Supplementary Information

Growth vector elaboration of fragments: regioselective functionalization of 5-hydroxy-6-azaindazole and 3-hydroxy-2,6-naphtyridine

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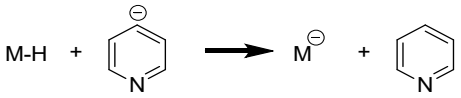
1. SOLUTION GIBBS ENERGIES (G_{sol})

pKa values were computed using the following isodesmic reaction:



pKa values were obtained in DMSO solvent system, performed by PCM model using single-point calculations with B3LYP/6-311++G(d,p)//B3LYP/6-31+G(d,p) model. The solvation Gibbs energies were obtained to deprotonation reaction using pyridine as reference compound.

Gibbs energies in solution for neutral and deprotonated species. All the values were obtained in B3LYP/6-311++G(d,p) using DMSO in PCM. Values in Hartree.

In order to predict the regioselectivity, we employed density-functional theory (DFT) calculations as previously done in several studies to describe radical functionalization in heterocycle compounds.[1] To estimate the reactivity of the hydroxypyridine moiety, pKa values were calculated using isodesmic reactions[2-7] in dimethyl sulfoxide (DMSO) using the proteochemometric (PCM) model and single-point calculations at the B3LYP/6-311++G(d,p) level using Gaussian 03.[8-16] The solvation Gibbs energies were obtained for deprotonation reactions using pyridine as a reference compound (see the Supporting Information). The most acidic C–H was found to be next to the pyridone oxygen and pyrazole nitrogen (Figure 2).

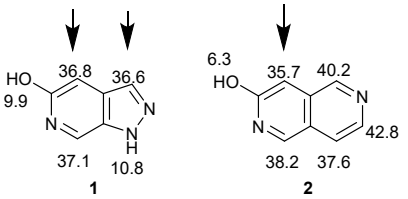


Figure 1. Calculated pKa values in DMSO for heterocycles **1** and **2** using DFT (PCM/B3LYP/6-311++G(d,p)/B3LYP/6-31+G(d,p)). Arrows indicate the predicted reactive sites for C–H activation.

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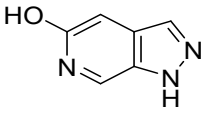
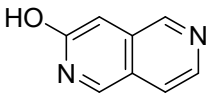
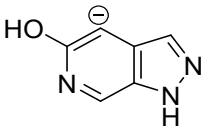
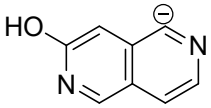
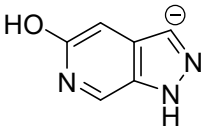
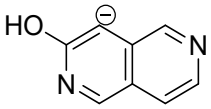
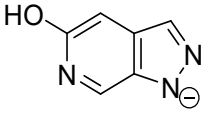
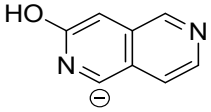
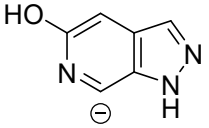
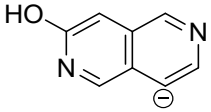
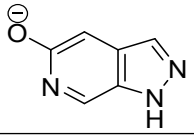
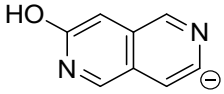
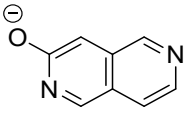
	-471,258395	Neutral 	-493,339949
dp1 	-470,717020	dp1 	-492,791189
dp2 	-470,717400	dp2 	-492,800921
dp3 	-470,773624	dp3 	-492,795532
dp4 	-470,716286	dp4 	-492,796742
dpOH 	-470,775542	dp5 	-492,785520
		dpOH 	-492,864918
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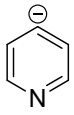
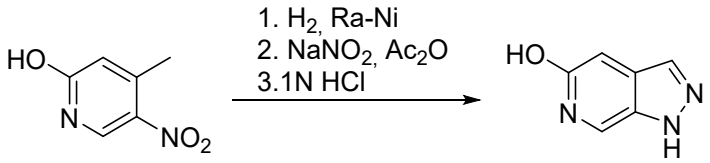
			-247,808111

2. SYNTHETIC PROCEDURES – for compounds already published in the literature

All solvents used for extraction and chromatography procedures were used as received from commercial suppliers without further purification. All reagents were purchased and used as received unless otherwise noted. The physicochemical properties were calculated using Vortex (2015.07.42634, Dotmatics Ltd.) and MarvinSketch (15.7.20, 2015, ChemAxon).

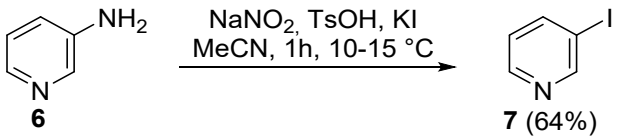
1H-Pyrazolo[3,4-c]pyridin-5-ol (**1**)



3 **1** (82%)

To a solution of 4-methyl-5-nitropyridin-2-ol **3** (3.52 g, 22.83 mmol) in methanol (500 mL) was added Raney® 2800 nickel (excess, 15 mL of the slurry in water) at room temperature. This suspension was purged with hydrogen and stirred for 5 hours. The solid material was filtered off and the filtrate was concentrated. Then, acetic anhydride (80 mL, 846 mmol) was added to the crude solid, the reaction was stirred for 17 hours at room temperature under nitrogen atmosphere. Then, $NaNO_2$ (7.879 g, 114.2 mmol) was added to the mixture at vigorous stirring at room temperature for 3 hours and after this time, the mixture was heated to 90°C for 3 hours. The insoluble material was filtered off and washed with EtOAc (3x20 mL), the solvent was removed under reduced pressure to give brown solid as the crude product. 1 N HCl (100 mL) aqueous solution was added to crude product and it was stirred for 17 hours at room temperature. The solvent was distilled off under reduced pressure resulting in the crude hydrochloride form. The product was purified by flash chromatography (dichloromethane to remove impurities, and then methanol – dichloromethane, 4:1), to yield and orange solid, 3.23 g (82%). ^{1}H NMR (400 MHz, XXXyridin-d_4) δ 8.89 (s, 1H), 8.30 (s, 1H), 7.44 (s, 1H).^{13}C NMR (101 MHz, Methanol-d_4) δ 152.6, 135.1, 134.2, 133.0, 127.5, 99.5. IR (solid, ν/cm^{-1}): 3154, 1656, 1537, 1402, 607. HRMS (EI) m/z $[M+H]^+$ calcd for $C_6H_6N_3O^+$: 136.0505; found: 136.0506. The obtained spectroscopic data are in accordance with those reported in the literature.[1]

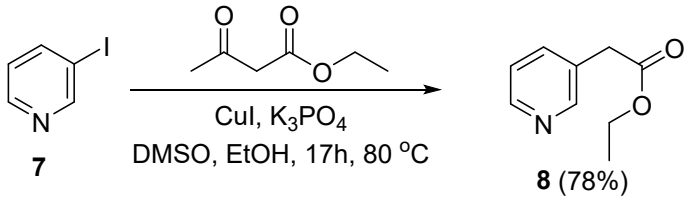
3-iodopyridine (**7**)



6 **7** (64%)

To a solution of p-TsOH.H_2O (244.5 g, 1.28 mol) in MeCN (2 L) was added **6** (40.1 g, 0.42 mol). The resulting suspension was cooled to 10-15 °C, then a solution of $NaNO_2$ (58.6 g, 0.85 mmol) and KI (176.3 g, 1.06 mol) in H_2O (200 mL) was added. The reaction mixture was stirred for 10 min, then allowed to stir at 20 °C for 1 hour. To the reaction mixture was then added a solution of $NaHCO_3$ aq. (1M, until pH = 9-10) and $Na_2S_2O_3$ (2M, 100 mL). The reaction was extracted with EtOAc (3 x 250 mL) and purified by flash chromatography (ethyl acetate – dichloromethane, 1:4), resulting in 55g of **7** (64%) as a pale solid. The obtained spectroscopic data are in accordance with those reported in the literature.[2]

Ethyl-2-(pyridinyl)-3-acetate (**8**)



7 **8** (78%)

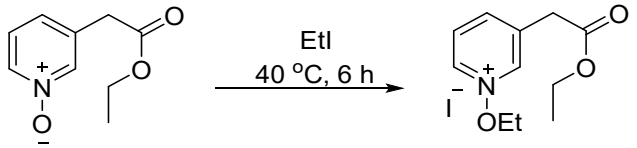
A mixture of **7** (57.2 g, 0.278 mol), ethyl acetoacetate (72 mL, 0.834 mmol), CuI (5.2 g, 10 mol%), K_3PO_4 (175.4 g, 0.834 mol) and ethanol (48 mL, 0.834 mol) in DMSO (200 mL) was stirred under N_2 atmosphere at 80 °C for 17 h. After completion of the reaction, the mixture was diluted with water (200 mL) and extracted with ethyl acetate (3 x 100 mL). The pure product was obtained by flash column chromatography (methanol – dichloromethane, 1:19), resulting in 45.9 g of **8** (78%) as an orange oil. The obtained spectroscopic data are in accordance with those reported in the literature.[3]

3-(2-ethoxy-2-oxoethyl)pyridine 1-oxide (**8.1**)

8 **8.1** (88%)

A solution of mCPBA (61 mmol, 10.5 g) in chloroform (100 mL) was added dropwise to a stirring solution of **8** (41 mmol, 6.82g) in methanol (50 ml), at room temperature. The reaction was followed by LCMS. After 4 hours the reaction was completed, the solvent was removed under reduced pressure and then dissolved in 2M Na_2CO_3 solution and extracted with chloroform (3x 20 mL). The organic layer was dried with $MgSO_4$ and the solvent removed under reduced pressure to give 6,59 g of **8** (88%) as a pale crystal. M.p. 103 ^oC. The obtained spectroscopic data are in accordance with those reported in the literature.[1]

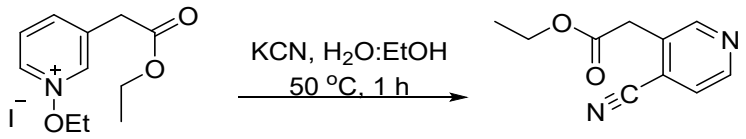
1-ethoxy-3-(2-ethoxy-2-oxoethyl)XXXyridine-1-ium iodide (**8.2**)



8.1 **8.2** (83%)

Iodoethane (10 mL, 134 mmol) was added to **8.1** (6.48 g, 35 mmol), the mixture was stirred for 6 hours at 40 ^oC under nitrogen atmosphere. The mixture was concentred under reduced pressure, resulting in 9.79 g (83%) of crude product **8.2** as a dark orange oil. ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, *J* = 5 Hz, 3H,), 3,57 (s, 2H), 4.36 (q, *J* = 5Hz, 2H), 7.26 (s, 1H), 7.26 (s, 1H), 8.19 (s, 1H), 8.2 (s, 1H). The obtained spectroscopic data are in accordance with those reported in the literature.[1]

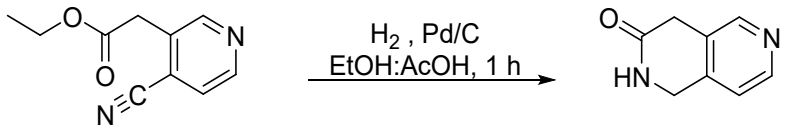
ethyl 2-(4-cyanopyridin-3-yl)acetate (**8.3**)



8.2 **8.3** (69%)

KCN solution (3.55 g, 54.5 mmol) in water (20 mL) was added dropwise for 20 minutes to a solution of **8.2** (18.37, 54.5 mmol) in EtOH:H_2O (7:3, 30 mL) at 50 °C. After 1h, the reaction mixture was poured in ice and extracted with DCM (3x30), dried over $MgSO_4$ and concentrated under reduced pressure. The product was purified by Flash chromatography (Hexane – ethyl acetate, 6:4) to give 7.14 g of **8.3** (69%) of a dark orange oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, *J* = 6 Hz, 3H,), 3.82 (s, 2H), 4.45 (q, *J* = 6Hz, 2H), 7.5 (d, *J* =2Hz, 1H), 8.65 (d, *J*= 6Hz, 1H), 8.68 (s, 1H). IR (cm^{-1}): 2355, 1732, 1166, 1024, 773, 769, 578. HRMS (EI) m/z [M+] calcd for $C_{10}H_{11}N_2O_2^+$: 191.0815; found: 191.0831. The obtained spectroscopic data are in accordance with those reported In the literature.[1]

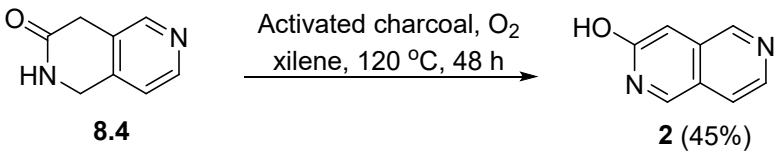
1,4-dihydro-2,6-naphthyridin-3(2H)-one (**8.4**)



8.3 **8.4** (38%)

A solution of **8.3** (2.79 g, 14.63 mmol) in acetic acid : ethanol (150 mL, 1: 4) was hydrogenated by 10% Pd/C (300 mg) and H_2 balloons. The reaction was stirred for 24 h at 50 °C. The reaction was filtered through celite, and the residue washed with hot acetic acid (3 x 10 mL). The solution was evaporated under reduced pressure, the residue was poured into a 10% aqueous K_2CO_3 solution and extracted with ethyl acetate (6x20mL). The crude product was purified by flash column chromatography (ethyl acetate), 1.77 g of **8.4** (82%) as a light brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.24 (t, *J* = 6 Hz, 3H,), 3.82 (s, 2H), 4.45 (q, *J* = 6Hz, 2H), 7.5 (d, *J* = 2Hz, 1H), 8.65 (d, *J* = 6Hz, 1H), 8.68 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.4, 44.5, 120.5, 127.6, 140.3, 146.8, 147.8, 176.2. IV (cm^{-1}): 3398, 2357, 1647, 1217, 1020, 771, 667, 576. HRMS (EI) m/z [M+] calcd for $C_8H_9N_2O^+$:149,0709; found: 149,0711. The obtained spectroscopic data are in accordance with those reported in the literature.[1]

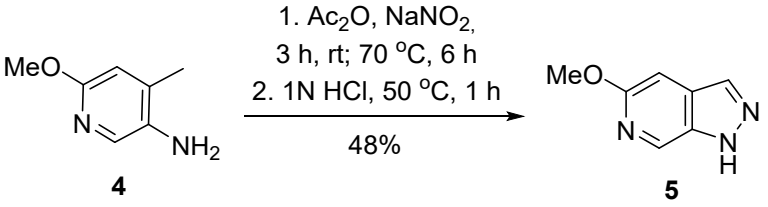
2,6-naphthyridin-3-ol (**2**)



8.4 **2** (45%)

Activated charcoal (640 mg) was added to a solution of **6.4** (6.4 g, 44 mmol) in xylene (200 mL) at 120 °C under an oxygen saturated atmosphere. The reaction was kept under stirring for 48 h. The reaction was filtered through celite and washed with MeOH. The solvent was removed under reduced pressure and the product was purified by flash chromatography (ethyl acetate–- methanol, 9: 1) resulting in 2.89 g (45%) of a yellow solid**.** The obtained spectroscopic data are in accordance with those reported in the literature.[1]

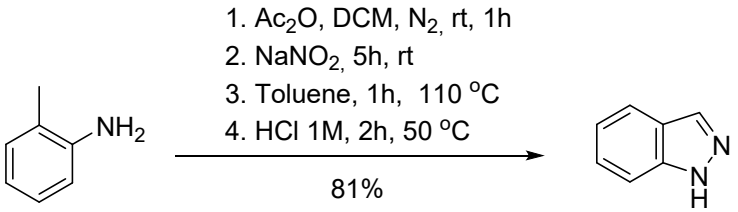
5-methoxy-1H-pyrazolo [3,4-c] pyridine (**5**)



4 **5**

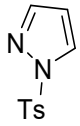
4 (2 g, 17.3 mmol) was added to a round bottom flask equipped with a rubber septum. The flask was purged with N_2 and dry DCM (20 mL) was added. Acetic anhydride (1.7 mL, 19.4 mmol) was added and the reaction was stirred at room temperature. After 2 hours, $NaNO_2$ (7 g, 101 mmol) and acetic anhydride (6.5 mL, 69.4 mmol) were added to the reaction mixture. The reaction was kept under vigorous stirring at room temperature for 5 hours. Thereafter, DCM was removed under reduced pressure and the residue was suspended in toluene (50 mL), the reaction mixture was stirred for 1h at 110 °C. The solvent was removed under reduced pressure, and the residue was dissolved in 1 mL of concentrated aqueous HCl solution (20 mL) and stirred for 1h at 50 °C. The mixture was cooled to room temperature and basified with 1M $NaOH_{aq}$ to pH 8-9, extracted with chloroform (4 x 40 mL), the organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by flash chromatography (Hexane–- ethyl acetate, 2 : 1) yielding 600 mg of **5** (48%) as an orange solid. The obtained spectroscopic data are in accordance with those reported in the literature.[1]

General procedure for one-pot to 1H-indazole



o-toluidine (400µL, 3.72 mmol) was added to a round-bottom flask via syringe and fitted with a rubber septum. The flask was purged with nitrogen and dry DCM (10 mL) was added. Acetic anhydride (2 mL, 18.2 mmol) was added and the reaction was stirred at room temperature for 1 hour and monitored by LCMS. After the total consumption of the amine, $NaNO_2$ (136 mg, 26 mmol) and acetic anhydride (2 mL, 18.2 mmol) were added to the reaction mixture. The reaction was left under vigorous stirring at room temperature for 5 hours. After that, the DCM was removed under reduced pressure and the residue was suspended in toluene (20 mL), the reaction mixture was stirred for 1h at 110 °C. The solvent was removed under reduced pressure, and the residue was solved in 1M $HCl_{aq.}$ (20 mL) and stirred for 2h at 50 °C. The mixture was cooled to room temperature and basified with saturated aqueous solution $NaHCO_3$ to pH 8-9, then the mixture was extracted with chloroform (3x50mL). The organic phase was dried over $MgSO_4$ and the solvent removed under reduced pressure. The product was purified by Flash chromatography (Hexane - ethyl acetate, 2:1) to give 179 mg of indazole (81%, orange powder). The spectral data are consistent with those reported in the literature.[6]

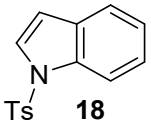
1-tosyl-1H-pyrazole (**17**)



17

202 mg, yield 89% as yellowish solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, *J* = 2.7 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 0.9 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.37 (dd, *J* = 2.7, 1.6 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 145.9, 145.2, 133.9, 131.1, 130.1, 128.1, 108.8, 77.1, 21.7. The spectral data are consistent with those reported in the literature.[7]

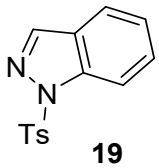
1-tosyl-1H-indole (**18**)



18

178 mg, yield 81% as white solid. m.p. 94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 6.65 (d,*J* = 3.2 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.21 (t,*J* = 6.8 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.51 (d,*J* = 7.6 Hz, 1H), 7.56 (d,*J* = 3.6 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.97 (d,*J* = 8.0 Hz, 1H). The spectral data are consistent with those reported in the literature.[8]

1-tosyl-1H-indazole (**19**)



19

242 mg, yield 89% as yellowish solid. m.p. 102 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (dt, *J* = 8.5, 0.9 Hz, 1H), 8.20 (d, *J* = 0.9 Hz, 1H), 7.92 – 7.86 (m, 2H), 7.71 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.4, 7.1, 1.2 Hz, 1H), 7.34 (ddd, *J* = 8.0, 7.1, 0.9 Hz, 1H), 7.30 – 7.20 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 141.3, 140.3, 134.6, 129.8, 129.2, 127.5, 125.8, 124.2, 121.3, 113.2, 21.6. The spectral data are consistent with those reported in the literature.[9]

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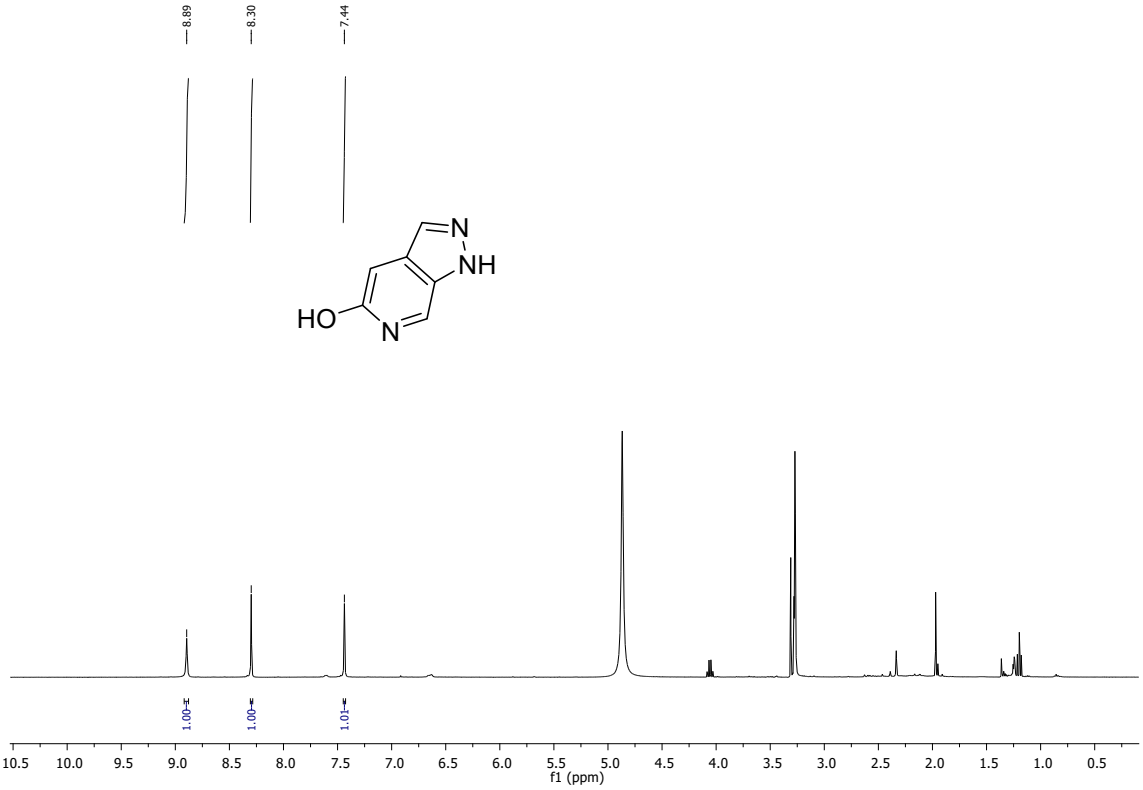
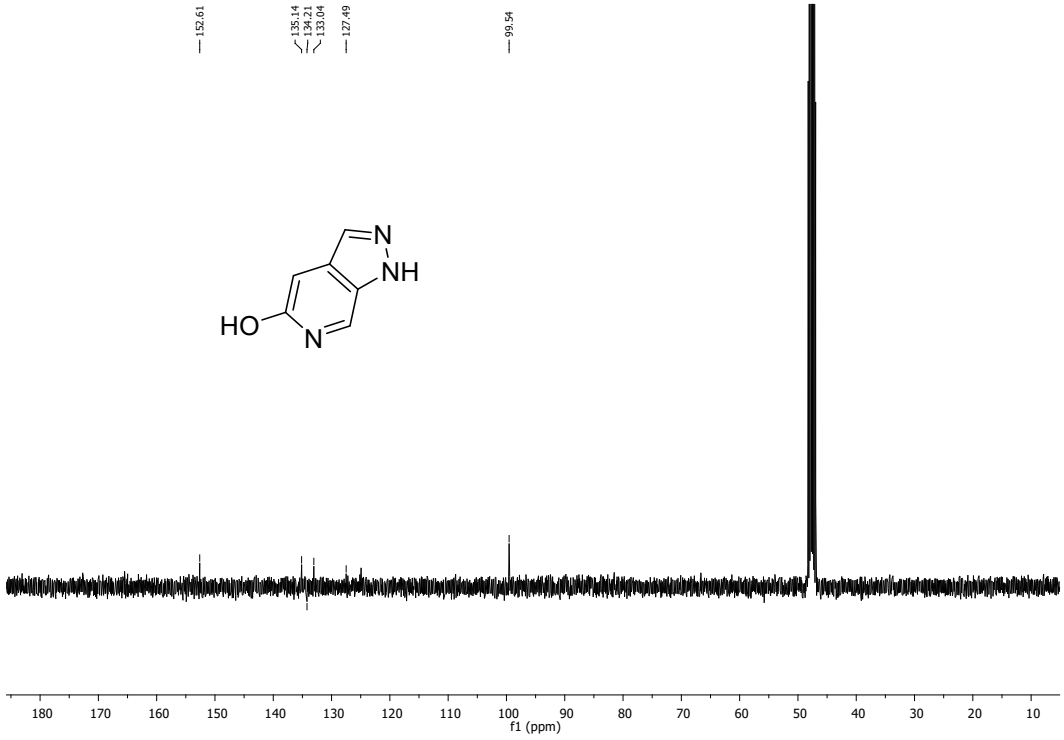
3. NMR-SPECTRA

