

# Diastereoselective Synthesis and Spin-Dependent Photodecarbonylation of di(3-Phenyl-2-pyrrolidinon-3-yl)ketones: Synthesis of Nonadjacent and Adjacent Stereogenic Quaternary Centers

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## Supporting Information

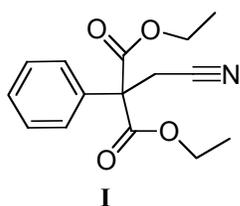
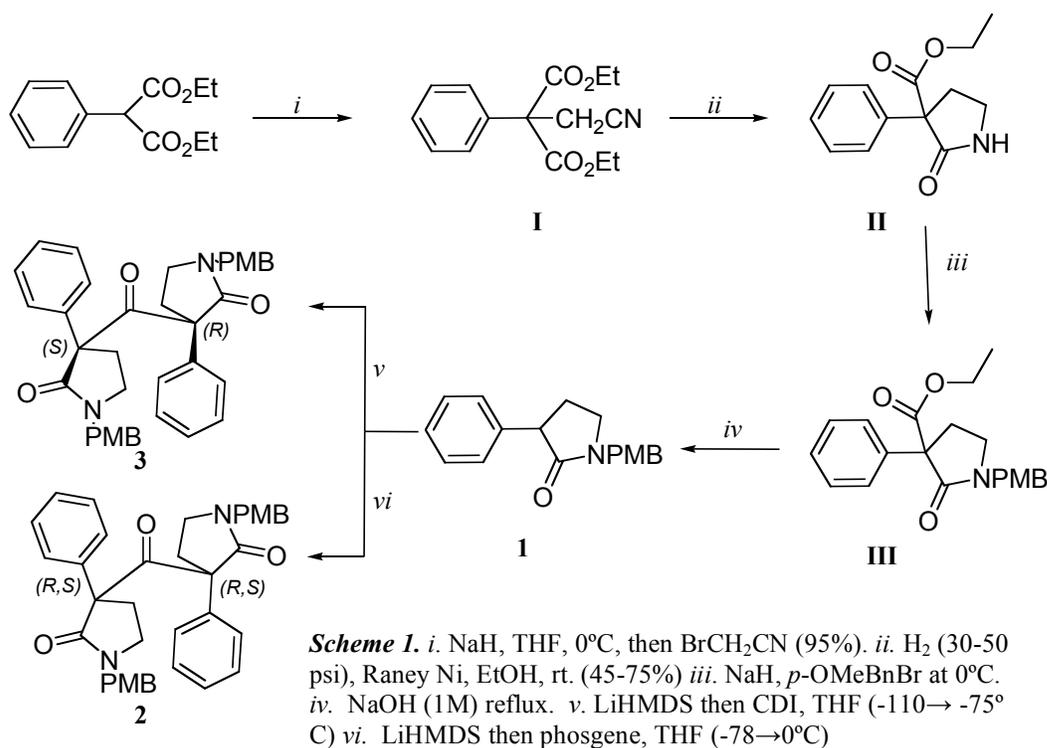
### Experimental

**Materials.** Tetrahydrofuran (THF) was dried by distillation from the sodium ketyl of benzophenone. All other reagents were commercial products that were used without further purification. Gas chromatography (GC) was conducted on a 0.2 mm × 25 m × 0.11 μm HP-1 (cross linked methyl silicon gum) capillary column. IR spectra were obtained with a Perkin-Elmer Spectrum 100 FT-IR spectrometer as neat samples. <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained with a Bruker ARX 500 and Avance 500 spectrometers in CDCl<sub>3</sub> and C<sub>6</sub>D<sub>6</sub>. Mass-Spectra were obtained both on an Agilent 190915-433 HP-SMS 5% phenyl methyl siloxane capillary: 30m × 250μm × 0.25μm for GC-MS and an AB/PerSpective DE-STR TOF for MALDI-TOF.

**General procedure for solution photolyses.** Milimolar solutions of **2** and **3** were prepared by dissolving milligram quantities into equivalent number of milliliters of degassed benzene, benzene/acetone, benzene/isoprene, acetone or isoprene solutions in

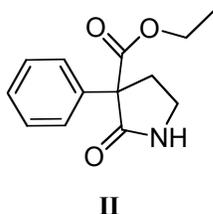
vials or pressure flasks. All samples were placed at similar distances from a medium pressure Hg Hanovia lamp ( $\lambda > 290$  nm). Samples were analyzed by NMR upon evaporation of the solvent and dissolution in  $\text{CDCl}_3$ . Actinometry experiments were performed in optically dense deuterated benzene solutions of **2** and **3** transferred into dry Pyrex 7 mm internal diameter (i.d.) NMR tubes using a RAYONET apparatus at  $\lambda = 300$  nm.

### Synthesis of ketones **2** and **3**.



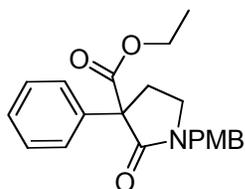
**Diethyl (2-cyanomethyl)-2-phenylpropanedioate (I).** Compound **I** was obtained by following a procedure reported by Prager *et al.*<sup>i</sup> Commercial (Aldrich) diethyl phenylmalonate (3.65g, 8.45 mmol)

was added slowly to a stirring suspension of sodium hydride (0.711 g of a 60% dispersion in mineral oil, 8.45 mmol) in anhydrous tetrahydrofuran (100 ml) under an Ar atmosphere at 0 °C. After 0.5 h, bromoacetonitrile (1.77 ml, 8.45 mmol) was added drop wise to the reaction mixture and stirred for 2 hours. The reaction was quenched with 100 ml of a saturated NH<sub>4</sub>Cl solution and the aqueous fraction extracted with ether (3 × 30 ml). The organic fractions were combined and washed with saturated aqueous sodium chloride (50 ml). The solution was then dried over MgSO<sub>4</sub> and concentrated under reduced pressure to obtain a yellow oil (95%) matching the reported spectral data for **I**. <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.3-7.4 (m, 5H), 4.26-4.34 (m, 4H, diastereotopic CH<sub>2</sub>), 3.22 (s, 2H), 1.27 (t, *J* = 7.06, 6H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 168.0, 134.9, 128.6, 128.4, 127.2, 116.6, 62.8, 60.6, 26.0 and 13.8 ppm. FTIR (neat) 1725, 1691, 1447, 1234 and 1179 cm<sup>-1</sup>.



**Ethyl 2-oxo-3-phenylpyrrolidin-2-one-3-carboxylate (II)** was obtained by following a procedure reported by Michael *et al.*<sup>ii</sup>. Hydrogenation (20-40 psi, rt) of diethyl (2-cyanomethyl)-2-phenylpropanedioate **I** (2.2 g, 8 mmol) in absolute ethanol (40 ml) over Raney nickel (1.0 g) was stirred vigorously for 24 hours while maintaining the H<sub>2</sub> pressure constant. The opaque white suspension was filtered through a frit and washed with ethyl acetate (3 × 20 ml). The organic residues were evaporated under reduced pressure. Purification of the residue by column chromatography (silica, CH<sub>3</sub>COOC<sub>2</sub>H<sub>5</sub> (15%)/hexanes (85%)) resulted in a white crystalline powder (1.32 g, 5.2 mmol, 65 %), mp = 98-102° C matching the known spectral information for **II**. <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.45-7.26 (m, 5H), 6.6 (br s, 1H), 4.31-4.23 (m, 2H), 3.48-3.46 (m, 1H), 3.35-3.32 (m, 1H),

3.17-3.12 (m, 1H), 2.57-2.50 (m, 1H) and 1.31-1.24 (m, 3H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 174.3, 170.5, 137.6, 128.6, 128.4, 127.4, 62.0, 59.7, 39.2, 34.6 and 13.8 ppm. FTIR (neat) 3251, 1712, 1678, 1444, 1247 and 1215  $\text{cm}^{-1}$ ; GC-MS (EI)  $m/z$  calculated for  $\text{C}_{13}\text{H}_{15}\text{NO}_3$ , 233.11, found 233.

