Supporting Information for

Asymmetric Synthesis of (–)-Martinellic Acid

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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.

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

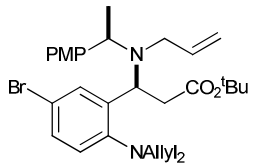
tert-Butyl (*E*)-3-(2'-*N*,*N*-diallylamino-5'-bromophenyl)propenoate 5

Step 1: $Pd(OAc)_2$ (80 mg, 0.36 mmol) was added to a stirred, degassed solution of **3** (10.6 g, 35.5 mmol), P(*o*-Tol)$_3$ (216 mg, 0.71 mmol), *tert*-butyl acrylate (5.72 mL, 39.1 mmol) and Et_3N (9.89 mL, 71.0 mmol) in MeCN (200 mL). The resultant mixture was heated at 70 °C for 16 h, then allowed to cool to rt and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (200 mL) and the resultant solution was washed with H_2O (2 × 200 mL). The combined aqueous layers were extracted with CH_2Cl_2 (200 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give **4** as a brown oil (10.7 g, >99:1 dr);[2] δ_H (400 MHz, $CDCl_3$) 1.53 (9H, s, C*Me*$_3$), 3.95 (2H, s, N*H*$_2$), 6.28 (1H, d, *J* 15.7, C(2)*H*), 6.58 (1H, d, *J* 8.7, C(3')*H*), 7.23 (1H, dd, *J* 8.7, 2.3, C(4')*H*), 7.48 (1H, d, *J* 2.3, C(6')*H*), 7.61 (1H, d, *J* 15.7, C(3)*H*).

Step 2: Allyl iodide (9.80 mL, 107 mmol) was added to a solution of **4** (10.7 g, >99:1 dr) and K_3PO_4 (18.8 g, 88.7 mmol) in acetone (200 mL), and the resultant mixture was heated at reflux for 48 h. The reaction mixture was then allowed to cool to rt, diluted with Et_2O (300 mL), and washed with H_2O (2 × 200 mL). The combined aqueous layers were extracted with Et_2O (200 mL) and the combined organic extracts were dried and concentrated *in vacuo*. The residue was passed through a short plug of silica (eluent 30–40 °C petrol/Et_2O, 20:1) and the filtrate was concentrated *in vacuo* to give **5** as a yellow oil (12.1 g, 90% from **3**, >99:1 dr); $C_{19}H_{24}BrNO_2$ requires C, 60.3; H, 6.4; N, 3.7%; found C, 60.4; H, 6.4; N, 3.8%; ν_{max} (ATR) 3078, 2978, 2931, 2822 (C–H), 1705 (C=O), 1631, 1585 (C=C); δ_H (400 MHz, $CDCl_3$) 1.54 (9H, s, C*Me*$_3$), 3.61 (4H, d, *J* 6.3, N(C*H*$_2$CH=CH$_2$)$_2$), 5.10–5.21 (4H, m, N(CH$_2$CH=C*H*$_2$)$_2$), 5.72–5.84 (2H, m, N(CH$_2$C*H*=CH$_2$)$_2$), 6.30 (1H, d, *J* 15.9, C(2)*H*), 6.89 (1H, d, *J* 8.6, C(3')*H*), 7.36 (1H, dd, *J* 8.6, 2.3, C(4')*H*), 7.63 (1H, d, *J* 2.3, C(6')*H*), 7.92 (1H, d, *J* 15.9, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 28.2 (C*Me*$_3$), 56.0 (N(*C*H$_2$CH=CH$_2$)), 80.5 (*C*Me$_3$), 115.5 (*C*(5')), 118.0 (N(CH$_2$CH=*C*H$_2$)$_2$), 120.8 (*C*(2)), 123.2 (*C*(3')), 130.4 (*C*(6')), 131.7 (*C*(1')), 132.4 (*C*(4')), 134.2 (N(CH$_2$*C*H=CH$_2$)$_2$), 139.9 (*C*(3)), 149.6 (*C*(2')), 166.2 (*C*(1)); *m/z* (ESI$^+$) 779 ([M(^{81}Br)+M(^{79}Br)+Na]$^+$, 100%), 400 ([M(^{79}Br)+Na]$^+$, 85%), 380 ([M(^{81}Br)+H]$^+$, 60%); HRMS (ESI$^+$) $C_{19}H_{24}{}^{81}BrNNaO_2^+$ ([M(^{81}Br)+Na]$^+$) requires 402.0862; found 402.0867.

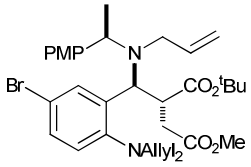
[2] A synthesis of **4** has previously been reported, see: Slavish, P. J.; Jiang, Q.; Xiaoli. C.; Morris, S. W.; Webb, T. R. *Bioorg. Med. Chem.* **2009**, *17*, 3308.

***tert*-Butyl (3*S*,α*R*)-3-[*N*-allyl-*N*-(α-methyl-4''-methoxybenzyl)amino]-3-(2'-*N*,*N*-diallylamino-5'-bromophenyl)propanoate 7**



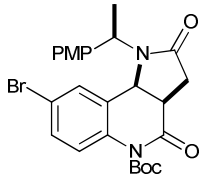
BuLi (2.3 M in hexanes, 29.2 mL, 68.7 mmol) was added dropwise to a solution of (*R*)-*N*-allyl-*N*-(α-methyl-4-methoxybenzyl)amine (13.1 g, 68.7 mmol, >99:1 er) in THF (200 mL) at –78 °C and the resultant mixture was stirred at –78 °C for 30 min. A solution of **5** (16.3 g, 42.9 mmol, >99:1 dr) in THF (200 mL) at –78 °C was added dropwise via cannula. The reaction mixture was stirred for 2 h at –78 °C then satd aq NH_4Cl (10 mL) was added. The resultant mixture was washed with 10% aq citric acid (2 × 150 mL) and the combined aqueous layers were extracted with Et_2O (200 mL). The combined organic extracts were then washed sequentially with satd aq $NaHCO_3$ (200 mL) and brine (100 mL), then dried and concentrated *in vacuo* to give **7** as a brown oil (25.0 g, quant, >99:1 dr). Purification of an aliquot via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 4:1) gave an analytical sample of **7** as a pale yellow oil (>99:1 dr); $C_{31}H_{41}BrN_2O_3$ requires C, 65.4; H, 7.3; N, 4.9%; found C, 65.45; H, 7.3; N, 4.9%; $[\alpha]_D^{20}$ –5.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3075, 2977, 2931, 2834 (C–H), 1727 (C=O), 1641, 1610, 1584 (C=C); δ_H (400 MHz, $CDCl_3$) 1.25 (3H, d, *J* 6.6, C(α)*Me*), 1.36 (9H, s, C*Me*$_3$), 2.54 (1H, dd, *J* 15.2, 6.3, C(2)H_A), 2.86 (1H, dd, *J* 15.2, 8.3, C(2)H_B), 3.13–3.23 (1H, m, NCH_AH$_B$CH=CH$_2$), 3.30–3.39 (1H, m, NCH$_A$$H_B$CH=CH$_2$), 3.47–3.64 (4H, m, N(C$H_2$CH=CH$_2$)$_2$), 3.80 (3H, s, O*Me*), 3.89 (1H, q, *J* 6.6, C(α)*H*), 4.92–5.20 (7H, m, C(3)*H*, NCH$_2$CH=CH_2, N(CH$_2$CH=CH_2)$_2$), 5.72–5.88 (3H, m, NCH$_2$C*H*=CH$_2$, N(CH$_2$C*H*=CH$_2$)$_2$), 6.84 (1H, d, *J* 8.7, C(3'')*H*, C(5'')*H*), 6.96 (1H, d, *J* 8.6, C(3')*H*), 7.28 (2H, d, *J* 8.7, C(2'')*H*, C(6'')*H*), 7.31 (1H, dd, *J* 8.6, 2.5, C(4')*H*), 7.67 (1H, d, *J* 2.5, C(6')); δ_C (100 MHz, $CDCl_3$) 15.8 (C(α)*Me*), 28.0 (C*Me*$_3$), 39.9 (*C*(2)), 48.8 (N*C*H$_2$CH=CH$_2$), 53.6 (*C*(3)), 55.2 (O*Me*), 56.0 (*C*(α)), 56.9 (N(*C*H$_2$CH=CH$_2$)$_2$), 80.2 (*C*Me$_3$), 113.2 (*C*(3''), *C*(5'')), 114.6 (NCH$_2$CH=*C*H$_2$), 117.4 (*Ar*), 118.1 (N(CH$_2$CH=*C*H$_2$)$_2$), 125.6 (*C*(3')), 128.7 (*C*(2''), *C*(6'')), 130.0 (*C*(4')), 132.1 (*C*(6')), 134.5 (N(CH$_2$*C*H=CH$_2$)$_2$), 136.7 (*Ar*), 139.8 (NCH$_2$*C*H=CH$_2$), 141.9, 148.9 (*Ar*), 158.2 (*C*(4'')), 171.2 (*C*(1)); *m*/*z* (ESI$^+$) 571 ([M(^{81}Br)+H]$^+$, 100%), 569 ([M(^{79}Br)+H]$^+$, 95%); HRMS (ESI$^+$) $C_{31}H_{42}{}^{79}BrN_2O_3^+$ ([M(^{79}Br)+H]$^+$) requires 569.2373; found 569.2367.

***tert*-Butyl (2*R*,3*S*,α*R*)-2-(2'-methoxy-2'-oxoethyl)-3-[*N*-allyl-*N*-(α-methyl-4'''-methoxybenzyl)amino]-3-(2''-*N*,*N*-diallylamino-5''-bromophenyl)propanoate 8**



BuLi (2.3 M in hexane, 27.4 mL, 64.4 mmol) was added dropwise to a solution of $^{i}Pr_2NH$ (9.02 mL, 64.5 mmol) in THF (200 mL) at 0 °C. The resultant mixture was stirred at 0 °C for 15 min then cooled to –78 °C and stirred at –78 °C for 30 min. A solution of **7** (24.5 g, 42.9 mmol, >99:1 dr) in THF (150 mL) at –78 °C was added dropwise via canula and the resultant mixture was stirred at –78 °C for 1 h. Methyl bromoacetate (12.2 mL, 128 mmol) was then added dropwise and the resultant mixture was allowed to warm to rt over 16 h. Satd aq NH_4Cl (10 mL) was then added and the reaction mixture was washed with 10% aq citric acid (2 × 100 mL). The combined aqueous layers were extracted with Et_2O (100 mL) and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (200 mL) and brine (200 mL), then dried and concentrated *in vacuo* to give **8** in >98:2 dr. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 83:17) gave **8** as a yellow oil (27.5 g, 81%, >98:2 dr); $[\alpha]_D^{20}$ –47.5 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3076, 2977, 2951, 2835 (C–H), 1741 (C=O), 1641, 1610, 1585 (C=C); δ_H (400 MHz, $CDCl_3$) 1.08 (3H, d, *J* 6.6, C(α)*Me*), 1.49 (9H, s, C*Me*$_3$), 2.17 (1H, dd, *J* 15.7, 3.5, C(1')H_A), 2.52 (1H, dd, *J* 15.7, 11.1, C(1')H_B), 3.09–3.25 (2H, m, NCH_2CH=CH$_2$), 3.43–3.64 (5H, m, C(2)*H*, N(CH_2CH=CH$_2$)$_2$), 3.61 (3H, s, CO_2Me), 3.77 (3H, s, ArO*Me*), 4.05 (1H, q, *J* 6.6, C(α)*H*), 4.82–4.97 (3H, m, C(3)*H*, NCH$_2$CH=CH_2), 5.10–5.21 (4H, m, N(CH$_2$CH=CH_2)$_2$), 5.64–5.89 (3H, m, NCH$_2$C*H*=CH$_2$, N(CH$_2$C*H*=CH$_2$)$_2$), 6.76 (2H, d, *J* 8.8, *C*(3''')*H*, *C*(5''')*H*), 7.03 (1H, d, *J* 8.6, C(3'')*H*), 7.13 (2H, d, *J* 8.8, *C*(2''')*H*, *C*(6''')*H*), 7.36 (1H, dd, *J* 8.6, 2.5, C(4'')*H*), 7.49 (1H, d, *J* 2.5, C(6'')*H*); δ_C (100 MHz, $CDCl_3$) 18.7 (C(α)*Me*), 28.0 (C*Me*$_3$), 35.7 (*C*(1')), 46.3 (*C*(2)), 49.9 (NCH_2CH=CH$_2$), 51.7 (CO_2Me), 55.2 (ArO*Me*), 56.3 (*C*(α)), 57.1 (N(*C*H$_2$CH=CH$_2$)$_2$), 57.4 (*C*(3)), 80.8 (*C*Me$_3$), 113.1 (*C*(3'''), *C*(5''')), 114.9 (NCH$_2$CH=*C*H$_2$), 117.7 (*Ar*), 118.8 (N(CH$_2$CH=*C*H$_2$)$_2$), 126.3 (*C*(3'')), 128.9 (*C*(2'''), *C*(6''')), 130.5 (*Ar*), 132.1 (*C*(6'')), 133.7 (N(CH$_2$*C*H=CH$_2$)$_2$), 137.0, 137.4 (*Ar*), 138.6 (NCH$_2$*C*H=CH$_2$), 150.1 (*Ar*), 158.1 (*C*(4''')), 171.8, 173.4 (*C*(1), *C*(2')); *m*/*z* (ESI^+) 643 ([M(^{81}Br)+H]$^+$, 100%), 641 ([M(^{79}Br)+H]$^+$, 95%); HRMS (ESI^+) $C_{34}H_{46}{}^{79}BrN_2O_5^+$ ([M(^{79}Br)+H]$^+$) requires 641.2585; found 641.2590.

(3a*R*,9b*S*,α*R*)-*N*(1)-(4'-Methoxy-α-methylbenzyl)-5-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2,4-dione 11

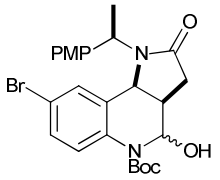


Step 1: $Pd(PPh_3)_4$ (357 mg, 0.31 mmol) was added to a stirred, degassed solution of **8** (3.97 g, 6.19 mmol, >98:2 dr) and DMBA (8.68 g, 55.7 mmol) in CH_2Cl_2 (80 mL) under argon and the resultant mixture was stirred at 35 °C for 16 h. Additional $Pd(PPh_3)_4$ (357 mg, 0.31 mmol) was then added and the resultant mixture was stirred at 35 °C for 16 h. The reaction mixture was then concentrated *in vacuo* and the residue was dissolved in Et_2O (200 mL). The resultant solution was washed with satd aq K_2CO_3 (2 × 100 mL) and the combined aqueous layers were extracted with Et_2O (2 × 100 mL). The combined organic extracts were washed with 3.0 M aq HCl (5 × 50 mL) and 2.0 M aq NaOH was added to the combined aqueous layers until pH >10 was achieved. The aqueous layer was then extracted with $CHCl_3$/IPA (3:1, 3 × 50 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give **9** as a yellow oil (3.97 g, >98:2 dr); δ_H (400 MHz, $CDCl_3$) [selected peaks] 2.23 (1H, dd, *J* 16.9, 4.6, C(1')H_A), 2.42 (1H, dd, *J* 16.9, 4.4, C(1')H_B), 3.34 (1H, app dt, *J* 9.5, 4.7, C(2)*H*), 3.96 (1H, d, *J* 9.5, C(3)*H*), 6.37 (1H, d, *J* 8.5, *Ar*), 6.96 (1H, d, *J* 2.4, *Ar*).

Step 2: $PhCO_2H$ (76 mg, 0.62 mmol) was added to a solution of **9** (3.97 g, >98:2 dr) in PhMe (50 mL). The resultant solution was heated at reflux for 16 h, then allowed to cool to rt and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (100 mL) and the resultant solution was washed with satd aq K_2CO_3 (2 × 50 mL). The combined aqueous layers were extracted with CH_2Cl_2 (50 mL) and the combined organic extracts were then dried and concentrated *in vacuo* to give **10** as a brown solid (1.72 g, >99:1 dr). An aliquot was purified by recrystallisation (PhMe) to give an analytical sample of **10** as a white solid; $C_{20}H_{19}BrN_2O_3$ requires C, 57.8; H, 4.6; N, 6.75%; found C, 57.8; H, 4.7; N, 6.7%; mp 258–262 °C; $[\alpha]_D^{20}$ +155 (*c* 0.7 in $CHCl_3$); ν_{max} (ATR) 3228 (N–H), 3076, 2935 (C–H), 1687 (C=O); δ_H (400 MHz, $CDCl_3$) 0.99 (3H, d, *J* 7.3, C(α)*Me*), 2.79 (1H, dd, *J* 16.7, 8.1, C(3)H_A), 3.02–3.09 (1H, m, C(3a)*H*), 3.28 (1H, app d, *J* 16.7, C(3)H_B), 3.87 (3H, s, O*Me*), 4.62 (1H, d, *J* 5.3, C(9b)*H*), 5.53 (1H, q, *J* 7.3, C(α)*H*), 6.24 (1H, d, *J* 2.3, C(9)*H*), 6.80 (1H, d, *J* 8.3, C(6)*H*), 6.97 (2H, d, *J* 9.0, C(3')*H*, C(5')*H*), 7.02 (2H, d, *J* 8.7, C(2')*H*, C(6')*H*), 7.42 (1H, dd, *J* 8.7, 2.3, C(7)*H*), 9.97 (1H, s, N*H*); δ_C (100 MHz, $CDCl_3$) 17.3 (C(α)*Me*), 34.0 (*C*(3)), 38.3 (*C*(3a)), 48.5 (*C*(α)), 55.4 (O*Me*), 57.1 (*C*(9b)), 114.1 (*C*(3'), *C*(5')), 114.8 (*Ar*), 117.3 (*C*(6)), 119.2 (*Ar*), 128.8 (*C*(2'), *C*(6')), 130.2 (*Ar*), 133.4 (*C*(7)), 134.6 (*C*(9)), 136.6 (*Ar*), 158.9 (*C*(4')), 170.8, 173.3 (*C*(2), *C*(4)); *m/z* (ESI^+) 439 ([M(^{81}Br)+Na]$^+$, 95%), 437 ([M(^{79}Br)+Na]$^+$, 100%); HRMS (ESI^+) $C_{20}H_{19}{}^{79}BrN_2NaO_3^+$ ([M(^{79}Br)+Na]$^+$) requires 437.0471; found 437.0473.

Step 3: Boc_2O (1.13 g, 5.16 mmol) was added to a solution of **10** (1.72 g, >99:1 dr), Et_3N (1.31 mL, 9.38 mmol) and DMAP (57 mg, 0.50 mmol) in CH_2Cl_2 (50 mL) and the resultant mixture was stirred at 35 °C for 16 h. The reaction mixture was then washed with 1.0 M aq HCl (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (50 mL) and brine (50 mL), then dried and concentrated *in vacuo*. Purification via recrystallisation (PhMe) gave **11** as a white solid (1.19 g, 49% from **8**, >99:1 dr); mp 178–182 °C; $[\alpha]_D^{20}$ +97.7 (*c* 1.2 in $CHCl_3$); ν_{max} (ATR) 2976 (C–H), 1749, 1737 (C=O); δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 7.3, C(α)*Me*), 1.58 (9H, s, C*Me*$_3$), 2.70 (1H, dd, *J* 16.4, 7.3, C(3)H_A), 3.01–3.12 (1H, m, C(3a)*H*), 3.24 (1H, app d, *J* 16.4, C(3)H_B), 3.84 (3H, s, O*Me*), 4.50 (1H, d, *J* 5.1, C(9b)*H*), 5.50 (1H, q, *J* 7.3, C(α)*H*), 6.18 (1H, d, *J* 2.0, C(9)*H*), 6.77 (1H, d, *J* 8.7, C(6)*H*), 6.93 (2H, d, *J* 8.8, C(3')*H*, C(5')*H*), 6.98 (2H, d, *J* 8.8, C(2')*H*, C(6')*H*), 7.42 (1H, dd, *J* 8.7, 2.0, C(7)*H*); δ_C (100 MHz, $CDCl_3$) 17.3 (C(α)*Me*), 27.5 (C*Me*$_3$), 34.4 (*C*(3)), 39.4 (*C*(3a)), 48.3 (*C*(α)), 55.4 (O*Me*), 56.9 (*C*(9b)), 86.1 (*C*Me$_3$), 114.1 (*C*(3'), *C*(5')), 116.1 (*Ar*), 117.7 (*C*(6)), 120.6 (*Ar*), 128.7 (*C*(2'), *C*(6')), 130.1 (*Ar*), 133.2 (*C*(7)), 134.8 (*C*(9)), 136.1 (*Ar*), 150.4 (N*C*O), 159.0 (*C*(4')), 167.4, 172.9 (*C*(2), *C*(4)); *m*/*z* (ESI^+) 539 ([M(^{81}Br)+Na]$^+$, 95%), 537 ([M(^{79}Br)+Na]$^+$, 100%); HRMS (ESI^+) $C_{25}H_{27}{}^{79}BrN_2NaO_5^+$ ([M(^{79}Br)+Na]$^+$) requires 537.0996; found 537.0998.

(3a*R*,4*R*,9b*S*,α*R*)- or (3a*R*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4'-methoxybenzyl)-4-hydroxy-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 12[3]

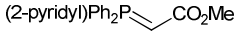


$LiAl(O^tBu)_3H$ (659 mg, 2.59 mmol) was added portionwise to a solution of **11** (891 mg, 1.72 mmol, >99:1 dr) in THF (20 mL) at 0 °C and the resultant mixture was stirred at 0 °C for 1 h. H_2O (1 mL) was then added and the reaction mixture was diluted with EtOAc (20 mL) and stirred at rt for 30 min, then filtered through Celite (eluent EtOAc/Et_3N, 100:1, 100 mL). The filtrate was then concentrated *in vacuo* to give **12** as a white foam (900 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ +67.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3311 (O–H), 2976, 2933, 2838 (C–H), 1699, 1665 (C=O); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, s, C(α)*Me*), 1.45 (9H, s, C*Me*$_3$), 2.51 (1H, d, *J* 15.4, C(3)H_A), 2.75–2.90 (2H, m, C(3)H_B, C(3a)*H*), 3.83 (3H, s, O*Me*), 4.39 (1H, d, *J* 7.3, C(9b)*H*), 5.30 (1H, q, *J* 7.1, C(α)*H*), 5.78 (1H, s, C(4)*H*), 6.35 (1H, d, *J* 2.2, C(9)*H*), 6.91 (2H, d, *J* 8.8, C(3'')*H*, C(5'')*H*), 6.97 (2H, d, *J* 8.8, C(2'')*H*, C(6'')*H*), 7.21 (1H, d, *J* 8.5, C(6)*H*), 7.36 (1H, dd, *J* 8.5, 2.2, C(7)*H*); δ_C (100 MHz, $CDCl_3$) 25.3 (C(α)*Me*), 28.2 (C*Me*$_3$), 36.0 (*C*(3)), 42.1 (*C*(3a)), 49.4 (*C*(α)), 55.4 (O*Me*), 56.4 (*C*(9b)), 81.8 (*C*(4)), 82.3

[3] Compound **12** was isolated as a single diastereoisomer of unknown configuration at C(4).

(*C*Me$_3$), 113.9 (*C*(3′), *C*(5′)), 116.9 (*Ar*), 127.3 (*C*(6)), 129.1 (*C*(2′), *C*(6′)), 129.9, 130.4 (*Ar*), 131.9 (*C*(7)), 133.5 (*C*(9)), 136.6 (*Ar*), 152.5 (*C*O$_2$^{t}Bu), 158.9 (*C*(4′)), 173.3 (*C*(2)); *m*/*z* (ESI$^+$) 541 ([M(^{81}Br)+Na]$^+$, 100%), 539 ([M(^{79}Br)+Na]$^+$, 95%); HRMS $C_{25}H_{29}{}^{79}BrN_2NaO_5^+$ ([M(^{79}Br)+Na]$^+$) requires 539.1152; found 539.1158.

