Supplementary Information

The first catalytic asymmetric cycloadditions of imines with an enolisable anhydride

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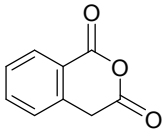
1. General

Proton Nuclear Magnetic Resonance spectra were recorded on Bruker DPX 400 MHz spectrometer in $CDCl_3$ referenced relative to residual $CHCl_3$ (δ = 7.26 ppm). Chemical shifts are reported in ppm and coupling constants in Hertz. Carbon NMR spectra were recorded on the same instruments (100 MHz) with total proton decoupling. All melting points are uncorrected. Infrared spectra were obtained using neat samples on a Perkin Elmer Spectrum 100 FT-IR spectrometer equipped with a universal ATR sampling accessory. Flash chromatography was carried out using silica gel, particle size 0.04-0.063 mm. TLC analysis was performed on precoated $60F_{254}$ slides, and visualised by either UV irradiation or $KMnO_4$ staining. Optical rotation measurements were made on a Rudolph Research Analytical Autopol IV instrument, and are quoted in units of 10^{-1} deg cm^2 g^{-1}. Analytical CSP-HPLC was performed using Daicel CHIRALCEL AD (4.6 mm x 25 cm), CHIRALCEL IA (4.6 mm x 25 cm) and CHIRALCEL OD-H (4.6 mm x 25 cm) columns. The data for the crystal structure of ***anti*-47** was collected on a Bruker Smart Apex2 CCD diffractometer. A suitable crystal was selected and mounted using inert oil on a 0.3mm MiTeGen loop and placed on the goniometer head in a 100K N_2 gas stream. The dataset was collected using Bruker APEX2 v2011.8-0 software. Data integrations, reductions and corrections for absorption and polarization effects were all performed using APEX2 v2011.8-0 software. Space group determination, structure solution and refinement were obtained using Bruker Shelxtl* Ver. 6.14 software. The structure was solved with Direct Methods using the SHELXTL program and refined against IF2I with the program XL from SHELX-97 using all data. Non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were placed into geometrically calculated positions and refined using a riding model. (*Software Reference Manual, version 5.625; Bruker Analytical X-Ray Systems Inc.: Madison, WI, 2001. Sheldrick, G. M. SHELXTL, An Integrated System for Data Collection, Processing, Structure Solution and Refinement; Bruker Analytical X-Ray Systems Inc., Madison, WI, 2001.) Unless otherwise stated, all chemicals were obtained from commercial sources and used as received. All reactions were carried out in oven-dried glassware with magnetic stirrers under an atmosphere of argon, unless specified. Anhydrous CH_2Cl_2 was obtained by using Pure Solv MD-4EN Solvent Purification System. Anhydrous MTBE was obtained by distillation over calcium hydride (CaH_2). Commercially available anhydrous ethanol (EtOH) was used.

2. Synthesis of homophthalic anhydride



Homophthalic anhydride (**4**) was synthesised according to the reported literature procedure.[1] The isolated compound exhibited identical spectroscopic data to those reported in the literature.[1]

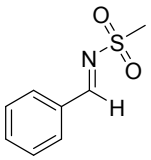
M.p. 140-144 °C (lit.,[2] m.p. 140-145 °C); δ_H (400 MHz, DMSO-d_6) 4.27 (s, 2H), 7.44 (d, *J* 7.8,1H), 7.52 (app. t, 1H), 7.75 (app. t, 1H), 8.05 (d, *J* 8.2, 1H).

3. Synthesis of imines

General procedure A for the synthesis of imines

An oven dried round bottomed flask was charged with methanesulfonamide (1 equiv.) fitted with a septum and placed under an atmosphere of argon. Dry CH_2Cl_2 was then added *via* syringe followed by NEt_3 (3 equiv.) and the appropriate aldehyde (1 equiv.). The resulting solution was cooled to 0 ºC. $TiCl_4$ (0.5 equiv.) was then added drop-wise to the solution at 0 ºC and it was allowed to stir for 1 h at this temperature. The reaction mixture was filtered through celite and washed with CH_2Cl_2. The filtrate was concentrated *in vacuo* and the resulting solid was suspended in toluene and then filtered to remove NEt_3.HCl. The filtrate was then concentrated *in vacuo* to afford the desired imine which was purified by recrystallisation.

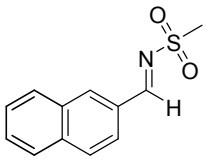
(*E*)-*N*-Benzylidenemethanesulfonamide (32)



Prepared according to general procedure **A** using methanesulfonamide (950.0 mg, 10 mmol), NEt_3 (4.2 mL, 30 mmol), benzaldehyde (1.2 mL, 10 mmol) in dry CH_2Cl_2 (25 mL) and $TiCl_4$ (547 µL, 5 mmol). The product was purified by recrystallization from CH_2Cl_2:hexane to afford **32** as an off-white solid (695 mg, 38%). NMR spectral data of **32** matches with the literature data.[3] M.p. 92-93 °C (lit.[4] 90-92 ºC).

δ_H (400 MHz, $CDCl_3$) 3.14 (s, 3H), 7.55 (t, *J* 7.4, 1H), 7.64-7.68 (m, 2H) 7.96 (d, *J* 7.4, 2H), 9.04 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 184.0430. $C_8H_{10}NO_2S$ requires 184.0432

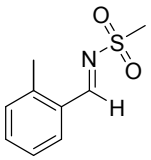
(*E*)-*N*-(Naphthalen-2-ylmethylene) methanesulfonamide (S1)



Prepared according to general procedure **A** using methanesulfonamide (950 mg, 10 mmol), NEt_3 (4.2 mL, 30 mmol), 2-naphthaldehyde (1.56 g, 10 mmol) and $TiCl_4$ (547 µL, 5 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S1** as a pale yellow solid (746 mg, 32%). NMR spectral data of **S1** matches with the literature data.[5] M.p. 120-122 ºC (lit.[5] 119-121 ºC).

δ_H (400 MHz, $CDCl_3$) 3.18 (s, 3H), 7.57-7.62 (m, 2H), 7.89-7.99 (m, 3H), 8.05-8.08 (m, 1H), 8.35 (app. d, 1H), 9.17 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 234.0590. $C_{12}H_{12}NO_2S$ requires 234.0589.

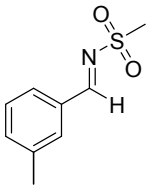
(*E*)-*N*-(2-Methylbenzylidene) methanesulfonamide (S2)



Prepared according to general procedure **A** using methanesulfonamide (951.2 mg, 10 mmol), NEt_3 (4.2 mL, 30 mmol), 2-methyl-benzaldehyde (1.1 mL, 10 mmol) and $TiCl_4$ (547 µL, 5 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S2** as a pale yellow solid (746 mg, 32%). NMR spectral data of **S2** matches with the literature data.[6]

δ_H (400 MHz, $CDCl_3$) 2.62 (s, 3H), 3.14 (s, 3H), 7.24-7.27 (m, 1H), 7.30-7.35 (m, 1H), 7.46-7.50 (m, 1H), 7.78-7.80 (m, 1H), 8.82 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 198.0594. $C_9H_{12}NO_2S$ requires 198.0589

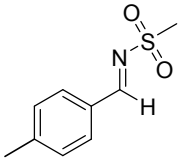
(*E*)-*N*-(3-Methylbenzylidene) methanesulfonamide (S3)



Prepared according to general procedure **A** using methanesulfonamide (806.7 mg, 8.5 mmol), NEt_3 (3.5 mL, 25.4 mmol), 3-methyl-benzaldehyde (1 mL, 8.5 mmol) and $TiCl_4$ (470 µL, 4.3 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by vacuum distillation to afford **S3** as a pale yellow oil (600 mg, 36%). NMR spectral data of **S3** matches with the literature data.[7]

δ_H (400 MHz, $CDCl_3$) 2.46 (s, 3H), 3.16 (s, 3H), 7.38-7.50 (m, 2H), 7.71-7.78 (m, 2H), 9.03 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 198.0595. $C_9H_{12}NO_2S$ requires 198.0589.

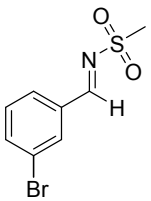
(*E*)-*N*-(4-Methylbenzylidene) methanesulfonamide (S4)



Prepared according to general procedure **A** using methanesulfonamide (806.7 mg, 8.5 mmol), NEt_3 (3.5 mL, 25.4 mmol), 4-methyl-benzaldehyde (1 mL, 8.5 mmol) and $TiCl_4$ (470 µL, 4.3 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S4** as a pale yellow solid (850 mg, 50%). NMR spectral data of **S4** matches with the literature data.[8]

δ_H (400 MHz, $CDCl_3$) 2.48 (s, 3H), 3.15 (s, 3H), 7.35 (d, *J* 7.9, 2H), 7.86 (d, *J* 7.9, 2H), 9.02 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 198.0580. $C_9H_{12}NO_2S$ requires 198.0589.

(*E*)-*N*-(3-Bromobenzylidene) methanesulfonamide (S5)

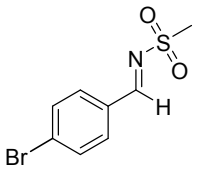


Prepared according to general procedure **A** using methanesulfonamide (815.7 mg, 8.6 mmol), NEt_3 (3.9 mL, 25.7 mmol), 3-bromo-benzaldehyde (1 mL, 8.6 mmol) and $TiCl_4$ (470 µL, 4.3 mmol) in

dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S5** as a white solid (625 mg, 39%). M.p. 95-97 °C.

δ_H (400 MHz, $CDCl_3$) 3.18 (s, 3H), 7.46 (t, *J* 7.9, 1H), 7.81 (d, *J* 7.9, 1H), 7.89 (d, *J* 7.9, 1H), 8.18 (s, 1H), 9.01 (s, 1H). δ_C (100 MHz, $CDCl_3$) 40.3, 123.4, 130.3, 130.8, 133.3, 133.9, 137.9, 170.1. ν_{max} (neat)/cm^{-1} 1606, 1430, 1302. *m/z* (ESI): $[M+H]^+$ found 261.9540. $C_8H_9NO_2SBr$ requires 261.9537.

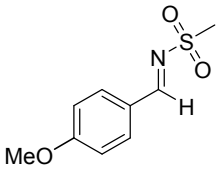
(*E*)-*N*-(4-Bromobenzylidene) methanesulfonamide (S6)



Prepared according to general procedure **A** using methanesulfonamide (950 mg, 10 mmol), NEt_3 (4.2 mL, 30 mmol), 4-bromobenzaldehyde (1.85 g, 10 mmol) and $TiCl_4$ (547 µL, 5 mmol) in dry CH_2Cl_2 (25 mL).The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S6** as a pale yellow solid (940 mg, 34%). NMR spectral data of **S6** matches with the literature data.[9]

δ_H (400 MHz, $CDCl_3$) 3.16 (s, 3H), 7.66 (d, *J* 7.4, 2H), 7.82 (d, *J* 7.4, 2H) 8.97 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 261.9530. $C_8H_9BrNO_2S$. Requires 261.9532.

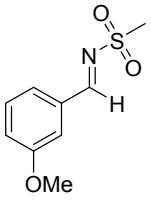
(*E*)-*N*-(4-Methoxybenzylidene) methanesulfonamide (S7)



Prepared according to general procedure **A** using methanesulfonamide (950 mg, 10 mmol), NEt_3 (4.2 mL, 30 mmol), 4-methoxybenzaldehyde (1.2 mL, 10 mmol) and $TiCl_4$ (547 µL, 5 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S7** as a pale yellow solid (852.0 mg, 40%). NMR spectral data of **S7** matches with the literature data.[6]

δ_H (400 MHz, $CDCl_3$) 3.09 (s, 3H), 3.89 (s, 3H), 7.00 (d, *J* 8.6, 2H), 7.90 (d, *J* 8.6, 2H), 8.91 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 214.0538. $C_9H_{12}NO_3S$ requires 214.0538.

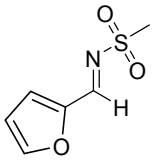
(*E*)-*N*-(3-Methoxybenzylidene) methanesulfonamide (S8)



Prepared according to general procedure **A** using methanesulfonamide (780.0 mg, 8.2 mmol), NEt_3 (3.4 mL, 25 mmol), *m*-anisaldehyde (1.0 mL, 8.2 mmol) and $TiCl_4$ (442 µL, 4.1 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S8** as a white solid (717 mg, 41%). Mp. 87-88 ºC (lit.[10] 88-90 ºC) NMR spectral data of **S8** matches with the literature data.[10]

δ_H (400 MHz, $CDCl_3$) 3.13 (s, 3H), 3.83 (s, 3H), 7.19 (ddd, *J* 1.2, 2.6, 8.1, 1H), 7.42 (app. t, 1H), 7.45-7.52 (m, 2H) 8.98 (s, 1H).

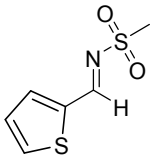
(*E*)-*N*-(Furan-2-ylmethylene) methanesulfonamide (S9)



Prepared according to general procedure **A** using methanesulfonamide (1.51 g, 12.1 mmol), NEt_3 (5.1 mL, 36.3 mmol), furfuraldehyde (1.0 mL, 12.1 mmol) and $TiCl_4$ (663 µL, 6.05 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S9** as a white solid (819 mg, 39%). Mp. 93-94 ºC.

δ_H (400 MHz, $CDCl_3$) 3.12 (s, 3H), 6.67 (dd, *J* 1.8, 3.6, 1H), 7.36 (d, *J* 3.6, 1H), 7.77-7.80 (m, 1H), 8.77 (s, 1H). δ_C (100MHz, $CDCl_3$) 40.5, 113.9, 125.2, 148.9, 150.0, 156.7. ν_{max} (neat)/cm^{-1} 3029, 2916, 1648, 1543, 1474, 1341, 1141, 1030, 964, 813. *m/z* (ESI): $[M+H]^+$ Found 174.0221 $C_6H_8NO_3S$ requires 174.0225.

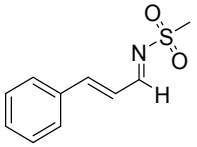
(*E*)-*N*-(Thiophen-2-ylmethylene) methanesulfonamide (S10)



Prepared according to general procedure **A** using methanesulfonamide (951.2 mg, 10 mmol), NEt_3 (4.2 mL, 30 mmol), 2-thiophenecarbaldehyde (930 μL, 10 mmol) and $TiCl_4$ (547 μL, 5 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S10** as a pale yellow solid (643 mg, 34%). NMR spectral data of **S10** matches with the literature data.[6]

δ_H (400 MHz, $CDCl_3$) 3.11 (s, 3H), 7.23-7.25 (m, 1H), 7.79 -7.83 (m, 2H), 9.08 (s, 1H). *m/z* (ESI): $[M+H]^+$ found 189.9998. $C_6H_8NO_2S_2$ requires 189.9996.

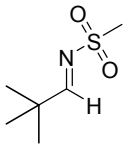
***N*-((1*E*,2*E*)-3-Phenylallylidene) methanesulfonamide (S11)**



Prepared according to general procedure **A** using methanesulfonamide (751.4 mg, 7.9 mmol), NEt_3 (3.3 mL, 23.7 mmol), cinammaldehyde (1 mL, 7.9 mmol) and $TiCl_4$ (433 μL, 4.0 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S11** as a pale yellow solid (700 mg, 42%). NMR spectral data of **S11** matches with the literature data.[11]

δ_H (400 MHz, $CDCl_3$) 3.11 (s, 3H), 7.03 (dd, *J* 9.5, 15.8, 1H), 7.46-7.63 (m, 6H), 8.79 (d, *J* 9.5, 1H). δ_C (100 MHz, $CDCl_3$) 40.3, 124.4, 128.8, 129.3, 131.8, 134.0, 154.5, 172.3. *m/z* (ESI): $[M+H]^+$ found 210.0582. $C_{10}H_{12}NO_2S$ requires 210.0589.

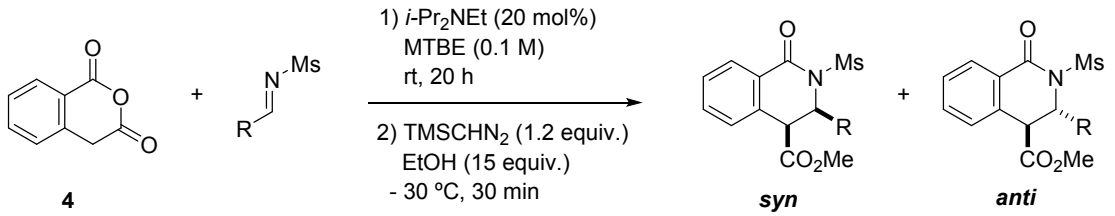
(*E*)-*N*-(2,2-Dimethylpropylidene) methanesulfonamide (S12)



Prepared according to general procedure **A** using methanesulfonamide (802 mg, 8.43 mmol), NEt_3 (3.9 mL, 27.6 mmol), pivalaldehyde (915 μL, 8.43 mmol) and $TiCl_4$ (799 μL, 4.21 mmol) in dry CH_2Cl_2 (25 mL). The product was purified by recrystallisation from CH_2Cl_2:hexane to afford **S12** as a brown solid (427 mg, 31%). Mp. 67-68 ºC.

δ_H (400 MHz, $CDCl_3$) 1.56 (s, 9H), 3.02 (s, 3H), 8.45 (s, 1H). δ_C (100MHz, $CDCl_3$) 25.9, 38.0, 40.0, 185.6. ν_{max} (neat)/cm^{-1} 2972, 1632, 1301, 114, 963, 804, 784. *m/z* (ESI): $[M+H]^+$ Found 164.0739 $C_6H_{14}NO_2S$ requires 164.0745.

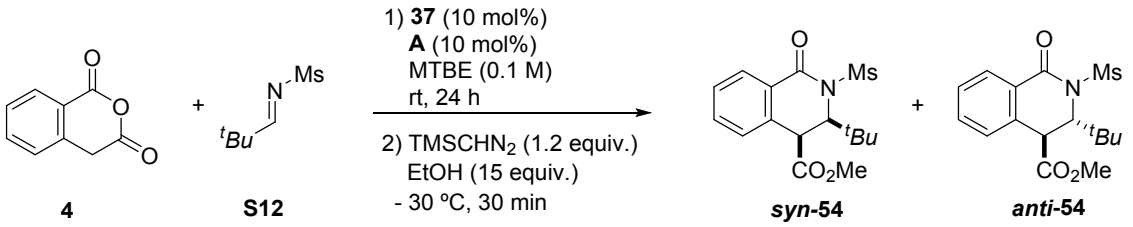
4. General procedure B: general protocol for the preparation of racemic lactams by annulation reactions between anhydride 4 and imines



An oven dried 10 mL round-bottomed flask containing a stirring bar under argon atmosphere was charged with the appropriate imine (0.25 mmol) and anhydrous MTBE (2.5 mL, 0.1 M). Anhydride **4** (39.9 mg, 0.25 mmol) was then added to the reaction followed by *N*,*N*-diisopropylethylamine (4.3 µL, 0.02 mmol, 10 mol%) and the resulting mixture was stirred for 24 h at room temperature. The reaction mixture containing the corresponding carboxylic acids was placed at -30 ºC and anhydrous EtOH (220.0 µL), followed by trimethylsilyldiazomethane (2.0 M solution in diethyl ether, 150.0 µL, 0.30 mmol) were added *via* syringe and the reaction was allowed to stir for exactly 30 min at -30 ºC. The solvent was then removed *in vacuo* at room temperature and the crude mixture of diastereomeric esters was purified immediately by flash chromatography to isolate the racemic diastereomers.

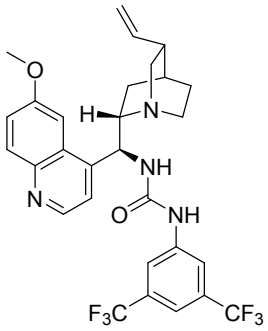
Attempts to synthesise rac-***syn*-54** using general procedure **B** were unsuccessful. As such, rac-***syn*-54** was obtained using the following procedure:

Rac-*syn*-54



An oven dried 10 mL round-bottomed flask containing a stirring bar under argon atmosphere was charged with the appropriate imine (0.25 mmol) and anhydrous MTBE (2.5 mL, 0.1 M). Anhydride **4** (39.9 mg, 0.25 mmol) was then added to the reaction followed by equal amounts of catalyst **37**[12] (10 mol%) and its pseudoenantiomer catalyst **A**[12] (10 mol %) and the resulting mixture was stirred for 24 h at room temperature. The reaction mixture containing the corresponding carboxylic acids was placed at -30 ºC and anhydrous EtOH (220.0 µL), followed by trimethylsilyldiazomethane (2.0 M solution in diethyl ether, 150.0 µL, 0.30 mmol) were added *via* syringe and the reaction was allowed to stir for exactly 30 min at -30 ºC. The solvent was then removed *in vacuo* at room

temperature and the crude mixture of diastereomeric esters was purified immediately by flash chromatography to isolate the racemic diastereomers.



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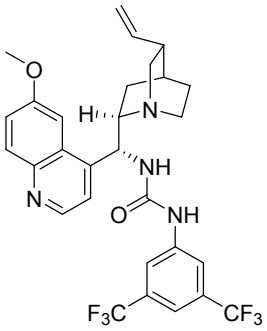
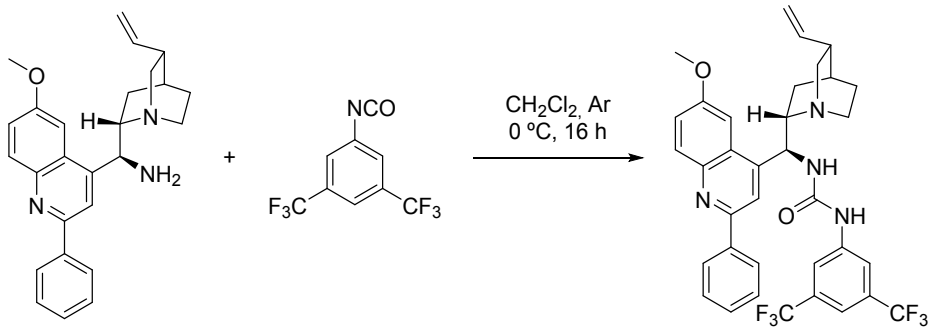


A

5. Synthesis of catalyst 30



B **C** **30**

A round-bottomed flask containing a stirring bar under argon atmosphere was charged with **B**[13] (1 g, 2.5 mmol) followed by dry CH_2Cl_2 (20 mL) and the reaction mixture was cooled in an icebath. 3,5-*bis*-(Trifluoromethyl)phenyl isocyanate (**C**) (520 µL, 3.00 mmol) was added *via* syringe and the reaction was stirred at 0 ºC to room temperature for 16 h. The solvent was removed *in vacuo* and the crude residue was purified by flash chromatography (CH_2Cl_2:MeOH 95:5) to yield **30** as a white solid (1.2 g, 73%), M.p. 152-153 °C. $[\alpha]_D^{20}$= +14.8 (*c* 0.6 $CHCl_3$).

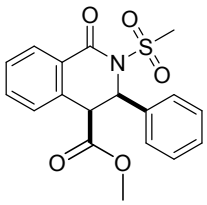
δ_H (400 MHz, $CDCl_3$) 1.06-1.09 (m, 1H), 1.70-1.79 (m, 4H), 2.33 (m, 1H), 2.50-2.52 (m, 1H), 2.73-2.75 (m, 1H), 3.08 (br t, 1H), 3.54-3.68 (m, 2H), 4.05 (s, 3H), 4.88-4.93 (m, 2H), 5.51-5.60 (m, 1H), 5.78 (br s, 1H), 6.75 (m, 1H), 7.02 (s, 1H), 7.36-7.56 (m, 4H), 7.75-7.90 (m, 4H), 8.15-8.19 (m, 3H), 8.37 (br s, 1H). δ_C (100 MHz,$CDCl_3$) 26.1, 26.7, 29.6, 37.4, 41.2, 49.6, 54.8, 55.8, 60.2, 101.5, 115.3, 115.4, 116.7, 117.8, 121.7, 123.3 (q, CF_3 $J_{C\text{-}F}$ 272.9), 127.2, 127.3, 128.8, 129.2, 131.7 (q, $J_{C\text{-}F}$ 33), 132.2, 139.1, 139.2, 140.8, 143.7, 145.0, 154.6, 154.7, 158.4. δ_F NMR (376.5 MHz, $CDCl_3$) -63.09 *m/z* (ESI): $[M+H]^+$ found 655.2498. $C_{35}H_{33}N_4O_2F_6$ requires 655.2508.

6. General procedure C: asymmetric cycloaddition reaction of imines with homophthalic anhydride (4) (Table 2 and Scheme 3)

Note: it is important to adhere to the procedure precisely to obtain reproducible results from a stereocontrol standpoint. This is especially true of the esterification protocol.

An oven dried 10 mL reaction vessel containing a stirring bar was charged with anhydride **4** (39.9 mg, 0.25 mmol) then placed under an argon atmosphere. Anhydrous MTBE (2.5 mL) was added *via* syringe and the reaction mixture was then cooled to -30 °C. The appropriate imine (0.25 mmol) was added followed by catalyst **30** (0.01 mmol, 5 mol%) and the reaction was stirred at -30 °C until completion. The conversion of the reaction was determined by ^{1}H NMR spectroscopic analysis using *p*-iodoanisole (28.8 mg, 0.12 mmol) as an internal standard. To the reaction mixture containing the diastereomeric mixture of carboxylic acid lactam products, anhydrous EtOH (220 μL), followed by trimethylsilyldiazomethane (2.0 M solution in diethyl ether, 150 μL, 0.30 mmol) were added *via* syringe and the reaction was allowed to stir for exactly 30 min at -30 ºC. The solvent was then removed *in vacuo* at room temperature and the crude mixture of diastereomeric esters was purified immediately by column chromatography.

syn-Methyl 2-(methylsulfonyl)-1-oxo-3-phenyl-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-33)

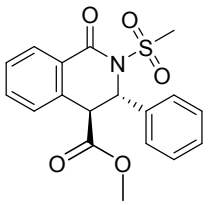


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **32** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 48 h to give a diastereomeric mixture of carboxylic acids in a 64:36 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-33** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (24 mg, 27 %, 27 % *ee*). M.p. 156-158 °C. $[\alpha]^{20}_D$ = -34.0 (c 0.05, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 70/30, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 8.9 min (major enantiomer) and 10.1 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.07 (s, 3H), 3.67 (s, 3H), 4.88 (d, *J* 6.2, 1H), 6.07 (d, *J* 6.2, 1H), 7.01 (d, *J* 7.2, 2H), 7.17-7.27 (m, 3H), 7.49-7.62 (m, 3H), 8.30 (d, *J* 7.9, 1H). δ_C (100 MHz, $CDCl_3$) 42.1, 48.9, 52.3, 59.8, 127.4, 127.5, 128.3, 128.6, 128.8, 129.1, 129.2, 133.5, 134.4, 135.5, 163.6, 168.7. ν_{max} (neat)/cm^{-1} 3019, 2924, 1732, 1060, 1599, 1499, 1340, 1235, 1155, 1027, 967, 767, 692. *m/z* (ESI): $[M+H]^+$ found 360.0896. $C_{18}H_{18}NO_5S$ requires 360.0900.

anti-Methyl 2-(methylsulfonyl)-1-oxo-3-phenyl-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-33)

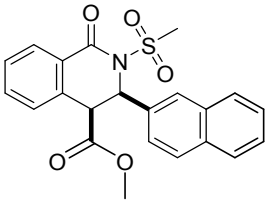


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **32** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 48 h to give a diastereomeric mixture of carboxylic acids in a 64:36 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-33** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (42 mg, 47 %, 70 % ee). M.p. 130-135 °C. $[\alpha]^{20}_D$ = 15.3 (c 0.15, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 70/30, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 18.2 min (major enantiomer) and 30.1 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.45 (s, 3H) 3.74 (app. s, 3H), 4.12 (app. s, 1H), 6.22 (s, 1H), 7.14-7.25 (m, 6H), 7.45-7.51 (m, 2H), 8.18 (d, *J* 7.9, 1H). δ_C (100 MHz, $CDCl_3$) 41.8, 50.7, 53.0, 59.0, 125.9, 128.0, 128.1, 128.8, 128.9, 129.0, 129.4, 133.0, 134.1, 138.0, 163.6, 170.4. ν_{max} (neat)/cm^{-1} 3011, 2931, 1736, 1682, 1602, 1458, 1320, 1245, 1158, 1010, 959, 839, 718. *m/z* (ESI): $[M+H]^+$ found 360.0908. $C_{18}H_{18}NO_5S$ requires 360.0900.

syn-Methyl 2-(methylsulfonyl)-3-naphthalen-2-yl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-43)

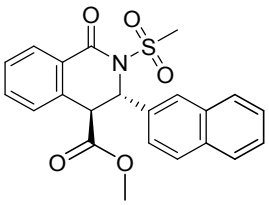


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S1** (57.4 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 72 h to give a diastereomeric mixture of carboxylic acids in a 65:35 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-43** was purified by column chromatography eluting with 70/30 hexane/EtOAc and was isolated as a colourless oil (30 mg, 34%, 6% ee). $[\alpha]^{20}_{D}$ = -1.2 (c = 0.20, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 60/40, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 10.0 min (minor enantiomer) and 14.5 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.06 (s, 3H), 3.64 (s, 3H), 4.96 (d, *J* 6.5, 1H), 6.25 (d, *J* 6.5, 1H), 7.03-7.06 (m, 1H), 7.45-7.43 (m, 2H), 7.52-7.58 (m, 3H), 7.61-7.69 (m, 3H), 7.72-7.74 (m, 1H), 8.35 (d, *J* 7.7, 1H). δ_C (100 MHz, $CDCl_3$) 42.2, 49.0, 53.3, 60.0, 124.2, 126.6, 126.8, 127.4, 127.6, 127.7, 128.1, 128.4, 128.6, 128.9, 129.1, 132.8, 132.9, 133.2, 133.6, 134.5, 163.6, 168.7. ν_{max} (neat)/cm^{-1} 3018, 2980, 1728, 1672, 1563, 1448, 1350, 1250, 1050, 955, 816, 731, 688. *m/z* (ESI): $[M+H]^+$ found 410.1064. $C_{22}H_{20}NO_5S$ requires 410.1057.

anti-Methyl 2-(methylsulfonyl)-3-naphthalen-2-yl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-43)

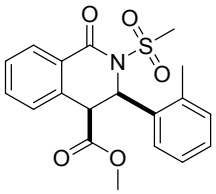


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S1** (57.4 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 72 h to give a diastereomeric mixture of carboxylic acids in a 65:35 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-43** was purified by column chromatography eluting with 70/30 hexane/EtOAc and was isolated as a colourless oil (51 mg, 55%, 63% *ee*). $[\alpha]^{20}_{D}$ = 40.6 (c = 0.33, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 60/40, 0.30 mL min^{-1}, RT, UV detection at 254 nm, retention times: 74.8 min (major enantiomer) and 80.6 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.48 (s, 3H), 3.76 (s, 3H), 4.24 (app. s, 1H), 6.38 (app. s, 1H), 7.18-7.27 (m, 2H), 7.41-7.46 (m, 4H), 7.61 (s, 1H), 7.69-7.74 (m, 3H), 8.19-8.21 (m, 1H). δ_C (100 MHz, $CDCl_3$) 41.8, 50.6, 50.2, 53.0, 59.2, 123.3, 125.3, 126.5, 127.4, 128.0, 128.1, 128.9, 129.0, 129.1, 129.4, 132.7, 132.9, 133.0, 134.1, 135.4, 163.7, 170.4. ν_{max} (neat)/cm^{-1} 3022, 2950, 1735, 1685, 1599, 1435, 1335, 1250, 1160, 1030, 935, 816, 731, 661. *m/z* (ESI): $[M+H]^+$ found 410.1064. $C_{22}H_{20}NO_5S$ requires 410.1057.

syn-Methyl-2-(methylsulfonyl)-1-oxo-3-(o-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-44)

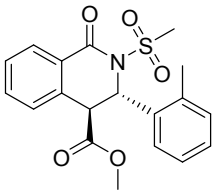


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S2** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 180 h to give a diastereomeric mixture of carboxylic acids in a 53:47 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-44** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (33 mg, 36 %, 25 % *ee*). M.p. 175-178 °C. $[\alpha]^{20}_D$ = 9.3 (c 0.14, acetone).

CSP-HPLC analysis, Chiralcel ODH (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 26.6 min (major enantiomer) and 42.0 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 2.40 (s, 3H), 2.99 (s, 3H), 3.63 (s, 3H), 4.93 (d, *J* 6.8, 1H), 6.36 (d, *J* 6.8, 1H), 6.83-6.91 (m, 2H), 7.12-7.28 (m, 3H), 7.48-7.59 (m, 2H), 8.33 (d, *J* 7.7, 1H). δ_C (100 MHz, $CDCl_3$) 18.9, 41.9, 49.4, 52.2, 54.8, 126.3, 126.5, 127.3, 128.3, 128.4, 128.8, 128.9, 131.1, 133.6, 134.0, 134.4, 136.5, 163.7, 169.1. ν_{max} (neat)/cm^{-1} 3010, 2914, 2863, 1721, 1682, 1604, 1457, 1348, 1214, 1156, 1063, 962, 778. *m/z* (ESI): $[M+H]^+$ found 374.1059. $C_{19}H_{20}NO_5S$ requires 374.1057.

***anti*-Methyl-2-(methylsulfonyl)-1-oxo-3-(o-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-44)**

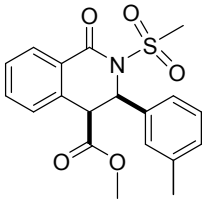


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S2** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 180 h to give a diastereomeric mixture of carboxylic acids in a 53:47 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-44** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a colourless oil (39 mg, 42 %, 33 % ee). $[\alpha]^{20}_{D}$ = -3.2 (c 0.05, acetone).

CSP-HPLC analysis, Chiralcel ODH (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 21.30 min (major enantiomer) and 30.9 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$): 2,22 (s, 3H), 3.42 (s, 3H), 3.72 (s, 3H), 4.11 (app. s, 1H), 6.18 (app. s, 1H), 6.99-7.00 (m, 4H), 7.20-7.22 (m, 1H), 7.41-7.51 (m, 2H), 8.15 (d, *J* 7.8, 1H). δ_C (100 MHz, $CDCl_3$): 19.1, 41.9, 49.2, 53.1, 56.2, 125.3, 126.3, 128.0, 128.1, 128.7, 129.0, 129.7, 131.3, 132.6, 134.0, 134.2, 135.9, 164.0, 170.4. ν_{max} (neat)/cm^{-1} 2925, 2863, 1732, 1680, 1604, 1457, 1348, 1214, 1156, 1061, 962, 766. *m/z* (ESI) $[M+H]^+$ found 374.1059. $C_{19}H_{20}NO_5S$ requires 373.1062.

***syn*-Methyl 2-(methylsulfonyl)-1-oxo-3-(*m*-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-45)**



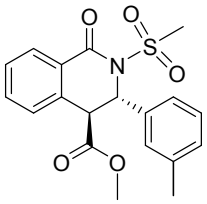
Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S3** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 144 h to give a diastereomeric mixture of carboxylic acids in a 59:41 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-45** was purified by

column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (28 mg, 31%, 36% *ee*). M.p. 117-120°C. $[\alpha]^{20}_D$ = 2.3 (c 0.15, acetone).

CSP-HPLC analysis, Chiralcel ODH (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 24.6 min (minor enantiomer) and 33.7 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 2.20 (s, 3H), 3.08 (s, 3H), 3.68 (s, 3H), 4.86 (d, *J* 6.3, 1H), 6.02, (d, *J* 6.3, 1H), 6.75-6.81 (m, 2H), 7.04-7.05 (m, 2H), 7.47-7.63 (m, 3H), 8.29 (dd, *J* 1.0, 7.7, 1H). δ_C (100 MHz, $CDCl_3$) 21.4, 42.2, 49.0, 52.2, 59.9, 124.3, 127.4, 128.3, 128.4, 128.6, 128.7, 129.0, 129.9, 133.6, 134.4, 135.4, 138.4, 163.7, 168.8. ν_{max} (neat)/cm^{-1} 1746, 1181, 1354, 1158. *m/z* (ESI): $[M+H]^+$ found 374.1059. $C_{19}H_{20}NO_5S$ requires 374.1057.

anti-Methyl 2-(methylsulfonyl)-1-oxo-3-(*m*-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-45)

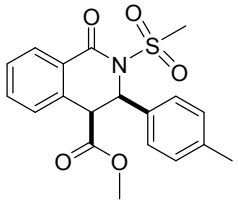


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S3** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 144 h to give a diastereomeric mixture of carboxylic acids in a 59:41 ratio (*syn*:*anti*). After esterification, the diastereomer ***anti*-45** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (44 mg, 48%, 70% *ee*). M.p. 157-160°C. $[\alpha]^{20}_D$ = 14.1 (c 0.27, acetone).

CSP-HPLC analysis, Chiralcel ODH (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 28.2 min (minor enantiomer) and 31.3 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 2.23 (s, 3H), 3.44 (s, 3H), 3.73 (s, 3H), 4.11 (d, *J* 1.4, 1H), 6.16, (d, *J* 1.4, 1H), 6.88-7.10 (m, 4H), 7.20-7.22 (m, 1H), 7.42-7.51 (m, 2H), 8.15 (dd, *J* 1.2, 7.5, 1H). δ_C (100 MHz, $CDCl_3$) 21.4, 41.8, 50.8, 53.0, 59.1, 122.8, 126.7, 128.0, 128.8, 128.8, 129.0, 129.0, 129.5, 133.0, 134.1, 138.0, 138.7, 163.7, 170.5. ν_{max} (neat)/cm^{-1} 1736, 1682, 1343, 1161. *m/z* (ESI): $[M+H]^+$ found 374.1062. $C_{19}H_{20}NO_5S$ requires 374.1057.

***syn*-Methyl 2-(methylsulfonyl)-1-oxo-3-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-46)**

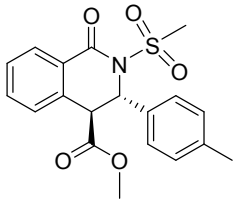


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S4** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 180 h to give a diastereomeric mixture of carboxylic acids in a 53:47 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-46** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (37 mg, 40%, 34% *ee*). M.p. 140-142°C. $[\alpha]^{20}_{D} = 50$ (c = 0.07, acetone).

CSP-HPLC analysis, Chiralcel ODH (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 23.0 min (minor enantiomer) and 33.7 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 2.23 (s, 3H), 3.07 (s, 3H), 3.68 (s, 3H), 4.85 (d, *J* 6.3, 1H), 6.03, (d, *J* 6.3, 1H), 6.87-6.99 (m, 4H), 7.48-7.63 (m, 3H), 8.29 (dd, *J* 1.1, 7.8, 1H). δ_C (100 MHz, $CDCl_3$) 21.1, 42.1, 49.0, 52.3, 59.7, 127.4, 127.4, 128.3, 128.6, 129.0, 129.5, 132.5, 133.7, 134.4, 139.1, 163.7, 168.8. ν_{max} (neat)/cm^{-1} 1747, 1682, 1341, 1160. *m/z* (ESI): $[M+H]^+$found 374.1062. $C_{19}H_{20}NO_5S$ requires 374.1057.

***anti*-Methyl 2-(methylsulfonyl)-1-oxo-3-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-46)**

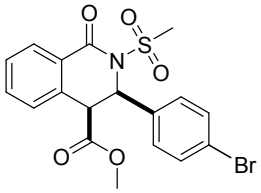


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S4** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 180 h to give a diastereomeric mixture of carboxylic acids in a 53:47 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-46** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (43 mg, 47%, 74% *ee*). M.p. 170-173°C. $[\alpha]^{20}_{D} = 36.0$ (c 0.20, acetone).

