Supplementary Material (ESI) for Chemical Communications

Kinetic Resolution of Racemic Pyrrolidine-2,5-diones Using Chiral Oxazaborolidine Catalysts

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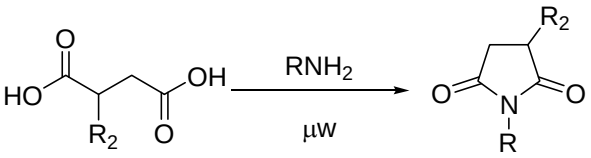
Supporting Information

I. General

All solvents were obtained dry from a Grubbs dry solvent system except 1,4-dioxane which was freshly distilled from sodium. All glassware was flame dried and cooled under vacuum before use. All reactions were carried out under nitrogen. TLC was carried out using Merck aluminium TLC sheets (silica gel 60 F_{254}), visualisation of TLC plates was performed using a UV lamp or by dipping in $KMnO_4$ then exposure to heat. Flash column chromatography was carried out with Silica Gel 40-63u 60Å (Fluorochem Limited). ^{1}H and ^{13}C NMR spectra were measured using $CDCl_3$ as a solvent unless otherwise stated, on a Bruker AC250 or AC400 machine with an automated sample changer. Chemical shifts for carbon and hydrogen are given on the δ scale relative to TMS (tetramethylsilane, δ = 0ppm). Coupling constants were measured in Hz. ^{13}C NMR spectra were recorded using the JMOD method. Specific rotations were performed on an Optical Activity Ltd. AA-10 automatic polarimeter at 589nm (Na D-Line) and measured at 20°C unless otherwise stated. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded on a Perkin-Elmer 1600 FT-IR machine using 0.5mm NaCl cells and mass spectra were recorded on a Kratos instrument. HPLC was carried out on a Gilson analytical system using a chiral stationary phase as described for each compound below. The flow rate was 1.00 cm^3 per minute (unless otherwise stated) and the detector was set at 254 nm. All chemicals were used as received without further purification except (1*R*,2*S*)-*cis*-1-amino-2-indanol which was recrystallised from hot toluene prior to use. Borane-THF was used as a 1M solution in THF.

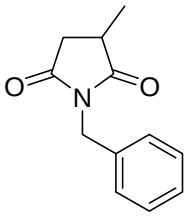
II. Racemic Imide Synthesis.

General procedure A for the synthesis of C-3 substituted imides.



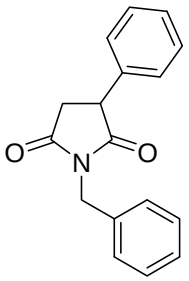
A mixture of succinic acid (20 mmol) and amine (20 mmol) were heated in a Biotage microwave reactor at 200 °C for 1 hour. The imide was purified via flash column chromatography eluting with 30% EtOAc : petroleum ether (40-60).

(±)-1-Benzyl-3-methyl-pyrrolidine-2,5-dione 4a.[1]



The title compound was obtained a colourless oil using general procedure **A**, (2.40 g, 79%); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.31 (3H, d, *J* 7.3, C*H*$_3$), 2.29 (1H, dd, *J* 17.1, 3.6, C*H*), 2.78 – 2.92 (2H, m, C*H*$_2$), 4.59 – 4.66 (2H, m, NC*H*$_2$), 7.25 – 7.36 (5H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 16.6 (*C*H$_3$), 34.7 (*C*HCH$_3$), 36.4 (*C*H$_2$), 42.3 (N*C*H$_2$), 127.9 (Ar*C*H), 128.7 (2 × Ar*C*H), 135.8 (Ar*C*), 176.1 (CH$_2$*C*=O), 180.2 (CH*C*=O). All data was in accordance with the literature.

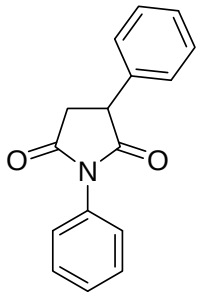
(±)-1-Benzyl-3-phenyl-pyrrolidine-2,5-dione 4b.[2]



The title compound was obtained as a white solid using general procedure **A**, (2.60 g, 50%); Mpt. 58-59 °C (lit.[3] 59–60 °C); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 2.74 (1H, dd, *J* 4.8, 18.5, C*H*$_2$), 3.12 (1H, dd, *J* 9.5, 18.5, C*H*$_2$), 3.94 (1H, dd, *J* 9.5, 4.8, C*H*), 4.61 (1H, d, *J* 14.0, NC*H*$_2$), 4.68 (1H, d, *J* 14.0, NC*H*$_2$), 7.07 – 7.37 (10H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 37.1 (*C*H$_2$), 42.7 (N*C*H$_2$), 45.8 (*C*HAr), 127.3 (Ar*C*H),

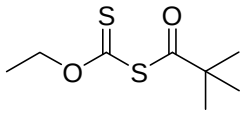
127.8 (Ar*C*H), 128.1 (Ar*C*H), 128.6 (Ar*C*H), 128.7 (Ar*C*H), 129.1 (Ar*C*H), 135.8 (Ar*C*), 137.2 (Ar*C*), 175.7 (CH_2*C*=O), 177.4 (CH*C*=O). All data was in accordance with the literature.

(±)-1-Phenyl-3-phenyl-pyrrolidine-2,5-dione 4h.[2]



The title compound was obtained as a white powder using general procedure **A**, (3.41 g, 57%); Mpt. 129-130°C; υ_{max} (film)/cm^{-1} 1775, 1698, 1595, 1495, 1454; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 3.00 (1H, dd, *J* 18.6, 4.8, C*H*$_2$), 3.38 (1H, dd, *J* 18.6, 9.5, C*H*$_2$), 4.19 (1H, dd, *J* 9.5, 4.8, C*H*), 7.25 – 7.38 (10H, m, C_6*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 36.8 (*C*H), 45.5 (*C*H_2), 125.9 (Ar*C*H), 126.8 (Ar*C*H), 127.6 (Ar*C*H), 128.2 (Ar*C*H), 128.7 (Ar*C*H), 128.8 (Ar*C*H), 131.4 (Ar*C*), 136.8 (Ar*C*), 174.6 (CH_2*C*=O), 176.1 (CH*C*=O); *m/z* (EI) 251.0958 (69%, M^+ $C_{16}H_{13}NO_2$ requires 251.0946), 119 (12), 104 (100), 103 (29), 91 (14), 78 (22), 64 (7). NMR data was in accordance with the literature.

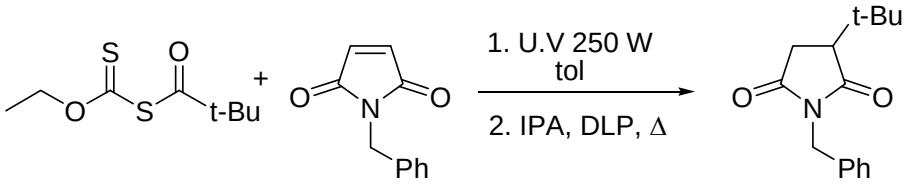
***O*-Ethyl-*S*-pivaloyl-dithiocarbonate.**[4]



A solution of potassium ethyl xanthate (10.0 g, 62.5 mmol) in acetone (100 cm^3) was added dropwise over the space of 1 hour to a solution of pivaloyl chloride (11.4 cm^3, 93.7 mmol, 1.5 eq) in acetone (20 cm^3) at -15 °C. The solution was allowed to warm to room temperature and stirred for a further 18 hours. The solvent was removed by rotary evaporation, water (50 cm^3) was added and the product extracted with CH_2Cl_2 (3 × 15 cm^3). The combined organic extracts were washed with saturated Na_2CO_3 (15 cm^3), dried over $MgSO_4$ and the solvent removed under reduced pressure. The title compound was obtained as a golden yellow liquid (11.57 g, 89%); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.26 (9H, s, *t*-Bu), 1.48 (3H, t, *J* 7.1, C*H*$_3$), 4.69 (2H, q, *J* 7.1, C*H*$_2$),

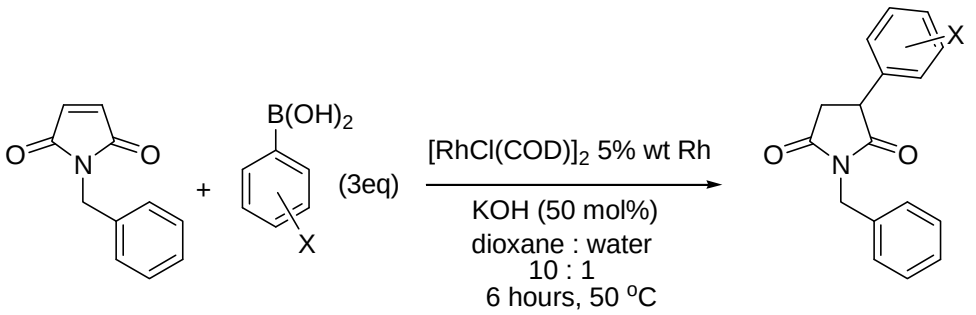
^{13}C NMR (63 MHz; $CDCl_3$) δ_C 13.0 (*C*H_3), 26.3 (3 × *C*H_3), 47.3 (*C*), 70.5 (*C*H_2), 197.9 (*C*=O), 204.2 (*C*=S); *m/z* (EI) 203 (100% M^+), 175 (23), 160 (42), 132 (27), 104 (48), 91 (47), 77 (21). No NMR data was recorded in the literature.

Synthesis of 1-benzyl-3-t-butyl-pyrrolidine-2,5-dione 4e.



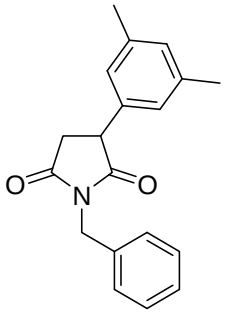
A solution of *N*-benzylmaleimide (2.33 g, 12.5 mmol) and *S*-acyl dithiocarbonate (4.05 g, 15 mmol, 1.5 eq) in dry degassed toluene (20 cm^3) was irradiated with a 250 W tungsten lamp, until no starting materials were detected by TLC. The solvent was removed under reduced pressure to give crude solid, which was recrystallised from hot toluene. The dithiocarbonate was dissolved in propan-2-ol (50 cm^3) and heated to reflux, then lauroyl peroxide (approximately 0.370g portions) was added until complete consumption of starting material was detected by TLC. The solvent was removed by rotary evaporation and the crude material re-dissolved in a THF:H_2O mixture (1:1, 50 cm^3). Lithium hydroxide (1.68 g, 0.41 mmol) was added and the reaction left to stir for 1 hour, acidified with 1M HCl to pH 3, then extracted with CH_2Cl_2 (3 × 15 cm^3). The combined organic extracts were dried over $MgSO_4$, the solvent removed and product purified by column chromatography eluting with 20% EtOAc : petroleum ether (40-60) to provide the title compound as a white solid, (1.83 g, 60%); Mpt. 63-65 ^oC; υ_{max} (film)/cm^{-1} 1764, 1685, 1433; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.01 (9H, s, 3 × C*H*$_3$), 2.51 – 2.74 (3H, m, C*H* & C*H*$_2$), 4.62 (2H, s, NC*H*$_2$), 7.27 – 7.37 (5H, m, C_6H_5), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 26.6 (3 × *C*H_3), 31.2 (*C*H), 32.9 (*C*), 41.7 (*C*H_2), 49.3 (N*C*H_2), 127.3 (Ar*C*H), 128.0 (Ar*C*H), 128.2 (Ar*C*H), 138.3 (Ar*C*), 175.6 (CH*C*=O), 177.6 (CH_2*C*=O); *m/z* (EI) 245.1416 (37%, M^+ $C_{15}H_{19}NO_2$ requires 245.1417), 200 (18), 189 (68), 111 (29), 97 (33), 91 (52), 83 (49), 55(100).

