J* 2.8, C(3)*H*); δ_C (100 MHz, D_2O) 43.4 (*C*(1)), 54.4 (*C*(5)), 60.9 (*C*(6)), 67.8 (*C*(2)), 68.3 (*C*(4)), 71.3 (*C*(3)); *m/z* (FI^+) 163 ($[M]^+$, 100%); HRMS (FI^+) $C_6H_{13}NO_4^+$ ($[M]^+$) requires 163.0839; found 163.0852.

[17] Kim, I. S.; Lee, H. Y.; Jung, Y. H. *Heterocycles* **2007**, *71*, 1787.

2. X-ray crystal structure determination for 13, 19·$CHCl_3$ and 25

Data were collected using either an Oxford Diffraction SuperNova diffractometer with graphite monochromated Cu-Kα radiation (for **13** and **25**), or a Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation (for **19**·$CHCl_3$), using standard procedures at 150 K. The structures were solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[18,19]

X-ray crystal structure data for **13** [$C_{28}H_{33}NO_3$]: M = 431.57, monoclinic, space group $P\ 2_1$, a = 12.8417(4) Å, b = 6.6522(1) Å, c = 14.8628(5) Å, β = 109.357(4)°, V = 1197.89(6) Å^3, Z = 2, μ = 0.605 mm^{-1}, colourless block, crystal dimensions = 0.05 × 0.06 × 0.19 mm. A total of 4855 unique reflections were measured for $3 < \theta < 80$ and 4265 reflections were used in the refinement. The final parameters were wR_2 = 0.110 and R_1 = 0.047 [$I > -3.0\sigma(I)$].

X-ray crystal structure data for **19**·$CHCl_3$ [$C_{21}H_{26}Cl_3NO_4$]: M = 462.80, monoclinic, space group $P\ 2_1$, a = 11.1676(4) Å, b = 8.2551(3) Å, c = 12.4524(5) Å, β = 90.8174(16)°, V = 1147.87(7) Å^3, Z = 2, μ = 0.425 mm^{-1}, colourless block, crystal dimensions = 0.23 × 0.26 × 0.27 mm. A total of 5050 unique reflections were measured for $5 < \theta < 27$ and 2656 reflections were used in the refinement. The final parameters were wR_2 = 0.062 and R_1 = 0.051 [$I > -3.0\sigma(I)$], with Flack enantiopole = –0.09(12).[20]

X-ray crystal structure data for **25** [$C_{20}H_{25}NO_4$]: M = 343.43, monoclinic, space group $P\ 2_1$, a = 10.3223(3) Å, b = 6.9861(2) Å, c = 12.9927(3) Å, β = 101.708(3)°, V = 917.44(4) Å^3, Z = 2, μ = 0.698 mm^{-1}, colourless block, crystal dimensions = 0.07 × 0.09 × 0.16 mm. A total of 3813 unique reflections were measured for $3 < \theta < 77$ and 3796 reflections were used in the refinement. The final parameters were wR_2 = 0.064 and R_1 = 0.033 [$I > -3.0\sigma(I)$], with Flack enantiopole = –0.05(16).[20]

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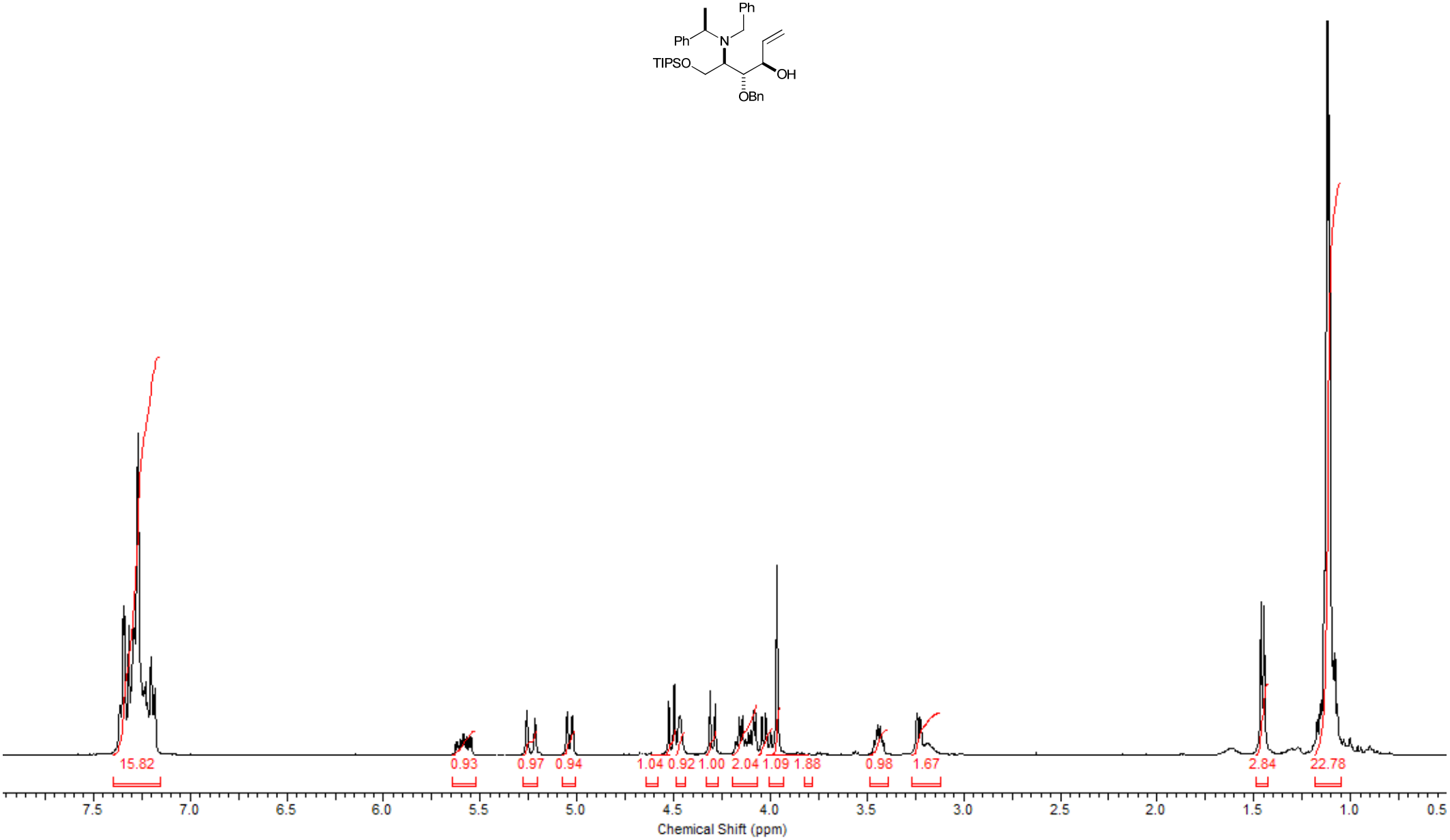
[19] Crystallographic data (excluding structure factors) for compounds **13**, **19**·$CHCl_3$ and **25** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 926152–926154, respectively. Copies of these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

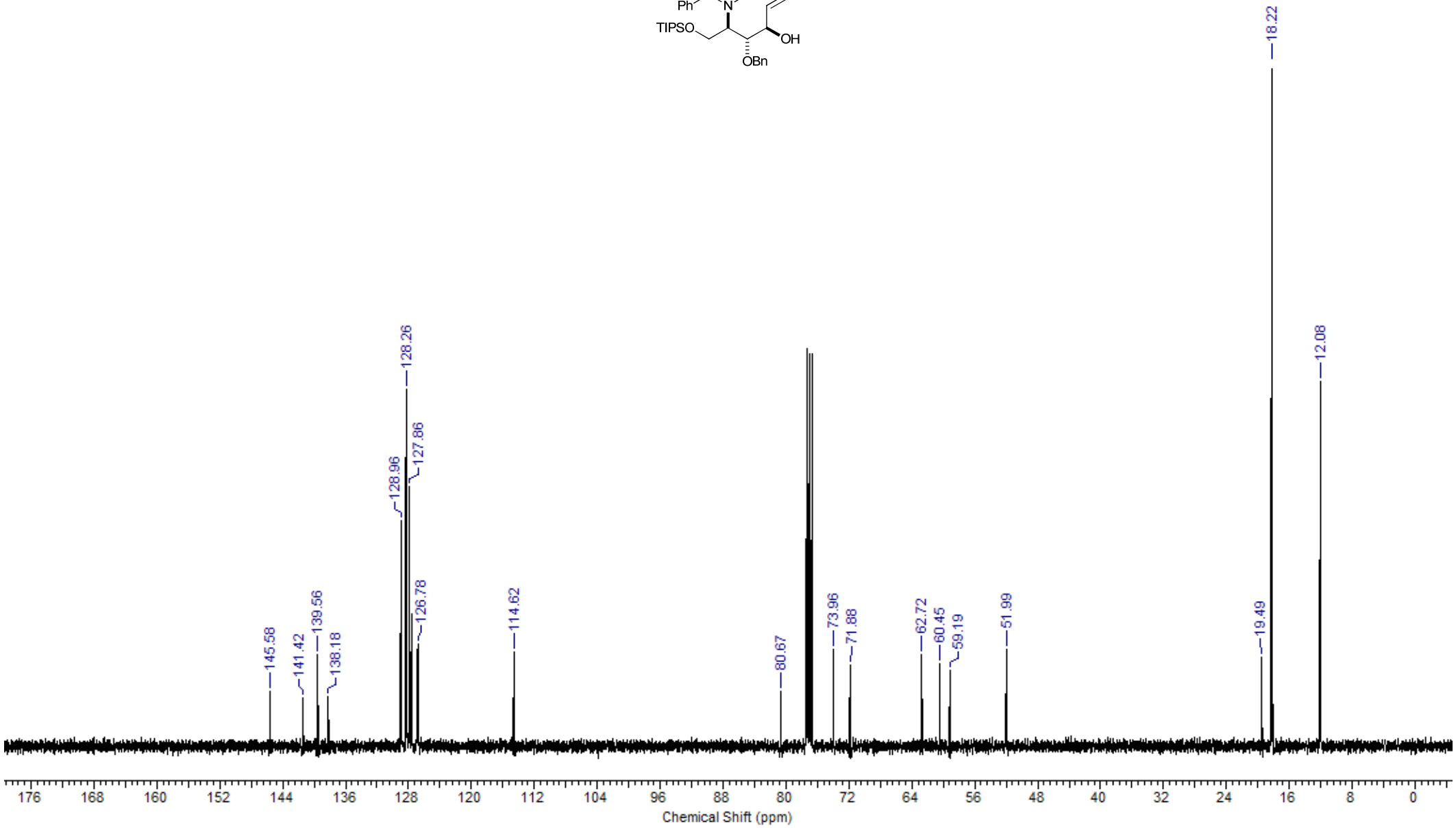
[20] (a) Flack, H. D. *Acta. Crystallogr., Sect. A* **1983**, *39*, 876. (b) Flack, H. D.; Bernardelli, G. *Acta. Crystallogr., Sect. A* **1999**, *55*, 908. (c) Flack, H. D.; Bernardinelli, G. *J. Appl. Crystallogr.* **2000**, *33*, 1143.

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

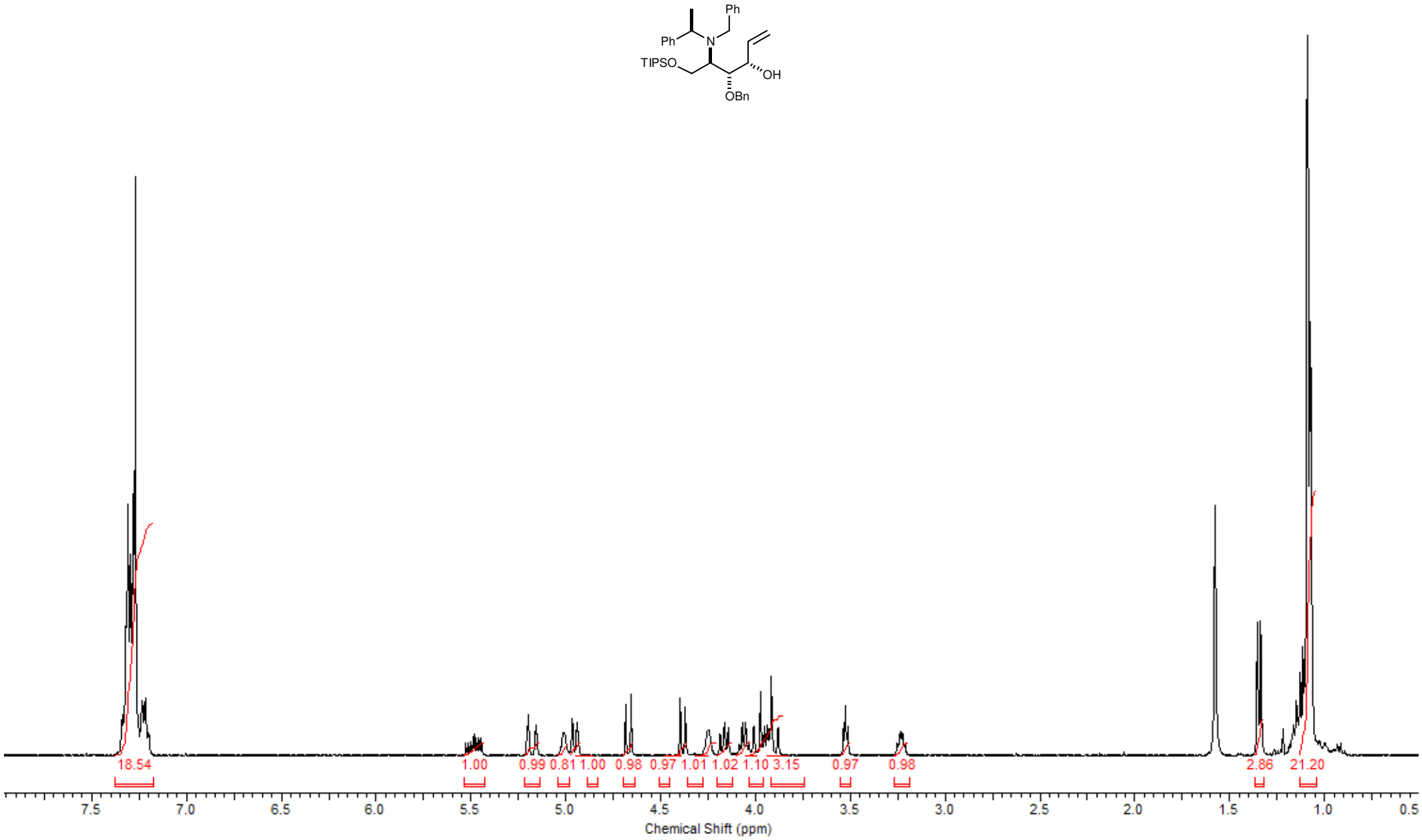
(*R*,*R*,*R*,*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-6-(triisopropylsilyloxy)hex-1-en-3-ol 11 (400 MHz ^{1}H, $CDCl_3$)



