Supporting Information

Palladium-Catalysed Enantioselective α-Hydroxylation of β-Ketoesters

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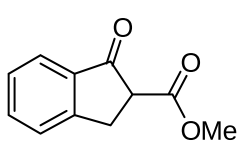
Contents

General Experimental. Solvents were dried by passing through columns of molecular sieves in a solvent purification system. Unless otherwise stated, all precursors and reagents were procured commercially and used as received. Substrates ethyl cyclopentanone-2-carboxylate (**IIa**) and ethyl 3-phenyl-2-acetylpropionate (**Vb**) were purchased from Sigma Aldrich. Palladium salts were provided by Johnson Matthey plc through a precious metals loan agreement. All manipulations involving air-sensitive reagents were performed using standard Schlenk techniques and oven-dried glassware.

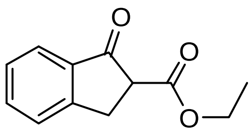
Asymmetric α-hydroxylation reactions were carried out without any special precautions for the exclusion of air or moisture, unless otherwise stated. Column chromatography and TLC were performed on silica gel (Kieselgel 60). α-Hydroxy products were visualised with ceric ammonium molybdate dip.

^{1}H, ^{13}C and ^{31}P NMR spectra were obtained on Bruker AVACE400 (Imperial) or Varian Inova 400 instruments (Pfizer) with ^{1}H at 400 MHz, ^{31}P at 161.9 MHz and ^{13}C at 100.6 MHz. Chemical shifts are reported in δ (ppm), referenced to residual protons and ^{13}C signals of deuterated chloroform. Multiplicity is abbreviated to s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Melting points were determined using an Electrothermal Gallenhamp apparatus fitted with a calibrated thermometer with an error of ±2°C. Infrared spectra were recorded using a Perkin Elmer 100 series FT-IR spectrometer, equipped with a beam-condensing accessory (samples were sandwiched between diamond compressor cells). HPLC analyses were performed on Gilson or Hewlett Packard HPLC machines. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Mass spectra (MS) were recorded on either a Micromass Autospec Premier or a VG Platform II spectrometer using FAB^+, EI, ESI or CI techniques.

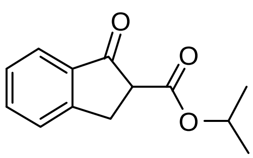


Methyl 1-indanone-2-carboxylate (Ia).[1] A round bottom flask was charged with NaH (60% suspension in mineral oil, 2.86 g, 71.5 mmol) and purged with nitrogen. The solid was then washed with pentane (3 x 20mL) and suspended in toluene (40mL). Dimethyl carbonate (14.4 mL, 171.6 mmol) was added, and the mixture was warmed to 60°C, whereupon a solution of 1-indanone (3.78 g, 28.6 mmol) in toluene (40 mL) was added dropwise over 1 h. After stirring for a further 1 h at 60°C, the reaction mixture was cooled to rt, and quenched by the addition of acetic acid (5 mL) and 2M HCl (60 mL). The aqueous phase was extracted into toluene (2 x 50 mL) and the combined organic extracts washed with H_2O (2 x 30 mL), dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by distillation (140°C, 0.1 Torr) to afford the ketoester (3.59 g, 66%, keto/enol, 4/1) as a colourless oil that solidified on standing. Mp 50-55°C (lit.,[1] 51-60°C); ν_{max}/cm^{-1} 2956, 1737 (C=O), 1708 (C=O), 1606, 1436, 1319, 1210, 1161; δ_H (400 MHz, $CDCl_3$) 7.80 (1H, d, *J* 7.6, Ar), 7.68-7.63 (1H, m, Ar), 7.54-7.40 (2H, m, Ar), 3.82 (3H, s, CH_3), 3.76 (1H, dd, *J* 8.4, 4.2, CHC=O), 3.59 (1H, dd, *J* 17.4, 4.2, CH_2), 3.40 (1H, dd, *J* 17.4, 8.4, CH_2). Minor peaks due to enol observed at 10.42 (1H, br s, OH), 3.88 (3H, s, CH_3), 3.54 (2H, s, CH_2); δ_C (100 MHz, $CDCl_3$) 199.44 (C=O), 169.57 (OC=O), 153.60 (Ar), 135.48 (Ar), 135.24 (Ar), 127.85 (Ar), 126.57 (Ar), 124.74 (2C, Ar), 53.16 (*C*HC=O), 52.80 (CH_3), 30.28 (CH_3). Minor peaks due to enol observed at 129.43 (Ar), 126.85 (Ar), 120.78 (Ar), 32.53 (CH_2); *m/z* (EI) 190 (M^+, 71%), 159 (23), 130 (100).

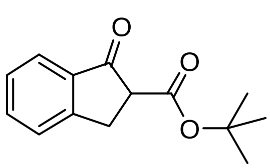
General method for the transesterification of methyl 1-indanone-2-carboxylate. A flask was charged with methyl 1-indanone-2-carboxylate (1.00 g, 5.26 mmol), the corresponding alcohol (50 mL) and dibutyl tin oxide (131 mg, 0.526 mmol). The mixture was refluxed until complete conversion was observed by TLC, then concentrated in vacuo and purified by column chromatography.



Ethyl 1-indanone-2-carboxylate (Ib).[2] Prepared by the general method (4 h reflux) and purified by column chromatography (hexane/ethyl acetate, 50/1 to 6/1) to give the ethyl ester (851 mg, 79%, keto/enol, 4/1) as a pink oil. ν_{max}/cm^{-1} 1738 (C=O), 1708 (C=O), 1367, 1206, 1151, 1008, 760; δ_H (400 MHz, $CDCl_3$) 7.77 (1H, d, *J* 7.8, Ar), 7.62 (1H, m, Ar), 7.50 (1H, d, *J* 7.8, Ar), 7.41-7.38 (1H, m, Ar), 4.25 (2H, q, *J* 7.0, CH_2O), 3.71 (1H, dd, *J* 8.2, 4.4, CHC=O), 3.56 (1H, dd, *J* 17.2, 4.4, ArCH_2), 3.37 (1H, dd, *J* 17.2, 8.2, ArCH_2), 1.31 (3H, t, *J* 7.0, CH_3). Minor peaks due to enol observed at 10.45 (1H, br s, OH enol), 4.32 (2H, q, *J* 7.0, CH_2O enol), 3.52 (2H, s, ArCH_2 enol), 1.37 (0.6H, t, *J* 7.0, CH_3); δ_C (100 MHz, $CDCl_3$) 199.77 (C=O), 169.34 (OC=O), 153.84 (Ar), 135.60 (Ar), 135.50 (Ar), 127.99 (Ar), 126.77 (Ar), 124.87 (Ar), 61.93 (CH_2O), 53.54 (*C*HC=O), 30.52 (CH_2), 14.43 (CH_3 keto); Minor peaks due to enol observed at 129.53 (Ar), 127.00 (Ar), 124.92 (Ar), 120.90 (Ar), 60.30 (CH_2O), 32.77 (CH_2), 14.69 (CH_3); *m/z* (EI) 204.0779 (M^+ $C_{12}H_{12}O_3$ requires 204.0786), 159 (23%), 131 (72), 130 (100), 103 (32).

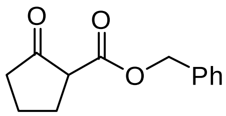


***iso*-Propyl 1-indanone-2-carboxylate (Ic).**[3] Prepared by the general method (18 h reflux) and purified by column chromatography (hexane/ethyl acetate, 25/1 to 8/1) to give the *iso*-propyl ester (791 mg, 69%, keto/enol, 8/1) as a pink oil. ν_{max}/cm^{-1} 1736 (C=O), 1708 (C=O), 1256, 1207, 1103, 988, 920, 760; δ_H (400 MHz, $CDCl_3$) 7.76 (1H, d, *J* 7.8, Ar), 7.64-7.59 (1H, m, Ar), 7.50-7.36 (2H, m, Ar), 5.08 (1H, septet, *J* 6.2, OCH), 3.67 (1H, dd, *J* 8.2, 4.4, CHC=O), 3.53 (1H, dd, *J* 17.2, 4.4, CH_2), 3.35 (1H, dd, *J* 17.2, 8.2, ArCH_2), 1.28 (3H, d, *J* 6.2, CH_3), 1.27 (3H, d, *J* 6.2, CH_3), Minor peaks due to enol observed at 10.48 (1H, br s, OH), 5.20 (1H, septet, *J* 6.2, OCH), 3.49 (2H, s, ArCH_2), 1.33 (6H, d, *J* 6.4, CH_3); δ_C (100 MHz, $CDCl_3$) 199.86 (C=O), 168.92 (OC=O), 153.85 (Ar), 135.57 (Ar), 127.96 (Ar), 126.76 (Ar), 124.84 (Ar), 69.50 (OCH), 53.74 (*C*HC=O), 30.51 (CH_2), 21.99 (CH_3), 21.95 (CH_3). Minor peaks due to enol observed at 129.44 (Ar), 126.97 (Ar), 124.89 (Ar), 120.85 (Ar), 67.75 (OCH), 32.82 (CH_2), 22.33 (CH_3); *m/z* (EI), 218.0943 (M^+ $C_{13}H_{14}O_3$ requires 218.0943), 192 (18%), 176 (38), 159 (33), 130 (100).



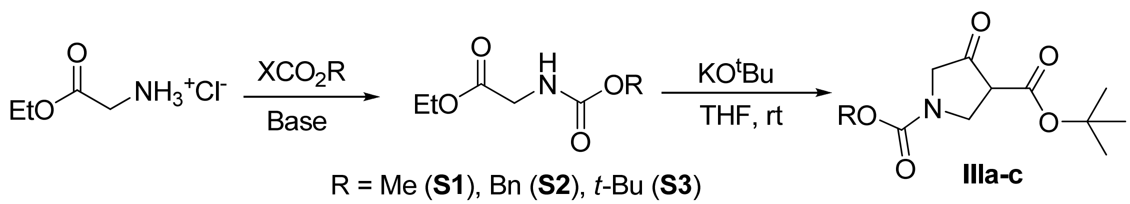
***tert*-Butyl 1-indanone-2-carboxylate (Id).**[3] A flask equipped with an air condenser was charged with methyl 1-indanone-2-carboxylate (627 mg, 3.30 mmol), *tert*-butanol (3.16 mL, 33.0 mmol), dibutyl tin oxide (82 mg, 0.33 mmol) and toluene (33 mL). The mixture was refluxed vigorously for 3 h, then concentrated in vacuo and purified by column chromatography (hexane/ethyl acetate, 20/1) to give **Id** (621 mg, 81%, keto/enol, 9/1) as pink crystals; Mp 43-44°C (lit.,[3] 44-46°C); ν_{max}/cm^{-1} 2975, 2932, 1713 (C=O), 1650 (C=O), 1373, 1265, 1151; δ_H (400 MHz, $CDCl_3$) 7.78 (1H, d, *J* 8.0, Ar), 7.63 (1H, m, Ar), 7.52 (1H, d, *J* 8.0, Ar), 7.42-7.39 (1H, m, Ar), 3.65 (1H, dd, *J* 8.4, 4.0, CHC=O), 3.52 (1H, dd, *J* 17.2, 4.0, CH_2), 3.36 (1H, dd, *J* 17.2, 8.4, CH_2), 1.51 (9H, s, CH_3). Minor peaks due to enol observed at 3.49 (2H, s, CH_2), 1.60 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 200.06 (C=O), 168.35 (OC=O), 153.71 (Ar), 135.47 (Ar), 135.24 (Ar), 127.68 (Ar), 126.54

(Ar), 124.58 (Ar), 82.07 (CCH_3), 54.29 (CHC=O), 30.34 (CH_2), 28.03 (CH_3). Minor peaks due to enol observed at 129.03 (Ar), 126.71 (Ar), 120.52 (Ar), 32.89 (CH_2), 28.51 (CH_3); *m/z* (EI) 232 (M^+, 12%), 176 (16), 130 (17), 43 (100).

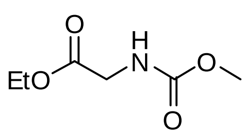


Benzyl cyclopentanone-2-carboxylate (IIb).[4] A flask equipped with a short air condenser was charged with methyl cyclopentanone-2-carboxylate (500 μL, 3.71 mmol), benzyl alcohol (442 μL, 4.08 mmol), DMAP (23 mg, 0.186 mmol) and toluene (10 mL), and was refluxed strongly for 8 h. The mixture was then cooled, concentrated in vacuo and purified by column chromatography (CH_2Cl_2/hexane, 1/1) to give the benzyl ester (438 mg, 55%) as a yellow oil. ν_{max}/cm^{-1} 2966, 1753 (C=O), 1726 (C=O), 1455, 1337, 1253, 1182; δ_H (400 MHz, $CDCl_3$) 7.39-7.35 (5H, m, Ar), 5.20 (2H, s, CH_2O), 3.23 (1H, t, *J* 9.2, CH), 2.34-2.32 (4H, m, CH_2), 2.16-2.13 (1H, m, CH_2), 1.91-1.86 (1H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 212.15 (C=O), 169.28 (OC=O), 135.64 (Ar), 128.60 (Ar), 128.31 (Ar), 128.11 (Ar), 67.03 (OCH_2), 54.81 (CHC=O), 38.10 (CH_2), 27.44 (CH_2), 21.00 (CH_2); *m/z* (EI) 218 (M^+, 11%), 190 (19), 91 (100), 84 (50).

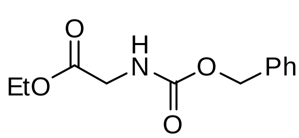
***tert*-Butyl cyclopentanone-2-carboxylate (IIc)** was synthesised by a literature method.[5]



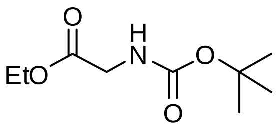
Scheme S1. General route to *tert*-butyl 3-pyrrolidinone-4-carboxylates (**III**).



***N*-(methoxycarbonyl)glycine ethyl ester (S1).**[6] A mixture of glycine ethyl ester hydrochloride (10 g, 71.6 mmol), methyl chloroformate (22.2 mL, 287 mmol) and K_2CO_3 (59.4 g, 430 mmol) was refluxed in acetone (150 mL) for 18 h. Upon cooling the mixture was diluted with H_2O (400 mL) and extracted using Et_2O (2 x 150 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuuo. The residue was purified by short path distillation (75°C, 0.1 mmHg) to give the **S1** (9.83 g, 85%) as a colourless oil. ν_{max}/cm^{-1} 1748 (C=O), 1703 (C=O), 1528, 1281, 1191, 1051, 782; δ_H (400 MHz, $CDCl_3$) 5.22 (1H, s, NH), 4.23 (2H, q, *J* 7.2, CH_2O), 3.97 (2H, d, *J* 5.8), 3.71 (3H, s, OCH_3), 1.30 (3H, t, *J* 7.2, CH_2CH_3); δ_C (100 MHz, $CDCl_3$) 170.20 (C=O), 157.02 (NC=O), 61.48 (CH_2CH_3), 52.46 (OCH_3), 42.75 (NCH_2), 14.11 (CH_2CH_3); *m/z* (EI) 161 M^+, 11%), 146 (18), 115 (14), 102 (15), 88 (100).

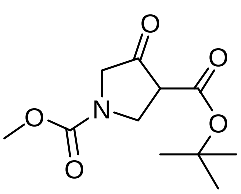


***N*-(benzyloxycarbonyl)glycine ethyl ester (S2).**[7] Benzyl chloroformate (11.1 mL, 78.8 mmol) was added dropwise to a solution of glycine ethyl ester hydrochloride (11.0 g, 78.8 g) and triethylamine (21.9 mL, 157.6 mmol) in THF (200 mL) at 0°C. The mixture was allowed to warm to room temperature, stirred for 18 h, and warmed to 50°C for 3h. Upon cooling, the solution was concentrated in vacuuo, dissolved in CH_2Cl_2 (200 mL) and washed with aq. K_2CO_3 (100 mL) then 1 M HCl (100 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by column chromatography (hexane/ethyl acetate, 5/1) to give the carbamate **S2** (2.68 g, 14%) as a colourless oil. ν_{max}/cm^{-1} 1737 (C=O), 1725 (C=O), 1524, 1374, 1354, 1202, 1052, 696; δ_H (400 MHz, $CDCl_3$) 7.45-7.29 (5H, m, Ar), 5.32 (1H, s, NH), 5.15 (2H, s, C*H*$_2$Ph), 4.24 (2H, q, *J* 7.2, C*H*$_2$CH$_3$), 4.00 (2H, d, *J* 5.6, CH_2N), 1.31 (3H, t, *J* 7.2, CH_3). δ_C (100 MHz, $CDCl_3$) 170.03 (C=O), 156.29 (NC=O), 136.23 (Ar), 128.57 (Ar), 128.23 (Ar), 128.15 (Ar), 67.11 (*C*H$_2$Ph), 61.54 (*C*H$_2$CH$_3$), 42.81 (CH_2N), 14.15 (CH_3); *m/z* (EI) 237 (M^+, 17%), 108 (62), 91 (100).

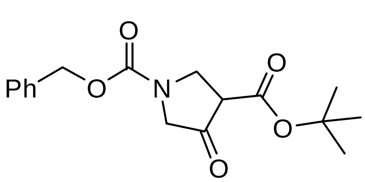


***N*-(*tert*-butoxycarbonyl)glycine ethyl ester (S3).**[8] Similarly prepared from di-*tert*-butyldicarbonate (17.2 g, 78.8 mmol), glycine ethyl ester hydrochloride (11 g, 78.8 mmol) and triethylamine (21.9 mL, 157.6 mmol) as a colourless oil (16.0 g, 100%). ν_{max}/cm^{-1} 1739 (C=O), 1724 (C=O), 1514, 1366, 1205, 1158, 1026; δ_H (400 MHz, $CDCl_3$) 5.02 (1H, s, NH), 4.23 (2H, q, *J* 7.2, CH_2O), 3.92 (2H, d, *J* 5.6, CH_2C=O), 1.47 (9H, s, ^{t}Bu), 1.30 (3H, t, *J* 7.2, CH_3); δ_C (100 MHz, $CDCl_3$) 170.40 (C=O), 155.73 (NC=O), 79.90 (*C*(CH$_3$)$_3$), 61.31 (CH_2O), 42.42 (CH_2N), 28.28 (C(*C*H$_3$)$_3$), 14.13 (CH_3); *m/z* (EI) 203 (M^+, <1%), 148 (20), 130 (18), 104 (11), 102 (12), 57 (100).

General method for the synthesis of 3-pyrrolidinones (III, Scheme S1). Potassium *tert*-butoxide (3.04 g, 27.1 mmol) was added portionwise to a solution of an *N*-(alkoxyoxycarbonyl)glycine ethyl ester (24.6 mmol) and *tert*-butyl acrylate (3.60 mL, 24.6 mmol) in THF (50 mL) at 0°C. After stirring at room temperature for 24 h the slurry was diluted with hexane (50 mL) and filtered. The residue was dissolved in 2 M HCl (100 mL), extracted to CH_2Cl_2 (3 x 80 mL) and the combined extracts was dried ($MgSO_4$) and concentrated.

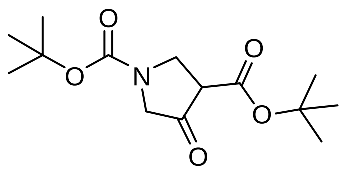


***N*-(methoxycarbonyl)-4-(*tert*-butoxycarbonyl)-3-pyrrolidinone (IIIa).** Prepared by the general method and purified by column chromatography (hexane/ethyl acetate, 1/1) to give the 3-pyrrolidinone (51%, 1.15 g) as a yellow oil which was stored in the freezer. NMR shows a keto-enol mixture as a mixture of rotamers. ν_{max}/cm^{-1} 1710 (C=O), 1444, 1369, 1247, 1145, 771; δ_H (400 MHz, $CDCl_3$) 10.22 (0.5H, br, s, enol OH), 4.29-4.21 (1.5H, m), 4.07 (1.5H, br, s), 3.91 (1.5H, br, s), 3.79 (3H, br, s, keto CH_3), 3.77-3.76 (1.5H, m, enol CH_3), 1.53 (4.5H, s, enol C(CH_3)$_3$), 1.50 (9H, s, keto C(CH_3)$_3$); δ_C (100 MHz, $CDCl_3$) 203.80, 203.14, 166.55, 166.42, 166.26, 165.22, 154.65, 154.49, 154.41, 97.77, 97.70, 82.13, 81.28, 54.30, 53.73, 52.18, 51.96, 51.81, 51.61, 50.80, 50.40, 48.61, 48.27, 45.61, 27.59, 27.22; *m/z* (CI, NH_3) 261.1455 (MNH_4^+ $C_{11}H_{21}N_2O_5$ requires 261.1450), 205 (100%), 193 (20), 179 (12), 151 (13).