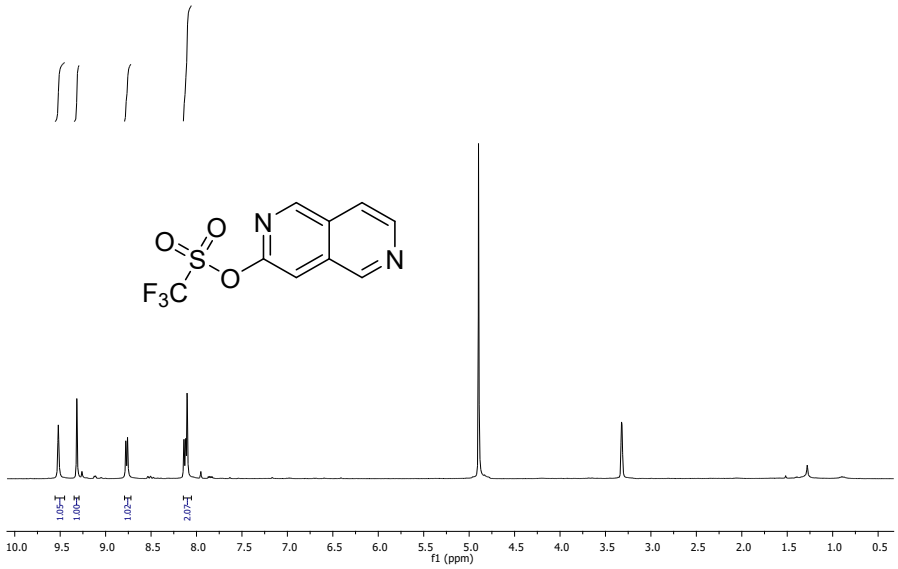
1H-NMR – 400 MHz in Methanol-d4: 1H-Pyrazolo[3,4-c]pyridin-5-ol (**1**)



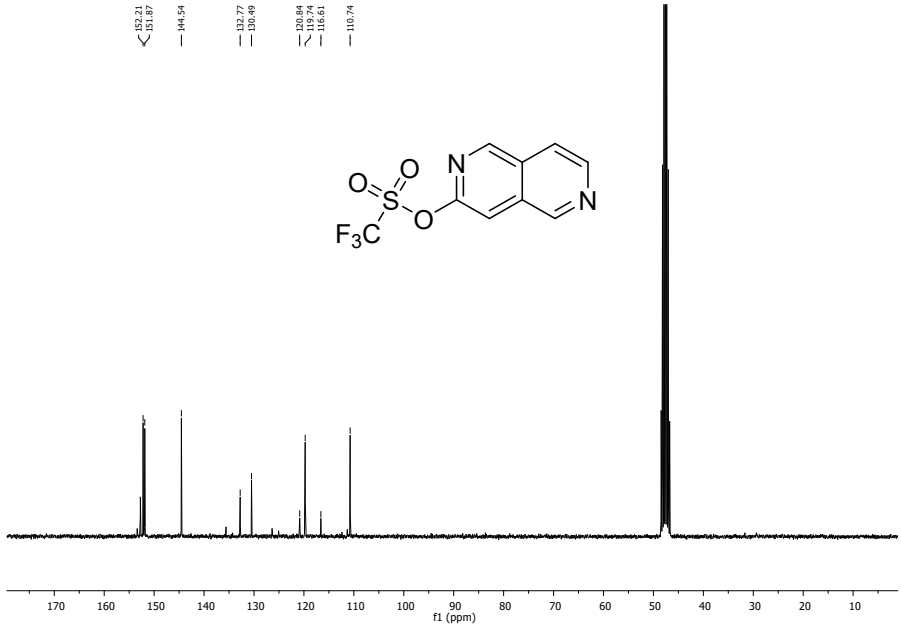
^{13}C NMR - 101 MHz in Methanol-d4: 1*H*-Pyrazolo[3,4-c]pyridin-5-ol (**1**)



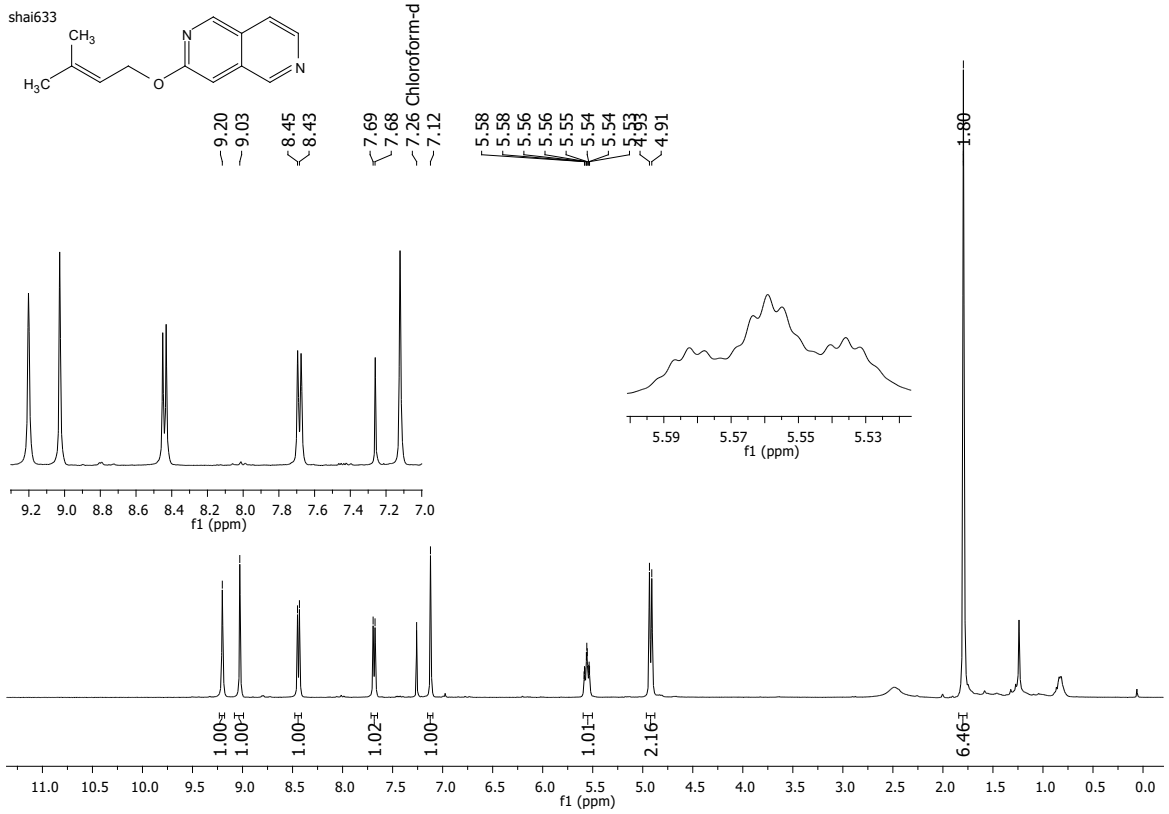
^{1}H-NMR – 300 MHz in $CDCl_3$: 2,6-naphthyridin-3-yl trifluoromethanesulfonate (**9**)



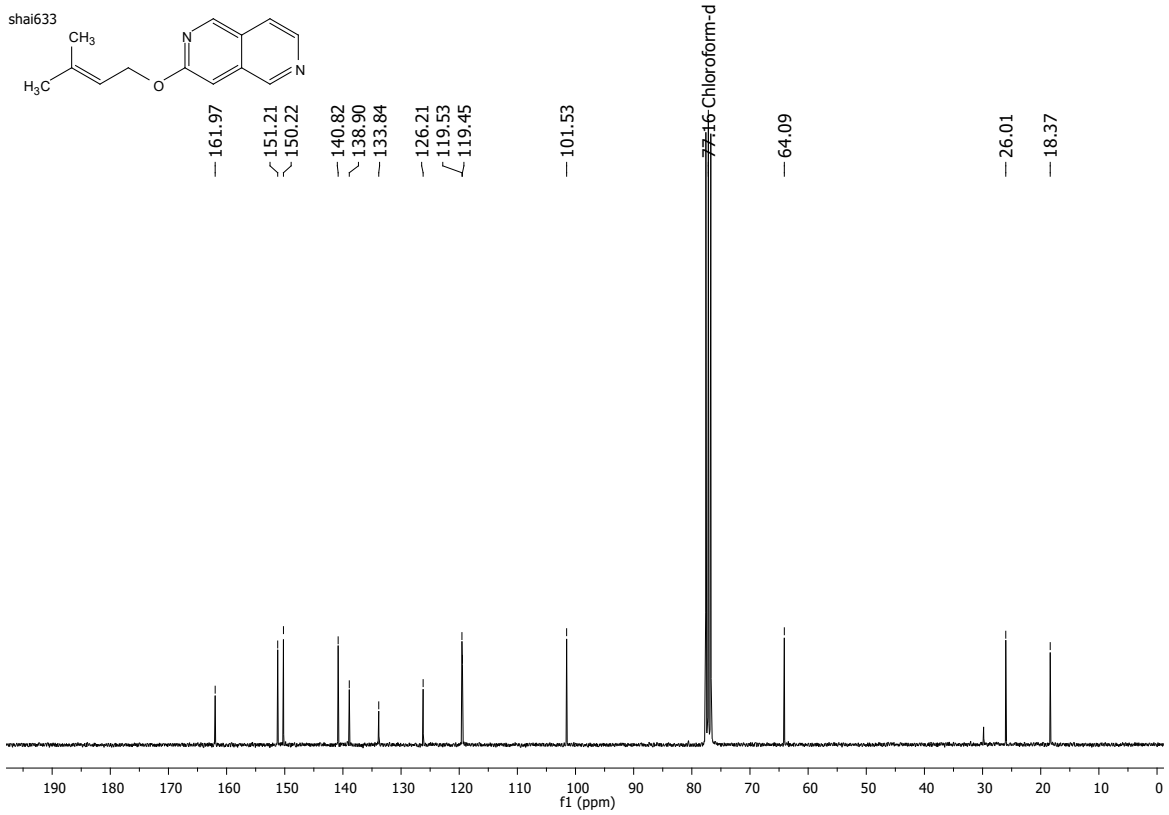
^{13}C-NMR – 101 MHz in $CDCl_3$: 2,6-naphthyridin-3-yl trifluoromethanesulfonate (**9**)



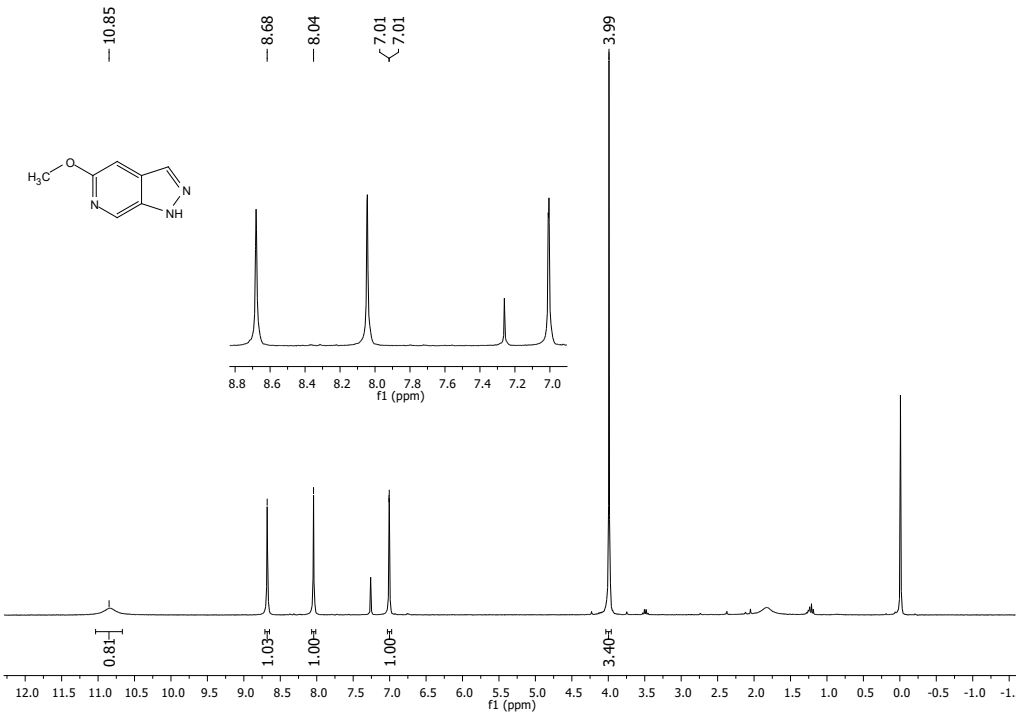
^{1}H-NMR – 300 MHz in $CDCl_3$: 3 - ((3-methylbut-2-en-1-yl) oxy) -2,6-naphthyridine (**10**)



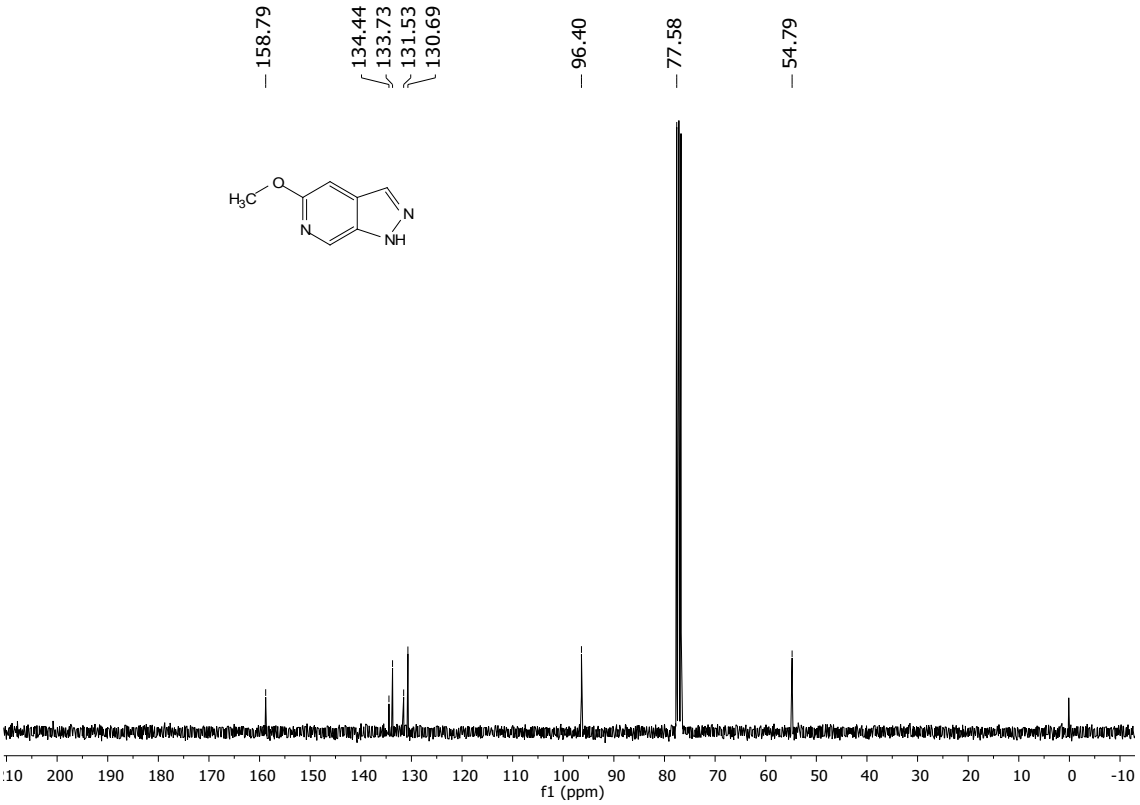
^{13}C-NMR – 75 MHz in $CDCl_3$: 3-((3-methylbut-2-en-1-yl) oxy) -2,6-naphthyridine (**10**)



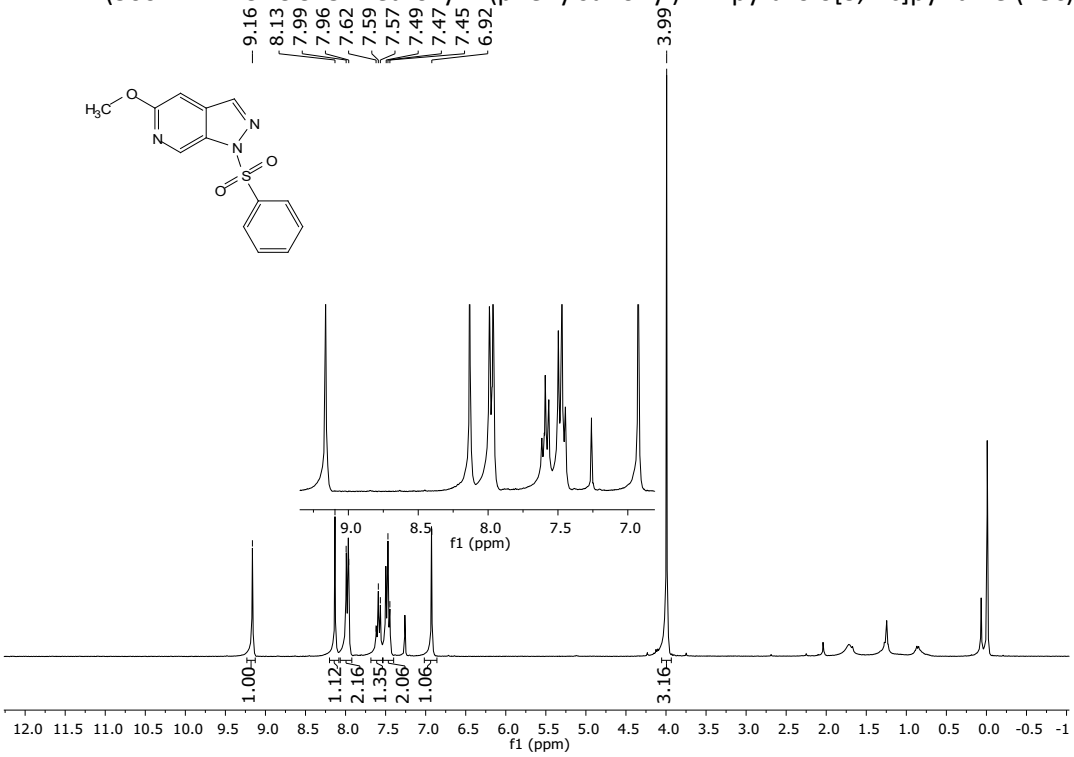
^{1}H NMR (300 MHz, $CDCl_3$) - 5-methoxy-1H-pyrazolo [3,4-c] pyridine (**5**)



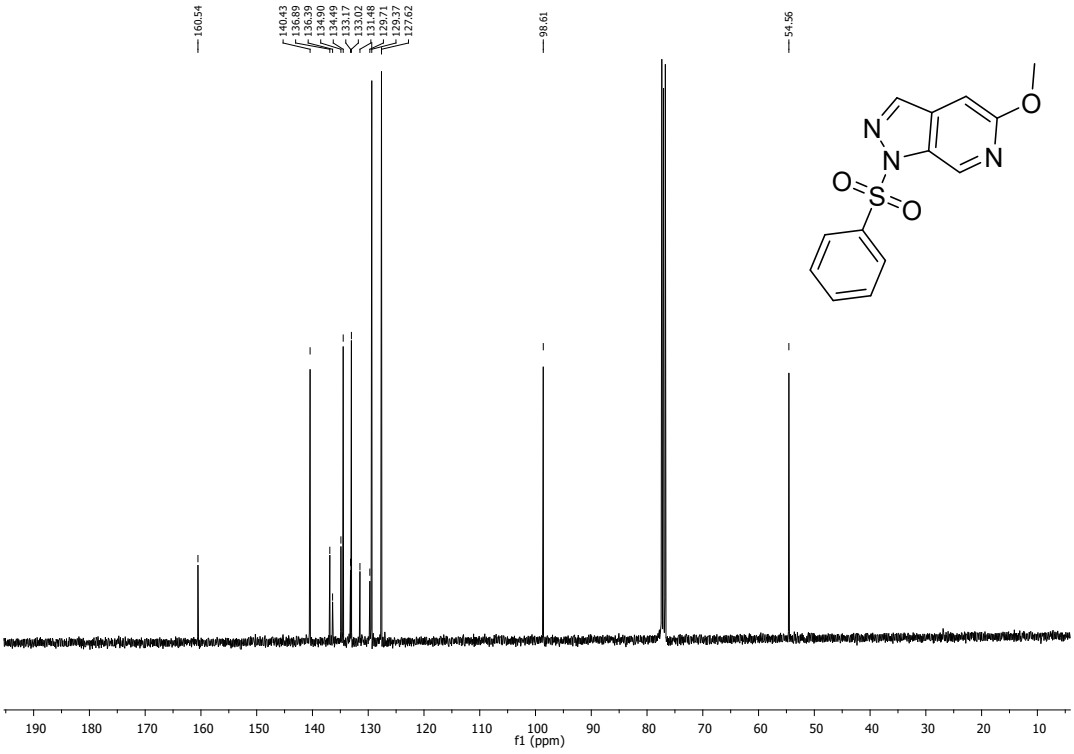
^{13}C NMR (75 MHz, $CDCl_3$) - 5-methoxy-1H-pyrazolo [3,4-c] pyridine (**5**)



