Supporting Information

Exploring the Scope of Asymmetric Synthesis of *β*-Hydroxy-*γ*-lactams via Noyori-type Reductions

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General Information

Solvents were distilled prior to use as follows: dichloromethane was distilled from phosphorus pentoxide; ethyl acetate was distilled from potassium carbonate; tetrahydrofuran was distilled from sodium–benzophenone ketyl; ethanol and methanol were distilled from the corresponding magnesium alkoxide. Isopropanol was dried before use with activated 4 Å molecular sieves. Anhydrous 2-methyltetrahydrofuran was purchased from Sigma–Aldrich and was not subjected to additional drying protocols prior to use. Butyl lithium was also purchased from Sigma–Aldrich, as a 2.5M solution in hexanes, and its concentration was determined by the Gilman double titration method[1] not more than 4 days prior to use. Organic phases were dried using anhydrous magnesium sulfate. All commercial reagents were used without further purification.

^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75.5 MHz respectively on a Bruker Avance 300 spectrometer, while ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100.6 MHz respectively on a Bruker Avance 400 spectrometer. All NMR spectra were recorded at 300K. Chemical shifts are given in ppm relative to tetramethylsilane (TMS) as an internal standard. Coupling constants (*J*) are given in hertz (Hz). Infrared spectra were measured using a Perkin–Elmer FTIR UATR2 Spectrometer. Melting points were measured using a Uni-Melt Thomas Hoover capillary melting point apparatus and are not corrected. Optical rotations were measured using Perkin–Elmer 141 polarimeter at 20 °C at 589 nm in a 10 cm cell; concentrations (*c*) are expressed in g/100 mL, and [α] is expressed in units of 10^{-1} deg cm^{2} g^{-1}. High resolution mass spectra (HRMS) were recorded on a Waters LCT Premier Time of Flight (ToF) spectrometer in electrospray ionization (ESI) mode. Samples were prepared for HRMS using acetonitrile as solvent. Single crystal X-ray data was collected at University College Cork on a Bruker APEX II DUO diffractometer using Cu Kα radiation (Incoatec Montel Multilayer Mirror monochromator, λ = 1.54178 Å). All calculations were performed using the APEX2 software suite and the diagrams prepared with Mercury 3.8. The N–H and O–H hydrogen atoms were found and refined were possible and the positions of the other hydrogen atoms were calculated and allowed to ride on the parent atom.

Wet flash chromatography was performed using silica gel 60. Thin-layer chromatography (TLC) was carried out on precoated silica gel plates (60 PF254). Visualization was achieved by UV (254 nm) detection and/or staining with phosphomolybdic acid. 1-Benzyl-3-(3-methylbutanoyl)pyrrolidin-2-one **3a**,[2] 1-benzyl-3-(1-hydroxy-3-methyl-butyl)pyrrolidin-2-one (±)-**4/9a**,[2] methyl cyclopropylacetate,[3] and methyl cyclohexylcarboxylate[4] were prepared

as described in the literature—the isolated products product demonstrating identical physical and spectroscopic properties to those previously described. All reactions were conducted under a nitrogen atmosphere, unless otherwise stated.

Preparation of *β*-Keto-*γ*-lactams

Method A

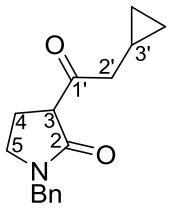
Diisopropylamine (2.2 equiv) was combined with 2-MeTHF, cooled to −7 °C, and *n*-BuLi in hexanes (2.2 equiv) was added over 30 min. 1-Benzylpyrrolidin-2-one **(1)** (1 equiv), ester (1.17 equiv), and 2-MeTHF were combined and added to the LDA/2-MeTHF mixture over 30 min, while maintaining the reaction temperature between −10 to 5 °C, to afford a slurry. After 45 min, heptane was added to the mixture over 30 min at −5 to 5 °C. The slurry was filtered and the off-white solids were rinsed with 1:1 heptane/2-Me-THF. The solids were then suspended in MTBE, 10% aqueous citric acid was added, and the mixture stirred for 30 min to give two homogeneous phases (aq. phase pH 4−5). A further portion of MTBE was added and the organic phase was separated, washed with water, dried and concentrated to afford the crude *β*-keto-γ-lactam product. In agreement with an earlier report,[2] the NMR spectra of the purified products **3e** and **7c** showed evidence for the presence of a minor enol tautomer (<10% in both cases): some characteristic signals were seen for the enol form and are listed in both cases, in addition the integration of the C-3H signal of the *β*-keto-*γ*-lactams were decreased relative to those of their other ^{1}H signals.

Method B

Diisopropylamine (1.05 equiv) was combined with THF, cooled to −20 °C, and *n*-BuLi in hexanes (1 equiv) was added over approximately 15 min, while maintaining the temperature below 0 °C. The LDA/THF mixture was then cooled to −75 °C, before a solution of 1-benzylpyrrolidin-2-one **(1)** (1 equiv) in THF was added over 30 min. During this addition the reaction temperature was maintained below −60 °C. The resulting mixture was stirred for 40 min at −75 °C, after which a solution the ester (1.17 equiv) in THF was added over approximately 20 min, again while maintaining the reaction temperature between below −60 °C. After the addition was complete, the mixture was stirred for 1 h at −75 °C, affording a homogenous mixture. The reaction was then allowed to warm slowly to 0 °C, over approximately 1.5 h, whereupon 10% aqueous citric acid was added to the resulting slurry. This mixture was stirred vigorously for 1 h to give two homogenous phases, to which MTBE was added. The organic phase was separated, washed with water and brine, dried, and

concentrated to afford the crude *β*-keto-γ-lactam product. In agreement with an earlier report,[2] the NMR spectra of the purified products **3b–d** and **7a, 7b** and **7d** showed evidence for the presence of a minor enol tautomer (<10% in all cases): some characteristic signals were seen for the enol form, and are listed in all cases, in addition the integration of the C-3H signal of the *β*-keto-*γ*-lactams were decreased relative to those of their other ^{1}H signals.

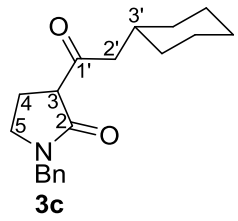
1-Benzyl-3-(2-cyclopropylacetyl)pyrrolidin-2-one (3b)



3b

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (6.16 mL, 46.0 mmol) with THF (44 mL), and adding 2.51M *n*-BuLi in hexanes (17.5 mL, 43.9 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (7.68 mL, 43.8 mmol) in (10 ml) THF and methyl 2-cyclopropylacetate (5.0 g, 43.8 mmol) in THF (9 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (40 mL) was added to the resulting slurry at 0 °C. MTBE (60 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 25 mL) and brine (30 mL), dried, and concentrated to afford the crude product (5.71 g, 93%) as a viscous yellow oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **3b** (2.50 g, 41%) as a yellow oil: ν_{max} (UATR)/cm^{-1} 3008, 2889, 1674, 1429, 1384, 1261, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10–0.25 (2H, sym m, one of each cyclopropyl CH_2), 0.48–0.64 (2H, sym m, one of each cyclopropyl CH_2), 0.97–1.13 (1H, sym m, C-3′H), 1.94–2.09 (1H, sym m, one of C-4H_2), 2.47–2.60 (1H, sym m, one of C-4H_2), 2.64 (1H, dd, J = 17.5, 6.8, one of C-2′H_2), 2.83 (1H, dd, J = 15.7, 7.0, C-2′H_2), 3.15–3.25 (1H, sym m, one of C-5H_2), 3.28–3.38 (1H, td, J = 9.2, 5.6, one of C-5H_2), 3.70 (1H, dd, J = 9.2, 5.8, C-3H), 4.34–4.51 (2H, ABq, δ_{Ha} = 4.38 and δ_{Hb} = 4.47, J = 14.7, NCH_2Ph), 7.16–7.23 (2H, m, 2 × *ortho*-ArH), 7.23–7.39 (3H, m, 3 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 4.2 (CH_2 of cyclopropyl), 4.5 (CH_2 of cyclopropyl), 5.8 (C-3′H), 19.6 (C-4H_2), 45.1 (C-5H_2), 46.9 (N*C*H_2Ph), 47.7 (C-2′H_2), 54.5 (C-3H), 127.6 (aromatic CH), 128.0 (aromatic CH), 128.7 (aromatic CH), 135.9 (aromatic C), 169.9 (C-2), 205.8 (C-1′). HRMS (ESI+): Exact mass calcd for $C_{16}H_{20}NO_2$ $(M+H)^+$ 258.1494. Found: 258.1498. A small amount of the enol tautomer is indicated in the ^{1}H NMR spectra of **3b** by the reduced integration of the C-3H signal relative to those of the other *β*-keto-*γ*-lactam signals, although no characteristic signals were identified for the enol form.

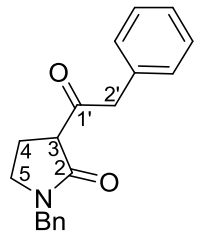
1-Benzyl-3-(2-cyclohexylacetyl)pyrrolidin-2-one (3c)



3c

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (3.94 mL, 28.1 mmol) with THF (15 mL), and adding 2.10M *n*-BuLi in hexanes (12.2 mL, 25.6 mmol). Solutions of 1-benzylpyrrolidin-2-one (**1)** (3.74 mL, 25.6 mmol) in THF (32 ml) and ethyl cyclohexylacetate (5.38 mL, 30.0 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (30 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (20 mL), dried, and concentrated to afford the crude product (7.51 g, 98%) as a viscous orange oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **3c** (4.83 g, 63%) as an orange oil: ν_{max} (UATR)/cm^{-1} 2921, 2851, 1714, 1678, 1448, 1428, 1260, 729, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86–1.06 (2H, m, cyclohexyl), 1.06–1.38 (3H, m, cyclohexyl), 1.56–1.81 (5H, m, cyclohexyl), 1.81–2.08 (2H, m, one of cyclohexyl and one of C-4H_2), 2.42–2.53 (1H, m, one of C-4H_2), 2.56 (1H, dd, J = 17.0, 6.2, one of C-2′H_2), 2.83 (1H, dd, J = 17.0, 7.3, one of C-2′H_2), 3.19 (1H, td, J = 9.1, 5.5, one of C-5H_2), 3.32 (1H, td, J = 9.1, 5.5, one of C-5H_2), 3.60 (1H, dd, J = 9.2, 5.7, C-3H), 4.36–4.49 (2H, ABq, δ_{Ha} = 4.39 and δ_{Hb} = 4.46, J = 14.7, NCH_2Ph), 7.16–7.23 (2H, m, 2 × *ortho*-ArH), 7.23–7.37 (3H, m, 3 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.8 (C-4H_2), 26.0 (cyclohexyl CH_2), 26.1 (cyclohexyl CH_2), 26.2 (cyclohexyl CH_2), 32.9 (cyclohexyl CH_2), 33.2 (cyclohexyl CH_2), 33.4 (C-3′H), 45.1 (C-5H_2), 46.9 (NCH_2Ph), 50.2 (C-2′H_2), 55.3 (C-3H) 127.7 (aromatic CH), 128.0 (aromatic CH), 128.7 (aromatic CH), 136.0 (aromatic C), 170.0 (C-2), 205.6 (C-1′). HRMS (ESI+): Exact mass calcd for $C_{19}H_{26}NO_2$ $(M+H)^+$ 300.1964. Found: 300.1952. A small amount of the enol tautomer appears in the NMR spectra of **7c** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.78 (1H, br s, OH).

1-Benzyl-3-(2-phenylacetyl)pyrrolidin-2-one (3d)

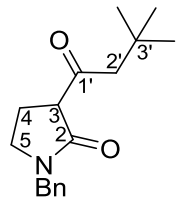


3d

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (3.36 mL, 24.0 mmol) with THF (15 mL), and adding 2.51M *n*-BuLi in hexanes (9.1 mL, 22.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (3.65 mL, 22.83 mmol) in THF (32 mL) and methyl phenylacetate (4.0 g, 26.7 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10%

Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried, and concentrated to afford the crude product (5.56 g, 83%) as a viscous orange oil. Purification by wet flash chromatography (20% EtOAc/hexanes), afforded **3d** (4.62 g, 69%) as an orange oil: ν_{max} (UATR)/cm^{-1} 3030, 2892, 2887, 1717, 1675, 1495, 1453, 1429, 1384, 1260, 697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85–2.01 (1H, sym m, one of C-4H$_2$), 2.42–2.56 (1H, sym m, one of C-4H$_2$), 3.11–3.22 (1H, sym m, one of C-5H$_2$), 3.29 (1H, td, J = 9.2, 5.3, one of C-5H$_2$), 3.75 (1H, dd, J = 9.3, 6.1, C-3H), 4.07–4.23 (2H, ABq, δ_{Ha} = 4.11 and, δ_{Hb} = 4.19, J = 15.7, C-2′H$_2$), 4.34–4.52 (2H, ABq, δ_{Ha} = 4.39 and δ_{Hb} = 4.48, J = 14.7, NC*H*$_2$Ph), 7.14–7.39 (10H, m, 10 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.6 (C-4H$_2$), 44.9 (C-5H$_2$), 47.0 (N*C*H$_2$Ph), 49.4 (C-2′H$_2$), 53.8 (C-3H), 127.0 (aromatic CH), 127.7 (aromatic CH), 128.0 (aromatic CH), 128.6 (aromatic CH), 128.7 (aromatic CH), 129.8 (aromatic CH), 133.8 (aromatic C), 135.8 (aromatic C), 169.7 (C-2), 203.3 (C-1′). HRMS (ESI+): Exact mass calcd for $C_{19}H_{20}NO_2$ $(M+H)^+$ 294.1494. Found: 294.1497. A small amount of the enol tautomer appears in the NMR spectra of **7c** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.58–2.65 (2H, t, J =7.4, C-4H$_2$), 11.82 (1H, br s, OH).

1-Benzyl-3-(3,3-dimethylbutanoyl)pyrrolidin-2-one (3e)

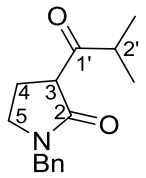


3e

This compound was prepared following the general procedure *(Method A)*, starting by combining diisopropylamine (7.04 mL, 50.2 mmol) with 2-MeTHF (22 mL), and adding 2.02M *n*-BuLi in hexanes (24.5 mL, 49.5 mmol). 1-Benzylpyrrolidin-2-one **(1)** (3.65 mL, 22.83 mmol, ethyl 3,3-dimethylbutyrate (3.83 mL, 22.83 mmol), and 2-MeTHF (18 mL) were combined and added to the LDA/2-MeTHF mixture. Heptane (40 mL) was used to precipitate the enolate and 1:1 heptane/2-Me-THF (8 mL) was used to rinse the resulting filtered off-white solids. The solids were suspended in MTBE (40 mL) and 10% aqueous citric acid (40 mL) was added. MTBE (16 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL), dried, and concentrated to afford the crude product (4.82 g, 77%) as a viscous purple oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **3e** (4.13 g, 66%) as a purple oil: ν_{max} (UATR)/cm^{-1} 2953, 1716, 1679, 1428, 1362, 1259, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (9H, s, 3 × CH_3), 1.90–2.05 (1H, m, one of C-4H$_2$), 2.41–2.54 (1H, sym m, one of C-4H$_2$), 2.64 (1H, d, J = 16.4, one of C-2′H$_2$), 2.86 (1H, d, J = 16.4, one of C-2′H$_2$), 3.18 (1H, td, J = 9.2, 5.5, one of

C-5H_2), 3.31 (1H, td, *J* = 9.1, 5.5, one of C-5H_2), 3.60 (1H, dd, *J* = 9.2, 5.6, C-3H), 4.35–4.49 (2H, ABq, δ_{Ha} = 4.39 and δ_{Hb} = 4.46, *J* = 14.7, NCH_2Ph), 7.15–7.22 (2H, m, 2 × *ortho*-ArH), 7.22–7.40 (3H, m, 3 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) *δ* 19.5 (C-4H_2), 29.4 (CH_3), 30.7 (C-3′), 44.9 (C-5), 46.8 (N*C*H_2Ph), 54.6 (C-2′), 56.1 (C-3H), 127.5 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 135.9 (aromatic C), 169.9 (C-2), 205.2 (C-1′); HRMS (ESI+): Exact mass calcd for $C_{17}H_{24}NO_2$ $(M+H)^+$ 274.1807. Found: 274.1802. A small amount of the enol tautomer appears in the NMR spectra of **3e** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 11.85 (1H, br s, OH).

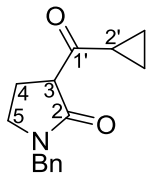
1-Benzyl-3-isobutyrylpyrrolidin-2-one (7a)



7a

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (3.36 mL, 24.0 mmol) with THF (15 mL), and adding 2.10M *n*-BuLi in hexanes (10.9 mL, 22.89 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (3.65 mL, 22.83 mmol) in THF (32 mL) and methyl ethyl isobutyrate (3.58 mL, 26.7 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (4.42 g, 79%) as a viscous orange oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **7a** (3.52 g, 63%) as an orange oil: ν_{max} (UATR)/cm^{-1} 2970, 1714, 1678, 1428, 1260, 700; ^{1}H NMR (300 MHz, DMSO-d_6) *δ* 1.02 (3H, d, *J* = 6.8, CH_3), 1.08 (3H, d, *J* = 7.1, CH_3), 1.97–2.13 (1H, m, one of C-4H_2), 2.14–2.29 (1H, m, one of C-4H_2), 3.06 (1H, sept, *J* = 6.9, C-2′H), 3.15–3.31 (2H, m, C-5H_2), 4.00 (1H, dd, *J* = 9.2, 6.7, C-3H), 4.31–4.45 (2H, ABq, δ_{Ha} = 4.35 and δ_{Hb} = 4.42, *J* = 15.0, NCH_2Ph), 7.17–7.24 (2H, m, 2 × *ortho*-ArH), 7.24–7.40 (3H, m, 3 × ArH); ^{13}C NMR (75.5 MHz, DMSO-d_6) *δ* 17.1 (CH_3), 18.0 (CH_3), 20.5 (C-4H_2), 39.8 (C-2′H), 44.6 (C-5H_2), 45.7 (N*C*H_2Ph), 52.1 (C-3H), 127.2 (aromatic CH), 127.5 (aromatic CH), 128.5 (aromatic CH), 136.5 (aromatic C), 170.1 (C-2), 210.5 (C-1′); HRMS (ESI+): Exact mass calcd for $C_{15}H_{20}NO_2$ $(M+H)^+$ 246.1494. Found: 246.1490. A small amount of the enol tautomer appears in the NMR spectra of **7c** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, DMSO-d_6) *δ* 2.56–2.63 (2H, t, *J* =7.4, C-4H_2), 11.97 (1H, br s, OH).

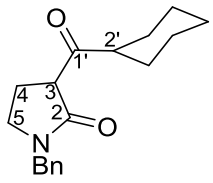
1-Benzyl-3-(cyclopropanecarbonyl)pyrrolidin-2-one (7b)



7b

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (3.36 mL, 24.0 mmol) with THF (15 mL), and adding 1.77M *n*-BuLi in hexanes (12.9 mL, 22.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (3.65 mL, 22.83 mmol) in THF (32 mL) and methyl cyclopropylcarboxylate (2.67 g, 26.7 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (4.33 g, 78%) as a viscous yellow oil. Purification by wet flash chromatography (20% EtOAc/hexanes), afforded **7b** (3.66 g, 66%) as an orange oil: ν_{max} (UATR)/cm^{-1} 3007, 2921, 1674, 1429, 1384, 1261, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95–1.22 (4H, m, 2 × CH_2 of cyclopropyl), 1.97–2.11 (1H, sym m, C-2′H), 2.45–2.60 (2H, m, C-4H_2), 3.15–3.25 (1H, sym m, one of C-5H_2), 3.25–3.36 (1H, sym m, one of C-5H_2), 3.80 (1H, dd, J = 9.3, 5.5, C-3H), 4.36–4.54 (2H, ABq, δ_{Ha} = 4.41 and δ_{Hb} = 4.50, J = 14.7, NCH_2Ph), 7.18–7.37 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 11.7 (CH_2 of cyclopropyl), 12.2 (CH_2 of cyclopropyl), 19.8 (C-4H_2), 20.4 (C-2′H), 45.0 (C-5H_2), 46.9 (NCH_2Ph), 55.6 (C-3H), 127.6 (aromatic CH), 128.0 (aromatic CH), 128.7 (aromatic CH), 136.0 (aromatic C), 170.2 (C-2), 205.9 (C-1′). HRMS (ESI+): Exact mass calcd for $C_{15}H_{18}NO_2$ $(M+H)^+$ 244.1338. Found: 244.1331. A small amount of the enol tautomer appears in the NMR spectra of **7c** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.19–0.29 (2H, m, one of CH_2 of cyclopropyl), 0.58–0.66 (2H, m, one of CH_2 of cyclopropyl), 2.81–2.90 (2H, t, J =9.0, C-4H_2).

1-Benzyl-3-(cyclohexanecarbonyl)pyrrolidin-2-one (7c)

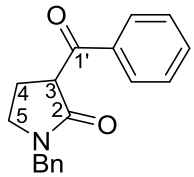


7c

This compound was prepared following the general procedure *(Method A)*, starting by combining diisopropylamine (17.25 mL, 123 mmol) with 2-MeTHF (55 mL), and adding 2.51M *n*-BuLi in hexanes (49 mL, 123 mmol). 1-Benzylpyrrolidin-2-one **(1)** (9.13 mL, 57.1 mmol), methyl cyclohexylcarboxylate (9.74 g, 68.5 mmol), and 2-MeTHF (45 mL) were combined and added to the LDA/2-MeTHF mixture. Heptane (60 mL) was used to precipitate

the enolate and 1:1 heptane/2-Me-THF (30 mL) was used to rinse the resulting filtered off-white solids. The solids were suspended in MTBE (100 mL) and 10% aqueous citric acid (100 mL) was added. MTBE (40 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 50 mL), dried, and concentrated to afford the crude product (6.50 g, 40%) as a viscous purple oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **7c** (5.50 g, 34%) as a purple oil: ν_{max} (UATR)/cm^{-1} 2921, 2850, 1714, 1679, 1447, 1428, 1260, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11–1.53 (5H, m, cyclohexyl), 1.63–1.92 (4H, m, cyclohexyl), 1.93–2.08 (2H, m, one of cyclohexyl and one of C-4H_2), 2.37–2.51 (1H, sym m, one of C-4H_2), 2.98 (1H, tt, J = 11.2, 3.3, C-2′H), 3.19 (1H, ddd, J = 9.6, 8.8, 5.4, one of C-5H_2), 3.34 (1H, td, J = 9.1, 5.4, one of C-5H_2), 3.81 (1H, dd, J = 9.2, 5.6, C-3H), 4.34–4.51 (2H, ABq, δ_{Ha} = 4.38 and δ_{Hb} = 4.47, J = 14.8, NCH_2Ph), 7.16–7.23 (2H, m, 2 × *ortho*-ArH), 7.24–7.37 (3H, m, 3 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.3 (C-4H_2), 25.1 (cyclohexyl CH_2), 25.9 (cyclohexyl CH_2), 26.0 (cyclohexyl CH_2), 27.3 (cyclohexyl CH_2), 29.1 (cyclohexyl CH_2), 45.1 (C-5H_2), 46.9 (N*C*H_2Ph), 50.0 (C-2′H), 52.8 (C-3H) 127.6 (aromatic CH), 128.0 (aromatic CH), 128.7 (aromatic CH), 136.0 (aromatic C), 170.2 (C-2), 209.4 (C-1′); HRMS (ESI+): Exact mass calcd for $C_{18}H_{24}NO_2$ $(M+H)^+$ 286.1807. Found: 286.1801. A small amount of the enol tautomer appears in the NMR spectra of **7c** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.58–2.65 (2H, t, J =7.5, C-4H_2), 11.82 (1H, br s, OH).

3-Benzoyl-1-benzylpyrrolidin-2-one (7d)

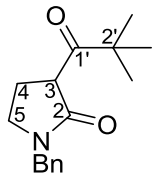


7d

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (6.72 mL, 48.2 mmol) with THF (30 mL), and adding 2.51M *n*-BuLi in hexanes (18.2 mL, 45.7 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (7.30 mL, 45.7 mmol) in THF (40 mL) and methyl benzoate (6.68 mL, 53.4 mmol) in THF (8 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (40 mL) was added to the resulting slurry at 0 °C. MTBE (40 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 30 mL) and brine (50 mL), dried, and concentrated to afford the crude product (10.58 g, 83%) as a viscous orange oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **7d** (6.12 g 48%) as an orange oil: ν_{max} (UATR)/cm^{-1} 2921, 2891, 1691, 1668, 1448, 1428, 1261, 1223, 699, 687; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.15–2.31 (1H, sym m, one of C-4H_2), 2.52–2.66 (1H, sym m, one of C-4H_2),

3.29 (1H, td, J = 9.1, 4.4, one of C-5H_2), 3.43–3.58 (1H, sym m, one of C-5H_2), 4.39–4.54 (2H, ABq, δ_{Ha} = 4.43 and δ_{Hb} = 4.51, J = 14.6, NCH_2Ph), 4.54 (1H, dd, J = 9.1, 4.8, C-3H), 7.21–7.37 (5H, m, ArCH), 7.46–7.54 (2H, sym m, 2 × ArH), 7.55–7.63 (1H, sym m, ArH), 8.14 (2H, d, J = 7.0, 2 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9 (C-4H_2), 45.4 (C-5H_2), 47.0 (NCH$_2$Ph), 50.6 (C-3H), 127.6 (aromatic CH), 128.0 (aromatic CH), 128.5 (aromatic CH), 128.7 (aromatic CH), 129.5 (aromatic CH), 133.5 (aromatic CH), 136.0 (aromatic C), 136.2 (aromatic C), 170.2 (C-2), 196.3 (C-1′). HRMS (ESI+): Exact mass calcd for $C_{18}H_{18}NO_2$ $(M+H)^+$ 280.1338. Found: 280.1332. A small amount of the enol tautomer appears in the NMR spectra of **7c** and the following characteristic signals were identified: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.91–2.99 (2H, t, J = 7.0, C-4H_2), 7.66–7.72 (3H, m, 3 × ArH), 7.84–7.92 (3H, m, 3 × ArH),8.02 (2H, t, J = 7.5, 2 × ArH), 12.72 (1H, br s, OH).

1-Benzyl-3-pivaloylpyrrolidin-2-one (7e)



7e

This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (3.36 mL) with THF (15 mL), and adding 2.51M *n*-BuLi in hexanes (9.1 mL, 22.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (3.65 mL, 22.83 mmol) in THF (32 mL) and methyl pivalate (3.55 g, 26.7 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried, and concentrated to afford the crude product (4.61 g, 78%) as a viscous orange oil. Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **7e** (3.61 g, 61%) as an orange oil: ν_{max} (ATR)/cm^{-1} 3400, 3005, 2877, 1657, 1432, 1280, 1258, 1028, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (9H, s, 3 × CH_3), 2.09–2.18 (2H, sym m, C-4H_2), 3.22 (1H, td, J = 9.4, 6.9, one of C-5H_2), 3.43 (1H, td, J = 9.4, 6.9, one of C-5H_2), 4.08 (1H, t, J = 7.5, C-3H), 4.39–4.52 (2H, ABq, δ_{Ha} = 4.42 and δ_{Hb} = 4.49, J = 14.9, NCH_2Ph), 7.21–7.37 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 23.8 (C-4H), 25.7 (CH_3), 44.9 (C-2′), 45.5 (C-5H), 46.7 (NCH$_2$Ph), 48.8 (C-3H), 127.5 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 136.1 (aromatic C), 171.4 (C-2), 213.3 (C-1′). HRMS (ESI+): Exact mass calcd for $C_{16}H_{22}NO_2$ $(M+H)^+$ 260.1651. Found: 260.1651.

Racemic Synthesis of *β*-Hydroxy-*γ*-lactams

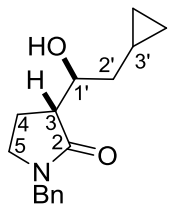
Method A

To a stirred suspension of $NaBH_4$ (1 equiv.) in EtOH, cooled to approximately 0 °C on an ice bath, was added a solution of *β*-keto-γ-lactam in EtOH over approximately 15 min. The reaction mixture was stirred for 2 h, before the ice bath (not replenished in the intervening period) was removed and the reaction was stirred for a further 2 hours at room temperature. The reaction mixture was re-cooled on an ice bath, prior to its quenching by the dropwise addition 5M aqueous HCl (accompanied by brisk effervescence) until the mixture reached pH 2. The solvent was then evaporated under reduced pressure, to leave a residue which was taken up into a mixture of CH_2Cl_2 and water. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2. The organic layers were combined, washed with brine, dried, and concentrated to afford the crude *β*-hydroxy-γ-lactam product.

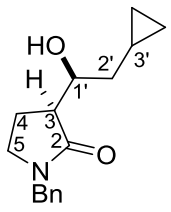
Method B

Diisopropylamine (1.05 equiv) was combined with THF, cooled to −20 °C, and *n*-BuLi in hexanes (1 equiv) was added over approximately 15 min, while maintaining the temperature below 0 °C. The LDA/THF mixture was then cooled to −75 °C, before a solution of 1-benzylpyrrolidin-2-one **(1)** (1 equiv) in THF was added over 30 min. During this addition the reaction temperature was maintained below −60 °C. The resulting mixture was stirred for 40 min at −75 °C, after which a solution the aldehyde (1.2 equiv) in THF was added over approximately 20 min, again while maintaining the reaction temperature between below −60 °C. After the addition was complete, the mixture was stirred for 1 h at −75 °C, affording a homogenous mixture. The reaction was then allowed to warm slowly to 0 °C, over approximately 1.5 h, whereupon 10% aqueous citric acid was added to the resulting slurry. This mixture was stirred for 30 min to give two homogenous phases, to which MTBE was added. The organic phase was separated, washed with water and brine, dried and concentrated under reduced pressure to afford the crude *β*-hydroxy-γ-lactam product.

1-Benzyl-3-(2-cyclopropyl-1-hydroxyethyl)pyrrolidin-2-one ((±)-4/9b)



(±)-4b



(±)-9b

This compound was prepared following the general procedure *(Method A)*, starting by combining $NaBH_4$ (74 mg) with EtOH (30 mL) and adding a solution of **3b** (500 mg, 1.94 mmol) in EtOH (10 mL). After evaporation of the solvent, the resulting residue was taken up into CH_2Cl_2 (20 mL) and water (10 mL). The organic phase was separated and the aqueous phase was

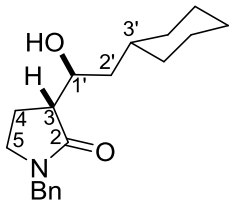
extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried and concentrated to afford the crude product (327 mg, 65%) as an orange oil (55:45 d.r.). A portion of the crude material (211 mg) was purified by wet flash chromatography (20–50% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, major diastereomer (±)-**9b** (81 mg) was recovered as a pale yellow oil: ν_{max} (UATR)/cm^{-1} 3411, 2907, 1658, 1427, 700; ^{1}H NMR (300 MHz, $CDCl_3$)* δ –0.04 to 0.14 (2H, m, cyclopropyl), 0.40–0.58 (2H, m, cyclopropyl), 0.86–1.07 (1H, sym m, C-3′H), 1.18–1.32 (1H, m, one of C-2′H_2), 1.44–1.70 (2H, m, one of C-2′H_2 and one of C-4H_2), 1.99–2.12 (1H, m, one of C-4H_2), 2.49–2.62 [1H, sym m (apparent q), C-3H], 3.14–3.26 (2H, m, C-5H_2), 3.84 (1H, ddd, J = 9.2, 7.8, 3.2, C-1′H), 4.39–4.51 (2H, ABq, δ_{Ha} = 4.41 and δ_{Hb} = 4.47, J = 14.8, NCH_2Ph), 5.15 (1H, br s, OH), 7.16–7.37 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 3.9 (cyclopropyl CH_2), 4.9 (cyclopropyl CH_2), 6.8 (C-3′H), 22.0 (C-4H_2), 39.8 (C-2′H_2), 44.8 (C-5H_2), 45.6 (C-3H), 46.5 (NCH$_2$Ph), 73.7 (C-1′H), 127.7 (aromatic CH), 128.0 (aromatic CH), 128.7 (aromatic CH), 135.9 (aromatic C), 176.8 (C-2). HRMS (ESI+): Exact mass calcd for $C_{16}H_{22}NO_2$ $(M+H)^+$ 260.1651. Found: 260.1640.

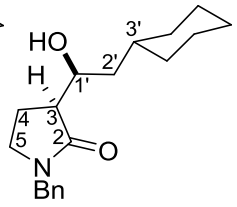
The slower eluting, minor diastereomer (±)-**4b** (78 mg) was recovered as a white solid (m.p. 71–74 °C): ν_{max} (UATR)/cm^{-1} 3372, 2925, 2904, 1663, 1454, 1438, 735, 699; ^{1}H NMR (300 MHz, $CDCl_3$)* δ –0.04 to 0.18 (2H, m, cyclopropyl), 0.38–0.55 (2H, sym m, cyclopropyl), 0.68–0.85 (1H, sym m, C-3′H), 1.18–1.30 (1H, sym m, one of C-2′H_2), 1.49–1.62 (1H, m, one of C-2′H_2), 1.86–2.15 (2H, m, C-4H_2), 2.56–2.80 [2H, overlapping signals, δ_{Ha} = 2.56–2.80 (1H, br s, OH) and δ_{Hb} = 2.70 (1H, td, J = 9.2, 2.9, C-3H)], 3.12–3.27 (2H, m, C-5H_2), 4.26–4.37 (1H, m, C-1′H), 4.47 (1H, s, NCH_2Ph), 7.17–7.37 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 4.1 (cyclopropyl CH_2), 4.4 (cyclopropyl CH_2), 7.6 (C-3′H), 18.1 (C-4H_2), 39.2 (C-2′H_2), 45.1 (C-5H_2), 46.6 (NCH$_2$Ph), 47.2 (C-3H), 70.3 (C-1′H), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 136.3 (aromatic C), 175.4 (C-2). HRMS (ESI+): Exact mass calcd for $C_{16}H_{22}NO_2$ $(M+H)^+$ 260.1651. Found: 260.1647.

*Due to overlap of the cyclopropyl hydrogen resonances with the TMS signal, the sample was subsequently spiked with $CHCl_3$ and the ^{1}H NMR spectrum recorded again to allow the chemical shifts of each resonance to be determined relative to the $CHCl_3$ signal at 7.26 ppm.

1-Benzyl-3-(2-cyclohexyl-1-hydroxyethyl)pyrrolidin-2-one ((±)-4/9c)



(±)-4c



(±)-9c

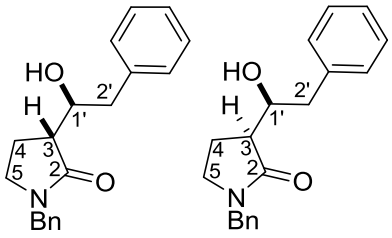
This compound was prepared following the general procedure *(Method A)*, starting by combining $NaBH_4$ (63 mg, 1.67 mmol) with EtOH (30 mL) and adding a solution of **3c** (500 mg, 1.67 mmol) in EtOH (10 mL). After evaporation of the solvent, the resulting residue was taken up into CH_2Cl_2 (20 mL) and water (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried and concentrated to afford the crude product (352 mg, 70%) as a white solid (53:47 d.r.). A portion of the crude material (262 mg) was purified by wet flash chromatography (1–2% MeOH/CH_2Cl_2), affording an isolated sample of each diastereomer.

The faster eluting, major diastereomer (±)-**9c** (44 mg) was recovered as a pale yellow solid (m.p. 54–56 °C): ν_{max} (UATR)/cm^{-1} 3385, 2921, 2848, 1653, 1435, 719, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74–0.87 (1H, m, cyclohexyl), 0.87–1.03 (1H, m, cyclohexyl), 1.07–1.35 (4H, m, 3 × cyclohexyl and one of C-2′H_2), 1.35–1.46 (1H, sym m, one of C-2′H_2), 1.51–1.75 (6H, m, 5 × cyclohexyl and one of C-4H_2), 1.89 (1H, br d, J = 11.6, cyclohexyl), 2.01–2.15 (1H, sym m, one of C-4H_2), 2.36–2.47 [1H, sym m (apparent q), C-3H], 3.11–3.28 (2H, m, C-5H_2), 3.57 (1H, br td, J = 9.6, 1.7, C-1′H), 4.40–4.50 (2H, ABq, δ_{Ha} = 4.43 and δ_{Hb} = 4.47, J = 14.7, NCH_2Ph), 5.14 (1H, s, OH), 7.19–7.39 (5H, m, 5 × ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 22.0 (C-4H_2), 26.0 (cyclohexyl CH_2), 26.3 (cyclohexyl CH_2), 26.6 (cyclohexyl CH_2), 31.3 (cyclohexyl CH_2), 33.1 (C-3′H), 34.7 (cyclohexyl CH_2), 42.9 (C-2′H_2), 44.8 (C-5H_2), 46.5 (N*C*H_2Ph), 46.6 (C-3H), 70.8 (C-1′H), 127.7 (aromatic CH), 128.1 (aromatic CH), 128.7 (aromatic CH), 136.0 (aromatic C), 176.9 (C-2); HRMS (ESI+): Exact mass calcd for $C_{19}H_{28}NO_2$ $(M+H)^+$ 302.2120. Found: 302.2110.

The slower eluting, minor diastereomer (±)-**4c** (19 mg) was recovered as a white solid (m.p. 114–116 °C): Found: C, 75.62; H, 8.98; N, 4.57; $C_{19}H_{27}NO_2$ requires C, 75.71; H, 9.03; N, 4.65%; ν_{max} (ATR)/cm^{-1} 3377, 2914, 1659, 1437, 1089, 745, 703; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78–1.05 (2H, sym m, cyclohexyl), 1.06–1.34 (4H, m, 3 × cyclohexyl and one of C-2′H_2), 1.35–1.56 (2H, m, 1 × cyclohexyl and one of C-2′H_2), 1.59–1.77 (4H, m, cyclohexyl), 1.77–1.88 (1H, m, cyclohexyl), 1.88–2.12 (2H, m, C-4H_2), 2.44 (1H, d, J = 5.5, OH), 2.62 (1H, td, J = 9.3, 2.9, C-3H), 3.12–3.30 (2H, m, C-5H_2), 4.26–4.36 (1H, sym m, C-1′H), 4.47 (2H, s, NCH_2Ph), 7.17–7.37 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ

18.1 (C-4H_2), 26.1 (cyclohexyl CH_2), 26.2 (cyclohexyl CH_2), 26.5 (cyclohexyl CH_2), 32.7 (cyclohexyl CH_2), 34.0 (C-3′H), 34.1 (cyclohexyl CH_2), 41.6 (C-2′H_2), 45.1 (C-5H_2), 46.5 (N*C*H_2Ph), 47.8 (C-3H), 67.0 (C-1′H), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.5 (aromatic CH), 136.2 (aromatic C), 175.4 (C-2); HRMS (ESI+): Exact mass calcd for $C_{19}H_{28}NO_2$ $(M+H)^+$ 302.2120. Found: 302.2115.

1-Benzyl-3-(1-hydroxy-2-phenylethyl)pyrrolidin-2-one ((±)-4/9d)



(±)-4d **(±)-9d**

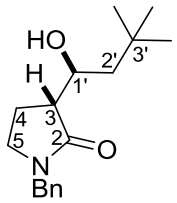
This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (2.62 mL, 18.7 mmol) with THF (15 mL) and adding 2.51M *n*-BuLi in hexanes (7.1 mL, 17.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (2.85 mL, 17.8 mmol) in THF (32 mL) and phenylacetaldehyde (2.48 mL, 21.4 mmol) in THF (10 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (4.05 g, 77%) as a viscous orange oil (57:43 d.r.). A portion of the crude material (254 mg) was purified by wet flash chromatography (10–40% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, minor diastereomer (±)-**9d** (44 mg) was isolated as an off-white solid (m.p. 71–75 °C): ν_{max} (UATR)/cm^{-1} 3376, 2914, 2890, 1648, 1425, 1261, 713, 697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60–1.77 (1H, sym m, one of C-4H_2), 2.03–2.15 (1H, sym m, one of C-4H_2), 2.42–2.54 [1H, sym m (apparent q), C-3H], 2.75 (1H, dd, J = 14.0, 7.3, one of C-2′H_2), 2.93 (1H, dd, J = 14.0, 3.8, one of C-2′H_2), 3.13–3.17 (2H, m, C-5H_2), 3.96–4.03 (1H, sym m, C-1′H), 4.44 (2H, s, NCH_2Ph), 5.09 (1H, s, OH), 7.16–7.36 (10H, m, 10 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.1 (C-4H_2), 41.1 (C-2′H_2), 44.9 (C-5H_2), 45.4 (C-3H), 46.6 (N*C*H_2Ph), 74.2 (C-1′H), 126.4 (aromatic CH), 127.7 (aromatic CH), 128.1 (aromatic CH), 128.2 (aromatic CH), 128.8 (aromatic CH), 129.7 (aromatic CH), 135.9 (aromatic C), 137.9

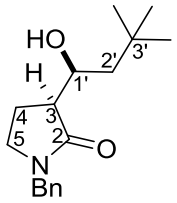
(aromatic C), 176.6 (C-2); HRMS (ESI+): Exact mass calcd for $C_{19}H_{22}NO_2$ $(M+H)^+$ 296.1651. Found: 296.1638.

The slower eluting, major diastereomer (±)-**4d** (25 mg) was isolated as a white solid (m.p. 75–77 °C): Found: C, 77.29; H, 7.15; N, 4.70; $C_{19}H_{21}NO_2$ requires C, 77.26; H, 7.17; N, 4.74%; ν_{max} (UATR)/cm^{-1} 3401, 3335, 2942, 2929, 1663, 1454, 1441, 697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.94–2.08 (1H, m, one of C-4H_2), 2.12–2.27 (1H, m, one of C-4H_2), 2.49 (1H, br d, J = 4.5, OH), 2.59 (1H, td, J = 9.2, 2.9, C-3H), 2.71–2.91 (2H, sym m, C-2′H_2), 3.12–3.29 (2H, sym m, C-5H_2), 4.42–4.53 [2H, overlapping signals, δ_{Ha} = 4.42–4.53 (1H, m, C-1′H) and δ_{Hb} = 4.45 (1H, s, NCH_2Ph)], 7.16–7.36 (10H, m, 10 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.0 (C-4H_2), 41.0 (C-2′H_2), 45.1 (C-5H_2), 46.7 (N*C*H_2Ph), 46.9 (C-3H), 70.9 (C-1′H), 126.5 (aromatic CH), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.5 (aromatic CH), 128.6 (aromatic CH), 129.2 (aromatic CH), 136.3 (aromatic C), 138.1 (aromatic C), 175.1 (C-2); HRMS (ESI+): Exact mass calcd for $C_{19}H_{22}NO_2$ $(M+H)^+$ 296.1651. Found: 296.1646.

1-Benzyl-3-(1-hydroxy-3,3-dimethylbutyl)pyrrolidin-2-one ((±)-4/9e)



(±)-4e



(±)-9e

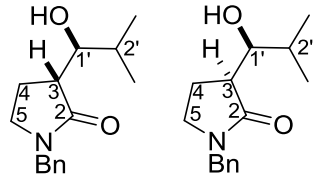
This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (2.62 mL, 18.7 mmol) with THF (15 mL) and adding 2.02M *n*-BuLi in hexanes (8.8 mL, 17.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (2.85 mL, 17.8 mmol) in THF (32 mL) and 3,3-dimethylbutanal (2.68 mL, 21.4 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (4.17 g, 85%) as a white solid (51:49 d.r.). A portion of the crude material (252 mg) was purified by wet flash chromatography (20% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, minor diastereomer (±)-**9e** (78 mg) was recovered as a clear oil: ν_{max} (UATR)/cm^{-1} 3408, 2949, 1660, 1429, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (9H, s, 3 × CH_3), 1.24 (1H, d, J = 14.3, one of C-2′H_2), 1.45 (1H, dd, J = 14.3, 9.3, one of C-2′H_2), 1.50–1.67 (1H, sym m, one of C-4H_2), 2.00–2.14 (1H, sym m, one of C-4H_2), 2.37–2.50 [1H, sym m (apparent q), C-3H], 3.13–3.25 (2H, m, C-5H_2), 3.84 (1H, br t, J = 9.3, C-1′H), 4.38–4.53

(2H, ABq, δ_{Ha} = 4.42 and δ_{Hb} = 4.48, J = 15.5, NCH_2Ph), 5.09 (1H, s, OH), 7.17–7.39 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.3 (C-4H_2), 30.1 (CH_3), 30.2 [$C(CH_3)_3$], 44.6 (C-5H_2), 46.5 (NCH$_2$Ph), 46.7 (C-3H), 48.6 (C-2′H_2), 71.3 (C-1′H), 127.7 (aromatic CH), 128.1 (aromatic CH), 128.7 (aromatic CH), 135.9 (aromatic C), 176.8 (C-2); HRMS (ESI+): Exact mass calcd for $C_{17}H_{26}NO_2$ $(M+H)^+$ 276.1964. Found: 276.1959.

The slower eluting, major diastereomer (±)-**4e** (60 mg) was recovered as a white solid, m.p. 154–156 °C): ν_{max} (ATR)/cm^{-1} 3375, 2953, 1664, 1451, 727, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (9H, s, 3 × CH_3), 1.24 (1H, dd, J = 14.4, 1.8, one of C-2′H_2), 1.45 (1H, dd, J = 14.4, 9.1, one of C-2′H_2), 1.90–2.13 (2H, m, C-4H_2), 2.46 (1H, br d, J = 5.2, OH), 2.60 (1H, td, J = 9.3, 2.9, C-3H), 3.14–3.27 [2H, sym m (apparent t), C-5H_2], 4.28–4.38 (1H, sym m, C-1′H), 4.37–4.57 (2H, ABq, δ_{Ha} = 4.41 and δ_{Hb} = 4.52, J = 14.8, NCH_2Ph), 7.17–7.36 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.5 (C-4H_2), 30.1 (CH_3), 30.2 [$C(CH_3)_3$], 45.1 (C-5H_2), 46.6 (NCH$_2$Ph), 47.3 (C-2′H_2), 49.3 (C-3H), 67.6 (C-1′H), 127.5 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 136.3 (aromatic C), 175.2 (C-2); HRMS (ESI+): Exact mass calcd for $C_{17}H_{26}NO_2$ $(M+H)^+$ 276.1964. Found: 276.1964.

1-Benzyl-3-(1-hydroxy-2-methylpropyl)pyrrolidin-2-one ((±)-8/10a)



(±)-8a **(±)-10a**

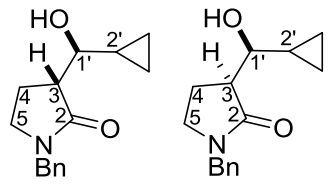
This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (2.62 mL, 18.7 mmol) with THF (15 mL) and adding 2.50M *n*-BuLi in hexanes (7.12 mL, 17.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (2.85 mL, 17.8 mmol) in THF (32 mL) and isobutanal (1.95 mL, 21.4 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (3.65 g, 83%) as a viscous orange oil (73:27 d.r.). The crude material was purified by wet flash chromatography (20–50% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, major diastereomer (±)-**10a** (1.93 g) was isolated as a pale yellow oil: ν_{max} (UATR)/cm^{-1} 3422, 2960, 1658, 1423, 1270, 1001, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (3H, d, J = 6.9, CH_3), 1.06 (3H, d, J = 6.9, CH_3), 1.54–1.78 (2H, m, C-2′H and one of C-4H_2), 1.95–2.13 (1H, m, one of C-4H_2), 2.48–2.61 [1H, sym m (apparent q), C-3H], 3.17–

3.25 (2H, m, C-5H_2), 3.60 (1H, dd, *J* = 9.7, 2.3, C-1′H), 4.45 (2H, s, NC*H*$_2$Ph), 5.14 (1H, s, OH), 7.18–7.38 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.2 (CH_3), 19.5 (CH_3), 21.5 (C-4H_2), 30.1 (C-2′H), 43.7 (C-3H), 44.7 (C-5H_2), 46.3 (N*C*H$_2$Ph), 76.9 (C-1′H), 127.5 (aromatic CH), 127.8 (aromatic CH), 128.5 (aromatic CH), 135.8 (aromatic C), 177.3 (C-2). HRMS (ESI+): Exact mass calculated for $C_{15}H_{22}NO_2$ $(M+H)^+$ 248.1651. Found: 248.1640.

The slower eluting, minor diastereomer (±)-**8a** (0.62 g) was recovered as a white solid (m.p. 104–106 °C): Found: C, 72.80; H, 8.46; N, 5.64; $C_{15}H_{21}NO_2$ requires C, 72.84; H, 8.56; N, 5.66%; ν_{max} (ATR)/cm^{-1} 3346, 2958, 2944, 2864, 1668, 1454, 1441, 697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (3H, d, *J* = 6.7, CH_3), 1.04 (3H, d, *J* = 6.7, CH_3), 1.68 (1H, dsept, *J* = 9.0, 6.7, C-2′H), 1.86–2.00 (1H, m, one of C-4H_2), 2.06–2.23 (1H, sym m, one of C-4H_2), 2.65 (1H, br d, *J* = 4.1, OH), 2.74 (1H, td, *J* = 9.4, 2.6, C-3H), 3.13–3.27 (2H, m, C-5H_2), 3.87 (1H, br d, *J* = 8.9, C-1′H), 4.48 (2H, s, NC*H*$_2$Ph), 7.18–7.36 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.7 (C-4H_2), 19.0 (CH_3), 19.4 (CH_3), 31.5 (C-2′H), 45.1 (C-5H_2), 45.7 (C-3H), 46.6 (N*C*H$_2$Ph), 74.9 (C-1′H), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 136.3 (aromatic C), 175.8 (C-2). HRMS (ESI+): Exact mass calcd for $C_{15}H_{22}NO_2$ $(M+H)^+$ 248.1651. Found: 248.1641.

1-Benzyl-3-(cyclopropyl(hydroxy)methyl)pyrrolidin-2-one ((±)-8/10b)



(±)-8b **(±)-10b**

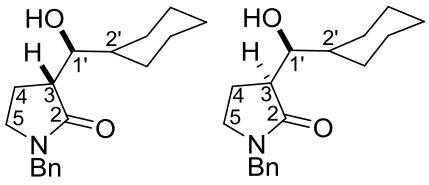
This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (2.62 mL, 18.7 mmol) with THF (15 mL) and adding 2.51M *n*-BuLi in hexanes (7.12 mL, 17.8 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (2.85 mL, 17.8 mmol) in THF (32 mL) and cyclopropylcarboxaldehyde (1.60 mL, 21.4 mmol) in THF (10 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (4.72 g, 98%) as a white solid (57:43 d.r.). A portion of the crude material (320 mg) was purified by wet flash chromatography (10–30% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, major diastereomer (±)-**10b** (85 mg) was recovered as a pale yellow oil: ν_{max} (UATR)/cm^{-1} 3008, 2921, 2890, 1674, 1384, 1261, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.28–0.58 (4H, m, 2 × cyclopropyl CH_2), 0.87–1.01 (1H, sym m, C-2′H), 1.72–1.89 (1H, sym m, one of C-4H_2), 2.14–2.28 (1H, sym m, one of C-4H_2), 2.59–2.71 [1H, sym m (apparent q),

C-3H], 3.11 (1H, t, J = 8.4, C-1′H), 3.16–3.29 (2H, m, C-5H_2), 4.46 (2H, s, NCH_2Ph), 4.95 (1H, s, OH), 7.19–7.38 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 1.1 (cyclopropyl CH_2), 2.1 (cyclopropyl CH_2), 15.3 (C-2′H), 21.8 (C-4H_2), 45.0 (C-5H_2), 46.4 (NCH_2Ph), 47.2 (C-3H), 76.8 (C-1′H), 127.5 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 135.9 (aromatic C), 176.4 (C-2); HRMS (ESI+): Exact mass calcd for $C_{15}H_{20}NO_2$ $(M+H)^+$ 246.1494. Found: 246.1487.