General procedure B for the synthesis of 1-benzyl-3-(aryl)-pyrrolidine-2,5-diones.[5]



Potassium hydroxide (2.5 mmol) in distilled water (1 cm^3) was added to a pale orange solution of chloro(1,5-cyclooctadiene) rhodium^{I} dimer (0.25 mmol, 5 mol% wt Rh) in dry dioxane (5 cm^3). The resulting yellow solution was stirred for 15 mins under an N_2 atmosphere. After this time the boronic acid (15 mmol) was added to the solution and stirred for a further 5 mins to give a deep orange solution. *N*-Benzylmaleimide (5 mmol) in dry dioxane (5 cm^3) was then added and the orange solution heated at 50 ^oC for 6 hours to give a yellow solution. The solution was filtered through a pad of silica, washed with Et_2O (3 × 10 cm^3) and the solvent removed under reduced pressure to give a crude yellow solid, which was purified by column chromatography eluting with 25% EtOAc : petroleum ether (40 : 60).

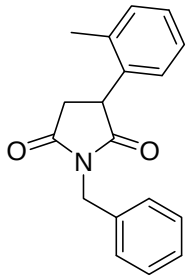
(±)-1-Benzyl-3-(3,5-dimethyl phenyl)-pyrrolidine-2,5-dione 4c.[2]



The title compound was obtained as an clear oil using general procedure **B** (1.11g, 76%); υ_{max} (film)/cm^{-1} 1775, 1689, 1604; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 2.17 (6H, s, C*H*$_3$), 2.67 (1H, dd, *J* 18.5, 4.4, C*H*$_2$), 3.06 (1H, dd, *J* 18.5, 9.4, C*H*$_2$), 3.82 (1H, dd, *J* 9.4, 4.4, C*H*), 4.59 (1H, d, *J* 14.5, NC*H*$_2$), 4.67 (1H,d, *J* 14.5, NC*H*$_2$), 6.63 (2H, s, C$_6$*H*$_3$), 6.82 (1H, s, C$_6$*H*$_3$), 7.16 – 7.34 (5H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 21.3 (2 × *C*H$_3$), 37.4 (*C*H$_2$), 42.6 (N*C*H$_2$), 45.8 (*C*H), 125.1 (Ar*C*H), 128.0 (Ar*C*H), 128.7 (Ar*C*H), 128.8 (Ar*C*H), 129.6 (Ar*C*H), 135.9 (Ar*C*), 137.3 (Ar*C*), 138.8 (2 × Ar*C*), 176.1 (CH$_2$*C*=O), 177.7 (CH*C*=O); *m/z* (EI) 293.1415 (78%, M^+ $C_{19}H_{19}NO_2$

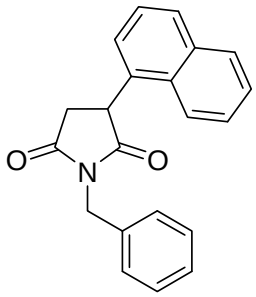
requires 293.1423), 160 (10), 132 (100), 117 (20), 91 (32), 72 (9). NMR data was in accordance to the literature.

(±)-1-Benzyl-3-(*o*-tolyl)-pyrrolidine-2,5-dione 4d.[2]



The title compound was obtained as a clear oil using general procedure **B** (819 mg, 59%); υ_{max} (film)/cm^{-1} 1770, 1691, 1499, 1422, 1401; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 2.22 (3H, s, C*H*$_3$), 2.60 (1H, dd, *J* 18.6, 4.9, C*H*$_2$), 3.13 (1H, dd, *J* 18.6, 9.6, C*H*$_2$), 4.15 (1H, dd, *J* 9.6, 4.9, C*H*), 4.63 (1H, d, *J* 14.7, NC*H*$_2$), 4.70 (1H, d, *J* 14.7, NC*H*$_2$), 6.83 (1H, app. d, *J* 6.8, C$_6$*H*$_4$), 7.02 – 7.37 (8H, m, C$_6$*H*$_4$ / C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 19.8 (*C*H$_3$), 37.1 (*C*H$_2$), 42.7 (N*C*H$_2$), 43.1 (*C*H), 126.4 (Ar*C*H), 126.8 (Ar*C*H), 127.8 (Ar*C*H), 128.1 (Ar*C*H), 128.7 (Ar*C*H), 128.9 (Ar*C*H), 131.1 (Ar*C*H), 135.7 (Ar*C*), 136.2 (Ar*C*), 148.1 (Ar*C*), 175.8 (CH$_2$*C*=O), 177.9 (CH*C*=O); *m/z* (EI) 279.1268 (100%, M$^+$ $C_{18}H_{17}NO_2$ requires 279.1259), 202 (13), 187 (8), 172 (7), 146 (47), 118 (86), 106 (33), 91 (65). NMR data was in accordance to the literature.

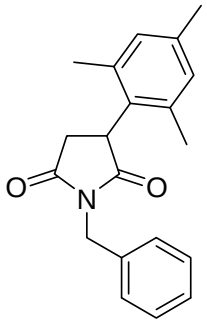
(±)-1-Benzyl-3-(1-napthyl)-pyrrolidine-2,5-dione 4f.



The title compound was obtained as a white powder using general procedure **B** (818 mg, 52%); Mpt. 134-136 ^{o}C; υ_{max} (film)/cm^{-1} 1774, 1703, 1511, 1496, 1430; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 2.81 (1H, dd, *J* 18.4, 5.0, C*H*$_2$), 3.35 (1H, dd, *J* 18.4, 9.5, C*H*$_2$), 4.71 (1H, dd, *J* 9.5, 5.0, C*H*), 4.79 (1H, d, *J* 14.6, NC*H*$_2$), 4.85 (1H, d, *J* 14.6, NC*H*$_2$), 7.18 – 7.89 (12H, m, ArC*H*), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 37.6 (*C*H$_2$), 42.8 (N*C*H$_2$), 43.4 (*C*H), 122.7 (Ar*C*H), 125.1 (Ar*C*H), 125.5 (Ar*C*H), 126.1 (Ar*C*H),

126.8 (Ar*C*H), 128.1 (Ar*C*H), 128.8 (Ar*C*H), 129.1 (Ar*C*H), 129.3 (Ar*C*H), 131.1 (Ar*C*), 133.7 (Ar*C*), 134.2 (Ar*C*), 135.8 (Ar*C*), 175.5 (CH_2C=O), 177.7 (CH*C*=O); *m/z* (EI) 315.1273 (61%, M^+ $C_{21}H_{17}NO_2$ requires 315.1259), 182 (29), 154 (100), 127 (100), 104 (16), 91 (59), 77 (28), 65 (24).

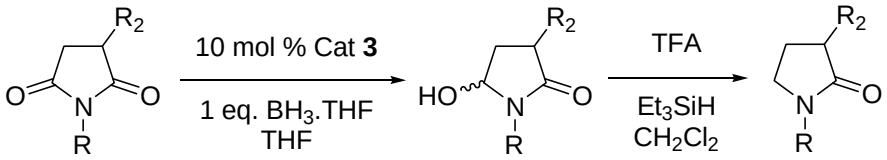
(±)-1-Benzyl-3-(2,4,6-trimethylphenyl)-pyrrolidine-2,5-dione 4g.



The title compound was obtained as a gum using general procedure **B** (1.39 g, 91%) υ_{max} (film)/cm^{-1} 1774, 1703, 1431; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.80 (3H, s, C*H*$_3$), 2.22 (3H, s, C*H*$_3$), 2.32 (3H, s, C*H*$_3$), 2.63 (1H, dd, *J* 18.3, 6.4, C*H*$_2$), 3.12 (1H, dd, *J* 18.3, 9.8, C*H*$_2$), 4.32 (1H, dd, *J* 9.8, 6.4, C*H*), 4.71 (1H, d, *J* 13.7, NC*H*$_2$), 4.77 (1H, d, *J* 13.7, NC*H*$_2$), 6.77 (1H, s, C_6H_2), 6.86 (1H, s, C_6H_2), 7.29 – 7.47 (5H, m, ArC*H*), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 19.7 (*C*H_3), 20.7 (*C*H_3), 21.0 (*C*H_3), 35.5 (*C*H_2), 41.4 (*C*H), 42.7 (N*C*H_2), 128.1 (Ar*C*H), 128.6 (Ar*C*H), 129.3 (Ar*C*H), 130.7 (Ar*C*H), 135.4 (Ar*C*), 135.7 (Ar*C*), 137.1 (Ar*C*), 137.4 (Ar*C*), 175.7 (CH_2C=O), 176.2 (CH*C*=O), *m/z* (EI) 307.1578 (100%, M^+ $C_{20}H_{21}NO_2$ requires 307.1572), 200 (7), 187 (19), 174 (34), 160 (32), 146 (82), 131 (62), 119 (75), 91 (95).

III. Regioselective Reductions.

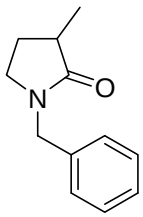
General procedure C for the regioselective reduction of C-3 substituted imides.



