Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Metal-Free Direct Oxidative C−C Bond Coupling of Quinoxalinones and Pyrazolones

Saowanee Toonchue,[a] Ladawan Sumunnee,[a] Khamphee Phomphrai[b] and Sirilata Yotphan[a]*

[a]*Center of Excellence for Innovation in Chemistry (PERCH-CIC), Department of Chemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*
E-mail: sirilata.yot@mahidol.ac.th

[b]*Department of Materials Science and Engineering, School of Molecular Science and Engineering, Vidyasirimedhi Institute of Science and Technology (VISTEC), Wangchan, Rayong, 21210, Thailand*

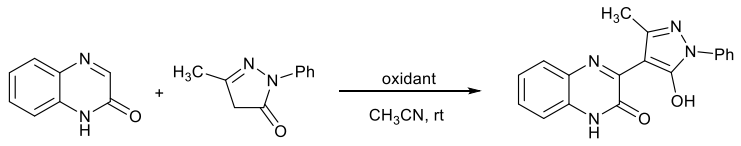
Table of Contents

I. General Procedure, Screening of Oxidants and Substrate Preparation

General Information:

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. All experiments were carried out under air atmosphere, and oven-dried glasswares were used in all cases. Column chromatography was performed over silica gel (SiO2; 60 Å silica gel, Merck Grade, 70–230 Mesh). ^{1}H and ^{13}C NMR spectra were recorded on Bruker-AV400 spectrometers in DMSO-d_6 or acetone-d_6 solution, at 400 and 100 MHz, respectively. NMR chemical shifts are reported in ppm, and were measured relative to DMSO (2.50 ppm for ^{1}H and 39.51 ppm for ^{13}C) or acetone (2. 05 ppm for ^{1}H and 29.92 ppm for ^{13}C). IR spectra were recorded on Bruker FT-IR Spectrometer Model ALPHA by neat method, and only partial data are listed. Melting points were determined on Buchi Melting Point M-565 apparatus. High resolution mass spectroscopy (HRMS) data were analysed by a high-resolution micrOTOF instrument with electrospray ionization (ESI).

Table S1. Effect of Oxidant.[a]

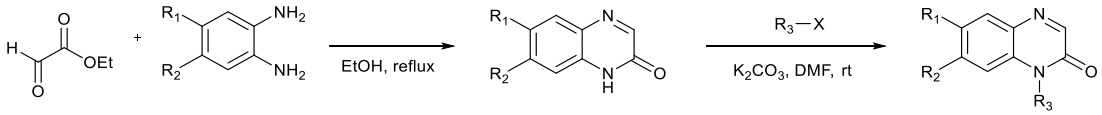


1a 2a 3a

entry	oxidant	equiv.	time (h)	%yield[b]
1	*m*-CPBA	2	16	60
2	Oxone	2	16	56
3	Benzoquinone	2	16	29
4	H_2O_2	2	16	52
5	TBHP	2	16	22
6	DTBP	2	16	31
7	$(NH_4)_2S_2O_8$	2	1	96
8	$Na_2S_2O_8$	2	1	72
9	**$K_2S_2O_8$**	**2**	**1**	**98**
10	$K_2S_2O_8$	1	1	80
11	$K_2S_2O_8$	3	1	99
12	air		16	25
13	No oxidant (under Ar)		16	trace

[a] Conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), oxidant (1−3 equiv.), CH_3CN (0.4 mL), rt, under air. [b] NMR yield.

General Procedure for the Preparation of Quinoxalinones:

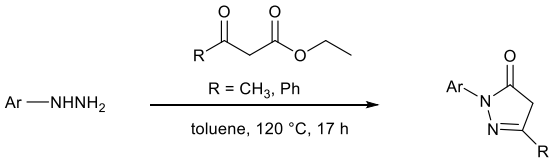


Ethyl 2- oxoacetate (1.1 equiv.) was added to a suspension of *o*-arylenediamine (4 mmol, 1 equiv.) in ethanol (1 mol/L). The reaction mixture was stirred and heated at reflux in an oil bath for 1 h, then at room temperature for 16 h. Upon completion (as monitored by

TLC), the precipitate was filtered and washed with ethanol, then dried to give quinoxalinone. For alkylation, the corresponding halogenoalkane (1.6 equiv.) was added to a suspension of quinoxalinone (1 equiv.) and potassium carbonate (1.2 equiv.) in DMF (16 mL). The mixture was stirred at room temperature for 16 h. Upon completion (as monitored by TLC), the reaction mixture was washed with saturated solution of ammonium chloride (NH_4Cl, 5 mL), ethyl acetate (10 mL) and water (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting organic residue was purified by flash chromatography column over silica gel (SiO_2) to afford the alkylated quinoxalinone.

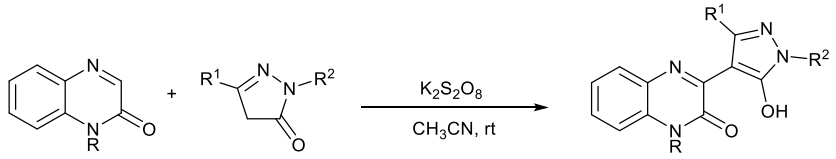
Quinoxalinone substrates employed in this work are known compounds and their ^1H NMR data agreed with the literature.[1]

Procedure for Preparation of Pyrazolone Substrates[2]:



A reaction mixture containing hydrazine (5 mmol), ethyl acetoacetate or ethyl 3-oxo-3-phenylpropanoate (5 mmol) and toluene(10 ml) was stirred at 120 °C in an oil bath. After 17 h, the reaction mixture was cooled to room temperature and the solvent was evaporated *in vacuo*. The organic residue was purified by flash column chromatography to yield a desired pyrazolone.

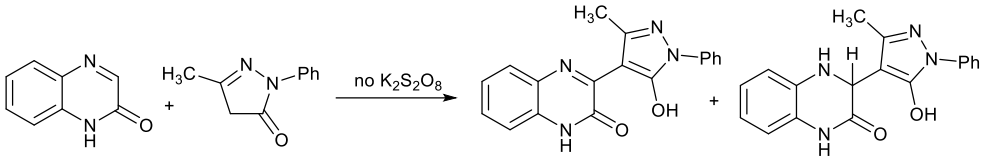
General Procedure for the Direct Oxidative C−C Bond Coupling of Pyrazolones and Quinoxalinones:



To a 2-dram vial equipped with a magnetic stir bar, quinoxalinone (0.5 mmol, 1.0 equiv.), pyrazolone (7.5 mmol, 1.5 equiv.), potassium persulfate ($K_2S_2O_8$) (270 mg, 1.0 mmol, 2.0 equiv.) and acetonitrile (CH_3CN) (2.00 mL) were added, respectively. The reaction mixture was stirred at room temperature or at 70 °C for 8 h. Upon completion, distilled deionized H_2O (10 mL) was added, and the mixture was extracted with ethyl acetate (EtOAc) (2 × 20 mL). The combined organic layer was washed with saturated NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by SiO_2 column chromatography to afford the hydroxy-pyrazolylquinoxalinone product.

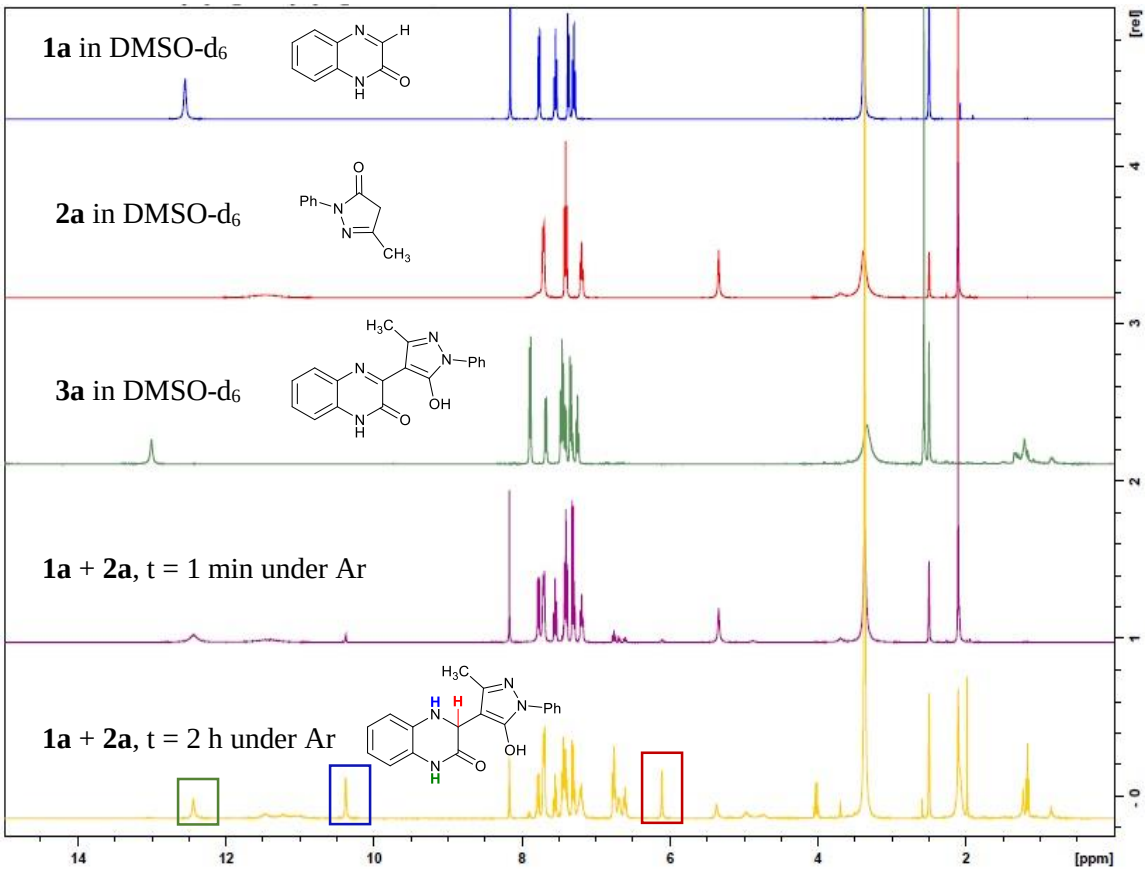
II. Miscellaneous Experiment

Control experiment in the absence of $K_2S_2O_8$

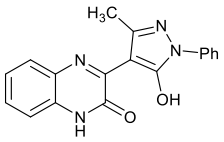


In the presence of $K_2S_2O_8$ oxidant, quinoxalinone and pyrazolone substrates underwent spontaneous C−C coupling to give the corresponding product. However, in the absence of $K_2S_2O_8$, approximately 25% of product **3a** was obtained from the reaction of **1a** and **2a** under air, and we could detect a reaction intermediate briefly by NMR. Meanwhile, the rest of starting materials could not be recovered from this reaction, indicating that a decomposition is likely to take place.

On the other hand, under an inert atmosphere of argon, we could not obtain the product from the reaction of **1a** and **2a** without the persulfate oxidant. However, we observed the possible reaction intermediate by NMR (shown below). This intermediate is unstable, could not be isolated, and underwent readily decomposition overtime. We suspected that this intermediate is likely to be the adduct (intermediate **I** or **II**) between quinoxalinone and pyrazolone.

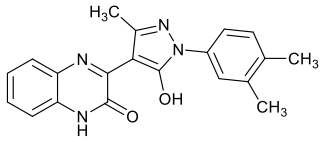


III. Characterization of Products



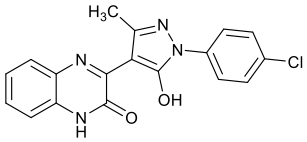
3a

3-(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3a). Orange solid (156 mg, 98% yield); mp = 274.3−274.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.48−7.43 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.35−7.31 (m , 8.4 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.7, 155.9, 148.7, 147.7, 138.3, 128.9 (2), 128.3, 127.7, 125.3, 124.6, 123.3, 119.9, 115.7, 98.3, 18.6; IR (neat, cm^{-1}): *ν* = 3042, 2995, 2851, 1681, 1611, 1587, 1383, 1015, 873, 818, 739, 713, 688; HRMS (ESI): calcd for $C_{18}H_{15}N_4O_2$ $[M+H]^+$ 319.1190, found 319.1199.



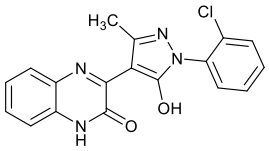
3b

3-(1-(3,4-Dimethylphenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3b). Orange solid (170 mg, 98% yield); mp = 273.3−273.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.04 (s, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.65 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.45−7.41 (m, 1H), 7.36−7.33 (m, 2H), 7.20 (d, *J* = 8.0 Hz, 1H), 2.57 (s, 3H), 2.27 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.9, 156.0, 148.4, 147.9, 136.7, 136.1, 133.4, 129.7, 129.4, 128.3, 127.8, 124.7, 123.7, 121.2, 117.6, 115.8, 98.3, 19.6, 18.9, 18.4; IR (neat, cm^{-1}): *ν* = 3039, 2920, 2870, 1682, 1605, 1499, 1382, 1125, 1016, 983, 870, 722, 671; HRMS (ESI): calcd for $C_{20}H_{19}N_4O_2$ $[M+H]^+$ 347.1503, found 347.1509.



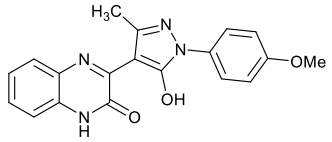
3c

3-(1-(4-Chlorophenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3c). Orange solid (123 mg, 70% yield); mp = 272.0–272.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.95 (s, 1H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 9.2 Hz, 2H), 7.44−7.40 (m, 1H), 7.35−7.31 (m, 2H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.3, 155.5, 148.8, 147.3, 137.0, 129.5, 128.9, 128.6, 128.2, 127.4, 124.3, 122.6, 121.0, 120.1, 115.6, 108.2, 98.1, 18.2; IR (neat, cm^{-1}): ν = 3099, 2954, 2918, 2849, 1681, 1611, 1382, 1088, 1016, 866, 737, 666, 563; HRMS (ESI): calcd for $C_{18}H_{14}ClN_4O_2$ $[M+H]^+$ 353.0800, found 353.0802.



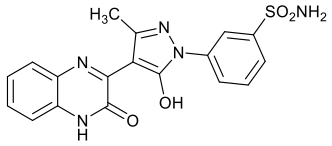
3d

3-(1-(2-Chlorophenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3d). Orange solid (74 mg, 42% yield); mp = 304.9 °C (decomposed); ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.16 (s, 1H), 7.71−7.66 (m, 2H), 7.56−7.49 (m, 3H), 7.48−7.43 (m, 1H), 7.38−7.34 (m, 2H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.3, 156.3, 149.1, 148.5, 135.1, 131.2, 130.7, 130.5, 130.1, 129.9,128.4, 128.1, 128.0, 124.9, 124.8, 115.8, 97.3, 18.1; IR (neat, cm^{-1}): *v* = IR ; 3169, 2925, 2849, 1693, 1601, 1486, 1366, 1261, 1013, 797, 754, 736, 644; HRMS (ESI): calcd for $C_{18}H_{14}ClN_4O_2$ $[M+H]^+$ 353.0800, found 353.0813.



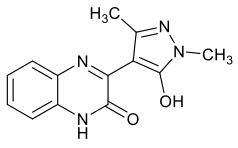
3e

3-(5-Hydroxy-1-(4-methoxyphenyl)-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3e). Orange solid (173 mg, 99% yield); mp = 175.1−175.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.08 (s, 1H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.46−7.42 (m, 1H), 7.37−7.33 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.0, 157.0, 156.1, 148.4, 148.1, 131.5, 129.5, 128.4, 127.9, 124.7, 124.2, 122.0, 115.8, 114.0, 98.3, 55.3, 18.3; IR (neat, cm^{-1}): *v* = 3039, 2919, 2773, 1682, 1504, 1383, 1297, 1242, 1163, 875, 754, 723, 666; HRMS (ESI): calcd for $C_{19}H_{17}N_4O_3$ $[M+H]^+$ 349.1295, found 349.1303.



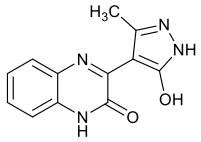
3f

3-(5-Hydroxy-3-methyl-4-(3-oxo-3,4-dihydroquinoxalin-2-yl)-1*H*-pyrazol-1-yl)benzenesulfonamide (3f). Orange solid (197 mg, 99% yield); mp = 299.5−300.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.93 (s, 1H), 8.46 (s, 1H), 8.21−8.18 (m, 1H), 7.70 (d, *J* = 8.4, 1H), 7.68−7.63 (m, 2H), 7.47 (s, 2H), 7.44−7.40 (m, 1H), 7.36−7.31 (m, 2H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.8, 155.6, 149.3(2), 147.3, 144.9, 138.6, 129.8(2), 127.6, 124.6, 122.2, 121.9, 121.8, 116.2, 116.0, 98.1, 19.0; IR (neat, cm^{-1}): *v* = 3189, 2919, 2855, 1863, 1589, 1445, 1366, 1156, 881, 795, 756, 746, 681; HRMS (ESI): calcd for $C_{18}H_{15}N_5NaO_4S$ $[M+Na]^+$ 420.0737, found 420.0748.



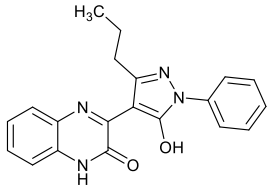
3g

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3g). Orange solid (110 mg, 86% yield); mp = 163.4−164.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.18 (s, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.45−7.41 (m, 1H), 7.36−7.32 (m, 2H), 3.47 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.6, 155.3, 149.2, 147.2, 132.4, 128.2, 128.1, 126.3, 124.8, 115.8, 97.4, 32.7, 17.4; IR (neat, cm^{-1}): *ν* = 3041, 2995, 2850, 1681, 1612, 1588, 1490, 1384, 1124, 1015, 874, 740, 688; HRMS (ESI): calcd for $C_{13}H_{13}N_4O_2$ $[M+H]^+$ 257.1033, found 257.1038.



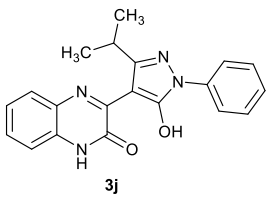
3h

3-(5-Hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3h). Yellow solid (89 mg, 73% yield); mp = 292.7−293.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.14 (s, 1H), 12.14 (s, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.49−7.45(m, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.4, 150.9, 133.0, 130.7, 128.8, 128.5, 127.3, 124.5, 123.2, 115.7, 100.4, 14.0; IR (neat, cm^{-1}): ν = 3032, 2914, 2793, 1641, 1515, 1476, 1391, 1147, 1062, 946, 871, 762, 666; HRMS (ESI): calcd for $C_{12}H_{12}N_4O_2$ $[M+H]^+$ 243.0877, found 243.0877.



3i

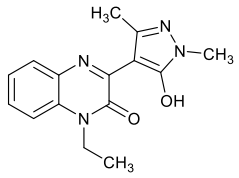
3-(5-Hydroxy-1-phenyl-3-propyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3i). Orange solid (121 mg, 70% yield); mp = 251.0−251.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.19 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.50−7.45 (m, 3H), 7.40−7.36 (m, 2H), 7.27 (t, *J* = 7.6 Hz, 1H), 3.02 (t, *J* = 7.6 Hz, 2H), 1.73−1.63 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.0, 156.2, 152.7, 148.1, 138.3, 130.5, 128.9, 128.3, 128.1, 125.6, 124.9, 124.6, 120.4, 115.8, 98.1, 32.9, 21.6, 14.1; IR (neat, cm^{-1}): *ν* = 3047, 2954, 2864, 1683, 1589, 1498, 1381, 1168, 987, 882, 752, 688, 655; HRMS (ESI): calcd for $C_{20}H_{19}N_4O_2$ $[M+H]^+$ 347.1503, found 347.1504.



3j

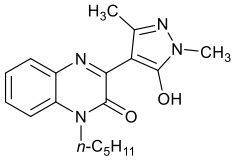
3-(5-Hydroxy-3-isopropyl-1-phenyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3j). Orange solid (85 mg, 49% yield); mp = 236.2−236.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.27 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.50−7.46 (m, 3H), 7.41−7.37 (m, 2H), 7.28 (t, *J* = 7.2 Hz, 1H),

4.05−3.98 (m, 1H), 1.29 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 157.5, 156.4, 148.3, 138.4, 131.3, 129.9, 129.4, 128.9, 128.7, 128.2, 125.6, 125.3, 124.9, 120.5, 118.8, 116.1, 97.8, 28.3, 21.6; IR (neat, cm^{-1}): *v* = 3192, 3139, 2917, 2849, 1680, 1492, 1373, 1138, 1011, 925, 836, 738, 674; HRMS (ESI): calcd for $C_{20}H_{19}N_4O_2$ $[M+H]^+$ 347.1503, found 347.1505.