The slower eluting, minor diastereomer (±)-**8b** (38 mg) was recovered as a white solid (m.p. 131–134 °C): ν_{max} (UATR)/cm^{-1} 3331, 2957, 2912, 1659, 1454, 1442, 738, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.23–0.33 (1H, m, one of cyclopropyl), 0.37–0.62 (3H, m, cyclopropyl), 0.86–0.99 (1H, sym m, C-2′H), 2.02–2.15 (1H, m, one of C-4H_2), 2.15–2.30 (1H, one of C-4H_2), 2.53 (1H, br d, J = 5.0, OH), 2.81 (1H, td, J = 9.2, 2.9, C-3H), 3.17–3.31 (2H, m, C-5H_2), 3.40–3.48 (1H, sym m, C-1′H), 4.49 (2H, s, NCH_2Ph), 7.20–7.36 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 2.5 (cyclopropyl CH_2), 3.1 (cyclopropyl CH_2), 14.8 (C-2′H), 18.7 (C-4H_2), 45.3 (C-5H_2), 46.7 (NCH_2Ph), 47.6 (C-3H), 74.8 (C-1′H), 127.5 (aromatic CH), 128.0 (aromatic CH), 128.7 (aromatic CH), 136.3 (aromatic C), 175.3 (C-2); HRMS (ESI+): Exact mass calcd for $C_{15}H_{20}NO_2$ $(M+H)^+$ 246.1494. Found: 246.1491.

1-Benzyl-3-(cyclohexyl(hydroxy)methyl)pyrrolidin-2-one ((±)-8/10c)



(±)-8c **(±)-10c**

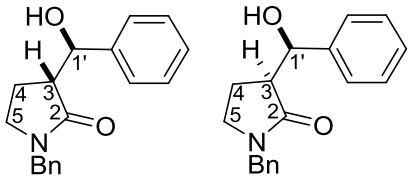
This compound was prepared following the general procedure *(Method A)*, starting by combining $NaBH_4$ (132 mg, 3.5 mmol) with EtOH (30 mL) and adding a solution of **7c** (1.0 g, 3.5 mmol) in EtOH (10 mL). After evaporation of the solvent, the resulting residue was taken up into CH_2Cl_2 (20 mL) and water (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried and concentrated to afford the crude product (825 mg, 82%) as an orange oil (58:42 d.r.). A portion of the crude material (498 mg) was purified by wet flash chromatography (10–20% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, major diastereomer (±)-**10c** (37 mg) was recovered as a white solid (m.p. 99–101 °C): ν_{max} (UATR)/cm^{-1} 3354, 2918, 2846, 1663, 1449, 730, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01–1.40 (5H, m, cyclohexyl), 1.41–1.88 (7H, m, 6 × cyclohexyl and one of C-4H_2), 1.99–2.12 (1H, sym m, one of C-4H_2), 2.54–2.67 [1H, sym m (apparent q), C-3H], 3.15–3.27 (2H, m, C-5H_2), 3.57 (1H, br d, J = 9.7, C-1′H), 4.45 (2H, s, NCH_2Ph), 5.07 (1H,

s, OH), 7.18–7.38 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9 (C-4H_2), 25.0 (cyclohexyl CH_2), 26.4 (2 × cyclohexyl CH_2), 26.7 (cyclohexyl CH_2), 30.1 (cyclohexyl CH_2), 40.6 (C-2′H), 43.3 (C-3H), 44.9 (C-5H_2), 46.6 (N*C*H_2Ph), 77.1 (C-1′H), 127.7 (aromatic CH), 128.1 (aromatic CH), 128.7 (aromatic CH), 136.0 (aromatic C), 177.7 (C-2); HRMS (ESI+): Exact mass calcd for $C_{18}H_{26}NO_2$ $(M+H)^+$ 288.1964. Found: 288.1960.

The slower eluting, minor diastereomer (±)-**8c** (30 mg) was recovered as a white solid (m.p. 145–148 °C): Found: C, 75.23; H, 8.62; N, 4.84; $C_{18}H_{25}NO_2$ requires C, 75.22; H, 8.77; N, 4.87%; ν_{max} (UATR)/cm^{-1} 3331, 2924, 2846, 1673, 1450, 1437, 732, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86–1.45 (6H, m, cyclohexyl), 1.52–1.83 (4H, m, cyclohexyl), 1.85–2.00 (1H, m, one of C-4H_2), 2.00–2.21 (2H, m, one of C-4H_2 and one of cyclohexyl), 2.54 (1H, br s, OH), 2.73 (1H, td, J = 7.3, 2.5, C-3H), 3.12–3.27 (2H, m, C-5H_2), 3.93 (1H, br d, J = 8.9, C-1′H), 4.41–4.54 (2H, ABq, δ_{Ha} = 4.45 and δ_{Hb} = 4.50, J = 15.3, NC*H*$_2$Ph), 7.17–7.36 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.7 (C-4H_2), 25.8 (cyclohexyl CH_2), 26.1 (cyclohexyl CH_2), 26.3 (cyclohexyl CH_2), 29.1 (cyclohexyl CH_2), 29.6 (cyclohexyl CH_2), 40.9 (C-2′H), 45.1 (C-5H_2), 45.4 (C-3H), 46.7 (N*C*H_2Ph), 73.8 (C-1′H), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 136.4 (aromatic C), 175.9 (C-2); HRMS (ESI+): Exact mass calcd for $C_{18}H_{26}NO_2$ $(M+H)^+$ 288.1964. Found: 288.1956.

1-Benzyl-3-(hydroxy(phenyl)methyl)pyrrolidin-2-one ((±)-8/10d)



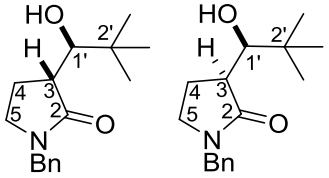
(±)-8d **(±)-10d**

This compound was prepared following the general procedure *(Method A)*, starting by combining $NaBH_4$ (135 mg, 3.58 mmol) with EtOH (30 mL) and adding a solution of **7d** (1.0 g, 3.58 mmol) in EtOH (10 mL). After evaporation of the solvent, the resulting residue was taken up into CH_2Cl_2 (20 mL) and water (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried and concentrated to afford the crude product (910 mg, 91%) as an orange oil (51:49 d.r.). A portion of the crude material (280 mg) was purified by wet flash chromatography (5–20% EtOAc/hexanes), affording an isolated sample of each diastereomer. The faster eluting, minor diastereomer (±)-**10d** (52 mg) was recovered as a viscous clear oil: ν_{max} (UATR)/cm^{-1} 3322, 3029, 2923, 1658, 1495, 1442, 1264, 698; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54–1.77 (2H, m, C-4H_2), 2.72–2.85 [1H, sym m (apparent q), C-3H], 3.09–3.20 (2H, m, C-5H_2), 4.48 (2H, s, NC*H*$_2$Ph), 4.72 (1H, d, J = 9.7, C-1′H), 5.60 (1H, s, OH), 7.21–7.42 (10H, m, 10 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9 (C-4H_2), 44.8 (C-5H_2), 46.7

(N*C*H$_2$Ph), 47.8 (C-3H), 76.4 (C-1′H), 126.8 (aromatic CH), 127.8 (aromatic CH), 128.0 (aromatic CH), 128.1 (aromatic CH), 128.4 (aromatic CH), 128.8 (aromatic CH), 135.9 (aromatic C), 141.2 (aromatic C), 176.4 (C-2); HRMS (ESI+): Exact mass calcd for $C_{18}H_{20}NO_2$ $(M+H)^+$ 282.1494. Found: 282.1482.

The slower eluting, major diastereomer (±)-**8d** (24 mg) was recovered as a white solid (m.p. 117–119 °C): Found: C, 76.46; H, 6.71; N, 4.85; $C_{18}H_{19}NO_2$ requires C, 76.84; H, 6.81; N, 4.98%; ν_{max} (UATR)/cm^{-1} 3333, 2857, 1658, 1495, 1437, 1264, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64–1.80 (1H, m, one of C-4H$_2$), 1.96–2.12 (1H, sym m, one of C-4H$_2$), 2.93 (1H, td, J = 9.1, 3.1, C-3H), 3.02–3.15 (2H, m, C-5H$_2$), 3.82 (1H, br s, OH), 4.43 (2H, s, NC*H*$_2$Ph), 5.36 (1H, br s, C-1′H), 7.14–7.40 (10H, m, 10 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.0 (C-4H$_2$), 45.1 (C-5H$_2$), 46.7 (N*C*H$_2$Ph), 49.3 (C-3H), 71.5 (C-1′H), 125.7 (aromatic CH), 127.1 (aromatic CH), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.2 (aromatic CH), 128.6 (aromatic CH), 136.1 (aromatic C), 142.3 (aromatic C), 174.9 (C-2); HRMS (ESI+): Exact mass calcd for $C_{18}H_{20}NO_2$ $(M+H)^+$ 282.1494. Found: 282.1480.

1-Benzyl-3-(1-hydroxy-2,2-dimethylpropyl)pyrrolidin-2-one ((±)-8/10e)



(±)-8e **(±)-10e**

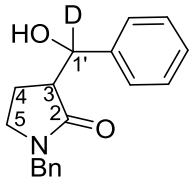
This compound was prepared following the general procedure *(Method B)*, starting by combining diisopropylamine (2.62 mL, 18.7 mmol) with THF (15 mL) and adding 2.10M *n*-BuLi in hexanes (8.50 mL, 17.9 mmol). Solutions of 1-benzylpyrrolidin-2-one **(1)** (2.85 mL, 17.8 mmol) in THF (32 mL) and pivaldehyde (2.32 mL, 21.4 mmol) in THF (4 mL) were added sequentially to the LDA/THF mixture. 10% Aqueous citric acid (25 mL) was added to the resulting slurry at 0 °C. MTBE (25 mL) was added to the two homogeneous phases and the organic phase was separated, washed with water (2 × 15 mL) and brine (30 mL), dried and concentrated to afford the crude product (4.55 g, 98%) as a white solid (88:12 d.r.). A portion of the crude material (300 mg) was purified by wet flash chromatography (20% EtOAc/hexanes), affording an isolated sample of each diastereomer.

The faster eluting, major diastereomer (±)-**10e** (124 mg) was recovered as a white solid (m.p. 75–77 °C): Found: C, 73.67; H, 8.79; N, 4.91; $C_{16}H_{23}NO_2$ requires C, 73.53; H, 8.87; N, 5.36%;ν_{max} (UATR)/cm^{-1} 3329, 2956, 1645, 1430, 703; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (9H, s, 3 × CH$_3$), 1.73–1.90 (1H, sym m, one of C-4H$_2$), 2.09–2.25 (1H, sym m, one of C-4H$_2$), 2.54 (1H, dt, J = 11.2, 8.7, C-3H), 3.11–3.24 (2H, m, C-5H$_2$), 3.43 (1H, dd, J = 8.9, 1.7,

C-1′H), 4.46 (2H, s, NC*H*$_2$Ph), 6.06 (1H, d, *J* = 1.7 OH), 7.19–7.38 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) *δ* 25.2 (C-4H$_2$), 26.2 (CH_3), 35.6 (C-2′), 42.9 (C-3H), 45.0 (C-5H$_2$), 46.7 (N*C*H$_2$Ph), 80.7 (C-1′H), 127.7 (aromatic CH), 128.1 (aromatic CH), 128.8 (aromatic CH), 135.9 (aromatic C), 177.7 (C-2); HRMS (ESI+): Exact mass calculated for $C_{16}H_{24}NO_2$ $(M+H)^+$ 262.1807. Found: 262.1798.

The slower eluting, minor diastereomer (±)-**8e** (30 mg) was recovered as an off-white solid (m.p. 125–127 °C): ν_{max} (ATR)/cm^{-1} 3368, 2958, 1670, 1452, 1438, 736, 696; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 0.97 (9H, s, 3 × CH_3), 1.90–2.12 (2H, overlapping m and br s, one of C-4H$_2$ and OH), 2.20–2.37 (1H, m, one of C-4H$_2$), 2.72 (1H, t, *J* = 9.6, C-3H), 3.11–3.25 (2H, m, C-5H$_2$), 4.05 (1H, br s, C-1′H), 4.49 (2H, s, NC*H*$_2$Ph), 7.18–7.36 (5H, m, 5 × ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) *δ* 19.0 (C-4H$_2$), 26.7 (CH_3), 35.1 (C-2′), 44.5 (C-3H), 45.1 (C-5H$_2$), 46.8 (N*C*H$_2$Ph), 76.4 (C-1′H), 127.4 (aromatic CH), 127.9 (aromatic CH), 128.6 (aromatic CH), 136.4 (aromatic C), 176.2 (C-2); HRMS (ESI+): Exact mass calculated for $C_{16}H_{24}NO_2$ $(M+H)^+$ 262.1807. Found: 262.1801.

1-Benzyl-3-[hydroxy(phenyl)methyl-*d*]pyrrolidin-2-one (11d)



11d

This compound was prepared following the general procedure *(Method A)*, starting by combining $NaBD_4$ (0.87 g, 20.8 mmol) with EtOH (50 mL) and adding a solution of **7d** (5.81 g, 20.8 mmol) in EtOH (50 mL). After evaporation of the solvent, the resulting residue was taken up into CH_2Cl_2 (100 mL) and water (50 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The organic layers were combined, washed with brine (30 mL), dried and concentrated to afford the crude product as an orange oil (57:43 d.r.). Purification by wet flash chromatography (20% EtOAc/hexanes) afforded **11d** (5.02 g, 93%), a mixture of diastereomers, as a viscous clear oil (60:40 d.r.): ν_{max} (UATR)/cm^{-1} 3336, 2922, 2859, 1657, 1494, 1445, 1436, 1255, 699; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 1.52–1.78 [1.4H, m, one of C-4H$_2$ (major diastereomer) and C-4H$_2$ (minor diastereomer)], 1.96–2.12 [0.6H, sym m, one of C-4H$_2$ (major diasteomer)], 2.77 [0.4H, t, *J* = 9.6, C-3H (minor diastereomer)], 2.90 [0.6H, t, *J* = 9.1, C-3H (major diastereomer)], 2.99–3.16 [2H, m, C-5H$_2$ (both diastereomers)], 3.86–4.05 [0.6H, br d, OH (major diastereomer)], 4.35–4.48 {2H, overlapping signals, δ = 4.35–4.48 [1.2H, ABq, $\delta_{Ha'}$ = 4.39 and $\delta_{Hb'}$ = 4.44, *J* = 15.5, NC*H*$_2$Ph (major diastereomer)] and δ = 4.44 [0.8H, s, NC*H*$_2$Ph (minor diastereomer)]}, 5.57 [0.4H, s, OH (minor diastereomer)], 6.97–7.52 [10H, m, 10 × ArH

(both diastereomers)]; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.6 [C-4H_2 (major diastereomer)], 21.6 [C-4H_2 (minor diastereomer)], 44.7 [C-5H_2 (minor diastereomer)], 45.0 [C-5H_2 (major diastereomer)], 46.5 [N*C*H_2Ph (minor diastereomer)], 46.6 [N*C*H_2Ph (major diastereomer)], 47.7 [C-3H (minor diastereomer)], 49.2 [C-3H (major diastereomer)], 71.0 [t, J = 22.2, C-1′H (major diastereomer)], 75.5 [t, J = 22.2, C-1′H (minor diastereomer)], 125.7 [aromatic CH (major diastereomer)], 126.6 [aromatic CH (minor diastereomer)], 127.0 [aromatic CH (major diastereomer)], 127.3 [aromatic CH (major diastereomer)], 127.6 [aromatic CH (minor diastereomer)], 127.8 [aromatic CH (major diastereomer)], 127.9 [aromatic CH (minor diastereomer)], 128.0 [aromatic CH (minor diastereomer)], 128.1 [aromatic CH (major diastereomer)], 128.3 [aromatic CH (minor diastereomer)], 128.5 [aromatic CH (major diastereomer)], 128.6 [aromatic CH (minor diastereomer)], 135.7 [aromatic C (minor diastereomer)], 136.0 [aromatic C (major diastereomer)], 141.1 [aromatic C (minor diastereomer)], 142.2 [aromatic C (major diastereomer)] 174.9 [C-2 (major diastereomer)], 176.2 [C-2 (minor diastereomer)]. HRMS (ESI+): Exact mass calculated for $C_{18}H_{19}DNO_2$ $(M+H)^+$ 283.1551. Found: 283.1559.

General Procedures for Asymmetric Synthesis of *β*-Hydroxy-*γ*-lactams

Hydrogenations in Methanol or Ethanol

β-Keto-*γ*-lactam substrate (1.0 g), lithium chloride solution (0 or 1 mol%, 0.1M solution in IPA) and ($Ru(OAc)_2$[(*S*)-tol-BINAP)])[5] (0.35 mol%) were combined with solvent (55 mL) in a 100 mL round bottom flask and stirred while a steady stream of nitrogen gas was bubbled through the resultant solution for 2 h to achieve full deoxygenation. The deoxygenated solution was then transferred via syringe (in 2 batches) to a hydrogenation reactor which had also been purged of oxygen by means of a stream of nitrogen, which was flowed through the reactor for 15 min prior to the transfer of reactants and was still flowing during the transfer. After the transfer of reactants was complete, hydrochloric acid [6 mol%, 1.2M hydrochloric acid in solvent (35% aqueous hydrochloric acid diluted to 3.5% with solvent)] was added to the hydrogenation reactor, which was then further purged with a steady stream of nitrogen for 30 min. The reactor was then purged with H_2 (3 × 85 psi) and heated to 65 °C under 85–90 psi of H_2 for 16 h. The reaction solution was allowed to cool to room temperature, vented,

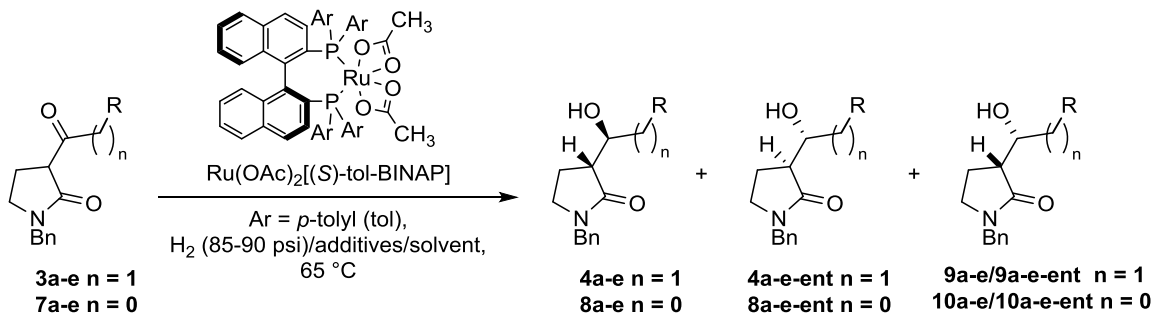
purged with nitrogen*, and an aliquot was removed for HPLC analysis. The reaction solution was then concentrated under reduced pressure to afford the crude product, which was purified by wet flash chromatography using an EtOAc–hexane mixture as eluent.

Hydrogenations in Isopropanol

β-Keto-*γ*-lactam substrate (4.4 g), lithium chloride solution (0 or 1 mol%, 0.1M solution in IPA) and ($Ru(OAc)_2$[(*S*)-tol-BINAP)])[5] (0.35 mol%) were combined with IPA (55 mL) in a 100 mL round bottom flask and stirred while a steady stream of nitrogen gas was bubbled through the resultant solution for 2 h to achieve full deoxygenation. The deoxygenated solution was then transferred via syringe (in 2 batches) to a hydrogenation reactor, which had also been purged of oxygen by means of a stream of nitrogen which was flowed through the reactor for 15 min prior to the transfer of reactants and was still flowing during the transfer. When the transfer of reactants was complete, hydrochloric acid [6 mol%, 1.2M hydrochloric acid in IPA (35% aqueous hydrochloric acid diluted to 3.5% with IPA)] was added to the hydrogenation reactor, which was then further purged with a steady stream of nitrogen for 30 min. The reactor was then purged with H_2 (3 × 85 psi), and heated to 65 °C under 85–90 psi of H_2 for 16 h (in instances where conversion of starting material was incomplete after this time, the reaction was continued for a further 20–24 h under identical conditions). The reaction solution was allowed to cool to room temperature, vented, purged with nitrogen*, and an aliquot was removed for HPLC analysis. The reaction solution was then concentrated under reduced pressure to afford the crude product, which was purified by wet flash chromatography using an EtOAc–hexane mixture as eluent.

*In instances where precipitation was observed after purging with nitrogen, the mixture was re-heated to dissolve the product.

Table S1(A). DKR-Hydrogenation Substrate Screen



3a-e n = 1
7a-e n = 0

4a-e n = 1
8a-e n = 0

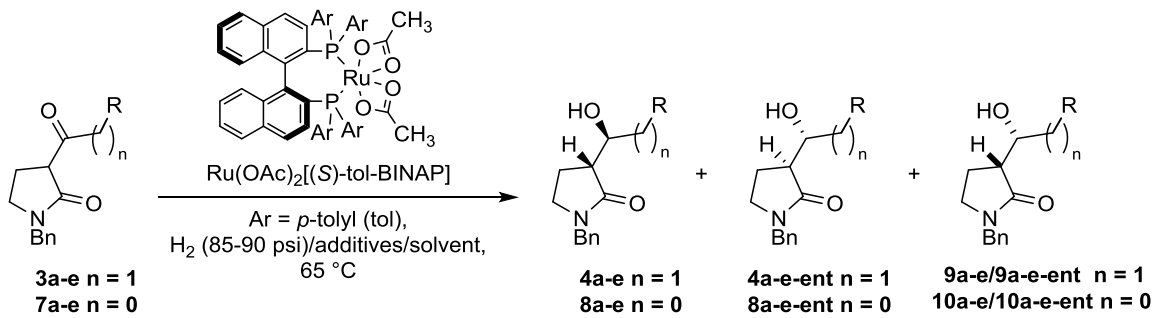
4a-e-ent n = 1
8a-e-ent n = 0

9a-e/9a-e-ent n = 1
10a-e/10a-e-ent n = 0

				n = 1						n = 0					
entry[a]	R	LiCl[b]	solvent	substrate (product)	Time (%[c])	% ee[d]	% de[d]	Yield[e] (%)	$[\alpha]_D^{20}$[f]	substrate (product)	Time (%[c])	% ee[d]	% de[d]	Yield[e] (%)	$[\alpha]_D^{20}$[f]
1	*i*-propyl	0	MeOH	**3a (4a)**	16 h	93.6	90.2	90		**7a (8a)**	16 h	78.7	>98.0	89	
2	cyclohexyl	0	MeOH	**3c (4c)**	16 h	94.5	96.5	88		-	-	-	-		
3	*t*-butyl	0	MeOH	**3e (4e)**	16 h (<2.0)	39.0	NA[g]			-	-	-	-		
4	*i*-propyl	0	EtOH	**3a (4a)**	16 h	94.3	94.4	85		**7a (8a)**	16 h	74.6	88.7	84	
5	cyclopropyl	0	EtOH	**3b (4b)**	16 h	84.2	97.5	88		**7b (8b)**	16 h	96.8	95.8	79	
6	cyclohexyl	0	EtOH	**3c (4c)**	16 h	95.0	94.7	87	–6.95°	**7c (8c)**	16 h	35.5	>98.0	90	
7	phenyl	0	EtOH	**3d (4d)**	16 h	84.7	91.6	83		**7d (8d)**	16 h	18.2	>98.0	86	
8	*t*-butyl	0	EtOH	**3e (4e)**	16 h (<2.0)	63.9	NA[g]			**7e (8e)**	16 h (<2.0)	NA[g]	NA[g]		
9	*t*-butyl	1	EtOH	**3e (4e)**	16 h (<2.0)	NA[g]	NA[g]			**7e (8e)**	16 h (<2.0)	NA[g]	NA[g]		
10	*t*-butyl	0	CF_3CH_2OH	**3e (4e)**	16 h (<2.0)	42.1	NA[g]			-	-	-	-		

[a]Screening reactions run with *β*-keto-*γ*-lactam **3** or **7** (1 g), diacetato[(*S*)-(−)-2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl]ruthenium(II) ($Ru(OAc)_2$[(*S*)-tol-BINAP)])[5] (substrate to catalyst mole ratio (S/C): 280), HCl (6 mol%), and solvent (55 mL) at 65 °C under 85–90 psi of H_2. [b]Mole percent relative to substrate **3** or **7**. [c]Extent of reaction as determined by ^{1}H NMR analysis. [d]Determined by chiral HPLC (see SI). [e]Isolated yield after chromatography. [f]Optical rotations measured in MeOH at a concentration of c=1.0. [g]Not applicable (too small to accurately measure).

Table S1(B). DKR-Hydrogenation Substrate Screen



				n = 1						n = 0					
entry[a]	R	LiCl[b]	solvent	substrate (product)	Time (%[c])	% ee[d]	% de[d]	Yield[e] (%)	$[\alpha]_D^{20}$[f]	substrate (product)	Time (%[c])	% ee[d]	% de[d]	Yield[e] (%)	$[\alpha]_D^{20}$[f]
11	*i*-propyl	0	IPA[h]	-	-	-	-			**7a (8a)**	16 h	72.1	>98.0	89	+6.30°
12	*i*-propyl	1	IPA[h]	**3a (4a)**	16 h (63.5)	-	-			**7a (8a)**	16 h	67.1	93.4	91	–6.50°
					36 h[i]	96.5	95.6	91	+1.70°						
13	cyclopropyl	1	IPA[h]	**3b (4b)**	16 h	86.1	>98.0	90	+4.70°	**7b (8b)**	16 h	94.9	92.6	87	
14	cyclohexyl	1	IPA[h]	**3c (4c)**	16 h (95.4)	-	-			**7c (8c)**	16 h	38.5	>98.0	90	+5.20°
					32 h[i]	97.4	96.2	89							
15	phenyl	1	IPA[h]	**3d (4b)**	16 h (75.1)	-	-			**7d (8d)**	16 h	15.3[j]	>98.0	92	+14.15°
					36 h[i]	87.5	97.0	92	+5.75°						

[a]Screening reactions run with *β*-keto-*γ*-lactam **3** or **7** (1 g), diacetato[(*S*)-(−)-2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl]ruthenium(II) ($Ru(OAc)_2$[(*S*)-tol-BINAP)])[5] (substrate to catalyst mole ratio (S/C): 280), HCl (6 mol%), and solvent (55 mL) at 65 °C under 85–90 psi of H_2. [b]Mole percent relative to substrate **3** or **7**. [c]Extent of reaction as determined by ^{1}H NMR analysis. [d]Determined by chiral HPLC (see SI). [e]Isolated yield after chromatography. [f]Optical rotations measured in MeOH at a concentration of c=1.0. [h]Reactions in IPA were run at a concentration of 88 mg/mL (4.4 g of substrate **3** or **7**) as a dilution effect caused ineffective hydrogenation at the lower concentration employed when using other solvents. [i]Second charge of catalyst (S/C: 280) was added after 16 h. [j]This reaction was repeated with a value of 8.3% ee recorded.

References

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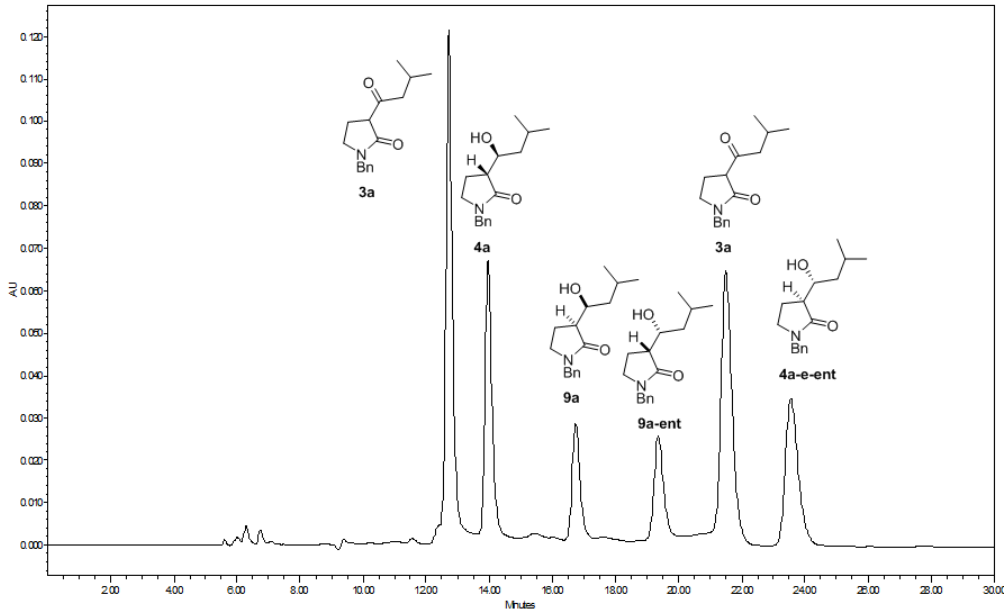
Chiral HPLC Chromatograms

Asymmetric Reduction of 1-Benzyl-3-(3-methylbutanoyl)pyrrolidin-2-one (3a)

Chiral HPLC method used:

Column: Chiralpak IA-3, 4.6 x 250 mm 3 µm particle. Mobile Phase: 80/20 Heptane/Ethanol. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 5 µL or 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **3a** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**4a** and (±)-**9a**:



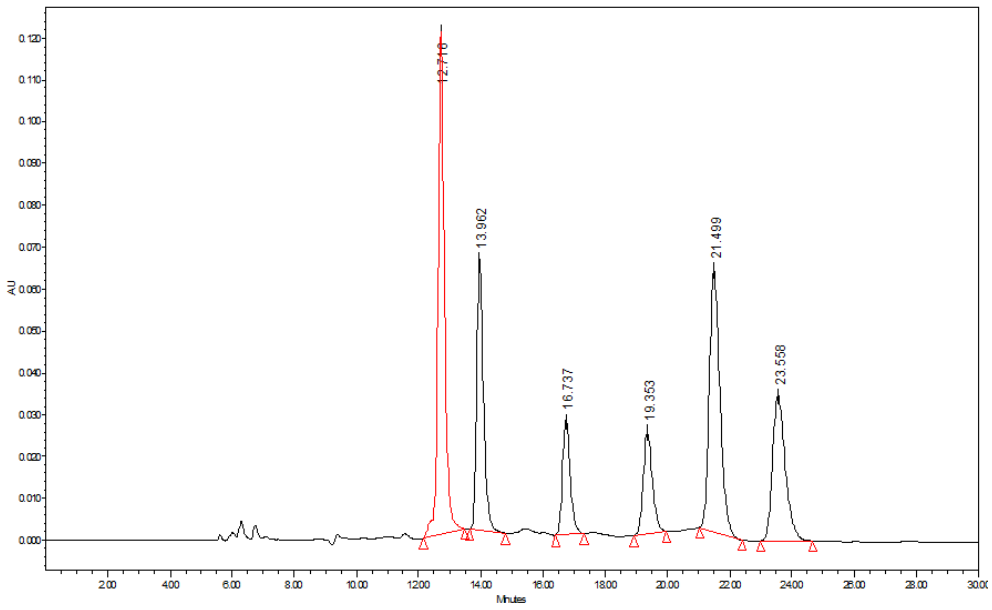
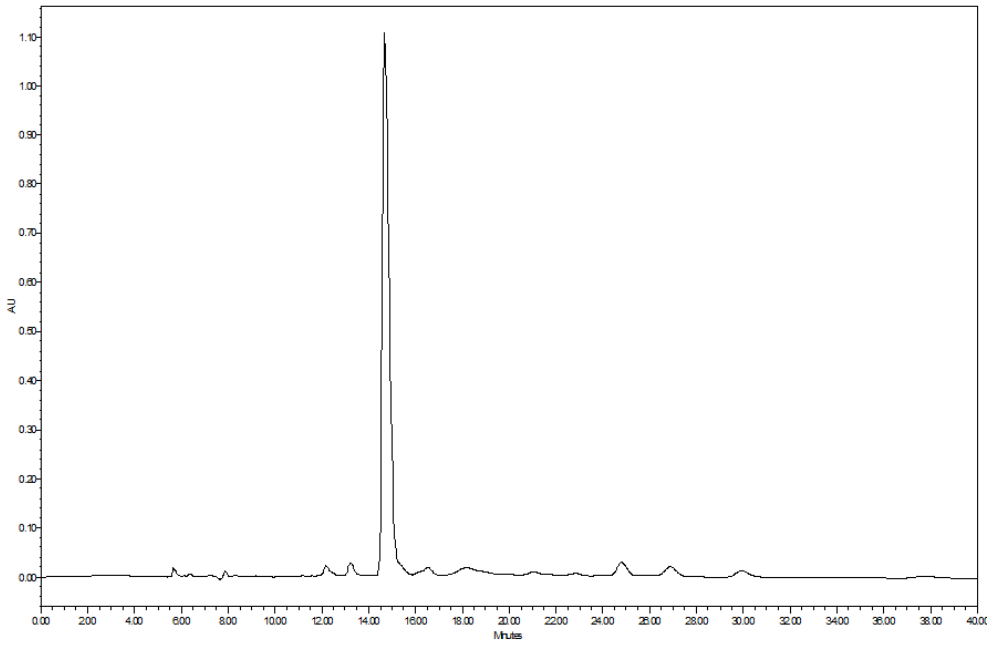
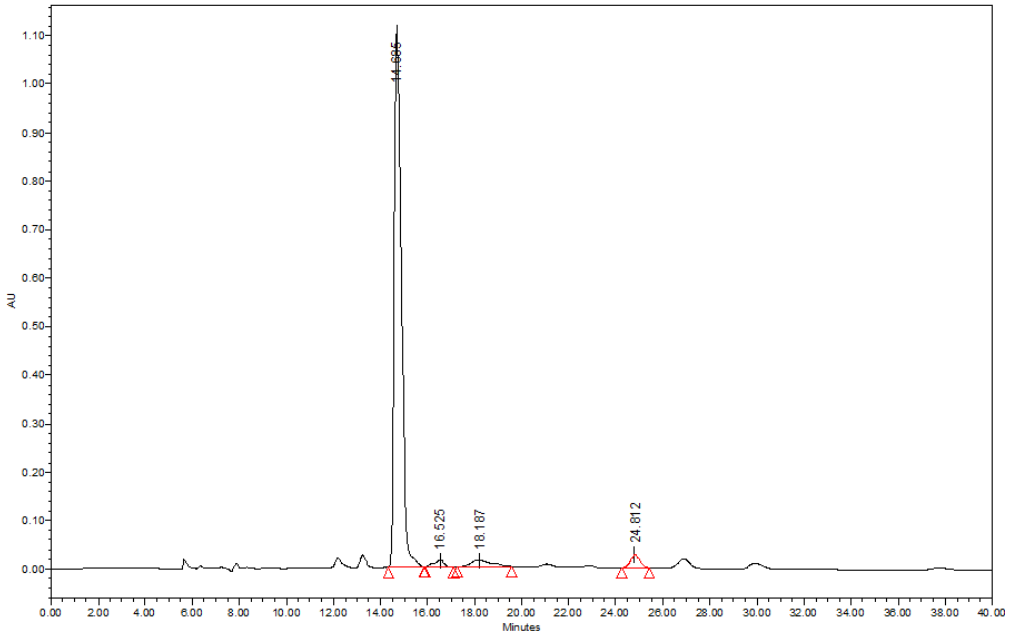


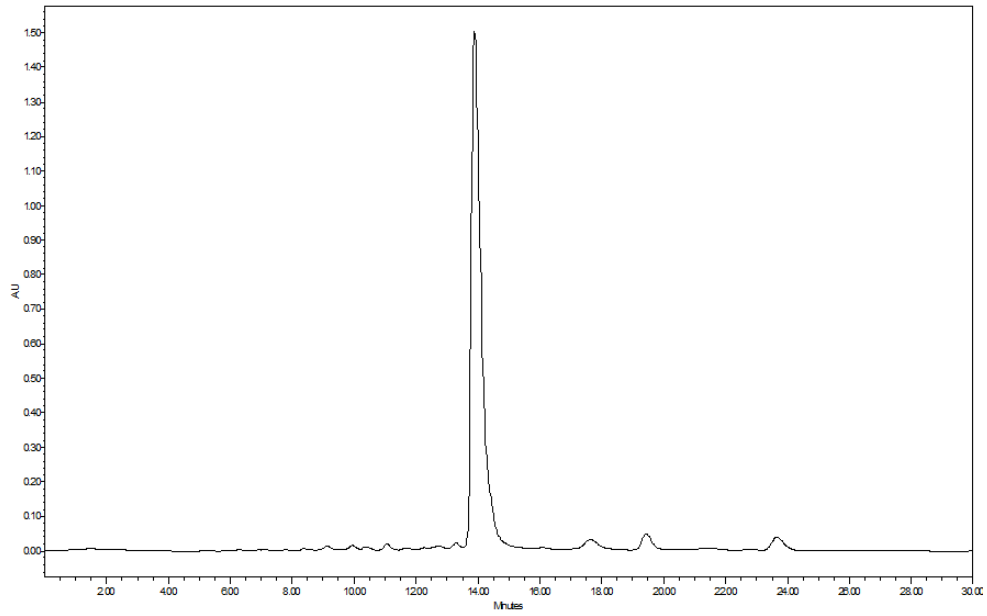
Table 2, entry 1: **3a** (1 g, 3.86 mmol); MeOH (55 mL); 35% HCl (requires 19 µL, 0.23 mmol: therefore charged 0.19 mL of a 10% stock solution of 35% HCl in MeOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (12.4 mg, 0.0138 mmol).

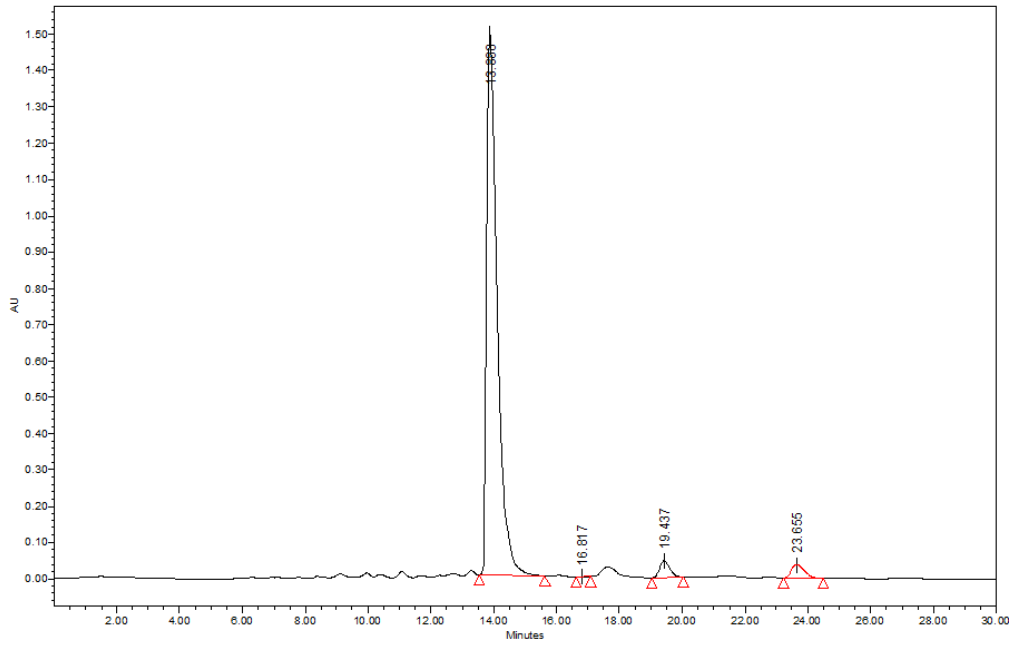




4a = 92.06A% **9a** = 1.72A% **9a-ent** = 3.16A% **4a-ent** = 3.05A%

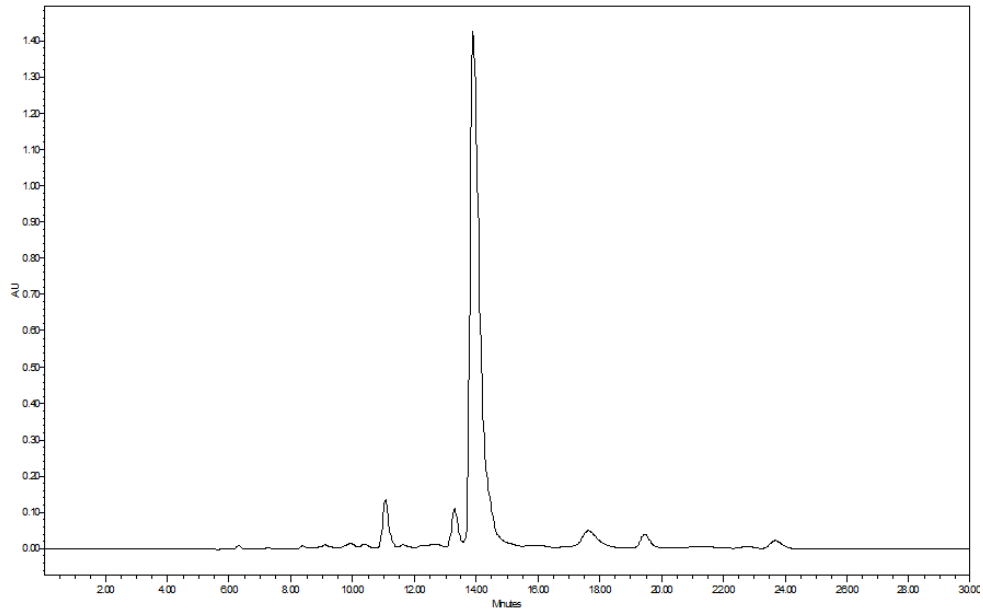
Table 2, entry 4: **3a** (1 g, 3.86 mmol); EtOH (55 mL); 35% HCl (requires 19 µL, 0.23 mmol: therefore charged 0.19 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (12.4 mg, 0.0138 mmol).

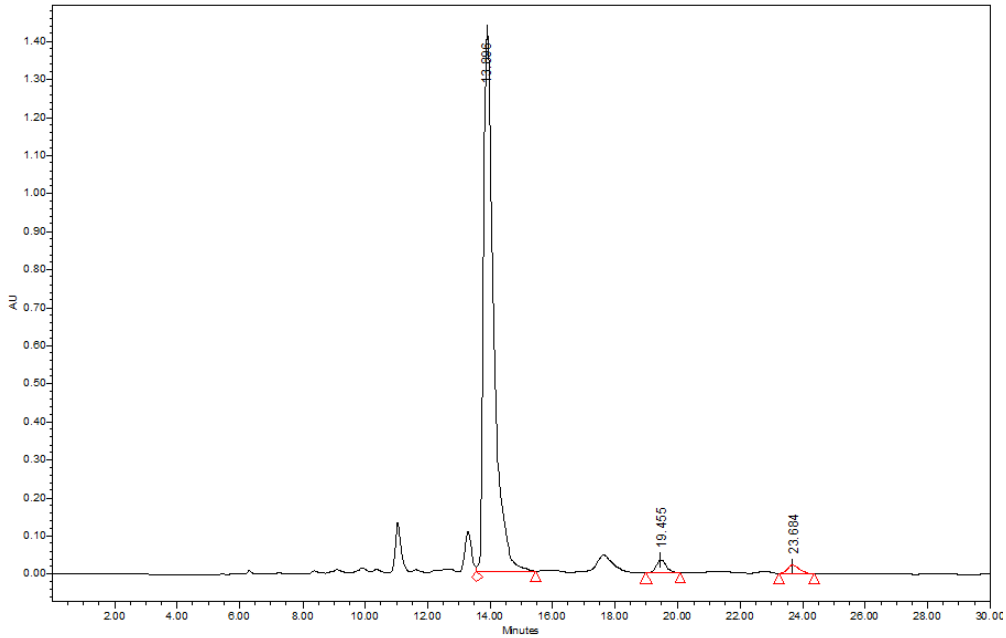




4a = 94.43A% **9a** = 0.15A% **9a-ent** = 2.63A% **4a-ent** = 2.80A%

Table 2, entry 12: **3a** (4.4 g, 17.0 mmol); IPA (55 mL); 35% HCl (requires 85 µL, 1.02 mmol: therefore charged 0.85 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.17 mL = 7.2 mg, 0.17 mmol); $Ru(OAc)_2$[(S)-tol-BINAP)] (54.5 mg, 0.0607 mmol).





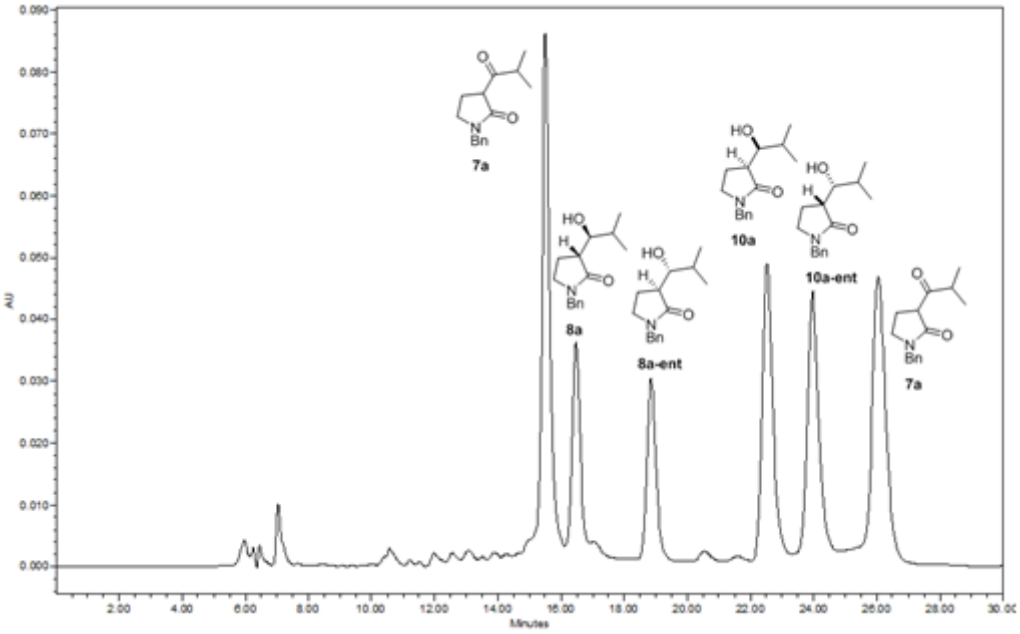
4a = 96.12A% **9a** = ND **9a-ent** = 2.18A% **4a-ent** = 1.70A%

Asymmetric Reduction of 1-Benzyl-3-isobutyrylpyrrolidin-2-one (7a)

Chiral HPLC method used:

Column: Chiralpak IA-3, 4.6 x 250 mm 3 µm particle. Mobile Phase: 85/15 Heptane/Ethanol. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 5 µL or 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **4a** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**8a** and (±)-**10a**:



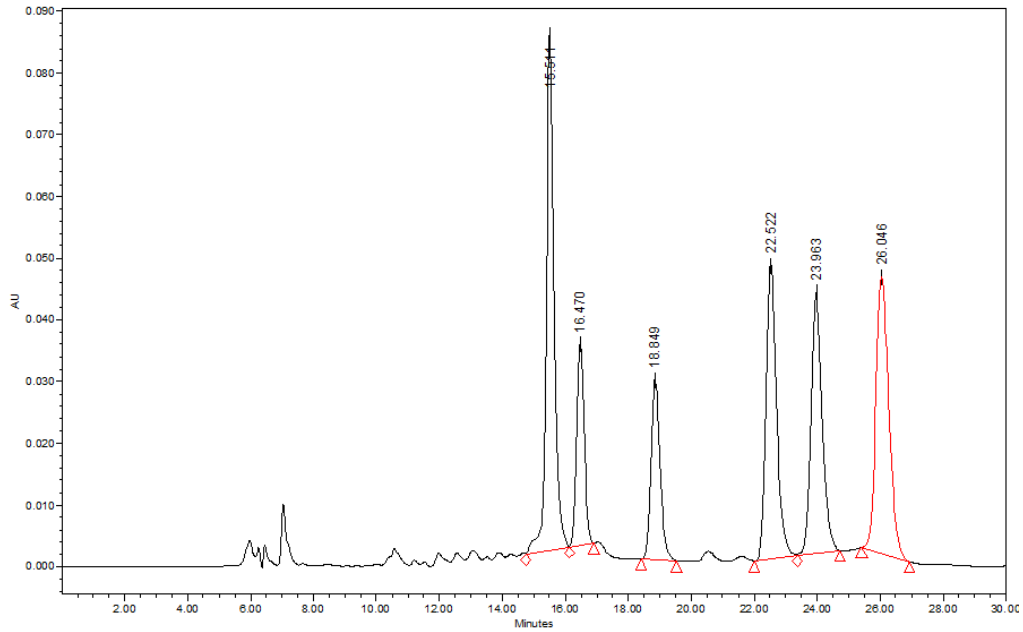
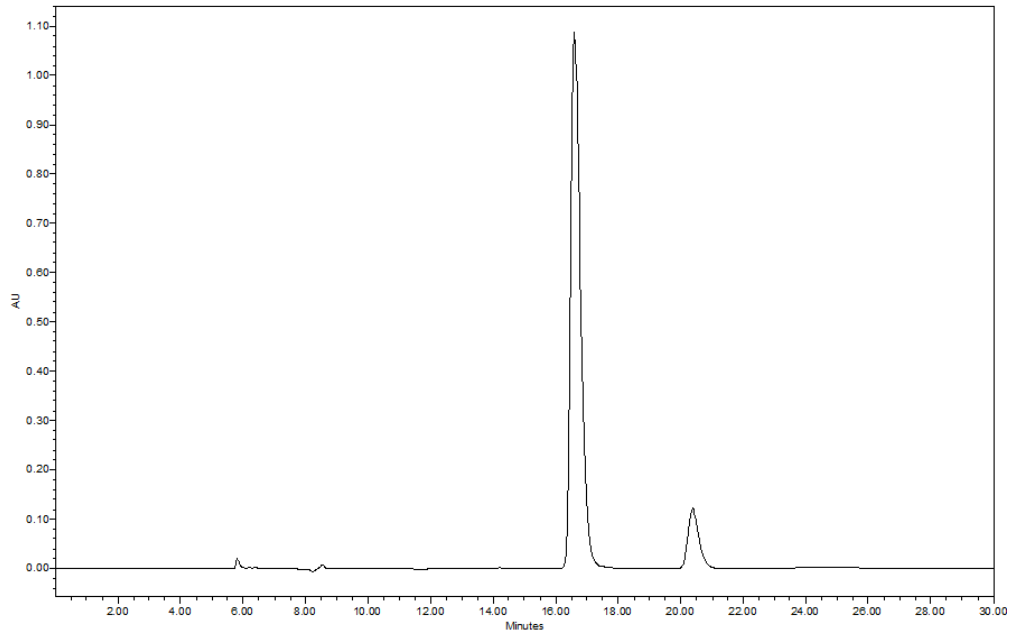
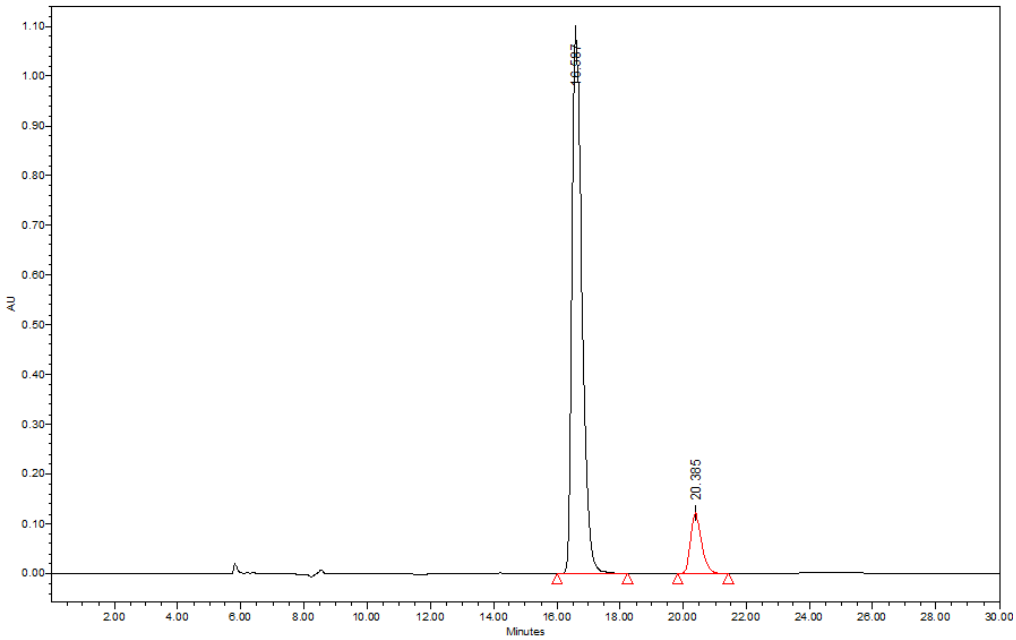


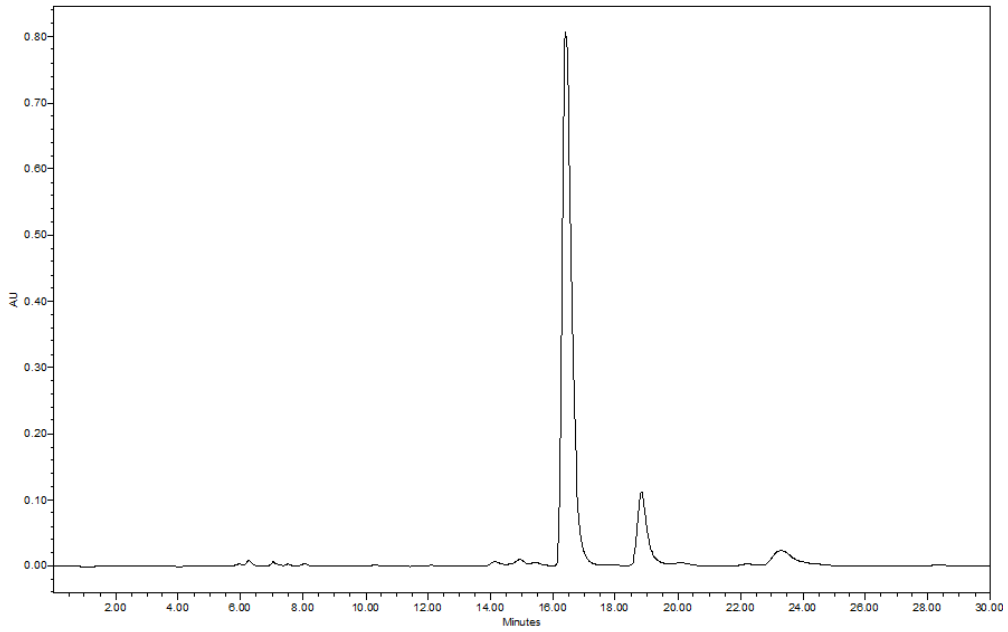
Table 2, entry 1: **7a** (1 g, 4.08 mmol); MeOH (55 mL); 35% HCl (requires 20 µL, 0.24 mmol: therefore charged 0.20 ml of a 10% stock solution of 35% HCl in MeOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (13.1 mg, 0.0146 mmol).

