Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for

An efficient asymmetric synthesis of (–)-lupinine

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1. Experimental

1.1. General Experimental

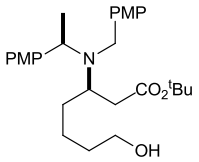
All reactions involving organometallic or other moisture sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs 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.

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

1.2. Experimental Data

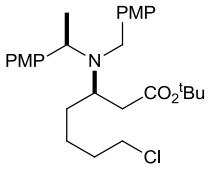
tert-Butyl (*R,R*)-3-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]-7-hydroxyheptanoate 18



BuLi (2.2 M in hexanes, 0.60 mL, 1.3 mmol) was added dropwise to a stirred solution of (*R*)-*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amine[2] (325 mg, 1.30 mmol, >99:1 er) in THF (4 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **15**[3,4] (100 mg, 0.50 mmol, >99:1 dr) in THF (4 mL) at −78 °C was then added via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq NH_4Cl (0.5 mL) was added and the reaction mixture was allowed to warm to rt, then concentrated in vacuo. The residue was partitioned between Et_2O (15 mL) and H_2O (10 mL), the aqueous layer was extracted with Et_2O (2 × 10 mL), and the combined organic extracts were washed sequentially with 10% aq citric acid (10 mL), satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried and concentrated in vacuo to give **18** in >99:1 dr. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 1:1) gave **18** as a colourless oil (102 mg, 43%, >99:1 dr); $[\alpha]_D^{22}$ +30.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3433 (O−H), 2971, 2933, 2864, 2836 (C−H), 1720 (C=O); δ_H (400 MHz, $CDCl_3$) 1.23–1.70 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 1.33 (3H, d, *J* 6.9, C(α)*Me*), 1.41 (9H, s, CMe_3) 1.87 (1H, dd, *J* 14.7, 9.4, C(2)H_A), 1.95 (1H, dd, *J* 14.7, 3.5, C(2)H_B), 3.27–3.34 (1H, m, C(3)*H*), 3.40 (1H, d, *J* 14.8, NC$H_A$$H_B$Ar), 3.63 (2H, t, *J* 6.3, C(7)H_2), 3.70 (1H, d, *J* 14.8, NCH$_A$$H_B$Ar), 3.75–3.80 (1H, q, *J* 6.9, C(α)*H*), 3.80 (3H, s, O*Me*), 3.82 (3H, s, O*Me*), 6.85 (2H, d, *J*, 8.6, C(3')*H*, C(5')*H*), 6.89 (2H, d, *J*, 8.6, C(3'')*H*, C(5'')*H*), 7.22 (2H, d, *J*, 8.6, C(2')*H*, C(6')*H*), 7.32 (2H, d, *J*, 8.6, C(2'')*H*, C(6'')*H*); δ_C (100 MHz, $CDCl_3$) 20.5 (C(α)*Me*), 23.0, 32.7, 33.2 (*C*(4), *C*(5), *C*(6)), 28.1 (CMe_3), 37.8 (*C*(2)), 49.3 (NCH_2Ar), 53.3 (*C*(3)), 55.2, 55.3 (2 × O*Me*), 57.0 (*C*(α)), 62.9 (*C*(7)), 80.0 (*C*Me$_3$), 113.4, 113.6, 128.9, 129.1 (*C*(2'), *C*(3'), *C*(5'), *C*(6'), *C*(2''), *C*(3''), *C*(5''), *C*(6'')), 133.8, 135.1 (*C*(1'), *C*(1'')), 158.3, 158.5 (*C*(4'), *C*(4'')), 172.4 (*C*(1)); *m/z* (ESI$^+$) 472 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{42}NO_5^+$ ([M+H]$^+$) requires 472.3057; found 472.3051.

[2] J. Podlech, *Synth. Commun.*, 2000, **30**, 1779.
[3] S. G. Davies, A. M. Fletcher, D. G. Hughes, J. A. Lee, P. D. Price, P. M. Roberts, A. J. Russell, A. D. Smith, J. E. Thomson and O. M. H. Williams, *Tetrahedron*, 2011, **67**, 9975.
[4] M. Baenzinger, L. Gobbi, B. P. Riss, F. Schaefer and A. Vaupel, *Tetrahedron: Asymmetry*, 2000, **11**, 2231.

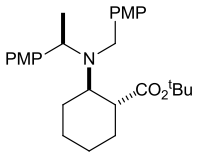
***tert*-Butyl (*R*,*R*)-3-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]-7-chloroheptanoate 19**



BuLi (2.2 M in hexanes, 3.2 mL, 7.1 mmol) was added dropwise to a stirred solution of (*R*)-*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amine[5] (1.98 g, 7.31 mmol, >99:1 er) in THF (40 mL) at –78 °C and the resultant mixture was stirred at –78 °C for 30 min. A solution of **16**[6,7] (1.00 g, 4.57 mmol, >99:1 dr) in THF (40 mL) at –78 °C was added via cannula, and the resultant mixture was stirred at –78 °C for 2 h. Satd aq NH_4Cl (4 mL) was added and the reaction mixture was allowed to warm to rt, then concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (40 mL) and H_2O (20 mL), the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic extracts were washed sequentially with 10% citric acid (40 mL), satd aq Na_2CO_3 (40 mL) and brine (40 mL), then dried and concentrated in vacuo to give **19** in >99:1 dr. Purification via flash column chromatography (eluent 30–40°C petrol/Et_2O, 15:1) gave **19** as a colourless oil (1.84 g, 82%, >99:1 dr); $[\alpha]_D^{22}$ +34.3 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2970, 2933, 2868, 2835 (C−H), 1720 (C=O); δ_H (400 MHz, $CDCl_3$) 1.20–1.55 (4H, m, C(4)H_2, C(5)H_2), 1.33 (3H, d, *J* 7.1, C(α)*Me*), 1.42 (9H, s, CMe_3), 1.65–1.80 (2H, m, C(6)H_2), 1.87 (1H, dd, *J* 14.7, 9.4, C(2)H_A), 1.96 (1H, dd, *J* 14.7, 3.0, C(2)H_B), 3.25–3.35 (1H, m, C(3)*H*), 3.41 (1H, d, *J* 14.8, NC$H_A$$H_B$Ar), 3.53 (2H, t, *J* 6.3, C(7)H_2), 3.71 (1H, d, *J* 14.8, NCH$_A$$H_B$Ar), 3.76–3.81 (1H, q, *J* 7.1, C(α)*H*), 3.81 (3H, s, O*Me*), 3.83 (3H, s, O*Me*), 6.86 (2H, d, *J*, 8.7, C(3')*H*, C(5')*H*), 6.90 (2H, d, *J*, 8.6, C(3'')*H*, C(5'')*H*), 7.23 (2H, d, *J*, 8.7, C(2')*H*, C(6')*H*), 7.33 (2H, d, *J*, 8.6, C(2'')*H*, C(6'')*H*); δ_C (100 MHz, $CDCl_3$) 20.6 (C(α)*Me*), 24.2, 32.4, 32.7 (*C*(4), *C*(5), *C*(6)), 28.1 (CMe_3), 37.7 (*C*(2)), 45.1 (*C*(7)), 49.3 (N*C*H$_2$Ar), 53.2 (*C*(3)), 55.2, 55.3 (2 × O*Me*), 57.1 (*C*(α)), 80.0 (*C*Me$_3$), 113.4, 113.7, 128.9, 129.1 (*C*(2'), *C*(3'), *C*(5'), *C*(6'), *C*(2''), *C*(3''), *C*(5''), *C*(6'')), 133.7, 135.0 (*C*(1'), *C*(1'')), 158.4, 158.5 (*C*(4'), *C*(4'')), 172.2 (*C*(1)); *m*/*z* (ESI$^+$) 514 ([M(^{37}Cl)+Na]$^+$, 26%), 512 ([M(^{35}Cl)+Na]$^+$, 66%), 492 ([M(^{37}Cl)+H]$^+$, 35%), 490 ([M(^{35}Cl)+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{41}{}^{37}ClNO_4^+$ ([M(^{37}Cl)+H]$^+$) requires 492.2689; found 492.2698; HRMS (ESI$^+$) $C_{28}H_{41}{}^{35}ClNO_4^+$ ([M(^{35}Cl)+H]$^+$) requires 490.2719; found 490.2719.

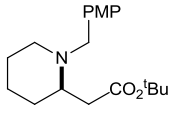
[5] J. Podlech, *Synth. Commun.*, 2000, **30**, 1779.
[6] S. G. Davies, A. M. Fletcher, D. G. Hughes, J. A. Lee, P. D. Price, P. M. Roberts, A. J. Russell, A. D. Smith, J. E. Thomson and O. M. H. Williams, *Tetrahedron*, 2011, **67**, 9975.
[7] D. Enders and J. Wiedemann, *Liebigs Ann.* 1997, 699.