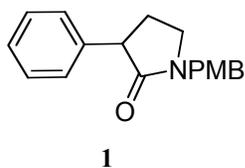


**III**

**Ethyl 1-(4-methoxybenzyl)-2-oxo-3-phenylpyrrolidine-3-carboxylate (III).** Ethyl 2-oxo-3-phenylpyrrolidine-3-carboxylate **II** (4.1 g, 17.6 mmol) dissolved in 50 mL dry tetrahydrofuran was added dropwise to a cooled solution ( $0^\circ\text{C}$ ) of sodium hydride (1.6 g of a

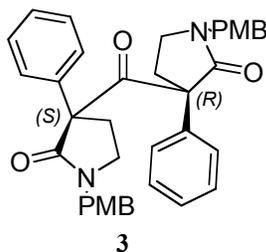
60% dispersion in mineral oil, 40 mmol) in THF (100 ml) over a period of 10 min. The reaction mixture was stirred for 0.5 h and *p*-methoxybenzyl bromide (2.6 mL, 17.8 mmol) was added dropwise and warmed to room temperature over a period of 90 min. The solution was then quenched with a saturated ammonium chloride solution and the organic components were extracted with ether (3×40 ml). The combined extracts were washed with saturated aqueous sodium chloride (60 ml). The solution was then dried over  $\text{MgSO}_4$  and purified by column chromatography (silica,  $\text{CH}_3\text{COOC}_2\text{H}_5$  (30%)/hexanes (70%)) resulting in a white crystalline powder of the desired N-protected pyrrolidinone **III** (0.3 g, 1.1 mmol, 85 %), mp =  $85\text{-}87^\circ\text{C}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 7.46 (d,  $J = 7.3$ , 2H), 7.35 (t,  $J = 7.3$ , 2H), 7.3-7.27 (m, 1H), 7.18 (d,  $J = 8.6$ , 2H), 6.85 (d,  $J = 8.6$ ), 4.52 (d,  $J = 14.5$ , 1H), 4.45 (d,  $J = 14.5$ , 1H), 4.22 (q,  $J = 7.1, 14.2$ , 2H), 3.8 (s, 3H), 3.31-3.27 (m, 1H), 3.16-3.13 (m, 1H), 2.98-2.95 (m, 1H), 2.39-2.34 (m, 1H) and 1.22 (t,  $J = 7.1$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 170.8, 170.5, 159.1, 138.0, 129.4, 128.3, 128.0, 127.4, 127.2,

114.0, 61.9, 60.5, 55.2, 46.6, 43.4, 32.0 and 13.9. FTIR (neat) 1733, 1669, 1509, 1438, 1243 and 1025  $\text{cm}^{-1}$ ; GC-MS (EI)  $m/z$  calculated for  $\text{C}_{21}\text{H}_{23}\text{NO}_4$ , 353.16, found 353.



**1-(4-Methoxybenzyl)-3-phenylpyrrolidin-2-one (1).** *p*-

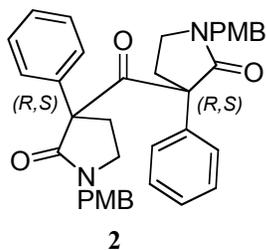
Methoxybenzyl protected pyrrolidinone **III** (0.45 g, 1.27 mmol) was refluxed in an aqueous NaOH solution (1M, 50 ml) for 1 h, after cooling, pH was raised to  $\sim 7$  using a saturated ammonium chloride solution. The organic components were then extracted with ether (3 $\times$ 30 ml) and the combined extracts washed with a saturated aqueous sodium chloride solution (50 ml). The organics were then dried over  $\text{MgSO}_4$  and concentrated under reduced pressure resulting in the desired PMB protected pyrrolidinone as a colorless oil (0.32 mg, 1.25 mmol, quant).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 7.43-7.38 (m, 2H), 7.34-7.29 (m, 3H), 7.26 (d,  $J = 8.5$ , 2H), 6.92 (d,  $J = 8.5$ , 2H), 4.58 (d,  $J = 14.5$ , 1H), 4.46 (d,  $J = 14.5$ , 1H), 3.85 (s, 3H), 3.75 (dd,  $J = 8.6, 8.6$ , 1H), 3.4-3.3 (m, 2H), 2.55-2.48 (m, 1H) and 2.16-2.08 (m, 1H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 174.6, 159.0, 139.8, 129.5, 128.6, 128.5, 127.8, 126.9, 113.9, 55.16, 48.2, 46.3, 44.7 and 27.7 ppm. FTIR (neat) 1677, 1511 and 1242  $\text{cm}^{-1}$ ; GC-MS (EI)  $m/z$  calculated for  $\text{C}_{18}\text{H}_{19}\text{NO}_2$ , 281.14, found 281.



**(*meso*)-1,1-Di-{3-[1-(4-methoxybenzyl)-3-phenylpyrrolidin-2-one]yl}methanone (3).** To a cooled solution of ( $-100^\circ\text{C}$ ) PMB-

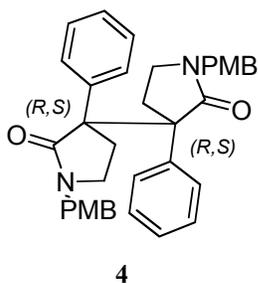
protected pyrrolidinone (0.46 g, 1.635 mmol) in tetrahydrofuran (40 ml), lithium bis(trimethylsilyl)amide (2 ml, 1M) was added at once and the reaction stirred for 20 min. Carbonyl diimidazole (CDI) (0.132 g, 0.82

mmol) was added at once and the reaction mixture was left stirring with constant warming and cooling from  $-115^{\circ}\text{C}$  to  $-75^{\circ}\text{C}$  over 4 hours. The reaction was then quenched with a saturated ammonium chloride solution and the organic components were extracted with ether ( $3 \times 10$  ml). The combined extracts were washed with saturated aqueous sodium chloride (20 ml). The solution was then dried over  $\text{MgSO}_4$ , concentrated under reduced pressure and purified by column chromatography (silica,  $\text{CH}_3\text{COOC}_2\text{H}_5$  (50%)/Hexanes (50%)) resulting in a colorless oil of **3** which was further crystallized by dissolving in minimum amounts of methylene chloride followed by addition of diethyl ether (0.25 g, 0.85 mmol, 52 %), mp =  $121\text{-}123^{\circ}\text{C}$ . Single crystals from these mixtures were separated and analyzed *via* X-ray diffraction (cif files and crystallographic data are included in the sup. inf.).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 7.52 (d,  $J = 7.65$ , 2H), 7.38-7.35 (m, 2H), 7.33-7.3 (m, 1H), 7.06 (d,  $J = 8.61$ , 2H), 6.84 (d,  $J = 8.63$ , 2H), 4.34 (d,  $J = 14.6$ , 1H), 3.87 (d,  $J = 14.6$ , 1H), 3.82 (s, 3H), 3.32-3.27 (m, 1H), 2.9-2.85 (m, 1H), 2.68-2.63 (m, 1H) and 2.32-2.27 (m, 1H) ppm.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 200.9, 170.1, 158.9, 137.5, 129.3, 128.5, 128.3, 128.0, 127.5, 113.8, 66.9, 55.2, 46.2, 42.7 and 31.2 ppm. FTIR (neat) 1708, 1676, 1611, 1511, 1449, 1255 and  $1237\text{ cm}^{-1}$ ; MALDI-TOF: calculated for  $\text{C}_{37}\text{H}_{36}\text{N}_2\text{O}_5$ , 588.26, found 588.6.