A solution of (±)-*cis*-1-aminoindan-2-ol (0.25 mmol) in dry THF (5 cm^3) was treated with trimethylborate (0.25 mmol) and the resulting solution allowed to stir at room temperature for 30 mins. BH_3.THF (1M, 2.5 mmol) was added, followed by a solution of the pyrrolidine (2.5 mmol) in THF (16 cm^3) and the solution allowed to stir at rt for 18 hours. The reaction was quenched by addition of 1M HCl (10 cm^3). The crude

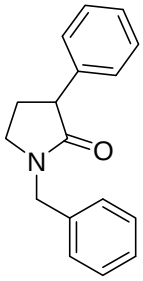
reaction mixture was extracted with CH_2Cl_2 (3 × 15 cm^3), and the combined organic extracts were dried over $MgSO_4$. The solvent was removed under vacuum to give the crude hydroxylactam which was immediately redissolved in CH_2Cl_2 (30 cm^3) and treated with TFA (1 cm^3) and triethylsilane (1 cm^3) in CH_2Cl_2 (5 cm^3). This was allowed to stir at rt for 1 hour and the solution added to an ice-water mixture (15 cm^3) followed by extraction with CH_2Cl_2 (3 × 15 cm^3). The combined organic extracts were washed with saturated $NaHCO_3$ (3 × 15 cm^3) and dried over $MgSO_4$. The solvent was removed under vacuum and purified via flash column chromatography eluting with 20% EtOAc : petroleum ether (40-60).

(±)-1-Benzyl-3-methyl-pyrrolidin-2-one 5a.[6]



The title compound was obtained as a clear oil from pyrrolidine **4a** (510 mg) using general procedure **C**, (53 mg, 11%); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.25 (3H, d, *J* 7.5, C*H*$_3$), 1.64, (1H, dq, *J* 14.1, 8.2, C*H*$_2$), 2.18 – 2.26 (1H, m, C*H*$_2$), 2.51 (1H, dq, *J* 14.1, 7.5, C*H*), 3.18 (2H, dd, *J* 8.2, 5.8, NC*H*$_2$), 4.43 (1H, d, *J* 14.5, NC*H*$_2$Ph), 4.49 (1H, d, *J* 14.5, NC*H*$_2$Ph), 7.23 – 7.33 (5H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 15.9 (*C*H$_3$), 26.6 (*C*H$_2$), 36.3 (*C*H), 44.2 (N*C*H$_2$), 46.3 (*C*H$_2$Ph), 127.0 (Ar*C*H), 127.6 (Ar*C*H), 128.2 (Ar*C*H), 136.2 (Ar*C*), 176.9 (*C*=O). All data was in accordance to the literature.

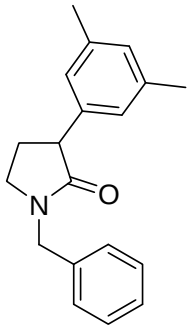
(±)-1-Benzyl-3-phenyl-pyrrolidin-2-one 5b.[7]



The title compound was obtained as a clear oil from pyrrolidine **4b** (665 mg) using general procedure **C**, (211 mg, 34%); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 2.05 – 2.15 (1H, m, C*H*$_2$), 2.45 – 2.53 (1H, m, C*H*$_2$), 3.27 – 3.37 (2H, m, NC*H*$_2$), 3.72 (1H, dd, *J*

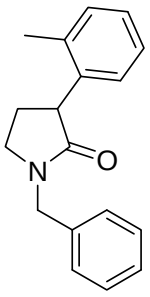
8.1, 8.2, C*H*), 4.47 (1H, d, *J* 14.8, C*H*$_2$Ph), 4.60 (1H, d, *J* 14.8, C*H*$_2$Ph), 7.25 – 7.33 (10H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 27.4 (*C*H$_2$), 44.4 (*C*H), 46.6 (N*C*H$_2$), 47.7 (*C*H$_2$Ph), 126.5 (Ar*C*H), 127.1 (Ar*C*H), 127.4 (Ar*C*H), 127.6 (Ar*C*H), 127.8 (Ar*C*H), 128.4 (Ar*C*H), 136.1 (Ar*C*), 139.4 (Ar*C*), 174.3 (*C*=O). All data was in accordance to the literature.

(±)-1-Benzyl-3-(3,5-dimethyl)-pyrrolidin-2-one 5c.



The title compound was obtained as a clear oil from pyrrolidine **4c** using general procedure **C**, (200 mg, 29%). υ_{max} (film)/cm^{-1} 1682, 1605, 1495, 1428; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.92 – 2.06 (1H, m, C*H*$_2$), 2.22 (6H, s, 2 x C*H*$_3$), 2.29 – 2.47 (1H, m, C*H*$_2$), 3.16 – 3.32 (2H, m, NC*H*$_2$), 3.56 (1H, app. t, *J* 8.6, C*H*), 4.38 (1H, d, *J* 14.6, C*H*$_2$Ph), 4.53 (1H, d, *J* 14.6, C*H*$_2$Ph), 6.77 (2H, s, C$_6$*H*$_3$), 6.81 (1H, s, C$_6$*H*$_3$), 7.17 – 7.31 (5H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 21.4 (2 × *C*H$_3$), 27.9 (*C*H$_2$), 44.9 (N*C*H$_2$), 47.1 (*C*H$_2$Ph), 48.2 (*C*H), 125.7 (Ar*C*H), 127.6 (Ar*C*H), 128.3 (Ar*C*H), 128.7 (Ar*C*H), 136.6 (Ar*C*), 138.2 (Ar*C*), 139.9 (Ar*C*), 175.1 (*C*=O); *m/z* (EI) 279.1632 (100%, M$^+$ $C_{19}H_{21}NO$ requires 279.1623) 188 (24), 173 (9), 146 (46), 145 (15), 131 (32), 119 (81), 91 (74).

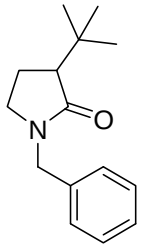
(±)-1-Benzyl-3-(*o*-tolyl)-pyrrolidin-2-one 5d.



The title compound was obtained as a clear oil from pyrrolidine **4d** using general procedure **C**, (275 mg, 42%). υ_{max} (film)/cm^{-1} 1686, 1603, 1493, 1454, 1428; ^{1}H

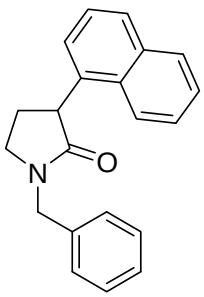
NMR (400 MHz; $CDCl_3$) δ_H 1.96 (1H, dtd, *J* 12.9, 8.8, 7.4, C*H*$_2$), 2.36 (3H, s, C*H*$_3$), 2.52 (1H, dddd, *J* 12.9, 8.8, 7.4, 4.2, C*H*$_2$), 3.30 – 3.40 (2H, m, NC*H*$_2$), 3.96 (1H, app. t, *J* 8.8, C*H*), 4.51 (1H, d, *J* 14.7, C*H*$_2$Ph), 4.66 (1H, d, *J* 14.7, C*H*$_2$Ph), 7.11 – 7.40 (9H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 19.7 (*C*H$_3$), 27.4 (*C*H$_2$), 44.8 (N*C*H$_2$), 45.4 (*C*H$_2$Ph), 47.1 (*C*H), 126.5 (Ar*C*H), 126.9 (Ar*C*H), 127.2 (Ar*C*H), 127.6 (Ar*C*H), 128.3 (Ar*C*H), 128.7 (Ar*C*H), 130.5 (Ar*C*H), 136.4 (Ar*C*), 136.6 (Ar*C*), 138.6 (Ar*C*), 175.1 (*C*=O); *m/z* (EI) 265.1479 (100%, M^+ $C_{18}H_{19}NO$ requires 265.1467) 174 (15), 132 (18), 117 (38), 105 (63), 91 (74), 77 (11), 65 (21).

(±)-1-Benzyl-3-*t*-butyl-pyrrolidin-2-one 5e.



The title compound was obtained as a clear oil from pyrrolidine **4e** (612 mg) using general procedure **C**, (217 mg, 37%); υ_{max} (film)/cm^{-1} 1703, 1640, 1607, 1586, 1508, 1440; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.07 (9H, s, 3 × C*H*$_3$), 1.84 (1H, ddd, *J* 13.1, 9.0, 8.6, C*H*$_2$), 1.98 – 2.06 (1H, m, C*H*$_2$), 2.31 (1H, app. t, *J* 9.0, C*H*), 3.07 – 3.17 (2H, m, NC*H*$_2$), 4.37 (1H, d, *J* 14.6, C*H*$_2$Ph), 4.52 (1H, d, *J* 14.6, C*H*$_2$Ph), 7.22 – 7.34 (5H, m, C$_6$*H*$_5$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 20.7 (*C*H$_2$), 26.8 (*C*H$_3$), 32.2 (*C*), 43.9 (*C*H), 46.1 (N*C*H$_2$), 50.6 (*C*H$_2$Ph), 126.9 (Ar*C*H), 127.6 (Ar*C*H), 128.1 (Ar*C*H), 136.4 (Ar*C*), 174.8 (*C*=O); *m/z* (EI) 231.1634 (30%, M^+ $C_{15}H_{21}NO$ requires 231.1623) 216 (7), 175 (100), 106 (4), 91 (77), 84 (4), 69 (6), 65 (11).

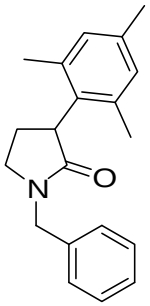
(±)-1-Benzyl-3-(1-napthyl)-pyrrolidin-2-one 5f.



The title compound was obtained as a clear oil from pyrrolidine **4f** using general procedure **C** (293 mg, 39%). υ_{max} (film)/cm^{-1} 1685, 1494, 1454, 1428; ^{1}H NMR (250

MHz; $CDCl_3$) δ_H 2.05 – 2.19 (1H, ddd, *J* 15.3, 13.0, 7.8, C*H*$_2$), 2.60 – 2.75 (1H, m, C*H*$_2$), 3.39 – 3.45 (2H, m, NC*H*$_2$), 4.48 (1H, dd, *J* 9.4, 7.8, C*H*), 4.57 (1H, d, *J* 14.8, PhC*H*$_2$), 4.74 (1H, d, *J* 14.8, PhC*H*$_2$), 7.36 – 7.55 (9H, m, C_6H_5 & $C_{10}H_7$), 7.78 – 7.98 (3H, m, C_6H_5 & $C_{10}H_7$), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 27.9 (*C*H$_2$), 44.9 (N*C*H$_2$), 45.3 (*C*H), 47.2 (Ph*C*H$_2$), 123.4 (Ar*C*H), 125.0 (Ar*C*H), 125.6 (Ar*C*H), 126.1 (Ar*C*H), 127.7 (Ar*C*H), 128.4 (Ar*C*H), 128.8 (Ar*C*H), 129.0 (Ar*C*H), 131.7 (Ar*C*), 134.2 (Ar*C*), 136.2 (Ar*C*), 136.6 (Ar*C*), 174.9 (*C*=O). *m/z* (EI) 301.1469 (100%, M^+ $C_{21}H_{19}NO$ requires 301.1467) 287 (12), 210 (24), 168 (38), 167 (47), 153 (59), 141 (67), 91 (73).