***tert*-Butyl (*R*,*R*,*R*)-2-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]cyclohexane-1-carboxylate 20**



LiHMDS (1.0 M in THF, 2.00 mL, 2.00 mmol) was added to a stirred solution of **19** (100 mg, 0.31 mmol, >99:1 dr) in THF (4 mL) at −78 °C. The reaction mixture was left to stir at −78 °C for 1 h before 1-iodo-3-(*tert*-butyldimethylsilyloxy)propane[8] (0.57 mL, 2.4 mmol) was added. The resultant mixture was allowed to warm to rt over 12 h, then partitioned between Et_2O (15 mL) and H_2O (10 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL), and the combined organic extracts were washed with brine (10 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/acetone, 25:1) gave **20** as a yellow oil (88 mg, 97%, >99:1 dr); $[\alpha]_D^{20}$ −9.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2972, 2932, 2856, 2834 (C−H), 1722 (C=O); δ_H (400 MHz, $CDCl_3$) 0.95–1.08 (1H, m, C(4)H_A), 1.10–1.22 (1H, m, C(3)H_A), 1.24–1.35 (1H, m, C(5)H_A), 1.36 (3H, d, *J* 6.8, C(α)*Me*), 1.37–1.47 (1H, m, C(6)H_A), 1.48 (9H, s, CMe_3), 1.60 (1H, app d, *J* 14.7, C(4)H_B), 1.65–1.75 (2H, m, C(3)H_B, C(5)H_B), 1.80 (1H, app d, *J* 12.6, C(6)H_B), 2.23 (1H, app t, *J* 11.1, C(1)*H*), 3.02 (1H, app t, *J* 11.1, C(2)*H*), 3.61 (1H, d, *J* 16.6, NCH_AH$_B$Ar), 3.66 (1H, d, *J* 16.6, NCH$_A$$H_B$Ar), 3.68 (6H, s, 2 × O*Me*), 4.03 (1H, q, *J* 6.8, C(α)*H*), 6.78–6.80 (4H, m, *Ar*), 7.20–7.22 (4H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 19.1 (C(α)*Me*), 25.2 (*C*(4)), 25.8 (*C*(3)), 27.9 (*C*(5)), 28.2 (CMe_3), 30.7 (*C*(6)), 48.5 (NCH_2Ar), 50.2 (*C*(1)), 55.2 (2 × O*Me*), 59.1 (*C*(α)), 60.1 (*C*(2)), 79.4 (*C*Me$_3$), 113.0, 113.1, 128.9, 129.9 (*C*(2'), *C*(3'), *C*(5'), *C*(6'), *C*(2''), *C*(3''), *C*(5''), *C*(6'')), 134.0, 136.9 (*C*(1'), *C*(1'')), 158.1 (*C*(4'), *C*(4'')), 175.1 (*C*O_2^{t}Bu); *m/z* (ESI$^+$) 454 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_4^+$ ([M+H]$^+$) requires 454.2952; found 454.2949.

***tert*-Butyl (*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]acetate 22**



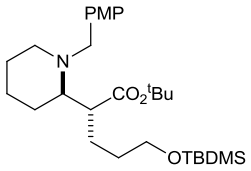
Method A: I_2 (464 mg, 1.83 mmol), imidazole (124 mg, 1.83 mmol) and PPh_3 (480 mg, 1.83 mmol) were added to a stirred solution of **18** (173 mg, 0.367 mmol, >99:1 dr) in MeCN (7.5 mL). The resultant mixture was heated at 80 °C for 16 h then allowed to cool to rt and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (20 mL) and the resultant solution was washed sequentially with satd aq $Na_2S_2O_3$ (10 mL), H_2O (10 mL) and brine (10 mL), then concentrated in vacuo. Purification via flash column chromatography (eluent 30–

[8] T. Hu, J. V. Schaus, K. Lam, M. G. Palfreyman, M. Wuonola, G. Gustafson and J. S. Panek, *J. Org. Chem.*, 1998, **63**, 2401.

40 °C petrol) gave 4-methoxystyrene as a colourless oil (20 mg, 40%);[9] δ_H (400 MHz, $CDCl_3$) 3.82 (3H, s, O*Me*), 5.14 (1H, d, *J* 10.9, CH=CH_AH_B), 5.62 (1H, d, *J* 17.6, CH=CH_AH_B), 6.67 (1H, dd, *J* 17.6, 10.9, C*H*=CH_2), 6.87 (2H, *J* 8.6, C(3)*H*, C(5)*H*), 7.35 (2H, *J* 8.6, C(2)*H*, C(6)*H*). Further elution (eluent 30–40 °C petrol/NEt_3, 100:1, then 30–40 °C petrol/acetone/NEt_3, 100:4:1) gave **22** as a yellow oil (80 mg, 68%); $[\alpha]_D^{21}$ +20.1 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2976, 2932, 2857, 2835, 2797 (C−H), 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.35–1.55 (4H, m, C(3')H_A, C(4')H_2, C(5')H_A), 1.45 (9H, s, CMe_3), 1.58–1.65 (1H, m, C(5')H_B), 1.75–1.80 (1H, m, C(3')H_B), 2.11–2.18 (1H, m, C(6')H_A), 2.33 (1H, dd, *J* 14.5, 8.0, C(2)H_A), 2.55–2.70 (2H, m, C(2)H_B, C(6')H_B), 2.91 (1H, m, C(2')*H*), 3.30 (1H, d, *J* 13.5, NCH_AH_BAr), 3.73 (1H, d, *J* 13.5, NCH_AH_BAr), 3.80 (3H, s, O*Me*), 6.85 (2H, d, *J* 8.6, C(3")*H*, C(5")*H*), 7.23 (2H, d, *J* 8.6, C(2")*H*, C(6")*H*); δ_C (100 MHz, $CDCl_3$) 22.3, 25.3 (*C*(4'), *C*(5')), 28.1 (CMe_3), 31.0 (*C*(3')), 37.3 (*C*(2)), 50.0 (*C*(6')), 55.2 (*C*(2')), 57.6 (N*C*H_2Ar), 57.8 (O*Me*), 80.2 (*C*Me_3), 113.5, 129.9 (*C*(2"), *C*(3"), *C*(5"), *C*(6")), 131.4 (*C*(1")), 158.5 (*C*(4")), 172.3 (*C*(1)); *m*/*z* (ESI^+) 320 ($[M+H]^+$, 100%), 264 ($[M-C_4H_8]^+$, 90%); HRMS (ESI^+) $C_{19}H_{30}NO_3^+$ ($[M+H]^+$) requires 320.2220; found 320.2220.

Method B: NaI (844 mg, 5.63 mmol) was added to a stirred solution of **19** (1.38 g, 2.82 mmol, >99:1 dr) in MeCN (65 mL) and the resultant mixture was heated at reflux for 24 h. The reaction mixture was then allowed to cool to rt and diluted with Et_2O (65 mL). The resultant mixture was washed with H_2O (50 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/acetone, 15:1) gave 4-methoxystyrene as a colourless oil (200 mg, 53%). Further elution (eluent 30–40 °C petrol/acetone, 3:1) gave **22** as a yellow oil (793 mg, 88%).

tert-Butyl (*R*,*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]-5-(_tert_-butyldimethylsiloxy)pentanoate 24

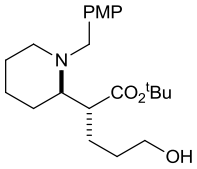


LiHMDS (1.0 M in THF, 5.15 mL, 5.15 mmol) was added to a stirred solution of **22** (235 mg, 0.736 mmol) in THF (10 mL) at –78 °C and the resultant mixture was stirred at –78 °C for 1 h. 1-Iodo-3-(*tert*-butyldimethylsilyloxy)propane[10] (1.10 g, 3.68 mmol) was then added and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h. Satd aq NH_4Cl (5 mL) was then added and the reaction mixture was concentrated in vacuo. The residue was partitioned between CH_2Cl_2 (10 mL) and H_2O (5 mL), and the organic layer was then dried and concentrated in vacuo. Purification by flash column chromatography (eluent 30–40

[9] M. Davi and H. Lebel, *Org. Lett.*, 2009, **11**, 41.
[10] T. Hu, J. V. Schaus, K. Lam, M. G. Palfreyman, M. Wuonola, G. Gustafson and J. S. Panek, *J. Org. Chem.*, 1998, **63**, 2401.

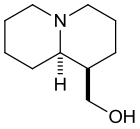
°C petrol/acetone/NH_4OH, 100:5:1) gave **24** as a colourless oil (271 mg, 75%, >99:1 dr); $[\alpha]_D^{20}$ +24.9 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2930, 2857 (C−H), 1728 (C=O); δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, Si*Me*$_2$), 0.89 (9H, s, SiC*Me*$_3$), 1.26–1.70 (10H, m, C(3)*H*$_2$, C(4)*H*$_2$, C(3')*H*$_2$, C(4')*H*$_2$, C(5')*H*$_2$), 1.47 (9H, s, OC*Me*$_3$), 2.07–2.14 (1H, m, C(6')*H*$_A$), 2.64–2.68 (1H, m, C(2')*H*), 2.82–2.87 (1H, m, C(6')*H*$_B$), 2.87–2.93 (1H, m, C(2)*H*), 3.38 (1H, d, *J* 13.1, NC*H*$_A$H$_B$Ar), 3.56–3.68 (2H, m, C(5)*H*$_2$), 3.80 (3H, s, O*Me*), 3.82 (1H, d, *J* 13.1, NCH$_A$*H*$_B$Ar), 6.83 (2H, d, *J* 8.5, C(3")*H*, C(5")*H*), 7.23 (2H, d, *J* 8.5, C(2")*H*, C(6")*H*); δ_C (100 MHz, $CDCl_3$) −5.1 (Si*Me*$_2$), 18.5 (Si*C*Me$_3$), 23.1, 23.3, 24.6 (*C*(4), *C*(4'), *C*(5')), 26.1 (SiC*Me*$_3$), 28.4 (OC*Me*$_3$), 31.7 (*C*(3), *C*(3')), 47.6 (*C*(2)), 49.8 (*C*(6')), 55.4 (O*Me*), 56.5 (N*C*H$_2$Ar), 62.6 (*C*(2')), 63.5 (*C*(5)), 80.1 (O*C*Me$_3$), 113.5, 130.2 (*C*(2"), *C*(3"), *C*(5"), *C*(6")), 131.7 (*C*(1")), 158.6 (*C*(4")), 174.4 (*C*(1)); *m/z* (ESI^+) 492 ($[M+H]^+$, 100%), 436 ($[M-C_4H_8]^+$, 25%); HRMS (ESI^+) $C_{28}H_{50}NO_4Si^+$ ($[M+H]^+$) requires 492.3504; found 492.3498.

