**Supporting Information.**

# Synthesis of 1- and 4-substituted piperazin-2-ones *via* Jocic-type reactions with *N*-substituted diamines.

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# 1. Experimental procedures.

## General Information.

Room temperature refers to ambient temperature (20-22 °C), 5 ºC refers to a cold water bath and 0 °C refers to an ice slush bath. Heated experiments were conducted using thermostatically controlled oil baths. All commercially available solvents and chemicals were used without any further purification. pH 2 buffer is an aqueous solution (0.25 M $H_2SO_4$ and 0.75 M $Na_2SO_4$).

NMR spectra were recorded on Bruker Advance DRX 250, 300, 400 and 600 MHz spectrometers at room temperature (298 K). Chemical shifts are reported in parts per million (ppm) referenced from $CDCl_3$ ($\delta_H$: 7.26 ppm and $\delta_C$: 77.0 ppm). Coupling constants (*J*) are rounded to the nearest 0.5 Hertz (Hz). Multiplicities are given as multiplet (m), singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin.), sextet (sext.), septet (sept.), octet (oct.) and nonet (non.). $^{1}H$ and $^{13}C$ assignments were established on the basis of COSY, DEPT, HMQC and HMBC correlations.

Infra-red spectra were recorded using either a Perkin Elmer Spectrum 100 FT-IR spectrometer or an Alpha Bruker Platunium ATR single reflection diamond ATR module.

Optical rotations were measured using an Optical Activity Ltd AA-1000 millidegree auto-ranging polarimeter (589 nm). Specific rotations are given in units of $10^{-1}$ deg $cm^2$ $g^{-1}$.

Melting points were recorded on a Stuart scientific melting point apparatus and are uncorrected.

Silica column chromatography was performed on 40-60 Å silica gel. Thin layer chromatography (TLC) was carried out aluminium sheets coated with 0.2 mm silica gel 60 $F_{254}$. Visualisation was effected by UV light (254 nm) or by potassium permanganate solution followed by heating.

Low resolution mass spectra (LRMS) were recorded using an Agilent 6130B single Quad (ESI). High resolution mass spectra (HRMS) were obtained were recorded using a Bruker micro-TOF ESI spectrometer.

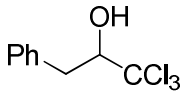
Chiral HPLC was performed on Chiralcel OD-H or AD-H columns (Diacel Industries Ltd) using a Varian Prostar 335 Photodiode Array Detector, a Varian Prostar Solvent Delivery Module and a Varian Prostar 420 Autosampler.

Chiral GC was performed on a CP-Chirasil-Dex Cβ column (Chrompak) using either a Hewlett Packard 5890 chromatograph fitted with a flame ionisation detector linked to a Hewlett Packard HP3396A integrator or a Perkin-Elmer 8500 chromatograph fitted with a flame ionisation detector linked to a PC running DataApex Clarity software.

Single X-ray crystal structures were performed on an Oxford Diffraction Gemini XRD.

## 1.1. Synthesis of trichlorocarbinols 22, 4 and 25.

### 1,1,1-trichloro-3-phenylpropan-2-ol 22.




Method modified from the literature.[1]

To a solution of phenylacetaldehyde (1.20 g, 10 mmol, 1 equiv.) in DMF (13.5 mL), cooled to 5 °C, was added trichloroacetic acid (2.45 g, 15 mmol, 1.5 equiv.). After stirring for 10 minutes, sodium trichloroacetate (2.78 g, 15 mmol, 1.5 equiv.) was added portionwise. The mixture was stirred at 5 °C for 30 minutes and then allowed warmed to room temperature where it was stirred for 17 hours. The reaction mixture was cooled to 5 °C before being quenched with water (10 mL). The reaction mixture was extracted with diethyl ether (3 x 40 mL). Organic extracts were combined and washed with sat. aq. sodium hydrogen carbonate (50 mL) and water (50 mL). The organics were dried ($MgSO_4$), filtered and concentrated *in*

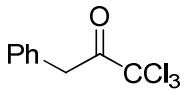
*vacuo*. The residues were purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether) to give a colourless oil (1.65 g, 69 %).

$\nu_{max}$/cm$^{-1}$ (neat) 3401 (br., OH st.), 1430 (m, C-O st.), 789 (C-Cl st.); $\delta_H$ (300 MHz; $CDCl_3$) 7.49-7.25 (5H, m, Ar*H*), 4.26 (1H, dd, *J* 9.5 and 1.5, C*H*OH), 3.44 (1H, dd, *J* 14 and 1.5, C*H*HPh), 2.89 (1H, dd, *J* 14 and 9.5, CH*H*Ph), 2.81 (1H, br. s, O*H*); $\delta_C$ (100 MHz; $CDCl_3$) 137.0 (Ar$C_{quat.}$), 129.4 (Ar*C*), 128.6 (Ar*C*), 127.0 (Ar*C*), 103.4 (*C*$Cl_3$), 83.9 (*C*HOH), 38.0 (*C*$H_2$Ph).

1,1,1-Trichloro-4-phenylbutan-2-ol **4** and 1,1,1-trichloro-4-methylpentan-2-ol **25** were synthesised according to the method previously described.[1]

## 1.2. Synthesis of trichloroketones 21, 24 and 1,1,1-trichloro-4-phenylbutan-2-one.

### 1,1,1-trichloro-3-phenylpropan-2-one 21.




Method modified from the literature.[1]

To a solution of 1,1,1-trichloro-3-phenylpropan-2-ol (0.52 g, 2.2 mmol, 1 equiv.) in acetic acid (10 mL), cooled to 5 °C, was added dropwise a solution of $NaCr_2O_7.2H_2O$ (0.79 g, 2.7 mmol, 1.2 equiv.) and concentrated sulfuric acid (0.23 mL, 4.4 mmol, 2 equiv.) in glacial acetic acid (10 mL). The mixture was stirred at 5 °C for 15 minutes before being allowed to warm to room temperature and stirred for 17 hours. The resulting solution was stirred at room temperature for 10 minutes. To the reaction mixture was added sat. aq. ammonium chloride (25 mL) which was extracted with dichloromethane (2 x 20 mL). The organic layers were combined and washed four times with 5 % aq. sodium hydrogen carbonate (3 x 40 mL), sat. aq. sodium hydrogen carbonate (50 mL) and then water (25 mL). Organic layer was dried

($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether) to give a colourless oil (0.44 g, 84 %).

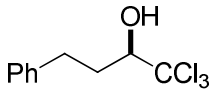
$\nu_{max}$/cm$^{-1}$ (neat) 1754 (s, C=O st.), 749 (s, C-Cl st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.44-7.28 (5H, m, Ar*H*), 4.29 (1H, s, C$H_2$); $\delta_C$ (100 MHz; $CDCl_3$) 187.8 (*C*O), 132.8 (Ar$C_{quat.}$), 129.5 (Ar*C*), 128.7 (Ar*C*), 127.5 (Ar*C*), 96.4 (*C*$Cl_3$), 40.2 (*C*$H_2$).

1,1,1-Trichloro-4-phenylbutan-2-one and 1,1,1-trichloro-4-methylpentan-2-one **24** were synthesised according the method previously reported.[1]

## 1.3. Asymmetric Reductions.

**Asymmetric Transfer Hydrogenation of Trichloroketones with [Ru(*p*-cymene)$Cl_2$]$_2$, (*R*,*R*)-TsDPEN in formic acid/triethylamine (5:2).[1]**

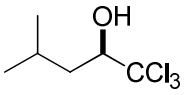
**(*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-4.**




The title compound was synthesised according to the method previously reported[1] with 1,1,1-trichloro-4-phenylbutan-2-one (4.68 g, 18.6 mmol) to give a colourless solid (4.26 g, 90 %, 95 % e.e.).

Spectroscopic data similar to that previously reported;[1] enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 10.31 min., (*R*)-isomer 17.51 min.). Chiral HPLC trace of racemate has been previously reported.[1]

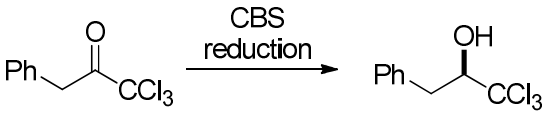
**(*R*)-1,1,1-trichloro-4-methylpentan-2-ol (*R*)-25.**




The title compound was synthesised according to the method previously reported[1] with 1,1,1-trichloro-4-methylpentan-2-one (2.08 g, 10 mmol) to give a colourless oil (1.45 g, 70 %, 97 % e.e.).

Spectroscopic data similar to that previously reported;*e*nantiomeric excess determined by GC analysis (CP-cyclodextrin-β-2,3,6-M-19, 50m 0.25mm 0.25μm, T = 120 °C, P = 15 psi ($H_2$ gas), (*S*)-isomer 16.5 min., (*R*)-isomer 17.9 min.). Chiral GC traces have been previously reported.[1]

**CBS Reduction of 1,1,1-trichloro-3-phenylpropan-2-one 22.**




Method modified from the literature.[2]

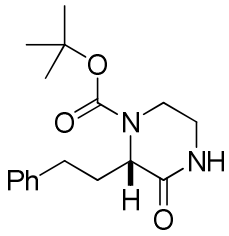
(*S*)-α,α-Diphenylprolinol (244 mg, 0.75 mmol), *n*-butylboronic acid (98 mg, 0.96 mmol) and toluene (30 mL) were heated at reflux under 4 Å molecular sieves and nitrogen for 16 hours. The reaction mixture was allowed to cool to room temperature and then a solution of 1,1,1-trichloro-3-phenylpropan-2-one **22** (1.78 g, 7.50 mmol) in dry toluene (35 mL) was added. This mixture was cooled to - 78 °C and a 1 M solution of catecholborane in THF (15 mL, 15 mmol) was added slowly. The mixture was stirred at -78 °C for 8 h and then at room temperature for 16 h. The reaction mixture was diluted with distilled water (20 mL) and extracted with ethyl acetate (20 mL). The organic phase was washed with 1 M sodium hydroxide (3 x 15 mL) and then with 1 M HCl (2 x 15 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by silica column chromatography (5 % ethyl

acetate in 40-60 petroleum ether) to afford (*R*)-1,1,1-trichloro-3-phenylpropan-2-ol (*R*)-**24** as a colourless oil (0.72 g, 40 %, 98 % e.e.).

Spectroscopic data similar to that of racemate. $[\alpha]_D^{26}$ (*c* 0.46, $CHCl_3$): + 29.5 (*R*); enantiomeric excess determined by GC analysis (CP-cyclodextrin-β-2,3,6-M-19, 50m 0.25mm 0.25μm, T = 160 °C, P = 15 psi ($H_2$ gas), (*S*)-isomer 52.0 min., (*R*)-isomer 53.6 min.).

## 1.4. Synthesis of 1-Substituted Piperazin-2-ones *via N*-Amino Alkylation.

### *N*-Boc-protection of (*S*)-3-Phenethylpiperazin-2-one (*S*)-1.




Method modified from the literature.[3] (*S*)-3-Phenethylpiperazin-2-one (*S*)-**1** was synthesised according to the method previously reported.[1]

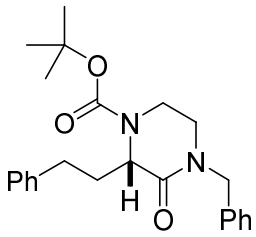
To a solution of (*S*)-3-phenethylpiperazin-2-one (*S*)-**1** (750 mg, 3.66 mmol, 96 % e.e.) in dry THF (35 mL) was added 40 % aq. NaOH (0.77 mL, 7.68 mmol, 2.1 equiv.). To this solution was added dropwise di-*tert*-butyl dicarbonate (960 mg, 4.39 mmol, 1.2 equiv.) in dry THF (3 mL). The reaction mixture was stirred at room temperature for 17 hours. THF was removed *in vacuo*, the residue taken up in ethyl acetate (40 mL) and washed with pH 2 buffer (2 x 40 mL). Organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford (*S*)-*tert*-butyl-3-oxo-2-phenethylpiperazine-1-carboxylate (*S*)-**2** as an orange solid (994 mg, 89 %, 94 % e.e.).

m.p. 138-140 ºC; $\nu_{max}/cm^{-1}$ (neat) 3189 (br., NH st.), 1695 (s, C=O st.), 1658 (s, C=O st.), 1333 (s, C-N st.), 1153 (s, C-O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.35-7.31 (2H, m, Ar*H*), 7.26-7.11

(3H, m, Ar*H*), 6.98 (1H, br. s, N*H*), 4.69 (1H, br. s, C*H*CO), 4.27 (1H, br. s, C*H*HNBoc), 3.52 (1H, td, *J* 11.5 and 3.5, C*H*HNH), 3.32-3.27 (1H, m, CH*H*NH), 3.25-3.19 (1H, m, CH*H*NBoc), 2.87-2.71 (2H, m, C$H_2$Ph), 2.35 (1H, dddd, *J* 14, 9.5, 6 and 4.5, C*H*HCHCO), 2.07 (1H, dddd, *J* 14, 11, 9.5 and 5, CH*H*CHCO), 1.51 (9H, s, 3 x C$H_3$); $\delta_C$ (100 MHz; $CDCl_3$) 171.0 (*C*O lactam), 154.1 (*C*O Boc), 151.3 (Ar$C_{quat.}$), 128.4 (Ar*C*), 128.3 (Ar*C*), 126.0 (Ar*C*), 80.8 (*C*$(CH_3)_3$), 57.1 (C*H*N), 41.3 (*C*$H_2$NH), 36.4 (*C*$H_2$NBoc), 33.8 (*C*$H_2$CHCO), 32.5 ($CH_2$*C*$H_2$Ph), 28.3 (3 x *C*$H_3$); HRMS (ESI) calc. for $C_{17}H_{24}N_2NaO_3$ ($M+Na^+$) 327.1684, found 327.1679; enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 22.41 min., (*R*)-isomer 28.93 min.).

Racemic **2** was synthesised according to this procedure with 3-phenethylpiperazin-2-one **1** (355 mg, 1.74 mmol) to give an orange solid (300 mg, 57 %).

***N*-Alkylation of (*S*)-*tert*-butyl-3-oxo-2-phenethylpiperazine-1-carboxylate (*S*)-2.**




Method modified from the literature.[4]

60 % Sodium hydride in mineral oil (200 mg, 5 mmol, 2.5 equiv.) in dry THF (16 mL) was stirred at 0 °C for 10 minutes under nitrogen. To this (*S*)-*tert*-butyl-3-oxo-2-phenethylpiperazine-1-carboxylate (*S*)-**2** (608 mg, 1 mmol, 94 % e.e.) in dry THF (9 mL) was added dropwise over 10 minutes and left to stir at 0 °C for 90 minutes. Benzyl bromide (0.48 mL, 4 mmol, 2 equiv.) was then added dropwise. The reaction mixture was stirred for a further 10 minutes at 0 °C before being allowed to warm to room temperature where it was stirred for 18 hours. To the reaction mixture was added distilled water (20 mL), which was

then extracted with diethyl ether (3 x 30 mL). The organic extracts were combined and washed with water (50 mL) and brine (50 mL). Organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The yellow oil was purified by silica column chromatography (10 % ethyl acetate in 40-60 petroleum ether) to give *tert*-butyl (*S*)-4-benzyl-3-oxo-2-phenethylpiperazine-1-carboxylate as a yellow solid (*S*)-**3** (299 mg, 38 %).

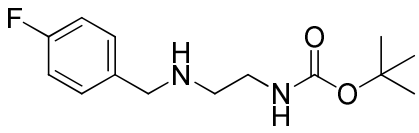
m.p. 129-130 ºC; $\nu_{max}/cm^{-1}$ (neat) 1694 (s, C=O st.), 1649 (s, C=O st.), 1162 (m, N-CO-O st.), 1125 (m, C-N st.), 1004 (w, N-CO-O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.37-7.20 (10H, m, Ar*H*), 4.94 (1H, br. d, *J* 12.5, NC*H*HPh), 4.81-4.68 (1H, br. m, C*H*N), 4.29 (1H, br. d, *J* 13, NCH*H*Ph), 4.22-4.09 (1H, br. m, C*H*HNBoc), 3.42 (1H, td, *J* 11 and 3.5, C*H*HNBn) 3.26-3.16 (1H, m, CH*H*NBoc), 3.15-3.10 (1H, m, CH*H*NBn), 2.83 (1H, td, *J* 13.5 and 5.5, $CH_2$C*H*HPh), 2.72 (1H, td, *J* 12 and 5, $CH_2$CH*H*Ph), 2.45-2.36 (1H, m, C*H*HCHCO), 2.11-2.01 (1H, m, CH*H*CHCO), 1.48 (9H, s, 3 x C$H_3$); $\delta_C$ (100 MHz; $CDCl_3$) 168.5 (*C*O lactam), 154.0 (*C*O Boc), 141.4 (Ar$C_{quat.}$), 136.4 (Ar$C_{quat.}$), 128.8 (Ar*C*), 128.4 (Ar*C*), 128.3 (Ar*C*), 128.1 (Ar*C*), 127.7 (Ar*C*), 126.0 (Ar*C*), 77.2 (*C*$(CH_3)_3$), 57.3 (C*H*N), 50.0 (N*C*$H_2$Ph), 45.6 (*C*$H_2$NBn), 40.8 (*C*$H_2$NBoc), 34.3 (*C*$H_2$CHCO), 32.6 ($CH_2$*C*$H_2$Ph), 28.3 (3 x *C*$H_3$); HRMS (ESI) calc. for $C_{24}H_{31}N_2O_3$ ($M+H^+$) 395.2329, found 395.2332; enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 209 nm, (*R*)-isomer 10.85 min., (*S*)-isomer 13.73 min.).

Racemic **3** was synthesised according to this procedure with *tert*-butyl-3-oxo-2-phenethylpiperazine-1-carboxylate (304 mg, 1 mmol) to give a yellow solid (197 mg, 50 %).

### 1.5. Synthesis of diamines.

*N*-phenyl-1,2-ethylenediamine and *N*-phenyl-1,3-propanediamine were synthesised according to the literature method by Yin *et al*.[5] *tert*-Butyl (3-aminoethyl)carbamate and *tert*-butyl (3-aminopropyl)carbamate were synthesised according to the literature method by Muller *et al*.[6]

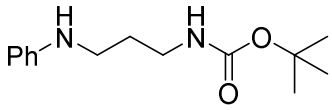
***tert*-butyl (2-((4-fluorobenzyl)amino)ethyl)carbamate.**



To a solution of *tert*-butyl-(3-aminoethyl)carbamate (3.5 g, 22 mmol, 1 equiv.) in methanol (30 mL) at 0 °C was added 4-fluorobenzaldehyde (2.58 mL, 24.1 mmol, 1.1 equiv.). The reaction mixture was allowed to warm to room temperature where it was stirred for a further 17 hours before being cooled to 0 °C for the portionwise addition of sodium borohydride (4.97 g, 131.4 mmol, 6 equiv.). The resulting mixture was stirred at 0 °C for 1 hour before being allowed to warm to room temperature over 17 hours. The reaction mixture was concentrated *in vacuo*, dissolved in ethyl acetate (50 mL) and washed with 0.5 M hydrochloric acid (2 x 50 mL). Aqueous extracts were combined, cooled to 0 °C and basified with sat. aq. sodium hydrogen carbonate. Resulting basic solution was extracted with chloroform (3 x 50 mL). Combined organics were dried ($MgSO_4$) and concentrated *in vacuo* to afford *tert*-butyl (2-((4-fluorobenzyl)amino)ethyl)carbamate as a viscous cream oil (2.60 g, 44 %).

$\nu_{max}/cm^{-1}$ (neat) 3337 (br., NH st.), 1691 (s, C=O st.), 1220 (s, CF st.); $\delta_F$ (300 MHz; $CDCl_3$) -116.6; $\delta_H$ (400 MHz; $CDCl_3$) 7.26 (2H, dd, J 8.5 and 6, Ar*H*), 7.00 (2H, t, *J* 8.5, Ar*H*), 3.74 (2H, s, C*H*$_2$Ar), 3.23 (2H, q, *J* 6, C*H*$_2$NHBoc), 2.73 (2H, t, *J* 6, C*H*$_2$NHCH$_2$Ar), 1.44 (9H, s, 3 x C*H*$_3$); $\delta_C$ (100 MHz; $CDCl_3$) 161.9 (d, $^1J_{CF}$ 245, Ar*C*F), 156.1 (*C*O), 135.9 (d, $^4J_{CF}$ 3, Ar$C_{quat.}$), 129.6 (d, $^3J_{CF}$ 8, Ar*C*), 115.1 (d, $^2J_{CF}$ 21, Ar*C*), 77.2 (*C*(CH$_3$)$_3$), 52.8 (*C*H$_2$Ar), 48.5 (*C*H$_2$NHAr), 40.2 (*C*H$_2$NHBoc), 28.4 (3 x *C*H$_3$); HRMS (ESI) cald. for $C_{14}H_{22}FN_2O_2$ ($M+H^+$) 269.1660, found 269.1654.

***tert*-Butyl (3-(phenylamino)propyl)carbamate.**

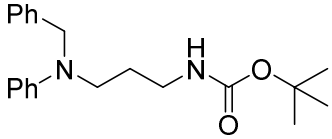


Method modified from the literature.[7]

To *N*-phenyl-1,3-diaminopropane (3.16 g, 21.1 mmol, 1 equiv.) in methanol (60 mL) was added dropwise di-*tert*-butyl dicarbonate (4.69 g, 21.5 mmol, 1.02 equiv.) in methanol (24 mL) and resulting solution stirred at room temperature for 16 hours. The reaction mixture was concentrated *in vacuo* and purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether to 40 % ethyl acetate in 40-60 petroleum ether) to give a colourless oil (4.06 g, 77 %).

$\nu_{max}$/cm$^{-1}$ (neat) 3367 (br., NH st.), 1688 (s, C=O st.); $\delta_H$ (300 MHz; $CDCl_3$) 7.20-7.14 (2H, m, Ar*H*), 6.70 (1H, t, *J* 7.5, *p*-Ar*H*), 6.61 (2H, d, *J* 8, Ar*H*), 4.68 (1H, br. s, N*H*Boc), 3.81 (1H, br. s, N*H*Ph), 3.23 (2H, q, *J* 6.5, C*H*$_2$NHBoc), 3.18 (2H, t, *J* 6.5, C*H*$_2$NHPh), 1.78 (2H, quin. J 6.5, C*H*$_2$CH$_2$NHPh), 1.45 (9H, m, 3 x C*H*$_3$); $\delta_C$ (75 MHz; $CDCl_3$) 156.2 (*C*O), 148.0 (Ar*C*$_{quat.}$), 129.2 (Ar*C*), 117.3 (Ar*C*), 112.9 (Ar*C*), 79.3 (*C*(CH$_3$)$_3$), 41.0 (*C*H$_2$), 38.1 (*C*H$_2$), 29.6 (*C*H$_2$), 28.4 (3 x *C*H$_3$); HRMS (ESI) calc. for $C_{14}H_{23}N_2O_2$ (M+H$^+$) 251.1754, found 251.1757.

***tert*-Butyl (3-(benzyl(phenyl)amino)propyl)carbamate.**



To *tert*-Butyl (3-(benzylamino)propyl)carbamate (2.36 g, 9.4 mmol, 1 equiv.) and potassium carbonate (1.96 g, 14.2 mmol, 1.5 equiv.) in ethanol (38 mL) was added benzyl bromide (1.68 mL, 14.2 mmol, 1.5 equiv.). The resulting mixture was heated to reflux for 3 hours before being allowed to cool to room temperature. Reaction mixture was concentrated *in*

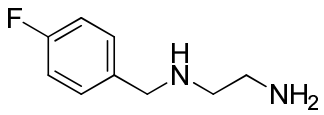
*vacuo* and partitioned between distilled water (40 mL) and ethyl acetate (3 x 30 mL). Combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Residue was purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether to 10 % ethyl acetate in 40-60 petroleum ether) to give a light yellow oil (1.91 g, 60 %).

$\nu_{max}/cm^{-1}$ (neat) 3354 (br., NH st.), 1692 (s, C=O st.); $\delta_H$ (300 MHz; $CDCl_3$) 7.62-7.29 (7H, m, Ar*H*), 6.91-6.78 (3H, m, Ar*H*), 4.71-4.63 (3H, m, C*H*$_2$Ph and N*H*Boc), 3.57 (2H, t, *J* 7.5, $CH_2$NPh), 3.31 (2H, br. q, *J* 7, C*H*$_2$NHBoc), 1.98 (2H, quin., *J* 7, $CH_2$C*H*$_2$$CH_2$), 1.58 (9H, s, 3 x C*H*$_3$); $\delta_C$ 129.2 (Ar*C*), 128.6 (Ar*C*), 128.3 (Ar*C*), 126.6 (Ar*C*), 116.5 (Ar*C*), 112.5 (Ar*C*), 69.4 (*C*$H_2$), 64.1 (*C*$H_2$), 54.8 (*C*$H_2$), 48.5 (*C*$H_2$), 28.3 (3 x *C*$H_3$); HRMS (ESI) calc. for $C_{21}H_{29}N_2O_2$ ($M+H^+$) 341.2224, found 341.2222. Four quaternary peaks in the $^{13}C$ NMR spectrum were not resolvable; *C*O, 2 x Ar$C_{quat.}$ and *C*$(CH_3)_3$.

## Boc-deprotection. General Procedure 1:

To a solution of Boc-protected amine (5.82 mmol, 1 equiv.) in $CH_2Cl_2$ (10 mL) at 5 °C was added dropwise trifluoroacetic acid (5 mL) in $CH_2Cl_2$ (20 mL). The reaction mixture was allowed to warm to room temperature where it was stirred for a further 6 hours. Reaction mixture was concentrated *in vacuo*, diluted with distilled water (10 mL) and the pH was adjusted to 14 with 4 M sodium hydroxide. Resulting solution was extracted with $CH_2Cl_2$ (3 x 30 mL). Combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford product, which was used without further purification.

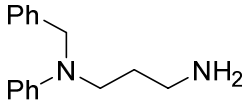
**$N^1$-4-fluorobenzylethane-1,3-diamine.**



The title compound was synthesised using General Procedure 1 with *tert*-butyl (2-((4-fluorobenzyl)amino)ethyl)carbamate (2.03 g, 7.6 mmol, 1 equiv.) to give a yellow oil (1.08 g, 85 %).

$\nu_{max}$/cm$^{-1}$ (neat) 3279 (br., NH st.), 1266 (s, CF st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.27 (2H, dd, *J* 8.5 and 5.5, Ar*H*), 7.00 (2H, t, *J* 8.5, Ar*H*), 3.75 (2H, s, C$H_2$Ar), 2.80 (2H, t, *J* 5.5, C$H_2$NH$_2$), 2.67 (2H, t, *J* 5.5, C$H_2$NHAr); $\delta_C$ (100 MHz; $CDCl_3$) 140.0 (Ar$C_{quat.}$), 161.9 (d, $^1J_{CF}$ 245, Ar*C*F), 136.1 (Ar$C_{quat.}$), 129.6 (d, $^3J_{CF}$ 8, Ar*C*), 115.1 (d, $^2J_{CF}$ 21, Ar*C*), 53.1 (*C*H$_2$Ar), 51.7 (*C*H$_2$NHAr), 41.6 (*C*H$_2$NH$_2$); HRMS (ESI) cald. for $C_9H_{14}FN_2$ (M+H$^+$) 169.1136, found 169.1137.

**$N^1$-Benzyl-$N^1$-phenylpropane-1,3-diamine.**



The title compound was synthesised according to General Procedure 1 with *tert*-butyl (3-(benzyl(phenyl)amino)propyl)carbamate (1.98 g, 5.82 mmol) to give a yellow oil (0.55 g, 39 %), which was used without further purification.

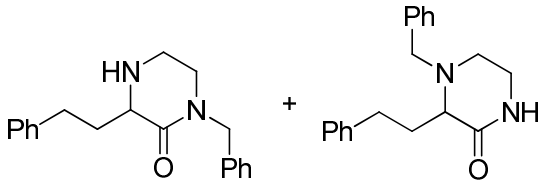
$\nu_{max}$/cm$^{-1}$ (neat) 3304 (br., NH$_2$ st.), 1596 (m, NH$_2$ bend), 1503 (m, C-N st.); $\delta_H$ (250 MHz; $CDCl_3$) 7.34-7.13 (7H, m, Ar*H*), 6.76-6.59 (3H, m, Ar*H*), 4.55 (2H, s, C$H_2$Ph), 3.52-3.41 (2H, m, CH$_2$N), 2.77 (2H, t, *J* 7, CH$_2$N), 1.81 (2H, quin., *J* 7, CH$_2$C$H_2$CH$_2$), 1.33 (2H, br. s, NH$_2$); $\delta_C$ (75 MHz; $CDCl_3$) 148.5 (Ar$C_{quat.}$), 138.9 (Ar$C_{quat.}$), 128.5 (Ar*C*), 126.7 (Ar*C*), 126.5 (Ar*C*), 116.2 (Ar*C*), 112.7 (Ar*C*), 112.3 (Ar*C*), 54.5 (*C*H$_2$), 48.7 (*C*H$_2$), 40.0 (*C*H$_2$), 31.1 (*C*H$_2$); HRMS (ESI) calc. for $C_{16}H_{21}N_2$ (M+H$^+$) 241.1699, found 241.1704.

## 1.6. Jocic-type Reactions with Unsymmetrical Diamines. General Procedure 2:

Trichlorocarbinol (1 mmol, 1 equiv.) and benzyltriethylammonium chloride (4.6 mg, 0.02 mmol, 0.02 equiv.) were stirred in $CH_2Cl_2$ (1 mL) on ice. Diamine was added, and the mixture was stirred for 10 minutes before the dropwise addition of 40 % aq. NaOH (5 mmol). The reaction mixture was stirred for a further 15 minutes on ice before being allowed to warm to room temperature where it was stirred for 17 hours. Distilled water (15 mL) was added and the reaction mixture was extracted with $CH_2Cl_2$ (3 x 15 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by silica column chromatography.

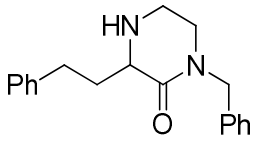
**Racemic Products.**

**1-Benzyl-3-phenethylpiperazin-2-one 5 and 4-benzyl-3-phenethylpiperazin-2-one 6.**



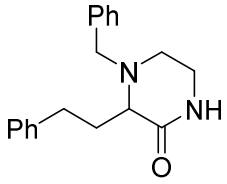

The title compounds were synthesised in a 93 : 7 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-benzyl-1,2-ethylenediamine (0.75 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 10 % MeOH in ethyl acetate) to give 1-benzyl-3-phenethylpiperazin-2-one **5** as a yellow solid (230 mg, 78 %) and 4-benzyl-3-phenethylpiperazin-2-one **6** as a yellow solid (14 mg, 5 %).

**1-Benzyl-3-phenethylpiperazin-2-one 5.**




m.p. 58-61 ºC; $\nu_{max}$/cm$^{-1}$ (neat) 3328 (br. m, NH st.), 1629 (s, C=O st.), 1227 (s, C-N st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.36-7.17 (10H, m, Ar*H*), 4.64 (1H, d, *J* 14.5, NC*H*HPh), 4.57 (1H, d, *J* 14.5, NCH*H*Ph), 3.51 (1H, dd, *J* 8.5 and 4, C*H*N), 3.31 (1H, ddd, *J* 11.5, 8.5 and 4.5, C*H*HNBn), 3.16-3.13 (1H, m, C*H*HNH), 3.10-3.06 (1H, m, CH*H*NBn), 2.95 (1H, ddd, *J* 13.5, 10.5 and 5, CH*H*NH), 2.85-2.71 (2H, m, $CH_2CH_2$Ph), 2.37 (1H, dddd, *J* 14, 10.5, 7 and 4, C*H*HCHCO), 2.03 (1H, dddd, *J* 14, 9.5, 8.5 and 6, CH*H*CHCO); $\delta_C$ (100 MHz; $CDCl_3$) 171.2 (*C*O), 141.6 ($(CH_2)_2$Ar$C_{quat.}$), 136.9 ($NCH_2$Ar$C_{quat.}$), 128.6 (Ar*C*), 128.5 (Ar*C*), 128.4 (Ar*C*), 128.1 (Ar*C*), 127.4 (Ar*C*), 125.9 (Ar*C*), 58.7 (*C*HN), 50.1 (N*C*$H_2$Ph), 47.6 (*C*$H_2$NBn), 41.7 (*C*$H_2$NH), 34.1 (*C*$H_2$CHCO), 32.3 ($CH_2$*C*$H_2$Ph); HRMS (ESI) calc. for $C_{19}H_{23}N_2O$ ($M+H^+$) 295.1805, found 295.1807.

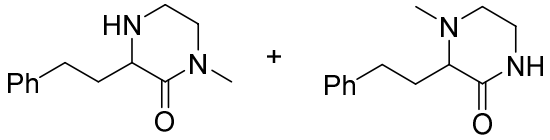
**4-Benzyl-3-phenethylpiperazin-2-one 6.**




m.p. 125-127 ºC; $\nu_{max}$/cm$^{-1}$ (neat) 3201 (br., NH st.), 1666 (s, C=O st.), 1494 (m, NH bend); $\delta_H$ (400 MHz; $CDCl_3$) 7.28-7.04 (10H, m, Ar*H*), 6.73 (1H, br. s, N*H*), 3.89 (1H, d, *J* 13.5, NC*H*HPh), 3.33 (1H, d, *J* 13.5, NCH*H*Ph), 3.24-3.21 (2H, m, C$H_2$NH), 3.09 (1H, t, *J* 5, C*H*N), 2.89 (1H, dt, *J* 12.5 and 5, C*H*HNBn), 2.79 (1H, ddd, *J* 14, 11 and 5.5, $CH_2$C*H*HPh), 2.62 (1H, ddd, *J* 13.5, 11 and 5.5, $CH_2$CH*H*Ph), 2.42 (1H, dt, *J* 12.5 and 6, CH*H*NBn), 2.22 (1H, ddt, *J* 14, 11 and 5, C*H*HCHCO), 2.04 (1H, ddt, *J* 14, 10.5 and 5, CH*H*CHCO); $\delta_C$ (100 MHz; $CDCl_3$) 172.4 (*C*O), 142.2 ($(CH_2)_2$Ar$C_{quat.}$), 138.1 ($NCH_2$Ar$C_{quat.}$), 128.8 (Ar*C*), 128.5 (Ar*C*), 128.4 (Ar*C*), 128.3 (Ar*C*), 127.3 (Ar*C*), 125.7 (Ar*C*), 64.1 (*C*HN), 58.2 (N*C*$H_2$Ph),

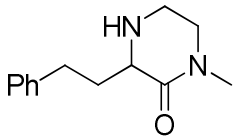
45.0 (*C*$H_2$NBn), 39.9 (*C*$H_2$NH), 32.0 (*C*$H_2$CHCO), 31.4 ($CH_2$*C*$H_2$Ph); HRMS (ESI) calc. for $C_{19}H_{23}N_2O$ ($M+H^+$) 295.1805, found 295.1815.

**1-Methyl-3-phenethylpiperazin-2-one 7 and 4-Methyl-3-phenethylpiperazin-2-one 8.**



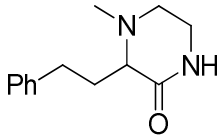

The title compounds were synthesised in a 50 : 50 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-methyl-1,2-ethylenediamine (0.44 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (ethyl acetate to 10 % MeOH in ethyl acetate) to give 1-methyl-3-phenethylpiperazin-2-one **7** as a yellow oil (103 mg, 47 %) and 4-methyl-3-phenethylpiperazin-2-one **8** as a yellow oil (78 mg, 36 %).

**1-Methyl-3-phenethylpiperazin-2-one 7.**



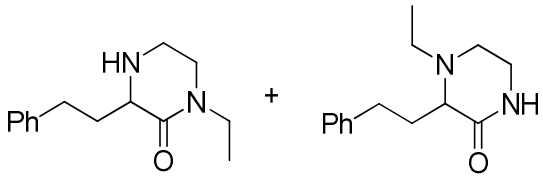

$\nu_{max}$/$cm^{-1}$ (neat) 3429 (br., amine NH st.), 1635 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.32-7.18 (5H, m, Ar*H*), 3.49-3.41 (2H, m, C*H*N and C*H*HNH), 3.24-3.14 (2H, m, CH*H*NH and C*H*HNC$H_3$), 3.07-2.98 (1H, m, CH*H*NC$H_3$), 2.97 (1H, s, NC$H_3$), 2.84-2.70 (2H, m, C$H_2$Ph), 2.39-2.30 (1H, m, C*H*HCHCO), 2.12 (1H, br. s, N*H*), 1.98 (1H, ddt, *J* 15, 9 and 6, CH*H*CHCO); $\delta_C$ (100 MHz; $CDCl_3$) 170.3 (*C*O), 141.6 (Ar$C_{quat.}$), 128.4 (Ar*C*), 128.3 (Ar*C*), 125.8 (Ar*C*), 58.5 (*C*HN), 50.2 (*C*$H_2$NH), 41.5 (*C*$H_2$NC$H_3$), 34.6 (NC$H_3$), 33.8 (*C*$H_2$CHCO), 32.3 (*C*$H_2$Ph); HRMS (ESI) calc. for $C_{13}H_{18}N_2NaO$ ($M+Na^+$) 241.1311, found 241.1317.

**4-Methyl-3-phenethylpiperazin-2-one 8.**



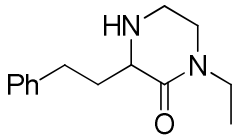

$\nu_{max}$/cm$^{-1}$ (neat) 3243 (br., lactam NH st.), 1666 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.29-7.15 (5H, m, Ar*H*), 5.98 (1H, br. s, N*H*), 3.49 (1H, m, C*H*HNH), 3.28 (1H, dq, *J* 11.5 and 3.5, CH*H*NH), 3.00-2.88 (2H, m, C*H*HNCH$_3$ and C*H*N), 2.80 (1H, m, CH*H*CH$_3$), 2.64-2.56 (2H, m, C*H*$_2$Ph), 2.41 (3H, s, C*H*$_3$), 2.31 (1H, dddd, *J* 14, 11.5, 5.5 and 4, C*H*HCHCO), 2.02 (1H, m, CH*H*CHCO); $\delta_C$ (100 MHz; $CDCl_3$) 173.7 (*C*O), 134.4 (Ar*C*$_{quat.}$), 128.6 (Ar*C*), 128.3 (Ar*C*), 125.7 (Ar*C*), 66.5 (*C*HN), 50.3 (*C*H$_2$NCH$_3$), 42.9 (*C*H$_3$), 40.4 (*C*H$_2$NH), 31.2 (*C*H$_2$CHCO), 30.8 (*C*H$_2$Ph); HRMS (ESI) calc. for $C_{13}H_{18}N_2NaO$ (M+Na$^+$) 241.1311, found 241.1303.

**1-Ethyl-3-phenethylpiperazin-2-one 9 and 4-Ethyl-3-phenethylpiperazin-2-one 10.**



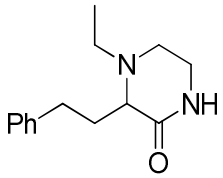

The title compounds were synthesised in a 75 : 25 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **25** (254 mg, 1 mmol, 1 equiv.) and *N*-ethyl-1,2-ethylenediamine (0.53 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (ethyl acetate to 10 % MeOH in ethyl acetate) to give 1-ethyl-3-phenethylpiperazin-2-one **9** as a light yellow oil (169 mg, 72 %) and 4-ethyl-3-phenethylpiperazin-2-one **10** as a yellow oil (19 mg, 8 %).

**1-Ethyl-3-phenethylpiperazin-2-one 9.**




$\nu_{max}$/cm$^{-1}$ (neat) 3457 (br., amine NH st.), 1626 (s, C=O st.); $\delta_H$ (600 MHz; $CDCl_3$) 7.30 (2H, t, *J* 7.5, 2 x *o*-Ar*H*), 7.25 (2H, d, *J* 7, 2 x *m*-Ar*H*), 7.20 (1H, t, *J* 7, *p*-Ar*H*), 3.50-3.38 (4H, m, C*H*N, NC*H*$_2$CH$_3$ and C*H*HNCH$_2$CH$_3$), 3.23-3.17 (2H, m, CH*H*NCH$_2$CH$_3$ and C*H*HNH), 3.01 (1H, ddd, *J* 14.5, 11 and 5.5, CH*H*NH), 2.82-2.73 (2H, m, C*H*$_2$Ph), 2.33 (1H, dddd, *J* 14, 10.5, 6.5 and 4, C*H*HCHCO), 1.98 (1H, dtd, *J* 14, 9 and 6, CH*H*CHCO), 1.87 (1H, br. s, N*H*), 1.15 (1H, t, *J* 7, C*H*$_3$); $\delta_C$ (150 MHz; $CDCl_3$) 169.6 (*C*O), 141.6 (Ar*C*$_{quat.}$), 128.4 (Ar*C*), 128.3 (Ar*C*), 125.8 (Ar*C*), 58.6 (*C*HN), 47.4 (*C*H$_2$NCH$_2$CH$_3$), 41.8 (N*C*H$_2$CH$_3$), 41.7 (*C*H$_2$NH), 34.0 (*C*H$_2$CHCO), 32.2 (*C*H$_2$Ph), 12.1 (*C*H$_3$); HRMS (ESI) calc. for $C_{14}H_{21}N_2O$ (M+H$^+$) 233.1648, found 233.1649.

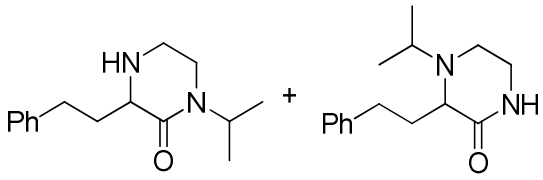
**4-Methyl-3-phenethylpiperazin-2-one 10.**




$\nu_{max}$/cm$^{-1}$ (neat) 3232 (br., lactam NH st.), 1656 (s, C=O st.); $\delta_H$ (600 MHz; $CDCl_3$) 7.30 (2H, t, *J* 7, 2 x *m*-Ar*H*), 7.25 (2H, t, *J* 7, 2 x *o*-Ar*H*), 7.20 (1H, t, *J* 7, *p*-Ar*H*), 6.70 (1H, br. s, N*H*), 3.44-3.35 (2H, m, C*H*$_2$NH), 3.16-3.10 (2H, m, C*H*N and C*H*HNCH$_2$CH$_3$), 2.83 (1H, ddd, *J* 14, 11 and 5.5, C*H*HPh), 2.81-2.76 (1H, m, NC*H*HCH$_3$), 2.71 (1H, ddd, *J* 13.5, 11 and 5.5, CH*H*Ph), 2.66 (1H, ddd, *J* 12, 7 and 4, CH*H*NCH$_2$CH$_3$), 2.56 (1H, dq, *J* 14 and 7, NCH*H*CH$_3$), 2.23 (1H, ddt, *J* 14, 11 and 5.5, C*H*HCHCO), 2.09 (1H, ddt, *J* 14, 11 and 5, CH*H*CHCO), 1.11 (3H, t, *J* 7, C*H*$_3$); $\delta_C$ (150 MHz; $CDCl_3$) 172.7 (*C*O), 142.3 (Ar*C*$_{quat.}$), 128.5 (Ar*C*), 128.2 (Ar*C*), 125.7 (Ar*C*), 63.4 (*C*HN), 47.4 (N*C*H$_2$CH$_3$), 44.7 (*C*H$_2$NCH$_2$CH$_3$),

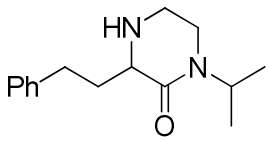
39.8 (*C*$H_2$NH), 31.8 (*C*$H_2$CHCO), 31.5 (*C*$H_2$Ph), 11.9 (*C*$H_3$); HRMS (ESI) calc. for $C_{14}H_{20}N_2NaO$ ($M+Na^+$) 255.1468, found 255.1470.

**1-Isopropyl-3-phenethylpiperazin-2-one 11 and 4-isopropyl-3-phenethylpiperazin-2-one.**




The title compounds were synthesised in a 95 : 5 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-isopropyl-1,2-ethylenediamine (0.62 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (ethyl acetate to 5 % MeOH in ethyl acetate) to give 1-isopropyl-3-phenethylpiperazin-2-one **11** as a colourless oil (157 mg, 64 %) and 4-isopropyl-3-phenethylpiperazin-2-one as a light yellow oil (4 mg, 2 %).

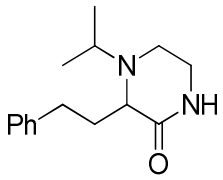
**1-Isopropyl-3-phenethylpiperazin-2-one 11.**




$\nu_{max}$/$cm^{-1}$ (neat) 3304 (br., amine NH st.), 1620 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.31-7.17 (5H, m, Ar*H*), 4.89 (1H, sept., *J* 7, C*H*($CH_3$)$_2$), 3.44 (1H, dd, *J* 8.5 and 3.5, C*H*NH), 3.30-3.13 (3H, m, C*H*HNH, C*H*HNCH($CH_3$)$_2$ and CH*H*NCH($CH_3$)$_2$), 2.99-2.92 (1H, m, CH*H*NH), 2.84-2.72 (2H, m, C$H_2$Ph), 2.34 (1H, dddd, *J* 14, 10.5, 7 and 4, C*H*HCHCO), 1.98 (1H, dtd, *J* 15, 9 and 6, CH*H*CHCO), 1.67 (1H, br. s, N*H*), 1.14 (3H, d, *J* 3.5, CH(C$H_3$)($CH_3$)), 1.12 (1H, d, *J* 3.5, CH($CH_3$)(C$H_3$)); $\delta_C$ (100 MHz; $CDCl_3$) 169.3 (*C*O), 141.7 (Ar$C_{quat.}$), 128.5 (Ar*C*), 128.3 (Ar*C*), 125.8 (Ar*C*), 58.8 (*C*HNH), 43.7 (*C*H($CH_3$)$_2$),

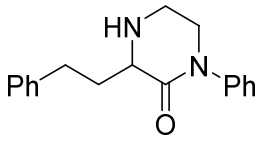
42.0 (*C*$H_2$NH), 41.0 (*C*$H_2$NCH($CH_3$)$_2$), 34.3 (*C*$H_2$CHCO), 32.2 (*C*$H_2$Ph), 19.2 (*C*$H_3$), 19.0 (*C*$H_3$); HRMS (ESI) calc.. for $C_{15}H_{23}N_2O$ ($M+H^+$) 247.1805, found 247.1796.

**4-Isopropyl-3-phenethylpiperazin-2-one.**




$\delta_H$ (400 MHz; $CDCl_3$) 7.28-7.14 (5H, m, Ar*H*), 5.99 (1H, br. s, N*H*), 3.37-3.27 (3H, m, C*H*NCH($CH_3$)$_2$, C*H*HNH and C*H*HNCHC($CH_3$)$_2$), 3.08 (1H, sept., *J* 6.5, C*H*($CH_3$)$_2$), 2.98 (1H, dt, *J* 12.5 and 4.5, CH*H*NH), 2.79 (1H, ddd, *J* 11.5, 7.5 and 5, C*H*HPh), 2.66-2.59 (2H, m, CH*H*Ph and CH*H*NCH($CH_3$)$_2$), 2.26 (1H, dddd, *J* 14, 11.5, 5.5 and 4.5, C*H*HCHCO), 2.05 (1H, ddt, *J* 14, 11 and 5, CH*H*CHCO), 1.13 (3H, d, *J* 6.5, CH(C*H*$_3$)($CH_3$)), 0.97 (3H, d, *J* 6.5, CH($CH_3$)(C*H*$_3$)); $\delta_C$ (100 MHz; $CDCl_3$) 172.8 (*C*O), 142.4 (Ar*C*$_{quat.}$), 128.5 (Ar*C*), 128.2 (Ar*C*), 125.7 (Ar*C*), 61.5 (*C*HN), 48.7 (*C*H($CH_3$)$_2$), 41.2 (*C*$H_2$NCH($CH_3$)$_2$), 40.0 (*C*$H_2$NH), 32.1 (*C*$H_2$CHCO), 31.1 (*C*$H_2$Ph), 21.6 (*C*$H_3$), 15.1 (*C*$H_3$); HRMS (ESI) calc. for $C_{15}H_{23}N_2O$ ($M+H^+$) 247.1805, found 247.1807.

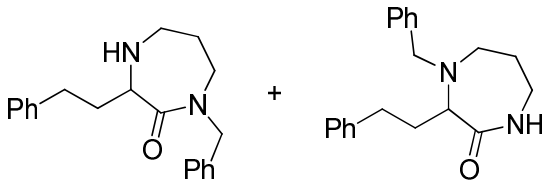
**1-Phenyl-3-phenethylpiperazin-2-one 12.**




The title compound was synthesised using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-phenyl-1,2-ethylenediamine (0.68 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (10 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to give 3-phenethyl-1-phenylpiperazin-2-one **12** as a beige solid (140 mg, 51 %).

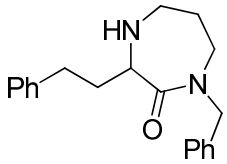
m.p. 102-103 ºC; $\nu_{max}$/cm$^{-1}$ (neat) 3294 (br., amine NH st.), 1629 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.41-7.37 (2H, m, Ar*H*), 7.31-7.27 (7H, m, Ar*H*), 7.21-7.16 (1H, m, Ar*H*), 3.81 (1H, ddd, *J* 11.5, 9.5 and 5, C*H*HNH), 3.61 (1H, dd, *J* 8 and 4, C*H*N), 3.57 (1H, dt, *J* 11.5 and 4, CH*H*NH), 3.28 (1H, dt, *J* 13 and 4, C*H*HNPh), 3.17 (1H, ddd, *J* 13.5, 9.5 and 4, CH*H*NPh), 2.89-2.78 (2H, m, C$H_2$Ph), 2.37 (1H, dddd, J 16.5, 9.5, 7 and 4, C*H*HCHCO), 2.08 (1H, dtd, *J* 15, 8.5 and 7, CH*H*CHCO), 1.74 (1H, br. s, N*H*); $\delta_C$ (100 MHz; $CDCl_3$) 170.1 (*C*O), 142.7 (ArC$_{quat.}$), 141.6 (Ar*C*$_{quat.}$), 129.1 (Ar*C*), 128.5 (Ar*C*), 128.4 (Ar*C*), 126.8 (Ar*C*), 126.0 (Ar*C*), 125.9 (Ar*C*), 59.1 (*C*HN), 51.8 (*C*$H_2$NPh), 42.3 (*C*$H_2$NH), 34.2 (*C*$H_2$CHCO), 32.3 (*C*$H_2$Ph); HRMS (ESI) calc. for $C_{18}H_{21}N_2O$ ($M+H^+$) 281.1648, found 281.1646.

**1-Benzyl-3-phenethyl-1,4-diazepan-2-one 13 and 4-benzyl-3-phenethyl-1,4-diazepan-2-one 14.**



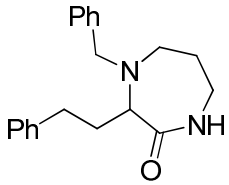

The title compounds were synthesised in a 73 : 27 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-benzyl-1,3-propylenediamine (0.83 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 10 % MeOH in ethyl acetate) to give 1-benzyl-3-phenethyl-1,4-diazepan-2-one **13** as a colourless oil (147 mg, 48 %) and 4-benzyl-3-phenethyl-1,4-diazepan-2-one **14** as a white solid (27 mg, 9 %).

**1-benzyl-3-phenethyl-1,4-diazepan-2-one 13.**




$\nu_{max}$/cm$^{-1}$ (neat) 3273 (br., NH st.), 1637 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.32-7.15 (10H, m, Ar*H*), 4.68 (1H, d, *J* 14.5, NC*H*HPh), 4.45 (1H, d, *J* 14.5, NCH*H*Ph), 3.47 (1H, dd, *J* 15 and 11.5, C*H*HNC$H_2$Ph), 3.31-3.19 (3H, m, C*H*N, CH*H*NC$H_2$Ph and C*H*HNH), 2.86-2.76 (3H, m, CH*H*NH and C$H_2$C*H*$_2$Ph), 2.24 (1H, dtd, *J* 15.5, 7.5 and 6, C*H*HCHCO), 1.84 (1H, dq, *J* 15 and 7.5, CH*H*CHCO), 1.55-1.41 (1H, m, $CH_2$C*H*HC$H_2$), 1.41-1.26 (2H, m, $CH_2$CH*H*C$H_2$ and N*H*); $\delta_C$ (100 MHz; $CDCl_3$) 175.4 (*C*O), 142.1 (Ar$C_{quat.}$), 137.7 (Ar*C*), 128.6 (Ar*C*), 128.5 (Ar*C*), 128.3 (Ar*C*), 128.2 (Ar*C*), 127.3 (Ar*C*), 125.7 (Ar*C*), 59.1 (*C*HNH), 51.2 (N*C*$H_2$Ph), 50.1 (*C*$H_2$NH), 47.4 (*C*$H_2$NC$H_2$Ph), 34.2 (*C*$H_2$CHCO), 32.5 (C$H_2$*C*$H_2$Ph), 29.8 (C$H_2$*C*$H_2$C$H_2$); HRMS (ESI) calc. for $C_{20}H_{25}N_2O$ ($M+H^+$) 309.1961, found 309.1959.

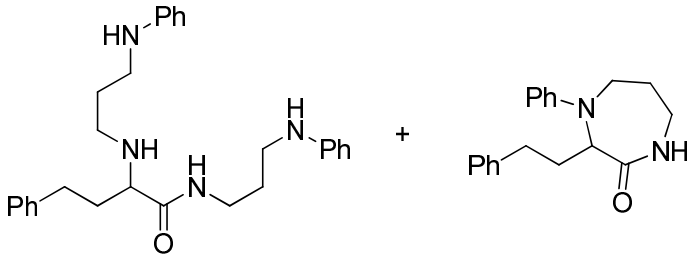
**4-Benzyl-3-phenethyl-1,4-diazepan-2-one 14.**




$\nu_{max}$/cm$^{-1}$ (neat) 3250 (br., NH st.), 1666 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.32-7.06 (10H, m, Ar*H*), 5.96 (1H, br. t, *J* 5.5, CON*H*), 3.76 (1H, d, *J* 14, NC*H*HPh), 3.47-3.41 (2H, m, C*H*N and NCH*H*Ph), 3.25 (1H, dddd, *J* 16, 11, 5 and 1, C*H*HNH), 3.20-3.05 (2H, m, CH*H*NH and C*H*HNC$H_2$Ph), 2.85-2.67 (3H, m, $CH_2$C$H_2$Ph and CH*H*NC$H_2$Ph), 2.04 (2H, q, *J* 7.5, C$H_2$CHCHO), 1.92-1.77 (1H, m, NC$H_2$*C*$H_2$), 1.27-1.21 (1H, m, NC$H_2$C$H_2$); $\delta_C$ (100 MHz; $CDCl_3$) 177.0 (*C*O), 142.2 (Ar$C_{quat.}$), 139.3 (Ar$C_{quat.}$), 128.7 (Ar*C*), 128.5 (Ar*C*), 128.4 (Ar*C*), 128.3 (Ar*C*), 126.9 (Ar*C*), 125.8 (Ar*C*), 62.8 (*C*HN), 52.2 (*C*$H_2$NC$H_2$Ph), 49.7

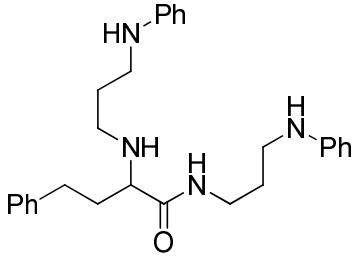
(N*C*$H_2$Ph), 41.9 (NH*C*$H_2$), 32.3 ($CH_2$*C*$H_2$Ph), 30.4 (*C*$H_2$CHCO), 23.0 (NC$H_2$*C*$H_2$); HRMS (ESI) calc. for $C_{20}H_{25}N_2O$ ($M+H^+$) 309.1961, found 309.1964.

**4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide 16 and 4-phenyl-3-phenethyl-1,4-diazepan-2-one 17.**



The title compounds were synthesised using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-phenyl-1,3-propanediamine (0.75 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 10 % MeOH in ethyl acetate) to give 4-phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide **16** as a colourless oil (221 mg, 50 %) and 4-phenyl-3-phenethyl-1,4-diazepan-2-one **17** as a colourless oil (10 mg, 3 %).

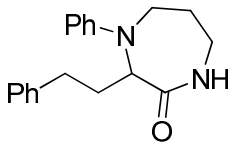
**4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide 16.**



$\nu_{max}$/$cm^{-1}$ (neat) 3324 (br., NH st.), 1600 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.37-7.33 (3H, m, CON*H* and Ar*H*), 7.28-7.21 (7H, m, Ar*H*), 6.79-6.70 (2H, m, Ar*H*), 6.66-6.61 (4H, m, Ar*H*), 3.43-3.30 (2H, m, CONHC$H_2$), 3.29-3.12 (5H, m, C*H*N, CHNHC$H_2$, CONH$(CH_2)_2$C$H_2$), 2.82-2.62 (4H, m, C$H_2$Ph, CHNH$(CH_2)_2$C$H_2$), 2.20-2.11 (1H, m, C*H*HC$H_2$Ph), 1.97-1.87 (1H, m, CH*H*C$H_2$Ph), 1.80-1.70 (4H, m, CHNHC$H_2$C$H_2$ and

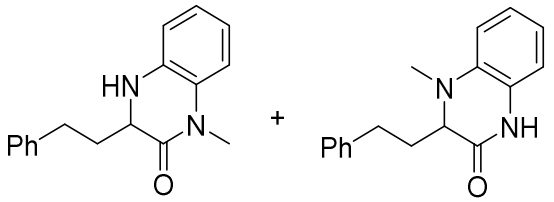
CONHCH$_2$C*H$_2$*); $\delta_C$ (100 MHz; CDCl$_3$) 174.4 (*C*O), 148.2 (Ar*C$_{quat.}$*), 148.1 (Ar*C$_{quat.}$*), 141.1 (Ar*C$_{quat.}$*), 129.3 (Ar*C*), 129.2 (Ar*C*), 128.5 (Ar*C*), 128.3 (Ar*C*), 126.1 (Ar*C*), 117.5 (Ar*C*), 117.2 (Ar*C*), 112.8 (Ar*C*), 112.7 (Ar*C*), 63.1 (*C*HN), 46.7 (CHNH(CH$_2$)$_2$*C*H$_2$Ph), 42.1 (CHNH*C*H$_2$), 40.9 (CONH(CH$_2$)$_2$*C*H$_2$), 36.5 (CONH*C*H$_2$), 35.3 (*C*H$_2$CH$_2$Ph), 32.5 (*C*H$_2$Ph), 29.6 (NH$_{amine}$CH$_2$*C*H$_2$), 29.1 (CONHCH$_2$*C*H$_2$); HRMS (ESI) calc. for $C_{28}H_{37}N_4O$ ($M+H^+$) 445.2962, found 445.2957.

**4-Phenyl-3-phenethyl-1,4-diazepan-2-one 17.**



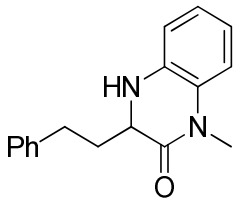

$v_{max}$/cm$^{-1}$ (neat) 3284 (br., NH st.), 1655 (s, C=O st.); $\delta_H$ (500 MHz; CDCl$_3$) 7.28-7.14 (7H, m, Ar*H*), 6.89 (2H, d, *J* 8.5, Ar*H*), 6.79 (1H, t, *J* 7.5, Ar*H*), 5.81 (1H, br. t, *J* 4.5,CON*H*), 4.25-4.16 (1H, m, C*H*N), 3.75-3.67 (2H, m, C*H$_2$*NPh), 3.22 (2H, q, *J* 6, CONHC*H$_2$*), 2.77 (1H, ddd, *J* 12, 9 and 4, C*H*HPh), 2.72-2.65 (1H, m, CH*H*Ph), 2.40-2.23 (2H, m, COCHC*H$_2$*), 2.00-1.90 (1H, br. m, NCH$_2$C*H*H), 1.83-1.75 (1H, m, NCH$_2$CH*H*); $\delta_C$ (100 MHz; CDCl$_3$) 177.4 (*C*O), 147.7 (Ar*C$_{quat.}$*), 141.4 (Ar*C$_{quat.}$*), 129.4 (Ar*C*), 128.6 (Ar*C*), 128.4 (Ar*C*), 126.0 (Ar*C*), 118.4 (Ar*C*), 114.9 (Ar*C*), 62.4 (*C*HN), 48.0 (*C*H$_2$NPh), 40.9 (CONH*C*H$_2$), 32.4 (*C*H$_2$Ph), 30.8 (COCH*C*H$_2$), 27.0 (NCH$_2$*C*H$_2$); HRMS (ESI) calc. for $C_{19}H_{22}N_2NaO$ ($M+Na^+$) 317.1624, found 317.1628.

**1-Methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one 18 and 4-methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one 19.**



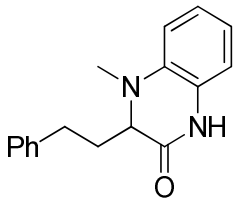

The title compounds were synthesised in a 78 : 22 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) and *N*-methyl-1,2-phenylenediamine (0.57 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether to 20 % ethyl acetate in 40-60 petroleum ether) to give 1-methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one **17** as a yellow oil (140 mg, 53 % ) and 4-methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one **18** as a red oil (31 mg, 12 %).

**1-Methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one 18.**



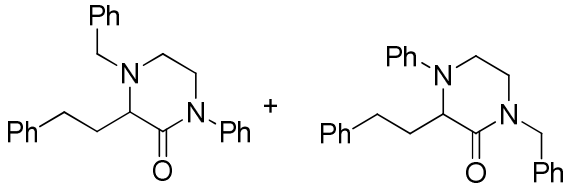

$\nu_{max}$/cm$^{-1}$ (neat) 3202 (br., NH st.), 1672 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.22-7.19 (2H, m, Ar*H*), 7.14-7.10 (3H, m, Ar*H*), 6.85-6.80 (2H, m, Ar*H*), 6.77-6.73 (1H, m, Ar*H*), 6.49 (1H, d, *J* 7.5, Ar*H*), 3.82 (1H, dd, *J* 8 and 4.5, C*H*N), 3.77 (1H, br. s, N*H*), 3.27 (3H, s, NC*H*$_3$), 2.77-2.64 (2H, m, C*H*$_2$Ph), 2.09 (1H, dddd, *J* 14, 8.5, 6.5 and 4.5, C*H*HCH$_2$Ph), 1.96-1.86 (1H, m, CH*H*CH$_2$Ph); $\delta_C$ (100 MHz; $CDCl_3$) 167.5 (*C*O), 141.0 (Ar*C*$_{quat.}$), 134.3 (Ar*C*$_{quat.}$), 128.8 (Ar*C*$_{quat.}$), 128.6 (Ar*C*), 128.4 (Ar*C*), 126.1 (Ar*C*), 123.5 (Ar*C*), 119.5 (Ar*C*), 114.5 (Ar*C*), 114.3 (Ar*C*), 56.4 (*C*HN), 33.0 (*C*H$_2$CH$_2$Ph), 32.0 (*C*H$_2$Ph), 29.0 (N*C*H$_3$); HRMS (ESI) calc. for $C_{17}H_{18}N_2NaO$ (M+Na$^+$) 289.1311, found 289.1309.

