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Supporting Information

Regioselective Synthesis of Novel Nitroso-pyrazolylquinoxalines *via* HOAc-Mediated Cyclocondensation of 2-Hydroxyimino-1,3-diketones with Hydrazinylquinoxalines

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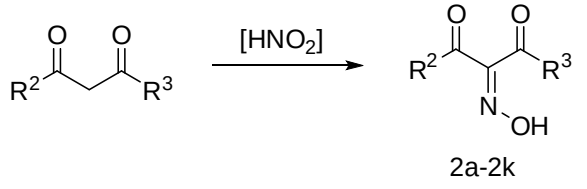
General procedure

Preparation of the starting materials. Synthesis of 2-Hydroxyimino-1,3-diketones 2a-2k [1].



2a-2k

2a: R^2= R^3= Me
2b: R^2= Ph, R^3= Me
2c: R^2= 4-Br-C_6H_4, R^3= Me
2d: R^2= 4-Cl-C_6H_4, R^3= Me
2e: R^2= 4-F-C_6H_4, R^3= Me
2f: R^2= 4-Tolyl, R^3= Me
2g: R^2= Naphthalen-1-yl, R^3= Me
2h: R^2= 4-Pyridyl, R^3= Me
2i: R^2= R^3= Ph
2j: R^2= Ph, R^3= CH_2OMe
2k: R^2= Naphthalen-1-yl, R^3= CH_2OMe

Synthesis of 3-(hydroxyimino)pentane-2,4-dione (2a). Finely crushed ice (340 g), concentrated hydrochloric acid (60 ml), and acetylacetone (50.21 g, 501.5 mmol) were placed into a beaker equipped with a mechanical stirrer and an ice bath. Sodium nitrite (35 g, 507 mmol) was added in portions to the reaction mass with effective stirring at 0-5 °C. After sodium nitrite was loaded, the reaction mixture was stirred for 30 minutes, the resulting white precipitate was filtered off, washed with cold water (20 ml) and dried. Additional 3-hydroxyminopentan-2,4-dione can be isolated by salting out the filtrate with NaCl (125 g). Purification of 3-hydroxyminopentan-2,4-dione was carried out by recrystallization from ethyl acetate (55 ml). Yield 51.75 g (80%), white crystals, M.p. = 72-74 °C.

Synthesis of 2-(hydroxyimino)-1-phenylbutane-1,3-dione (2b). Sodium nitrite (3.6 g, 52.2 mmol, 1.2 eq.) was slowly added to the solution of 1-phenylbutane-1,3-dione (7.0 g, 43.5 mmol, 1 eq.) in acetic acid (20 ml) at 14 °C. After 2 h the reaction mixture was poured in water, filtered off the precipitate of 2-(hydroxyimino)-1-phenylbutane-1,3-dione, washed with water and dried in air. Yield 6.92 g (84%), white crystals, M.p. = 124-126 °C ($EtOH/H_2O$).

Synthesis of 1-(4-bromophenyl)-2-(hydroxyimino)butane-1,3-dione (2c). Sodium nitrite (2.15 g, 23.3 mmol, 1.6 eq.) was slowly added to the solution of 1-(4-bromophenyl)butane-1,3-dione (4.68 g, 19.4 mmol, 1 eq.) in acetic acid (46 ml) at 14 °C. After 3 h the reaction mixture was poured in water, filtered off the precipitate of 1-(4-bromophenyl)-2-(hydroxyimino)butane-1,3-dione, washed with water and dried in air. Yield 4.28 g (82 %), white crystals, M.p. = 162 °C ($EtOH/H_2O$).

Synthesis of 1-(4-chlorophenyl)-2-(hydroxyimino)butane-1,3-dione (2d). Sodium nitrite (0.632 g, 9.2 mmol, 1.2 eq.) was slowly added to the solution of 1-(4-chlorophenyl)butane-1,3-dione (1.5 g, 7.6 mmol, 1 eq.) in acetic acid (25 ml) at 14 °C. After 2.5 h the reaction mixture was poured in water, filtered off the precipitate of 1-(4-chlorophenyl)-2-(hydroxyimino)butane-1,3-dione, washed with water and dried in air. Yield 1.24 g (72 %), light yellow crystals, M.p. = 160-161 °C (EtOH/H_2O).

Synthesis of 1-(4-fluorophenyl)-2-(hydroxyimino)butane-1,3-dione (2e). Sodium nitrite (2.51 g, 36.38 mmol) was slowly added to the solution of 1-(4-fluorophenyl)butane-1,3-dione (5.467 g, 30.37 mmol) in acetic acid (30 ml) at 14 °C. After 2 h the reaction mixture was poured in cold water, filtered off the precipitate of 1-(4-fluorophenyl)-2-(hydroxyimino)butane-1,3-dione, washed with water and dried in air. Yield 5.41 g (85 %), white crystals, M.p. = 144-146 °C (EtOH).

Synthesis of 2-(hydroxyimino)-1-p-tolylbutane-1,3-dione (2f). Sodium nitrite (4.21 g, 61 mmol, 1.2 eq.) was slowly added to the solution of 1-p-tolylbutane-1,3-dione (8.95 g, 50.9 mmol, 1 eq.) in acetic acid (25 ml) at 14 ° C. After 3 h the reaction mixture was poured in water (100 ml), the precipitate of 2-(hydroxyimino)-1-p-tolylbutane-1,3-dione was filtered off, washed with water and dried in air. Yield 9.17 g (88%), white crystals, M.p. = 154-156 °C (EtOH/H_2O).

Synthesis of 2-(hydroxyimino)-1-(naphthalen-1-yl)butane-1,3-dione (2g). Sodium nitrite (2.95 g, 42.7 mmol, 1.2 eq.) was slowly added to the solution of 1-(naphthalen-1-yl)butane-1,3-dione (7.55 g, 35.6 mmol, 1 eq.) in acetic acid (90 ml) at 14 °C. After 4 h the reaction mixture was poured in water (150 ml), filtered off beige precipitate of 2-(hydroxyimino)-1-(naphthalen-1-yl)butane-1,3-dione, washed with water and dried in air. Yield 7.98 g (93 %), beige crystals, M.p. = 166-167 °C (EtOH/H_2O).

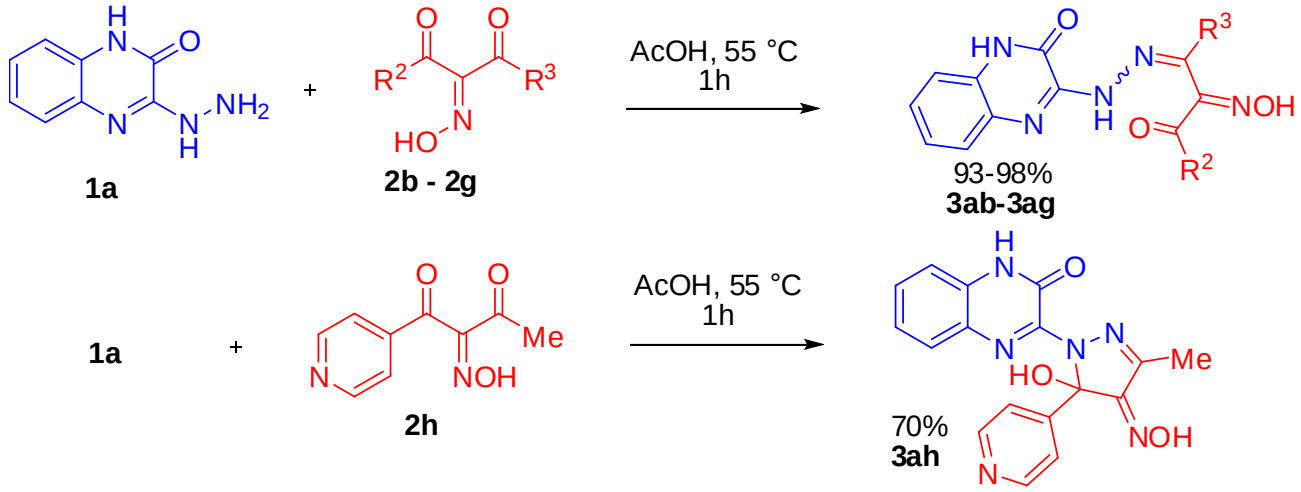
Synthesis of 2-(hydroxyimino)-1,3-diphenylpropane-1,3-dione (2i). A solution of 1,3-diphenylpropane-1,3-dione (20.0 g, 89.29 mmol) in chloroform (60 mL) was placed into a beaker equipped with a mechanical stirrer, cooled to 17°C, and then freshly distilled isoamyl nitrite (12.0 g, 113.21 mmol) and absolute ethanol (2 ml) saturated with dry hydrogen chloride were added in 2 portions. The reaction mixture was stirred for 1 h, then diluted with hexane (60 ml), the precipitate was filtered off, washed with hexane (20 ml) and dried. Yield 19.00 g (84%), white crystals, M.p. = 146 °C [2].

Synthesis of 2-(hydroxyimino)-4-methoxy-1-phenylbutane-1,3-dione (2j). Sodium nitrite (5.84 g, 84.63 mmol) was slowly added to the solution of 4-methoxy-1-phenylbutane-1,3-dione (14.77 g, 76.94 mmol) in acetic acid (60 ml) at 14 °C. After 3

h the reaction mixture was poured in water (250 ml), the precipitate of 2-(hydroxyimino)-4-methoxy-1-phenylbutane-1,3-dione was filtered off, washed with water and dried in air. Yield 12.373 g (73%), beige crystals, M.p. = 129-130 °C.

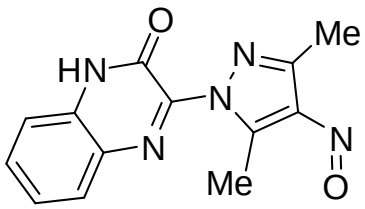
Synthesis of 2-(hydroxyimino)-4-methoxy-1-(naphthalen-1-yl)butane-1,3-dione (2k). Sodium nitrite (3.795 g, 55.00 mmol) was slowly added to the solution of 4-methoxy-1-(naphthalen-1-yl)butane-1,3-dione (10.635 g, 43.95 mmol) in acetic acid (50 ml) at 14 °C. After 3 h the reaction mixture was poured in water (250 ml), the precipitate of 2-(hydroxyimino)-4-methoxy-1-(naphthalen-1-yl)butane-1,3-dione was filtered off, washed with water and dried in air. Yield 10.38 g (86%), beige crystals, M.p. = 152-153 °C.

General procedure for the synthesis of hydrazone intermediates 3ab-3ag and 5-hydroxypyrazoline intermediate 3ah [3].



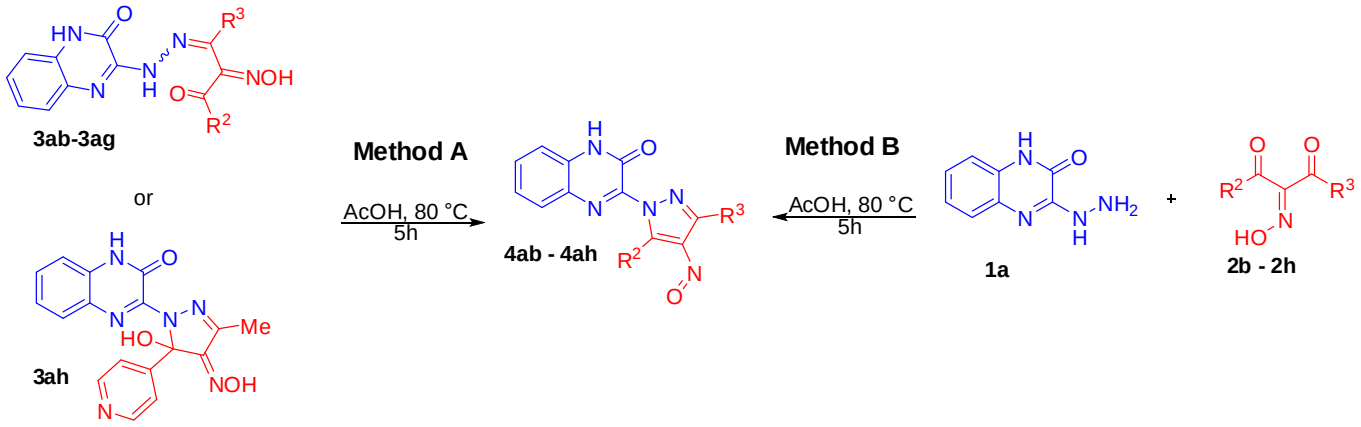
The mixture of 3-hydrazinylquinoxalin-2(1H)-one **1a** (0.4 g, 2.27 mmol, 1.0 eq), 2-(hydroxyimino)-1,3-dione **2b-h** (2.27 mmol, 1.0 eq) and glacial acetic acid (7 mL) was stirred during 1 h at 50-55 °C. The reaction mixture was cooled, the resulting precipitate was filtered off, washed with 1 ml of acetic acid, 20 ml of water, and dried. Yields 70-99%, yellow or beige solids. Physical, spectral data and structure for hydrazones 3aa-3ag, 5-hydroxypyrazoline 3ah were described in our recent report [3].

Gram-scale synthesis of nitrosopyrazole 4aa



3-Hydrazinylquinoxalin-2(1H)-one **1a** (5.18 g, 29.4 mmol, 1.0 eq) was dissolved in boiling ethanol (1150 mL), the resulting hot saturated solution was cooled to 60 °C, then 3-(hydroxyimino)pentane-2,4-dione **2a** (4.00 g, 31 mmol, 1.05 eq) and hydrochloric acid (0.2 mL) was added. The resulting solution was stirred for 2 h without heating and then allowed to stand for 72 h. The resulting green crystals were filtered off, washed with ethanol (15 mL) and dried in air. Green crystals, yield 6.25 g (79%); mp 216 °C (dec.)

General procedure for the synthesis of nitrosopyrazoles 4ab-4ah



Method A. The intermediate **3ab-3ah** (0.55 mmol) was suspended in glacial acetic acid (6 mL) and stirred during 5 h at 80 °C. The reaction mixture was filtered, the resulting green filtrate was poured into cold water (35 mL), then sodium chloride (0.6 g) was added and stirred for 1 min. The precipitate was filtered off, washed with water (10 mL) and dried in air. The obtained solid was purified by column chromatography on silica gel (70-230 mesh) using toluene - acetonitrile as eluent (gradient 15:1 - 10:1) to yield the desired product.

Method B. The mixture of 3-hydrazinylquinoxalin-2(1H)-one **1a** (0.097g, 0.55 mmol, 1.0 eq), 2-(hydroxyimino)-1,3-dione **2** (0.55 mmol, 1.0 eq) and glacial acetic acid (6 mL) was stirred during 5 h at 80 °C. The reaction mixture was filtered, the resulting green filtrate was poured into cold water (35 mL), then sodium chloride (0.6 g) was added and stirred during 1 min. The precipitate was filtered off, washed with water

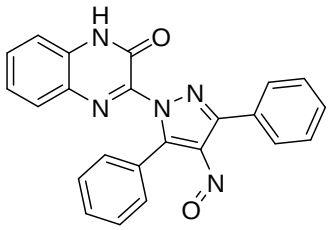
(10 mL) and dried in air. The obtained solid was purified by column chromatography on silica gel (70-230 mesh) using toluene - acetonitrile as eluent (gradient 15:1 - 10:1) to yield the desired product.

Table 1. Synthesis of nitrosopyrazoles **4ab-4ah**

compd	R^2	R^3	yield[a], % **Method A**	yield[a], % **Method B**	mp, °C (EtOH)
4ab	Ph	Me	33	39	237-240 (dec.)
4ac	4-Br-C_6H_4	Me	50	49	236-237 (dec.)
4ad	4-Cl-C_6H_4	Me	35	37	222-224 (dec.)
4ae	4-F-C_6H_4	Me	58	40	204-207
4af	4-Tolyl	Me	54	47	218-220 (dec.)
4ag	Naphthalen-1-yl	Me	39	44	200-204 (dec.)
4ah	4-Pyridyl	Me	25	traces	251-253 (dec.)

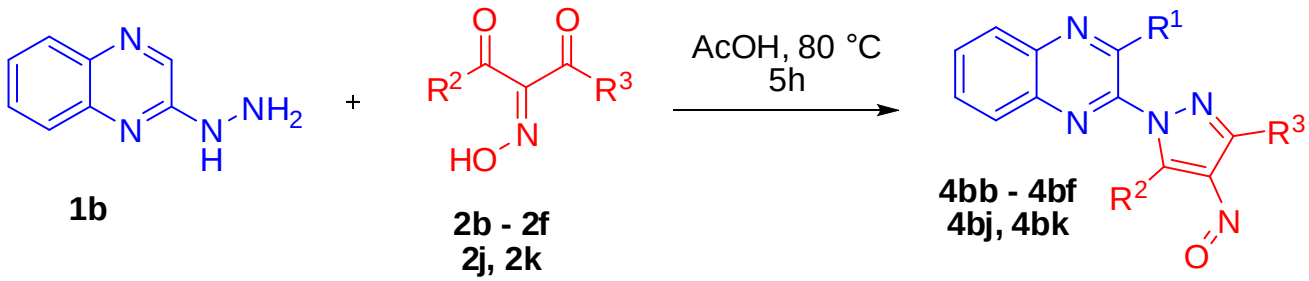
[a] Isolated yield.

Gram-scale synthesis of nitrosopyrazole 4ai



The mixture of 3-hydrazinylquinoxalin-2(1H)-one **1a** (3.872 g, 22 mmol, 1.0 eq), 2-(hydroxyimino)-1,3-diphenylpropane-1,3-dione **2i** (6.123 g, 24.2 mmol, 1.1 eq), acetic acid (40 mL) and TFA (0.2 mL) was stirred during 96 h at 25°C. The resulting yellow precipitate was filtered off and washed with acetic acid (5 mL). Yellow solid was suspended in acetic acid (250 mL) and stirred during 5 hours at 80°C. The hot mixture was filtered and the green filtrate was allowed to stand at 25 °C during 24 h. After the crystallization was completed, the precipitate was filtered off, washed with acetic acid (2 mL), and dried in air. Light green solid, yield 1.73 g (20 %); mp 238-240 °C (dec.) (EtOH).

General procedure for nitrosopyrazoles 4bb-4bf, 4bj, 4bk synthesis



1b + **2b - 2f, 2j, 2k** → **4bb - 4bf, 4bj, 4bk**

The mixture of 2-hydrazinylquinoxaline **1b** (0.088g, 0,55 mmol, 1.0 eq), 2-(hydroxyimino)-1,3-dione **2** (0.55 mmol, 1.0 eq) and glacial acetic acid (2 mL) was stirred during 1 h at 25 °C. Acetic acid (4 mL) was added to the resulting yellow suspension. The reaction mixture was heated to 80 °C and stirred during 5 h. After cooling down to room temperature, the resulting green solution was poured into water (25 mL) and extracted ($CHCl_3$, 2*10 mL). The combined organic layers were washed with 5% aqueous $NaHCO_3$ (10 mL) then brine (10 mL) and dried over Na_2SO_4. The resulting extract was evaporated and chromatographed on a silica gel column (70-230 mesh) using toluene-acetonitrile as eluent (gradient 25:0 - 25:1) to yield the desired product.

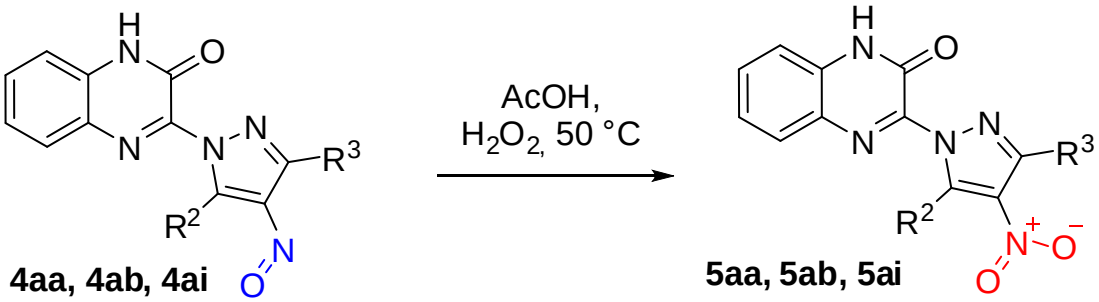
Table 2. Synthesis of nitrosopyrazoles **4bb-4bf, 4bj, 4bk**

compd	R^2	R^3	yield[a], %	mp, °C
4bb	Ph	Me	78	156-158 (CCl_4)
4bc	4-Br-C_6H_4	Me	74	160-162 (CCl_4)
4bd	4-Cl-C_6H_4	Me	65	160-162 (CCl_4)
4be	4-F-C_6H_4	Me	64	148-150 (CCl_4)
4bf	4-Tolyl	Me	65	132-134 (CCl_4)
4bj	Ph	CH_2OMe	86	106-108 (CCl_4)
4bk	Naphthalen-1-yl	CH_2OMe	53	140-142 (CCl_4)

[a] Isolated yield.

Substrates screening showed the reaction was tolerant to sterically bulky substituents (**4ag, 4bk**). At the same time, the introduction of electron-donating substituents into hydrazinylquinoxaline should increase the nucleophilicity of the amino group. Taking this into account, we assume successful cyclocondensation when R^1 is an alkyl or an aryl group.

Oxidation of nitrosopyrazoles



4aa, 4ab, 4ai **5aa, 5ab, 5ai**

Oxidation of 4aa

The mixture of **4aa** (0.162 g, 0.6 mmol), acetic acid (20 mL) and hydrogen peroxide 30% (2 mL) was stirred during 4 h at 50 °C, then the reaction mixture was evaporated to 10 mL and poured into cold water (30 mL). The resulting precipitate was filtered off, washed with water and dried. Beige solid, yield 0.045 g (23%); mp 295-300 °C (dec.) (EtOH).

Oxidation of 4ab

Hydrogen peroxide 30% (2 mL) was added dropwise to a solution of compound **4ab** (0.2 g, 0.6 mmol) in acetic acid (17 mL) and stirred during 4 h at 50 °C, then the reaction mixture was evaporated to 10 mL and poured into cold water (30 mL). The resulting precipitate was filtered off, washed with water, and recrystallized from ethanol. Yellow solid, yield 0.15 g (71%); mp 222-224 °C (EtOH).

Oxidation of 4ai

Hydrogen peroxide 30% (2 mL) was added dropwise to a solution of compound **4ai** (0.237 g, 0.6 mmol) in acetic acid (20 mL) and stirred during 4 h at 50 °C, then the reaction mixture was evaporated to 10 mL and poured into cold water (30 mL). The resulting precipitate was filtered off, washed with water, and recrystallized from ethanol. Beige solid, yield 0.134 g (54%); mp 242-244 °C (EtOH).

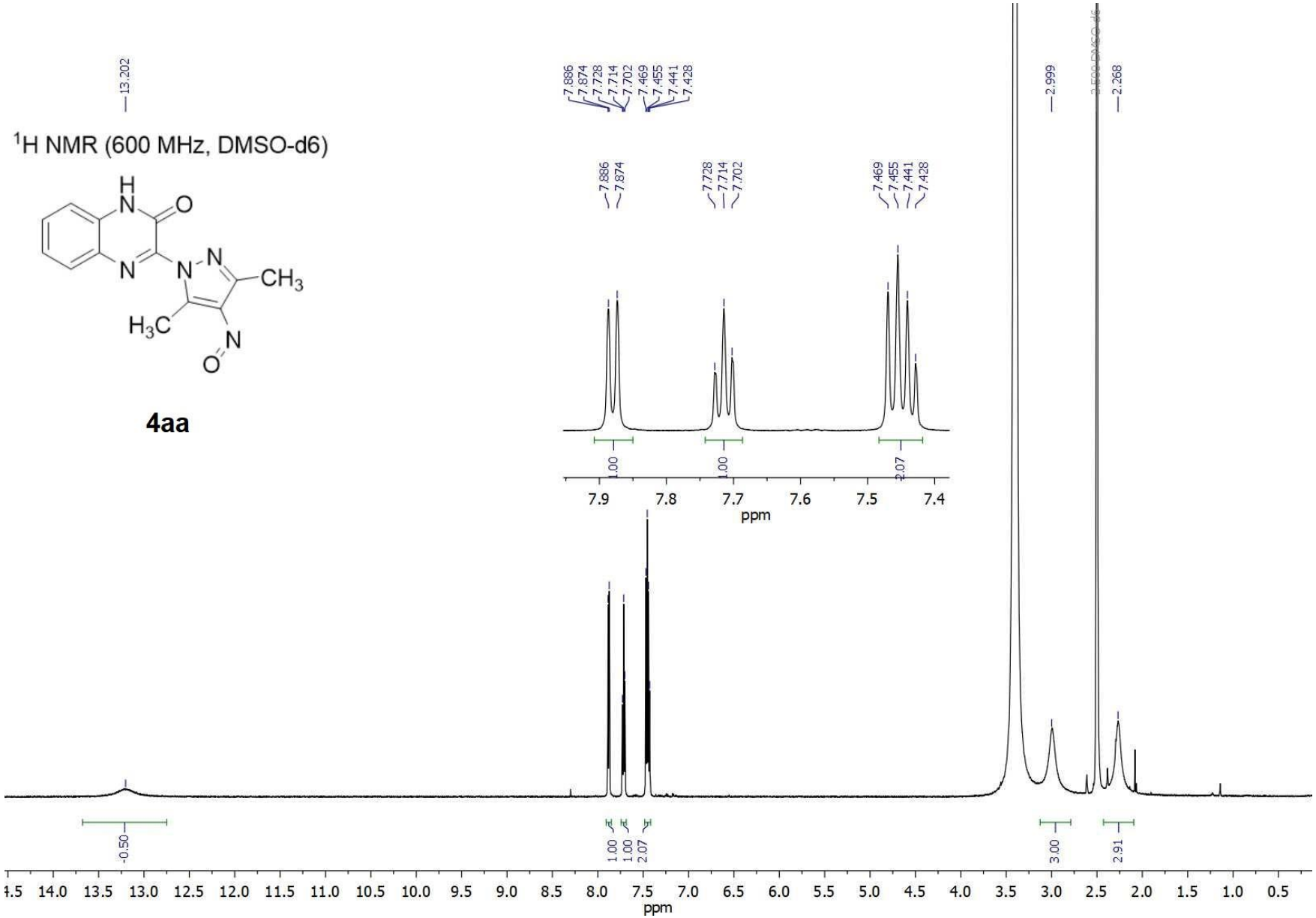
REFERENCES

[1] P.S. Bobrov, S.D. Kirik, A.V. Lyubyashkin, G.A. Suboch, M.S. Tovbis. Molecular packing peculiarities in 2-hydroxyimino-1,3-diketones by X-ray powder diffraction. *Butlerov Communications B.* **2022**, *3 (2),* Id.1. https://doi.org/10.37952/ROI-jbc-B/22-3-2-1

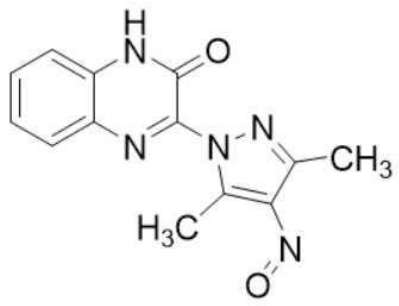
[2] R. Neufville, H. Pechmann. Ueber das Diphenyltriketon. *Chem. Ber.* **1890,** *23,* 3375-3387. https://doi.org/10.1002/cber.189002302302

