

One-pot synthesis of γ -lactams from ketoaziridines

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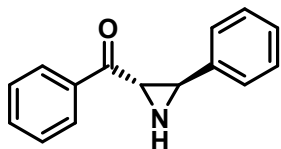
1. General information

All reagents used were commercially available from Sigma-Aldrich, Synth, Exodus and Merck. The solvents used are from commercial sources and when necessary dry solvents were treated as recommended in the literature.¹ Purification of the products was performed by flash column chromatography, with silica gel 60, 230-400 mesh ASTM Merck, silica gel 60 A, 70-230 mesh AldrichCo and silica gel chromatoplates 60 F₂₅₄ Merck KGaA. Nuclear Magnetic Resonance spectra were recorded on Bruker ARX 400 MHz spectrometers. Chemical shifts (δ) are expressed in ppm referenced by the residual solvent signal and coupling constants (J) in Hertz (Hz). To indicate the multiplicity of signs, the following abbreviation was used: *s* (singlet), *brs* (broad singlet), *d* (doublet), *t* (triplet), *q* (quadruplet), *m* (multiplet). HRMS-ESI analyzes were performed on an Agilent 6545 qTOF MS system (Agilent Technologies, Santa Clara, CA, USA) equipped with a Jet electrospray interface (ESI) in positive mode. The enantiomeric ratios were determined using UltraPerformance Convergence Chromatography (UPC²) from Waters ACQUITY. IR spectra were generated on a Shimadzu spectrophotometer, model IR Prestige-21. The samples were diluted in dichloromethane and applied in a NaCl cell used to obtain the absorption spectra. Melting points were obtained using a Büchi equipment, model M-560, and reported in degrees Celsius (°C). X-ray analysis was performed using a Bruker APEX-II CCD diffractometer at the Institute of Chemistry of São Carlos-University of São Paulo (IQSC-USP).

2. General procedure for obtaining aziridines (2a-r)²

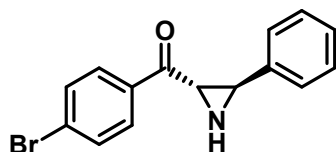
To a 250 mL flask provided with magnetic stirring, 4-nitrobenzoylhydroxylamine (2.73 g, 15 mmol), DMF (160 mL) and *N*-methyldmorpholine (12 mL, 110 mmol) were added. After 15 minutes of stirring, NaOH (0.8 g, 20 mmol) and chalcone (2.08 g, 10 mmol) were added and then the reaction mixture was stirred for 21 hours at room temperature. Then an 5% aqueous solution of LiCl (200 mL) was added and the product was extracted with AcOEt (3 x 5 mL). The organic phase was dried with anhydrous Na₂SO₄ and concentrated under vacuum. The crude was purified by column chromatography with silica gel and Hexane-AcOEt 9:1 with 1% triethylamine as eluent.

phenyl(3-phenylaziridin-2-yl)methanone (2a)²



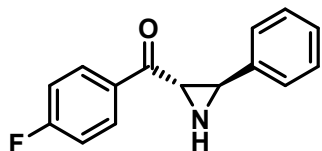
The product was obtained as a white solid in 61% yield (1.36 g). ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.41 – 7.30 (m, 2H), 3.53 (d, *J* = 2.2 Hz, 1H), 3.19 (d, *J* = 2.2 Hz, 1H), 2.45 (brs, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 195.9, 138.5, 136.0, 134.0, 129.0, 128.7, 128.5, 128.0, 126.4, 44.2, 43.7.

(4-bromophenyl)(3-phenylaziridin-2-yl)methanone (2c)³



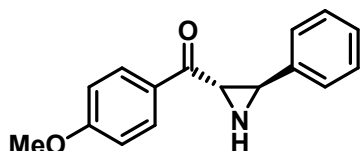
The product was obtained as a white solid in 56% yield (271 mg). ¹H NMR (400 MHz, CDCl₃) δ: 7.85 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.40 – 7.30 (m, 5H), 3.45 (brs, 1H), 3.19 (brs, 1H), 2.65 (s, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 194.8, 138.1, 134.6, 132.2, 129.8, 129.2, 128.6, 128.0, 126.2, 44.1, 43.8.

(4-fluorophenyl)(3-phenylaziridin-2-yl)methanone (2d)⁴



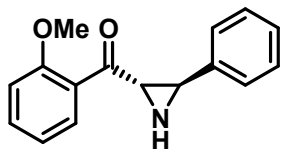
The product was obtained as a white solid in 71% yield (341 mg). ¹H NMR (400 MHz, CDCl₃) δ: 8.03 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.41 – 7.35 (m, 4H), 7.35 – 7.29 (m, 1H), 7.16 (t, *J* = 8.6 Hz, 2H), 3.47 (d, *J* = 1.9 Hz, 1H), 3.18 (d, *J* = 1.8 Hz, 1H), 2.58 (s, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 194.2, 166.2 (d, *J* = 256.5 Hz), 138.2, 132.4, 131.1 (d, *J* = 9.5 Hz), 128.6, 128.0, 126.2, 116.1 (d, *J* = 22.1 Hz), 43.6. ¹⁹F{¹H} NMR (376 MHz, CDCl₃): -103.5.

(4-methoxyphenyl)(3-phenylaziridin-2-yl)methanone (2e)²



The product was obtained as an off-white solid in 91% yield (462 mg). ¹H NMR (400 MHz, CDCl₃) δ: 7.99 (d, *J* = 8.9 Hz, 2H), 7.36 (d, *J* = 4.2 Hz, 4H), 7.34 – 7.27 (m, 2H), 6.96 (d, *J* = 8.8 Hz, 1H), 3.88 (s, 3H), 3.47 (d, *J* = 2.1 Hz, 1H), 3.15 (d, *J* = 2.1 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 193.9, 164.2, 138.5, 130.7, 129.0, 128.6, 127.8, 126.2, 114.0, 55.6, 43.7, 43.1.

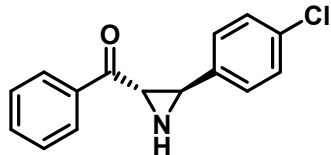
(2-methoxyphenyl)(-3-phenylaziridin-2-yl)methanone (2f)⁵



The product was obtained as a yellow oil in 75% yield (459 mg). ¹H NMR (400 MHz, CDCl₃) δ: 7.75 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.40 – 7.31 (m, 4H), 7.30 – 7.24 (m, 1H). 7.02 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.60 (s, 3H), 3.53 (d, *J* = 2.1 Hz, 1H), 3.14 (d, *J* = 2.1 Hz, 1H), 2.61 (s, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 197.6, 159.6, 139.1, 134.6, 130.6, 128.3, 127.5, 126.4, 126.2, 120.8, 111.7, 55.5, 48.5, 43.6.

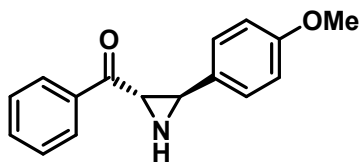
(3-(4-chlorophenyl)aziridin-2-yl)(phenyl)methanone (2g)²



The product was obtained as a white solid in 37% yield (289 mg). ¹H NMR (400 MHz, CDCl₃) δ: 7.98 (d, *J* = 7.8 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.28 (m, 4H), 3.46 (d, *J* = 1.8 Hz, 1H), 3.15 (d, *J* = 1.5 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 195.4, 136.9, 135.8,

134.0, 133.7, 128.9, 128.8, 128.4, 127.6, 44.1, 42.8.

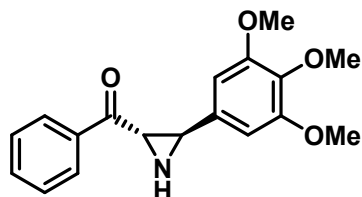
(3-(4-methoxyphenyl)aziridin-2-yl)(phenyl)methanone (2h)²



The product was obtained as an orange solid in 60% yield (456 mg). ¹H NMR (400 MHz, CDCl₃) δ: 7.99 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 3.82 (s, 3H), 3.48 (d, *J* = 2.2 Hz, 1H), 3.14 (d, *J* = 2.0 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃)

δ: 195.8, 159.4, 136.0, 133.8, 130.4, 128.8, 128.3, 127.4, 114.0, 55.4, 44.2, 43.4.

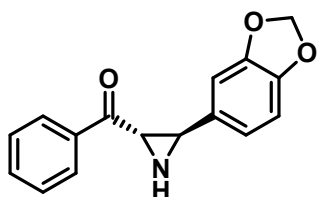
phenyl(3-(3,4,5-trimethoxyphenyl)aziridin-2-yl)methanone (2i)



The product was obtained as an orange solid in 44% yield (277 mg). ¹H NMR (400 MHz, CDCl₃) δ: 8.03 (d, *J* = 7.7 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.80 (s, 3H), 3.43 (brs, 1H), 3.39 (brs,

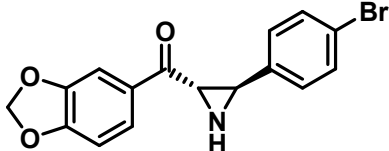
1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 196.1, 153.4, 152.8, 141.8, 136.1, 133.7, 128.8, 128.3, 124.4, 120.5, 107.4, 61.2, 60.9, 56.1, 43.5, 39.0.

Benzo[d][1,3]dioxol-5-yl(-3-(4-bromophenyl)aziridin-2-yl)methanone (2j)



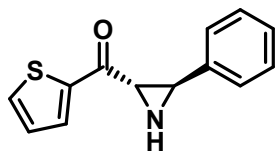
The product was obtained as an off-white solid in 38% yield (301 mg). ^1H NMR (400 MHz, CDCl_3) δ : 7.99 (dt, J = 8.5, 1.6 Hz, 2H), 7.67 – 7.56 (m, 1H), 7.55 – 7.42 (m, 2H), 6.90 – 6.80 (m, 2H), 6.77 (dd, J = 7.6, 0.7 Hz, 1H), 5.95 (s, 2H), 3.44 (brs, 1H), 3.10 (brs, 1H), 2.64 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 195.7, 148.0, 147.4, 135.9, 133.8, 132.4, 128.9, 128.3, 120.1, 108.3, 106.1, 101.2, 44.1, 43.5.

Benzo[d][1,3]dioxol-5-yl(-3-(4-bromophenyl)aziridin-2-yl)methanone (2k)



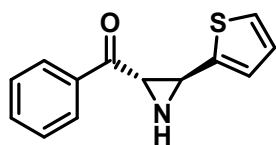
The product was obtained as a yellow solid in 57% yield (334 mg). ^1H NMR (400 MHz, CDCl_3) δ : 7.60 (d, J = 8.2 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.25 (d, J = 8.3 Hz, 2H), 6.88 (d, J = 8.2 Hz, 1H), 6.08 (s, 2H), 3.37 (d, J = 1.9 Hz, 1H), 3.11 (d, J = 1.6 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 193.2, 152.6, 148.5, 137.5, 131.7, 130.6, 127.9, 125.0, 121.7, 108.2, 107.9, 102.1, 43.8, 42.5.

(3-phenylaziridin-2-yl)(thiophen-2-yl)methanone (2l)⁴



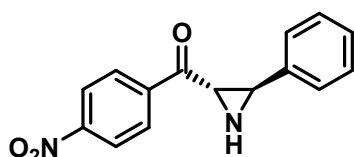
The product was obtained as an orange solid in 65% yield (448 mg). ^1H NMR (400 MHz, CDCl_3) δ : 7.85 (d, J = 3.8 Hz, 1H), 7.74 (d, J = 4.9 Hz, 1H), 7.38 – 7.28 (m, 5H), 7.17 (t, J = 4.4 Hz, 1H), 3.40 (d, J = 2.0 Hz, 1H), 3.27 (d, J = 1.9 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 188.3, 142.8, 138.2, 134.9, 133.0, 128.6, 127.9, 126.3, 44.4, 43.3.

phenyl(3-(thiophen-2-yl)aziridin-2-yl)methanone (2m)²



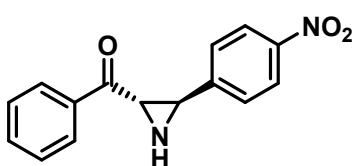
The product was obtained as an orange solid in 81% yield (555 mg). ¹H NMR (400 MHz, CDCl₃) δ: 8.02 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 7.1 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 5.1 Hz, 1H), 7.10 (d, *J* = 3.4 Hz, 1H), 7.03 – 6.96 (m, 1H), 3.62 (brs, 1H), 3.42 (brs, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 195.1, 143.2, 135.8, 134.0, 128.9, 128.4, 127.2, 125.3, 124.5, 44.9, 40.0.

(4-nitrophenyl)(-3-phenylaziridin-2-yl)methanone (2n)⁶



The product was obtained as a brown oil in 43% yield (345 mg). ¹H NMR (400 MHz, CDCl₃) δ: 8.34 (d, *J* = 8.7 Hz, 2H), 8.14 (d, *J* = 8.7 Hz, 2H), 7.44 – 7.32 (m, 5H), 3.50 (brs, 1H), 3.26 (brs, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 194.6, 150.7, 140.3, 137.7, 129.4, 128.7, 128.3, 126.2, 124.1, 44.6, 44.6.

(3-(4-nitrophenyl)aziridin-2-yl)(phenyl)methanone (2o)²



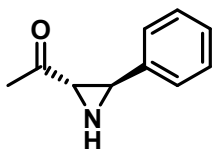
The product was obtained as a yellow solid in 60% yield (480 mg). ¹H NMR (400 MHz, CDCl₃) δ: 8.22 (d, *J* = 8.6 Hz, 2H), 7.99 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.61 – 7.45 (m, 4H), 3.51 (brs, 1H), 3.26 (brs, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ: 194.9, 147.6, 145.8, 135.6, 134.3, 129.0, 128.4, 127.1, 123.9, 44.2, 42.3.

3. Synthesis of alkyl aziridines (2p-q)⁷

To a 10 mL vial with 4-nitrobenzoylhydroxylamine (91.1 mg, 0.5 mmol) and dichloromethane (2 mL) was added dropwise *N*-methylmorpholine (302 μL, 2.75 mmol). After 30 minutes of stirring, 60% NaH in mineral oil (30 mg, 0.75 mmol), *i*PrOH (57 μL, 0.75 mmol) and a solution of (*E*)-4-phenylbut-3-en-2-one (36.5 mg, 0.25 mmol) and dichloromethane (2 mL). The reaction mixture was stirred for 48 hours. After this period the reaction was extracted with DCM (3 x 5 mL), and the organic

phase were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude was purified by column chromatography with silica gel and Hexane-AcOEt (9:1) with 1% triethylamine as eluent.

1-(3-phenylaziridin-2-yl)ethanone (2p)⁵

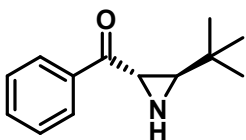


The product was obtained as a yellow oil in 68% yield (27.5 mg). ¹H NMR (400 MHz, CDCl_3) δ : 7.40 – 6.83 (m, 5H), 2.97 (brs, 1H), 2.79 (brs, 1H), 2.30 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl_3) δ : 204.7, 138.3, 128.6, 128.0, 126.2, 46.9, 43.1,

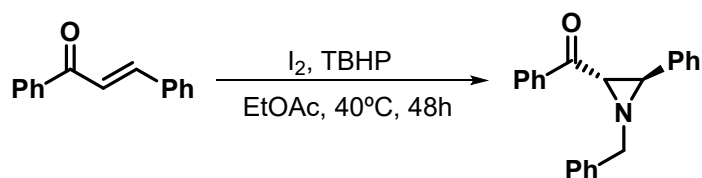
29.6.

(3-(tert-butyl)aziridin-2-yl)(phenyl)methanone (2q)²



The product was obtained as a pale yellow solid in 53% yield (322mg). ¹H NMR (400 MHz, CDCl_3) δ : 8.02 (d, J = 7.8 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 3.36 (d, J = 2.0 Hz, 1H), 2.03 (d, J = 2.2 Hz, 1H), 0.99 (s, 9H). ¹³C{¹H} NMR (100 MHz, CDCl_3) δ : 197.7, 136.1, 133.6, 128.8, 128.1, 52.7, 36.8, 31.3, 26.8.

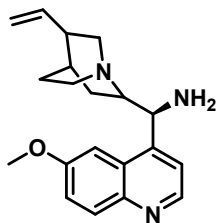
4. Synthesis of (1-benzyl-3-phenylaziridin-2-yl)(phenyl)methanone (2b)⁸



In a sealed tube provided with magnetic stirring, chalcone (41.7 mg, 0.2 mmol), benzylamine (44 μL , 0.4 mmol), I_2 (5.08 mg, 0.02 mmol), EtOAc (2 mL) and TBHP (36.4 μL , 0.2 mmol) were added. The mixture was stirred at 40°C for 2 days and then washed with saturated aqueous sodium thiosulfate solution (30 mL) and saturated aqueous NaCl solution (5 mL) and extracted with AcOEt (3 x 5 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude was purified by column chromatography with silica gel and Hexane-AcOEt 9:1 with 1% triethylamine as eluent. The product was obtained as a yellow solid in 31% yield (20.3 mg). ¹H NMR (400 MHz, CDCl_3)

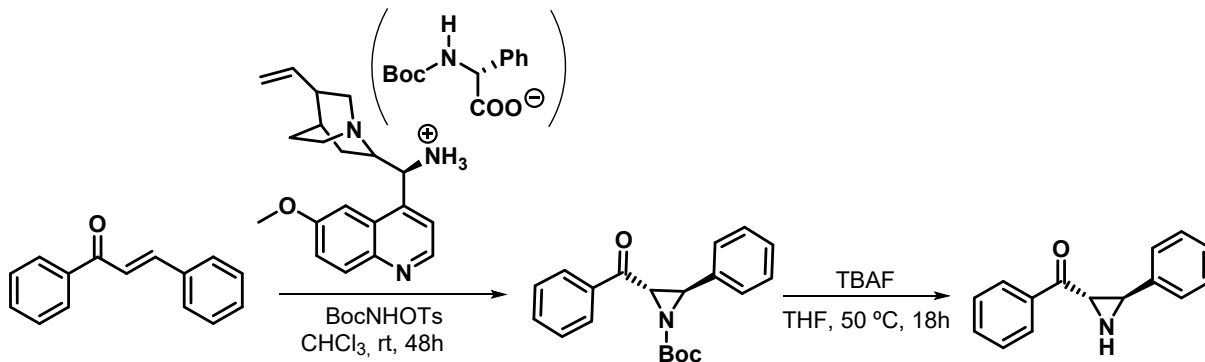
δ : 7.80 (d, J = 8.0 Hz, 2H), 7.46 – 7.40 (m, 3H), 7.35 – 7.27 (m, 5H), 7.20 (t, J = 7.4 Hz, 2H), 7.13 (t, J = 7.5 Hz, 2H), 7.10 – 7.04 (m, 1H), 3.97 (d, J = 13.9 Hz, 1H), 3.76 (d, J = 14.0 Hz, 1H), 3.34 (d, J = 6.9 Hz, 1H), 3.26 (d, J = 7.0 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 193.2, 137.8, 137.0, 135.0, 133.0, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 127.4, 127.2, 63.9, 51.1, 49.8.

5. Synthesis of (1S)-(6-methoxyquinolin-4-yl)(5-vinylquinuclidin-2-yl)methanamine (B)⁹



In a flask under nitrogen atmosphere and ice bath, a solution of quinine (1.62 g; 5 mmol), triphenylphosphine (1.58 g; 6 mmol), DIAD (1.22 g; 6 mmol) in THF dry (mL) was prepared. To this mixture, a solution of DPPA (1.65 g; 6 mmol) in THF dry (25 mL) was added slowly. The reaction mixture was kept under stirring at room temperature for 12 hours and after this period, it was heated to 50 °C for 2 hours and then triphenylphosphine (1.70 g; 6.5 mmol) was added and heating continued for another 2 hours. The reaction was cooled to room temperature, water (1 mL) added and stirred for 3 hours. The reaction was concentrated under vacuum and subsequently solubilized in DCM (25 mL) and HCl 10% (25 mL). The aqueous phase was washed with DCM (4 x 25 mL), basified with excess NH_4OH 28-30% solution (10 mL) and then extracted with DCM (4 x 25 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated in vacuum. The crude was purified by column chromatography with silica gel and in a gradient of 10 to 100% AcOEt-MeOH. The product was obtained a viscous yellow oil in 73% yield (1.18 g). ^1H NMR (400 MHz, CDCl_3) δ : 8,75 (d, J = 4,3 Hz, 1H), 8,04 (d, J = 9,2 Hz, 1H), 7,65 (d, J = 7,3 Hz, 1H), 7,47 (sl, 1H), 7,39 (dd, J = 9,1, 2,3 Hz, 1H), 5,80 (dd, J = 16,1, 8,7 Hz, 1H), 5,03-4,96 (m, 2H), 4,60 (d, J = 8.9 Hz, 1H), 3,97 (s, 3H), 3,28 (dd, J = 13,6, 10,2 Hz, 1H), 3,22 (s, 1H), 3,08 (s, 1H), 2,87 – 2,75 (m, 2H), 2,22 (d, J = 49.8 Hz, 4H), 1,63 (s, 1H), 1,58 - 1,55 (m, 1H), 1,43 (s, 1H), 0,77 (dd, J = 13.3, 7.3 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 157.6, 147.9, 147.1, 144.7, 141.8, 131.8, 128.8, 121.3, 119.9, 114.4, 102.0, 61.9, 56.4, 55.6, 41.0, 39.8, 28.2, 27.6, 26.1.

6. Synthesis of phenyl (2*S*,3*R*)-3-phenylaziridin-2-yl)methanone (**2a**)¹⁰



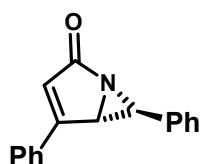
In a 5 mL vial, 9-amino(9-deoxy)epiquinine (64.7 mg, 0.2 mmol), *D*-Boc-phenylglycine³ (75.4 mg, 0.3 mmol) and CHCl₃ (4 mL). After 10 minutes of stirring at room temperature, chalcone (208 mg, 1 mmol) was added and stirred for a further 10 minutes. Then BocNHOTs (345 mg, 1.2 mmol) was added and stirred for 5 minutes and then NaHCO₃ (168 mg, 2 mmol) was added. The reaction mixture was stirred for 48 hours at room temperature. After this period, the reaction was filtered on silica with DCM:Et₂O (1:1), concentrated under vacuum, and purified on a chromatographic column with silica gel and Hexane-AcOEt 9:1 with 1% triethylamine as eluent. The product was obtained as a yellow solid in 21% yield (67.8 mg).

To a two-way flask was added *tert*-butyl (2*S*,3*R*)-2-benzoyl-3-phenylaziridine-1-carboxylate (67.8 mg, 0.2 mmol), 0.1M solution of tetrabutylammonium fluoride in THF (70 μ L, 0.2 mmol), and THF (1 mL). The reaction mixture was heated to 50°C and stirred for 18 hours. After this period, the reaction was extracted with AcOEt (3 x 5 mL). The organic phase was dried with anhydrous Na₂SO₄ and concentrated under vacuum. The crude was purified by column chromatography with silica gel and Hexane-AcOEt (85:15) with 1% triethylamine as eluent. The product **2a** was obtained as a yellow solid in 75% yield (34.8 mg). *ee*: 70% of reaction crude determined by UPC² on a Trefoil AMY column, CO₂/iPrOH gradient [CO₂ (1 min), CO₂ at 60:40 (2 min), 60:40 (5 min), CO₂ (1 min)], 0.8 mL/min, 35 °C, 137.89 bar, λ = 254 nm, t_{majority} = 4.89 min, t_{minority} = 4.71 min.

7. General procedure for obtaining γ -lactams (5a-q)

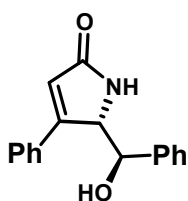
A suspension of 60% NaH in mineral oil (30 mg, 0.75 mmol) and anhydrous THF (1 mL) was added to a Schlenk flask provided with magnetic stirring and under N₂ atmosphere. Triethyl phosphonoacetate (95 μ L, 0.48 mmol) was added to this solution and allowed to stir for 10 minutes with a needle attached to the system to release the generated H₂. In another flamed Schlenk flask and under N₂ atmosphere, a solution of aziridine **2** (67 mg, 0.3 mmol) in anhydrous THF (1 mL) was prepared. This solution was added to the reaction mixture and stirred at 17°C for 15-18 hours. After this period the reaction mixture was neutralized with saturated NH₄Cl solution (5 mL), extracted with AcOEt (4 x 5 mL). The organic phase was dried with anhydrous Na₂SO₄ and concentrated under vacuum. The reaction crude was purified in column chromatography with silica gel and as eluent Hexane-AcOEt 8:2 for **4a** and Hexane-AcOEt 4:6 for **5**. Triethylamine (100:3) was added to the eluent since the product proved to be unstable in silica gel.

4,6-diphenyl-1-azabicyl[3.1.0]hex-3-en-2-one (**4a**)



The product was obtained as a yellow solid in 67% yield (49.7 mg). ¹H NMR (400 MHz, CDCl₃) δ : 7.74 – 7.59 (m, 2H), 7.53 – 7.41 (m, 5H), 7.41 – 7.35 (m, 3H), 6.21 (brs, 1H), 3.78 (d, J = 2.6 Hz, 1H), 3.46 (d, J = 2.6 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ : 189.6, 169.7, 136.1, 131.9, 131.3, 129.3, 129.0, 128.6, 127.2, 126.7, 117.4, 68.3, 50.1. mp: 114.3-116.3 °C. HRMS-ES⁺ *m/z*: calcd. for [C₁₇H₁₃NO + H] 248.1070; found: 248.1064 (Error: 2.77 ppm). IR (ν_{\max}): 3388, 3317, 1712, 1452 cm⁻¹.

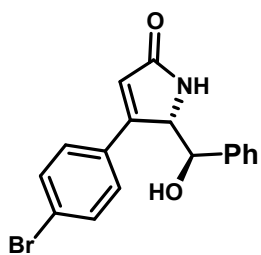
5-(hydroxy(phenyl)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (**5a**)



The product was obtained as a yellow oil in 78% yield (62 mg). ¹H NMR (400 MHz, CDCl₃) δ : 7.50 (dd, J = 6.4, 2.8 Hz, 2H), 7.44 – 7.40 (m, 3H), 7.38 – 7.35 (m, 4H), 7.34 – 7.29 (m, 1H), 6.26 (s, 1H), 5.58 (d, J = 4.2 Hz, 1H), 4.36 (d, J = 4.2 Hz, 1H), 2.00 (brs, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ : 163.8, 157.3, 137.3, 135.0, 130.6, 129.1, 128.8, 128.6, 126.7, 126.3, 115.9, 85.1, 51.1. HRMS-ES⁺ *m/z*: calcd. for [C₁₇H₁₅NO₂ + H] 266.1175;

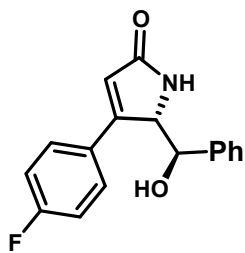
found: 266.1172 (Error: 1.44 ppm). IR(ν_{\max}): 3388, 3317, 3066, 3034, 1708, 1620, 1448, 1222 cm^{-1} . The enantiomerically enriched product was obtained as a yellow oil in 73% yield (29.2 mg). *ee*: 72% determined by UPC² on a Trefoil AMY column, CO₂/iPrOH gradient [CO₂ (1 min), CO₂ at 60:40 (2 min), 60:40 (5 min), CO₂ (1 min)], 0.8 mL/min, 35°C, 137.89 bar, λ = 280 nm, t_{majority} = 6.39 min, t_{minority} = 5.62 min.

4-(4-bromophenyl)-5-hydroxy(phenyl)methyl-1,5-dihydro-2H-pyrrol-2-one (5c)



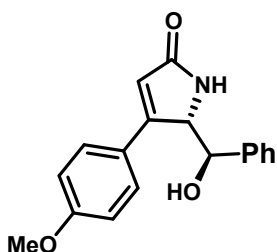
The product was obtained as a light-yellow solid in 61% yield (63.4 mg). ¹H NMR (400 MHz, CDCl₃) δ : 7.54 (d, J = 8.4 Hz, 2H), 7.41 – 7.31 (m, 7H), 6.24 (s, 1H), 5.50 (d, J = 4.3 Hz, 1H), 4.26 (d, J = 4.2 Hz, 1H), 1.64 (brs, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ : 163.5, 156.3, 137.1, 134.0, 132.3, 128.9, 128.7, 128.3, 126.3, 125.0, 116.3, 85.4, 51.2. **mp**: 106.4-107.8 °C. **HRMS-ES⁺ m/z** : calcd. for [C₁₇H₁₄BrNO₂ + H] 344.0286; found: 344.0281 (Error: 0.09 ppm).