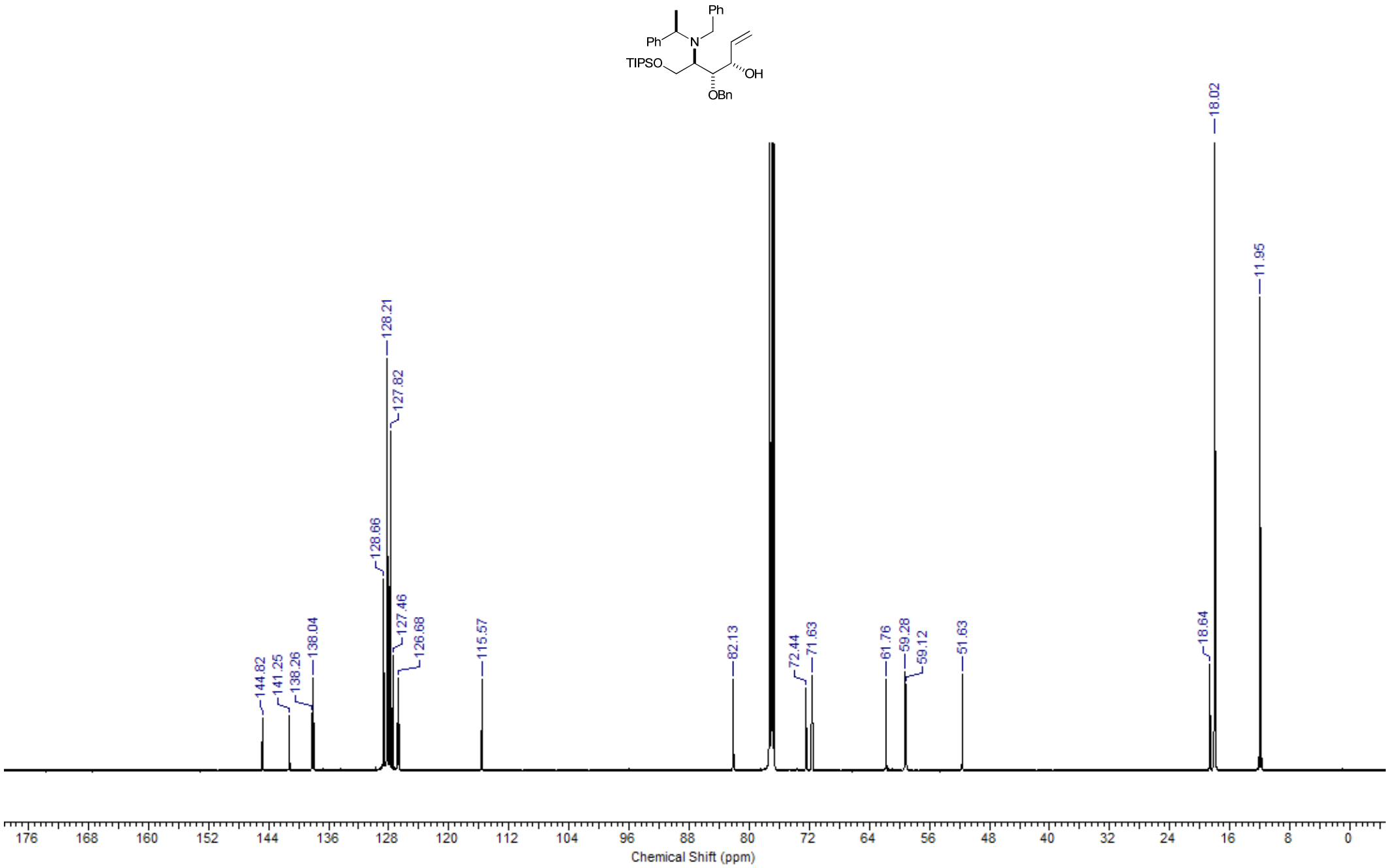
(*R*,*R*,*R*,*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-6-(triisopropylsilyloxy)hex-1-en-3-ol 11 (100 MHz ^{13}C, $CDCl_3$)



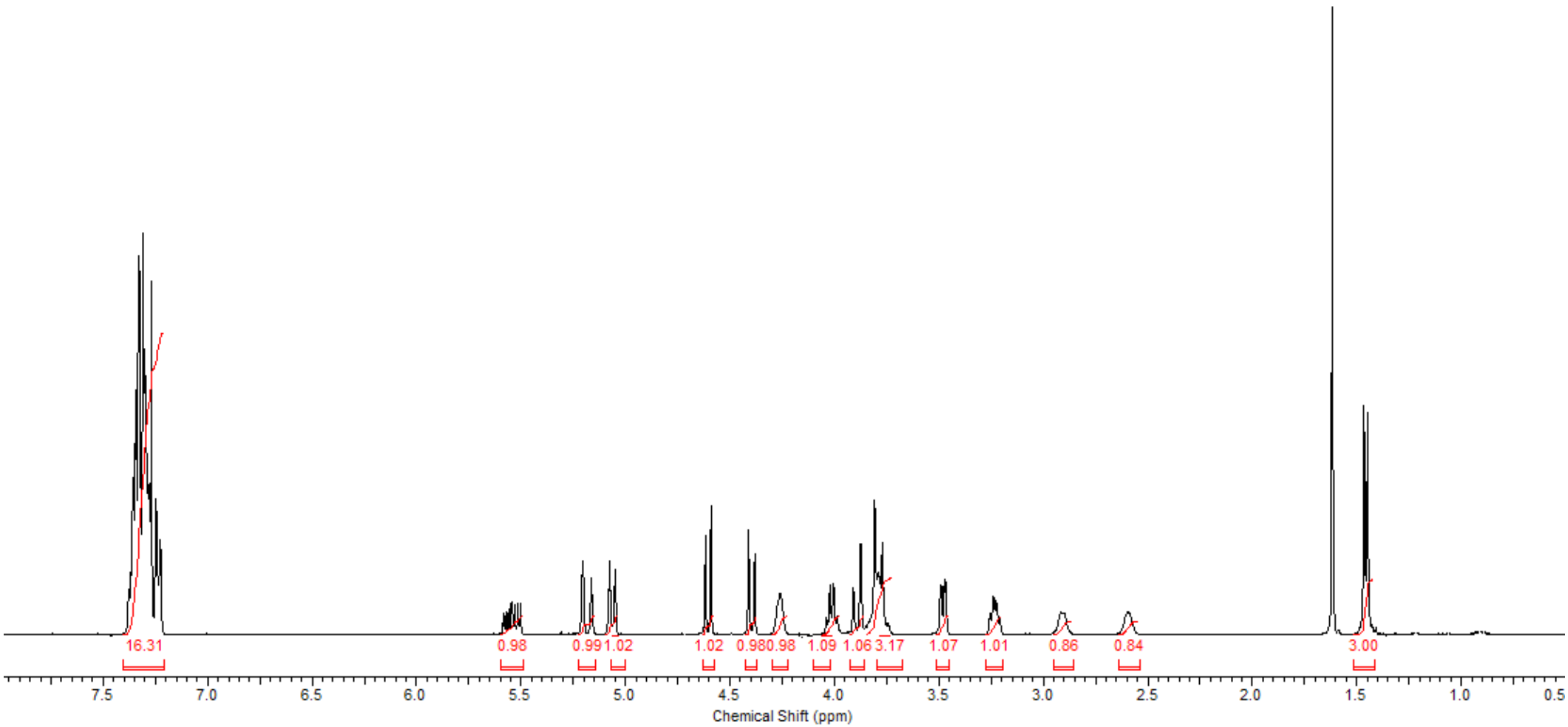
(3*S*,4*R*,5*R*,α*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-6-(triisopropylsilyloxy)hex-1-en-3-ol 12 (400 MHz ^{1}H, $CDCl_3$)



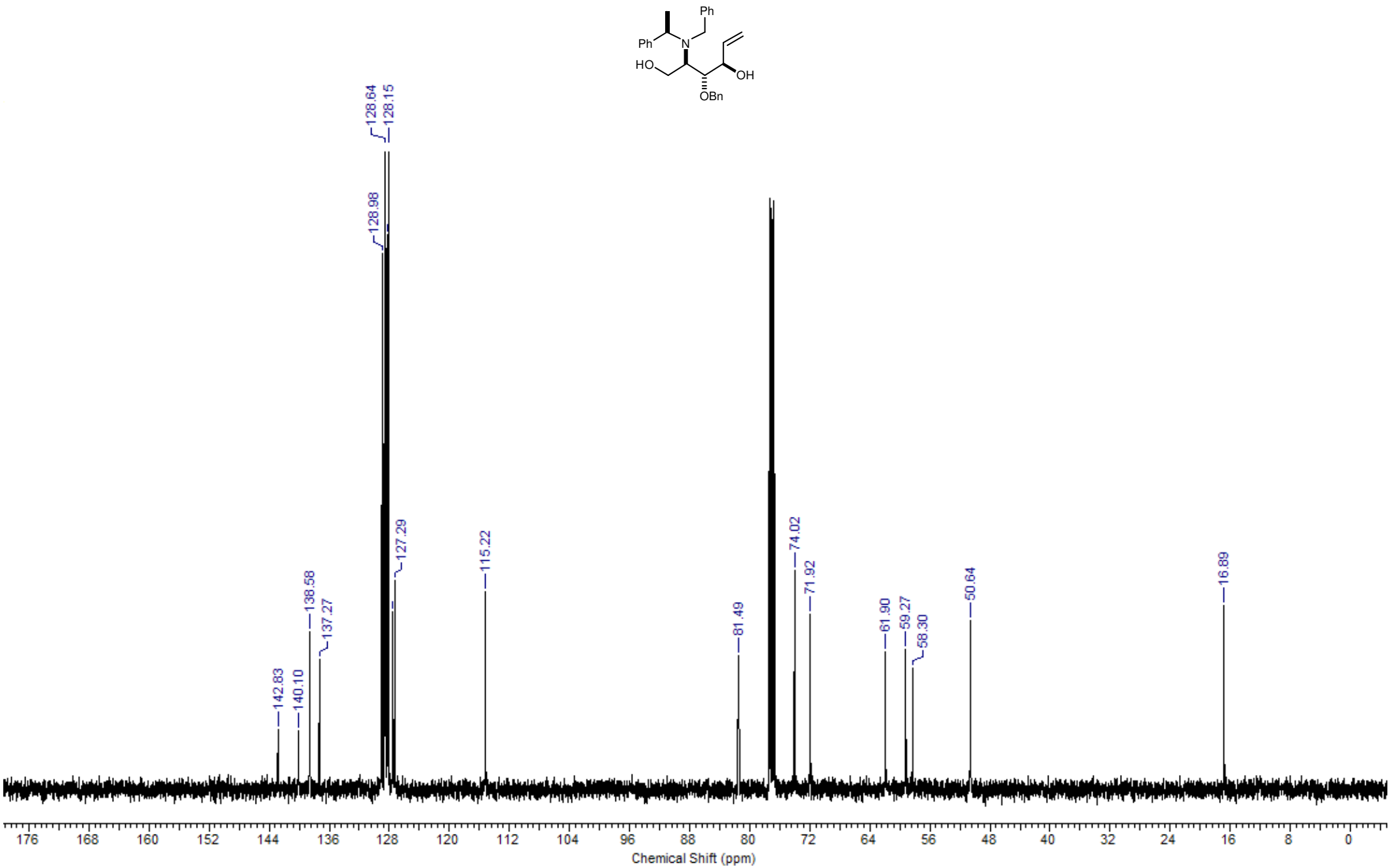
(3*S*,4*R*,5*R*,α*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-6-(triisopropylsilyloxy)hex-1-en-3-ol 12 (100 MHz ^{13}C, $CDCl_3$)