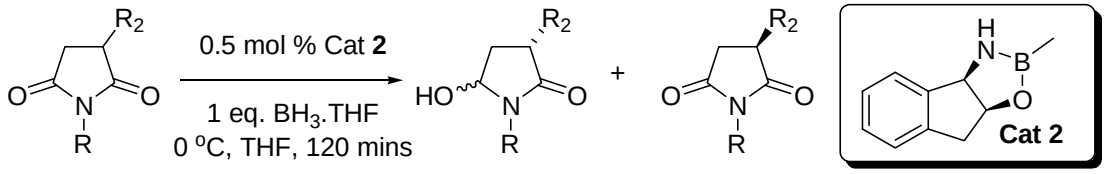
(±)-1-Benzyl-3-(2,4,6-trimethylphenyl)-pyrrolidin-2-one 5g.



The title compound was obtained as a clear oil from pyrrolidine **4g** using general procedure **C** (360 mg, 48%). υ_{max} (film)/cm^{-1} 1686, 1611, 1494, 1428; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.94 – 2.11 (1H, m, C*H*$_2$), 2.24 (3H, s, C*H*$_3$), 2.27 (3H, s, C*H*$_3$), 2.33 – 2.45 (4H, m, C*H*$_2$ & C*H*$_3$), 3.42 – 3.29 (2H, m, NC*H*$_2$), 4.09 (1H, app. t, *J* 10.5, C*H*), 4.37 (1H, d, *J* 14.0, C*H*$_2$Ph), 4.73 (1H, d, *J* 14.0, C*H*$_2$Ph), 6.87 (2H, s, C_6H_2), 7.31 – 7.42 (5H, m, C_6H_5), ^{13}C NMR (63 MHz; $CDCl_3$) δ_C 19.0 (*C*H$_3$), 19.7 (*C*H$_3$), 19.9 (*C*H$_3$), 23.9 (*C*H$_2$), 42.7 (*C*H), 43.6 (N*C*H$_2$), 46.1 (*C*H$_2$Ph), 126.6 (Ar*C*H), 127.4 (Ar*C*H), 127.6 (Ar*C*H), 127.9 (Ar*C*H), 129.7 (Ar*C*H), 131.8 (Ar*C*), 135.4 (Ar*C*), 135.6 (Ar*C*), 136.1 (Ar*C*), 174.1 (*C*=O); *m/z* (EI) 293.1793 (100%, M^+ $C_{20}H_{23}NO$ requires 293.1780), 173 (14), 145 (32), 133 (27), 119 (22), 91 (53).

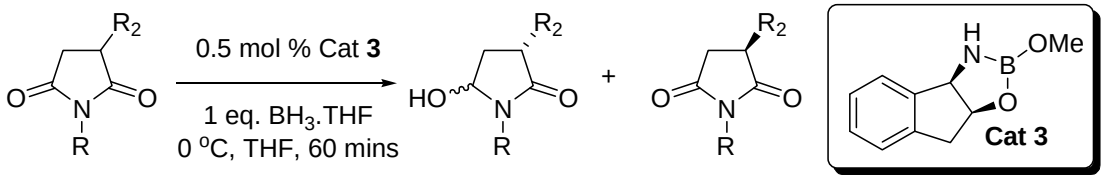
IV. Kinetic Resolutions

General Procedure D for the kinetic resolution of C-3 imides with *B*-Me catalyst.



A suspension of (1*R*,2*S*)-*cis*-1-aminoindan-2-ol (149 mg, 1 mmol) in dry toluene (3 cm^3) was treated with trimethylboroxine (88 μl, 0.33 mmol) and allowed to stir for 30 mins., followed by addition of toluene (5 cm^3) and subsequent distillation until approximately 2 cm^3 of solvent remained. This procedure was repeated twice more after which the toluene was removed under reduced pressure to give a white solid. THF (20 cm^3) was added to give solution of catalyst **2** which was used immediately thus no analytical data was obtained. A aliquot of catalyst **2** (0.1 cm^3) was added to a solution of imide (1 mmol) in THF (8 cm^3) at 0 °C followed by BH_3.THF (1 cm^3, 1 mmol). The solution was allowed to stir for 120 mins at 0 °C, then quenched by addition of MeOH (2 cm^3) and 1M HCl (2 cm^3). The product was extracted with CH_2Cl_2 (1 × 10 cm^3, 3 × 5 cm^3), the organic extracts dried over $MgSO_4$ and solvent removed under reduced pressure. The crude material which was purified via column chromatography eluting with 25% EtOAc : petroleum ether (40 : 60).

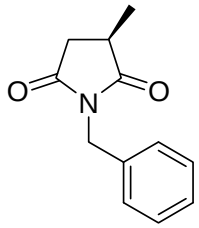
General Procedure E for the kinetic resolution of C-3 imides with *B*-OMe catalyst.



A solution of (1*R*,2*S*)-*cis*-1-aminoindan-2-ol (149 mg, 1mmol) in THF (3 cm^3) was treated with trimethylborate (110 μl, 1mmol) and allowed to stir for 30 mins. The solution was then diluted to 20 cm^3 by further addition of THF. The imide (1 mmol) in THF (8 cm^3) was cooled to 0 °C, then catalyst **3** (0.1 cm^3) was added followed by BH_3.THF (1 cm^3, 1 mmol). The resulting solution was stirred for 60 mins at 0 °C then quenched by addition of MeOH (2 cm^3) and 1M HCl (2 cm^3). The product was extracted with CH_2Cl_2 (1 × 10 cm^3, 3 × 5 cm^3), the organic extracts dried over $MgSO_4$

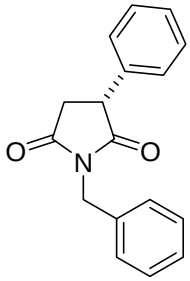
and solvent removed under reduced pressure to give crude product. Purification was carried out by column chromatography eluting with 25% EtOAc : petroleum ether (40 : 60).

(*R*)-1-Benzyl-3-methyl-pyrrolidine-2,5-dione 4a.[1]



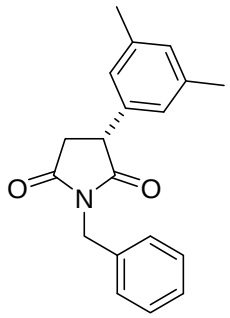
The title compound was obtained as a clear oil using general procedure **D** (46%, ee 16%) or **E** (32%, ee 11%). $[\alpha]_D$ + 8.1 (*c* 0.2, $CHCl_3$, ee 63%), lit.[1] +14 (*c* 0.18, $CHCl_3$, ee 99%). All other data as previously stated. Chiral HPLC: CHIRALPAK AD, 1.3% IPA in hexane, t_R (R) enantiomer 34.5 min and (*S*) enantiomer 38.7 min.

(*R*)-1-Benzyl-3-phenyl-pyrrolidine-2,5-dione 4b.[2]



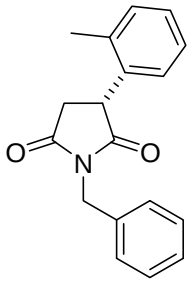
The title compound was obtained as a white powder using general procedure **D** (52%, ee 45%) or **E** (36%, ee 28%). $[\alpha]_D$ -40.0 (*c* 0.3, $CHCl_3$, ee 75%), lit.[2] +46.9 (*c* 0.83, $CHCl_3$, ee 93% *S* enantiomer). All other data as previously stated. Chiral HPLC: CHIRALPAK AD, 8% IPA in hexane, t_R (*R*) enantiomer 17.6 min (*S*) enantiomer 22.6 min.

(*R*)-1-Benzyl-3-(3,5-dimethylphenyl)-pyrrolidine-2,5-dione 4c.[2]



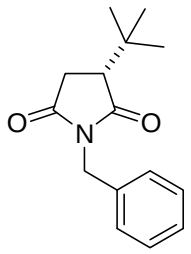
The title compound was obtained as a clear oil using either general procedure **D** (48%, ee 41%), or **E** (39%, ee 42%). $[\alpha]_D$ -38 (*c* 2.4, $CHCl_3$, 91%), lit.[2] +44 (*c* 2.42, $CHCl_3$, ee 92% *S* enantiomer). All other data as previously stated. Chiral HPLC, CHIRALPAK AD, 5% IPA in hexane, t_R (*R*) enantiomer 15.3 mins (*S*) enantiomer 20.7 mins.

(*R*)-1-Benzyl-3-(*o*-tolyl)-pyrrolidine-2,5-dione 4d.[2]



The title compound was obtained as a clear oil using general procedure **D** (23%, ee 24%) or **E** (43%, ee 57%). $[\alpha]_D$ +4.8 (*c* 2.5, $CHCl_3$, ee 90%), lit.[2] -5.2 (*c* 2.68, $CHCl_3$, ee 95% *S* enantiomer). All other data as previously stated. Chiral HPLC, CHIRALCEL OD, 20% IPA in hexane flow rate 0.8 ml/min, t_R (*S*) enantiomer 13.3 min (*R*) enantiomer 18.9 min.

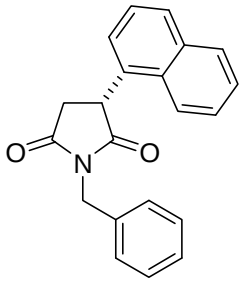
(*R*)-1-Benzyl-3-*t*-butyl-pyrrolidine-2,5-dione 4e.



The title compound was obtained as a white powder using general procedure **D** (38%, ee 52%) or **E** (35%, ee 47%). $[\alpha]_D$ -18 (*c* 0.1, $CHCl_3$, 99%). All other data was as

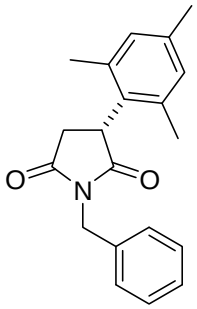
previously stated. Chiral HPLC, CHIRALPAK AD, 8% IPA in hexane, t_R (*R*) enantiomer 7.32 min (*S*) enantiomer 8.76.

(*R*)-1-Benzyl-3-(naphthyl)-pyrrolidine-2,5-dione 4f.



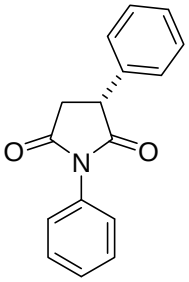
The title compound was obtained as a off white powder using either general procedure **D** (21%, ee 26%) or **E** (30%, ee 37%). $[\alpha]_D$ 31.3 (*c* 0.25, $CHCl_3$, ee 93%). Chiral HPLC, CHIRALCEL OD, 20% IPA in hexane at flow rate 0.8 ml/min, t_R (*S*) enantiomer 30.6 min (*R*) enantiomer 35.7 min.

(*S*)-1-Benzyl-3-(2,4,6-trimethylphenyl)-pyrrolidine-2,5-dione 4g.