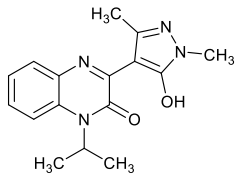
4a

1-Ethyl-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1H)-one (4a). Yellow solid (103 mg, 72% yield); mp = 148.9−149.1 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.76−7.70 (m, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.45−7.41 (m, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 3.50 (s, 3H), 2.46 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 155.6, 150.6, 133.3, 131.6, 130.4, 129.0, 127.8, 125.3, 123.8, 115.5, 115.1, 38.6, 33.2, 17.9, 12.7; IR (neat, cm^{-1}): *v* = 3078, 2961, 2920, 1663, 1550, 135, 131, 1165, 904, 821, 743, 688, 652; HRMS (ESI): calcd for $C_{15}H_{17}N_4O_2$ $[M+H]^+$ 285.1346, found 285.1355.



4b

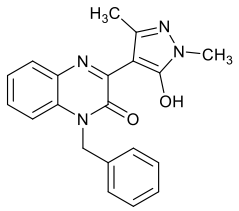
3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-1-pentylquinoxalin-2(1*H*)-one (4b). Yellow solid (152 mg, 93% yield); mp = 274.3−274.8 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.74 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.57−7.53 (m, 1H), 7.45−7.41 (m, 1H), 4.32 (t, *J* = 7.6 Hz, 2H), 3.50 (s, 3H), 2.45 (s, 3H), 1.73−1.66 (m, 2H), 1.44−1.33 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 155.4, 155.1, 148.3, 147.3, 132.8, 128.9, 128.5, 127.3, 124.8, 115.1, 97.3, 42.8, 32.8, 28.3, 26.5, 21.9, 17.4, 13.8; IR (neat, cm^{-1}): *v* = 3064, 2954, 2919, 2852, 1619, 1402, 1342, 1166, 901, 759, 692, 657, 576; HRMS (ESI): calcd for $C_{18}H_{23}N_4O_2$ $[M+H]^+$ 327.1816, found 327.1825.



4c

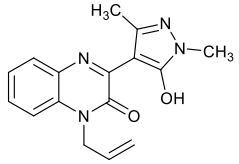
3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-1-isopropylquinoxalin-2(1*H*)-one (4c). Orange solid (18 mg, 12% yield); mp = 103.4−103.7 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.84−7.82 (m, 1H), 7.74−7.72 (m, 1H), 7.60−7.53 (m, 2H), 5.57−5.51 (m, 1H), 3.48 (s, 3H), 2.28 (s, 3H), 1.41 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 157.4, 153.7, 144.7, 141.4, 136.7, 133.6, 127.9, 127.0, 126.1, 124.0, 94.9, 69.7, 32.1, 21.4, 16.5; IR (neat, cm^{-1}): *v* = 3066, 2954, 2853, 1731, 1595, 1538, 1463,

1375, 1178, 1106, 939, 755, 628; HRMS (ESI): calcd for $C_{16}H_{19}N_4O_2$ $[M+H]^+$ 299.1503, found 299.1512.



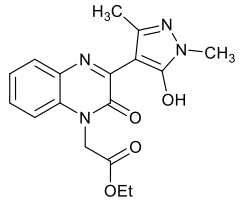
4d

1-Benzyl-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1H)-one (4d). Yellow solid (156 mg, 90% yield); mp = 161.0−161.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.73 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.45−7.38 (m, 2H), 7.36−7.31 (m, 4H), 7.28−7.26 (m, 1H), 5.61 (s, 2H), 3.48 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.9, 155.6, 148.3, 147.3, 135.2, 132.4, 129.0, 128.8, 128.2, 127.5, 126.8(2), 125.0, 115.5, 97.4, 46.0, 32.7, 17.6; IR (neat, cm^{-1}): *v* = 3078, 2958, 2918, 1554, 1439, 1375, 1330, 1116, 941, 857, 820, 755, 690; HRMS (ESI): calcd for $C_{20}H_{19}N_4O_2$ $[M+H]^+$ 347.1503, found 347.1510.



4e

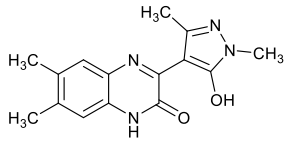
1-Allyl-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4e). Yellow solid (101 mg, 68% yield); mp = 128.4−129.0 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.53−7.48 (m, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 6.03−5.93 (m, 1H), 5.22−5.13 (m, 2H), 4.99 (d, *J* = 4.8 Hz, 2H), 3.49 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.5, 155.4, 148.3, 147.2, 132.4, 131.1, 128.9, 128.3, 126.9, 124.9, 117.5, 115.5, 97.3, 45.0, 32.7, 17.5; IR (neat, cm^{-1}): *v* = 2980, 2925, 1721, 1690, 1622, 1411, 1342, 1164, 994, 912, 887, 758, 693; HRMS (ESI): calcd for $C_{16}H_{17}N_4O_2$ $[M+H]^+$ 297.1346, found 297.1351.



4f

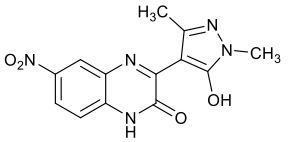
Ethyl 2-(3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (4f). Yellow solid (170 mg, 99% yield); mp = 191.9−192.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.80 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.55−7.51 (m, 1H), 7.47−7.43 (m, 1H), 5.23 (s, 2H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.50 (s, 3H), 2.46 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.7, 155.6, 155.3, 147.6, 147.0, 131.8, 129.1, 128.2, 126.5, 124.9, 114.7, 97.0, 61.3, 44.6, 32.5,

17.0, 13.7; IR (neat, cm^{-1}): ν = 3011, 2978, 2918, 1741, 1554, 1383, 1168, 1114, 1024, 947, 874, 756, 692; HRMS (ESI): calcd for $C_{17}H_{19}N_4O_4$ $[M+H]^+$ 343.1401, found 343.1408.



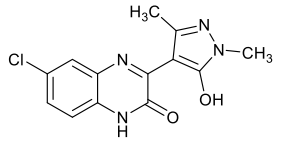
4g

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-6,7-dimethylquinoxalin-2(1*H*)-one (4g). Orange solid (93 mg, 65% yield); mp = 325.4−326.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.12 (s, 1H), 7.47 (s, 1H), 7.12 (s, 1H), 3.48 (s, 3H), 2.44 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.5, 154.8, 148.3, 147.0, 137.8, 133.7, 131.3, 126.6, 126.3, 115.8, 97.3, 32.8, 19.7, 19.1, 17.3; IR (neat, cm^{-1}): ν = 3591, 2917, 2852, 1640, 1563, 1510, 1445, 1415, 1147, 928, 882, 722, 677; HRMS (ESI): calcd for $C_{15}H_{17}N_4O_2$ $[M+H]^+$ 285.1346, found 285.1358.



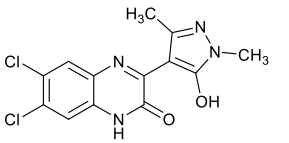
4h

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-6-nitroquinoxalin-2(1*H*)-one (4h). Orange solid (149 mg, 99% yield); mp = 144.5−144.9 °C; ^{1}H NMR (400 MHz, Acetone-d_6): δ 14.42 (s, 1H), 8.31 (d, J = 2.4 Hz, 1H), 8.18 (dd, J = 8.8, 2.4 Hz, 1H), 7.90 (d, J = 8.8 Hz, 1H), 3.53 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, Acetone-d_6): δ 156.2, 149.5, 129.0, 128.1, 125.8, 120.1, 119.5, 118.4, 116.5, 111.6, 99.5, 33.2, 18.2; IR (neat, cm^{-1}): ν = 3079, 2918, 2849, 1638, 1562, 1518, 1339, 1161, 1085, 904, 817, 711, 660; HRMS (ESI): calcd for $C_{13}H_{12}N_5O_4$ $[M+H]^+$ 302.0884, found 302.0885.



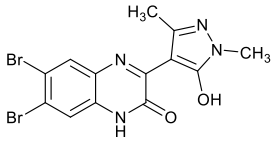
4i

6-Chloro-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4i). Yellow solid (142 mg, 98% yield); mp = 327.5−328.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.24 (s, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.37 (dd, J = 8.4, 2.4 Hz, 1H), 7.33 (d, J = 2.4 Hz, 1H), 3.48 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.7, 155.0, 149.7, 147.4, 131.8, 131.6, 129.3, 128.2, 124.9, 115.0, 97.4, 32.9, 17.4; IR (neat, cm^{-1}): ν = 3128, 2915, 1645, 1562, 1545, 1483, 1118, 1004, 817, 738, 666, 615, 549; HRMS (ESI): calcd for $C_{13}H_{12}ClN_4O_2$ $[M+H]^+$ 291.0643, found 291.0647.



4j

6,7-Dichloro-3-(5-hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)quinoxalin-2(1H)-one (4j). Yellow solid 115 mg, 71% yield); mp = 334.7−335.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.32 (s, 1H), 7.92 (s, 1H), 7.47 (s, 1H), 3.49 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.6, 154.9, 150.8, 147.6, 132.5, 129.6, 128.2, 127.5, 126.6, 116.7, 97.6, 32.8, 17.3; IR (neat, cm^{-1}): *ν* = 2924, 2769, 1684, 1562, 1148, 1114, 1052, 983, 899, 856, 766, 719, 669;HRMS (ESI): calcd for $C_{13}H_{11}Cl_2N_4O_2$ $[M+H]^+$ 325.0254, found 325.0256.



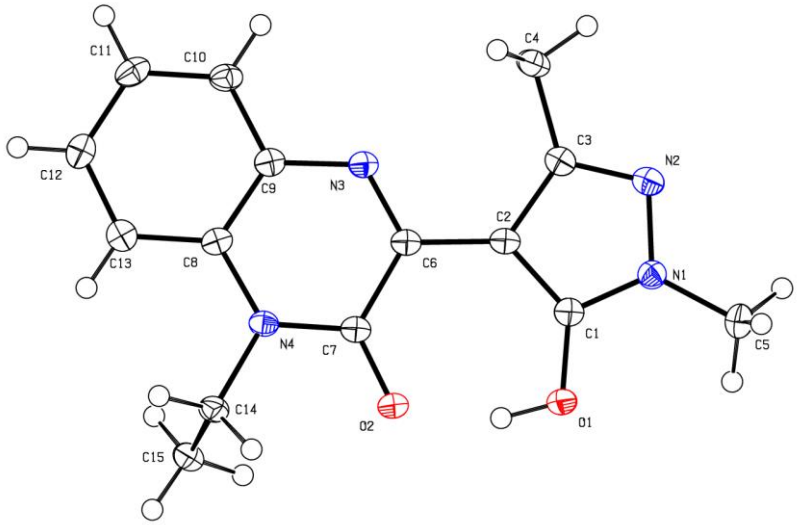
4k

6,7-Dibromo-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4k). Yellow solid (183 mg, 89% yield); mp = 160.5−160.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.29 (s, 1H), 8.04 (s, 1H), 7.62 (s, 1H), 3.49 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.4, 155.0, 150.5, 147.5, 132.9, 130.2, 128.5, 121.7, 119.7, 118.3, 97.4, 32.6, 17.0; IR (neat, cm^{-1}): *ν* = 2922, 2757, 1645, 1557, 1514, 1178, 1096, 1005, 951, 886, 913, 659, 543; HRMS (ESI): calcd for $C_{13}H_{11}Br_2N_4O_2$ $[M+H]^+$ 414.9223, found 414.9228.

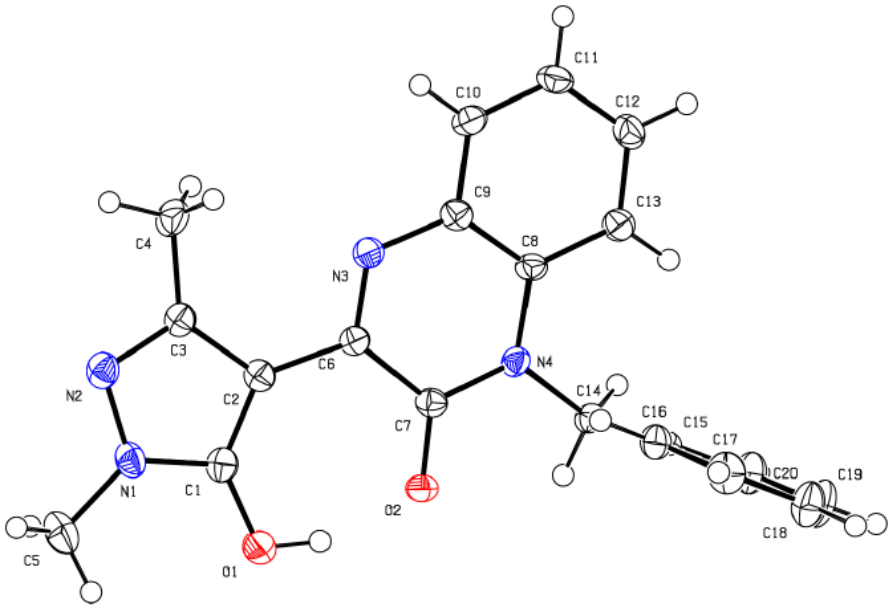
IV. X-Ray Crystallography

Data integration was performed with the SAINT software,[3] and intensity data were corrected based on the intensities symmetry-related reflections measured at different angular setting (SADABS).[4] The space group was determined with the XPREP software. The crystal structure was solved by intrinsic phasing method (SHELXT)[5] and refined by full-matrix least squares against F^2 using SHELXL[6] based on ShelXle engine or Olex2 software package.[7] All non-hydrogen atoms were refined anisotropically while the hydrogen atoms were placed in calculated positions and not refined. The crystallographic images were processed by Ortep3 program.[8]

Compound 4a:



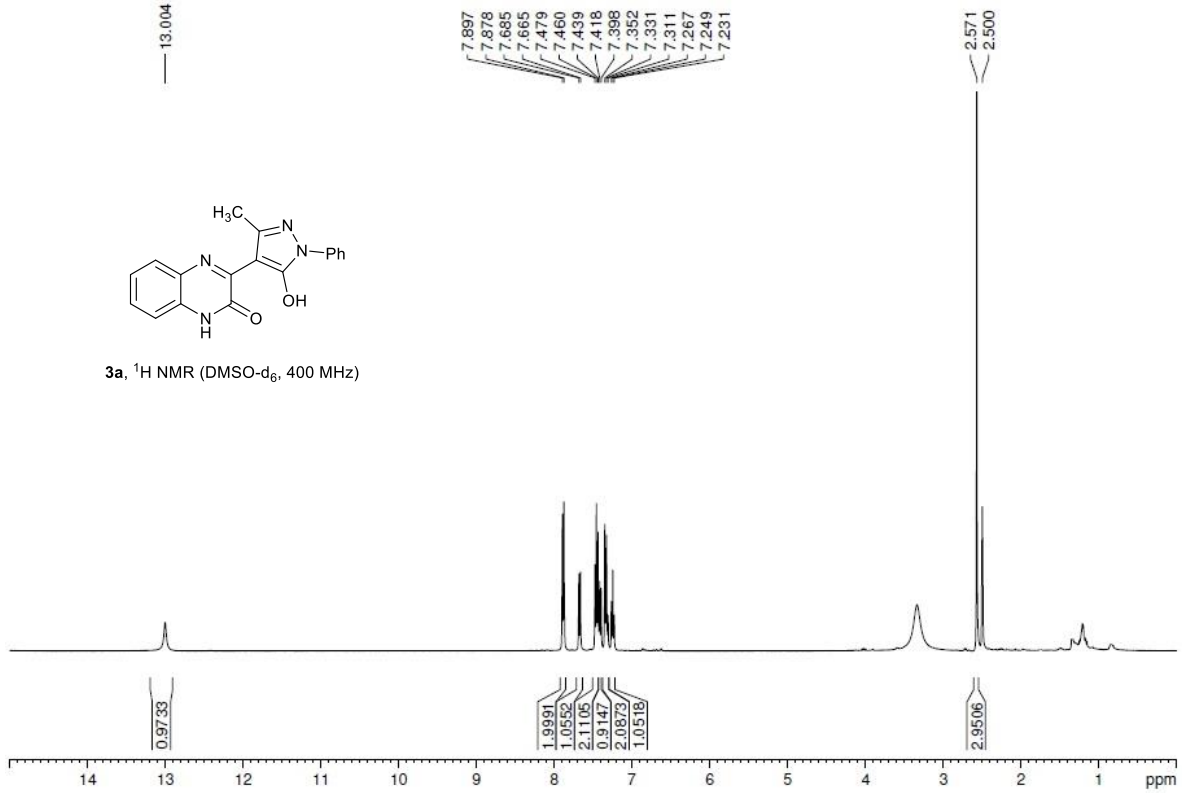
Compound 4d:



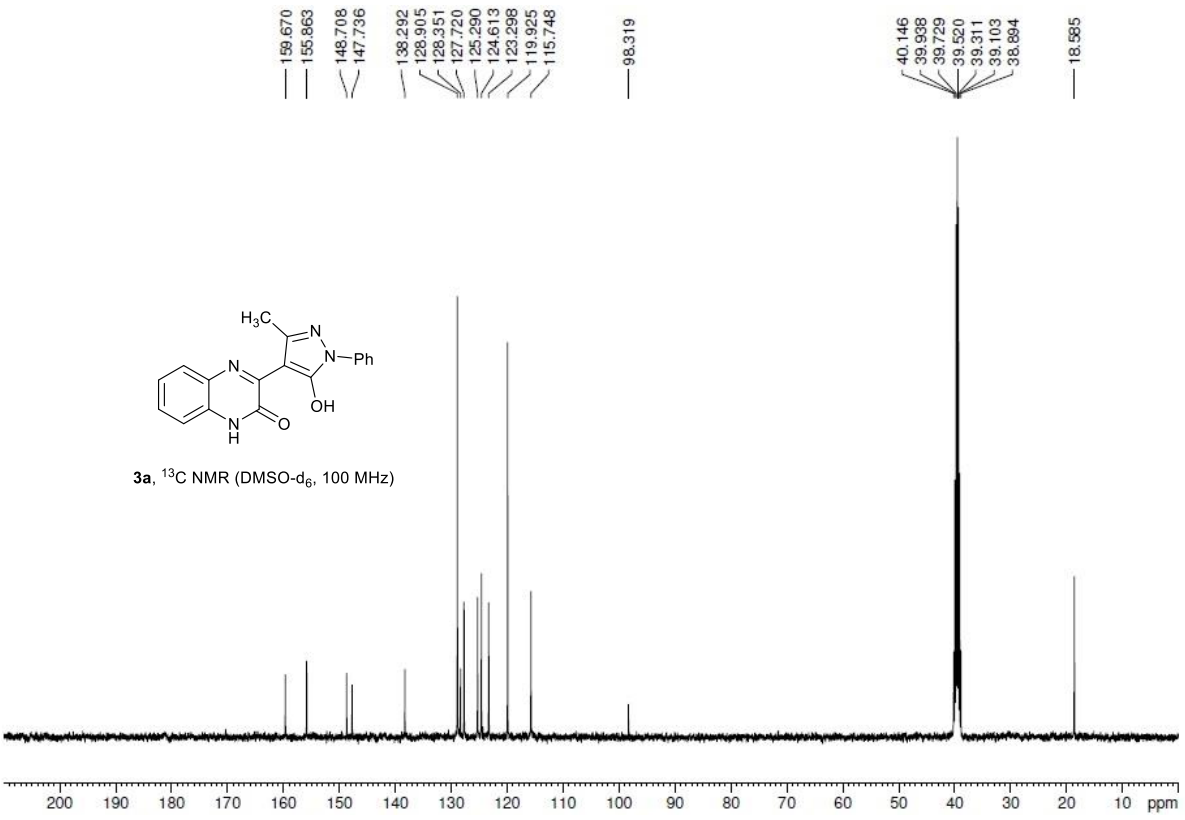
(See CIF files for more detail)

V. ^{1}H and ^{13}C Spectra of Products

3-(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3a)