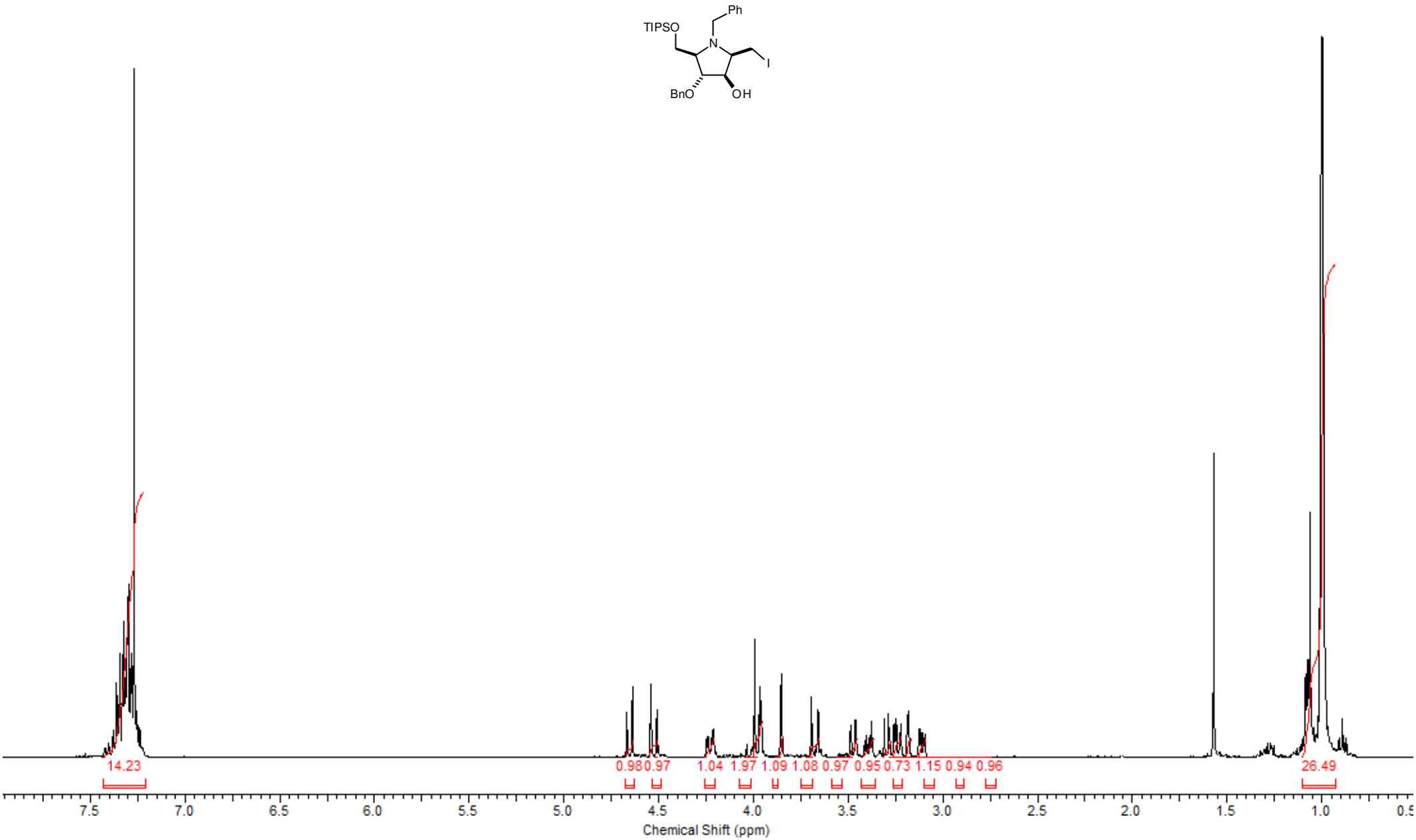
(*R*,*R*,*R*,*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]hex-1-en-3,6-diol 13 (400 MHz ^{1}H, $CDCl_3$)



(*R*,*R*,*R*,*R*)-4-Benzyloxy-5-[*N*-benzyl-*N*-(α-methylbenzyl)amino]hex-1-en-3,6-diol 13 (100 MHz ^{13}C, $CDCl_3$)



(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4-hydroxy-5-(iodomethyl)pyrrolidine 14 (400 MHz ^{1}H, $CDCl_3$)



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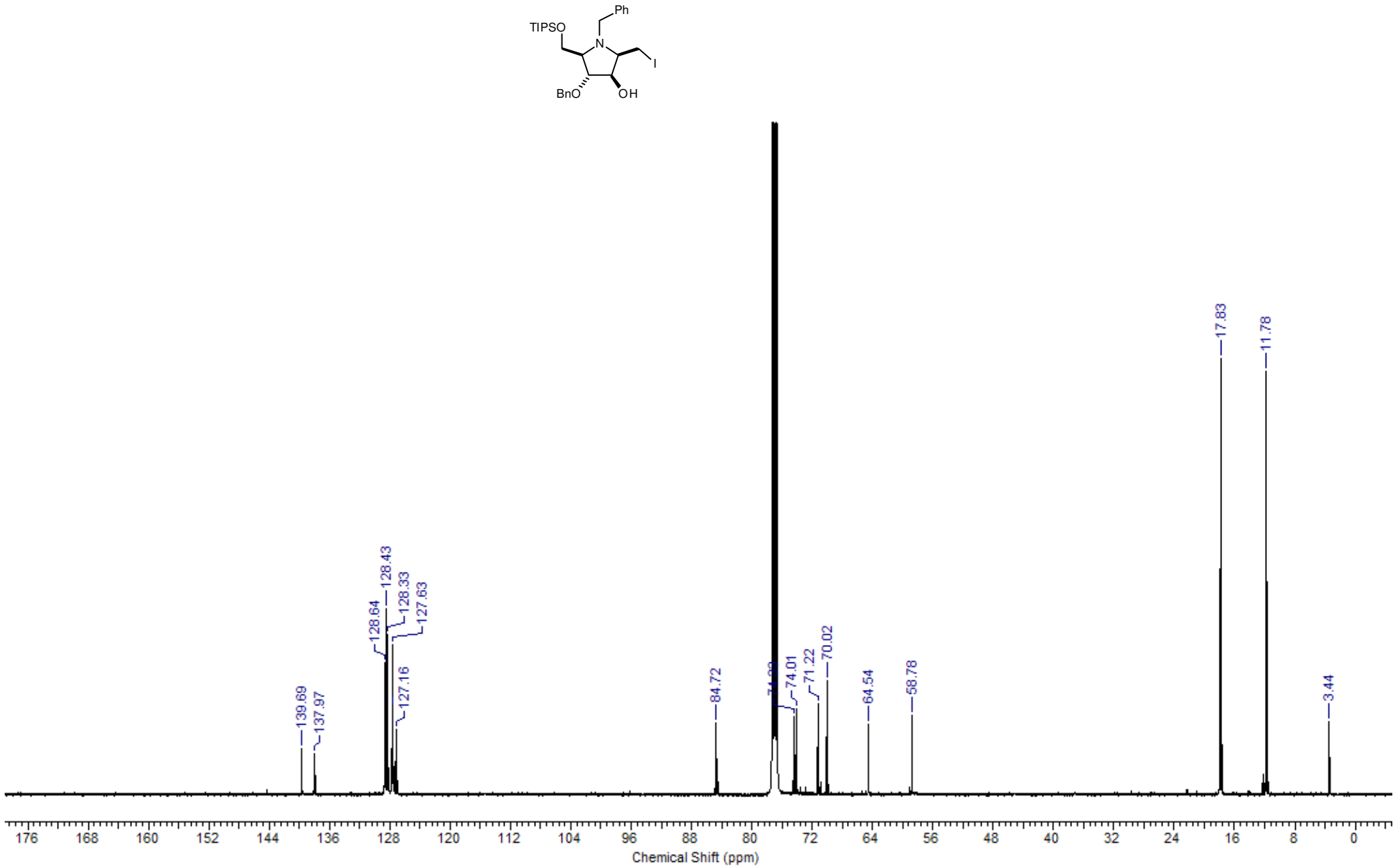
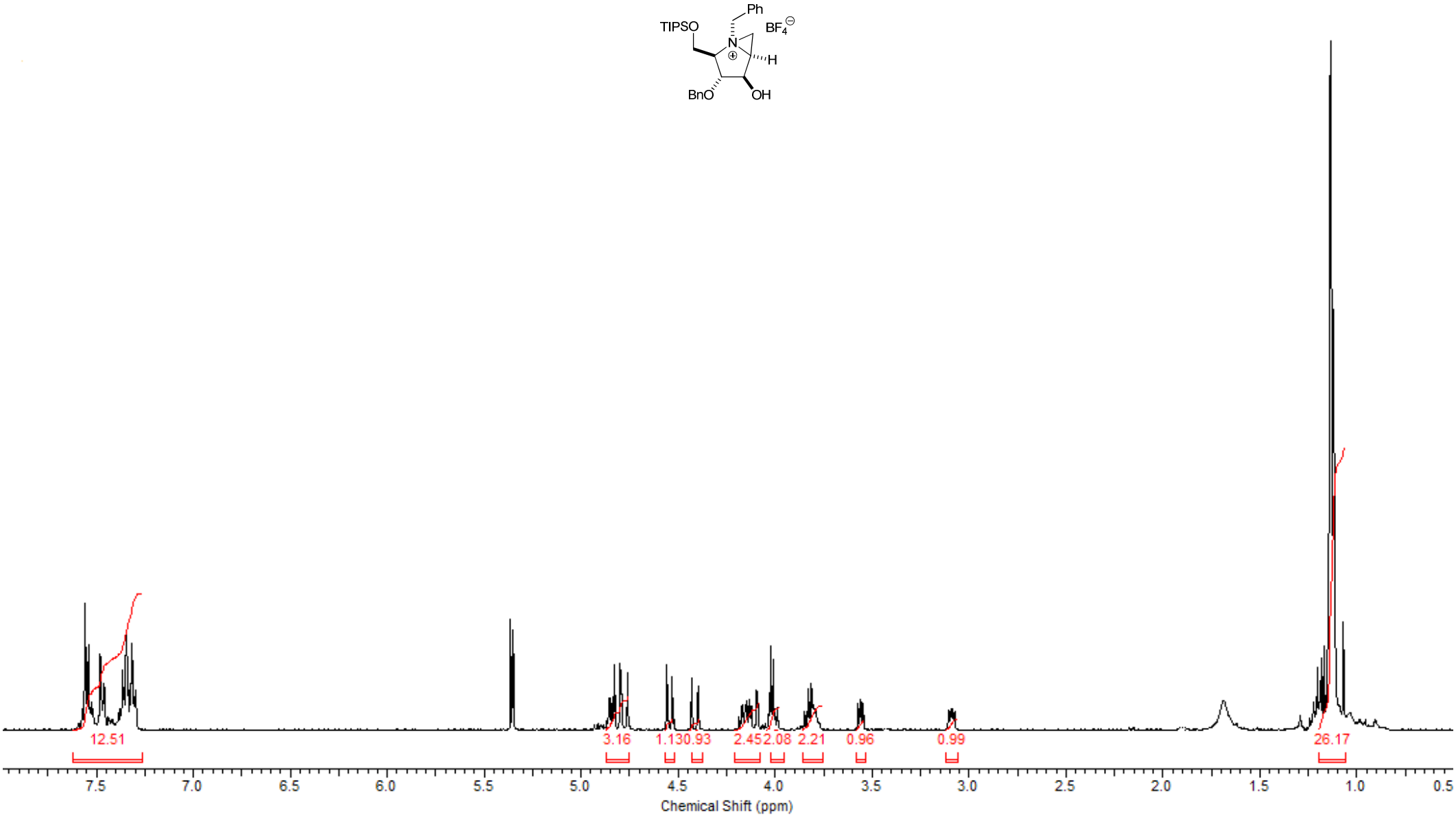
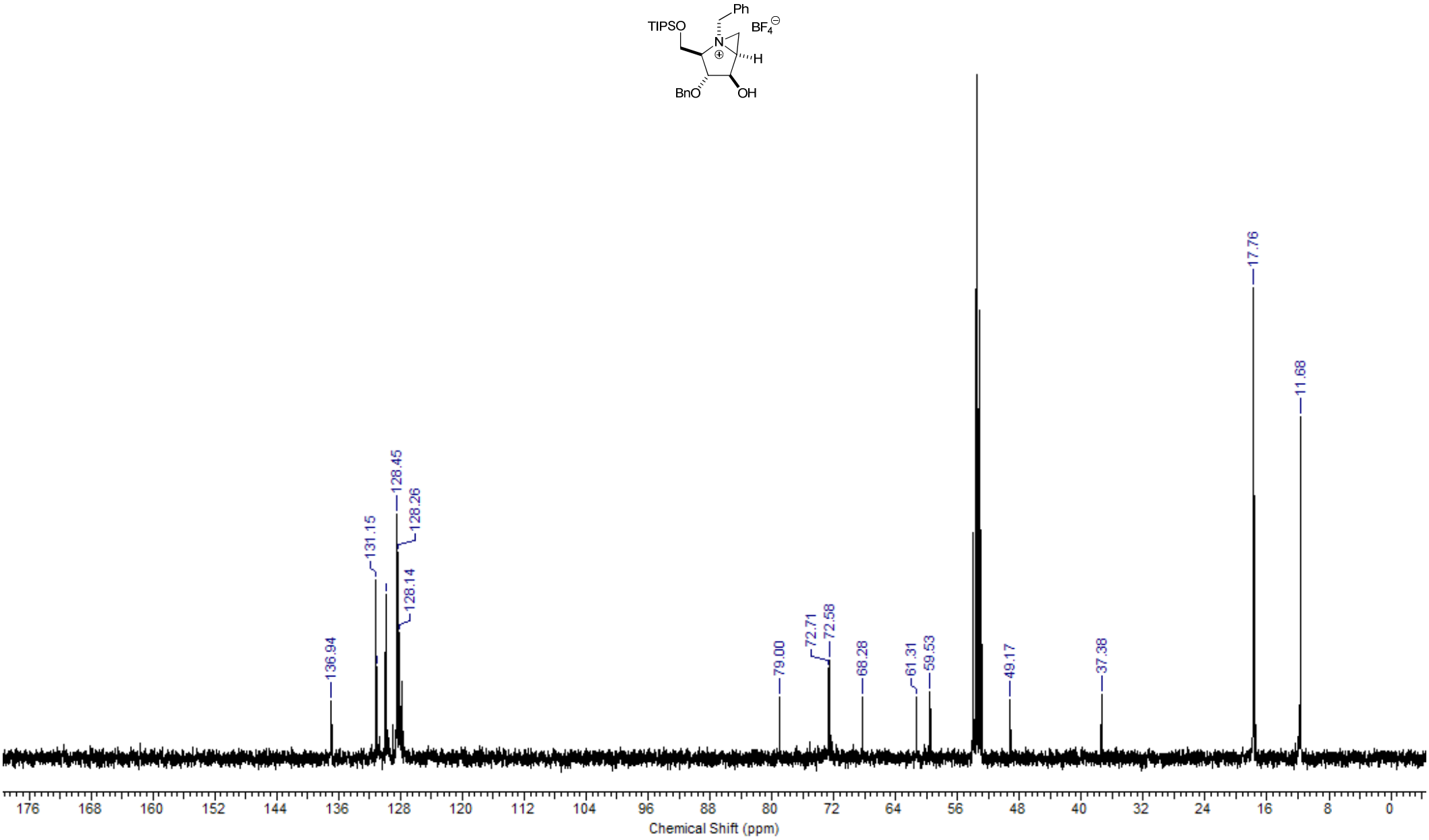


