

## *Supporting Information*

### **2-Aryl-1-hydroxyimidazoles possessing antiviral activity against wide range of orthopoxviruses including *Variola virus*.**

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## Single crystal x-ray analysis.

**Table S1.** Crystallographic characteristics, details of the experiments and structure refinement for compounds **5a-5c**

Parameter/substance	<b>5a</b>	<b>5b</b>	<b>5c</b>	<b>semihydrate 5c</b>
Chemical formula	C <sub>12</sub> H <sub>11</sub> N <sub>3</sub> O <sub>4</sub>	C <sub>13</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	C <sub>13</sub> H <sub>11</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub>	C <sub>26</sub> H <sub>24</sub> F <sub>6</sub> N <sub>4</sub> O <sub>5</sub>
<i>M</i> , g/mol	261.24	241.25	284.24	586.49
Temperature, K	295(4)	293(2)	295(4)	295(4)
Crystal system	triclinic	monoclinic	monoclinic	triclinic
Space group	P-1	P2 <sub>1</sub> /c	Ia	P-1
<i>a</i> , Å	6.2902(6)	13.6508(11)	15.7230(16)	9.7912(6)
<i>b</i> , Å	7.3546(7)	6.9360(8)	14.3769(9)	11.5563(9)
<i>c</i> , Å	12.9978(11)	12.6244(12)	23.665(2)	12.0456(8)
<i>α</i> , deg	85.350(7)	90	90	91.342(6)
<i>β</i> , deg	88.976(7)	93.350(8)	105.339(10)	101.399(5)
<i>γ</i> , deg	83.526(7)	90	90	97.183(6)
<i>V</i> , Å <sup>3</sup>	595.47(9)	1193.3(2)	5159.0(8)	1323.97(16)
<i>Z</i>	2	4	4	2
<i>ρ</i> <sub>calc</sub> , g/cm <sup>3</sup>	1.457	1.343	1.464	1.471
<i>μ</i> , mm <sup>-1</sup>	0.112	0.094	0.129	0.130
<i>F</i> (000)	272.0	504.0	2336.0	604.0
Crystal size, mm <sup>3</sup>	0.07 × 0.05 × 0.02	0.2 × 0.04 × 0.04	0.3 × 0.025 × 0.01	0.5 × 0.02 × 0.02
2 $\theta$ range for data collection, deg	5.592 to 56.13	6.466 to 56.282	5.61 to 56.454	4.282 to 52.766
<i>h</i> , <i>k</i> , <i>l</i> intervals	-8 ≤ <i>h</i> ≤ 8, -9 ≤ <i>k</i> ≤ 9, -17 ≤ <i>l</i> ≤ 15	-16 ≤ <i>h</i> ≤ 18, -9 ≤ <i>k</i> ≤ 9, -16 ≤ <i>l</i> ≤ 15	-20 ≤ <i>h</i> ≤ 20, -18 ≤ <i>k</i> ≤ 18, -30 ≤ <i>l</i> ≤ 30	-12 ≤ <i>h</i> ≤ 12, -14 ≤ <i>k</i> ≤ 13, -14 ≤ <i>l</i> ≤ 15
Measured reflections	6217	12229	16053	13672
Independent reflections [ <i>R</i> <sub>int</sub> , <i>R</i> <sub>σ</sub> ]	2379 [ <i>R</i> <sub>int</sub> = 0.0212, <i>R</i> <sub>sigma</sub> = 0.0361]	2501 [ <i>R</i> <sub>int</sub> = 0.0422, <i>R</i> <sub>sigma</sub> = 0.0367]	9353 [ <i>R</i> <sub>int</sub> = 0.0466, <i>R</i> <sub>sigma</sub> = 0.0710]	5051 [ <i>R</i> <sub>int</sub> = 0.0496, <i>R</i> <sub>sigma</sub> = 0.0744]
Data/restraints/parameters	2379/0/175	2501/0/168	9353/25/836	5051/6/406
<i>GOOF</i> on <i>F</i> <sup>2</sup>	1.027	1.037	1.001	1.055
<i>R</i> factor ( <i>I</i> > 2σ( <i>I</i> ))	<i>R</i> <sub>1</sub> = 0.0488, w <i>R</i> <sub>2</sub> = 0.1285	<i>R</i> <sub>1</sub> = 0.0479, w <i>R</i> <sub>2</sub> = 0.1230	<i>R</i> <sub>1</sub> = 0.0515, w <i>R</i> <sub>2</sub> = 0.1119	<i>R</i> <sub>1</sub> = 0.0559, w <i>R</i> <sub>2</sub> = 0.1510
<i>R</i> factor (all data)	<i>R</i> <sub>1</sub> = 0.0721, w <i>R</i> <sub>2</sub> = 0.1400	<i>R</i> <sub>1</sub> = 0.0739, w <i>R</i> <sub>2</sub> = 0.1354	<i>R</i> <sub>1</sub> = 0.0993, w <i>R</i> <sub>2</sub> = 0.1299	<i>R</i> <sub>1</sub> = 0.0740, w <i>R</i> <sub>2</sub> = 0.1625
$\Delta\rho_{\max} / \Delta\rho_{\min}$ , e/Å <sup>-3</sup>	0.17/-0.15	0.14/-0.20	0.12/-0.15	0.28/-0.25
CCDC deposition number	2340418	2340435	2331165	2340465

**Table S2.** Crystallographic characteristics, details of the experiments and structure refinement for compounds **4b,c, 6a and 11b**

Parameter/substance	<b>4b</b>	<b>4c</b>	<b>6a</b>	<b>11b</b>
Chemical formula	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	C <sub>16</sub> H <sub>15</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub>	C <sub>16</sub> H <sub>17</sub> N <sub>3</sub> O <sub>4</sub>	C <sub>22</sub> H <sub>20</sub> BrN <sub>3</sub> O <sub>4</sub>
<i>M</i> , g/mol	281.31	324.30	315.32	470.32
Temperature, K	298(4)	298(4)	293(2)	295(4)
Crystal system	monoclinic	monoclinic	triclinic	triclinic
Space group	P2 <sub>1</sub> /n	P2 <sub>1</sub> /c	P-1	P-1
<i>a</i> , Å	5.7707(9)	5.8260(13)	8.7742(9)	9.339(2)
<i>b</i> , Å	24.525(3)	25.780(3)	9.1629(9)	13.222(2)
<i>c</i> , Å	10.1461(17)	11.897(3)	10.6026(10)	18.311(4)
$\alpha$ , deg	90	90	86.044(8)	78.539(16)
$\beta$ , deg	93.696(17)	122.66(3)	88.978(8)	77.793(19)
$\gamma$ , deg	90	90	65.694(9)	77.049(17)
<i>V</i> , Å <sup>3</sup>	1432.9(4)	1504.4(7)	774.96(14)	2126.5(8)
<i>Z</i>	4	4	2	4
$\rho_{\text{calc}}$ , g/cm <sup>3</sup>	1.304	1.432	1.351	1.469
$\mu$ , mm <sup>-1</sup>	0.089	0.120	0.099	1.967
<i>F</i> (000)	592.0	672.0	332.0	960.0
Crystal size, mm <sup>3</sup>	0.1 × 0.05 × 0.02	0.25 × 0.18 × 0.01	0.25 × 0.18 × 0.01	0.2 × 0.05 × 0.05
2 $\Theta$ range for data collection, deg	4.352 to 56.456	5.15 to 56.384	5.094 to 56.522	4.232 to 52.804
<i>h, k, l</i> intervals	-7 ≤ <i>h</i> ≤ 7, -31 ≤ <i>k</i> ≤ 29, -13 ≤ <i>l</i> ≤ 13	-7 ≤ <i>h</i> ≤ 7, -30 ≤ <i>k</i> ≤ 33, -15 ≤ <i>l</i> ≤ 15	-11 ≤ <i>h</i> ≤ 11, -11 ≤ <i>k</i> ≤ 11, -13 ≤ <i>l</i> ≤ 14	-11 ≤ <i>h</i> ≤ 11, -15 ≤ <i>k</i> ≤ 16, -22 ≤ <i>l</i> ≤ 22
Measured reflections	14927	15466	8302	16882
Independent reflections [ <i>R</i> <sub>int</sub> , <i>R</i> <sub>σ</sub> ]	3107 [ <i>R</i> <sub>int</sub> = 0.0904, <i>R</i> <sub>σ</sub> = 0.0832]	3203 [ <i>R</i> <sub>int</sub> = 0.0620, <i>R</i> <sub>σ</sub> = 0.0575]	3097 [ <i>R</i> <sub>int</sub> = 0.0189, <i>R</i> <sub>σ</sub> = 0.0252]	7829 [ <i>R</i> <sub>int</sub> = 0.0916, <i>R</i> <sub>σ</sub> = 0.1519]
Data/restraints /parameters	3107/1/195	3203/36/238	3097/0/211	7829/0/545
<i>GOOF</i> on <i>F</i> <sup>2</sup>	1.039	1.058	1.046	1.018
<i>R</i> factor ( <i>I</i> > 2σ( <i>I</i> ))	<i>R</i> <sub>1</sub> = 0.0590, <i>wR</i> <sub>2</sub> = 0.1404	<i>R</i> <sub>1</sub> = 0.0836, <i>wR</i> <sub>2</sub> = 0.2347	<i>R</i> <sub>1</sub> = 0.0399, <i>wR</i> <sub>2</sub> = 0.1072	<i>R</i> <sub>1</sub> = 0.0895, <i>wR</i> <sub>2</sub> = 0.2353
<i>R</i> factor (all data)	<i>R</i> <sub>1</sub> = 0.1159, <i>wR</i> <sub>2</sub> = 0.1615	<i>R</i> <sub>1</sub> = 0.1079, <i>wR</i> <sub>2</sub> = 0.2493	<i>R</i> <sub>1</sub> = 0.0513, <i>wR</i> <sub>2</sub> = 0.1137	<i>R</i> <sub>1</sub> = 0.2227, <i>wR</i> <sub>2</sub> = 0.2957
$\Delta\rho_{\text{max}} / \Delta\rho_{\text{min}}$ , e/Å <sup>-3</sup>	0.33/-0.2	0.41/-0.25	0.15/-0.20	1.06/-0.68
CCDC deposition number	2340467	2336792	2331158	2340466