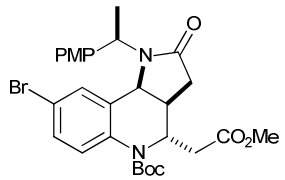
Methyl 2-[diphenyl(pyridin-2-yl)phosphoranylidene]acetate 13



Step 1: Methyl bromoacetate (1.89 mL, 19.9 mmol) was added dropwise to a solution of diphenyl-2-pyridylphosphine (5.26 g, 19.9 mmol) in PhMe (50 mL) and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then filtered to collect the white precipitate, which was then washed with cold PhMe (20 mL). The filtrate was allowed to stand at rt for 16 h during which time a second crop of crystals formed. Both crops of crystals were then combined to give (2-methoxy-2-oxoethyl)diphenyl-2-pyridylphosphonium bromide as a white crystalline solid (6.87 g, 83%); mp 162–168 °C; ν_{max} (ATR) 2802, 2738 (C–H), 1721 (C=O); δ_H (400 MHz, $CDCl_3$) 3.62 (3H, s, O*Me*), 5.62 (2H, d, *J* 13.5, C(2)*H*$_2$), 7.61–7.72 (5H, m, *Ar*), 7.73–7.82 (2H, m, *Ar*), 7.87–7.98 (4H, m, *Ar*), 8.05–8.13 (1H, m, *Ar*), 8.41–8.48 (1H, m, *Ar*), 8.87 (1H, d, *J* 4.6, *Ar*); δ_C (100 MHz, $CDCl_3$) 31.8 (d, *J* 59.1, *C*(2)), 53.5 (O*Me*), 117.1 (d, *J* 88.7, *Ar*), 128.2 (d, *J* 3.2, *Ar*), 130.1 (d, *J* 12.8, *Ar*), 131.9 (d, *J* 24.8, *Ar*), 134.3 (d, *J* 10.4, *Ar*), 135.2, (d, *J* 3.2, *Ar*), 138.3 (d, *J* 10.4, *Ar*), 144.1 (d, *J* 121.4, *Ar*), 151.7 (d, *J* 20.0, *Ar*), 165.3 (d, *J* 3.2, *C*(1)); δ_P (162 MHz, $CDCl_3$) 16.0.

Step 2: Phosphorane **13** was prepared, as required, by treatment of a solution of (2-methoxy-2-oxoethyl)diphenyl-2-pyridylphosphonium bromide in CH_2Cl_2 with 2.0 M aq NaOH. The aqueous layer was then extracted with CH_2Cl_2 and the combined organic extracts were dried and concentrated *in vacuo* to give **13** as a pink solid.

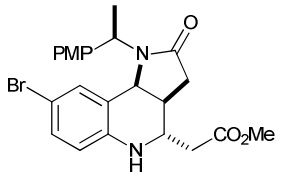
(3a*S*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4''-methoxybenzyl)-4-(2'-methoxy-2'-oxoethyl)-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 14



Phosphorane **13** (2.36 g, 7.05 mmol) was added to a solution of **12** (1.03 g, 2.35 mmol, >99:1 dr) in PhMe (50 mL) and the resultant mixture was heated at 80 °C for 72 h, then allowed to cool to rt and concentrated *in vacuo*. The residue was dissolved in EtOAc (20 mL) and the resultant solution was washed with 3.0 M aq HCl (6 × 10 mL). The combined aqueous layers were extracted with EtOAc (10 mL) and the combined organic extracts were dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 50:50) gave **14** as a colourless oil (1.01 g, 75%, >99:1 dr); $[\alpha]_D^{20}$ +109.8 (*c* 1.1 in $CHCl_3$);

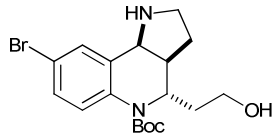
ν_{max} (ATR) 2978, 2935, 2838 (C–H), 1739, 1696 (C=O); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, d, *J* 7.3, C(α)*Me*), 1.49 (9H, s, C*Me*$_3$), 2.11 (2H, d, *J* 7.6, C(1')*H*$_2$), 2.60–2.76 (2H, m, C(3)*H*$_A$, C(3a)*H*), 2.85–2.97 (1H, m, C(3)*H*$_B$), 3.59 (3H, s, CO_2*Me*), 3.84 (3H, s, ArO*Me*), 4.36 (1H, d, *J* 7.8, C(9b)*H*), 4.78–4.91 (1H, m, C(4)*H*), 5.42 (1H, q, *J* 7.3, C(α)*H*), 6.40 (1H, d, *J* 2.3, C(9)*H*), 6.93 (2H, d, *J* 8.8, C(3")*H*, C(5")*H*), 7.00 (2H, d, *J* 8.8, C(2")*H*, C(6")*H*), 7.25 (1H, br s, C(6)*H*), 7.41 (1H, dd, *J* 8.6, 2.3, C(7)*H*); δ_C (100 MHz, $CDCl_3$) 17.1 (C(α)*Me*), 28.2 (C*Me*$_3$), 38.2 (*C*(3)), 38.9 (*C*(1')), 39.7 (*C*(3a)), 49.4 (*C*(α)), 51.8 (CO_2*Me*), 55.3 (ArO*Me*), 55.8, 56.2 (*C*(4), *C*(9b)), 81.9 (*C*Me$_3$), 113.8 (*C*(3"), *C*(5")), 117.1 (*C*(8)), 128.1 (*C*(6)), 129.1 (*C*(2"), *C*(6")), 130.0, 131.0 (*Ar*), 132.0 (*C*(7)), 133.4 (*C*(9)), 137.6 (*Ar*), 152.5, 158.9 (*C*(4"), N*C*O), 170.5, 173.5 (*C*(2), *C*(2')); *m*/*z* (ESI$^+$) 597 ([M(^{81}Br)+Na]$^+$, 95%), 595 ([M(^{79}Br)+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{33}{}^{79}BrN_2NaO_6^+$ ([M(^{79}Br)+Na]$^+$) requires 595.1414; found 595.1412.

(3a*S*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4''-methoxybenzyl)-4-(2'-methoxy-2'-oxoethyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 15



A solution of **14** (162 mg, 0.28 mmol, >99:1 dr) in methanolic HCl (1.25 M, 4 mL) was stirred at rt for 16 h, then concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (20 mL) and the resultant solution was washed with 2.0 M aq NaOH (2 × 10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL) and the combined organic extracts were then dried and concentrated *in vacuo*. Purification via recrystallisation ($CHCl_3$/hexane) gave **15** as a yellow solid (98 mg, 73%, >99:1 dr); mp 206–209 °C; $[\alpha]_D^{20}$ +16.3 (*c* 0.7 in $CHCl_3$); ν_{max} (ATR) 3392, 3318 (N–H), 2952, 2935, 2938 (C–H), 1735, 1680 (C=O); δ_H (400 MHz, $CDCl_3$) 1.20 (3H, d, *J* 7.1, C(α)*Me*), 2.09–2.18 (1H, m, C(3a)*H*), 2.26–2.42 (2H, m, C(3)*H*$_A$, C(1')*H*$_A$), 2.63 (1H, dd, *J* 16.3, 2.4, C(1')*H*$_B$), 2.71 (1H, dd, *J* 16.7, 6.8, C(3)*H*$_B$), 3.71 (3H, s, CO_2*Me*), 3.82 (3H, s, ArO*Me*), 4.50 (1H, d, *J* 5.1, C(9b)*H*), 4.96 (1H, br s, C(4)*H*), 5.46 (1H, q, *J* 7.1, C(α)*H*), 6.28 (1H, d, *J* 2.0, C(9)*H*), 6.21 (1H, d, *J* 2.2, N*H*), 6.42 (1H, d, *J* 8.6, C(6)*H*), 6.92 (2H, d, *J* 8.7, C(3")*H*, C(5")*H*), 7.06 (2H, d, *J* 8.7, C(2")*H*, C(6")*H*), 7.12 (1H, dd, *J* 8.6, 2.0, C(7)*H*); δ_C (100 MHz, $CDCl_3$) 17.3 (C(α)*Me*), 35.6 (*C*(3a)), 35.7 (*C*(3)), 38.0 (*C*(1')), 48.0 (*C*(4)), 48.7 (*C*(α)), 52.1 (CO_2*Me*), 55.3 (ArO*Me*), 56.1 (*C*(9b)), 108.0 (*Ar*), 114.0 (*C*(3"), *C*(5")), 116.4 (*C*(6)), 117.4 (*C*(8)), 128.5 (*C*(2"), *C*(6")), 131.4 (*Ar*), 132.5 (*C*(7)), 134.9 (*C*(9)), 143.2 (*Ar*), 158.7 (*C*(4")), 172.4, 173.3 (*C*(2), *C*(2')); *m*/*z* (ESI$^+$) 497 ([M(^{81}Br)+Na]$^+$, 95%), 495 ([M(^{79}Br)+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{23}H_{25}{}^{79}BrN_2NaO_4^+$ ([M(^{79}Br)+Na]$^+$) requires 495.0890; found 495.0889.

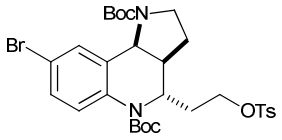
(3a*R*,4*S*,9b*S*)-4-(2'-Hydroxyethyl)-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 17



Step 1: A solution of CAN (5.64 g, 10.3 mmol) in H_2O (30 mL) was added to a solution of **14** (1.97 g, 3.44 mmol, >99:1 dr) in MeCN (30 mL) and the resultant mixture was stirred at rt for 1 h. The MeCN was then removed *in vacuo* and the residue was diluted with $CHCl_3$/IPA (3:1, 100 mL). The resultant mixture was washed with brine (2 × 50 mL) and the combined aqueous layers were extracted with $CHCl_3$/IPA (3:1, 2 × 50 mL). The combined organic extracts were then dried and concentrated *in vacuo* to give **16** as a pale yellow oil (1.95 g, >99:1 dr); δ_H (400 MHz, $CDCl_3$) [selected peaks] 1.50 (9H, s, C*Me*$_3$), 3.05 (1H, app ddd, *J* 18.3, 9.4, 1.4, C(3a)*H*), 3.65 (3H, s, CO_2*Me*), 4.70 (1H, d, *J* 8.9, C(9b)*H*), 5.05 (1H, app t, *J* 7.5, C(4)*H*), 6.73 (1H, s, N*H*), 7.32 (1H, d, *J* 2.2, C(9)*H*), 7.36 (1H, dd, *J* 8.9, 2.2, C(7)*H*), 7.47 (1H, br d, *J* 8.9, C(6)*H*).

Step 2: BH_3·THF (1.0 M in THF, 34.0 mL, 34.0 mmol) was added dropwise to a solution of **16** (1.95 g, >99:1 dr) in THF (35 mL) at 0 °C. The resultant mixture was heated at reflux for 4 h then allowed to cool to rt before being cooled further to 0 °C. Satd aq K_2CO_3 (20 mL) and EtOAc (20 mL) were then carefully added and the resultant mixture was heated at 60 °C for 1 h. The reaction mixture was then allowed to cool to rt and washed with satd aq K_2CO_3 (2 × 30 mL). The combined aqueous layers were extracted with EtOAc (50 mL) then the organic extract was dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc/Et_3N, 66:34:1) gave **17**·BH_3 as a white foam (554 mg, >99:1 dr). Further elution ($CHCl_3$/MeOH/Et_3N, 95:5:1) gave **17** as a pale yellow oil (288 mg, 21% from **14**, >99:1 dr); $C_{18}H_{25}BrN_2O_3$ requires C, 54.4; H, 6.3; N, 7.05%; found C, 54.4; H, 6.3; N, 6.9%; $[\alpha]_D^{20}$ +125 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3310 (O–H, N–H), 2974, 2934, 2878, 2730 (C–H), 1694 (C=O); δ_H (400 MHz, $CDCl_3$) 1.40–1.56 (1H, m, C(1')H_A), 1.45 (9H, s, C*Me*$_3$), 1.56–1.70 (2H, m, C(3)H_A, C(1')H_B), 2.00–2.10 (1H, m, C(3)H_B), 2.52 (1H, app q, *J* 8.8, C(3a)*H*), 2.76–2.86 (1H, m, C(2)H_A), 2.86–2.95 (1H, m, C(2)H_B), 3.23 (1H, br s, O*H*), 3.43–3.54 (2H, m, C(2')H_2), 4.24 (1H, d, *J* 8.8, C(9b)*H*), 4.65–4.74 (1H, m, C(4)*H*), 7.24–7.34 (2H, m, C(6)*H*, C(7)*H*), 7.42 (1H, s, C(9)*H*); δ_C (100 MHz, $CDCl_3$) 28.3 (C*Me*$_3$), 31.6 (*C*(3)), 34.8 (*C*(1')), 43.7 (*C*(3a)), 45.6 (*C*(2)), 52.9 (*C*(4)), 55.7 (*C*(9b)), 58.8 (*C*(2')), 82.0 (*C*Me$_3$), 117.3, 126.5, 130.5, 132.1, 133.2, 134.8 (*Ar*), 154.9 (N*C*O); *m/z* (FI$^+$) 398 ([M(^{81}Br)]$^+$, 95%), 396 ([M(^{79}Br)]$^+$, 100%); HRMS (FI$^+$) $C_{18}H_{25}{}^{79}BrN_2O_3{}^+$ ([M(^{79}Br)]$^+$) requires 396.1043; found 396.1049. A solution of **17**·BH_3 (554 mg, 1.34 mmol) in MeOH (30 mL) was heated at reflux for 48 h then allowed to cool to rt and concentrated *in vacuo* to give **17** as a colourless oil (525 mg, 39% from **14**, >99:1 dr).

(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-[2'-(4''-toluenesulfonyloxy)ethyl]-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 19

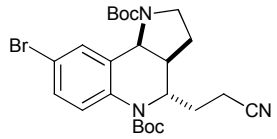


Step 1: Boc_2O (148 mg, 0.68 mmol), DMAP (8 mg, 62 μmol) and Et_3N (0.26 mL, 1.85 mmol) were added sequentially to a solution of **17** (245 mg, 0.62 mmol, >99:1 dr) in CH_2Cl_2 (10 mL) and the resultant mixture was stirred at 35 °C for 5 h. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and the resultant solution was washed with 1.0 M aq HCl (10 mL). The aqueous layer was extracted with $CHCl_3$/IPA (3:1, 2 × 20 mL) and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried and concentrated *in vacuo* to give **18** (300 mg, >99:1 dr); δ_H (400 MHz, $CDCl_3$) 1.27–1.89 (3H, m, C(3a)*H*, C(1')H_2), 1.52 (18H, s, 2 × CMe_3), 2.00–2.15 (1H, br m, C(3)H_A), 2.40–2.58 (1H, m, C(3)H_B), 3.27–3.49 (2H, br m, C(2)H_2), 3.50–3.69 (2H, br m, C(2')H_2), 4.62–5.17 (2H, br m, C(4)*H*, C(9b)*H*), 7.21–7.43 (2H, br m, C(6)*H*, C(7)*H*), 8.09 (1H, s, C(9)*H*).

Step 2: TsCl (141 mg, 0.74 mmol), DMAP (8 mg, 62 μmol) and Et_3N (0.26 mL, 1.85 mmol) were added sequentially to a solution of **18** (300 mg, >99:1 dr) in CH_2Cl_2 (10 mL) and the resultant mixture was stirred at 35 °C for 16 h. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and was washed with 1.0 M aq HCl (10 mL). The aqueous layer was extracted with $CHCl_3$/IPA (3:1, 2 × 20 mL) and the combined organic extracts were washed sequentially with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O/Et_3N, 50:50:1) gave **19** as a colourless oil (275 mg, 69% from **17**, >99:1 dr); $[\alpha]_D^{20}$ –57.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2976, 2933 (C–H), 1693 (C=O); δ_H (500 MHz, PhMe-d_8, 363K) 1.29–1.30 (2H, m, C(1')H_2), 1.45 (9H, s, CMe_3), 1.50 (9H, s, CMe_3), 1.54–1.66 (2H, m, C(3)H_2), 1.79–1.89 (1H, m, C(3a)*H*), 2.04 (3H, s, C(4'')*Me*), 2.99–3.13 (1H, m, C(2)H_A), 3.18–3.34 (1H, m, C(2)H_B), 3.80–3.90 (1H, m, C(2')H_A), 3.90–3.99 (1H, m, C(2')H_B), 4.47–4.60 (1H, m, C(4)*H*), 4.86 (1H, br d, *J* 6.9, C(9b)*H*), 6.88 (2H, d, *J* 8.4, C(3'')*H*, C(5'')*H*), 7.15 (1H, dd, *J* 8.8, 2.2, C(7)*H*), 7.39 (1H, d, *J* 8.8, C(6)*H*), 7.68 (2H, d, *J* 8.4, C(2'')*H*, C(6'')*H*), 8.32 (1H, br s, C(9)*H*); δ_C (125 MHz, PhMe-d_8, 363K) 21.0 (C(4'')*Me*), 27.9 (*C*(3)), 28.2, 28.5 (2 × CMe_3), 32.1 (*C*(1')), 42.6 (*C*(3a)), 45.6 (*C*(2)), 52.3 (*C*(4)), 54.3 (*C*(9b)), 67.0 (*C*(2')), 79.8, 81.4 (2 × *C*Me_3), 117.7 (*Ar*), 127.1 (*C*(6)), 129.7 (*C*(3''), *C*(5'')), 130.6 (*C*(7)), 132.2 (*Ar*), 133.9 (*C*(9)), 134.7, 135.1, 144.1 (*Ar*), 153.8, 155.2 (2 × N*C*O);[4] *m*/*z* (ESI^+) 675 ([M(^{81}Br)+Na]$^+$, 100%), 673 ([M(^{79}Br)+Na]$^+$, 95%); HRMS (ESI^+) $C_{30}H_{39}{}^{79}BrN_2NaO_7S^+$ ([M(^{79}Br)+Na]$^+$) requires 673.1554; found 673.1559.

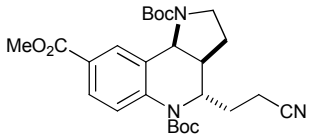
[4] The remaining peak in the ^{13}C NMR spectrum, corresponding to *C*(2'') and *C*(6'') within **19**, was obscured by the resonances corresponding to PhMe-d_8.

(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-(2'-cyanoethyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 20



NaCN (28 mg, 0.58 mmol) was added to a solution of **19** (252 mg, 0.39 mmol, >99:1 dr) in NMP (4 mL) and the resultant mixture was stirred at 60 °C for 16 h.[5] The reaction mixture was then diluted with EtOAc (20 mL) and washed with H_2O (2 × 10 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL) and the combined organic extracts were dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc/Et_3N, 83:17:1) gave **20** as a colourless oil (167 mg, 86%, >99:1 dr); $C_{24}H_{32}BrN_3O_4$ requires C, 56.9; H, 6.4; N, 8.3%; found C, 57.1; H, 6.5; N, 8.3%; $[\alpha]_D^{20}$ –61.3 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2976, 2933 (C–H), 2247 (C≡N), 1693 (C=O); δ_H (500 MHz, PhMe-d_8, 363K) 0.81–0.90 (1H, m, C(1')H_A), 0.98–1.09 (1H, m, C(1')H_B), 1.29 (9H, s, CMe_3), 1.34 (9H, s, CMe_3), 1.38–1.68 (5H, m, C(3)H_2, C(3a)*H*), C(2')H_2), 1.51–1.68 (1H, m, C(2)H_A), 2.86–2.95 (1H, m, C(2)H_B), 4.21 (1H, app d, *J* 10.7, C(4)*H*), 4.68 (1H, d, *J* 6.3, C(9b)*H*), 7.03 (1H, dd, *J* 8.8, 1.9, C(7)*H*), 7.25 (1H, d, *J* 8.8, C(6)*H*), 8.15 (1H, br s, C(9)*H*); δ_C (125 MHz, PhMe-d_8, 363K) 9.3 (*C*(2')), 23.1 (*C*(3)), 23.3, 23.6 (2 × CMe_3), 40.5 (*C*(3a)), 49.3, 49.6 (*C*(4), *C*(9b)), 72.6, 74.9 (2 × *C*Me_3), 113.0, 113.3, 122.3, 125.8, 127.1, 128.9, 129.3 (*Ar*, *C*(3')), 149.1 (2 × N*C*O);[6] *m*/*z* (ESI$^+$) 530 ([M(^{81}Br)+Na]$^+$, 95%), 528 ([M(^{79}Br)+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{24}H_{32}{}^{79}BrN_3NaO_4^+$ ([M(^{79}Br)+Na]$^+$) requires 528.1468; found 528.1475.

(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-(2'-cyanoethyl)-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 21

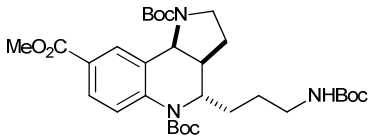


$Pd(OAc)_2$ (15 mg, 68 μmol) and Xantphos (79 mg, 0.14 mmol) were added sequentially to a round bottomed flask containing **20** (342 mg, 0.68 mmol, >99:1 dr). Degassed Et_3N (5 mL) and degassed MeOH (1 mL) were then added sequentially.[7] The resultant mixture was stirred at rt and the apparatus was evacuated and refilled with N_2 three times; the apparatus was then evacuated and refilled with CO three times. The reaction mixture was stirred vigorously under CO (1 atm) at 70 °C for 16 h, then allowed to cool to rt and filtered through a pad

[5] For an example of the use of NMP as the solvent in displacement reactions with NaCN, see: Davies, S. G.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2279.
[6] The remaining peaks in the ^{13}C NMR spectrum, corresponding to *C*(2) and *C*(1') within **20**, were obscured by the resonances corresponding to PhMe-d_8.
[7] These solvents were dried over 4 Å molecular sieves and degassed using the vacuum-refill technique under N_2 gas.

of Celite (eluent MeOH/Et_3N, 100:1). The filtrate was then concentrated *in vacuo* and the residue was resubjected to the reaction conditions twice more, using the procedure described above. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc/Et_3N, 75:25:1) gave **21** as a white foam (228 mg, 69%, >99:1 dr); $[\alpha]_D^{20}$ –39.1 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2977, 2953, 2933 (C–H), 2247 (C≡N), 1717, 1693 (C=O); δ_H (500 MHz, PhMe-d_8, 363K) 1.07–1.17 (1H, m, C(1')H_A), 1.23–1.35 (1H, m, C(1')H_B), 1.45 (9H, s, CMe_3), 1.50 (9H, s, CMe_3), 1.52–1.71 (2H, m, C(3)H_2), 1.74–1.96 (3H, m, C(3a)*H*, C(2')H_2), 3.11 (1H, br td, *J* 9.6, 3.5, C(2)H_A), 3.31–3.42 (1H, br m, C(2)H_B), 3.63 (3H, s, O*Me*), 4.39–4.45 (1H, br m, C(4)*H*), 4.97 (1H, d, *J* 7.6, C(9b)*H*), 7.64 (1H, d, *J* 8.8, C(6)*H*), 7.91 (1H, dd, *J* 8.8, 1.6, C(7)*H*), 8.80 (1H, m, C(9)*H*); δ_C (125 MHz, PhMe-d_8, 363 K) 13.8 (*C*(2')), 27.4, 27.5, 27.8, 28.1, 28.2 (*C*(3), *C*(3a), *C*(1'), 2 × CMe_3), 45.0 (*C*(2)), 50.8 (O*Me*), 53.9 (*C*(9b)), 54.5 (*C*(4)), 79.6, 81.6 (2 × *C*Me_3), 118.0 (*C*(3')), 126.7 (*C*(6)), 127.8 (*Ar*), 128.7 (*C*(7)), 129.2 (*Ar*), 132.4 (*C*(9)), 138.8 (*Ar*), 153.7, 165.7 (2 × N*C*O), 175.3 (*C*O_2Me); *m/z* (ESI^+) 508 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{26}H_{35}N_3NaO_6^+$ ($[M+Na]^+$) requires 508.2418; found 508.2414.