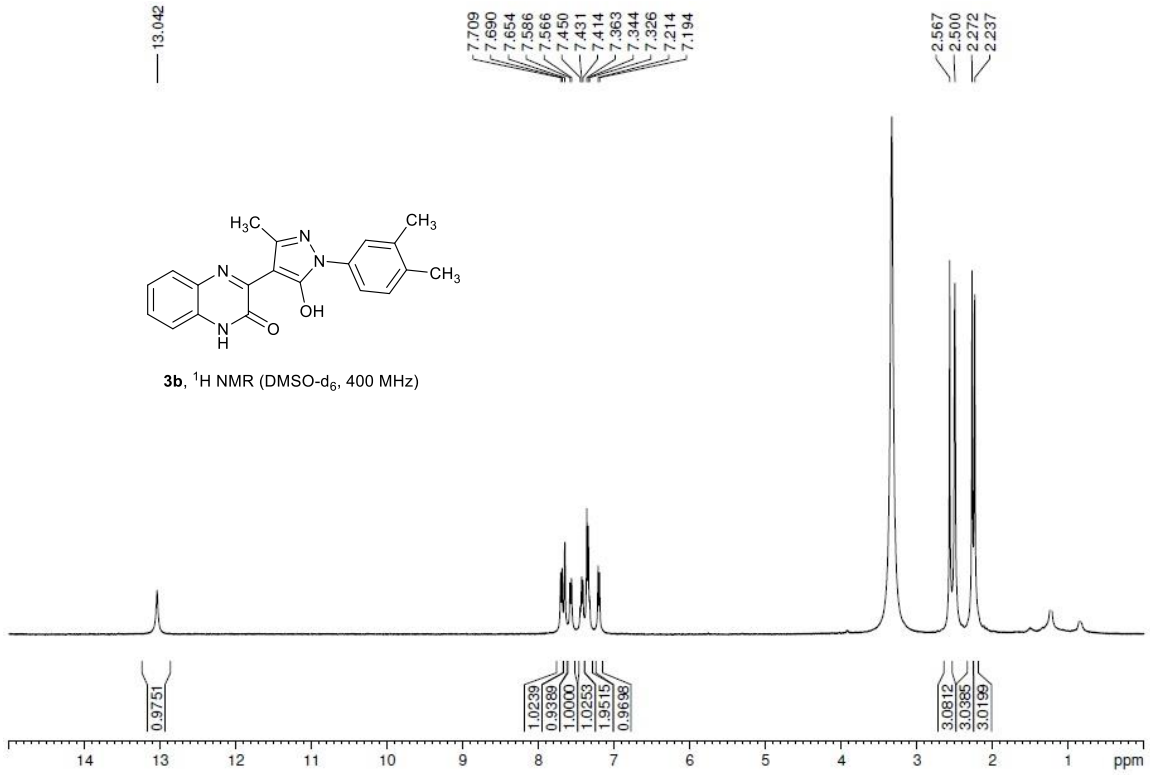


3a, ^{1}H NMR (DMSO-d_6, 400 MHz)

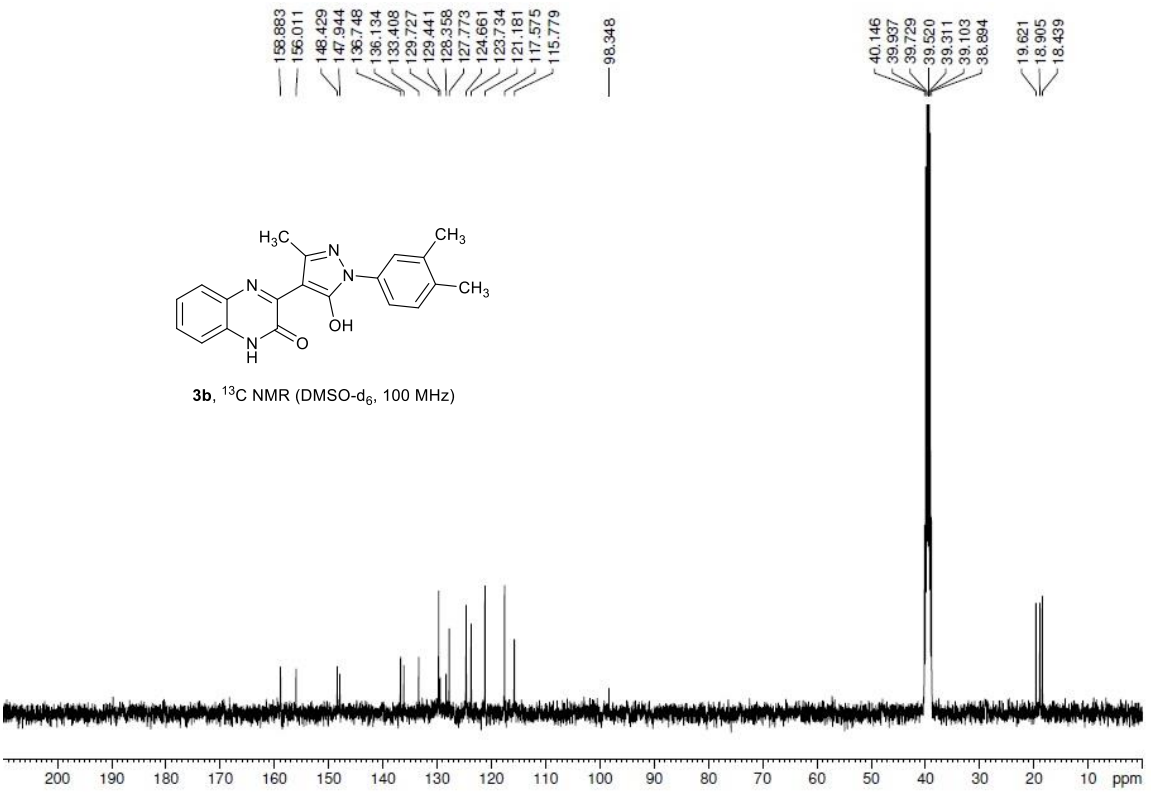


3a, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(1-(3,4-Dimethylphenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3b)

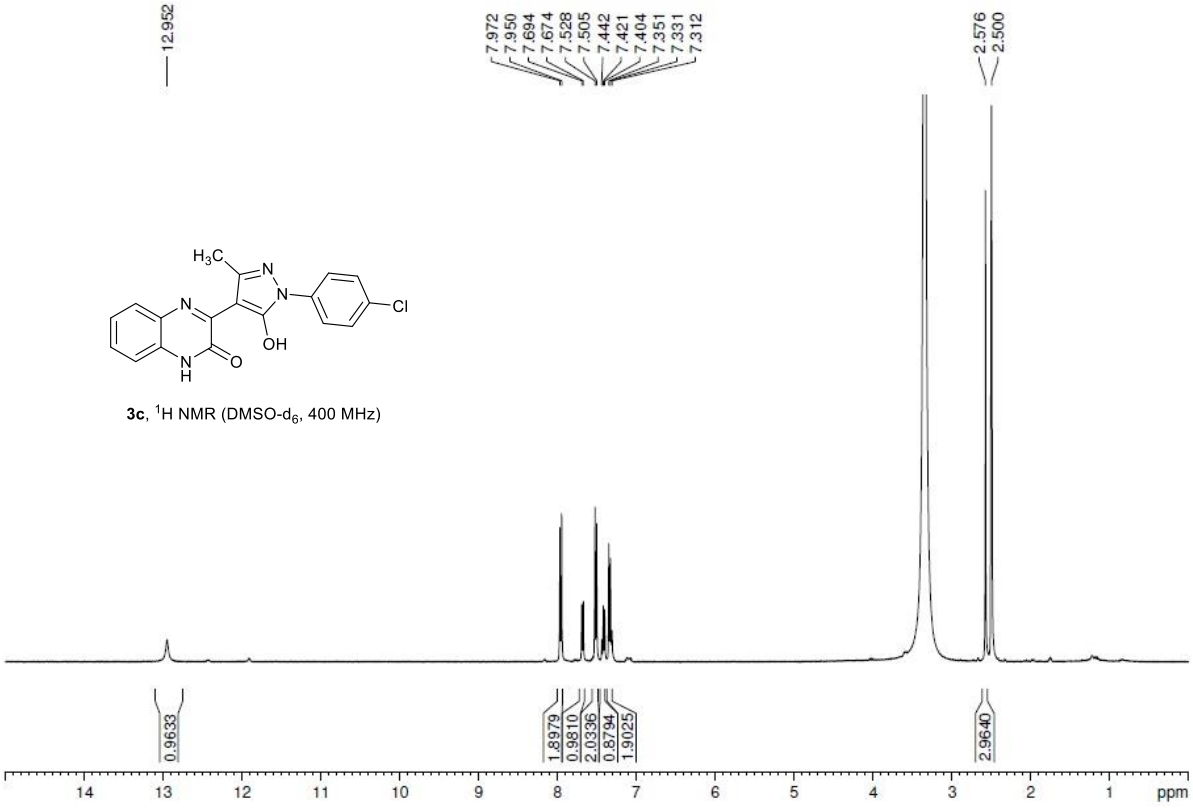


3b, ^{1}H NMR (DMSO-d_6, 400 MHz)

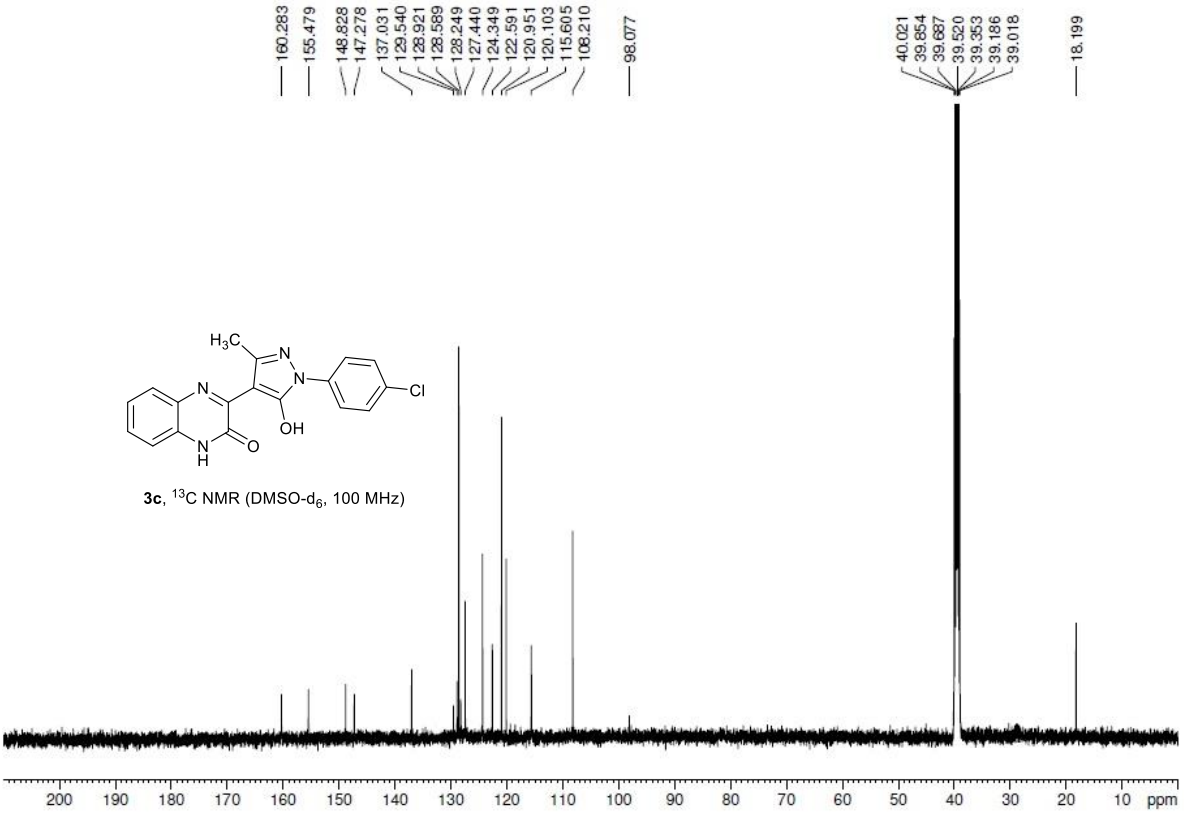


3b, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(1-(4-Chlorophenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3c)

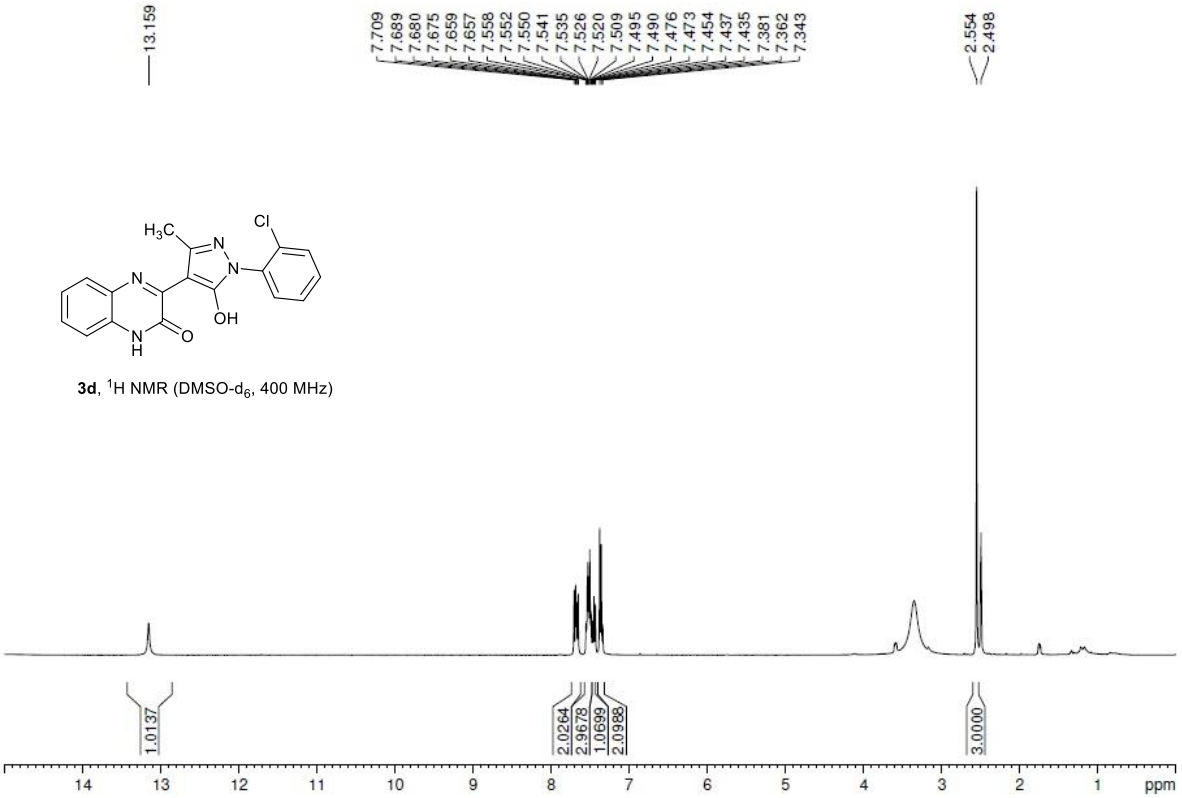


3c, ^{1}H NMR (DMSO-d_6, 400 MHz)

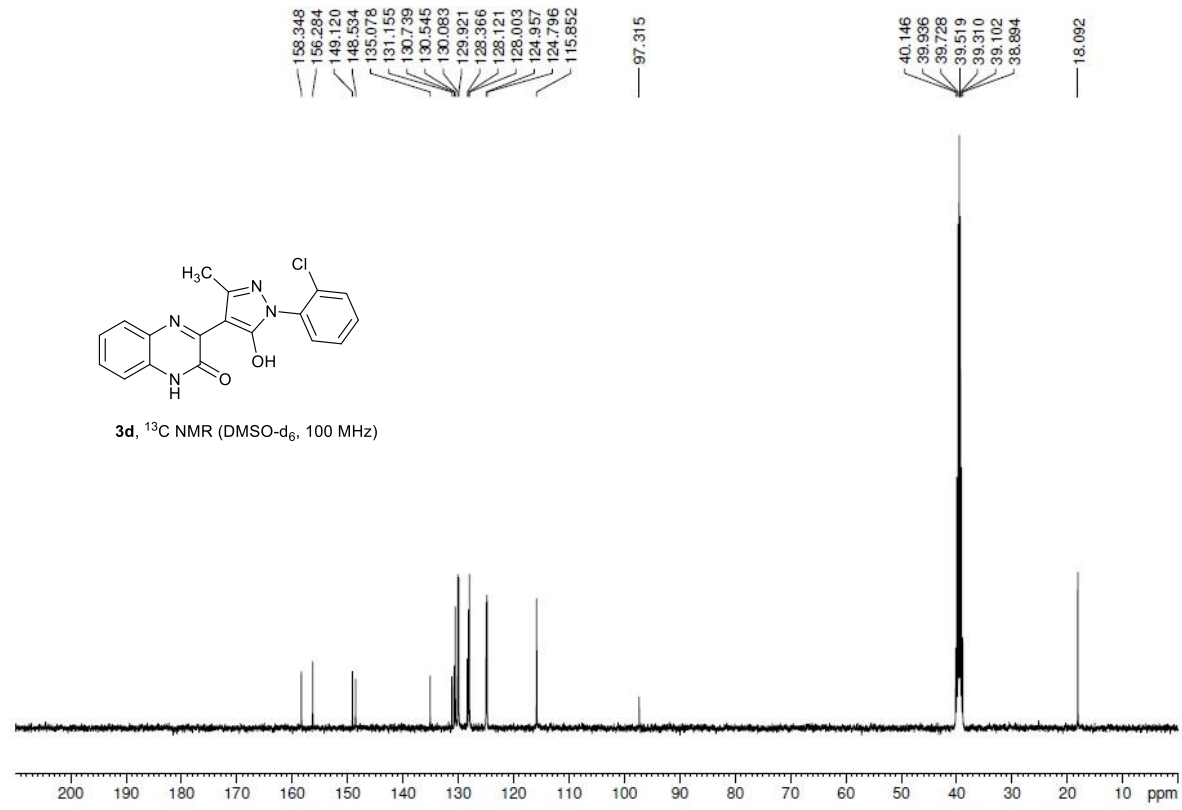


3c, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(1-(2-Chlorophenyl)-5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3d)

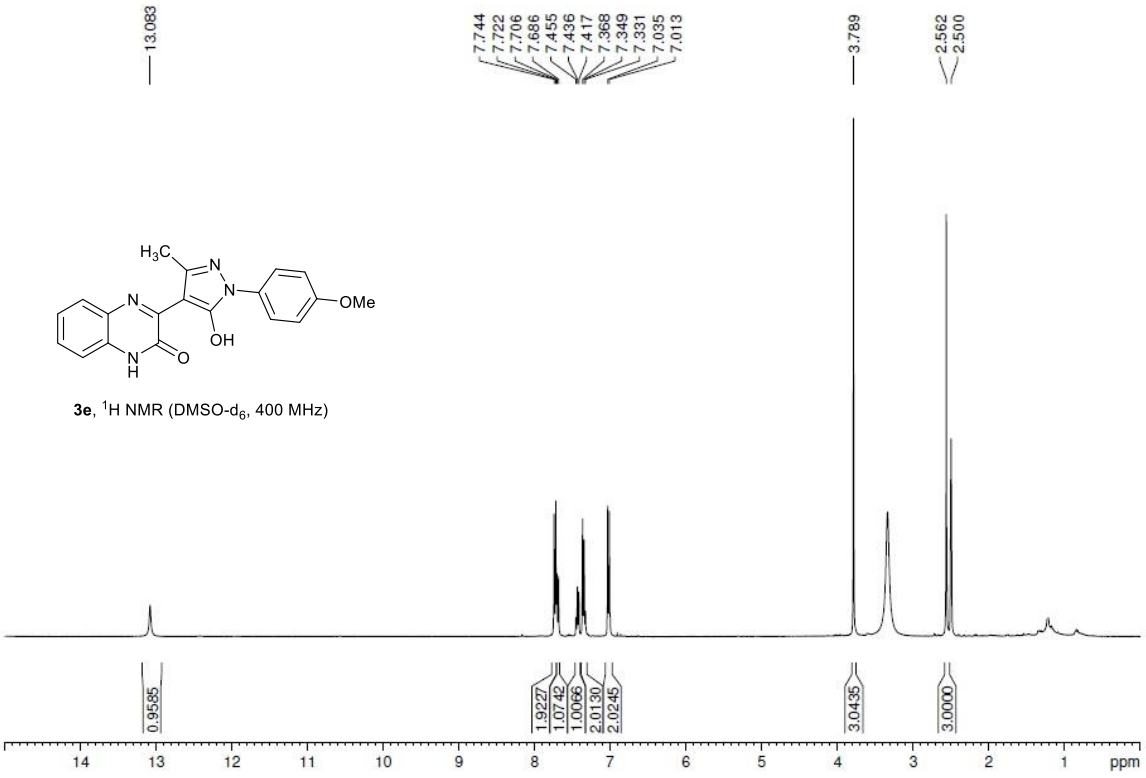


3d, ^{1}H NMR (DMSO-d_6, 400 MHz)