[3] a) P.S. Bobrov, E.S. Semichenko, A.A. Kondrasenko, G.A. Suboch. Interaction of 3-Hydrazinylquinoxaline-2(1H)-one with 2-Hydroxyimino-1,3-dicarbonyl Compounds. *Zhurnal Organicheskoi Khimii*, **2022**, *58(11)*, 1214–1223. https://doi.org/10.31857/S0514749222110106; b) P.S. Bobrov, E.S. Semichenko, A.A. Kondrasenko, G.A. Suboch. Reaction of 3-Hydrazinylquinoxaline-2(1H)-one with 2-Hydroxyimino-1,3-dicarbonyl Compounds. *Russ. J. Org. Chem.*, **2022**, *58 (11), 1628-1636*. https://doi.org/10.1134/S1070428022110100

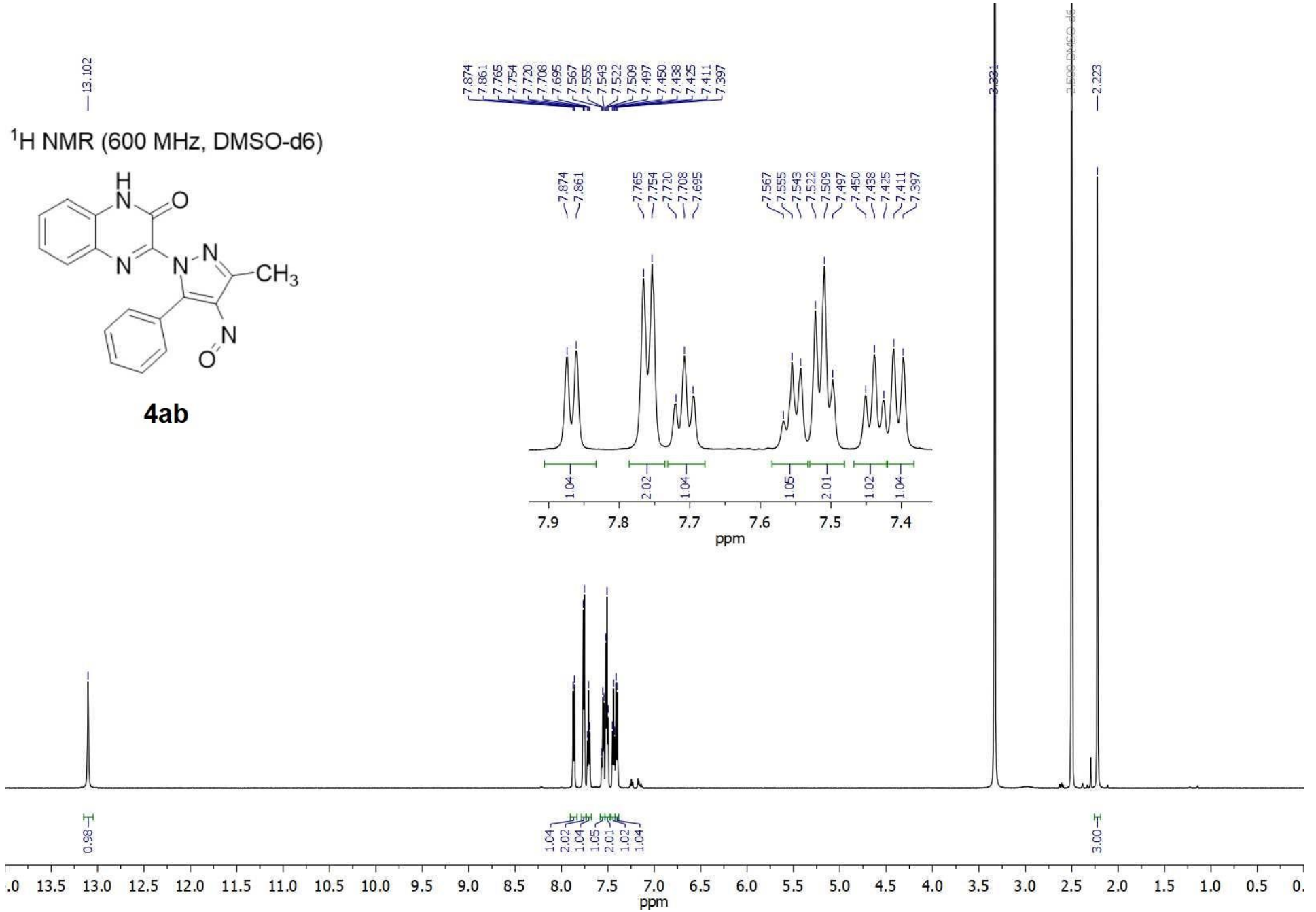
NMR spectra copies



^{13}C NMR (150 MHz, DMSO-d6)



4aa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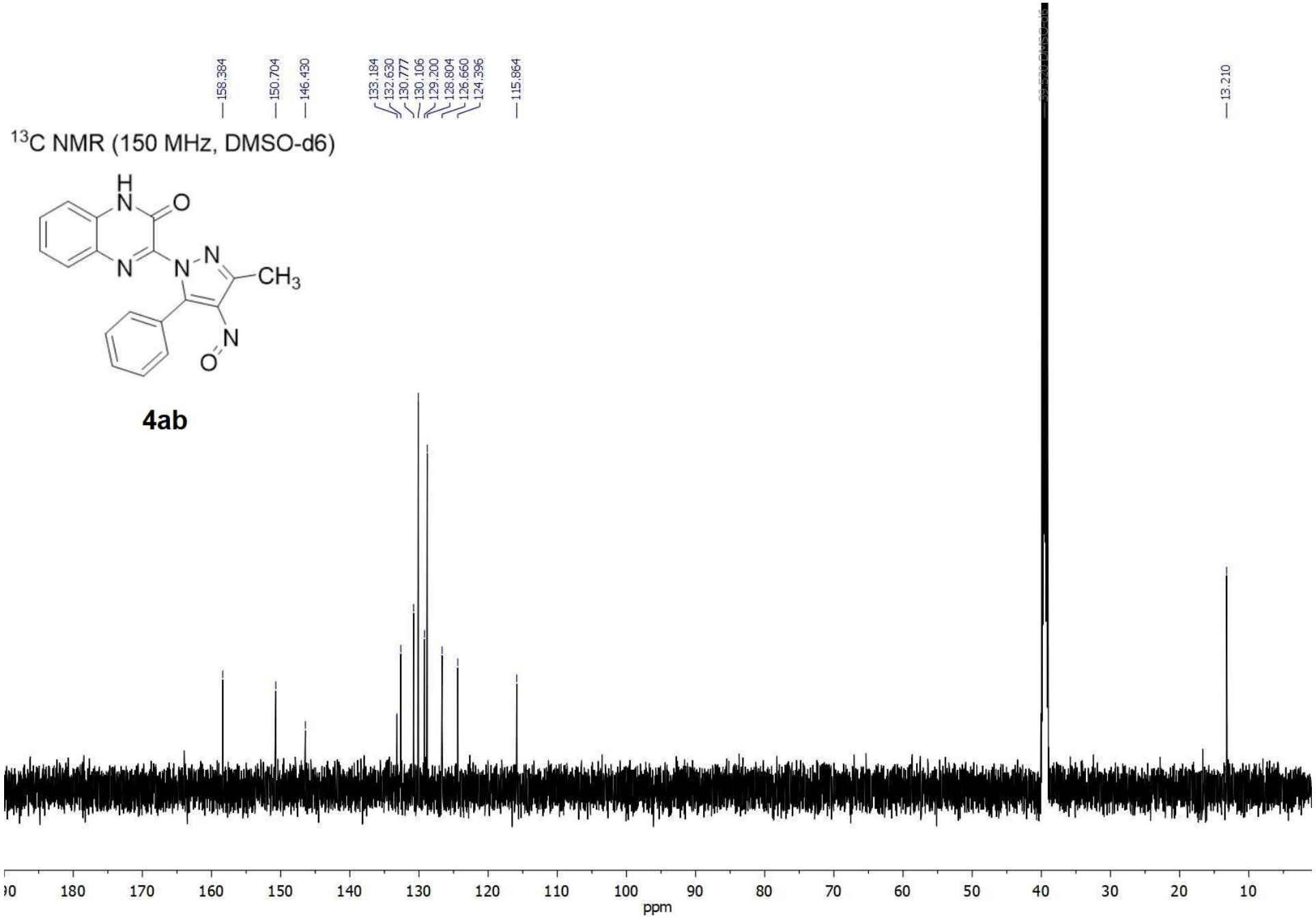
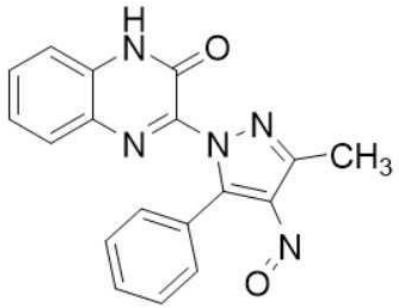
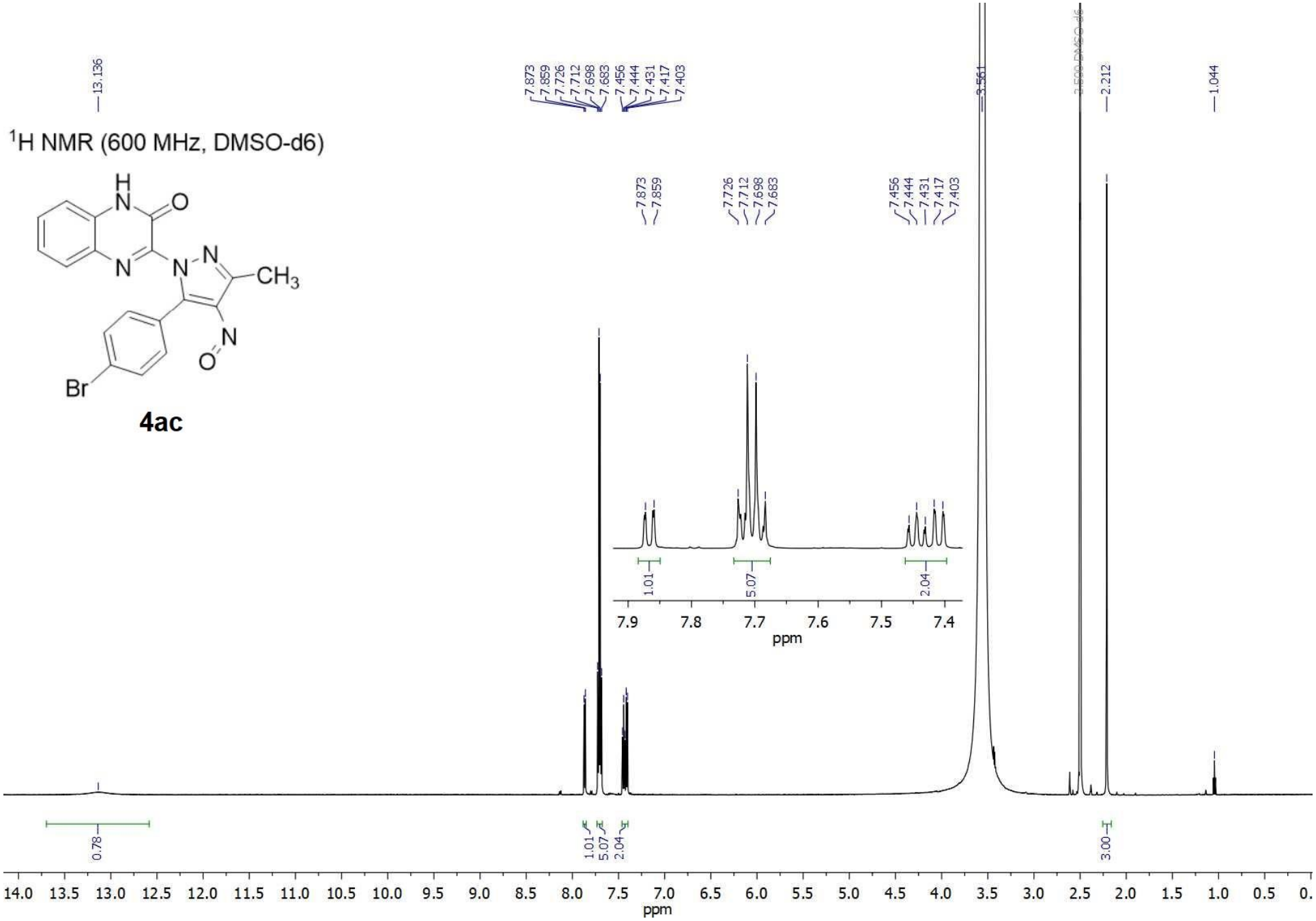
4ab
13.102
7.874
7.861
7.765
7.754
7.720
7.708
7.695
7.567
7.555
7.543
7.522
7.509
7.497
7.450
7.438
7.425
7.411
7.397
3.331
2.500 DMSO-d6
2.223
1.04
2.02
1.04
1.05
2.01
1.02
1.04
0.98
3.00
ppm


158.384
150.704
146.430
133.184
132.630
130.777
130.106
129.200
128.804
126.660
124.396
115.864
39.520 DMSO-d6
13.210
^{13}C NMR (150 MHz, DMSO-d6)
H
N
O
N
N
N
CH$_3$
N
O
4ab
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

HSQC (DMSO-d6)



4ab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7.726
7.712
7.698
7.683
7.456
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7.431
7.417
7.403
3.561
3.500 DMSO-d6
2.212
1.044
1H NMR (600 MHz, DMSO-d6)
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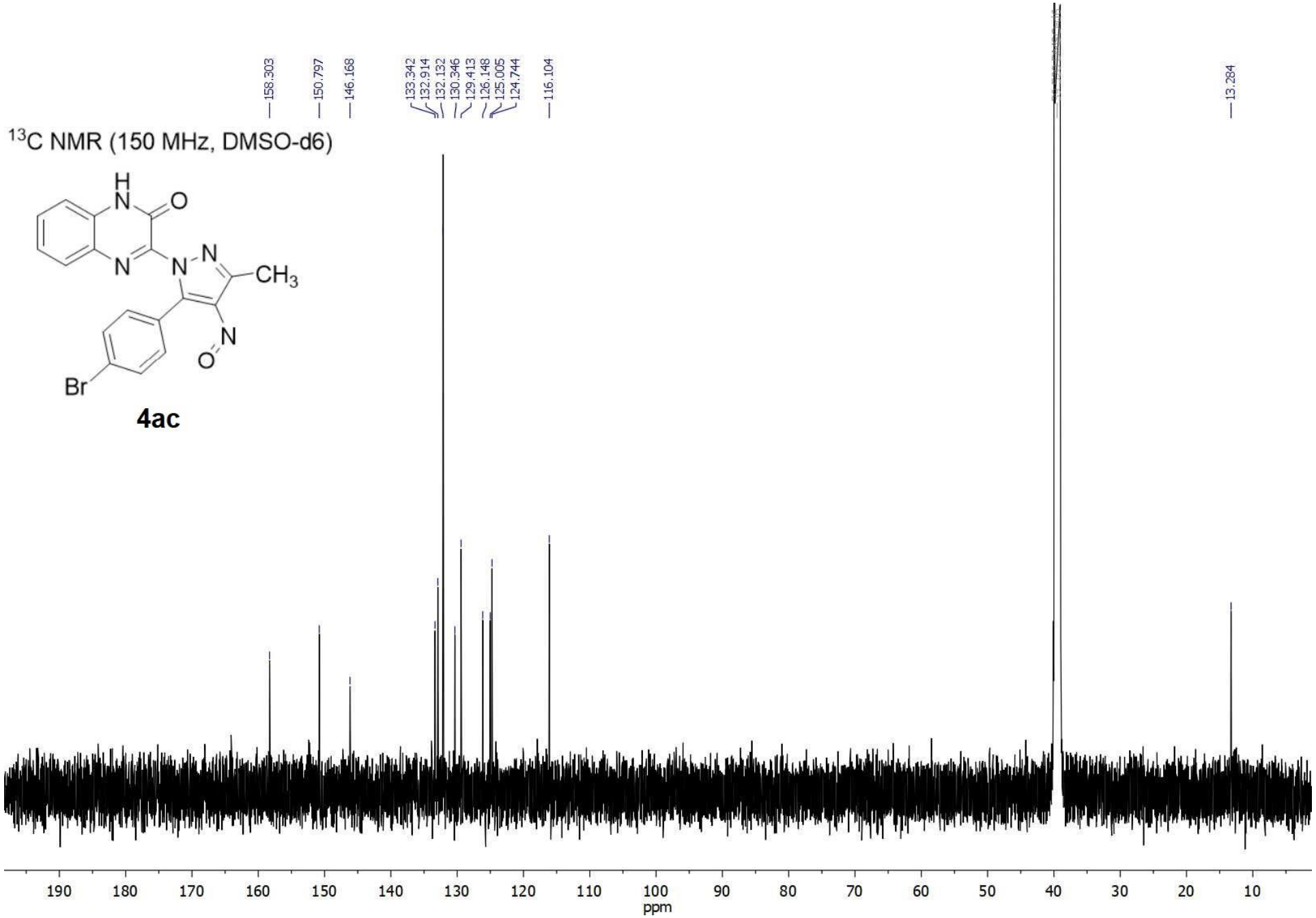
5.07
2.04
0.78
3.00
ppm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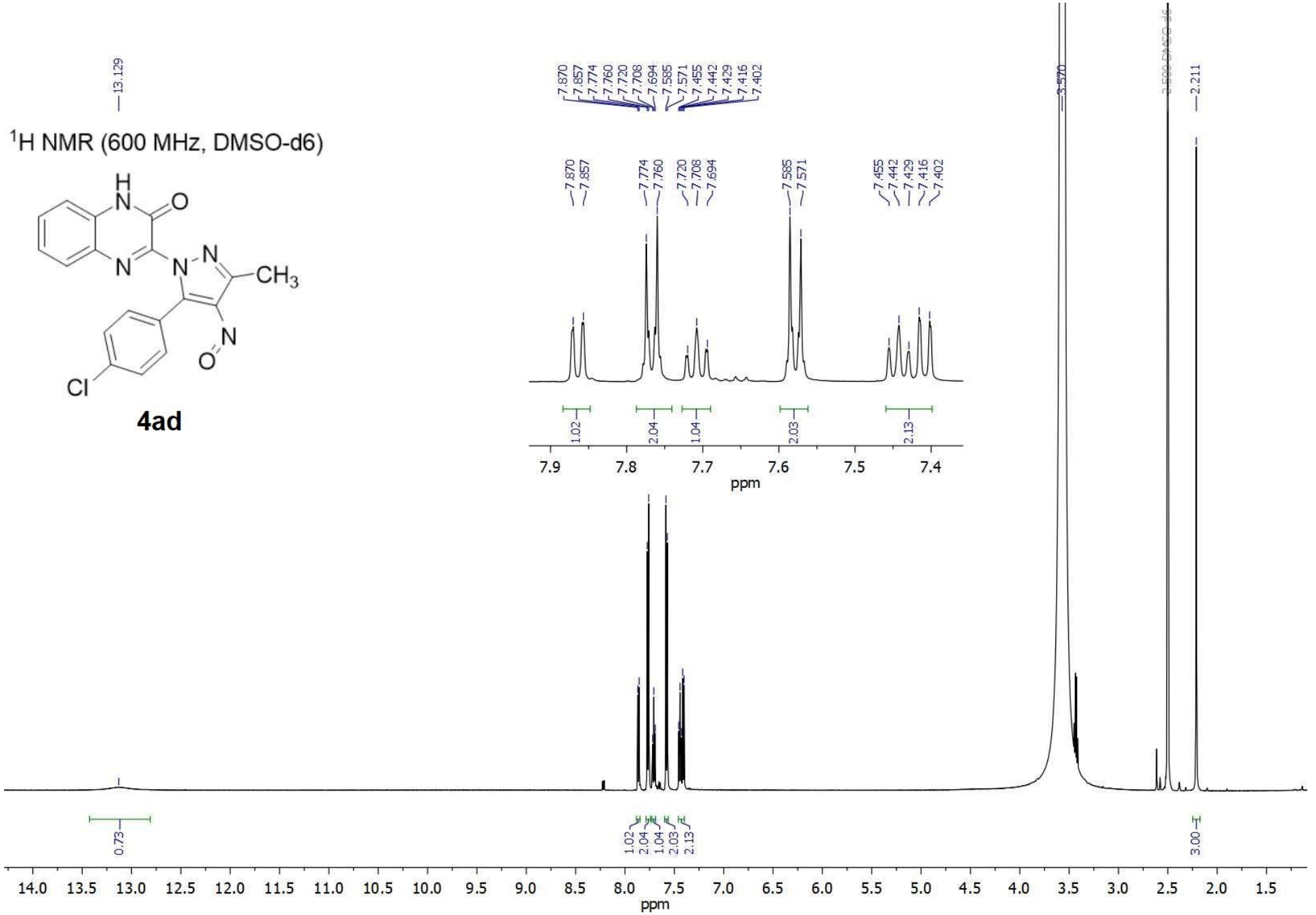
146.168
133.342
132.914
132.132
130.346
129.413
126.148
125.005
124.744
116.104
13.284
^{13}C NMR (150 MHz, DMSO-d6)
H
N
O
N
N
N
CH$_3$
N
O
Br
4ac
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.857
7.774
7.760
7.720
7.708
7.694
7.585
7.571
7.455
7.442
7.429
7.416
7.402
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1.02
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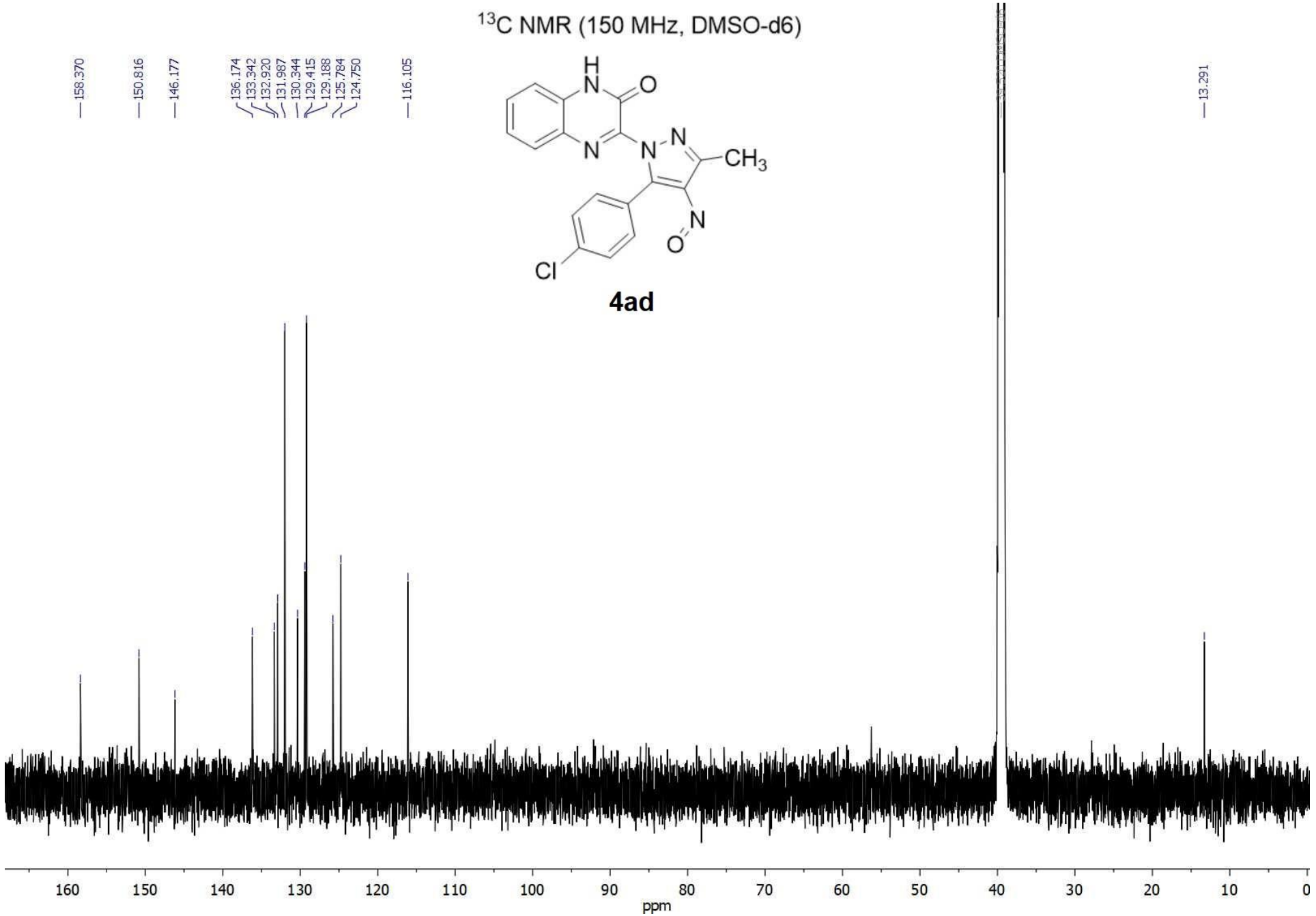
2.03
2.13
0.73
3.00
ppm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146.177
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132.920
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130.344
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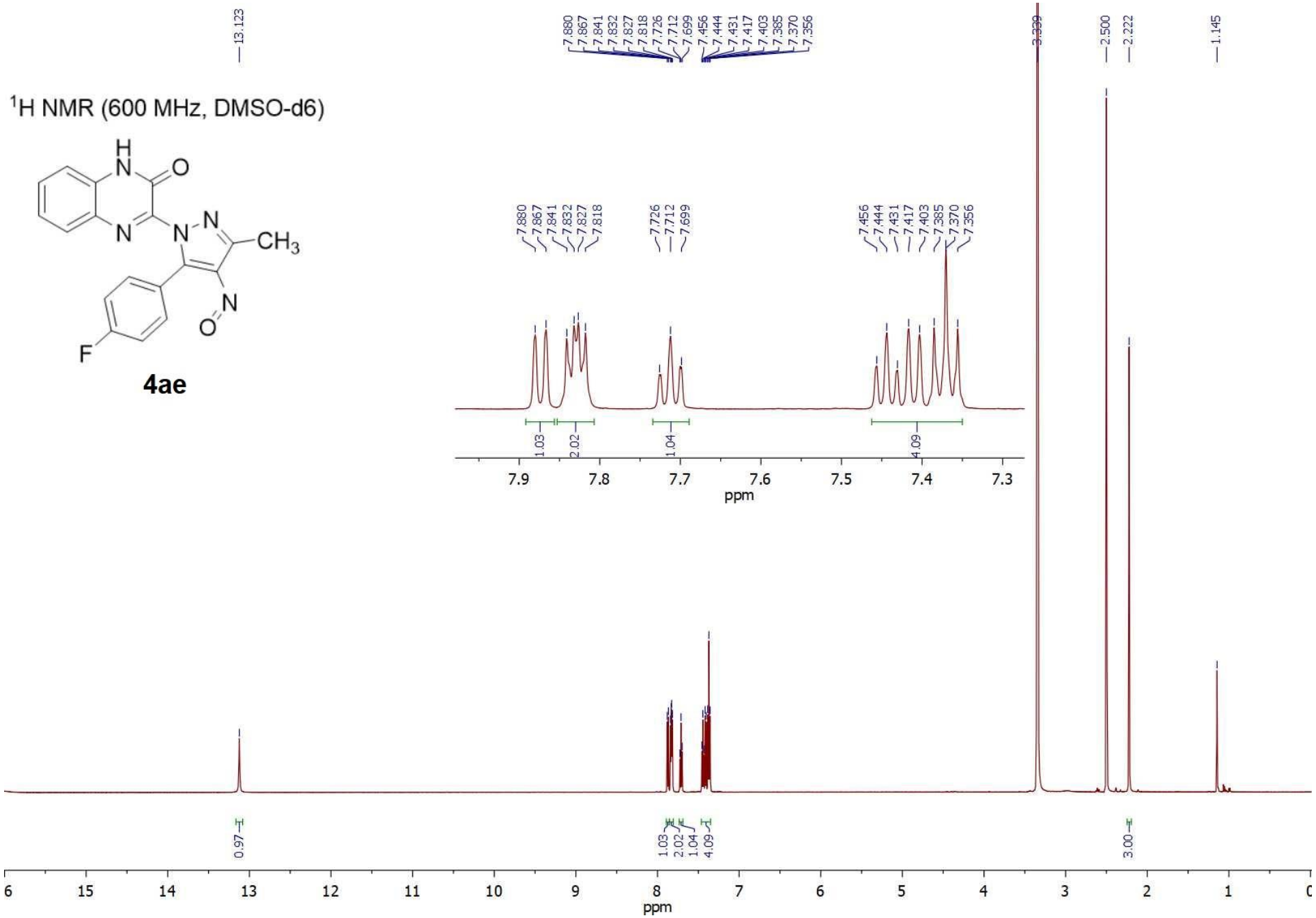
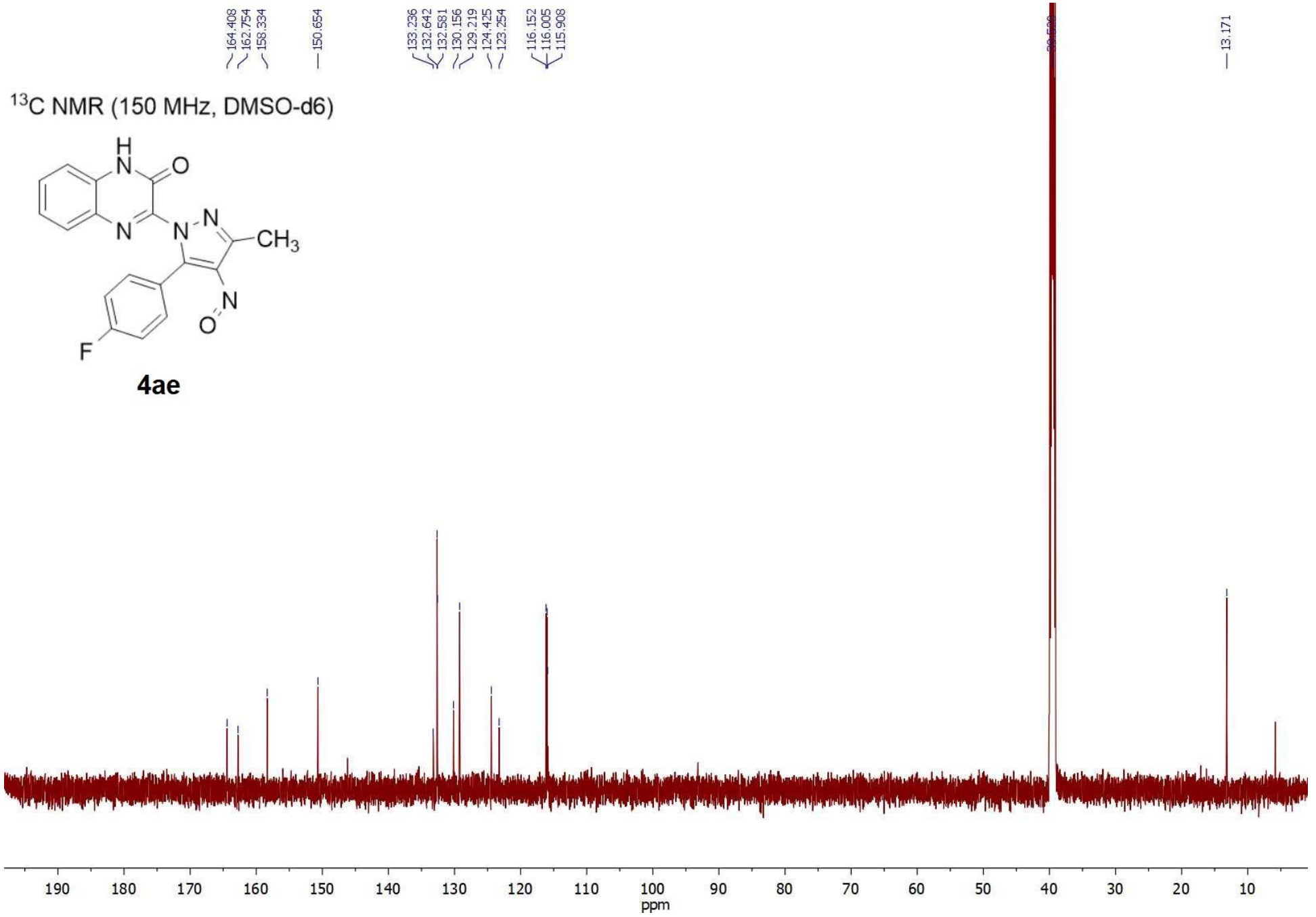
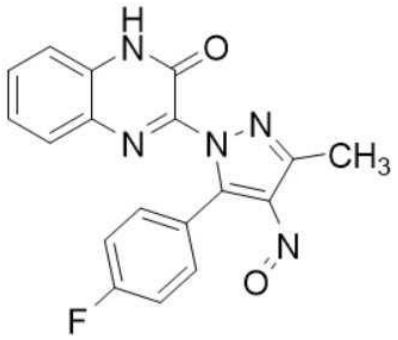
125.784
124.750
116.105
13.291
H
N
O
N
N
N
CH3
N
O
Cl
4ad
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


