Supporting Information

Copper(I)-Catalyzed Oxyamination of β,γ-Unsaturated Hydrazones : Synthesis of Dihydropyrazoles

Shanshan Chen,[†] Wenming Chen,[‡] Xu Chen,[†] Guifang Chen,[†] Lutz Ackermann,[§] and Xu Tian*[†]

[†]Key Laboratory of Molecular Target & Clinical Pharmacology and the State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong 511436, China.

Email: xtian@gzhmu.edu.cn

[‡] Department of Pharmaceutical Production Center, The First Affiliated Hospital of Hunan University of Chinese Medicine, Changsha, Hunan 410007, China

[§]Institut für Organische und Biomolekulare Chemie, Georg-August-Universität, Tammannstraße 2, 37077 Göttingen, Germany.

Table of Contents

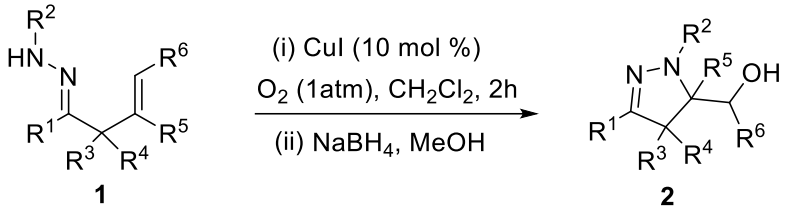
1. General Information

Catalytic reactions were carried out in Schlenk tubes under an oxygen atmosphere using pre-dried glassware. Toluene was dried and distilled over CaH_2 under nitrogen. All the imine **1** have been synthesized following procedures reported in the literature[1]. Other chemicals were obtained from commercial sources and were used without further purification. The ^1H and ^{13}C NMR spectra were recorded on JEOL at 400 MHz for ^1H or at 100 MHz for ^{13}C, respectively. The chemical shifts (δ) for ^1H and ^{13}C are given in ppm relative to residual signals of the solvents ($CHCl_3$ 7.26 ppm ^1H NMR, 77.16 ppm ^{13}C NMR). Mass spectra and high-resolution mass spectra were measured on a Thermo-DFS mass spectrometer. Analysis of crude reaction mixture was done on an Agilent 7890 GC System with an Agilent 5975 Mass Selective Detector. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used, Silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) were used for general chromatography, using UV light as the visualizing agent and an acidic mixture of ceric ammonium molybdate or basic aqueous potassium permangante ($KMnO_4$), and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

2. Materials.

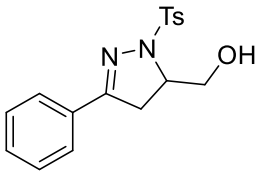
Commercial grade reagents and solvents were purchased from Sigma Aldrich, Fluka, and Alfa Aesar and used as received without further purification, β,γ-unsaturated hydrazones were prepared following the literature procedure.[1]

3. General procedure for the Copper-Catalyzed One-Pot Oxyamination of β, γ-unsaturated Hydrazones



1 2

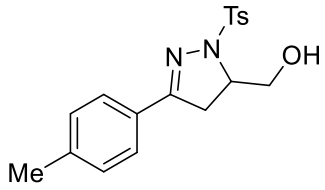
A solution of **1** (0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %) in dry DCM (1.0 mL) was stirred under O_2 for 2 h at 25 °C. Then the $NaBH_4$ (1.5 eq) and MeOH (1.0 mL) was added to the mixture and the mixture was stirred at room temperature for another 30 min. After quenched with saturated NH_4Cl solution and washed by saturated NaCl, then extracted with DCM three times. The combined organic layers were dried over anhydrous Na_2SO_4 and then evaporated. The crude product was purified by column chromatography (Petroleum Ether /EtOAc 4/1-3/1) to afford the desired product **2**.



(3-phenyl-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2a)

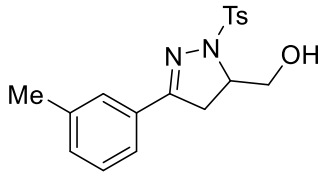
The reaction was carried out following the general procedure using substrate **1a** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2a** (50 mg, 76%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.69-7.62 (m, 2H), 7.43-7.34 (m, 3H), 7.28 (d, *J* = 8.08 Hz, 2H), 4.11-4.05 (m, 1H), 3.99-3.94 (m, 1H), 3.93-3.83 (m, 1H), 3.20-3.08 (m, 2H), 2.76 (bs, 1H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 144.7, 131.6, 130.8, 130.6, 129.8, 128.8, 128.7, 127.1, 64.4, 63.7, 36.6, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{18}N_2O_3S$ $[M+H]^+$ 331.11164, found: 331.11152. The analytical data are in accordance with these reported in the literature[1].

***1 mmol scale reaction**:* A solution of **1a** (314 mg, 1 mmol), CuI (19 mg, 0.1 mmol, 10.0 mol %) in dry DCM (5.0 mL) was stirred under O_2 for 2 h at 25 °C. Then the $NaBH_4$ (57mg, 1.5 eq) and MeOH (5.0 mL) was added to the mixture and the mixture was stirred at room temperature for another 30 min. After quenched with saturated NH_4Cl solution and washed by saturated NaCl, then extracted with DCM three times. The combined organic layers were dried over anhydrous Na_2SO_4 and then evaporated. The title product was isolated by column chromatography (petroleum ether /ethyl acetate 4/1) yielded **2a** (220 mg, 67%) as a white solid.



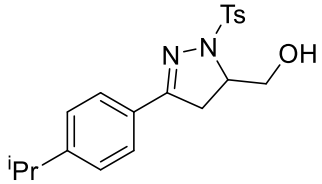
(3-(*p*-tolyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2b)

The reaction was carried out following the general procedure using substrate **1b** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2b** (49 mg, 71%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.18-7.16 (m, 2H), 4.06 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.98-3.90 (m, 1H), 3.86 (dd, *J* = 11.7, 4.0 Hz, 1H), 3.15-3.0 (m, 1H), 2.67 (bs, 1H), 2.36 (s, 2H), 2.35 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 144.6, 141.3, 131.6, 129.7, 129.4, 128.7, 127.9, 127.1, 64.4, 63.6, 36.7, 21.7, 21.6 ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{20}N_2O_3S$ $[M+H]^+$ 345.12729, found: 345.12599. The analytical data are in accordance with these reported in the literature[1].



(3-(*m*-tolyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2c)

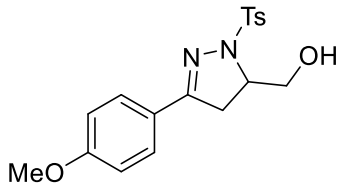
The reaction was carried out following the general procedure using substrate **1c** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2c** (42 mg, 61%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.52 (s, 1H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.29-7.21 (m, 4H), 4.08 (dd, *J* = 11.8, 4.1 Hz, 1H), 4.00 -3.91 (m, 1H), 3.87 (dd, *J* = 11.8, 4.2 Hz, 1H), 3.17-3.03 (m, 2H), 2.39 (s, 3H), 2.36 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 144.7, 138.5, 131.7, 131.6, 130.6, 129.8, 128.8, 128.6, 127.6, 124.3, 64.5, 63.6, 36.7, 21.7, 21.4 ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{20}N_2O_3S$ $[M+H]^+$ 345.12729, found: 345.12644.



(3-(4-isopropylphenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2d)

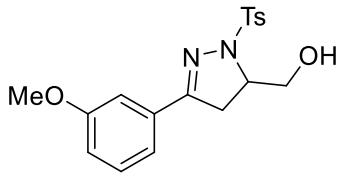
The reaction was carried out following the general procedure using substrate **1d** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2d** (54 mg, 73%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.08 (dd, *J* = 11.8, 4.1 Hz, 1H), 3.99-3.90 (m, 1H), 3.87 (dd, *J* = 11.8, 4.2 Hz, 1H), 3.17-3.01 (m, 2H), 2.93-2.90 (m, 1H), 2.38 (s, 3H), 1.24 (d, *J* = 6.91 Hz, 6H) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$): δ 158.6, 152.2, 144.6, 131.5, 129.7, 128.8, 128.2, 127.2, 126.8, 64.4, 63.7, 36.8, 34.2, 23.9, 23.8, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{20}H_{24}N_2O_3S$ $[M+H]^+$ 373.15859, found: 373.15693.



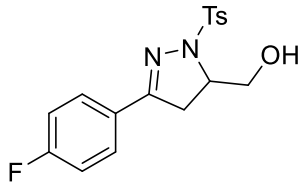
(3-(4-methoxyphenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2e)

The reaction was carried out following the general procedure using substrate **1e** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2e** (53 mg, 74%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.9 Hz, 2H), 7.27 (d, *J* = 9.0 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 4.06 (dd, *J* = 11.7, 3.2 Hz, 1H), 4.00-3.90 (m, 1H), 3.86 (dd, *J* = 11.7, 4.2 Hz, 1H), 3.82 (s, 3H), 3.14-3.0 (m, 2H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 158.4, 158.4, 144.6, 131.9, 129.7, 128.82, 128.80, 123.3, 114.2, 64.5, 63.5, 55.5, 36.7, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{20}N_2O_4S$ $[M+H]^+$ 361.12220, found: 361.12118.



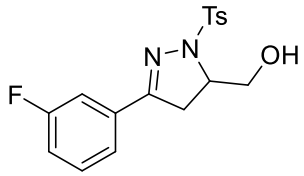
(3-(3-methoxyphenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2f)

The reaction was carried out following the general procedure using substrate **1f** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2f** (46 mg, 64%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.30-7.24 (m, 3H), 7.24-7.23 (m, 1H), 7.18-7.16 (m, 1H), 6.95 (ddd, *J* = 8.26, 2.64, 0.96 Hz, 1H), 4.08 (dd, *J* = 11.8, 4.3 Hz, 1H), 4.02-3.92 (m, 1H), 3.87 (dd, *J* = 11.8, 4.1 Hz, 1H), 3.83 (s, 3H), 3.24 -2.92 (m, 2H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 158.6, 144.7, 131.9, 131.6, 129.8, 129.7, 128.7, 119.7, 116.9, 111.8, 64.4, 63.7, 55.5, 36.7, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{20}N_2O_4S$ $[M+H]^+$ 361.12220, found: 361.12116. The analytical data are in accordance with these reported in the literature[1].



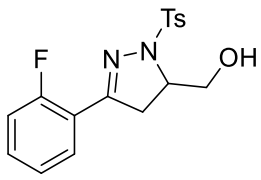
(3-(4-fluorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2g)

The reaction was carried out following the general procedure using substrate **1g** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2g** (51 mg, 73%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.68-7.60 (m, 2H), 7.34 (d, *J* = 8.08 Hz, 2H), 7.05 (t, *J* = 8.36 Hz, 2H), (m, 2H), 4.09 (dd, *J* = 11.8, 3.4 Hz, 1H), 4.01-3.94 (m, 1H), 3.87 (dd, *J* = 11.9, 4.0 Hz, 1H), 3.18-3.05 (m, 2H), 2.76 (bs, 1H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 163.0, 157.6, 144.8, 131.6, 129.8, 129.2, 129.1, 128.8, 127.0, 126.9, 116.1, 115.8, 64.3, 63.7, 36.6, 21.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) *δ* -108.54 - -108.60 (m) ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}FN_2O_3S$ $[M+H]^+$ 349.10222, found: 349.10059.



(3-(3-fluorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2h)

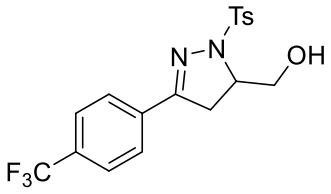
The reaction was carried out following the general procedure using substrate **1h** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2h** (41 mg, 59%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.42-7.28 (m, 5H), 7.10 (t, *J* = 8.0 Hz, 1H), 4.10 (dd, *J* = 12.0, 3.3 Hz, 1H), 4.05-3.96 (m, 1H), 3.87 (dd, *J* = 11.9, 3.9 Hz, 1H), 3.19-3.03 (m, 2H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 161.6, 157.4, 144.9, 132.8, 131.7, 130.4, 129.9, 128.8, 122.9, 117.9, 113.9, 113.7, 64.3, 63.9, 36.5, 21.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.93 - -111.99 (m) ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}FN_2O_3S$ $[M+H]^+$ 349.10222, found: 349.10126.



(3-(2-fluorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2i)

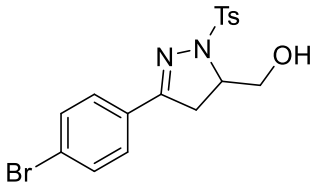
The reaction was carried out following the general procedure using substrate **1i** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2i** (33 mg, 47%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.87 (m, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.41-7.34 (m,

1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.18-7.14 (m, 1H), 7.07-7.02 (m, 1H), 4.08 (dd, *J* = 11.9, 4.1 Hz, 1H), 4.01-3.92 (m, 1H), 3.88 (dd, *J* = 11.8, 4.2 Hz, 1H), 3.29-3.12 (m, 2H), 2.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 159.9, 155.5, 144.8, 132.6, 132.5, 131.6, 129.8, 129.3, 128.8, 124.6, 118.7, 116.4, 64.4, 63.9, 39.0, 21.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.75 (s) ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}FN_2O_3S$ $[M+H]^+$ 349.10222, found: 349.10149.



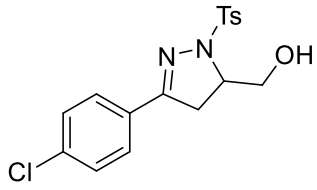
(1-tosyl-3-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-pyrazol-5-yl)methanol (2j)

The reaction was carried out following the general procedure using substrate **1j** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2j** (45 mg, 57%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (t, *J* = 8.32 Hz, 4H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.15-4.10 (m, 1H), 4.07-3.97 (m, 1H), 3.93-3.82 (m, 1H), 3.24-3.08 (m, 2H), 2.57 (s, 1H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 145.0, 134.0, 132.5, 132.2, 131.6, 129.9, 128.7, 127.3, 125.8, 125.7, 125.7, 125.2, 122.5, 64.2, 64.0, 36.4, 21.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.85 (s) ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{17}F_3N_2O_3S$ $[M+H]^+$ 399.09902, found: 399.09747. The analytical data are in accordance with these reported in the literature[1].



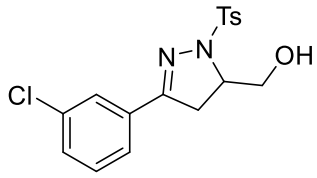
(3-(4-bromophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2k)

The reaction was carried out following the general procedure using substrate **1k** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2k** (58 mg, 71%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.53-7.47 (m, 4H), 7.28 (d, *J* = 8.24 Hz, 2H), 4.10 (dd, *J* = 11.9, 3.3 Hz, 1H), 4.04-3.92 (m, 1H), 3.87 (dd, *J* = 11.9, 3.9 Hz, 1H), 3.18-3.02 (m, 2H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 144.8, 132.0, 131.6, 129.8, 129.6, 128.7, 128.5, 125.3, 64.2, 63.8, 36.4, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}BrN_2O_3S$ $[M+H]^+$ 409.02215, found: 409.02119. The analytical data are in accordance with these reported in the literature[1].



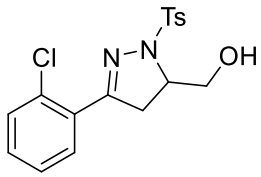
(3-(4-chlorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2l)

The reaction was carried out following the general procedure using substrate **1l** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2l** (52 mg, 72%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79-7.75 (m, 2H), 7.60-7.56 (m, 2H), 7.35-7.32 (m, 2H), 7.29 (d, *J* = 7.95 Hz, 2H), 4.10 (dd, *J* = 11.9, 3.2 Hz, 1H), 4.04-3.94 (m, 1H), 3.87 (dd, *J* = 11.9, 3.9 Hz, 1H), 3.18-3.05 (m, 2H), 2.67 (bs, 1H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 144.8, 136.9, 131.6, 129.8, 129.2, 129.1, 128.7, 128.3, 64.3, 63.8, 36.5, 21.8 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}ClN_2O_3S$ $[M+H]^+$ 365.07267, found: 365.07225. The analytical data are in accordance with these reported in the literature[1].



(3-(3-chlorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2m)

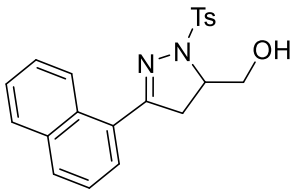
The reaction was carried out following the general procedure using substrate **1m** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2m** (47 mg, 65%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.65 (t, *J* = 1.8 Hz, 1H), 7.60 (dt, *J* = 7.8, 1.32 Hz, 1H), 7.39-7.36 (m, 1H), 7.32-7.28 (m, 3H), 4.12-4.06 (m, 1H), 4.04-3.94 (m, 1H), 3.92-3.82 (m, 1H), 3.18-3.03 (m, 2H), 2.62 (bs, 1H), 2.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.3, 144.9, 134.9, 132.4, 131.6, 130.8, 130.1, 129.9, 128.7, 127.0, 125.2, 64.3, 63.8, 36.5, 21.8 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}ClN_2O_3S$ $[M+H]^+$ 365.07267, found: 365.07124.



(3-(2-chlorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2n)

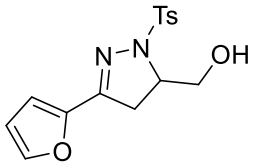
The reaction was carried out following the general procedure using substrate **1n** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2n** (23 mg, 32%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.58 (dd, *J* = 7.62, 1.9 Hz, 1H), 7.37-7.29 (m, 4H), 7.29-7.24 (m, 1H), 4.09 (dd, *J* = 11.9, 4.1 Hz, 1H), 4.03-3.93 (m, 1H), 3.89 (dd, *J* = 11.9, 4.2

Hz, 1H), 3.26-3.19 (m, 2H), 2.43 (s, 3H), 2.21 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 144.9, 132.9, 131.6, 131.3, 130.7, 130.7, 130.2, 129.8, 128.9, 127.1, 64.4, 64.3, 39.7, 21.8 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{17}ClN_2O_3S$ $[M+H]^+$ 365.07267, found: 365.07184. The analytical data are in accordance with these reported in the literature[1].



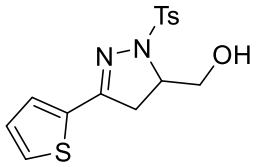
(3-(naphthalen-1-yl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2o)

The reaction was carried out following the general procedure using substrate **1o** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2o** (35 mg, 46%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.99 (d, *J* = 8.6 Hz, 1H), 7.90-7.85 (m, 4H), 7.61 (t, *J* = 7.1 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.47-7.38 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.17 (dd, *J* = 11.8, 3.9 Hz, 1H), 4.10-4.01 (m, 1H), 3.95 (dd, *J* = 11.8, 4.0 Hz, 1H), 3.43-3.24 (m, 2H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 144.9, 134.0, 132.0, 131.6, 130.6, 129.9, 128.9, 128.8, 128.6, 127.8, 127.4, 126.9, 126.5, 124.7, 64.4, 62.8, 39.6, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{21}H_{20}N_2O_3S$ $[M+H]^+$ 381.12729, found: 381.12622.



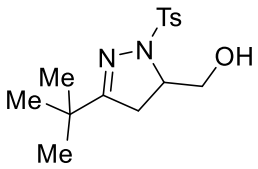
(3-(furan-2-yl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2p)

The reaction was carried out following the general procedure using substrate **1p** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2p** (26 mg, 41%) as a pale brown solid,. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 1.5 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.78 (d, *J* = 3.4 Hz, 1H), 6.45 (dd, *J* = 3.5, 1.8 Hz, 1H), 4.05 (dd, *J* = 11.8, 4.3 Hz, 1H), 3.99-3.89 (m, 1H), 3.84 (dd, *J* = 11.8, 4.1 Hz, 1H), 3.15-3.0 (m, 2H), 2.49 (bs, 1H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3, 146.3, 145.0, 144.7, 131.6, 129.8, 128.8, 113.1, 112.1, 64.3, 63.1, 36.5, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{15}H_{16}N_2O_4S$ $[M+H]^+$ 321.09090, found: 321.09018.



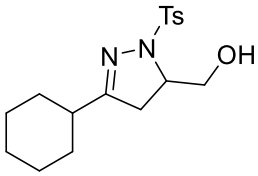
(3-(thiophen-2-yl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2q)

The reaction was carried out following the general procedure using substrate **1q** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2q** (50 mg, 75%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.42-7.41 (m, 1H), 7.30-7.28 (m, 2H), 7.17-7.16 (m, 1H), 7.03-7.00 (m, 1H), 4.07 (d, *J* = 12.0 Hz, 1H), 4.00-3.93 (m, 1H), 3.86 (d, *J* = 11.6 Hz, 1H), 3.20-3.03 (m, 2H), 2.61 (bs, 1H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 144.8, 144.7, 134.2, 131.5, 129.8, 129.7, 129.5, 128.9, 127.6, 64.3, 63.8, 37.3, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{15}H_{16}N_2O_3S_2$ $[M+H]^+$ 337.06806, found: 337.06679.



(3-(tert-butyl)-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2r)

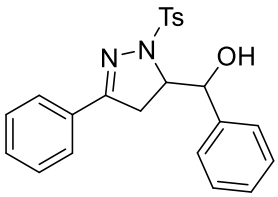
The reaction was carried out following the general procedure using substrate **1r** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2r** (35 mg, 57%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.32-7.28 (m, 2H), 3.97-3.90 (m, 1H), 3.81-3.69 (m, 2H), 2.73-2.56 (m, 2H), 2.41 (s, 3H), 2.25 (bs, 1H), 1.07-1.03 (m, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 144.5, 131.3, 129.4, 128.9, 64.5, 63.3, 35.7, 34.4, 28.0, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{15}H_{22}N_2O_3S$ $[M+H]^+$ 311.14294, found: 311.14163. The analytical data are in accordance with these reported in the literature[1].



(3-cyclohexyl-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2s)

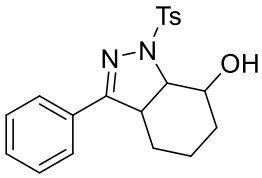
The reaction was carried out following the general procedure using substrate **1s** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2s** (17 mg, 26%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.95 (d, *J* = 9.1 Hz, 1H), 3.78-3.70 (m, 2H), 2.71-2.53 (m, 2H), 2.43 (s, 3H), 2.29-2.25 (m, 1H), 1.72-1.65 (m, 4H), 1.25-1.18 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 131.4, 129.8, 129.5, 128.9, 126.6, 64.5, 62.6, 39.3, 37.0, 30.4,

30.1, 25.8, 25.7, 25.6, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{24}N_2O_3S$ $[M+H]^+$ 337.15859, found: 337.15751. The analytical data are in accordance with these reported in the literature[1].



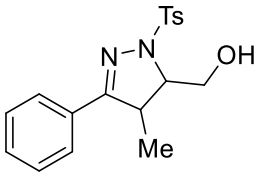
phenyl(3-phenyl-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2t)

The reaction was carried out following the general procedure using substrate **1t** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 3/1) yielded **2t** (16 mg, 20%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.08 Hz, 2H), 7.71-7.69 (m, 2H), 7.38-7.35 (m, 3H), 7.23-7.17 (m, 5H), 7.01 (d, *J* = 7.48 Hz, 2H), 5.53 (s, 1H), 4.36 (s, 1H), 2.66 (d, *J* = 18.1 Hz, 1H), 2.38 (s, 3H), 2.31 (dd, *J* = 18.4, 3.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 144.0, 138.0, 136.9, 135.8, 129.6, 129.4, 129.0, 128.6, 128.41, 128.0, 126.1, 125.5, 65.1, 62.2, 26.3, 21.7 ppm. HR-MS (ESI) m/z calcd for $C_{23}H_{22}N_2O_3S$ $[M+H]^+$407.14294, found: 407.14167. The analytical data are in accordance with these reported in the literature[1].



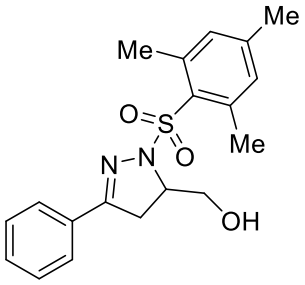
3-phenyl-1-tosyl-3a,4,5,6,7,7a-hexahydro-1H-indazol-7-ol (2u)

The reaction was carried out following the general procedure using substrate **1u** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 3/1) yielded **2u** (22_{major}+11_{minor} = 33 mg, 45%, dr = 2/1) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, major): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.69-7.65 (m, 2H), 7.41-7.35 (m, 3H), 7.28 (d, *J* = 8.03 Hz, 2H), 4.58-4.55 (m, 1H), 3.40-3.37 (m, 2H), 2.38 (s, 3H), 1.99-1.94 (m, 1H), 1.86-1.82 (m, 1H), 1.73-1.61 (m, 3H), 1.42-1.32 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 144.7, 130.8, 130.7, 130.1, 129.7, 129.2, 128.9, 127.3, 69.3, 67.5, 44.4, 27.3, 23.6, 21.7, 17.2 ppm. HR-MS (ESI) m/z calcd for $C_{20}H_{22}N_2O_3S$ $[M+H]^+$ 371.14294, found: 371.14213. ^{1}H NMR (400 MHz, $CDCl_3$, minor): δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.71-7.62 (m, 2H), 7.42-7.34 (m, 3H), 7.28 (d, *J* = 8.2 Hz, 2H), 4.07-4.03 (m, 1H), 3.64 (dd, *J* = 8.62, 3.04 Hz, 1H), 3.38-3.32 (m,1H), 2.38 (s, 3H), 1.99-1.82 (m, 2H), 1.81-1.75 (m, 2H), 1.53-1.46 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 144.9, 130.8, 129.9, 129.8, 129.2, 128.9, 127.3, 68.2, 68.2, 47.1, 27.7, 23.5, 21.8, 20.3 ppm. HR-MS (ESI) m/z calcd for $C_{20}H_{22}N_2O_3S$ $[M+H]^+$ 371.14294, found: 371.14205.



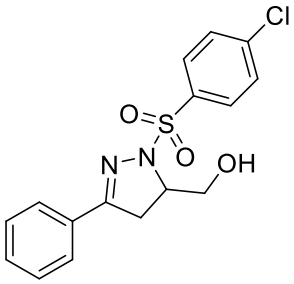
(4-methyl-3-phenyl-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2w)

The reaction was carried out following the general procedure using substrate **1w** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2w** (22_{major}+18_{minor}= 40 mg, 58%, dr = 1.2/1) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, major): δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.65-7.62 (m, 2H), 7.42-7.35 (m, 3H), 7.32 (d, *J* = 8.2 Hz, 2H), 3.96 (dd, *J* = 11.8, 3.7 Hz, 1H), 3.83 (dd, *J* = 11.8, 4.6 Hz, 1H), 3.61-3.57 (m, 1H), 3.52-3.45 (m, 1H), 2.40 (s, 3H), 0.76 (d, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 144.7, 132.0, 130.7, 130.0, 129.7, 128.8, 128.6, 127.6, 70.7, 64.6, 44.0, 21.7, 19.0 ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{20}N_2O_3S$ $[M+H]^+$ 345.12729, found: 345.12608. ^{1}H NMR (400 MHz, $CDCl_3$, minor): δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.73-7.63 (m, 2H), 7.43-7.34 (m, 3H), 7.28 (d, *J* = 7.9 Hz, 2H), 4.26 (dd, *J* = 12.4, 6.0 Hz, 1H), 4.06 (dd, *J* = 12.5, 3.4 Hz, 1H), 3.61-3.56 (m, 1H), 3.53-3.37 (m, 1H), 2.39 (s, 3H), 1.20 (d, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 144.8, 130.7, 129.8, 129.7, 129.2, 128.9, 127.3, 68.5, 61.1, 43.4, 21.7, 11.7 ppm. HR-MS (ESI) m/z calcd for $C_{18}H_{20}N_2O_3S$ $[M+H]^+$ 345.12729, found: 345.12598.



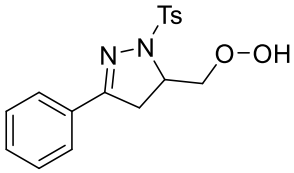
(1-(mesitylsulfonyl)-3-phenyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2y)

The reaction was carried out following the general procedure using substrate **1y** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2y** (39 mg, 55%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.57 (m, 2H), 7.40-7.33 (m, 3H), 7.01 (s, 2H), 4.65-4.55 (m, 1H), 4.10 (dd, *J* = 11.8, 3.8 Hz, 1H), 3.91 (dd, *J* = 11.8, 4.6 Hz, 1H), 3.41 (dd, *J* = 17.0, 11.2 Hz, 1H), 3.17 (dd, *J* = 17.1, 8.8 Hz, 1H), 2.74 (s, 6H), 2.32 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 143.7, 141.5, 132.2, 131.0, 130.9, 130.7, 128.7, 127.0, 64.7, 61.7, 36.9, 23.5, 21.2 ppm. HR-MS (ESI) m/z calcd for $C_{19}H_{22}N_2O_3S$ $[M+H]^+$ 359.14294, found: 359.14233.



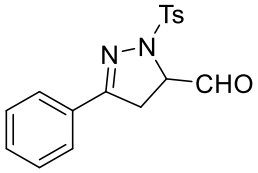
(1-((4-chlorophenyl)sulfonyl)-3-phenyl-4,5-dihydro-1H-pyrazol-5-yl)methanol (2z)

The reaction was carried out following the general procedure using substrate **1z** to furnish the crude product. The title compound was isolated by column chromatography (petroleum ether/ethyl acetate: 4/1) yielded **2z** (47 mg, 67%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.84 (m, 2H), 7.68-7.64 (m, 2H), 7.49-7.46 (m, 2H), 7.44-7.35 (m, 3H), 4.10 (dd, *J* = 11.9, 4.3 Hz, 1H), 4.02-3.89 (m, 1H), 3.88 (dd, *J* = 11.9, 4.0 Hz, 1H), 3.24-3.10 (m, 2H), 2.10 (bs, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 140.5, 133.3, 131.1, 130.5, 130.2, 129.5, 128.9, 127.1, 64.3, 63.8, 36.7 ppm. HR-MS (ESI) m/z calcd for $C_{16}H_{15}ClN_2O_3S$ $[M+H]^+$ 351.05702, found: 351.05649.



5-(hydroperoxymethyl)-3-phenyl-1-tosyl-4,5-dihydro-1H-pyrazole (4)

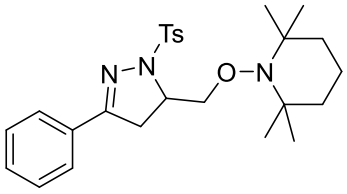
The reaction was carried out following the first step of general procedure using substrate **1a** to furnish the crude product. The title compound was isolated by preparative TLC (petroleum ether/ethyl acetate: 2/1) yielded **4** (28 mg, 40%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.68-7.64 (m, 2H), 7.43-7.35 (m, 3H), 7.28 (d, *J* = 8.3 Hz, 2H), 4.54-4.41 (m, 1H), 4.30 (dd, *J* = 12.7, 6.6 Hz, 1H), 4.17 (dd, *J* = 12.7, 5.9 Hz, 1H), 3.18 (dd, *J* = 17.6, 11.2 Hz, 1H), 2.97 (dd, *J* = 17.6, 7.4 Hz, 1H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 144.7, 132.5, 131.0, 130.6, 129.8, 128.8, 128.7, 127.2, 78.5, 58.5, 37.4, 21.8 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{18}N_2O_4S$ $[M+H]^+$ 347.10655, found: 347.10563. The analytical data are in accordance with these reported in the literature[1].