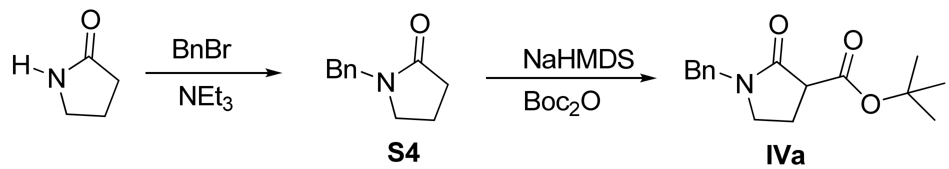


***N*-(benzyloxycarbonyl)-4-(*tert*-butoxycarbonyl)-3-pyrrolidinone (IIIb).** Prepared by the general method and purified by column chromatography (hexane/ethyl acetate, 5/1) to give the 3-pyrrolidinone (33%, 660 mg) as a yellow oil which was stored in the freezer. NMR shows keto enol mixture as a mixture of rotamers. ν_{max}/cm^{-1} 1768 (C=O), 1705 (C=O), 1418, 1367, 1146, 697; δ_H (400 MHz, $CDCl_3$) 7.41-7.33 (5H, m, Ar), 5.22-5.19 (2H, m, C*H*$_2$Ph), 4.30-4.09 (3.25H, br, m), 4.10-4.09 (1.25H, br, m), 3.94-3.93 (1.25H, br, s), 3.52-3.48 (0.5H, br, m), 1.52 (4H, s, CH_3), 1.48 (5H, s, CH_3); δ_C (100 MHz, $CDCl_3$)

203.77, 203.16, 169.70, 166.75, 166.65, 166.38, 165.32, 156.12, 154.09, 153.99, 136.23, 136.15, 136.06, 135.87, 128.13, 128.09, 128.05, 127.81, 127.65, 127.51, 97.98, 97.85, 82.46, 81.54, 66.95, 66.64, 66.43, 60.84, 54.44, 53.87, 51.97, 51.77, 50.98, 50.61, 48.80, 48.43, 45.76, 42.34, 27.82, 27.80, 27.43, 20.52, 13.77; *m/z* (CI, NH_3) 337.1763 (MNH_4^+ $C_{17}H_{25}N_2O_5$ requires 337.1763), 297 (100), 281 (75), 255 (32), 197 (46), 108 (40), 91 (9).



1,4-(di-*tert*-butoxycarbonyl)-3-pyrrolidinone (IIIc). The crude oil was purified by dissolving in hexane (10 mL) and left in the freezer overnight. The crystallised product was collected by filtration as a white solid (5.96 g, 85%). NMR shows keto enol mixture as a mixture of rotamers. Mp 86°C; ν_{max}/cm^{-1} 1766 (C=O), 1727 (C=O), 1699 (C=O), 1667 (C=O), 1643 (C=O), 1411, 1360, 1319, 1143; δ_H (400 MHz, $CDCl_3$) 10.19-10.14 (0.33H, br, m, enol OH), 4.22-4.12 (1.3H, m), 4.03-3.95 (1.3H, m), 3.85 (1.3H, br, s), 3.49 (0.66H, t, *J* 7.6, keto CH), 1.52-1.48 (18H, m, CH_3); δ_C (100 MHz, Tol, 373 K) 203.29, 168.66, 167.95, 166.25, 154.12, 82.28, 81.80, 80.09, 79.56, 55.21, 52.65, 51.67, 49.34, 46.61, 42.73, 36.66, 31.53, 28.73, 28.69, 28.64, 28.48, 28.14, 27.90; *m/z* (CI, NH_3) 303.1923 (MNH_4^+ $C_{14}H_{27}N_2O_5$ requires 303.1920), 286 (MH^+, 16%), 247 (100), 230 (10), 191 (22).

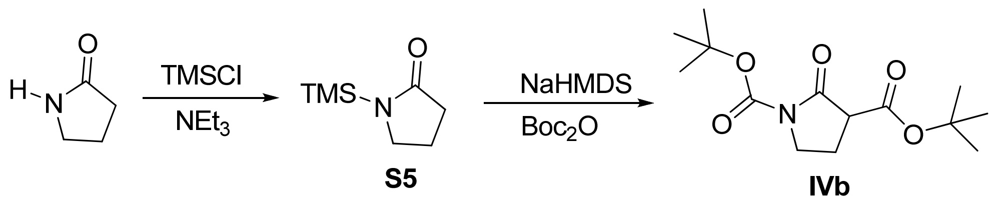


Scheme S2. Preparation of **IVa**.

***tert*-Butyl *N*-benzyl-2-pyrrolidinone-3-carboxylate (IVa)** was prepared in two steps (Scheme S2):[9]

***N*-benzyl-2-pyrrolidinone (S4).**[10] In an oven-dried flask, NaH (60% dispersion in mineral oil, 5.16 g, 129 mmol) was washed with hexane (5 x 20 mL). THF (200 mL) was added and the suspension cooled to 0 °C. 2-Pyrrolidinone (10 g, 118 mmol) was added dropwise, followed by benzyl bromide (15.3 mL, 129 mmol). After stirring for 1 h the mixture was warmed to 60 °C and stirred for 24 h. The solvent was removed in vacuuo and the residue partitioned between CH_2Cl_2 (200 mL) and H_2O (200 mL). The organic layer was separated, washed with H_2O (100 mL), dried ($MgSO_4$) and concentrated in vacuuo, heating to 60°C at 0.2 mmHg to remove the remaining benzyl bromide impurity, giving **S5** (16.4 g, 79%) as an orange oil. This was used in the next step without further purification. ν_{max}/cm^{-1} 1673 (C=O), 1495, 1422, 1286, 1264, 699; δ_H (400 MHz, $CDCl_3$) 7.44-7.21 (5H, m, Ar), 4.45 (2H, s, CH_2O), 3.26 (2H, t, *J* 7.2, CH_2N), 2.44 (2H, t, *J* 8.2, CH_2C=O), 2.02-1.89 (2H, m, CH_2CH_2N); δ_C (100 MHz, $CDCl_3$) 174.91 (C=O), 136.59 (Ar), 128.66 (Ar), 128.10 (Ar), 127.53 (Ar), 46.57 (CH_2Ph, CH_2N), 30.94 (CH_2C=O), 17.72 (CH_2CH_2N); *m/z* (EI) 175 (M^+, 100%), 146 (44), 104 (30), 91 (100).

Sodium hexamethyldisilylamide (1M in THF, 34.2 mL) was added dropwise to a solution of **S4** (6.00 g, 34.2 mmol) in THF (40 mL) at -78 °C. After stirring for 1 h a solution of di-*tert*-butyldicarbonate (3.73 g, 17.1 mmol) in THF (20 mL) was added dropwise over 30 min. The solution was stirred at -78 °C for a further 30 min then quenched with sat. NH_4Cl (30 mL), and extracted to ether (3 x 30 mL). The combined organic extracts were dried ($MgSO_4$), concentrated and the crude material was purified by column chromatography (hexane/ethyl acetate, 2/1 to 1/1) to give the pyrrolidinone **IVa** (3.78 g) as a yellow oil. ν_{max} (thin film)/cm^{-1} 1740 (C=O), 1670 (C=O), 1490, 1454, 1439, 1260, 1139, 843, 696; δ_H (400 MHz, $CDCl_3$) 7.31-7.21 (5H, m, Ar), 4.52 (1H, d, *J* 14.8, CH_2Ph), 4.40 (1H, d, *J* 14.8, CH_2Ph), 3.36-3.33 (2H, m, CH_2N), 3.23-3.18 (1H, m, CH), 2.28-2.16 (2H, m, CH_2CH), 1.48 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.31 (C=O), 169.55 (C=O), 136.11 (Ar), 128.68 (Ar), 128.05 (Ar), 127.61 (Ar), 81.82 (*C*(CH_3)$_3$), 49.58, 46.86, 45.21, 27.97 (CH_3), 22.34 (CH_2); *m/z* (EI) 275 (M^+, 4%), 265 (18), 219 (81), 202 (33), 174 (49), 91 (100).

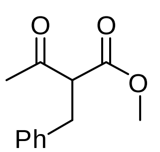


Scheme S3. Synthesis of **IVb.**

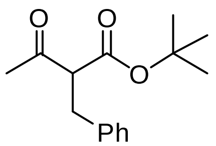
***tert*-Butyl *N*-(*tert*-butoxycarbonyl)-2-pyrrolidinone-3-carboxylate (IVb)** was prepared in two steps by following a reported procedure for the synthesis of *tert*-butyl 2-pyrrolidinone-3-carboxylate,[11] however only *tert*-butyl *N*-(*tert*-butoxycarbonyl)-2-pyrrolidinone-3-carboxylate **IVb** was isolated:

***N*-trimethylsilyl-2-pyrrolidinone (S5).**[12] A mixture of 2-pyrrolidinone (7.59 mL, 100 mmol), triethylamine (17.4 mL, 125 mmol) and chlorotrimethylsilane (14.0 mL, 110 mmol) was stirred in toluene (100 mL) at room temperature for 4 h. The solution was cooled to 0°C, diluted with hexane (50 mL) and ether (50 mL) and filtered through a pad of Celite, rinsing with hexane/ether, 1/1. The filtrate was concentrated in vacuuo and purified by distillation (72-82 °C, 7 mmHg) to give **S5** (11.2 g, 71%) as an orange oil. ν_{max}/cm^{-1} 1673 (C=O), 1381, 1246, 1122, 832; δ_H (400 MHz, $CDCl_3$) 3.37 (2H, t, *J* 7.0, CH_2N), 2.34 (2H, t, *J* 8.2, CH_2C=O), 2.08-2.00 (2H, m, C$H_2$$CH_2N$), 0.28 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 183.42 (C=O), 46.54 (CH_2N), 32.77 (*C*H_2C=O), 21.63 (*C*$H_2$$CH_2N$), -1.16 ($CH_3$); *m/z* (EI) 157 ($M^+$, 20%), 142 (100).

Sodium hexamethyldisilylamide (1M in THF, 15.9 mL) was added dropwise to a solution of **S5** (2.5 g, 15.9 mmol) in THF (15 mL) at -78 °C. After stirring for 1 h, a solution of di-*tert*-butyldicarbonate (1.74 g, 7.95 mmol) in THF (10 mL) was added dropwise over 30 min. The solution was stirred at -78 °C for a further 30 min then quenched with sat. NH_4Cl (30 mL), and extracted to ether (3 x 30 mL). The combined organic extracts were dried ($MgSO_4$), concentrated and the residue was purified by column chromatography (hexane/ethyl acetate, 5/1 to 3/1) to give **IVb** (386 mg, 34%) as a white crystalline solid. Mp 62-64°C; ν_{max}/cm^{-1} 1768 (C=O), 1724 (C=O), 1366, 1281, 1153, 1013, 940, 776; δ_H (400 MHz, $CDCl_3$) 3.94-3.79 (1H, m, CH_2N), 3.74-3.61 (1H, m, CH_2N), 3.48-3.36 (1H, m, CH), 2.42-2.26 (1H, m, CH_2CH), 2.26-2.12 (1H, m, CH_2CH), 1.62-1.44 (18H, m, CH_3); *m/z* (EI) 308.1473 (MNa^+ $C_{14}H_{23}NO_5Na$ requires 308.1471), 229 (9%), 212 (8), 173 (31), 156 (17), 130 (22), 112 (22).

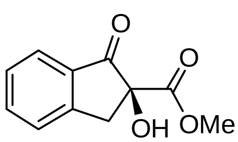


Methyl 3-phenyl-2-acetylpropionate (Va). A solution of ethyl 3-phenyl-2-acetylpropionate (2.00 g, 9.08 mmol) and dibutyltin oxide (226 mg, 0.908 mmol) in methanol (400 mL) was heated to reflux for 24 h. The mixture was then concentrated in vacuuo, diluted with methanol (400 mL), and refluxed for a further 24 h. This process was repeated twice, giving complete conversion (monitored by NMR). The mixture was then concentrated and purified by column chromatography (hexane/ethyl acetate, 16/1 to 10/1) to give the methyl ester **Va** (1.20 g, 64%) as a colourless oil. ν_{max}/cm^{-1} 1740 (C=O), 1715 (C=O), 1435, 1359, 1217, 1145, 749, 399; δ_H (400 MHz, $CDCl_3$) 7.29-7.25 (2H, m, Ar), 7.22-7.16 (3H, m, Ar), 3.80 (1H, t, *J* 7.4, CH), 3.69 (3H, s, CH_3O), 3.16 (2H, d, *J* 7.2, CH_2), 2.17 (3H, s, CH_3C=O); δ_C (100 MHz, $CDCl_3$) 202.59 (C=O), 169.78 (OC=O), 138.29 (Ar), 128.95 (Ar), 128.83 (Ar), 126.94 (Ar), 61.34 (CH_3O), 52.68 (CH), 34.26 (CH_2), 29.92 (CH_3C=O); *m/z* (EI) 206.0936 (M^+ $C_{12}H_{14}O_3$ requires 206.0943), 163 (100), 147 (32), 131 (100), 104 (43), 91 (53).

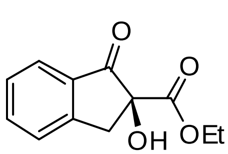


***tert*-Butyl 3-phenyl-2-acetylpropionate (Vc).** A mixture of *tert*-butyl acetoacetate (2.00 mL, 12.1 mmol), benzyl bromide (2.88 mL, 24.2 mmol) and K_2CO_3 (3.34 g, 24.2 mmol) (40 mL) was refluxed in acetonitrile for 18 h. The mixture was then cooled, quenched with H_2O (100 mL), and extracted to ether (2 x 80 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexane/ethyl acetate, 50/1 to 6/1) to give the ketoester (2.12 g, 72%) as a colourless oil. ν_{max}/cm^{-1} 1732 (C=O), 1713 (C=O), 1368, 1252, 1136, 843, 699; δ_H (400 MHz, $CDCl_3$) 7.29-7.25 (2H, m, Ar), 7.19-7.17 (3H, m, Ar), 3.68 (1H, dd, *J* 7.2, 7.8, CH), 3.14 (1H, dd, *J* 14.4, 7.2, C*H*$_2$Ph), 3.09 (1H dd, *J* 14.4, 7.8, C*H*$_2$Ph), 2.18 (3H, s, CH_3C=O), 1.38 (9H, s, $C(CH_3)_3$); δ_C (100 MHz, $CDCl_3$) 203.01 (C=O), 168.50 (OC=O), 138.57 (Ar), 129.06 (Ar), 128.68 (Ar), 126.75 (Ar), 82.28 (*C*($CH_3)_3$), 62.52 (CH), 34.11 (*C*H_2Ph), 29.66 (*C*H_3C=O), 28.04 (C(*C*$H_3)_3$); *m/z* (EI) 248.1408 (M^+ $C_{15}H_{20}O_3$ requires 248.1412), 192 (72), 175 (37), 149 (100), 131 (55).

General method A for hydroxylation of β-ketoesters. A Radley's reaction tube was charged with β-ketoester (0.123 mmol), $[Pd(R\text{-BINAP})(H_2O)_2]^{2+}[TfO]^-_2$ (6.6 mg, 12.3 μmol) and CH_2Cl_2 (0.5 mL) and cooled to -20°C. A solution of DMD in acetone (0.05-0.09 M, 2.95-1.64 mL, 0.147 mmol) at -20°C was then added dropwise. After 30 min the mixture was concentrated, and filtered through a plug of silica. The crude product was either judged to be pure enough by ^1H NMR, or purified by column chromatography.

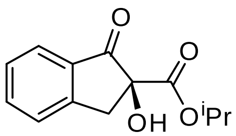


Methyl 2-hydroxy-1-indanone-2-carboxylate (2a, table 1, entry 1).[13] White crystalline solid. Mp 132-134°C (lit.,[14] 131-132°C); ν_{max}/cm^{-1} 1749 (C=O), 1708 (C=O), 1603, 1260, 1207, 1114; δ_H (400 MHz, $CDCl_3$) 7.83 (1H, d, *J* 7.6, Ar), 7.70 (1H, t, *J* 7.6, Ar), 7.53 (1H, d, *J* 7.6, Ar), 7.46 (1H, t, *J* 7.6, Ar), 3.98 (1H, br s, OH), 3.76 (3H, s, CH_3), 3.75 (1H, d, *J* 17.2, CH_2), 3.28 (1H, d, *J* 17.2, CH_2); δ_C (100 MHz, $CDCl_3$) 200.82 (C-1), 171.94 (OC=O), 152.22 (Ar), 136.22 (Ar), 133.54 (Ar), 128.20 (Ar), 126.50 (Ar), 125.37 (Ar), 80.39 (C), 53.50 (CH_2), 39.26 (CH_3); *m/z* (EI) 206 (M^+, 47%), 147 (57%), 118 (100%), 91 (41%); HPLC conditions: Chiracel OD-H column (250 x 4.6 mm), Hexane/^{i}PrOH = 90/10, 1 mL/min, 254 nm, t_R (major) = 11.9 min, t_R (minor) = 13.7 min; $[\alpha]_D^{25}$ +19.9 (*c*=1.21, $CHCl_3$, 26% ee).

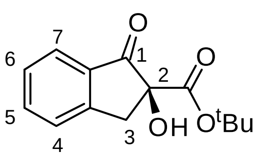


Ethyl 2-hydroxy-1-indanone-2-carboxylate (2b, table 1, entry 2). Colourless oil. ν_{max}/cm^{-1} 1738 (C=O), 1709 (C=O), 1607, 1299, 1249, 1184, 928, 751; δ_H (400 MHz, $CDCl_3$) 7.79 (1H, d, *J* 7.8, Ar), 7.68-7.64 (1H, m, Ar), 7.48 (1H, t, *J* 7.8, Ar), 7.44-7.42 (1H, t, *J* 7.4, Ar), 4.26-4.17 (2H, m, CH_2O), 4.01 (1H, s, OH), 3.72 (1H, d, *J* 17.4, CH_2), 3.24 (1H, d, *J* 17.4, CH_2), 1.17 (3H, t, *J* 7.6, CH_3). δ_C (100 MHz,

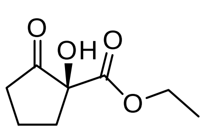
$CDCl_3$) 201.27 (C=O), 171.69 (OC=O), 152.51 (Ar), 136.33 (Ar), 133.81 (Ar), 128.33 (Ar), 126.67 (Ar), 125.50 (Ar), 80.52 (C-2), 63.01 (CH_2O), 39.51 (C-3), 14.19 (CH_3); *m/z* (EI) 220.0732 (M^+ $C_{12}H_{12}O_4$ requires 220.0736), 147 (95%), 135 (50), 118 (100), 91 (68); HPLC conditions: Chiracel OD-H column (250 x 4.6 mm), Hexane/^{i}PrOH=98/2, 1 mL/min, 254 nm, t_R (major) = 24.4 min, t_R (minor) = 29.1 min; $[\alpha]_D^{25}$ +24.4 (*c*=1.11, $CHCl_3$, 48% ee).