4-(4-fluorophenyl)-5-(hydroxy(phenyl)methyl)-1,5-dihydro-2H-pyrrol-2-one (5d)



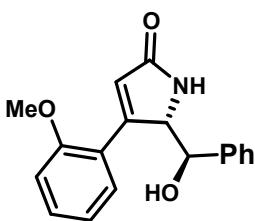
The product was obtained as a pale-yellow solid in 88% yield (74.7 mg). ¹H NMR (400 MHz, CDCl₃) δ : 7.57 – 7.47 (m, 2H), 7.43 – 7.27 (m, 5H), 7.14 – 7.06 (m, 2H), 6.22 (s, 1H), 5.53 (d, J = 4.3 Hz, 1H), 4.28 (d, J = 4.3 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ : 165.4, 163.3 (d, J = 81.3 Hz), 156.3, 137.3, 131.3, 128.9, 128.9, 128.8 (d, J = 10.6 Hz), 126.3, 116.4 (d, J = 21.7 Hz), 115.8, 85.4, 51.4. ¹⁹F{¹H} NMR (376 MHz, CDCl₃): -109.3. **mp**: 104.3-106.1 °C. **HRMS-ES⁺ m/z** : calcd. for [C₁₇H₁₄FNO₂ + H] 284.1081; found: 284.1083 (Error: 0.35 ppm).

5-(hydroxy(phenyl)methyl)-4-(4-methoxyphenyl)-1,5-dihydro-2H-pyrrol-2-one (5e)



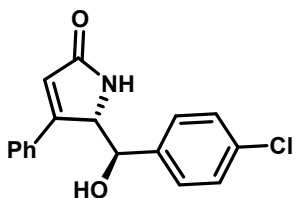
The product was obtained as a yellow oil in 63% yield (55.4 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.53 – 7.47 (m, 2H), 7.34 (t, $J = 3.95$ Hz, 4H), 7.33 – 7.27 (m, 2H), 6.97 – 6.88 (m, 2H), 6.22 (s, 1H), 5.61 (d, $J = 3.4$ Hz, 1H), 4.34 (d, $J = 3.2$ Hz, 1H), 3.82 (s, 3H), 2.20 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 164.0, 161.7, 137.5, 128.8, 128.4, 128.3, 126.9, 126.1, 114.6, 113.6, 84.8, 55.5, 50.7. HRMS-ES⁺ m/z : calcd. for $[\text{C}_{18}\text{H}_{17}\text{NO}_3 + \text{H}]$ 296.1287; observ 296.1282 (Error: 0.27 ppm).

5-(hydroxy(phenyl)methyl)-4-(2-methoxyphenyl)-1,5-dihydro-2H-pyrrol-2-one (5f)



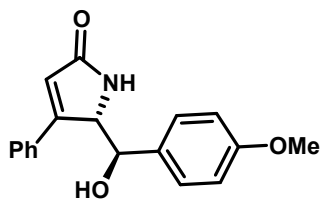
The product was obtained as an orange oil in 58% yield (51.6 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.49 (d, $J = 7.2$ Hz, 2H), 7.46 – 7.36 (m, 4H), 7.27 (d, $J = 7.5$ Hz, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 6.94 (d, $J = 8.3$ Hz, 1H), 6.11 (s, 1H), 5.34 (d, $J = 8.0$ Hz, 1H), 4.42 (d, $J = 7.9$ Hz, 1H), 3.80 (s, 3H), 1.65 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 164.0, 160.7, 156.4, 137.3, 131.4, 130.0, 128.9, 128.7, 127.3, 125.3, 121.5, 117.9, 111.1, 85.2, 55.6, 52.6. HRMS-ES⁺ m/z : calcd. For $[\text{C}_{18}\text{H}_{17}\text{NO}_3 + \text{H}]$ 296.1287; found: 296.1283 (Error: 0.61 ppm).

5-(4-chlorophenyl)(hydroxy)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5g)



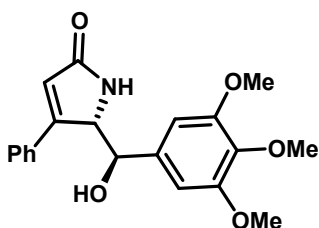
The product was obtained as a yellow oil in 66% yield (59.3 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.51 – 7.46 (m, 2H), 7.45 – 7.39 (m, 3H), 7.35 – 7.27 (m, 4H), 6.24 (s, 1H), 5.51 (d, $J = 4.2$ Hz, 1H), 4.29 (d, $J = 4.1$ Hz, 1H), 1.78 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.5, 157.5, 135.9, 134.8, 134.5, 130.7, 129.2, 129.0, 127.8, 126.6, 115.7, 84.5, 51.1. HRMS-ES⁺ m/z : calcd. for $[\text{C}_{17}\text{H}_{14}\text{ClNO}_2 + \text{H}]$ 300.0791; found: 300.0788 (Error: 0.73 ppm).

5-(hydroxy(4-methoxyphenyl)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5h)



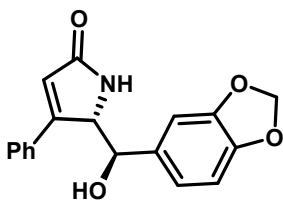
The product was obtained as an orange oil in 58% yield (51 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.54 – 7.48 (m, 2H), 7.45 – 7.40 (m, 3H), 7.30 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.26 (s, 1H), 5.50 (d, J = 2.1 Hz, 1H), 4.35 (brs, 1H), 3.78 (s, 3H), 1.95 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.9, 159.8, 135.1, 130.5, 129.2, 129.1, 127.9, 126.7, 116.0, 114.2, 84.9, 55.3, 51.0. HRMS-ES⁺ m/z : calcd. for $[\text{C}_{18}\text{H}_{17}\text{NO}_3 + \text{H}]$ 296.1287; found: 296.1284 (Error: 0.94 ppm).

5-(hydroxy(2,3,4-trimethoxyphenyl)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5i)



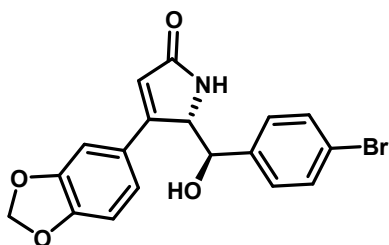
The product was obtained as a yellow solid in 70% yield (74.4 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.57 – 7.50 (m, 2H), 7.44 – 7.36 (m, 3H), 6.89 (d, J = 8.7 Hz, 1H), 6.60 (s, 1H), 6.29 (s, 1H), 5.72 (d, J = 4.3 Hz, 1H), 4.35 (d, J = 4.3 Hz, 1H), 3.99 (s, 3H), 3.86 (s, 3H), 3.82 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 164.3, 157.7, 154.1, 151.4, 142.1, 135.3, 130.4, 129.0, 126.8, 122.9, 121.7, 115.5, 107.1, 81.6, 61.3, 60.8, 56.0, 50.3. HRMS-ES⁺ m/z : calcd. for $[\text{C}_{20}\text{H}_{21}\text{NO}_5 + \text{H}]$ 356.1498; found: 356.1494. (Error: 0.42 ppm).

5-(benzo[d][1,3]dioxol-5-yl(hydroxy)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5j)



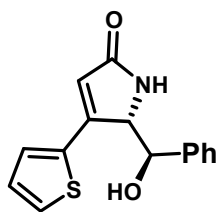
The product was obtained as an orange oil in 74% yield (69 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.52 – 7.47 (m, 2H), 7.47 – 7.42 (m, 3H), 6.88 (d, J = 1.7 Hz, 1H), 6.83 (dd, J = 8.2, 1.5 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 6.24 (s, 1H), 5.95 (s, 2H), 5.39 (d, J = 5.1 Hz, 1H), 4.28 (d, J = 5.1 Hz, 1H), 1.72 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.7, 158.0, 148.1, 147.90, 135.1, 131.0, 130.5, 129.1, 126.7, 120.4, 115.9, 108.4, 107.0, 101.4, 85.2, 51.1. HRMS-ES⁺ m/z : calcd. for $[\text{C}_{18}\text{H}_{15}\text{NO}_4 + \text{H}]$ 310.1079; found: 310.1076 (Error: 0.71 ppm).

4-(benzo[d][1,3]dioxol-5-yl)-5-(4-bromophenyl)(hydroxy)methyl)-1,5-dihydro-2H-pyrrol-2-one (5k)



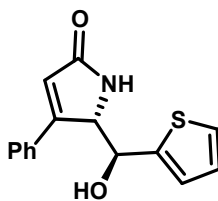
The product was obtained as a yellow oil in 67% yield (77.6 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.48 (d, $J = 8.5$ Hz, 2H), 7.22 (d, $J = 8.4$ Hz, 2H), 7.05 (dd, $J = 8.2, 1.8$ Hz, 1H), 6.98 (d, $J = 1.8$ Hz, 1H), 6.84 (d, $J = 8.1$ Hz, 1H), 6.16 (s, 1H), 6.01 (s, 1H), 5.50 (d, $J = 3.7$ Hz, 1H), 4.18 (d, $J = 3.8$ Hz, 1H), 1.69 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.5, 156.5, 150.0, 148.6, 136.5, 131.9, 128.7, 127.8, 122.6, 121.3, 114.1, 108.8, 106.7, 101.8, 84.4, 51.0. HRMS-ES $^+$ m/z : calcd. for $[\text{C}_{18}\text{H}_{14}\text{BrNO}_4 + \text{H}]$ 388.0179 found: 388.0174 (Error: 1.29 ppm).

5-(hydroxy(phenyl)methyl)-4-(thiophen-2-yl)-1,5-dihydro-2H-pyrrol-2-one (5l)



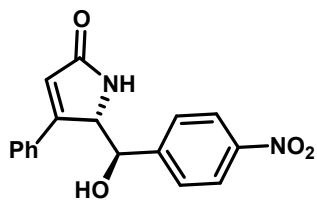
The product was obtained as an orange oil in 48% yield (39 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.47 (d, $J = 4.5$ Hz, 2H), 7.38 – 7.27 (m, 5H), 7.12 – 7.07 (m, 1H), 6.24 (s, 1H), 5.66 (d, $J = 2.6$ Hz, 1H), 4.27 (d, $J = 2.5$ Hz, 1H), 2.28 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.7, 150.0, 138.9, 137.4, 130.1, 128.8, 128.6, 128.5, 128.4, 125.9, 112.2, 84.6, 51.6. HRMS-ES $^+$ m/z : calcd. for $[\text{C}_{15}\text{H}_{13}\text{NO}_2\text{S} + \text{H}]$ 272.0745; found: 272.0741 (Error: 0.44 ppm).

5-(hydroxy(thiophen-2-yl)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5m)



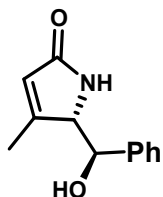
The product was obtained as an orange oil with 74% yield (60.2 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.53 (dd, $J = 6.3, 2.7$ Hz, 3H), 7.44 – 7.30 (m, 1H), 7.19 (d, $J = 4.7$ Hz, 1H), 7.02 (d, $J = 3.2$ Hz, 1H), 6.96 – 6.83 (m, 1H), 6.24 (s, 1H), 5.72 (d, $J = 2.9$ Hz, 1H), 4.26 (d, $J = 2.3$ Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.1, 157.3, 140.1, 135.0, 130.8, 129.2, 127.0, 126.9, 126.7, 126.2, 115.7, 81.8, 51.2. HRMS-ES $^+$ m/z : calcd. for $[\text{C}_{15}\text{H}_{13}\text{NO}_2\text{S} + \text{H}]$ 272.0740; found: 272.0742 (Error: 0.73 ppm).

5-(hydroxy(4-nitrophenyl)methyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5o)



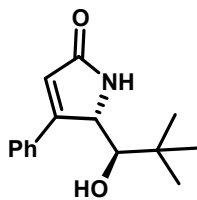
The product was obtained as an orange solid in 34% yield (31.6 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 8.27 (d, $J = 8.7$ Hz, 2H), 7.69 (d, $J = 8.7$ Hz, 2H), 7.42 – 7.33 (m, 5H), 6.34 (s, 1H), 5.48 (d, $J = 5.2$ Hz, 1H), 4.30 (d, $J = 5.0$ Hz, 1H), 1.71 (brs, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 162.9, 148.7, 141.7, 136.6, 129.0, 129.0, 128.0, 126.4, 124.1, 119.0, 85.7, 51.7. **mp**: 121.1–122.6 °C. **HRMS–ES⁺ m/z** : calcd. for $[\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_4 + \text{H}]$ 311.1032; found: 311.1027 (Error: 0.22 ppm).

5-(hydroxy(phenyl)methyl)-4-methyl-1,5-dihydro-2H-pyrrol-2-one (5p)



The product was obtained as a yellow solid in 31% yield (18.7 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.41 – 7.34 (m, 5H), 5.91 – 5.84 (m, 1H), 5.04 (d, $J = 8.8$ Hz, 1H), 3.70 (d, $J = 8.8$ Hz, 1H), 2.05 (t, $J = 1.2$ Hz, 3H), 1.39 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 163.7, 160.3, 136.8, 129.1, 128.8, 127.3, 116.8, 85.5, 53.8, 19.9. **mp**: 94.8 – 96.3 °C. **HRMS–ES⁺ m/z** : calcd. for $[\text{C}_{12}\text{H}_{13}\text{NO}_2 + \text{H}]$ 204.1025; found: 204.1020 (Error: 0.44 ppm).

5-(1-hydroxy-2,2-dimethylpropyl)-4-phenyl-1,5-dihydro-2H-pyrrol-2-one (5q)



The product was obtained as a pale yellow oil in 14% yield (10.2 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 7.53 – 7.36 (m, 5H), 6.34 (d, $J = 1.5$ Hz, 1H), 5.79 (brs, 1H), 2.68 (brs, 1H), 1.09 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ : 173.4, 167.6, 131.3, 130.2, 129.4, 127.2, 115.5, 81.4, 60.6, 35.3, 27.2. **HRMS–ES⁺ m/z** : calcd. for $[\text{C}_{15}\text{H}_{19}\text{NO}_2 + \text{H}]$ 246.1489; found: 246.1490 (Error: 0.41 ppm).

8. References

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9. NMR spectra, IR and chromatograms

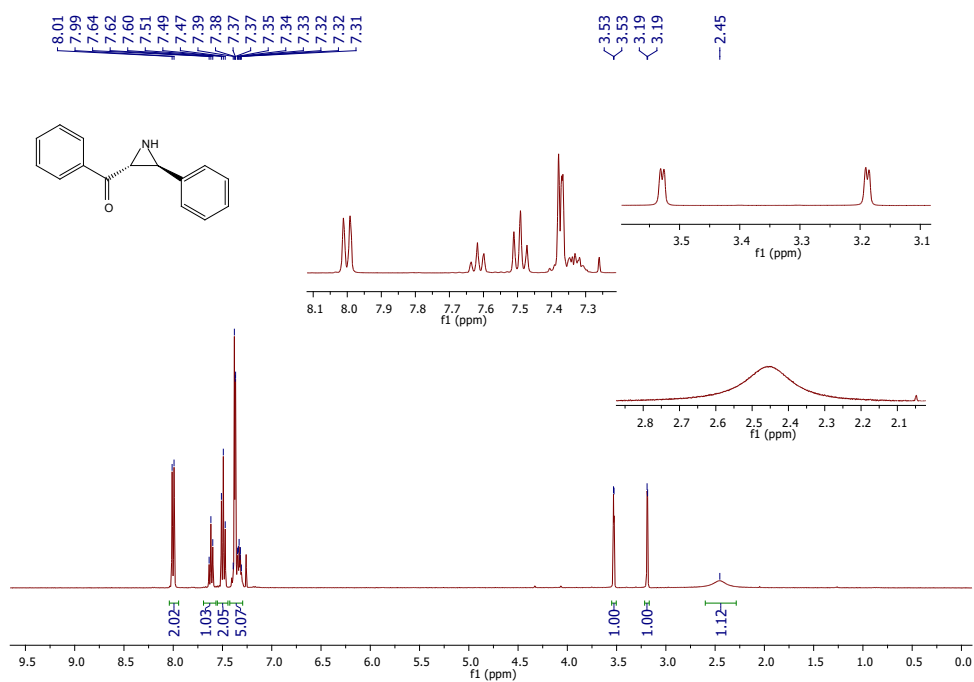


Fig. S1. ¹H NMR spectrum of compound 2a in CDCl₃ at 400 MHz.

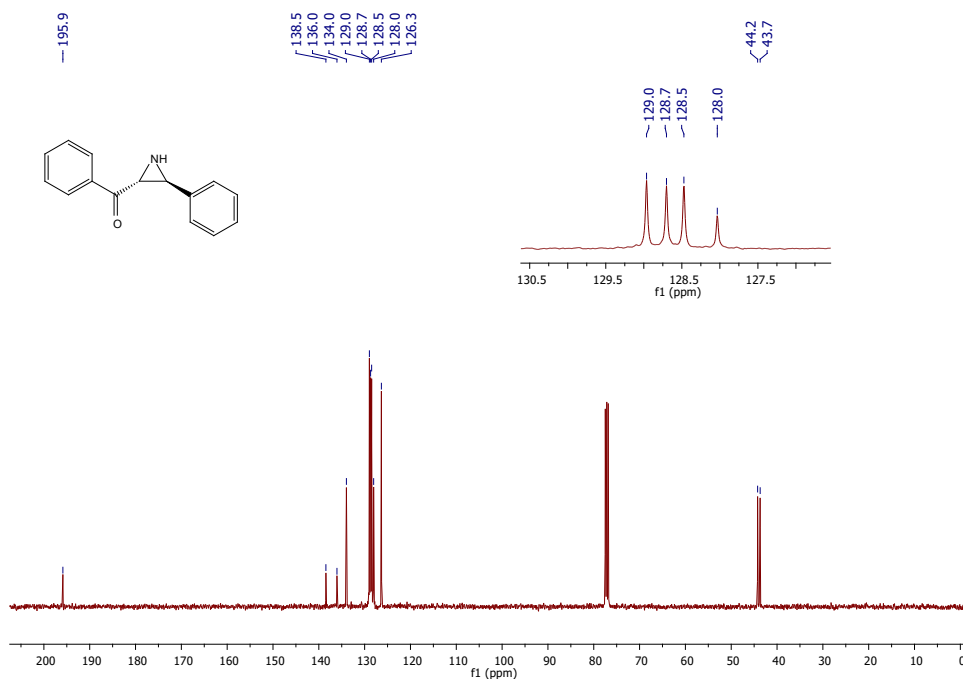
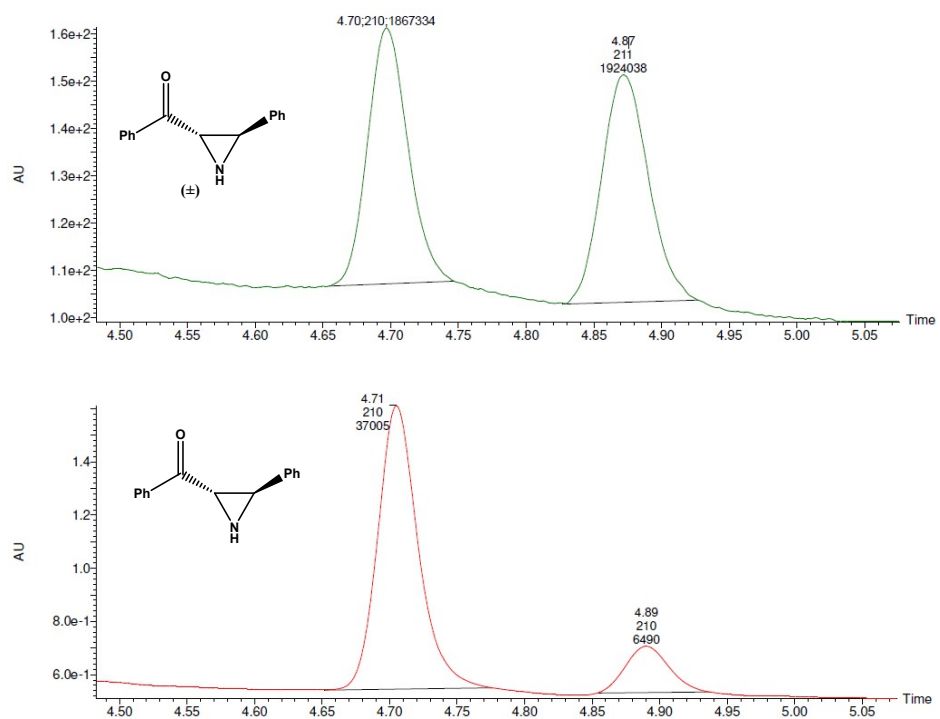


Fig. S2. ¹³C{¹H} NMR spectrum of compound 2a in CDCl₃ at 100 MHz.



	Retention time	Area	% Area
1	4.71	37005.01	85.08
2	4.89	6490.07	14.92

Fig. S3. Chromatogram of compound **(2S,3R)-2a** obtained by UPC².

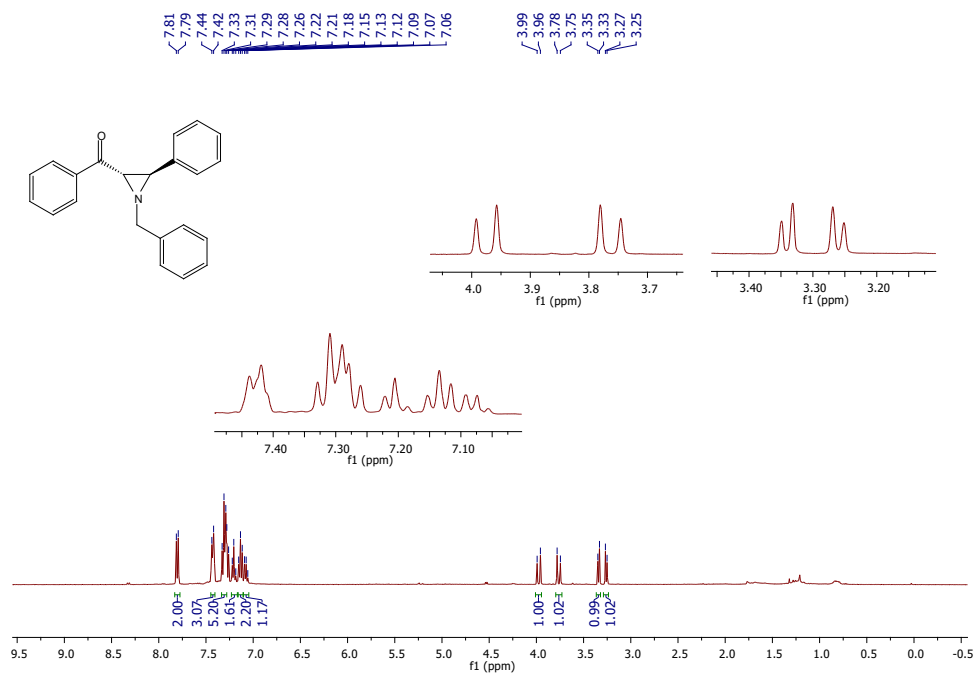


Fig. S4. ^1H NMR spectrum of compound **2b** in CDCl_3 at 400 MHz.

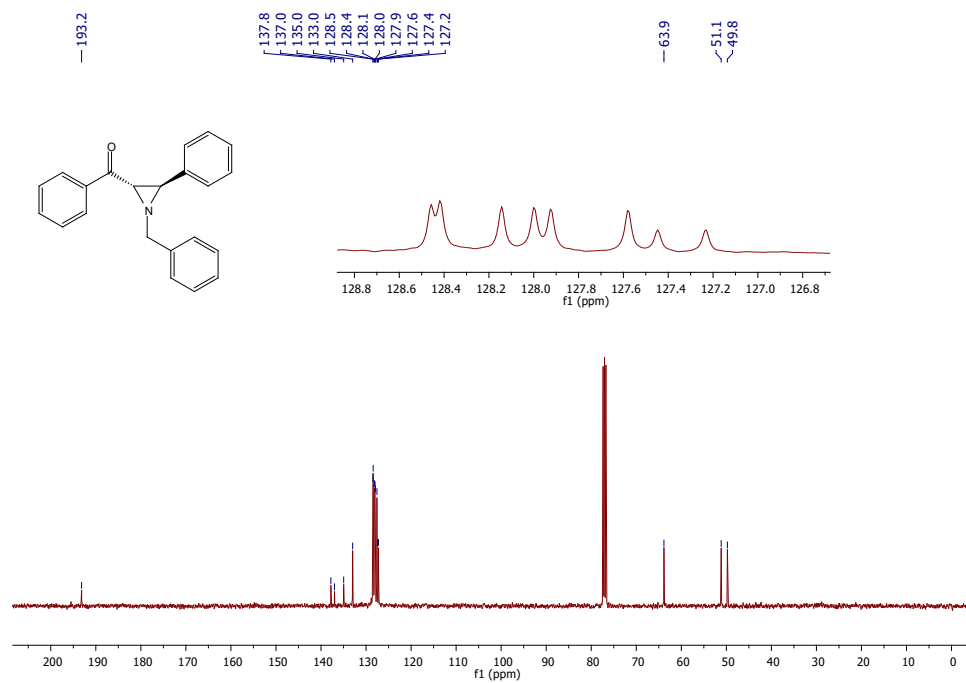


Fig. S5. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2b** in CDCl_3 at 100 MHz.

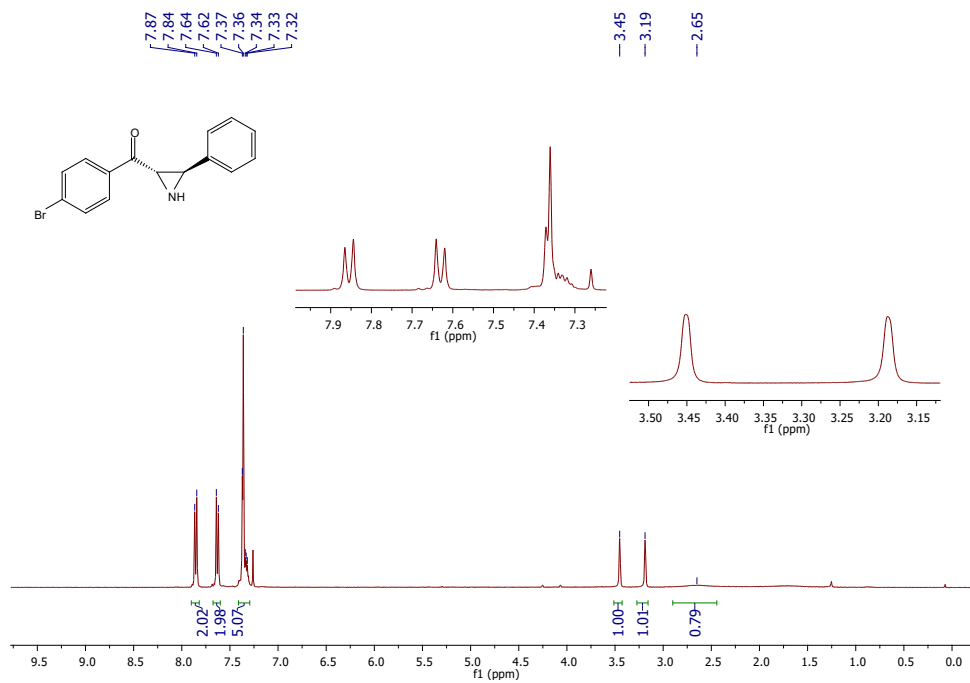


Fig. S6. ¹H NMR spectrum of compound **2c** in CDCl₃ at 400 MHz.

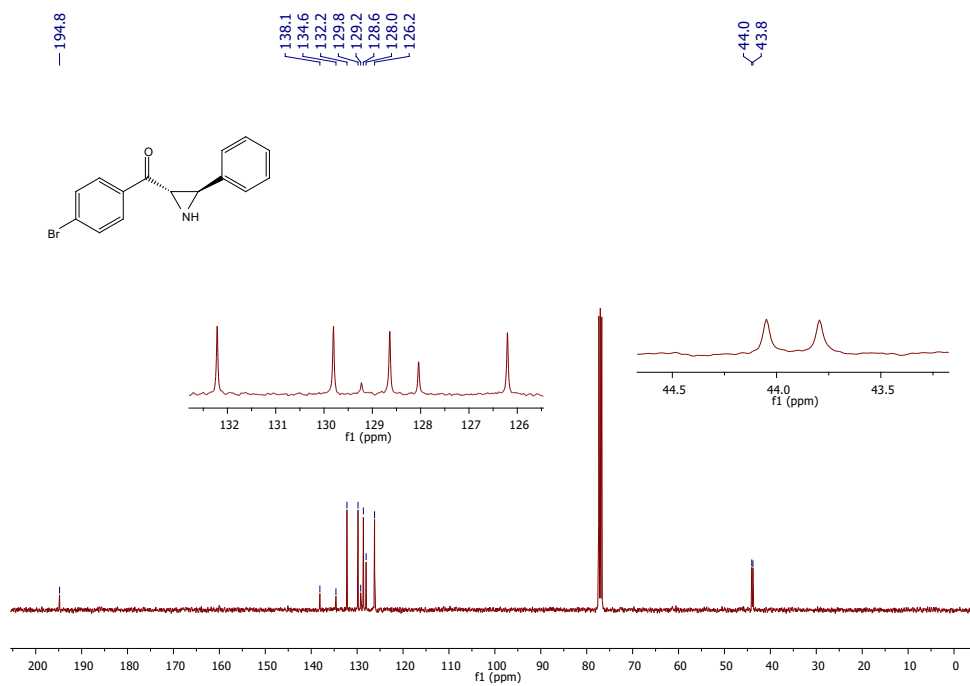


Fig. S7. ¹³C{¹H} NMR spectrum of compound **2c** in CDCl₃ at 100 MHz.

