

Supporting Information

Highly Efficient and Enantioselective Synthesis of β -Heteroaryl Amino Alcohols via Ru-Catalyzed Asymmetric Hydrogenation

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1. General Information

Unless otherwise mentioned, all experiments were carried out under an atmosphere of argon in a glovebox or using standard Schlenk techniques. Solvents were dried with standard procedures and degassed with Ar₂. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 300-400 mesh). NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for ¹H NMR, 101 MHz for ¹³C NMR and 162 MHz for ³¹P NMR or a Bruker DPX 600 spectrometer at 600 MHz for ¹H NMR, 150 MHz for ¹³C NMR in CDCl₃, DMSO-*d*₆ and CD₃OD with tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz.

2. Experimental Details

2.1 General Procedure for the Synthesis of Substrate

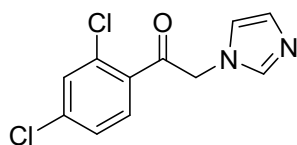
Procedure A: Preparation of ketones 1a~1q, 1t.¹

To a solution of substituted α -bromo aryl ketone (10 mmol, 1.0 eq) in dichloromethane (10 mL), was added slowly to a suspension of imidazole (24.5 g, 0.36 mol) in dichloromethane (10 mL), and the mixture was heated to 40 °C for 2 h and then overnight at room temperature. The reaction mixture was washed with water and brine (100 mL) and dried (Na_2SO_4), and solvent was removed under vacuum to give a red oil. The desired product was purified by silica gel column chromatography with a mixture of petroleum ether and ethyl acetate as eluent.

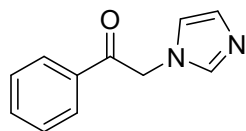
Procedure B: Preparation of ketones 1r, 1s, 1u.²

Potassium carbonate (1.5 mmol), nitrogen heterocyclic (1.2 mmol) and α -bromo aryl ketone (1.0 mmol) were heated at 80 °C in acetonitrile (10 mL) for 10 hours. After solvents evaporation under vacuum, water was added to the reaction mixture followed by extraction with DCM. The combined organic phases were dried over Na_2SO_4 , filtered, and concentrated in vacuo. The desired product was purified by silica gel column chromatography.

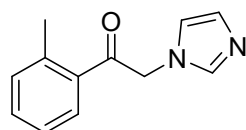
2.2 Characterization Data of 1



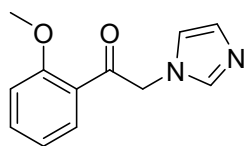
1-(2,4-dichlorophenyl)-2-(1H-imidazol-1-yl)ethan-1-one (1a)¹: white solid; 83% yield. ¹H NMR (600 MHz, CDCl_3) δ 7.57 (d, $J = 8.3$ Hz, 1H), 7.54 – 7.49 (m, 2H), 7.38 (dd, $J = 8.4, 1.9$ Hz, 1H), 7.12 (s, 1H), 6.94 (s, 1H), 5.33 (s, 2H). ¹³C NMR (151 MHz, CDCl_3) δ 193.68, 139.27, 138.03, 134.10, 132.49, 131.14, 130.79, 129.83, 127.99, 119.99, 55.51.



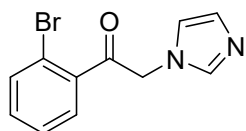
2-(1H-imidazol-1-yl)-1-phenylethan-1-one (1b)¹: white solid; 63% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.01 – 7.93 (m, 2H), 7.71 – 7.62 (m, 1H), 7.58 – 7.48 (m, 3H), 7.12 (s, 1H), 6.94 (d, *J* = 1.4 Hz, 1H), 5.40 (d, *J* = 2.1 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 191.73, 138.17, 134.40, 134.18, 129.55, 129.13, 127.98, 120.34, 52.48.



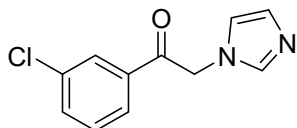
2-(1H-imidazol-1-yl)-1-(o-tolyl)ethan-1-one (1c)³: white solid; 79% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 7.8 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.13 (s, 1H), 6.94 (s, 1H), 5.30 (s, 2H), 2.53 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 194.37, 139.95, 138.13, 133.95, 132.85, 132.76, 129.67, 128.30, 126.07, 120.21, 54.05, 21.70.



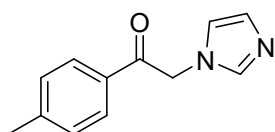
2-(1H-imidazol-1-yl)-1-(2-methoxyphenyl)ethan-1-one (1d)⁴: white solid; 81% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.56 (ddd, *J* = 8.4, 7.3, 1.9 Hz, 1H), 7.47 (s, 1H), 7.10 (t, *J* = 1.1 Hz, 1H), 7.09 – 7.01 (m, 2H), 6.91 (s, 1H), 5.32 (s, 2H), 4.00 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 193.15, 159.34, 138.22, 135.32, 131.28, 129.27, 124.54, 121.29, 120.30, 111.66, 56.90, 55.70.



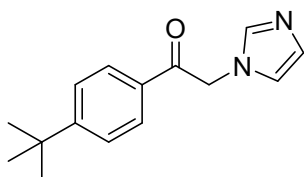
1-(2-bromophenyl)-2-(1H-imidazol-1-yl)ethan-1-one (1e): white solid; 61% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.65 (d, *J* = 7.1 Hz, 1H), 7.52 (s, 1H), 7.43 – 7.34 (m, 3H), 7.10 (s, 1H), 6.96 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 196.18, 138.49, 137.96, 133.88, 132.85, 129.78, 128.98, 127.88, 119.95, 118.91, 55.01. HRMS (ESI) calcd. for C₁₁H₉BrN₂O [M+H]⁺: 264.9898, Found: 264.9970.



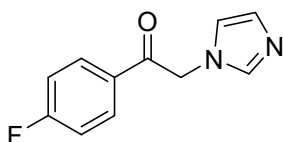
1-(3-chlorophenyl)-2-(1H-imidazol-1-yl)ethan-1-one (1f)⁵: white solid; 84% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.94 (t, *J* = 1.9 Hz, 1H), 7.84 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.63 (ddd, *J* = 8.0, 2.1, 1.0 Hz, 1H), 7.54 – 7.43 (m, 2H), 7.13 (s, 1H), 6.93 (s, 1H), 5.38 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 190.56, 138.10, 135.64, 135.57, 134.36, 130.50, 129.70, 128.14, 126.01, 120.26, 52.52.



2-(1H-imidazol-1-yl)-1-(*p*-tolyl)ethan-1-one (1g)³: white solid; 85% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.49 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 1H), 6.93 (s, 1H), 5.35 (s, 2H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 191.20, 145.48, 138.16, 131.71, 129.78, 129.57, 128.07, 120.29, 52.33, 21.79.

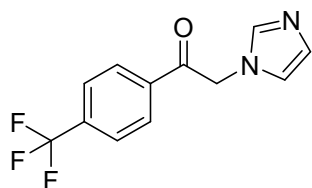


1-(4-(tert-butyl)phenyl)-2-(1H-imidazol-1-yl)ethan-1-one (1h): white solid, 86% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.95 – 7.86 (m, 2H), 7.58 – 7.46 (m, 3H), 7.13 (d, *J* = 1.3 Hz, 1H), 6.94 (q, *J* = 1.3 Hz, 1H), 5.38 (s, 2H), 1.36 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 191.19, 158.45, 138.15, 131.63, 129.56, 127.99, 126.09, 120.29, 52.38, 35.33, 31.02. HRMS (ESI) calcd. for C₁₅H₁₈N₂O [M+H]⁺: 242.1419, Found: 243.1492.

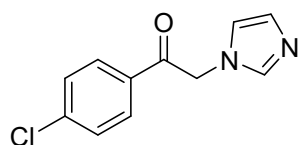


1-(4-fluorophenyl)-2-(1H-imidazol-1-yl)ethan-1-one (1i)⁵: white solid; 80% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.05 – 7.96 (m, 2H), 7.50 (s, 1H), 7.24 – 7.15 (m, 2H), 7.13 (s, 1H), 6.93 (t, *J* = 1.3 Hz, 1H), 5.37 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ

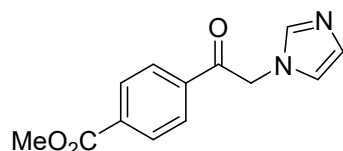
190.09, 167.69, 165.14, 138.13, 130.80, 130.71, 130.67, 130.64, 129.75, 120.24, 116.54, 116.32, 52.35. ^{19}F NMR (376 MHz, CDCl_3) δ -102.27.



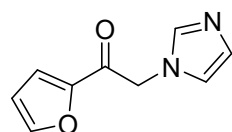
2-(1H-imidazol-1-yl)-1-(4-(trifluoromethyl)phenyl)ethan-1-one (1j): white solid; 80% yield. ^1H NMR (600 MHz, CDCl_3) δ 8.09 (d, $J = 8.0$ Hz, 2H), 7.81 (d, $J = 8.8$ Hz, 2H), 7.56 (s, 1H), 7.15 (s, 1H), 6.96 (s, 1H), 5.46 (s, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 191.14, 138.11, 136.78, 135.53 (q, $J = 33.1$ Hz), 129.43, 128.43, 126.17 (q, $J = 3.7$ Hz), 123.31 (q, $J = 272.9$ Hz), 120.36, 52.76. ^{19}F NMR (376 MHz, CDCl_3) δ -63.31. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_9\text{F}_3\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 254.0667, Found: 255.0739.



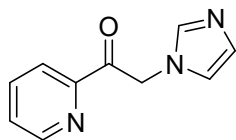
1-(4-chlorophenyl)-2-(1H-imidazol-1-yl)ethan-1-one (1k)³: white solid; 83% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 8.6$ Hz, 2H), 7.56 – 7.47 (m, 3H), 7.14 (s, 1H), 6.94 (s, 1H), 5.37 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 190.49, 141.05, 138.12, 132.49, 129.81, 129.53, 129.37, 120.21, 52.41.



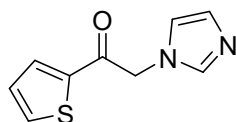
methyl 4-(2-(1H-imidazol-1-yl)acetyl)benzoate (1l): white solid, 87% yield. ^1H NMR (400 MHz, CDCl_3) δ 8.22 – 8.16 (m, 2H), 8.06 – 8.01 (m, 2H), 7.53 (s, 1H), 7.15 (s, 1H), 6.96 (s, 1H), 5.44 (s, 2H), 3.97 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 191.28, 165.83, 138.11, 137.26, 135.07, 130.27, 129.78, 127.94, 120.23, 52.73, 52.68. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 244.0848, Found: 245.0921.



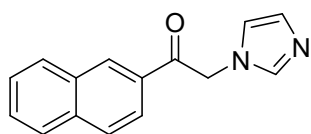
1-(furan-2-yl)-2-(1H-imidazol-1-yl)ethan-1-one (1m)⁶: white solid; 51% yield. ¹H NMR (600 MHz, DMSO-*d*₆) δ 8.10 (s, 1H), 7.59 (s, 2H), 7.12 (d, *J* = 2.6 Hz, 1H), 6.91 (d, *J* = 2.5 Hz, 1H), 6.80 (s, 1H), 5.50 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 182.64, 150.39, 148.88, 138.82, 128.44, 121.31, 119.72, 113.23, 52.07.



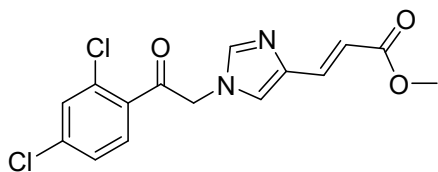
2-(1H-imidazol-1-yl)-1-(pyridin-2-yl)ethan-1-one (1n)⁶: white solid; 57% yield. ¹H NMR (600 MHz, CDCl₃) δ 8.70 (s, 1H), 8.06 (d, *J* = 6.7 Hz, 1H), 7.89 (t, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 19.7 Hz, 2H), 7.12 (s, 1H), 6.96 (s, 1H), 5.65 (s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 193.48, 151.33, 149.24, 138.27, 137.37, 129.50, 128.29, 122.38, 120.29, 52.28.



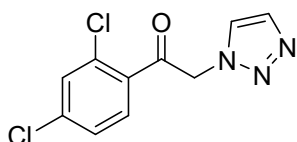
2-(1H-imidazol-1-yl)-1-(thiophen-2-yl)ethan-1-one (1o)⁷: white solid; 73% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.76 (ddd, *J* = 7.8, 4.4, 1.1 Hz, 2H), 7.54 (s, 1H), 7.20 (dd, *J* = 4.9, 3.8 Hz, 1H), 7.13 (s, 1H), 6.97 (d, *J* = 1.4 Hz, 1H), 5.29 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 184.73, 140.59, 138.11, 135.36, 132.52, 129.74, 128.65, 120.24, 52.57.



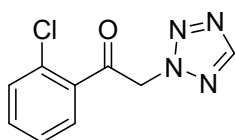
2-(1H-imidazol-1-yl)-1-(naphthalen-2-yl)ethan-1-one (1p)⁷: white solid; 85% yield; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, *J* = 1.7 Hz, 1H), 8.03 – 7.88 (m, 4H), 7.72 – 7.51 (m, 3H), 7.16 (d, *J* = 1.1 Hz, 1H), 6.99 (s, 1H), 5.53 (s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 193.99, 138.86, 135.78, 132.58, 132.24, 130.50, 130.07, 129.46, 129.03, 128.39, 128.27, 127.68, 123.81, 121.43, 53.10.



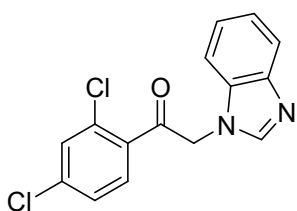
Methyl (E)-3-(1-(2-(2,4-dichlorophenyl)-2-oxoethyl)-1H-imidazol-4-yl)acrylate (1q): white solid, 79% yield. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.98 (d, $J = 8.4$ Hz, 1H), 7.83 (d, $J = 2.0$ Hz, 1H), 7.71 (s, 1H), 7.67 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.59 – 7.53 (m, 2H), 6.37 (d, $J = 15.5$ Hz, 1H), 5.64 (s, 2H), 3.69 (s, 3H). ^{13}C NMR (151 MHz, $\text{DMSO-}d_6$) δ 194.01, 167.09, 140.26, 137.36, 137.30, 136.67, 133.62, 132.05, 131.49, 130.54, 127.71, 124.78, 113.61, 54.99, 51.19. HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 338.0225, Found: 339.0299.



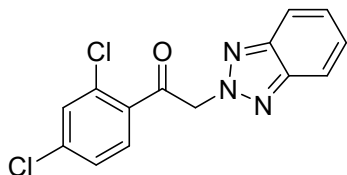
1-(2,4-dichlorophenyl)-2-(1H-1,2,3-triazol-1-yl)ethan-1-one (1r)⁸: white solid; 69% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.70 (s, 2H), 7.62 (d, $J = 8.4$ Hz, 1H), 7.49 (d, $J = 2.0$ Hz, 1H), 7.35 (dd, $J = 8.4, 2.0$ Hz, 1H), 5.88 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 192.52, 139.16, 135.37, 133.80, 132.92, 131.38, 130.78, 127.73, 62.91.



1-(2-chlorophenyl)-2-(2H-tetrazol-2-yl)ethan-1-one (1s)⁹: white solid; 60% yield. ^1H NMR (400 MHz, CDCl_3) δ 8.63 (s, 1H), 7.77 – 7.72 (m, 1H), 7.54 (dd, $J = 6.2, 1.7$ Hz, 2H), 7.44 (ddd, $J = 7.8, 6.2, 2.3$ Hz, 1H), 6.17 (s, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 190.99, 153.34, 134.73, 133.94, 132.11, 131.11, 130.67, 127.52, 77.31, 77.10, 76.88, 60.78, 25.37.



2-(1H-benzo[d]imidazol-1-yl)-1-(2,4-dichlorophenyl)ethan-1-one (1t)¹⁰: white solid; 80% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.07 – 8.00 (m, 2H), 7.93 (s, 1H), 7.88 – 7.82 (m, 1H), 7.72 – 7.66 (m, 1H), 7.56 (dd, *J* = 8.5, 7.1 Hz, 2H), 7.33 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 5.57 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 191.24, 143.77, 143.63, 134.50, 134.25, 129.20, 128.07, 123.30, 122.37, 120.62, 109.23, 77.36, 77.04, 76.73, 50.39.

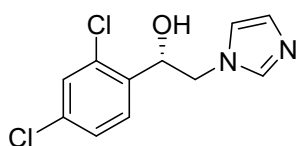


2-(2H-benzo[d][1,2,3]triazol-2-yl)-1-(2,4-dichlorophenyl)ethan-1-one (1u): white solid; 65% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.47 – 7.35 (m, 3H), 6.06 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 192.06, 146.06, 139.50, 133.69, 133.63, 132.87, 131.41, 130.92, 128.03, 127.99, 124.17, 120.31, 109.29, 77.35, 77.04, 76.72, 56.63. HRMS (ESI) calcd. for C₁₄H₉Cl₂N₃O [M+H]⁺: 306.0123, Found: 306.0200.

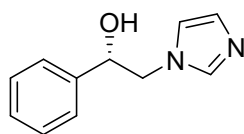
3. General procedure for the asymmetric hydrogenation

3.1 General procedure for the asymmetric hydrogenation conducted with S/C = 100

To a 4.0 mL vial was added the catalyst (2×10^{-2} mmol, 24 mg) and anhydrous THF (2.0 mL) under argon atmosphere. The mixture was stirred in the argon-filled glovebox. The resulting solution (200 μ L) and KOH (0.1 mg) were transferred by syringe into a 5.0 mL vial charged with substrate (0.2 mmol) in 0.5 mL anhydrous THF. The vials were transferred to an autoclave, which was then charged with 50 atm of H₂ and stirred at room temperature for 24 h. The hydrogen gas was released slowly in a well-ventilated hood and the solution was concentrated and passed through a short column of silica gel to remove the metal complex.

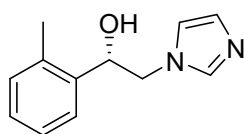


(S)-1-(2,4-dichlorophenyl)-2-(1H-imidazol-1-yl)ethan-1-ol (2a)¹: white solid; 99% yield, >99% ee, $[\alpha]_{\text{D}}^{25} = +85$ (*c* 1.0, MeOH) (lit.¹ $[\alpha]_{\text{D}}^{25} = +83.8$ (*c* 0.998, MeOH), 91% ee, *S*); ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.59 (d, *J* = 3.3 Hz, 1H), 7.45 (dt, *J* = 23.0, 5.4 Hz, 3H), 7.05 (s, 1H), 6.84 (s, 1H), 6.06 (s, 1H), 5.13 – 5.04 (m, 1H), 4.17 (dd, *J* = 14.1, 2.9 Hz, 1H), 4.05 (ddd, *J* = 14.3, 6.8, 3.3 Hz, 1H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 139.12, 138.21, 133.22, 132.28, 129.85, 128.88, 128.42, 127.93, 120.50, 69.16, 52.08. The enantiomeric excess of **2a** was determined by HPLC analysis on Chiralpak AS-H column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 208$ nm, *t*_R = 10.4 min (major), 13.1 min (minor).

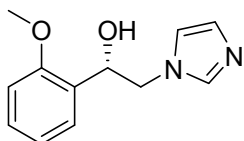


(S)-2-(1H-imidazol-1-yl)-1-phenylethan-1-ol (2b)¹: white solid; 97% yield, >99% ee, $[\alpha]_{\text{D}}^{25} = +81$ (*c* 0.5, MeOH) (lit.¹ $[\alpha]_{\text{D}}^{25} = +46.1$ (*c* 0.98, EtOH), 97% ee, *S*); ¹H

NMR (600 MHz, DMSO- d_6) δ 7.49 (d, J = 8.5 Hz, 1H), 7.35 (d, J = 6.9 Hz, 4H), 7.30 – 7.24 (m, 1H), 7.11 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 5.72 (s, 1H), 4.82 (td, J = 8.5, 4.0 Hz, 1H), 4.14 (tt, J = 9.2, 4.3 Hz, 1H), 4.04 (dt, J = 13.7, 8.3 Hz, 1H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 143.12, 138.18, 128.54, 128.19, 127.80, 126.49, 120.50, 72.55, 54.01. The enantiomeric excess of **2b** was determined by HPLC analysis on Chiralpak AS-H column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at λ = 208 nm, t_R = 10.4 min (major), 13.1 min (minor).

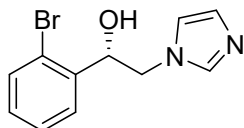


(S)-2-(1H-imidazol-1-yl)-1-(o-tolyl)ethan-1-ol (2c): white solid; 98% yield, >99% ee, $[\alpha]_D^{25} = +67$ (c 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.50 (s, 1H), 7.41 – 7.38 (m, 1H), 7.18 – 7.12 (m, 3H), 7.04 (s, 1H), 6.90 (s, 1H), 5.16 – 5.11 (m, 1H), 4.21 – 4.14 (m, 2H), 2.28 (s, 3H). ^{13}C NMR (151 MHz, CD_3OD) δ 139.53, 137.61, 134.55, 129.92, 127.33, 126.98, 125.87, 125.43, 120.16, 69.34, 52.86, 17.62. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 203.1106, Found: 203.1177. The enantiomeric excess of **2c** was determined by HPLC analysis on Chiralpak IB column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 208 nm, t_R = 11.4 min (minor), 23.6 min (major).

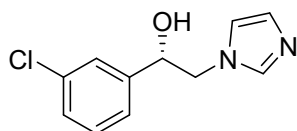


(S)-2-(1H-imidazol-1-yl)-1-(2-methoxyphenyl)ethan-1-ol (2d): white solid; 98% yield, >99% ee, $[\alpha]_D^{25} = +80$ (c 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.50 (s, 1H), 7.38 – 7.34 (m, 1H), 7.28 (td, J = 7.8, 1.7 Hz, 1H), 7.03 (s, 1H), 6.99 (d, J = 7.3 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H), 6.90 (s, 1H), 5.25 (dd, J = 7.1, 3.4 Hz, 1H), 4.26 (dd, J = 14.1, 3.4 Hz, 1H), 4.12 (dd, J = 14.0, 7.1 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, CD_3OD) δ 155.97, 137.56, 129.29, 128.49, 126.84, 126.09, 120.22, 120.12, 109.88, 67.70, 54.47, 52.57. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 219.1055,

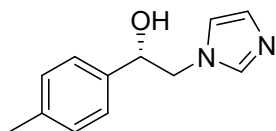
Found: 219.1126. The enantiomeric excess of **2d** was determined by HPLC analysis on Chiralpak AS-H column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 208$ nm, $t_R = 16.3$ min (major), 22.2 min (minor).



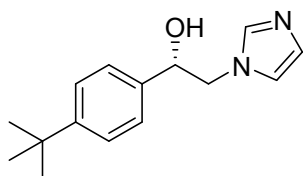
(S)-1-(2-bromophenyl)-2-(1H-imidazol-1-yl)ethan-1-ol (2e): white solid; 97% yield, >99% ee, $[\alpha]_D^{25} = +65$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.57 (d, $J = 7.5$ Hz, 2H), 7.49 (dd, $J = 7.8, 1.7$ Hz, 1H), 7.34 (t, $J = 7.5$ Hz, 1H), 7.20 (td, $J = 7.7, 1.8$ Hz, 1H), 7.07 (s, 1H), 6.92 (s, 1H), 5.25 (dd, $J = 7.3, 3.0$ Hz, 1H), 4.30 (dd, $J = 14.3, 3.1$ Hz, 1H), 4.13 (dd, $J = 14.3, 7.3$ Hz, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 140.38, 137.58, 132.27, 129.21, 127.66, 127.52, 126.86, 121.26, 120.17, 71.69, 52.38. HRMS (ESI) calcd. for $\text{C}_{11}\text{H}_{11}\text{BrN}_2\text{O}$ $[\text{M}+\text{H}]^+$: 267.0055, Found: 267.0124. The enantiomeric excess of **2e** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 3.0$ min (major), 3.6 min (minor).



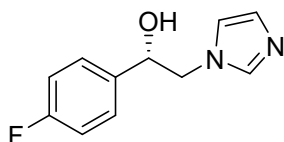
(S)-1-(3-chlorophenyl)-2-(1H-imidazol-1-yl)ethan-1-ol (2f): white solid; 98% yield, >99% ee, $[\alpha]_D^{25} = +23$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.71 (s, 1H), 7.35 (s, 1H), 7.33 – 7.24 (m, 3H), 7.15 (s, 1H), 7.00 (s, 1H), 4.95 (dd, $J = 7.3, 4.1$ Hz, 1H), 4.28 (dd, $J = 14.1, 4.0$ Hz, 1H), 4.19 (dd, $J = 14.1, 7.3$ Hz, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 143.93, 137.37, 134.04, 129.61, 127.53, 125.79, 125.74, 124.07, 120.61, 53.99. HRMS (ESI) calcd. for $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}$ $[\text{M}+\text{H}]^+$: 223.0560, Found: 223.0641. The enantiomeric excess of **2f** was determined by HPLC analysis on Chiralpak IB column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 208$ nm, $t_R = 18.3$ min (major), 23.9 min (minor).



(S)-2-(1H-imidazol-1-yl)-1-(p-tolyl)ethan-1-ol (2g): white solid; 99% yield, >99% ee, $[\alpha]_D^{25} = +35$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, DMSO- d_6) δ 7.49 (s, 1H), 7.22 (d, $J = 7.9$ Hz, 2H), 7.13 (d, $J = 7.8$ Hz, 2H), 7.10 (s, 1H), 5.63 (s, 1H), 4.77 (dd, $J = 7.9, 4.1$ Hz, 1H), 4.10 (dd, $J = 13.9, 4.2$ Hz, 1H), 4.01 (dd, $J = 13.9, 7.9$ Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 140.11, 138.15, 136.83, 129.09, 128.09, 126.41, 120.51, 72.37, 54.05, 21.18. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 203.1106, Found: 203.1177. The enantiomeric excess of **2g** was determined by HPLC analysis on Chiralpak AS-H column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 21.8$ min (major), 24.3 min (minor).

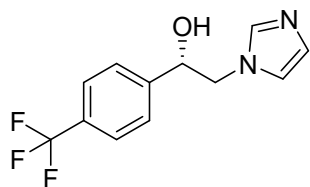


(S)-1-(4-(tert-butyl)phenyl)-2-(1H-imidazol-1-yl)ethan-1-ol (2h): white solid, 98% yield, >99% ee, $[\alpha]_D^{25} = +33$ (*c* 0.1, MeOH). ^1H NMR (400 MHz, CDCl_3) δ 7.50 (s, 1H), 7.38 (dt, $J = 8.4, 2.0$ Hz, 2H), 7.25 (dt, $J = 8.5, 2.1$ Hz, 2H), 7.08 (t, $J = 1.3$ Hz, 1H), 6.91 (s, 1H), 4.86 (d, $J = 2.3$ Hz, 1H), 4.25 – 4.11 (m, 2H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 154.58, 142.51, 141.56, 130.90, 129.40, 128.88, 124.03, 76.64, 57.84, 37.91, 34.33. HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 244.1576, Found: 245.1649. The enantiomeric excess of **2h** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 75/25, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 220$ nm, $t_R = 3.40$ min (major), 3.91 min (minor).

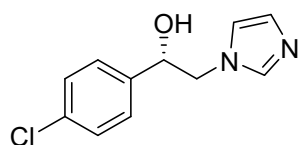


(S)-1-(4-fluorophenyl)-2-(1H-imidazol-1-yl)ethan-1-ol (2i): white solid; 98% yield, >99% ee, $[\alpha]_D^{25} = +41$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.48 (s, 1H), 7.32 (dd, $J = 8.4, 5.4$ Hz, 2H), 7.07 – 7.01 (m, 3H), 6.89 (s, 1H), 4.92 (dd, $J = 7.2, 4.5$ Hz, 1H), 4.20 (dd, $J = 14.1, 4.4$ Hz, 1H), 4.15 (dd, $J = 14.1, 7.1$ Hz, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 163.22, 161.60, 137.64, 127.63, 127.57, 127.02, 120.13,

114.74, 114.60, 72.11, 53.82. ^{19}F NMR (377 MHz, CD_3OD) δ -116.94. HRMS (ESI) calcd. for $\text{C}_{11}\text{H}_{11}\text{FN}_2\text{O}$ $[\text{M}+\text{H}]^+$: 207.0855, Found: 207.0924. The enantiomeric excess of **2i** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 230$ nm, $t_R = 3.2$ min (major), 3.7 min (minor).

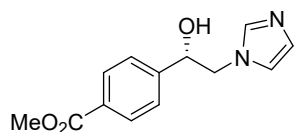


(S)-2-(1H-imidazol-1-yl)-1-(4-(trifluoromethyl)phenyl)ethan-1-ol (2j): white solid; 98% yield, >99% ee, $[\alpha]^{25}_D = +30$ (c 0.1, MeOH). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.70 (d, $J = 8.1$ Hz, 2H), 7.56 (d, $J = 8.0$ Hz, 2H), 7.48 (s, 1H), 7.12 (s, 1H), 6.83 (s, 1H), 5.92 (d, $J = 4.6$ Hz, 1H), 4.95 (dt, $J = 8.2, 4.4$ Hz, 1H), 4.19 (dd, $J = 14.0, 4.1$ Hz, 1H), 4.07 (dd, $J = 13.9, 7.6$ Hz, 1H). ^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) δ 147.78, 138.22, 128.42 (q, $J = 31.6$ Hz), 128.27, 127.29, 125.40 (q, $J = 3.8$ Hz), 124.79 (q, $J = 271.9, 270.7$ Hz), 120.54, 71.90, 53.63. ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$) δ -59.99. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_{11}\text{F}_3\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 256.0823, Found: 257.0895. The enantiomeric excess of **2j** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 75/25, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 220$ nm, $t_R = 2.38$ min (major), 2.84 min (minor).

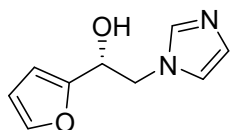


(S)-1-(4-chlorophenyl)-2-(1H-imidazol-1-yl)ethan-1-ol (2k): white solid; 97% yield, >99% ee, $[\alpha]^{25}_D = +86$ (c 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.48 (s, 1H), 7.30 (q, $J = 8.5$ Hz, 4H), 7.05 (s, 1H), 6.89 (s, 1H), 4.92 (dd, $J = 7.1, 4.3$ Hz, 1H), 4.22 (dd, $J = 14.1, 4.4$ Hz, 1H), 4.16 (dd, $J = 14.1, 7.1$ Hz, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 140.47, 137.66, 133.16, 128.08, 127.34, 127.04, 120.14, 72.05, 53.68. HRMS (ESI) calcd. for $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}$ $[\text{M}+\text{H}]^+$: 223.0560, Found: 223.0641. The enantiomeric excess of **2k** was determined by HPLC analysis on Chiralpak IB column.

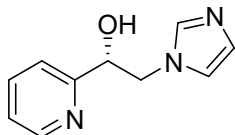
Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at λ = 208 nm, t_R = 20.3 min (major), 23.5 min (minor).



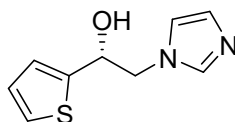
methyl (S)-4-(1-hydroxy-2-(1H-imidazol-1-yl)ethyl)benzoate (2l): white solid, 99% yield, >99% ee, $[\alpha]_D^{25} = +120$ (*c* 0.1, MeOH). $^1\text{H NMR}$ (400 MHz, CD_3OD) δ 7.97 (d, $J = 8.4$ Hz, 2H), 7.49 (s, 1H), 7.44 (d, $J = 8.3$ Hz, 2H), 7.06 (s, 1H), 6.90 (s, 1H), 5.01 (dd, $J = 7.0, 4.2$ Hz, 1H), 4.27 (dd, $J = 14.1, 4.3$ Hz, 1H), 4.19 (dd, $J = 14.1, 7.0$ Hz, 1H), 3.89 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CD_3OD) δ 166.91, 147.14, 137.68, 129.40, 129.22, 127.06, 128.89, 120.19, 72.29, 53.62, 51.26. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 246.1004, Found: 247.1077. The enantiomeric excess of **2l** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 75/25, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 4.53$ min (major), 5.33 min (minor).



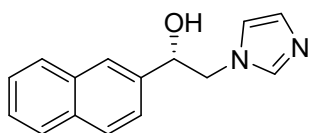
(R)-1-(furan-2-yl)-2-(1H-imidazol-1-yl)ethan-1-ol (2m): white solid; 96% yield, >99% ee, $[\alpha]_D^{25} = +34$ (*c* 0.5, MeOH). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.41 (d, $J = 1.8$ Hz, 1H), 7.31 (s, 1H), 6.84 – 6.80 (m, 2H), 6.35 (dd, $J = 3.3, 1.8$ Hz, 1H), 6.29 (d, $J = 3.3$ Hz, 1H), 5.05 (s, 1H), 4.92 (dd, $J = 7.7, 3.9$ Hz, 1H), 4.27 (dd, $J = 14.1, 4.0$ Hz, 1H), 4.20 (dd, $J = 14.1, 7.7$ Hz, 1H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 153.78, 142.24, 137.61, 128.42, 119.61, 110.55, 107.18, 67.32, 52.07. HRMS (ESI) calcd. for $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 179.0742, Found: 179.0813. The enantiomeric excess of **2m** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 1.9$ min (major), 2.5 min (minor).



(R)-2-(1H-imidazol-1-yl)-1-(pyridin-2-yl)ethan-1-ol (2n): white solid; 97% yield, >99% ee, $[\alpha]_D^{25} = +18$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 8.53 (s, 1H), 7.80 (t, $J = 7.8$ Hz, 1H), 7.54 – 7.45 (m, 2H), 7.35 – 7.29 (m, 1H), 7.03 (s, 1H), 6.88 (s, 1H), 5.01 – 4.95 (m, 1H), 4.42 (dt, $J = 14.3, 3.3$ Hz, 1H), 4.32 – 4.21 (m, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 160.42, 148.23, 137.68, 137.39, 127.04, 122.86, 120.92, 120.10, 73.07, 52.66. HRMS (ESI) calcd. for $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$: 190.0902, Found: 190.0973. The enantiomeric excess of **2n** was determined by UPLC analysis on Chiralpak IG-3 column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 5.3$ min (major), 5.7 min (minor).

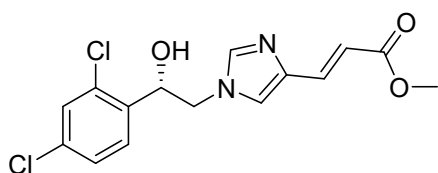


(R)-2-(1H-imidazol-1-yl)-1-(thiophen-2-yl)ethan-1-ol (2o): yellow solid; 96% yield, >99% ee, $[\alpha]_D^{25} = +10$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.54 (s, 1H), 7.33 (dd, $J = 4.9, 1.3$ Hz, 1H), 7.10 (s, 1H), 6.96 (dt, $J = 7.4, 3.5$ Hz, 2H), 6.91 (s, 1H), 5.17 (dd, $J = 7.4, 4.5$ Hz, 1H), 4.30 (dd, $J = 14.0, 4.5$ Hz, 1H), 4.23 (dd, $J = 14.1, 7.4$ Hz, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 145.30, 137.66, 127.06, 126.37, 124.47, 123.77, 120.08, 69.05, 53.99. HRMS (ESI) calcd. for $\text{C}_9\text{H}_9\text{N}_2\text{S}$ $[\text{M}+\text{H}]^+$: 195.0514, Found: 195.0585. The enantiomeric excess of **2o** was determined by UPLC analysis on Chiralpak AS-H column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 2.4$ min (major), 2.9 min (minor).

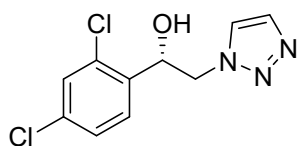


(S)-2-(1H-imidazol-1-yl)-1-(naphthalen-2-yl)ethan-1-ol (2p): white solid; 99% yield, >99% ee, $[\alpha]_D^{25} = +43$ (*c* 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.67 (s, 2H), 7.58 (d, $J = 8.4$ Hz, 1H), 7.43 (d, $J = 2.1$ Hz, 1H), 7.35 (d, $J = 8.6$ Hz, 1H), 5.57 (dd, $J = 8.1, 3.9$ Hz, 1H), 4.65 (dd, $J = 13.8, 3.9$ Hz, 1H), 4.57 (dd, $J = 13.8, 8.0$ Hz,

1H). ¹³C NMR (151 MHz, CD₃OD) δ 137.83, 134.08, 133.84, 132.43, 128.85, 128.54, 127.25, 68.55, 59.31. HRMS (ESI) calcd. for C₁₅H₁₄N₂O [M+H]⁺: 239.1106, Found: 239.1177. The enantiomeric excess of **2p** was determined by HPLC analysis on Chiralpak IB column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at λ = 208 nm, t_R = 26.6 min (major), 30.9 min (minor).

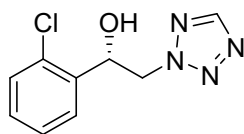


methyl (S, E)-3-(1-(2-(2,4-dichlorophenyl)-2-hydroxyethyl)-1H-imidazol-4-yl)acrylate (2q): white solid, 98% yield, >99% ee, [α]_D²⁵ = +21 (c 0.1, MeOH). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.62 (t, *J* = 1.2 Hz, 1H), 7.59 – 7.58 (m, 1H), 7.55 (s, 1H), 7.50 (d, *J* = 15.6 Hz, 1H), 7.45 (d, *J* = 1.5 Hz, 2H), 6.33 (d, *J* = 15.6 Hz, 1H), 6.08 (d, *J* = 4.6 Hz, 1H), 5.08 (ddd, *J* = 7.7, 4.7, 3.3 Hz, 1H), 4.20 (dd, *J* = 14.1, 3.3 Hz, 1H), 4.05 (dd, *J* = 14.1, 7.3 Hz, 1H), 3.68 (s, 3H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 167.59, 140.30, 138.83, 137.88, 137.06, 133.34, 132.26, 129.82, 128.97, 128.01, 124.73, 113.81, 68.93, 52.31, 51.63. HRMS (ESI) calcd. for C₁₅H₁₄Cl₂N₂O₃ [M+H]⁺: 340.0381, Found: 341.0455. The enantiomeric excess of **2q** was determined by UPLC analysis on Chiralpak IA-U column. Conditions: hexane/isopropanol = 75/25, flow rate = 0.5 mL/min, uv-vis detection at λ = 280 nm, t_R = 1.92 min (major), 3.02 min (minor).

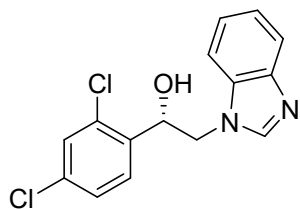


(S)-1-(2-(2,4-dichlorophenyl)-2-(1H-1,2,3-triazol-1-yl)ethan-1-ol (2r): white solid; 98% yield, >99% ee, [α]_D²⁵ = +22 (c 0.5, MeOH). ¹H NMR (600 MHz, CD₃OD) δ 7.67 (s, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 2.1 Hz, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 5.57 (dd, *J* = 8.1, 3.9 Hz, 1H), 4.65 (dd, *J* = 13.8, 3.9 Hz, 1H), 4.57 (dd, *J* = 13.8, 8.0 Hz, 1H). ¹³C NMR (151 MHz, CD₃OD) δ 137.83, 134.08, 133.84, 132.43, 128.85, 128.54, 127.25, 68.55, 59.31. HRMS (ESI) calcd. for C₁₀H₉Cl₂N₃O [M+H]⁺: 258.0123, Found: 258.0194. The enantiomeric excess of **2r** was determined by HPLC analysis on

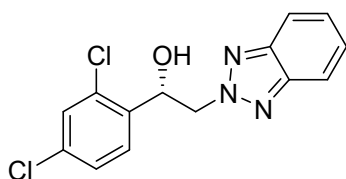
Chiralpak IB column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 208$ nm, $t_R = 11.6$ min (major), 12.2 min (minor).



(S)-1-(2-chlorophenyl)-2-(2H-tetrazol-2-yl)ethan-1-ol (2s): white solid; 98% yield, 98.5% ee, $[\alpha]_D^{25} = +66$ (c 0.25, MeOH). ^1H NMR (600 MHz, CDCl_3) δ 8.54 (s, 1H), 7.63 (dd, $J = 7.7, 1.8$ Hz, 1H), 7.40 (dd, $J = 7.8, 1.5$ Hz, 1H), 7.32 (dtd, $J = 22.8, 7.5, 1.6$ Hz, 2H), 5.73 (dt, $J = 8.5, 3.3$ Hz, 1H), 4.99 (dd, $J = 13.9, 2.7$ Hz, 1H), 4.79 (dd, $J = 13.9, 8.7$ Hz, 1H), 3.26 (d, $J = 4.2$ Hz, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 152.91, 136.63, 131.78, 129.79, 129.71, 127.51, 127.37, 69.25, 58.00. HRMS (ESI) calcd. for $\text{C}_9\text{H}_9\text{ClN}_4\text{O}$ $[\text{M}+\text{H}]^+$: 224.0456, Found: 224.0527. The enantiomeric excess of **2s** was determined by HPLC analysis on Chiralpak IC column. Conditions: hexane/isopropanol = 75/25, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 208$ nm, $t_R = 6.8$ min (major), 7.6 min (minor).

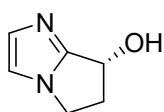


(S)-2-(1H-benzo[d]imidazol-1-yl)-1-(2,4-dichlorophenyl)ethan-1-ol (2t): white solid; 98% yield, >99% ee, $[\alpha]_D^{25} = +10$ (c 0.5, MeOH). ^1H NMR (600 MHz, CD_3OD) δ 7.99 (s, 1H), 7.65 (dd, $J = 7.2, 1.5$ Hz, 1H), 7.51 (dd, $J = 7.4, 1.5$ Hz, 1H), 7.36 – 7.31 (m, 4H), 7.30 – 7.24 (m, 3H), 5.07 (dd, $J = 7.2, 4.8$ Hz, 1H), 4.51 – 4.43 (m, 2H). ^{13}C NMR (151 MHz, CD_3OD) δ 144.01, 142.32, 141.65, 133.91, 128.10, 127.57, 125.71, 122.71, 121.91, 118.51, 110.23, 71.83, 51.89. HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 307.0329, Found: 307.0400. The enantiomeric excess of **2t** was determined by HPLC analysis on Chiralpak IB column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 14.2$ min (major), 17.2 min (minor).



(S)-2-(2H-benzo[d][1,2,3]triazol-2-yl)-1-(2,4-dichlorophenyl)ethan-1-ol (2u):

white solid; 98% yield, 97% ee, $[\alpha]^{25}_D = +34$ (*c* 0.5, MeOH). $^1\text{H NMR}$ (600 MHz, DMSO-*d*₆) δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.61 (d, *J* = 2.1 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.45 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.42 – 7.36 (m, 1H), 6.08 (s, 1H), 5.40 (dd, *J* = 7.6, 3.8 Hz, 1H), 4.88 (dd, *J* = 14.4, 3.8 Hz, 1H), 4.82 (dd, *J* = 14.4, 7.6 Hz, 1H). $^{13}\text{C NMR}$ (151 MHz, CD₃OD) δ 145.10, 137.87, 133.94, 132.26, 128.83, 128.55, 127.26, 127.16, 124.10, 118.28, 110.68, 68.72, 53.35. HRMS (ESI) calcd. for C₁₄H₁₁Cl₂N₃O [M+H]⁺: 308.0279, Found: 308.0350. The enantiomeric excess of **2u** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 2.9$ min (minor), 3.2 min (major).



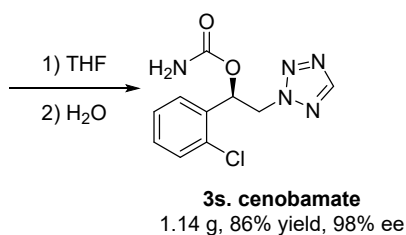
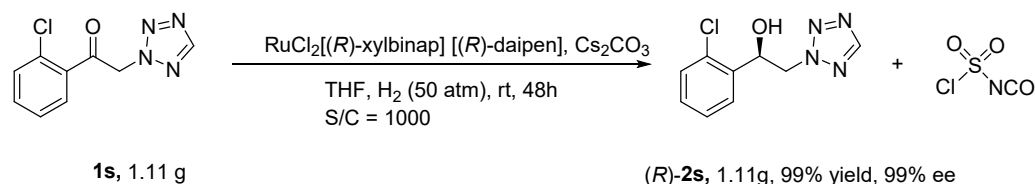
(R)-6,7-dihydro-5H-pyrrolo[1,2-a]imidazol-7-ol (2v)¹¹: white solid; 65% yield, >99% ee, $[\alpha]^{25}_D = +35.4$ (*c* 0.125, MeOH) (lit.¹¹ $[\alpha]^{24}_D = +11$ (*c* 0.48, MeOH), 99% ee, *R*). $^1\text{H NMR}$ (600 MHz, CD₃OD) δ 7.04 (s, 2H), 5.04 – 5.00 (m, 1H), 4.16 (ddt, *J* = 10.2, 7.6, 3.6 Hz, 1H), 3.96 (td, *J* = 8.4, 4.2 Hz, 1H), 2.93 (dq, *J* = 14.4, 7.4 Hz, 1H), 2.42 (ddd, *J* = 13.8, 7.4, 3.6 Hz, 1H). $^{13}\text{C NMR}$ (151 MHz, CD₃OD) δ 154.36, 131.51, 114.44, 64.12, 42.05, 36.45. HRMS (ESI) calcd. for C₆H₈N₂O [M+H]⁺: 125.0637, Found: 125.0708. The enantiomeric excess of **2v** was determined by UPLC analysis on Chiralpak OD column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 210$ nm, $t_R = 1.9$ min (major), 3.4 min (minor).

3.2 General procedure for the asymmetric hydrogenation conducted with S/C =

4000

$\text{RuCl}_2[(R)\text{-xylbinap}] [(R)\text{-daipen}]$ (1.25×10^{-4} mmol) and KOH (0.1 mg) transferred by syringe into a 10 mL vial charged with substrate (1.27 g, 5 mmol) in 2.0 mL anhydrous THF. The vial was transferred to an autoclave, which was then charged with 50 atm of H_2 and stirred at room temperature for 48 h. The hydrogen gas was released slowly in a well-ventilated hood and the solution was concentrated and passed through a short column of silica gel to remove the metal complex.

4. Synthetic Applications



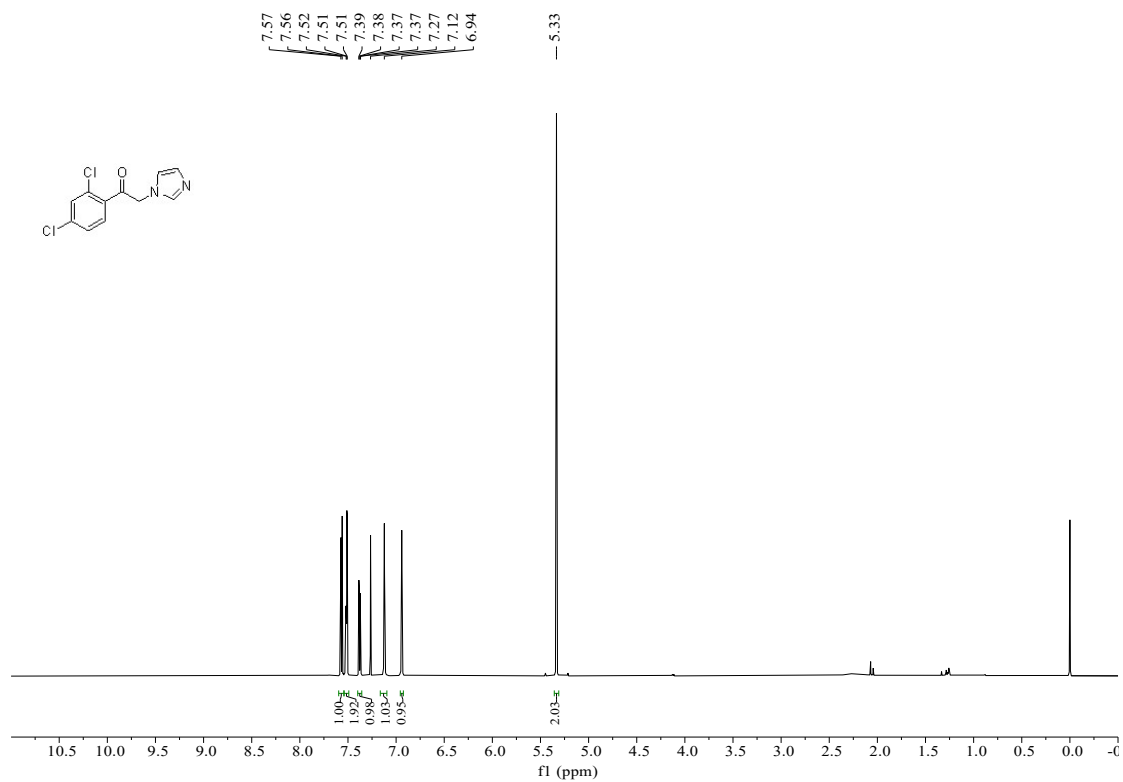
Step 1: $\text{RuCl}_2[(R)\text{-xylbinap}] [(R)\text{-daipen}]$ (5×10^{-4} mmol) and Cs_2CO_3 (0.3 mg) transferred by syringe into a 10 mL vial charged with substrate (1.11 g, 5 mmol) in 2.0 mL anhydrous THF. The vial was transferred to an autoclave, which was then charged with 50 atm of H_2 and stirred at room temperature for 48 h. The hydrogen gas was released slowly in a well-ventilated hood and the solution was concentrated and passed through a short column of silica gel to remove the metal complex.

Step 2¹²: Chlorosulfonylisocyanate (1.5 equiv) was dissolved in dry THF (0.1-0.15 M) and placed in an ice bath. The **(R)-2s** (1 equiv) dissolved in dry THF (0.3 M) was added slowly to the reaction. The ice bath was removed and stirred until consumption of alcohol was apparent by TLC. The reaction was placed back in an ice bath and water was added. The reaction flask was fitted with a reflux condenser and refluxed

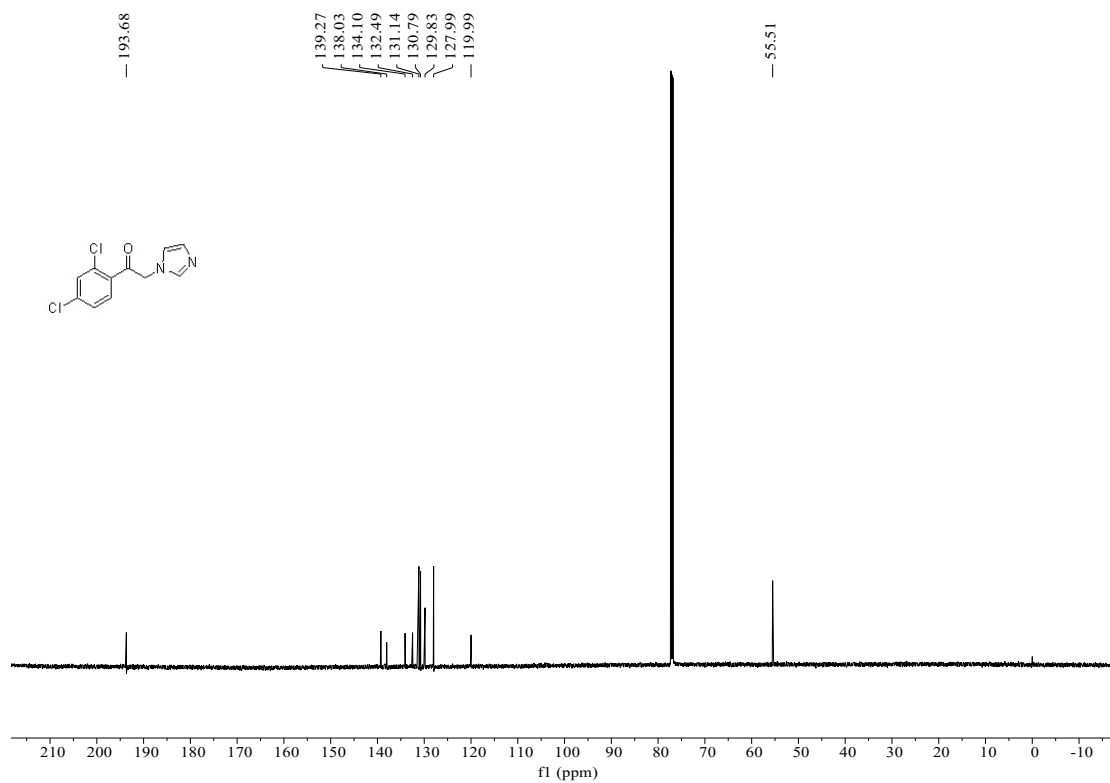
until TLC indicated complete conversion of the starting material. Water was added and the organic phase separated collected. The aqueous layer was extracted with 3 portions of ethyl acetate, the organics combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography. The products **3s**¹³ were obtained as oil (1.14 g, 86% yield, 98% ee). $[\alpha]_{\text{D}}^{25} = 3.4$ (c 0.5, MeOH). ¹H NMR (400 MHz, CD₃OD) δ 8.70 (s, 1H), 7.45 (ddd, $J = 9.5, 5.5, 3.5$ Hz, 2H), 7.39 – 7.27 (m, 2H), 6.54 (dd, $J = 8.1, 3.6$ Hz, 1H), 5.10 (dd, $J = 14.2, 8.2$ Hz, 1H), 5.03 (dd, $J = 14.3, 3.6$ Hz, 1H), 4.85 (s, 2H). ¹³C NMR (151 MHz, CD₃OD) δ 156.19, 152.77, 134.57, 131.75, 129.84, 129.46, 127.31, 127.08, 70.46, 55.34. The enantiomeric excess of **3s** was determined by UPLC analysis on Chiralpak IB-U column. Conditions: hexane/isopropanol = 80/20, flow rate = 0.5 mL/min, uv-vis detection at $\lambda = 230$ nm, $t_R = 2.8$ min (minor), 3.9 min (major).