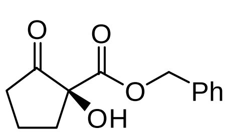
***iso*-Propyl 2-hydroxy-1-indanone-2-carboxylate (2c, table 1, entry 3).** White crystalline solid. Mp 68-74 °C; ν_{max}/cm^{-1} 3458, 1729 (C=O), 1711 (C=O), 1606, 1374, 1273, 1207, 1101, 922; δ_H (400 MHz, $CDCl_3$) 7.79 (1H, d, *J* 7.6, Ar), 7.68-7.64 (1H, m, Ar), 7.48 (1H, t, *J* 7.8, Ar), 7.46-7.42 (1H, m, Ar), 5.11-5.01 (1H, m, C*H*Me_2), 4.01 (1H, s, OH), 3.69 (1H, d, *J* 17.2, CH_2), 3.23 (1H, d, *J* 17.2, CH_2), 1.17 (3H, d, *J* 6.2, CH_3), 1.12 (3H, d, *J* 6.2, CH_3); δ_C (100 MHz, $CDCl_3$) 201.23 (C=O), 171.23 (OC=O), 152.56 (Ar), 136.25 (Ar), 133.87 (Ar), 128.28 (Ar), 126.63 (Ar), 125.43 (Ar), 80.51 (C), 71.11 (*C*HMe_2), 39.50 (CH_2), 21.76 (CH_3), 21.56 (CH_3); *m/z* (EI) 234.0890 (M^+ $C_{13}H_{14}O_4$ requires 234.0892), 192 (100), 147 (100), 136 (55), 118 (88), 91 (56); HPLC conditions: Chiracel OJ-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 254 nm, t_R (major) = 13.0 min, t_R (minor) = 23.7 min; $[\alpha]_D^{25}$ +20.6 (*c*=1.02, $CHCl_3$, 48% ee).



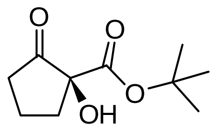
***tert*-Butyl 2-hydroxy-1-indanone-2-carboxylate (2d, table 1, entry 4).**[13] White crystalline solid. Mp 128-129 °C; ν_{max}/cm^{-1} 1736 (C=O), 1711 (C=O), 1605, 1459, 1307, 1160; δ_H (400 MHz, $CDCl_3$) 7.80 (1H, d, *J* 7.6, H-7), 7.66 (1H, t, *J* 7.6, H-5), 7.49 (1H, d, *J* 7.6, H-4), 7.42 (1H, t, *J* 7.6, H-6), 4.04 (1H, br s, OH), 3.66 (1H, d, *J* 17.0, H-3), 3.23 (1H, d, *J* 17.0, H-3'), 1.37 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 201.38 (C-1), 170.56 (OC=O), 152.34 (Ar), 135.86 (Ar), 133.93 (Ar), 127.94 (Ar), 126.29 (Ar), 125.06 (Ar), 83.92 (C-2), 80.54 (*C*(CH_3)), 39.46 (C-3), 27.69 (CH_3); *m/z* (EI) 248 (M^+, <1%), 192 (75), 147 (71), 57 (100); HPLC conditions: Chiracel OD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 98/2, 1 mL/min, 254 nm, t_R (major) = 12.0 min, t_R (minor) = 14.6 min; $[\alpha]_D^{25}$ +32.4 (*c*=1.85, $CHCl_3$, 85% ee).



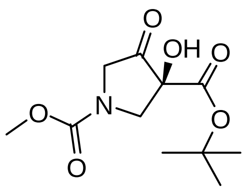
Ethyl 2-hydroxycyclopentanone-2-carboxylate (3a, table 1, entry 5).[15] Colourless oil. ν_{max}/cm^{-1} 2923, 2853, 1728 (C=O), 1457, 1155; δ_H (400 MHz, $CDCl_3$) 4.28 (2H, dq, *J* 7.2, 1.3, OCH_2), 3.67 (1H, s, OH), 2.54-2.46 (3H, m), 2.20-2.07 (3H, m), 1.31 (3H, t, *J* 7.2, CH_3); δ_C (100 MHz, $CDCl_3$) 213.43 (C=O), 171.60 (OC=O), 79.76 (COH), 62.62 (CH_2O), 35.85 (CH_2), 34.73 (CH_2), 18.40 (CH_2), 14.06 (CH_3); *m/z* (EI) 172 (M^+, <1%), 167 (45), 97 (36), 83 (37); HPLC conditions: Chiracel OJ-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 220 nm, t_R (major) = 9.82 min, t_R (minor) = 11.47 min; $[\alpha]_D^{25}$ -12.0 (*c*=1.00, $CHCl_3$, 87% ee).



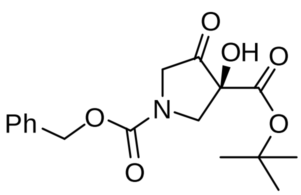
Benzyl 2-hydroxycyclopentanone-2-carboxylate (3b, table 1, entry 6).[16] Colourless oil. ν_{max}/cm^{-1} 1755 (C=O), 1736, 1263, 1164; δ_H (400 MHz, $CDCl_3$) 7.38-7.31 (5H, m, Ar), 5.25 (1H, d, *J* 12.4, CH_2O), 5.16 (1H, d, *J* 12.4, CH_2O), 3.73 (1H, br s, OH), 2.53-2.42 (3H, m, CH_2), 2.17-2.04 (3H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 213.41 (C=O), 171.54 (OC=O), 134.88 (Ar), 128.72 (Ar), 128.63 (Ar), 128.11 (Ar), 79.99 (COH), 67.98 (CH_2O), 35.90 (CH_2), 34.84 (CH_2), 18.43 (CH_2); *m/z* (EI) 234 (M^+, 4%), 216 (5), 206 (5), 143 (20), 115 (17), 91 (100); HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 254 nm, t_R (major) = 17.4 min, t_R (minor) = 21.0 min; $[\alpha]_D^{25}$ -17.4 (*c*=1.84, $CHCl_3$, 66% ee).



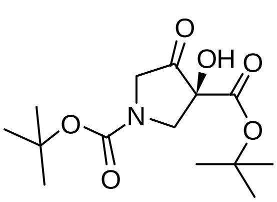
***tert*-Butyl 2-hydroxycyclopentanone-2-carboxylate (3c, table 1, entry 7).**[15] Colourless oil. ν_{max}/cm^{-1} 1753 (C=O), 1725 (C=O), 1370, 1258, 1142, 844; δ_H (400 MHz, $CDCl_3$) 2.45-2.41 (3H, m, CH_2), 2.12-2.07 (3H, m, CH_2), 1.48 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 213.94 (C=O), 170.84 (OC=O), 83.96, 79.77, 35.93 (CH_2), 34.88 (CH_2), 27.88 (CH_3), 18.44 (CH_2); *m/z* (EI) 200 (M^+, <1%), 191 (10), 132 (80), 91 (100); GC conditions: Chiraldex G-TA (20 m x 0.25 mm), 90°C, t_R (major) 19.84, t_R (minor) 20.97; $[\alpha]_D^{25}$ -4.6 (*c*=0.87, $CHCl_3$, 94% ee).



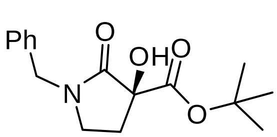
***N*-(Methoxycarbonyl)-4-(*tert*-butoxycarbonyl)-4-hydroxy-3-pyrrolidinone (4a, table 1, entry 8).** Colourless oil. Unstable at room temperature, and was analysed within 1h of isolation. ν_{max}/cm^{-1} 1716, 1154; ^{1}H NMR showed a mixture of rotamers: δ_H (400 MHz, $CDCl_3$) 4.46-4.14 (2H, m), 3.95-3.79 (2H, m), 3.63-3.57 (1H, m), 1.48 (9H, s, CH_3); *m/z* (CI, NH_3) 277.1404 (MNH_4^+ $C_{11}H_{21}N_2O_6$ requires 277.1400), HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 240 nm, t_R (major) = 14.7 min, t_R (minor) = 17.7 min; $[\alpha]_D^{25}$ +16.6 (*c*=0.56, $CHCl_3$, 84% ee).



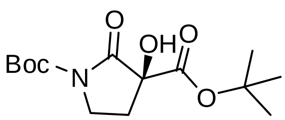
***N*-(Benzyloxycarbonyl)-4-(*tert*-butoxycarbonyl)-4-hydroxy-3-pyrrolidinone (4b, table 1, entry 9).** Purified by column chromatography (hexane/ethyl acetate, 2/1). Colourless oil. ν_{max}/cm^{-1} 1737 (C=O), 1703 (C=O), 1370, 1216, 1148, 734; ^{1}H NMR showed a mixture of rotamers: δ_H (400 MHz, $CDCl_3$) 7.36-7.32 (5H, m, Ar), 5.20-5.14 (2H, m, C*H*$_2$Ph), 4.39-4.13 (2H, m), 3.91-3.84 (2H, m), 3.62-3.54 (1H, m), 1.39-1.36 (9H, m, CH_3); *m/z* (CI, NH_3) 353.1711 (MNH_4^+ $C_{17}H_{25}N_2O_6$ requires 353.1713), 339 (46), 297 (37), 255 (100), 227 (55), 197 (31), 164 (23); HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 240 nm, t_R (major) = 22.5 min, t_R (minor) = 25.8 min; $[\alpha]_D^{25}$ +7.5 (*c*=1.02, $CHCl_3$, 90% ee).



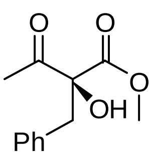
1,4-(Di-*tert*-butoxycarbonyl)-4-hydroxy-3-pyrrolidinone (4c, table 1, entry 10). Colourless oil. ν_{max}/cm^{-1} 1724 (C=O), 1700 (C=O), 1369, 1145, 841; ^{1}H NMR showed a mixture of rotamers: δ_H (400 MHz, $CDCl_3$) 4.39-4.07 (2H, m), 3.88-3.82 (2H, m), 3.63-3.45 (1H, m), 1.56-1.45 (18H, m); *m/z* (CI, NH_3) 319.1871 (MNH_4^+ $C_{14}H_{27}N_2O_6$ requires 319.1869), 305 (100%), 288 (13), 263 (17), 249 (48), 221 (41), 164 (44), 137 (22); HPLC conditions: Chiracel OD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 98/02, 1 mL/min, 220 nm, t_R (minor) = 25.0 min, t_R (major) = 32.0 min; $[\alpha]_D^{25}$ +18.7 (*c*=1.99, $CHCl_3$, 93% ee).



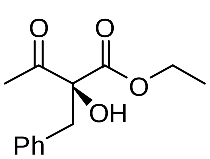
1-Benzyl-3-(*tert*-butoxycarbonyl)-3-hydroxy-2-pyrrolidinone (5a, table 1, entry 11). White crystalline solid. Mp 89-91 °C; ν_{max}/cm^{-1} 3446, 1740 (C=O), 1670 (C=O), 1454, 1260, 1139, 843, 697; δ_H (400 MHz, $CDCl_3$) 7.43-7.24 (5H, m, Ar), 4.78 (1H, d, *J* 14.6, C*H*$_2$Ph), 4.28 (1H, d, *J* 14.6, C*H*$_2$Ph), 3.91 (1H, s, OH), 3.40-3.25 (2H, m, NCH_2), 2.48 (ddd, *J* = 13.3, 7.0, 2.7, 1H, NCH_2CH_2), 2.28-2.12 (1H, m, NCH_2CH_2), 1.44 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.90 (C=O), 170.85 (C=O), 135.65 (Ar), 128.74 (Ar), 128.31 (Ar), 127.84 (Ar), 83.93 (*C*(CH_3)$_3$), 77.97, 47.44, 43.51, 30.87, 27.80 (CH_3); *m/z* (ESI) 314.1376 (MNa^+ $C_{16}H_{21}NO_4Na$ requires 314.1368), 265 (38%), 235 (22), 191 (31), 174 (61), 91 (100); HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 220 nm, t_R (major) = 27.0 min, t_R (minor) = 29.9 min; $[\alpha]_D^{25}$ +53.4 (*c*=1.63, $CHCl_3$, 77% ee).



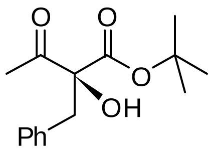
3-(*tert*-Butoxycarbonyl)-3-hydroxy-2-pyrrolidinone (5b, table 1, entry 12). White crystalline solid. Mp 70-72 °C; ν_{max}/cm^{-1} 3475, 1781 (C=O), 1726 (C=O), 1367, 1295, 1157, 1137, 951; δ_H (400 MHz, $CDCl_3$) 3.85 (1H, ddd, *J* 10.4, 9.2, 3.2, CH_2N), 3.78-3.72 (1H, m, CH_2N), 2.49 (1H, ddd, *J* 13.6, 7.6, 3.2, C*H*$_2$COH), 2.23-2.13 (1H, m, C*H*$_2$COH), 1.57 (9H, s, CH_3), 1.52 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.40 (NC=O), 169.57 (OC=O), 149.86 (N(C=O)O), 84.69, 83.69, 78.64, 43.10 (NCH_2), 29.64 (*C*H$_2$COH), 27.97 (CH_3), 27.83 (CH_3). *m/z* (ESI) 324.1416 (MNa^+ $C_{14}H_{23}NO_6Na$ requires 324.1423), 309 (8%), 265 (10), 238 (8), 224 (7); HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH=90/10, 1 mL/min, 220 nm, t_R (minor) = 15.8 min, t_R (major) = 22.0 min; $[\alpha]_D^{25}$ +4.8 (*c*=1.26, $CHCl_3$, 97% ee).



Methyl 3-phenyl-2-acetyl-2-hydroxypropionate (6a, table 1, entry 13). Purified by column chromatography (pentane/CH_2Cl_2/ether, 50/50/1 to 6/6/1). Colourless oil. ν_{max}/cm^{-1} 1717 (C=O), 1356, 1271, 1208, 1119, 7000; δ_H (400 MHz, $CDCl_3$) 7.29-7.19 (5H, m, Ar), 4.04 (1H, s, OH), 3.78 (3H, s, CH_3O), 3.42 (1H, d, *J* 14.2, CH_2Ph), 3.18 (1H, d, *J* 14.2, CH_2Ph), 2.29 (3H, s, CH_3C=O). δ_C (100 MHz, $CDCl_3$) 204.24 (C=O), 171.18 (OC=O), 134.71 (Ar), 130.33 (Ar), 128.53 (Ar), 127.47 (Ar), 84.64 (COH), 53.68 (CH_3O), 41.25 (CH_2Ph), 25.46 (*C*H$_3$C=O); *m/z* (EI) 222.0890 (M^+ $C_{12}H_{14}O_4$ requires 222.0892), 180 (72%), 119 (18), 102 (20), 91 (100); HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 90/10, 1 mL/min, 220 nm, t_R (major) = 16.7 min, t_R (minor) = 18.3 min; $[\alpha]_D^{25}$ +8.1 (*c*=0.74, $CHCl_3$, 48% ee).



Ethyl 3-phenyl-2-acetyl-2-hydroxypropionate (6b, table 1, entry 14).[17] Purified by column chromatography (pentane/ether, 20/1 to 3/2). Colourless oil. ν_{max}/cm^{-1} 1716 (C=O), 1356, 1268, 1203, 1119, 1013, 7000; δ_H (400 MHz, $CDCl_3$) 7.26-7.21 (5H, m, Ar), 4.21 (2H, q, *J* 7.0, CH_2O), 4.06 (1H, s, OH), 3.41 (1H, d, *J* 14.4, C*H*$_2$Ph), 3.17 (1H, d, *J* 14.4, C*H*$_2$Ph), 2.27 (3H, s, CH_3C=O), 1.27 (3H, t, *J* 7.0, C*H*$_3$CH$_2$); δ_C (100 MHz, $CDCl_3$) 204.24 (C=O), 170.74 (OC=O), 134.87 (Ar), 130.41 (Ar), 128.45 (Ar), 127.38 (Ar), 84.46 (COH), 63.10 (CH_2O), 40.97 (CH_2Ph), 25.37 (*C*H$_3$C=O), 14.26 (CH$_2$*C*H$_3$). *m/z* (EI) 236 (M^+, 3%), 194 (56), 119 (22), 91 (100); HPLC conditions: Chiracel OJ-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 98/02, 1 mL/min, 220 nm, t_R (minor) = 23.8 min, t_R (major) = 25.9 min; $[\alpha]_D^{25}$ +17.9 (*c*=0.67, $CHCl_3$, 61% ee).



***tert*-Butyl 3-phenyl-2-acetyl-2-hydroxypropionate (6c, table 1, entry 15).** Purified by column chromatography (pentane/CH_2Cl_2/ether, 50/50/1 to 6/6/1). Colourless oil. ν_{max}/cm^{-1} 3471, 1715 (C=O), 1370, 1281, 1149, 1119, 837, 700; δ_H (400 MHz, $CDCl_3$) 7.25-7.24 (5H, m, Ar), 4.02 (1H, s, OH), 3.36 (1H, d, *J* 14.0, CH_2Ph), 3.13 (1H, d, *J* 14.0, CH_2Ph), 2.24 (3H, s, CH_3C=O), 1.42 (9H, s, CH_3C); δ_C (100 MHz, $CDCl_3$) 204.01 (C=O), 169.71 (OC=O), 135.09 (Ar), 130.32 (Ar), 128.09 (Ar), 127.03 (Ar), 84.23, 84.10, 40.06 (CH_2), 27.74 (C(CH_3)$_3$), 24.92 (CH_3); *m/z* (EI) 264 (M^+, 1%), 221 (14), 208 (24), 166 (21), 148 (21), 120 (23), 91 (42); HPLC conditions: Chirapak AD-H column (250 x 4.6 mm), Hexane/^{i}PrOH, 98/02, 1 mL/min, 220 nm, t_R (major) = 10.8 min, t_R (minor) = 13.5 min; $[\alpha]_D^{25}$ +58.3 (*c*=0.72, $CHCl_3$, 88% ee).

Dimethyldioxirane (0.05-0.09 M in acetone).[18] A 3-necked round bottom flask was charged with H_2O (80 mL), acetone (50 mL) and $NaHCO_3$ (96 g). It was then fitted with an air condenser, a solid addition flask containing oxone (180 g, 0.29 mol) and a dropping funnel containing H_2O and acetone (1:1, 120 mL). The condenser outlet was connected to a cold trap (-78°C) and bubbler. Whilst stirring vigorously the acetone-water mixture was added dropwise and the oxone was simultaneously added in 10 g portions over 45 min, maintaining continuous evolution of gas. After a further 30 min (when the evolution has subsided), the bubbler was removed and DMD was distilled under a slight vacuum (50 mmHg), which was applied for 15 min. The distillate was dried (Na_2SO_4), assayed using phenyl methyl sulfide and stored at -25°C.

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Figure S1a. ^{1}H NMR of **2a**.