CSP-HPLC analysis, Chiralcel ODH (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 29.9 min (major enantiomer) and 33.6 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 2.22 (s, 3H), 3.42 (s, 3H), 3.73 (s, 3H), 4.09 (d, *J* 1.5, 1H), 6.17, (d, *J* 1.5, 1H), 7.02 (app. s, 4H), 7.20-7.21 (m, 1H), 7.41-7.50 (m, 2H), 8.15 (dd, *J* 1.5, 7.6, 1H). δ_C (100 MHz, $CDCl_3$) 20.9, 41.8, 50.8, 53.0, 58.9, 125.8, 128.1, 128.9, 129.0, 129.5, 129.6, 133.1, 134.1, 135.1, 138.0, 163.7, 170.4. ν_{max} (neat)/cm^{-1} 1735, 1682, 1341, 1160. *m/z* (ESI): $[M+H]^+$ found 374.1068. $C_{19}H_{20}NO_5S$ requires 374.1057.

syn-Methyl 3-(4-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-47)

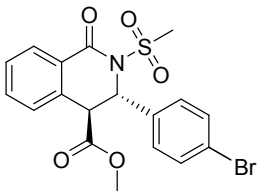


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S5** (64.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 17 h to give a diastereomeric mixture of carboxylic acids in a 66:34 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-47** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a colourless oil (28 mg, 30 %, 4 % *ee*). $[\alpha]^{20}_D$ = 14.3 (c 0.14, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 70/30, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 10.4 min (minor enantiomer) and 13.1 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.14 (s, 3H), 3.70 (s, 3H), 4.86 (d, *J* 6.2, 1H), 6.03 (d, *J* 6.2, 1H), 6.87-6.90 (m, 2H), 7.31-7.33 (m, 2H), 7.50-7.65 (m, 3H), 8.28 (d, *J* 7.4, 1H). δ_C (100 MHz, $CDCl_3$) 42.4, 48.7, 52.4, 59.0, 123.4, 127.2, 127.6, 128.5, 128.6, 129.3, 129.3, 133.2, 134.6, 134.7, 163.3, 168.5. ν_{max} (neat)/cm^{-1} 3320, 3232, 2948, 1736, 1685, 1589, 1437, 1365, 1254, 1176, 1024, 964, 836, 715. *m/z* (ESI): $[M+H]^+$ found 438.0018. $C_{18}H_{17}NO_5SBr$ requires 438.0005.

anti-Methyl 3-(4-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-47)

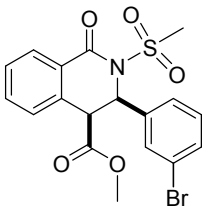


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S5** (64.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 17 h to give a diastereomeric mixture of carboxylic acids in a 66:34 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-47** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (60 mg, 55 %, 61 % *ee*). M.p. 178-181 °C. $[\alpha]^{20}_{D}$ = 29.4 (c 0.35, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 70/30, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 32.7 min (major enantiomer) and 37.4 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.46 (s, 3H), 3.73 (s, 3H), 4.07 (app. s, 1H), 6.15 (app. s, 1H), 7.03 (d, *J* 8.2, 2H), 7.22 (d, *J* 7.2, 1H), 7.36 (d, *J* 8.2, 2H), 7.42-7.53 (m, 2H), 8.15 (d, *J* 7.7, 1H). δ_C (100 MHz, $CDCl_3$) 46.1, 54.7, 57.4, 62.8, 126.5, 131.9, 132.2, 132.3, 133.5, 133.7, 136.3, 136.9, 138.5, 141.5, 167.7, 174.4. ν_{max} (neat)/cm^{-1} 3334, 3258, 2954, 1734, 1682, 1601, 1435, 1346, 1245, 1157, 1024, 964, 816, 735. *m/z* (ESI): $[M+H]^+$ found 438.0014. $C_{18}H_{17}NO_5SBr$ requires 438.0011.

syn-Methyl 3-(3-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-48)

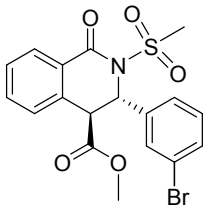


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S6** (64.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 17 h to give a diastereomeric mixture of carboxylic acids in a 61:39 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-48** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (28 mg, 26%, 3% *ee*). M.p. 157-160°C. $[\alpha]^{20}_{D}$ = 78.0 (c 0.10, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 20.2 min (major enantiomer) and 23.4 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.16 (s, 3H), 3.71 (s, 3H), 4.85 (d, *J* 6.2, 1H), 6.02, (d, *J* 6.2, 1H), 6.89-6.91 (m, 1H), 7.05 (t, *J* 7.9, 1H), 7.18 (m, 1H), 7.37-7.65 (m, 4H), 8.28 (m, 1H). δ_C (100 MHz, $CDCl_3$) 42.5, 48.8, 52.5, 59.0, 122.7, 125.7, 127.2, 128.5, 128.6, 129.2, 130.4, 131.0, 132.3, 133.2, 134.6, 137.9, 163.4, 168.5. ν_{max} (neat)/cm^{-1} 1746, 1682, 1456, 1350, 1158. *m/z* (ESI): $[M+H]^+$ found 438.0007. $C_{18}H_{17}NO_5SBr$ requires 438.0005.

anti-Methyl 3-(3-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-48)

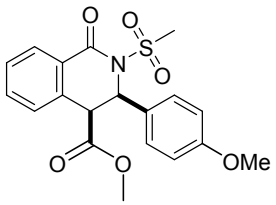


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S6** (64.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 17 h to give a diastereomeric mixture of carboxylic acids in a 61:39 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-48** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (55 mg, 51%, 69% *ee*). M.p. 180-182°C. $[\alpha]^{20}_D$ = 18.5 (c 0.13, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 43.7 min (major enantiomer) and 53.3 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.47 (s, 3H), 3.73 (s, 3H), 4.08 (d, *J* 1.4, 1H), 6.16, (d, *J* 1.4, 1H), 7.04-7.10 (m, 2H), 7.22-7.24 (m, 2H), 7.32-7.34 (m, 2H) 7.44-7.54 (m, 2H), 8.15 (dd, *J* 1.3, 7.6, 1H). δ_C (100 MHz, $CDCl_3$) 41.9, 50.5, 53.1, 58.4, 123.0, 124.5, 127.9, 129.0, 129.1, 129.3, 129.5, 130.5, 131.4, 132.6, 134.3, 140.5, 163.4, 170.1. ν_{max} (neat)/cm^{-1} 1735, 1682, 1341, 1160. *m/z* (ESI): $[M+H]^+$ found 438.0005. $C_{18}H_{17}NO_5SBr$ requires 438.0011.

syn-Methyl 3-(4-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-49)

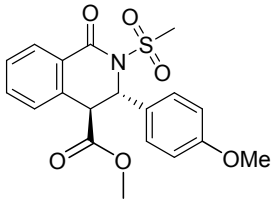


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S7** (48.9 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 168 h to give a diastereomeric mixture of carboxylic acids in a 56:44 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-49** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a colourless oil (20 mg, 26%, 35% *ee*). $[\alpha]^{20}_{D}$ = 21.9 (c = 0.19, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 60/40, 1 mL min-1, RT, UV detection at 254 nm, retention times: 8.5 min (minor enantiomer) and 9.6 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.06 (s, 3H), 3.68 (s, 3H), 3.70 (s, 3H), 4.85 (d, *J* 6.6, 1H), 6.03 (d, *J* 6.6, 1H), 6.69 (d, *J* 7.6, 2H), 6.94 (d, *J* 7.6, 2H), 7.50 (app. t, 1H), 7.56-7.62 (m, 2H), 8.29 (dd, *J* 1.7, 7.8, 1H). δ_C (100 MHz, $CDCl_3$) 42.1, 48.9, 52.3, 55.1, 59.4, 114.1, 127.3, 127.5, 128.3, 128.7, 128.9, 129.0, 133.7, 134.4, 159.9, 163.6, 168.8. ν_{max} (neat)/cm^{-1} 2961, 2918, 1735, 1678, 1604, 1459, 1320, 1254, 1176, 1063, 962, 767. *m/z* (ESI): $[M+H]^+$ found 390.1009. $C_{19}H_{20}NO_6S$ requires 390.1006.

anti-Methyl 3-(4-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-49)

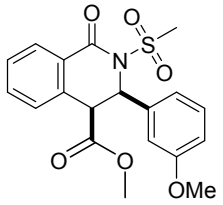


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S7** (48.9 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 168 h to give a diastereomeric mixture of carboxylic acids in a 56:44 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-49** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a colourless oil (36 mg, 38%, 66% *ee*). $[\alpha]^{20}_{D}$ = 24.2 (c = 0.32, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 60/40, 1 mL min-1, RT, UV detection at 254 nm, retention times: 21.3 min (major enantiomer) and 30.3 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.41 (s, 3H), 3.70 (s, 3H), 3.72 (s, 3H), 4.08 (app. s, 1H), 6.16 (app. s, 1H), 6.74 (d, *J* 7.8, 2H), 7.05 (d, *J* 7.8, 2H), 7.22-7.23 (m, 1H), 7.43-7.52 (m, 2H), 8.16 (d, *J* 8.0, 1H). δ_C (100 MHz, $CDCl_3$) 41.8, 50.7, 53.0, 55.1, 58.6, 114.2, 127.2, 127.5, 128.9, 129.0, 129.4, 130.1, 133.2, 134.1, 159.3, 163.6, 170.4. ν_{max} (neat)/cm^{-1} 2984, 2956, 1733, 1688, 1604, 1499, 1350, 1254, 1166, 1039, 962, 769. *m/z* (ESI): $[M+H]^+$ found 390.1009. $C_{19}H_{20}NO_6S$ requires 390.1006.

syn-Methyl 3-(3-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-50)

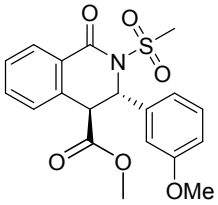


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S8** (48.9 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 60 h to give a diastereomeric mixture of carboxylic acids in a 60:40 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-50** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a white solid (19 mg, 21%, 23% *ee*). Mp. 125-127 ºC. $[\alpha]^{20}_D = 11.5$ (c = 0.20, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 80/20, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 12.8 min (major enantiomer) and 14.3 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.10 (s, 3H), 3.61 (s, 3H), 3.69 (s, 3H), 4.85 (d, *J* 6.2, 1H), 6.03 (d, *J* 6.2, 1H), 6.52 (app. t, 1H), 6.57 (d, *J* 7.7 1H), 6.76 (dd, *J* 2.3, 8.2, 1H), 7.09 (app. t, 1H), 7.46-7.52 (m, 1H), 7.56-7.64 (m, 2H), 8.28 (d, *J* 7.4, 1H). δ_C (100 MHz, $CDCl_3$) 42.2, 48.9, 52.3, 55.0, 59.7, 113.6, 114.2, 119.7, 127.4, 128.3, 128.6, 129.0, 129.9, 133.6, 134.4, 137.0, 159.5, 163.6, 168.7. ν_{max} (neat)/cm^{-1} 3063, 2951, 1740, 1678, 1601, 1458, 1345, 1320, 1249, 1151, 1117, 970, 766, 696. *m/z* (ESI): $[M+H]^+$ Found 390.1010 $C_{19}H_{20}NO_6S$ requires 390.1006.

anti-Methyl 3-(3-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-50)

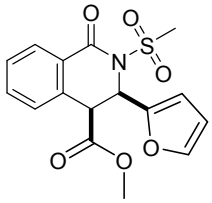


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S8** (48.9 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 60 h to give a diastereomeric mixture of carboxylic acids in a 60:40 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-50** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a white solid (60 mg, 62%, 65% *ee*). Mp. 140-142 ºC. $[\alpha]^{20}_{D}$ = 6.0 (c = 0.20, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 80/20, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 25.6 min (major enantiomer) and 32.0 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.43 (s, 3H), 3.67 (s, 3H), 3.72 (s, 3H), 4.12 (app. s, 1H), 6.17 (app. s, 1H), 6.65-6.74 (m, 3H), 7.12 (app. t, 1H), 7.21 (d, *J* 7.3, 1H), 7.39-7.52 (m, 2H), 8.14 (dd, *J* 1.3, 7.5, 1H) . δ_C (100 MHz, $CDCl_3$) 41.8, 50.6, 53.0, 55.1, 59.0, 111.9, 113.5, 118.1, 128.0, 128.8, 129.0, 129.4, 130.0, 133.1, 134.1, 139.7, 159.9, 163.6, 170.3. ν_{max} (neat)/cm^{-1} 3059, 2949, 1736, 1677, 1600, 1458, 1341, 1248, 1152, 1117, 971, 767, 735. *m/z* (ESI): $[M+H]^+$ Found 390.1010 $C_{19}H_{20}NO_6S$ requires 390.1006.

syn-Methyl 3-(furan-2-yl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-51)

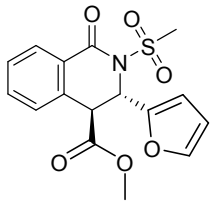


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S9** (42.6 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 48 h to give a diastereomeric mixture of carboxylic acids in a 41:59 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-51** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a pale yellow oil (45 mg, 50%, 88% *ee*). $[\alpha]^{20}_{D}$ = 50.0 (c = 0.20, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 95/5, 1 mL min-1, RT, UV detection at 254 nm, retention times: 33.7 min (major enantiomer) and 37.9 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.20 (s, 3H), 3.77 (s, 3H), 4.75 (d, *J* 5.5, 1H), 6.04 (d, *J* 3.3, 1H), 6.15 (d, *J* 5.5, 1H), 6.17 (dd, *J* 1.5, 3.3, 1H), 7.18 (d, *J* 1.5, 1H), 7.46 (app. t., 1H), 7.57-7.68 (m, 2H), 8.20 (dd, *J* 0.8, 7.7 1H). δ_C (100 MHz, $CDCl_3$) 41.8, 47.8, 52.6, 53.7, 109.8, 110.3, 127.4, 127.8, 128.2, 129.2, 134.0, 134.2, 143.2, 149.0, 163.7, 168.6. ν_{max} (neat)/cm^{-1} 3052, 2953, 1742, 1685, 1602, 1457, 1348, 1316, 1159, 964, 735. *m/z* (ESI): $[M+H]^+$ Found 350.0688 $C_{16}H_{16}NO_6S$ requires 350.0693.

anti-Methyl 3-(furan-2-yl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-51)

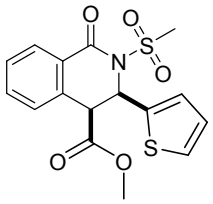


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S9** (42.6 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 48 h to give a diastereomeric mixture of carboxylic acids in a 41:59 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-51** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a white solid (39 mg, 46%, 76% *ee*). Mp. 154-155 ºC. $[\alpha]^{20}_D$ = 48.0 (c 0.12, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 85/15, 1 mL min-1, RT, UV detection at 254 nm, retention times: 20.5 min (major enantiomer) and 30.1 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.45 (s, 3H), 3.73 (s, 3H), 4.31 (d, *J* 1.4, 1H), 6.10 (d, *J* 3.1, 1H), 6.16 (dd, *J* 1.4, 3.1, 1H), 6.23 (s, 1H), 7.21 (s, 1H), 7.35 (d, *J* 7.5, 1H), 7.43 (app. t., 1H), 7.55 (app. t, 1H), 8.09 (d, *J* 7.5, 1H). δ_C (100 MHz, $CDCl_3$) 41.8, 47.2, 53.1, 53.6, 108.6, 110.5, 127.5, 128.9, 129.1, 129.3, 133.7, 134.1, 142.7, 150.8, 163.0, 169.7. ν_{max} (neat)/cm^{-1} 3055, 2950, 1735, 1678, 1600, 1458, 1344, 1250, 1152, 972, 766, 737. *m/z* (ESI): $[M+H]^+$ Found 350.0700 $C_{16}H_{16}NO_6S$ requires 350.0693.

***syn*-Methyl-2-(methylsulfonyl)-1-oxo-3-(thiophen-2-yl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-52)**

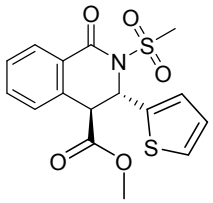


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S10** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 264 h to give a diastereomeric mixture of carboxylic acids in a 63:35 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn-52*** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a colourless oil (21 mg, 23 %, 50 % *ee*). $[\alpha]^{20}_{D}$ = 34.0 (c 0.10, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 95/5, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 6.4 min (major enantiomer) and 12.0 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.07 (s, 3H), 3.74 (s, 3H), 4.83 (d, *J* 5.6, 1H), 6.40 (d, *J* 5.6, 1H), 6.81-6.84 (m, 1H), 6.91-6.92 (m, 1H), 7.08-7.09 (m, 1H), 7.53 (app. t, 1H), 7.65-7.68 (m, 1H), 7.72-7.74 (m, 1H), 8.26 (d, *J* 8.0, 1H). δ_C (100 MHz, $CDCl_3$) 41.9, 48.9, 52.5, 56.1, 126.2, 126.8, 127.5, 128.6, 128.7, 128.8, 129.4, 133.6, 134.5, 137.4, 163.2, 168.3. *m/z* (ESI): $[M+H]^+$ found 366.0473. $C_{16}H_{16}NO_5S_2$ requires 366.0464.

***anti*-Methyl-2-(methylsulfonyl)-1-oxo-3-(thiophen-2-yl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-52)**

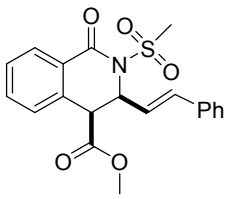


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S10** (48.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 264 h to give a diastereomeric mixture of carboxylic acids in a 63:35 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti-52*** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (40 mg, 40 %, 51 % *ee*). M.p. 106-109 °C. $[\alpha]^{20}_{D}$ = 70.0 (c 0.24, acetone).

CSP-HPLC analysis, Chiralcel AD (4.6 mm x 25 cm), hexane/IPA: 95/5, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 42.3 min (major enantiomer) and 48.1 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.36 (s, 3H), 3.74 (s, 3H), 4.21 (app. s, 1H), 6.49 (app. s, 1H), 6.8-6.84 (m, 1H), 6.98 (d, *J* 3.6, 1H), 7.08 (dd, *J* 0.8, 5.2, 1H), 7.39 (d, *J* 7.6, 1H), 7.49-7.53 (m, 1H), 7.58-7.62 (m, 1H), 8.15 (d, *J* 8.1, 1H). δ_C (100 MHz, $CDCl_3$) 46.1, 54.5, 57.3, 59.6, 129.9, 130.9, 131.4, 132.0, 133.4, 133.5, 134.1, 137.8, 138.5, 145.1, 167.0, 173.8. ν_{max} (neat)/cm^{-1} 3232, 2961, 2918, 1735, 1678, 1604, 1459, 1320, 1254, 1176, 1063, 962, 767. *m/z* (ESI): $[M+H]^+$ found 366.0467. $C_{16}H_{16}NO_5S_2$ requires 366.0464.

syn-Methyl 2-(methylsulfonyl)-1-oxo-3-((*E*)-styryl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-53)

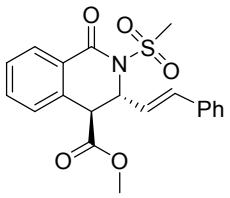


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S11** (51.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 72 h to give a diastereomeric mixture of carboxylic acids in a 17:81 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-53** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a white solid (62 mg, 65%, 35% ee). M.p. 140-143°C. $[\alpha]^{20}_D$ = 44.4 (c 0.27, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 19.2 min (minor enantiomer) and 23.8 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.36 (s, 3H), 3.80 (s, 3H), 4.65 (d, *J* 5.0, 1H), 5.63 (dd, *J* 5.0, 9.0, 1H), 6.04, (dd, *J* 9.0, 15.7, 1H), 6.70 (d, *J* 15.7, 1H), 7.23-7.24 (m, 5H), 7.46-7.65 (m, 3H), 8.21 (dd, *J* 1.1, 7.8, 1H). δ_C (100 MHz, $CDCl_3$) 42.7, 48.8, 52.6, 59.0, 121.7, 126.8, 127.1, 128.3, 128.3, 128.6, 128.7, 129.5, 134.1, 134.4, 135.2, 136.4, 163.3, 169.1. ν_{max} (neat)/cm^{-1} 1735, 1685, 1342, 1159. *m/z* (ESI): $[M+H]^+$ found 386.1064. $C_{20}H_{20}NO_5S$ requires 386.1057

***anti*-Methyl 2-(methylsulfonyl)-1-oxo-3-((*E*)-styryl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-53)**

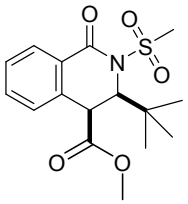


Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S11** (51.5 mg, 0.25 mmol) and catalyst **30** (8.2 mg, 0.01 mmol, 5 mol%). The reaction was stirred at -30 °C for 72 h to give a diastereomeric mixture of carboxylic acids in a 17:81 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-53** was purified by column chromatography eluting with 70/30 hexane/EtOAc. The product was isolated as a colourless oil (11 mg, 12%, 79% *ee*). $[\alpha]^{20}_{D}$ = -9.8 (c 0.05, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min^{-1}, RT, UV detection at 254 nm, retention times: 57.2 min (minor enantiomer) and 75.7 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 3.44 (s, 3H), 3.71 (s, 3H), 3.97 (d, *J* 1.8, 1H), 5.76 (m, 1H), 5.99 (dd, *J* 7.0, 15.7), 6.71 (dd, *J* 1.8, 15.7, 1H) 7.22-7.24 (m, 5H), 7.36 (app. d, 1H), 7.45-7.58 (m, 2H), 8.14 (dd, *J* 1.1, 7.7, 1H). δ_C (100 MHz, $CDCl_3$) 42.0, 48.8, 53.0, 58.1, 124.6, 126.7, 127.8, 128.4, 128.5, 129.0, 129.2, 129.5, 133.5, 134.1, 134.4, 135.3, 163.1, 170.0. ν_{max} (neat)/cm^{-1} 1695, 1666, 1327, 1139. *m/z* (ESI): $[M+H]^+$ found 386.1068. $C_{20}H_{20}NO_5S$ requires 386.1057.

***syn*-Methyl 3-(*tert*-butyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-54)**



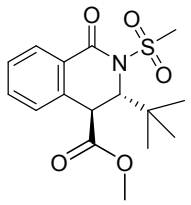
Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S12** (40.1 mg, 0.25 mmol) and catalyst **40** (16.4 mg, 0.02 mmol, 10 mol%). The reaction was stirred at room temperature for 120 h to give a diastereomeric mixture of carboxylic acids in a 61:39 ratio (*anti*:*syn*). After esterification, the diastereomer ***syn*-54** was

purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a colourless oil (25 mg, 29%, 66% *ee*). $[\alpha]^{20}_D = 47.1$ (c = 0.20, acetone).

CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min-1, RT, UV detection at 254 nm, retention times: 12.1 min (minor enantiomer) and 14.3 min (major enantiomer).

δ_H (400 MHz, $CDCl_3$) 0.81 (s, 9H), 3.54 (s, 3H), 3.83 (s, 3H), 4.53 (d, *J* 4.7, 1H), 5.06 (d, *J* 4.7, 1H), 7.41 (app. t., 1H), 7.56-7.63 (m, 1H), 8.05-8.12 (m, 2H). δ_C (100 MHz, $CDCl_3$) 28.8, 37.8, 43.1, 46.8, 52.0, 63.7, 126.9, 127.9, 128.5, 128.7, 134.2, 135.1, 164.8, 170.1. ν_{max} (neat)/cm^{-1} 3064, 2956, 1741, 1680, 1457, 1343, 1159, 965, 765. *m/z* (ESI): $[M+H]^+$ Found 340.1213 $C_{16}H_{22}NO_5S$ requires 340.1213.

anti-Methyl 3-(_tert_-butyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_anti_-54)



Prepared according to general procedure **C** using anhydride **4** (39.9 mg, 0.25 mmol), anhydrous MTBE (0.1 M, 2.5 mL), imine **S12** (40.1 mg, 0.25 mmol) and catalyst **30** (16.4 mg, 0.02 mmol, 10 mol%). The reaction was stirred at room temperature for 120 h to give a diastereomeric mixture of carboxylic acids in a 61:39 ratio (*anti*:*syn*). After esterification, the diastereomer ***anti*-54** was purified by column chromatography eluting with 70/30 hexane/EtOAc and isolated as a white solid (55mg, 65%, 46% *ee*). Mp. 153-155 ºC. $[\alpha]^{20}_D = 10.5$ (c = 0.20, acetone).

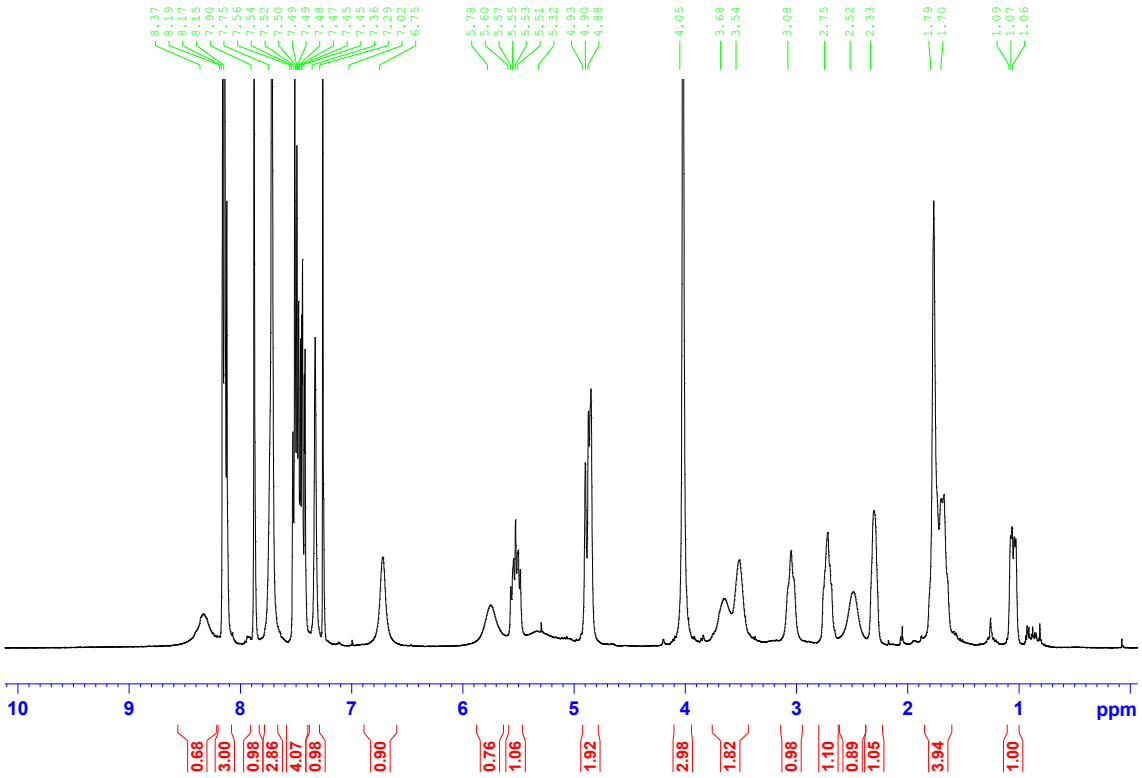
CSP-HPLC analysis, Chiralcel IA (4.6 mm x 25 cm), hexane/IPA: 90/10, 1 mL min-1, RT, UV detection at 254 nm, retention times: 17.6 min (major enantiomer) and 21.7 min (minor enantiomer).

δ_H (400 MHz, $CDCl_3$) 0.84 (s, 9H), 3.45 (s, 3H), 3.68 (s, 3H), 4.08 (d, *J* 1.1, 1H), 4.73 (d, *J* 1.1, 1H), 7.32 (d, *J* 7.5, 1H), 7.40-7.47 (m, 1H), 7.51-7.58 (m, 1H), 8.08 (dd, *J* 0.8, 7.5, 1H). δ_C (100 MHz, $CDCl_3$) 27.9, 36.7, 41.0, 44.2, 52.8, 64.0, 128.2, 128.7, 128.8, 128.8, 134.1, 135.0, 164.1, 171.5. ν_{max} (neat)/cm^{-1} 3060, 2972, 1732, 1685, 1465, 1340, 1249, 1157, 1027, 962, 768, 733. *m/z* (ESI): $[M+H]^+$ Found 340.1216 $C_{16}H_{22}NO_5S$ requires 340.1213.

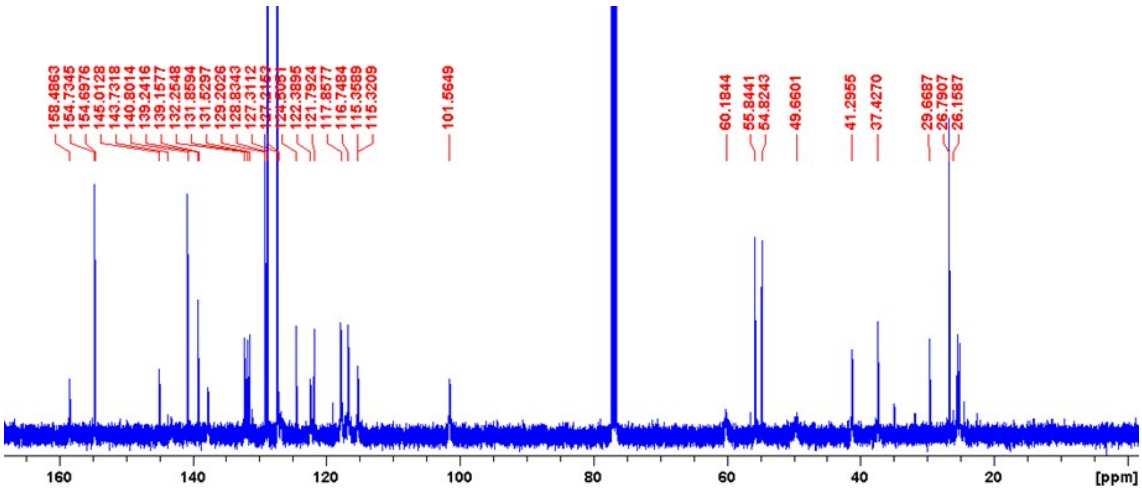
7. NMR spectra

1-(3,5-*bis*(trifluoromethyl)phenyl)-3-((1*S*)-(2-phenyl-6-methoxyquinolin-4-yl) ((2*S*) -5-vinylquinuclidin-2-yl)methyl)urea (cat 30)

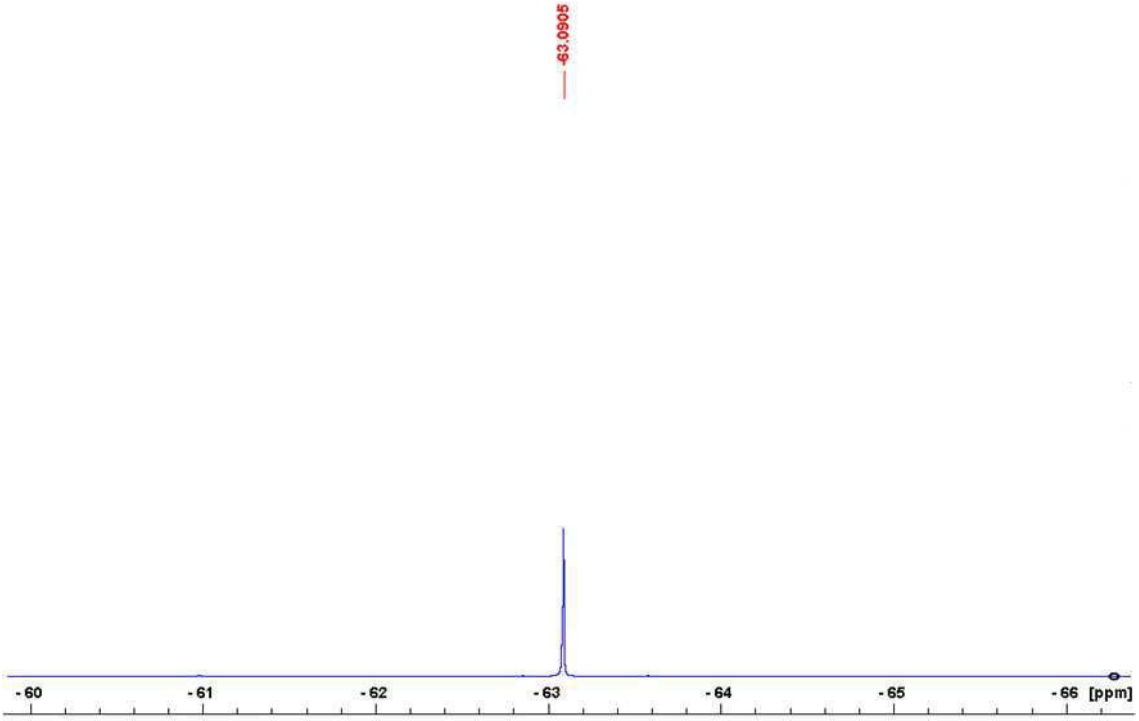
^{1}H NMR in $CDCl_3$ (400 MHz)



^{13}C NMR in $CDCl_3$ (100 MHz)

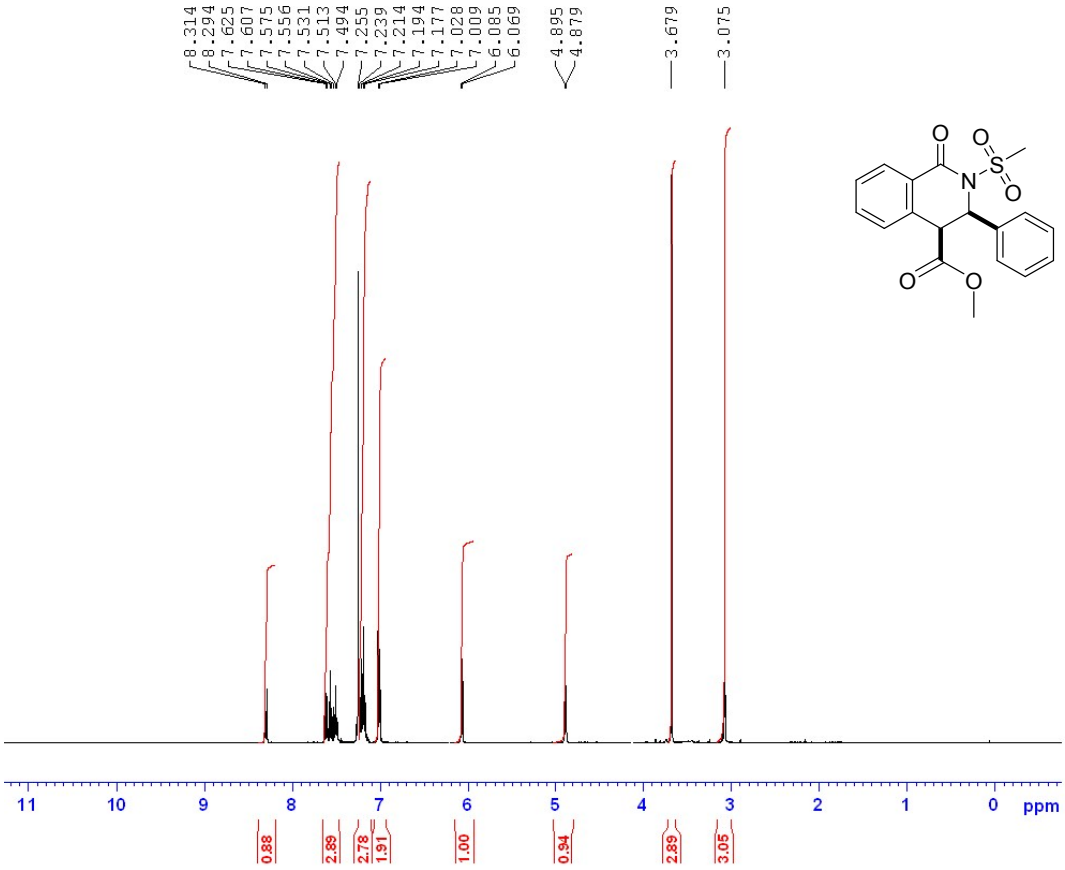


^{19}F NMR in $CDCl_3$ (376.5 MHz)

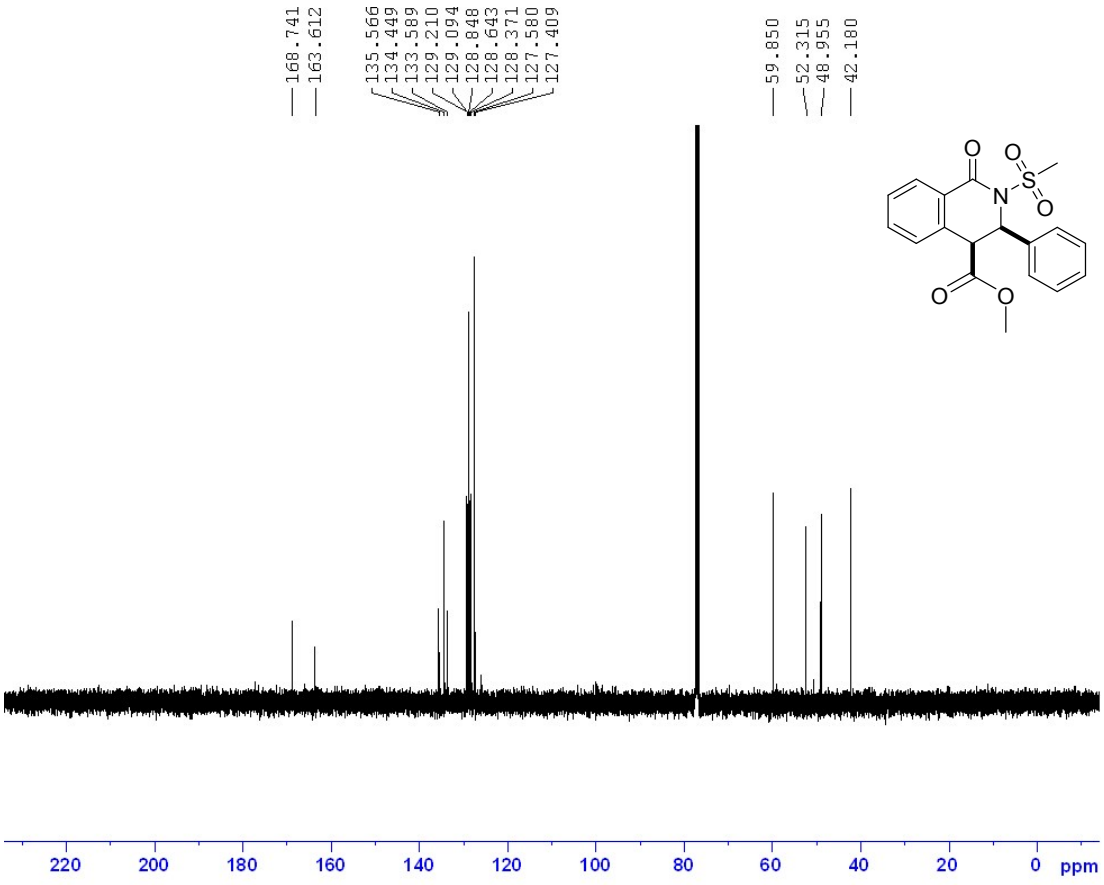


***syn*-Methyl 2-(methylsulfonyl)-1-oxo-3-phenyl-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-33)**

^{1}H NMR in $CDCl_3$ (400 MHz)

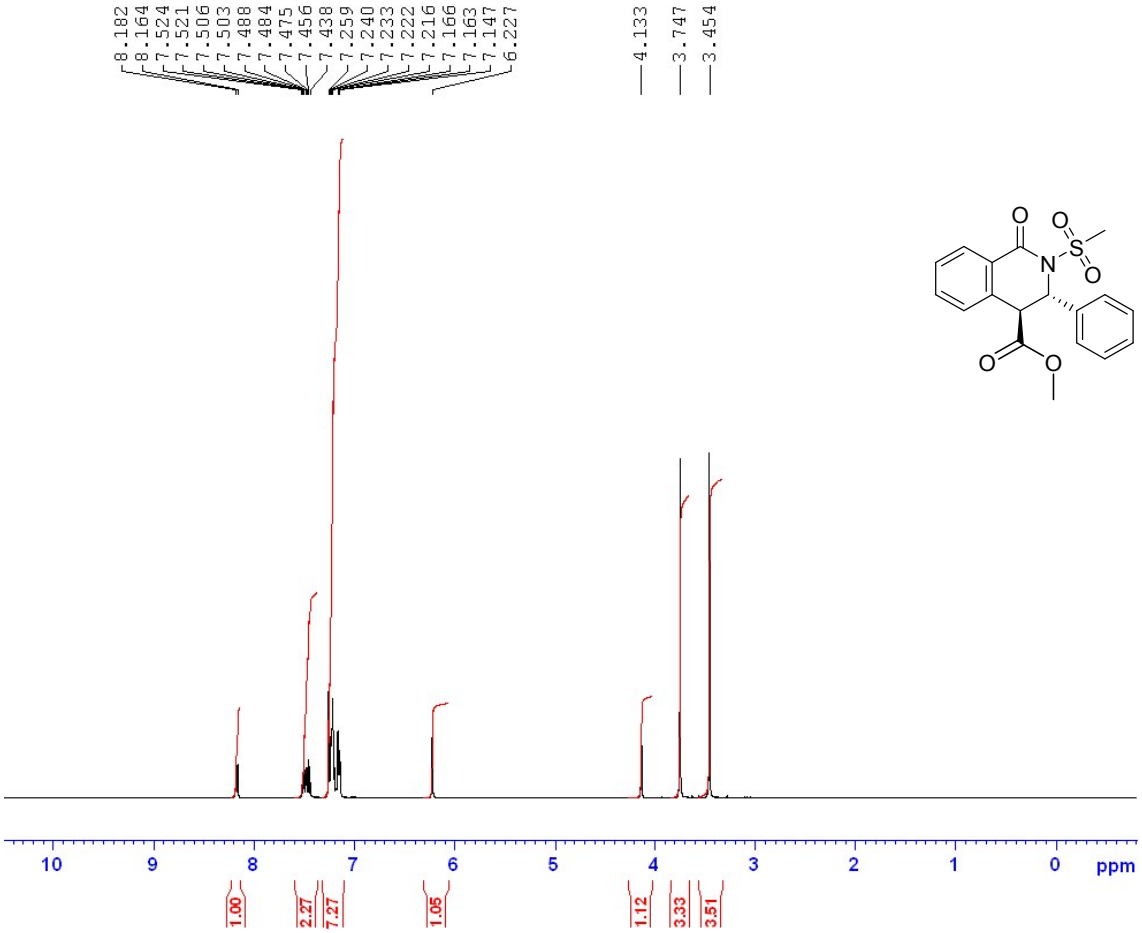


^{13}C NMR in $CDCl_3$ (100 MHz)

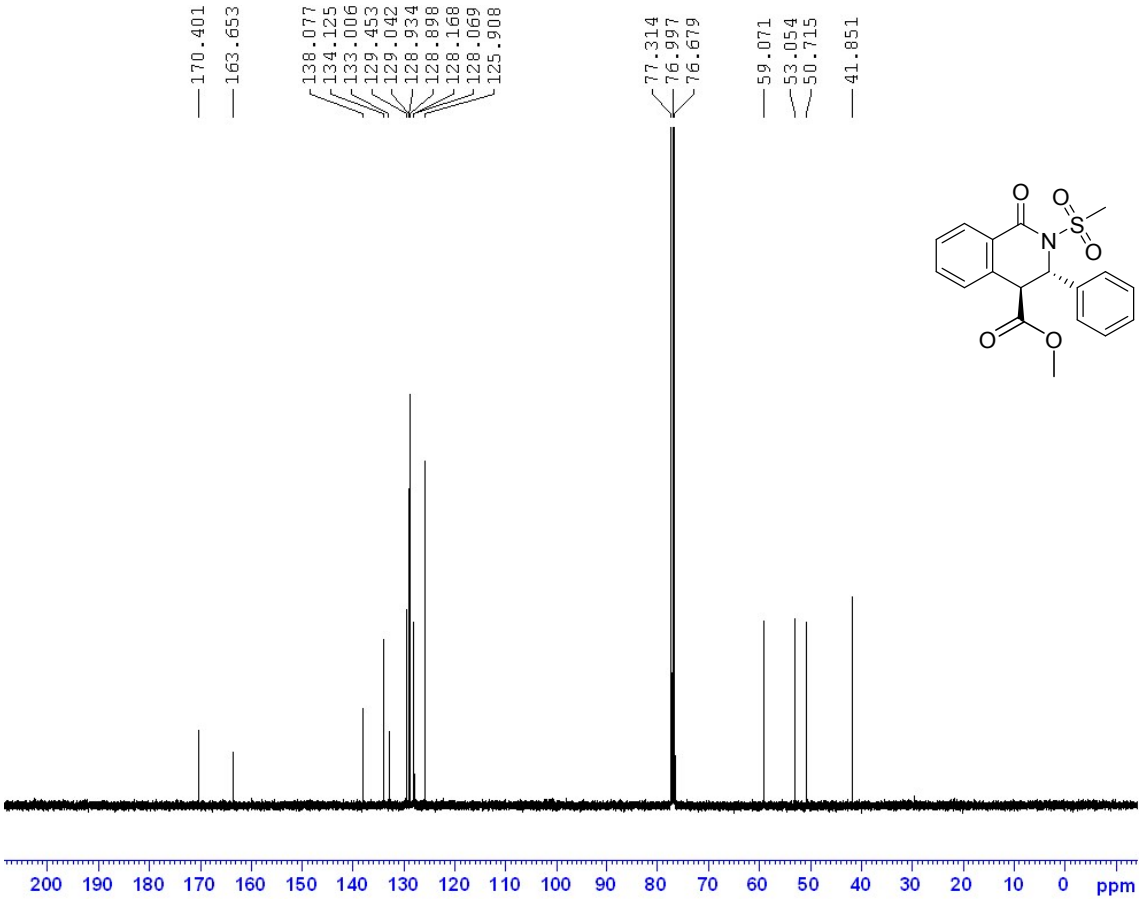


***anti*-Methyl 2-(methylsulfonyl)-1-oxo-3-phenyl-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-33)**

^{1}H NMR in $CDCl_3$ (400 MHz)