^{1}H NMR (600 MHz, DMSO-d6)
4ae
13.123
7.880
7.867
7.841
7.832
7.827
7.818
7.726
7.712
7.699
7.456
7.444
7.431
7.417
7.403
7.385
7.370
7.356
3.339
2.500
2.222
1.145
1.03
2.02
1.04
4.09
0.97
3.00
ppm

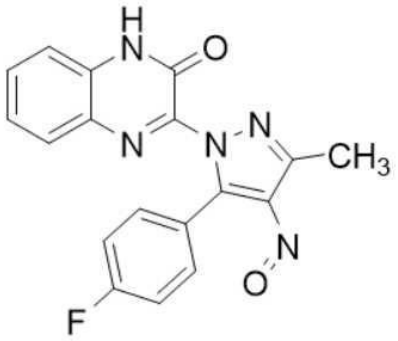

164.408
162.754
158.334
150.654
133.236
132.642
132.581
130.156
129.219
124.425
123.254
116.152
116.005
115.908
13.171
^{13}C NMR (150 MHz, DMSO-d6)
H
N
O
N
N
N
CH$_3$
O
N
F
4ae
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

^{19}F NMR (564 MHz, DMSO-d6)

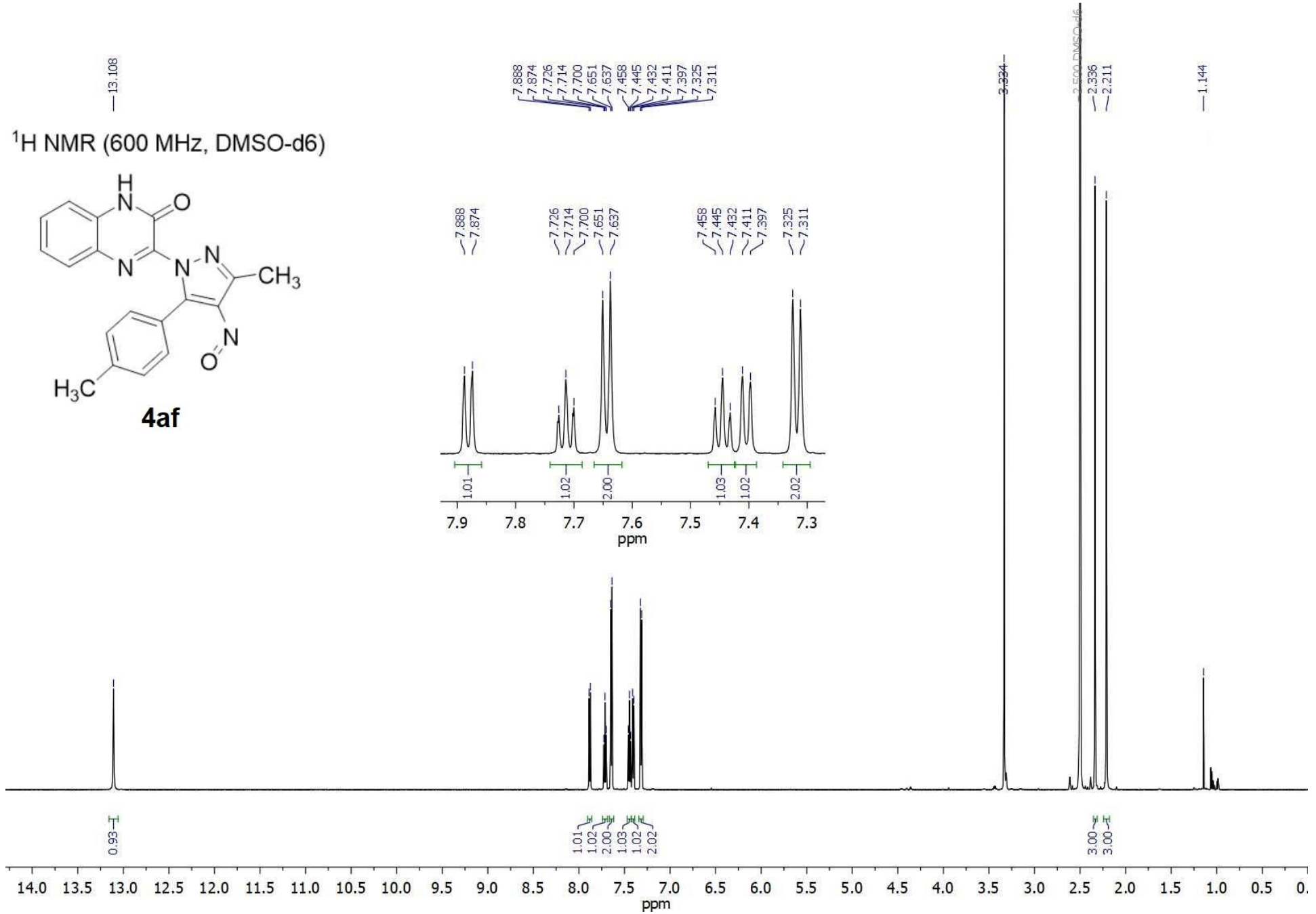


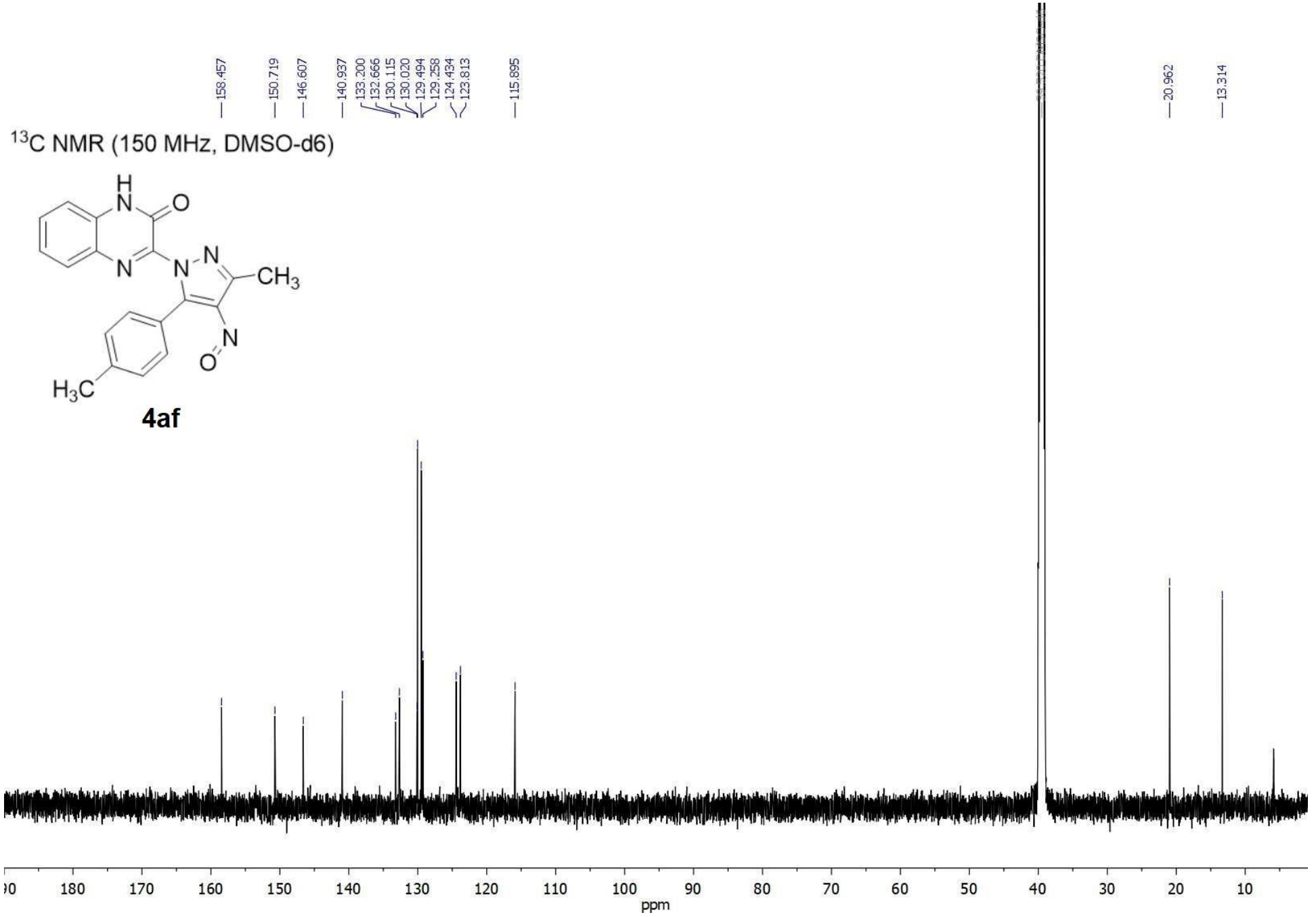
4ae

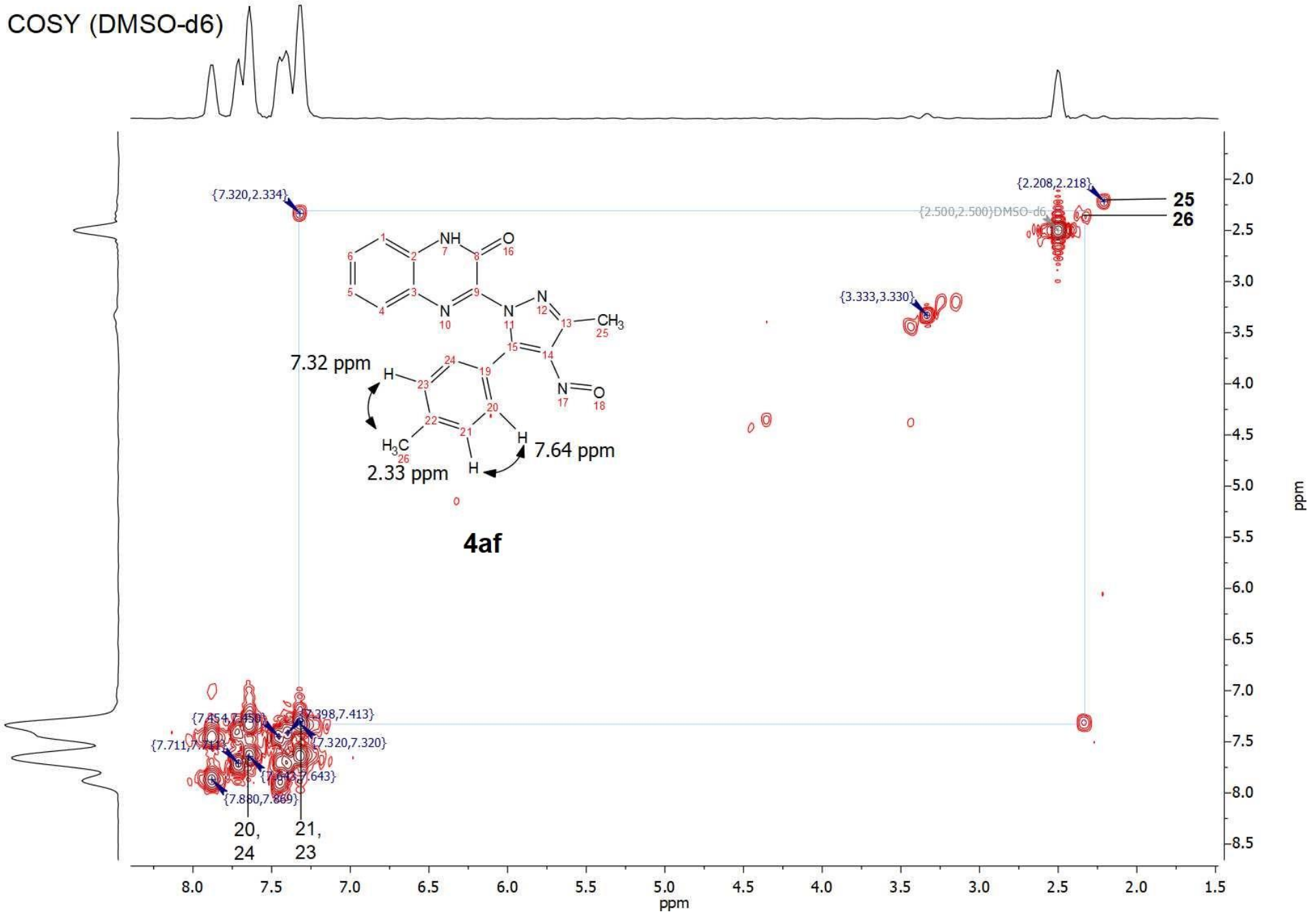
HSQC (DMSO-d6)

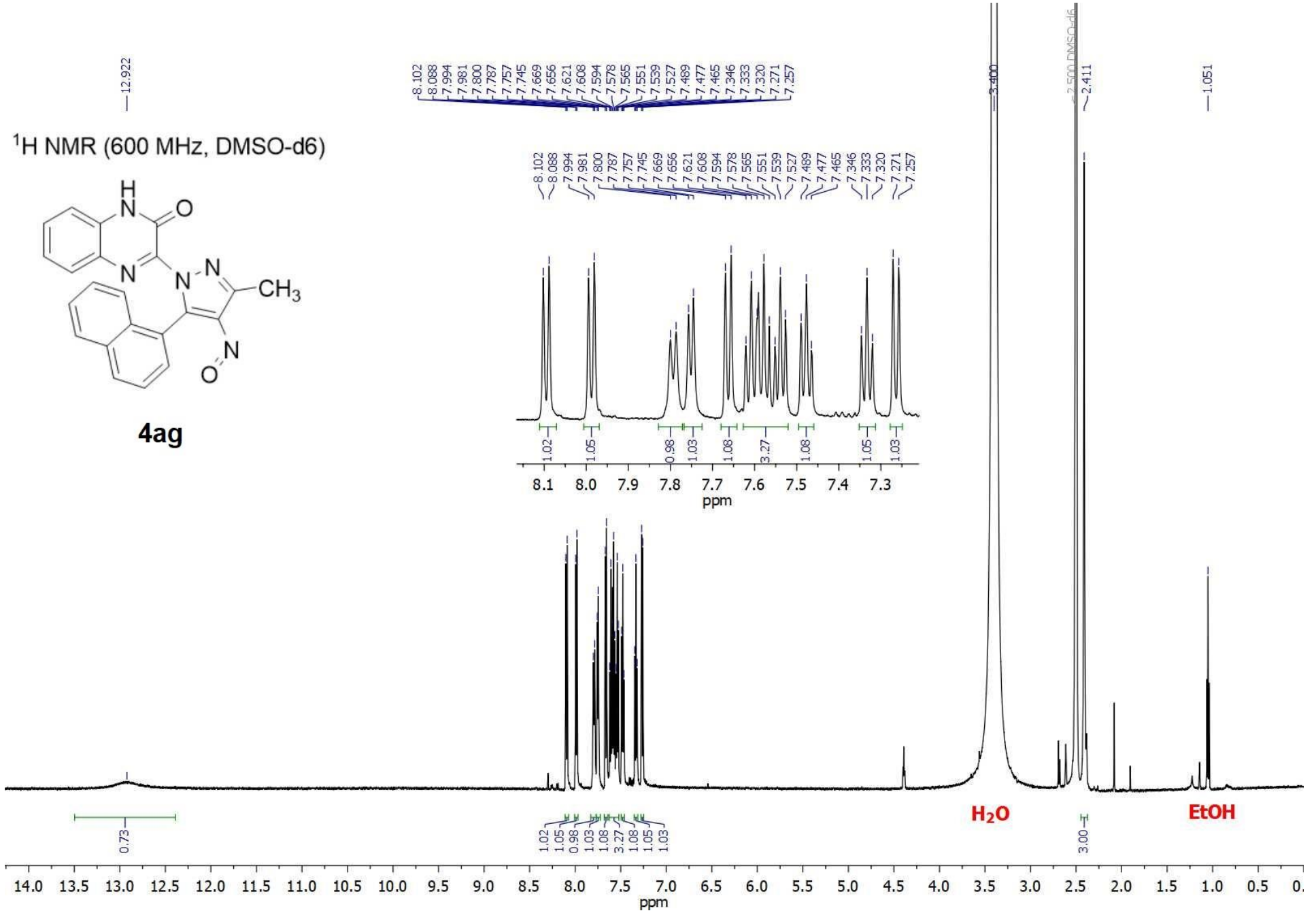


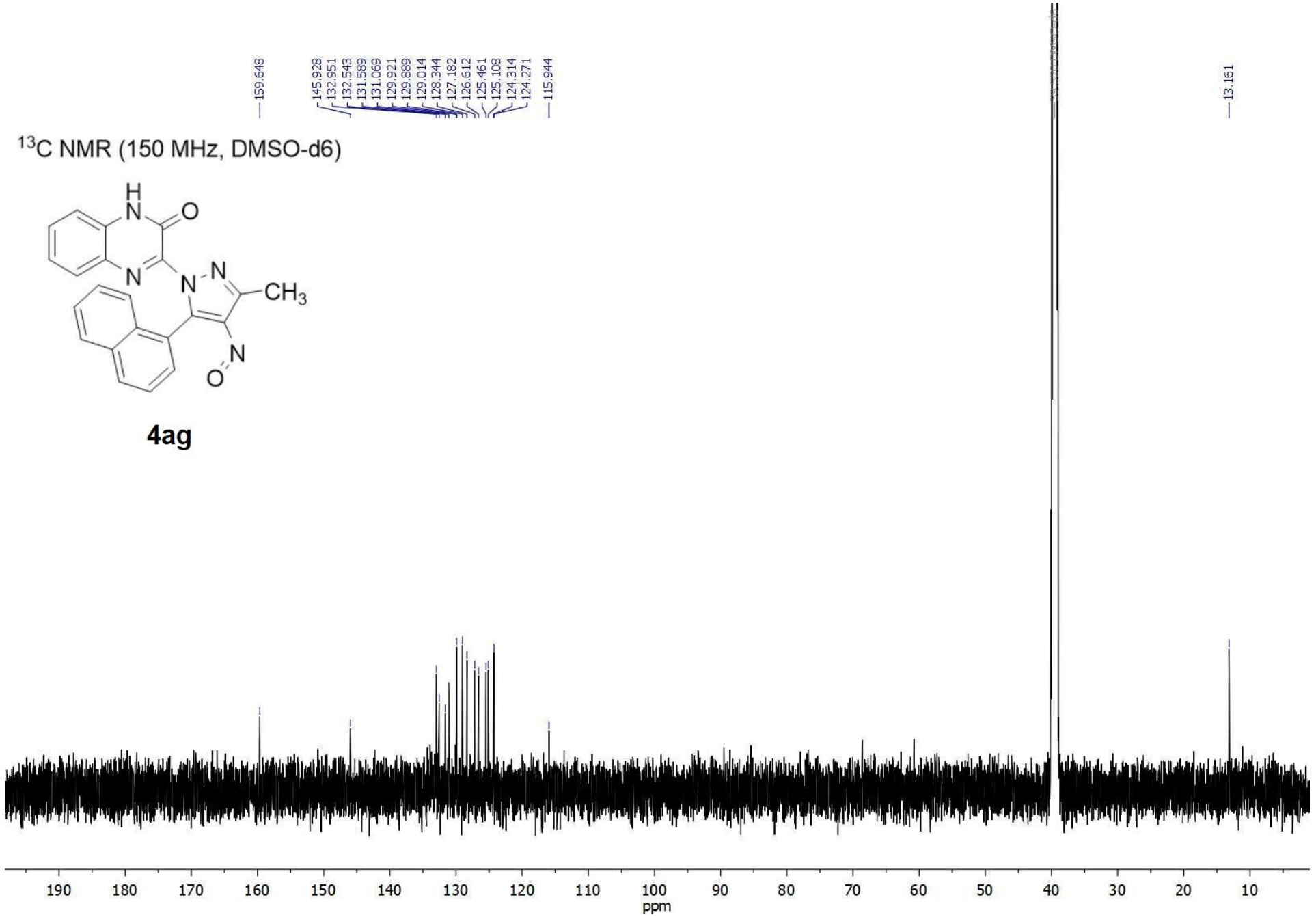
4ae


13.108
7.888
7.874
7.726
7.714
7.700
7.651
7.637
7.458
7.445
7.432
7.411
7.397
7.325
7.311
3.324
2.500 DMSO-d6
2.336
2.211
1.144
1H NMR (600 MHz, DMSO-d6)
4af
1.01
1.02
2.00
1.03
1.02
2.02
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm
0.93
3.00
3.00
14.0
13.5
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
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
ppm