**4-Methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one 19.**



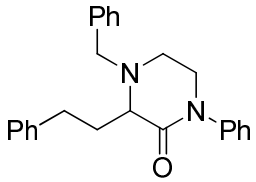
$\nu_{max}/cm^{-1}$ (neat) 3328 (br., NH st.), 1651 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 8.74 (1H, br. s, N*H*), 7.30-7.26 (2H, m, Ar*H*), 7.23-7.14 (3H, m, Ar*H*), 7.06-6.99 (1H, m, Ar*H*), 6.82-6.76 (2H, m, Ar*H*), 6.67 (1H, d, *J* 8, Ar*H*), 3.96 (1H, dd, *J* 8.5 and 5, C*H*N), 2.95 (3H, s, NC$H_3$), 2.78-2.66 (2H, m, $CH_2CH_2Ph$), 2.08-1.87 (2H, m, $CH_2CH_2Ph$); $\delta_C$ (100 MHz; $CDCl_3$) 167.8 (*C*O), 141.1 (Ar$C_{quat.}$), 134.8 (Ar$C_{quat.}$), 128.4 (Ar*C*), 128.3 (Ar*C*), 126.0 (Ar$C_{quat.}$), 125.5 (Ar*C*), 124.3 (Ar*C*), 118.4 (Ar*C*), 115.0 (Ar*C*), 111.9 (Ar*C*), 63.7 (*C*HN), 36.1 (N$CH_3$), 31.7 ($CH_2Ph$), 30.2 ($CH_2CH_2Ph$); HRMS (ESI) Cclc. for $C_{17}H_{18}N_2NaO$ ($M+Na^+$) 289.1311, found 289.1315.

**4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one 20 and 1-benzyl-3-phenethyl-4-phenylpiperazin-2-one 21.**



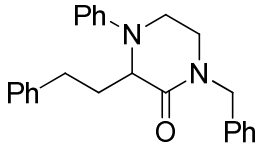
The title compounds were synthesised in a 81 : 19 ratio using General Procedure 6 with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (254 mg, 1 mmol, 1 equiv.) $N^1$-benzyl-$N^2$-phenylethane-1,2-diamine (1.13 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (10 % ethyl acetate in 40-60 petroleum ether to 50 % ethyl acetate in 40-60 petroleum ether) to give 4-benzyl-3-phenethyl-1-phenylpiperazin-2-one **20** as a colourless oil (150 mg, 41 %) and 1-benzyl-3-phenethyl-4-phenylpiperazin-2-one **21** as a colourless oil (42 mg, 11 %).

**4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one 20.**




$\nu_{max}$/cm$^{-1}$ (neat) 1639 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.43-7.16 (15H, m, Ar*H*), 4.09 (1H, d, *J* 13.5, NC*H*HPh), 3.87-3.71 (1H, br. m, C*H*HNPh), 3.57 (1H, dt, *J* 12 and 4, CH*H*NPh), 3.45 (1H, d, *J* 13.5, NCH*H*Ph), 3.40 (1H, t, *J* 4.5, C*H*N), 3.19-3.08 (1H, br. m, C*H*HNCH$_2$Ph), 3.00 (1H, ddd, *J* 13.5, 11 and 5, CH$_2$C*H*HPh), 2.76 (1H, ddd, *J* 13.5, 11 and 5.5, CH*H*CH$_2$Ph), 2.68 (1H, ddd, *J* 12, 9 and 3, CH*H*NCH$_2$Ph), 2.55-2.42 (1H, m, C*H*HCH$_2$Ph), 2.23 (1H, ddt, *J* 16, 10.5 and 5, CH*H*CH$_2$Ph); $\delta_C$ (100 MHz; $CDCl_3$) 169.7 (*C*O), 142.5 (Ar*C*$_{quat.}$), 142.2 (Ar*C*$_{quat.}$), 138.0 (Ar*C*$_{quat.}$), 129.1 (Ar*C*), 128.8 (Ar*C*), 128.6 (Ar*C*), 128.5 (Ar*C*), 128.3 (Ar*C*), 127.4 (Ar*C*), 126.8 (Ar*C*), 125.7 (Ar*C*), 65.2 (*C*HN), 58.6 (N*C*H$_2$Ph), 48.9 (*C*H$_2$NPh), 46.4 (*C*H$_2$NCH$_2$Ph), 32.6 (*C*H$_2$CH$_2$Ph), 31.4 (CH$_2$*C*H$_2$Ph); HRMS (ESI) calc. for $C_{25}H_{26}N_2NaO$ (M+Na$^+$) 393.1937, found 393.1925. One ArC peak in the $^{13}$C NMR was not resolable.

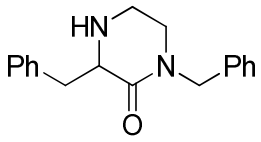
**1-Benzyl-3-phenethyl-4-phenylpiperazin-2-one 21.**




$\nu_{max}$/cm$^{-1}$ (neat) 1642 (s, C=O st.); $\delta_H$ (300 MHz; $CDCl_3$) 7.43-7.21 (12H, m, Ar*H*), 6.89 (1H, t, *J* 7.5, Ar*H*), 6.87-6.78 (2H, m, Ar*H*), 4.87 (1H, d, *J* 14.5, NC*H*HPh), 4.44 (1H, d, *J* 14.5, NCH*H*Ph), 4.37 (1H, t, *J* 6.5, C*H*N), 3.65-3.42 (3H, m, NC*H*$_2$ and NC*H*H), 3.28 (1H, dt, *J* 11 and 3, NCH*H*), 2.99-2.81 (2H, m, CH$_2$C*H*$_2$Ph), 2.41-2.15 (2H, m, C*H*$_2$CH$_2$Ph); $\delta_C$ (100 MHz; $CDCl_3$) 169.9 (*C*O), 148.4 (Ar*C*$_{quat.}$), 141.5 (Ar*C*$_{quat.}$), 136.6 (Ar*C*$_{quat.}$), 129.4 (Ar*C*), 128.7 (Ar*C*), 128.6 (Ar*C*), 128.3 (Ar*C*), 128.0 (Ar*C*), 127.6 (Ar*C*), 125.9 (Ar*C*), 119.4 (Ar*C*), 115.5

(Ar*C*), 60.6 (*C*HN), 49.9 (N*C*$H_2$Ph), 44.3 (*C*$H_2$), 42.4 (*C*$H_2$), 33.6 (*C*$H_2$$CH_2$Ph), 32.5 ($CH_2$*C*$H_2$Ph); HRMS (ESI) calc. for $C_{25}H_{26}N_2NaO$ ($M+Na^+$) 393.1937, found 393.1936.

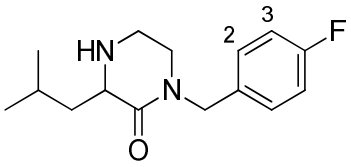
**1,3-Dibenzylpiperazin-2-one 22.**




The title compound was synthesised using synthesised using General Procedure A with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (240 mg, 1 mmol, 1 equiv.) and $N^1$-benzyl-1,2-ethylenediamine (0.76 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 5% MeOH in ethyl acetate) to give 1,3-dibenyzlpiperazin-2-one **22** as a yellow oil (168 mg, 60 %).

$\nu_{max}$/$cm^{-1}$ (neat) 3297 (br., amine NH st.), 1632 (s, C=O st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.34-7.23 (10H, m, Ar*H*), 4.65 (1H, d, *J* 14.5, NC*H*HPh), 4.57 (1H, d, *J* 14.5,NCH*H*Ph), 3.70 (1H, dd, *J* 9.5 and 3.5, C*H*N), 3.51 (1H, dd, *J* 13.5 and 3.5, CHC*H*HPh), 3.28 (1H, td, *J* 11.5 and 4.5, C*H*HC$H_2$NH), 3.12-3.03 (2H, m, CH*H*C$H_2$NH and C*H*HNH), 2.93 (1H, dd, *J* 13.5 and 9.5, CHCH*H*Ph), 2.90-2.85 (1H, m, CH*H*NH), 1.73 (1H, br. s, N*H*); $\delta_C$ (100 MHz; $CDCl_3$) 169.4 (*C*O), 138.3 (Ar$C_{quat.}$), 136.7 (Ar$C_{quat.}$), 129.4 (Ar*C*), 128.6 (Ar*C*), 128.6 (Ar*C*), 128.0 (Ar*C*), 127.4 (Ar*C*), 126.6 (Ar*C*), 60.7 (*C*HN), 50.1 (N*C*$H_2$Ph), 47.4 (*C*$H_2$$CH_2$NH), 41.9 (*C*$H_2$NH), 38.2 (CH*C*$H_2$Ph); HRMS (ESI) cald. for $C_{18}H_{21}N_2O$ ($M+H^+$) 281.1648, found 281.1639.

**1-(4-Fluorobenzyl)-3-Isobutylpiperazin-2-one 26.**

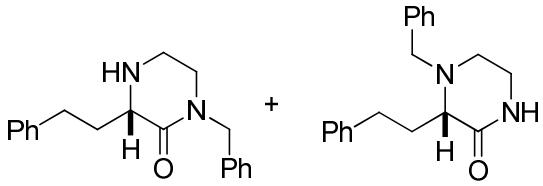



The title compound was synthesised using General Procedure 5 with 1,1,1-trichloro-4-methylpentan-2-ol **25** (205 mg, 1 mmol, 1 equiv.) and $N^1$-4-fluorobenzylethane-1,3-diamine (0.44 g, 2.4 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to afford an orange oil (55 mg, 21 %).

$\nu_{max}$/cm$^{-1}$ (neat) 3305 (br., amine NH st.), 1630 (s, C=O st.) 1219 (s, CF st.); $\delta_H$ (400 MHz; $CDCl_3$) 7.23-7.18 (2H, m, *m*-Ar*H*), 7.00-6.94 (2H, m, *o*-ArH), 4.61 (1H, d, *J* 14.5, ArC*H*H), 4.45 (1H, d, *J* 14.5, ArCH*H*), 3.46 (1H, dd, *J* 10 and 3.5, C*H*N), 3.30-3.24 (1H, m, C*H*HNC$H_2$Ar), 3.14-3.07 (2H, m, C*H*HNH and CH*H*NC$H_2$Ar), 2.95-2.89 (1H, m, CH*H*NH), 1.90 (1H, ddd, *J* 13.5, 10 and 3.5, CHC*H*H), 1.79-1.65 (2H, m, N*H* and C*H*($CH_3$)$_2$), 1.54 (1H, ddd, *J* 14, 10 and 4.5, CHCH*H*), 0.93 (3H, d, *J* 6.5, C*H*$_3$), 0.91 (3H, d, *J* 6.5, C*H*$_3$); $\delta_C$ (100 MHz; $CDCl_3$) 170.9 (*C*O), 162.2 (d, $^1J_{CF}$ 245, CF), 132.7 (d, $^4J_{CF}$ 3, ArC$_{quat.}$), 129.8 (d, $^3J_{CF}$ 8, *o*-Ar*C*), 115.4 (d, $^2J_{CF}$ 21, C3), 57.3 (CO*C*), 49.6 (Ar*C*$H_2$N), 47.5 (NHC$H_2$*C*), 41.6 (NH*C*$H_2$), 41.2 (COCH*C*), 24.6 (COCHC$H_2$*C*), 23.6 (C*H*$_3$CC$H_3$) 21.0 (C$H_3$CC*H*$_3$); HRMS (ESI) cald. for $C_{15}H_{22}FN_2O$ (M+H$_+$) 265.1711, found 265.1712.

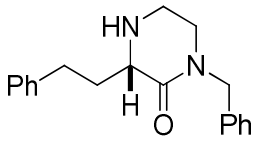
**Enantiomerically enriched products.**

**(*S*)-1-Benzyl-3-phenethylpiperazin-2-one (*S*)-5 and (*S*)-4-benzyl-3-phenethyl-piperazin-2-one (*S*)- 6.**



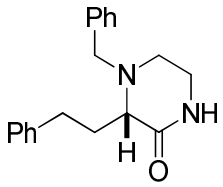

The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-benzyl-1,2-ethylenediamine (0.75 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 10 % MeOH in ethyl acetate) to give (*S*)-1-benzyl-3-phenethylpiperazin-2-one (*S*)-**5** as a yellow solid (224 mg, 76 %, 95 % e.e.) and (*S*)-4-benzyl-3-phenethylpiperazin-2-one (*S*)-**6** as a yellow solid (18 mg, 6 %, 98 % e.e.).

**(*S*)-1-Benzyl-3-phenethylpiperazin-2-one (*S*)-5.**



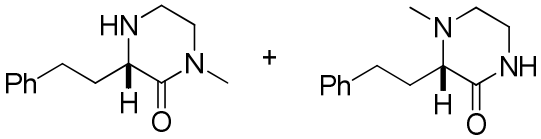

Spectroscopic data similar to that of racemate; $[\alpha]_D^{26}$ (*c* 0.24, $CHCl_3$): - 52.2 (*S*); Enantiomeric excess determined by HPLC analysis on *N*-Boc derivative (*S*)-**3**.

**(*S*)-4-Benzyl-3-phenethylpiperazin-2-one (*S*)-6.**



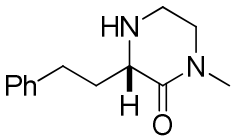

Spectroscopic data similar to that of racemate; $[\alpha]_D^{26}$ (*c* 0.28, $CHCl_3$): - 3.0 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 12.43 min., (*S*)-isomer 14.40 min.).

**(*S*)-1-Methyl-3-phenethylpiperazin-2-one (*S*)-7 and (*S*)-4-methyl-3-phenethylpiperazin-2-one (*S*)-8.**



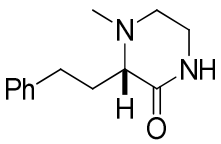
The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-methyl-1,2-ethylenediamine (0.44 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (ethyl acetate to 10 % MeOH in ethyl acetate) to give (*S*)-1-methyl-3-phenethylpiperazin-2-one (*S*)-**7** as a yellow oil (100 mg, 46 %, 94 % e.e.) and (*S*)-4-methyl-3-phenethylpiperazin-2-one (*S*)-**8** as a yellow oil (89 mg, 41 %, 96 % e.e.).

**(*S*)-1-Methyl-3-phenethylpiperazin-2-one (*S*)-7.**



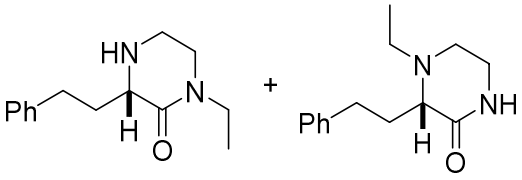
Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{28}$ (*c* 0.38, $CHCl_3$): - 60.5 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 24.30 min., (*R*)-isomer 27.84 min.).

**(*S*)-4-Methyl-3-phenethylpiperazin-2-one (*S*)-8.**



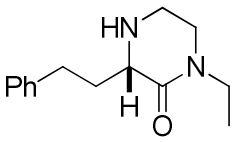
Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{28}$ (*c* 0.66, $CHCl_3$): - 7.1 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 12.64 min., (*R*)-isomer 23.53 min.).

**(*S*)-1-ethyl-3-phenethylpiperazin-2-one (*S*)-9 and (*S*)-4-ethyl-3-phenethylpiperazin-2-one (*S*)-10.**



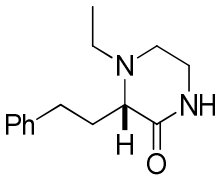
The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-ethyl-1,2-ethylenediamine (0.53 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (ethyl acetate to 10 % MeOH in ethyl acetate) to give (*S*)-1-ethyl-3-phenethylpiperazin-2-one (*S*)-**9** as a yellow oil (168 mg, 72 %, 96 % e.e.) and (*S*)-4-ethyl-3-phenethylpiperazin-2-one (*S*)-**10** as a yellow oil (12 mg, 5 %, 95 % e.e.).

**(*S*)-1-Ethyl-3-phenethylpiperazin-2-one (*S*)-9.**



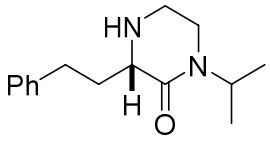
Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{28}$ (*c* 0.52, $CHCl_3$): - 53.6 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 210 nm, (*S*)-isomer 12.85 min., (*R*)-isomer 14.24 min.).

**(*S*)-4-Ethyl-3-phenethylpiperazin-2-one (*S*)-10.**



Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{30}$ (*c* 0.55, $CHCl_3$): + 11.1 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel AD-H column, 2-propanol : hexane = 5 : 95, 1 mL/min., 208 nm, (*R*)-isomer 20.63 min., (*S*)-isomer 21.51 min.).

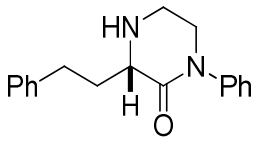
**(*S*)-1-Isopropyl-3-phenethylpiperazin-2-one (*S*)-11.**




The title compound was synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-isopropyl-1,2-ethylenediamine (0.62 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (ethyl acetate to 5 % MeOH in ethyl acetate) to give a yellow oil (168 mg, 72 %, 99 % e.e.).

Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{28}$ (*c* 0.38, $CHCl_3$): - 67.1 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 210 nm, (*S*)-isomer 15.20 min., (*R*)-isomer 16.83 min.).

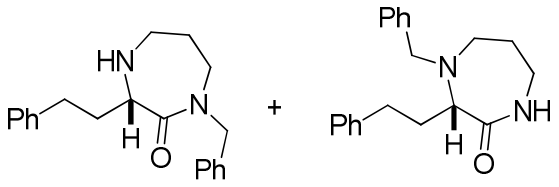
**(*S*)-1-Phenyl-3-phenethylpiperazin-2-one (*S*)-12.**




The title compound was synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-phenyl-1,2-ethylenediamine (0.68 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to give a colourless oil (145 mg, 52 %, 98 % e.e.).

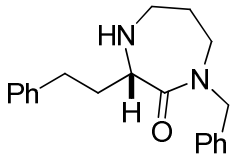
Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{26}$ (*c* 0.54, $CHCl_3$): - 57.5 (*S*); Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 20 : 80, 1 mL/min., 208 nm, (*S*)-isomer 20.09 min., (*R*)-isomer 21.96 min.).

**(*S*)-1-Benzyl-3-phenethyl-1,4-diazepan-2-one (*S*)-13 and (*S*)-4-benzyl-3-phenethyl-1,4-diazepan-2-one (*S*)-14.**



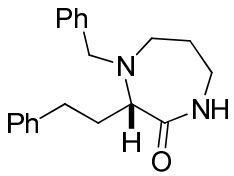
The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-benzyl-1,3-propylenediamine (0.0.83 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 10 % MeOH in ethyl acetate) to give (*S*)-1-benzyl-3-phenethyl-1,4-diazepan-2-one (*S*)-**13** as a colourless oil (163 mg, 53 %, 99 % e.e.) and 4-benzyl-3-phenethyl-1,4-diazepan-2-one (*S*)-**14** as a white solid (35 mg, 11 %, 97 % e.e).

**(*S*)-1-Benzyl-3-phenethyl-1,4-diazepan-2-one (*S*)-13.**



Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{26}$ (*c* 0.27, $CHCl_3$): - 12.0 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 20 : 80, 1 mL/min., 210 nm, (*S*)-isomer 13.23 min., (*R*)-isomer 26.41 min.).

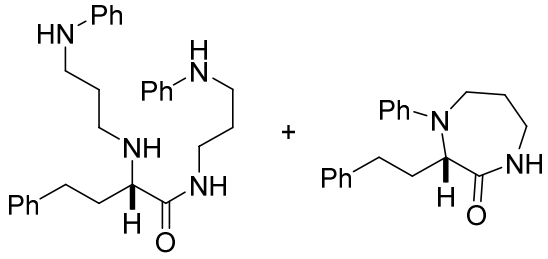
**(*S*)-4-Benzyl-3-phenethyl-1,4-diazepan-2-one (*S*)-14.**



Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{30}$ (*c* 0.11, MeOH): - 133.6 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel AD-H column, 2-

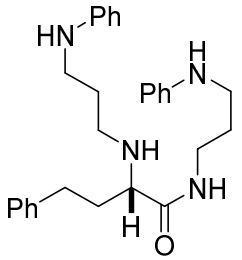
propanol : hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 10.95 min., (*R*)-isomer 13.87 min.).

**(*S*)-4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide (*S*)-16 and (*S*)-4-phenyl-3-phenethyl-1,4-diazepan-2-one (*S*)-17.**



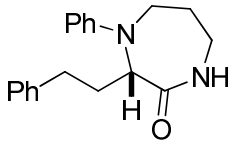
The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-phenyl-1,3-propanediamine (0.75 g, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 10 % MeOH in ethyl acetate) to give (*S*)-4-phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide (*S*)-**15** as a colourless oil (221 mg, 50 %) and (*S*)-4-phenyl-3-phenethyl-1,4-diazepan-2-one (*S*)-**16** as a colourless oil (10 mg, 3 %, 96 % e.e.).

**(*S*)-4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide (*S*)-16.**



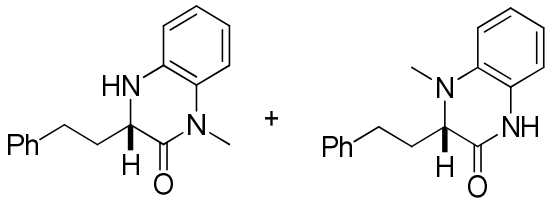
Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{30}$ (*c* 0.89, MeOH): - 4.2 (*S*).

**(*S*)-4-Phenyl-3-phenethyl-1,4-diazepan-2-one (*S*)-17.**



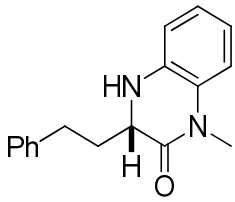

Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{30}$ (*c* 0.14, MeOH): + 18.8 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 207 nm, (*R*)-isomer 18.32 min., (*R*)-isomer 33.08 min.).

**(*S*)-1-Methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one (*S*)-18 and (*S*)-4-methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one (*S*)-19.**



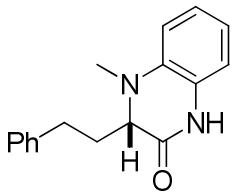

The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and *N*-methyl-1,2-phenylenediamine (0.57 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether to 20 % ethyl acetate in 40-60 petroleum ether) to give (*S*)-1-methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one (*S*)-**18** as a yellow oil (142 mg, 53 %, 96 % e.e.) and (*S*)-4-methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one (*S*)-**19** as a red oil (42 mg, 16 %, 98 % e.e.).

**(*S*)-1-Methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one (*S*)-18.**



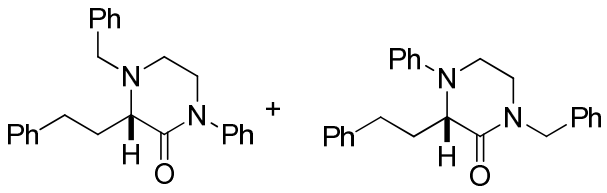

Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{28}$ (*c* 0.86, MeOH): + 54.8 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 222 nm, (*S*)-isomer 21.39 min., (*R*)-isomer 31.64 min.).

**(*S*)-4-Methyl-3-phenethyl-3,4-dihydroquinoxalin-2(1*H*)-one (*S*)-19.**




Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{28}$ (*c* 0.24, MeOH): + 131.5 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 222 nm, (*S*)-isomer 14.12 min., (*S*)-isomer 33.82 min.).

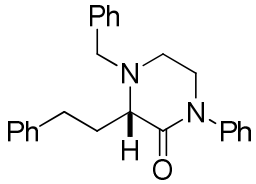
**(*S*)-4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-20 and (*S*)-1-benzyl-3-phenethyl-4-phenylpiperazin-2-one (*S*)-21.**




The title compounds were synthesised using General Procedure 6 with (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and $N^1$-benzyl-$N^2$-phenylethane-1,2-diamine (1.13 g, 5 mmol, 5 equiv.). The residue was purified by silica column

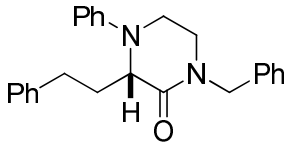
chromatography (10 % ethyl acetate in 40-60 petroleum ether) to give (*S*)-4-benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-**20** as a colourless oil (140 mg, 38 %, 94 % e.e.) and (*S*)-1-benzyl-3-phenethyl-4-phenylpiperazin-2-one (*S*)-**21** as a colourless oil (26 mg, 7 %, 95 % e.e.).

**(*S*)-4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-20.**



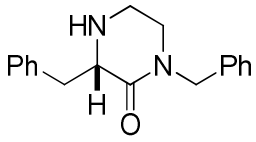

Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{25}$ (*c* 0.26, MeOH): - 27.9 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel AD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 208 nm, (*S*)-isomer 17.96 min., (*R*)-isomer 31.45 min.).

**(*S*)-1-Benzyl-3-phenethyl-4-phenylpiperazin-2-one (*S*)-21.**




Spectroscopic data similar to that of racemate; $[\alpha]_{D}^{25}$ (*c* 0.12, MeOH): + 54.6 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 13.87 min., (*S*)-isomer 20.27 min.).

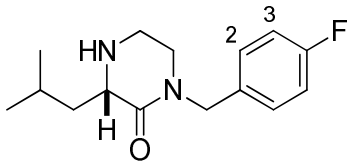
**(*S*)-1,3-Dibenzylpiperazin-2-one (*S*)-24.**




The title compound was synthesised using General Procedure A with (*R*)-1,1,1-trichloro-3-phenylpropan-2-ol (*R*)-**23** (240 mg, 1 mmol, 99 % e.e.) and $N^1$-benzyl-1,2-ethylenediamine (0.76 mL, 5 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to 5% MeOH in ethyl acetate) to give a yellow oil (171 mg, 61 %, 97 % e.e.).

Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{26}$ (*c* 0.42, $CHCl_3$): - 34.6 (*S*); Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 47.06 min., (*R*)-isomer 63.35 min.).

**(*S*)-1-(4-Fluorobenzyl)-3-Isobutylpiperazin-2-one (*S*)-27.**



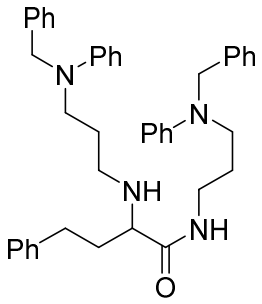

The title compound was synthesised using General Procedure 5 with (*R*)-1,1,1-trichloro-4-methylpentan-2-ol (*R*)-**26** (205 mg, 1 mmol, 1 equiv.) and $N^1$-4-fluorobenzylethane-1,3-diamine (0.44 g, 2.4 mmol, 5 equiv.). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to give an orange oil (63 mg, 24 %, 94 % e.e.).

Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{27}$ (*c* 0.54, MeOH): - 18.0 (*S*); Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-

propanol : hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 21.71 min., (*R*)-isomer 29.18 min.).

## 1.7. Independent Synthesis and Isolation of 4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl)butanamide.

**4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl) butanamide.**

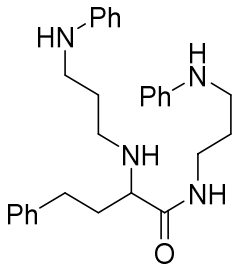



The title compound was synthesised using General Procedure A with 1,1,1-trichloro-4-phenylbutan-2-ol **4** (182 mg, 0.72 mmol, 1 equiv.) and $N^1$-phenyl-$N^1$-benzyl-1,3-propanediamine (864 mg, 3.6 mmol, 5 equiv.). The residue was purified by silica column chromatography (5 % ethyl acetate in 40-60 petroleum ether to 20 % ethyl acetate in petroleum ether) to afford a colourless oil (85 mg, 19 %).

$\nu_{max}$/cm$^{-1}$ (neat) 3324 (br., NH st.), 1598 (s, C=O st.); $\delta_H$ (300 MHz; $CDCl_3$) 7.33-7.14 (19H, m, Ar*H*), 7.04 (1H, t, *J* 5.5, CON*H*), 6.73-6.63 (6H, m, Ar*H*), 4.50 (2H, s, NC*H*$_2$Ph), 4.48 (2H, s, NC*H*$_2$Ph), 3.41-3.18 (6H, m, 3 x C*H*$_2$), 2.99 (1H, dd, *J* 7.5 and 5, C*H*NH), 2.73-2.60 (2H, m, $CH_2$C*H*$_2$Ph), 2.56-2.43 (2H, m, CHNHC*H*$_2$), 2.06-1.97 (1H, m, COCHC*H*H), 1.85-1.76 (3H, m, COCHCH*H* and $CH_2$C*H*$_2$$CH_2$), 1.74-1.64 (2H, m, $CH_2$C*H*$_2$$CH_2$); $\delta_C$ (75 MHz; $CDCl_3$) 174.5 (*C*O), 148.5 (Ar*C*$_{quat.}$), 148.4 (Ar*C*$_{quat.}$), 141.1 (Ar*C*$_{quat.}$), 138.73 (Ar*C*$_{quat.}$), 138.69 (Ar*C*$_{quat.}$), 129.3 (Ar*C*), 128.6 (Ar*C*), 128.5 (Ar*C*), 128.3 (Ar*C*), 126.8 (Ar*C*), 126.58 (Ar*C*), 126.56 (Ar*C*), 126.1 (Ar*C*), 116.6 (Ar*C*), 116.5 (Ar*C*), 112.5 (Ar*C*), 112.4 (Ar*C*), 63.2 (*C*HN), 54.7 (*C*$H_2$), 54.5 (*C*$H_2$), 48.8 (*C*$H_2$), 48.6 (*C*$H_2$), 46.6 (NHCH*C*$H_2$), 36.8 (*C*$H_2$), 35.2 (COCH*C*$H_2$), 32.5 ($CH_2$*C*$H_2$Ph), 27.9 ($CH_2$*C*$H_2$$CH_2$), 27.5 ($CH_2$*C*$H_2$$CH_2$); HRMS (ESI) calc.

for $C_{42}H_{49}H_4O$ ($M+H^+$) 625.3901, found 625.3907. Three of the Ar*C* peaks in the $^{13}C$ NMR spectrum were not resolvable.

**4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl) butanamide 15.**



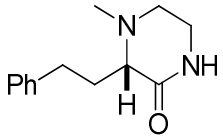

To a suspension of Pd/C (20 mg) in methanol (10 mL) was added 4-Phenyl-*N*-(3-phenylamino)propyl)-2-((3-(phenylamino)propyl) butanamide (54 mg, 0.09 mmol, 1 equiv.) and ammonium formate (57 mg, 0.9 mmol, 10 equiv.) and was heated to reflux for 3 hours. Reaction mixture was filtered through Celite and concentrated *in vacuo*. The residue was extracted with ethyl acetate (3 x 15 mL) and water (15 mL). Organic extracts were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford a colourless oil (25 mg, 60 %). Spectroscopic data similar to that of (*S*)-**15**.

## 1.8. *N*-Amino Alkylation of (*S*)-1, (*S*)-12 and 15. General Procedure 3:

Method modified from the literature.[8] (*S*)-3-phenethylpiperazin-2-one (*S*)-**1** and 3-phenethyl-1,4-diazepan-2-one **15** were synthesised according to the method previously described.[1]

To a solution of (*S*)-3-phenethylpiperazin-2-one (*S*)-**1** (205 mg, 1 mmol, 1 equiv.) in acetonitrile (13 mL) was added $K_2CO_3$ (275 mg, 2 mmol, 2 equiv.) and then alkylating agent (1.05 mmol, 1.05 equiv.). The reaction mixture was stirred at 55 ºC for 17 hours. After cooling, the reaction mixture was concentrated *in vacuo*. The residue was taken up in ethyl acetate (25 mL) and washed with water (2 x 30 mL). Organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by silica column chromatography.

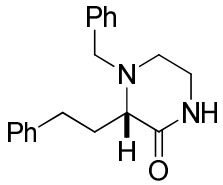
**(*S*)-4-Methyl-3-phenethylpiperazin-2-one (*S*)-8.**




The title compound was synthesised using General Procedure 3 with (*S*)-3-phenethylpiperazin-2-one (*S*)-1 (205 mg, 1 mmol, 95 % e.e.) and methyl iodide (19.5 µL, 1.05 mmol). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to give a yellow oil (80 mg, 37 %, 95 % e.e.).

Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{26}$ (*c* 0.58, $CHCl_3$): - 5.3 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 13.29 min., (*R*)-isomer 24.78 min.).

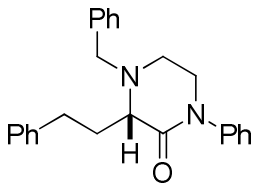
**(*S*)-4-Benzyl-3-phenethylpiperazin-2-one (*S*)-6.**




The title compound was synthesised using General Procedure 3 with (*S*)-3-phenethylpiperazin-2-one (*S*)-**1** (205 mg, 1 mmol, 95 % e.e.) and benzyl bromide (125 µL, 1.05 mmol). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to give a yellow solid (171 mg, 58 %, 95 % e.e.).

Spectroscopic data similar to that of racemate; $[\alpha]_{\mathrm{D}}^{26}$ (*c* 0.30, $CHCl_3$): - 6.6 (*S*); enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 12.32 min., (*R*)-isomer 14.09 min.).

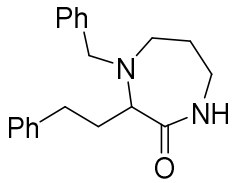
**(*S*)-4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-20.**




The title compound was synthesised using General Procedure 3 with (*S*)-1-phenyl-3-phenethylpiperazin-2-one (*S*)-**12** (16 mg, 0.06 mmol, 98 % e.e.) with benzyl bromide (7.5 µL, 0.063 mmol). The residue was purified by silica column chromatography (50 % ethyl acetate in 40-60 petroleum ether to ethyl acetate) to give a yellow oil (11 mg, 50 %, 98 % e.e.).

Spectroscopic data similar to that of racemate; enantiomeric excess determined by HPLC analysis (Daicel Chiralcel AD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 18.65 min., (*R*)-isomer 32.26 min.).

**4-Benzyl-3-phenethyl-1,4-diazepan-2-one 14.**



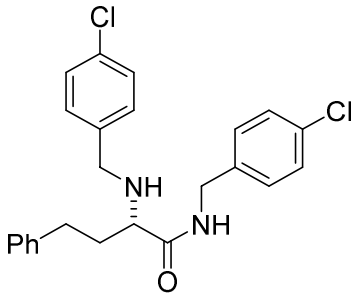

The title compound was synthesised using General Procedure 3 with 3-phenethyl-1,4-diazepan-2-one **15** (20 mg, 0.09 mmol) and benzyl bromide (12 µL, 0.1 mmol). The $^{1}$H NMR of the crude residue was consistent with that isolated from the Jocic-type reaction.

## 1.9. Synthesis of Amino-amides with Methanol and NaOH or NaOMe. General Procedure 4:

To (*R*)-1,1,1-trichloro-4-phenylbutan-2-ol (*R*)-**4** (254 mg, 1 mmol, 95 % e.e.) and amine (5 mmol, 5 equiv.) in methanol (4 mL) was added base (5 mmol, 5 equiv.) and resulting mixture stirred at stated temperature for 20 hours. Reaction mixture was cooled and concentrated *in*

*vacuo*. Residue was taken up in ethyl acetate (15 mL) and washed with water (15 mL). Aqueous layer was extracted a further two times with ethyl acetate (2 x 15 mL). Combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Residue was purified by silica column chromatography.

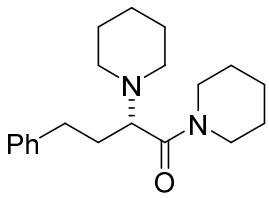
**(*S*)-*N*-(4-Chlorobenzyl)-2-((4-chlorobenzyl)amino)-4-phenylbutanamide (*S*)-28.**




The title compound was synthesised using General Procedure 4 with 4-chlorobenzylamine (0.61 mL, 5 mmol) and NaOH (200 mg, 5 mmol) at 55 ºC. The residue was purified by silica column chromatography (20 % ethyl acetate in 40-60 petroleum ether to 50 % ethyl acetate in 40-60 petroleum ether) to give a yellow solid (111 mg, 26 %, 88 % e.e.).

Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel AD-H column, 2-propanol : hexane = 10 : 90, 1 mL/min., 217 nm, (*S*)-isomer 19.32 min., (*R*)-isomer 24.24 min.). Spectroscopic data similar to that previously reported.[1]

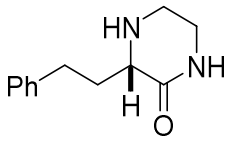
**(*S*)-4-Phenyl-1,2-di(piperidin-1-yl)butan-1-one (*S*)-29.**




The title compound was synthesised using General Procedure 4 with piperidine (0.49 mL, 5 mmol) and NaOH (200 mg, 5 mmol) at 55 ºC. The residue was purified by silica column chromatography (ethyl acetate) to give a colourless oil (116 mg, 37 %, 96 % e.e.).

Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 5 : 95, 0.5 mL/min., 212 nm, (*R*)-isomer 8.31 min., (*S*)-isomer 10.29 min.). Spectroscopic data similar to that previously reported.[1]

**(*S*)-3-phenethylpiperazin-2-one (*S*)-1.**



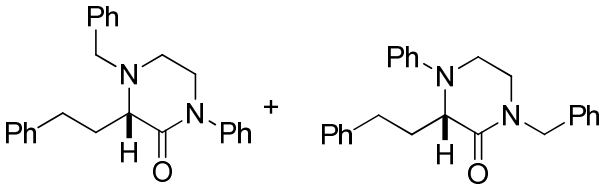

The title compound was synthesised using General Procedure 4 with 1,2-diaminoethane (0.67 mL, 10 mmol) and NaOH (200 mg, 5 mmol) at 55 ºC. The residue was purified by silica column chromatography ($CH_2Cl_2$ to 20 % MeOH in $CH_2Cl_2$) to give a yellow solid (92 mg, 45 %, 54 % e.e.).

Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 50 : 50, 0.5 mL/min., 210 nm, (*S*)-isomer 13.13 min., (*R*)-isomer 16.24 min.). Spectroscopic data similar to that previously reported.[1]

The title compound was synthesised using General Procedure 4 with 1,2-diaminoethane (0.67 mL, 10 mmol) and 25 % sodium methoxide in methanol (1.14 mL, 5 mmol) at room temperature. The residue was purified by silica column chromatography ($CH_2Cl_2$ to 20 % MeOH in $CH_2Cl_2$) to give a yellow solid (66 mg, 32 %, 91 % e.e.).

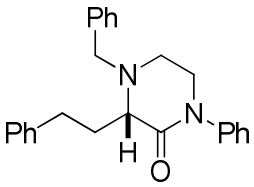
Enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 50 : 50, 0.5 mL/min., 210 nm, (*S*)-isomer 12.72 min., (*R*)-isomer 15.48 min.). Spectroscopic data similar to that previously reported.[1]

**(*S*)-4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-20 and (*S*)-1-benzyl-3-phen-ethyl-4-phenylpiperazin-2-one (*S*)-21.**



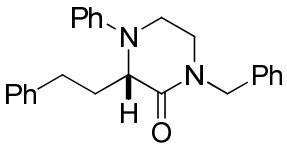
The title compounds were synthesised using General Procedure 4 with $N^1$-phenyl-$N^2$-benzyl-1,2-ethylenediamine (1.13 g, 5 mmol) and NaOH (200 mg, 5 mmol) at 55 ºC. The residue was purified by silica column chromatography (10 % ethyl acetate in 40-60 petroleum ether to 50 % ethyl acetate in 40-60 petroleum ether) to give (*S*)-4-benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-**20** as a colourless oil (104 mg, 28 %, 91 % e.e.) and (*S*)-1-benzyl-3-phenethyl-4-phenylpiperazin-2-one (*S*)-**21** as a colourless oil (37 mg, 10 %, 84 % e.e.).

**(*S*)-4-Benzyl-3-phenethyl-1-phenylpiperazin-2-one (*S*)-20.**



Spectroscopic data similar to that of racemate; enantiomeric excess determined by HPLC analysis (Daicel Chiralcel AD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 208 nm, (*S*)-isomer 11.96 min., (*R*)-isomer 25.69 min.).

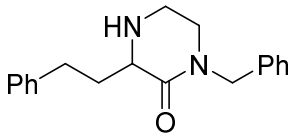
**(*S*)-1-Benzyl-3-phenethyl-4-phenylpiperazin-2-one (*S*)-21.**



Spectroscopic data similar to that of racemate; enantiomeric excess determined by HPLC analysis (Daicel Chiralcel OD-H column, 2-propanol : hexane = 15 : 85, 1 mL/min., 208 nm, (*R*)-isomer 14.56 min., (*S*)-isomer 22.25 min.).

## 2. Single X-ray Crystal Structures Determination of 5, 6 and 12.

### 2.1. X-ray Crystal Structure Determination of 5.




Single crystals of **5** were grown from ethyl acetate/hexane. A suitable crystal was selected and mounted on a Mitigen Micromount using Fromblin oil on an Oxford Diffraction Gemini Xcalibur diffractometer with a Ruby CCD area detector. The crystal was kept at 100(2) K during data collection. Using Olex2,[9] the structure was solved with the ShelXS[10] structure solution program using Direct Methods and refined with the ShelXL[10] refinement package using Least Squares minimisation.

Crystal data for **5**: orthorhombic, space group $Pca2_1$ (no. 29), $a$ = 9.2888(2) Å, $b$ = 6.04300(10) Å, $c$ = 27.8317(6) Å, $V$ = 1562.26(5) Å$^3$, $Z$ = 4, $T$ = 150.15 K, μ(Cu Kα) = 0.607 mm$^{-1}$, *Dcalc* = 1.252 g/mm$^3$, 7248 reflections measured ($6.352 \leq 2\Theta \leq 155.122$), 3120 unique ($R_{int}$ = 0.0273) which were used in all calculations. The final $R_1$ was 0.0309 ($I > 2\sigma(I)$) and $wR_2$ was 0.0833 (all data).

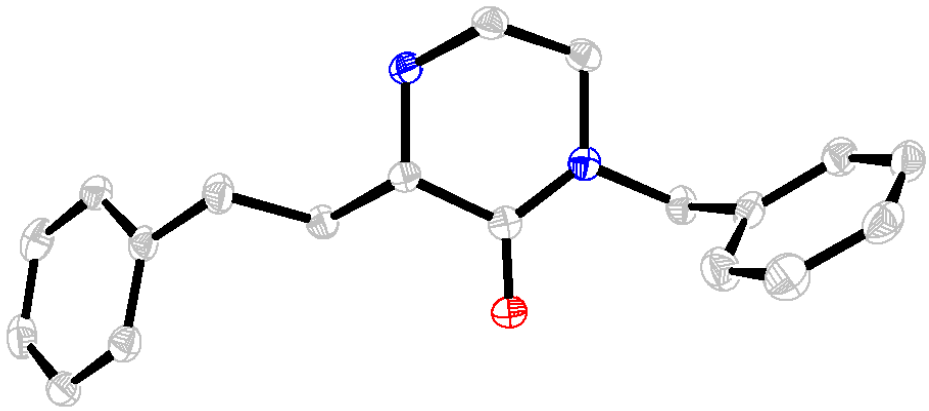
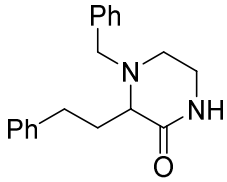


**Figure 1** Solid state structure of **5** with atom labelling. Thermal ellipsoids are drawn at 50% probability.

The asymmetric unit contains 4 molecules of **5** in the unit cell (2 of each enantiomer). The molecule has crystallised in a polar space group so both enantiomers are present. Since the space group is polar it has a related Flack parameter which is 0.203(298) by hole-in-one fit to

all intensities (Shelx 2013/14) and 0.015(132) from 1357 selected quotients (Parsons' method).[11] The Hooft y parameter refined to 0.07(12) (Olex2).[9] The NH was located in a difference map and allowed to refine freely but given a thermal parameter U*iso* equivalent to 1.5 times U*equiv* of the parent Nitrogen.

## 2.2. X-ray Crystal Structure Determination of 6.




Single crystals of **6** were grown from ethyl acetate/hexane. A suitable crystal was selected and mounted on a glass fibre with Fromblin oil and placed on an Oxford Diffraction Xcalibur Gemini diffractometer with a Ruby CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2,[9] the structure was solved with the ShelXS[10] structure solution program using Direct Methods and refined with the ShelXL[10] refinement package using Least Squares minimisation.

Crystal data for **6**: triclinic, space group P-1 (no. 2), $a$ = 5.3351(3) Å, $b$ = 10.0384(5) Å, $c$ = 15.6306(9) Å, $\alpha$ = 106.562(5)°, $\beta$ = 98.033(5)°, $\gamma$ = 95.518(4)°, $V$ = 786.30(8) Å$^3$, $Z$ = 2, $T$ = 150(2) K, μ(CuKα) = 0.603 mm$^{-1}$, *Dcalc* = 1.243 g/mm$^3$, 5168 reflections measured (5.992 ≤ 2Θ ≤ 154.62), 3220 unique ($R_{int}$ = 0.0200, $R_{sigma}$ = 0.0252) which were used in all calculations. The final $R_1$ was 0.0420 (I > 2σ(I)) and $wR_2$ was 0.1183 (all data).

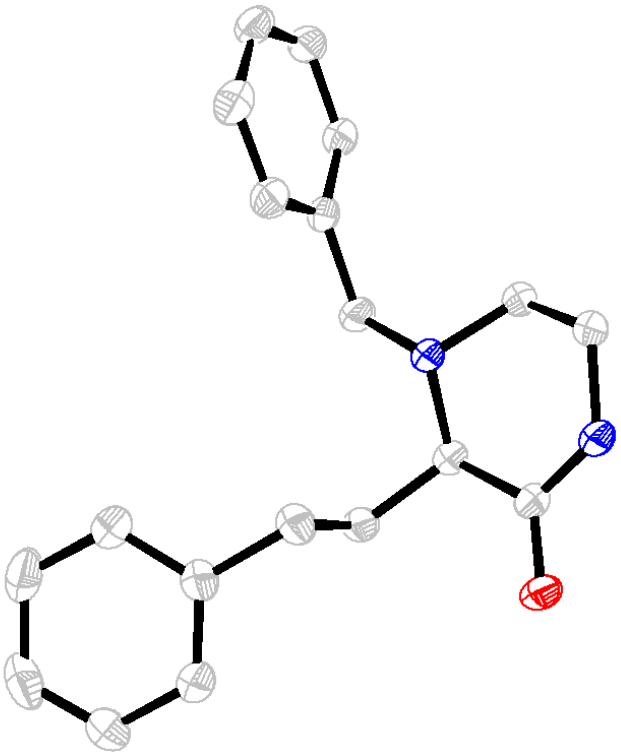
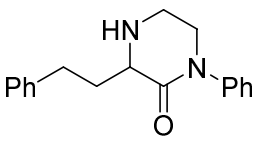


**Figure 2** Solid state structure of **6** with atom labelling. Thermal ellipsoids are drawn at 50 % probability.

The disorder in the ring of the phenylethyl chain is removed for clarity. The asymmetric unit contains **6**. There are 2 molecules in the unit cell related by an inversion centre. The ring of the phenylethyl chain was modeled as disordered over two positions by rotation about the C6-C7 bond (C3 and C6 belonged to both parts). The occupancies were refined to 47 : 53 (minor : major). The NH was located in a difference map and allowed to refine freely but given a thermal parameter Uiso 1.5 times the Uequiv of the parent nitrogen.

### 2.3. X-ray Crystal Structure Determination of 12.




Single crystals of **12** were grown from ethyl acetate/hexane. A suitable crystal was selected and mounted on a Mitegen loop with Fromblin oil on an Oxford Diffraction Xcalibur Gemini diffractometer with a Ruby CCD area detector. The crystal was kept at 100(2) K during data

collection. Using Olex2,[9] the structure was solved with the ShelXS[10] structure solution program using Direct Methods and refined with the ShelXL[10] refinement package using Least Squares minimisation.

Crystal data for **12**: orthorhombic, space group $Pca2_1$ (no. 29), $a$ = 27.3686(6) Å, $b$ = 6.32664(13) Å, $c$ = 8.74746(17) Å, $V$ = 1514.63(6) Å$^3$, $Z$ = 4, $T$ = 150.15 K, μ(Cu Kα) = 0.602 mm$^{-1}$, *Dcalc* = 1.229 g/mm$^3$, 4385 reflections measured ($6.46 \leq 2\Theta \leq 133.174$), 2162 unique ($R_{int}$ = 0.0194) which were used in all calculations. The final $R_1$ was 0.0343 ($I > 2\sigma(I)$) and $wR_2$ was 0.0915 (all data).

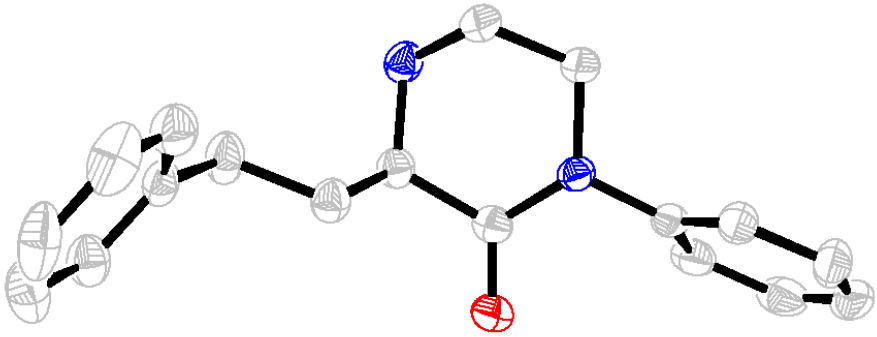


**Figure 3** Solid state structure of **12** with atom labelling. Thermal ellipsoids are drawn at 50% probability.

The asymmetric unit contains 4 molecules of **12** in the unit cell (2 of each enantiomer). The molecule has crystallised in a polar space group so both enantiomers are present. Since the space group is polar it has a related Flack parameter which is 0.2(2). The Hooft y parameter refined to 0.28(11) (Olex2).[9] The hydrogen on the amine was located in a difference map and was allowed to refine freely but given Uiso 1.5 times the Uequiv of the parent nitrogen.

## 3. References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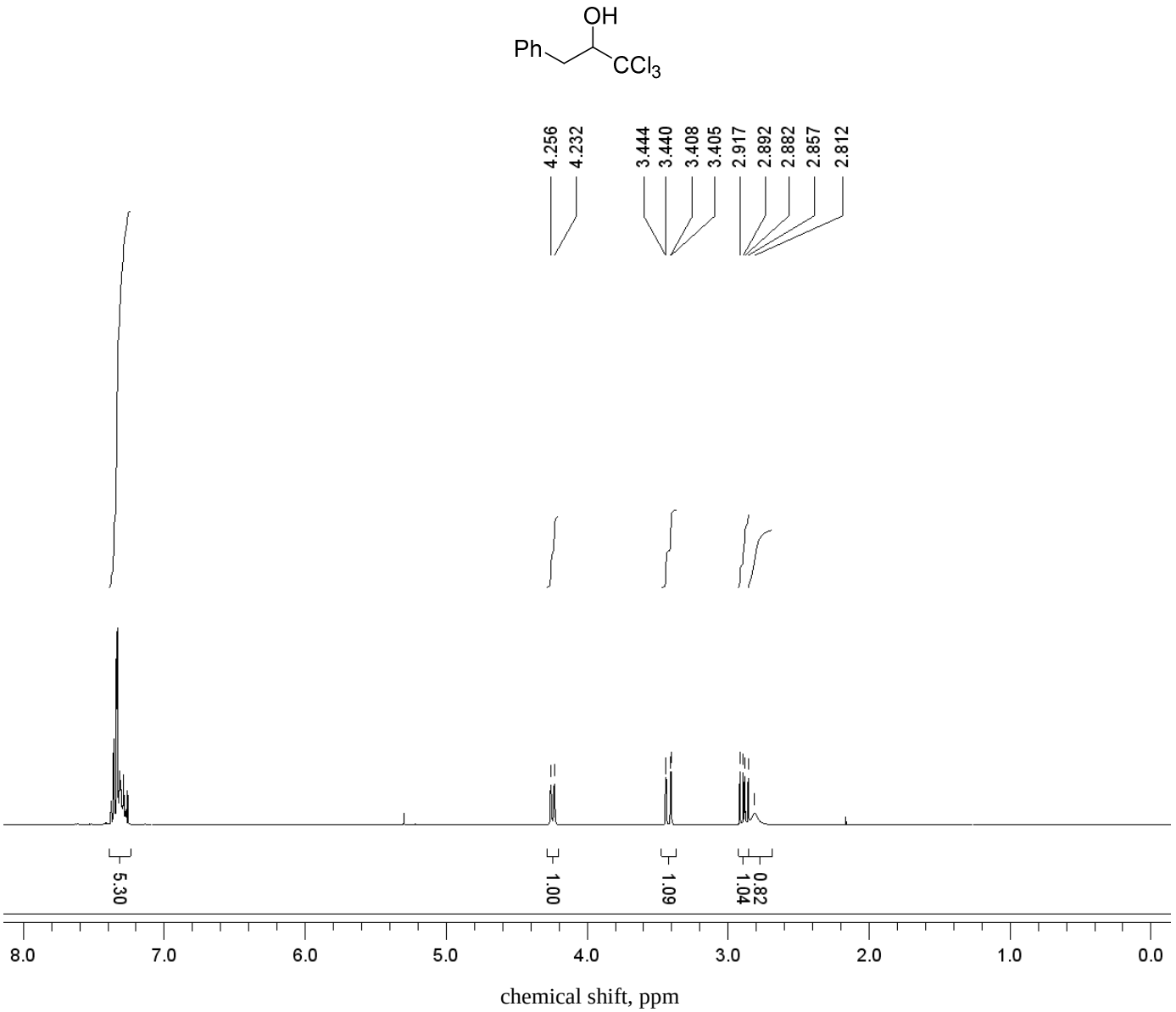
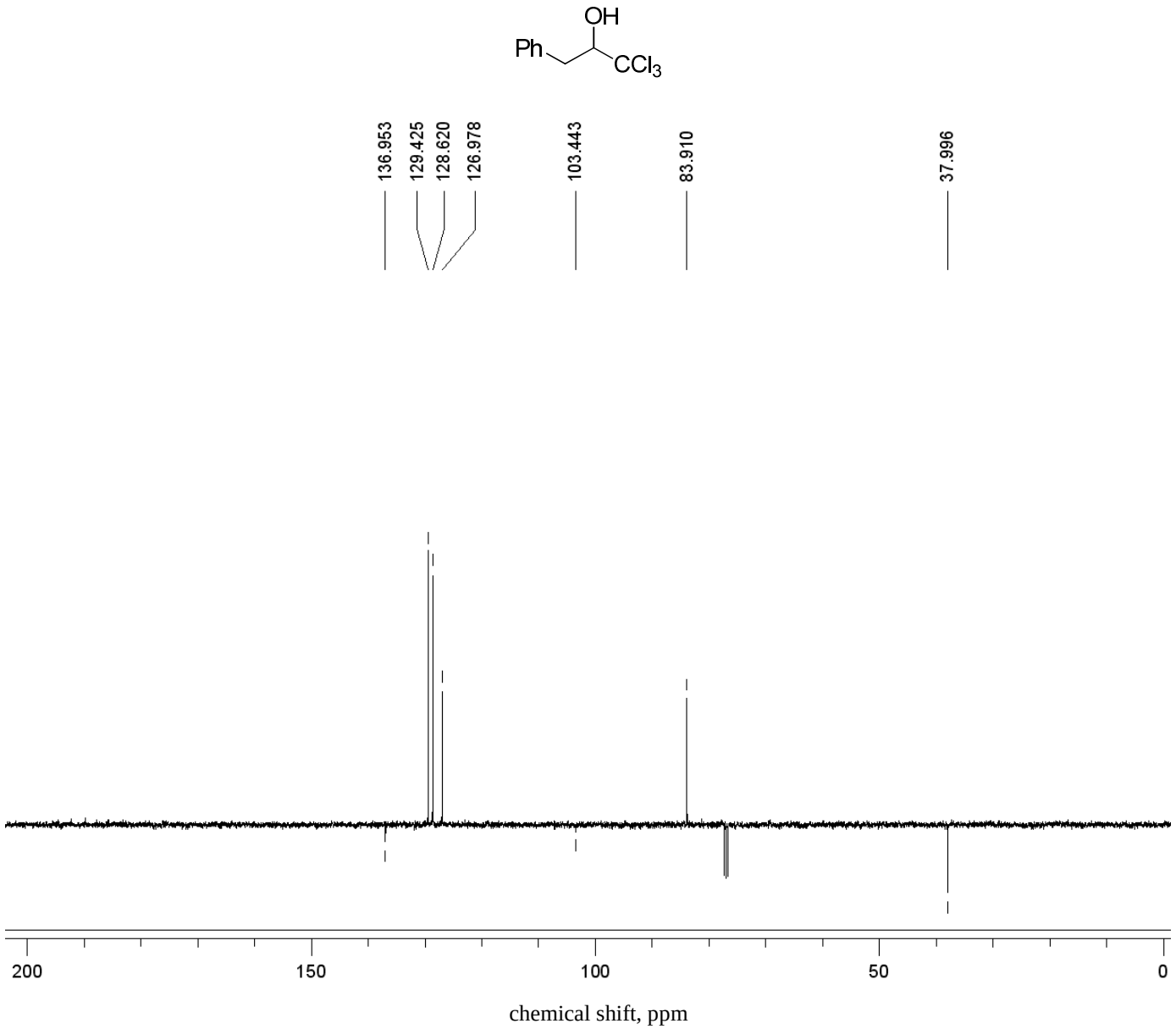
11. S. Parsons and H. Flack, *Acta Cryst.*, 2004, **A60**, s61.

## 4. $^{1}H$ and $^{13}C$ NMR Spectra.

### 4.1 $^{1}H$ and $^{13}C$ Spectra of 1,1,1-trichloro-3-phenylpropan-2-ol 23, 1,1,1-trichloro-3-phenylpropan-2-one 22, *tert*-butyl (2-((4-fluorobenzyl)amino)ethyl)carbamate and *N*-(4-fluorobenzyl)ethane-1,2-diamine.