## Evaluation of antiviral activity.

**Table S3.** Cytotoxicity and antiviral activity of 2-arylimidazoles **3a-c**, **4a-e**, **5a,b**, **6a-e**, **8a,c**, **9a,b**, **10a-e**, **12** against the Vaccinia virus (Copenhagen strain) in Vero cell culture.

No	R <sup>1</sup>	R <sup>2</sup>	CC <sub>50</sub> , µg/mL (M±SD, n=3)	IC <sub>50</sub> (VACV), µg/mL (M±SD, n=3)	SI
<b>4a</b>	NO <sub>2</sub>	H	42.9±14.6	0.04±0.01	1072
<b>4b</b>	CN	H	49.2±11.8	0.14±0.04	351
<b>4c</b>	CF <sub>3</sub>	H	15.0±2.8	0.05±0.01	300
<b>5a</b>	NO <sub>2</sub>	H	7.4±1.8	0.17±0.05	44
<b>5b</b>	CN	H	20.4±4.9	0.27±0.08	76
<b>5c</b>	CF <sub>3</sub>	H	1.1±0,5	0.020±0.009	55
<b>5d</b>	N(CH <sub>3</sub> ) <sub>2</sub>	H	77.5±17.6	3.35±0.74	23
<b>5e</b>	OCH <sub>3</sub>	H	151.3±36.1	4.41±0.67	34
<b>6a</b>	NO <sub>2</sub>	CH <sub>3</sub>	364.0±85.9	1.25±0.07	291
<b>6b</b>	CN	CH <sub>3</sub>	223.7±28.9	8.42±2.10	27
<b>7a</b>	NO <sub>2</sub>	CH <sub>3</sub>	122.1±28.1	1.31±0.03	93
<b>7b</b>	CN	CH <sub>3</sub>	270.0±71.8	58.21±12.22	<8
<b>7c</b>	CF <sub>3</sub>	CH <sub>3</sub>	52.5±10.5	1.76±0.53	30
<b>7d</b>	N(CH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub>	53.9±13.5	16.97±4.00	<8
<b>7e</b>	OCH <sub>3</sub>	CH <sub>3</sub>	92.9±23.5	53.97±7.94	<8
<b>9a</b>	NO <sub>2</sub>	–	769.7±192.4	57.83±13.30	13
<b>9c</b>	CF <sub>3</sub>	–	704.0±176.0	4.82±1.40	146
<b>10a</b>	NO <sub>2</sub>	–	820.0±180.4	N/A	–
<b>10b</b>	CN	–	385.0±88.6	N/A	–
<b>11a</b>	NO <sub>2</sub>	CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	455.0±70.5	2.50±0.62	182
<b>11b</b>	NO <sub>2</sub>	CH <sub>2</sub> (2-BrC <sub>6</sub> H <sub>4</sub> )	47.1±8.8	1.37±0.37	34
<b>11c</b>	NO <sub>2</sub>	CH <sub>2</sub> (3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> )	50.0±17.1	0.28±0.14	179
<b>11d</b>	NO <sub>2</sub>	CH <sub>2</sub> (2,6-F <sub>2</sub> C <sub>6</sub> H <sub>3</sub> )	22.1±4.4	0.52±0.32	43
<b>11e</b>	NO <sub>2</sub>	CH <sub>2</sub> (2,5-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> )	44.0±9.3	0.56±0.18	79
<b>13</b>	NO <sub>2</sub>	-	140.7±38.0	10.83±1.21	13
<b>Cidofovir</b>			276.2±45.6	9.07±0.63	34
<b>NIOCH-14</b>			470.6±90.2	0.003±0.001	157026

Notes: CC<sub>50</sub> – 50% cytotoxicity concentration, at which 50% of cells in uninfected monolayers are destroyed; IC<sub>50</sub> – 50% virus inhibitory concentration, at which 50% of cells in infected monolayers are preserved; SI – selectivity index, ratio CC<sub>50</sub>/IC<sub>50</sub>; M – mean value; SD – standard deviation; n=3 – the number of repeats of measurement of CC<sub>50</sub> and IC<sub>50</sub>; N/A – not active.



**Table S4.** Cytotoxicity and antiviral activity of 2-arylimidazoles **4a-c**, **5a**, **6a**, **7a**, **11a-c**, against the cowpox virus (Grishak strain) and the ectromelia virus (K-1 strain) in Vero cell culture.

<b>№</b>	<b>CC<sub>50</sub>, µg/mL (M±SD, n=3)</b>	<b>IC<sub>50</sub>(CPXV), µg/mL (M±SD, n=3)</b>	<b>SI (CPXV)</b>	<b>IC<sub>50</sub>(ECTV), µg/mL (M±SD, n=3)</b>	<b>SI (ECTV)</b>
<b>4a</b>	42.9±14.6	0.35±0.11	123	0.12±0.05	358
<b>4b</b>	49.2±11.8	4.82±1.20	10	0.70±0.24	70
<b>4c</b>	15.0±2.8	0.78±0.09	19	0.16±0.01	94
<b>5a</b>	7.4±1.8	1.54±0.37	<8	0.34±0.1	22
<b>6a</b>	364.0±85.9	5.65±1.54	65	3.95±0.18	92
<b>7a</b>	122.1±28.1	6.13±1.35	20	3.82±0.31	32
<b>11a</b>	455.0±70.5	30.6±7.65	15	12.08±1.03	38
<b>11b</b>	47.1±8.8	13.67±1.41	<8	13.51±1.32	<8
<b>11c</b>	50.0±17.1	3.24±0.71	15	0.83±0.27	60
<b>11d</b>	22.1±4.4	3.16±0.70	<8	1.92±0.57	12
<b>11e</b>	44.0±9.3	13.56±0.94	<8	6.05±2.08	<8
<b>Cidofovir</b>	276.2±45.6	13.47±1.24	23	11.01±0.90	28
<b>NIOCH-14</b>	470.6±90.2	0.004±0.002	132600	0.003±0.001	149175

Notes: CC<sub>50</sub> – 50% cytotoxicity concentration, at which 50% of cells in uninfected monolayers are destroyed; IC<sub>50</sub> – 50% virus inhibitory concentration, at which 50% of cells in infected monolayers are preserved; SI – selectivity index, ratio CC<sub>50</sub>/IC<sub>50</sub>; M – mean value; SD – standard deviation; n=3 – the number of repeats of measurement of CC<sub>50</sub> and IC<sub>50</sub>.