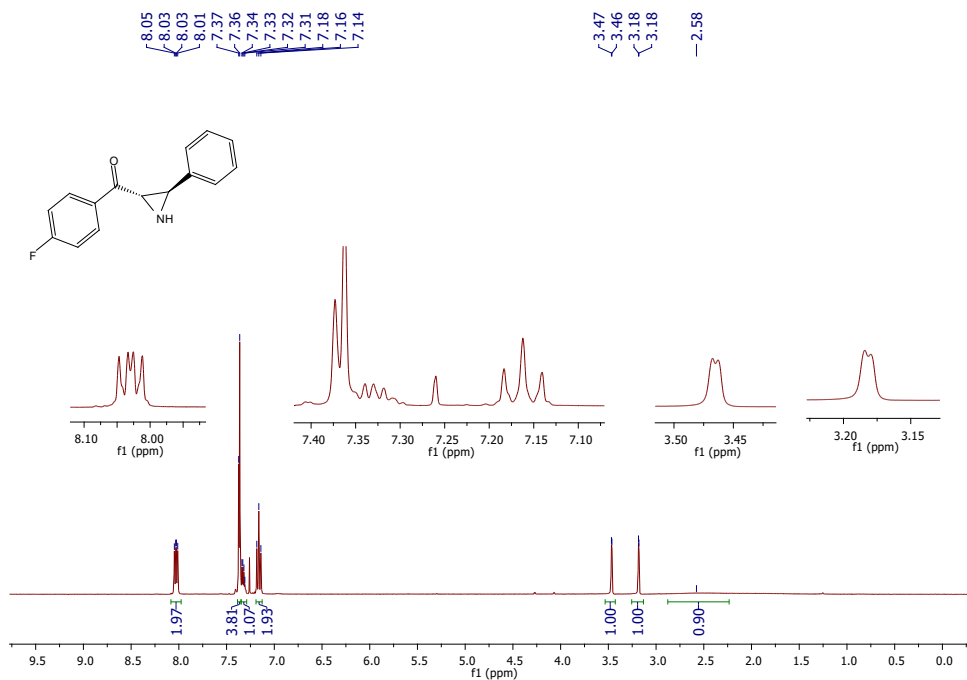


Fig. S8. ^1H NMR spectrum of compound **2d** in CDCl_3 at 400 MHz.

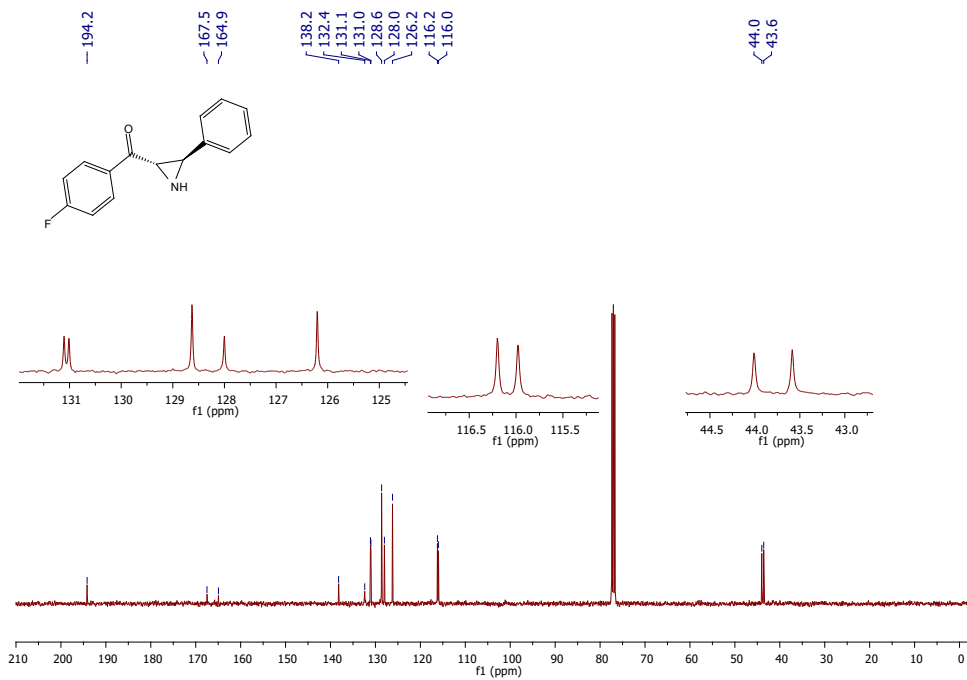


Fig. S9. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2d** in CDCl_3 at 100 MHz.

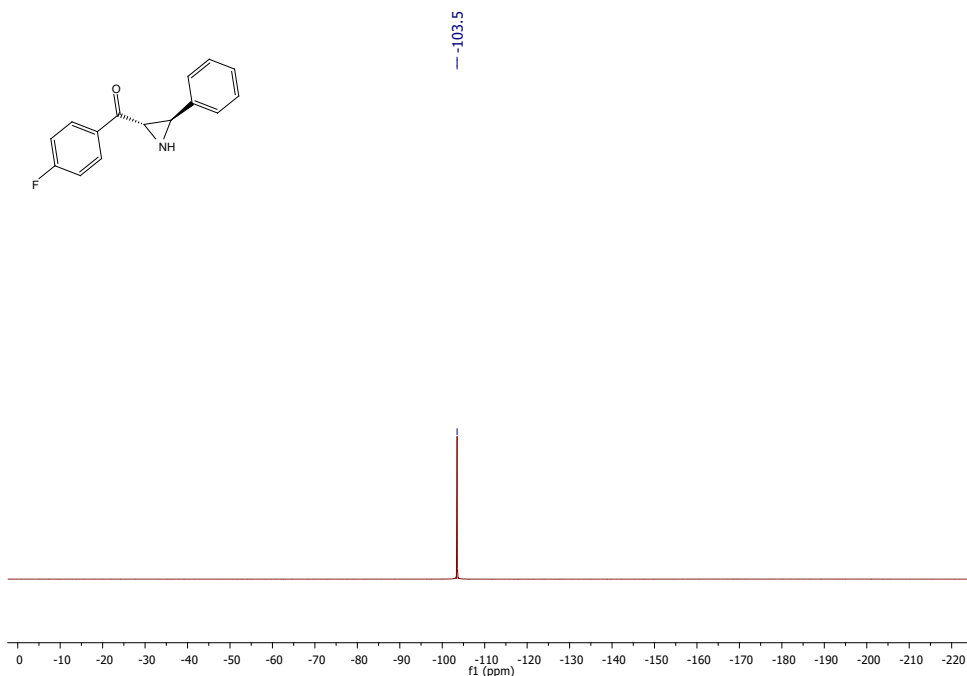


Fig. S10. $^{19}\text{F}\{^1\text{H}\}$ NMR spectrum of compound **2d** in CDCl_3 at 376 MHz.

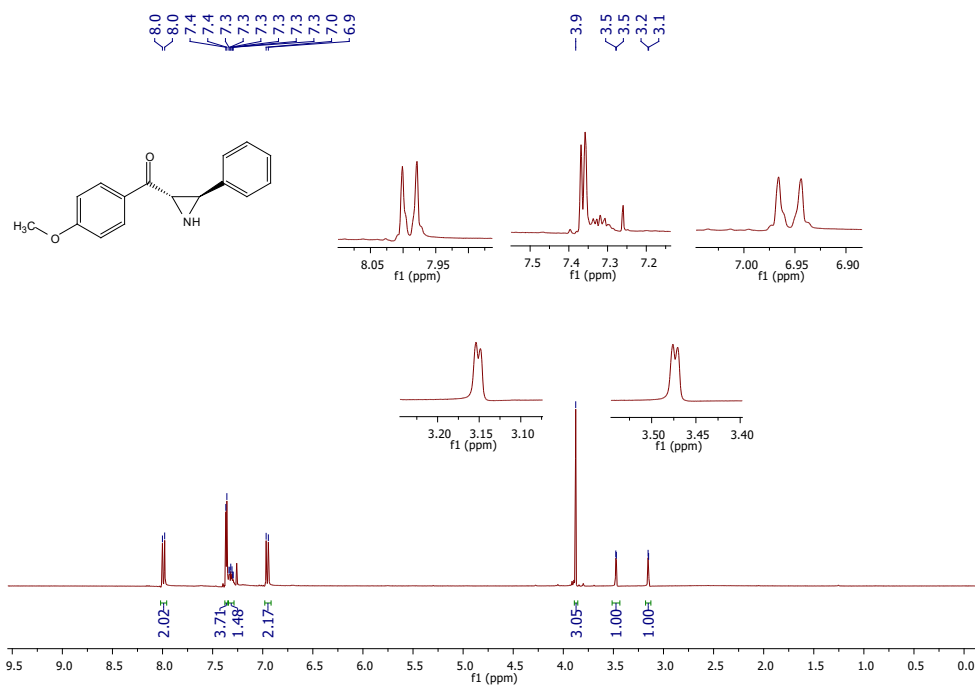


Fig. S11. ^1H NMR spectrum of compound **2e** in CDCl_3 at 400 MHz.

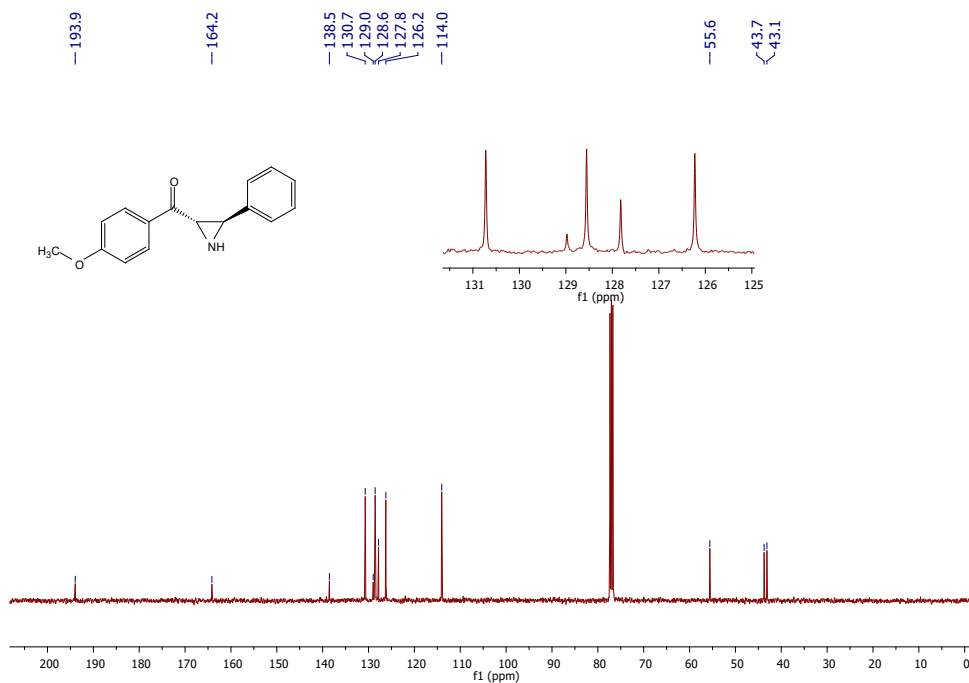


Fig. S12. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2e** in CDCl_3 at 100 MHz.

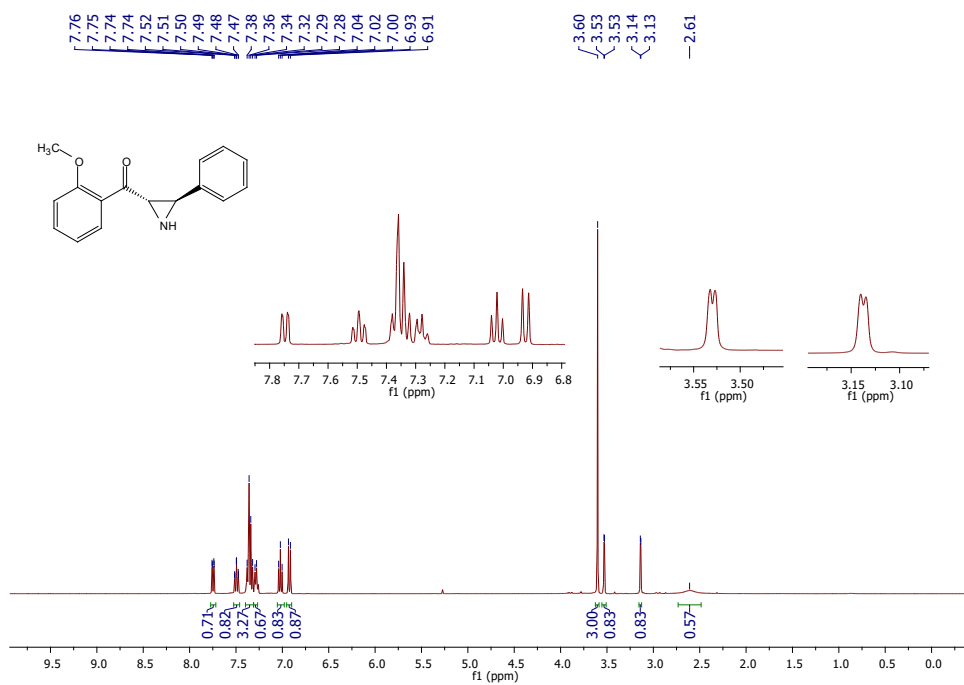


Fig. S13. ^1H NMR spectrum of compound **2f** in CDCl_3 at 400 MHz.

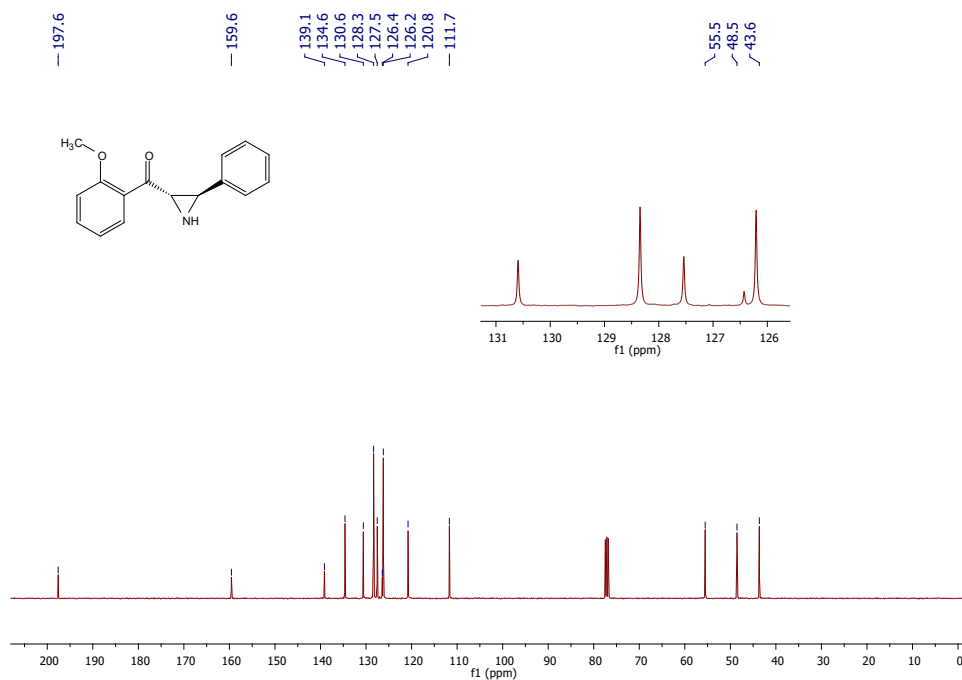


Fig. S14. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2f** in CDCl_3 at 100 MHz.

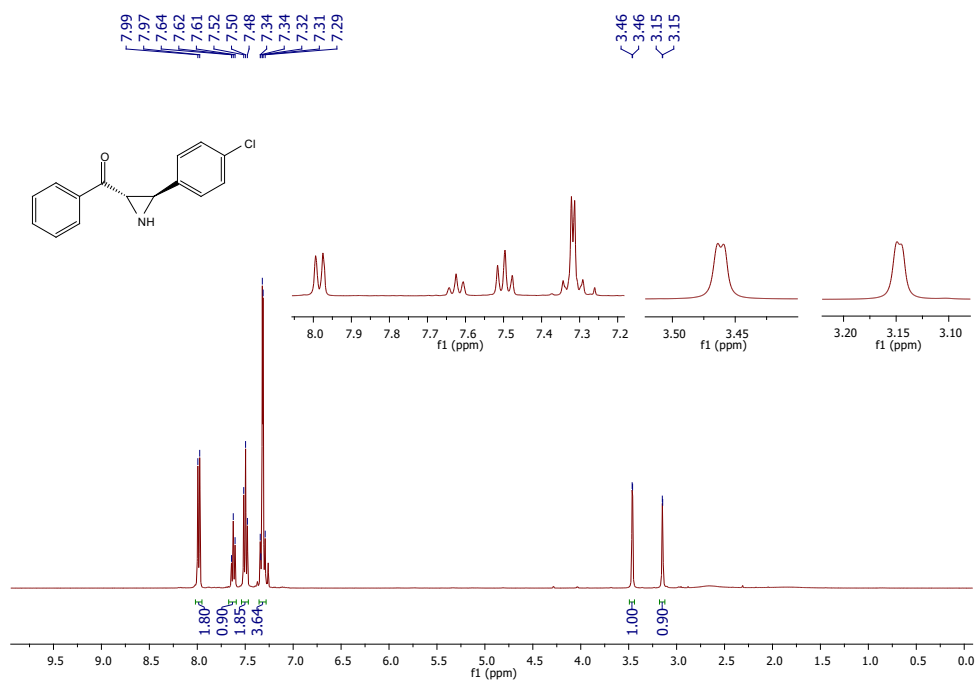


Fig. S15. ^1H NMR spectrum of compound **2g** in CDCl_3 at 400 MHz.

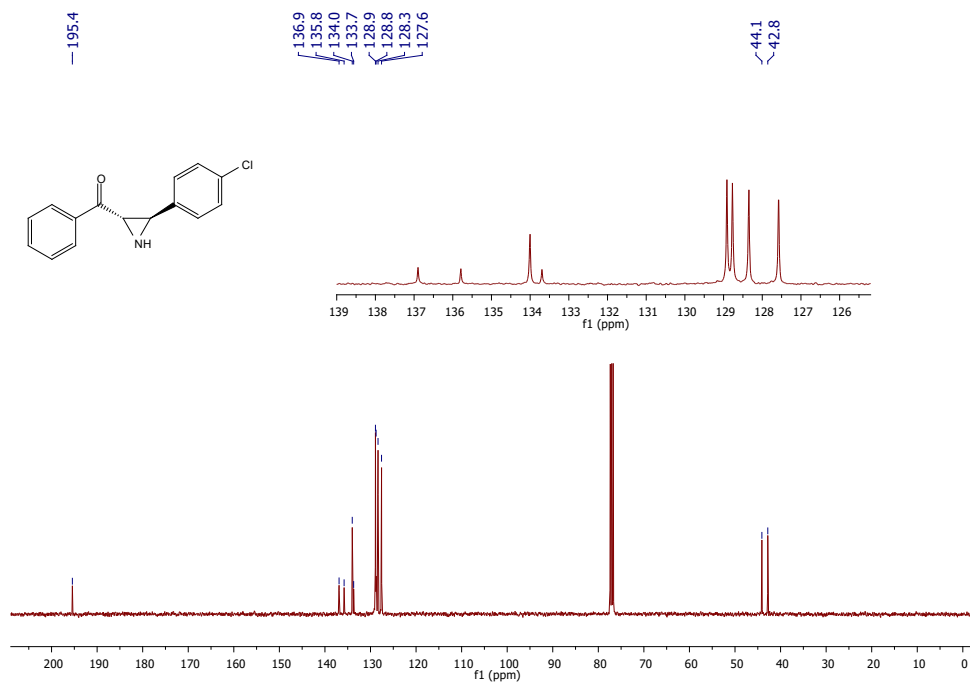


Fig. S16. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2g** in CDCl_3 at 100 MHz.

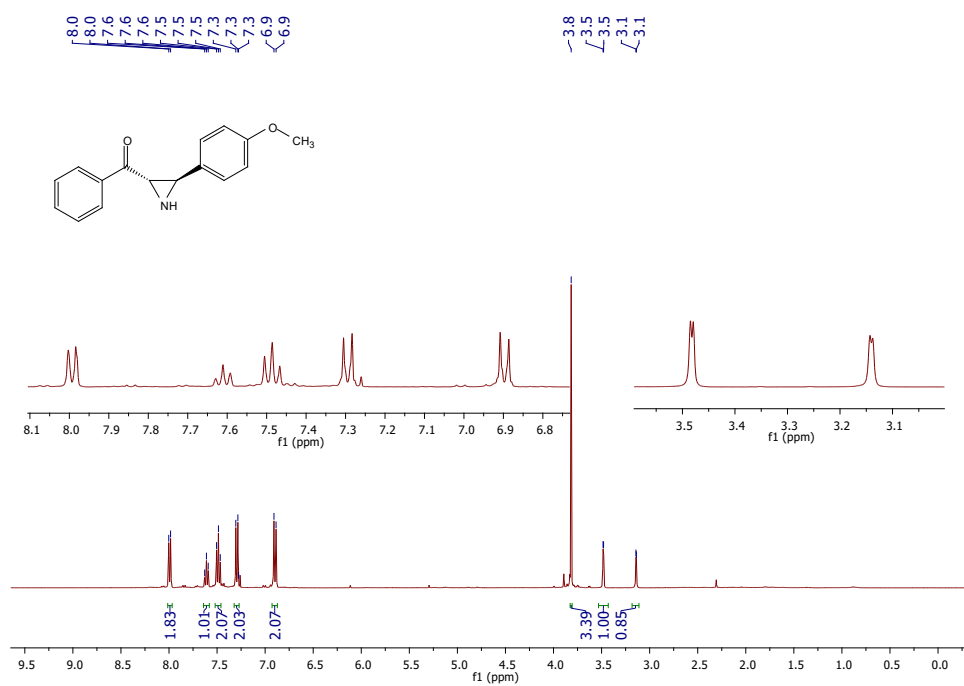


Fig. S17. ^1H NMR spectrum of compound **2h** in CDCl_3 at 400 MHz.

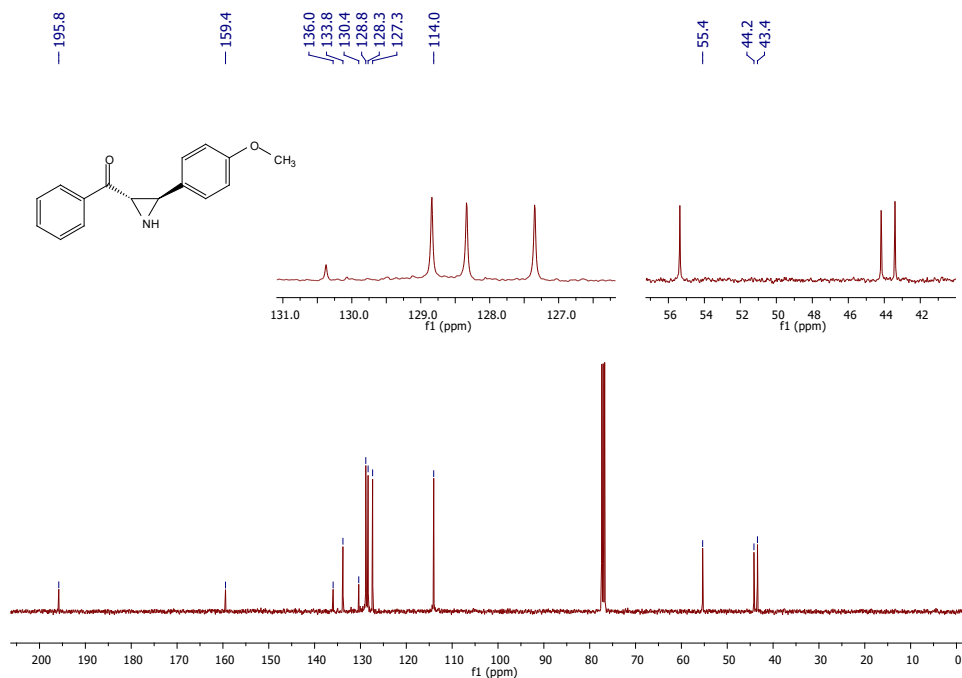


Fig. S18. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2h** in CDCl_3 at 100 MHz.

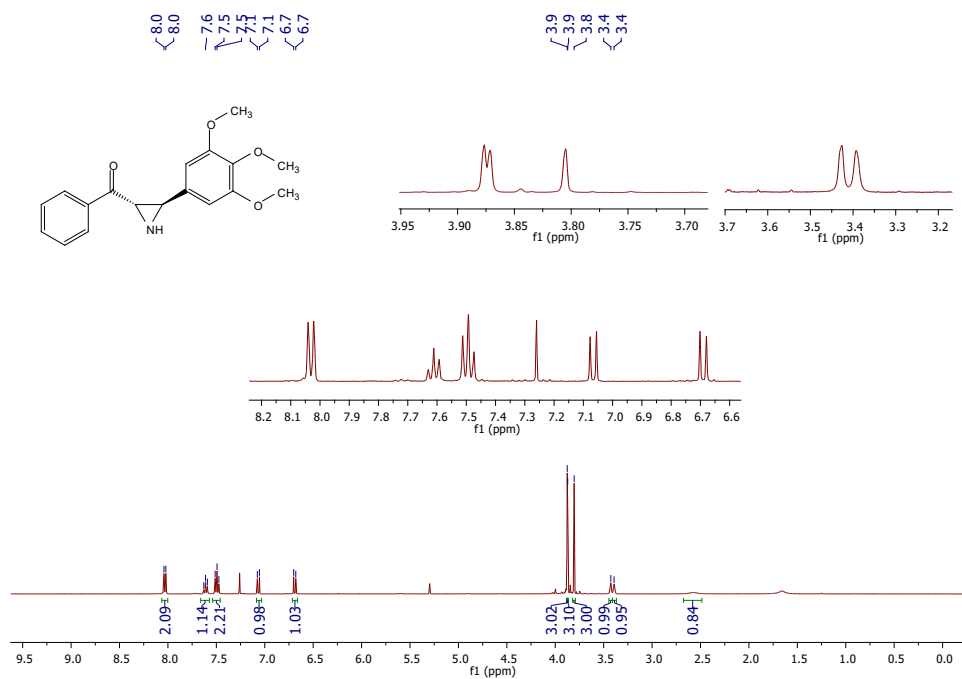


Fig. S19. ^1H NMR spectrum of compound **2i** in CDCl_3 at 400 MHz.

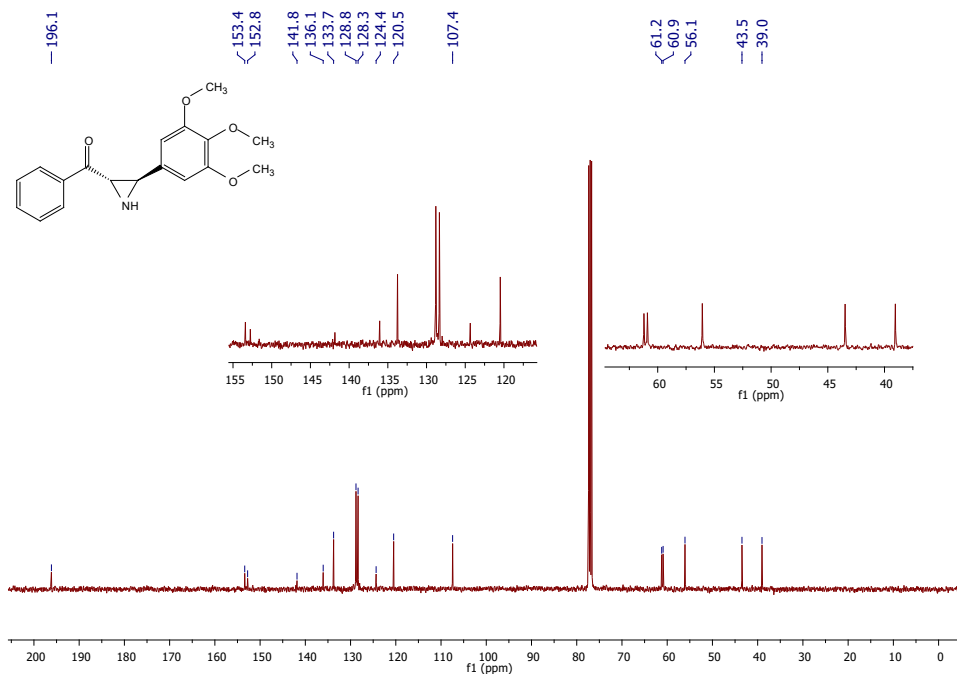


Fig. S20. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2i** in CDCl_3 at 100 MHz.