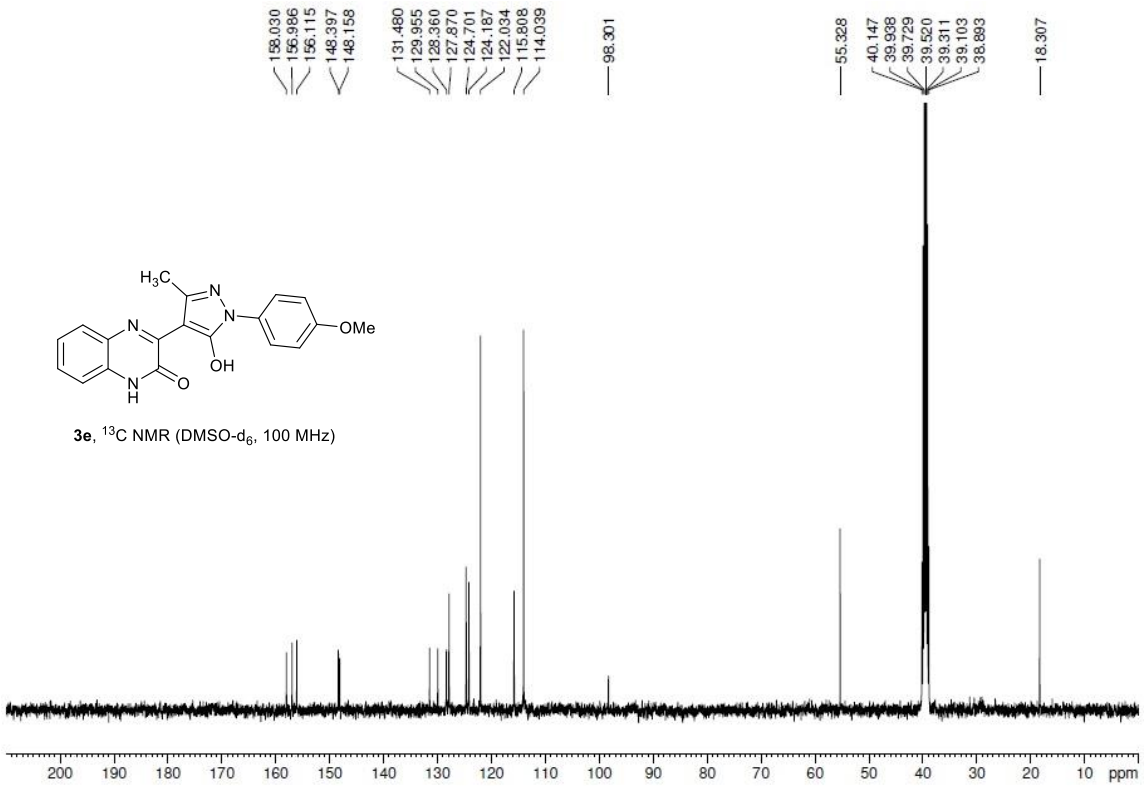


3d, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-1-(4-methoxyphenyl)-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3e)

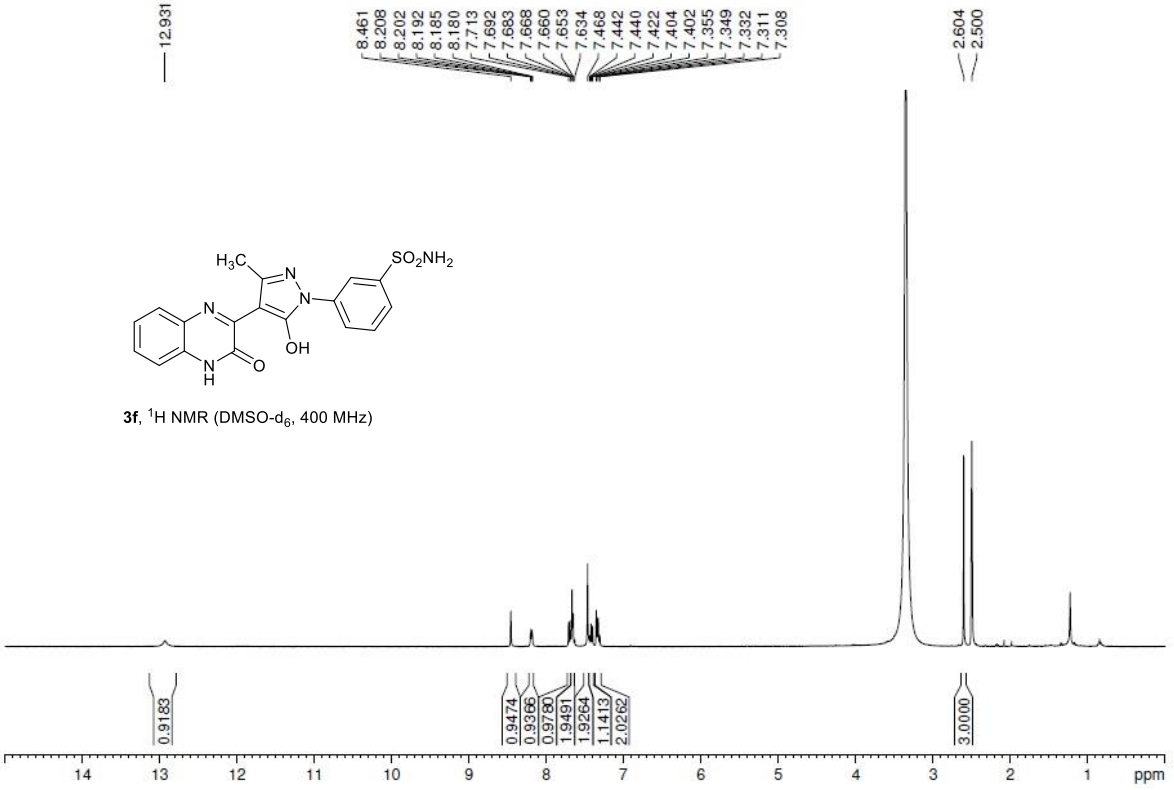


3e, ^{1}H NMR (DMSO-d$_6$, 400 MHz)

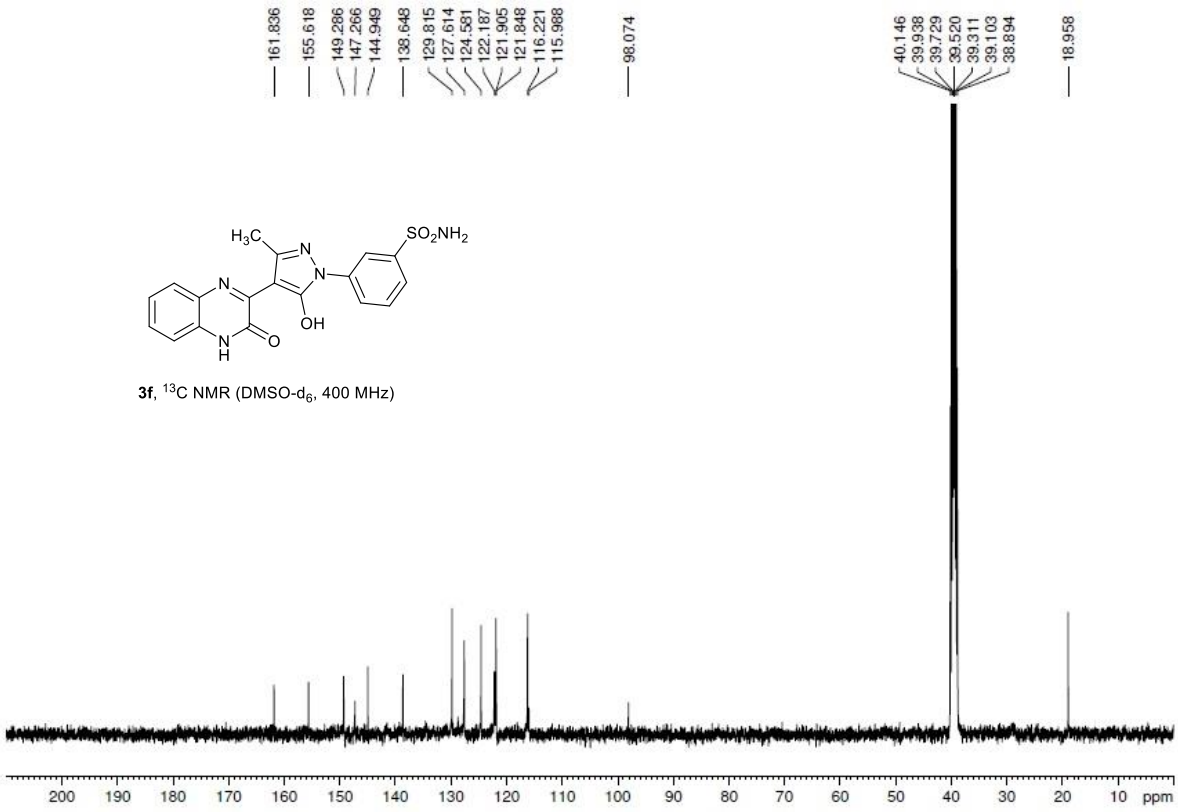


3e, ^{13}C NMR (DMSO-d$_6$, 100 MHz)

3-(5-Hydroxy-3-methyl-4-(3-oxo-3,4-dihydroquinoxalin-2-yl)-1*H*-pyrazol-1-yl)benzenesulfonamide (3f)

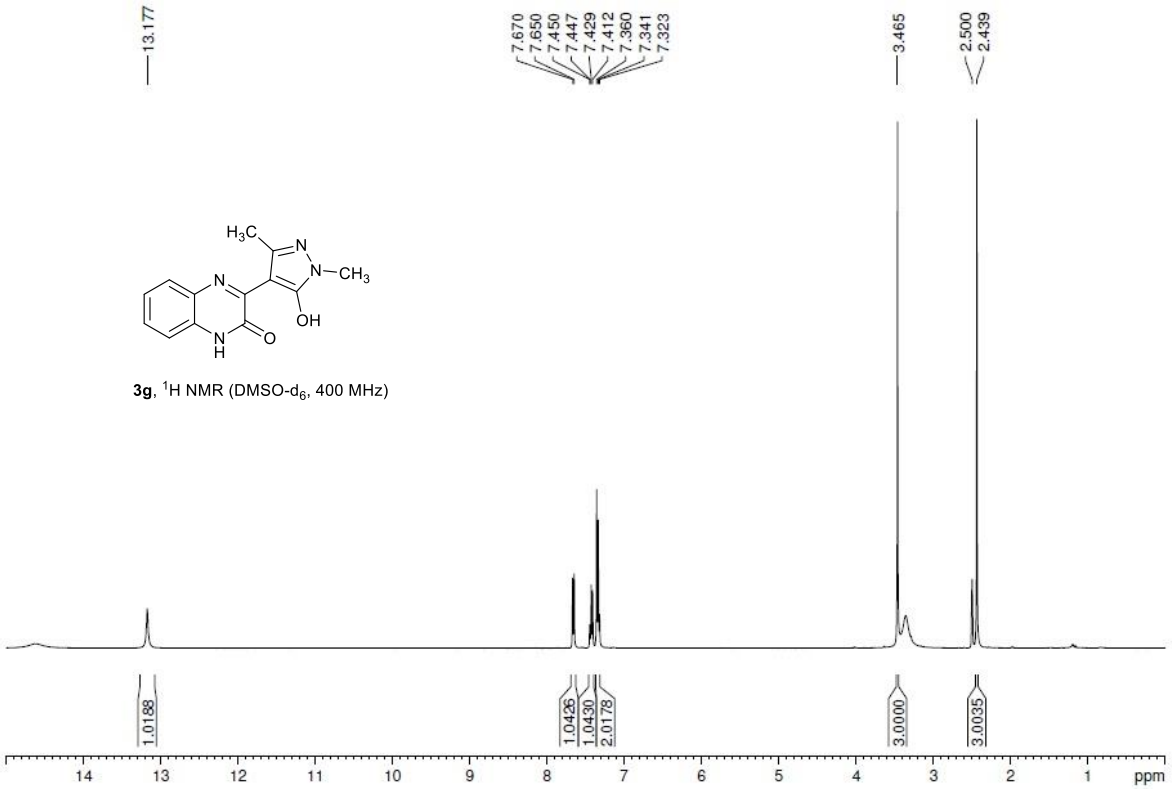


3f, ^{1}H NMR (DMSO-d_6, 400 MHz)

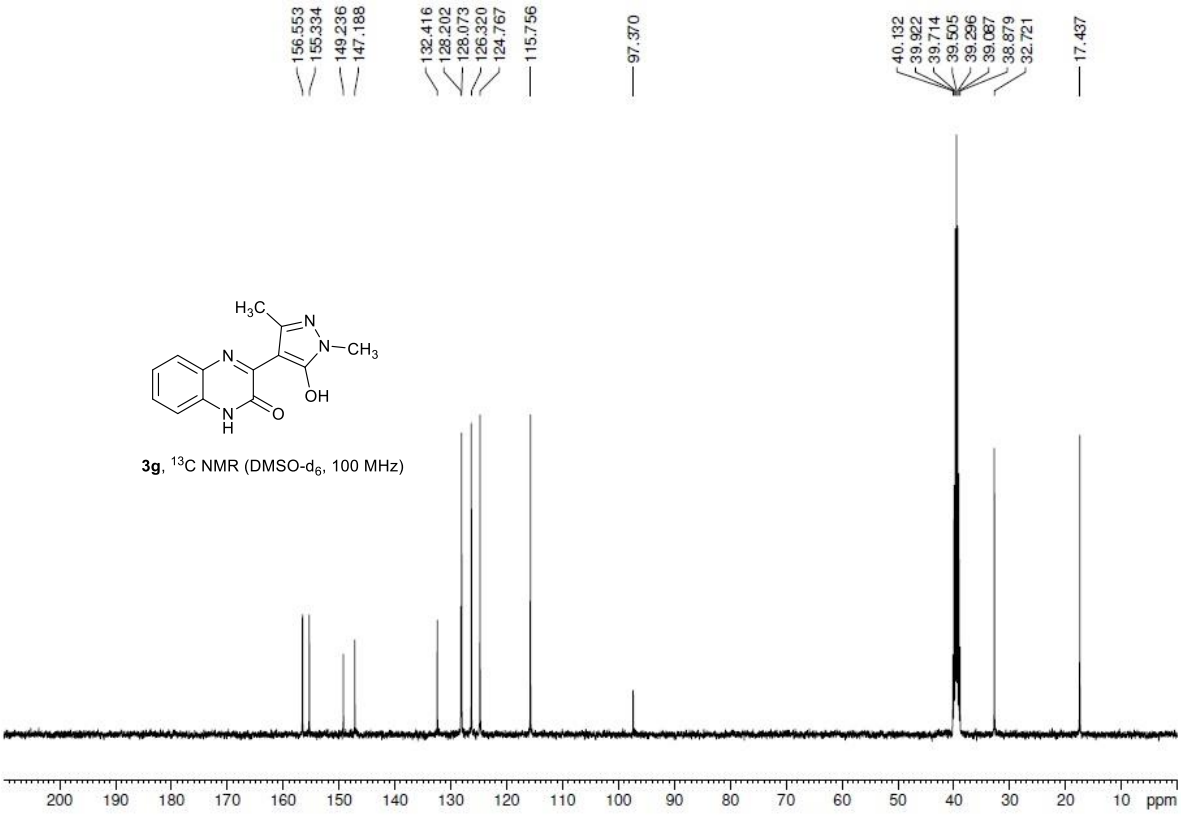


3f, ^{13}C NMR (DMSO-d_6, 400 MHz)

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3g)

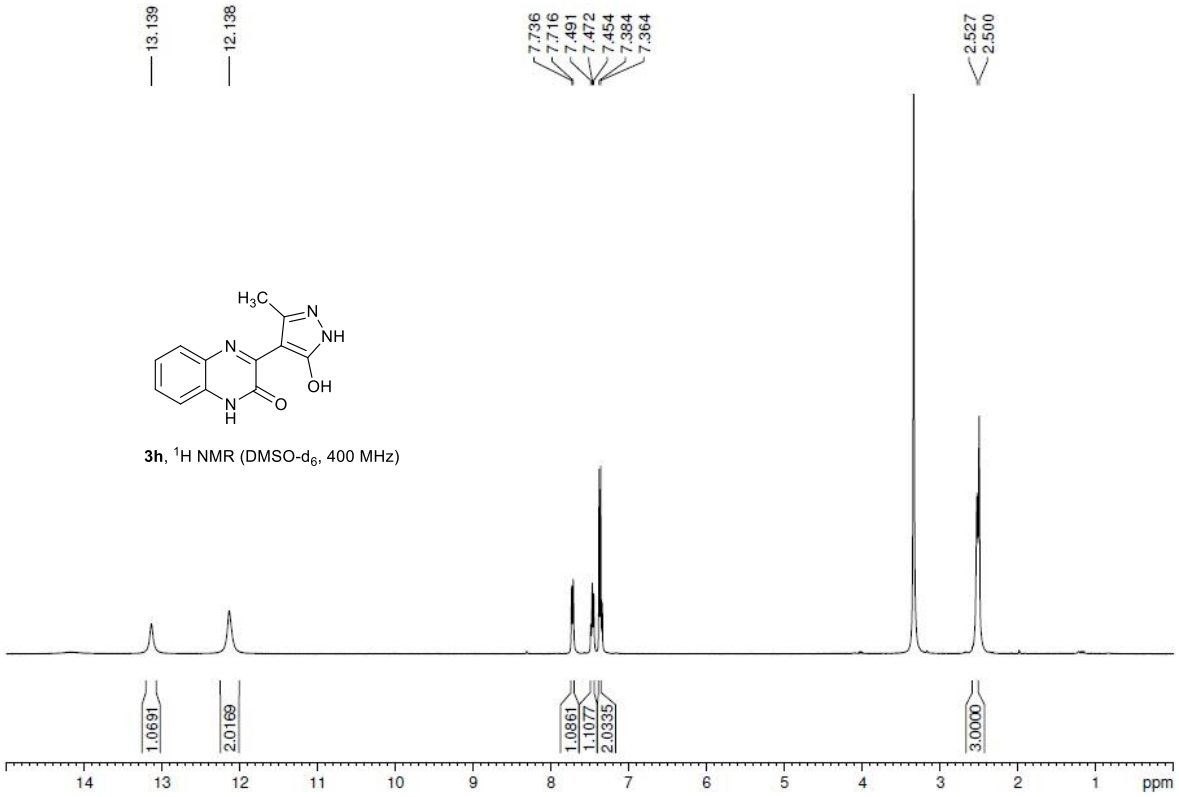


3g, ^{1}H NMR (DMSO-d_6, 400 MHz)

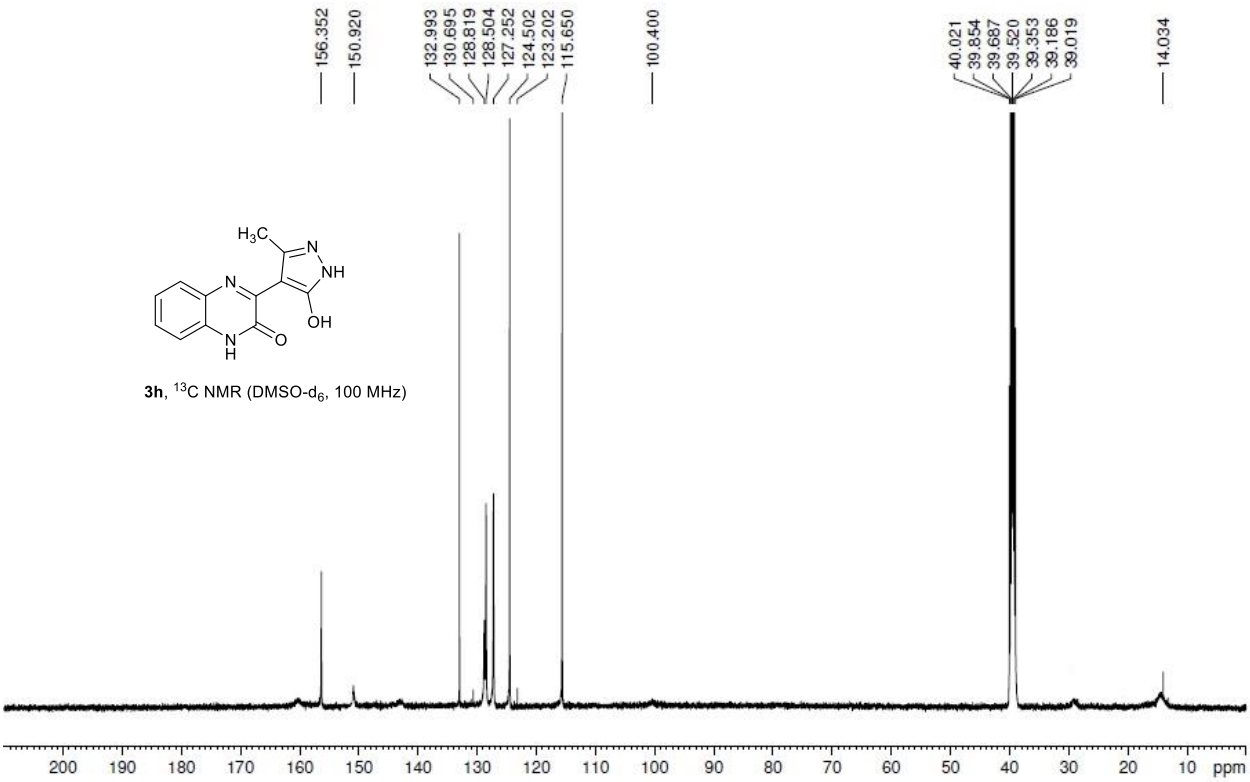


3g, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-3-methyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3h)