5-(hydroperoxymethyl)-3-phenyl-1-tosyl-4,5-dihydro-1H-pyrazole (5)

The reaction was carried out following the first step of general procedure using substrate **1a** to furnish the crude product. The title compound was isolated by preparative TLC (petroleum ether/ethyl acetate: 2/1) yielded **5** (13 mg,

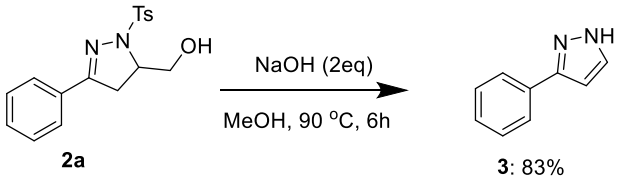
20%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.45-7.35 (m, 3H), 7.32 (d, *J* = 7.5 Hz, 2H), 4.29 (t, *J* = 11.0 Hz, 1H), 3.36 (dd, *J* = 17.12, 10.42 Hz, 1H), 3.16 (dd, *J* = 17.12, 12.0 Hz, 1H), 2.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.8, 157.9, 145.2, 131.5, 131.3, 130.1, 130.0, 128.9, 128.9, 127.2, 67.9, 34.7, 21.8 ppm. HR-MS (ESI) m/z calcd for $C_{17}H_{16}N_2O_3S$ $[M+H]^+$ 329.09599, found: 329.09540.



2,2,6,6-tetramethyl-1-((3-phenyl-1-tosyl-4,5-dihydro-1H-pyrazol-5-yl)methoxy)piperidine (2aa)

A solution of **1a** (62.8mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %), TEMPO (46.8mg, 1.5 eq) in dry DCM (1.0 mL) was stirred under O_2 for 2 h at 25 °C then monitored by TLC. The title compound was isolated by preparative TLC (petroleum ether/ethyl acetate: 5/1) yielded **2aa** (9 mg, 10%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.70 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.42-7.36 (m, 3H), 7.28-7.26 (m, 2H), 4.30 (dd, *J* = 9.2, 3.8 Hz, 1H), 4.14-4.09 (m, 1H), 4.00-3.92 (m, 1H), 3.21 -3.06 (m, 2H), 2.38 (s, 3H), 1.51-1.45 (m, 5H), 1.26-1.23 (m, 7H), 1.08-1.06 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 144.3, 132.4, 131.1, 130.6, 129.6, 128.8, 128.7, 127.1, 78.2, 60.1, 39.8, 37.6, 33.4, 21.7, 20.3, 17.2 ppm. HR-MS (ESI) m/z calcd for $C_{26}H_{35}N_3O_3S$ [M+H]+ 470.2477, found: 470.2484. The analytical data are in accordance with these reported in the literature[1].

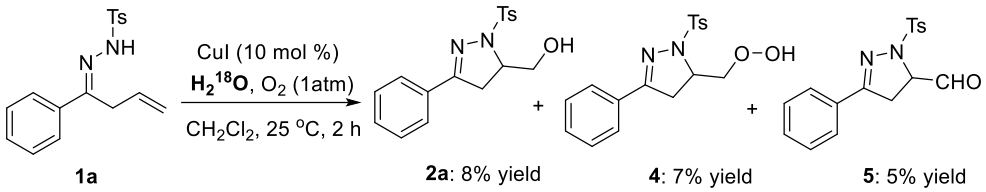
4. Transformation of Product 2a



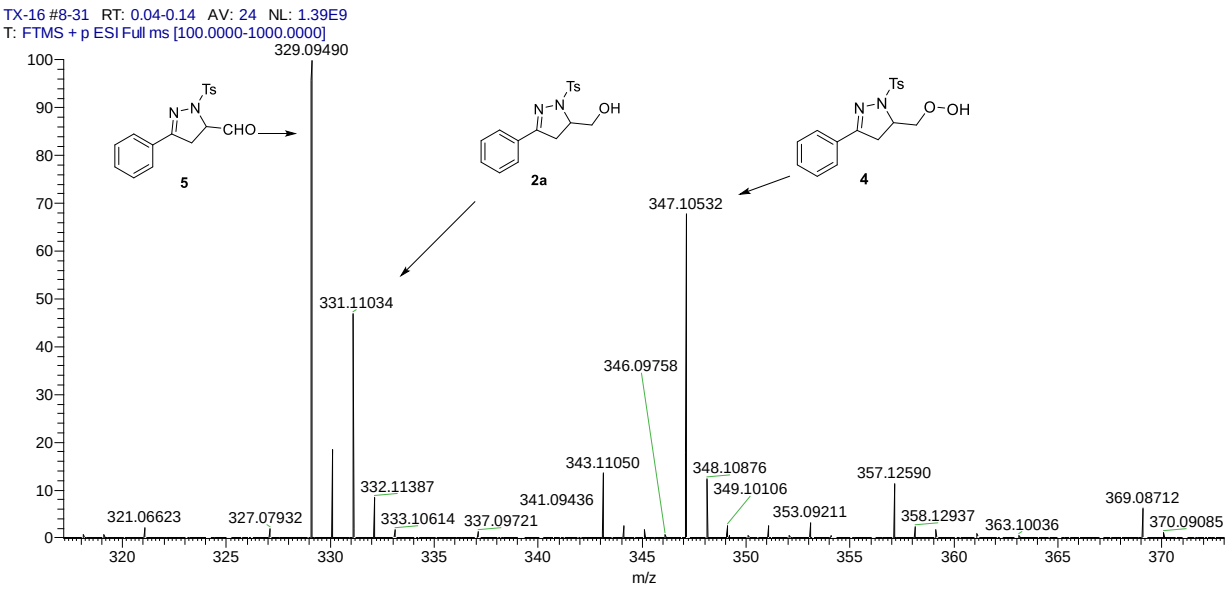
2a (0.3 mmol, 99 mg) were dissolved in MeOH (2.0 mL). Then, NaOH (2.0 equiv) was addded to the mixture then at 90°C for 6 h until the reaction was completed as monitored by TLC. The crude product was purified by column chromatography (petroleum ether/ethyl acetate: 5/1) yielded **3** (36 mg, 83%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.88 (bs, 1H), 7.77 (d, *J* = 7.2 Hz, 2H), 7.61 (s, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 6.62 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 133.4, 132.2, 128.9, 128.2, 126.0, 102.8 ppm. HR-MS (ESI) m/z calcd for $C_9H_8N_2$ $[M+H]^+$ 145.07657, found: 145.07594. The analytical data are in accordance with these reported in the literature[2].

5. Mechanistic Studies

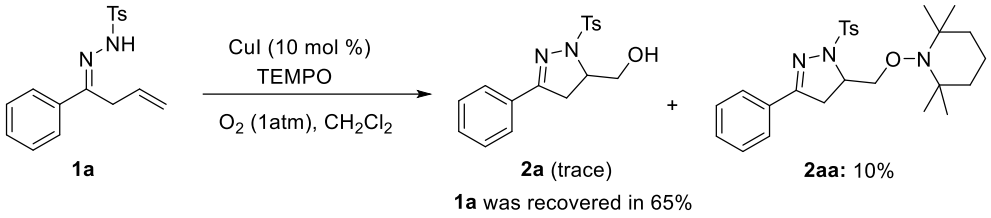
5.1. Labeling Experiments



A solution of **1a** (62.8mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %), $H_2{}^{18}O$ (8 mg, 0.04 mmol, 2 eq.) in dry DCM (1.0 mL) was stirred under O_2 for 2 h at 25 ºC. Then purified by preparative TLC (petroleum ether/ethyl acetate: 2/1) directly to give the products **2a** (6 mg, 8% yield), **4** (5 mg, 7% yield) and **5** (3 mg, 5% yield). Compound **5**: HR-MS (ESI) m/z calcd for $C_{17}H_{16}N_2O_3S$ $[M+H]^+$ 329.09599, found: 329.09490. Product **2a**: HR-MS (ESI) m/z calcd for $C_{17}H_{18}N_2O_3S$ $[M+H]^+$ 331.11164, found: 331.11034. Compound **4**: HR-MS (ESI) m/z calcd for $C_{17}H_{18}N_2O_4S$ $[M+H]^+$ 347.10655, found: 347.10532. This finding indicated that the $H_2{}^{18}O$ decreased the reactivity of the catalytic system, and only ^{16}O labeled products were determined in the mixture by HRMS.

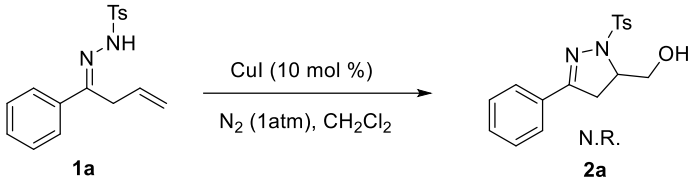


5.2. Radical-trapping Experiments

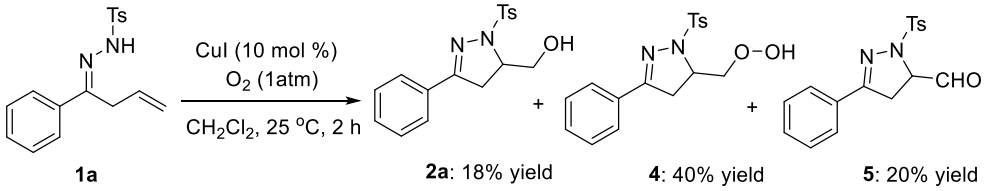


A solution of **1a** (62.8mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %), TEMPO (46.8mg, 1.5 eq) in dry DCM (1.0 mL) was stirred under O_2 for 2 h at 25 °C then monitored by TLC. The C-centered radical intermediate **III** was trapped by TEMPO in the formation of compound **2aa**, and the reactions were completely inhibited in the presence of TEMPO, which indicated that a radical process might be involved in the reaction.

5.3 Control Experiments

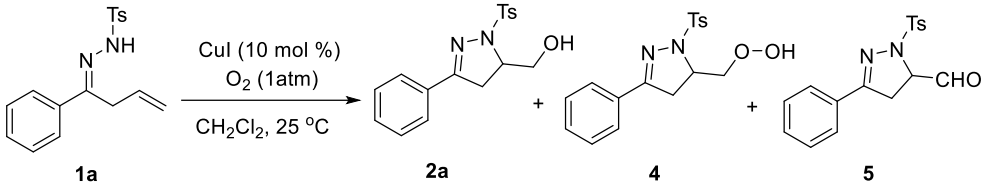


A solution of **1a** (62.8mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %) in dry DCM (1.0 mL) was stirred under N_2 for 2 h at 25 °C. the reaction did not take place.



A solution of **1a** (62.8mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %) in dry DCM (1.0 mL) was stirred under O_2 for 2 h at 25 °C. Then purified by preparative TLC (petroleum ether/ethyl acetate: 2/1) directly to give the products **2a** (12 mg, 18% yield), **4** (28 mg, 40% yield) and **5** (13 mg, 20% yield).

6. Kinetic Studies



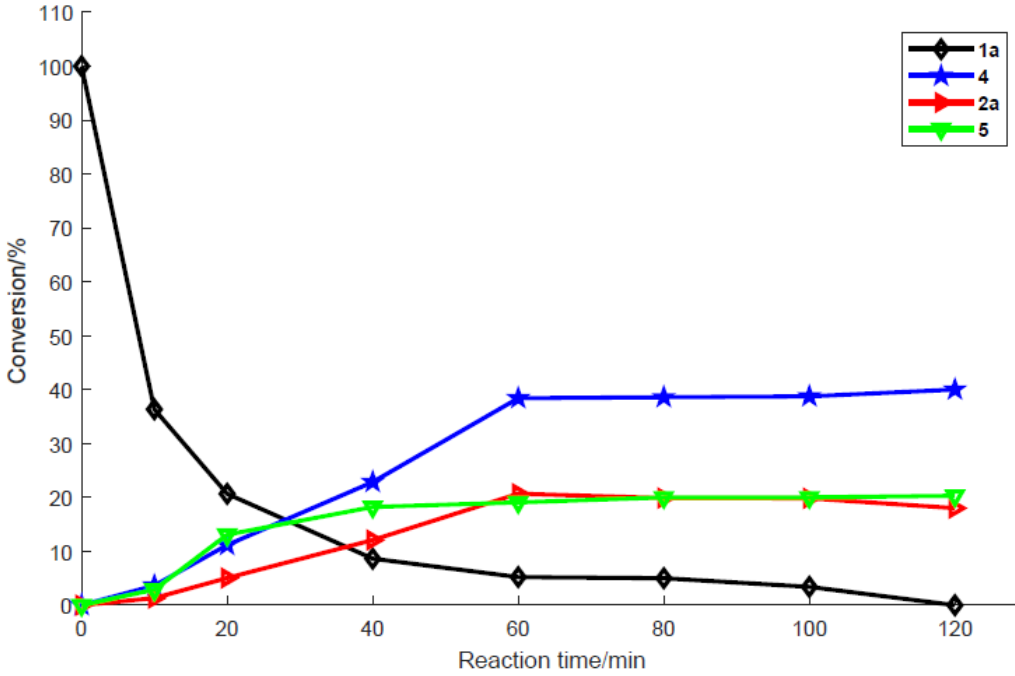


Figure S1. Kinetic profile of oxyamination reaction

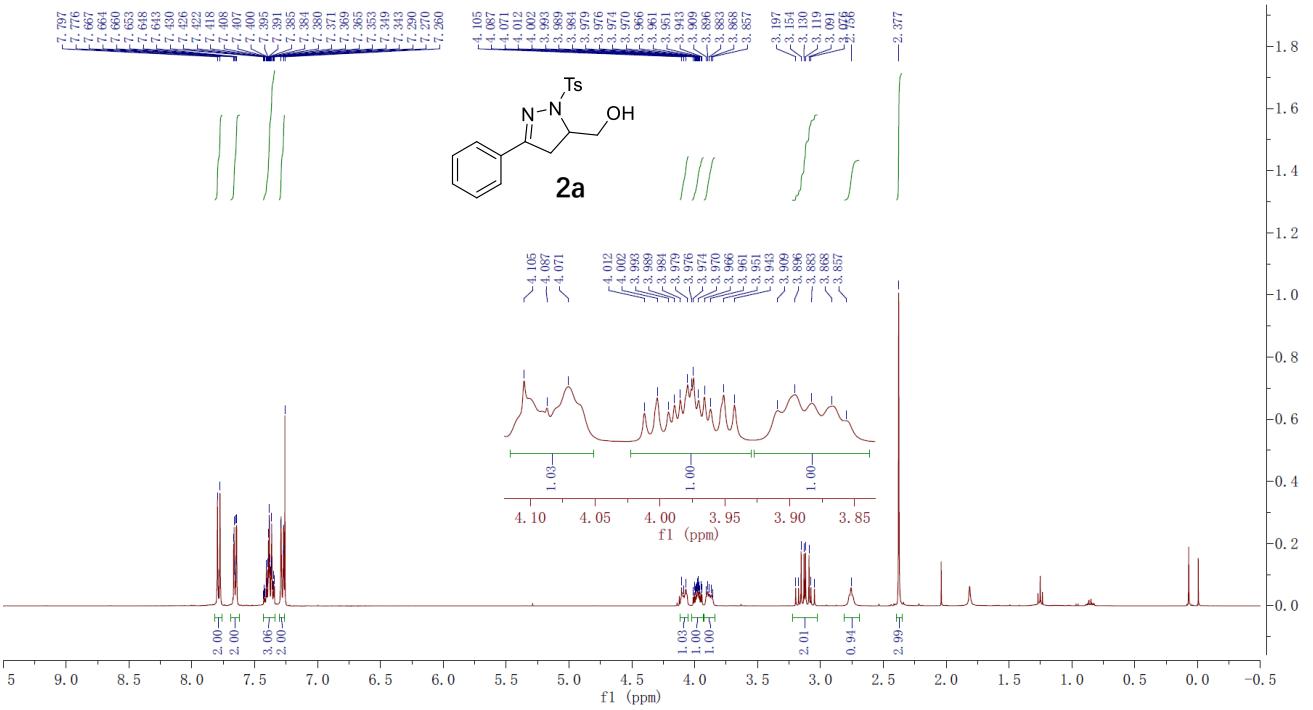
Reaction conditions: **1a** (62.8mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol, 10.0 mol %) in dry DCM (1.0 mL) was stirred under O_2. We conducted the kinetic experiment of transformation from **1a** into **2a, 4** and **5** under the first step of the standard conditions. The product of **2a, 4** and **5** was detected by GC-MS using the dodecane as the internal standard. The product of **2a** with yield of 2% (10 min), 5% (20 min), 12% (40 min), 20% (60 min), 20% (80 min), 20% (100 min), 19% (120 min). The yield of **4** was 4% (10 min), 11% (20 min), 22% (40 min), 38% (60 min), 39% (80 min), 39% (100 min), 40% (120 min). The yield of **5** was 3% (10 min), 13% (20 min), 18% (40 min), 19% (60 min), 20% (80 min), 20% (100 min), 20% (120 min). The results indicated that the intermediate **4** was not the main source in the formation of **2a**.

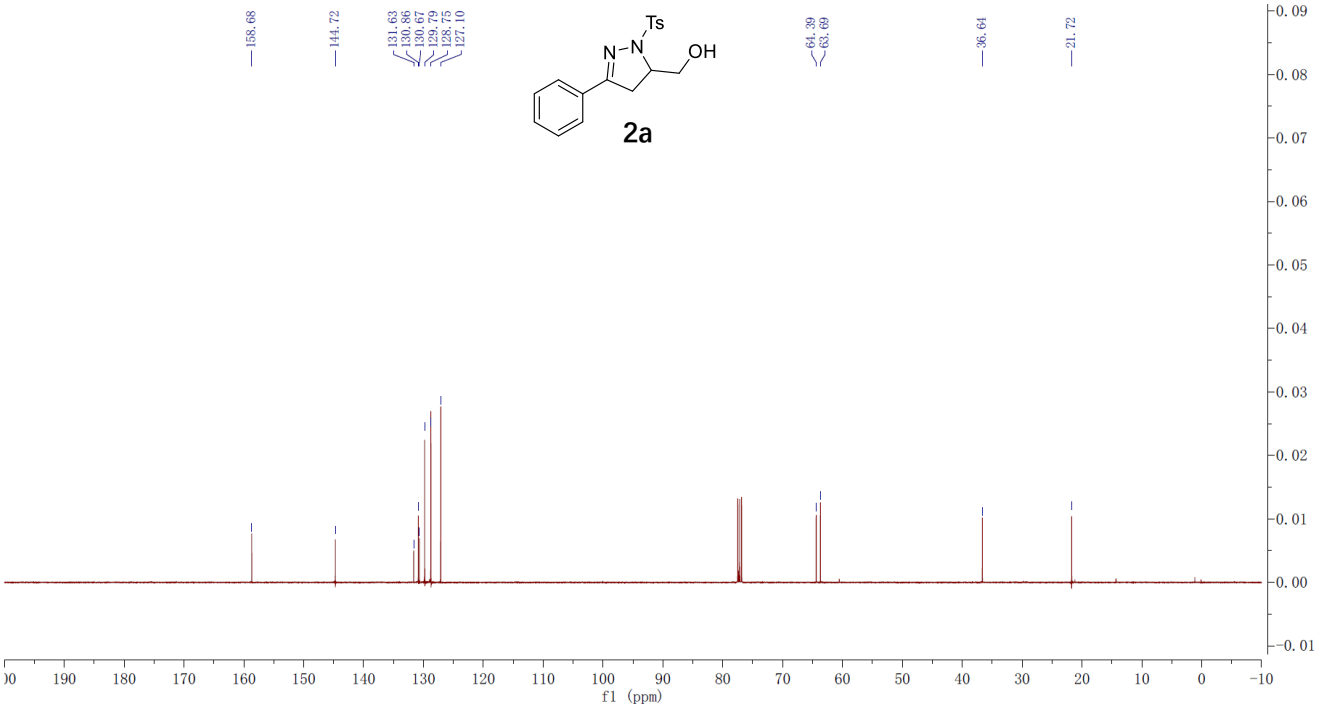
7. References

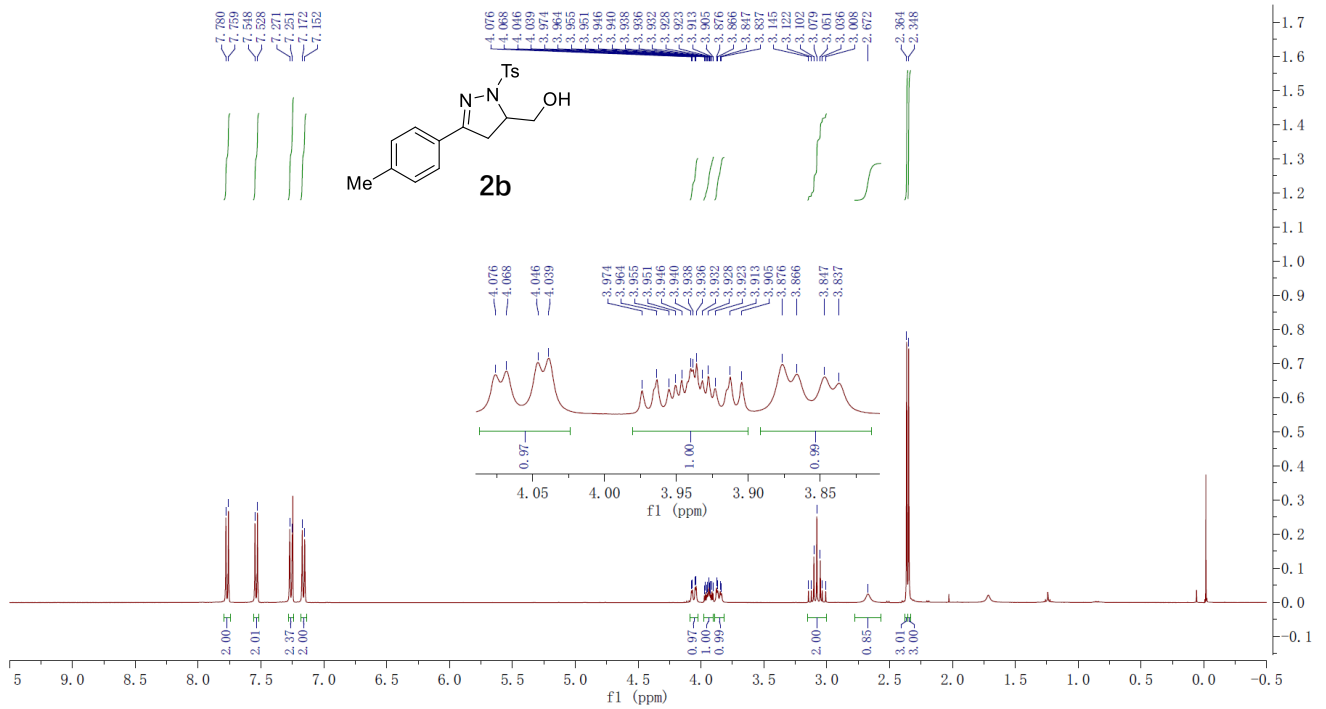
[1] Hu, X.-Q.; Chen, J.; Chen, J.-R.; Yan, D.-M.; Xiao, W.-J. *Chem. - Eur. J.* **2016**, *22*, 14141.

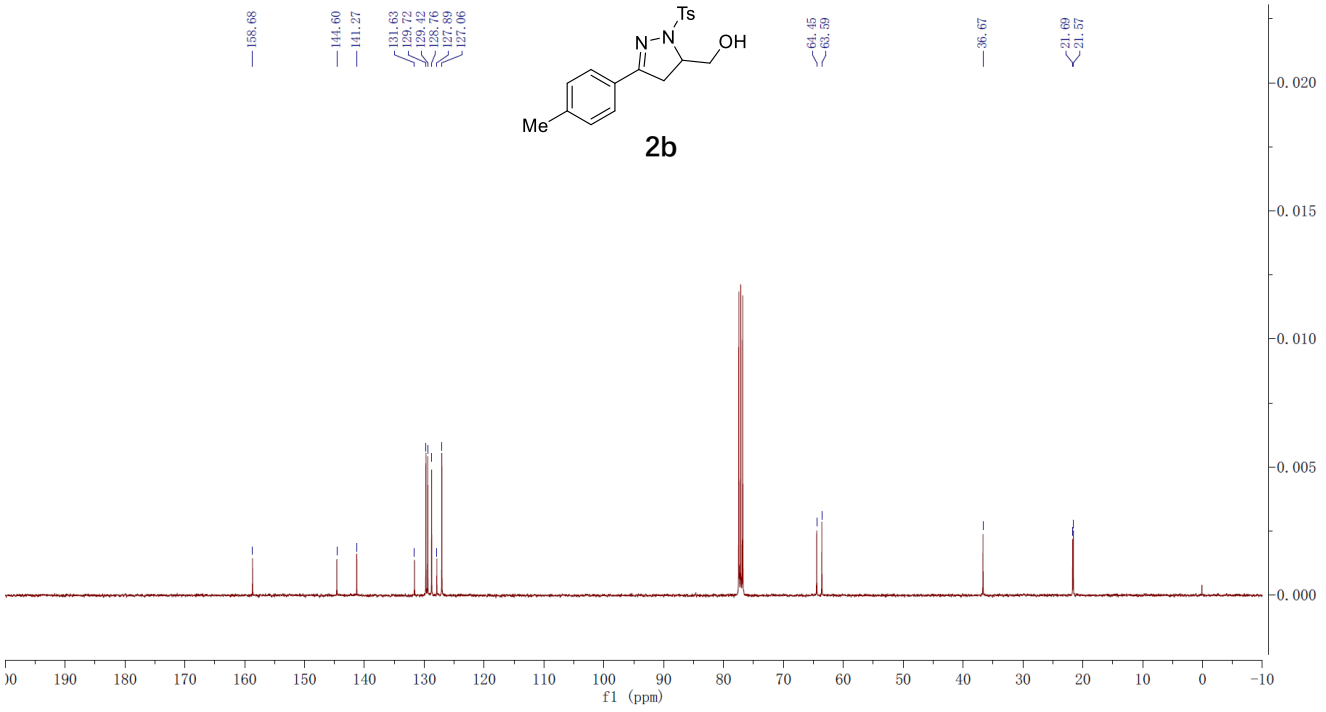
[2] Kumar, R.; Turcaud, S.; Micouin, L. *Org. Lett.* **2014**, *16*, 6192.