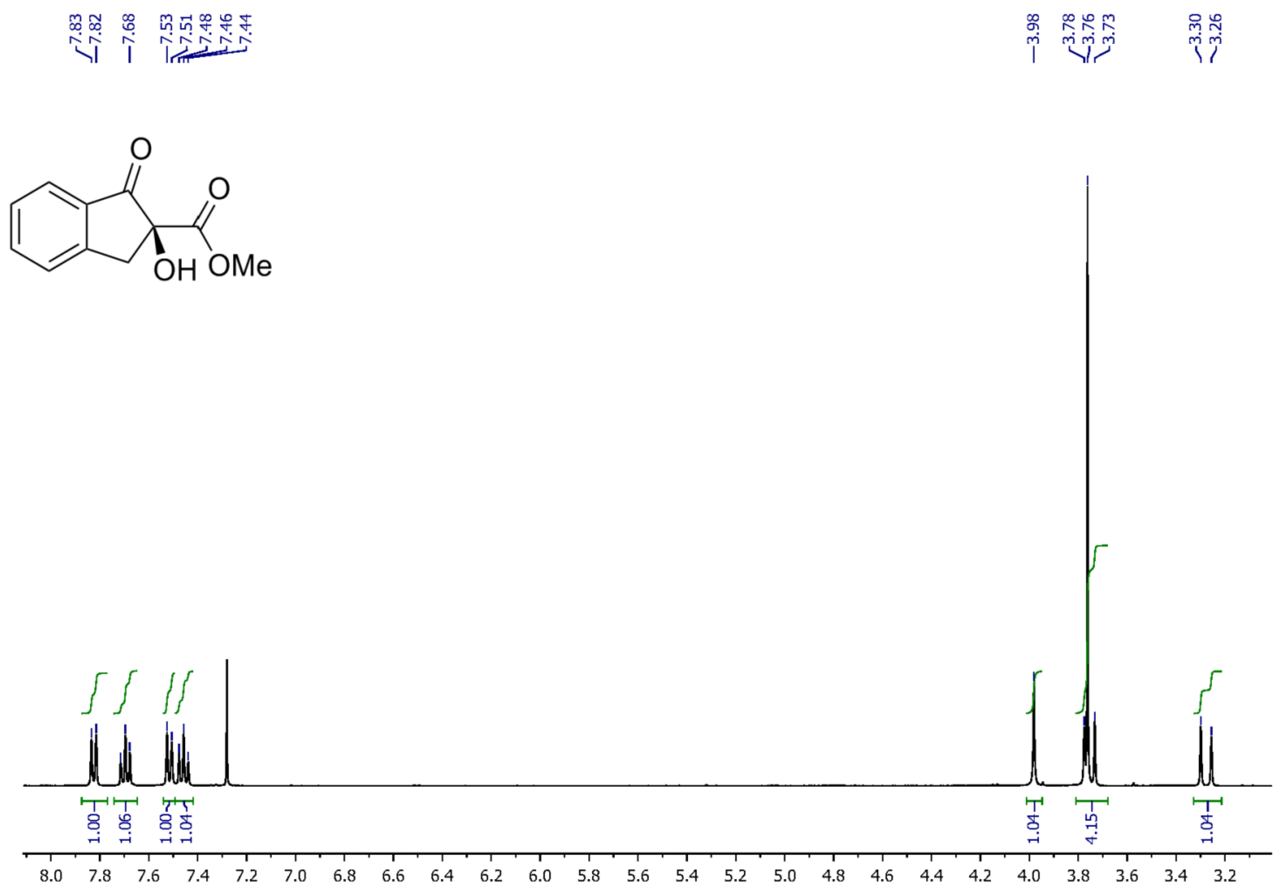


Figure S1b. ^{13}C NMR of **2a**.

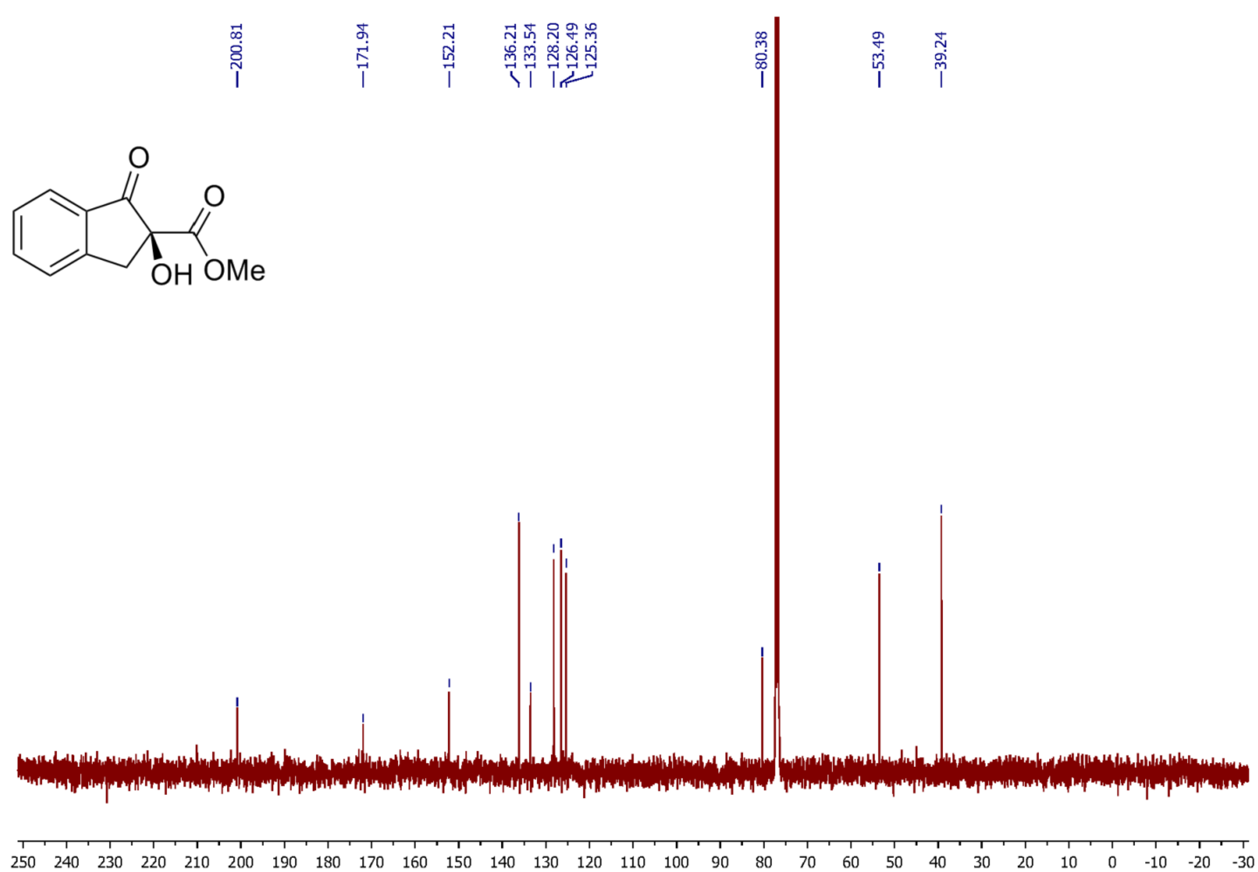


Figure S2a. [1]H NMR of **2b**.

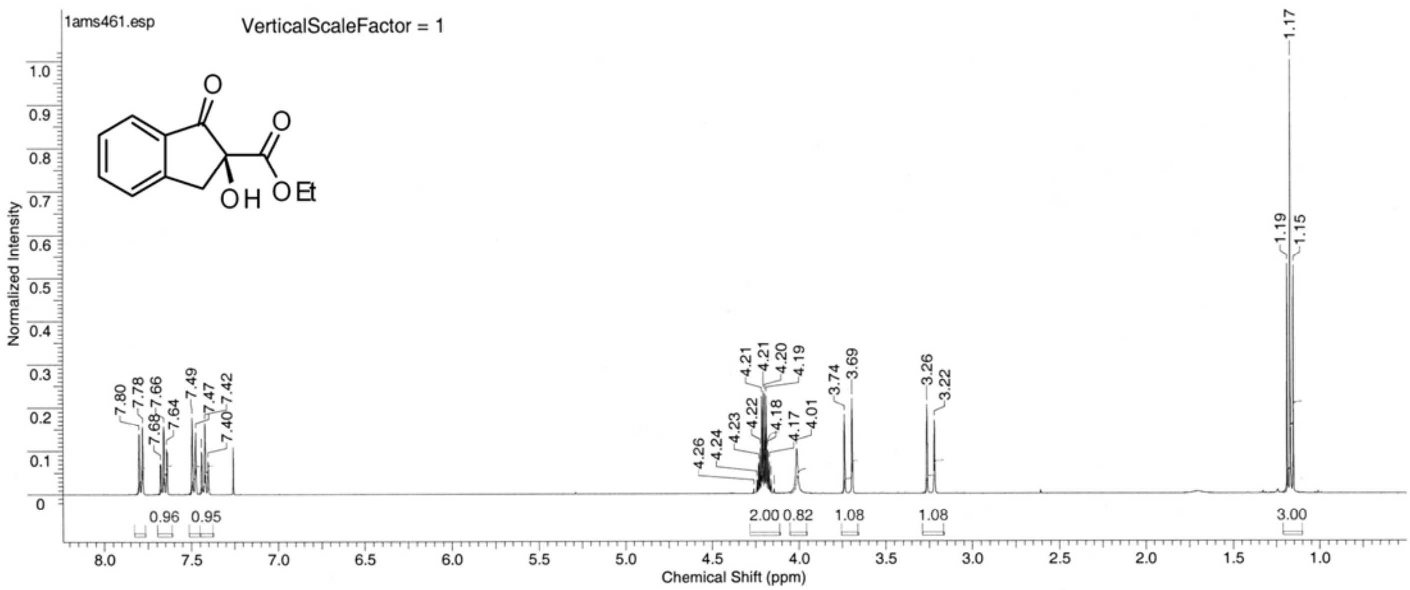


Figure S2b. [13]C NMR of **2b**.

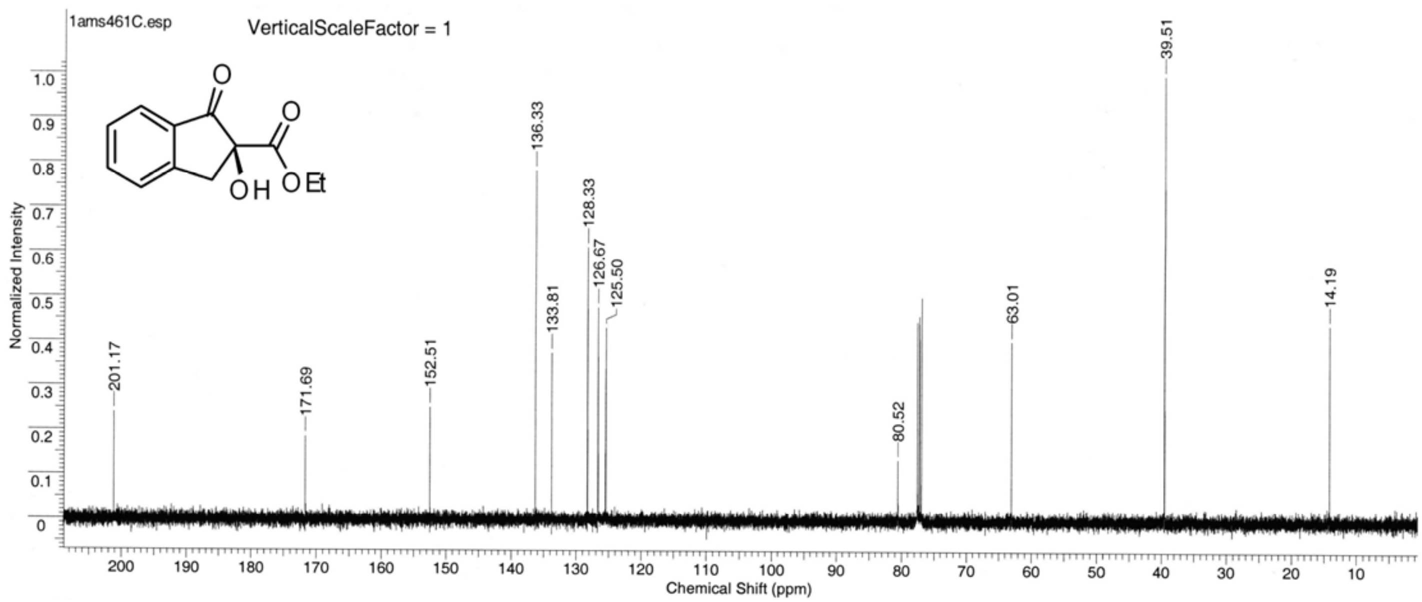


Figure S3a. ^{1}H NMR of **2c**.

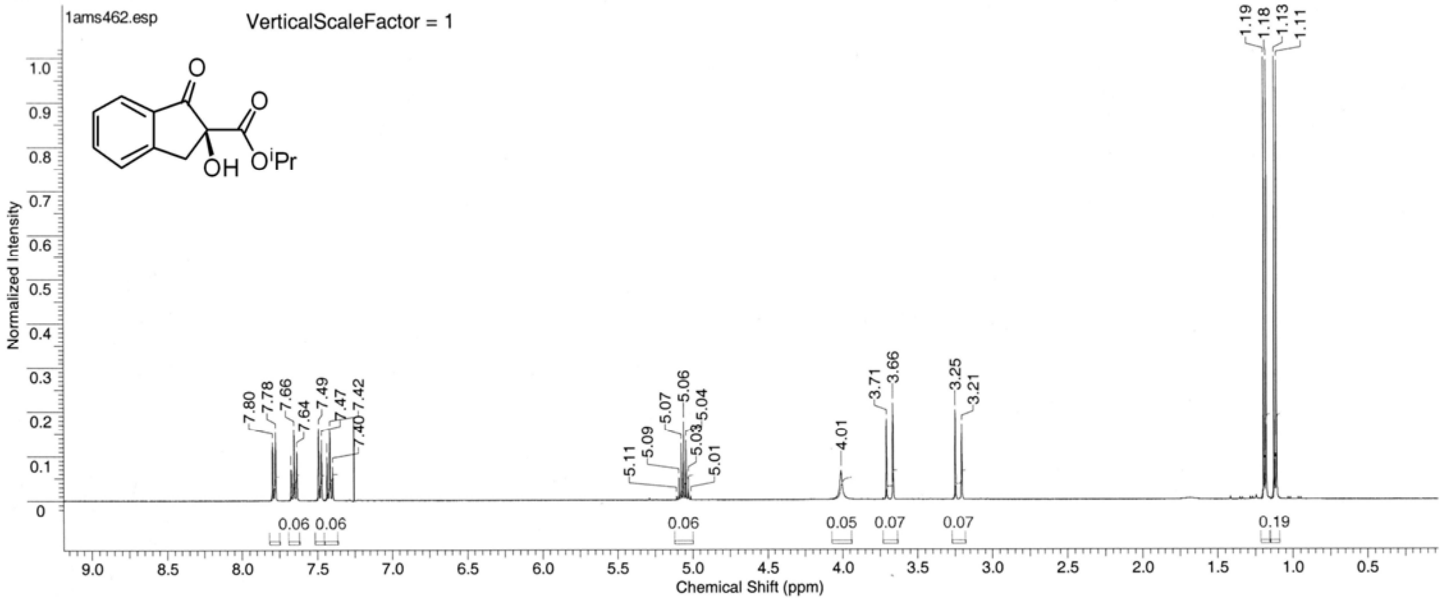


Figure S3b. ^{13}C NMR of **2c**.

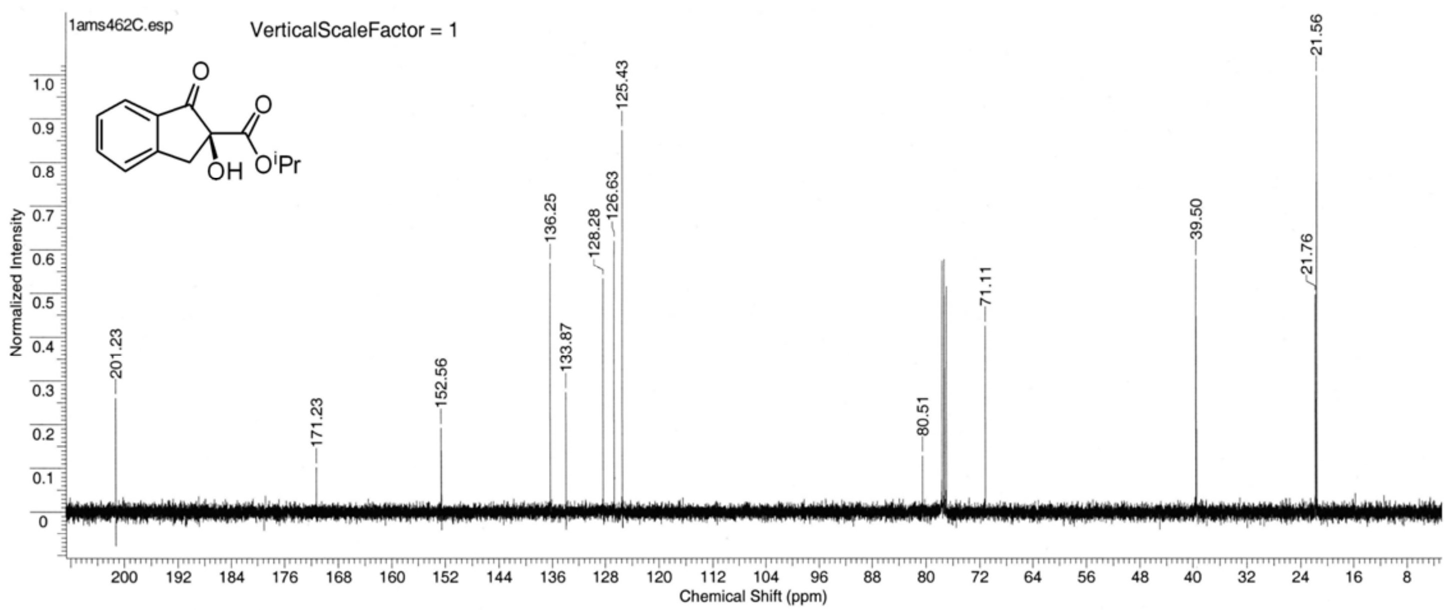


Figure S4a. ^{1}H NMR of **2d**.

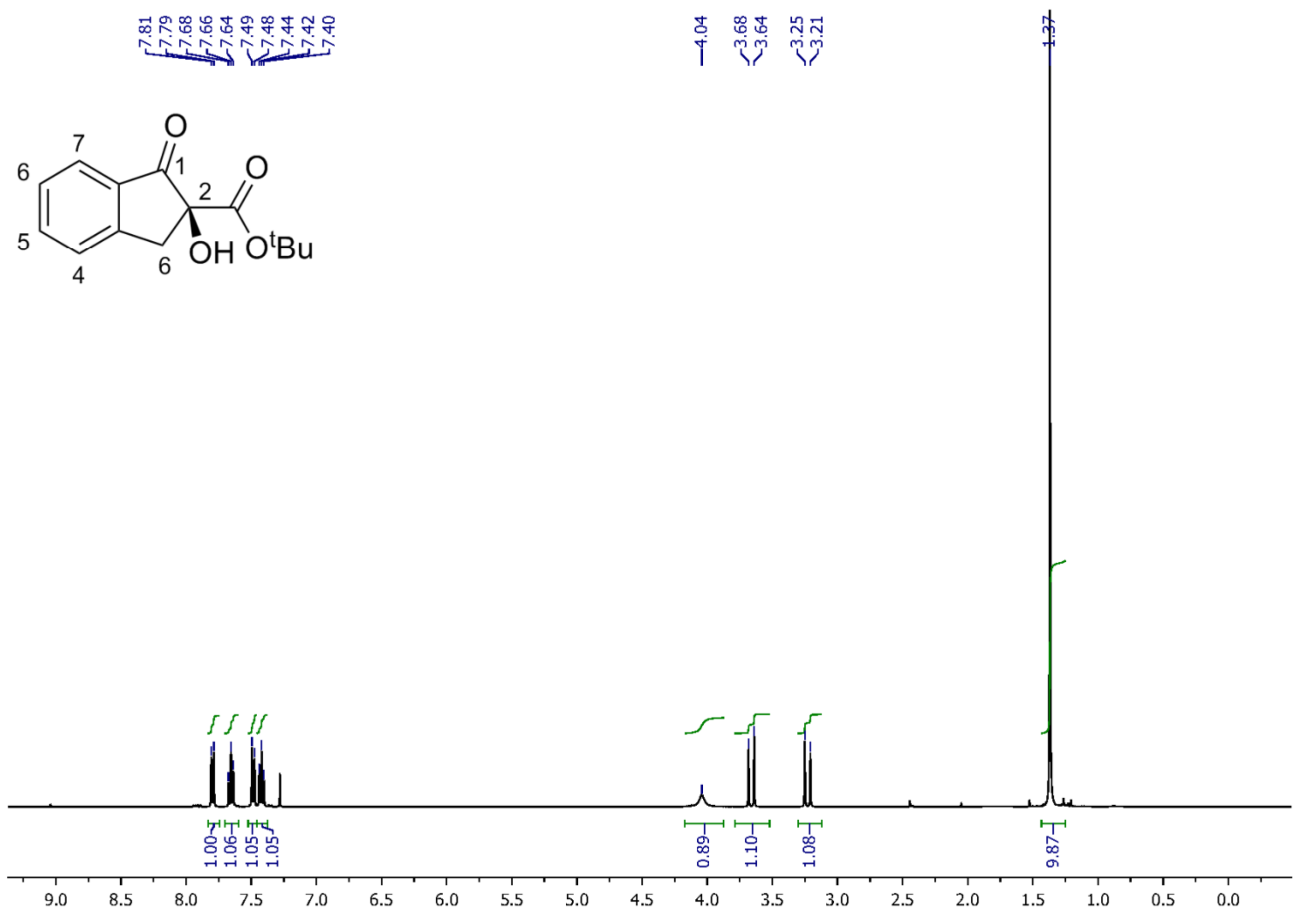


Figure S4b. ^{13}C NMR of **2d**.