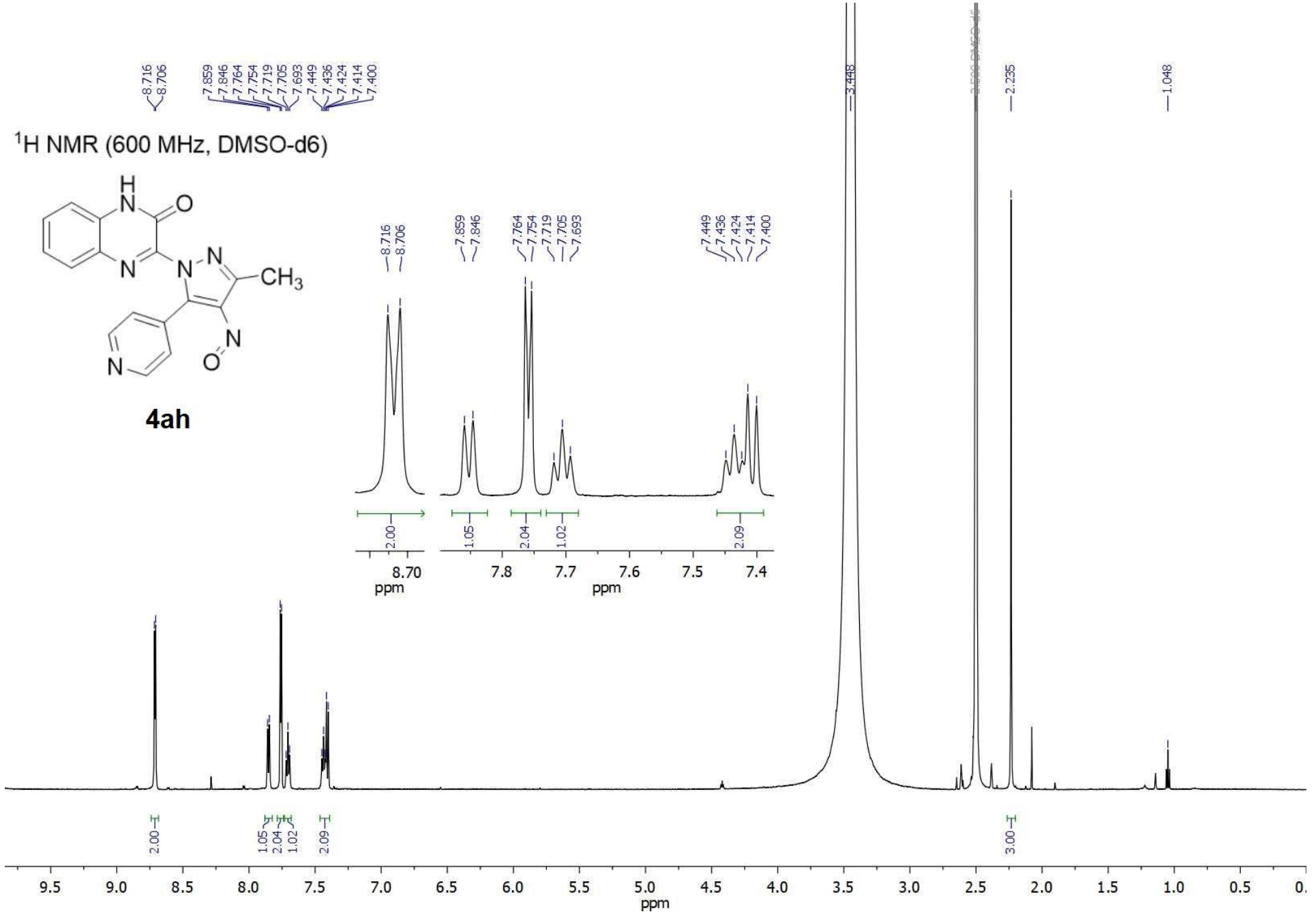

158.457
150.719
146.607
140.937
133.200
132.666
130.115
130.020
129.494
129.258
124.434
123.813
115.895
20.962
13.314
13C NMR (150 MHz, DMSO-d6)
4af
ppm


COSY (DMSO-d6)
{7.320,2.334}
{2.208,2.218}
25
26
{2.500,2.500}DMSO-d6
{3.333,3.330}
7.32 ppm
2.33 ppm
7.64 ppm
4af
{7.454,7.458}
{7.398,7.413}
{7.711,7.714}
{7.320,7.320}
{7.880,7.869}
20, 24
21, 23
ppm

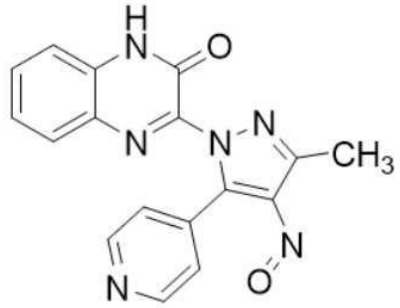

1H NMR (600 MHz, DMSO-d6)
4ag
H2O
EtOH
ppm


159.648
145.928
132.951
132.543
131.589
131.069
129.921
129.889
129.014
128.344
127.182
126.612
125.461
125.108
124.314
124.271
115.944
13.161
^{13}C NMR (150 MHz, DMSO-d6)
H
N
O
N
N
N
CH$_3$
N
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

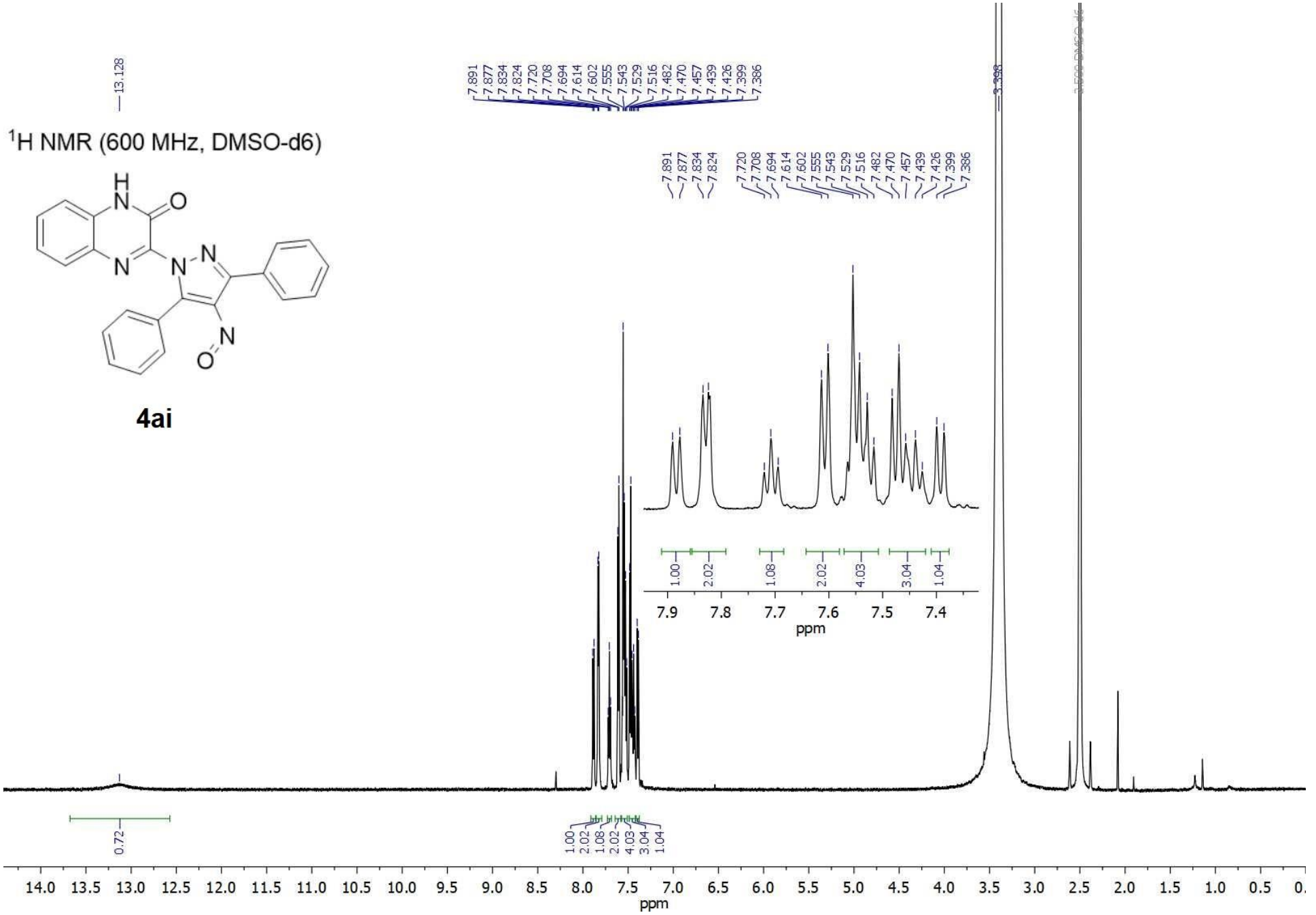
4ag


8.716
8.706
7.859
7.846
7.764
7.754
7.719
7.705
7.693
7.449
7.436
7.424
7.414
7.400
3.448
2.235
1.048
^{1}H NMR (600 MHz, DMSO-d6)
4ah
2.00
1.05
2.04
1.02
2.09
3.00
ppm

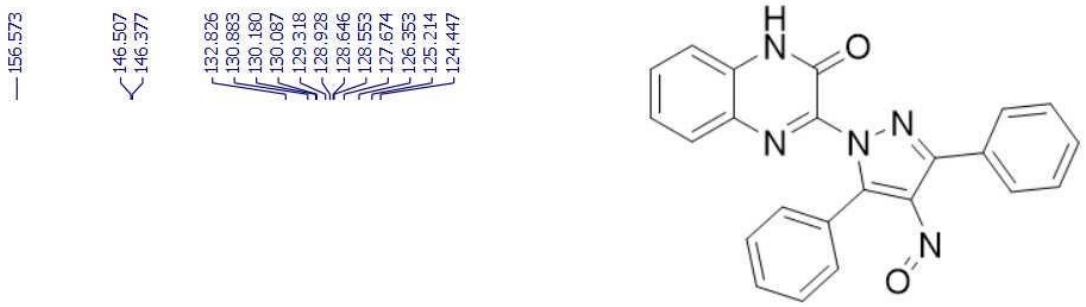
^{13}C NMR (150 MHz, DMSO-d6)



4ah

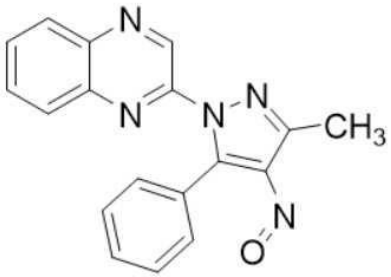

13.128
^{1}H NMR (600 MHz, DMSO-d6)
4ai
7.891
7.877
7.834
7.824
7.720
7.708
7.694
7.614
7.602
7.555
7.543
7.529
7.516
7.482
7.470
7.457
7.439
7.426
7.399
7.386
3.398
2.500
1.00
2.02
1.08
2.02
4.03
3.04
1.04
0.72
ppm

^{13}C NMR (150 MHz, DMSO-d6)

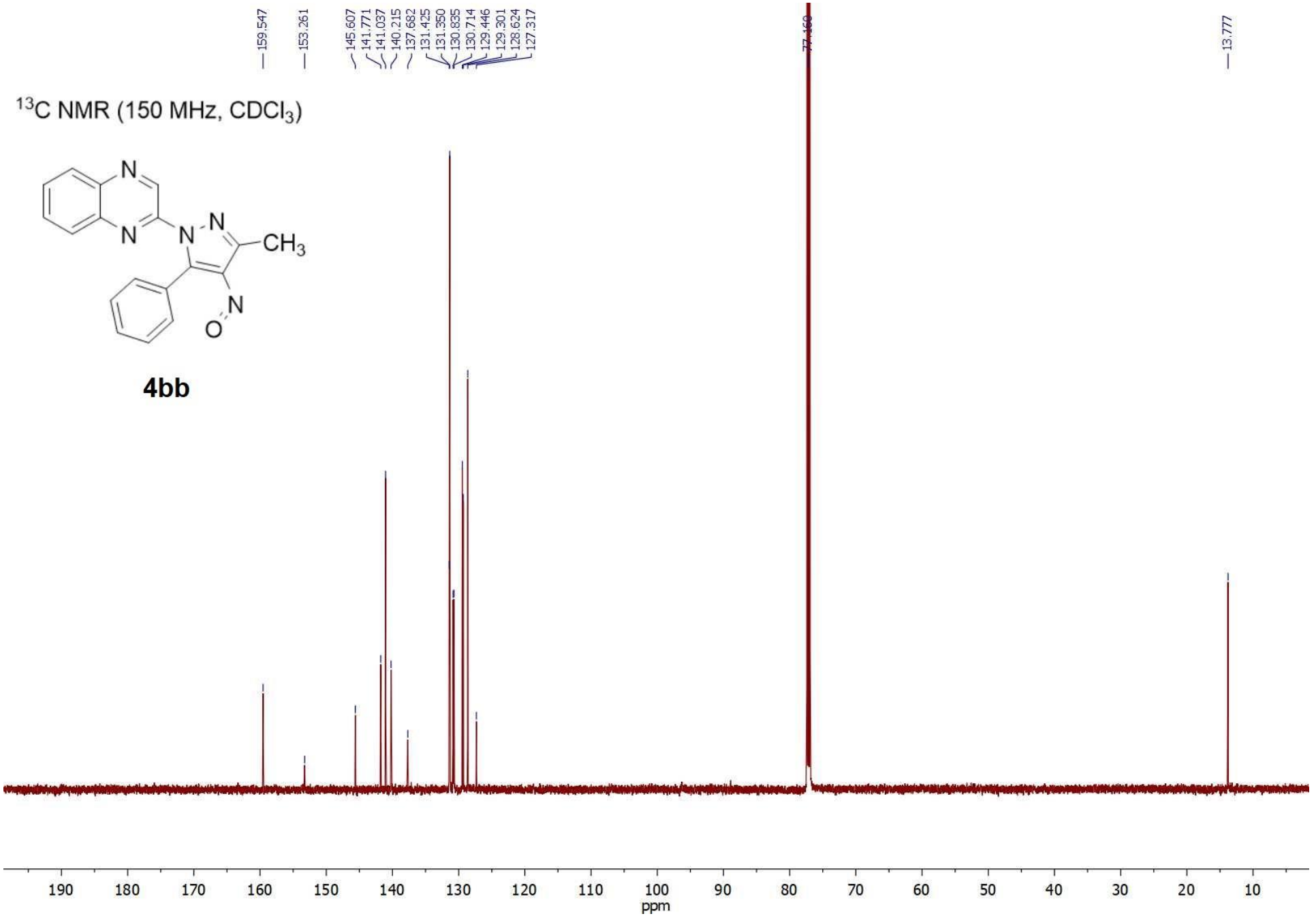


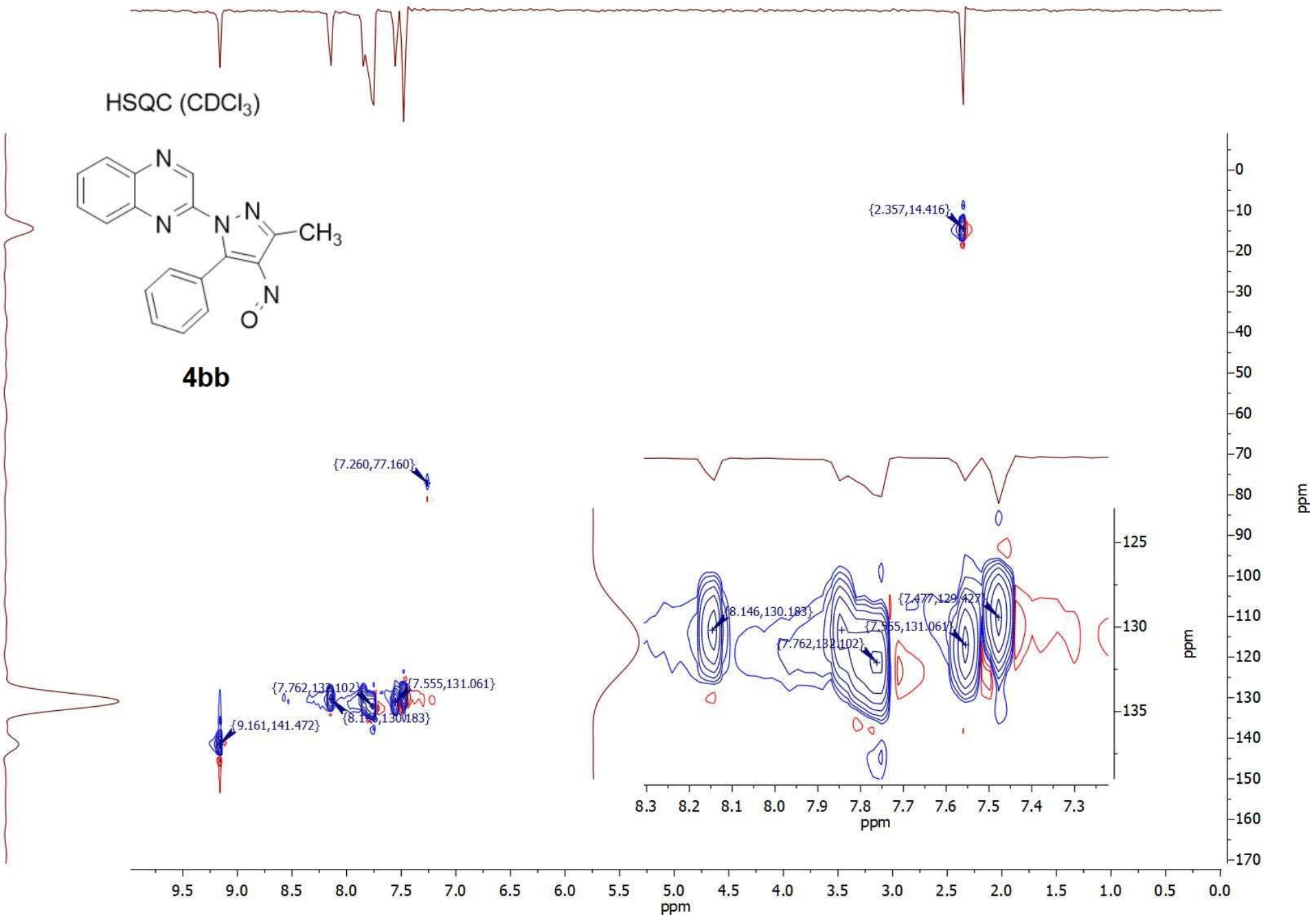
4ai

^{1}H NMR (600 MHz, $CDCl_3$)

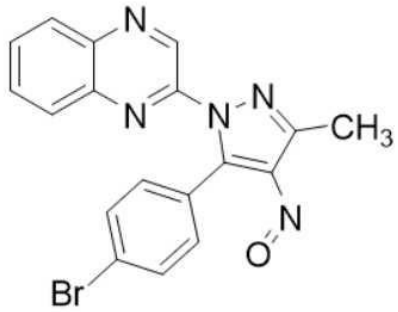


4bb

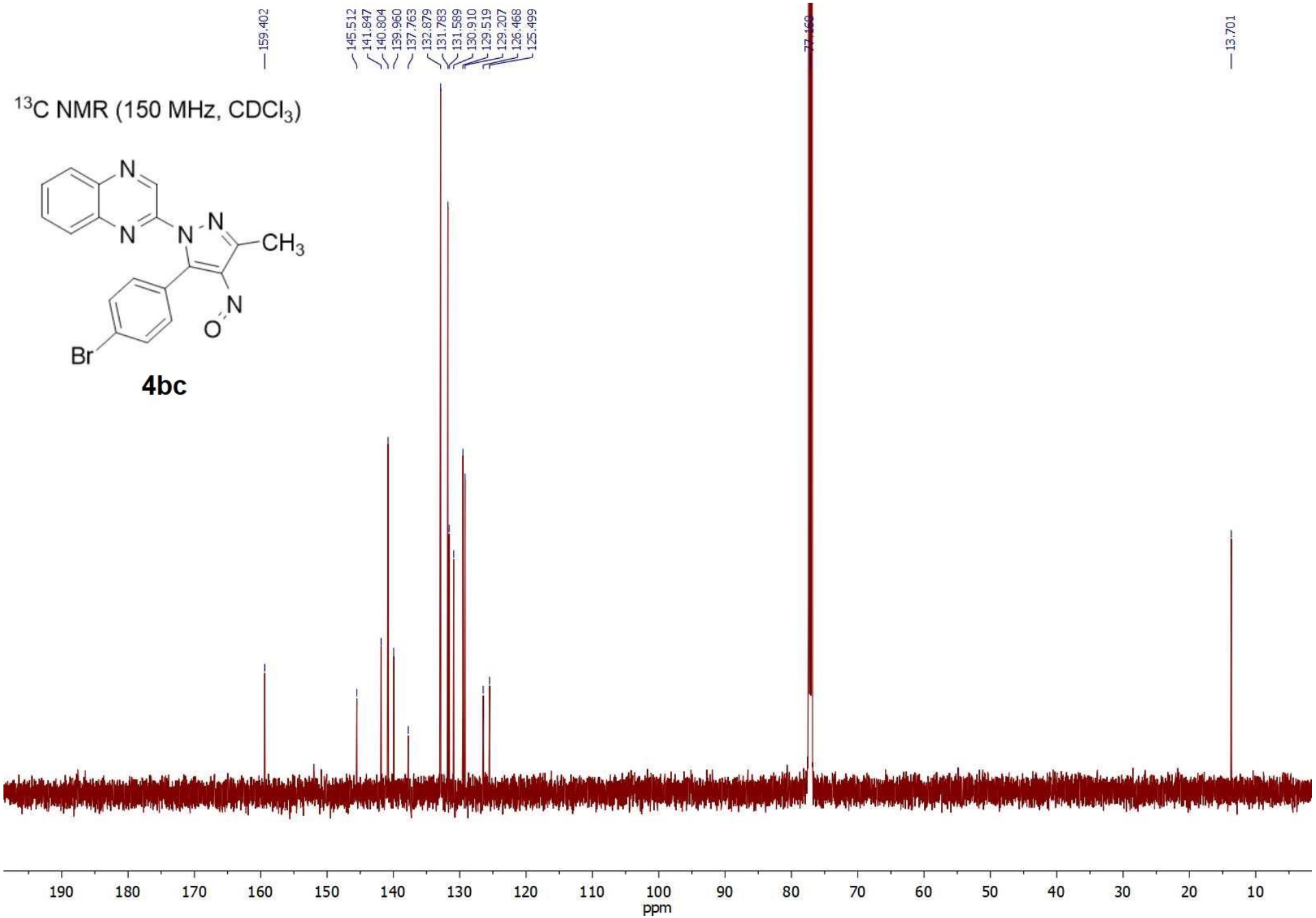

159.547
153.261
145.607
141.771
141.037
140.215
137.682
131.425
131.350
130.835
130.714
129.446
129.301
128.624
127.317
77.160
13.777
^{13}C NMR (150 MHz, $CDCl_3$)
N
N
N
N
CH_3
N
O
4bb
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


HSQC ($CDCl_3$)
4bb
{2.357,14.416}
{7.260,77.160}
{9.161,141.472}
{7.762,132.102}
{7.555,131.061}
{8.146,130.183}
{7.477,129.427}
ppm
ppm

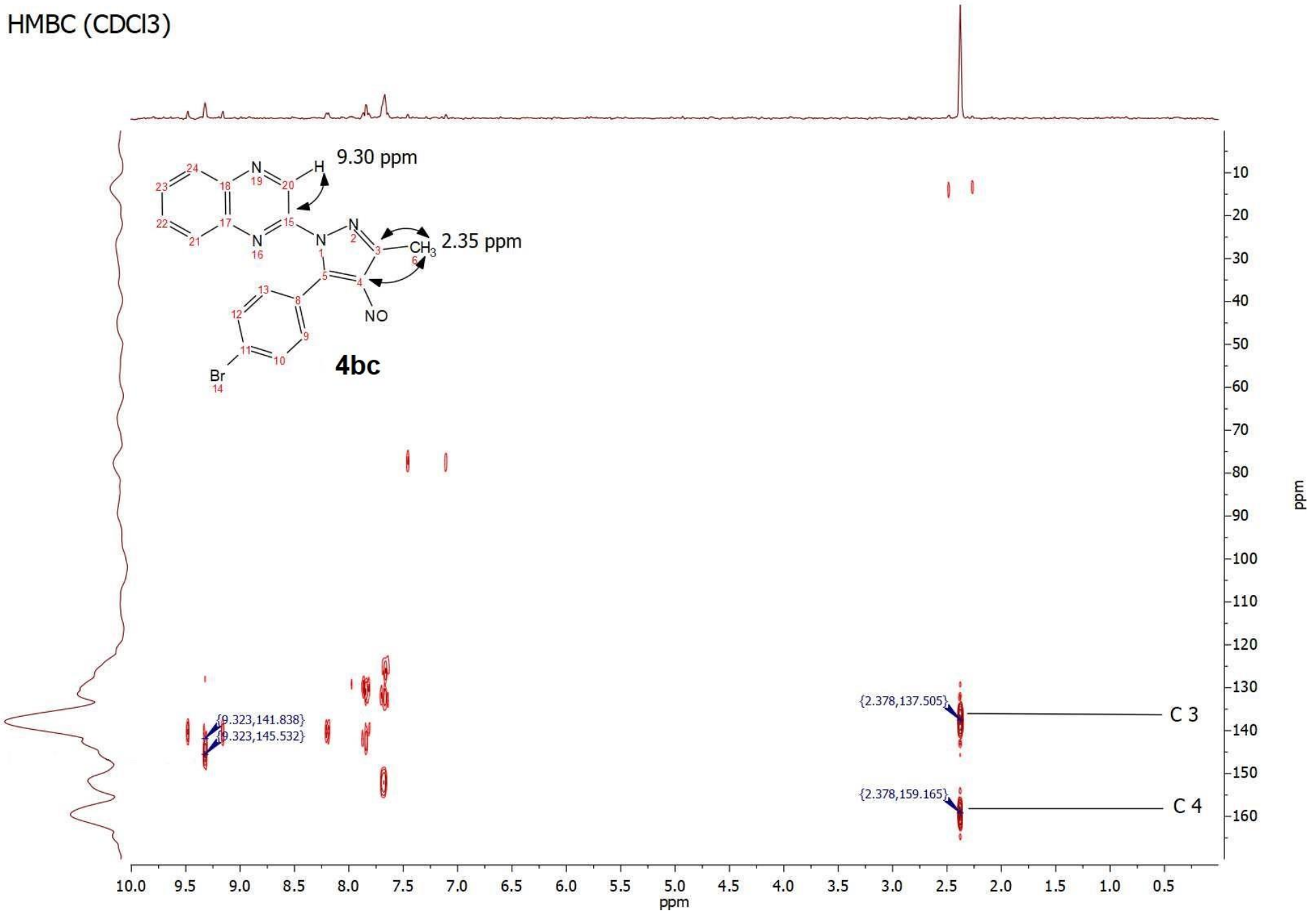
^{1}H NMR (600 MHz, $CDCl_3$)