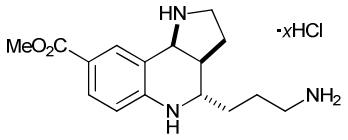
(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-[3'-(*N*-*tert*-butoxycarbonylamino)propyl]-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 22



Boc_2O (199 mg, 0.91 mmol) was added to a solution of $NiCl_2 \cdot 6H_2O$ (21.7 mg, 91 μmol) and **21** (222 mg, 0.45 mmol, >99:1 dr) in dry MeOH (5 mL) and the resultant mixture was stirred at 0 °C for 5 min. $NaBH_4$ (241 mg, 6.38 mmol) was then added portionwise over a period of 15 min, during which time a fine black precipitate formed and a gas was evolved. The reaction mixture was stirred at 0 °C for 1 h then diethylenetriamine (49 μL, 0.46 mmol) was added and the resultant mixture was allowed to stir for 30 min at 0 °C before being concentrated *in vacuo*. The residue was dissolved in EtOAc (30 mL) and the resultant solution was washed with satd aq $NaHCO_3$ (2 × 10 mL). The combined aqueous layers were extracted with EtOAc (30 mL) and the combined organic extracts were then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O/Et_3N, 75:25:1) gave **22** as a colourless oil (244 mg, 91%, >99:1 dr); $[\alpha]_D^{20}$ –9.3 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3362 (N–H), 2977, 2933 (C–H), 1695 (C=O); δ_H (400 MHz, C_6D_6) 0.87–1.05 (1H, br s, C(2')H_A), 1.05–1.18 (1H, br s, C(2')H_B), 1.71 (2H, app s, C(3)H_2), 1.39 (9H, s, CMe_3), 1.41 (9H, s, CMe_3), 1.42 (9H, s, CMe_3), 1.77–1.91 (1H, br s, C(3a)*H*), 2.69–3.32 (4H, br m, C(2)H_2, C(1')H_2), 3.51 (3H, s, O*Me*), 4.26–4.56 (2H, br m, C(3')H_2), 4.86–5.32 (2H, br m, C(4)*H*, C(9b)*H*), 7.72 (1H, d, *J* 8.6, C(6)*H*), 7.93–8.13 (1H, br m, C(7)*H*), 8.91 (1H, br s, C(9)*H*); δ_C (100 MHz, C_6D_6) [selected peaks] 26.8 (*C*(3)), 29.2 (*C*(2')), 27.8, 28.2, 28.2 (3 × CMe_3), 42.5 (*C*(3a)), 45.3 (*C*(2)), 51.1 (O*Me*), 53.9, 54.3 (*C*(4),

C(9b)), 125.0 (*C*(6)), 125.9 (*Ar*), 128.3 (*C*(7)), 129.5 (*Ar*), 132.3 (*C*(9)), 139.6 (*Ar*), 153.8, 155.6, 155.9 (3 × N*C*O), 166.0 (*C*O_2Me);[8] *m/z* (ESI$^+$) 590 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{31}H_{47}N_3NaO_8^+$ ([M+Na]$^+$) requires 612.3255; found 612.3258.

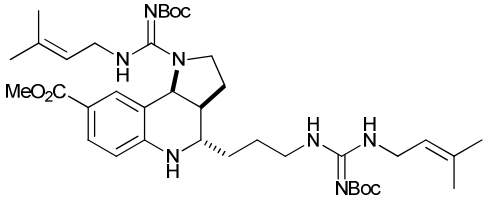
(*S*,*S*,*S*)-4-(3'-Aminopropyl)-8-(methoxycarbonyl)- 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]-quinoline·*x*HCl ["Ma's intermediate"] 23·*x*HCl



A solution of **22** (37 mg, 62 μmol, >99:1 dr) in methanolic HCl (1.25 M, 4 mL) was stirred at rt for 6 h then concentrated *in vacuo*. Methanolic HCl (1.25 M, 2 mL) was then added and the resultant mixture was concentrated *in vacuo* again to give **23**·*x*HCl as a white amorphous solid (24 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ –48.7 (*c* 0.3 in MeOH);[9] {lit.[10] $[\alpha]_D^{20}$ –49.9 (*c* 1.25 in MeOH); lit.[11] $[\alpha]_D^{18}$ –54.4 (*c* 0.29 in MeOH); lit.[12] $[\alpha]_D^{29}$ –57.7 (*c* 0.3 in MeOH)}; ν_{max} (ATR) 2950, 2892 (N–H), 2748, 2576 (C–H), 1704 (C=O); δ_H (500 MHz, MeOD-d_4) 1.67–1.79 (1H, br m, C(1')H_A), 1.81–2.01 (3H, br m, C(1')H_B, C(2')H_2), 2.12–2.23 (1H, br m, C(3)H_A), 2.39–2.54 (2H, br m, C(3)H_B, C(3a)*H*), 2.96–3.09 (2H, br m, C(3')H_2), 3.09–3.17 (1H, br m, C(4)*H*), 3.38–3.45 (2H, br m, C(2)H_2), 3.86 (3H, s, O*Me*), 4.66–4.73 (1H, br d, C(9b)*H*), 6.86 (1H, d, *J* 8.5, C(6)*H*), 7.76–7.82 (1H, br m, C(7)*H*), 8.02 (1H, d, *J* 1.3, C(9)*H*); δ_C (125 MHz, MeOD-d_4) 23.9 (*C*(2')), 28.0 (*C*(3)), 30.5 (*C*(1')), 39.4 (*C*(3a)), 40.9 (*C*(3')), 43.6 (*C*(2)), 50.9 (*C*(4)), 52.3 (O*Me*), 59.3 (*C*(9b)), 113.4 (*Ar*), 115.8 (*C*(6)), 119.3 (*Ar*), 132.8 (*C*(7)), 134.0 (*C*(9)), 151.1 (*Ar*), 168.5 (*C*O_2Me); *m/z* (ESI$^+$) 290 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{24}N_3O_2^+$ ([M+H]$^+$) requires 290.1863; found 290.1864.

[8] Some of the peaks in the ^{13}C NMR spectrum of **22** in C_6D_6 at rt are broad, and the peaks corresponding to the *C*(1'), *C*(3') and 3 × *C*Me_3 carbons were not observed in this spectrum.
[9] In our hands triamine **23**·*x*HCl was insoluble at concentrations of >3 mg/mL.
[10] Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189.
[11] Yoshitomi, Y.; Arai, H.; Makino, K.; Hamada, Y. *Tetrahedron* **2008**, *64*, 11568.
[12] Ikeda, S.; Shibuya, M.; Iwabuchi, Y. *Chem. Commun.* **2007**, 504.

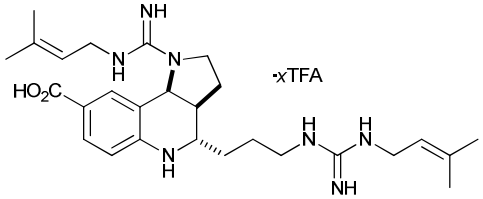
(*S*,*S*,*S*)-*N*(1)-[*N*'-(*tert*-Butoxycarbonyl)-*N*''-prenylcarbamimidoyl]-4-{3'-[*N*'-(*tert*-butoxycarbonyl)-*N*''-prenylguanidino]propyl}-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 25



Et_3N (0.38 mL, 2.75 mmol) was added to a solution of **23**·*x*HCl (92 mg, 0.23 mmol, >99:1 dr) and thiourea **24**[13] (296 mg, 1.14 mmol) in MeCN/MeOH (2:1, 7 mL) at 40 °C. A solution of $AgNO_3$ (272 mg, 1.60 mmol) in MeCN (2 mL) was added dropwise via syringe (in the dark) over a period of 30 min. The resultant mixture was stirred at 40 °C (in the dark) for 16 h. The reaction mixture was then filtered through a short pad of Celite (eluent $CHCl_3$/Et_3N, 100:1) and the filtrate was concentrated *in vacuo*. The residue was dissolved in $CHCl_3$ (20 mL) and the resultant solution was washed with H_2O (10 mL). The aqueous layer was extracted with $CHCl_3$ (20 mL) and the combined organic extracts were dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent $CHCl_3$/MeOH, 30:1) gave **25** as a colourless oil (104 mg, 64%, >99:1 dr); $[\alpha]_D^{20}$ –142.5 (*c* 0.8 in $CHCl_3$); {lit.[14] $[\alpha]_D^{20}$ –94.2 (*c* 0.28 in $CHCl_3$); lit.[15] $[\alpha]_D^{28}$ –179.1 (*c* 0.80 in $CHCl_3$); lit.[16] $[\alpha]_D$ –95.2 (*c* 0.58 in $CHCl_3$)}; ν_{max} (ATR) 3281 (N–H), 2974 (C–H), 1708, 1606 (C=O); δ_H (500 MHz, $CDCl_3$) 1.12–1.35 (2H, m, C(1')H_2), 1.49 (9H, s, CMe_3), 1.52 (9H, s, CMe_3), 1.54–1.68 (2H, m, C(2')H_2), 1.65 (6H, s, 2 × NCH_2CH=C$Me_A$$Me_B$), 1.68 (6H, s, 2 × NCH_2CH=C$Me_A$$Me_B$), 1.89–2.21 (2H, m, C(3)H_2), 2.31–2.42 (1H, m, C(3a)*H*), 3.10–3.20 (1H, m, C(3')H_A), 3.27–3.50 (4H, m, C(2)H_2, C(4)*H*, C(3')H_B), 3.67–3.93 (4H, m, 2 × NCH_2CH=CMe_2), 3.81 (3H, s, O*Me*), 5.16–5.33 (2H, m, 2 × NCH_2CH=CMe_2), 5.75 (1H, d, *J* 6.9, C(9b)*H*), 6.60 (1H, d, *J* 8.3, C(6)*H*), 7.10 (1H, br s, N*H*), 7.67 (1H, dd, *J* 8.3, 1.9, C(7)*H*), 7.97 (1H, br s, C(9)*H*), 8.95 (1H, br s, N*H*); δ_C (125 MHz, $CDCl_3$) 18.0, 18.0 (2 × NCH_2CH=C$Me_A$$Me_B$), 25.6, 25.6 (2 × NCH_2CH=C$Me_A$$Me_B$), 27.9 (*C*(3)), 28.3 (*C*(2')), 28.4, 28.5 (2 × CMe_3), 29.7 (*C*(1')), 39.4, 39.4 (*C*(3a), NCH_2CH=CMe_2), 42.5 (NCH_2CH=CMe_2), 46.8, 46.8 (*C*(2), *C*(3')), 50.5 (*C*(4)), 51.4 (O*Me*), 53.4 (*C*(9b)), 77.8, 78.3 (2 × *C*Me_3), 113.8 (*C*(6)), 118.1 (*Ar*), 119.5, 120.2 (2 × NCH_2*C*H=CMe_2), 127.8, 128.8 (*Ar*), 130.0 (*C*(7)), 131.7 (*C*(9)), 137.2, 137.3 (2 × NCH_2CH=*C*Me_2), 146.3, 159.9, 163.7 (2 × N*C*O, 2 × N*C*N), 167.4 (*C*O_2Me);[17] *m*/*z* (ESI^+) 710 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{38}H_{60}N_7O_6^+$ ($[M+H]^+$) requires 710.4600; found 710.4601.

[13] Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189.
[14] Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189.
[15] Ikeda, S.; Shibuya, M.; Iwabuchi, Y. *Chem Commun.* **2007**, 504.
[16] Badarinarayana, V.; Lovely, C. J. *Tetrahedron Lett.* **2007**, *48*, 2607.
[17] Some of the peaks in the ^{13}C NMR spectrum of **25** in $CDCl_3$ at rt are broad.

(*S*,*S*,*S*)-*N*(1)-[*N*''-Prenylcarbamimidoyl]-4-{3'-[*N*''-prenylguanidino]propyl}-8-carboxy-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline·*x*TFA [(–)-martinellic acid] 1·*x*TFA



Step 1: A solution of 0.2 M aq NaOH (2 mL) was added to a solution of **25** (39 mg, 55 μmol, >99:1 dr) in MeOH (6 mL) and the resultant mixture was heated at reflux for 16 h. The reaction mixture was then partially concentrated *in vacuo* to approximately 25% of its original volume and the residue was poured onto satd aq NH_4Cl (25 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic extracts were washed with brine (10 mL), then dried and concentrated *in vacuo*.

Step 2: Anisole (60 μL, 0.55 mmol) and TFA (0.12 mL, 1.62 mmol) were added sequentially to a solution of the residue in CH_2Cl_2 (3.5 mL) and the resultant mixture was stirred at rt for 16 h. The reaction mixture was then concentrated *in vacuo* and the residue was purified by preparative HPLC[18,19,20] to give **1**·*x*TFA as a pale yellow oil (13.3 mg, 34% from **25**, >99:1 dr); $[\alpha]_D^{20}$ –118 (*c* 0.3 in MeOH); {lit.[21] for sample isolated from natural source $[\alpha]_D$ –8.5 (*c* 0.01 in MeOH); lit.[22] $[\alpha]_D^{20}$ –122.7 (*c* 0.31 in MeOH); lit.[23] $[\alpha]_D^{29}$ –164.3 (*c* 0.14 in MeOH); lit.[24] $[\alpha]_D^{23}$ –164.8 (*c* 0.33 in MeOH)}; ν_{max}(ATR) 3338, 3207 (N–H, O–H) 2980, 2932 (C–H), 1673 (C=O), 1611, 1526, 1452; δ_H (500 MHz, DMSO-d_6) 1.35–1.52 (2H, m, C(1')H_2), 1.51–1.76 (3H, m, C(3)H_A, C(2')H_2), 1.63 (3H, s, NCH_2CH=C*Me*Me), 1.68 (3H, s, NCH_2CH=C*Me*Me), 1.69 (3H, s, NCH_2CH=C*Me*Me), 1.73 (3H, s, NCH_2CH=C*Me*Me), 2.03–2.14 (1H, m, C(3)H_B), 2.37–2.48 (1H, m, C(3a)*H*), 3.04–3.20 (2H, m, C(3')H_2), 3.27 (1H, br s, C(4)*H*), 3.33–3.43 (2H, m, C(2)H_2), 3.66–3.77 (2H, m, NCH_2CH=CMe_2), 3.79–3.87 (1H, m, NCH_AH_BCH=CMe_2), 3.88–3.89 (1H, m, NCH_AH_BCH=CMe_2), 5.13–5.20 (1H, m, NCH_2CH=CMe_2), 5.25 (1H, d, *J* 6.4, C(9b)*H*), 5.27–5.34 (1H, m, NCH_2CH=CMe_2), 6.58 (1H, d, *J* 8.5, C(6)*H*), 7.07 (1H, br s, N*H*), 7.43 (2H, br s, 2 × N*H*), 7.54 (1H, dd, *J* 8.5, 1.5, C(7)*H*), 7.51–7.62 (2H, br m, 2 × N*H*), 7.66 (1H, br s,

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[18] The authors would like to thank Veronique Gouverneur and Stefan Verhoog for their assistance with the purification of **1**·*x*TFA.

[19] Purification of **1**·*x*TFA was conducted using a SunFire™ preparative column (C_{18}, 10 μm, 10 × 250 mm) eluting with H_2O/MeOH/CF_3CO_2H (80:20:0.1 → 20:80:0.1, gradient elution) 40 mins with a flow rate of 2.50 mL/min. The detector was set to 330 nm and the major component had a rentention time of 19.1 min.

[20] Although several literature reports begin the solvent gradient in 80:20 H_2O/MeOH, this is not a suitable solvent system to load the crude material. After optimisation, it was found best to dissolve the crude sample in ~500μL of MeOH and perform purification with several ~125 μL injections.

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[22] Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189.

[23] Ikeda, S.; Shibuya, M.; Iwabuchi, Y. *Chem. Commun.* **2007**, 504.

[24] Shirai, A.; Miyata, O.; Tohnai, N.; Miyata, M.; Procter, D. J.; Sucunza, D.; Naito, T. *J. Org. Chem.* **2007**, *73*, 4464.

C(9)*H*), 7.70 (1H, br s, N*H*), 7.78 (1H, br s, N*H*); δ_C (125 MHz, DMSO-d_6) 17.8, 17.9, 25.2, 25.2 (2 × $NCH_2CH{=}CMe_2$), 25.3 (*C*(2')), 26.3 (*C*(3)), 33.4 (*C*(1')), 39.5, 39.8 (2 × $NCH_2CH{=}CMe_2$), 40.7 (*C*(3')), 45.8 (*C*(2)), 49.2 (*C*(4)), 53.0 (*C*(9b)), 113.3 (*C*(6)), 115.7 (*C*(9a)), 116.6 (br q, *J* 299, CF_3), 117.1 (*C*(8)), 119.2, 119.6 (2 × $NCH_2CH{=}CMe_2$), 130.0 (*C*(7)), 130.5 (*C*(9)), 135.6, 136.0 (2 × $NCH_2CH{=}CMe_2$), 146.3 (*C*(5a)), 154.3, 155.5 (2 × N*C*N), 158.2 (q, *J* 33.4, $CF_3CO_2^-$), 167.2 (CO_2H);[25] δ_F (470 MHz, DMSO-d_6) –73.7 (CF_3); *m*/*z* (ESI^+) 496 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{27}H_{42}N_7O_2^+$ ($[M+H]^+$) requires 496.3395; found 496.3377.

[25] The remaining peak in the ^{13}C NMR spectrum, corresponding to *C*(3a) within **1**·*x*TFA, was obscured by the resonances corresponding to PhMe-d_8.

2. X-ray crystal structure determination for 11 and 15

Data were collected using a Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation, 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.[26,27]

X-ray crystal structure data for **11** [$C_{25}H_{27}BrN_2O_5$]: M = 515.40, orthorhombic, space group $P\ 2_1\ 2_1\ 2_1$, a = 9.6810(2) Å, b = 12.7183(2) Å, c = 19.2223(4) Å, V = 2366.76(8) Å^3, Z = 4, μ = 1.446 mm^{-1}, colourless block, crystal dimensions = 0.14 × 0.17 × 0.36 mm. A total of 3028 unique reflections were measured for $5 < \theta < 27$ and 5258 reflections were used in the refinement. The final parameters were wR_2 = 0.076 and R_1 = 0.047 [$I > -3.0\sigma(I)$], with Flack enantiopole = 0.011(8).[28]

X-ray crystal structure data for **15** [$C_{23}H_{25}BrN_2O_4$]: M = 473.37, orthorhombic, space group $P\ 2_1\ 2_1\ 2_1$, a = 6.8274(1) Å, b = 11.2253(2) Å, c = 27.9028(5) Å, V = 2138.46(6) Å^3, Z = 4, μ = 1.955 mm^{-1}, colourless block, crystal dimensions = 0.17 × 0.21 × 0.30 mm. A total of 2774 unique reflections were measured for $5 < \theta < 27$ and 4675 reflections were used in the refinement. The final parameters were wR_2 = 0.082 and R_1 = 0.047 [$I > -3.0\sigma(I)$], with Flack enantiopole = 0.014(9).[29]

[26] Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, C. K.; Watkin, D. J. *J. Appl. Crystallogr.* **2003**, *36*, 1487.

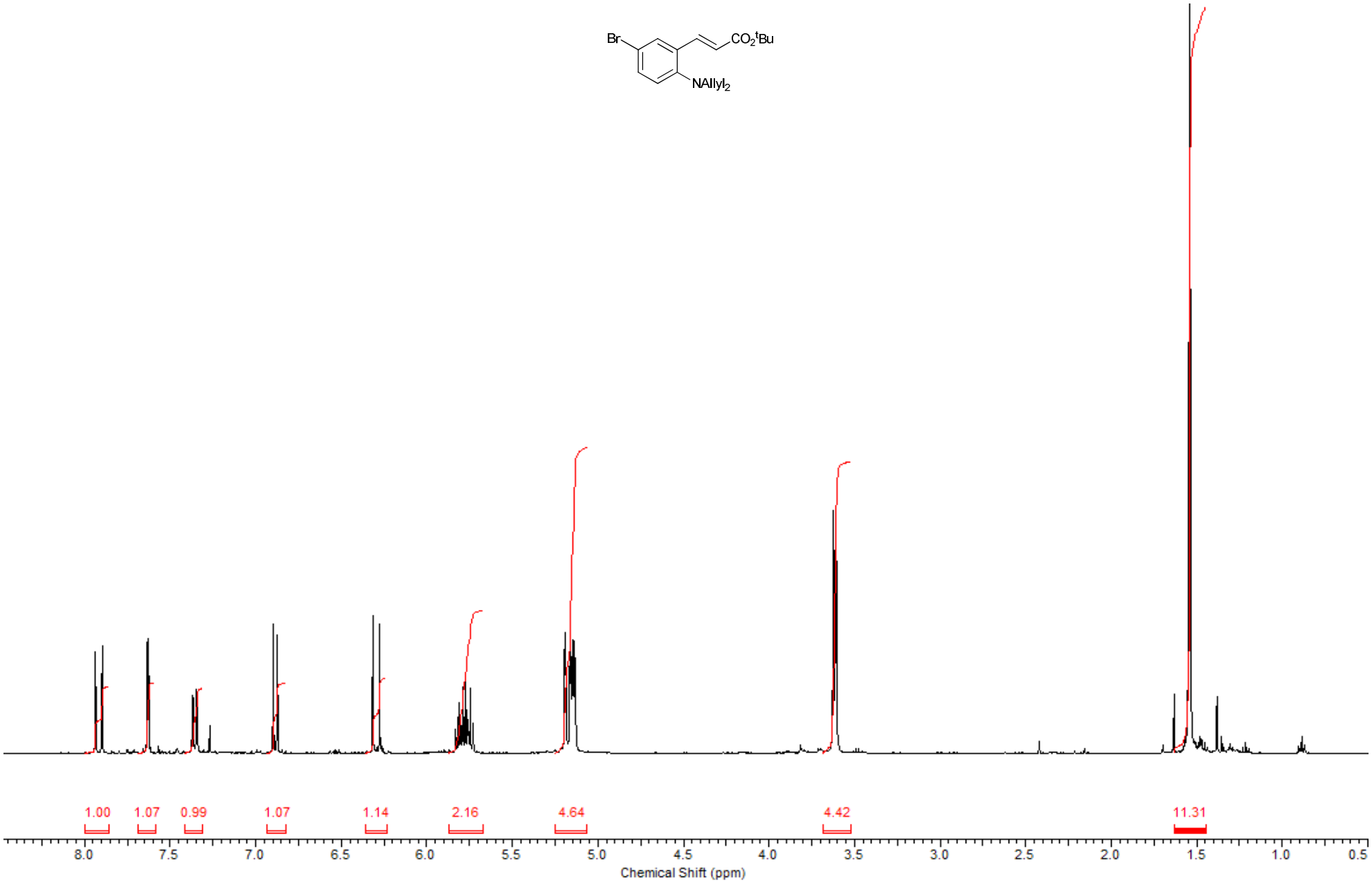
[27] Crystallographic data (excluding structure factors) for compounds **11** and **15** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 926034 and 926035, respectively. Copies of these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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

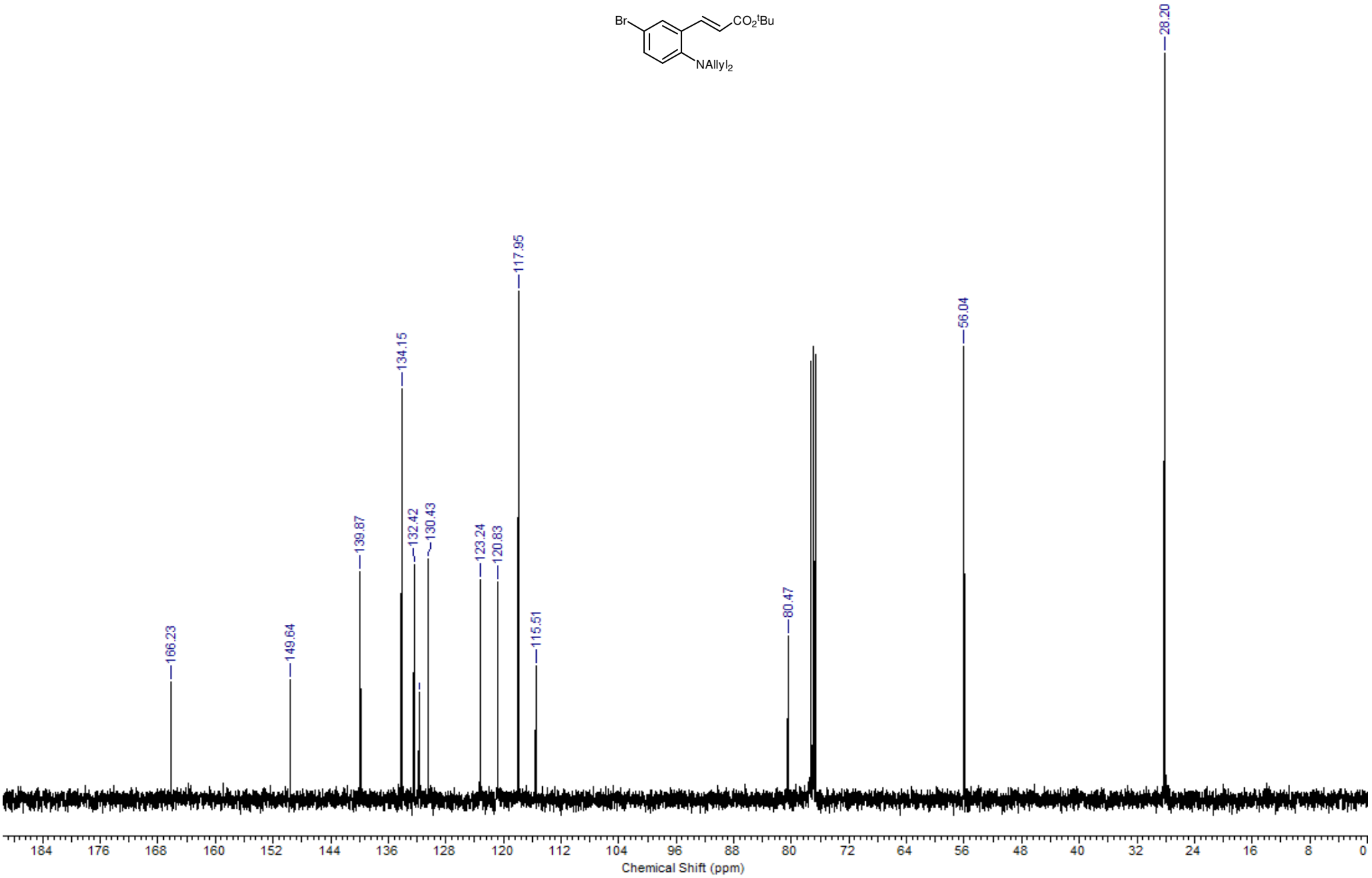
[29] (a) Flack, H. D. *Acta. Crystallogr., Sect. A* **1983**, *39*, 876. (b) Flack, H. D.; Bernardinelli, G. *Acta. Crystallogr., Sect. A* **1999**, *55*, 908. (c) Flack, H. D.; Bernardinelli, G. *J. Appl. Crystallogr.* **2000**, *33*, 1143.