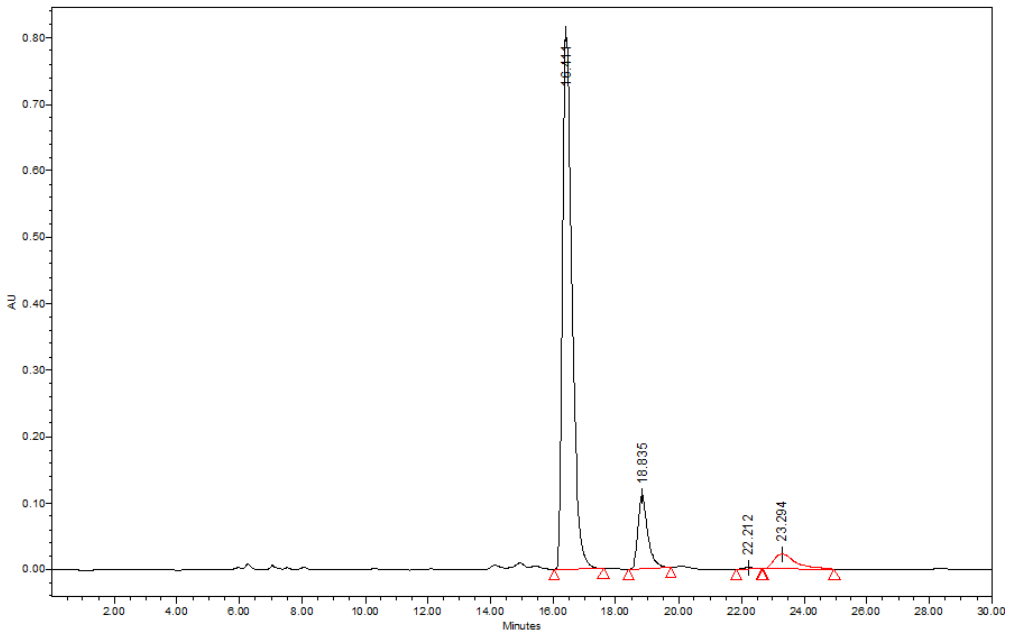




8a = 89.35A% **8a-ent** = 10.65A% **10a** = ND **10a-ent** = ND

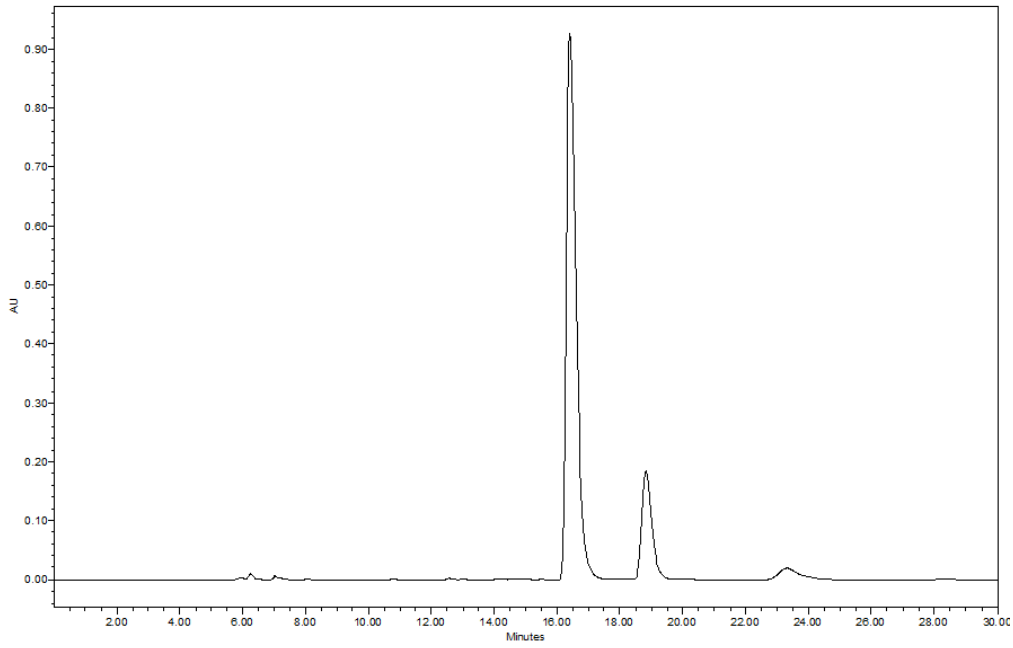
Table 2, entry 4: **7a** (1 g, 4.08 mmol); EtOH (55 mL); 35% HCl (requires 20 µL, 0.24 mmol: therefore charged 0.20 ml of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (13.1 mg, 0.0146 mmol).

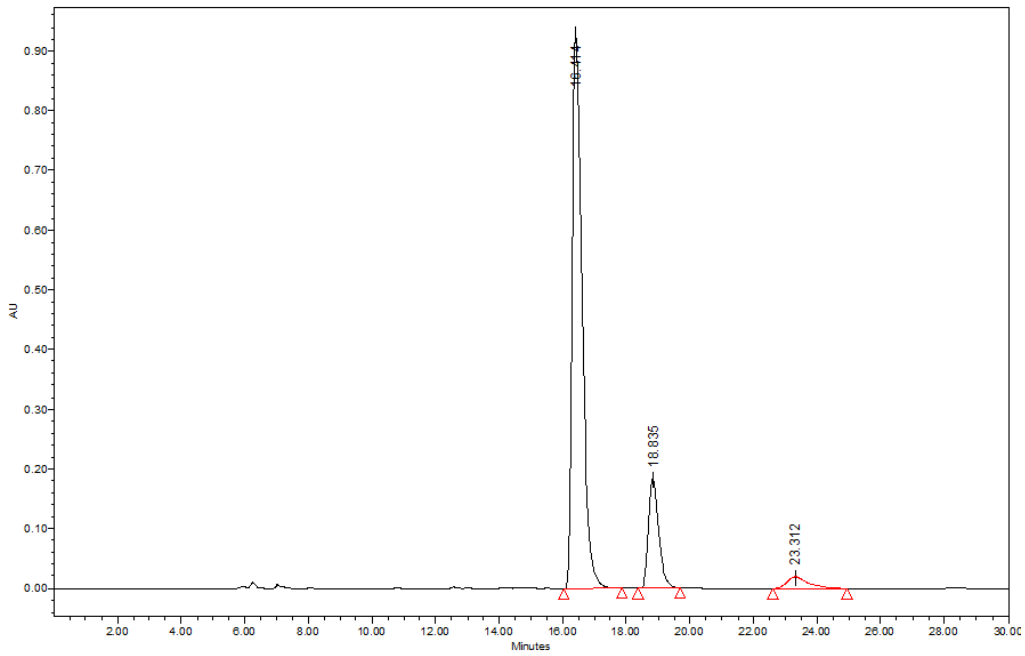




8a = 82.32A% **8a-ent** = 11.94A% **10a** = 0.36A% **10a-ent** = 5.37A%

Table 2, entry 12: **7a** (4.4 g, 18.0 mmol); IPA (55 mL); 35% HCl (requires 90 µL, 1.08 mmol: therefore charged 0.90 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.18 mL = 7.6 mg, 0.18 mmol); $Ru(OAc)_2$[(S)-tol-BINAP)] (57.7 mg, 0.0642 mmol).





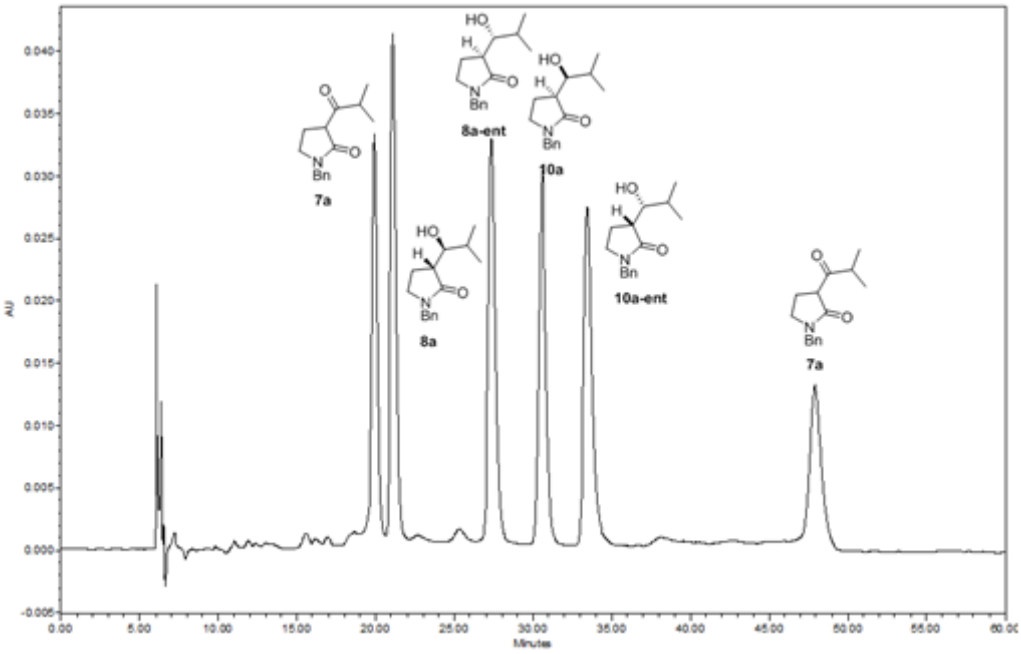
8a = 80.80A% **8a-ent** = 15.91A% **10a** = ND **10a-ent** = 3.29A%

Table 2, entry 11:

Chiral HPLC method used:

Column: Chiralpak IA-3, 4.6 x 250 mm 3 µm particle. Mobile Phase: 90/10 Heptane/Ethanol. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 2.5µL or 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **4a** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**8a** and (±)-**10a**:



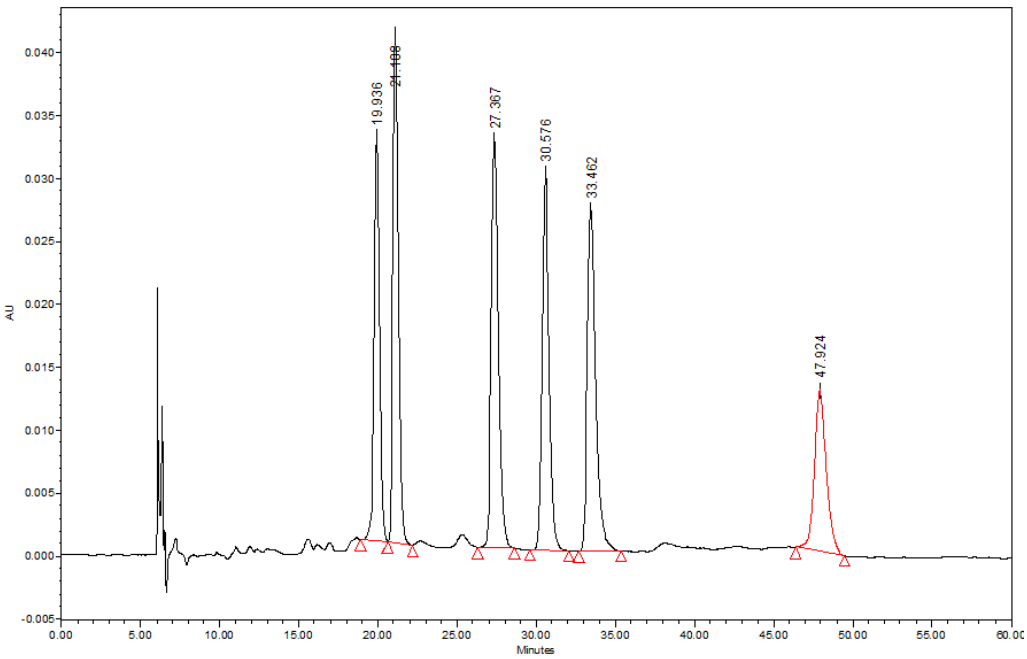
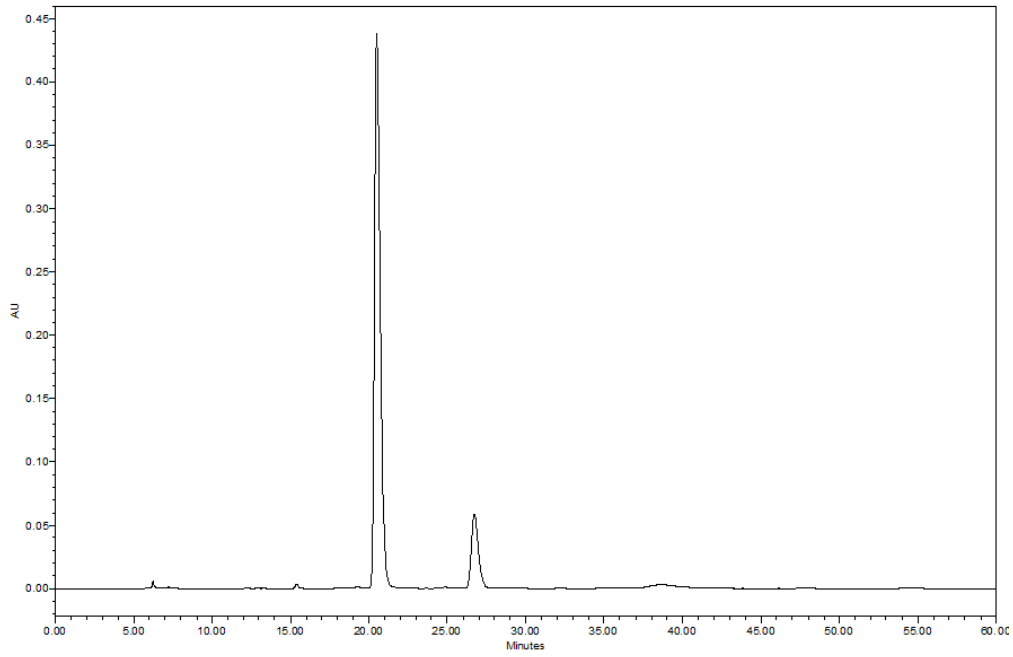
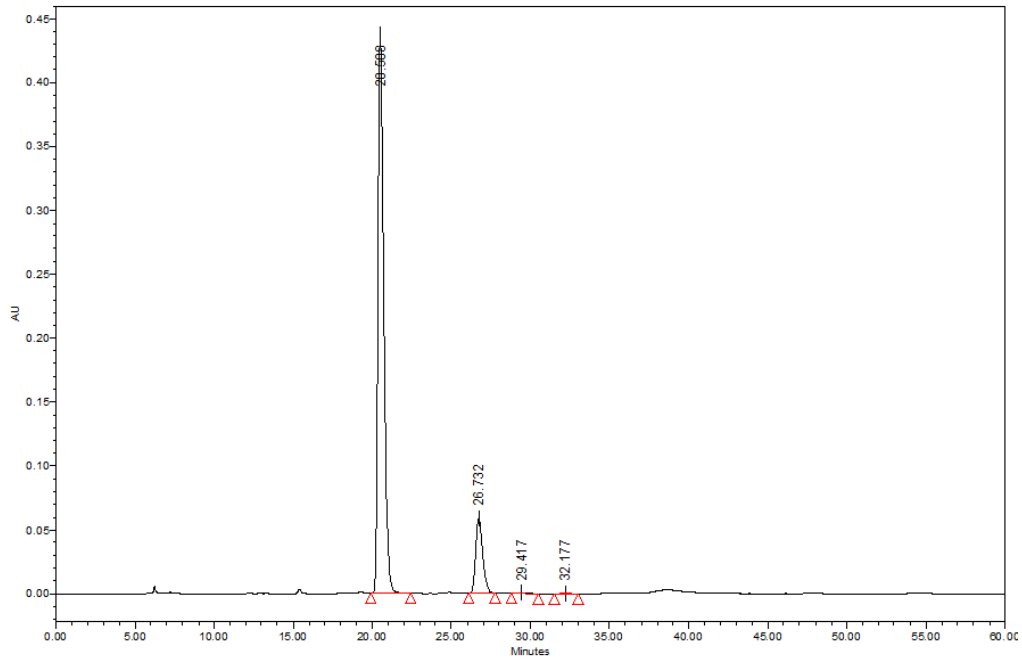


Table 2, entry 11: **7a** (4.4 g, 18.0 mmol); IPA (55 mL); 35% HCl (requires 90 µL, 1.08 mmol: therefore charged 0.90 mL of a 10% stock solution of 35% HCl in IPA); $Ru(OAc)_2$[(S)-tol-BINAP)] (57.7 mg, 0.0642 mmol).





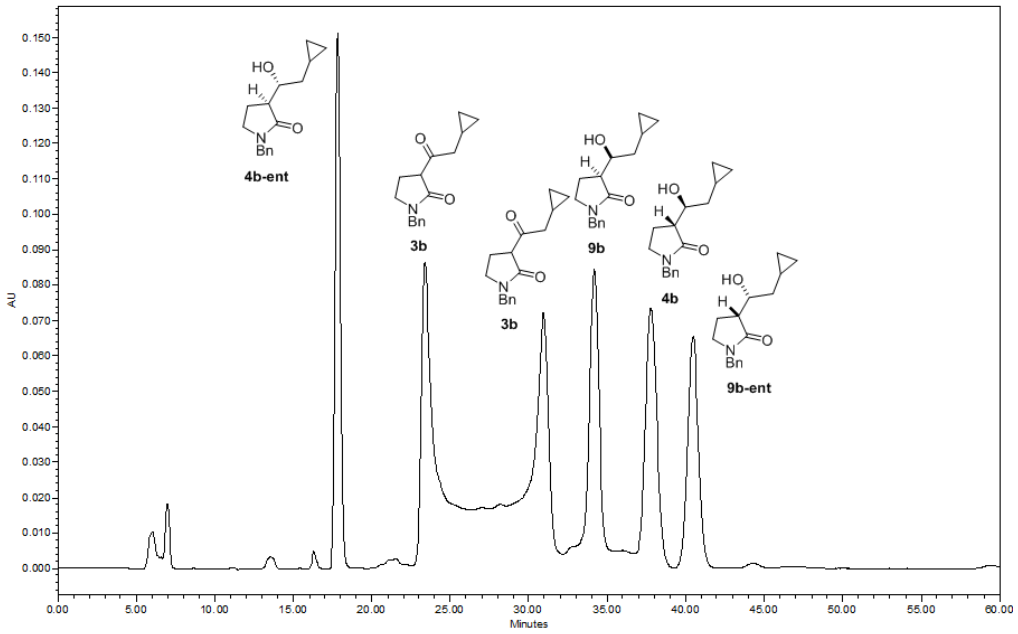
8a = 85.77A% **8a-ent** = 13.93A% **10a** = 0.19A% **10a-ent** = 0.11A%

Asymmetric Reduction of 1-Benzyl-3-(2-cyclopropylacetyl)pyrrolidin-2-one (3b)

Chiral HPLC method used:

Column: Lux-Cellulose-2, 4.6 x 250 mm 3 µm particle. Mobile Phase: 80/20 Hexane/IPA. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **3b** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**4b** and (±)-**9b**:



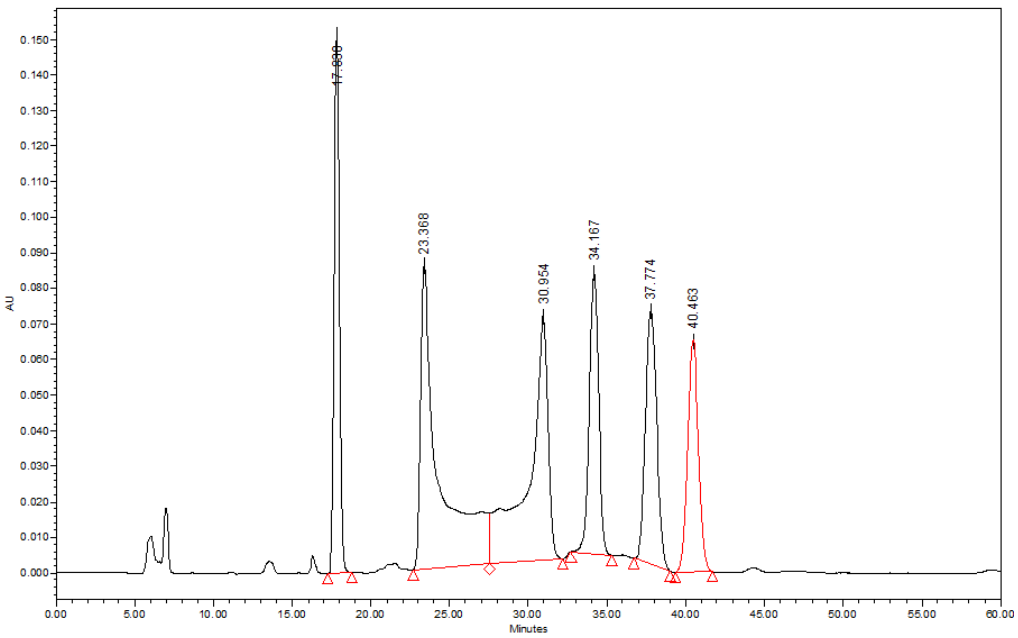
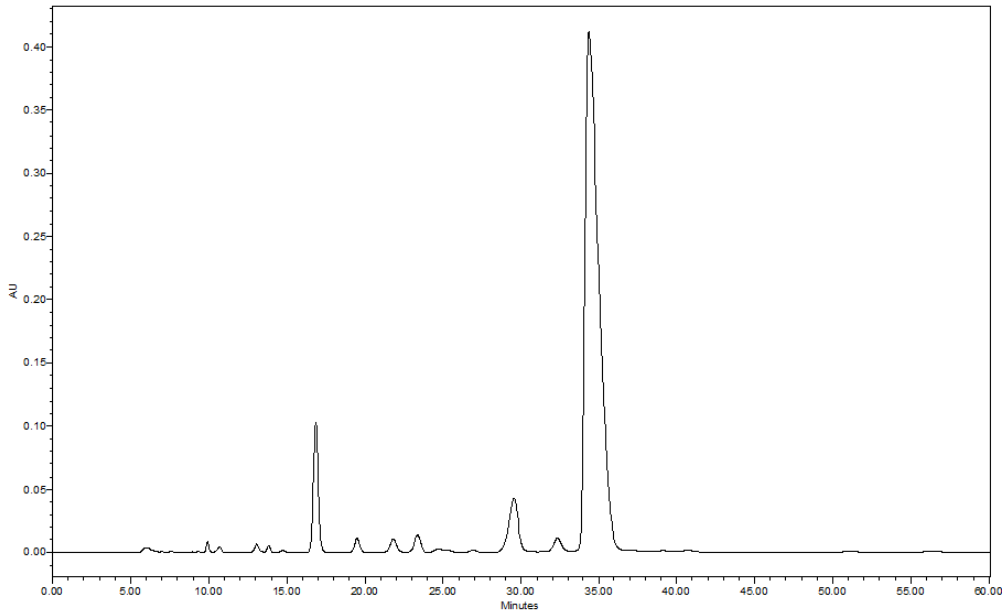
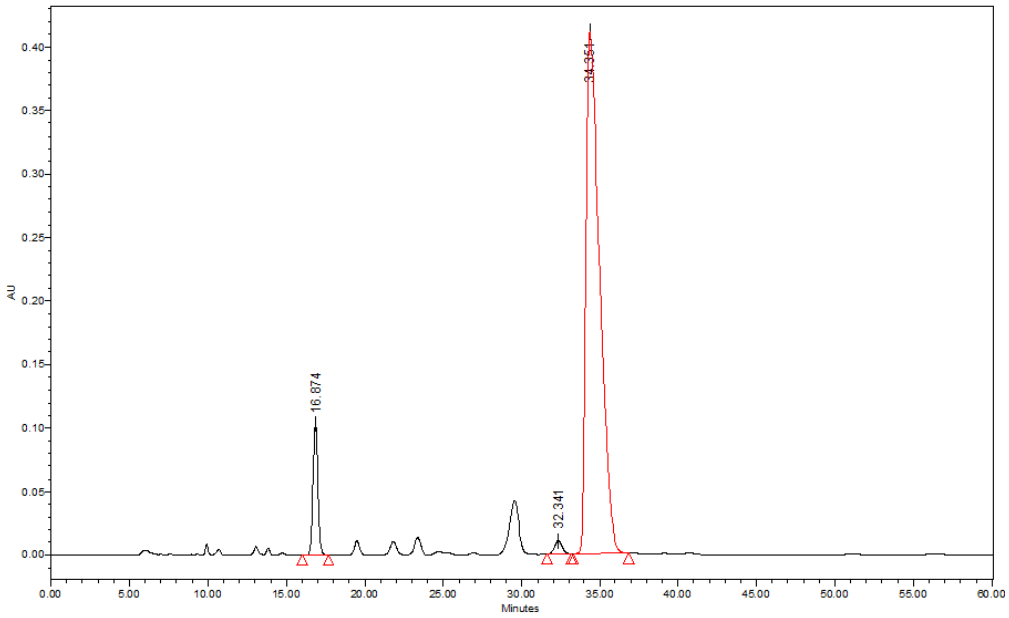


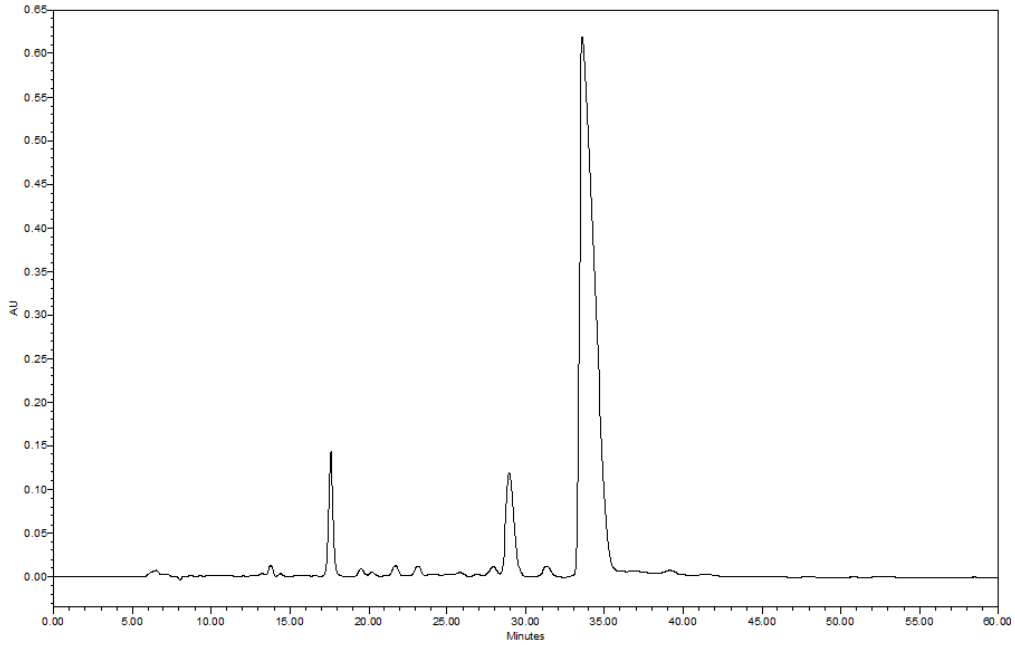
Table 2, entry 5: **3b** (1 g, 3.89 mmol); EtOH (55 mL); 35% HCl (requires 19 µL, 0.23 mmol: therefore charged 0.19 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (12.5 mg, 0.0139 mmol).

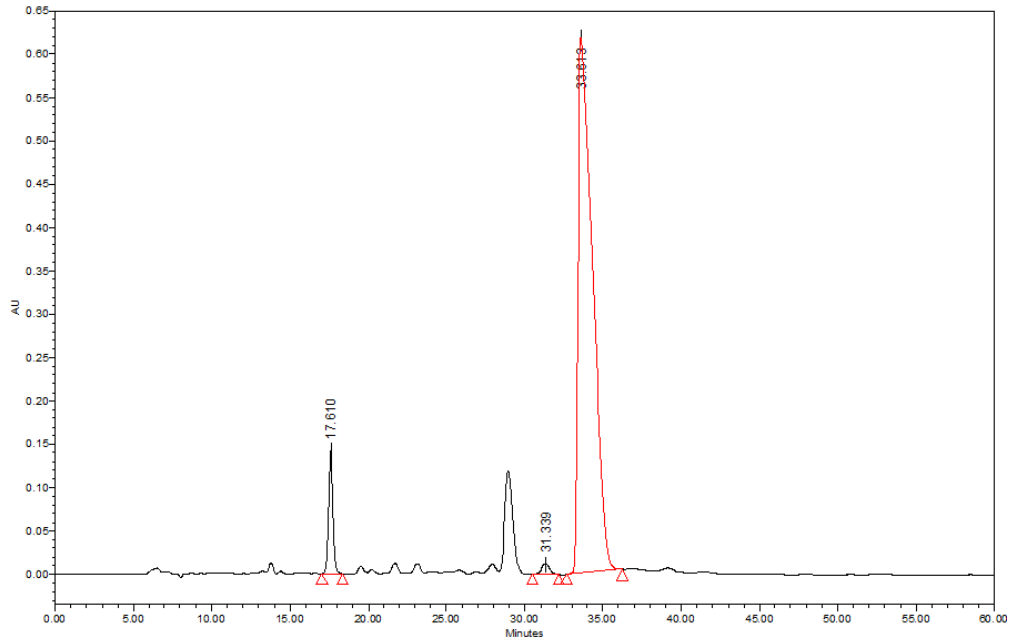




4b-ent = 7.78A% **9b** = 1.27A% **4b** = 90.95A% **9b-ent** = ND

Table 2, entry 13: **3b** (4.4 g, 17.1 mmol); IPA (55 mL); 35% HCl (requires 86 µL, 1.03 mmol: therefore charged 0.86 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.17 mL = 7.2 mg, 0.17 mmol); $Ru(OAc)_2$[(S)-tol-BINAP)] (54.9 mg, 0.0611 mmol).





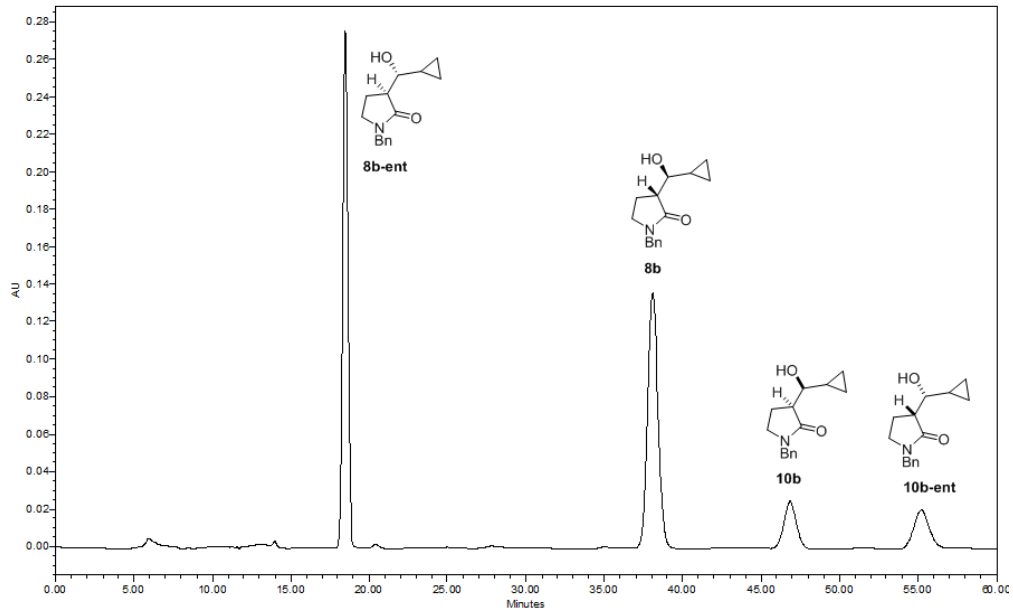
4b-ent = 6.90A% **9b** = 0.96A% **4b** = 92.14A% **9b-ent** = ND

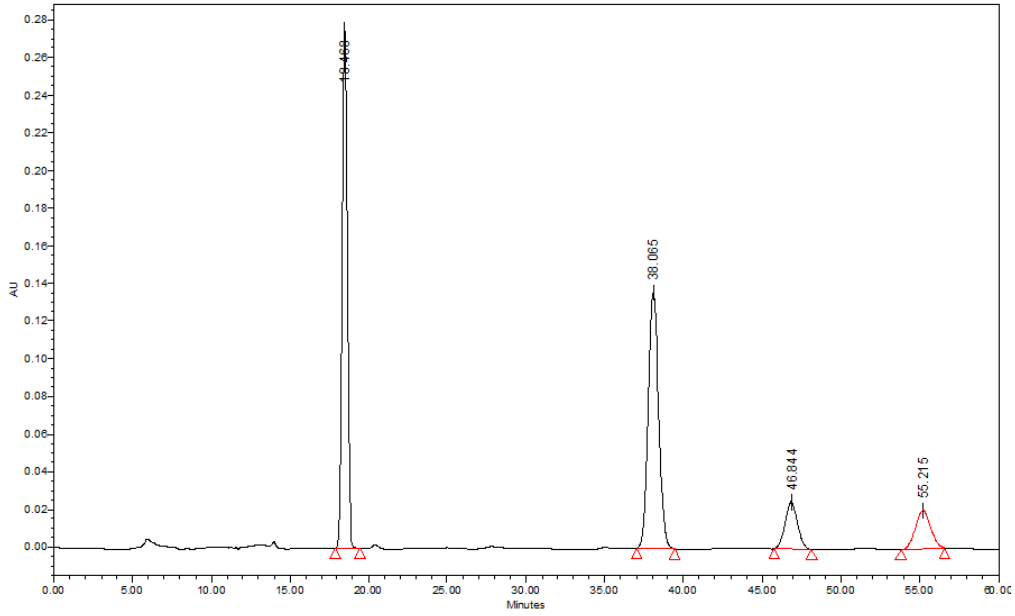
Asymmetric Reduction of 1-Benzyl-3-(cyclopropanecarbonyl)pyrrolidin-2-one (7b)

Chiral HPLC method used:

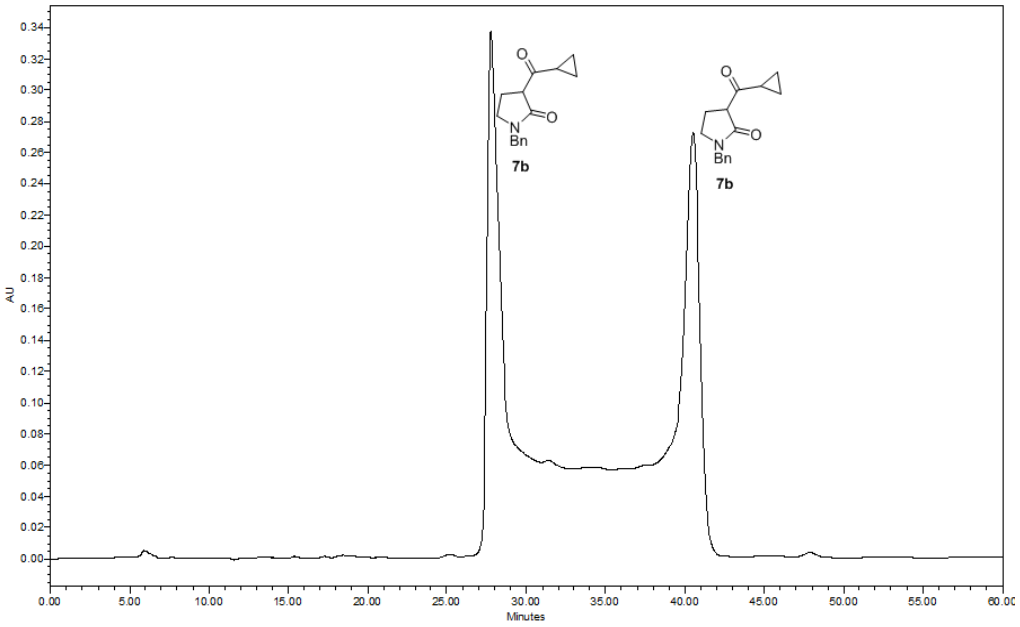
Column: Lux-Cellulose-2, 4.6 x 250 mm 3 µm particle. Mobile Phase: 80/20 Hexane/IPA. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of diastereomeric *β*-hydroxy-*γ*-lactams (±)-**8b** and (±)-**10b**:





β-Keto-*γ*-lactam **7b**:



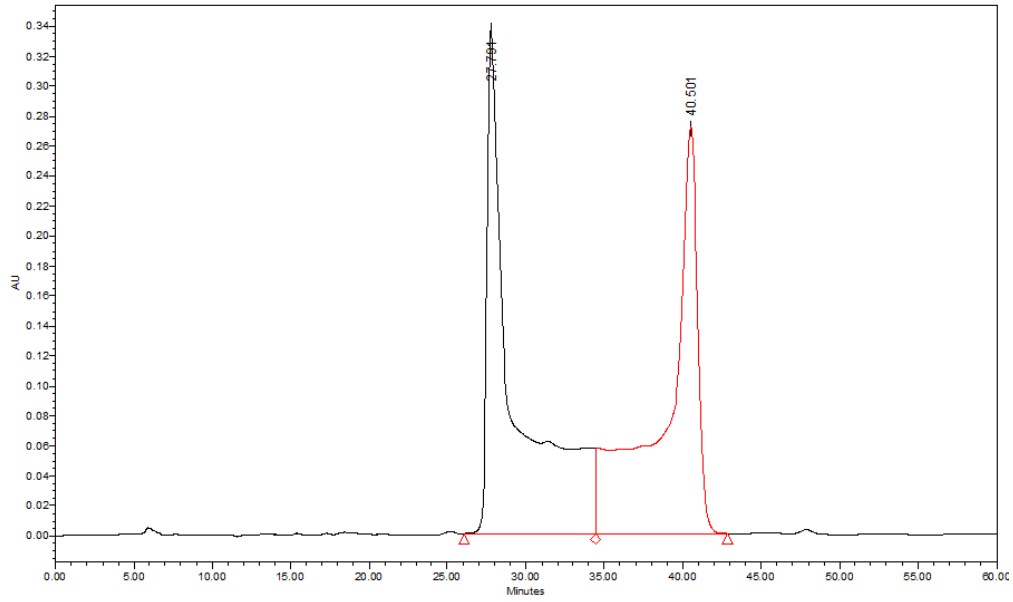
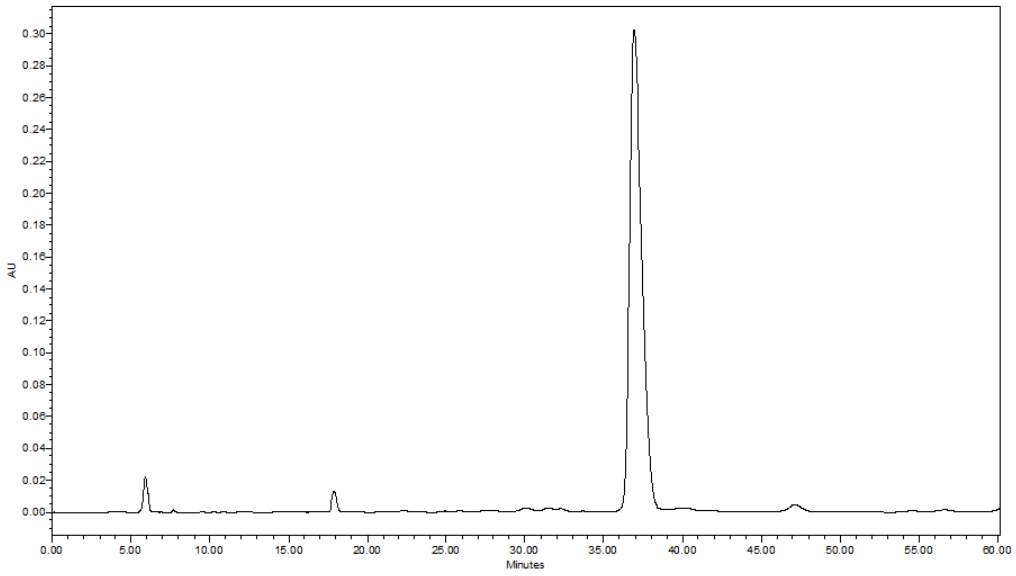
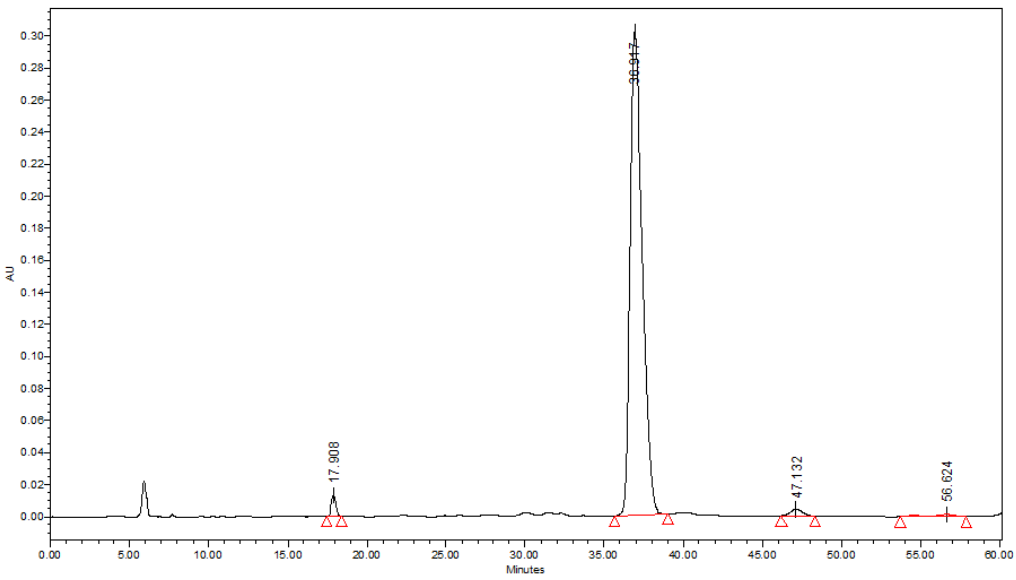


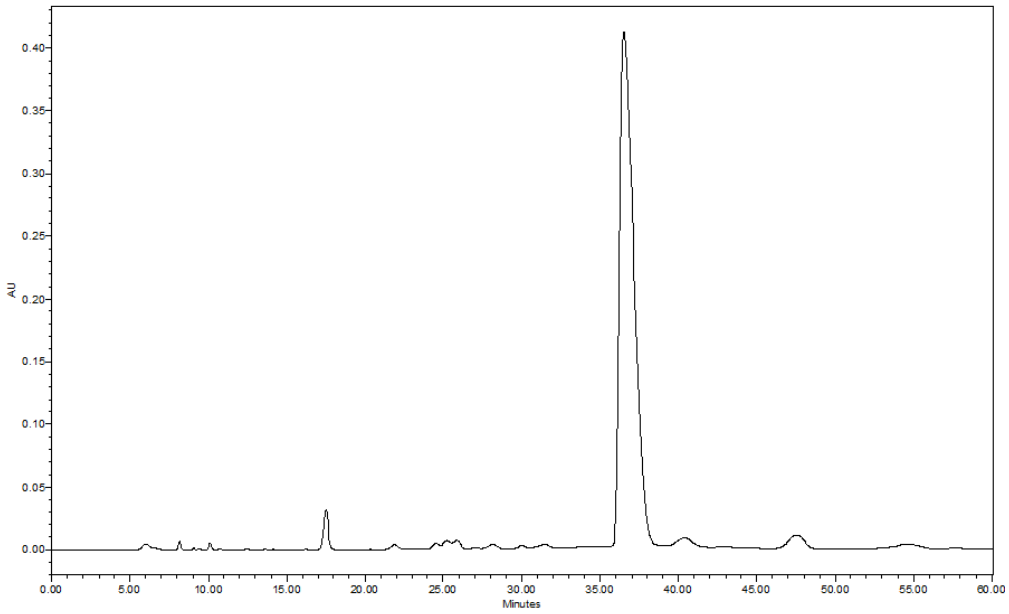
Table 2, entry 5: **7b** (1 g, 4.11 mmol); EtOH (55 mL); 35% HCl (requires 21 µL, 0.25 mmol: therefore charged 0.21 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (13.2 mg, 0.0147 mmol).

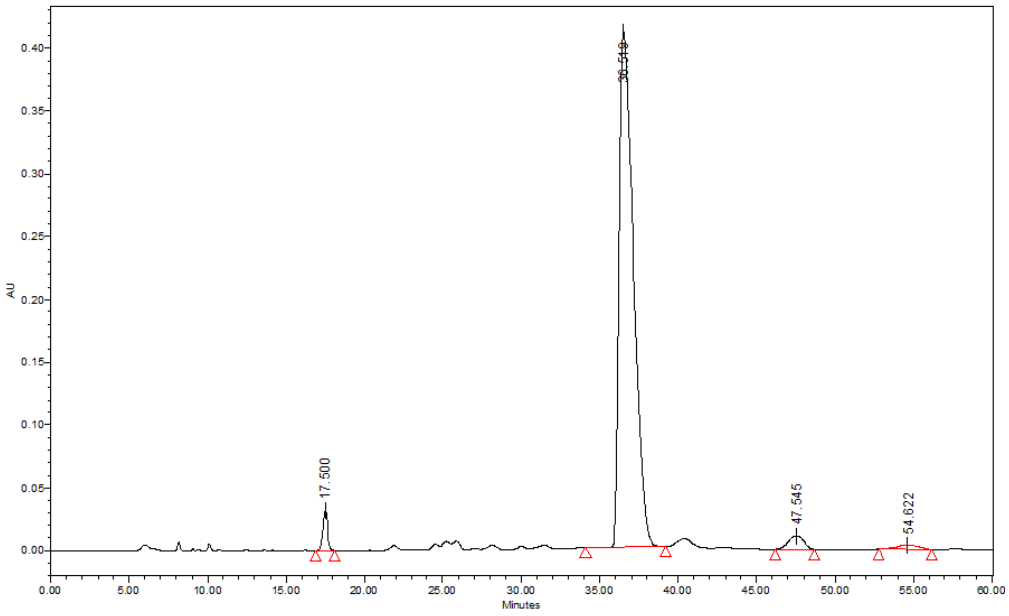




8b-ent = 1.56A% **8b** = 96.34A% **10b** = 1.29A% **10b-ent** = 0.81A%

Table 2, entry 13: **7b** (4.4 g, 18.0 mmol); IPA (55 mL); 35% HCl (requires 90 µL, 1.08 mmol: therefore charged 0.90 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.18 mL = 7.6 mg, 0.18 mmol); $Ru(OAc)_2$[(S)-tol-BINAP)] (57.7 mg, 0.0642 mmol).