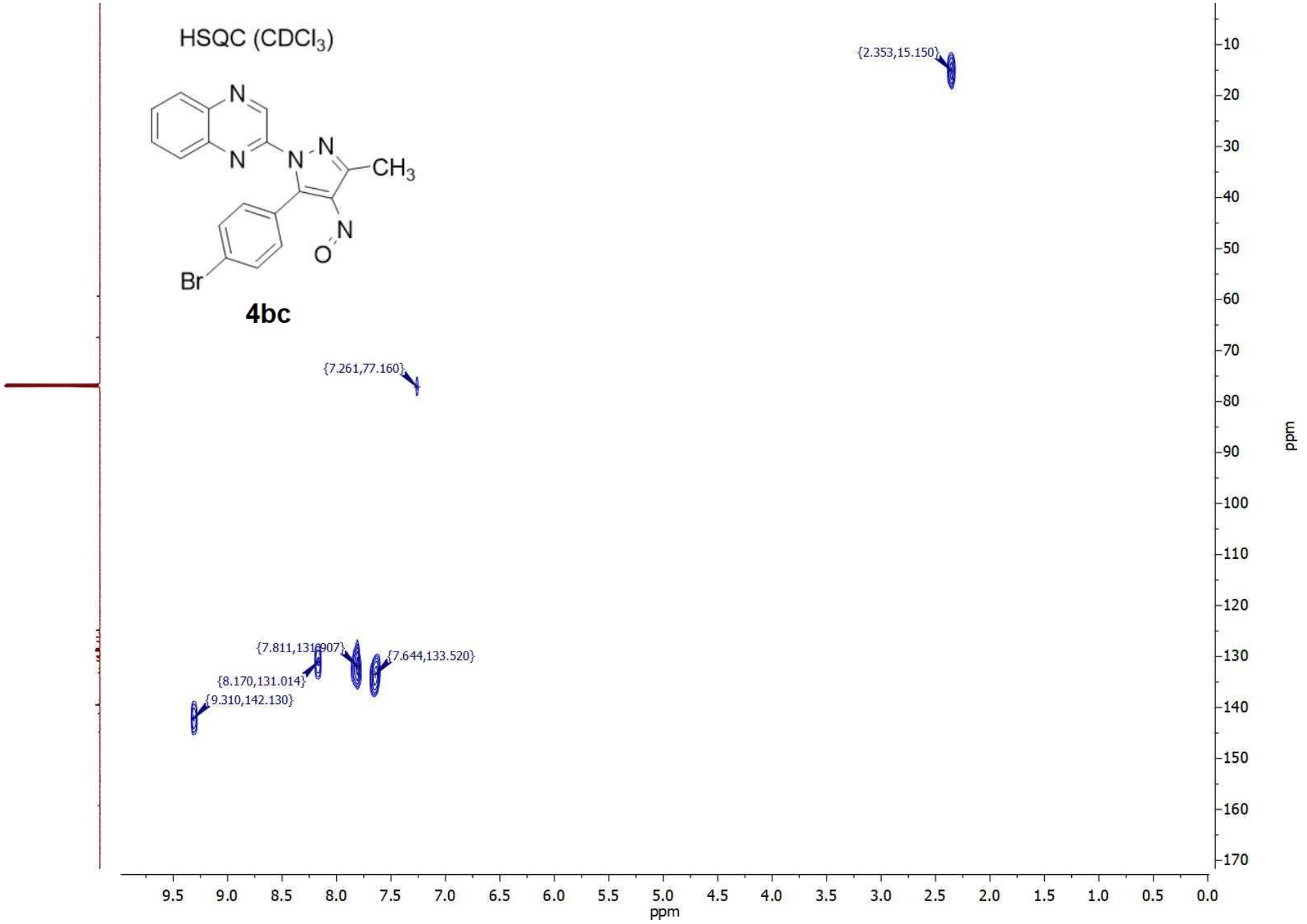


4bc

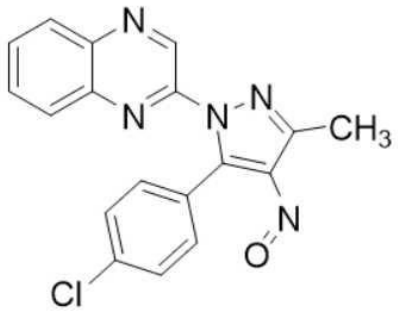

159.402
145.512
141.847
140.804
139.960
137.763
132.879
131.783
131.589
130.910
129.519
129.207
126.468
125.499
77.160
13.701
^{13}C NMR (150 MHz, $CDCl_3$)
N
N
N
N
CH_3
O
N
Br
4bc
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

HMBC (CDCl3)

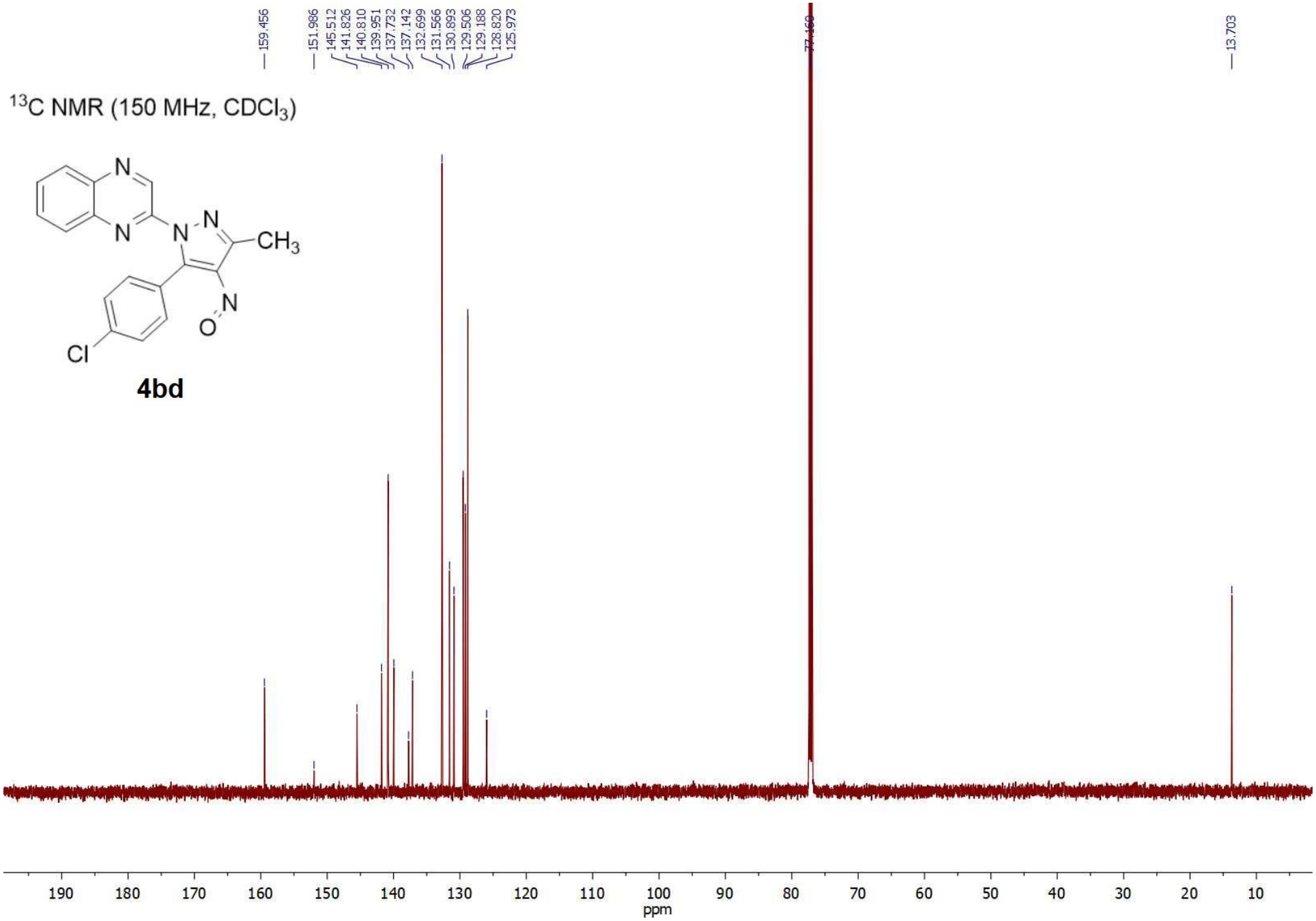

9.30 ppm
2.35 ppm
4bc
{9.323,141.838}
{9.323,145.532}
{2.378,137.505}
C 3
{2.378,159.165}
C 4
ppm
ppm

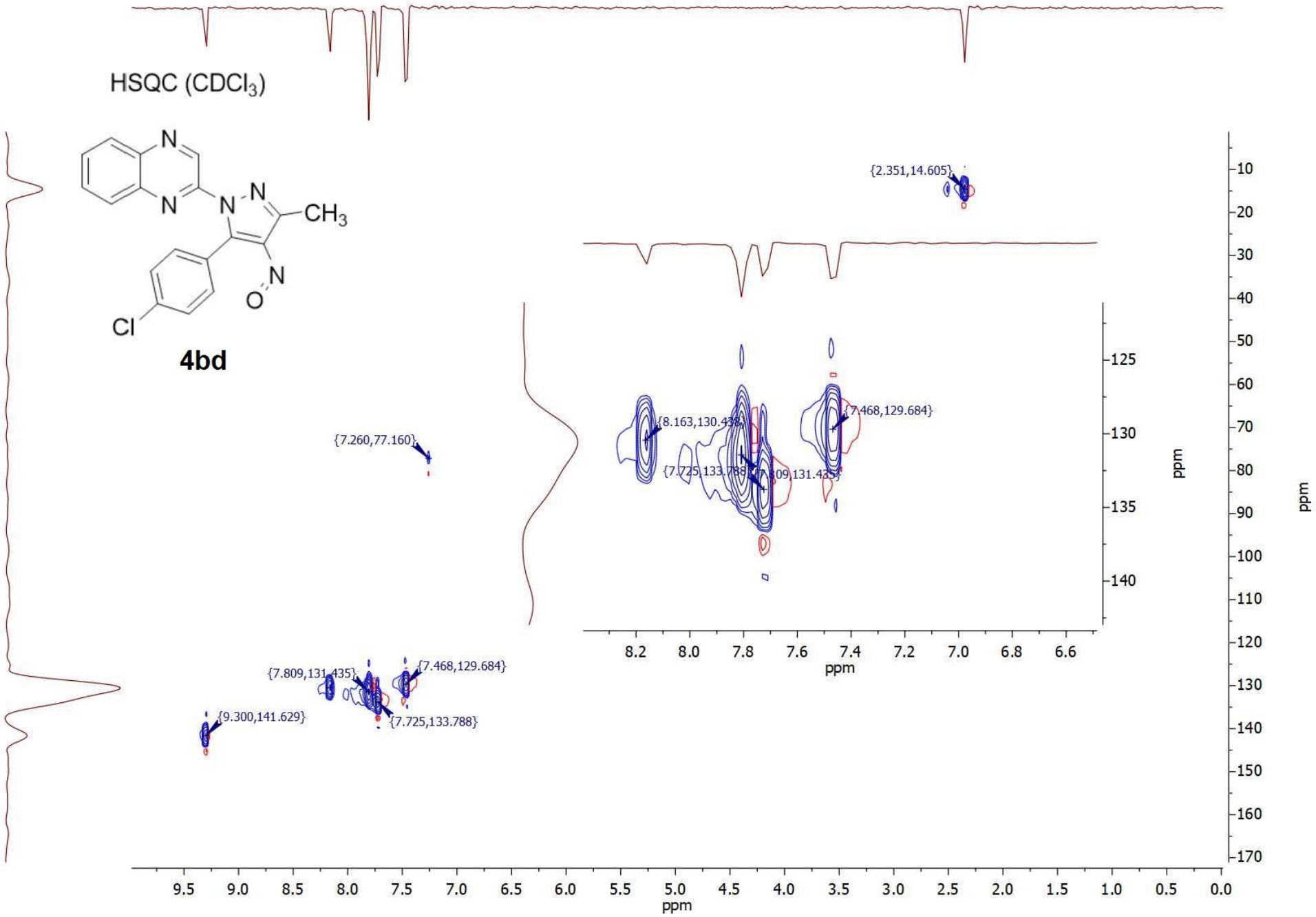

HSQC ($CDCl_3$)
N
N
N
N
CH_3
N
O
Br
4bc
{2.353,15.150}
{7.261,77.160}
{7.811,131.907}
{7.644,133.520}
{8.170,131.014}
{9.310,142.130}
ppm
ppm

^{1}H NMR (600 MHz, $CDCl_3$)

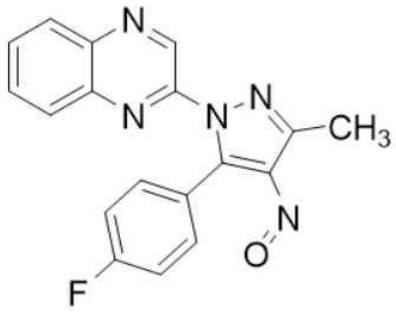


4bd

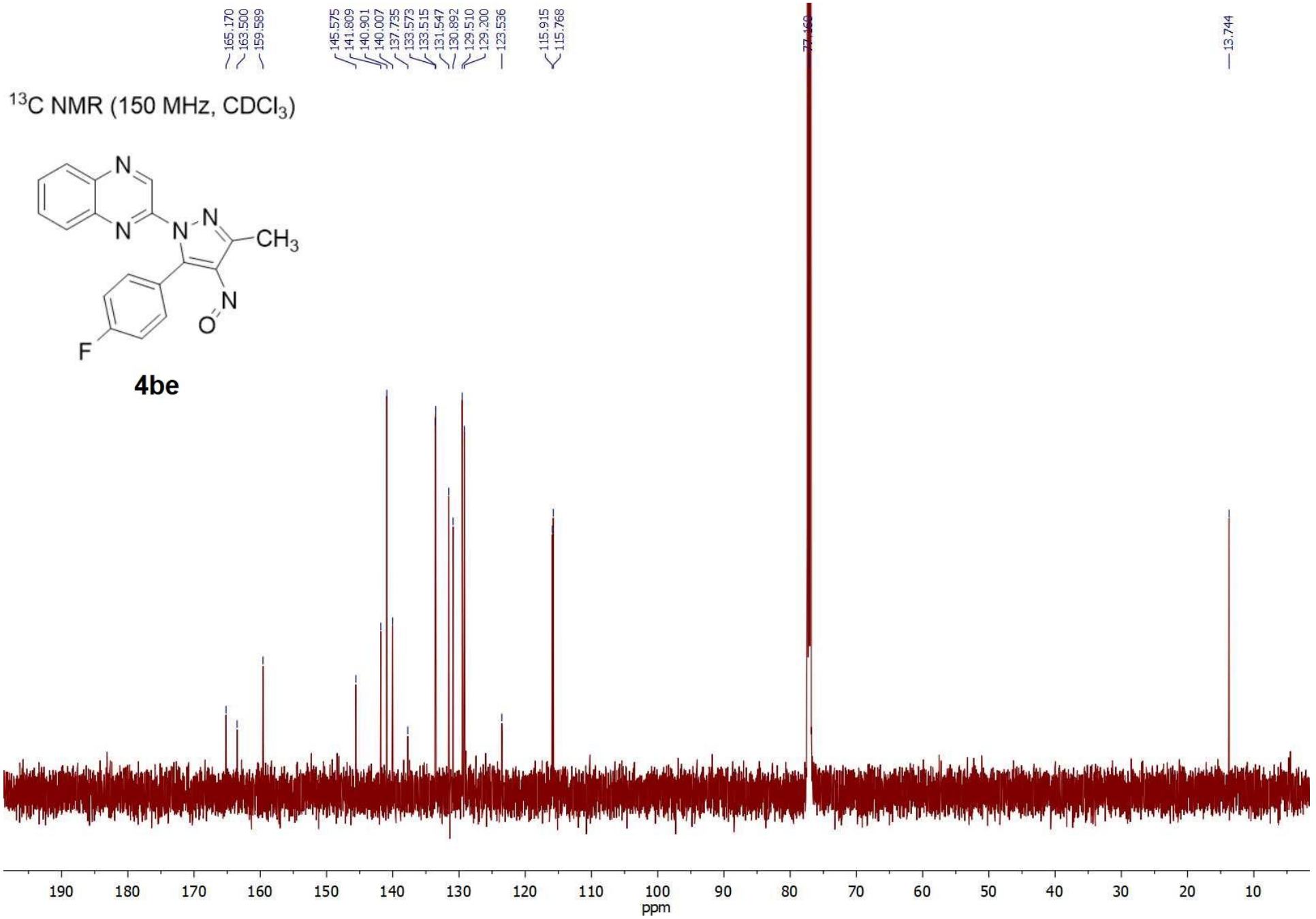

159.456
151.986
145.512
141.826
140.810
139.951
137.732
137.142
132.699
131.566
130.893
129.506
129.188
128.820
125.973
77.160
13.703
13C NMR (150 MHz, CDCl3)
N
N
N
N
CH3
O
N
Cl
4bd
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


HSQC ($CDCl_3$)
4bd
{2.351,14.605}
{7.260,77.160}
{8.163,130.438}
{7.468,129.684}
{7.725,133.788}
{7.809,131.435}
{7.468,129.684}
{9.300,141.629}
{7.725,133.788}
ppm
ppm
ppm
ppm

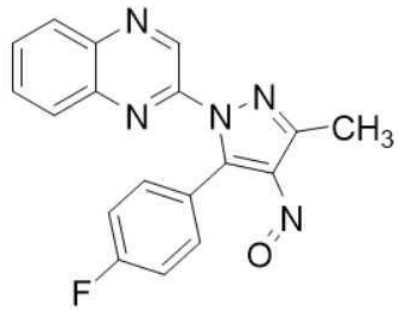
^{1}H NMR (600 MHz, $CDCl_3$)



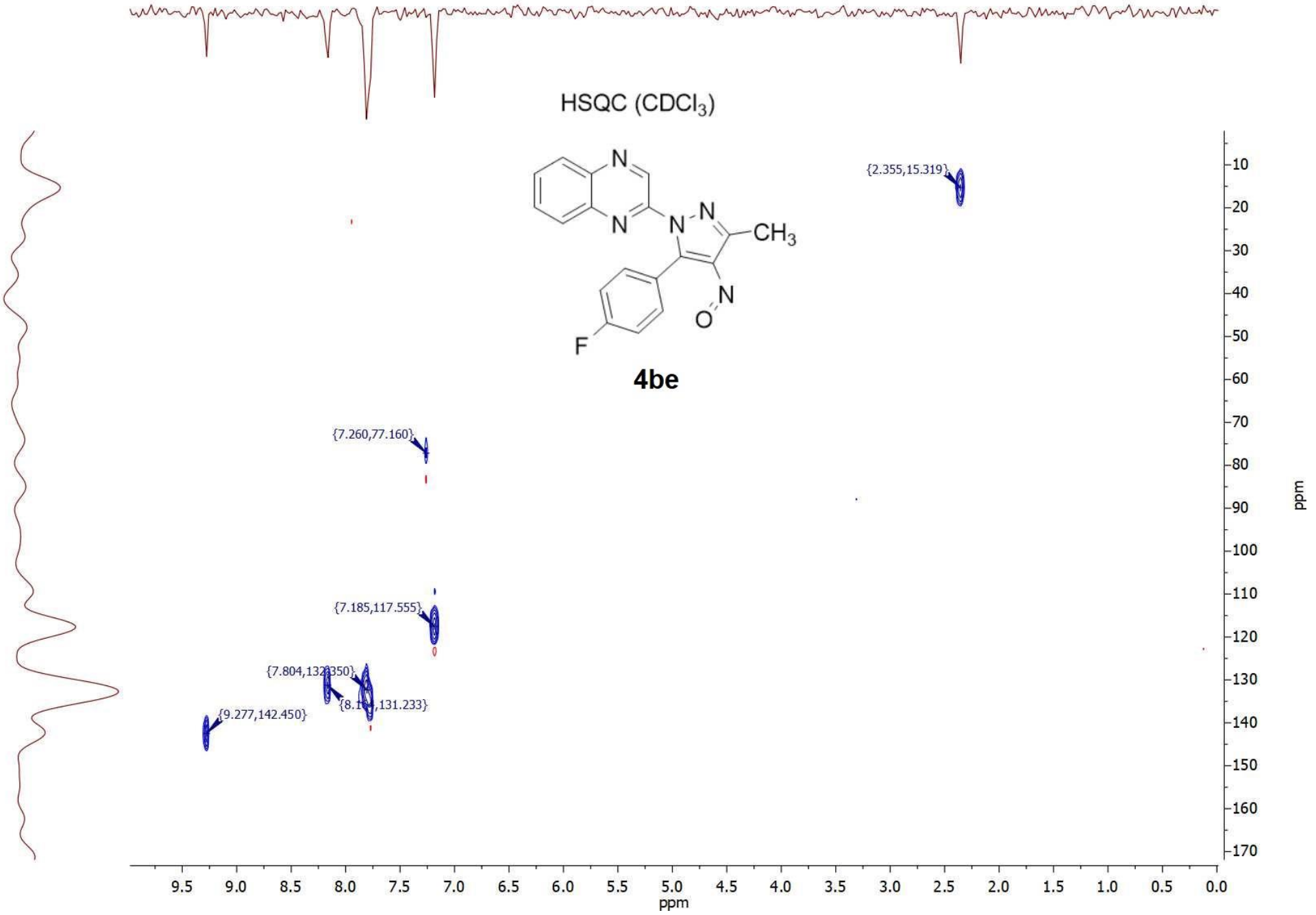
4be


165.170
163.500
159.589
145.575
141.809
140.901
140.007
137.735
133.573
133.515
131.547
130.892
129.510
129.200
123.536
115.915
115.768
77.160
13.744
13C NMR (150 MHz, CDCl3)
N
N
N
N
CH3
N
O
F
4be
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

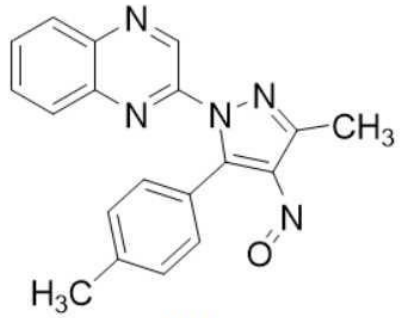
^{19}F NMR (564 MHz, $CDCl_3$)



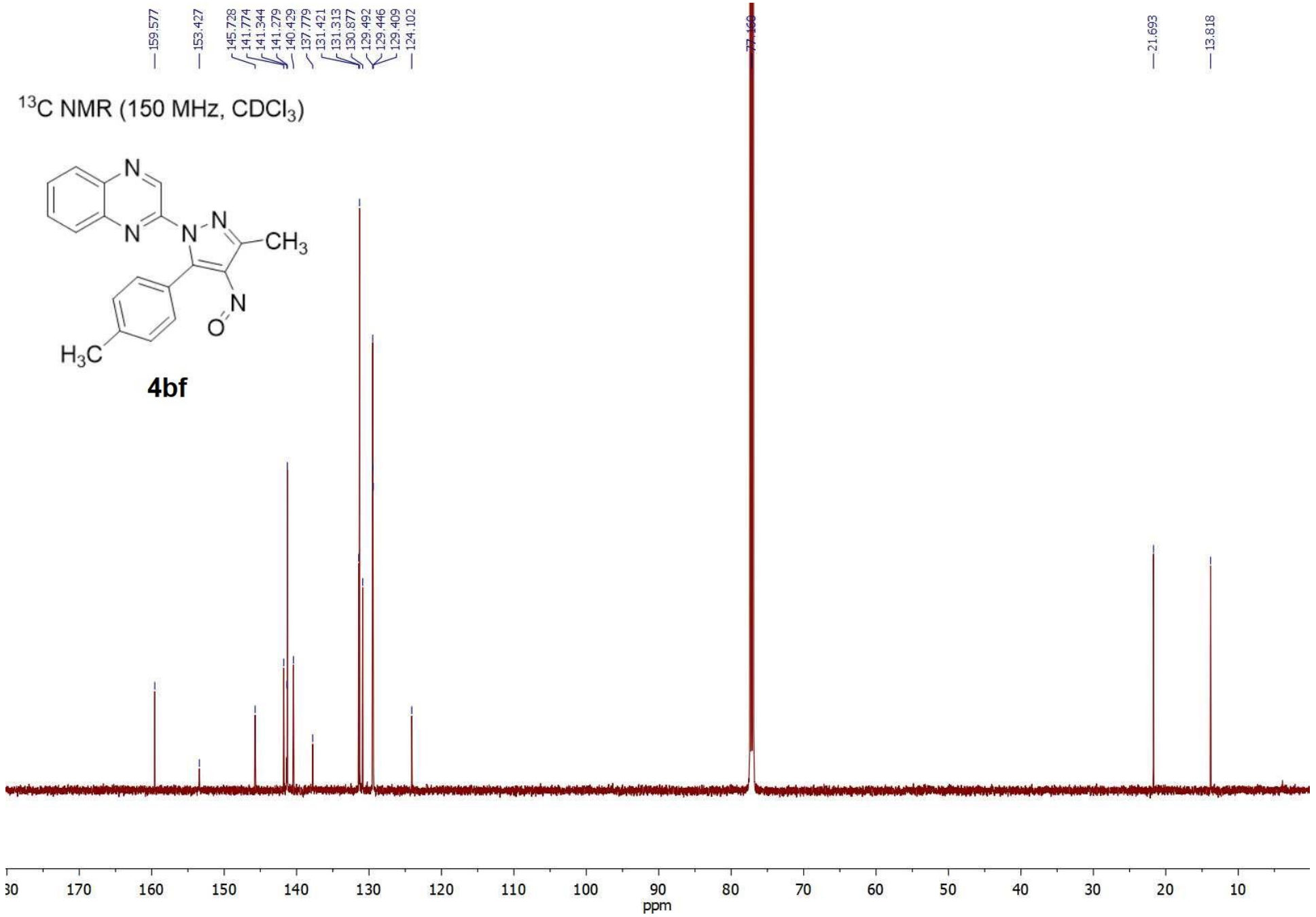
4be

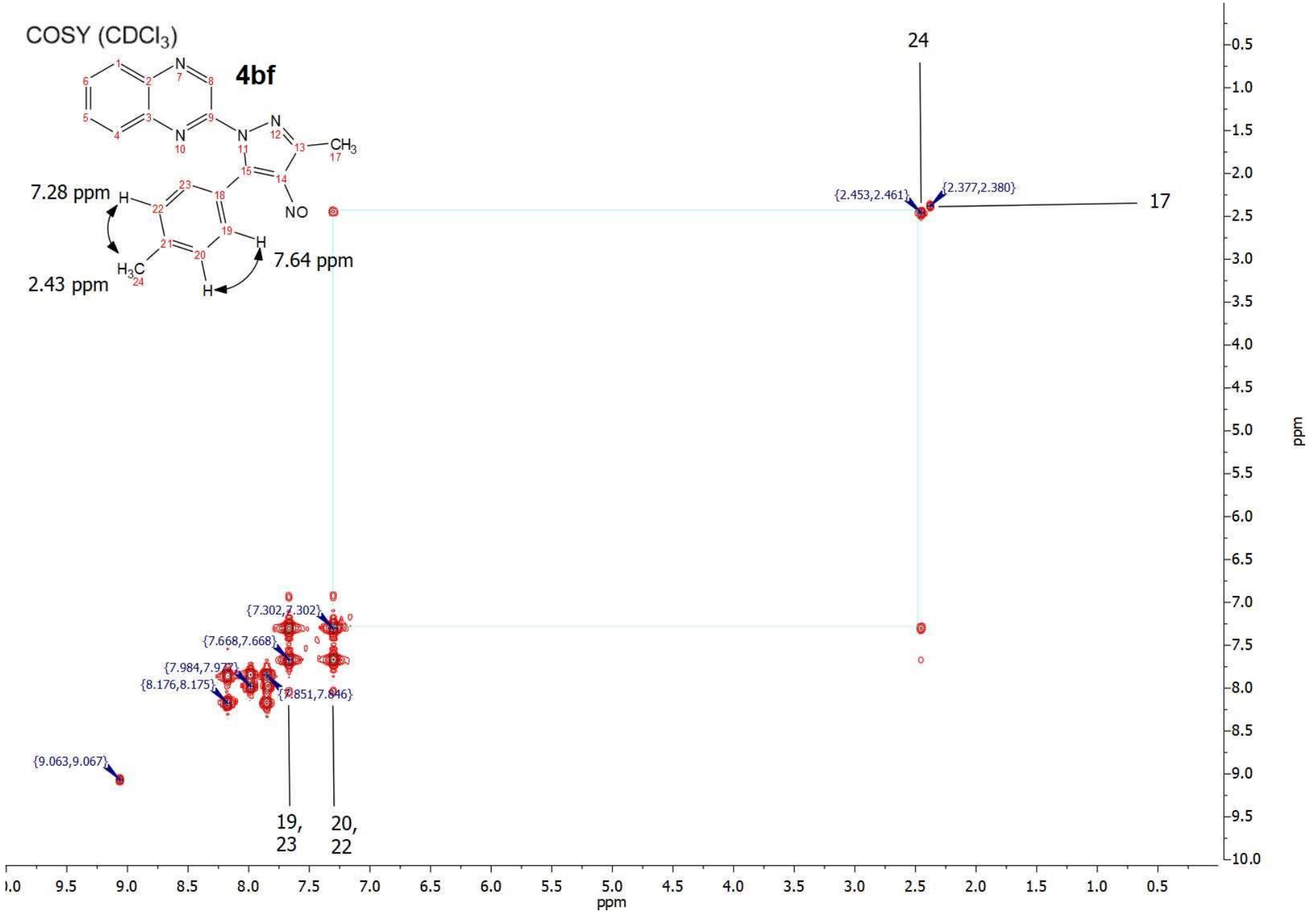

HSQC ($CDCl_3$)
{2.355,15.319}
{7.260,77.160}
{7.185,117.555}
{7.804,132.350}
{8.1[illegible],131.233}
{9.277,142.450}
4be
ppm
ppm