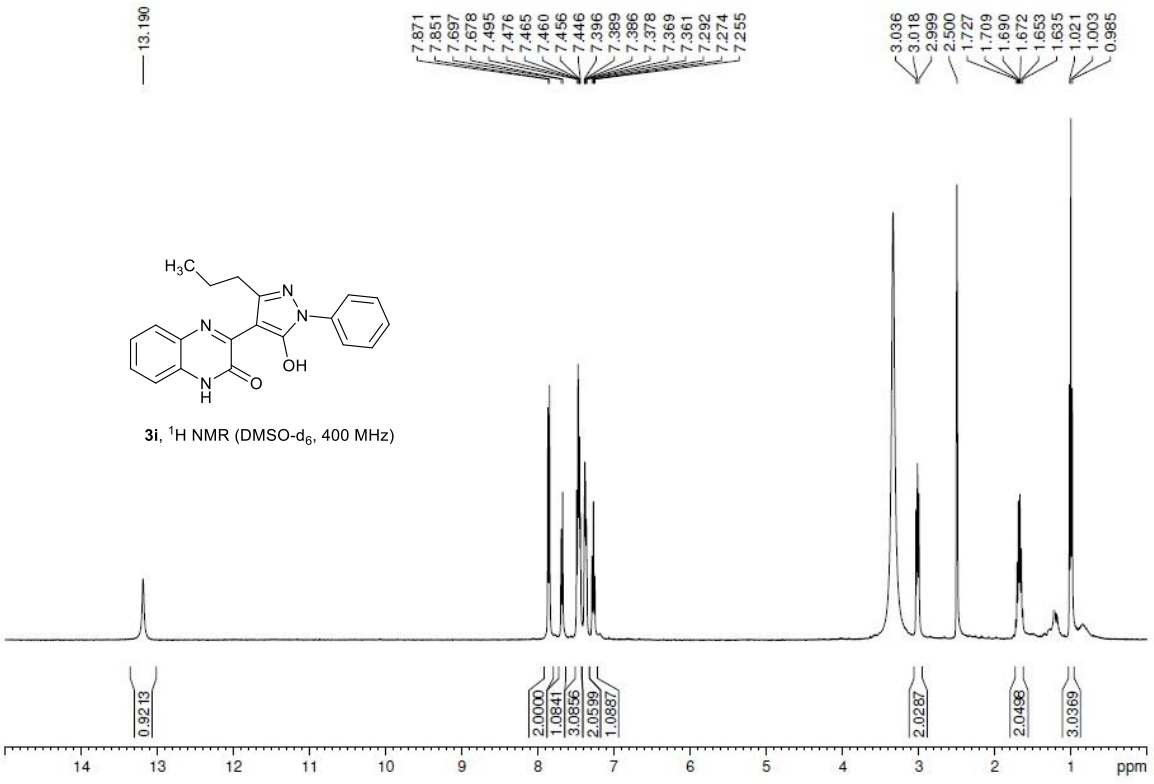


3h, ^{1}H NMR (DMSO-d_6, 400 MHz)

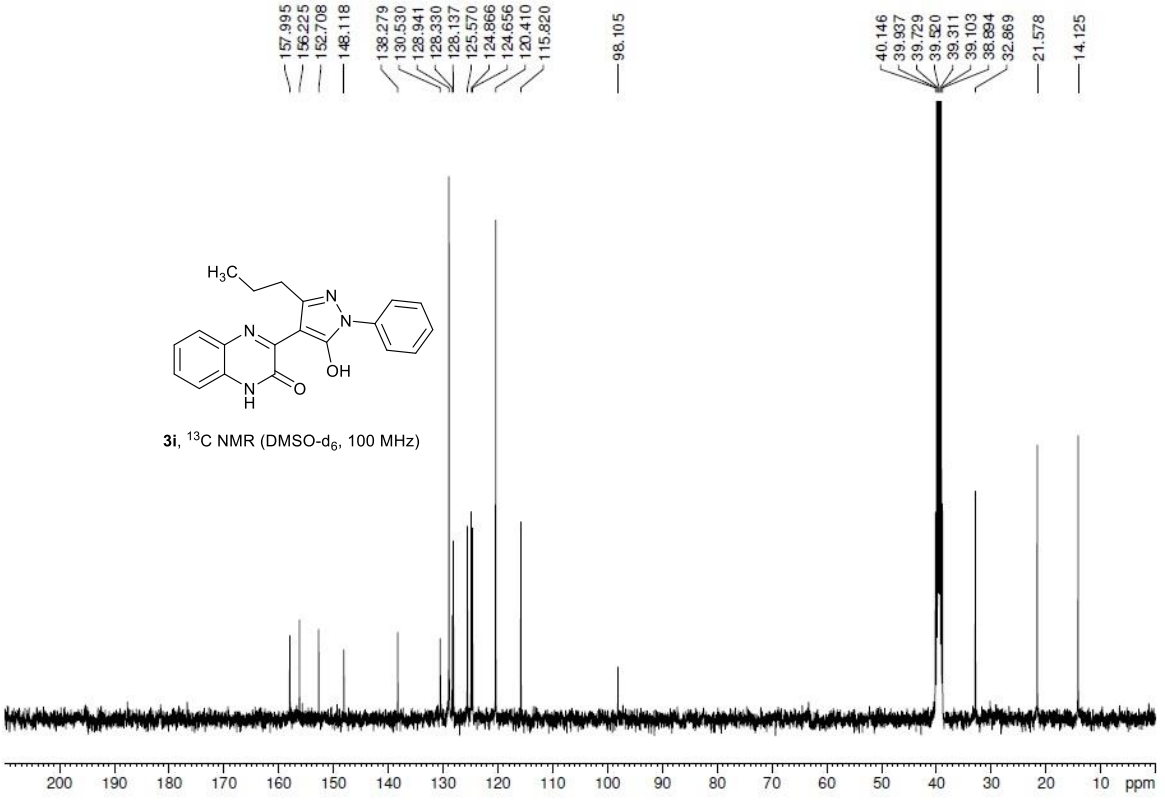


3h, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-1-phenyl-3-propyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3i)

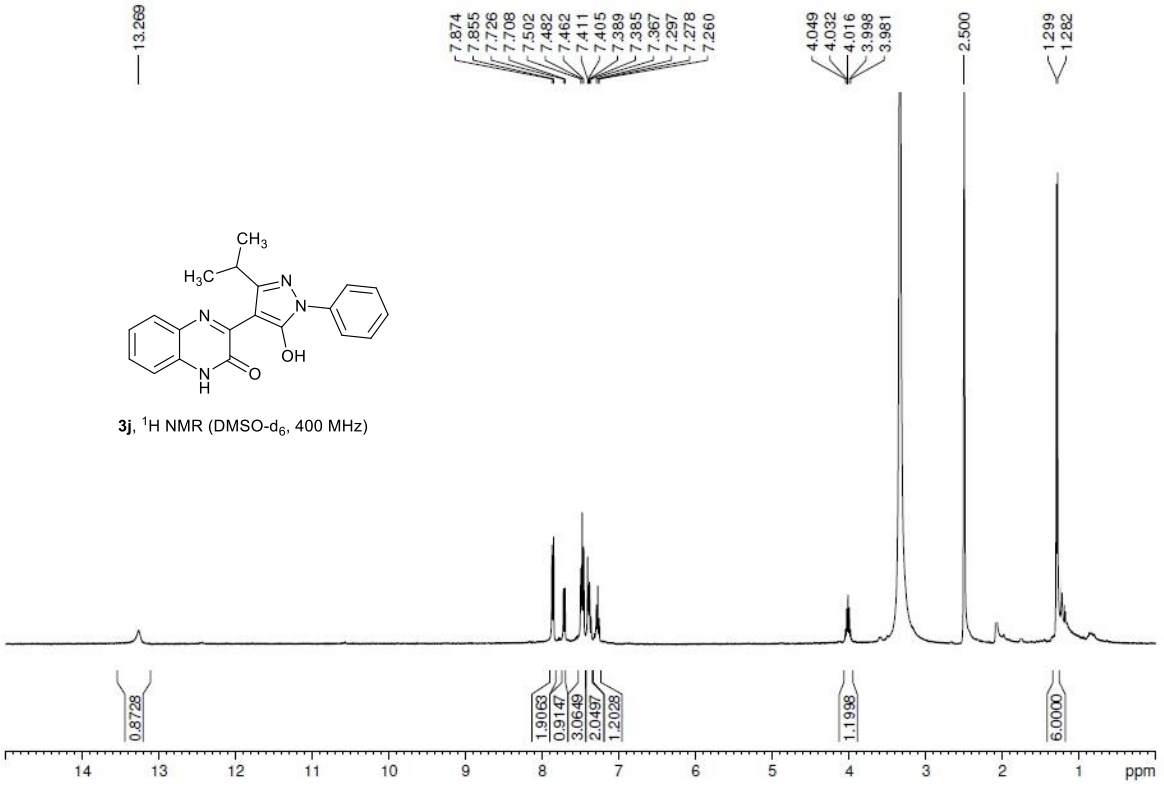


3i, ^{1}H NMR (DMSO-d_6, 400 MHz)

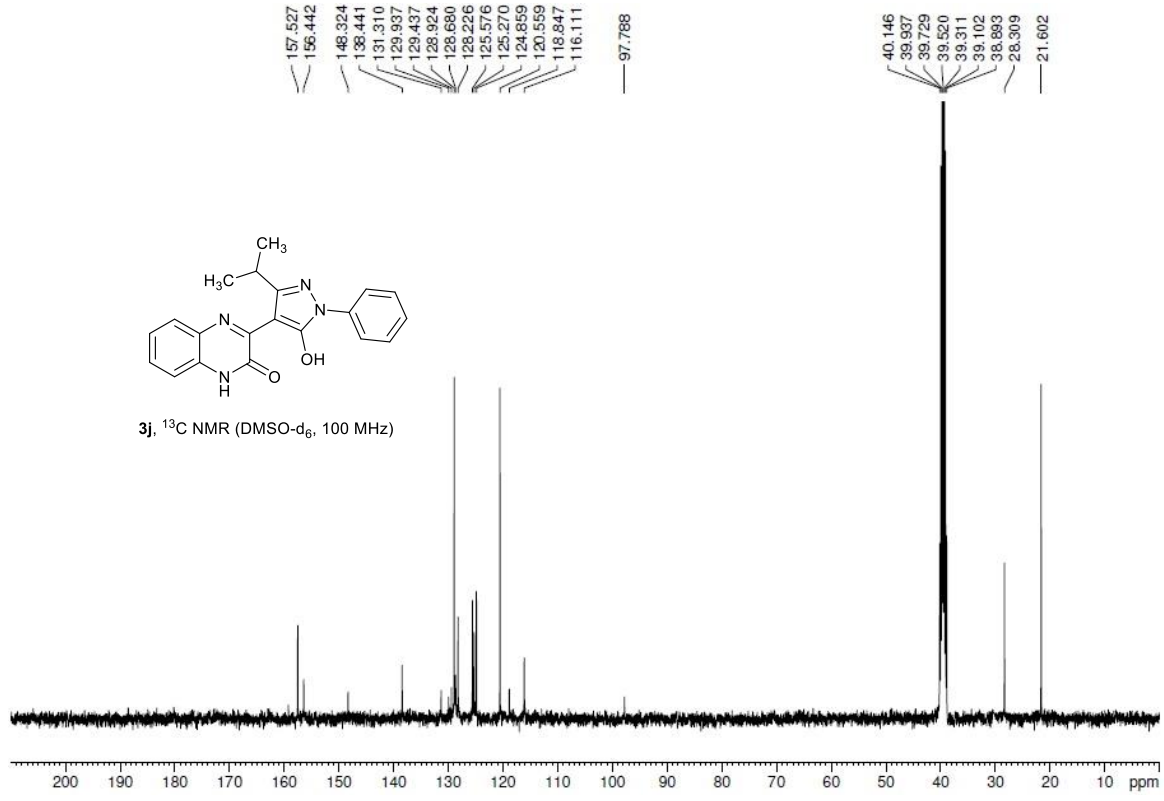


3i, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-3-isopropyl-1-phenyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (3j)

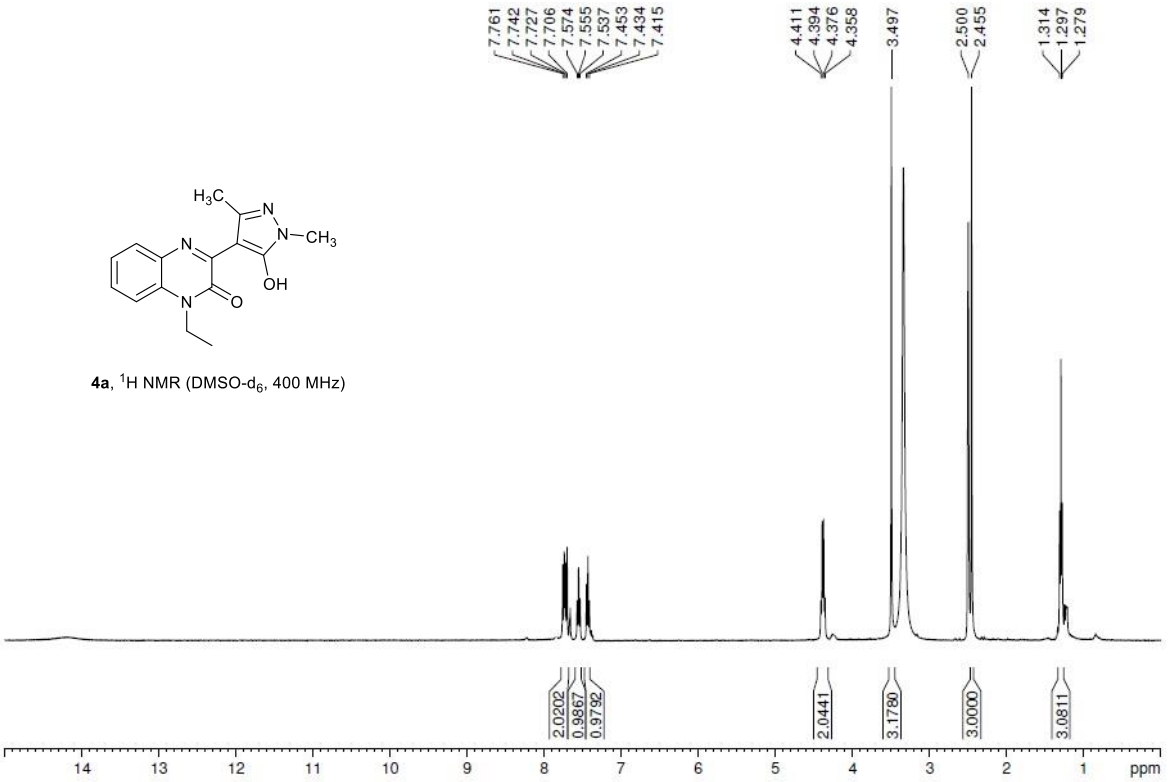


3j, ^{1}H NMR (DMSO-d_6, 400 MHz)

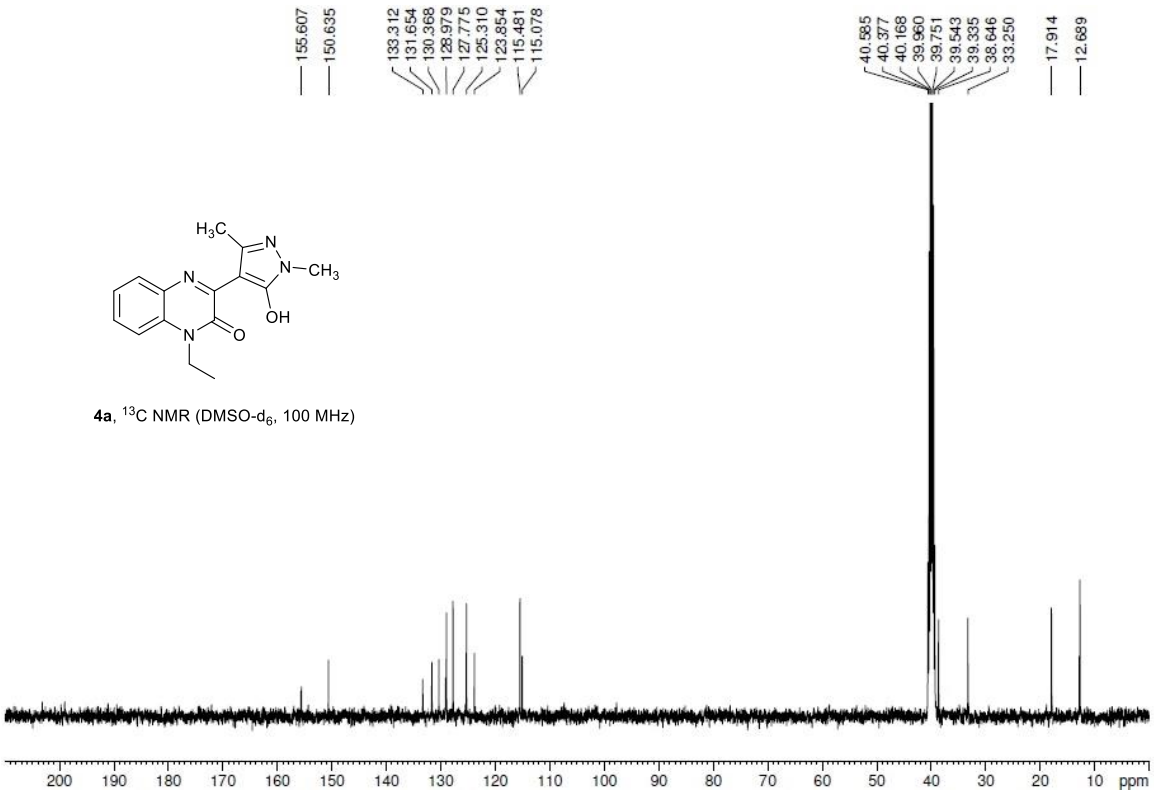


3j, ^{13}C NMR (DMSO-d_6, 100 MHz)

1-Ethyl-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4a)