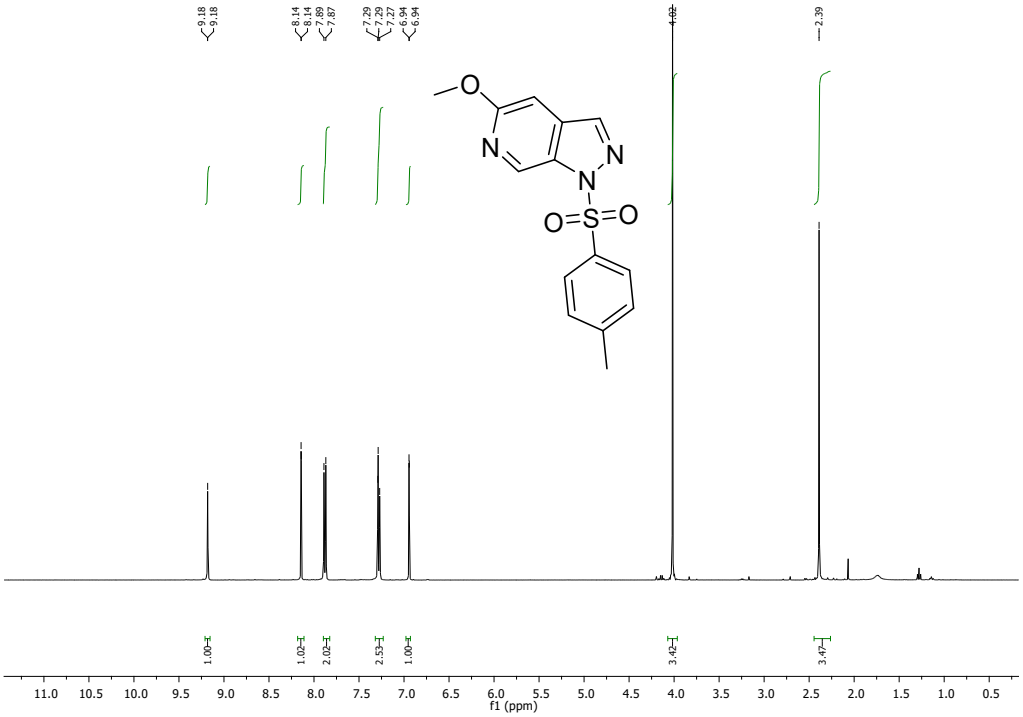
^{1}H NMR (300 MHz - CDCl3: 5-methoxy-1-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15c**)



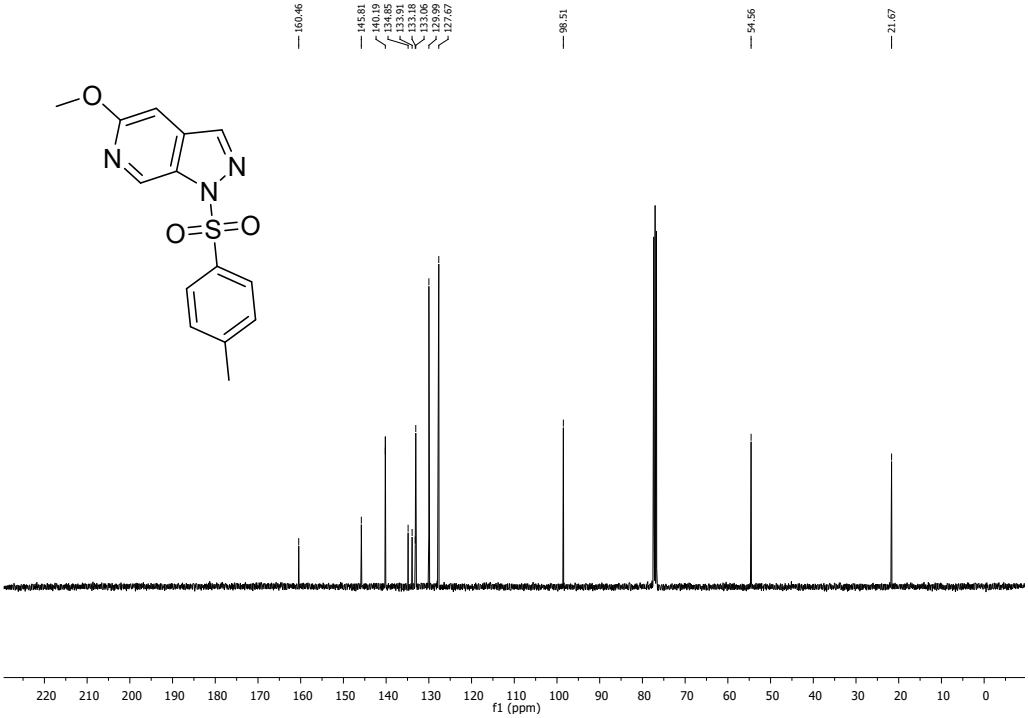
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-1-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15c**)



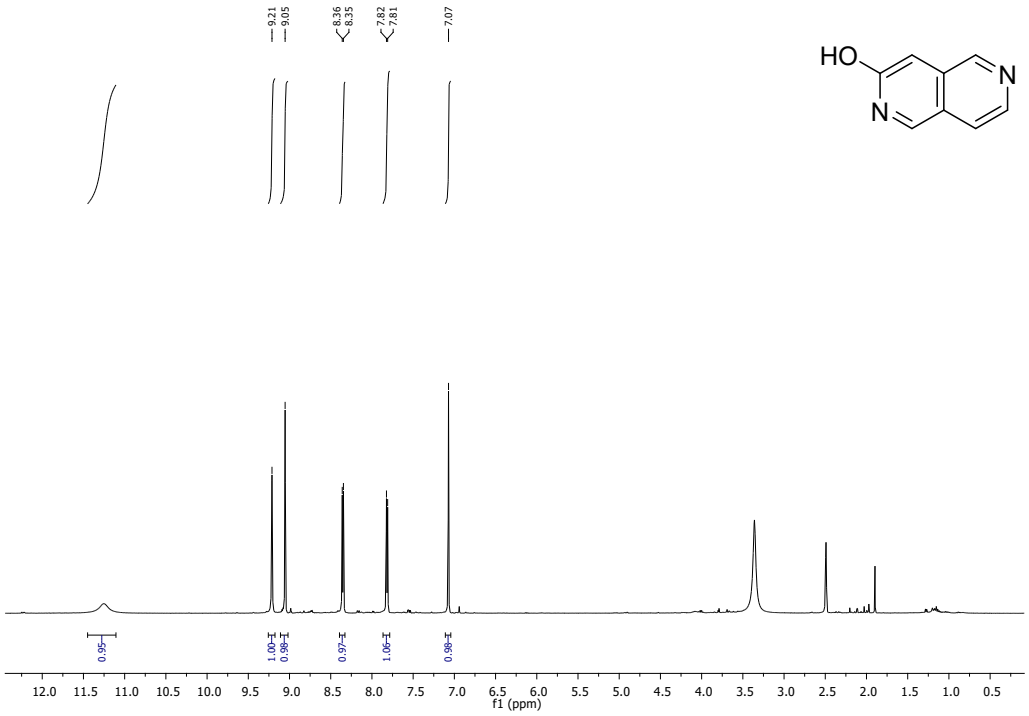
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-1-tosyl-1H-pyrazolo[3,4-c]pyridine (**11**)



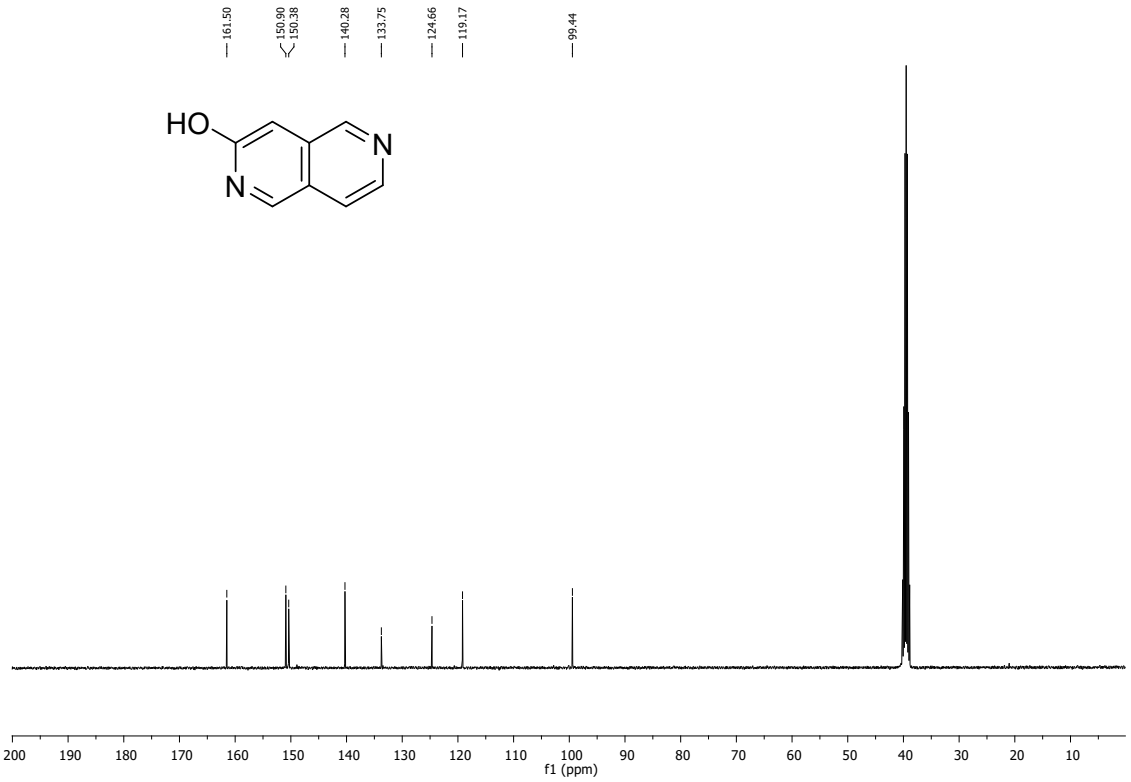
^{13}C NMR - 101 MHz in $CDCl_3$: 5-methoxy-1-tosyl-1H-pyrazolo[3,4-c]pyridine (**11**)



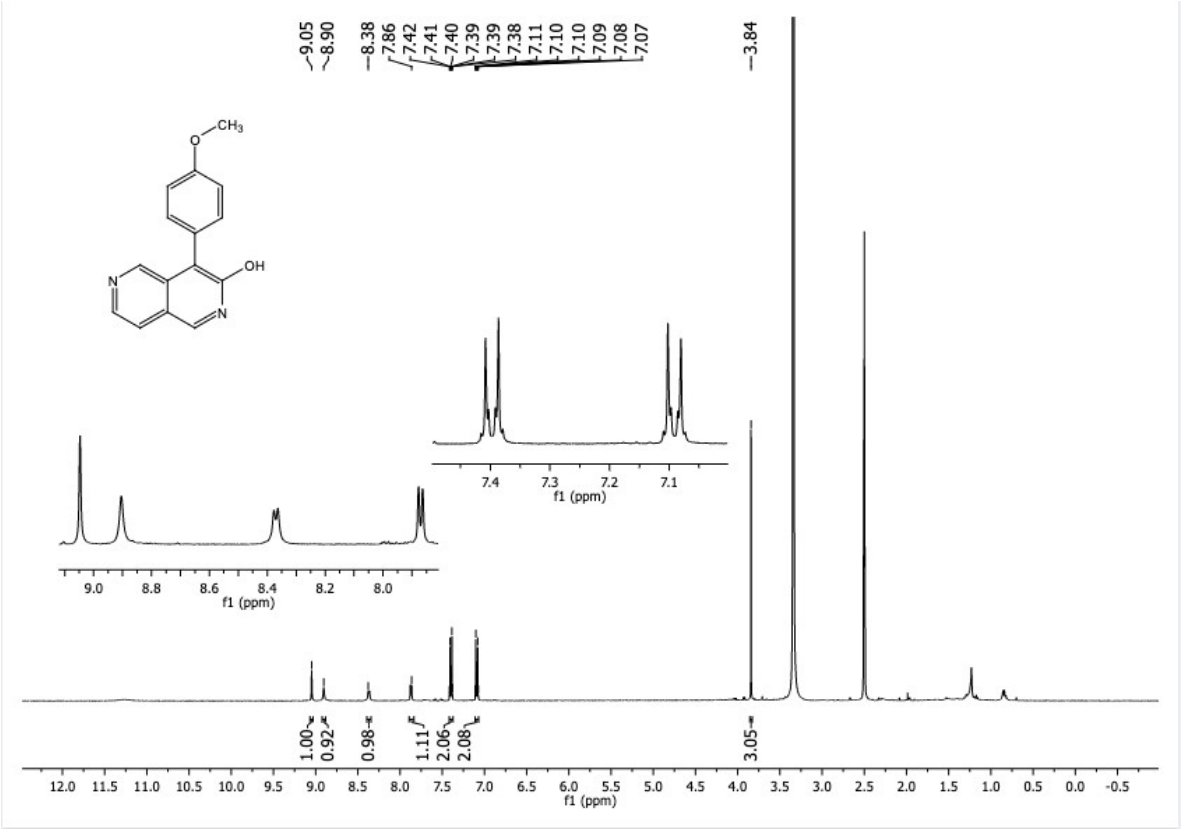
^{1}H-NMR – 400 MHz in DMSO-d$_6$: 2,6-naphthyridin-3-ol (**2**)



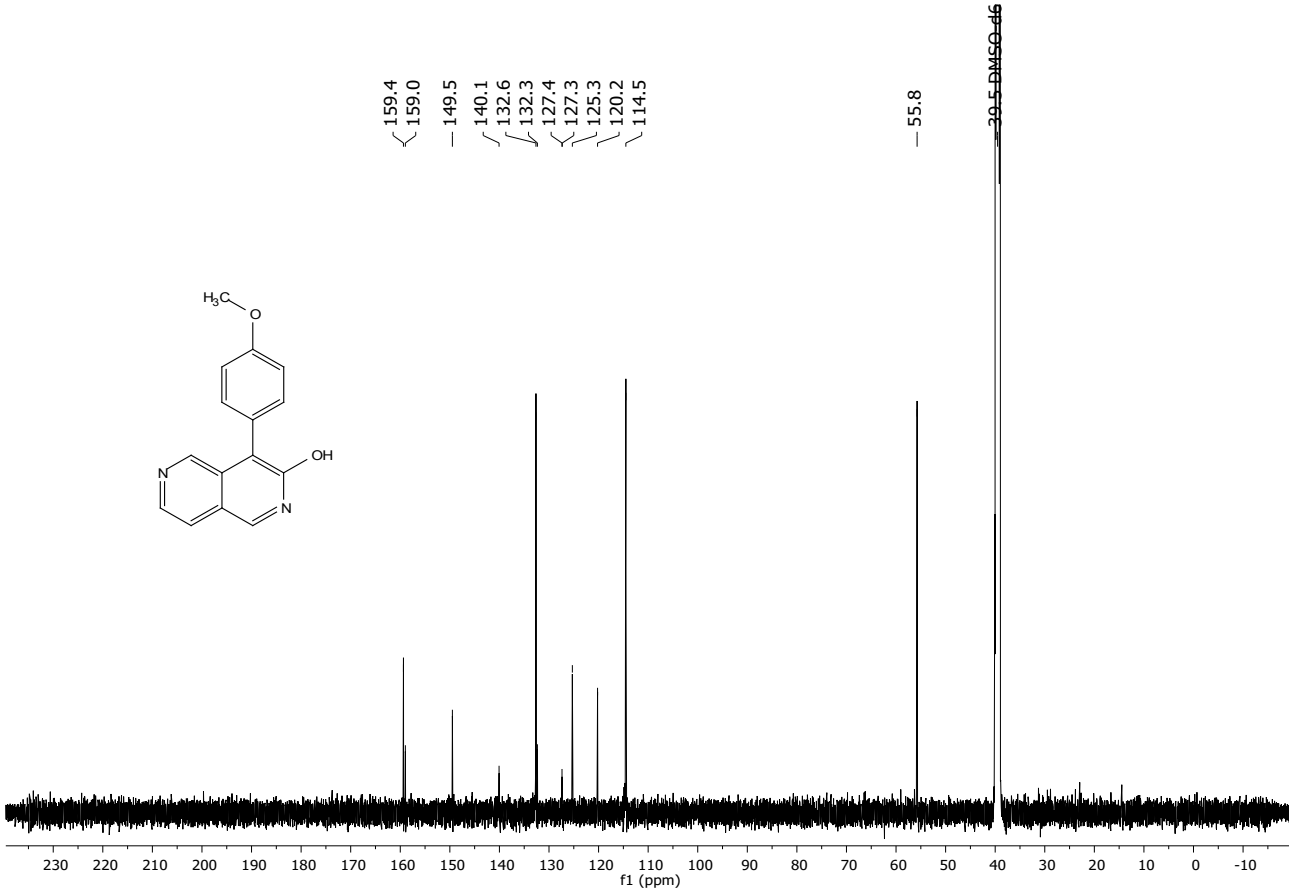
^{13}C NMR - 101 MHz in DMSO-d$_6$: 2,6-naphthyridin-3-ol (**2**)



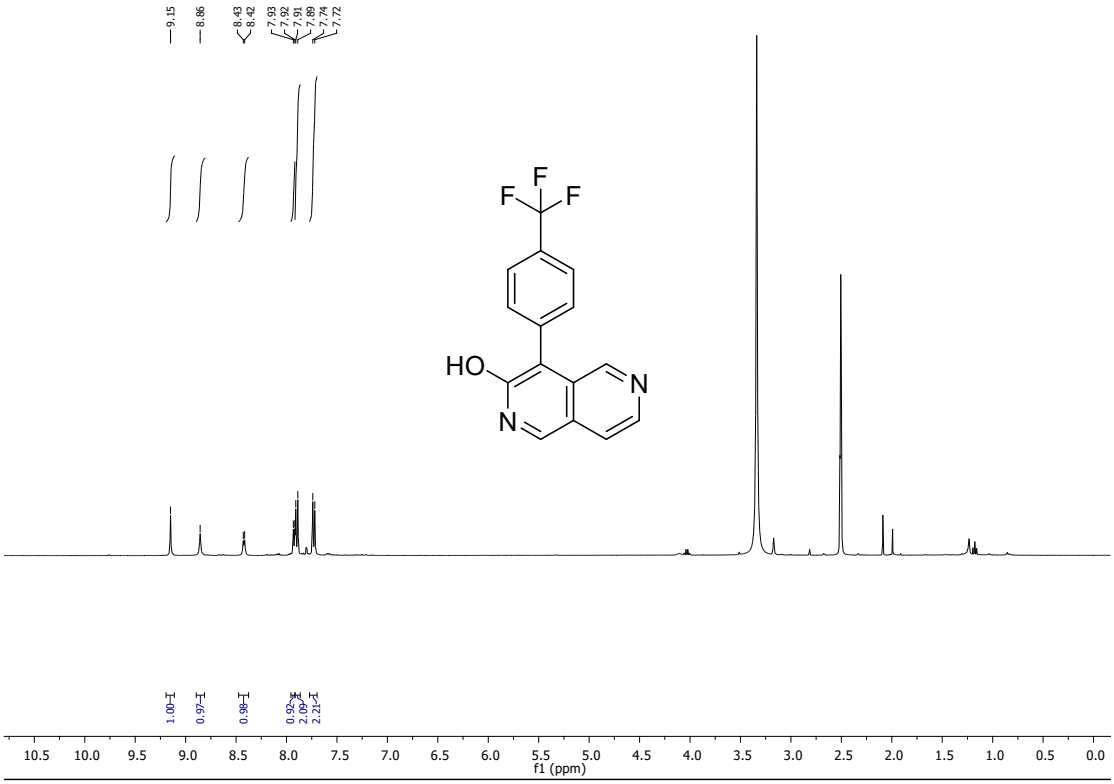
^{1}H-NMR – 300 MHz in DMSO-d_6: 4-(4-methoxyphenyl)-2,6-naphthyridin-3-ol (**12a**)


9.05
8.90
8.38
7.86
7.42
7.41
7.40
7.39
7.39
7.38
7.11
7.10
7.10
7.09
7.08
7.07
3.84
O
CH3
OH
N
N
f1 (ppm)
1.00
0.92
0.98
1.11
2.06
2.08
3.05

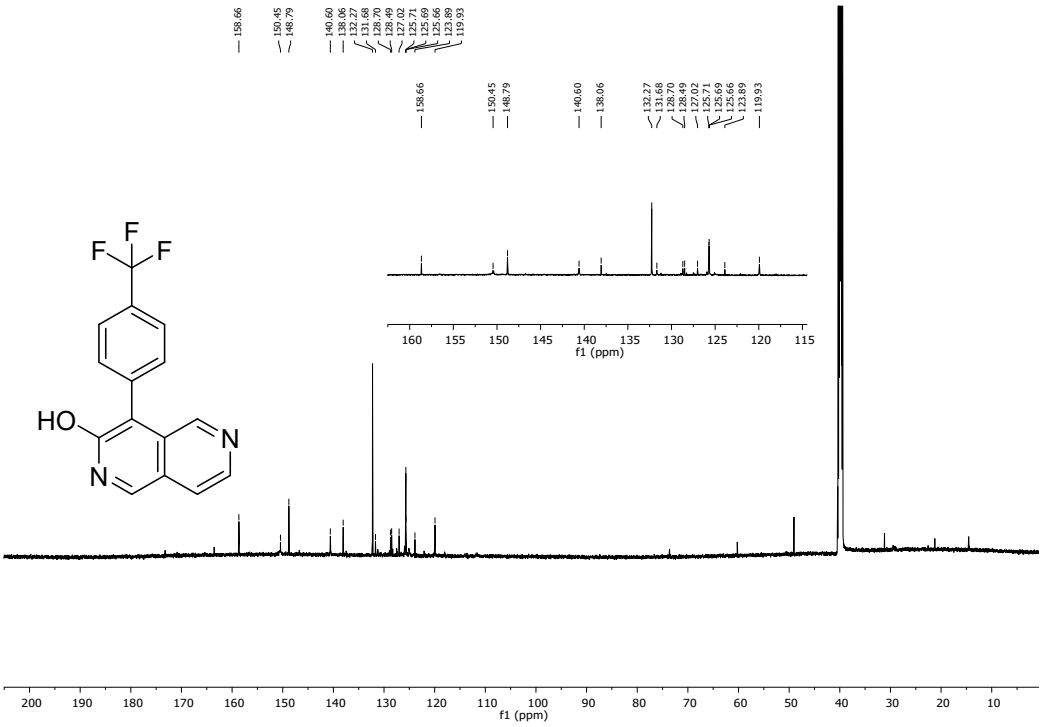
^{13}C NMR - 101 MHz in DMSO-d6: 4-(4-methoxyphenyl)-2,6-naphthyridin-3-ol (**12a**)