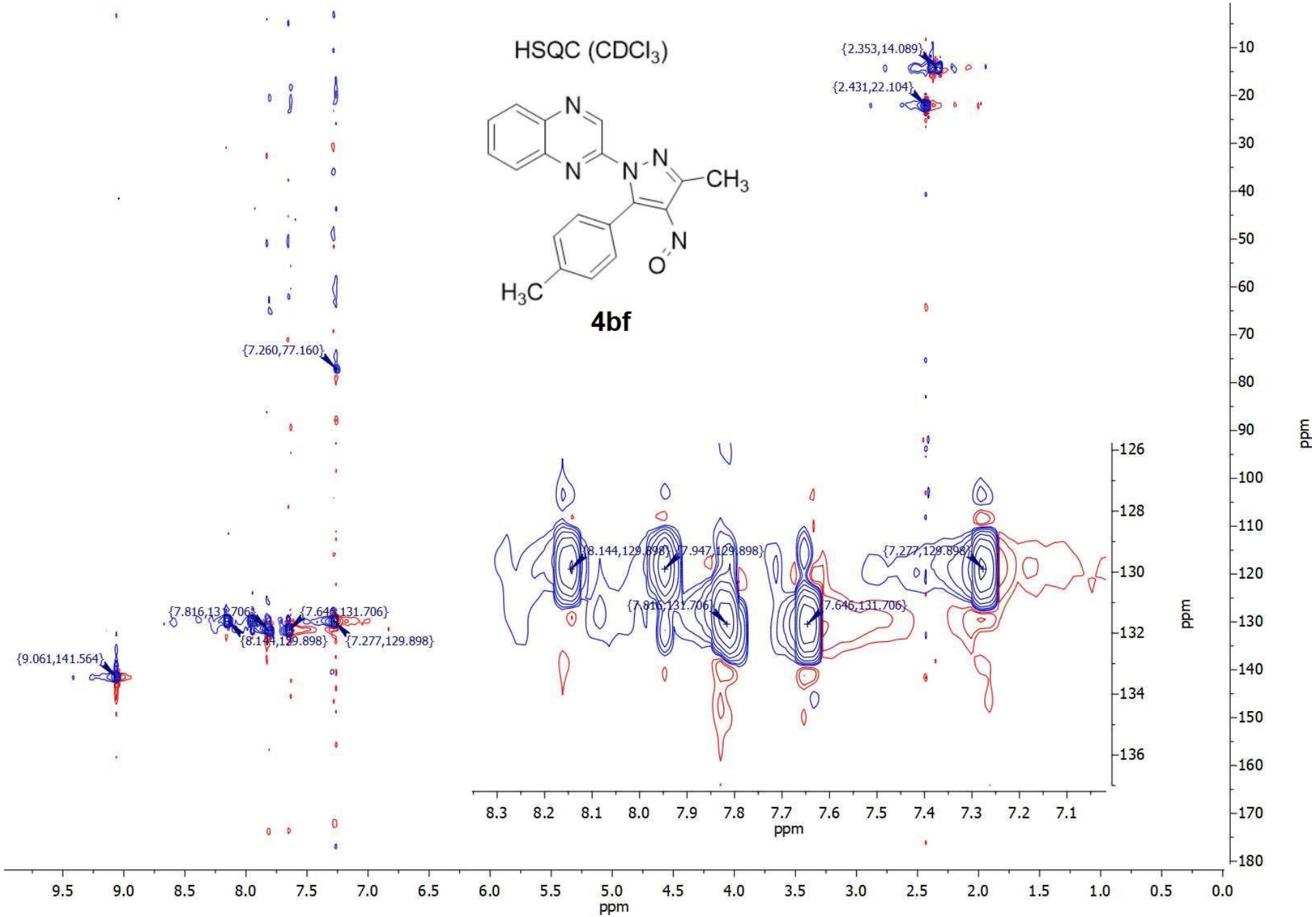
^{1}H NMR (600 MHz, $CDCl_3$)

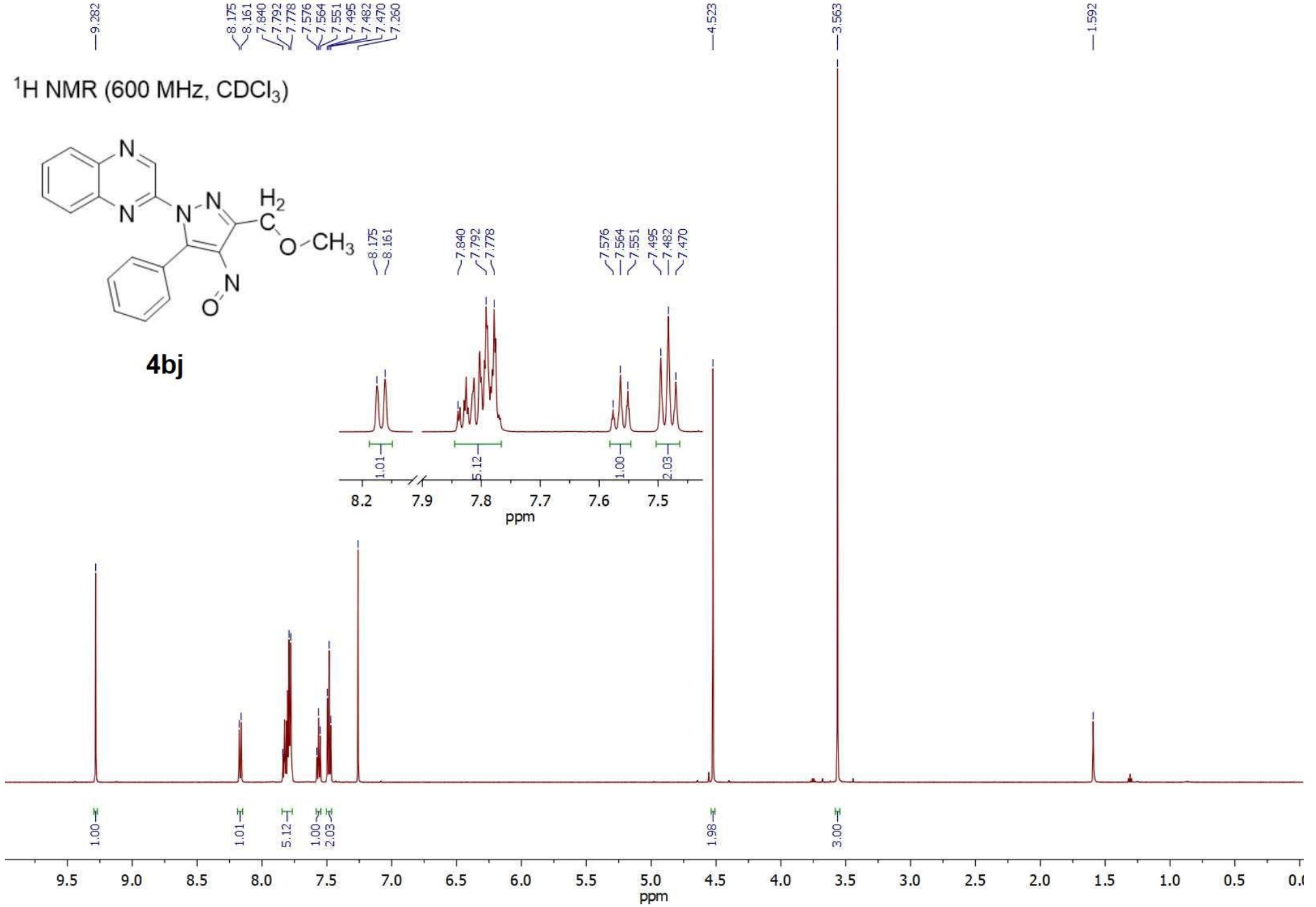


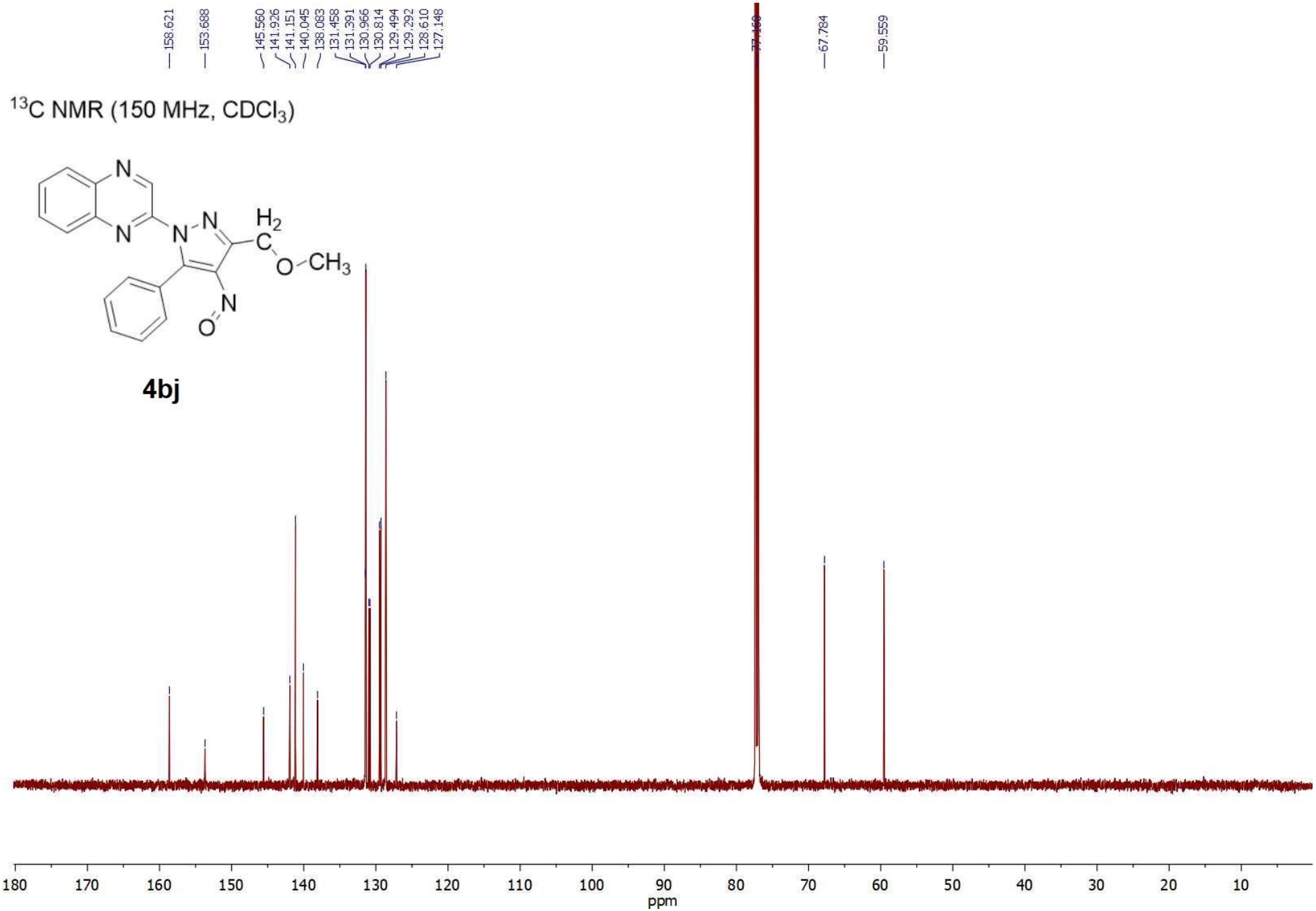
4bf

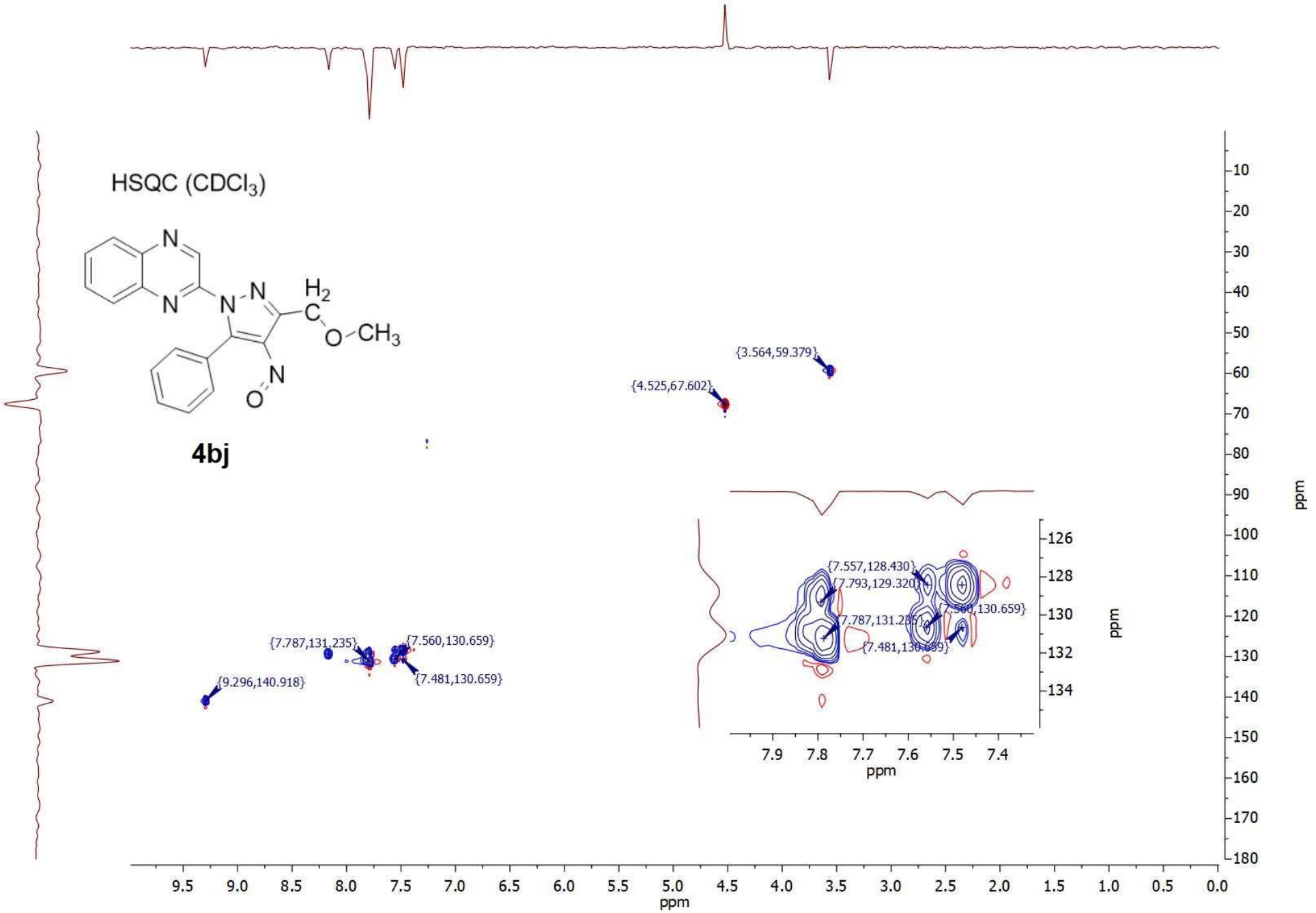

159.577
153.427
145.728
141.774
141.344
141.279
140.429
137.779
131.421
131.313
130.877
129.492
129.446
129.409
124.102
77.160
21.693
13.818
13C NMR (150 MHz, CDCl3)
4bf
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


COSY ($CDCl_3$)
4bf
7.28 ppm
2.43 ppm
7.64 ppm
24
17
{2.453,2.461}
{2.377,2.380}
{7.302,7.302}
{7.668,7.668}
{7.984,7.977}
{8.176,8.175}
{7.851,7.846}
{9.063,9.067}
19, 23
20, 22
ppm

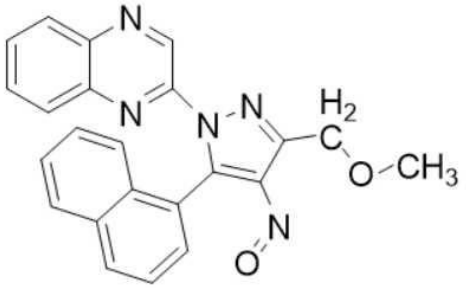

HSQC ($CDCl_3$)
4bf
{2.353,14.089}
{2.431,22.104}
{7.260,77.160}
{9.061,141.564}
{7.816,131.706}
{7.646,131.706}
{8.144,129.898}
{7.277,129.898}
{7.947,129.898}
ppm


9.282
8.175
8.161
7.840
7.792
7.778
7.576
7.564
7.551
7.495
7.482
7.470
7.260
4.523
3.563
1.592
1H NMR (600 MHz, CDCl3)
4bj
1.00
1.01
5.12
1.00
2.03
1.98
3.00
ppm

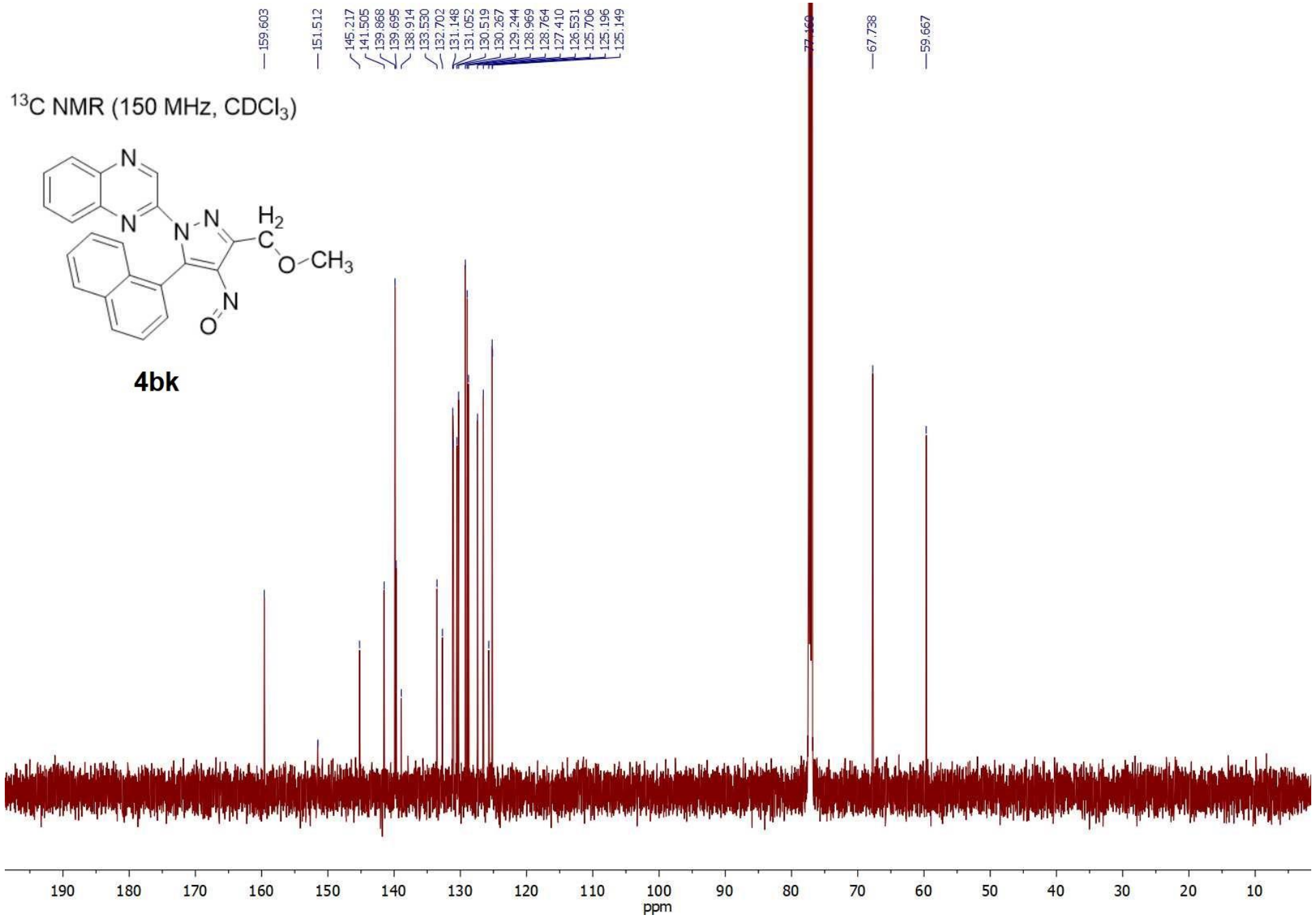

158.621
153.688
145.560
141.926
141.151
140.045
138.083
131.458
131.391
130.966
130.814
129.494
129.292
128.610
127.148
77.160
67.784
59.559
13C NMR (150 MHz, CDCl3)
4bj
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

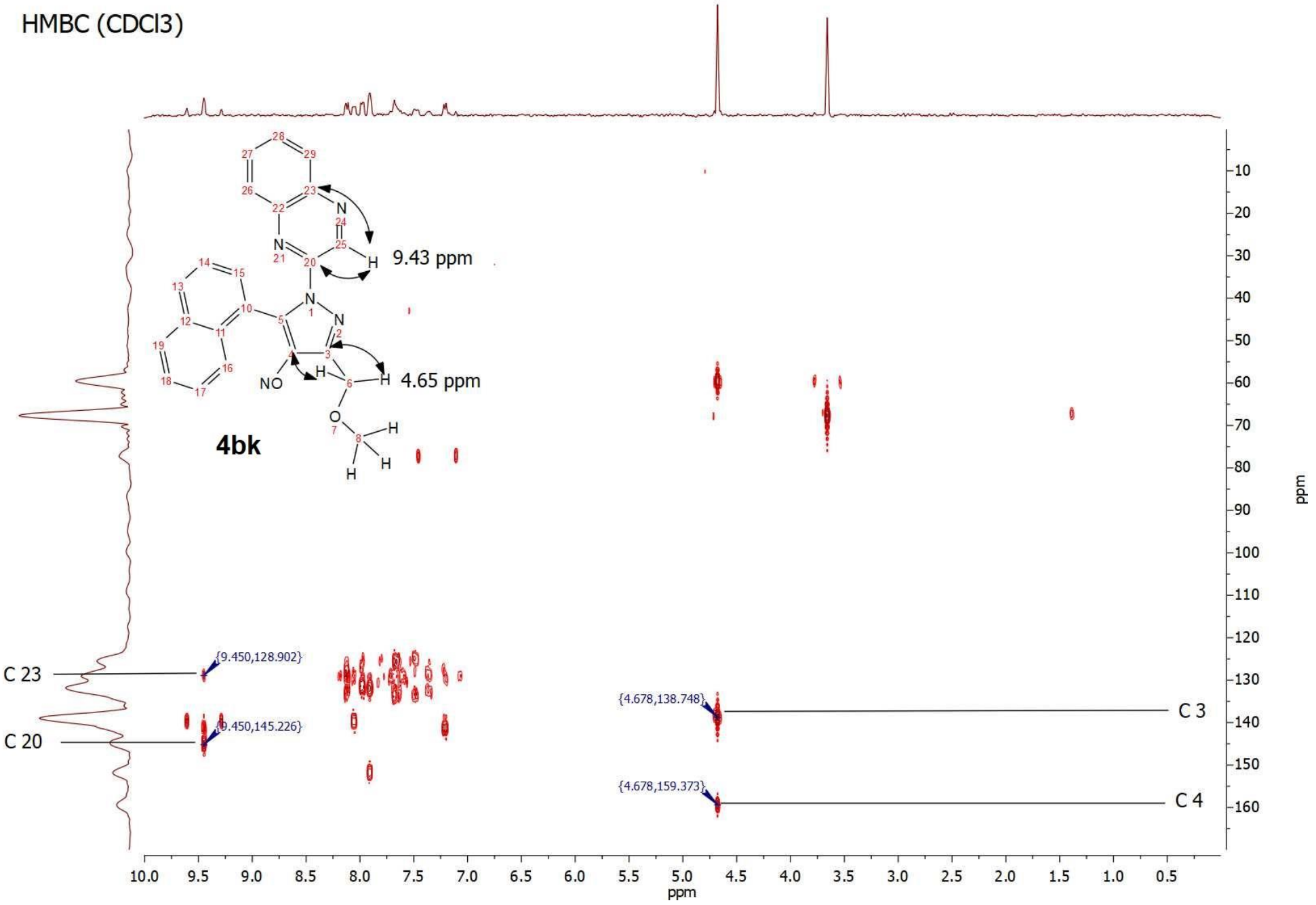

HSQC ($CDCl_3$)
4bj
{3.564,59.379}
{4.525,67.602}
{7.787,131.235}
{7.560,130.659}
{9.296,140.918}
{7.481,130.659}
{7.557,128.430}
{7.793,129.320}
{7.787,131.235}
{7.560,130.659}
{7.481,130.659}
ppm
ppm
ppm
ppm