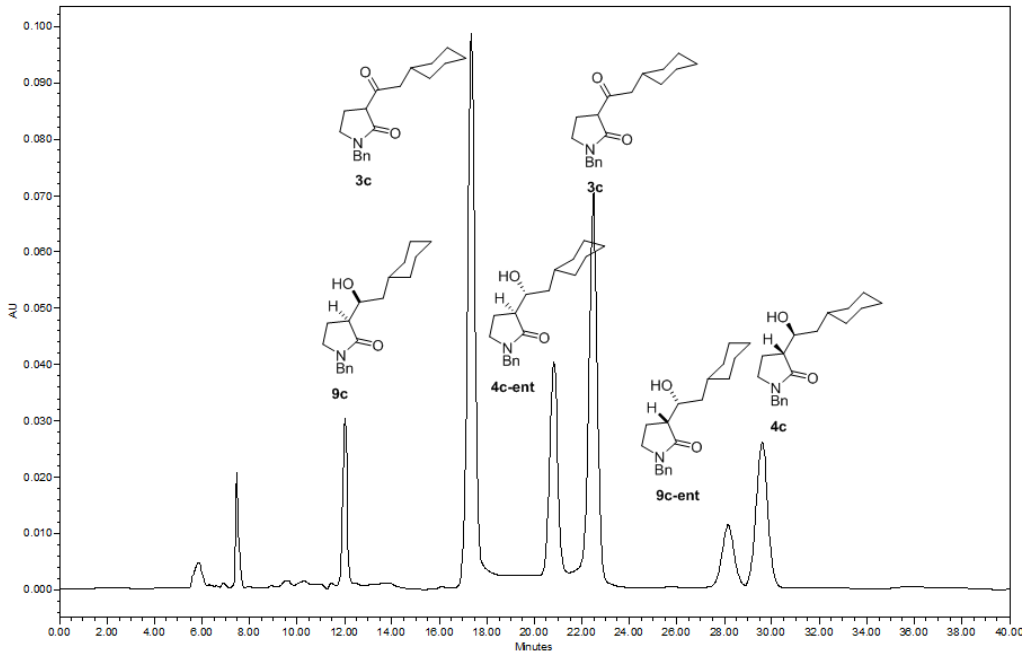
8b-ent = 2.42A% **8b** = 93.87A% **10b** = 2.52A% **10b-ent** = 1.20A%

Asymmetric Reduction of 1-Benzyl-3-(2-cyclohexylacetyl)pyrrolidin-2-one (3c)

Chiral HPLC method used:

Column: Lux-Cellulose-2, 4.6 x 250 mm 3 µm particle. Mobile Phase: 80/20 Hexane/IPA. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 5 µL or 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **3c** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**4c** and (±)-**9c**:



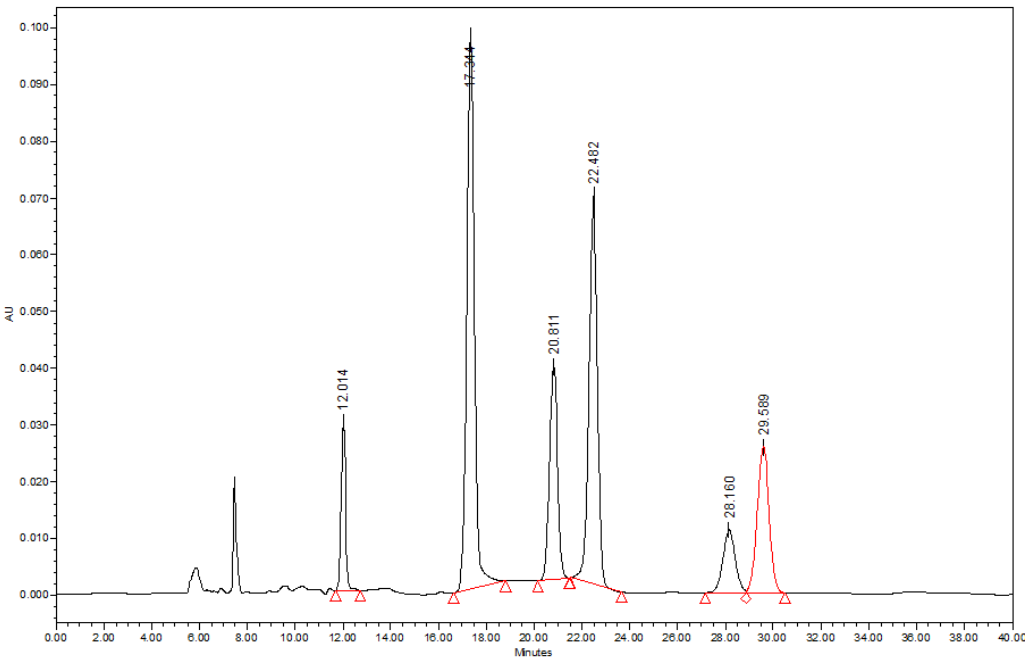
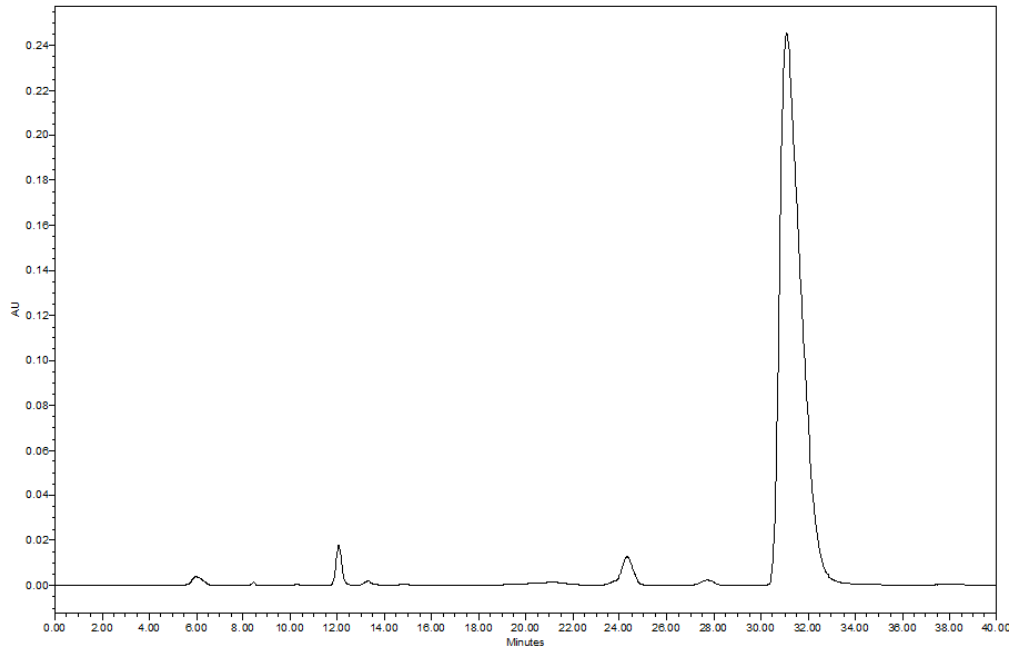
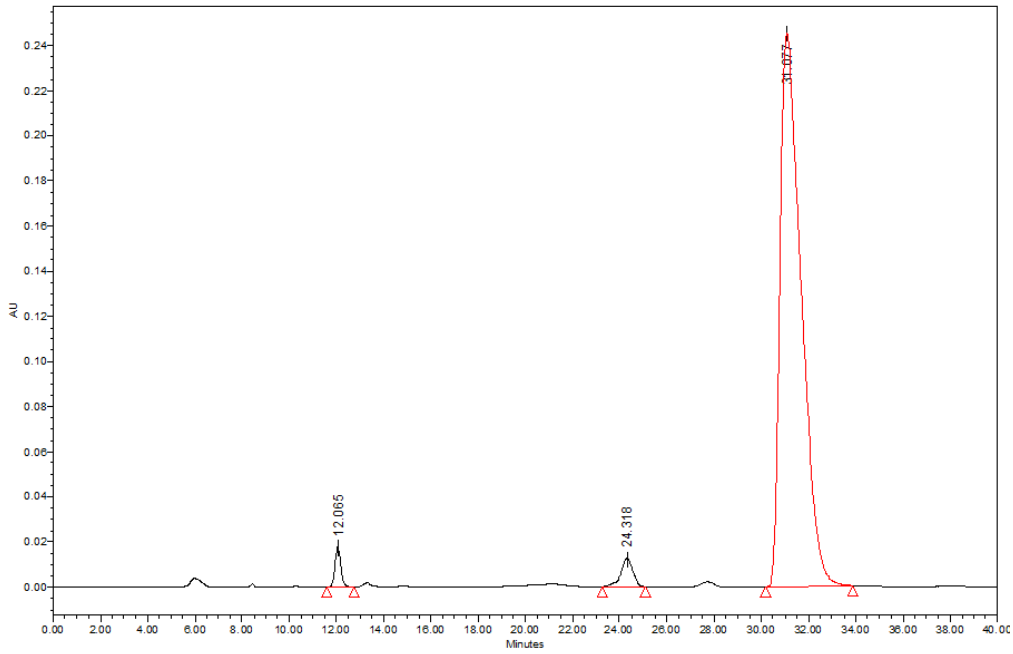


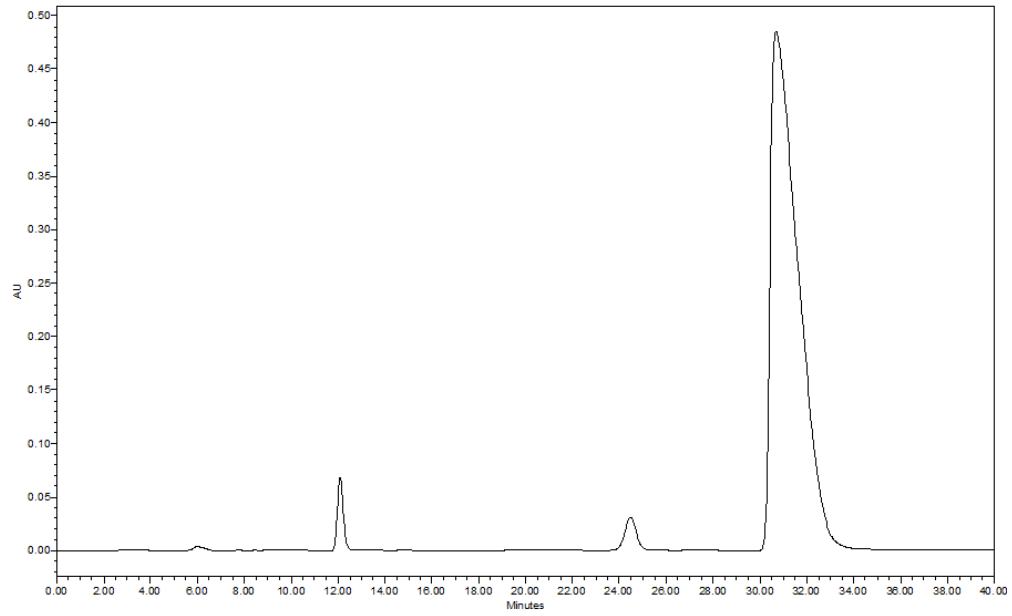
Table 2, entry 2: **3c** (1 g, 3.34 mmol); MeOH (55 mL); 35% HCl (requires 17 µL, 0.20 mmol: therefore charged 0.17 mL of a 10% stock solution of 35% HCl in MeOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (10.7 mg, 0.0119 mmol).

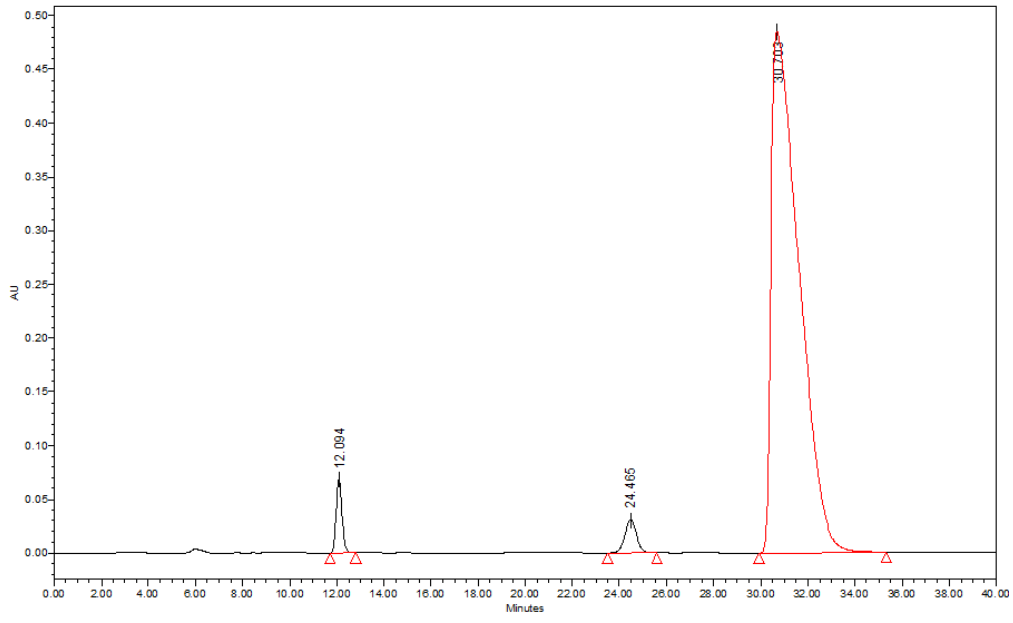




9c = 1.75A% **4c-ent** = 2.72A% **9c-ent** = ND **4c** = 95.53A%

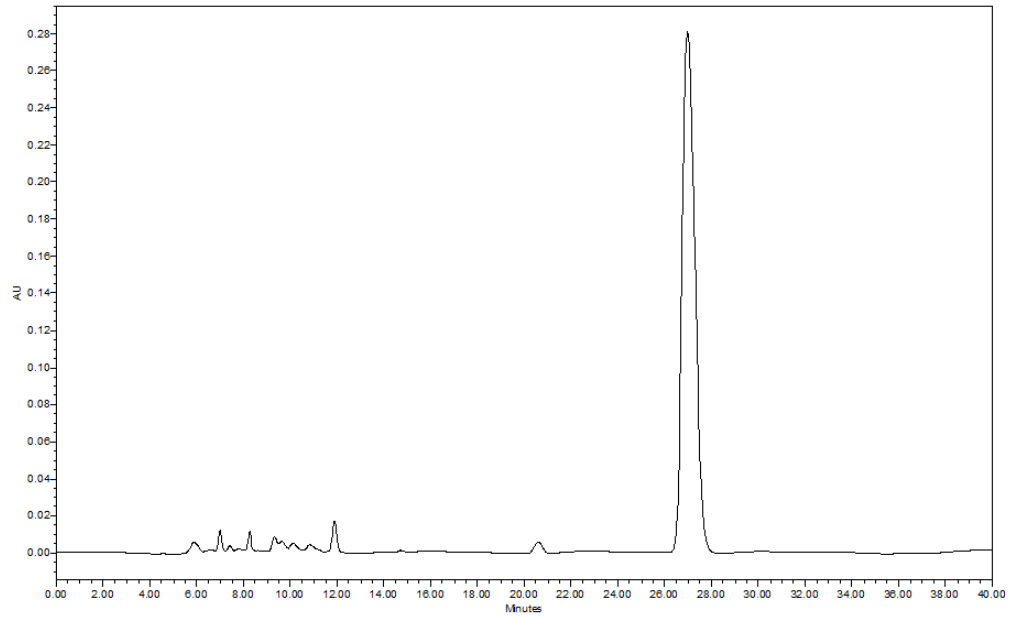
Table 2, entry 6: **3c** (1 g, 3.34 mmol); EtOH (55 mL); 35% HCl (requires 17 µL, 0.20 mmol: therefore charged 0.17 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (10.7 mg, 0.0119 mmol).

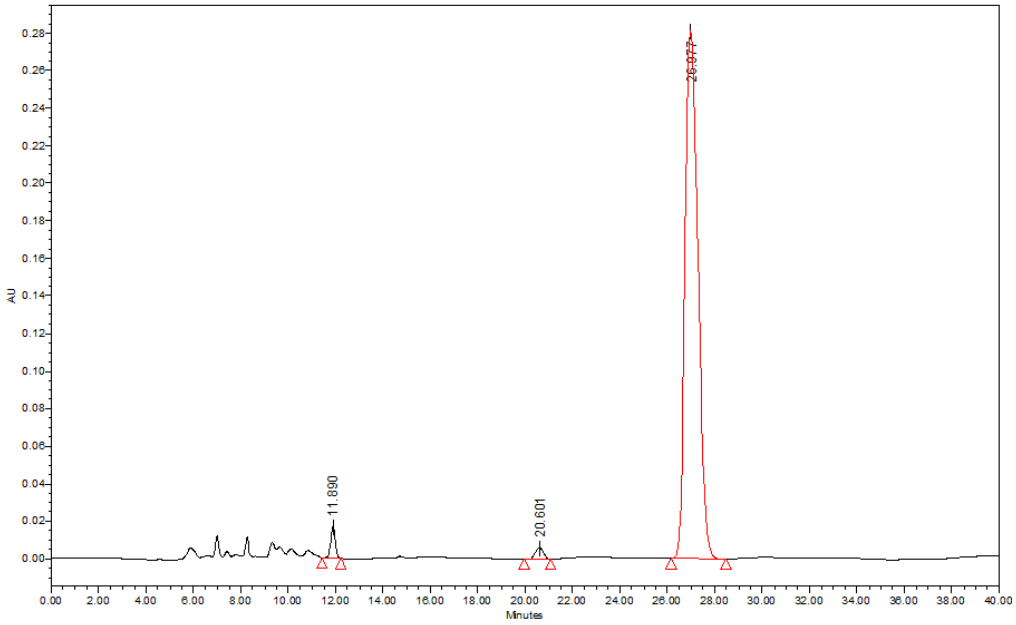




9c = 2.64A% **4c-ent** = 2.41A% **9c-ent** = ND **4c** = 94.95A%

Table 2, entry 14: **3c** (4.4 g, 14.7 mmol); IPA (55 mL); 35% HCl (requires 74 µL, 0.88 mmol: therefore charged 0.74 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.15 mL = 6.4 mg, 0.15 mmol); $Ru(OAc)_2$[(*S*)-tol-BINAP)] (47.1 mg, 0.0524 mmol).





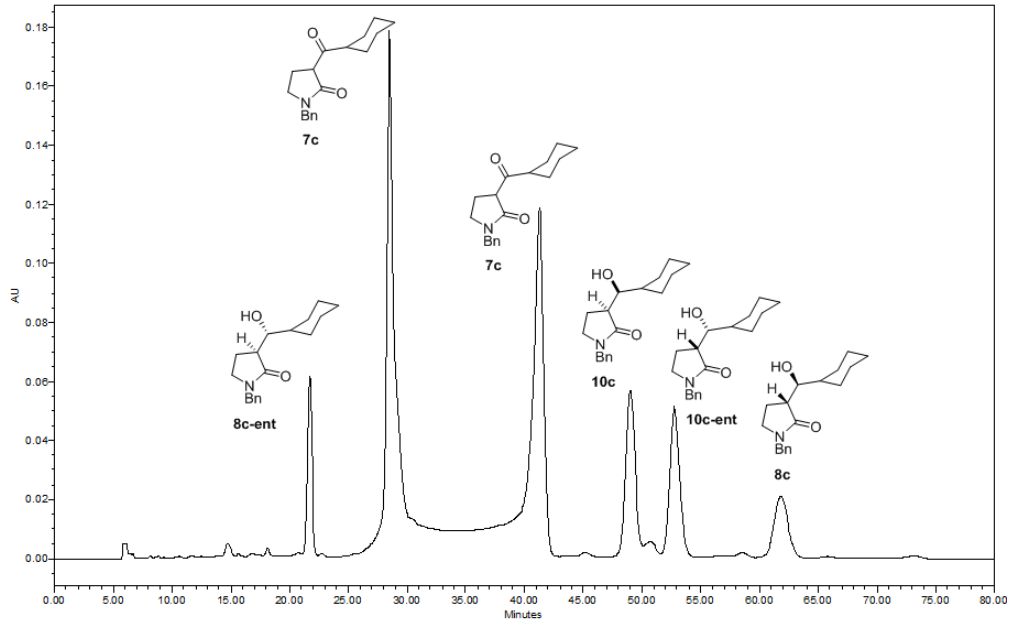
9c = 1.91A% **4c-ent** = 1.29A% **9c-ent** = ND **4c** = 96.80A%

Asymmetric Reduction of 1-Benzyl-3-(cyclohexanecarbonyl)pyrrolidin-2-one (7c)

Chiral HPLC method used:

Column: Lux-Cellulose-2, 4.6 x 250 mm 3 µm particle. Mobile Phase: 90/10 Hexane/IPA. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **7c** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**8c** and (±)-**10c**:



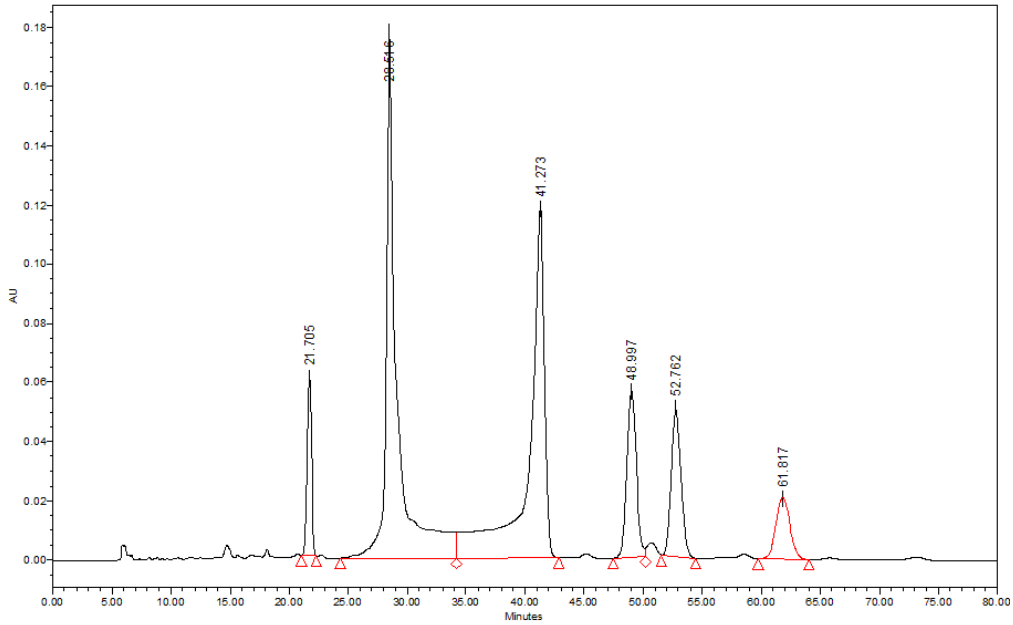
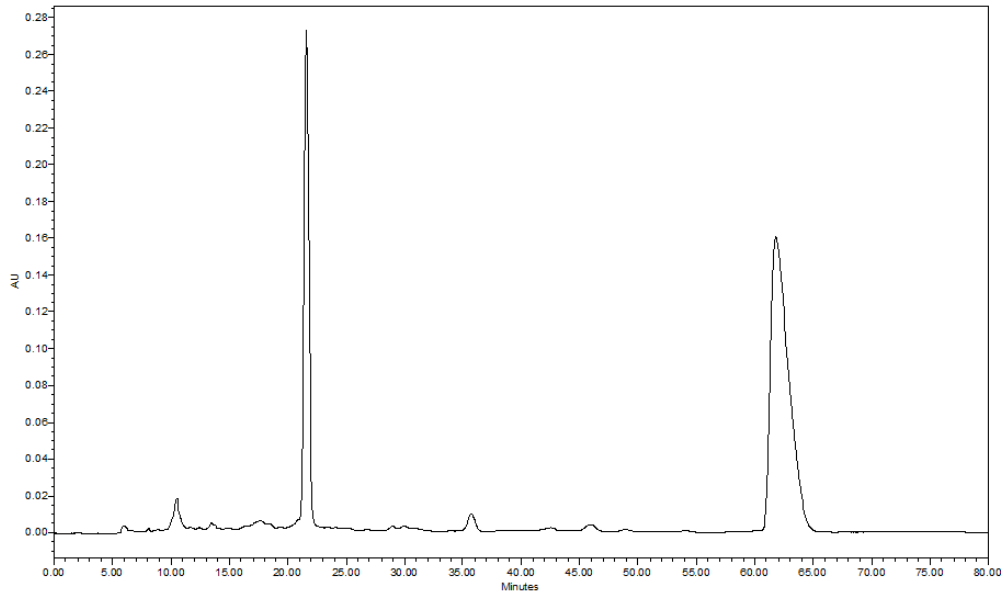
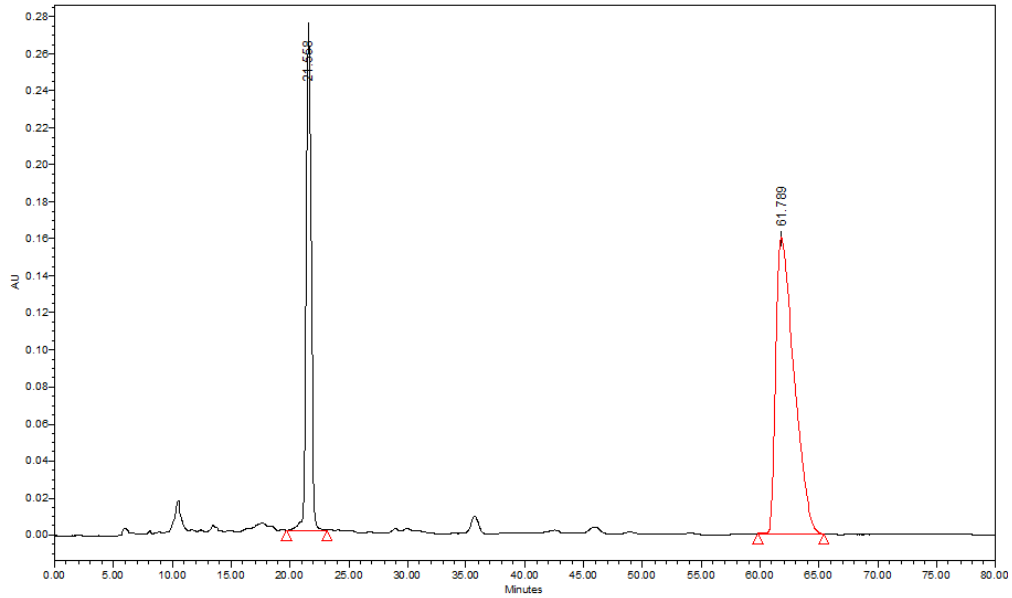


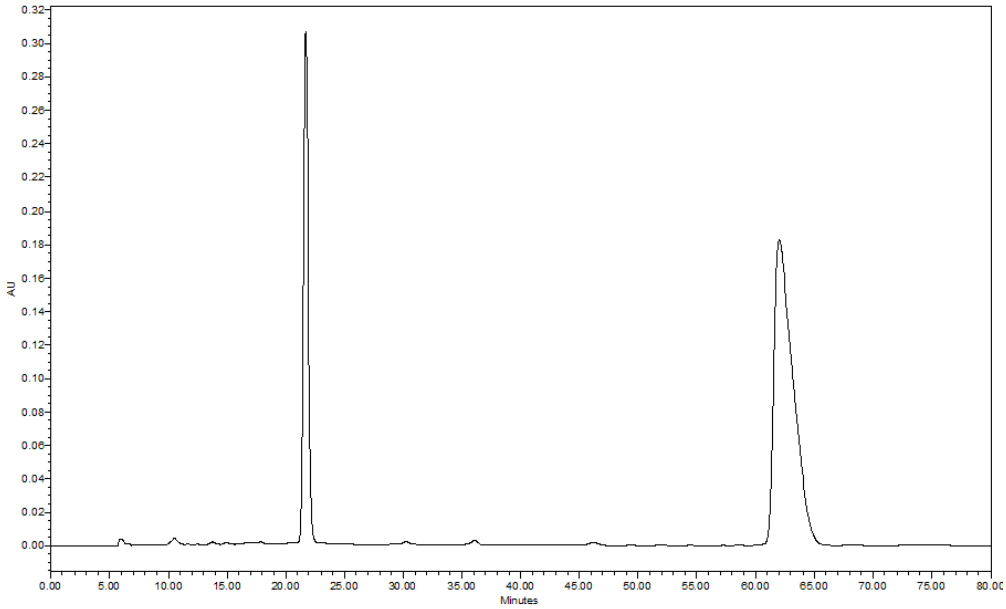
Table 2, entry 6: **7c** (1 g, 3.51 mmol); EtOH (55 mL); 35% HCl (requires 18 µL, 0.21 mmol: therefore charged 0.18 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (11.3 mg, 0.0125 mmol).

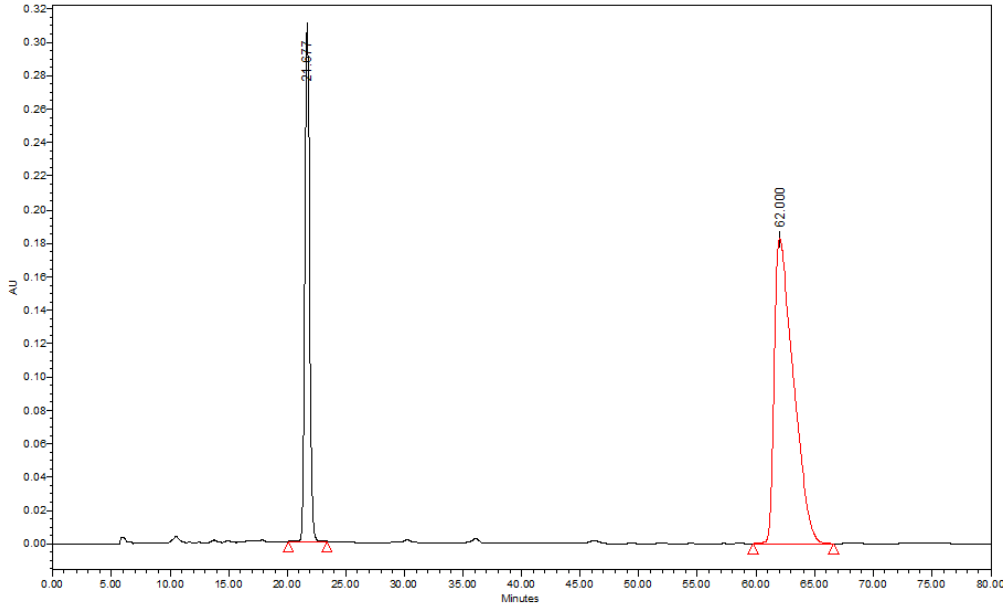




8c-ent = 32.25A% **10c** = ND **10c-ent** = ND **8c** = 67.75A%

Table 2, entry 14: **7c** (4.4 g, 15.4 mmol); IPA (55 mL); 35% HCl (requires 77 µL, 0.92 mmol: therefore charged 0.77 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.15 mL = 6.4 mg, 0.15 mmol); $Ru(OAc)_2$[(*S*)-tol-BINAP)] (49.4 mg, 0.055 mmol).





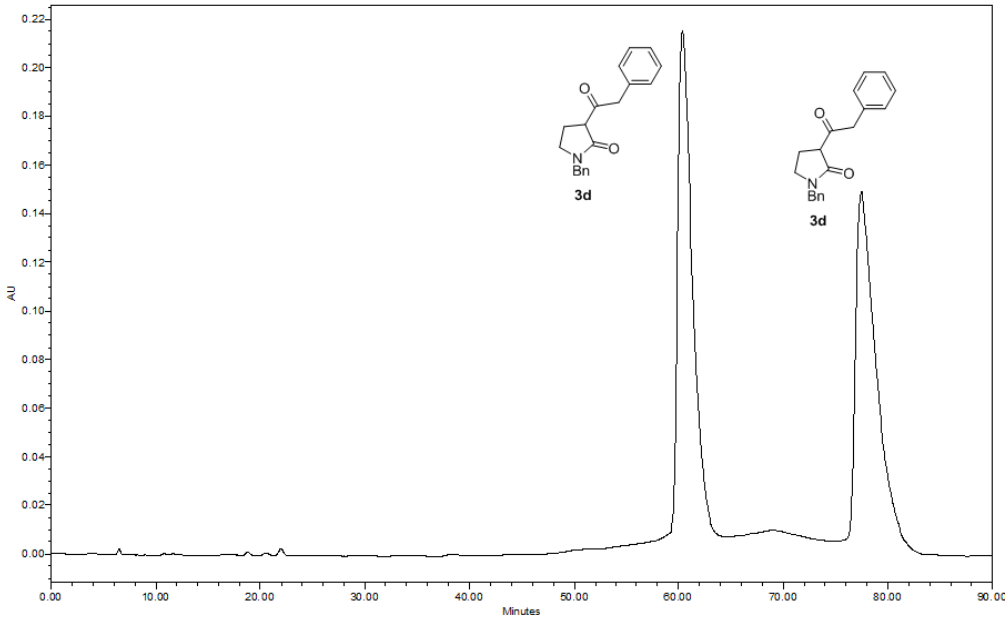
8c-ent = 30.73A% **10c** = ND **10c-ent** = ND **8c** = 69.27A%

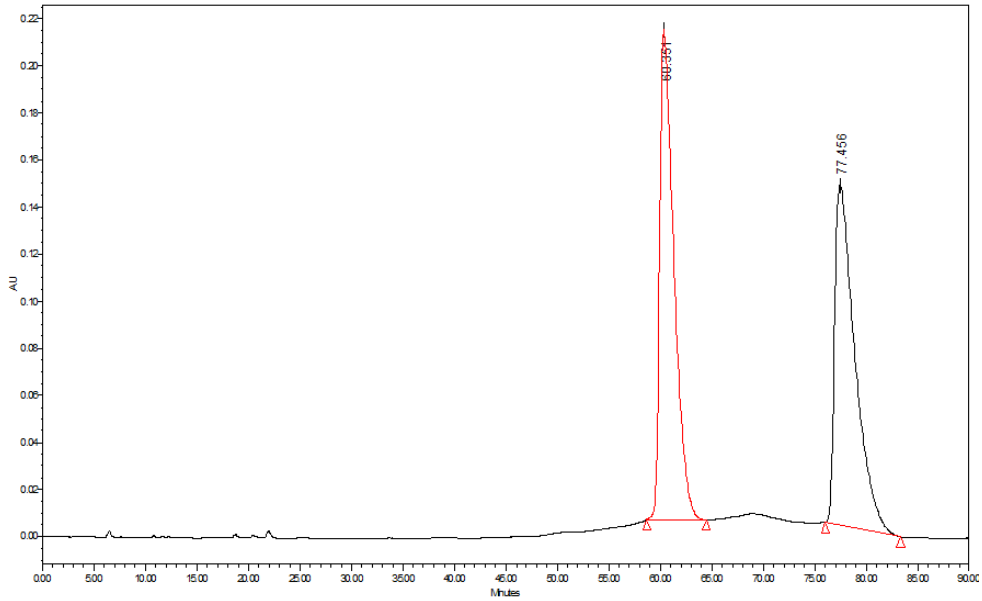
Asymmetric reduction of 1-Benzyl-3-(2-phenylacetyl)pyrrolidin-2-one (3d)

Chiral HPLC method used:

Column: OJH, 4.6 x 250 mm 3 µm particle. Mobile Phase: 80/20 Hexane/IPA. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 5 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

β-Keto-*γ*-lactam **3d:**

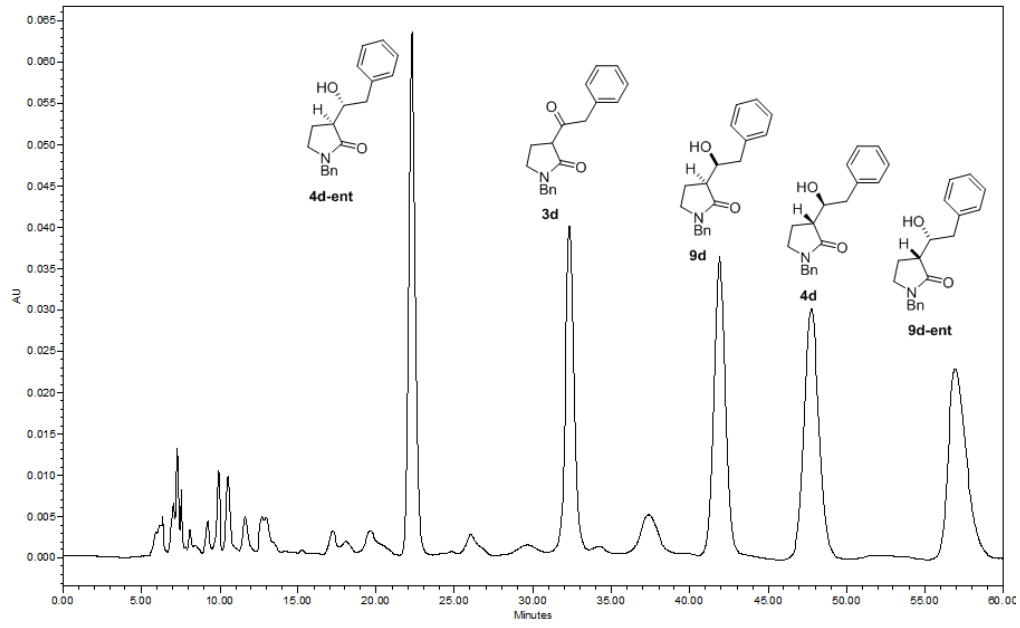




Chiral HPLC method used:

Column: Lux-Cellulose-2, 4.6 x 250 mm 3 µm particle. Mobile Phase: 80/20 Hexane/IPA. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 0.5 mL/min. Injection Volume: 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **3d** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**4d** and (±)-**9d**:



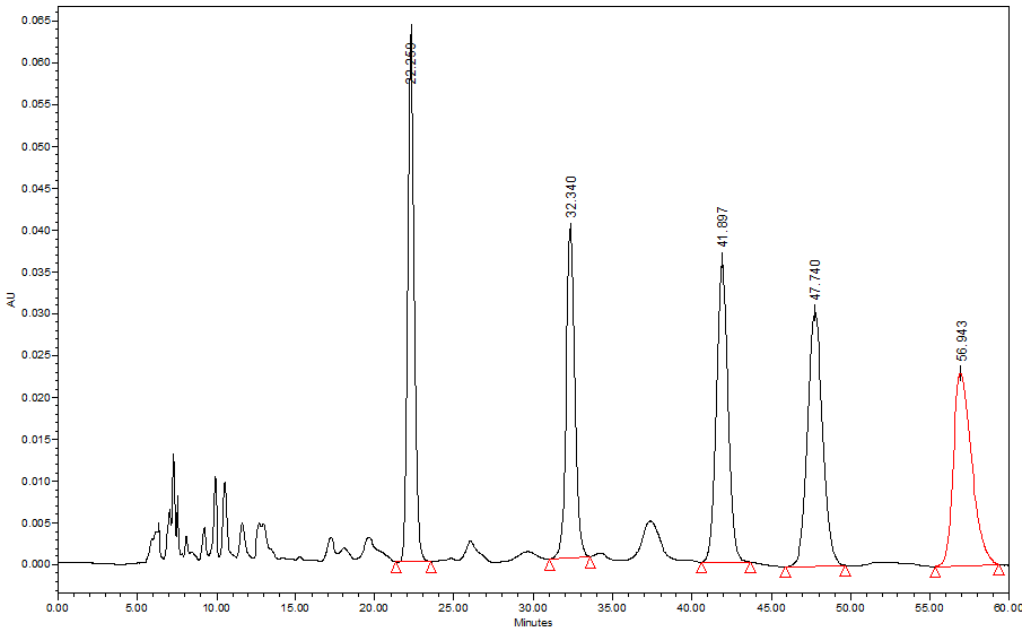
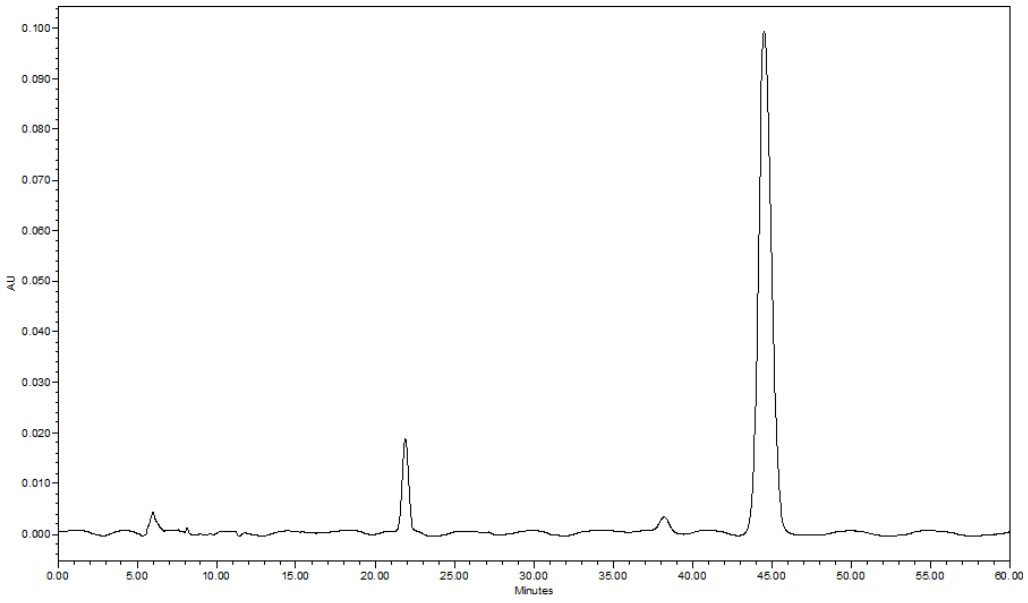
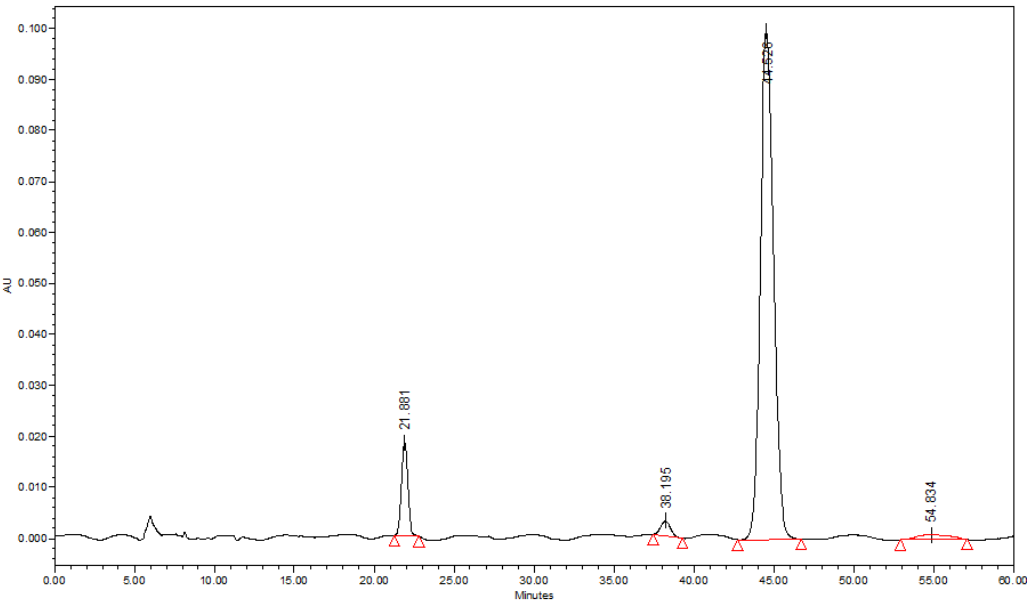


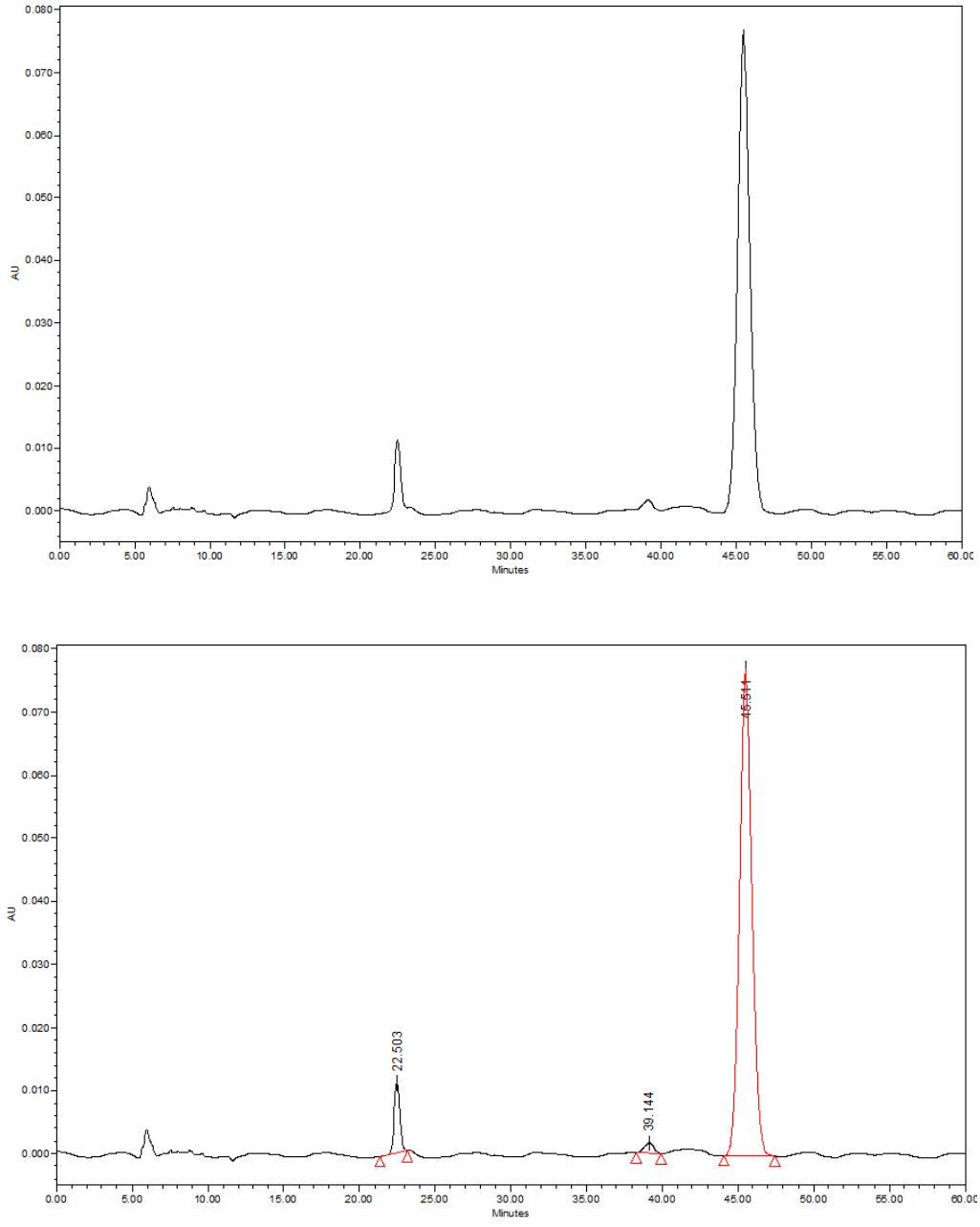
Table 2, entry 7: **3d** (1 g, 3.41 mmol); EtOH (55 mL); 35% HCl (requires 17 µL, 0.20 mmol: therefore charged 0.17 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (10.9 mg, 0.0122 mmol).





4d-ent = 7.35A% **9d** = 2.08A% **4d** = 88.47A% **9d-ent** = 2.10A%

Table 2, entry 15: **3d** (4.4 g, 15.0 mmol); IPA (55 mL); 35% HCl (requires 75 µL, 0.90 mmol: therefore charged 0.75 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.15 mL = 6.4 mg, 0.15 mmol); $Ru(OAc)_2$[(*S*)-tol-BINAP)] (48.1 mg, 0.0536 mmol).



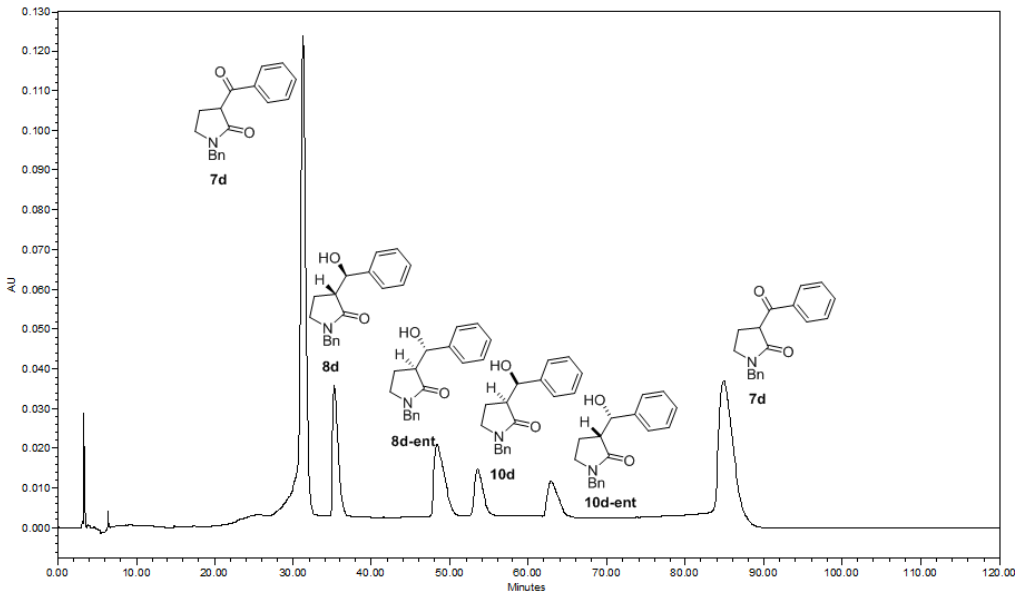
4d-ent = 6.16A% **9d** = 1.48A% **4d** = 92.36A% **9d-ent** = ND

Asymmetric Reduction of 3-Benzoyl-1-benzylpyrrolidin-2-one (7d)

Chiral HPLC method used:

Column: Chiralpak IA-3, 4.6 x 250 mm 3 µm particle. Mobile Phase: 95/5 Heptane/Ethanol. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 1 mL/min. Injection Volume: 5 µL or 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **7d** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**8d** and (±)-**10d**:



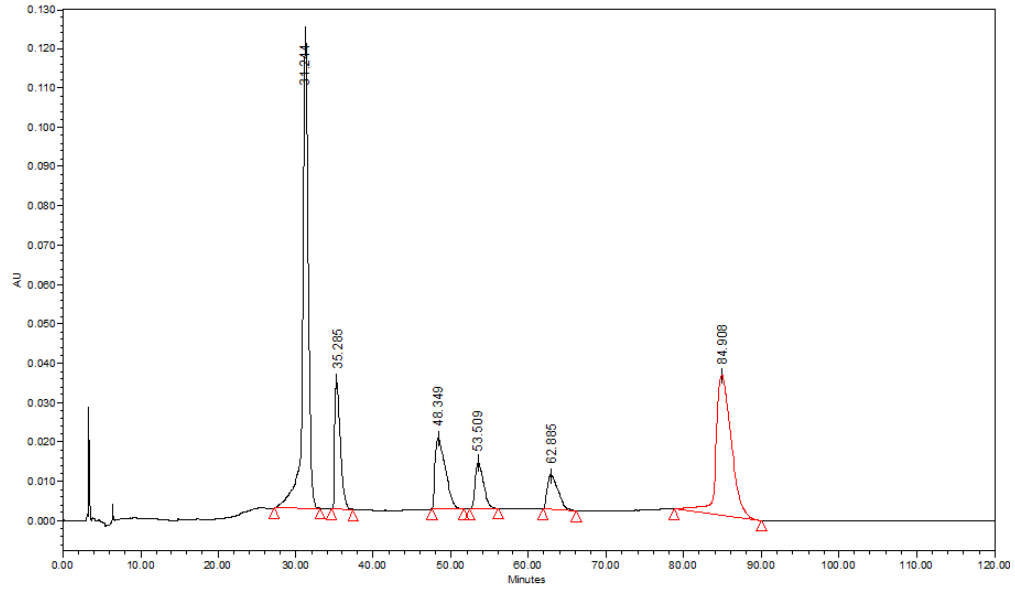
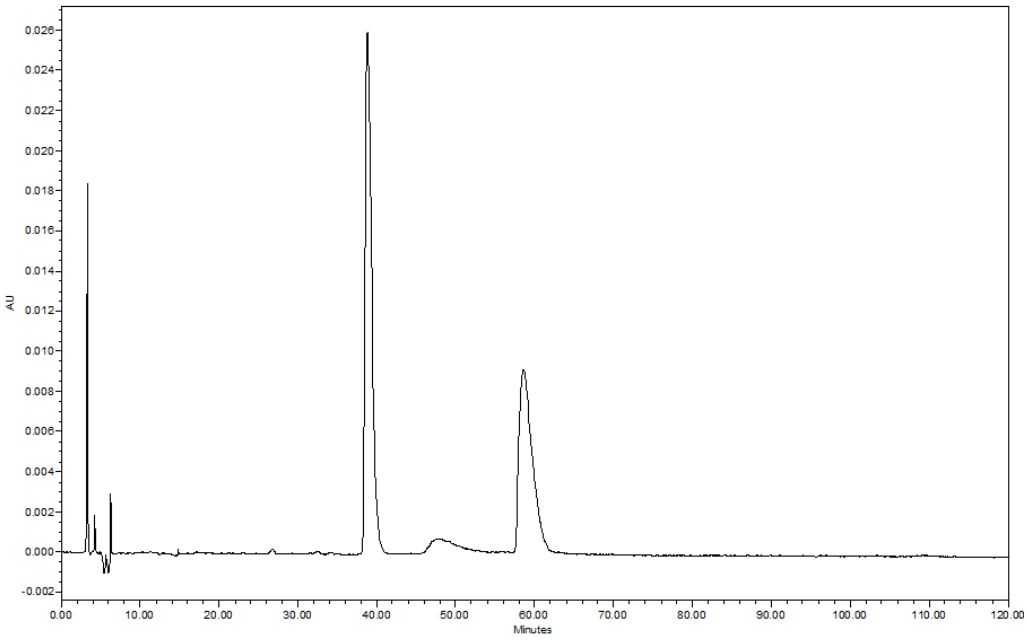
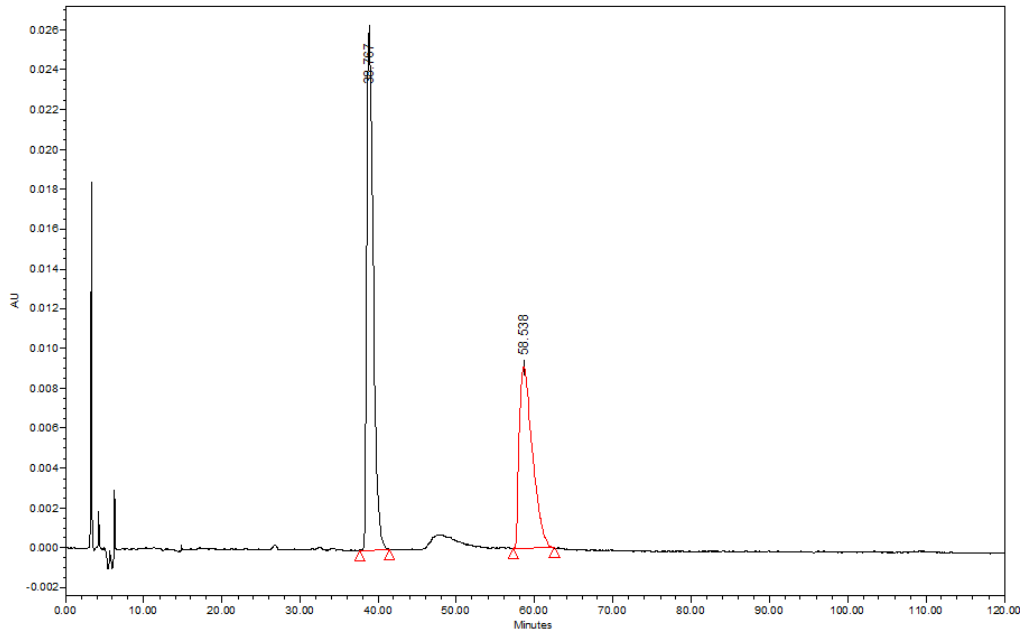


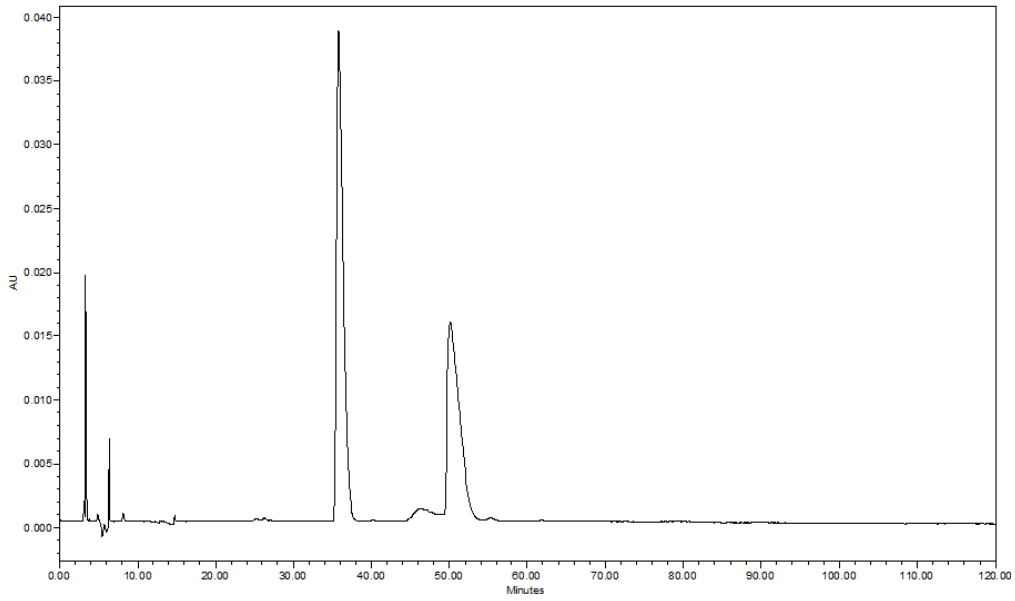
Table 2, entry 5: **7d** (1 g, 3.58 mmol); EtOH (55 mL); 35% HCl (requires 18 µL, 0.21 mmol: therefore charged 0.18 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (11.5 mg, 0.0128 mmol).