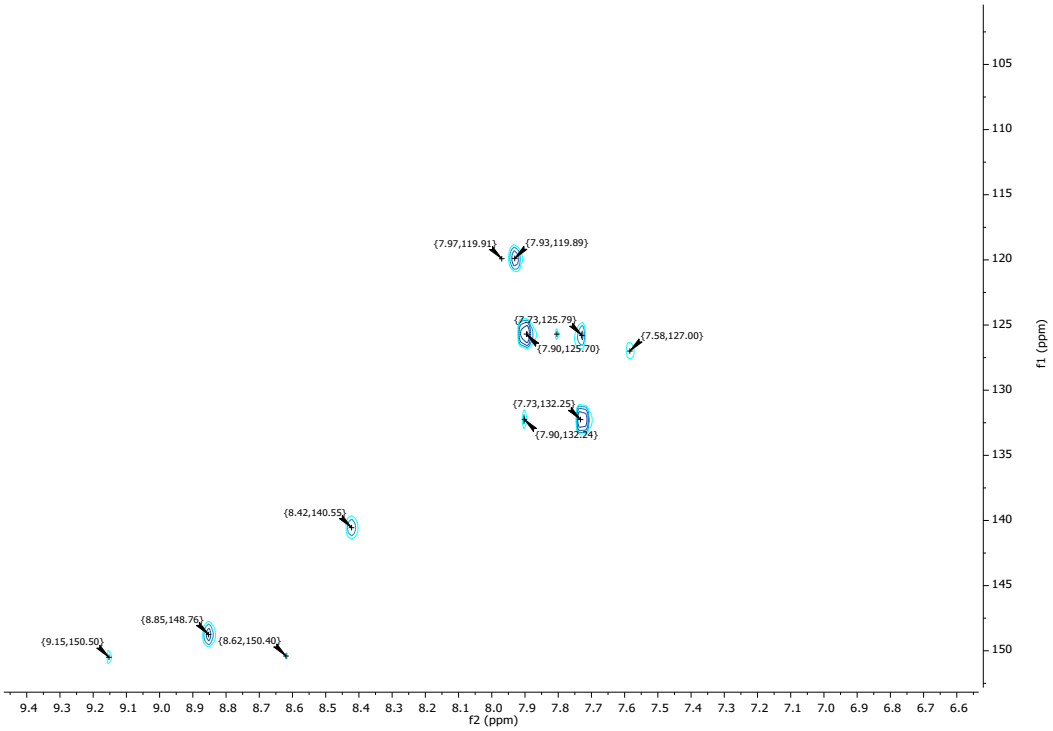
^{1}H-NMR – 300 MHz in DMSO-d_6: 4-(4-(trifluoromethyl)phenyl)-2,6-naphthyridin-3-ol (**12b**)



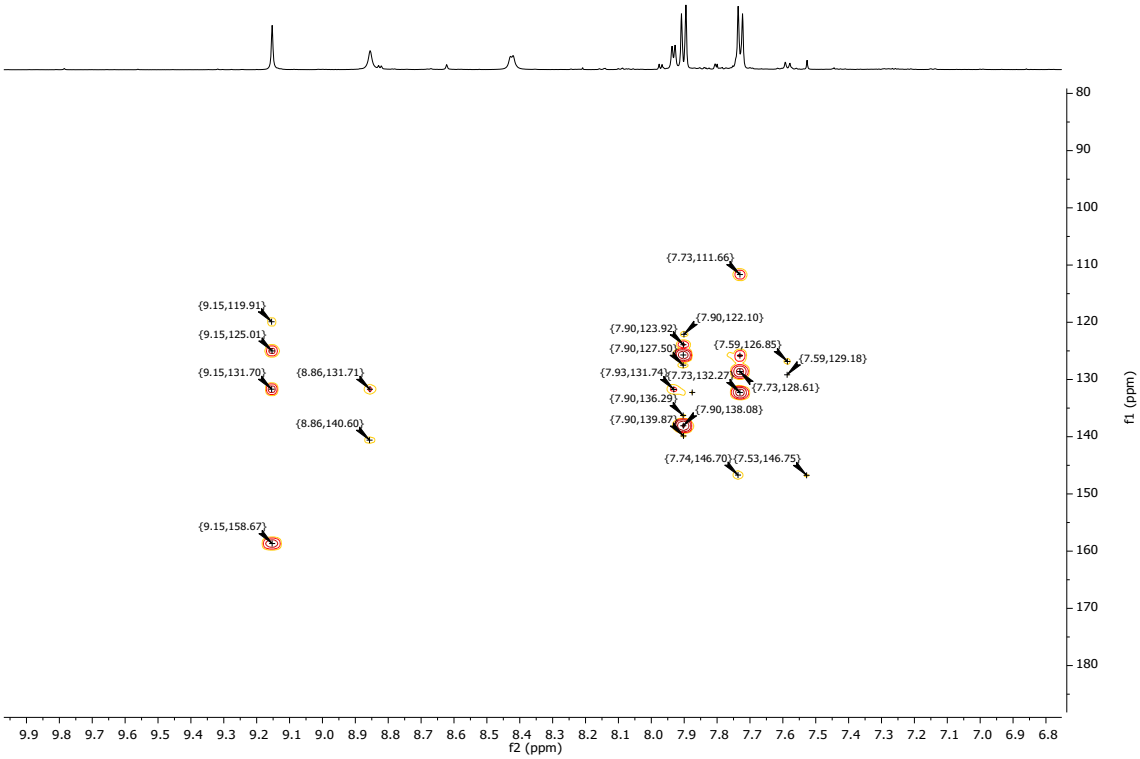
^{13}C NMR - 101 MHz in DMSO-d_6: 4-(4-(trifluoromethyl)phenyl)-2,6-naphthyridin-3-ol (**12b**)



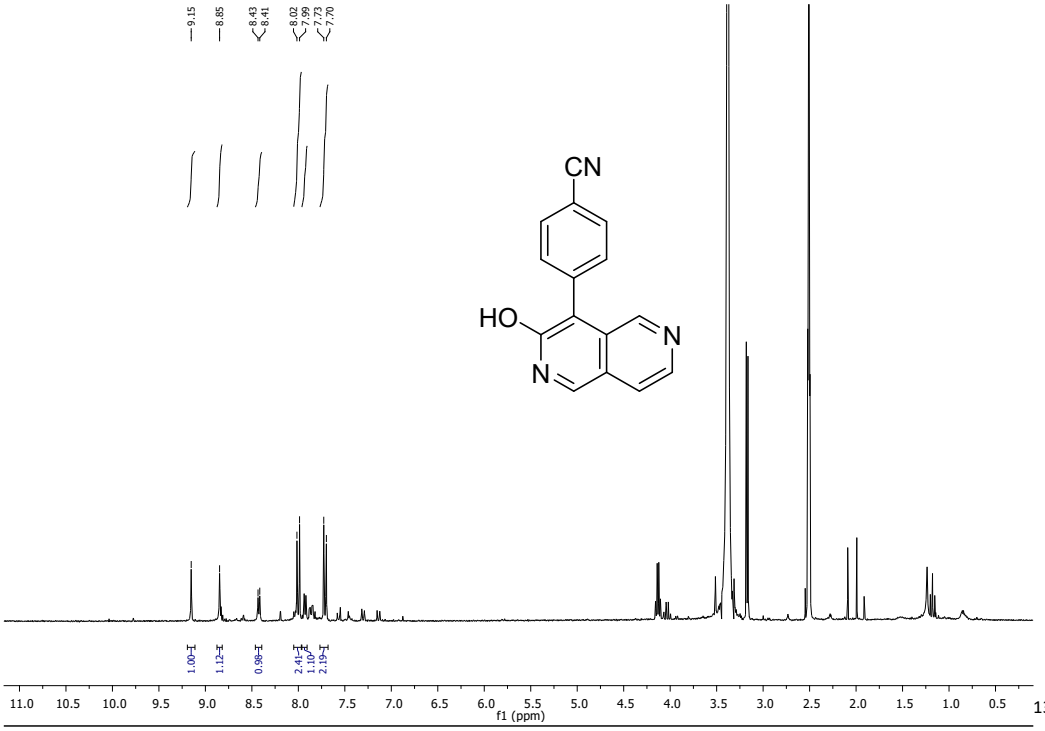
HSQC- 600 MHz in DMSO-d_6: 4-(4-(trifluoromethyl)phenyl)-2,6-naphthyridin-3-ol (**12b**)



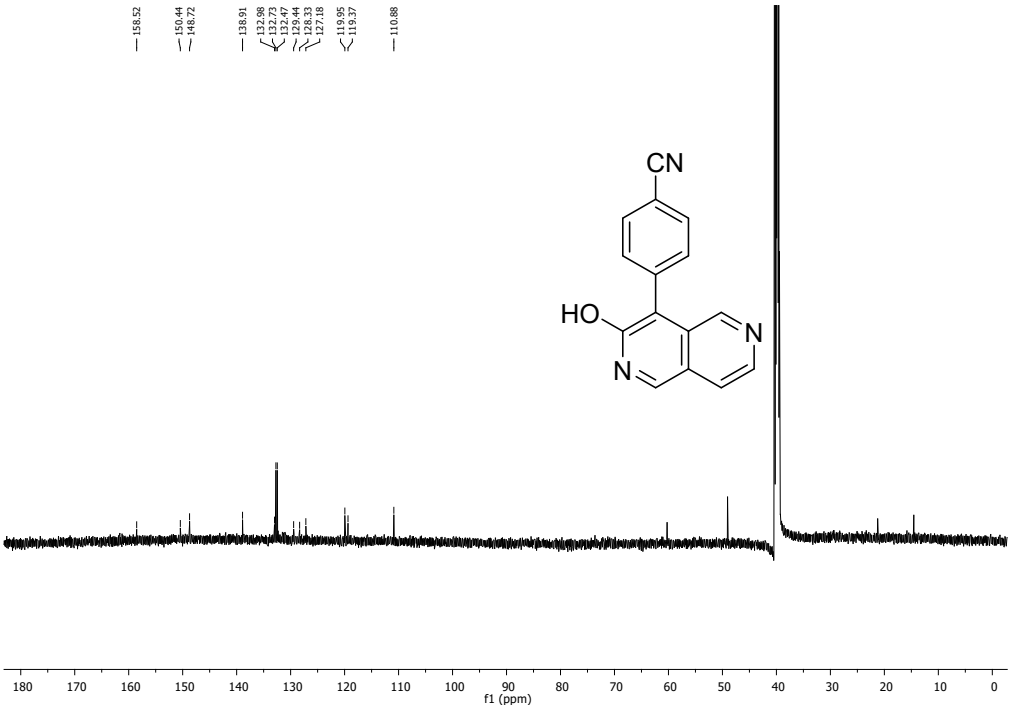
HMBC- 600 MHz in DMSO-d_6: 4-(4-(trifluoromethyl)phenyl)-2,6-naphthyridin-3-ol (**12b**)



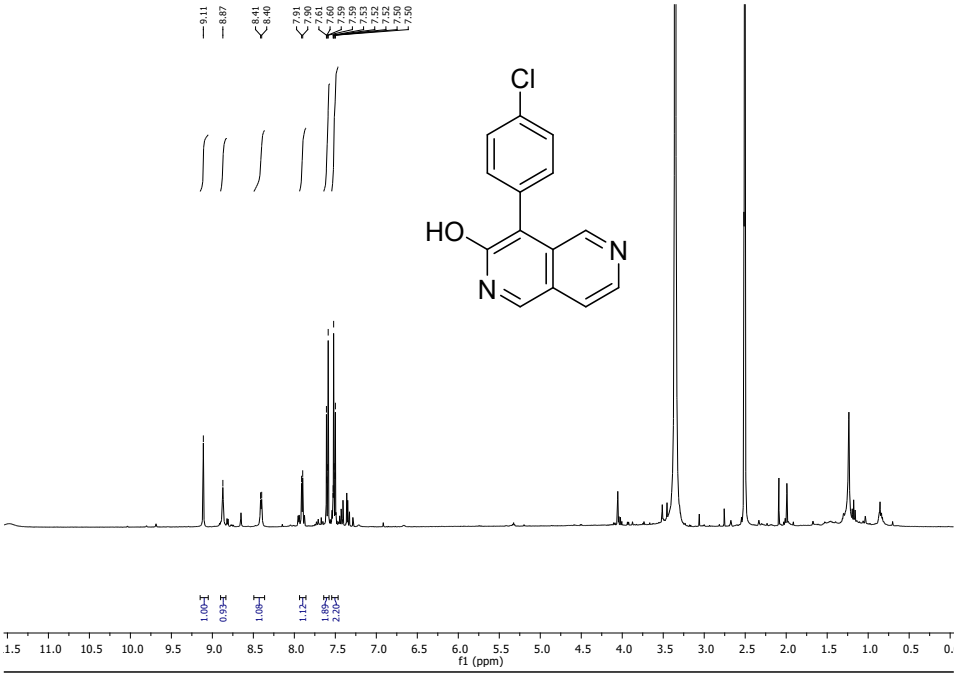
^{1}H-NMR – 300 MHz in DMSO-d_6: 4-(3-hydroxy-2,6-naphthyridin-4-yl)benzonitrile (**12c**)



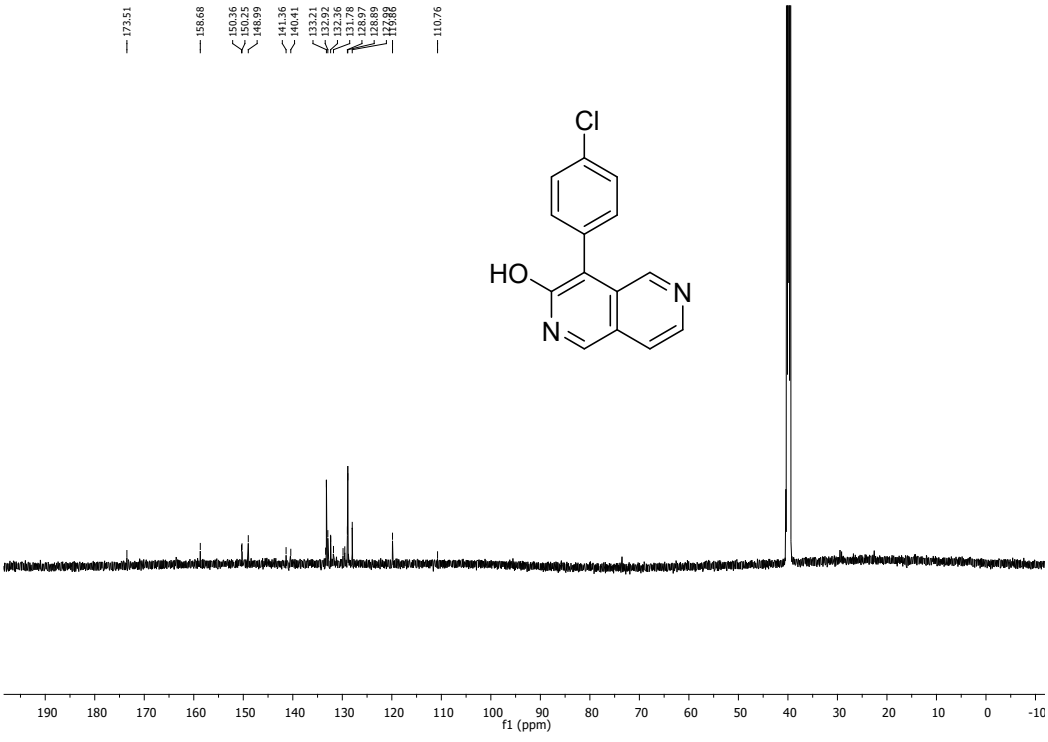
^{13}C NMR - 101 MHz in DMSO-d_6: 4-(3-hydroxy-2,6-naphthyridin-4-yl)benzonitrile (**12c**)



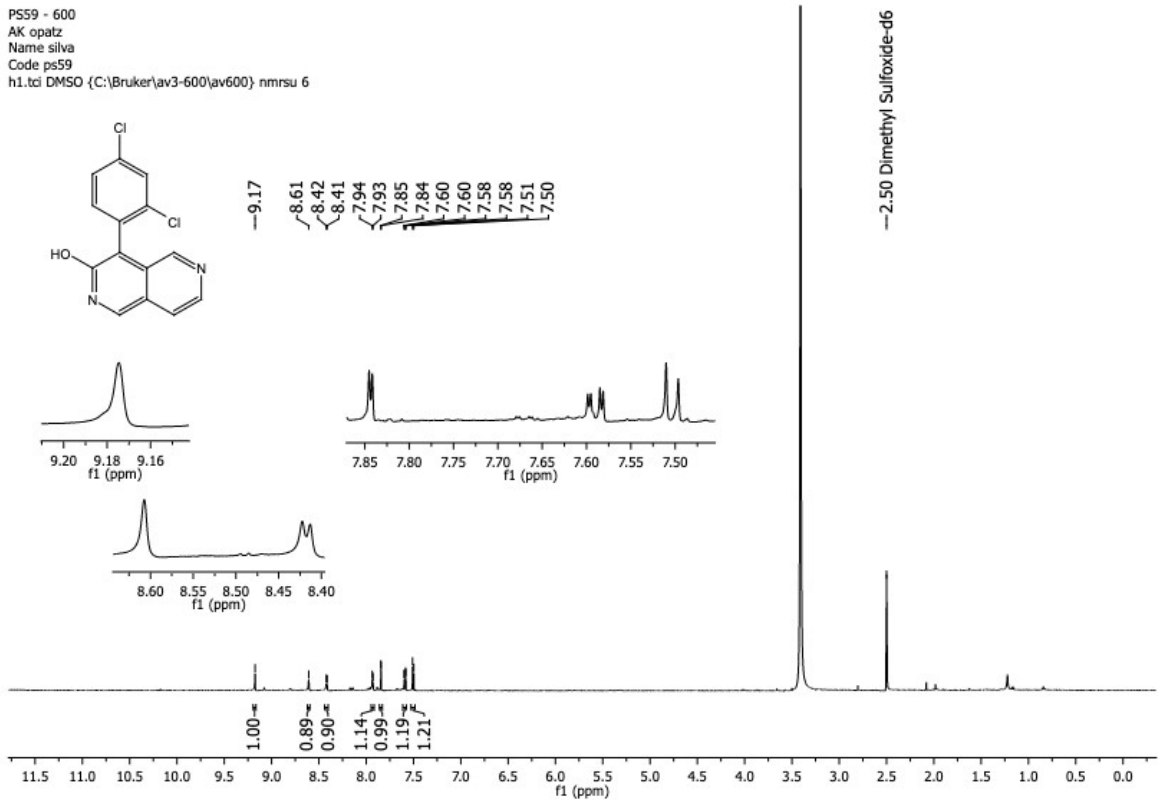
^{1}H-NMR – 300 MHz in DMSO-d_6: 4-(4-chlorophenyl)-2,6-naphthyridin-3-ol (**12d**)



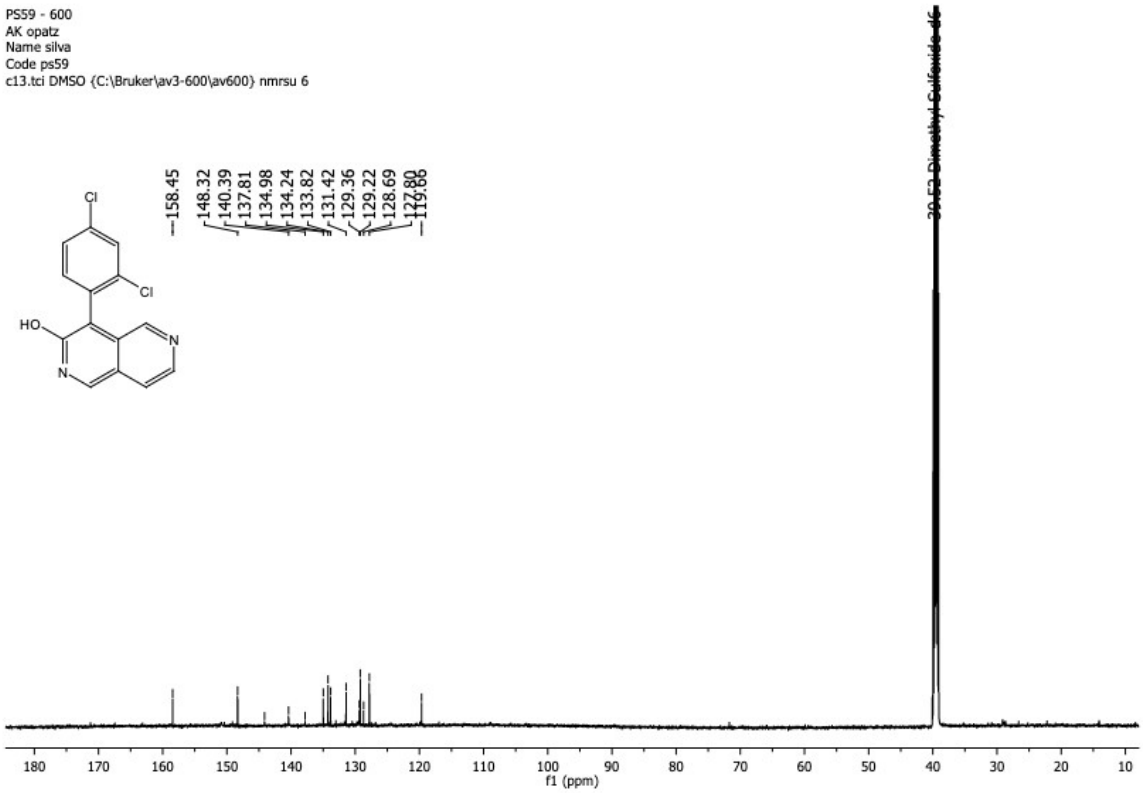
^{13}C NMR - 101 MHz in DMSO-d$_6$: 4-(4-chlorophenyl)-2,6-naphthyridin-3-ol (**12d**)



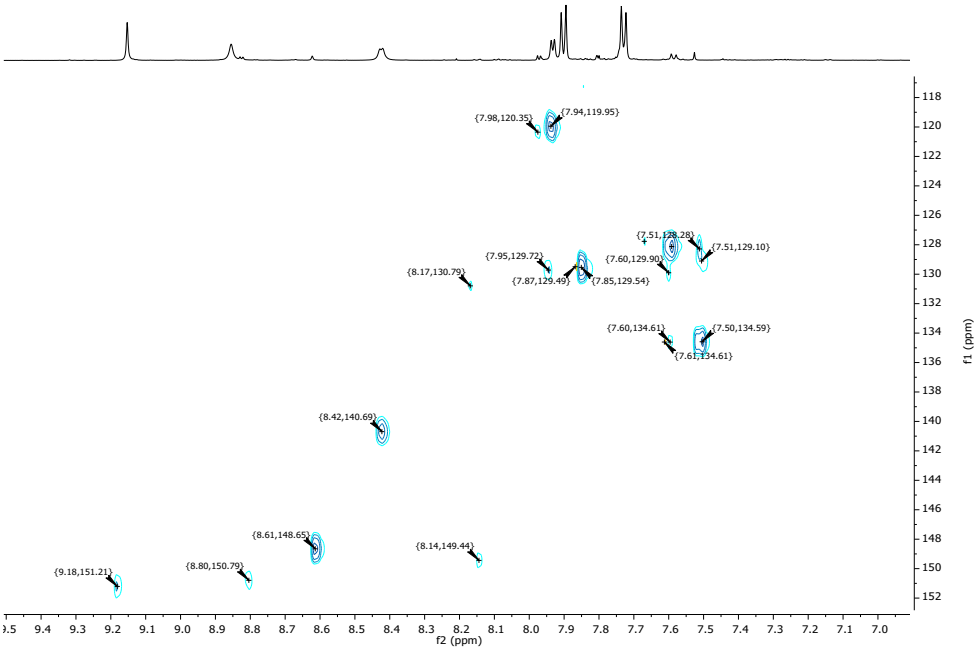
^{1}H-NMR – 600 MHz in DMSO-d_6: 4-(2,4-dichlorophenyl)-2,6-naphthyridin-3-ol (**12e**)