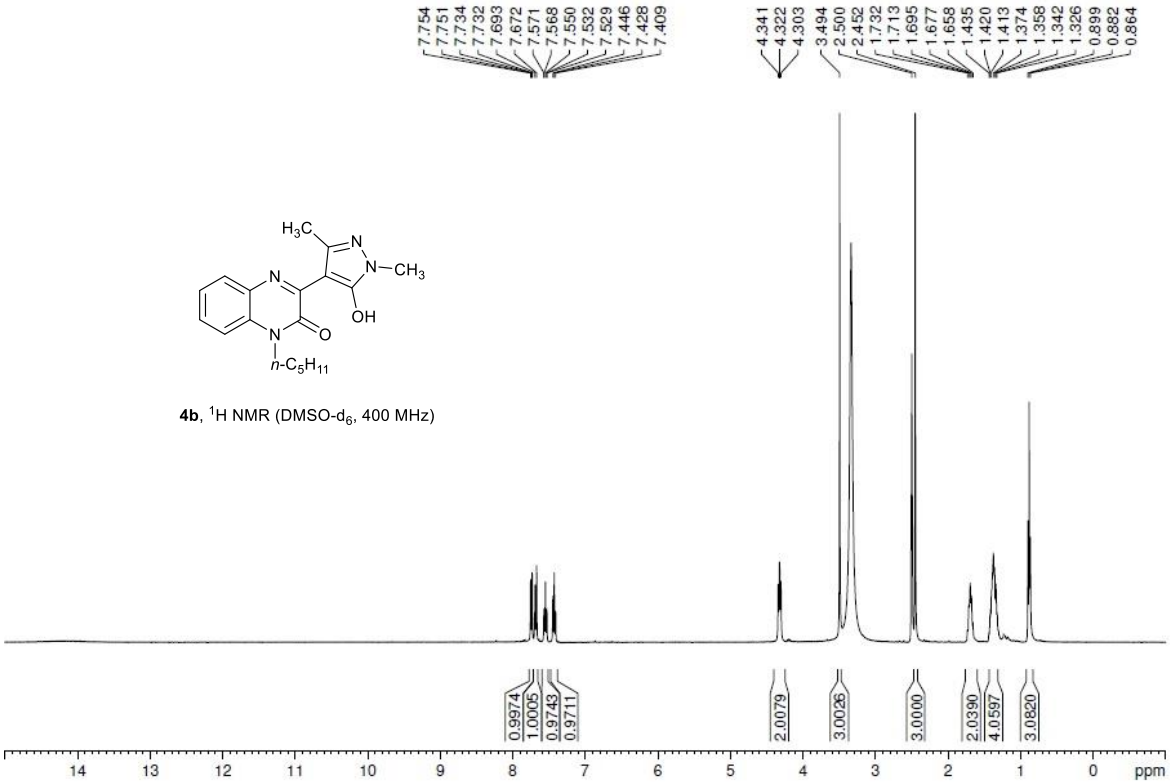


4a, ^{1}H NMR (DMSO-d_6, 400 MHz)

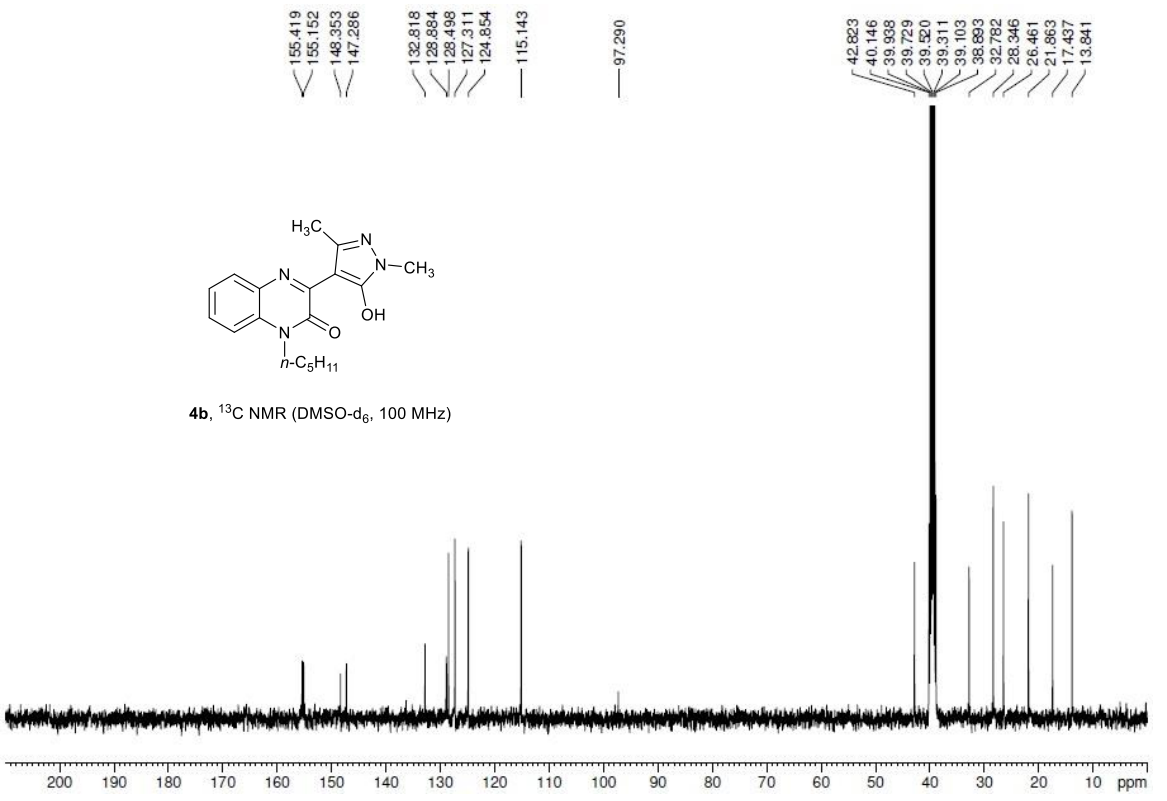


4a, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-1-pentylquinoxalin-2(1*H*)-one (4b)

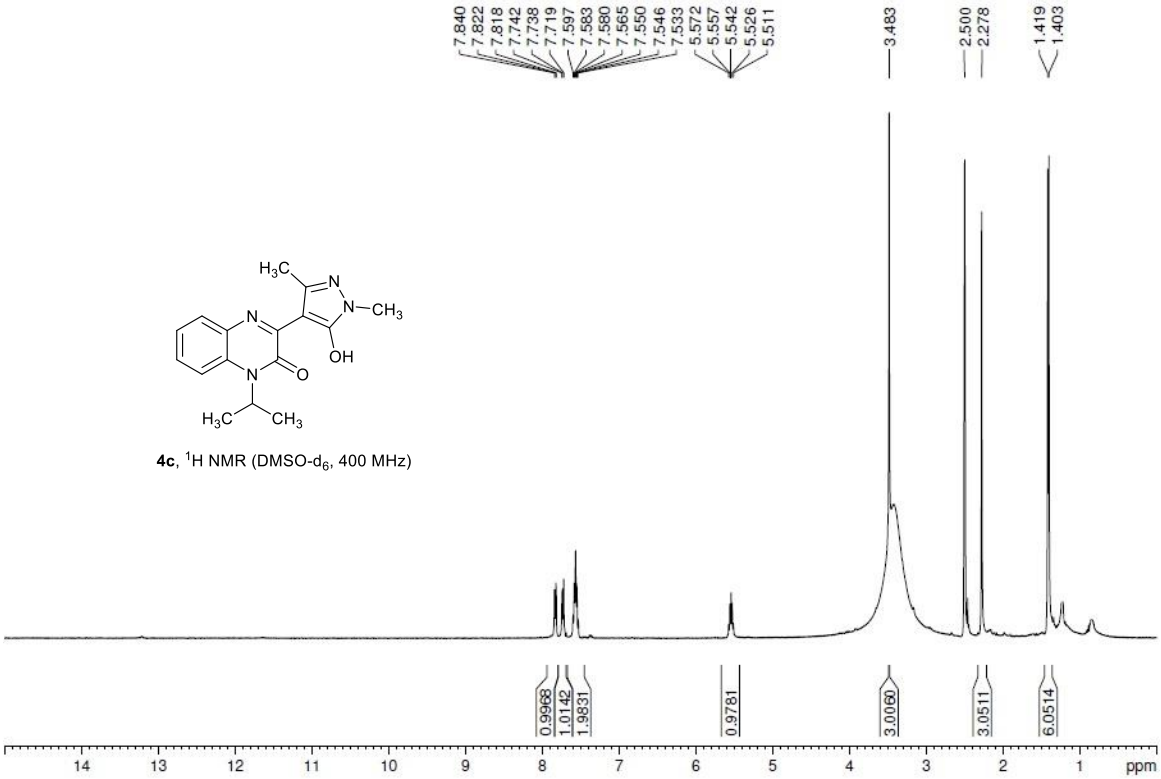


4b, ^{1}H NMR (DMSO-d$_6$, 400 MHz)

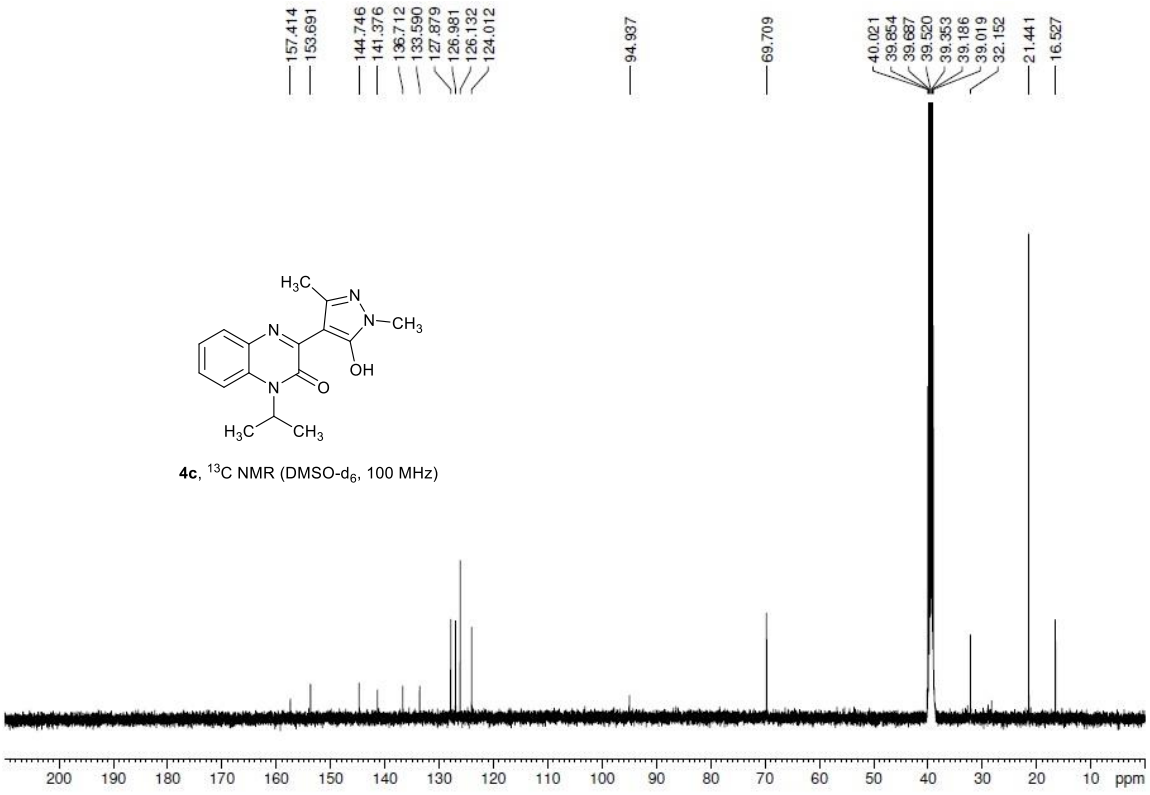


4b, ^{13}C NMR (DMSO-d$_6$, 100 MHz)

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-1-isopropylquinoxalin-2(1*H*)-one (4c)

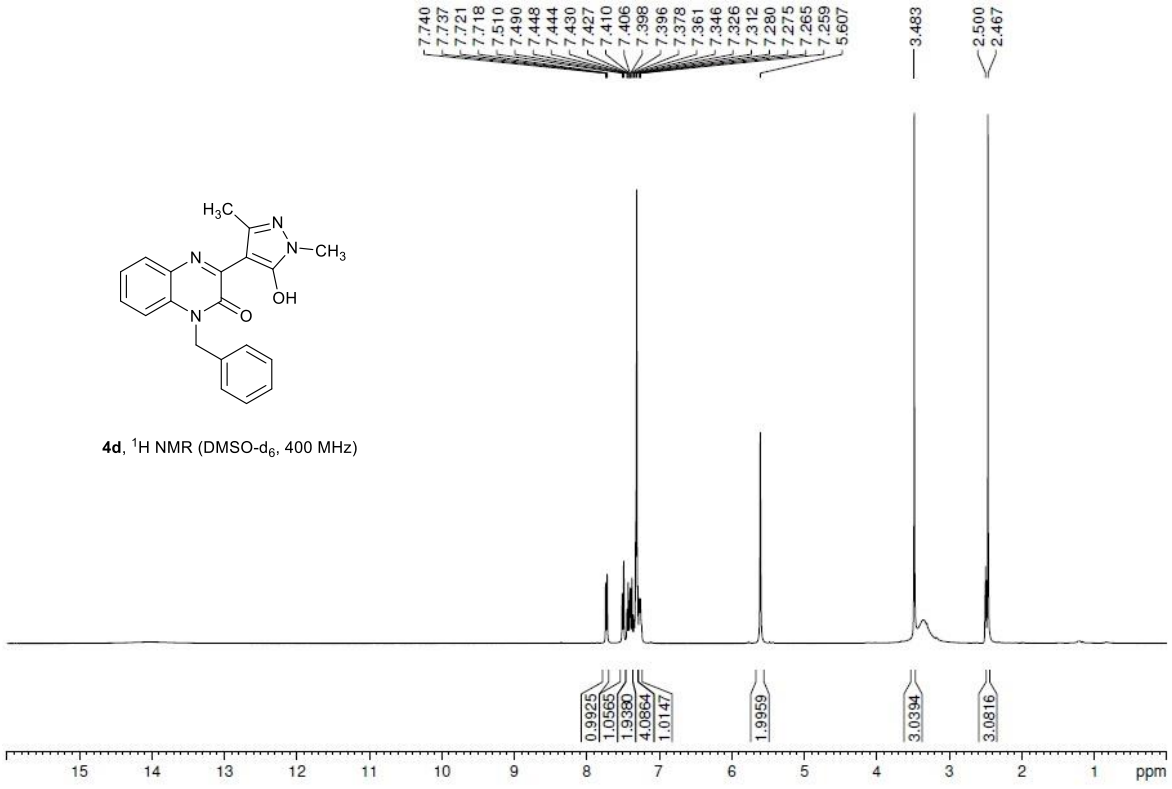


4c, ^{1}H NMR (DMSO-d_6, 400 MHz)

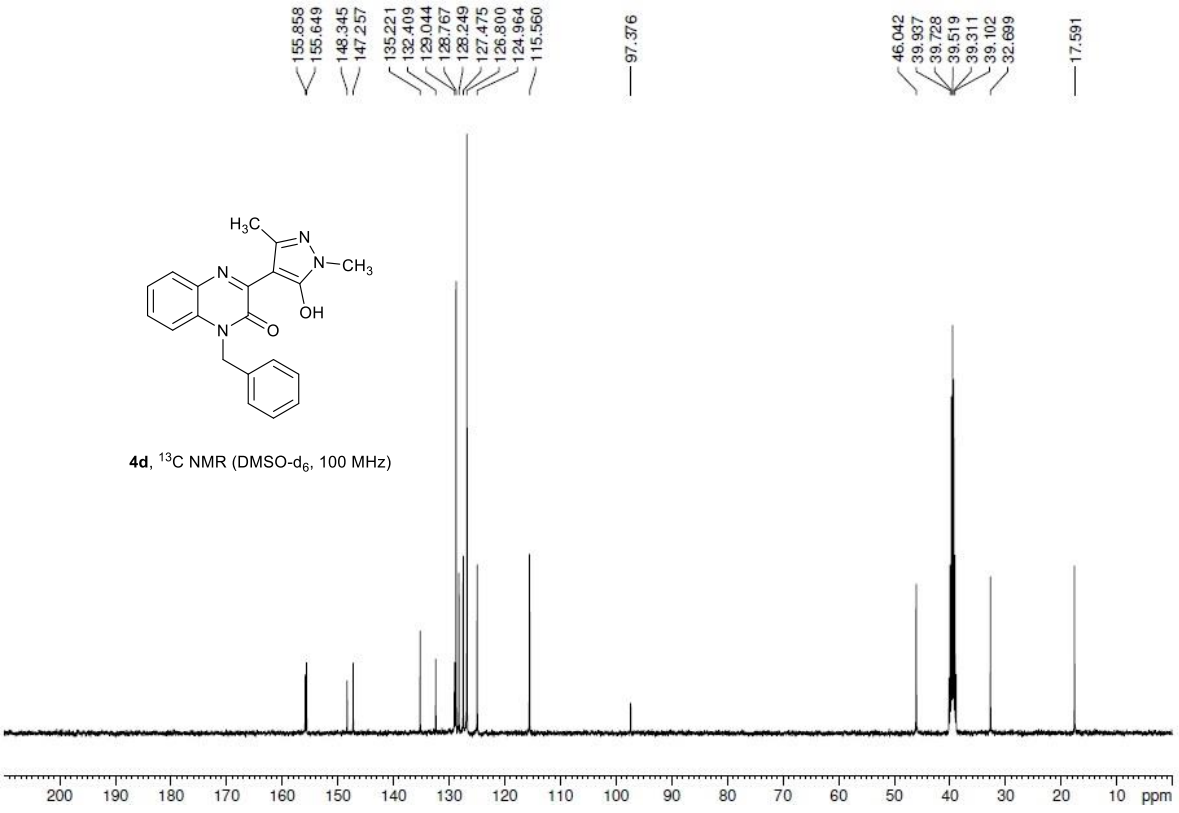


4c, ^{13}C NMR (DMSO-d_6, 100 MHz)

1-Benzyl-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4d)

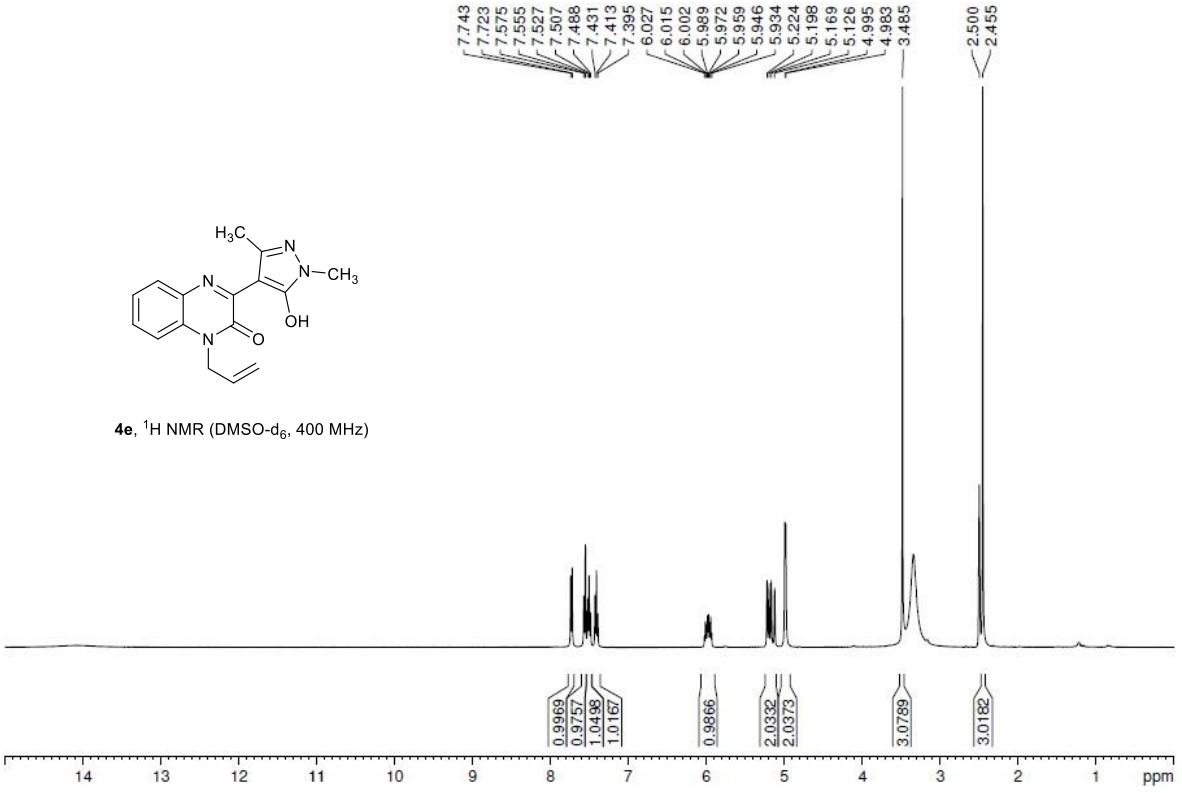


4d, ^{1}H NMR (DMSO-d_6, 400 MHz)