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

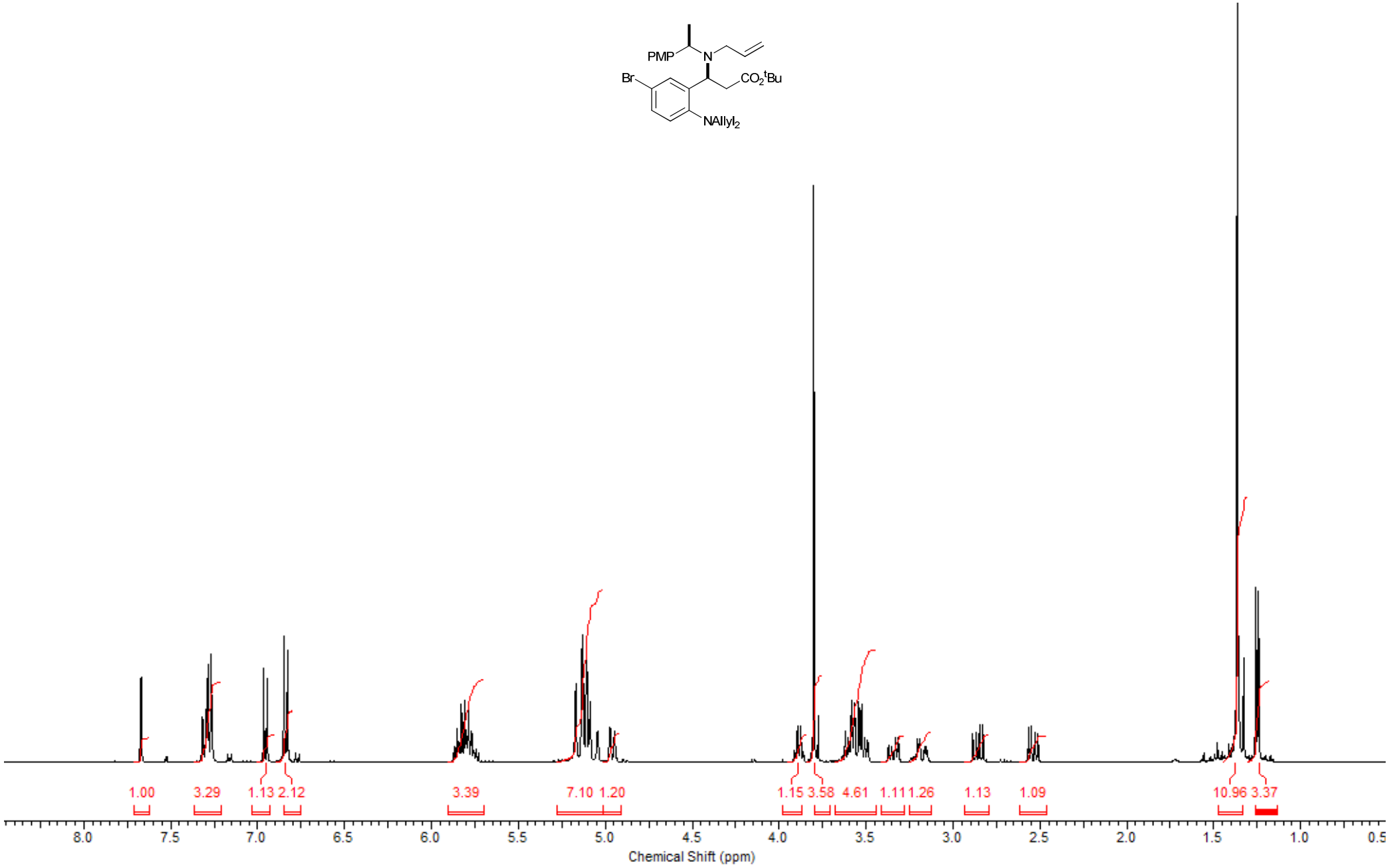
***tert*-Butyl (*E*)-3-(2'-*N*,*N*-diallylamino-5'-bromophenyl)propenoate 5 (400 MHz ^{1}H, $CDCl_3$)**



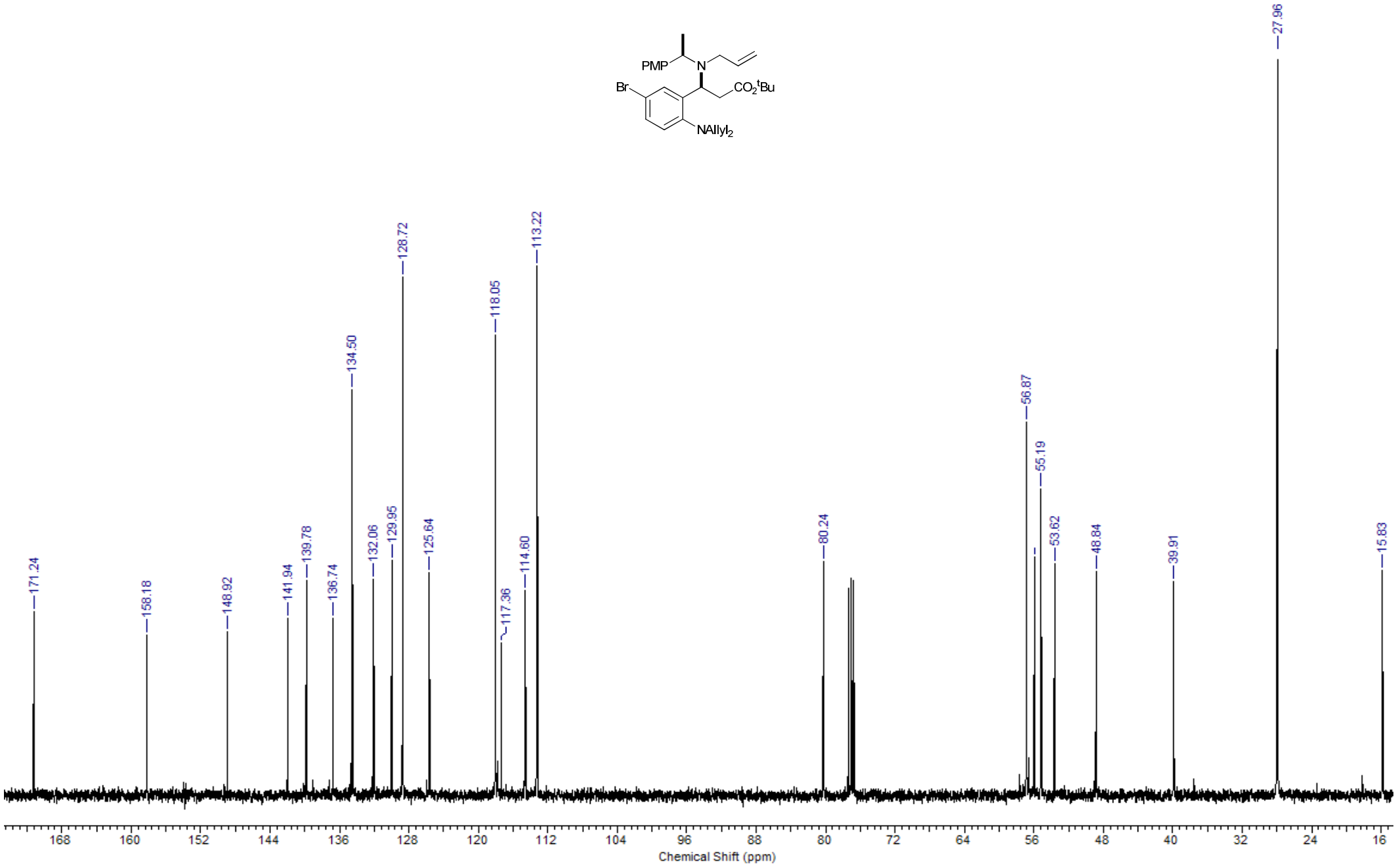
***tert*-Butyl (*E*)-3-(2'-*N*,*N*-diallylamino-5'-bromophenyl)propenoate 5 (100 MHz ^{13}C, $CDCl_3$)**



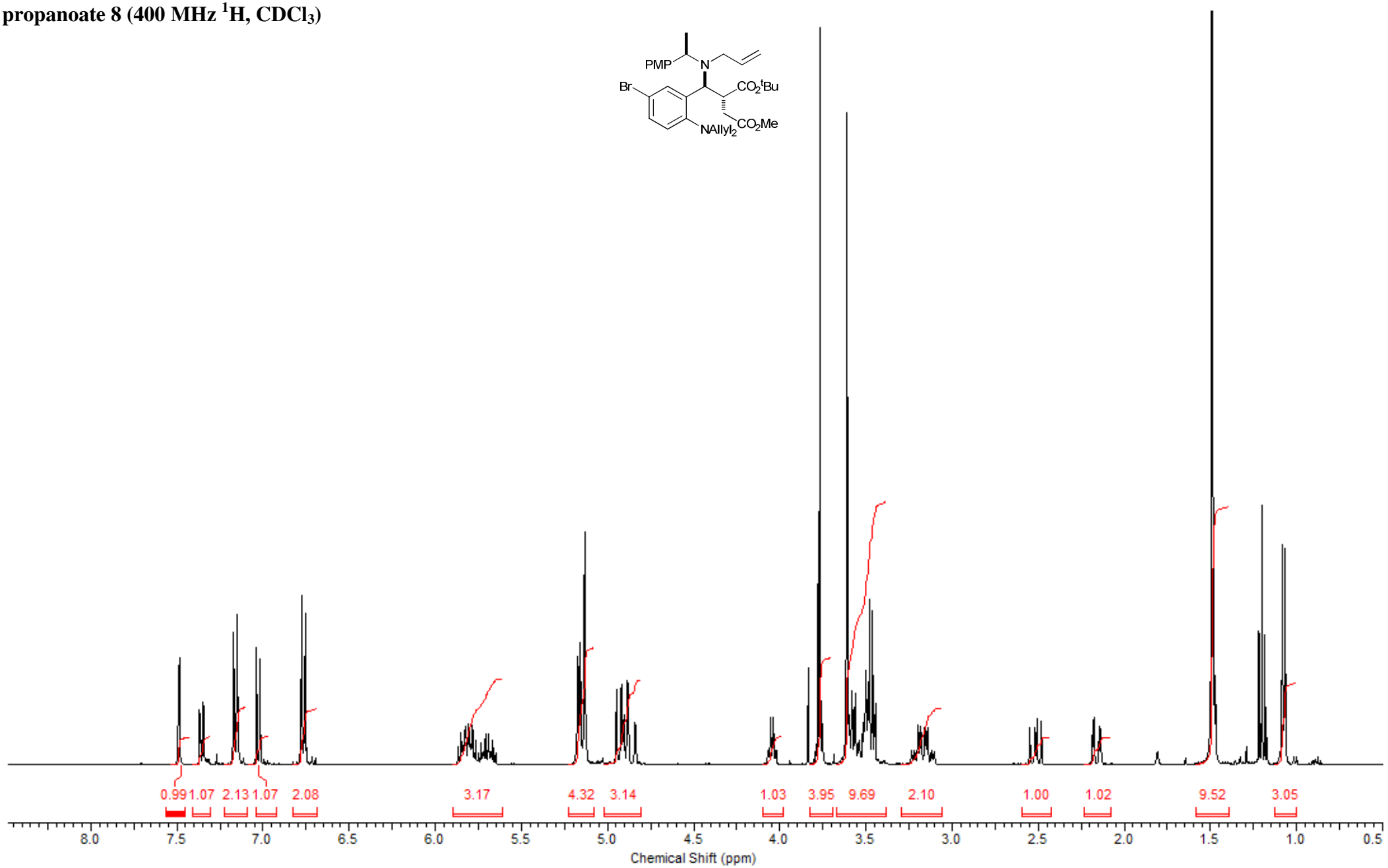
***tert*-Butyl (3*S*,*αR*)-3-[*N*-allyl-*N*-(α-methyl-4''-methoxybenzyl)amino]-3-(2'-*N*,*N*-diallylamino-5'-bromophenyl)propanoate 7 (400 MHz ^{1}H, $CDCl_3$)**



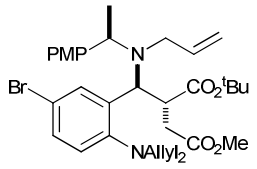
***tert*-Butyl (3*S*,α*R*)-3-[*N*-allyl-*N*-(α-methyl-4''-methoxybenzyl)amino]-3-(2'-*N*,*N*-diallylamino-5'-bromophenyl)propanoate 7 (100 MHz ^{13}C, $CDCl_3$)**



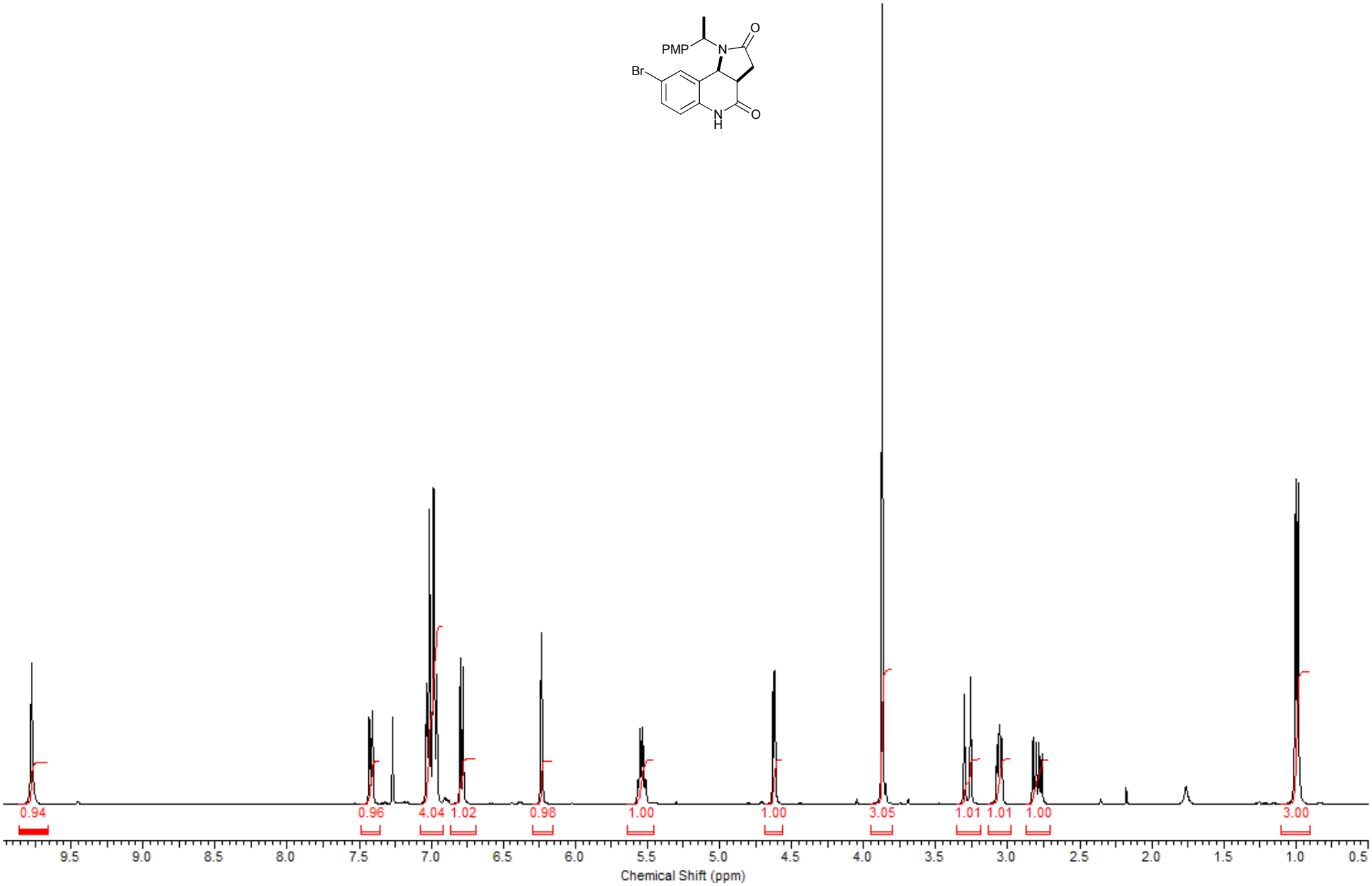
***tert*-Butyl (2*R*,3*S*,α*R*)-2-(2'-methoxy-2'-oxoethyl)-3-[*N*-allyl-*N*-(α-methyl-4'''-methoxybenzyl)amino]-3-(2''-*N*,*N*-diallylamino-5''-bromophenyl)-propanoate 8 (400 MHz ^{1}H, $CDCl_3$)**



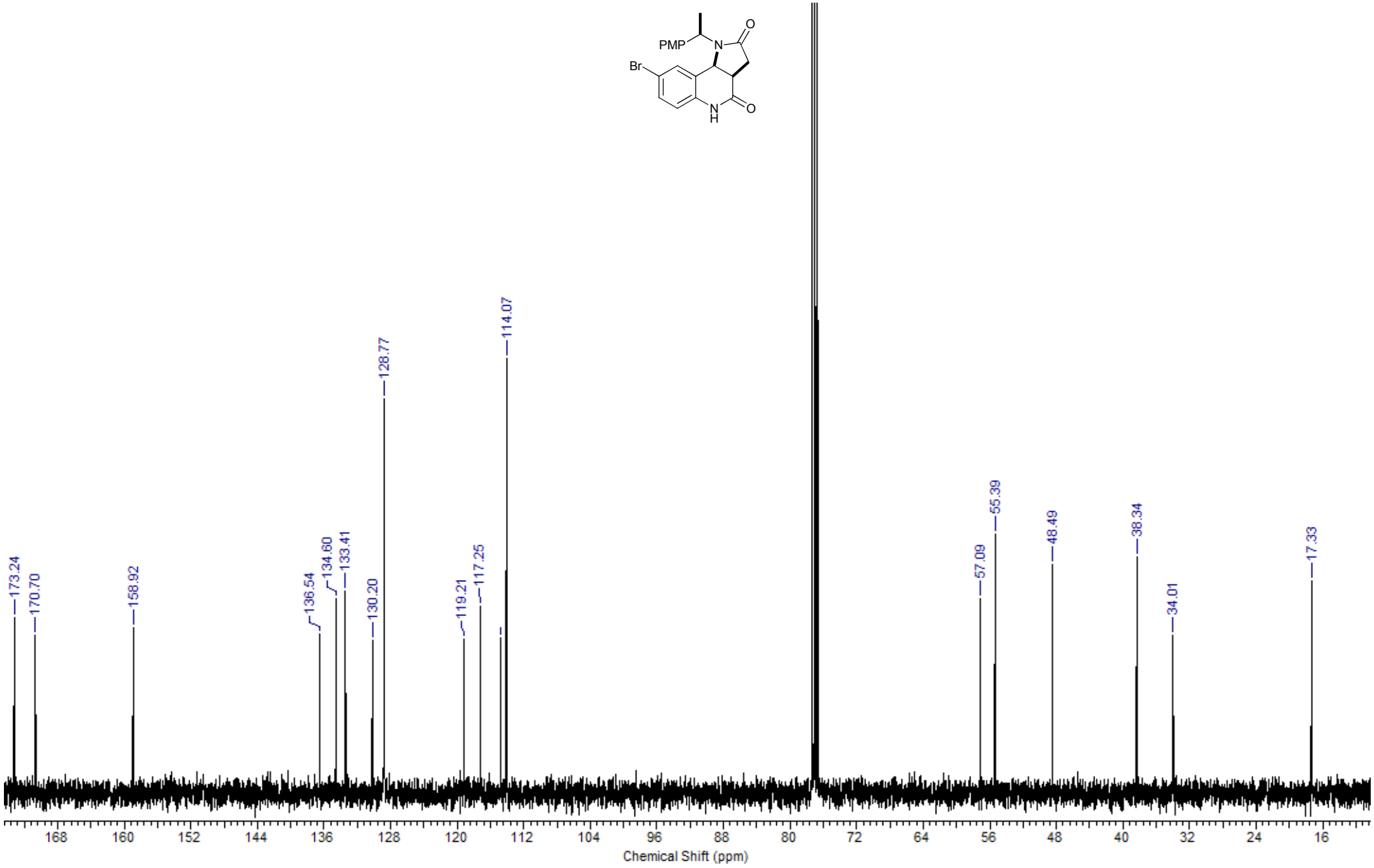
***tert*-Butyl (2*R*,3*S*,α*R*)-2-(2'-methoxy-2'-oxoethyl)-3-[*N*-allyl-*N*-(α-methyl-4'''-methoxybenzyl)amino]-3-(2''-*N*,*N*-diallylamino-5''-bromophenyl)-propanoate 8 (100 MHz ^{13}C, $CDCl_3$)**



(3a*R*,9b*S*,*αR*)-*N*(1)-(4'-Methoxy-α-methylbenzyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2,4-dione 10 (400 MHz ^{1}H, $CDCl_3$)

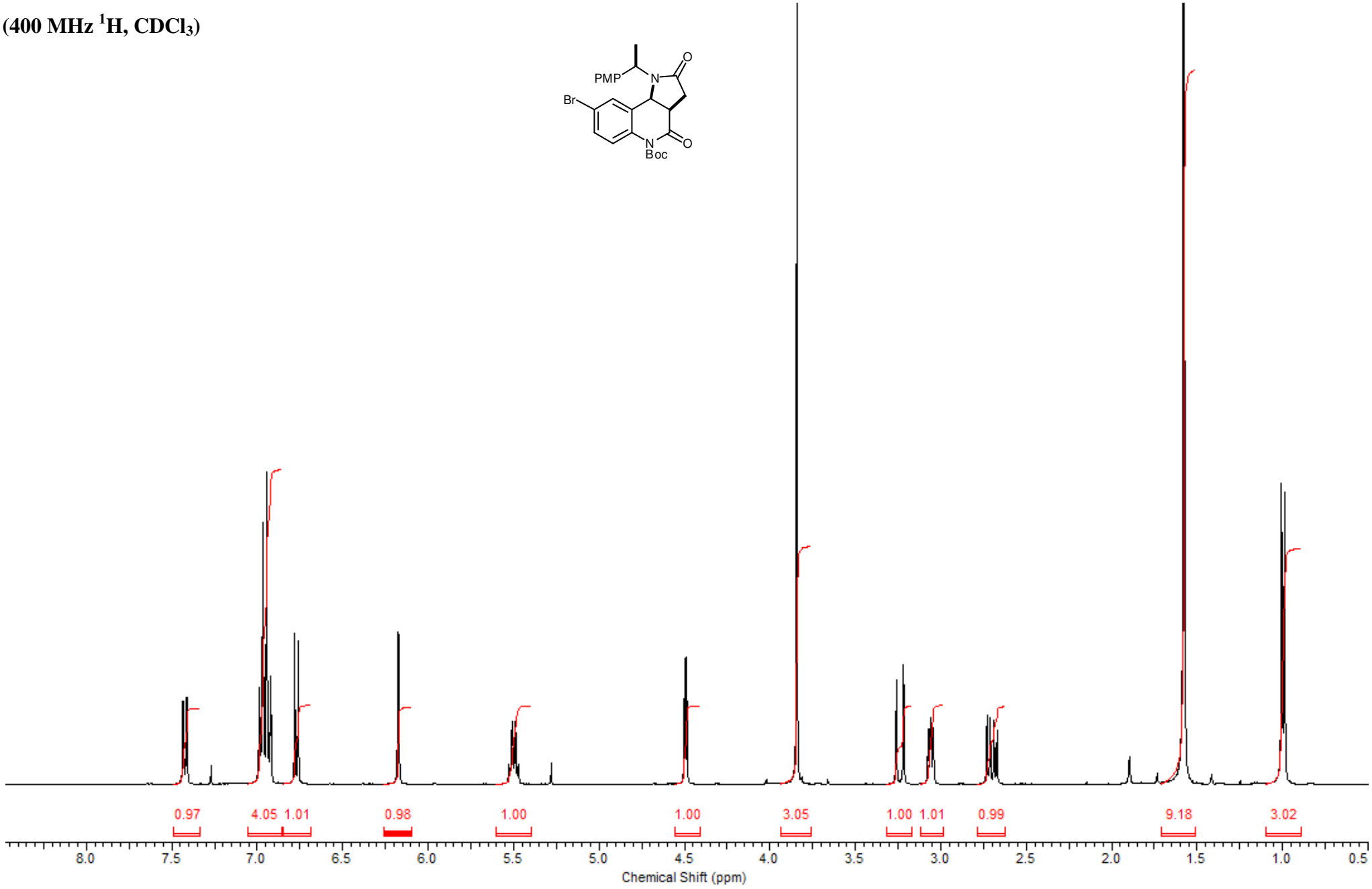


(3a*R*,9b*S*,*αR*)-*N*(1)-(4'-Methoxy-α-methylbenzyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2,4-dione 10 (100 MHz ^{13}C, $CDCl_3$)