**(*d,l*)-1,1-Di-{3-[1-(4-methoxybenzyl)-3-phenylpyrrolidin-2-one]methyl}methanone (2).** To a cooled solution of ( $-78^{\circ}\text{C}$ ) PMB-protected pyrrolidinone (1.06 g, 3.78 mmol) in tetrahydrofuran (70 ml), lithium bis(trimethylsilyl)amide (4 ml, 1M) was added at once and the reaction stirred for 45 min. Phosgene (0.1 ml, 20mol % soln) was added

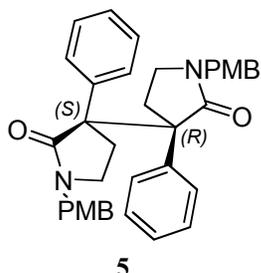
over ~5 min and the reaction mixture was left stirring upon warming up to -0° C. The reaction was then quenched with a saturated ammonium chloride solution and the organic components were extracted with ether (3×40 ml). The combined extracts were washed with saturated aqueous sodium chloride (60 ml). The solution was then dried over MgSO<sub>4</sub>, concentrated under reduced pressure and purified by column chromatography (silica, CH<sub>3</sub>COOC<sub>2</sub>H<sub>5</sub> (40%)/hexanes (60%)) resulted in a white waxy (glass-like) solid of **2** (1.36 g, 1.36 mmol, 72 %), mp = 121-123° C. <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.37-7.31 (m, 2H), 7.29-7.24 (m, 3H), 7.2 (d, *J* = 8.6, 2H), 6.85 (d, *J* = 8.6, 2H), 4.67 (d, *J* = 14.7, 1H), 4.24 (d, *J* = 14.7, 1H), 3.78 (s, 3H), 3.35-3.31 (m, 1H), 3.22-3.18 (m, 1H), 2.95-2.9 (m, 1H) and 1.93-1.88 (m, 1H) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>) 200.7, 171.0, 158.9, 138.4, 129.4, 128.6, 128.1, 127.3, 127.2, 113.9, 67.9, 55.1, 46.8, 43.7 and 32.7 ppm. FTIR (neat) 1685, 1610, 1512 and 1243 cm<sup>-1</sup>; MALDI-TOF: calculated for C<sub>37</sub>H<sub>36</sub>N<sub>2</sub>O<sub>5</sub>, 588.26, found 588.8.



**(*d,l*)-1,1'-bis(4-methoxybenzyl)-1,1'-bis(phenyl)-3,3'-bipyrrolidine-2,2'-dione (4).** The desired product was obtained upon column chromatography (silica, ethyl ether (40%)/hexanes (60%)) of the combined photolyses performed over the course of all photochemical experiments performed on **2** and **3**. **4** in the form of

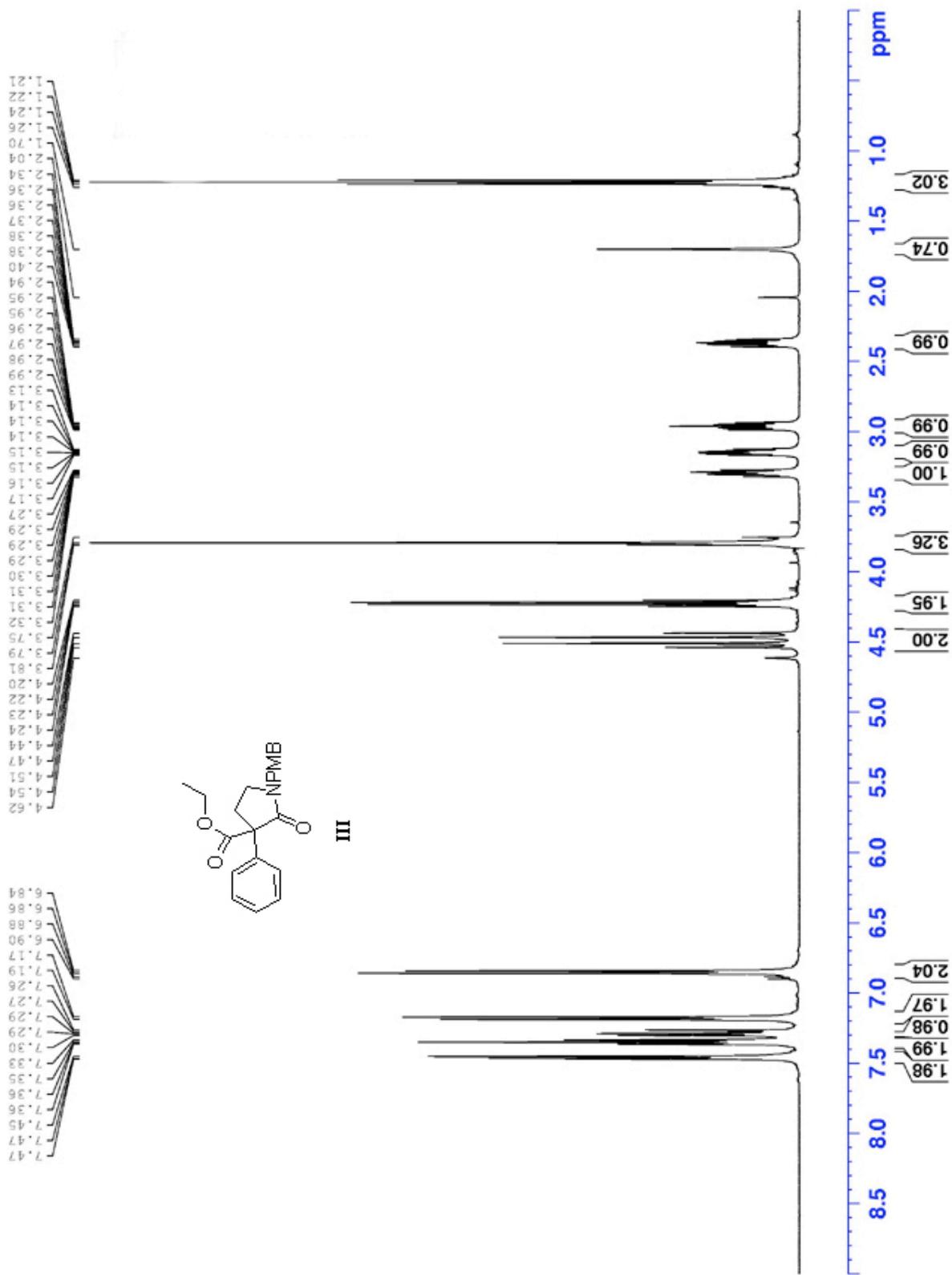
a soft solid was collected upon slow evaporation from ethyl acetate. High quality single crystals were obtained upon slow evaporation of chloroform/hexane mixtures and analyzed *via* X-ray diffraction (cif files and crystallographic data are included in the sup. inf.). <sup>1</sup>H NMR (CDCl<sub>3</sub>) 7.27 (s, 5H), 7.11 (d, *J* = 8.6, 2H), 6.78 (d, *J* = 8.6, 2H), 4.44 (dd, *J* = 14.8, 25.9, 2H), 3.75 (s, 3H), 3.53-3.46 (m, 1H), 3.05 (t, *J* = 8.92, 1H), 2.69-2.4

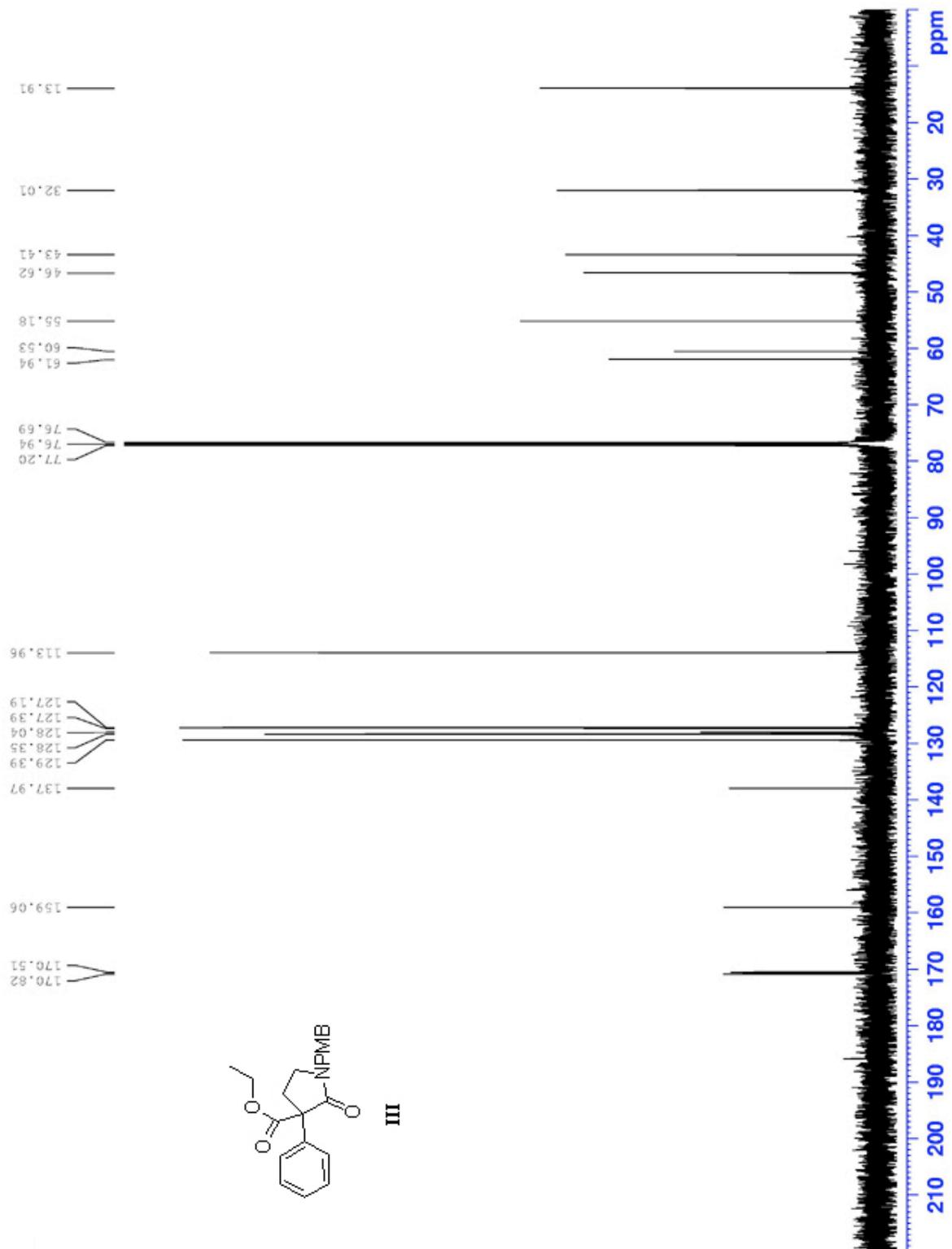
(m, 1H) and 1.77-1.74 (m, 1H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 175.7, 158.7, 136.8, 129.2, 128.9, 128.6, 127.4, 127.3, 113.8, 55.8, 55.1, 46.0, 43.4 and 29.2 ppm. MALDI-TOF: calculated for  $\text{C}_{36}\text{H}_{36}\text{N}_2\text{O}_4$ , 560.27, found 560.87.