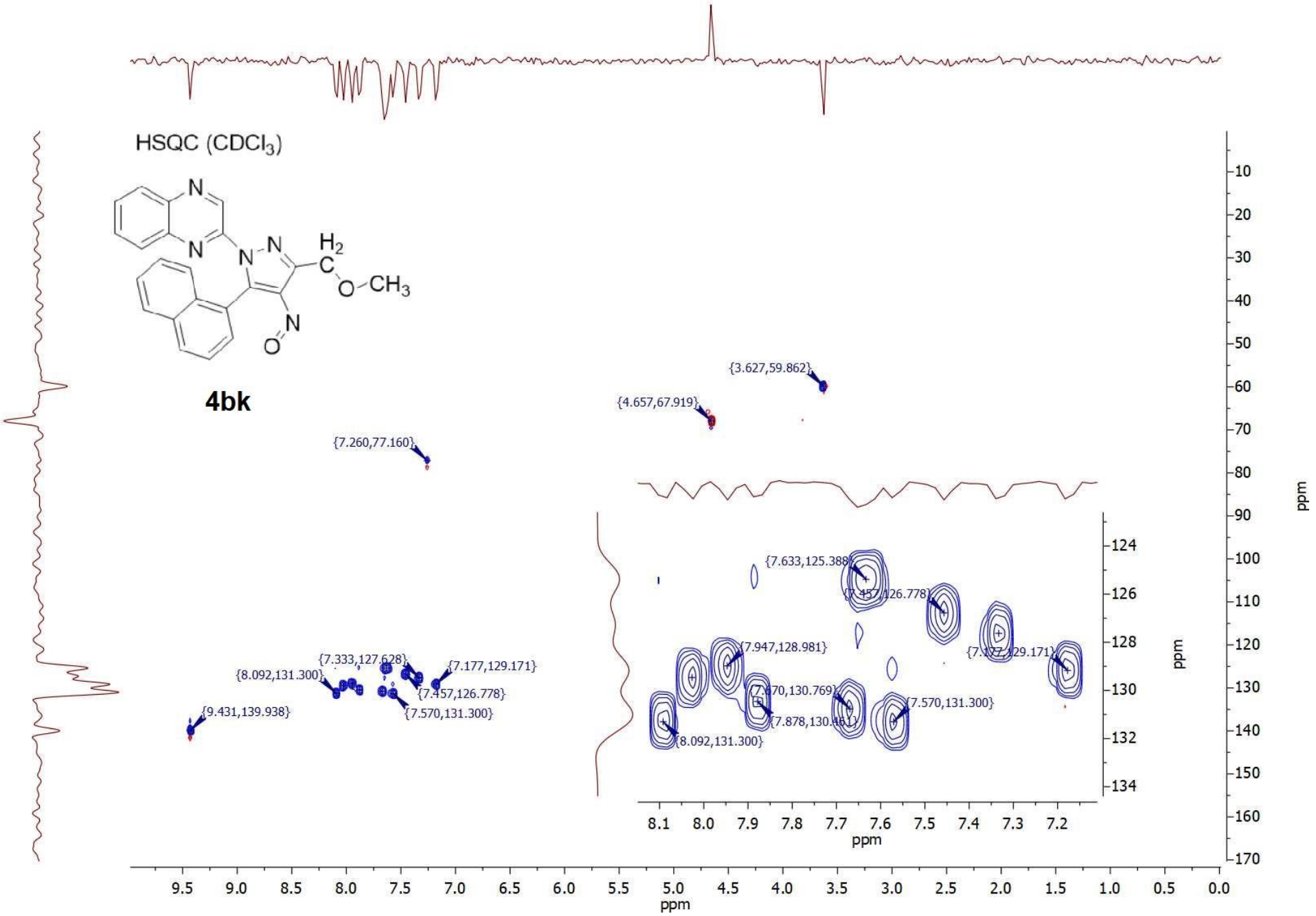
^{1}H NMR (600 MHz, $CDCl_3$)

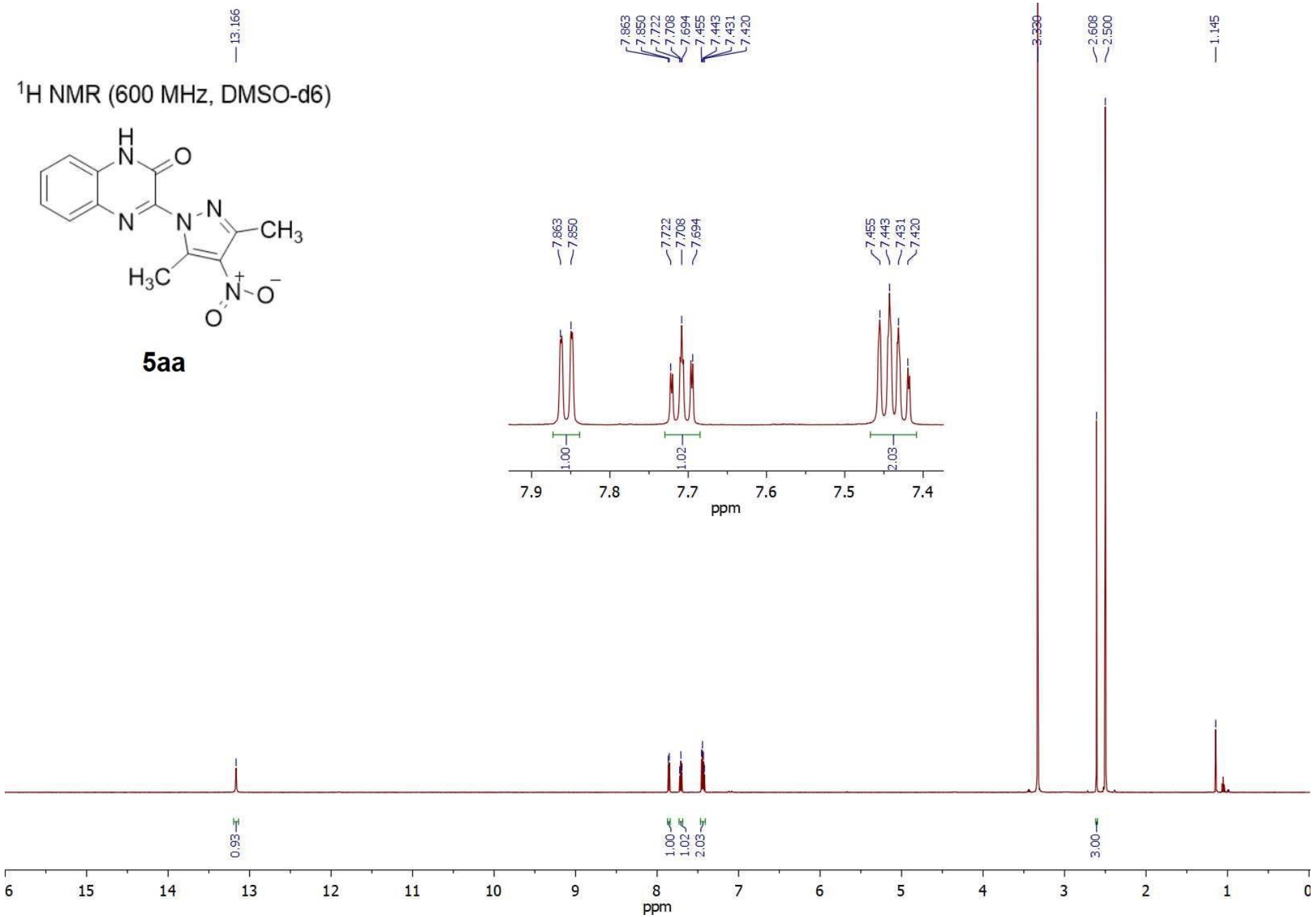


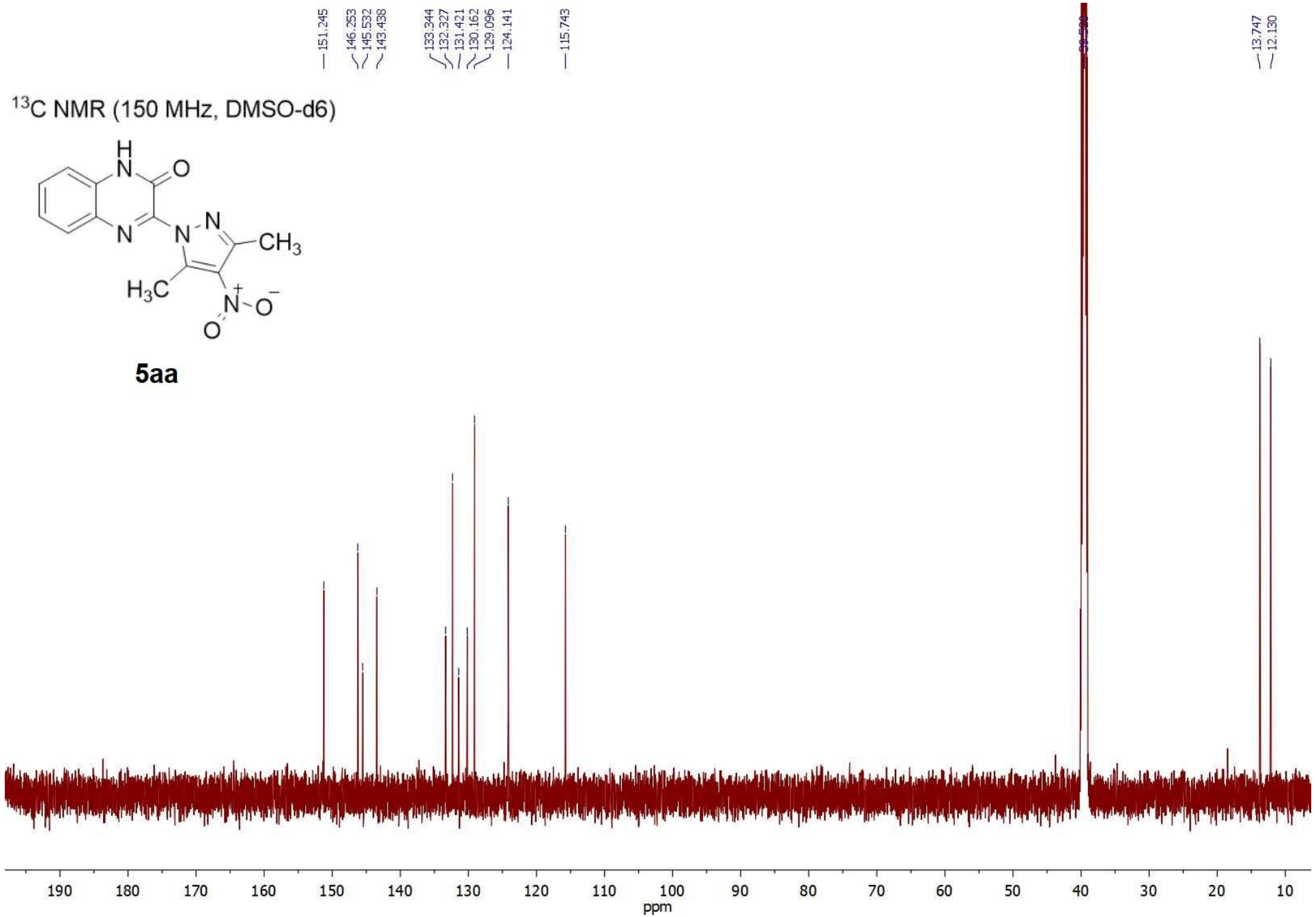
4bk

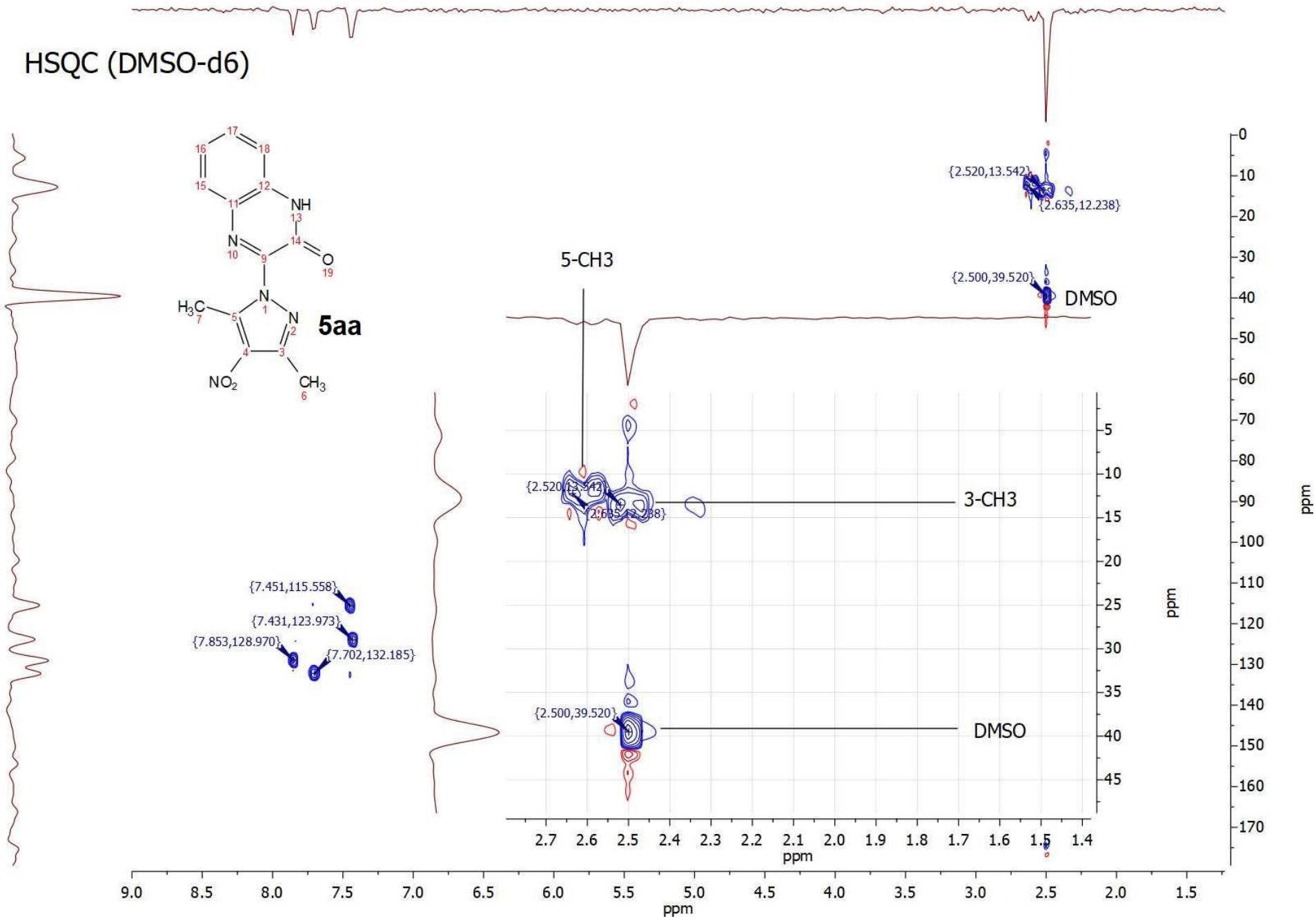

159.603
151.512
145.217
141.505
139.868
139.695
138.914
133.530
132.702
131.148
131.052
130.519
130.267
129.244
128.969
128.764
127.410
126.531
125.706
125.196
125.149
77.160
67.738
59.667
13C NMR (150 MHz, CDCl3)
4bk
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

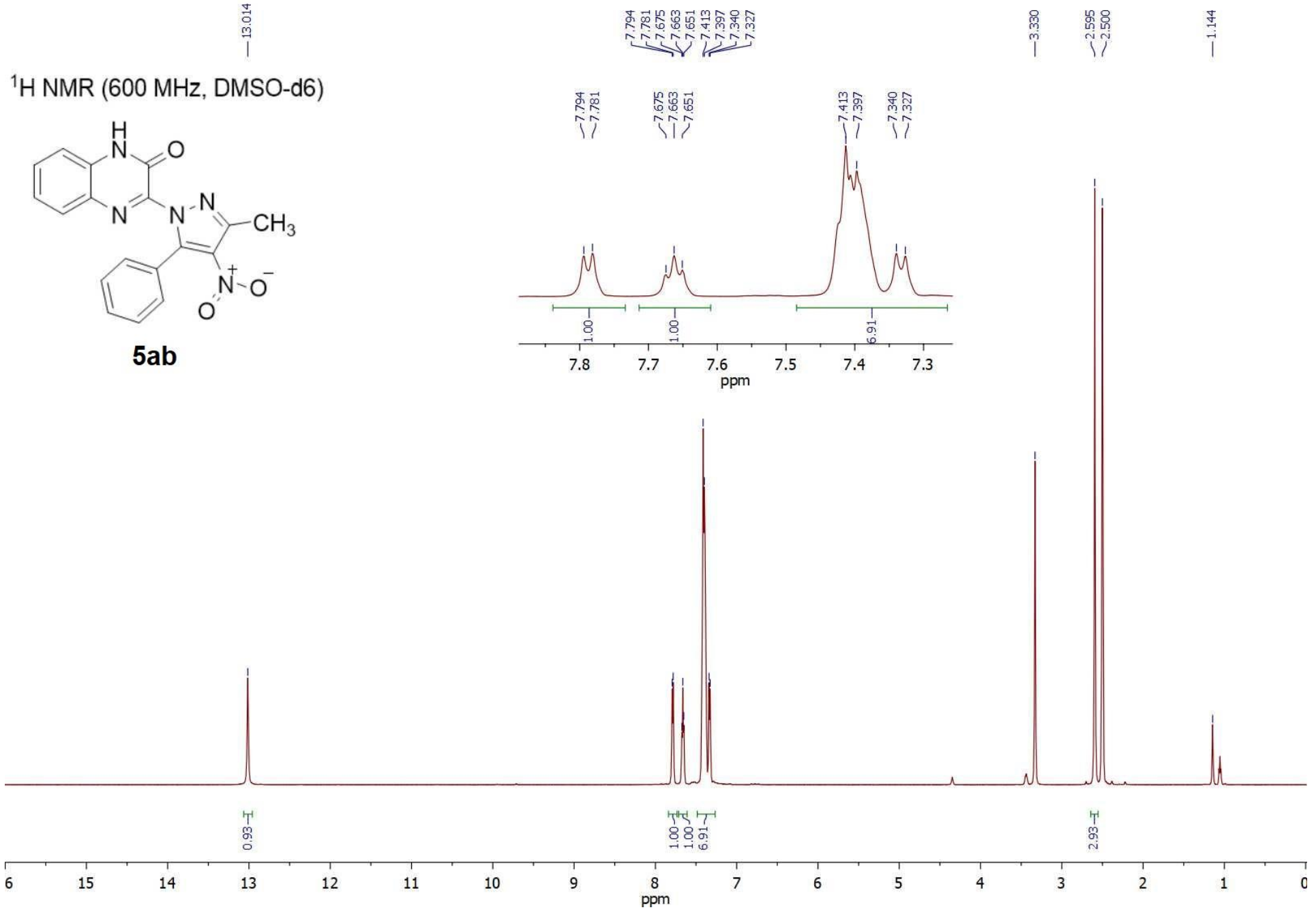

HMBC (CDCl3)
9.43 ppm
4.65 ppm
4bk
C 23
C 20
C 3
C 4
{9.450,128.902}
{9.450,145.226}
{4.678,138.748}
{4.678,159.373}
ppm
ppm

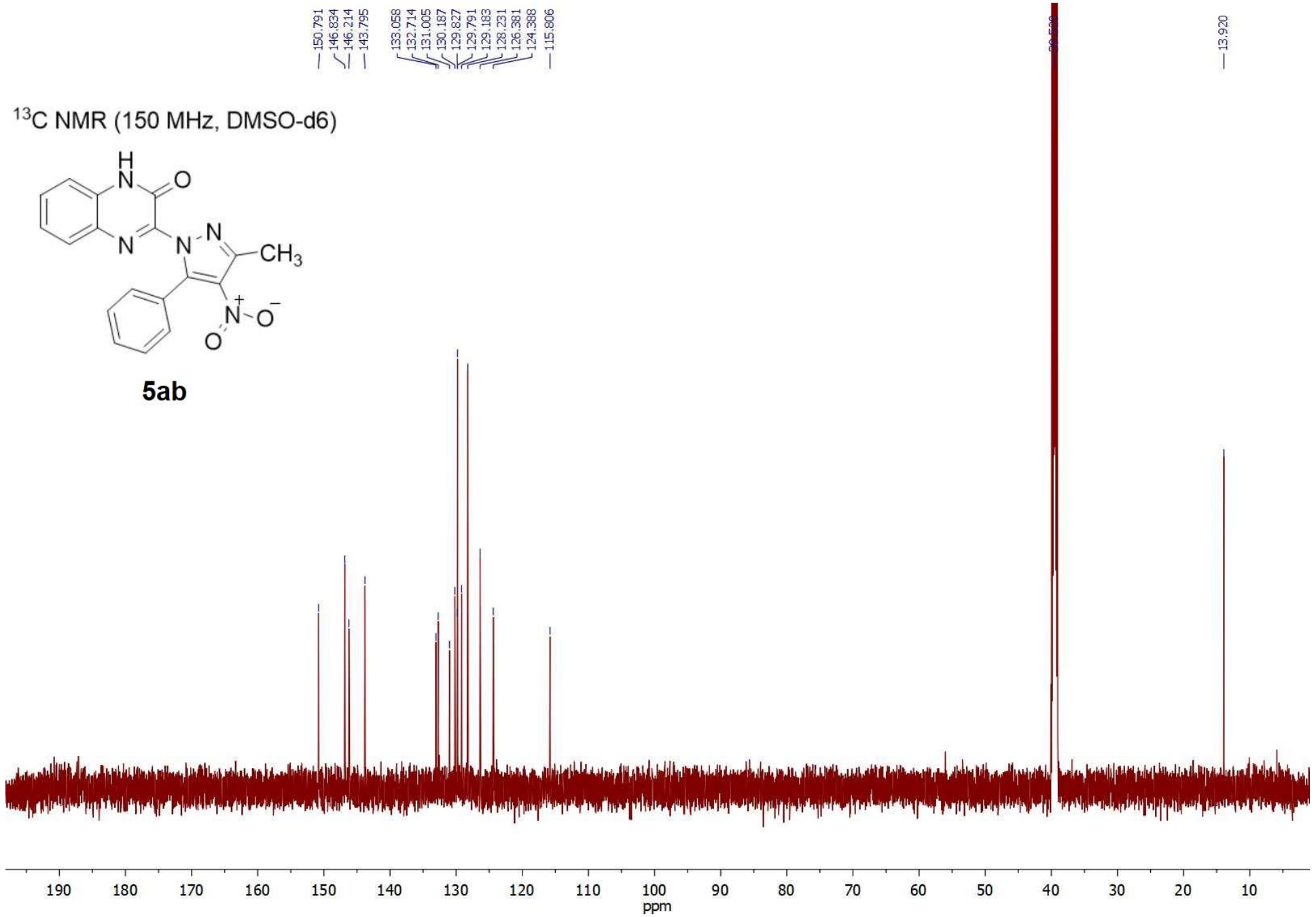

HSQC ($CDCl_3$)
4bk
{3.627,59.862}
{4.657,67.919}
{7.260,77.160}
{7.633,125.388}
{7.457,126.778}
{7.947,128.981}
{7.177,129.171}
{7.670,130.769}
{7.570,131.300}
{7.878,130.481}
{8.092,131.300}
{7.333,127.628}
{7.177,129.171}
{8.092,131.300}
{7.457,126.778}
{9.431,139.938}
{7.570,131.300}
ppm

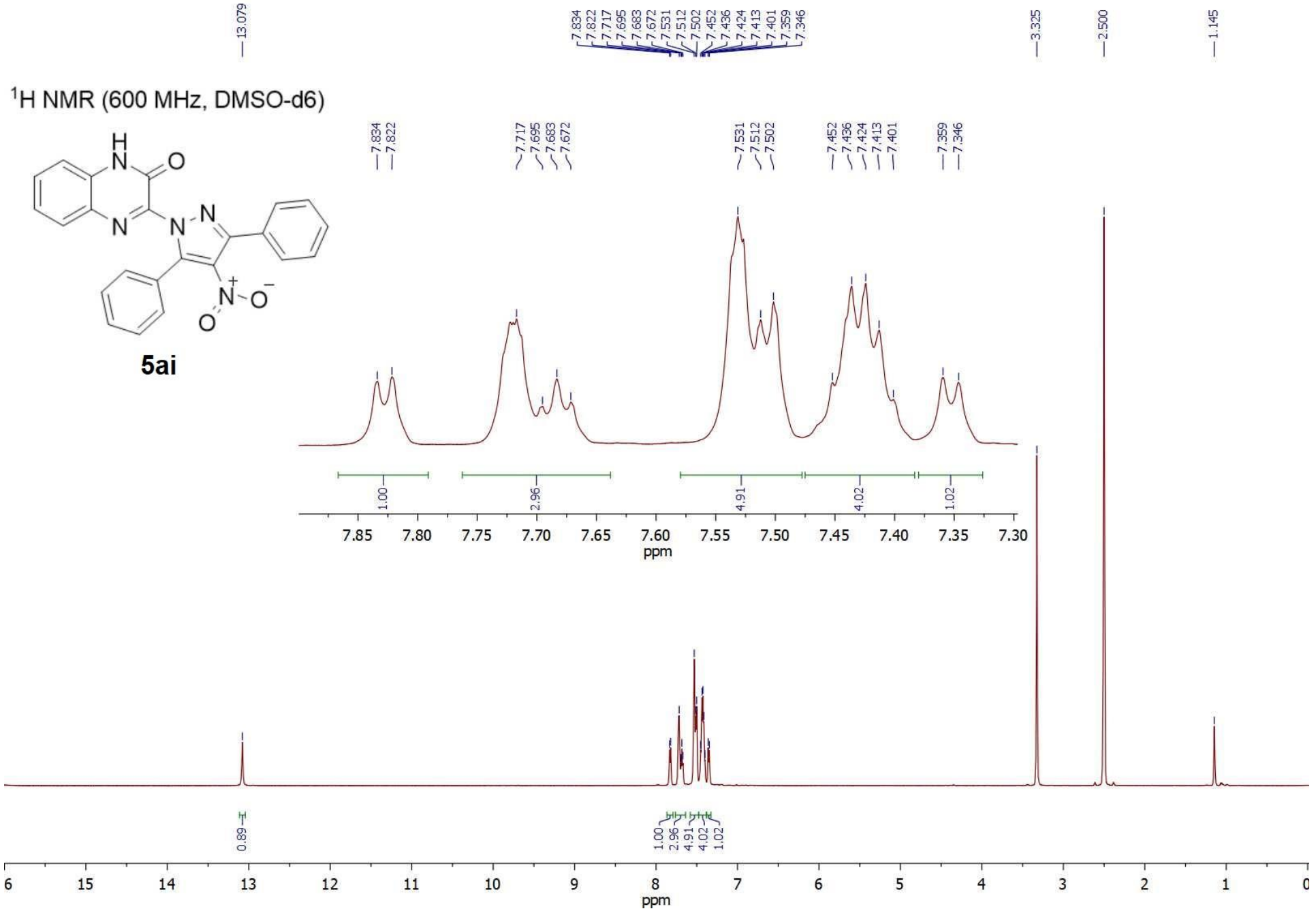

13.166
7.863
7.850
7.722
7.708
7.694
7.455
7.443
7.431
7.420
3.330
2.608
2.500
1.145
1H NMR (600 MHz, DMSO-d6)
5aa
1.00
1.02
2.03
7.9
7.8
7.7
7.6
7.5
7.4
ppm
0.93
3.00
6
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