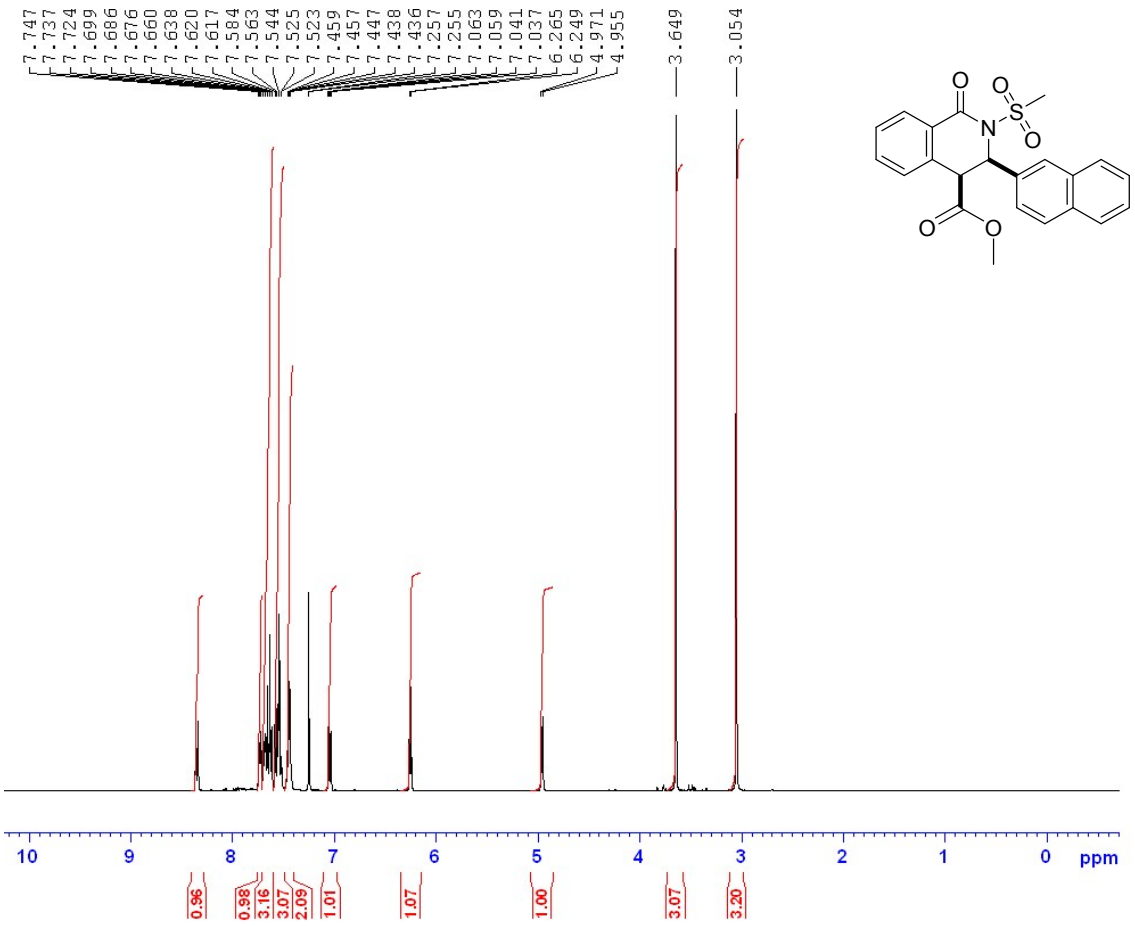


^{13}C NMR in $CDCl_3$ (100 MHz)

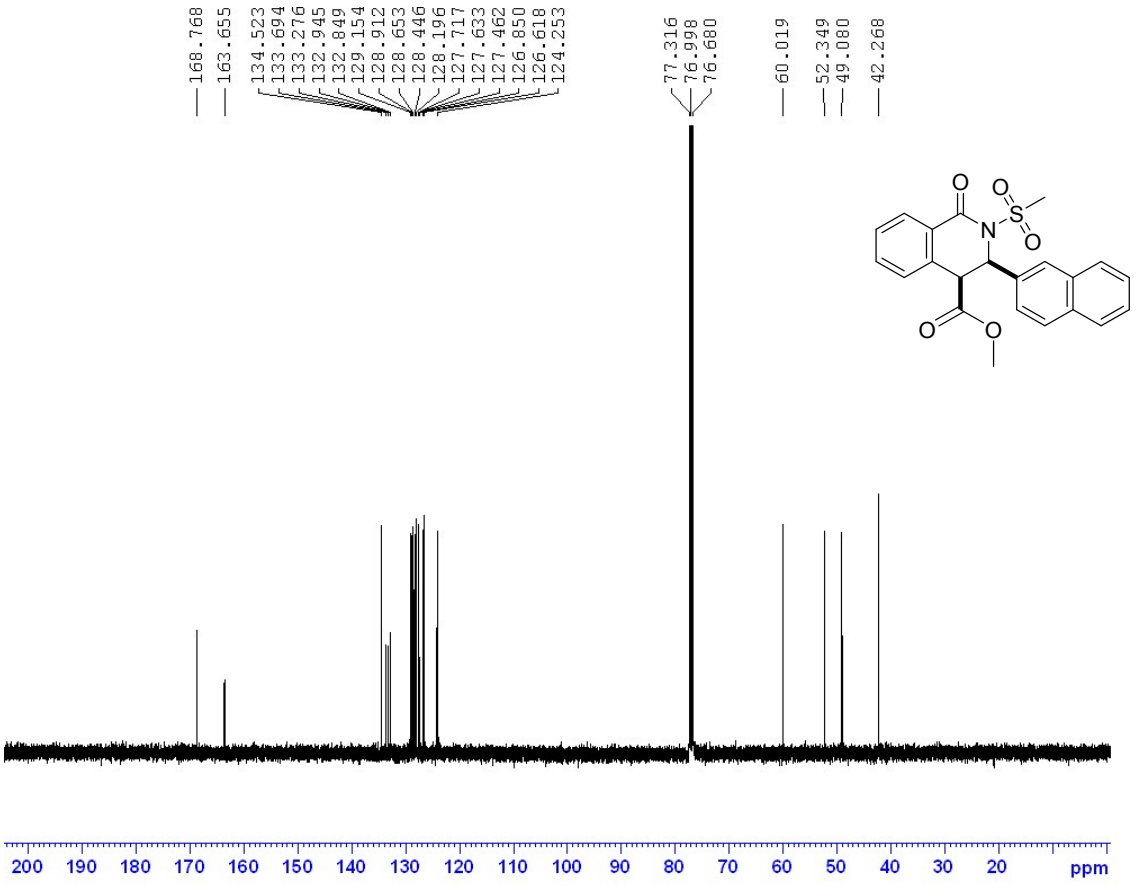


syn-Methyl 2-(methylsulfonyl)-3-naphthalen-2-yl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-43)

^{1}H NMR in $CDCl_3$ (400 MHz)

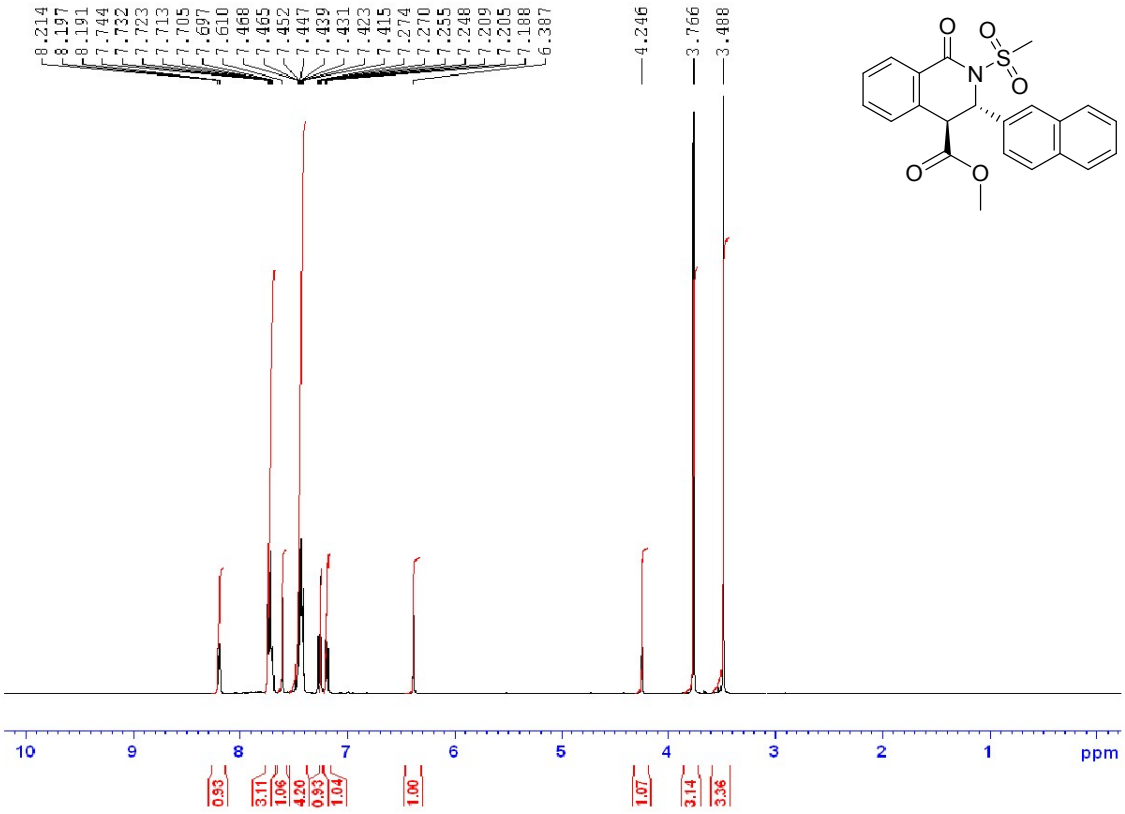


^{13}C NMR in $CDCl_3$ (100 MHz)

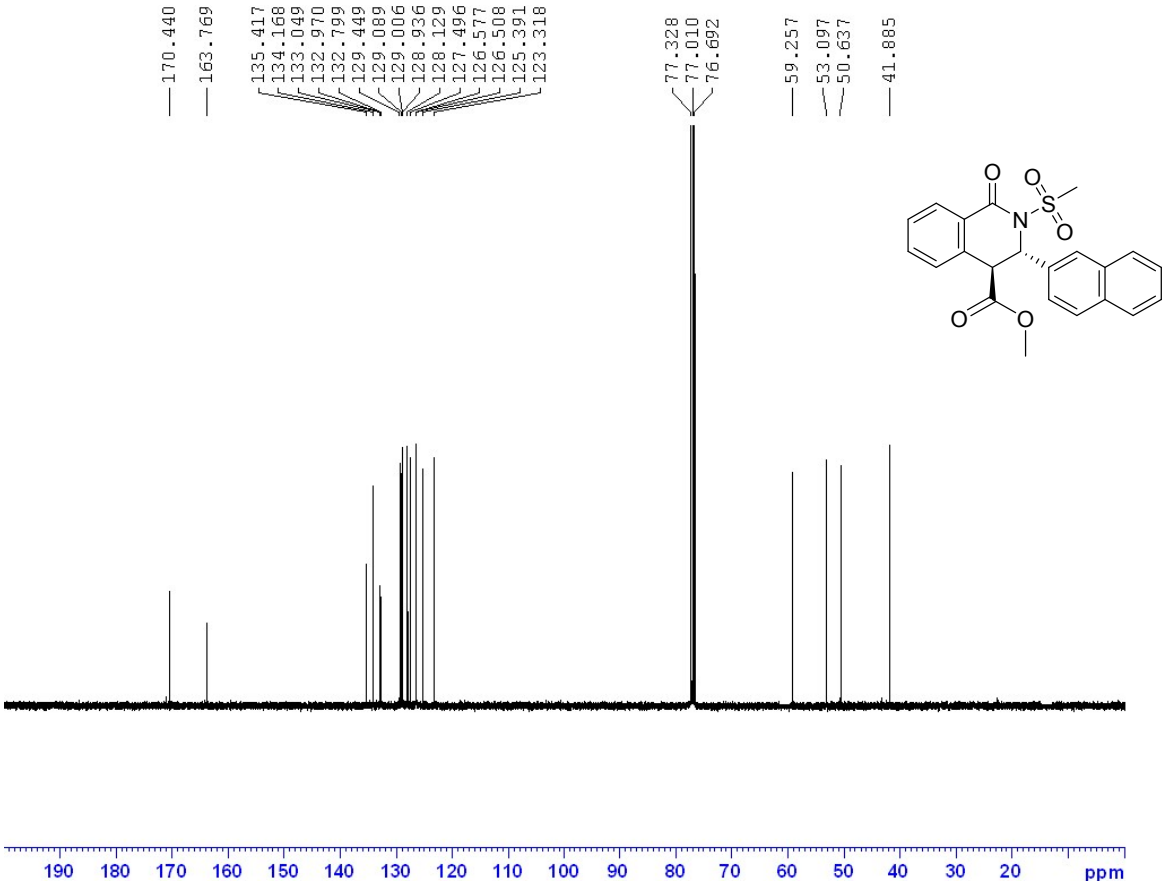


***anti*-Methyl 2-(methylsulfonyl)-3-naphthalen-2-yl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-43)**

^{1}H NMR in $CDCl_3$ (400 MHz)

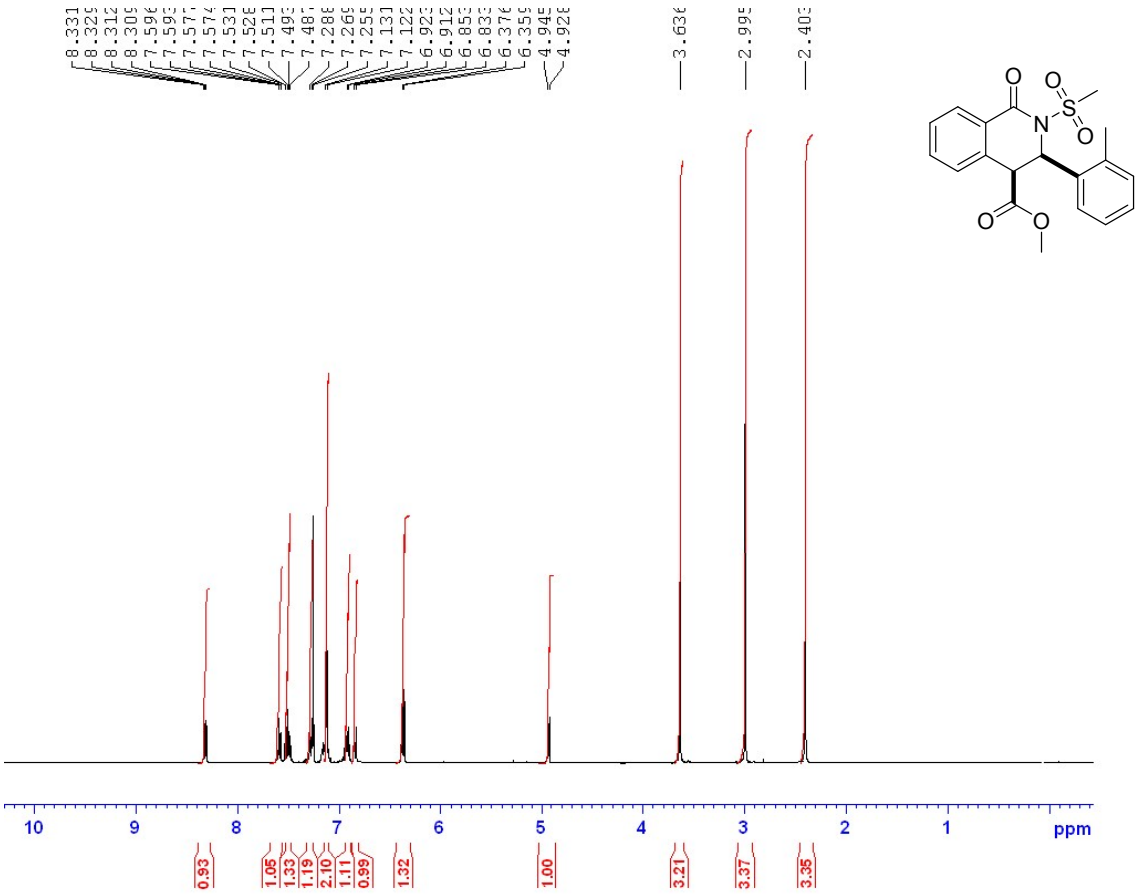


^{13}C NMR in $CDCl_3$ (100 MHz)

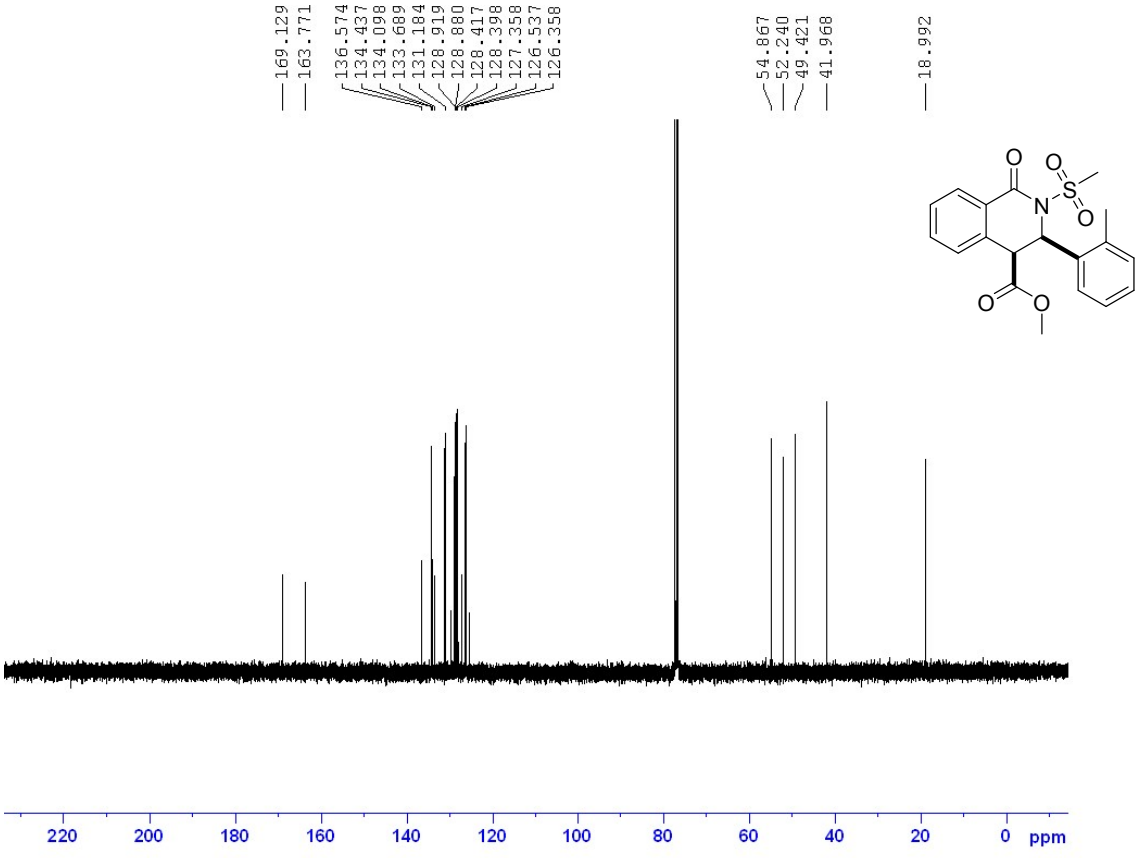


***syn*-Methyl-2-(methylsulfonyl)-1-oxo-3-(o-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-44)**

^{1}H NMR in $CDCl_3$ (400 MHz)

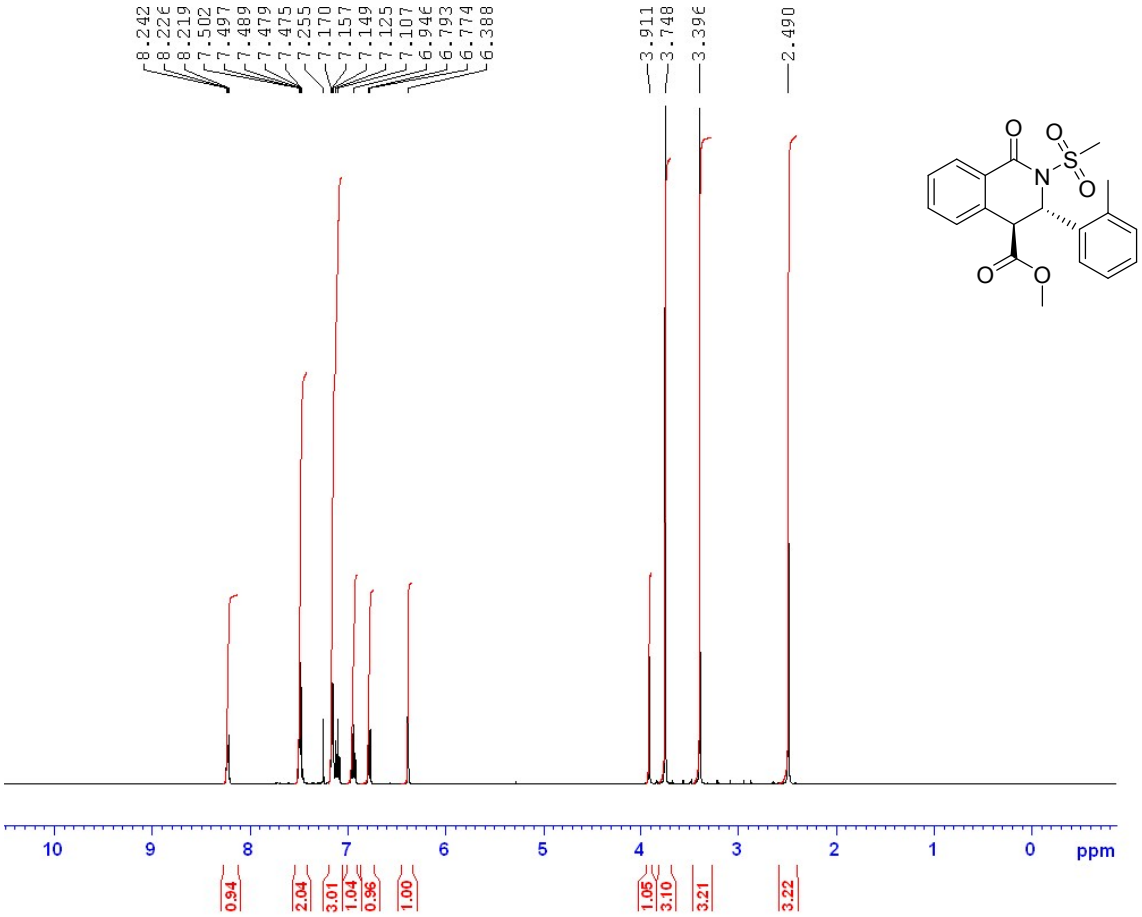


^{13}C NMR in $CDCl_3$ (100 MHz)

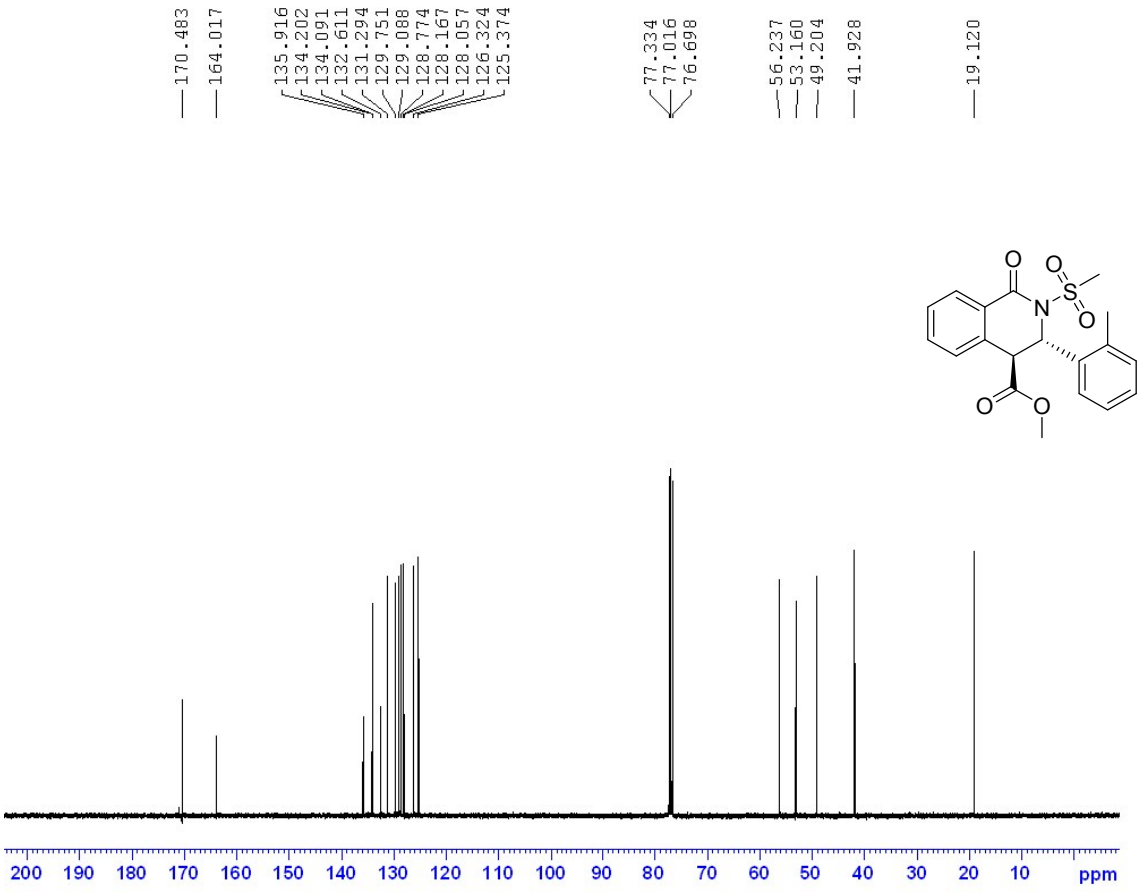


***anti*-Methyl-2-(methylsulfonyl)-1-oxo-3-(o-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-44)**

^{1}H NMR in $CDCl_3$ (400 MHz)

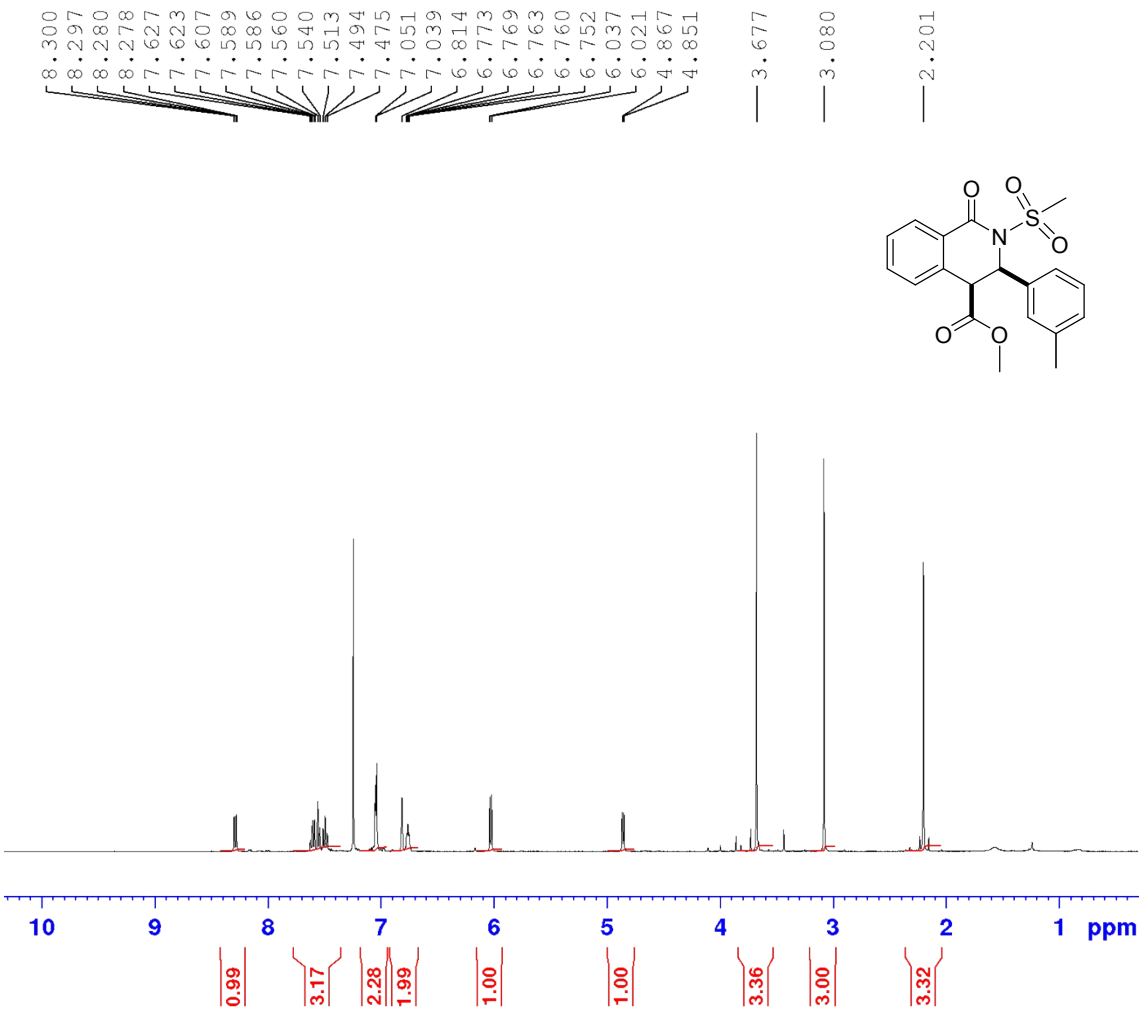


^{13}C NMR in $CDCl_3$ (100 MHz)

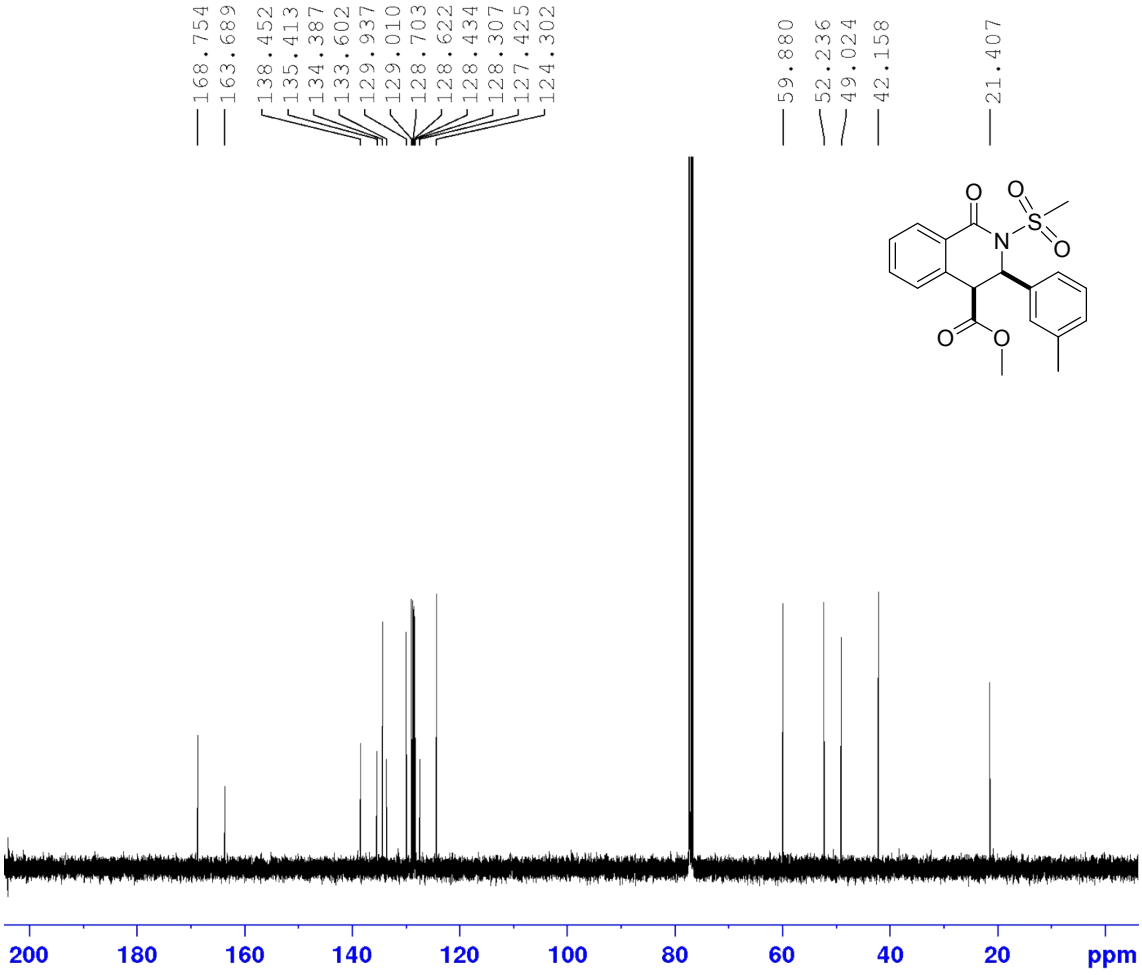


syn-Methyl 2-(methylsulfonyl)-1-oxo-3-(_m_-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-45)

^{1}H NMR in $CDCl_3$ (400 MHz)

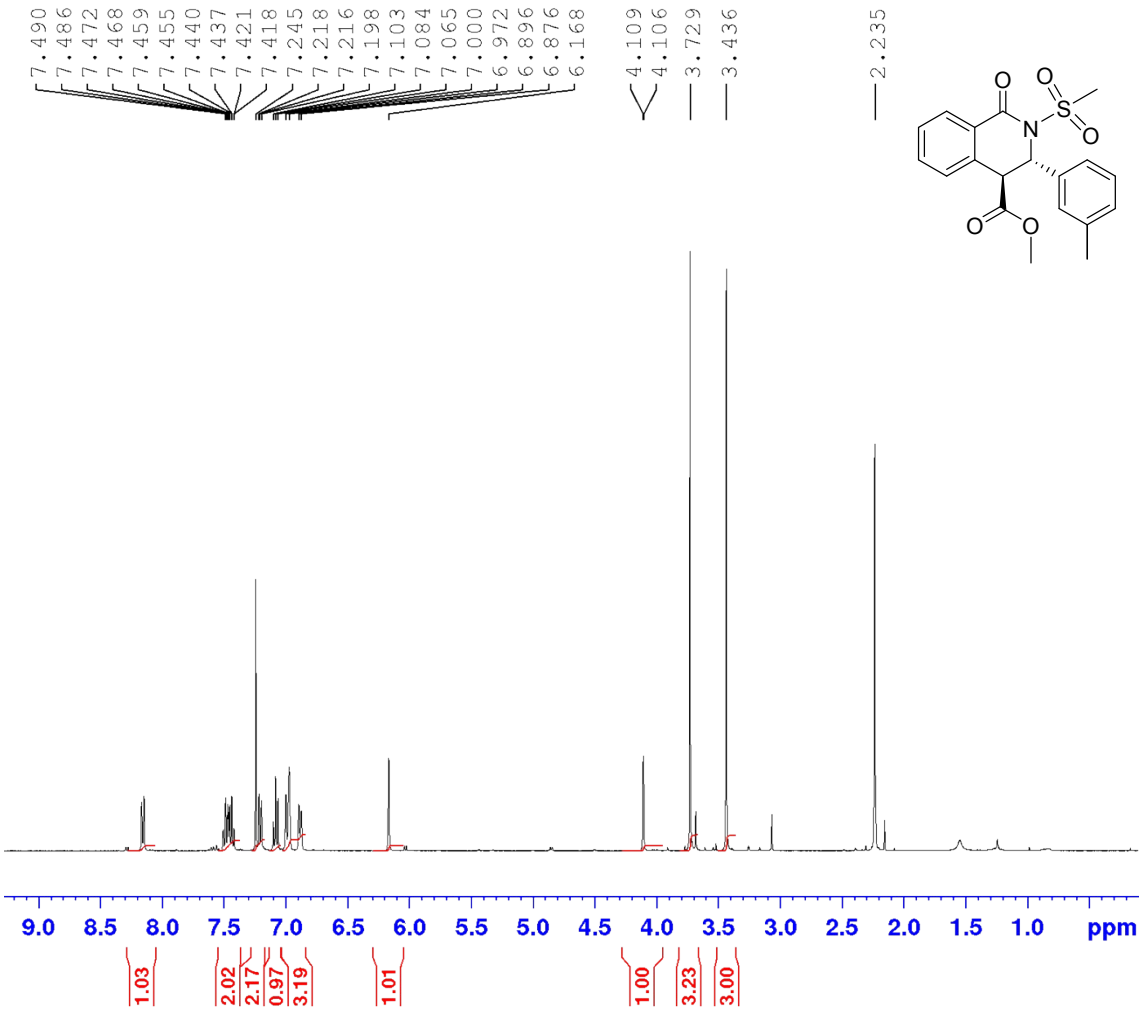


^{13}C NMR in $CDCl_3$ (100 MHz)

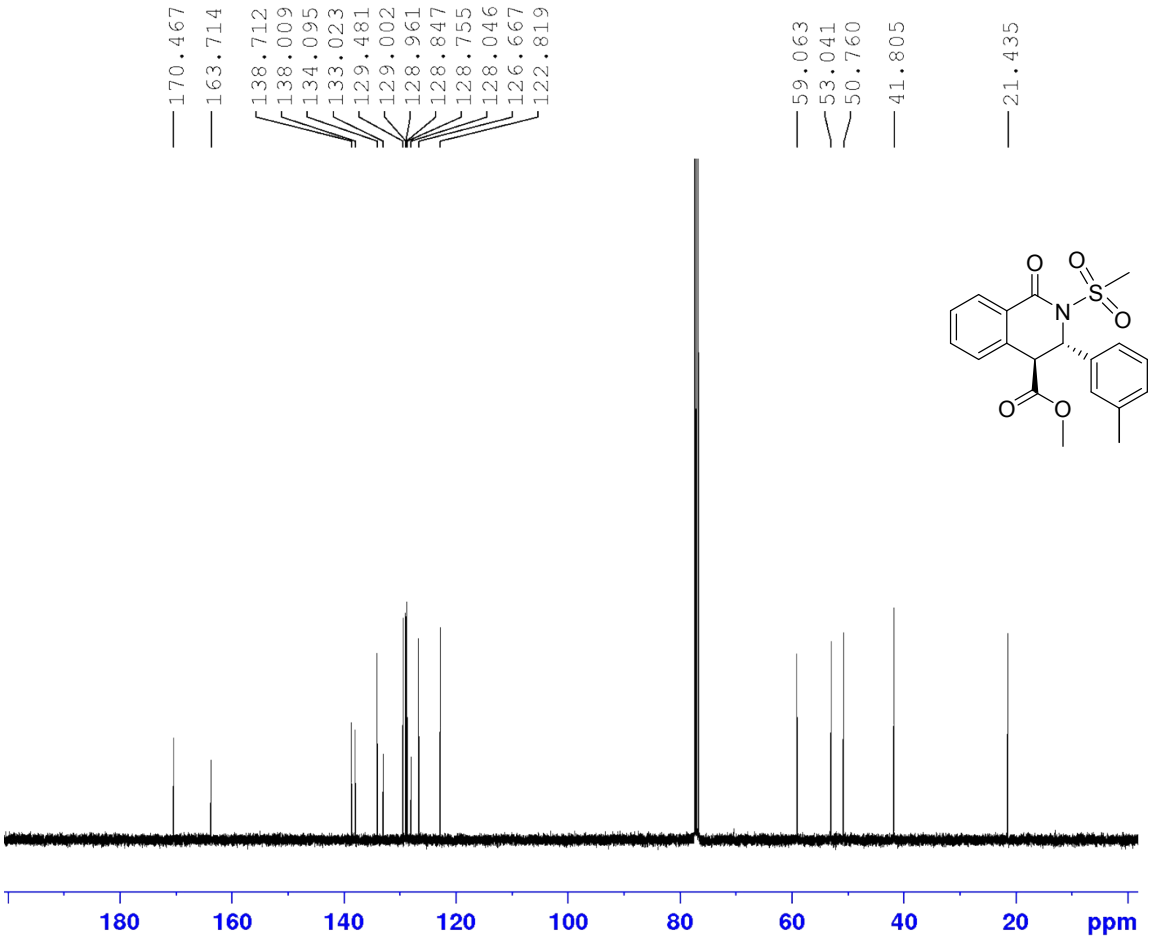


***anti*-Methyl 2-(methylsulfonyl)-1-oxo-3-(*m*-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-45)**

^{1}H NMR in $CDCl_3$ (400 MHz)