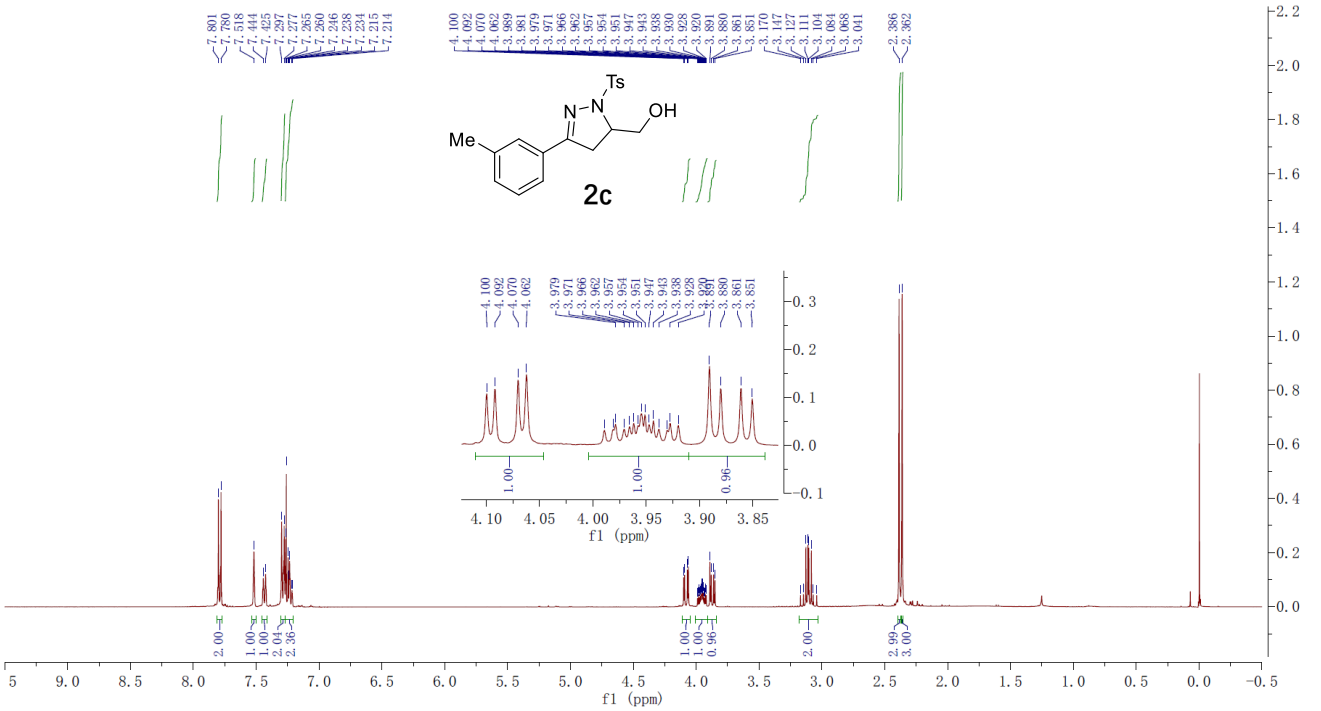
8. NMR Spectra

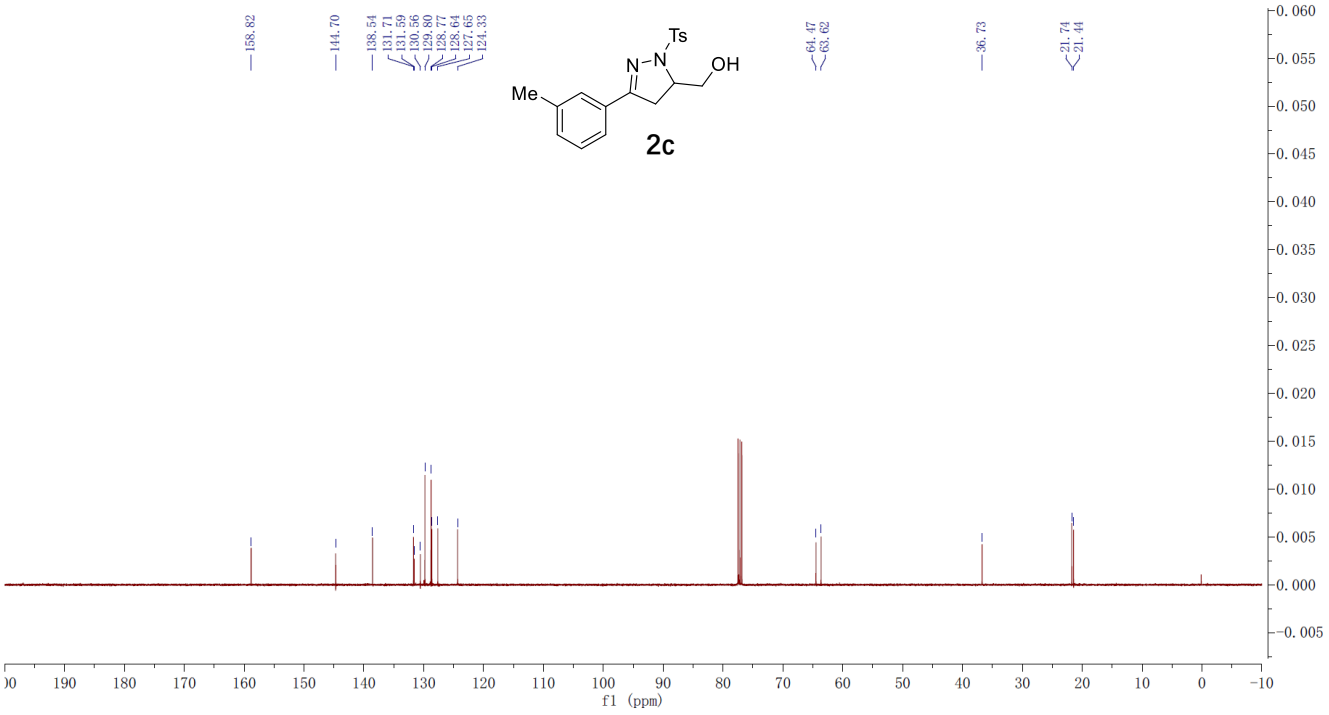


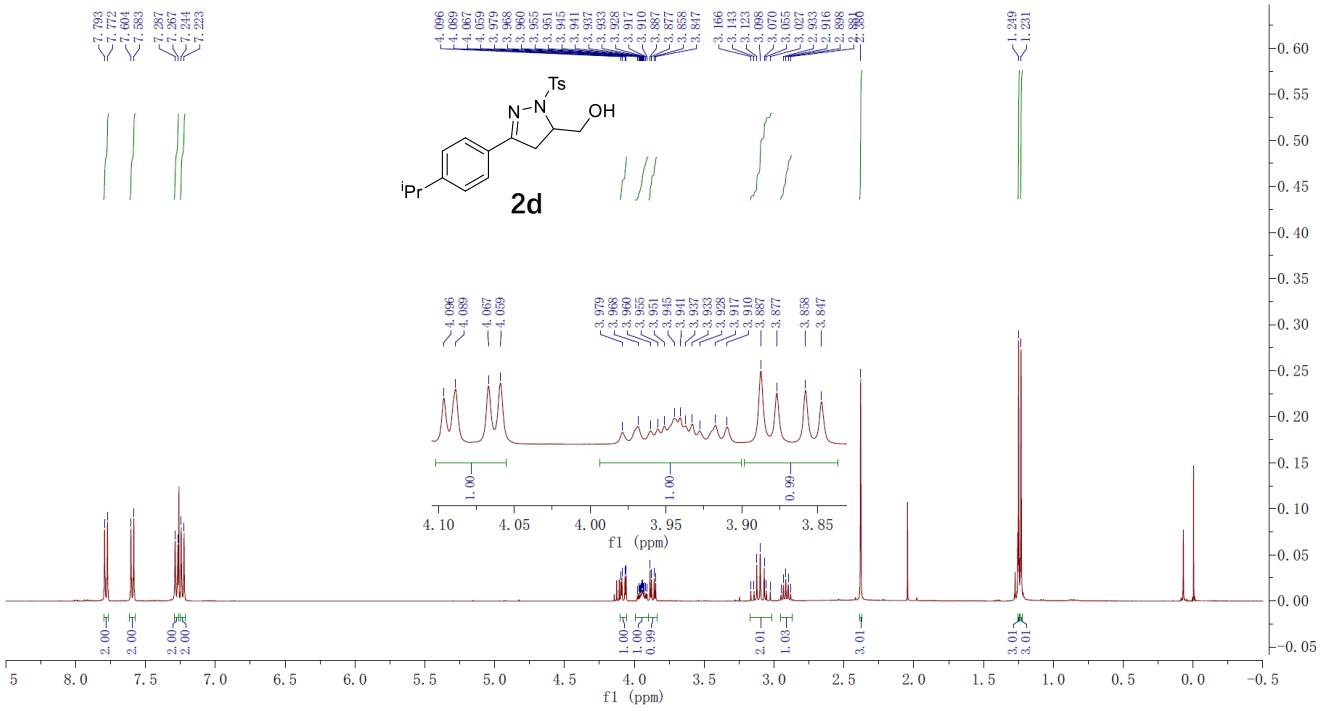


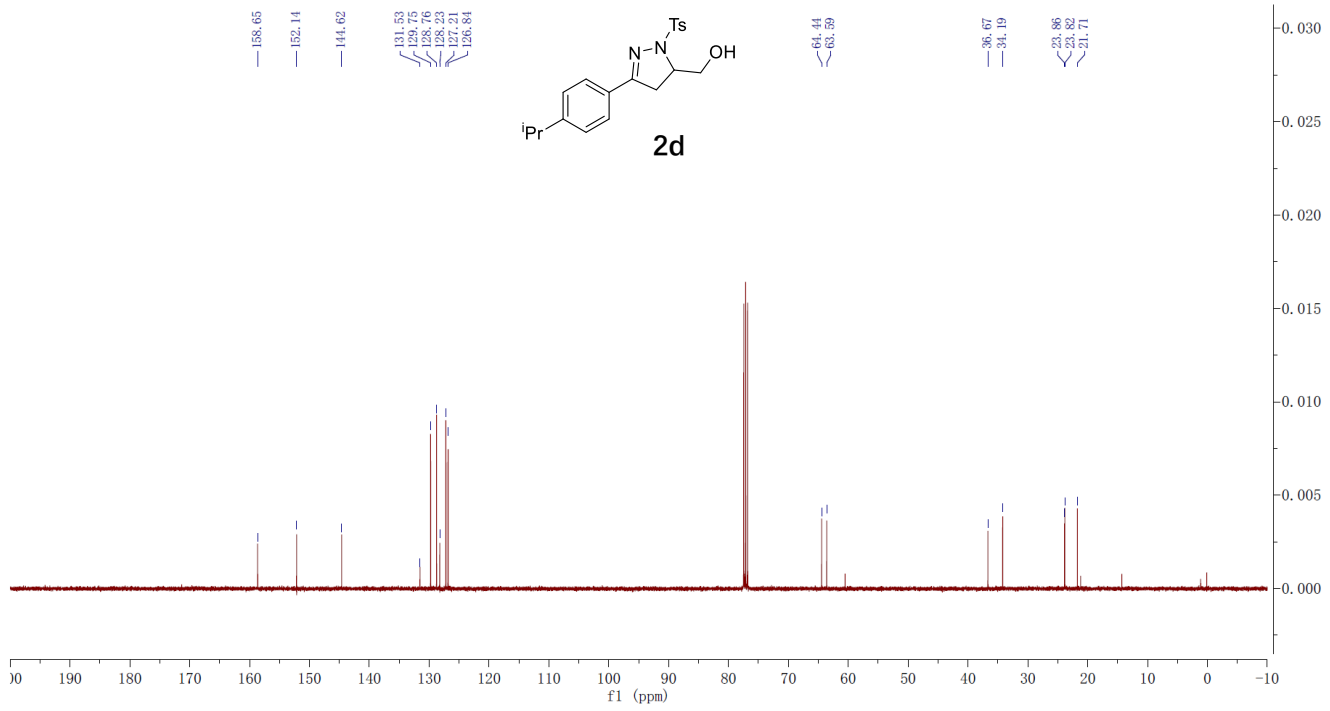

Ts
N
N
OH
Me
2b
f1 (ppm)

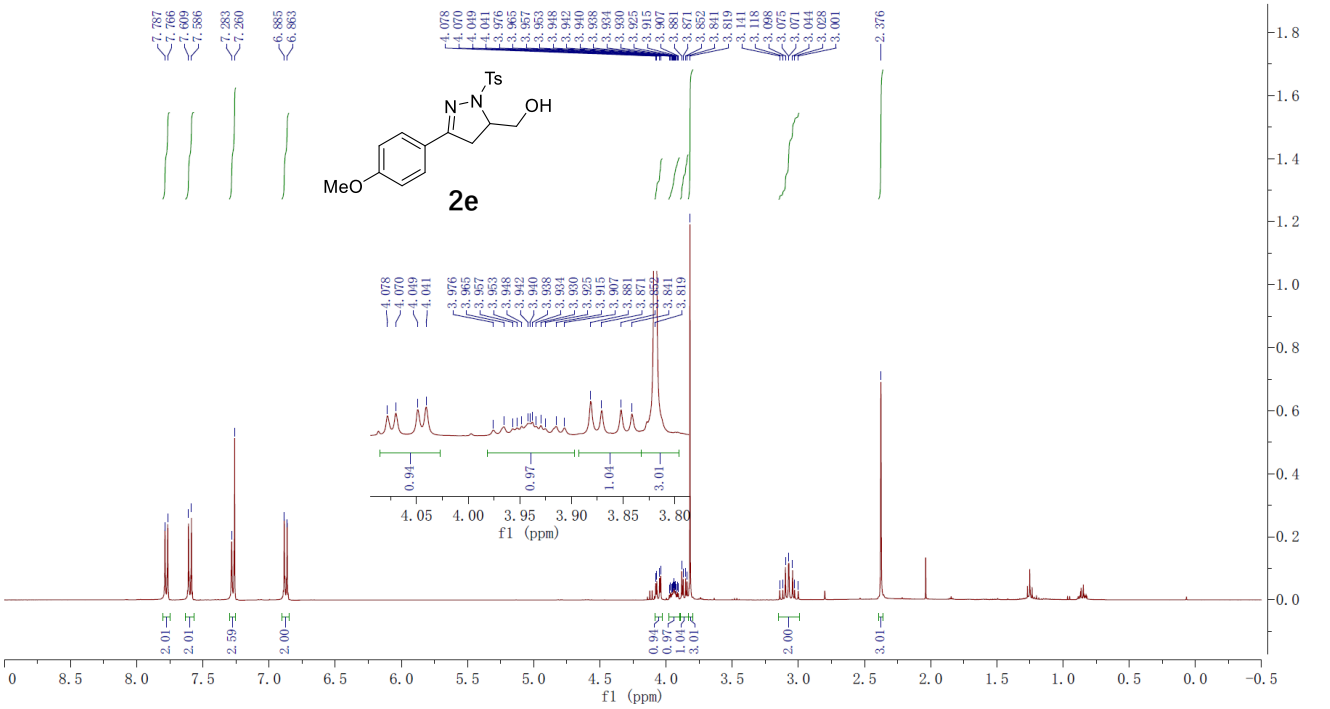

Ts
N
N
OH
Me
2b
f1 (ppm)

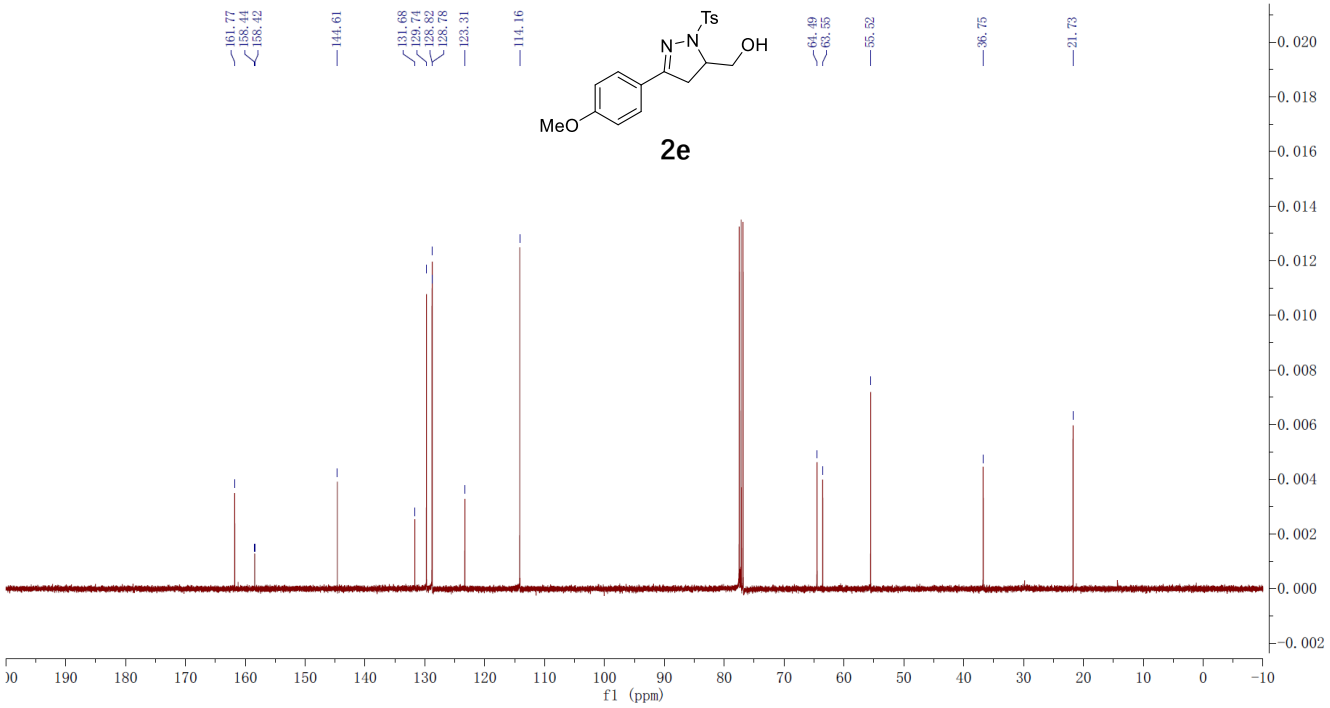

Ts
N
N
OH
Me
2c
f1 (ppm)

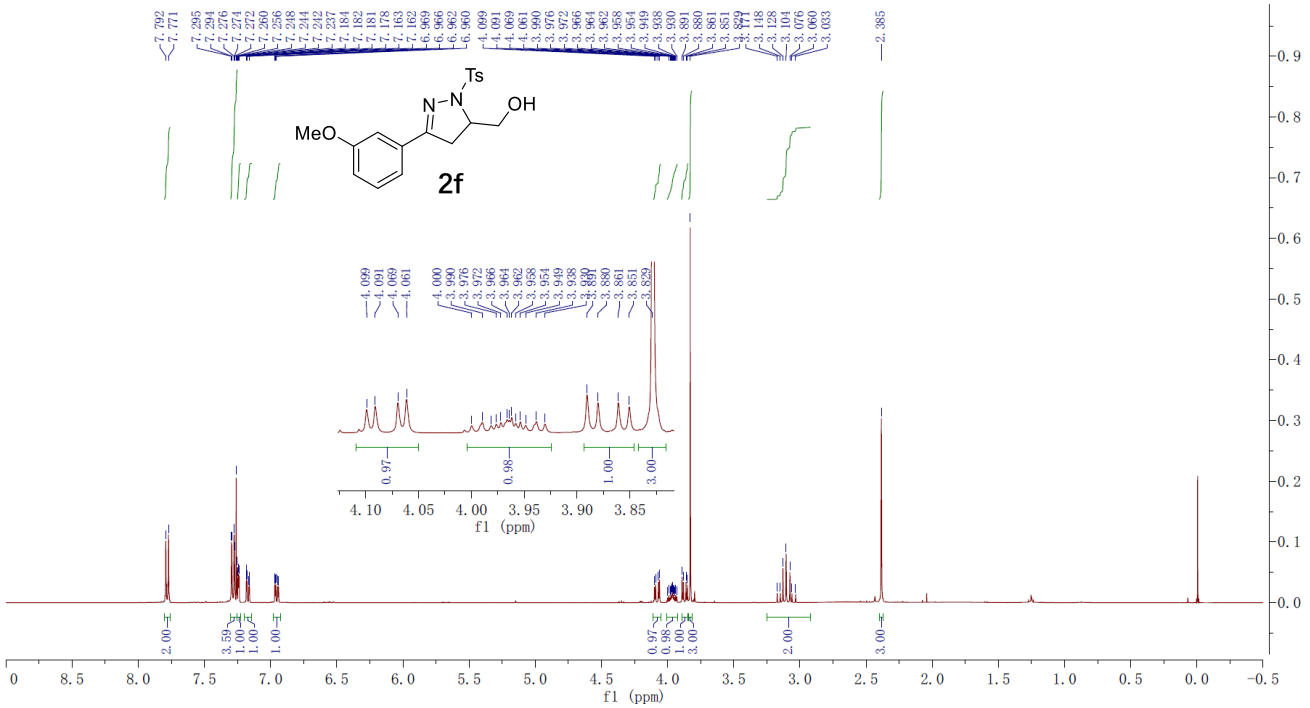

Ts
N
N
OH
Me
2c
f1 (ppm)

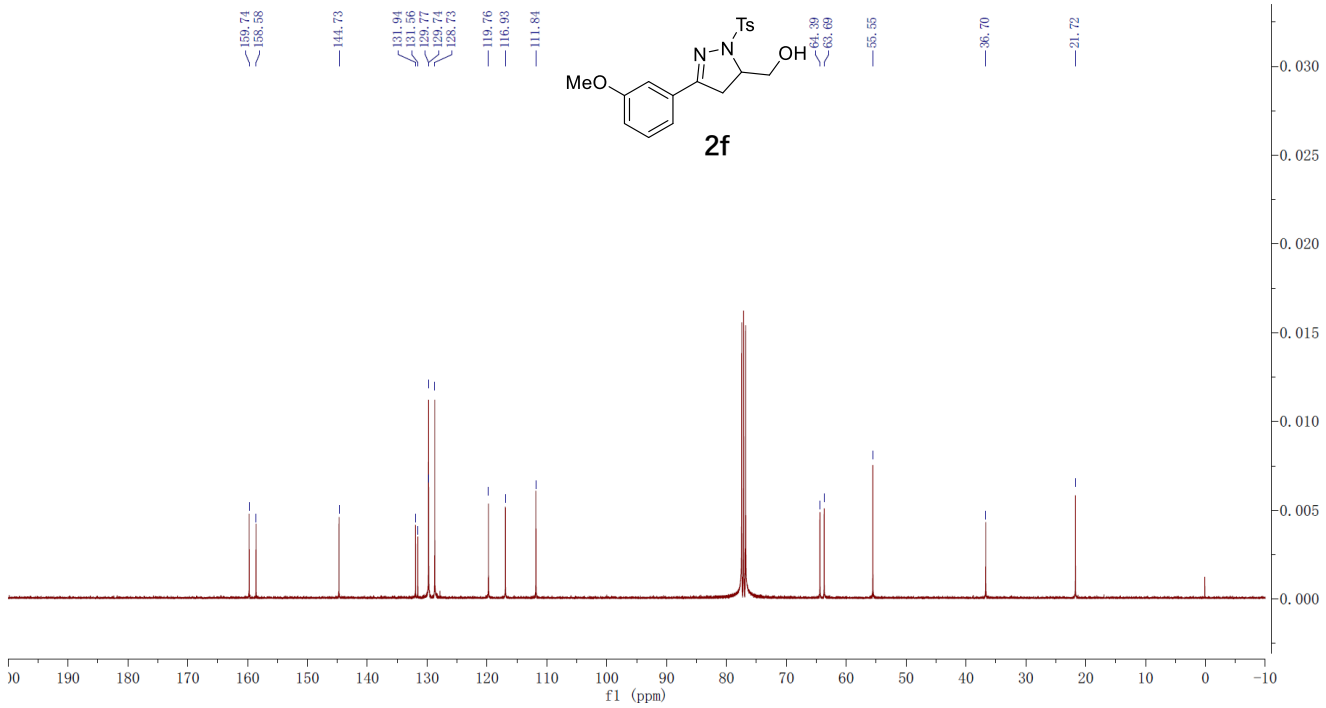

Ts
N
N
OH
iPr
2d
f1 (ppm)

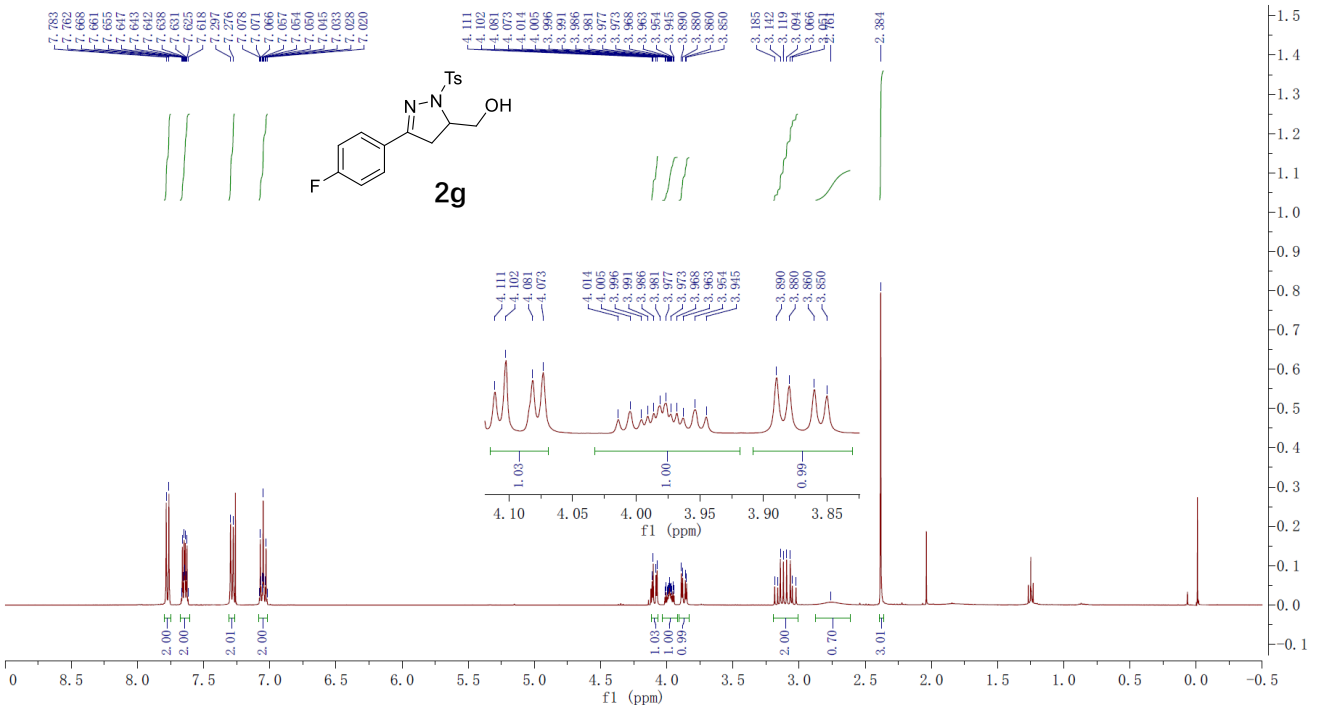

Ts
N
N
OH
iPr
2d
f1 (ppm)

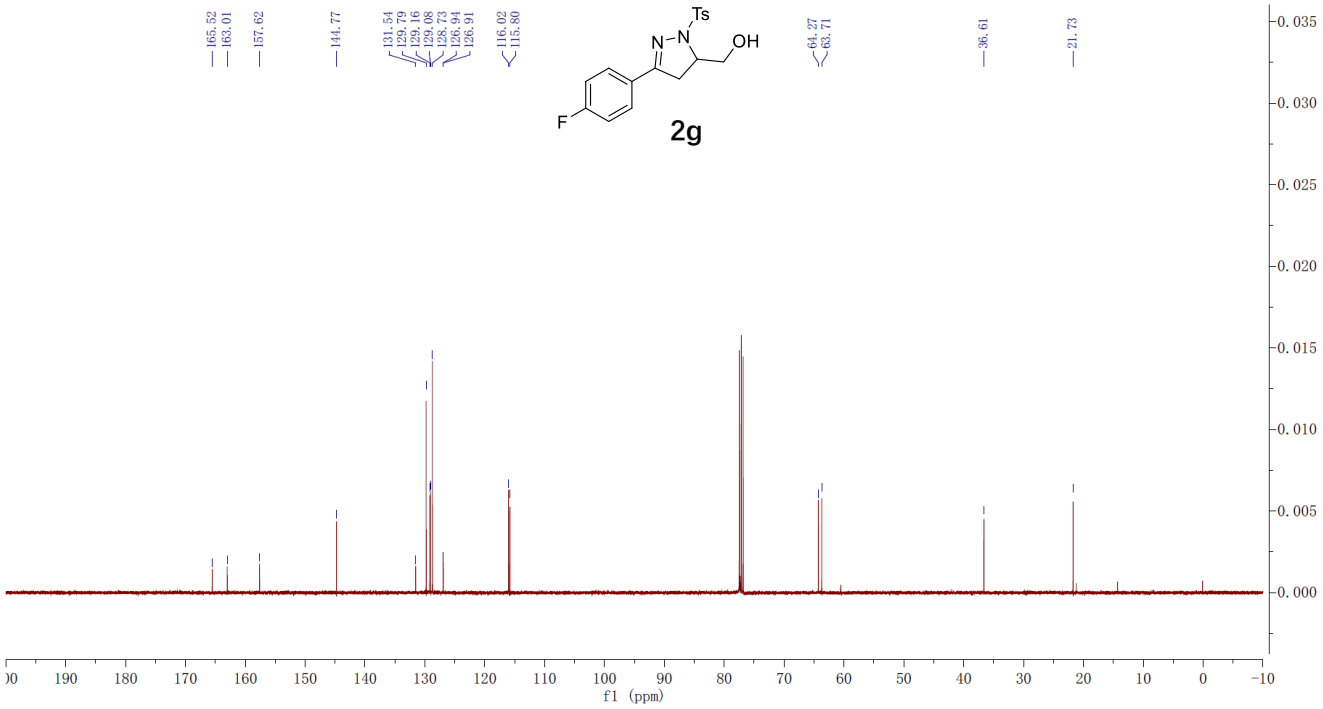

Ts
N
N
OH
MeO
2e
f1 (ppm)

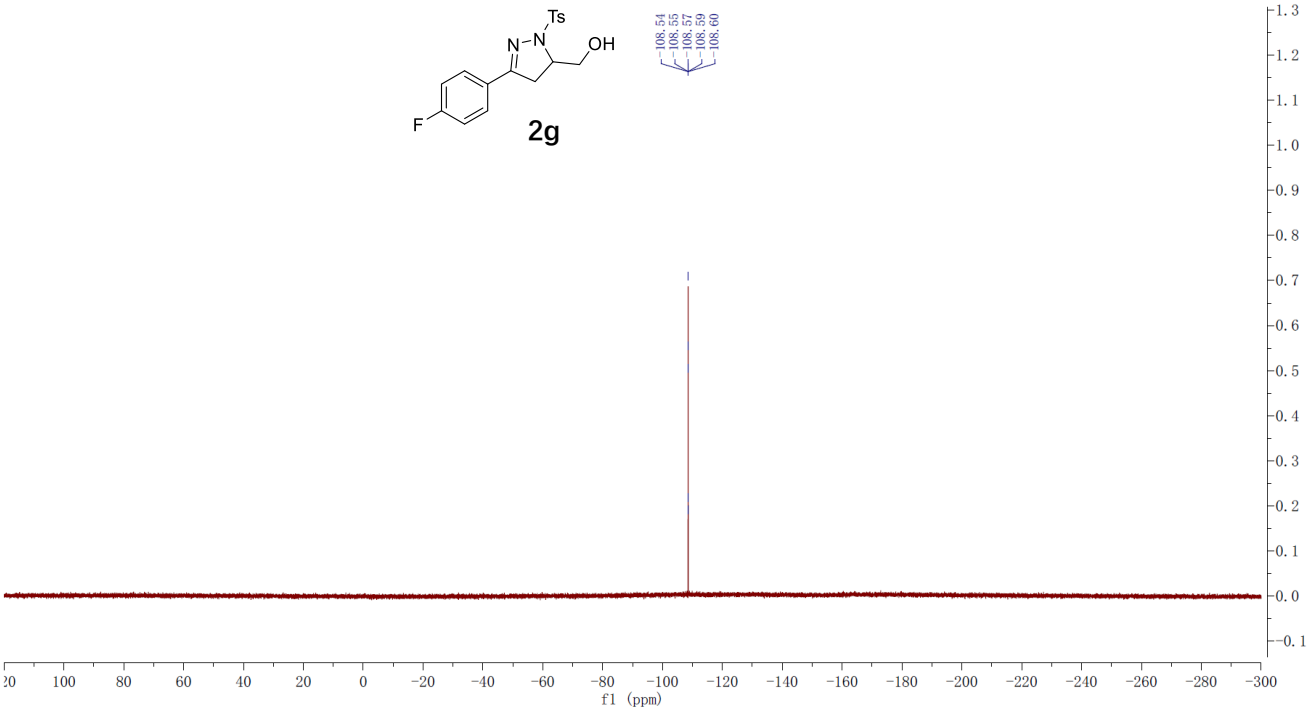

Ts
N
N
OH
MeO
2e
f1 (ppm)

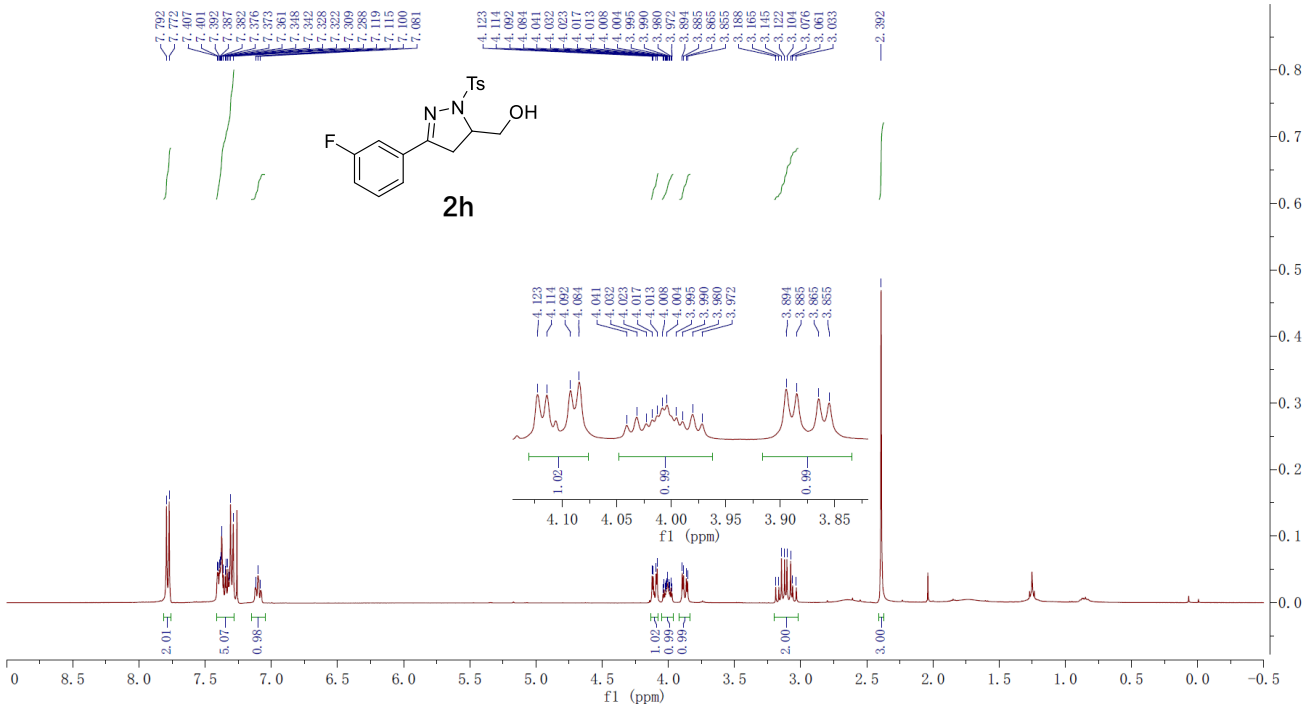

Ts
N
N
OH
MeO
2f
f1 (ppm)