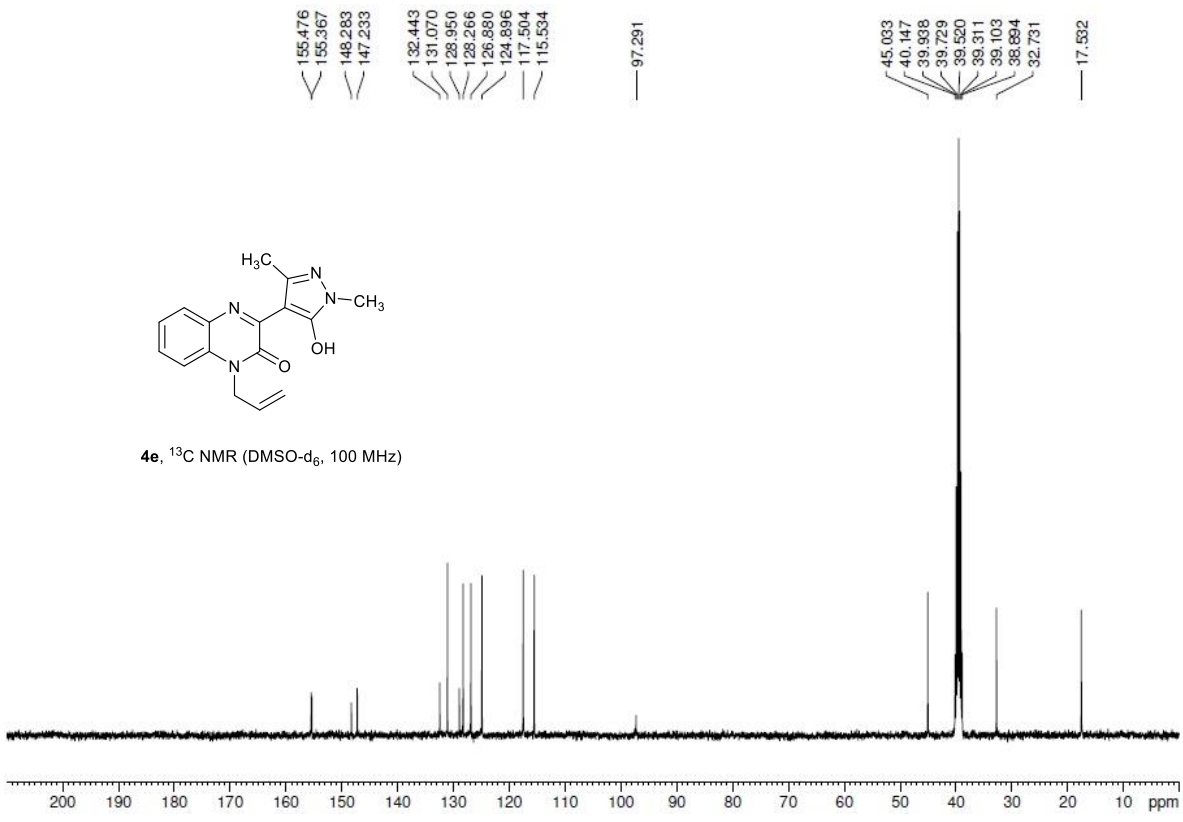


4d, ^{13}C NMR (DMSO-d_6, 100 MHz)

1-Allyl-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4e)

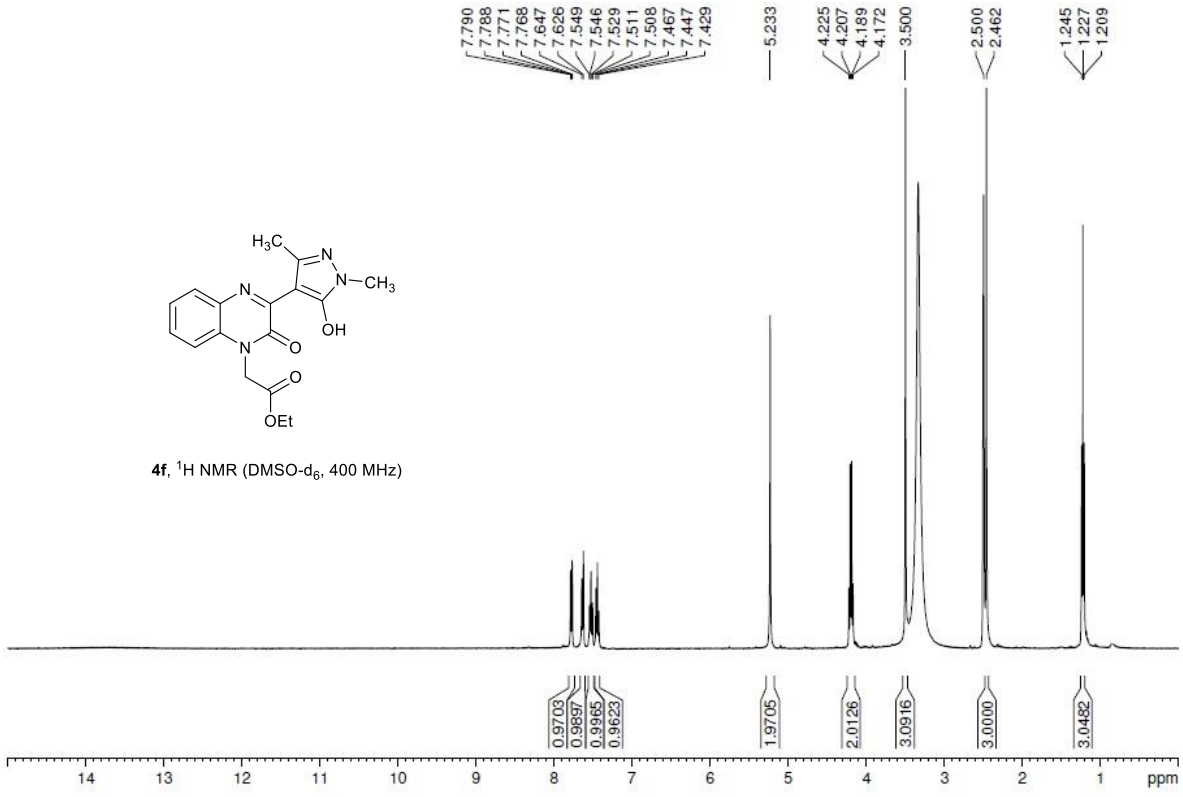


4e, ^{1}H NMR (DMSO-d_6, 400 MHz)

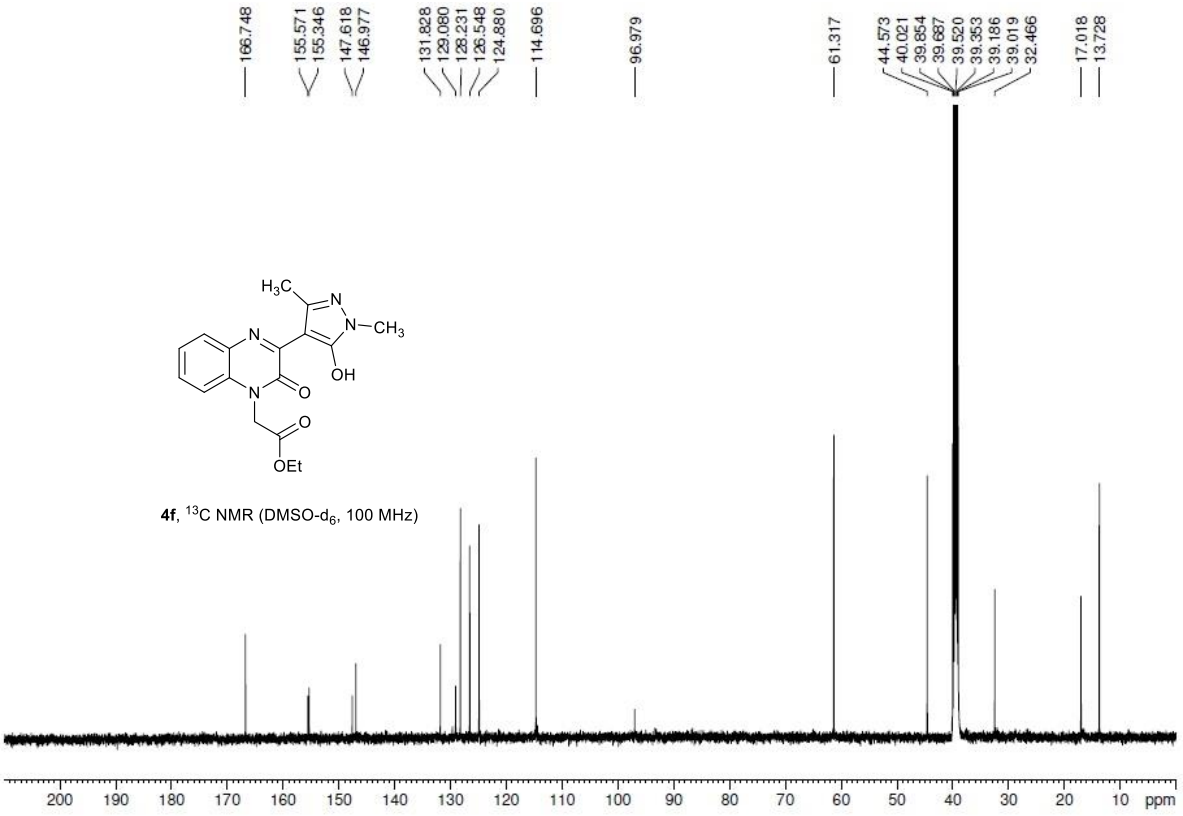


4e, ^{13}C NMR (DMSO-d_6, 100 MHz)

Ethyl 2-(3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (4f)

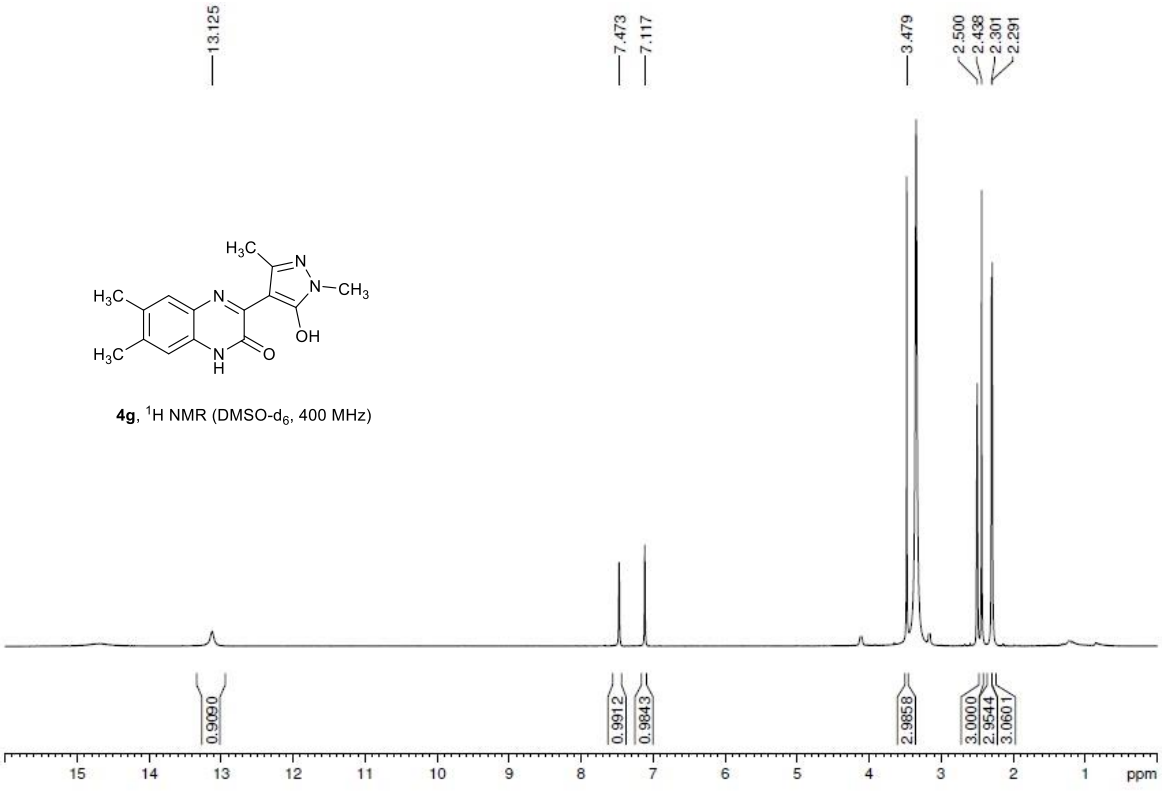


4f, ^{1}H NMR (DMSO-d_6, 400 MHz)

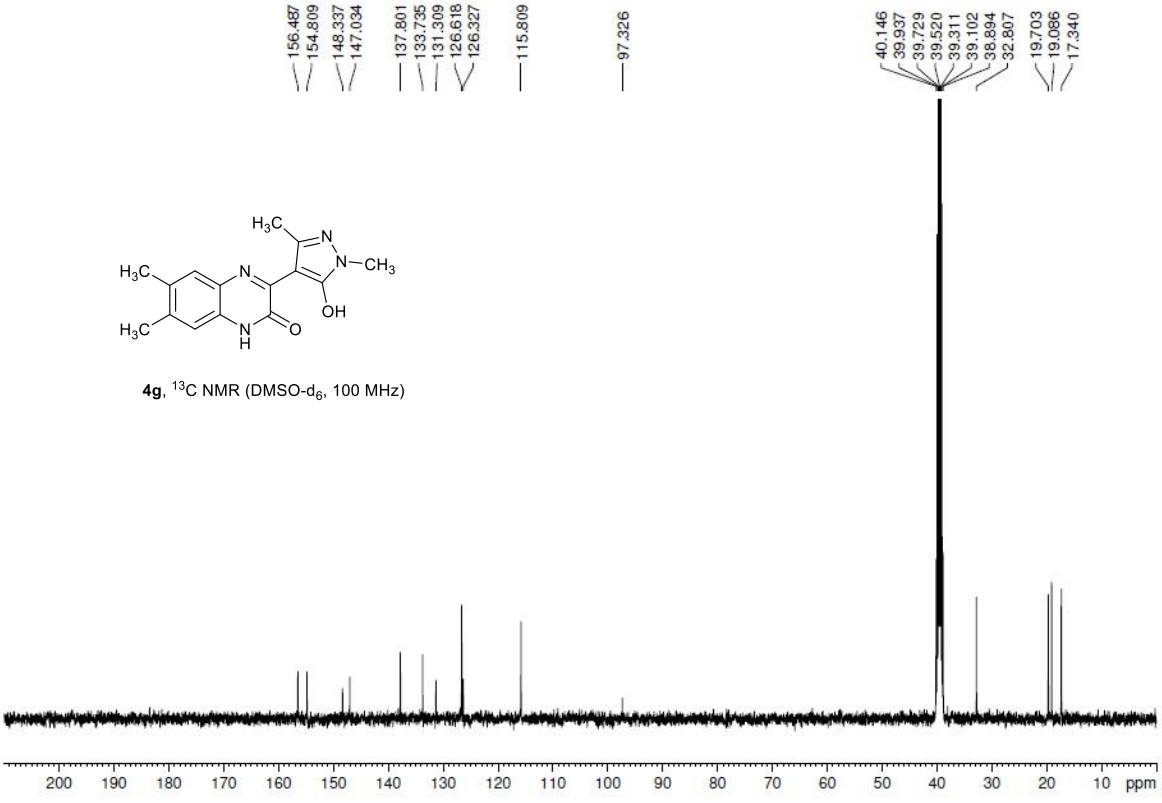


4f, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-6,7-dimethylquinoxalin-2(1*H*)-one (4g)

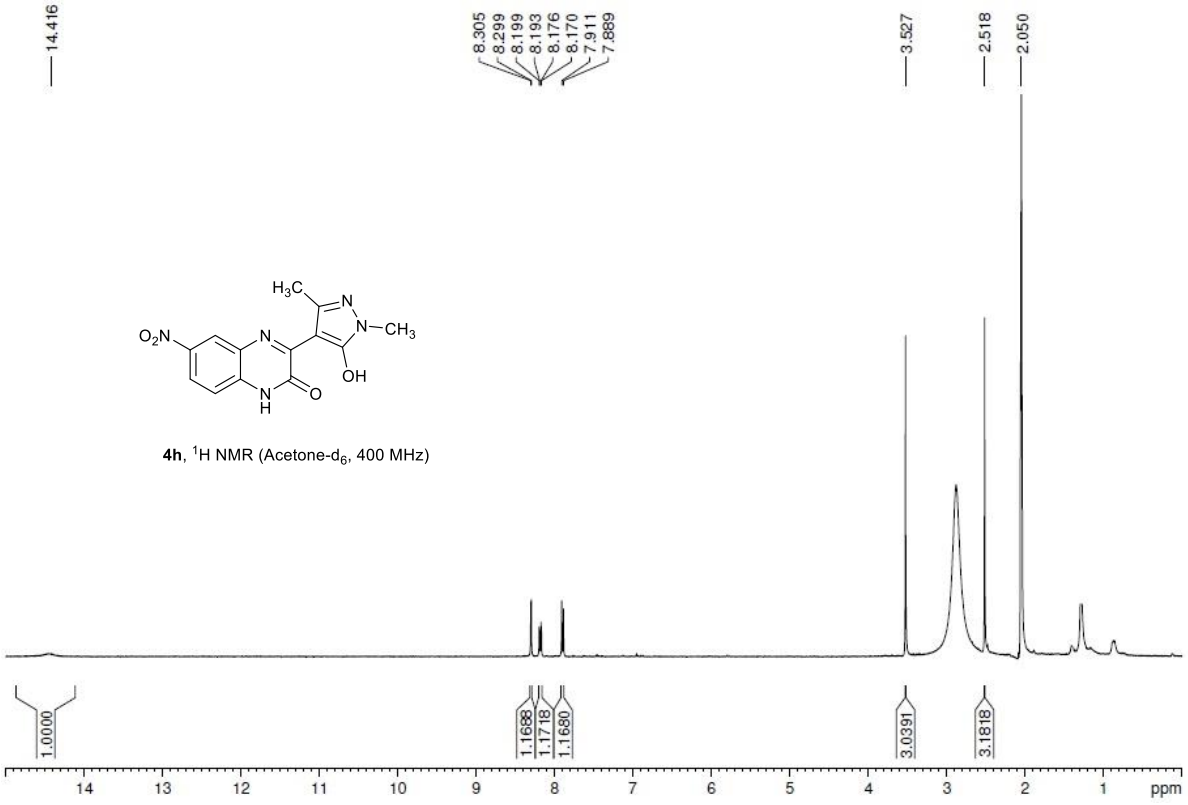


4g, ^{1}H NMR (DMSO-d_6, 400 MHz)

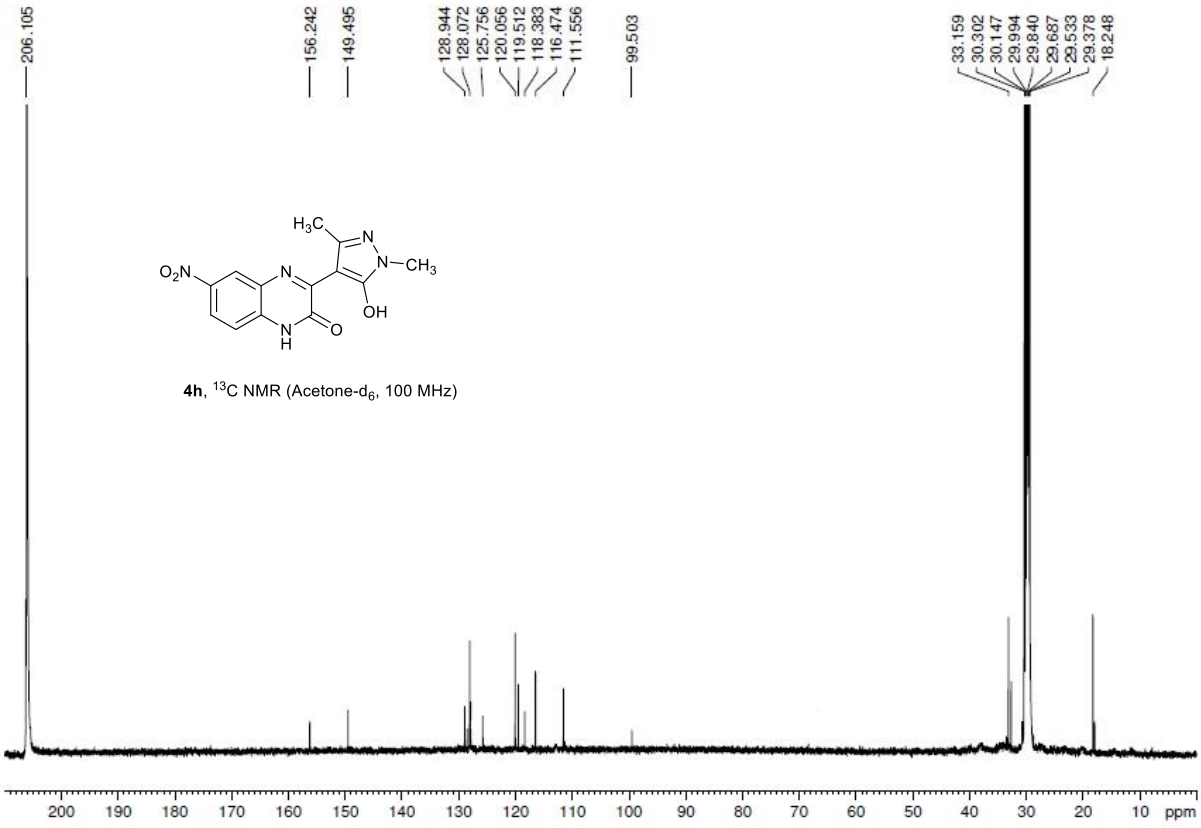


4g, ^{13}C NMR (DMSO-d_6, 100 MHz)