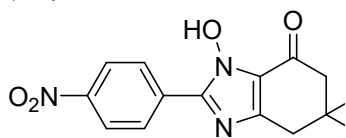
**Table S5.** Cytotoxicity and antiviral activity of 2-arylimidazoles **4a-c** and **6a** against the Variola virus (India3a strain) in Vero cell culture.

<b>No</b>	<b>CC<sub>50</sub>, µg/mL (M±SD, n=3)</b>	<b>IC<sub>50</sub>(VARV), µg/mL (M±SD, n=3)</b>	<b>SI (VARV)</b>
<b>4a</b>	42.9±14.6	0.115±0.033	374
<b>4b</b>	49.2±11.8	0.409±0.042	120
<b>4c</b>	15.0±2.8	0.06±0.01	257
<b>6a</b>	364.0±85.9	1.251±0.080	291
<b>Cidofovir</b>	276.2±45.6	12.05±1.53	26
<b>NIOCH-14</b>	470.6±90.2	0.003±0.001	149175

Notes: CC<sub>50</sub> – 50% cytotoxicity concentration, at which 50% of cells in uninfected monolayers are destroyed; IC<sub>50</sub> – 50% virus inhibitory concentration, at which 50% of cells in infected monolayers are preserved; SI – selectivity index, ratio CC<sub>50</sub>/IC<sub>50</sub>; M – mean value; SD – standard deviation; n=3 – the number of repeats of measurement of CC<sub>50</sub> and IC<sub>50</sub>.

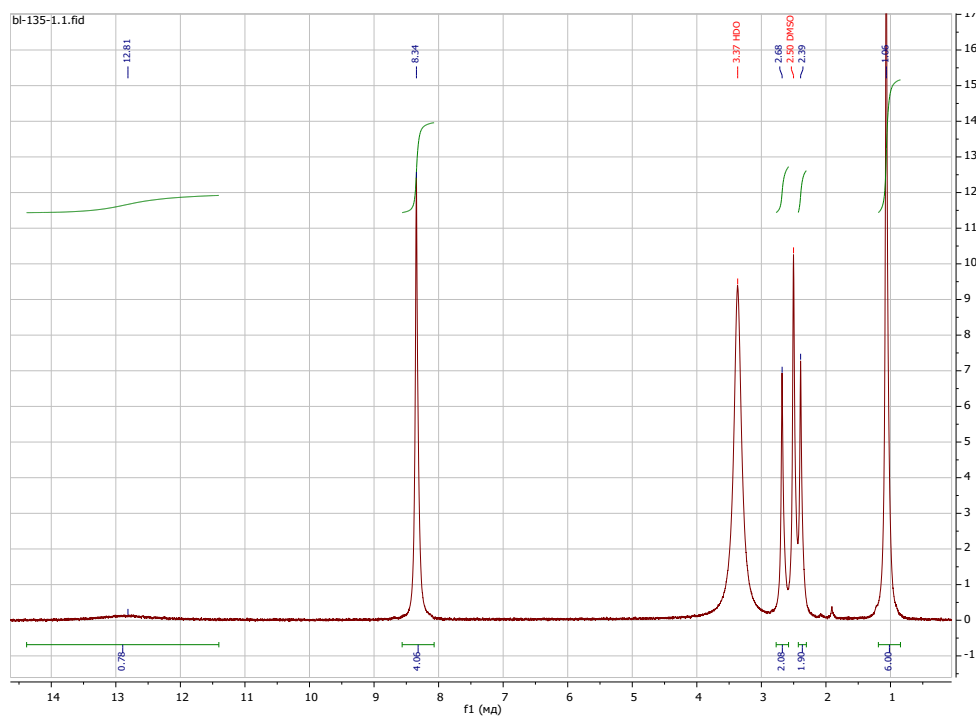
Copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR, HSQC, HMBC spectra, HRMS (ESI) and HRMS (EI) for 4a-c, 5a-e, 6a-b, 7a-e, 8a-c, 9a, 9c, 10a-b, 11a-e, 12 and 13.

3-hydroxy-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzimidazol-4-one (4a).

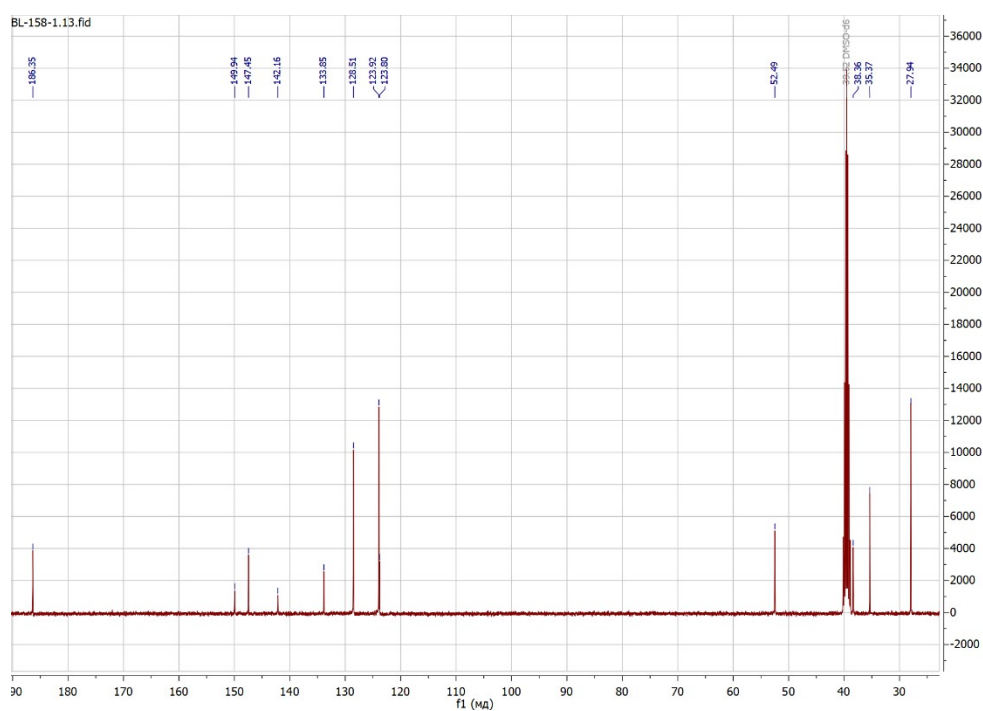


4a

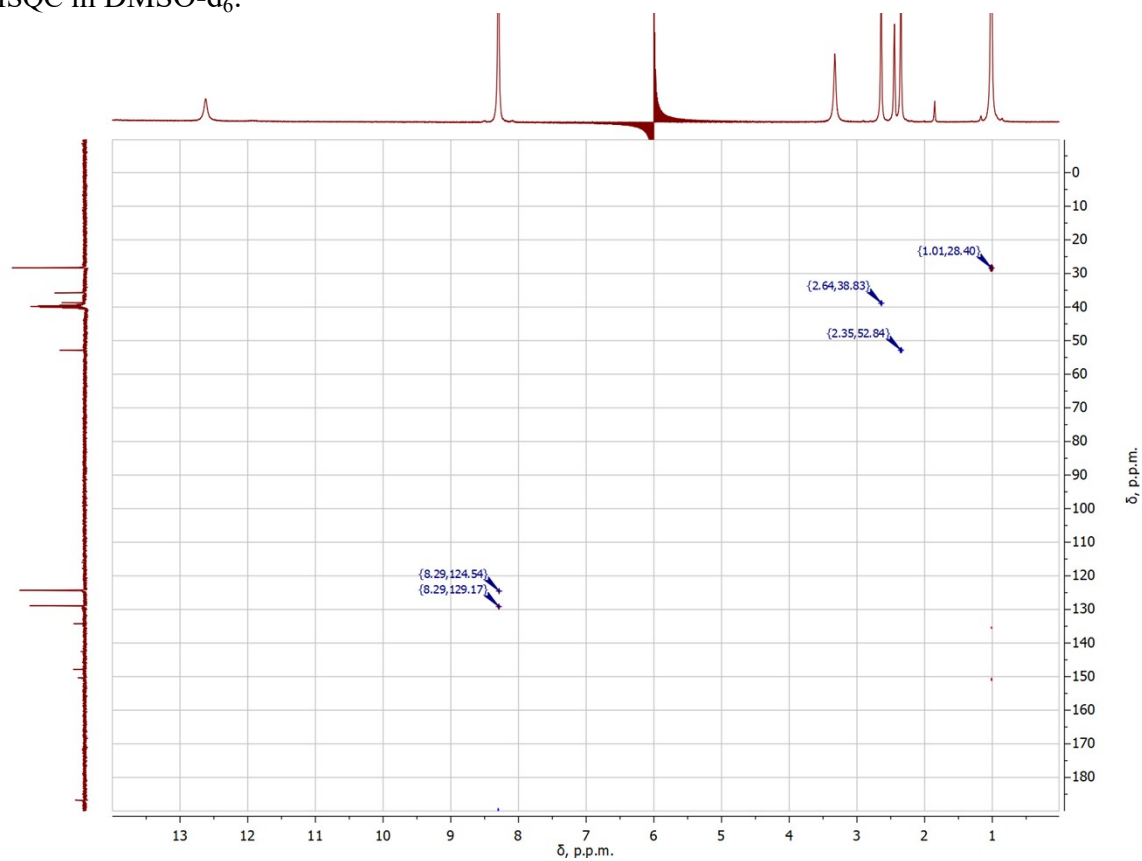
$^1\text{H}$  NMR spectrum in DMSO- $d_6$ :