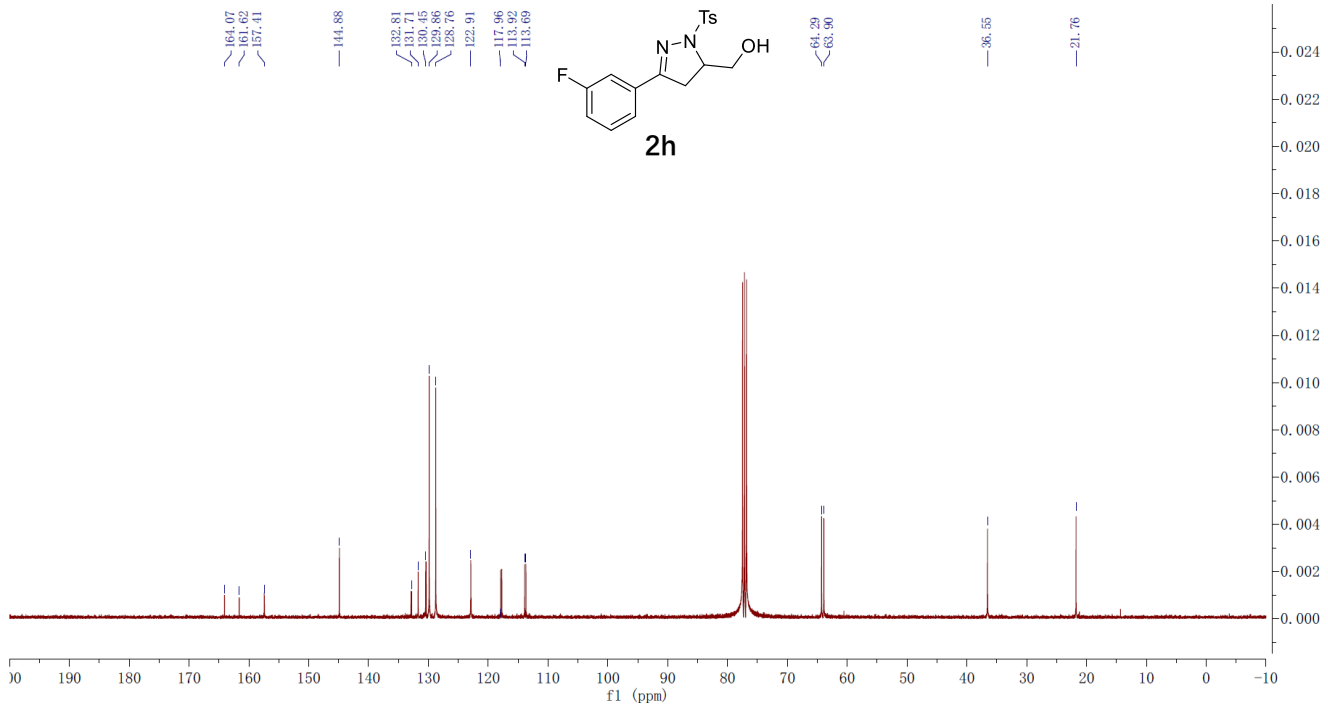

Ts
N
N
OH
MeO
2f
f1 (ppm)

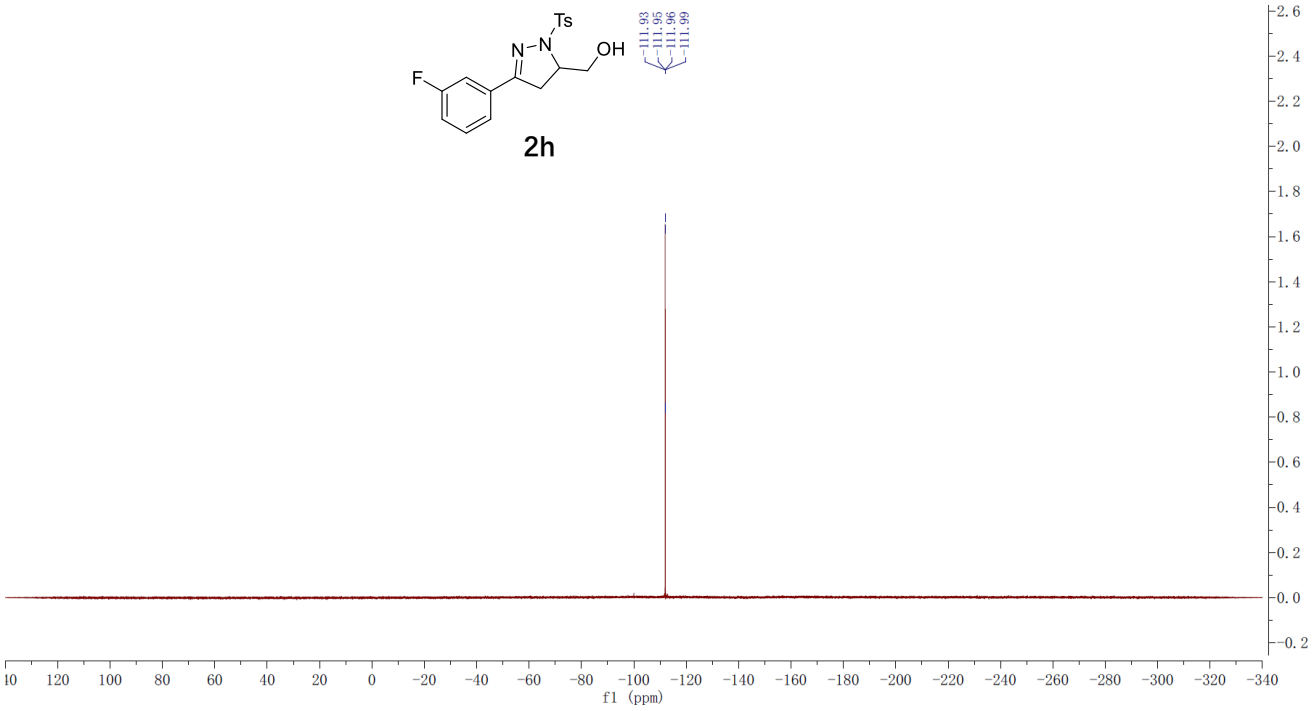

Ts
N
N
OH
F
2g
f1 (ppm)

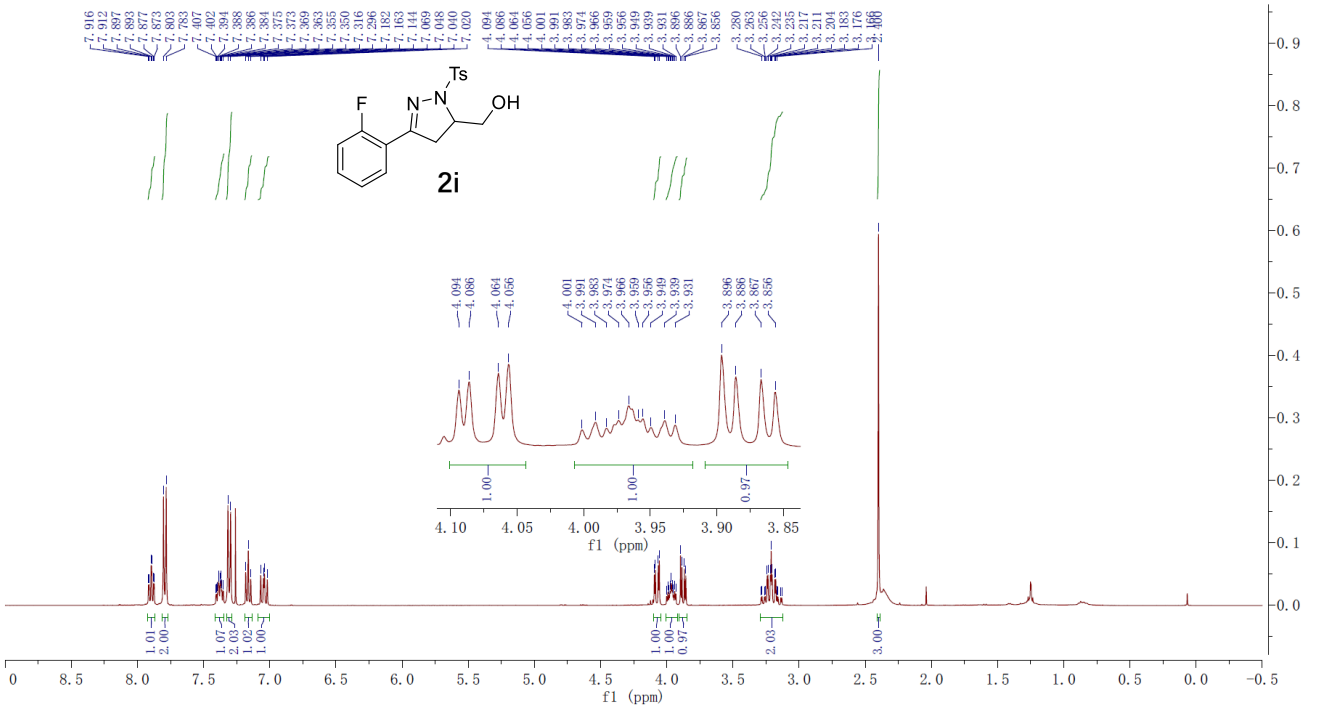

Ts
N
N
OH
F
2g
f1 (ppm)

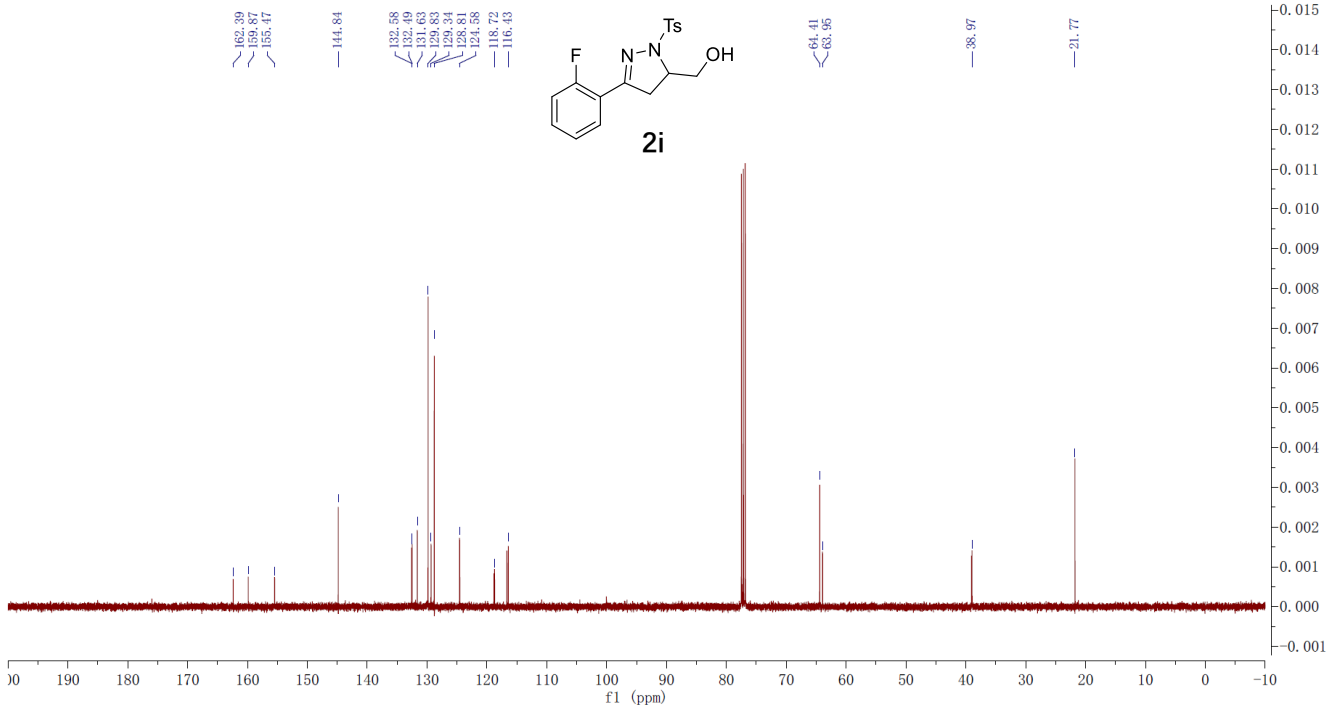

Ts
N
N
OH
F
2g
108.54
108.55
108.57
108.59
108.60
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
20
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
-280
-300
f1 (ppm)

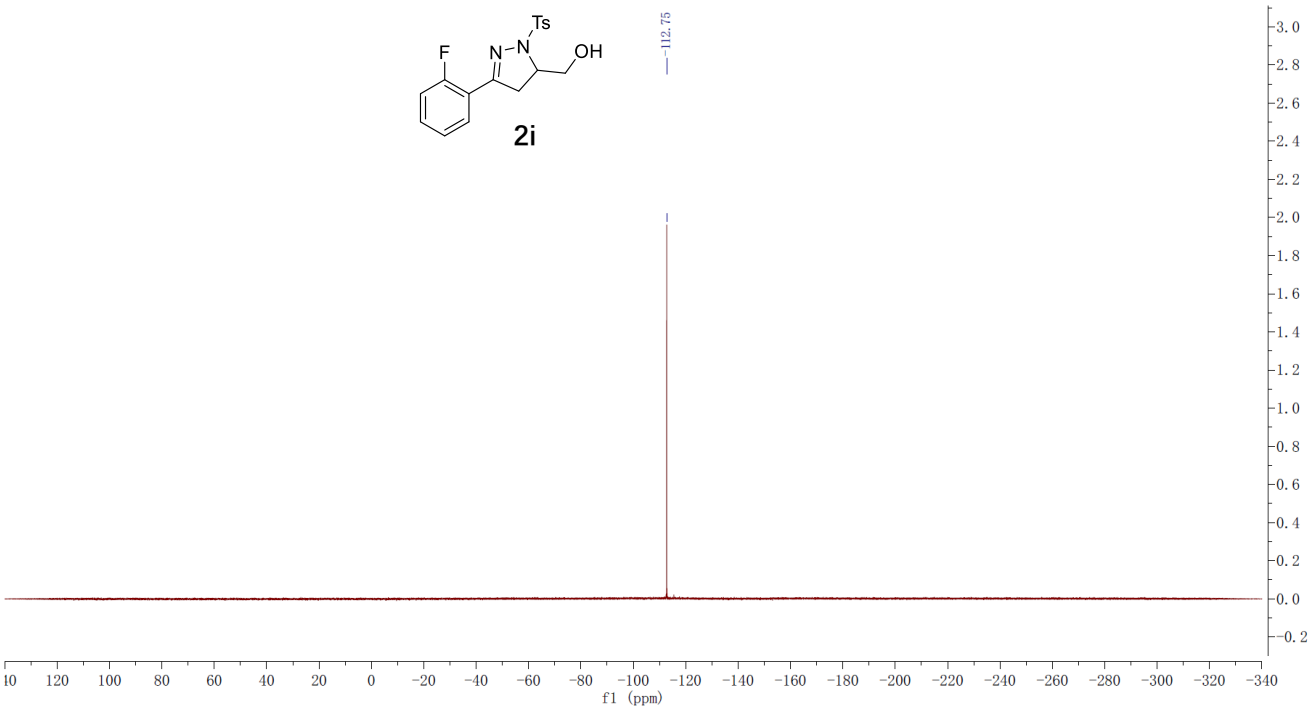

Ts
N
N
OH
F
2h
f1 (ppm)

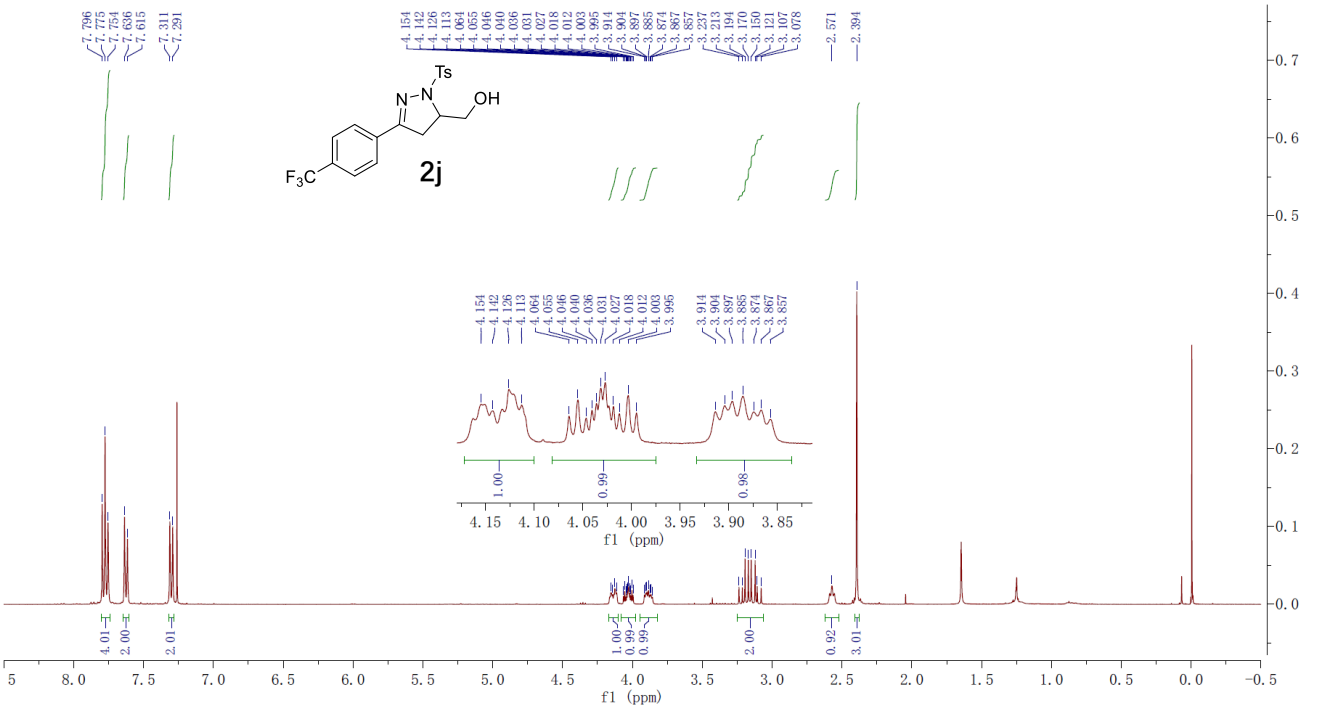

Ts
N
N
OH
F
2h
f1 (ppm)

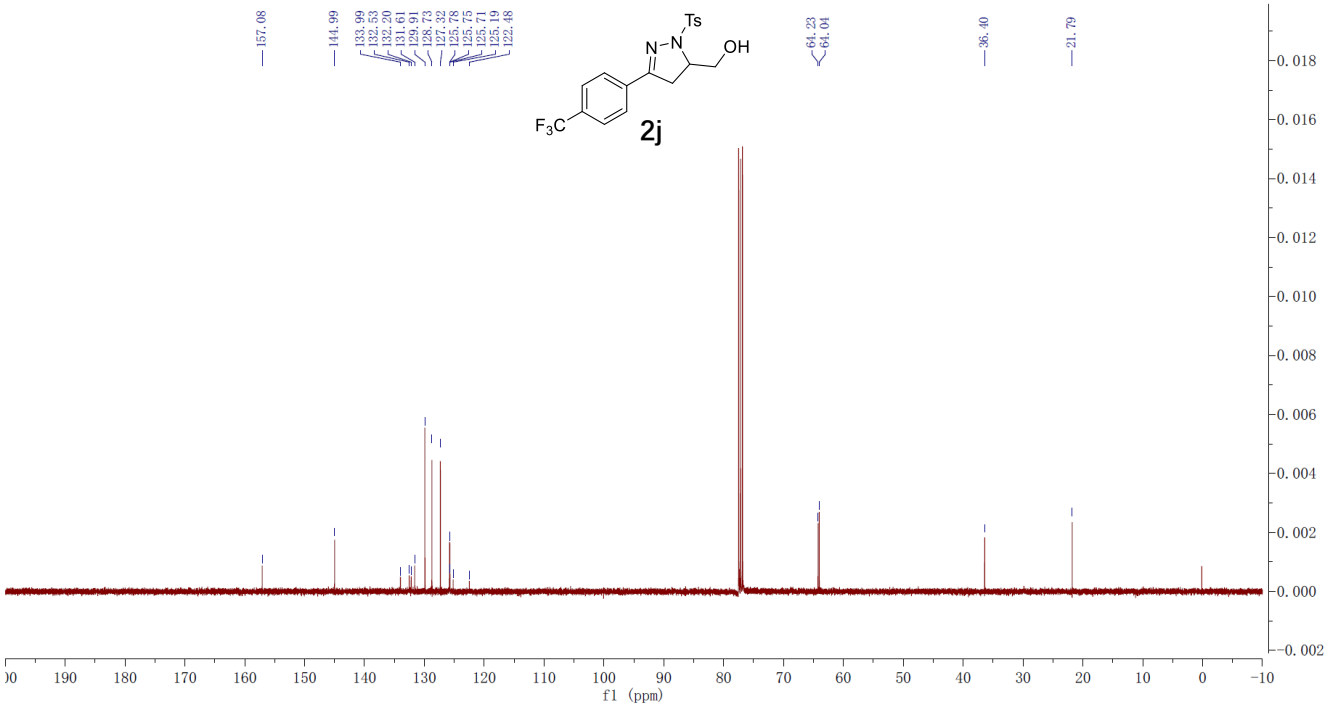

Ts
N
N
OH
F
2h
-111.93
-111.95
-111.96
-111.99
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
10 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300 -320 -340
f1 (ppm)

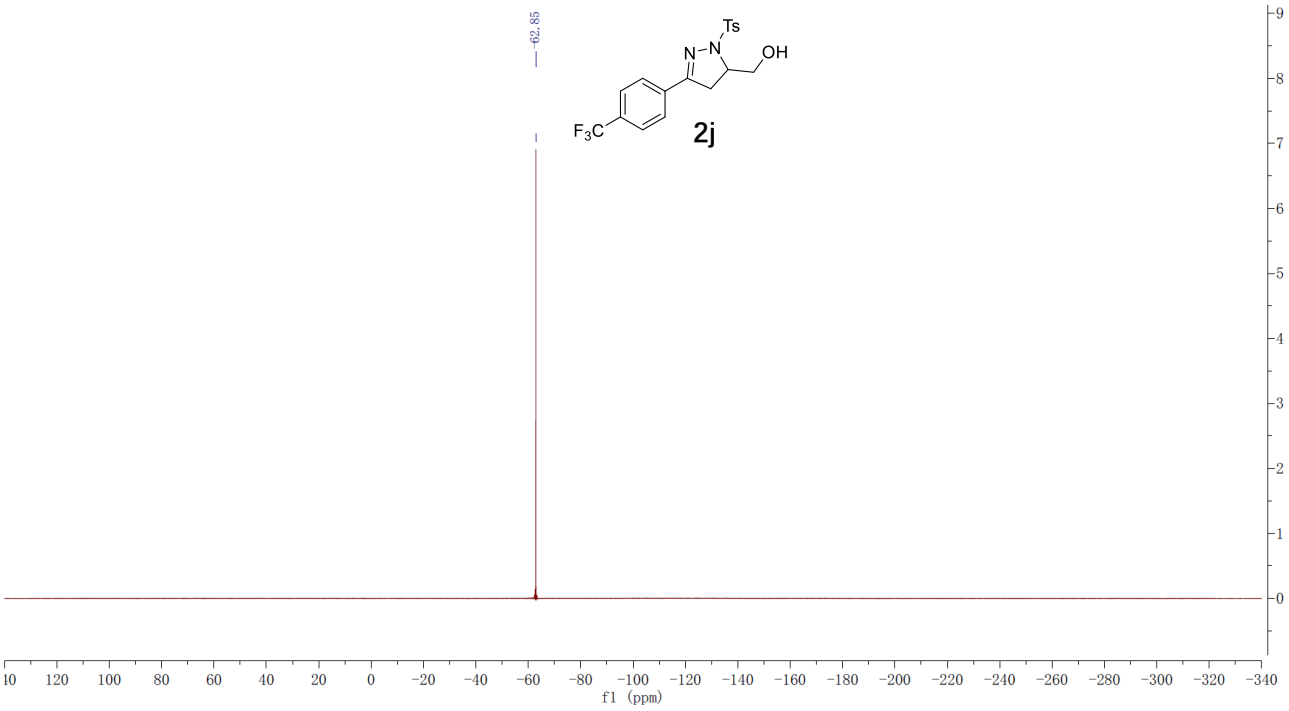

Ts
F
N
N
OH
2i
f1 (ppm)

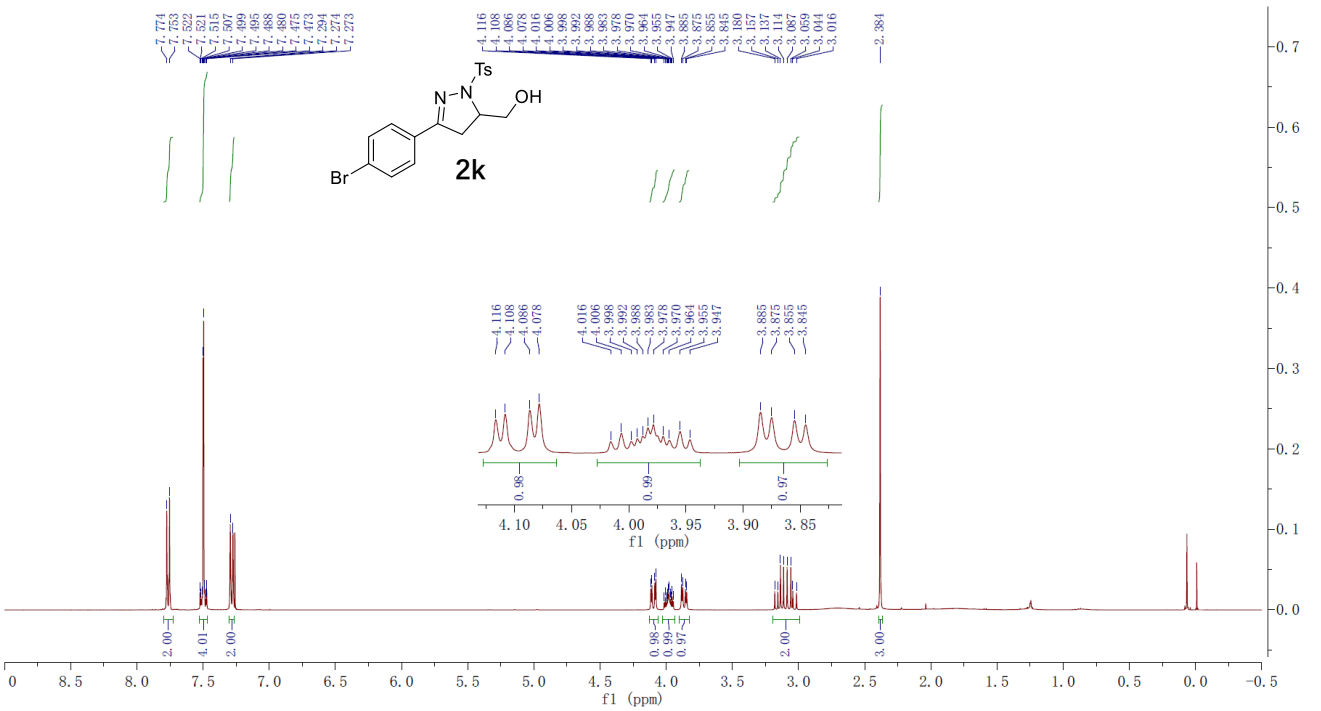

Ts
F
N
N
OH
2i
f1 (ppm)

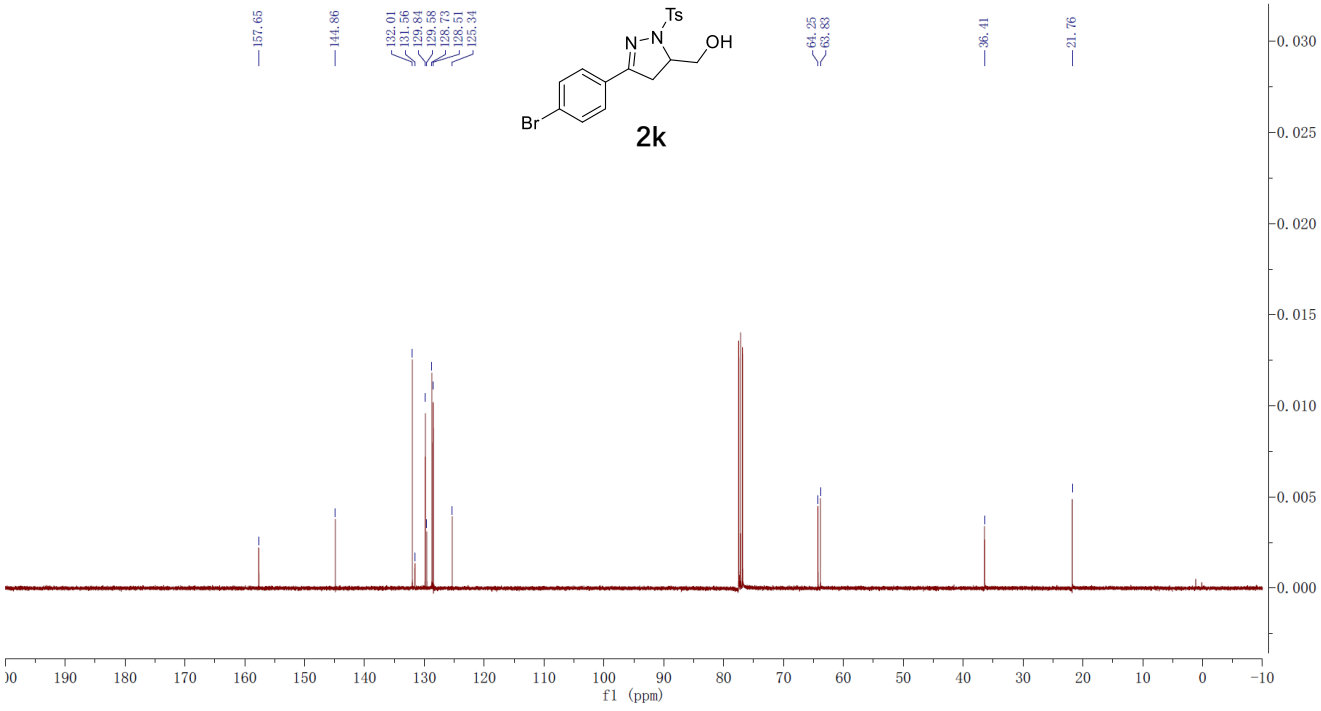

Ts
F
N
N
OH
2i
-112.75
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
40 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300 -320 -340
f1 (ppm)