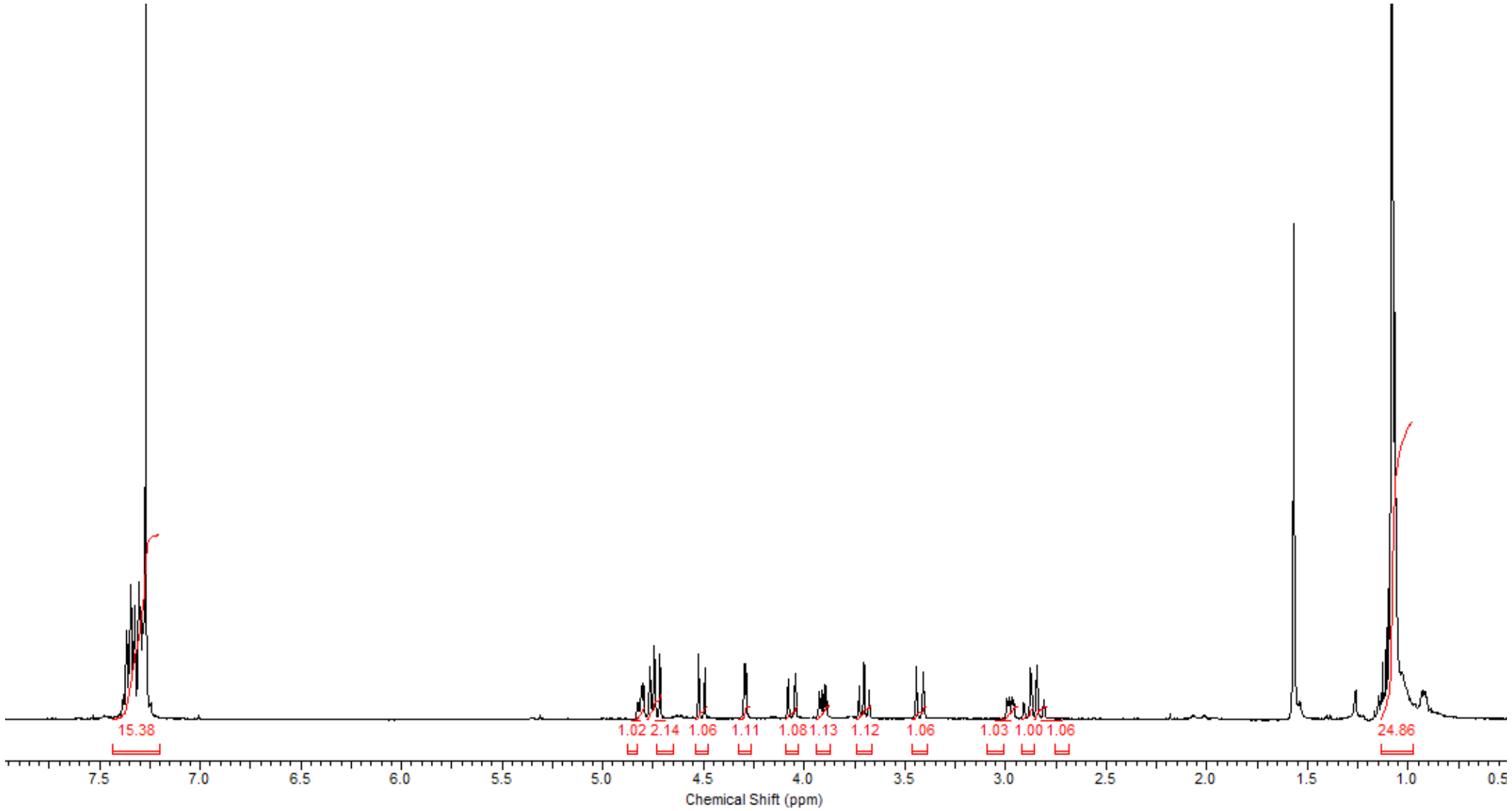
(1*S*,2*R*,3*R*,4*R*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4-hydroxy-1-azabicyclo[3.1.0]hexanium tetrafluoroborate 15
(400 MHz ^{1}H, CD_2Cl_2)



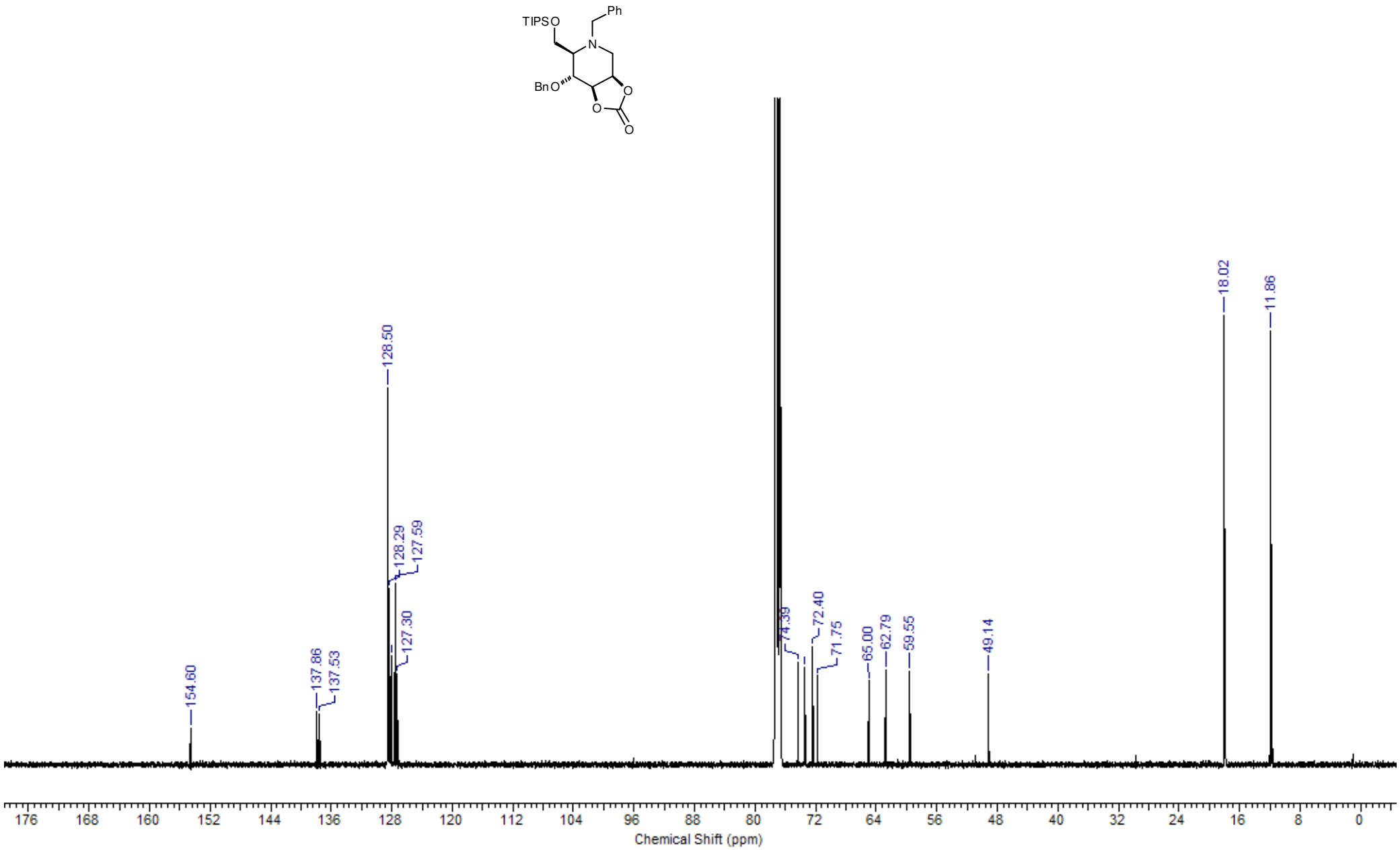
(1*S*,2*R*,3*R*,4*R*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4-hydroxy-1-azabicyclo[3.1.0]hexanium tetrafluoroborate 15
(100 MHz ^{13}C, CD_2Cl_2)



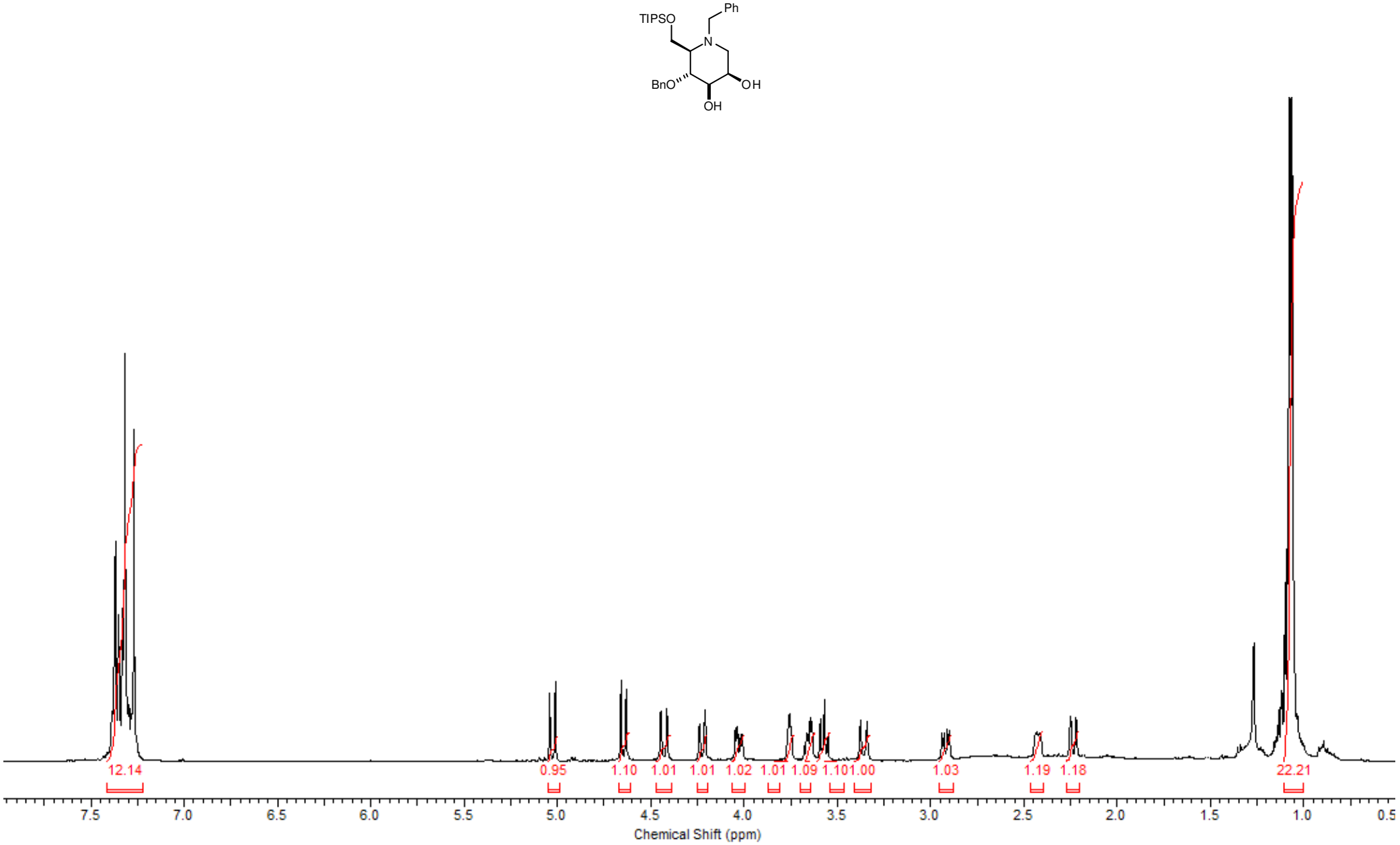
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxy-4,5-*O*-carbonylpiperidine 16 (400 MHz ^{1}H, $CDCl_3$)