OH
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CCl3
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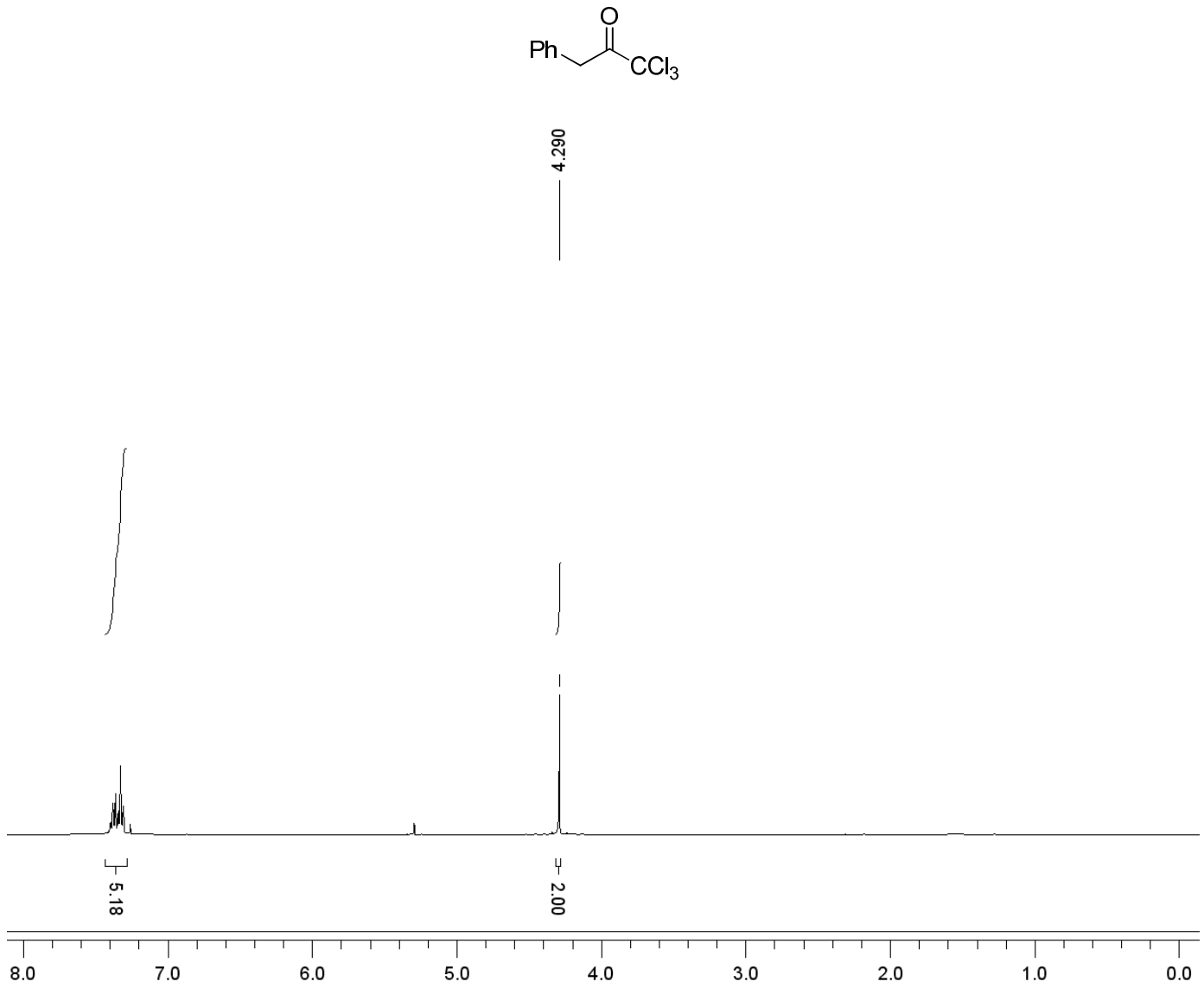
128.620
126.978
103.443
83.910
37.996
200
150
100
50
0
chemical shift, ppm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CCl3
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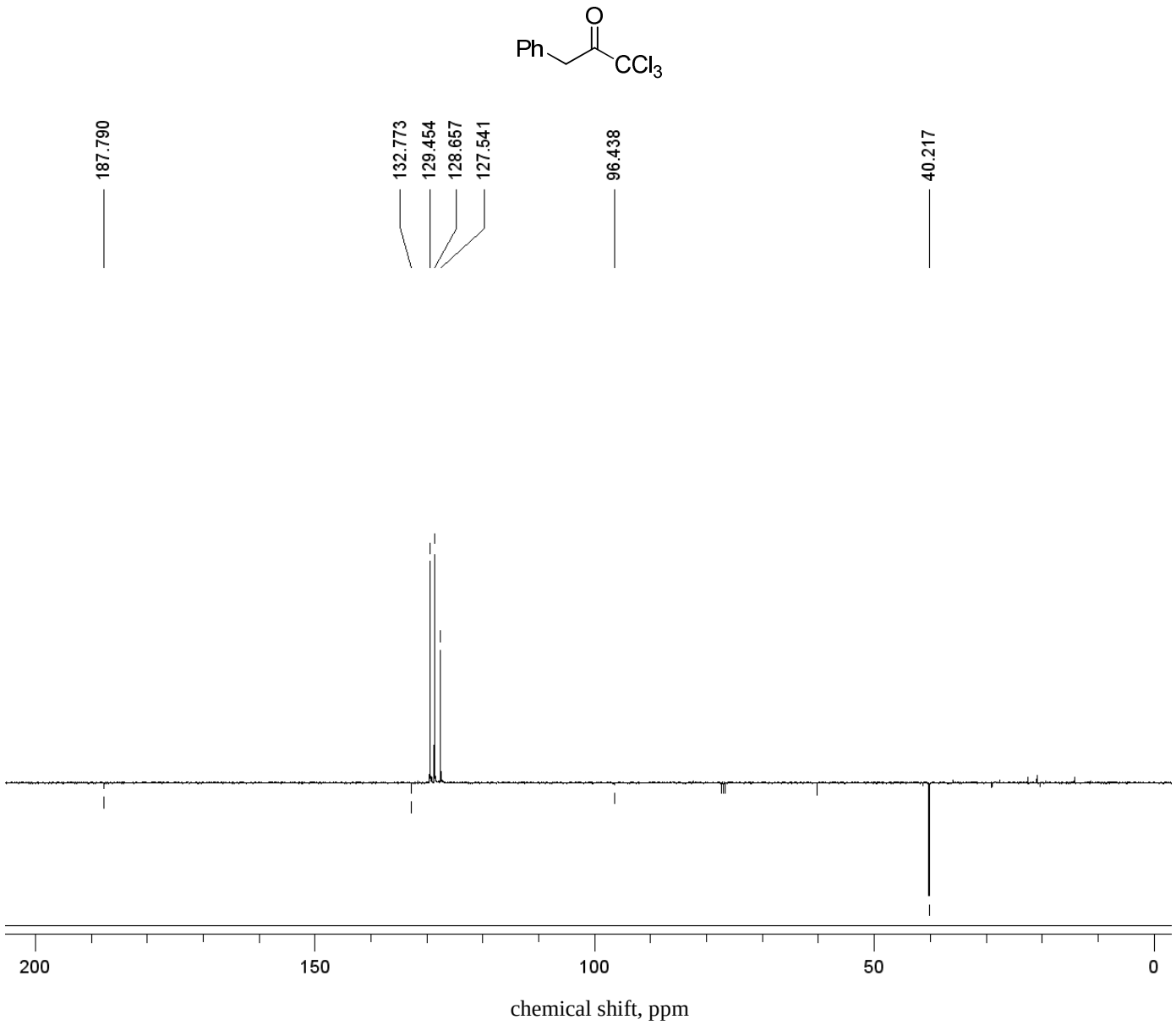
2.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm


O
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96.438
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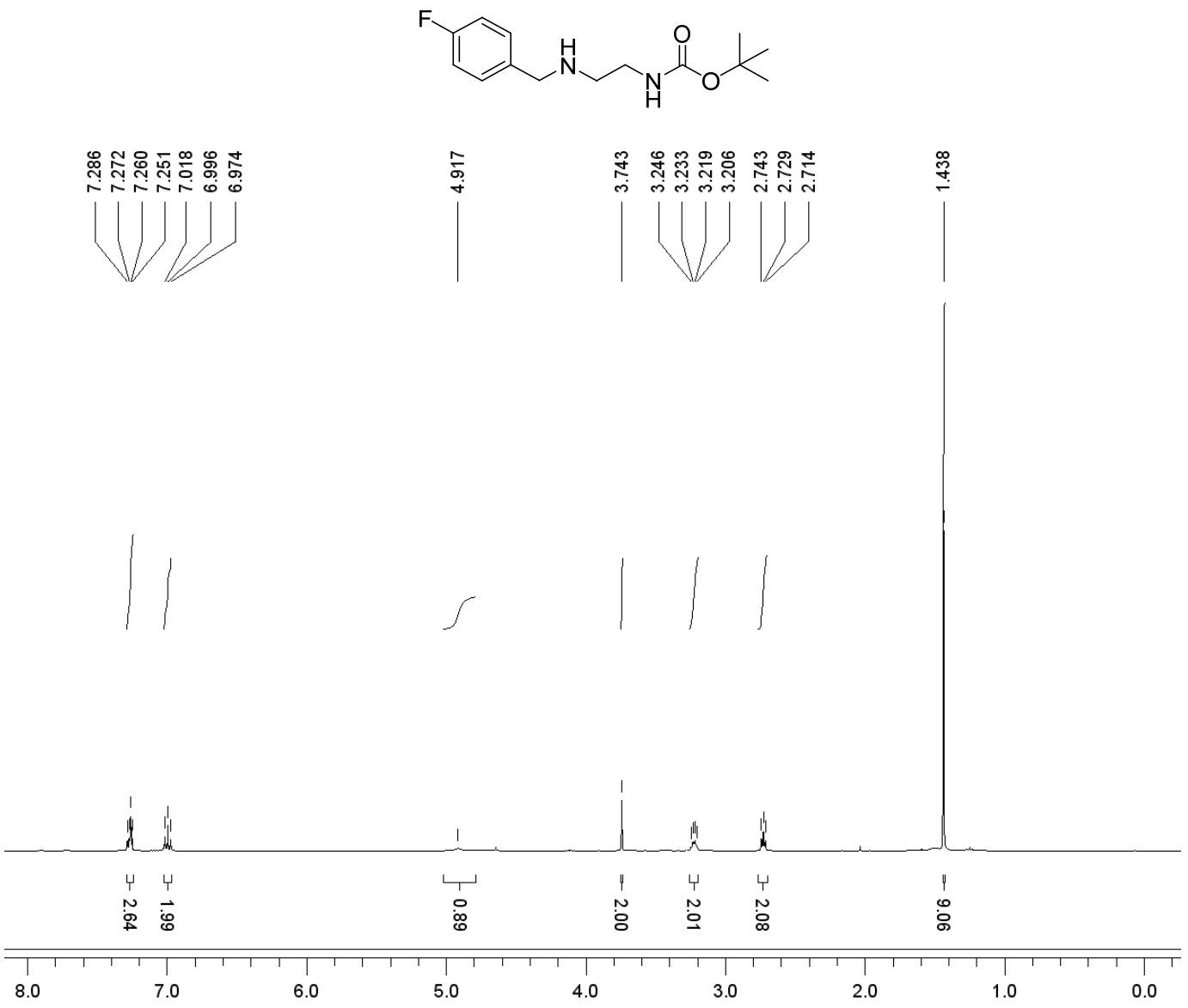
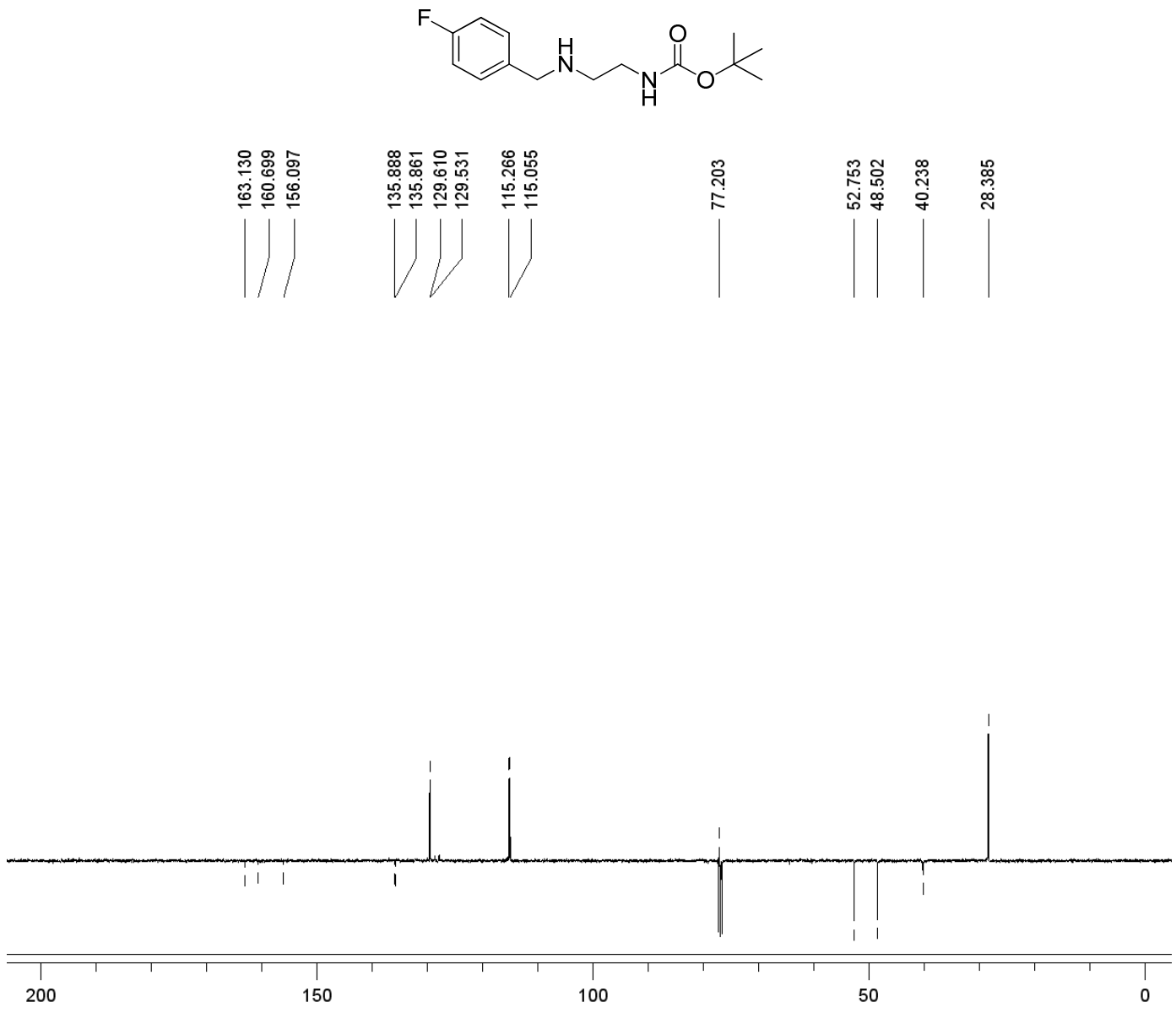
150
100
50
0
chemical shift, ppm




chemical shift, ppm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N
O
N
H
O
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160.699
156.097
135.888
135.861
129.610
129.531
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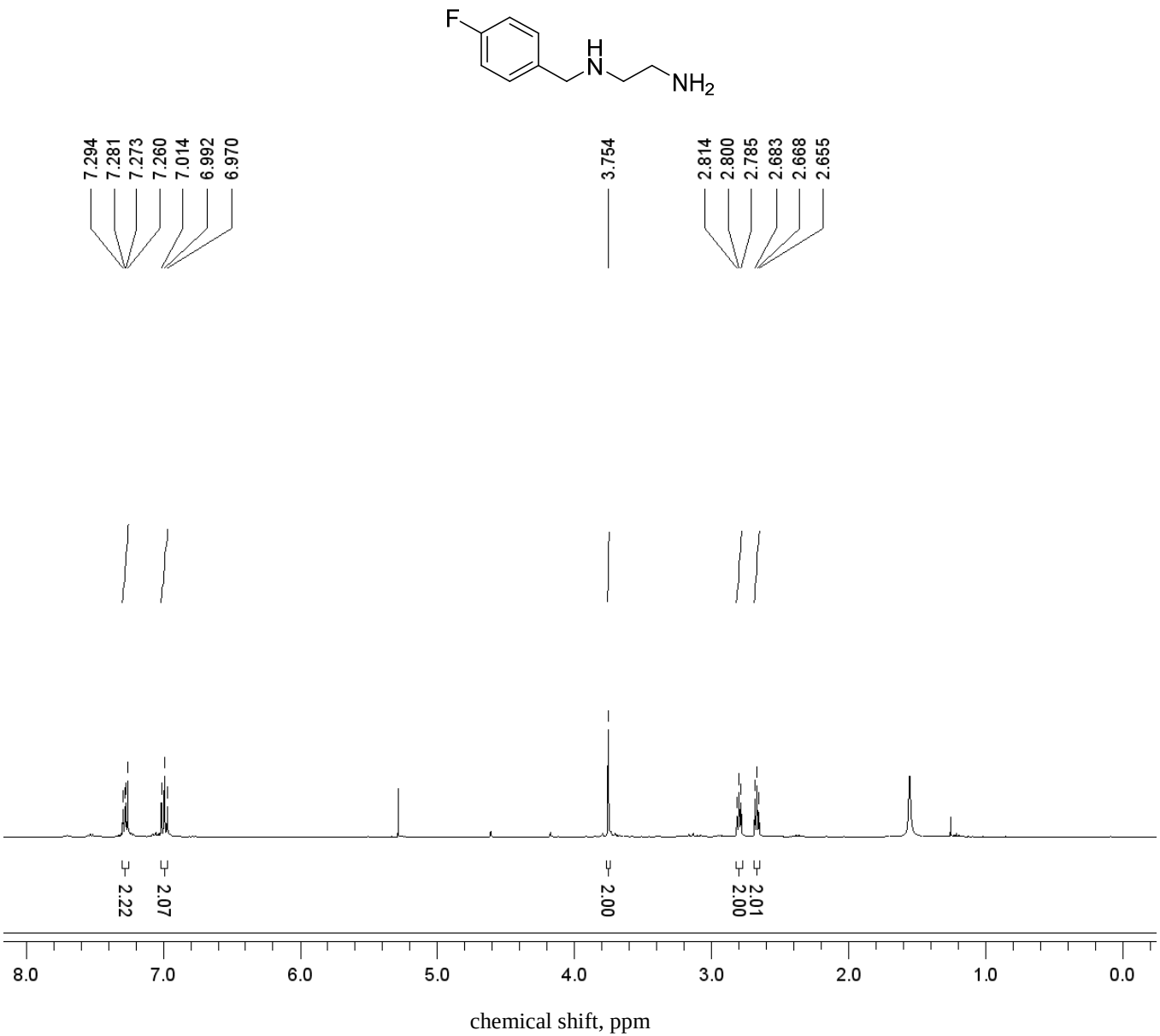
115.055
77.203
52.753
48.502
40.238
28.385
200
150
100
50
0
chemical shift, ppm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H
N
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7.273
7.260
7.014
6.992
6.970
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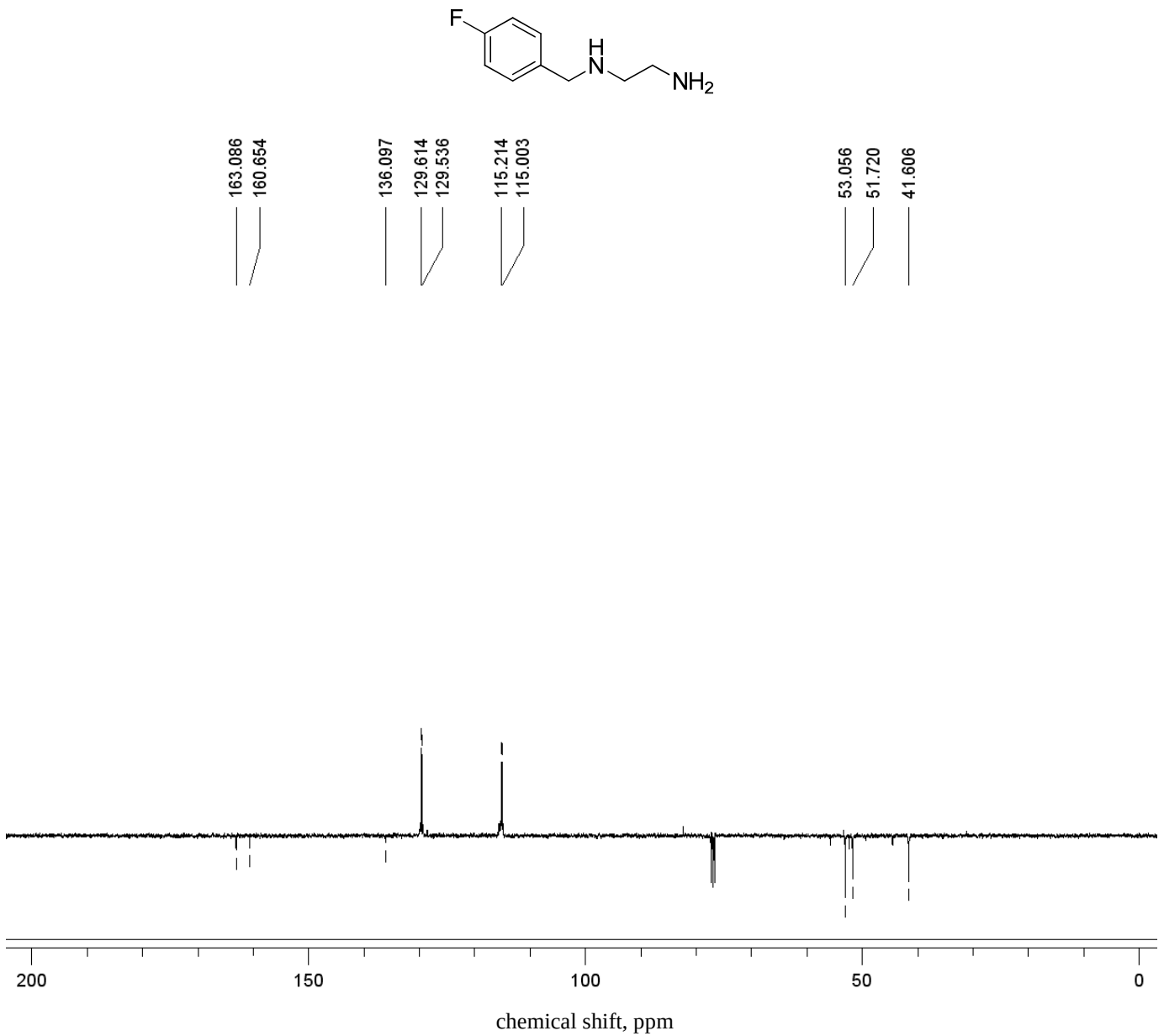
2.785
2.683
2.668
2.655
2.22
2.07
2.00
2.00
2.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm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H
N
NH2
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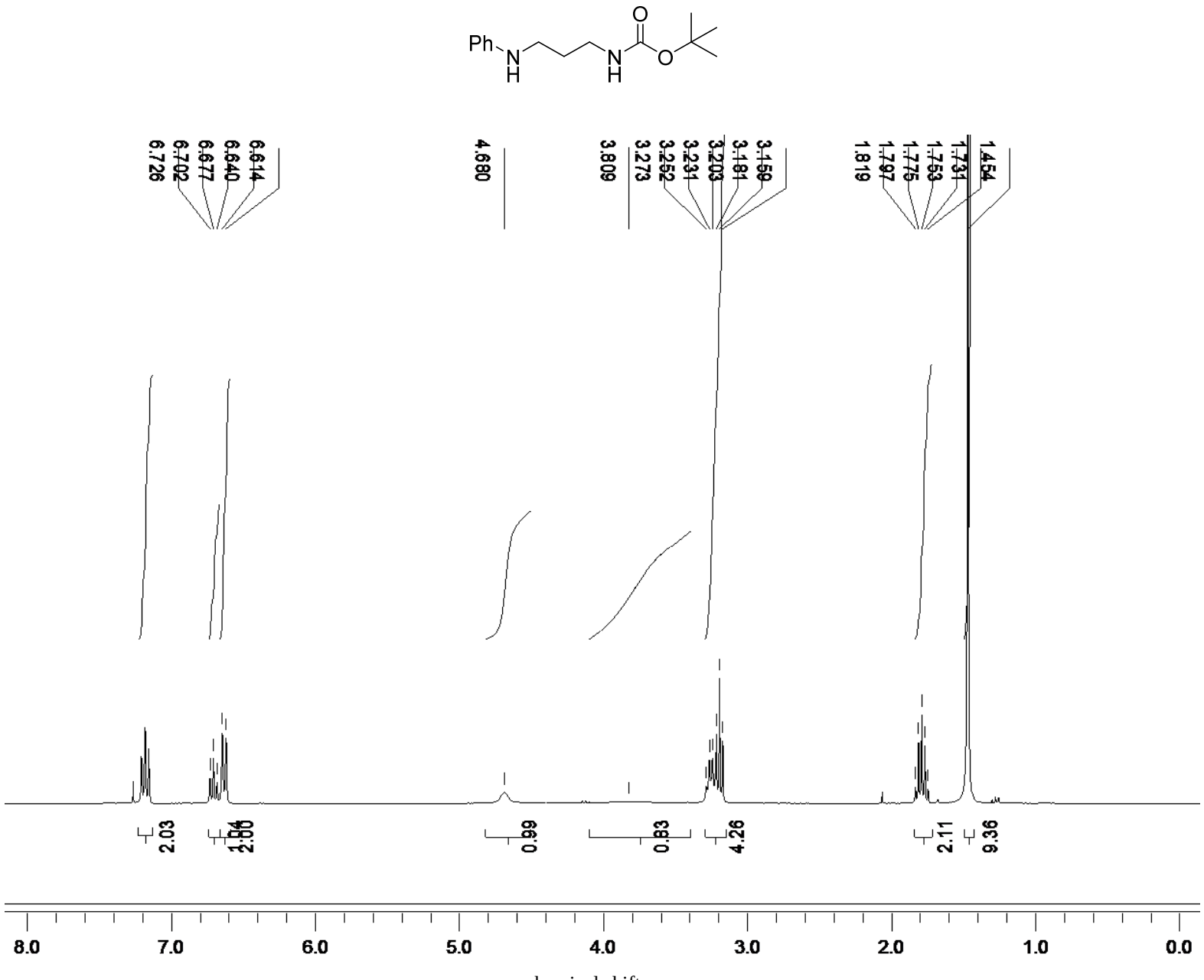
100
50
0
chemical shift, ppm


Ph
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H
N
H
O
O
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6.677
6.640
6.614
4.680
3.809
3.273
3.252
3.231
3.203
3.181
3.159
1.819
1.797
1.775
1.753
1.731
1.454
2.03
0.99
0.83
4.26
2.11
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7.0
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5.0
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3.0
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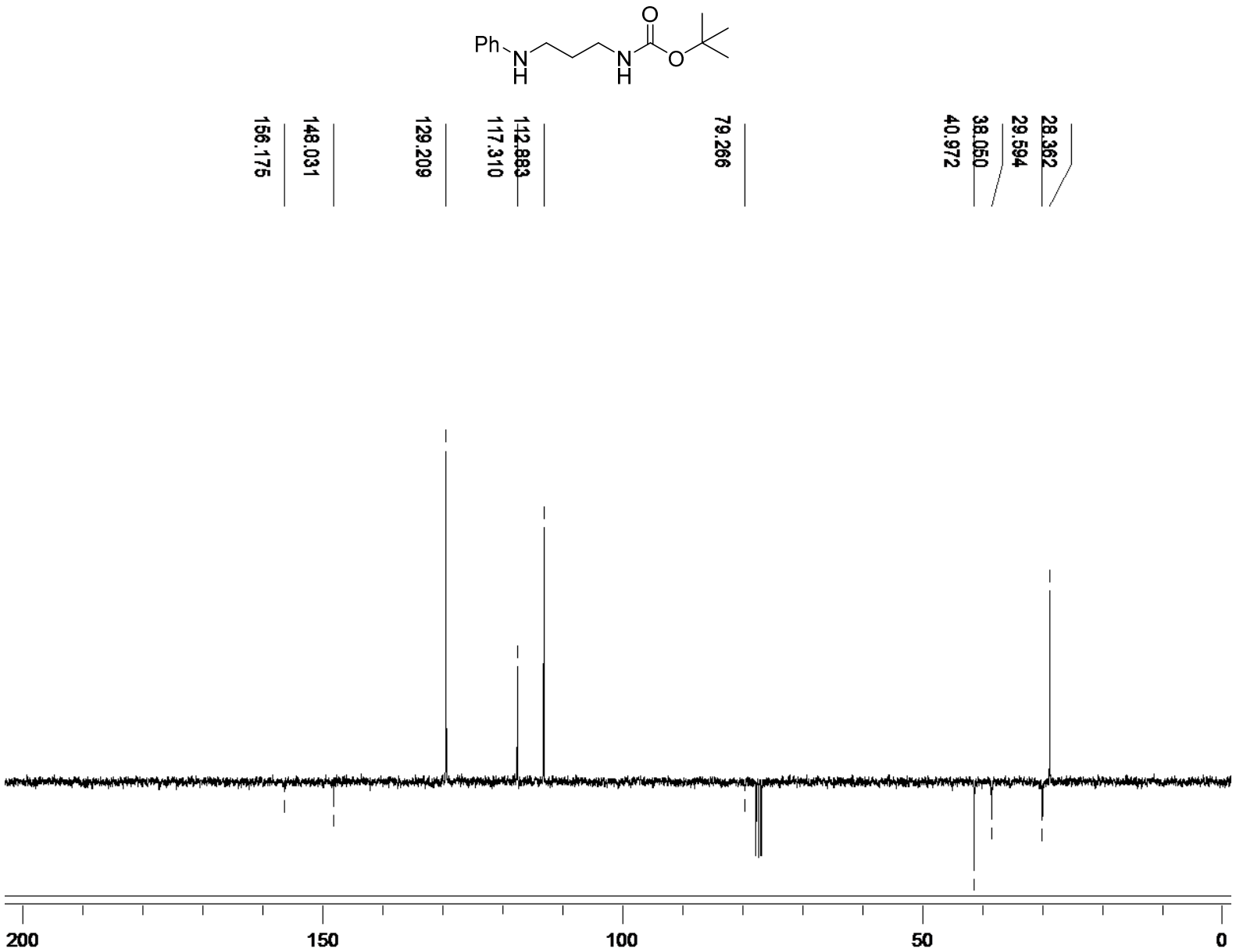
chemical shift, ppm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50
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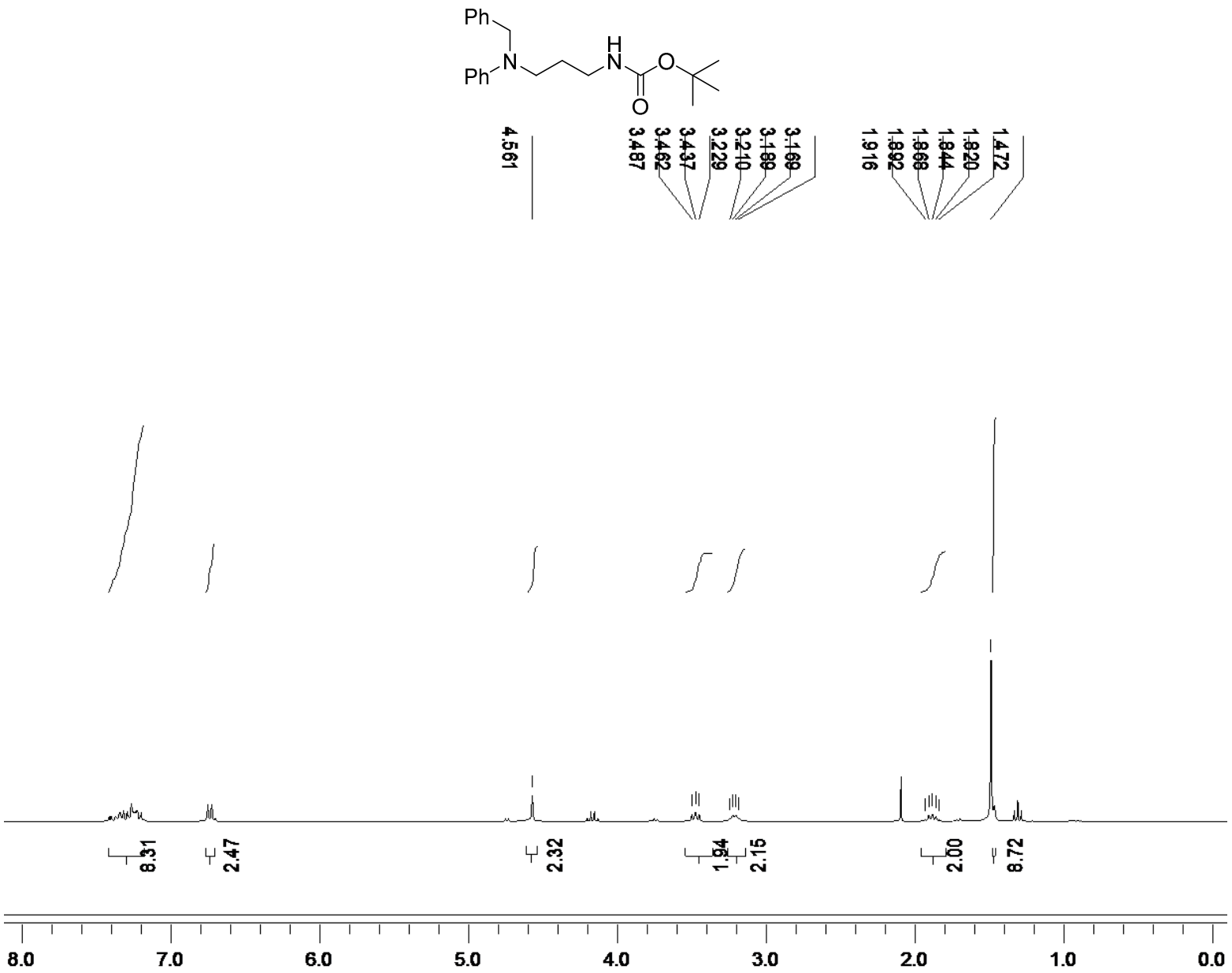
chemical shift, ppm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Ph
H
N
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1.916
1.892
1.868
1.844
1.820
1.472
8.31
2.47
2.32
1.94
2.15
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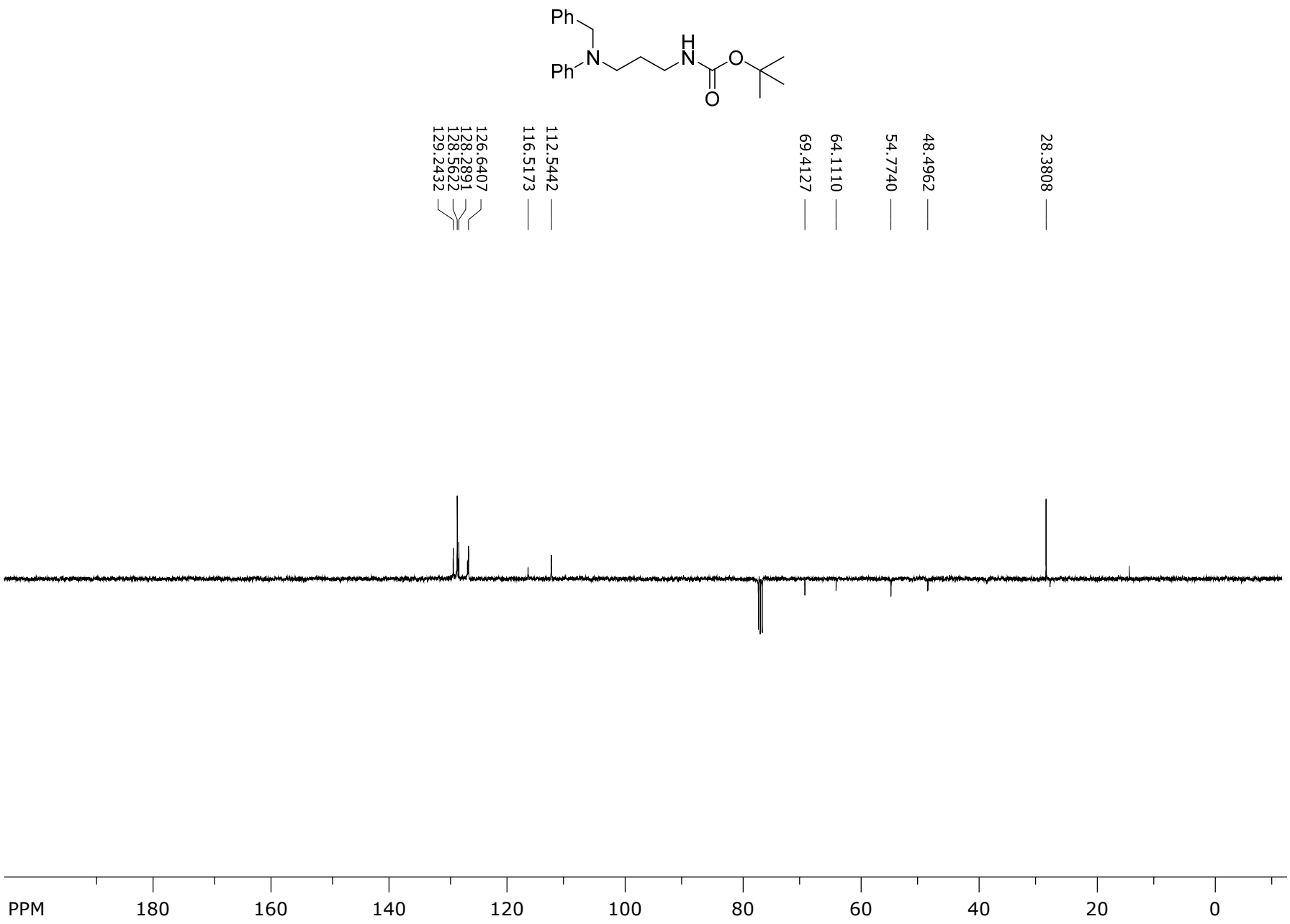
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm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Ph
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H
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116.5173
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69.4127
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48.4962
28.3808
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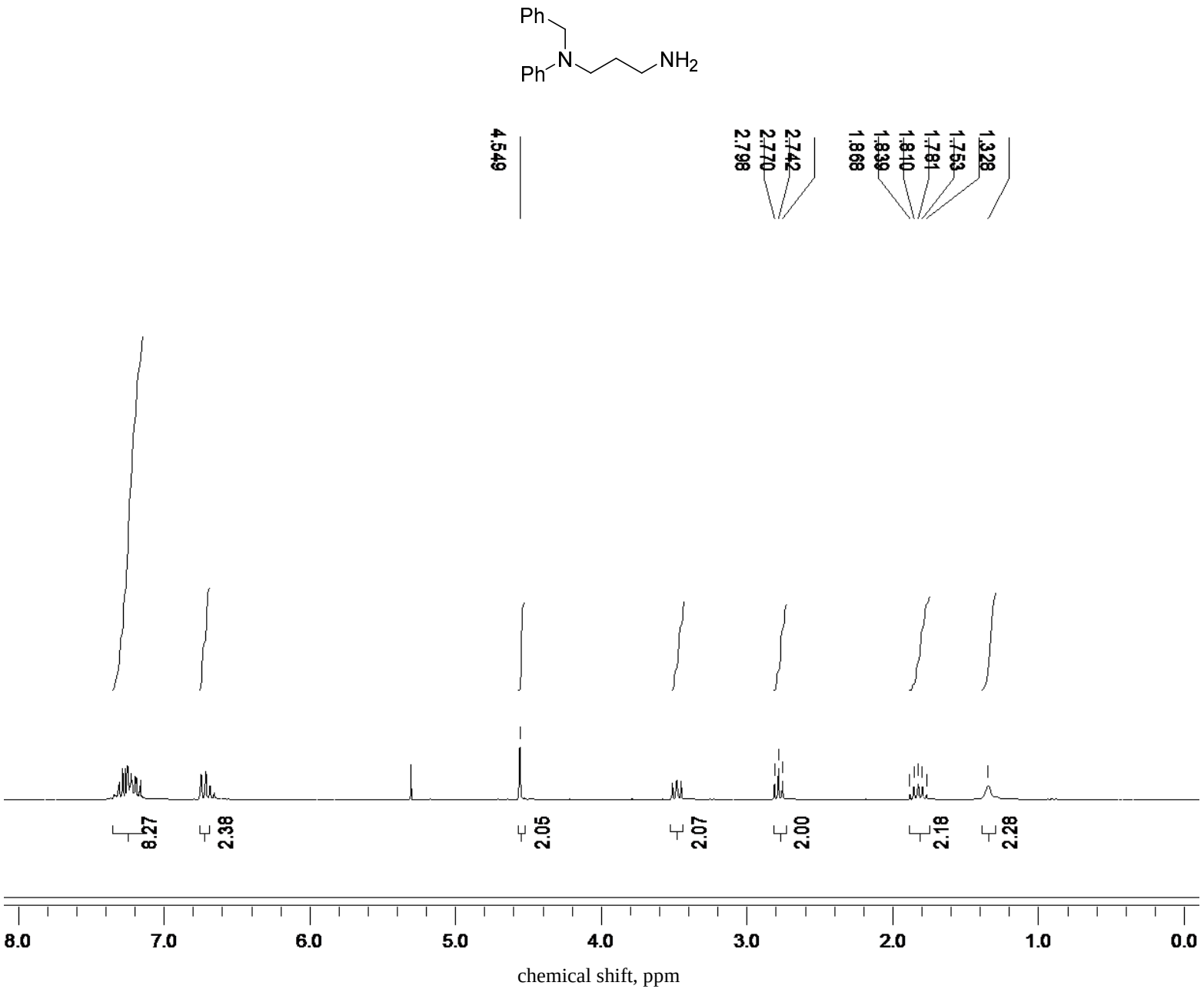
160
140
120
100
80
60
40
20
0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Ph
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1.810
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1.753
1.328
8.27
2.38
2.05
2.07
2.00
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3.0
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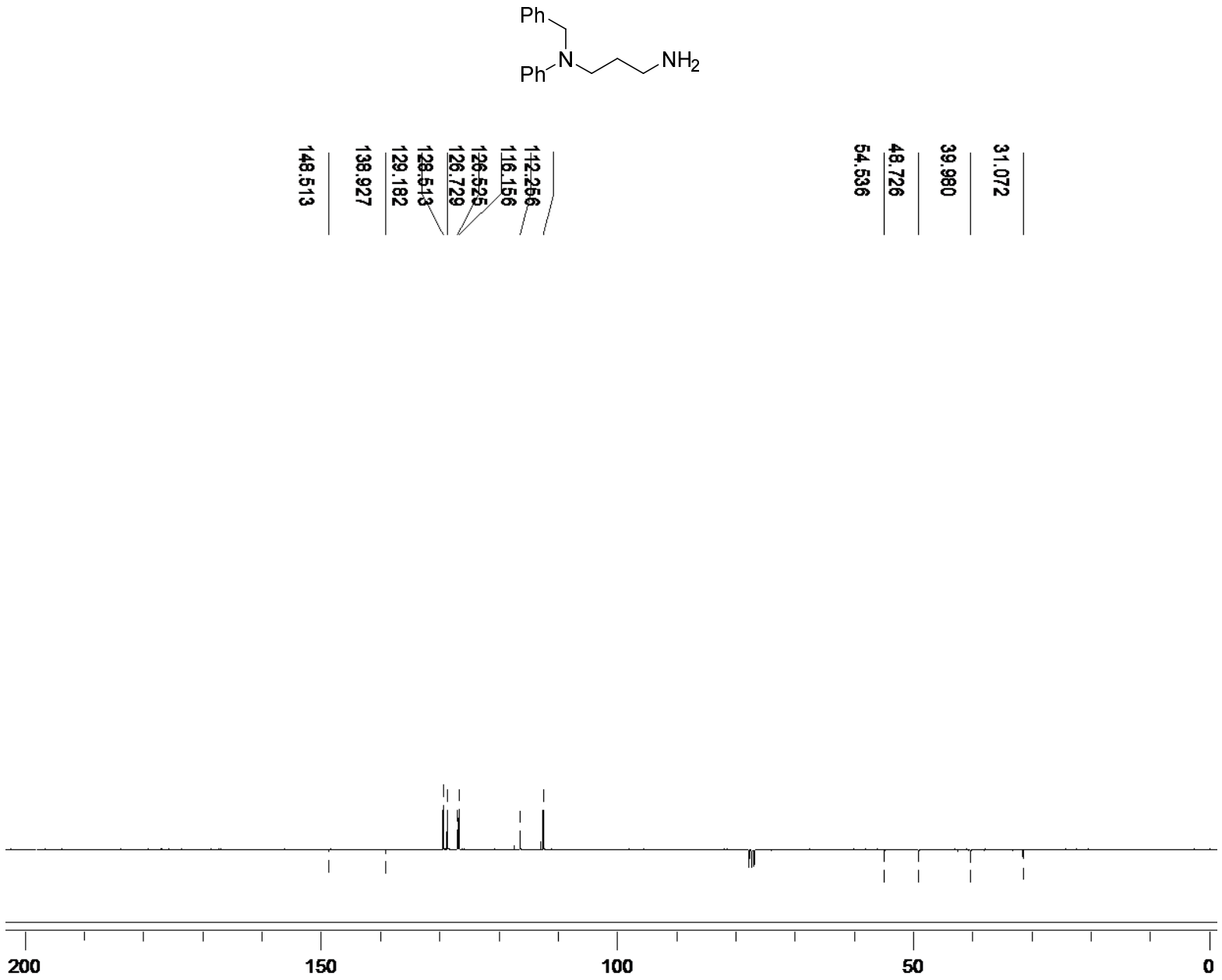
chemical shift, ppm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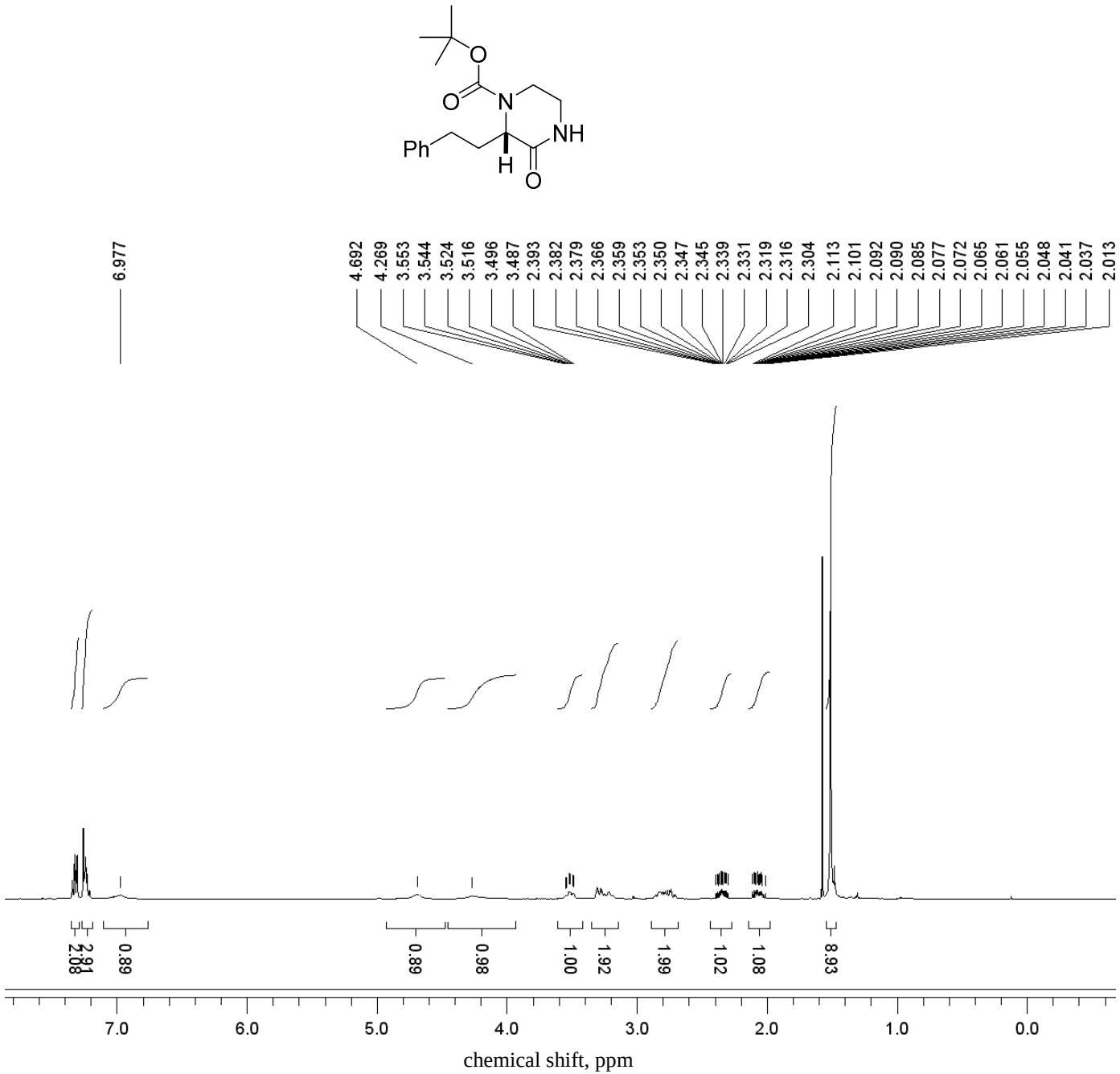
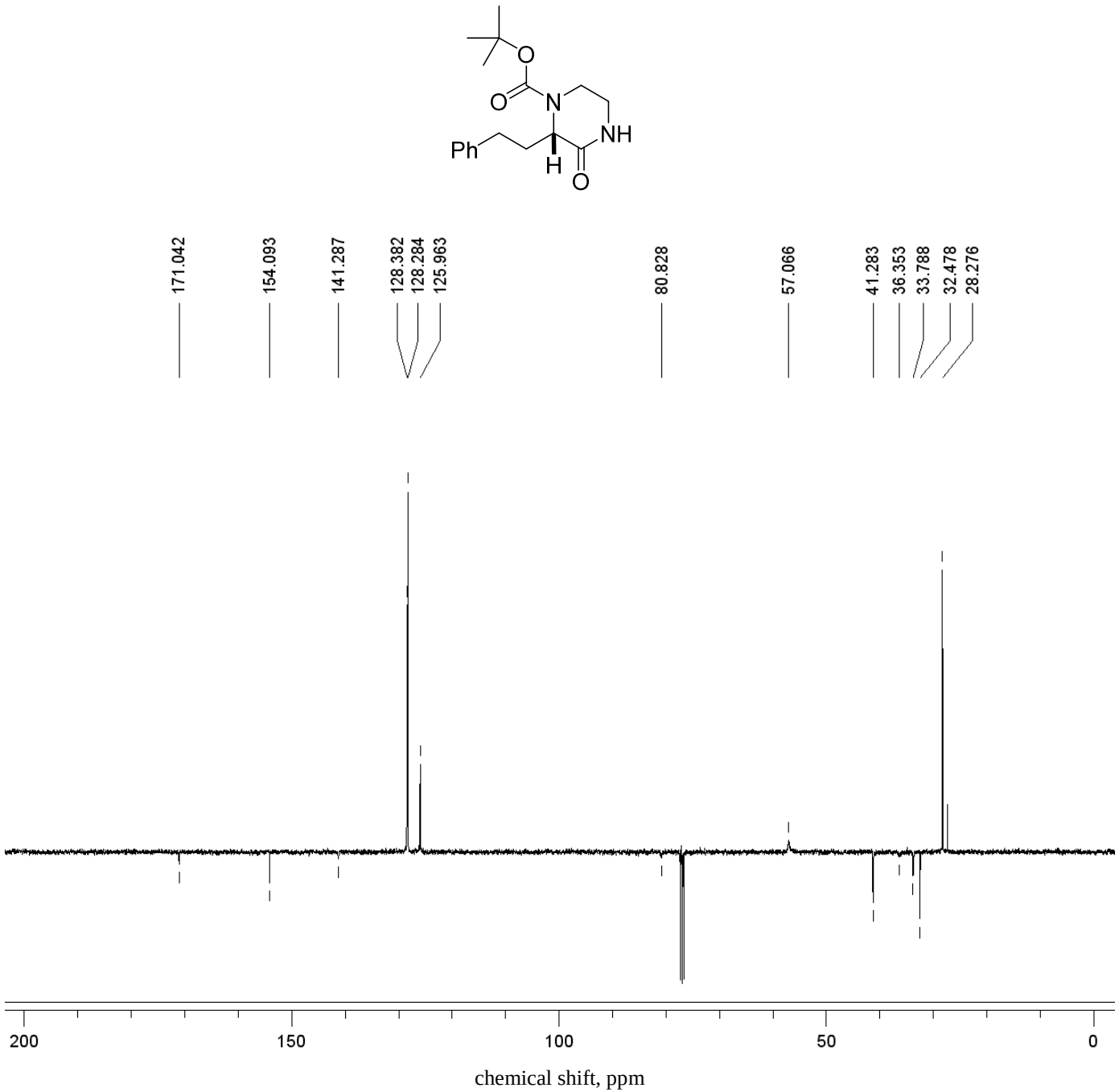
50
0
chemical shift, ppm

**4.2 $^{1}$H and $^{13}$C NMR Spectra for (*S*)-2 and (*S*)-3.**

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NH
Ph
H
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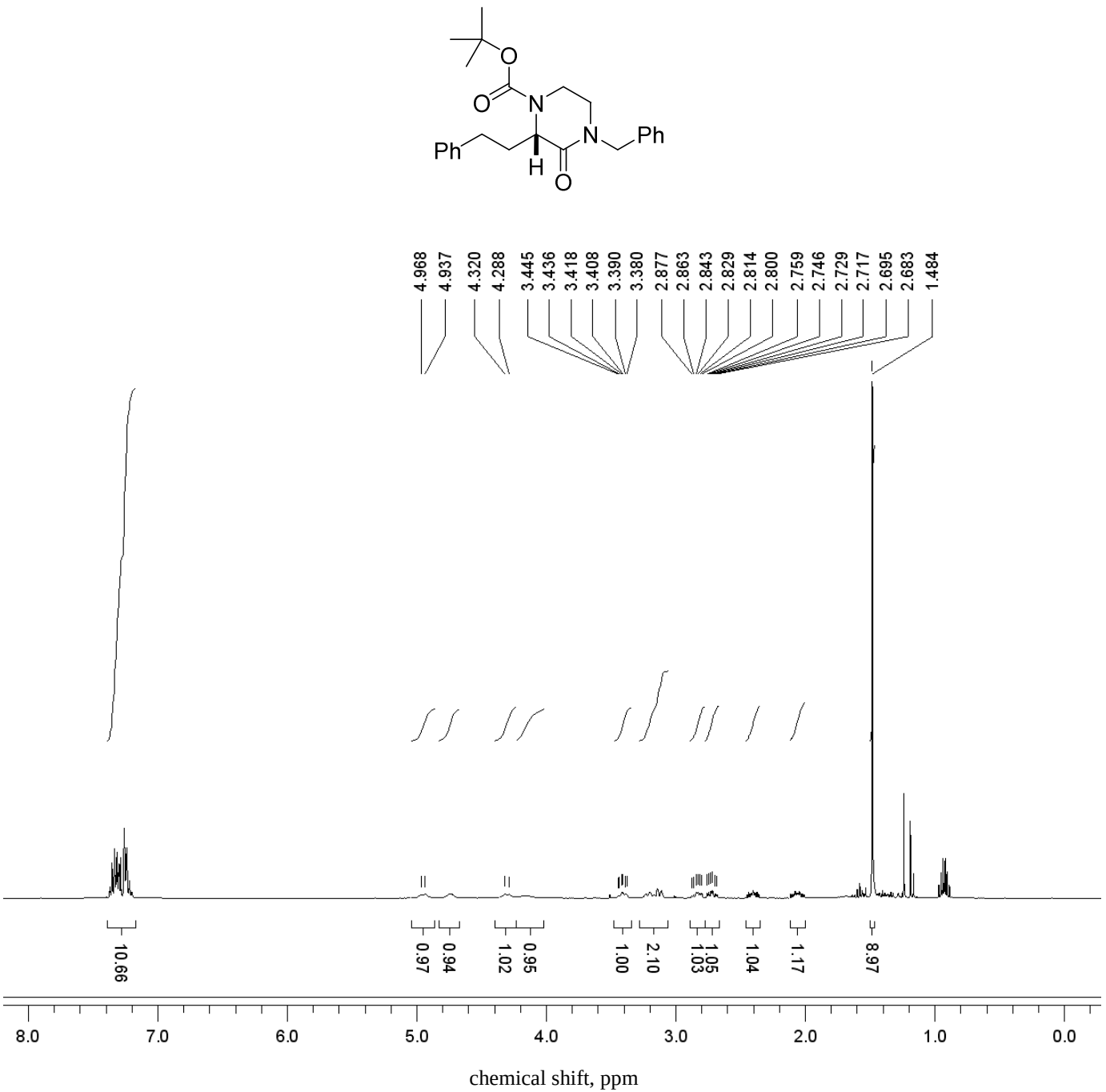
150
100
50
0
chemical shift, ppm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O
N
Ph
N
Ph
H
O
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3.436
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3.408
3.390
3.380
2.877
2.863
2.843
2.829
2.814
2.800
2.759
2.746
2.729
2.717
2.695
2.683
1.484
10.66
0.97
0.94
1.02
0.95
1.00
2.10
1.05
1.03
1.04
1.17
8.97
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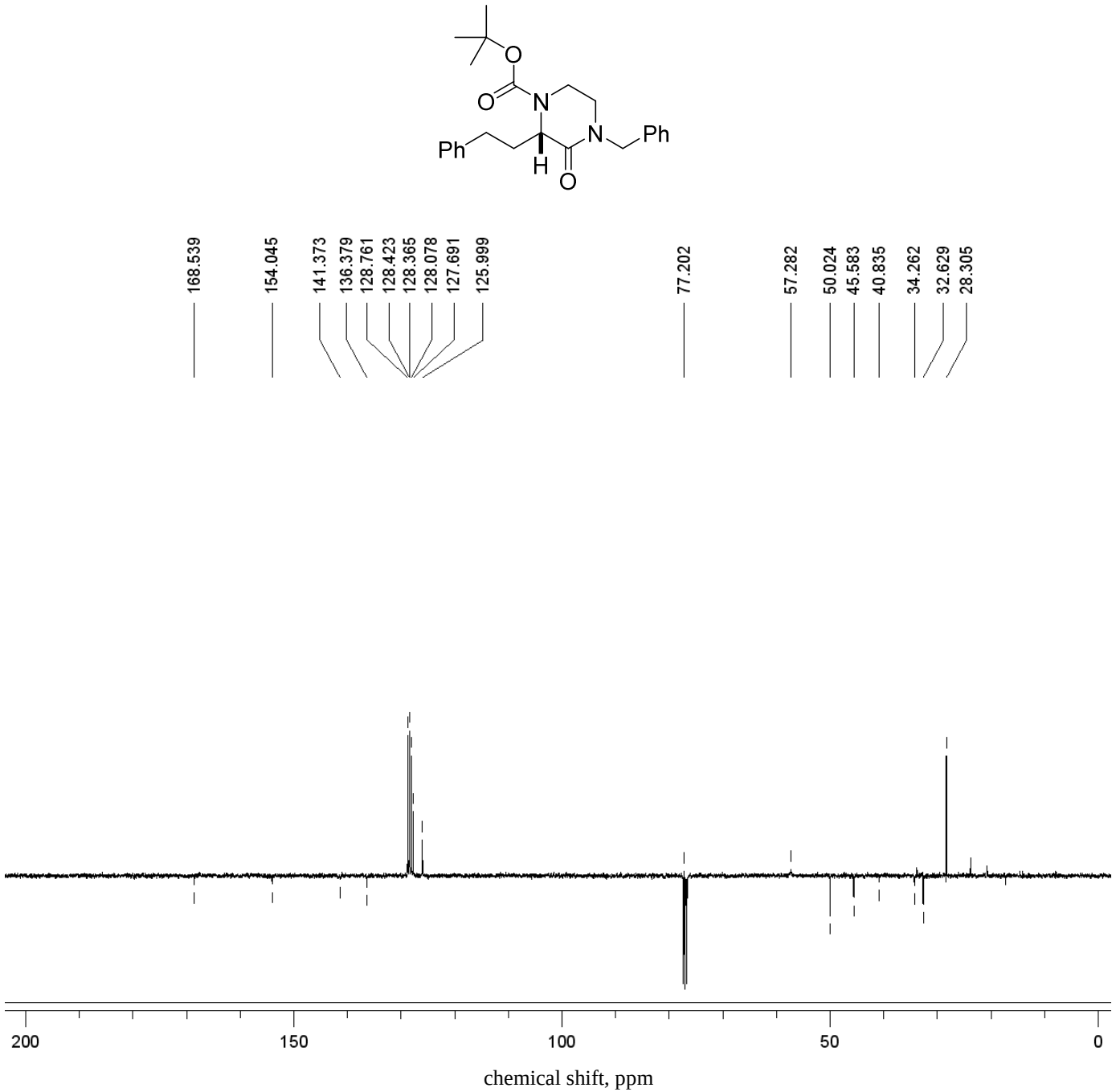
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm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O
N
N
Ph
Ph
H
O
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141.373
136.379
128.761
128.423
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127.691
125.999
77.202
57.282
50.024
45.583
40.835
34.262
32.629
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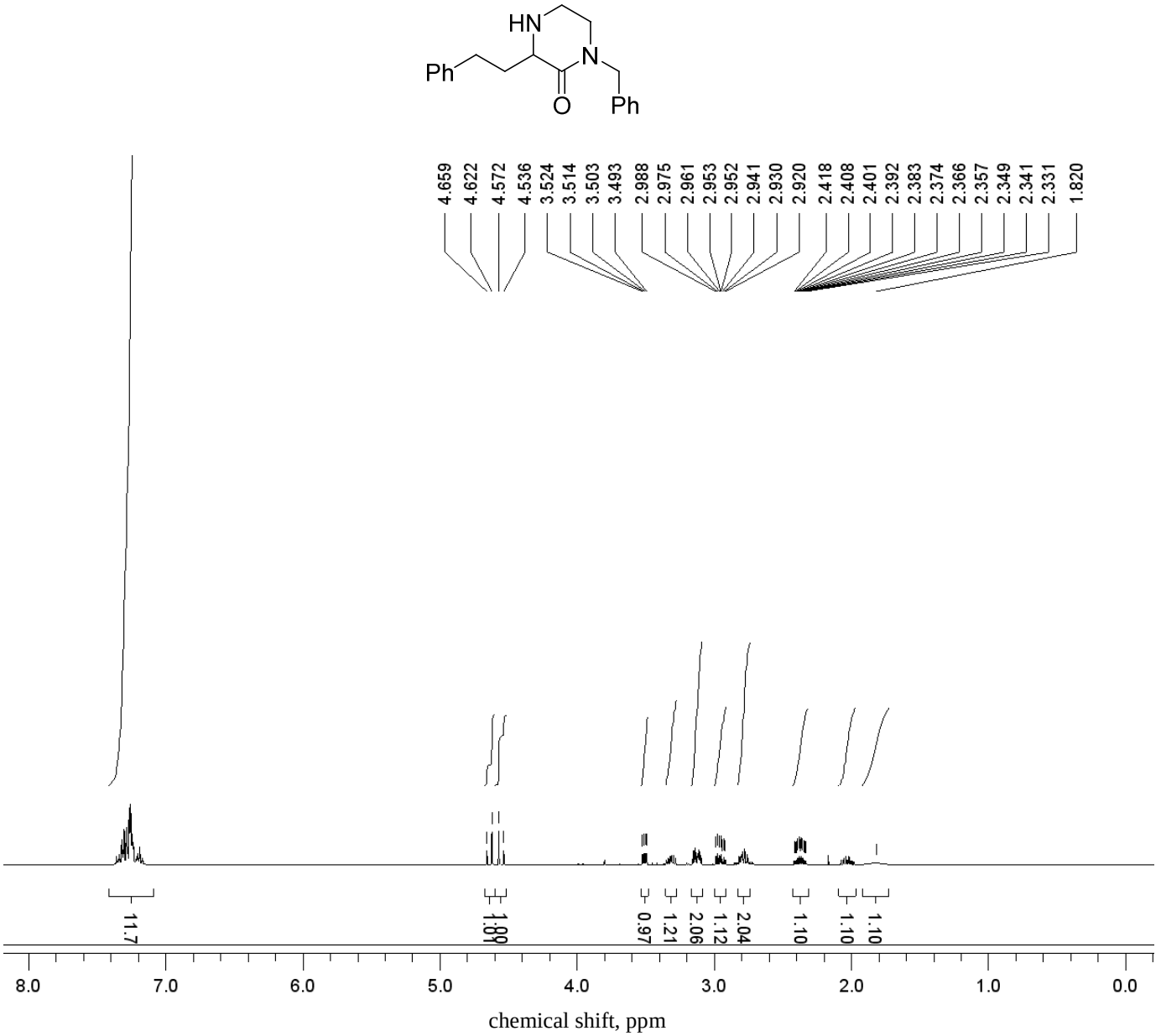
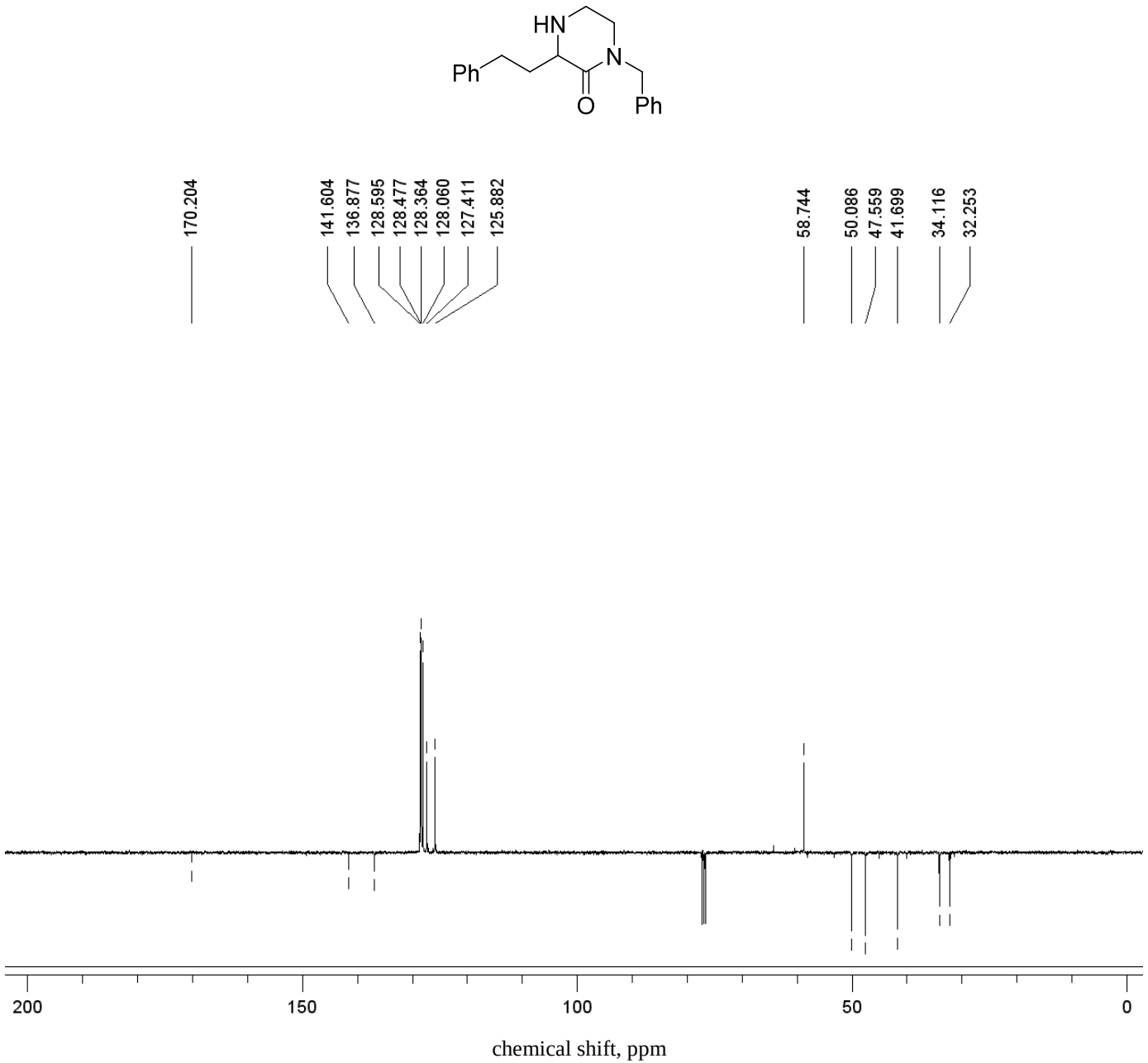
200
150
100
50
0
chemical shift, ppm