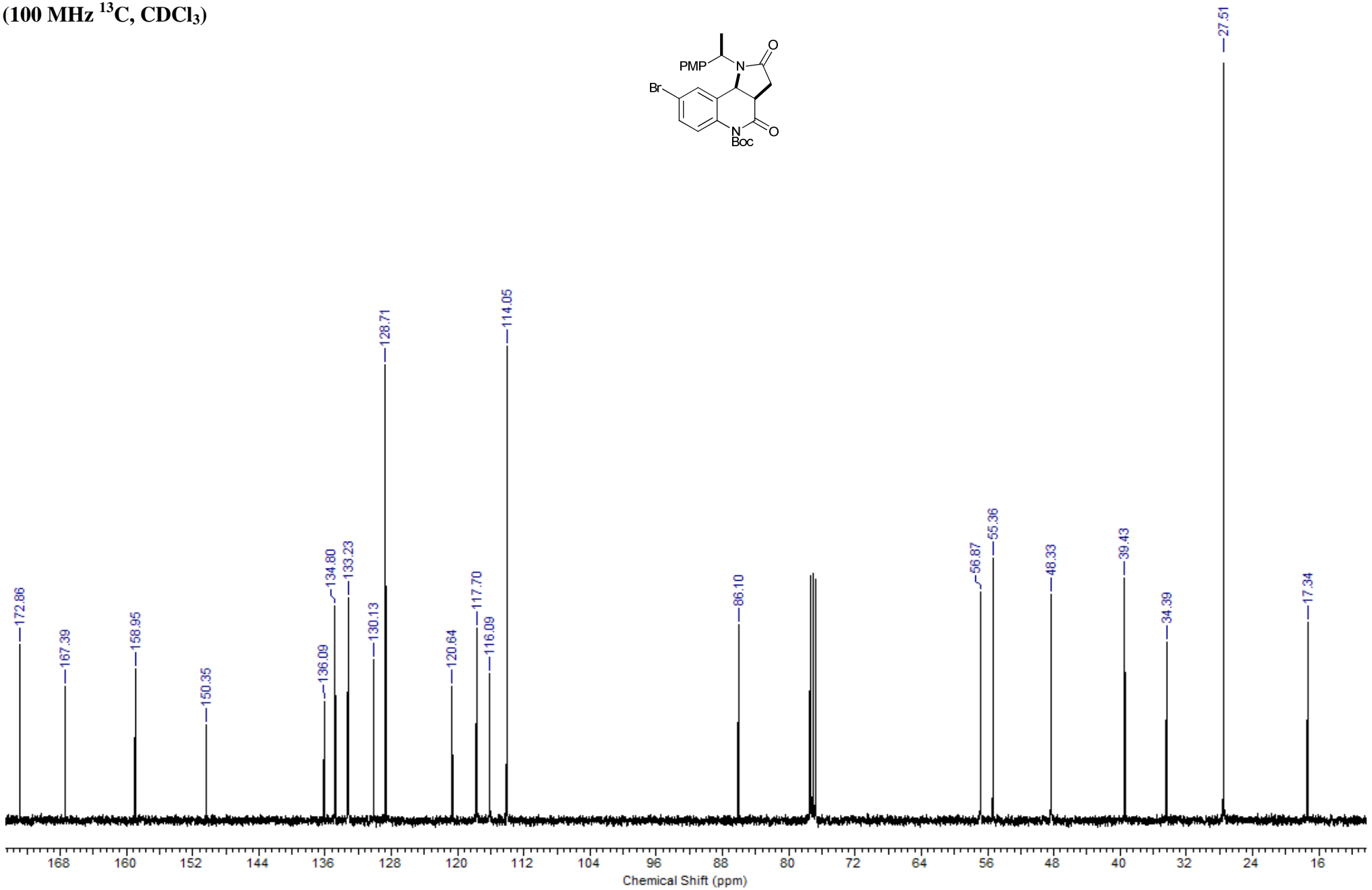
(3a*R*,9b*S*,*αR*)-1-(4'-Methoxy-α-methylbenzyl)-5-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2,4-dione 11

(400 MHz ^{1}H, $CDCl_3$)

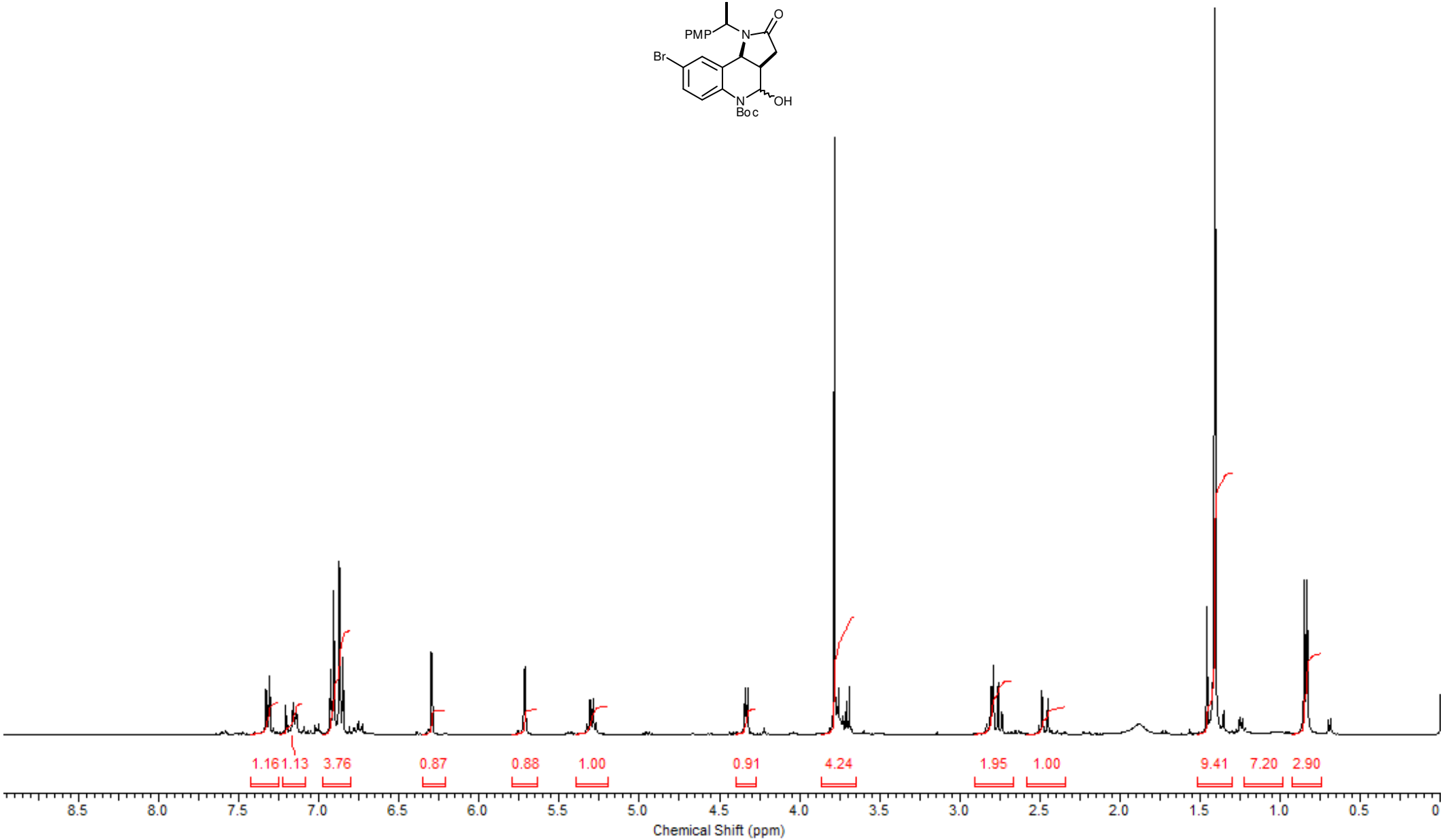


(3a*R*,9b*S*,*αR*)-1-(4'-Methoxy-α-methylbenzyl)-5-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2,4-dione 11

(100 MHz ^{13}C, $CDCl_3$)

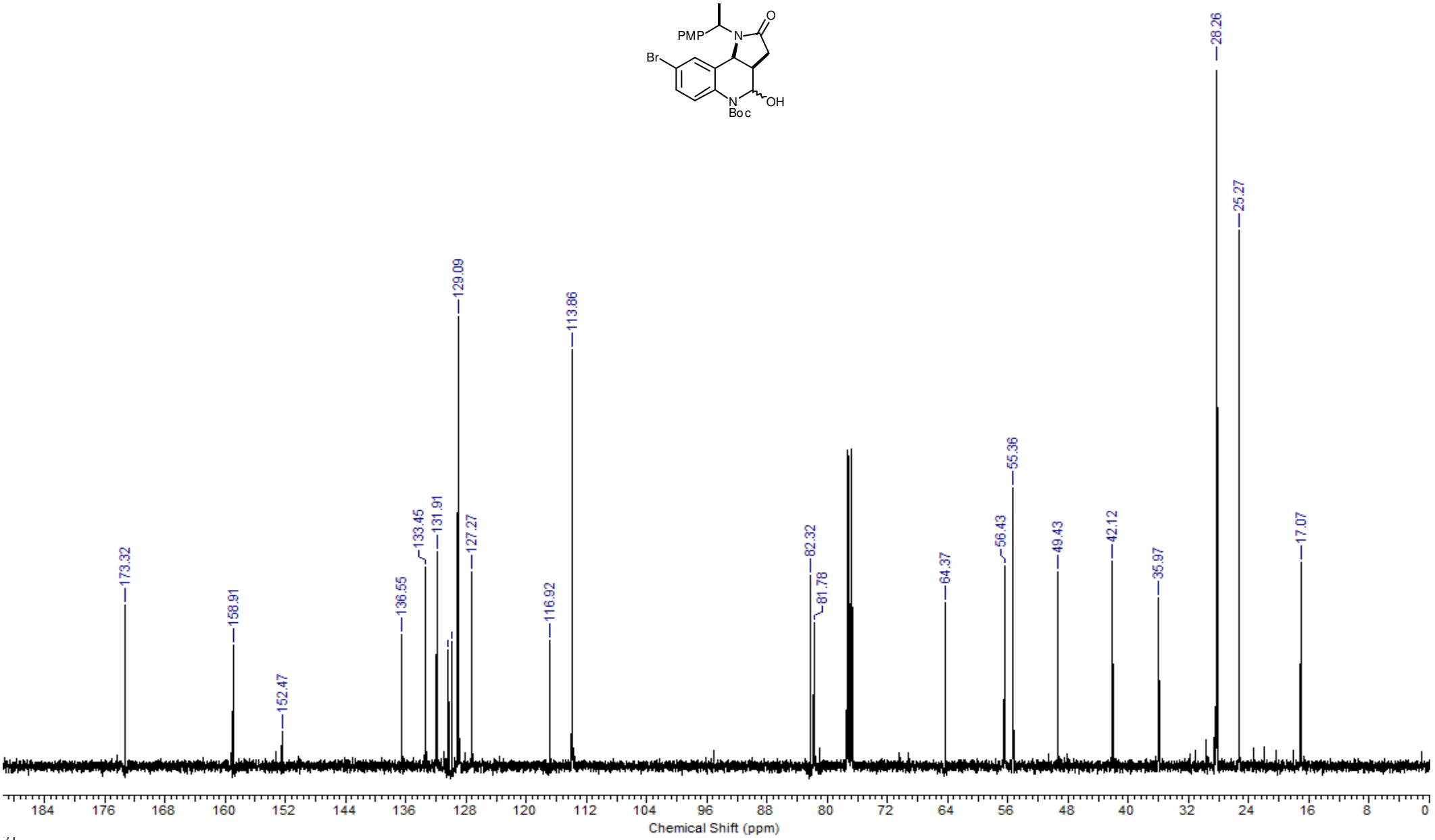


(3a*R*,4*R*,9b*S*,α*R*)- or (3a*R*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4'-methoxybenzyl)-4-hydroxy-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 12 (400 MHz ^{1}H, $CDCl_3$) [30]



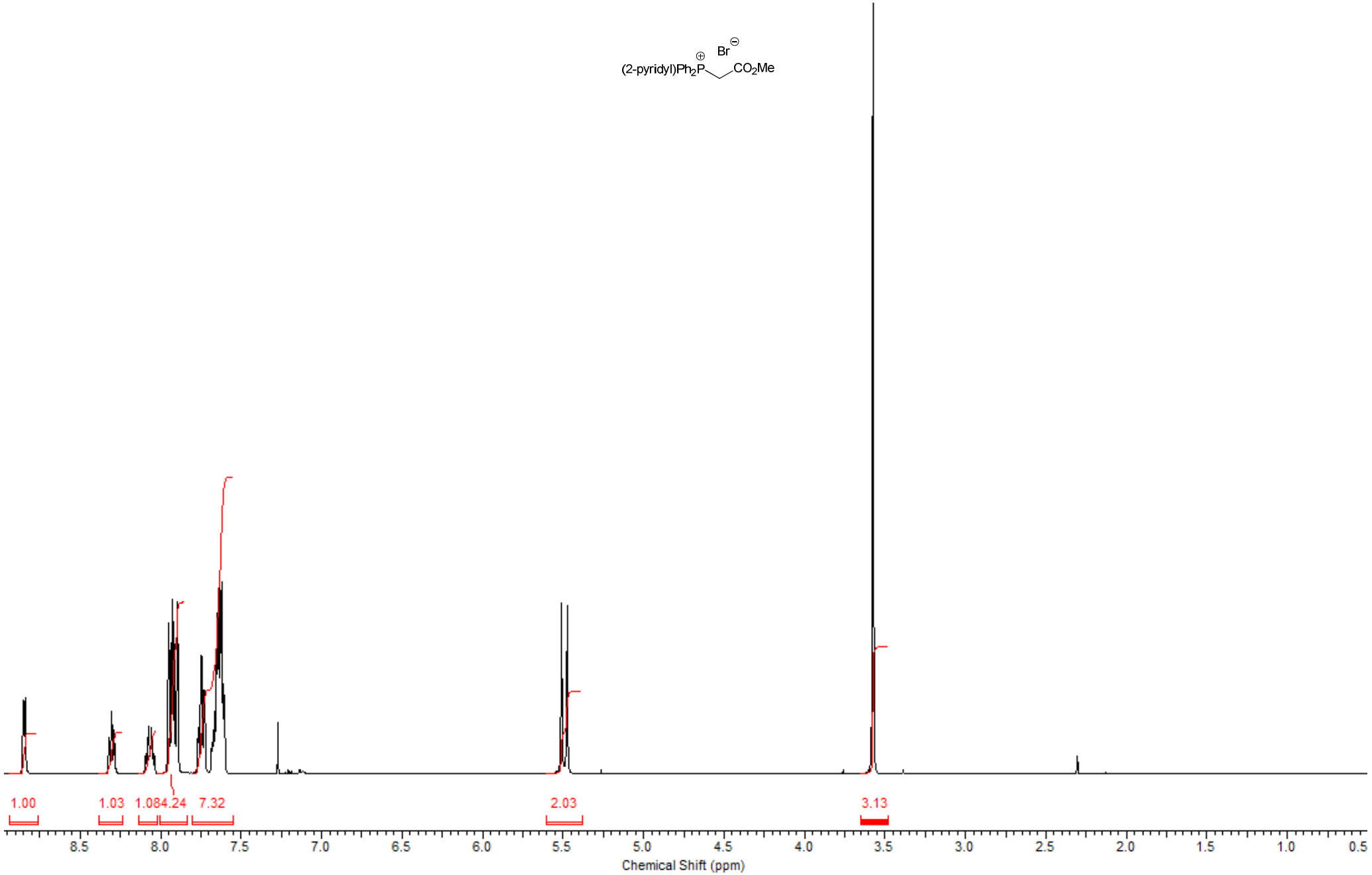
[30] Compound **12** was isolated as a single diastereoisomer of unknown configuration at C(4).

(3a*R*,4*R*,9b*S*,α*R*)- or (3a*R*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4'-methoxybenzyl)-4-hydroxy-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 12 (100 MHz ^{13}C, $CDCl_3$) [31]

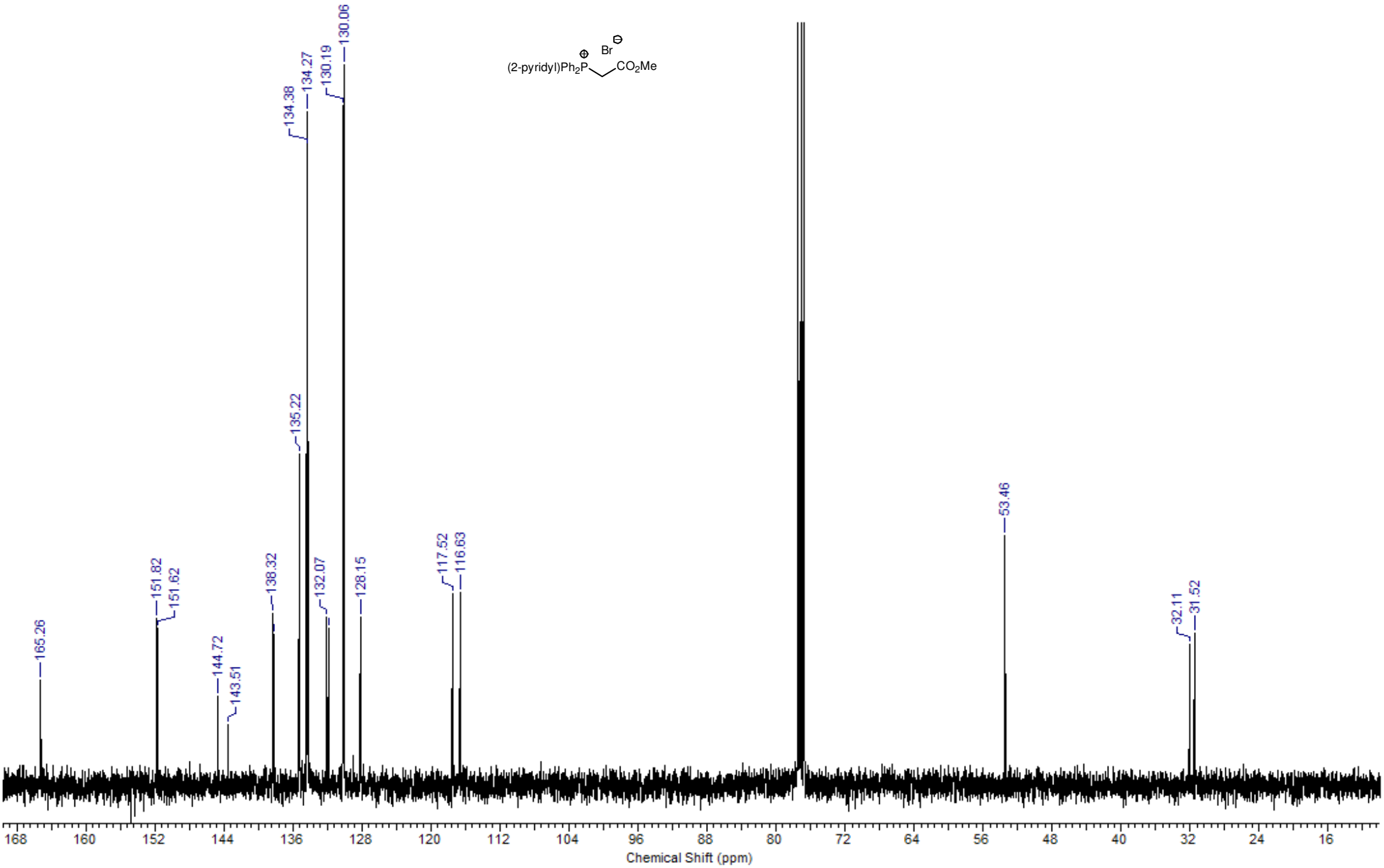


[31] Compound **12** was isolated as a single diastereoisomer of unknown configuration at C(4).