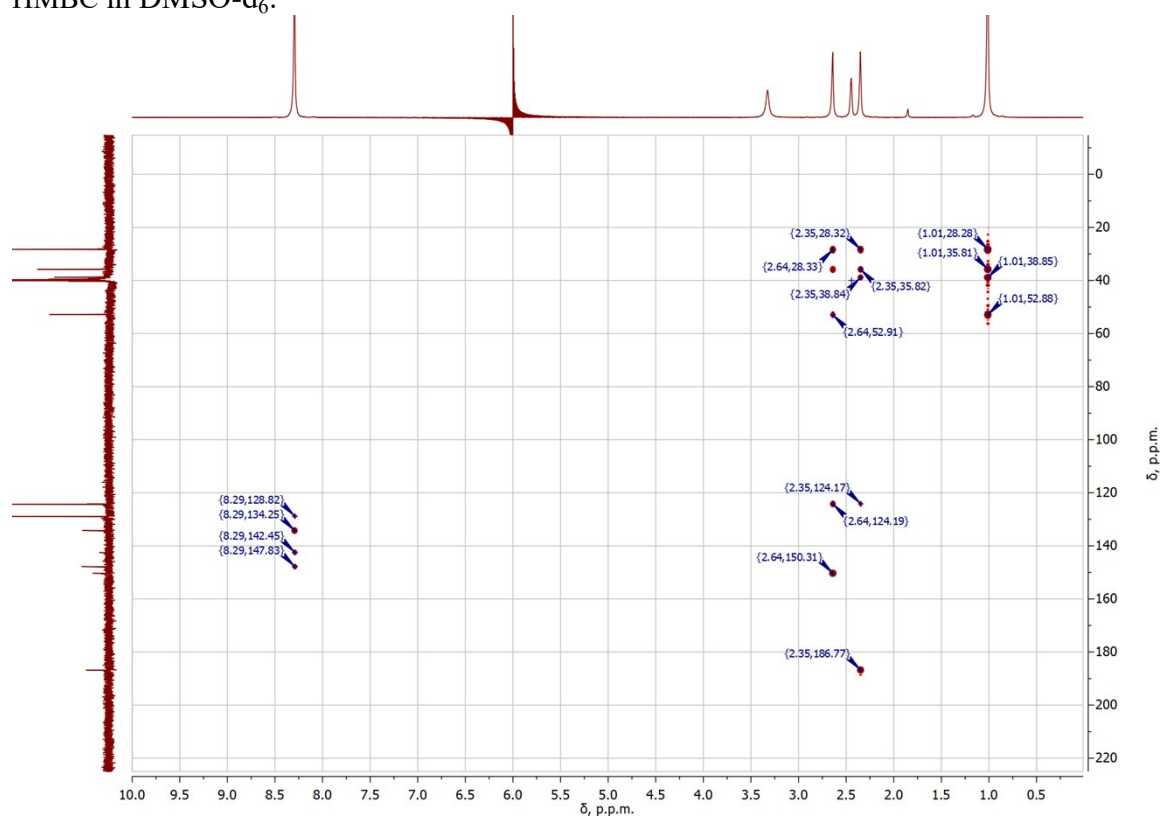
$^{13}\text{C}$  NMR spectrum in DMSO- $d_6$ :



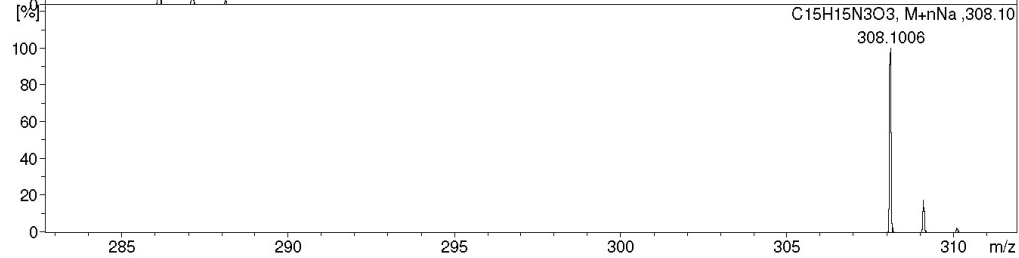
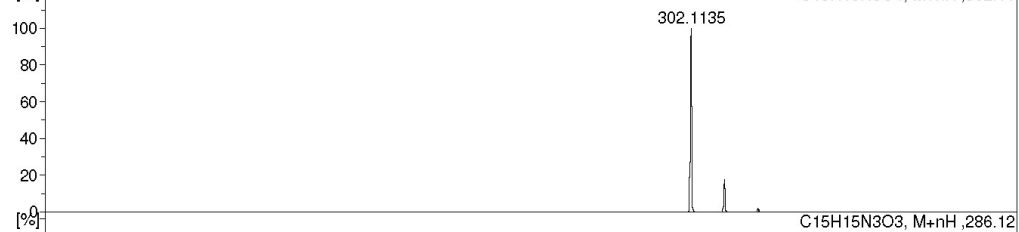
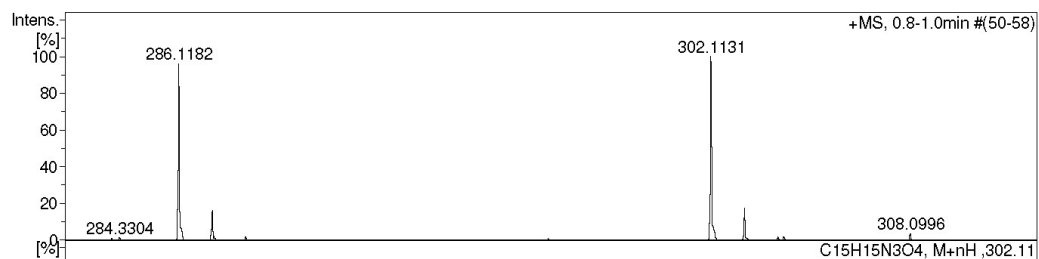
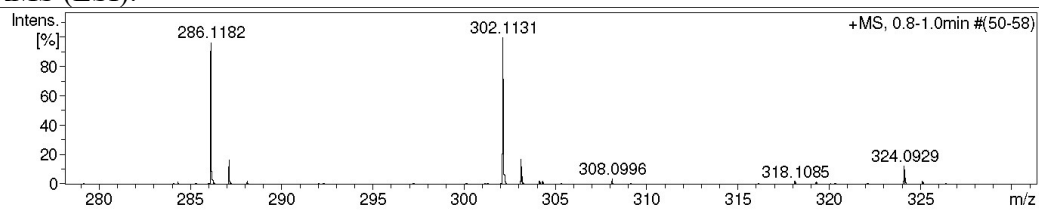
HSQC in DMSO-d<sub>6</sub>:



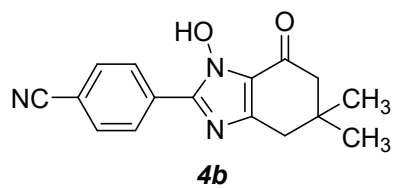
HMBC in DMSO-d<sub>6</sub>:



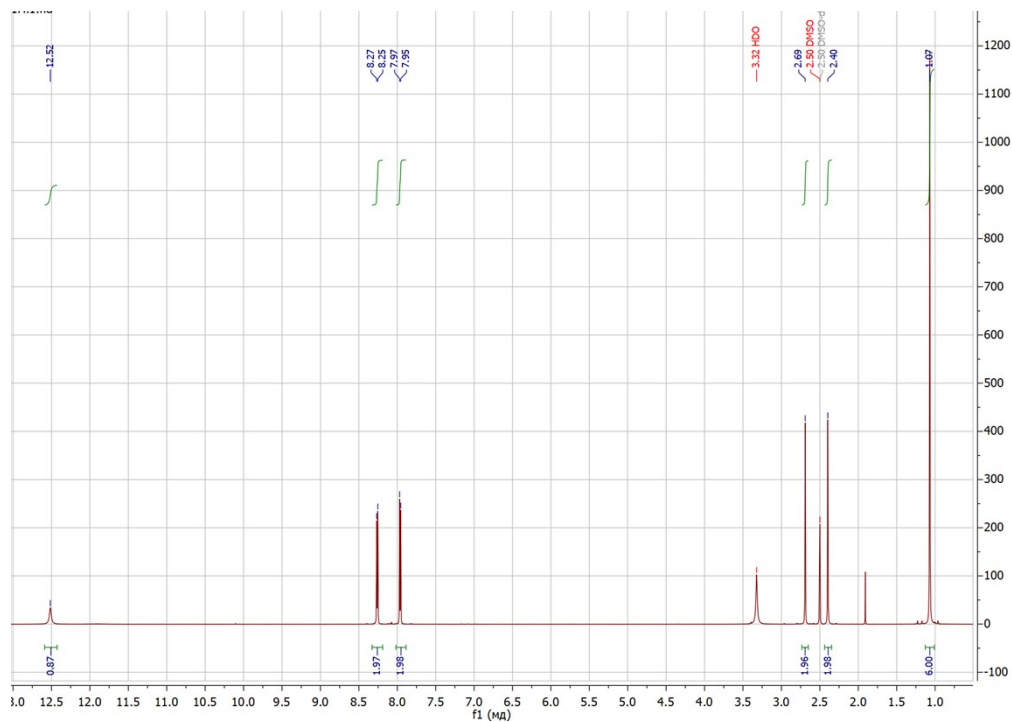
# HRMS (ESI):



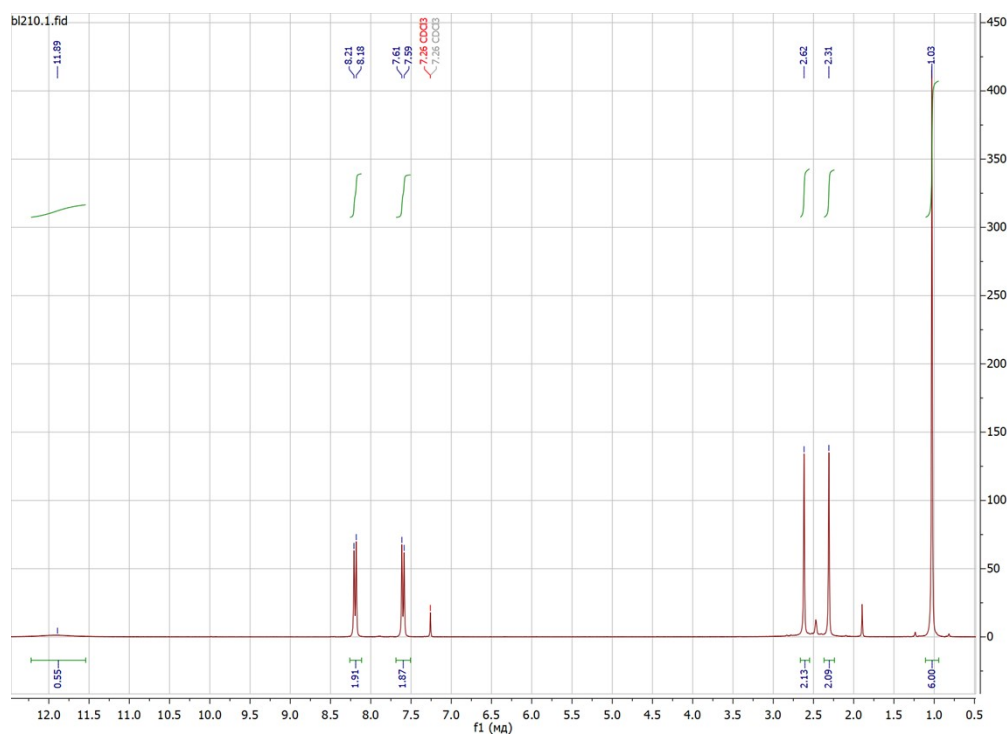
4-(1-hydroxy-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-1H-benzo[d]imidazol-2-yl)benzonitrile (**4b**)



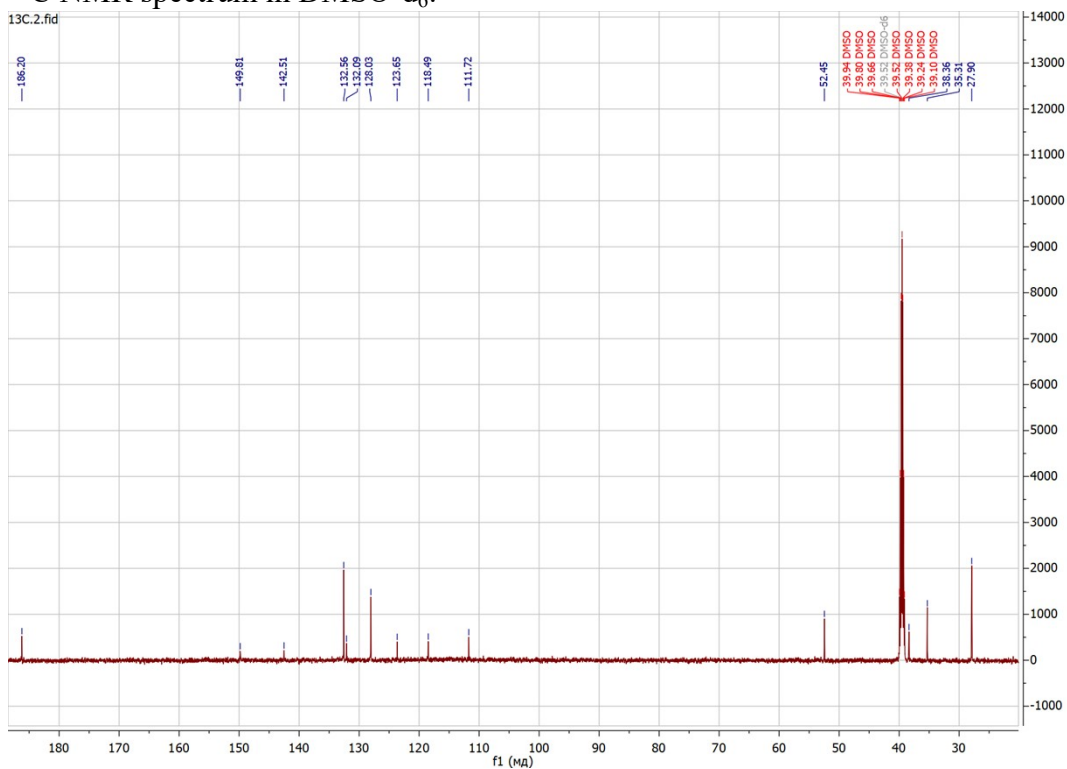
$^1\text{H}$  NMR spectrum in  $\text{DMSO-}d_6$ :



$^1\text{H}$  NMR spectrum in  $\text{CDCl}_3$ :