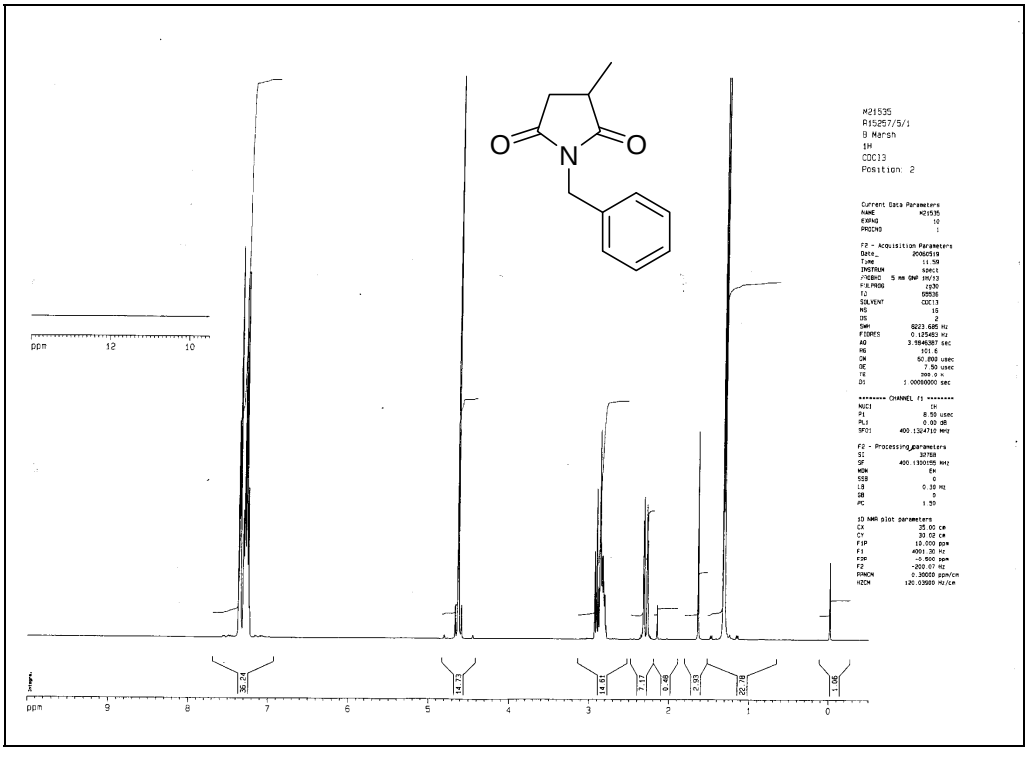
The title compound was obtained as an amorphous solid using either general procedure **D** (31%, ee 16%), or **E** (34%, ee 5%). $[\alpha]_D$ 4.7 (*c* 0.15, $CHCl_3$, ee 45%). All other data was as previously stated. Chiral HPLC, CHIRALPAK AD, 5% IPA in hexane, (*R*) enantiomer 16.0 min (*S*) enantiomer 18.0 min.

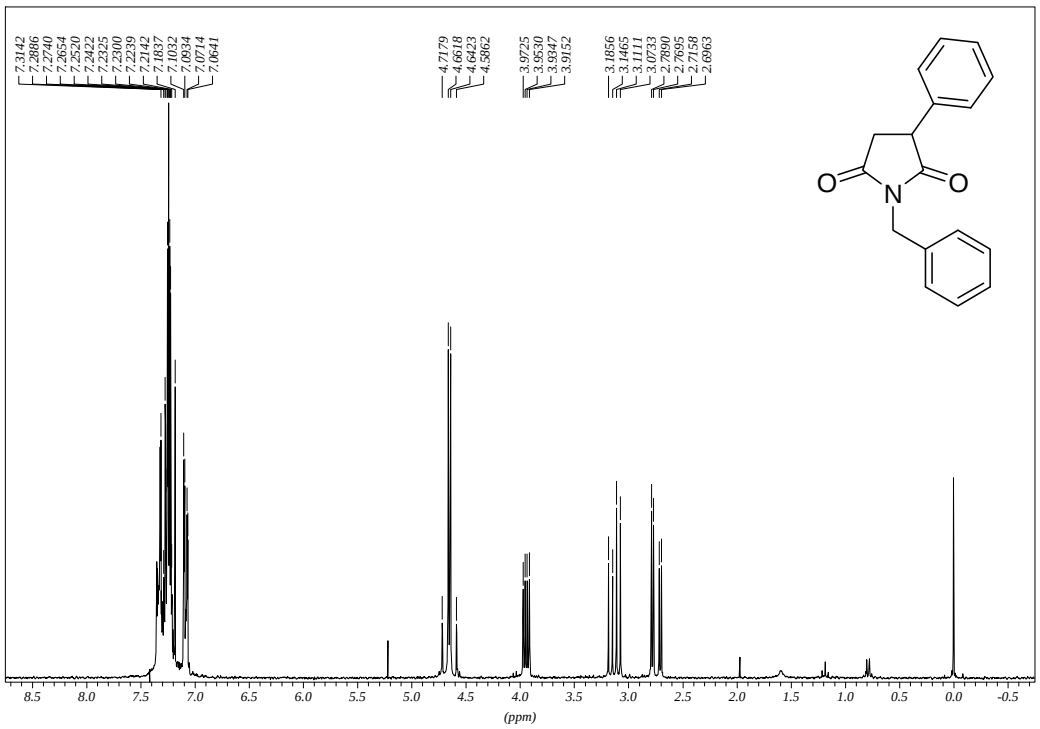
(*R*)-1-Phenyl-3-phenyl-pyrrolidine-2,5-dione 4h.[2]



The title compound was obtained as an off white powder using general procedure **E** (17%, ee 3%). $[\alpha]_D$ -7.1 (*c* 1.0, $CHCl_3$, 80%), lit.[2] +10.6 (*c* 1.06, $CHCl_3$, ee 90% *S* enantiomer). All other data was a previously stated. Chiral HPLC, CHIRALCEL OD, 5% IPA in hexane, t_R (*S*) enantiomer 47.3 min (*R*) enantiomer 53.1 min.