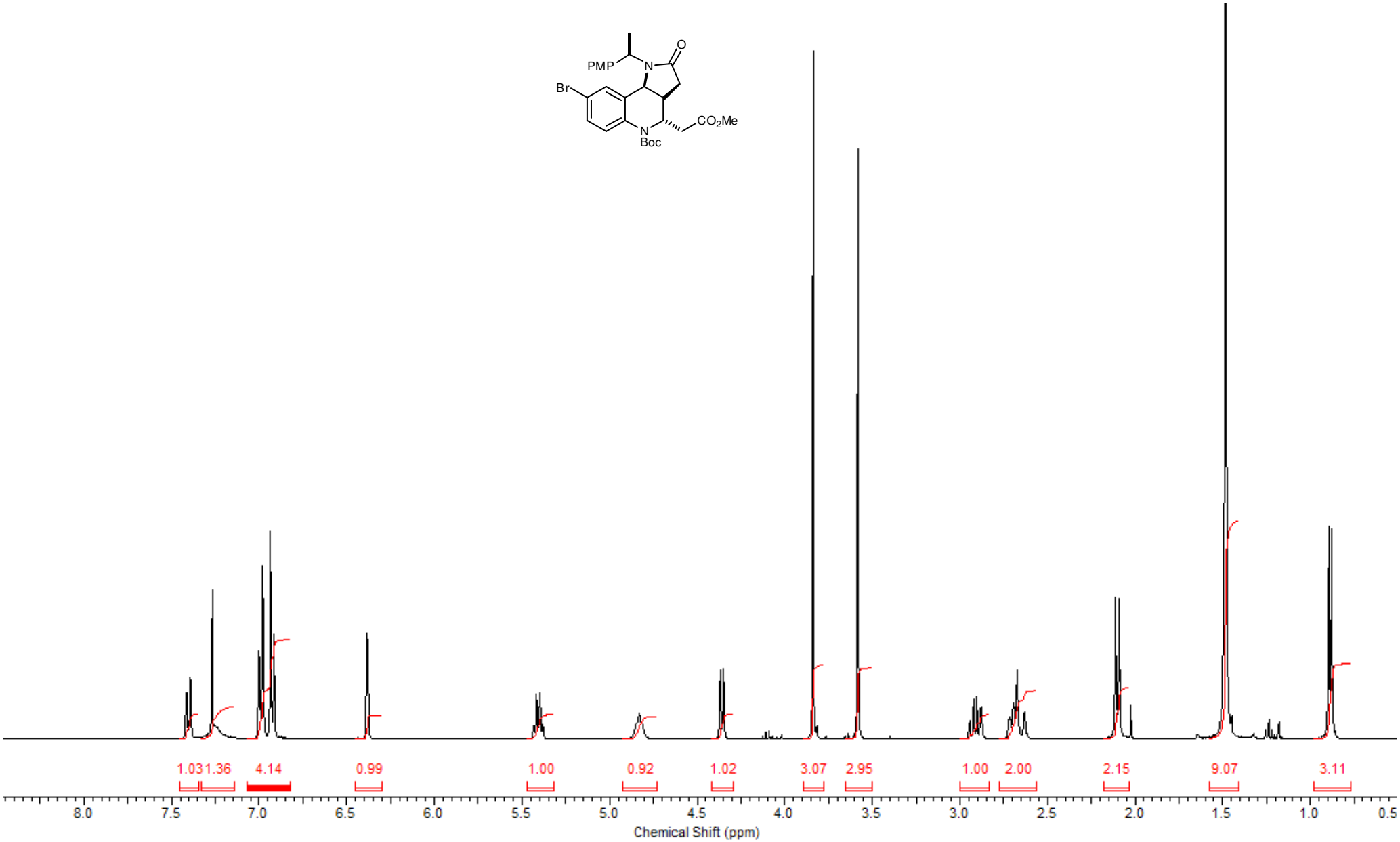
(2-Methoxy-2-oxoethyl)diphenyl-2-pyridylphosphonium bromide (400 MHz ^{1}H, $CDCl_3$)



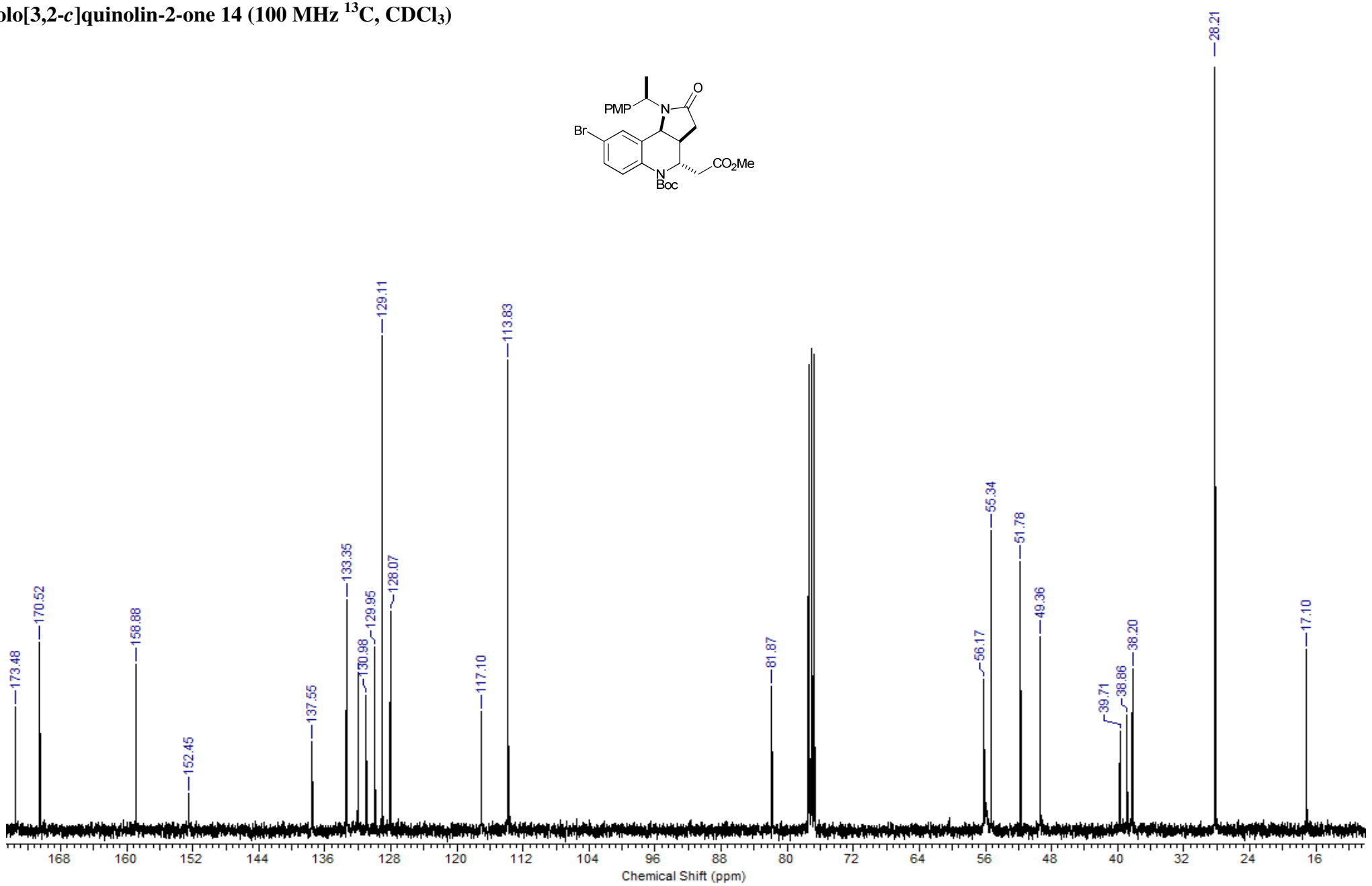
(2-Methoxy-2-oxoethyl)diphenyl-2-pyridylphosphonium bromide (100 MHz ^{13}C, $CDCl_3$)



(3a*S*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4''-methoxybenzyl)-4-(2'-methoxy-2'-oxoethyl)-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 14 (400 MHz ^{1}H, $CDCl_3$)

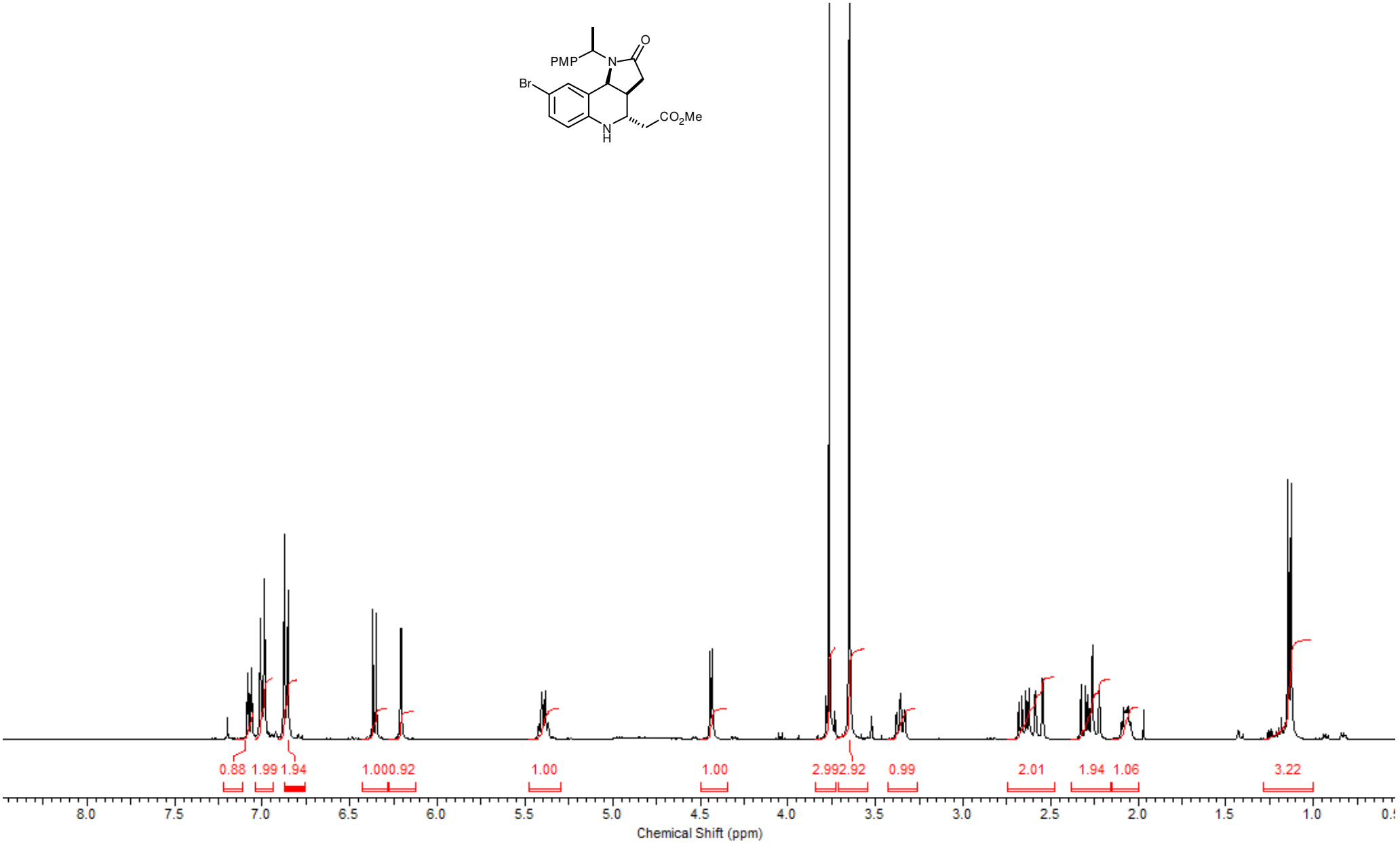


(3a*S*,4*S*,9b*S*,*αR*)-*N*(1)-(α-Methyl-4''-methoxybenzyl)-4-(2'-methoxy-2'-oxoethyl)-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 14 (100 MHz ^{13}C, $CDCl_3$)



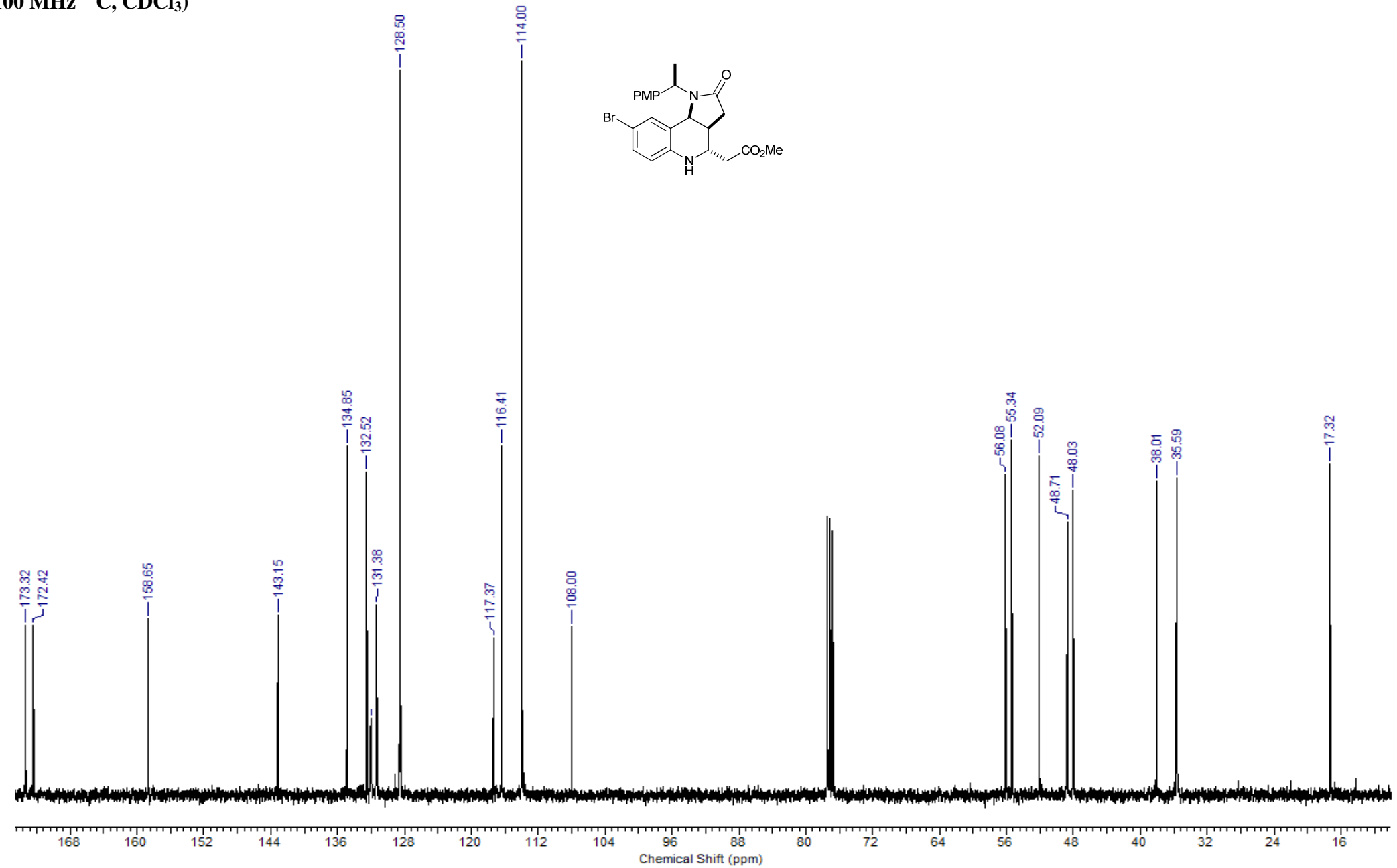
(3a*S*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4''-methoxybenzyl)-4-(2'-methoxy-2'-oxoethyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 15

(400 MHz ^{1}H, $CDCl_3$)



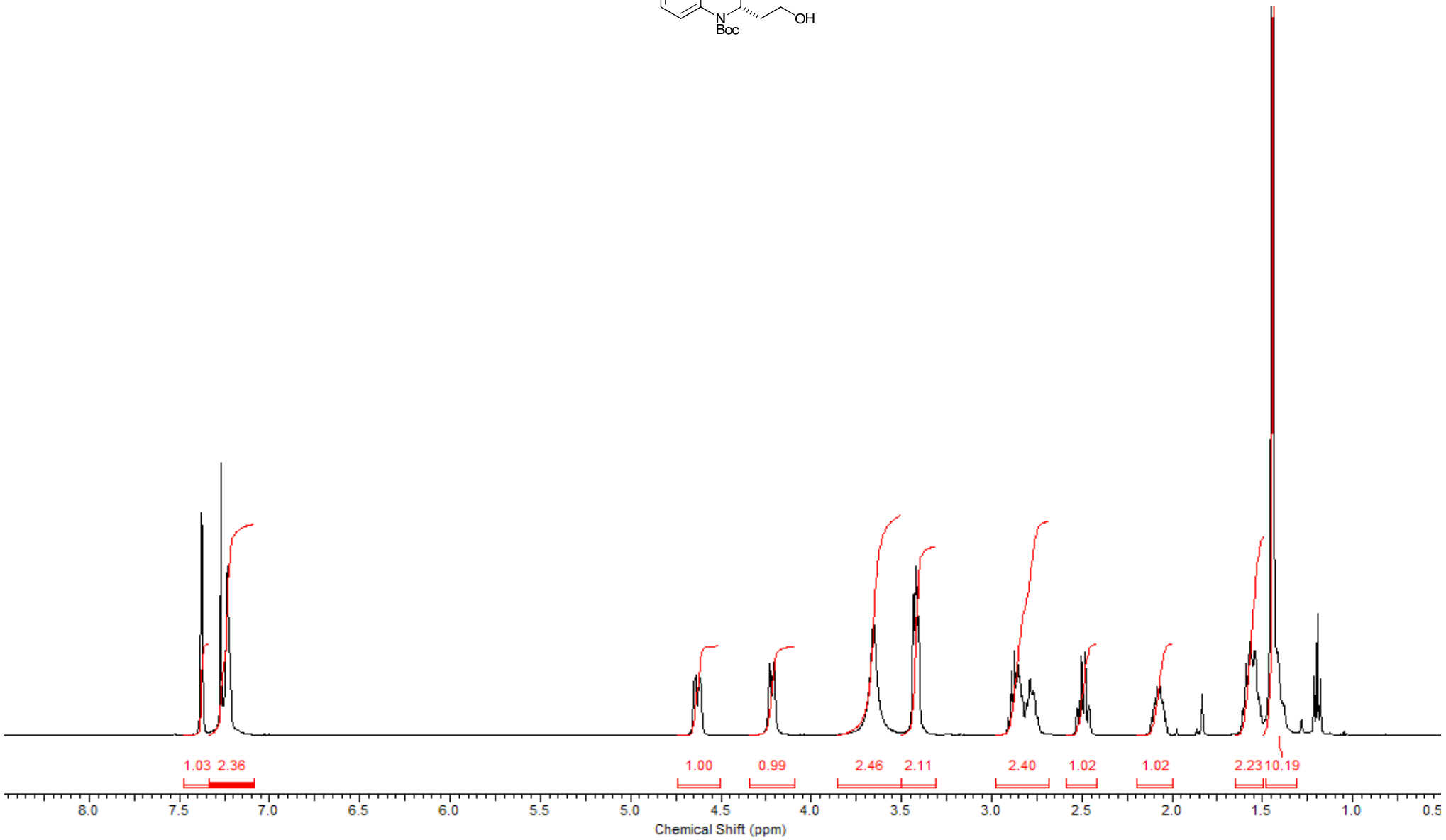
(3a*S*,4*S*,9b*S*,α*R*)-*N*(1)-(α-Methyl-4''-methoxybenzyl)-4-(2'-methoxy-2'-oxoethyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2-one 15

(100 MHz ^{13}C, $CDCl_3$)



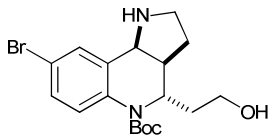
(3a*R*,4*S*,9b*S*)-4-(2'-Hydroxyethyl)-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 17

(400 MHz ^{1}H, $CDCl_3$)



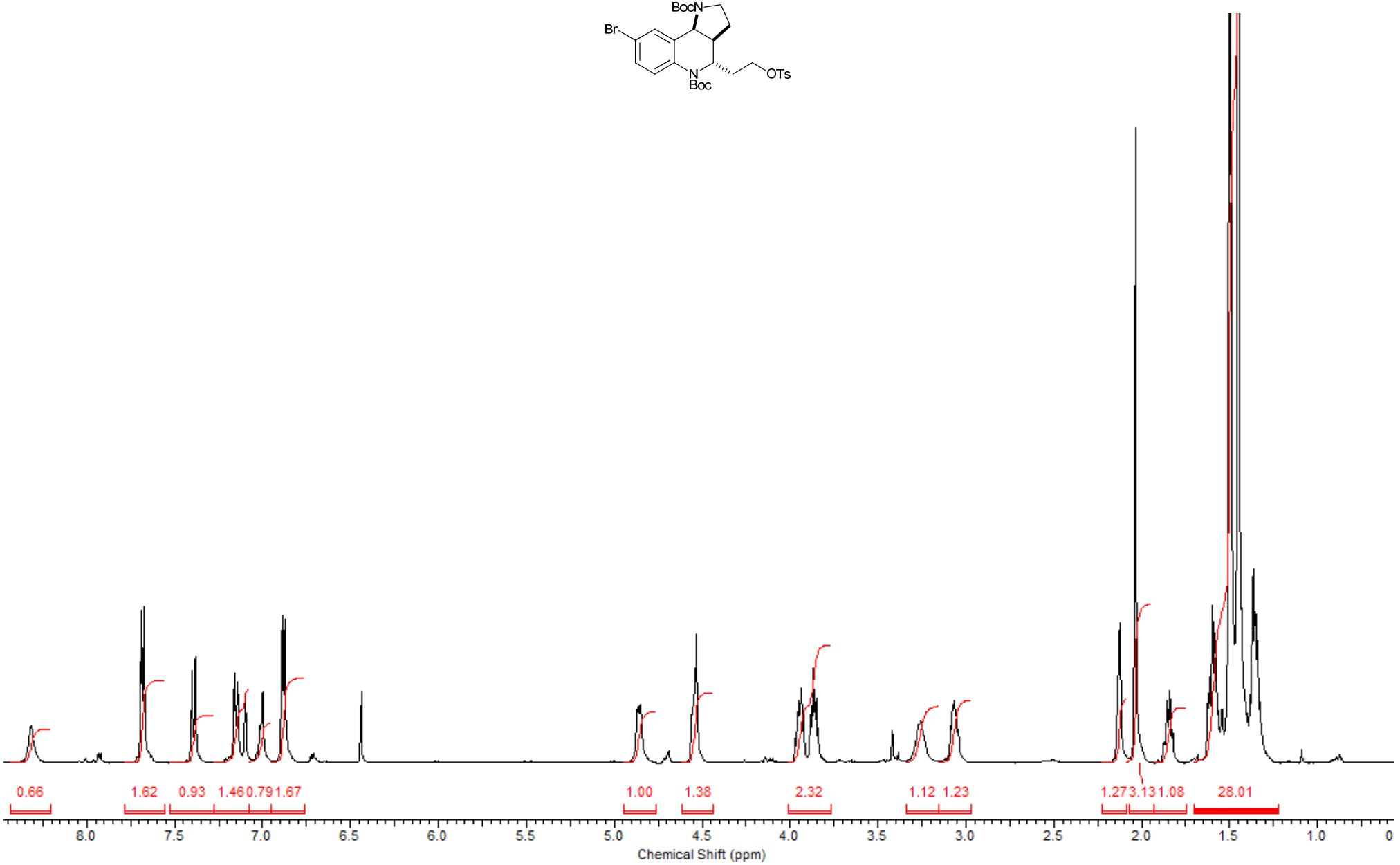
(3a*R*,4*S*,9b*S*)-4-(2'-Hydroxyethyl)-*N*(5)-(*tert*-butoxycarbonyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 17

(100 MHz ^{13}C, $CDCl_3$)



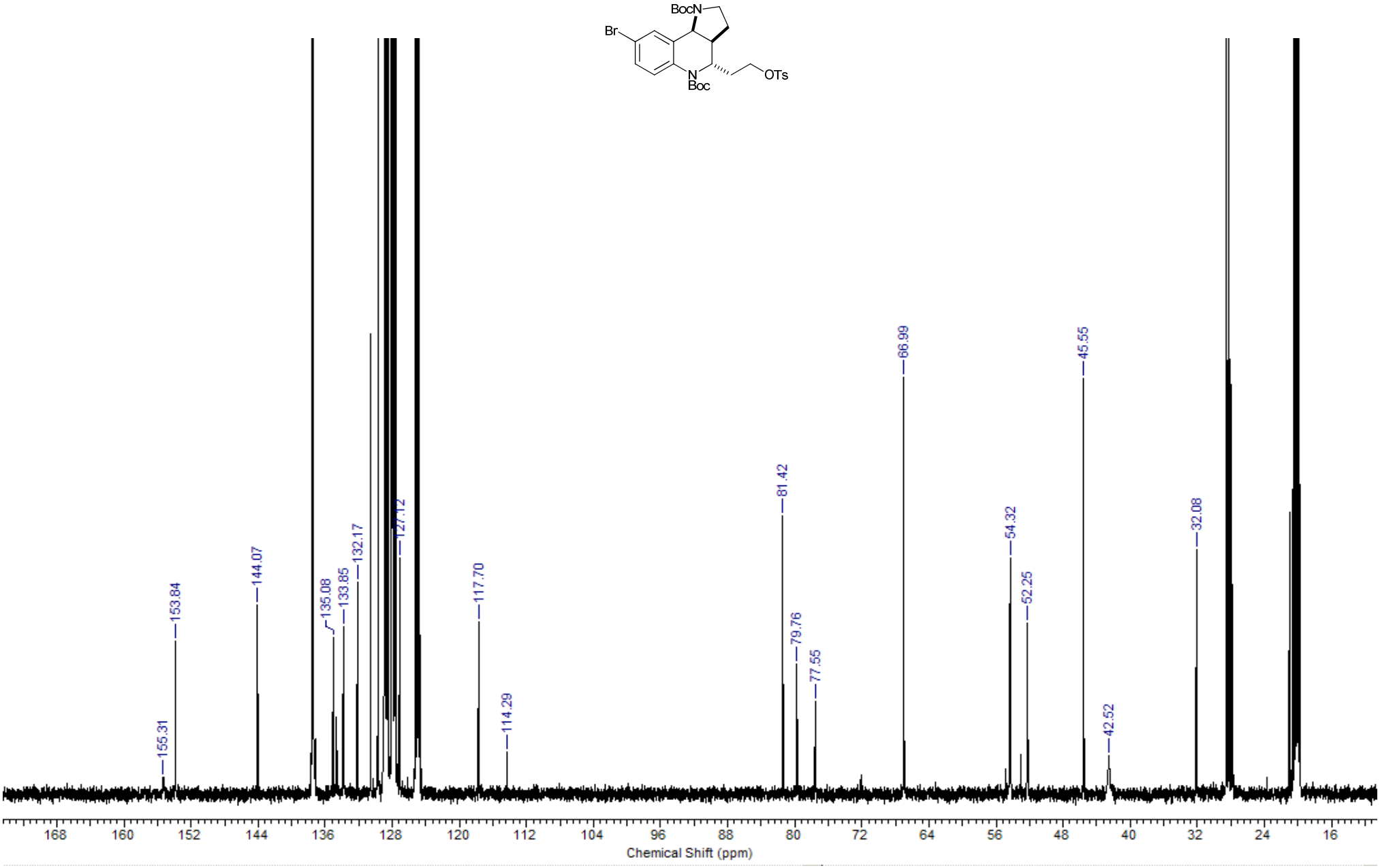
(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-[2'-(4''-toluenesulfonyloxy)ethyl]-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 19