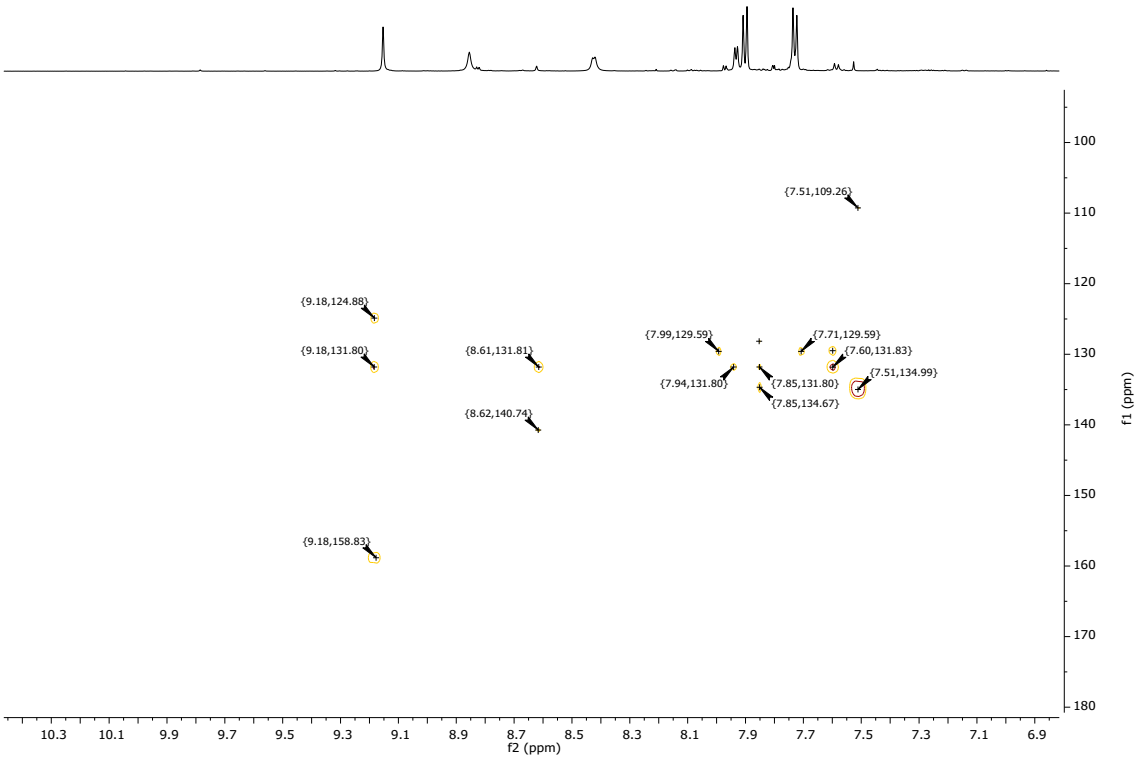
^{13}C NMR - 150 MHz in DMSO-d_6: 4-(2,4-dichlorophenyl)-2,6-naphthyridin-3-ol (**12e**)



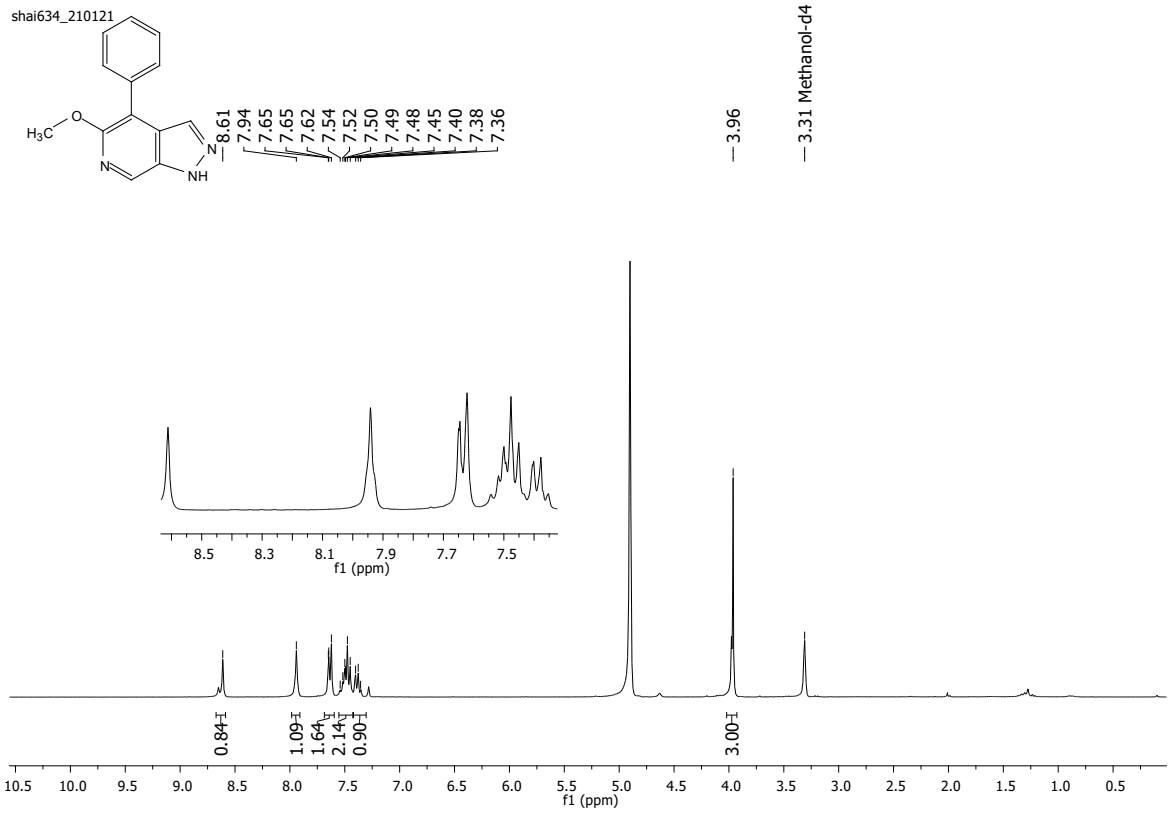
HSQC - 600 MHz in DMSO-d_6: 4-(2,4-dichlorophenyl)-2,6-naphthyridin-3-ol (**12e**)



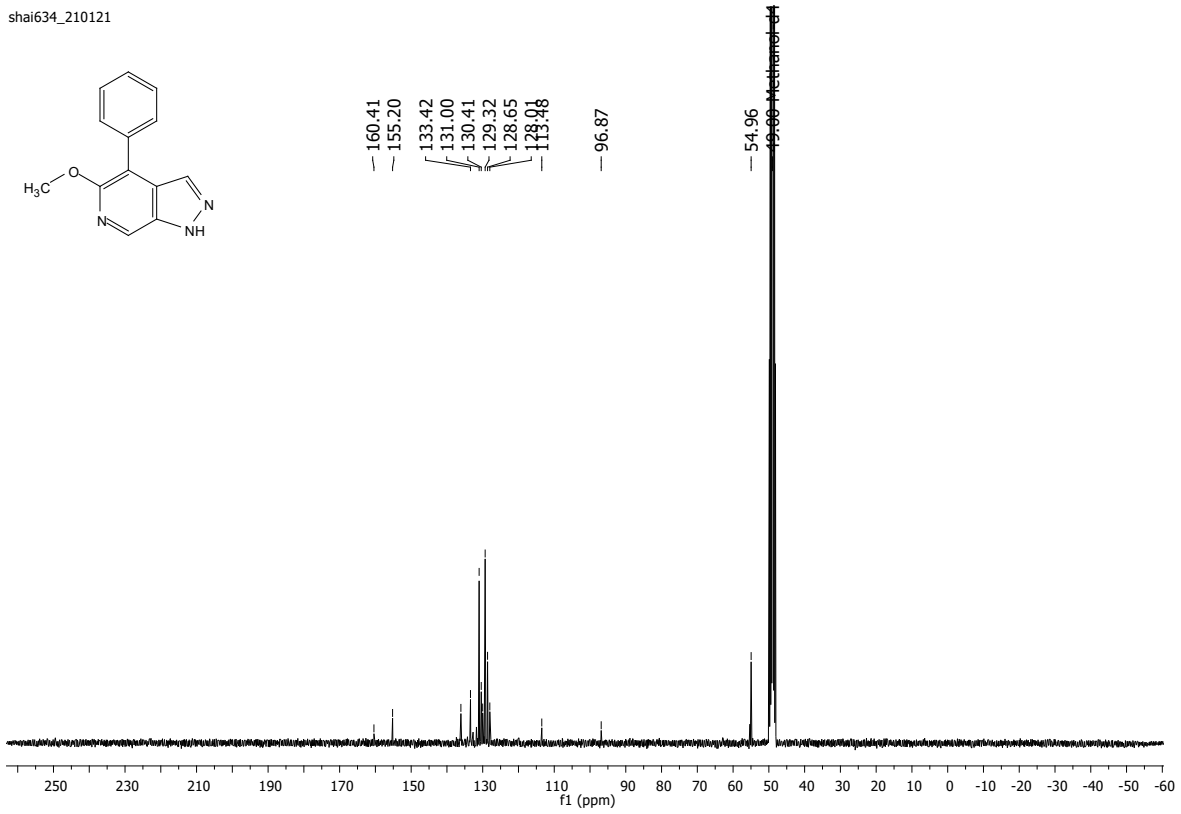
HMBC - 600 MHz in DMSO-d_6: 4-(2,4-dichlorophenyl)-2,6-naphthyridin-3-ol (**12e**)



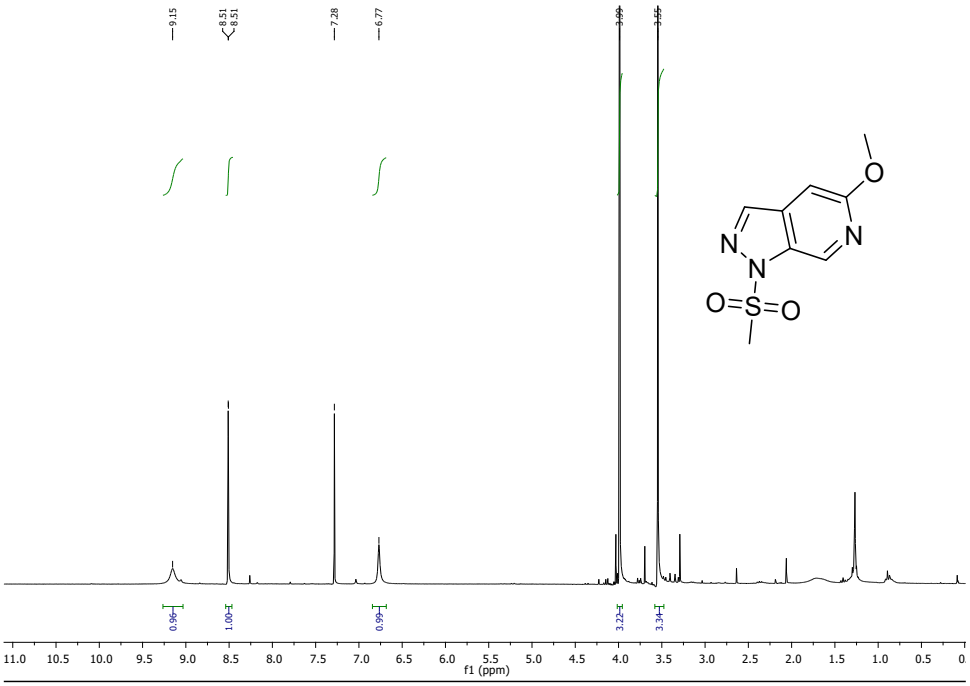
^{1}H-NMR – 300 MHz in $MeO\text{-}d_4$: 5-methoxy-4-phenyl-1H-pyrazolo[3,4-c]pyridine (**13**)



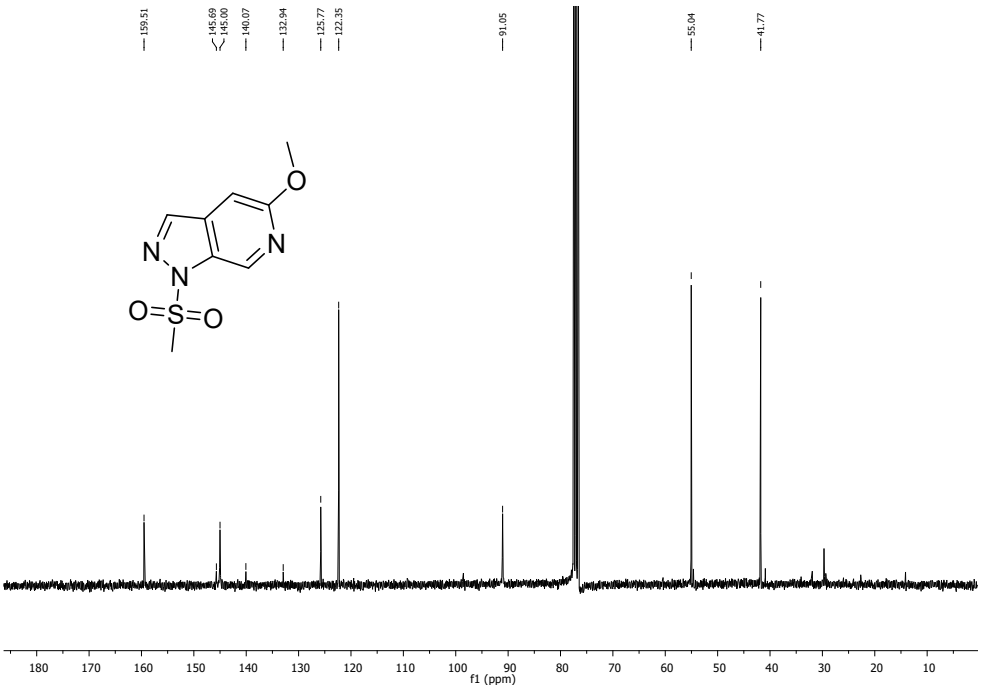
^{1}H-NMR – 75 MHz in $MeO\text{-}d_4$: 5-methoxy-4-phenyl-1H-pyrazolo[3,4-c]pyridine (**13**)



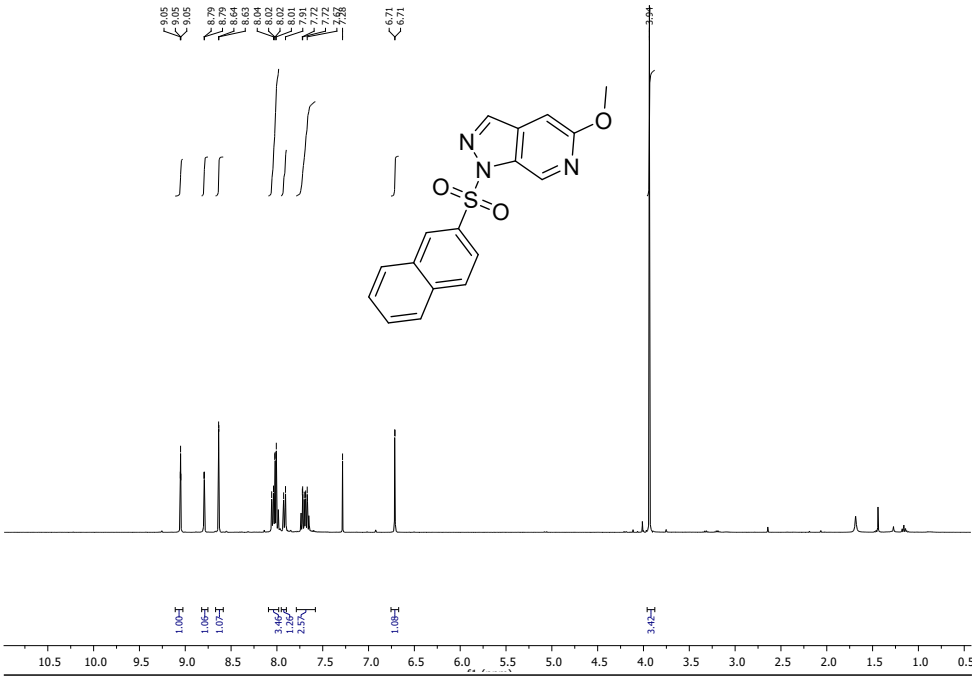
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-1-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15a**)



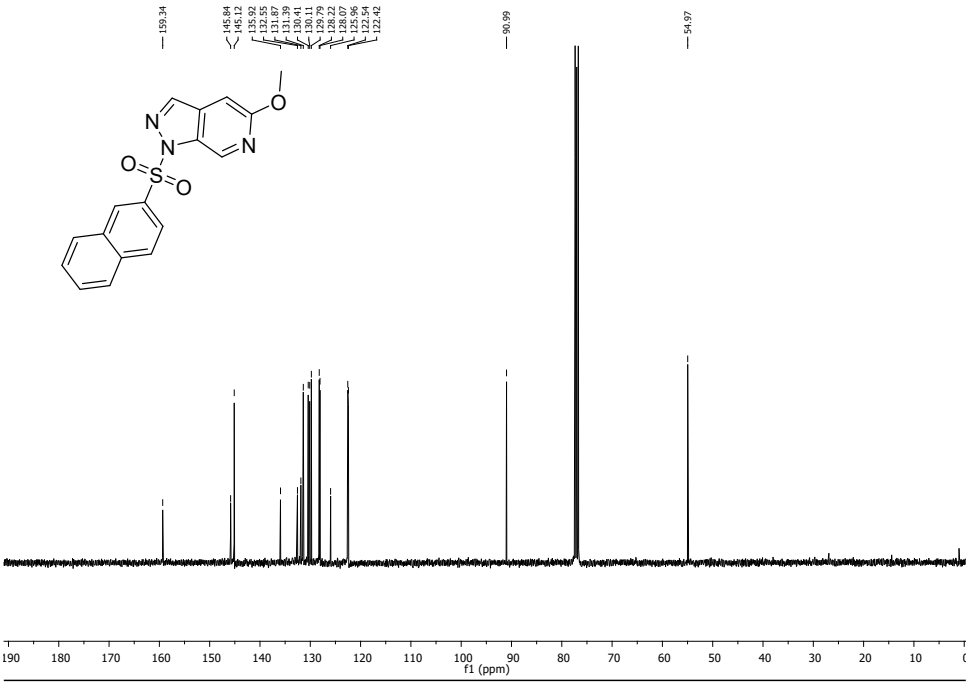
^{13}C NMR - 101 MHz in $CDCl_3$. 5-methoxy-1-(methylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15a**)



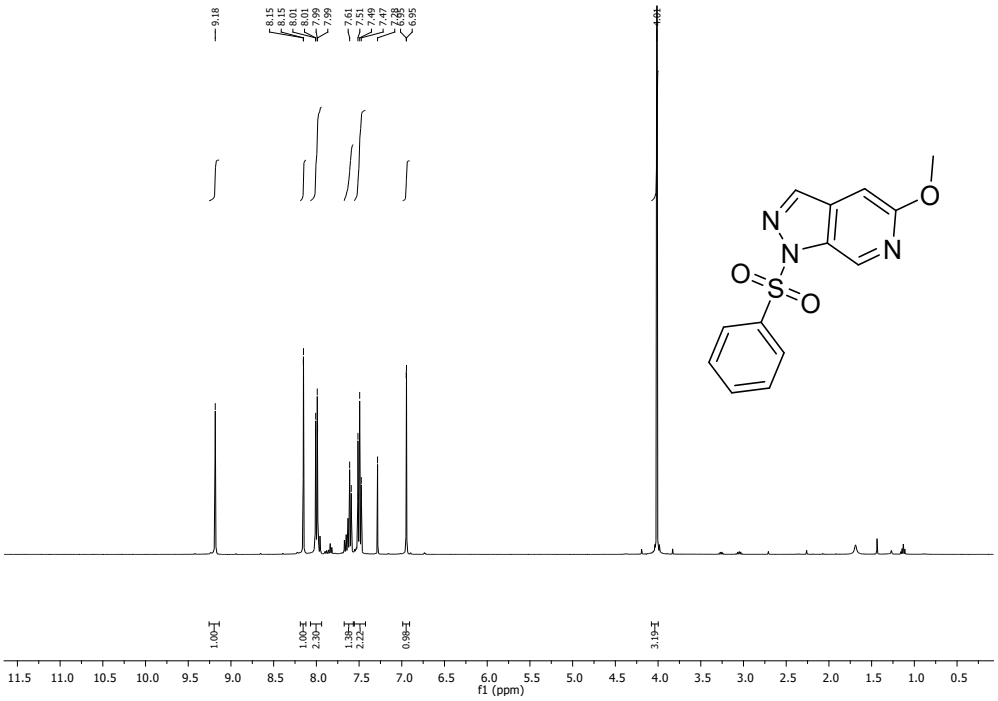
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-1-(naphthalen-2-ylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15b**)



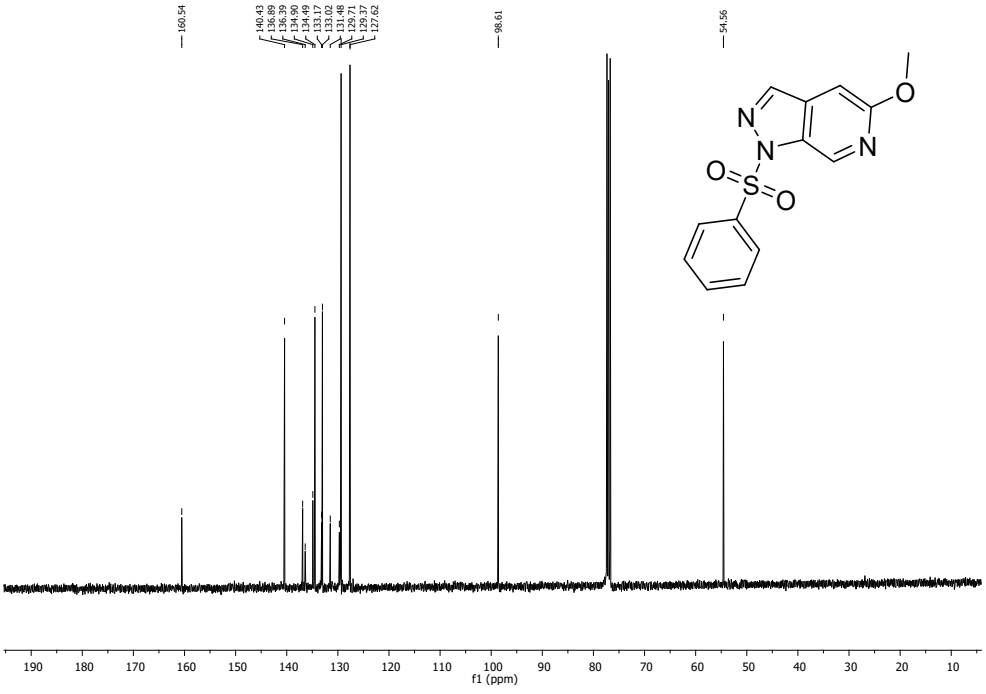
^{13}C NMR - 101 MHz in $CDCl_3$: 5-methoxy-1-(naphthalen-2-ylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15b**)