5. Spectroscopic data

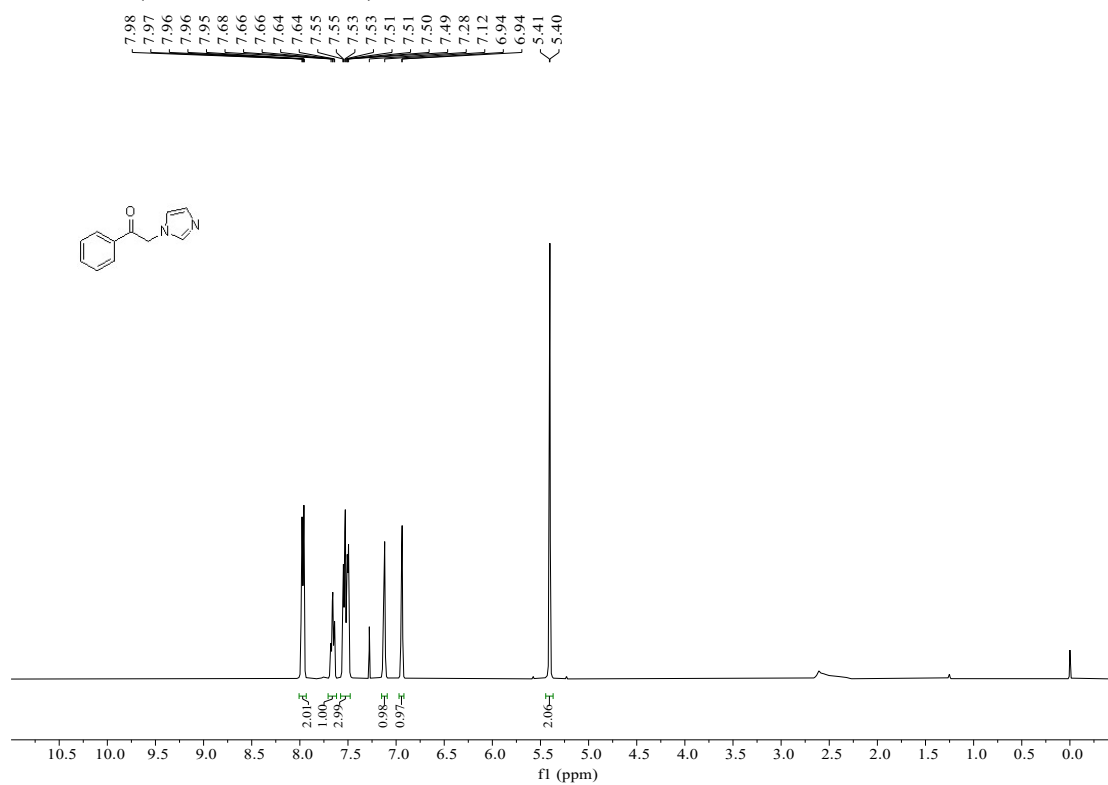
^1H NMR (600 MHz, CDCl_3) of **1a**:



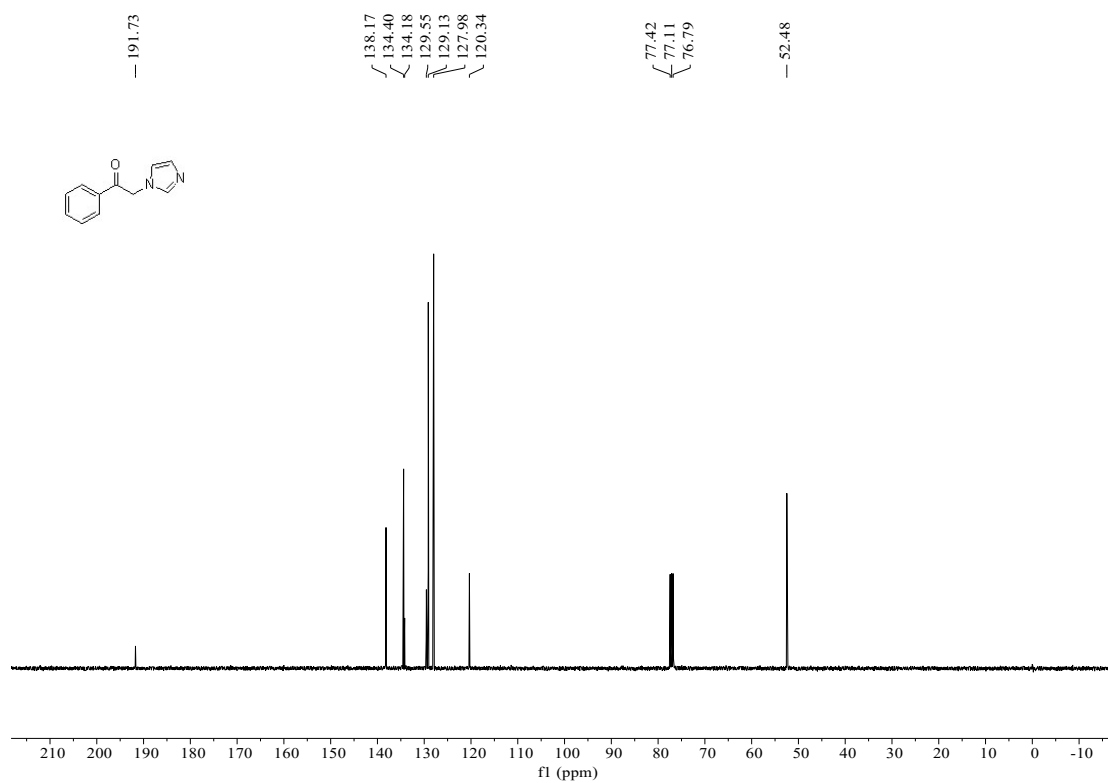
^{13}C NMR (151 MHz, CDCl_3) of **1a**:



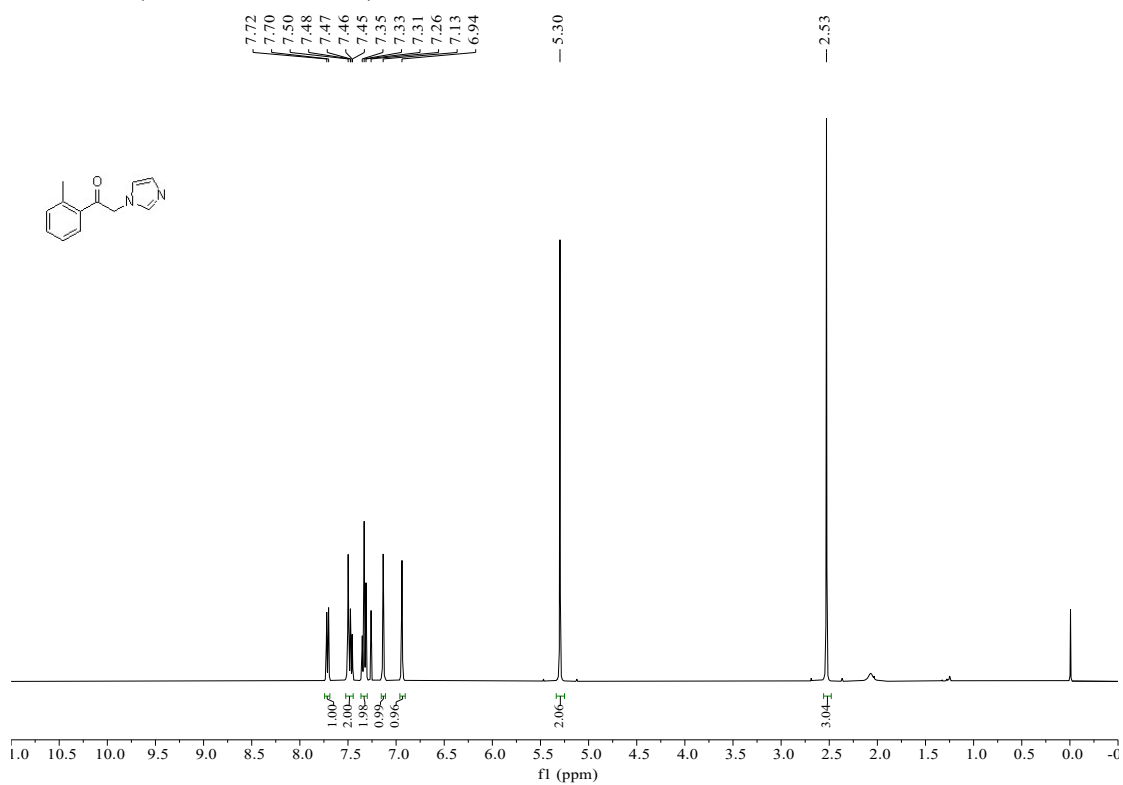
¹H NMR (400 MHz, CDCl₃) of **1b**:



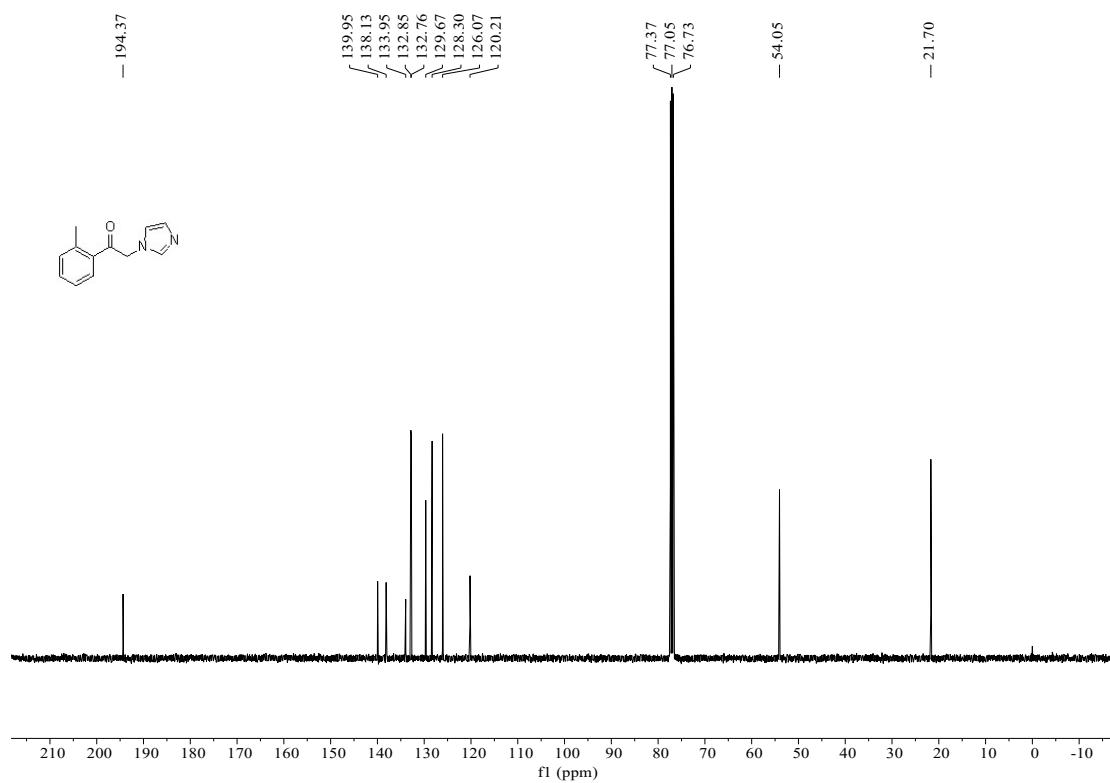
¹³C NMR (101 MHz, CDCl₃) of **1b**:



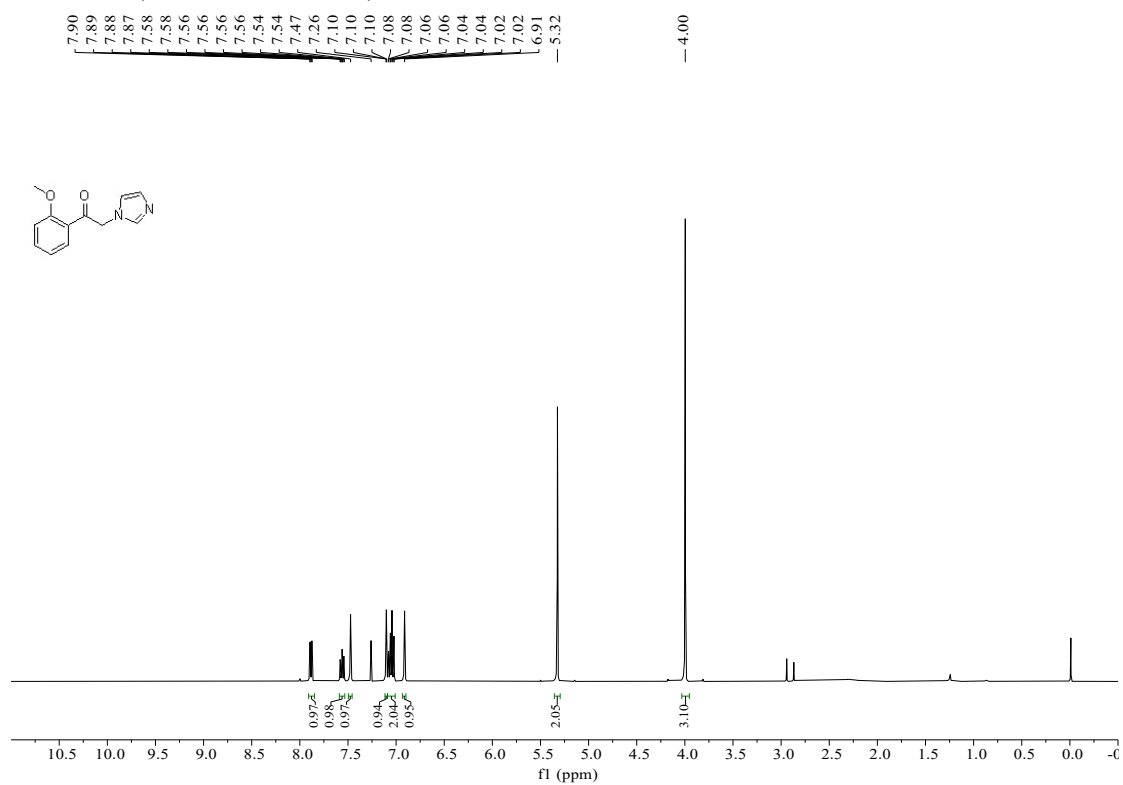
¹H NMR (400 MHz, CDCl₃) of **1c**:



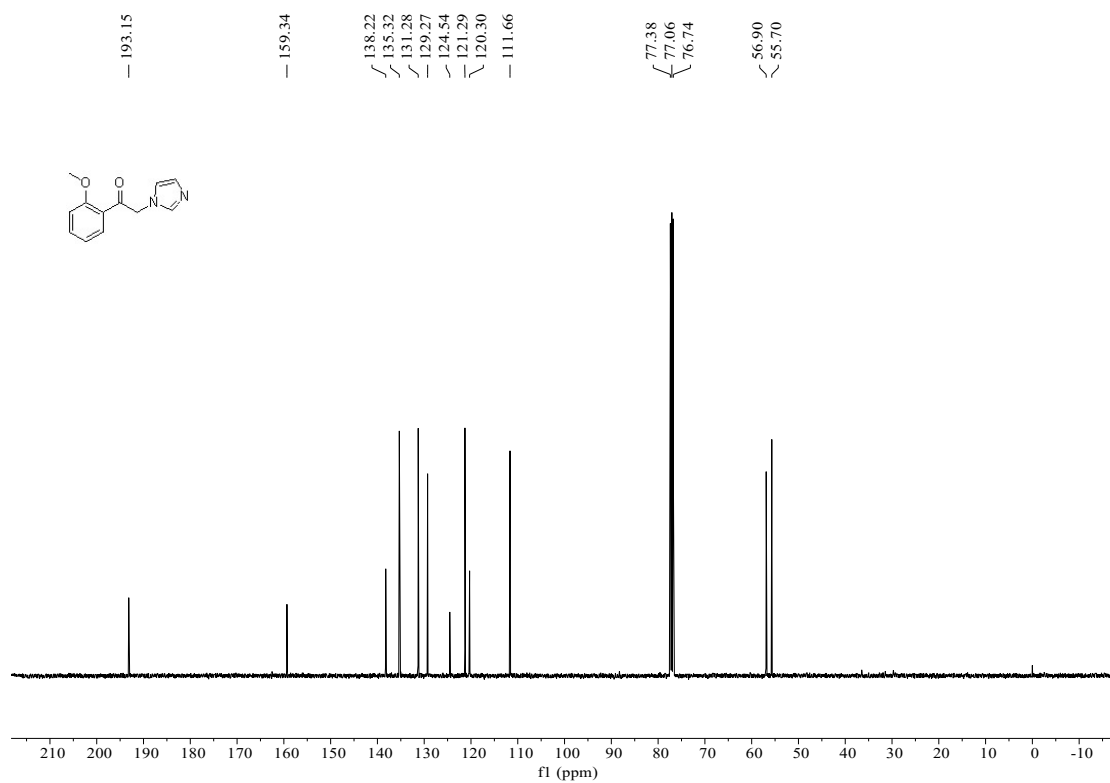
¹³C NMR (101 MHz, CDCl₃) of **1c**:



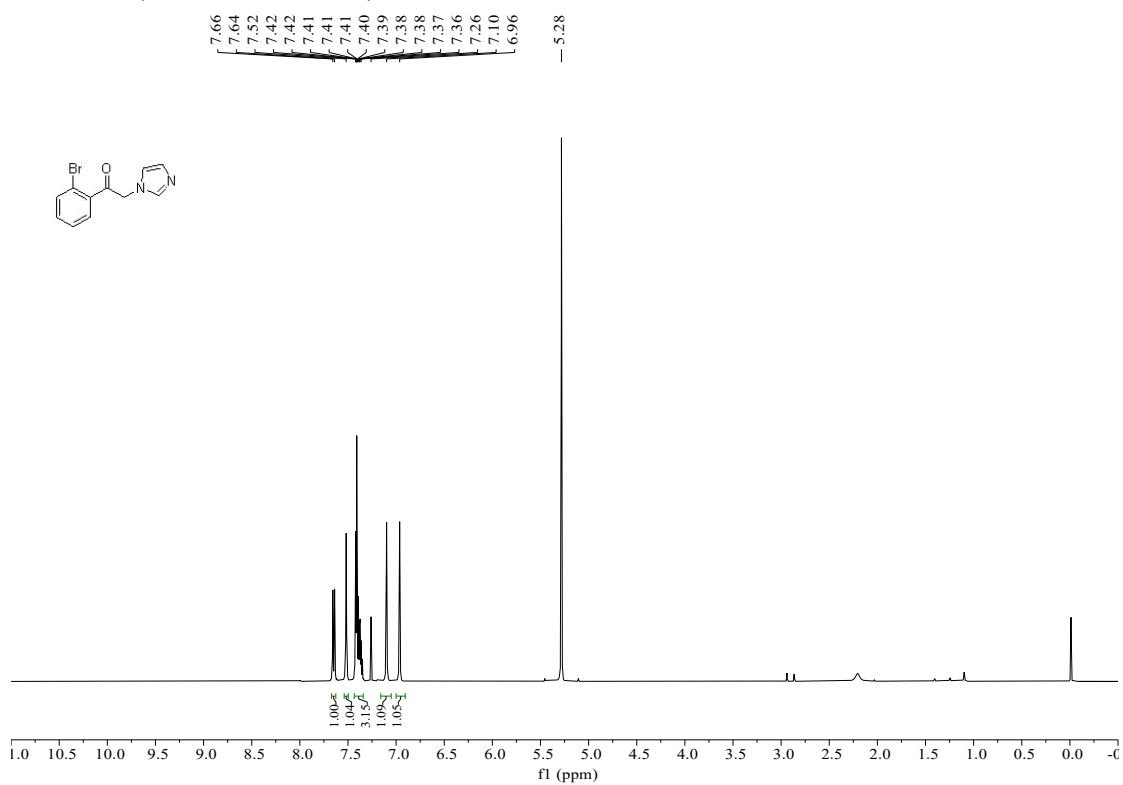
¹H NMR (400 MHz, CDCl₃) of **1d**:



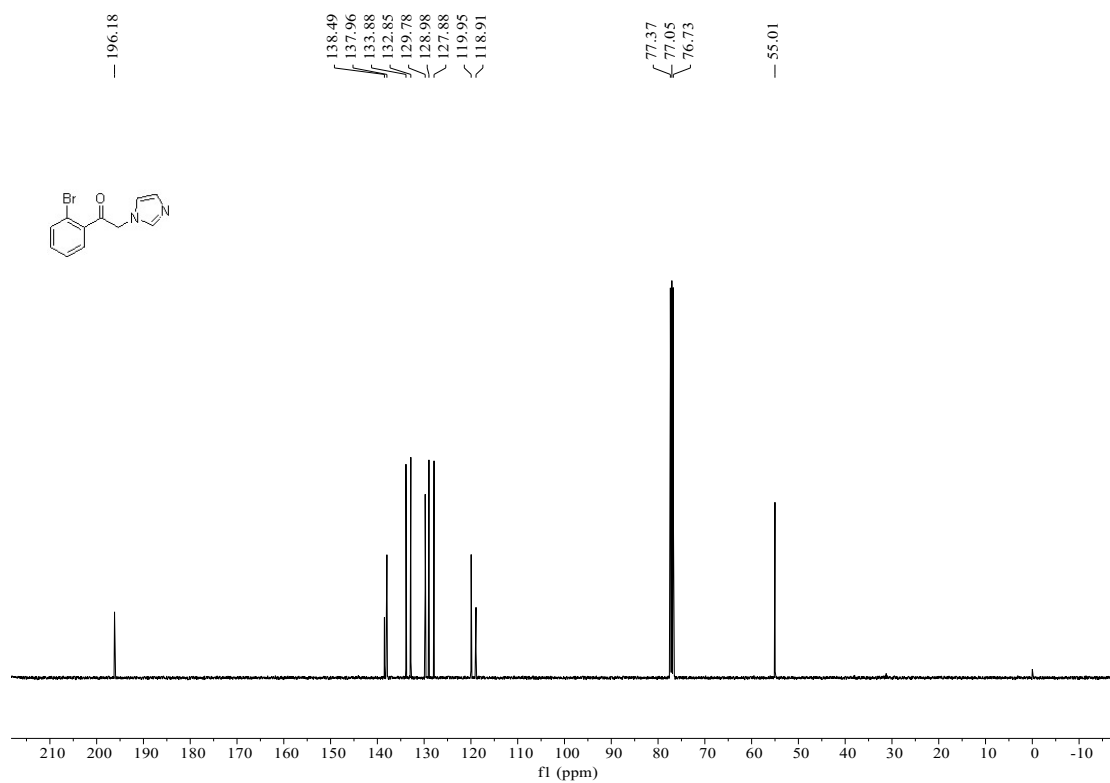
¹³C NMR (101 MHz, CDCl₃) of **1d**:



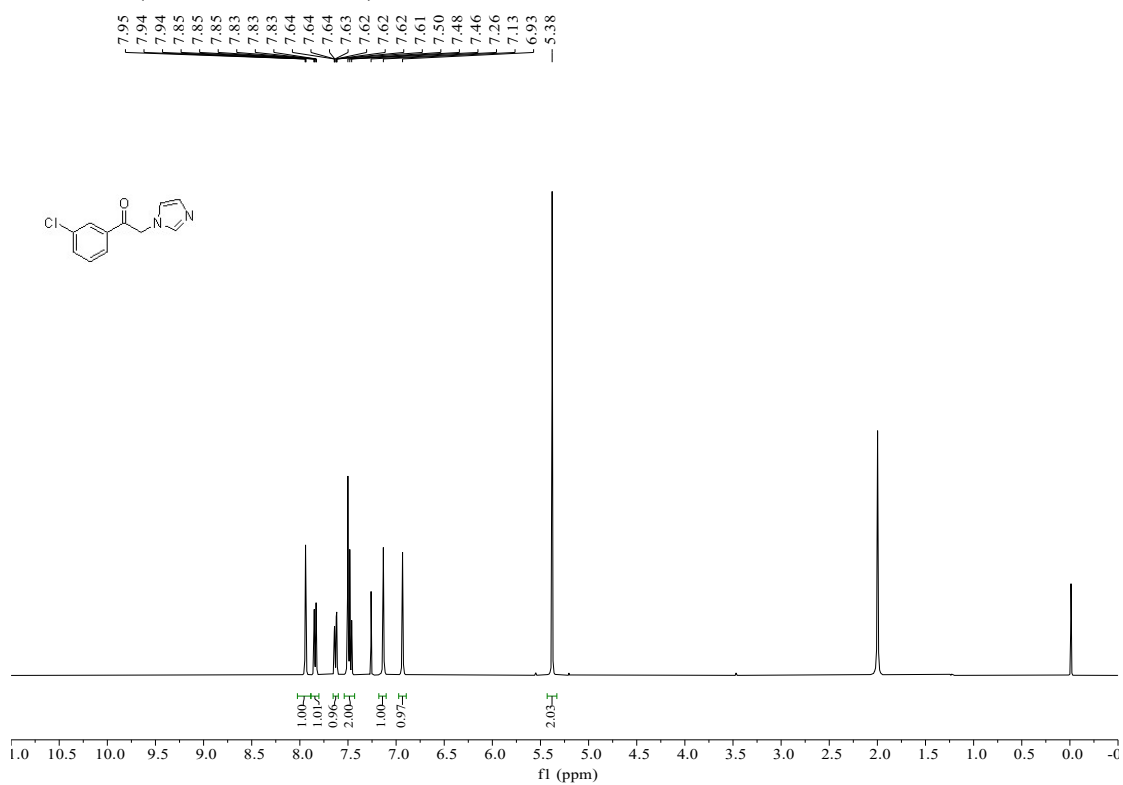
¹H NMR (400 MHz, CDCl₃) of **1e**:



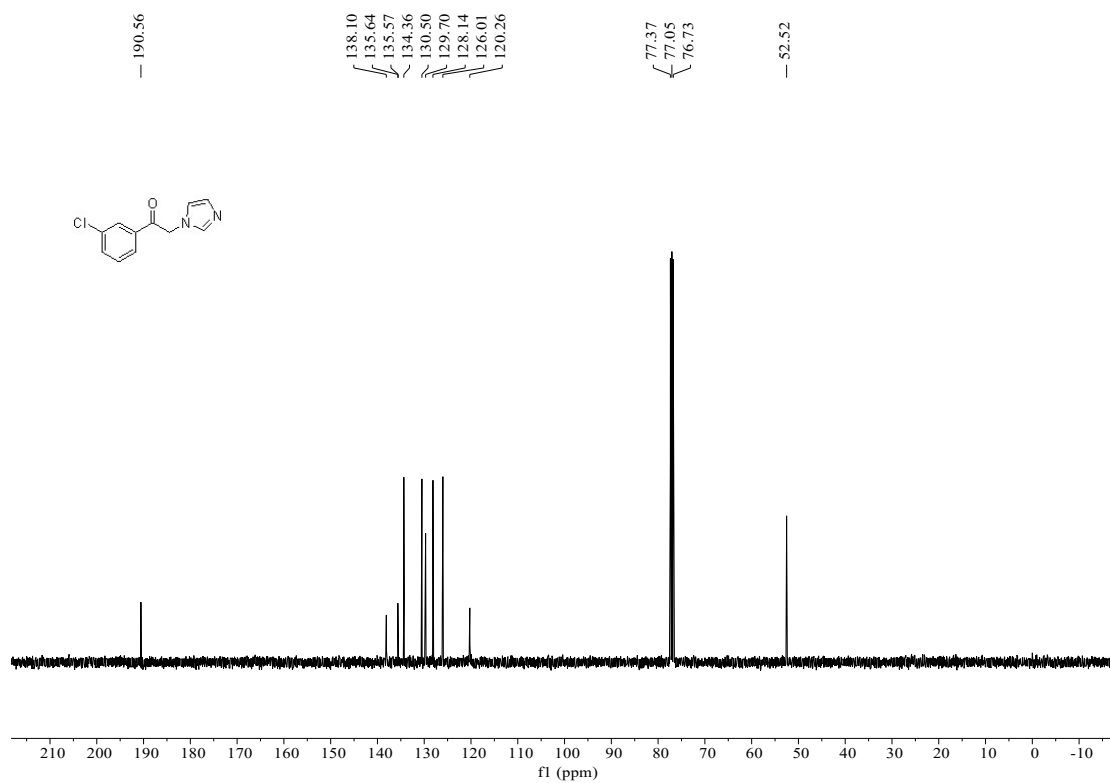
¹³C NMR (101 MHz, CDCl₃) of **1e**:



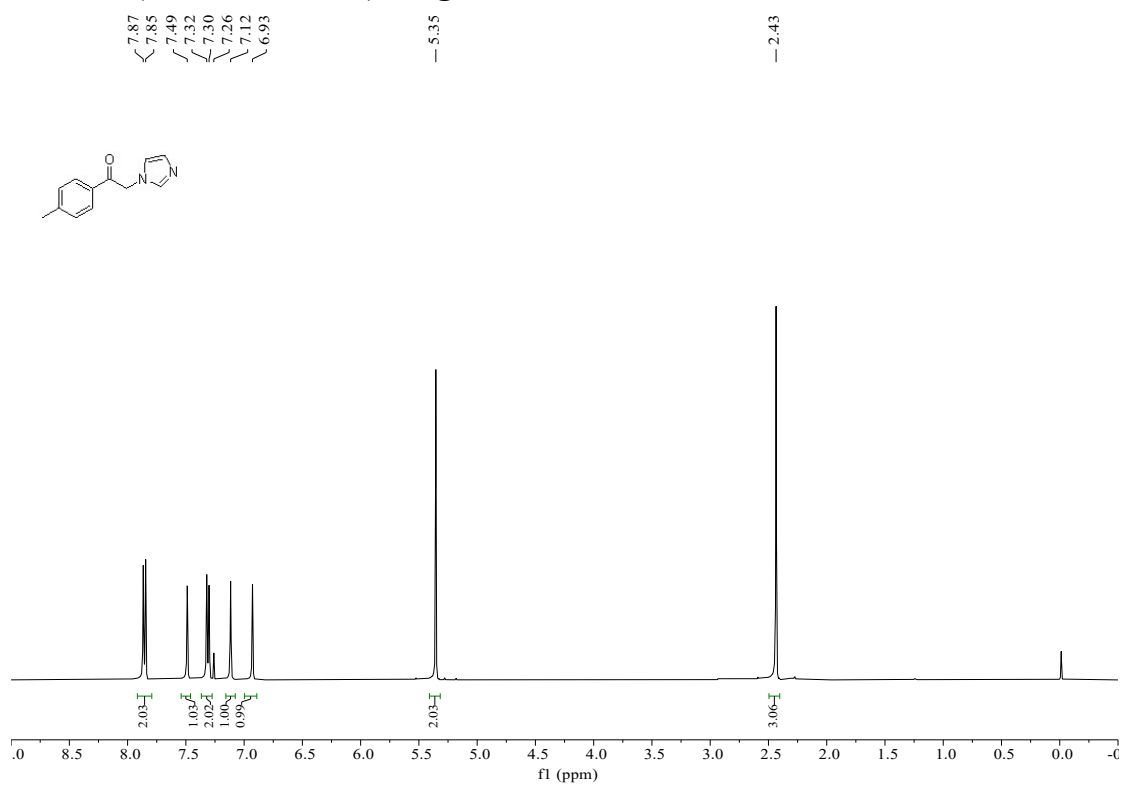
¹H NMR (400 MHz, CDCl₃) of **1f**:



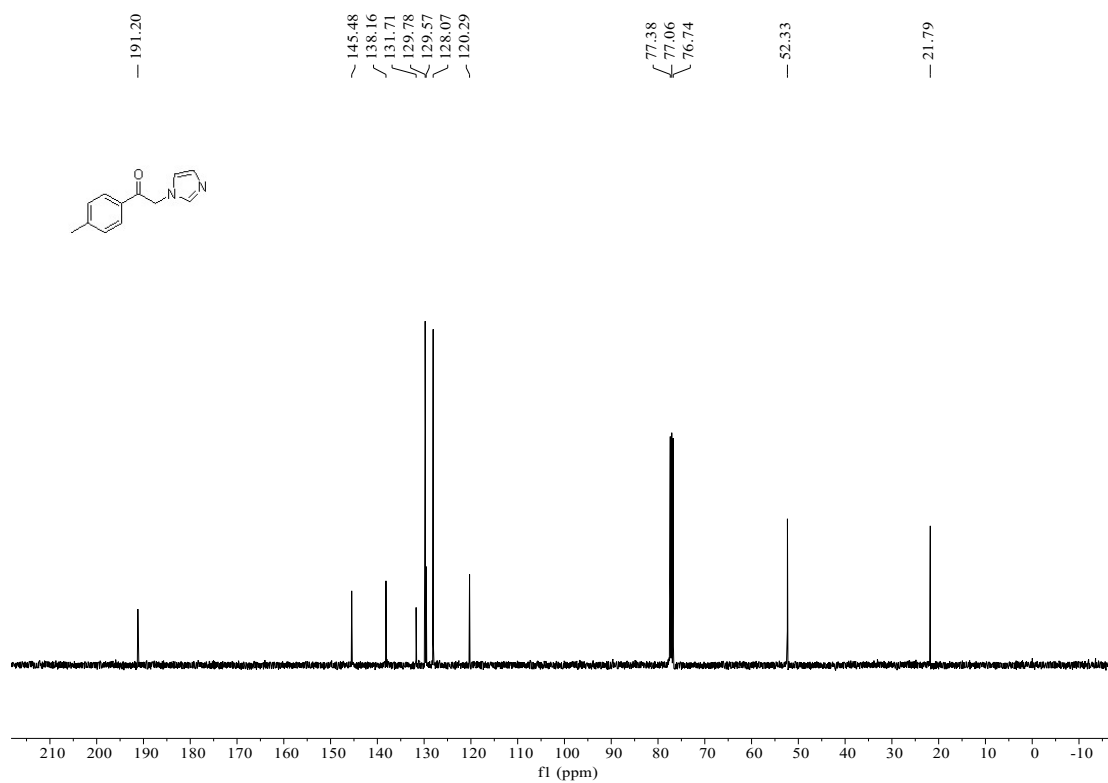
¹³C NMR (101 MHz, CDCl₃) of **1f**:



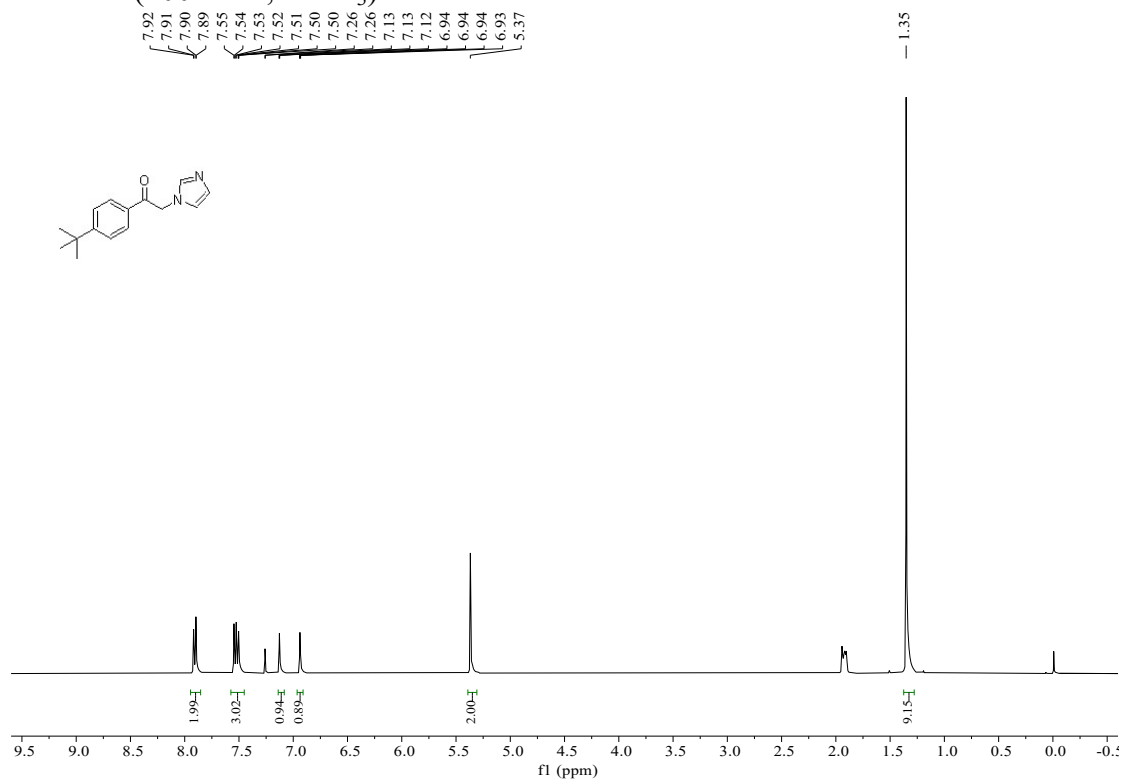
^1H NMR (400 MHz, CDCl_3) of **1g**:



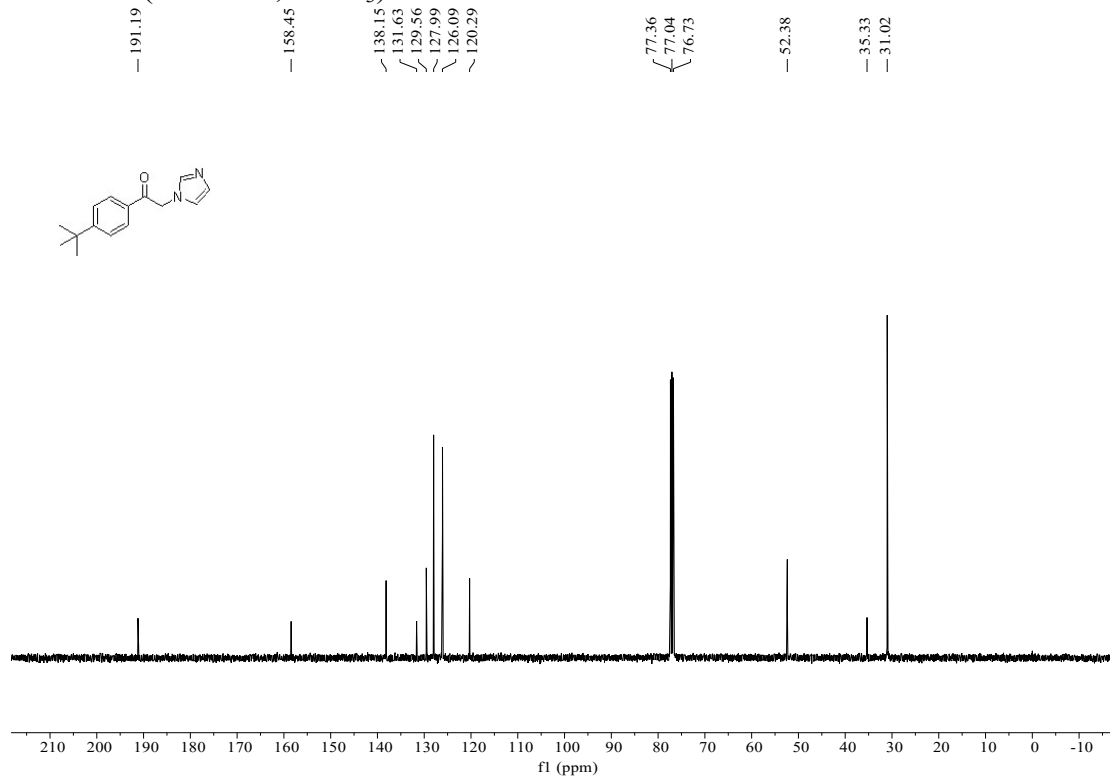
^{13}C NMR (101 MHz, CDCl_3) of **1g**:



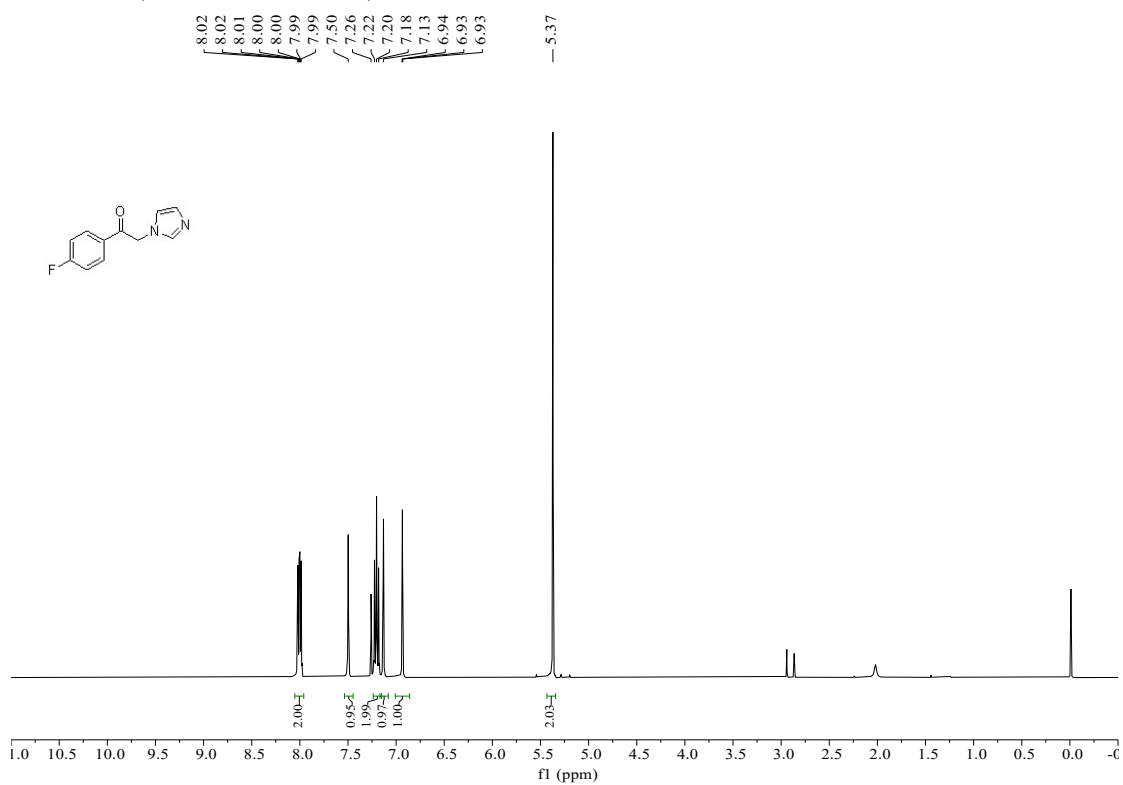
^1H NMR (400 MHz, CDCl_3) of **1h**:



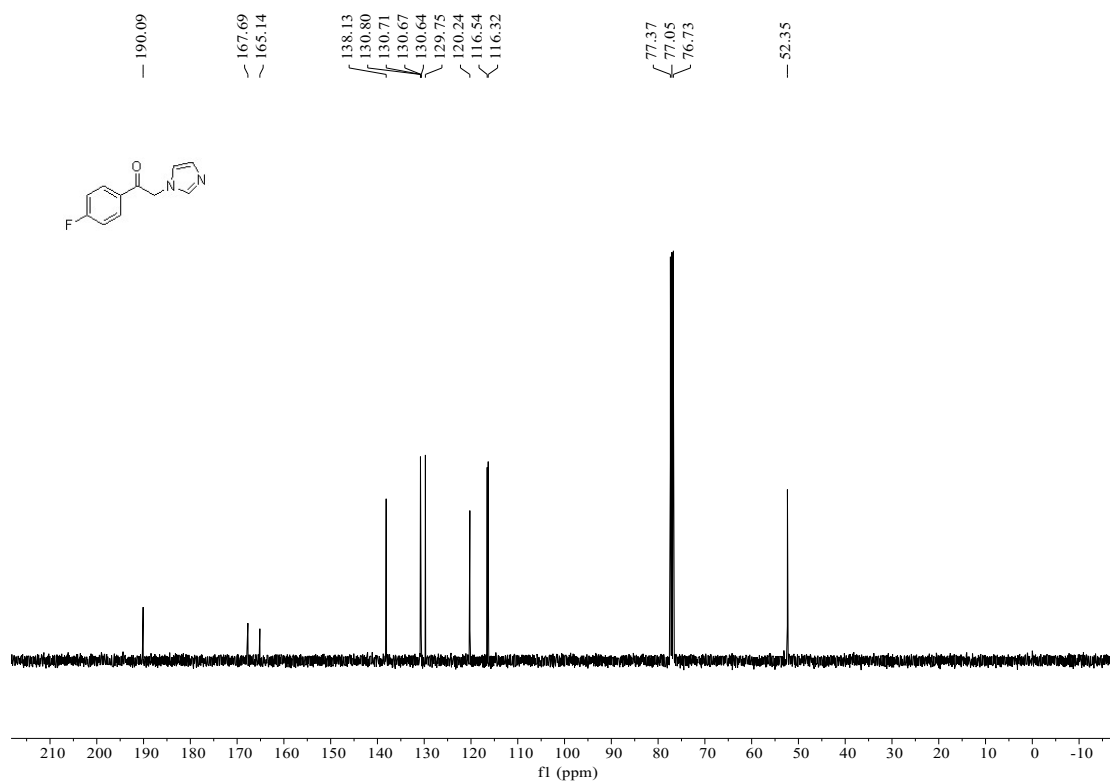
^{13}C NMR (101 MHz, CDCl_3) of **1h**:



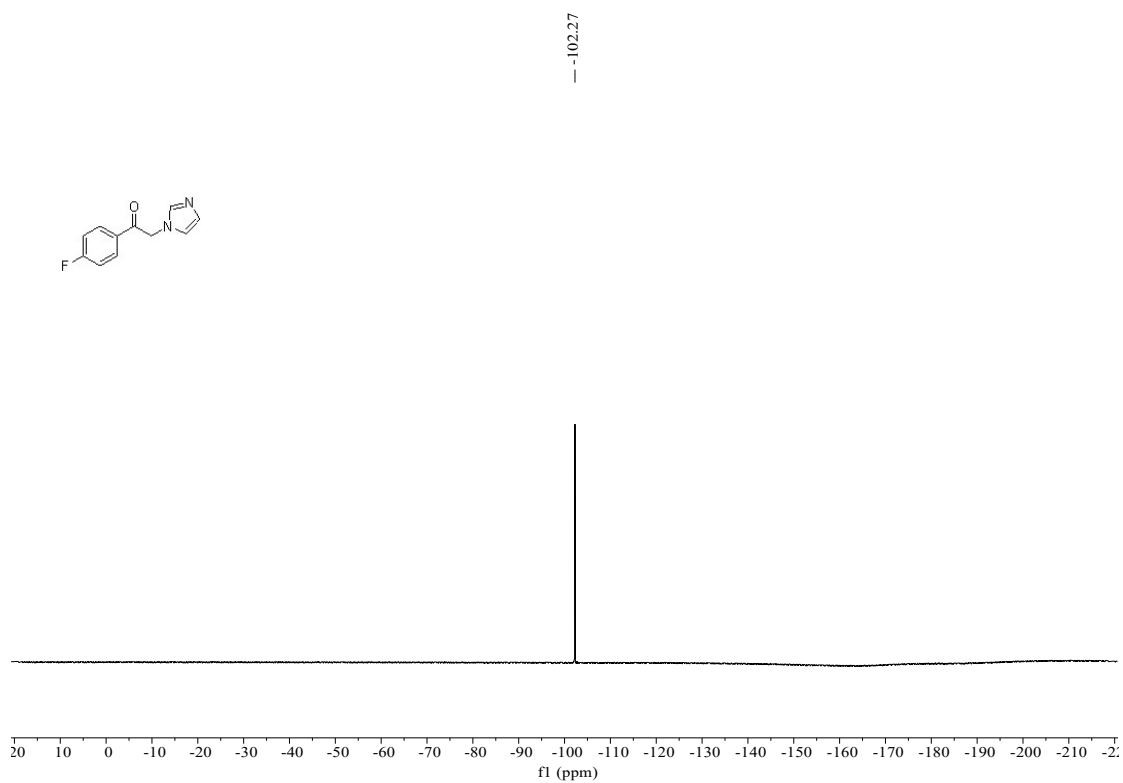
¹H NMR (400 MHz, CDCl₃) of **1i**:



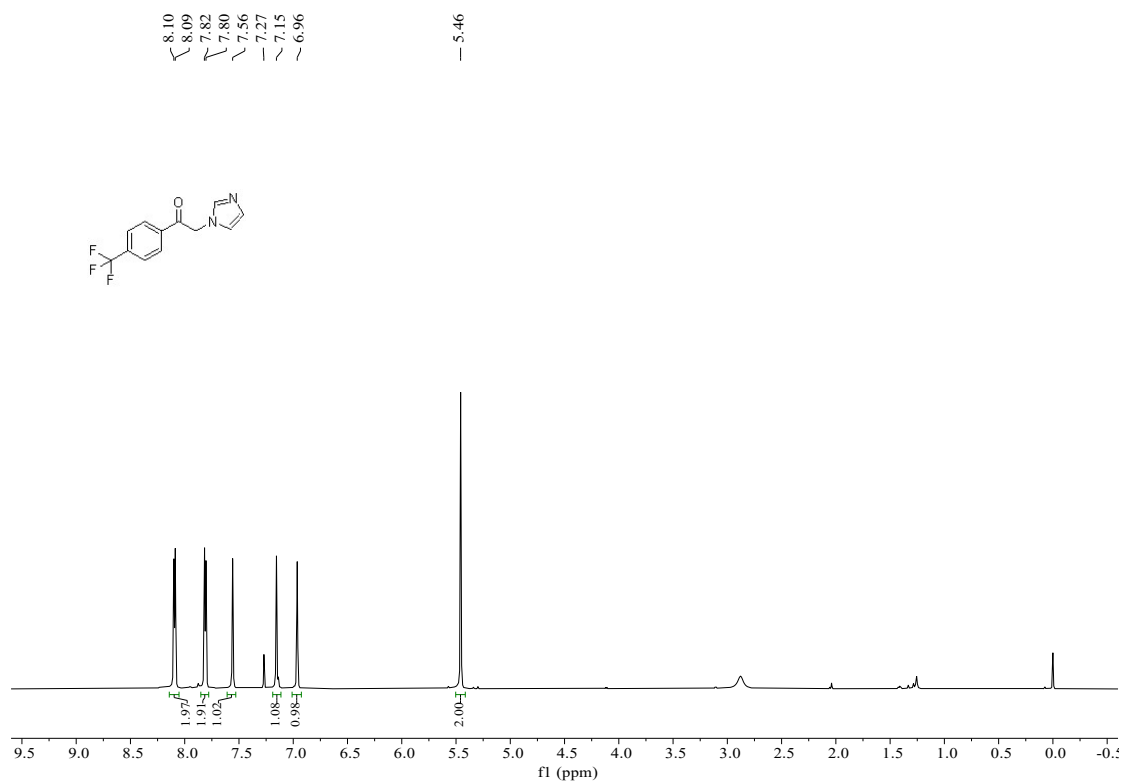
¹³C NMR (101 MHz, CDCl₃) of **1i**:



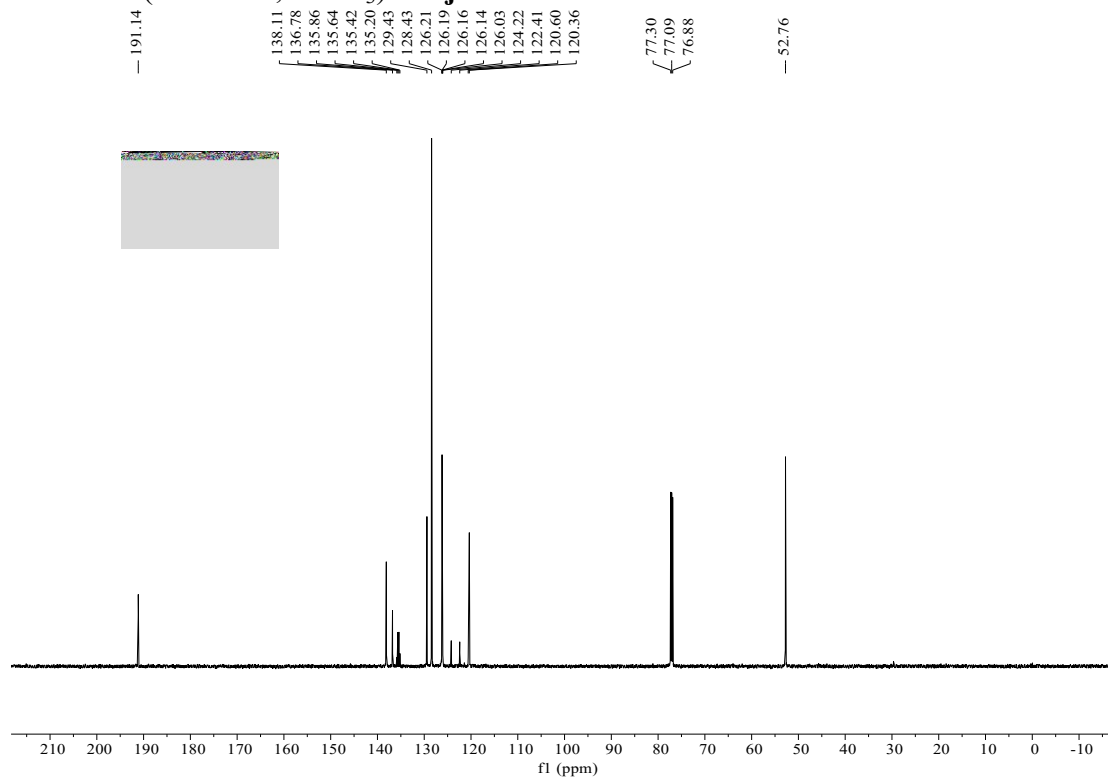
^{19}F NMR (376 MHz, CDCl_3) of **1i**:



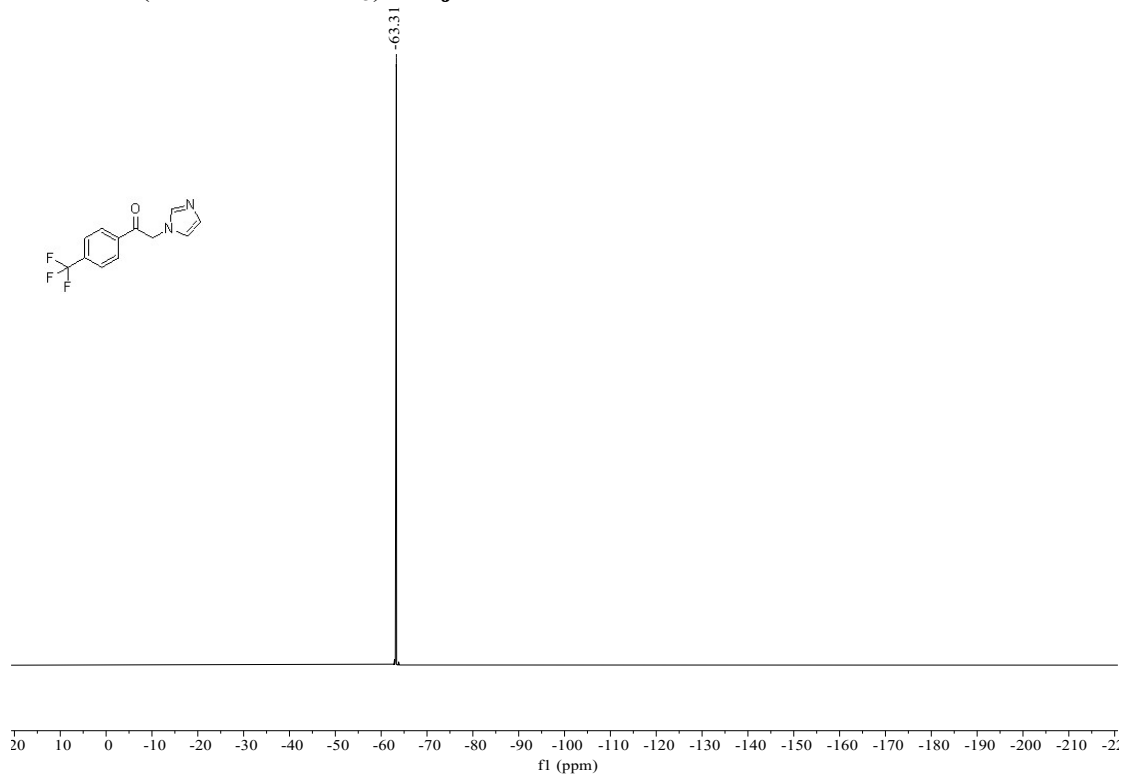
^1H NMR (600 MHz, CDCl_3) of **1j**:



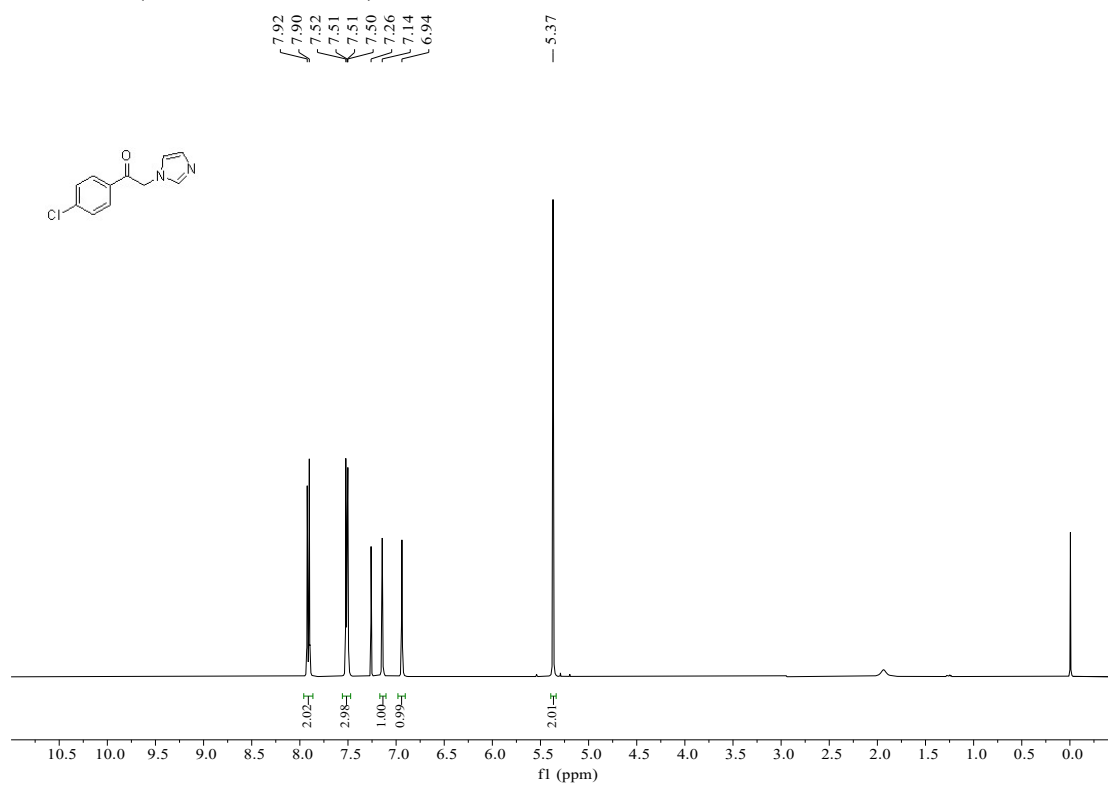
¹³C NMR (151 MHz, CDCl₃) of **1j**:



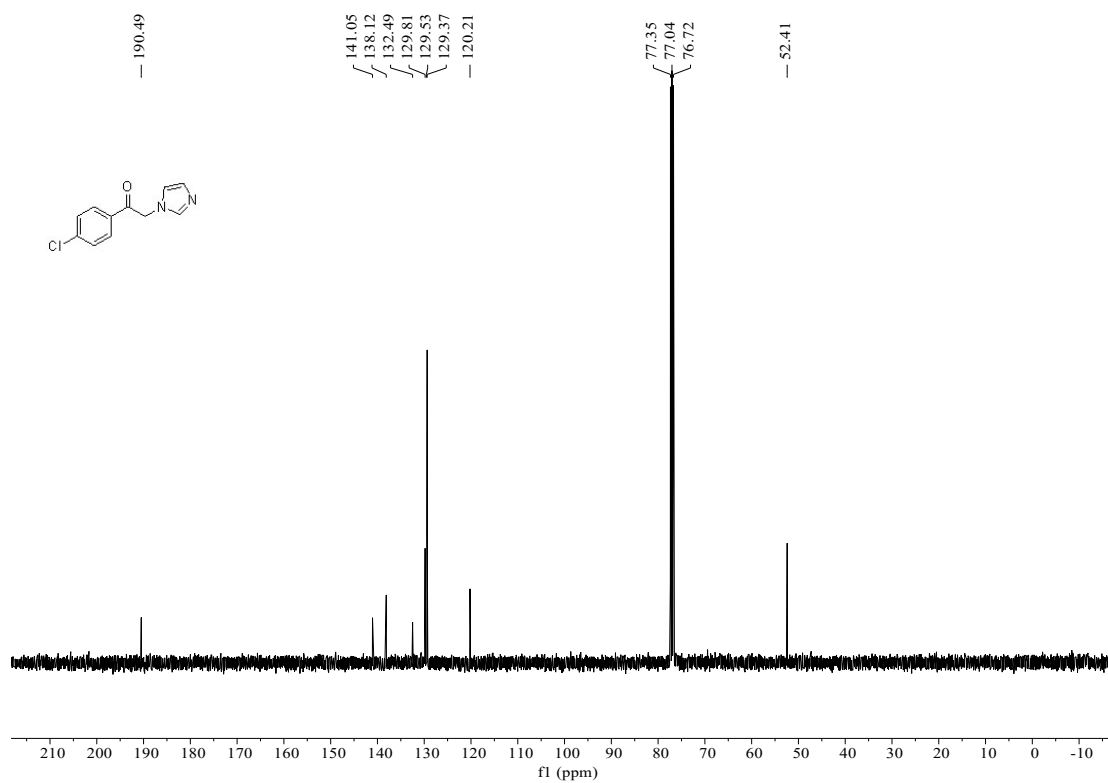
¹⁹F NMR (376 MHz, CDCl₃) of **1j**:



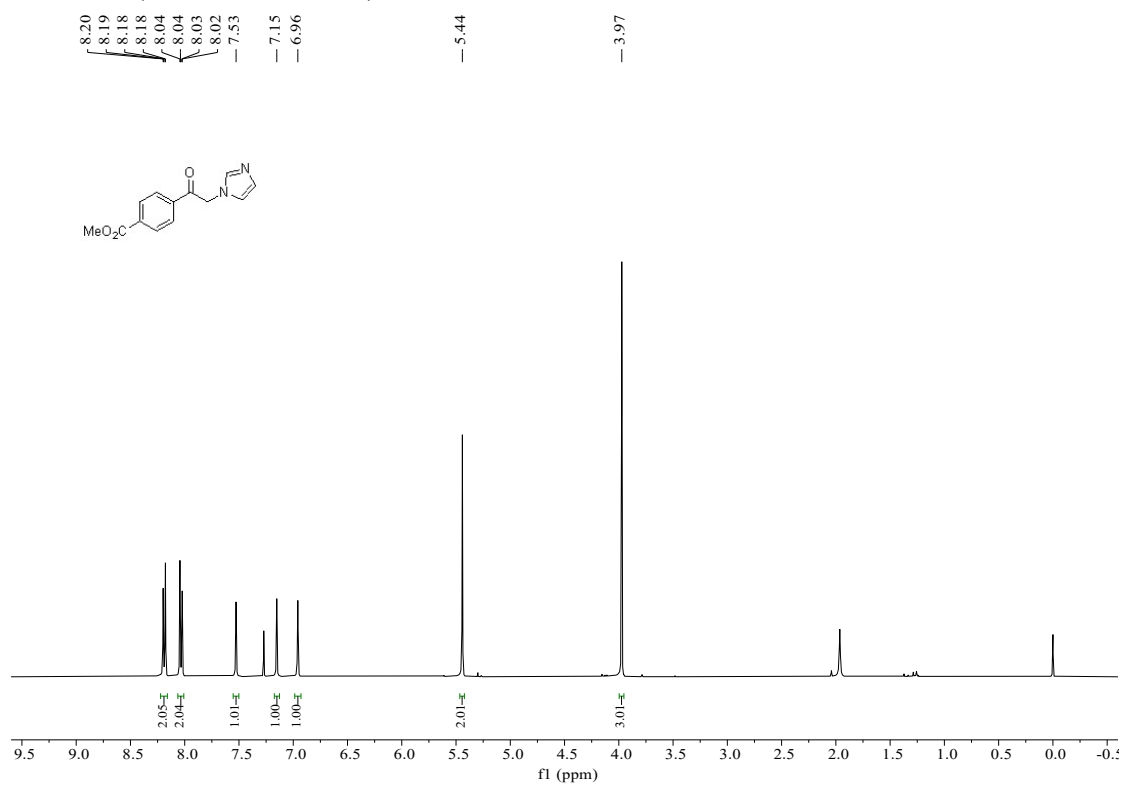
¹H NMR (400 MHz, CDCl₃) of **1k**:



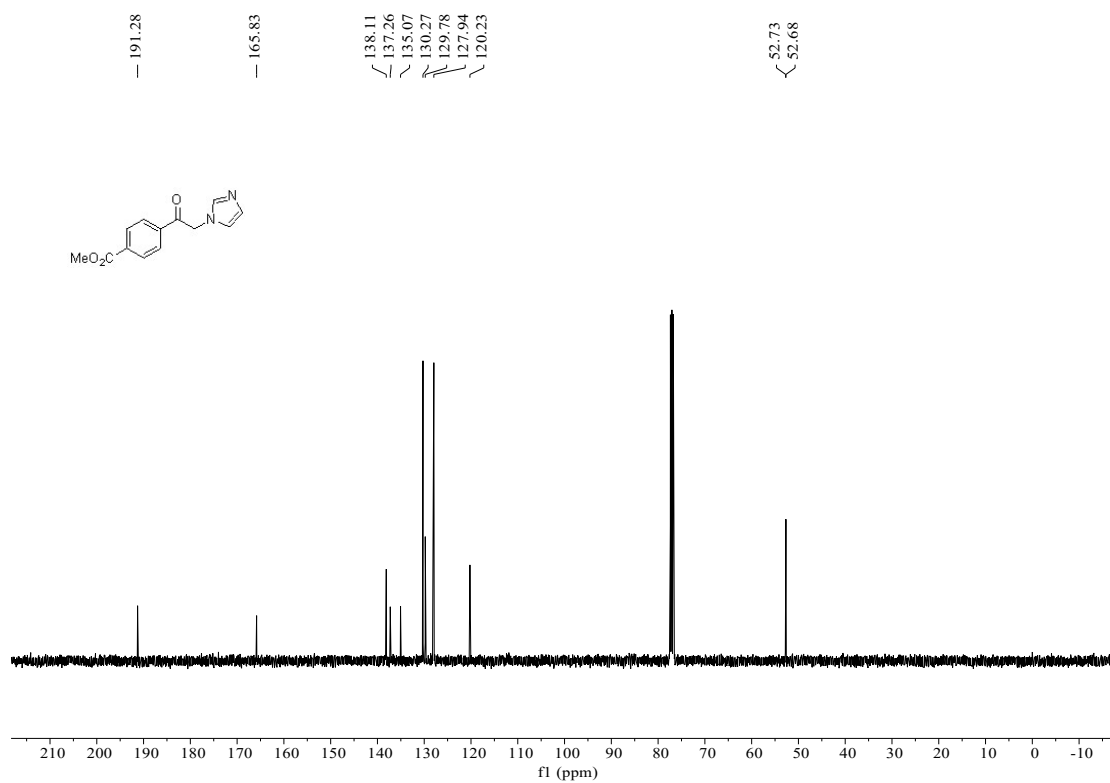
¹³C NMR (101 MHz, CDCl₃) of **1k**:



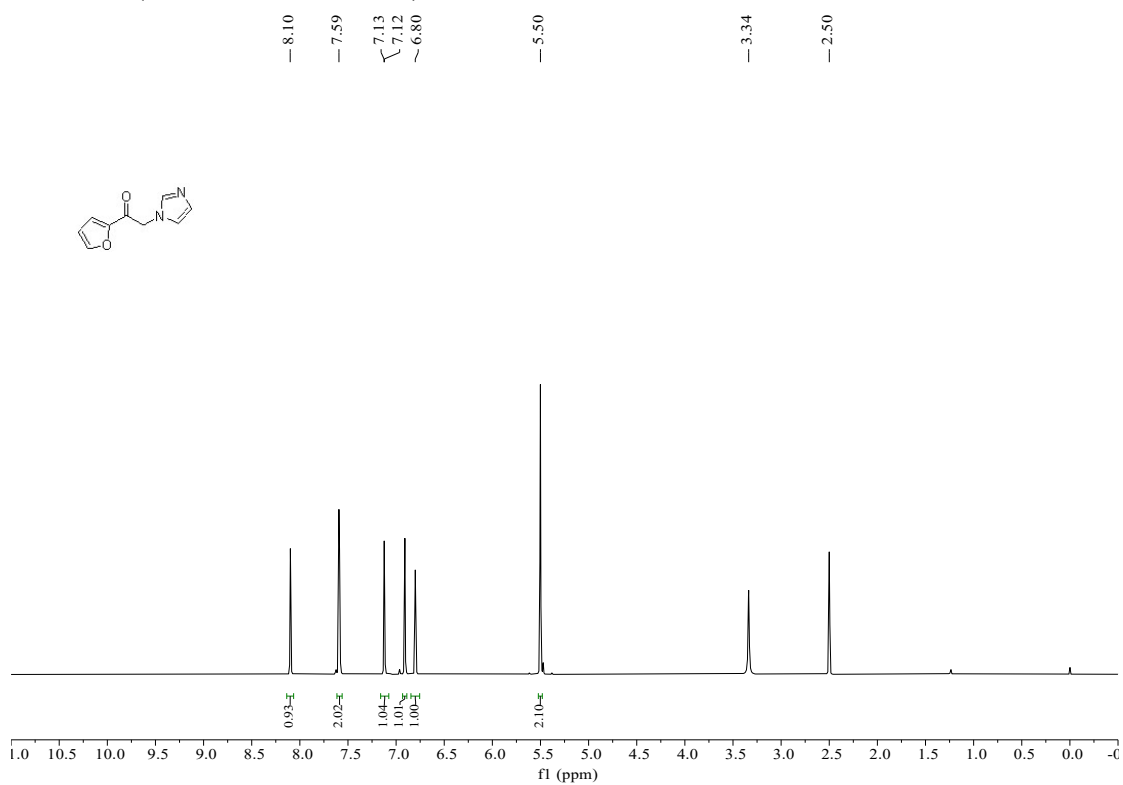
^1H NMR (400 MHz, CDCl_3) of **11**:



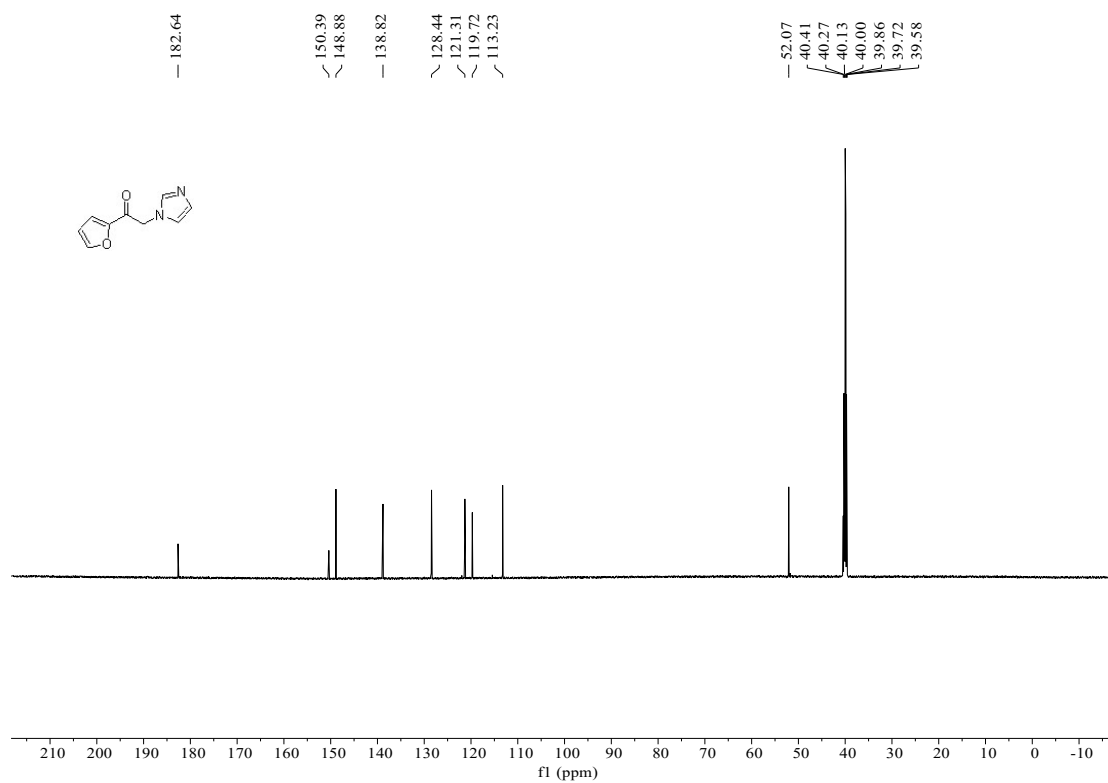
^{13}C NMR (101 MHz, CDCl_3) of **11**:



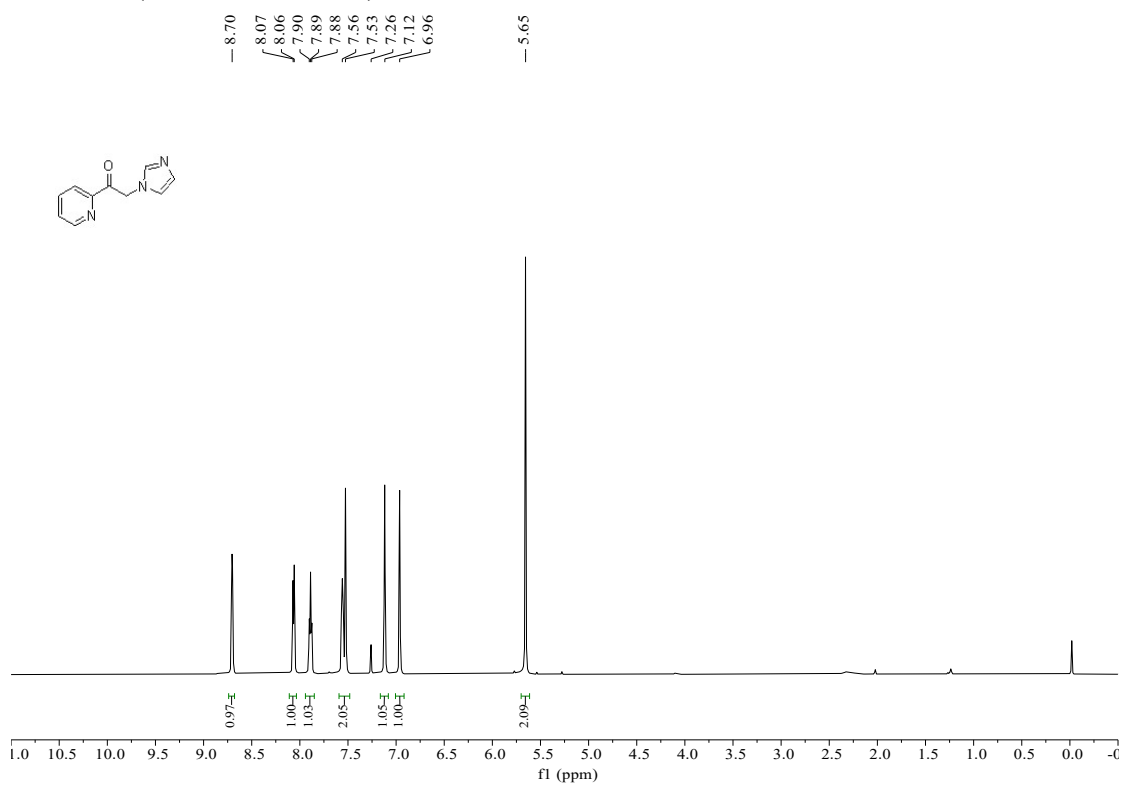
^1H NMR (600 MHz, $\text{DMSO-}d_6$) of **1m**:



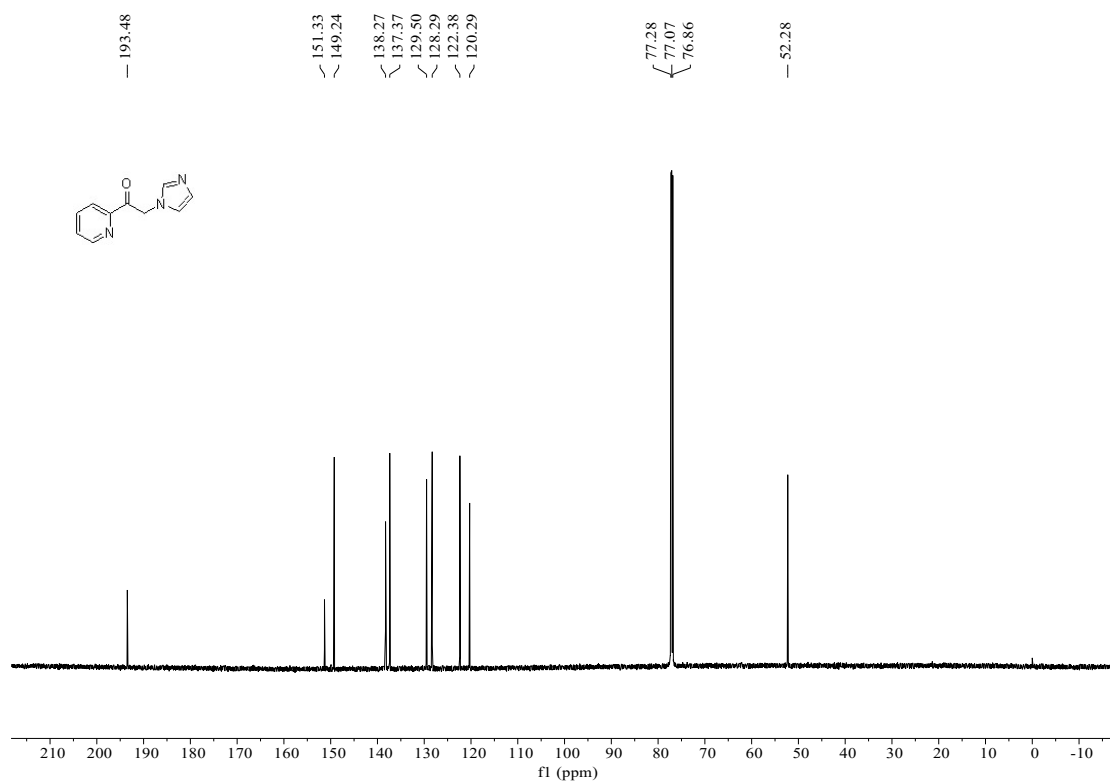
^{13}C NMR (151 MHz, $\text{DMSO-}d_6$) of **1m**:



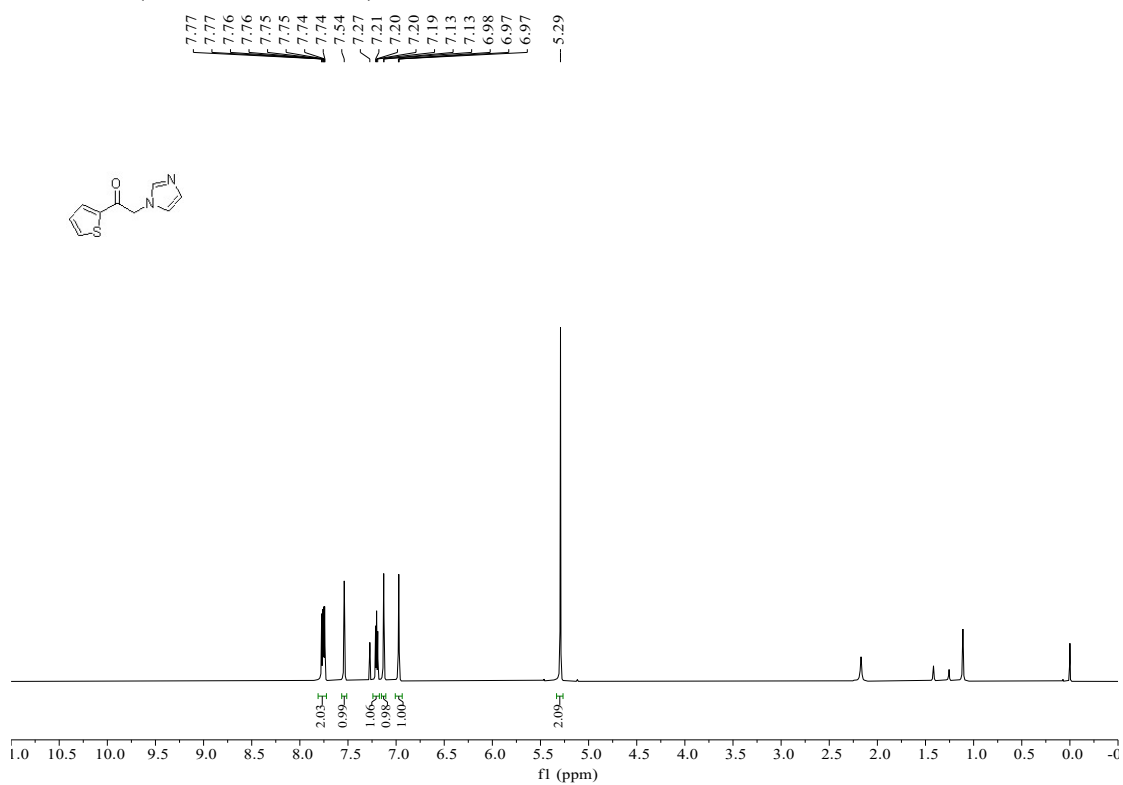
^1H NMR (600 MHz, CDCl_3) of **1n**:



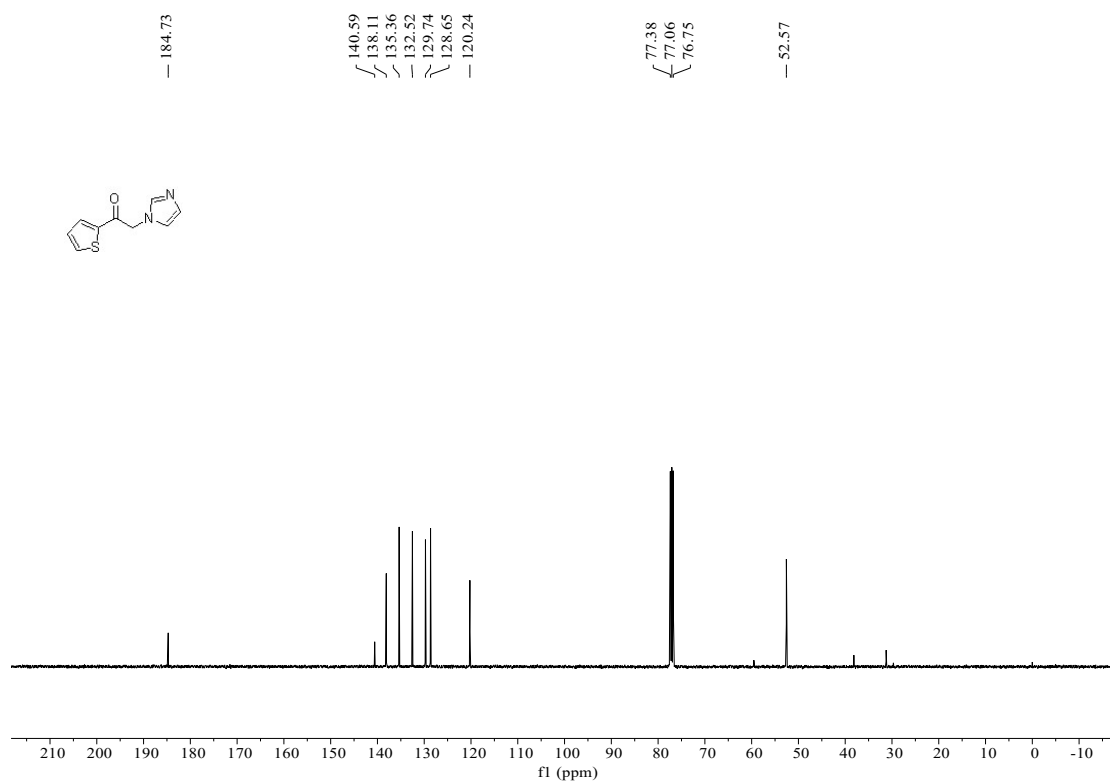
^{13}C NMR (151 MHz, CDCl_3) of **1n**:



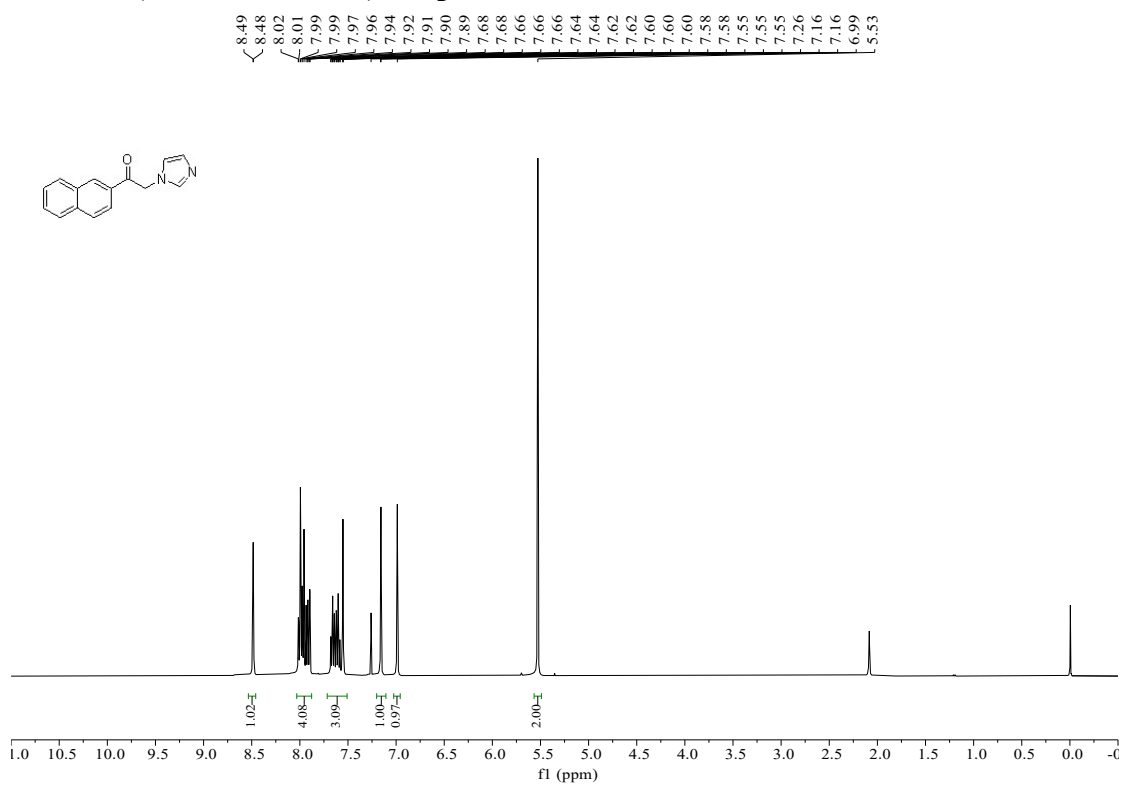
¹H NMR (400 MHz, CDCl₃) of **1o**:



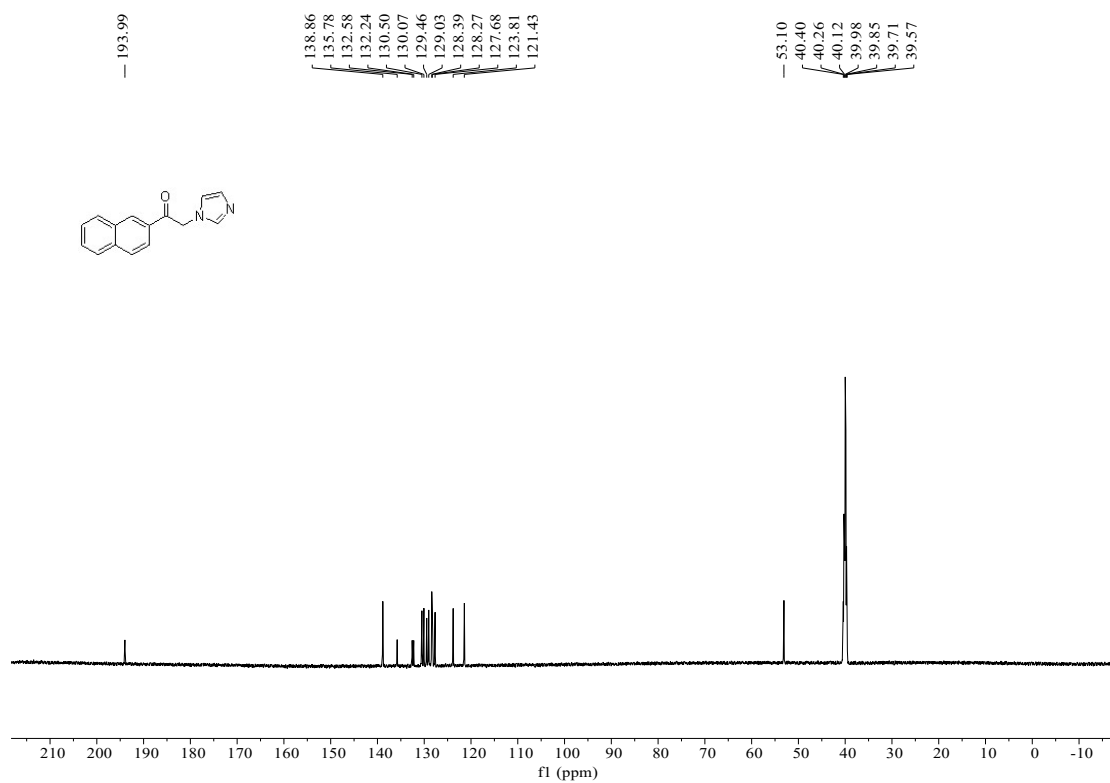
¹³C NMR (101 MHz, CDCl₃) of **1o**:



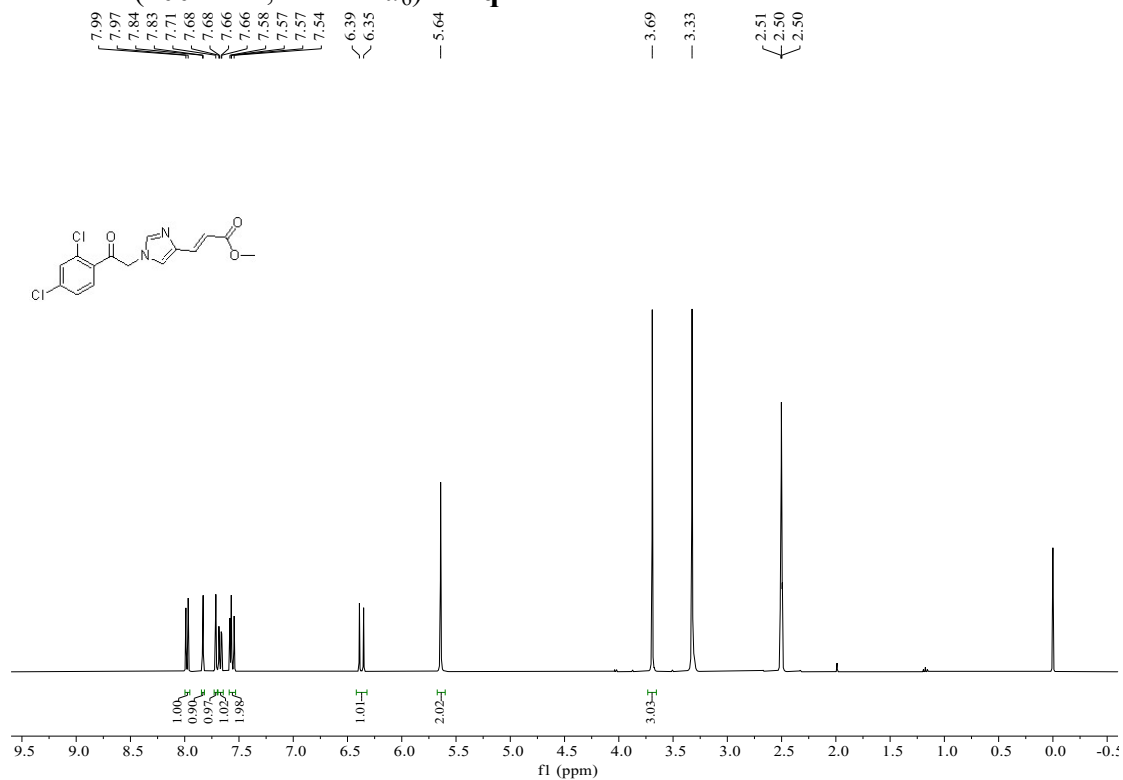
¹H NMR (400 MHz, CDCl₃) of **1p**:



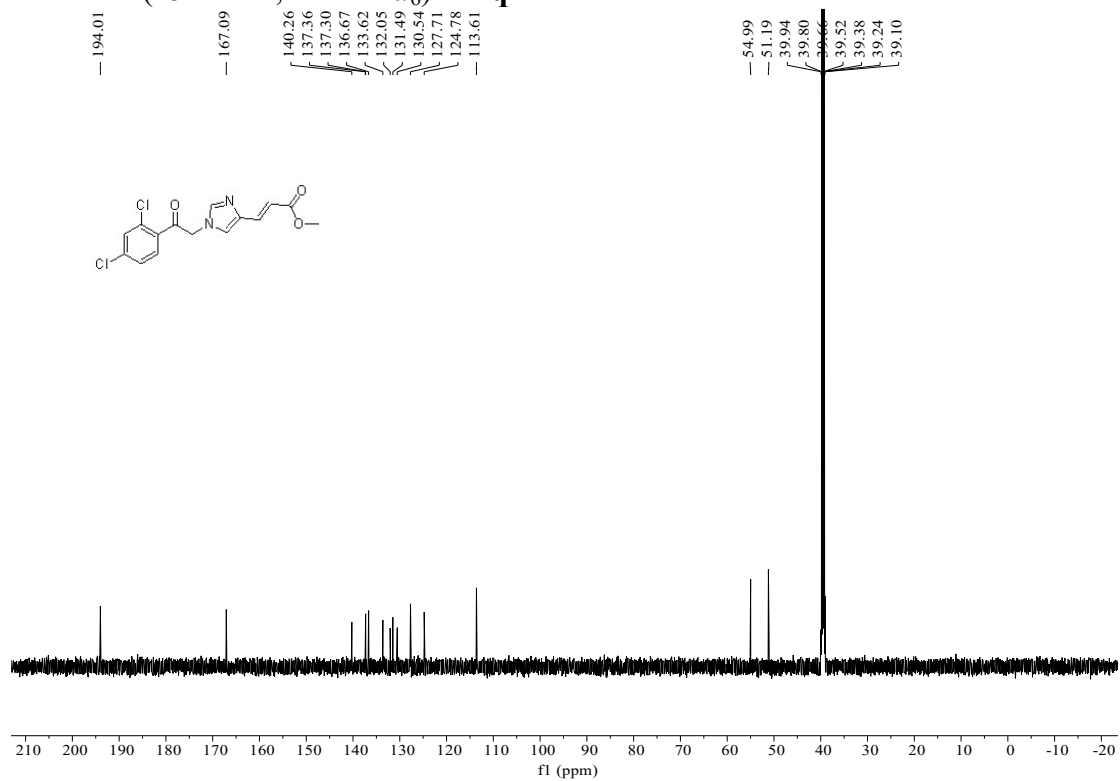
¹³C NMR (101 MHz, CDCl₃) of **1p**:



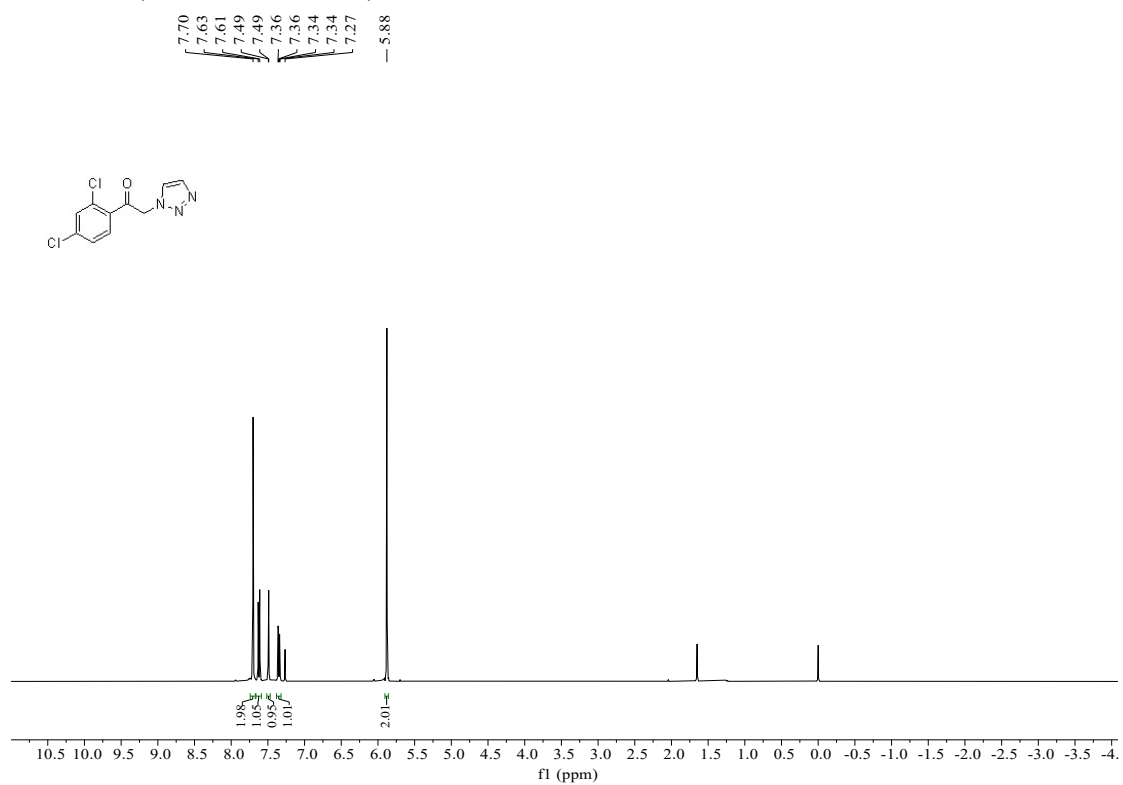
¹H NMR (400 MHz, DMSO-*d*₆) of **1q**:



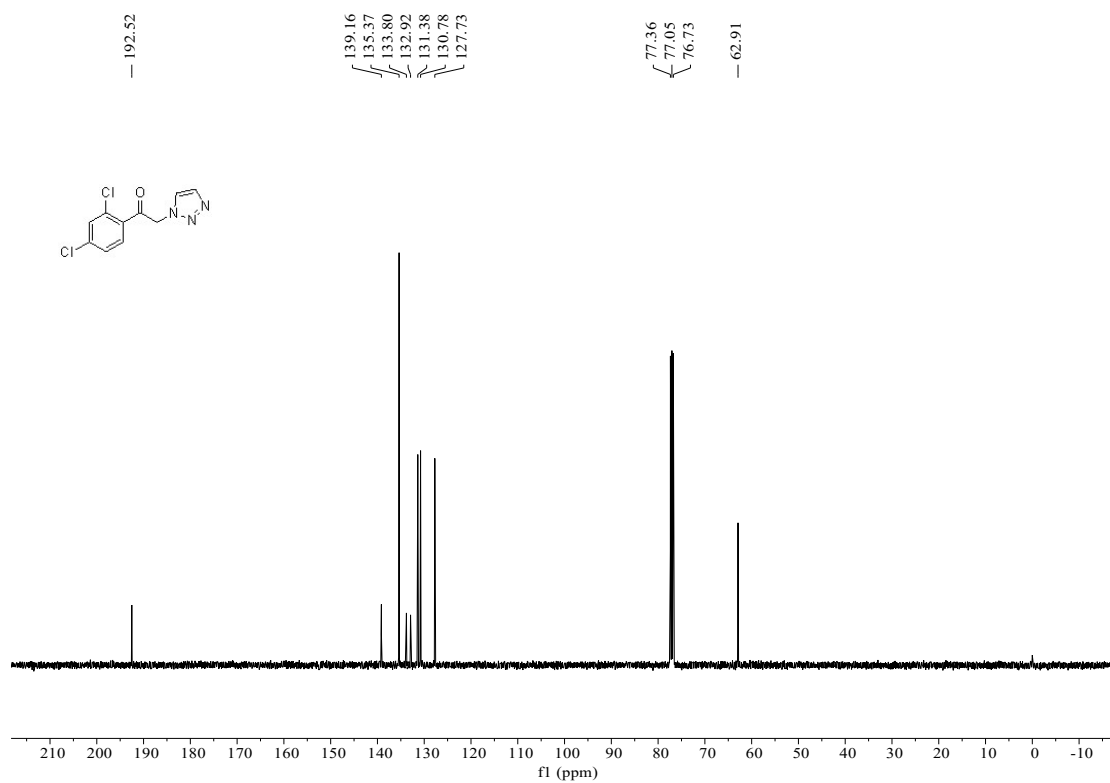
¹³C NMR (151 MHz, DMSO-*d*₆) of **1q**:



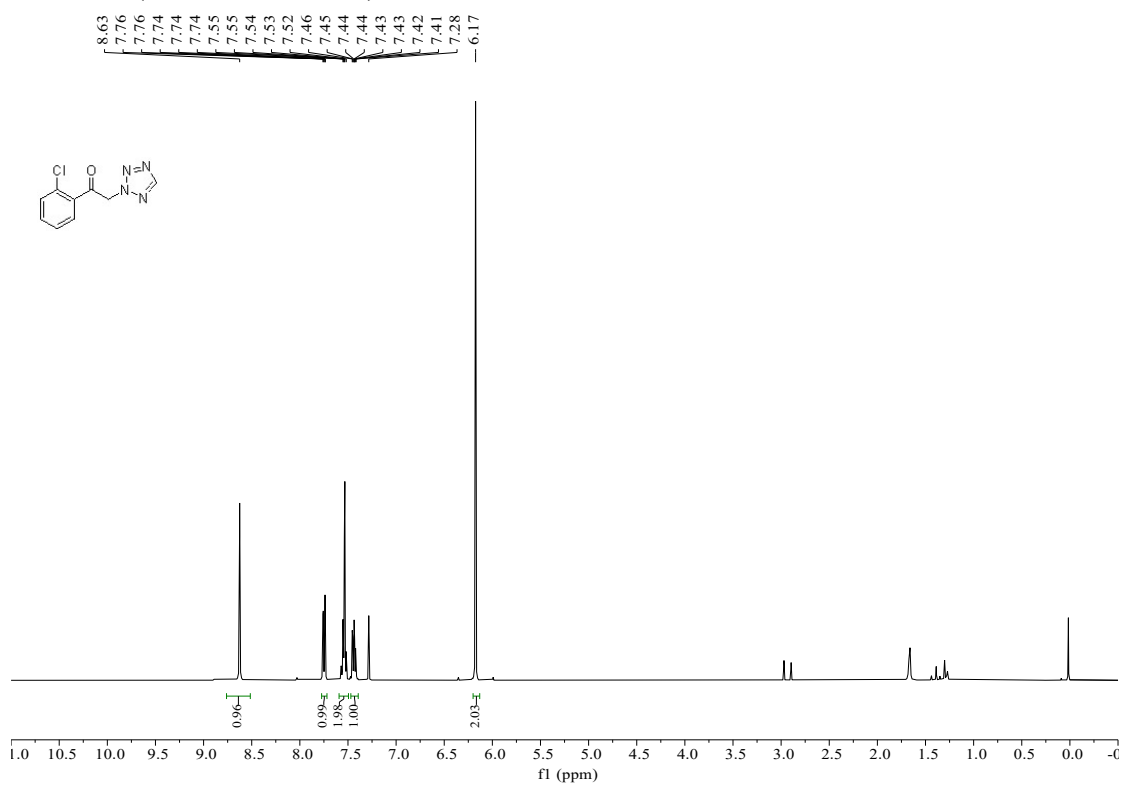
^1H NMR (400 MHz, CDCl_3) of **1r**:



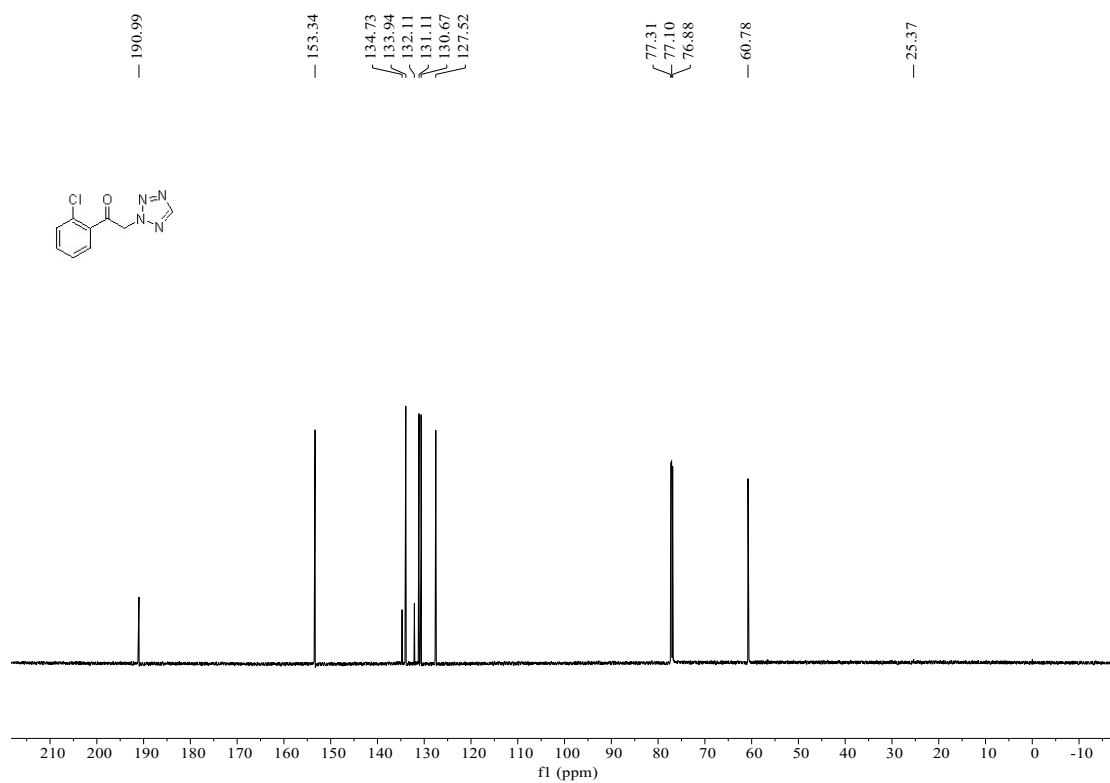
^{13}C NMR (101 MHz, CDCl_3) of **1r**:



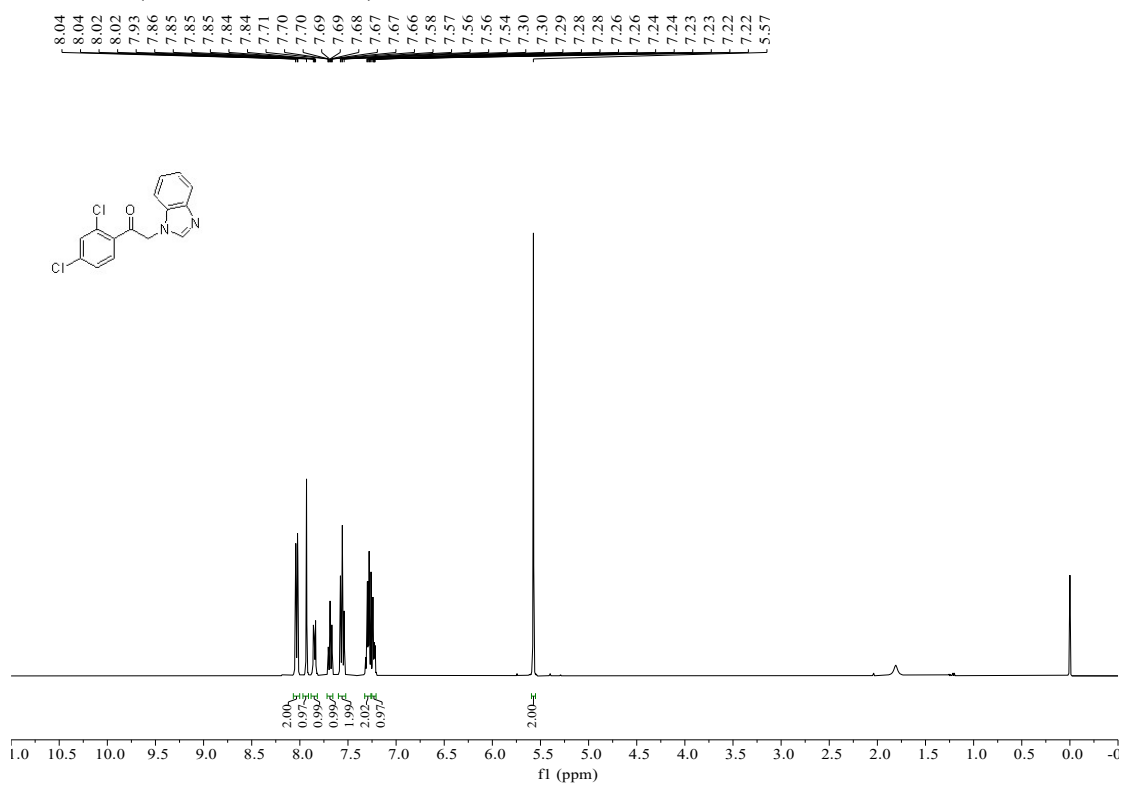
¹H NMR (400 MHz, CDCl₃) of **1s**:



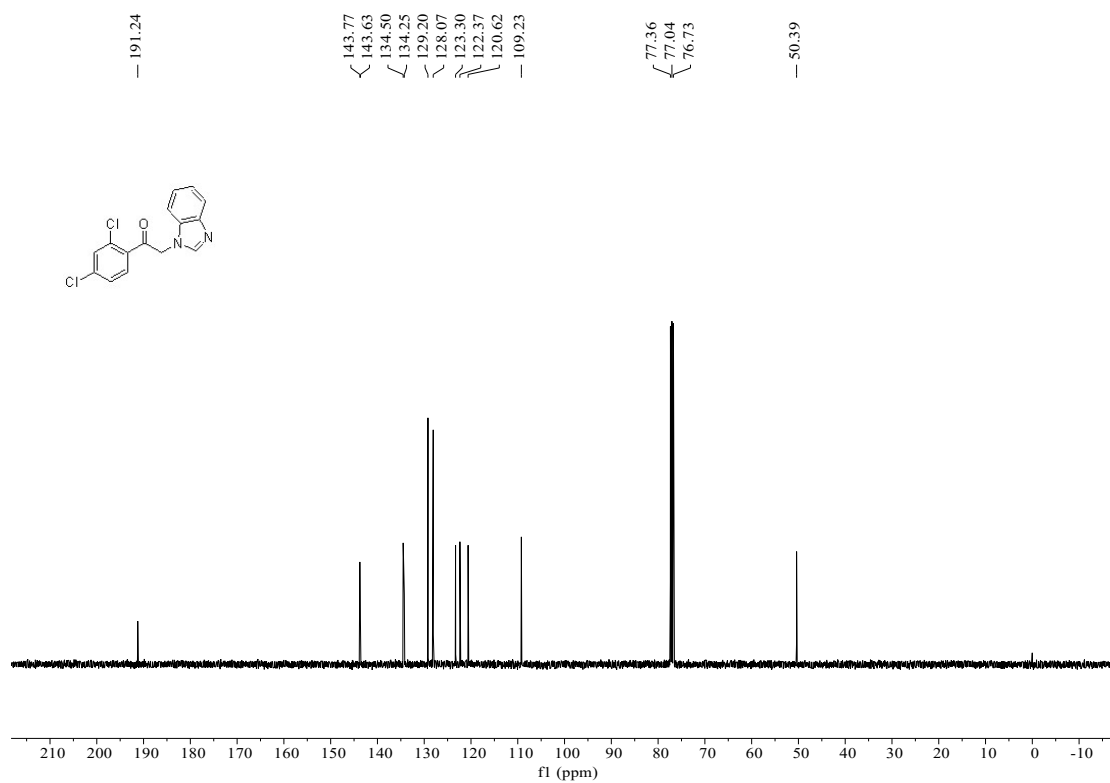
¹³C NMR (151 MHz, CDCl₃) of **1s**:



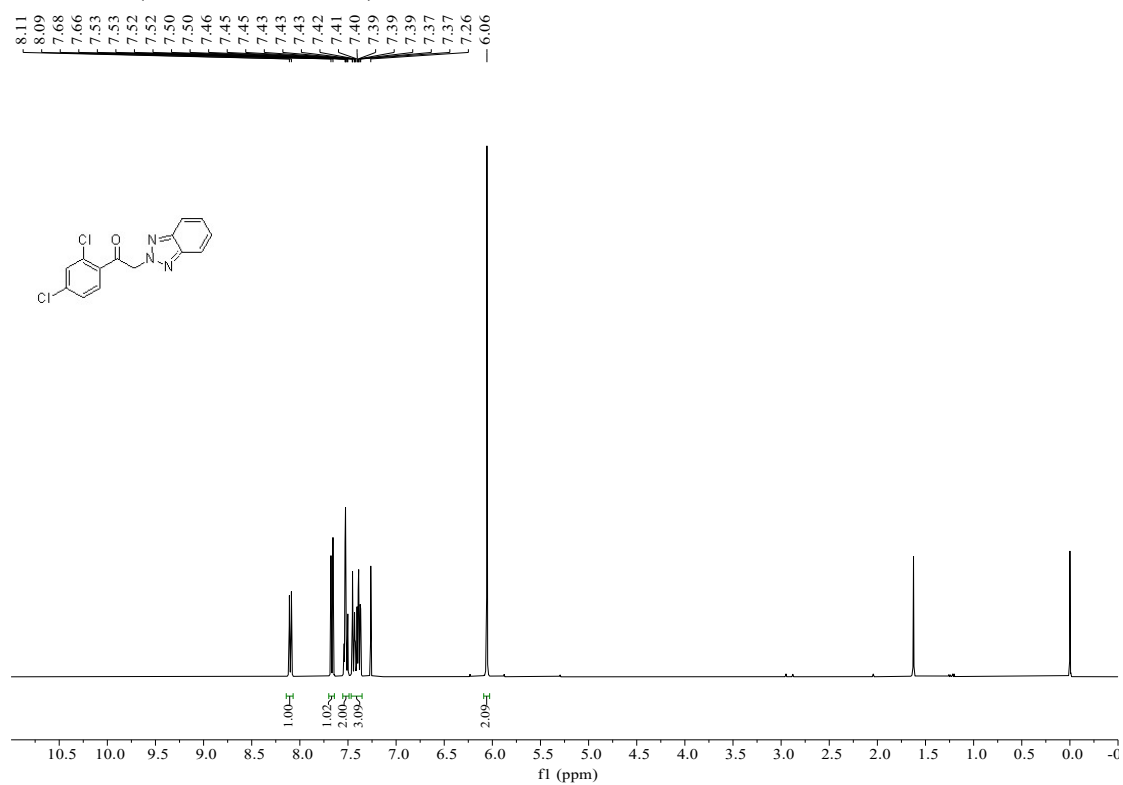
¹H NMR (400 MHz, CDCl₃) of **1t**:



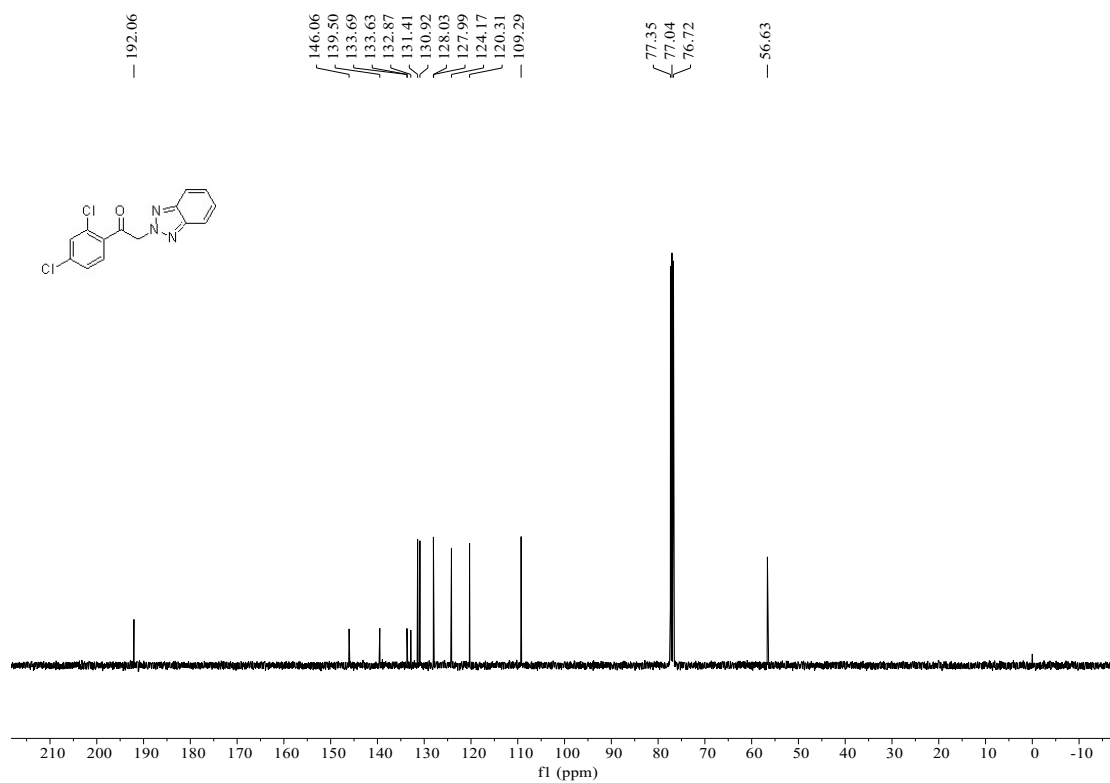
¹³C NMR (101 MHz, CDCl₃) of **1t**:



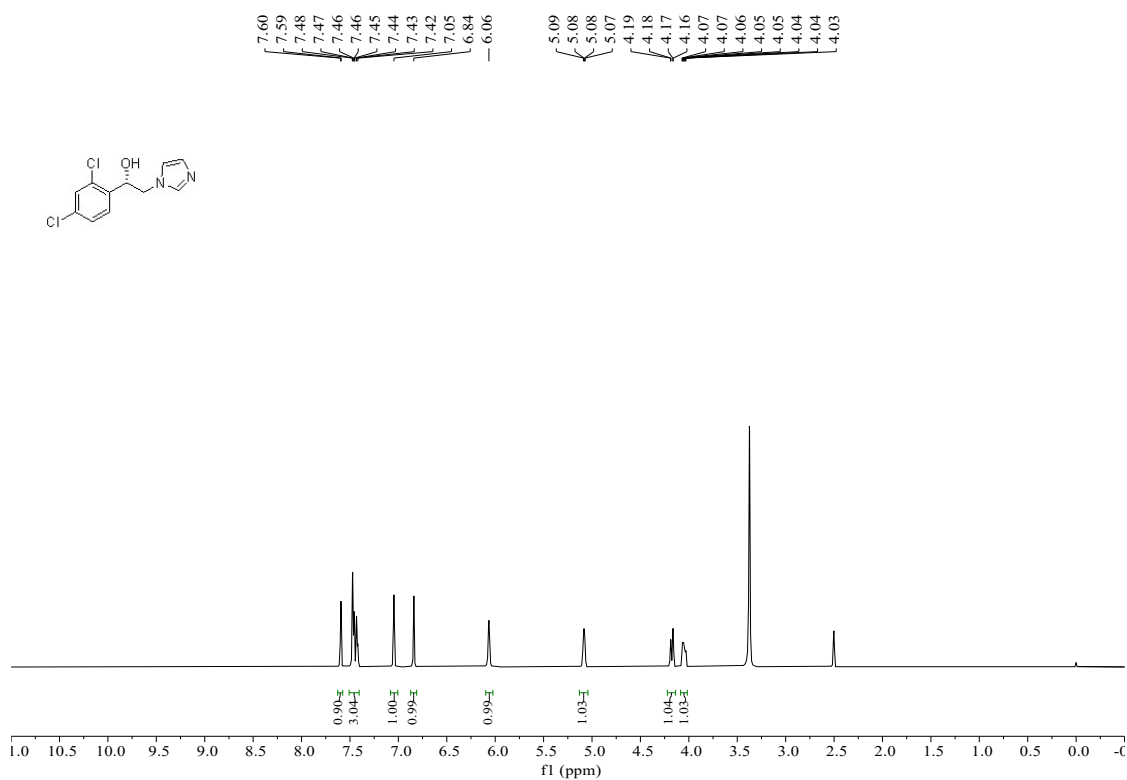
¹H NMR (400 MHz, CDCl₃) of **1u**:



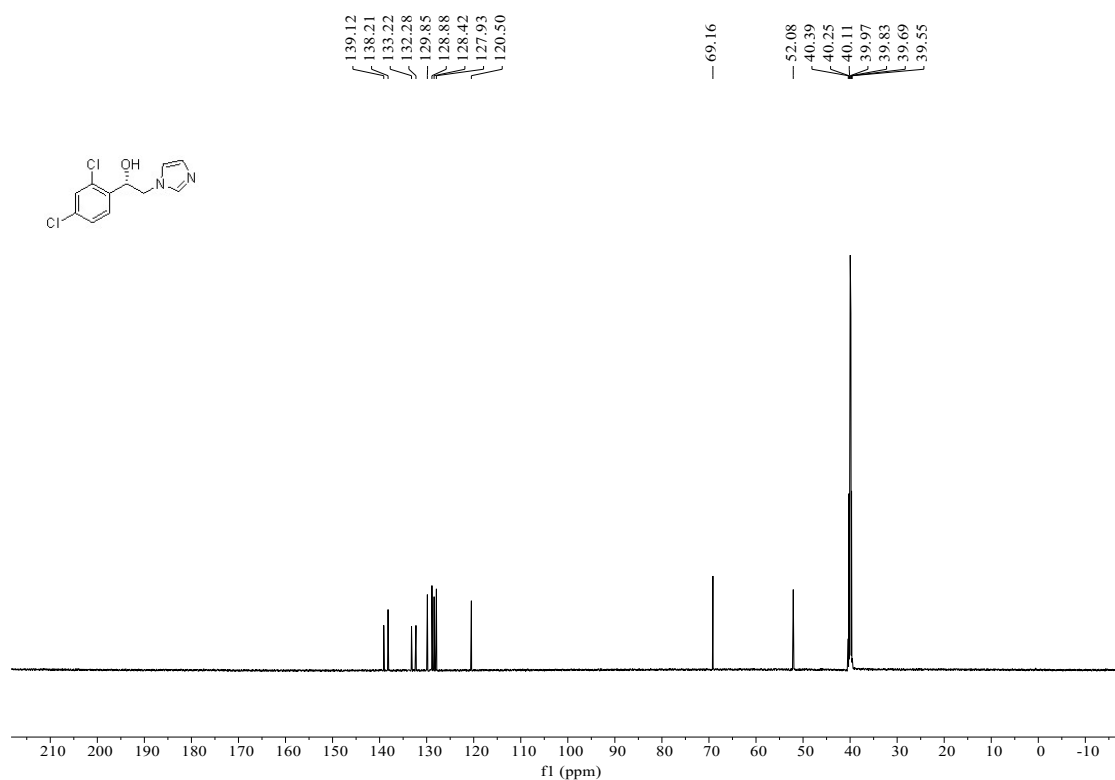
¹³C NMR (101 MHz, CDCl₃) of **1u**:



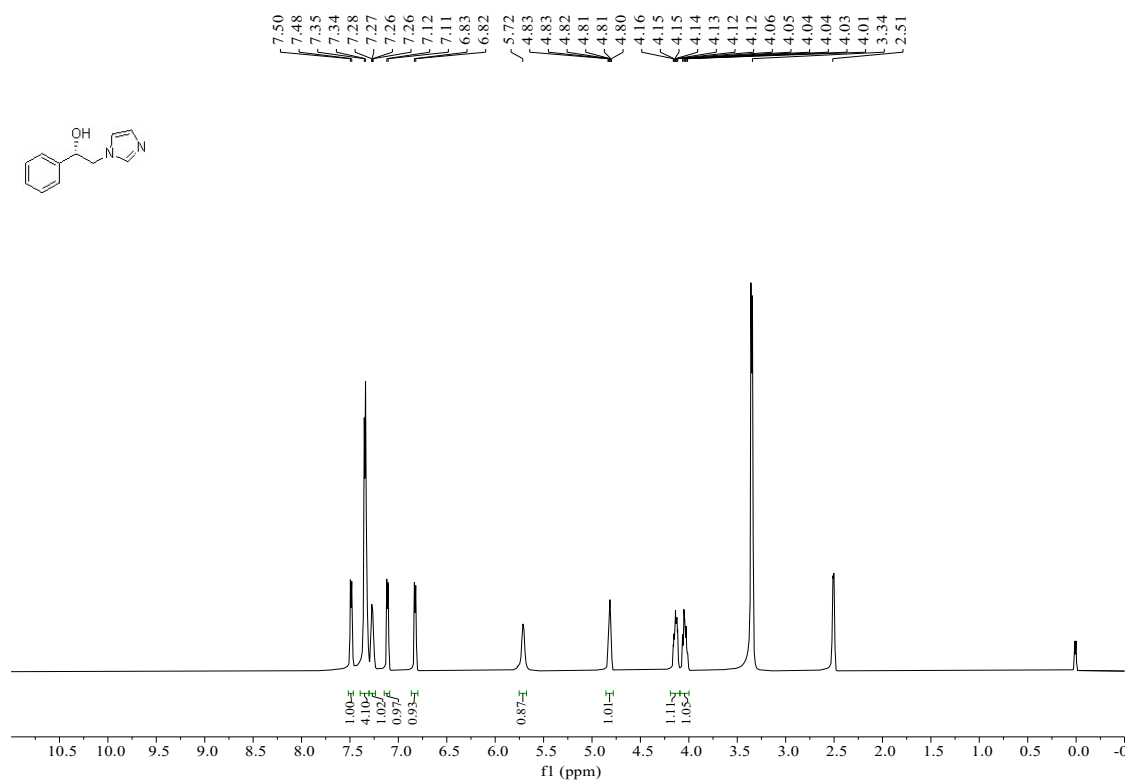
^1H NMR (600 MHz, $\text{DMSO-}d_6$) of **2a**:



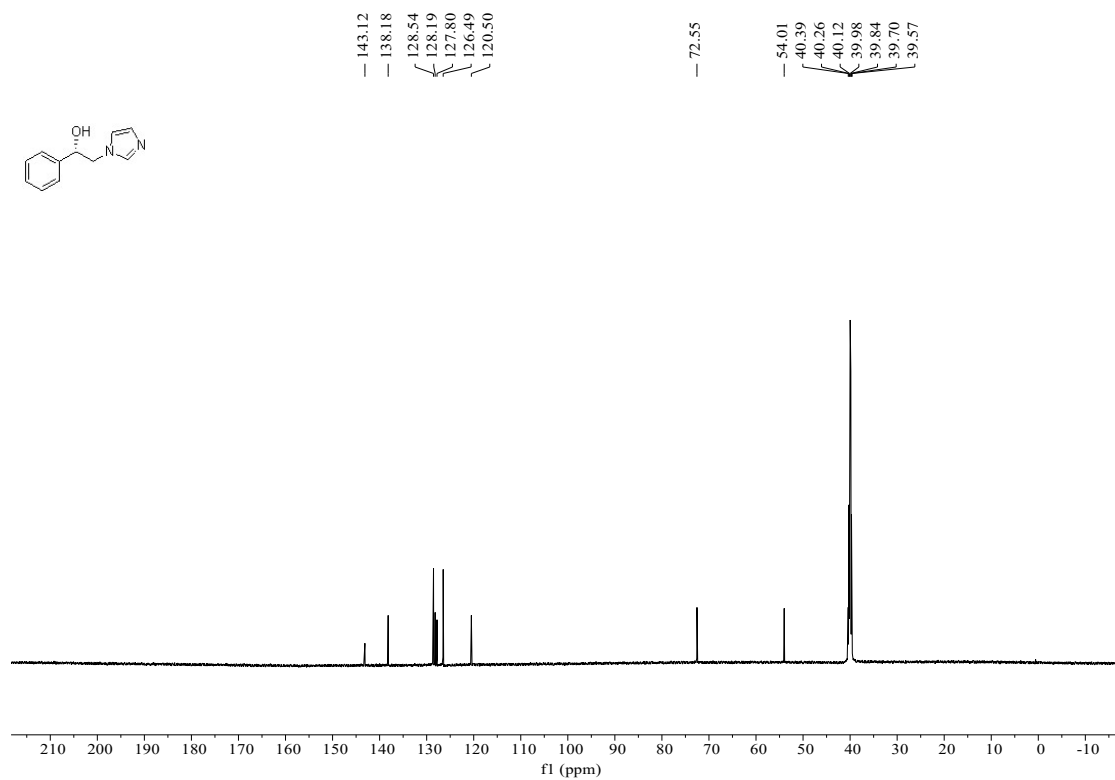
^{13}C NMR (151 MHz, $\text{DMSO-}d_6$) of **2a**:



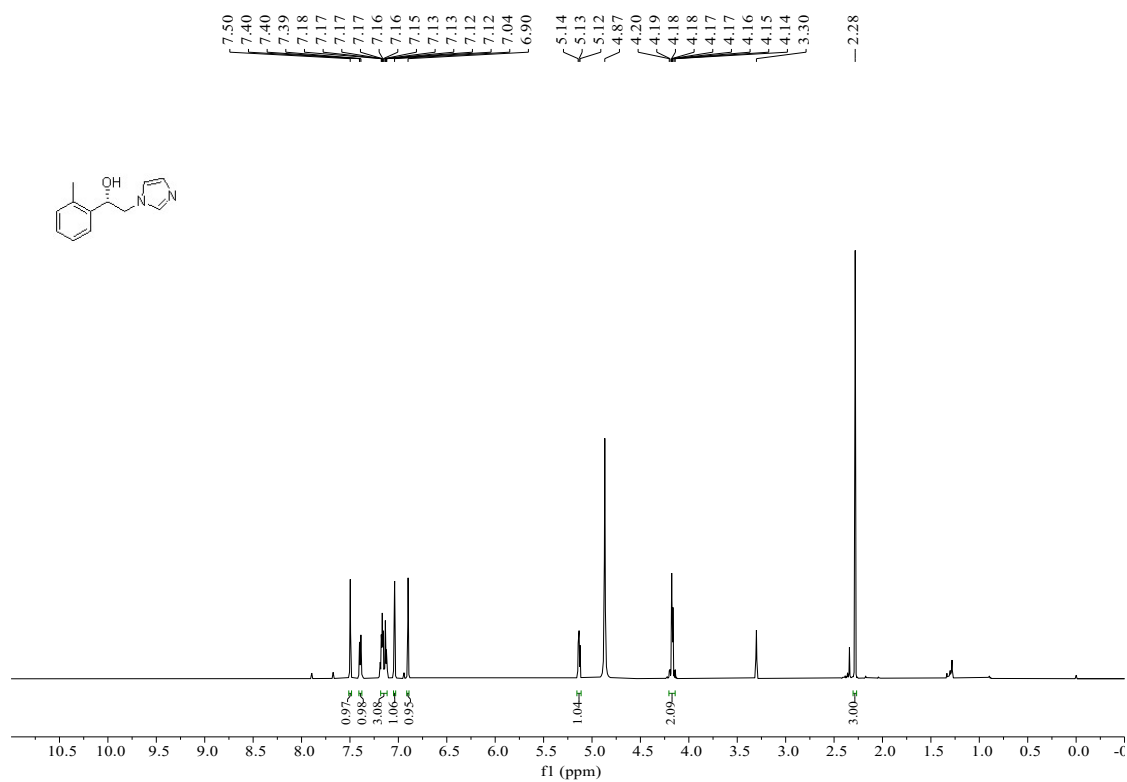
^1H NMR (600 MHz, $\text{DMSO-}d_6$) of **2b**:



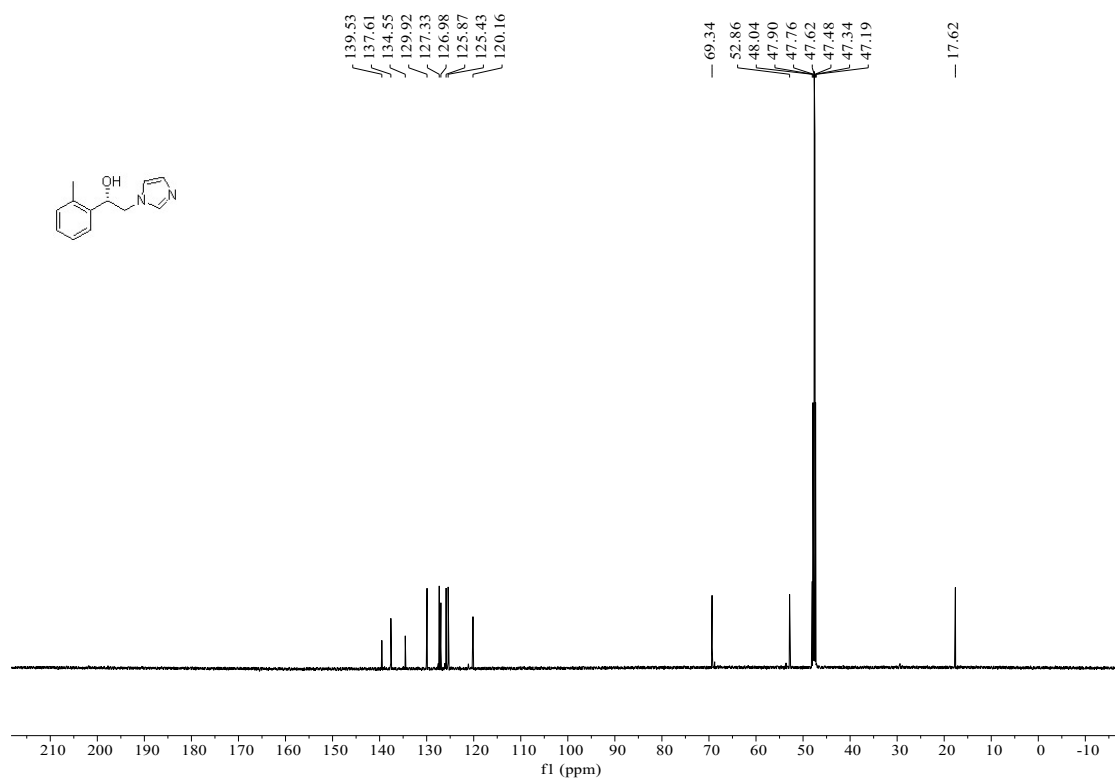
^{13}C NMR (151 MHz, $\text{DMSO-}d_6$) of **2b**:



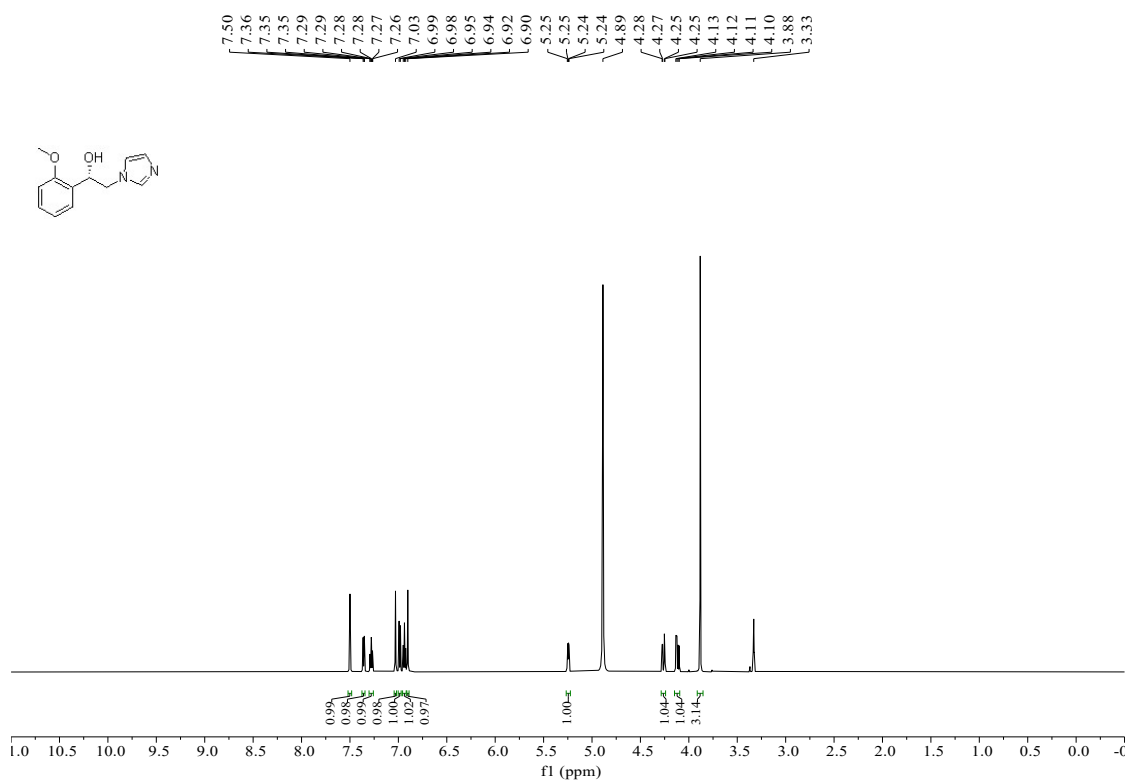
^1H NMR (600 MHz, CD_3OD) of **2c**:



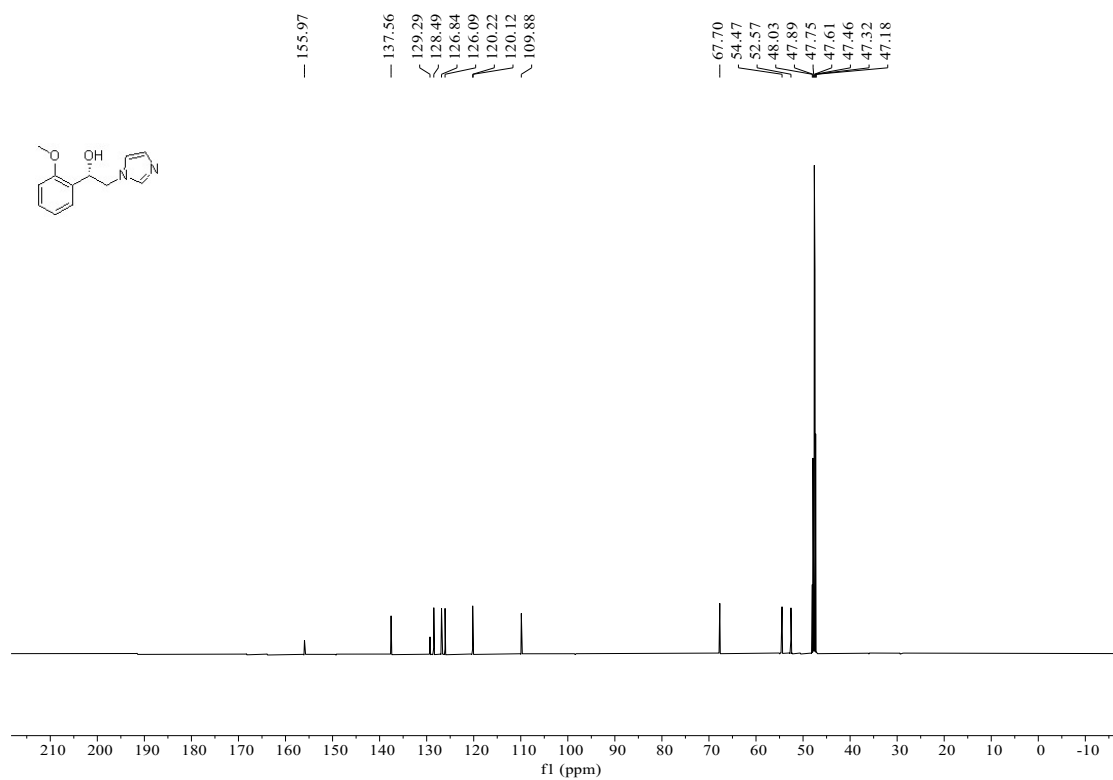
^{13}C NMR (151 MHz, CD_3OD) of **2c**:



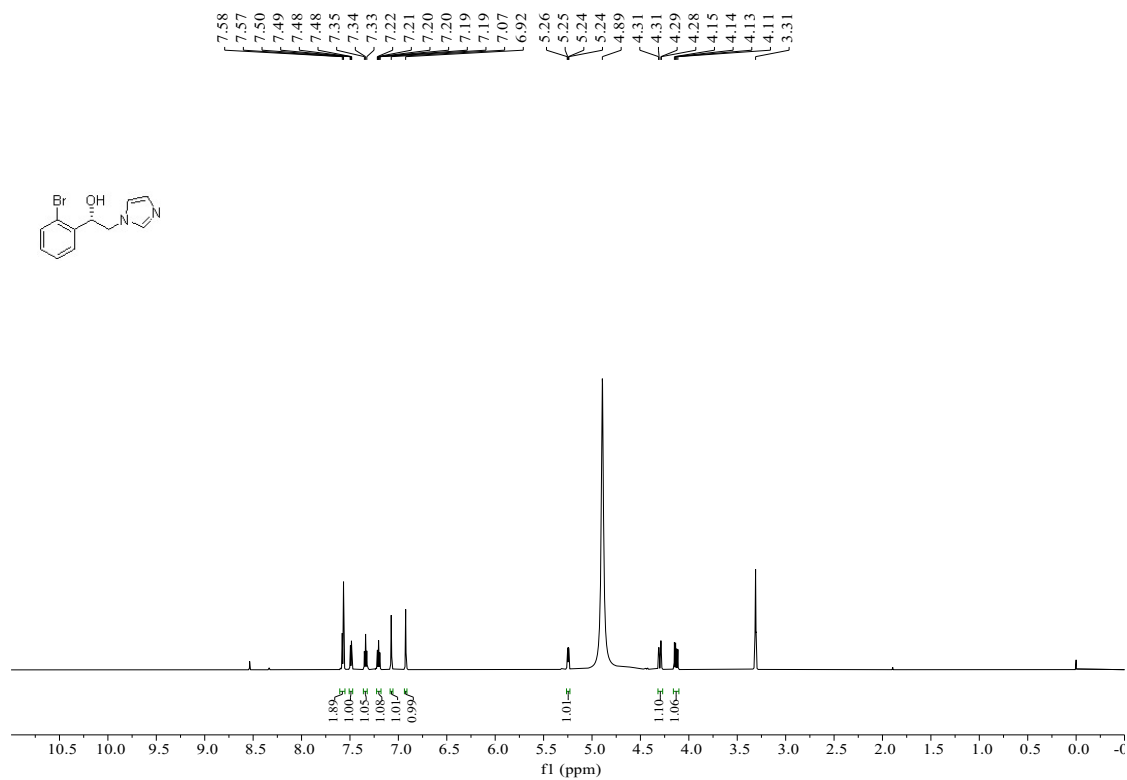
^1H NMR (600 MHz, CD_3OD) of **2d**:



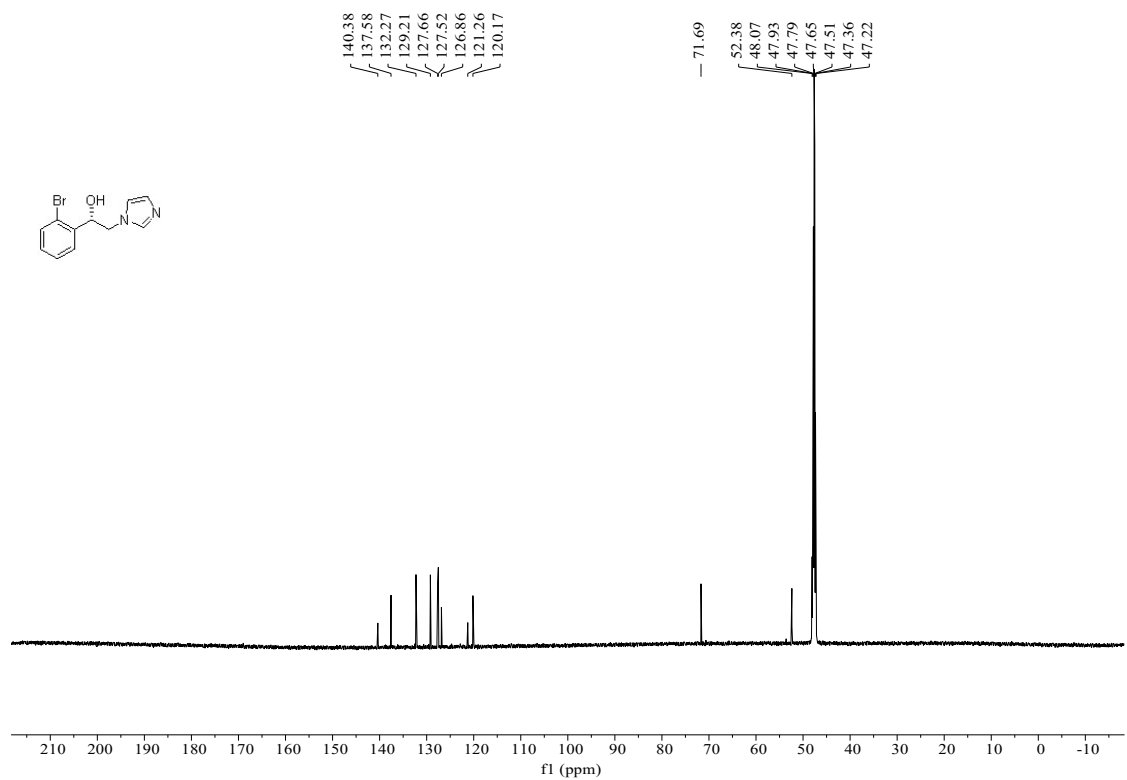
^{13}C NMR (151 MHz, CD_3OD) of **2d**:



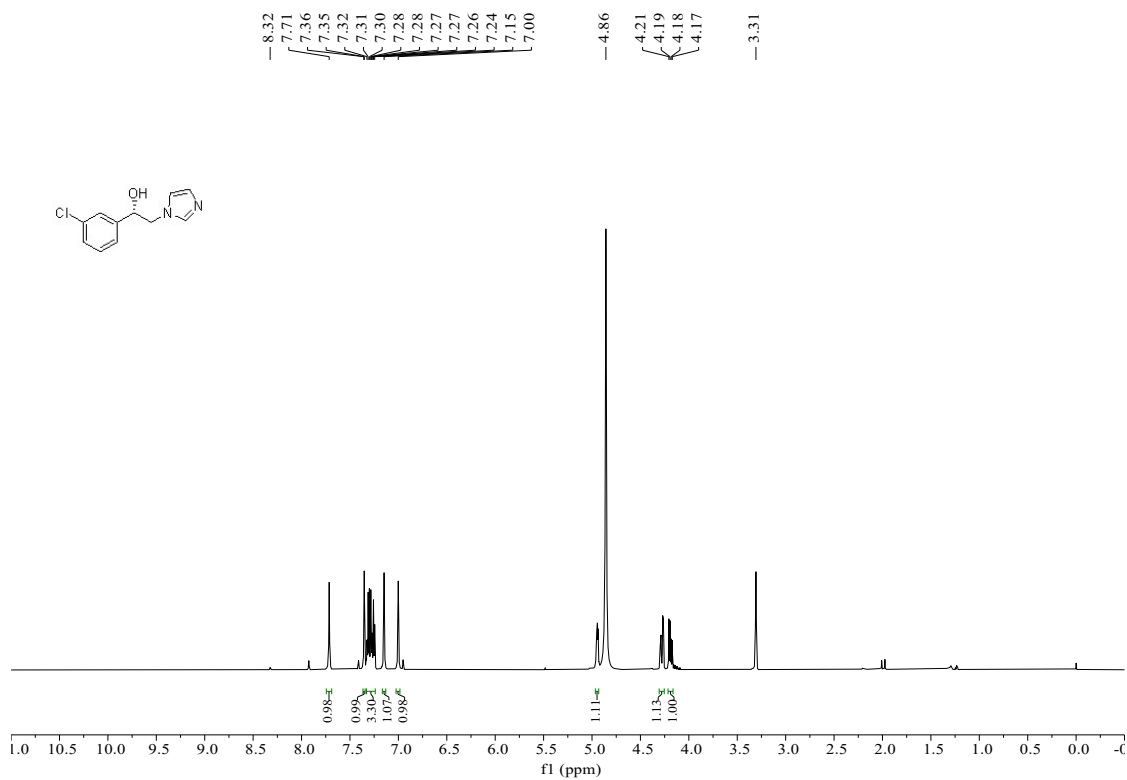
^1H NMR (600 MHz, CD_3OD) of **2e**:



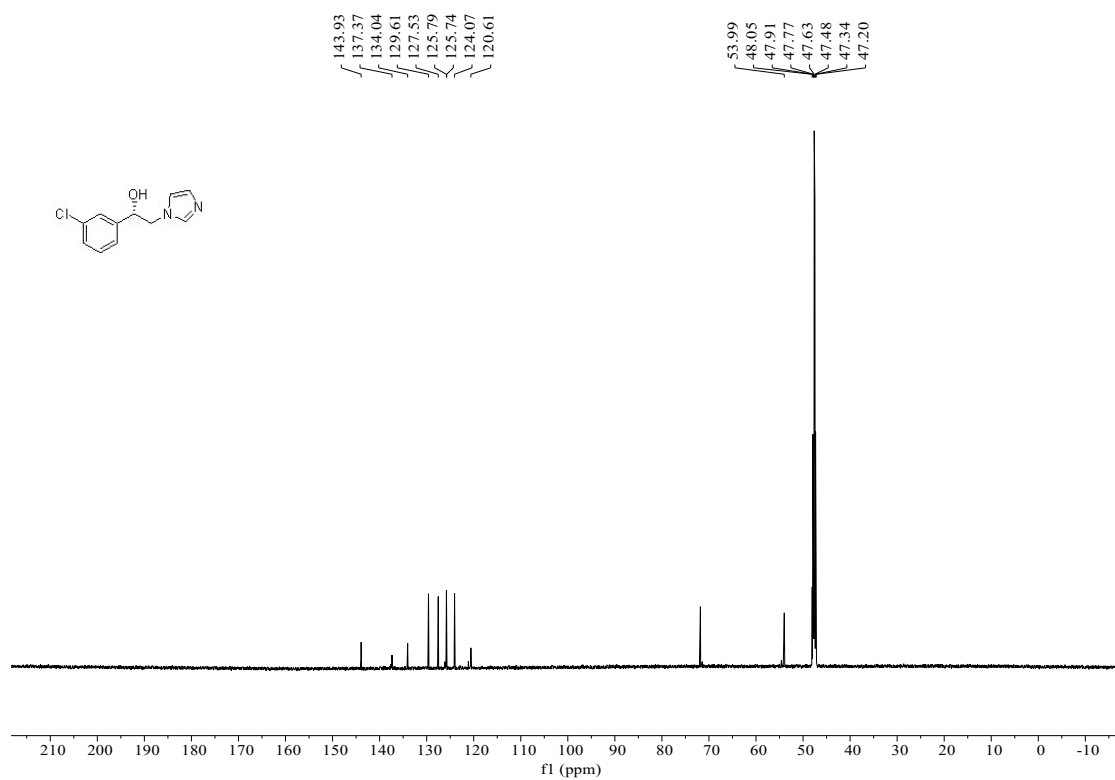
^{13}C NMR (151 MHz, CD_3OD) of **2e**:



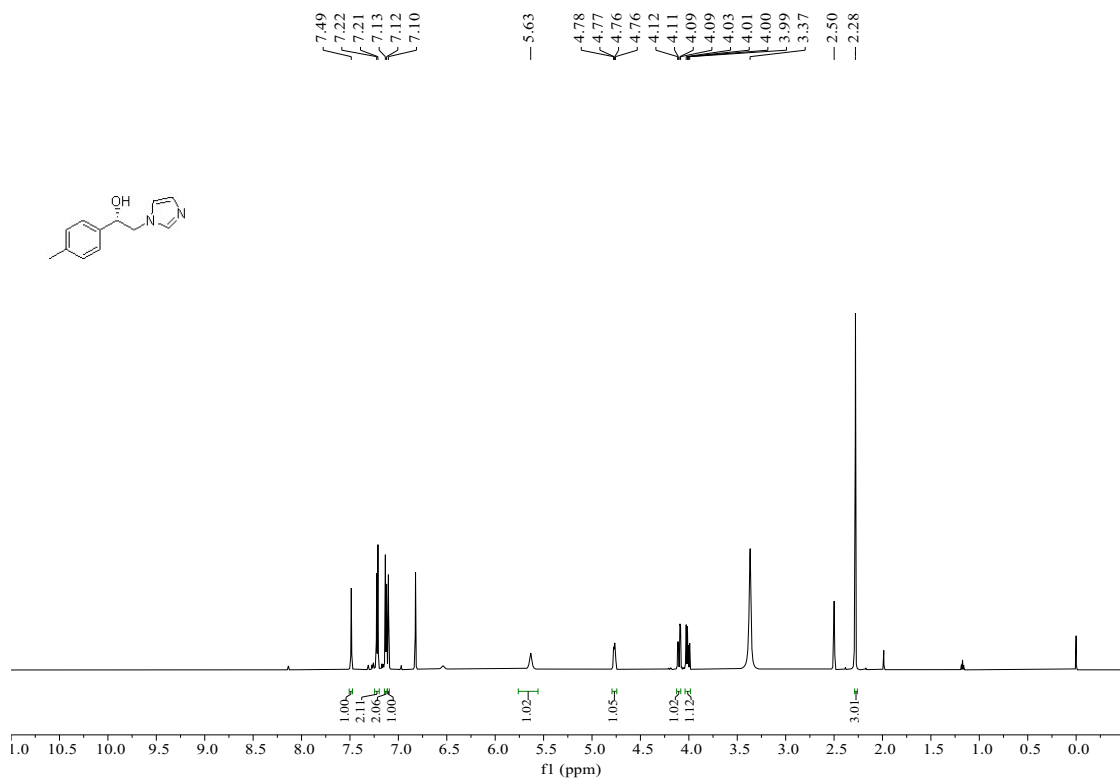
^1H NMR (600 MHz, CD_3OD) of **2f**:



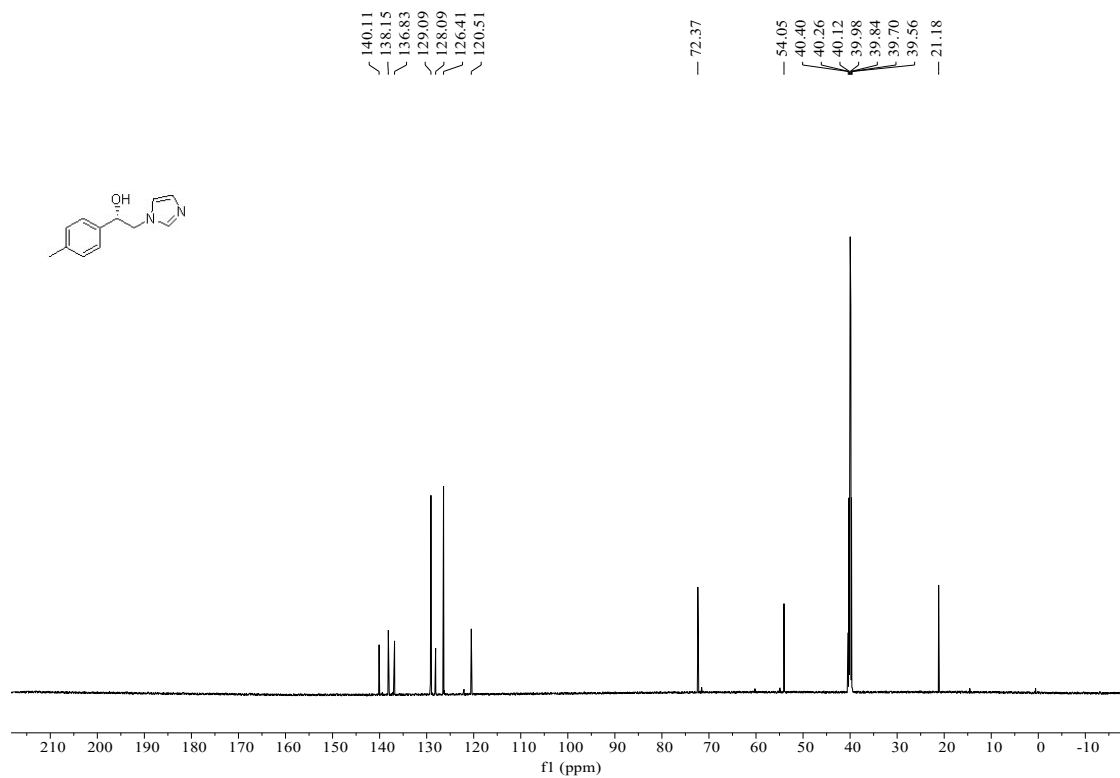
^{13}C NMR (151 MHz, CD_3OD) of **2f**:



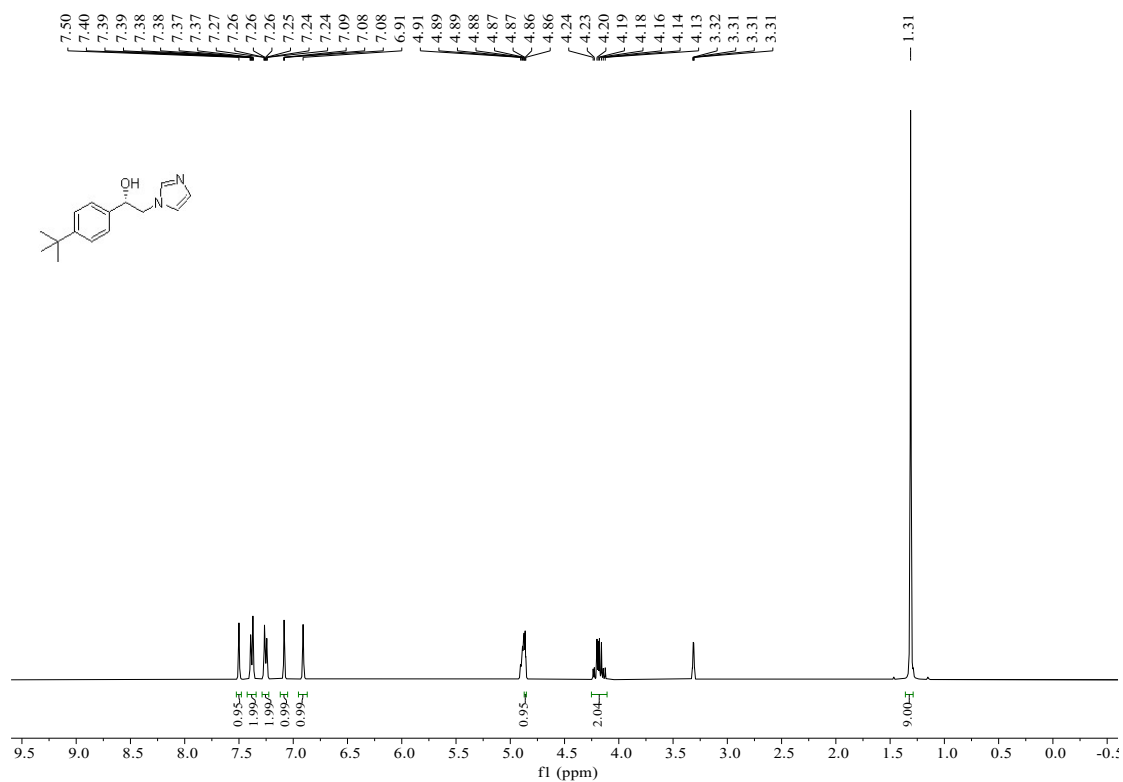
^1H NMR (600 MHz, $\text{DMSO}-d_6$) of **2g**:



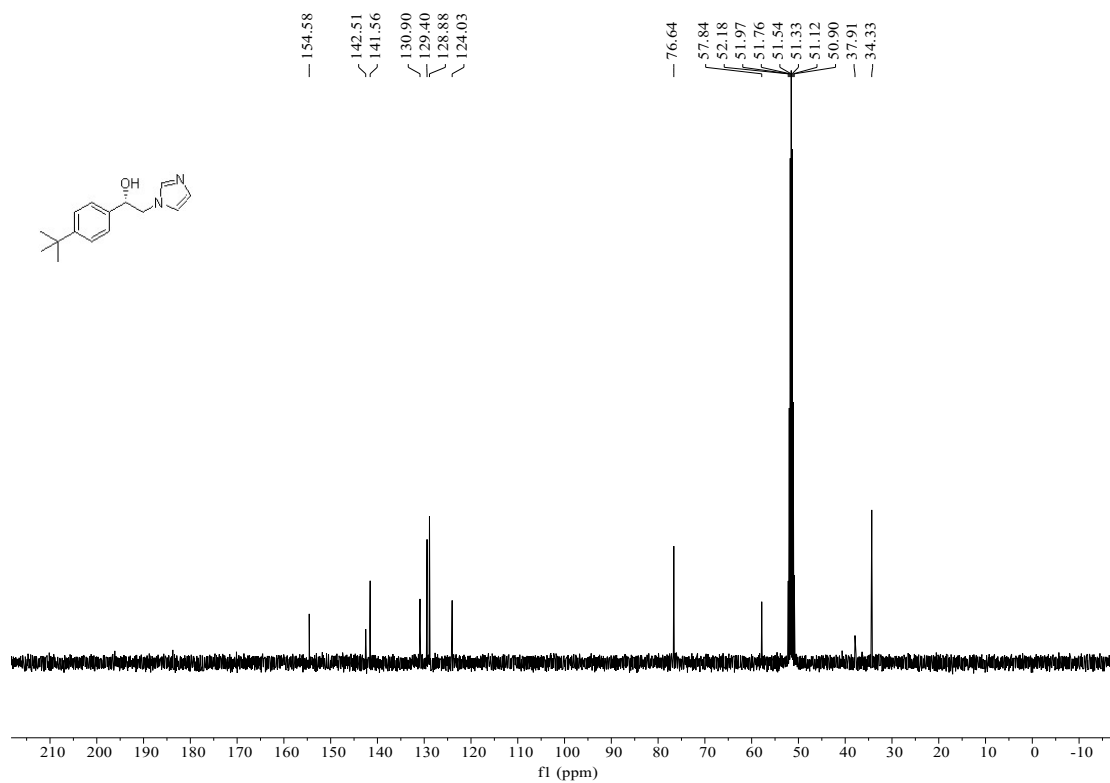
¹³C NMR (151 MHz, DMSO-*d*₆) of **2g**:



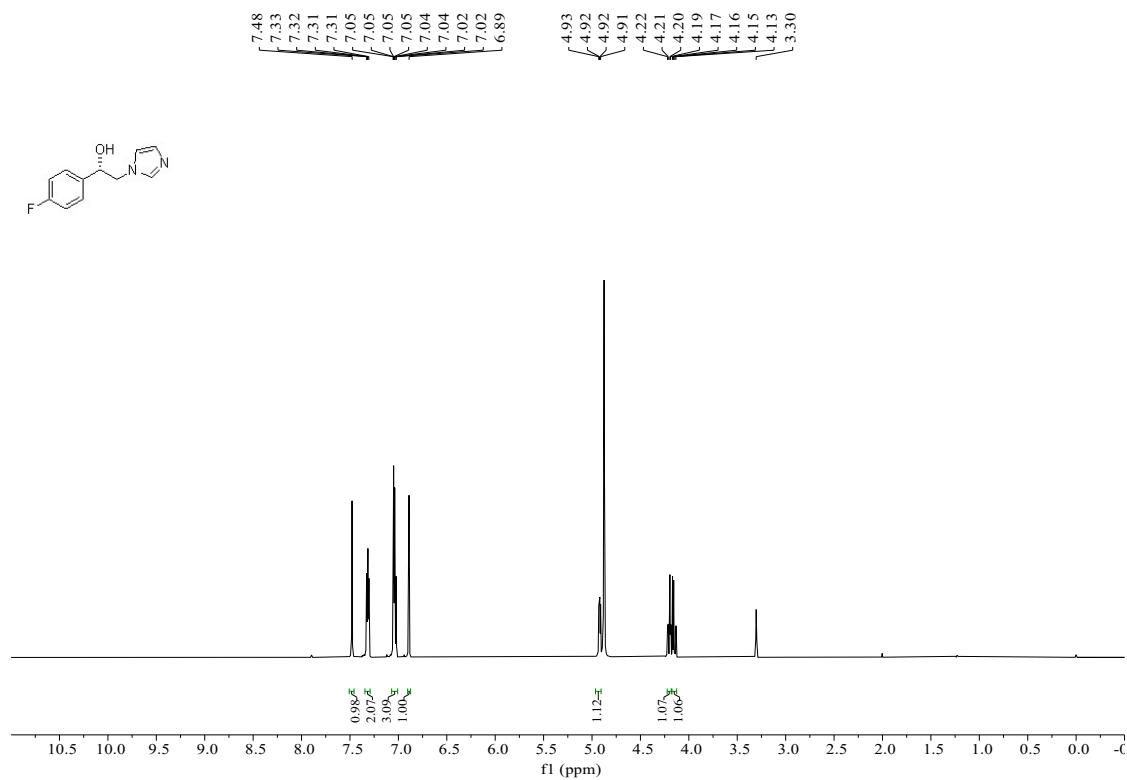
¹H NMR (400 MHz, CD₃OD) of **2h**:



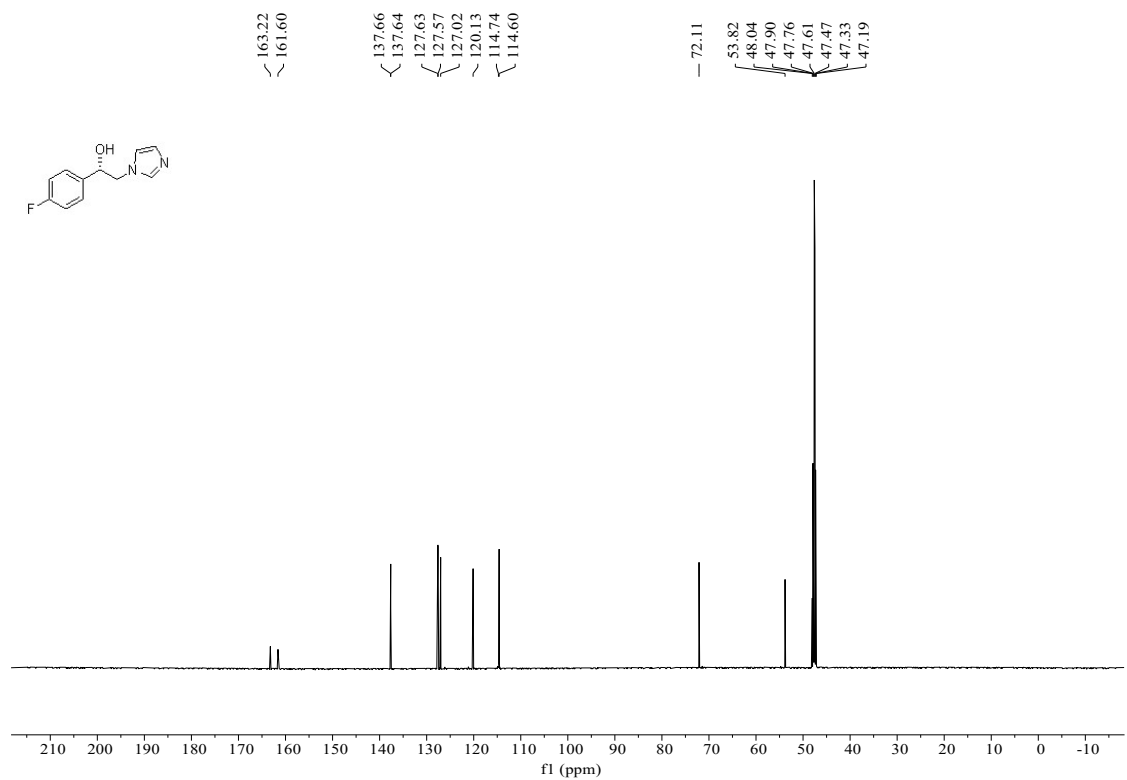
¹³C NMR (101 MHz, CD₃OD) of 2h:



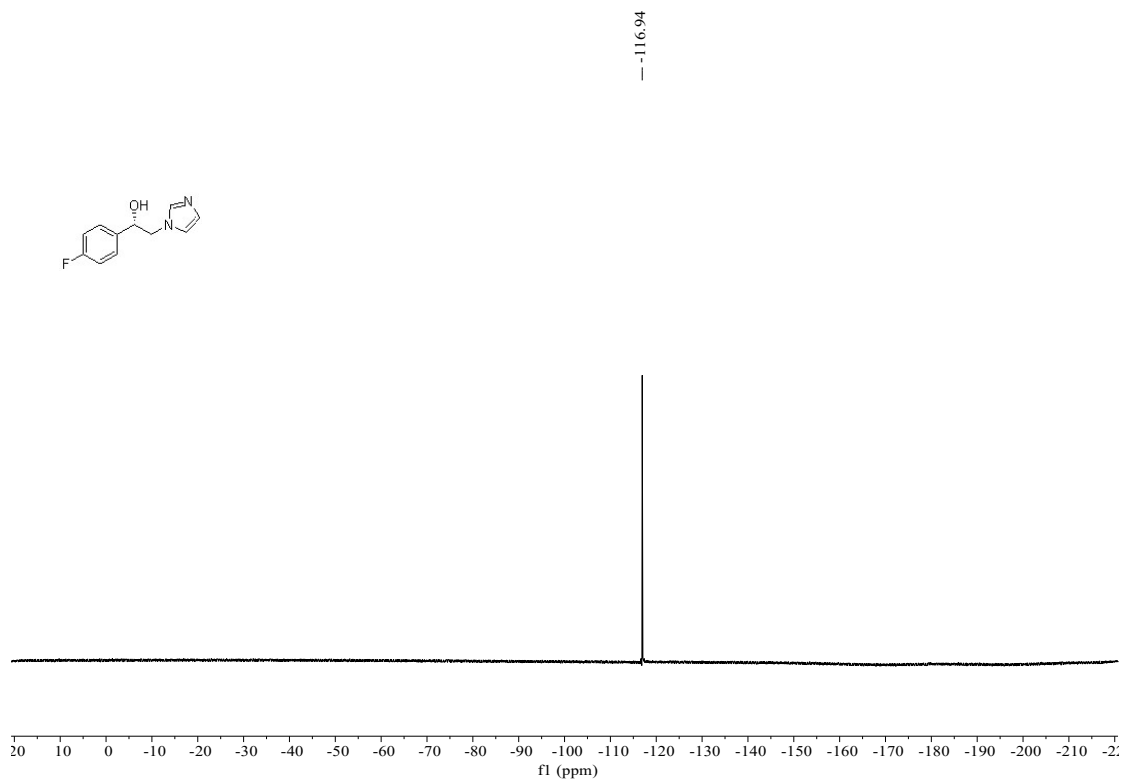
¹H NMR (600 MHz, CD₃OD) of 2i:



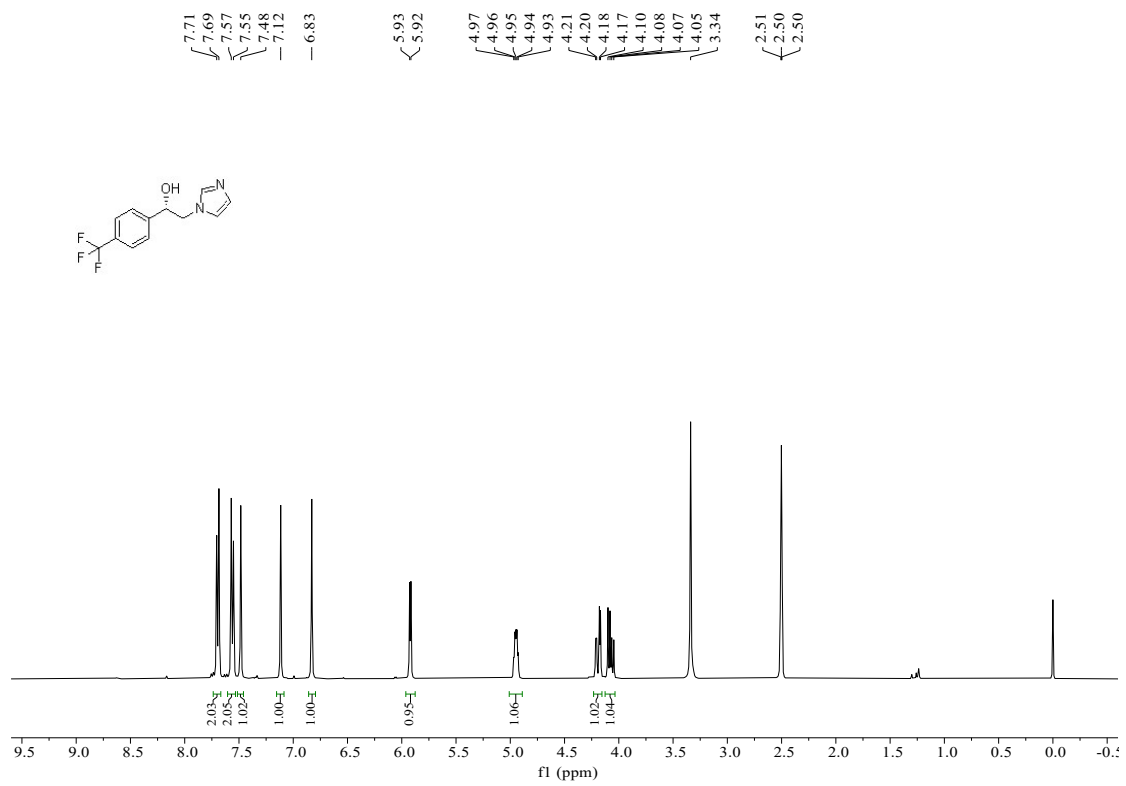
^{13}C NMR (151 MHz, CD_3OD) of **2i**:



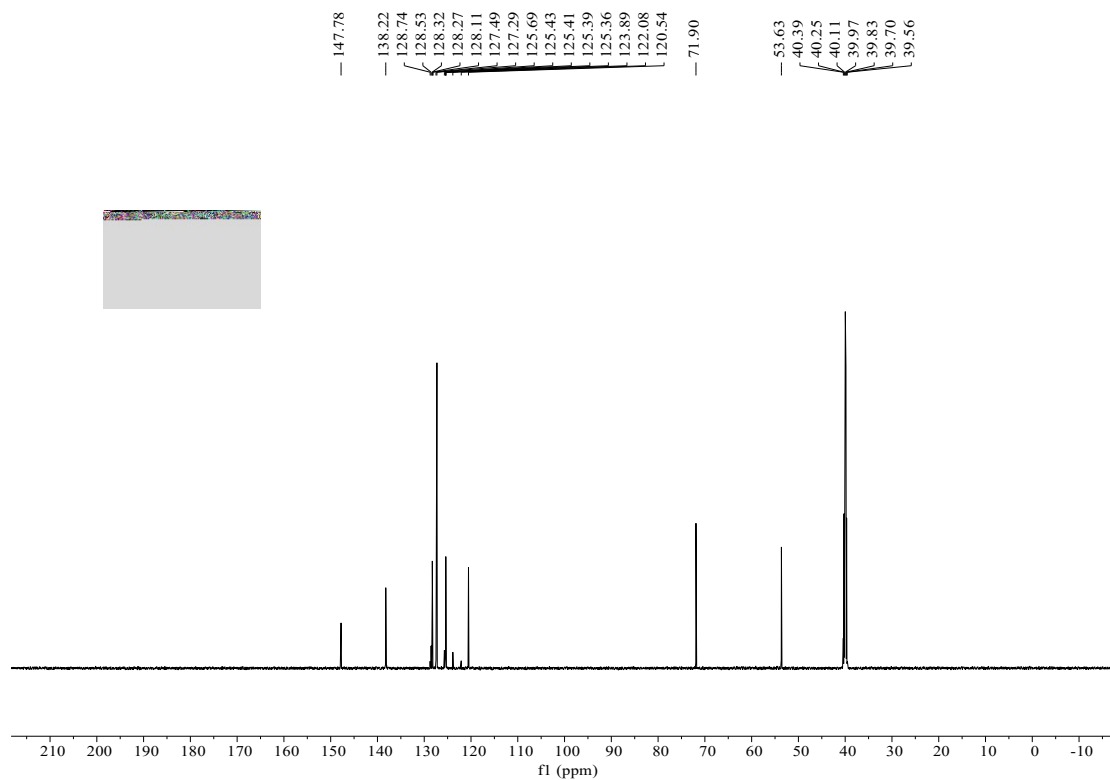
^{19}F NMR (377 MHz, CD_3OD) of **2i**:



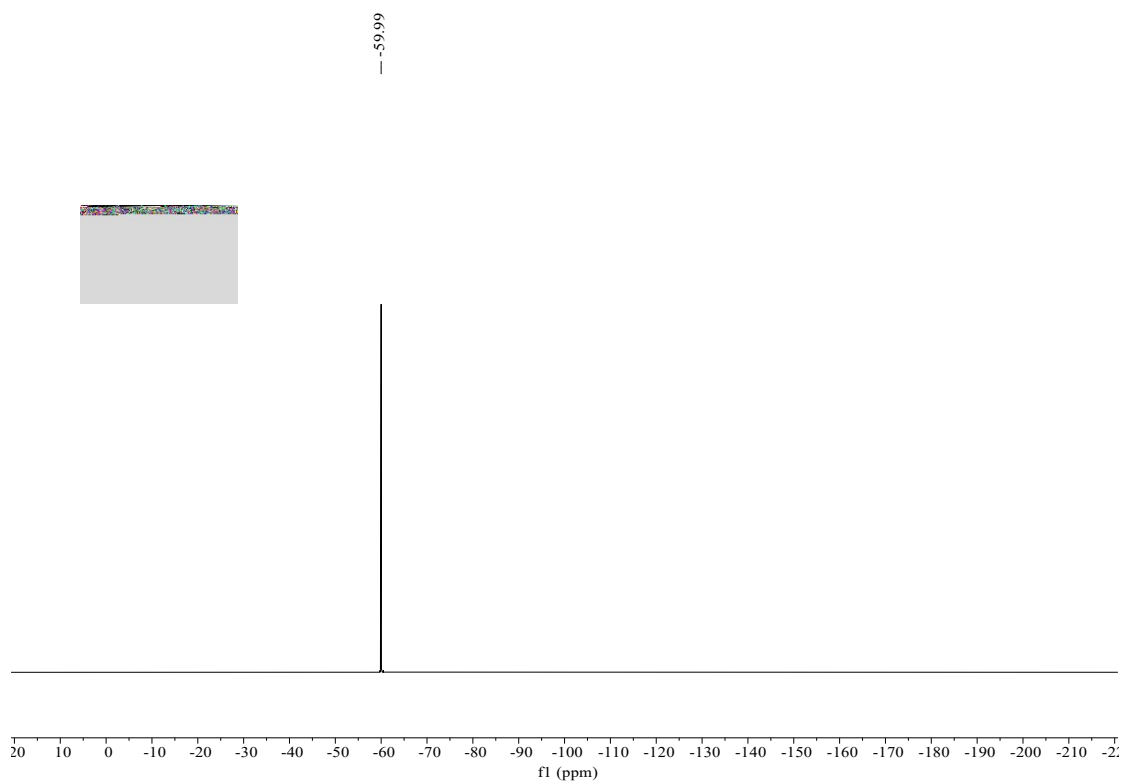
^1H NMR (400 MHz, DMSO- d_6) of 2j:



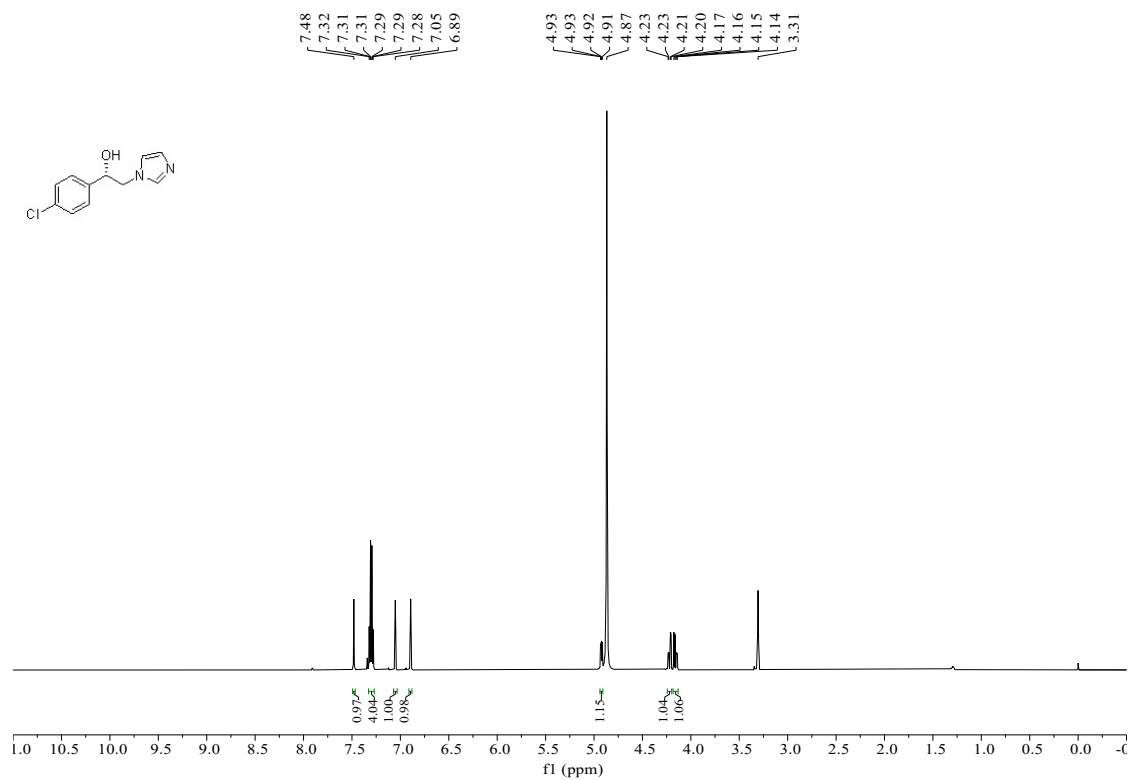
^{13}C NMR (151 MHz, DMSO- d_6) of 2j:



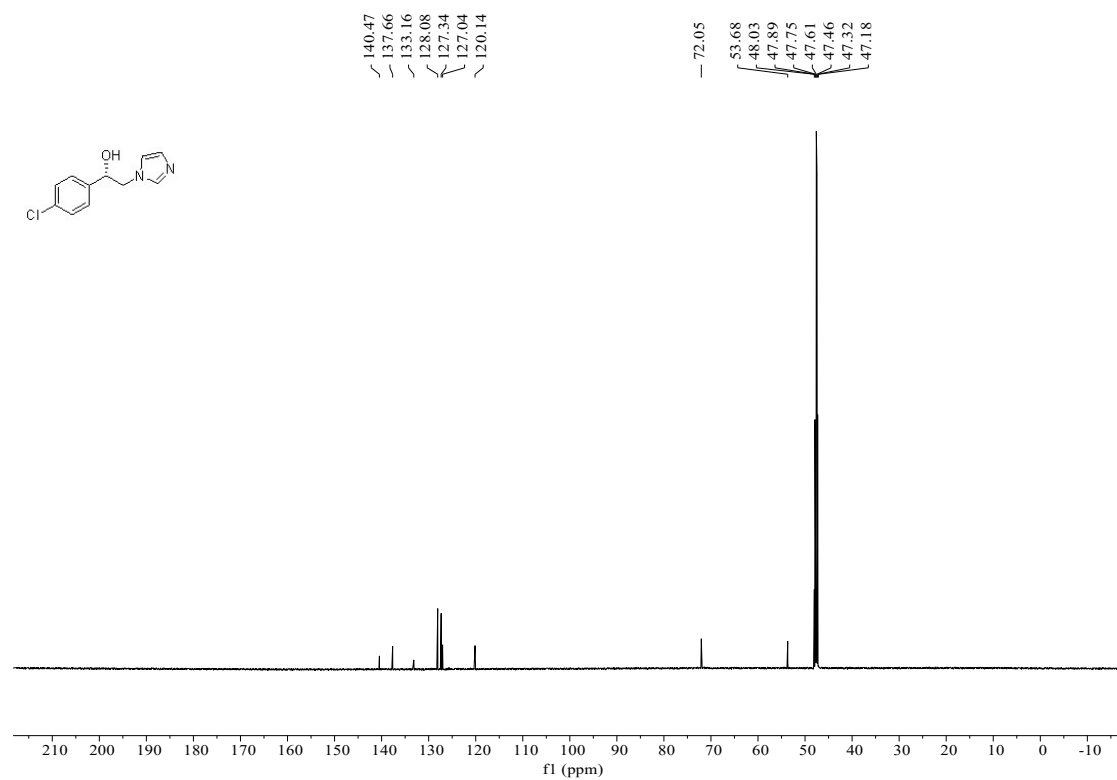
^{19}F NMR (376 MHz, $\text{DMSO-}d_6$) of **2j**:



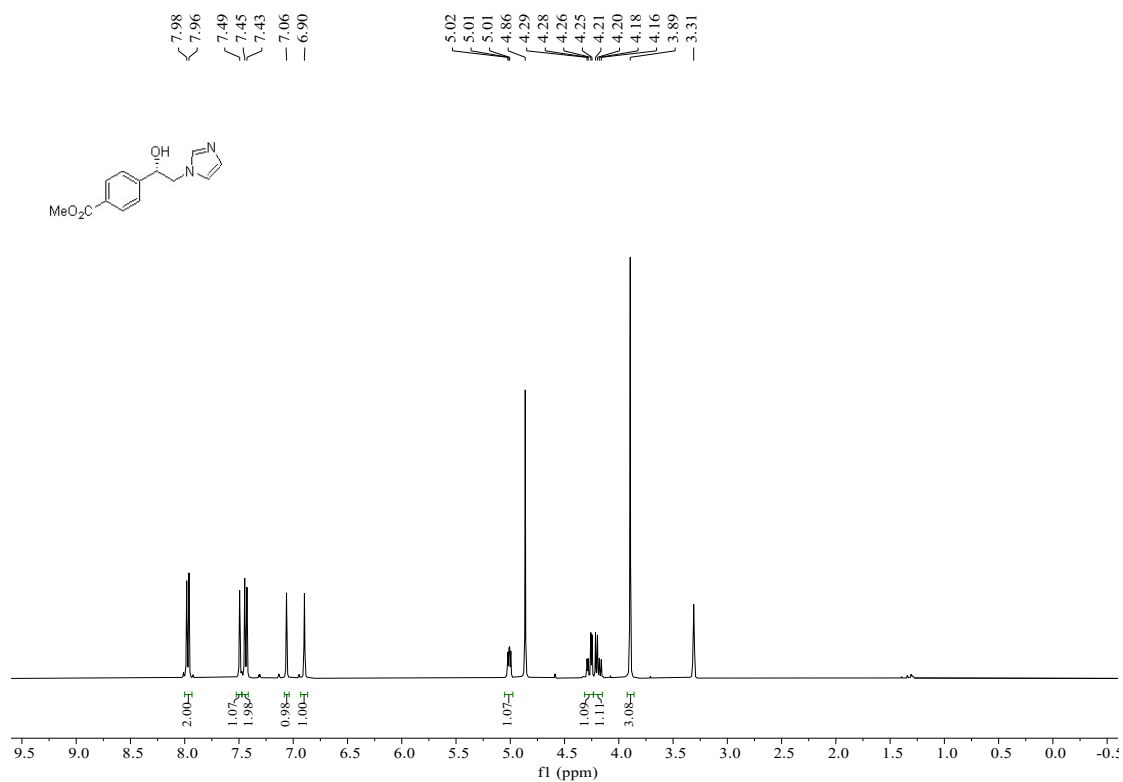
^1H NMR (600 MHz, CD_3OD) of **2k**:



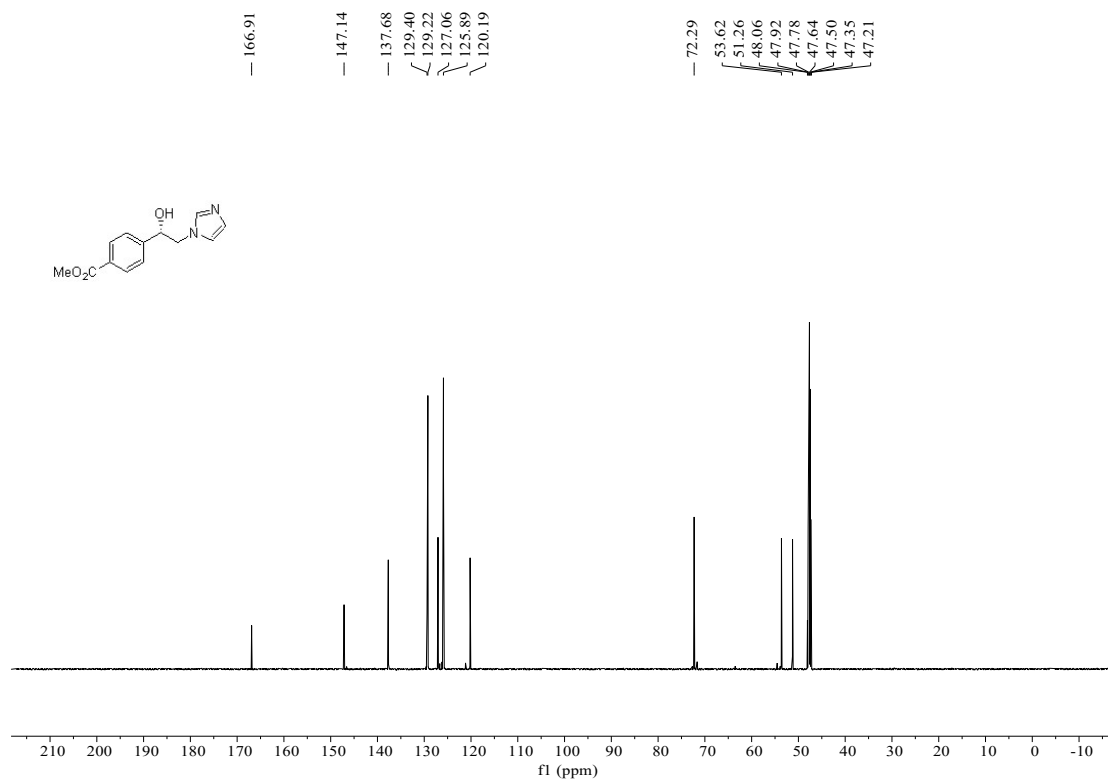
¹³C NMR (151 MHz, CD₃OD) of **2k**:



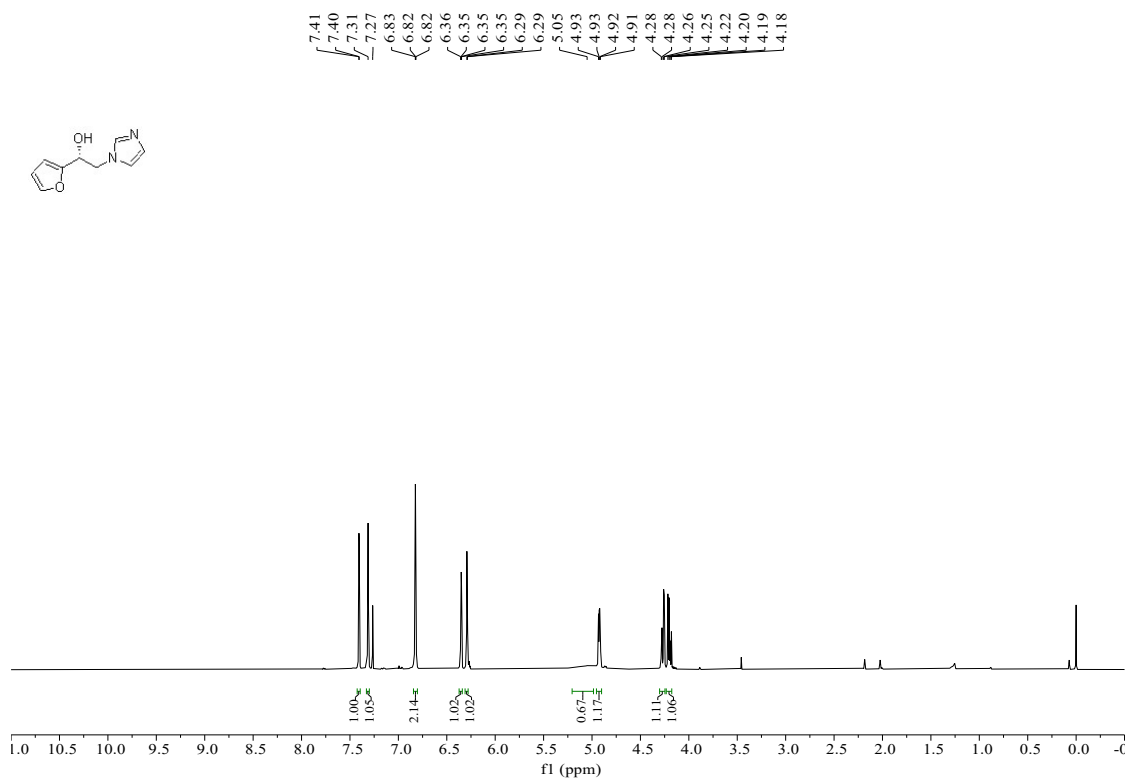
¹H NMR (400 MHz, CD₃OD) of **2l**:



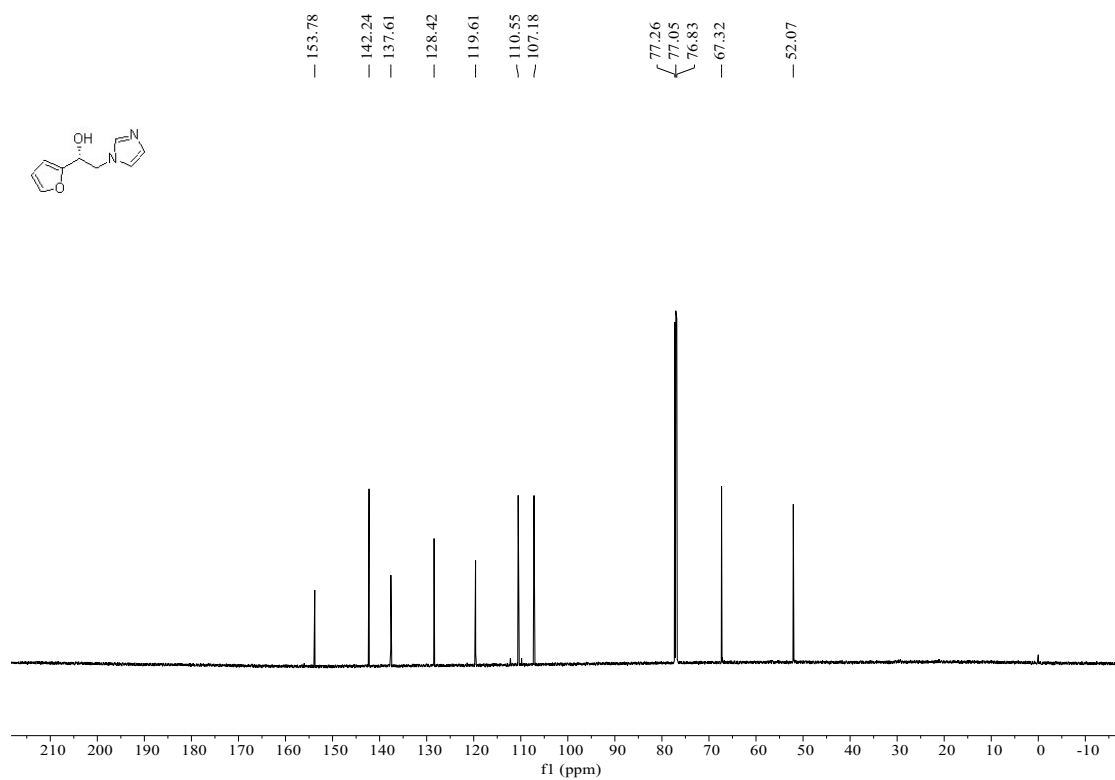
¹³C NMR (101 MHz, CD₃OD) of **2l**:



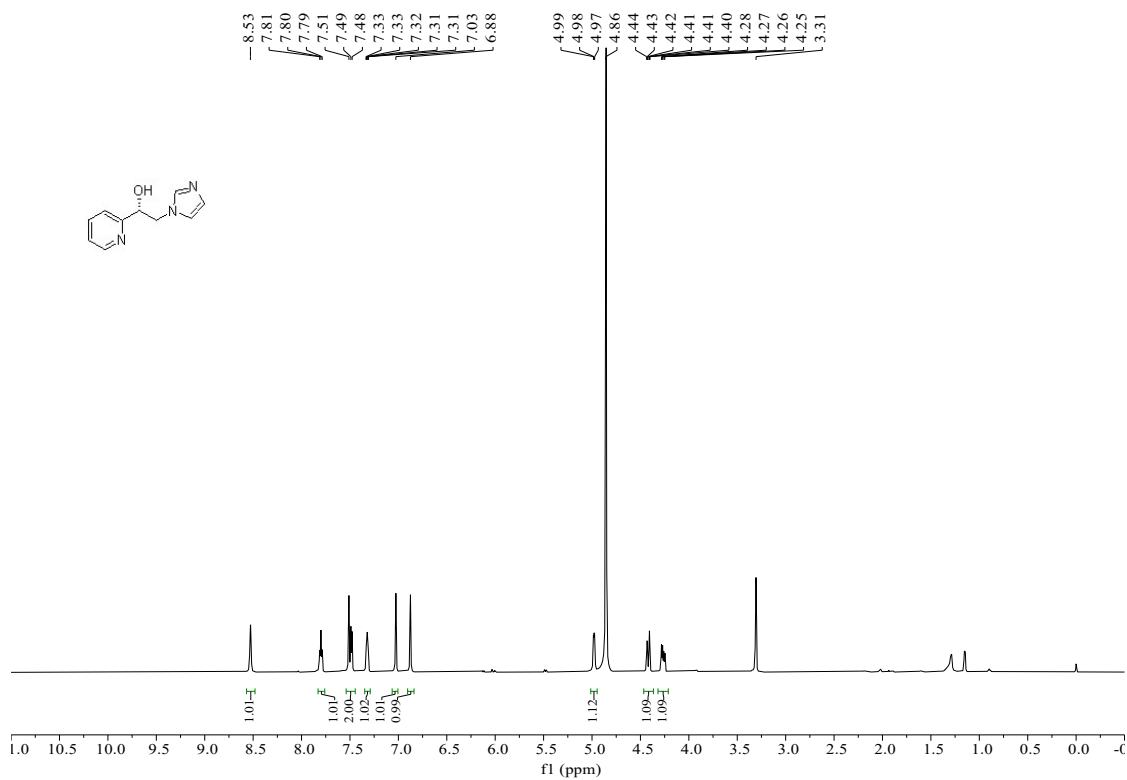
¹H NMR (600 MHz, CDCl₃) of **2m**:



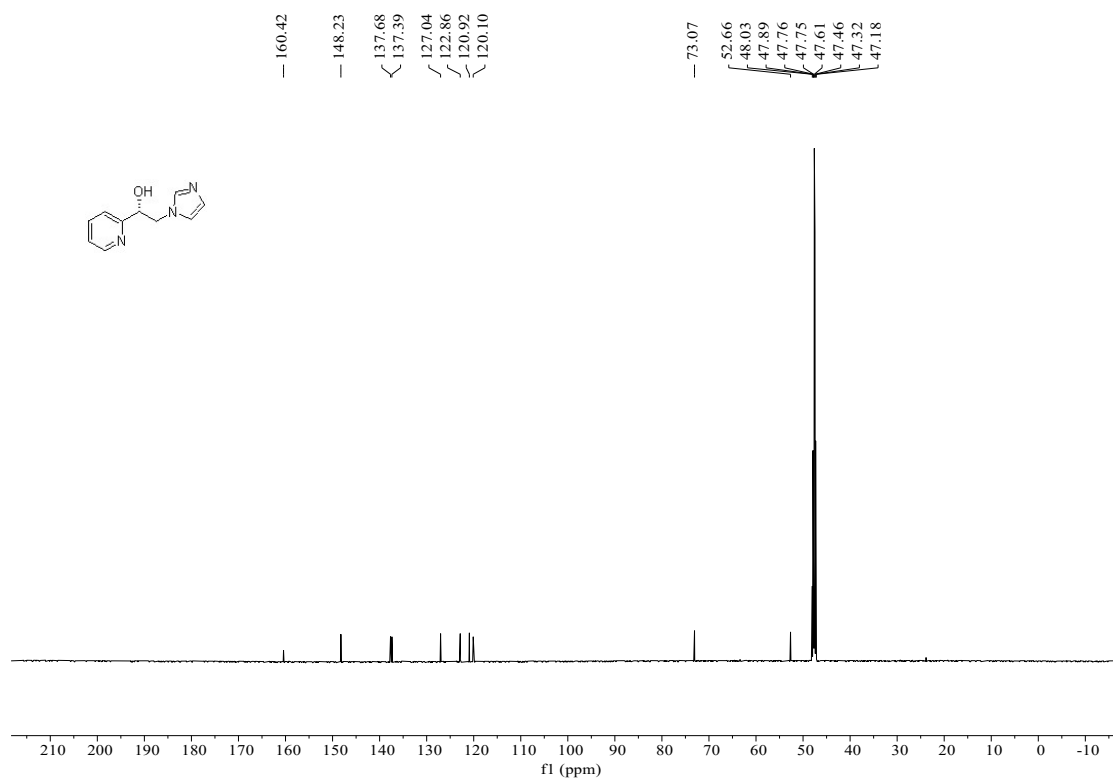
¹³C NMR (151 MHz, CDCl₃) of **2m**:



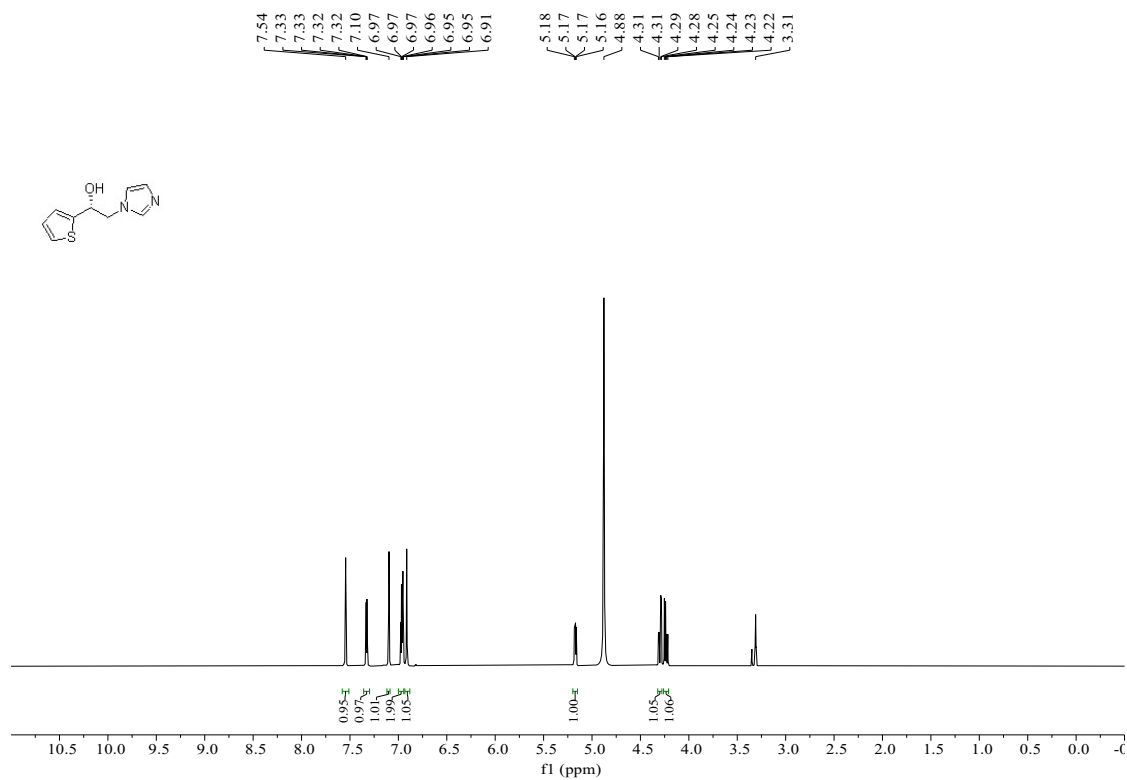
¹H NMR (600 MHz, CD₃OD) of **2n**:



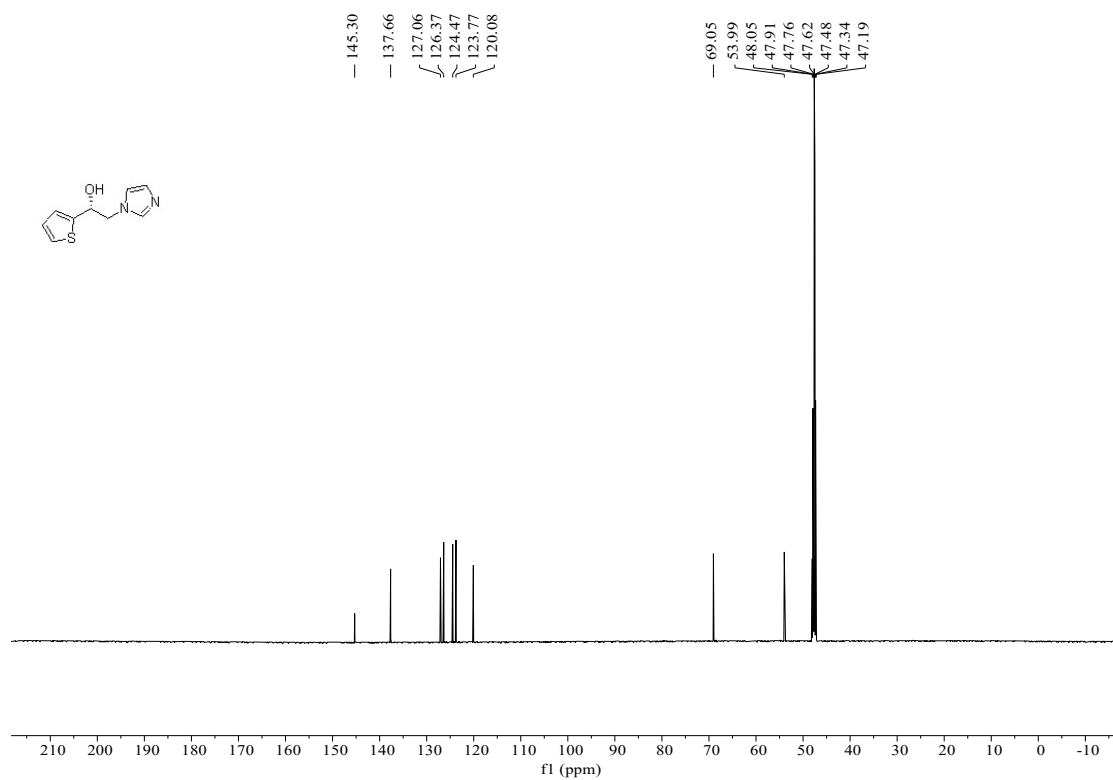
^{13}C NMR (151 MHz, CD_3OD) of **2n**:



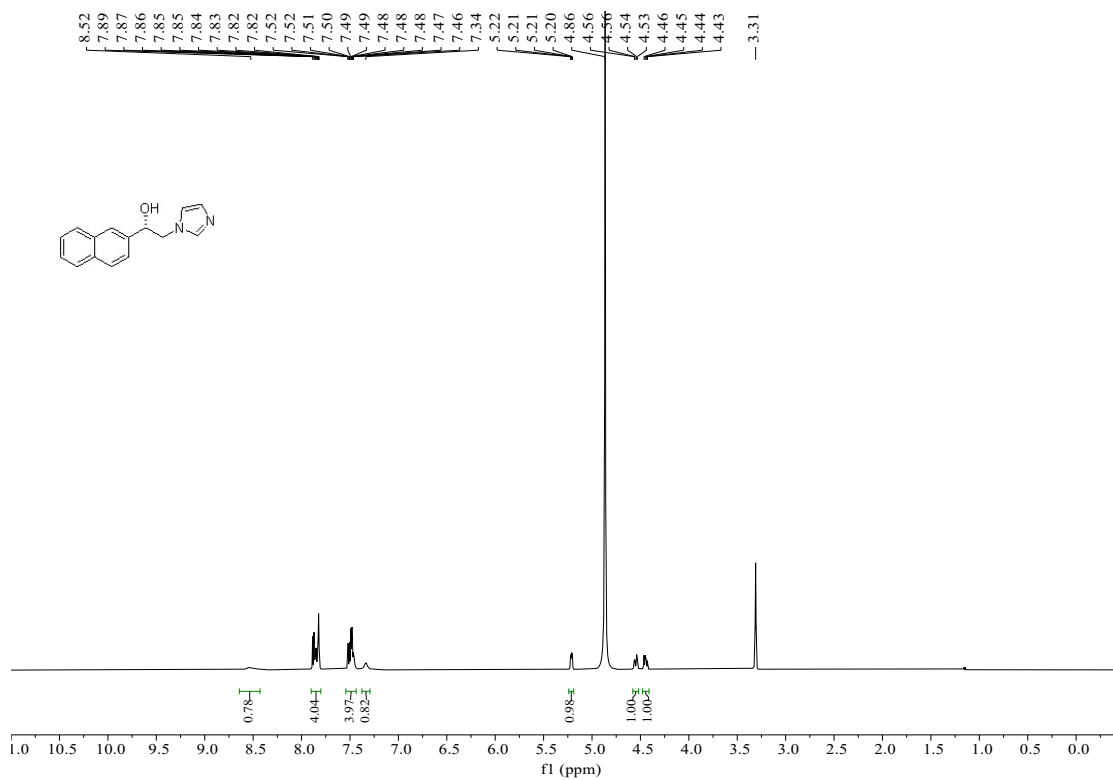
^1H NMR (600 MHz, CD_3OD) of **2o**:



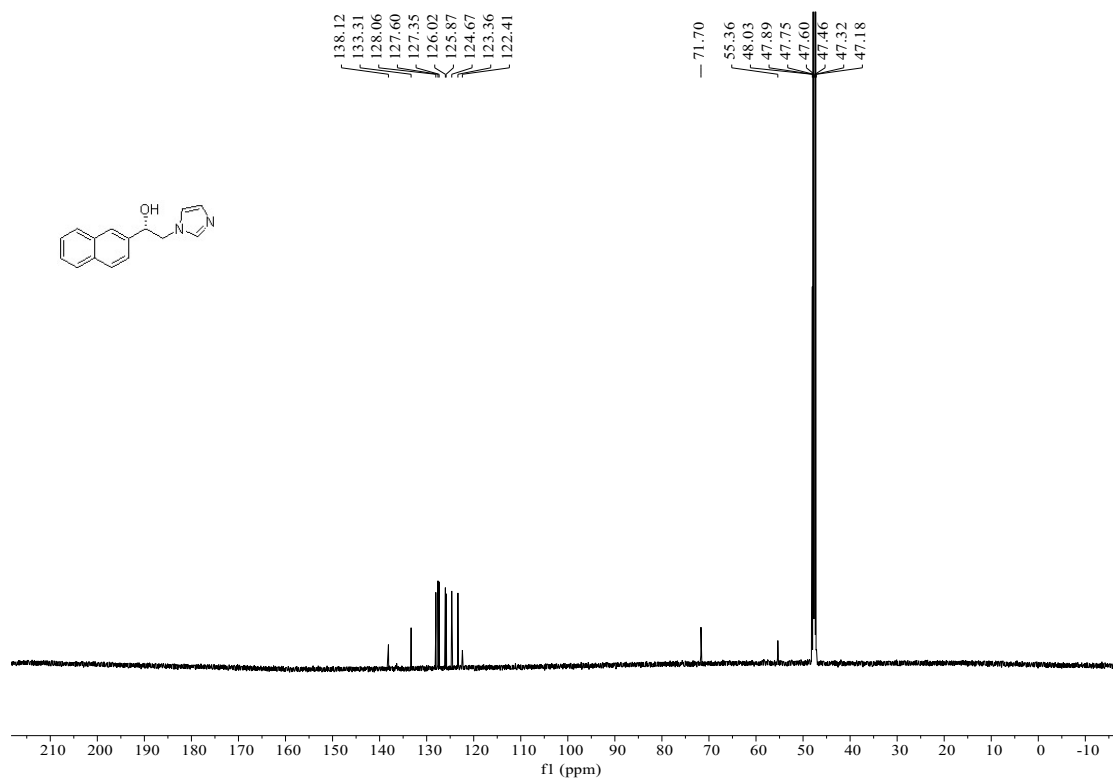
¹³C NMR (151 MHz, CD₃OD) of **2o**:



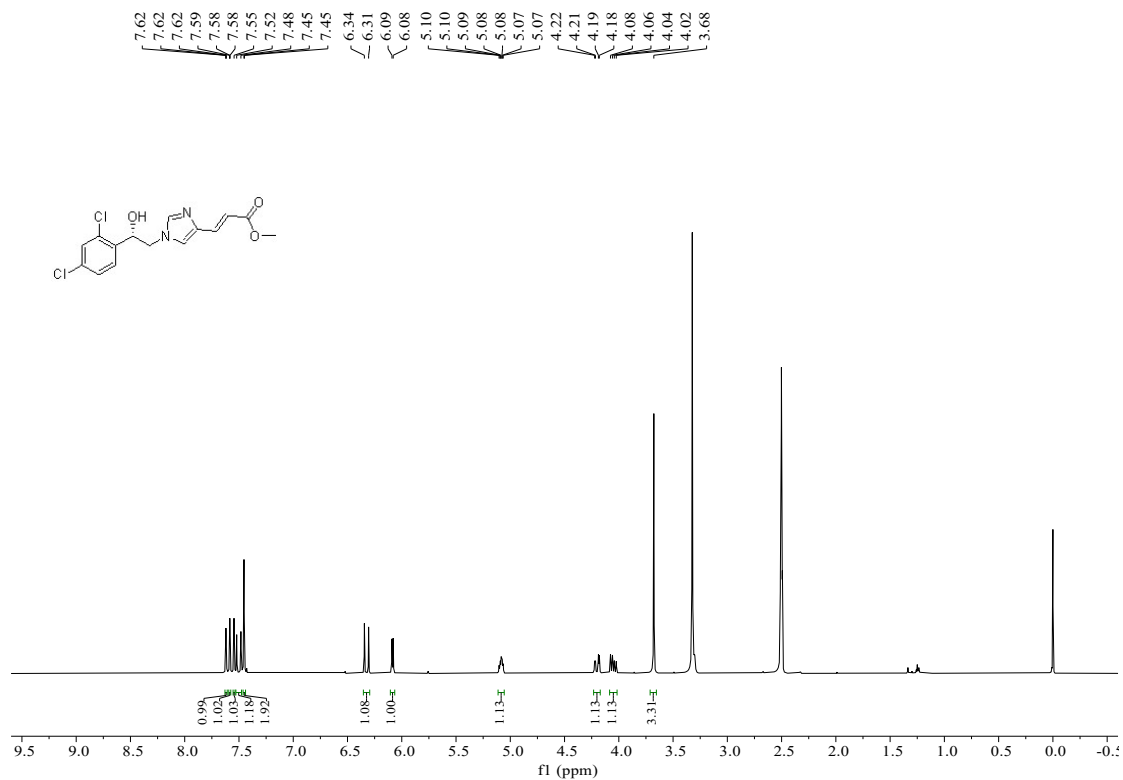
¹H NMR (600 MHz, CD₃OD) of **2p**:



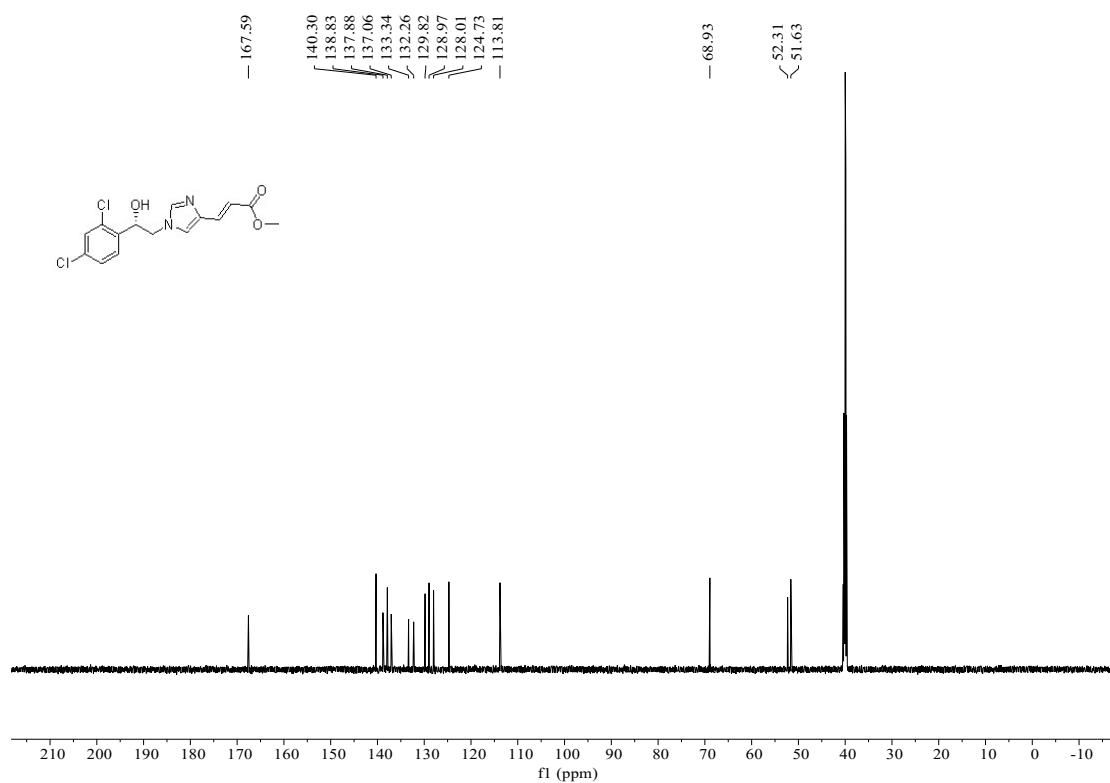
^{13}C NMR (151 MHz, CD_3OD) of **2p**:



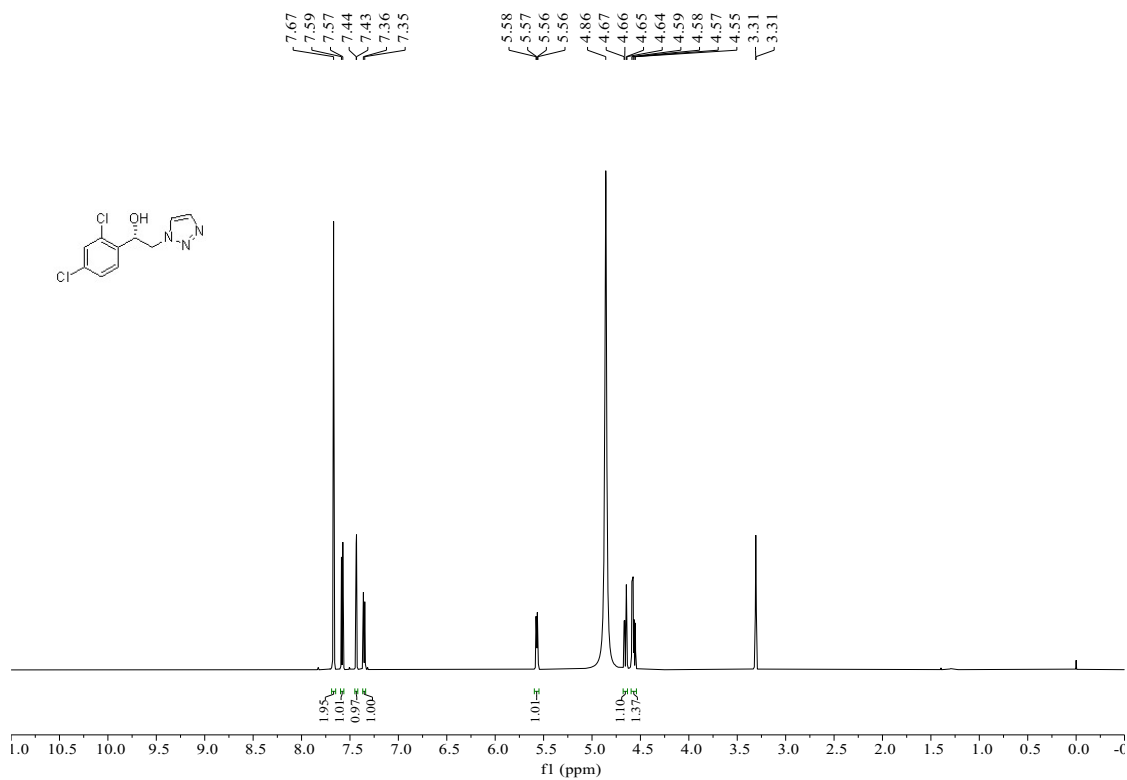
^1H NMR (400 MHz, $\text{DMSO}-d_6$) of **2q**:



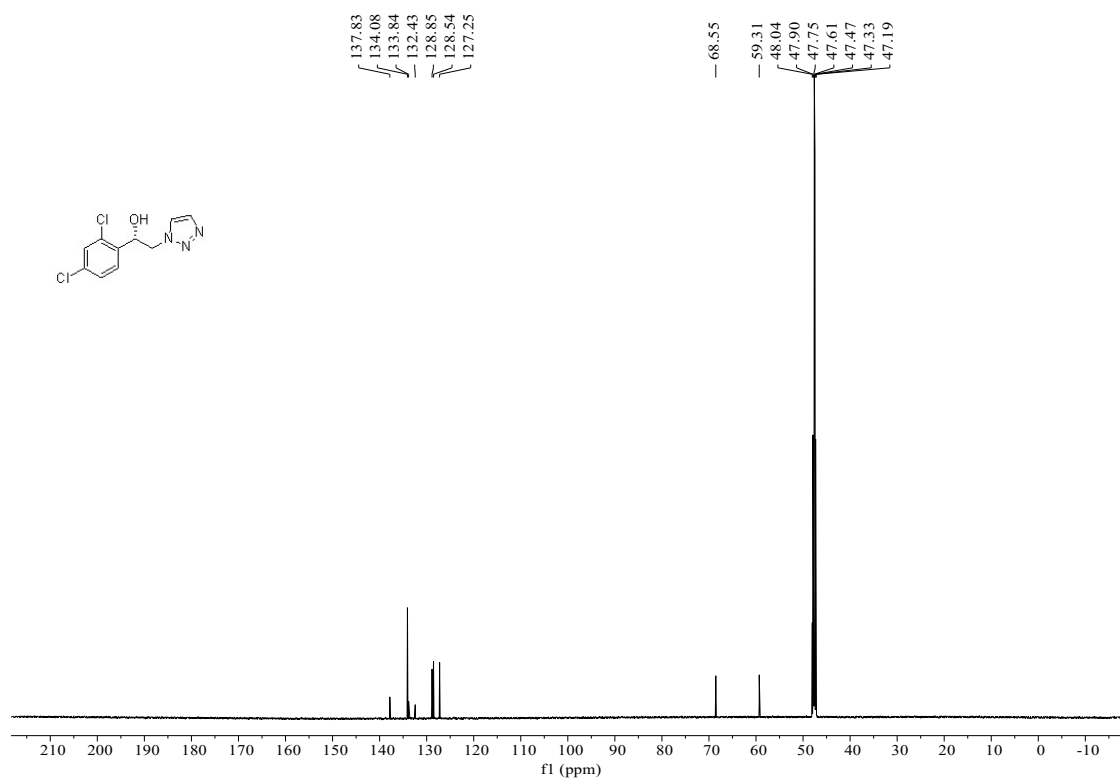
¹³C NMR (151 MHz, DMSO-*d*₆) of **2q**:



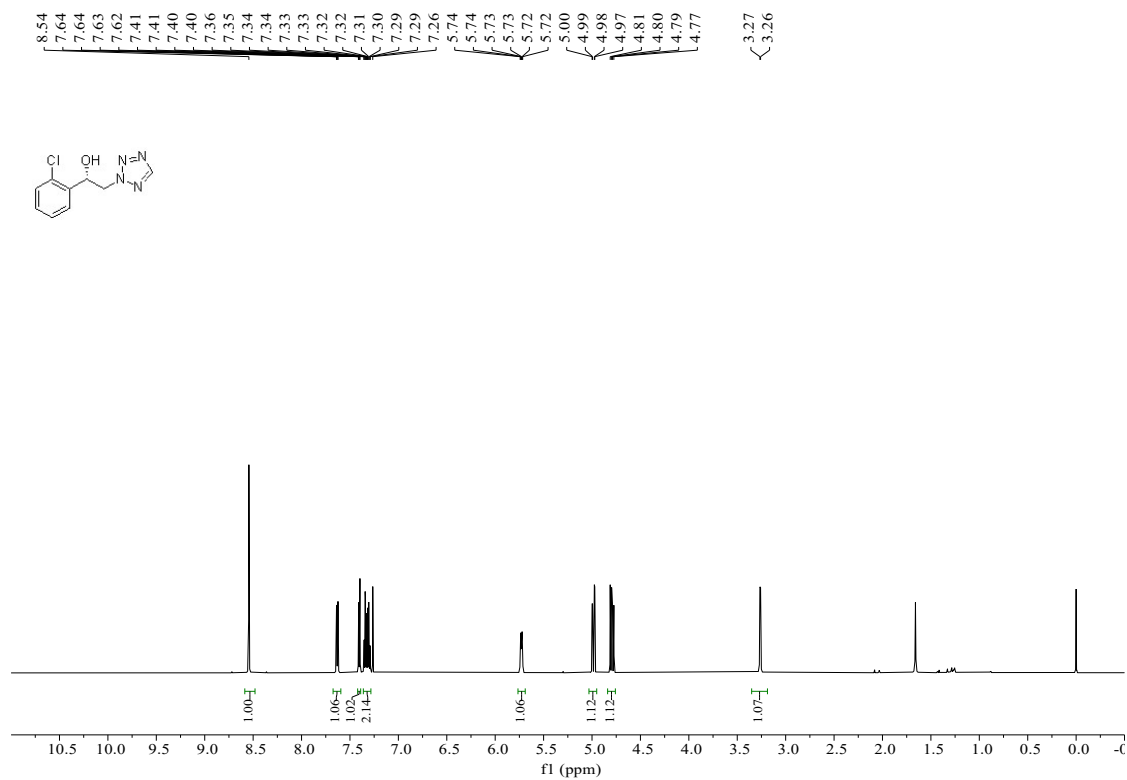
¹H NMR (600 MHz, CD₃OD) of **2r**:



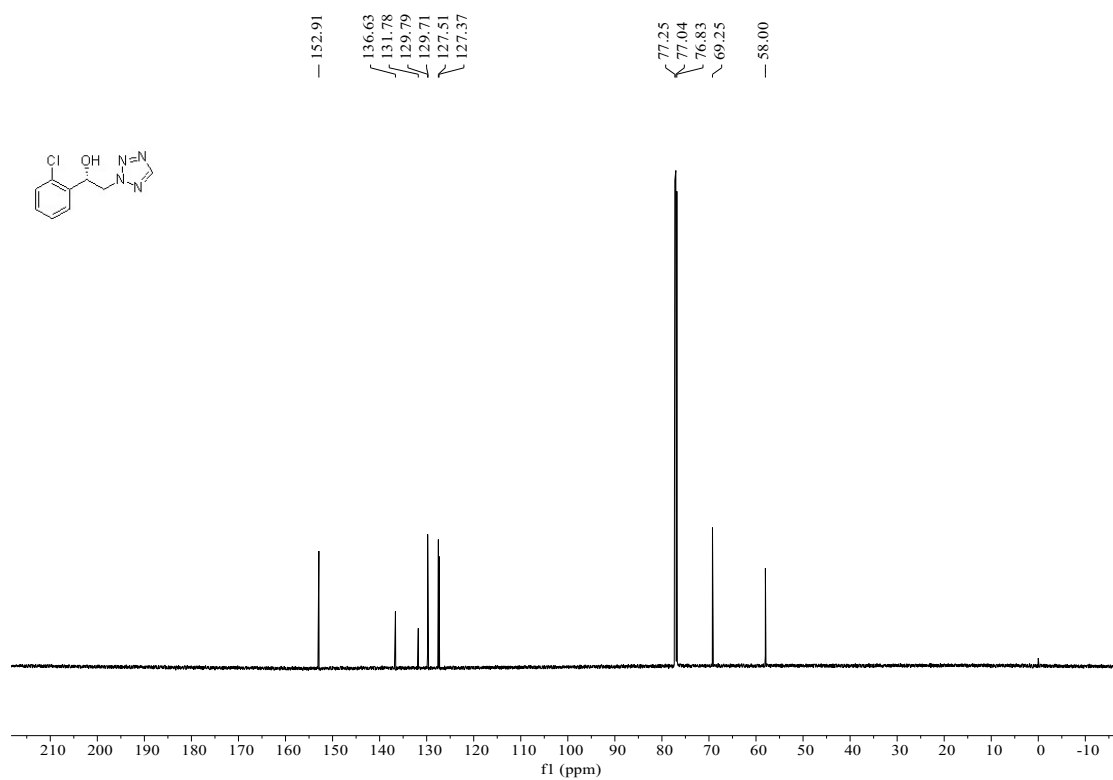
^{13}C NMR (151 MHz, CD_3OD) of **2r**:



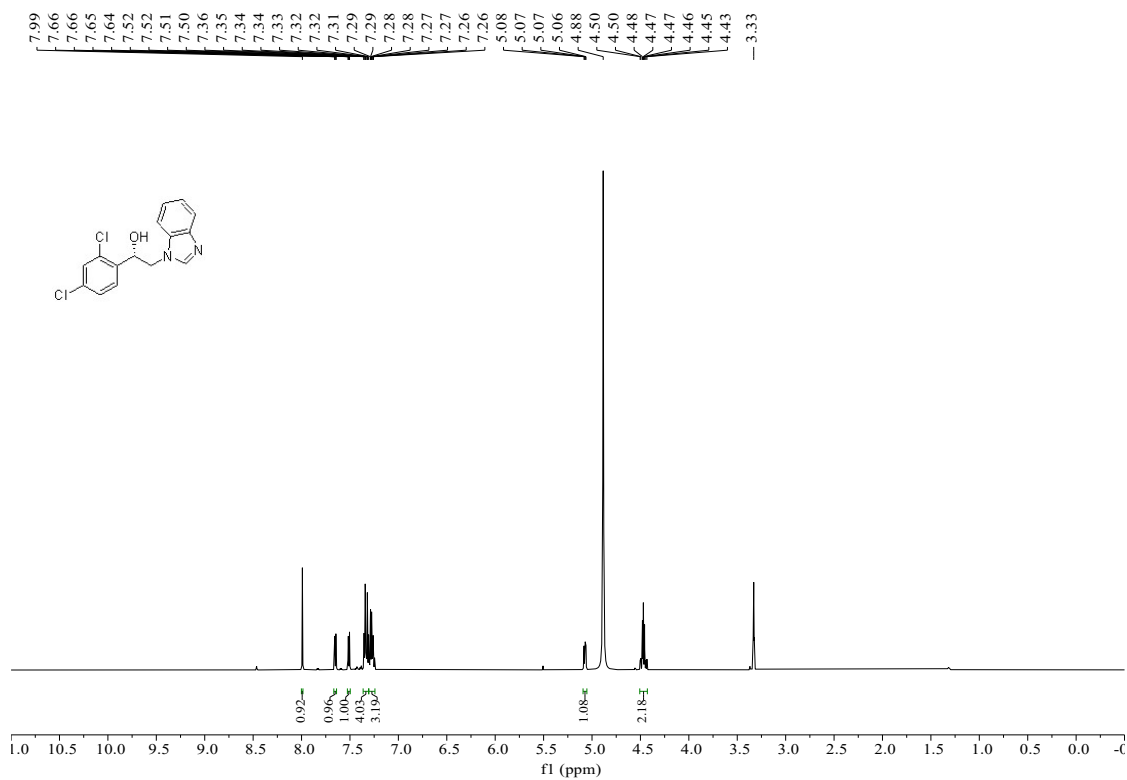
^1H NMR (600 MHz, CDCl_3) of **2s**:



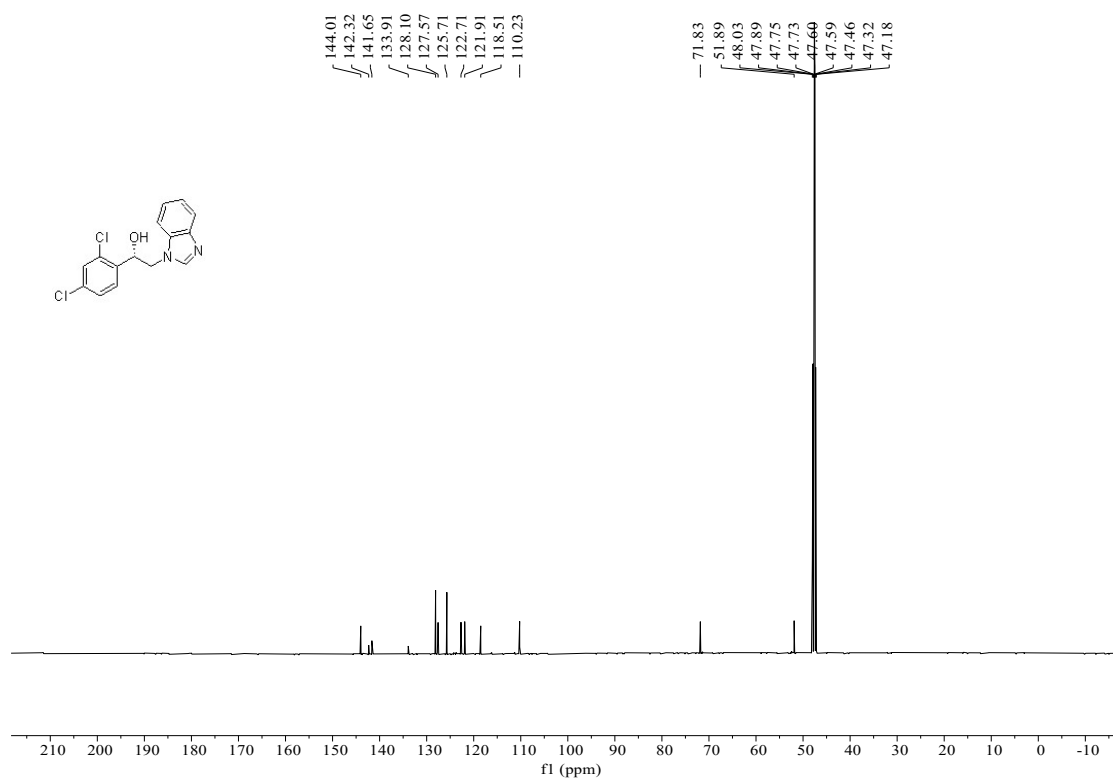
¹³C NMR (151 MHz, CDCl₃) of **2s**:



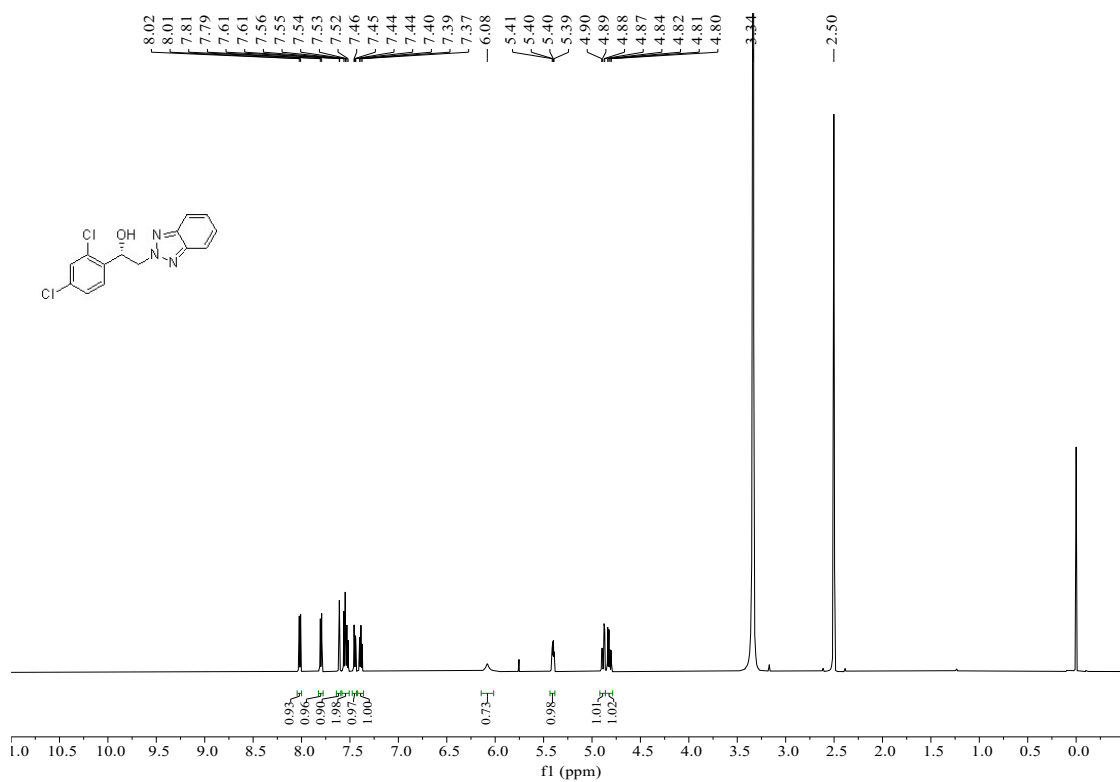
¹H NMR (600 MHz, CD₃OD) of **2t**:



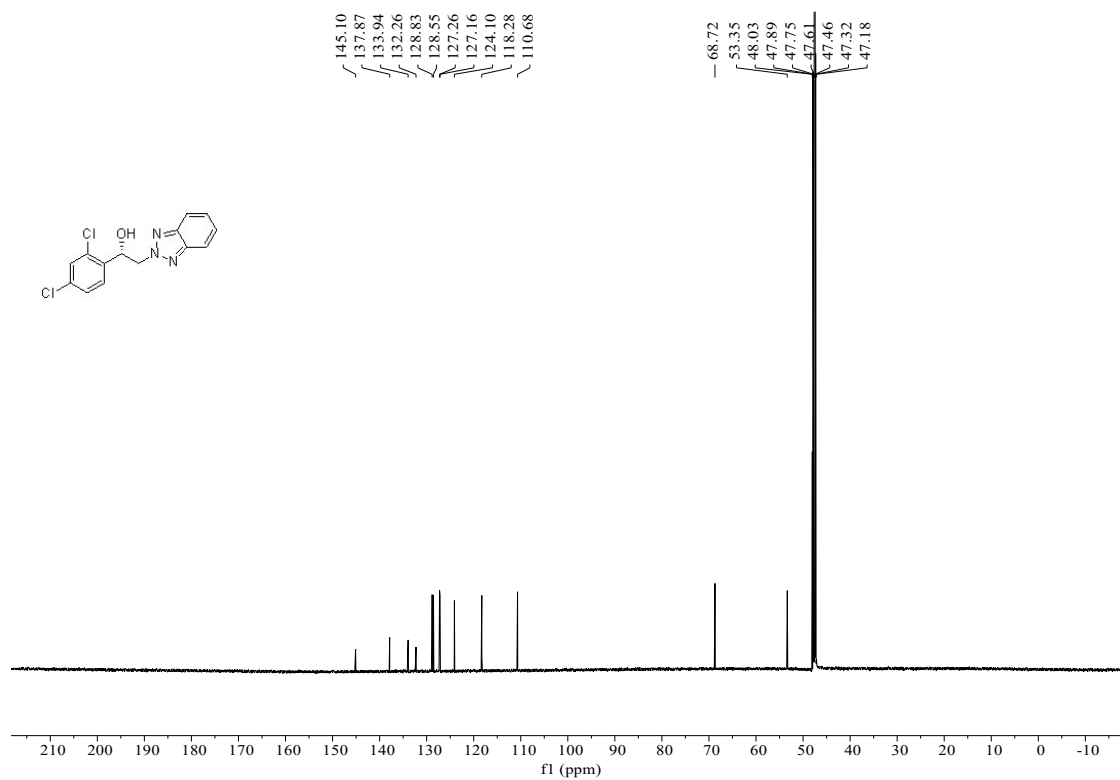
¹³C NMR (151 MHz, CD₃OD) of **2t**:



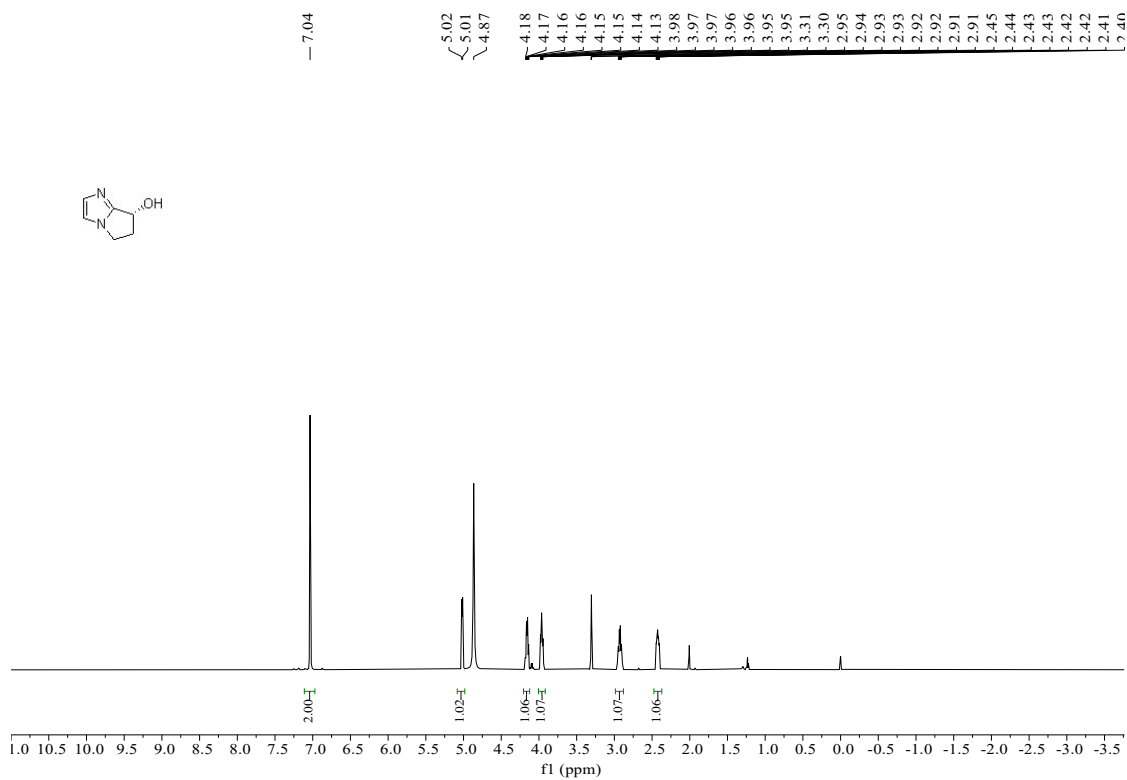
¹H NMR (600 MHz, DMSO-*d*₆) of **2u**:



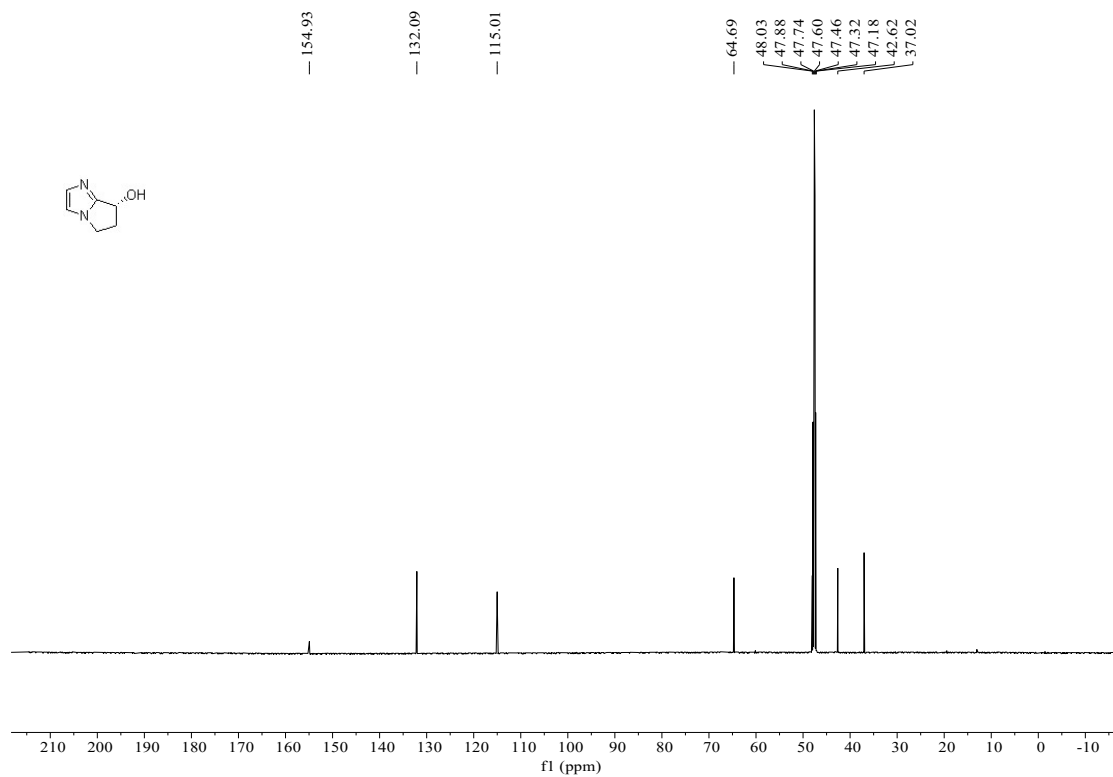
¹³C NMR (151 MHz, CD₃OD) of **2u**:



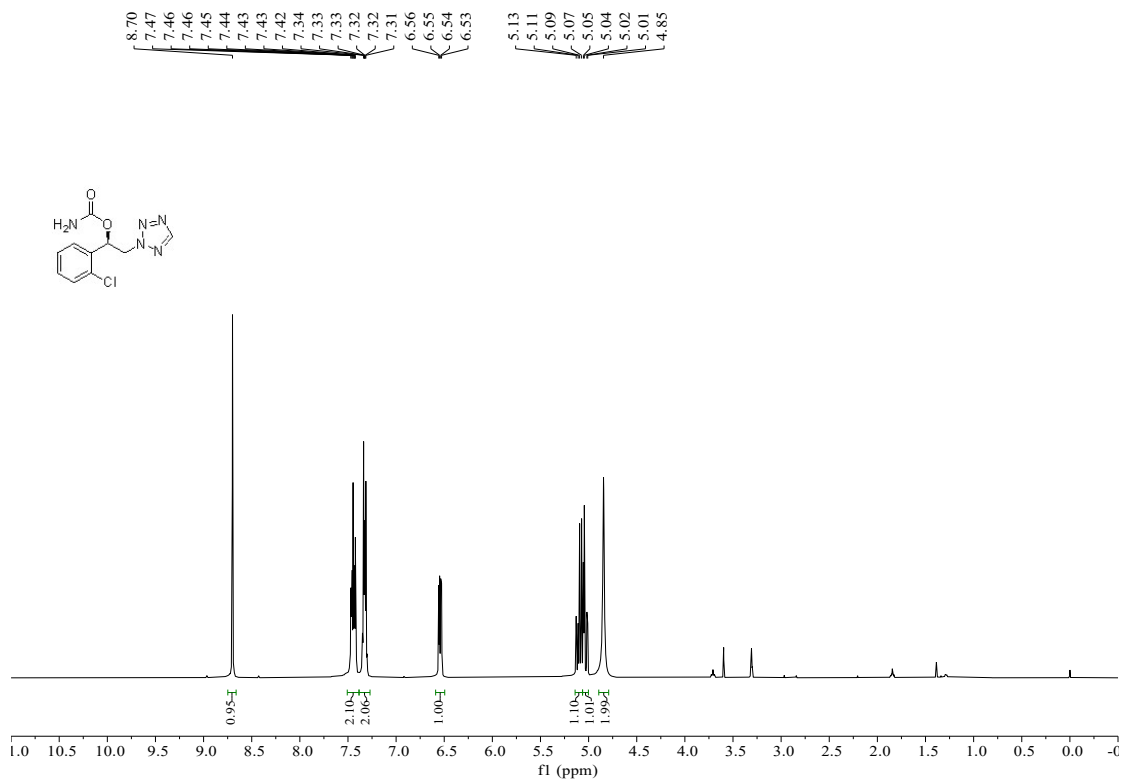
¹H NMR (600 MHz, CD₃OD) of **2v**:



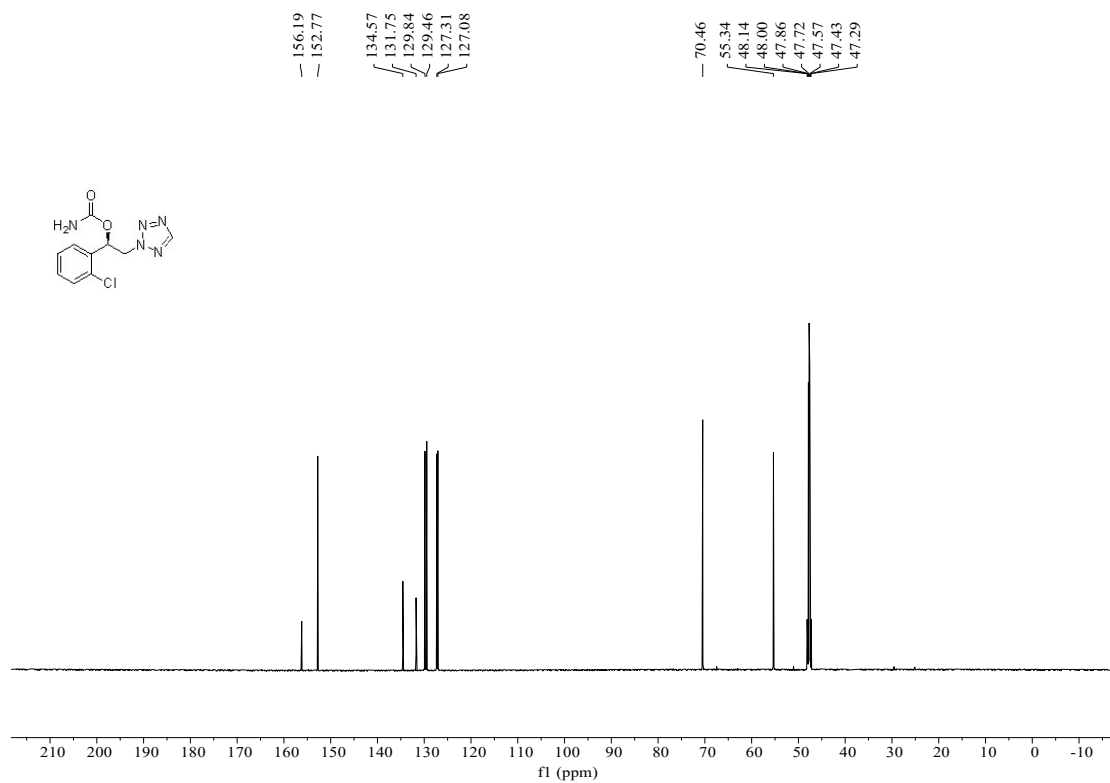
^{13}C NMR (151 MHz, CD_3OD) of **2v**:



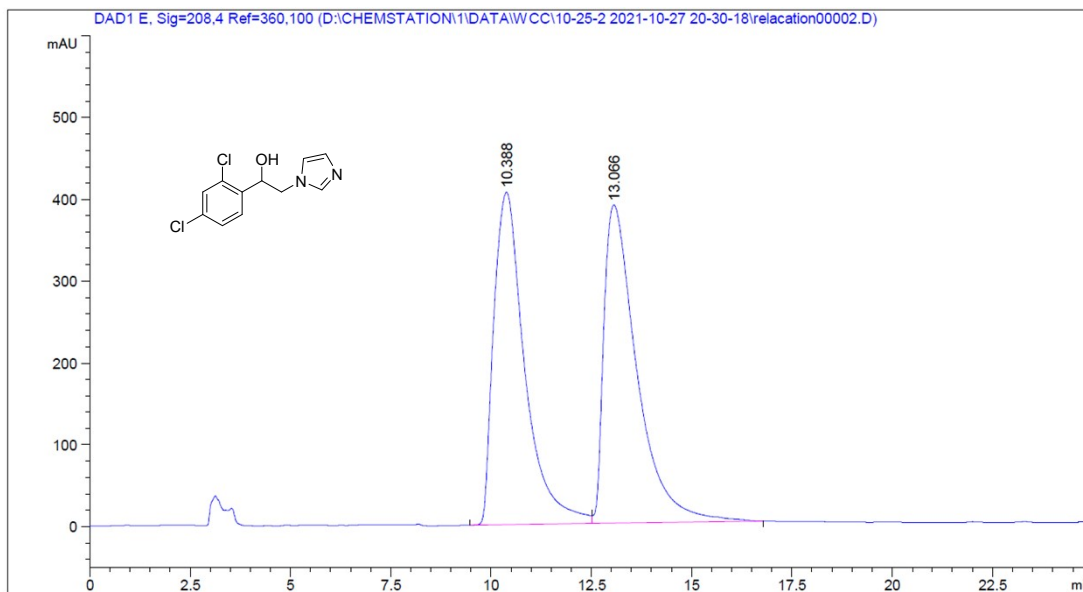
^1H NMR (400 MHz, CD_3OD) of **3s**:



¹³C NMR (101 MHz, CD₃OD) of 3s:

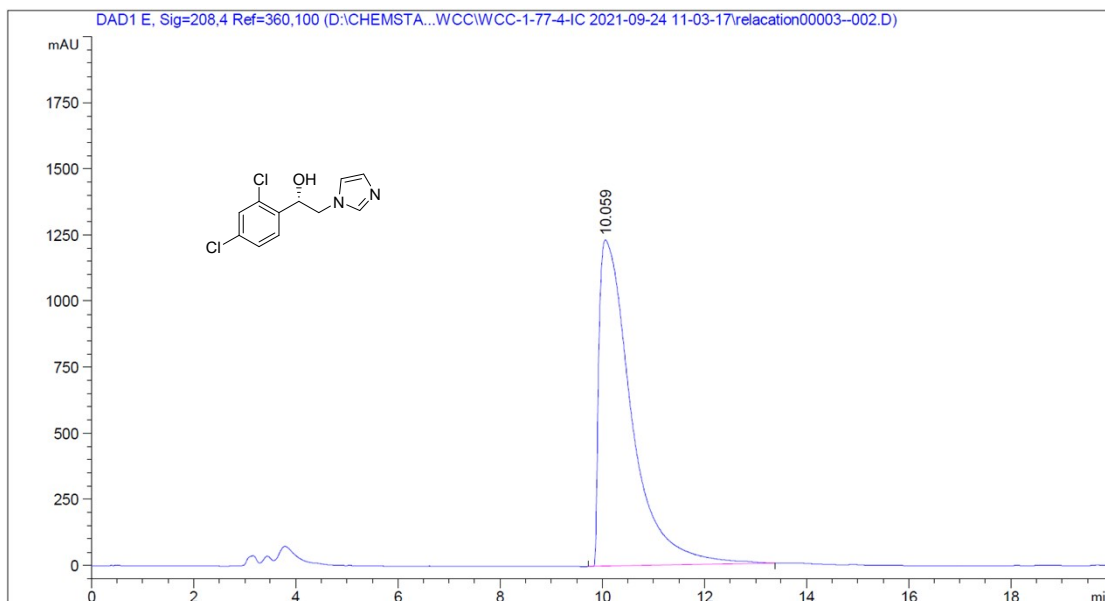


6. HPLC spectra



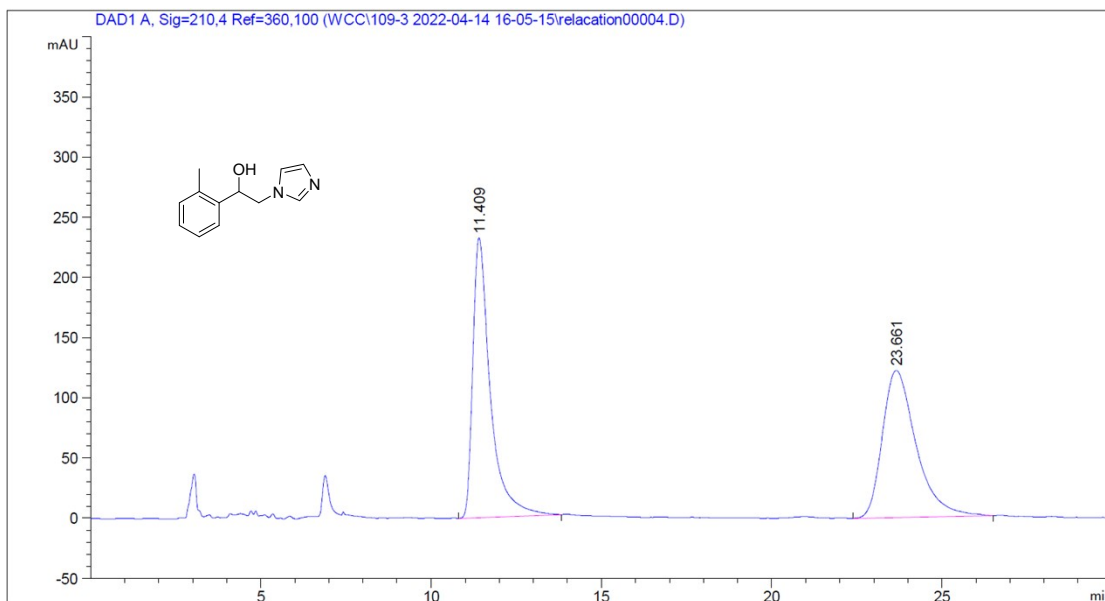
Signal 1: DAD1 E, Sig=208,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|----------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 10.388 | BV | 0.8300 | 2.18737e4 | 406.34833 | 49.4832 |
| 2 | 13.066 | VB | 0.8675 | 2.23306e4 | 389.11380 | 50.5168 |
| Totals : | | | | 4.42043e4 | 795.46213 | |



Signal 1: DAD1 E, Sig=208,4 Ref=360,100

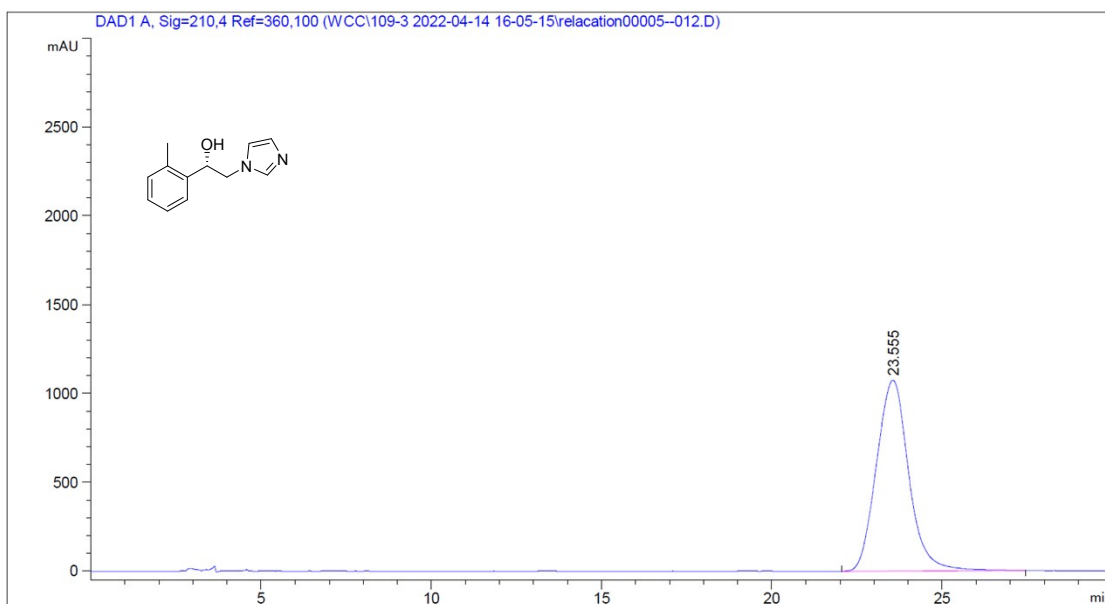
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 10.059 | BB | 0.6726 | 5.42146e4 | 1233.79675 | 100.0000 |



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 11.409 | BB | 0.5263 | 8291.38867 | 232.36989 | 49.6316 |
| 2 | 23.661 | BB | 1.0394 | 8414.48047 | 122.18788 | 50.3684 |

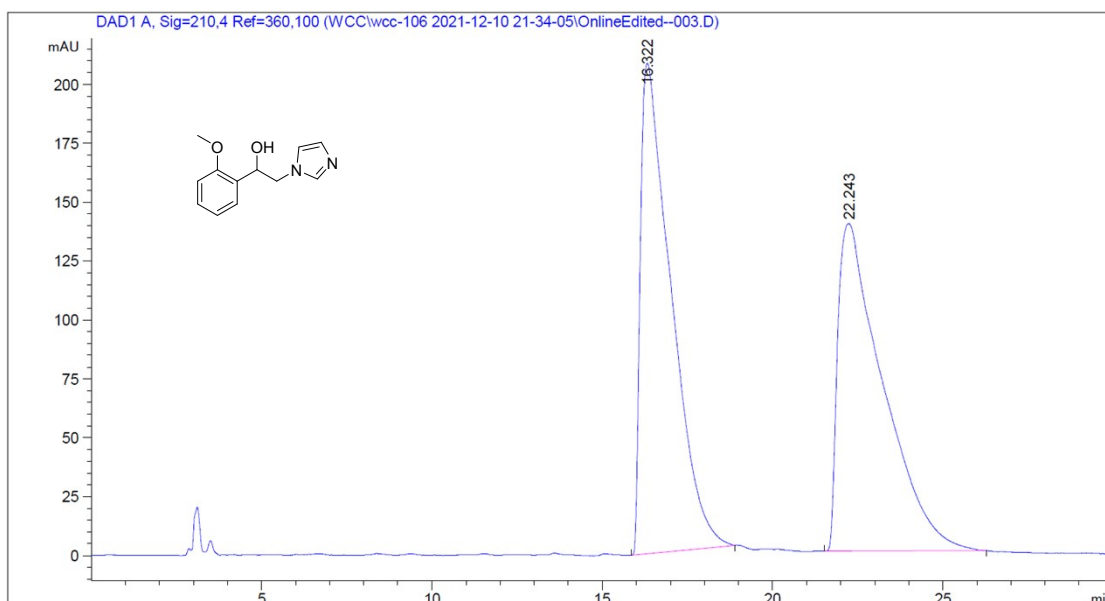
Totals : 1.67059e4 354.55777



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

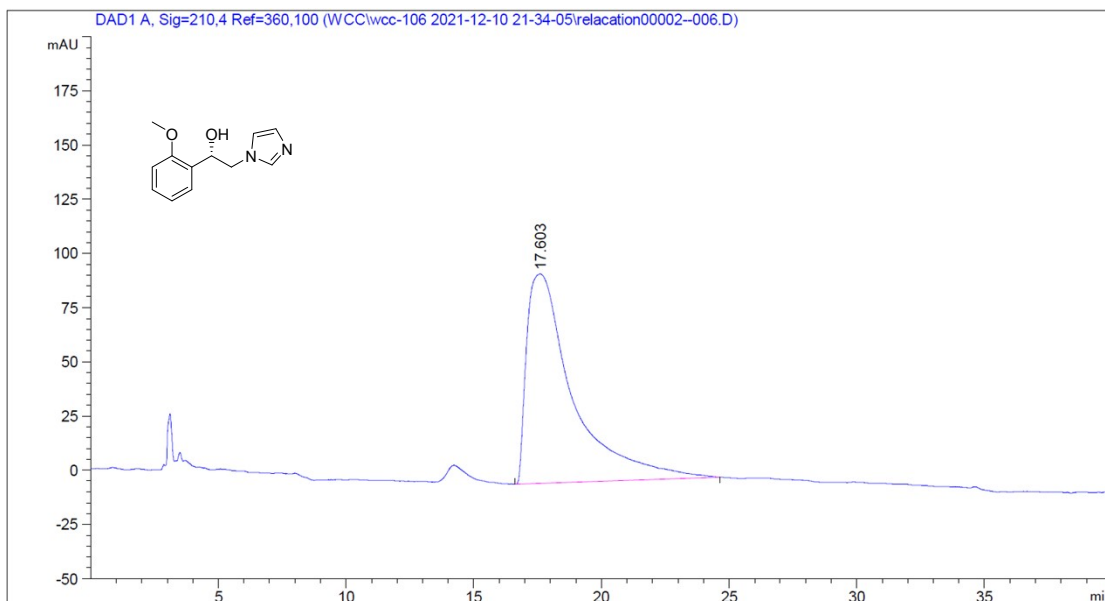
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 23.555 | BB | 1.0231 | 7.08493e4 | 1074.67920 | 100.0000 |

Totals : 7.08493e4 1074.67920



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

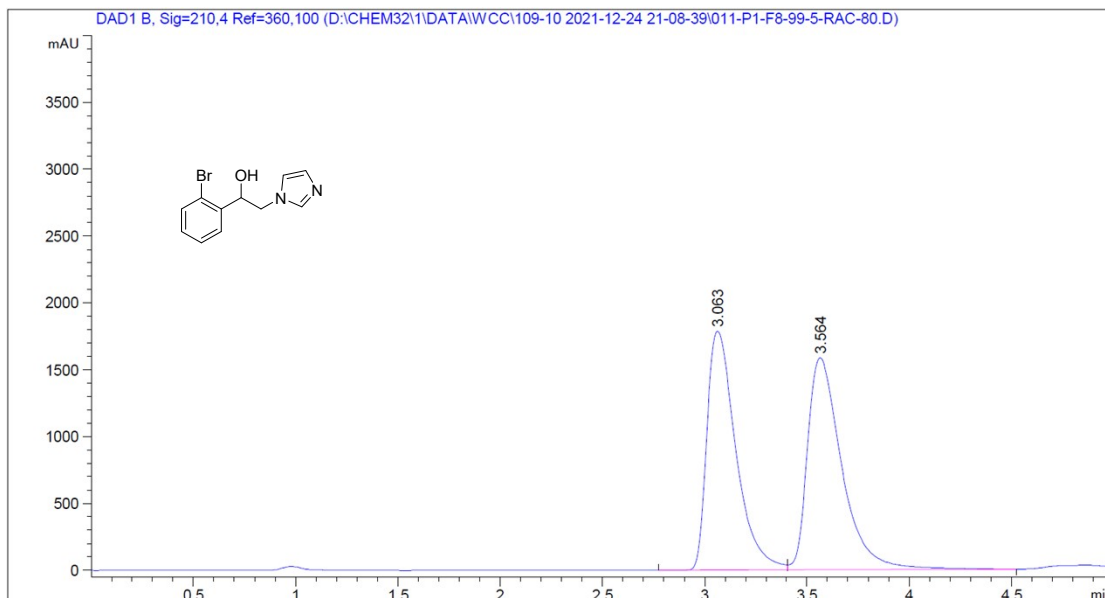
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 16.322 | BB | 0.8488 | 1.30053e4 | 208.18881 | 50.4193 |
| 2 | 22.243 | BB | 1.1455 | 1.27890e4 | 138.99339 | 49.5807 |



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 17.603 | BB | 1.5081 | 1.22038e4 | 96.58673 | 100.0000 |

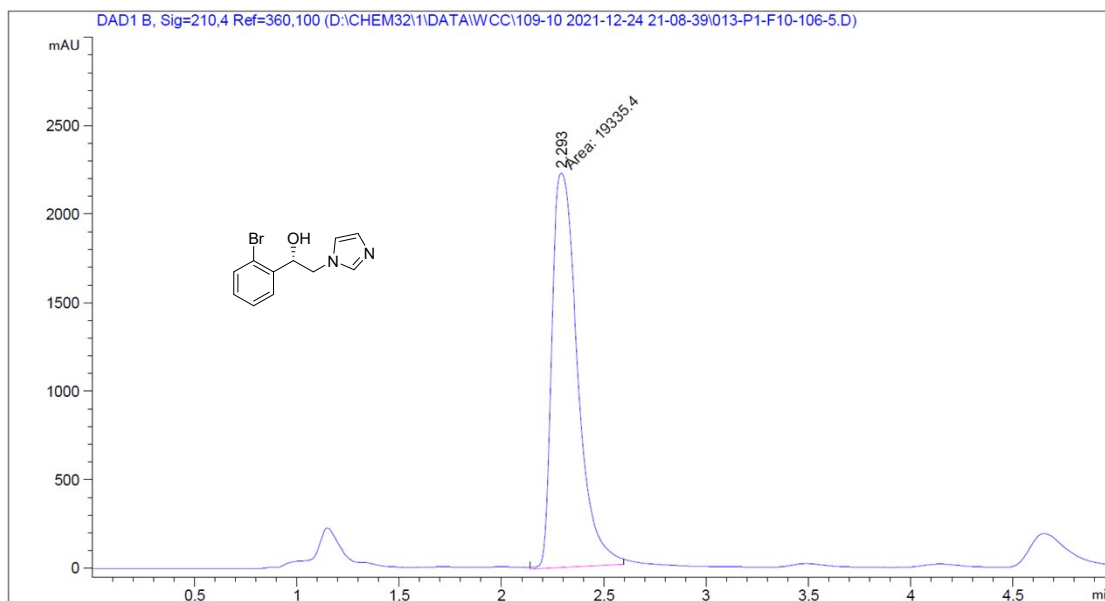
Totals : 1.22038e4 96.58673



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 3.063 | BV | 0.1508 | 1.76086e4 | 1789.19788 | 48.7634 |
| 2 | 3.564 | VB | 0.1781 | 1.85017e4 | 1586.24841 | 51.2366 |

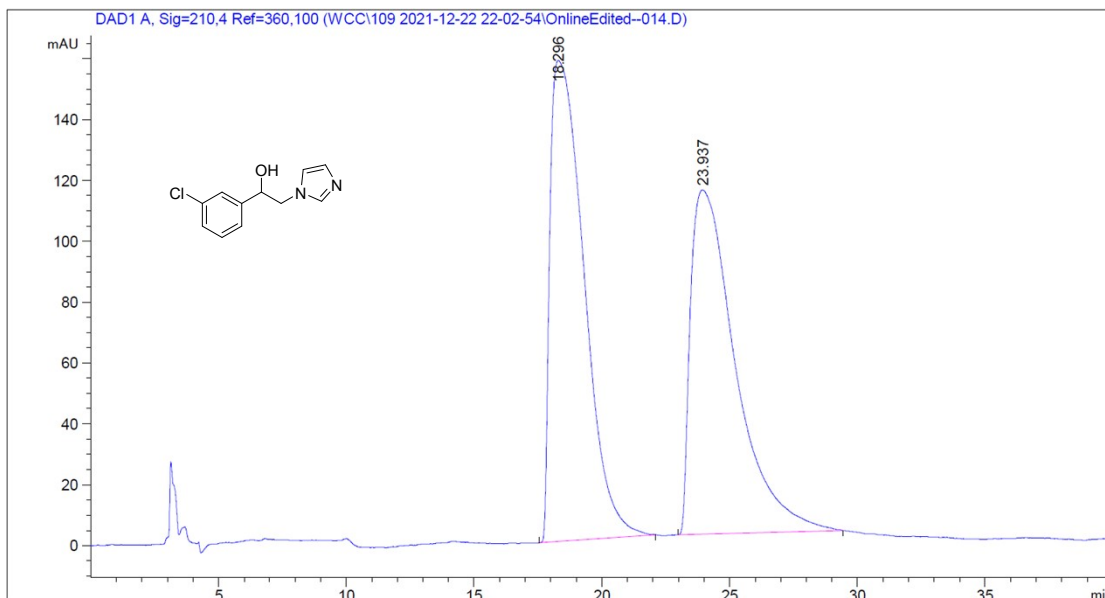
Totals : 3.61102e4 3375.44629



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 2.293 | MM | 0.1446 | 1.93354e4 | 2229.32056 | 100.0000 |

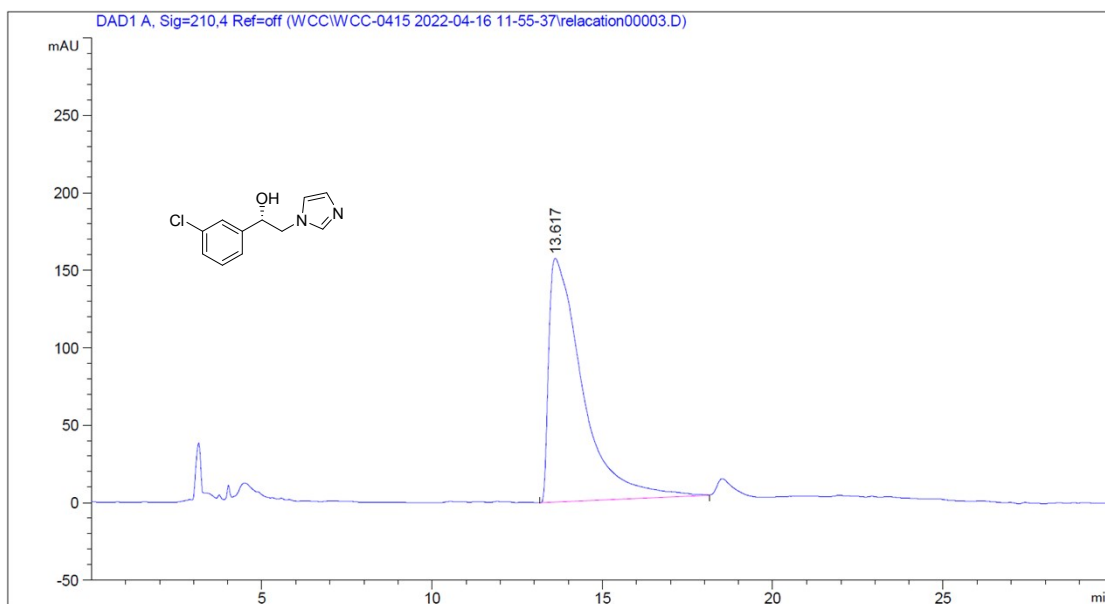
Totals : 1.93354e4 2229.32056



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 18.296 | BB | 1.2264 | 1.45578e4 | 158.08727 | 51.3504 |
| 2 | 23.937 | BB | 1.5067 | 1.37921e4 | 113.10023 | 48.6496 |

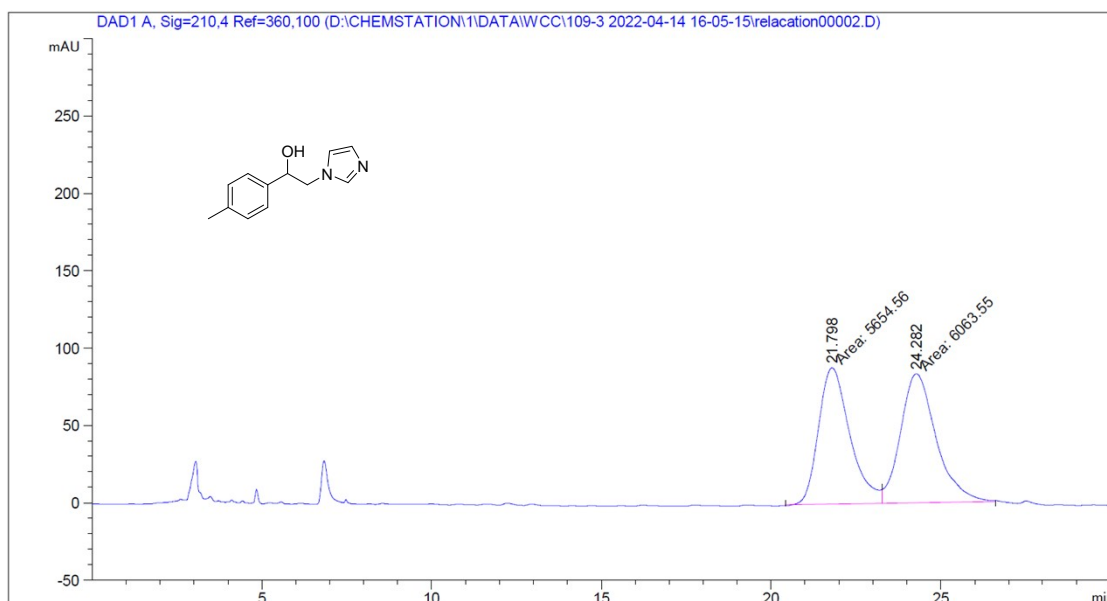
Totals : 2.83499e4 271.18750



Signal 1: DAD1 A, Sig=210,4 Ref=off

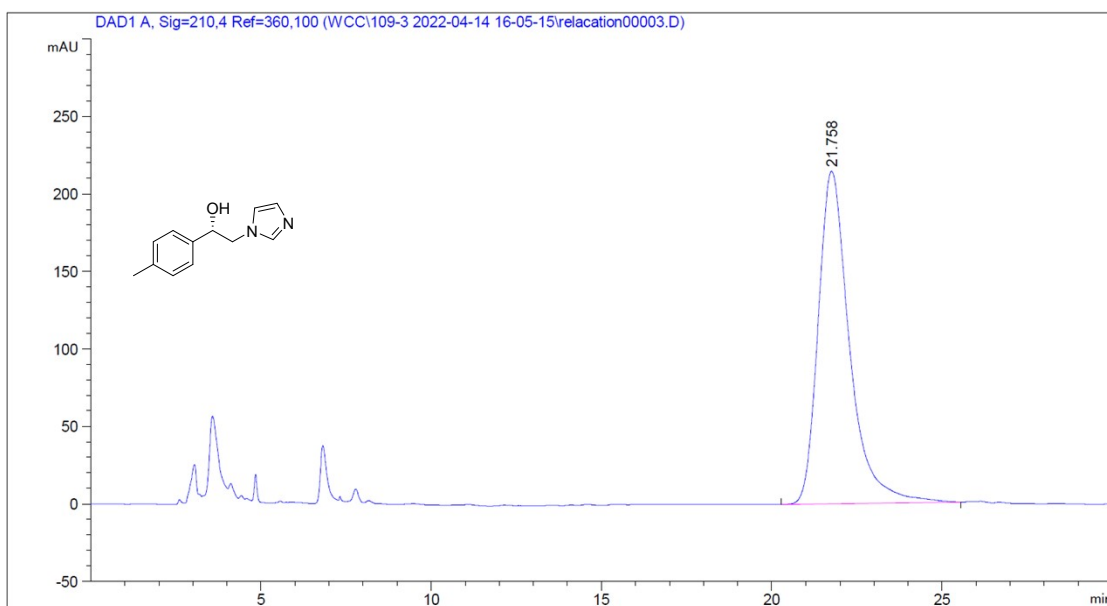
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 13.617 | BB | 0.9095 | 1.08159e4 | 157.44118 | 100.0000 |

Totals : 1.08159e4 157.44118



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

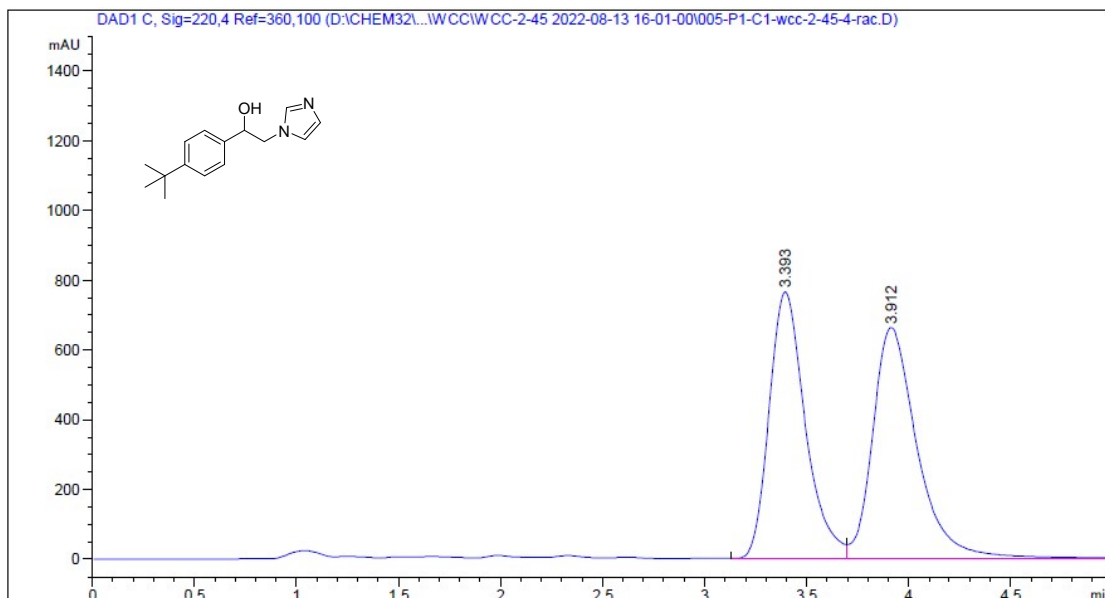
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 21.798 | MF | 1.0716 | 5654.55566 | 87.94574 | 48.2549 |
| 2 | 24.282 | FM | 1.2136 | 6063.55273 | 83.26916 | 51.7451 |



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 21.758 | BB | 0.9529 | 1.37448e4 | 214.70074 | 100.0000 |

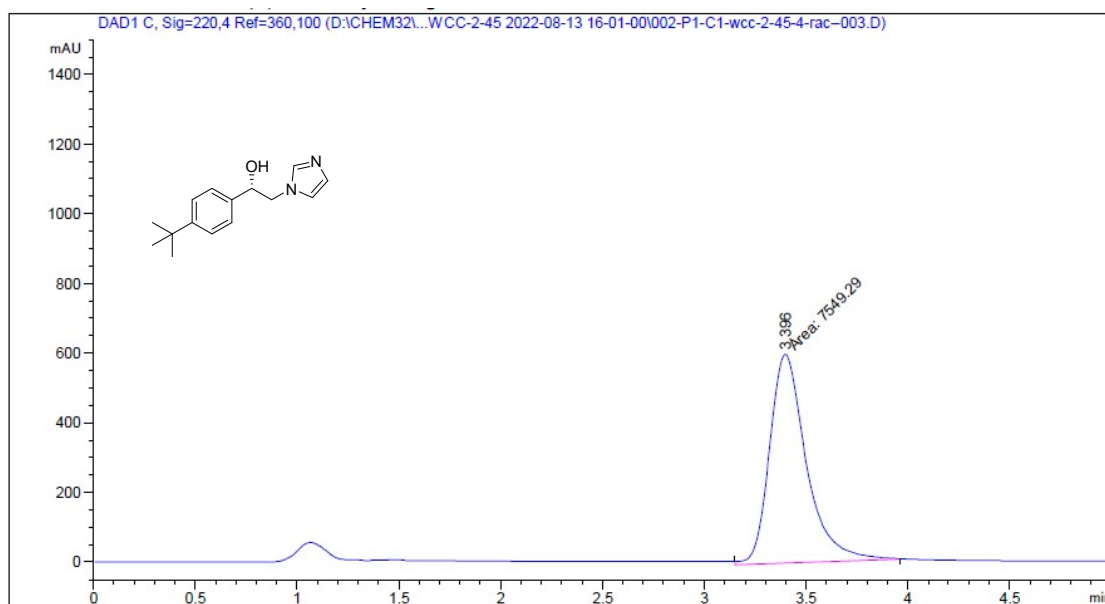
Totals : 1.37448e4 214.70074



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 3.393 | BV | 0.1870 | 9383.28320 | 765.69318 | 48.2830 |
| 2 | 3.912 | VB | 0.2289 | 1.00507e4 | 662.71301 | 51.7170 |

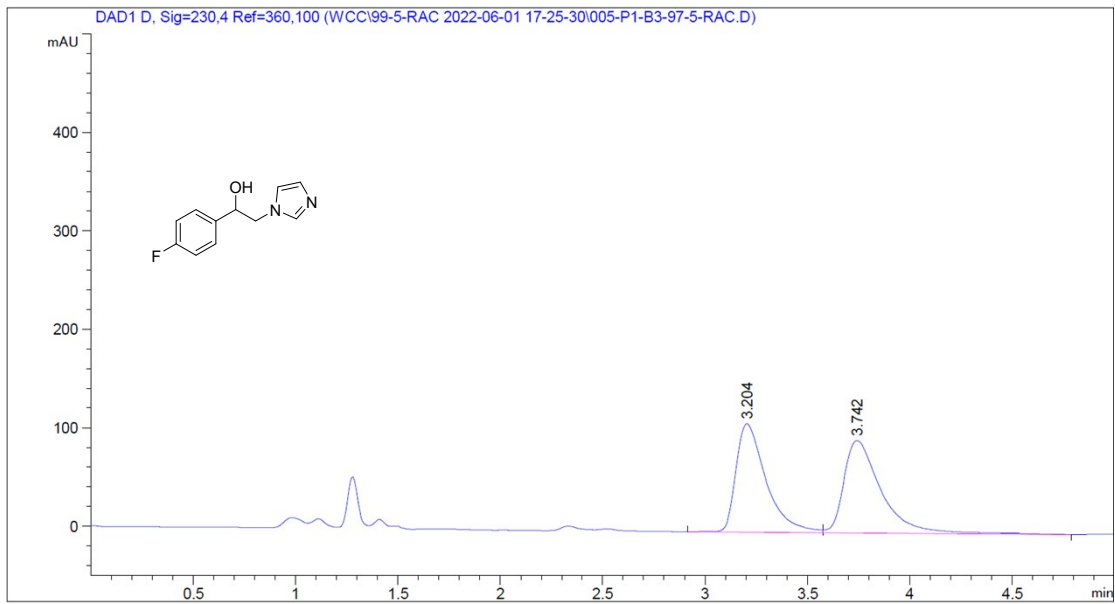
Totals : 1.94339e4 1428.40619



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 3.396 | MM | 0.2094 | 7549.28662 | 600.90680 | 100.0000 |

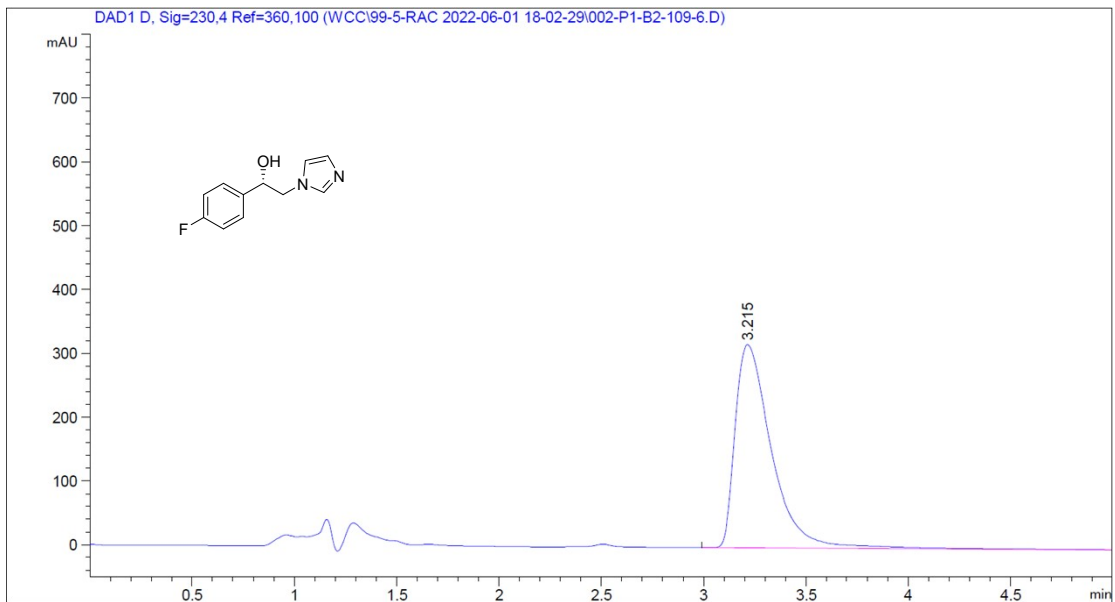
Totals : 7549.28662 600.90680



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 3.204 | BV | 0.1529 | 1124.43457 | 110.36457 | 48.6112 |
| 2 | 3.742 | VB | 0.1876 | 1188.68591 | 93.93526 | 51.3888 |

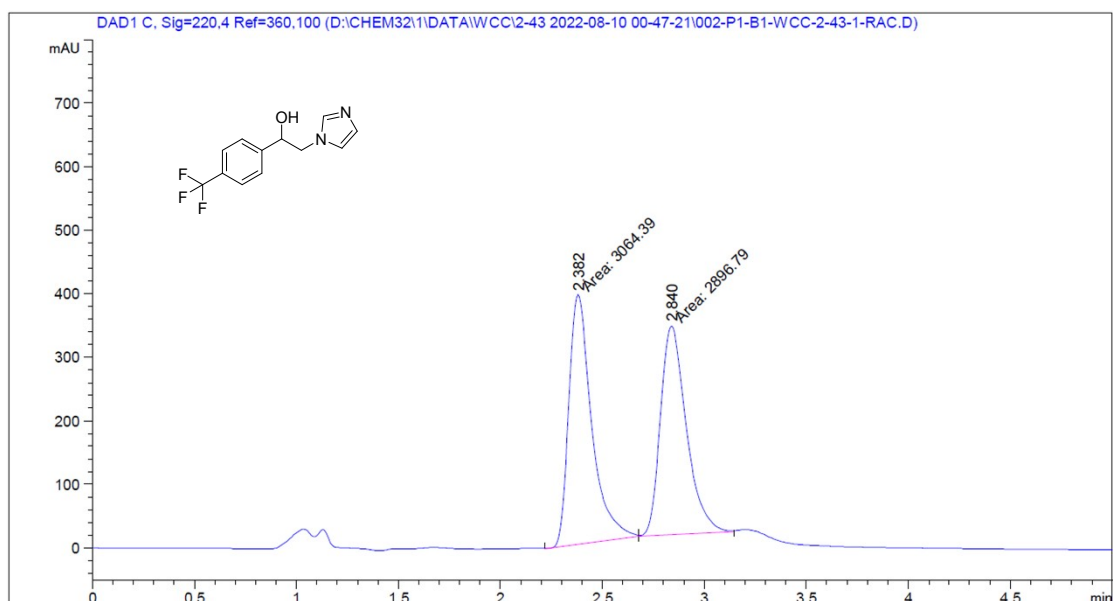
Totals : 2313.12048 204.29984



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 3.215 | BBA | 0.1909 | 3958.71265 | 318.76175 | 100.0000 |

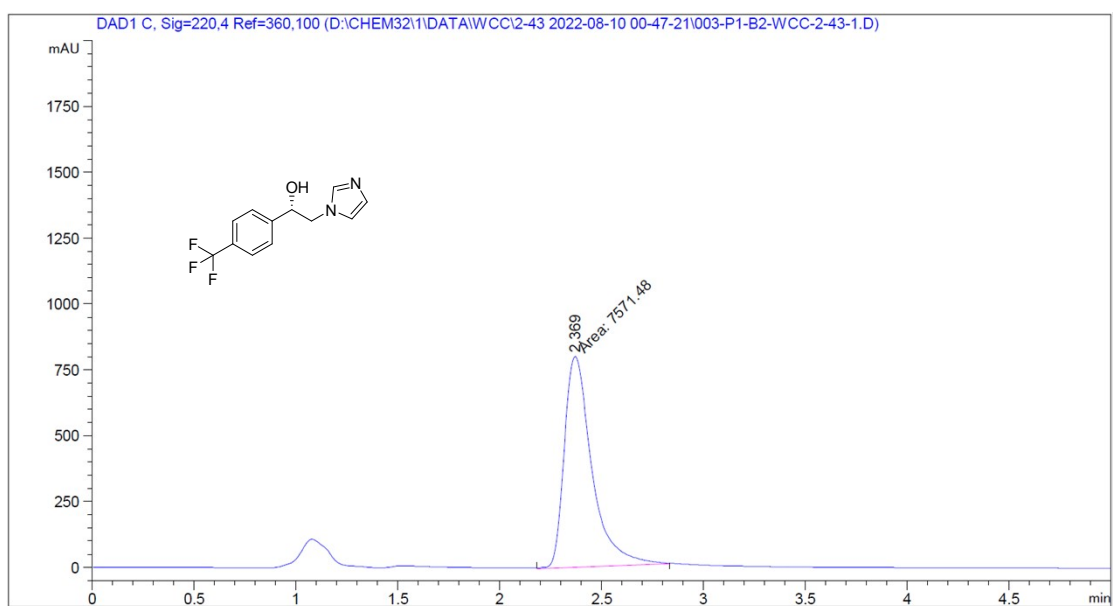
Totals : 3958.71265 318.76175



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 2.382 | MM | 0.1297 | 3064.38647 | 393.64590 | 51.4058 |
| 2 | 2.840 | MM | 0.1469 | 2896.78735 | 328.66504 | 48.5942 |

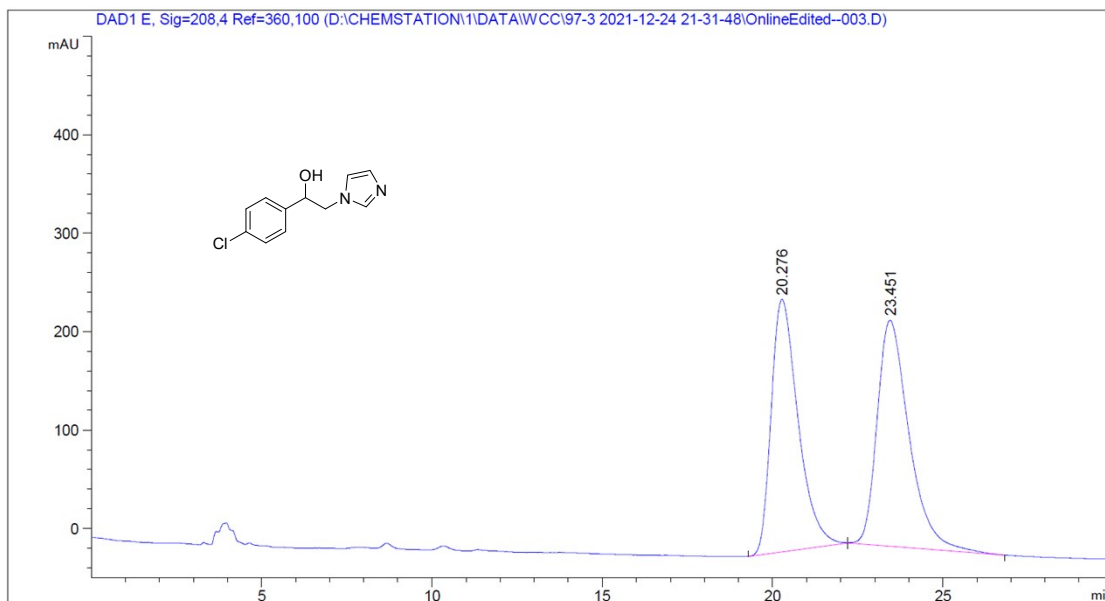
Totals : 5961.17383 722.31094



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

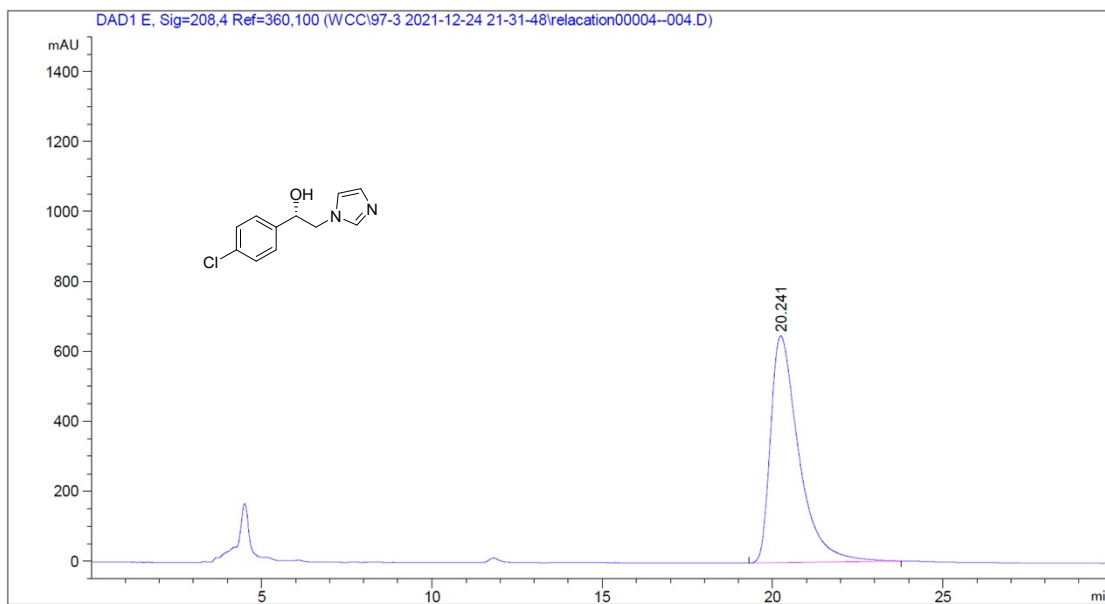
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 2.369 | MM | 0.1575 | 7571.47803 | 801.30267 | 100.0000 |

Totals : 7571.47803 801.30267



Signal 1: DAD1 E, Sig=208,4 Ref=360,100

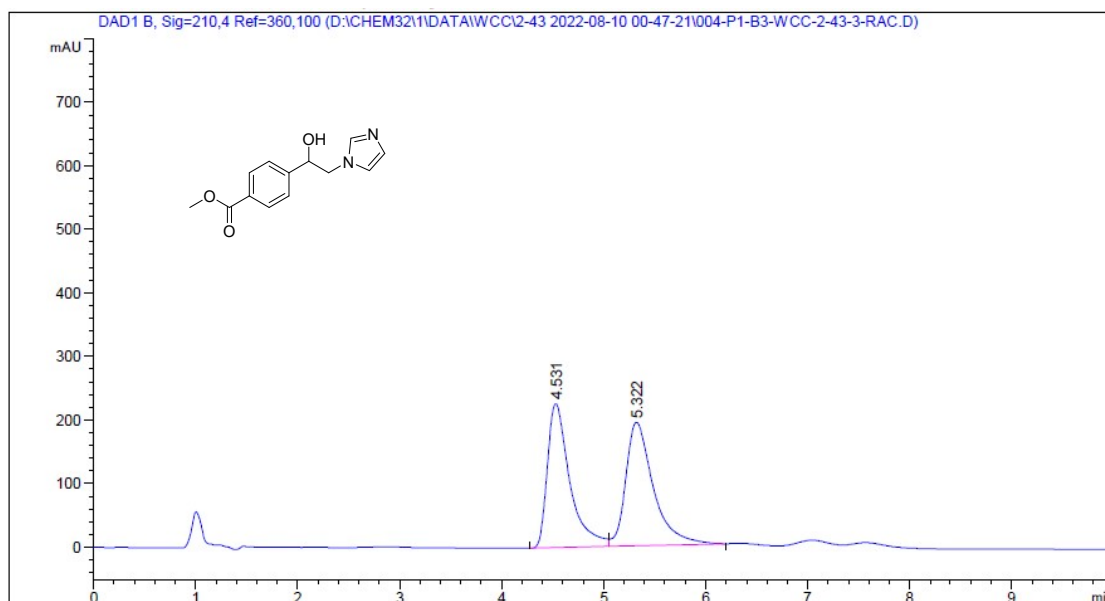
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 20.276 | BB | 0.8227 | 1.40428e4 | 256.52542 | 48.4773 |
| 2 | 23.451 | BB | 0.9292 | 1.49249e4 | 229.36137 | 51.5227 |



Signal 1: DAD1 E, Sig=208,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 20.241 | BB | 0.8369 | 3.74351e4 | 649.05475 | 100.0000 |

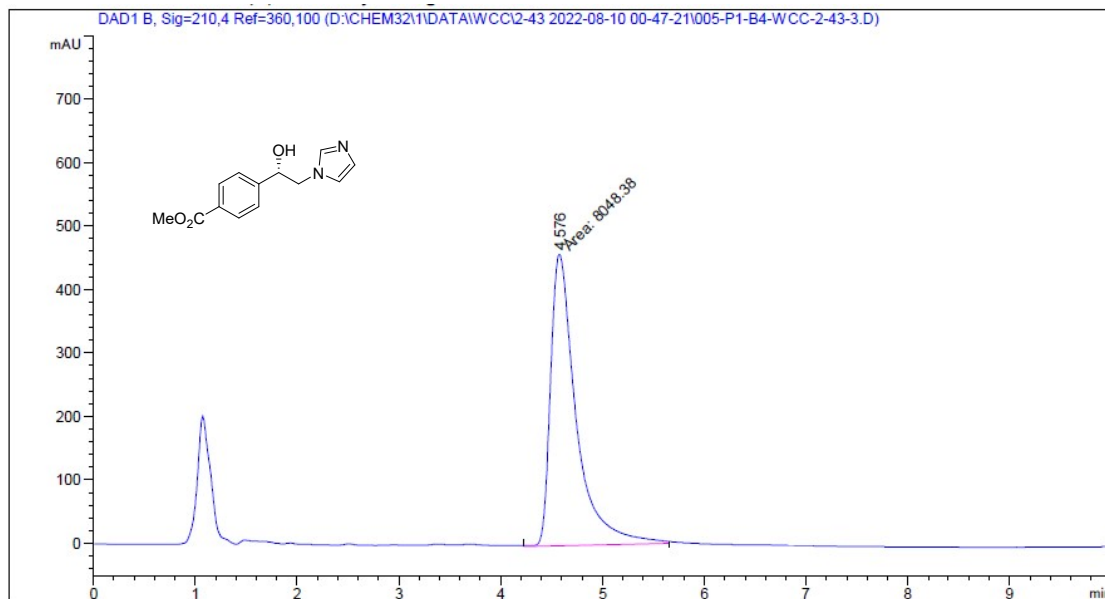
Totals : 3.74351e4 649.05475



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 4.531 | BV | 0.2286 | 3468.59229 | 226.54500 | 48.6715 |
| 2 | 5.322 | VB | 0.2817 | 3657.94824 | 194.20930 | 51.3285 |

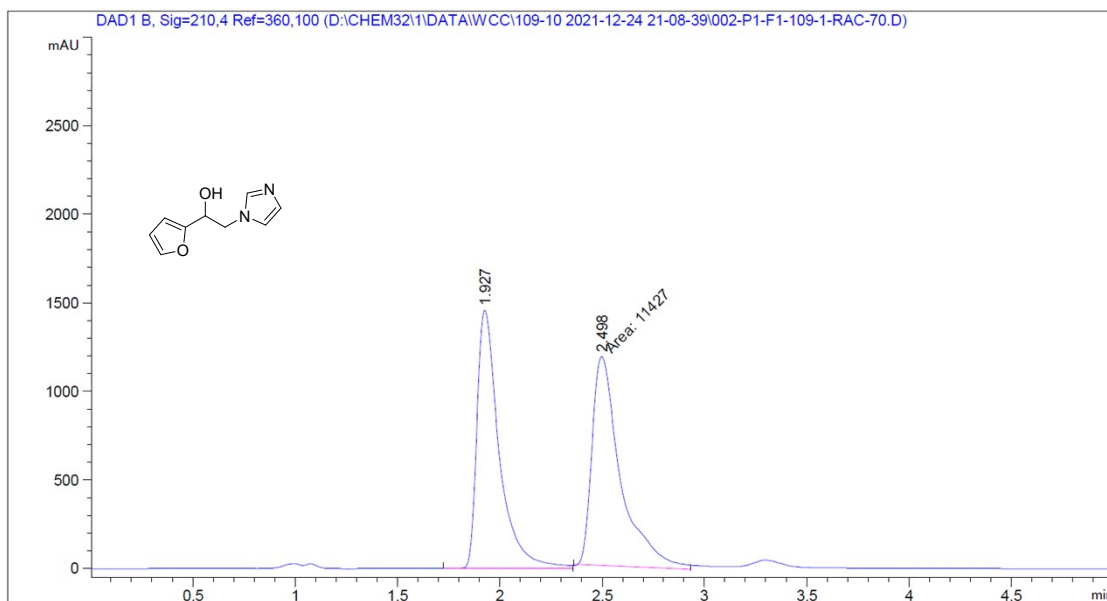
Totals : 7126.54053 420.75430



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

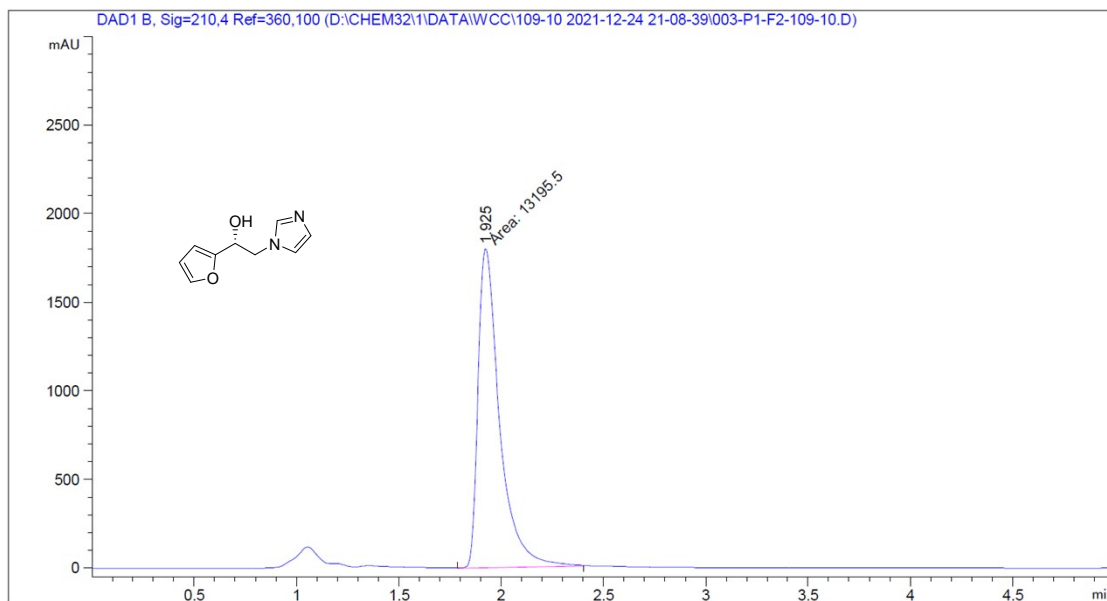
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 4.576 | MM | 0.2918 | 8048.38037 | 459.70197 | 100.0000 |