(500 MHz ^{1}H, PhMe-d_8, 363 K)



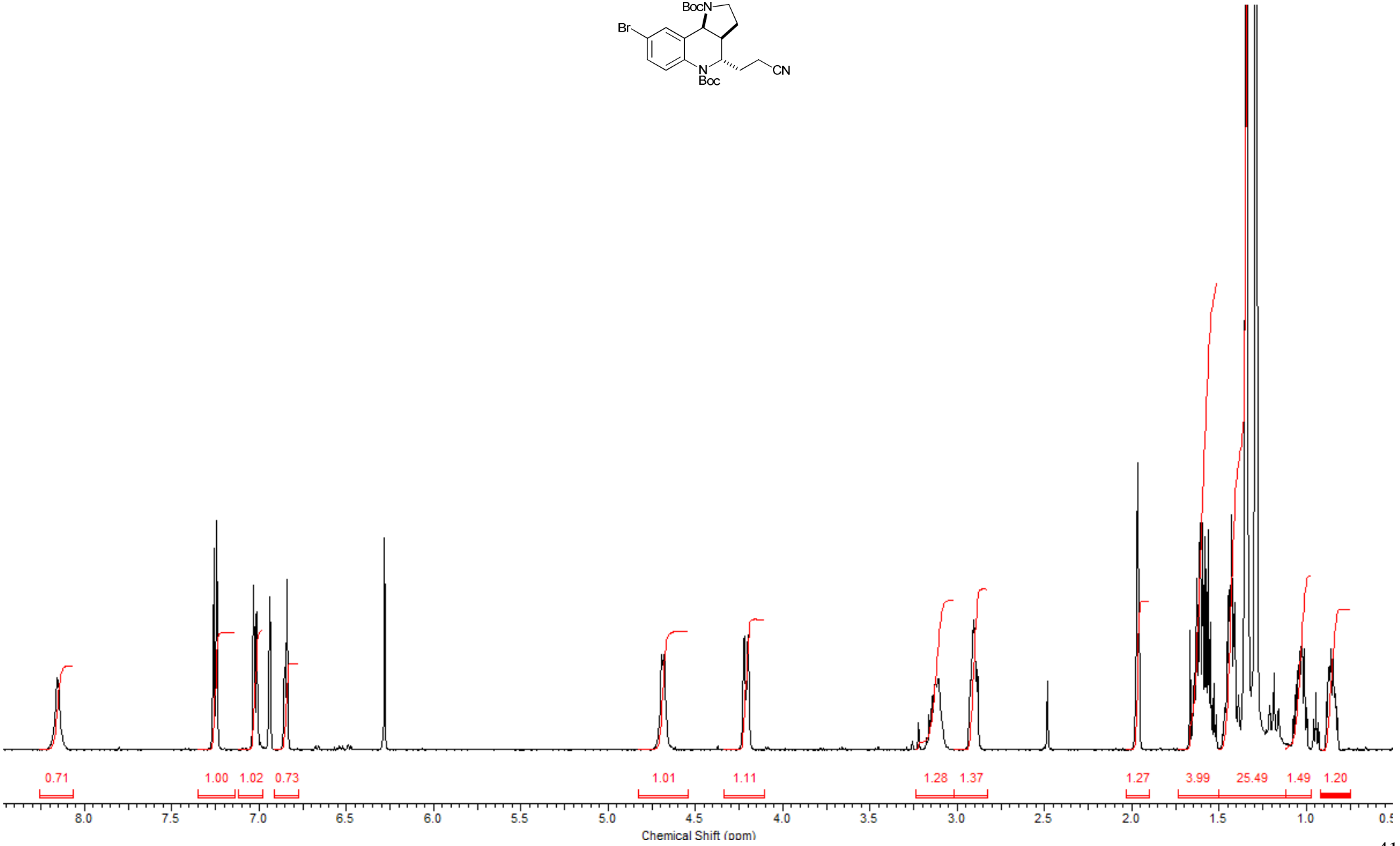
(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-[2'-(4''-toluenesulfonyloxy)ethyl]-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 19

(125 MHz ^{13}C, PhMe-d_8, 363 K)



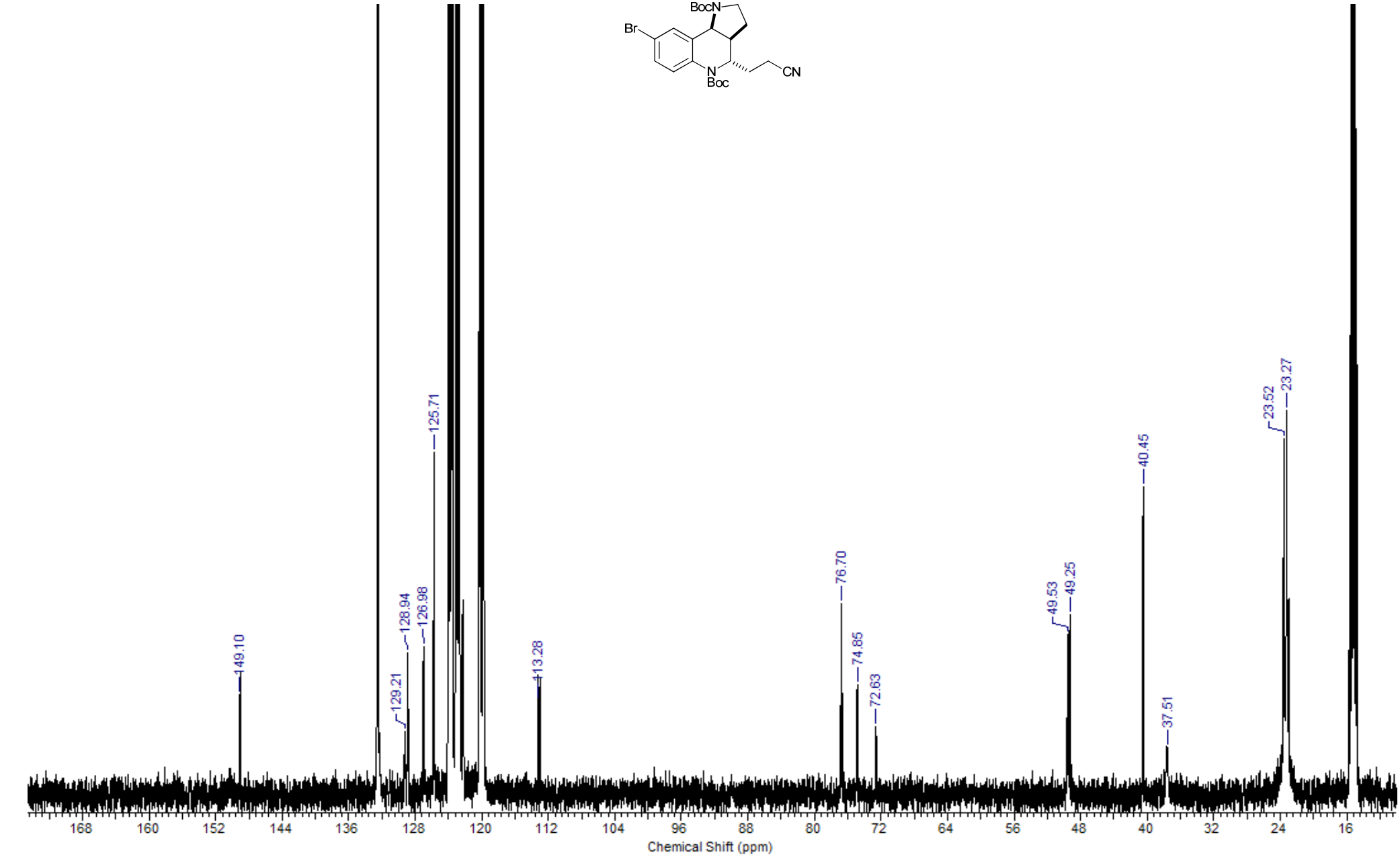
(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-(2'-cyanoethyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 20

(500 MHz ^{1}H, PhMe-d_8, 363 K)



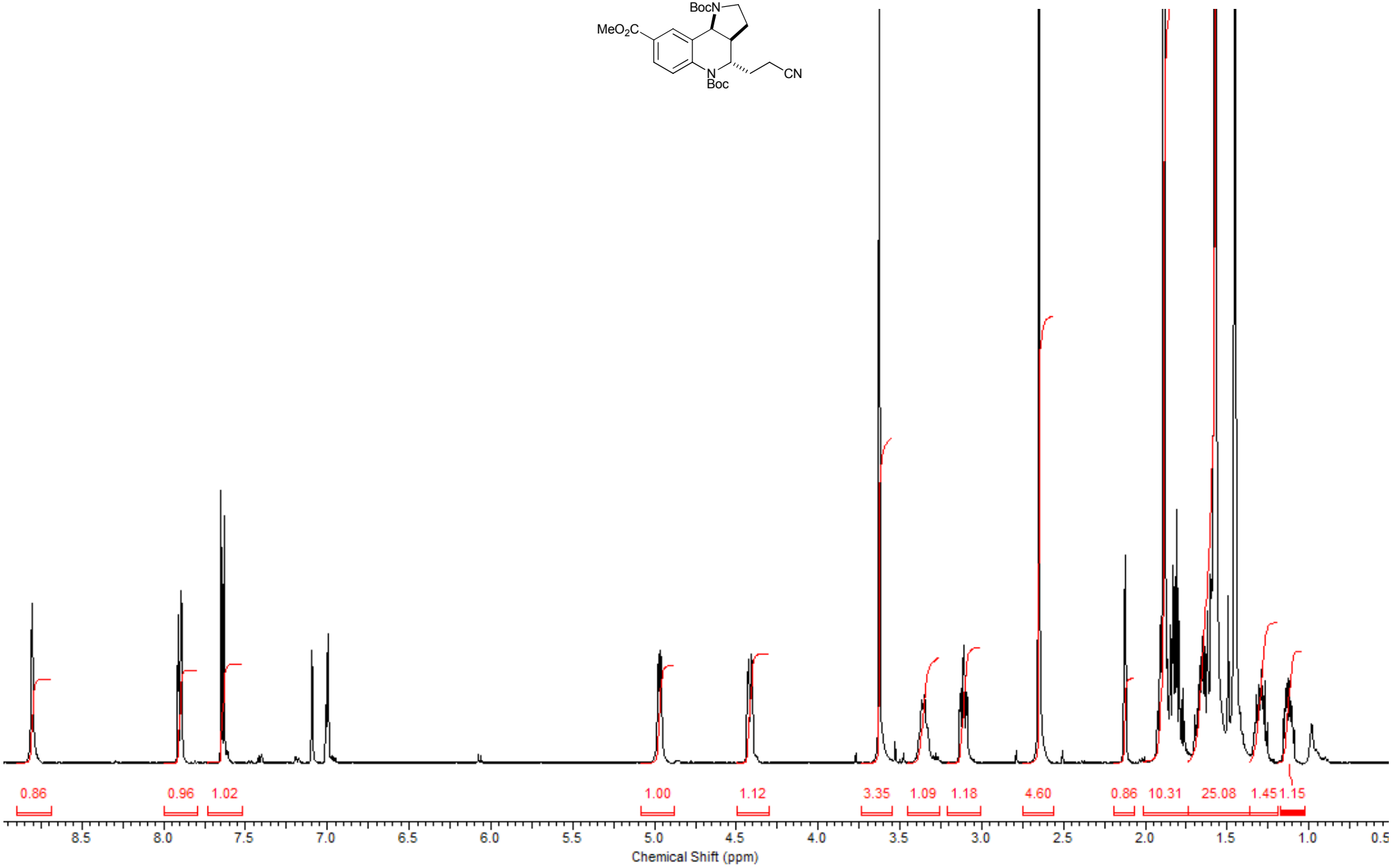
(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-(2'-cyanoethyl)-8-bromo-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 20

(125 MHz ^{13}C, PhMe-d_8, 363 K)



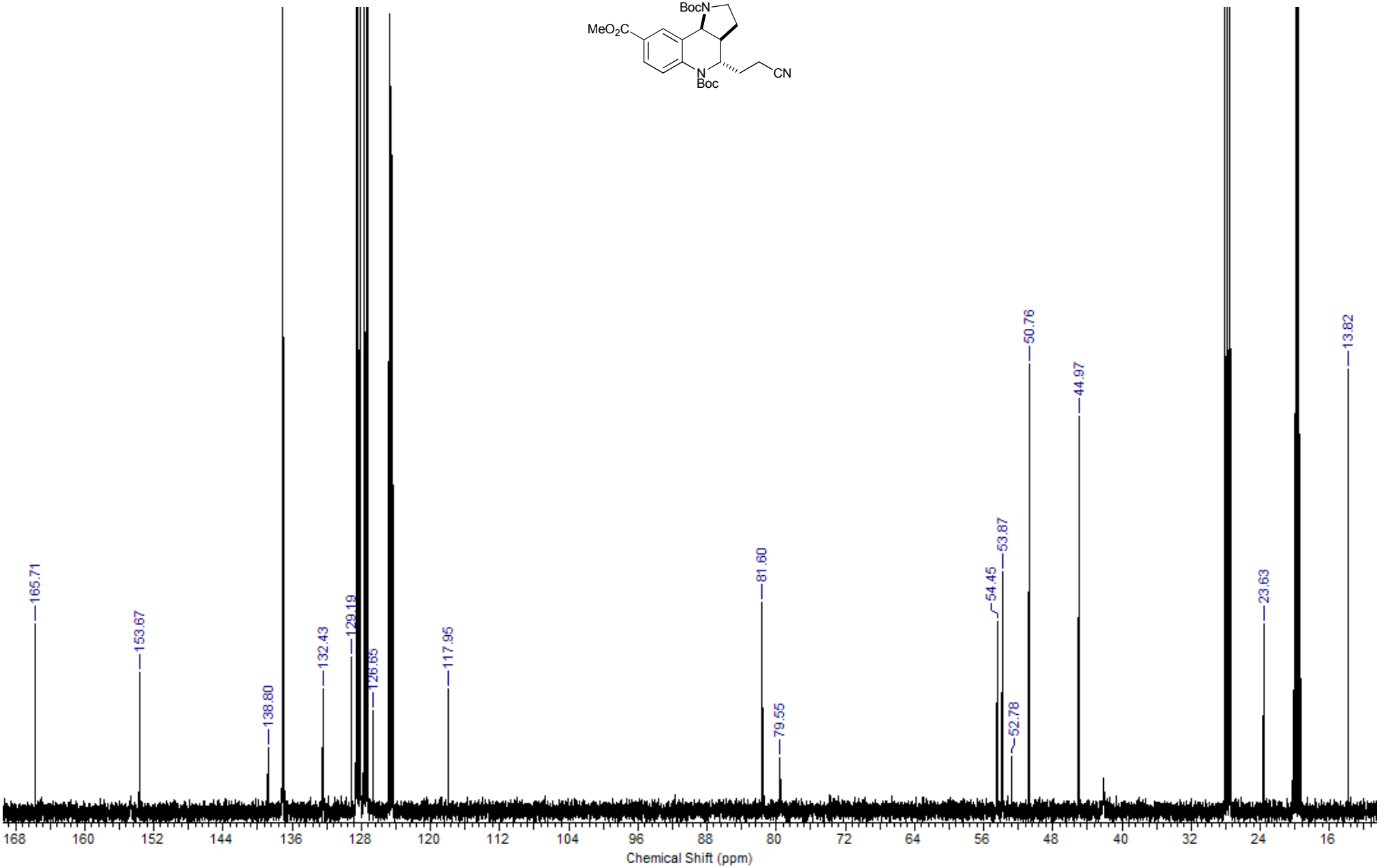
(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-(2'-cyanoethyl)-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 21

(500 MHz ^{1}H, PhMe-d_8, 363 K)

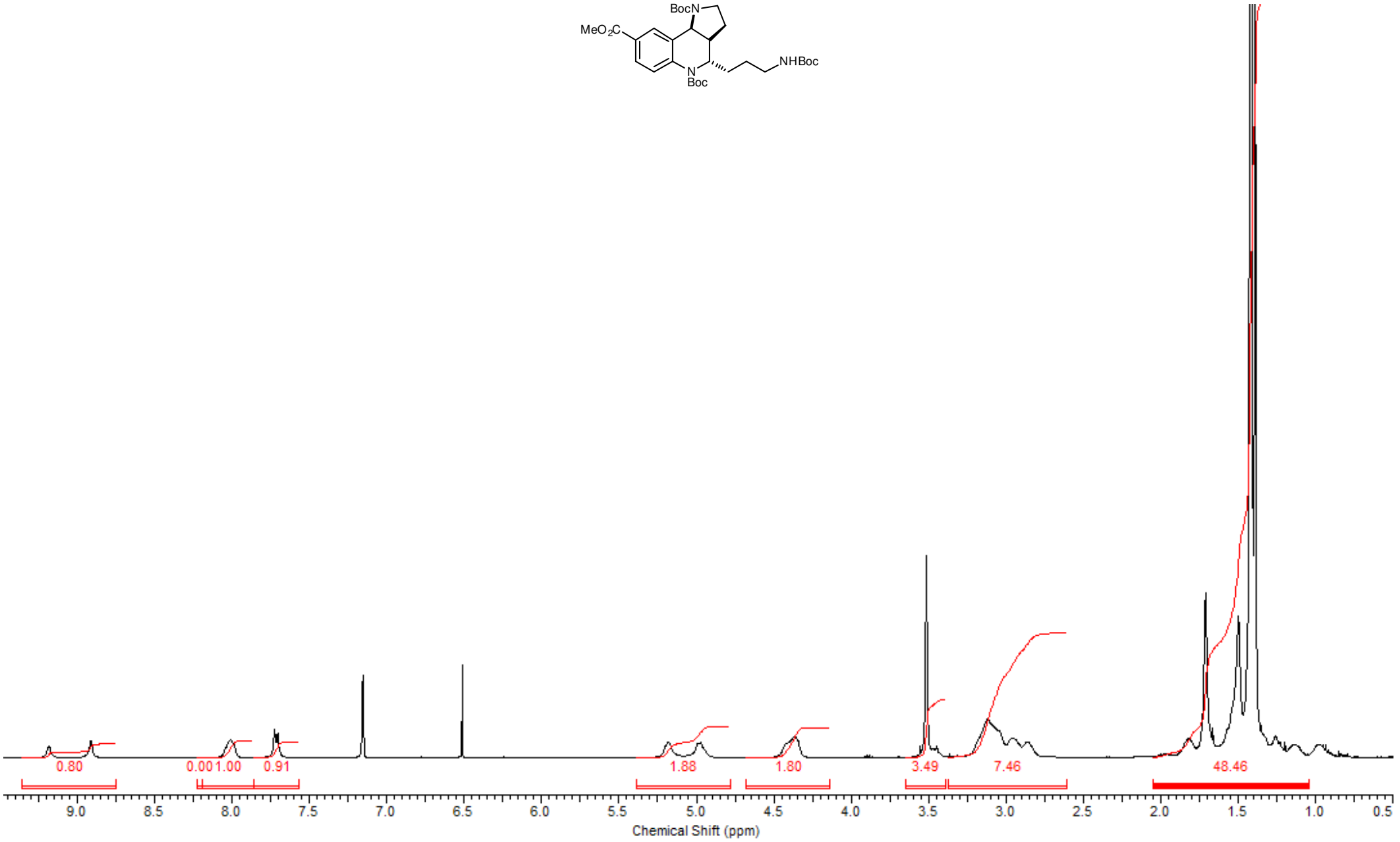


(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-(2'-cyanoethyl)-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 21

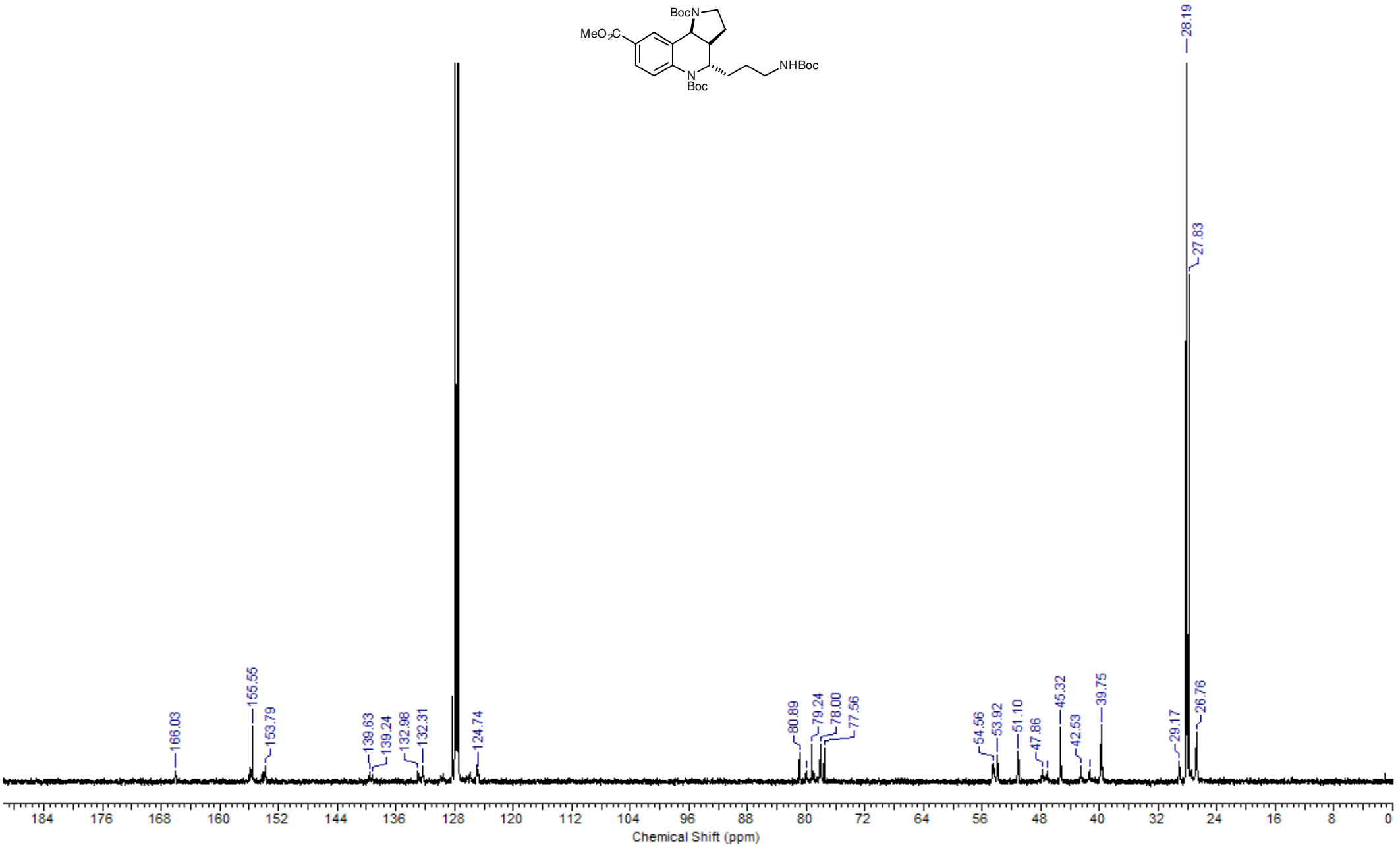
(125 MHz ^{13}C, PhMe-d_8, 363 K)



(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-[3'-(*N*-*tert*-butoxycarbonylamino)propyl]-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 22 (400 MHz ^{1}H, C_6D_6)