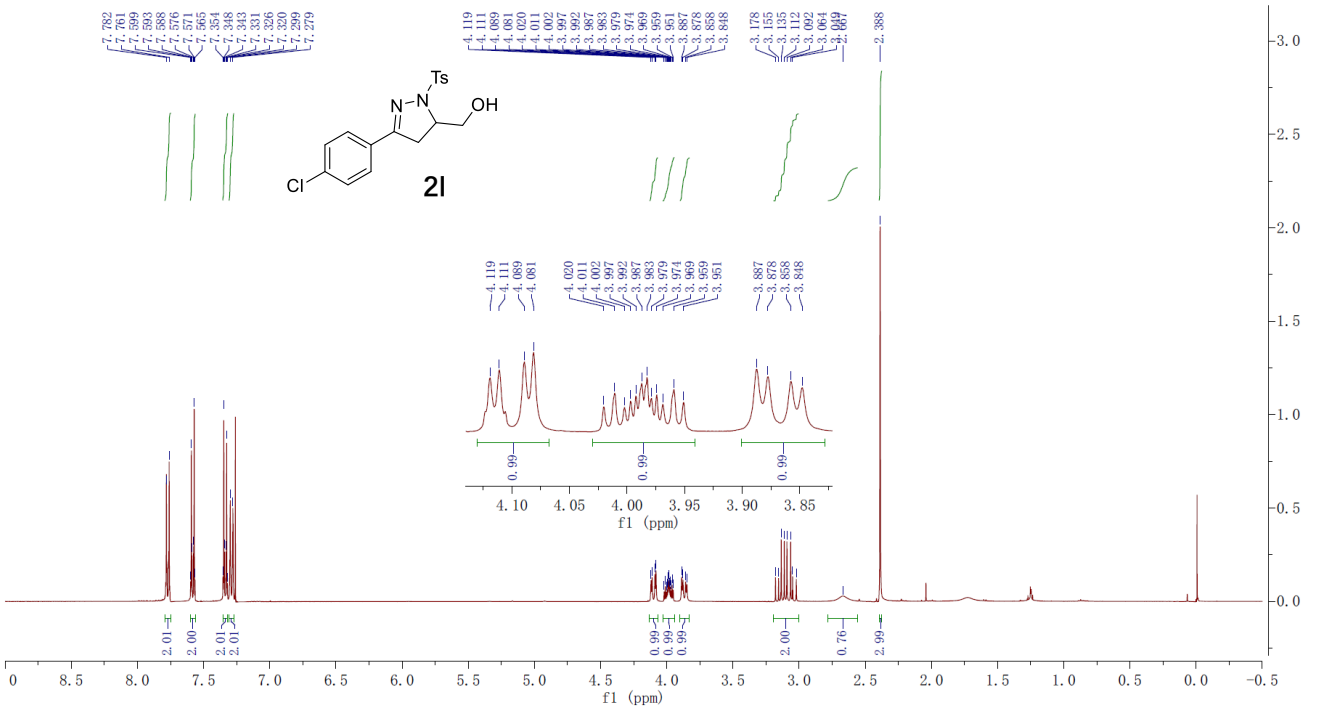

Ts
N
N
OH
F3C
2j
f1 (ppm)

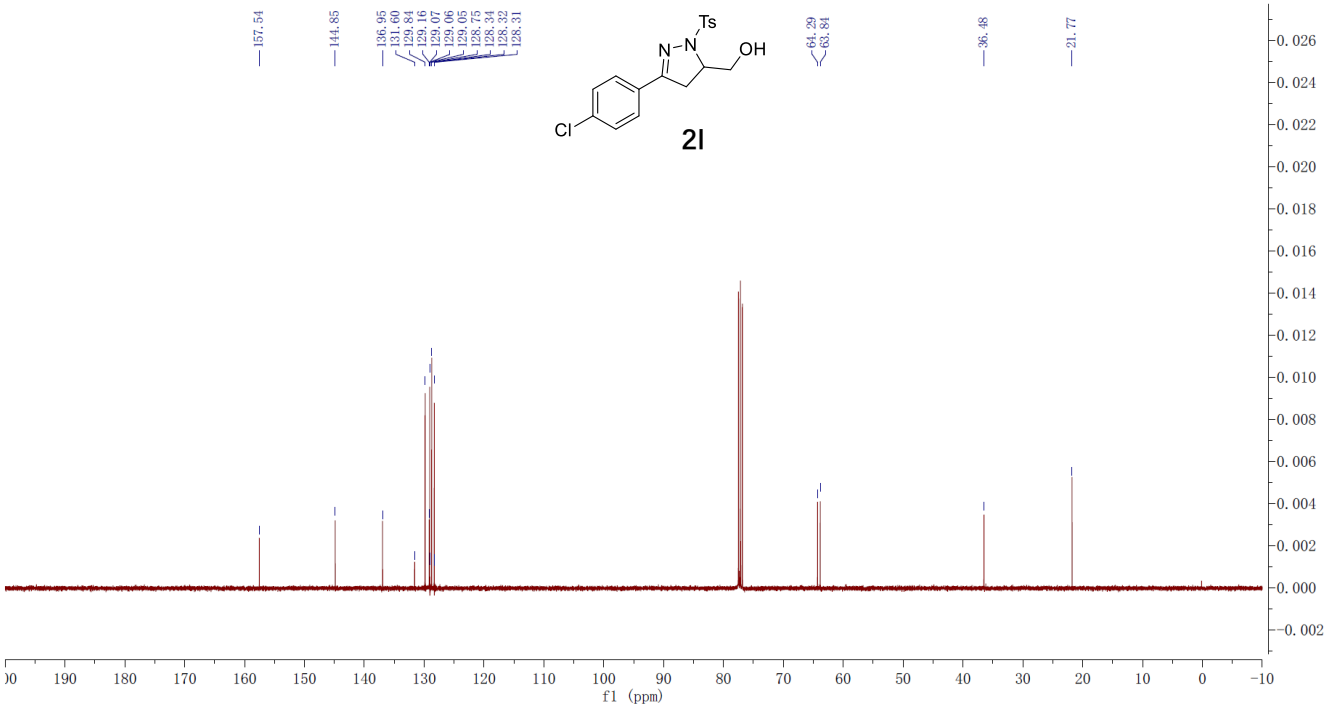

Ts
N
N
OH
F3C
2j
f1 (ppm)

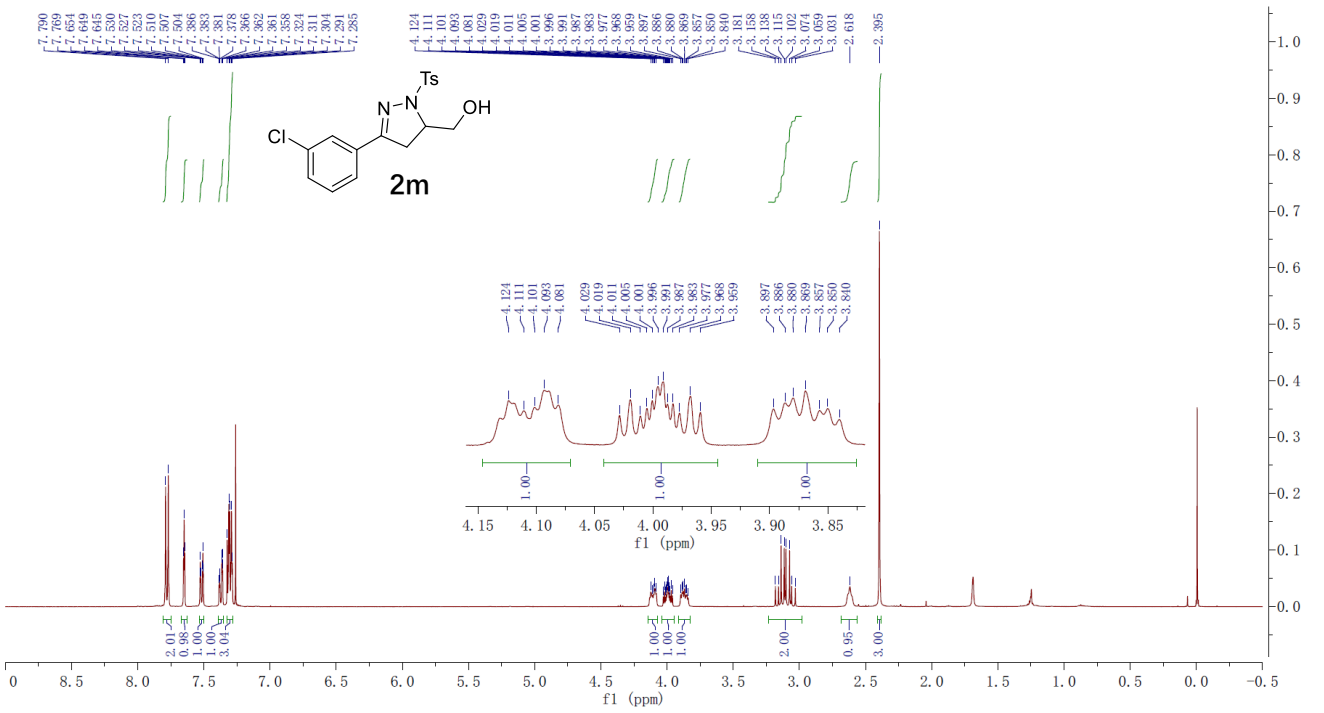

-62.85
Ts
N
N
OH
F3C
2j
9
8
7
6
5
4
3
2
1
0
10 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300 -320 -340
f1 (ppm)

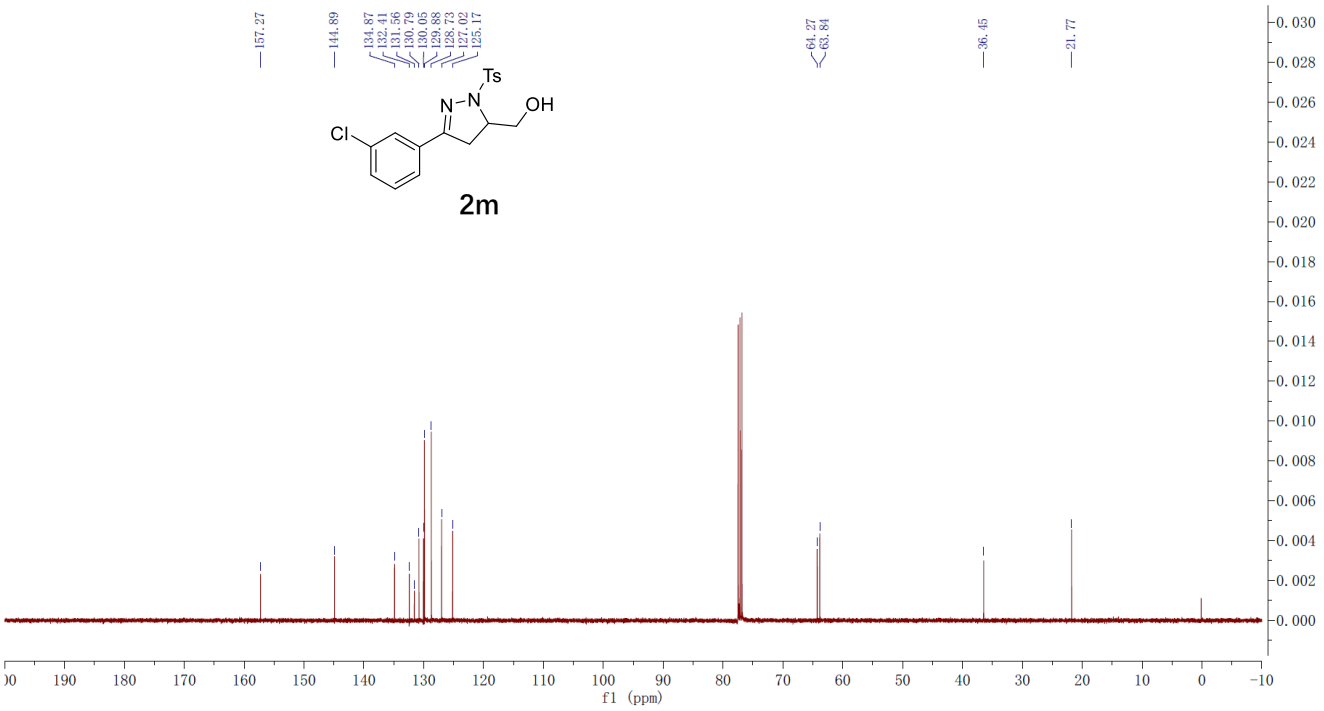

Ts
N
N
OH
Br
2k
f1 (ppm)

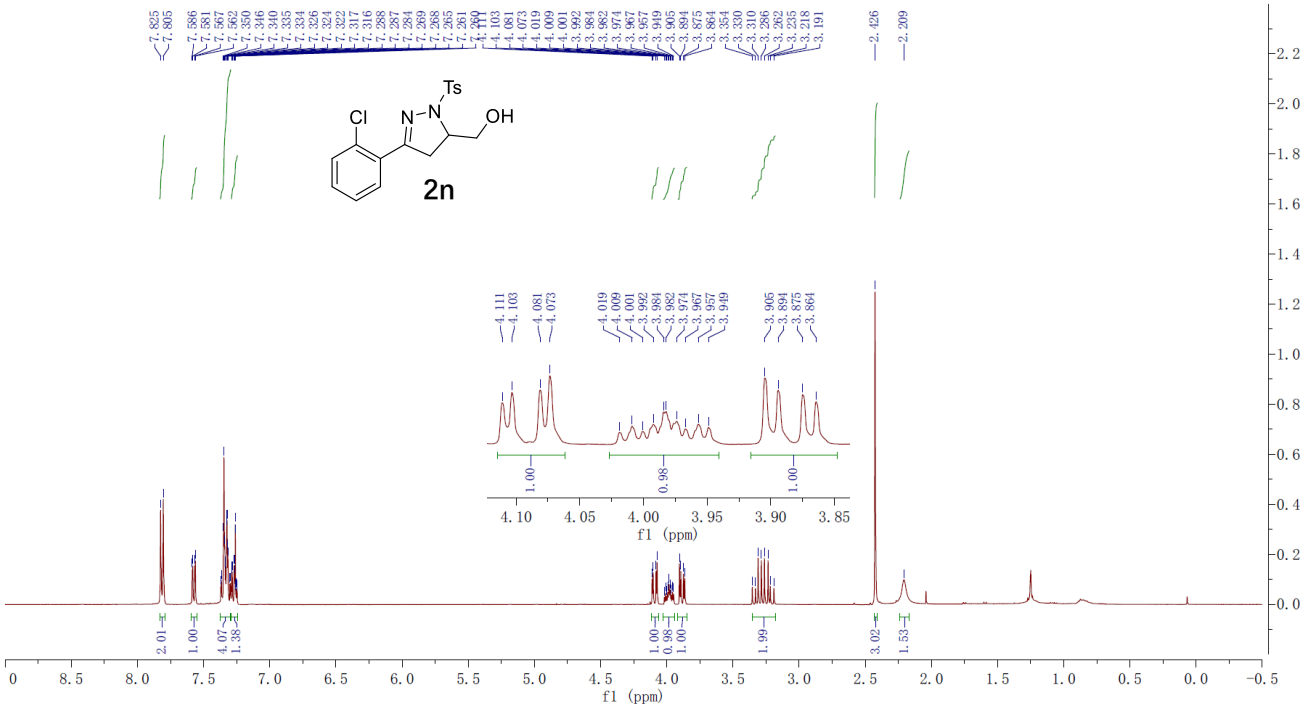

Ts
N
N
OH
Br
2k
f1 (ppm)

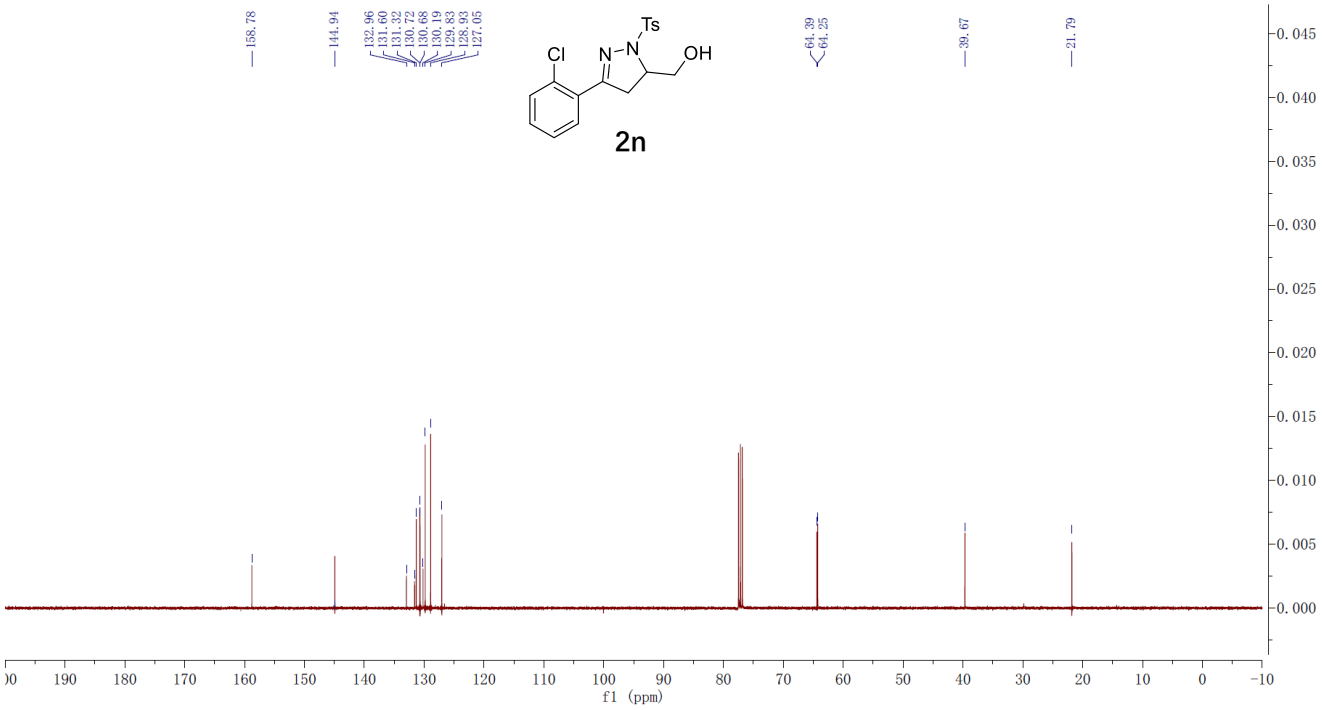

Ts
N
N
OH
Cl
2l
f1 (ppm)

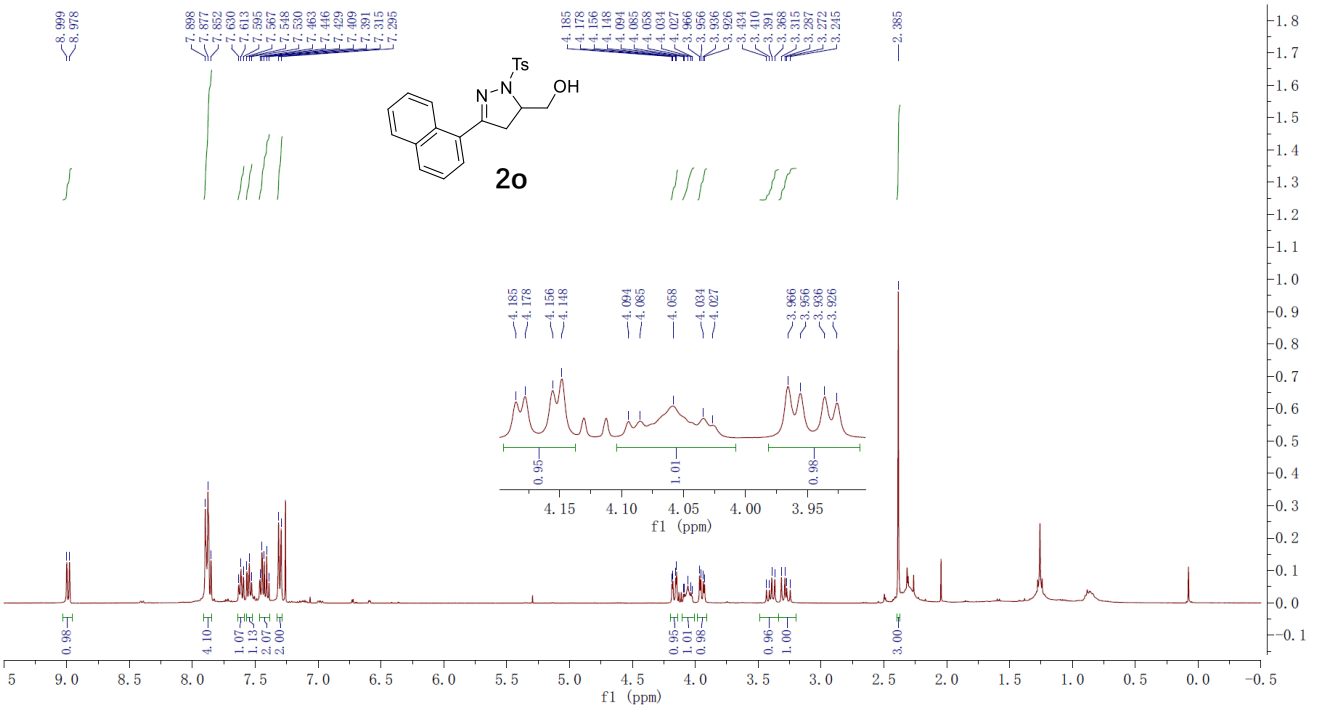

Ts
N
N
OH
Cl
2l
f1 (ppm)

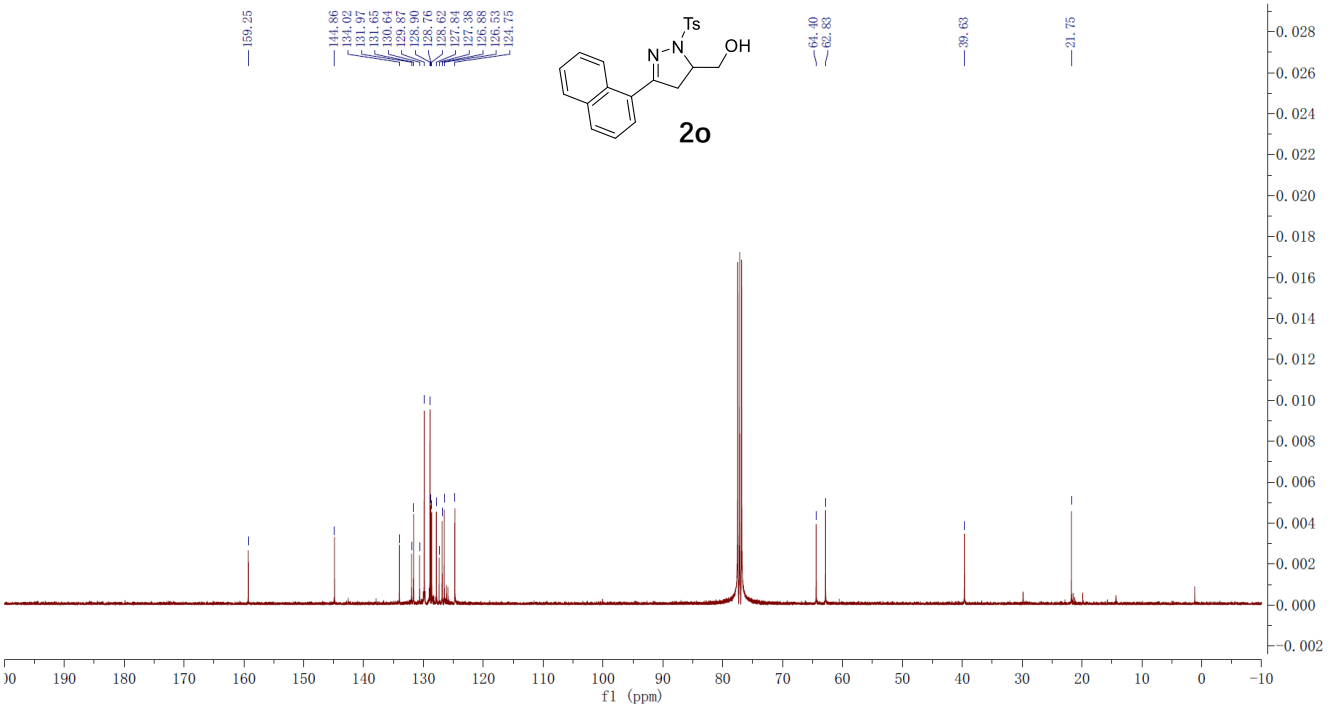

Ts
N
N
OH
Cl
2m
f1 (ppm)

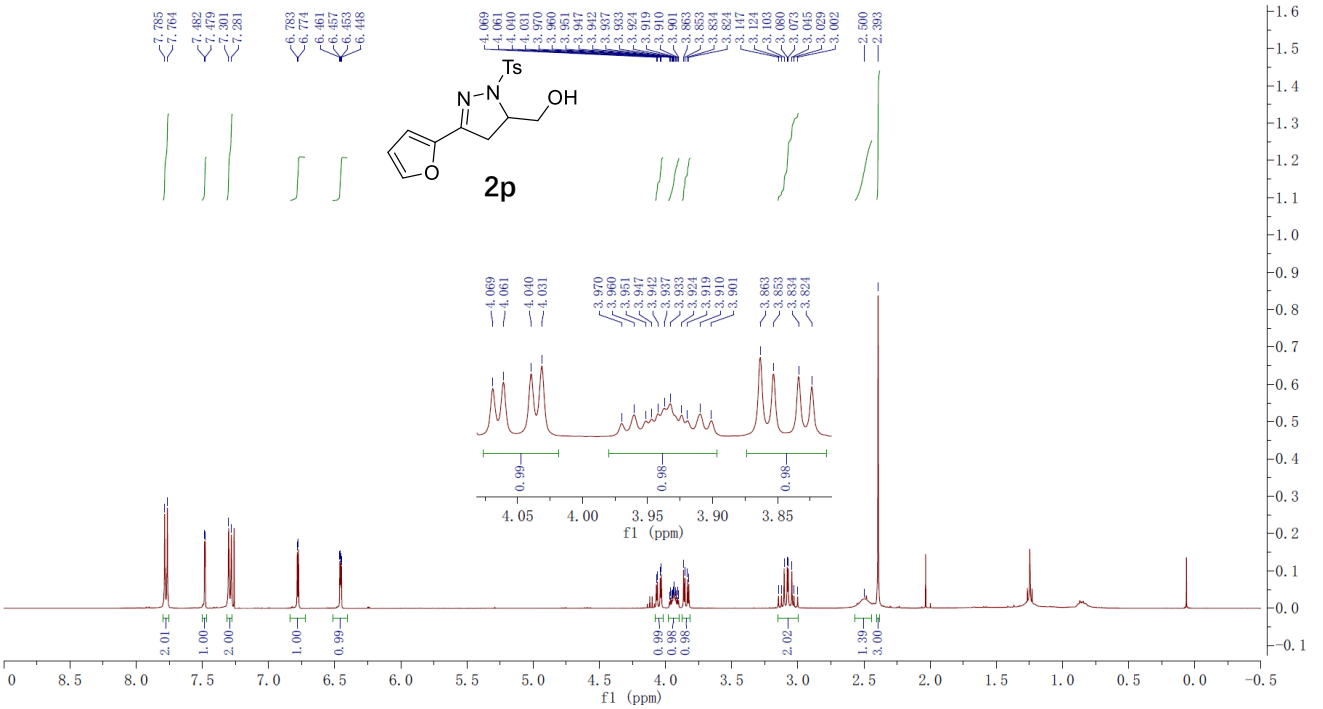

Ts
N
N
OH
Cl
2m
f1 (ppm)

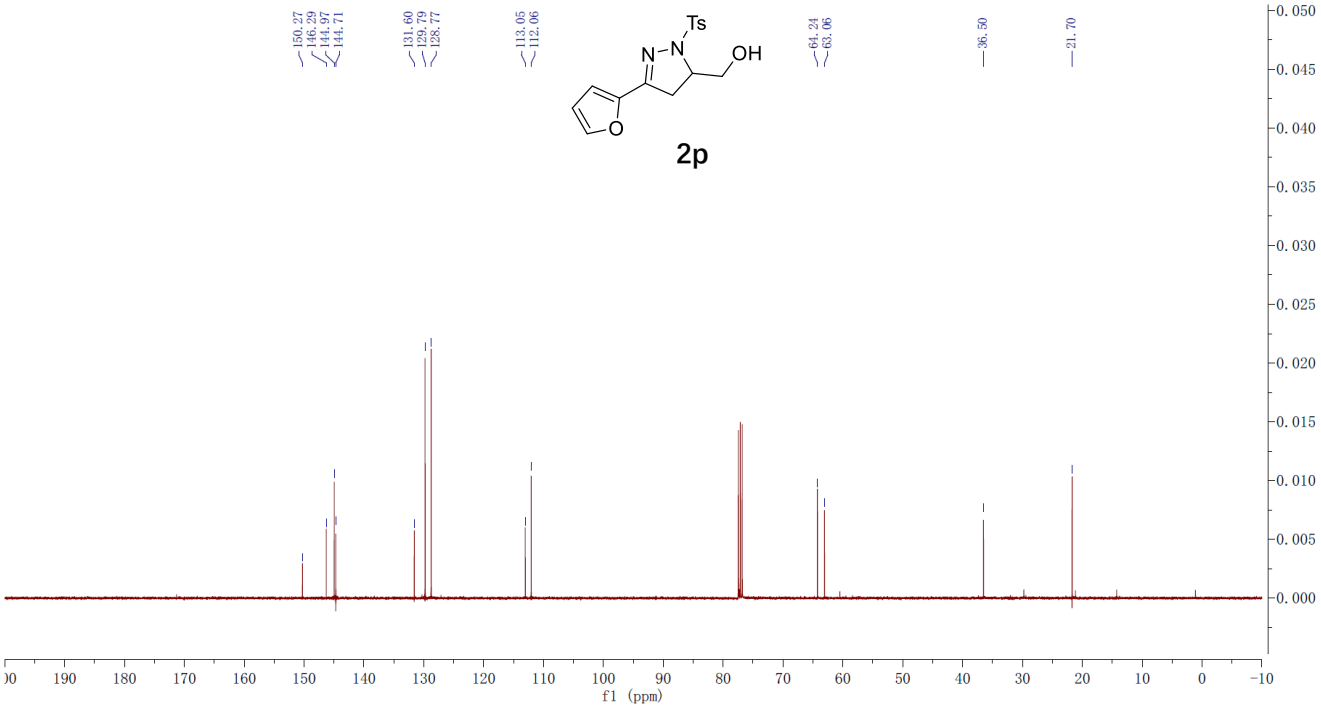

Ts
Cl
N
N
OH
2n
f1 (ppm)