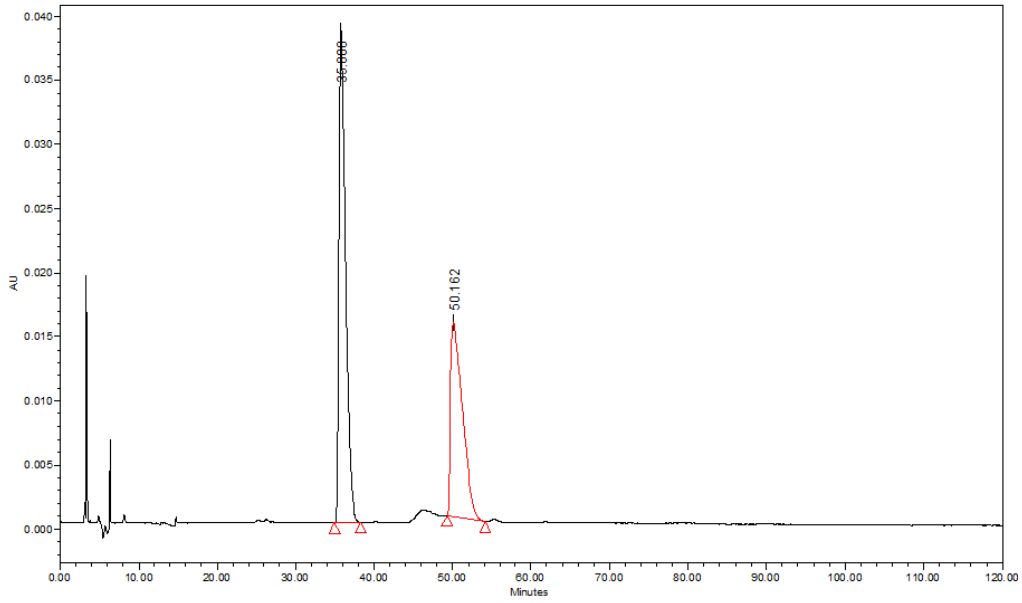




8d = 59.12A% **8d-ent** = 40.88A% **10a** = ND **10a-ent** = ND

Table 2, entry 15: **7d** (4.4 g, 15.8 mmol); IPA (55 mL); 35% HCl (requires 79 µL, 0.95 mmol: therefore charged 0.79 mL of a 10% stock solution of 35% HCl in IPA); LiCl 0.1M in IPA (0.16 mL = 6.8 mg, 0.16 mmol); $Ru(OAc)_2$[(*S*)-tol-BINAP)] (50.5 mg, 0.0563 mmol).





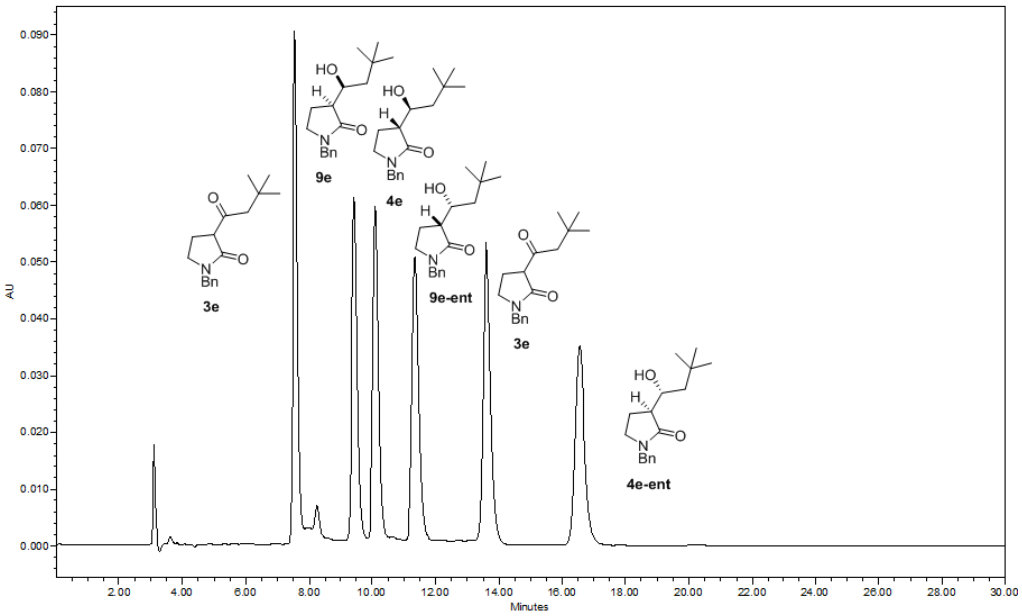
8d = 57.64A% **8d-ent** = 42.36A% **10d** = ND **10d-ent** = ND

Asymmetric Reduction of 1-Benzyl-3-(3,3-dimethylbutanoyl)pyrrolidin-2-one (3e)

Chiral HPLC method used:

Column: Chiralpak IA-3, 4.6 x 250 mm 3 µm particle. Mobile Phase: 90/10 Heptane/Ethanol. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 1 mL/min. Injection Volume: 5 µL or 10 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

Mixture of *β*-keto-*γ*-lactam **3e** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**4e** and (±)-**9e**:



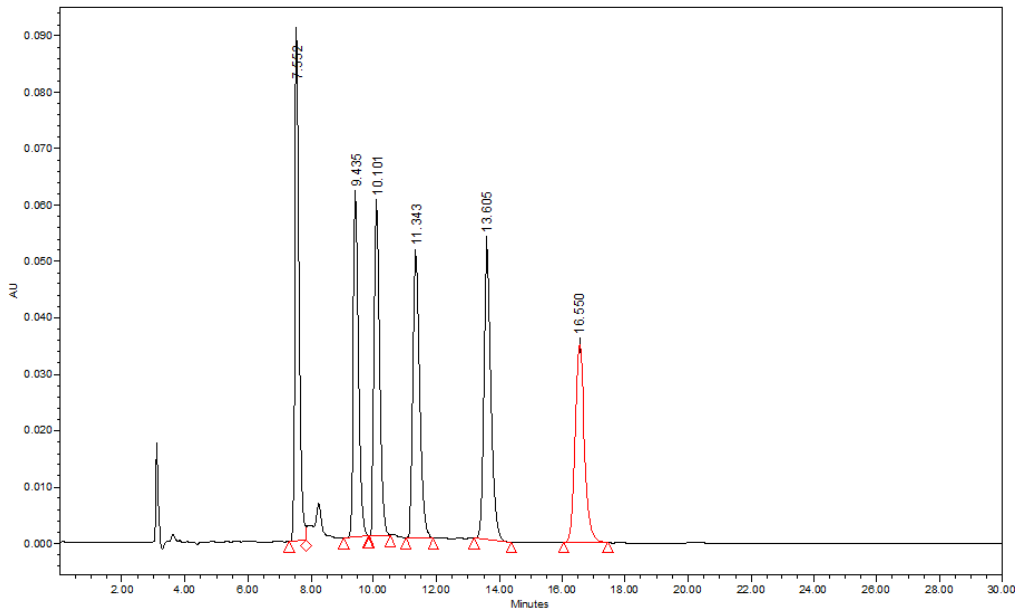
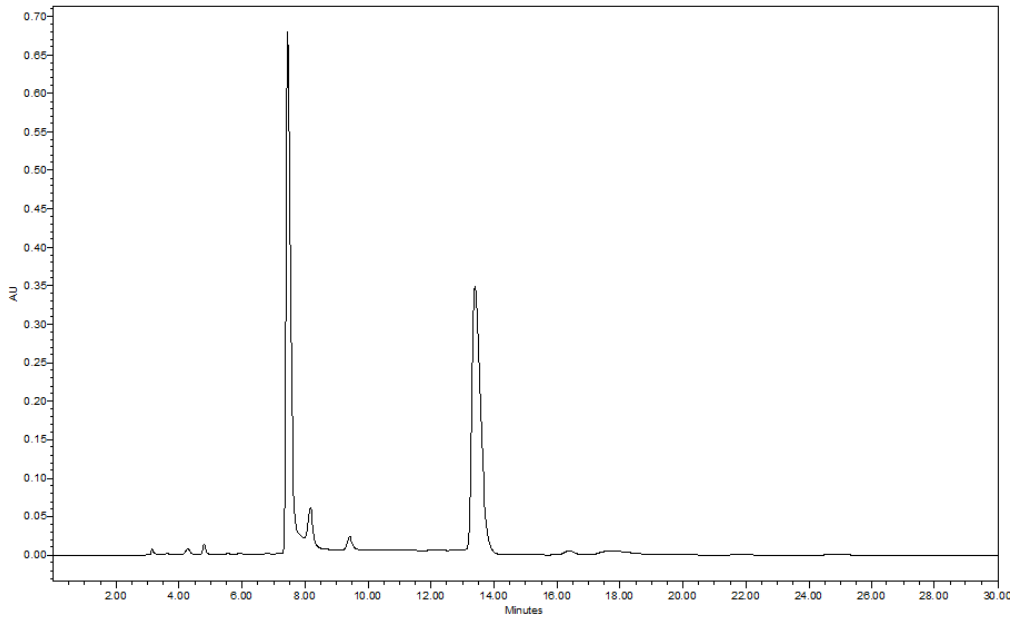
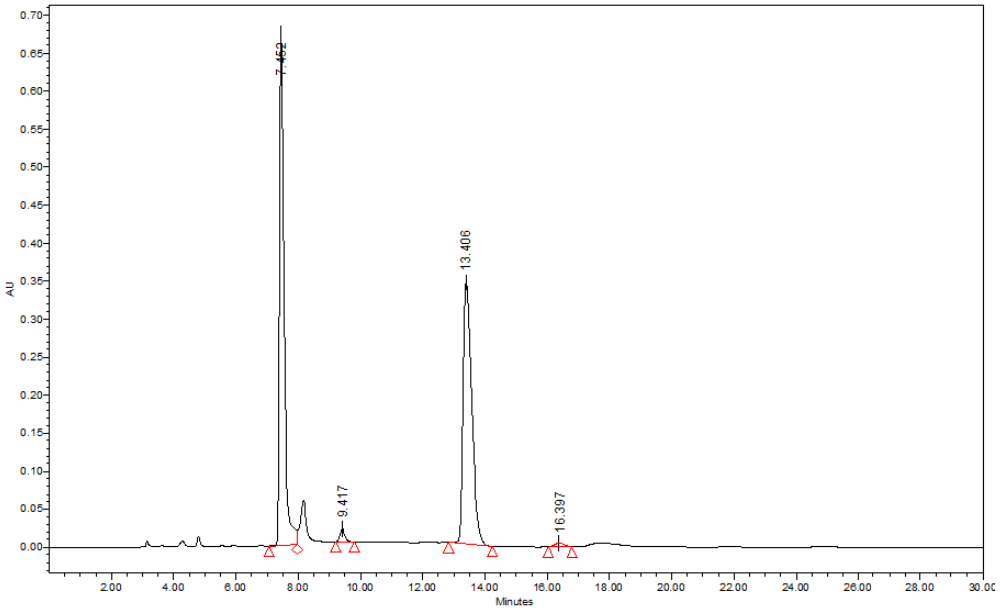


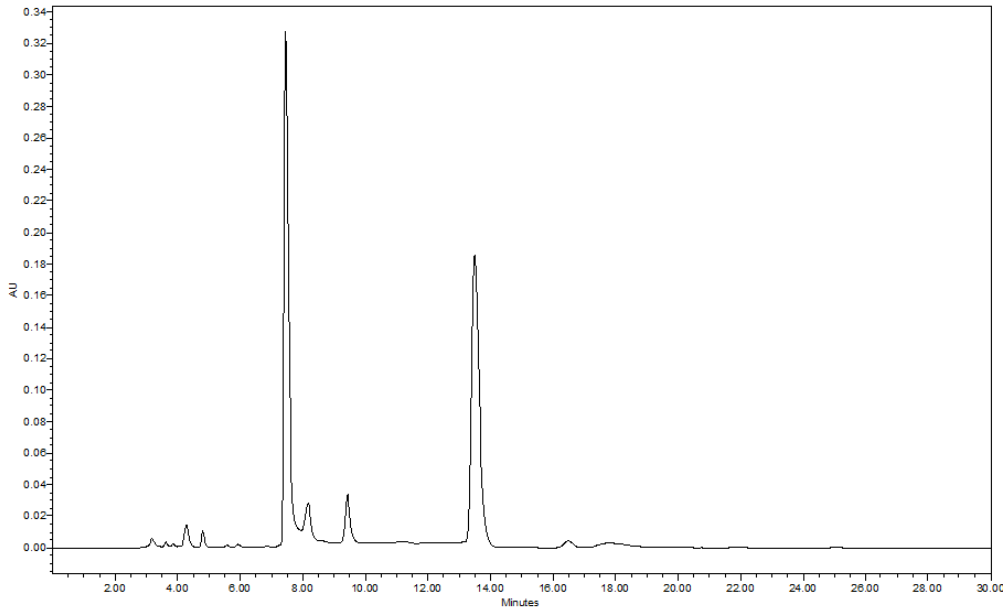
Table 2, entry 3: **3e** (1 g, 3.66 mmol); MeOH (55 mL); 35% HCl (requires 18 µL, 0.22 mmol: therefore charged 0.18 mL of a 10% stock solution of 35% HCl in MeOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (11.7 mg, 0.0131 mmol).

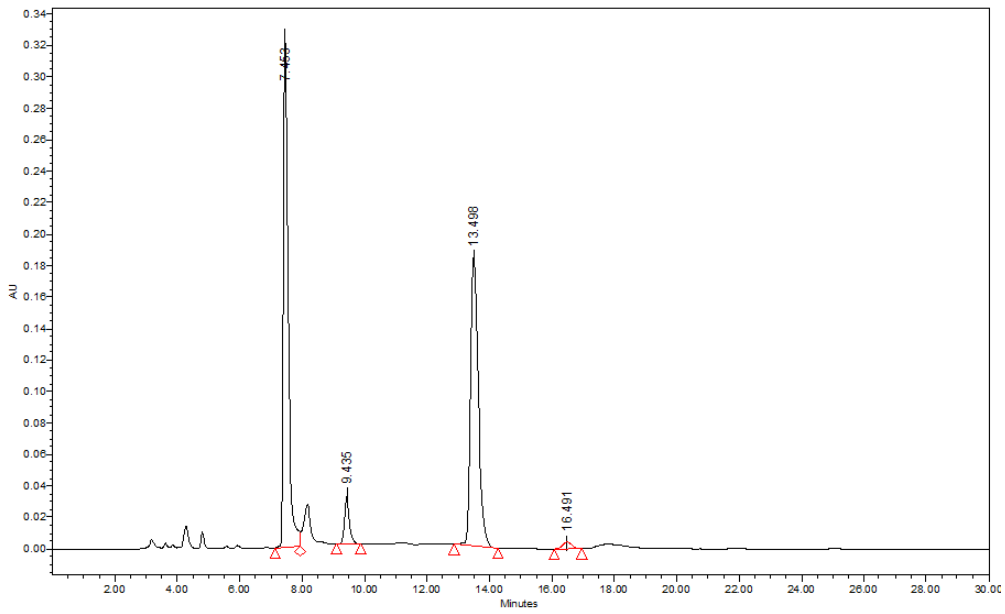




3e = 50.46A% **9e** = ND **4e** = 1.71A% **9e-ent** = ND **3e** = 47.08A% **4e-ent** = 0.75A%

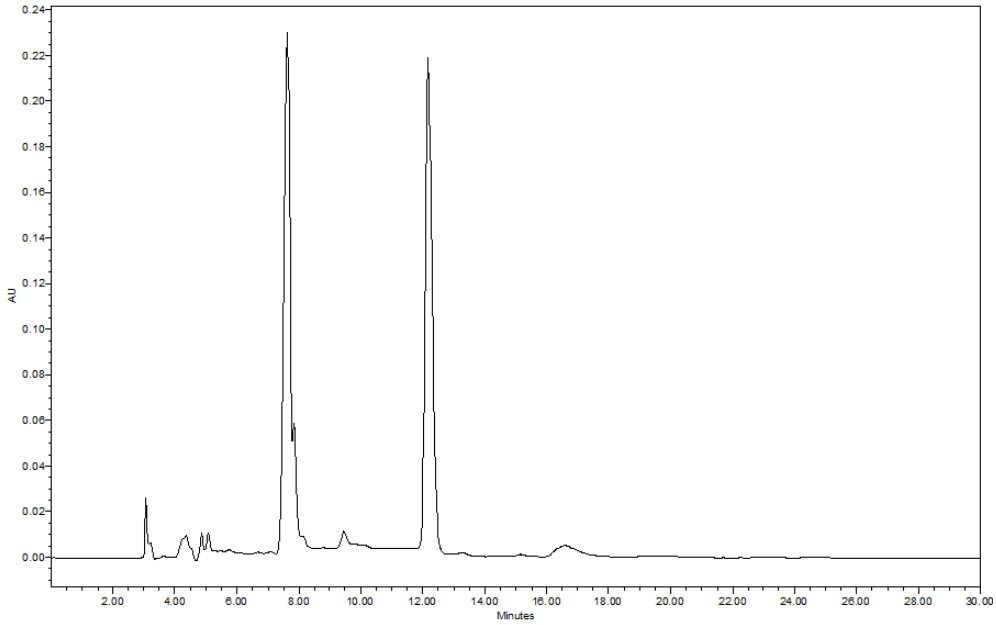
Table 2, entry 8: **3e** (1 g, 3.66 mmol); EtOH (55 mL); 35% HCl (requires 18 µL, 0.22 mmol: therefore charged 0.18 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (11.7 mg, 0.0131 mmol).

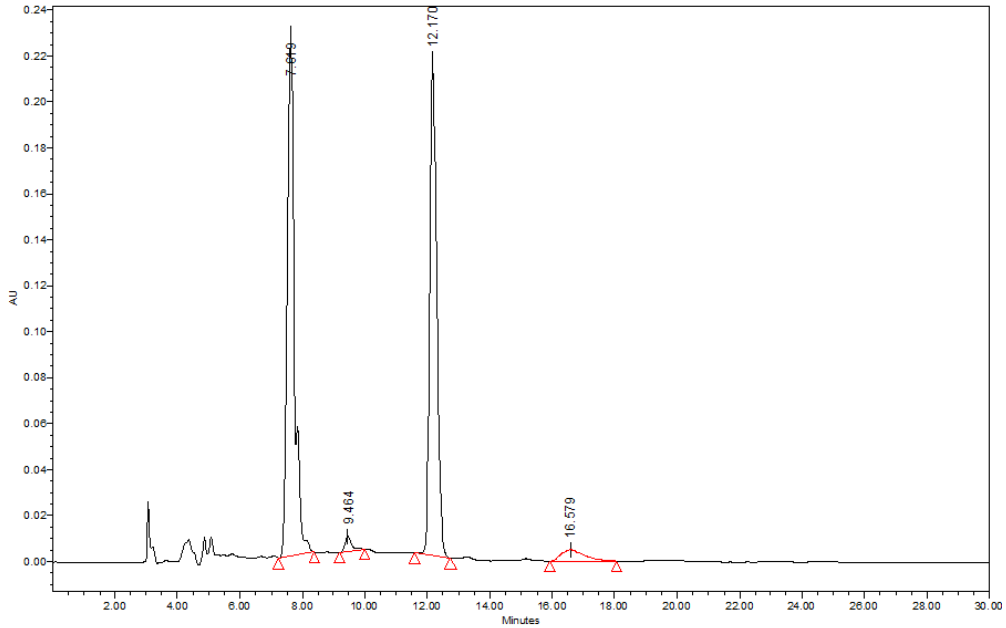




3e = 48.17A% **9e** = ND **4e** = 5.23A% **9e-ent** = ND **3e** = 45.45A% **4e-ent** = 1.15A%

Table 2, entry 10: **3e** (1 g, 3.66 mmol); CF_3CH_2OH (55 mL); 35% HCl (requires 18 µL, 0.22 mmol: therefore charged 0.18 mL of a 10% stock solution of 35% HCl in EtOH); $Ru(OAc)_2$[(S)-tol-BINAP)] (11.7 mg, 0.0131 mmol).





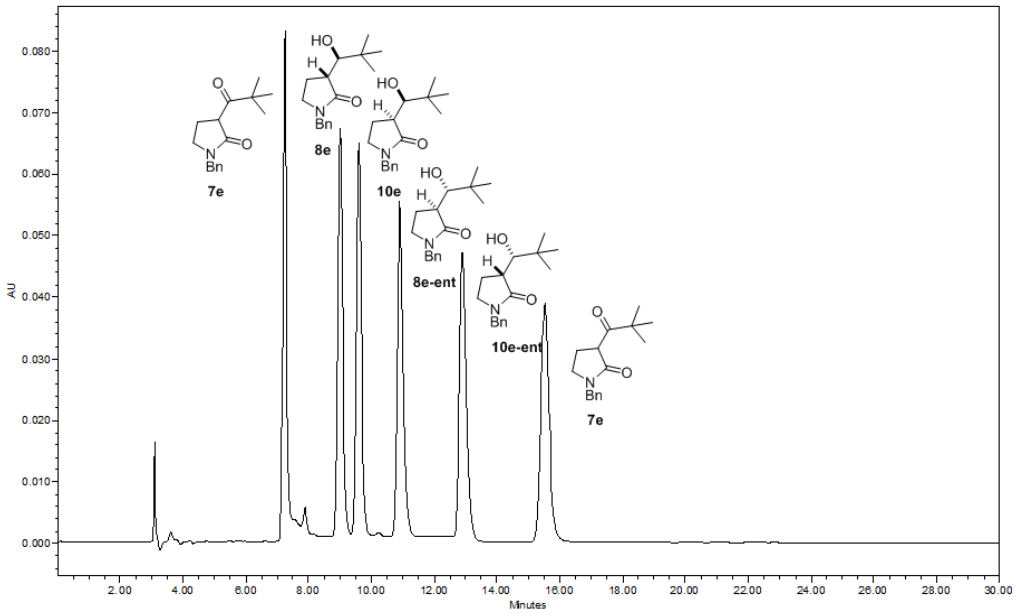
3e = 52.09A% **9e** = ND **4e** = 1.27A% **9e-ent** = ND **3e** = 43.52A% **4e-ent** = 3.12A%

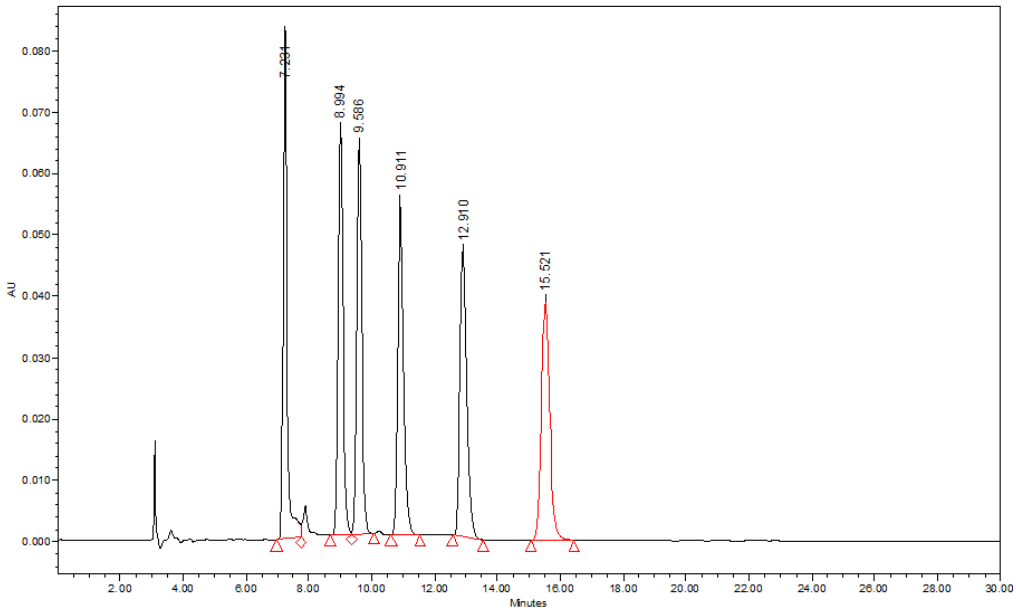
Asymmetric Reduction of 1-Benzyl-3-pivaloylpyrrolidin-2-one (7e)

Chiral HPLC method used:

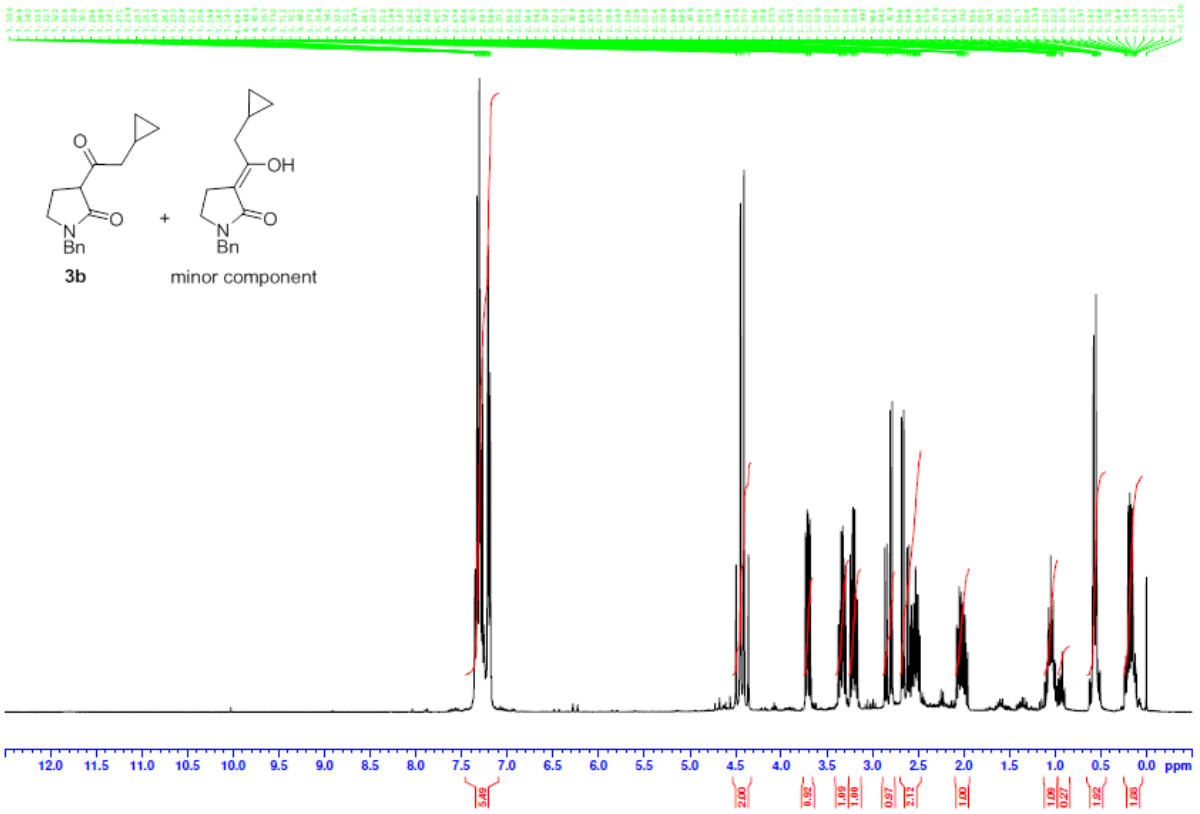
Column: Chiralpak IA-3, 4.6 x 250 mm 3 µm particle. Mobile Phase: 95/5 Heptane/Ethanol. Samples were prepared at a concentration of approximately 1 mg/mL in IPA. Flow Rate: 1 mL/min. Injection Volume: 5 µL. Column Temperature: 25 °C. Detection Wavelength: 220 nm.

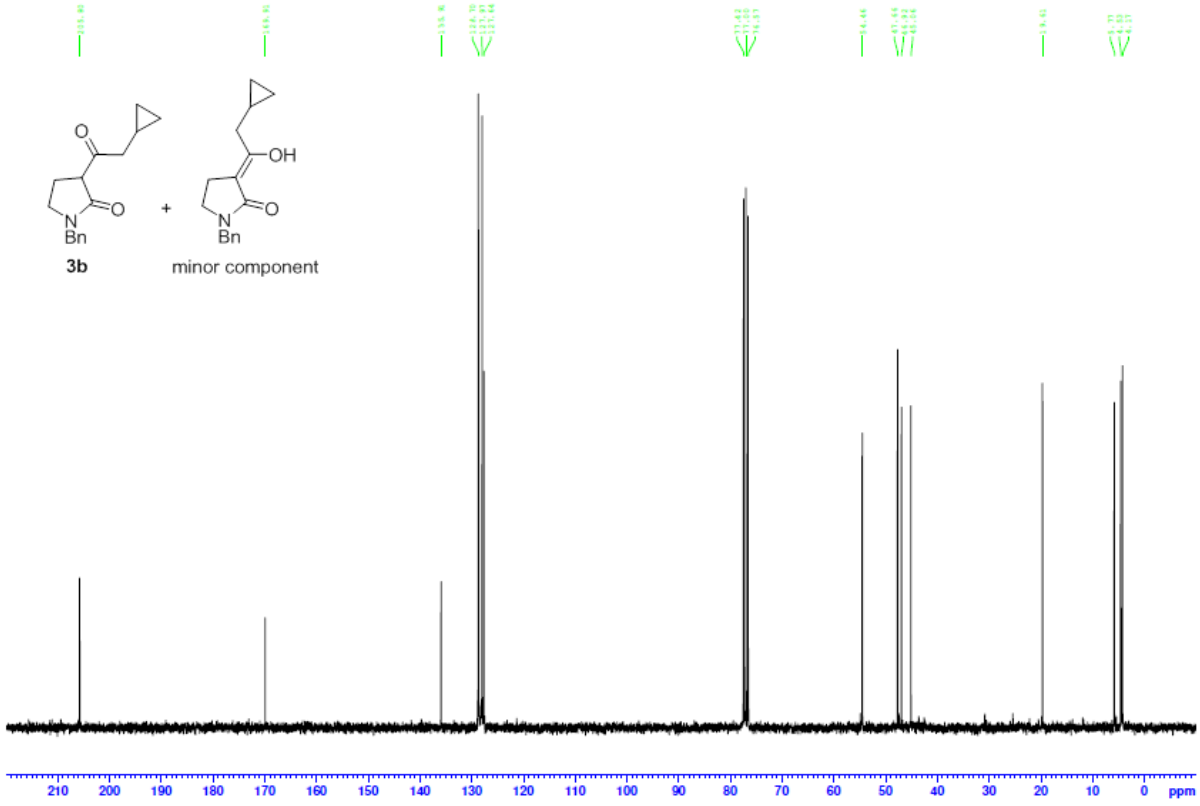
Mixture of *β*-keto-*γ*-lactam **7e** and diastereomeric *β*-hydroxy-*γ*-lactams (±)-**8e** and (±)-**10e**:

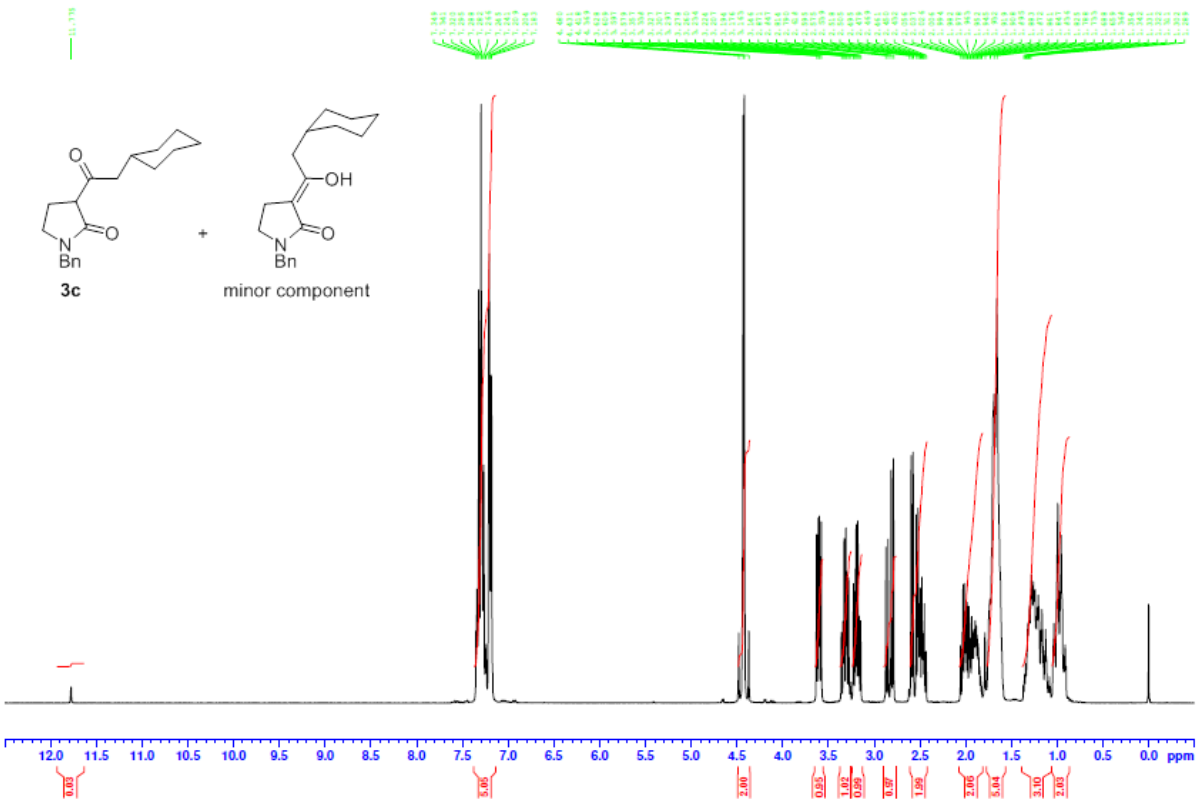


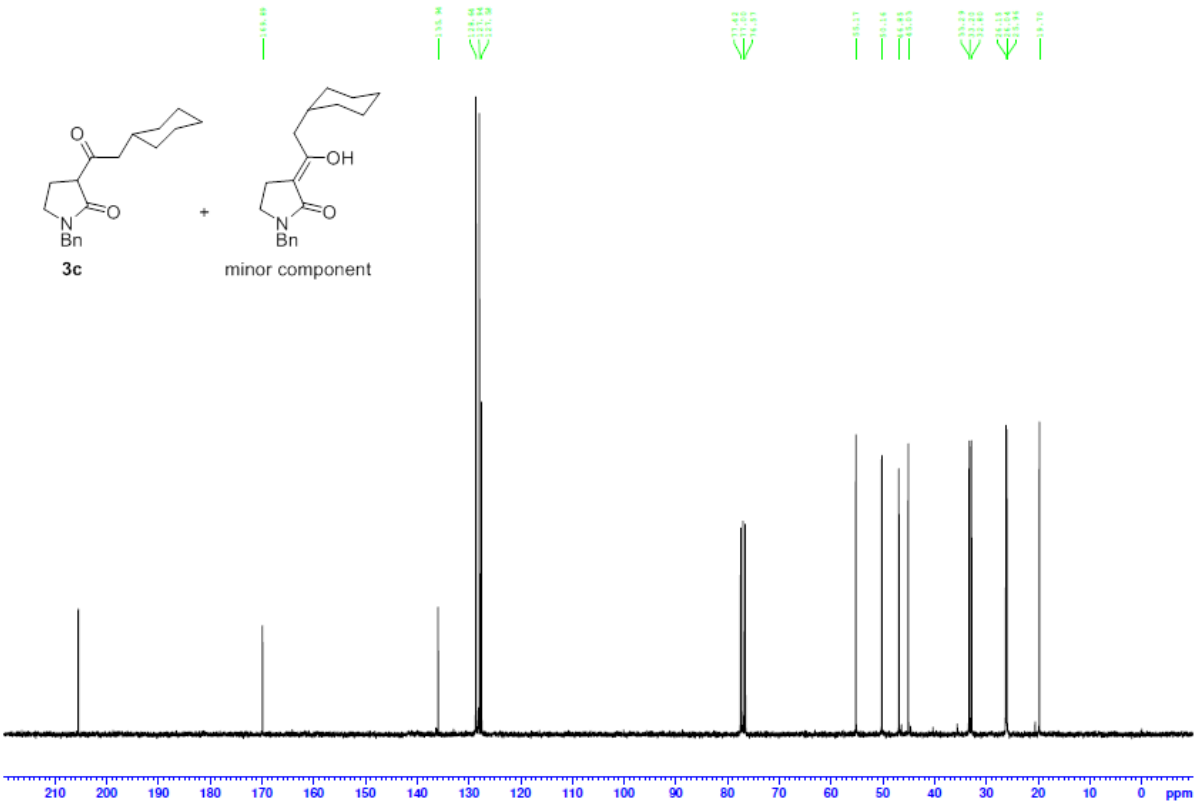


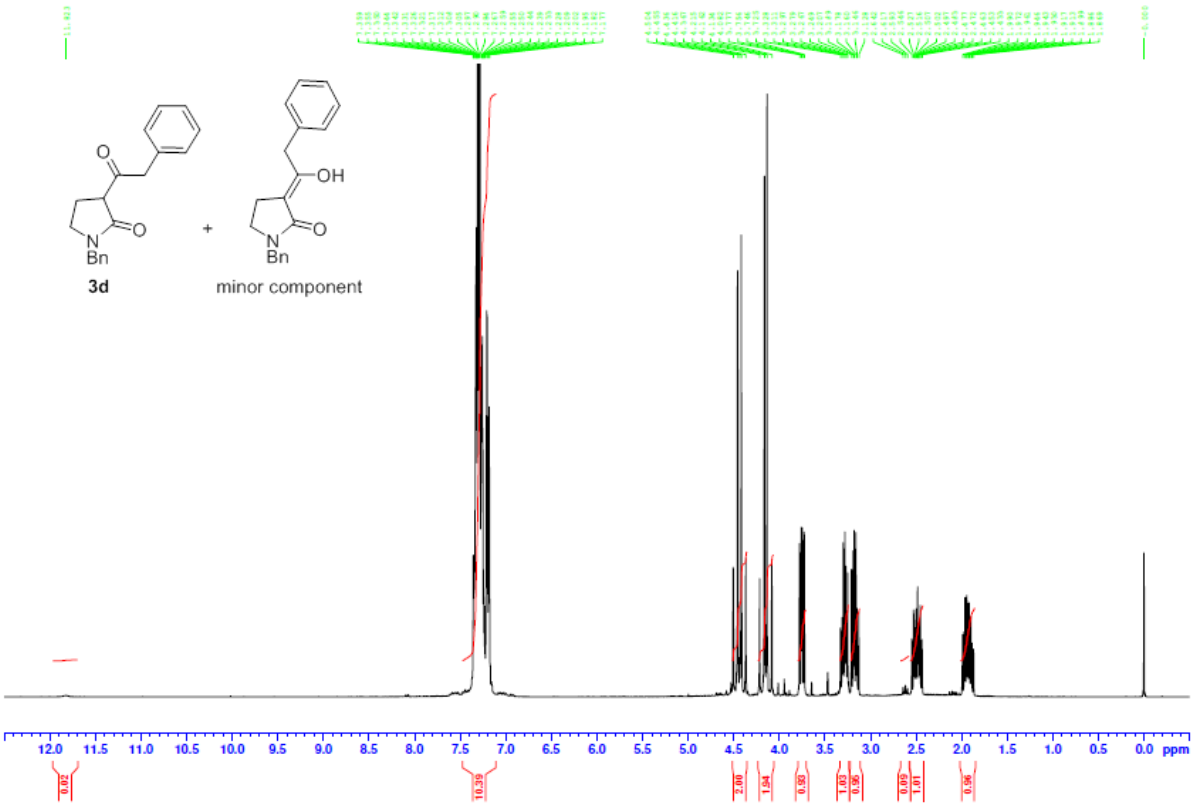
^{1}H and ^{13}C NMR Spectra






O
O
N
Bn
3c
+
OH
O
N
Bn
minor component
12.0 11.5 11.0 10.5 10.0 9.5 9.0 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 ppm