***tert*-Butyl (*R*,*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]-5-hydroxypentanoate 25**



TBAF (1.0 M in THF, 2.70 mL, 2.70 mmol) was added dropwise to a stirred solution of **24** (265 mg, 0.539 mmol, >99:1 dr) in THF (10 mL). The resultant solution was stirred at rt for 4 h, then partitioned between Et_2O (10 mL) and H_2O (10 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic extracts were washed with brine (30 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40°C petrol/acetone/NH_4OH, 100:20:1) gave **25** as a yellow oil (173 mg, 85%, >99:1 dr); $[\alpha]_D^{20}$ +30.3 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3414 (O−H), 3032, 2933, 2860, 2836, 2724 (C−H), 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.25–1.45 (3H, m, C(3')*H*$_A$, C(4')*H*$_A$, C(5')*H*$_A$), 1.46 (9H, s, C*Me*$_3$), 1.47–1.61 (4H, m, C(3)*H*$_2$, C(4)*H*$_2$), 1.61–1.80 (3H, m, C(3')*H*$_B$, C(4')*H*$_B$, C(5')*H*$_B$), 2.03–2.10 (1H, m, C(6')*H*$_A$), 2.60–2.66 (1H, m, C(2')*H*), 2.80–2.92 (2H, m, C(2)*H*, C(6')*H*$_B$), 3.34 (1H, d, *J* 13.1, NC*H*$_A$H$_B$Ar), 3.54–3.65 (2H, m, C(5)*H*$_2$), 3.78 (3H, s, O*Me*), 3.83 (1H, d, *J* 13.1, NCH$_A$*H*$_B$Ar), 6.83 (2H, d, *J* 8.4, C(3")*H*, C(5")*H*), 7.22 (2H, d, *J* 8.4, C(2")*H*, C(6")*H*); δ_C (100 MHz, $CDCl_3$) 21.7, 23.4, 23.7 (*C*(3'), *C*(4'), *C*(5')), 24.9 (*C*(3)), 28.1 (C*Me*$_3$), 31.6 (*C*(4)), 47.5 (*C*(2)), 50.5 (*C*(6')), 55.2 (O*Me*), 56.6 (N*C*H$_2$Ar), 62.4 (*C*(5)), 62.6 (*C*(2')), 80.3 (*C*Me$_3$), 113.4, 130.1 (*C*(2"), *C*(3"), *C*(5"), *C*(6")), 131.2 (*C*(1")), 158.5 (*C*(4")), 174.5 (*C*(1)); *m/z* (ESI^+) 378 ($[M+H]^+$, 100%), 322 ($[M-C_4H_8]^+$, 25%); HRMS (ESI^+) $C_{22}H_{36}NO_4^+$ $[M+H]^+$ requires 378.2639; found 378.2633.

(*R*,*R*)-1-(Hydroxymethyl)octahydro-1*H*-quinolizine [(–)-lupinine] 1



Method A – Step 1: I_2 (548 mg, 2.16 mmol), imidazole (147 mg, 2.16 mmol) and polymer-supported PPh_3 (720 mg, ~3.2 mmol/g,) were added to a solution of **25** (163 mg, 0.432 mmol, >99:1 dr) in PhMe/MeCN (4:1, 5 mL). The resultant mixture was heated at 65 °C for 16 h, then allowed to cool to rt and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL) and the resultant solution was washed with satd aq $Na_2S_2O_3$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic extracts were then concentrated in vacuo to give **26** as a brown oil (175 mg, >99:1 dr).

Method A – Step 2: $LiAlH_4$ (1.0 M in THF, 0.59 mL, 0.59 mmol) was added to a stirred solution of **26** (95 mg, >99:1 dr) in THF (4 mL) at 0 °C. The resultant mixture was heated at reflux for 48 h then allowed to cool to rt. 2.0 M aq NaOH (0.5 mL) was then added and the resultant mixture was heated at reflux for 3 h. The reaction mixture was then allowed to cool to rt and filtered through Celite® (eluent CH_2Cl_2), then concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/NH_4OH, 200:25:2) gave (–)-lupinine **1** as a pale yellow oil (26 mg, 66% from **25**, >99:1 dr);[11,12] $[\alpha]_D^{20}$ –12.0 (*c* 0.4 in EtOH); {lit.[11] for *ent*-**1** $[\alpha]_D^{30}$ +12.7 (*c* 0.35 in EtOH)}; ν_{max} (ATR) 3323 (O–H), 2933, 2857, 2807, 2763 (C–H); δ_H (400 MHz, C_6D_6) 0.94–1.06 (1H, m, C(8)H_A), 1.15–1.25 (2H, m, C(1)*H*, C(9)H_A), 1.25–1.44 (4H, m, C(2)H_A, C(3)H_A, C(7)H_2), 1.49–1.58 (2H, m, C(6)H_A, C(8)H_B), 1.63–1.80 (4H, m, C(2)H_B, C(4)H_A, C(9)H_B, C(9a)*H*), 2.23–2.37 (1H, m, C(3)H_B), 2.44–2.56 (2H, m, C(4)H_B, C(6)H_B), 3.75 (1H, app d, *J* 10.7, CH_AH$_B$OH), 4.18 (1H, dd, *J* 10.7, 4.8, CH$_A$$H_B$OH); δ_H (400 MHz, $CDCl_3$) 1.21–1.34 (1H, m, CH_2), 1.49–1.64 (6H, m, C(1)*H*, CH_2), 1.71–1.91 (4H, m, CH_2), 1.98–2.08 (1H, m, CH_2), 2.10–2.23 (2H, m, C(9a)*H*, CH_2), 2.79–2.88 (2H, m, C(4)H_A, C(6)H_A), 3.70 (1H, d, *J* 10.8, CH_AH$_B$OH), 4.17 (1H, ddd, *J* 10.8, 4.6, 1.2, CH$_A$$H_B$OH); δ_C (100 MHz, C_6D_6) 23.3 (*C*(3)), 25.0 (*C*(8)), 25.9 (*C*(7)), 29.9 (*C*(9)), 31.6 (*C*(2)), 38.9 (*C*(1)), 57.3 (*C*(6)), 57.4 (*C*(4)), 65.2 (*C*(9a)), 65.7 (*C*H$_2$OH); *m/z* (ESI$^+$) 170 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{10}H_{20}NO^+$ ([M+H]$^+$) requires 170.1539; found 170.1541.

Method B – Step 1: I_2 (343 mg, 1.35 mmol), imidazole (92 mg, 1.35 mmol) and polymer-supported PPh_3 (450 mg, ~3.2 mmol/g) were added to a solution of **25** (102 mg, 0.27 mmol, >99:1 dr) in PhMe/MeCN (4:1, 5 mL). The resultant mixture was heated at 65 °C for 60 h, then allowed to cool to rt and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (5 mL) and the resultant solution was washed sequentially with satd aq $Na_2S_2O_3$ (5 mL) and satd aq $NaHCO_3$ (5 mL). The combined aqueous layers were extracted with CH_2Cl_2 (3 × 5

[11] A. C. Cutter, I. R. Miller, J. F. Keily, R. K. Bellingham, M. E. Light and R. C. D. Brown, *Org. Lett.*, 2011, **13**, 3988.
[12] D. S. Rycroft, D. J. Robins and I. H. Sadler, *Magn. Reson. Chem.*, 1992, **30**, S15.

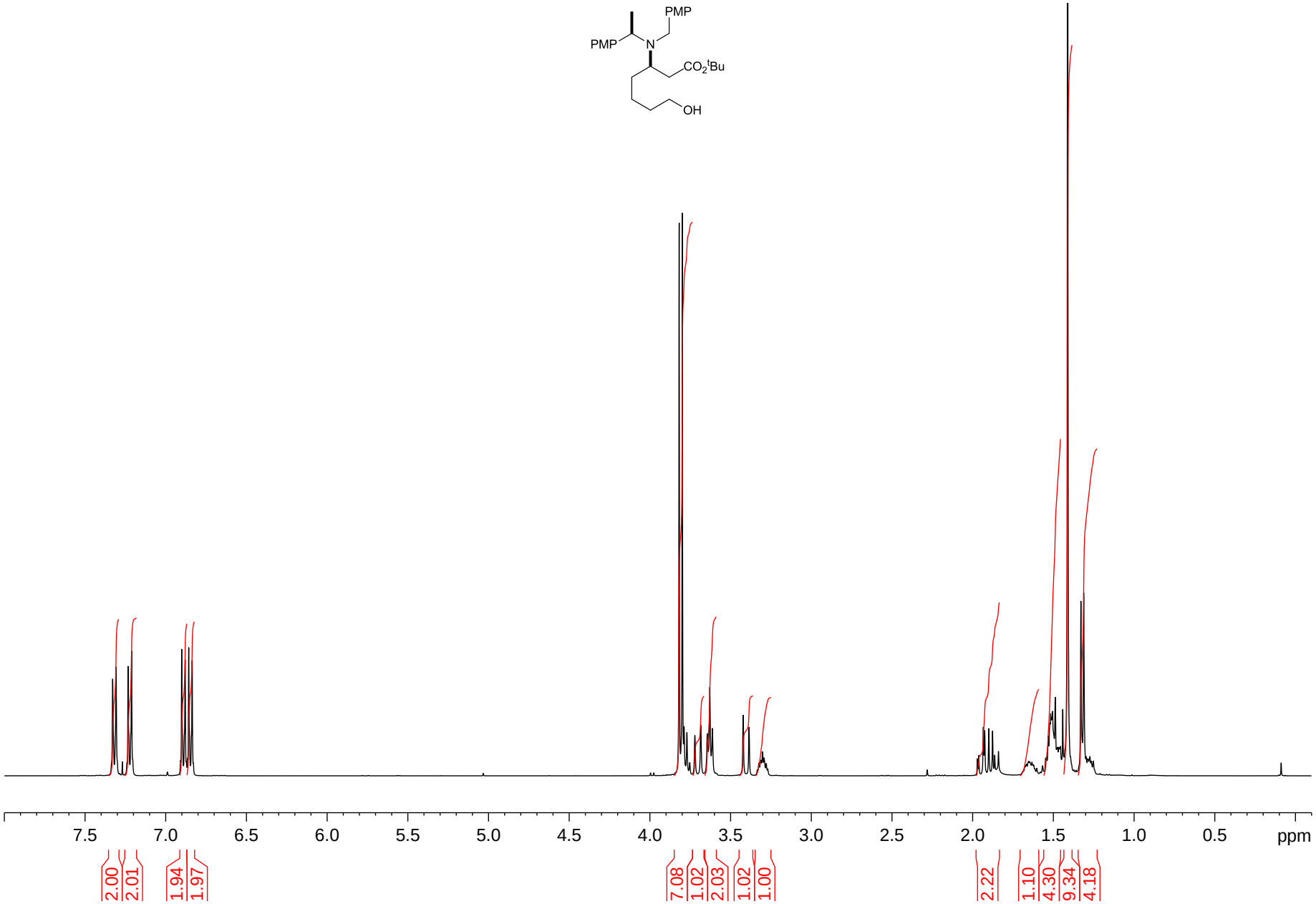
mL) and the combined organic extracts were then concentrated in vacuo to give **27** as a brown oil (118 mg, >99:1 dr).