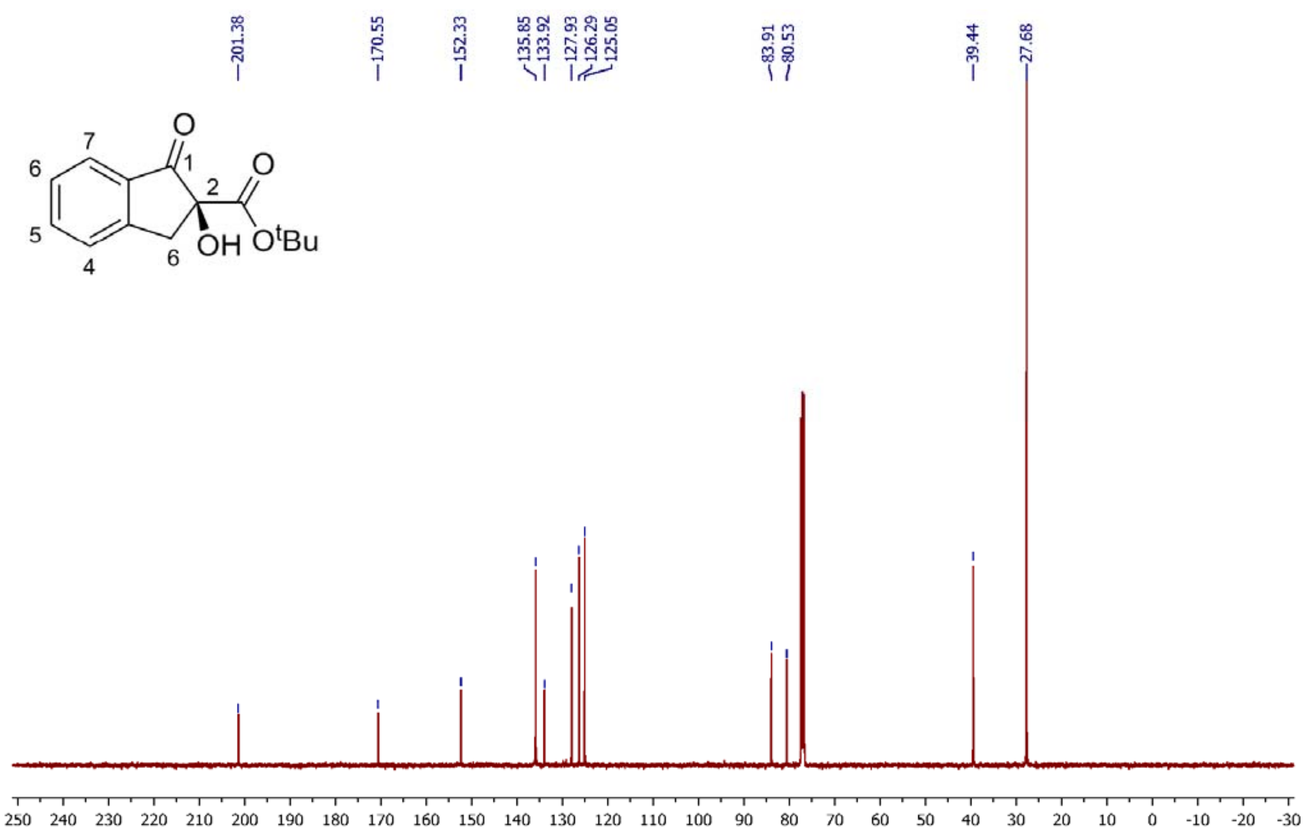


Figure S5a.^{1}H NMR of **3a**.

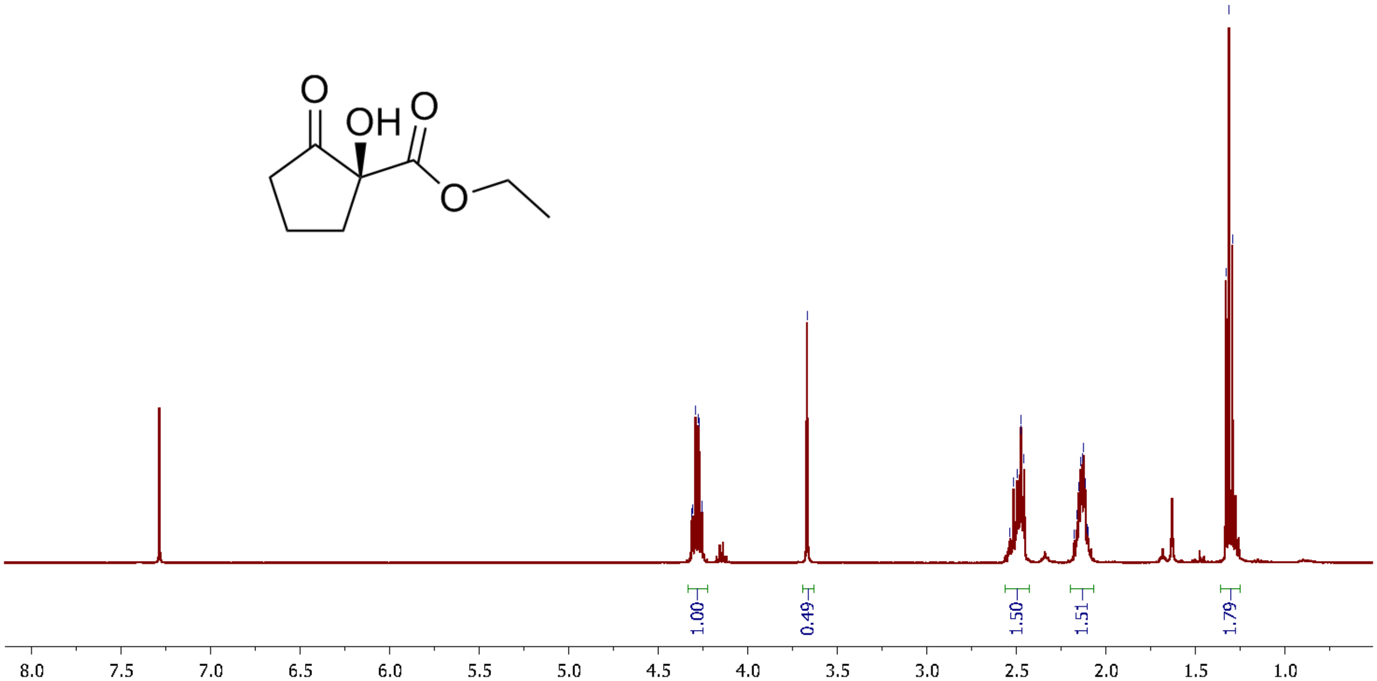


Figure S5b.^{13}C NMR of **3a**.

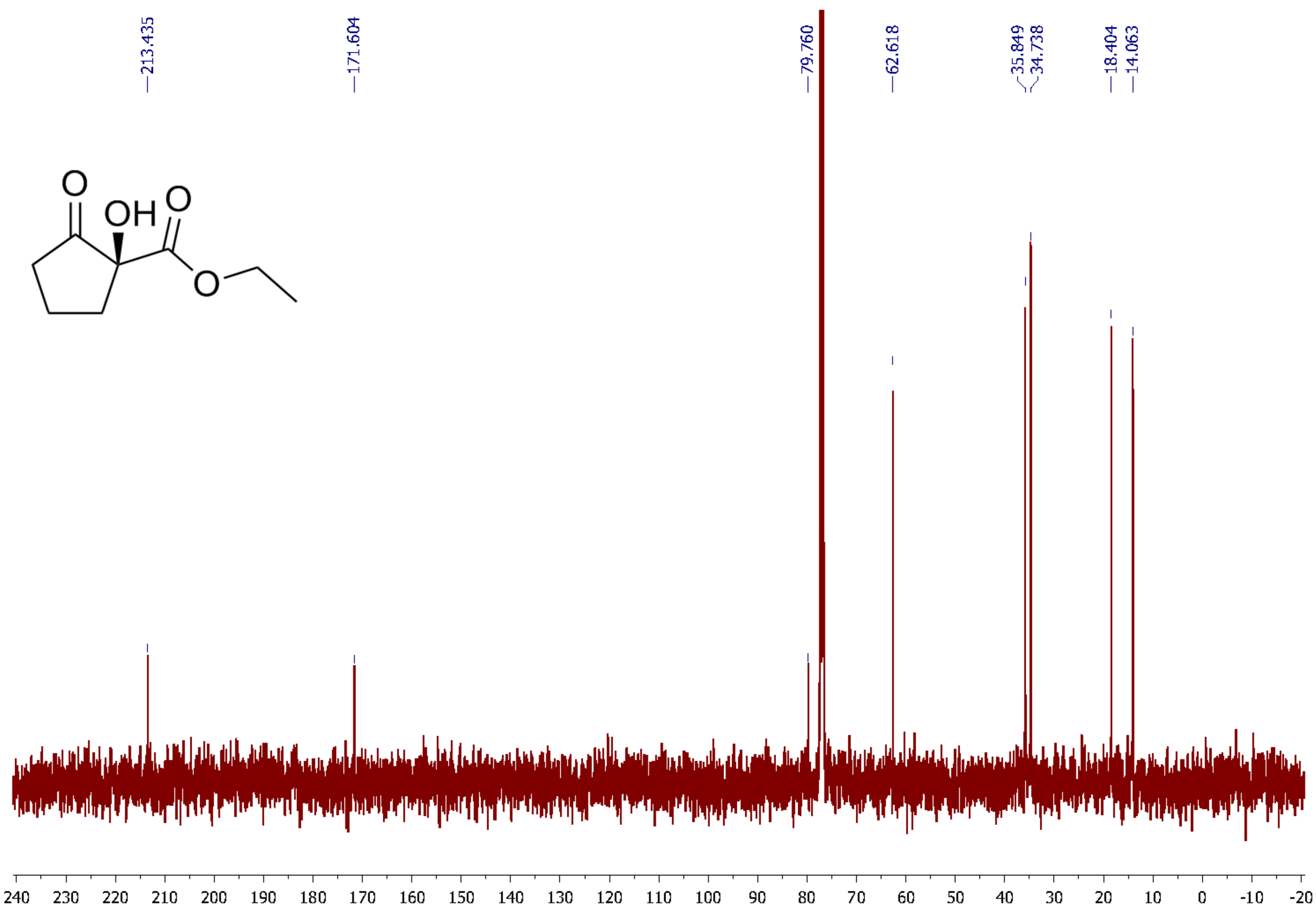


Figure S6a.[1]H NMR of **3b**.

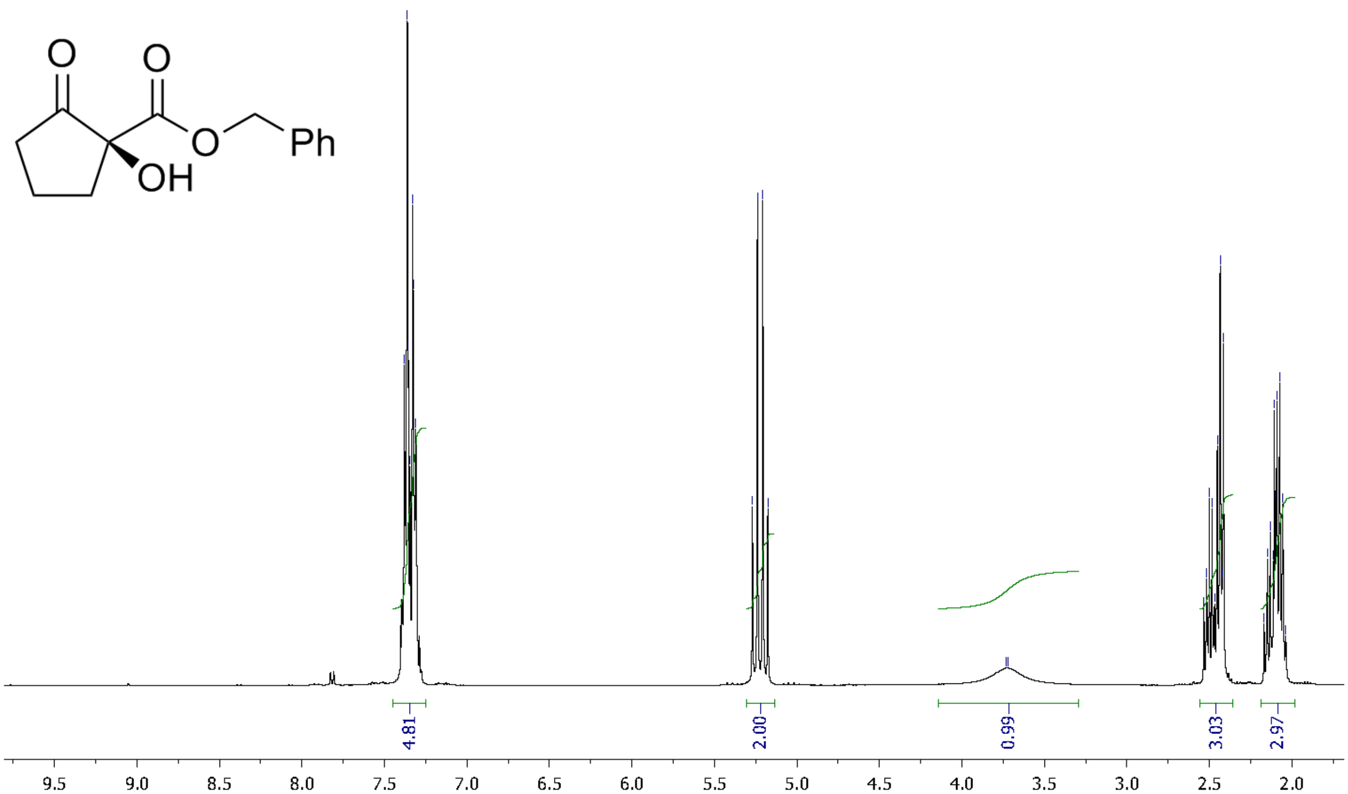


Figure S6b.[13]C NMR of **3b**.

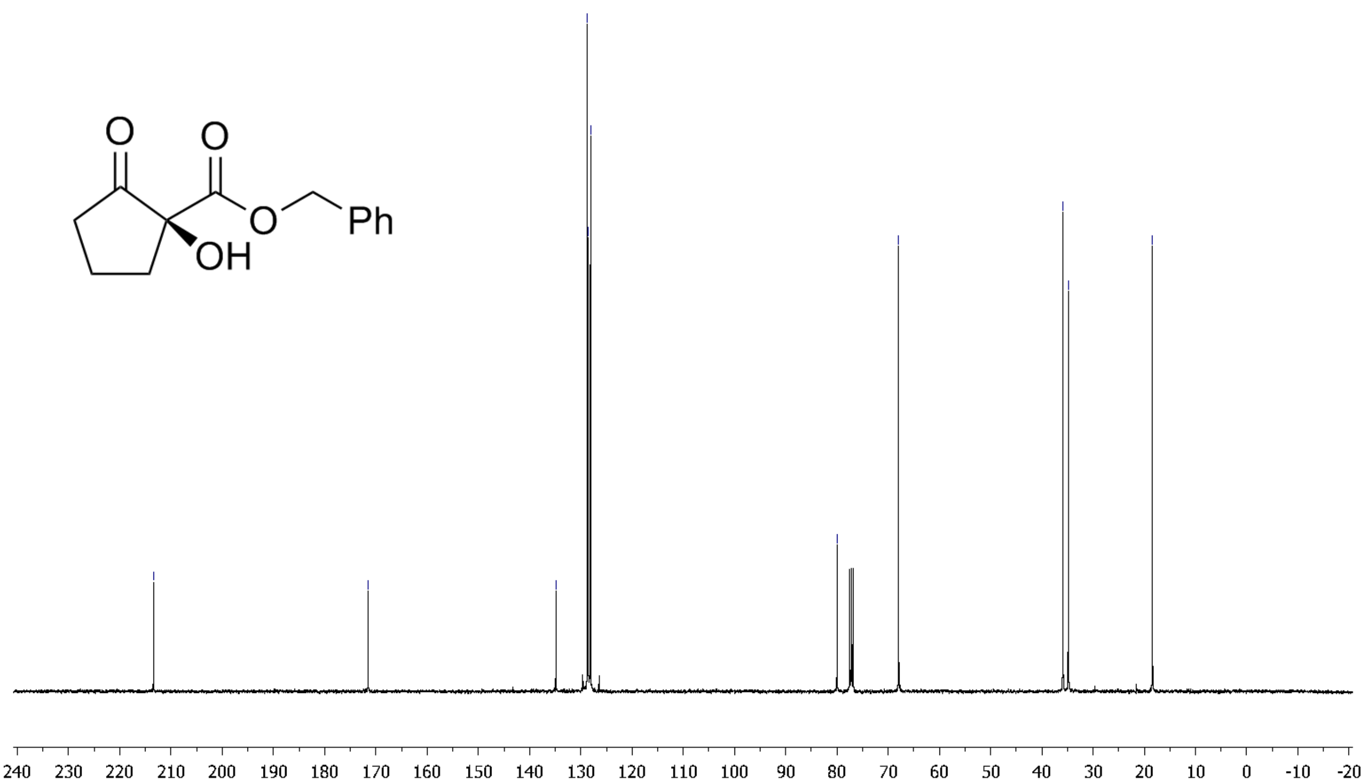


Figure S7a.^{1}H NMR of **3c**.

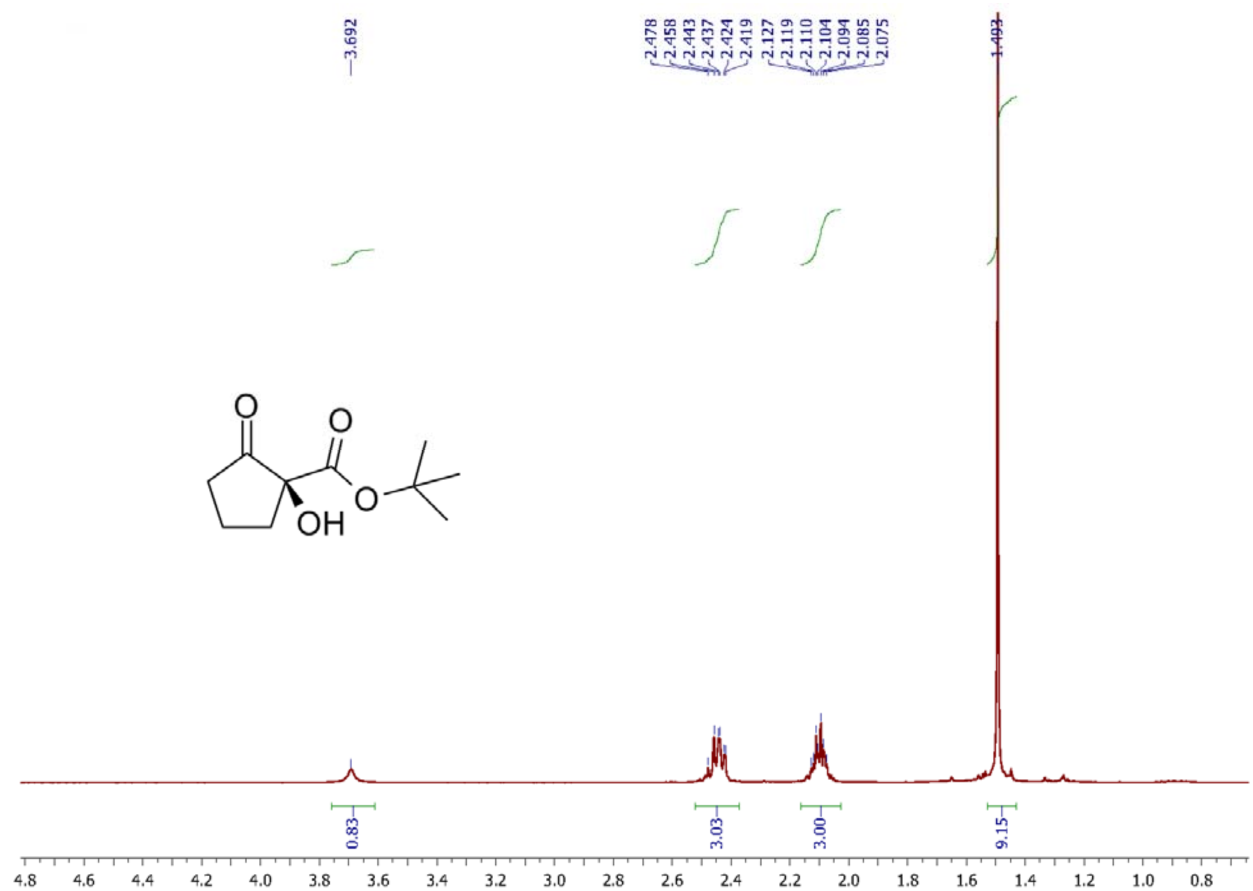


Figure S7b.^{13}C NMR of **3c**.