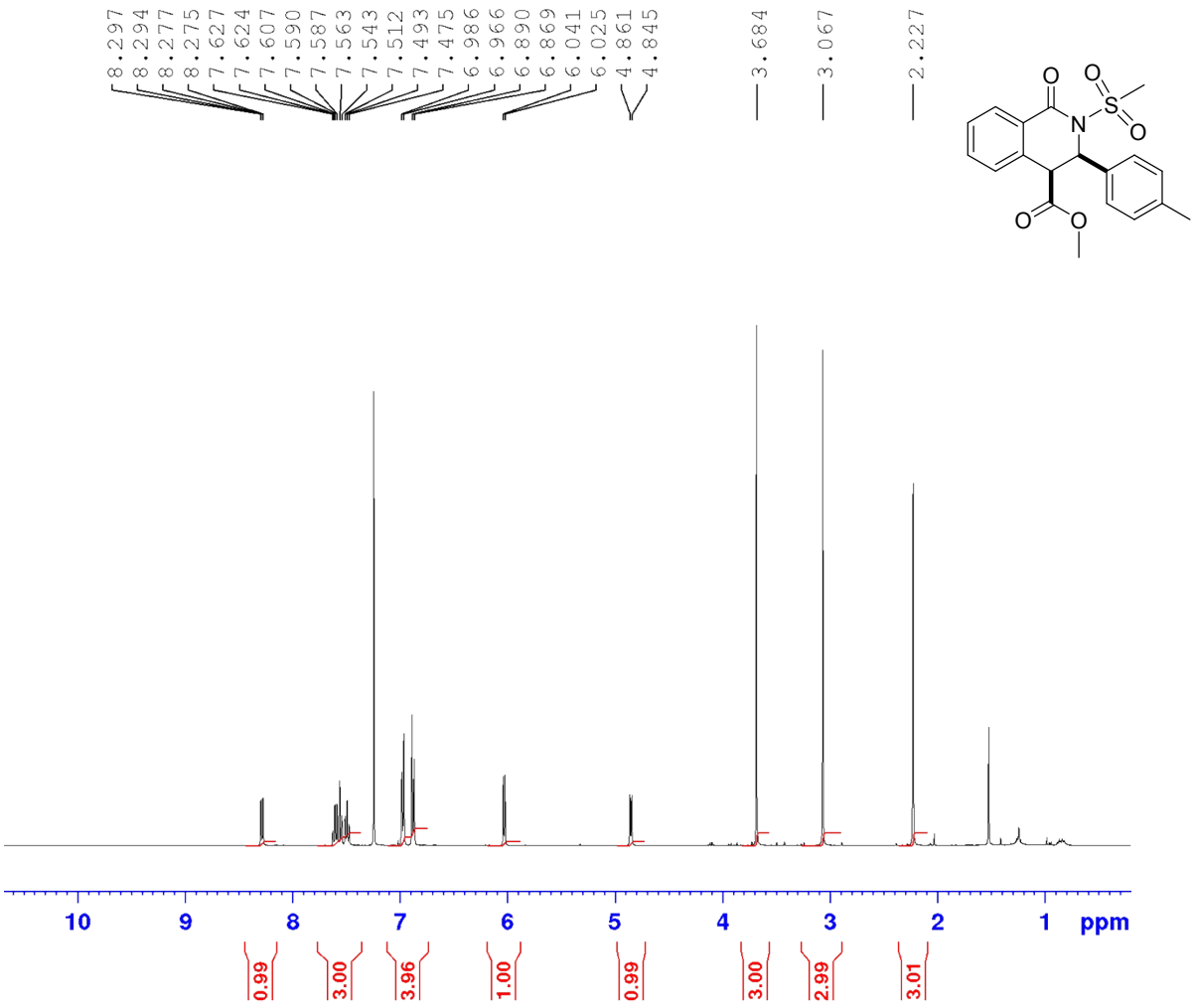


^{13}C NMR in $CDCl_3$ (100 MHz)

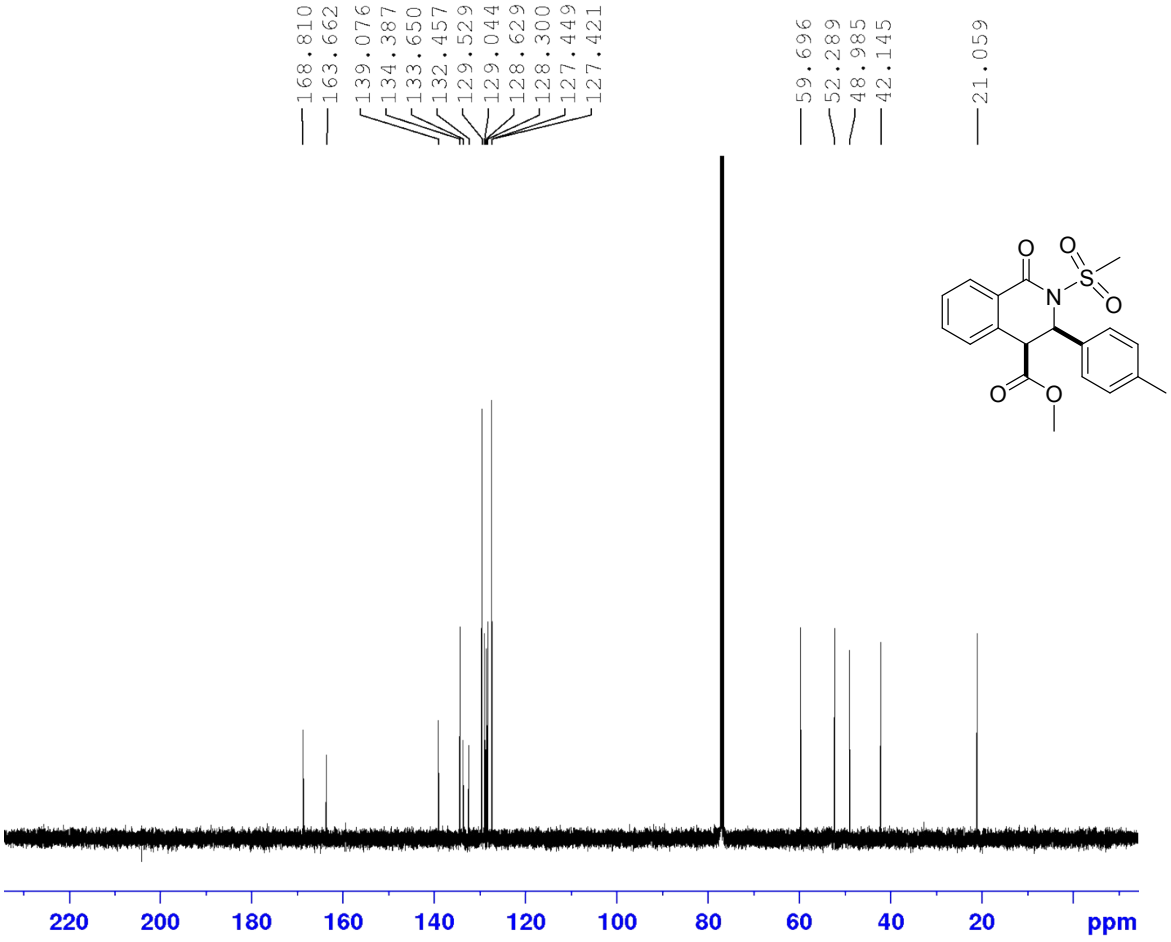


***syn*-Methyl 2-(methylsulfonyl)-1-oxo-3-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-46)**

^{1}H NMR in $CDCl_3$ (400 MHz)

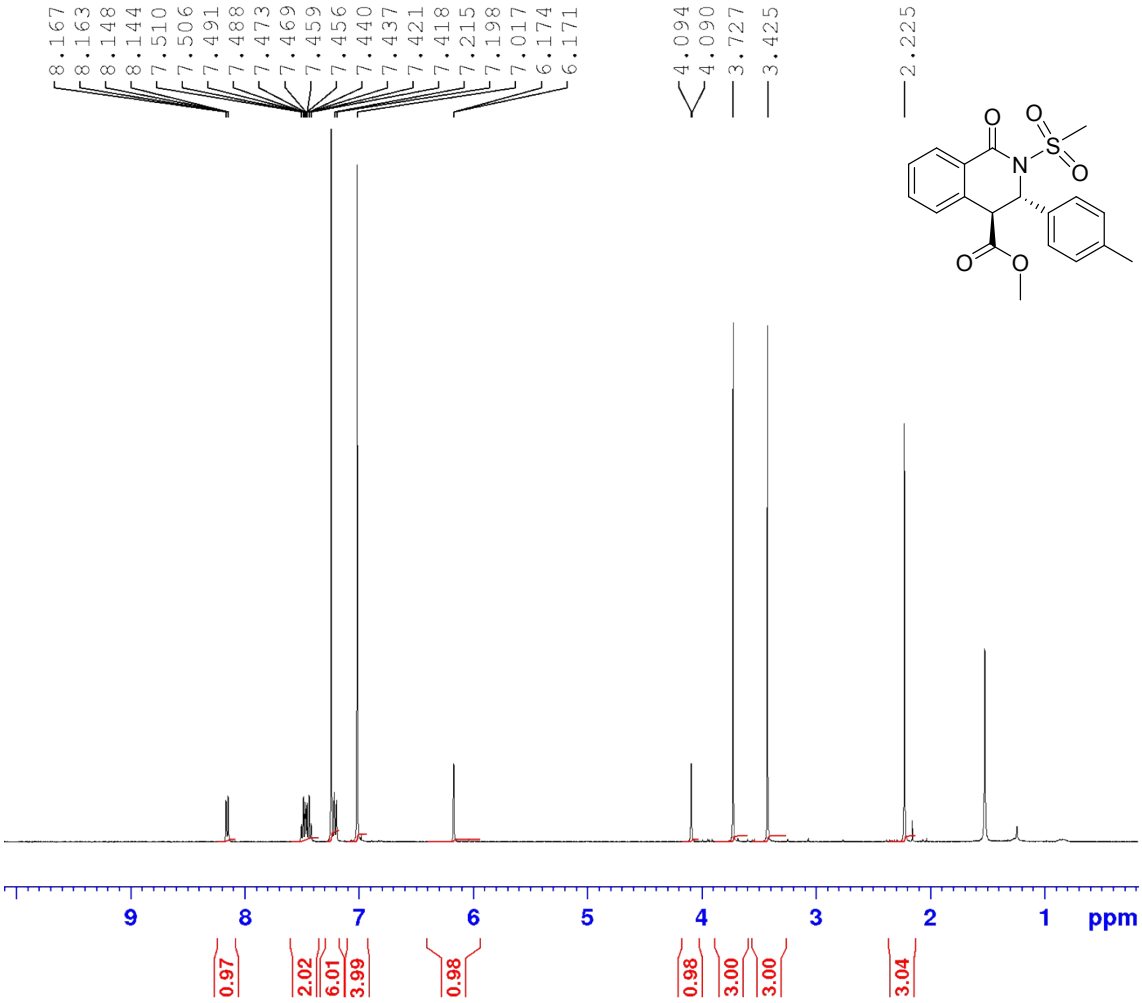


^{13}C NMR in $CDCl_3$ (100 MHz)

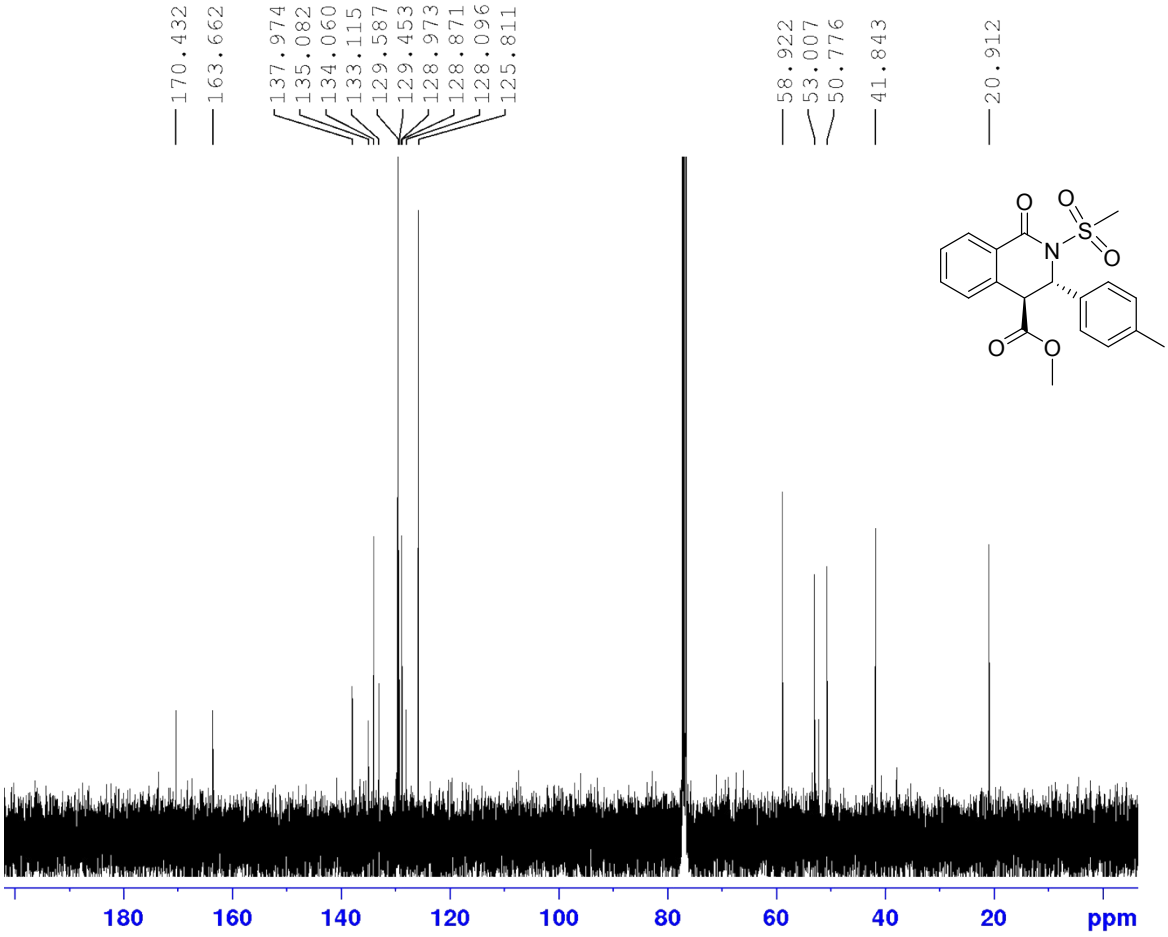


***anti*-Methyl 2-(methylsulfonyl)-1-oxo-3-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-46)**

^{1}H NMR in $CDCl_3$ (400 MHz)

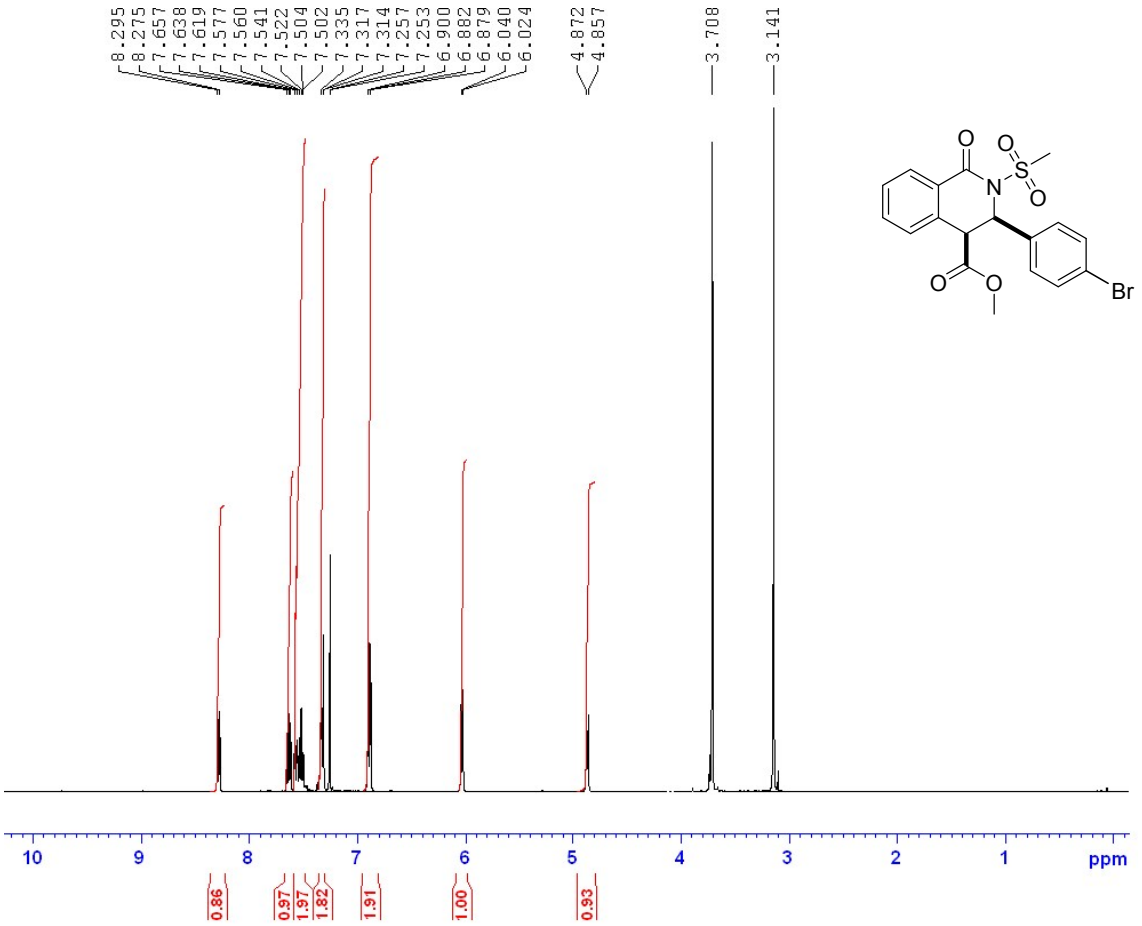


^{13}C NMR in $CDCl_3$ (100 MHz)

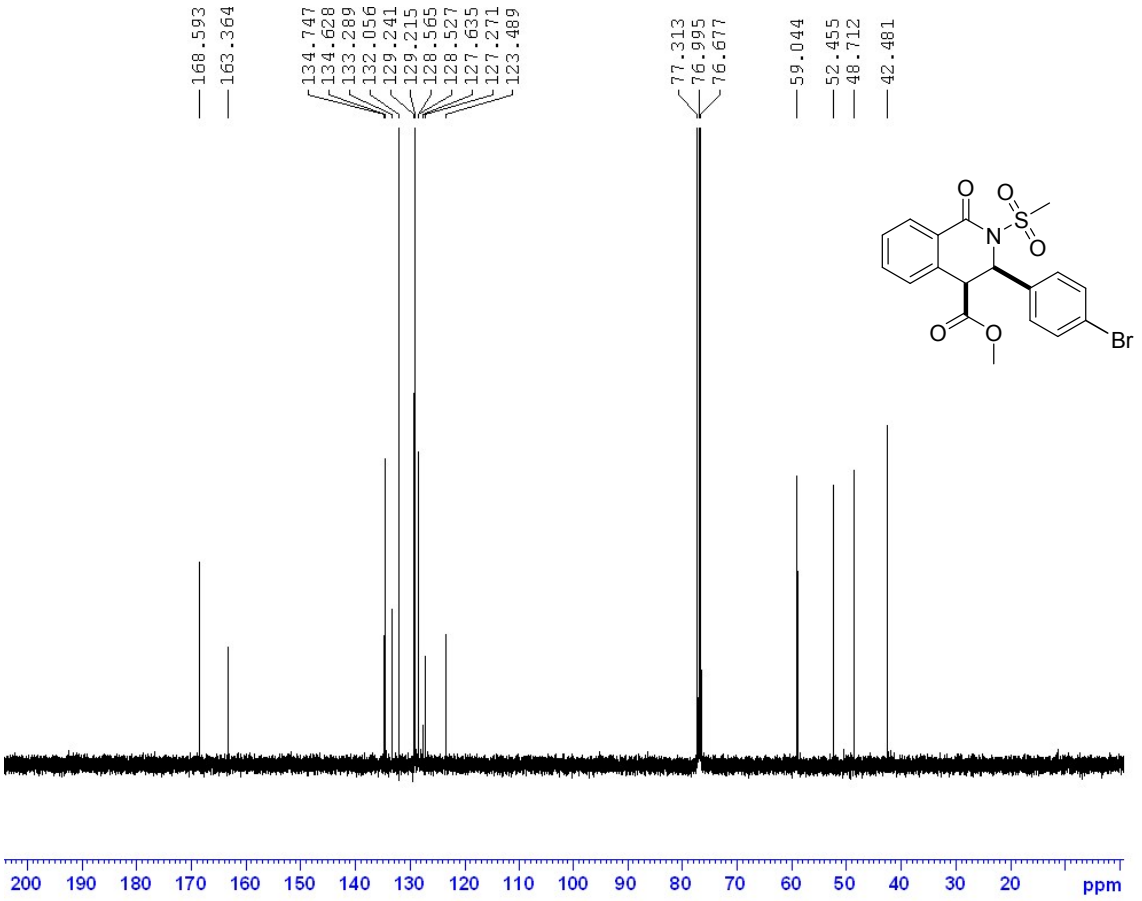


***syn*-Methyl 3-(4-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-47)**

^{1}H NMR in $CDCl_3$ (400 MHz)

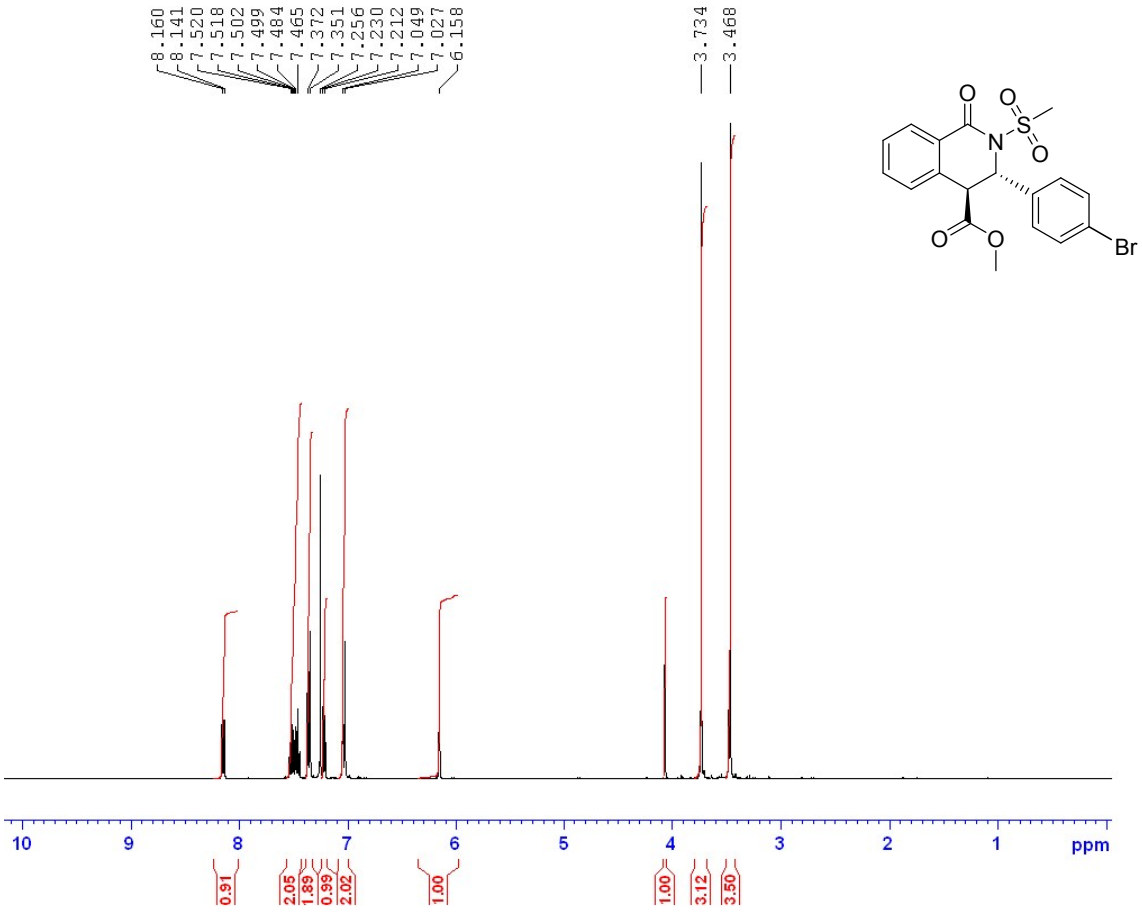


^{13}C NMR in $CDCl_3$ (100 MHz)

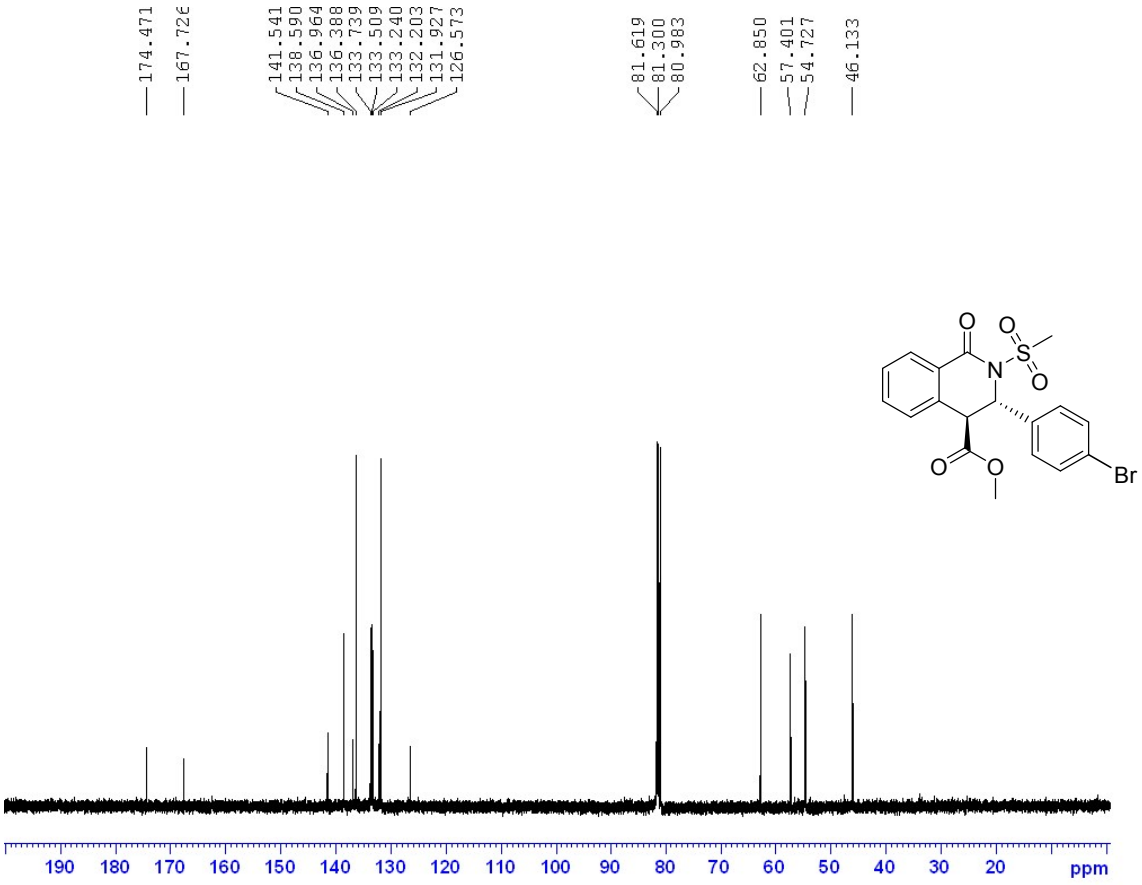


***anti*-Methyl 3-(4-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-47)**

^{1}H NMR in $CDCl_3$ (400 MHz)

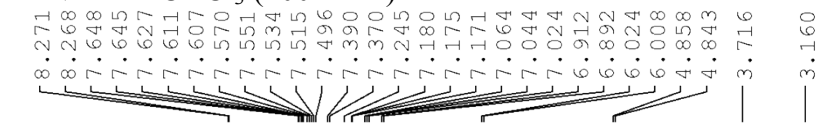


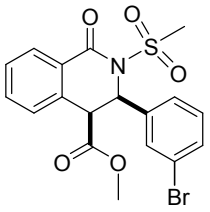
^{13}C NMR in $CDCl_3$ (100 MHz)

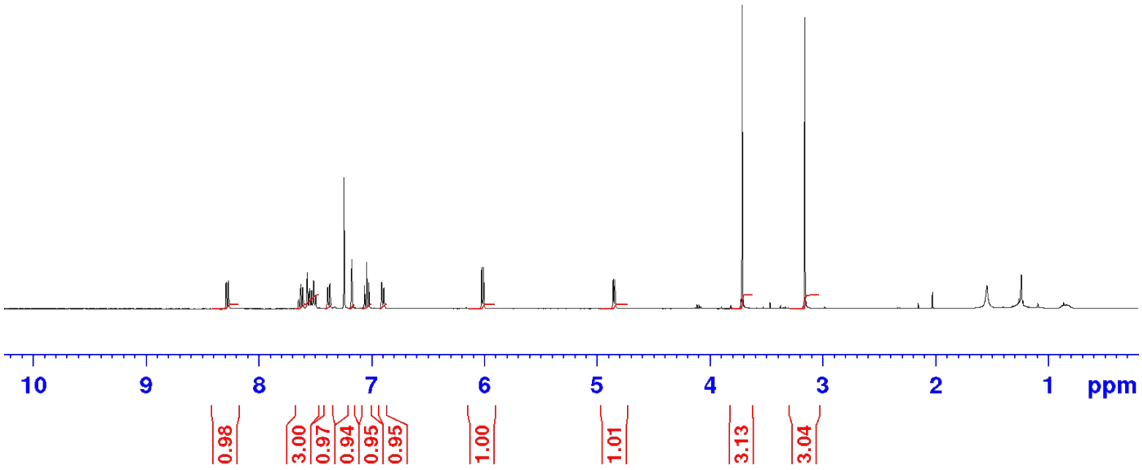


***syn*-Methyl 3-(3-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-48)**

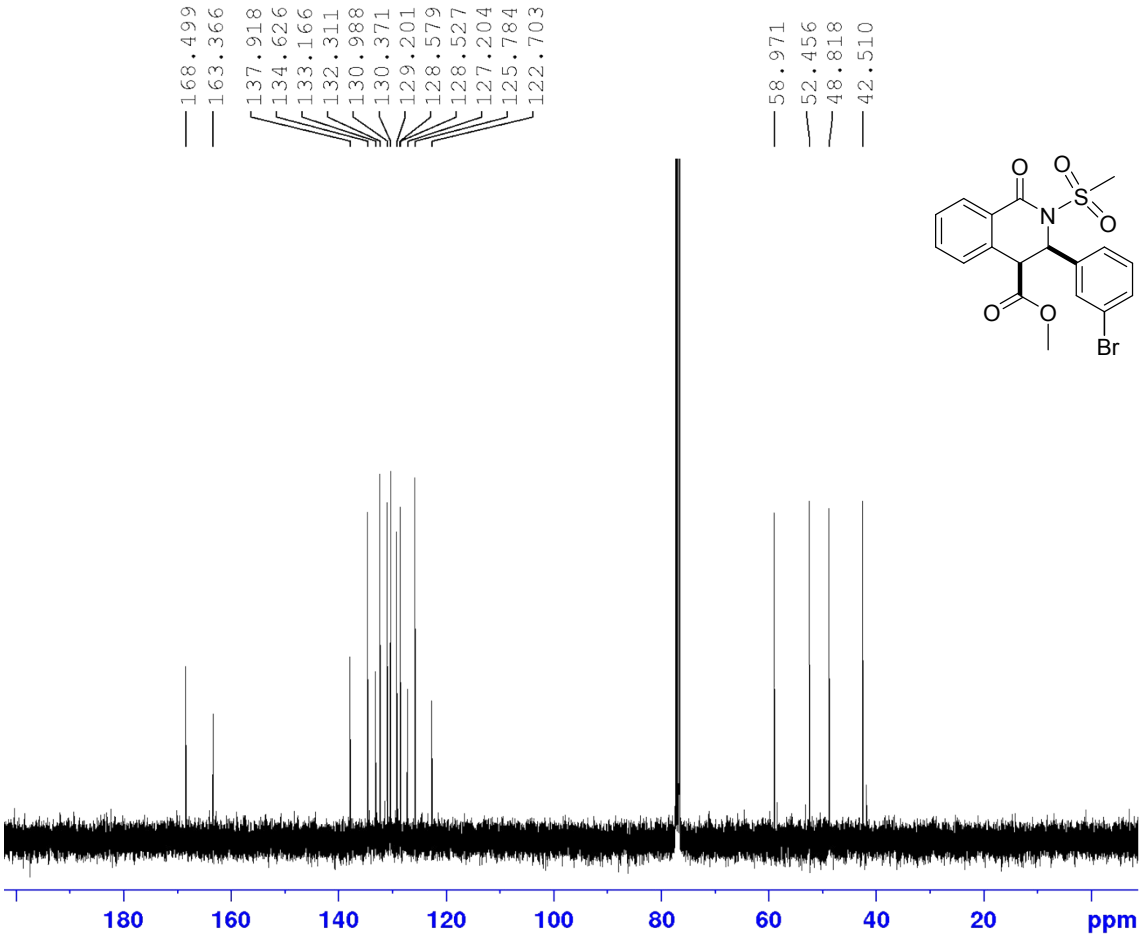
^{1}H NMR in $CDCl_3$ (400 MHz)





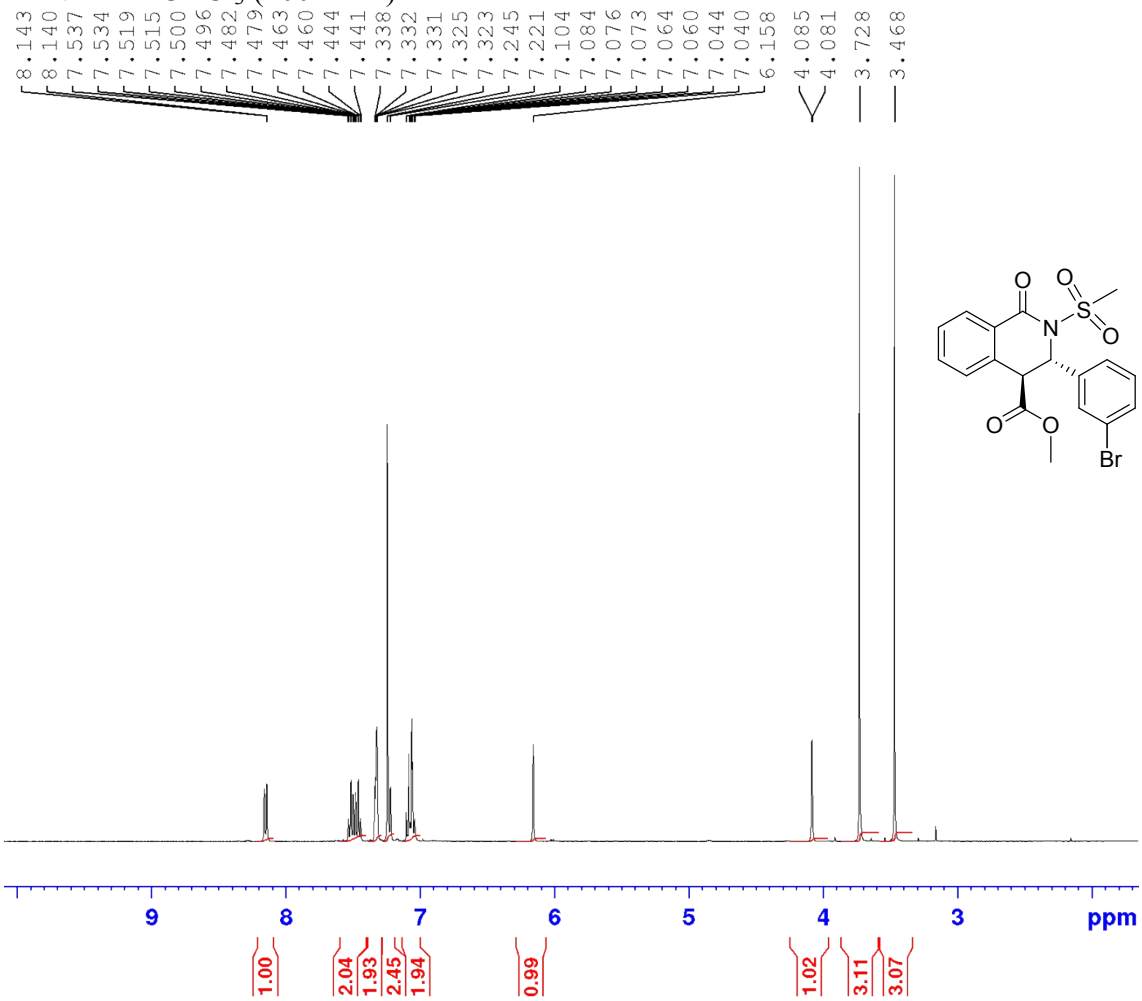


^{13}C NMR in $CDCl_3$ (100 MHz)

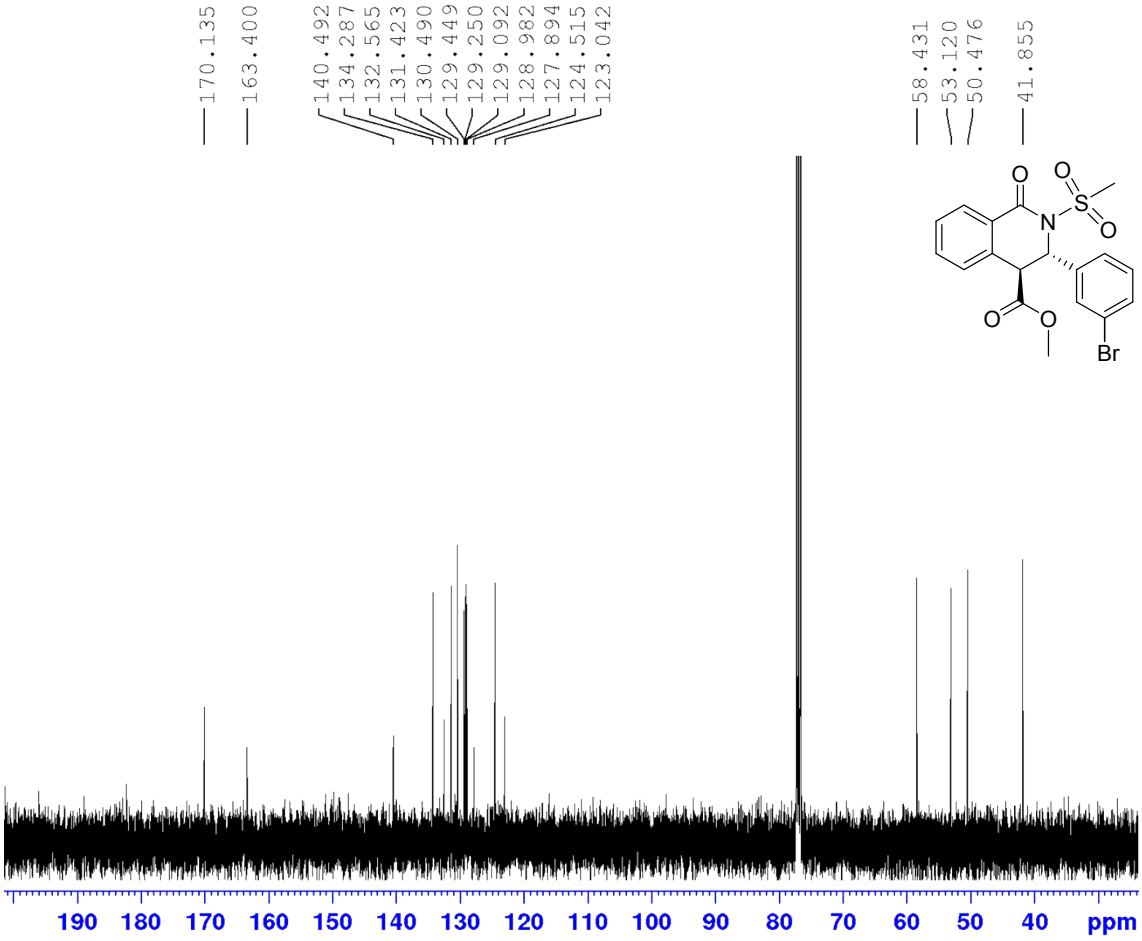


***anti*-Methyl 3-(3-bromophenyl)-2-(methylsulfonyl)1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-48)**

^{1}H NMR in $CDCl_3$ (400 MHz)

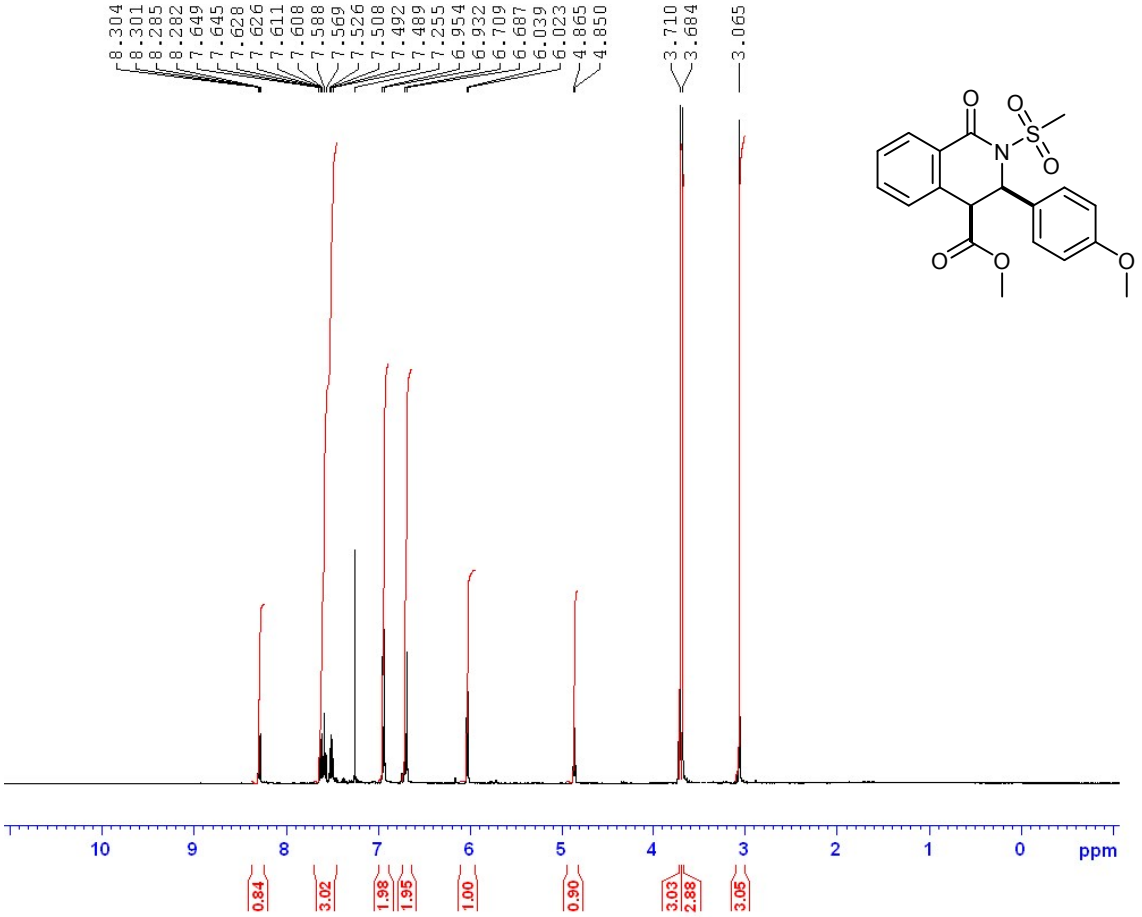


^{13}C NMR in $CDCl_3$ (100 MHz)