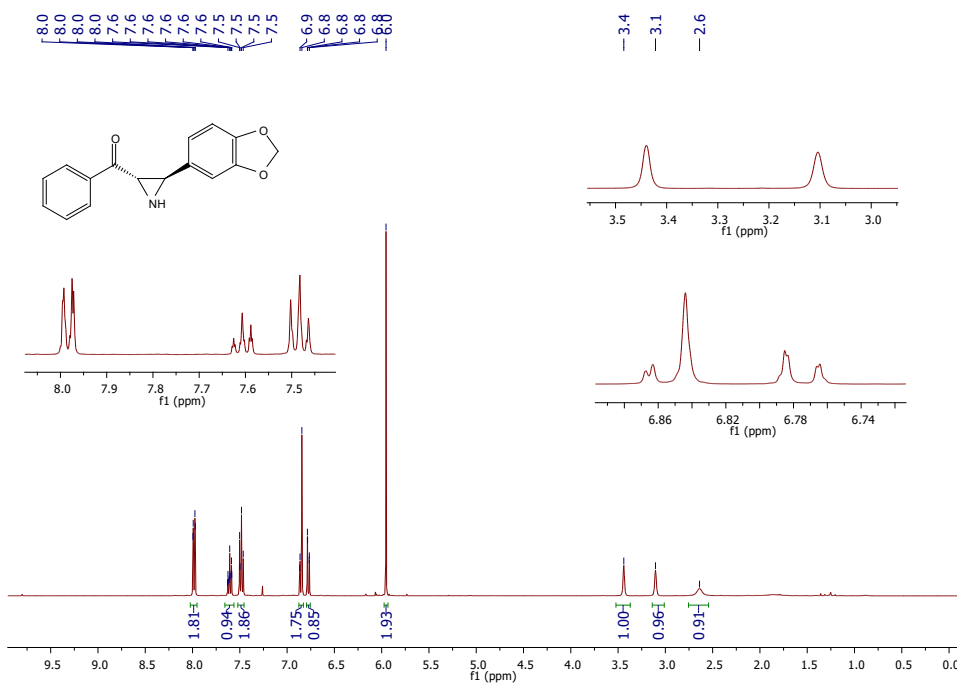


Fig. S21. ^1H NMR spectrum of compound **2j** in CDCl_3 at 400 MHz.

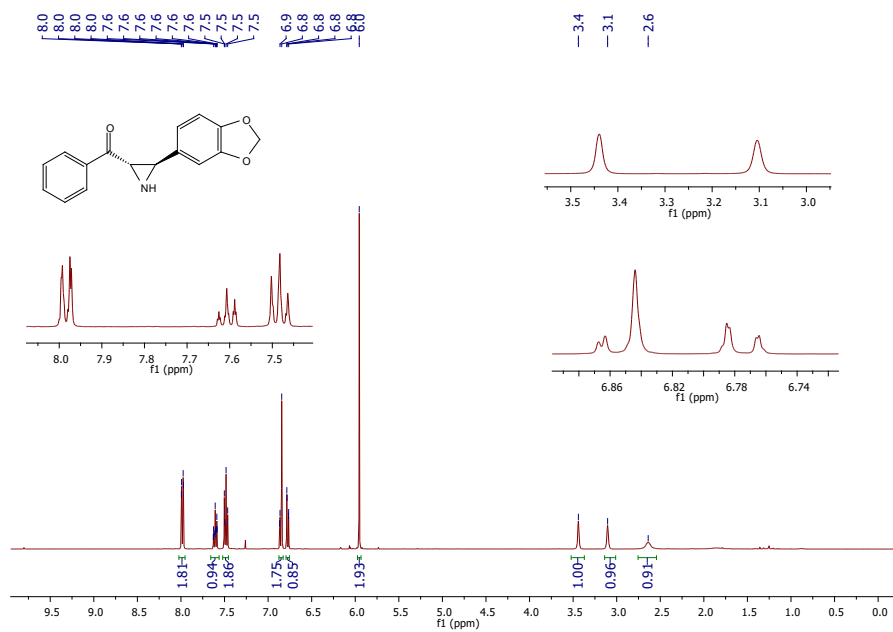


Fig. S22. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2j** in CDCl_3 at 100 MHz.

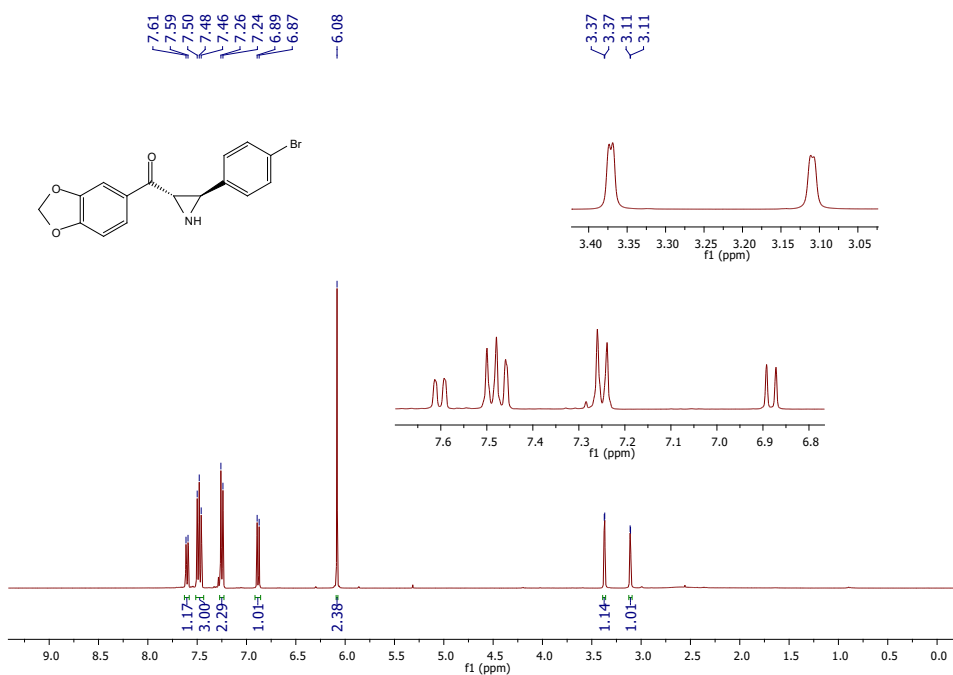


Fig. S23. ^1H NMR spectrum of compound **2k** in CDCl_3 at 400 MHz.

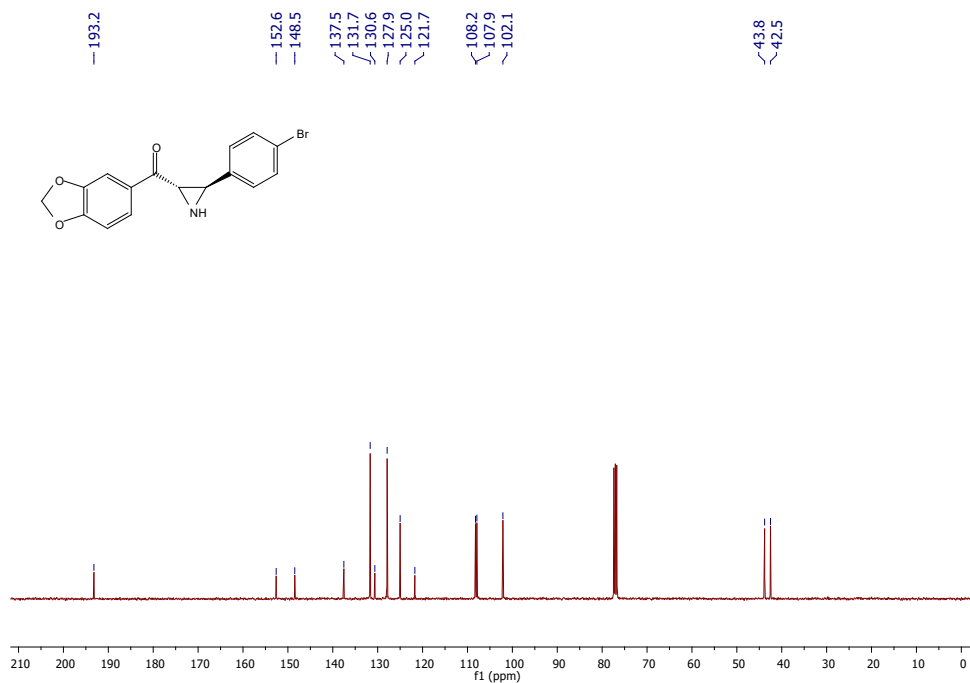


Fig. S24. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2k** in CDCl_3 at 100 MHz.

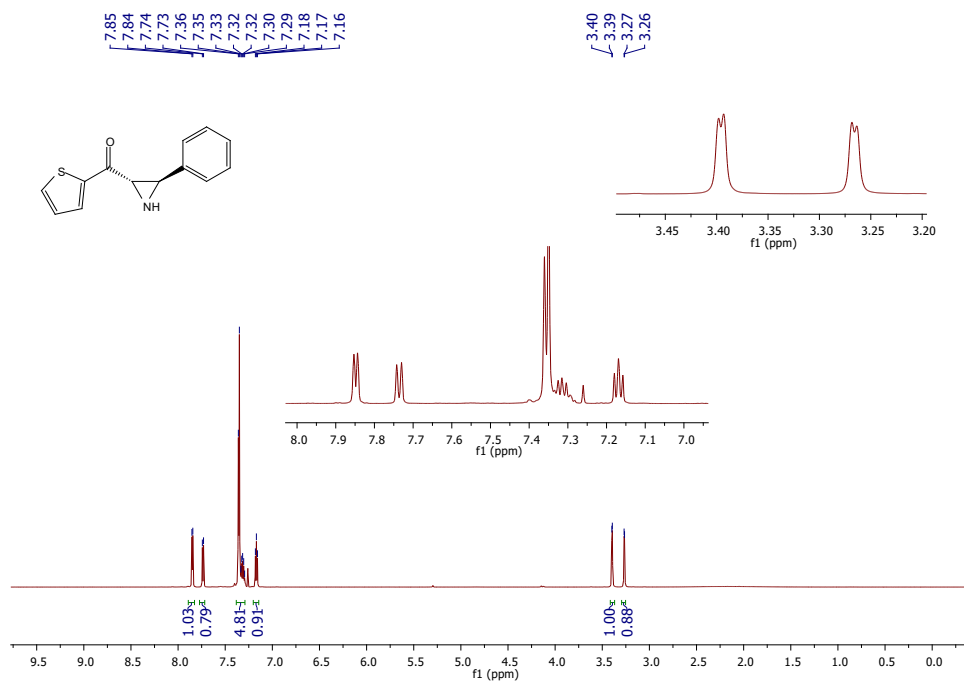


Fig. S25. ^1H NMR spectrum of compound **2l** in CDCl_3 at 400 MHz.

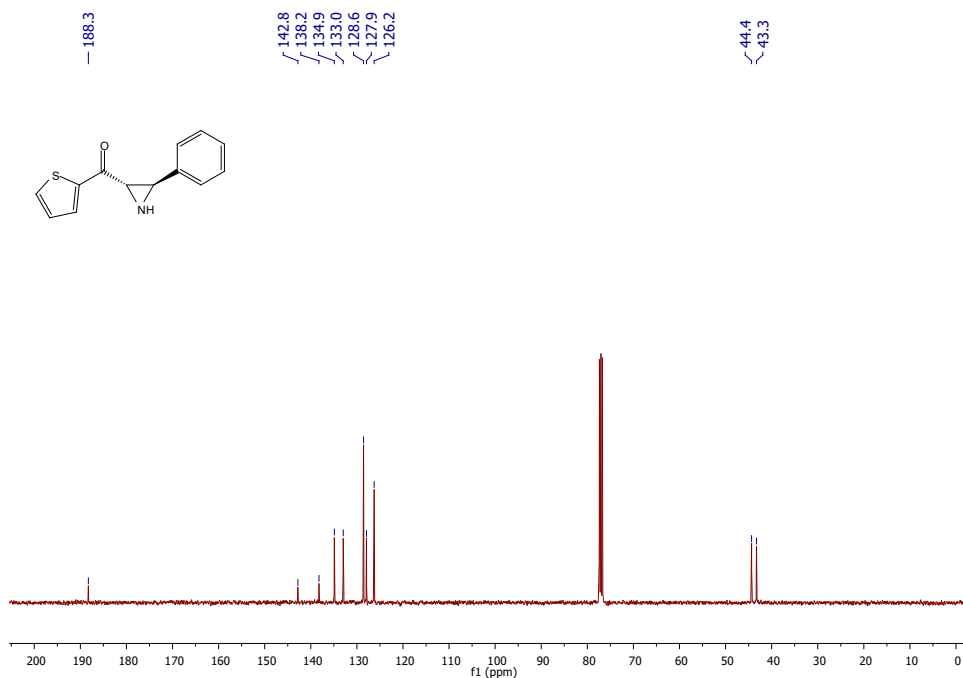


Fig. S26. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2l** in CDCl_3 at 100 MHz.

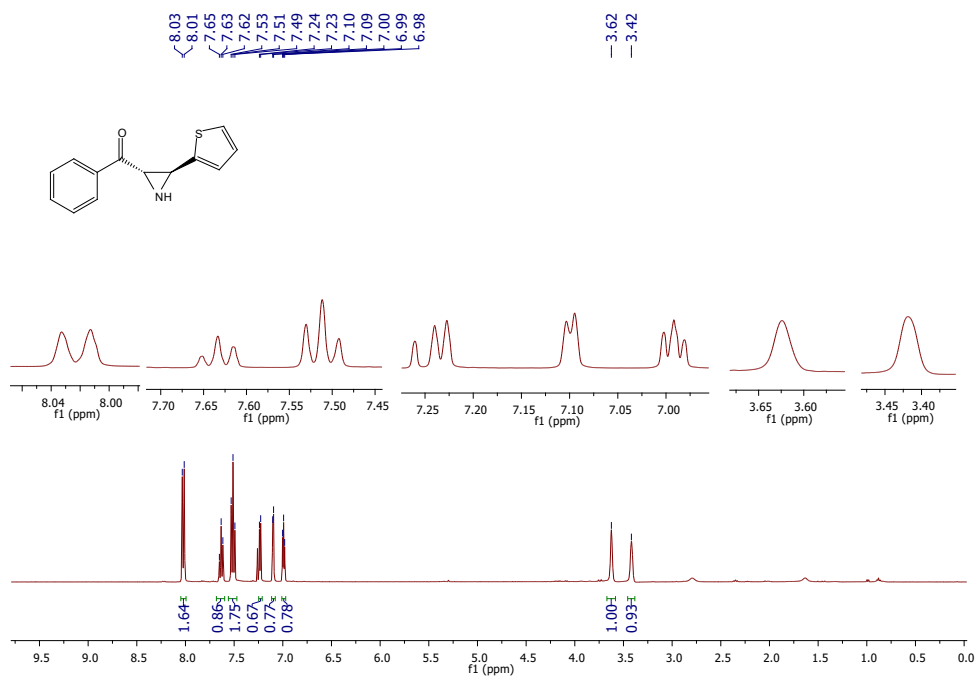


Fig. S27. ^1H NMR spectrum of compound **2m** in CDCl_3 at 400 MHz.

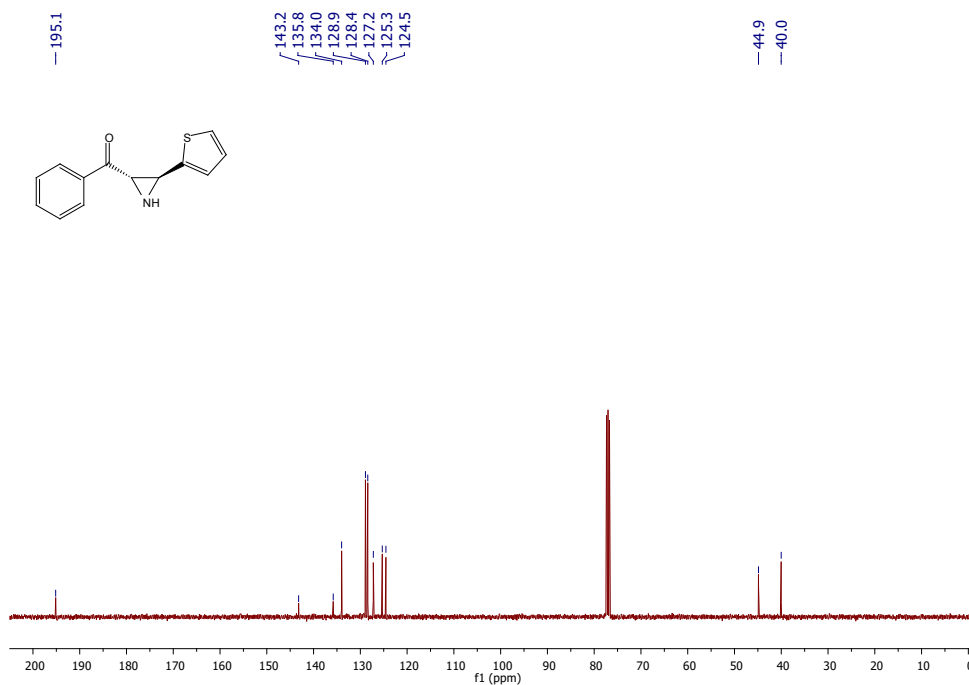


Fig. S28. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2m** in CDCl_3 at 100 MHz.

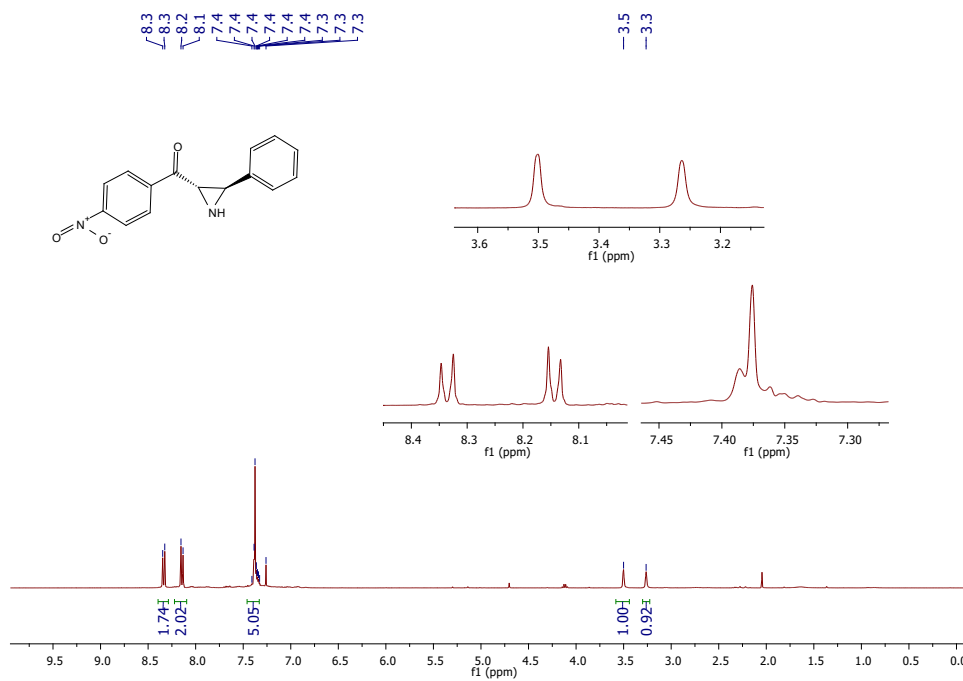


Fig. S29. ^1H NMR spectrum of compound **2n** in CDCl_3 at 400 MHz.

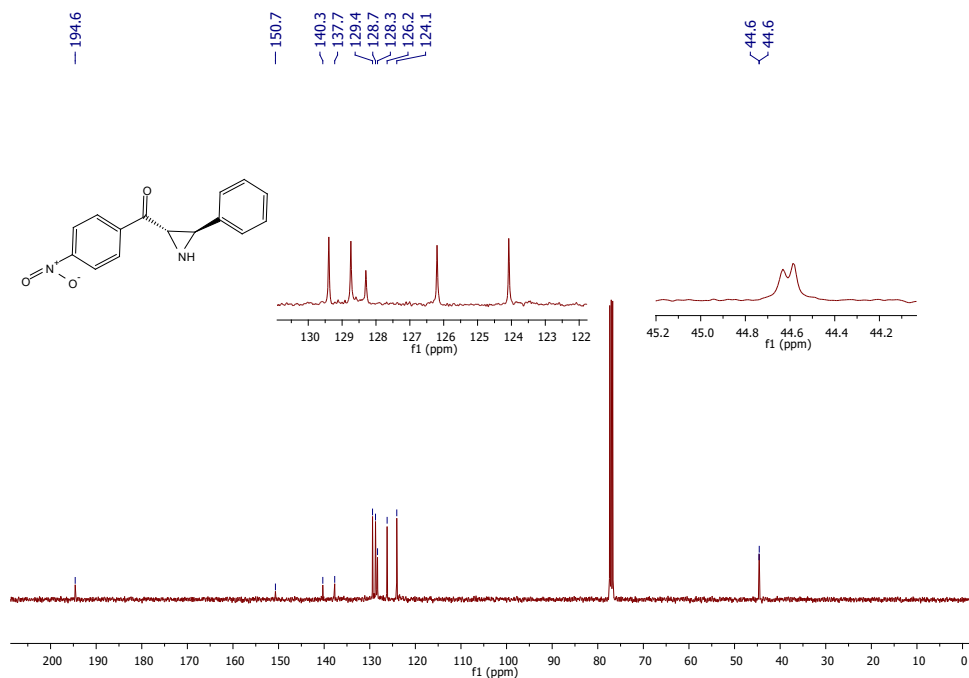


Fig. S30. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2n** in CDCl_3 at 100 MHz.

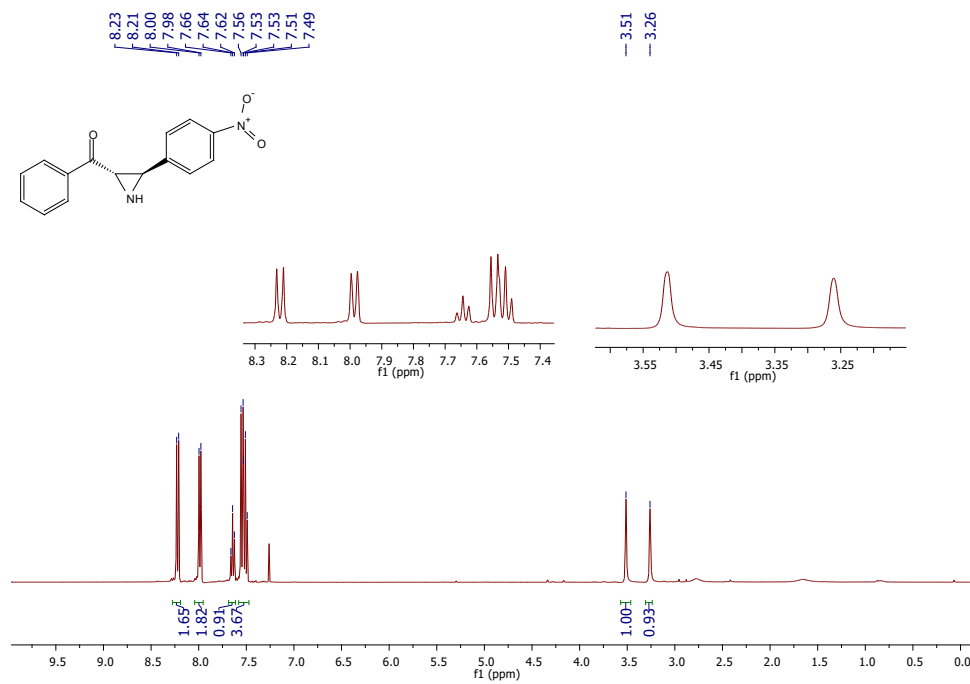


Fig. S31. ^1H NMR spectrum of compound **2o** in CDCl_3 at 400 MHz.

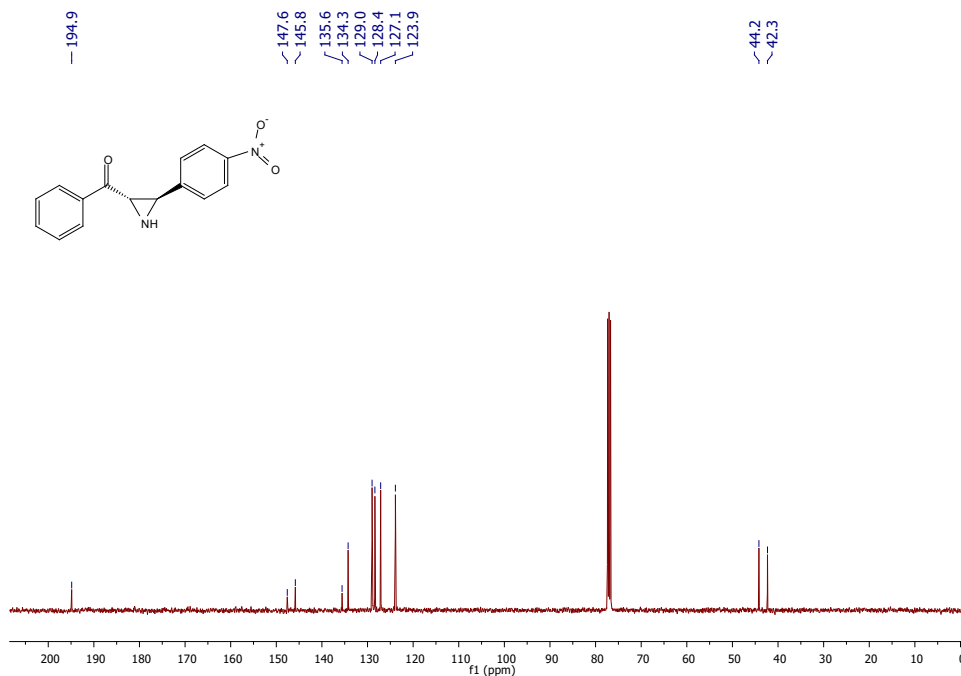


Fig. S32. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2o** in CDCl_3 at 100 MHz.

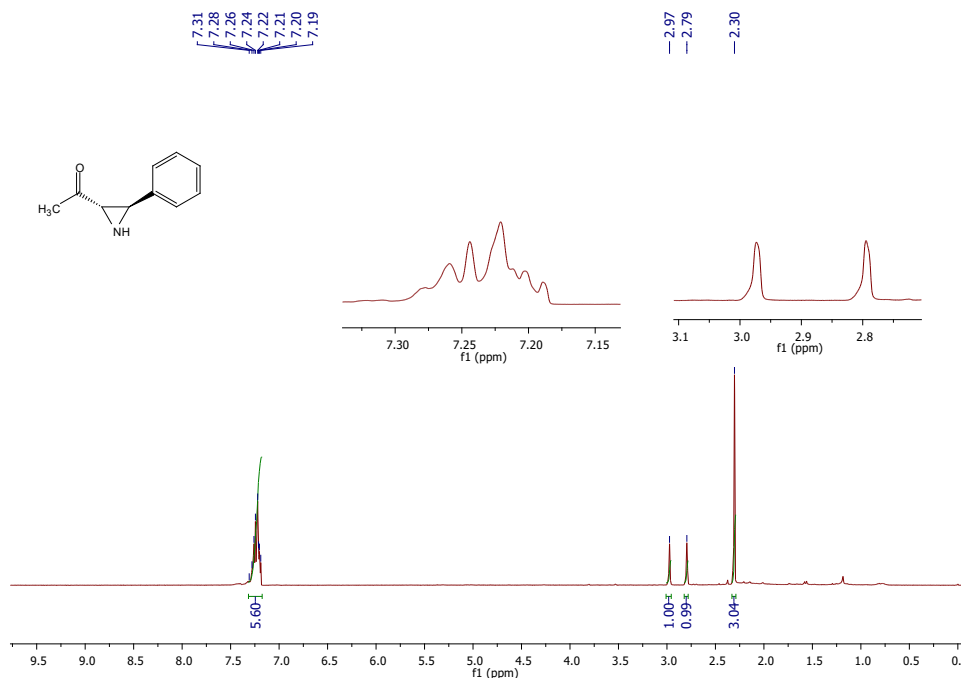


Fig. S33. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2p** in CDCl_3 at 100 MHz.