**4.3 $^{1}$H and $^{13}$C NMR Spectra for Substituted Piperazin-2-ones with Product Ratios.**




HN
Ph
N
O
Ph
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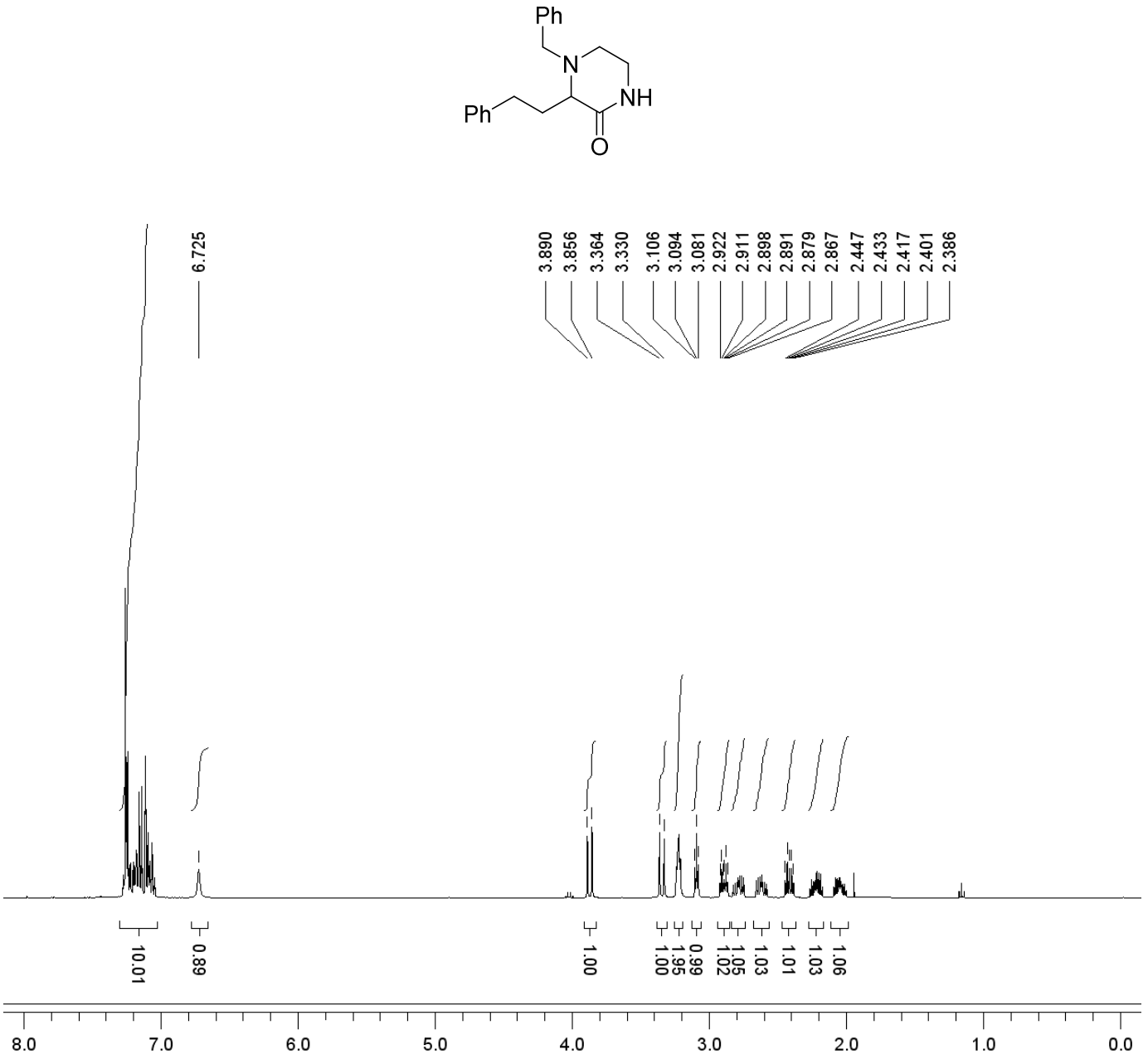
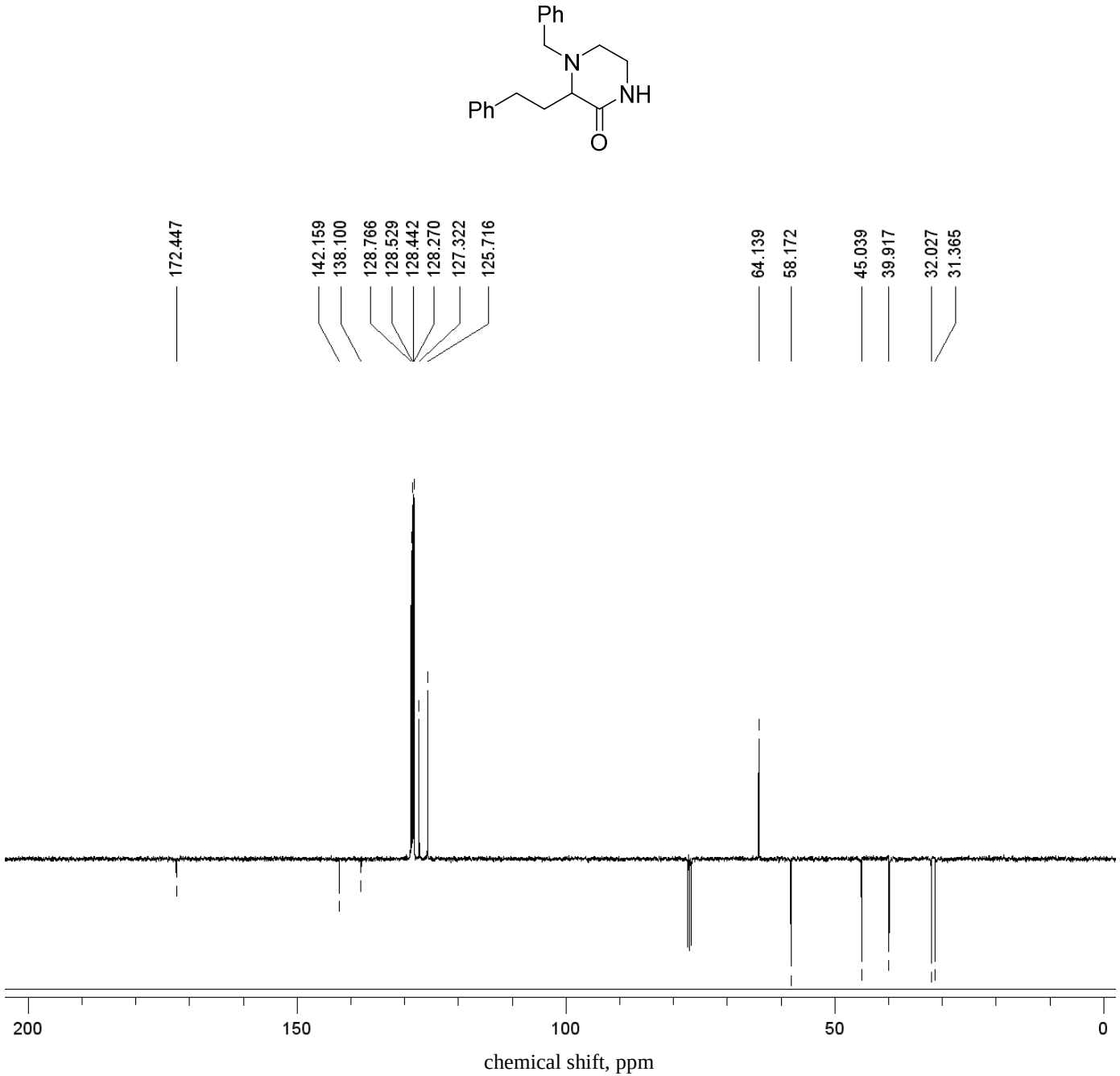
136.877
128.595
128.477
128.364
128.060
127.411
125.882
58.744
50.086
47.559
41.699
34.116
32.253
200
150
100
50
0
chemical shift, ppm


Ph
N
NH
Ph
O
6.725
3.890
3.856
3.364
3.330
3.106
3.094
3.081
2.922
2.911
2.898
2.891
2.879
2.867
2.447
2.433
2.417
2.401
2.386
10.01
0.89
1.00
1.00
1.65
0.99
1.02
1.05
1.03
1.01
1.03
1.06
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm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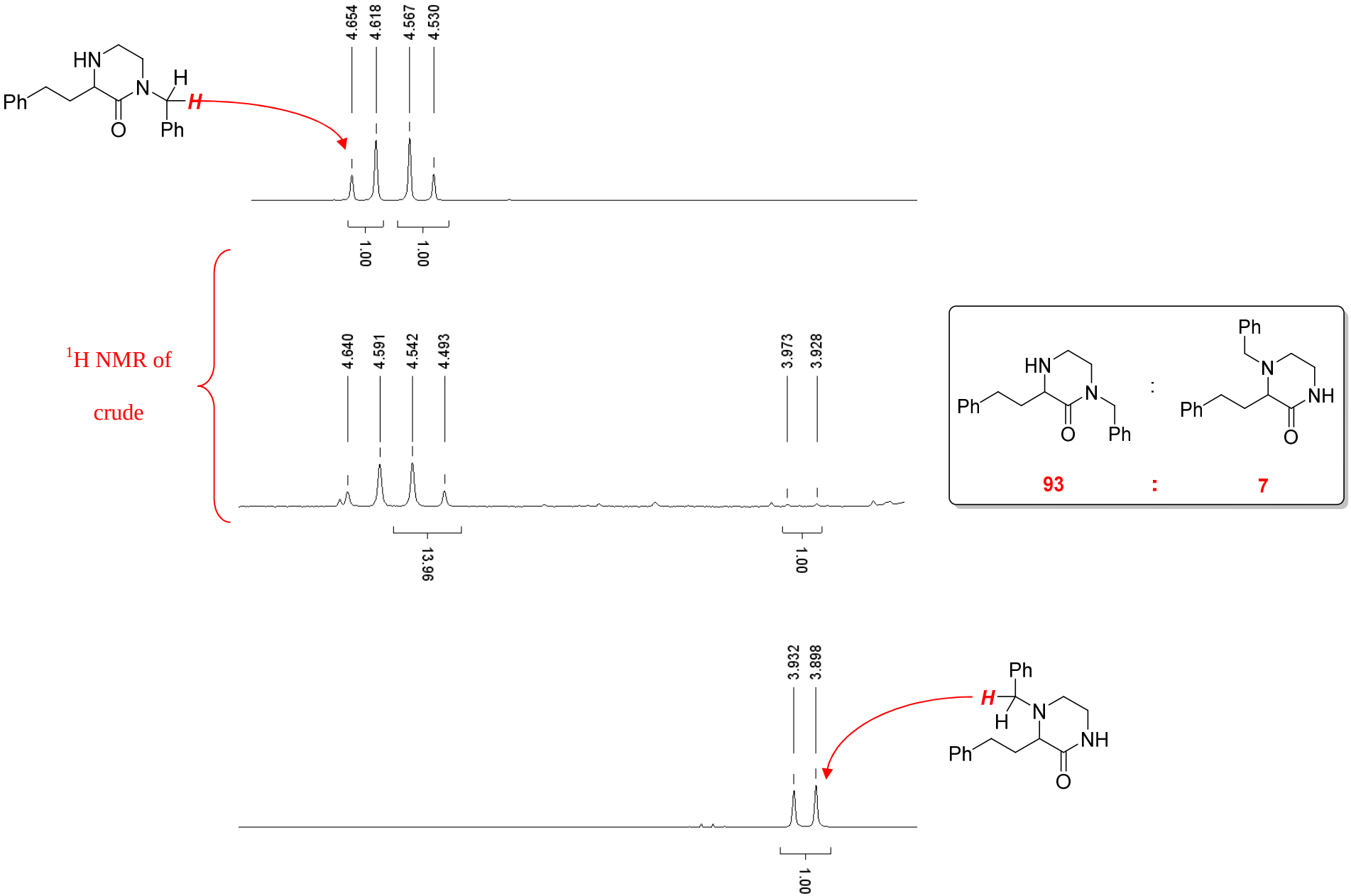
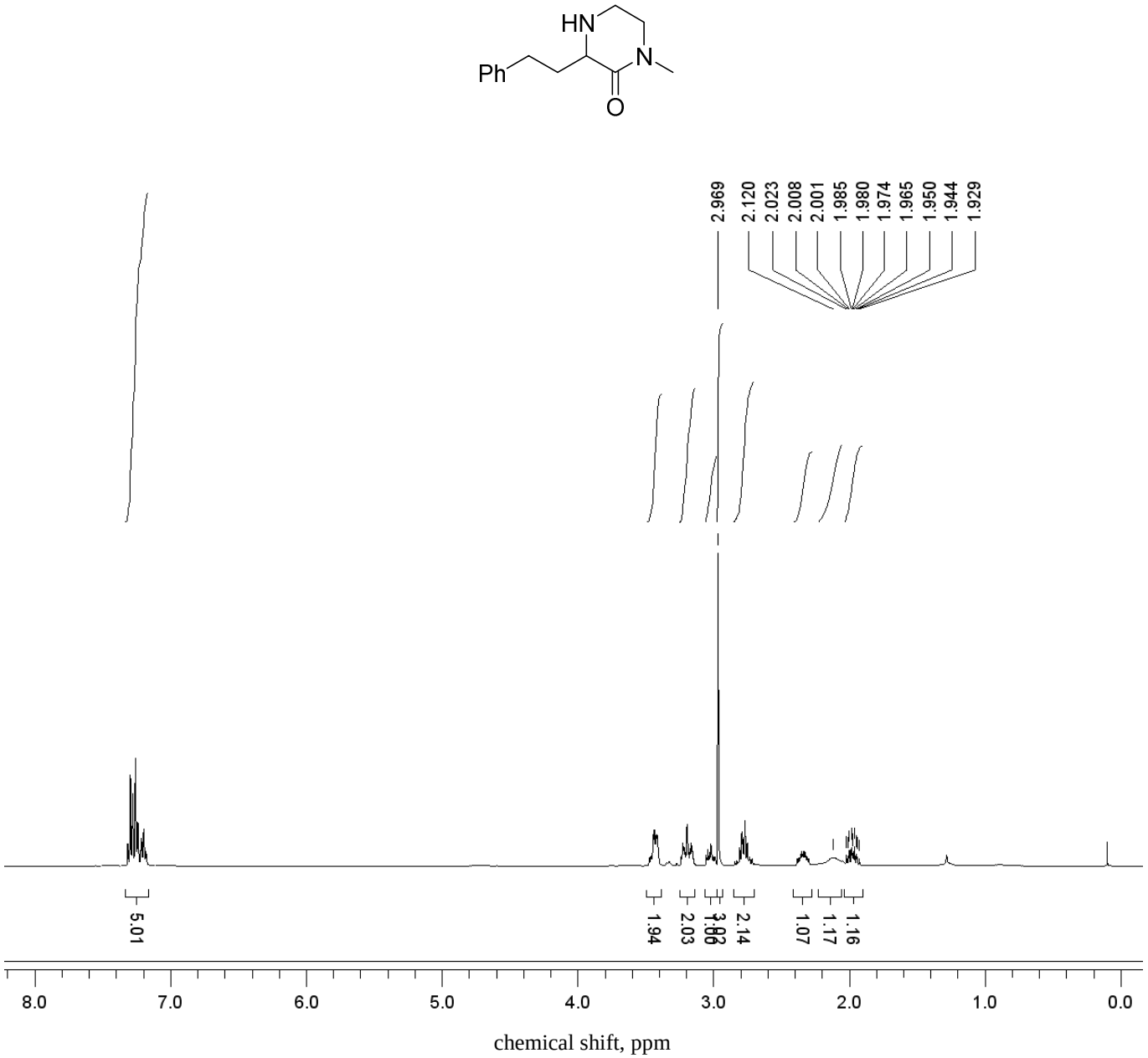
N
NH
Ph
O
172.447
142.159
138.100
128.766
128.529
128.442
128.270
127.322
125.716
64.139
58.172
45.039
39.917
32.027
31.365
200
150
100
50
0
chemical shift, ppm


4.654
4.618
4.567
4.530
1.00
1.00
HN
Ph
N
H
H
O
Ph
$^1$H NMR of
crude
4.640
4.591
4.542
4.493
3.973
3.928
13.96
1.00
HN
Ph
N
O
Ph
:
Ph
N
NH
Ph
O
93
:
7
3.932
3.898
1.00
Ph
H
H
N
NH
Ph
O


HN
N
Ph
O
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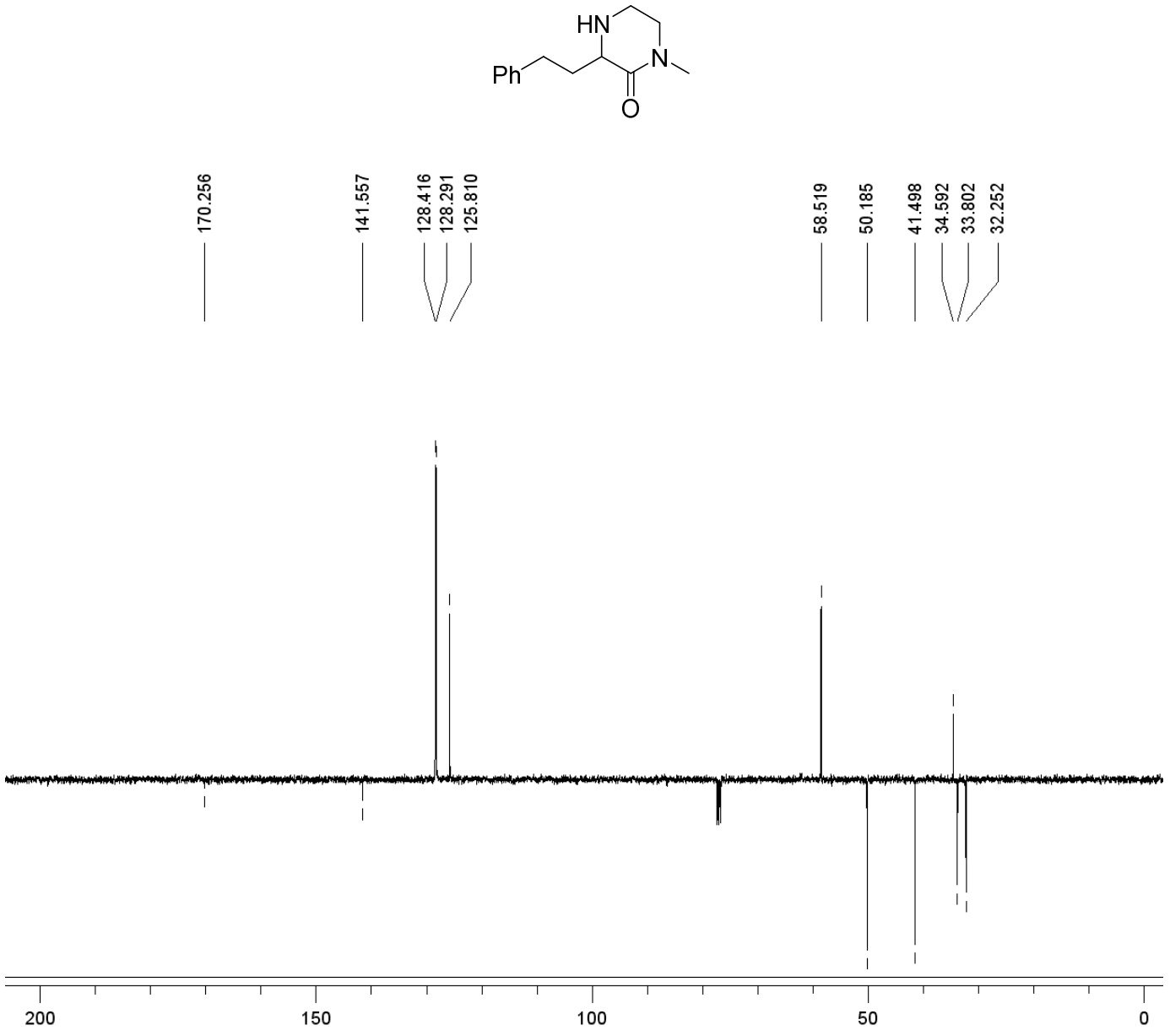
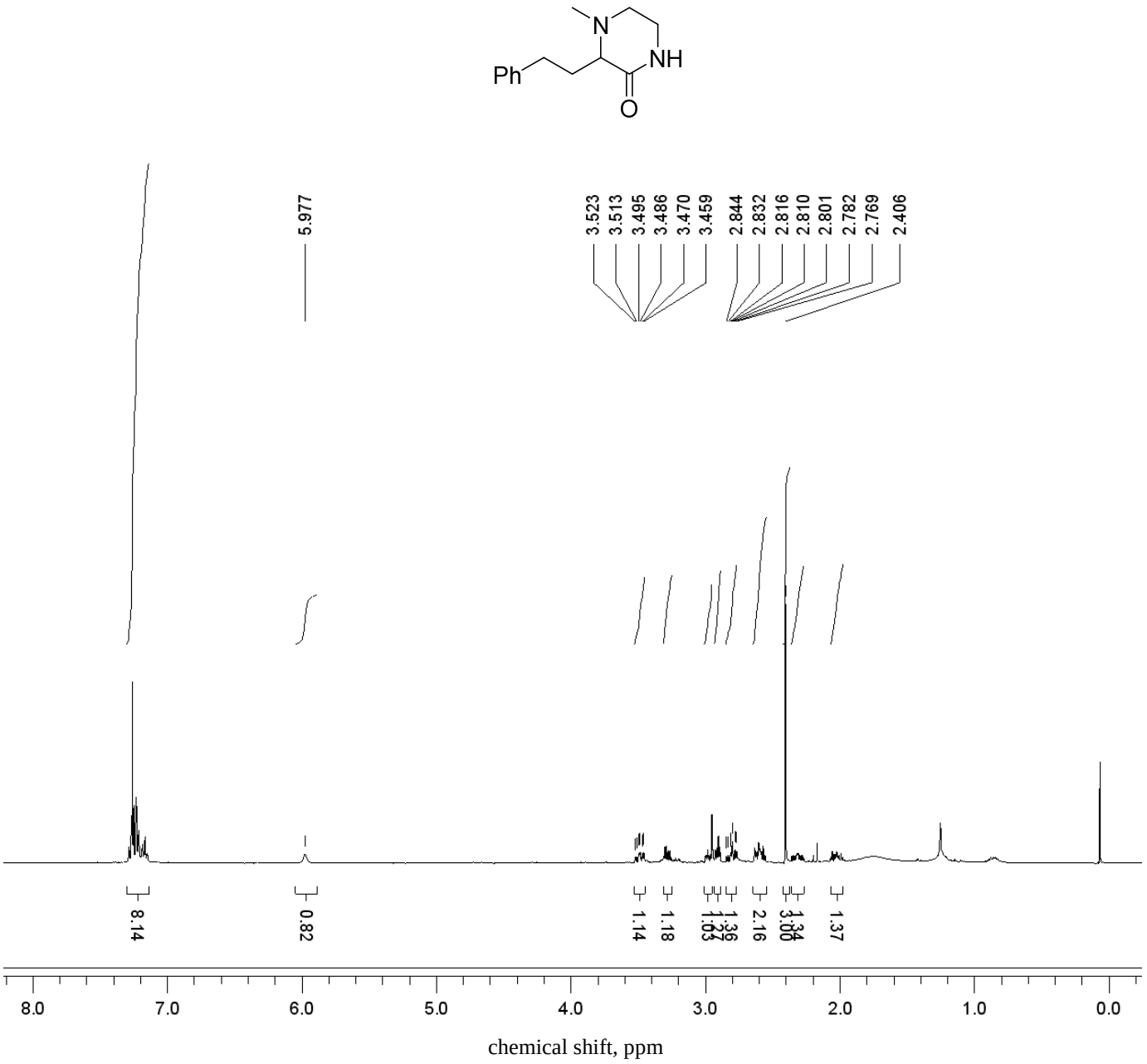
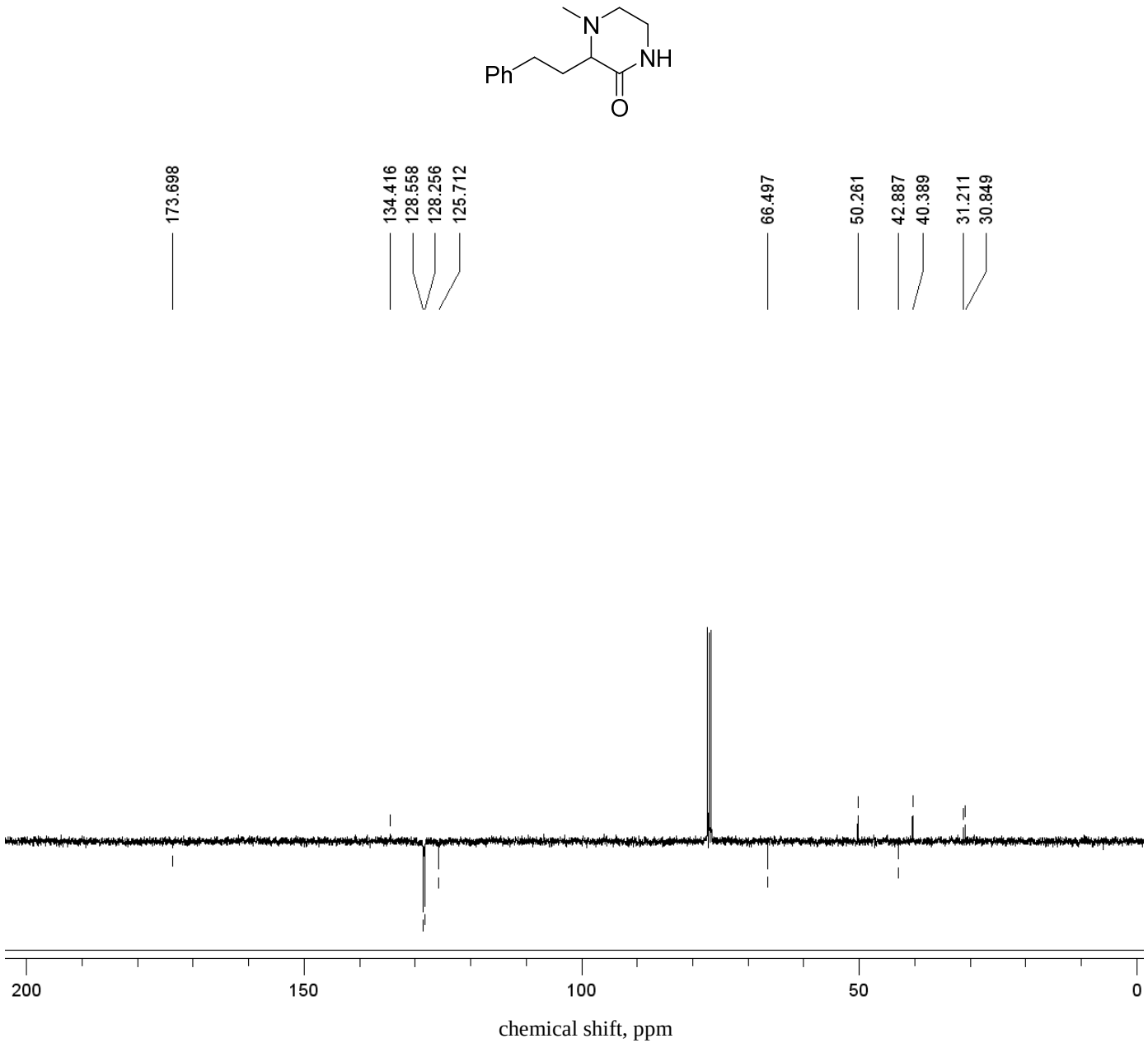
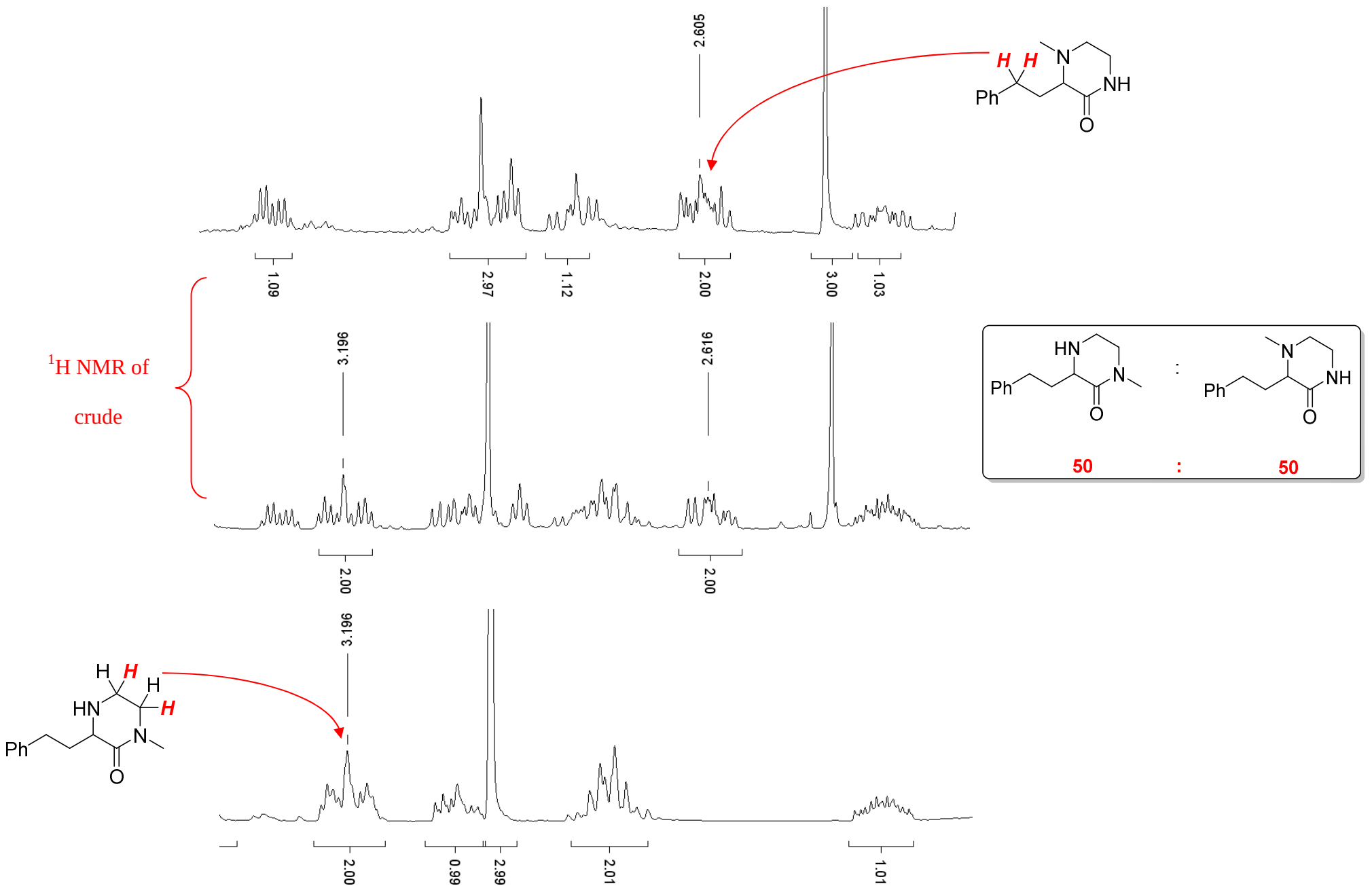
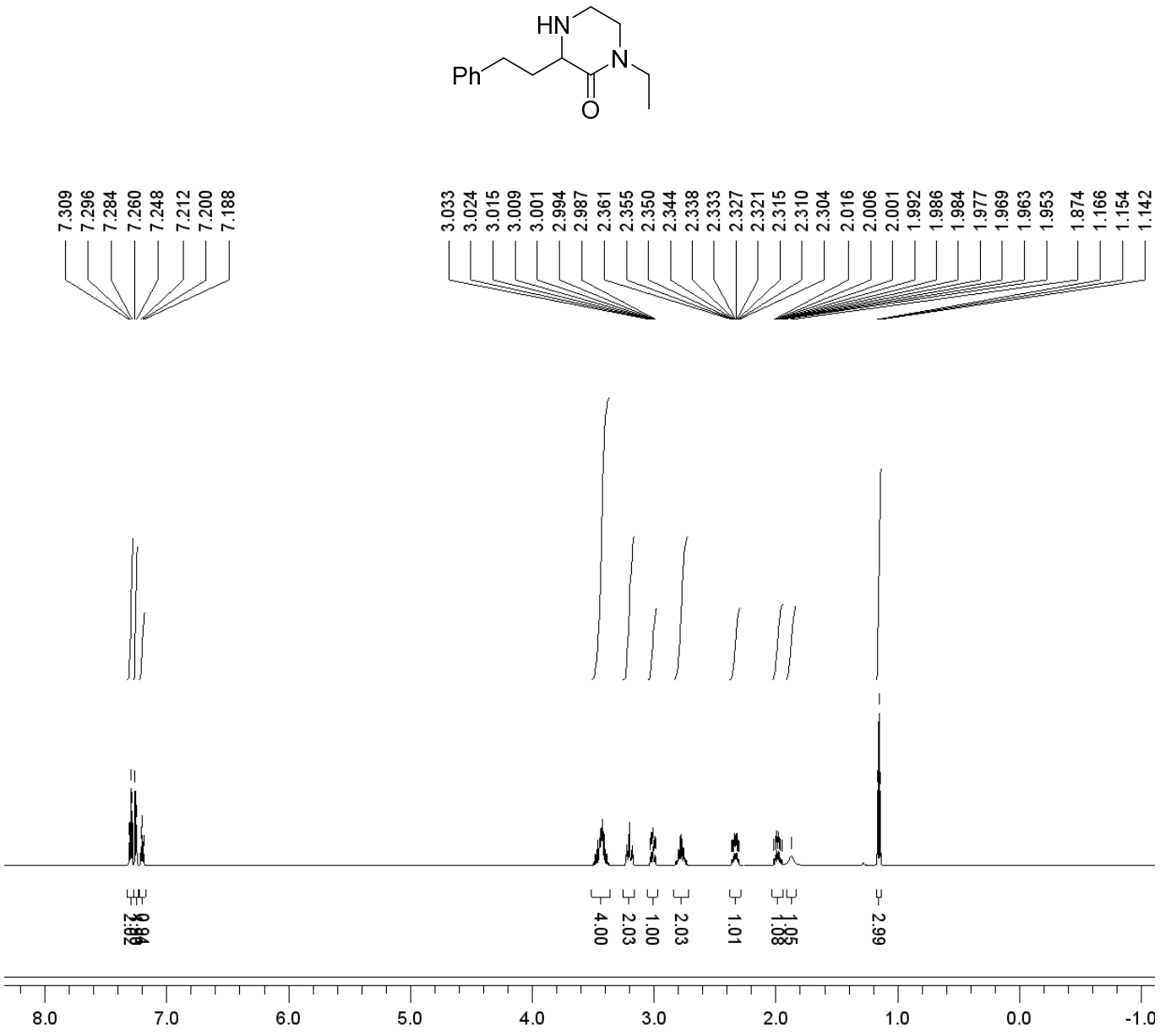
2.120
2.023
2.008
2.001
1.985
1.980
1.974
1.965
1.950
1.944
1.929
5.01
1.94
2.03
2.14
1.07
1.17
1.16
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

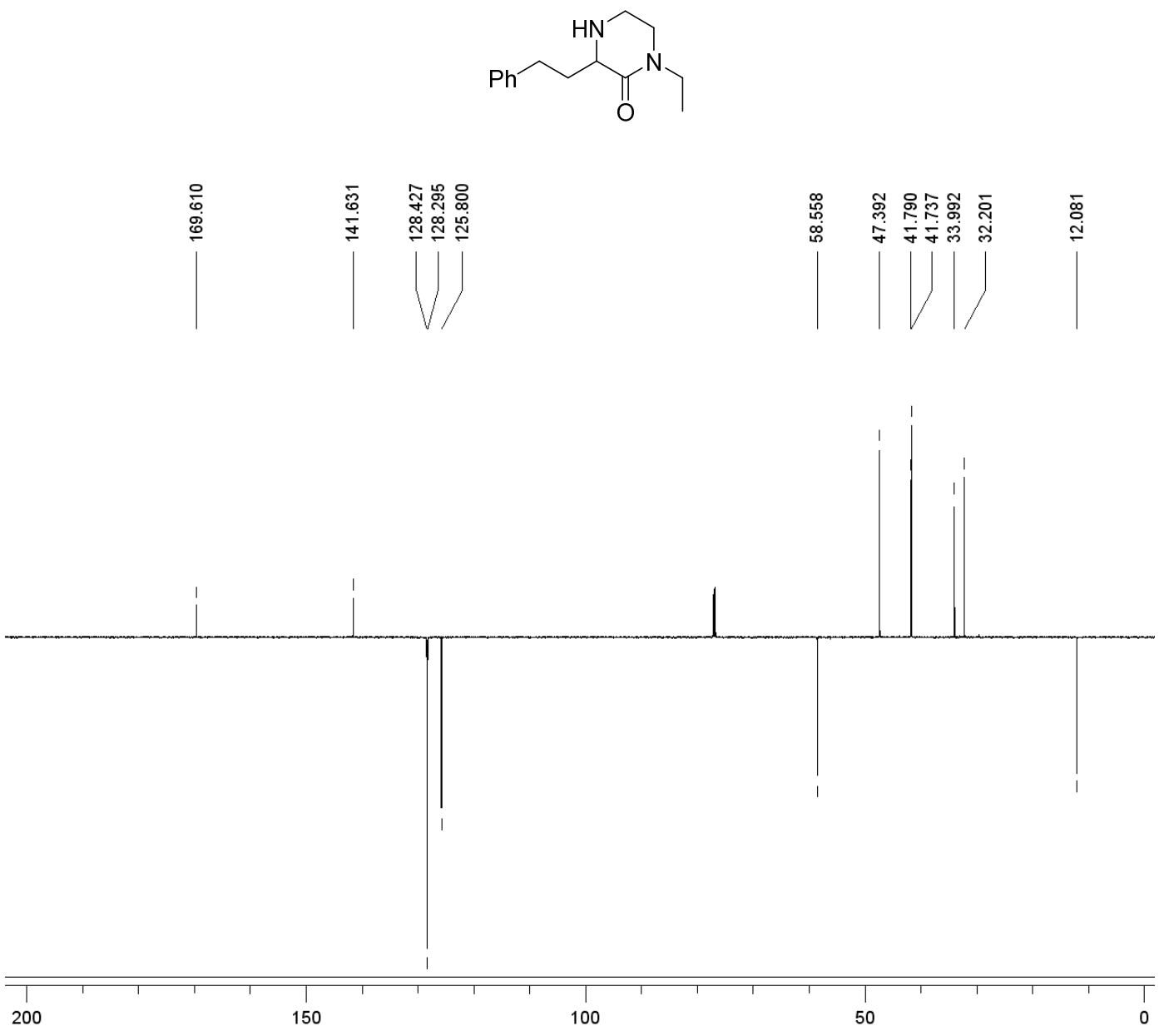

HN
N
Ph
O
170.256
141.557
128.416
128.291
125.810
58.519
50.185
41.498
34.592
33.802
32.252
200
150
100
50
0
chemical shift, ppm

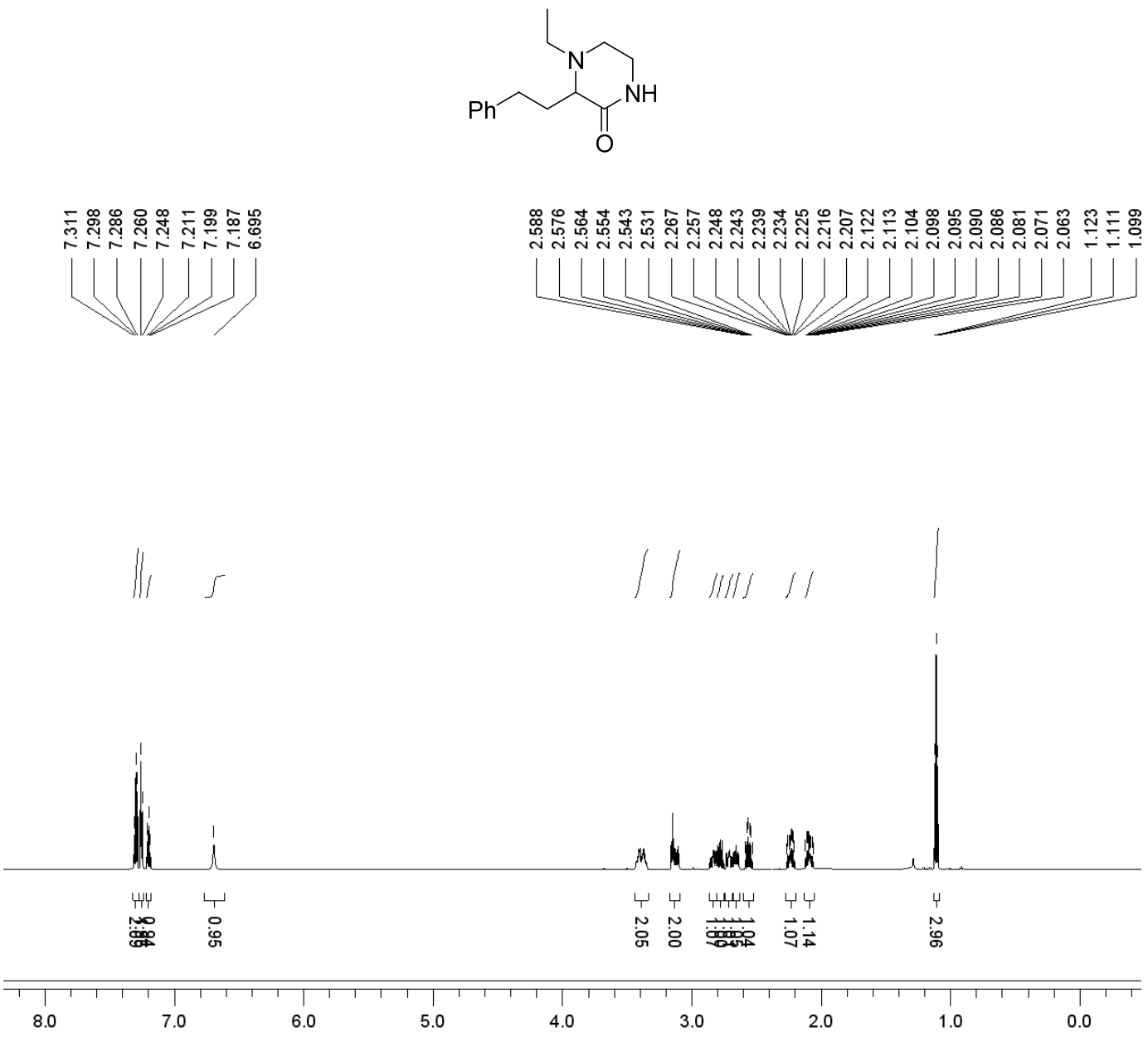

N
NH
Ph
O
5.977
3.523
3.513
3.495
3.486
3.470
3.459
2.844
2.832
2.816
2.810
2.801
2.782
2.769
2.406
8.14
0.82
1.14
1.18
1.03
1.36
2.16
3.00
3.34
1.37
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm


N
NH
Ph
O
173.698
134.416
128.558
128.256
125.712
66.497
50.261
42.887
40.389
31.211
30.849
200
150
100
50
0
chemical shift, ppm

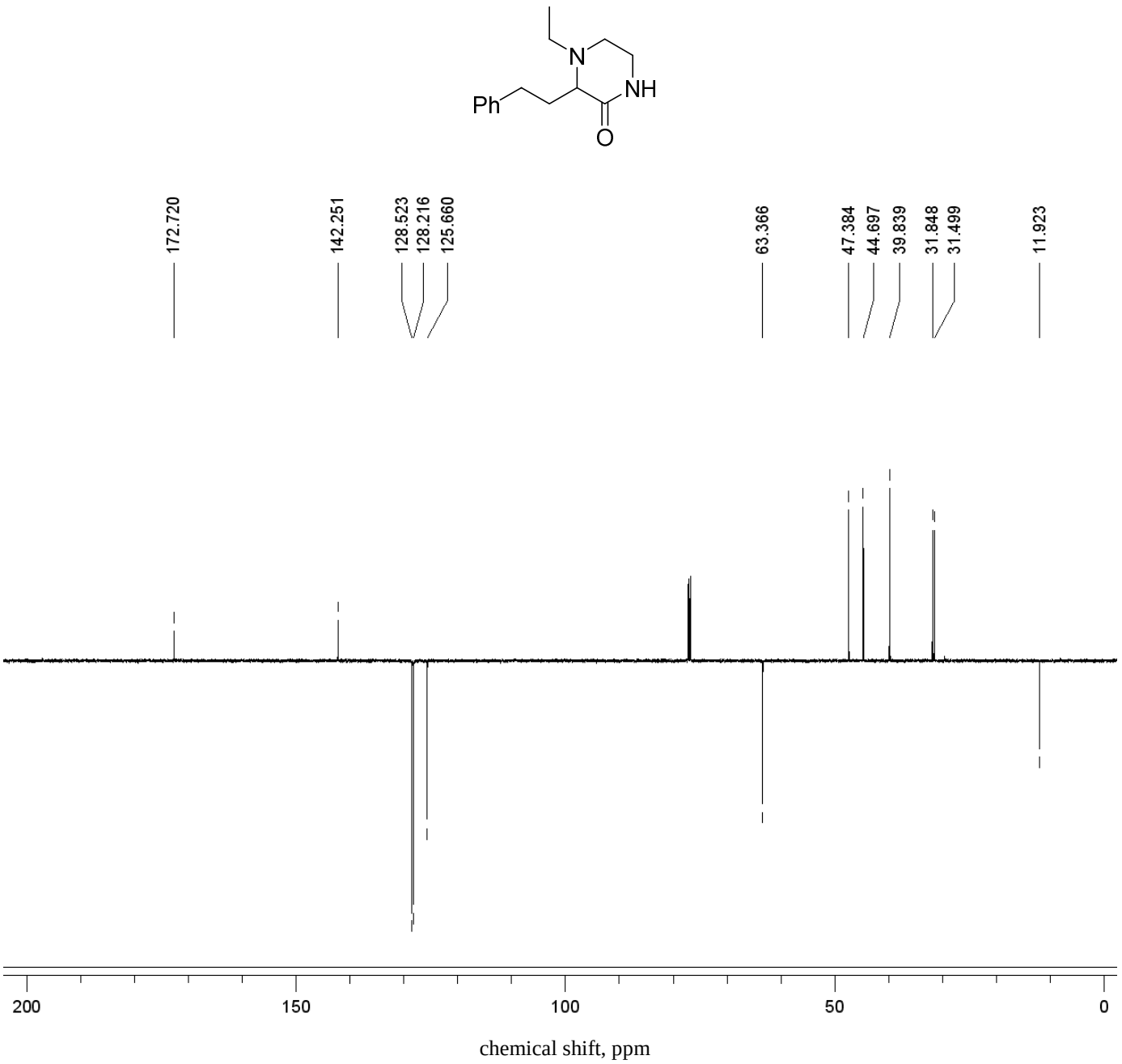

2.605
1.09
2.97
1.12
2.00
3.00
1.03
H H
N
NH
Ph
O
$^1$H NMR of
crude
3.166
2.616
2.00
2.00
HN
N
Ph
O
:
50
:
50
3.196
2.00
0.99
2.99
2.01
1.01
H H
H
HN
H
N
Ph
O

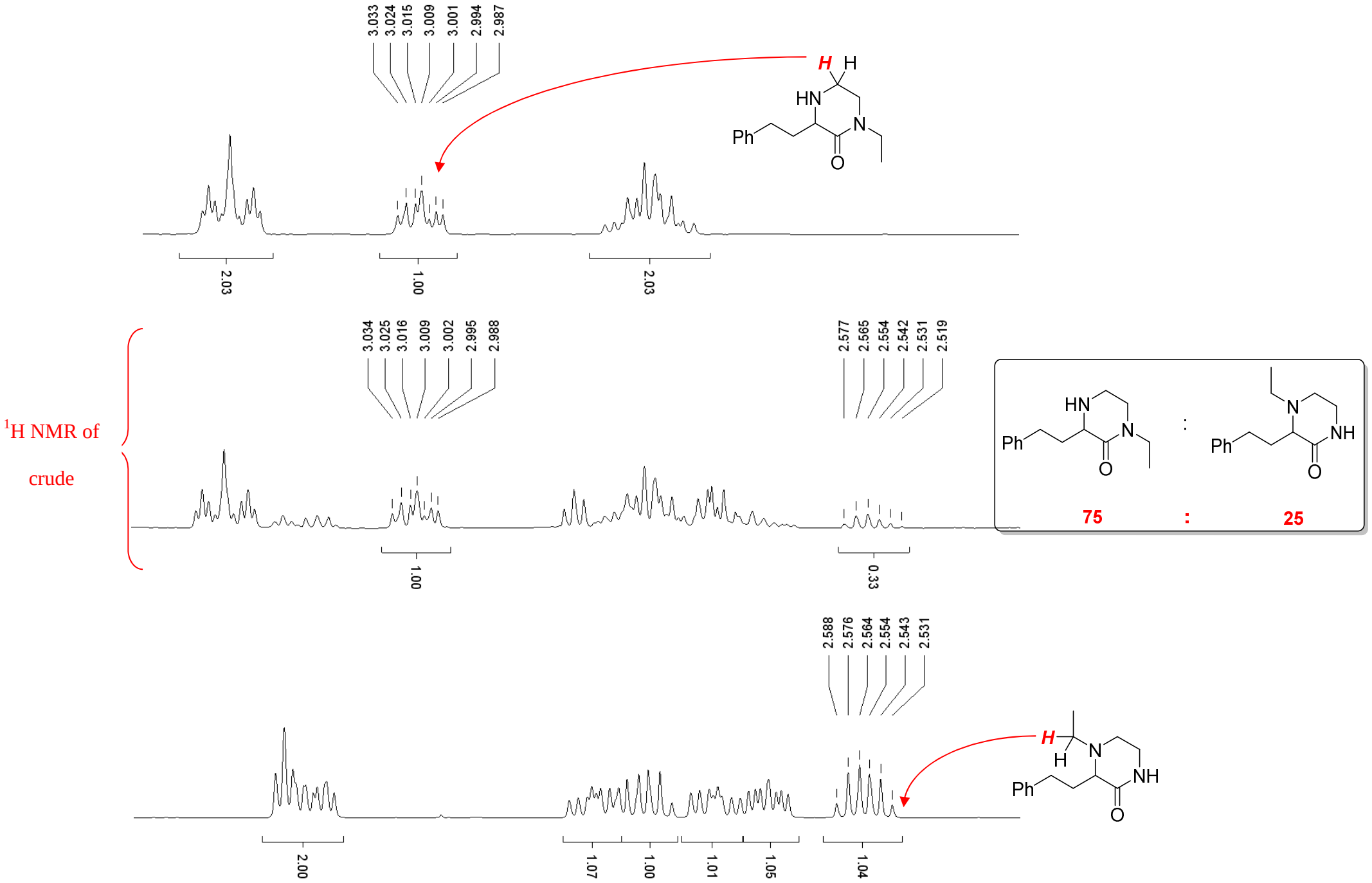

HN
N
Ph
O
7.309
7.296
7.284
7.260
7.248
7.212
7.200
7.188
3.033
3.024
3.015
3.009
3.001
2.994
2.987
2.361
2.355
2.350
2.344
2.338
2.333
2.327
2.321
2.315
2.310
2.304
2.016
2.006
2.001
1.992
1.986
1.984
1.977
1.969
1.963
1.953
1.874
1.166
1.154
1.142
4.00
2.03
1.00
2.03
1.01
2.99
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
chemical shift, ppm

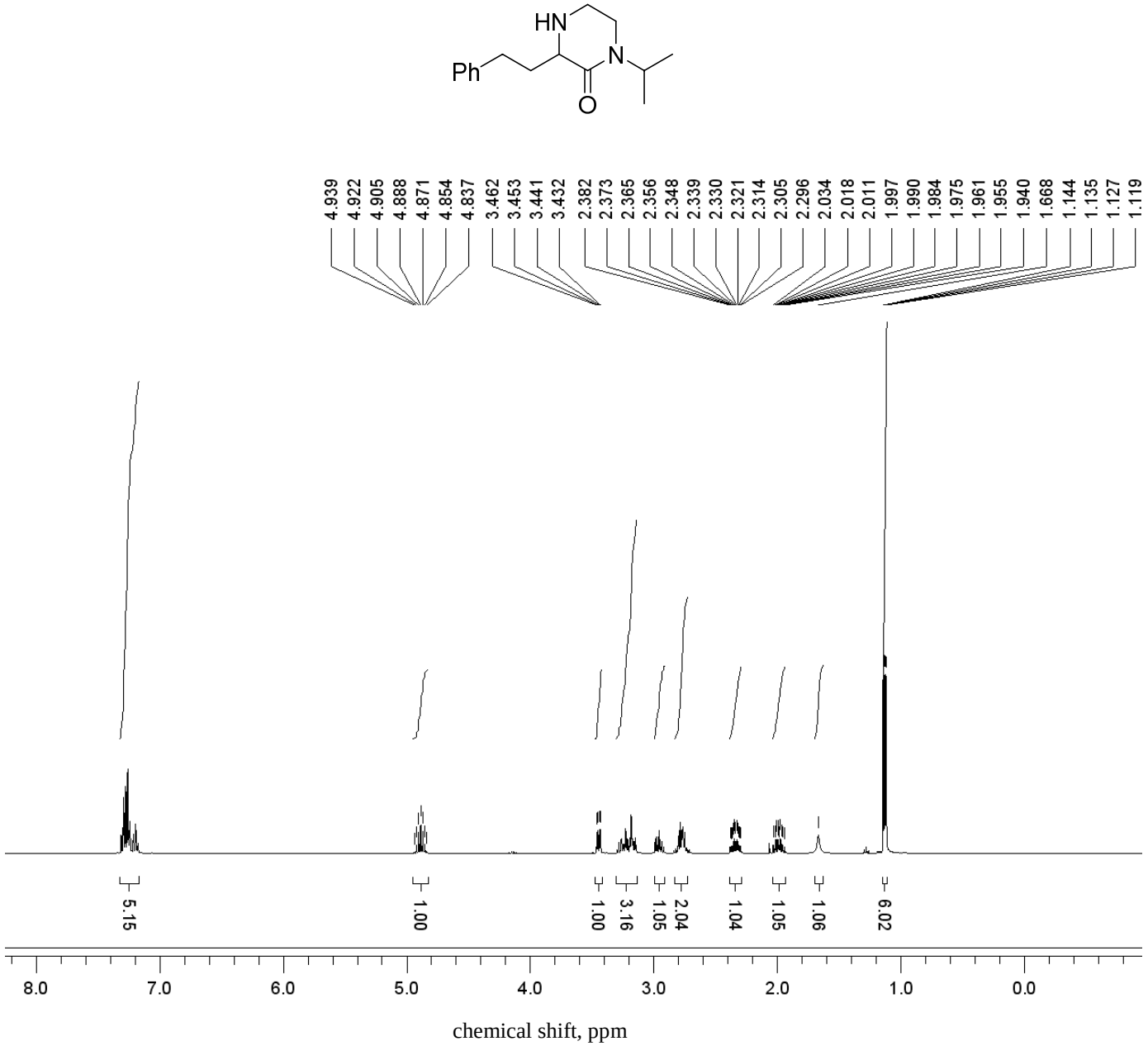

HN
N
Ph
O
169.610
141.631
128.427
128.295
125.800
58.558
47.392
41.790
41.737
33.992
32.201
12.081
200
150
100
50
0
chemical shift, ppm

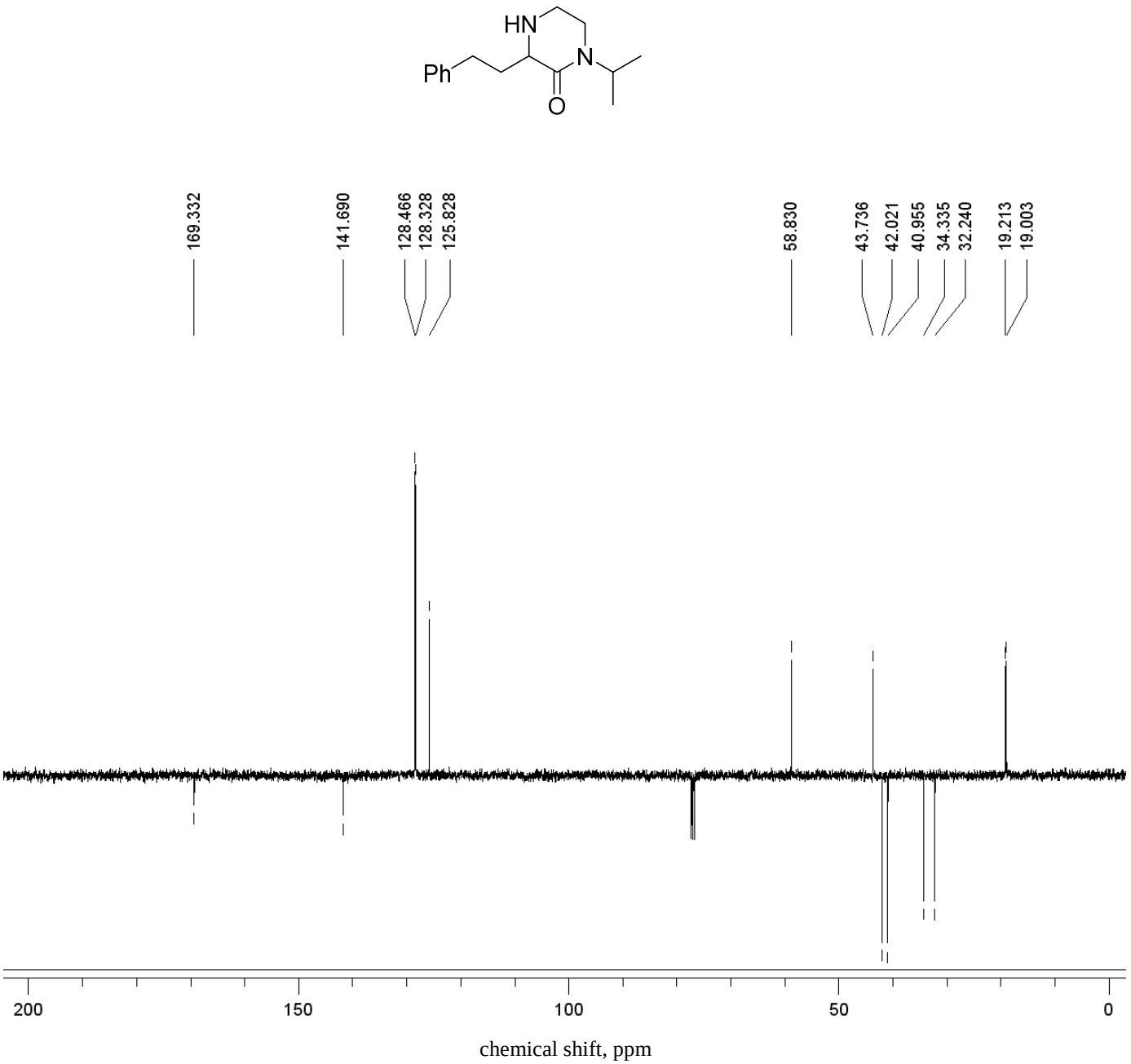


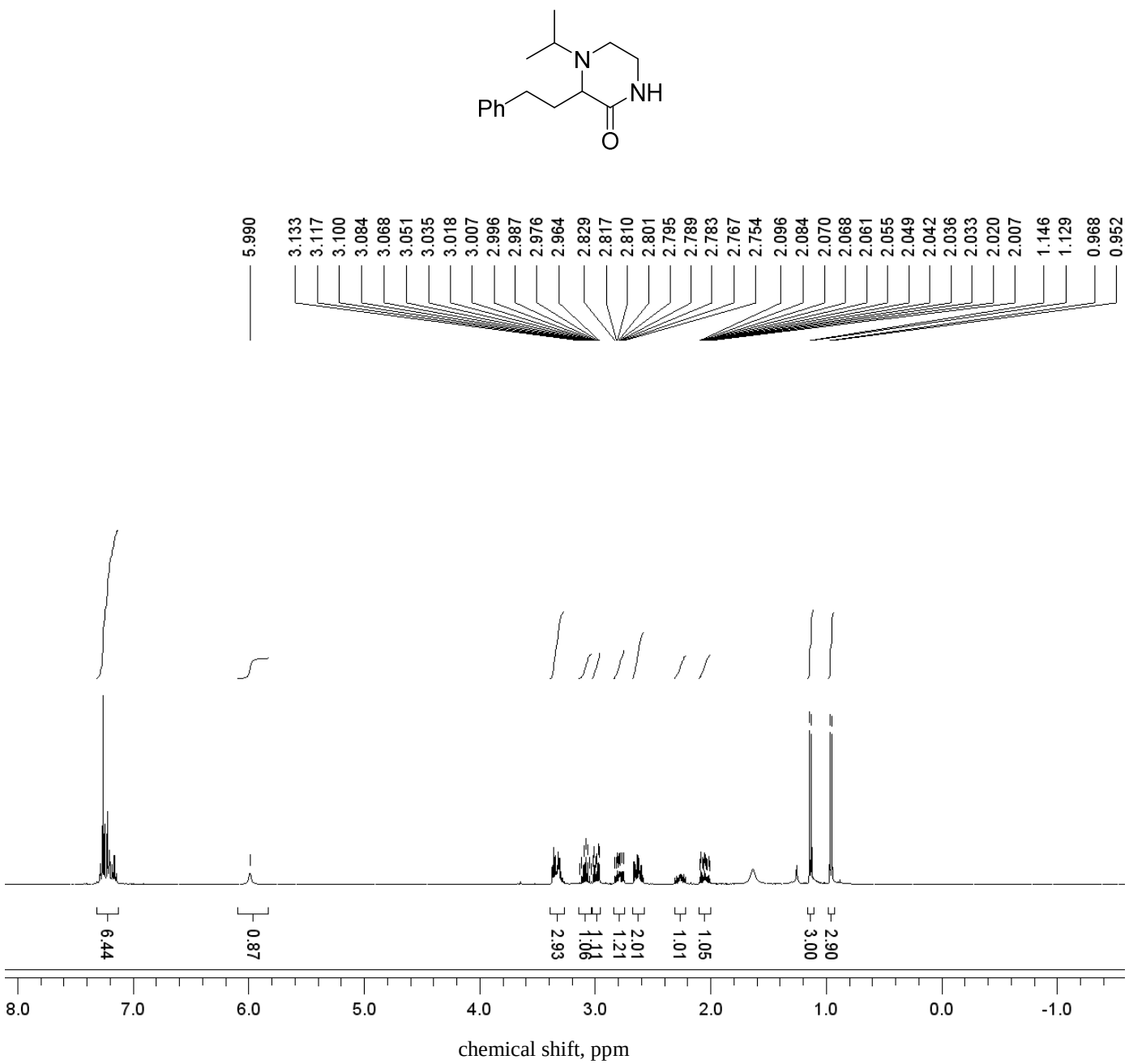

chemical shift, ppm

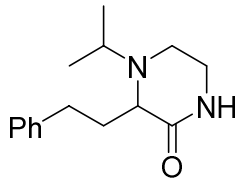

N
NH
Ph
O
172.720
142.251
128.523
128.216
125.660
63.366
47.384
44.697
39.839
31.848
31.499
11.923
200
150
100
50
0
chemical shift, ppm