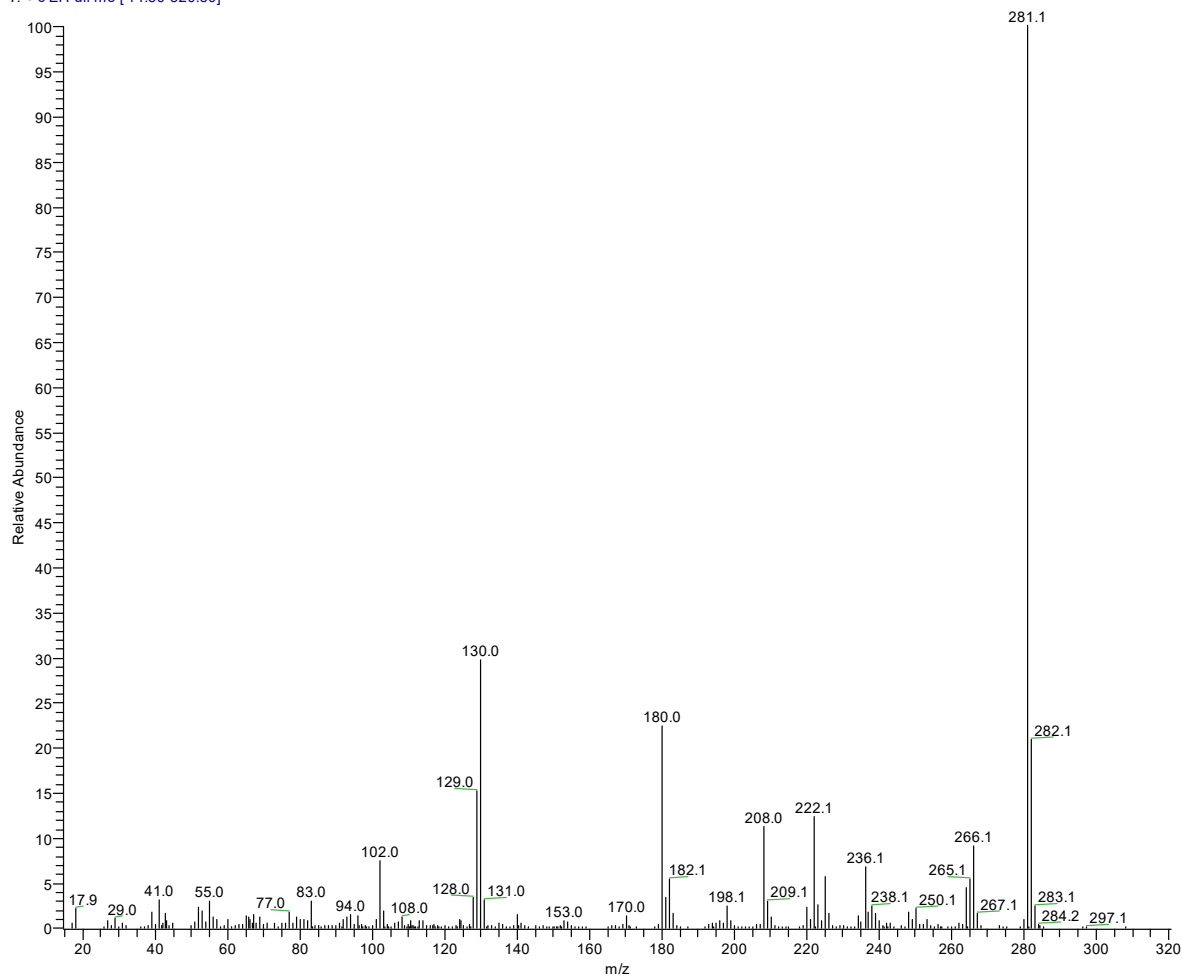


### <sup>13</sup>C NMR spectrum in DMSO-d<sub>6</sub>:

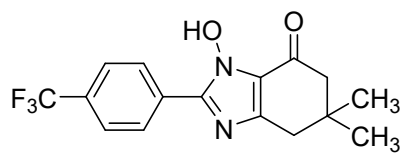


### HRMS (EI):

PANI-164 #4 RT: 0.22 AV: 1 NL: 4.43E6  
T: + c EI Full ms [ 14.50-320.50]

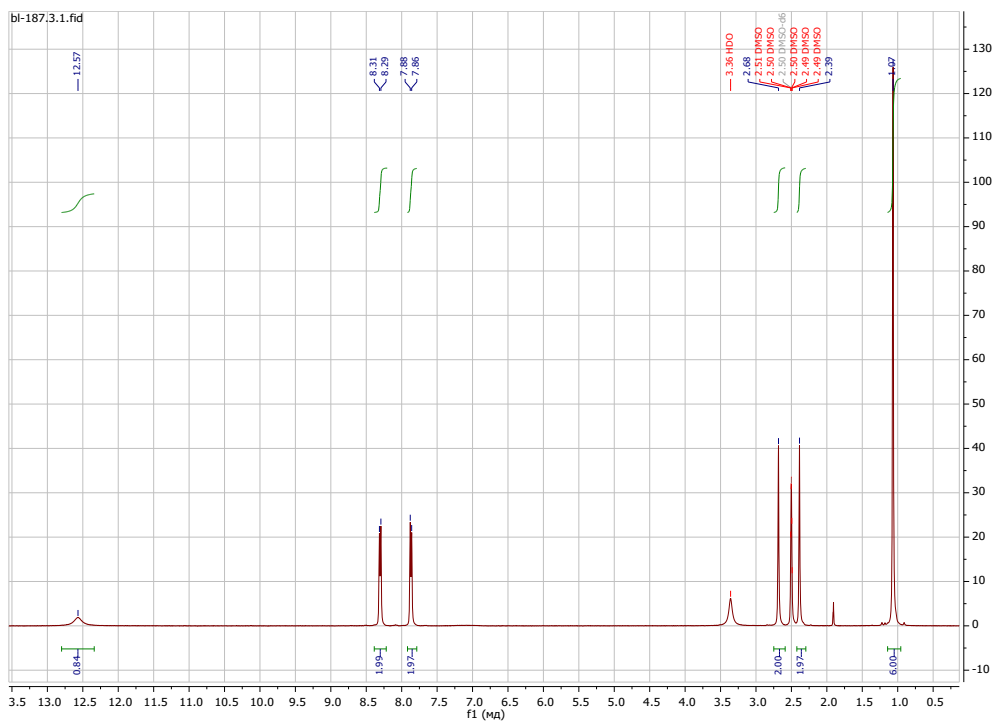


3-Hydroxy-6,6-dimethyl-2-(4-(trifluoromethyl)phenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one (**4c**)