Method B – Step 2: $LiAlH_4$ (1.0 M in THF, 0.81 mL, 0.81 mmol) was added to a stirred solution of **27** (118 mg, >99:1 dr) in THF (2.5 mL) at 0 °C. The resultant mixture was heated at reflux for 16 h then allowed to cool to rt. 2.0 M aq NaOH (0.8 mL) was then added and the resultant mixture was heated at reflux for 3 h. The reaction mixture was then allowed to cool to rt and filtered through Celite® (eluent CH_2Cl_2), then concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/NH_4OH, 200:25:2) gave (–)-lupinine **1** as a pale yellow oil (23 mg, 50% from **25**, >99:1 dr); $[\alpha]_D^{20}$ –9.5 (*c* 0.4 in EtOH); {lit.[13] for *ent*-**1** $[\alpha]_D^{30}$ +12.7 (*c* 0.35 in EtOH)}.

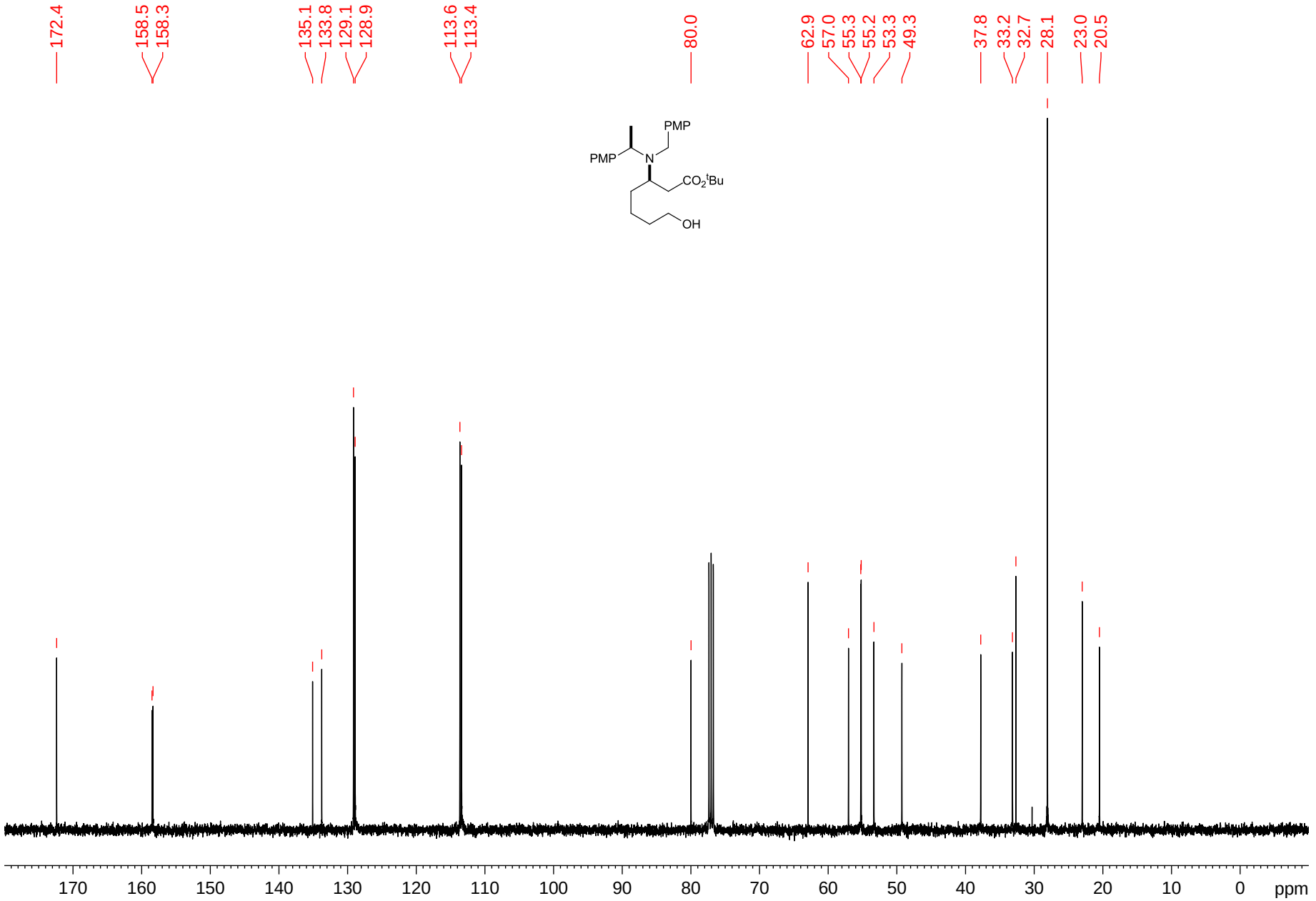
[13] A. C. Cutter, I. R. Miller, J. F. Keily, R. K. Bellingham, M. E. Light and R. C. D. Brown, *Org. Lett.*, 2011, **13**, 3988.

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

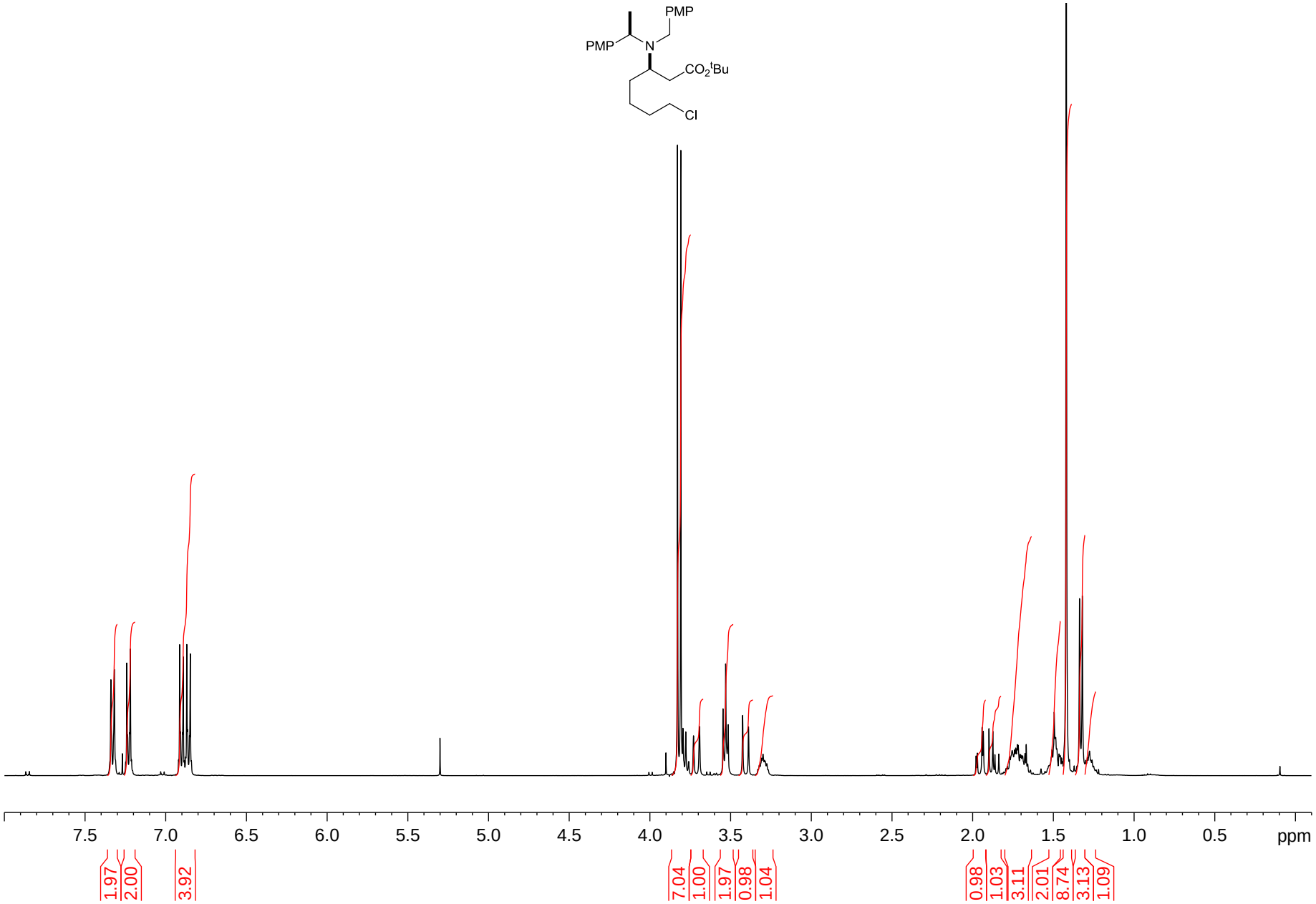
***tert*-Butyl (*R*,*R*)-3-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]-7-hydroxyheptanoate 18 (400 MHz ^{1}H, $CDCl_3$)**