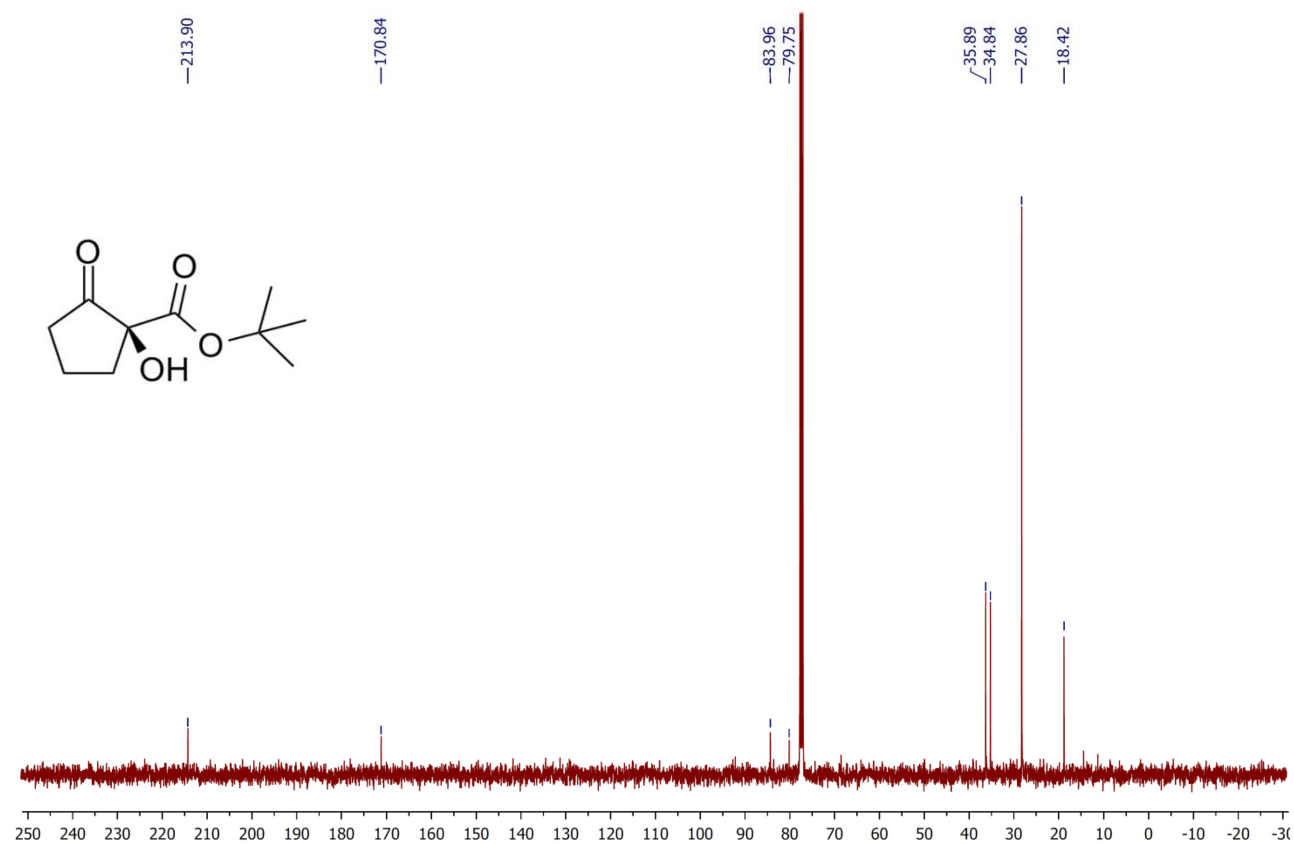
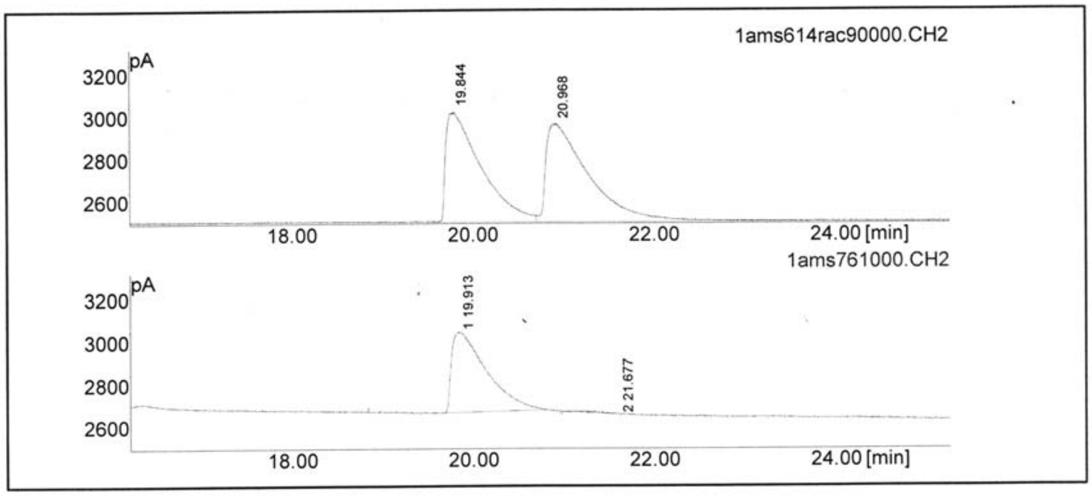


Figure 7c. Chiral GC chromatogram of **3c** (top: racemic, bottom: optically active): Chiraldex G-TA (20 m x 0.25 mm), isothermal 90°C, FID detector, t_R (major) 19.84, t_R (minor) 20.97.



#	Name	RT [min]	Area [pA*s]	Amount [%]
1	1	19.913	10039	99.1081
2	2	21.677	90	0.8919

98%

Figure S8a.^{1}H NMR of **4a**.

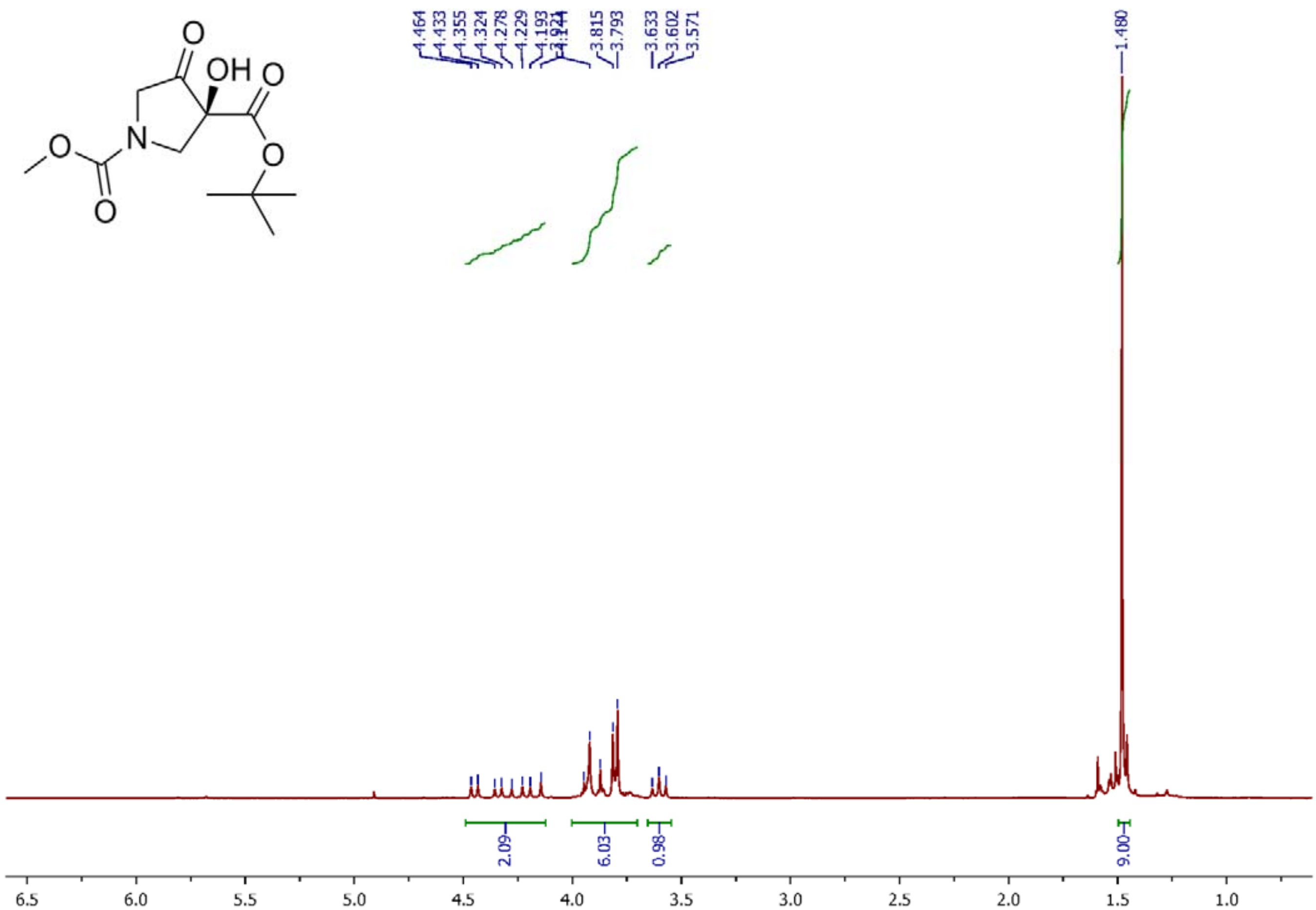
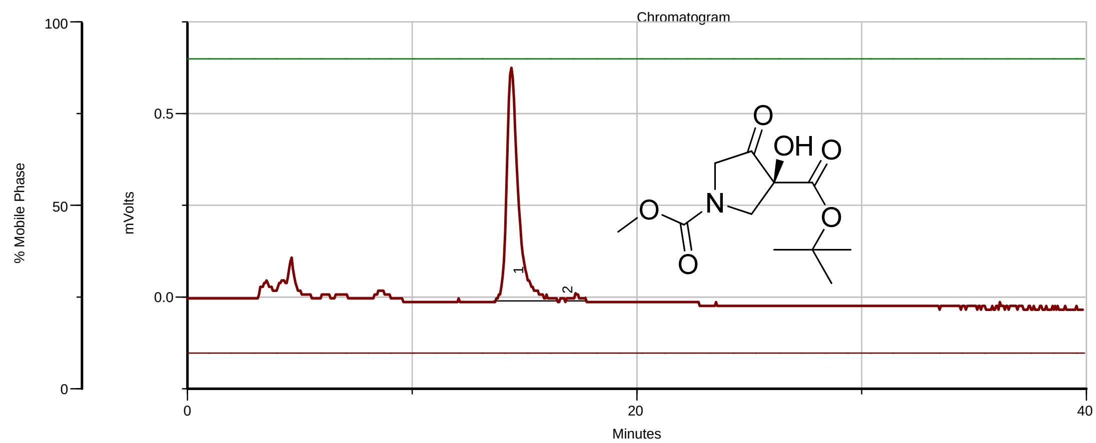


Figure S8b.Chiral HPLC chromatogram of **4a** (unstable): Chirapak AD-H column, Hexane/^{i}PrOH, 90/10, 1 mL/min, 240 nm, t_R (major) = 14.7 min, t_R (minor) = 17.7 min.



Sample Descrip.	Inj. Number	R. Time	Area	Area %	Sample Location
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1AMS770	4.00	17.21	1090.58	2.71	TUBES:2

Figure S9a.[1]H NMR of **4b**.

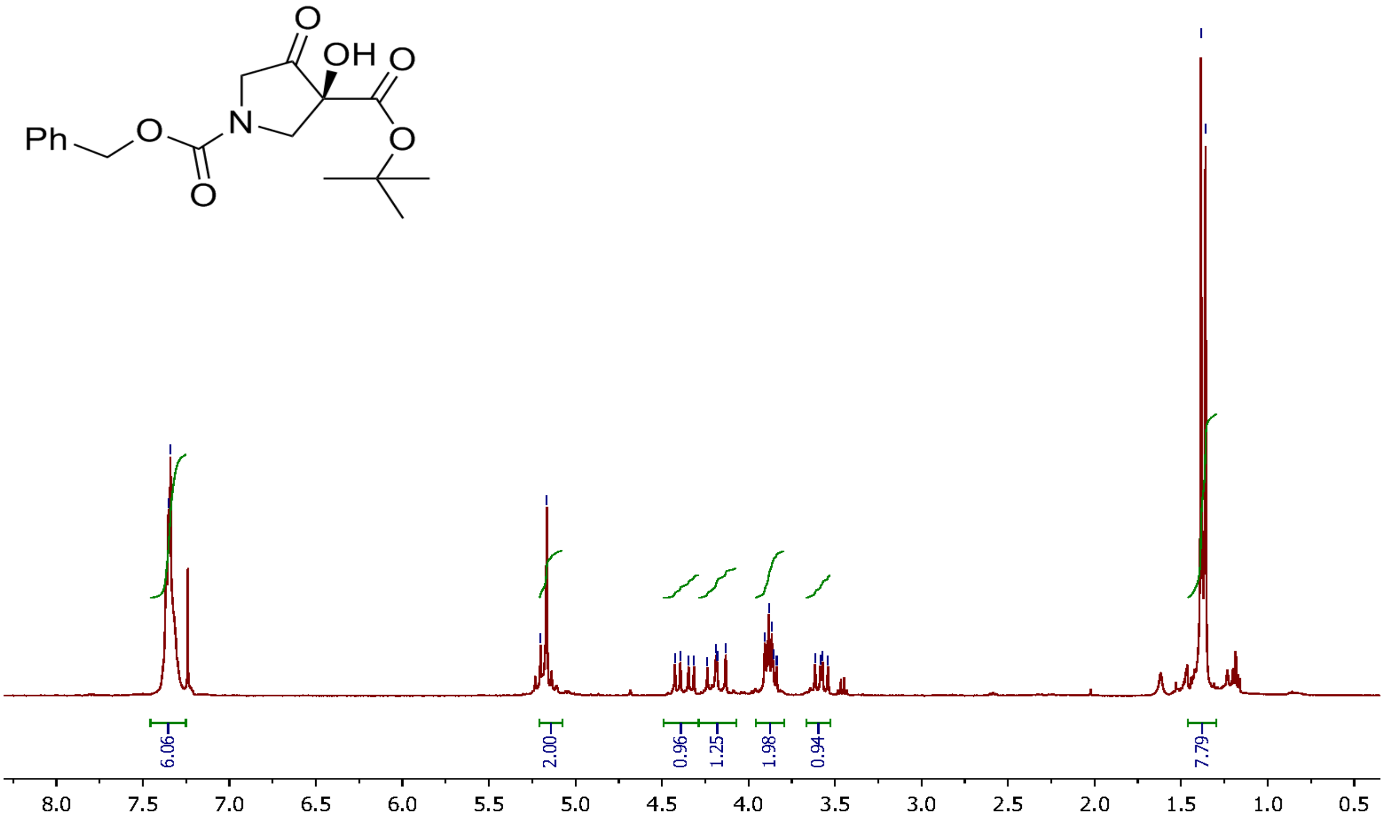
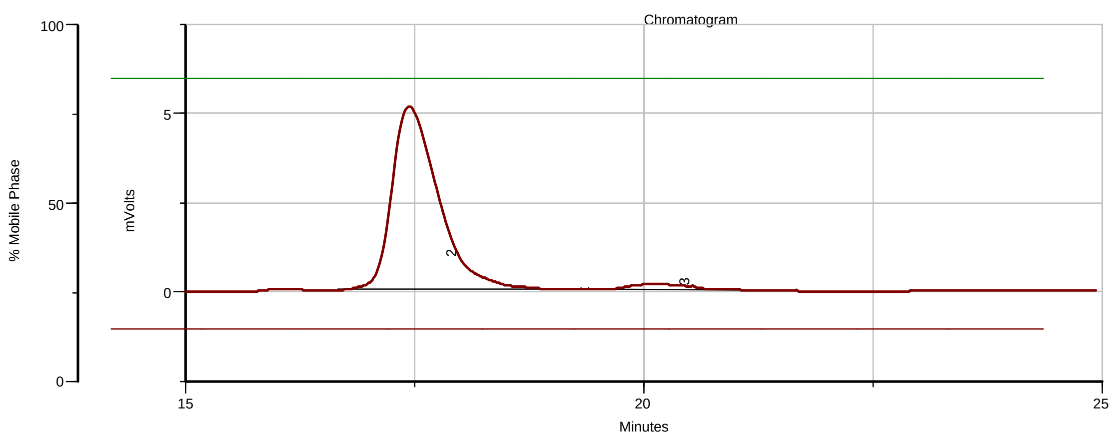


Figure S9b.Chiral HPLC chromatogram of **4b**: Chirapak AD-H column, Hexane/^{i}PrOH, 90/10, 1 mL/min, 240 nm, t_R (major) = 22.5 min, t_R (minor) = 25.8 min.



Sample Descrip.	Inj. Number	R. Time	Area	Area %	Sample Location
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1AMS769	1.00	20.19	15949.23	4.85	TUBES:1

Figure S10a.[1]H NMR of **4c**.