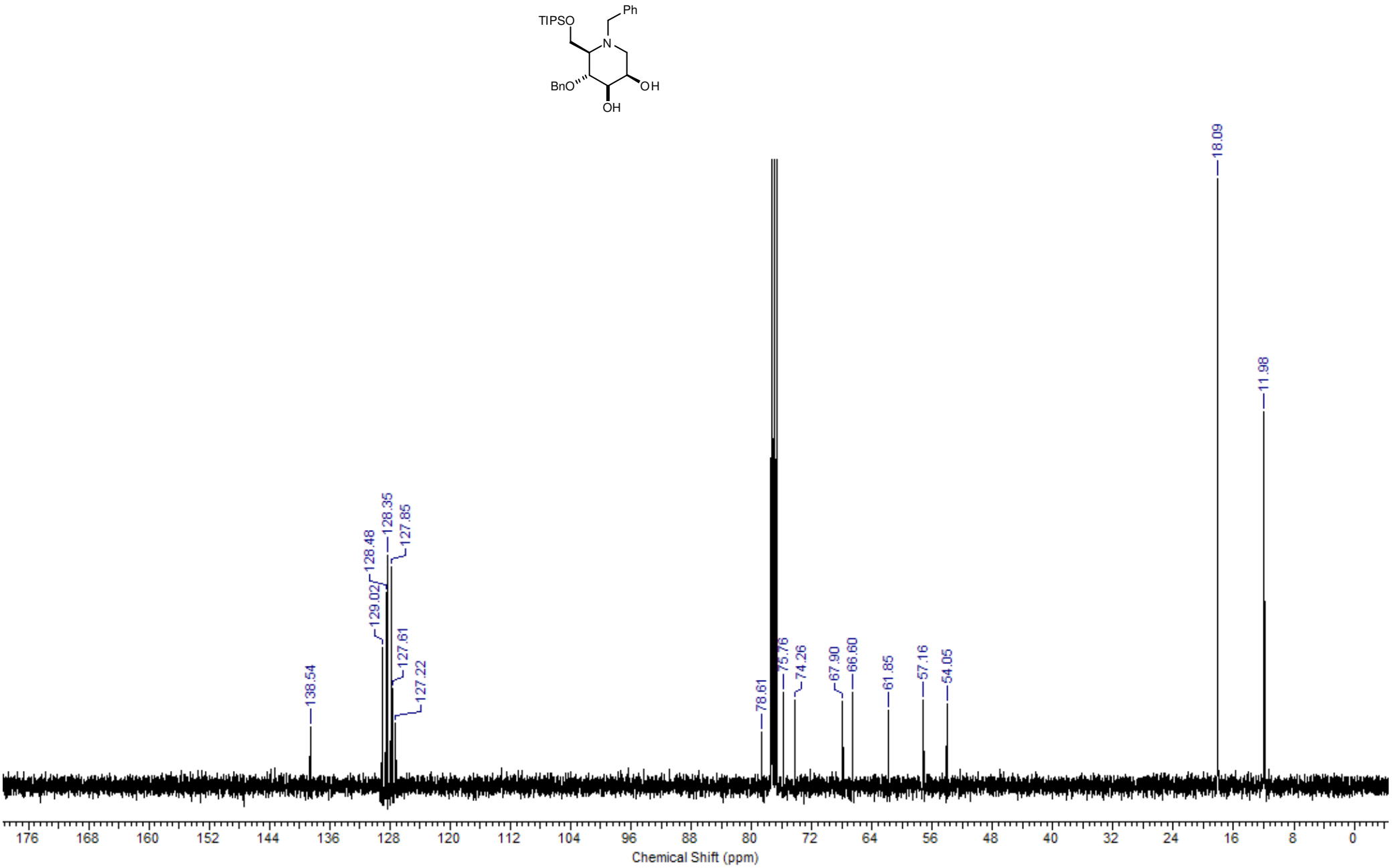
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxy-4,5-*O*-carbonylpiperidine 16 (100 MHz ^{13}C, $CDCl_3$)



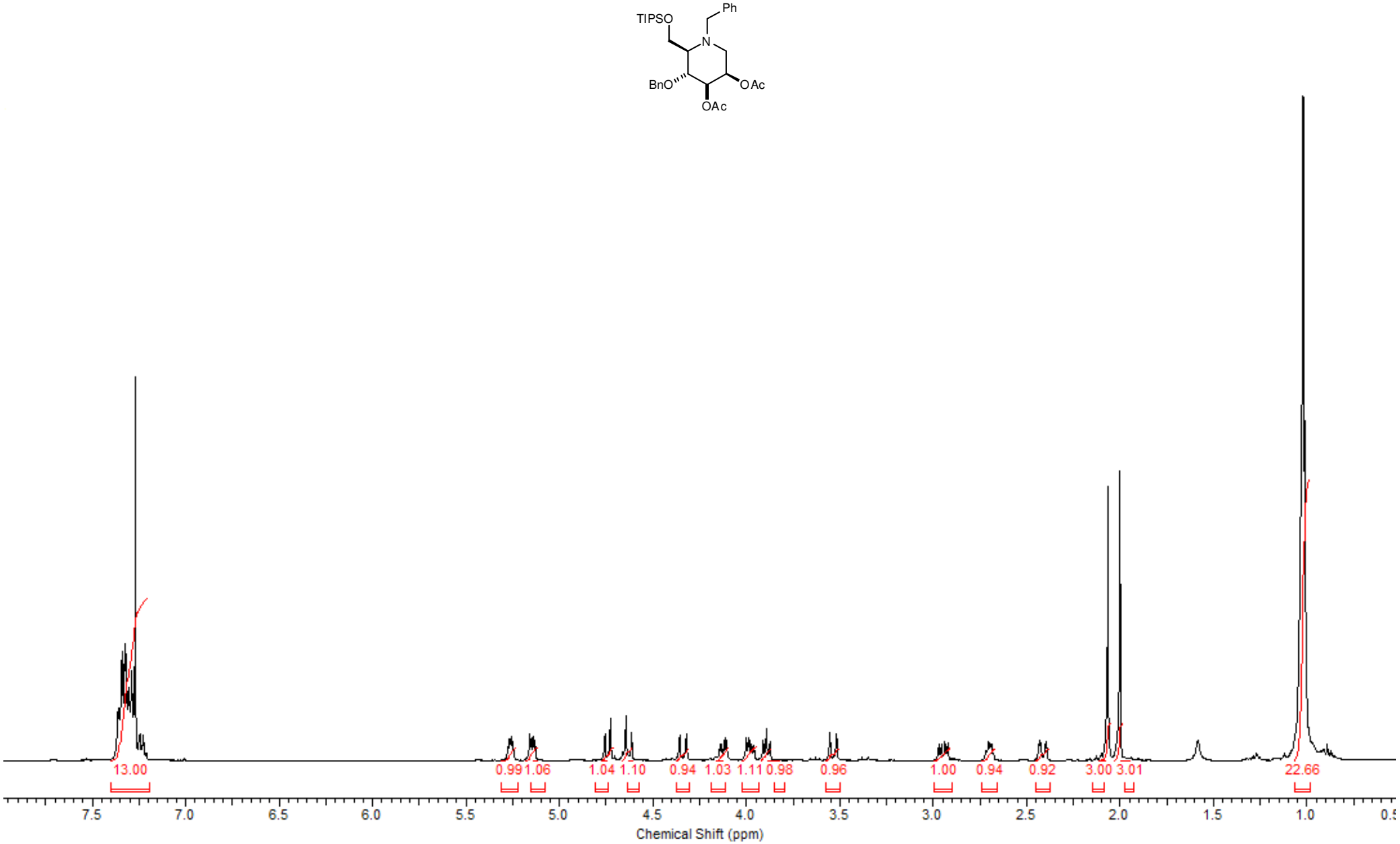
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxypiperidine 17 (400 MHz ^{1}H, $CDCl_3$)



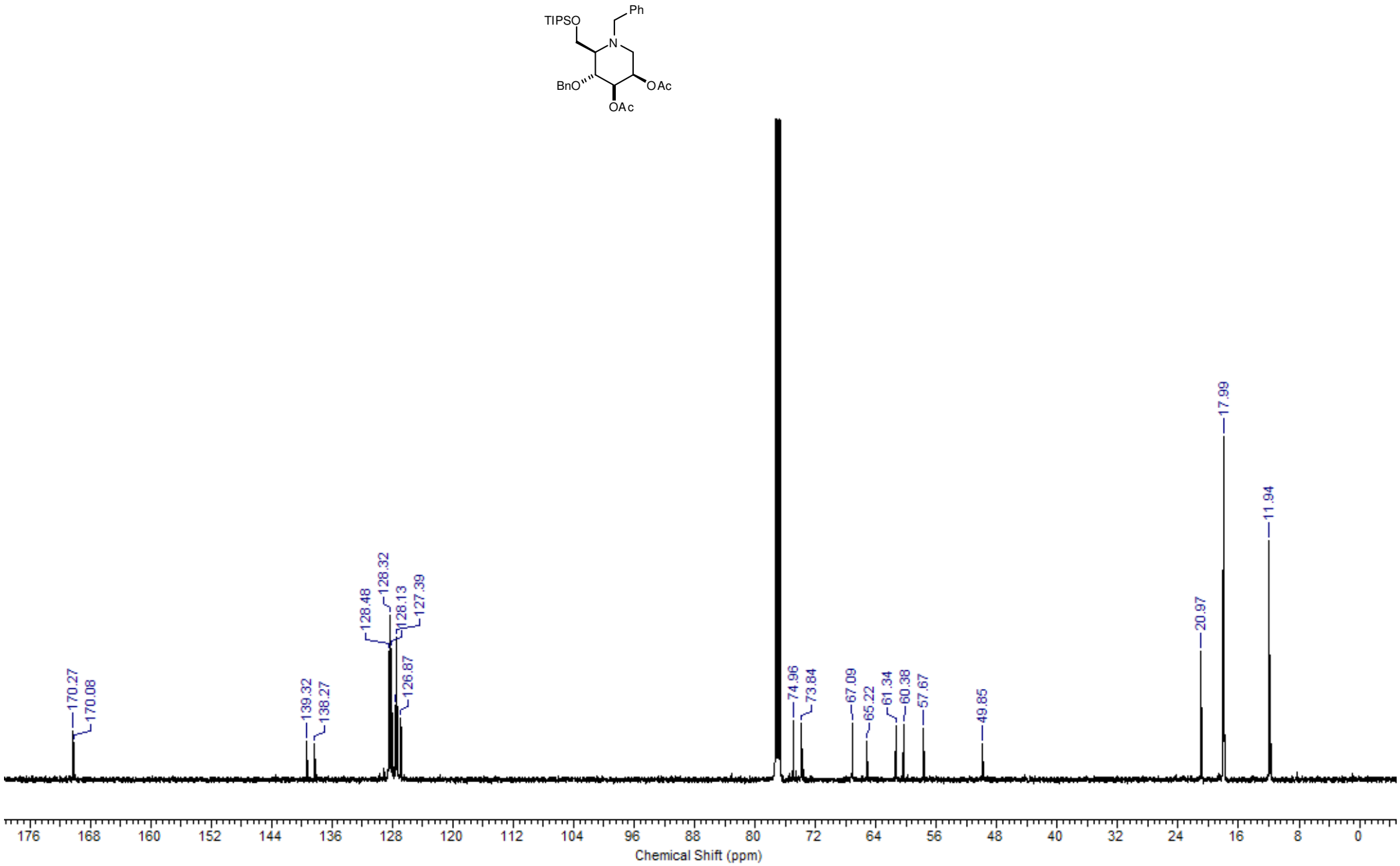
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxypiperidine 17 (100 MHz ^{13}C, $CDCl_3$)



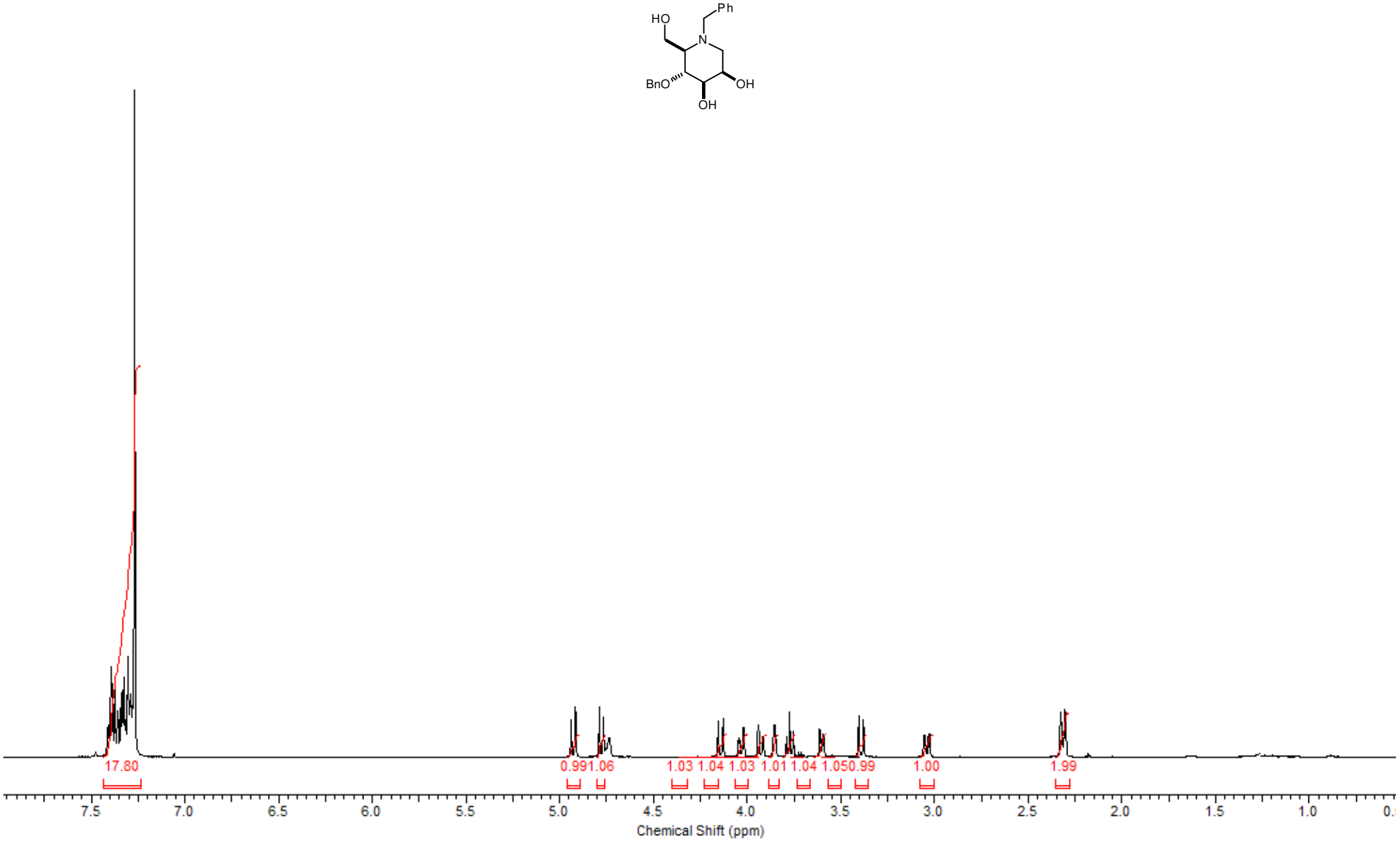
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-diacetoxypiperidine 18 (400 MHz ^{1}H, $CDCl_3$)