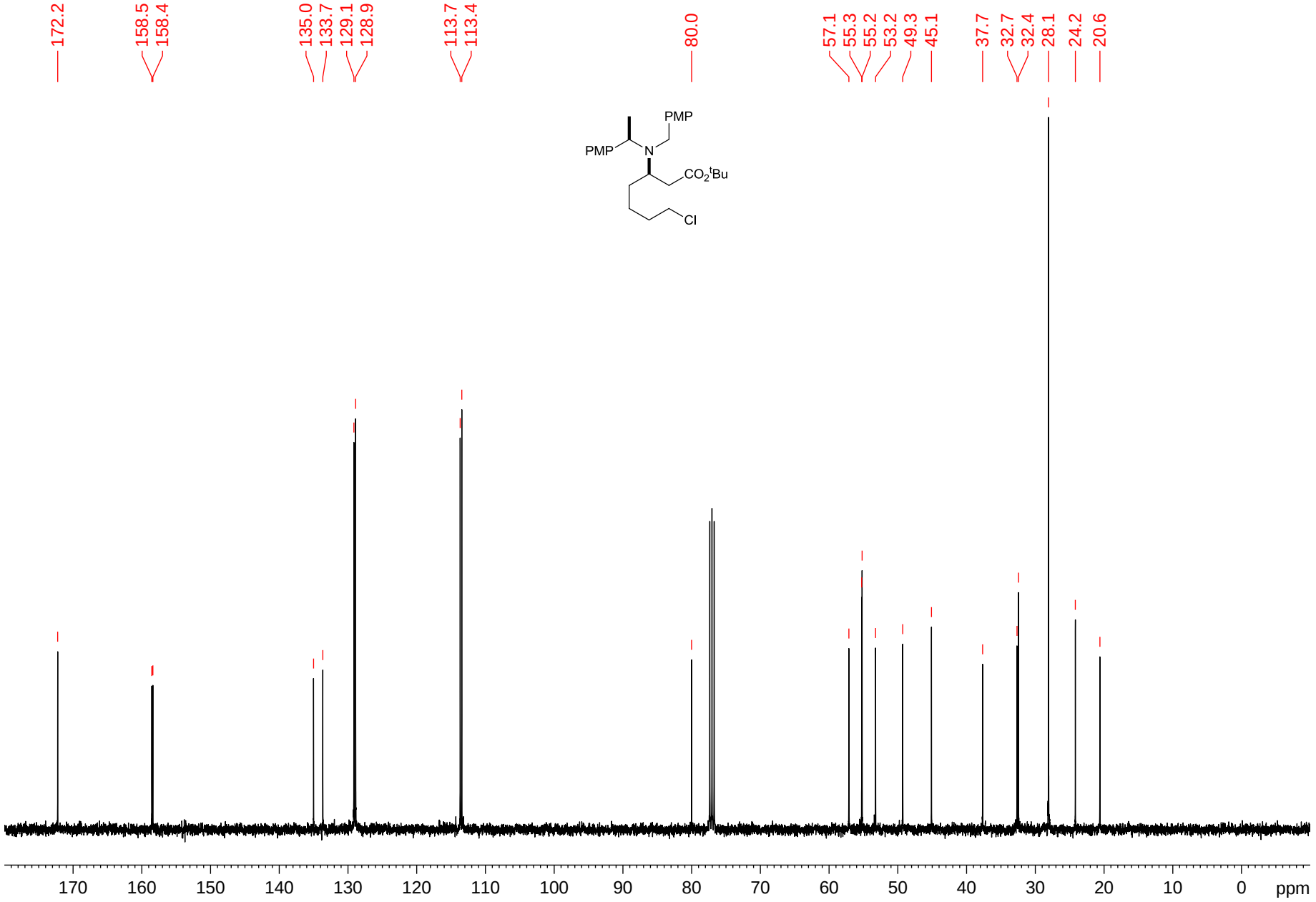
***tert*-Butyl (*R,R*)-3-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]-7-hydroxyheptanoate 18 (100 MHz ^{13}C, $CDCl_3$)**



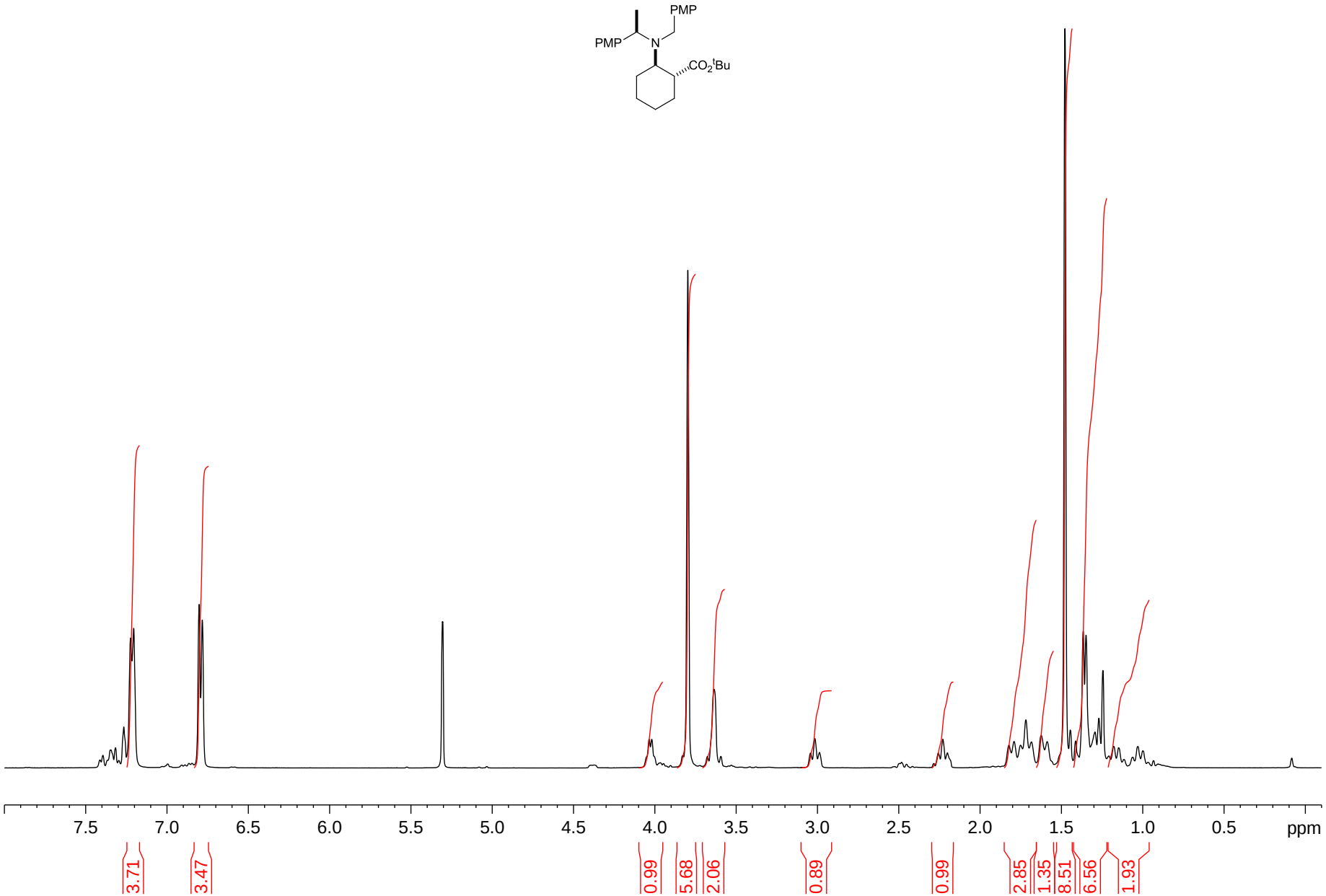
***tert*-Butyl (*R*,*R*)-3-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]-7-chloroheptanoate 19 (400 MHz ^{1}H, $CDCl_3$)**



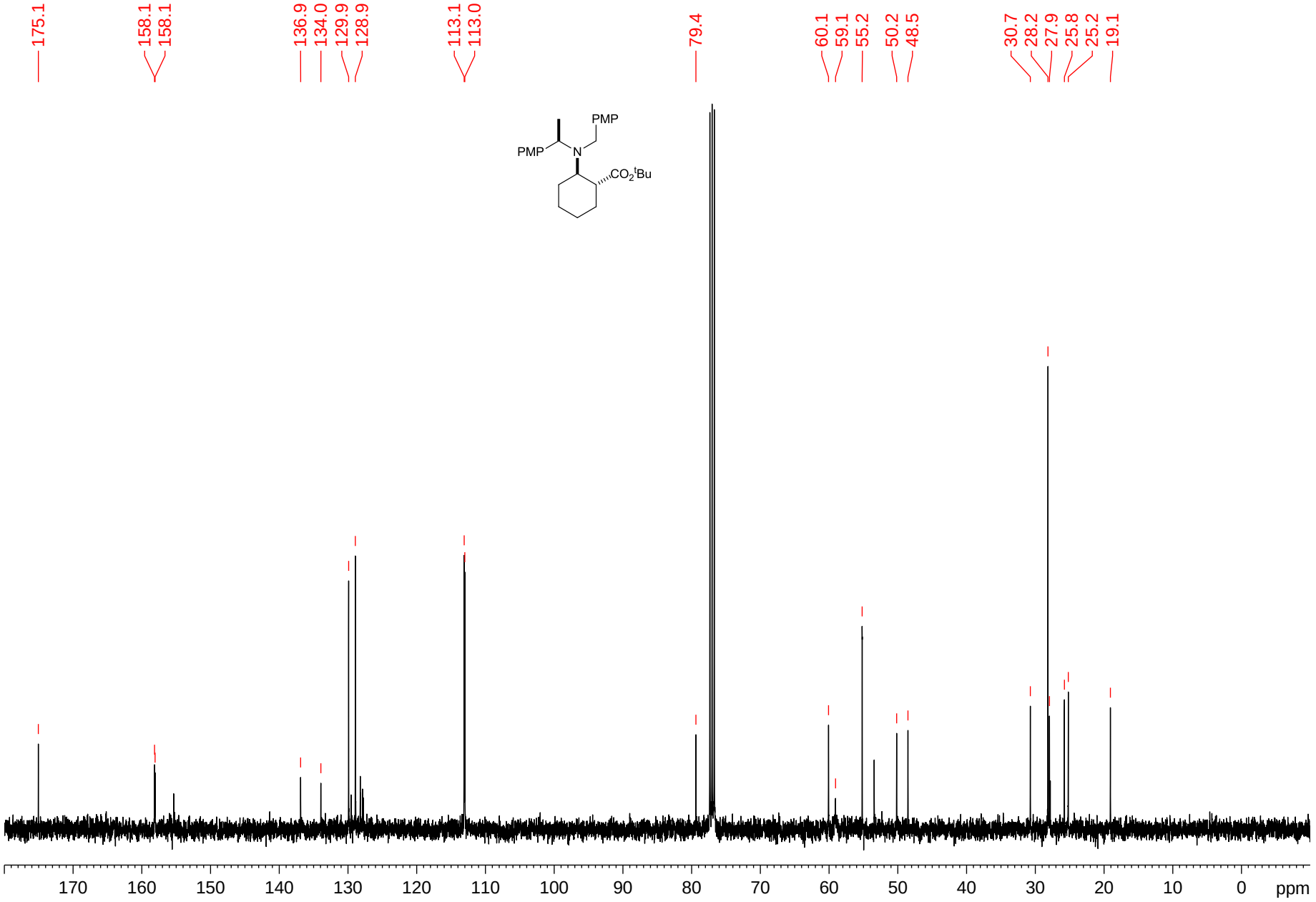
***tert*-Butyl (*R*,*R*)-3-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]-7-chloroheptanoate 19 (100 MHz ^{13}C, $CDCl_3$)**