V. 1H NMR Data

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7.2520
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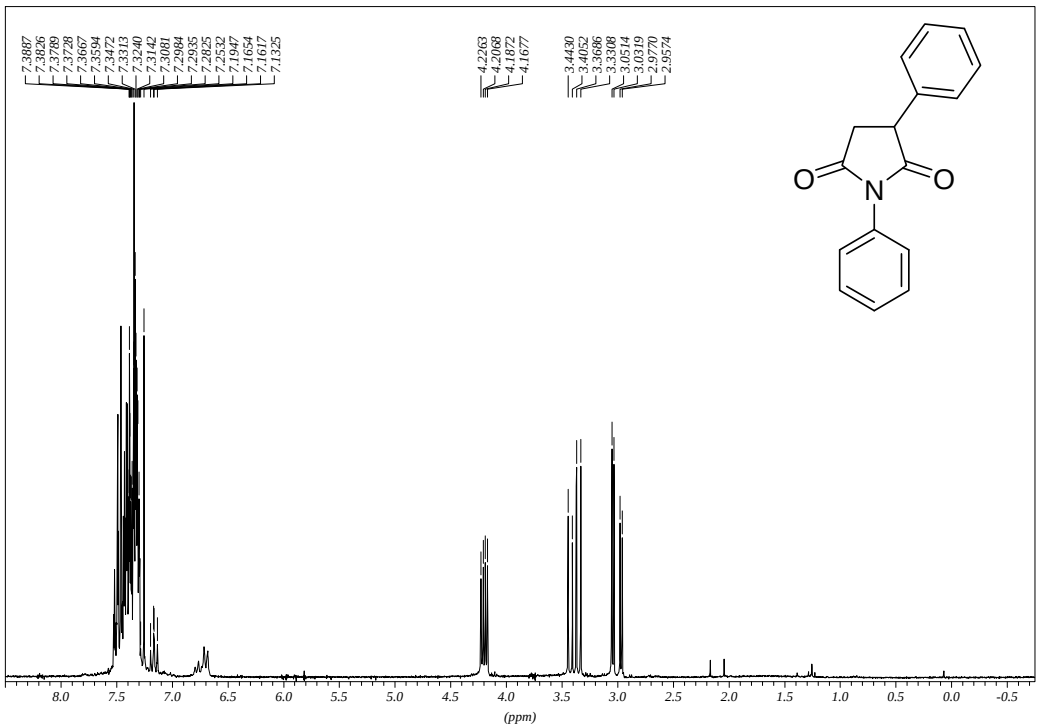
7.2325
7.2300
7.2239
7.2142
7.1837
7.1032
7.0934
7.0714
7.0641
4.7179
4.6618
4.6423
4.5862
3.9725
3.9530
3.9347
3.9152
3.1856
3.1465
3.1111
3.0733
2.7890
2.7695
2.7158
2.6963
O
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)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7.3728
7.3667
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7.3554
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7.3313
7.3240
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7.3091
7.3004
7.2935
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7.1654
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4.1872
4.1677
3.4430
3.4052
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O
N
O
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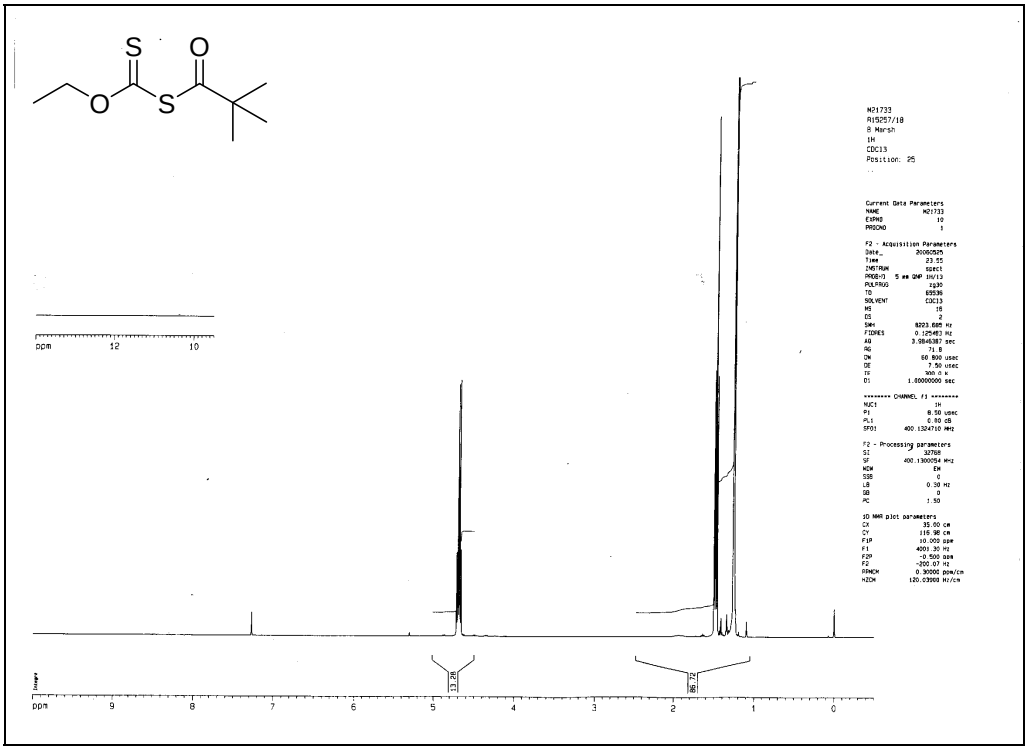
(ppm)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O
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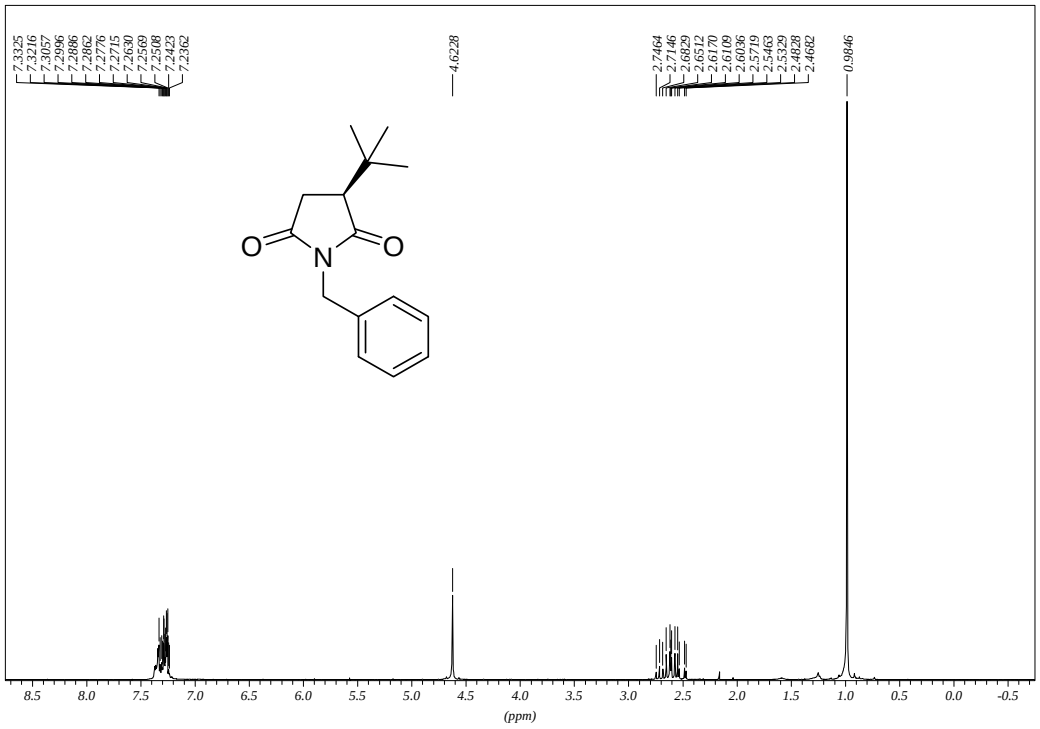
13.26
16.72
ppm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7.2362
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2.6109
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O
N
O
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6.0
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5.0
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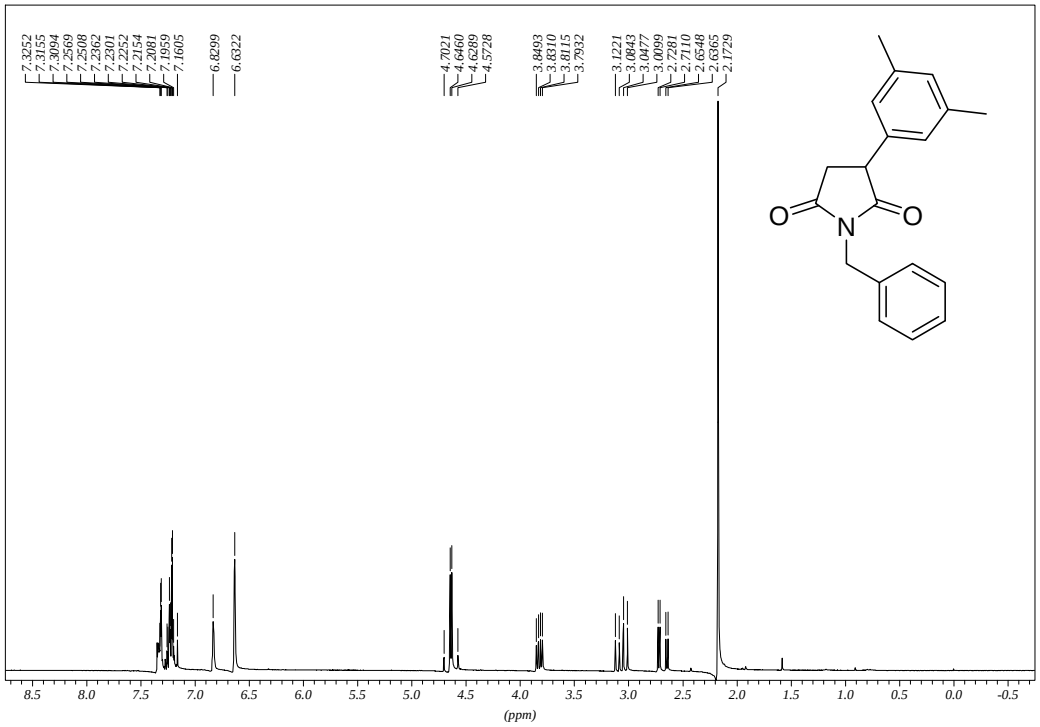
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7.1605
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6.6322
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4.5728
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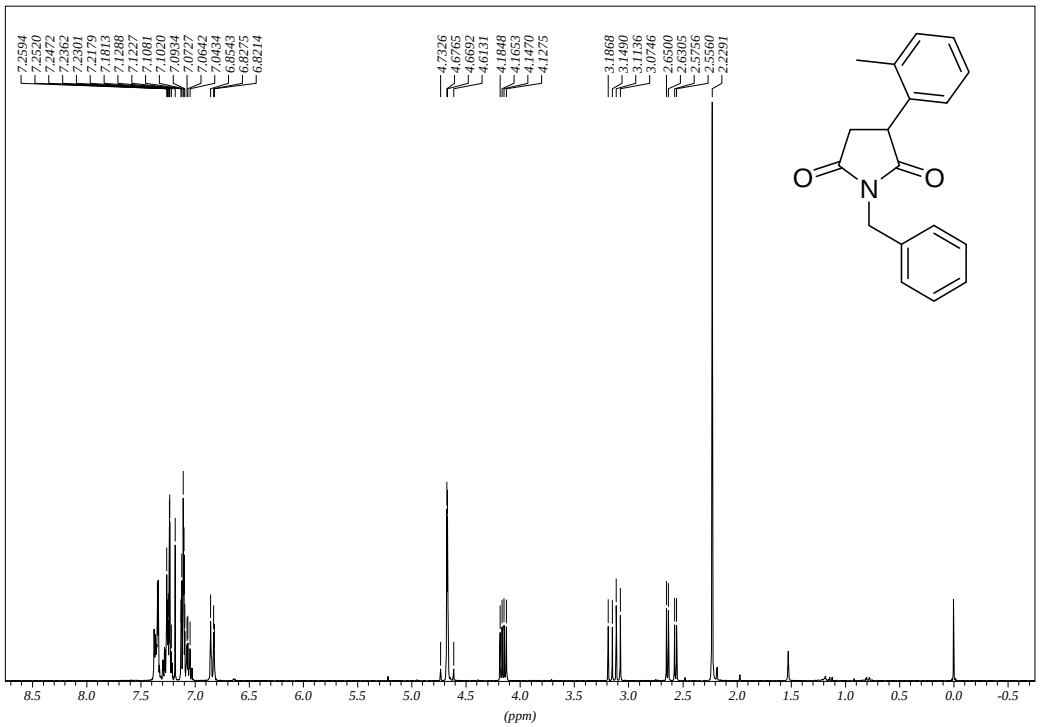
3.8115
3.7932
3.1221
3.0843
3.0477
3.0099
2.7281
2.7110
2.6548
2.6365
2.1729
O
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)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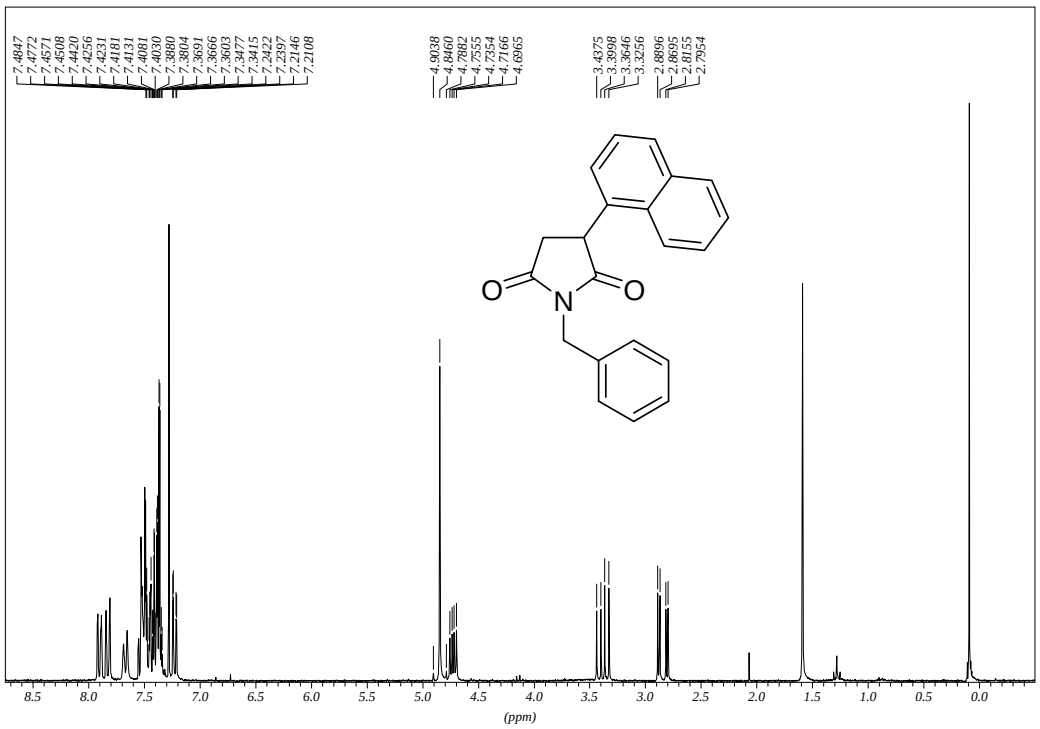
7.1020
7.0934
7.0727
7.0642
7.0434
6.8543
6.8275
6.8214
4.7326
4.6765
4.6692
4.6131
4.1848
4.1653
4.1470
4.1275
3.1868
3.1490
3.1136
3.0746
2.6500
2.6305
2.5756
2.5560
2.2291
O
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)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7.3477
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3.3646
3.3256
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2.8155
2.7954
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N
O
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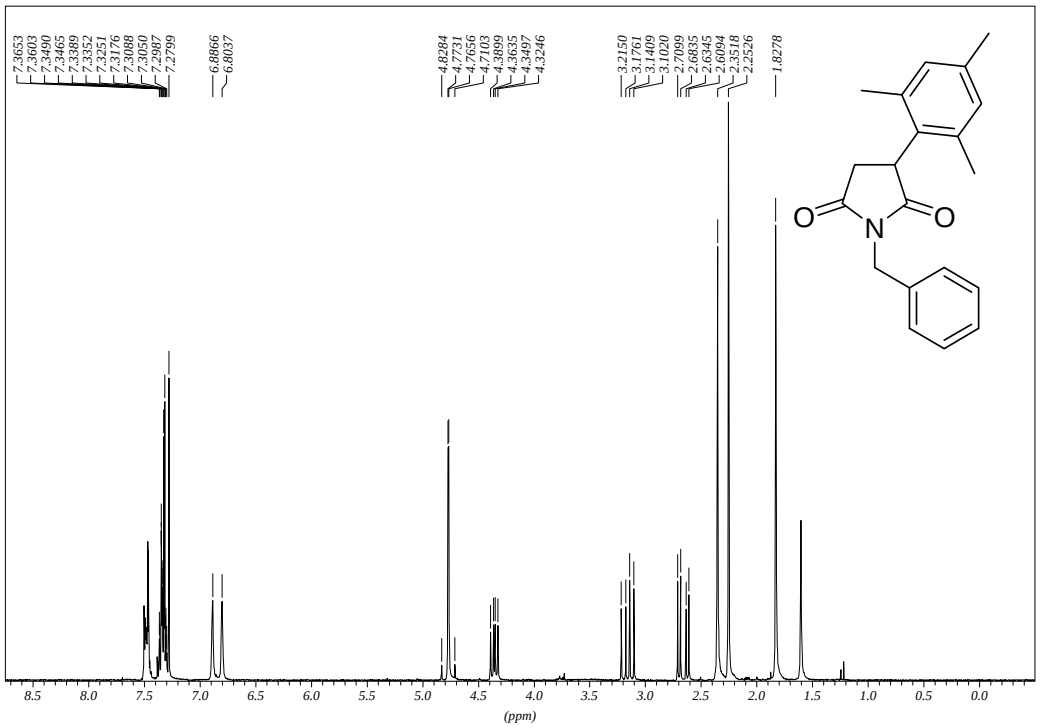
(ppm)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3.1020
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2.6835
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2.6094
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O
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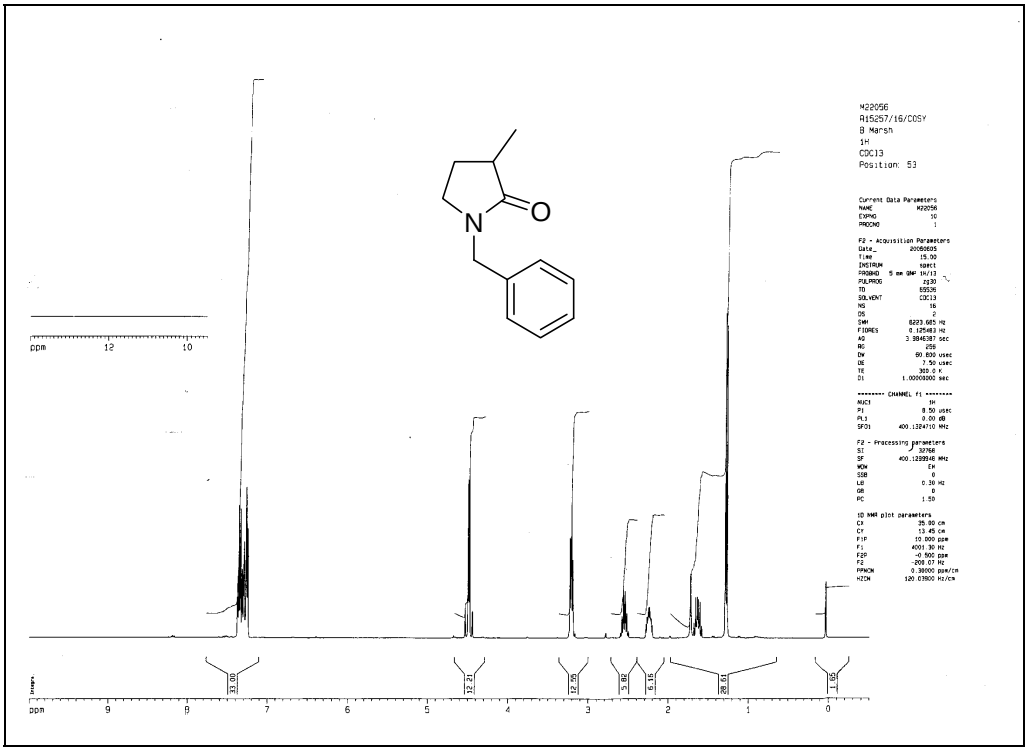
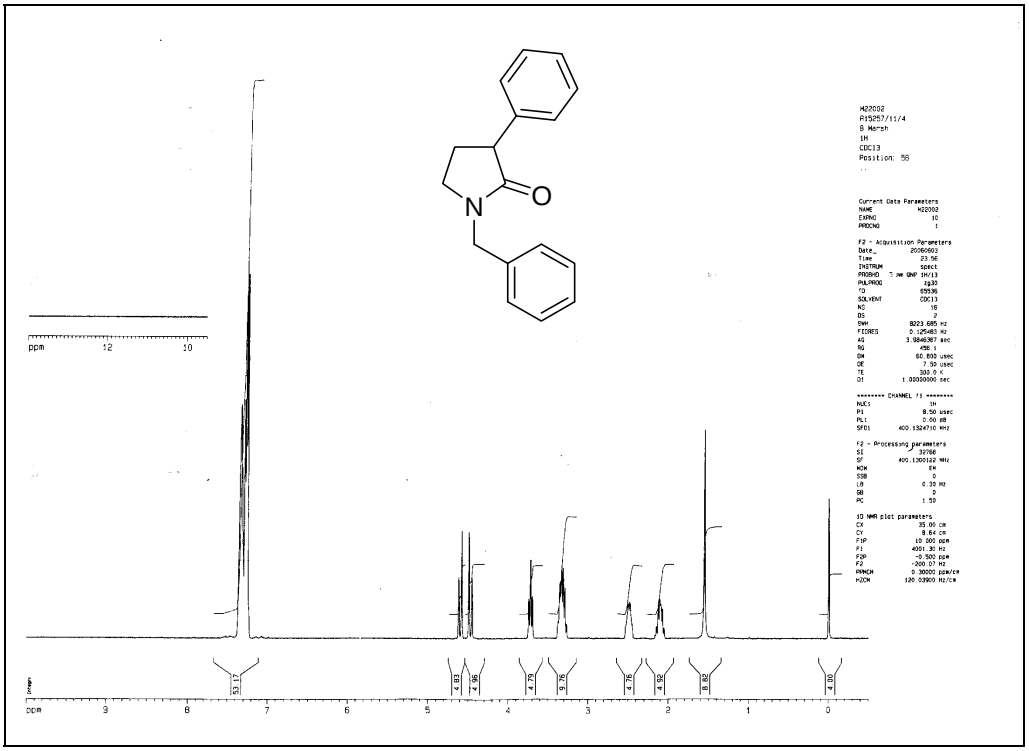
(ppm)