Totals : 8048.38037 459.70197



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 1.927 | BV | 0.1119 | 1.09902e4 | 1459.46130 | 49.0258 |
| 2 | 2.498 | MM | 0.1612 | 1.14270e4 | 1181.69531 | 50.9742 |

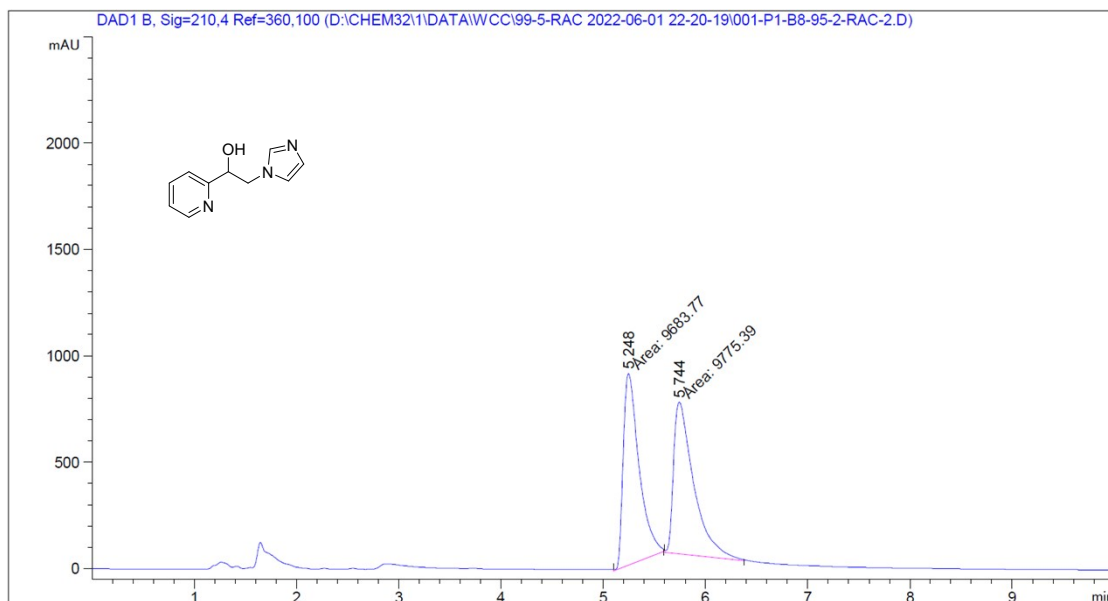
Totals : 2.24172e4 2641.15662



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 1.925 | MM | 0.1218 | 1.31955e4 | 1806.21582 | 100.0000 |

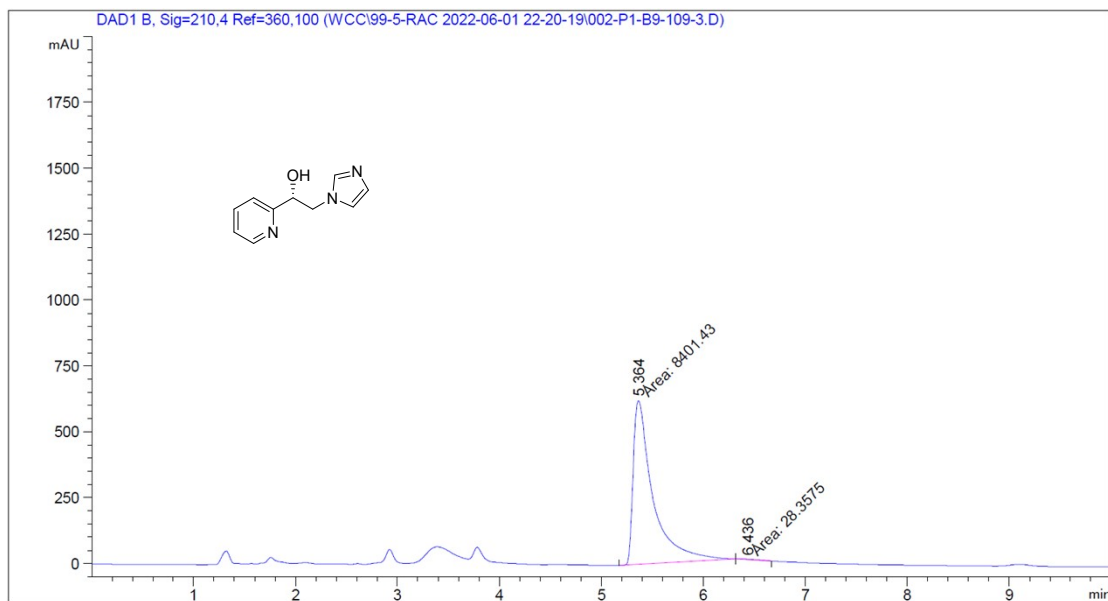
Totals : 1.31955e4 1806.21582



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 5.248 | MM | 0.1789 | 9683.76953 | 902.33600 | 49.7646 |
| 2 | 5.744 | MM | 0.2279 | 9775.38867 | 714.77600 | 50.2354 |

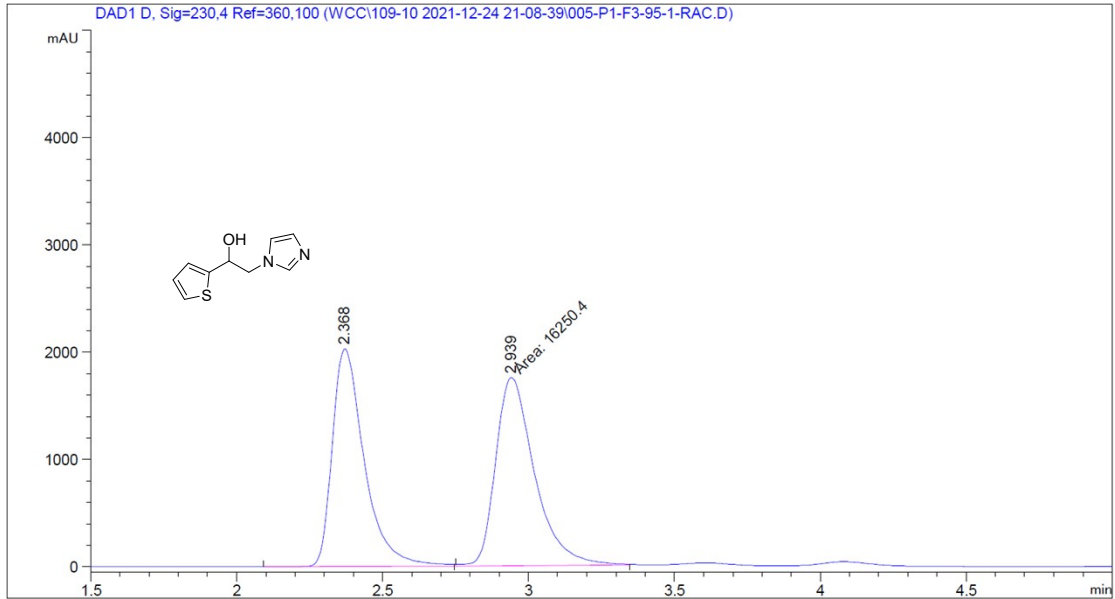
Totals : 1.94592e4 1617.11200



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 5.364 | MM | 0.2250 | 8401.42773 | 622.21075 | 99.6636 |
| 2 | 6.436 | MM | 0.2456 | 28.35750 | 1.92461 | 0.3364 |

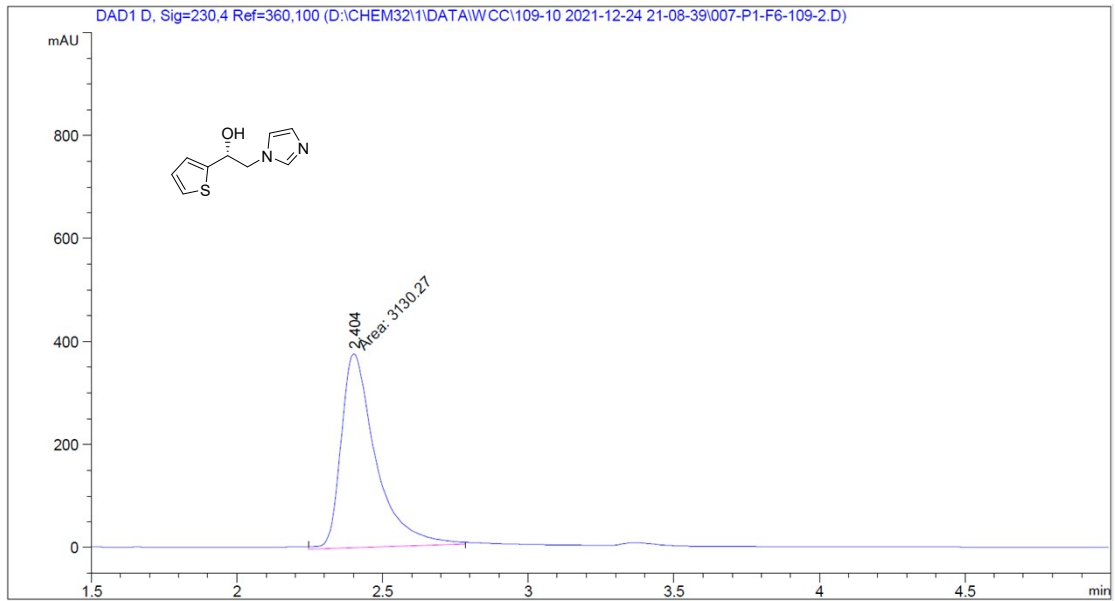
Totals : 8429.78523 624.13537



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 2.368 | MM | 0.1273 | 1.09782e4 | 1437.71606 | 49.0736 |
| 2 | 2.939 | MM | 0.1525 | 1.13927e4 | 1245.04895 | 50.9264 |

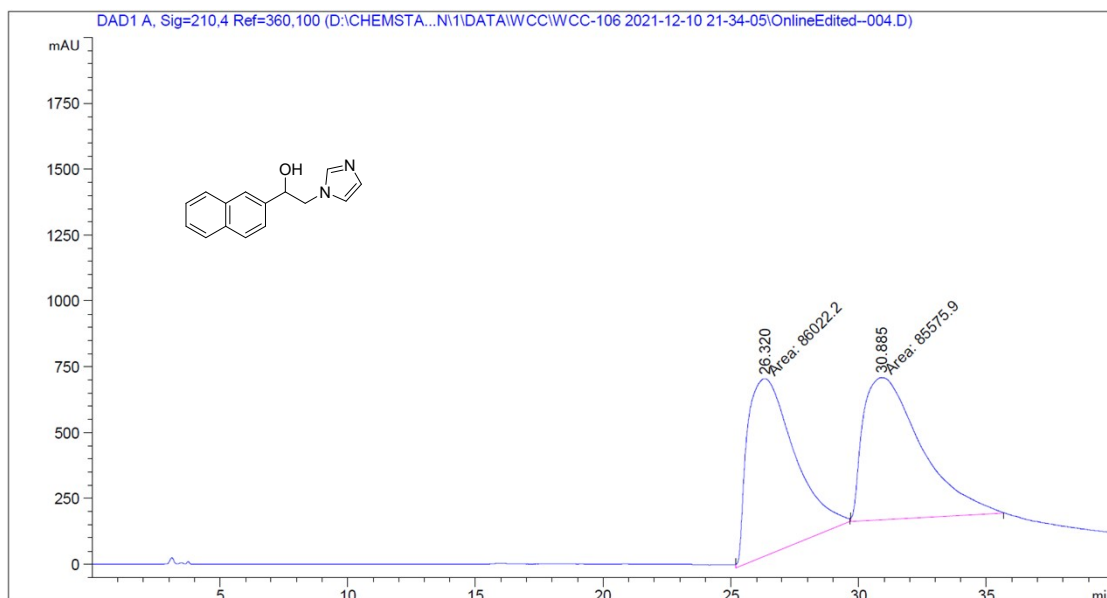
Totals : 2.23708e4 2682.76501



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

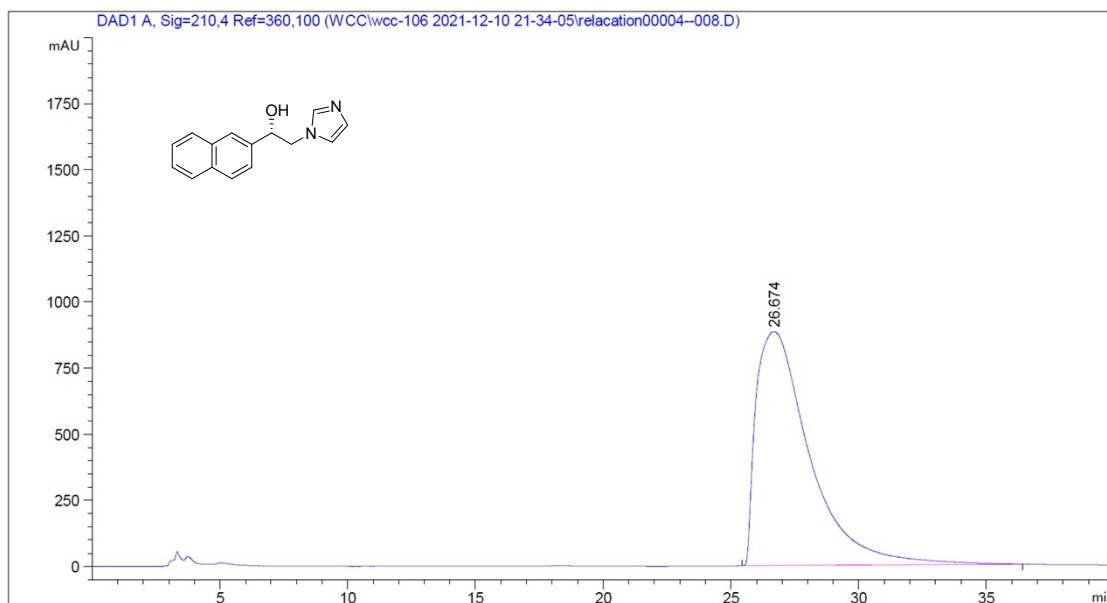
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 2.404 | MM | 0.1413 | 2323.25635 | 273.98352 | 100.0000 |

Totals : 2323.25635 273.98352



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

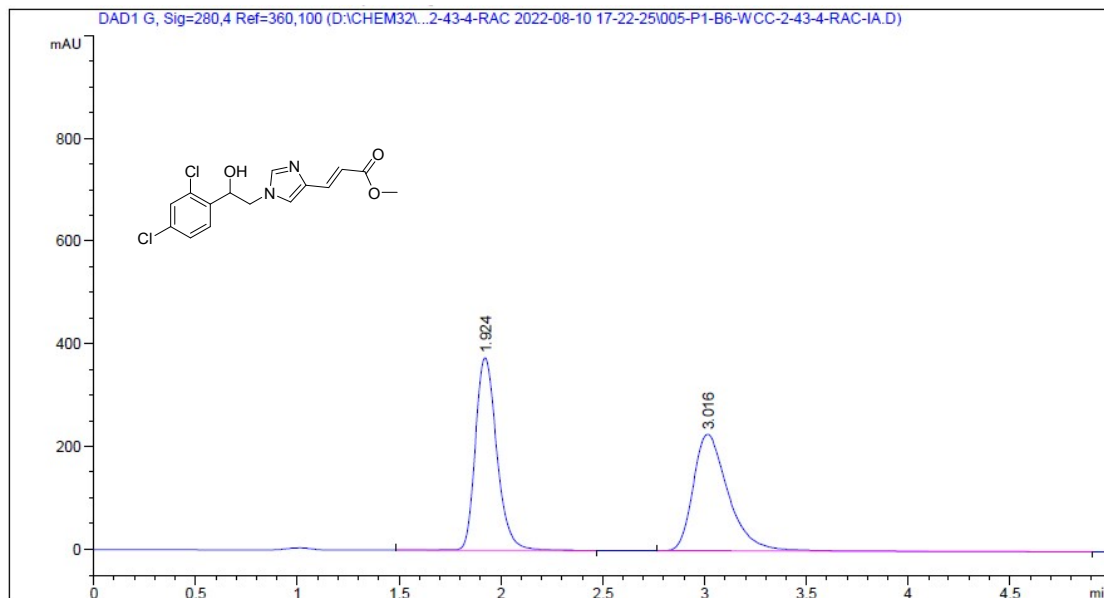
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 26.320 | MM | 2.1267 | 8.60222e4 | 674.15271 | 50.1301 |
| 2 | 30.885 | MM | 2.6425 | 8.55759e4 | 539.73499 | 49.8699 |



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 26.674 | BB | 1.7352 | 1.29459e5 | 884.68591 | 100.0000 |

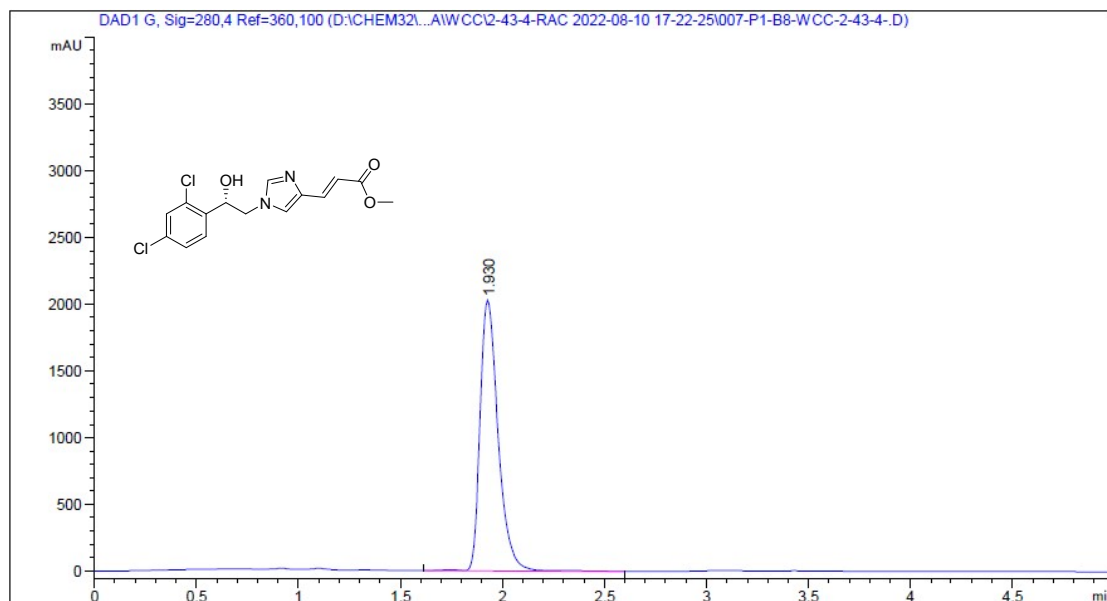
Totals : 1.29459e5 884.68591



Signal 1: DAD1 G, Sig=280,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 1.924 | BB | 0.1133 | 2742.44360 | 375.06287 | 50.2110 |
| 2 | 3.016 | BBA | 0.1817 | 2719.38965 | 227.06509 | 49.7890 |

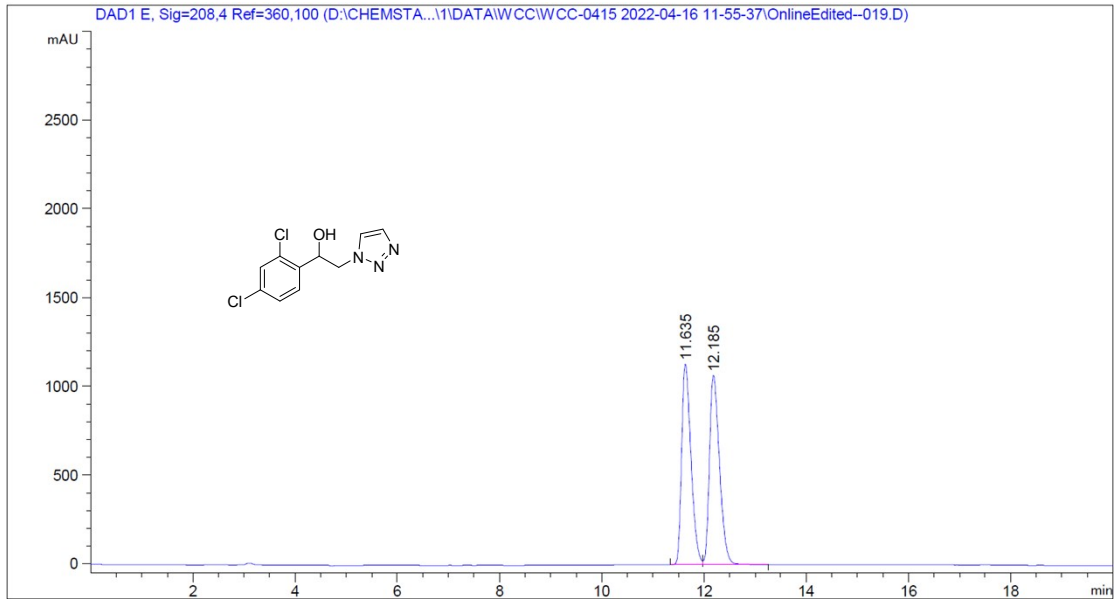
Totals : 5461.83325 602.12796



Signal 1: DAD1 G, Sig=280,4 Ref=360,100

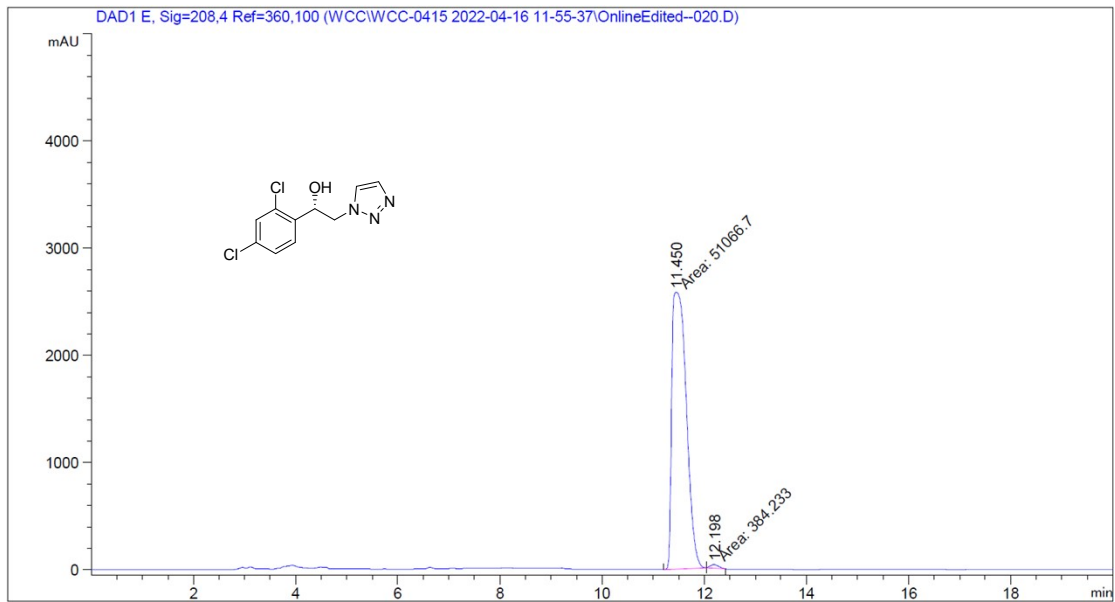
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 1.930 | VV R | 0.0931 | 1.24510e4 | 2026.74792 | 100.0000 |

Totals : 1.24510e4 2026.74792



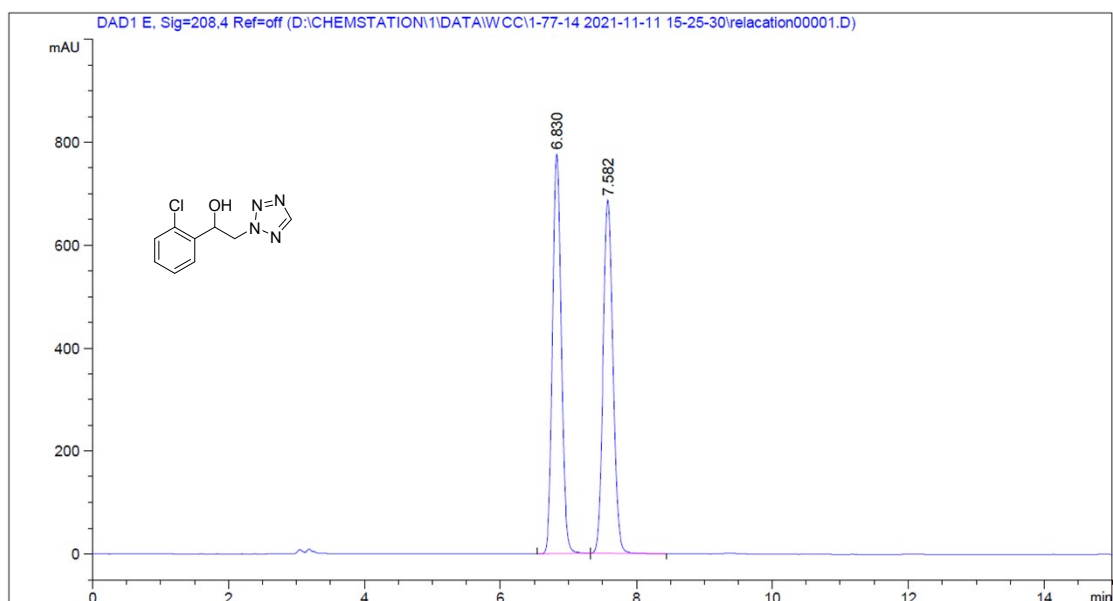
Signal 1: DAD1 E, Sig=208,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 11.635 | BV | 0.1962 | 1.43582e4 | 1130.05945 | 49.6172 |
| 2 | 12.185 | VB | 0.2094 | 1.45798e4 | 1066.79895 | 50.3828 |



Signal 1: DAD1 E, Sig=208,4 Ref=360,100

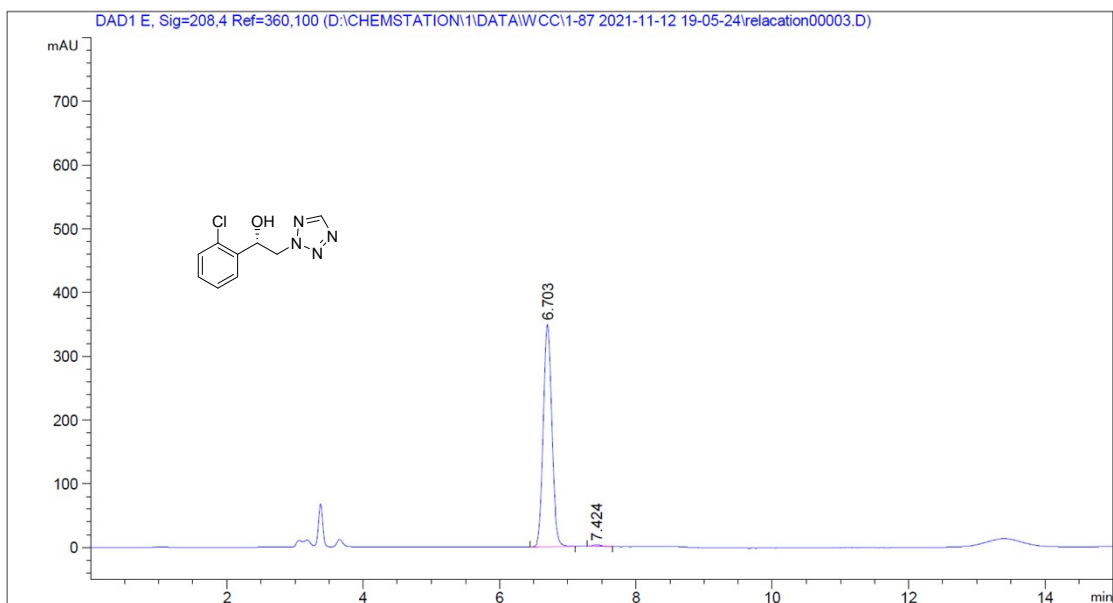
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 11.450 | MM | 0.3296 | 5.10667e4 | 2582.09473 | 99.2532 |
| 2 | 12.198 | MM | 0.1935 | 384.23291 | 33.09596 | 0.7468 |



Signal 1: DAD1 E, Sig=208,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 6.830 | BB | 0.1376 | 6897.81592 | 777.13690 | 49.9374 |
| 2 | 7.582 | BB | 0.1555 | 6915.10107 | 686.80951 | 50.0626 |

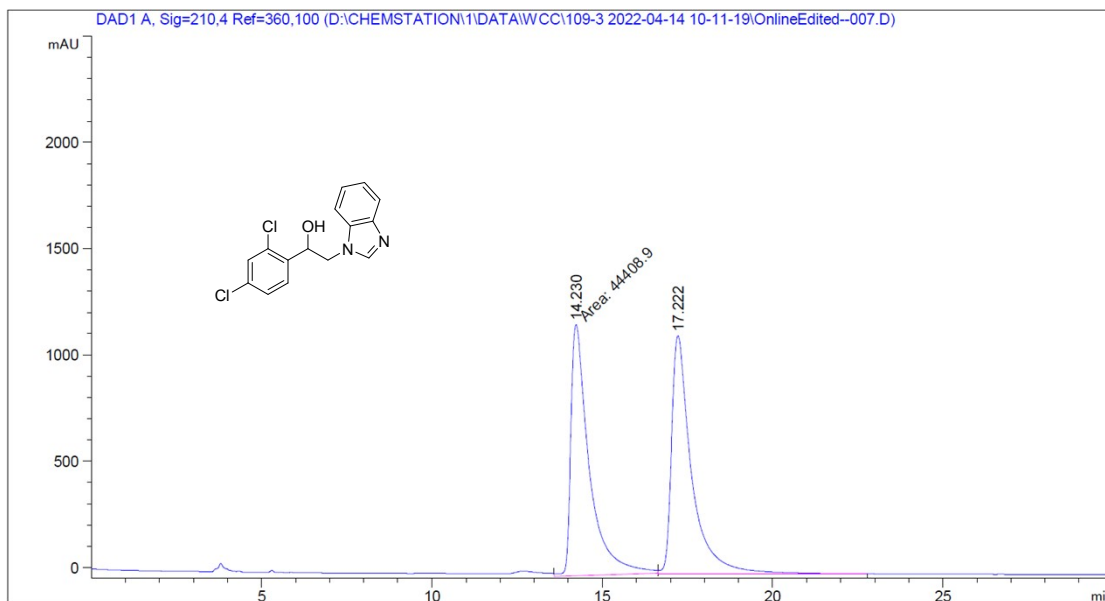
Totals : 1.38129e4 1463.94641



Signal 1: DAD1 E, Sig=208,4 Ref=360,100

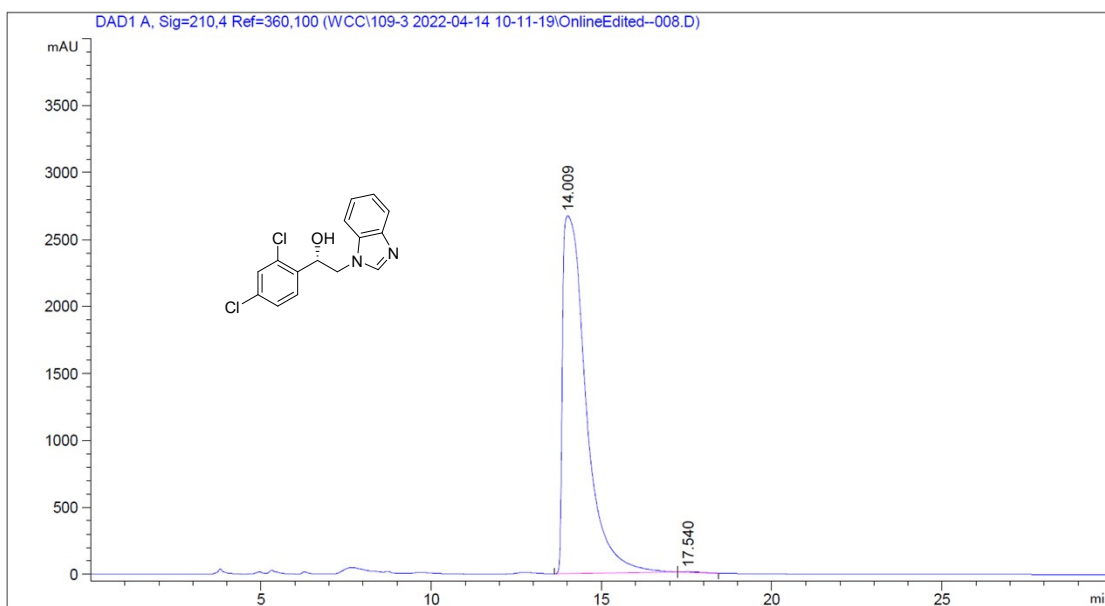
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 6.703 | BB | 0.1354 | 3028.35278 | 348.45911 | 99.3265 |
| 2 | 7.424 | BB | 0.1353 | 20.53299 | 2.31836 | 0.6735 |

Totals : 3048.88577 350.77747



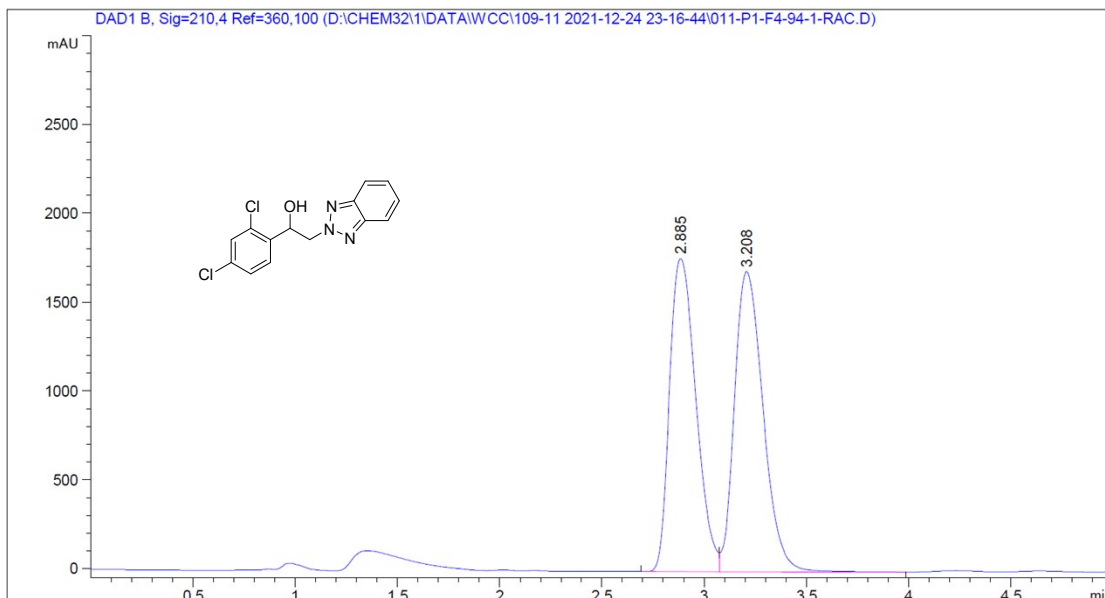
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 14.230 | MM | 0.6264 | 4.44089e4 | 1181.56445 | 49.1842 |
| 2 | 17.222 | VB | 0.5917 | 4.58820e4 | 1120.52917 | 50.8158 |



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

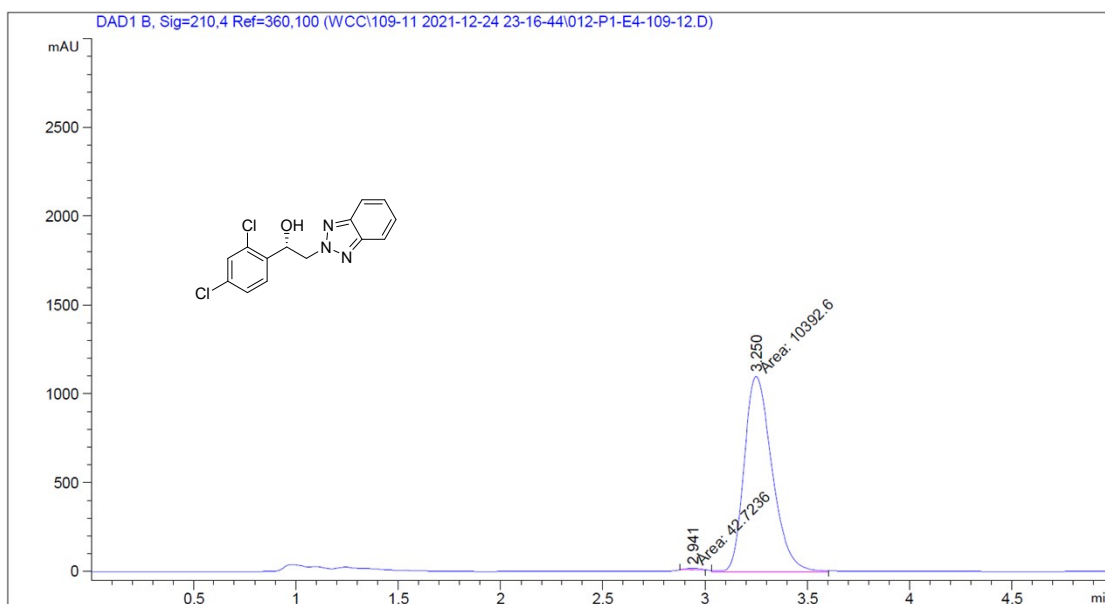
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 14.009 | BB | 0.6099 | 1.26449e5 | 2673.07446 | 99.8887 |
| 2 | 17.540 | BB | 0.5189 | 140.83405 | 3.69280 | 0.1113 |



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 2.885 | BV | 0.1421 | 1.57373e4 | 1763.17883 | 48.8532 |
| 2 | 3.208 | VB | 0.1537 | 1.64761e4 | 1690.78552 | 51.1468 |

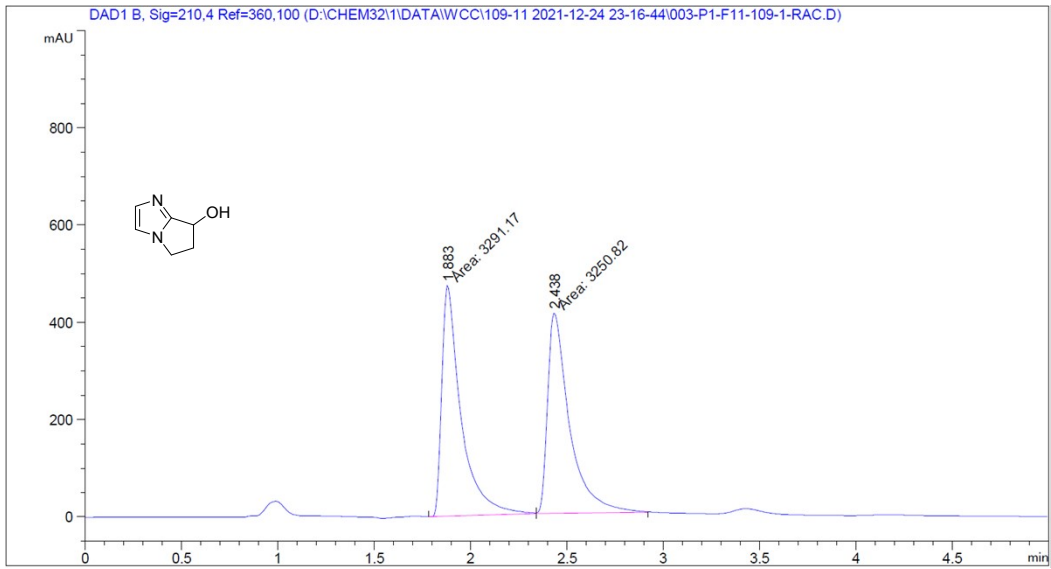
Totals : 3.22134e4 3453.96436



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 2.941 | MM | 0.0816 | 42.72357 | 8.72127 | 0.4094 |
| 2 | 3.250 | MM | 0.1576 | 1.03926e4 | 1099.19788 | 99.5906 |

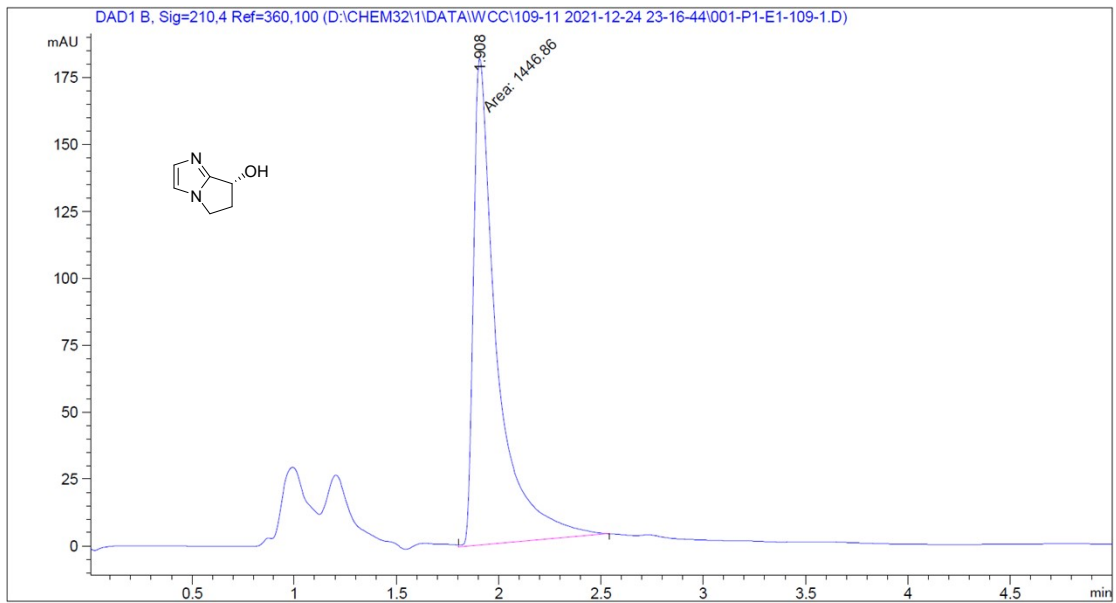
Totals : 1.04353e4 1107.91914



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 1.883 | MM | 0.1153 | 3291.16821 | 475.60983 | 50.3084 |
| 2 | 2.438 | MM | 0.1314 | 3250.82227 | 412.33521 | 49.6916 |

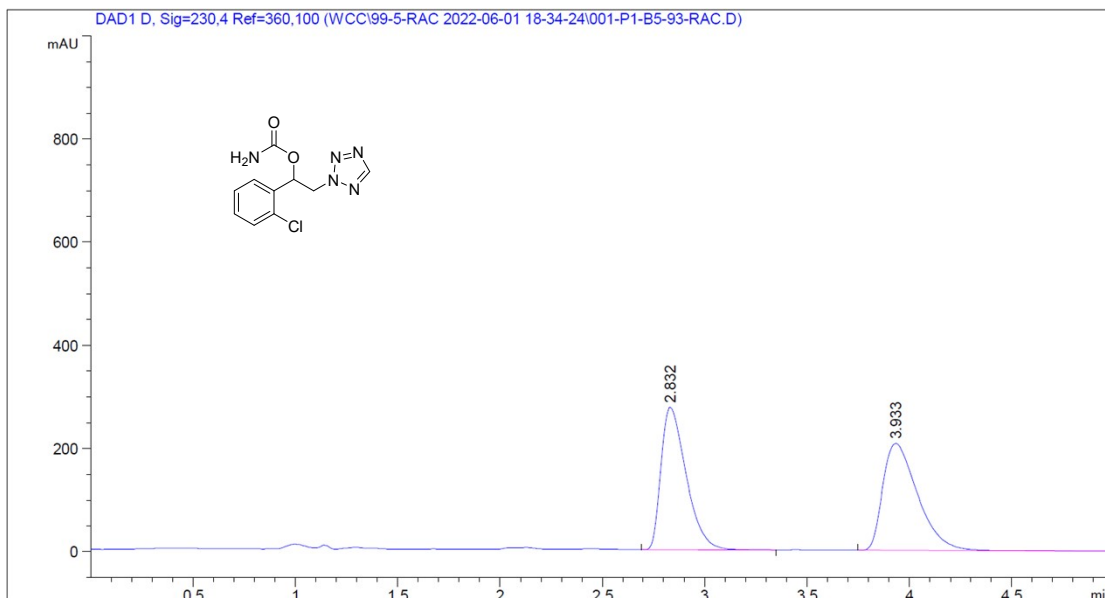
Totals : 6541.99048 887.94504



Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|----------|
| 1 | 1.908 | MM | 0.1322 | 1446.86353 | 182.44945 | 100.0000 |

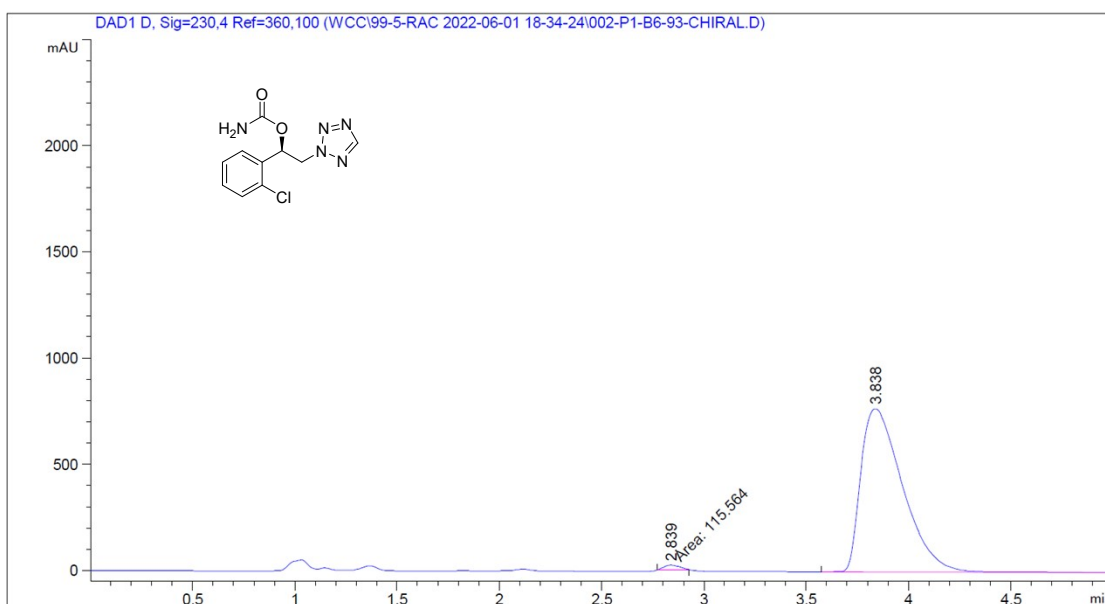
Totals : 1446.86353 182.44945



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 2.832 | BB | 0.1314 | 2351.97925 | 276.13885 | 48.9468 |
| 2 | 3.933 | BBA | 0.1819 | 2453.19067 | 207.51233 | 51.0532 |

Totals : 4805.16992 483.65118



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 2.839 | MM | 0.0885 | 115.56354 | 21.75784 | 1.0502 |
| 2 | 3.838 | BBA | 0.2212 | 1.08883e4 | 769.11243 | 98.9498 |

Totals : 1.10038e4 790.87026

7. References

1. I. C. Lennon and J. A. Ramsden, An Efficient Catalytic Asymmetric Route to 1-Aryl-2-imidazol-1-yl-ethanols, *Org. Process Res. Dev.*, 2005, **9**, 110-112.
2. L. Zhang, L. Fu, S. Zhang, J. Zhang, Y. Zhao, Y. Zheng, G. He, S. Yang, L. Ouyang and B. Liu, Discovery of a small molecule targeting ULK1-modulated cell death of triple negative breast cancer in vitro and in vivo, *Chemical Science*, 2017, **8**, 2687-2701.
3. S. Dhiman, K. Pericherla, N. K. Nandwana, D. Kumar and A. Kumar, Synthesis of Aza-Fused Isoquinolines through Domino Cross-Aldol Condensation and Palladium-Catalyzed Intramolecular Direct Arylation, *J. Org. Chem.*, 2014, **79**, 7399-7404.
4. A. S. Wagman, R. S. Boyce, S. P. Brown, E. Fang, D. Goff, J. M. Jansen, V. P. Le, B. H. Levine, S. C. Ng, Z.-J. Ni, J. M. Nuss, K. B. Pfister, S. Ramurthy, P. A. Renhowe, D. B. Ring, W. Shu, S. Subramanian, X. A. Zhou, C. M. Shafer, S. D. Harrison, K. W. Johnson and D. E. Bussiere, Synthesis, Binding Mode, and Antihyperglycemic Activity of Potent and Selective (5-Imidazol-2-yl-4-phenylpyrimidin-2-yl)[2-(2-pyridylamino)ethyl]amine Inhibitors of Glycogen Synthase Kinase 3, *J. Med. Chem.*, 2017, **60**, 8482-8514.
5. Y. Zhou, X. Lu, C. Du, Y. Liu, Y. Wang, K. H. Hong, Y. Chen and H. Sun, Novel BuChE-IDO1 inhibitors from sertaconazole: Virtual screening, chemical optimization and molecular modeling studies, *Bioorg. Med. Chem. Lett.*, 2021, **34**, 127756.
6. C. Liu, C. Shi, F. Mao, Y. Xu, J. Liu, B. Wei, J. Zhu, M. Xiang and J. Li, Discovery of New Imidazole Derivatives Containing the 2,4-Dienone Motif with Broad-Spectrum Antifungal and Antibacterial Activity, *Molecules*, 2014, **19**, 15653-15672.
7. G. Roman, J. Z. Vlahakis, D. Vukomanovic, K. Nakatsu and W. A. Szarek, Heme Oxygenase Inhibition by 1-Aryl-2-(1H-imidazol-1-yl/1H-1,2,4-triazol-1-yl)ethanones and Their Derivatives, *ChemMedChem*, 2010, **5**, 1541-1555.
8. V. K. Vyas and B. M. Bhanage, Catalytic asymmetric synthesis of β -triazolyl amino alcohols by asymmetric transfer hydrogenation of α -triazolyl amino alkanones, *Tetrahedron: Asymmetry*, 2017, **28**, 974-982.
9. Y. Li, K. K. Pasunooti, R.-J. Li, W. Liu, S. A. Head, W. Q. Shi and J. O. Liu,

- Novel Tetrazole-Containing Analogues of Itraconazole as Potent Antiangiogenic Agents with Reduced Cytochrome P450 3A4 Inhibition, *J. Med. Chem.*, 2018, **61**, 11158-11168.
10. L. Zhang, L. Fu, S. Zhang, J. Zhang, Y. Zhao, Y. Zheng, G. He, S. Yang, L. Ouyang and B. Liu, Discovery of a small molecule targeting ULK1-modulated cell death of triple negative breast cancer in vitro and in vivo, *Chem. Sci.*, 2017, **8**, 2687-2701.
 11. Z. Zhang, F. Xie, J. Jia and W. Zhang, Chiral Bicycle Imidazole Nucleophilic Catalysts: Rational Design, Facile Synthesis, and Successful Application in Asymmetric Steglich Rearrangement, *J. Am. Chem. Soc.*, 2010, **132**, 15939-15941.
 12. R. D. Grigg, J. W. Rigoli, S. D. Pearce and J. M. Schomaker, Synthesis of Propargylic and Allenic Carbamates via the C–H Amination of Alkynes, *Org. Lett.*, 2012, **14**, 280-283.
 13. J.-x. Huang, W. Hong-yi, W. Ze-nong, S. Xun and Z. Fu-li, Improved synthesis of cenobamate, *Chin. J. Med. Chem.*, 2021, **31**, 419-421.