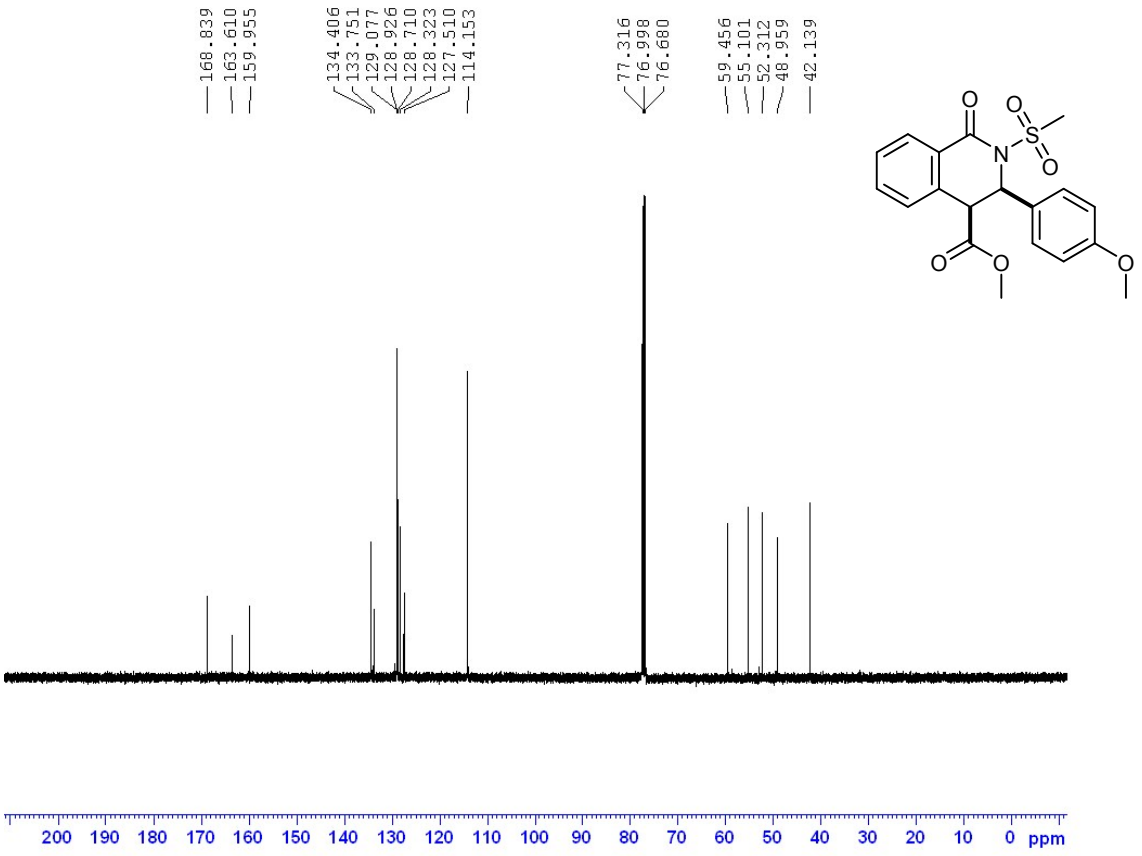


***syn*-Methyl 3-(4-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-49)**

^{1}H NMR in $CDCl_3$ (400 MHz)

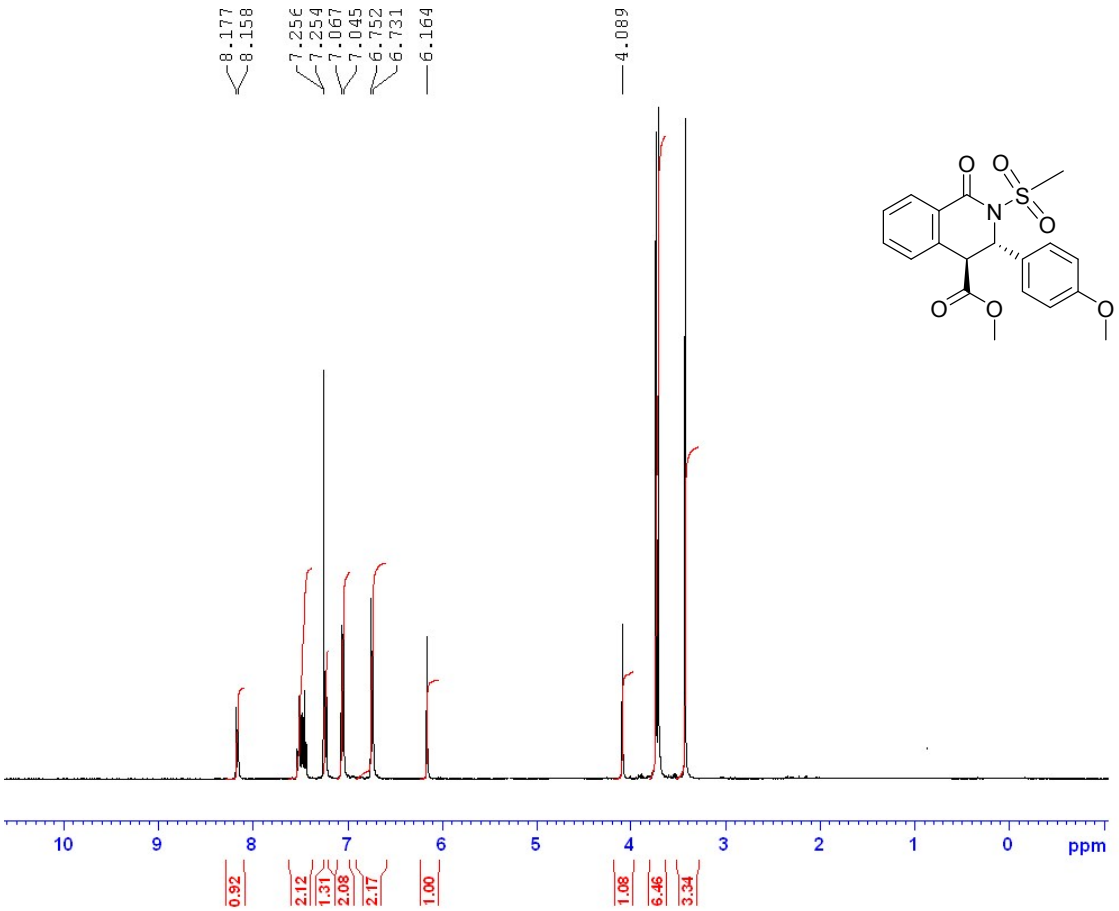


^{13}C NMR in $CDCl_3$ (100 MHz)

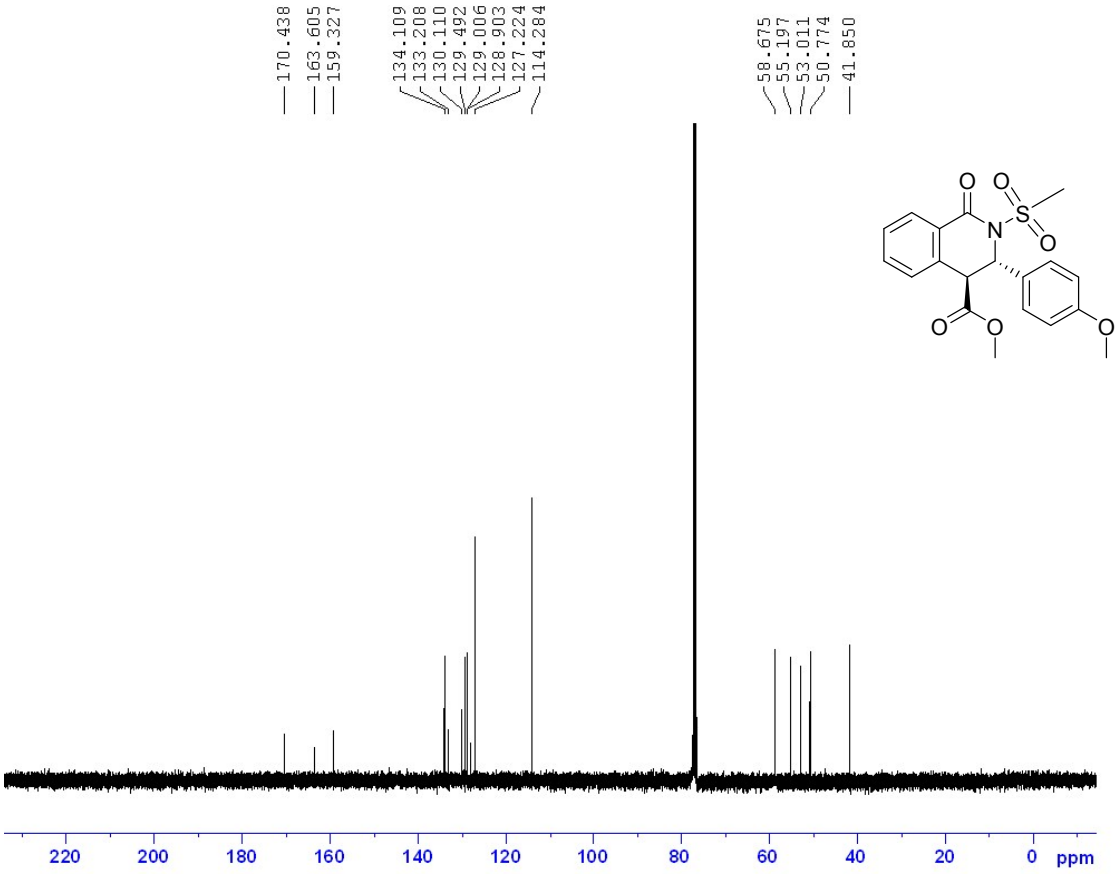


***anti*-Methyl 3-(4-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-49)**

^{1}H NMR in $CDCl_3$ (400 MHz)

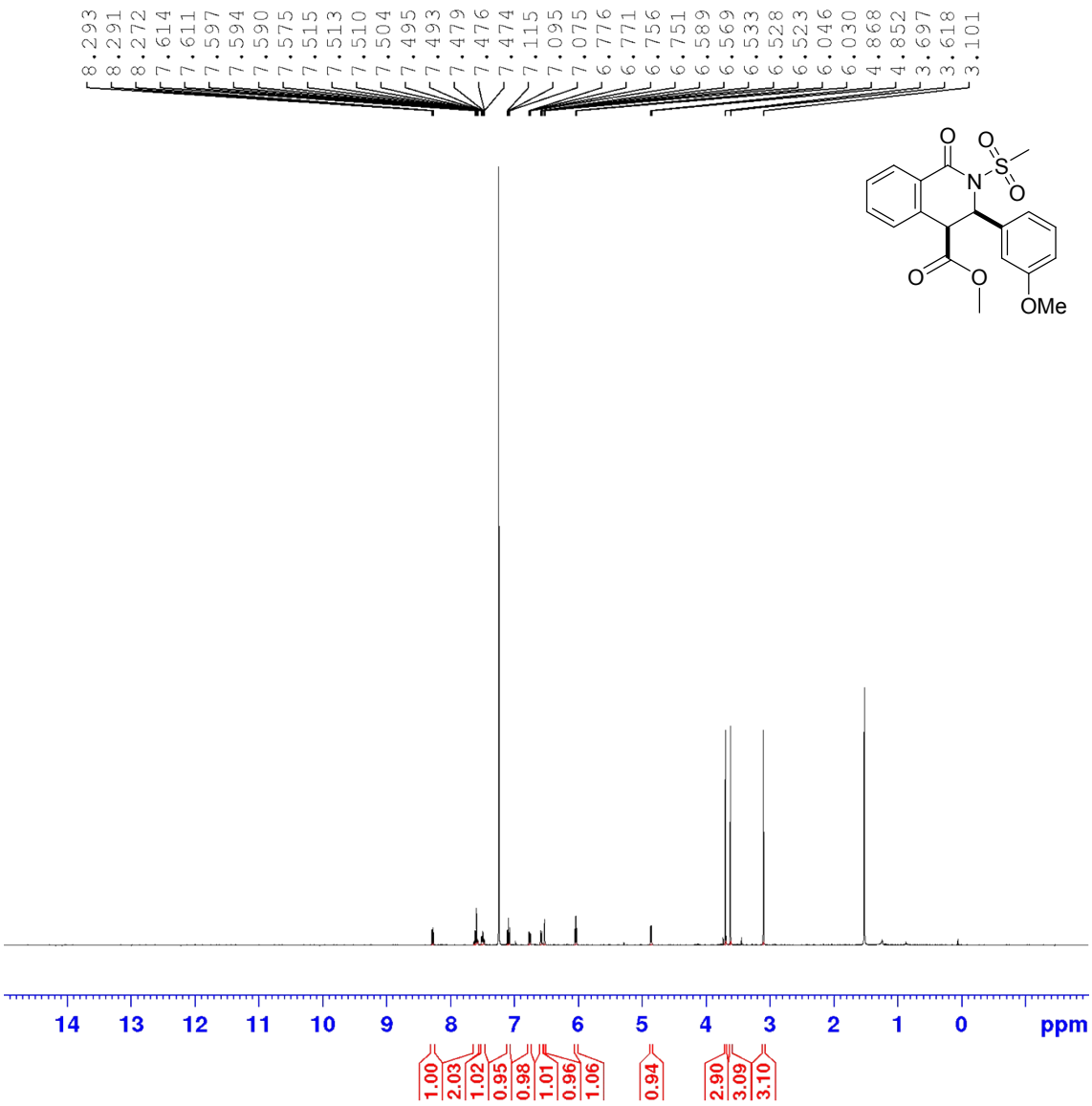


^{13}C NMR in $CDCl_3$ (100 MHz)

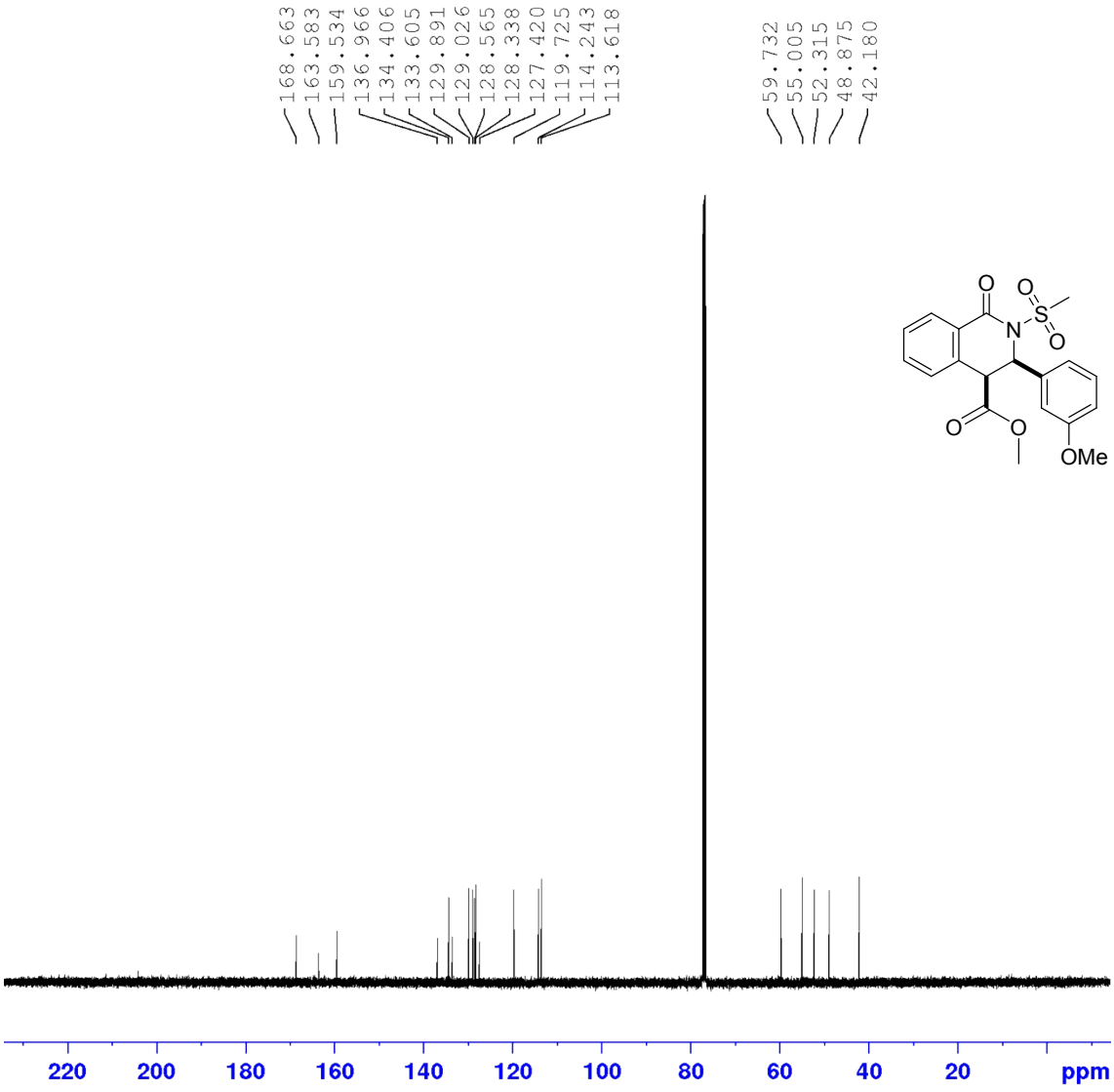


***syn*-Methyl 3-(3-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-50)**

^{1}H NMR in $CDCl_3$ (400 MHz)

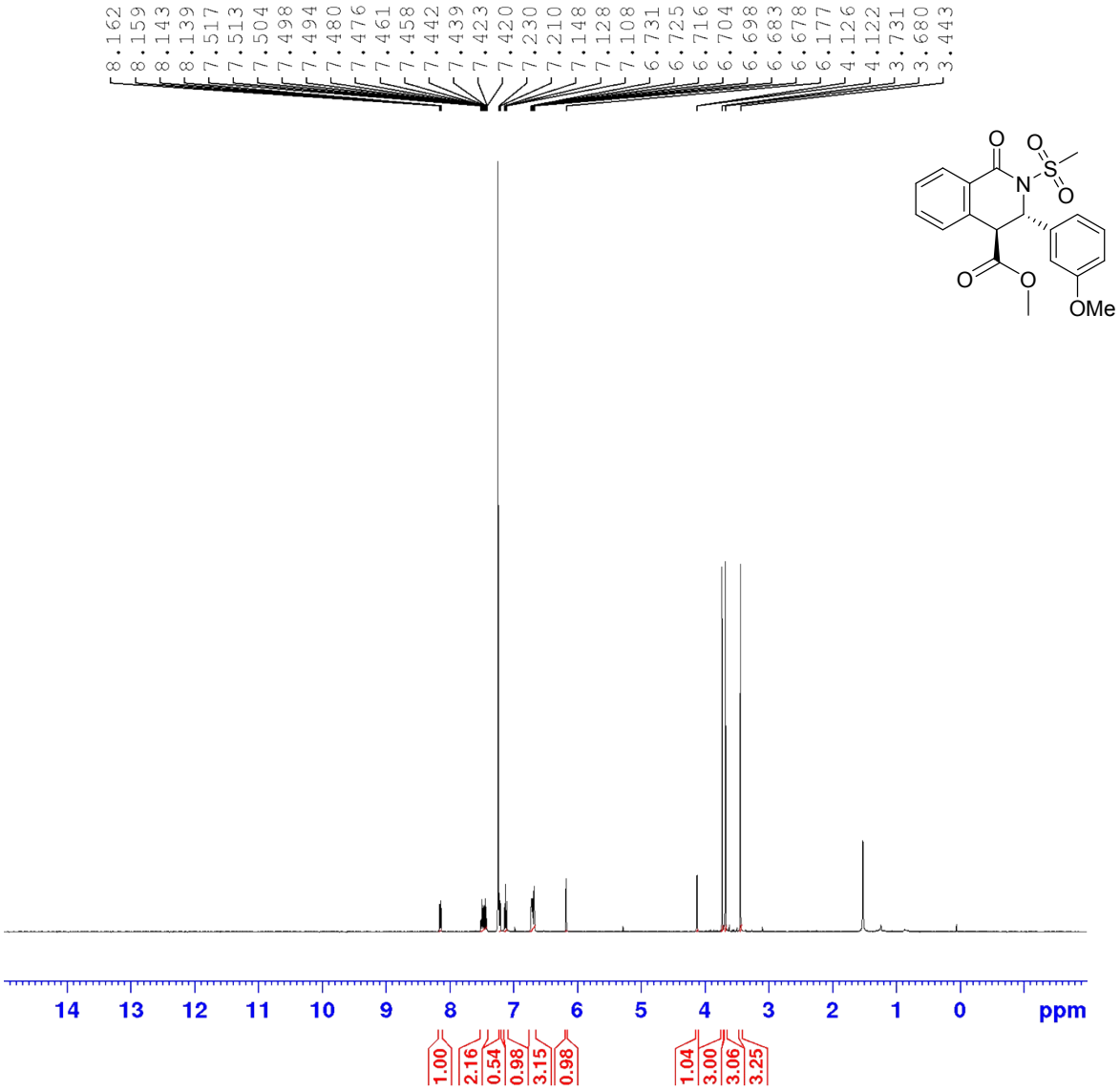


^{13}C NMR in $CDCl_3$ (100 MHz)

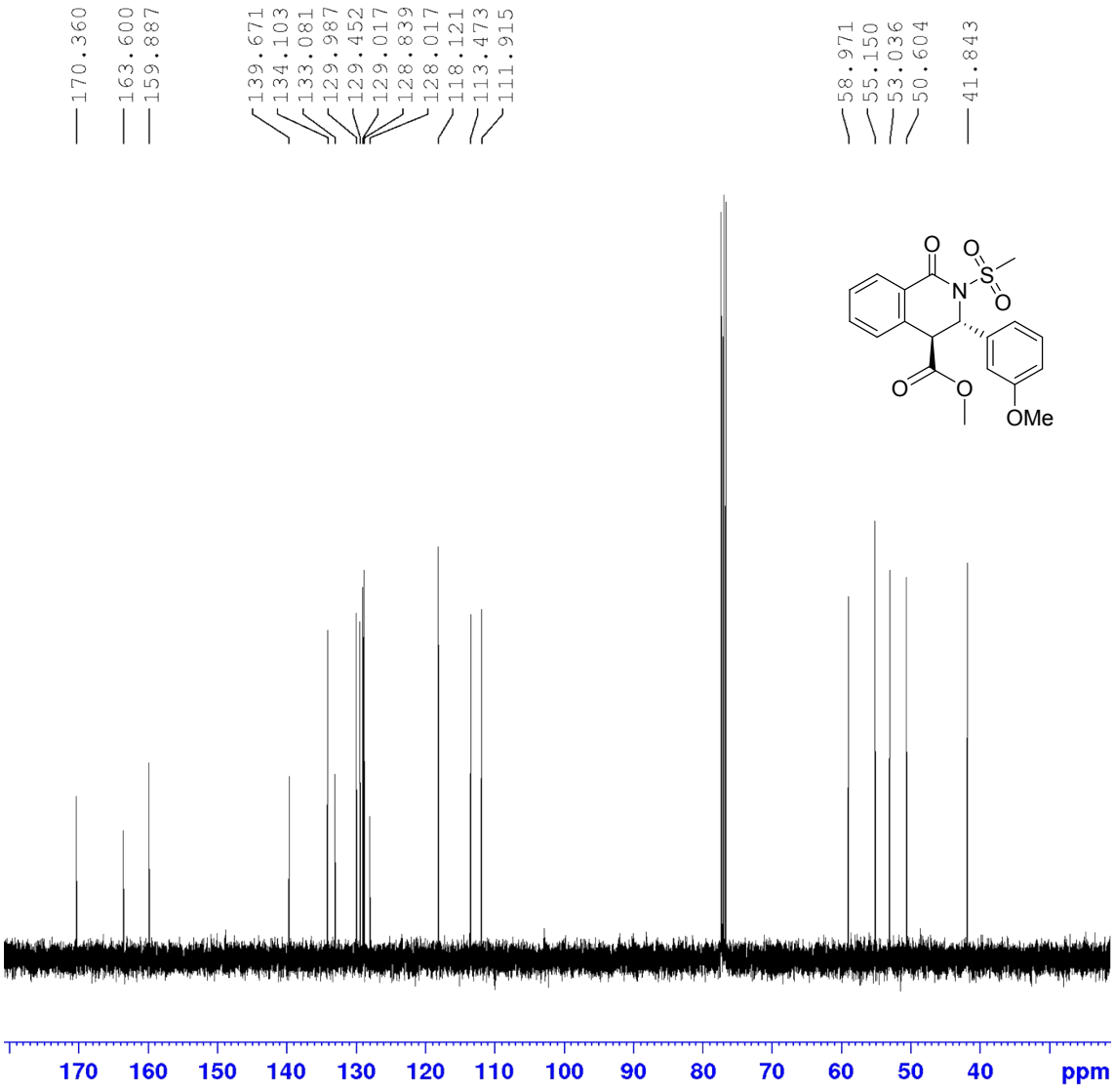


***anti*-Methyl 3-(3-methoxyphenyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-50)**

^{1}H NMR in $CDCl_3$ (400 MHz)

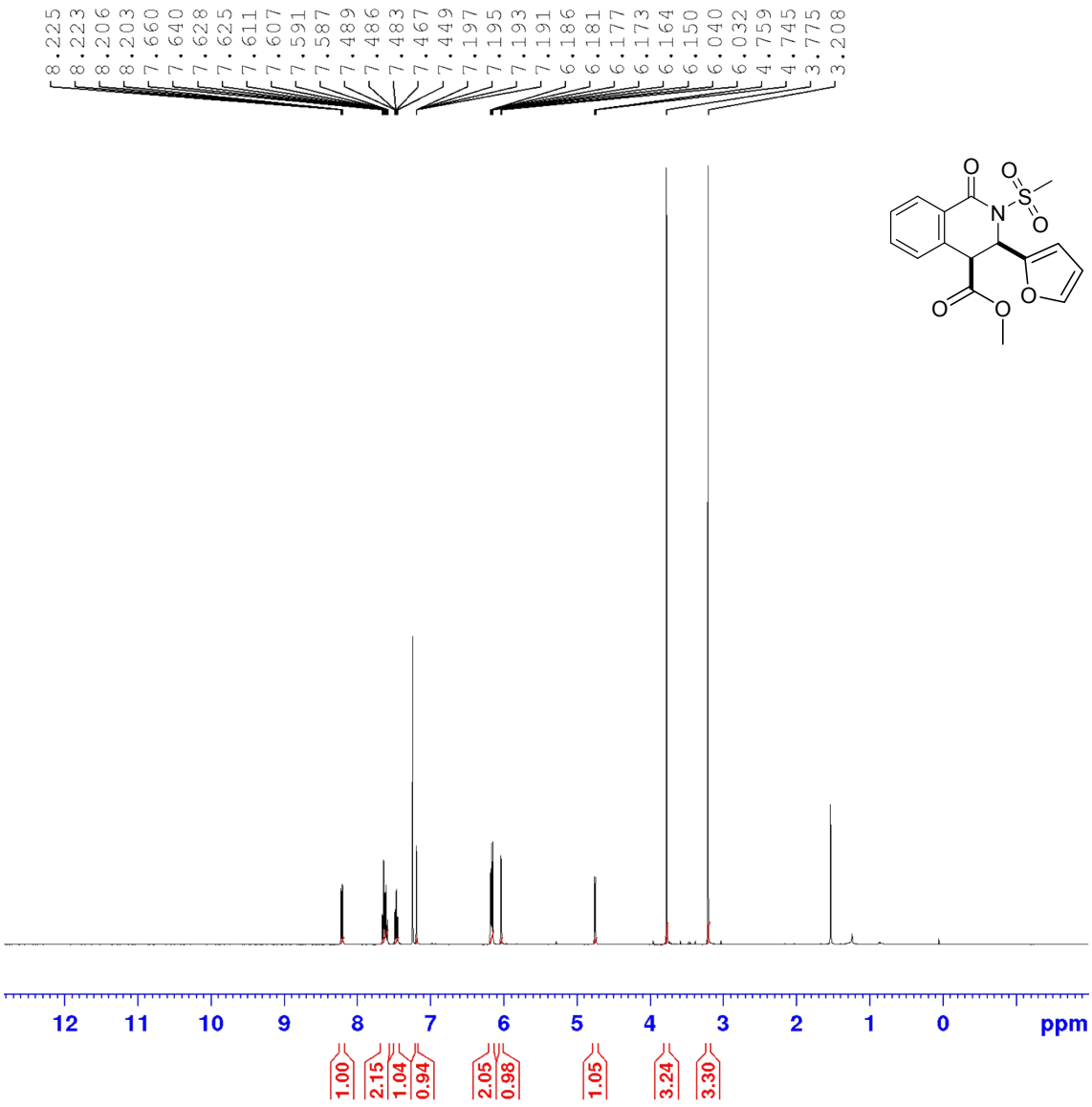


^{13}C NMR in $CDCl_3$ (100 MHz)

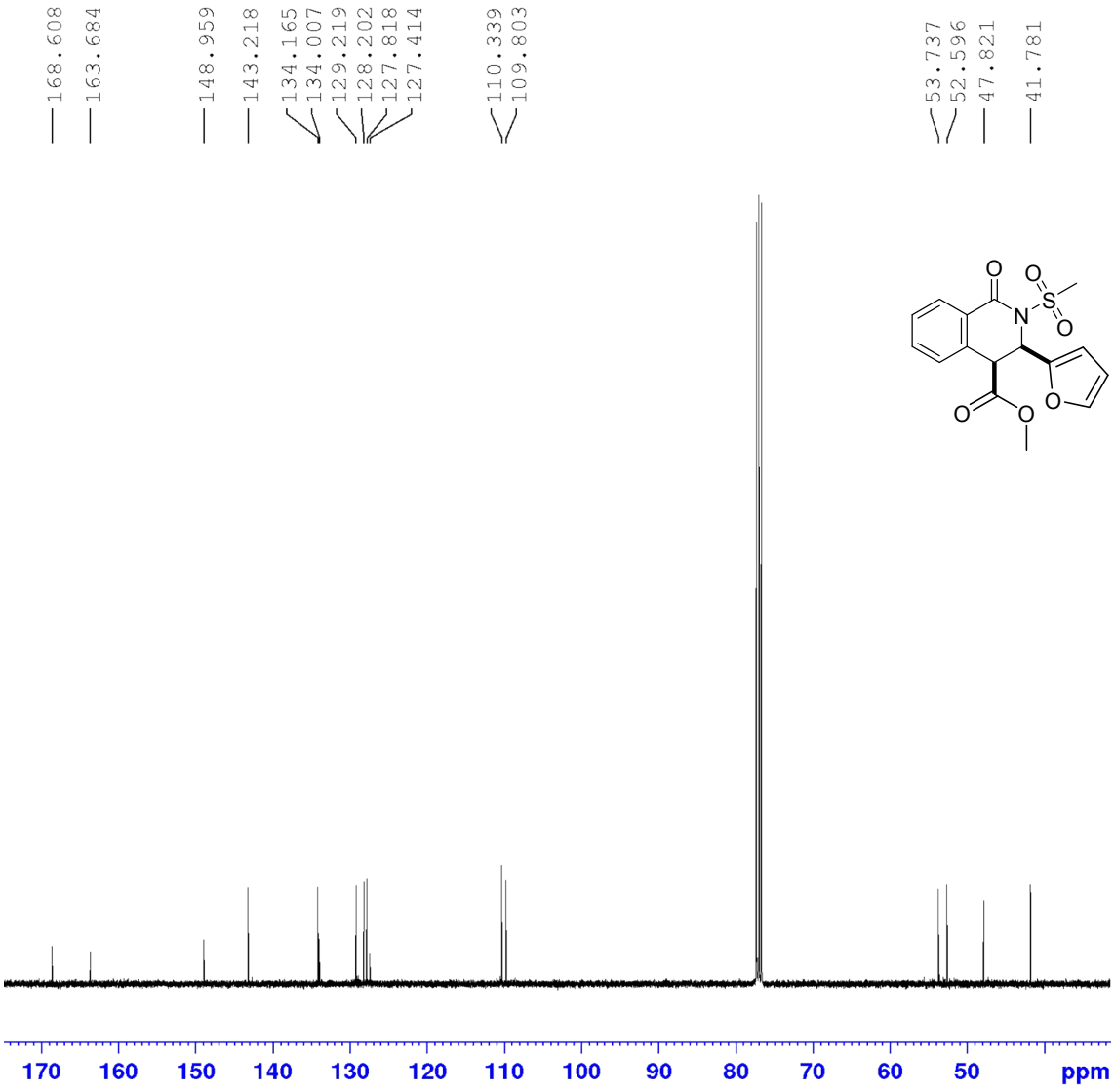


syn-Methyl 3-(furan-2-yl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-51)

^{1}H NMR in $CDCl_3$ (400 MHz)

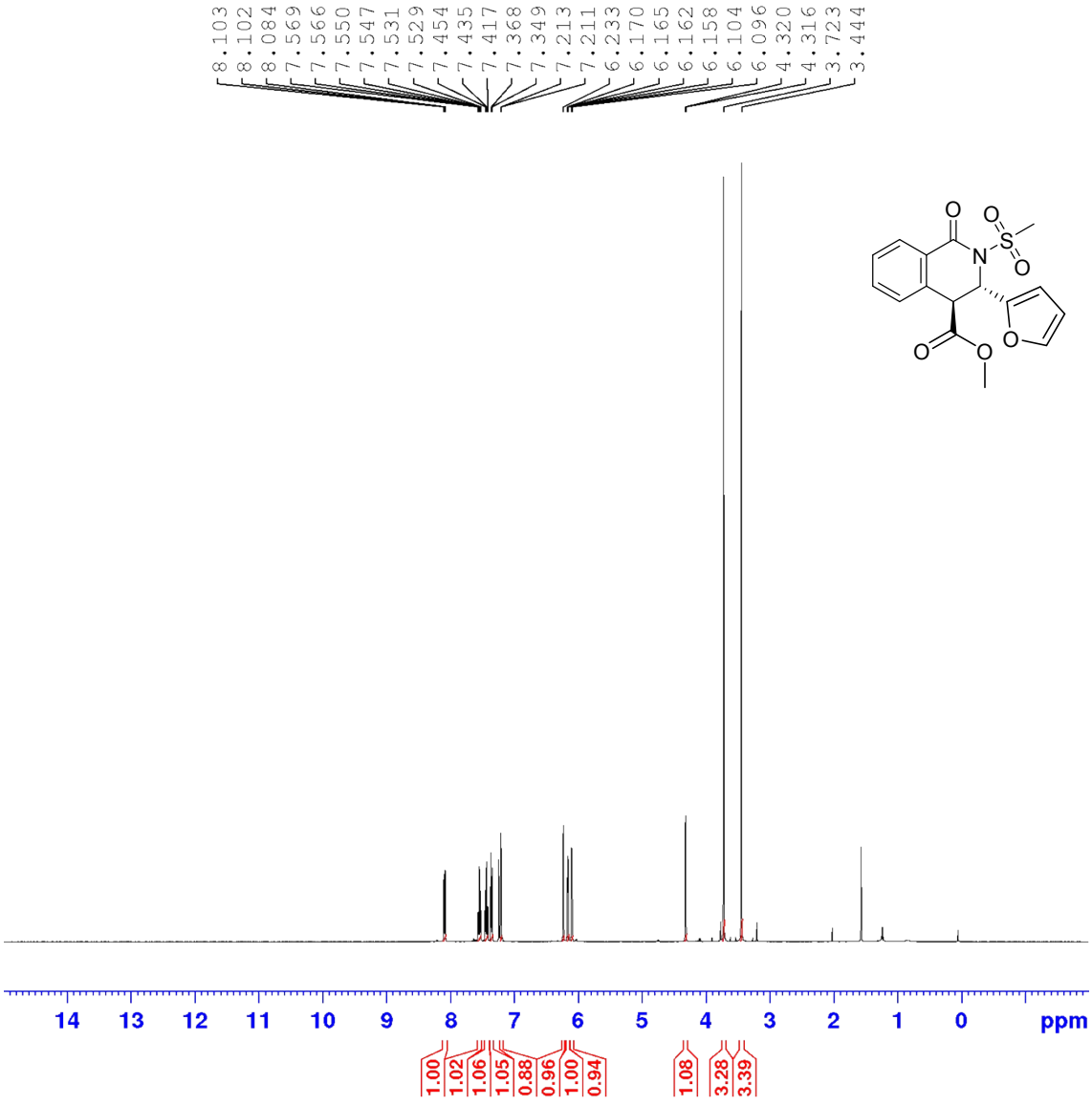


^{13}C NMR in $CDCl_3$ (100 MHz)

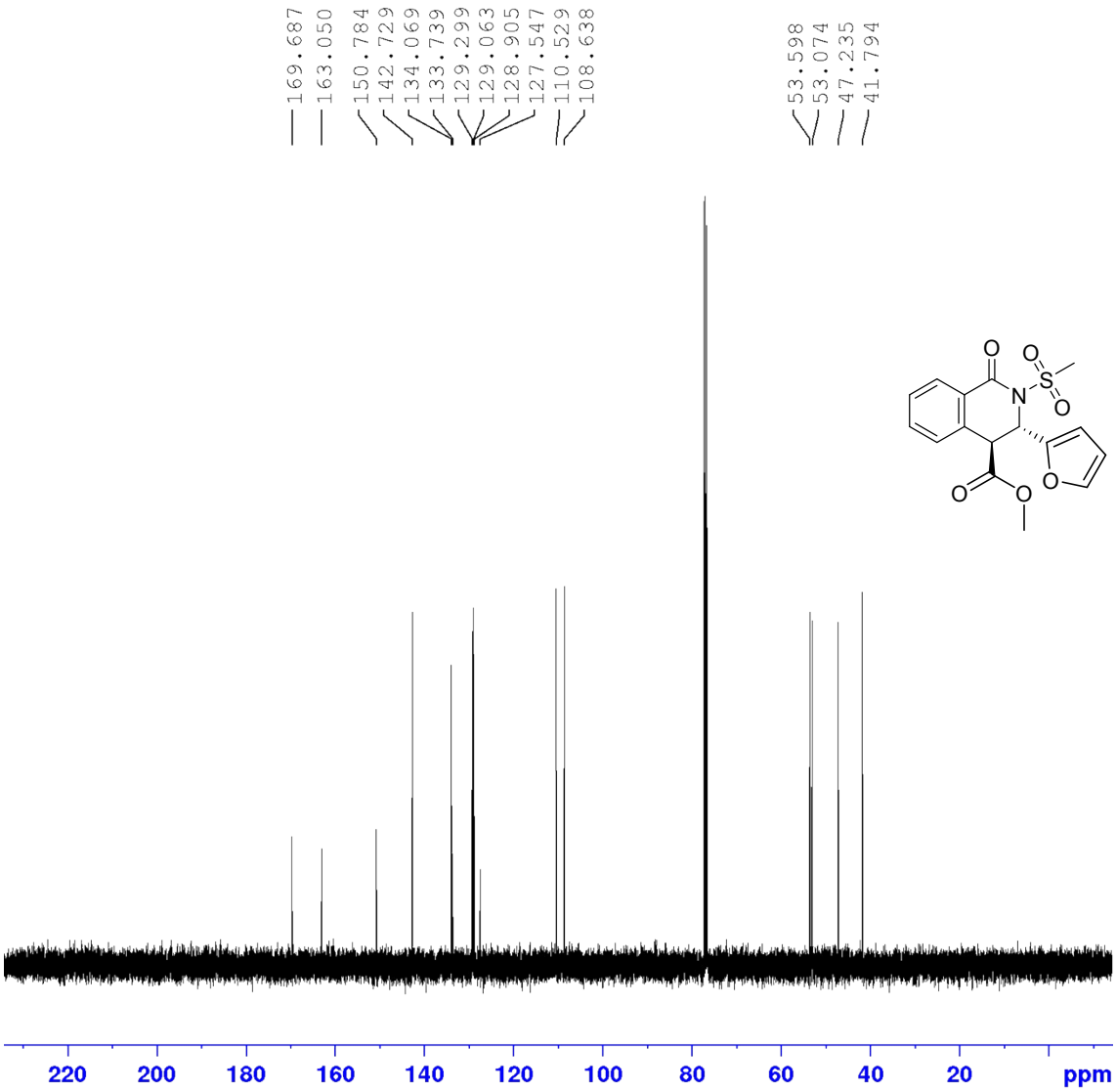


***anti*-Methyl 3-(furan-2-yl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-51)**

^{1}H NMR in $CDCl_3$ (400 MHz

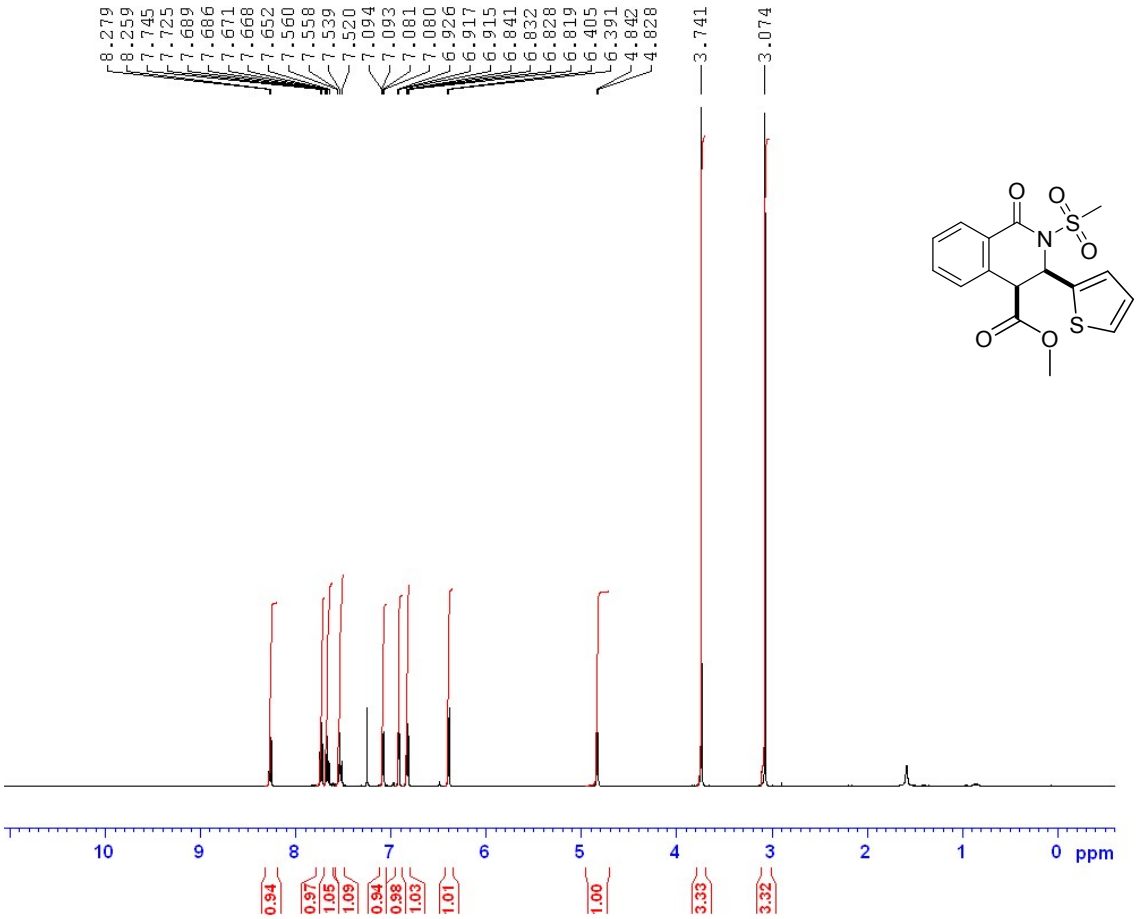


^{13}C NMR in $CDCl_3$ (100 MHz)