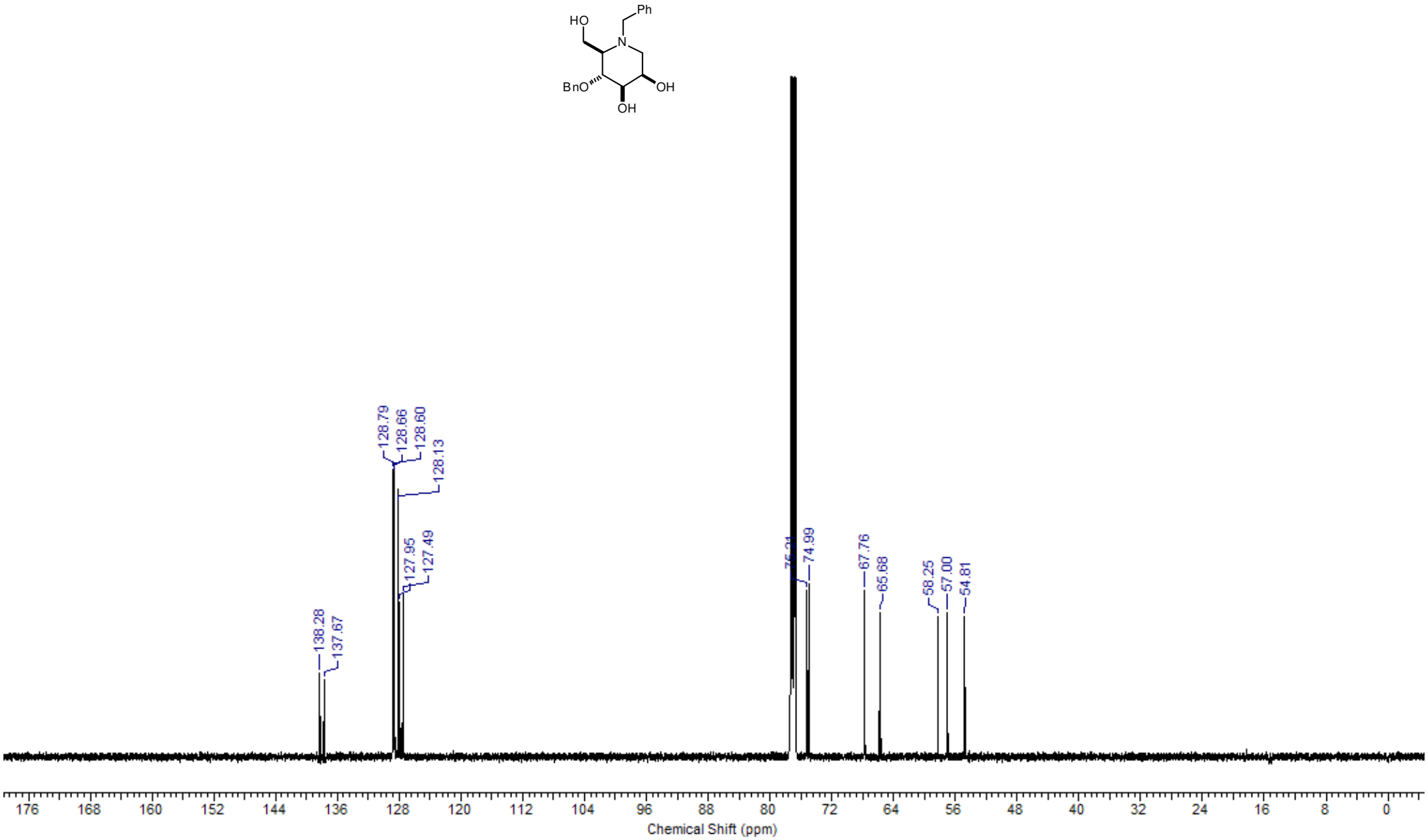
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-diacetoxypiperidine 18 (100 MHz ^{13}C, $CDCl_3$)



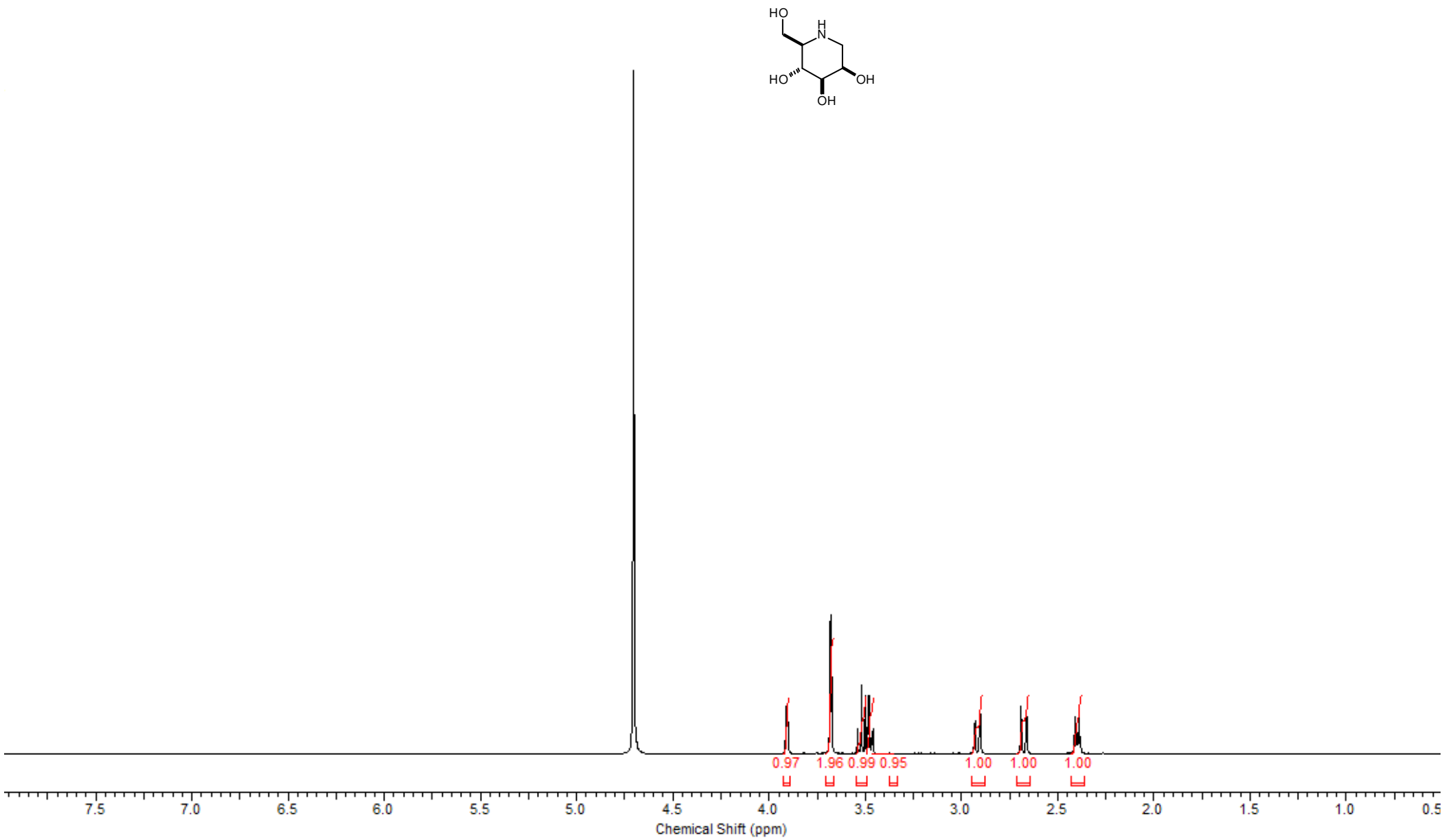
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-(hydroxymethyl)-3-benzyloxy-4,5-dihydroxypiperidine 19 (400 MHz ^{1}H, $CDCl_3$)



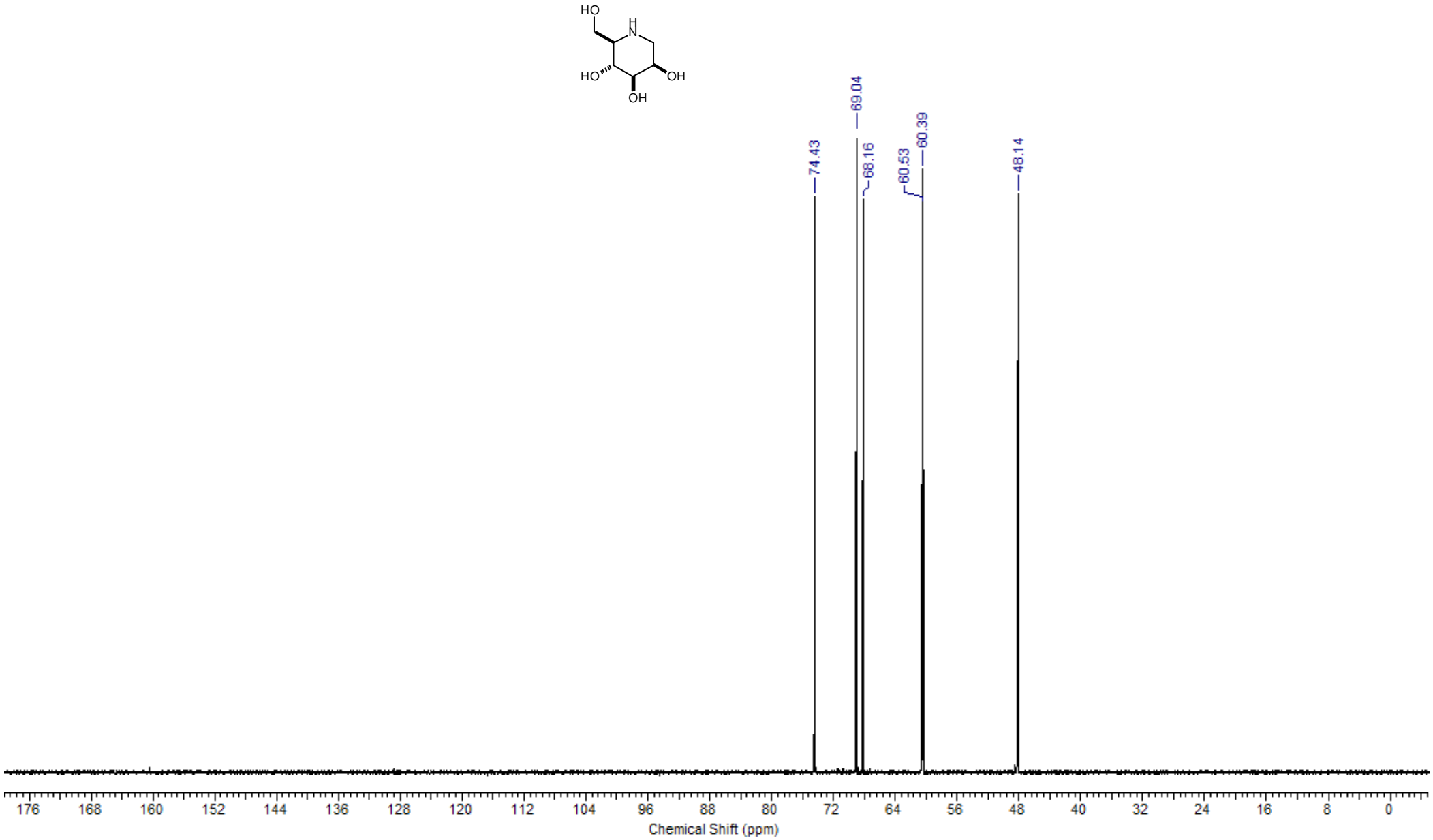
(*R*,*R*,*R*,*R*)-*N*(1)-Benzyl-2-(hydroxymethyl)-3-benzyloxy-4,5-dihydroxypiperidine 19 (100 MHz ^{13}C, $CDCl_3$)