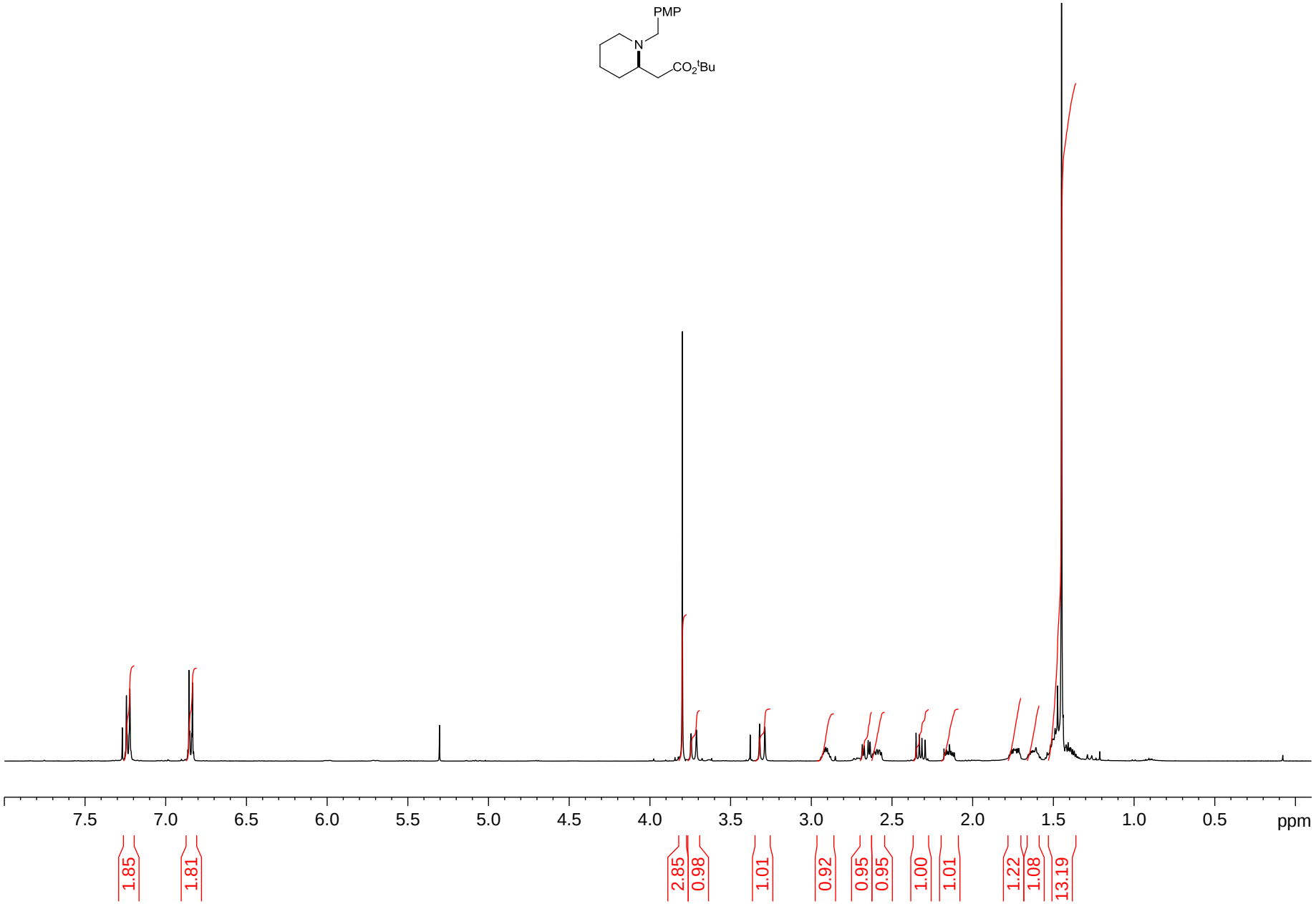
***tert*-Butyl (*R*,*R*,*R*)-2-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]cyclohexane-1-carboxylate 20 (400 MHz ^{1}H, $CDCl_3$)**



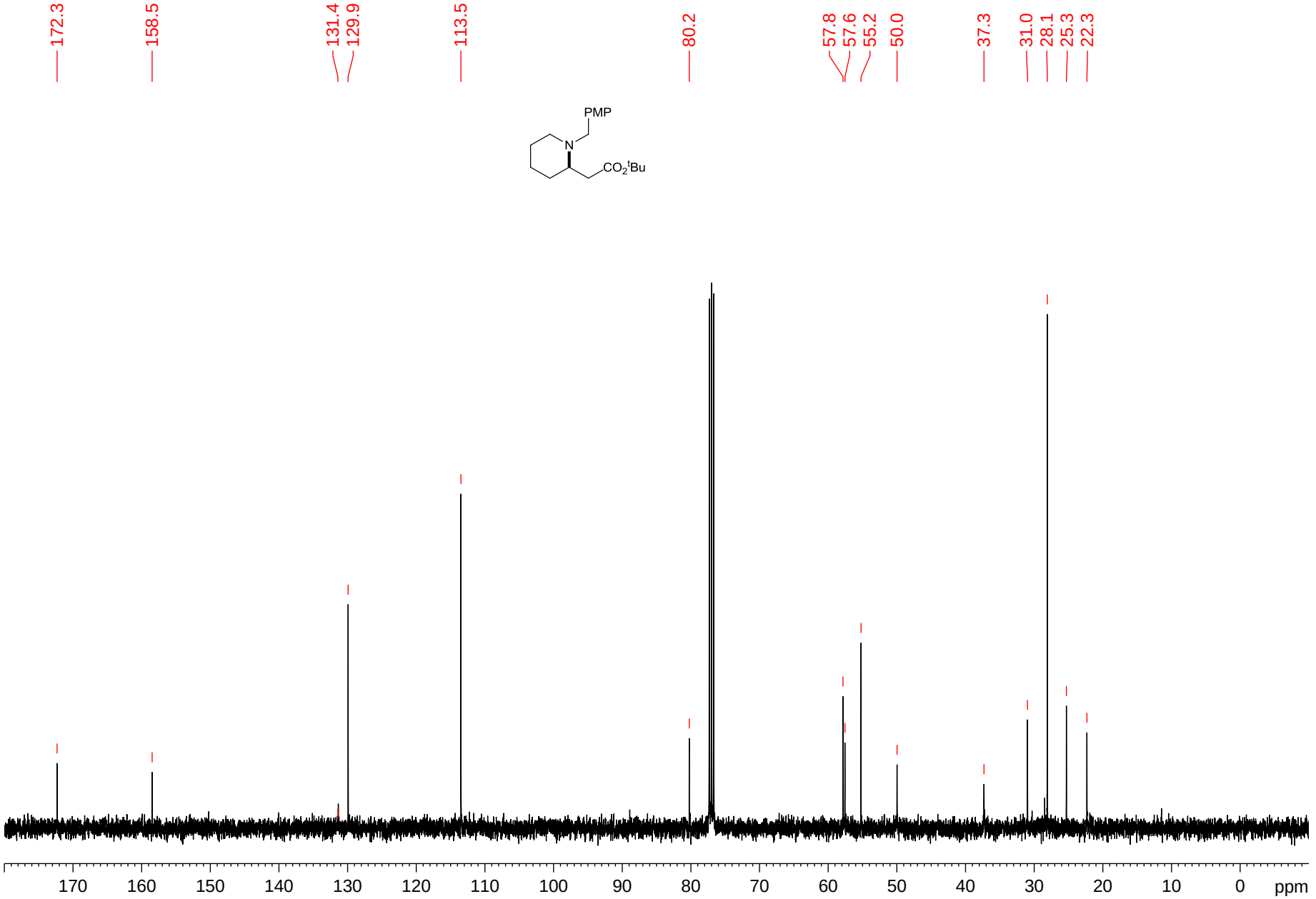
***tert*-Butyl (*R,R,R*)-2-[*N*-(*p*-methoxybenzyl)-*N*-(α-methyl-*p*-methoxybenzyl)amino]cyclohexane-1-carboxylate 20 (100 MHz ^{13}C, $CDCl_3$)**