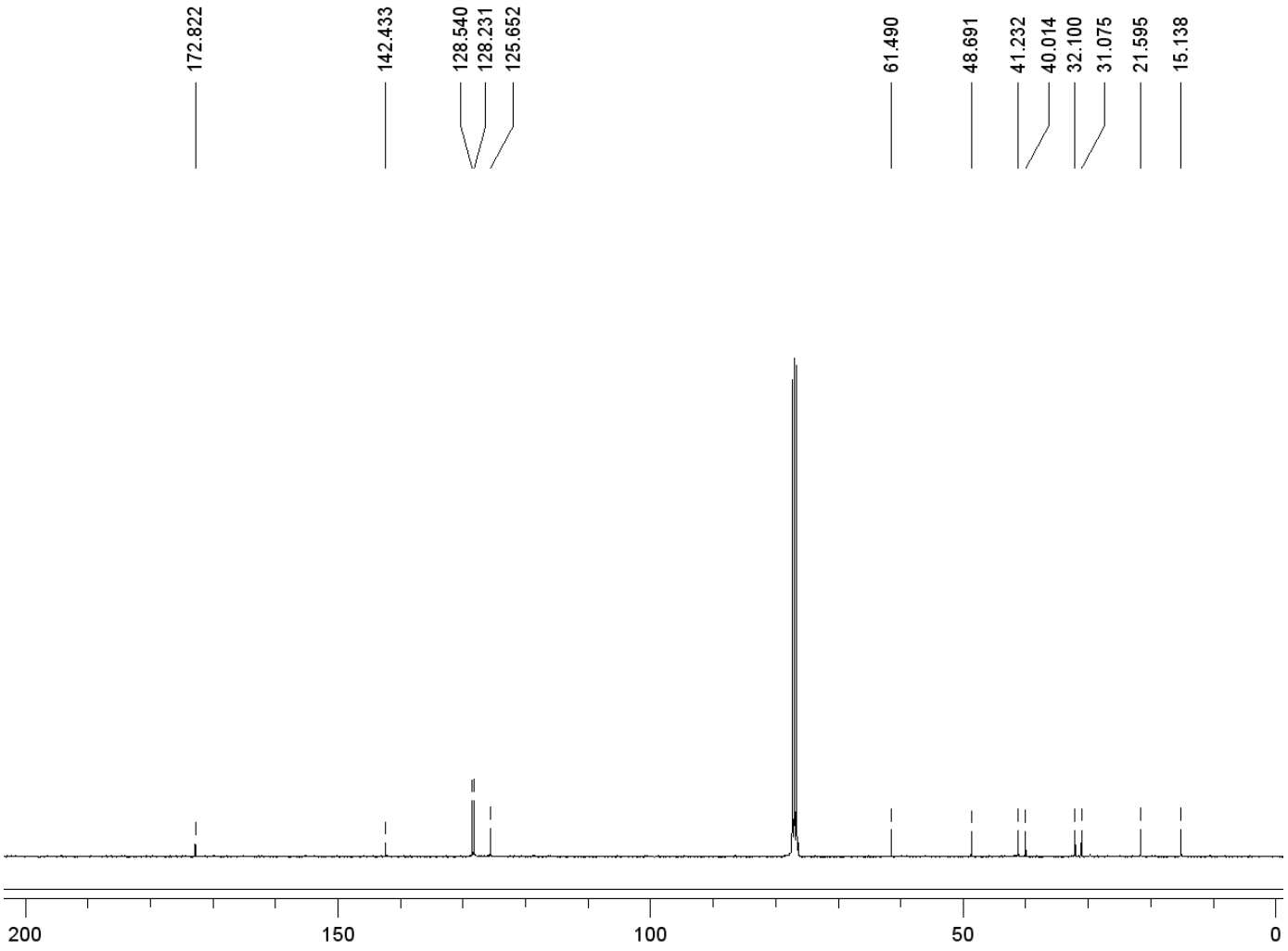

3.033
3.024
3.015
3.009
3.001
2.994
2.987
H
H
HN
N
Ph
O
2.03
1.00
2.03
$^1$H NMR of
crude
3.034
3.025
3.016
3.009
3.002
2.995
2.988
2.577
2.565
2.554
2.542
2.531
2.519
HN
N
Ph
O
:
N
NH
Ph
O
75
:
25
1.00
0.33
2.588
2.576
2.564
2.554
2.543
2.531
H
H
N
NH
Ph
O
2.00
1.07
1.00
1.01
1.05
1.04

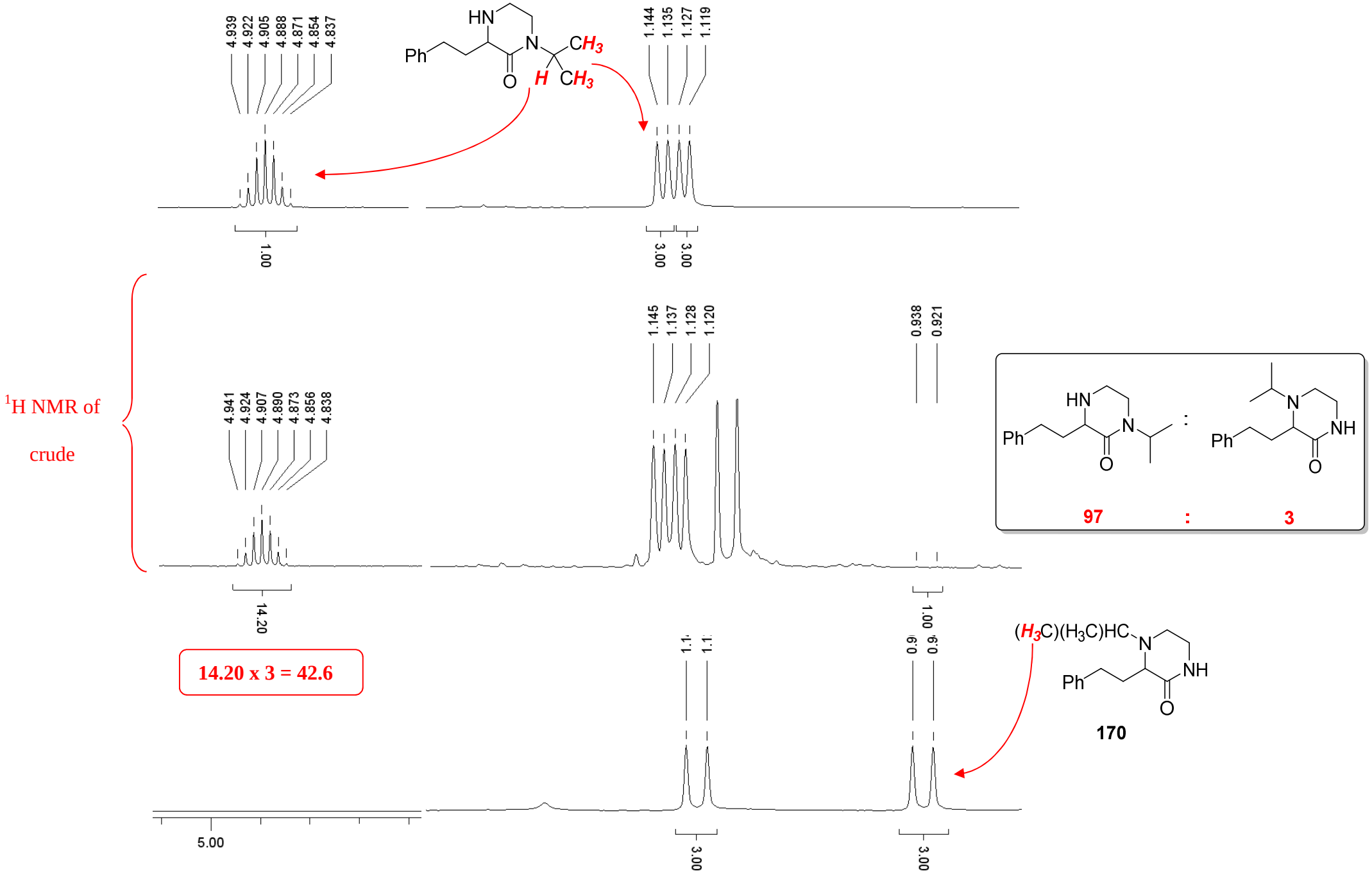

HN
N
Ph
O
4.939
4.922
4.905
4.888
4.871
4.854
4.837
3.462
3.453
3.441
3.432
2.382
2.373
2.365
2.356
2.348
2.339
2.330
2.321
2.314
2.305
2.296
2.034
2.018
2.011
1.997
1.990
1.984
1.975
1.961
1.955
1.940
1.668
1.144
1.135
1.127
1.119
5.15
1.00
1.00
3.16
1.05
2.04
1.04
1.05
1.06
6.02
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

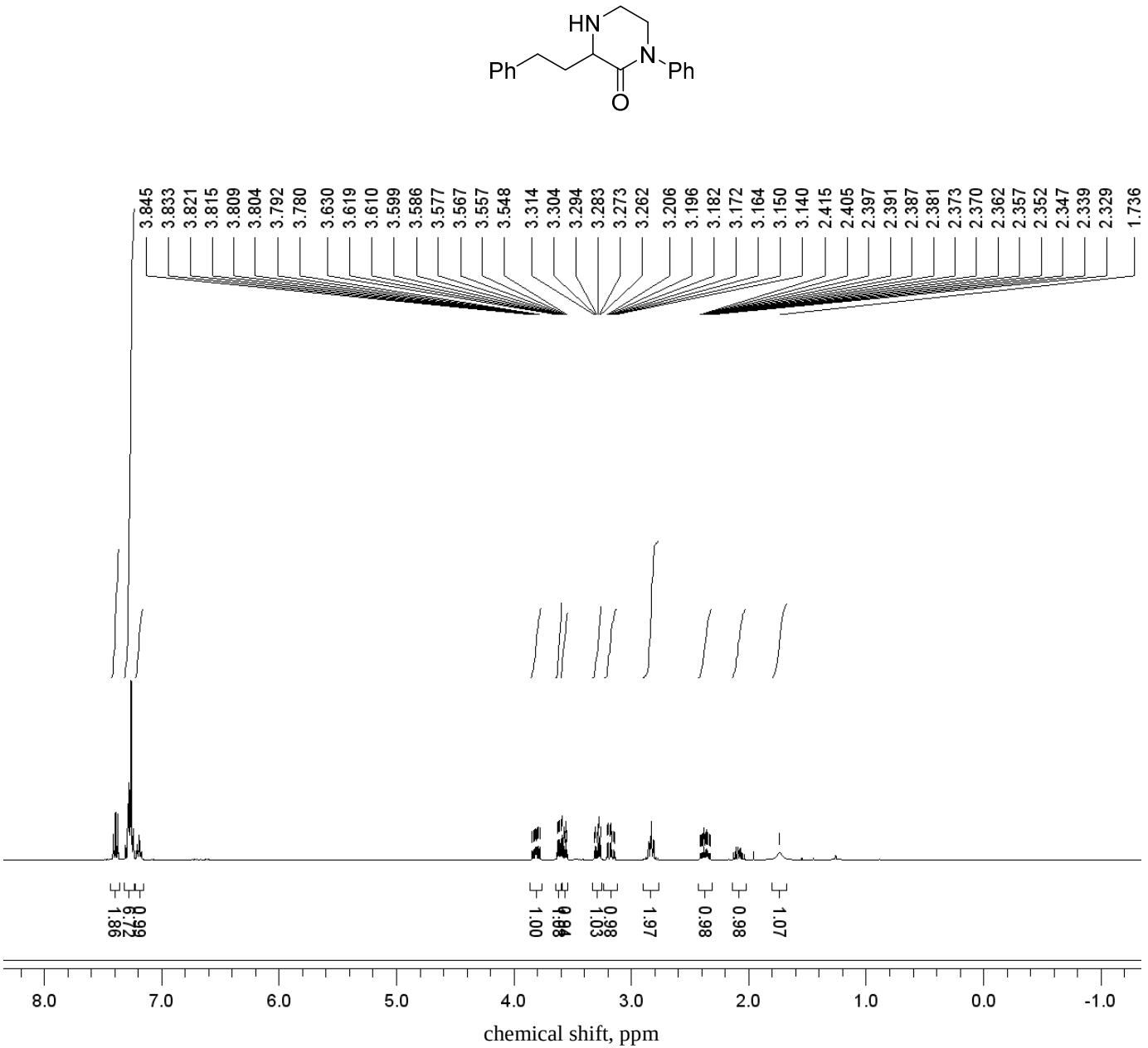

HN
N
Ph
O
169.332
141.690
128.466
128.328
125.828
58.830
43.736
42.021
40.955
34.335
32.240
19.213
19.003
200
150
100
50
0
chemical shift, ppm

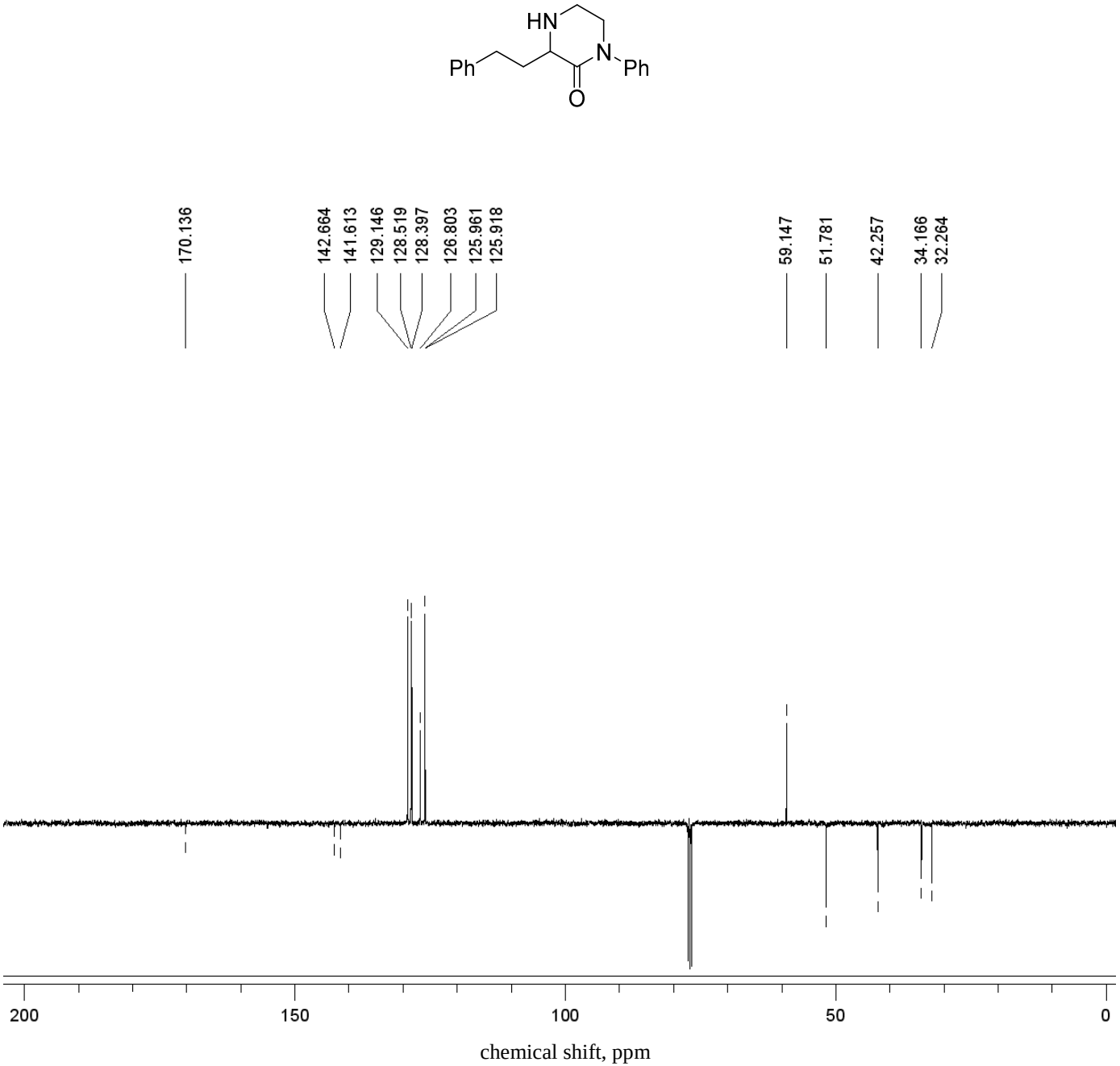

N
NH
Ph
O
5.990
3.133
3.117
3.100
3.084
3.068
3.051
3.035
3.018
3.007
2.996
2.987
2.976
2.964
2.829
2.817
2.810
2.801
2.795
2.789
2.783
2.767
2.754
2.096
2.084
2.070
2.068
2.061
2.055
2.049
2.042
2.036
2.033
2.020
2.007
1.146
1.129
0.968
0.952
6.44
0.87
2.93
1.06
1.11
1.21
2.01
1.01
1.05
3.00
2.90
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
chemical shift, ppm

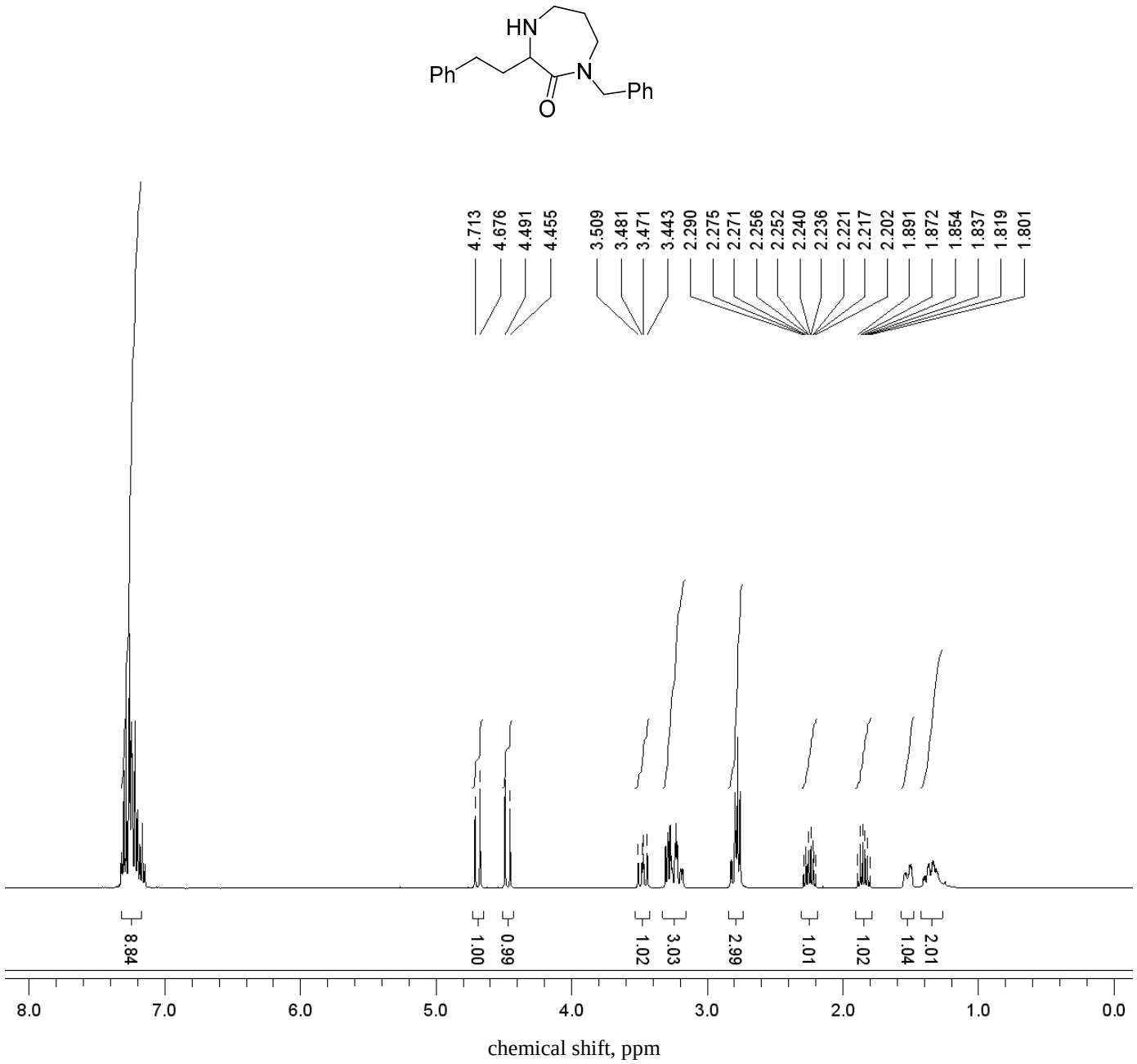

N
NH
Ph
O

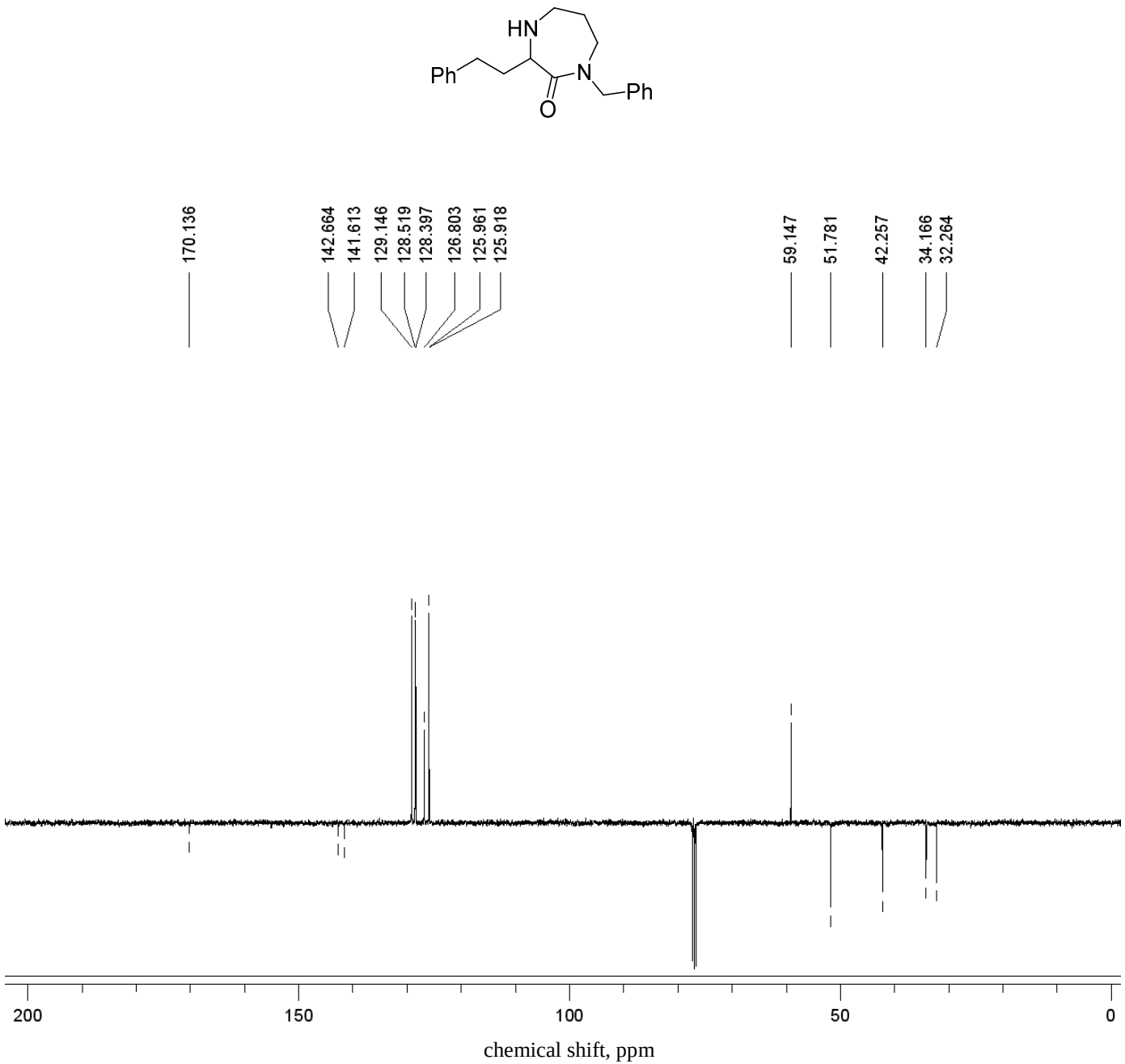

172.822
142.433
128.540
128.231
125.652
61.490
48.691
41.232
40.014
32.100
31.075
21.595
15.138
200
150
100
50
0
chemical shift, ppm

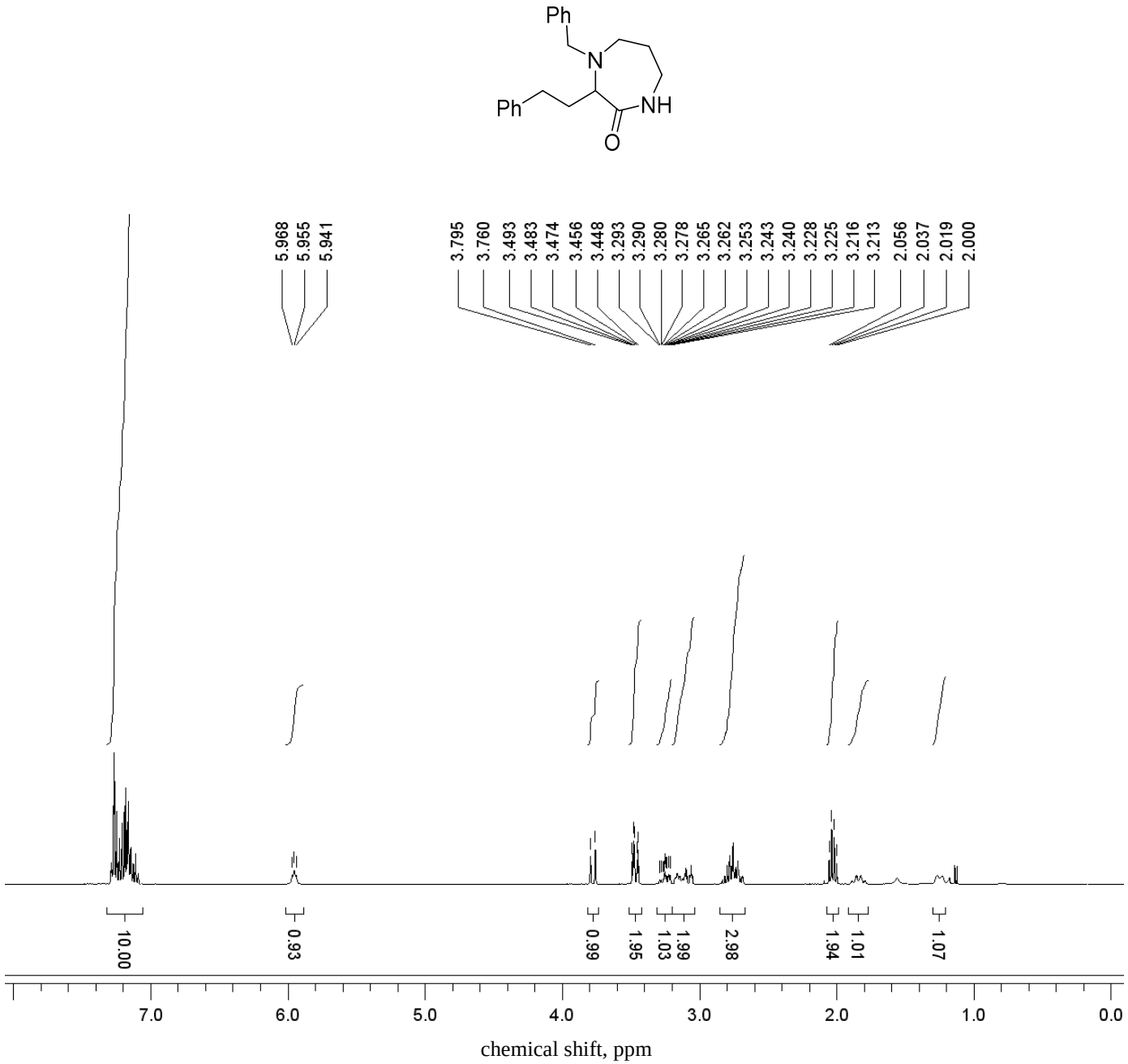

4.939
4.922
4.905
4.888
4.871
4.854
4.837
HN
Ph
N
O
CH3
H
CH3
1.144
1.135
1.127
1.119
1.00
3.00
3.00
1H NMR of
crude
4.941
4.924
4.907
4.890
4.873
4.856
4.838
1.145
1.137
1.128
1.120
0.938
0.921
14.20
1.00
HN
Ph
N
O
:
N
Ph
NH
O
97
:
3
14.20 x 3 = 42.6
(H3C)(H3C)HC
N
Ph
NH
O
170
5.00
3.00
3.00

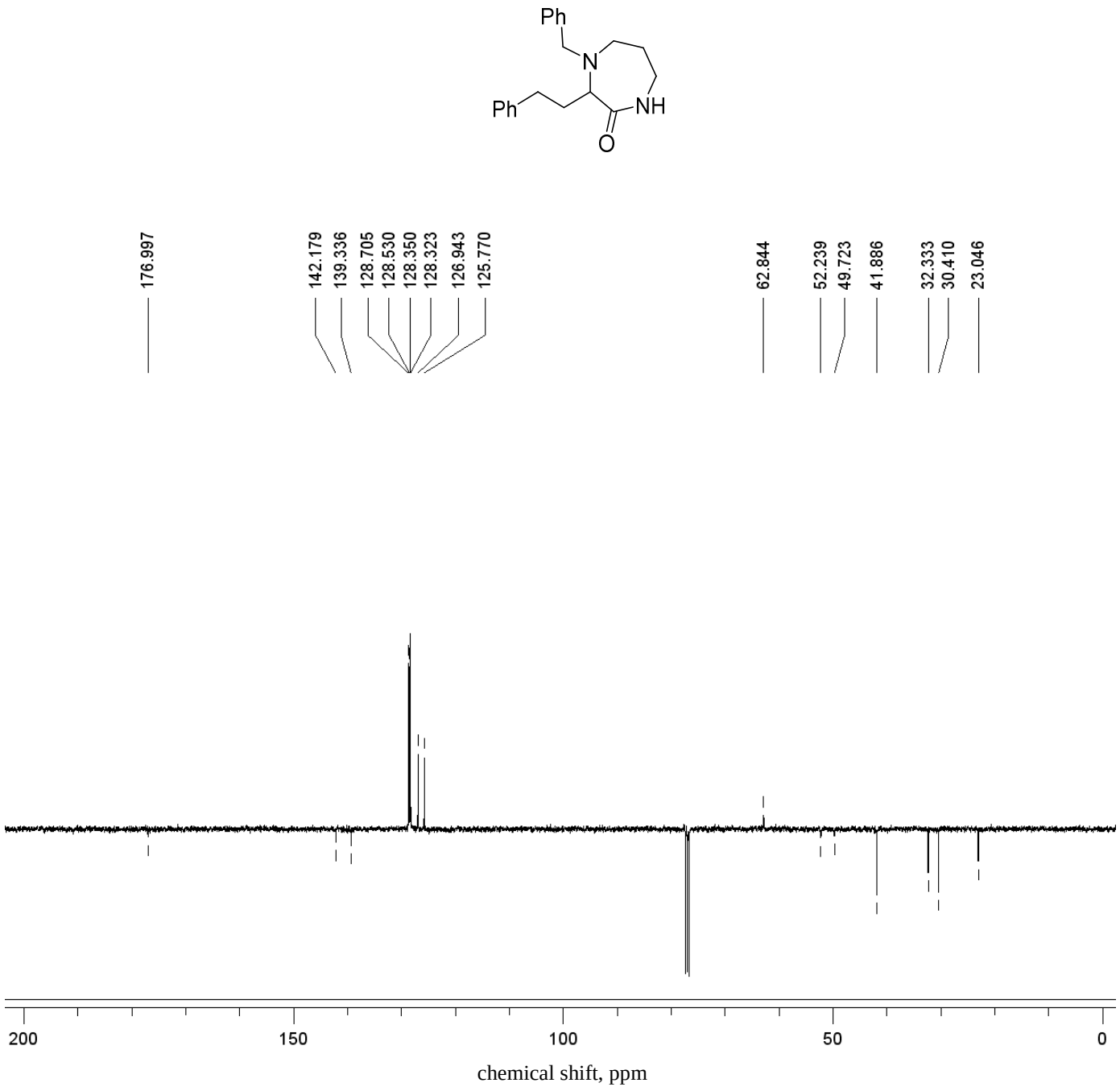

HN
N
Ph
Ph
O
3.845
3.833
3.821
3.815
3.809
3.804
3.792
3.780
3.630
3.619
3.610
3.599
3.586
3.577
3.567
3.557
3.548
3.314
3.304
3.294
3.283
3.273
3.262
3.206
3.196
3.182
3.172
3.164
3.150
3.140
2.415
2.405
2.397
2.391
2.387
2.381
2.373
2.370
2.362
2.357
2.352
2.347
2.339
2.329
1.736
1.86
2.74
0.99
1.00
0.88
0.98
1.03
0.88
1.97
0.98
0.98
1.07
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
chemical shift, ppm

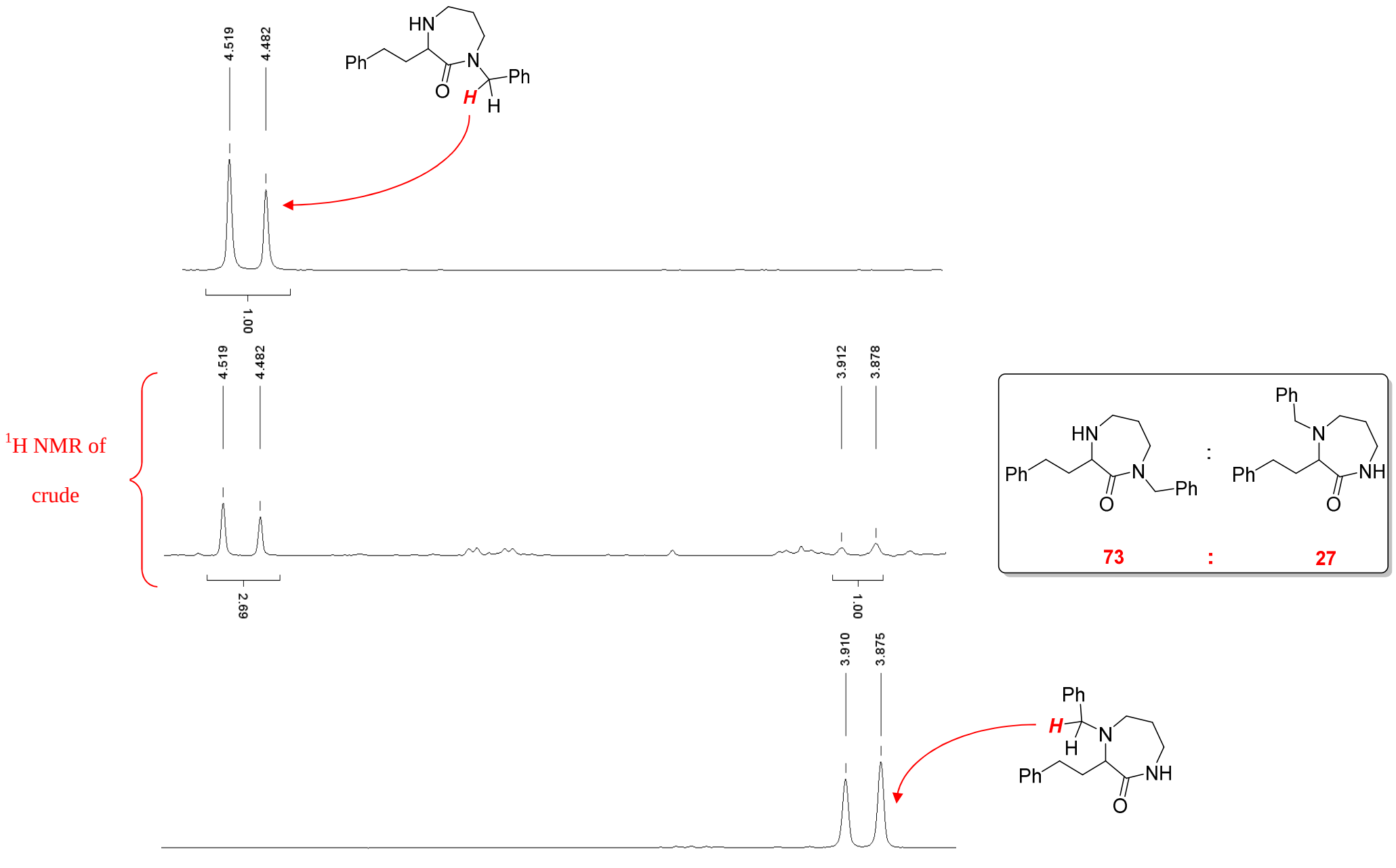

HN
N
Ph
Ph
O
170.136
142.664
141.613
129.146
128.519
128.397
126.803
125.961
125.918
59.147
51.781
42.257
34.166
32.264
200
150
100
50
0
chemical shift, ppm

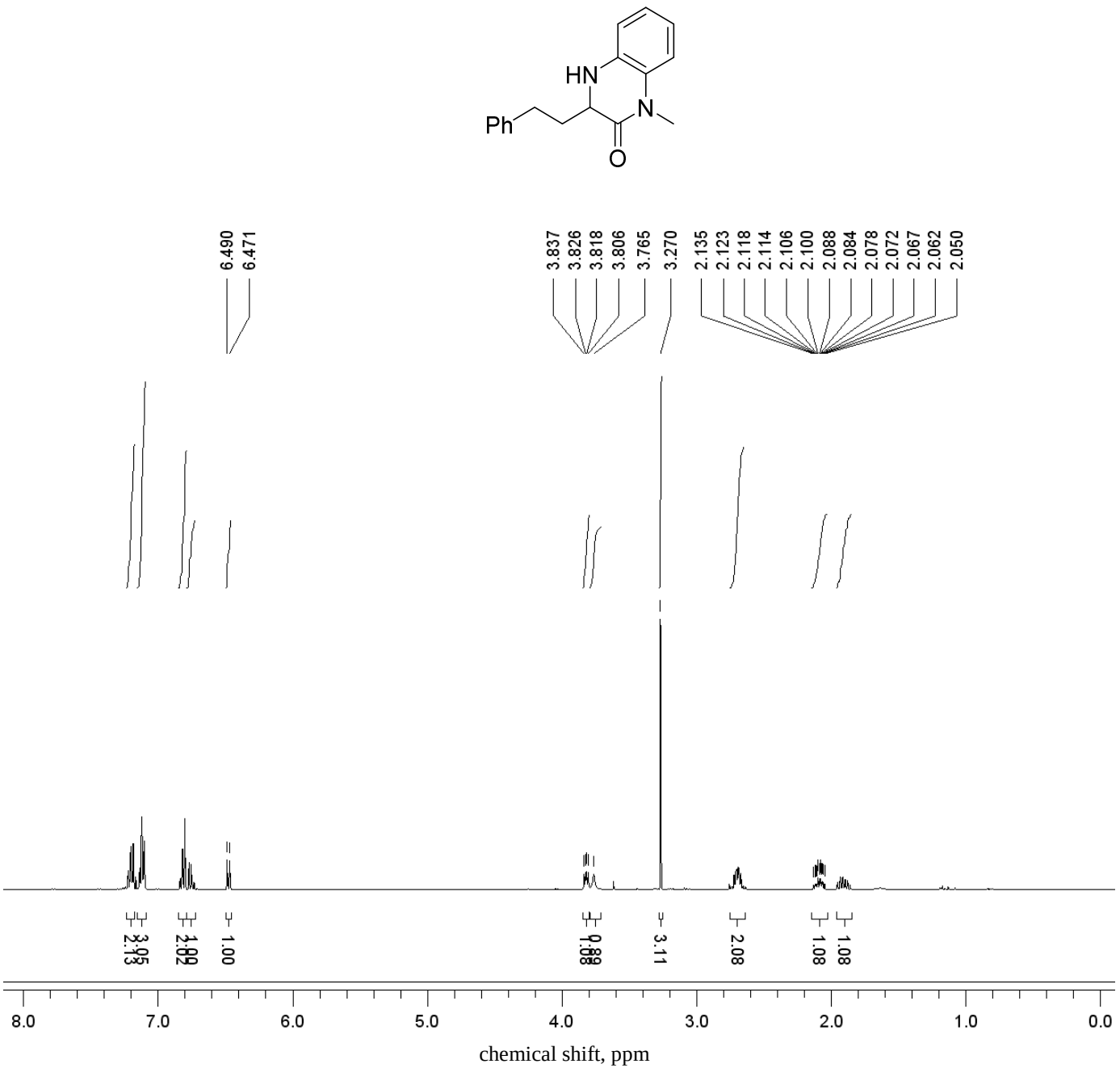

HN
Ph
N
Ph
O
4.713
4.676
4.491
4.455
3.509
3.481
3.471
3.443
2.290
2.275
2.271
2.256
2.252
2.240
2.236
2.221
2.217
2.202
1.891
1.872
1.854
1.837
1.819
1.801
8.84
1.00
0.99
1.02
3.03
2.99
1.01
1.02
1.04
2.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

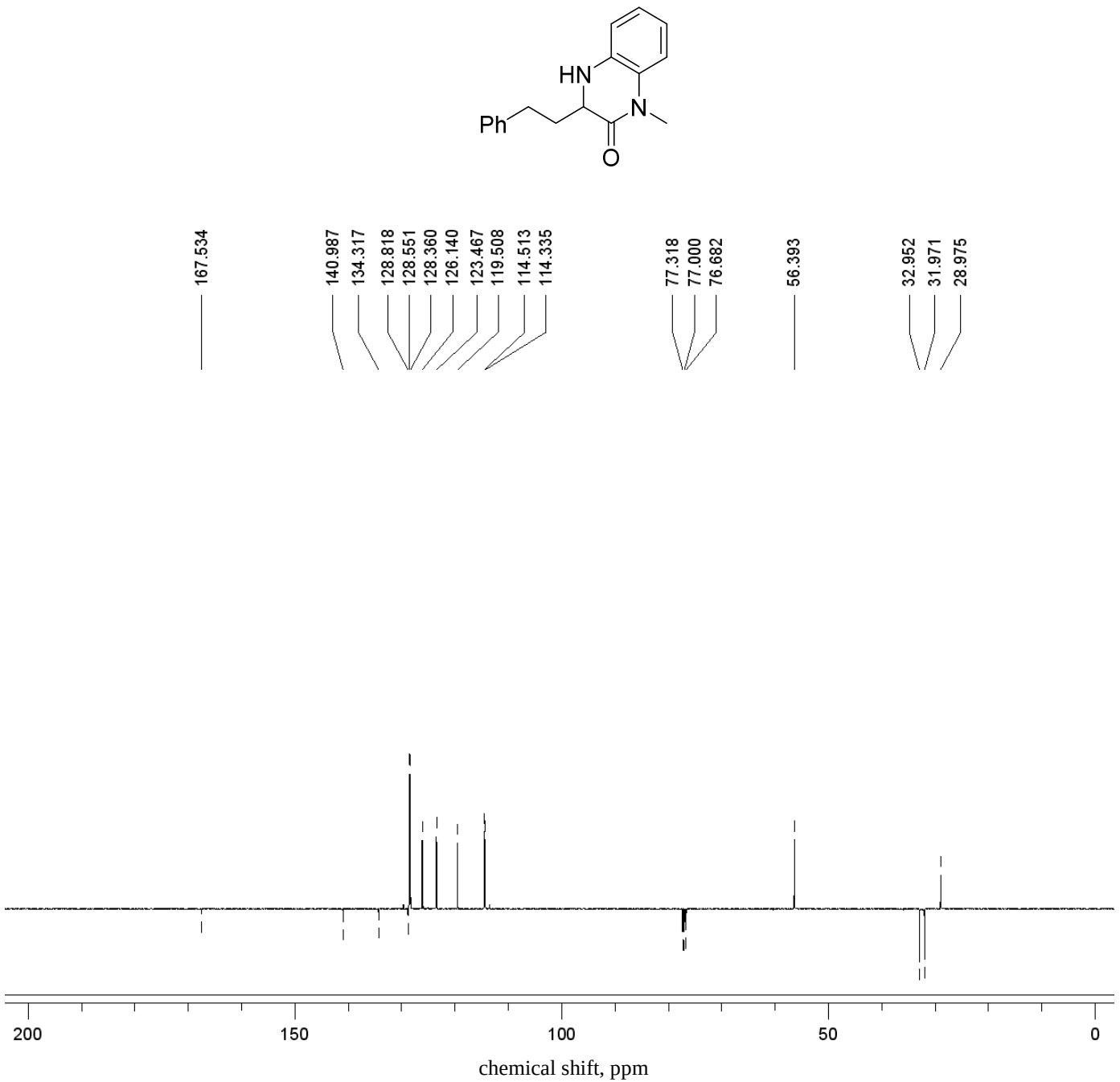

HN
Ph
N
Ph
O
170.136
142.664
141.613
129.146
128.519
128.397
126.803
125.961
125.918
59.147
51.781
42.257
34.166
32.264
200
150
100
50
0
chemical shift, ppm

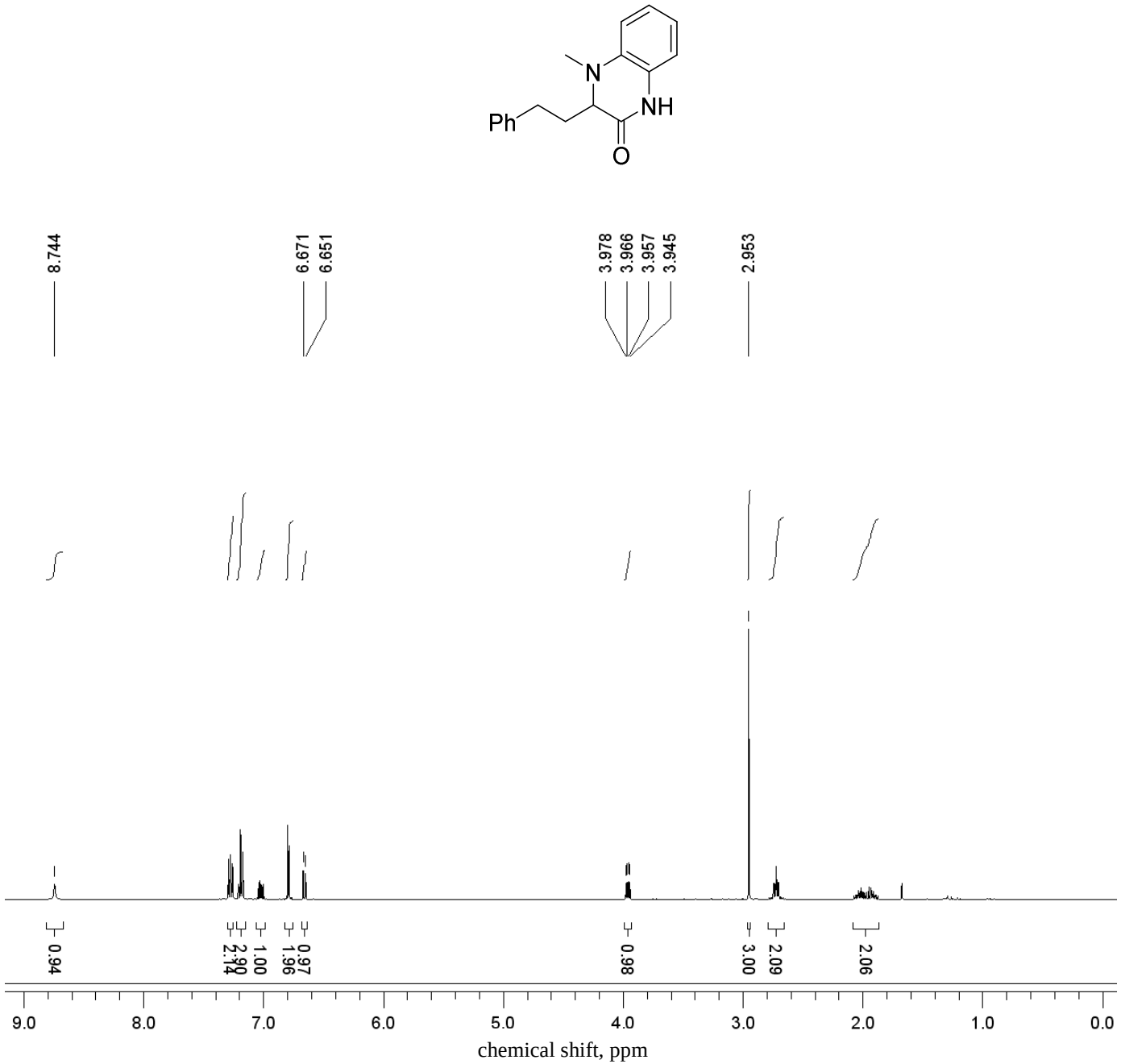

Ph
N
Ph
NH
O
5.968
5.955
5.941
3.795
3.760
3.493
3.483
3.474
3.456
3.448
3.293
3.290
3.280
3.278
3.265
3.262
3.253
3.243
3.240
3.228
3.225
3.216
3.213
2.056
2.037
2.019
2.000
10.00
0.93
0.99
1.95
1.03
1.99
2.98
1.94
1.01
1.07
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

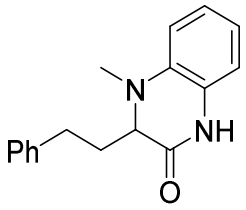

Ph
N
Ph
NH
O
176.997
142.179
139.336
128.705
128.530
128.350
128.323
126.943
125.770
62.844
52.239
49.723
41.886
32.333
30.410
23.046
200
150
100
50
0
chemical shift, ppm

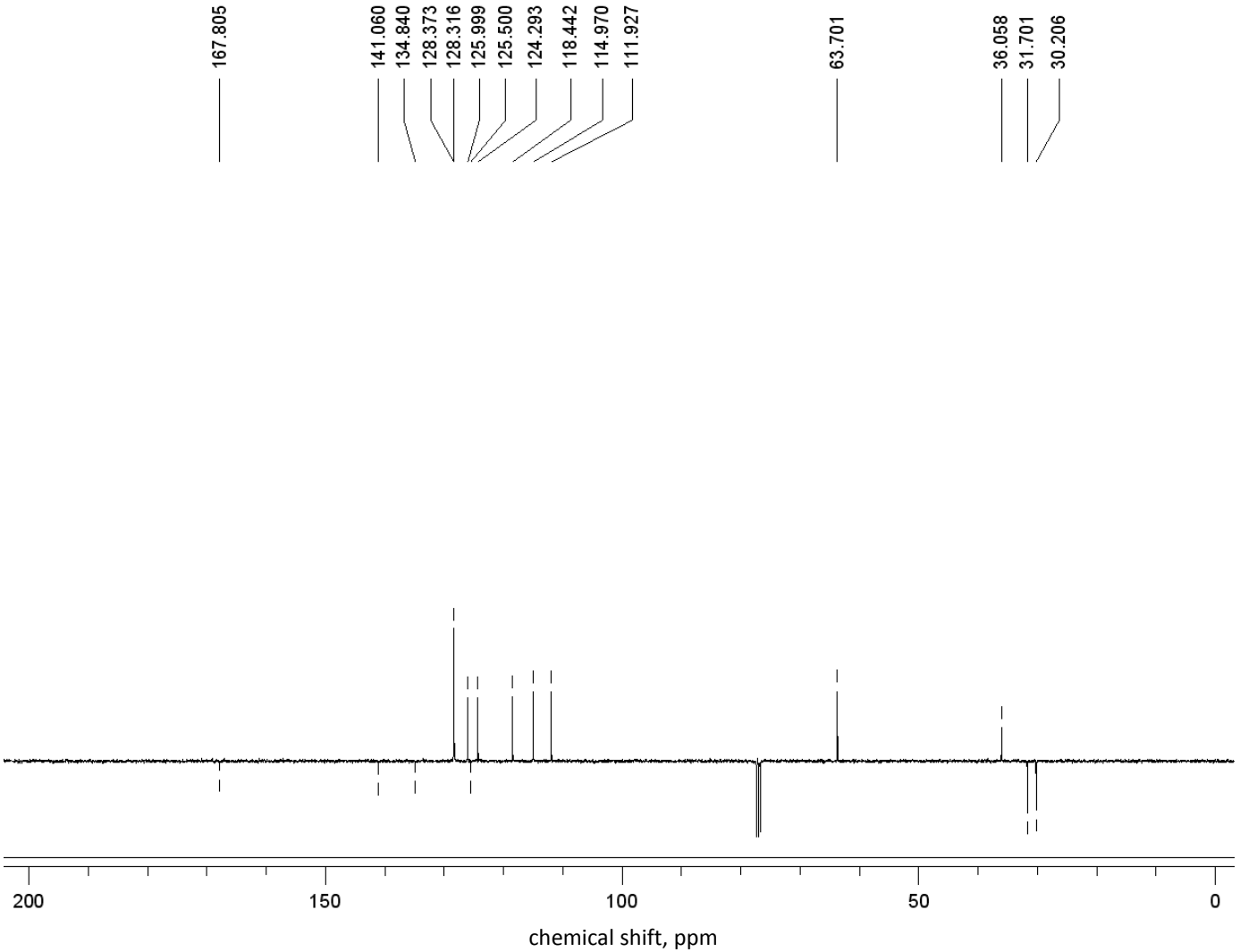

4.519
4.482
HN
Ph
N
Ph
O
H
H
1.00
4.519
4.482
3.912
3.878
$^1$H NMR of
crude
2.69
1.00
3.910
3.875
Ph
H
N
Ph
NH
O
HN
Ph
N
Ph
O
:
Ph
N
Ph
NH
O
73
:
27

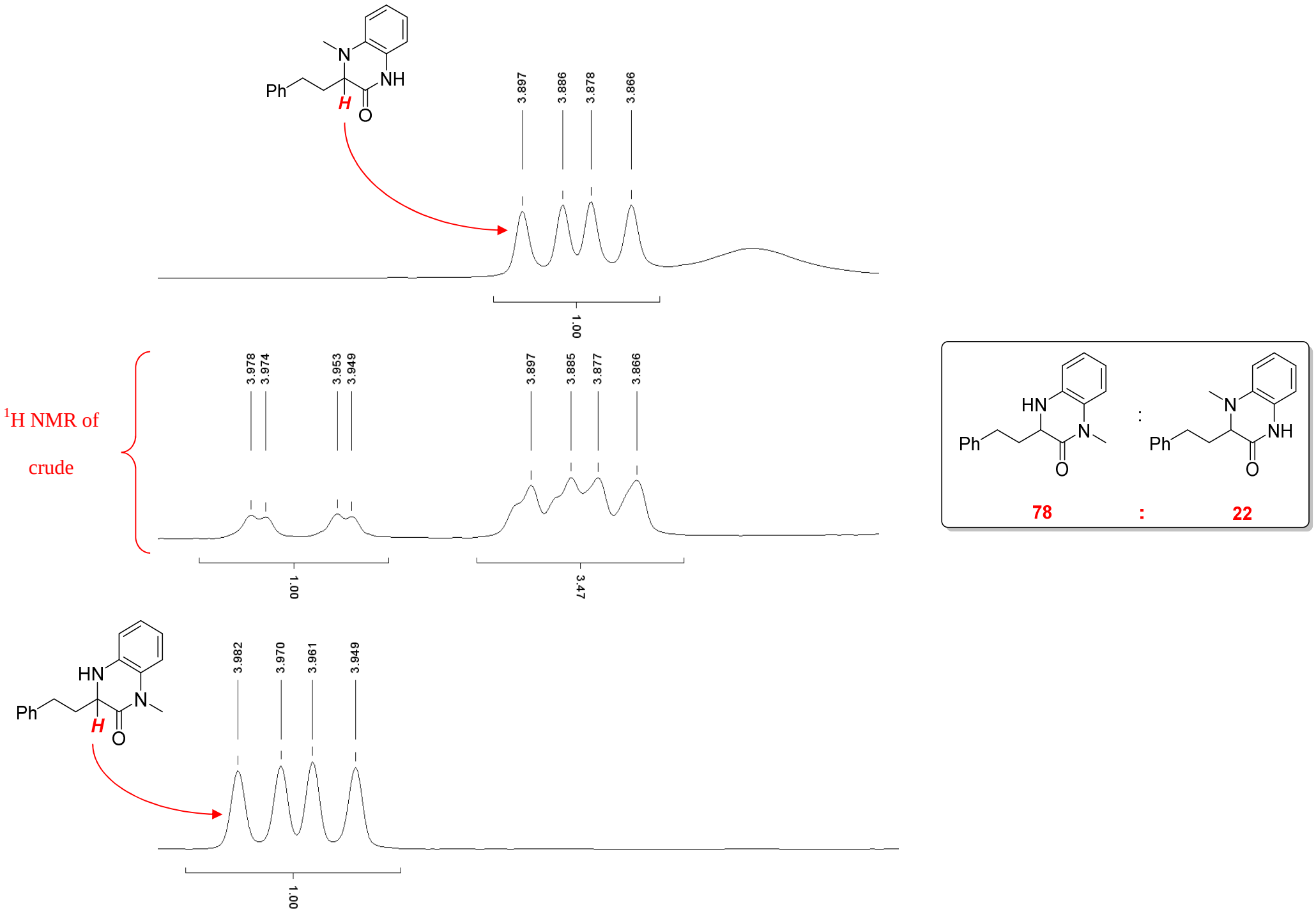

HN
N
Ph
O
6.490
6.471
3.837
3.826
3.818
3.806
3.765
3.270
2.135
2.123
2.118
2.114
2.106
2.100
2.088
2.084
2.078
2.072
2.067
2.062
2.050
3.05
2.13
2.02
1.92
1.00
0.89
0.88
3.11
2.08
1.08
1.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

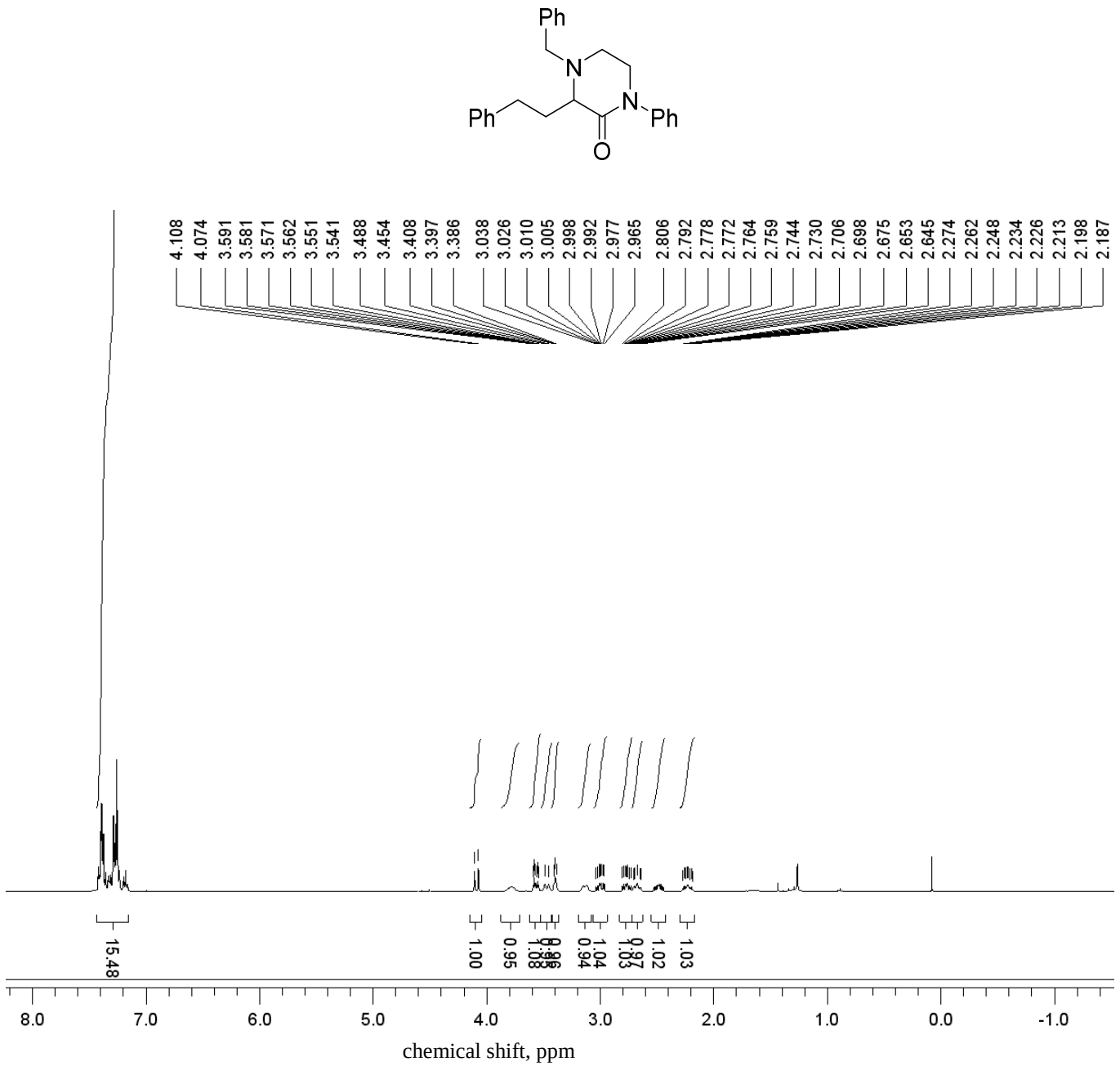

HN
N
Ph
O
167.534
140.987
134.317
128.818
128.551
128.360
126.140
123.467
119.508
114.513
114.335
77.318
77.000
76.682
56.393
32.952
31.971
28.975
200
150
100
50
0
chemical shift, ppm