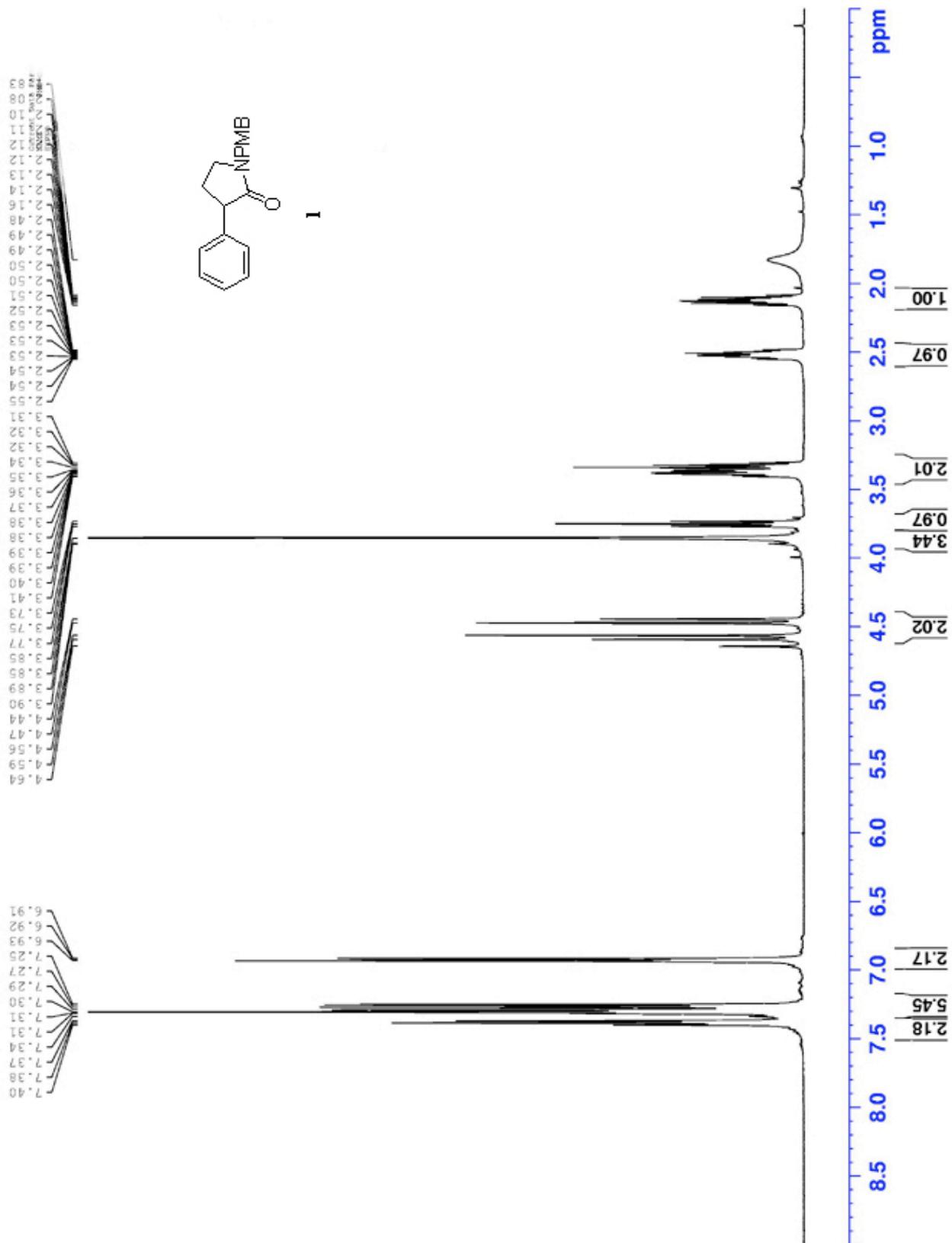
**(*meso*)-1,1'-bis(4-methoxybenzyl)-1,1'-bis(phenyl)-3,3'-bipyrrolidine-2,2'-dione (5).** The desired product was obtained upon column chromatography (silica, ethyl ether (40%)/hexanes (60%)) of the combined photolyses performed over the course of