O
O
N
Bn
3c
+
OH
O
N
Bn
minor component
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
O
N
Bn
3d
+
OH
O
N
Bn
minor component
12.0 11.5 11.0 10.5 10.0 9.5 9.0 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 ppm
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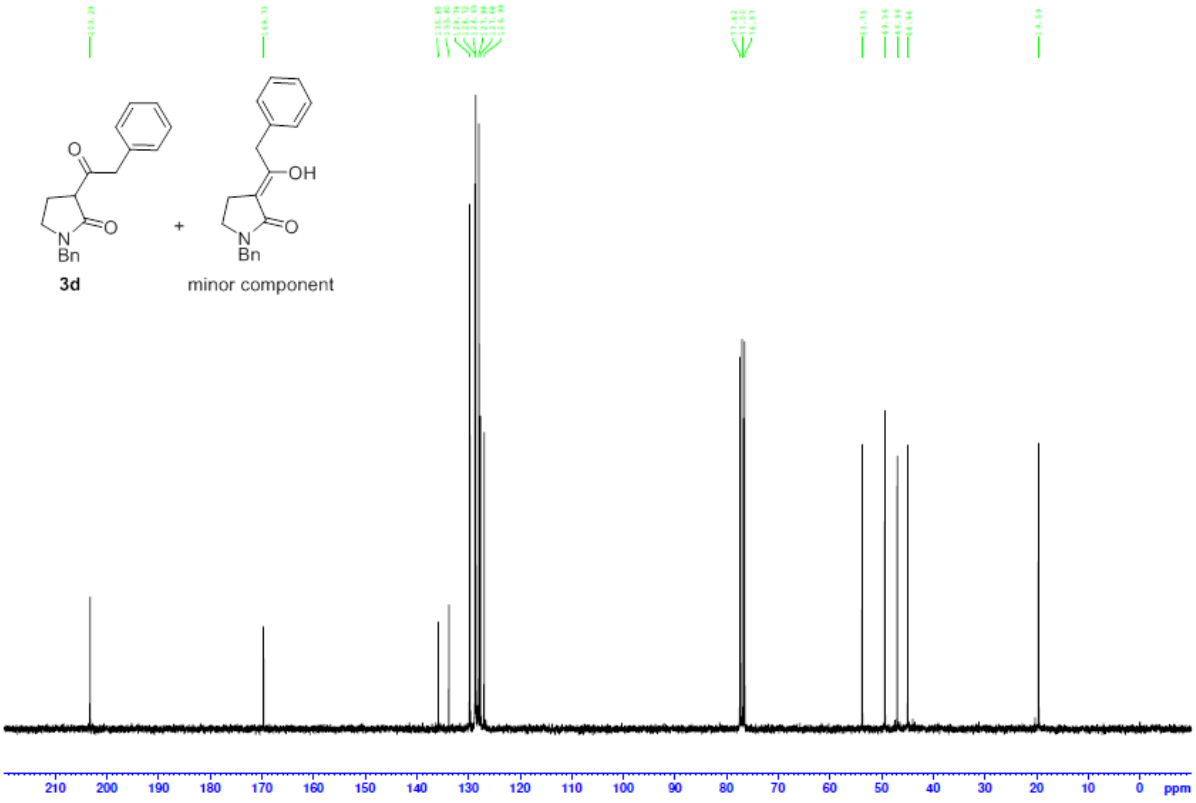
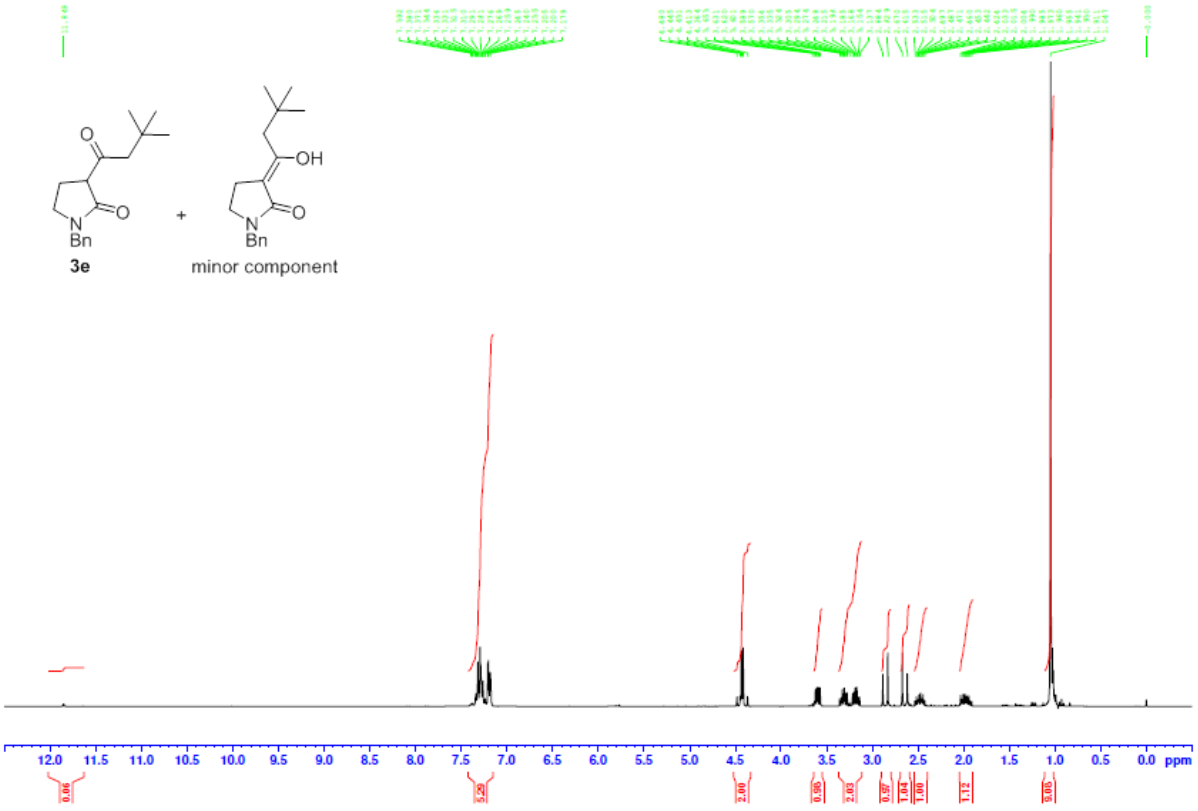
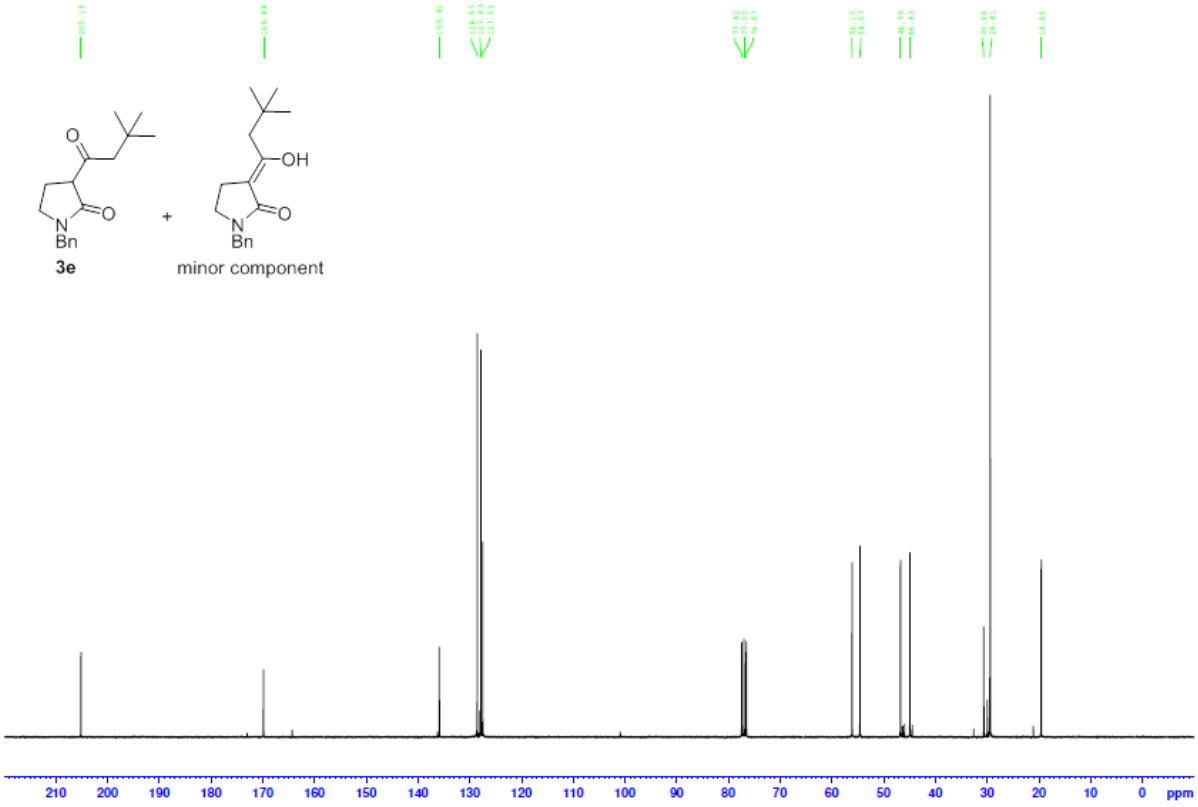
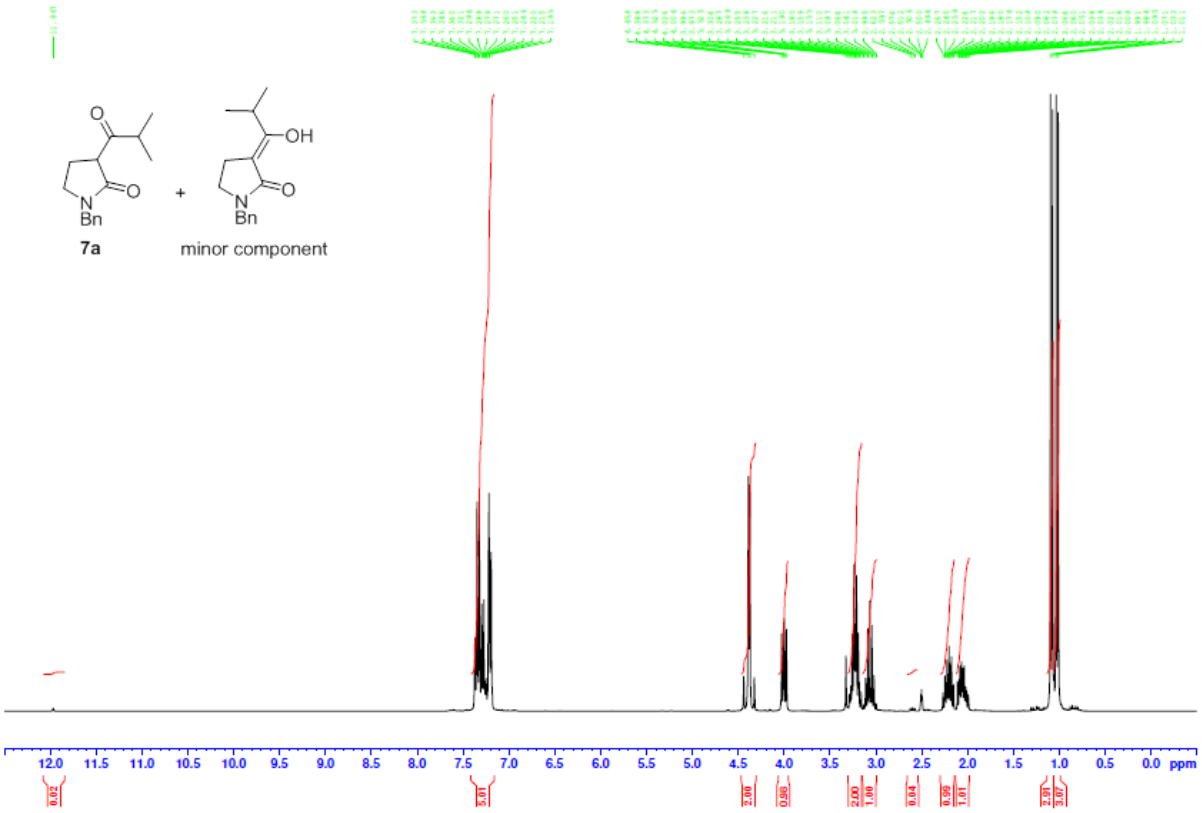
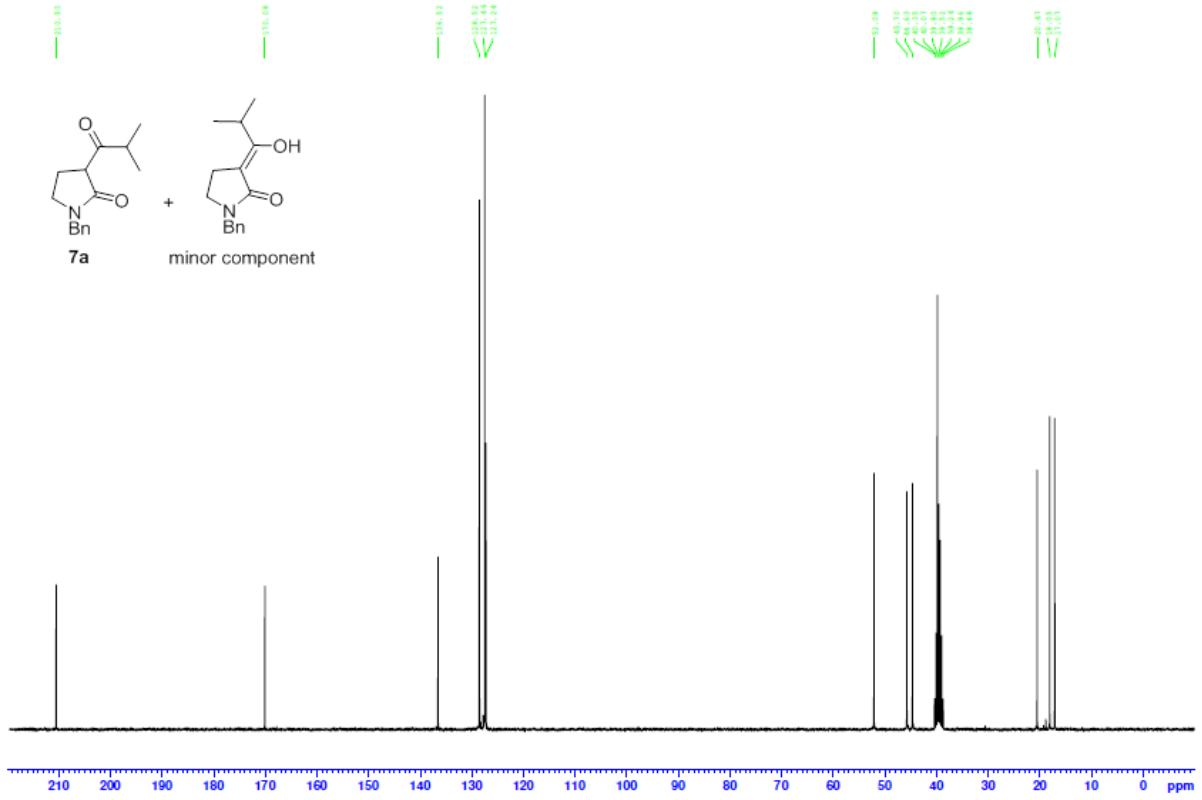
10.39
2.00
1.84
0.80
1.03
0.86
0.89
1.01
0.96

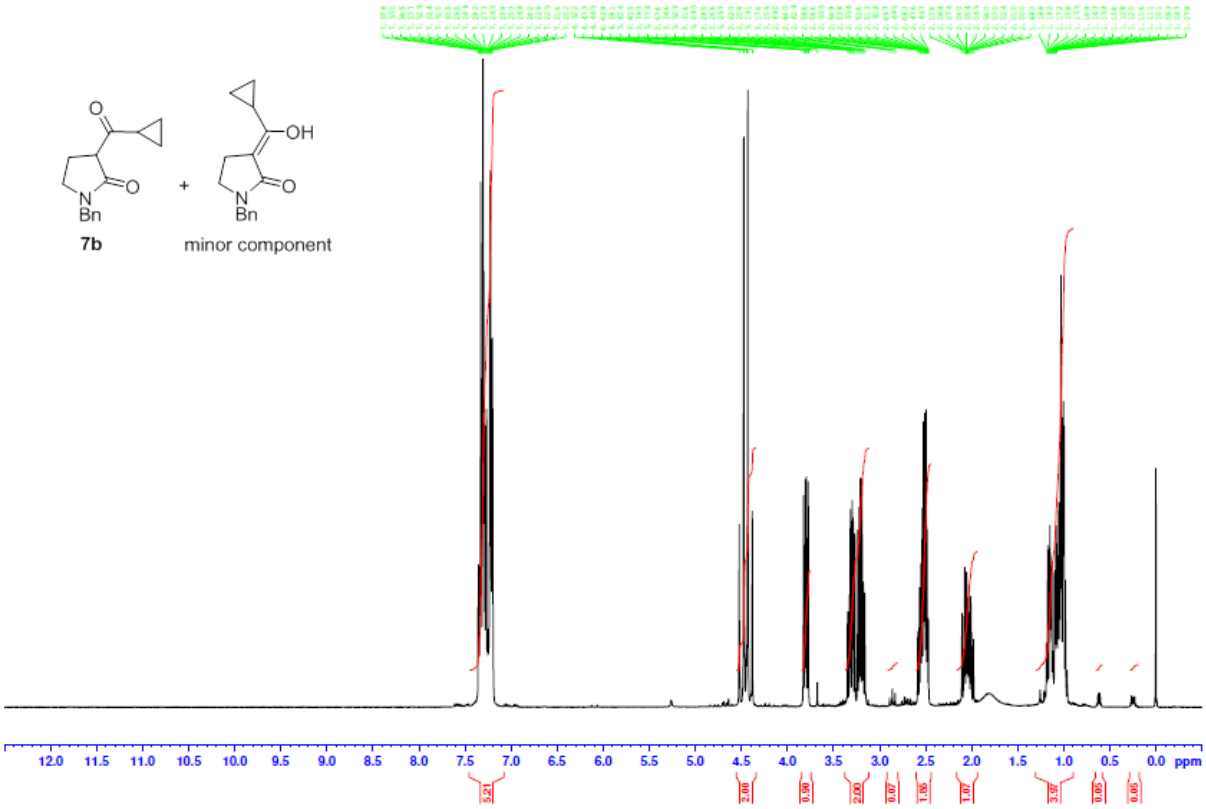

O
O
N
Bn
3d
+
OH
O
N
Bn
minor component
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

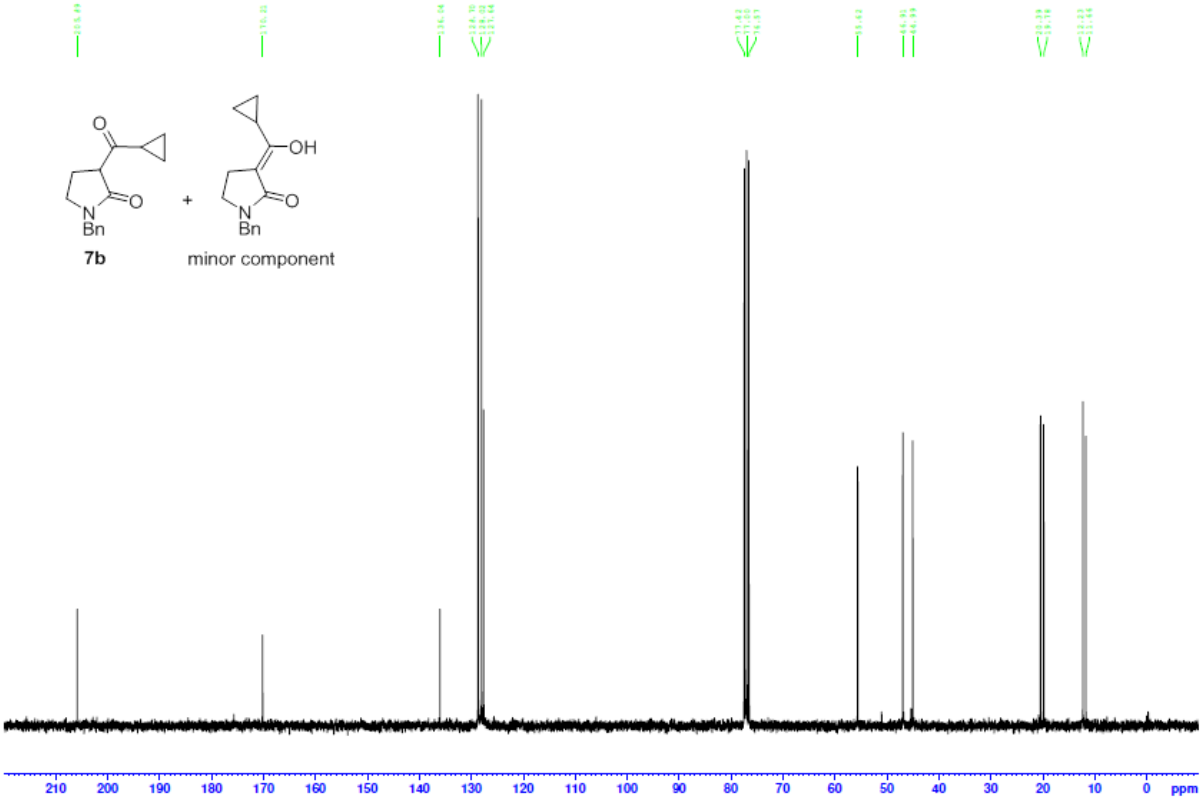

O
N
Bn
O
+
OH
N
Bn
O
3e
minor component
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


O
N
Bn
O
+
OH
N
Bn
O
3e
minor component
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7a
minor component
12.0 11.5 11.0 10.5 10.0 9.5 9.0 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 ppm


7a
minor component
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7b
minor component
12.0 11.5 11.0 10.5 10.0 9.5 9.0 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 ppm


7b
minor component
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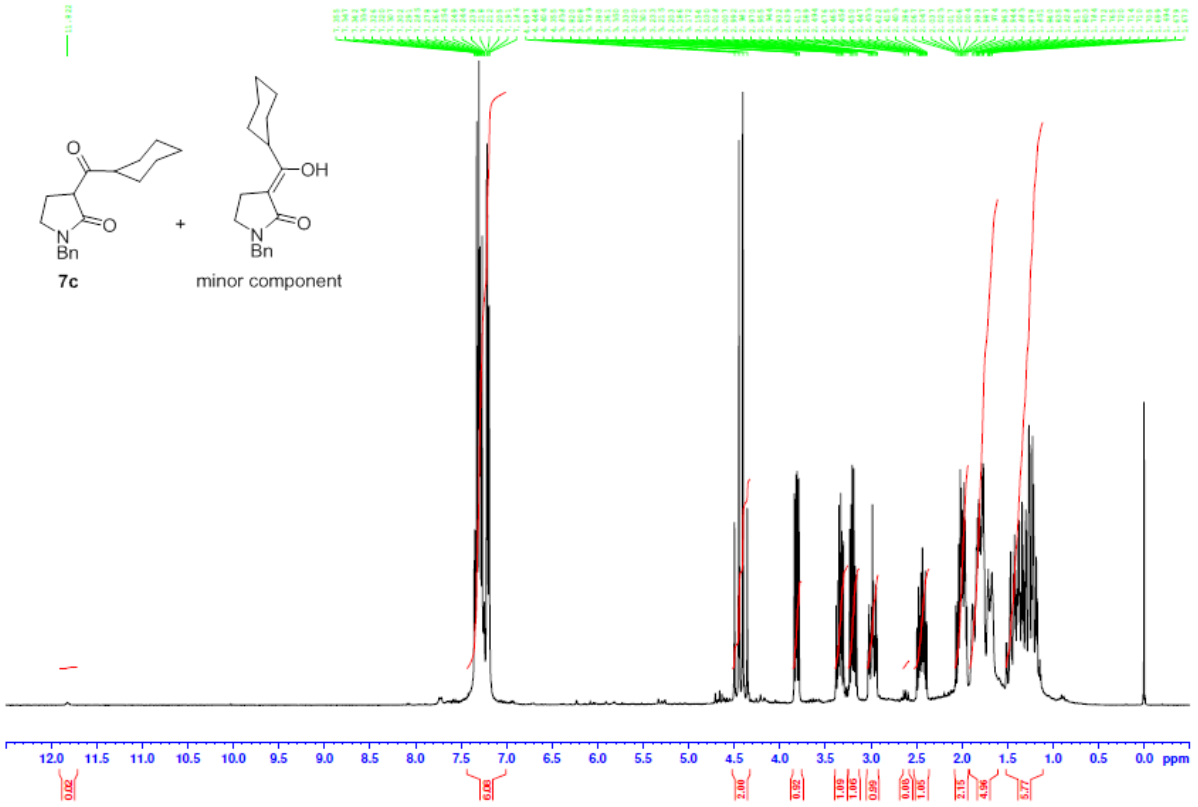
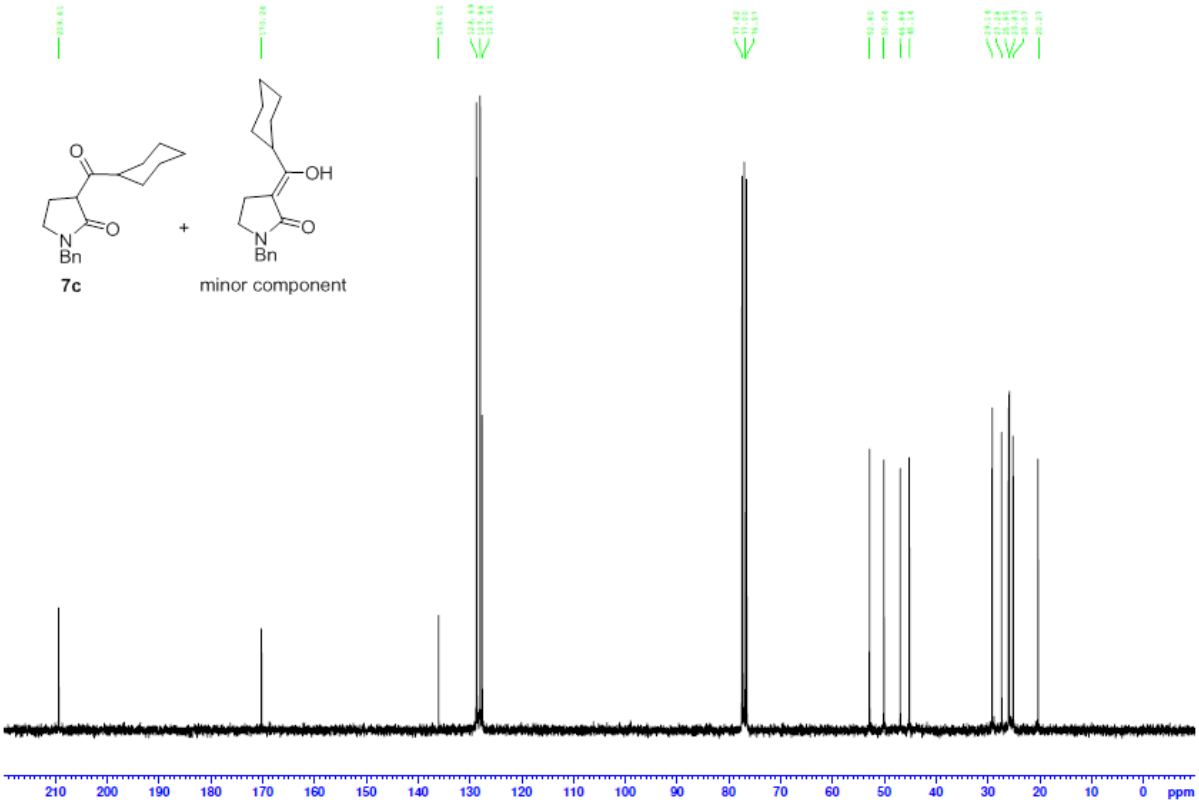
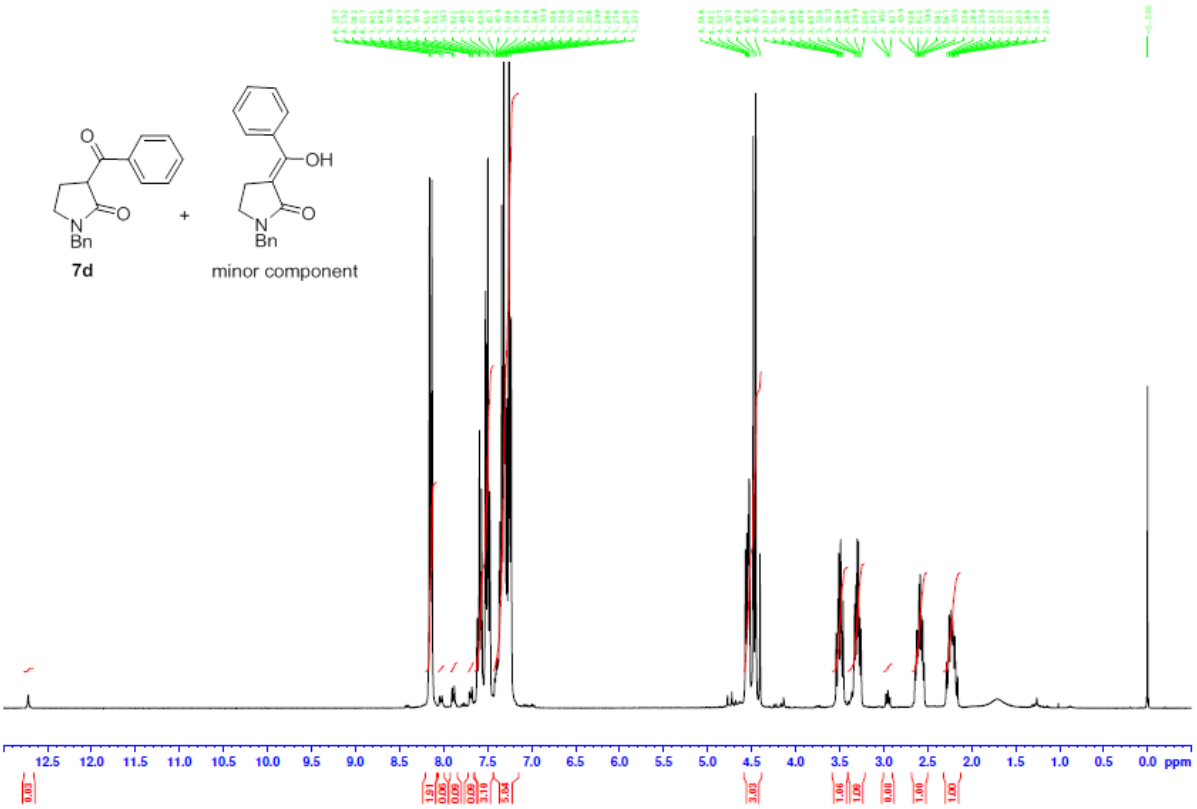
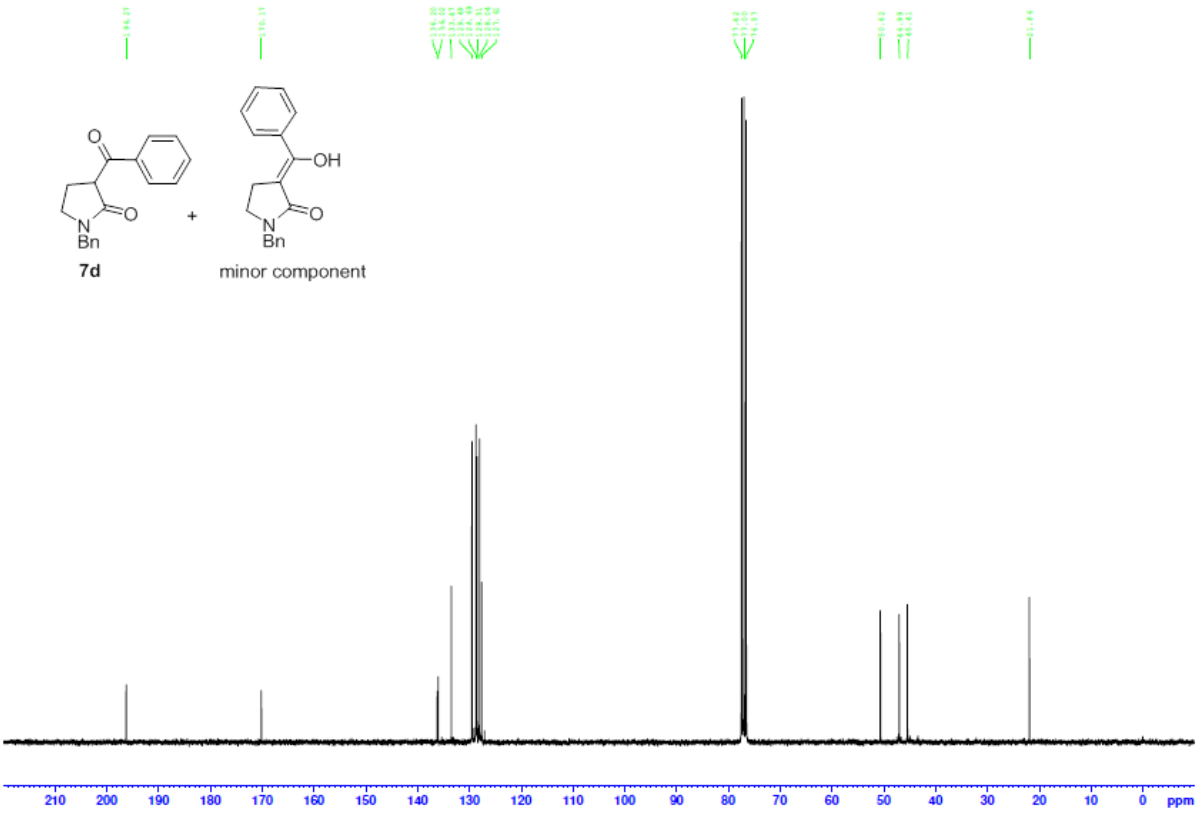
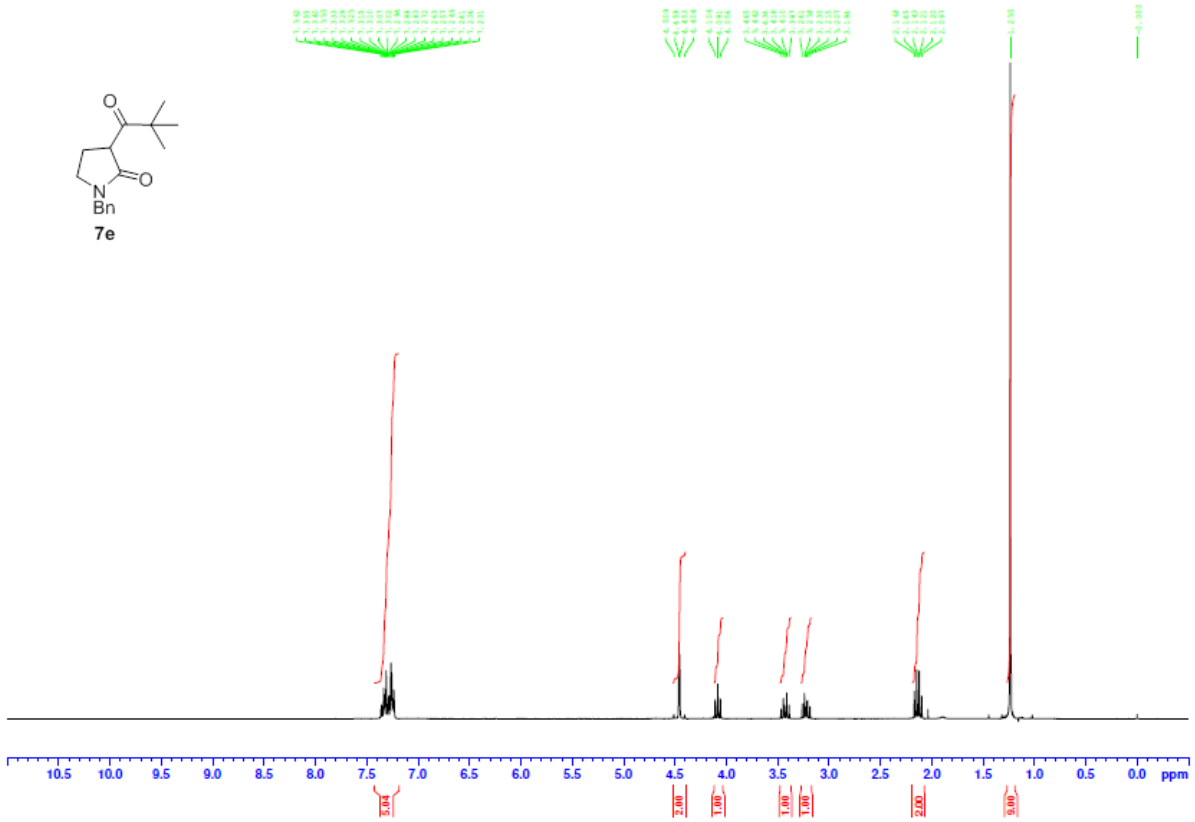
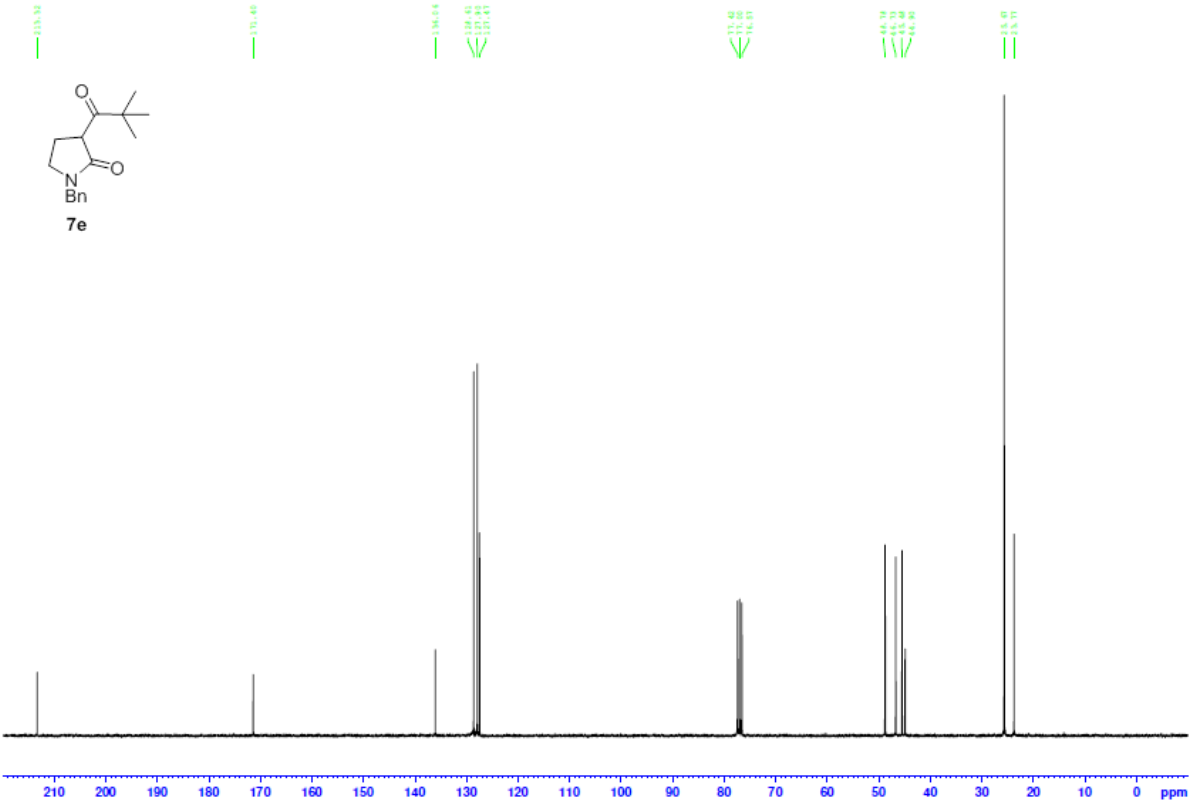

O
O
N
Bn
7c
+
OH
O
N
Bn
minor component
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

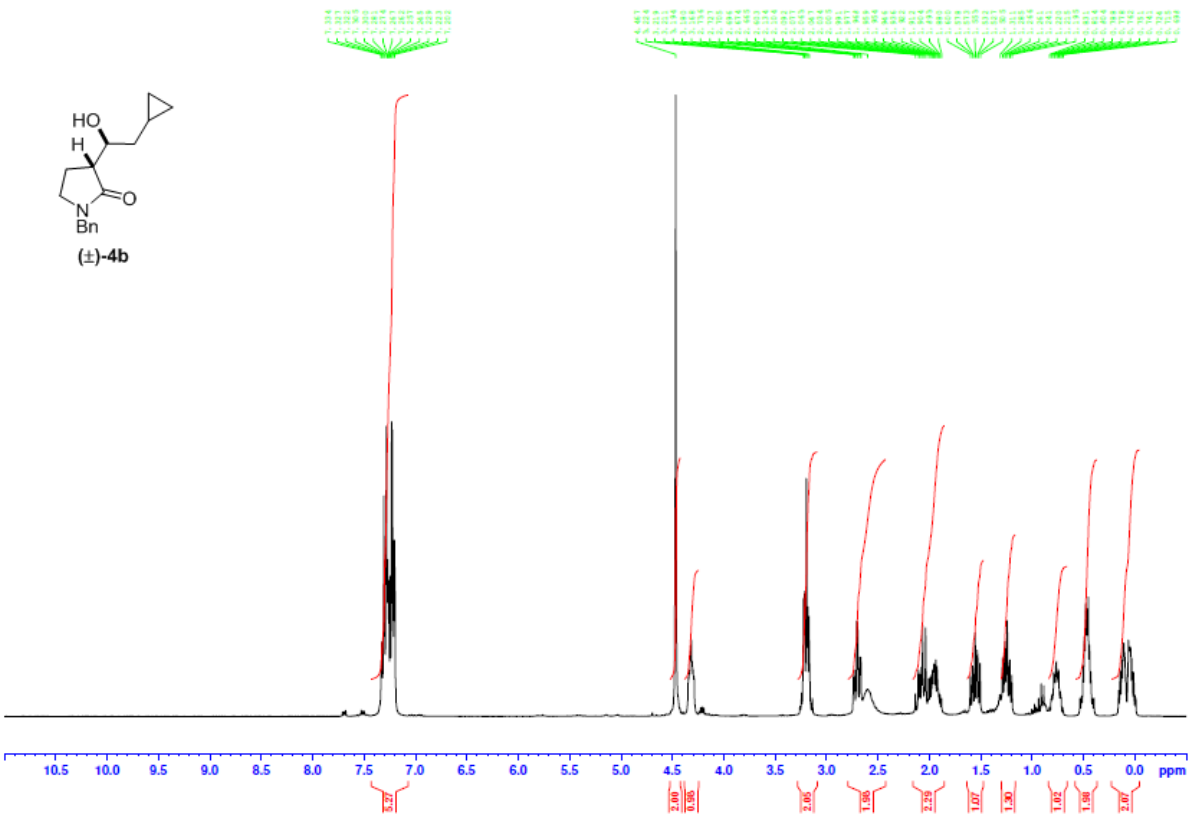

O
O
N
Bn
7c
+
OH
O
N
Bn
minor component
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

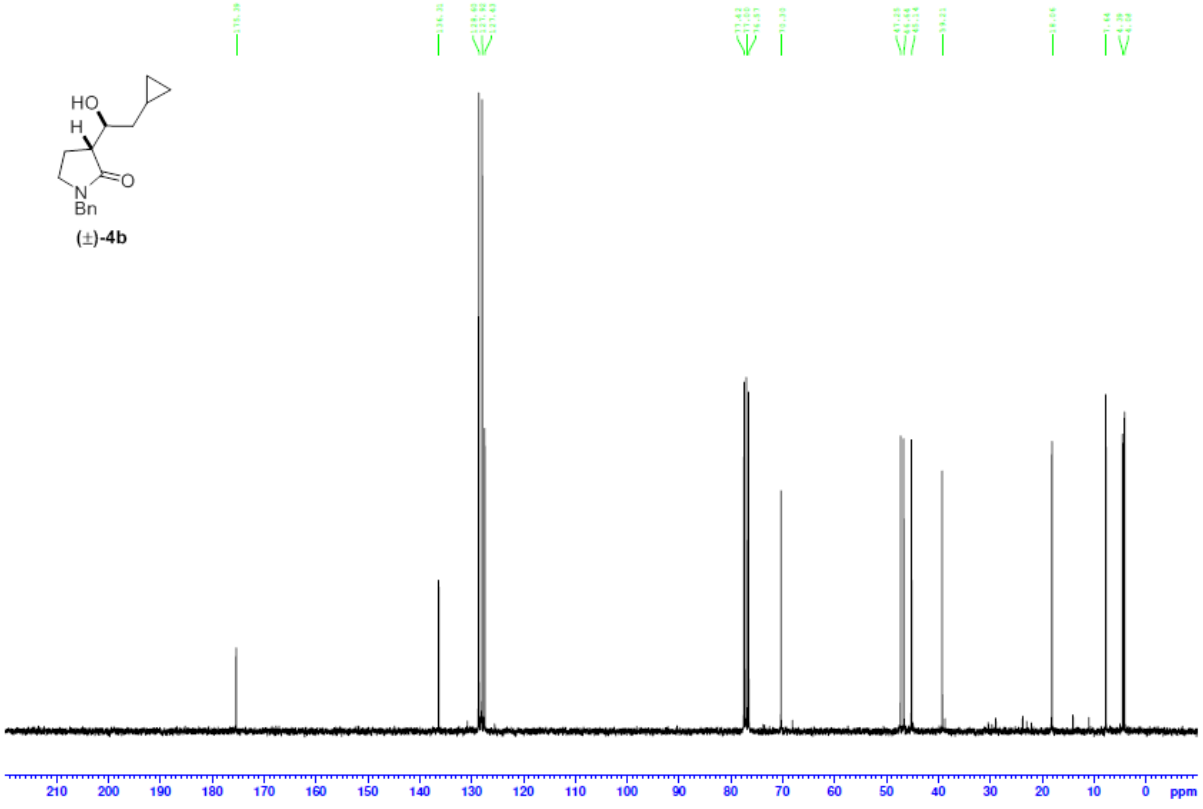

O
N
Bn
O
+
OH
O
N
Bn
7d
minor component
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

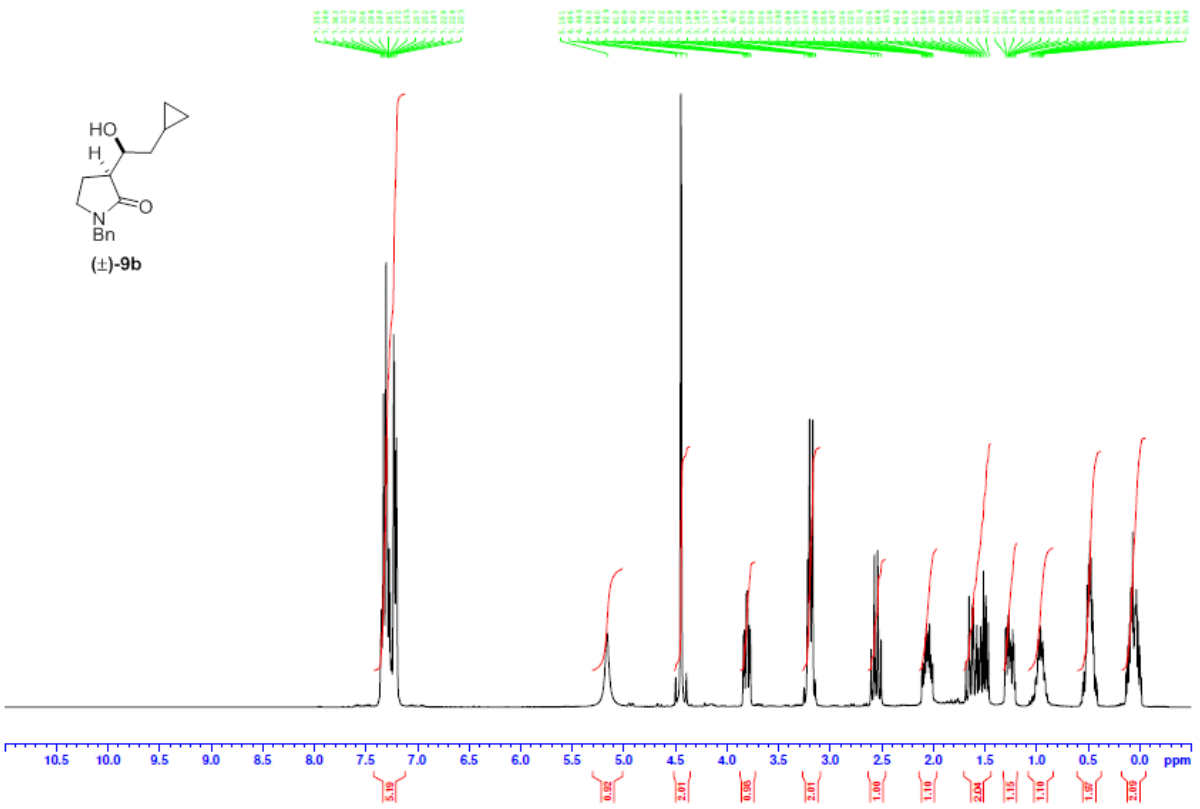

O
N
Bn
O
+
OH
O
N
Bn
7d
minor component
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

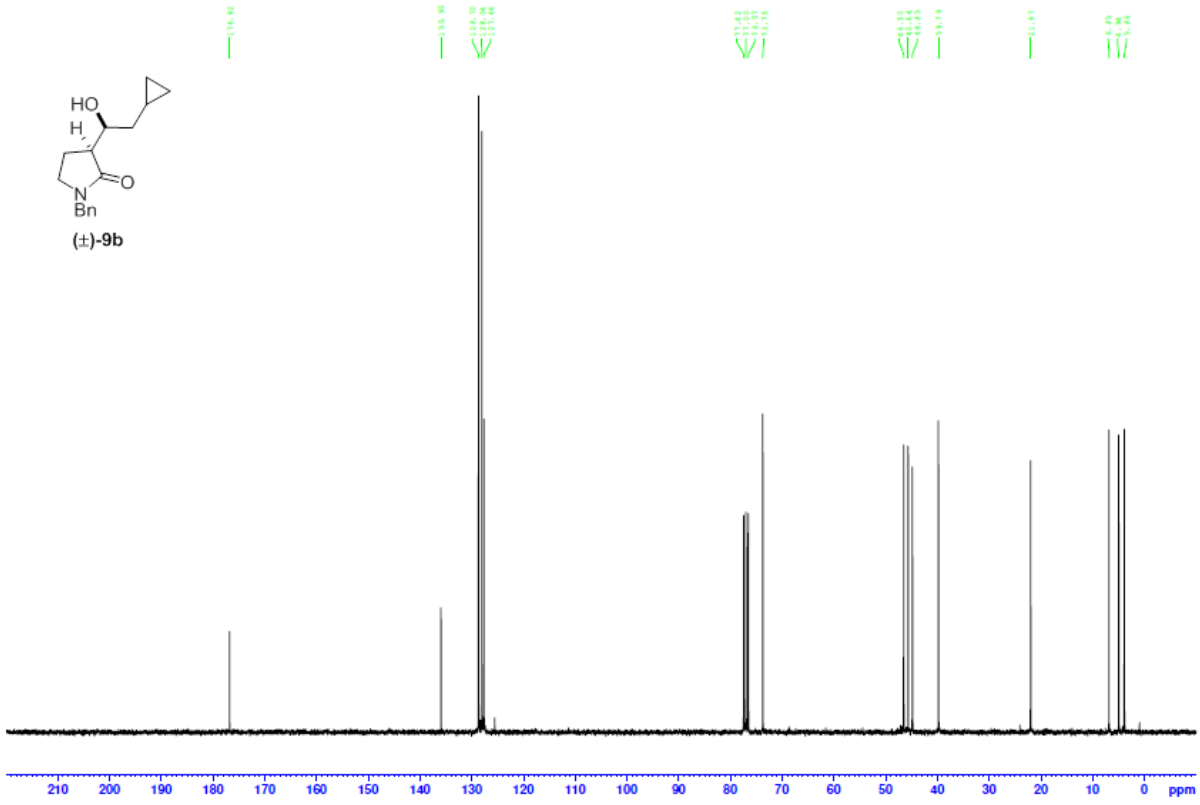

O
O
N
Bn
7e
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.04
2.00
1.00
1.00
1.00
2.00
9.00

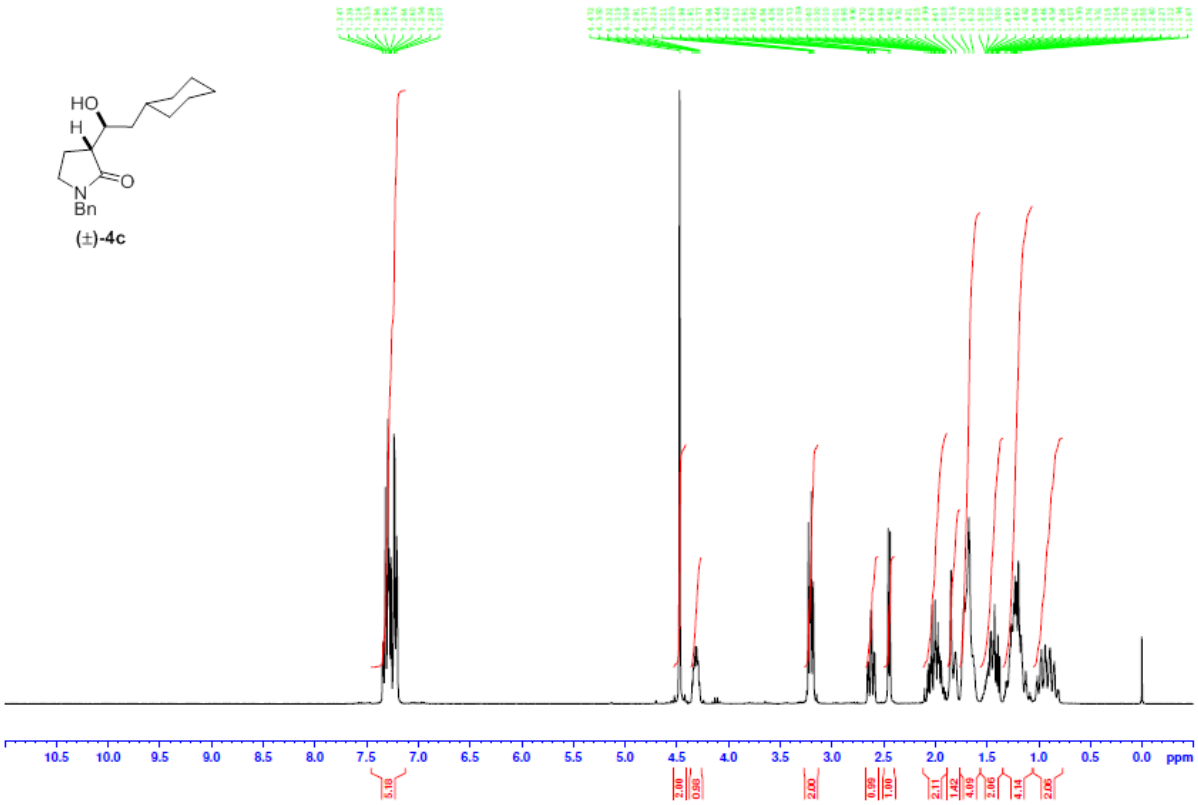

O
O
N
Bn
7e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

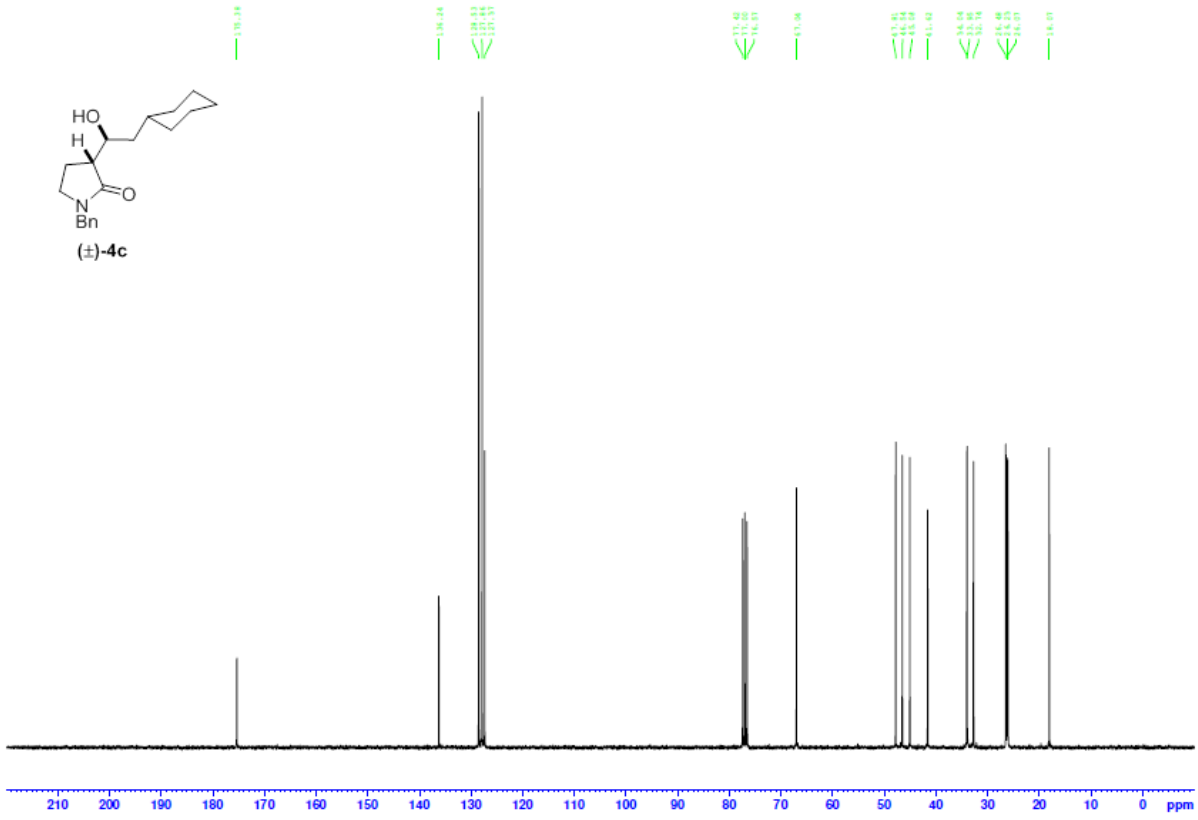

HO
H
O
N
Bn
(±)-4b
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.27
2.00
0.96
2.05
1.99
2.29
1.07
1.30
1.02
1.98
2.07