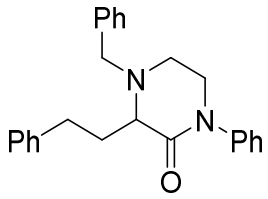

Ph
N
NH
O
8.744
6.671
6.651
3.978
3.966
3.957
3.945
2.953
0.94
2.14
2.90
1.00
1.96
0.97
0.98
3.00
2.09
2.09
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

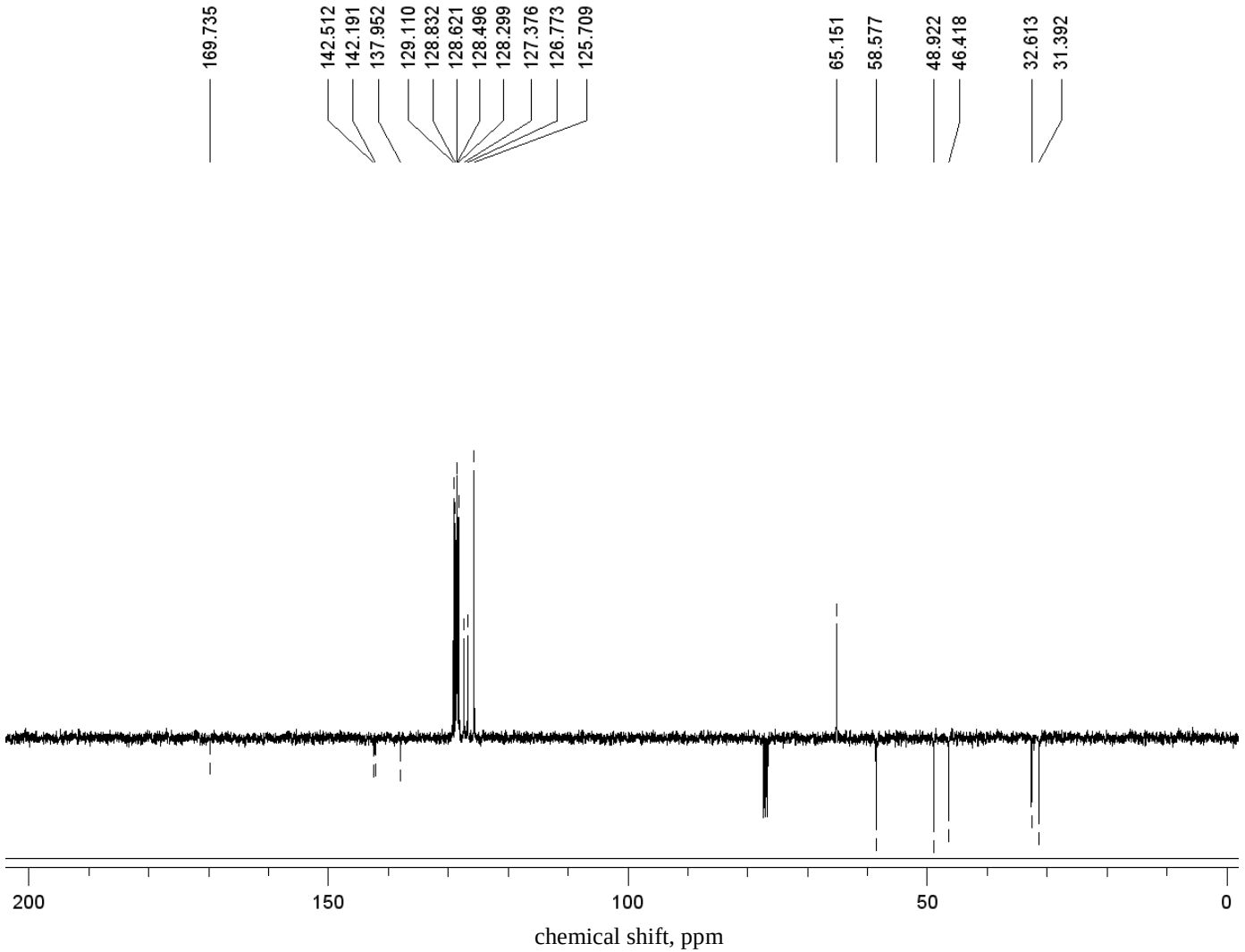

N
NH
Ph
O

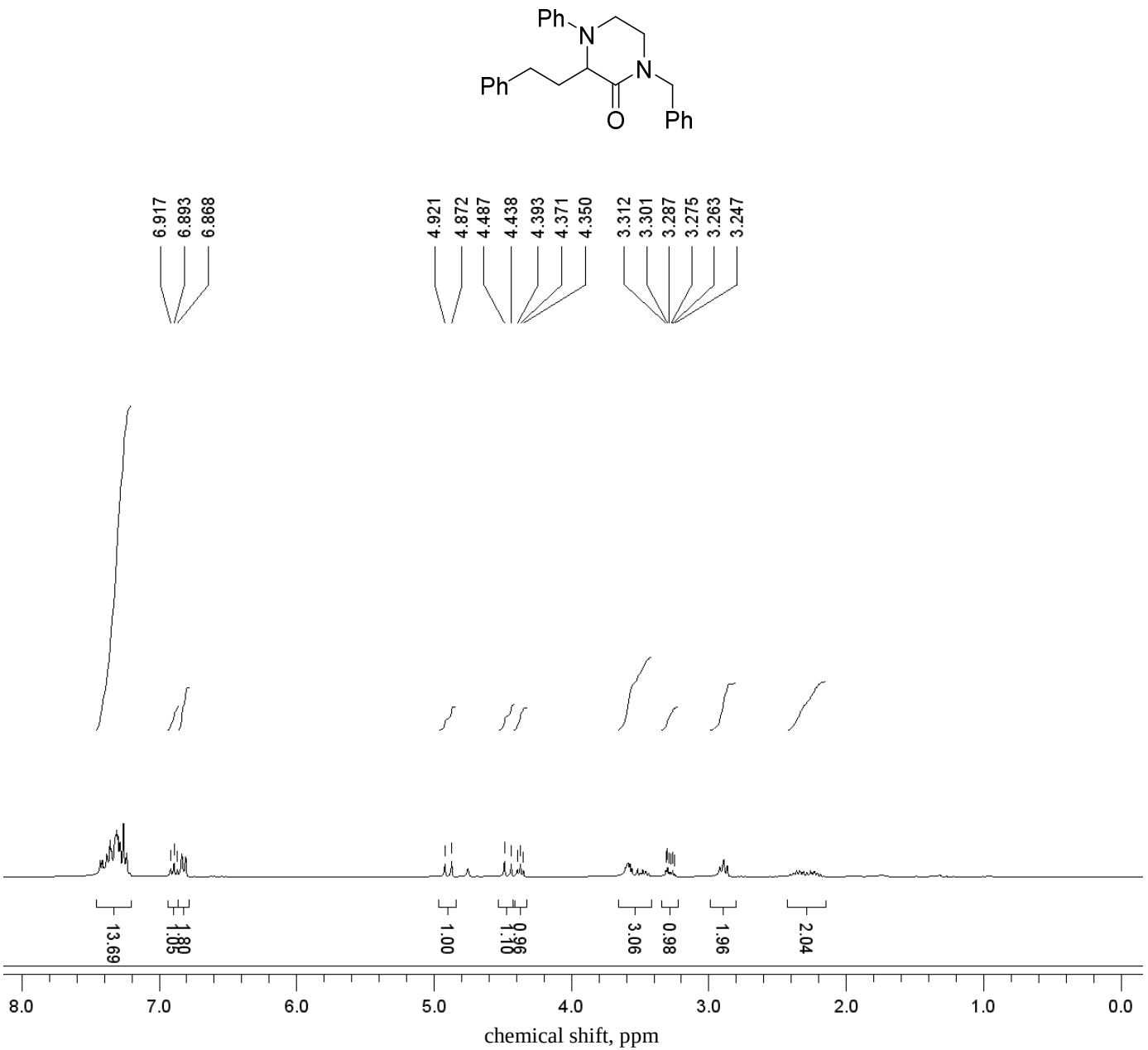

167.805
141.060
134.840
128.373
128.316
125.999
125.500
124.293
118.442
114.970
111.927
63.701
36.058
31.701
30.206
200
150
100
50
0
chemical shift, ppm

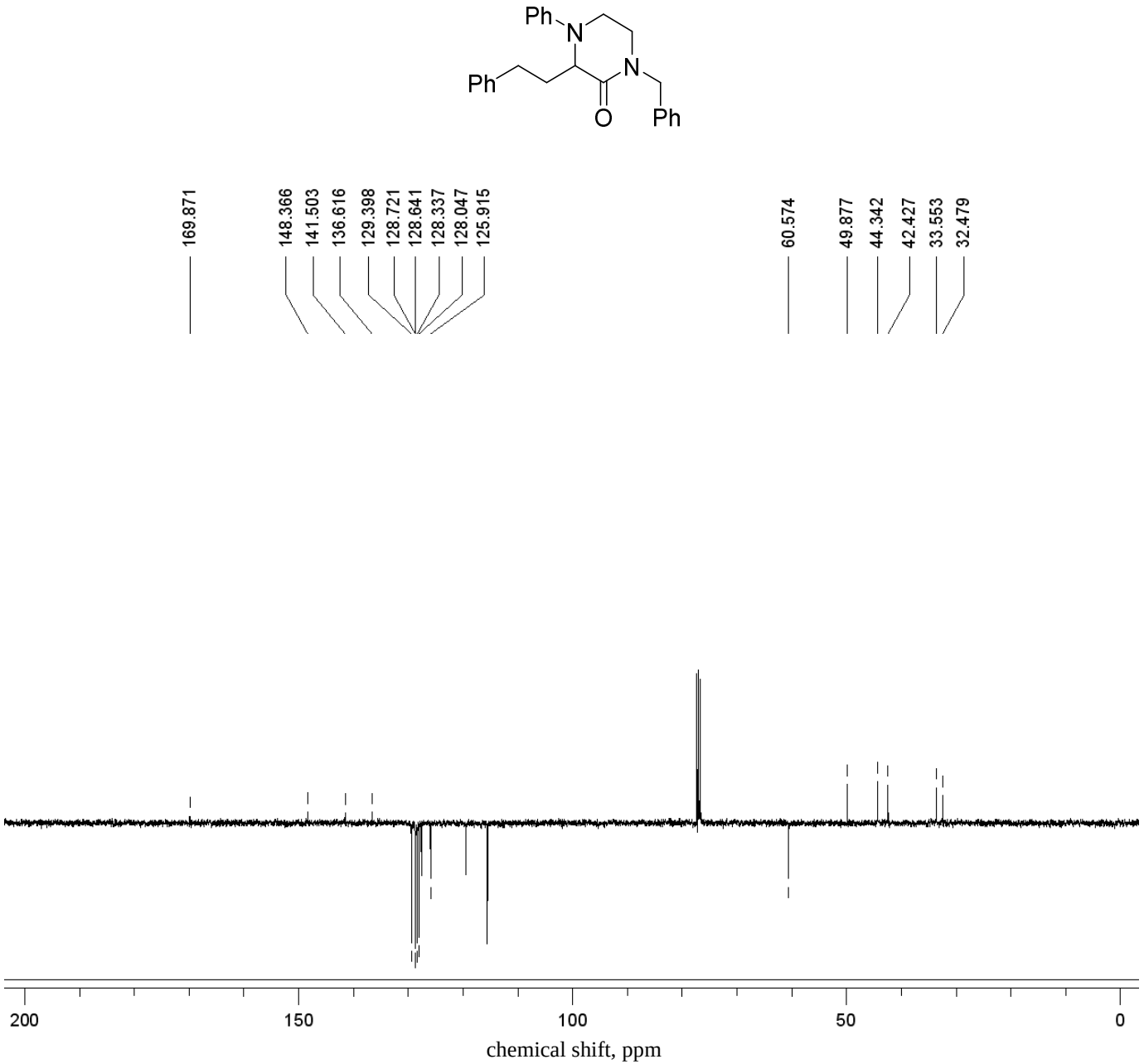

Ph
N
NH
H
O
3.897
3.886
3.878
3.866
1.00
$^1$H NMR of
crude
3.978
3.974
3.953
3.949
3.897
3.885
3.877
3.866
1.00
3.47
HN
N
Ph
H
O
3.982
3.970
3.961
3.949
1.00
HN
N
Ph
O
:
N
NH
Ph
O
78
:
22

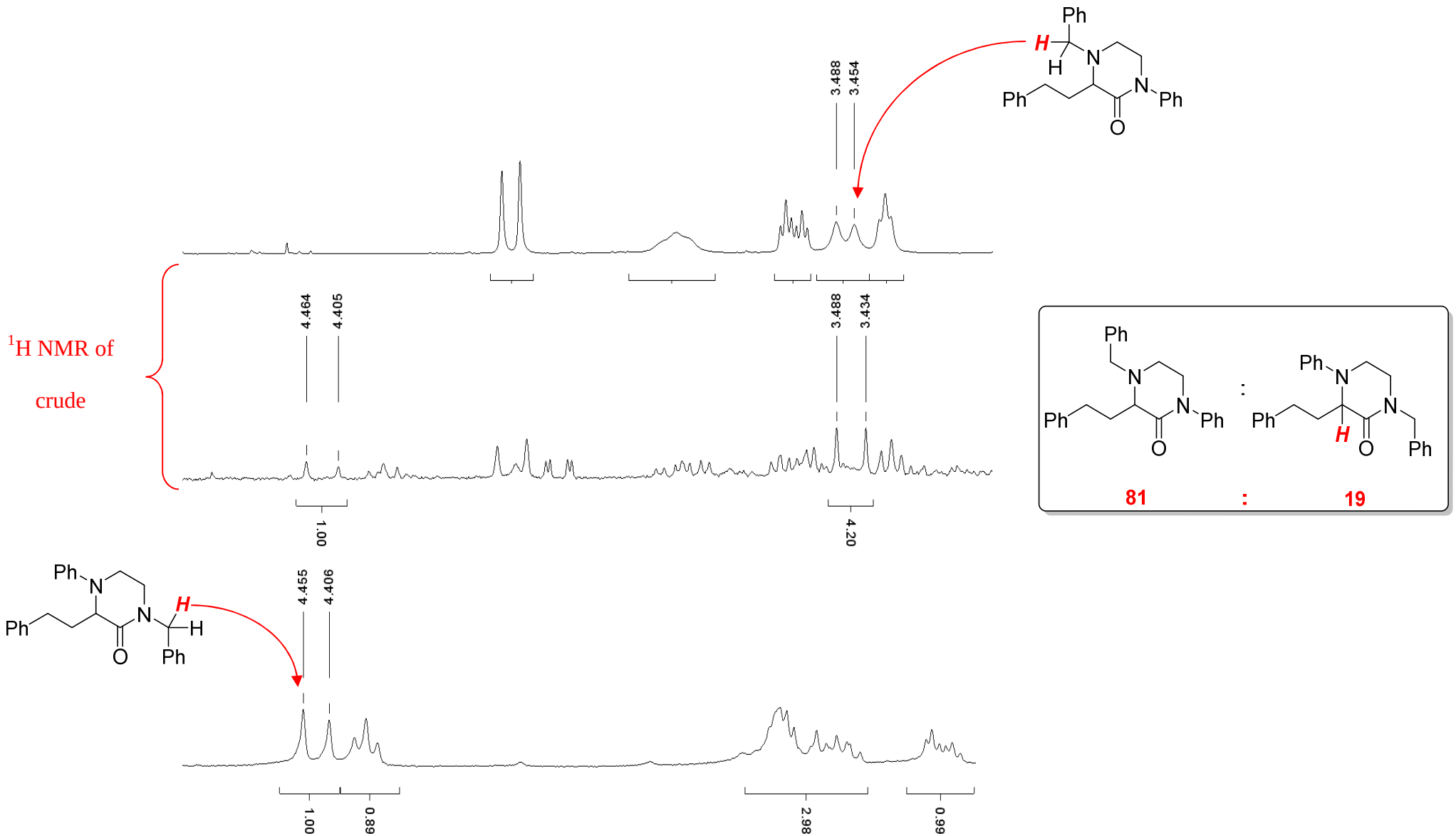

Ph
N
N
Ph
Ph
O
4.108
4.074
3.591
3.581
3.571
3.562
3.551
3.541
3.488
3.454
3.408
3.397
3.386
3.038
3.026
3.010
3.005
2.998
2.992
2.977
2.965
2.806
2.792
2.778
2.772
2.764
2.759
2.744
2.730
2.706
2.698
2.675
2.653
2.645
2.274
2.262
2.248
2.234
2.226
2.213
2.198
2.187
15.48
1.00
0.95
1.04
1.03
1.02
1.03
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
chemical shift, ppm

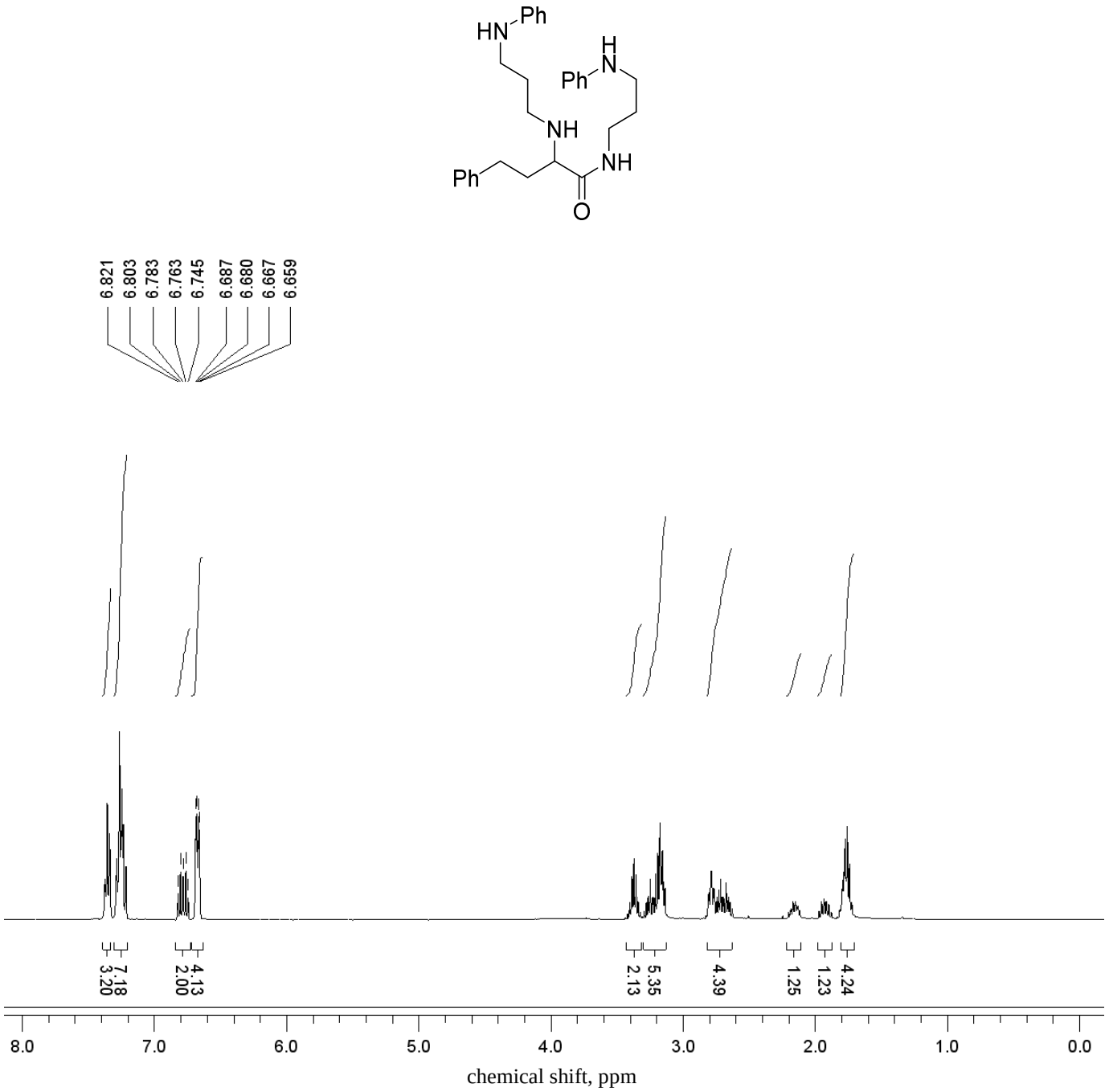

Ph
N
Ph
N
Ph
O

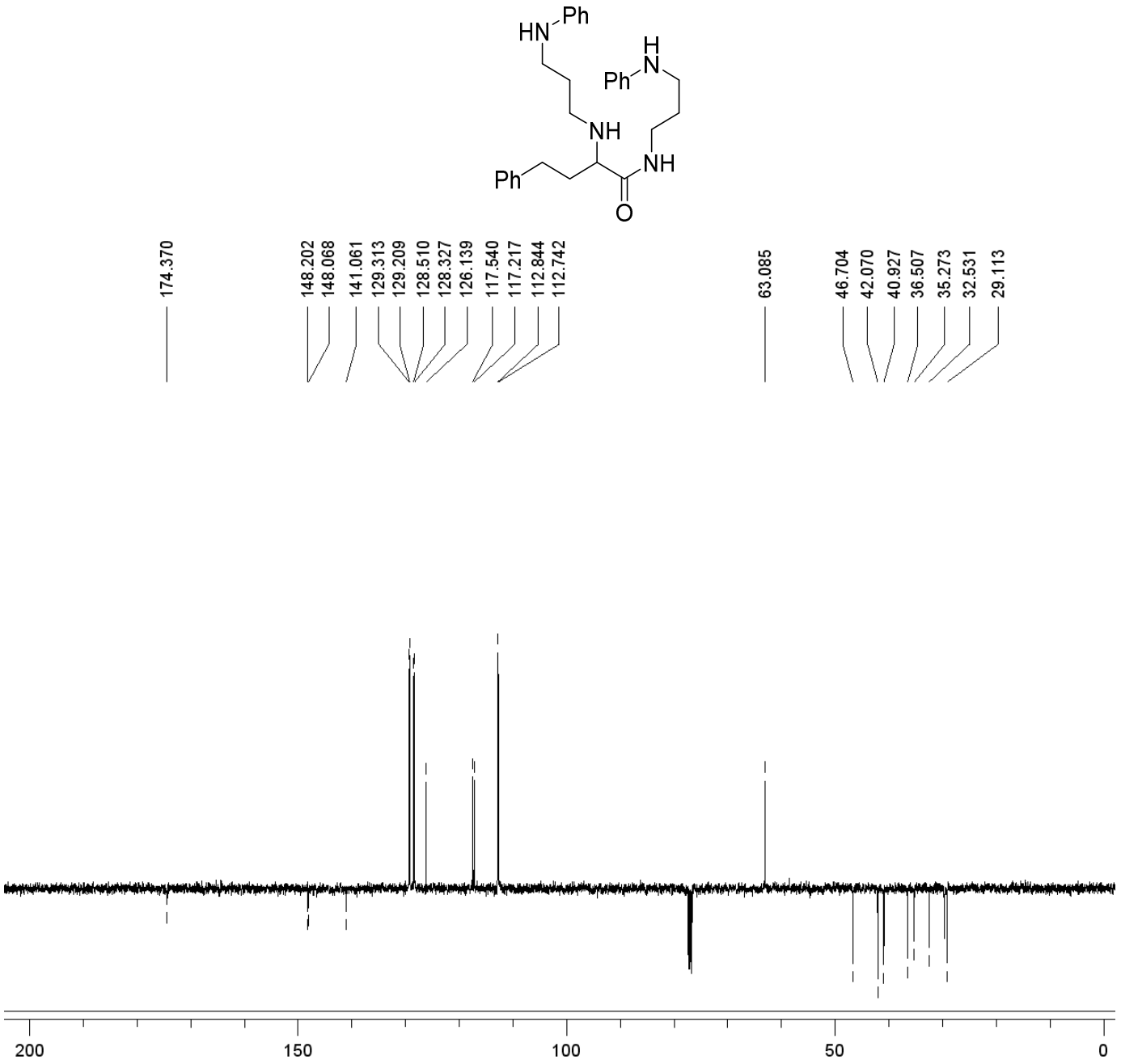

169.735
142.512
142.191
137.952
129.110
128.832
128.621
128.496
128.299
127.376
126.773
125.709
65.151
58.577
48.922
46.418
32.613
31.392
200
150
100
50
0
chemical shift, ppm


Ph
N
N
Ph
O
Ph
6.917
6.893
6.868
4.921
4.872
4.487
4.438
4.393
4.371
4.350
3.312
3.301
3.287
3.275
3.263
3.247
13.69
1.88
1.85
1.00
0.96
1.10
3.06
0.98
1.96
2.04
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

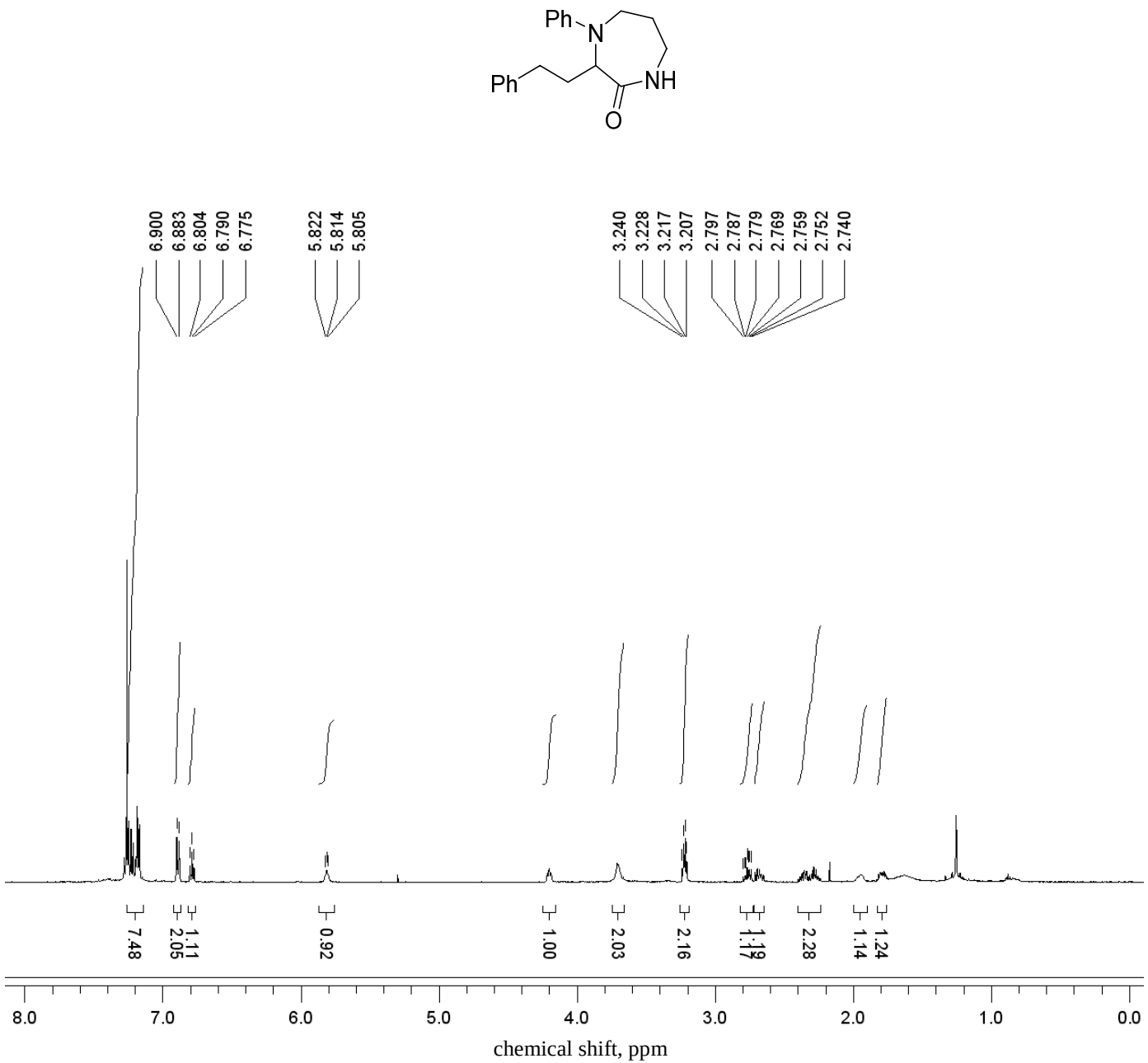

Ph
N
Ph
N
O
Ph
169.871
148.366
141.503
136.616
129.398
128.721
128.641
128.337
128.047
125.915
60.574
49.877
44.342
42.427
33.553
32.479
200
150
100
50
0
chemical shift, ppm

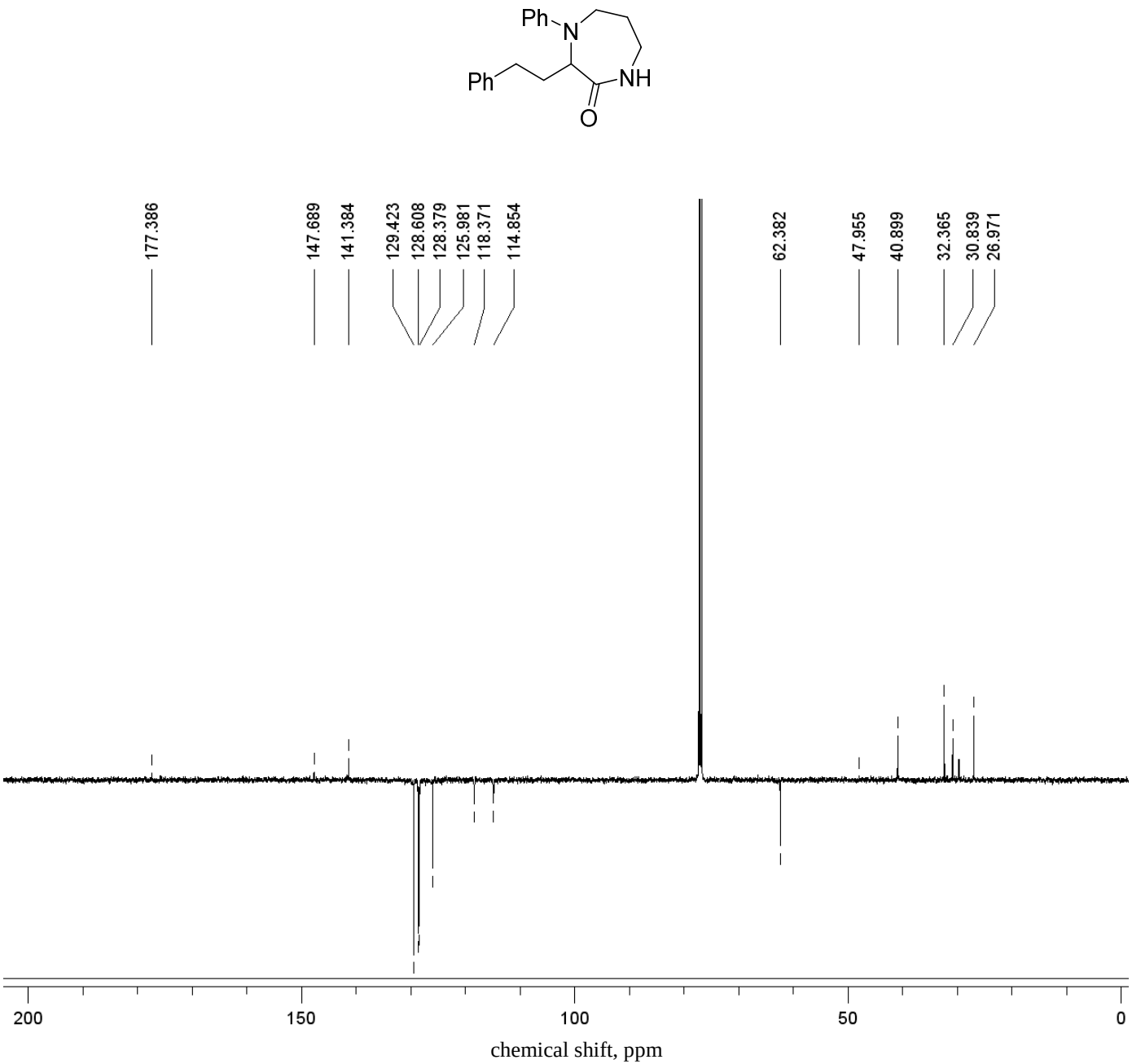

$^1$H NMR of
crude
3.488
3.454
4.464
4.405
3.488
3.434
1.00
4.20
4.455
4.406
1.00
0.89
2.98
0.99
81 : 19

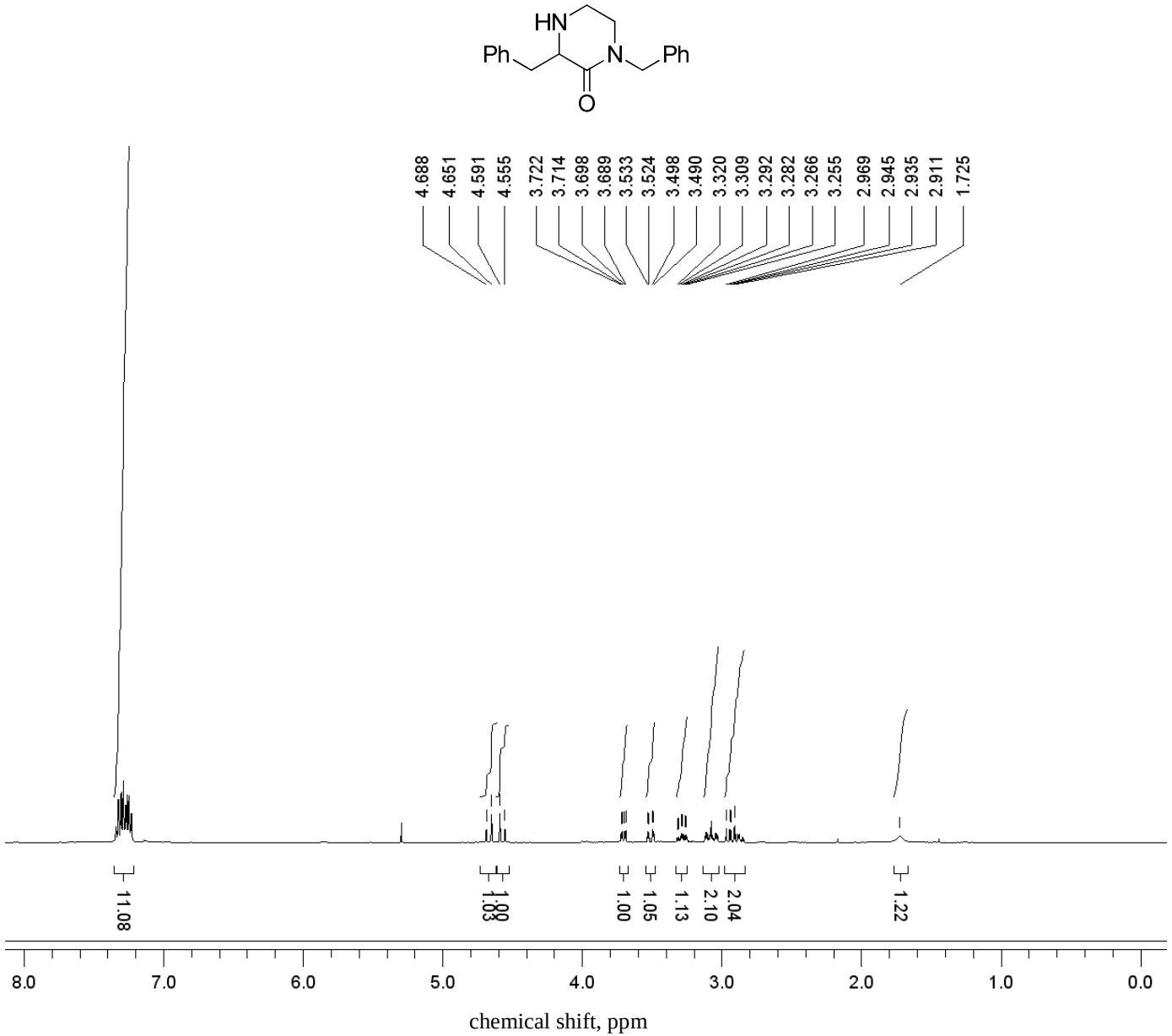

HN
Ph
H
N
Ph
NH
Ph
NH
O
6.821
6.803
6.783
6.763
6.745
6.687
6.680
6.667
6.659
3.20
7.18
2.00
4.13
2.13
5.35
4.39
1.25
1.23
4.24
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

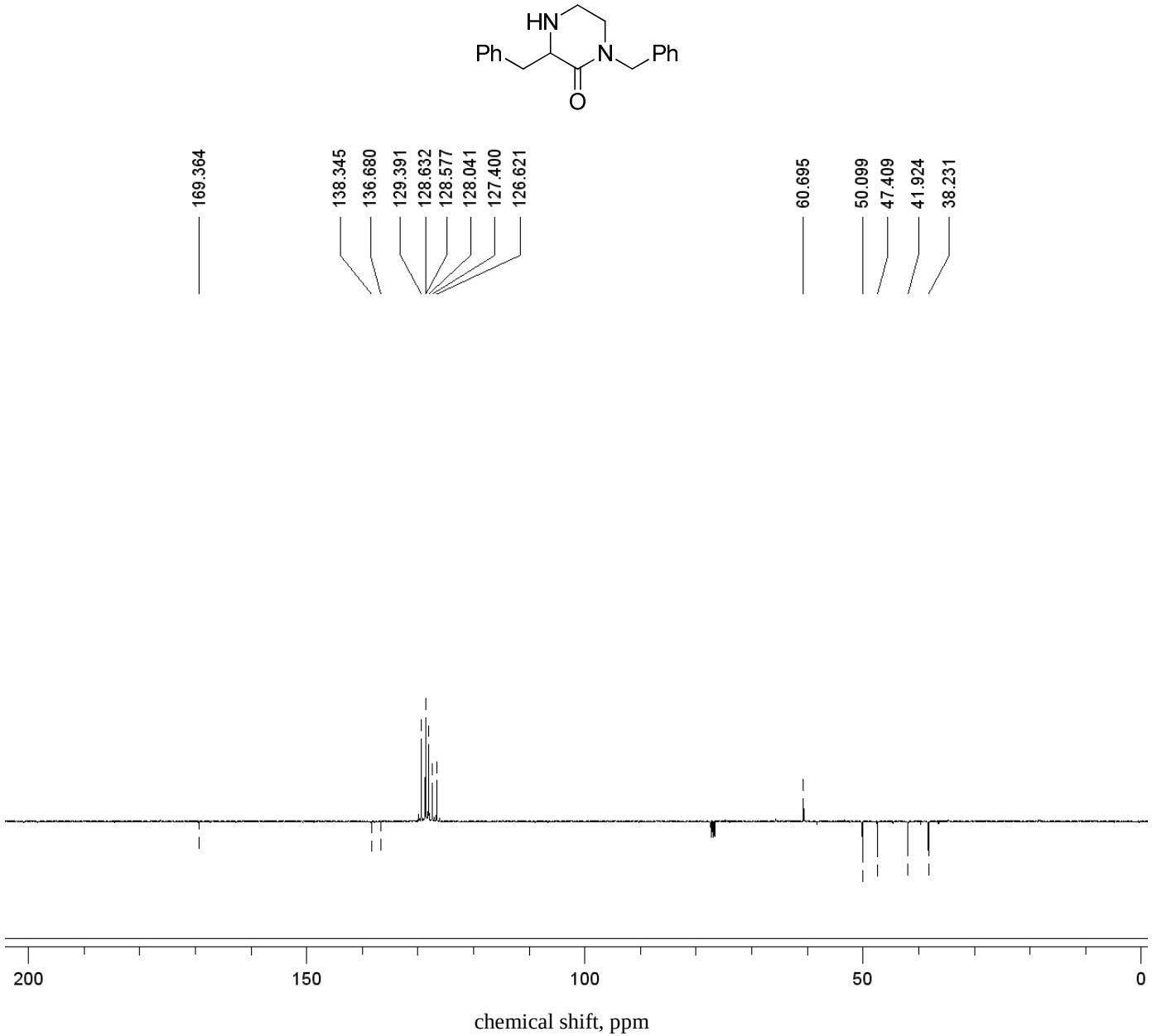


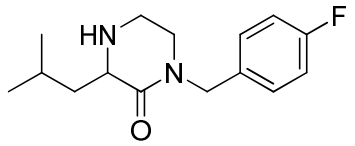

chemical shift, ppm

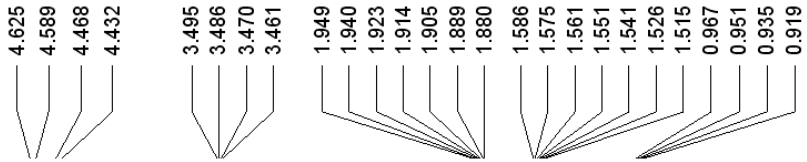

Ph
N
Ph
NH
O
6.900
6.883
6.804
6.790
6.775
5.822
5.814
5.805
3.240
3.228
3.217
3.207
2.797
2.787
2.779
2.769
2.759
2.752
2.740
7.48
2.05
1.11
0.92
1.00
2.03
2.16
1.19
1.17
2.28
1.14
1.24
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

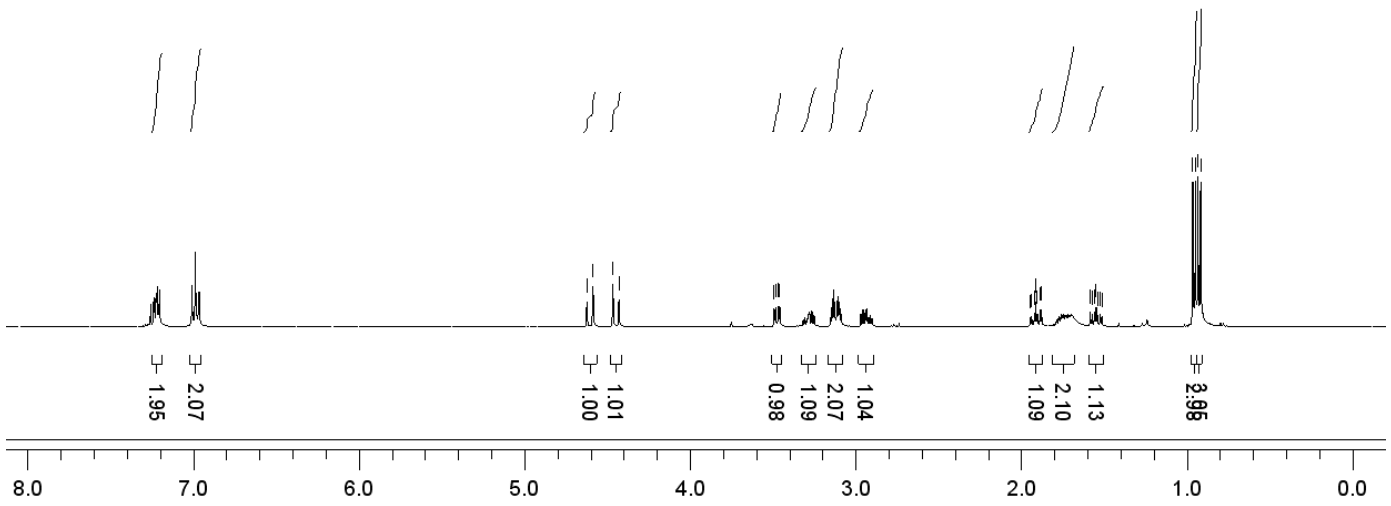

Ph
N
Ph
NH
O
177.386
147.689
141.384
129.423
128.608
128.379
125.981
118.371
114.854
62.382
47.955
40.899
32.365
30.839
26.971
200
150
100
50
0
chemical shift, ppm


HN
Ph
N
Ph
O
4.688
4.651
4.591
4.555
3.722
3.714
3.698
3.689
3.533
3.524
3.498
3.490
3.320
3.309
3.292
3.282
3.266
3.255
2.969
2.945
2.935
2.911
1.725
11.08
1.03
1.00
1.00
1.05
1.13
2.10
2.04
1.22
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
chemical shift, ppm

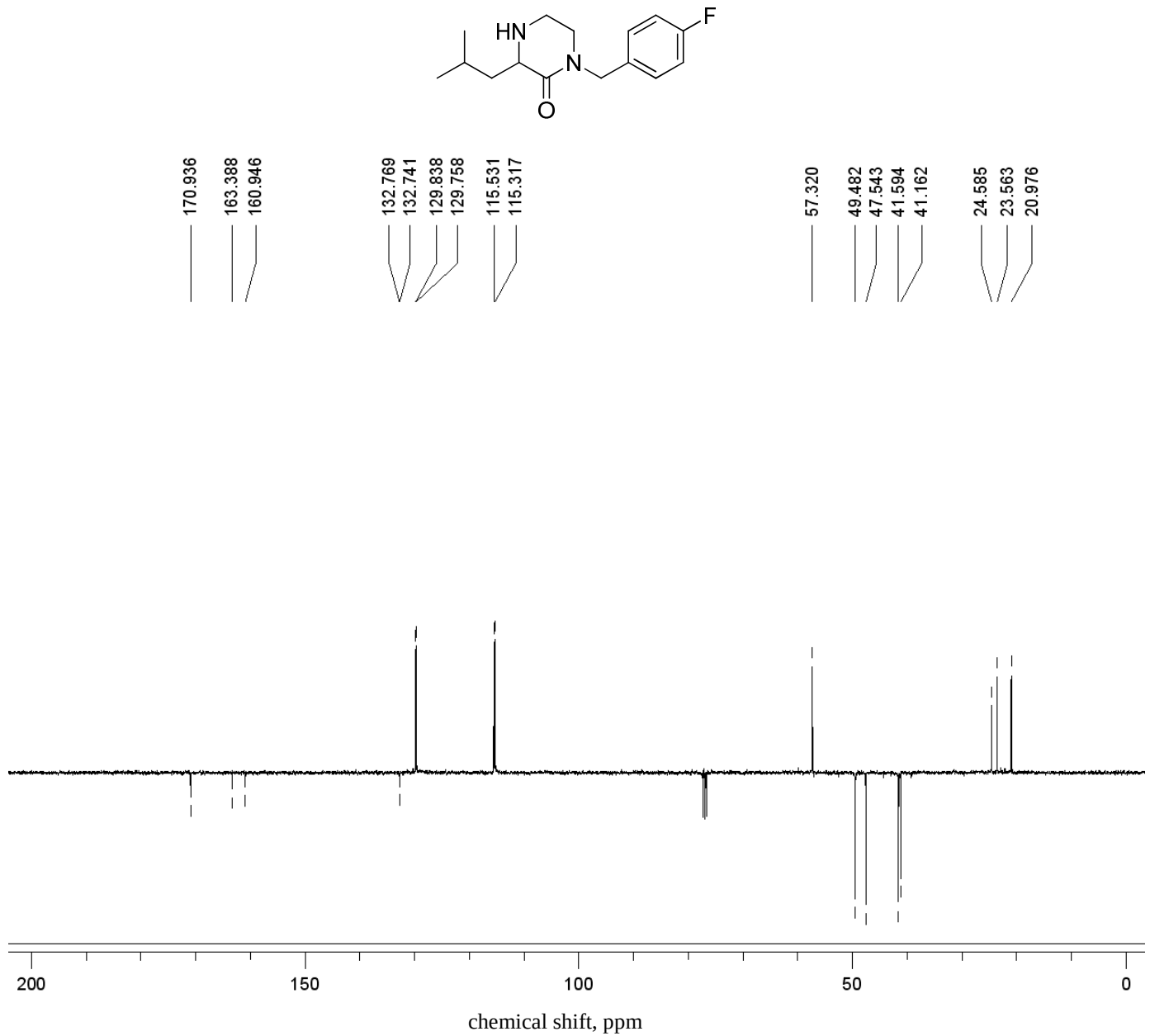

HN
Ph
N
Ph
O
169.364
138.345
136.680
129.391
128.632
128.577
128.041
127.400
126.621
60.695
50.099
47.409
41.924
38.231
200
150
100
50
0
chemical shift, ppm



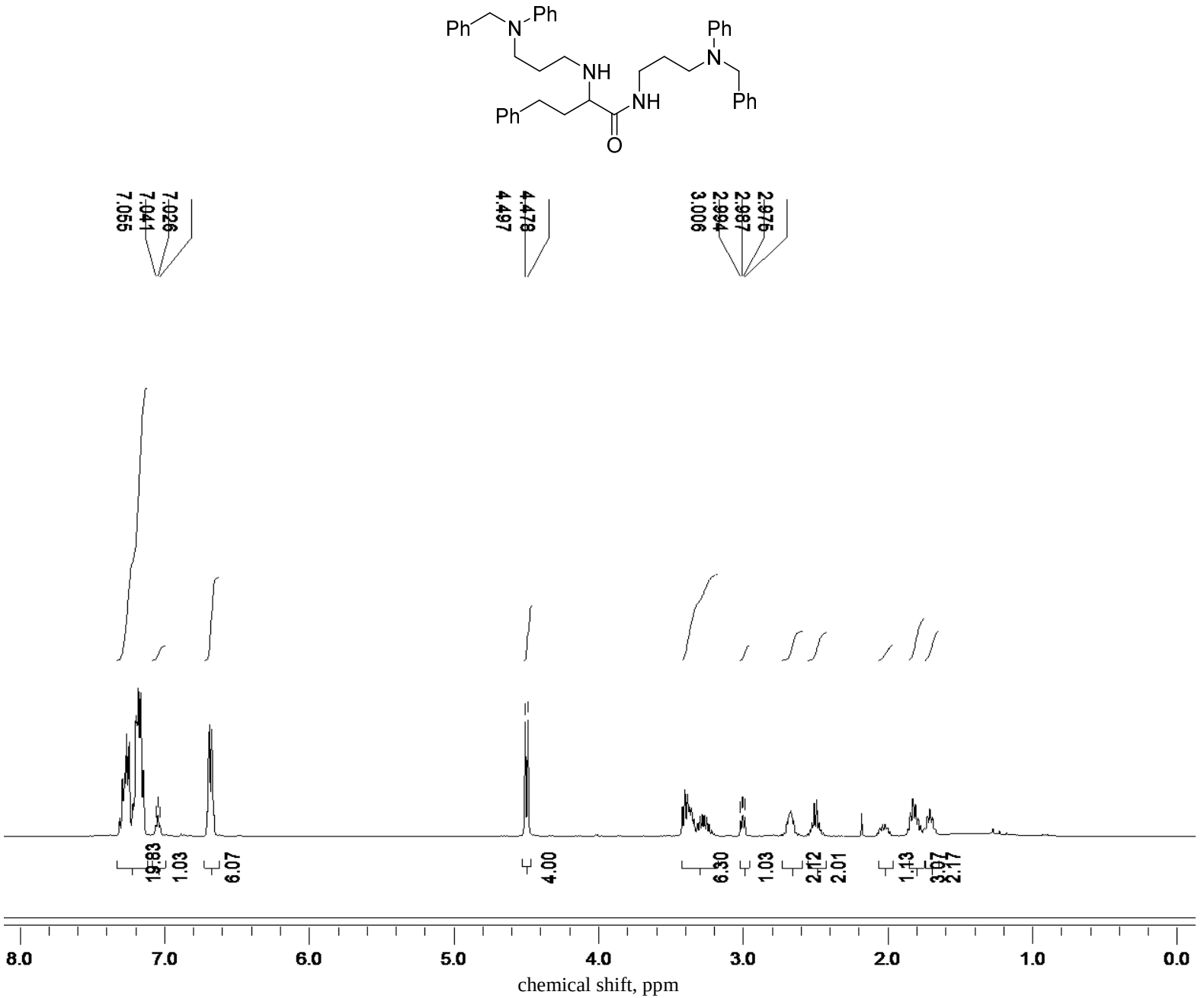



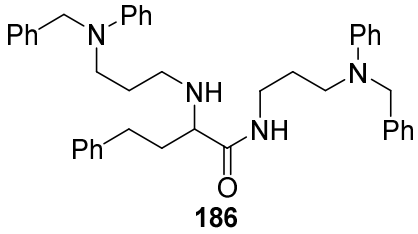




chemical shift, ppm

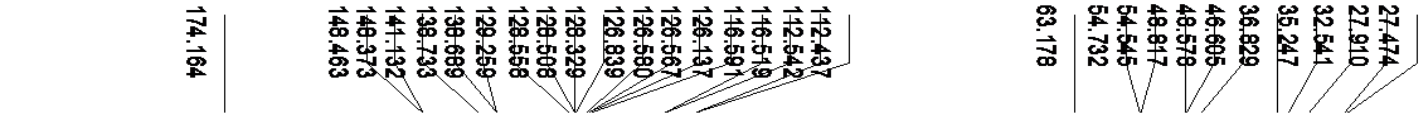

HN
N
O
F
170.936
163.388
160.946
132.769
132.741
129.838
129.758
115.531
115.317
57.320
49.482
47.543
41.594
41.162
24.585
23.563
20.976
200
150
100
50
0
chemical shift, ppm

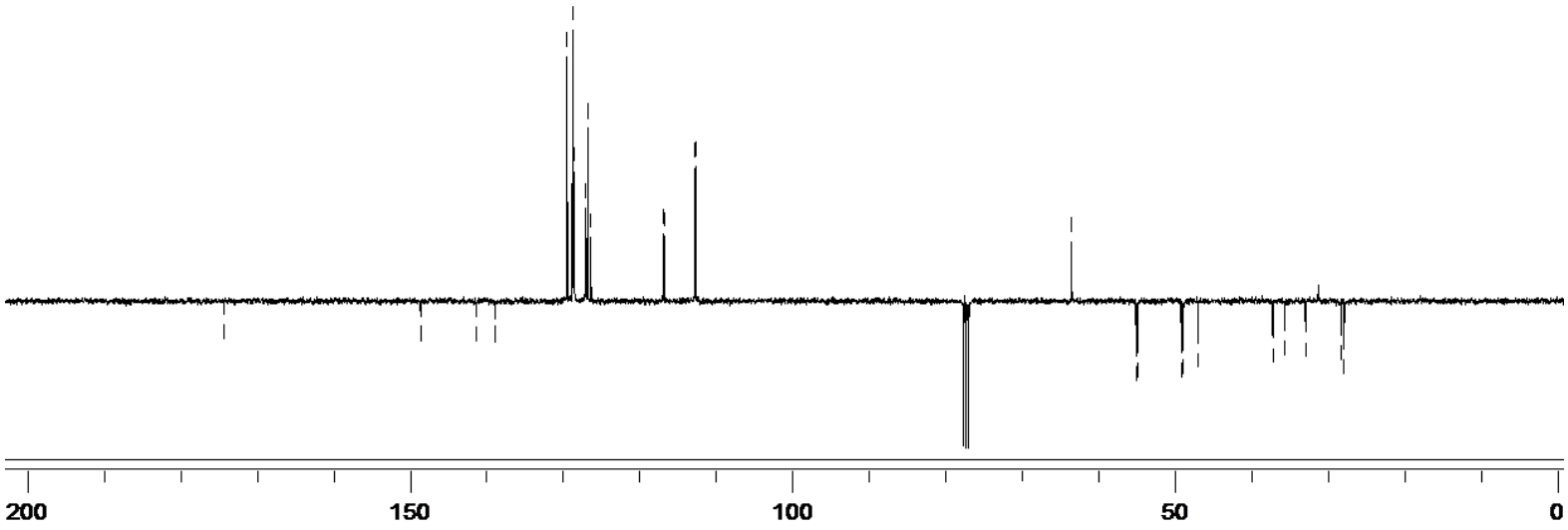
**4.4 $^{1}$H and $^{13}$C NMR Spectra for *N*-(3-(benzyl(phenyl)amino)propyl)-2-((3-(benzyl(phenyl)amino)propyl)amino)-4-phenylbutanamide.**





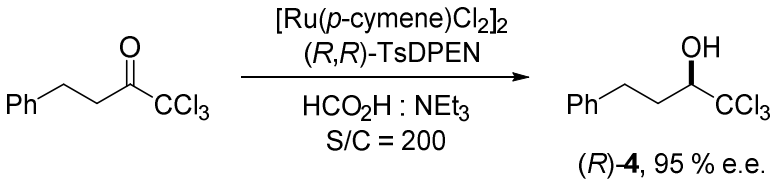

**186**



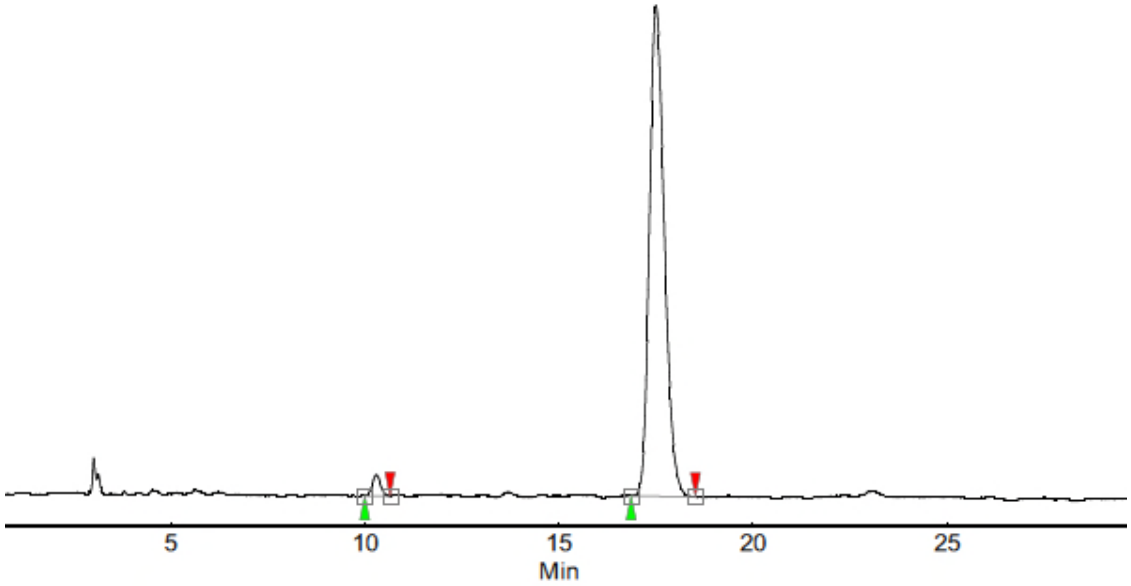




chemical shift, ppm

## 5. Chiral HPLC and GC Traces.

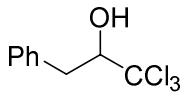



(*R*)-**4**, 95 % e.e.

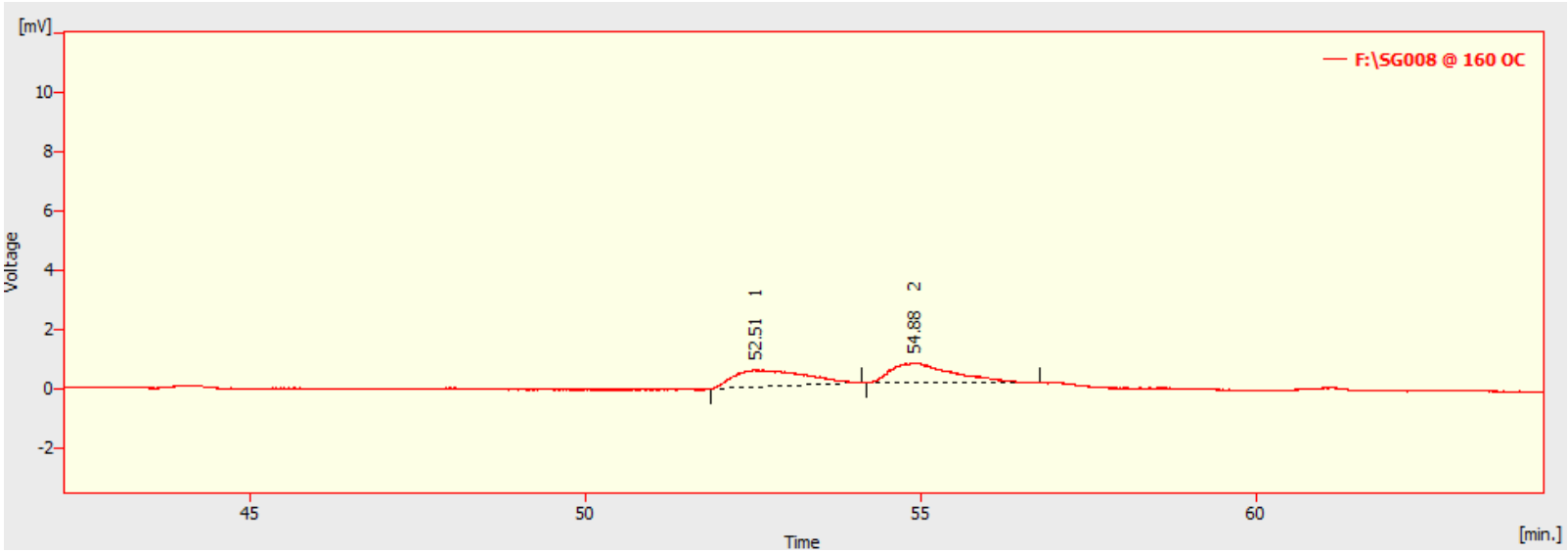



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 10.31 | 2.29 | 11.9 | 2.9 | 2.293 |
| 2 | UNKNOWN | 17.51 | 97.71 | 273.6 | 122.3 | 97.707 |
| | | | | | | |
| Total | | | 100.00 | 285.5 | 125.2 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 209 nm, (*S*)-isomer 10.31 min., (*R*)-isomer 17.51 min.