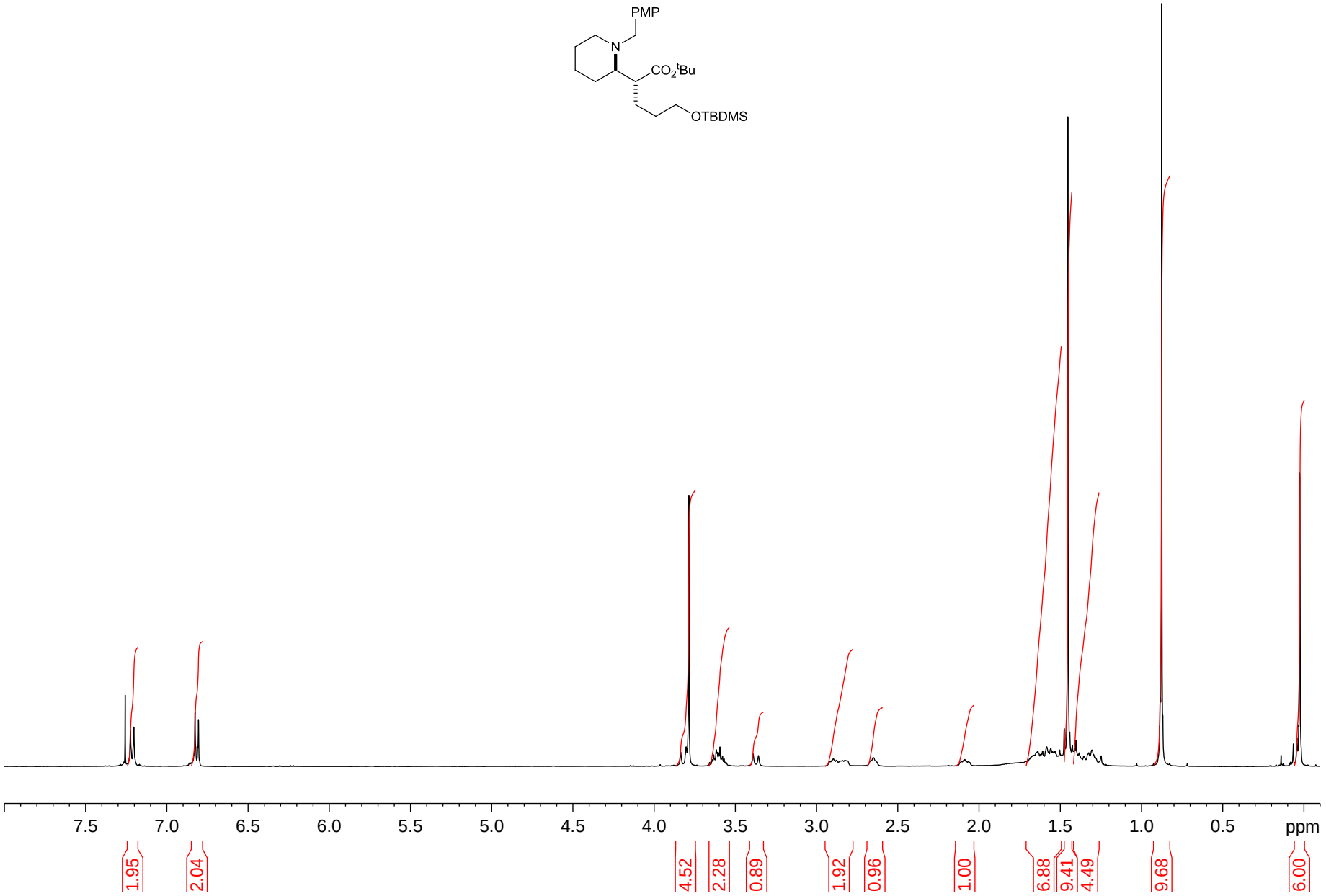
***tert*-Butyl (*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]acetate 22 (400 MHz ^{1}H, $CDCl_3$)**



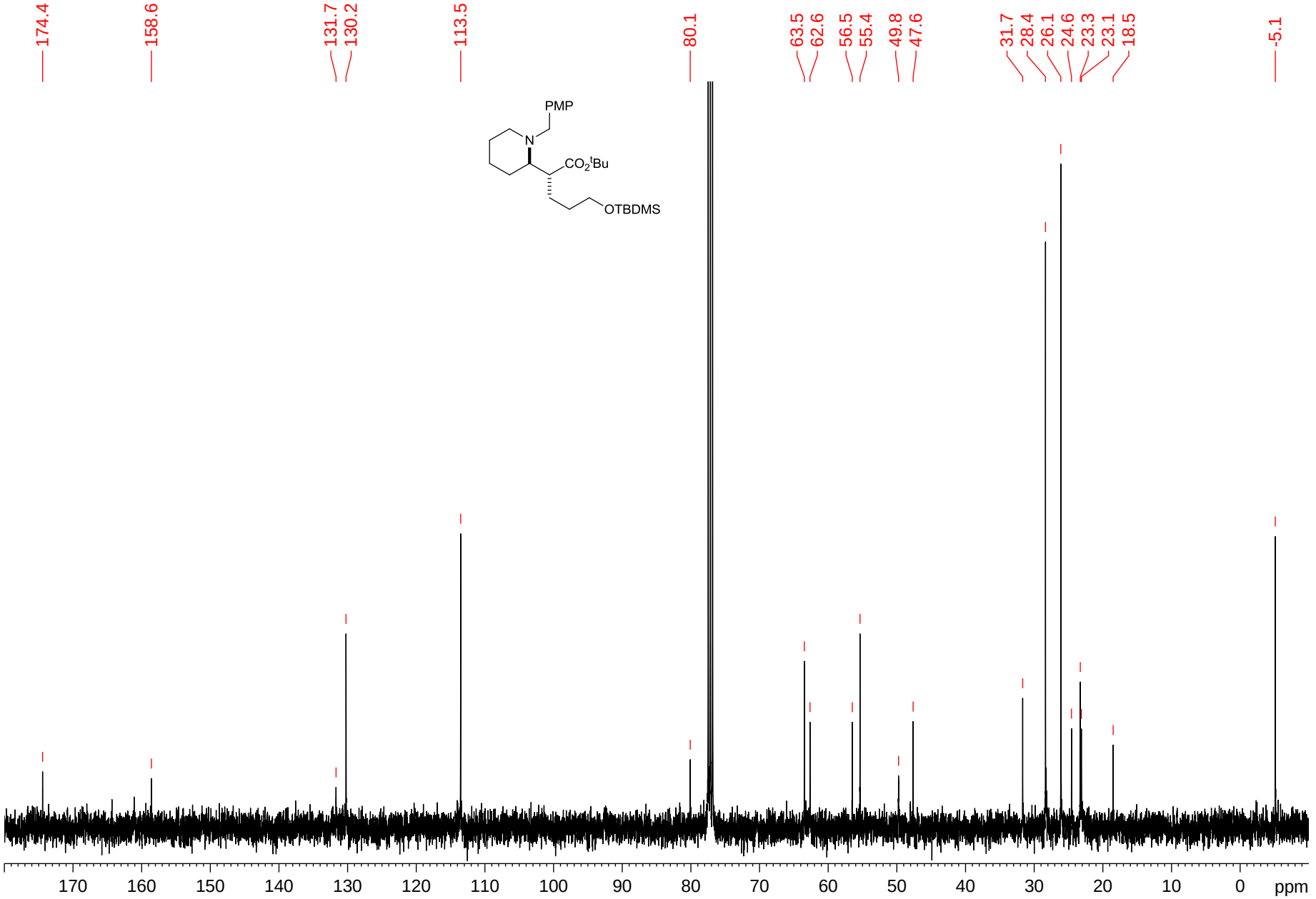
***tert*-Butyl (*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]acetate 22 (100 MHz ^{13}C, $CDCl_3$)**



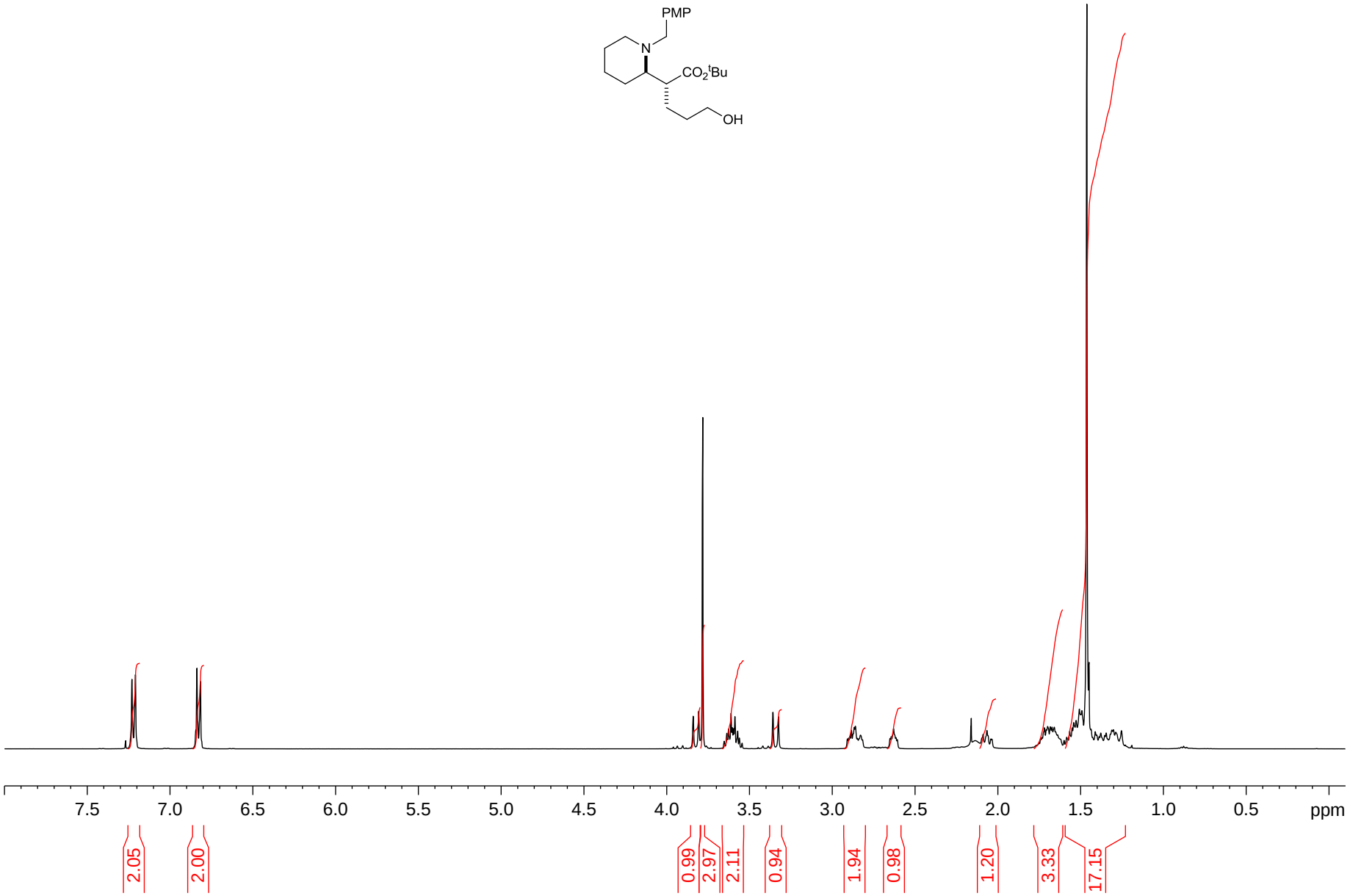
***tert*-Butyl (*R*,*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]-5-(*tert*-butyldimethylsiloxy)pentanoate 24 (400 MHz ^{1}H, $CDCl_3$)**