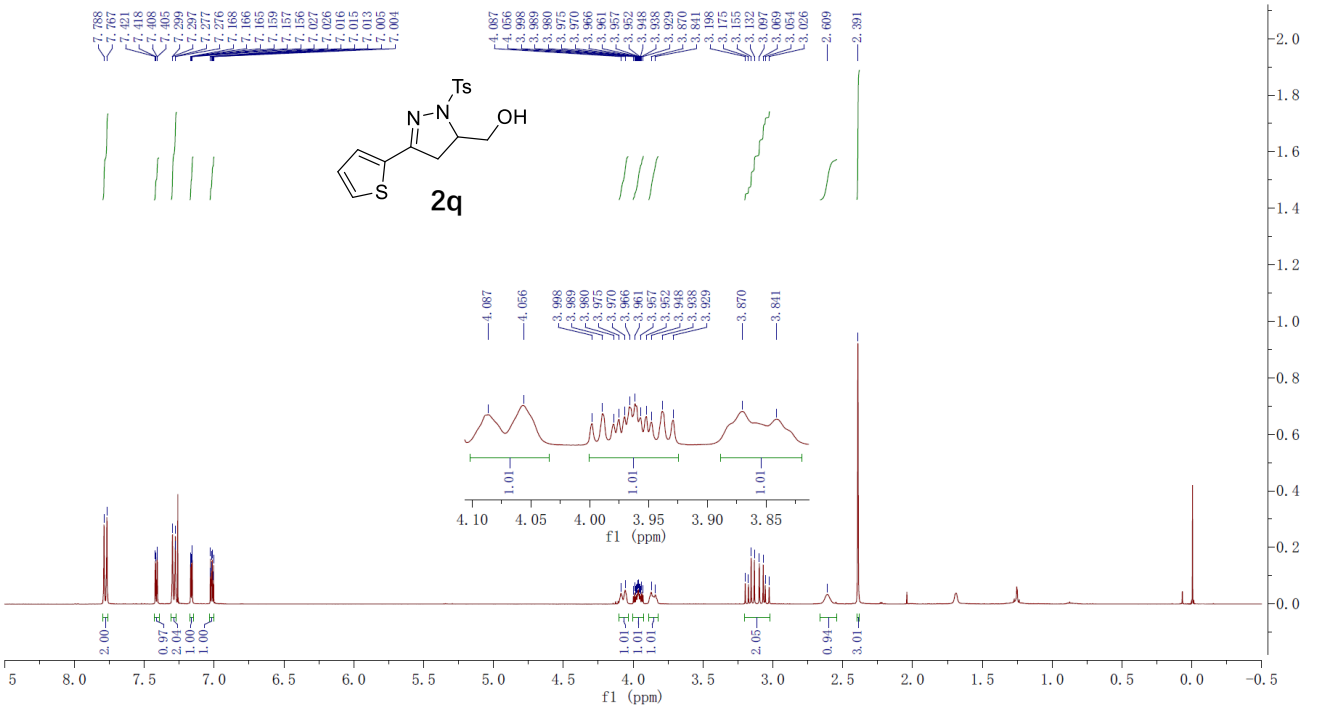

Ts
Cl
N
N
OH
2n
f1 (ppm)

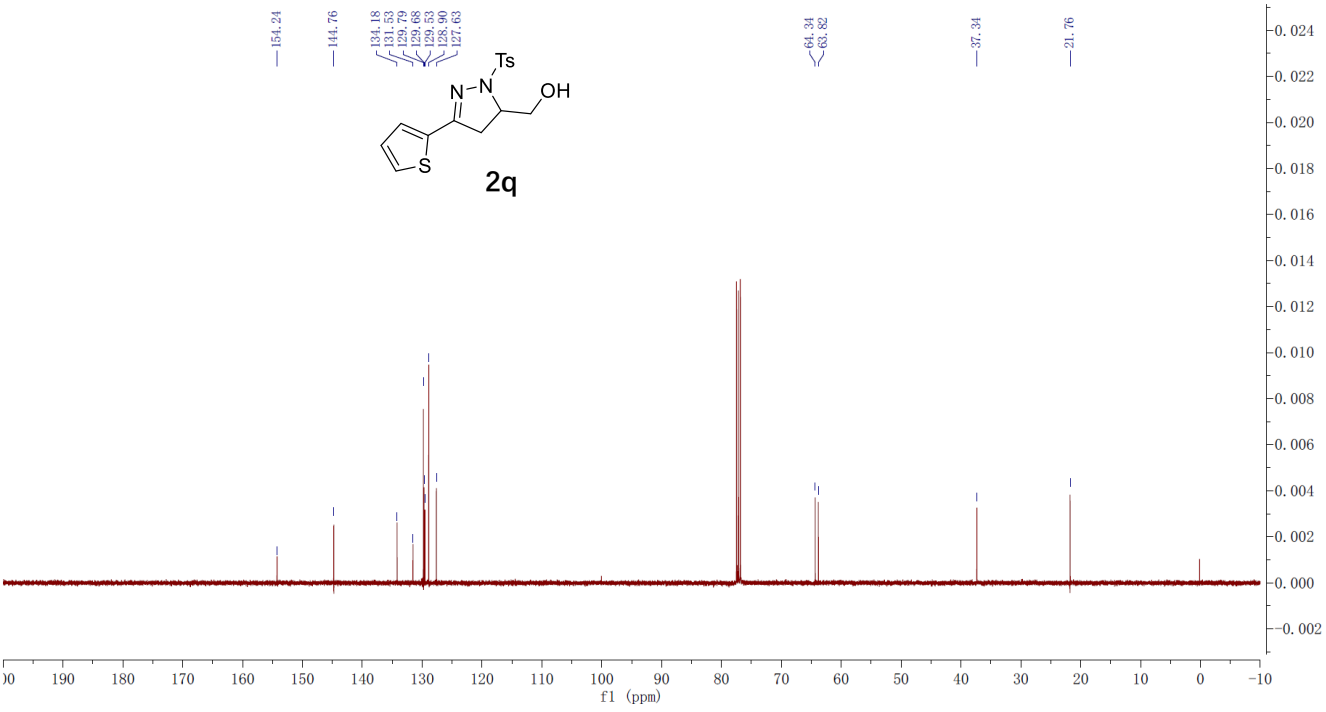

Ts
N
N
OH
2o
f1 (ppm)

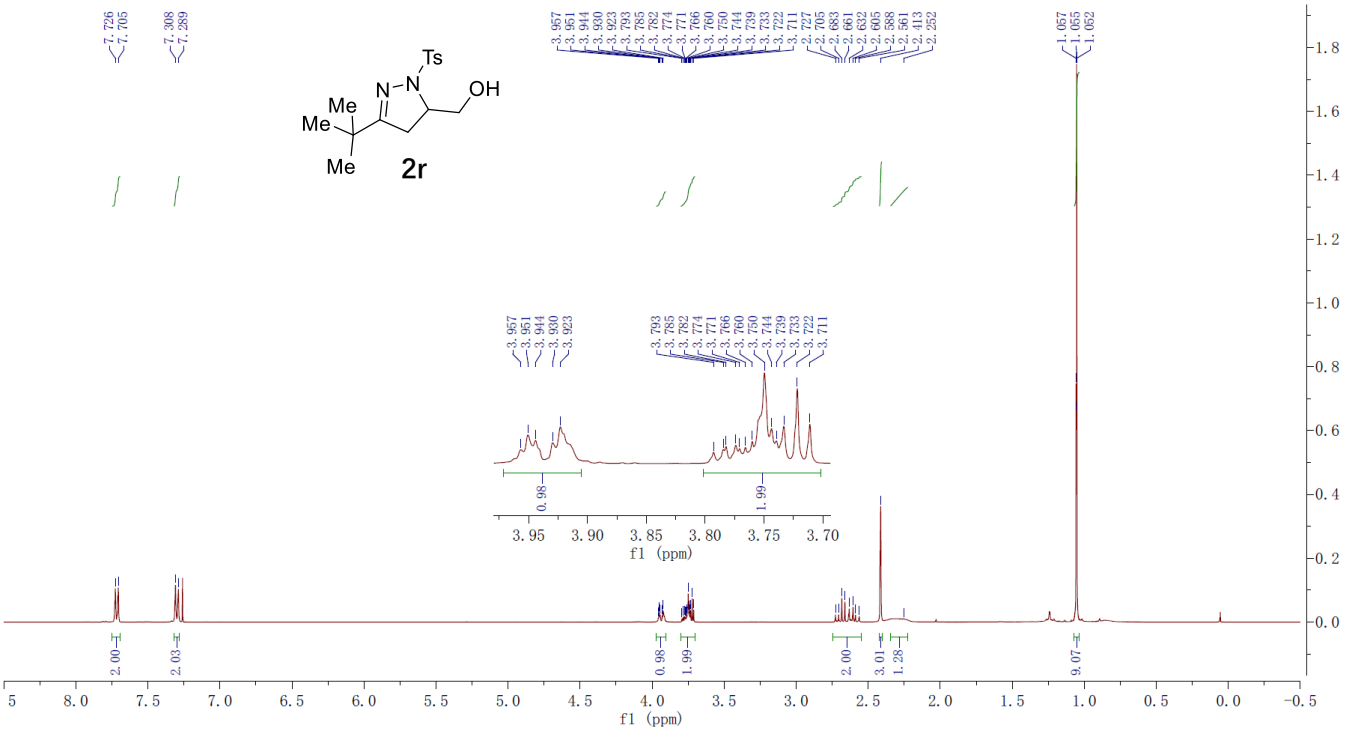

Ts
N
N
OH
2o
f1 (ppm)

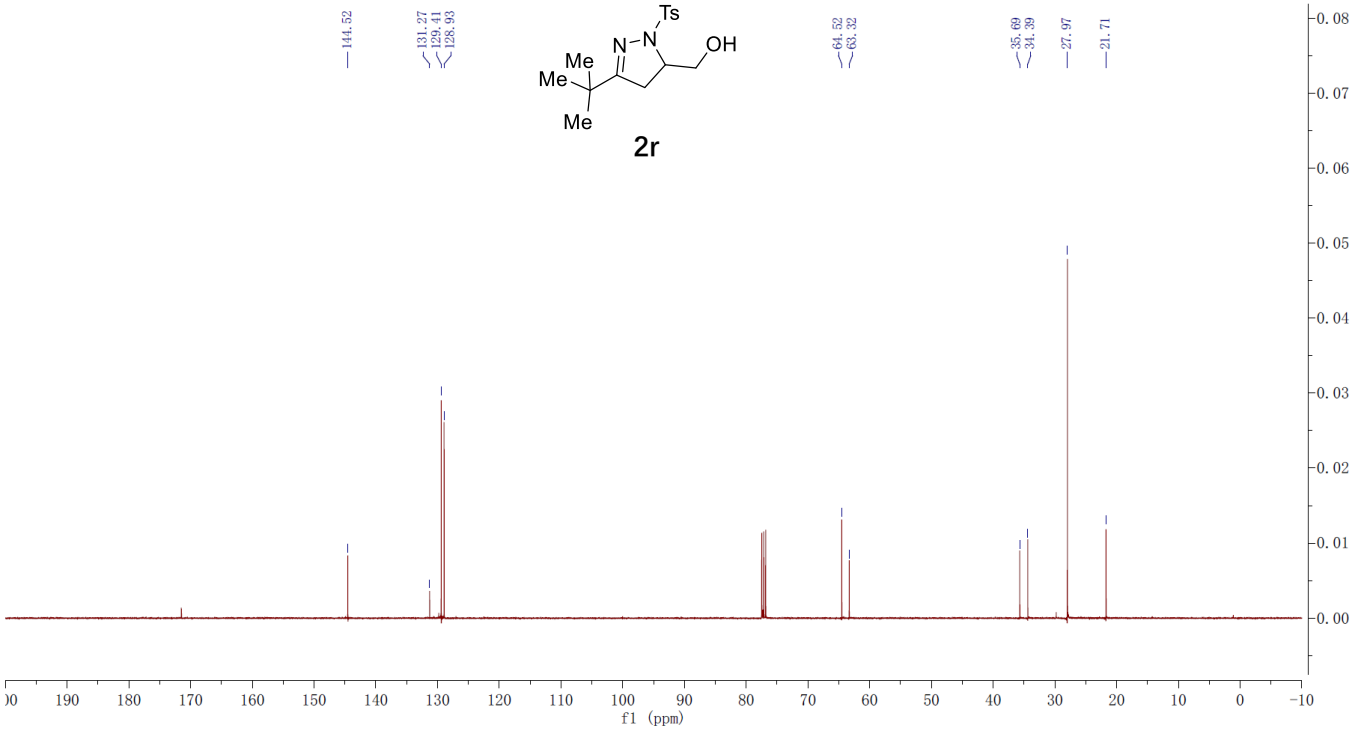

Ts
N
N
OH
O
2p
f1 (ppm)

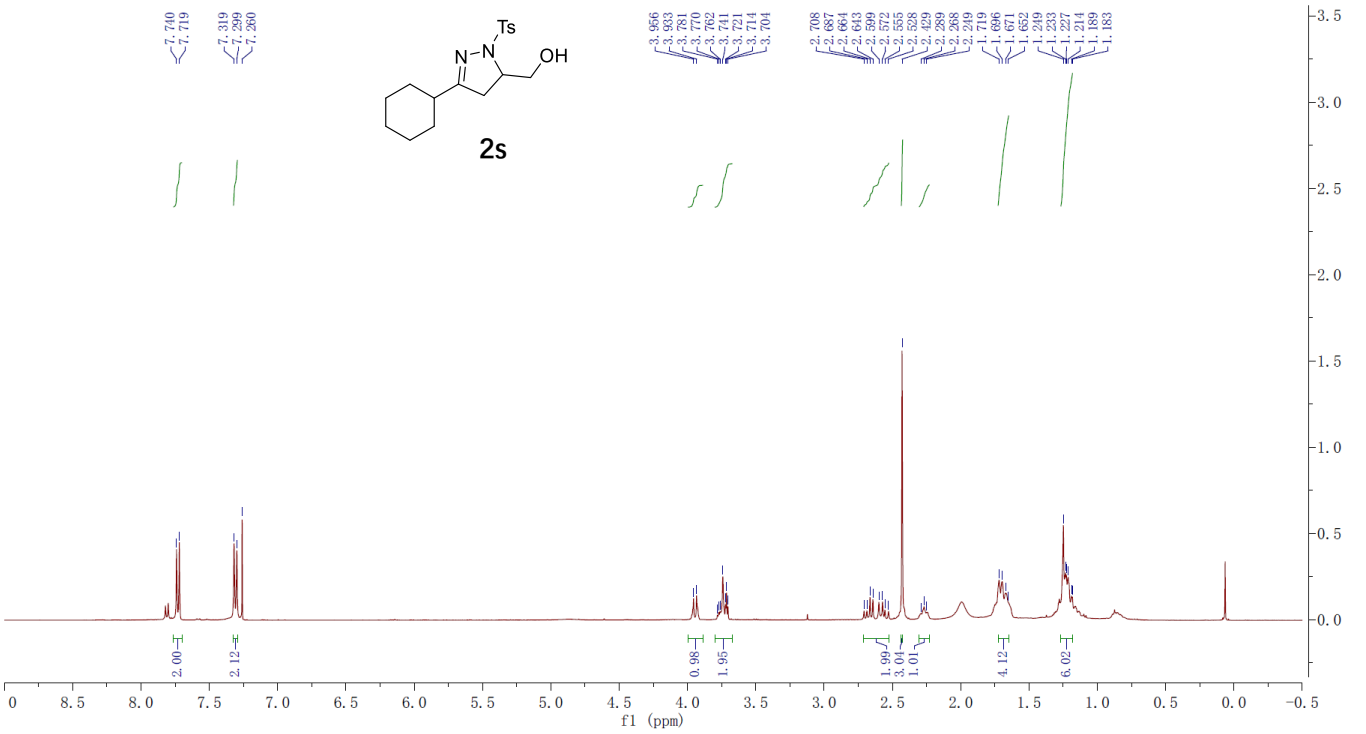

Ts
N
N
OH
O
2p
f1 (ppm)

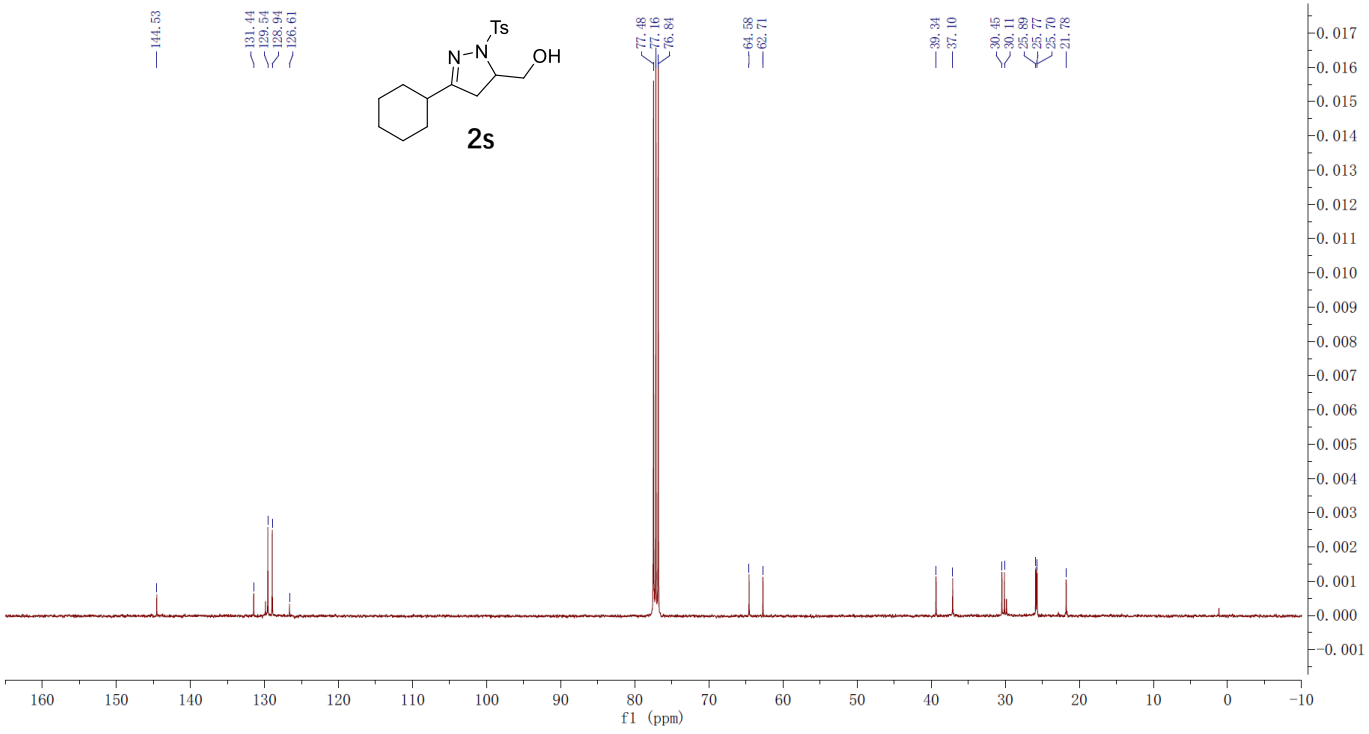

Ts
N
N
OH
S
2q
f1 (ppm)

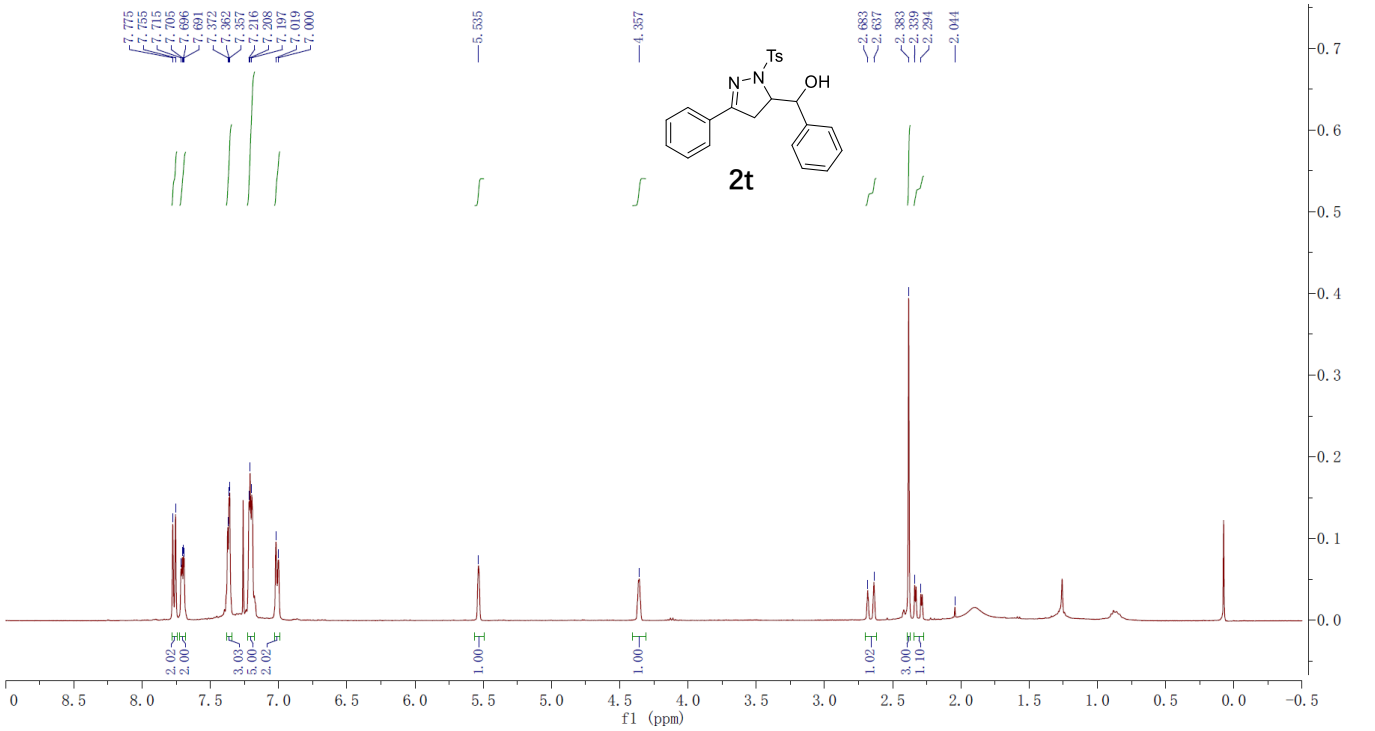

Ts
N
N
OH
S
2q
f1 (ppm)

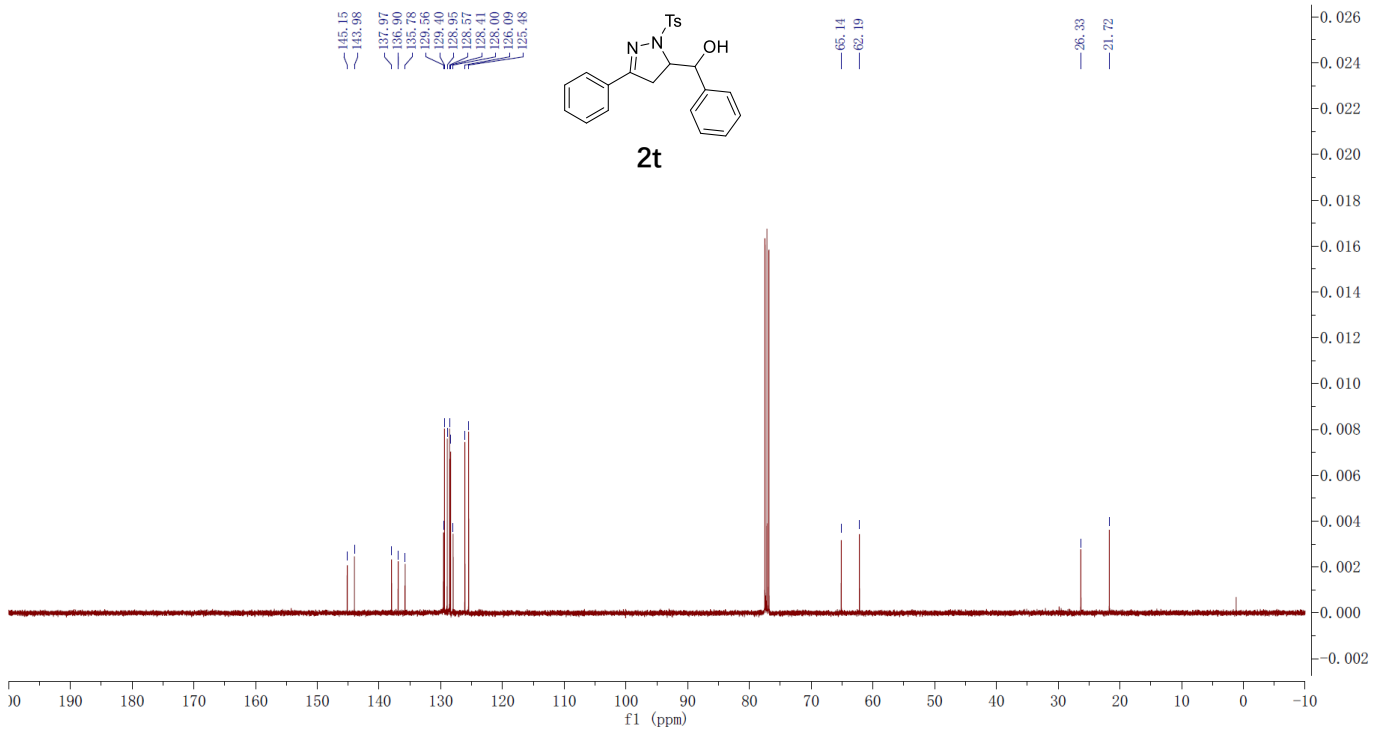

Ts
N
N
OH
Me
Me
Me
2r
f1 (ppm)

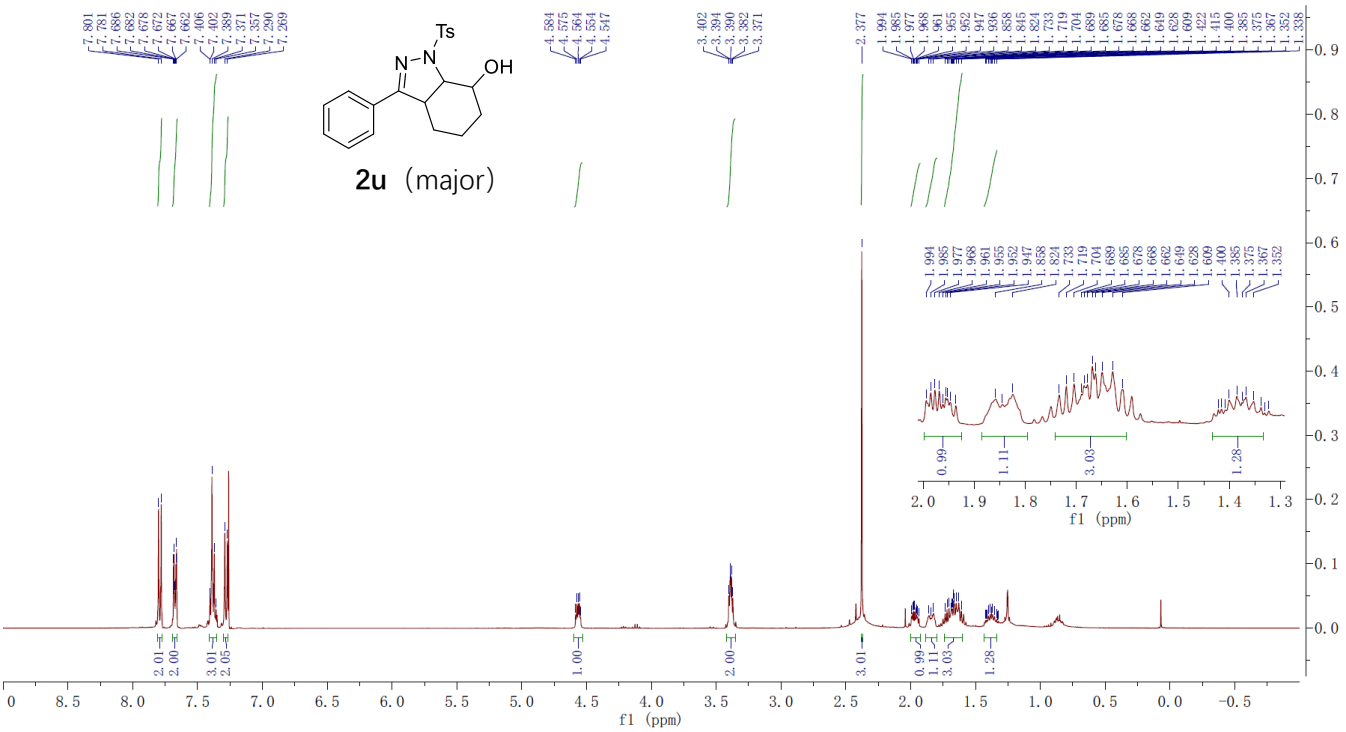

Ts
N
N
OH
Me
Me
Me
2r
f1 (ppm)

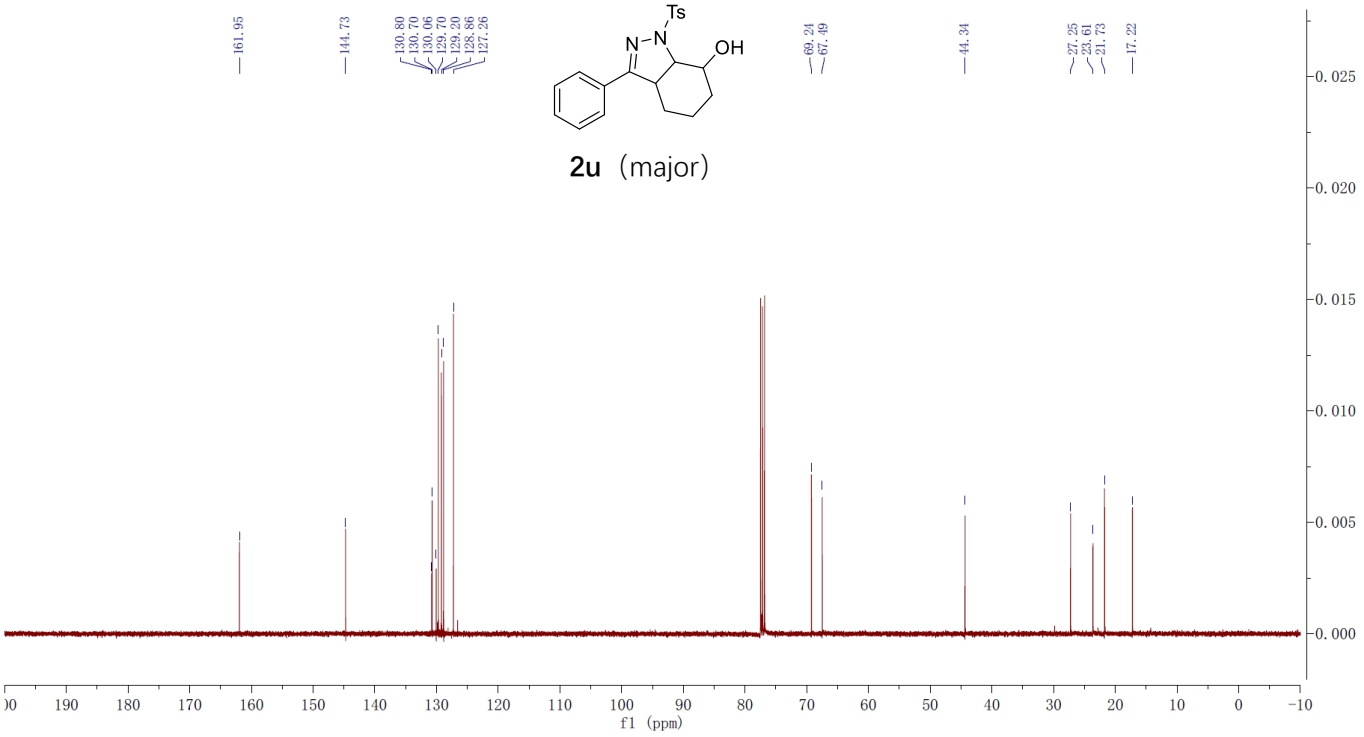

7.740
7.719
7.319
7.299
7.260
3.956
3.783
3.781
3.770
3.762
3.741
3.721
3.714
3.704
2.708
2.687
2.664
2.643
2.599
2.572
2.555
2.528
2.429
2.289
2.268
2.249
1.719
1.696
1.671
1.652
1.249
1.233
1.227
1.214
1.189
1.183
Ts
N
N
OH
2s
2.00
2.12
0.98
1.95
1.99
3.04
1.01
4.12
6.02
f1 (ppm)