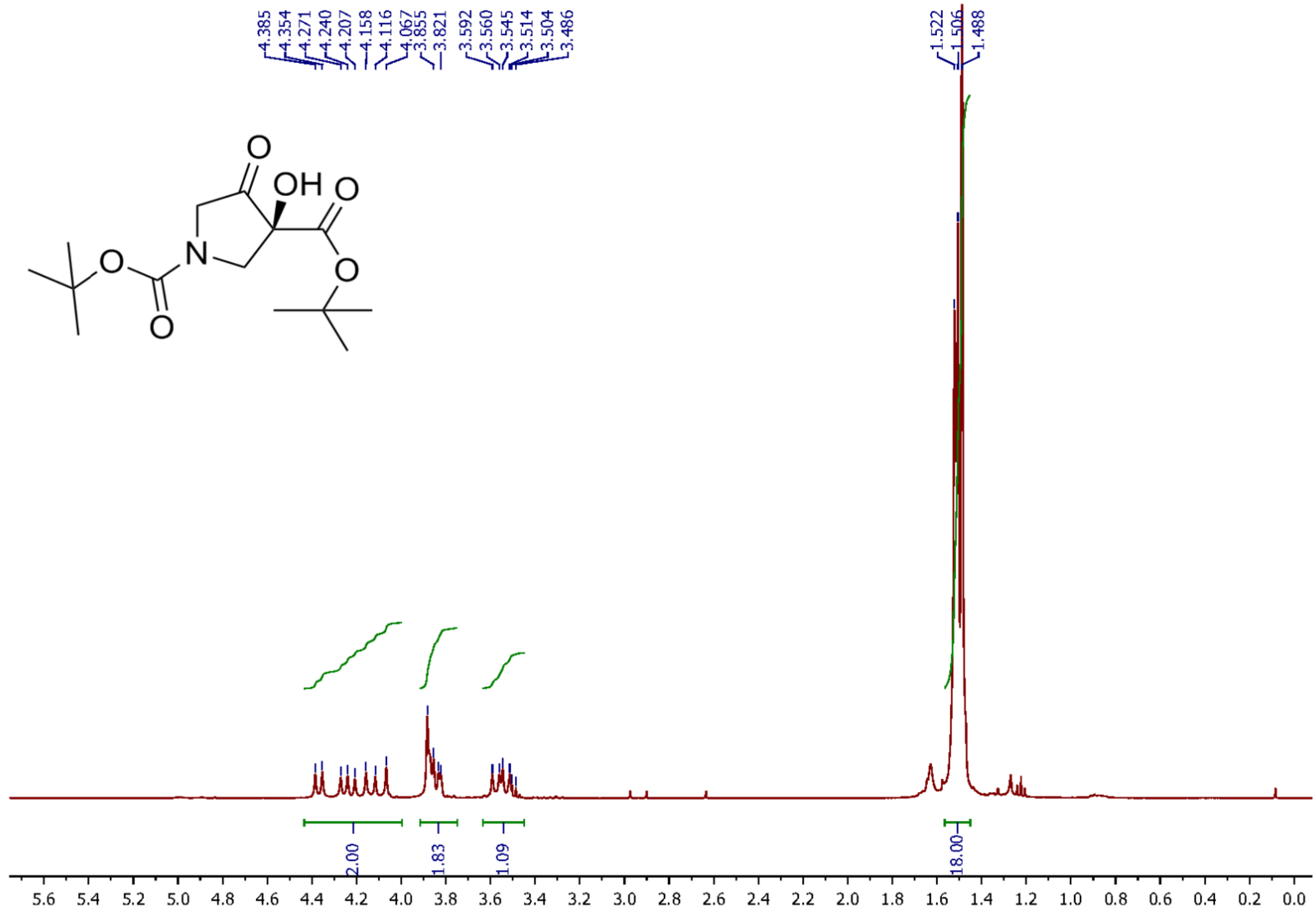
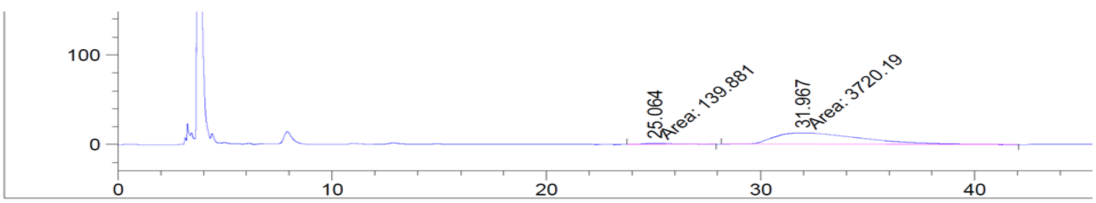


Figure S10b.Chiral HPLC chromatogram of 4c: Chiracel OD-H column, Hexane/^{i}PrOH, 98/2, 1 mL/min, 220 nm, t_R (minor) = 25.0 min, t_R (major) = 32.0 min.



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.064	MM	1.7691	139.88118	1.31782	3.6238
2	31.967	MM	4.8275	3720.18848	12.84381	96.3762
Totals :				3860.06966	14.16163	

Figure S11a. ^{1}H NMR of **5a**.

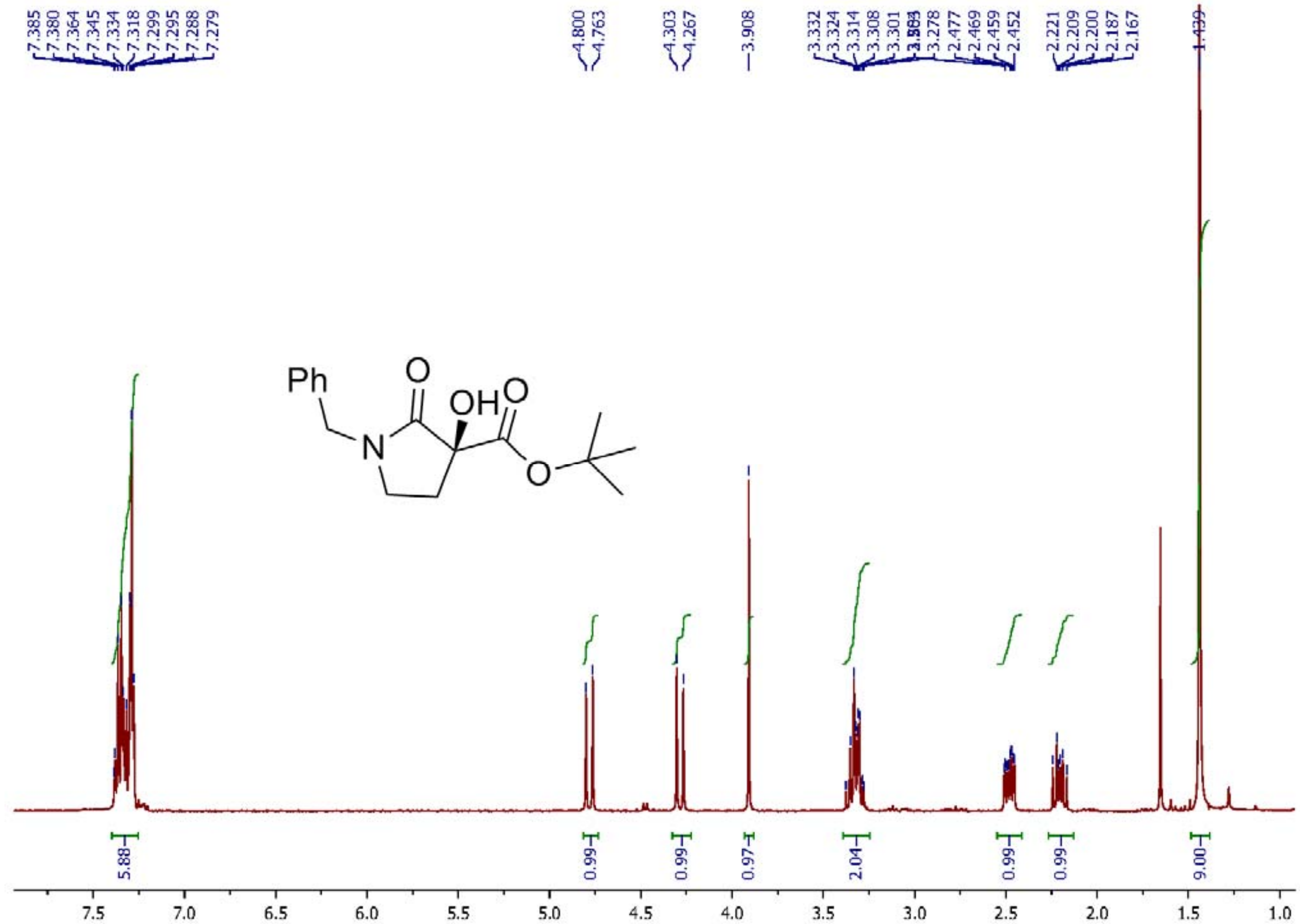


Figure S11b. ^{13}C NMR of **5a**.

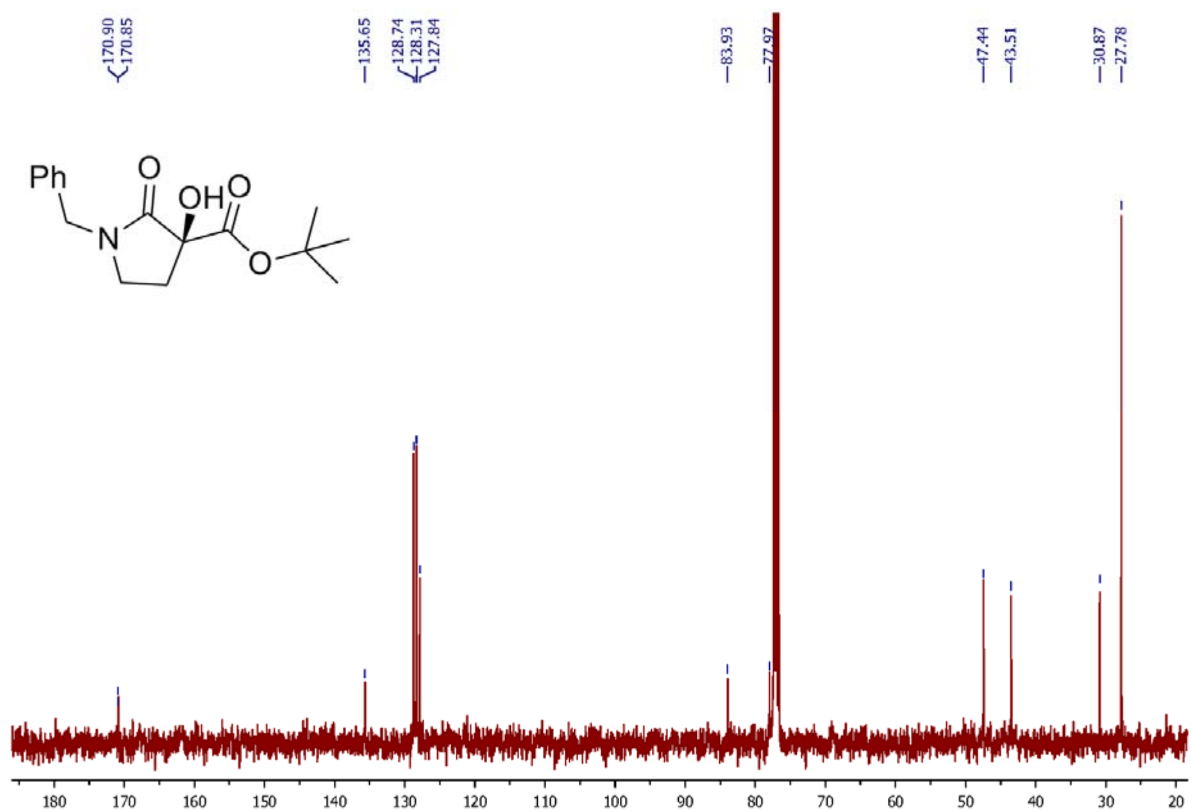
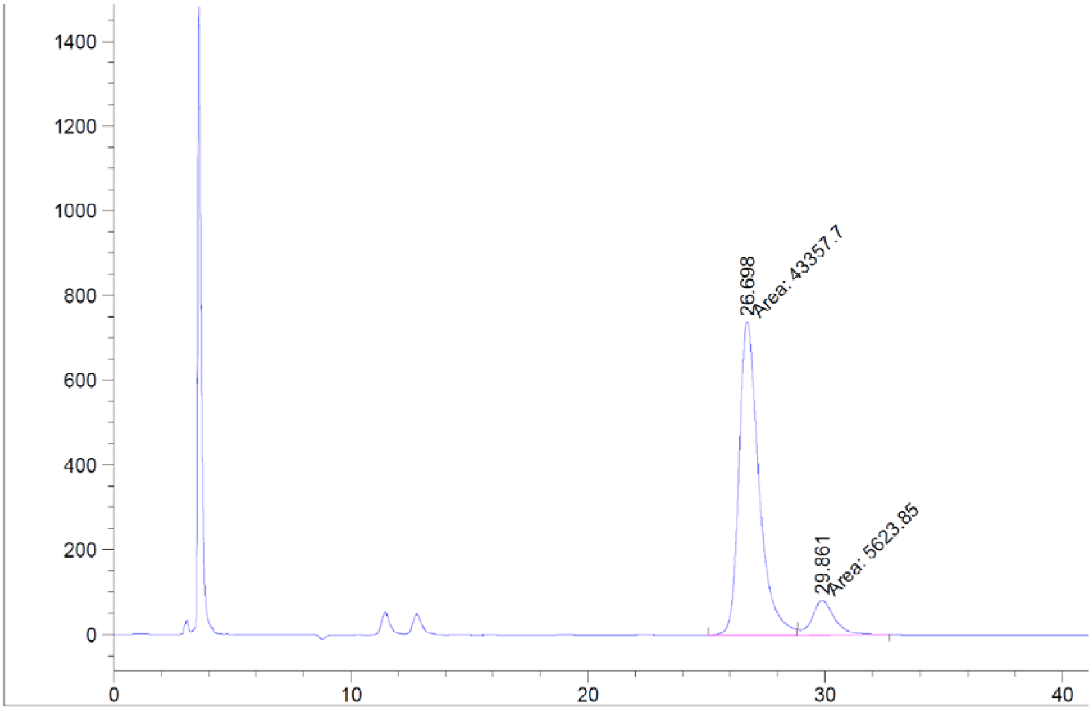