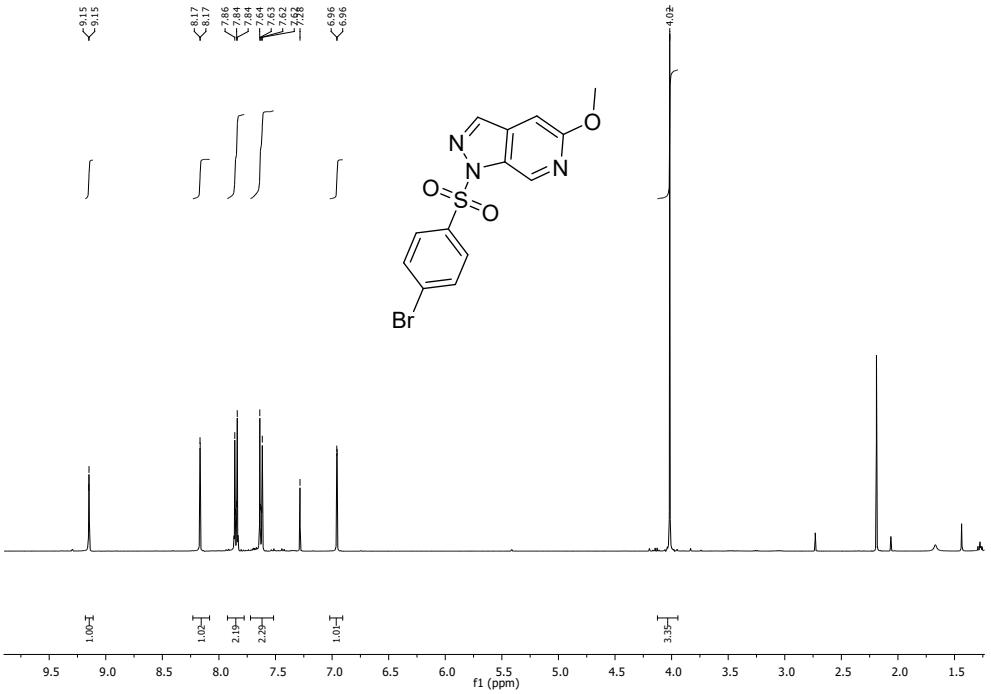
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-1-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15c**)



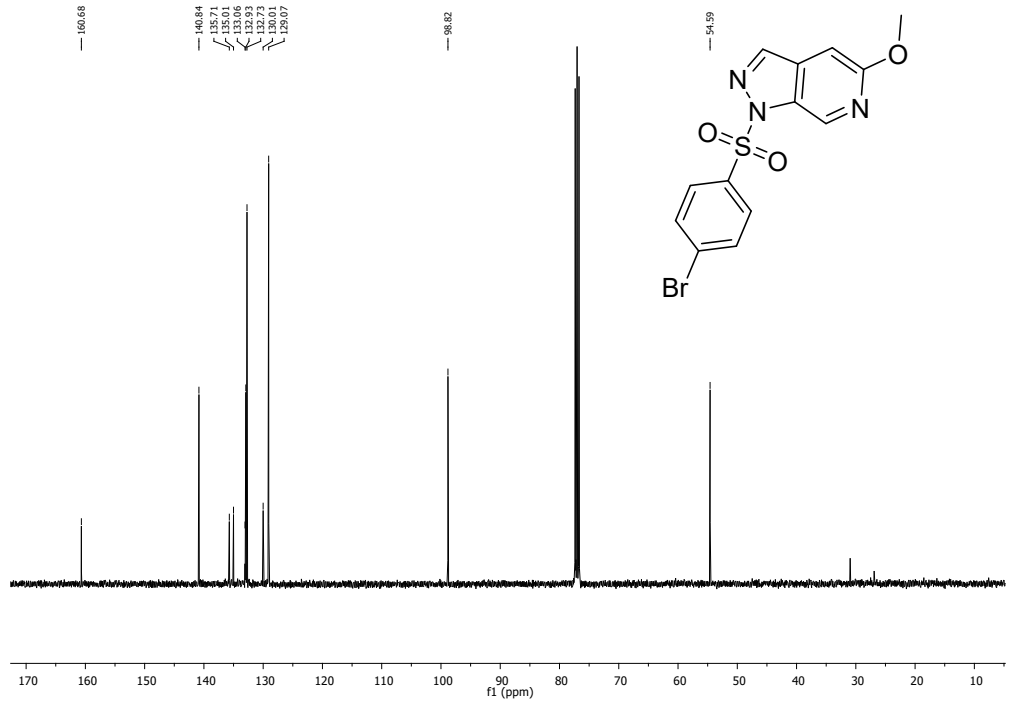
^{13}C NMR - 101 MHz in $CDCl_3$: *5-methoxy-1-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine* (**15c**)



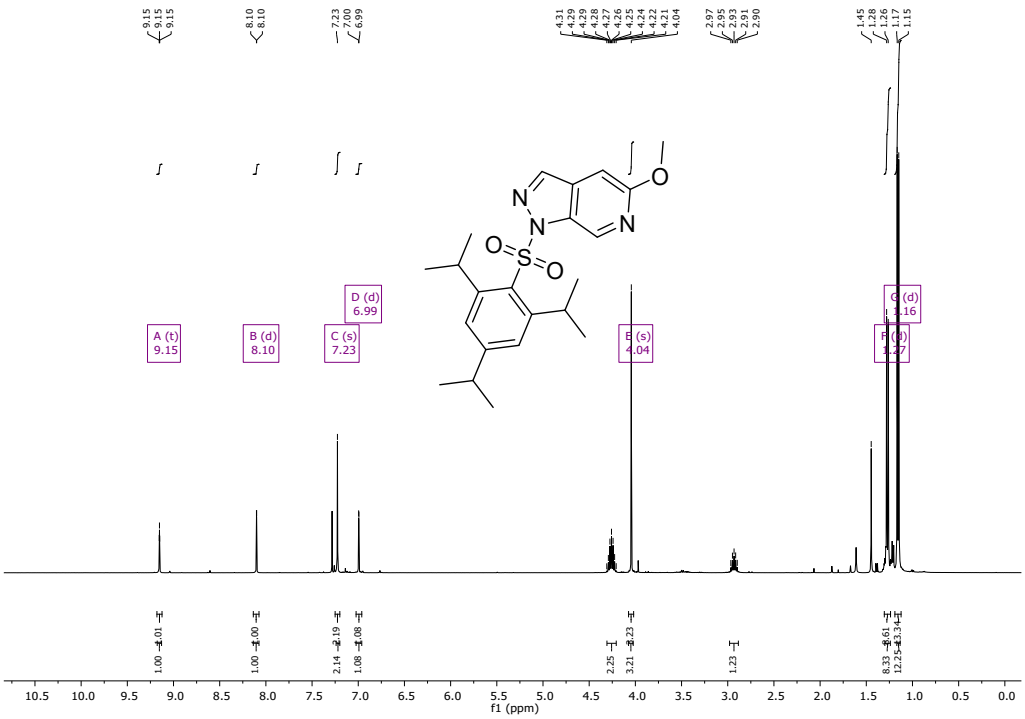
^{1}H-NMR – 400 MHz in $CDCl_3$: 1-((4-bromophenyl)sulfonyl)-5-methoxy-1H-pyrazolo[3,4-c]pyridine (**15d**)



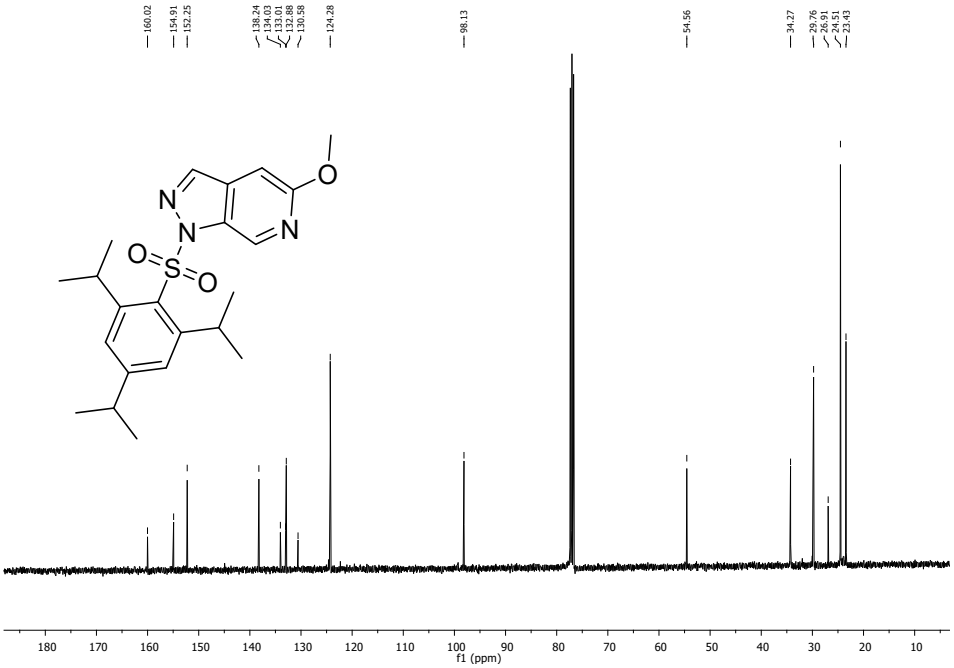
^{13}C NMR - 101 MHz in $CDCl_3$: 1-((4-bromophenyl)sulfonyl)-5-methoxy-1H-pyrazolo[3,4-c]pyridine (**15d**)



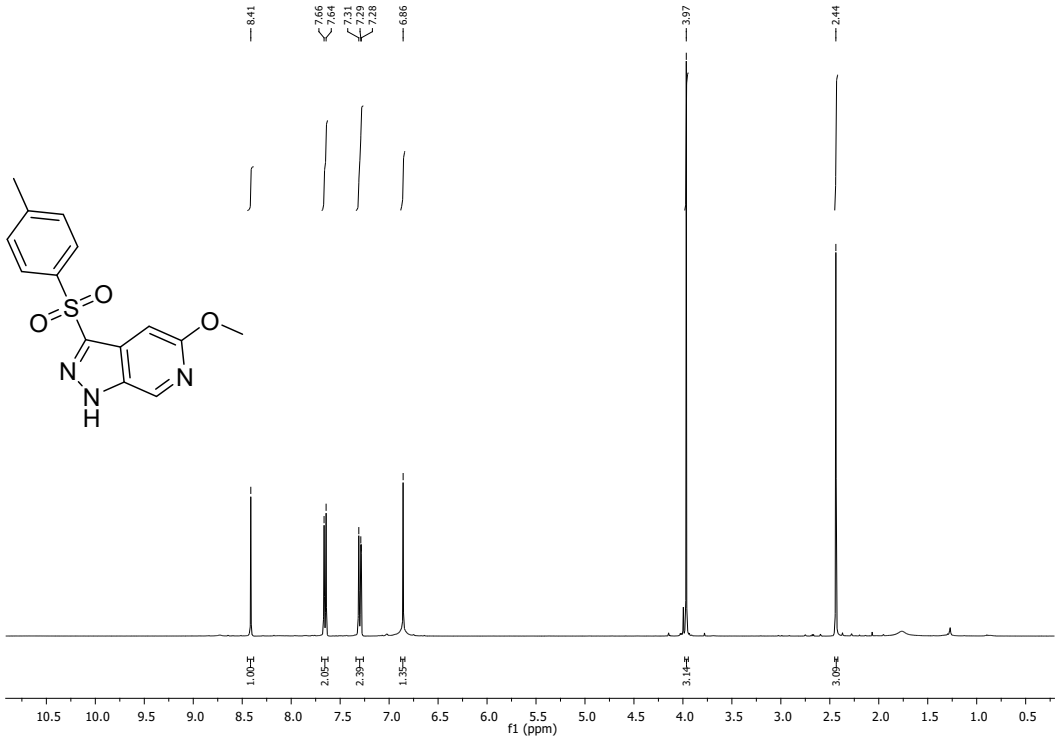
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-1-((2,4,6-triisopropylphenyl)sulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15e**)



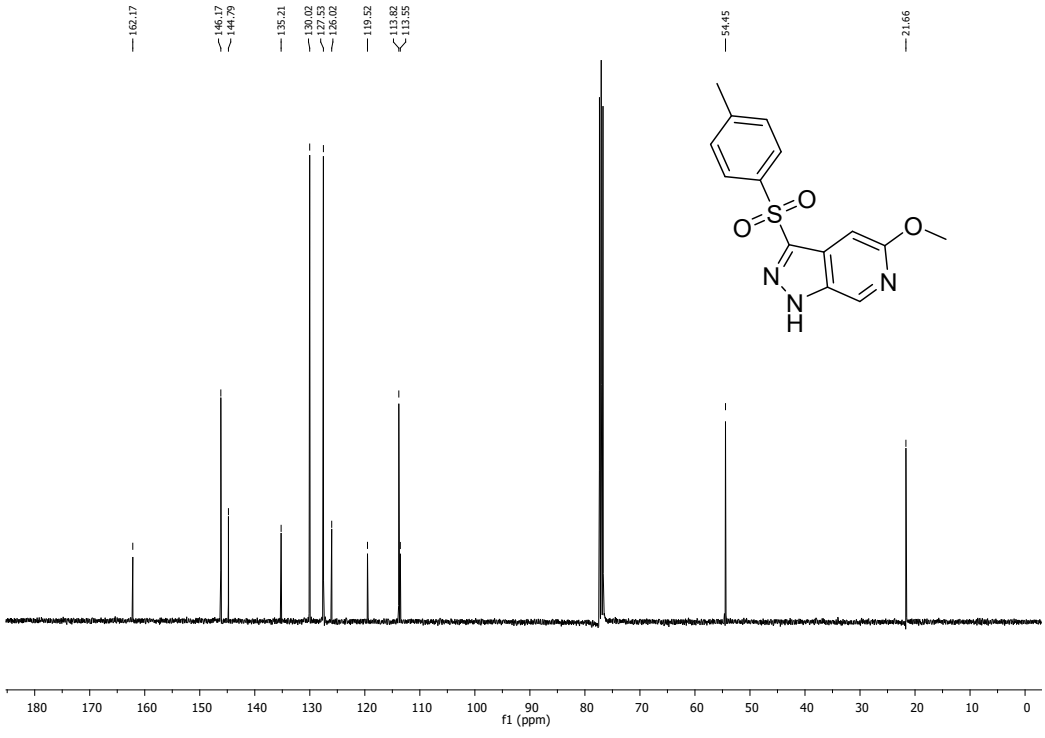
^{13}C NMR - 101 MHz in $CDCl_3$: 5-methoxy-1-((2,4,6-triisopropylphenyl)sulfonyl)-1H-pyrazolo[3,4-c]pyridine (**15e**)



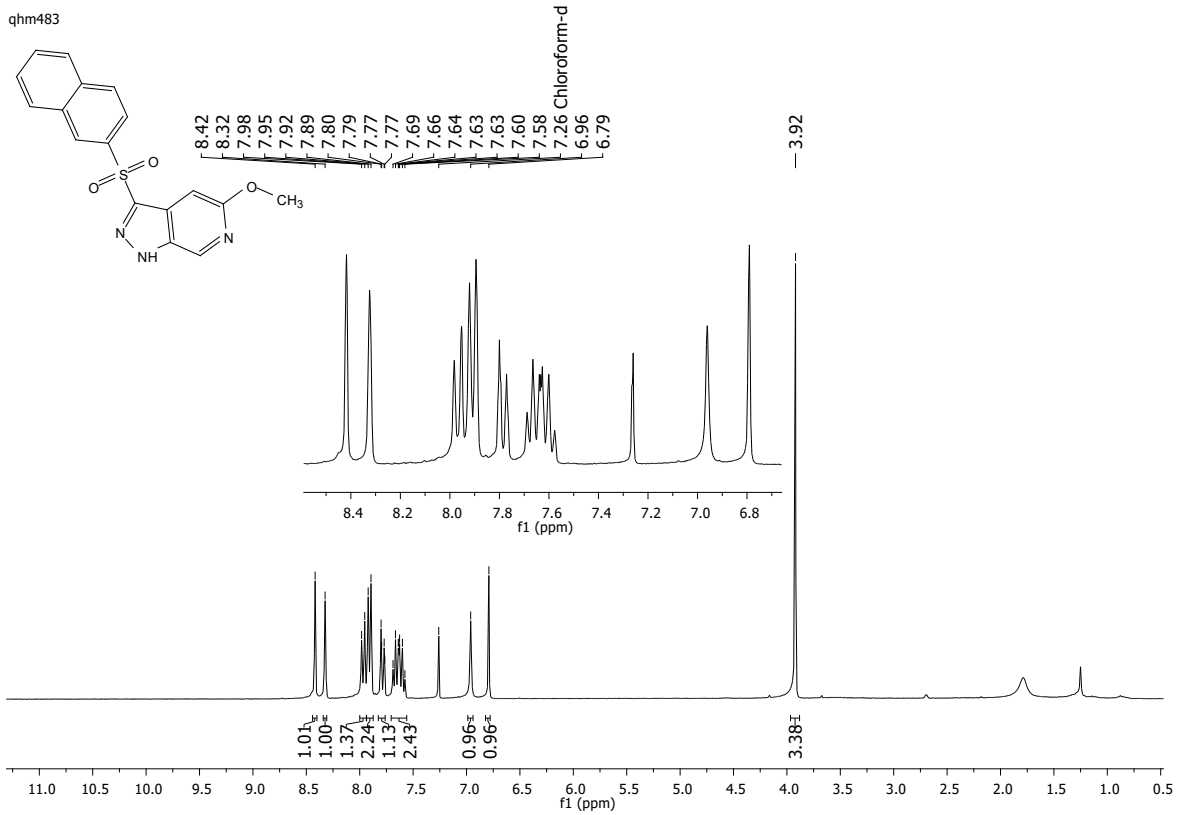
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-3-tosyl-1H-pyrazolo[3,4-c]pyridine (**14**)



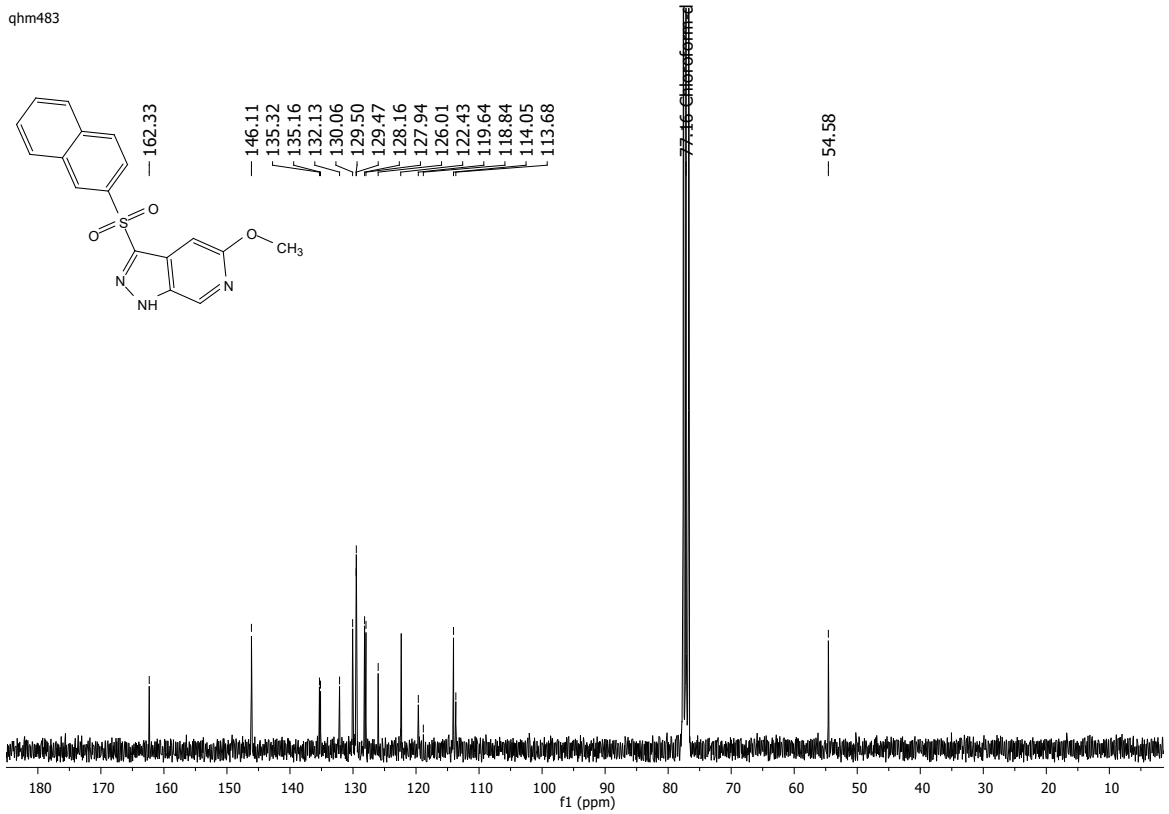
^{13}C NMR - 101 MHz in $CDCl_3$. 5-methoxy-3-tosyl-1H-pyrazolo[3,4-c]pyridine (**14**)



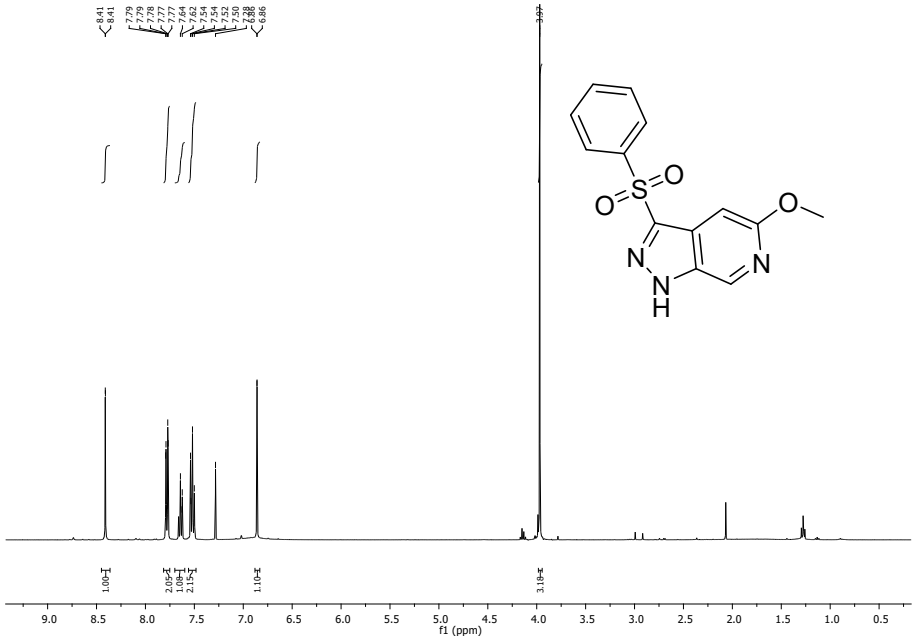
^{1}H-NMR – 300 MHz in $CDCl_3$: 5-methoxy-3-(naphthalen-2-ylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**16b**)