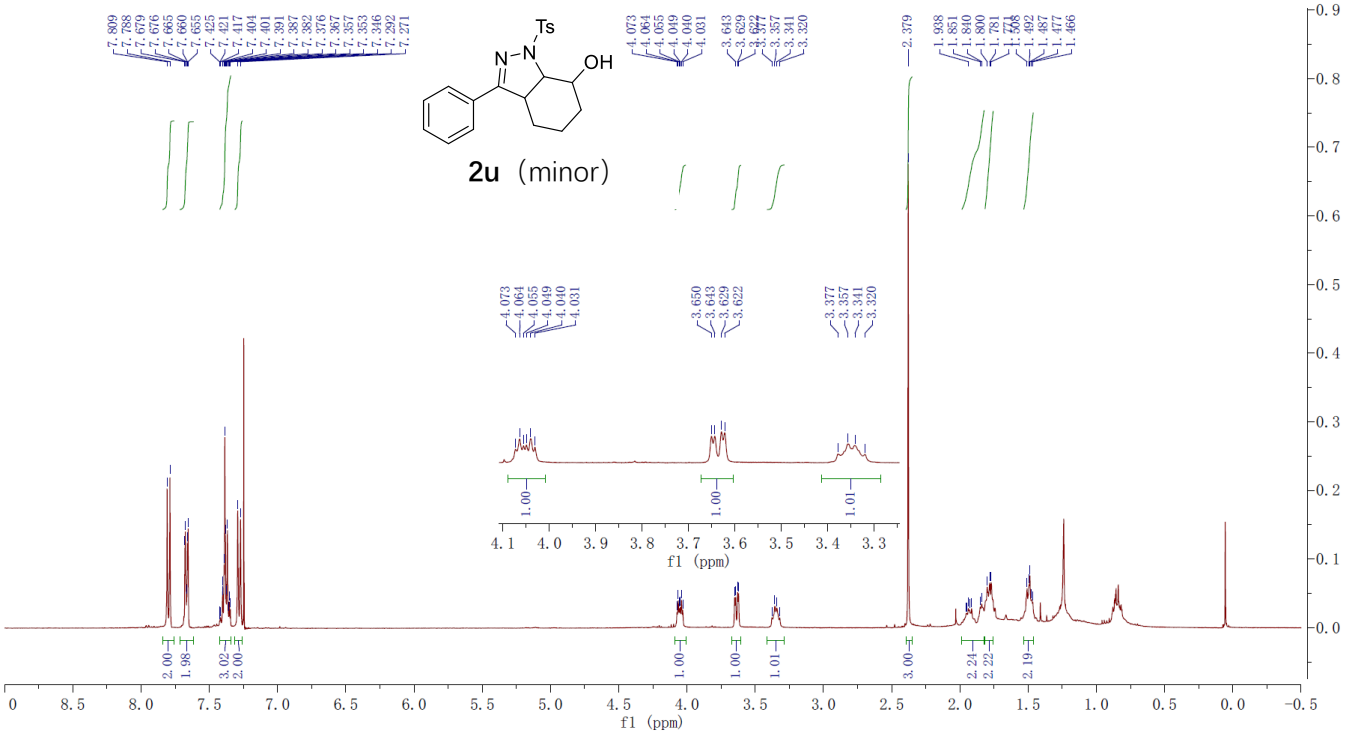

144.53
131.44
129.54
128.94
126.61
77.48
77.16
76.84
64.58
62.71
39.34
37.10
30.45
30.11
25.89
25.77
25.70
21.78
Ts
N
N
OH
2s
f1 (ppm)

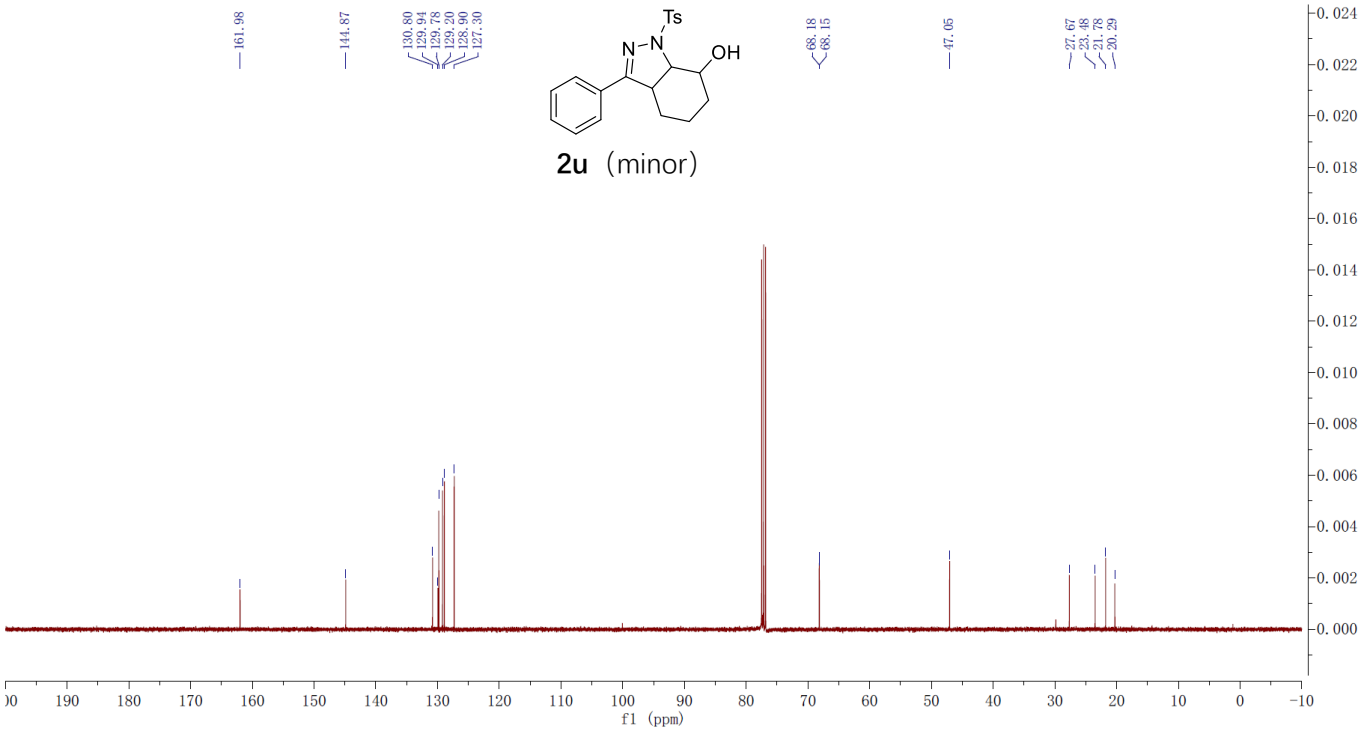

7.775
7.755
7.715
7.705
7.696
7.691
7.372
7.362
7.357
7.216
7.208
7.197
7.019
7.000
5.535
4.357
2.683
2.637
2.383
2.339
2.294
2.044
Ts
N
N
OH
2t
2.02
2.00
3.03
3.00
2.02
1.00
1.00
1.02
3.00
1.10
f1 (ppm)

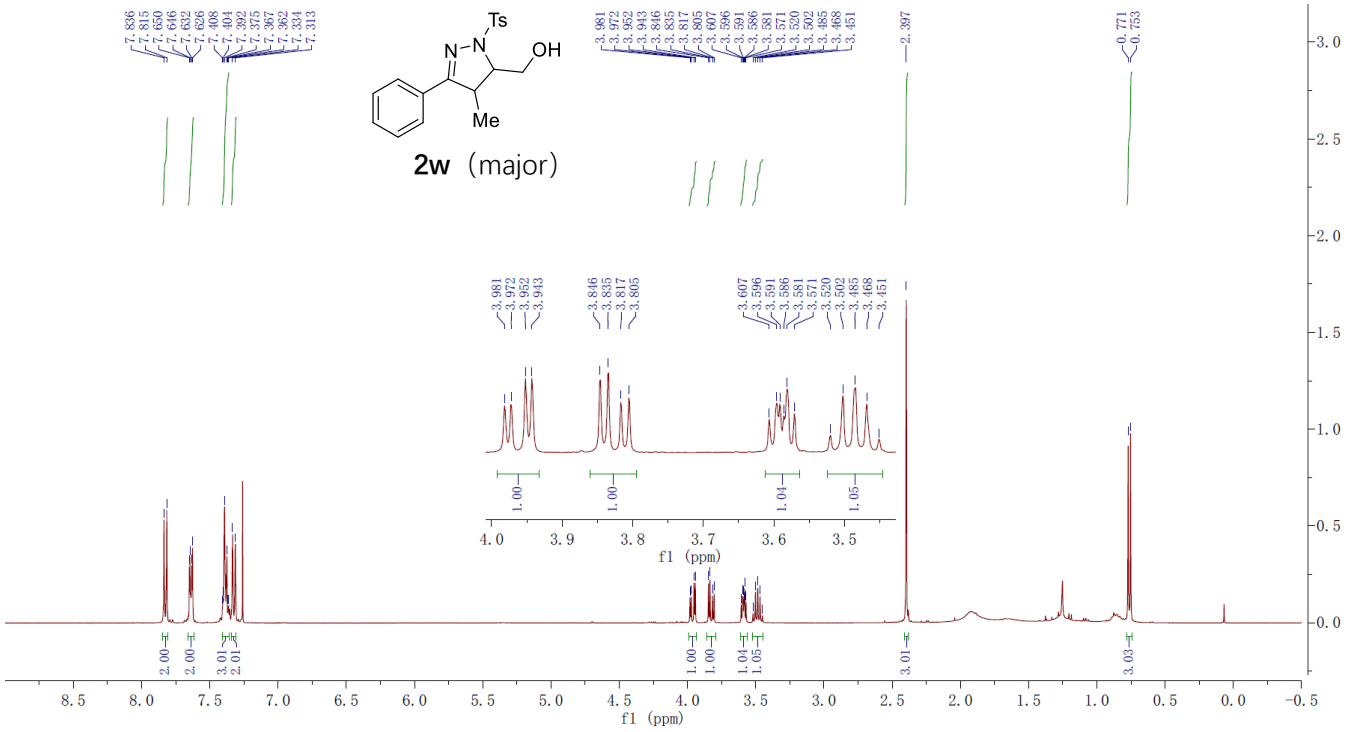

145.15
143.98
137.97
136.90
135.78
129.56
129.40
128.95
128.57
128.41
128.00
126.09
125.48
65.14
62.19
26.33
21.72
Ts
N
N
OH
2t
f1 (ppm)

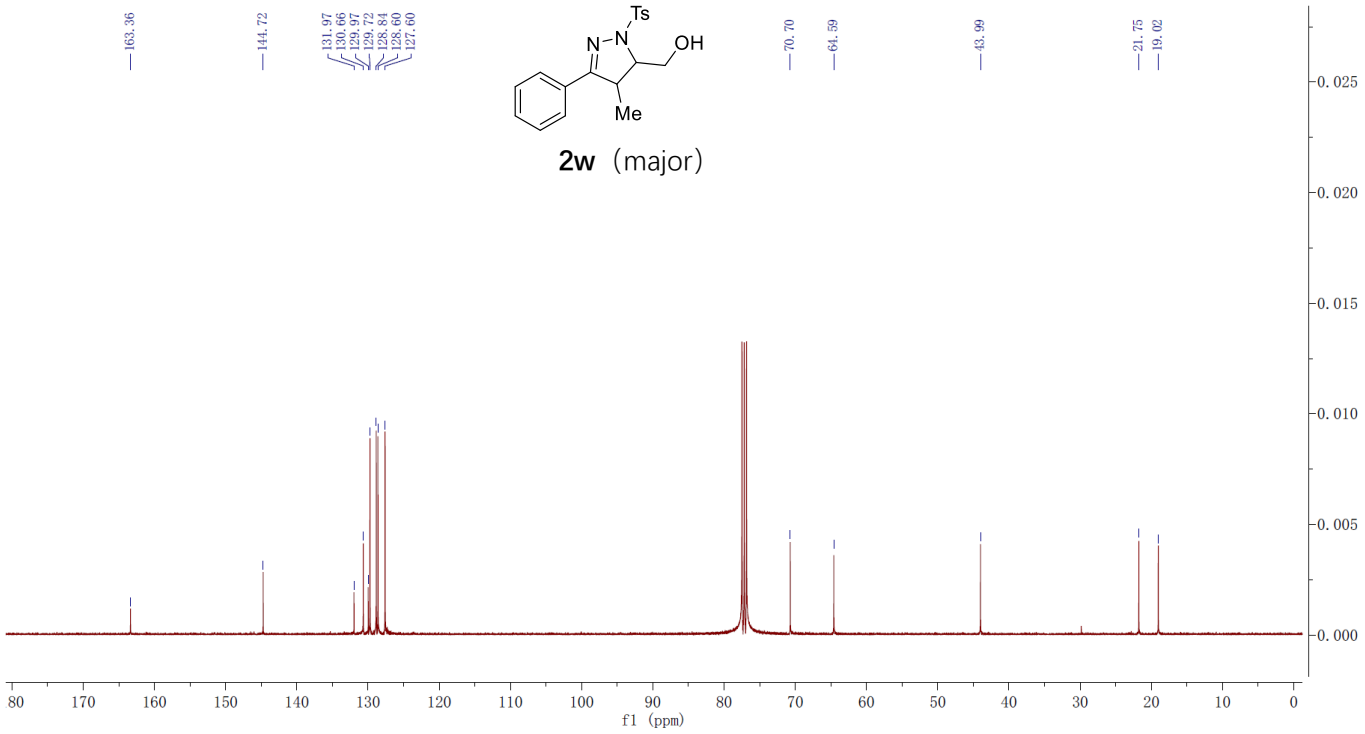

Ts
N
N
OH
2u (major)
f1 (ppm)

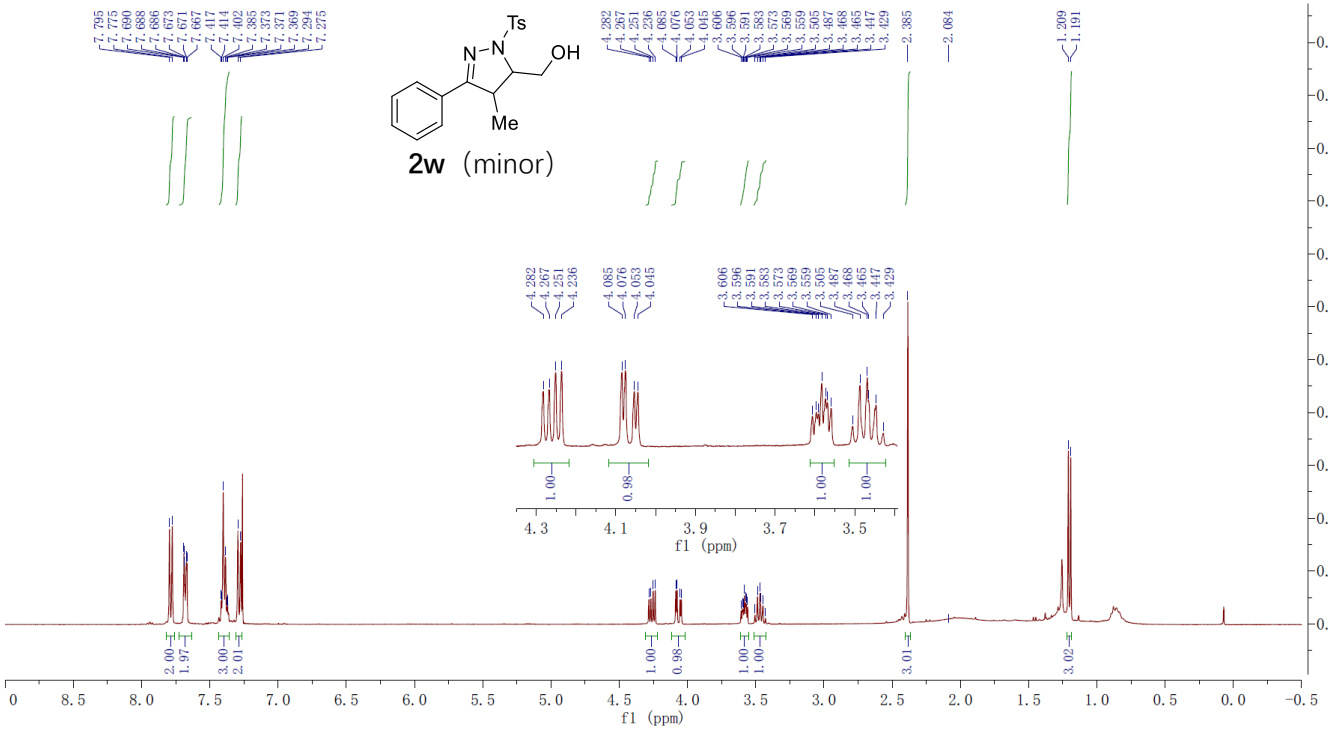

Ts
N
N
OH
2u (major)
f1 (ppm)

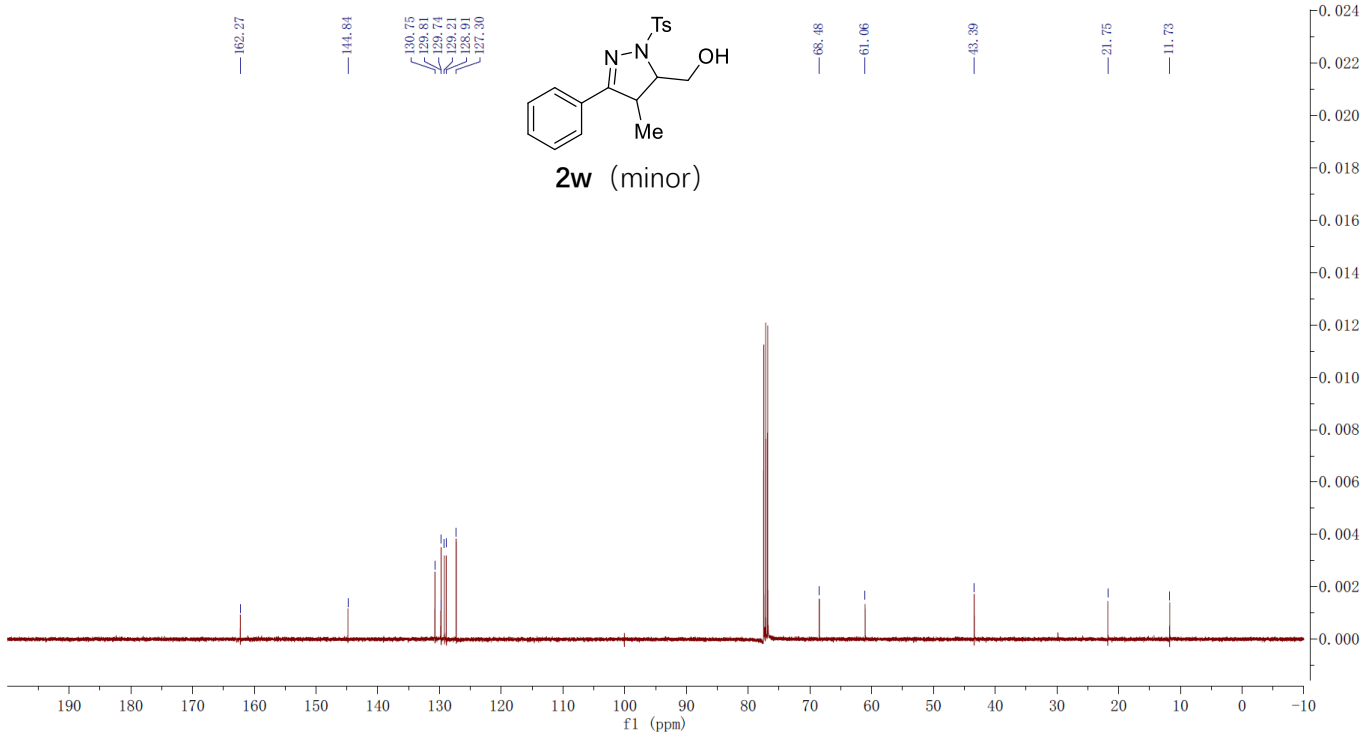

Ts
N
N
OH
2u (minor)
f1 (ppm)

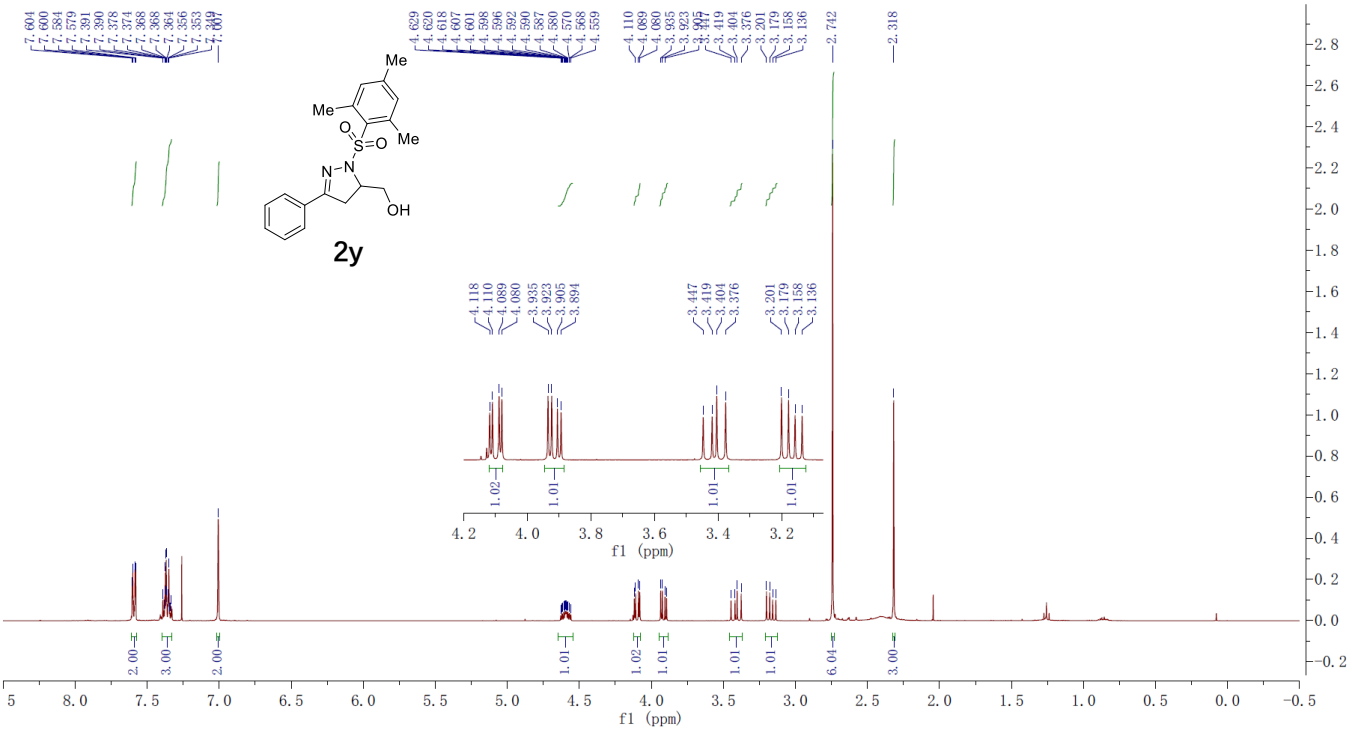

Ts
N
N
OH
2u (minor)
f1 (ppm)

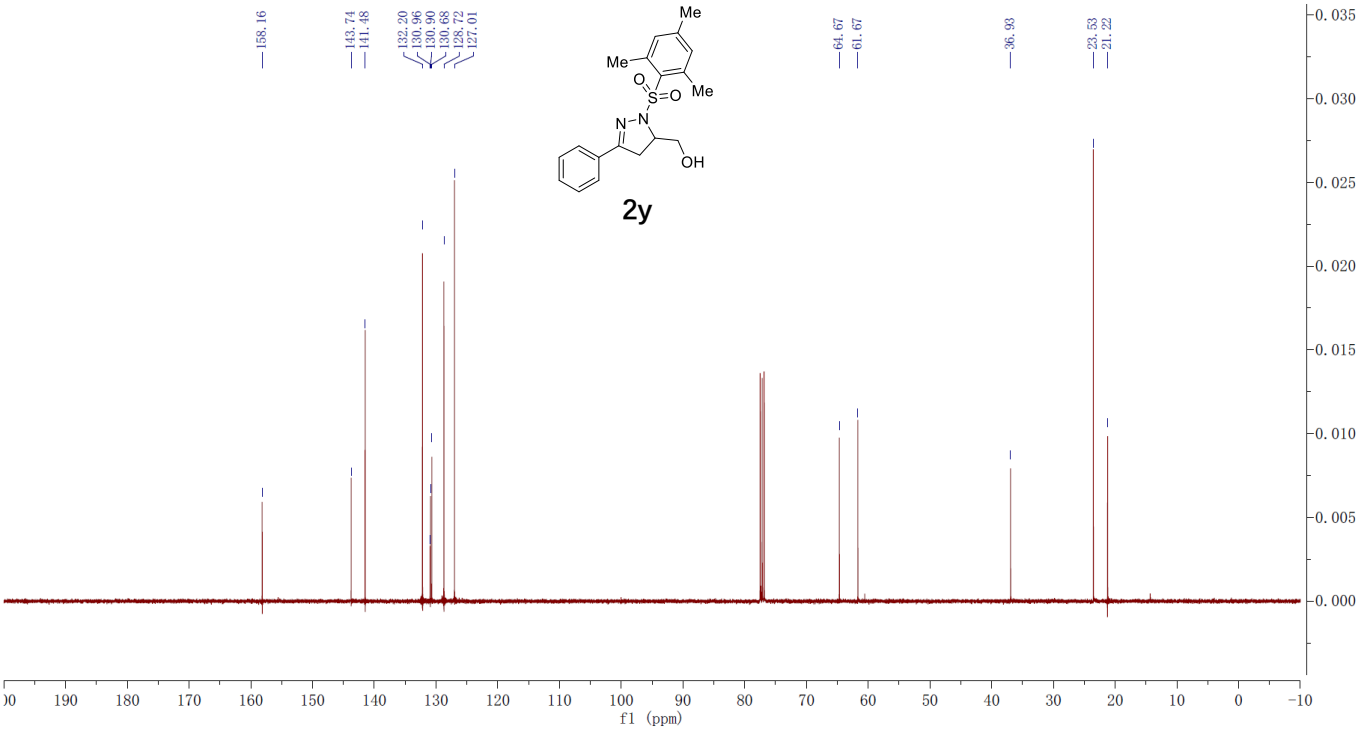

Ts
N
N
OH
Me
2w (major)
7.836
7.815
7.650
7.646
7.632
7.626
7.408
7.404
7.392
7.375
7.367
7.362
7.334
7.313
3.981
3.972
3.952
3.943
3.846
3.835
3.817
3.805
3.607
3.596
3.591
3.586
3.581
3.571
3.520
3.502
3.485
3.468
3.451
2.397
0.771
0.753
1.00
1.00
1.04
1.05
f1 (ppm)
2.00
2.00
3.01
2.01
1.00
1.00
1.04
1.05
3.01
3.03
f1 (ppm)

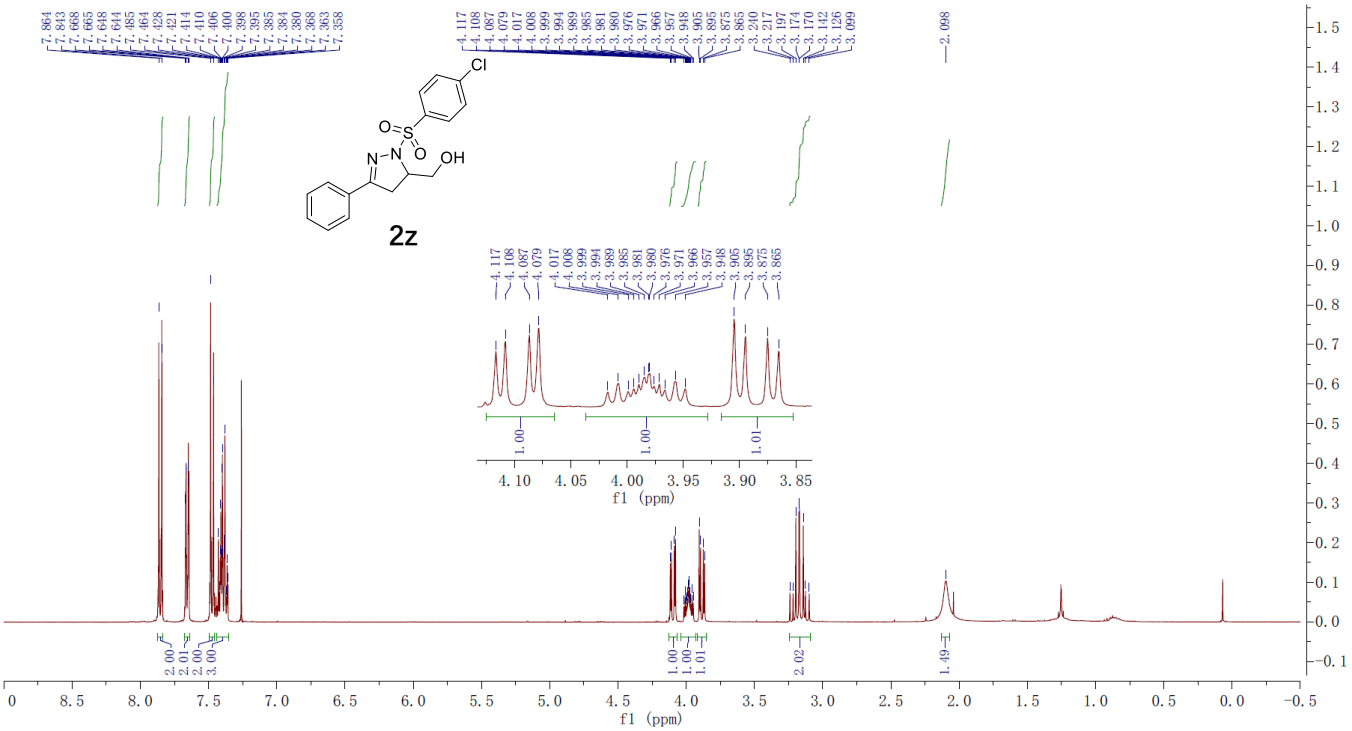

Ts
N
N
OH
Me
2w (major)
163.36
144.72
131.97
130.66
129.97
129.72
128.84
128.60
127.60
70.70
64.59
43.99
21.75
19.02
f1 (ppm)