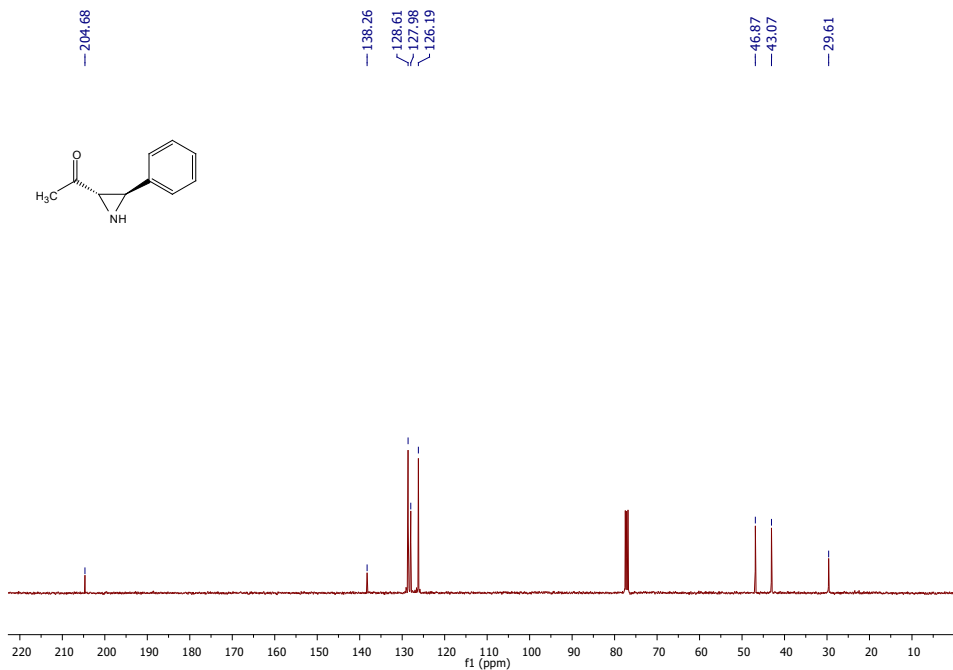


Fig. S34. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2p** in CDCl_3 at 100 MHz.

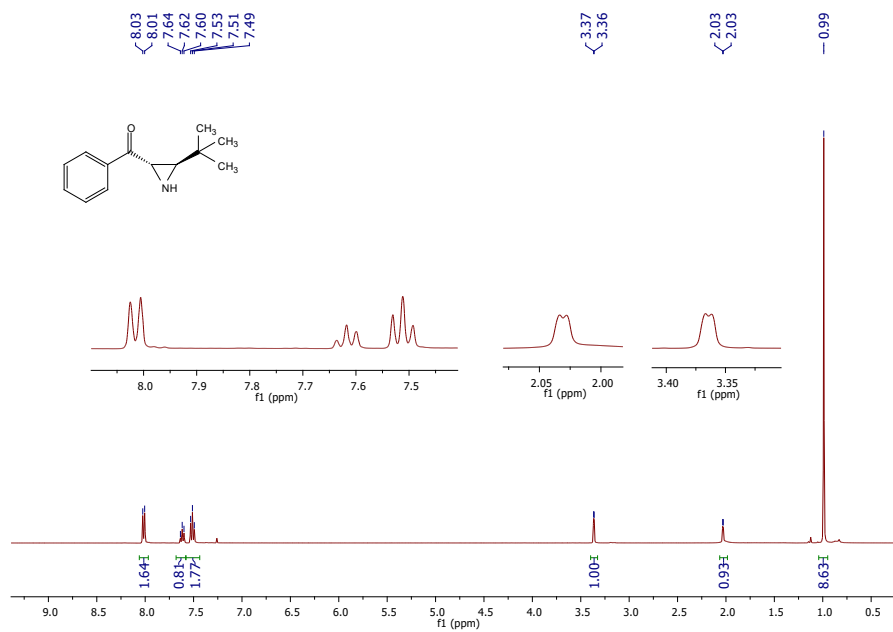


Fig. S35. ^1H NMR spectrum of compound **2q** in CDCl_3 at 400 MHz.

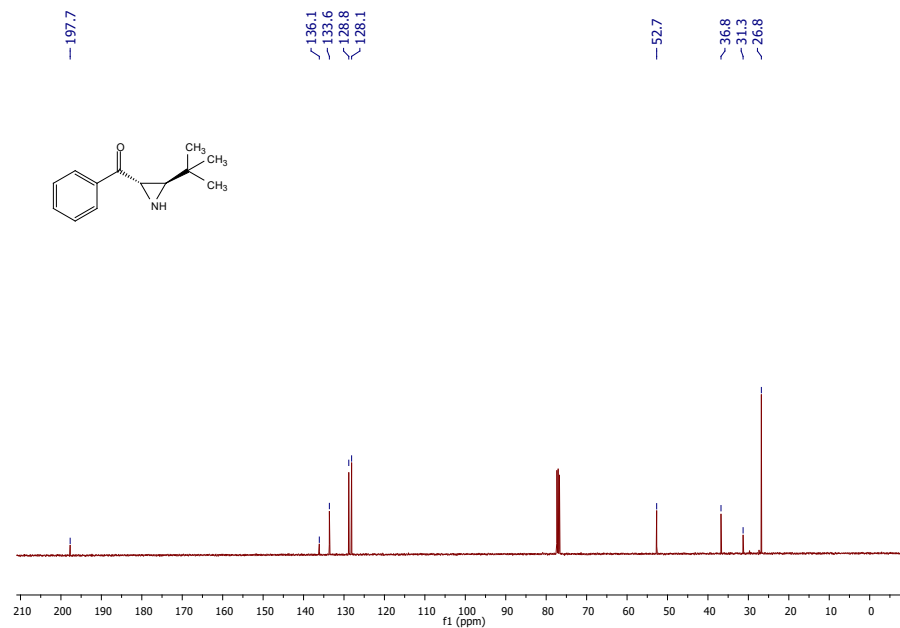


Fig. S36. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2q** in CDCl_3 at 100 MHz.

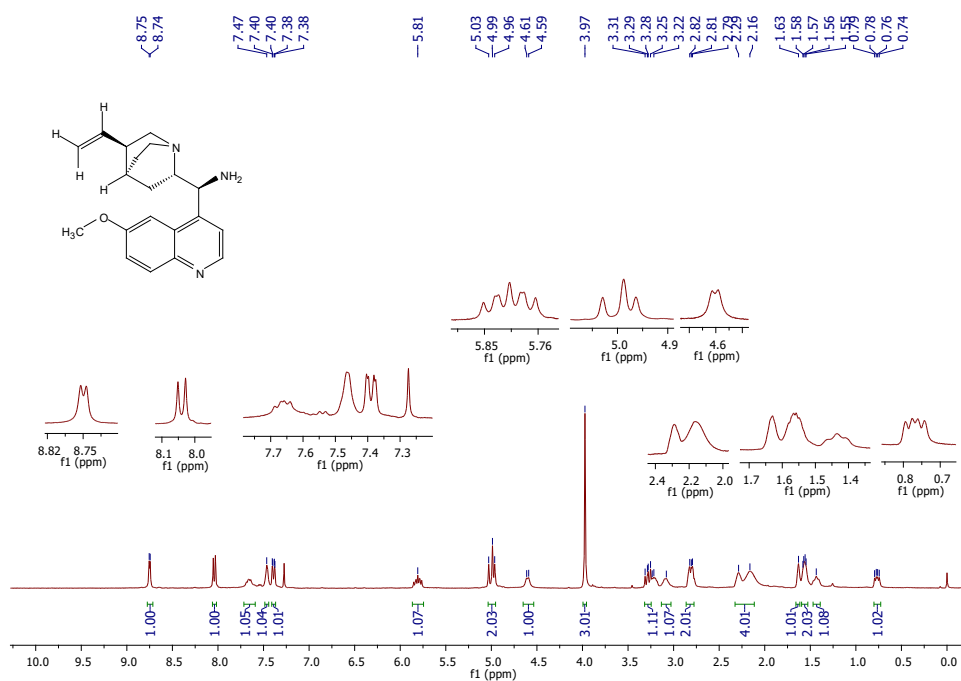


Fig. S37. ^1H NMR spectrum of catalyst **B** in CDCl_3 at 400 MHz.

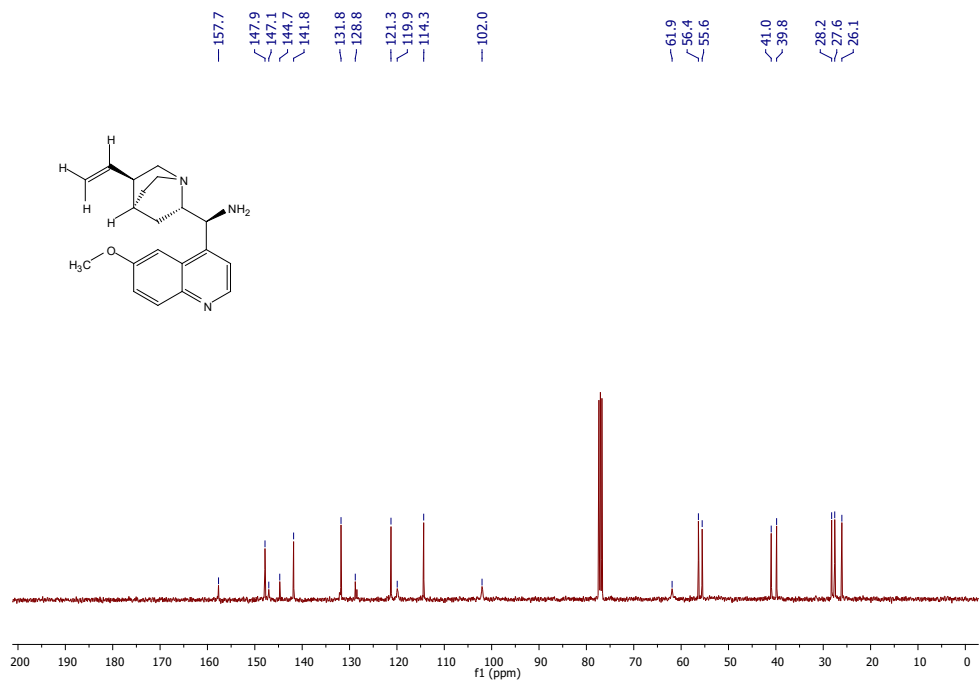


Fig. S38. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of catalyst B in CDCl_3 at 100 MHz.

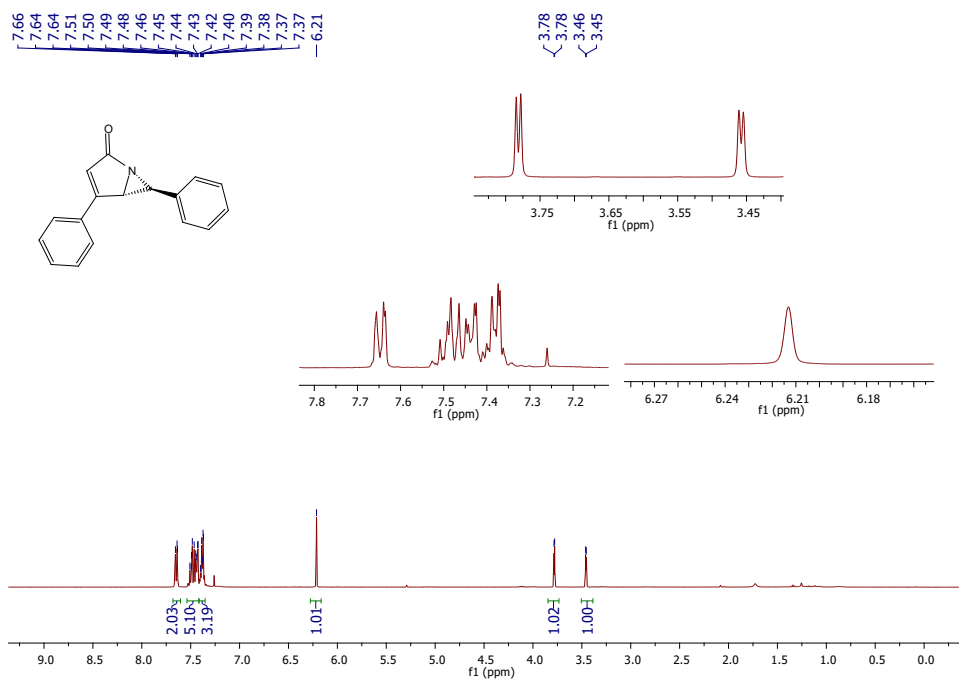


Fig. S39. ^1H NMR spectrum of compound 4a in CDCl_3 at 400 MHz.

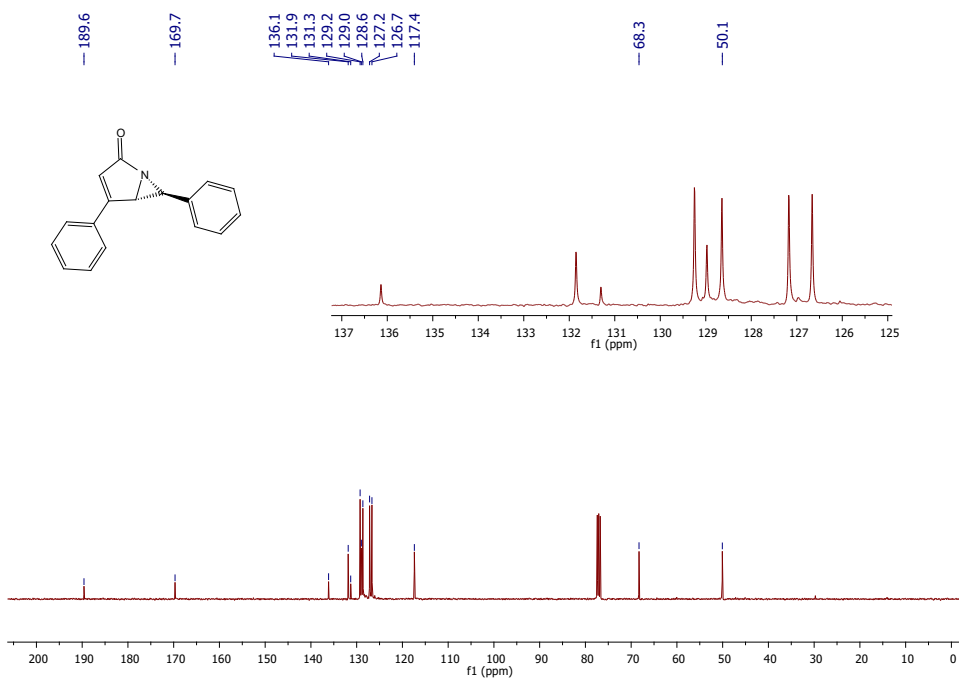


Fig. S40. ¹³C{¹H} NMR spectrum of compound 4a in CDCl₃ at 400 MHz.

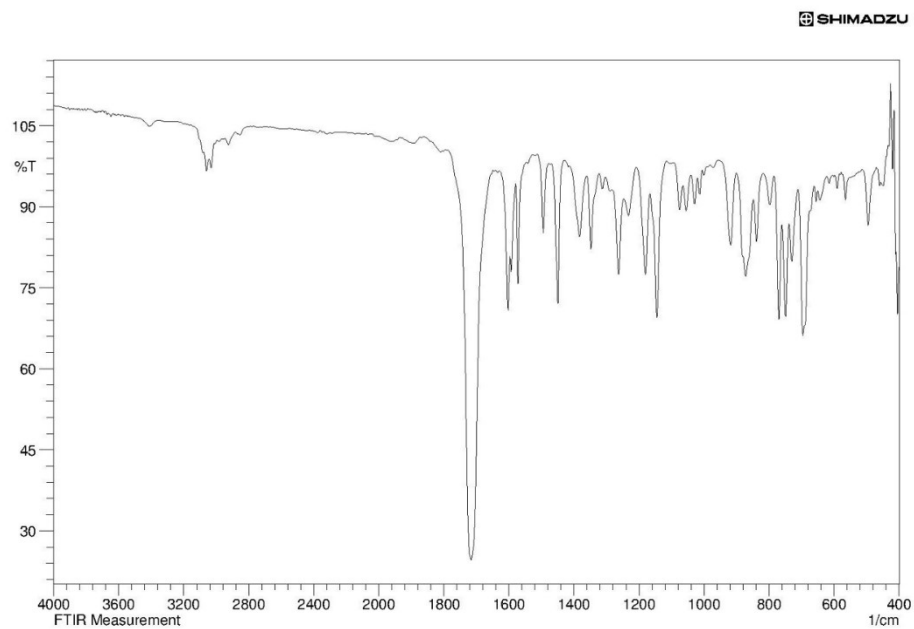


Fig. S41. IR spectrum of compound 4a in NaCl cell.

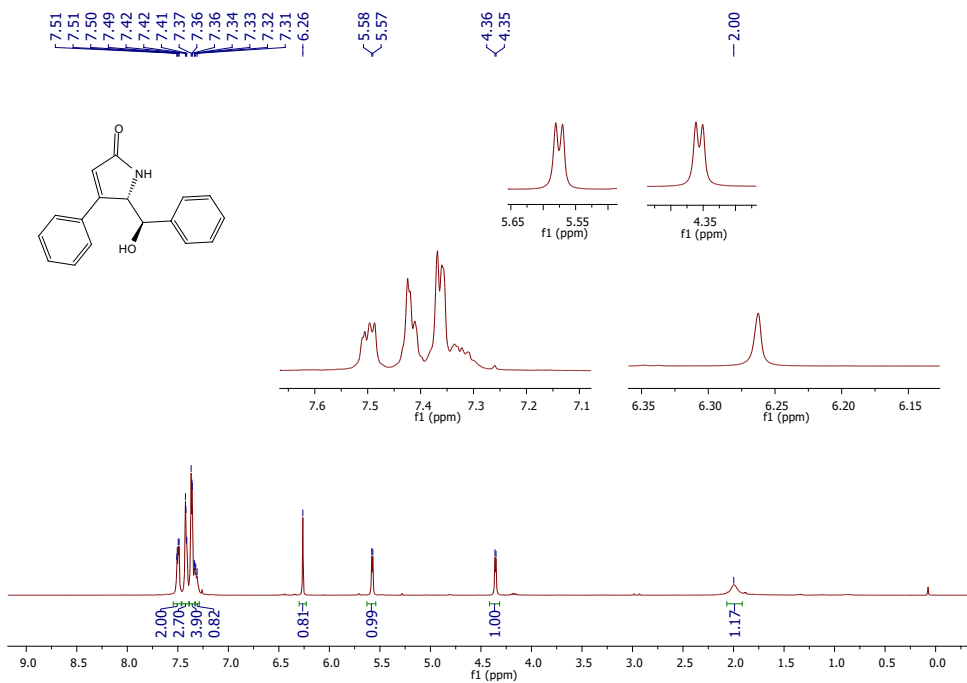


Fig. S42. ¹H NMR spectrum of compound 5a in CDCl₃ at 400 MHz.

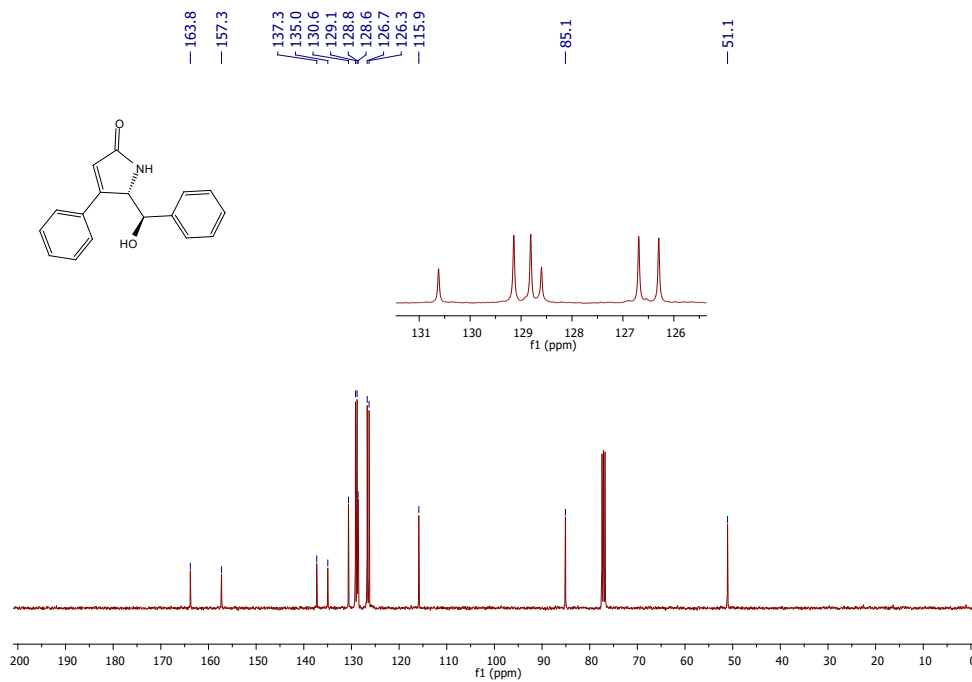
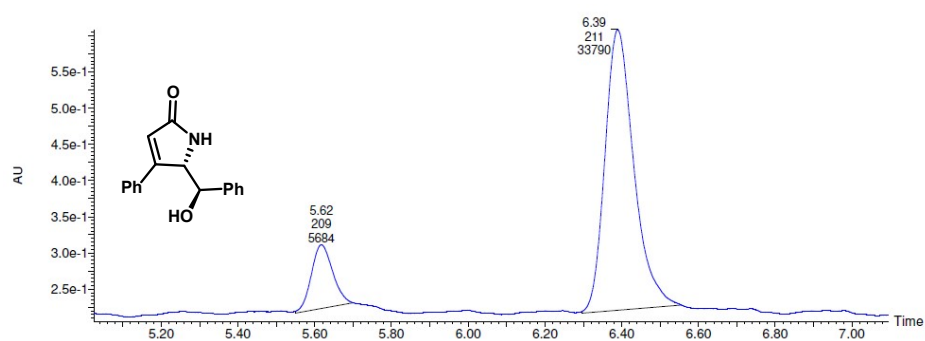
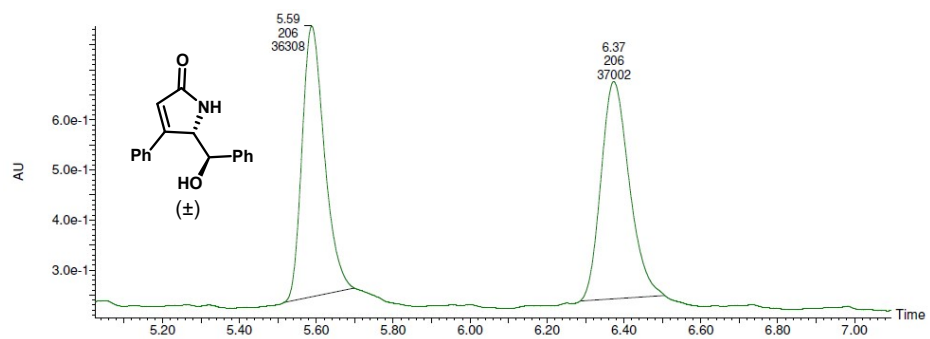


Fig. S43. ¹³C{¹H} NMR spectrum of compound 5a in CDCl₃ at 100 MHz.



	Retention time	Area	% Area
1	5.62	5683.61	14.40
2	6.39	33789.54	85.60

Fig. S44. Chromatogram of compound **5a** obtained by UPC².

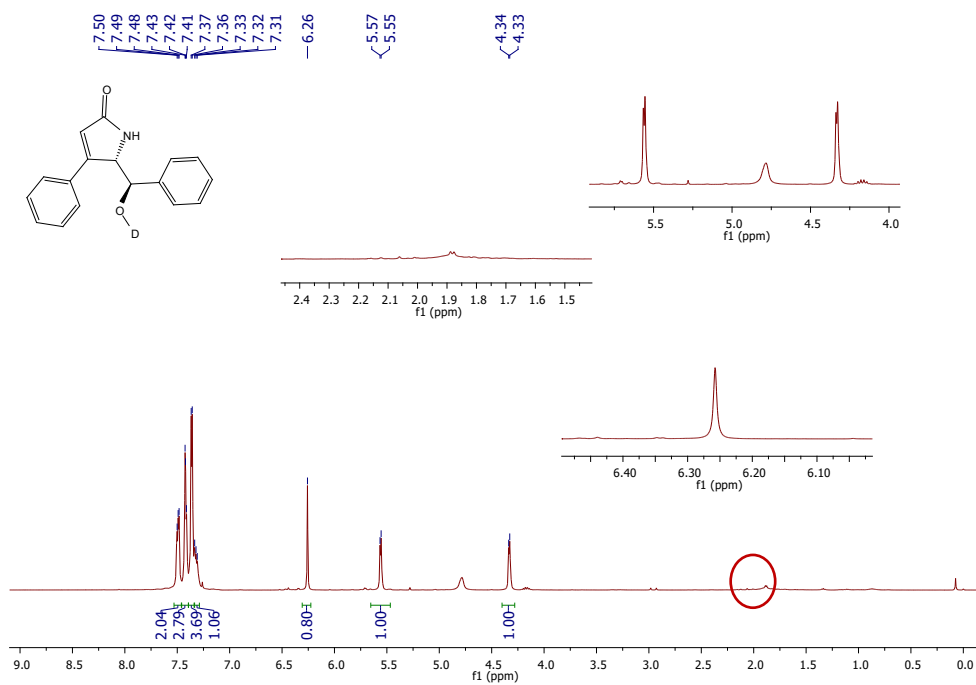


Fig. S45. ^1H NMR spectrum of compound 5a in D_2O at 400 MHz.

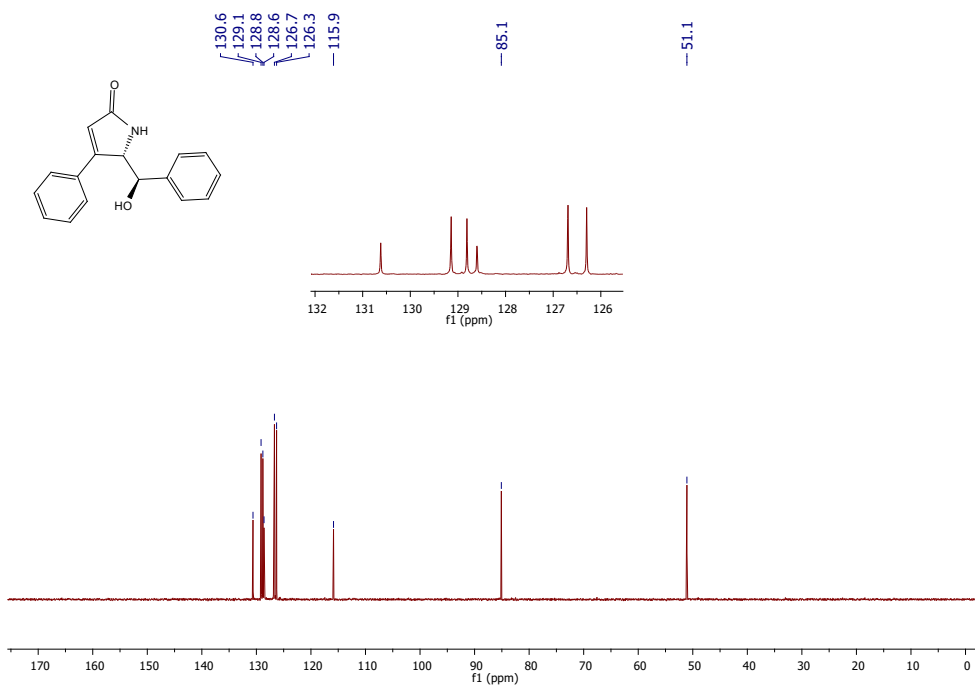


Fig. S46. $^{135}\text{DEPT}$ NMR spectrum of compound 5a and CDCl_3 at 100 MHz.