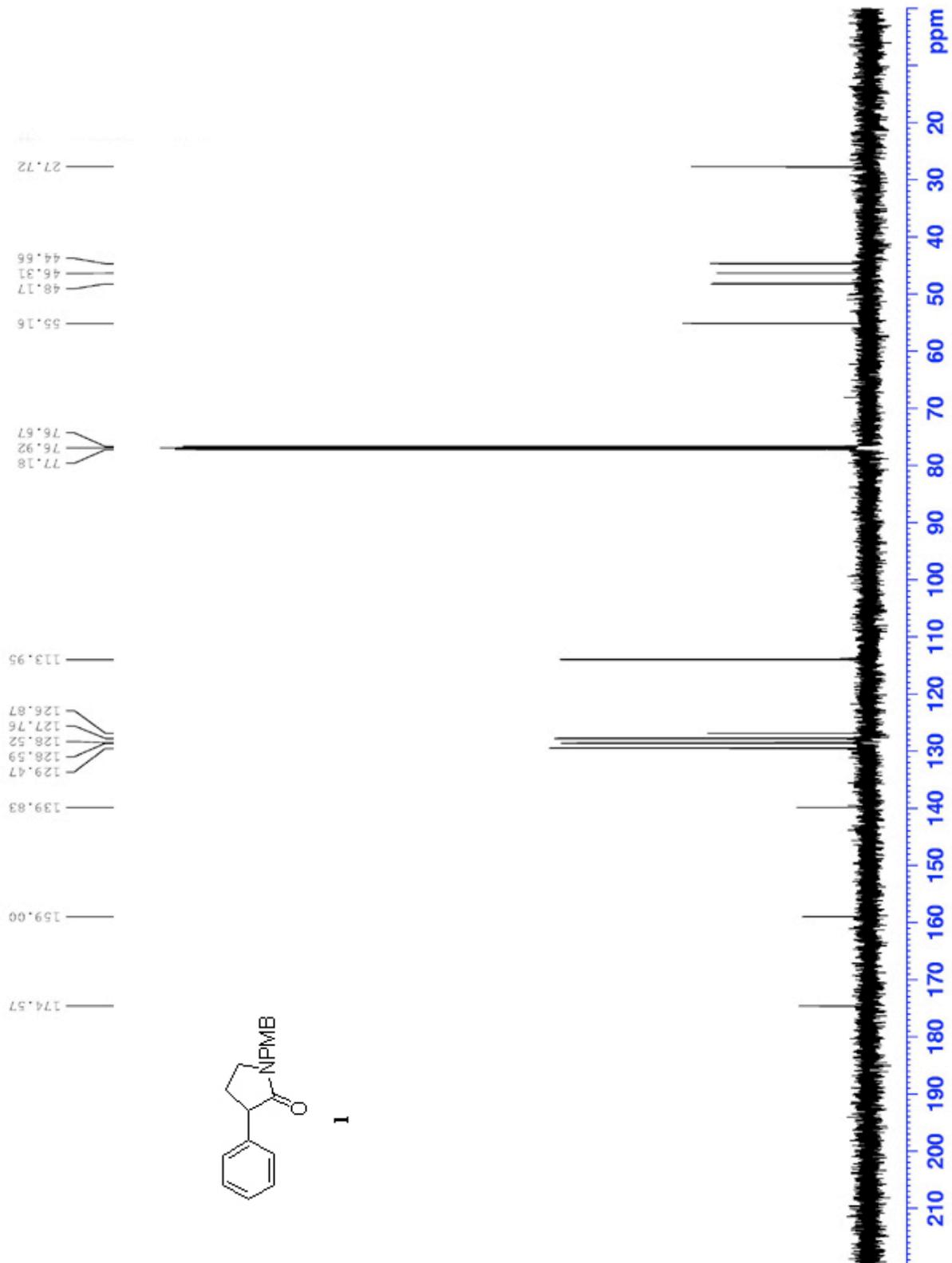
all photochemical experiments performed on **2** and **3** as a precipitate formed from acetone washes in the form of a white solid.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 7.98 (d,  $J = 6.8$ , 2H), 7.38 (m, 3H), 6.87 (d,  $J = 8.6$ , 2H), 6.74 (d,  $J = 6.8$ , 2H), 4.34 (d,  $J = 14.6$ , 1H), 4.09 (d,  $J = 14.6$ , 1H), 3.79 (s, 3H), 3.17-3.14 (m, 1H), 2.74-2.69 (m, 2H) and 2.29-2.26 (m, 1H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 173.8, 158.7, 139.5, 129.4, 128.9, 128.1, 127.7, 127.1, 113.7, 57.9, 55.1, 45.9, 43.3 and 29.5 ppm. MALDI-TOF: calculated for  $\text{C}_{36}\text{H}_{36}\text{N}_2\text{O}_4$ , 560.27, found 560.87.