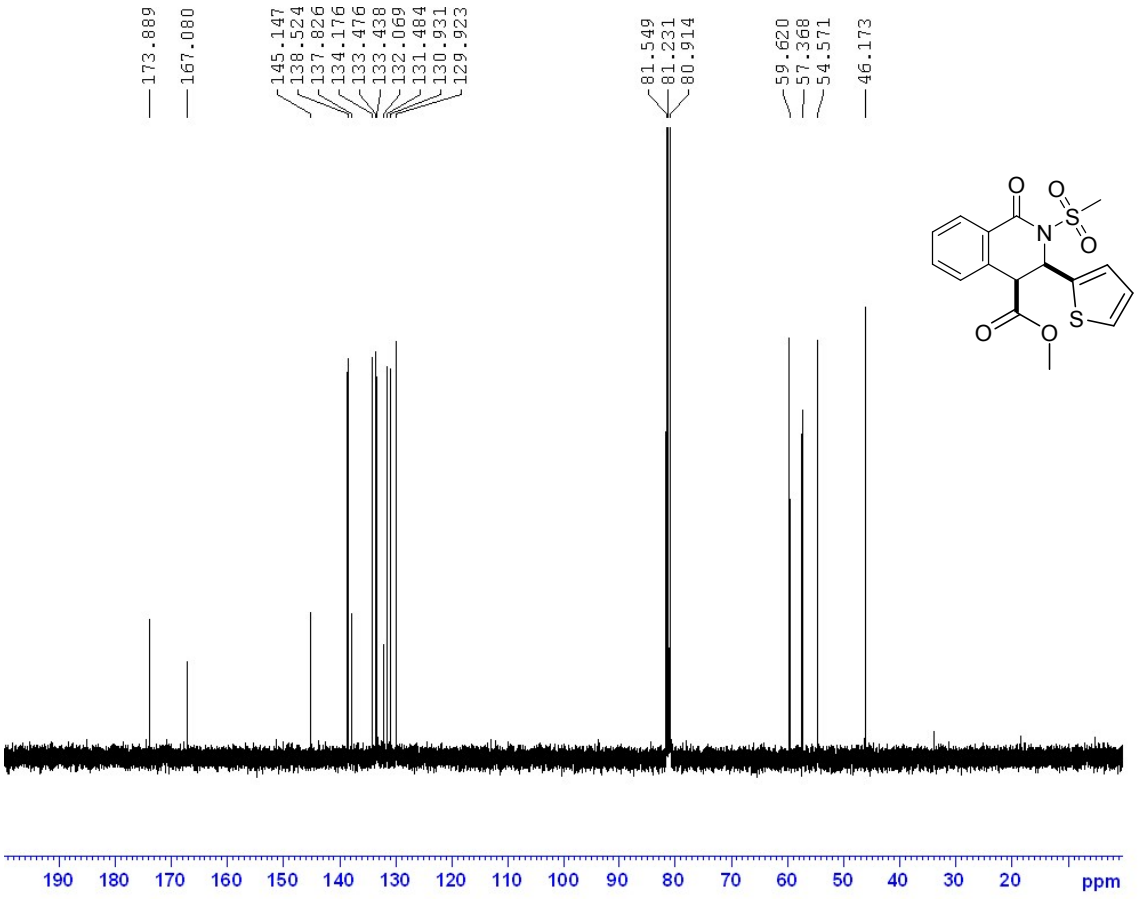


syn-Methyl-2-(methylsulfonyl)-1-oxo-3-(thiophen-2-yl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (_syn_-52)

^{1}H NMR in $CDCl_3$ (400 MHz)

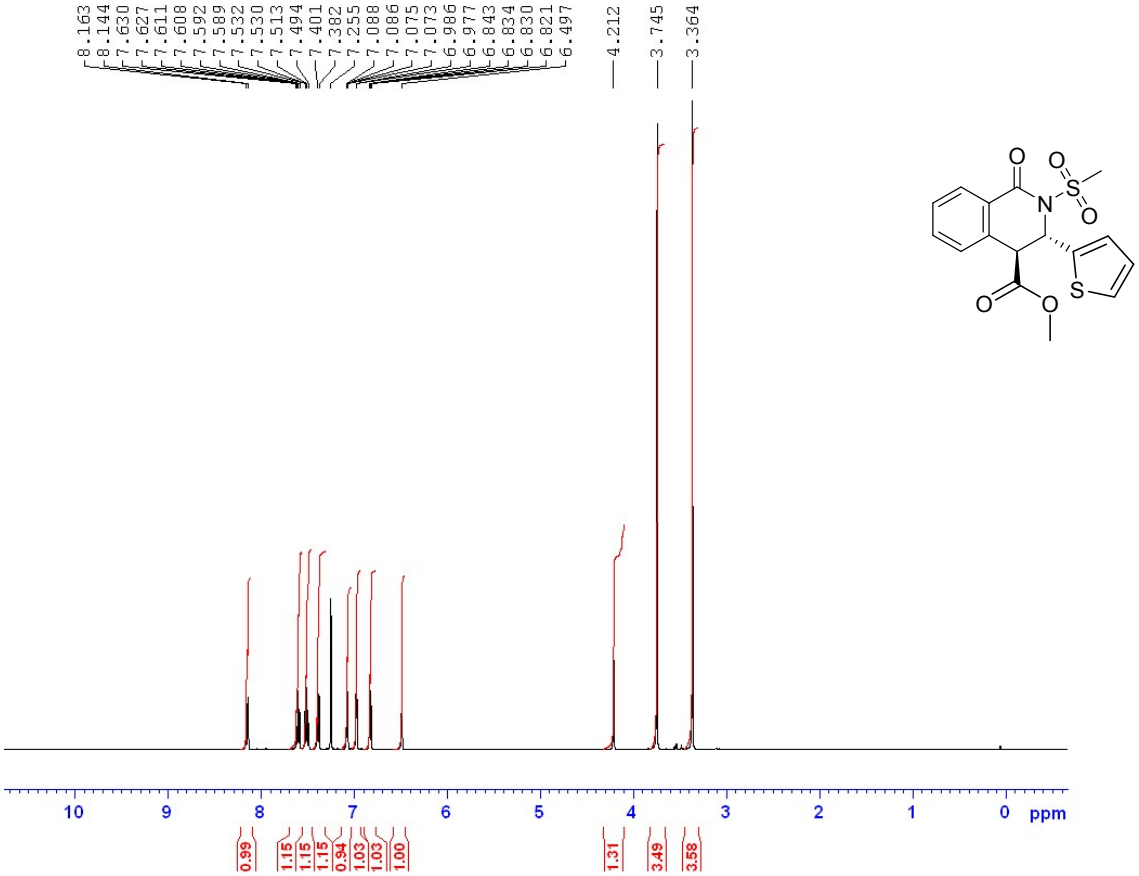


^{13}C NMR in $CDCl_3$ (100 MHz)

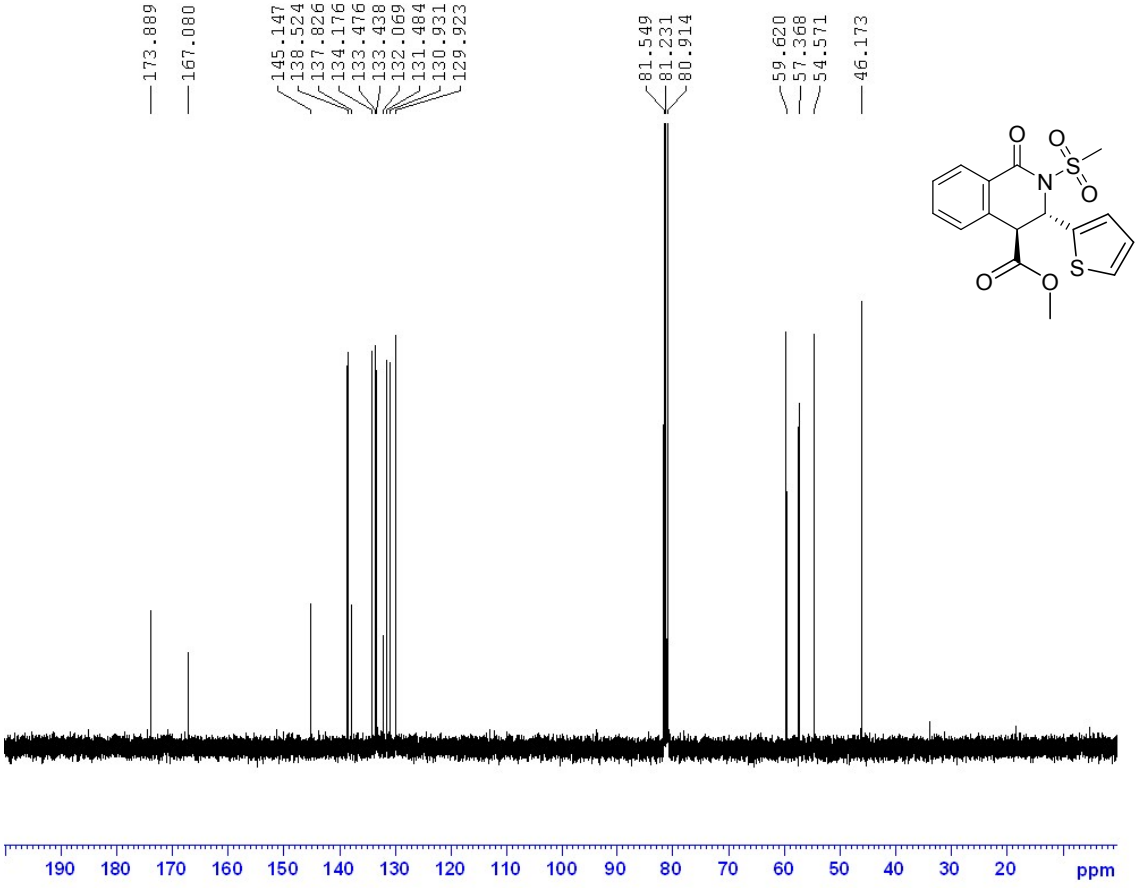


***anti*-Methyl-2-(methylsulfonyl)-1-oxo-3-(thiophen-2-yl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-52)**

^{1}H NMR in $CDCl_3$ (400 MHz)

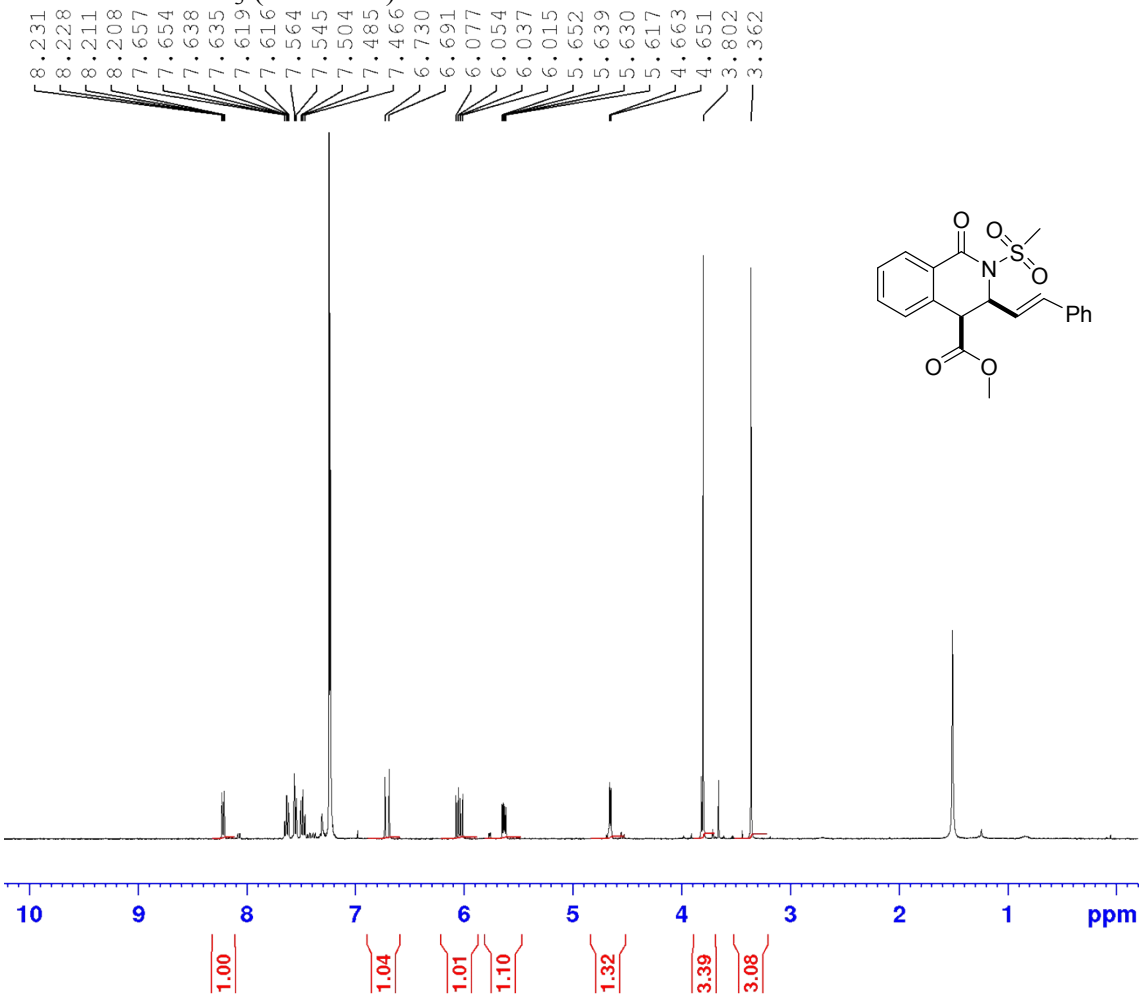


^{13}C NMR in $CDCl_3$ (100 MHz)

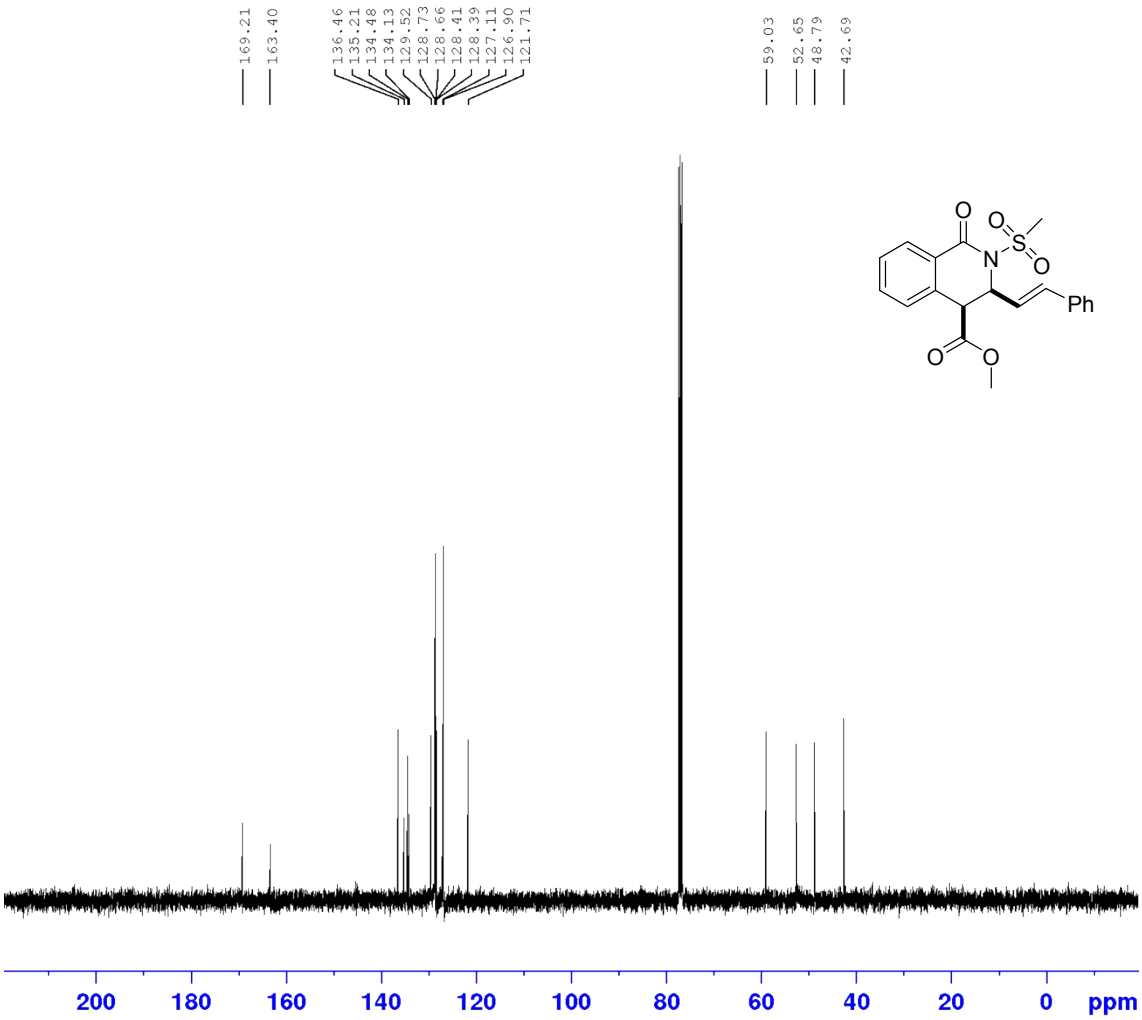


***syn*-Methyl 2-(methylsulfonyl)-1-oxo-3-((*E*)-styryl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-53)**

^{1}H NMR in $CDCl_3$ (400 MHz)

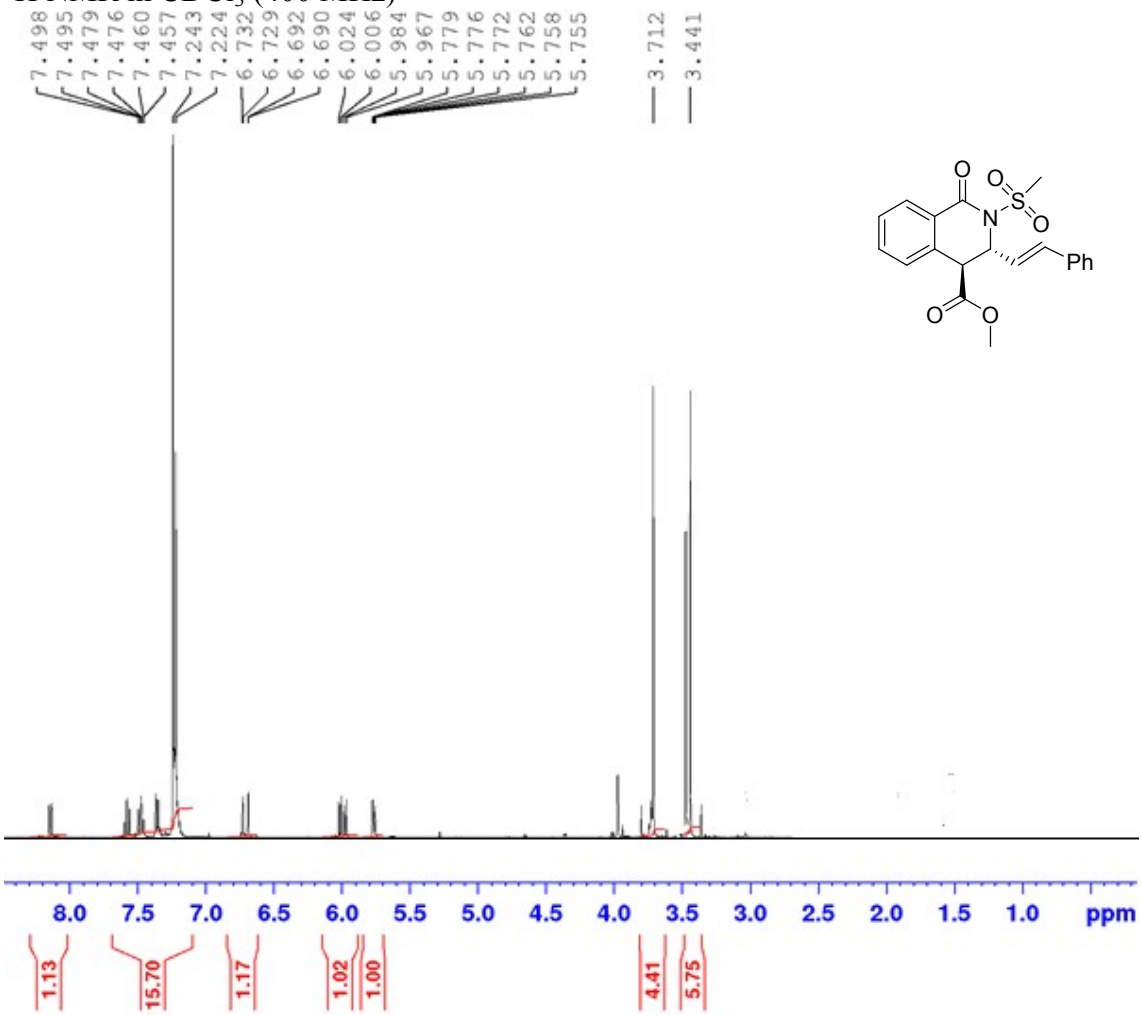


^{13}C NMR in $CDCl_3$ (100 MHz)

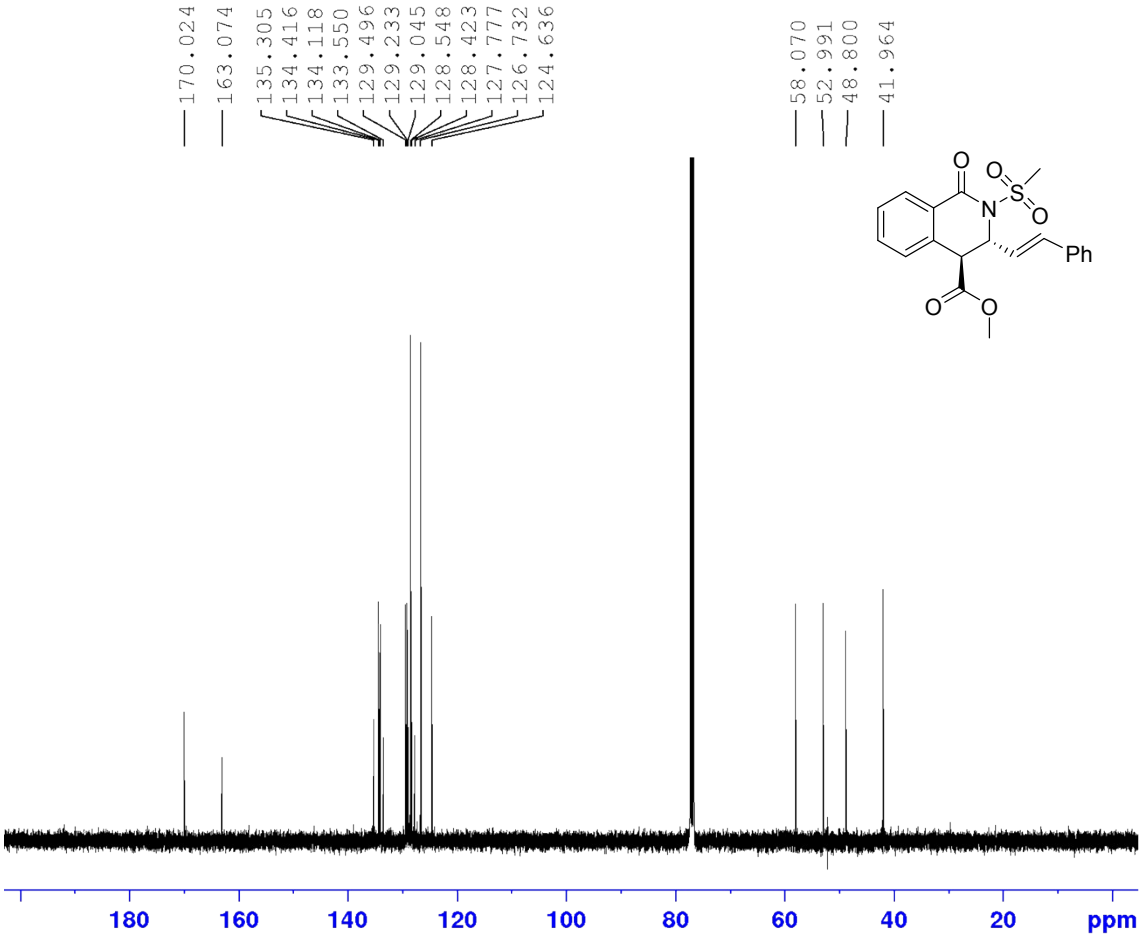


***anti*-Methyl 2-(methylsulfonyl)-1-oxo-3-((*E*)-styryl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-53)**

^{1}H NMR in $CDCl_3$ (400 MHz)

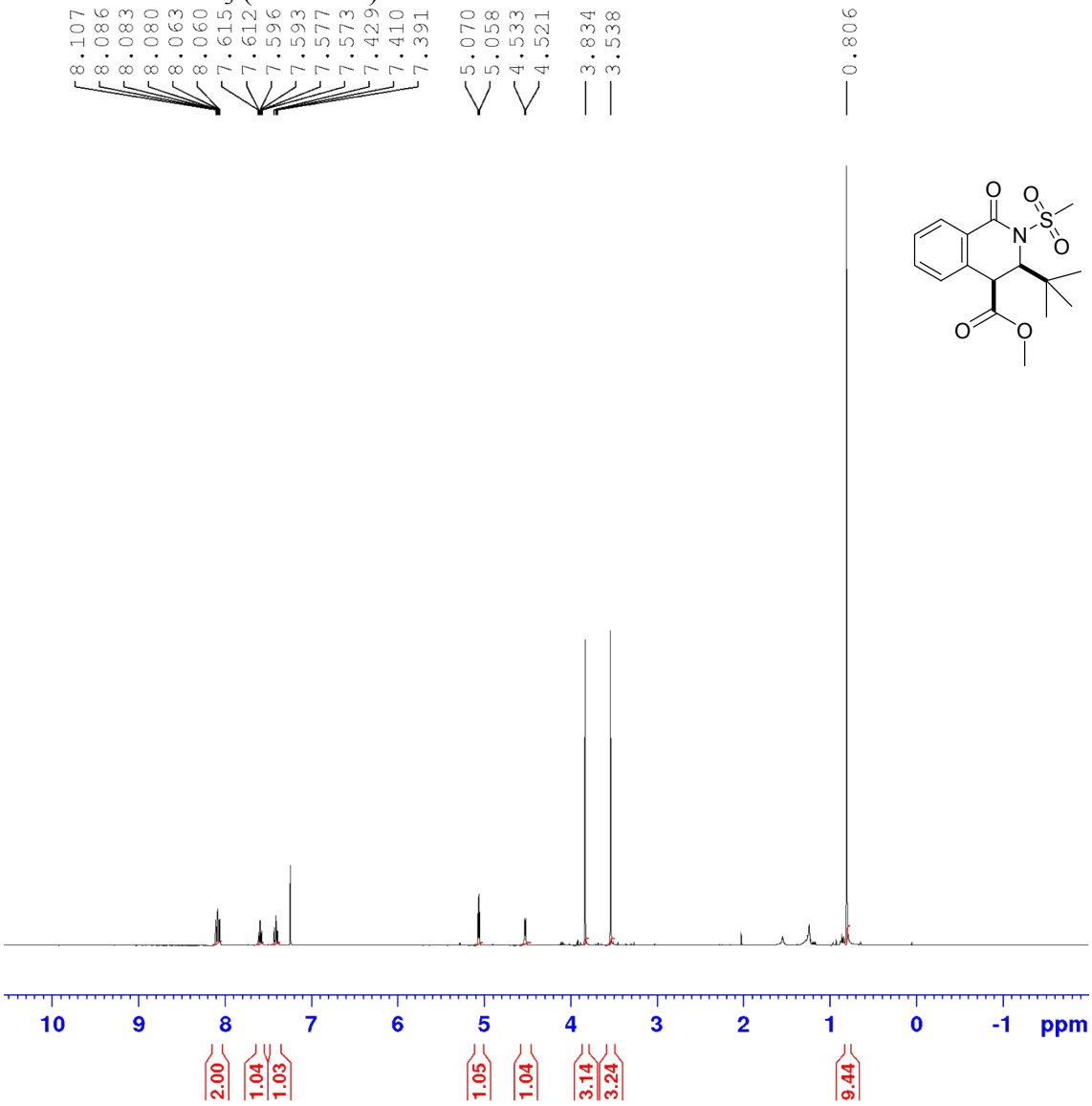


^{1}H NMR in $CDCl_3$ (400 MHz)

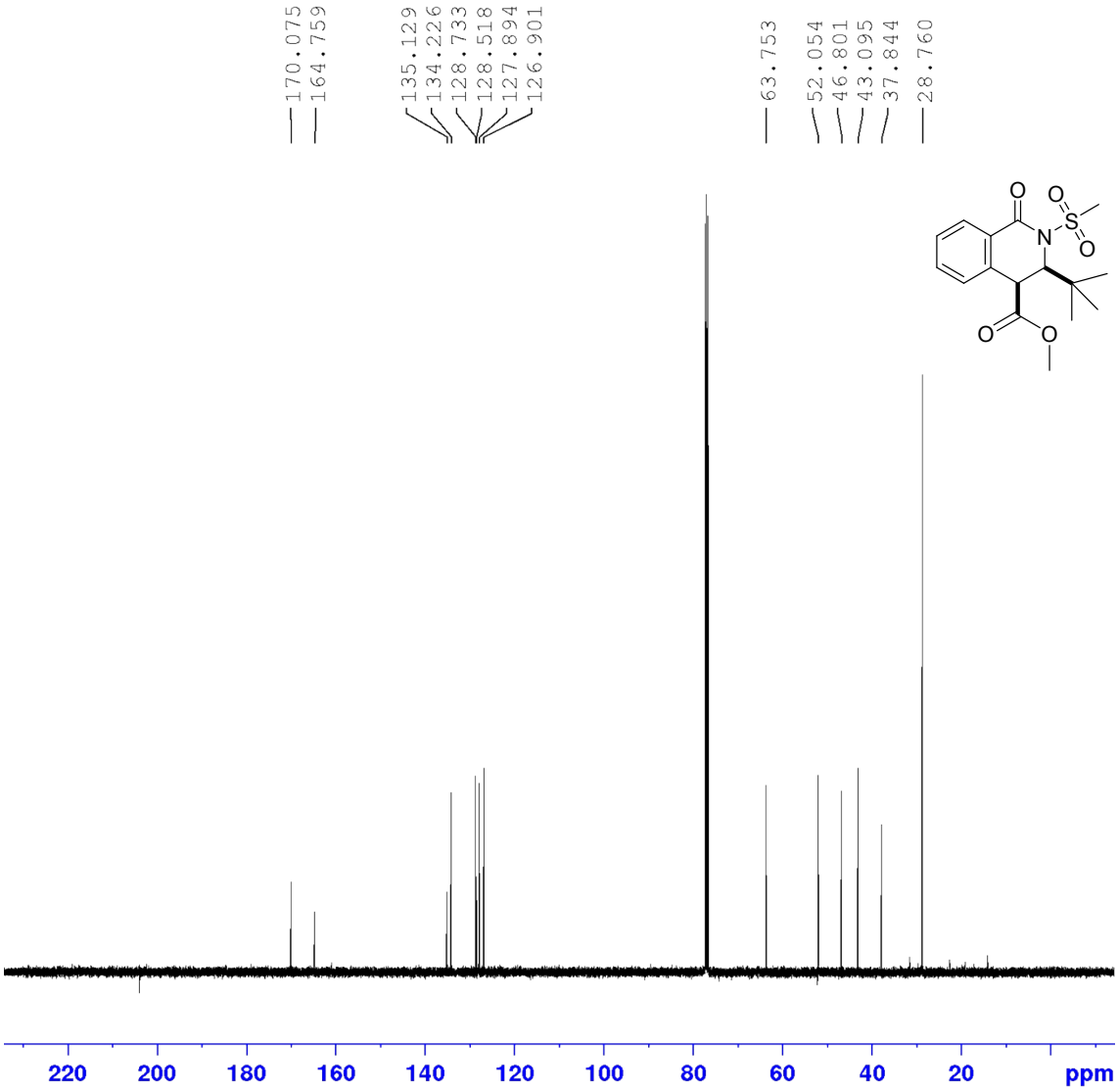


***syn*-Methyl 3-(*tert*-butyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*syn*-54)**

^{1}H NMR in $CDCl_3$ (400 MHz)

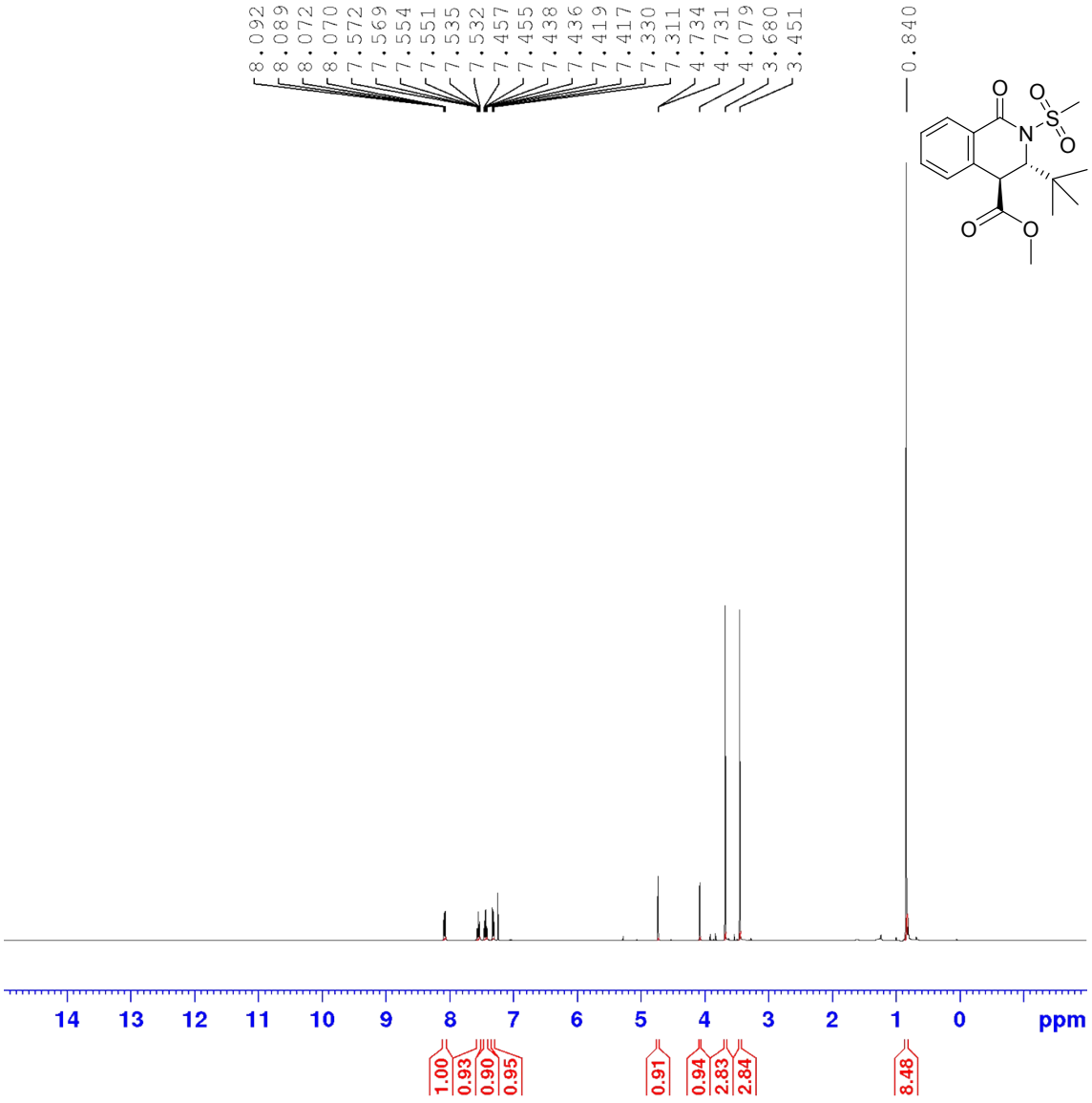


^{1}H NMR in $CDCl_3$ (400 MHz)

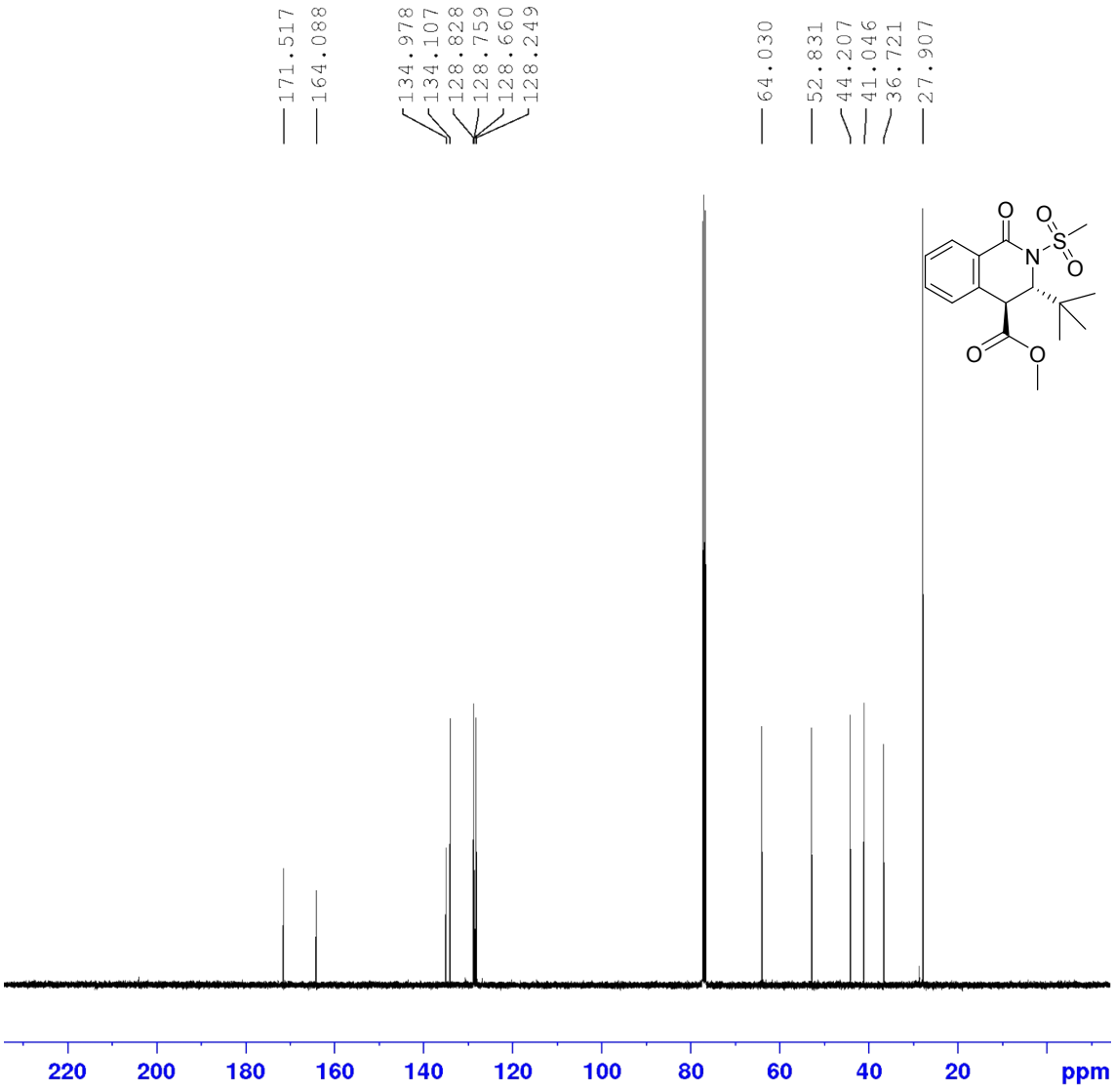


***anti*-Methyl 3-(*tert*-butyl)-2-(methylsulfonyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (*anti*-54)**

^{1}H NMR in $CDCl_3$ (400 MHz)



^{13}C NMR in $CDCl_3$ (100 MHz)



8. HPLC Chromatograms

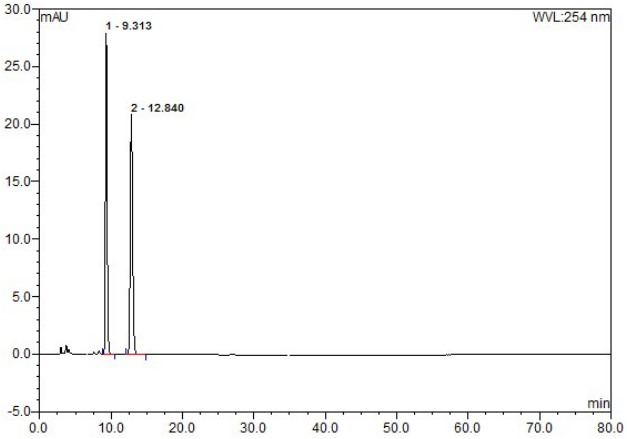
Resolved HPLC chromatogram for ***syn*-33** racemate

HPLC Chromatograms of ***syn*-33**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	9.31	49.00
2	12.84	51.00
Total:		100.00

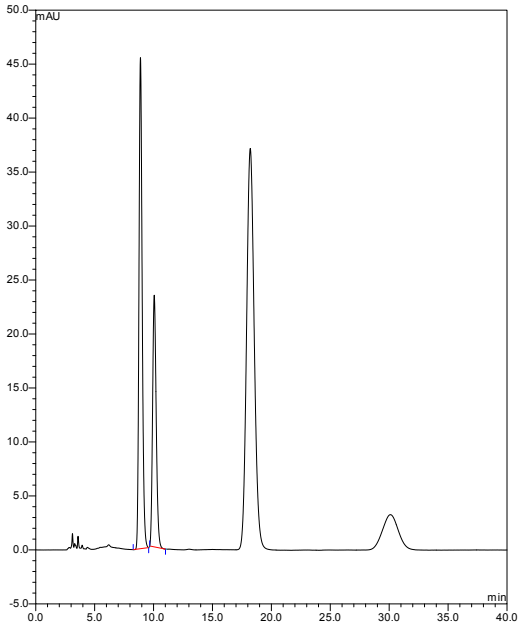
Resolved HPLC chromatogram for enantioenriched ***syn*-33**

HPLC Chromatograms of ***syn*-33**

Chiralcel AD (4.6 mm x 25 cm) cm),

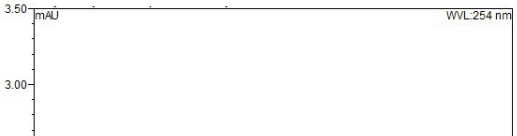
Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	8.88	64.55
2	10.06	35.45
Total:		100.00

Resolved HPLC chromatogram for ***anti*-33** racemate



HPLC Chromatograms of ***anti*-33**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.