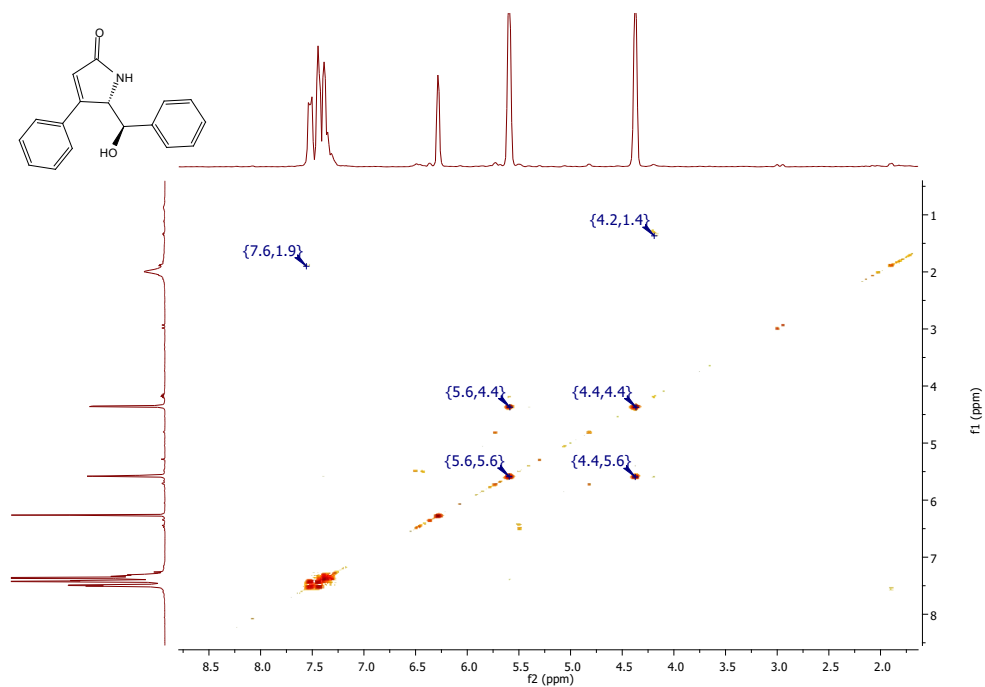


Fig. S47. COSY NMR spectrum of compound 5a in CDCl₃ at 400 MHz.

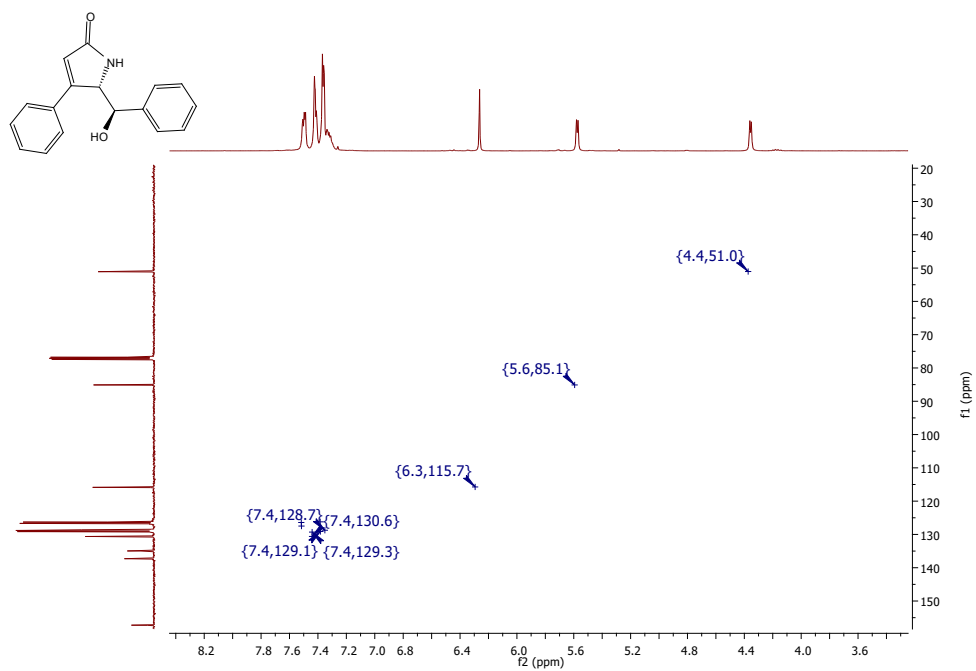


Fig. S48. HSQC NMR spectrum of compound 5a in CDCl₃ at 400 MHz.

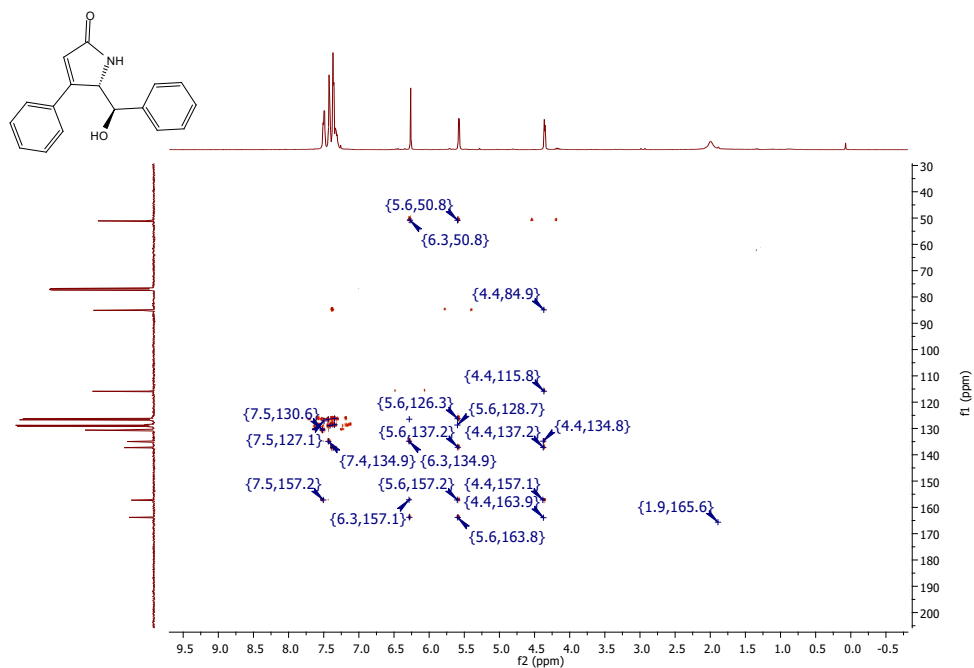


Fig. S49. HMBC NMR spectrum of compound 5a in CDCl₃ at 400 MHz.

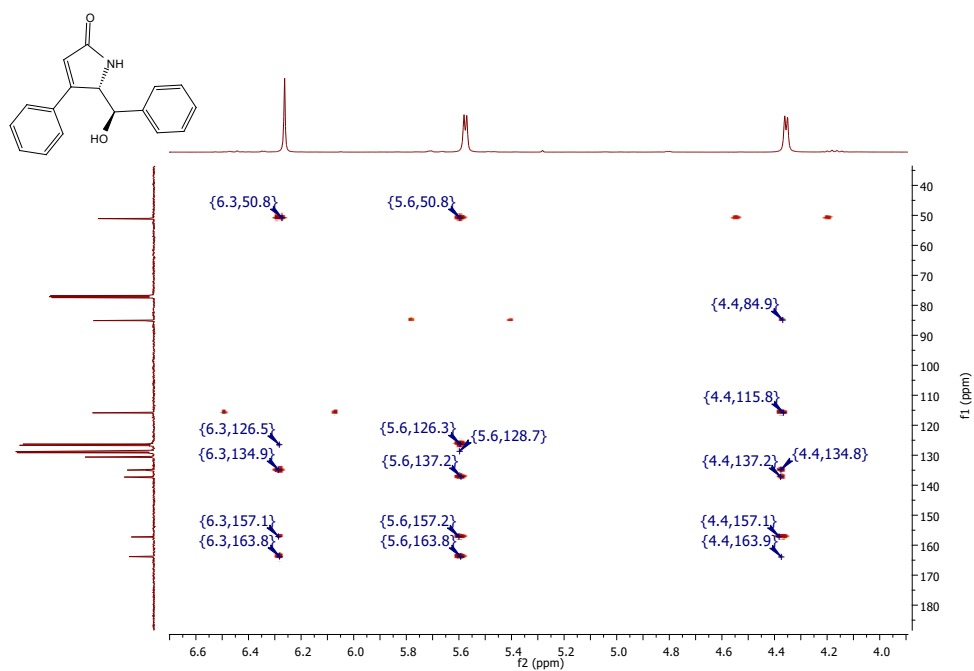


Fig. S50. HMBC NMR spectrum expansion of compound 5a in CDCl₃ at 400 MHz.

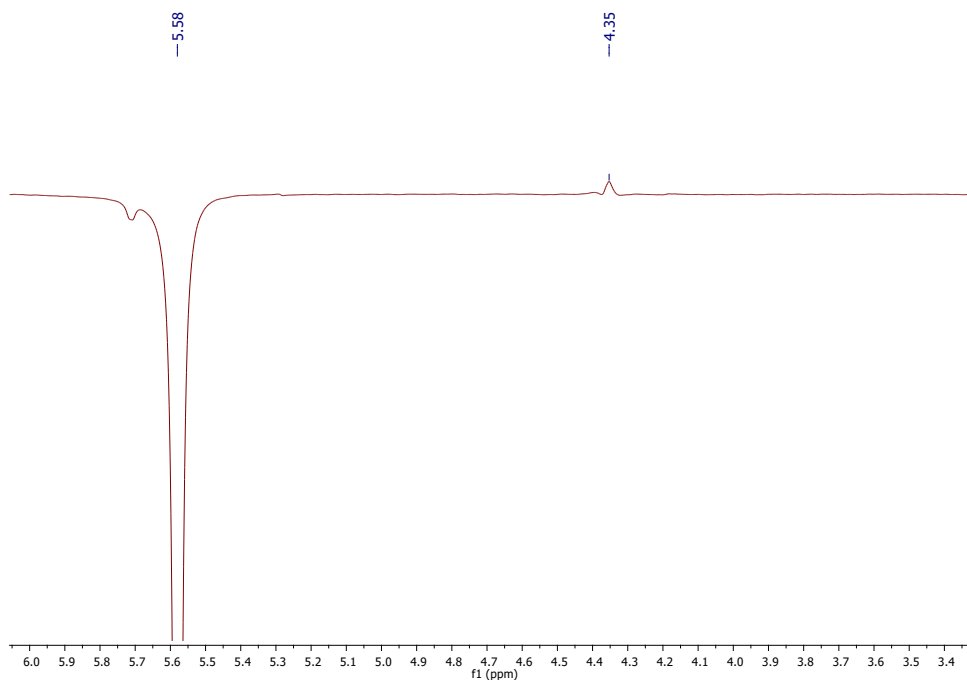


Fig. S51. 1D NOESY NMR spectrum of compound 5a for irradiation to 5.58 ppm in CDCl₃ at 400 MHz.

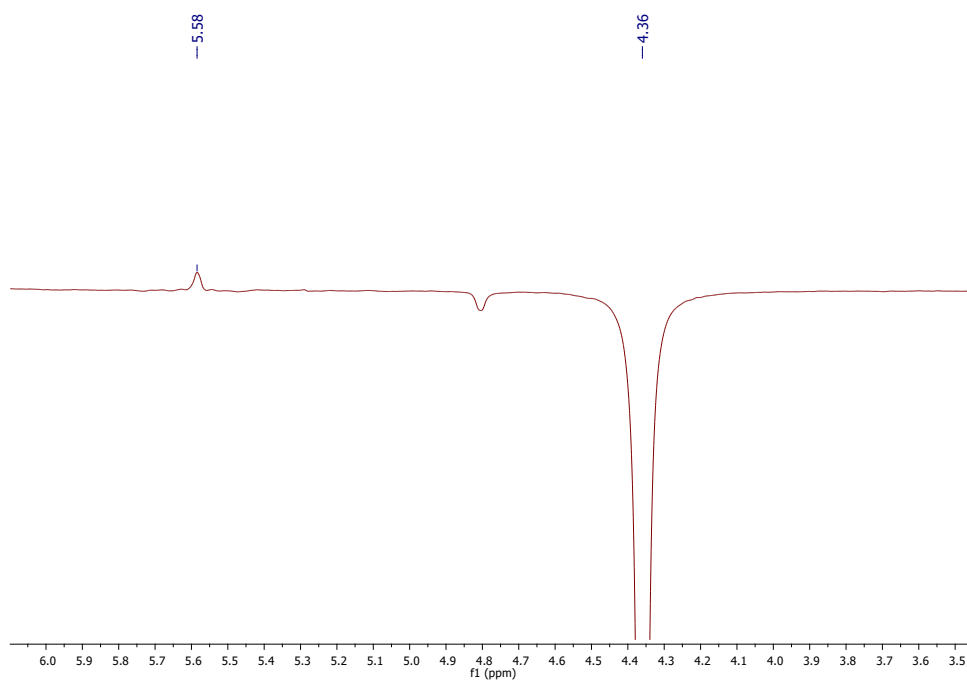


Fig. S52. 1D NOESY NMR spectrum of compound 5a for irradiation to 4.36 ppm in CDCl₃ at 400 MHz.

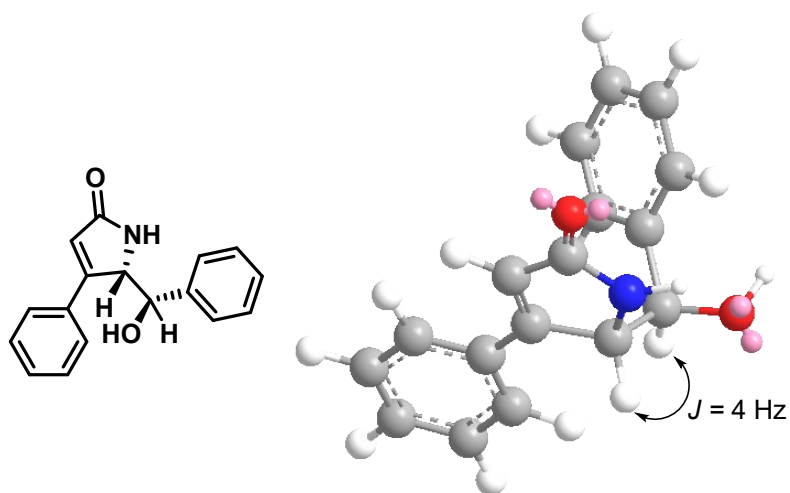


Fig. S53. Energy minimization in 3D Chemdraw for (S,R)-5a and compared with Kariuki *et al.*¹¹

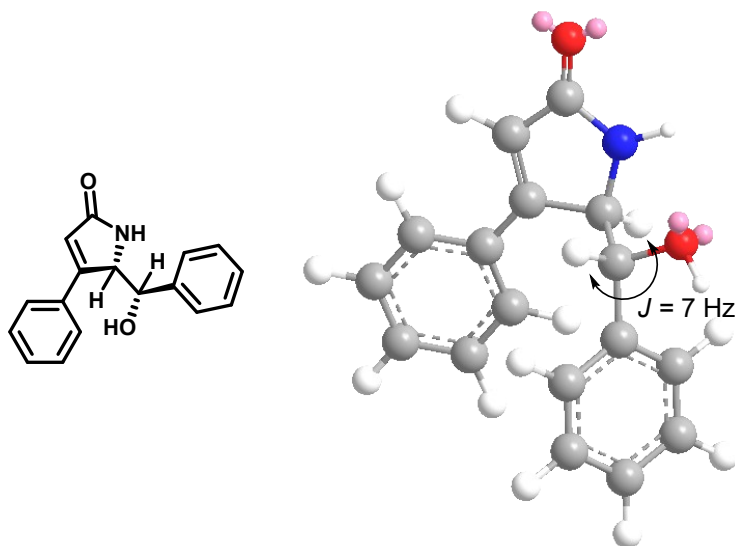


Fig. S54. Energy minimization in 3D Chemdraw for (R,R)-5a and compared with Kariuki *et al.*¹¹

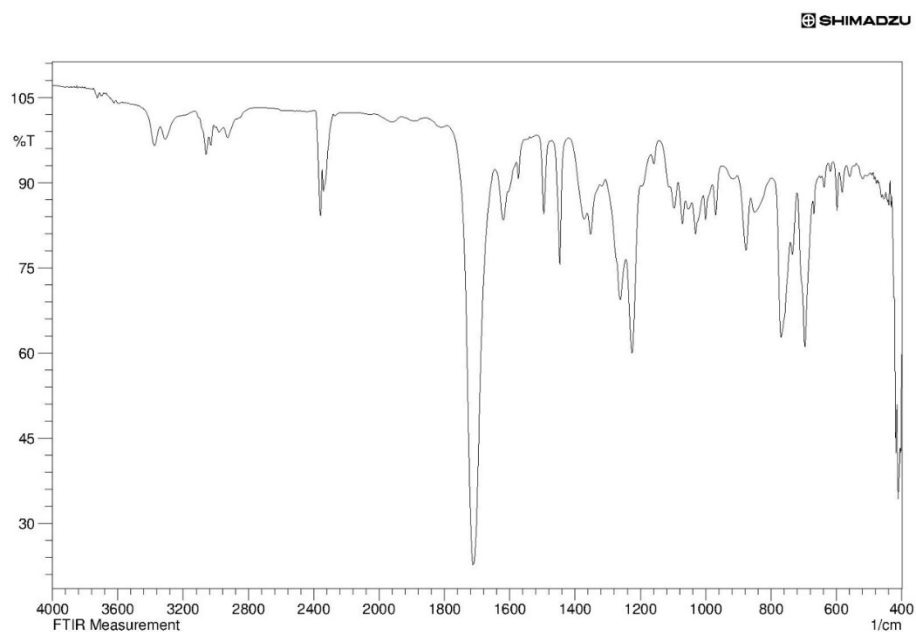


Fig. S55. IR spectrum of compound **5a** in NaCl cell.

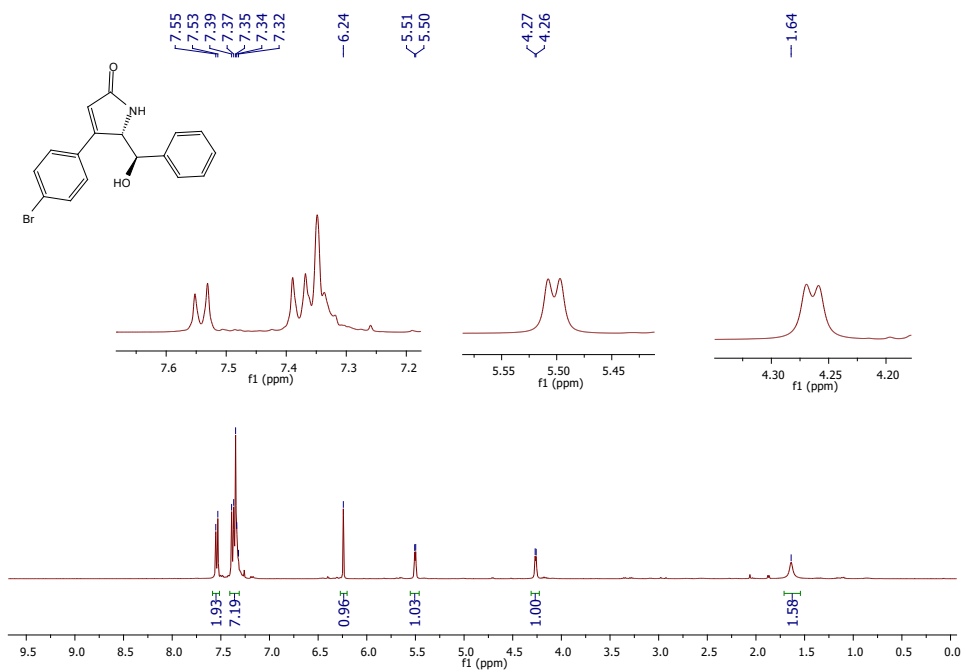


Fig. S56. ¹H NMR spectrum of compound **5c** in CDCl₃ at 400 MHz.

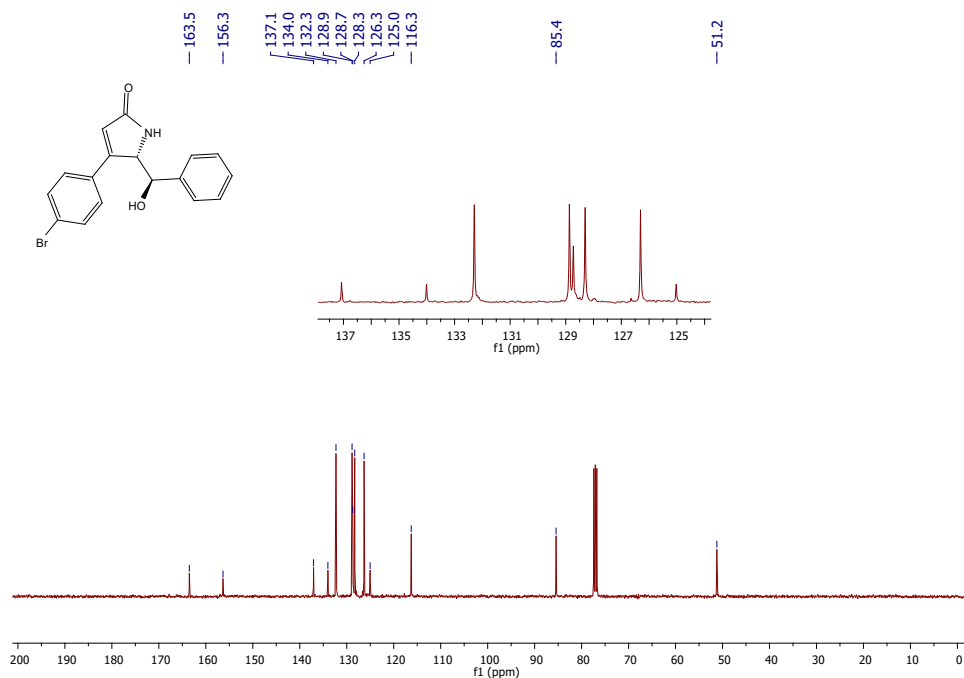


Fig. S7. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 5c in CDCl_3 at 100 MHz.

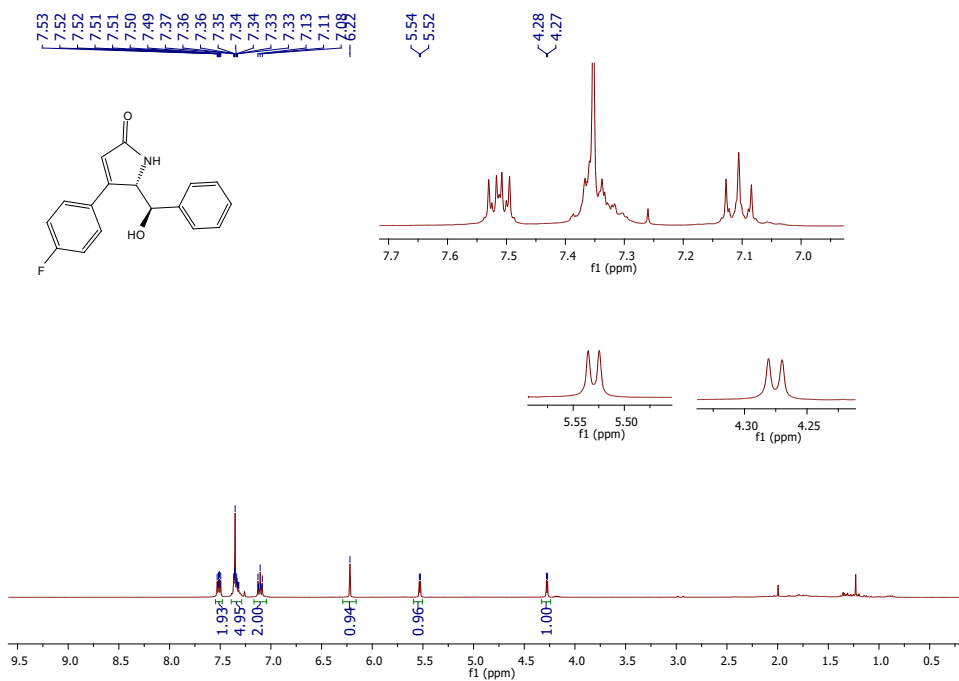


Fig. S58. ^1H NMR spectrum of compound 5d in CDCl_3 at 400 MHz.

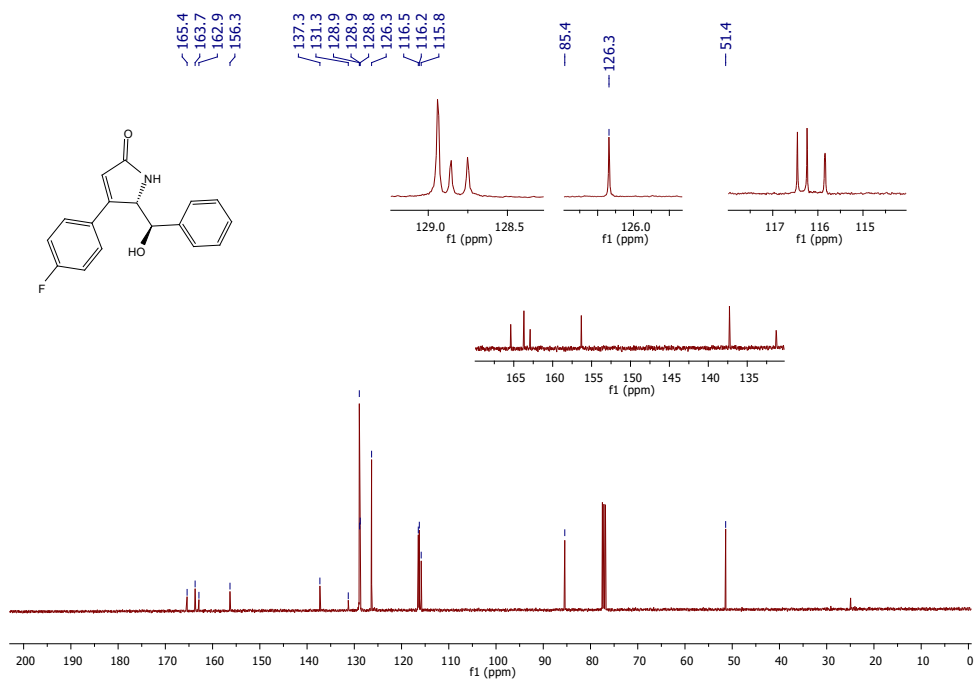


Fig. S59. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **5d** in CDCl_3 at 100 MHz.

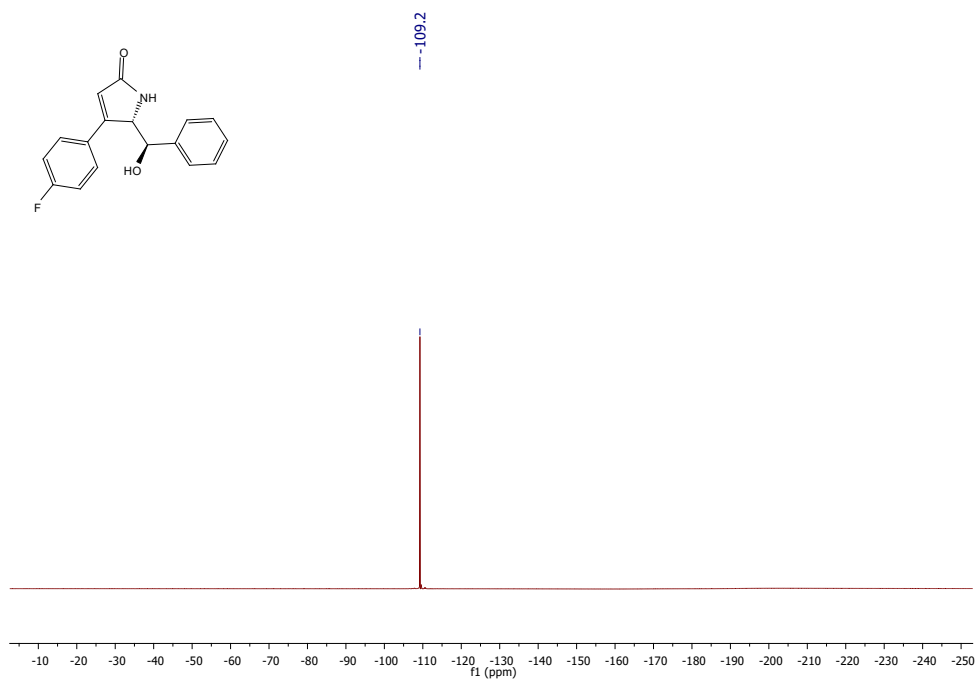


Fig. S60. $^{19}\text{F}\{^1\text{H}\}$ NMR spectrum of compound **5d** in CDCl_3 at 376 MHz.