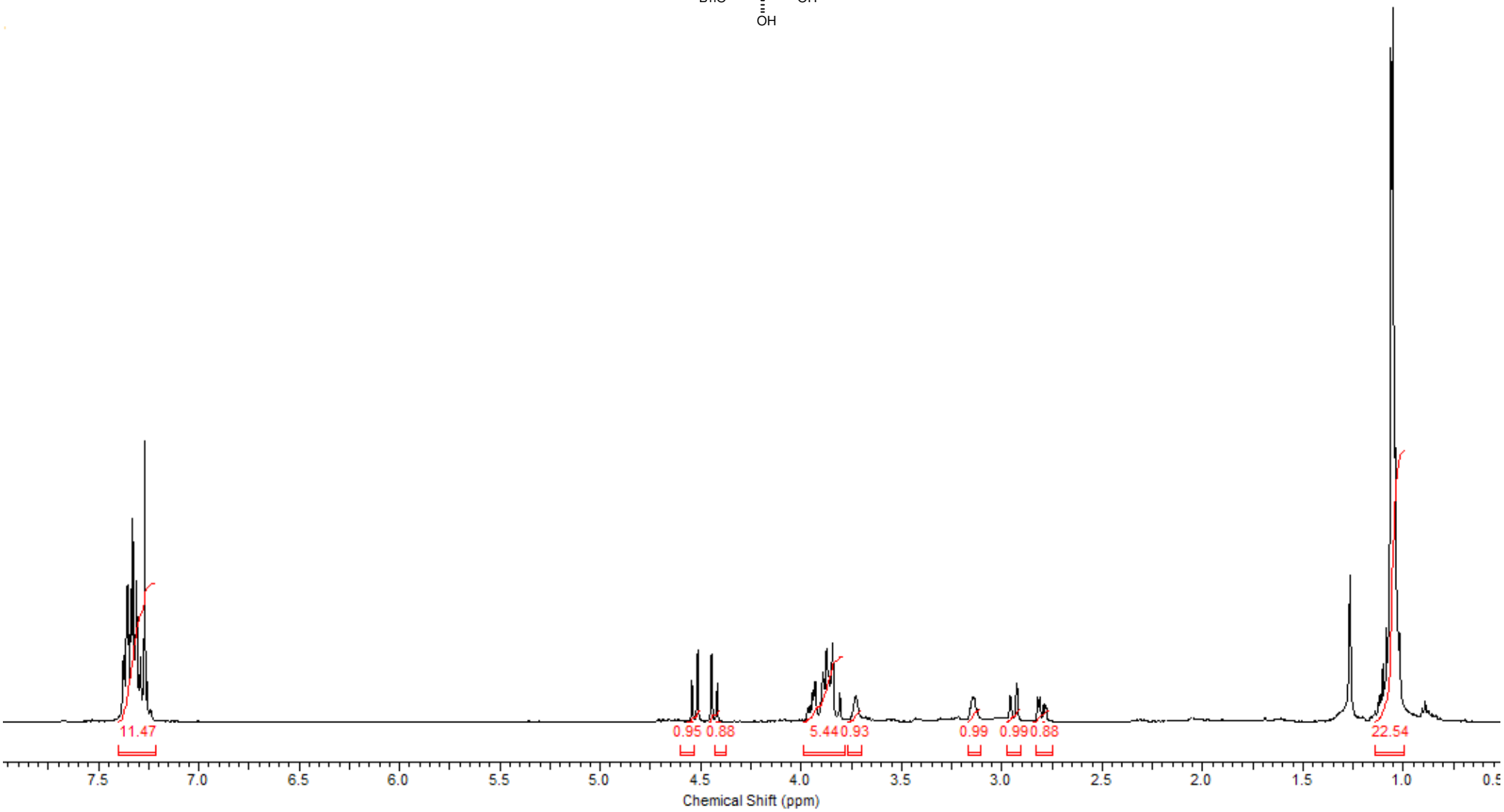
(*R*,*R*,*R*,*R*)-1,5-Dideoxy-1,5-imino-D-mannose [(–)-1-deoxymannojirimycin] 21 (400 MHz ^{1}H, D_2O)



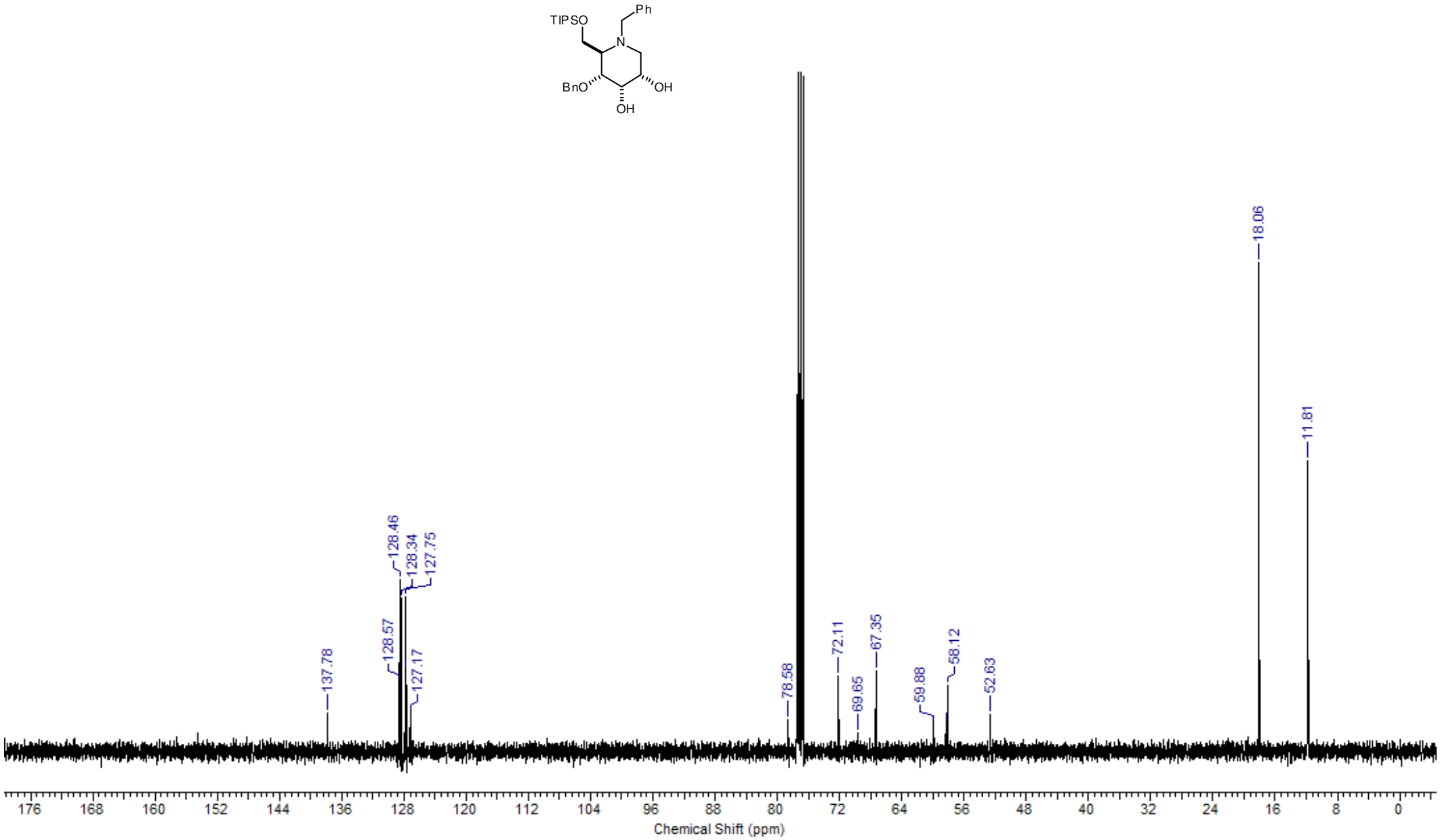
(*R*,*R*,*R*,*R*)-1,5-Dideoxy-1,5-imino-D-mannose [(–)-1-deoxymannojirimycin] 21 (100 MHz ^{13}C, D_2O)



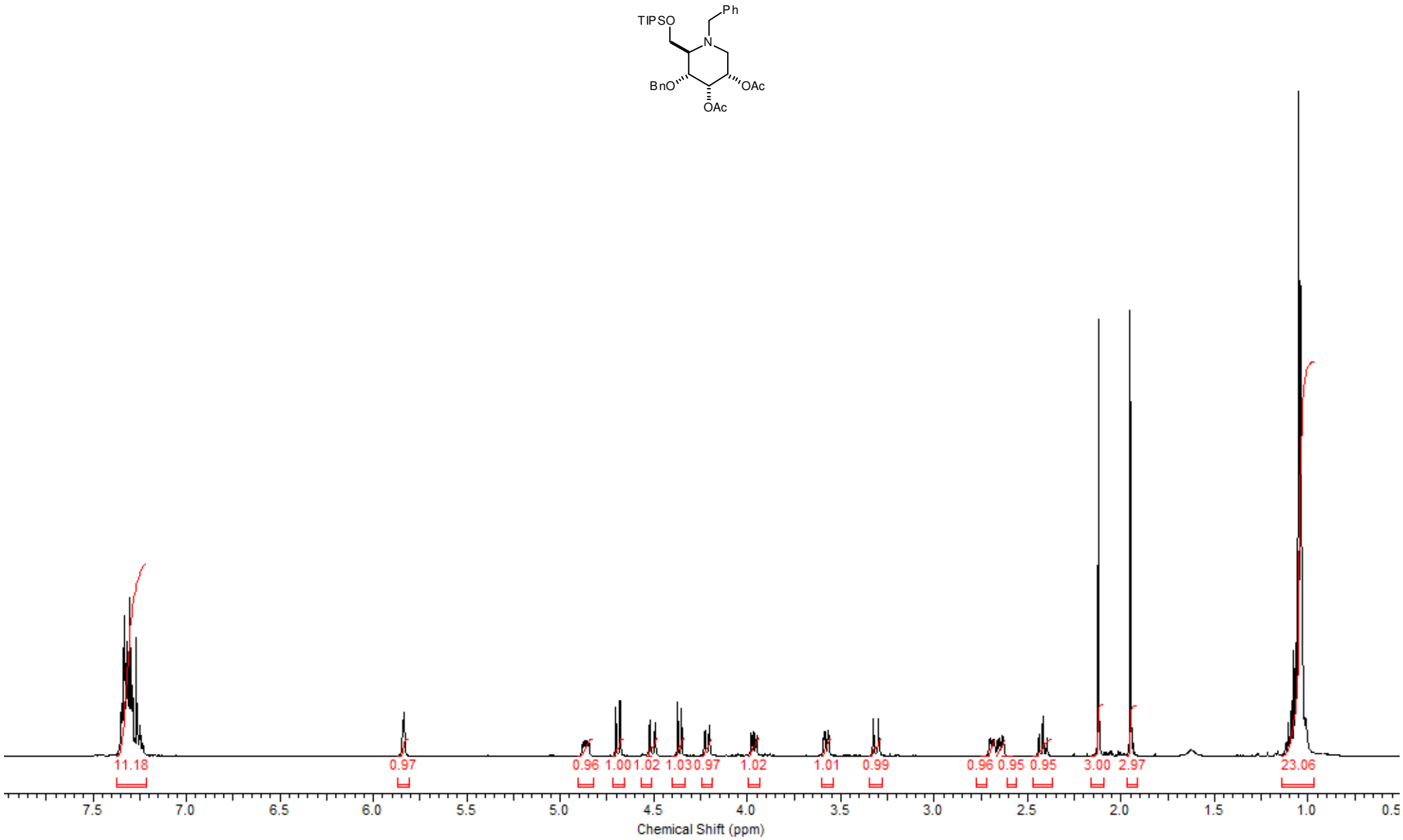
(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxypiperidine 22 (400 MHz ^{1}H, $CDCl_3$)



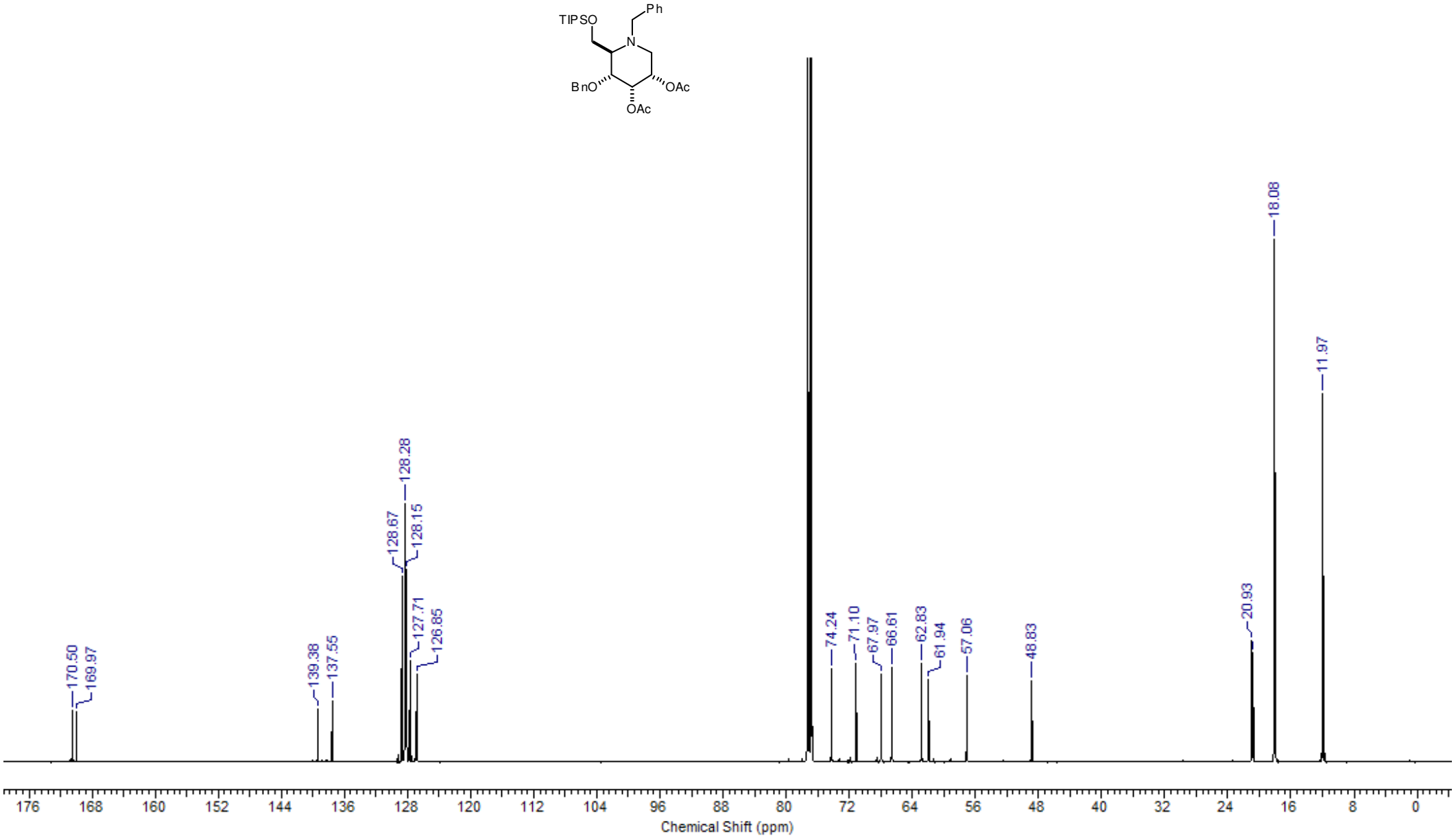
(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-dihydroxypiperidine 22 (100 MHz ^{13}C, $CDCl_3$)