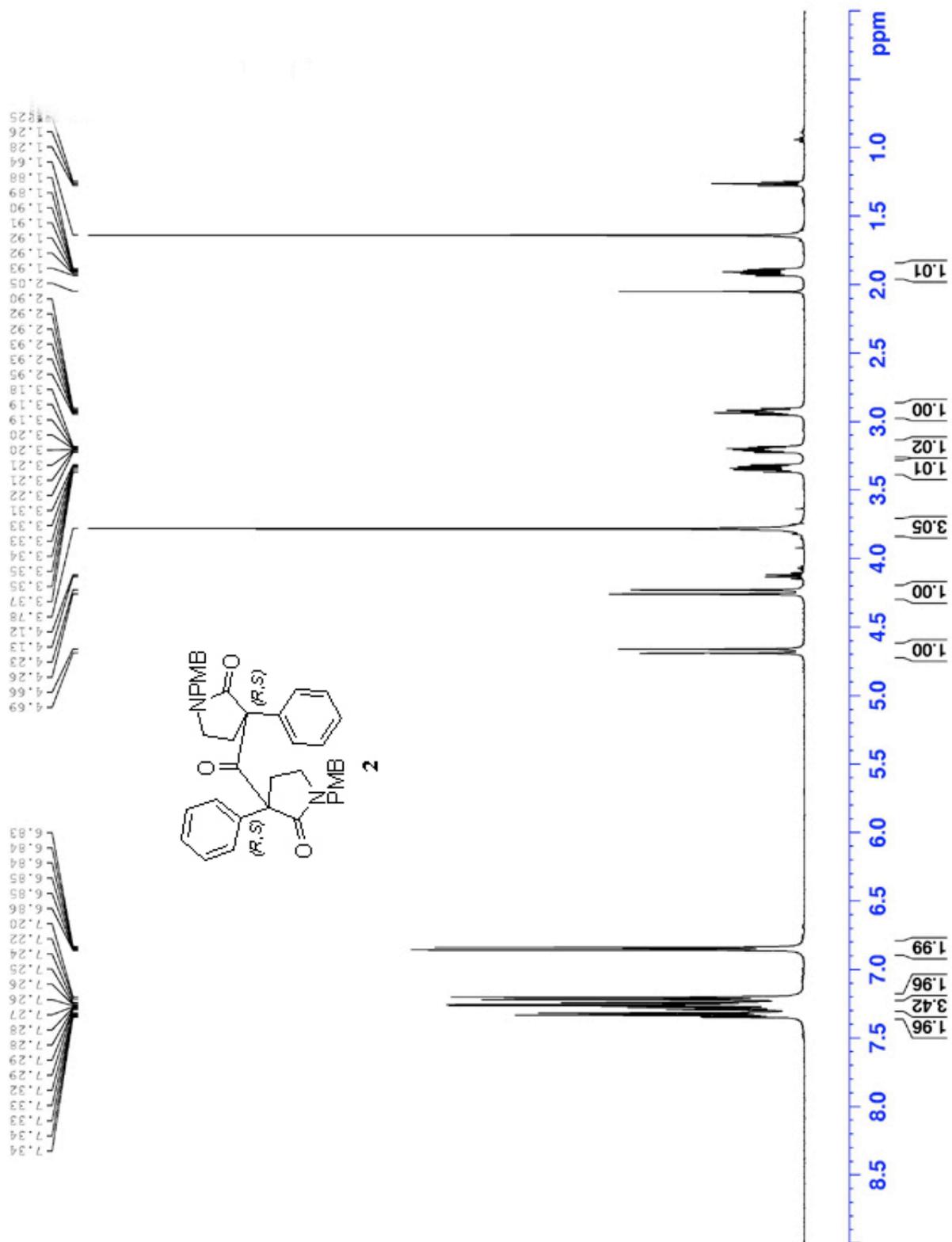


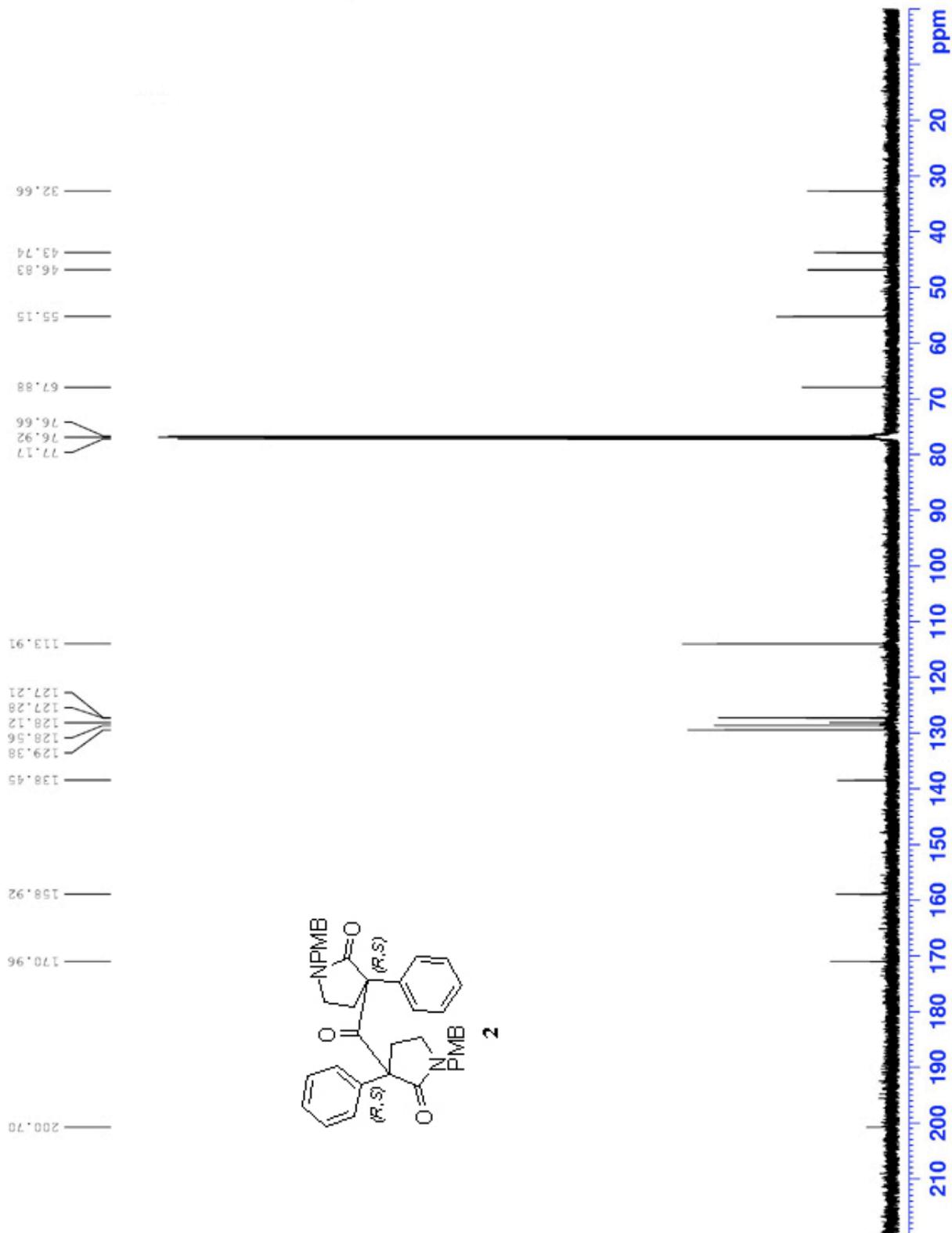


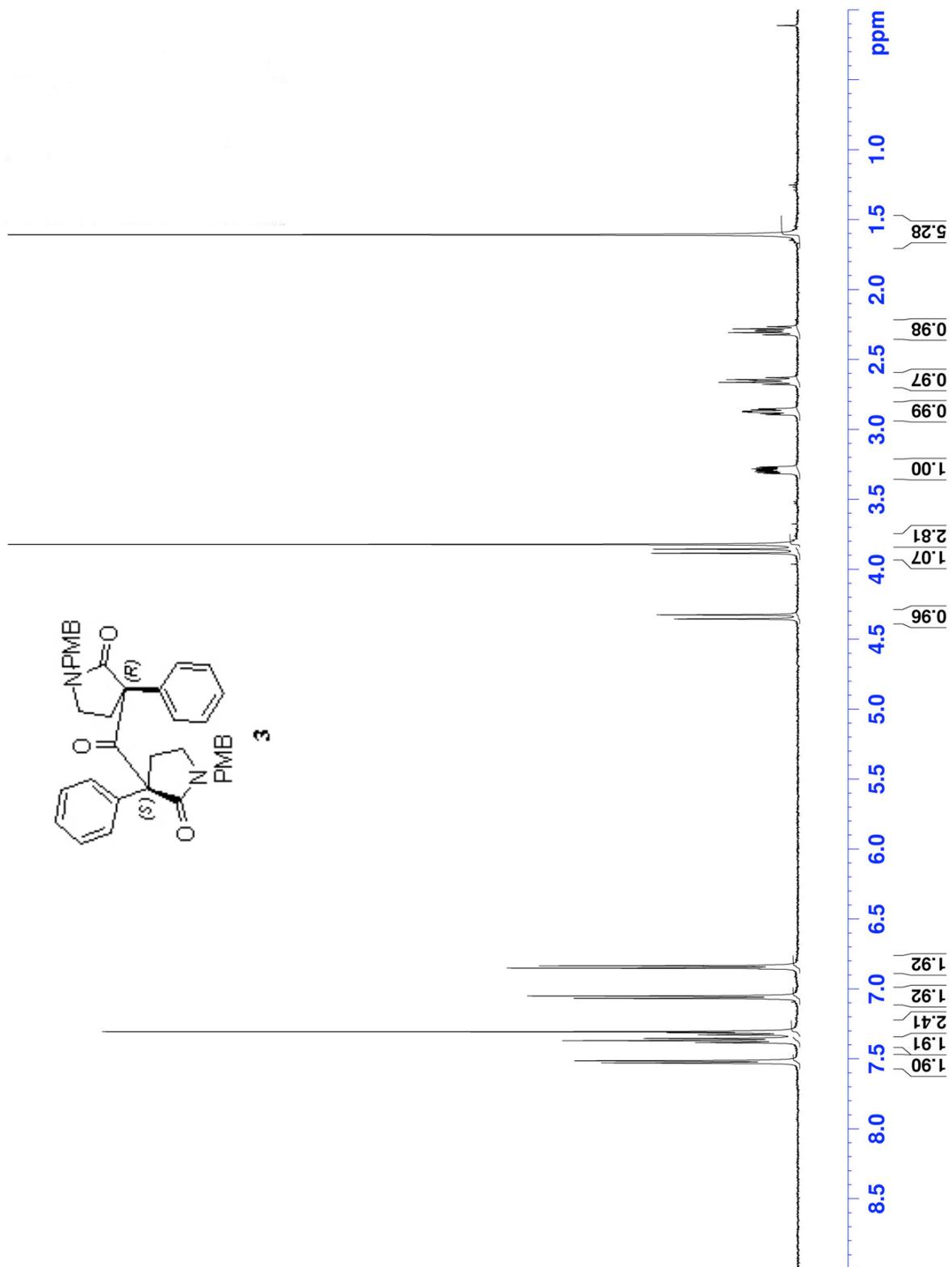


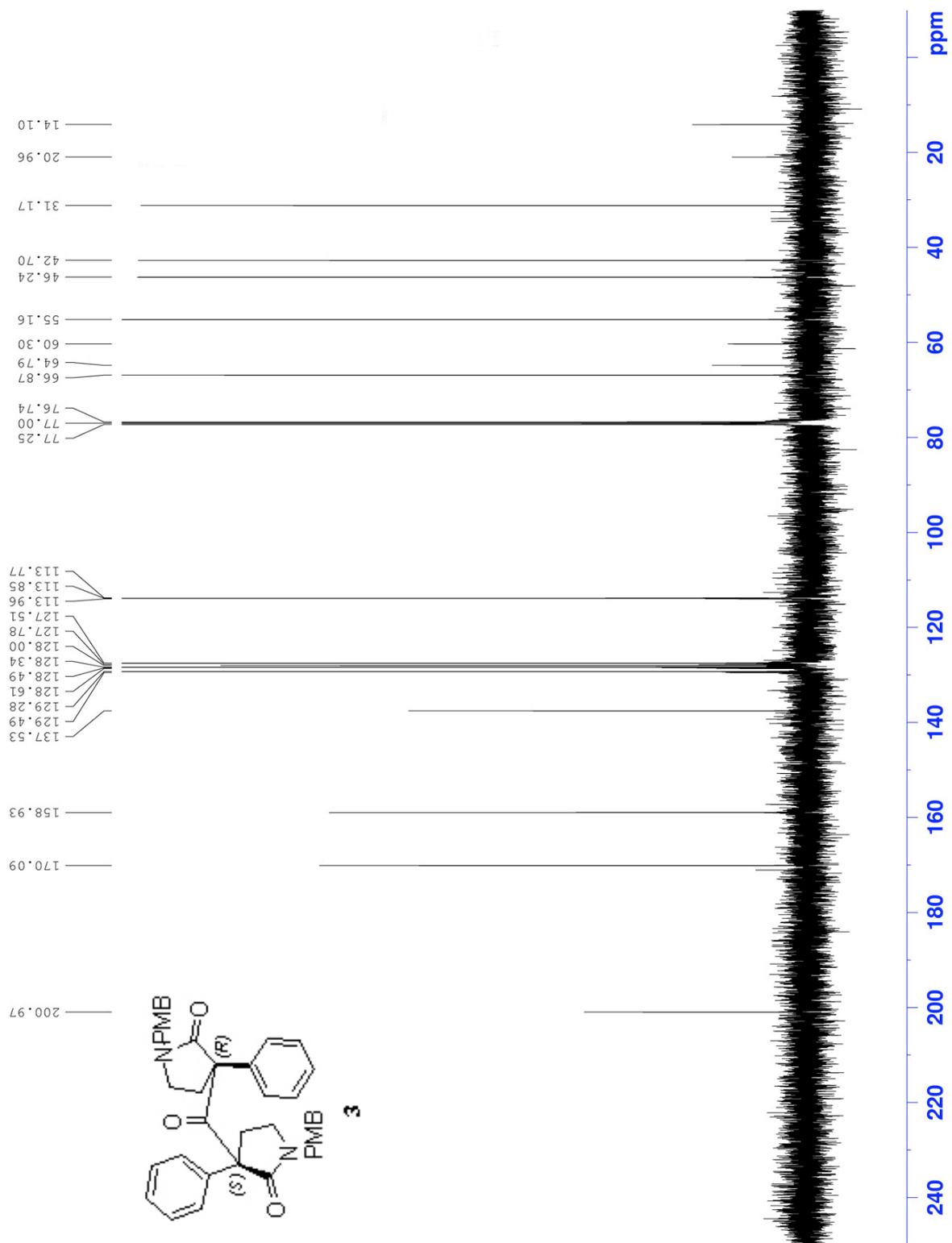


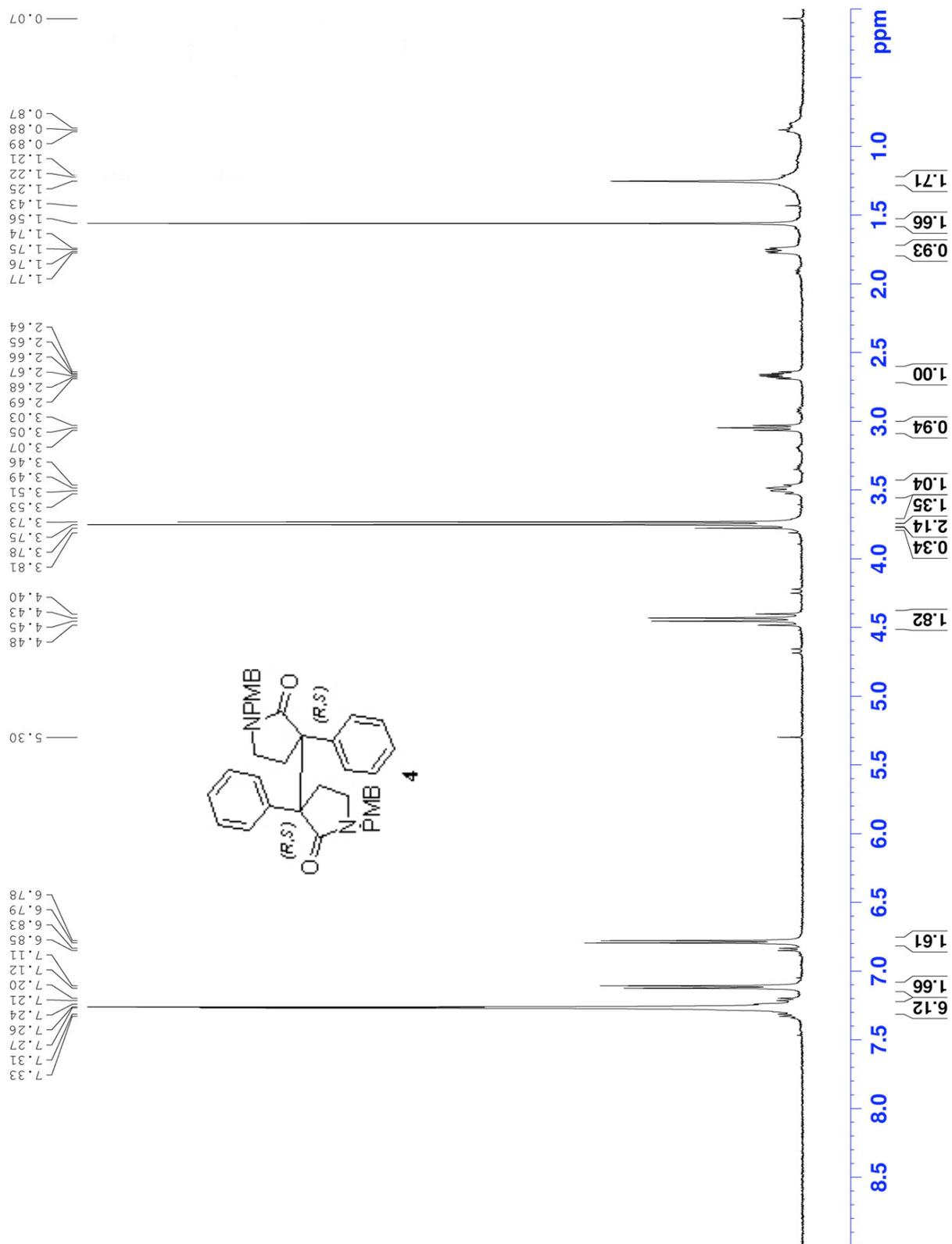