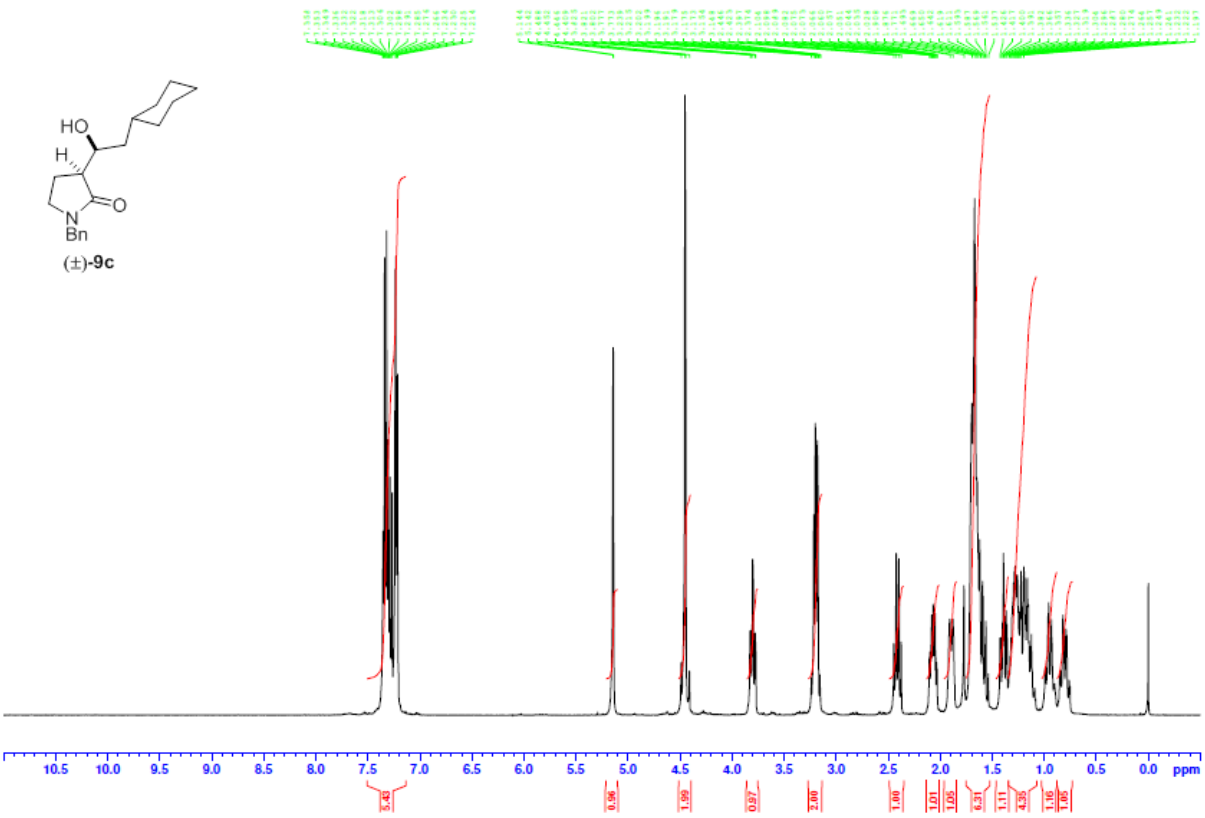

HO
H
O
N
Bn
(±)-4b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

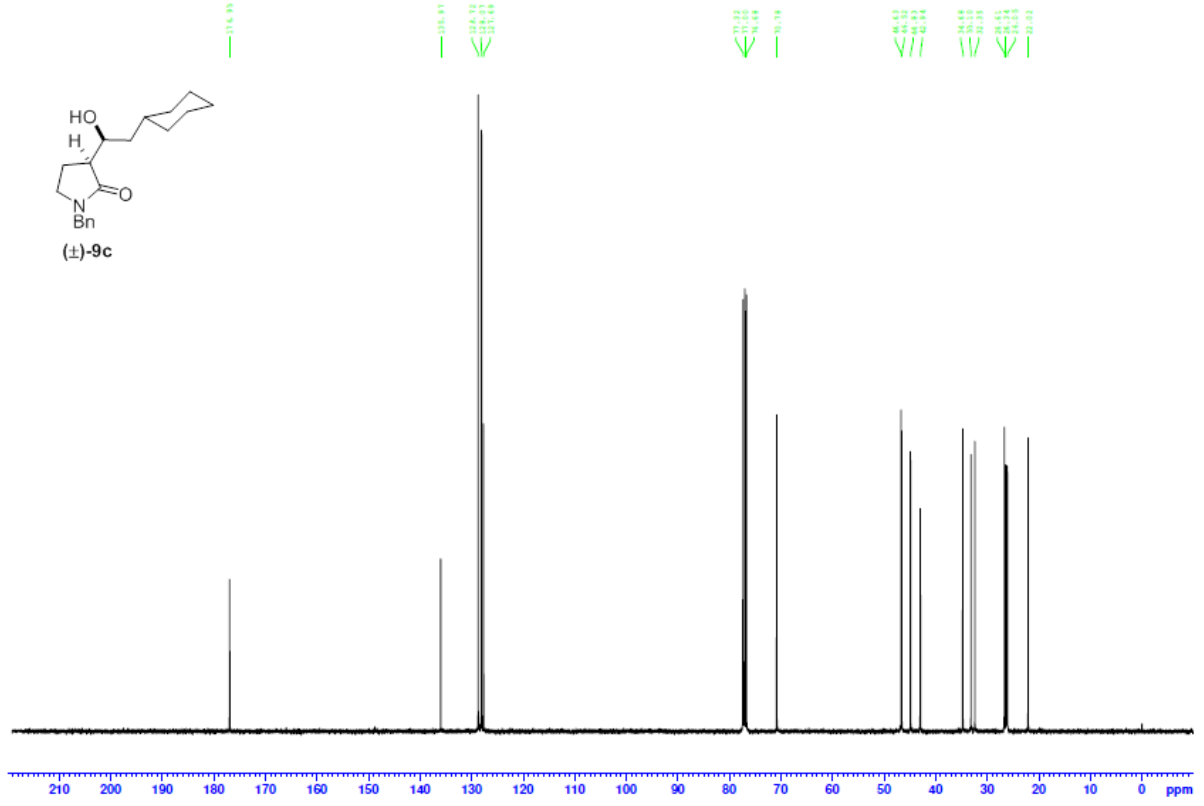

HO
H
O
N
Bn
(±)-9b
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.19 0.92 2.01 0.98 2.01 1.00 1.10 2.04 1.15 1.10 1.87 2.09

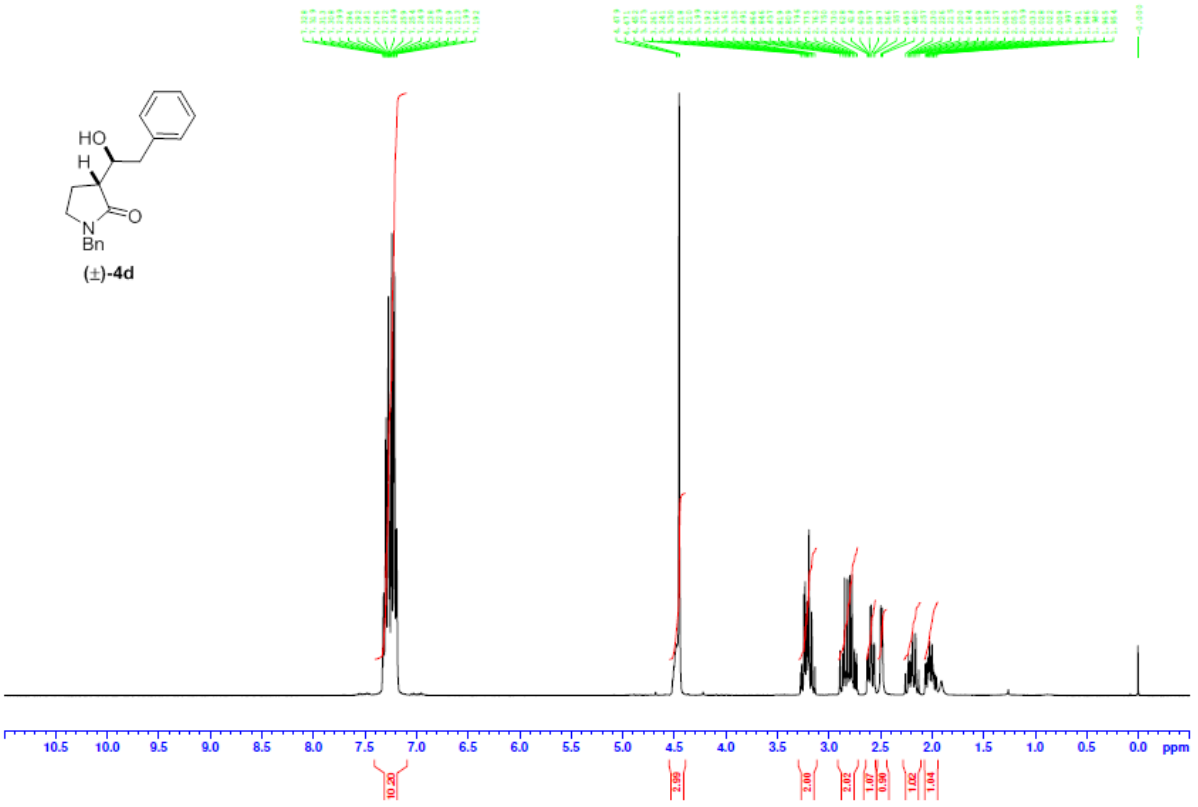

HO
H
O
N
Bn
(±)-9b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

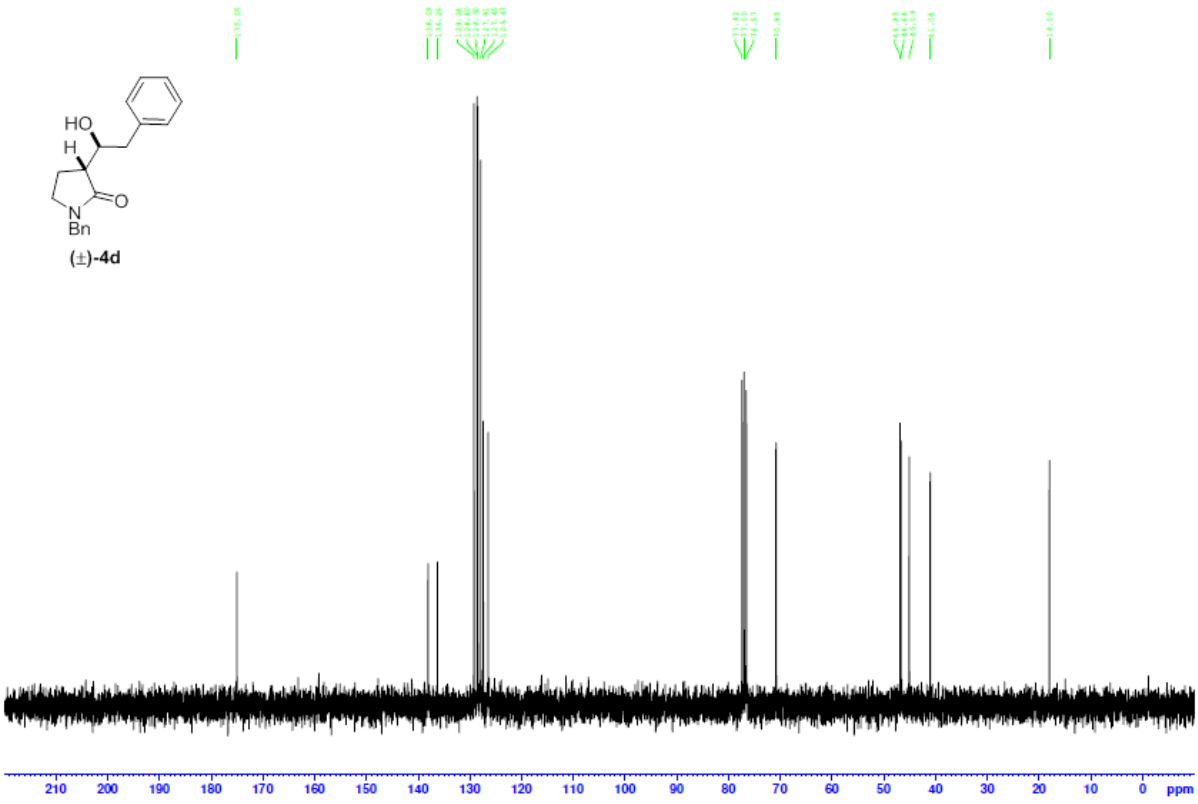

HO
H
O
N
Bn
(±)-4c
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.18
2.08
0.60
2.00
0.98
1.00
2.11
1.62
4.69
2.06
4.14
2.06

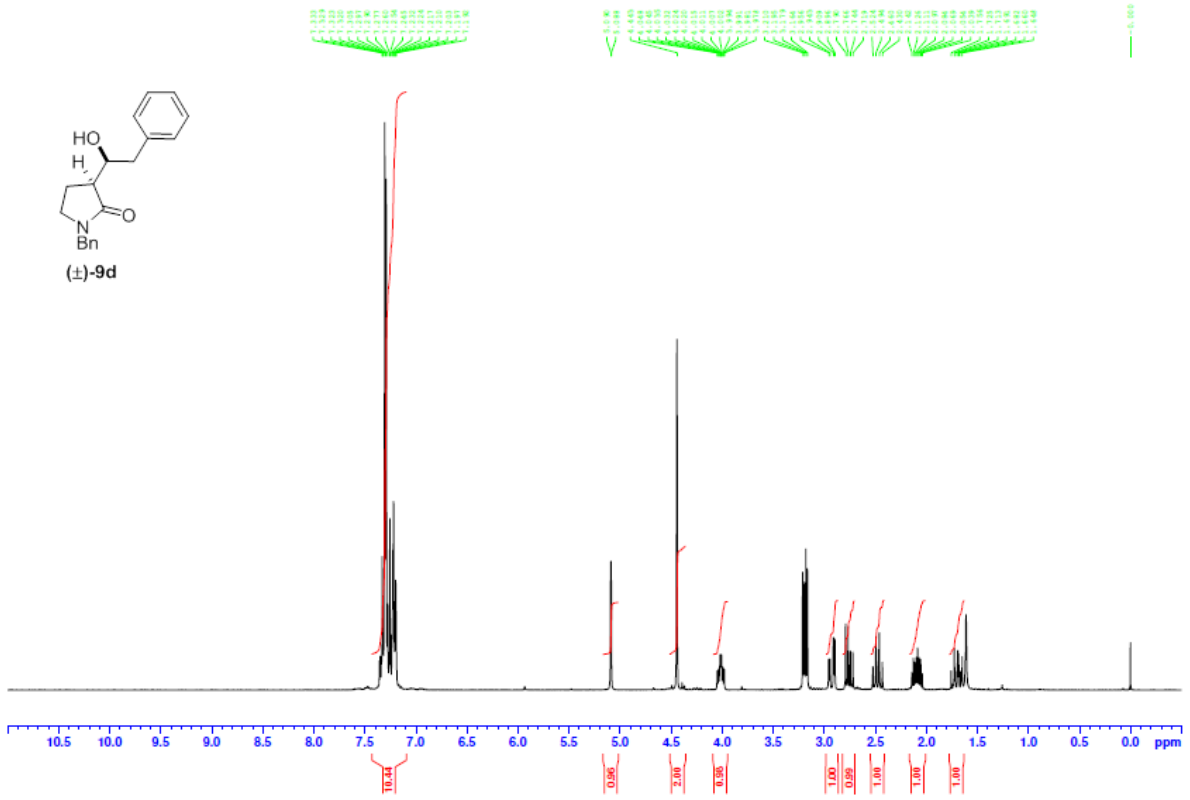

HO
H
O
N
Bn
(±)-4c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

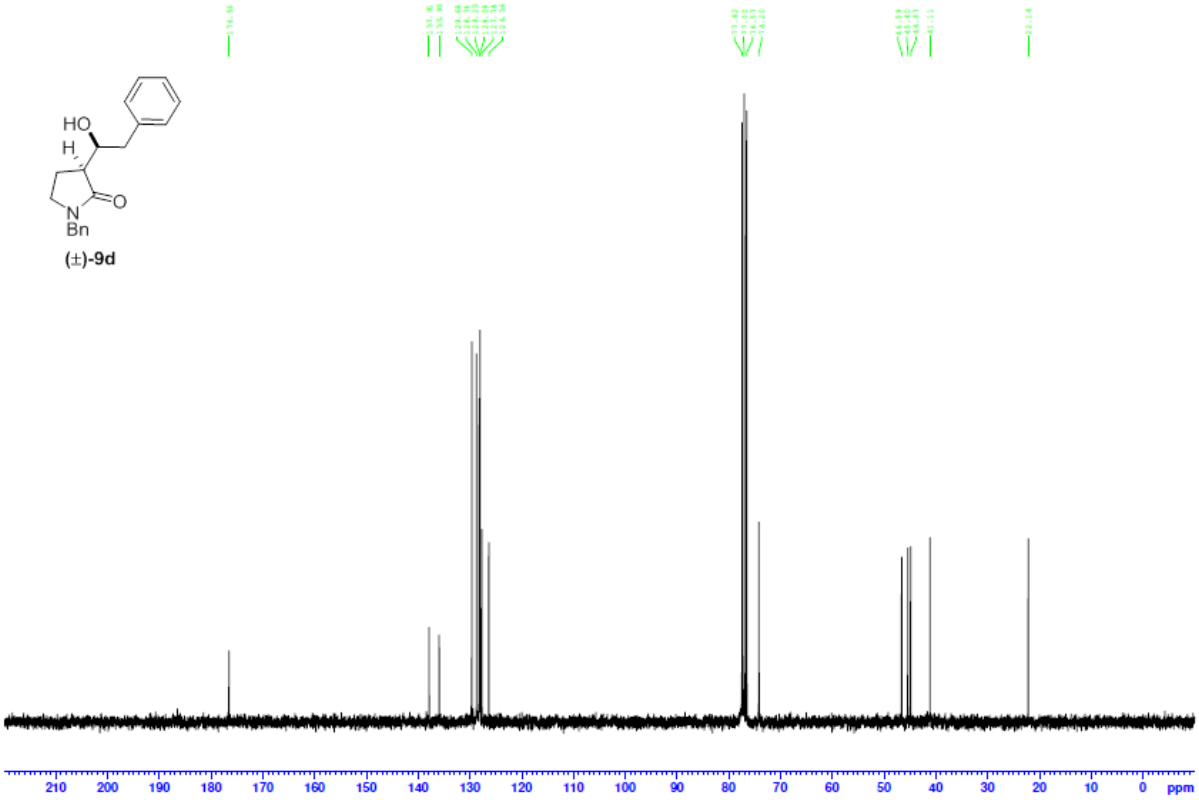

HO
H
O
N
Bn
(±)-9c
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.43
0.96
1.99
0.87
2.00
1.00
1.01
1.05
6.31
1.11
4.35
1.16
1.05

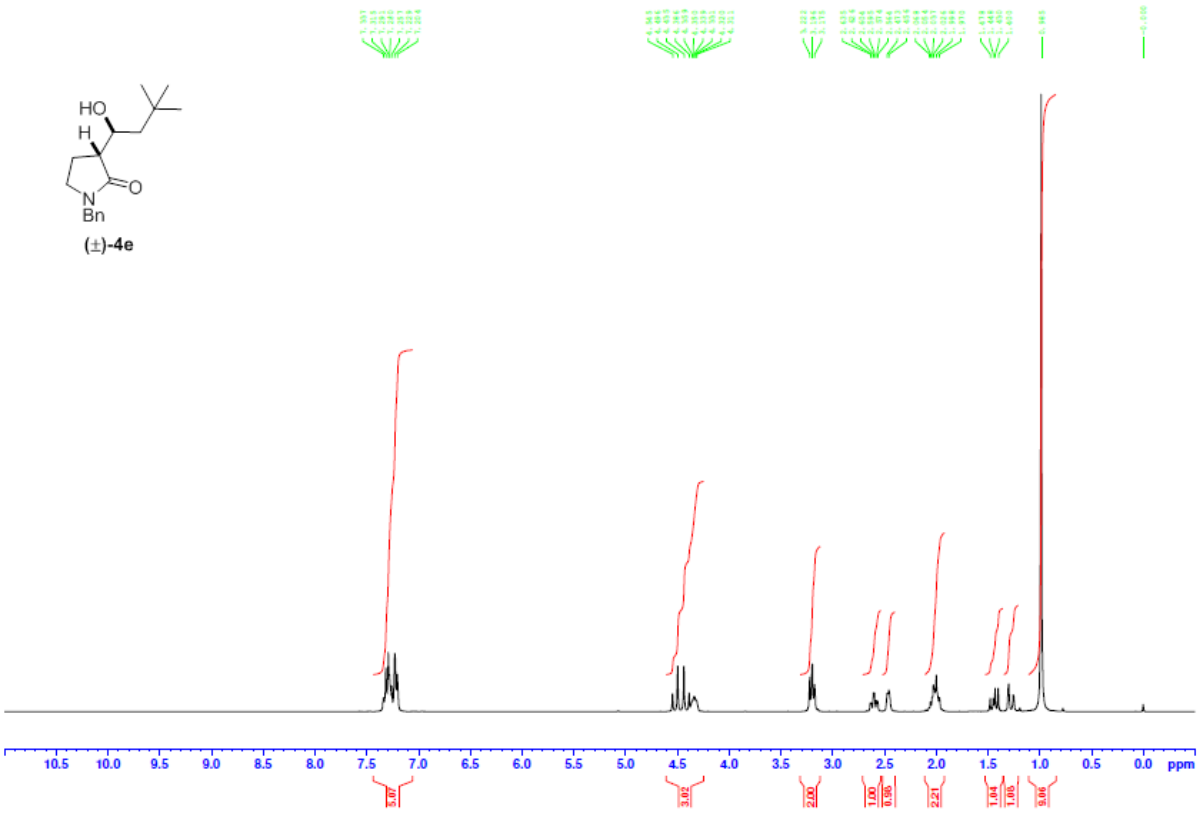

HO
H
O
N
Bn
(±)-9c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

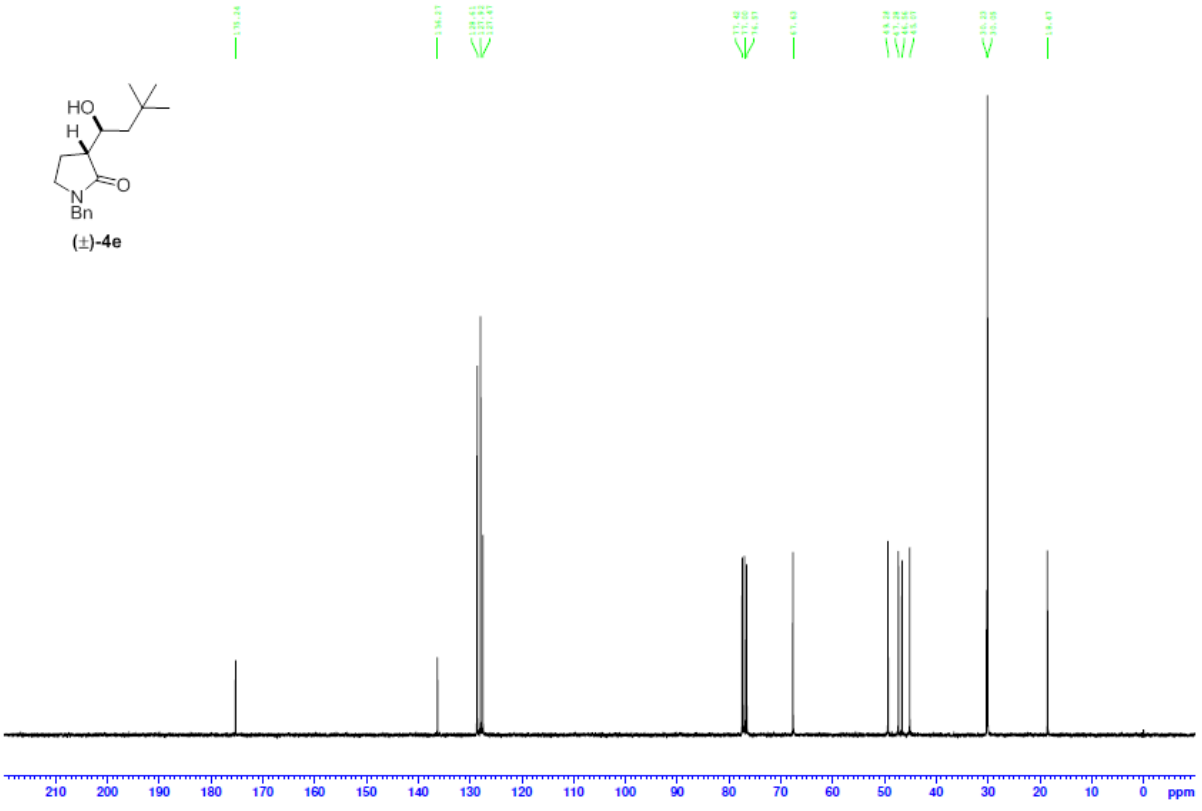

HO
H
N
O
Bn
(±)-4d
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
10.20
2.99
2.00
2.02
1.07
0.98
1.02
1.04

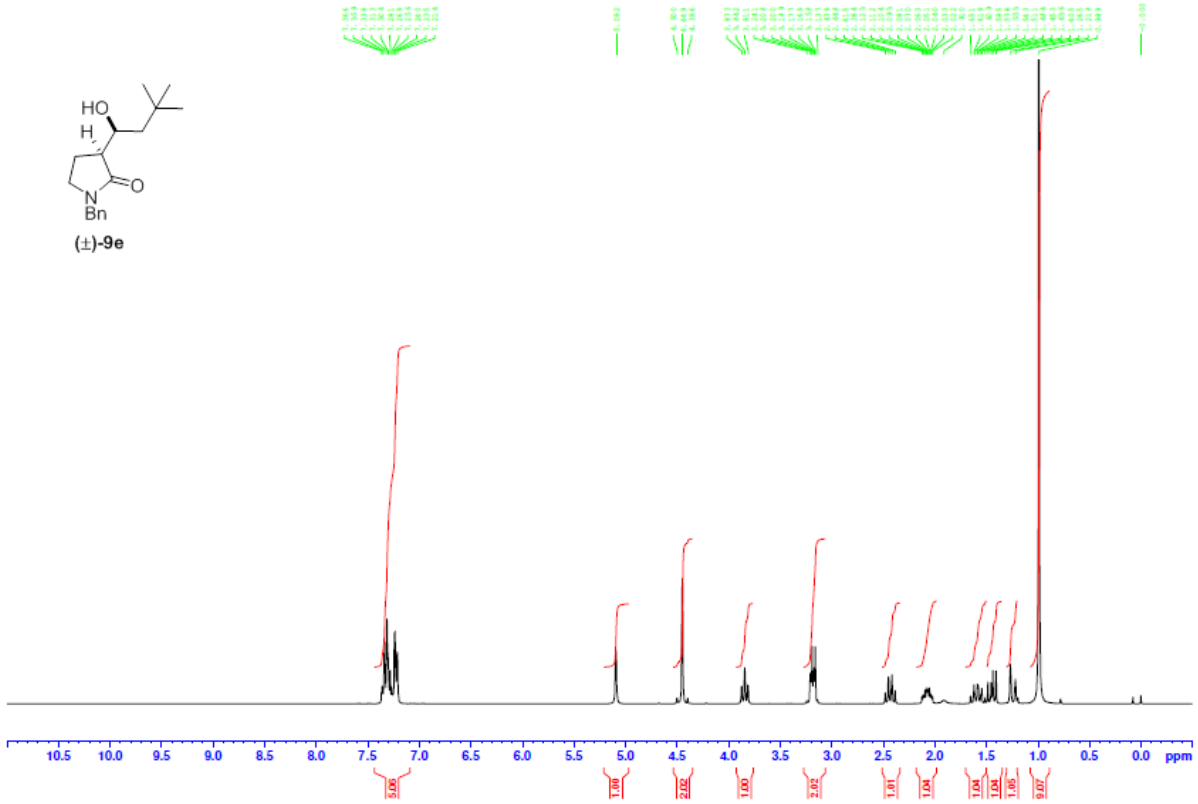

HO
H
N
O
Bn
(±)-4d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

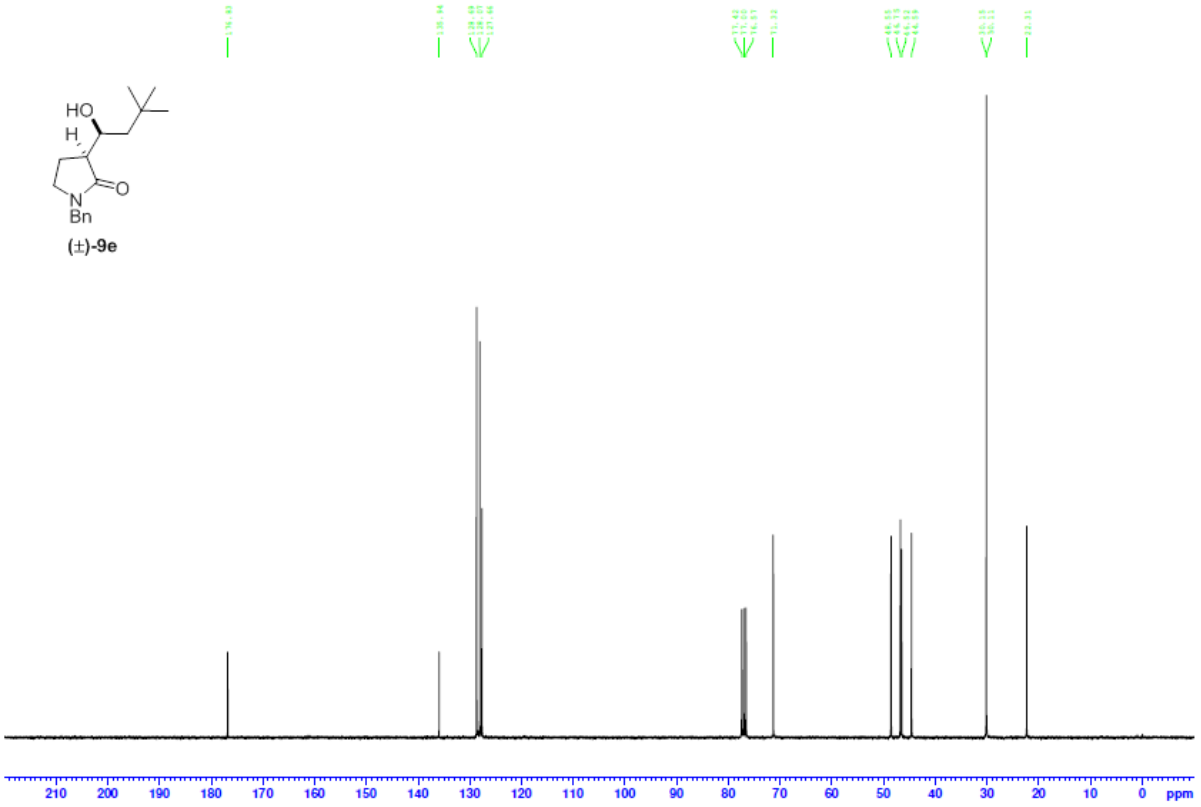

HO
H
O
N
Bn
(±)-9d
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
10.44
0.96
2.00
0.98
1.00
0.99
1.00
1.00
1.00

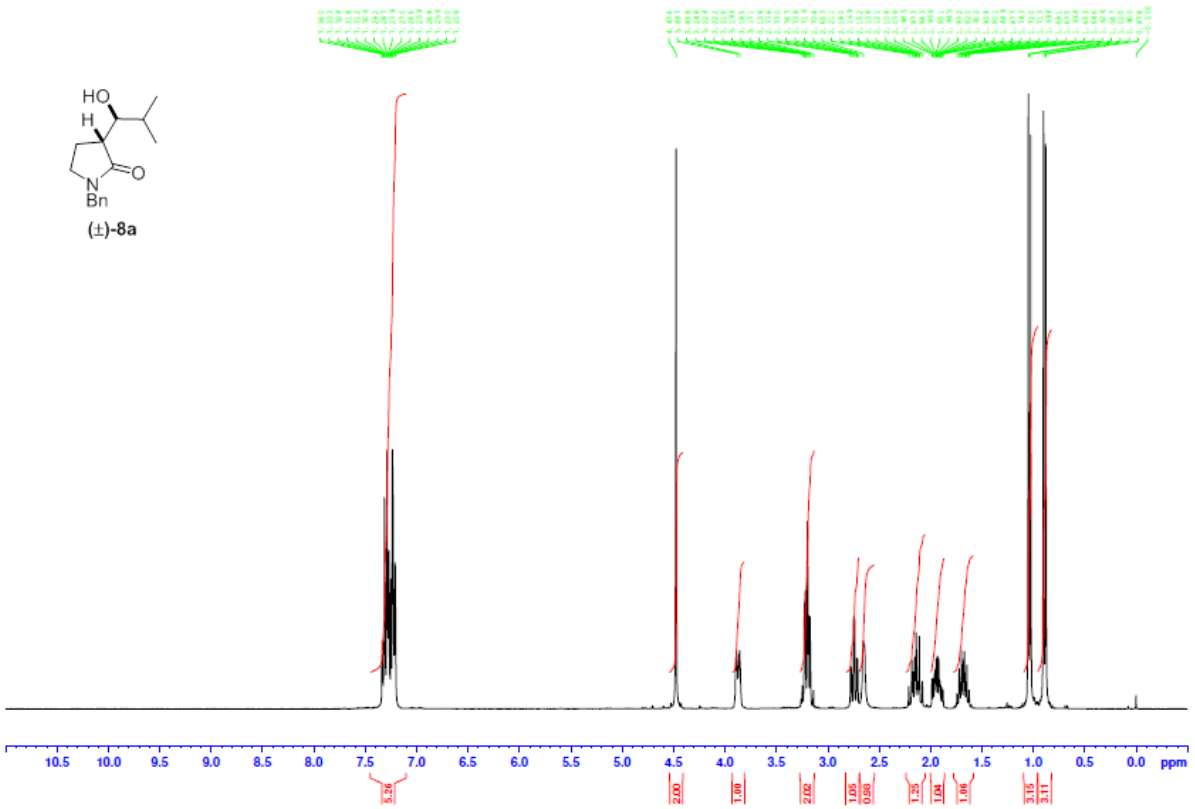

HO
H
O
N
Bn
(±)-9d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

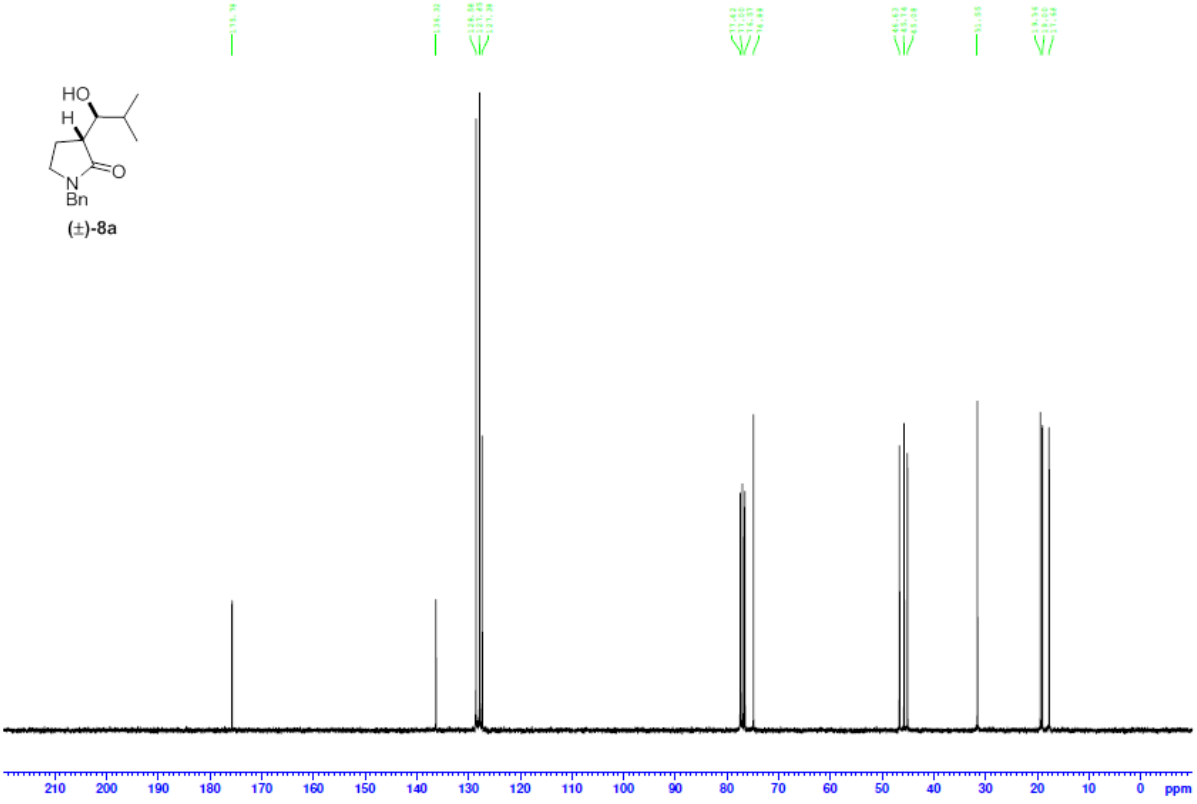

HO
H
O
N
Bn
(±)-4e
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.07
3.02
2.00
1.00
0.96
2.21
1.04
1.05
9.06

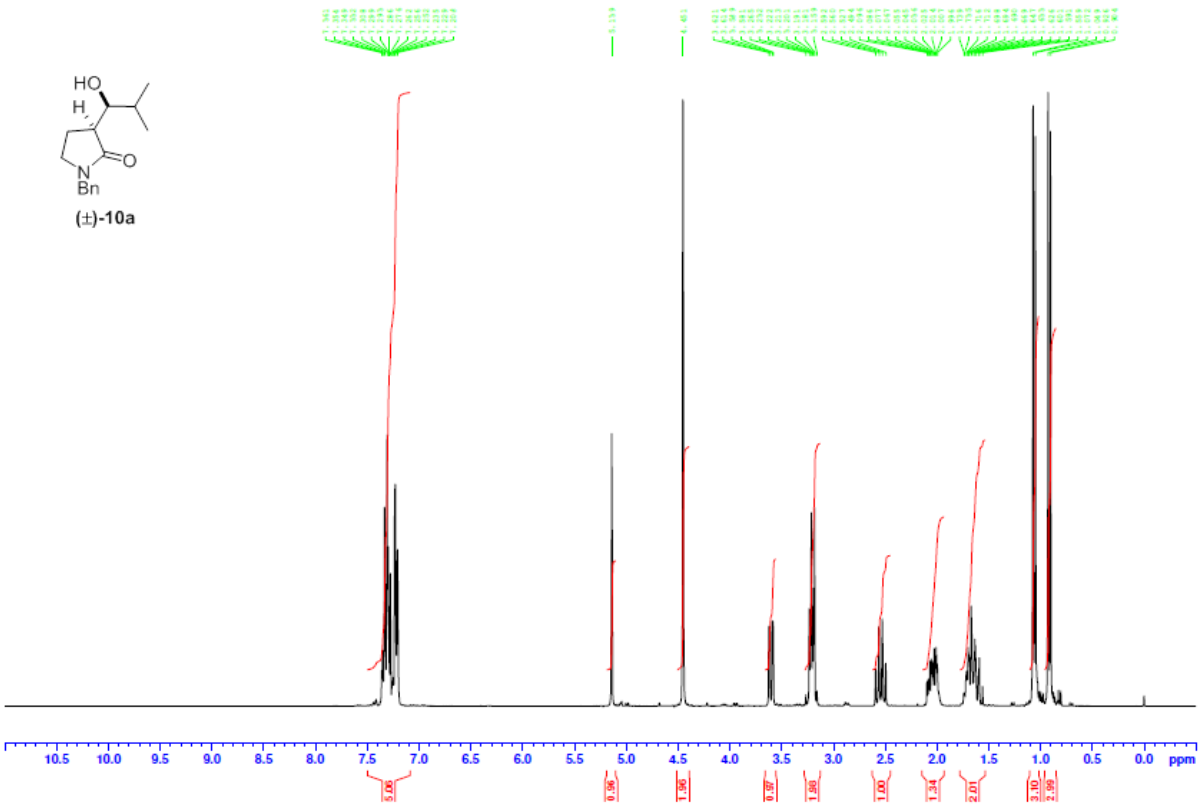

HO
H
O
N
Bn
(±)-4e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

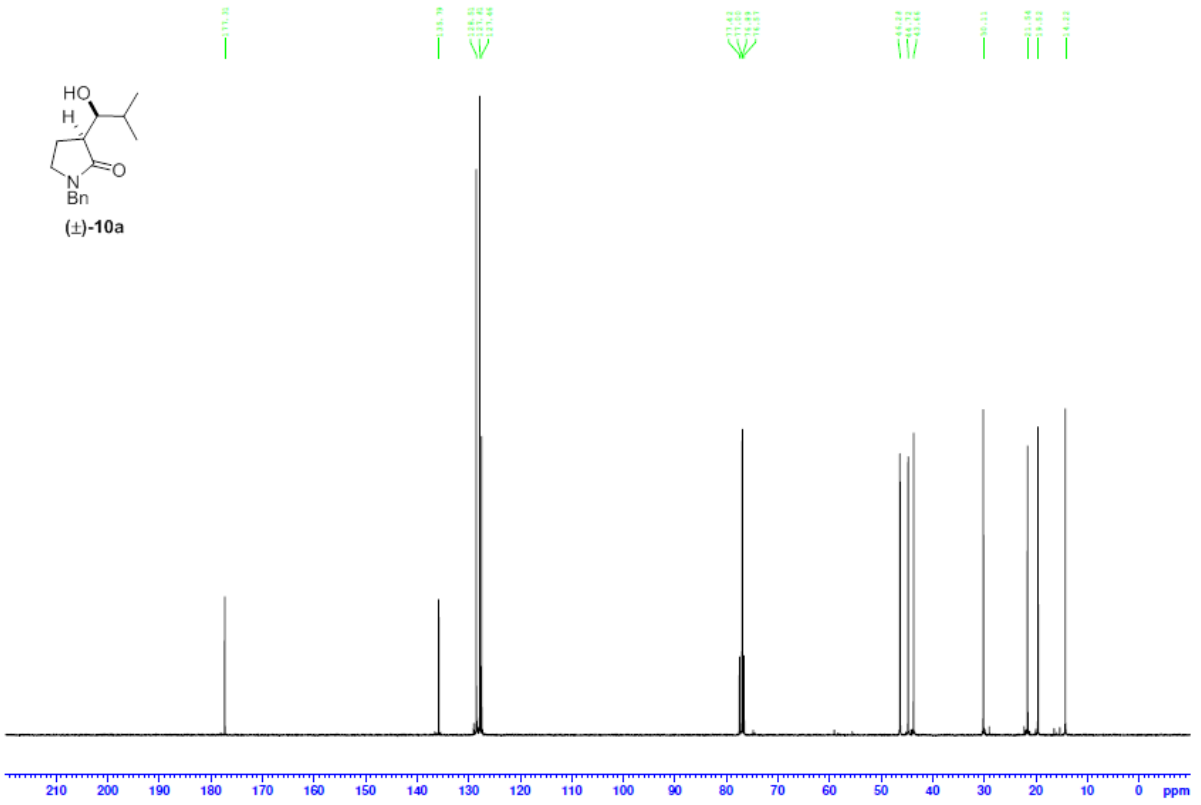

HO
H
O
N
Bn
(±)-9e
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.00 1.00 2.02 1.00 2.02 1.01 1.04 1.04 1.04 1.05 9.07

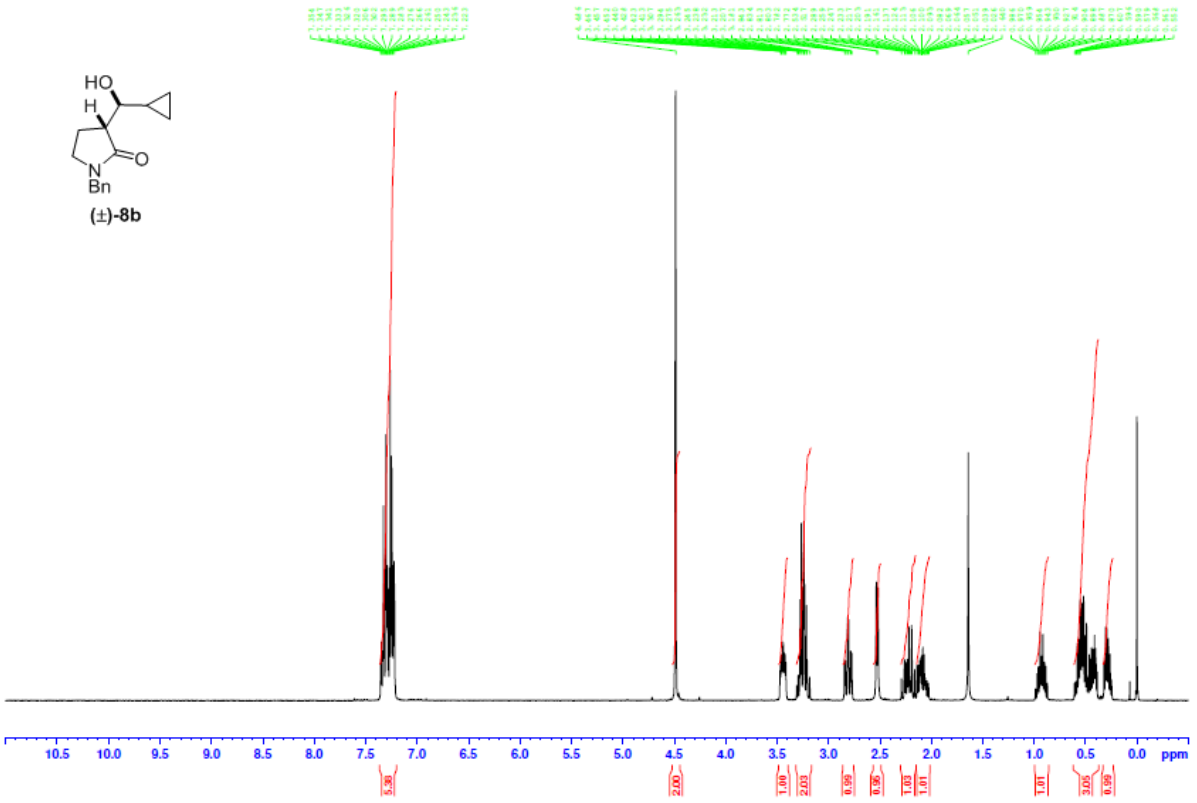

HO
H
O
N
Bn
(±)-9e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

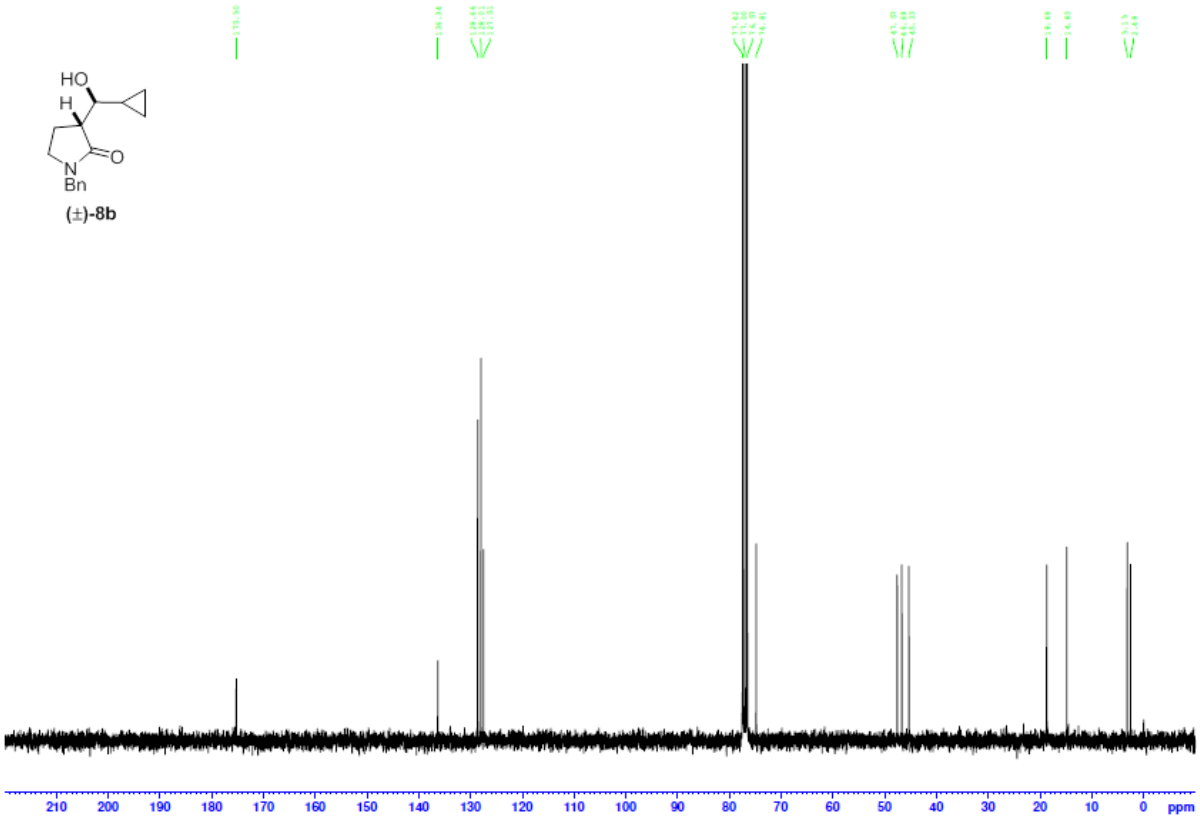

HO
H
O
N
Bn
(±)-8a
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.26
2.00
1.00
2.02
1.05
0.98
1.25
1.04
1.06
3.15
3.11