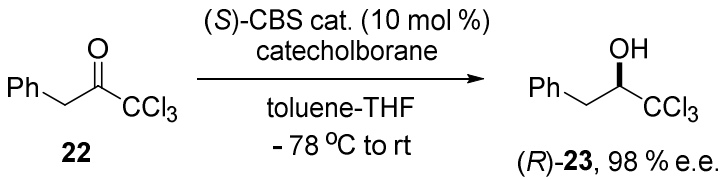


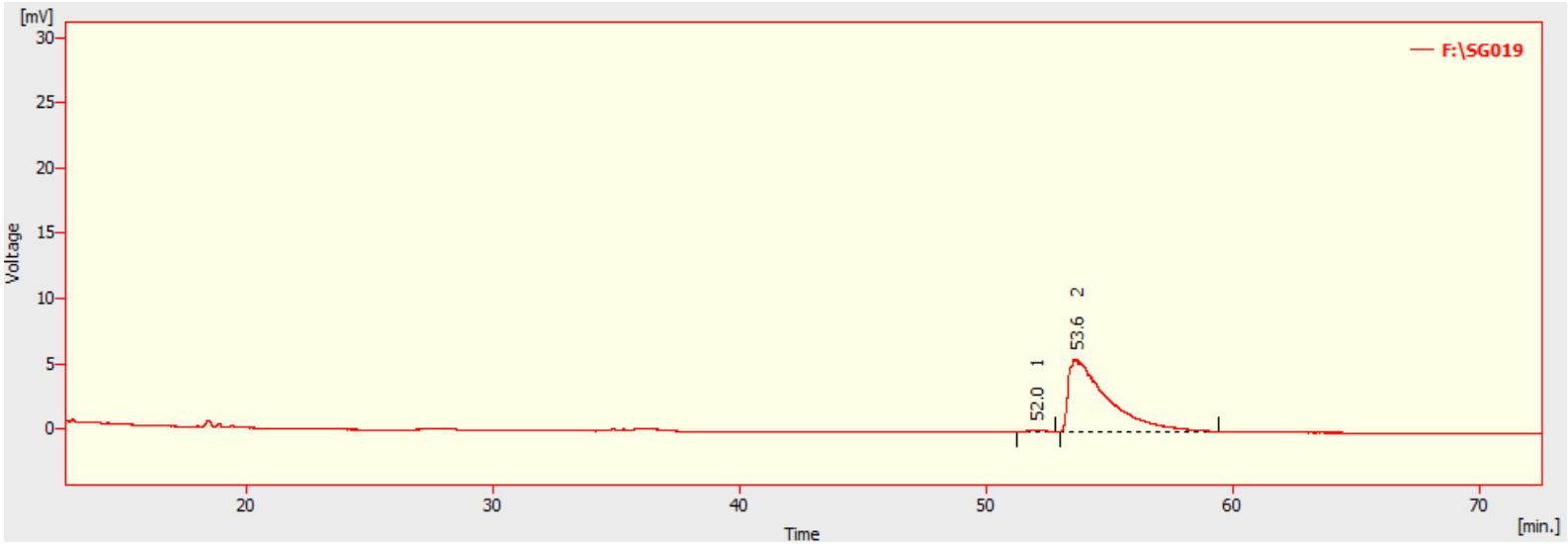

**23**




| | Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | W05 [min] | Compound Name |
|---|---|---|---|---|---|---|---|
| 1 | 52.513 | 43.759 | 0.598 | 49.7 | 46.8 | 1.47 | |
| 2 | 54.883 | 44.269 | 0.678 | 50.3 | 53.2 | 1.03 | |
| | Total | 88.028 | 1.276 | 100.0 | 100.0 | | |

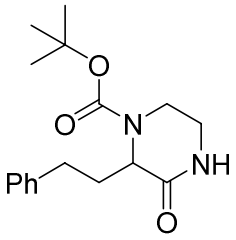
CP-cyclodextrin-β-2,3,6-M-19, 50m 0.25mm 0.25µm, T = 160 °C, P = 15 psi ($H_2$ gas), (*S*)-isomer 52.5 min., (*R*)-isomer 54.9 min.



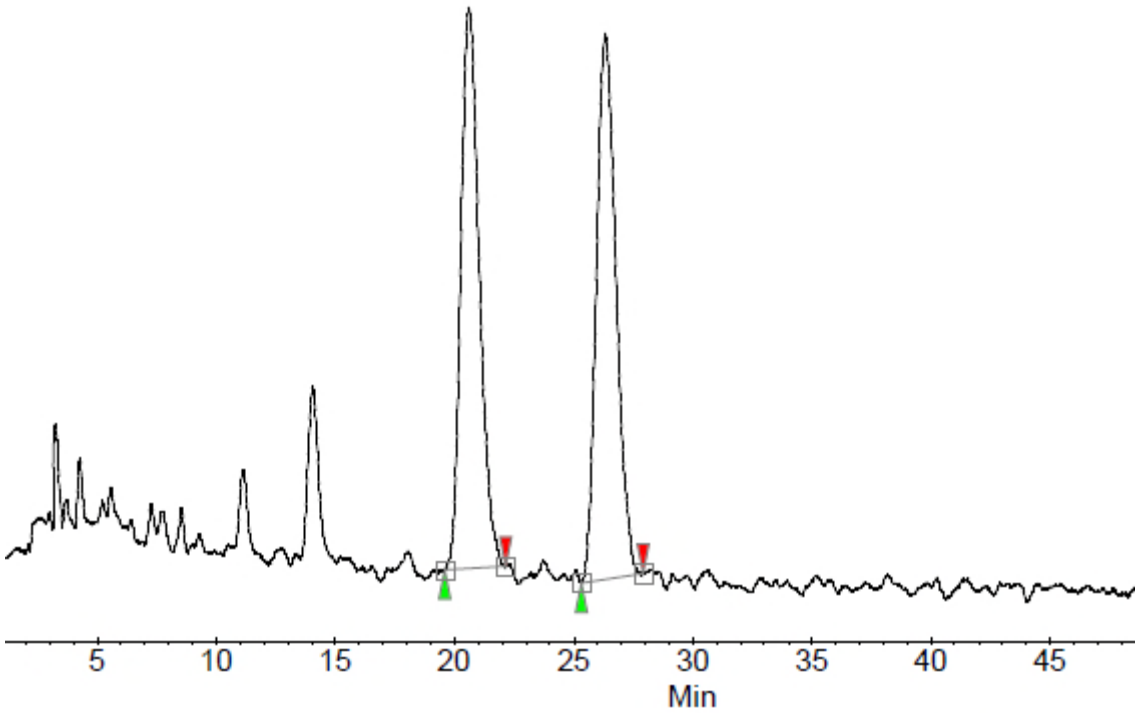




| | Reten. Time [min] | Area [mV.s] | Height [mV] | Area [%] | Height [%] | W05 [min] | Compound Name |
|---|---|---|---|---|---|---|---|
| 1 | 51.970 | 4.567 | 0.093 | 0.7 | 1.7 | 0.87 | |
| 2 | 53.627 | 609.977 | 5.498 | 99.3 | 98.3 | 1.52 | |
| | Total | 614.544 | 5.591 | 100.0 | 100.0 | | |

CP-cyclodextrin-β-2,3,6-M-19, 50m 0.25mm 0.25µm, T = 160 °C, P = 15 psi ($H_2$ gas), (*S*)-isomer 52.0 min., (*R*)-isomer 53.6 min.

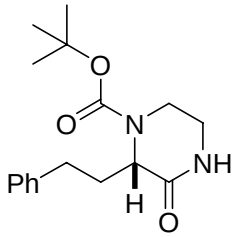



**2**

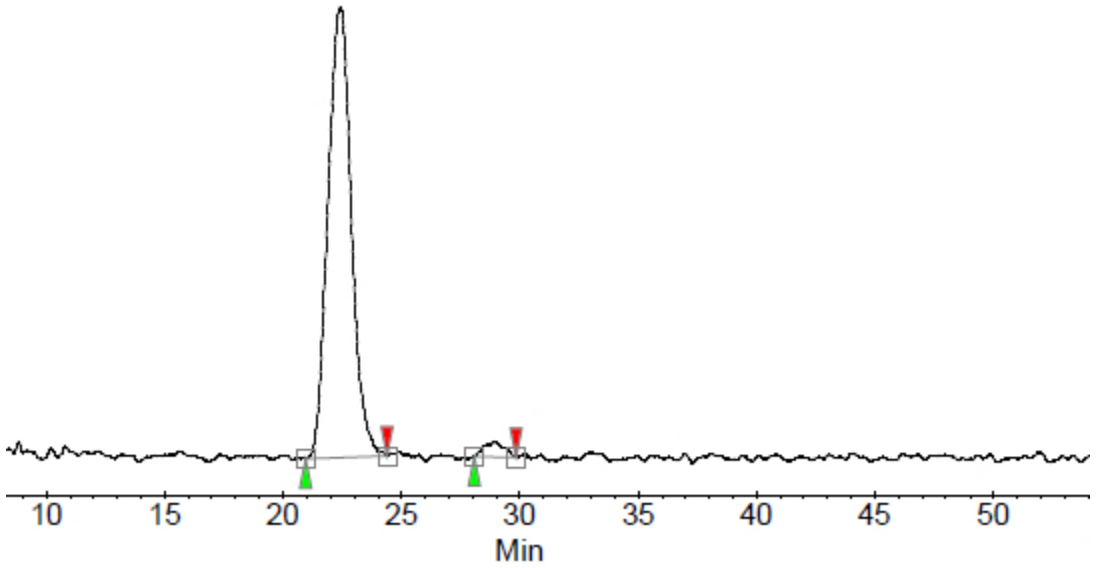



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 20.60 | 49.23 | 95.4 | 85.9 | 49.228 |
| 2 | UNKNOWN | 26.32 | 50.77 | 93.0 | 88.5 | 50.772 |
| | | | | | | |
| Total | | | 100.00 | 188.5 | 174.4 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 20.60 min., (*R*)-isomer 26.32 min.

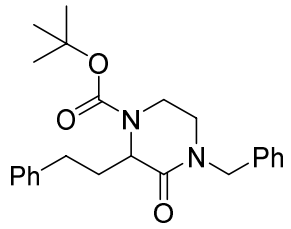



(*S*)-**2**, 94 % e.e.

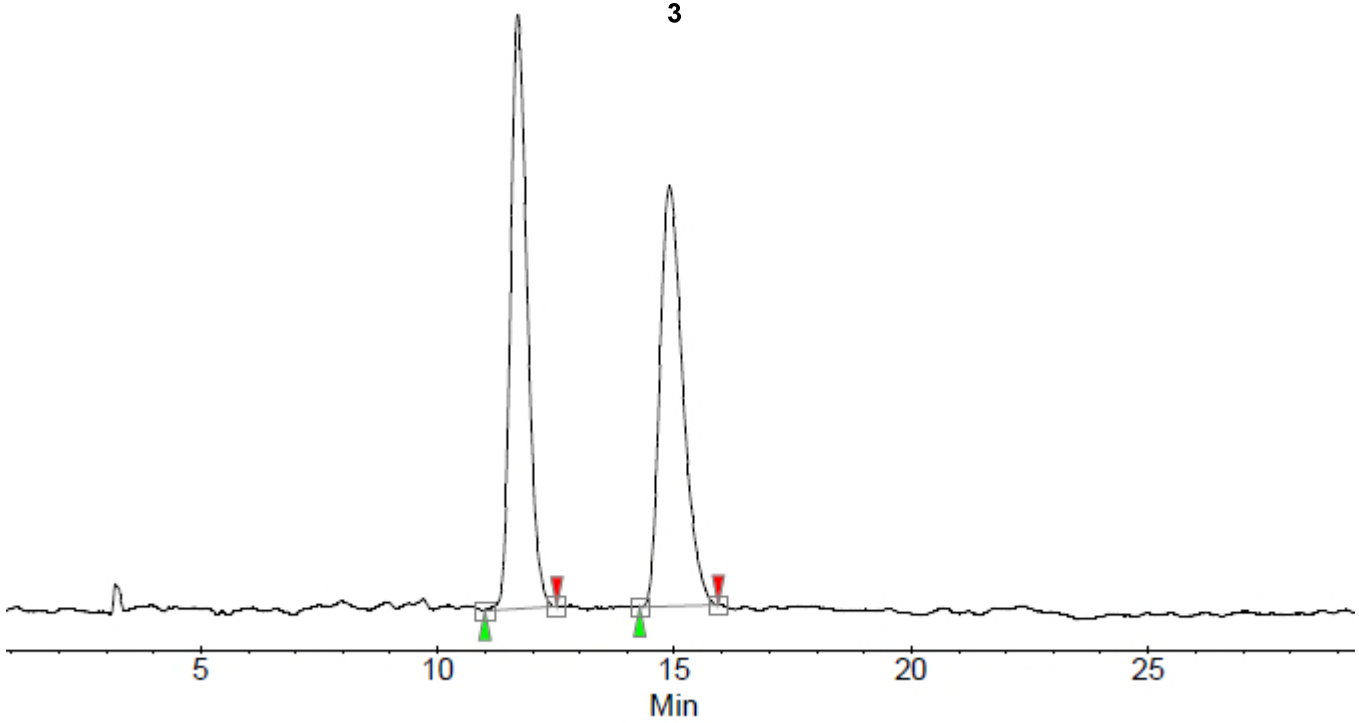



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 22.41 | 97.07 | 172.6 | 198.0 | 97.073 |
| 2 | UNKNOWN | 28.93 | 2.93 | 6.1 | 6.0 | 2.927 |
| | | | | | | |
| Total | | | 100.00 | 178.7 | 204.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 22.41 min., (*R*)-isomer 28.93 min.

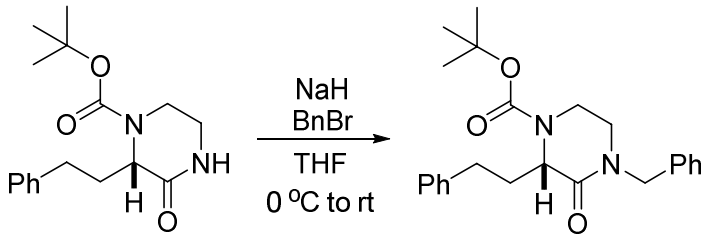


**3**

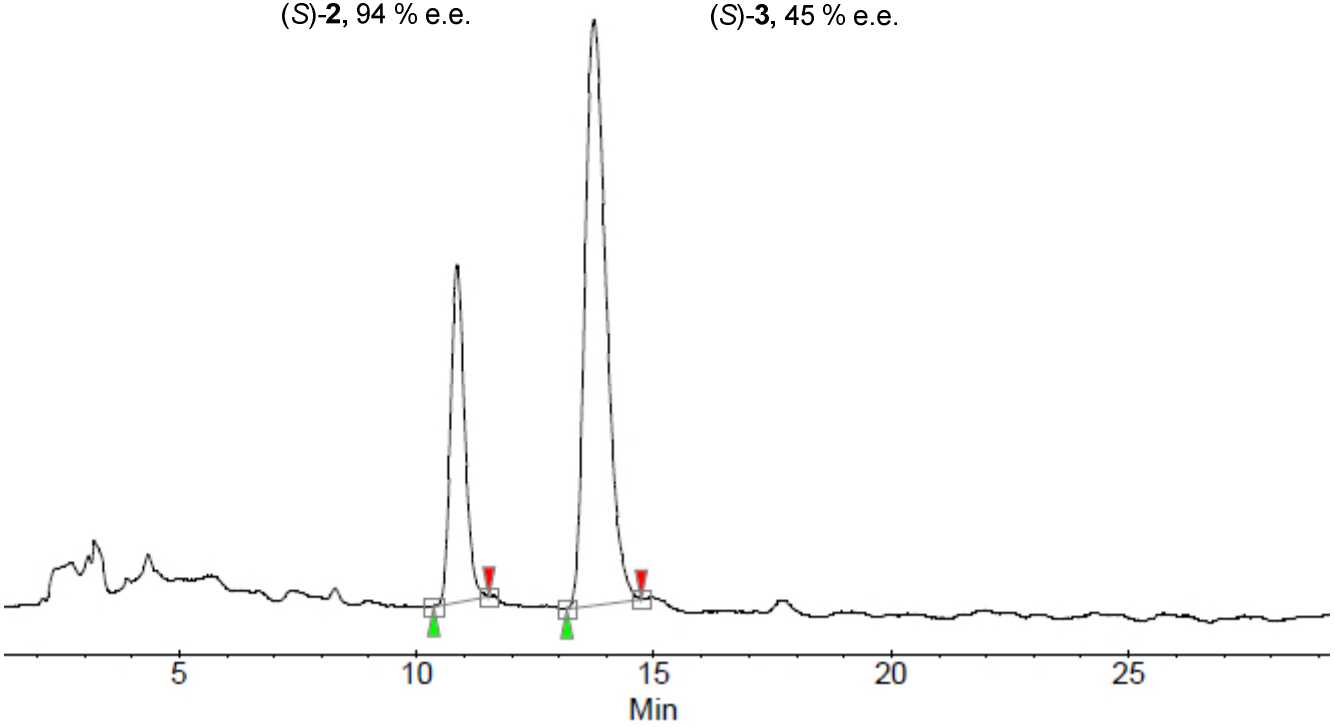



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 11.69 | 50.72 | 222.1 | 90.5 | 50.717 |
| 2 | UNKNOWN | 14.89 | 49.28 | 157.3 | 88.0 | 49.283 |
| | | | | | | |
| Total | | | 100.00 | 379.4 | 178.5 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*R*)-isomer 11.69 min., (*S*)-isomer 14.89 min.

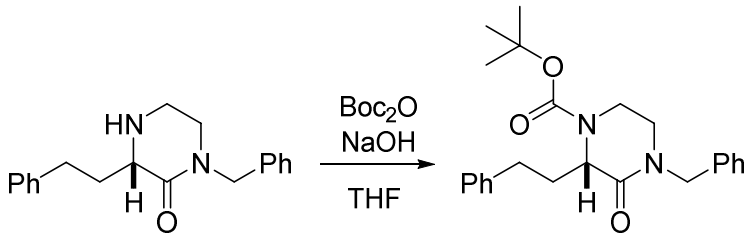



(*S*)-**2**, 94 % e.e. (*S*)-**3**, 45 % e.e.

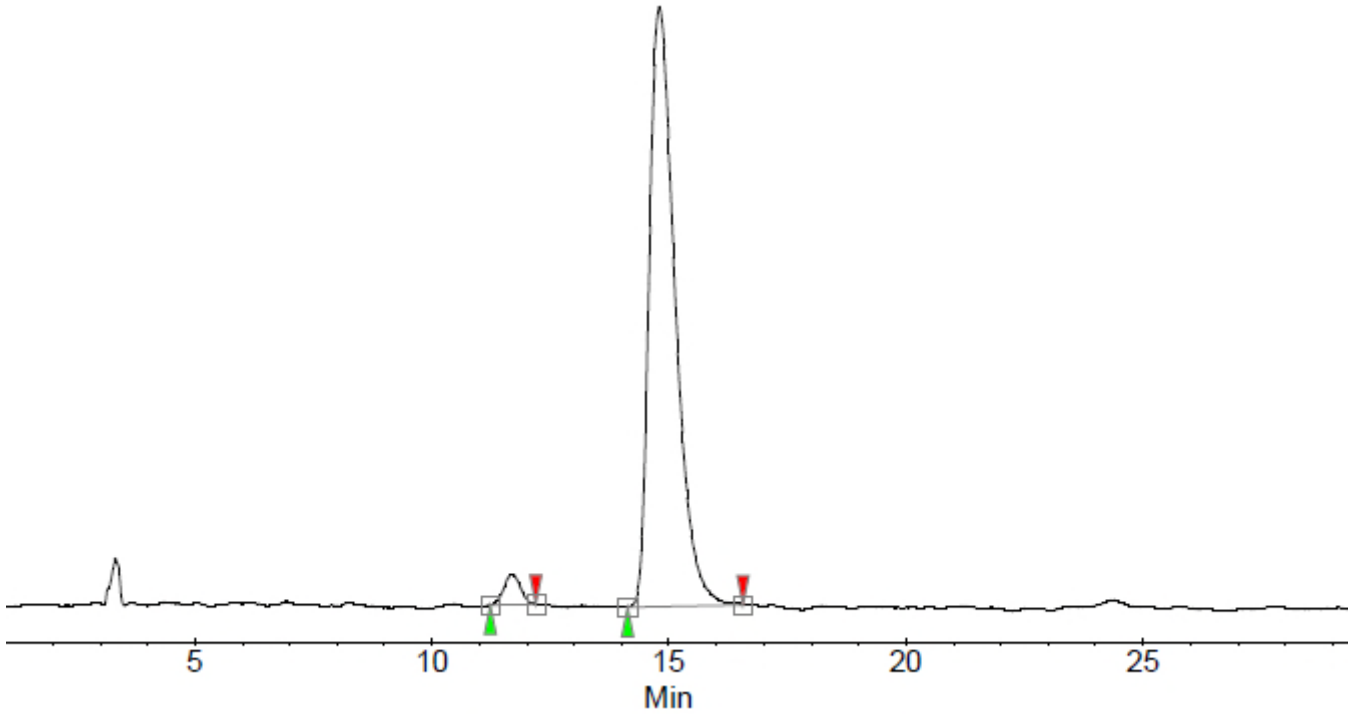



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 10.85 | 27.68 | 142.3 | 48.9 | 27.676 |
| 2 | UNKNOWN | 13.73 | 72.32 | 247.1 | 127.8 | 72.324 |
| | | | | | | |
| Total | | | 100.00 | 389.4 | 176.6 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*R*)-isomer 10.85 min., (*S*)-isomer 13.73 min.

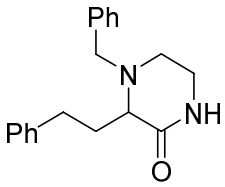



(*S*)-**5**, 95 % e.e. (*S*)-**3**, 94 % e.e.

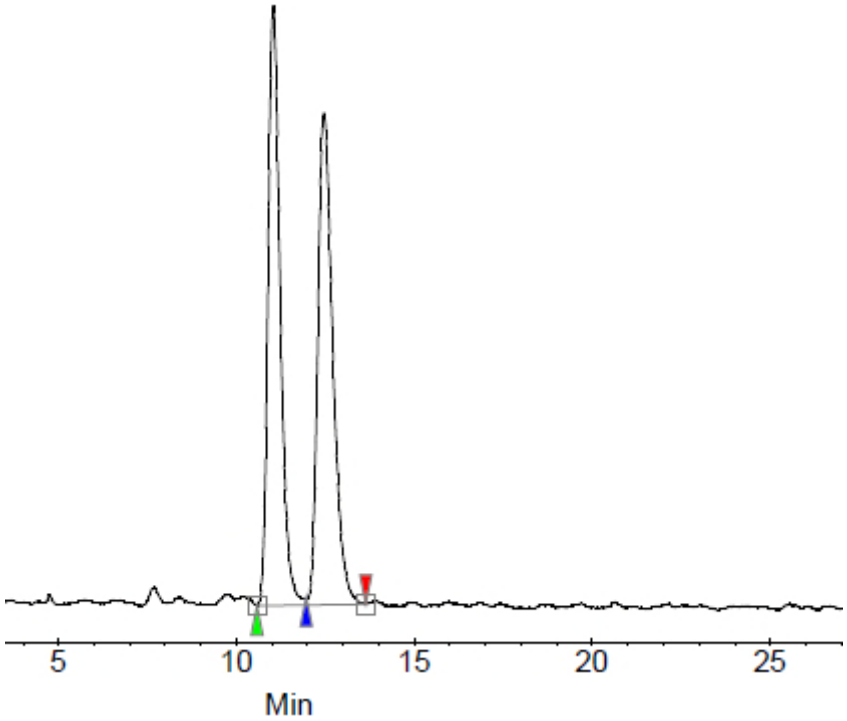



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 11.68 | 3.18 | 22.8 | 9.1 | 3.181 |
| 2 | UNKNOWN | 14.79 | 96.82 | 439.9 | 277.4 | 96.819 |
| | | | | | | |
| Total | | | 100.00 | 462.7 | 286.5 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*R*)-isomer 11.68 min., (*S*)-isomer 14.79 min.

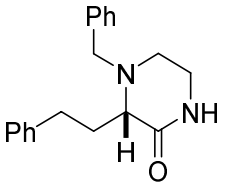



**6**

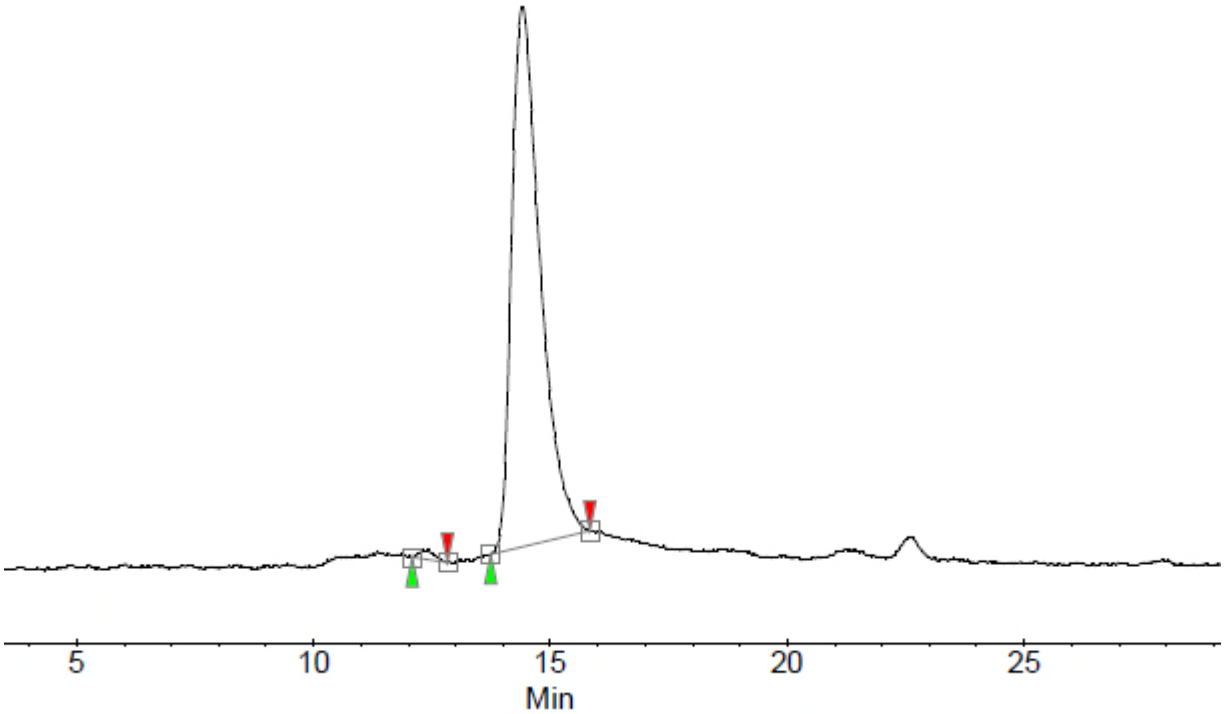



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 11.03 | 49.83 | 202.0 | 80.7 | 49.625 |
| 2 | UNKNOWN | 12.45 | 50.17 | 165.5 | 81.3 | 50.175 |
| | | | | | | |
| Total | | | 100.00 | 367.5 | 162.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 209 nm, (*S*)-isomer 11.03 min., (*R*)-isomer 12.45 min.

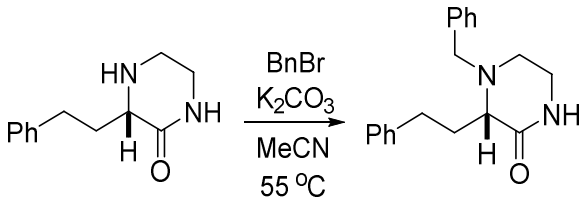



(*S*)-**6**, 98 % e.e.



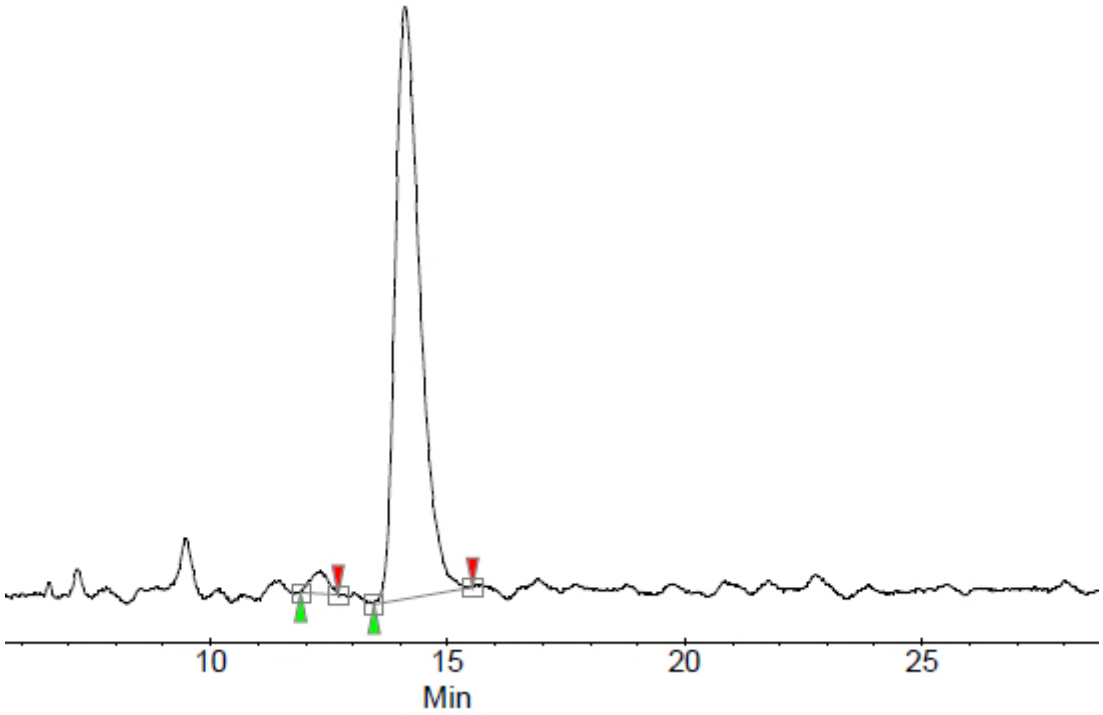

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 2 | UNKNOWN | 12.43 | 0.90 | 4.4 | 1.5 | 0.897 |
| 1 | UNKNOWN | 14.40 | 99.10 | 241.1 | 169.4 | 99.103 |
| | | | | | | |
| Total | | | 100.00 | 245.5 | 171.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 12.43 min., (*S*)-isomer 14.40 min.



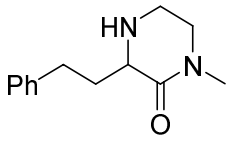

(*S*)-**1**, 95 % e.e.

(*S*)-**6**
58 %, 95 % e.e.

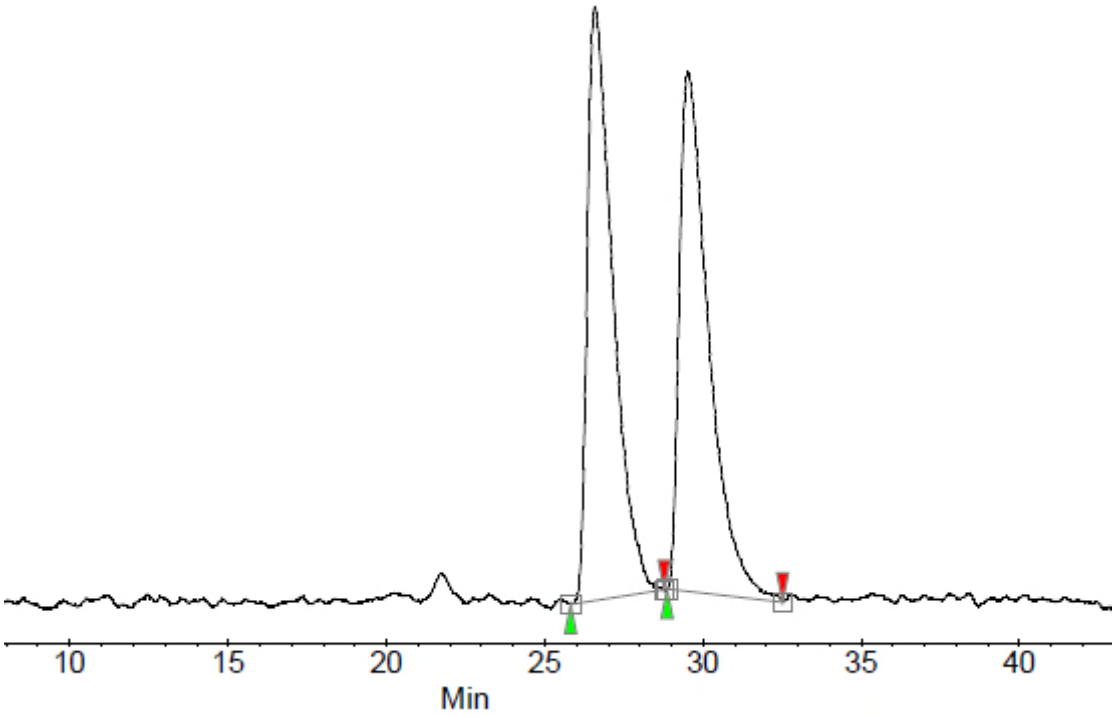



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 2 | UNKNOWN | 12.32 | 2.64 | 5.1 | 2.2 | 2.640 |
| 1 | UNKNOWN | 14.09 | 97.36 | 136.7 | 82.4 | 97.360 |
| | | | | | | |
| Total | | | 100.00 | 141.9 | 84.7 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 12.32 min., (*S*)-isomer 14.09 min.

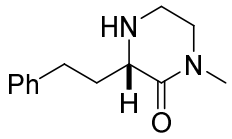



**7**

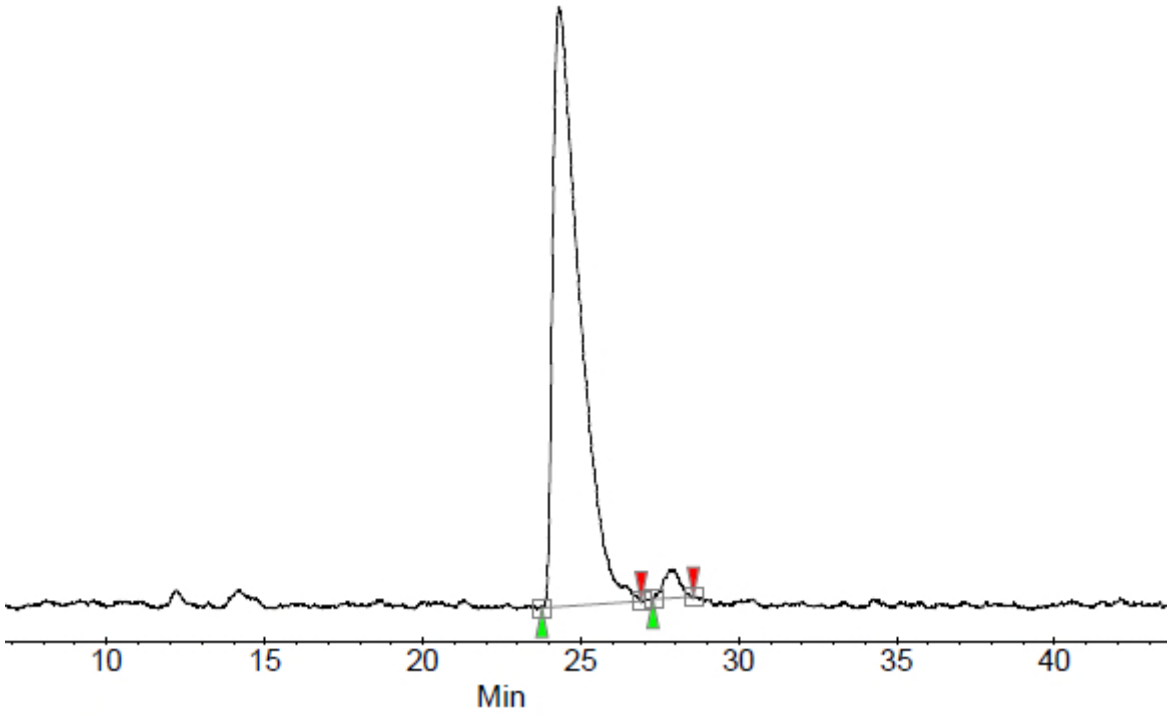



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 26.58 | 49.99 | 107.2 | 100.7 | 49.994 |
| 2 | UNKNOWN | 29.53 | 50.01 | 93.6 | 100.7 | 50.006 |
| | | | | | | |
| Total | | | 100.00 | 200.8 | 201.4 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 26.58 min., (*R*)-isomer 29.53 min.

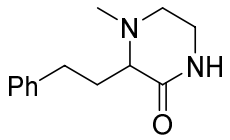



(*S*)-**7**, 94 % e.e.

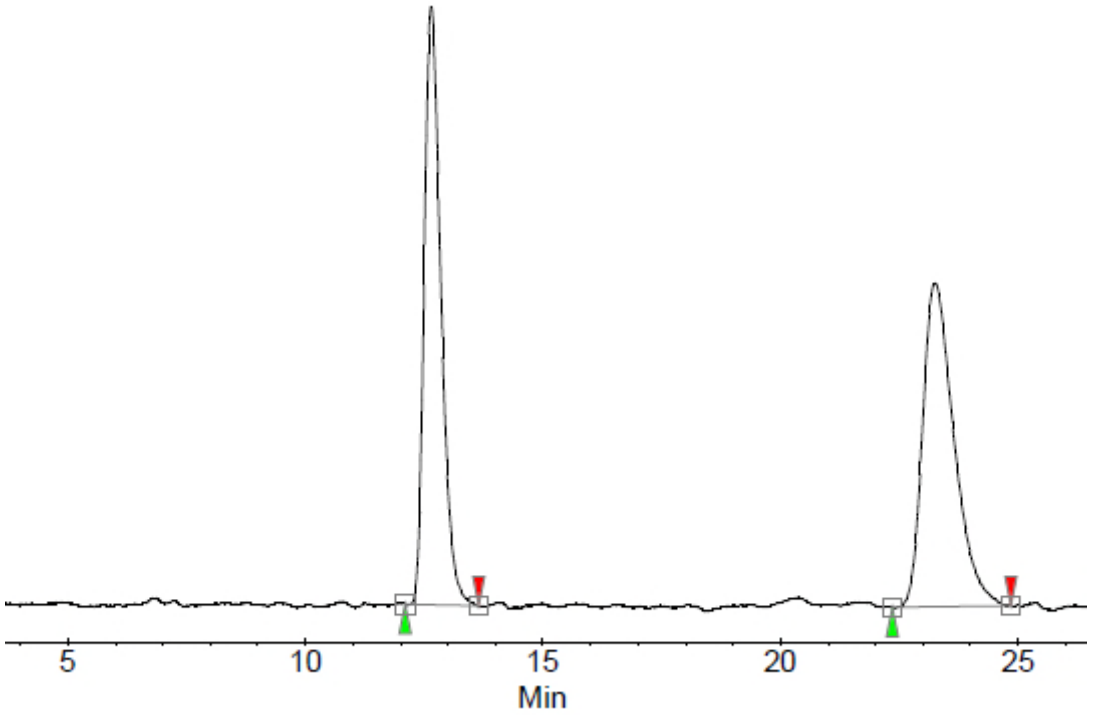



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 24.30 | 97.22 | 222.9 | 217.8 | 97.218 |
| 2 | UNKNOWN | 27.84 | 2.78 | 10.7 | 6.2 | 2.782 |
| | | | | | | |
| Total | | | 100.00 | 233.6 | 224.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 24.30 min., (*R*)-isomer 27.84 min.

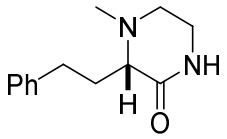



**8**

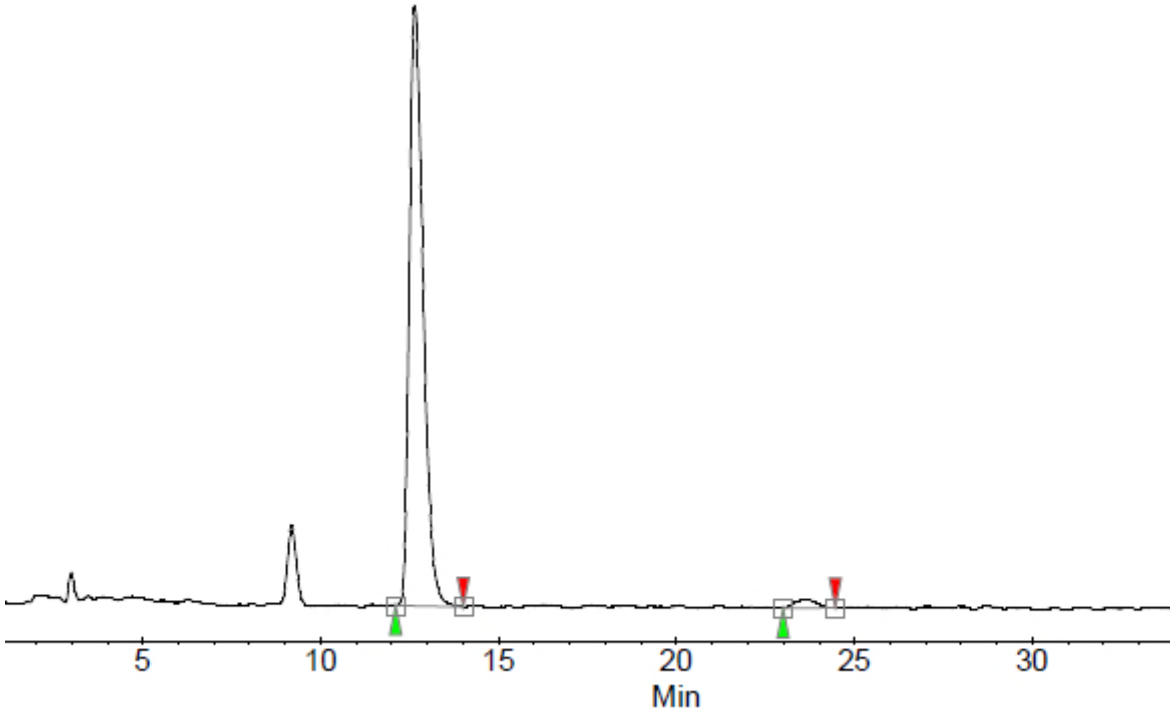



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 12.64 | 49.64 | 172.7 | 70.5 | 49.640 |
| 2 | UNKNOWN | 23.24 | 50.36 | 93.5 | 71.5 | 50.360 |
| | | | | | | |
| Total | | | 100.00 | 266.2 | 142.1 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 12.64 min., (*R*)-isomer 23.24 min.

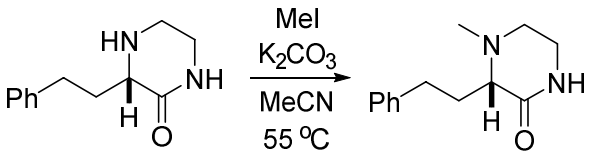



(*S*)-**8**, 95 % e.e.

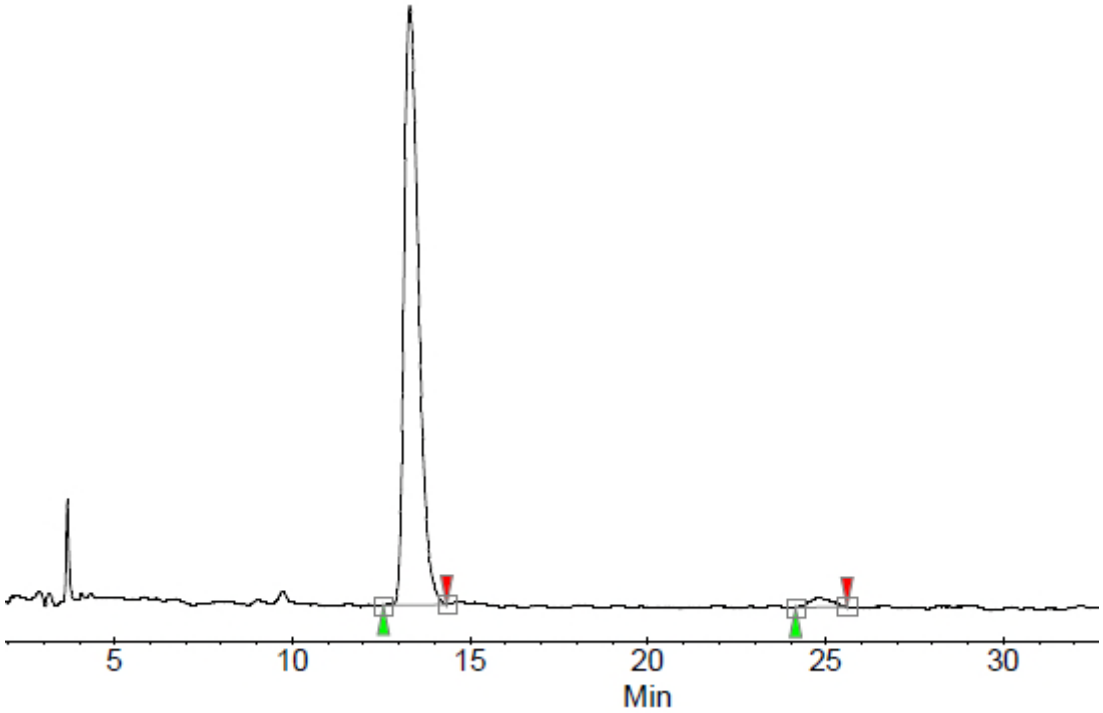



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 12.64 | 97.85 | 403.9 | 182.6 | 97.854 |
| 2 | UNKNOWN | 23.53 | 2.15 | 5.3 | 4.0 | 2.146 |
| | | | | | | |
| Total | | | 100.00 | 409.2 | 186.6 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 12.64 min., (*R*)-isomer 23.53 min.

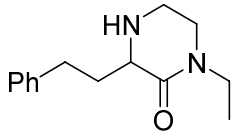



(*S*)-**1**, 95 % e.e. (*S*)-**8**, 95 % e.e.

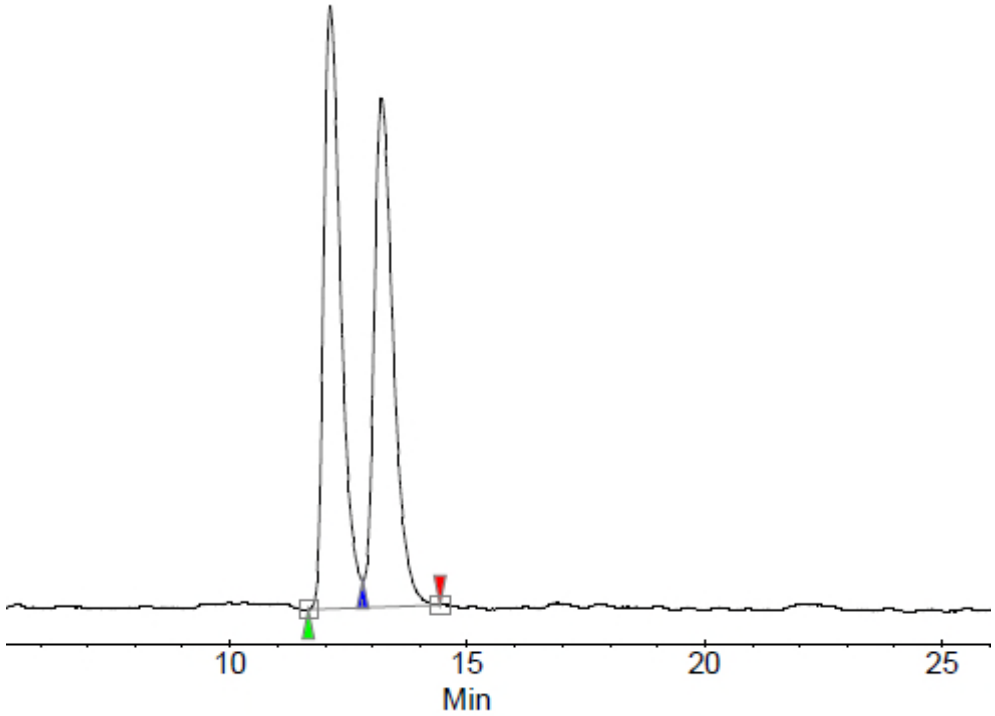



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 13.29 | 97.51 | 564.8 | 265.4 | 97.506 |
| 2 | UNKNOWN | 24.78 | 2.49 | 9.0 | 6.8 | 2.494 |
| | | | | | | |
| Total | | | 100.00 | 573.8 | 272.2 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 209 nm, (*S*)-isomer 13.29 min., (*R*)-isomer 14.78 min.

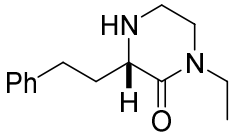



**9**

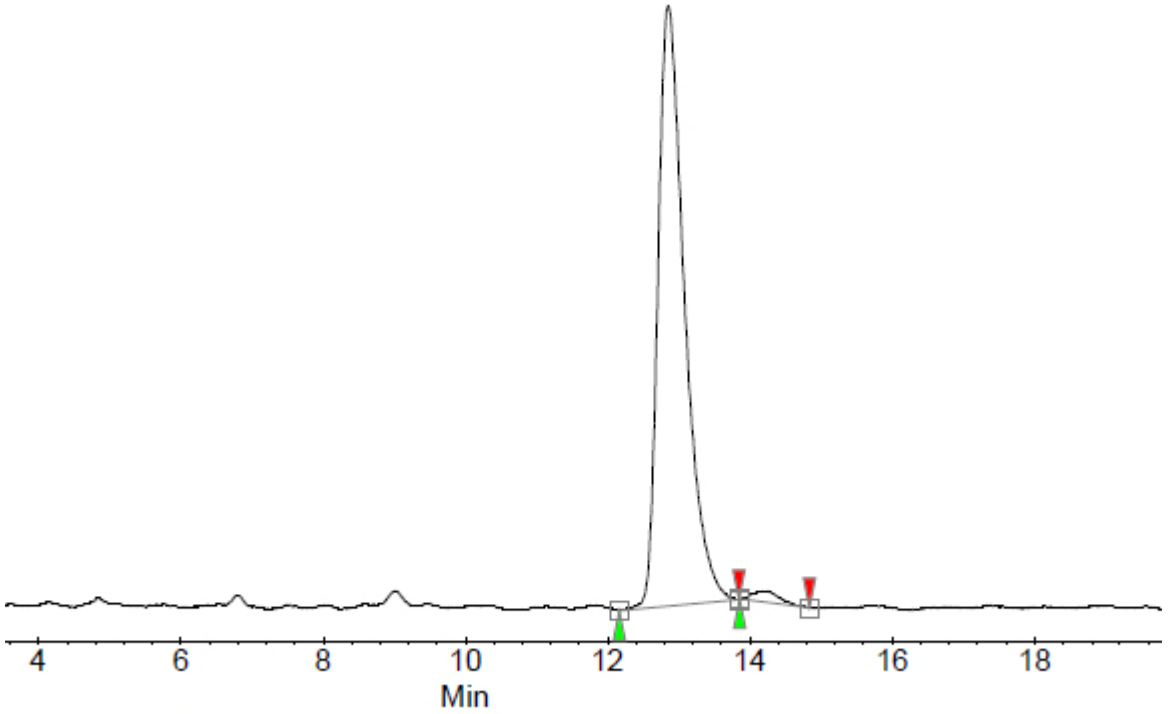



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 12.11 | 51.45 | 369.6 | 156.0 | 51.455 |
| 2 | UNKNOWN | 13.19 | 48.55 | 312.2 | 147.2 | 48.545 |
| | | | | | | |
| Total | | | 100.00 | 681.8 | 303.1 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 210 nm, (*S*)-isomer 12.11 min., (*R*)-isomer 13.19 min.

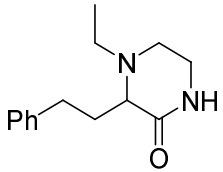



(*S*)-**9**, 96 % e.e.

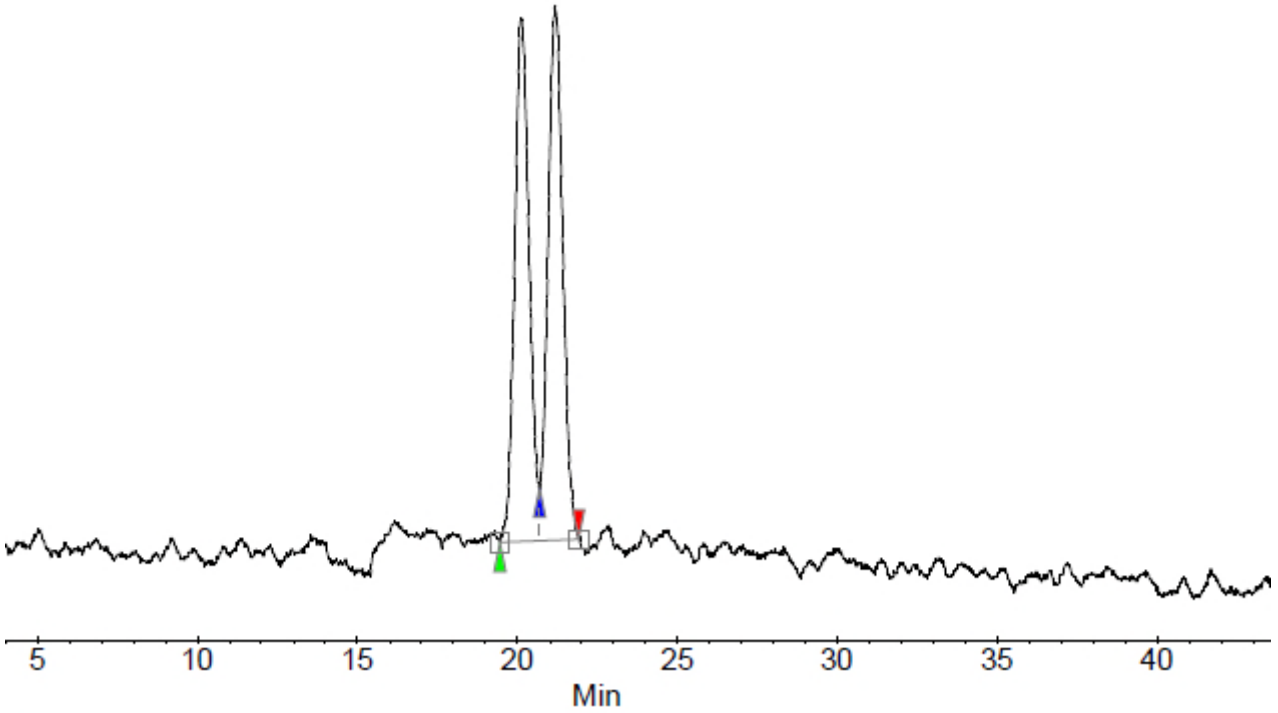



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 12.85 | 98.08 | 186.9 | 81.1 | 98.081 |
| 2 | UNKNOWN | 14.24 | 1.92 | 3.6 | 1.6 | 1.919 |
| | | | | | | |
| Total | | | 100.00 | 190.4 | 82.6 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 210 nm, (*S*)-isomer 12.85 min., (*R*)-isomer 14.24 min.

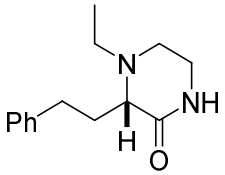



**10**

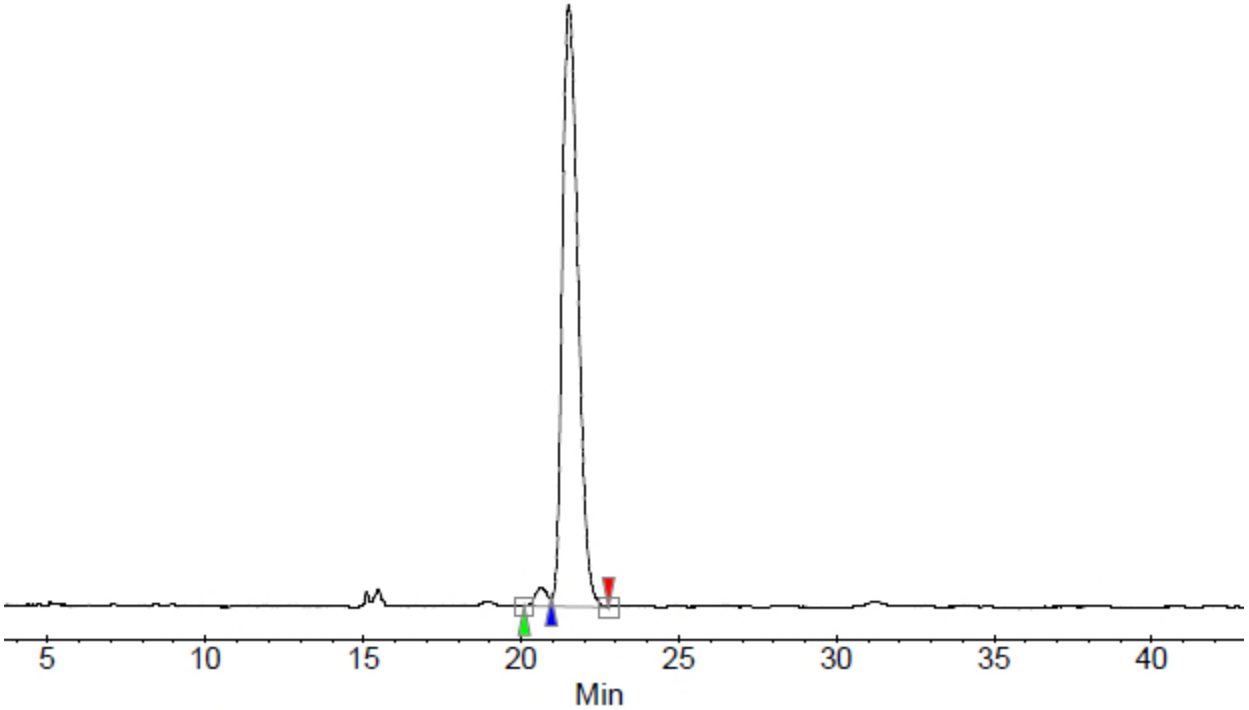



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 20.12 | 49.01 | 40.9 | 21.6 | 49.006 |
| 2 | UNKNOWN | 21.17 | 50.99 | 41.8 | 22.4 | 50.994 |
| | | | | | | |
| Total | | | 100.00 | 82.7 | 44.0 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 208 nm, (*R*)-isomer 20.12 min., (*S*)-isomer 21.17 min.

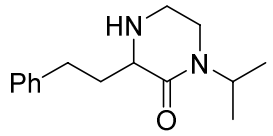



(*S*)-**10**, 95 % e.e.

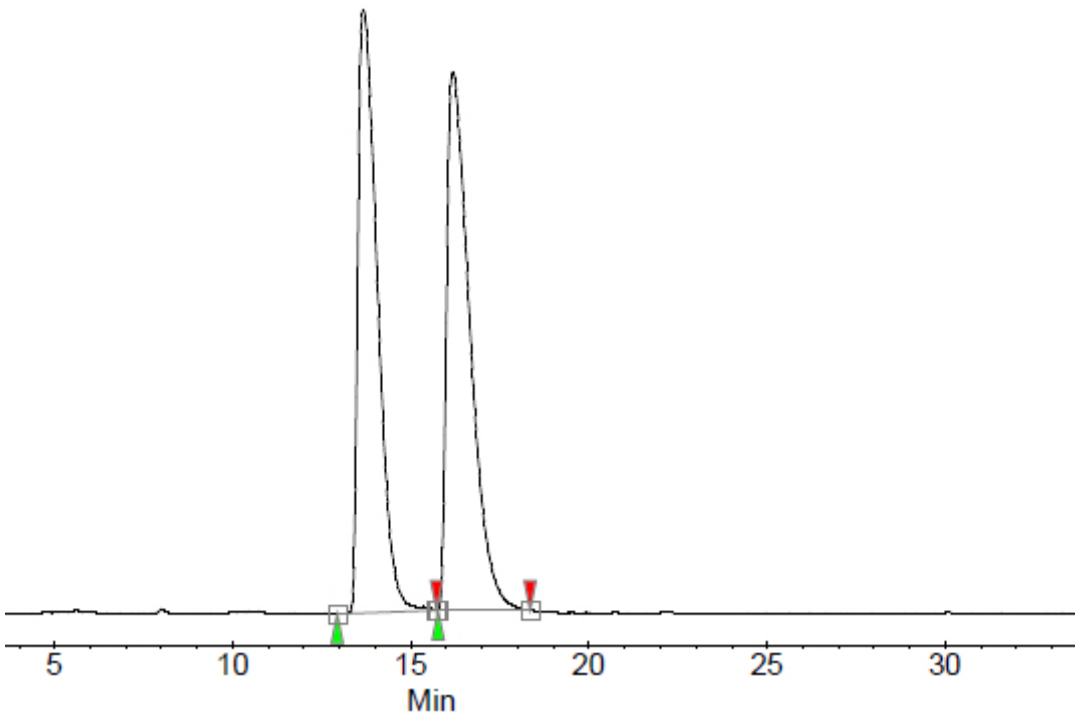



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 20.63 | 2.28 | 19.2 | 8.2 | 2.277 |
| 2 | UNKNOWN | 21.51 | 97.72 | 615.3 | 353.2 | 97.723 |
| | | | | | | |
| Total | | | 100.00 | 634.5 | 361.4 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 208 nm, (*R*)-isomer 20.63 min., (*S*)-isomer 21.51 min.

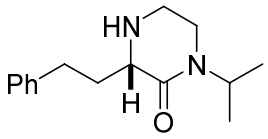



**11**

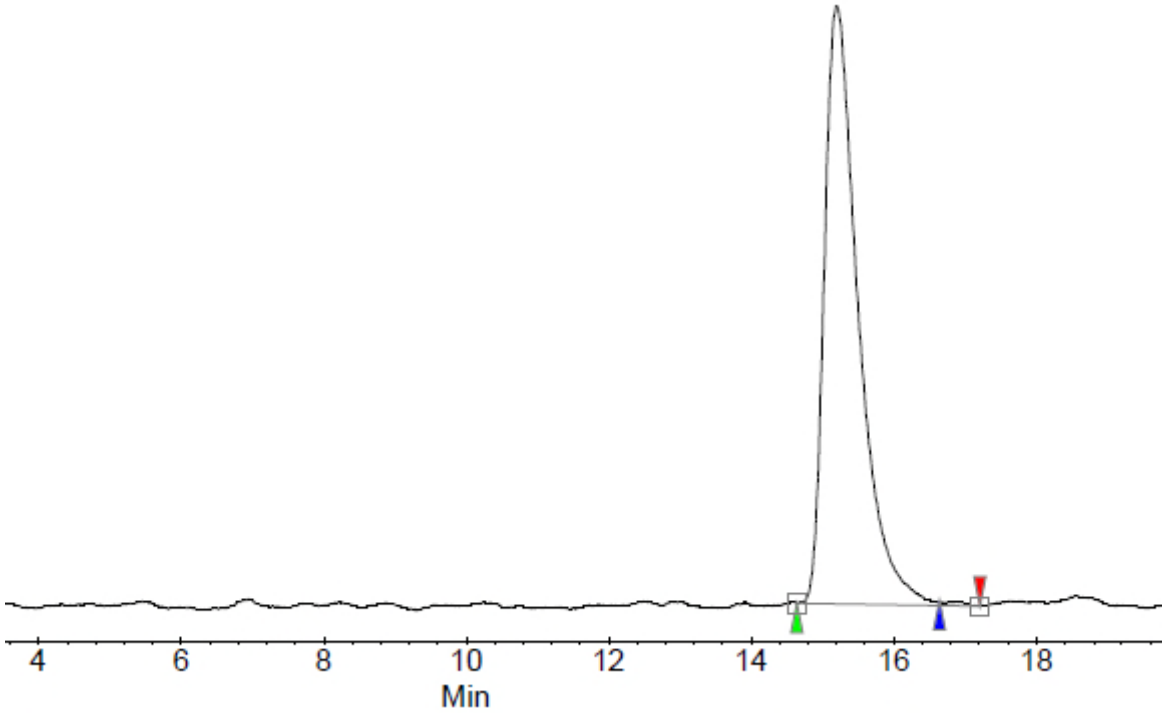



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 13.67 | 48.58 | 876.0 | 556.7 | 48.583 |
| 2 | UNKNOWN | 16.19 | 51.42 | 781.5 | 589.2 | 51.417 |
| | | | | | | |
| Total | | | 100.00 | 1657.4 | 1145.9 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 212 nm, (*S*)-isomer 13.67 min., (*R*)-isomer 16.19 min.