No.	Ret.Time	Rel.Area
	min	%
1	18.47	49.94
2	30.35	50.06
Total:		100.00

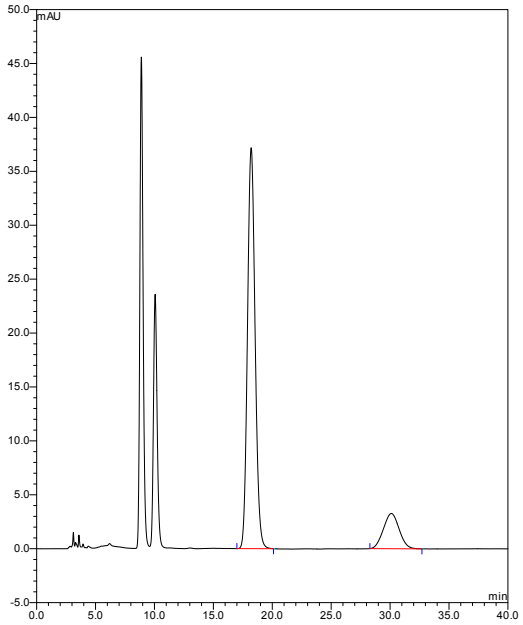
Resolved HPLC chromatogram for enantioenriched ***anti*-33**

HPLC Chromatograms of ***anti*-33**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	18.20	84.91
2	30.12	15.09
Total:		100.00

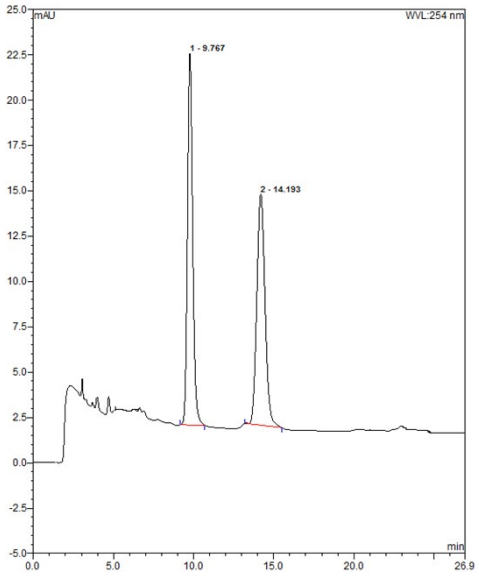
Resolved HPLC chromatograms for ***syn*-43** racemate

HPLC Chromatograms of ***syn*-43**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	9.76	50.92
2	14.19	49.08
Total:		100.00

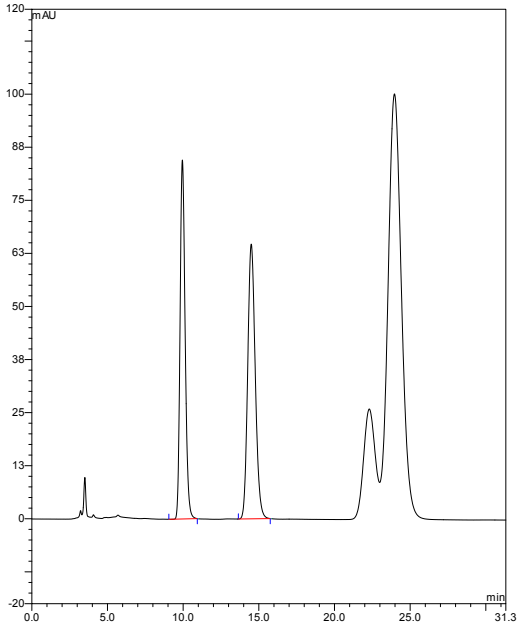
Resolved HPLC chromatograms for enantioenriched ***syn*-43**

HPLC Chromatograms of ***syn*-43**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 1.0 mL min^{-1},

RT, UV detectiom at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	9.95	46.81
2	14.50	53.19
Total:		100.00

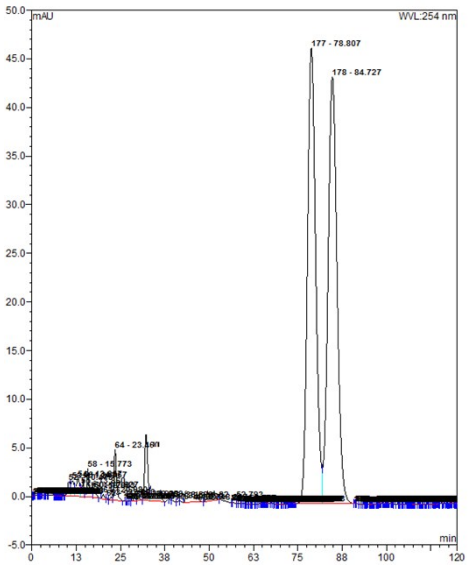
Resolved HPLC chromatograms for ***anti*-43** racemate

HPLC Chromatograms of ***anti*-43**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 0.3 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	68.81	48.95
2	84.73	51.05
Total:		100.00

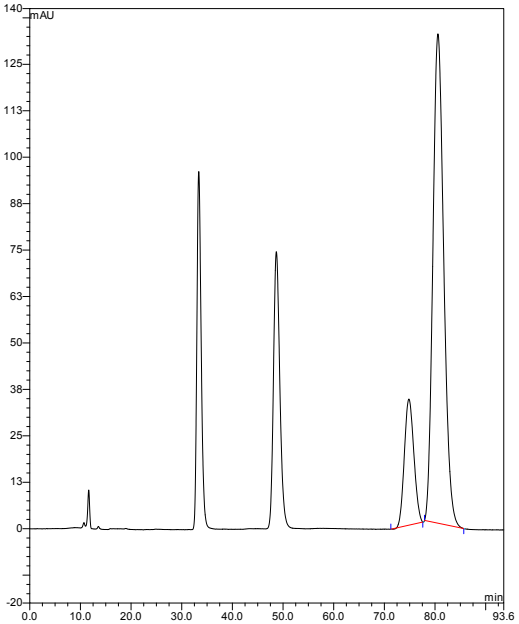
Resolved HPLC chromatograms for enantioenriched ***anti*-43**

HPLC Chromatograms of ***anti*-43**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 0.3 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	74.84	18.24
2	80.57	81.76
Total:		100.00

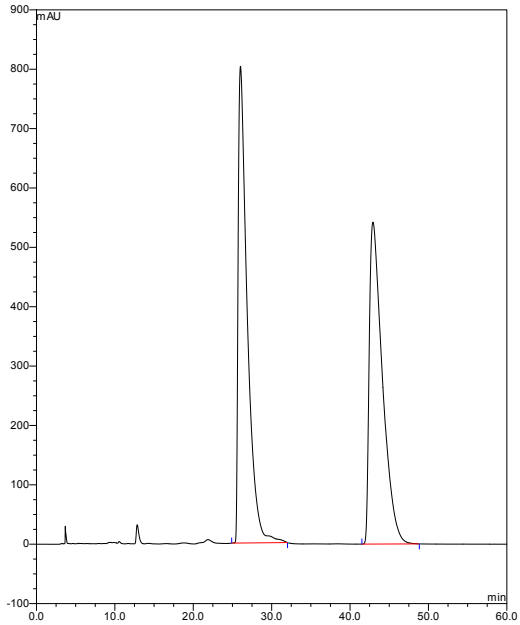
Resolved HPLC chromatogram for ***syn*-44** racemate

HPLC Chromatograms of ***syn*-44**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	26.02	50.66
2	42.92	49.34
Total:		100

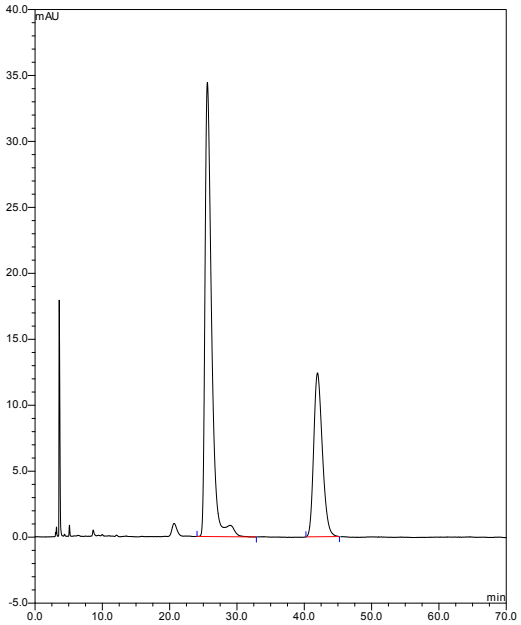
Resolved HPLC chromatogram for enantioenriched ***syn*-44**

HPLC Chromatograms of ***syn*-44**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	26.61	34.42
2	41.98	32.08
Total:		100

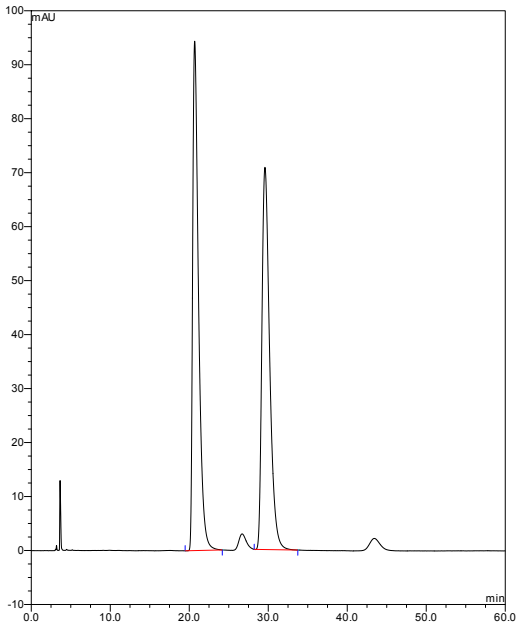
Resolved HPLC chromatogram for ***anti*-44** racemate

HPLC Chromatograms of ***anti*-44**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.68	50.27
2	29.58	49.73
Total:		100

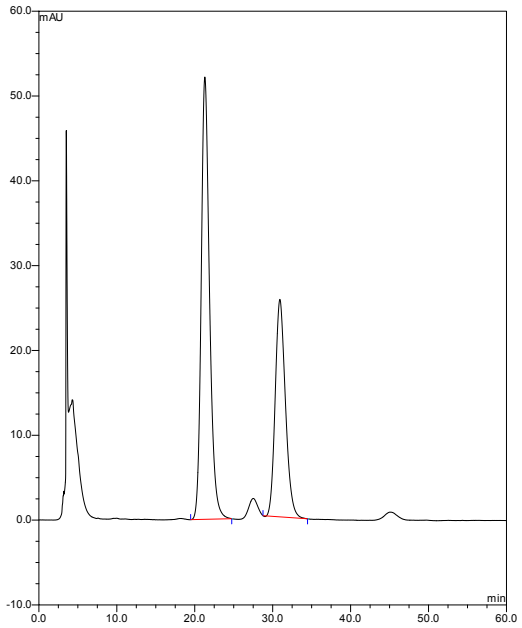
Resolved HPLC chromatogram for enantioenriched ***anti*-44**

HPLC Chromatograms of ***anti*-44**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	21.30	62.32
2	30.93	37.68
Total:		100

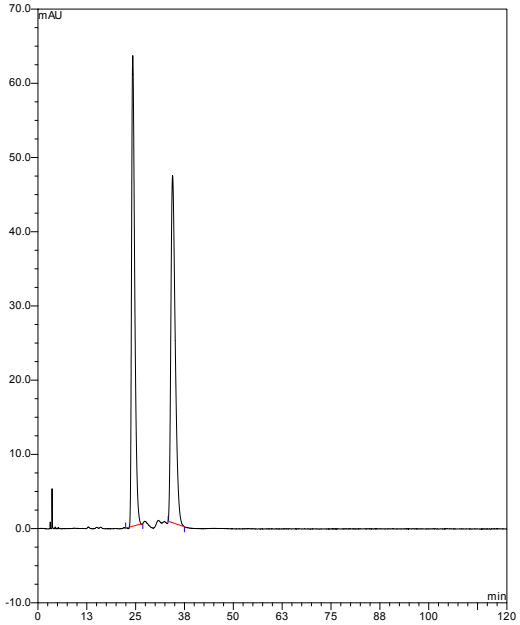
Resolved HPLC chromatogram for ***syn*-45** racemate

HPLC Chromatograms of ***syn*-45**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	24.27	49.59
2	34.46	50.41
Total:		100

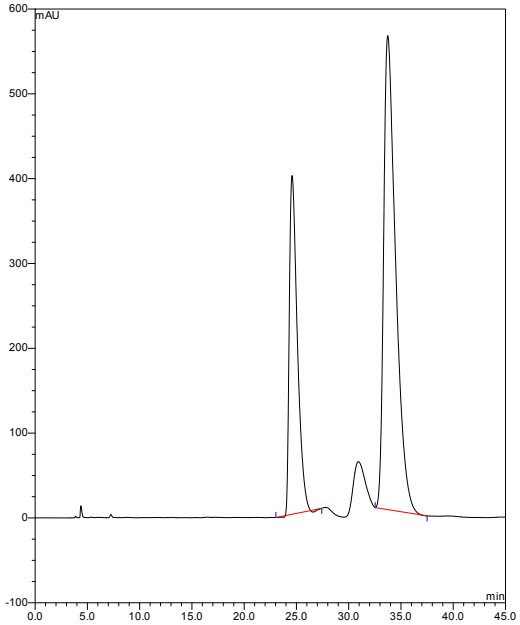
Resolved HPLC chromatogram for enantioenriched ***syn*-45**

HPLC Chromatograms of ***syn*-45**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	24.58	32.23
2	33.74	67.77
Total:		100

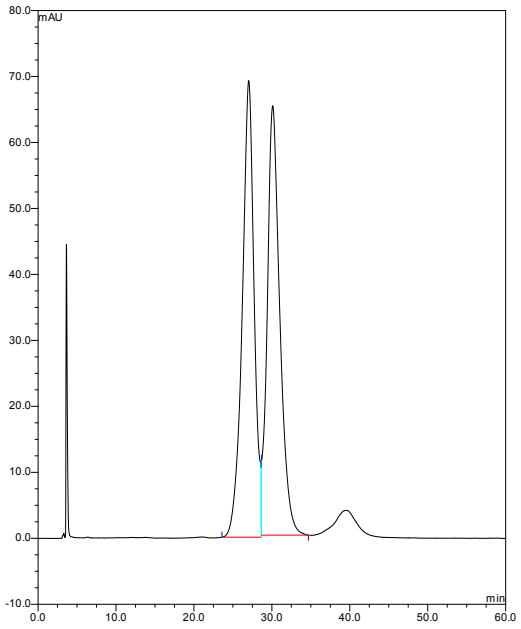
Resolved HPLC chromatogram for ***anti*-45** racemate

HPLC Chromatograms of ***anti*-45**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	27.03	50.50
2	30.11	49.95
Total:		100

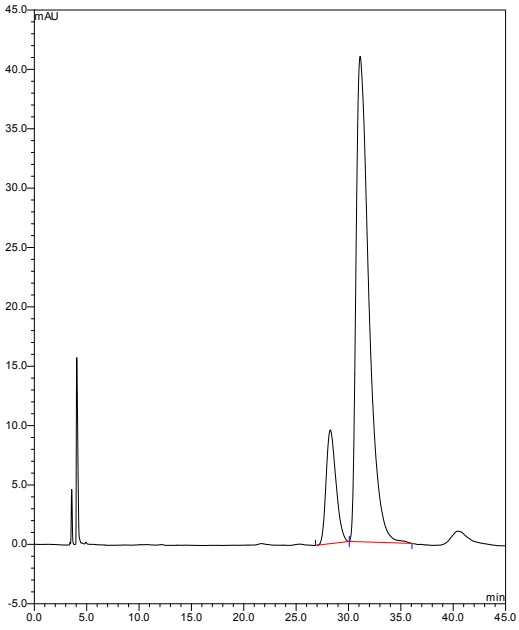
Resolved HPLC chromatogram for enantioenriched ***anti*-45**

HPLC Chromatograms of ***anti*-45**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	28.26	15.23
2	31.11	84.77
Total:		100

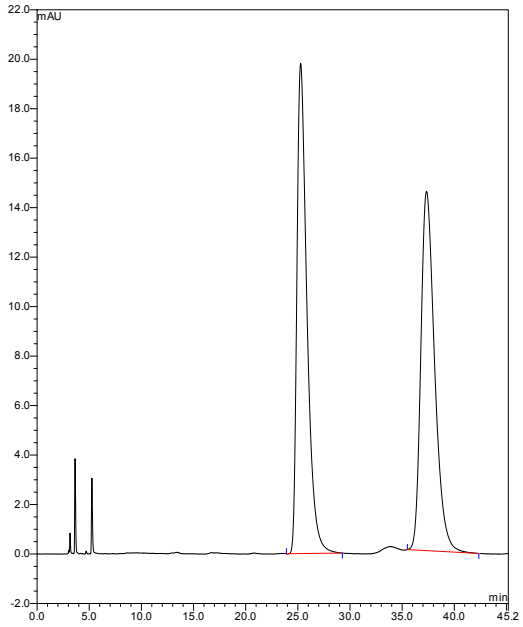
Resolved HPLC chromatogram for ***syn*-46** racemate

HPLC Chromatograms of ***syn*-46**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	25.26	49.81
2	37.32	50.19
Total:		100

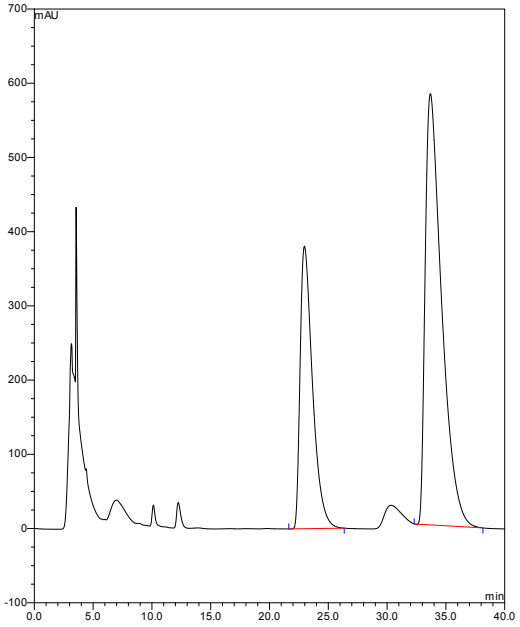
Resolved HPLC chromatogram for enantioenriched ***syn*-46**

HPLC Chromatograms of ***syn*-46**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	22.97	33.03
2	33.68	66.97
Total:		100

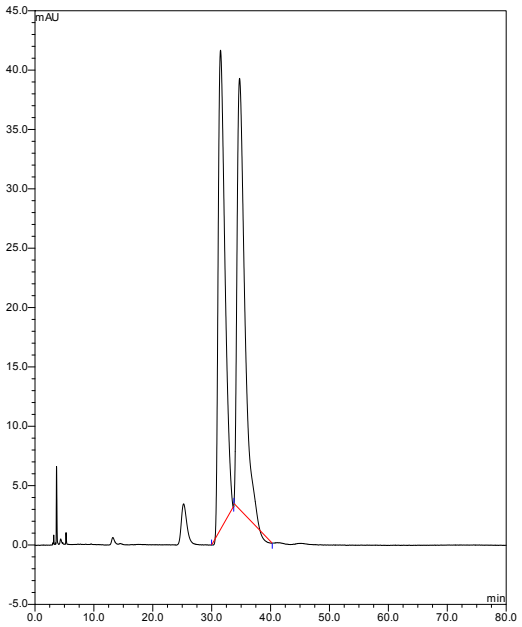
Resolved HPLC chromatogram for ***anti*-46** racemate

HPLC Chromatograms of ***anti*-46**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	31.50	49.43
2	34.73	50.57
Total:		100

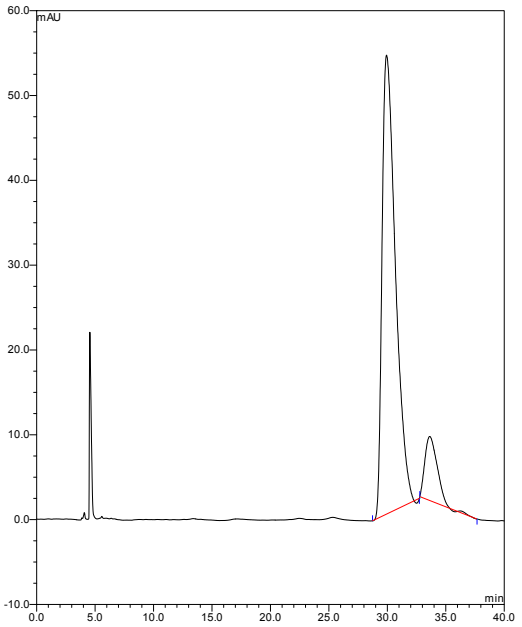
Resolved HPLC chromatogram for enantioenriched ***anti*-46**

HPLC Chromatograms of ***anti*-46**

Chiralcel ODH (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	29.92	88.45
2	33.62	11.55
Total:		100

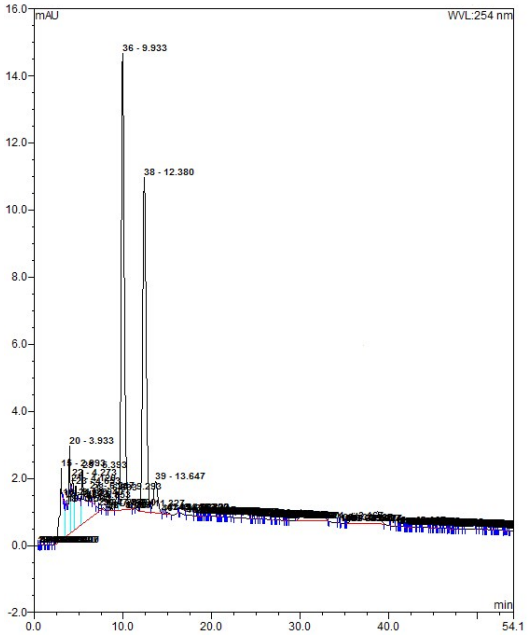
Resolved HPLC chromatogram for ***syn*-47** racemate

HPLC Chromatograms of ***syn*-47**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	9.93	52.90
2	12.38	47.10
Total:		100.00

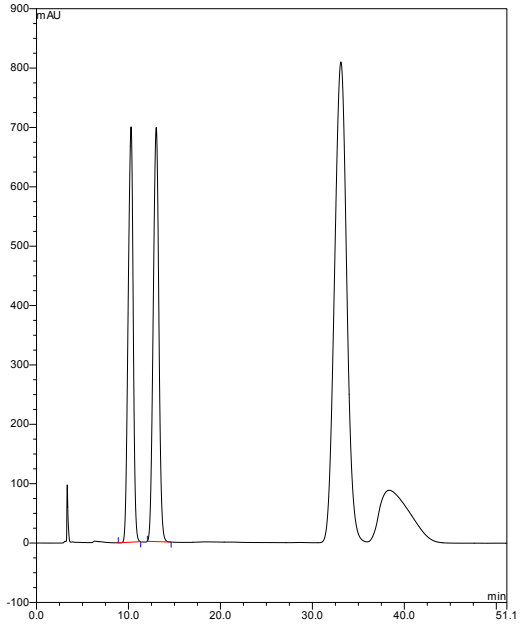
Resolved HPLC chromatogram for enantioenriched ***syn*-47**

HPLC Chromatograms of ***syn*-47**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	10.45	47.76
2	13.15	52.24
Total:		100

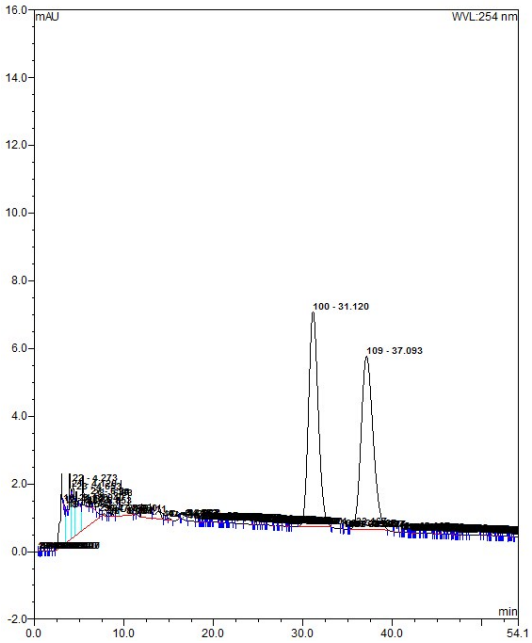
Resolved HPLC chromatogram for ***anti*-47** racemate

HPLC Chromatograms of ***anti*-47**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	31.12	50.72
2	37.09	49.28
Total:		100.00

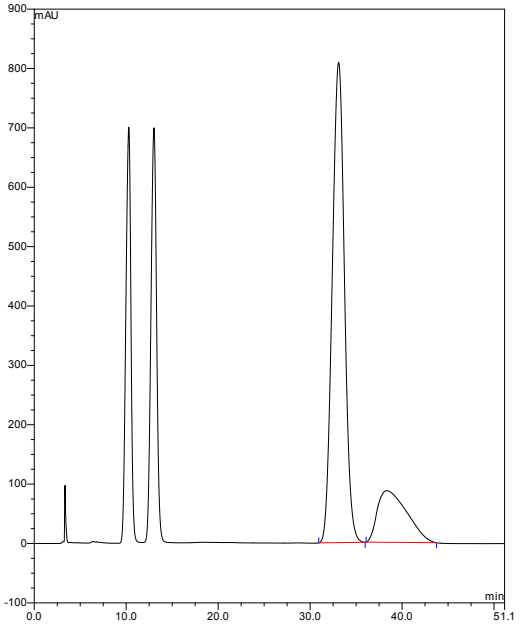
Resolved HPLC chromatogram for enantioenriched ***anti*-47**

HPLC Chromatograms of ***anti*-47**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 70/30, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	32.76	80.25
2	37.49	19.75
Total:		100

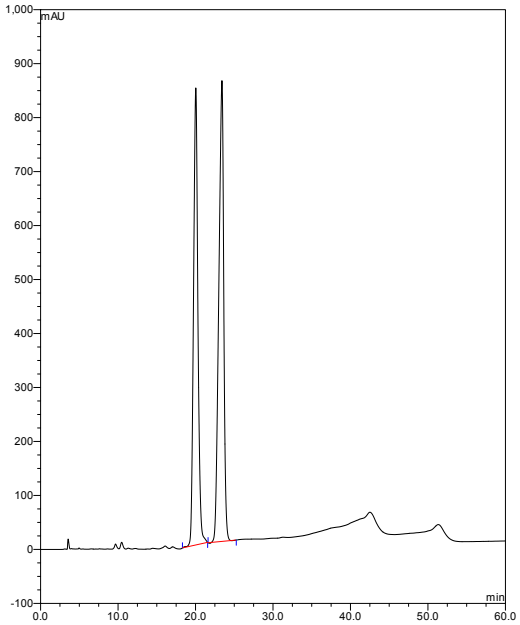
Resolved HPLC chromatogram for ***syn*-48** racemate

HPLC Chromatograms of ***syn*-48**

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.03	46.96
2	23.41	53.04
Total:		100

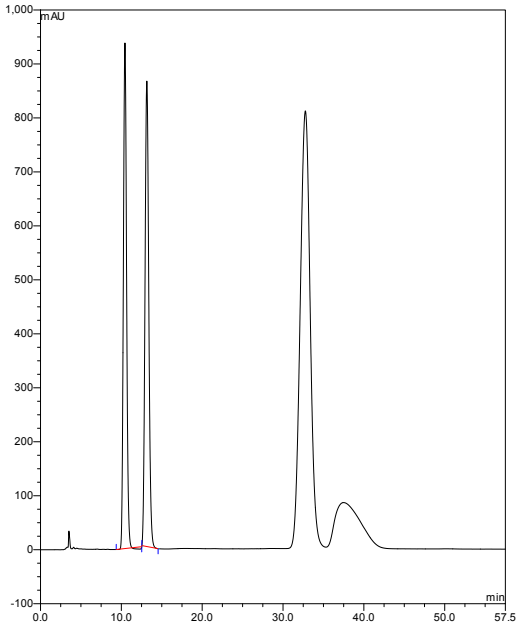
Resolved HPLC chromatogram for enantioenriched ***syn*-48**

HPLC Chromatograms of ***syn*-48**

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.21	52.26
2	23.43	47.74
Total:		100

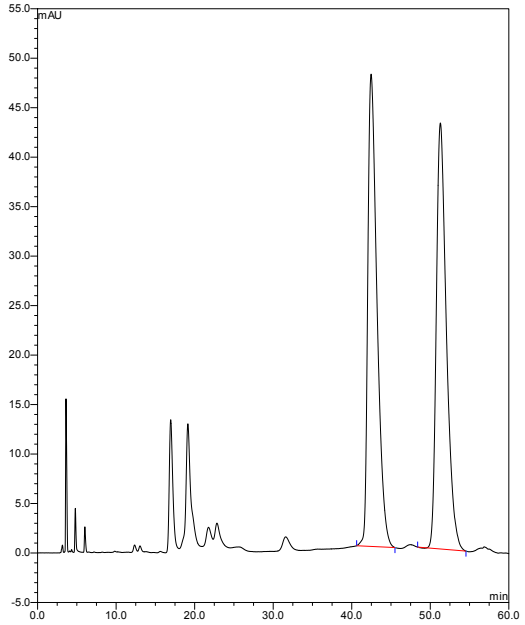
Resolved HPLC chromatogram for ***anti*-48** racemate

HPLC Chromatograms of ***anti*-48**

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	42.47	50.22
2	51.28	49.78
Total:		100

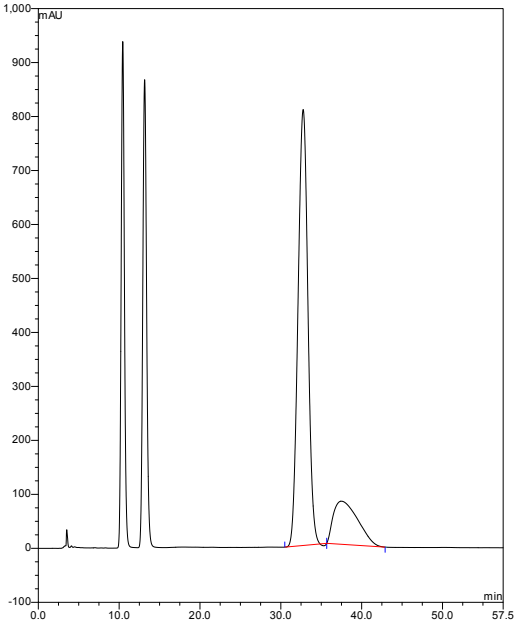
Resolved HPLC chromatogram for enantioenriched ***anti*-48**

HPLC Chromatograms of ***anti*-48**

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	43.73	83.87
2	53.28	16.13
Total:		100

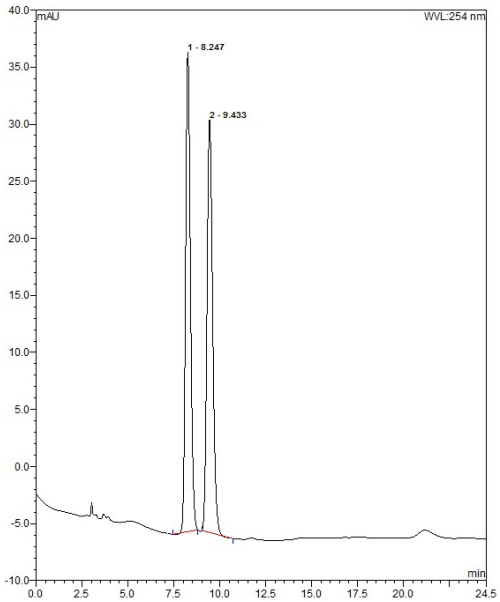
Resolved HPLC chromatogram for ***syn*-49** racemate

HPLC Chromatograms of ***syn*-49**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 1.0 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	8.25	50.05
2	9.43	49.95
Total:		100.00

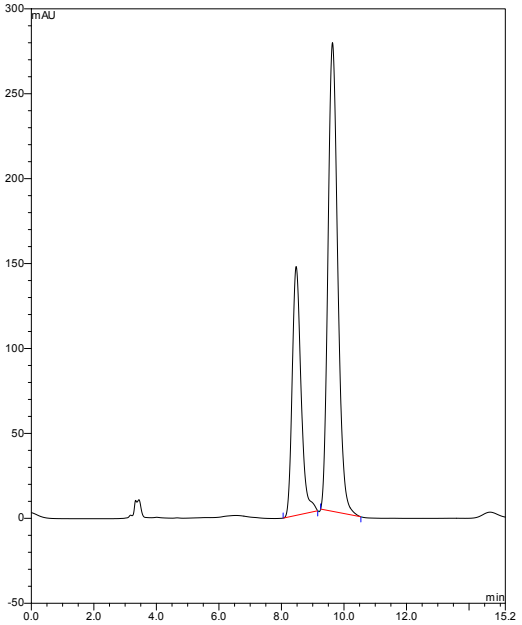
Resolved HPLC chromatogram for enantioenriched ***syn*-49**

HPLC Chromatograms of ***syn*-49**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	8.47	32.42
2	9.63	67.58
Total:		100.00

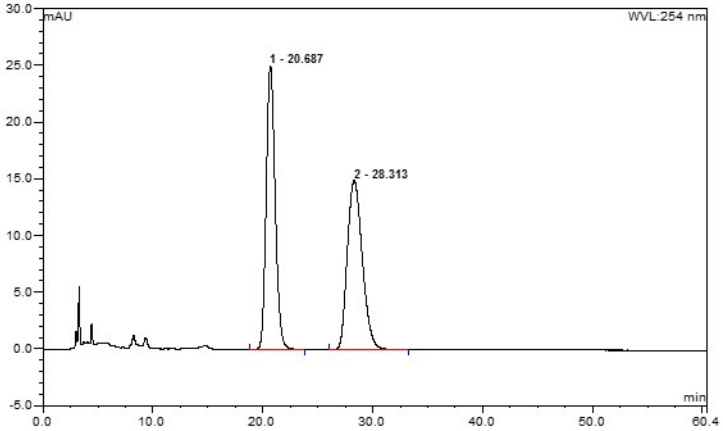
Resolved HPLC chromatograms for ***anti*-49** racemate

HPLC Chromatograms of ***anti*-49**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.69	49.94
2	28.31	50.06
Total:		100.00

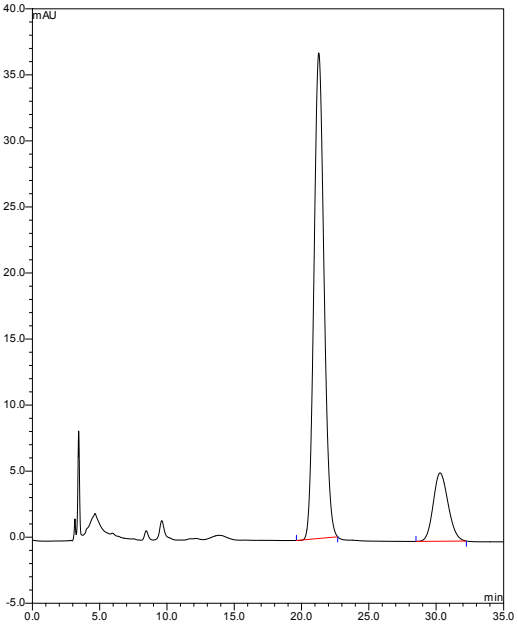
Resolved HPLC chromatogram for enantioenriched ***anti*-49**

HPLC Chromatograms of ***anti*-49**

Chiralcel AD (4.6 mm x 25 cm),

Hexane/IPA: 60/40, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	21.28	82.74
2	30.30	17.26
Total:		100.00

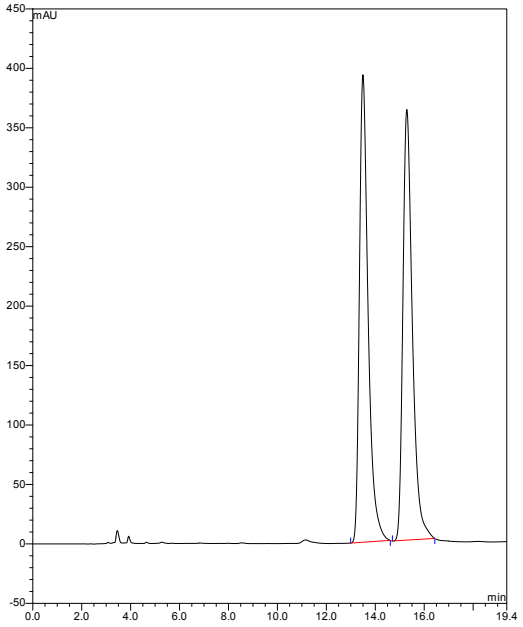
Resolved HPLC chromatograms for ***syn*-50** racemate

HPLC chromatograms of ***syn*-50**

Chiralcel IA (4.6mm x 25 cm),

Hexane/IPA: 80/20, 1 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	13.49	49.97
2	15.29	50.03
Total:		100.00

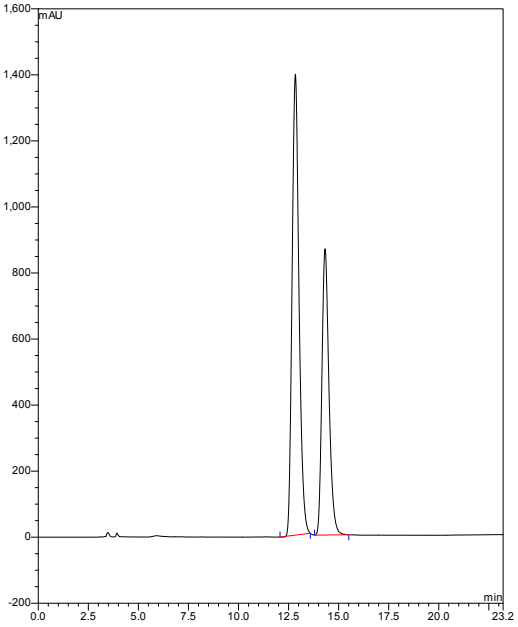
Resolved HPLC chromatograms for enantioenriched ***syn*-50**

HPLC chromatograms of ***syn*-50**

Chiralcel IA (4.6mm x 25 cm),

Hexane/IPA: 80/20, 1 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	12.84	61.24
2	14.32	38.76
Total:		100.00

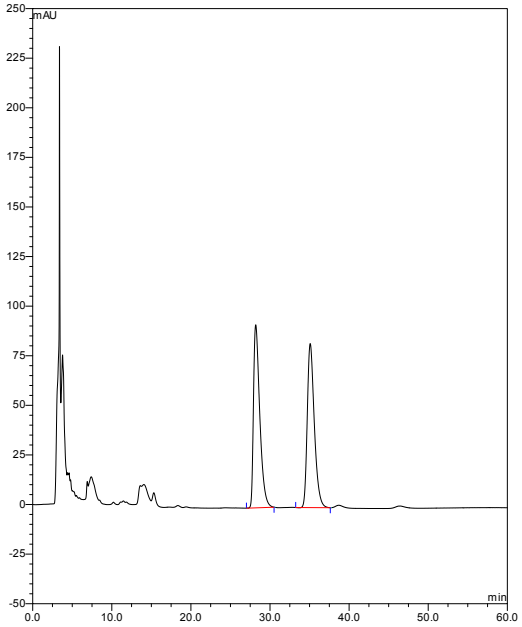
Resolved HPLC Chromatograms for ***anti*-50** racemate

HPLC Chromatograms of ***anti*-50**

Chiralcel IA (4.6mm x 25 cm),

Hexane/IPA: 80/20, 1 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	28.19	50.01
2	35.08	49.99
Total:		100.00

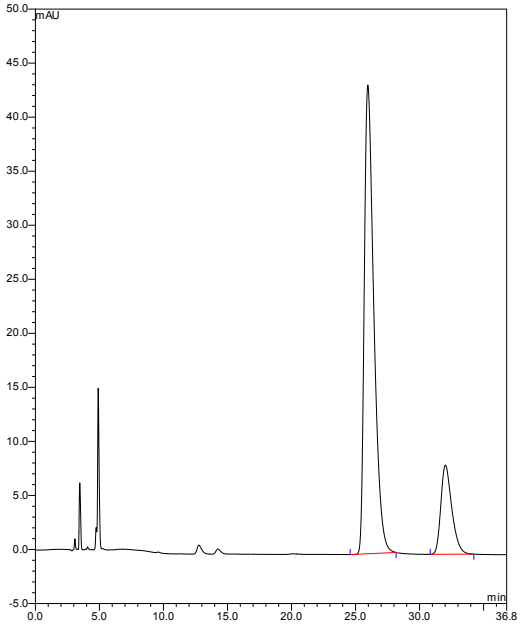
Resolved HPLC chromatogram for enantioenriched ***anti*-50**

HPLC Chromatograms of ***anti*-50**

Chiralcel IA (4.6mm x 25 cm),

Hexane/IPA: 80/20, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	25.76	83.25
2	32.03	16.75
Total:		100.00

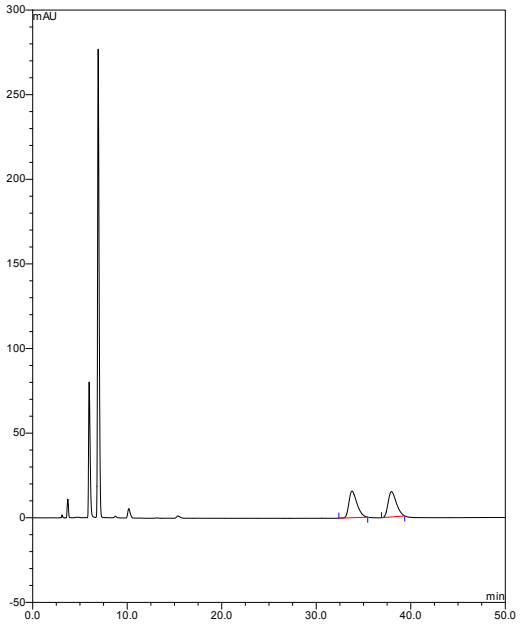
Resolved HPLC chromatograms for ***syn*-51** racemate