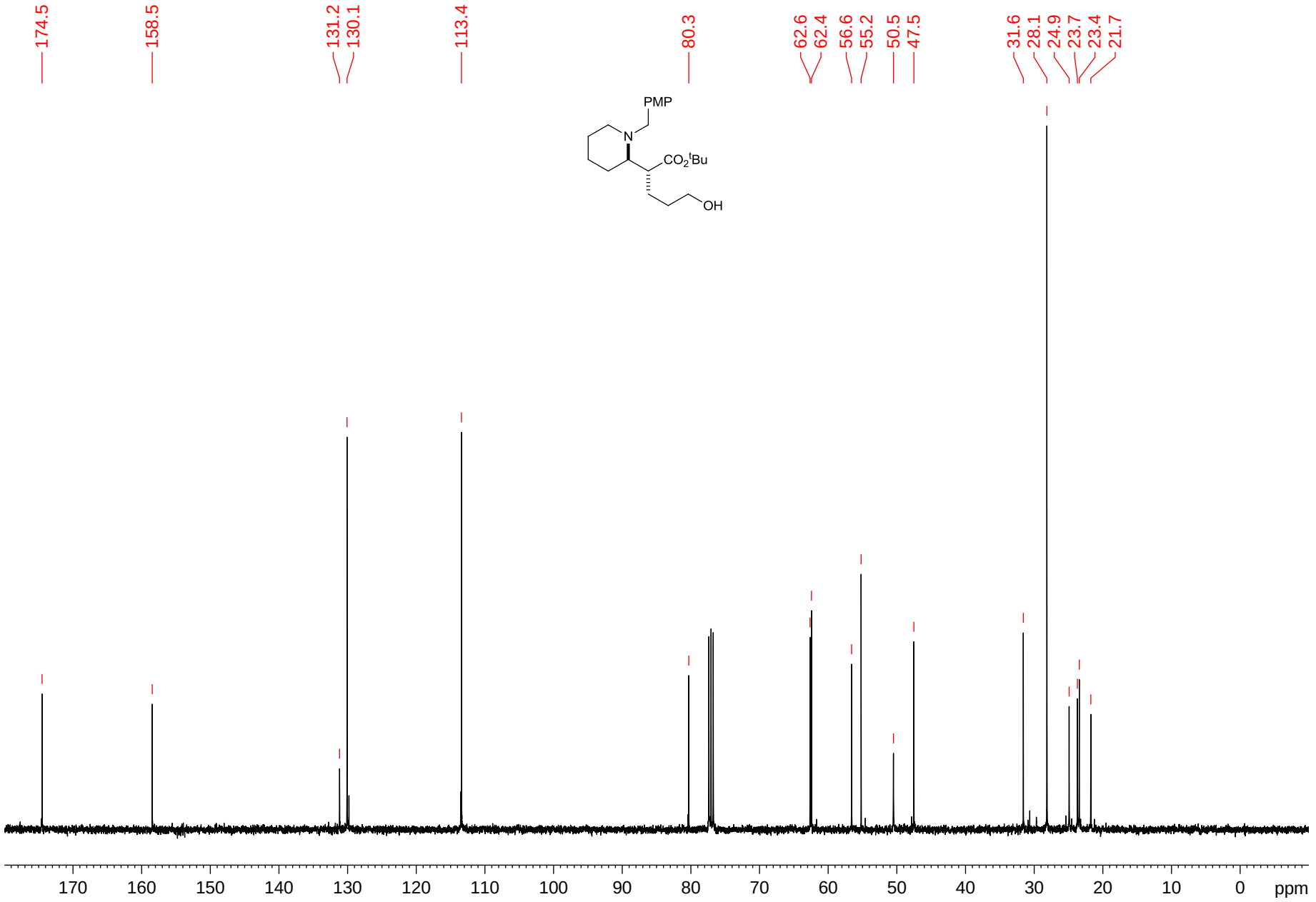
***tert*-Butyl (*R*,*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]-5-(*tert*-butyldimethylsiloxy)pentanoate 24 (100 MHz ^{13}C, $CDCl_3$)**



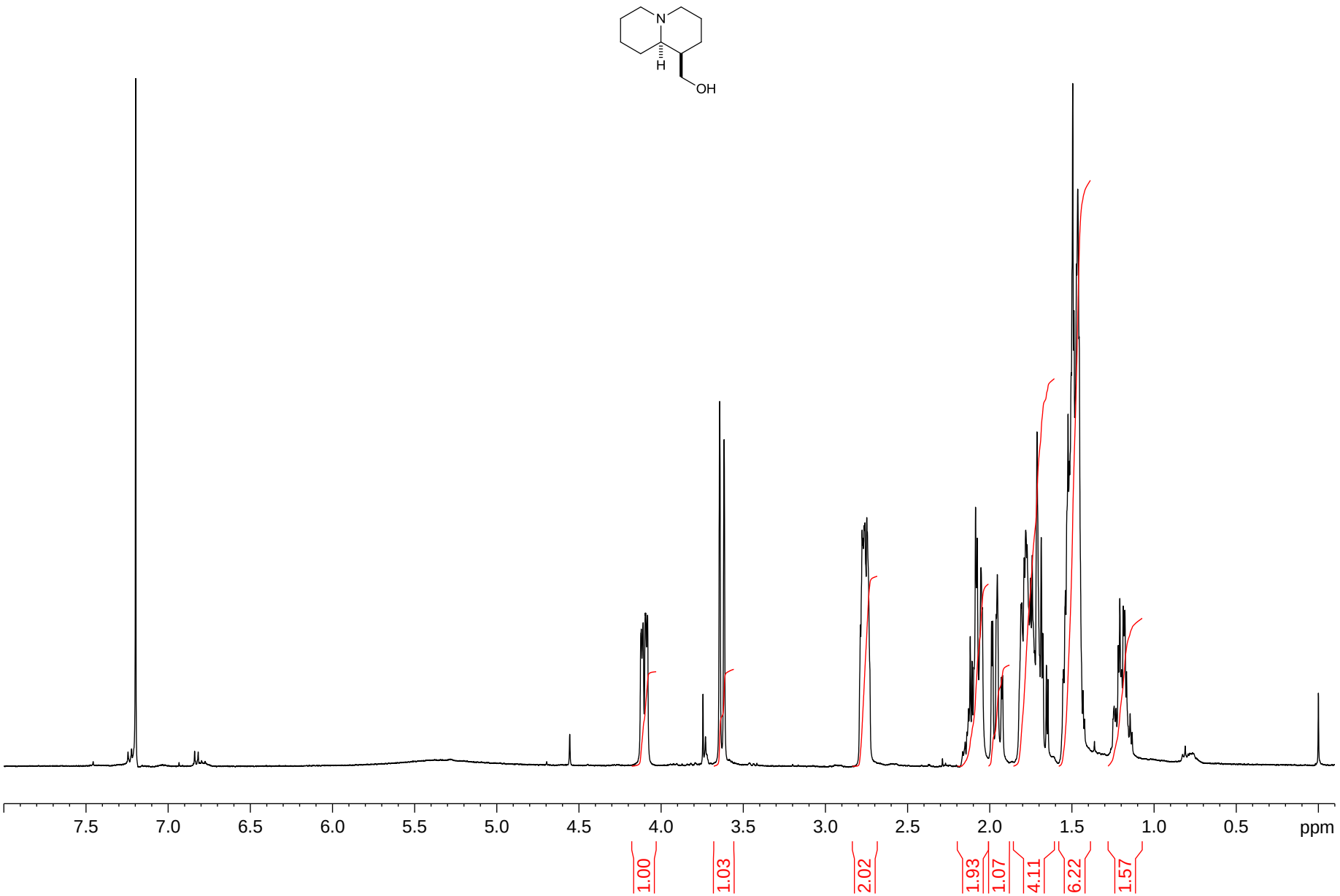
***tert*-Butyl (*R*,*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]-5-hydroxypentanoate 25 (400 MHz ^{1}H, $CDCl_3$)**



***tert*-Butyl (*R*,*R*)-2-[*N*(1')-(*p*-methoxybenzyl)piperidin-2'-yl]-5-hydroxypentanoate 25 (100 MHz ^{13}C, $CDCl_3$)**



(*R*,*R*)-1-(Hydroxymethyl)octahydro-1*H*-quinolizine [(–)-lupinine] 1 (400 MHz ^{1}H, $CDCl_3$)



(*R*,*R*)-1-(Hydroxymethyl)octahydro-1*H*-quinolizine [(–)-lupinine] 1 (100 MHz ^{13}C, C_6D_6)