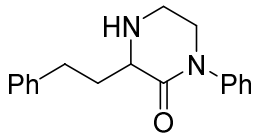



(*S*)-**11**, 99 % e.e.

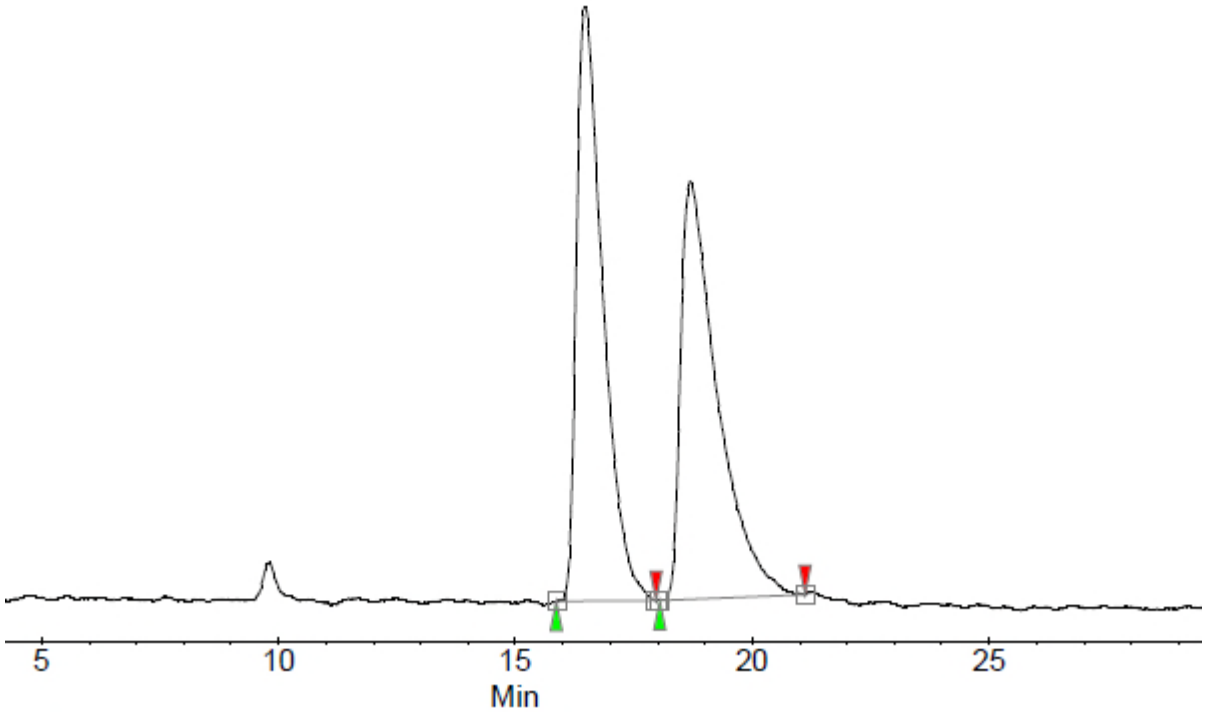



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 15.20 | 99.59 | 148.3 | 81.9 | 99.589 |
| 2 | UNKNOWN | 16.83 | 0.41 | 0.9 | 0.3 | 0.411 |
| | | | | | | |
| Total | | | 100.00 | 149.2 | 82.2 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 212 nm, (*S*)-isomer 15.20 min., (*R*)-isomer 16.83 min.

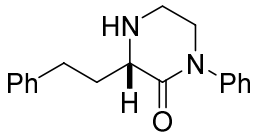



**12**

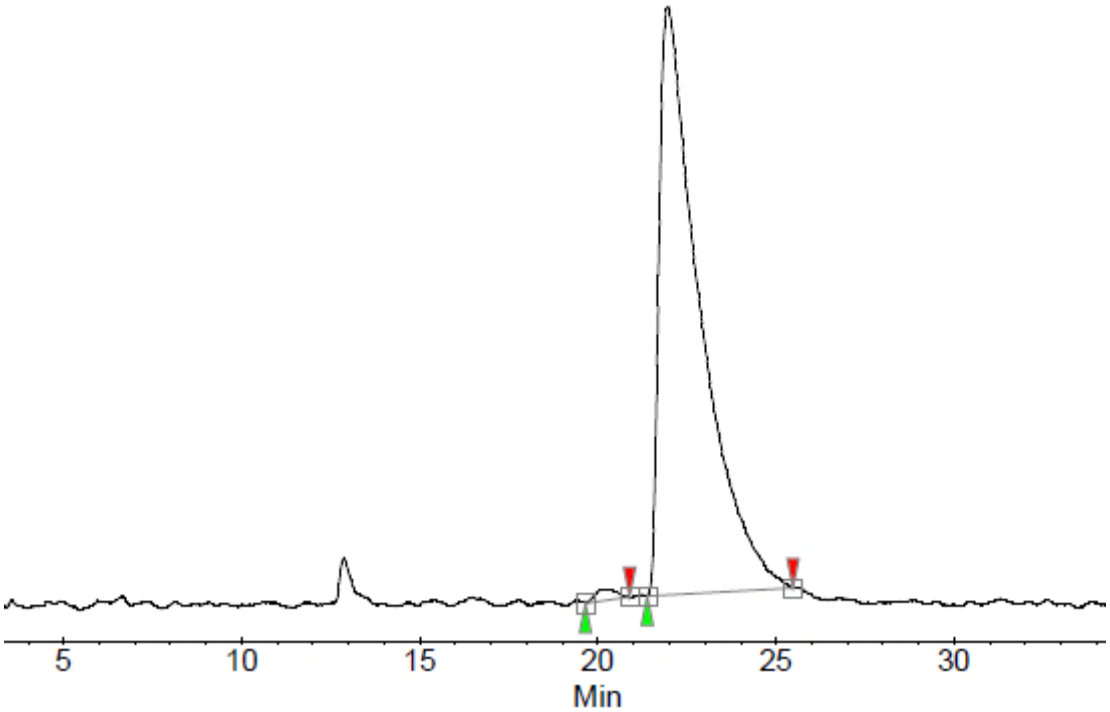



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 16.47 | 50.72 | 205.2 | 133.1 | 50.724 |
| 2 | UNKNOWN | 18.69 | 49.28 | 144.1 | 129.3 | 49.276 |
| | | | | | | |
| Total | | | 100.00 | 349.3 | 262.3 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 20 : 80, 1 mL/min., 208 nm, (*S*)-isomer 16.47 min., (*R*)-isomer 18.69 min.

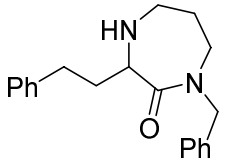



(*S*)-**12**, 98 % e.e.

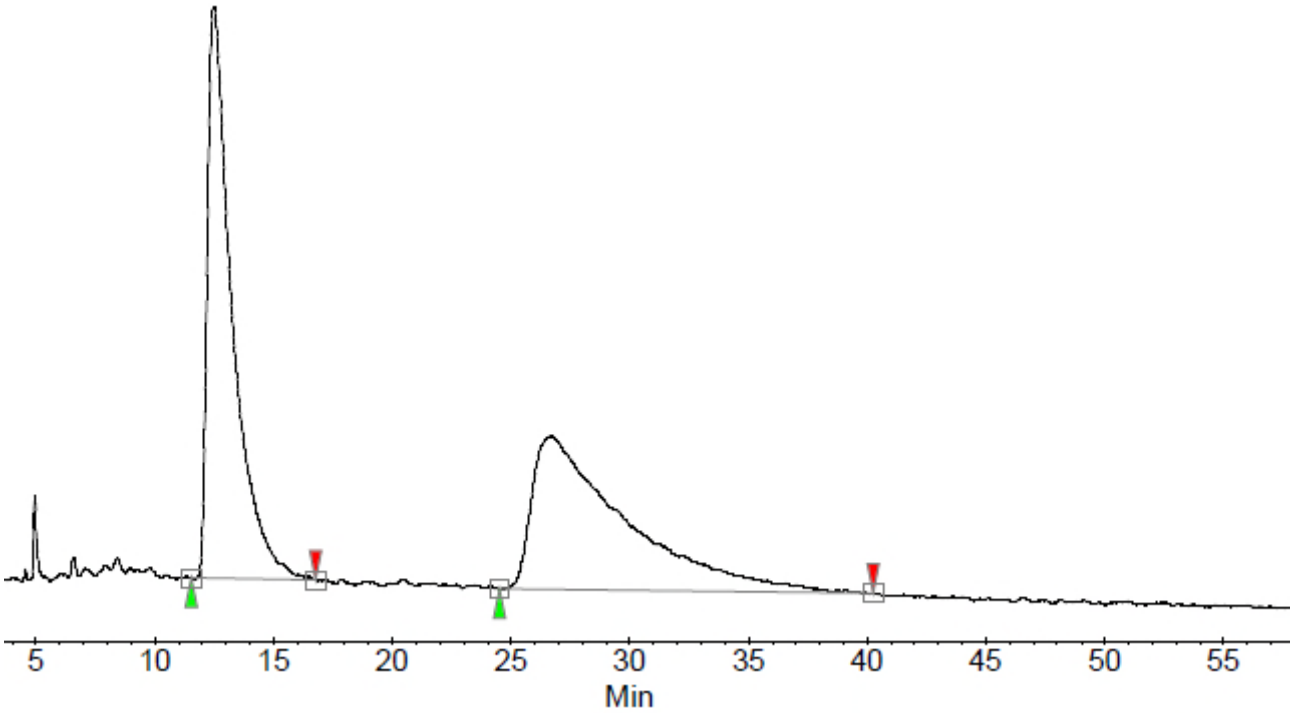



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 2 | UNKNOWN | 20.09 | 1.02 | 6.6 | 4.5 | 1.016 |
| 1 | UNKNOWN | 21.96 | 98.98 | 332.7 | 440.3 | 98.984 |
| | | | | | | |
| Total | | | 100.00 | 339.3 | 444.8 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 20 : 80, 1 mL/min., 208 nm, (*S*)-isomer 20.09 min., (*R*)-isomer 21.96 min.

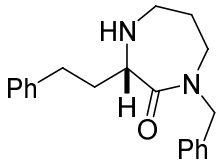



**13**

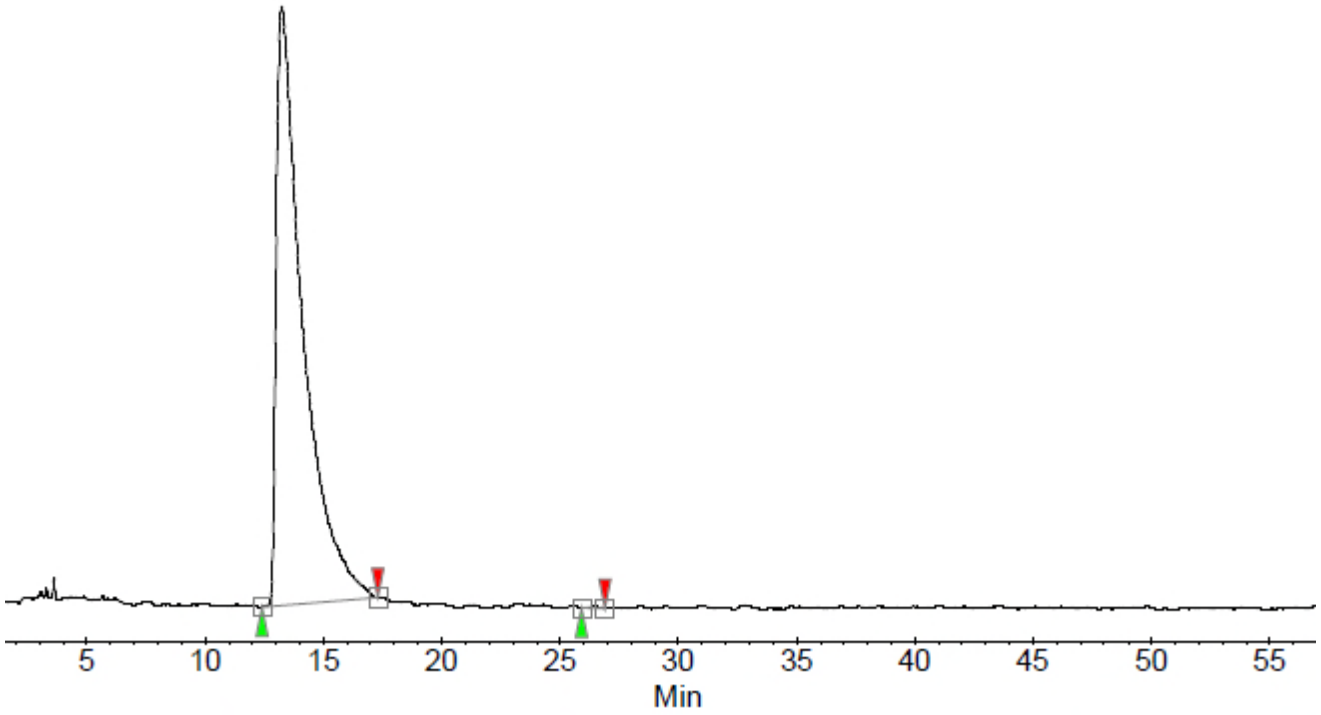



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 12.49 | 49.93 | 236.4 | 287.1 | 49.926 |
| 2 | UNKNOWN | 26.68 | 50.07 | 63.5 | 287.9 | 50.074 |
| | | | | | | |
| Total | | | 100.00 | 299.9 | 575.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 80 : 20, 1 mL/min., 210 nm, (*S*)-isomer 12.49 min., (*R*)-isomer 26.68 min.

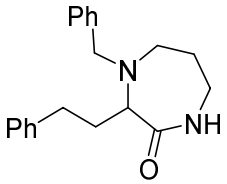



(*S*)-**13**, 99 % e.e.

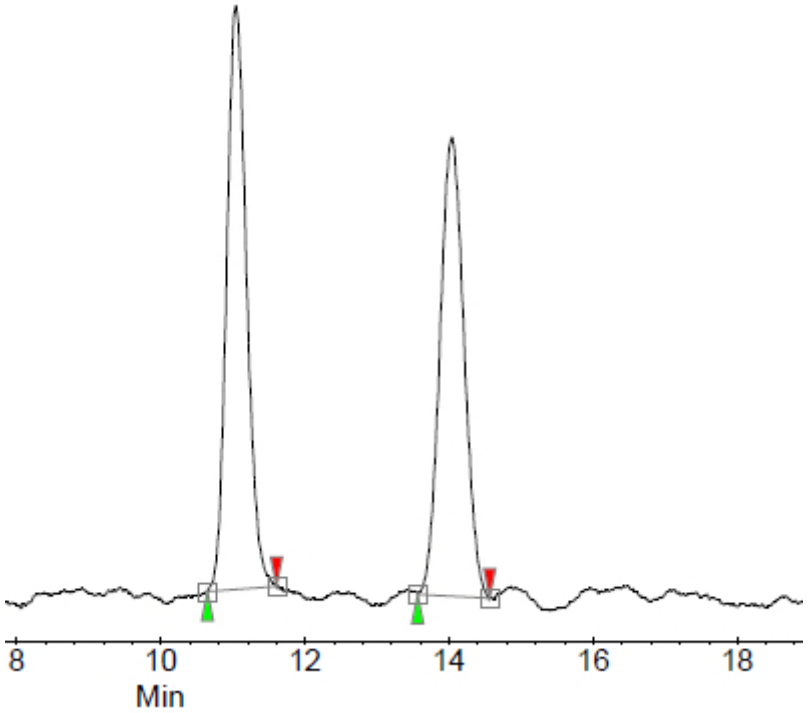



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 13.23 | 99.84 | 582.4 | 759.8 | 99.841 |
| 2 | UNKNOWN | 26.41 | 0.16 | 2.5 | 1.2 | 0.159 |
| | | | | | | |
| Total | | | 100.00 | 584.9 | 761.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 20 : 80, 1 mL/min., 210 nm, (*S*)-isomer 13.23 min., (*R*)-isomer 26.41 min.

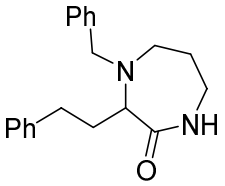



**14**

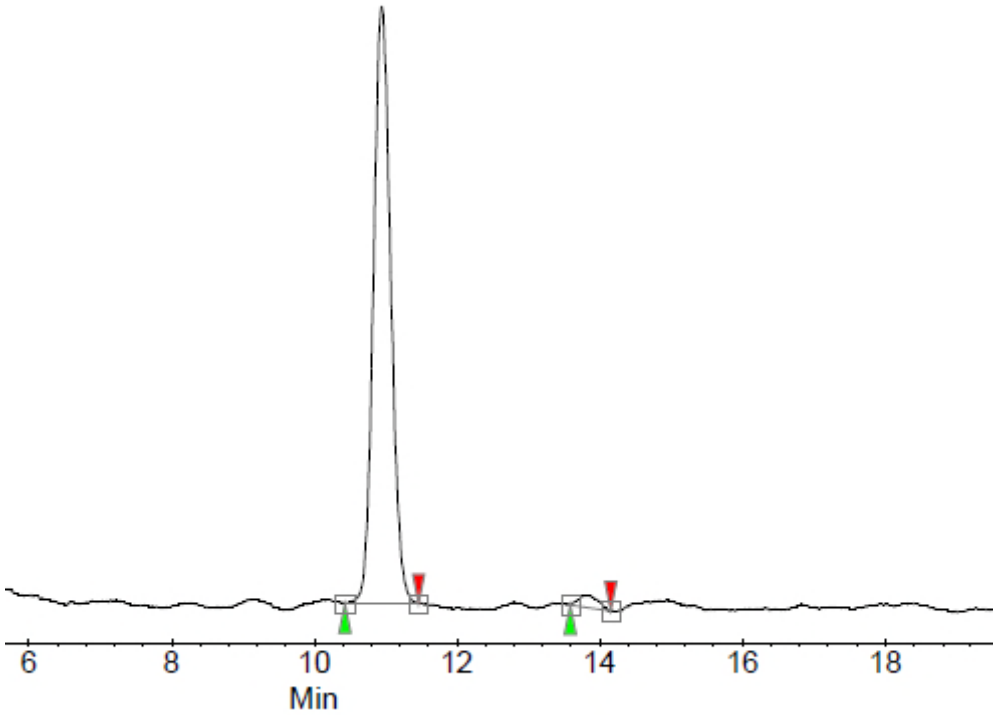



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 2 | UNKNOWN | 11.04 | 51.26 | 93.0 | 29.7 | 51.257 |
| 1 | UNKNOWN | 14.03 | 48.74 | 72.9 | 28.2 | 48.743 |
| | | | | | | |
| Total | | | 100.00 | 165.8 | 57.9 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 11.04 min., (*R*)-isomer 14.03 min.

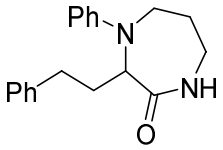



(*S*)-**14**, 96 % e.e.

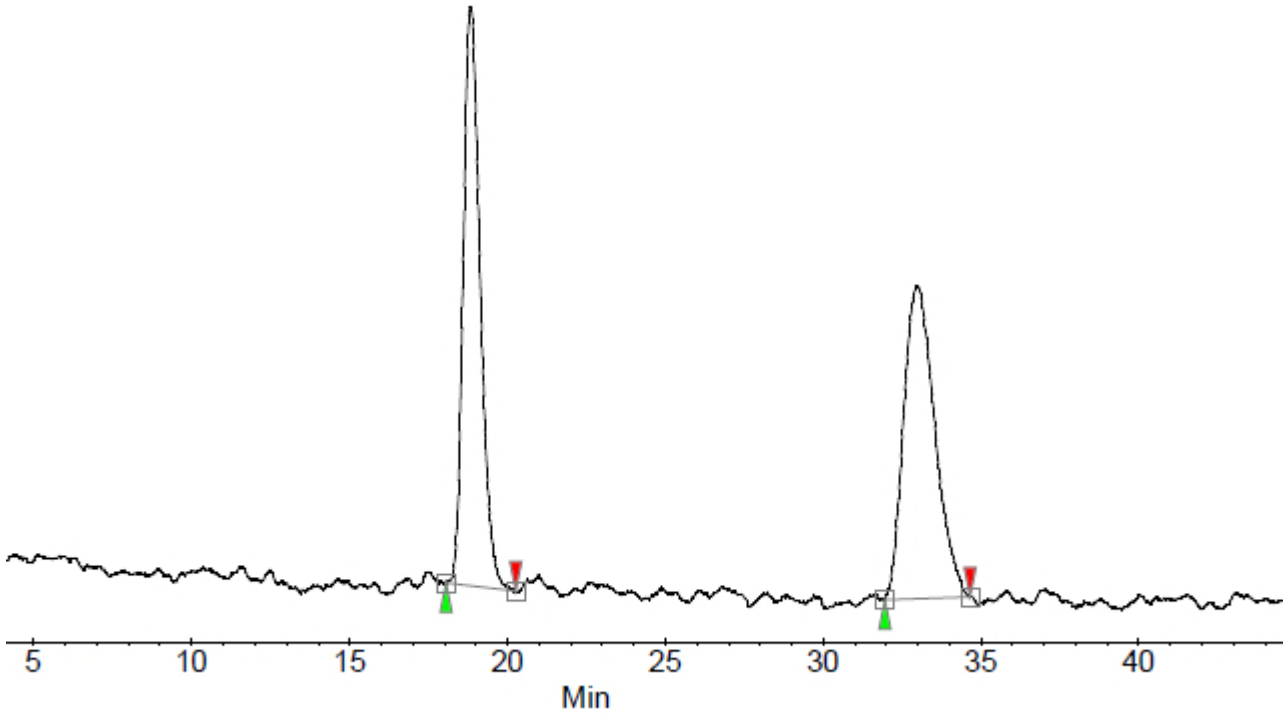



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 10.95 | 97.75 | 186.3 | 52.5 | 97.754 |
| 2 | UNKNOWN | 13.87 | 2.25 | 3.8 | 1.2 | 2.246 |
| | | | | | | |
| Total | | | 100.00 | 190.1 | 53.7 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 10.95 min., (*R*)-isomer 13.87 min.

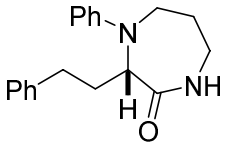



**17**

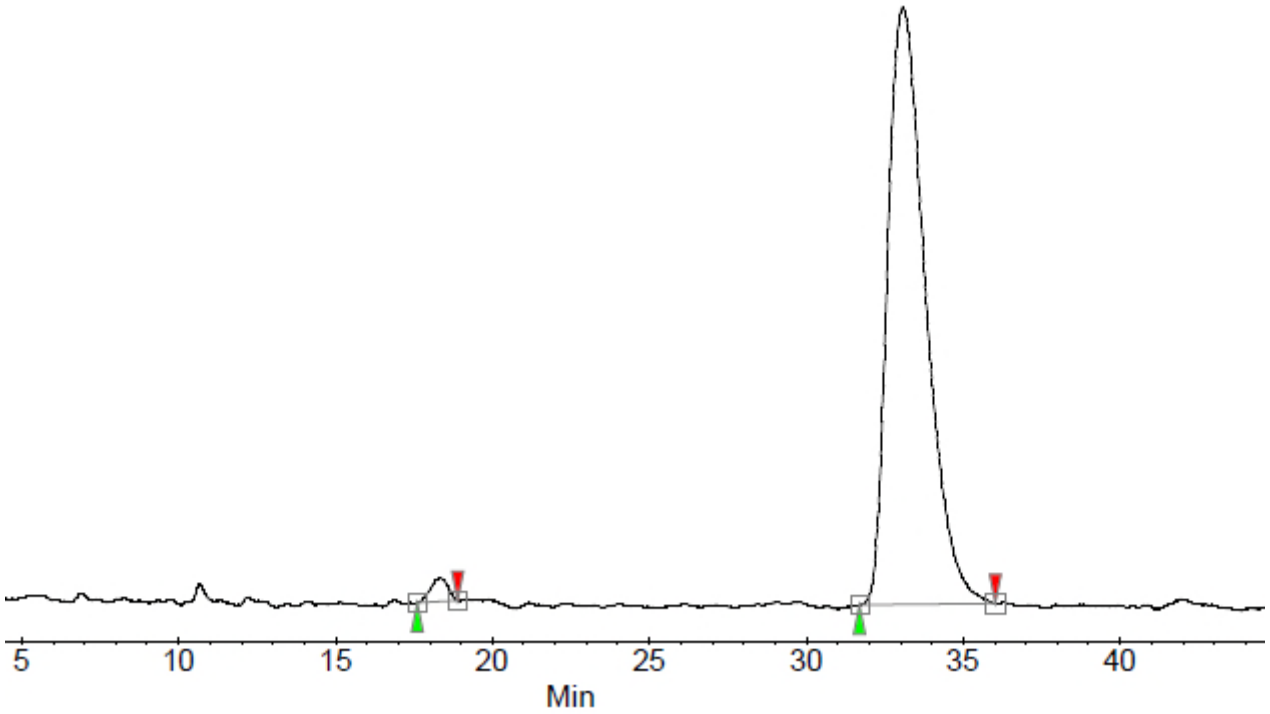



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 18.83 | 50.16 | 130.8 | 81.6 | 50.165 |
| 2 | UNKNOWN | 33.00 | 49.84 | 70.6 | 81.1 | 49.835 |
| | | | | | | |
| Total | | | 100.00 | 201.4 | 162.7 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 207 nm, (*R*)-isomer 18.83 min., (*S*)-isomer 33.00 min.

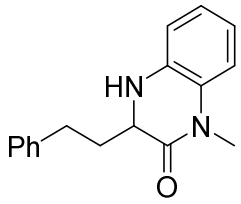



(*S*)-**17**, 96 % e.e.

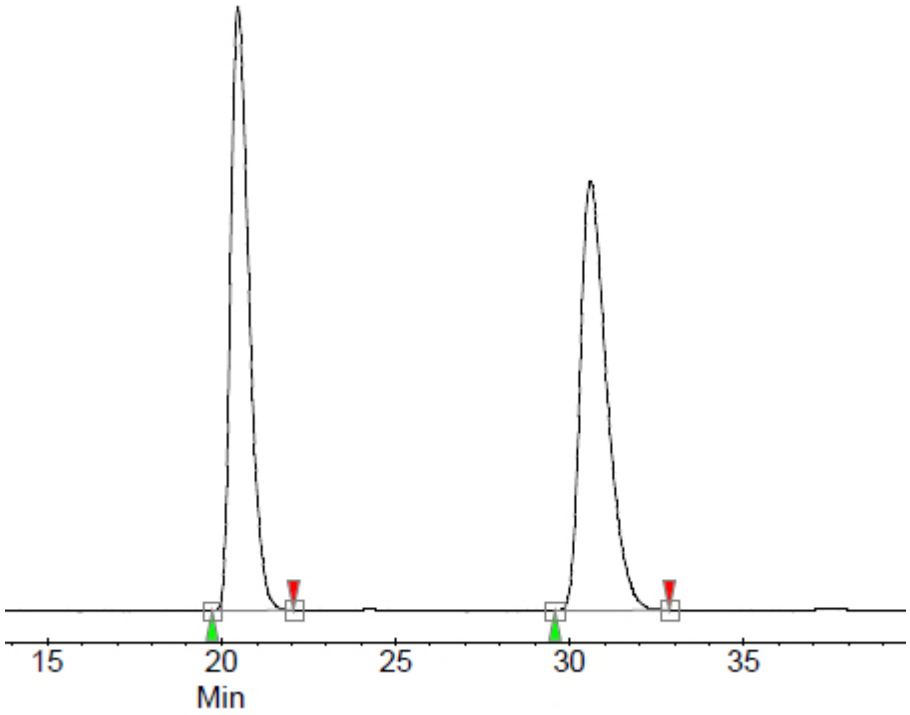



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 18.32 | 1.76 | 15.0 | 9.8 | 1.765 |
| 2 | UNKNOWN | 33.08 | 98.24 | 391.5 | 546.9 | 98.235 |
| | | | | | | |
| Total | | | 100.00 | 406.5 | 556.7 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 207 nm, (*R*)-isomer 18.32 min., (*S*)-isomer 33.08 min.

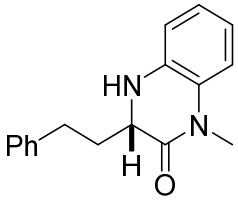



**18**

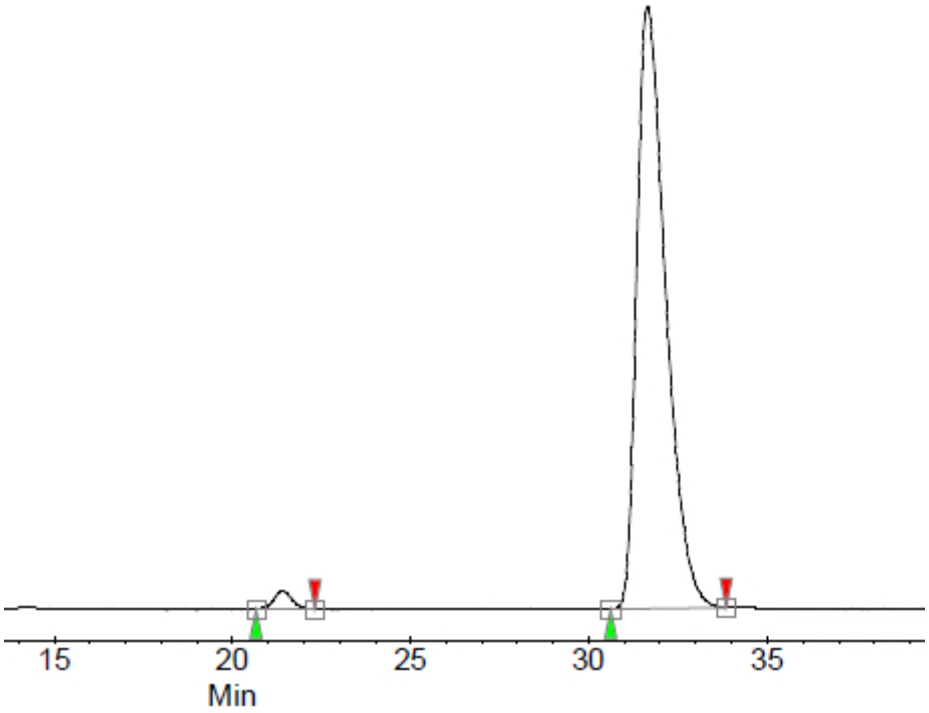



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 20.47 | 49.18 | 958.4 | 583.1 | 49.181 |
| 2 | UNKNOWN | 30.60 | 50.82 | 681.5 | 602.5 | 50.819 |
| | | | | | | |
| Total | | | 100.00 | 1639.8 | 1185.5 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 222 nm, (*R*)-isomer 20.47 min., (*S*)-isomer 30.60 min.

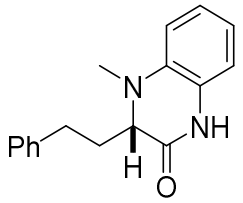



(*S*)-**18**, 96 % e.e.

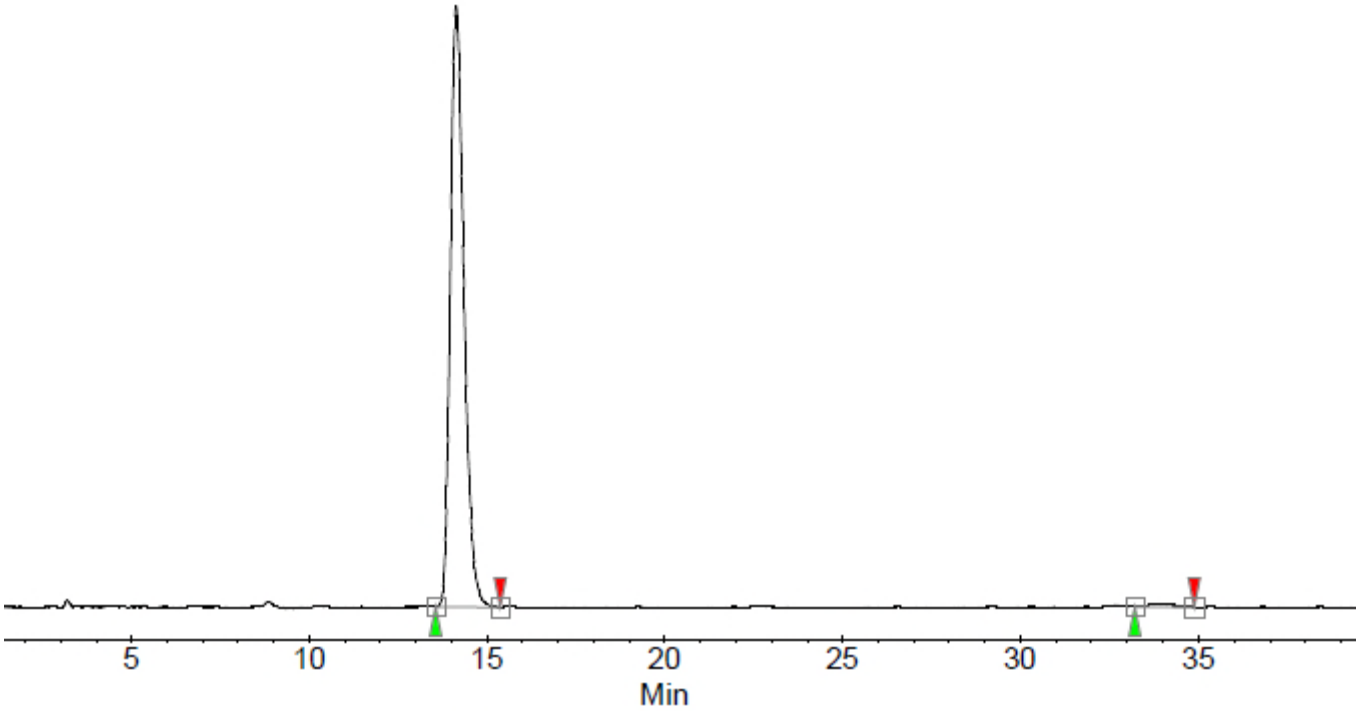



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 21.39 | 1.87 | 24.7 | 14.8 | 1.871 |
| 2 | UNKNOWN | 31.64 | 98.13 | 823.0 | 774.7 | 98.129 |
| | | | | | | |
| Total | | | 100.00 | 847.7 | 789.5 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 222 nm, (*R*)-isomer 21.39 min., (*S*)-isomer 31.64 min.

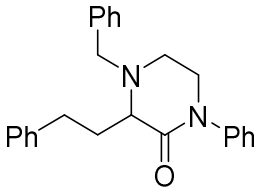



(*S*)-**19**, 98 % e.e.

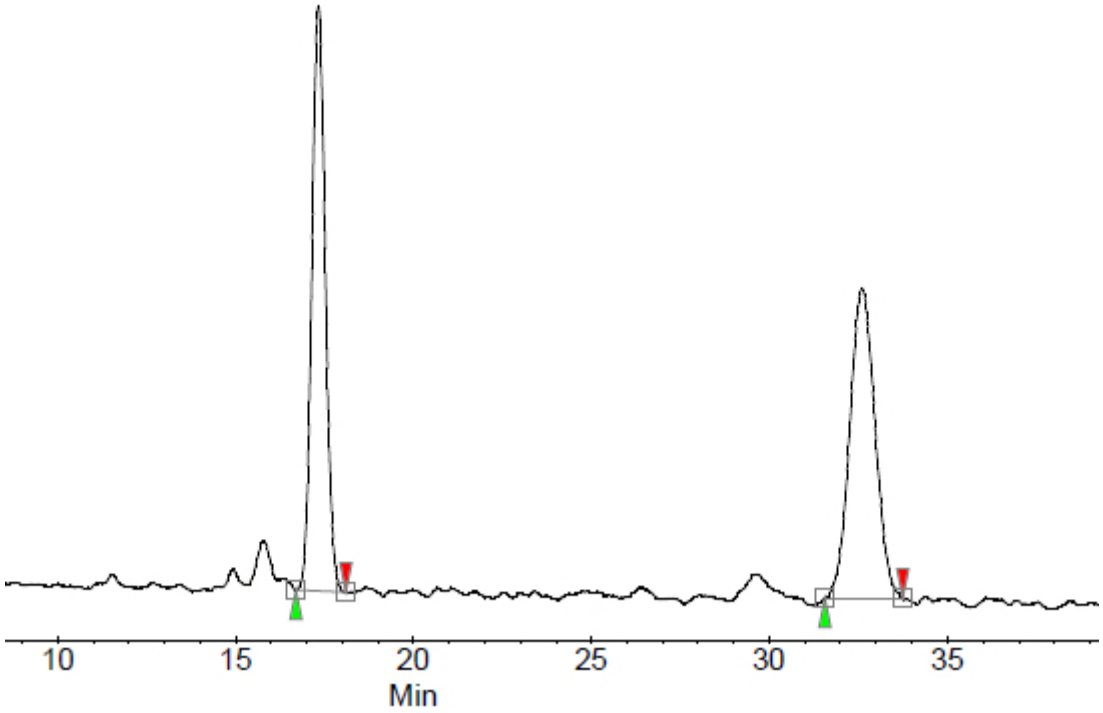



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 14.12 | 98.83 | 372.2 | 166.1 | 98.832 |
| 2 | UNKNOWN | 33.82 | 1.17 | 2.1 | 2.0 | 1.168 |
| | | | | | | |
| Total | | | 100.00 | 374.3 | 168.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 222 nm, (*S*)-isomer 14.12 min., (*R*)-isomer 33.82 min.

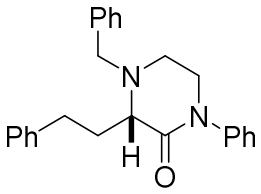



**20**

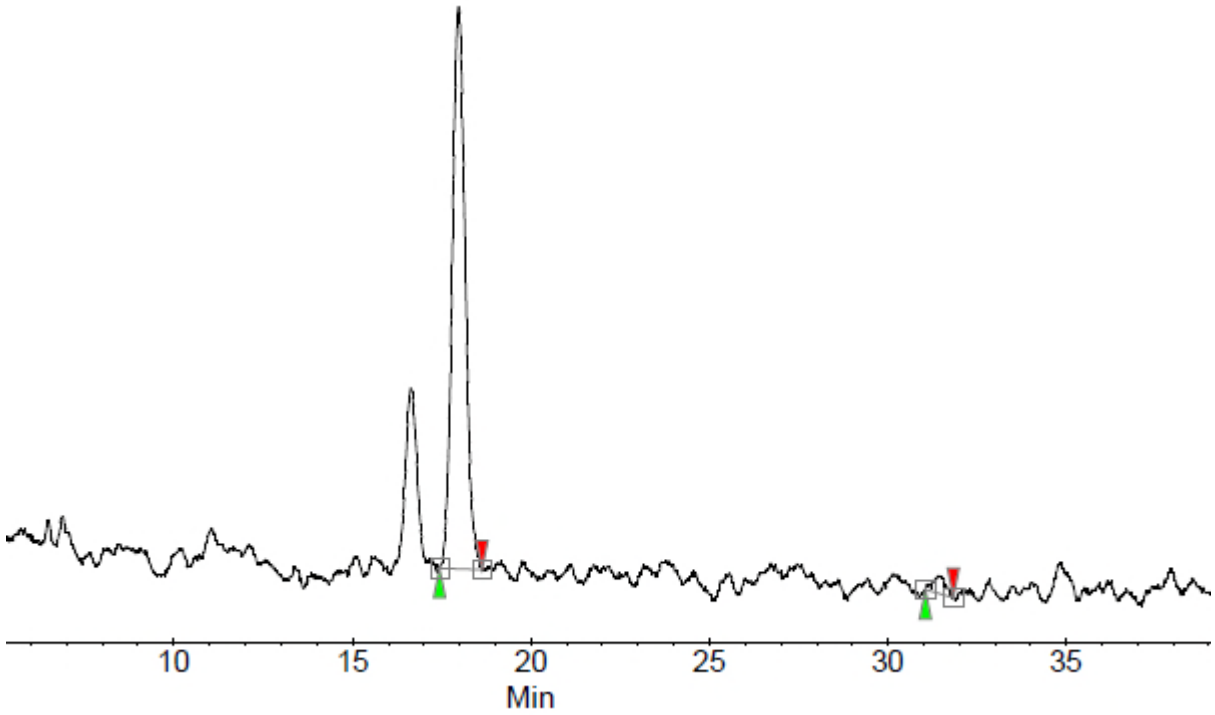



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 17.32 | 50.49 | 196.7 | 87.1 | 50.488 |
| 2 | UNKNOWN | 32.60 | 49.51 | 104.2 | 85.4 | 49.512 |
| | | | | | | |
| Total | | | 100.00 | 301.0 | 172.5 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 17.32 min., (*R*)-isomer 32.60 min.

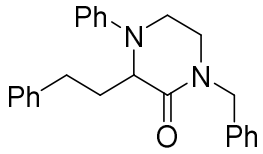



(*S*)-**20**, 94 % e.e.

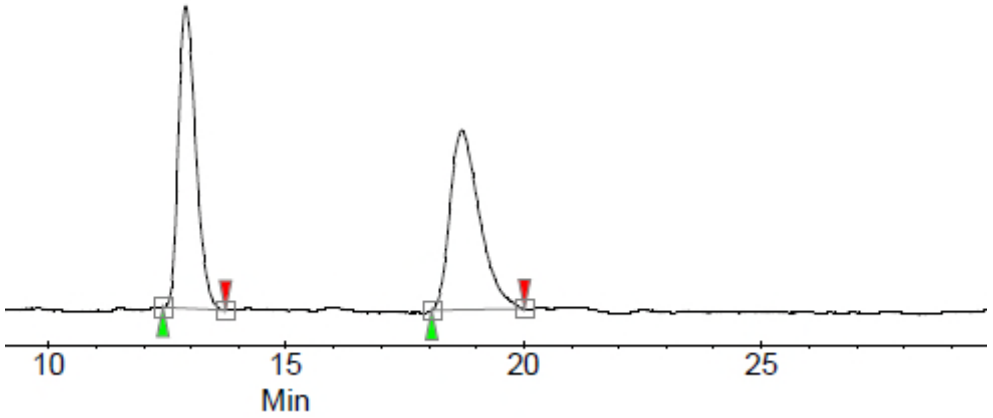



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 17.96 | 96.97 | 60.3 | 25.6 | 96.974 |
| 2 | UNKNOWN | 31.45 | 3.03 | 1.9 | 0.8 | 3.026 |
| | | | | | | |
| Total | | | 100.00 | 62.1 | 26.4 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 17.96 min., (*S*)-isomer 31.45 min.

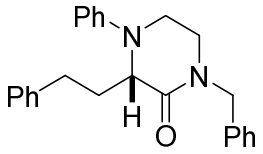



**21**

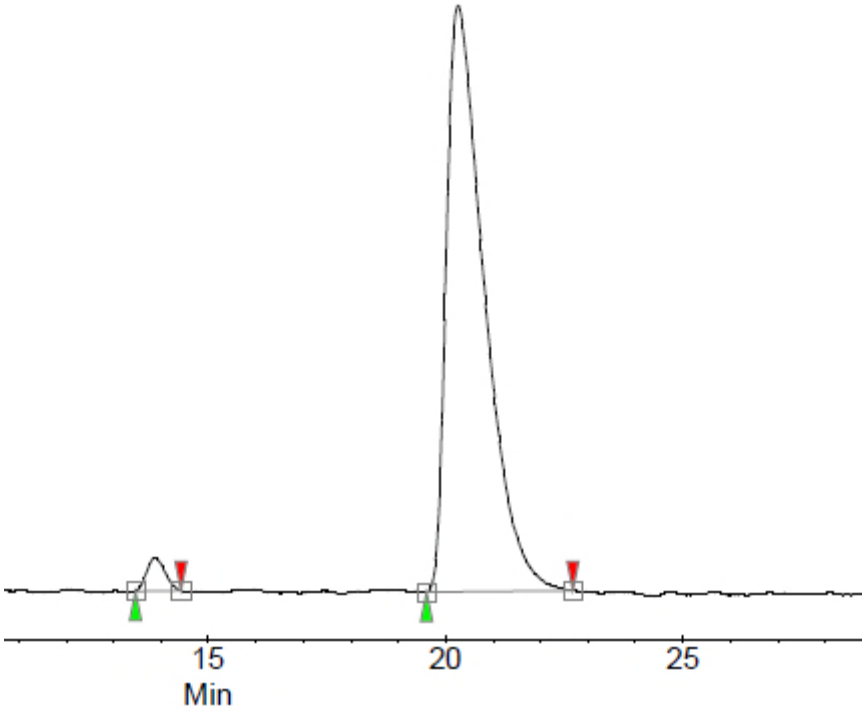



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 12.88 | 49.74 | 358.3 | 151.4 | 49.743 |
| 2 | UNKNOWN | 18.69 | 50.26 | 212.3 | 152.9 | 50.257 |
| | | | | | | |
| Total | | | 100.00 | 570.6 | 304.3 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 12.88 min., (*S*)-isomer 18.69 min.

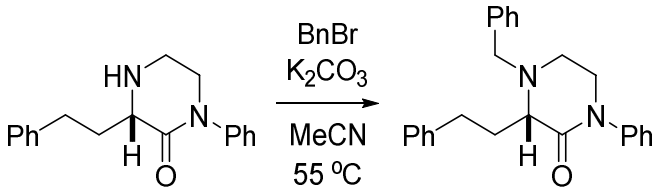



(*S*)-**21**, 95 % e.e.

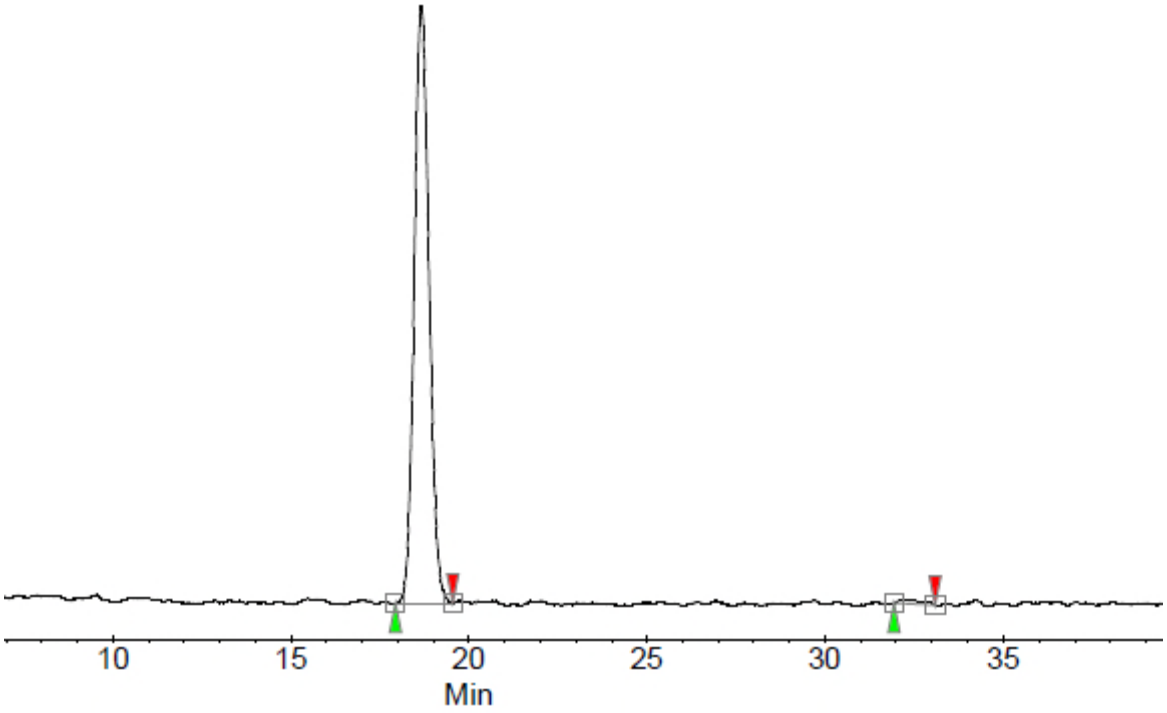



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 13.87 | 2.66 | 34.0 | 15.2 | 2.657 |
| 2 | UNKNOWN | 20.27 | 97.34 | 602.5 | 557.8 | 97.343 |
| | | | | | | |
| Total | | | 100.00 | 636.5 | 573.0 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 15 : 85, 1 mL/min., 209 nm, (*R*)-isomer 13.87 min., (*S*)-isomer 20.27 min.

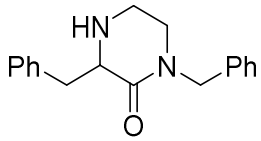



(*S*)-**12**, 99 % e.e. (*S*)-**20**, 98 % e.e.

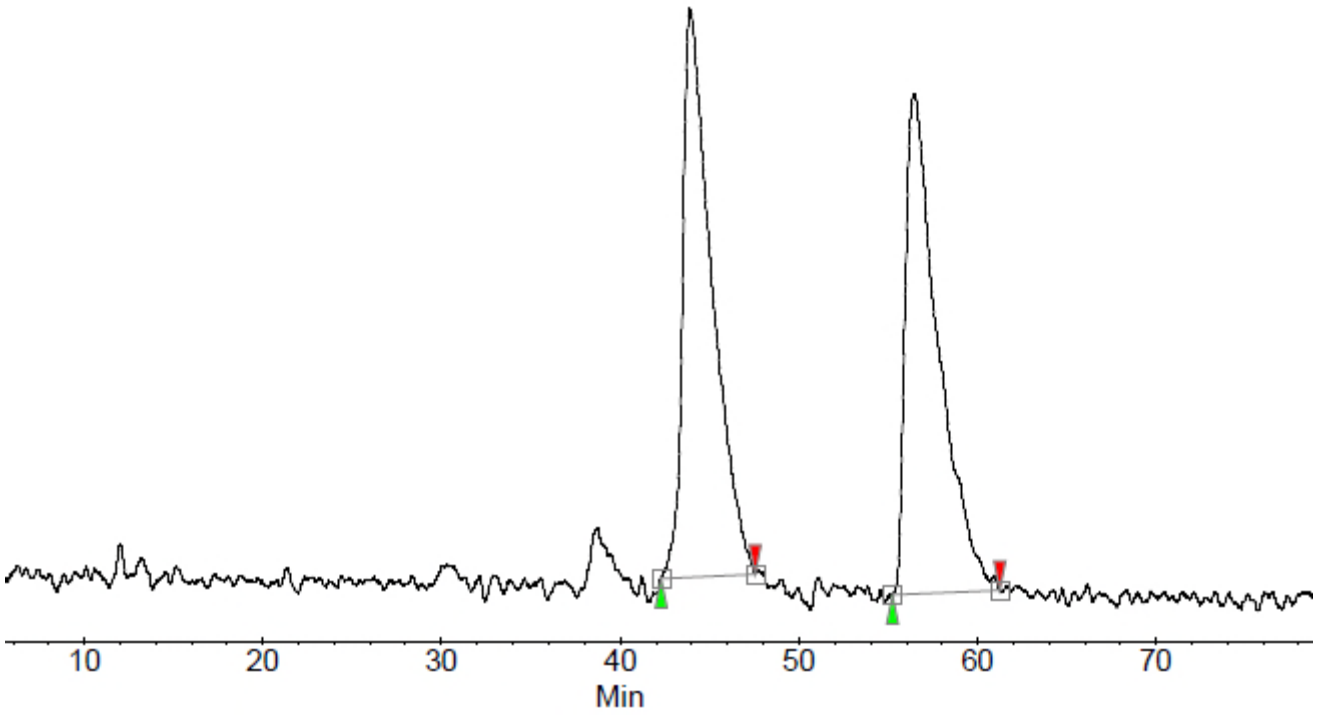



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 18.65 | 98.92 | 287.1 | 139.8 | 98.925 |
| 2 | UNKNOWN | 32.26 | 1.08 | 1.8 | 1.5 | 1.075 |
| | | | | | | |
| Total | | | 100.00 | 288.9 | 141.4 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 10 : 90, 1 mL/min., 208 nm, (*S*)-isomer 18.65 min., (*R*)-isomer 32.26 min.

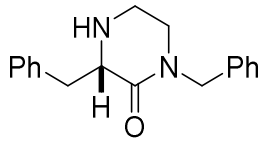



**24**

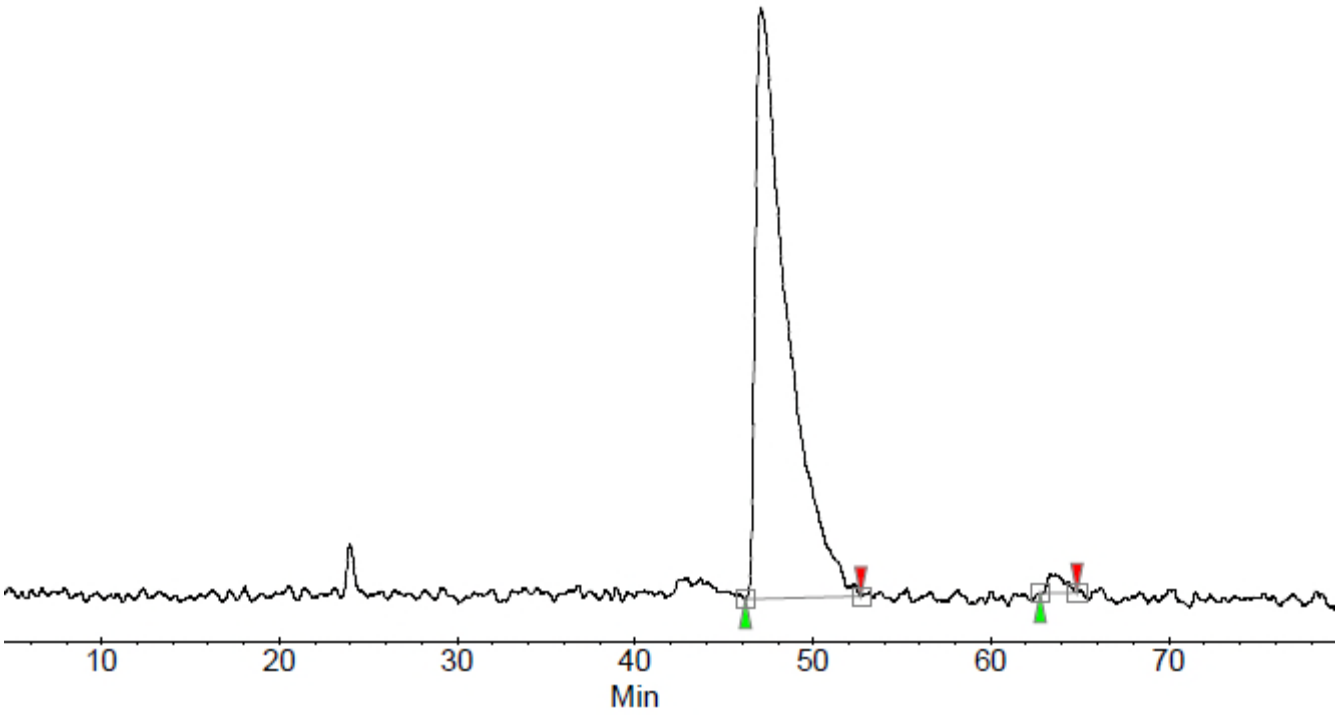



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 43.88 | 50.28 | 86.9 | 165.3 | 50.281 |
| 2 | UNKNOWN | 56.47 | 49.72 | 76.2 | 163.5 | 49.719 |
| | | | | | | |
| Total | | | 100.00 | 163.1 | 328.8 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 43.88 min., (*R*)-isomer 56.47 min.

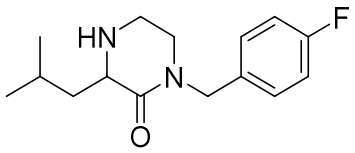



(*S*)-**24**, 97 % e.e.

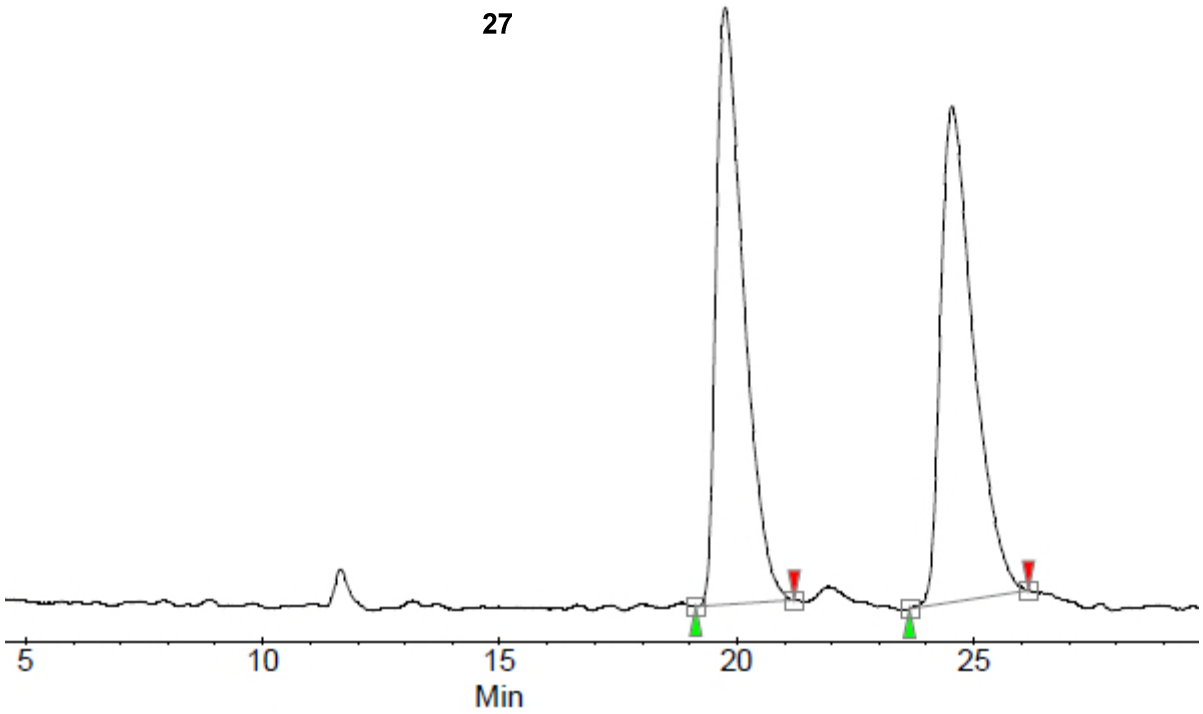



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 47.06 | 98.34 | 171.1 | 354.8 | 98.344 |
| 2 | UNKNOWN | 63.35 | 1.66 | 5.7 | 6.0 | 1.656 |
| | | | | | | |
| Total | | | 100.00 | 176.8 | 360.8 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 47.06 min., (*R*)-isomer 63.35 min.

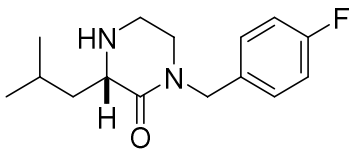



**27**

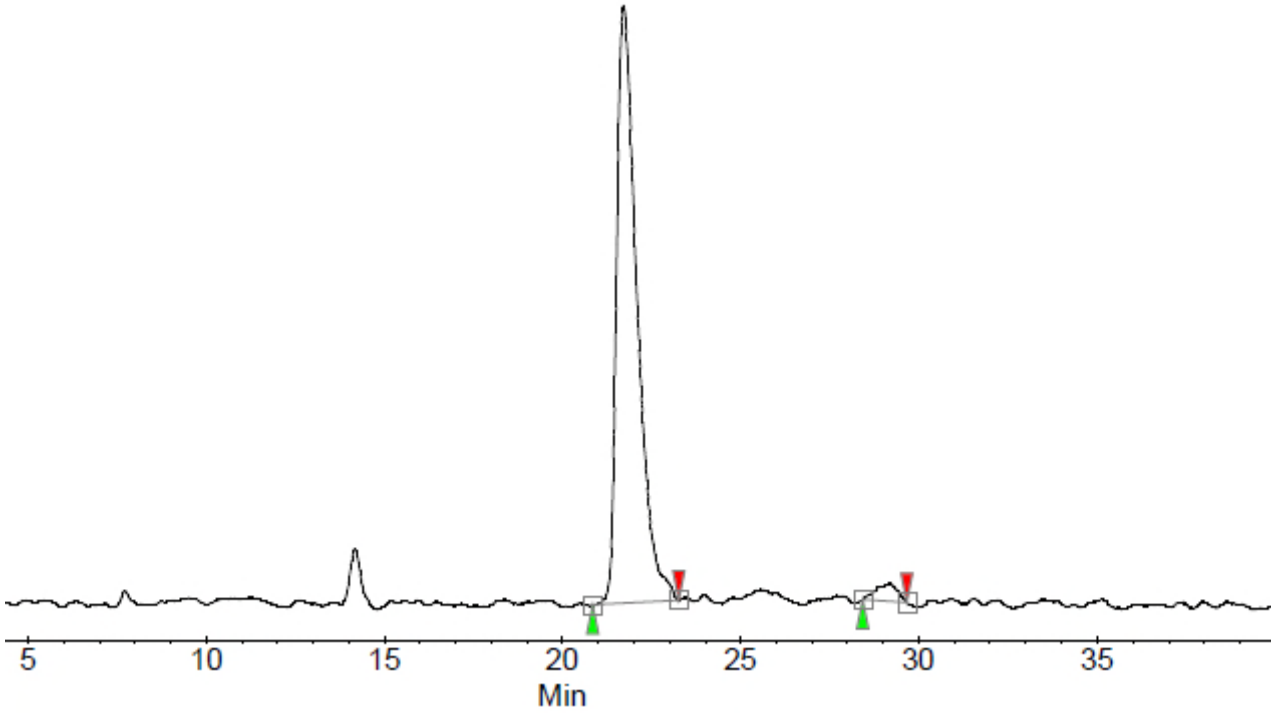



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 19.75 | 50.13 | 270.3 | 181.5 | 50.133 |
| 2 | UNKNOWN | 24.53 | 49.87 | 224.3 | 180.5 | 49.867 |
| | | | | | | |
| Total | | | 100.00 | 494.6 | 362.1 | 100.000 |

Daicel Chiralcel OD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 19.75 min., (*R*)-isomer 24.53 min.




(*S*)-**27**, 94 % e.e.




| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 21.71 | 97.03 | 225.4 | 149.6 | 97.033 |
| 2 | UNKNOWN | 29.18 | 2.97 | 6.9 | 4.6 | 2.967 |
| | | | | | | |
| Total | | | 100.00 | 232.3 | 154.2 | 100.000 |

Daicel Chiralcel AD-H column, 2-propanol : *n*-hexane = 5 : 95, 1 mL/min., 210 nm, (*S*)-isomer 21.71 min., (*R*)-isomer 29.18 min.