N
O
ppm
12
10
ppm
9
8
7
6
5
4
3
2
1
0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ppm
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10
ppm
9
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7
6
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3
2
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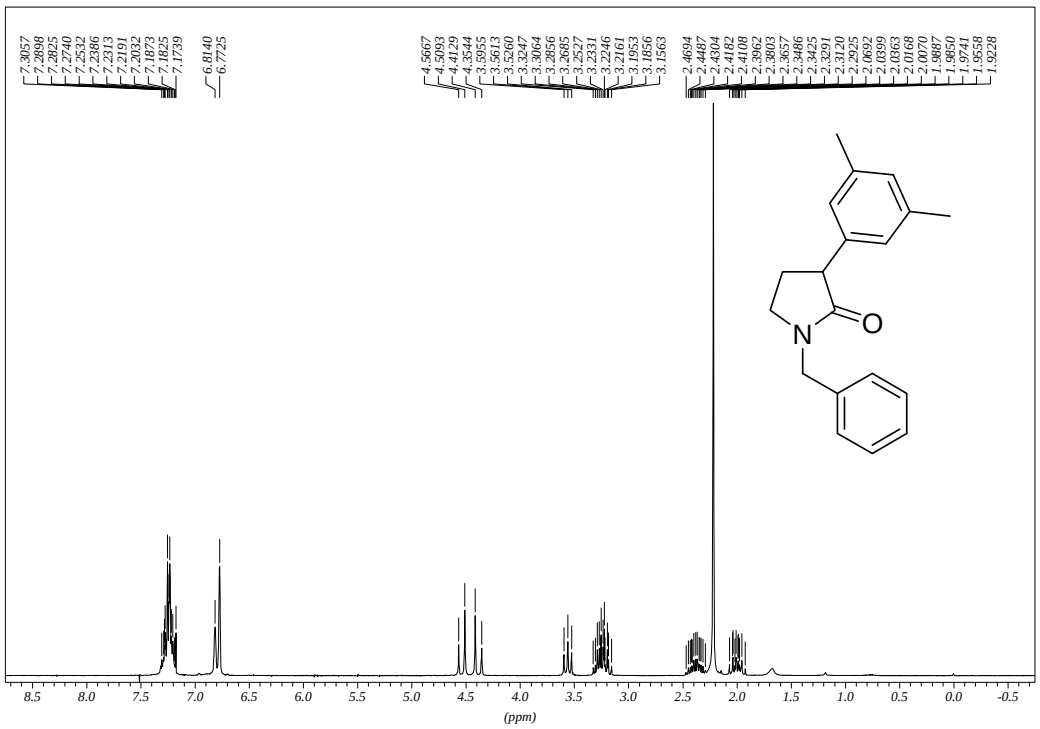
0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7.1825
7.1739
6.8140
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4.4129
4.3544
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3.5613
3.5260
3.3247
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3.2856
3.2685
3.2527
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3.2161
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2.3425
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2.0363
2.0168
2.0070
1.9887
1.9850
1.9741
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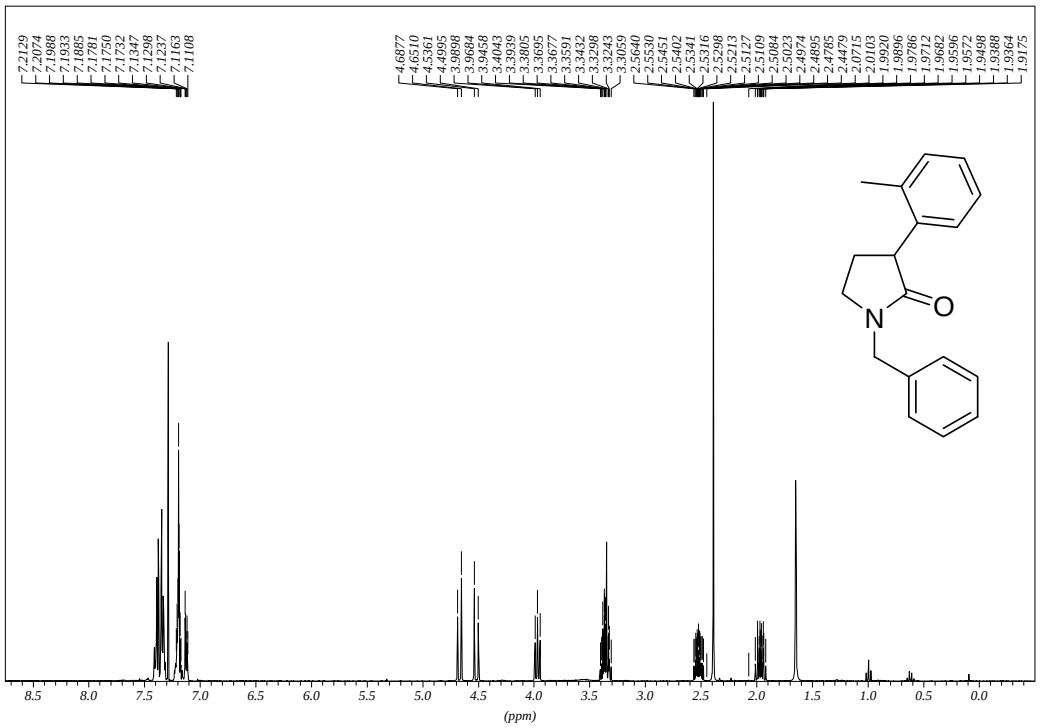
1.9228
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)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4.6510
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4.4995
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3.9684
3.9458
3.4043
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3.3695
3.3677
3.3591
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2.5341
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2.5298
2.5213
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2.5109
2.5084
2.5023
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2.4895
2.4785
2.4479
2.0715
2.0103
1.9920
1.9896
1.9786
1.9712
1.9682
1.9596
1.9572
1.9498
1.9388
1.9364
1.9175
N
O
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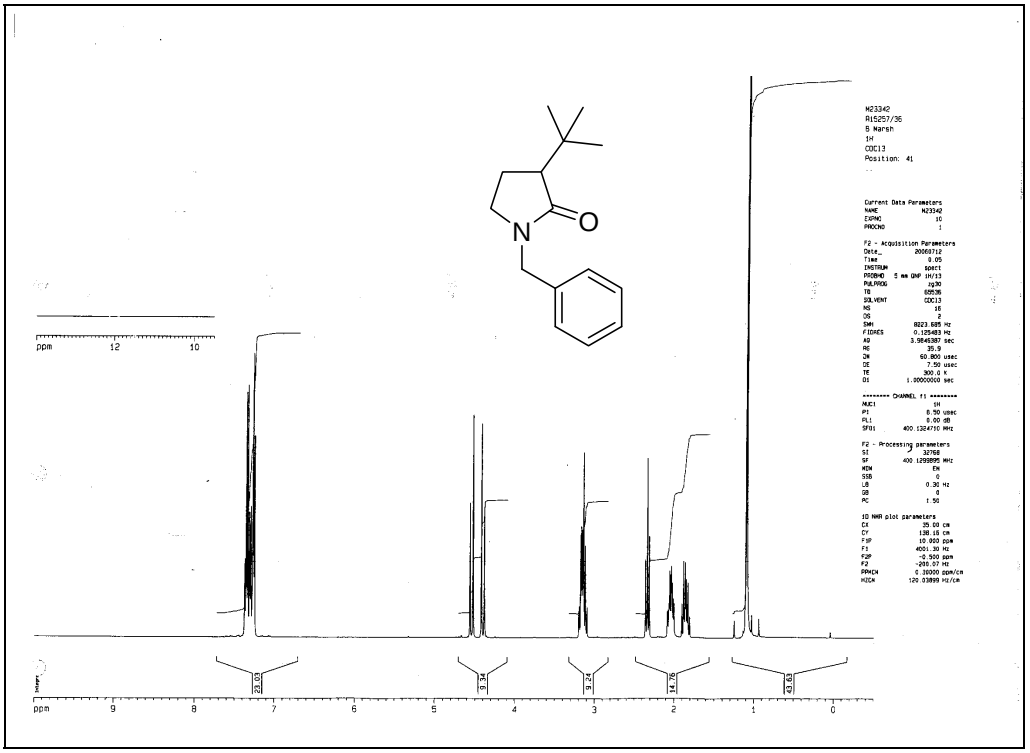
(ppm)