Figure S11c. Chiral HPLC chromatogram of **5a**: Chirapak AD-H column, Hexane/^{i}PrOH, 90/10, 1 mL/min, 220 nm, t_R (major) = 27.0 min, t_R (minor) = 29.9 min




```
=====================================================================
                     Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.698	MM	0.9761	4.33577e4	740.29681	88.5184
2	29.861	MM	1.1350	5623.84619	82.58150	11.4816
Totals :				4.89815e4	822.87832	

Figure S12a.[1]H NMR of **5b.**

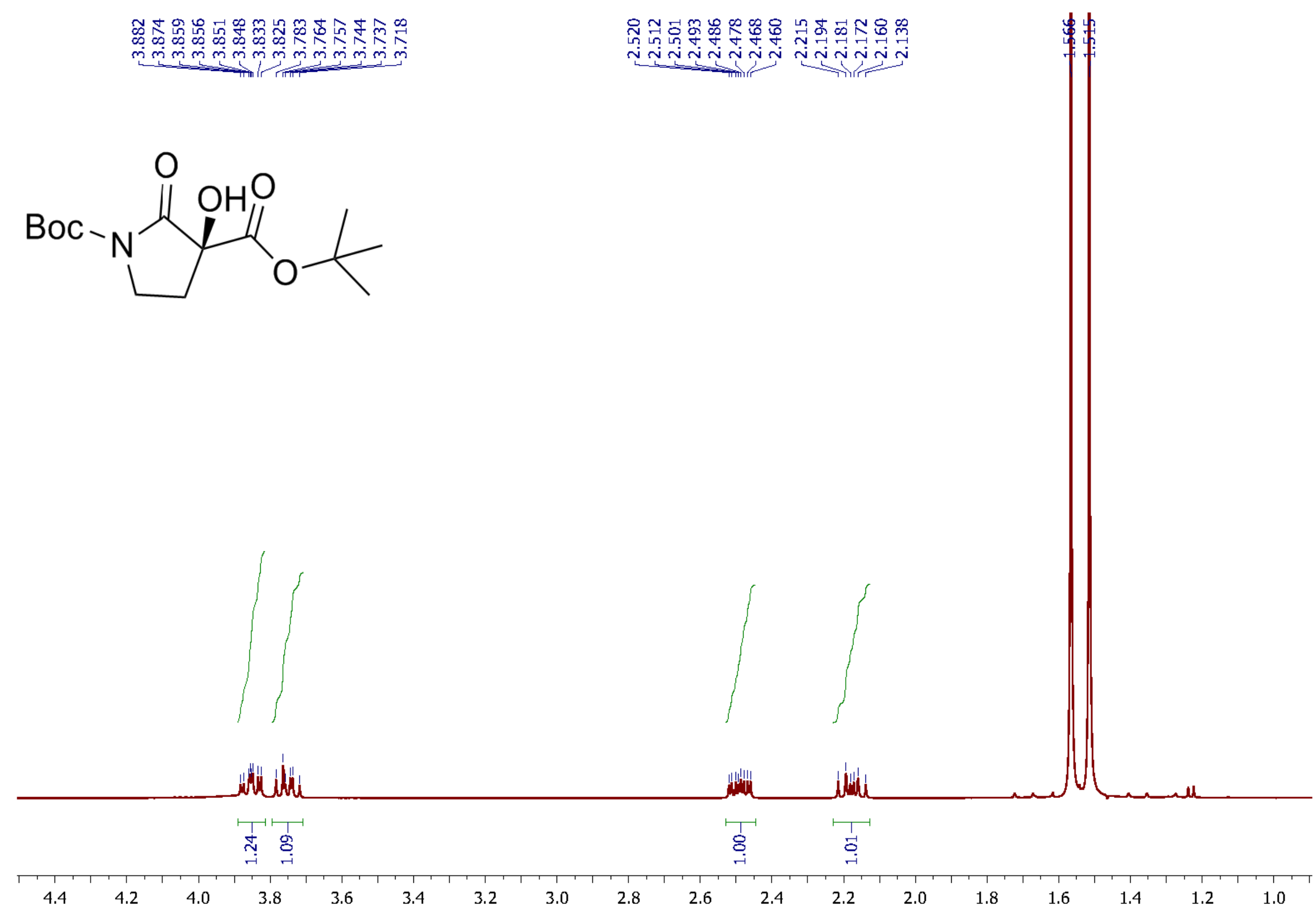


Figure S12b.[13]C NMR of **5b.**

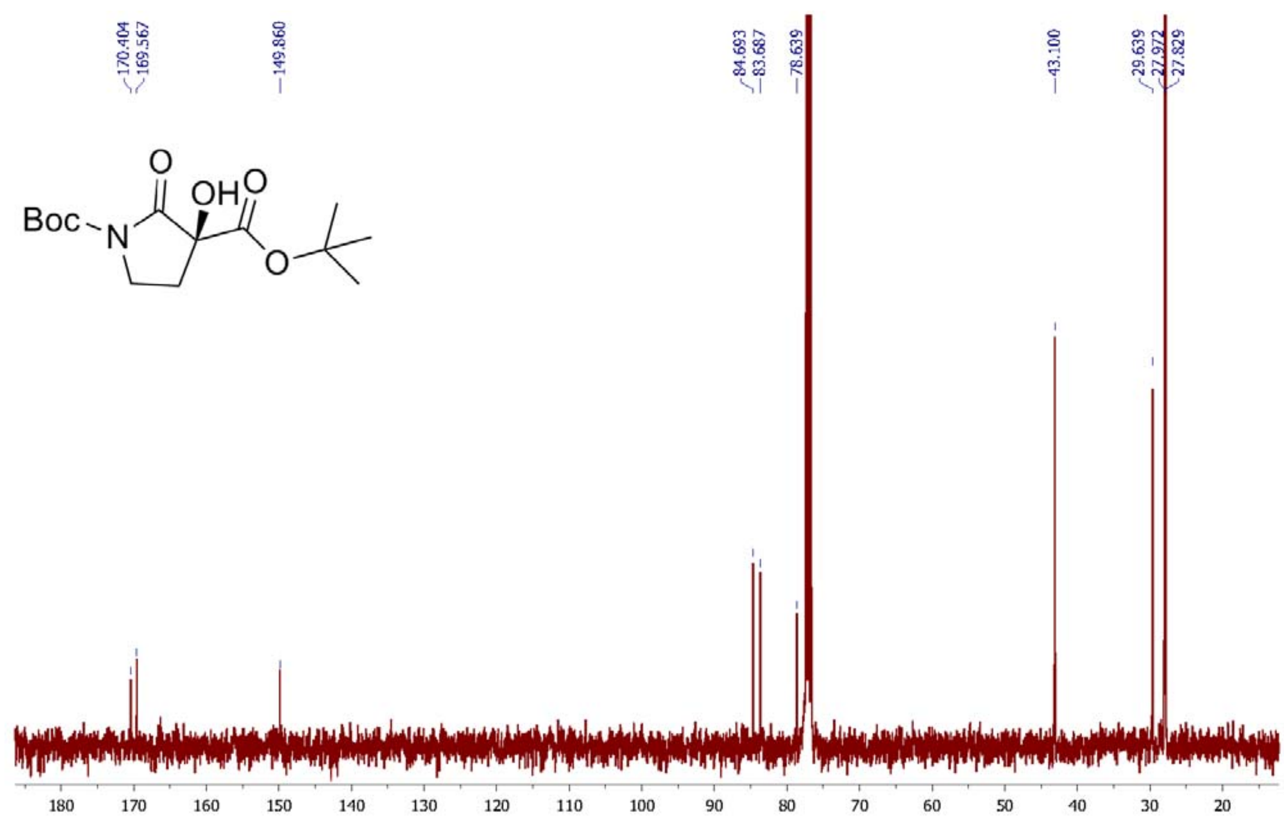


Figure S12a.^{1}H NMR of **6a.**

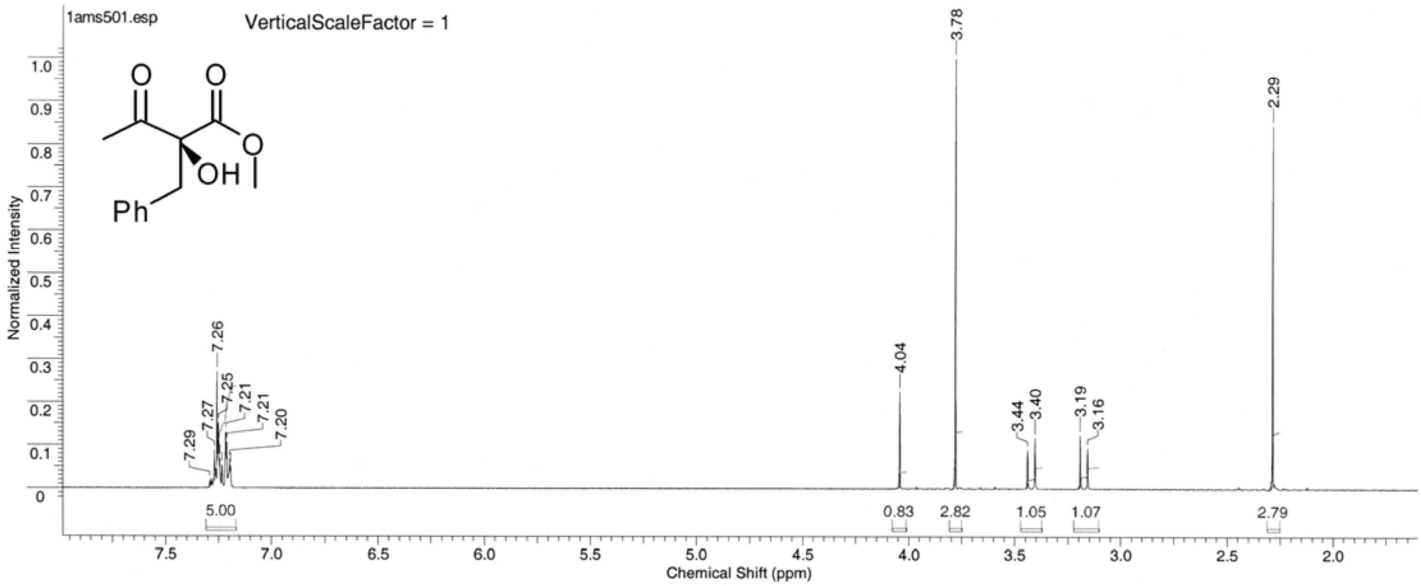


Figure S12b.^{13}C NMR of **6a.**

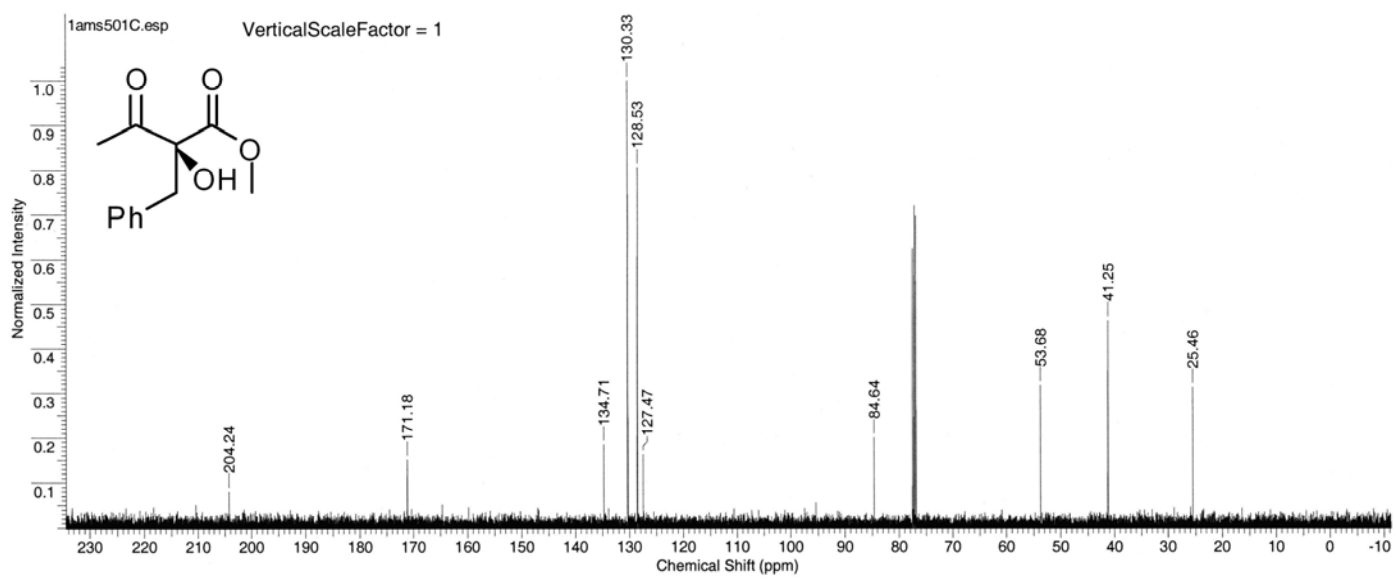


Figure S12a.[1]H NMR of **6b.**

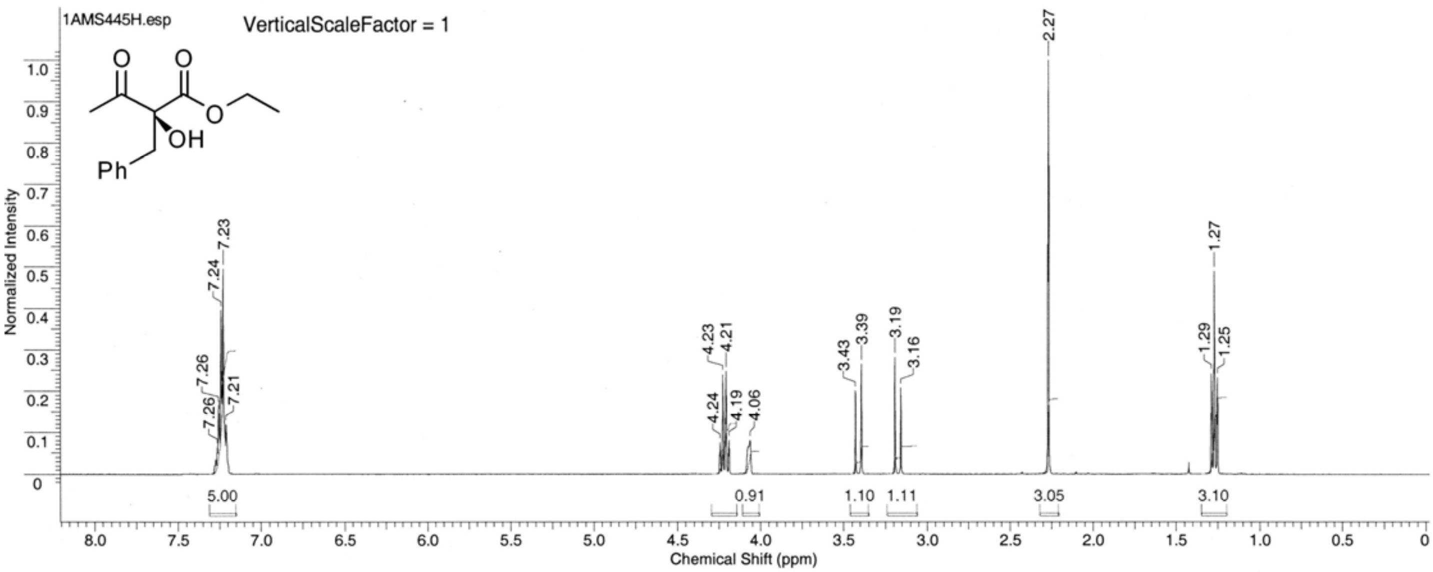


Figure S12b.[13]C NMR of **6b.**

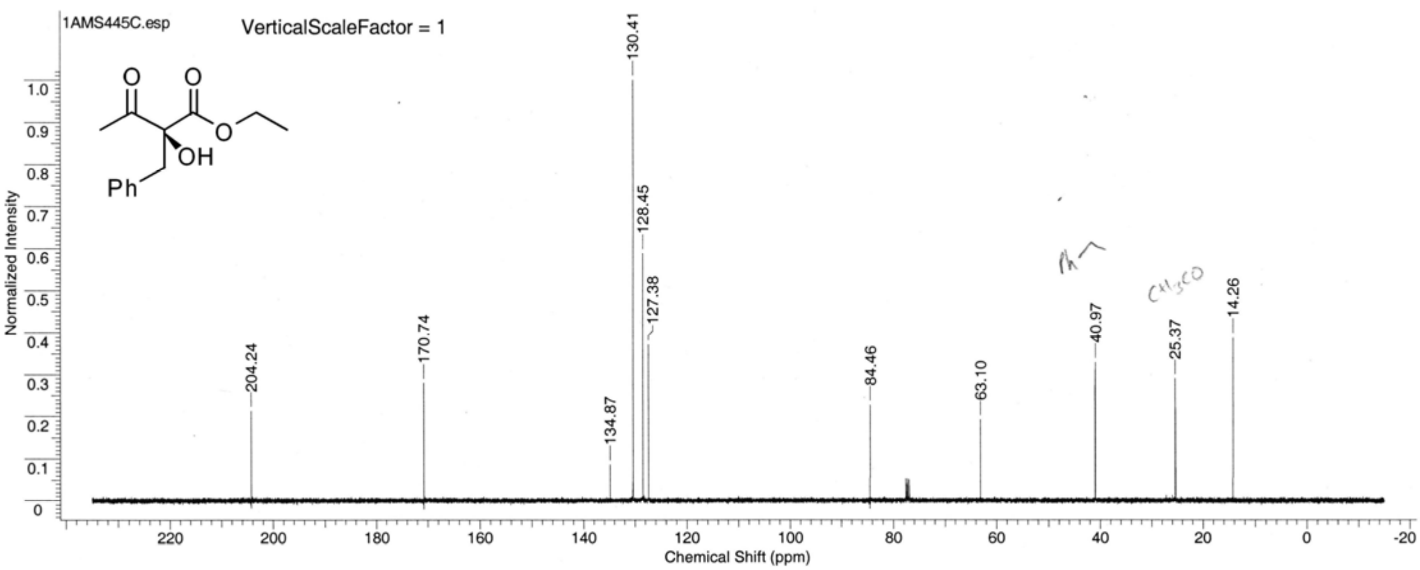


Figure S12a.[1]H NMR of **6c.**

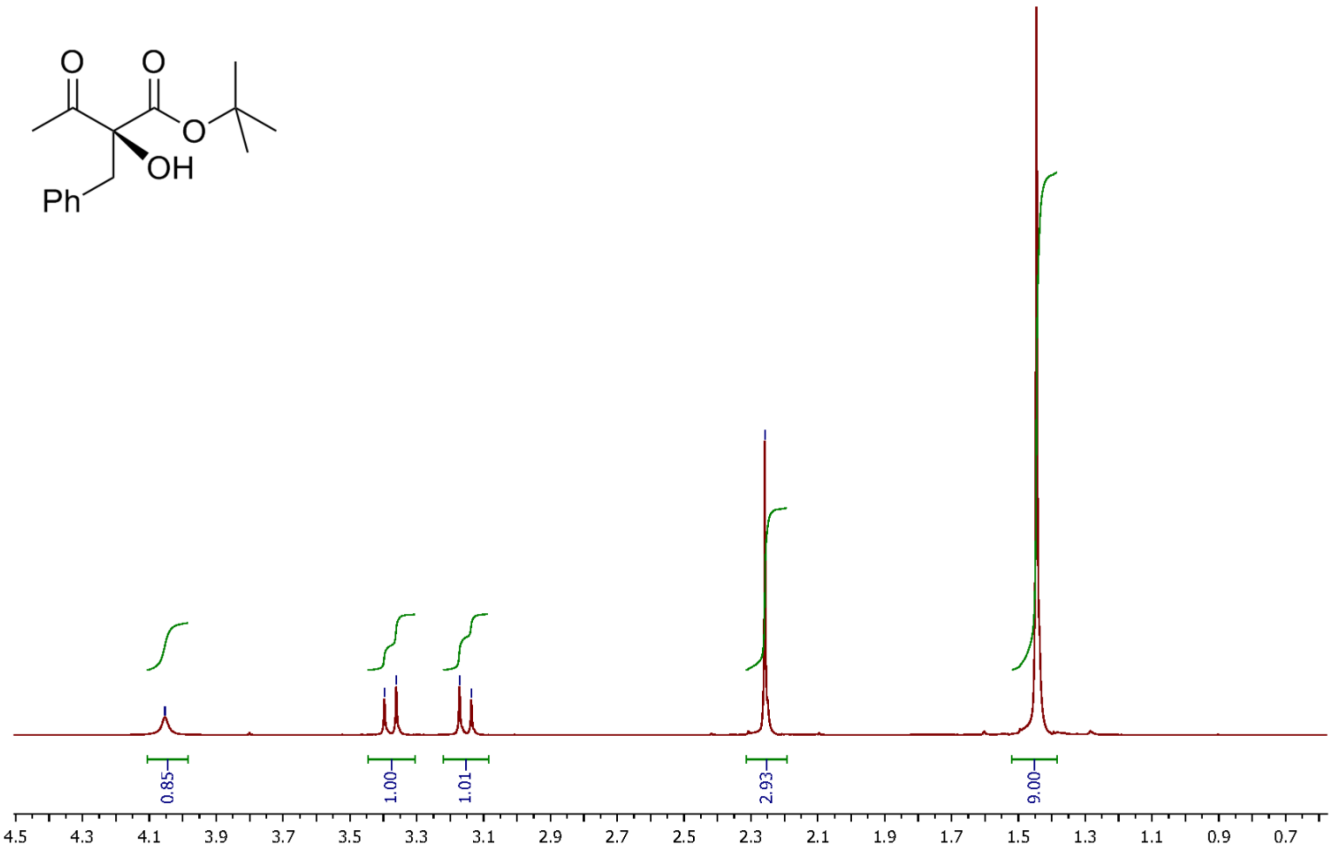


Figure S12b.[13]C NMR of **6c.**

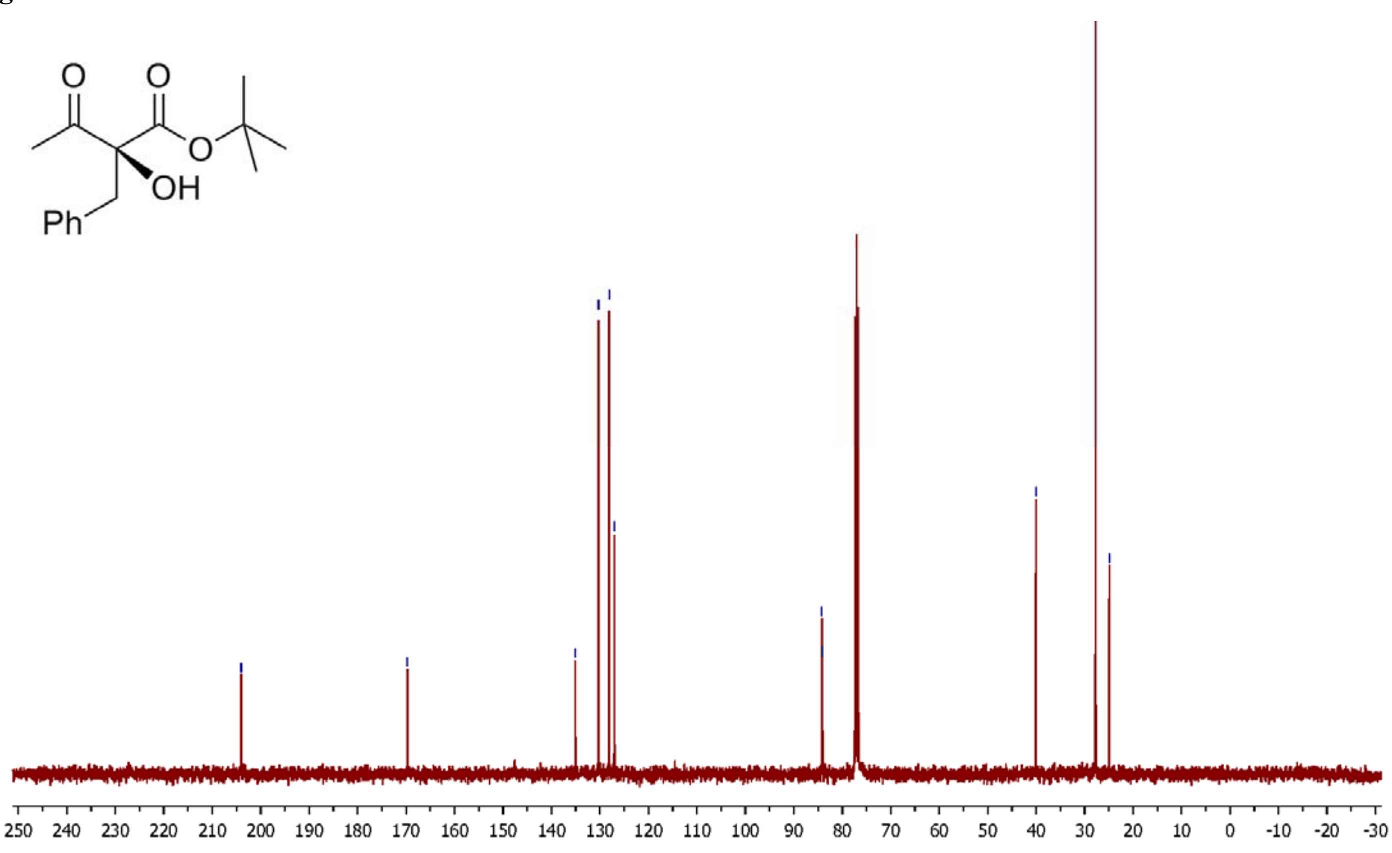
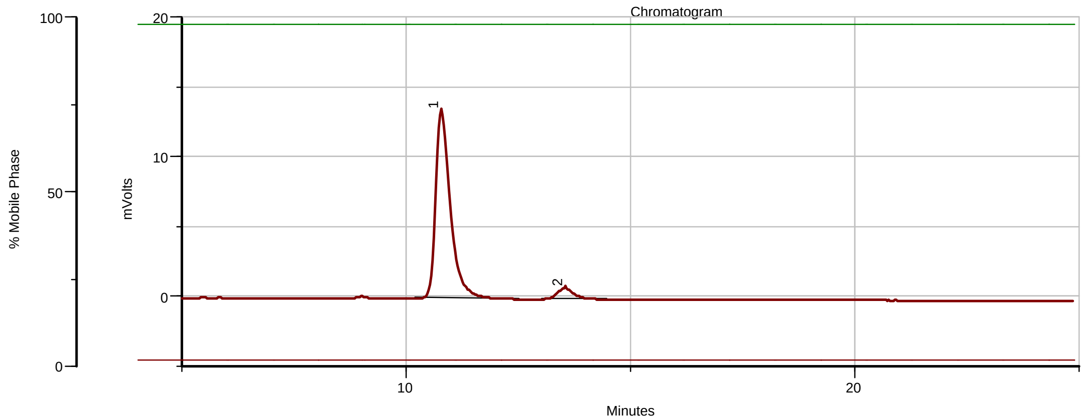


Figure S12c. Chiral HPLC chromatogram of **6c**: Chirapak AD-H column, Hexane/^{i}PrOH, 98/02, 1 mL/min, 220 nm, t_R (major) = 10.8 min, t_R (minor) = 13.5 min.



Sample Descrip.	Inj. Number	R. Time	Area	Area %	Sample Location
1AMS759	1.00	10.78	521764.66	93.76	TUBES:4
1AMS759	1.00	13.53	34717.92	6.24	TUBES:4