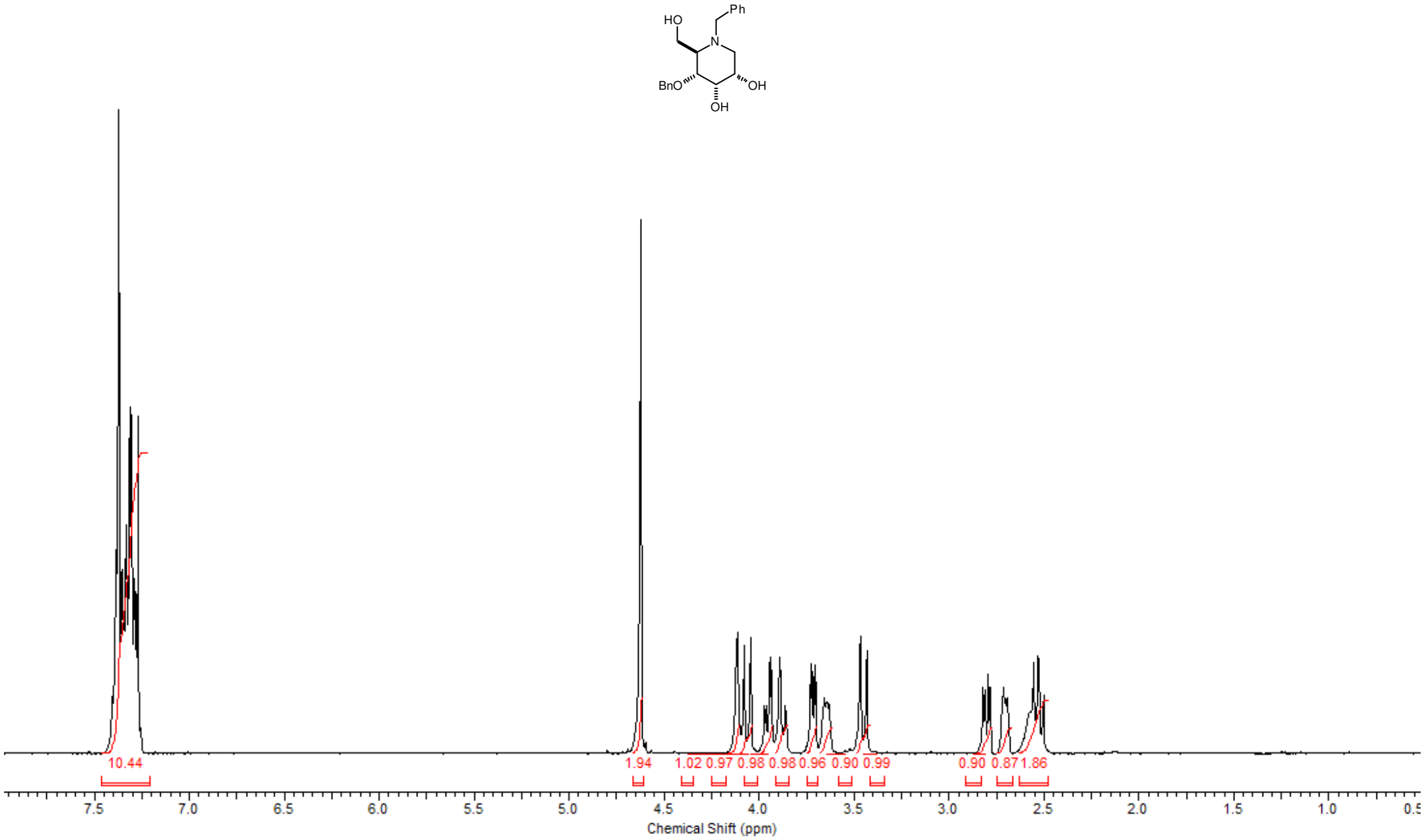
(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-diacetoxypiperidine 24 (400 MHz ^{1}H, $CDCl_3$)



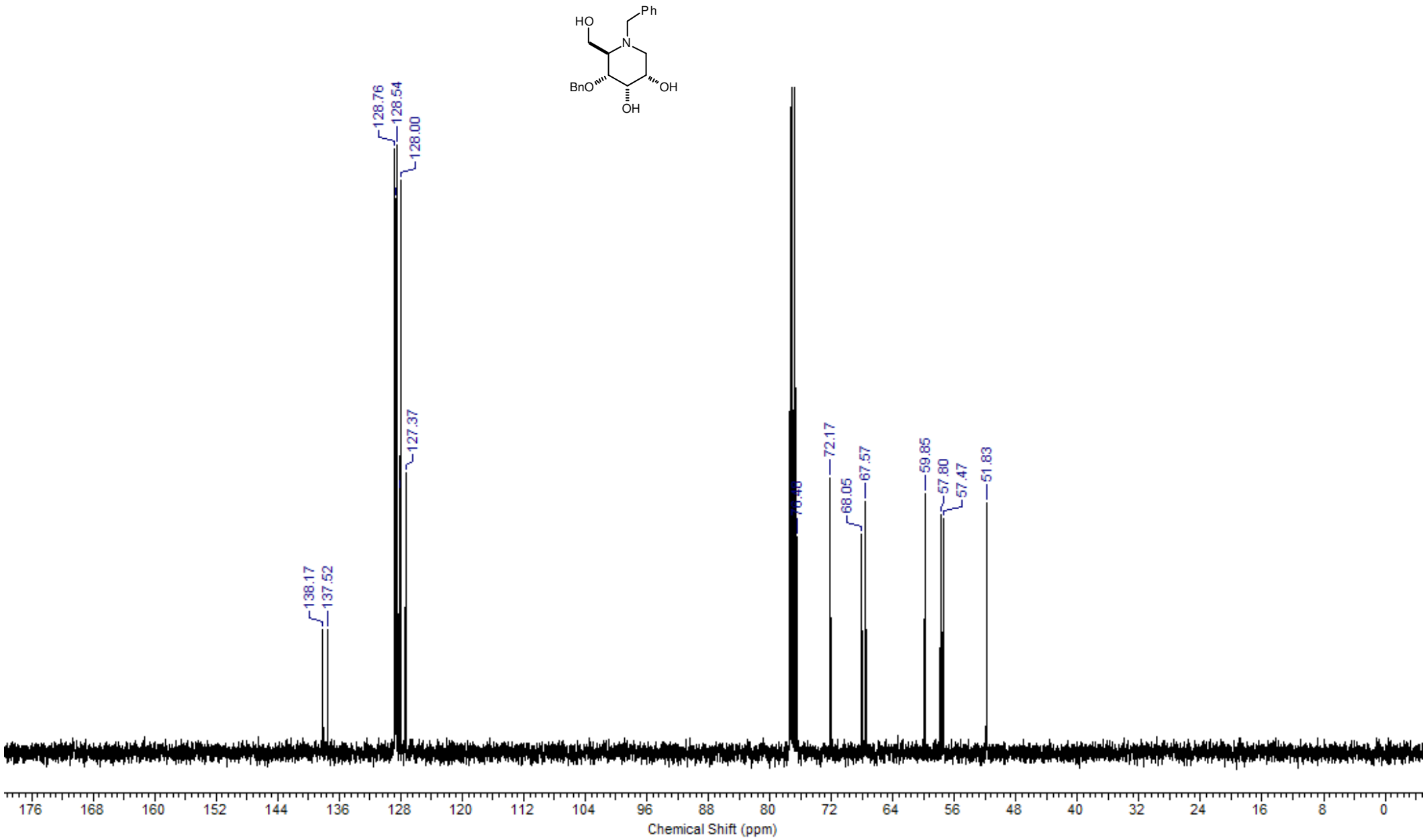
(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-[(triisopropylsilyloxy)methyl]-3-benzyloxy-4,5-diacetoxypiperidine 24 (100 MHz ^{13}C, $CDCl_3$)



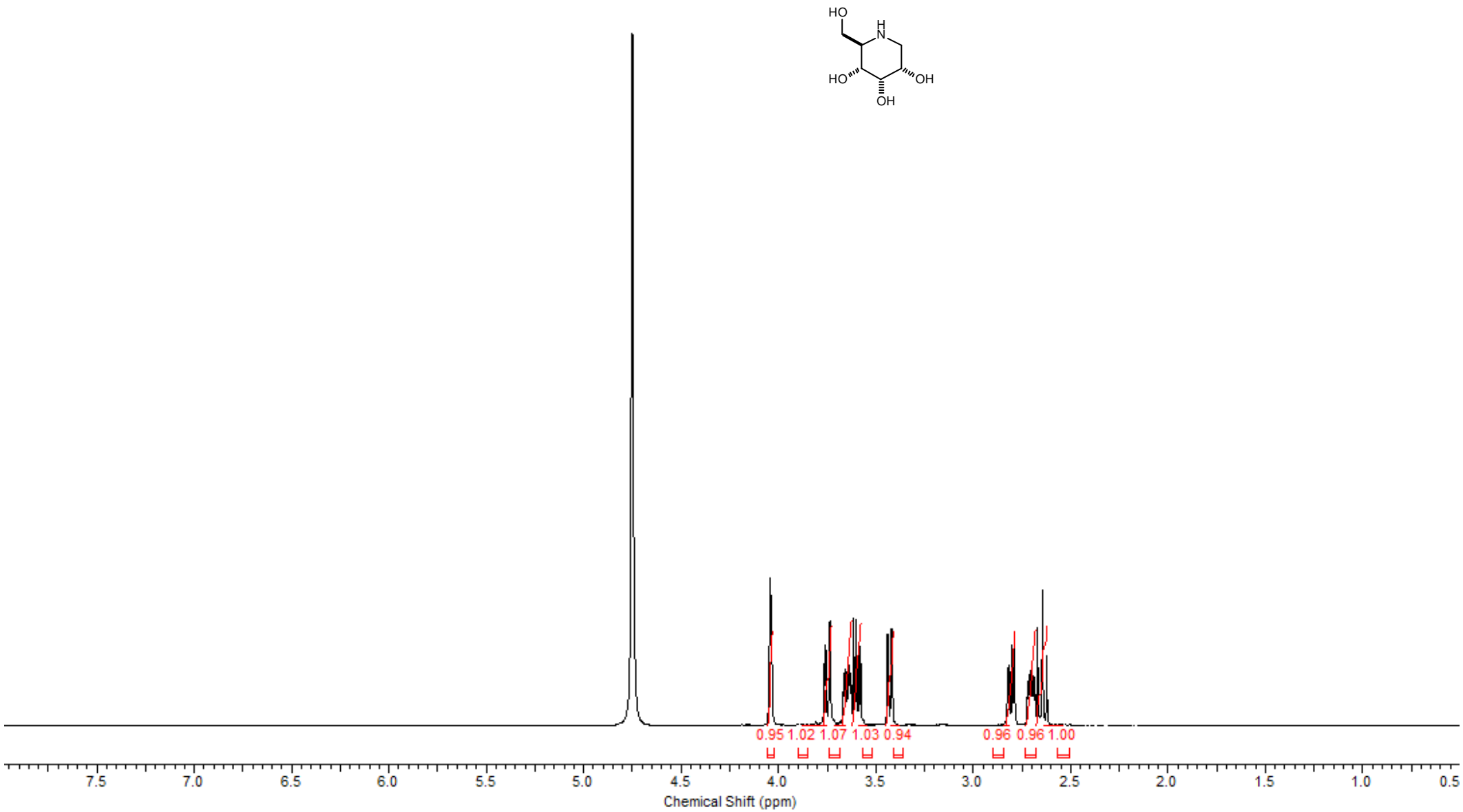
(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-(hydroxymethyl)-3-benzyloxy-4,5-dihydroxypiperidine 25 (400 MHz ^{1}H, $CDCl_3$)



(2*R*,3*R*,4*S*,5*S*)-*N*(1)-Benzyl-2-(hydroxymethyl)-3-benzyloxy-4,5-dihydroxypiperidine 25 (100 MHz ^{13}C, $CDCl_3$)



(2*S*,3*S*,4*R*,5*R*)-1,5-Dideoxy-1,5-imino-D-allose [(+)-1-deoxyallonojirimycin] 26 (400 MHz ^{1}H, D_2O)



(2*S*,3*S*,4*R*,5*R*)-1,5-Dideoxy-1,5-imino-D-allose [(+)-1-deoxyallonojirimycin] 26 (100 MHz ^{13}C, D_2O)