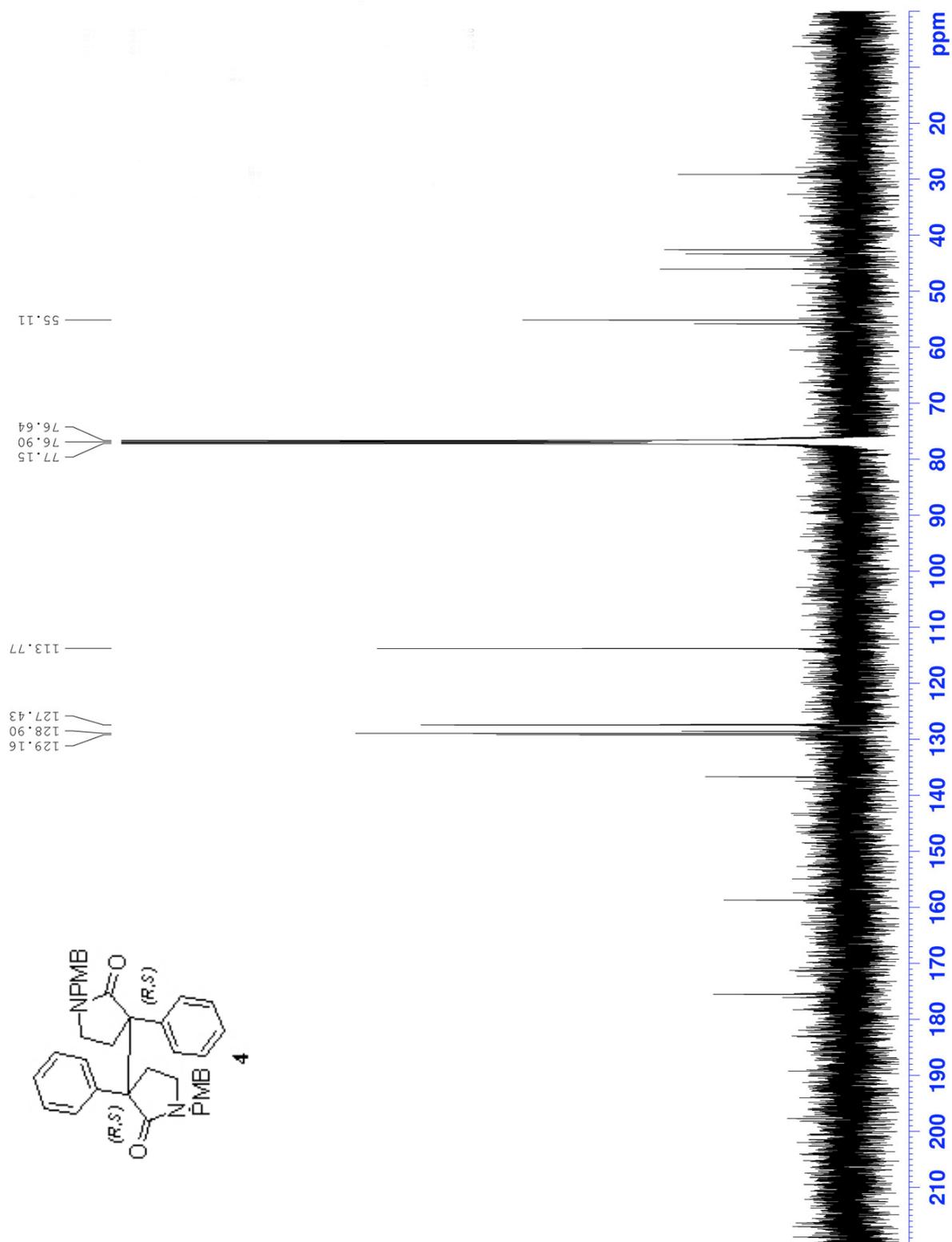


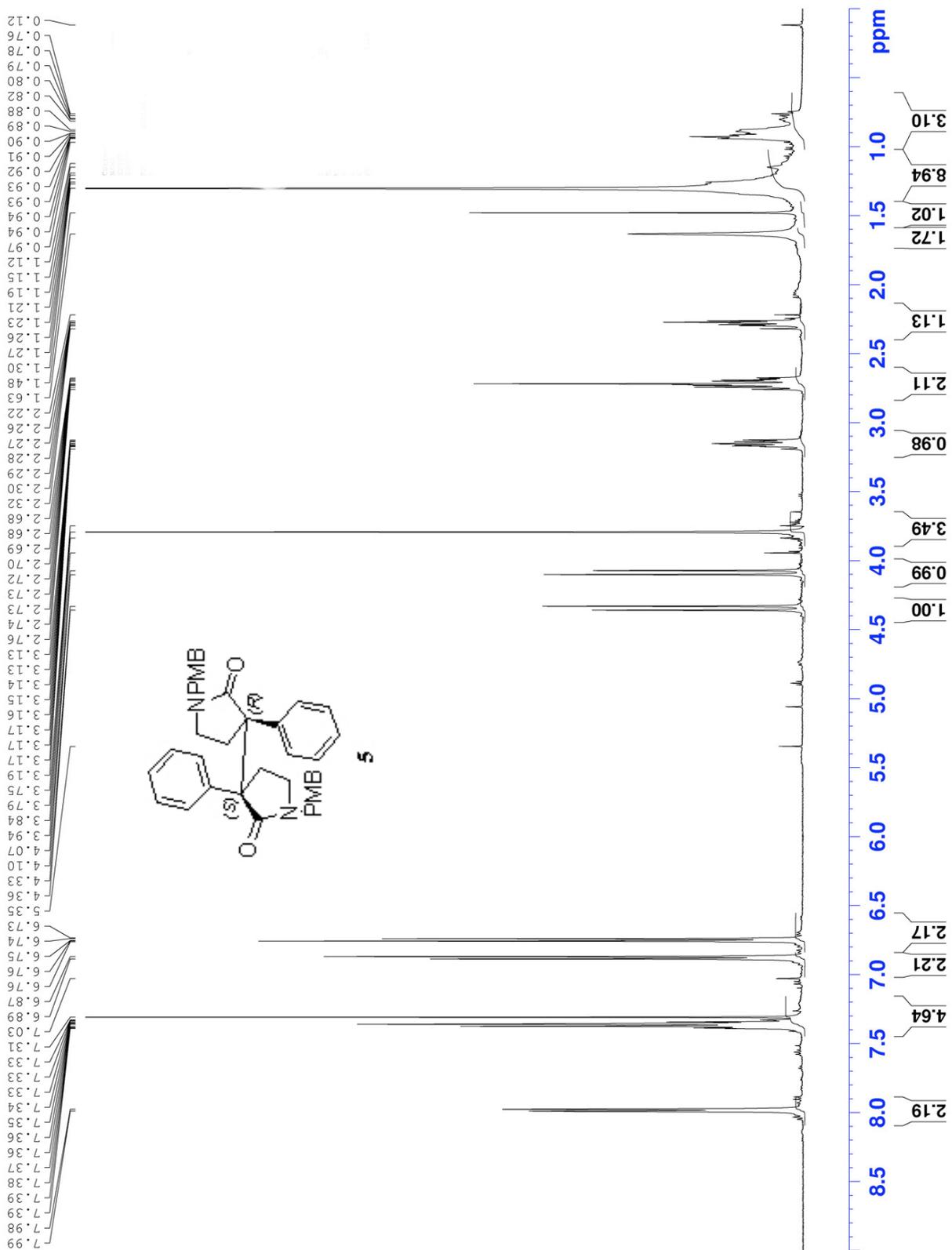


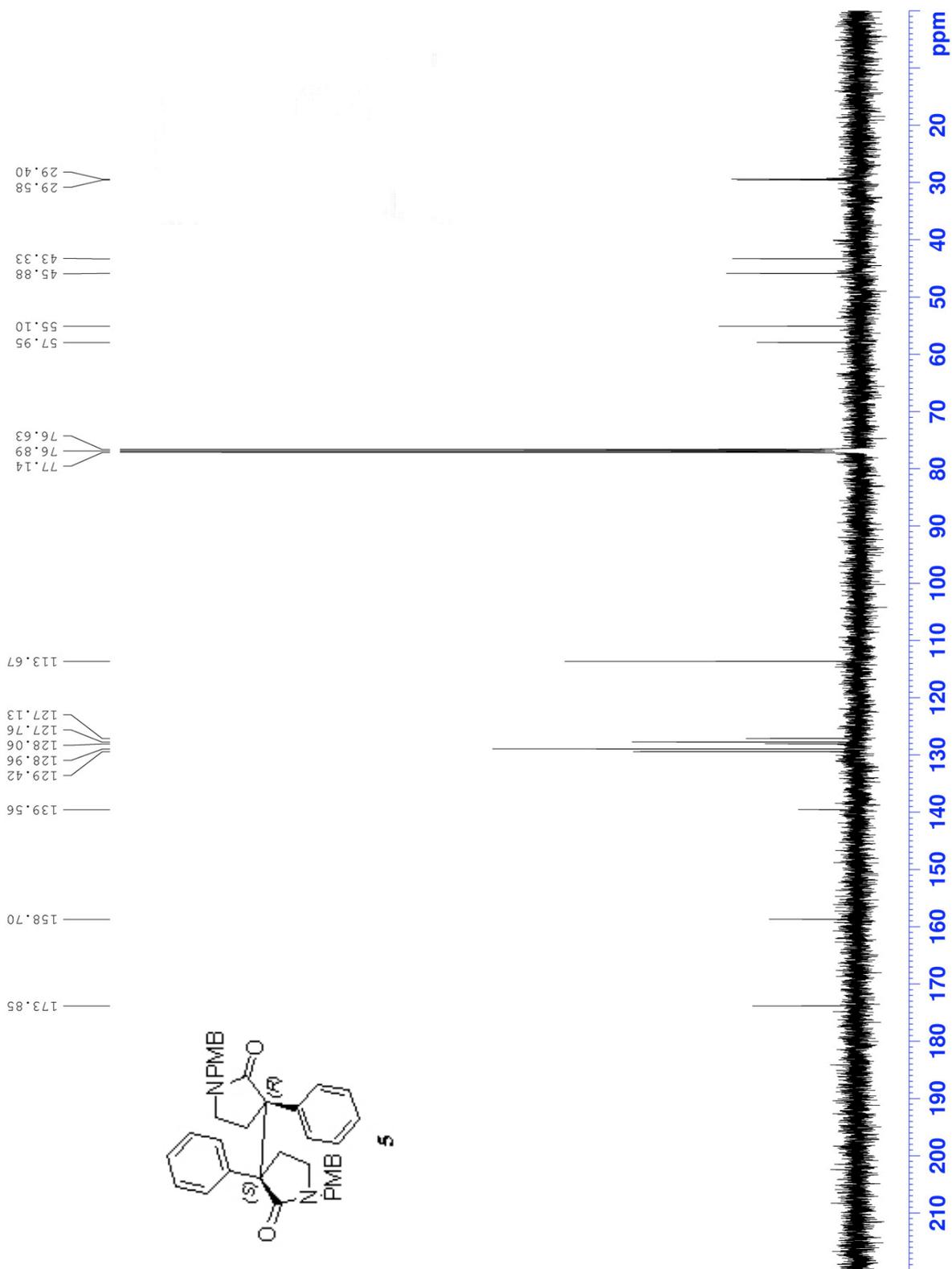












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<sup>i</sup> Prager, R. H.; Schafer, K., *Aust. J. Chem.*, **1997**, 50, 813.

<sup>ii</sup> Michael, J. P.; de Koning, C. B.; van der Westhuyzen, C. W.; Fernandes, M. A., *J. Chem. Soc., Perkin trans. 1*, **2001**, 2055.