N
O
ppm
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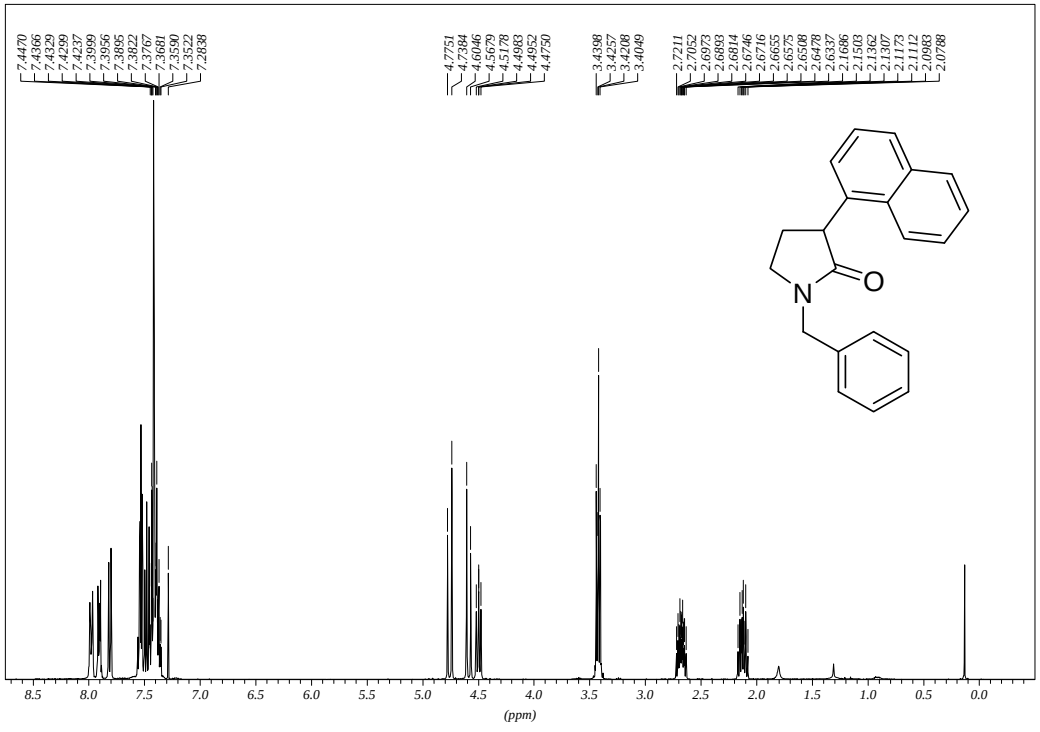
9.24
14.76
43.63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3.4208
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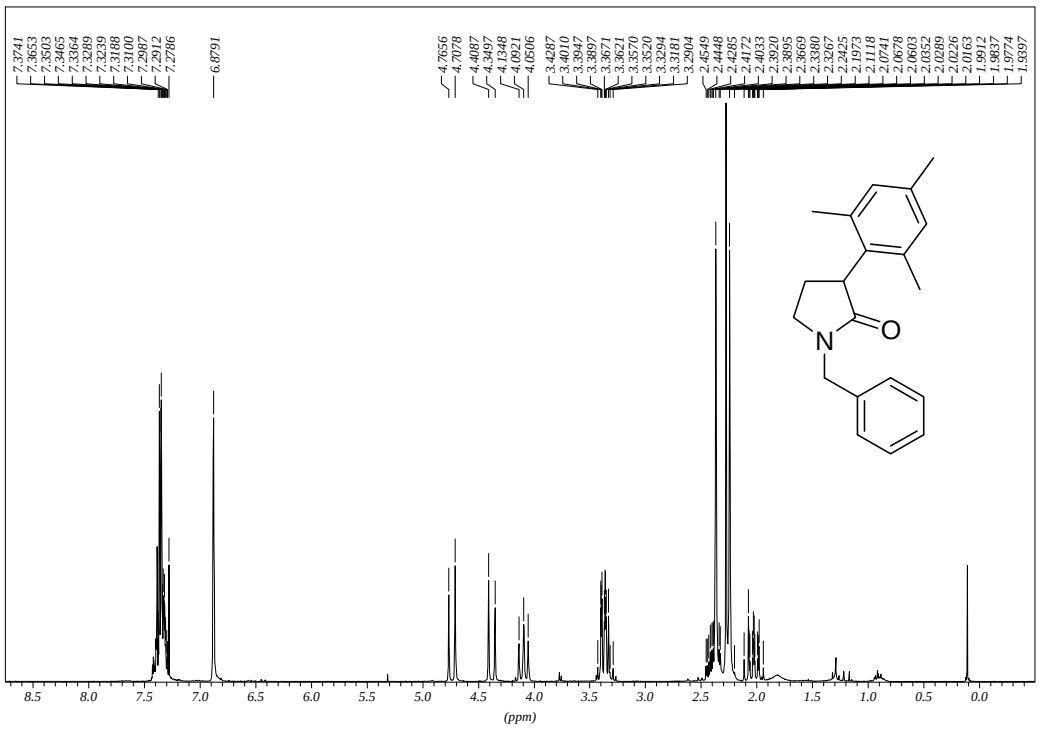
N
O
(ppm)



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