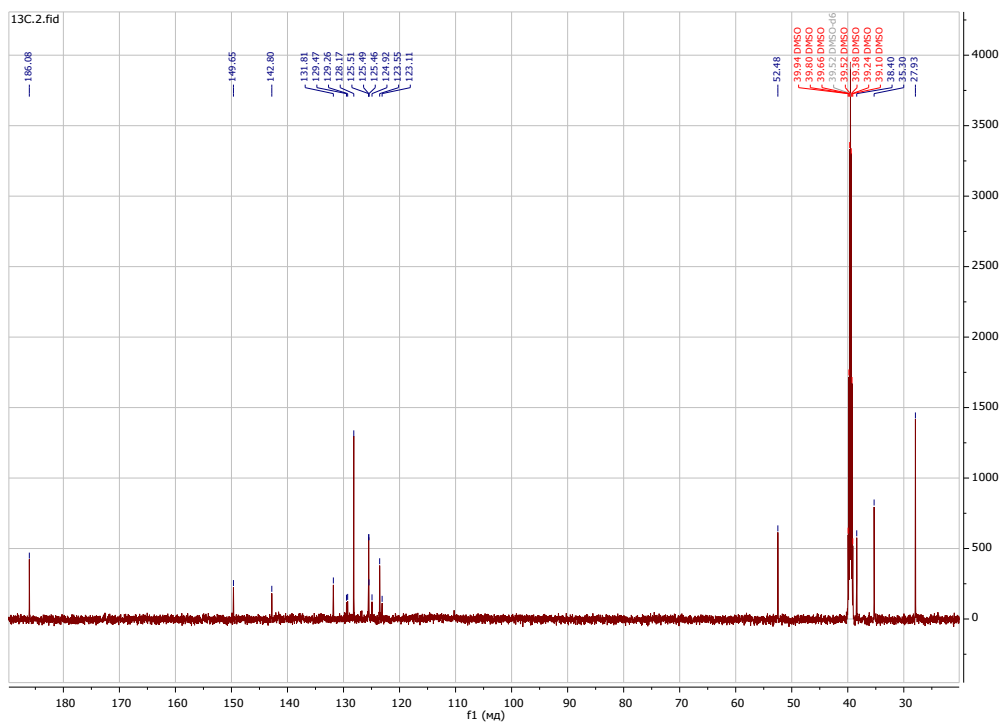


**4c**

$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



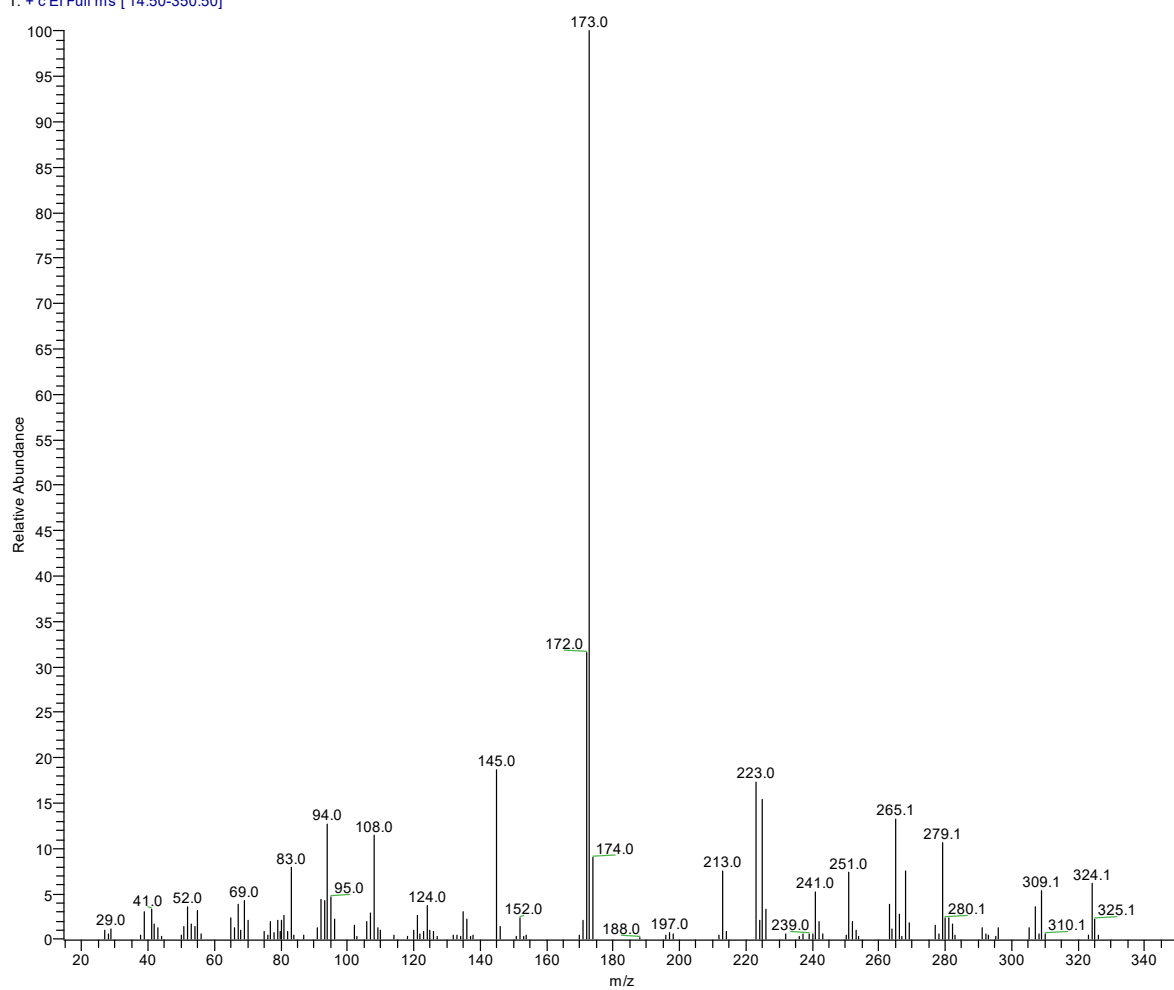
$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



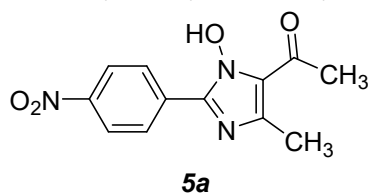


# HRMS (EI):

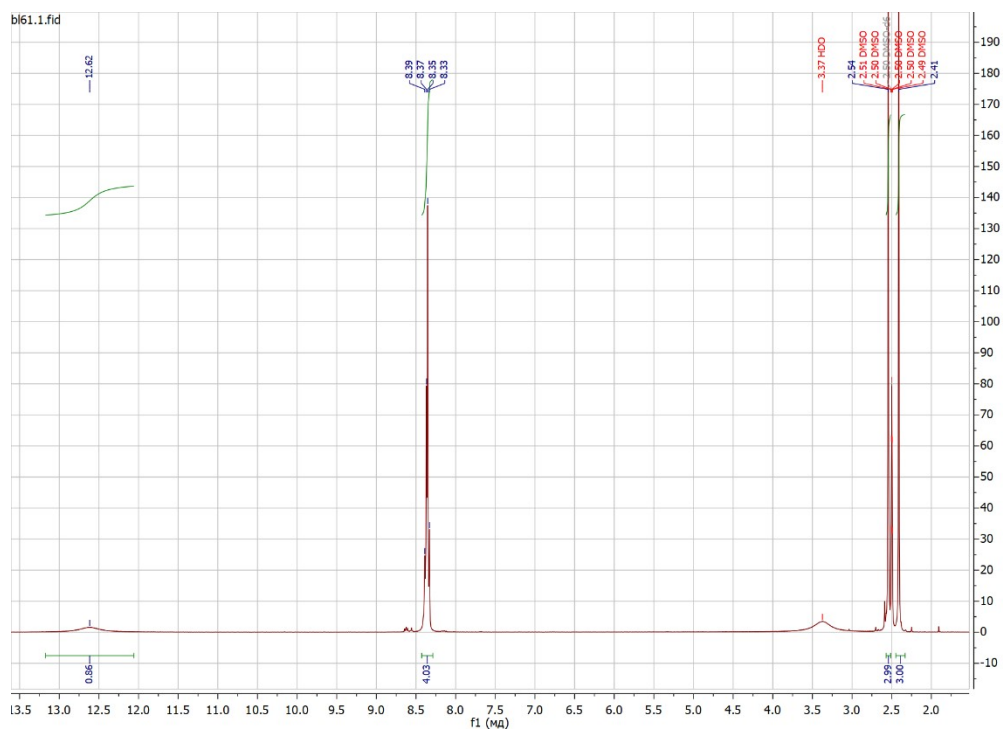
PANI-152\_230804151708 #4 RT: 0.22 AV: 1 NL: 5.93E5  
T: + c EI Full ms [ 14.50-350.50]



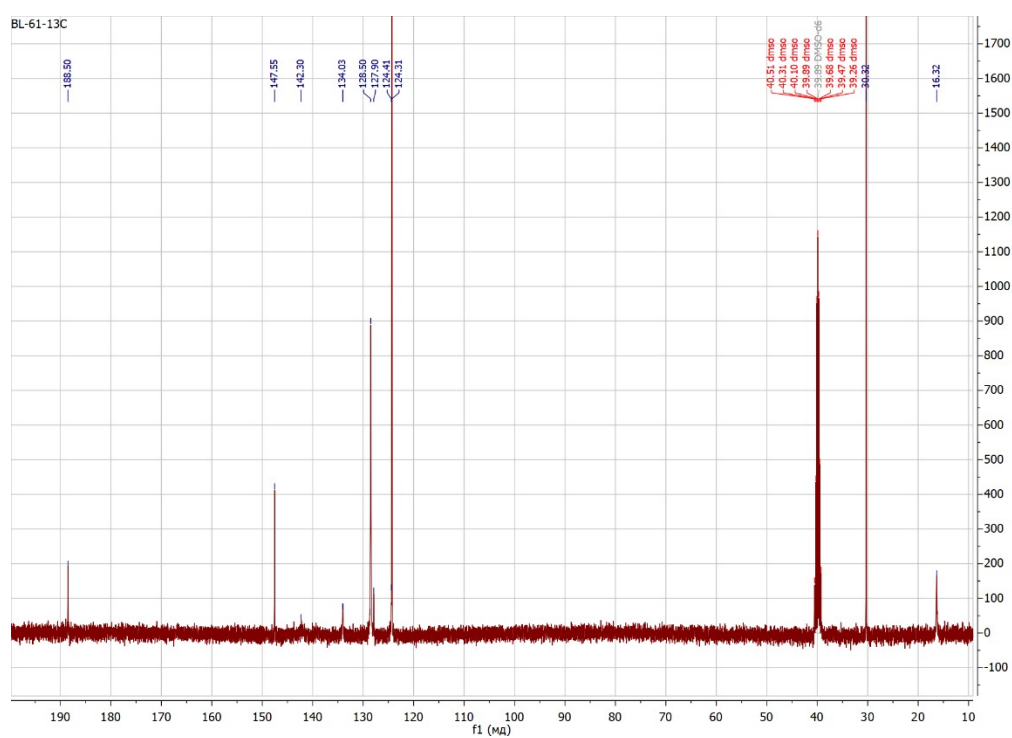
*1-[1-Hydroxy-4-methyl-2-(4-nitrophenyl)-1H-imidazol-5-yl]ethanone (5a).*