HPLC chromatograms of ***syn*-51**,

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 95/5, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	33.79	50.94
2	37.96	49.06
Total:		100.00

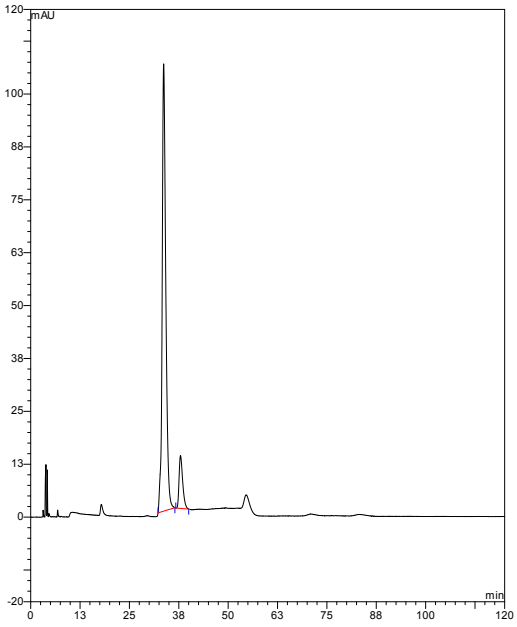
Resolved HPLC chromatograms for enantioenriched ***syn*-51**

HPLC chromatograms of ***syn*-51**,

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 95/5, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	33.67	89.49
2	37.93	10.51
Total:		100.00

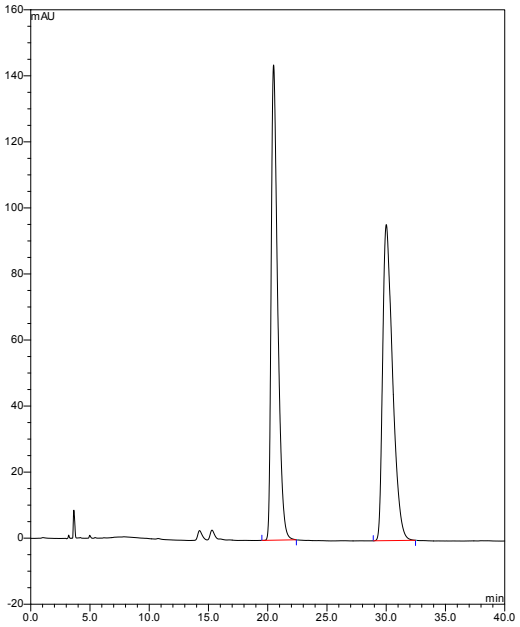
Resolved HPLC chromatograms for ***anti*-51** racemate

HPLC chromatograms of ***anti*-51**

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 85/15, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.49	49.65
2	30.01	50.35
Total:		100.00

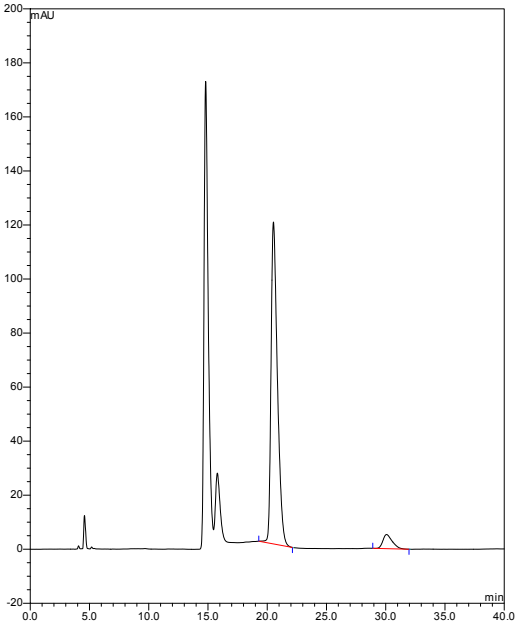
Resolved HPLC chromatograms for enantioenriched ***anti*-51**

HPLC chromatograms of ***anti*-51**

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 85/15, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.53	93.91
2	30.07	6.09
Total:		100.00

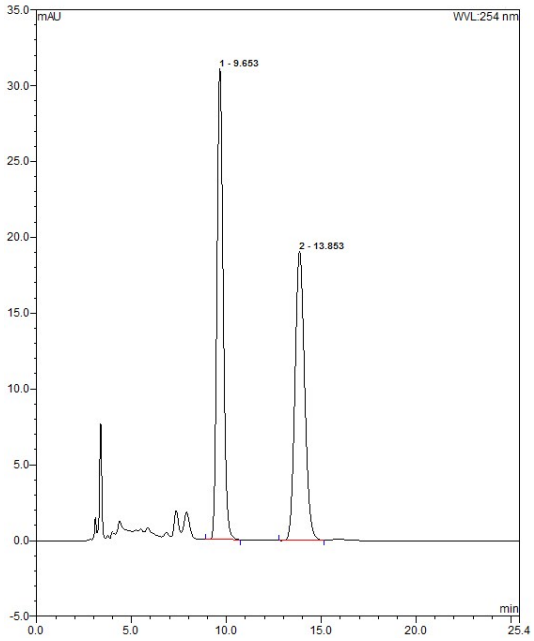
Resolved HPLC chromatogram for ***syn*-52** racemate

HPLC Chromatograms of ***syn*-52**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 95/5, 1.0 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	9.65	51.16
2	13.85	48.84
Total:		100

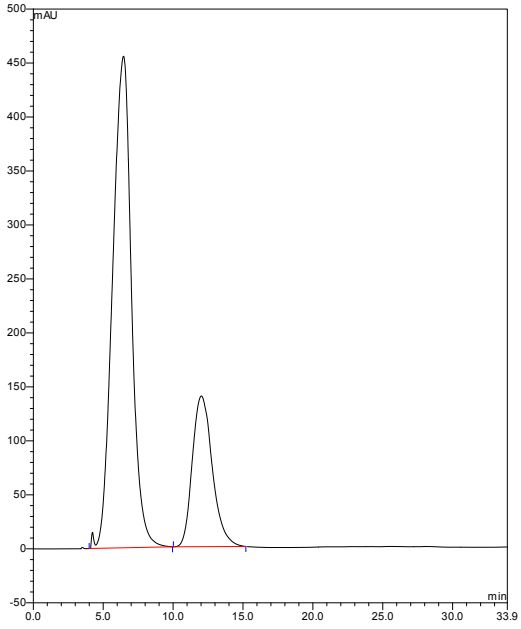
Resolved HPLC chromatogram for enantioenriched ***syn*-52**

HPLC Chromatograms of ***syn*-52**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 95/5, 1.0 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	6.45	75.47
2	12.04	24.53
Total:		100

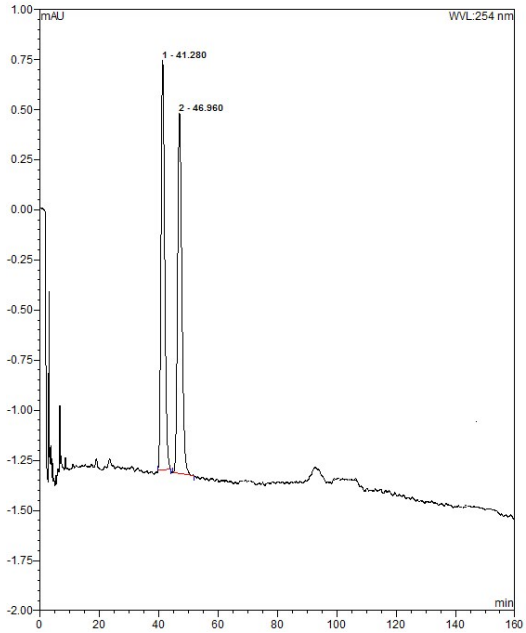
Resolved HPLC chromatogram for ***anti*-52** racemate

HPLC Chromatograms of ***anti*-52**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 95/5, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	41.28	49.62
2	46.96	50.38
Total:		100.00

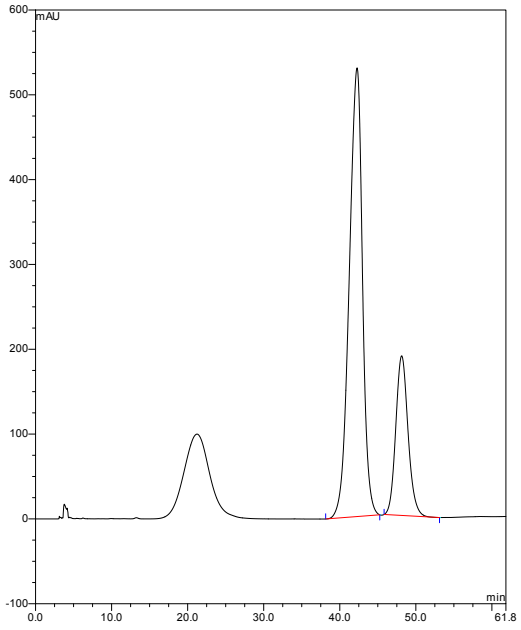
Resolved HPLC chromatogram for enantioenriched ***anti*-52**

HPLC Chromatograms of ***anti*-52**

Chiralcel AD (4.6 mm x 25 cm) cm),

Hexane/IPA: 95/5, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	42.27	75.10
2	48.15	24.90
Total:		100

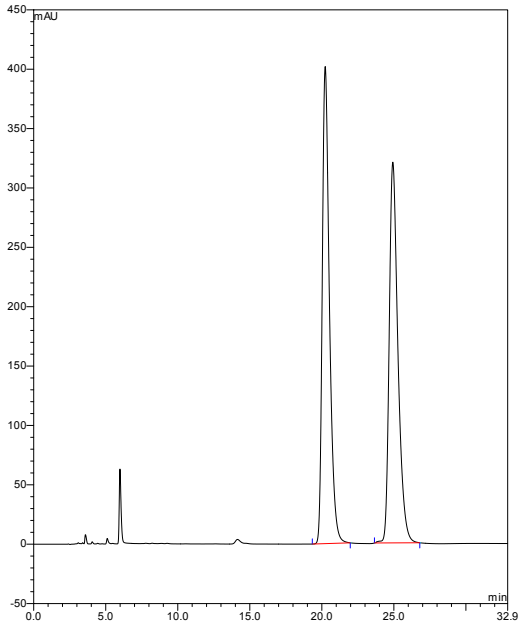
Resolved HPLC chromatogram for ***syn-53*** racemate

HPLC Chromatograms of ***syn-53***

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	20.23	50.68
2	24.93	49.32
Total:		100

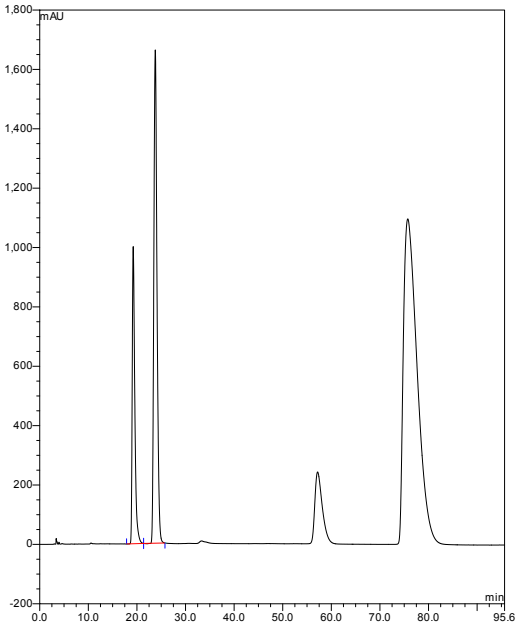
Resolved HPLC chromatogram for enantioenriched ***syn-53***

HPLC Chromatograms of ***syn-53***

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	19.24	32.43
2	23.78	67.57
Total:		100

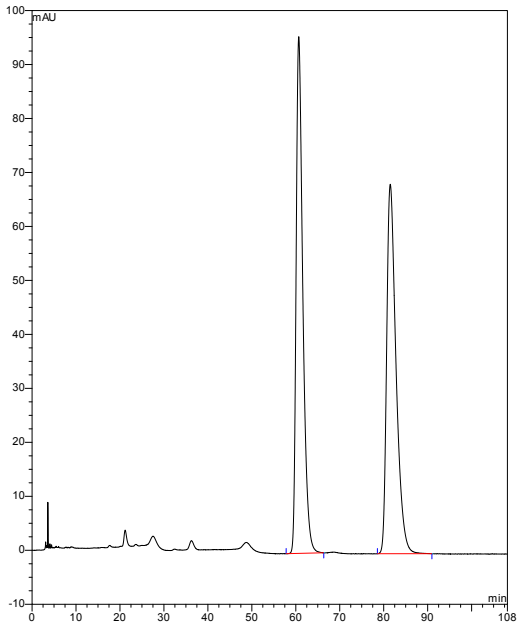
Resolved HPLC chromatogram for ***anti-53*** racemate

HPLC Chromatograms of ***anti-53***

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	60.67	50.01
2	81.49	49.99
Total:		100

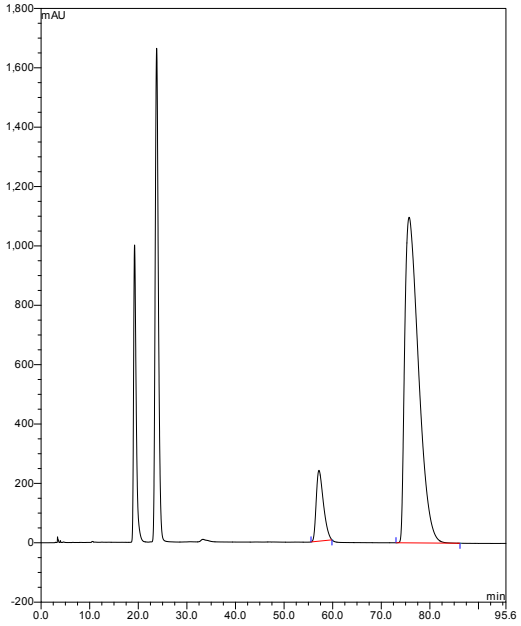
Resolved HPLC chromatogram for enantioenriched ***anti-53***

HPLC Chromatograms of ***anti-53***

Chiralcel IA (4.6 mm x 25 cm) cm),

Hexane/IPA: 90/10, 1.0 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	57.18	10.16
2	75.73	89.84
Total:		100

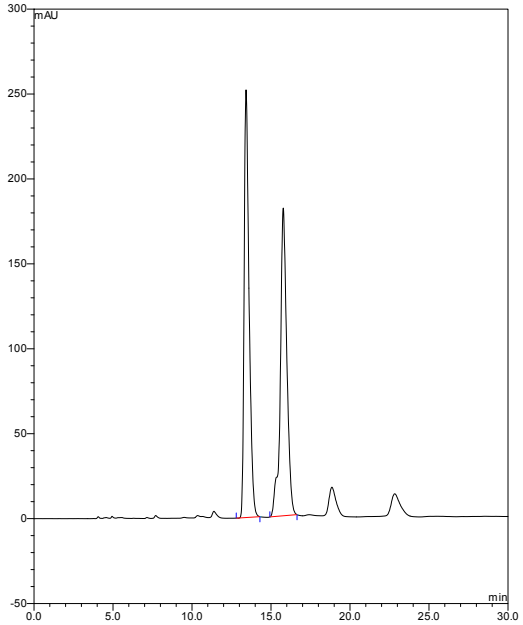
Resolved HPLC chromatograms for ***syn*-54**

HPLC chromatograms of ***syn*-54**

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 90/10, 1 mL min^{-1}

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	13.42	51.31
2	15.77	48.69
Total:		100.00

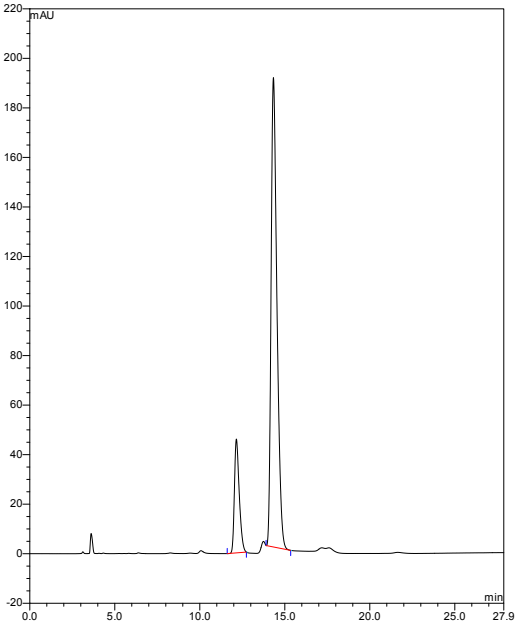
Resolved HPLC chromatograms for enantioenriched ***syn*-54**

HPLC chromatograms of ***syn*-54**

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 90/10, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	%
1	12.15	16.65
2	14.33	83.35
Total:		100.00

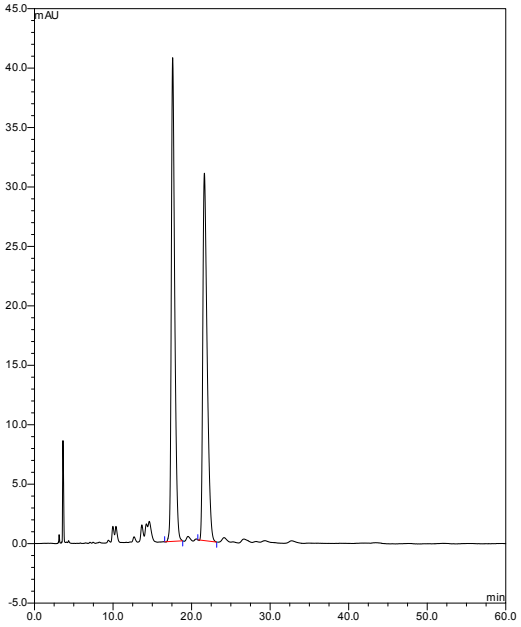
Resolved HPLC chromatograms for ***anti*-54**

HPLC chromatograms of ***anti*-54**

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 90/10, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	**%**
1	17.59	50.97
2	21.63	49.03
Total:		100.00

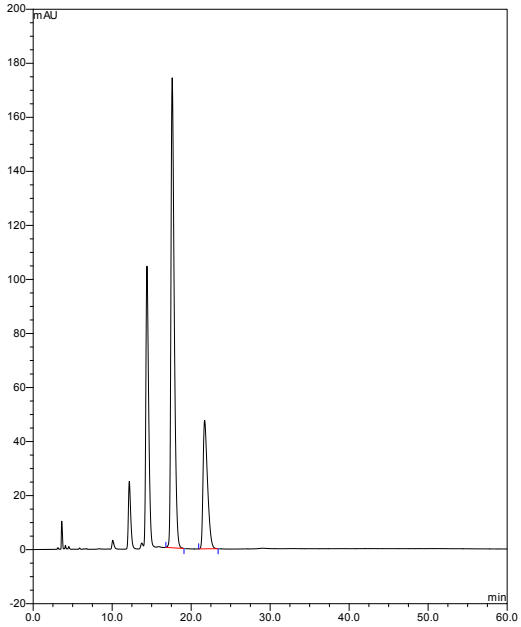
Resolved HPLC chromatograms for enantioenriched ***anti*-54**

HPLC chromatograms of ***anti*-54**

Chiralcel IA (4.6 mm x 25 cm),

Hexane/IPA: 90/10, 1 mL min^{-1},

RT, UV detection at 254 nm.



No.	Ret.Time	Rel.Area
	min	**%**
1	17.60	73.09
2	21.71	26.91
Total:		100.00

9. Crystal structure of *anti*-47

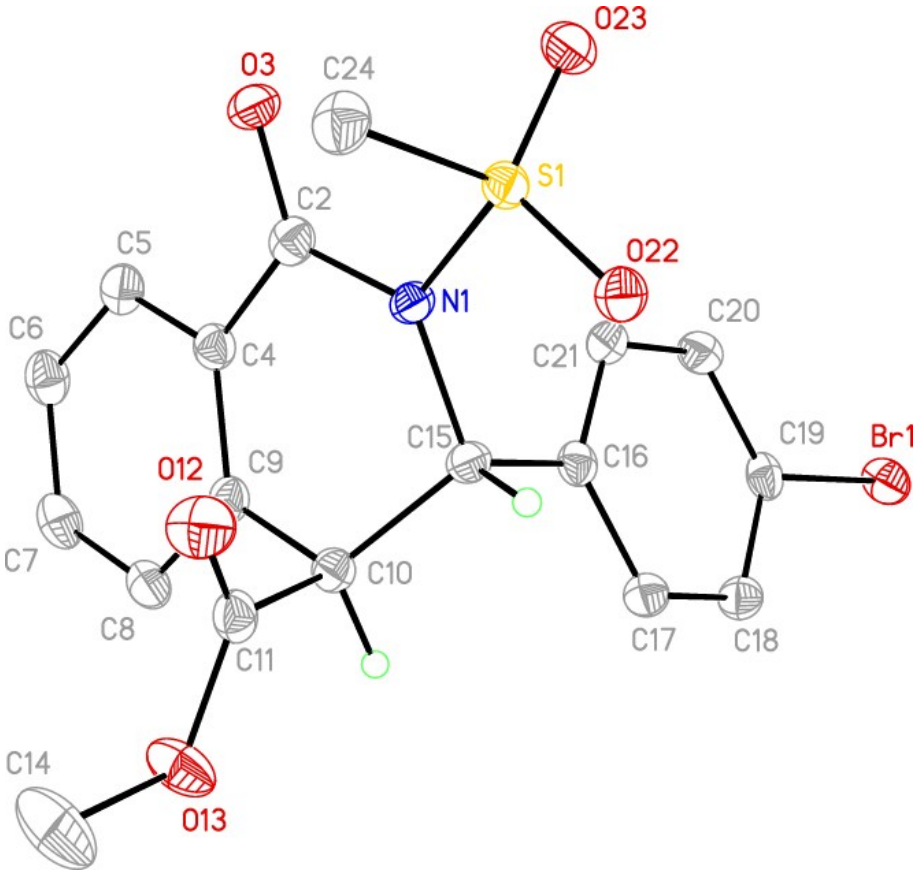


Fig. 1. Molecular structure of TCD504 with atomic displacement parameters shown at 50% probability. Only H atoms on chiral positions C10, C15 shown as S enantiomer. Racemic mixture.

Crystal Structure Report for TCD504

A specimen of $C_{18}H_{16}BrNO_5S$, approximate dimensions 0.050 mm x 0.090 mm x 0.200 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured at 100(2)K using an Oxford Cryosystems low temperature device using a MiTeGen micromount. See Table 1 for collection parameters and exposure time. Bruker APEX software was used to correct for Lorentz and polarization effects.

A total of 2888 frames were collected. The total exposure time was 10.90 hours. The integration of the data using a monoclinic unit cell yielded a total of 27629 reflections to a maximum θ angle of 70.09° (0.82 Å resolution), of which 3303 were independent (average redundancy 8.365, completeness = 99.0%, R_{int} = 3.92%, R_{sig} = 2.16%) and 3191 (96.61%) were greater than $2\sigma(F^2)$.The final cell constants of a = 8.9592(4) Å, b = 13.9166(6) Å, c = 14.1101(6) Å, β = 92.4338(13)°, volume = 1757.68(13) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I).Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.758. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.5659 and 0.7533.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_1/c$, with Z = 4 for the formula unit, $C_{18}H_{16}BrNO_5S$.The final anisotropic full-matrix least-squares refinement on F^2 with 237 variables converged at R1 = 2.88%, for the observed data and wR2 = 7.73% for all data. The goodness-of-fit was 1.072. The largest peak in the final difference electron density synthesis was 0.343 $e^-/Å^3$ and the largest hole was -0.461 $e^-/Å^3$ with an RMS deviation of 0.074 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.656 g/cm^3 and F(000), 888 e^-.

References: See CIF, CCDC No. 1481218.

Table 1: Data collection details for TCD504.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	50.000	109.57	95.80	341.18	-51.34	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	-49.35	299.47	36.00	-64.88	2.00	56	10.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	50.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Phi	50.000	-47.74	343.92	221.00	23.00	2.00	111	10.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	300.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	108.96	342.40	360.00	64.88	2.00	69	15.00	1.54184	45	0.6	100
Omega	50.000	106.72	91.92	264.49	-48.75	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	107.62	94.56	5.97	-55.69	2.00	67	15.00	1.54184	45	0.6	100
Phi	50.000	79.35	65.80	360.00	-57.06	2.00	180	15.00	1.54184	45	0.6	100
Omega	50.000	-49.35	299.47	180.00	-64.88	2.00	56	15.00	1.54184	45	0.6	100
Omega	50.000	108.96	342.40	250.00	64.87	2.00	69	15.00	1.54184	45	0.6	100
Phi	50.000	109.35	95.80	0.00	-57.06	2.00	180	15.00	1.54184	45	0.6	100
Omega	50.000	-11.25	229.18	240.00	54.74	2.00	66	10.00	1.54184	45	0.6	100
Phi	50.000	-64.35	58.14	0.00	-57.06	2.00	180	10.00	1.54184	45	0.6	100
Omega	50.000	-49.35	299.47	288.00	-64.88	2.00	56	10.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	175.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Phi	50.000	-47.74	325.81	360.00	57.06	2.00	180	10.00	1.54184	45	0.6	100
Omega	50.000	-11.25	337.52	60.00	-64.87	2.00	37	10.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	250.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Phi	50.000	94.35	80.80	360.00	-57.06	2.00	180	15.00	1.54184	45	0.6	100
Omega	50.000	108.96	342.40	25.00	64.87	2.00	69	15.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	325.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	275.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	200.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	-49.35	191.08	144.00	54.74	2.00	66	10.00	1.54184	45	0.6	100
Omega	50.000	108.96	96.53	150.00	-54.74	2.00	66	15.00	1.54184	45	0.6	100
Omega	50.000	-49.35	191.08	72.00	54.74	2.00	66	10.00	1.54184	45	0.6	100
Phi	60.000	110.97	90.26	360.00	-57.06	2.00	180	15.00	1.54184	45	0.6	100
Phi	60.000	95.97	75.26	360.00	-57.06	2.00	180	15.00	1.54184	45	0.6	100
Phi	65.000	110.96	86.96	360.00	-57.06	2.00	180	15.00	1.54184	45	0.6	100

Table 2. Crystal data and structure refinement for tcd504.

Identification code	tcd504	
Empirical formula	$C_{18}H_{16}BrNO_5S$	
Formula weight	438.29	
Temperature	99.98 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 8.9592(4) Å	α= 90°.
	b = 13.9166(6) Å	β= 92.4338(13)°.
	c = 14.1101(6) Å	γ = 90°.
Volume	1757.68(13) $Å^3$	
Z	4	
Density (calculated)	1.656 Mg/m^3	
Absorption coefficient	4.572 mm^{-1}	
F(000)	888	
Crystal size	0.2 x 0.09 x 0.05 mm^3	
Theta range for data collection	4.464 to 70.092°.	
Index ranges	$-10\leq h\leq 10$, $-16\leq k\leq 16$, $-17\leq l\leq 16$	
Reflections collected	27629	
Independent reflections	3303 [R(int) = 0.0392]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7533 and 0.5659	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3303 / 0 / 237	
Goodness-of-fit on F^2	1.072	
Final R indices [$I>2\sigma(I)$]	R1 = 0.0288, wR2 = 0.0767	
R indices (all data)	R1 = 0.0296, wR2 = 0.0773	
Largest diff. peak and hole	0.343 and -0.461 $e.Å^{-3}$	

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for tcd504. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	9889(1)	6619(1)	6254(1)	24(1)
C(2)	5506(2)	5071(2)	1919(1)	17(1)
C(4)	4308(2)	5655(2)	2331(1)	17(1)
C(5)	3032(2)	5184(2)	2626(2)	20(1)
C(6)	1836(2)	5712(2)	2933(2)	23(1)
C(7)	1913(3)	6708(2)	2958(2)	23(1)
C(8)	3185(2)	7181(2)	2678(2)	20(1)
C(9)	4388(2)	6659(1)	2366(2)	16(1)
C(10)	5757(2)	7158(1)	2012(1)	16(1)
C(11)	5428(2)	7425(2)	981(2)	18(1)
C(14)	4322(3)	8591(2)	-27(2)	40(1)
C(15)	7153(2)	6525(1)	2144(2)	16(1)
C(16)	7739(2)	6519(1)	3173(2)	15(1)
C(17)	8218(2)	7389(2)	3579(2)	18(1)
C(18)	8837(2)	7432(2)	4495(2)	19(1)
C(19)	8957(2)	6587(2)	5014(2)	18(1)
C(20)	8450(2)	5721(2)	4642(2)	20(1)
C(21)	7848(2)	5691(2)	3720(2)	18(1)
C(24)	7294(2)	4708(2)	67(2)	23(1)
N(1)	6848(2)	5542(1)	1778(1)	15(1)
O(3)	5313(2)	4238(1)	1680(1)	21(1)
O(12)	5606(2)	6908(1)	315(1)	27(1)
O(13)	4856(2)	8312(1)	919(1)	28(1)
O(22)	9311(2)	5685(1)	1040(1)	20(1)
O(23)	8608(2)	4105(1)	1658(1)	22(1)
S(1)	8186(1)	4972(1)	1171(1)	16(1)

Table 4. Bond lengths [Å] and angles [°] for tcd504.

Br(1)-C(19)	1.908(2)	C(21)-H(21)	0.9500
C(2)-C(4)	1.485(3)	C(24)-H(24A)	0.9800
C(2)-N(1)	1.391(3)	C(24)-H(24B)	0.9800
C(2)-O(3)	1.218(3)	C(24)-H(24C)	0.9800
C(4)-C(5)	1.396(3)	C(24)-S(1)	1.758(2)
C(4)-C(9)	1.399(3)	N(1)-S(1)	1.6996(17)
C(5)-H(5)	0.9500	O(22)-S(1)	1.4317(15)
C(5)-C(6)	1.384(3)	O(23)-S(1)	1.4307(16)
C(6)-H(6)	0.9500		
C(6)-C(7)	1.388(3)	N(1)-C(2)-C(4)	116.17(17)
C(7)-H(7)	0.9500	O(3)-C(2)-C(4)	122.25(19)
C(7)-C(8)	1.388(3)	O(3)-C(2)-N(1)	121.52(19)
C(8)-H(8)	0.9500	C(5)-C(4)-C(2)	118.26(19)
C(8)-C(9)	1.387(3)	C(5)-C(4)-C(9)	120.00(19)
C(9)-C(10)	1.513(3)	C(9)-C(4)-C(2)	121.58(18)
C(10)-H(10)	1.0000	C(4)-C(5)-H(5)	120.1
C(10)-C(11)	1.518(3)	C(6)-C(5)-C(4)	119.9(2)
C(10)-C(15)	1.534(3)	C(6)-C(5)-H(5)	120.1
C(11)-O(12)	1.200(3)	C(5)-C(6)-H(6)	120.0
C(11)-O(13)	1.339(3)	C(5)-C(6)-C(7)	120.0(2)
C(14)-H(14A)	0.9800	C(7)-C(6)-H(6)	120.0
C(14)-H(14B)	0.9800	C(6)-C(7)-H(7)	119.8
C(14)-H(14C)	0.9800	C(8)-C(7)-C(6)	120.5(2)
C(14)-O(13)	1.451(3)	C(8)-C(7)-H(7)	119.8
C(15)-H(15)	1.0000	C(7)-C(8)-H(8)	120.0
C(15)-C(16)	1.522(3)	C(9)-C(8)-C(7)	120.0(2)
C(15)-N(1)	1.483(2)	C(9)-C(8)-H(8)	120.0
C(16)-C(17)	1.400(3)	C(4)-C(9)-C(10)	119.17(18)
C(16)-C(21)	1.389(3)	C(8)-C(9)-C(4)	119.66(19)
C(17)-H(17)	0.9500	C(8)-C(9)-C(10)	121.09(18)
C(17)-C(18)	1.385(3)	C(9)-C(10)-H(10)	108.5
C(18)-H(18)	0.9500	C(9)-C(10)-C(11)	107.51(16)
C(18)-C(19)	1.387(3)	C(9)-C(10)-C(15)	111.39(16)
C(19)-C(20)	1.384(3)	C(11)-C(10)-H(10)	108.5
C(20)-H(20)	0.9500	C(11)-C(10)-C(15)	112.41(16)
C(20)-C(21)	1.388(3)	C(15)-C(10)-H(10)	108.5

O(12)-C(11)-C(10)	125.26(19)	C(20)-C(19)-Br(1)	119.45(16)
O(12)-C(11)-O(13)	124.4(2)	C(20)-C(19)-C(18)	121.4(2)
O(13)-C(11)-C(10)	110.32(18)	C(19)-C(20)-H(20)	120.3
H(14A)-C(14)-H(14B)	109.5	C(19)-C(20)-C(21)	119.3(2)
H(14A)-C(14)-H(14C)	109.5	C(21)-C(20)-H(20)	120.3
H(14B)-C(14)-H(14C)	109.5	C(16)-C(21)-H(21)	119.6
O(13)-C(14)-H(14A)	109.5	C(20)-C(21)-C(16)	120.76(19)
O(13)-C(14)-H(14B)	109.5	C(20)-C(21)-H(21)	119.6
O(13)-C(14)-H(14C)	109.5	H(24A)-C(24)-H(24B)	109.5
C(10)-C(15)-H(15)	107.5	H(24A)-C(24)-H(24C)	109.5
C(16)-C(15)-C(10)	111.44(16)	H(24B)-C(24)-H(24C)	109.5
C(16)-C(15)-H(15)	107.5	S(1)-C(24)-H(24A)	109.5
N(1)-C(15)-C(10)	110.48(16)	S(1)-C(24)-H(24B)	109.5
N(1)-C(15)-H(15)	107.5	S(1)-C(24)-H(24C)	109.5
N(1)-C(15)-C(16)	112.22(16)	C(2)-N(1)-C(15)	122.17(16)
C(17)-C(16)-C(15)	118.24(18)	C(2)-N(1)-S(1)	118.93(14)
C(21)-C(16)-C(15)	123.22(18)	C(15)-N(1)-S(1)	118.89(13)
C(21)-C(16)-C(17)	118.52(19)	C(11)-O(13)-C(14)	114.66(19)
C(16)-C(17)-H(17)	119.2	N(1)-S(1)-C(24)	103.90(9)
C(18)-C(17)-C(16)	121.51(19)	O(22)-S(1)-C(24)	109.06(10)
C(18)-C(17)-H(17)	119.2	O(22)-S(1)-N(1)	104.84(8)
C(17)-C(18)-H(18)	120.8	O(23)-S(1)-C(24)	110.52(10)
C(17)-C(18)-C(19)	118.39(19)	O(23)-S(1)-N(1)	109.22(9)
C(19)-C(18)-H(18)	120.8	O(23)-S(1)-O(22)	118.21(9)
C(18)-C(19)-Br(1)	119.10(15)		

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for tcd504. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	28(1)	24(1)	18(1)	-4(1)	-6(1)	5(1)
C(2)	19(1)	19(1)	14(1)	1(1)	-1(1)	-1(1)
C(4)	17(1)	19(1)	16(1)	1(1)	-2(1)	0(1)
C(5)	18(1)	23(1)	19(1)	2(1)	-1(1)	-2(1)
C(6)	18(1)	29(1)	23(1)	5(1)	1(1)	-1(1)
C(7)	18(1)	31(1)	21(1)	1(1)	2(1)	6(1)
C(8)	19(1)	22(1)	20(1)	0(1)	-1(1)	4(1)
C(9)	17(1)	19(1)	13(1)	1(1)	-2(1)	-1(1)
C(10)	16(1)	16(1)	16(1)	-1(1)	-1(1)	1(1)
C(11)	13(1)	21(1)	20(1)	2(1)	0(1)	-1(1)
C(14)	50(2)	46(2)	24(1)	13(1)	-1(1)	18(1)
C(15)	16(1)	14(1)	18(1)	-1(1)	2(1)	-1(1)
C(16)	12(1)	18(1)	16(1)	-1(1)	2(1)	1(1)
C(17)	18(1)	17(1)	20(1)	1(1)	1(1)	0(1)
C(18)	19(1)	18(1)	20(1)	-5(1)	1(1)	0(1)
C(19)	14(1)	24(1)	15(1)	-3(1)	-2(1)	3(1)
C(20)	22(1)	18(1)	22(1)	2(1)	-2(1)	2(1)
C(21)	17(1)	17(1)	20(1)	-2(1)	-2(1)	0(1)
C(24)	22(1)	28(1)	18(1)	-6(1)	1(1)	0(1)
N(1)	14(1)	14(1)	17(1)	-2(1)	1(1)	-1(1)
O(3)	21(1)	16(1)	24(1)	-3(1)	1(1)	-2(1)
O(12)	37(1)	26(1)	17(1)	-2(1)	0(1)	1(1)
O(13)	38(1)	25(1)	20(1)	5(1)	0(1)	11(1)
O(22)	16(1)	20(1)	23(1)	-1(1)	2(1)	-1(1)
O(23)	21(1)	20(1)	25(1)	1(1)	1(1)	3(1)
S(1)	14(1)	16(1)	16(1)	-2(1)	1(1)	1(1)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for tcd504.

	x	y	z	U(eq)
H(5)	2985	4502	2615	24
H(6)	963	5393	3127	28
H(7)	1089	7068	3167	28
H(8)	3232	7863	2701	24
H(10)	5923	7762	2385	19
H(14A)	5128	8513	-470	60
H(14B)	4004	9264	-22	60
H(14C)	3475	8183	-229	60
H(15)	7947	6811	1755	19
H(17)	8118	7964	3218	22
H(18)	9170	8025	4761	23
H(20)	8512	5153	5015	24
H(21)	7508	5096	3460	22
H(24A)	8023	4439	-358	34
H(24B)	6869	5299	-210	34
H(24C)	6494	4241	156	34

Table 7. Torsion angles [°] for tcd504.

Br(1)-C(19)-C(20)-C(21)	-176.41(16)	C(15)-N(1)-S(1)-C(24)	-122.36(16)
C(2)-C(4)-C(5)-C(6)	-174.15(19)	C(15)-N(1)-S(1)-O(22)	-7.92(17)
C(2)-C(4)-C(9)-C(8)	174.23(19)	C(15)-N(1)-S(1)-O(23)	119.70(15)
C(2)-C(4)-C(9)-C(10)	-2.6(3)	C(16)-C(15)-N(1)-C(2)	84.5(2)
C(2)-N(1)-S(1)-C(24)	57.97(17)	C(16)-C(15)-N(1)-S(1)	-95.16(18)
C(2)-N(1)-S(1)-O(22)	172.40(15)	C(16)-C(17)-C(18)-C(19)	-0.8(3)
C(2)-N(1)-S(1)-O(23)	-59.98(17)	C(17)-C(16)-C(21)-C(20)	-1.4(3)
C(4)-C(2)-N(1)-C(15)	8.7(3)	C(17)-C(18)-C(19)-Br(1)	177.14(15)
C(4)-C(2)-N(1)-S(1)	-171.59(14)	C(17)-C(18)-C(19)-C(20)	-1.3(3)
C(4)-C(5)-C(6)-C(7)	-0.7(3)	C(18)-C(19)-C(20)-C(21)	2.0(3)
C(4)-C(9)-C(10)-C(11)	93.9(2)	C(19)-C(20)-C(21)-C(16)	-0.6(3)
C(4)-C(9)-C(10)-C(15)	-29.7(3)	C(21)-C(16)-C(17)-C(18)	2.1(3)
C(5)-C(4)-C(9)-C(8)	-1.1(3)	N(1)-C(2)-C(4)-C(5)	-170.01(18)
C(5)-C(4)-C(9)-C(10)	-177.90(18)	N(1)-C(2)-C(4)-C(9)	14.6(3)
C(5)-C(6)-C(7)-C(8)	-0.2(3)	N(1)-C(15)-C(16)-C(17)	173.54(17)
C(6)-C(7)-C(8)-C(9)	0.4(3)	N(1)-C(15)-C(16)-C(21)	-5.1(3)
C(7)-C(8)-C(9)-C(4)	0.2(3)	O(3)-C(2)-C(4)-C(5)	12.9(3)
C(7)-C(8)-C(9)-C(10)	176.98(19)	O(3)-C(2)-C(4)-C(9)	-162.5(2)
C(8)-C(9)-C(10)-C(11)	-82.9(2)	O(3)-C(2)-N(1)-C(15)	-174.17(19)
C(8)-C(9)-C(10)-C(15)	153.56(19)	O(3)-C(2)-N(1)-S(1)	5.5(3)
C(9)-C(4)-C(5)-C(6)	1.3(3)	O(12)-C(11)-O(13)-C(14)	5.4(3)
C(9)-C(10)-C(11)-O(12)	-86.1(2)		
C(9)-C(10)-C(11)-O(13)	91.8(2)		
C(9)-C(10)-C(15)-C(16)	-76.8(2)		
C(9)-C(10)-C(15)-N(1)	48.7(2)		
C(10)-C(11)-O(13)-C(14)	-172.4(2)		
C(10)-C(15)-C(16)-C(17)	-62.0(2)		
C(10)-C(15)-C(16)-C(21)	119.4(2)		
C(10)-C(15)-N(1)-C(2)	-40.5(2)		
C(10)-C(15)-N(1)-S(1)	139.81(14)		
C(11)-C(10)-C(15)-C(16)	162.50(16)		
C(11)-C(10)-C(15)-N(1)	-72.0(2)		
C(15)-C(10)-C(11)-O(12)	36.9(3)		
C(15)-C(10)-C(11)-O(13)	-145.30(17)		
C(15)-C(16)-C(17)-C(18)	-176.63(18)		
C(15)-C(16)-C(21)-C(20)	177.31(19)		

Table 8. Hydrogen bonds for tcd504 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(15)-H(15)...Br(1)#1	1.00	2.90	3.810(2)	151.9
C(15)-H(15)...O(22)	1.00	2.25	2.790(2)	112.4
C(18)-H(18)...O(22)#2	0.95	2.55	3.425(3)	154.0
C(24)-H(24A)...O(22)#3	0.98	2.62	3.521(3)	153.1
C(24)-H(24B)...O(12)	0.98	2.63	3.438(3)	140.0
C(24)-H(24C)...O(3)	0.98	2.44	3.017(3)	117.4
C(24)-H(24C)...O(12)#4	0.98	2.54	3.462(3)	157.5

Symmetry transformations used to generate equivalent atoms:

#1 x,-y+3/2,z-1/2 #2 x,-y+3/2,z+1/2 #3 -x+2,-y+1,-z

#4 -x+1,-y+1,-z

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