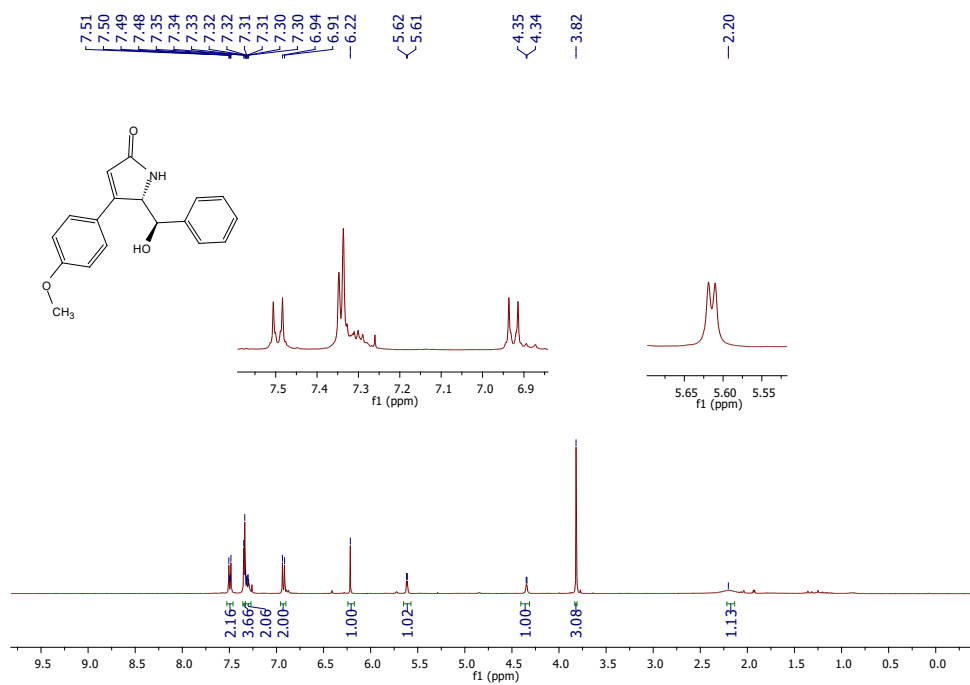


Fig. S61. ¹H NMR spectrum of compound 5e in CDCl₃ at 400 MHz.

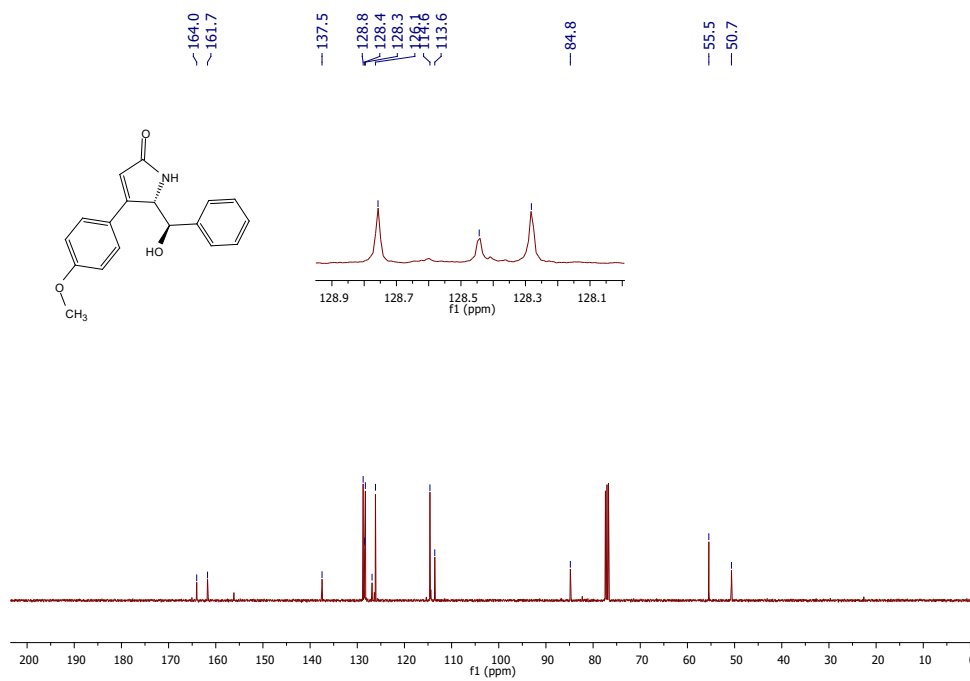


Fig. S62. ¹³C{¹H} NMR spectrum of compound 5e in CDCl₃ at 100 MHz.

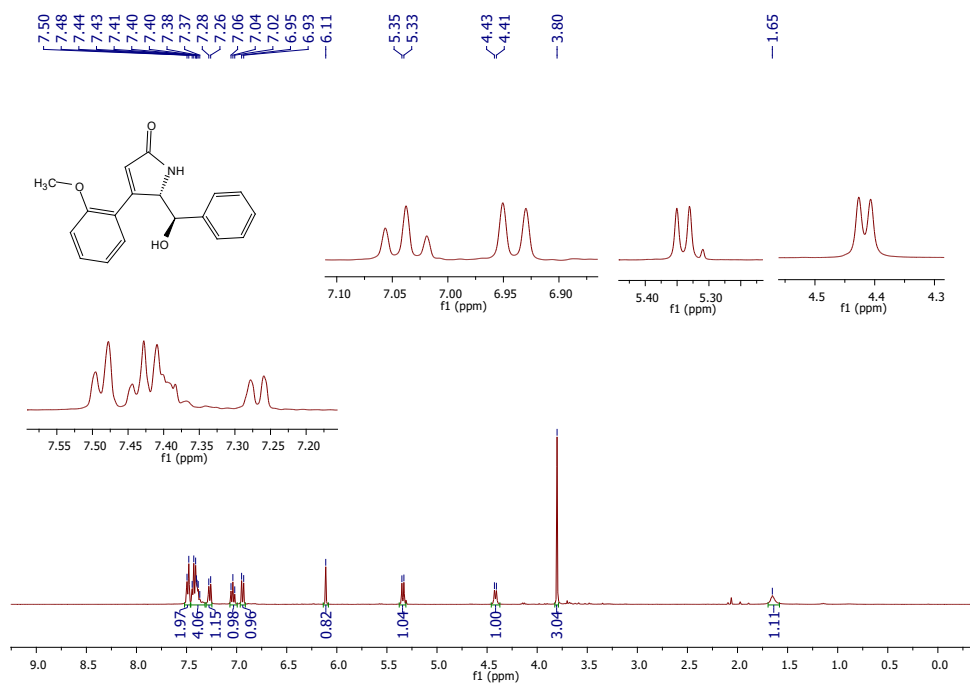


Fig. S63. ¹H NMR spectrum of compound **5f** in CDCl₃ at 400 MHz.

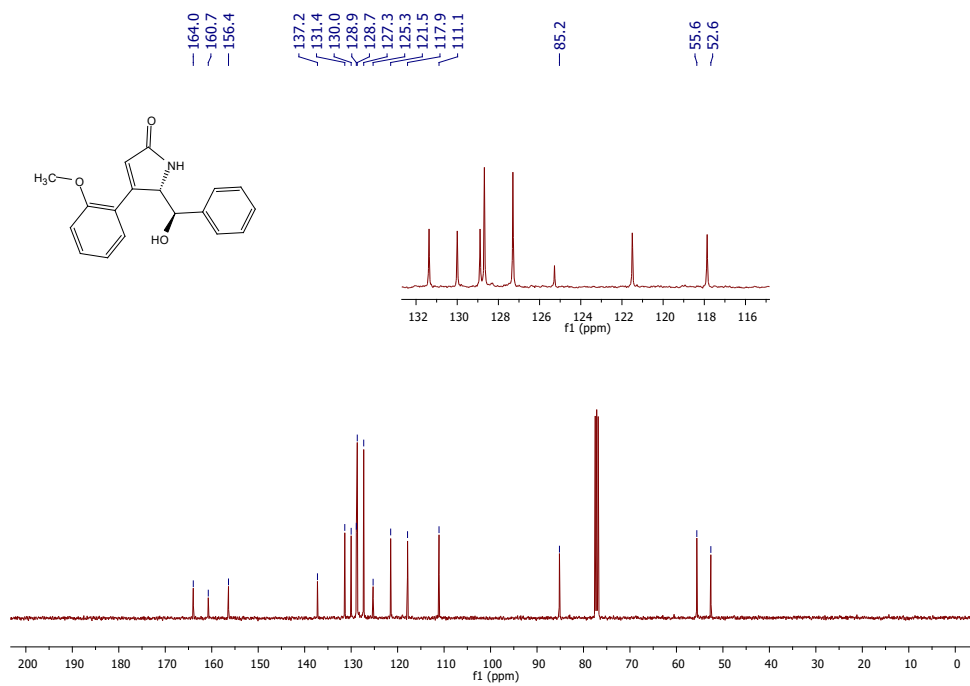


Fig. S64. ¹³C{¹H} NMR spectrum of compound **5f** in CDCl₃ at 100 MHz.

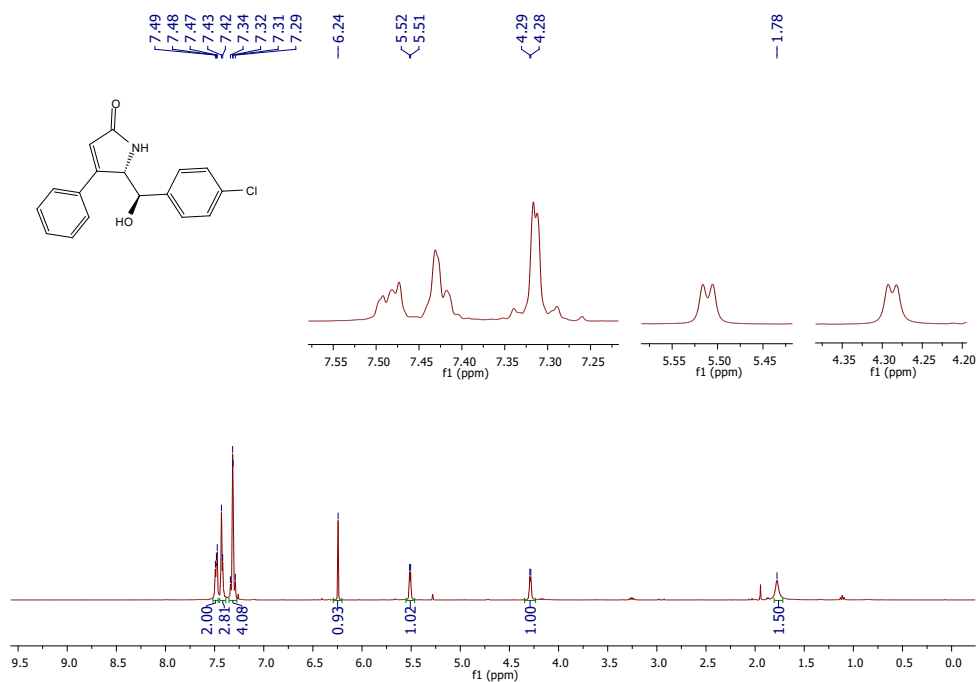


Fig. S65. ¹H NMR spectrum of compound **5g** in CDCl₃ at 400 MHz.

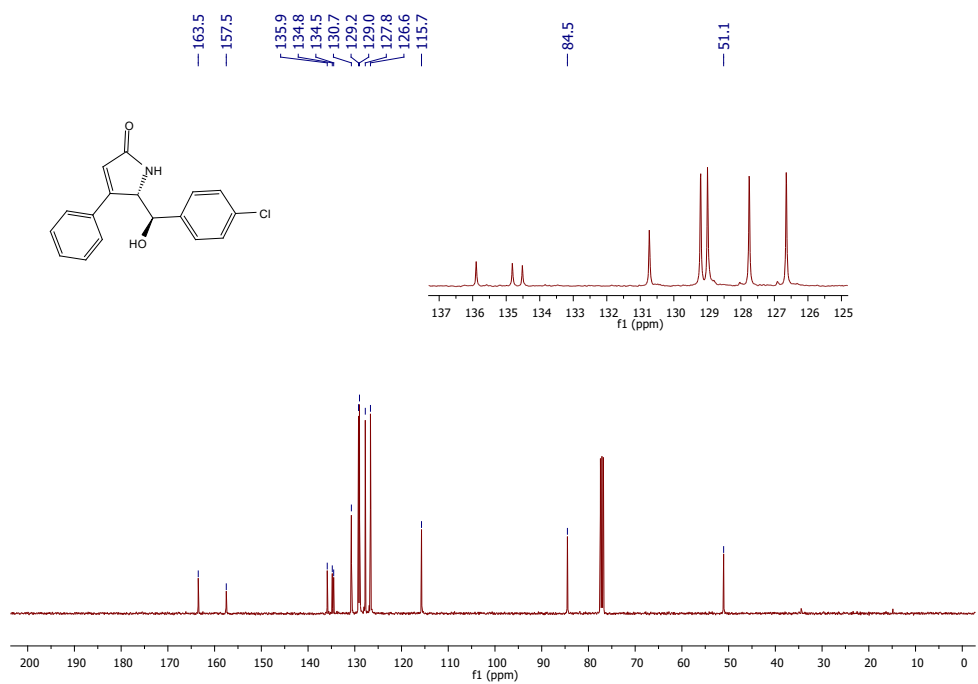


Fig. S66. ¹³C{¹H} NMR spectrum of compound **5g** in CDCl₃ at 100 MHz.

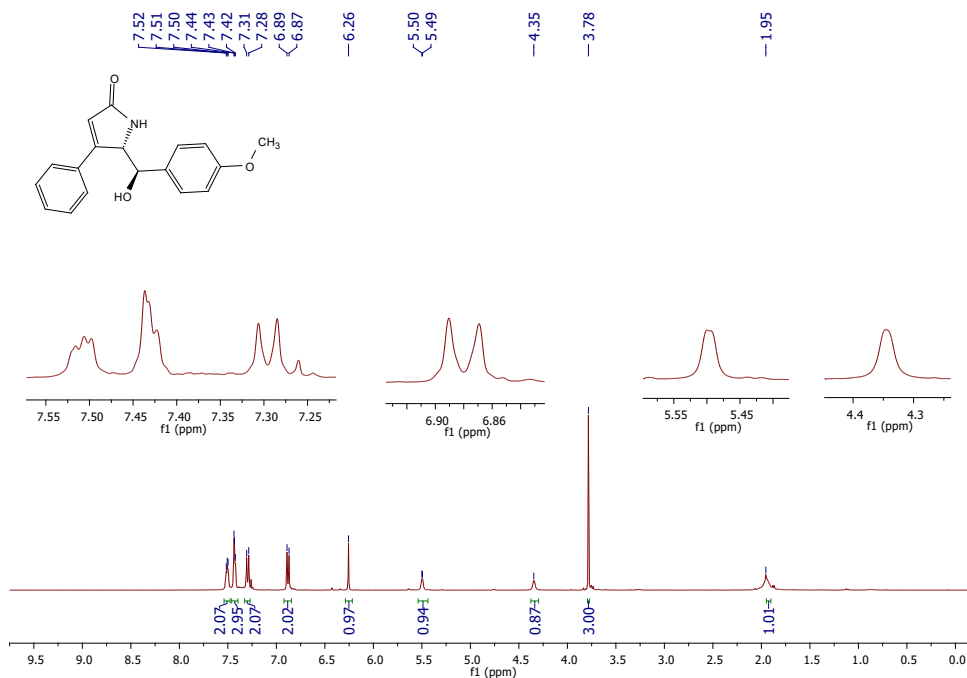


Fig. S67. ^1H NMR spectrum of compound **5h** in CDCl_3 at 400 MHz.

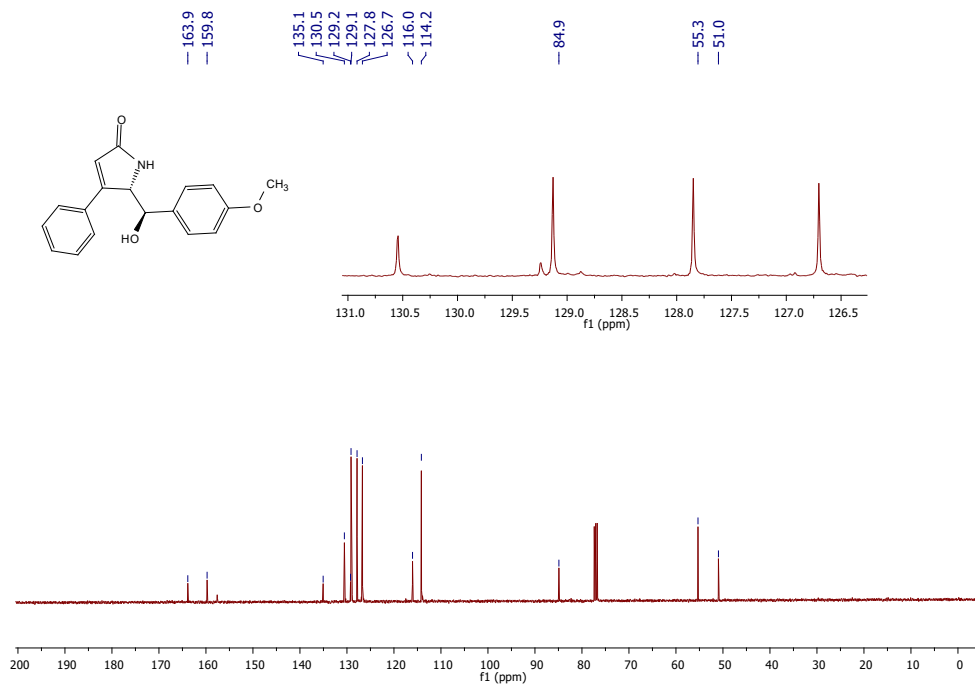


Fig. S68. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **5h** in CDCl_3 at 100 MHz.

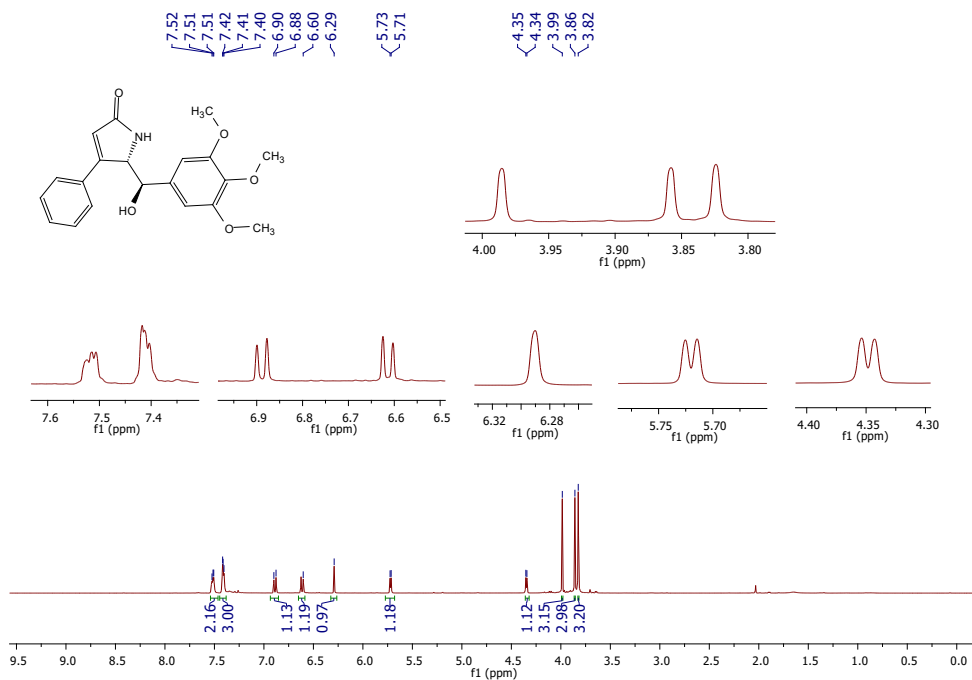


Fig. S69. ¹H NMR spectrum of compound 5i in CDCl₃ at 400 MHz.

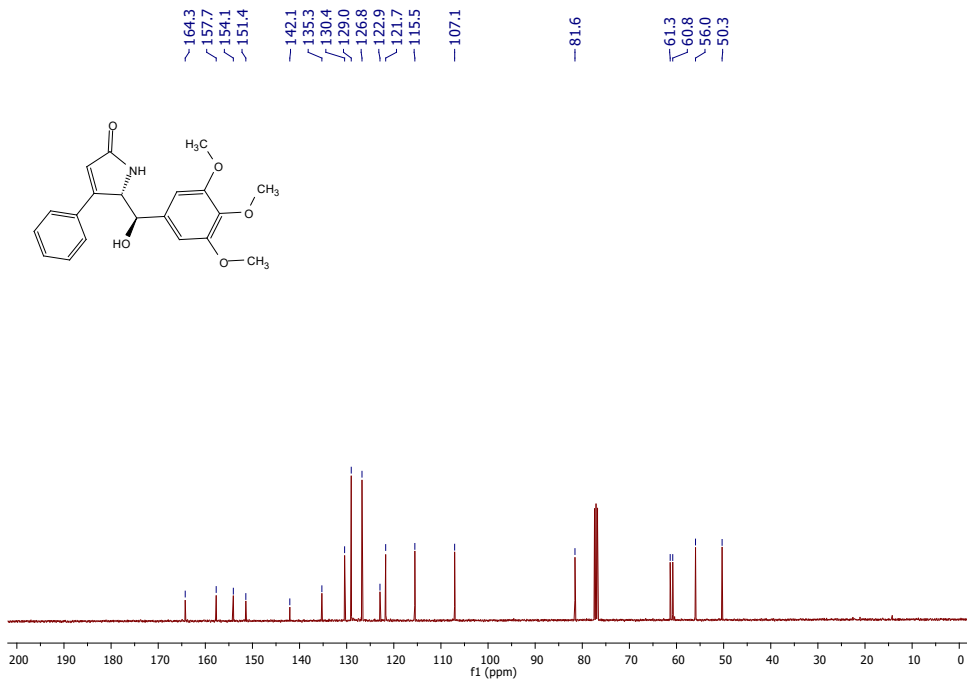


Fig. S70. ¹³C{¹H} NMR spectrum of compound 5i in CDCl₃ at 100 MHz.

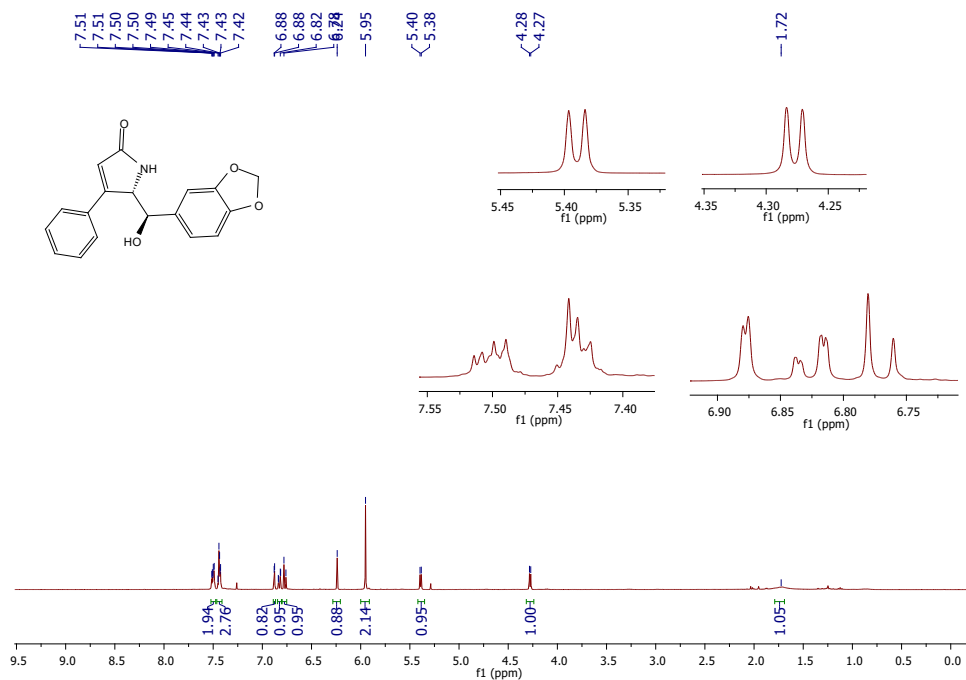


Fig. S71. ¹H NMR spectrum of compound **5j** in CDCl₃ at 400 MHz.

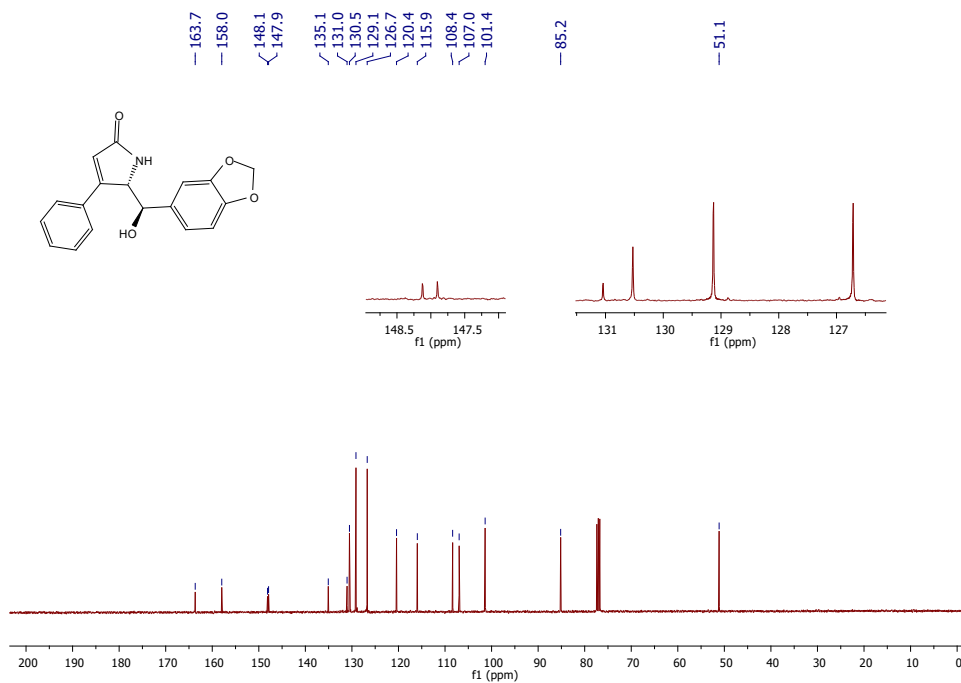


Fig. S72. ¹³C{¹H} NMR spectrum of compound **5j** in CDCl₃ at 100 MHz.

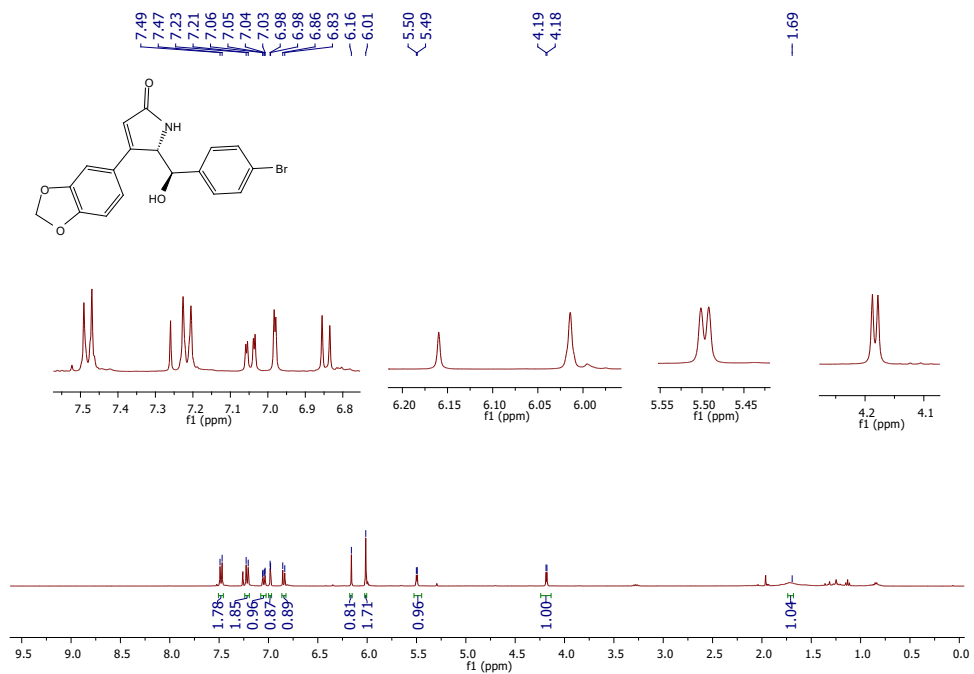


Fig. S73. ¹H NMR spectrum of compound **5k** in CDCl₃ at 400 MHz.