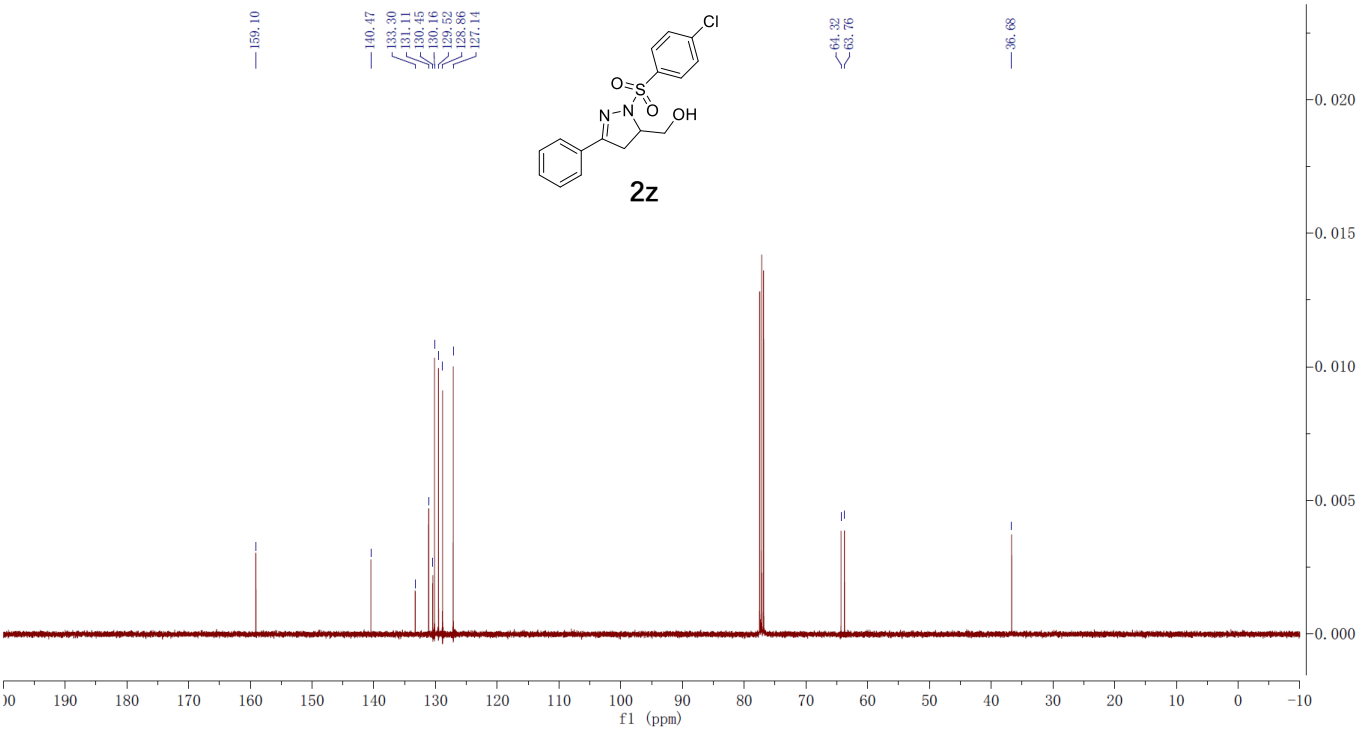

Ts
N
N
OH
Me
2w (minor)
f1 (ppm)

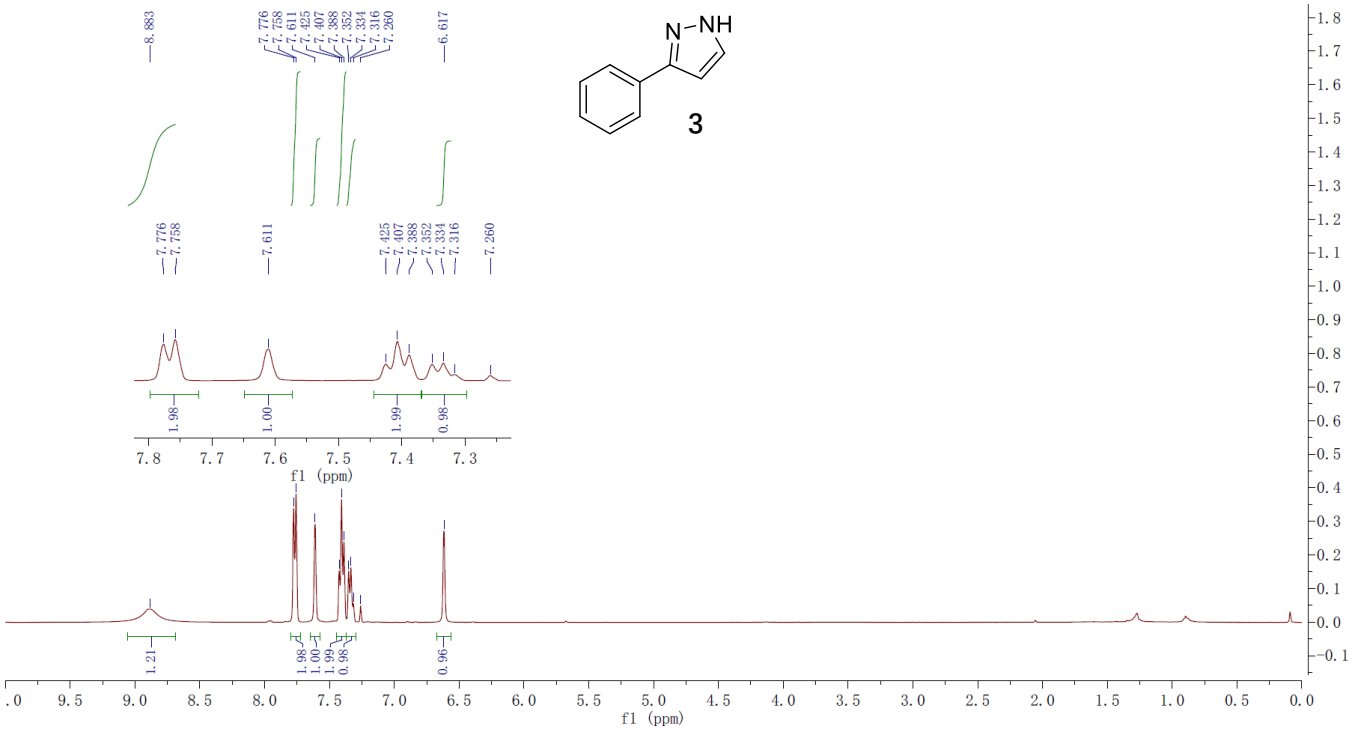

Ts
N
N
OH
Me
2w (minor)
f1 (ppm)

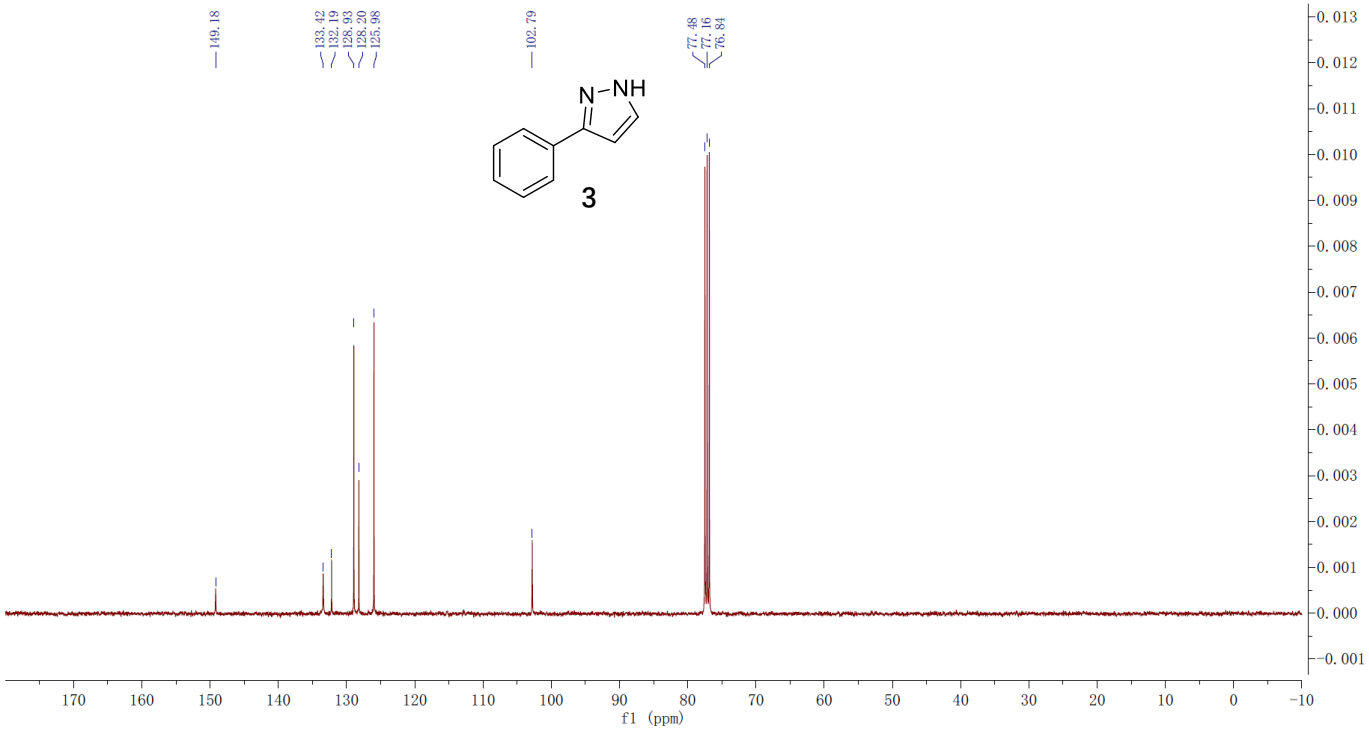

Me
Me
Me
O
S=O
N
N
OH
2y
f1 (ppm)

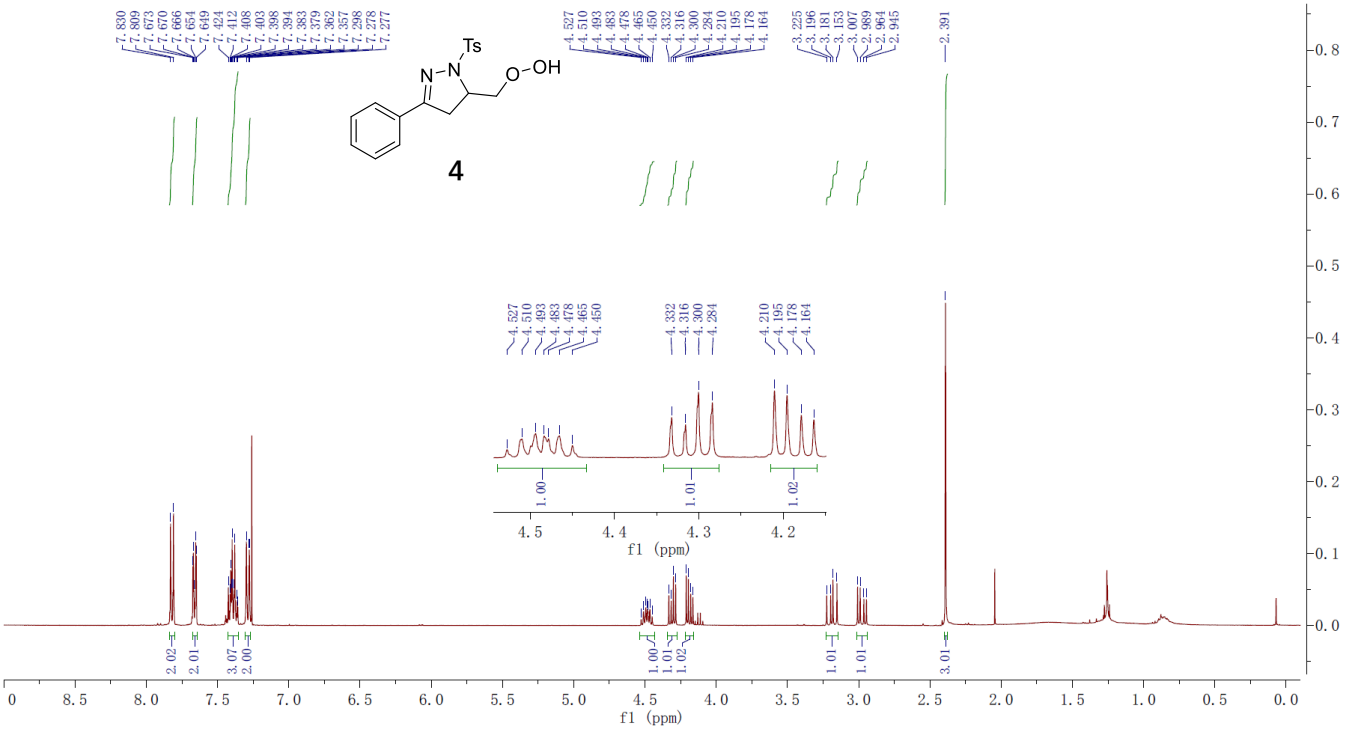

Me
Me
Me
O
S=O
N
N
OH
2y
f1 (ppm)

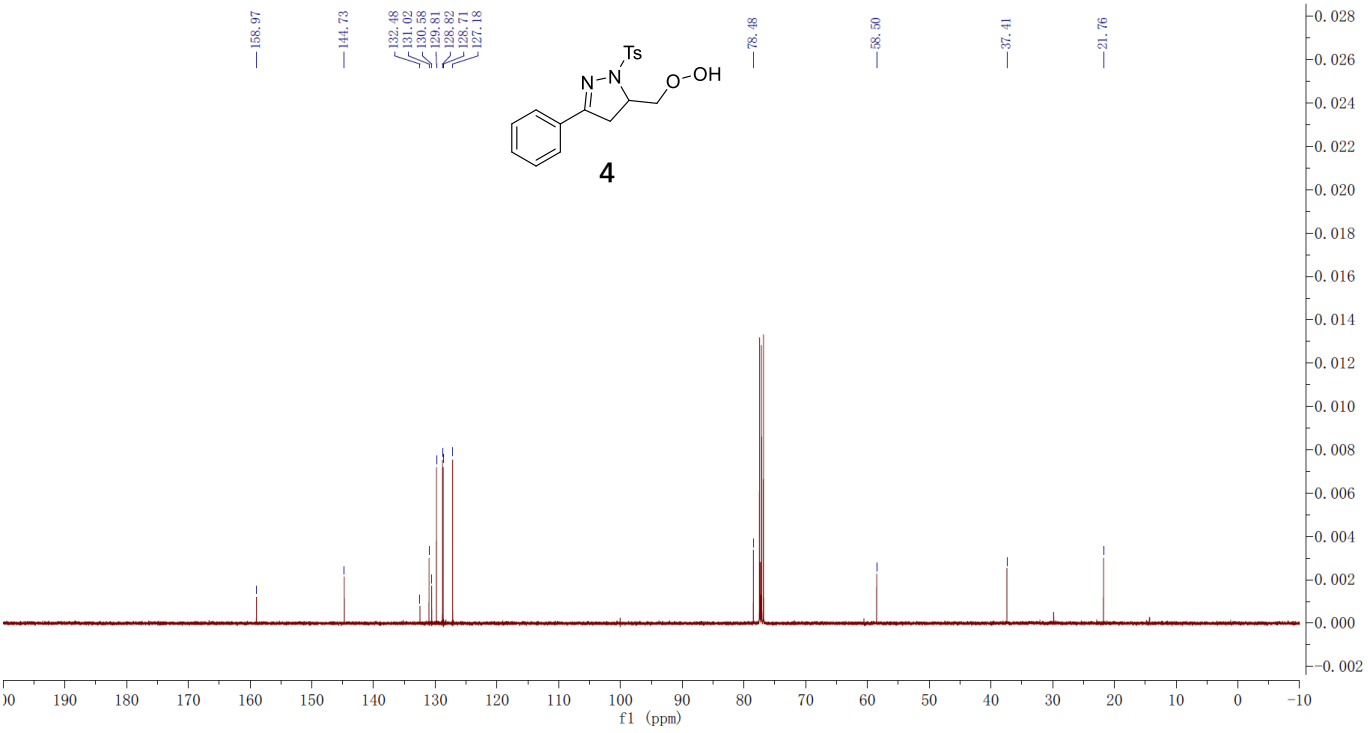

7.864
7.843
7.668
7.665
7.648
7.644
7.485
7.464
7.428
7.421
7.414
7.410
7.406
7.400
7.398
7.395
7.385
7.384
7.380
7.368
7.363
7.358
4.117
4.108
4.087
4.079
4.017
4.008
3.999
3.994
3.989
3.985
3.981
3.980
3.976
3.971
3.966
3.957
3.948
3.905
3.895
3.875
3.865
3.240
3.217
3.197
3.174
3.170
3.142
3.126
3.099
2.098
Cl
O
S
O
N
N
O
OH
2z
1.00
1.00
1.01
4.10
4.05
4.00
3.95
3.90
3.85
f1 (ppm)
2.00
2.01
2.00
2.00
3.00
1.00
1.00
1.01
2.02
1.49
f1 (ppm)

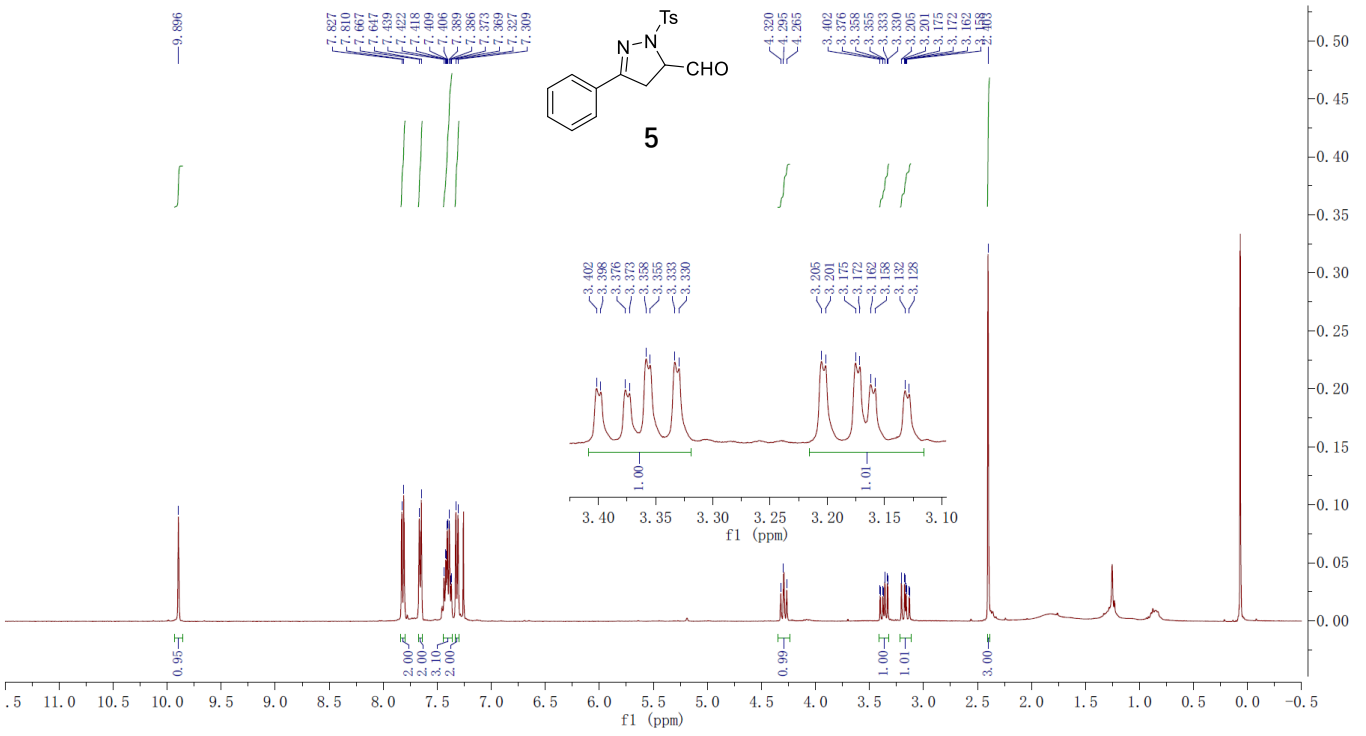

159.10
140.47
133.30
131.11
130.45
130.16
129.52
128.86
127.14
64.32
63.76
36.68
Cl
O
S
O
N
N
O
OH
2z
f1 (ppm)

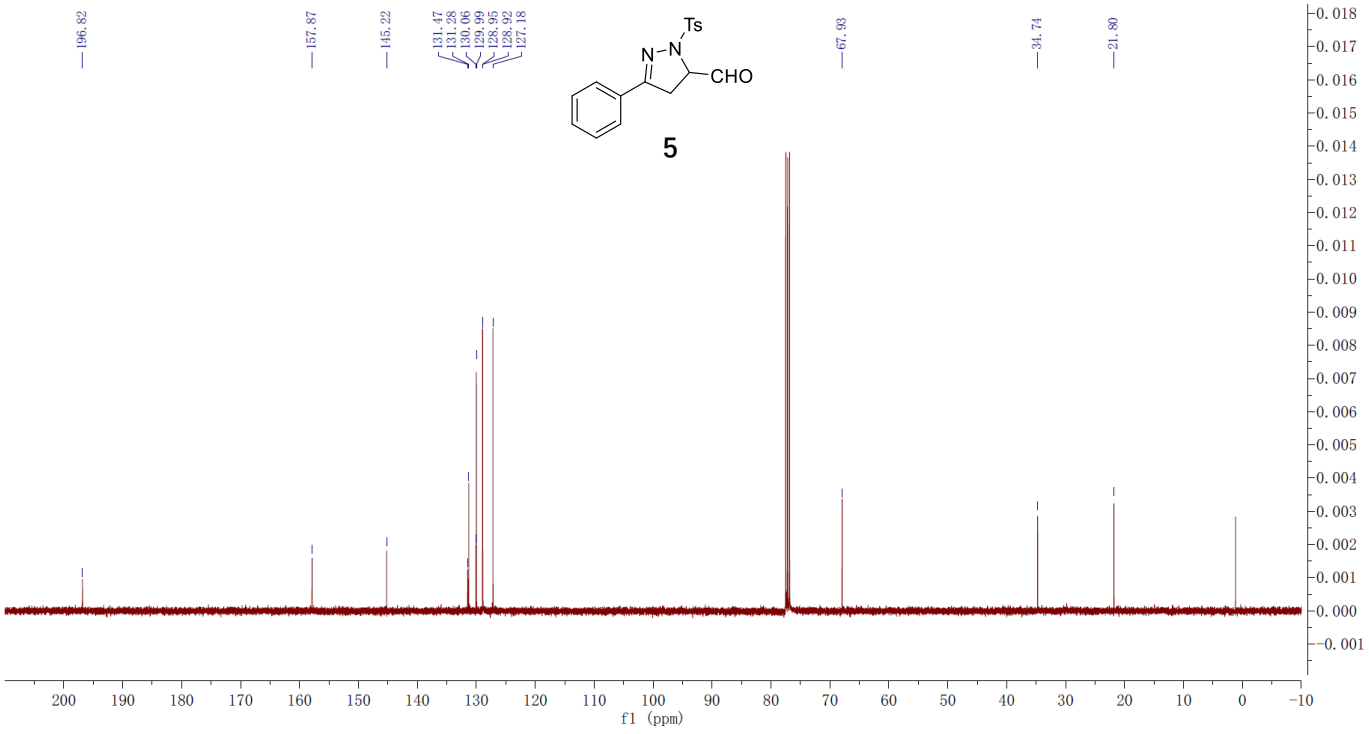

8.883
7.776
7.758
7.611
7.425
7.407
7.388
7.352
7.334
7.316
7.260
6.617
N-NH
3
1.98
1.00
1.99
0.98
f1 (ppm)
1.21
1.98
1.00
1.99
0.98
0.96
f1 (ppm)

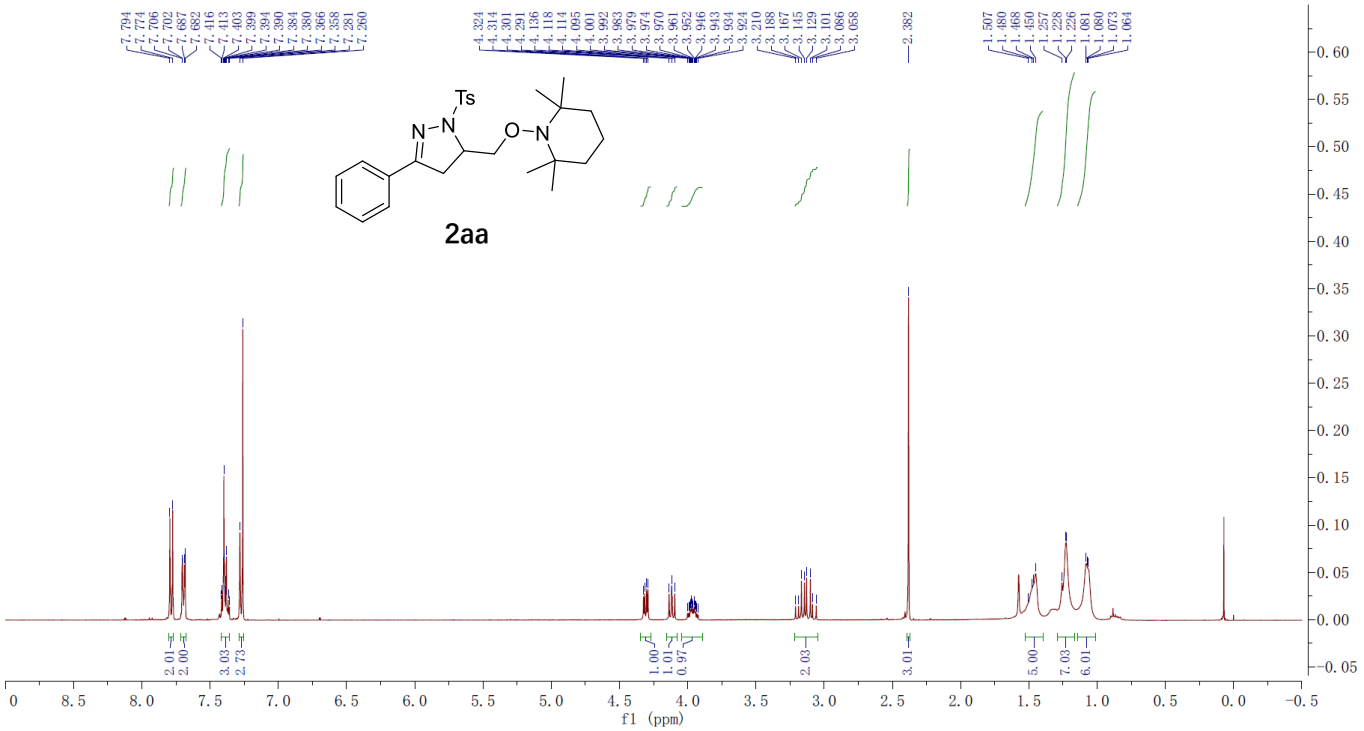

149.18
133.42
132.19
128.93
128.20
125.98
102.79
77.48
77.16
76.84
N-NH
3
f1 (ppm)

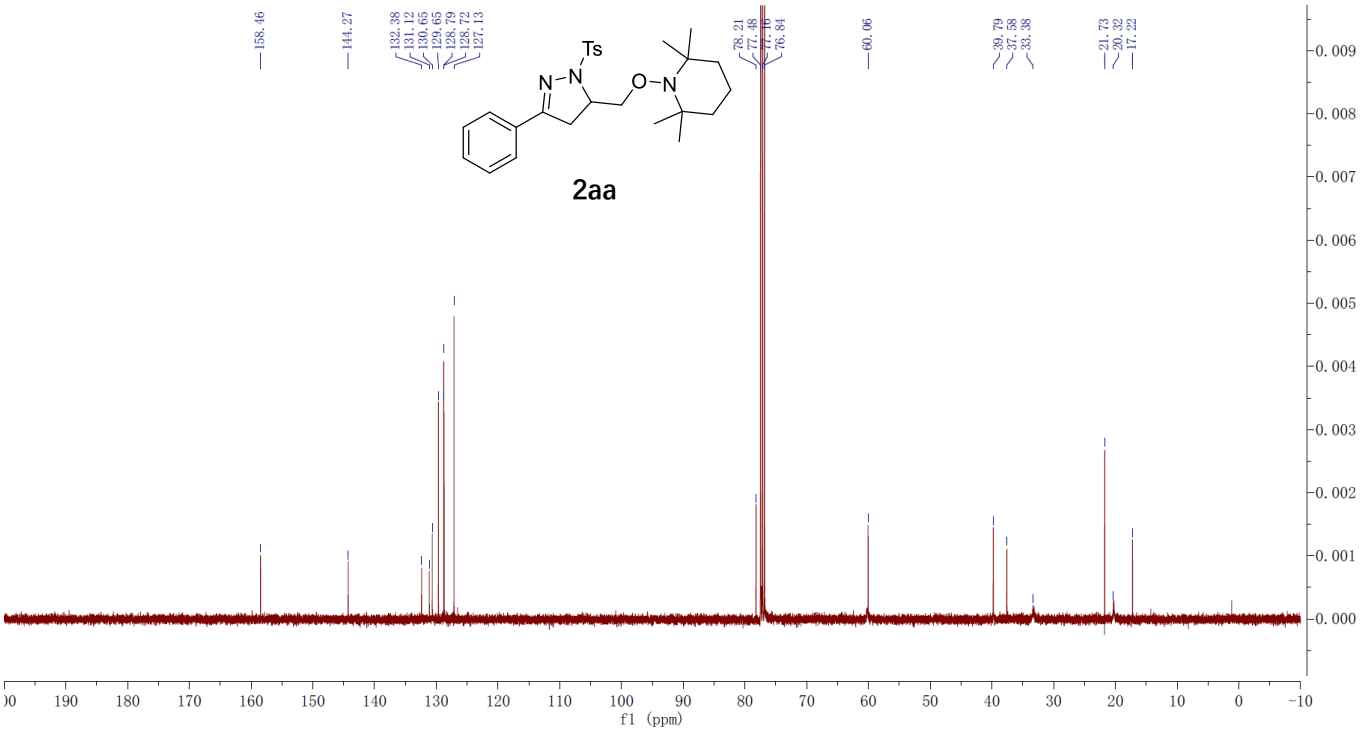

7.830
7.809
7.673
7.670
7.666
7.654
7.649
7.424
7.412
7.408
7.403
7.398
7.394
7.383
7.379
7.362
7.357
7.288
7.278
7.277
4.527
4.510
4.493
4.483
4.478
4.465
4.450
4.332
4.316
4.300
4.284
4.210
4.195
4.178
4.164
3.225
3.196
3.181
3.153
3.007
2.989
2.964
2.945
2.391
Ts
N-N
O-OH
4
1.00
1.01
1.02
4.5
4.4
4.3
4.2
f1 (ppm)
2.02
2.01
3.07
2.00
1.00
1.01
1.02
1.01
1.01
3.01
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0


158.97
144.73
132.48
131.02
130.58
129.81
128.82
128.71
127.18
78.48
58.50
37.41
21.76
Ts
N-N
O-OH
4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
0.028
0.026
0.024
0.022
0.020
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
-0.002


Ts
N
N
CHO
5
f1 (ppm)


Ts
N
N
CHO
5
f1 (ppm)


7.794
7.774
7.706
7.702
7.687
7.682
7.416
7.413
7.403
7.399
7.394
7.390
7.384
7.380
7.366
7.358
7.281
7.260
4.324
4.314
4.301
4.291
4.136
4.118
4.114
4.095
4.001
3.992
3.983
3.979
3.974
3.970
3.961
3.952
3.946
3.943
3.934
3.924
3.210
3.188
3.167
3.145
3.129
3.101
3.086
3.058
2.382
1.507
1.480
1.468
1.450
1.257
1.228
1.226
1.081
1.080
1.073
1.064
Ts
N
N
O
N
2aa
2.01
2.00
3.03
2.73
1.00
1.01
0.97
2.03
3.01
5.00
7.03
6.01
f1 (ppm)


158.46
144.27
132.38
131.12
130.65
129.65
128.79
128.72
127.13
78.21
77.48
77.16
76.84
60.06
39.79
37.58
33.38
21.73
20.32
17.22
Ts
N
N
O
N
2aa
f1 (ppm)