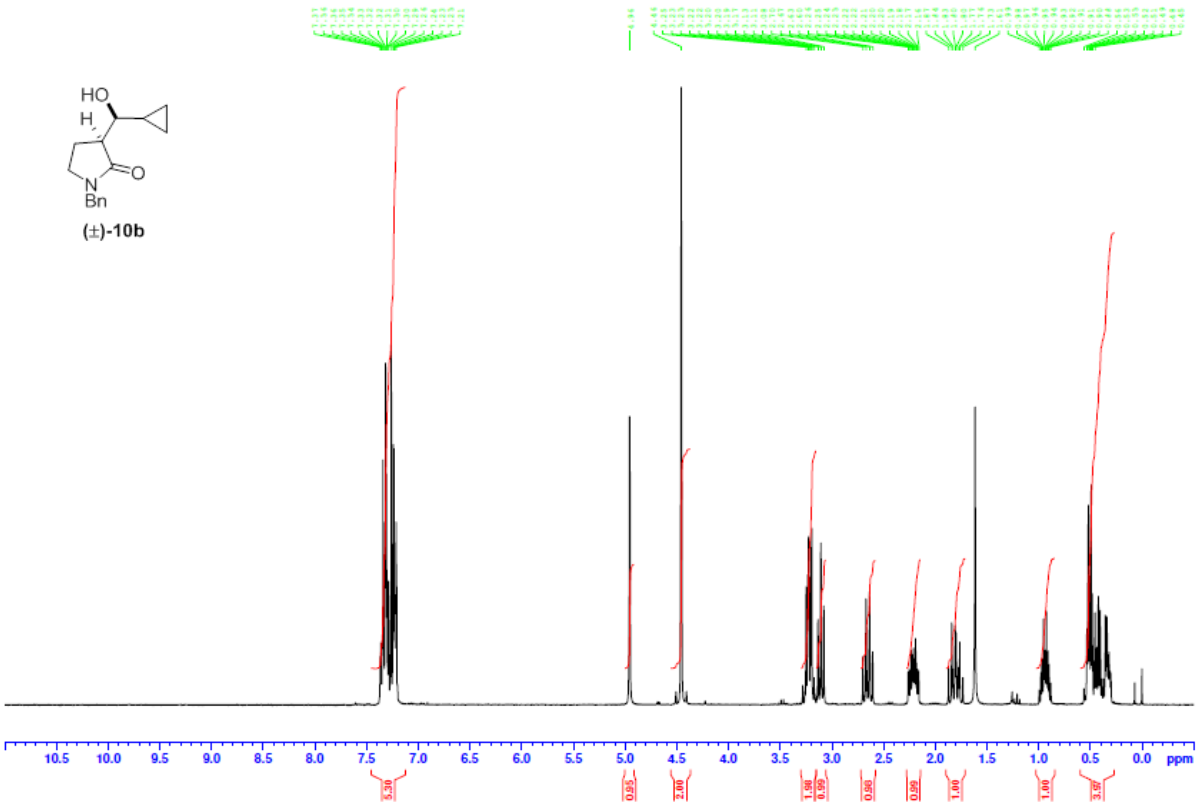

HO
H
O
N
Bn
(±)-8a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

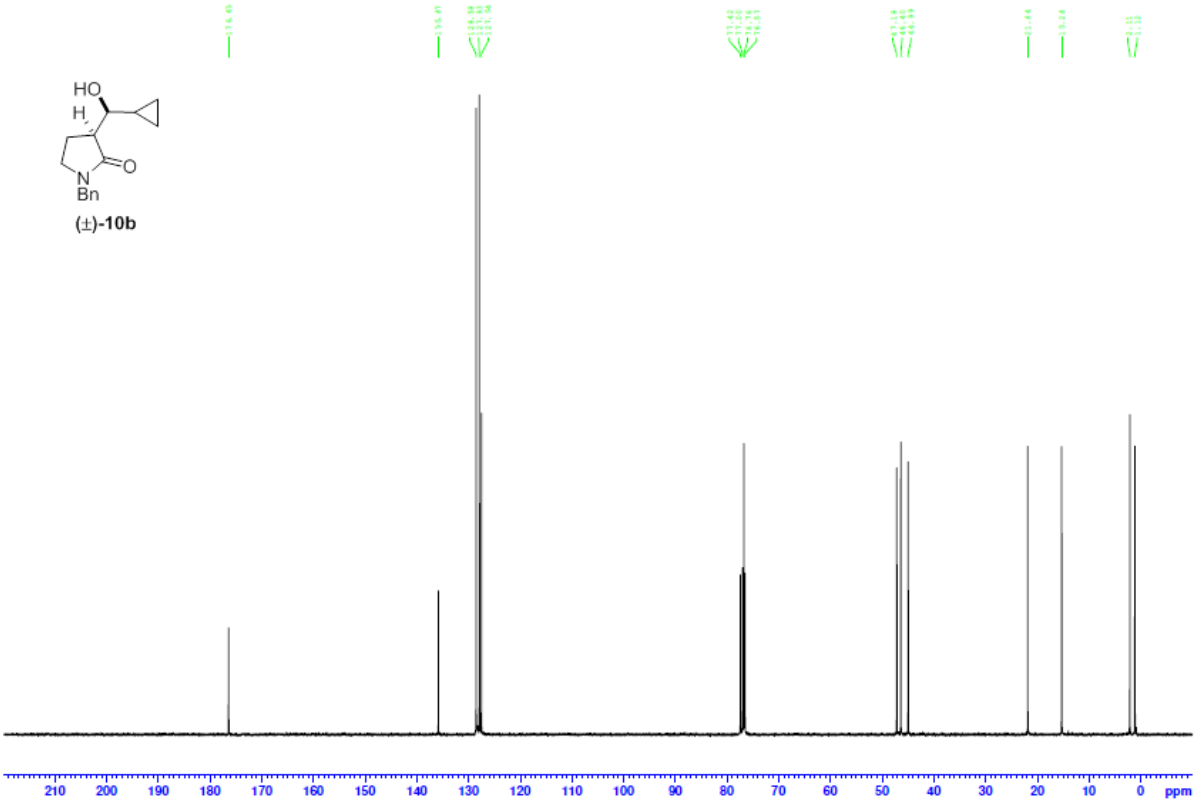

HO
H
O
N
Bn
(±)-10a
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.06
0.96
1.96
0.97
1.98
1.00
1.34
2.01
3.10
2.98

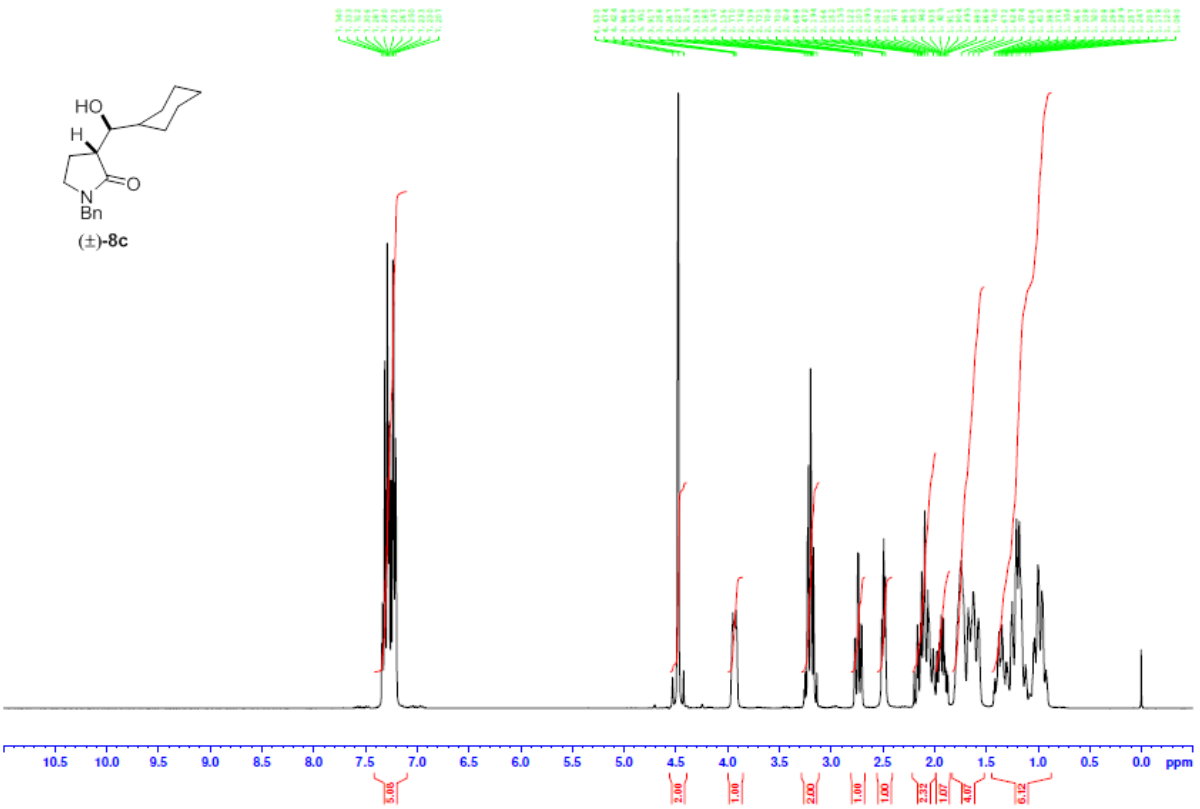

HO
H
O
N
Bn
(±)-10a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

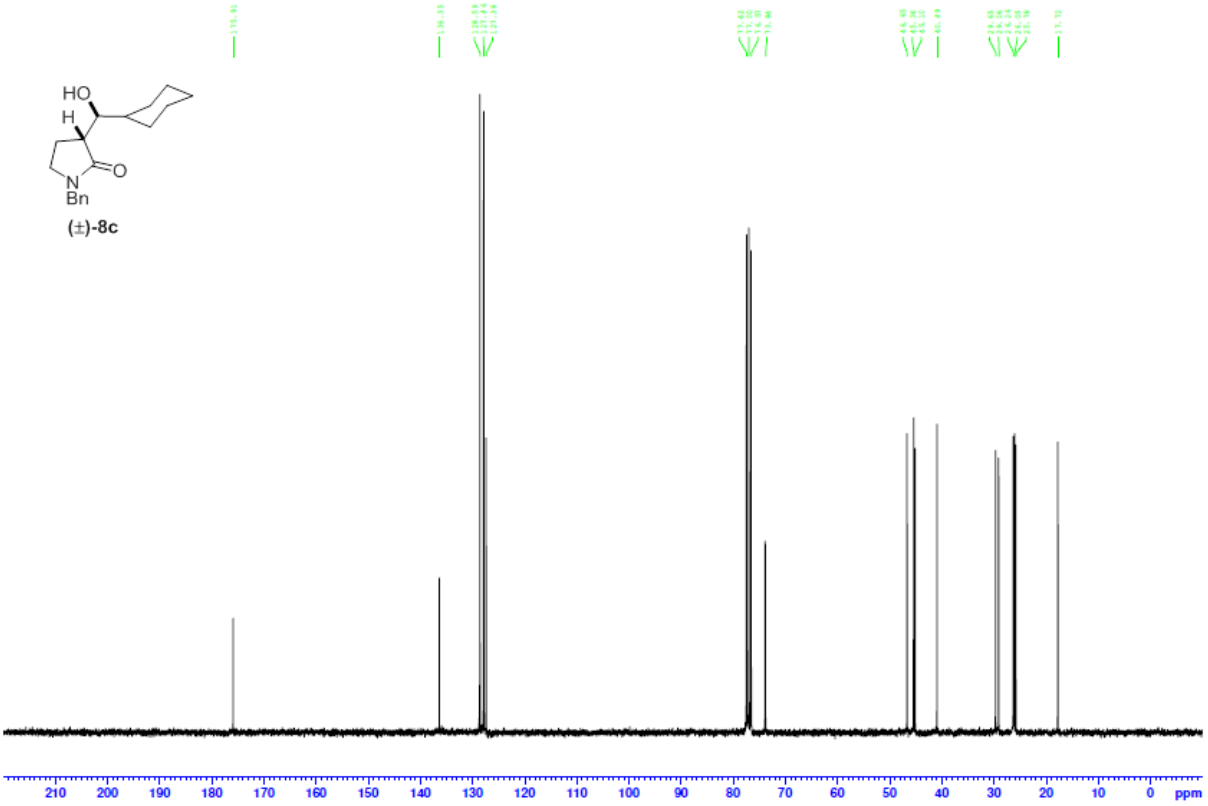

HO
H
O
N
Bn
(±)-8b
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.38
2.00
1.00
2.03
0.99
0.96
1.03
1.01
1.01
3.05
0.99

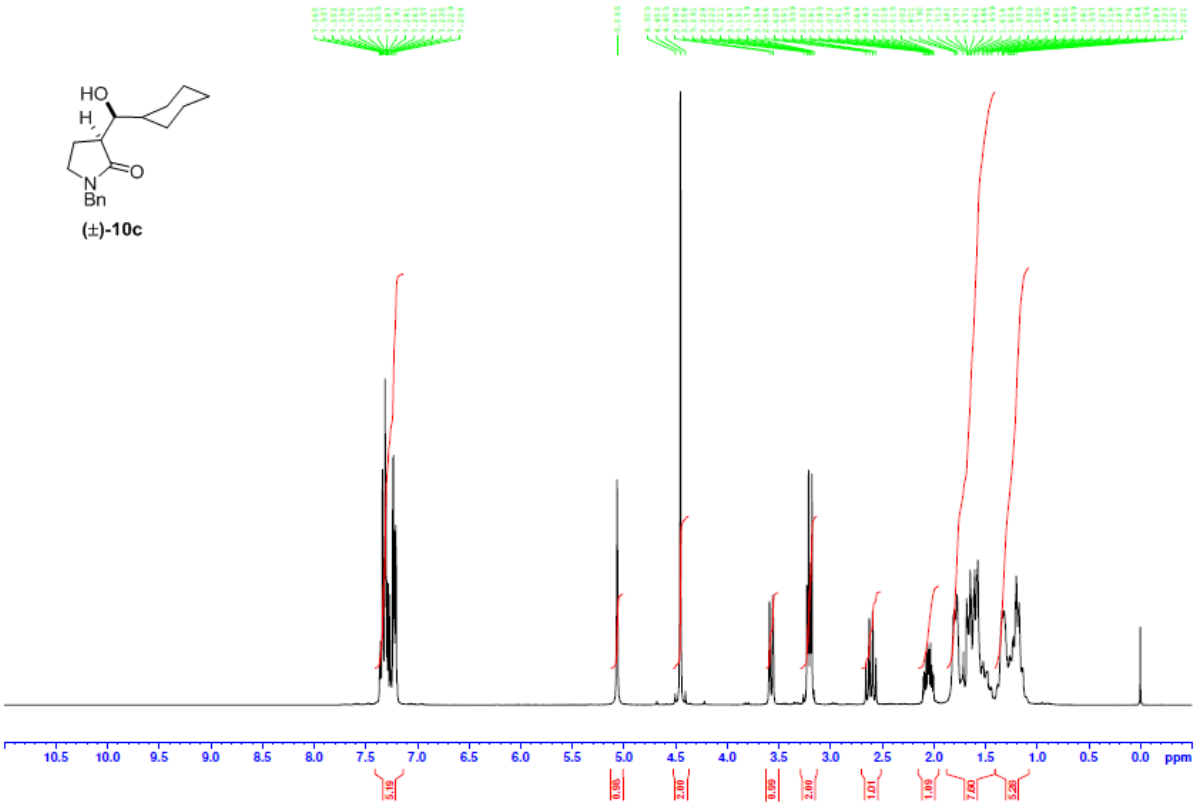

HO
H
O
N
Bn
(±)-8b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

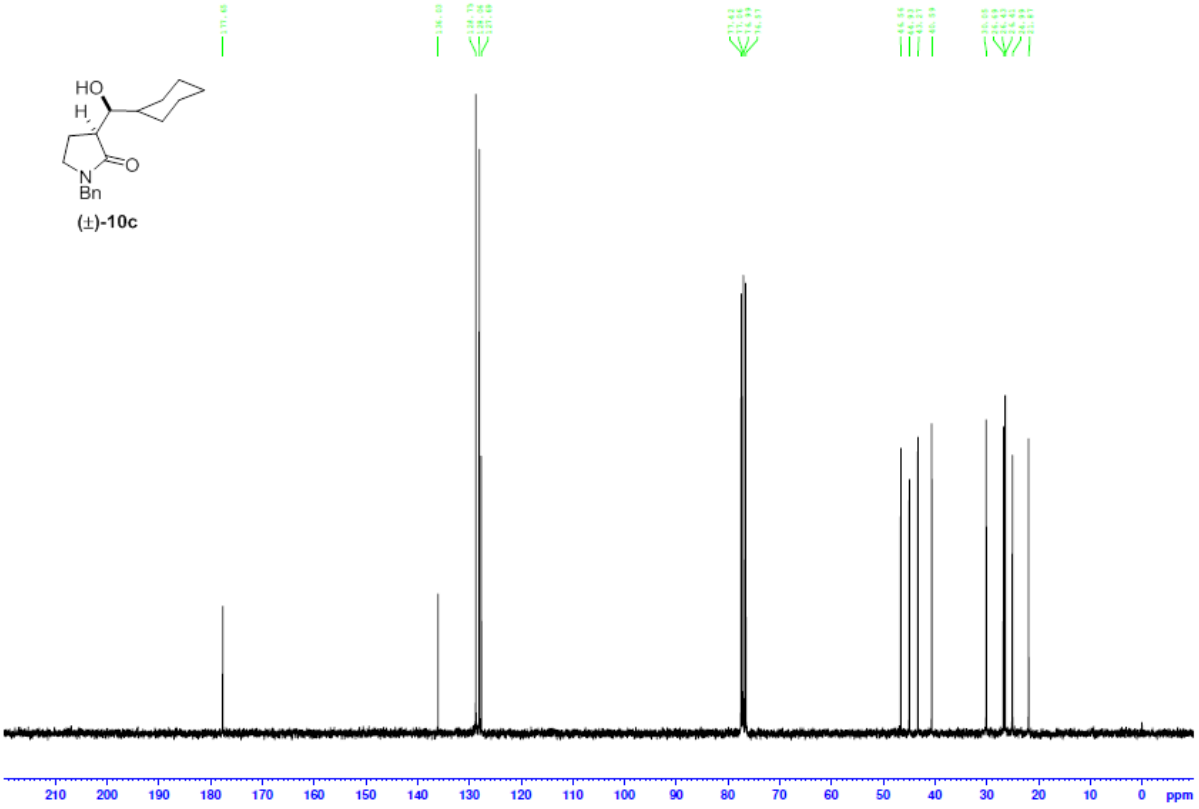

HO
H
N
Bn
O
(±)-10b
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.30
0.95
2.00
1.98
0.99
0.98
0.99
1.00
1.00
3.06

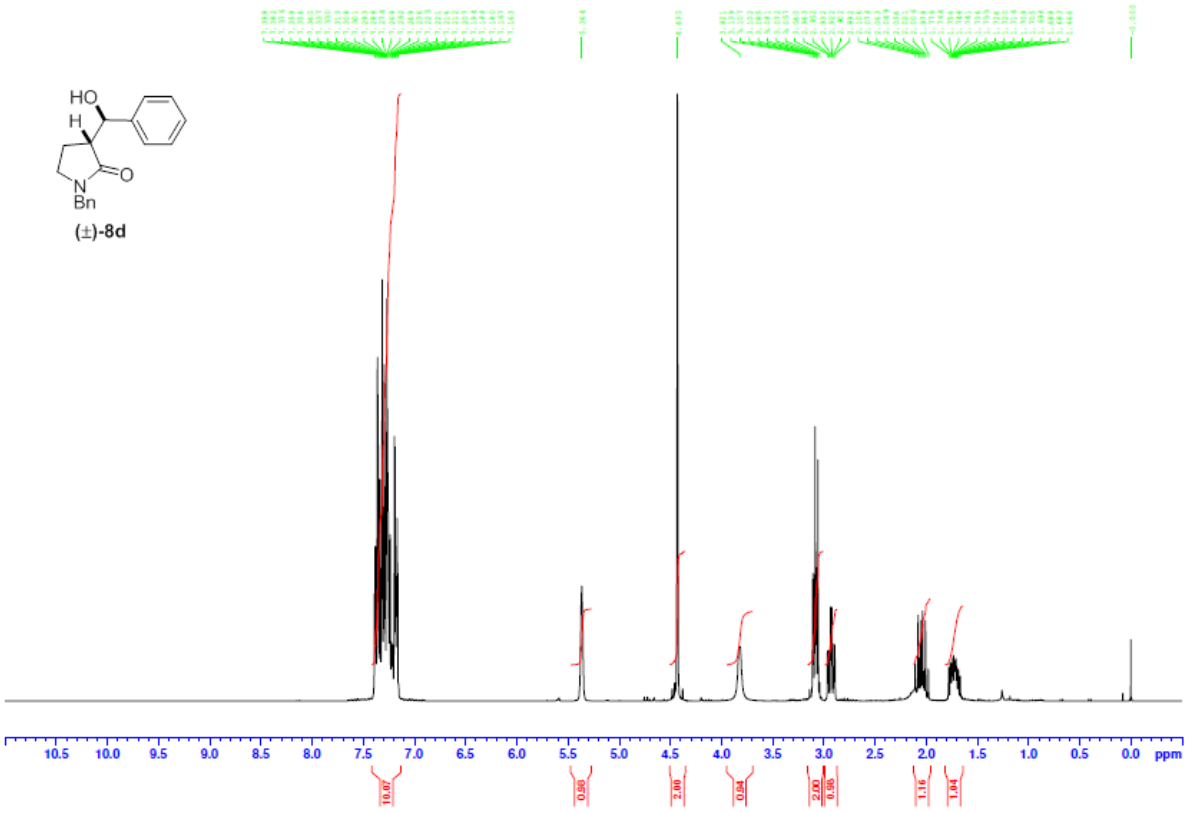

HO
H
N
Bn
O
(±)-10b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

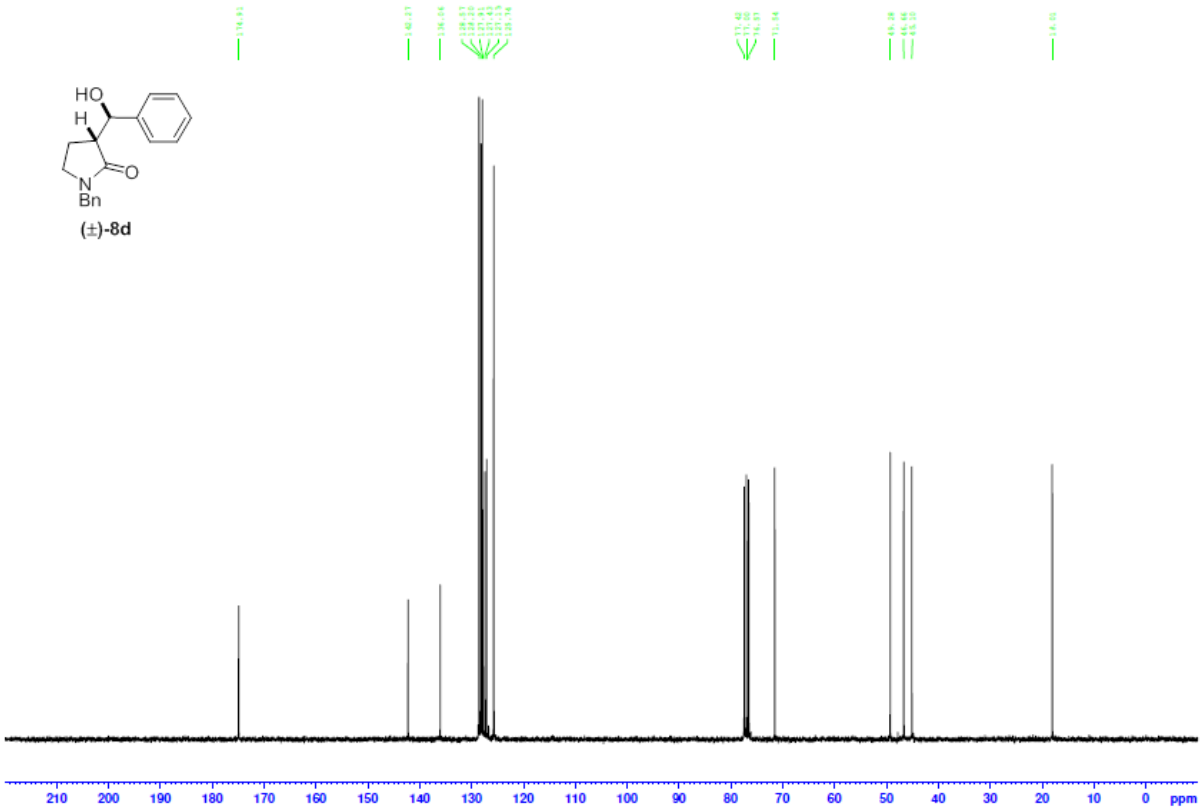

HO
H
O
N
Bn
(±)-8c
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.05 2.00 1.00 2.00 1.00 1.00 2.33 1.07 4.01 6.12

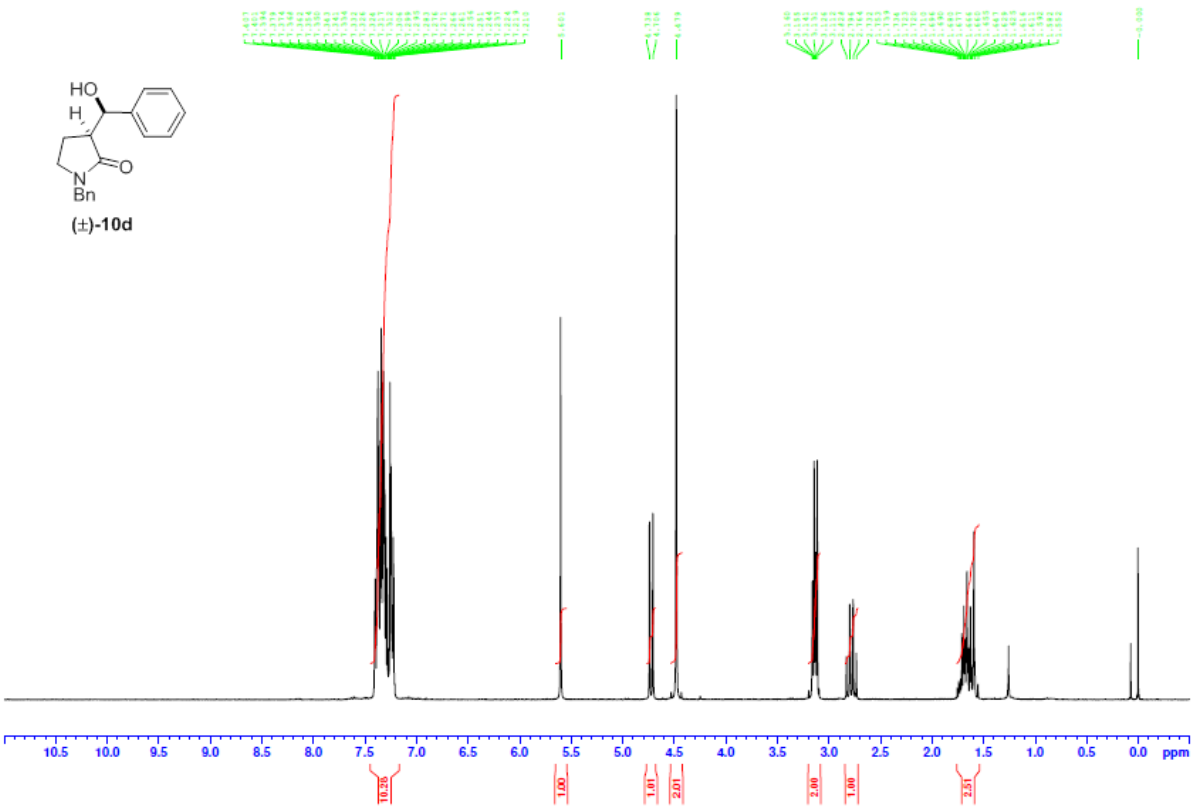

HO
H
O
N
Bn
(±)-8c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

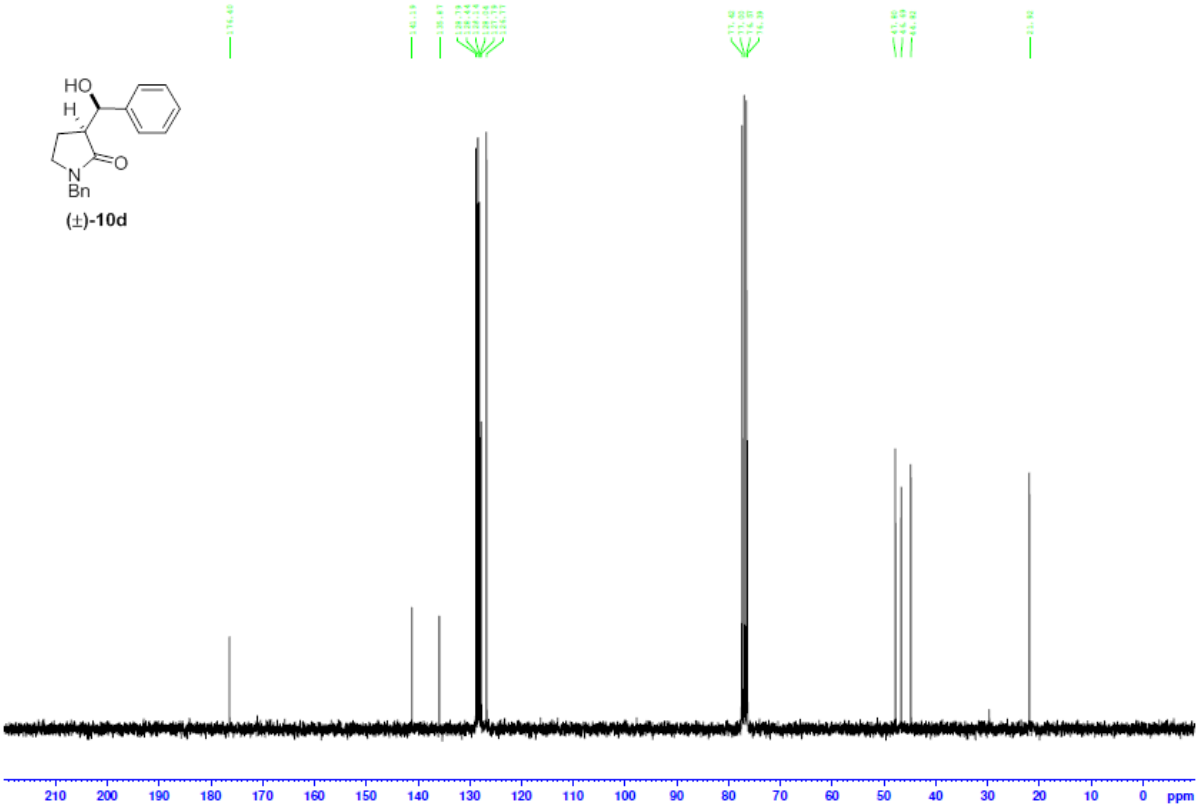

HO
H
N
Bn
O
(±)-10c
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.19
0.98
2.00
0.99
2.00
1.01
1.09
7.00
5.28

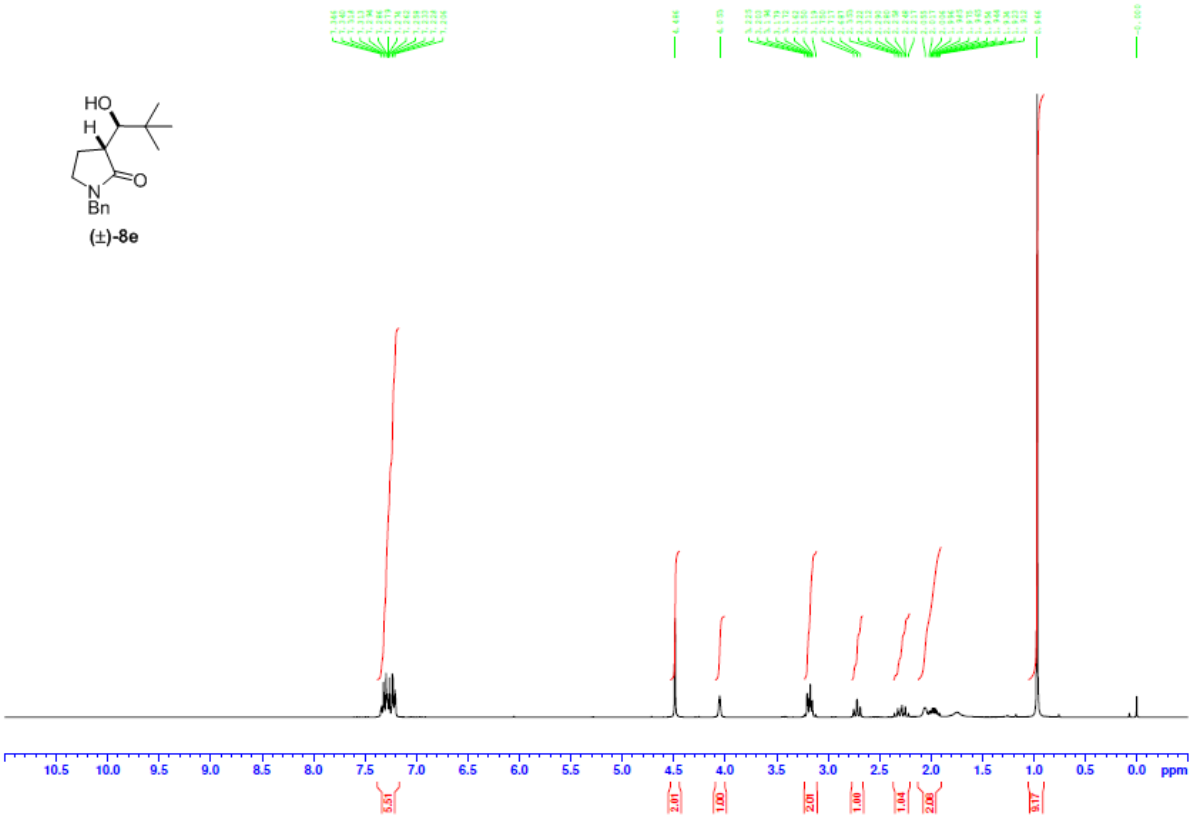

HO
H
N
Bn
O
(±)-10c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

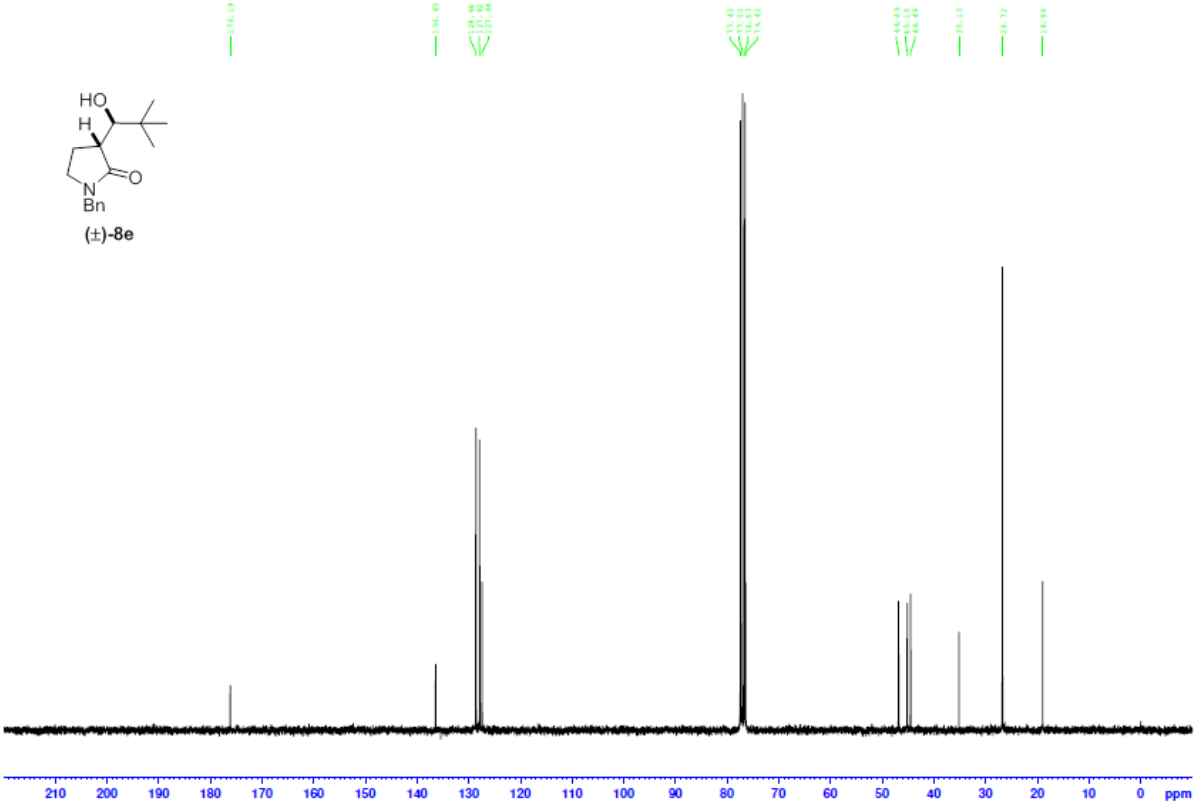

HO
H
N
O
Bn
(±)-8d
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
10.07
0.98
2.00
0.94
2.00
0.98
1.16
1.04

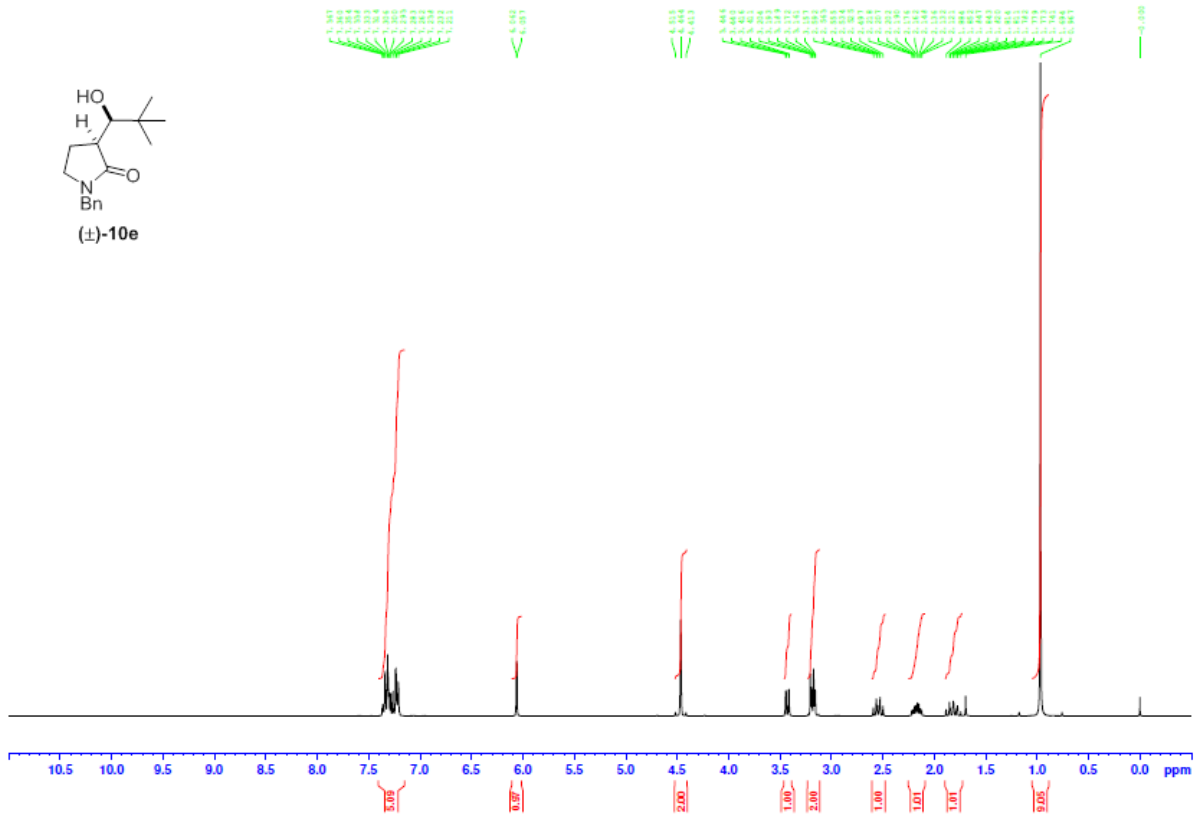

HO
H
N
O
Bn
(±)-8d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

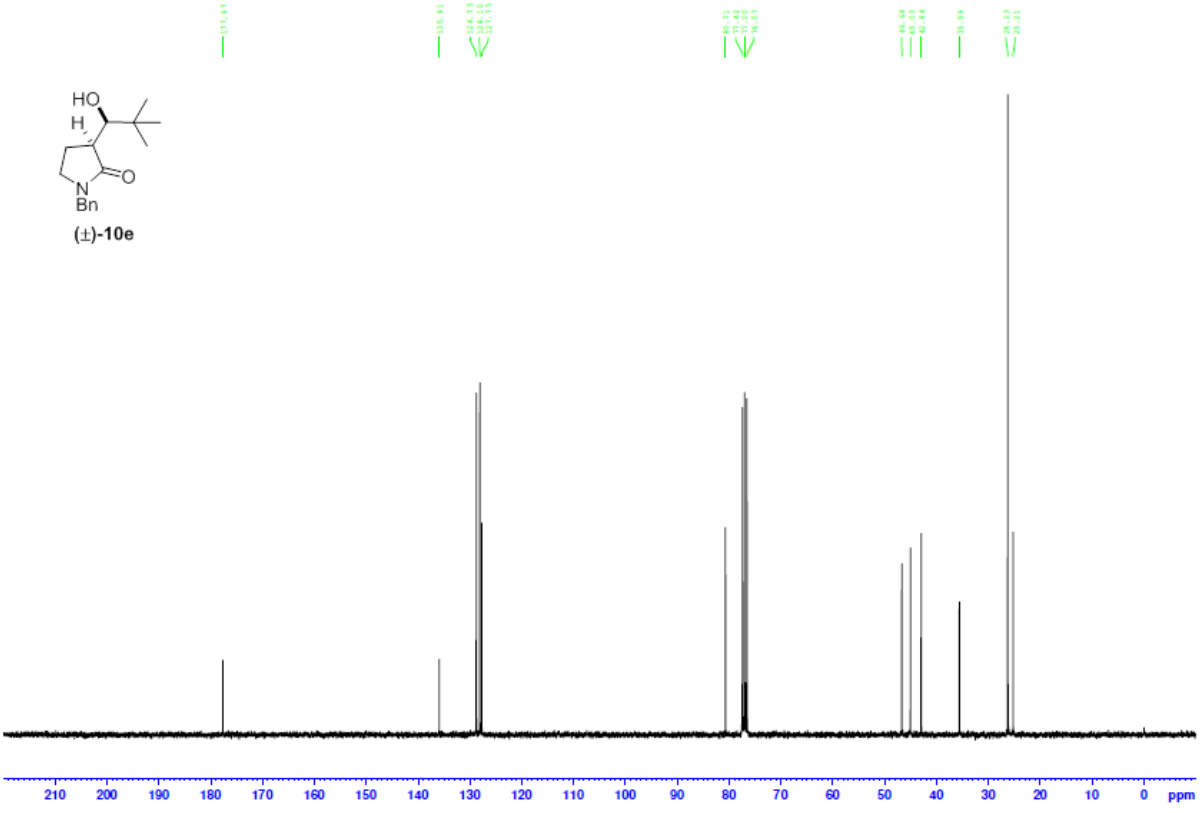

HO
H
O
N
Bn
(±)-10d
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
10.26
1.00
1.01
2.01
2.00
1.00
2.51

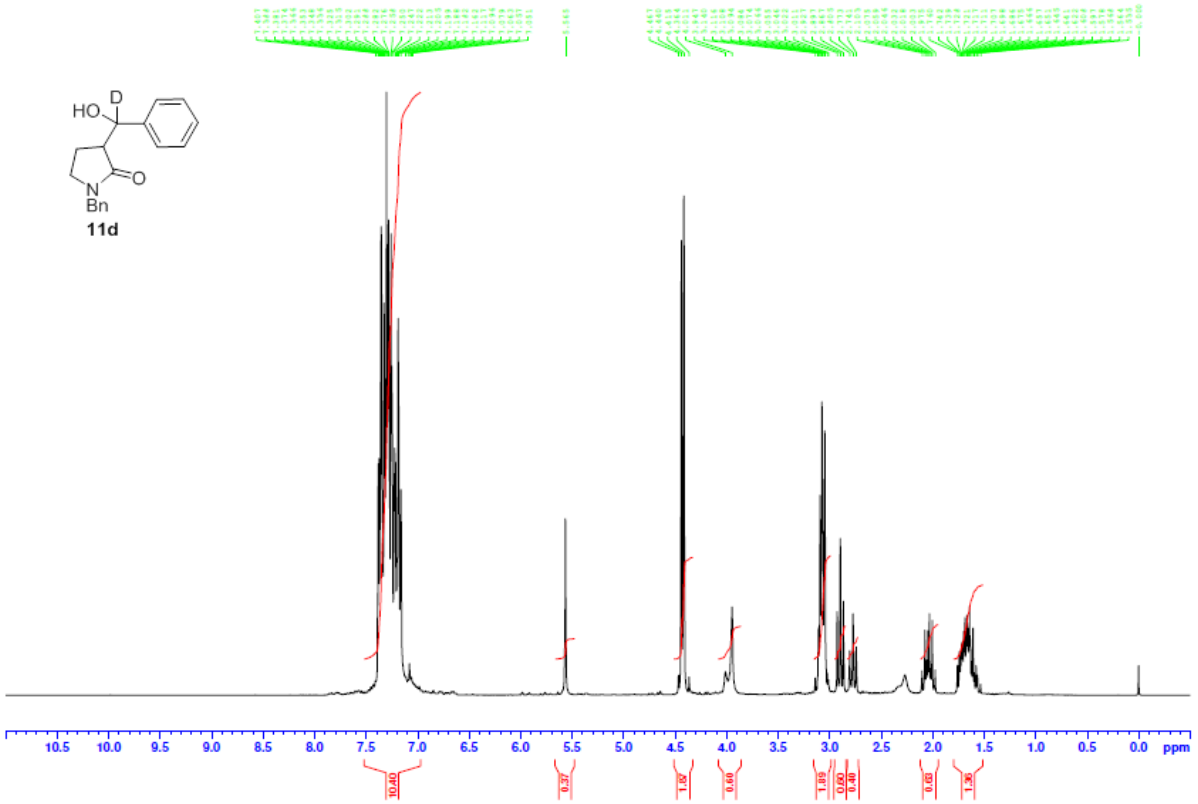

HO
H
O
N
Bn
(±)-10d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

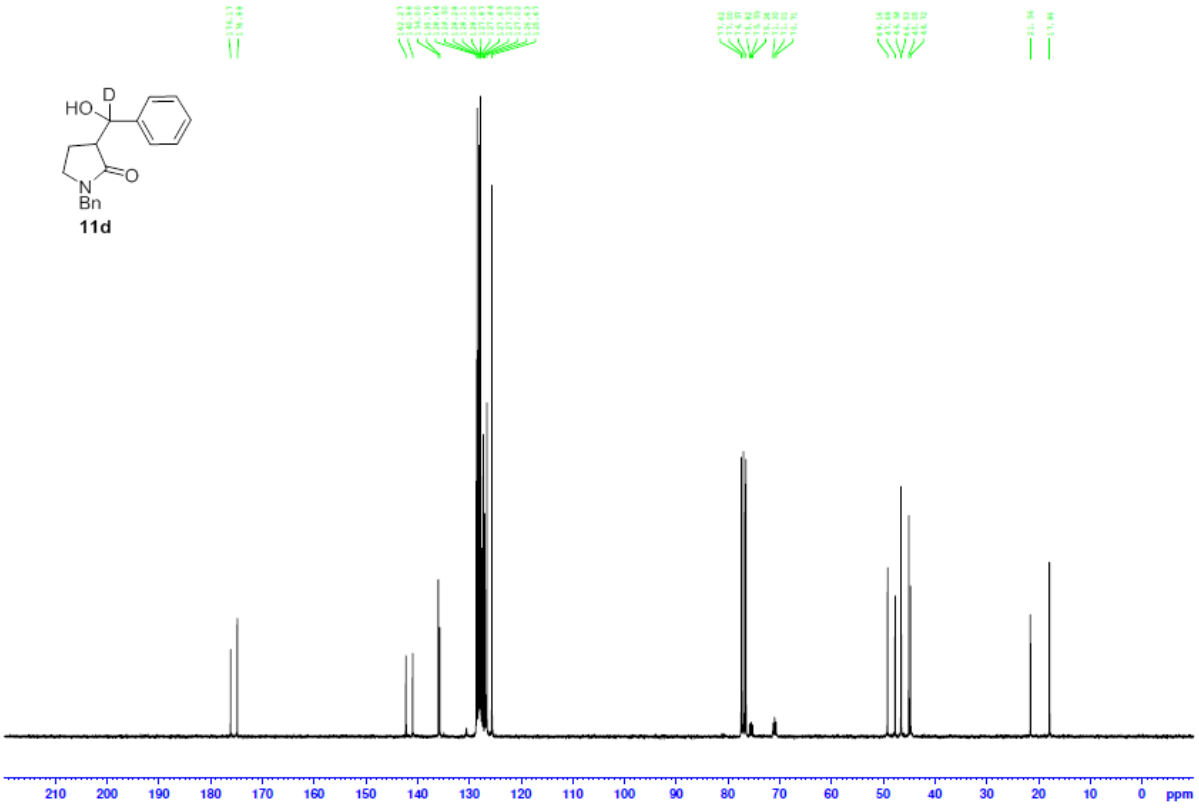

HO
H
N
O
Bn
(±)-8e
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.51
2.01
1.00
2.05
1.00
1.04
2.08
9.17


HO
H
N
O
Bn
(±)-8e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


HO
H
O
N
Bn
(±)-10e
10.5 10.0 9.5 9.0 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 ppm
5.09
0.97
2.00
1.00
2.00
1.00
1.01
1.01
9.05


HO
H
O
N
Bn
(±)-10e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


HO
D
O
N
Bn
11d
10.5 10.0 9.5 9.0 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 ppm
10.60
0.37
1.00
0.69
1.89
0.60
0.40
0.60
1.90


HO
D
O
N
Bn
11d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

X-Ray Crystallographic Structures

Crystals of **4c** and **4d**—suitable for single crystal X-ray diffraction and taken from samples of the chromatographically purified products of Table S1(A), entry 6 and Table S1(B) entry 15 respectively—were grown by solvent evaporation from a toluene solution over 14 d until the solvent had completely evaporated. Full crystallographic details are contained in the CIFs.

While both **4c** (CCDC 1505406) and **4d** (CCDC 1505405) have identical absolute and relative stereochemistry and both agree with the earlier stereochemical assignment of **4a**,[2] they display optical rotations of opposite sign.

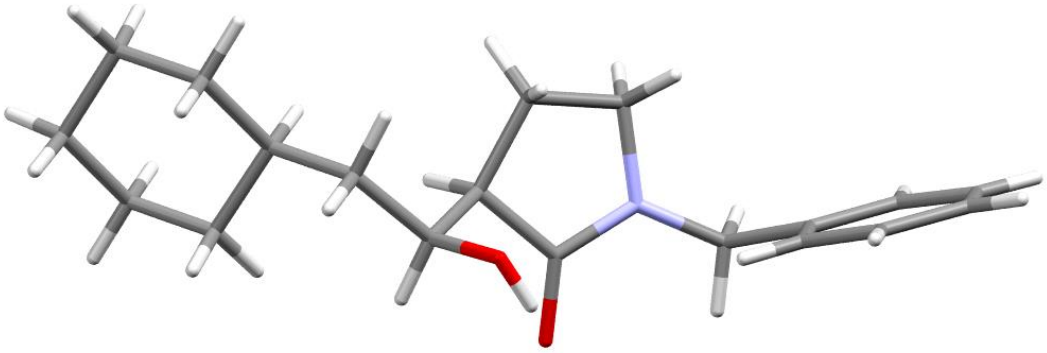


Figure *Image* **4c**, *(CCDC 1505406)*

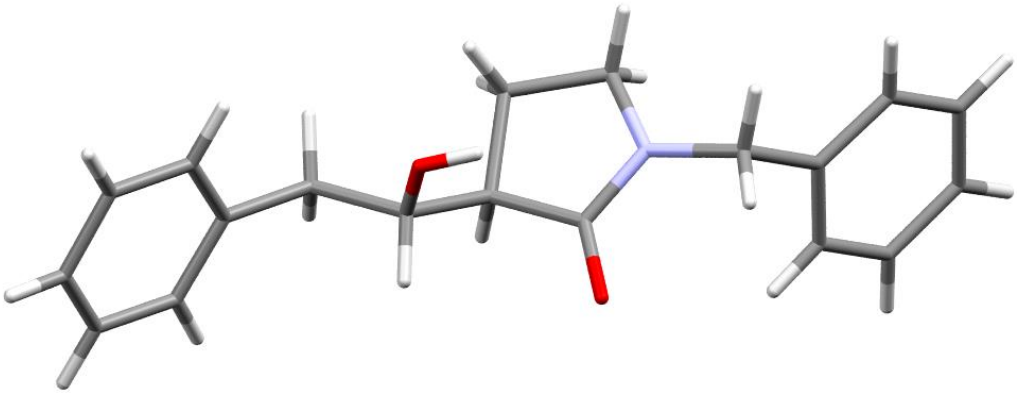


Figure *Image* **4d**, *(CCDC 1505405)*