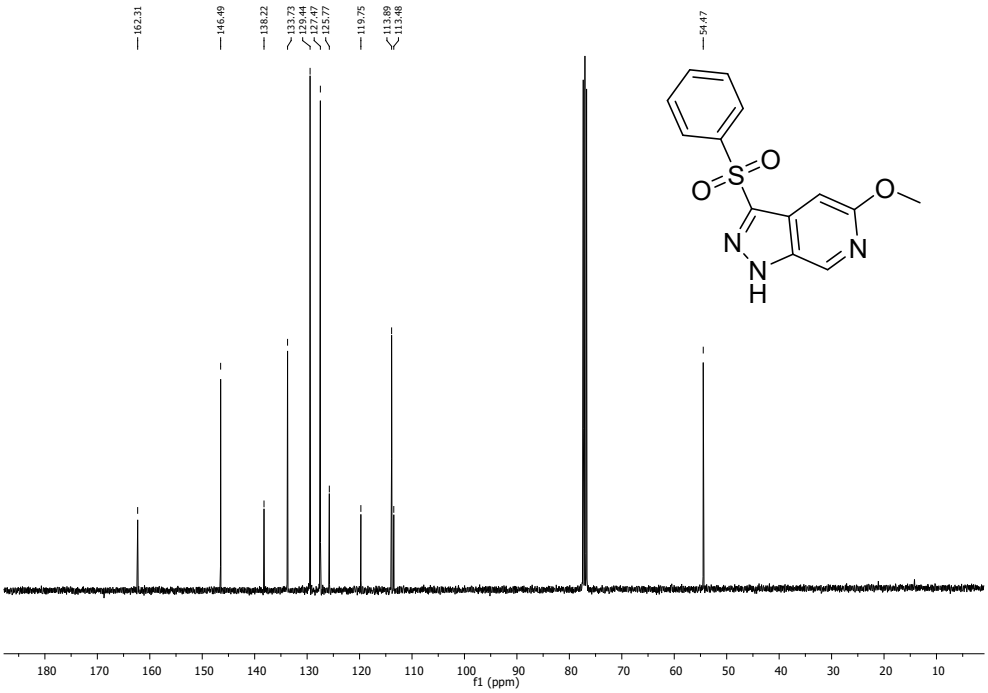
^{13}C NMR - 75 MHz in $CDCl_3$: 5-methoxy-3-(naphthalen-2-ylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**16b**)



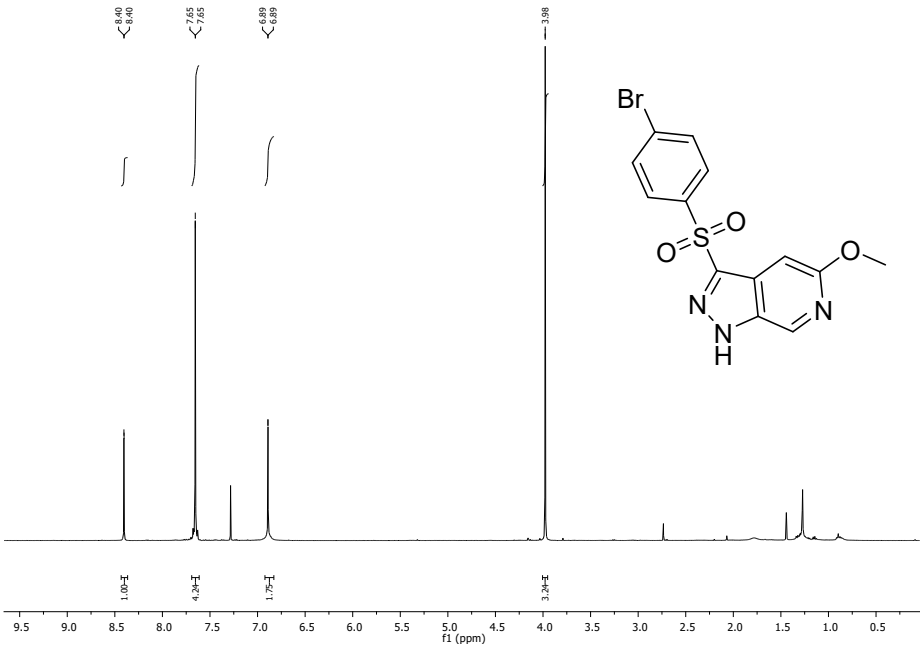
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-3-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**16c**)



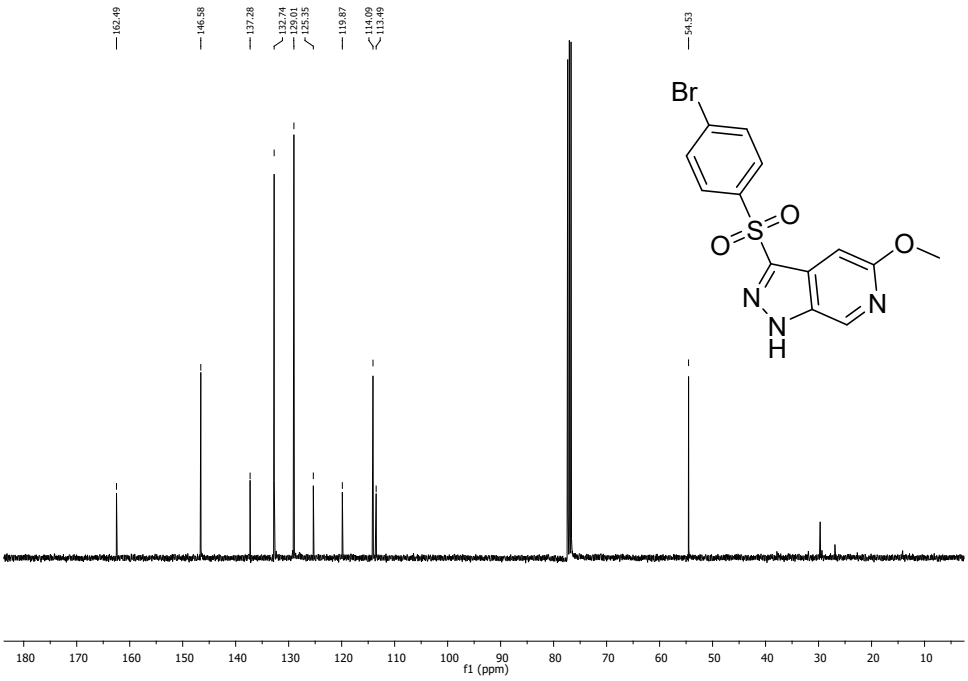
^{13}C NMR - 101 MHz in $CDCl_3$. 5-methoxy-3-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine (**16c**)



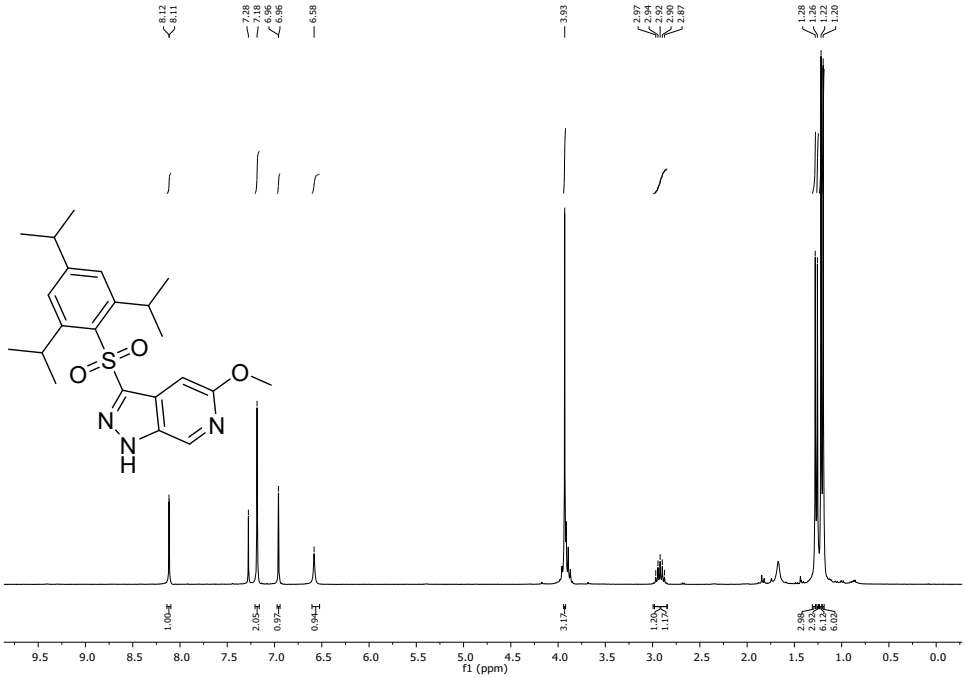
^{1}H-NMR – 400 MHz in $CDCl_3$: 3-((4-bromophenyl)sulfonyl)-5-methoxy-1H-pyrazolo[3,4-c]pyridine (**16d**)



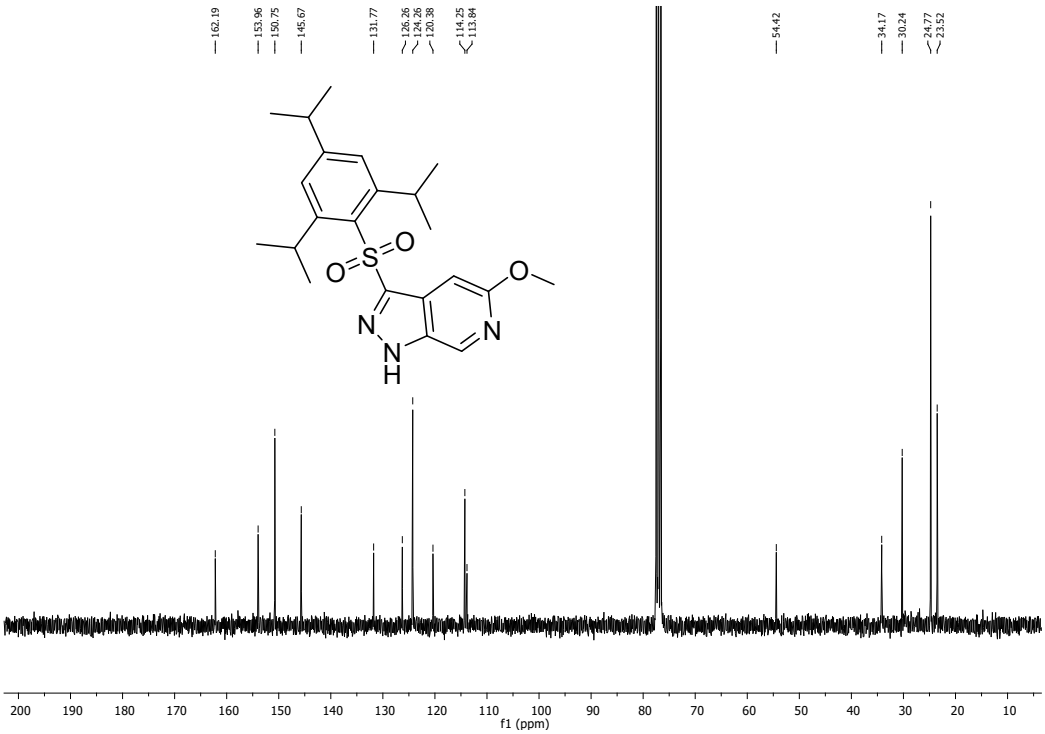
^{13}C NMR - 101 MHz in $CDCl_3$: 3-((4-bromophenyl)sulfonyl)-5-methoxy-1H-pyrazolo[3,4-c]pyridine (**16d**)



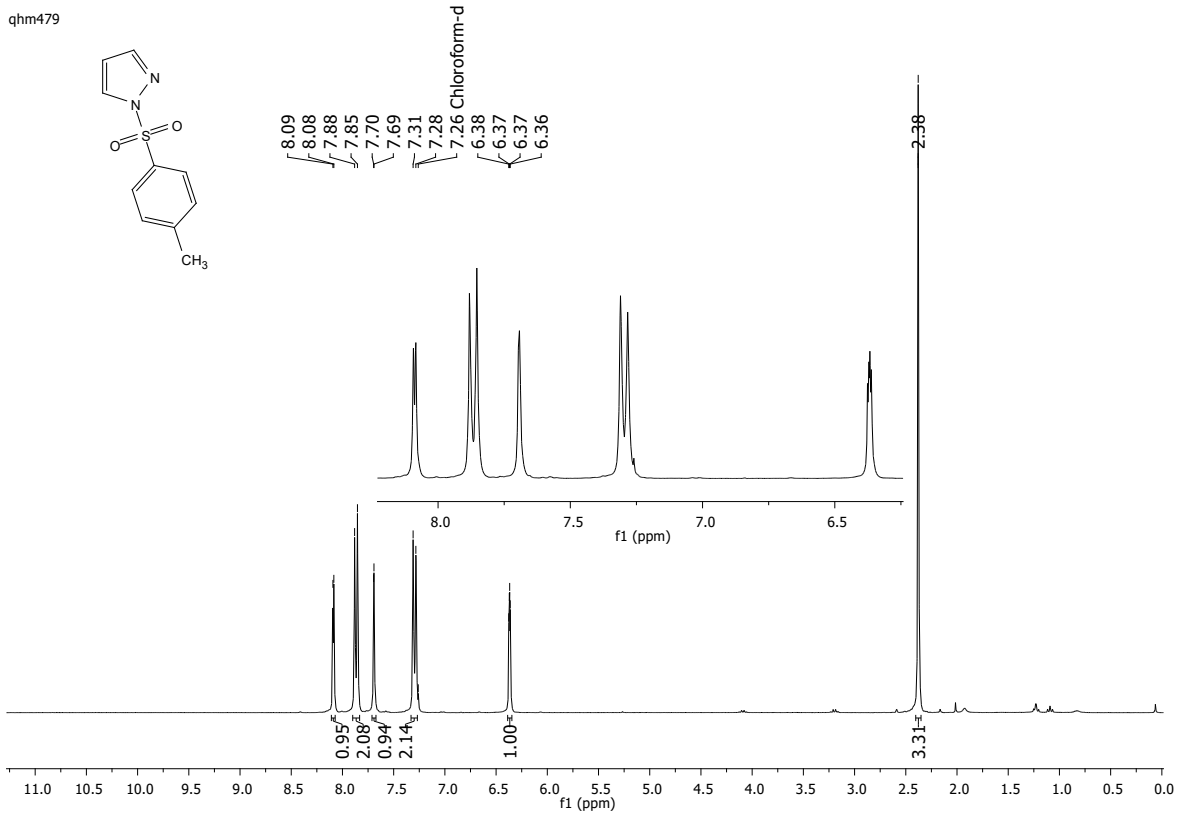
^{1}H-NMR – 400 MHz in $CDCl_3$: 5-methoxy-3-((2,4,6-triisopropylphenyl)sulfonyl)-1H-pyrazolo[3,4-c]pyridine (**16e**)



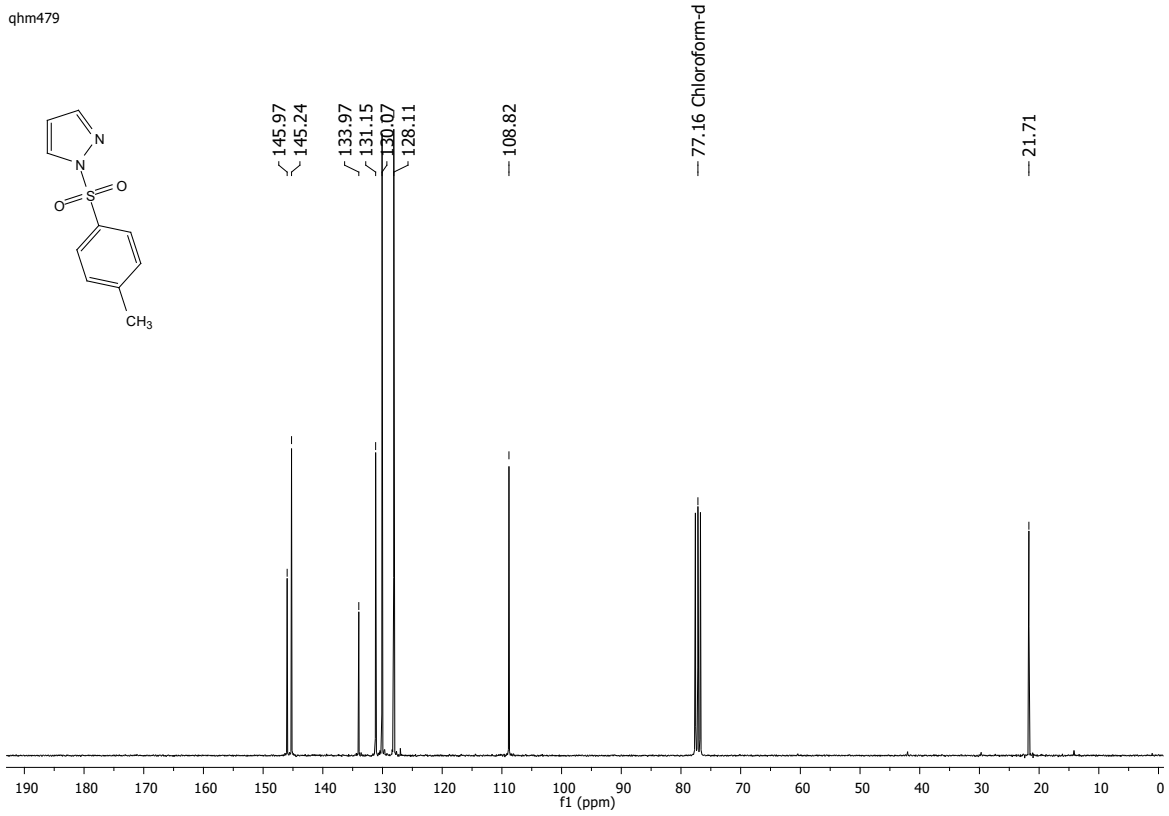
^{13}C NMR - 101 MHz in $CDCl_3$: 5-methoxy-3-((2,4,6-triisopropylphenyl)sulfonyl)-1H-pyrazolo[3,4-c]pyridine (**16e**)



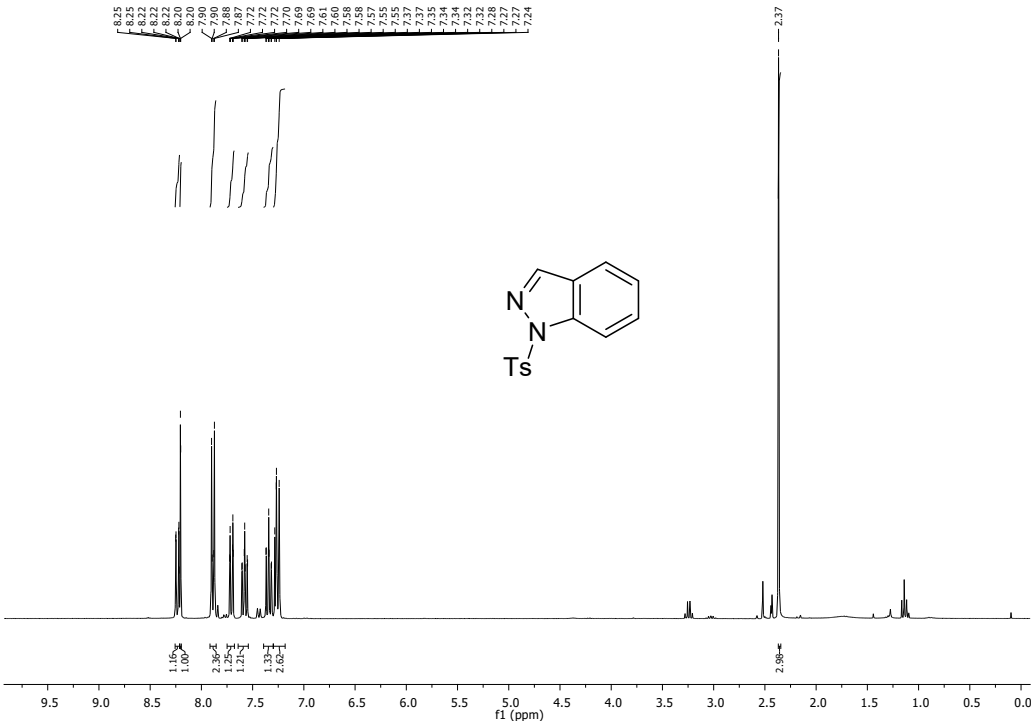
,,,^{1}H-NMR – 400 MHz in $CDCl_3$: 1-tosyl-1H-pyrazole (**17**)



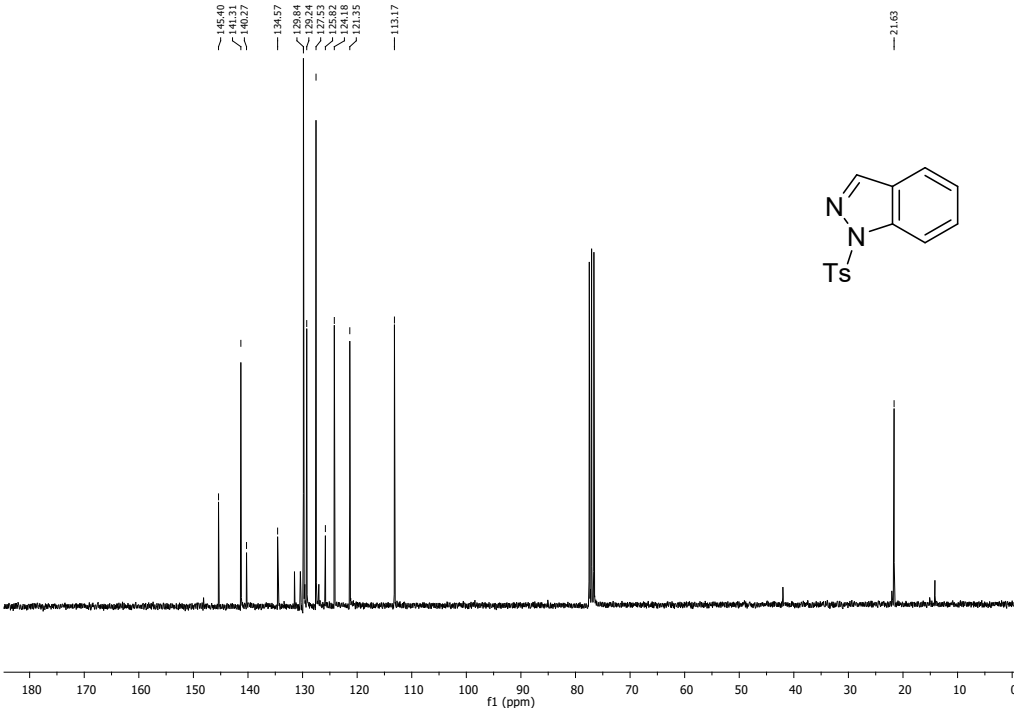
^{13}C NMR - 101 MHz in $CDCl_3$: 1-tosyl-1H-pyrazole (**17**)