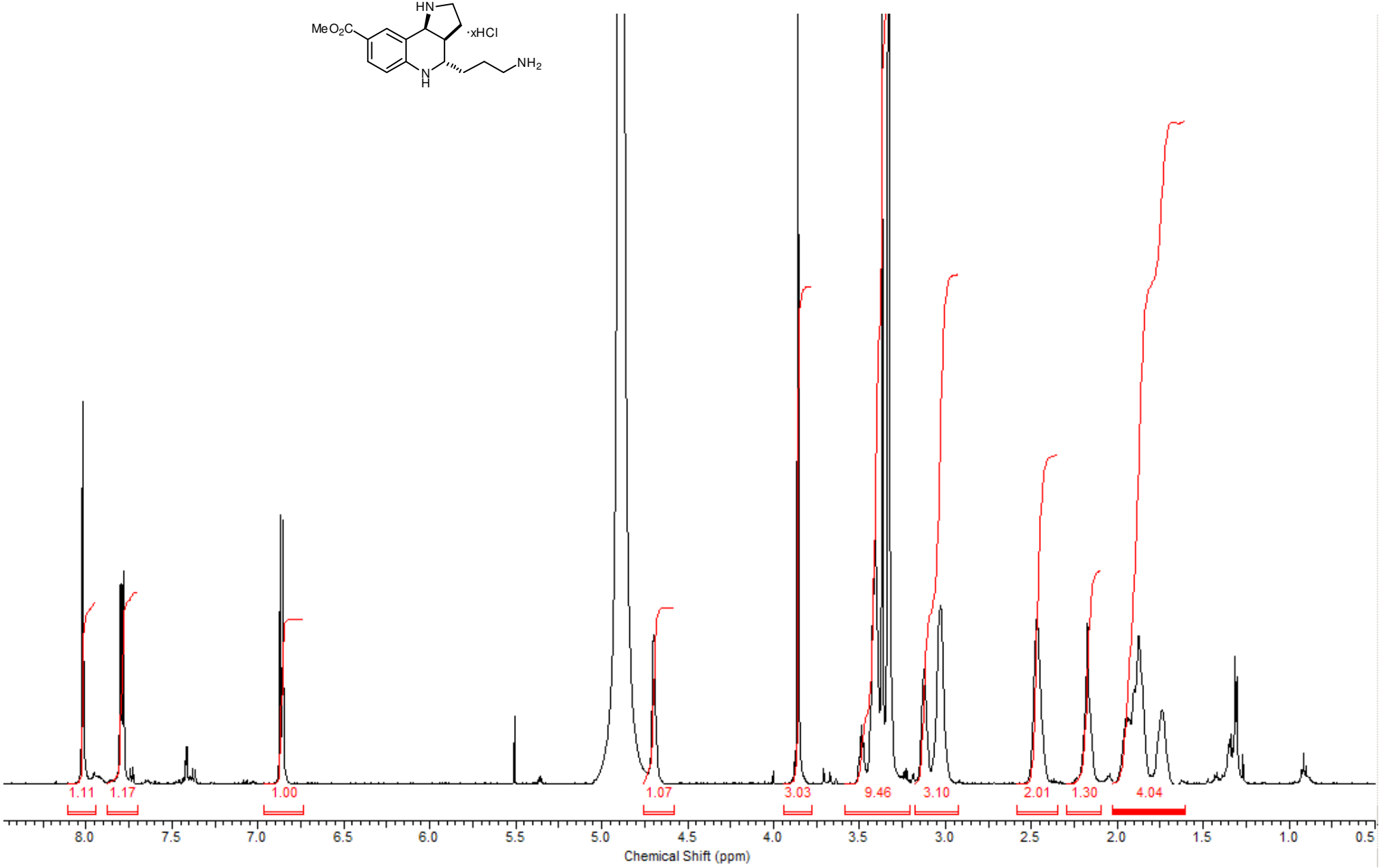


(*S*,*S*,*S*)-*N*(1),*N*(5)-(Di-*tert*-butoxycarbonyl)-4-[3'-(*N*-*tert*-butoxycarbonylamino)propyl]-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 22 (100 MHz ^{13}C, C_6D_6)



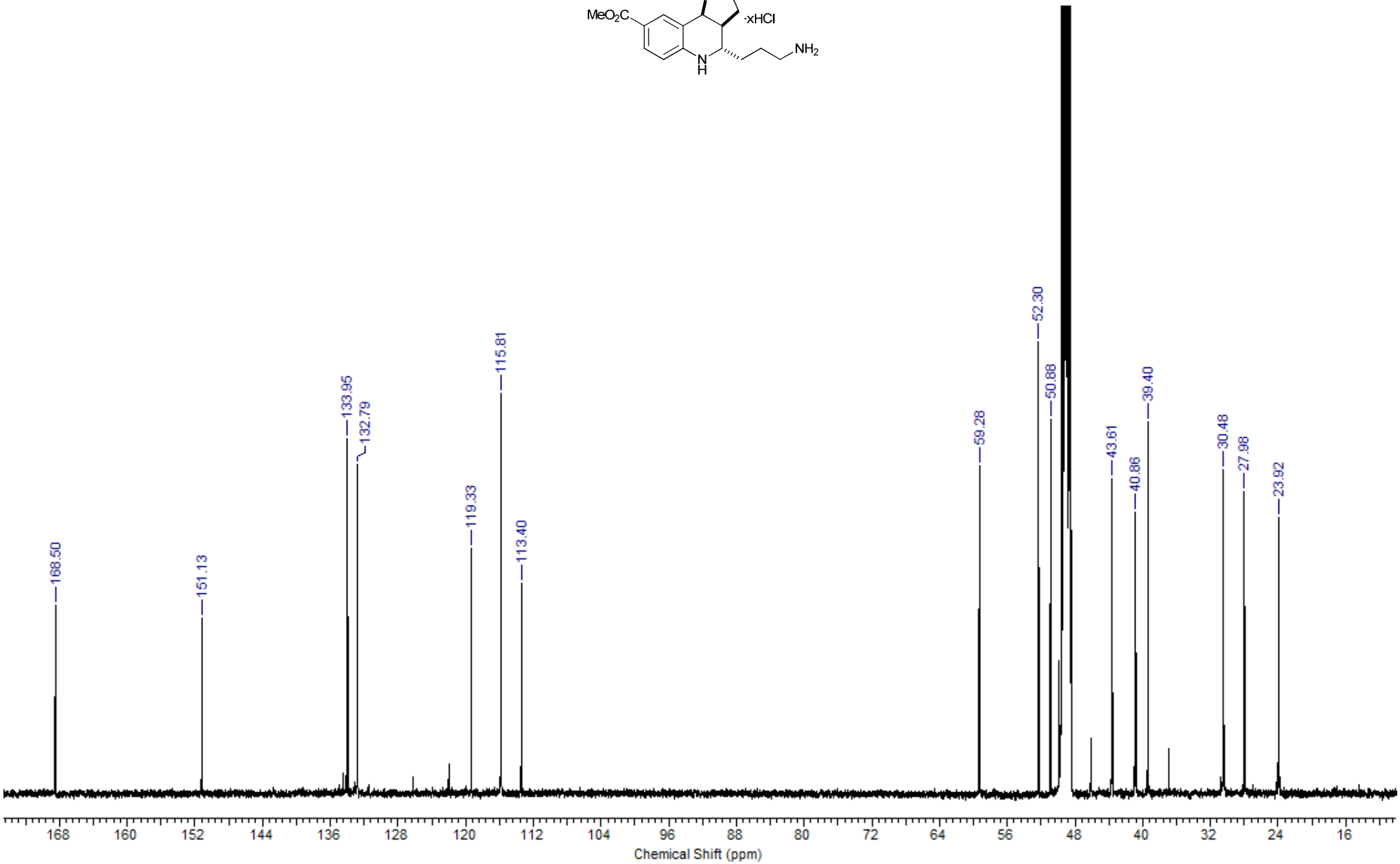
(*S*,*S*,*S*)-4-(3'-Aminopropyl)-8-(methoxycarbonyl)- 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]-quinoline·*x*HCl [“Ma’s intermediate”] 23·*x*HCl

(500 MHz ^{1}H, MeOD-d_4)

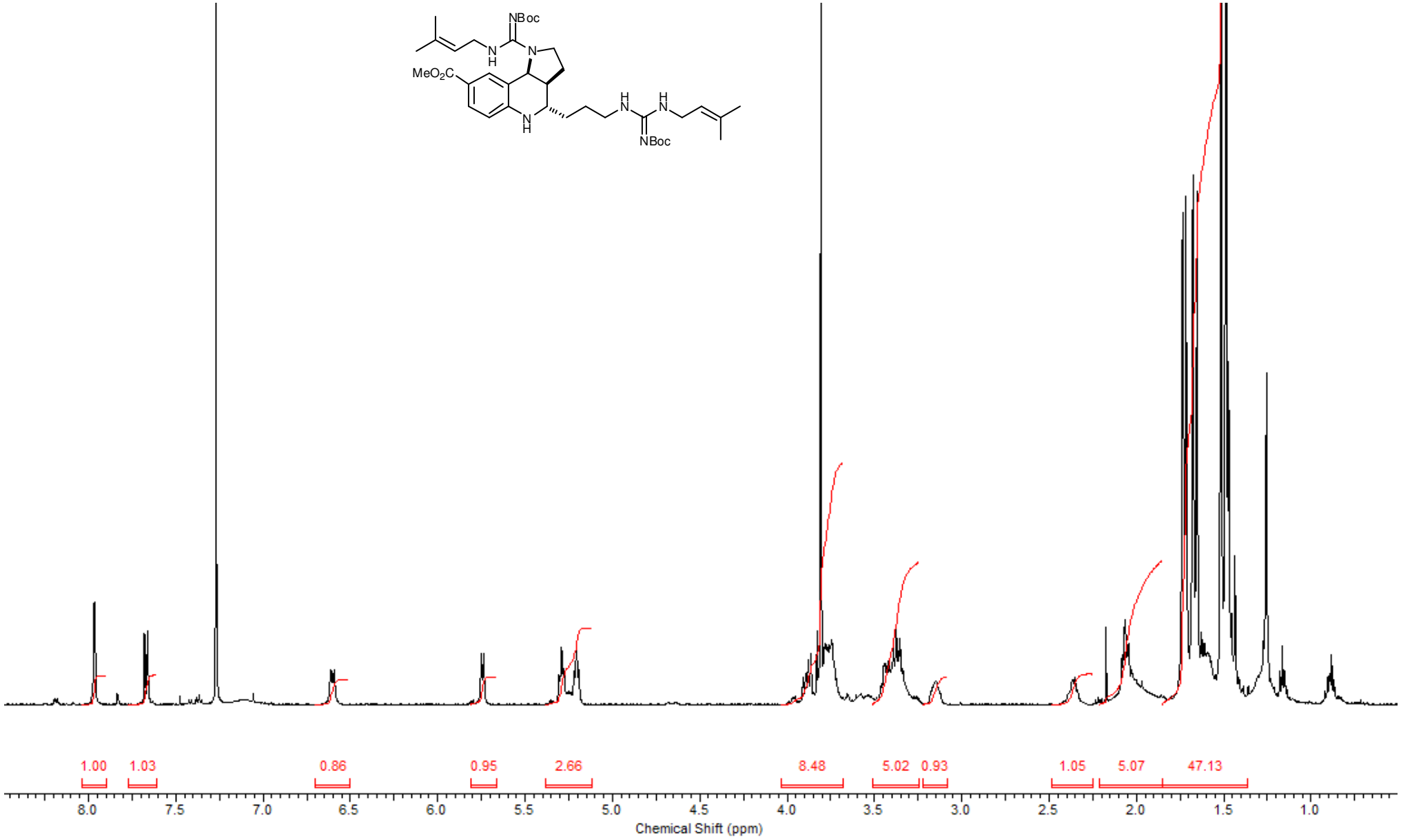


(*S*,*S*,*S*)-4-(3'-Aminopropyl)-8-(methoxycarbonyl)- 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]-quinoline·*x*HCl [“Ma’s intermediate”] 23·*x*HCl

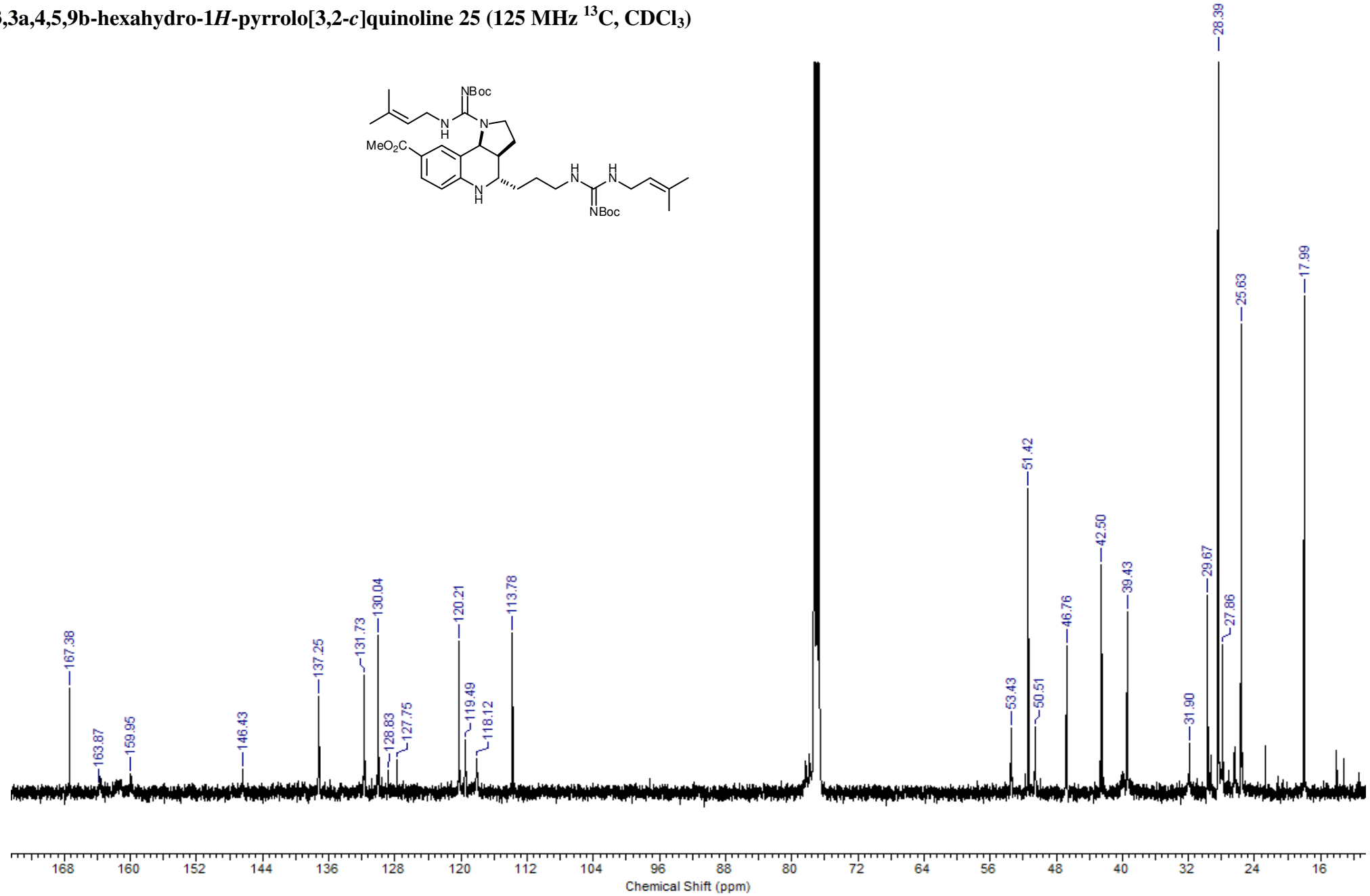
(125 MHz ^{13}C, MeOD-d_4)



(*S*,*S*,*S*)-*N*(1)-[*N*'-(*tert*-Butoxycarbonyl)-*N*''-prenylcarbamimidoyl]-4-{3'-[*N*'-(*tert*-butoxycarbonyl)-*N*''-prenylguanidino]propyl}-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 25 (500 MHz ^{1}H, $CDCl_3$)

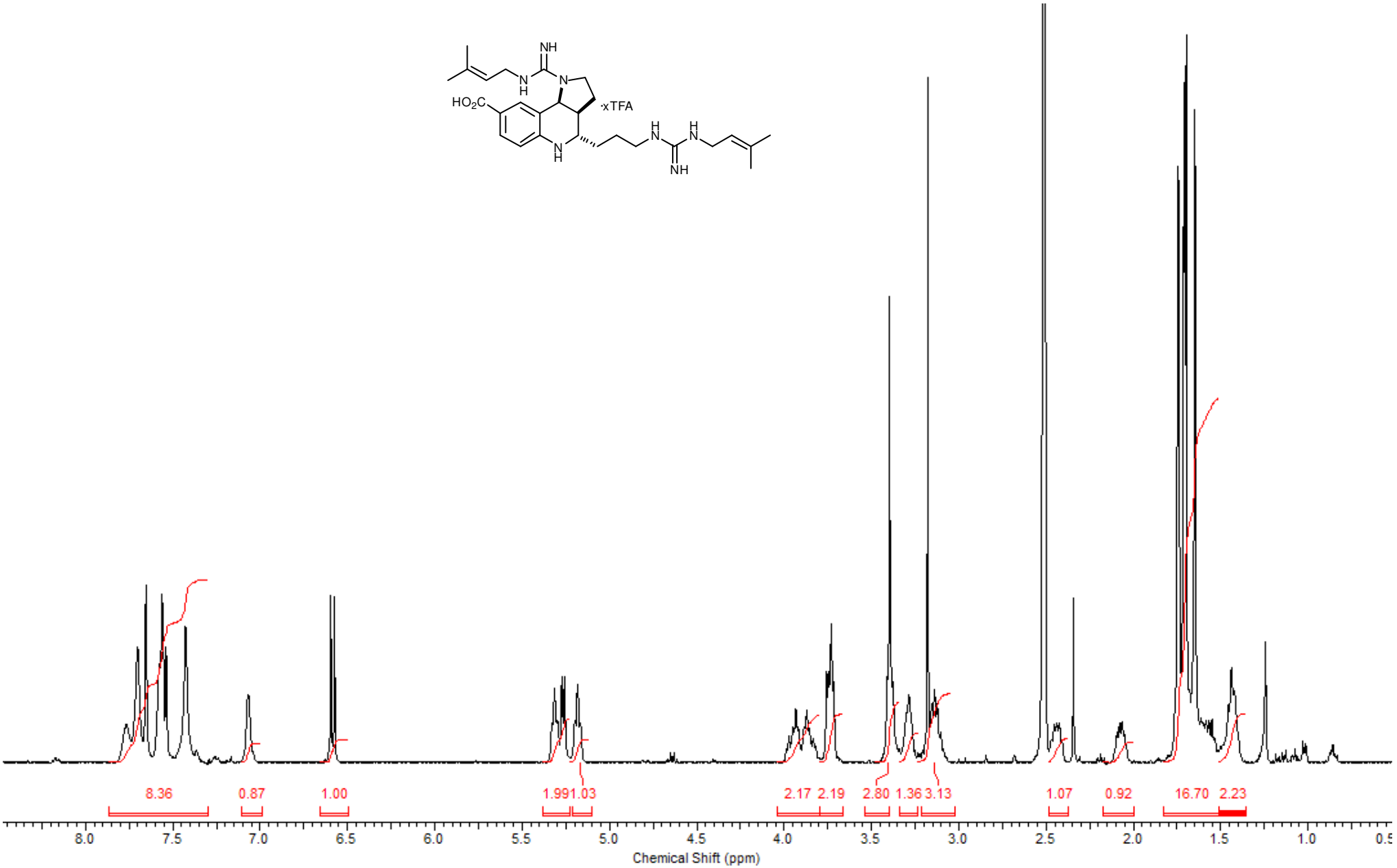


(*S*,*S*,*S*)-*N*(1)-[*N*'-(*tert*-Butoxycarbonyl)-*N*''-prenylcarbamimidoyl]-4-{3'-[*N*'-(*tert*-butoxycarbonyl)-*N*''-prenylguanidino]propyl}-8-(methoxycarbonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline 25 (125 MHz ^{13}C, $CDCl_3$)



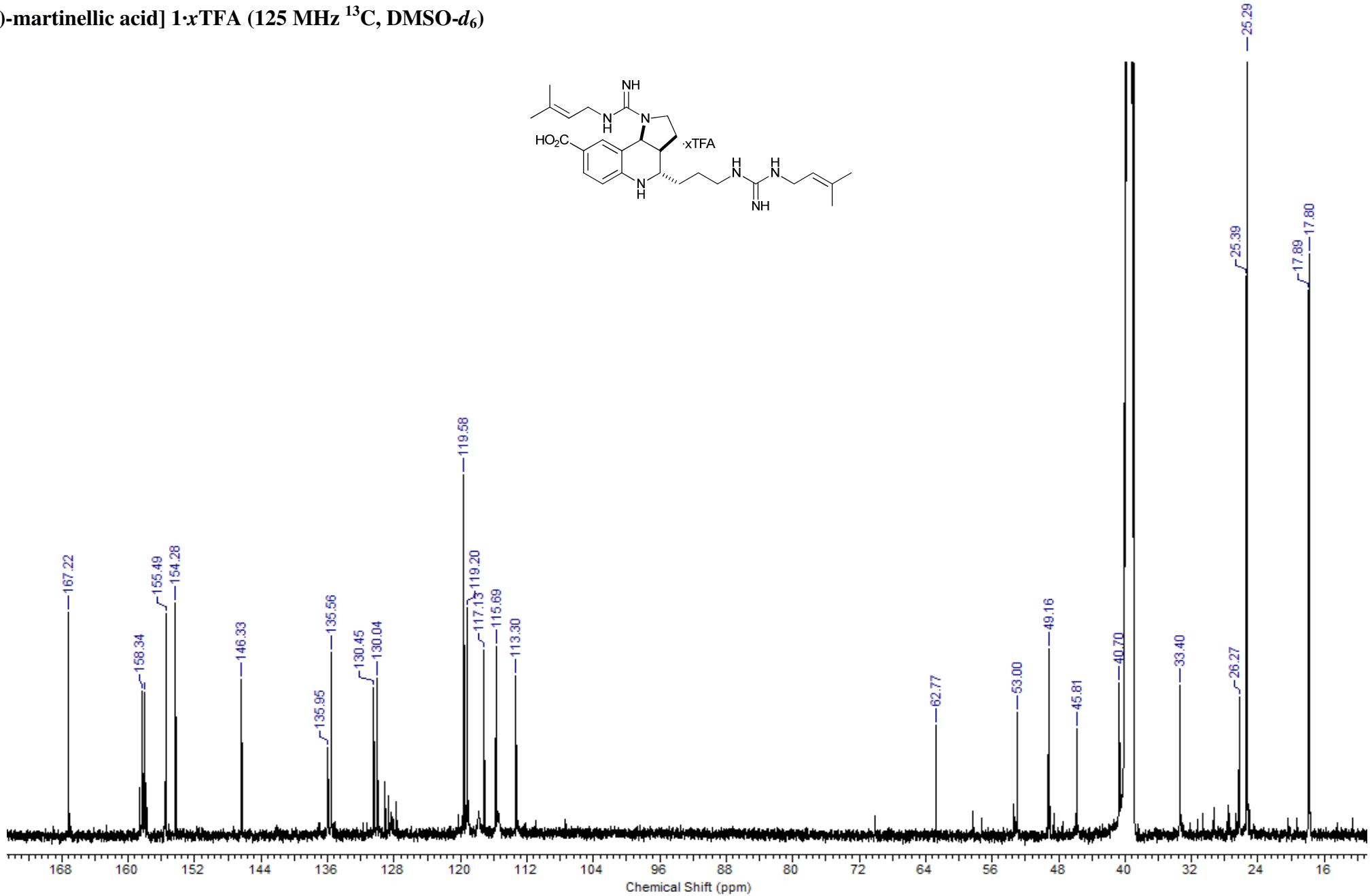
(*S*,*S*,*S*)-*N*(1)-[*N*''-Prenylcarbamimidoyl]-4-{3'-[*N*''-prenylguanidino]propyl}-8-carboxy-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline·*x*TFA

[(–)-martinellic acid] 1·*x*TFA (500 MHz ^{1}H, DMSO-d_6)



(*S*,*S*,*S*)-*N*(1)-[*N*''-Prenylcarbamimidoyl]-4-{3'-[*N*''-prenylguanidino]propyl}-8-carboxy-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline·*x*TFA

[(–)-martinellic acid] 1·*x*TFA (125 MHz ^{13}C, DMSO-d_6)



(*S*,*S*,*S*)-*N*(1)-[*N*''-Prenylcarbamimidoyl]-4-{3'-[*N*''-prenylguanidino]propyl}-8-carboxy-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline·*x*TFA

[(–)-martinellic acid] 1·*x*TFA (470 MHz ^{19}F, DMSO-d_6)