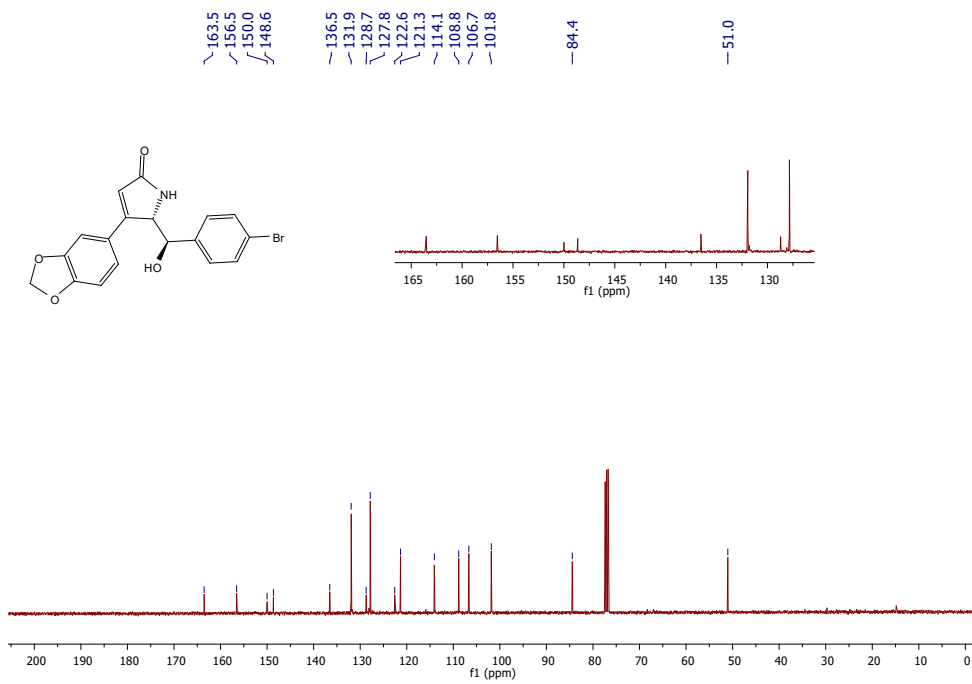


Fig. S74. ¹³C{¹H} NMR spectrum of compound **5k** in CDCl₃ at 100 MHz.

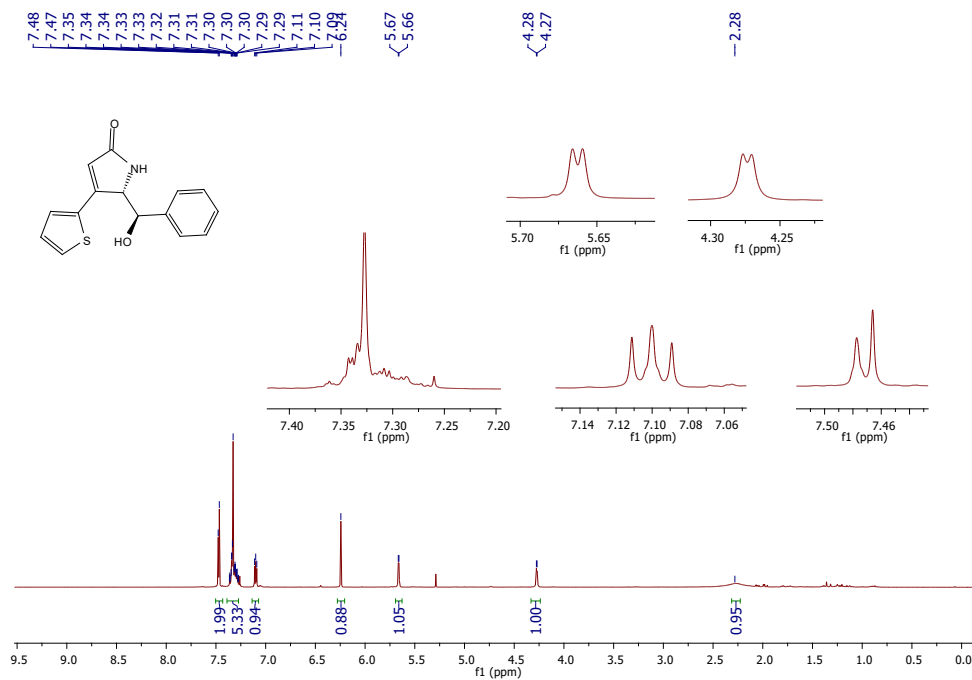


Fig. S75. ¹H NMR spectrum of compound 5I in CDCl₃ at 400 MHz.

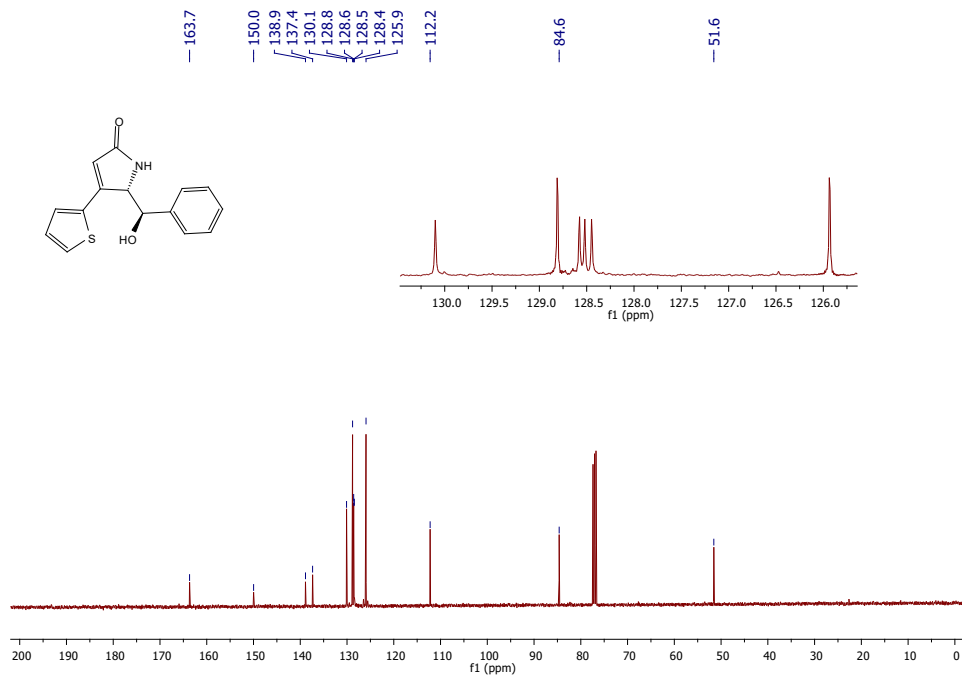


Fig. S76. ¹³C{¹H} NMR spectrum of compound 5I in CDCl₃ at 100 MHz.

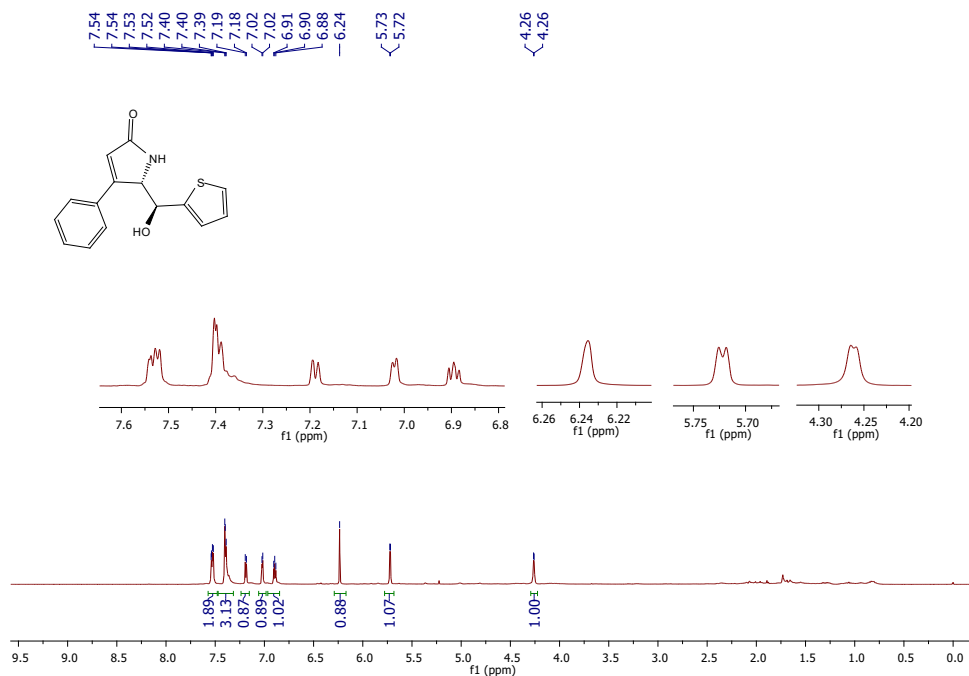


Fig. S77. ^1H NMR spectrum of compound **5m** in CDCl_3 at 400 MHz.

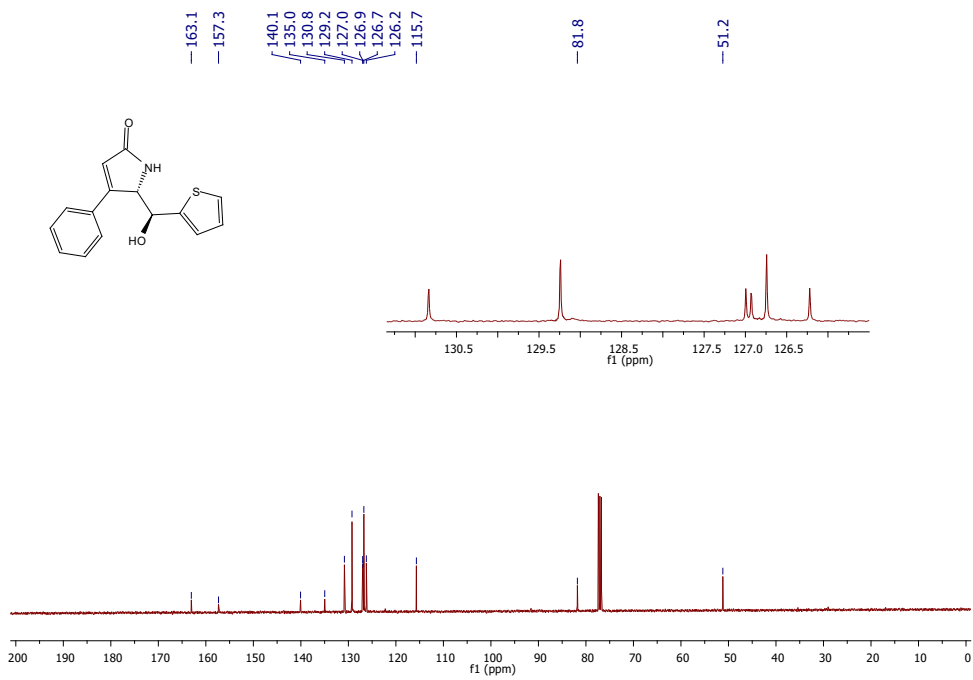


Fig. S78. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **5m** in CDCl_3 at 100 MHz.

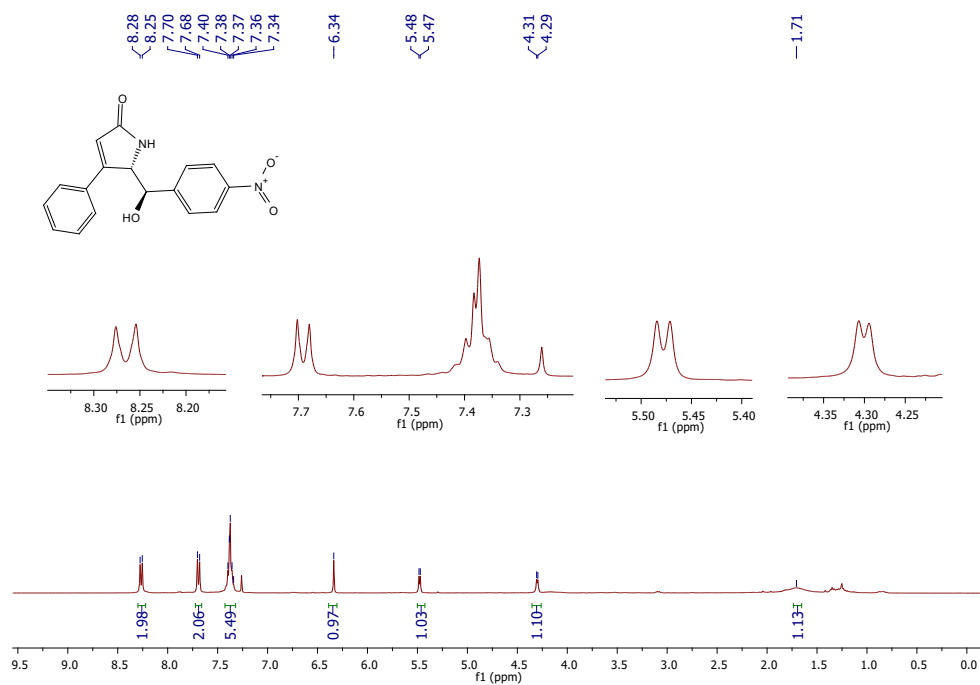


Fig. S79. ¹H NMR spectrum of compound **5o** in CDCl₃ at 400 MHz.

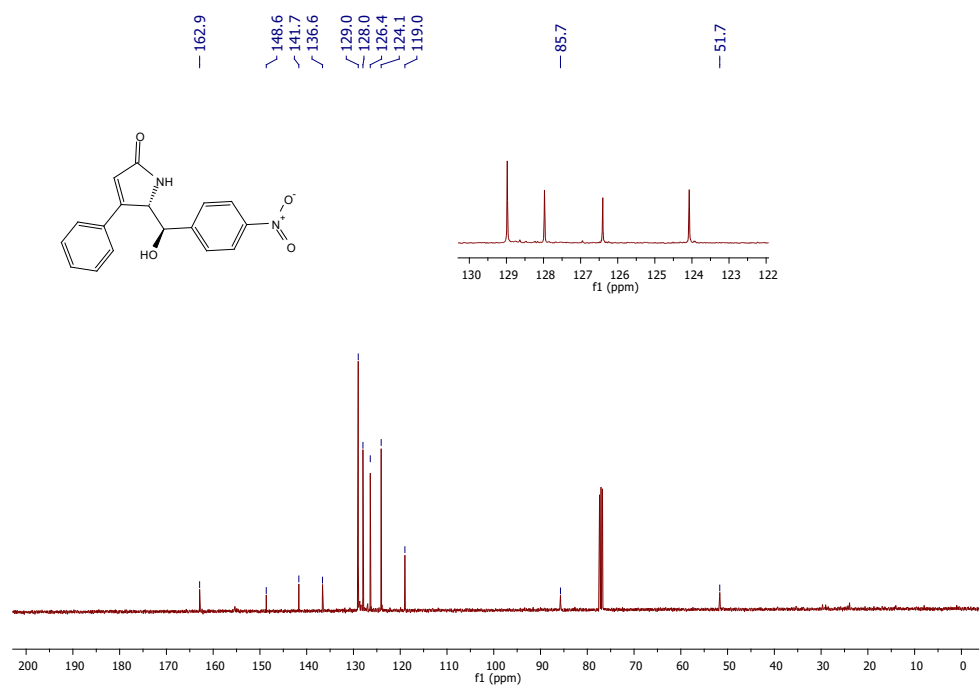


Fig. S80. ¹³C{¹H} NMR spectrum of compound **5o** in CDCl₃ at 100 MHz.

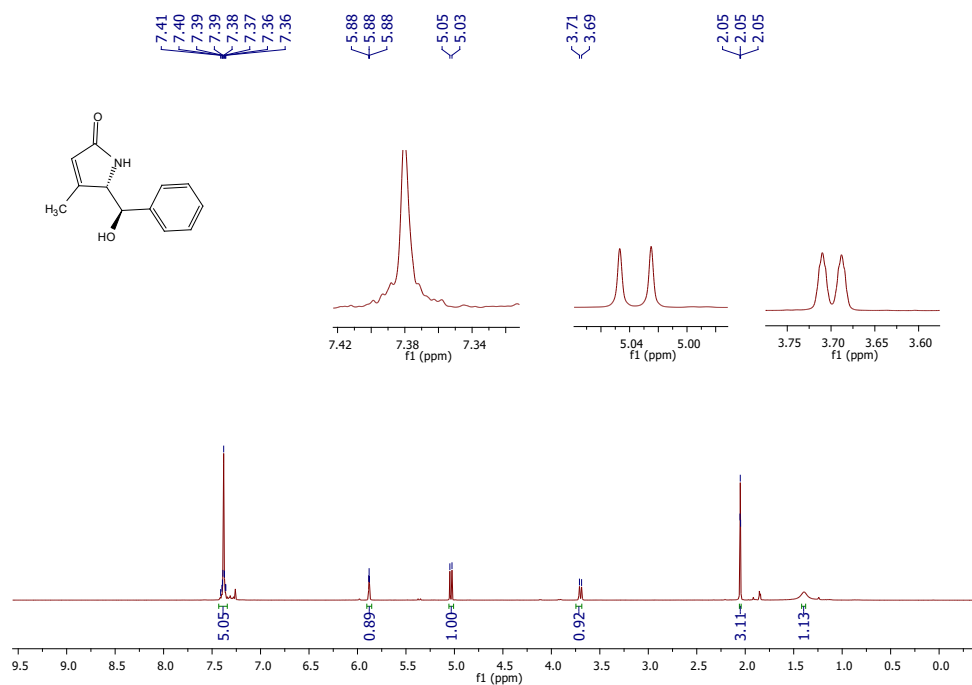


Fig. S81. ¹H NMR spectrum of compound **5p** in CDCl₃ at 400 MHz.

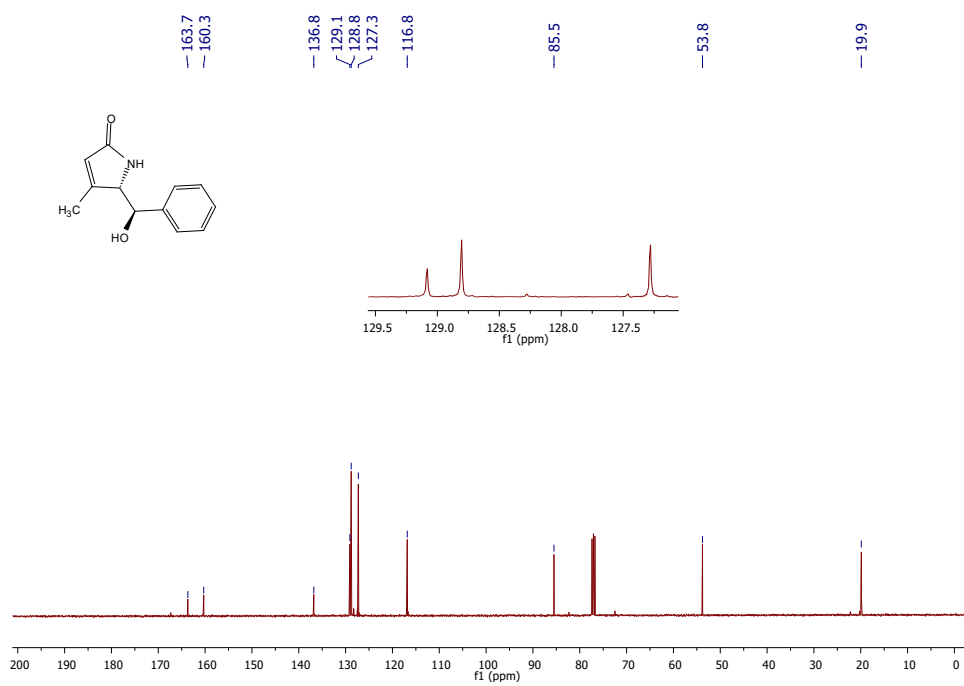


Fig. S82. ¹³C{¹H} NMR spectrum of compound **5p** in CDCl₃ at 100 MHz.

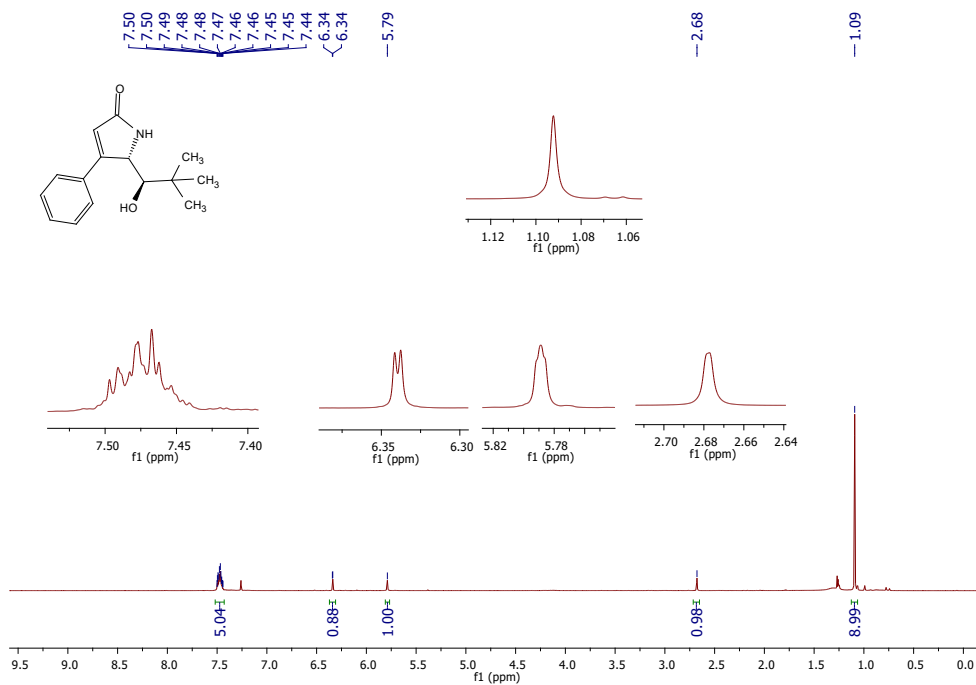


Fig. S83. ¹H NMR spectrum of compound **5q** in CDCl₃ at 400 MHz.

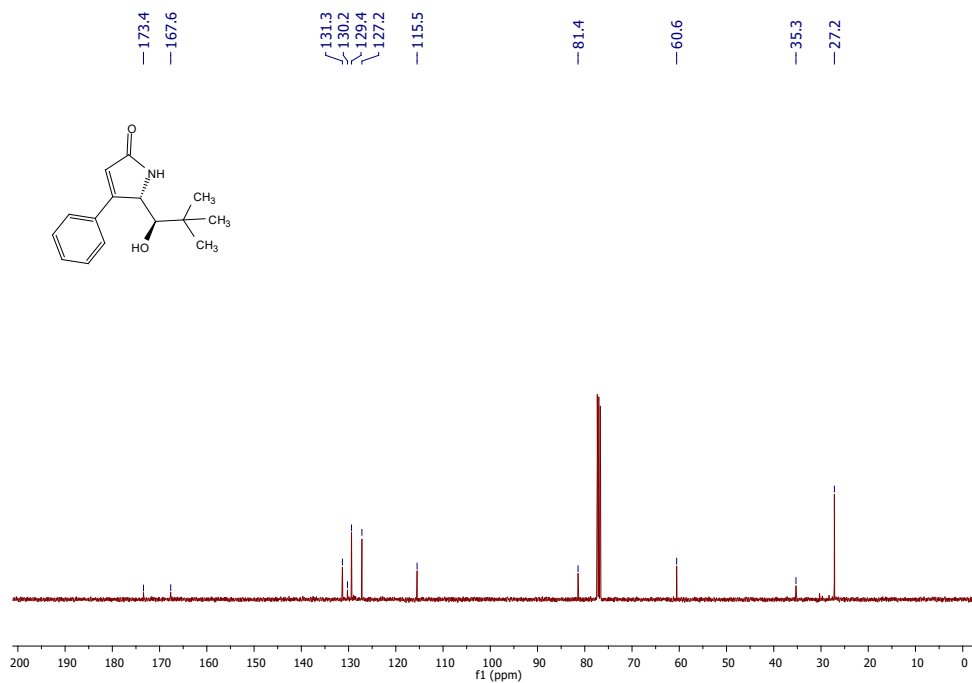


Fig. S84. ¹³C{¹H} NMR spectrum of compound **5q** in CDCl₃ at 100 MHz.

10. Crystallographic data

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) shelx

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: shelx

Bond precision: C-C = 0.0039 Å Wavelength=0.71073

Cell: a=11.280 (3) b=9.997 (3) c=11.637 (4)
 alpha=90 beta=91.08 (2) gamma=90
 290 K

Temperature:

	Calculated	Reported
Volume	1312.0 (7)	1312.0 (7)
Space group	P 21/c	P 21/c
group		
Moiety formula	-P 2ybc C17 H13 N	-P 2ybc C17 H13 N


		O		O
Sum formula	C17 H13 N	O	C17 H13 N	O
Mr	247.28		247.28	
Dx, g cm-3	1.252		1.252	
Z	4		4	
Mu (mm-1)	0.078		0.078	
F000	520.0		520.0	
F000'	520.21			
h, k, lmax	14, 12, 14		14, 11, 14	
Nref	2764		2093	
Tmin, Tmax	0.978, 0.991		0.375, 0.745	
Tmin'	0.974			

Correction method= # Reported T Limits: Tmin=0.375 Tmax=0.745 AbsCorr = MULTI-SCAN

Data completeness= 0.757 Theta(max)= 26.655


R(reflections)= 0.0495 (875) wR2(reflections)=
0.1104 (2093)
S = 0.703 Npar= 172

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

 **Alert level A**


PLAT029_ALERT_3_A _diffn_measured_fraction_theta_full value Low . 0.770 Why?

Author Response: Due to the very low diffraction quality of the crystal. Eventhough the main objective was attained which was confirming the structure and the number of reflections per parameteris over 10.


 **Alert level B**

PLAT911_ALERT_3_B Missing FCF Refl Between Thmin & STh/L= 0.600 544 Report

Author Response: Due to the very low diffraction quality of the crystal. Eventhough the main objective was attained which was confirming the structure and the number of reflections per parameteris over 10.

 **Alert level C**

GOODF01_ALERT_2_C The least squares goodness of fit parameter lies
outside the range 0.80 <> 2.00
Goodness of fit given = 0.703
PLAT026_ALERT_3_C Ratio Observed / Unique Reflections (too) Low ..42% Check
PLAT905_ALERT_3_C Negative K value in the Analysis of Variance ...-1.769 Report

 **Alert level G**

PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 94
Note PLAT913_ALERT_3_G Missing # of Very Strong Reflections in FCF
2 Note PLAT941_ALERT_3_G Average HKL Measurement Multiplicity
2.1 Low PLAT963_ALERT_2_G Both SHELXL WEIGHT Parameter Values Zero Please
CheckPLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.
0 Info

-
- 1 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
3 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
5 **ALERT level G** = General information/check it is not something unexpected
- 0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
6 ALERT type 3 Indicator that the structure quality may be low
1 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check
-

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 06/07/2023; check.def file version of 30/06/2023

Datablock shelx - ellipsoid plot

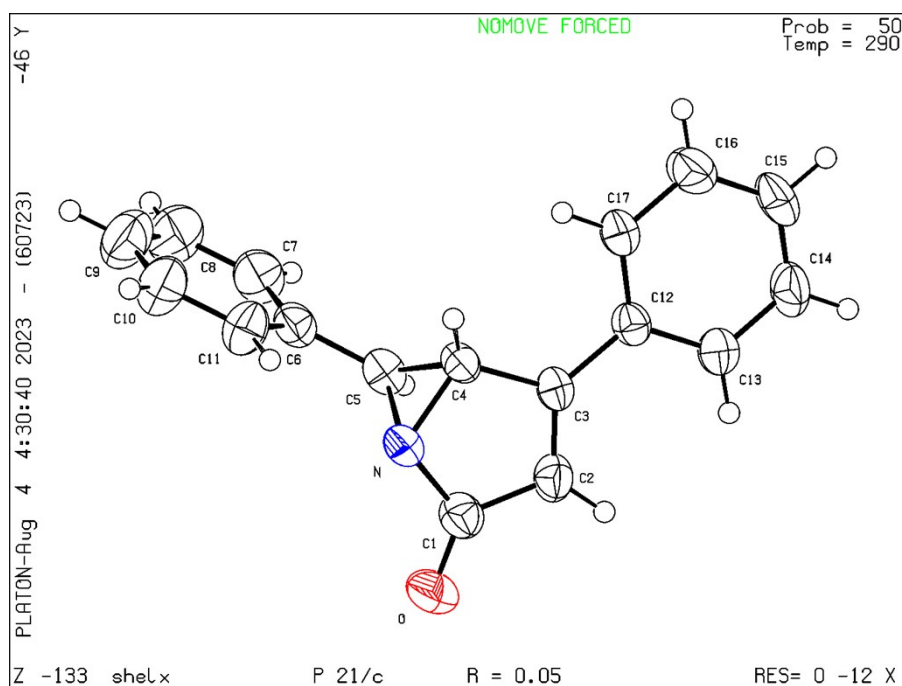


Fig. S85. X-ray crystallography of compound **4a**.