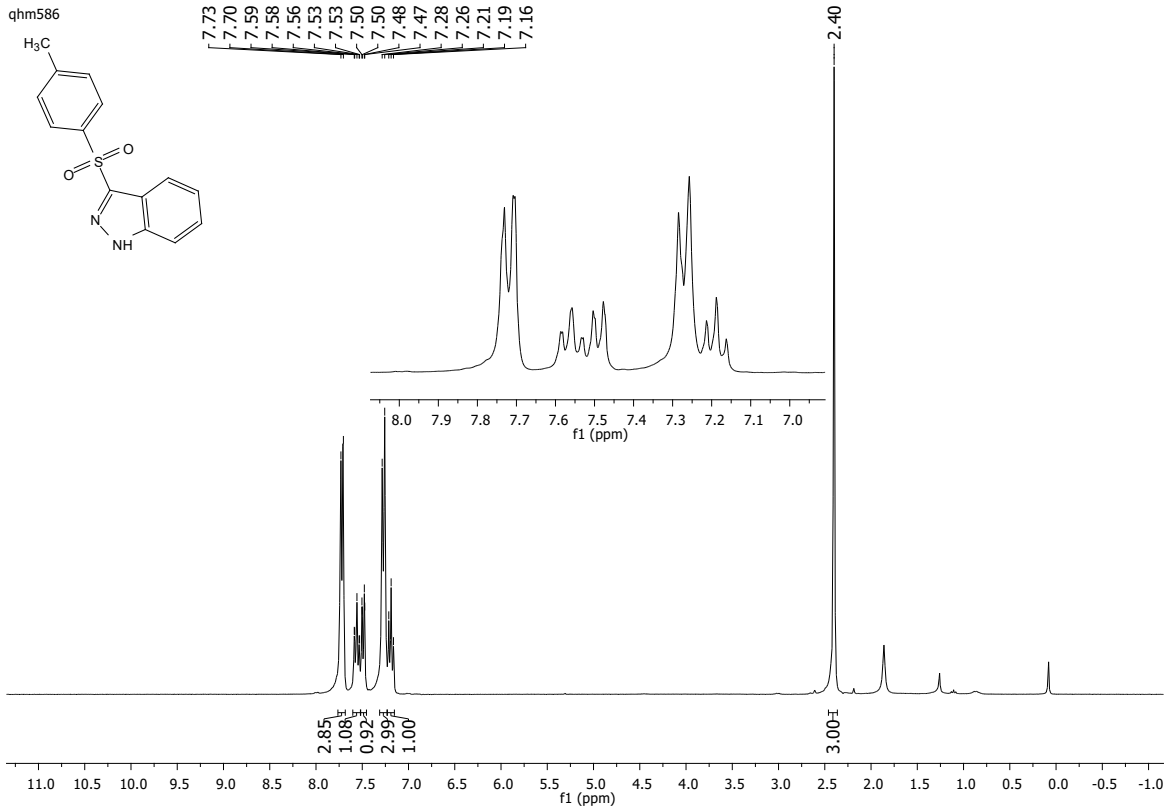
^{1}H-NMR – 400 MHz in $CDCl_3$: 1-tosyl-1H-indazole (**19**)



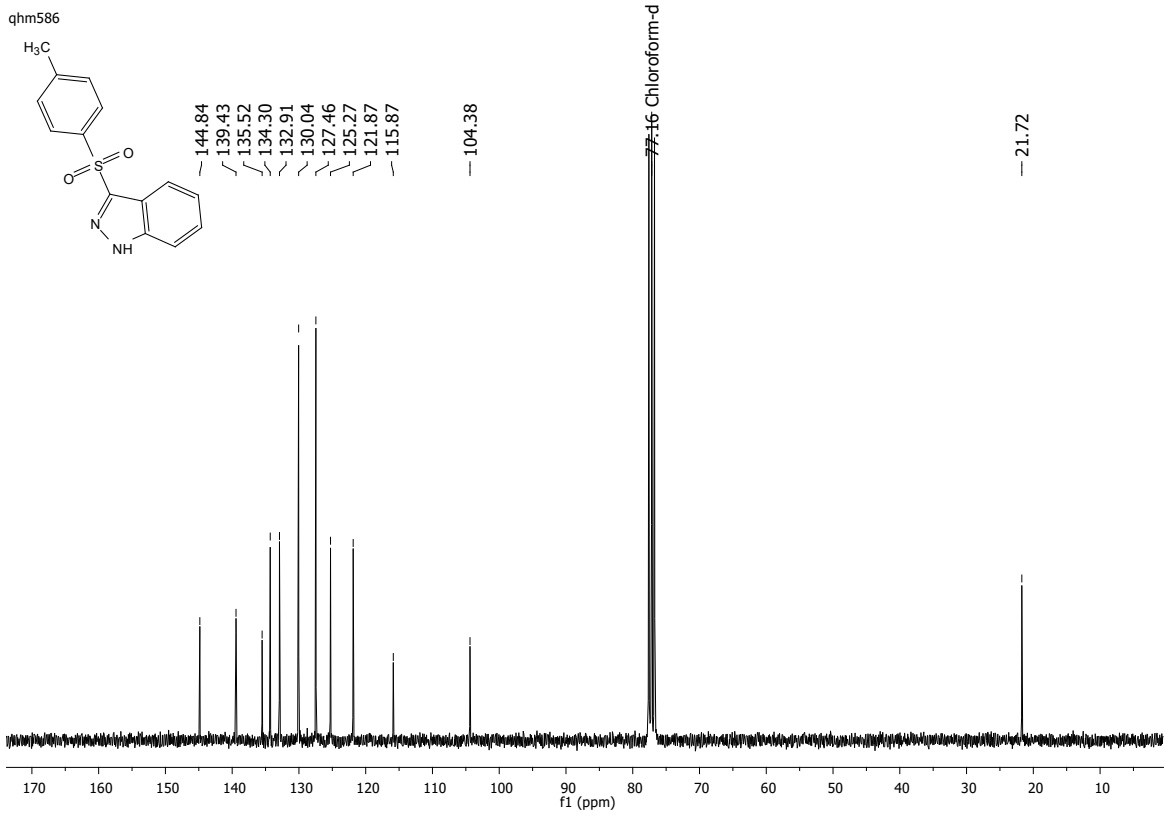
^{13}C NMR - 101 MHz in $CDCl_3$: 1-tosyl-1H-indazole (**19**)



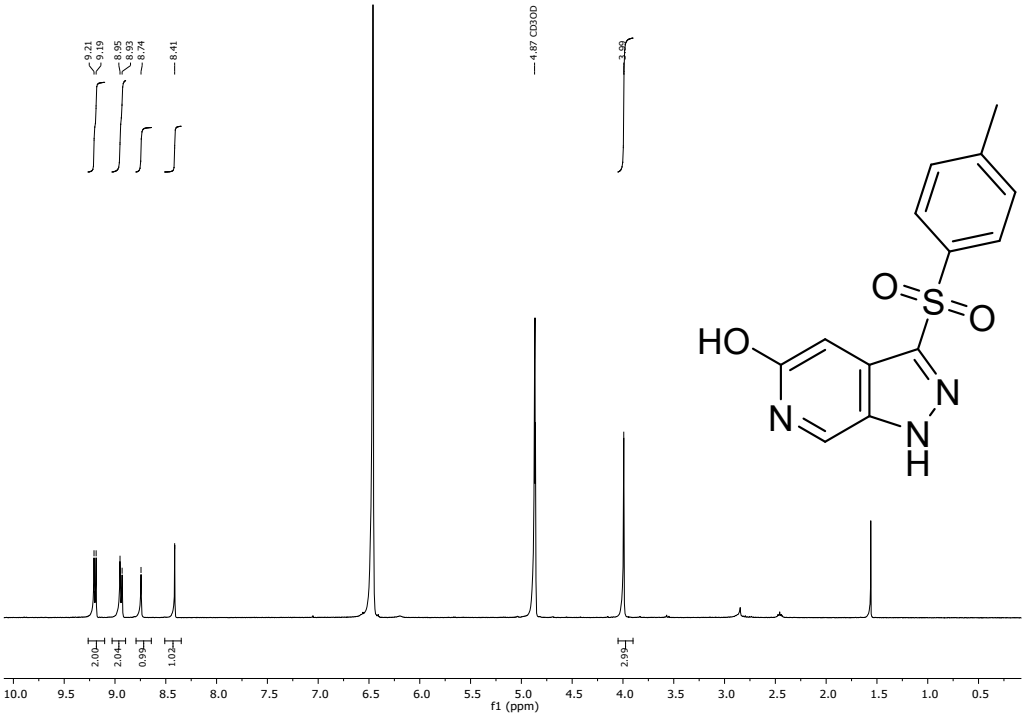
^{1}H-NMR – 300 MHz in $CDCl_3$: 3-tosyl-1H-indazole (**20**)



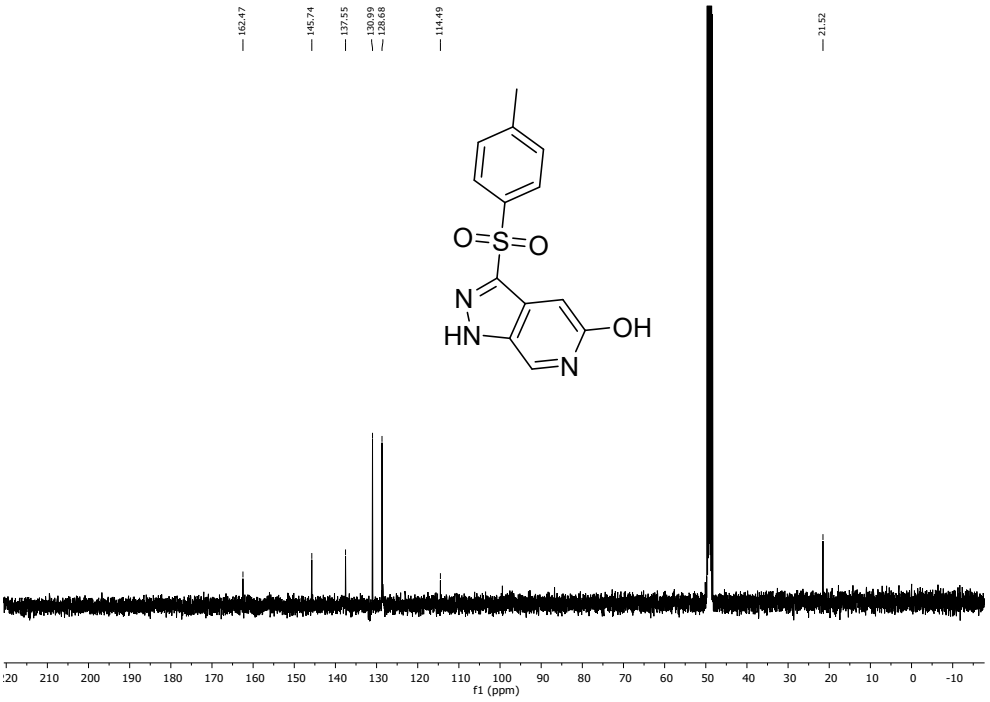
^{13}C NMR - 75 MHz in $CDCl_3$: 3-tosyl-1H-indazole (**20**)



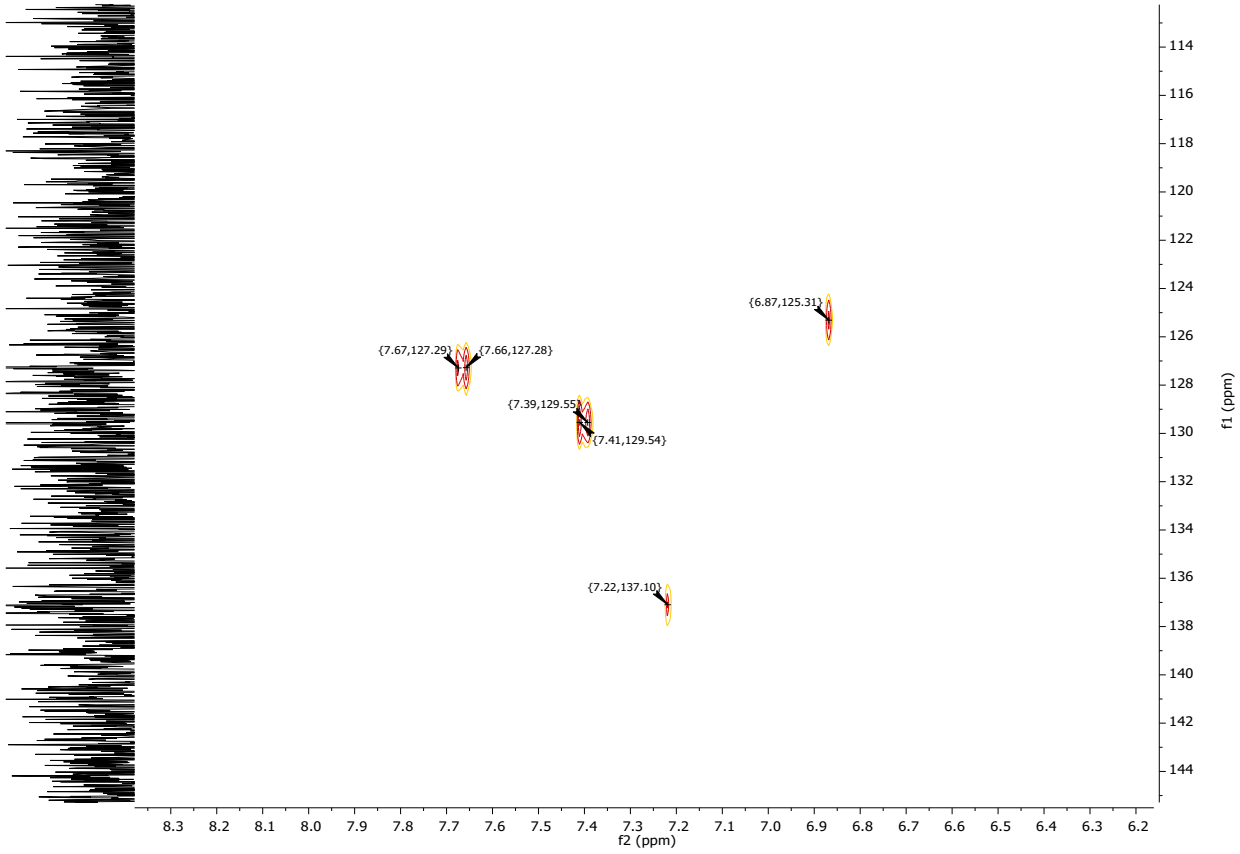
^{1}H-NMR – 400 MHz in CD_3OD: 3-tosyl-1H-pyrazolo[3,4-c]pyridin-5-ol (**21**)



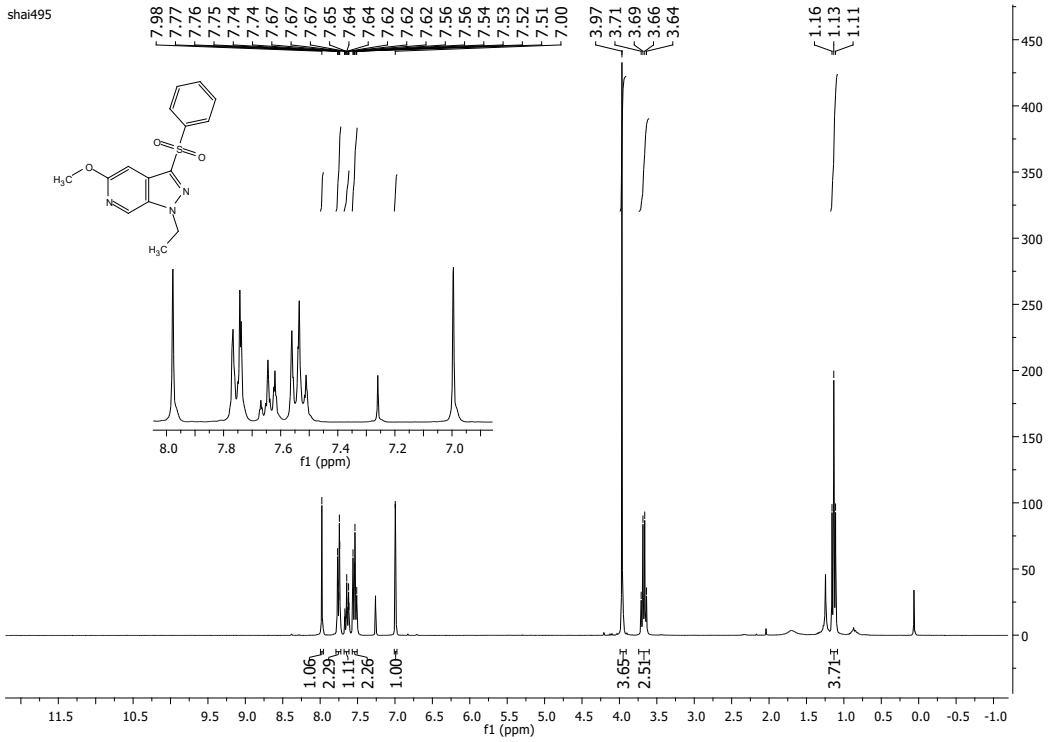
^{13}C NMR - 101 MHz in CD_3OD: 3-tosyl-1H-pyrazolo[3,4-c]pyridin-5-ol (**21**)



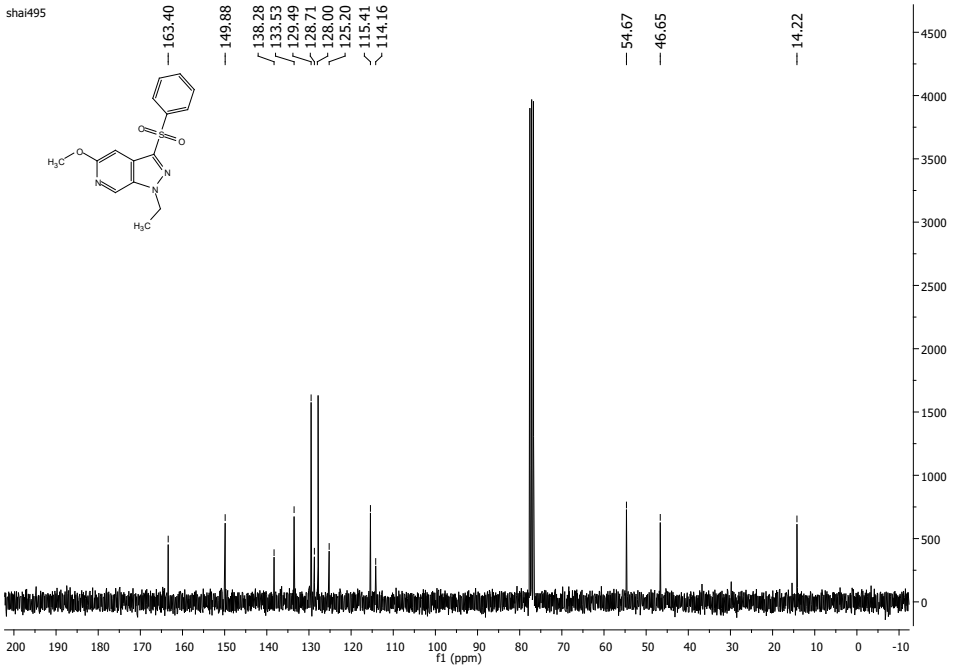
HMBC- 400 MHz in CD_3OD: 3-tosyl-1H-pyrazolo[3,4-c]pyridin-5-ol (**21**)



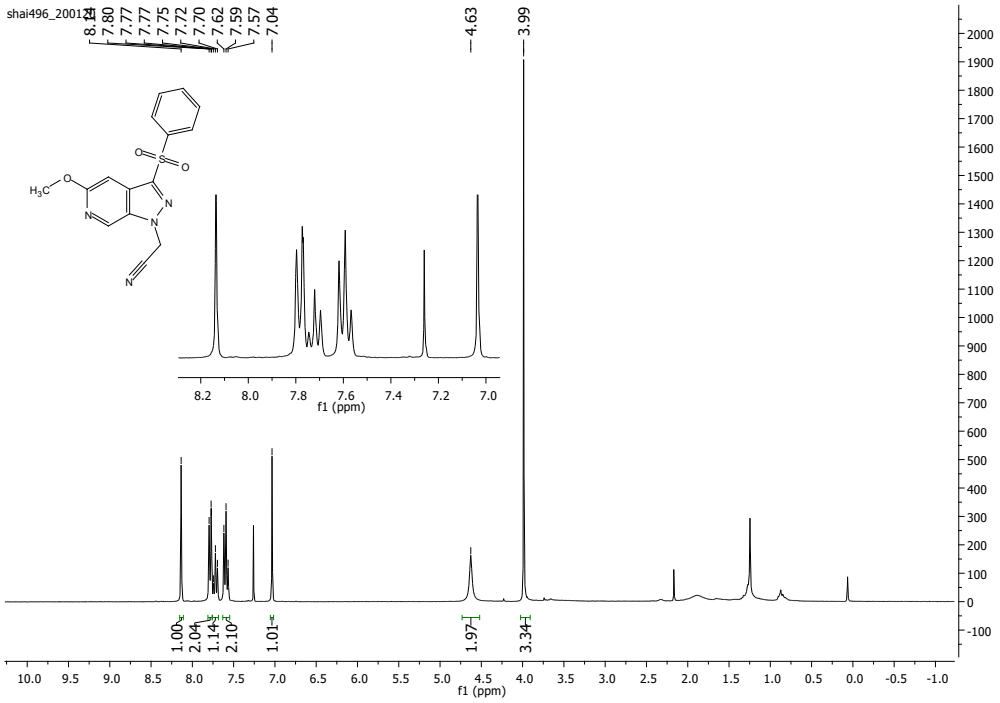
1-ethyl-5-methoxy-3-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine ^{1}H NMR (300 MHz, $CDCl_3$) (**22**)



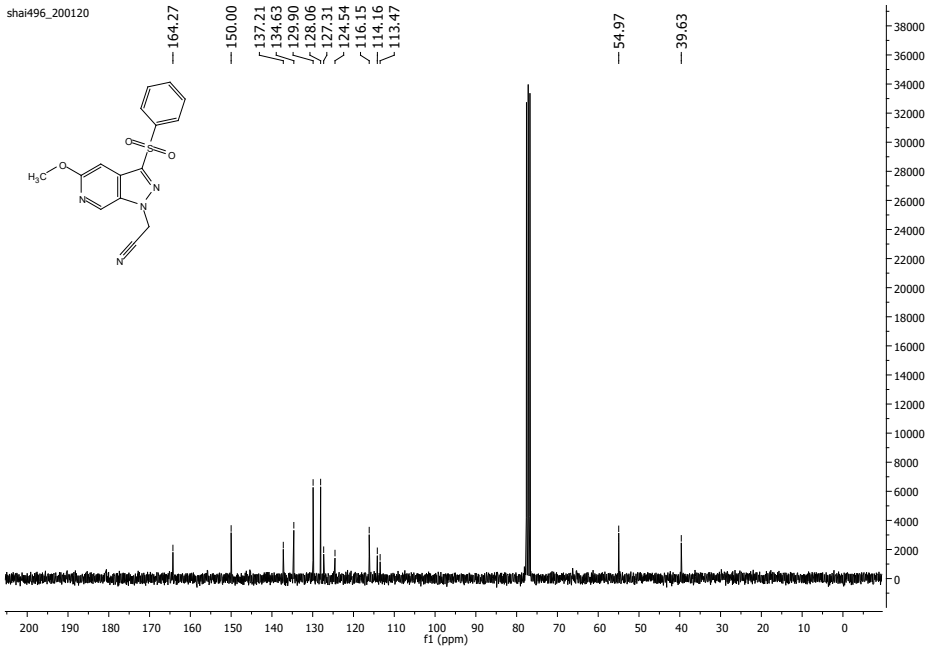
1-ethyl-5-methoxy-3-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridine. ^{13}C NMR (75 MHz, $CDCl_3$) (**22**)



2-(5-methoxy-3-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl)acetonitrile. ^{1}H NMR (300 MHz, $CDCl_3$) (**23**)



2-(5-methoxy-3-(phenylsulfonyl)-1H-pyrazolo[3,4-c]pyridin-1-yl)acetonitrile. ^{1}H ^{13}C NMR (75 MHz, $CDCl_3$) (**23**)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150.00
137.21
134.63
129.90
128.06
127.31
124.54
116.15
114.16
113.47
54.97
39.63
f1 (ppm)