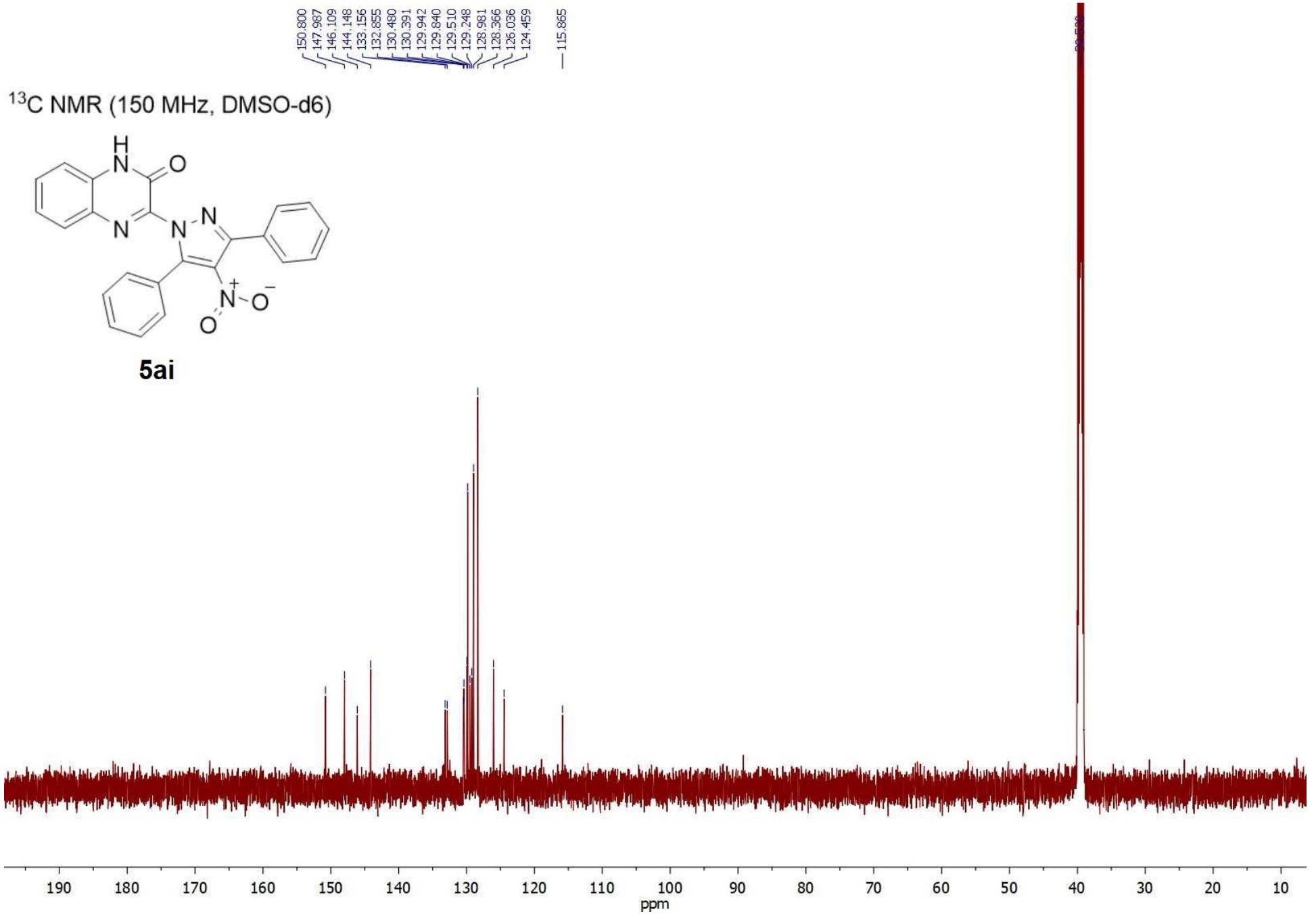

151.245
146.253
145.532
143.438
133.344
132.327
131.421
130.162
129.096
124.141
115.743
13.747
12.130
^{13}C NMR (150 MHz, DMSO-d6)
H
N
O
N
N
N
CH$_3$
H$_3$C
N$^+$
O$^-$
O
5aa
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

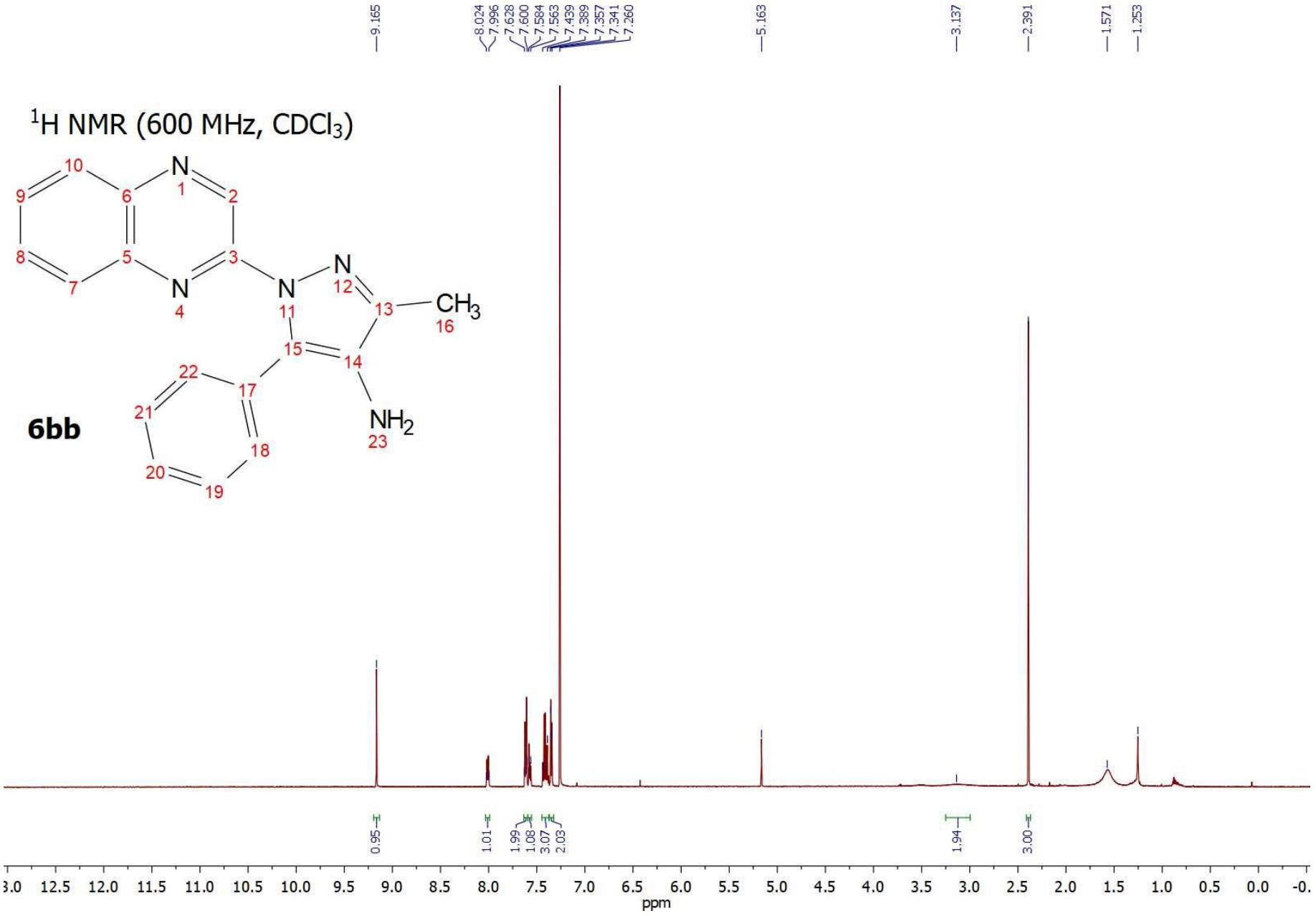

HSQC (DMSO-d6)
5aa
5-CH3
3-CH3
DMSO
DMSO
{2.520,13.542}
{2.635,12.238}
{2.500,39.520}
{7.451,115.558}
{7.431,123.973}
{7.853,128.970}
{7.702,132.185}
ppm
ppm
ppm

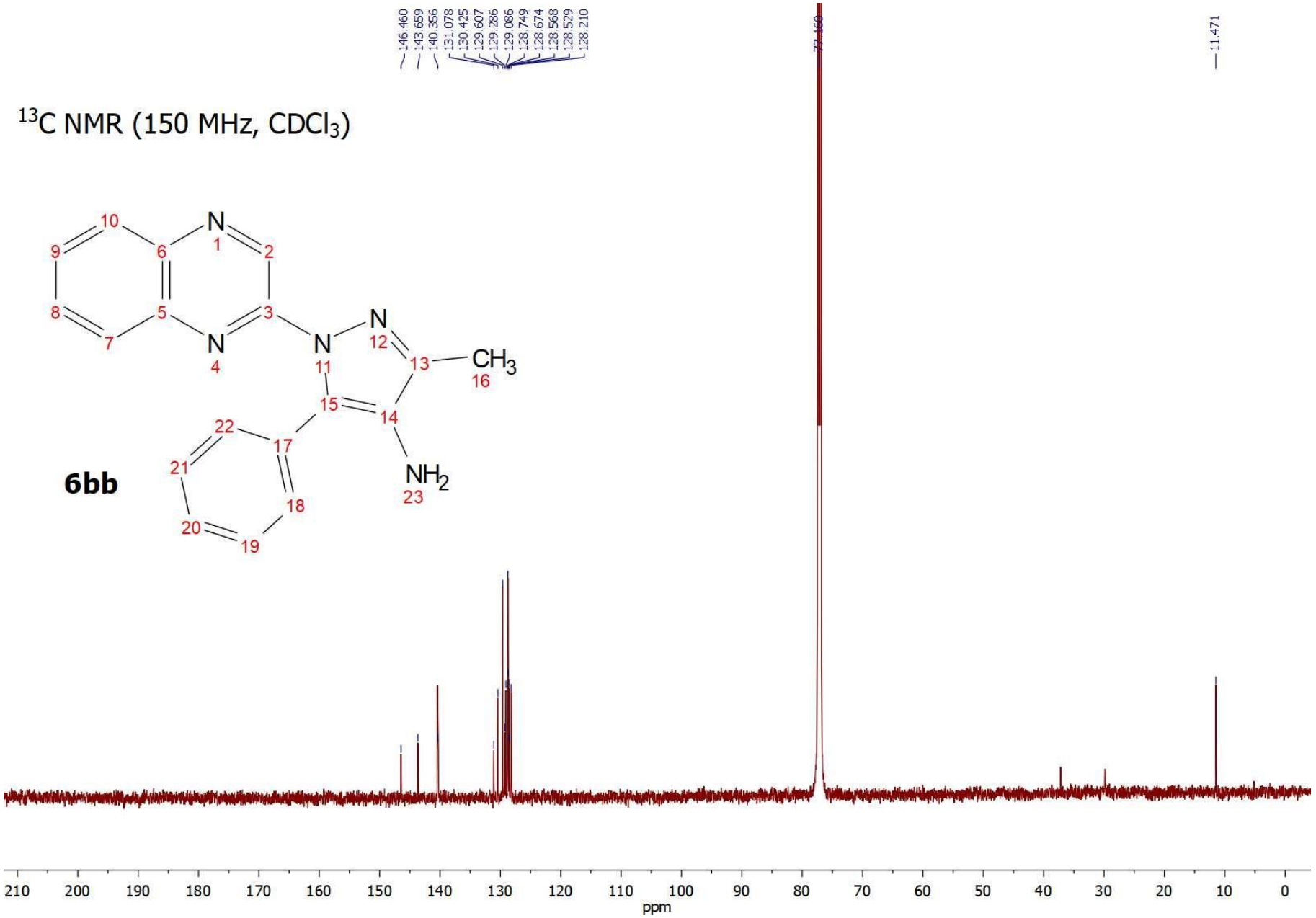

13.014
7.794
7.781
7.675
7.663
7.651
7.413
7.397
7.340
7.327
3.330
2.595
2.500
1.144
1H NMR (600 MHz, DMSO-d6)
5ab
1.00
1.00
6.91
0.93
1.00
1.00
6.91
2.93
ppm
ppm

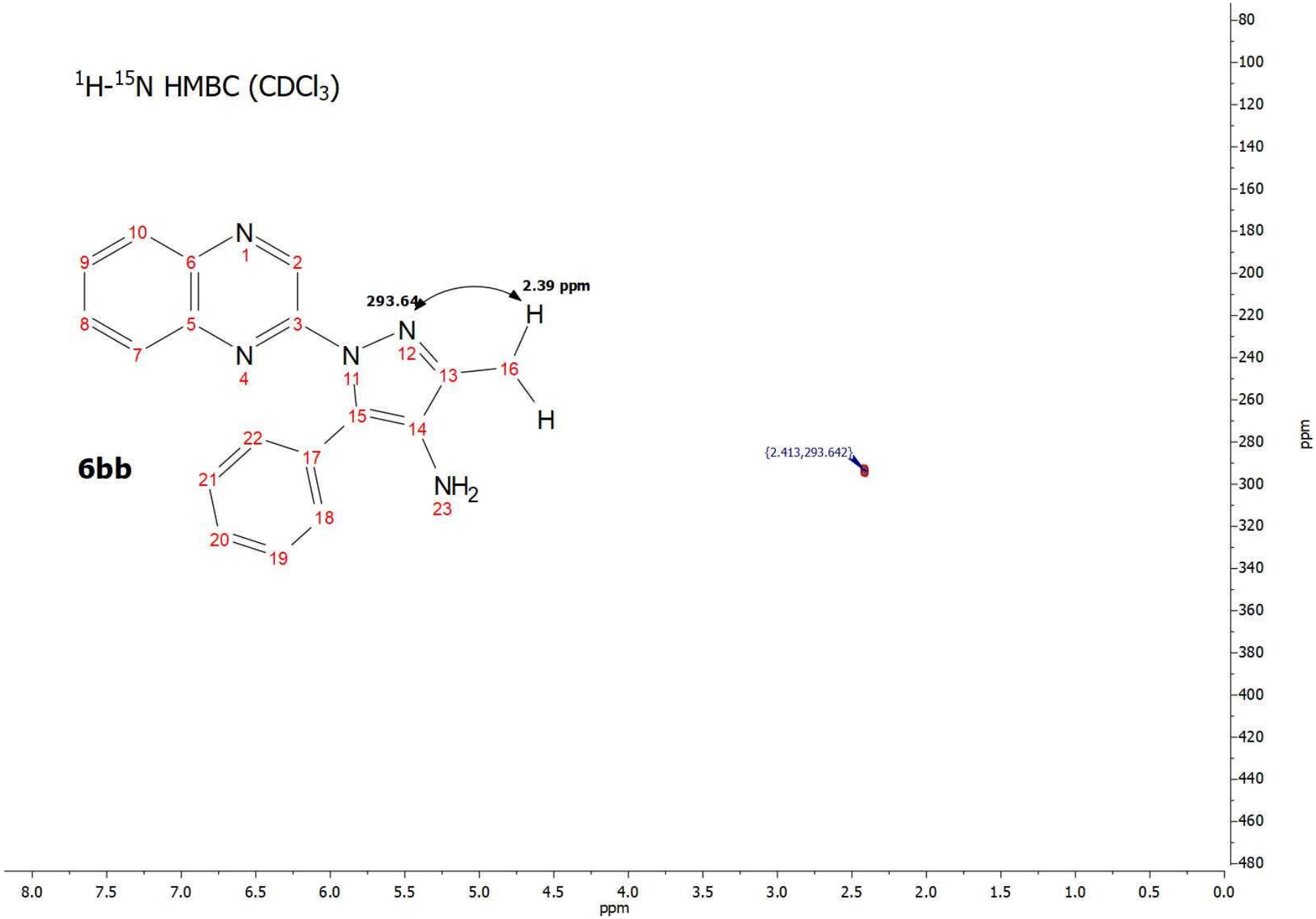

150.791
146.834
146.214
143.795
133.058
132.714
131.005
130.187
129.827
129.791
129.183
128.231
126.381
124.388
115.806
13.920
^{13}C NMR (150 MHz, DMSO-d6)
H
N
O
N
N
N
CH$_3$
N$^+$
O$^-$
O
5ab
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


13.079
7.834
7.822
7.717
7.695
7.683
7.672
7.531
7.512
7.502
7.452
7.436
7.424
7.413
7.401
7.359
7.346
3.325
2.500
1.145
1H NMR (600 MHz, DMSO-d6)
5ai
1.00
2.96
4.91
4.02
1.02
ppm
0.89
1.00
2.96
4.91
4.02
1.02
ppm


150.800
147.987
146.109
144.148
133.156
132.855
130.480
130.391
129.942
129.840
129.510
129.248
128.981
128.366
126.036
124.459
115.865
^{13}C NMR (150 MHz, DMSO-d6)
5ai
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

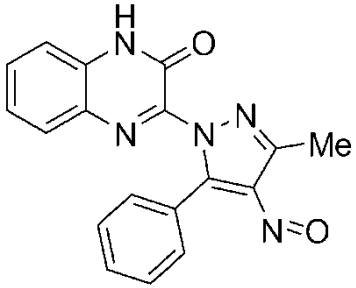

9.165
8.024
7.996
7.628
7.600
7.584
7.563
7.439
7.389
7.357
7.341
7.260
5.163
3.137
2.391
1.571
1.253
^{1}H NMR (600 MHz, $CDCl_3$)
6bb
0.95
1.01
1.99
1.08
3.07
2.03
1.94
3.00
ppm

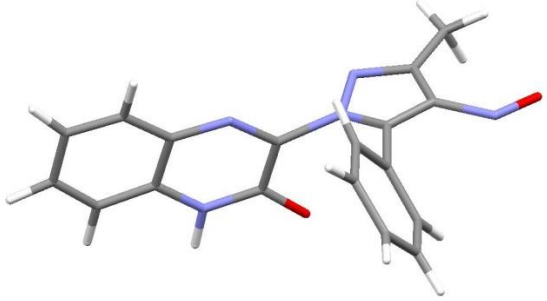

146.460
143.659
140.356
131.078
130.425
129.607
129.286
129.086
128.749
128.674
128.568
128.529
128.210
77.160
11.471
^{13}C NMR (150 MHz, $CDCl_3$)
6bb
ppm

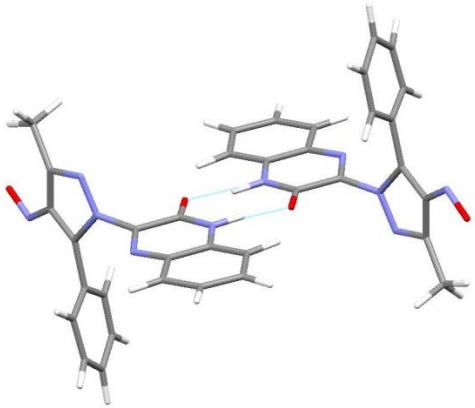

^{1}H-^{15}N HMBC ($CDCl_3$)
6bb
293.64
2.39 ppm
{2.413,293.642}
ppm
ppm

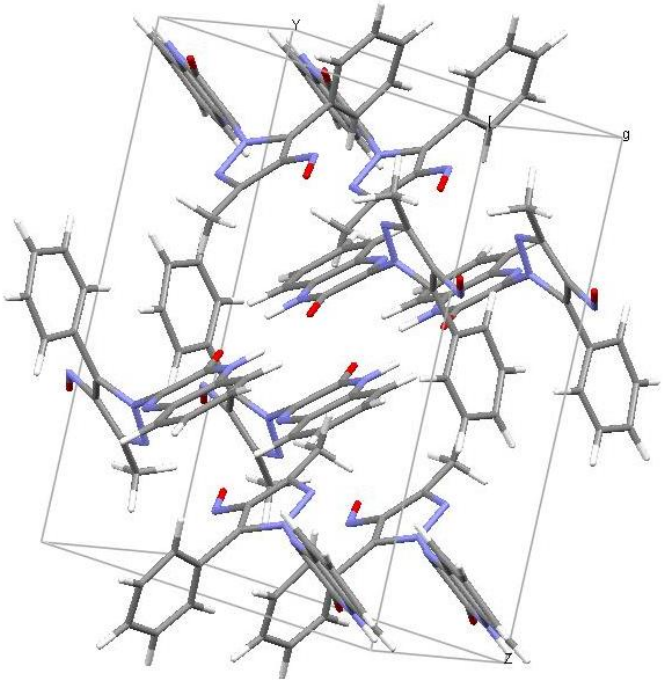
X-Ray crystallography data

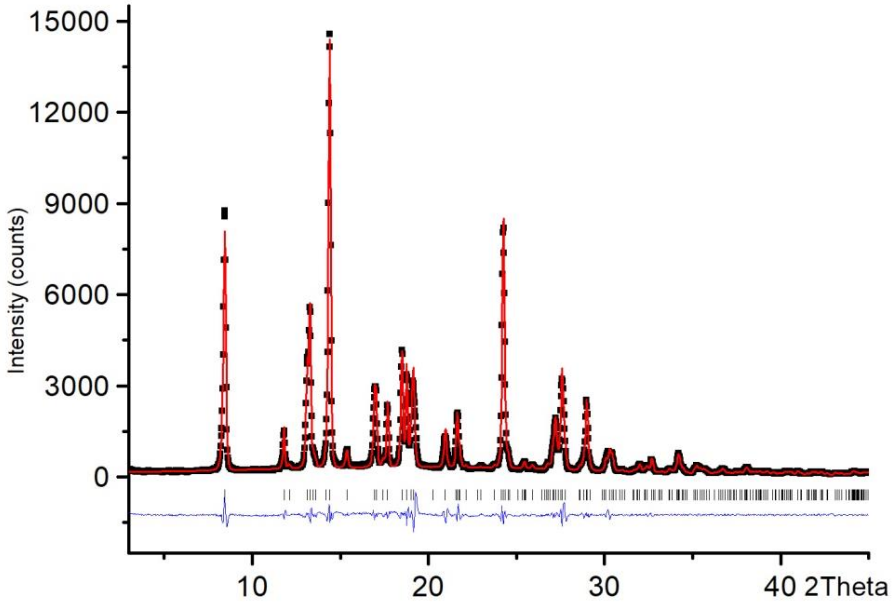
The crystal structure data of **4ab** was deposited in CSD (Deposition Number 2224867).











"Rietveld-plot" for **4ab**

Crystallographic parameters and experimental details of X-ray powder diffraction crystal structure investigation for **4ab**

Chemical formula	$C_{18}H_{13}N_5O_2$ (**4ab**)
Molecular weight	**331.33**
Space group	P 21/a
a, Å	15.7306(9)
b, Å	14.9839(8)
c, Å	7.2686(5)
α, (°)	90.0
β, (°)	111.748(8)
γ, (°)	90.0
$V_{un.cell}$, Å^3	1590.254
Z	4
V/Z, Å^3	397.5
$\rho_{calc.}$, g/cm^3	1.384
MAC μ/ρ	0.779
T, K	295
Diffractometer	X'PertPRO
Radiation	CuKα
λ, Å	λ_1 = 1.54056, λ_2 = 1.54439
Scanning area,2θ (°)	3.0–90.9
Number of Reflections	105
R_p, %	7.6%
R_{wp}, %	9.5%
R_{exp}, %	4.7%
$S = R_{wp}/R_{exp}$	2.02

The X-ray structural study was carried out by X-ray powder diffraction approach. This method does not allow creating a table of structural factors. In accordance with the accepted agreement IUCr, the reliability of the solution found is estimated by the correspondence between the experimental and calculated X-ray powder patterns (Rietveld-plot is given in the article) and the analysis of the crystal structure based on the software "PLATON " (CheckCif protocol).

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: C18H13N5O2

```
Bond precision:   C-C = 0.0140 A          Wavelength=1.54184

Cell:             a=15.7306(9)     b=14.9839(8)         c=7.2686(5)
                  alpha=90         beta=111.748(8)      gamma=90
Temperature:      295 K

                 Calculated                Reported
Volume           1591.31(19)               1591
Space group      P 21/a                    P 1 21/a 1
Hall group       -P 2yab                   -P 2yab
Moiety formula   C18 H13 N5 O2             ?
Sum formula      C18 H13 N5 O2             C18 H13 N5 O2
Mr               331.33                    331.33
Dx,g cm-3        1.383                     1.383
Z                4                         4
Mu (mm-1)        0.779                     0.779
F000             688.0                     688.0
F000'            690.15
h,k,lmax         14,13,6
Nref             1317
Tmin,Tmax
Tmin'

Correction method= Not given

Data completeness= 0.000           Theta(max)=

R(reflections)=                                    wR2(reflections)=
S =                      Npar=
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds ..... 0.014 Ang.

Alert level C

SHFSU01_ALERT_2_C The absolute value of parameter shift to su ratio > 0.05
Absolute value of the parameter shift to su ratio given 0.100
Additional refinement cycles may be required.
PLAT048_ALERT_1_C MoietyFormula Not Given (or Incomplete) ..... Please Check
PLAT080_ALERT_2_C Maximum Shift/Error ..... 0.10 Why ?
PLAT151_ALERT_1_C No s.u. (esd) Given on Volume ..... Please Do !
PLAT369_ALERT_2_C Long C(sp2)-C(sp2) Bond C12 - C18 . 1.55 Ang.
PLAT762_ALERT_1_C CIF Contains no X-Y-H or H-Y-H Angles ..... Please Check

---

Alert level G

PLAT128_ALERT_4_G Alternate Setting for Input Space Group P21/a P21/n Note
PLAT432_ALERT_2_G Short Inter X...Y Contact O24 ..C21 . 2.98 Ang.
1-x,-y,1-z = 3_656 Check
PLAT432_ALERT_2_G Short Inter X...Y Contact N15 ..C22 . 2.91 Ang.
1-x,-y,1-z = 3_656 Check
PLAT432_ALERT_2_G Short Inter X...Y Contact C3 ..C25 . 3.02 Ang.
1/2+x,1/2-y,z = 4_555 Check
PLAT432_ALERT_2_G Short Inter X...Y Contact C3 ..C14 . 3.07 Ang.
1/2+x,1/2-y,z = 4_555 Check
PLAT769_ALERT_4_G CIF Embedded explicitly supplied scattering data Please Note
PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 20 Note
PLAT982_ALERT_1_G The C-f'= 0.0170 Deviates from IT-value = 0.0181 Check
PLAT982_ALERT_1_G The N-f'= 0.0290 Deviates from IT-value = 0.0311 Check

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
6 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
9 **ALERT level G** = General information/check it is not something unexpected

5 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
7 ALERT type 2 Indicator that the structure model may be wrong or deficient
2 ALERT type 3 Indicator that the structure quality may be low
2 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 28/11/2022; check.def file version of 28/11/2022

Datablock C18H13N5O2 - ellipsoid plot