3-(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)-6-nitroquinoxalin-2(1*H*)-one (4h)

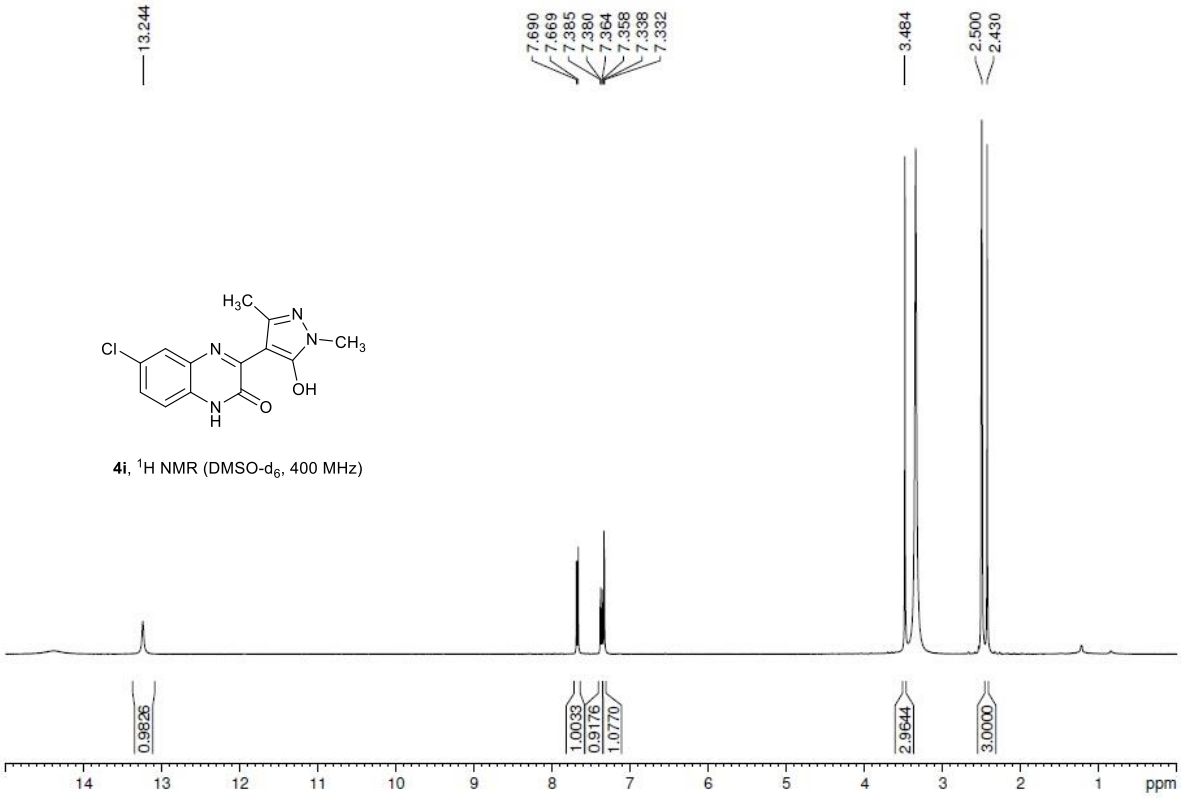


4h, ^{1}H NMR (Acetone-d_6, 400 MHz)

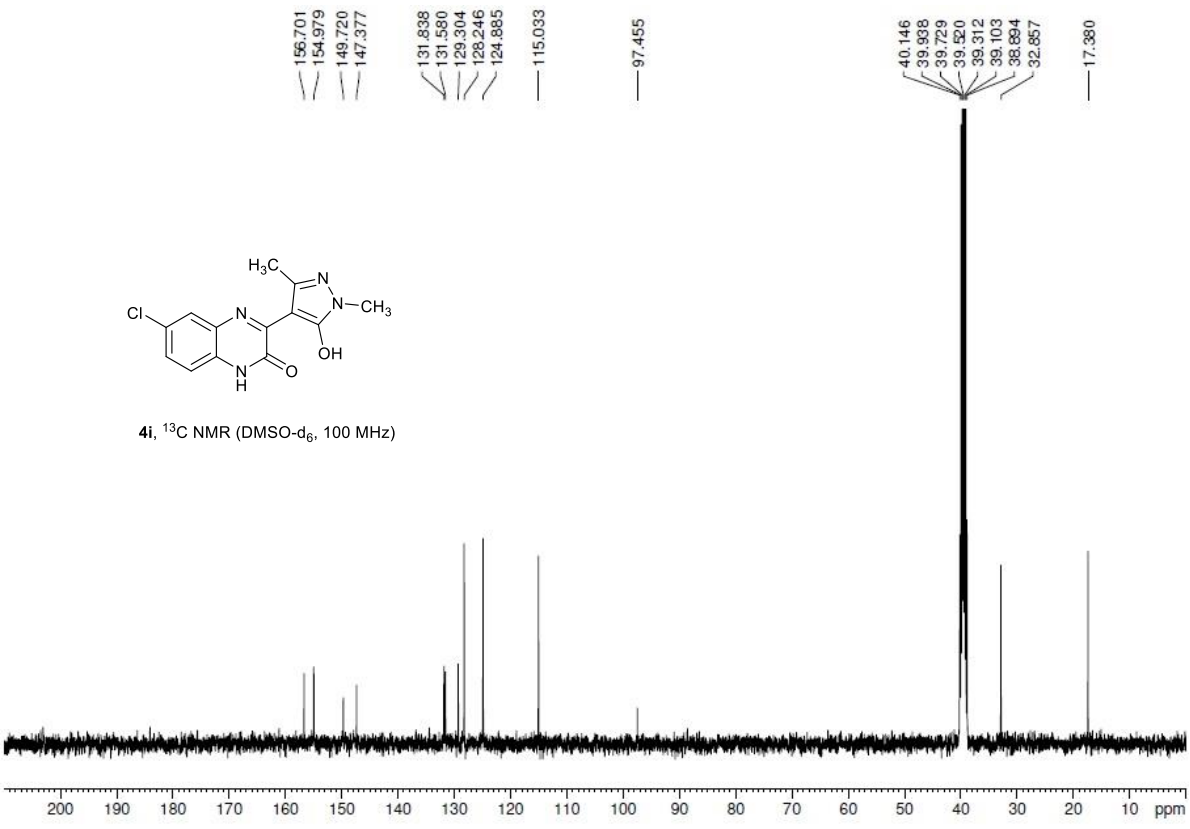


4h, ^{13}C NMR (Acetone-d_6, 100 MHz)

6-Chloro-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4i)

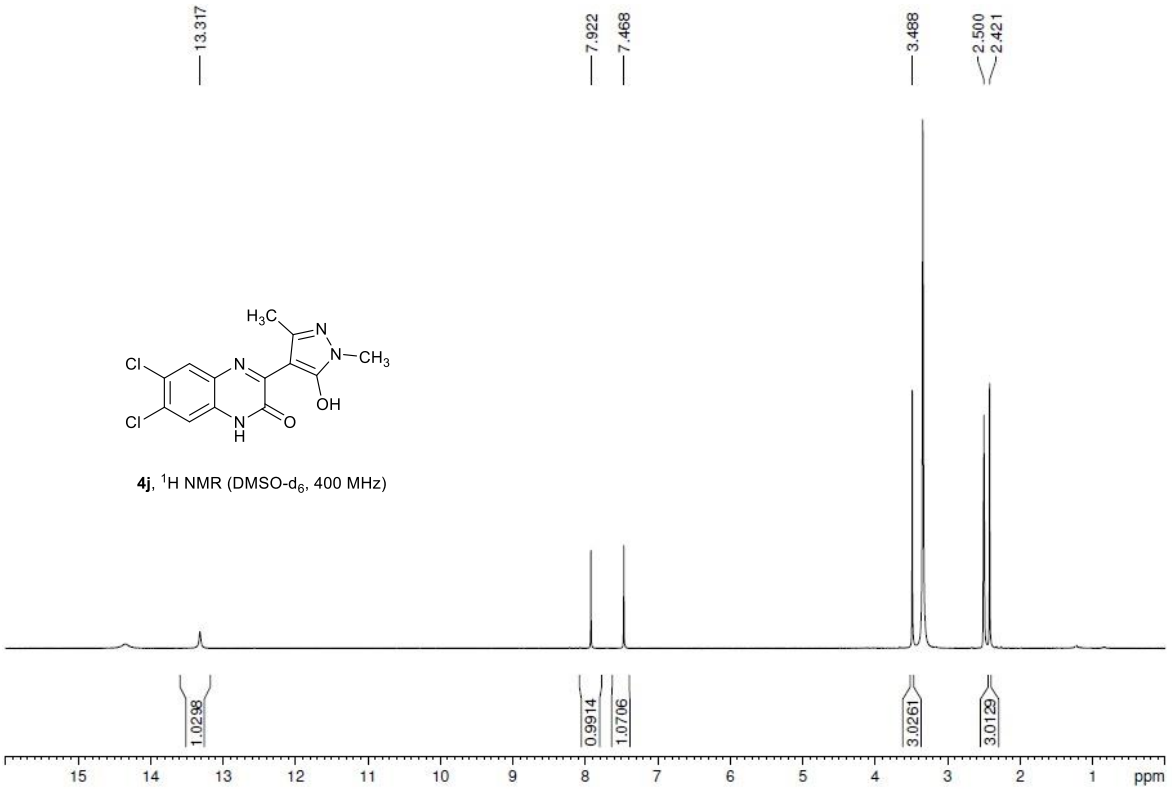


4i, ^{1}H NMR (DMSO-d_6, 400 MHz)

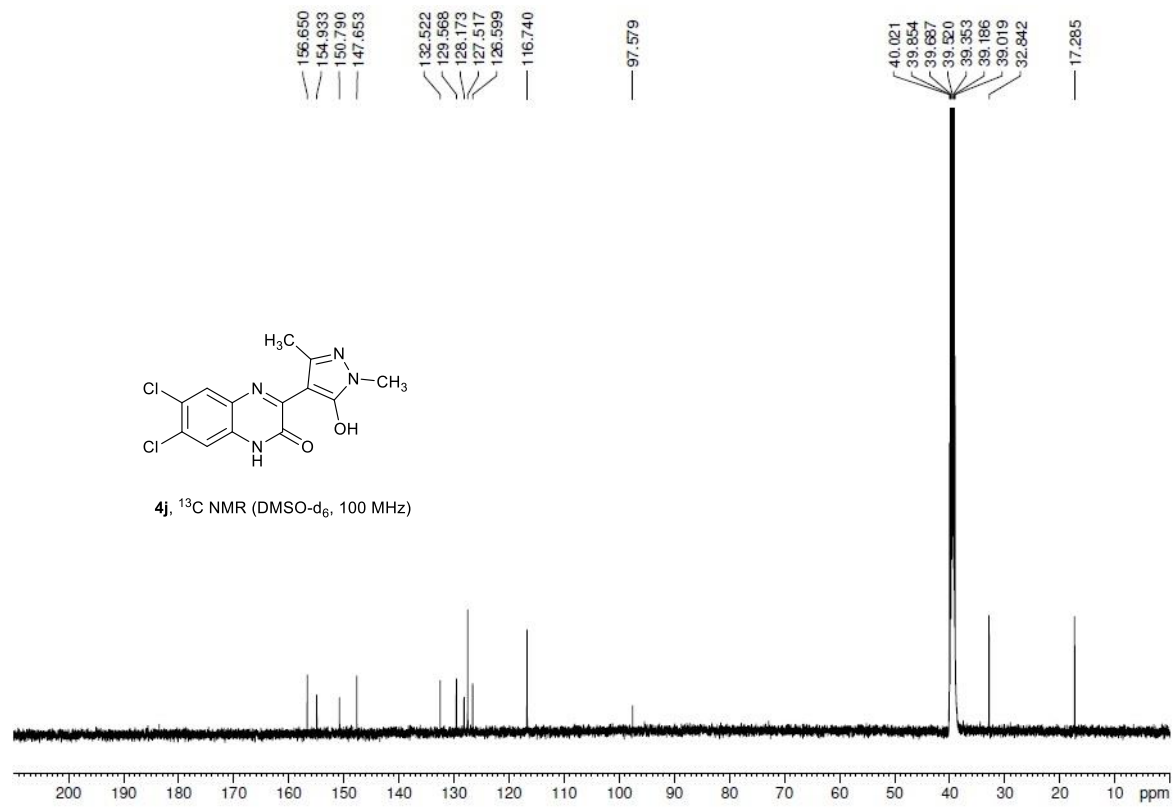


4i, ^{13}C NMR (DMSO-d_6, 100 MHz)

6,7-Dichloro-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4j)

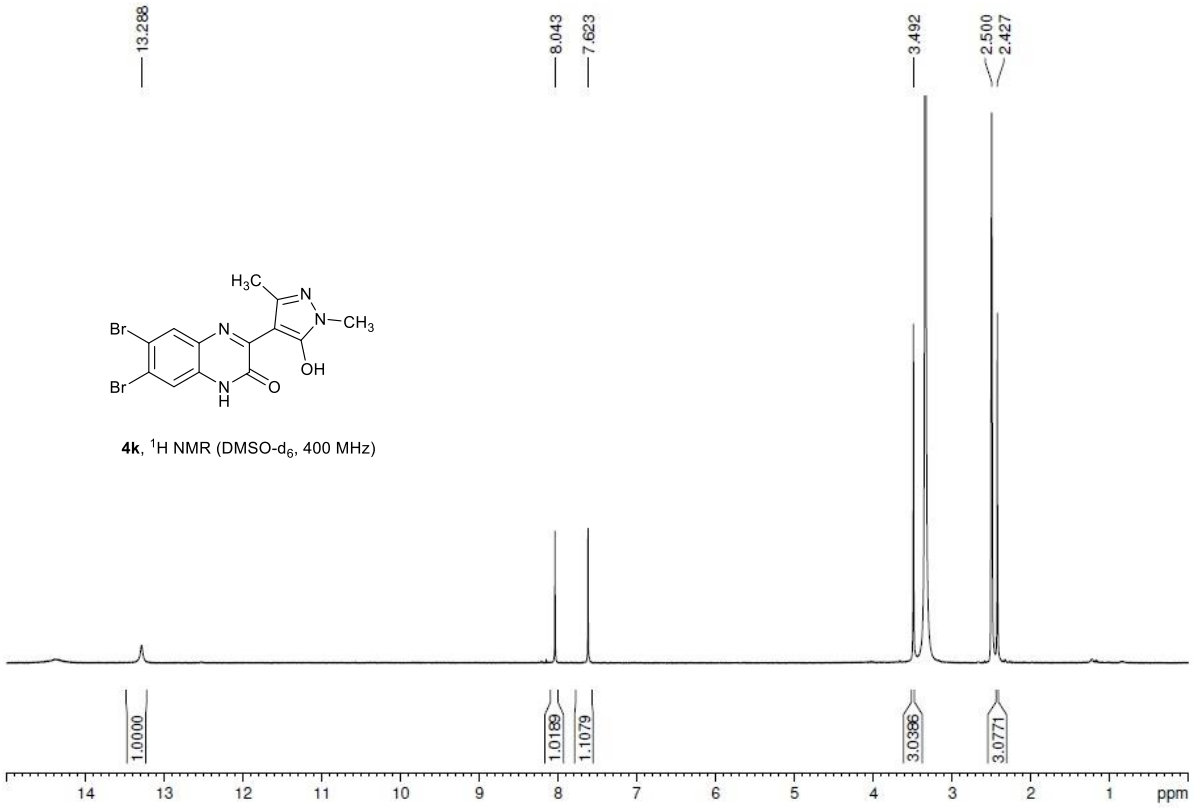


4j, ^{1}H NMR (DMSO-d_6, 400 MHz)

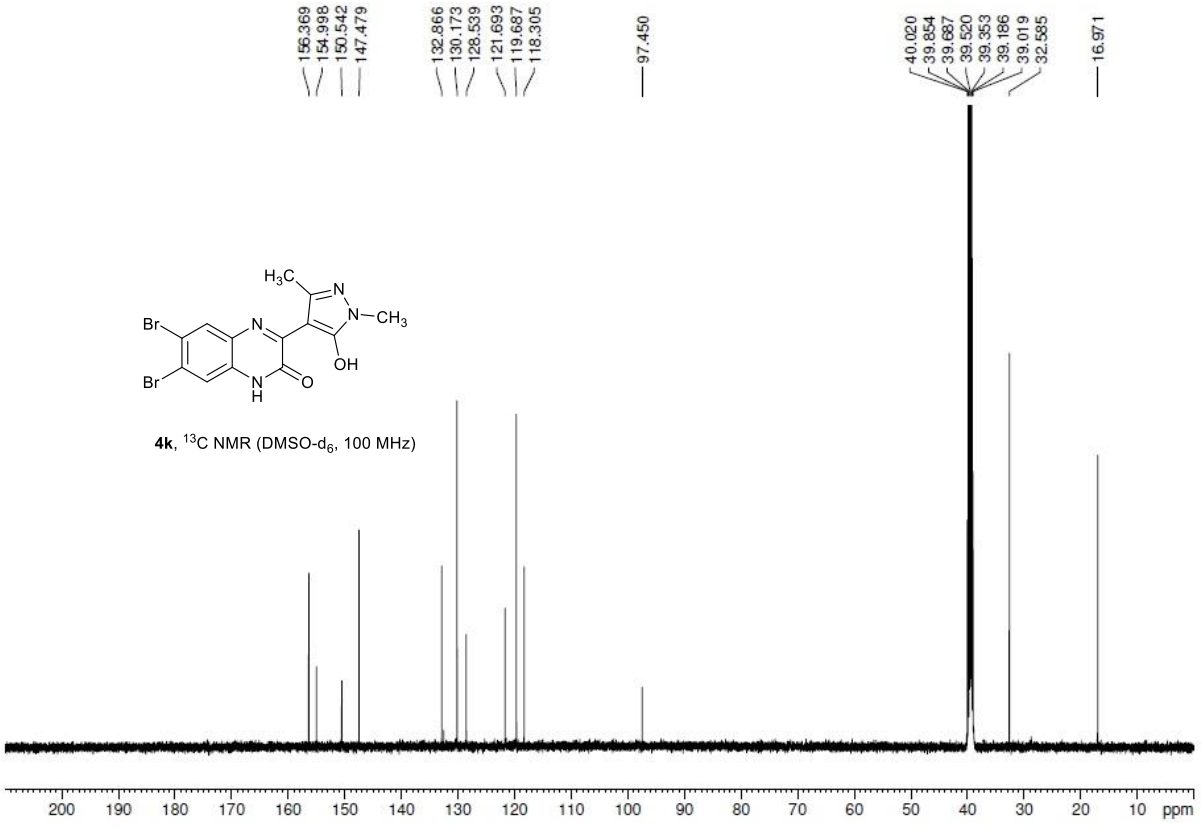


4j, ^{13}C NMR (DMSO-d_6, 100 MHz)

6,7-Dibromo-3-(5-hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)quinoxalin-2(1*H*)-one (4k)



4k, ^{1}H NMR (DMSO-d_6, 400 MHz)



4k, ^{13}C NMR (DMSO-d_6, 100 MHz)

VI. References

1. A. Carrër, J.-D. Brion, S. Messaoudi and M. Alami, *Org. Lett.*, 2013, **15**, 5606.
2. Y. Yang, H.Gong and C. Kuang, *Eur. J. Org. Chem.*, 2013, 5276.
3. SAINT V8.34A, Bruker-AXS, Madison WI, USA, 2013.
4. SADABS-2014/5, Bruker AXS, Madison WI, USA, 2014.
5. G. M. Sheldrick, *Acta Crystallogr. A*, 2015, **71**, 3−8.
6. G. M. Sheldrick, *Acta Crystallogr. A*, 2008, **64**, 112−122.
7. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339−341.
8. L. J. Farrugia, *J. Appl. Crystallogr.*, 2012, **45**, 849−854.