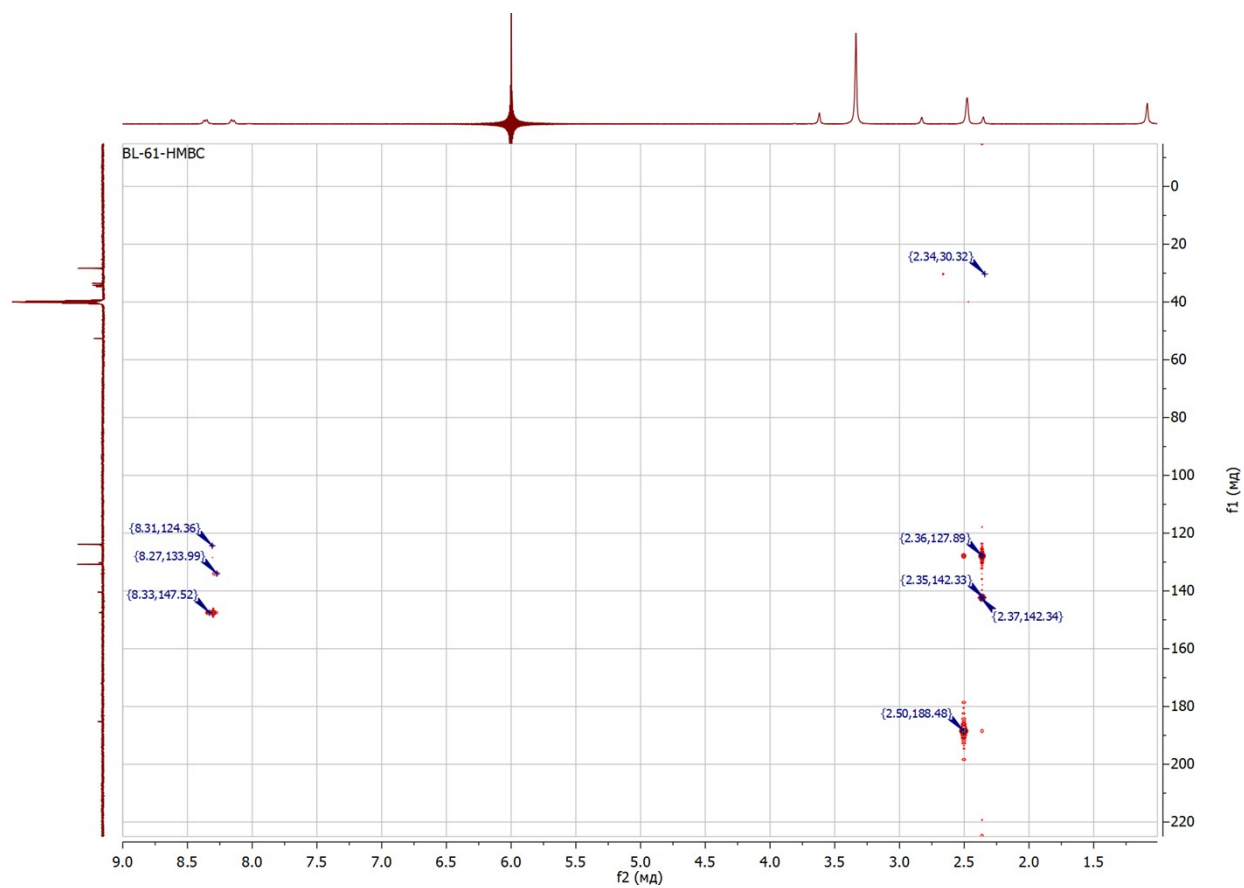
$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



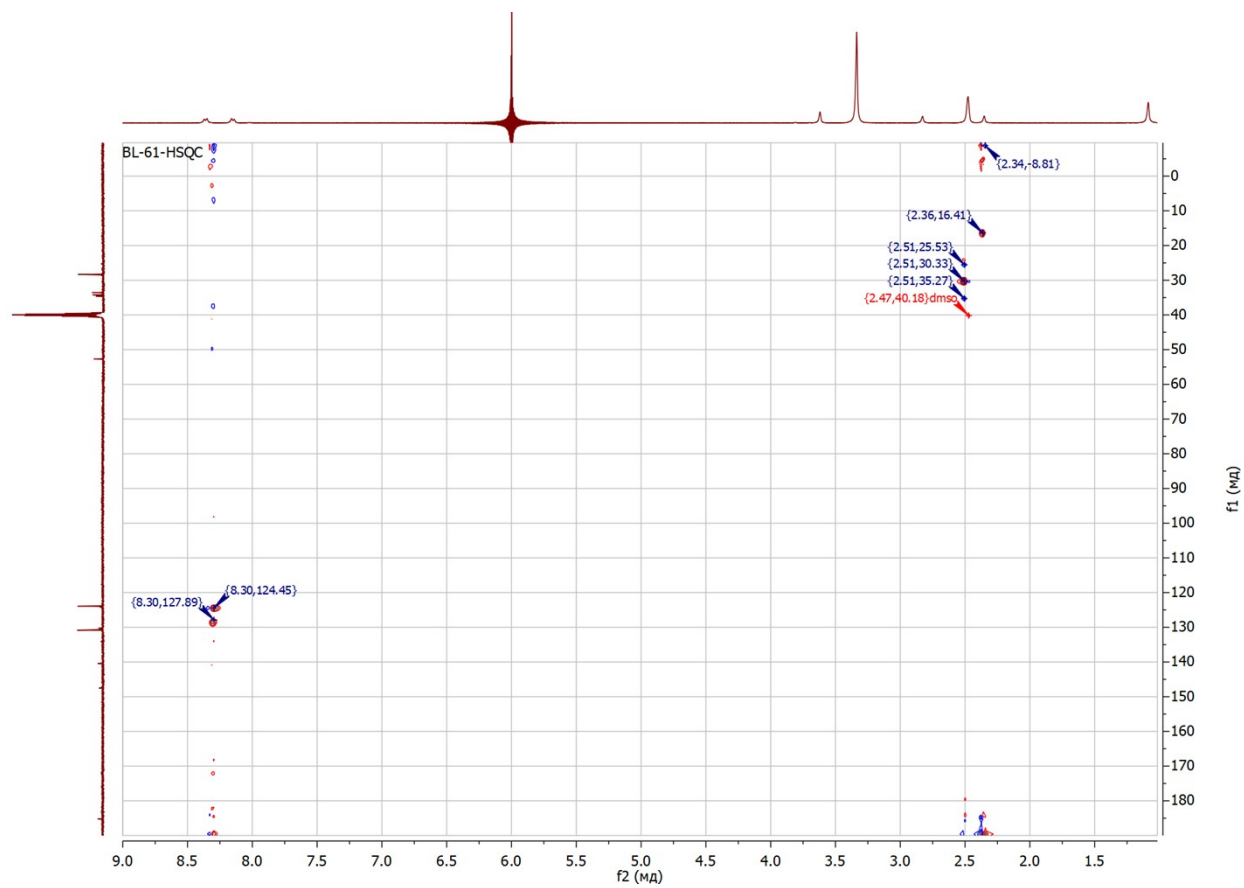
$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



HMBC in DMSO-d<sub>6</sub>:

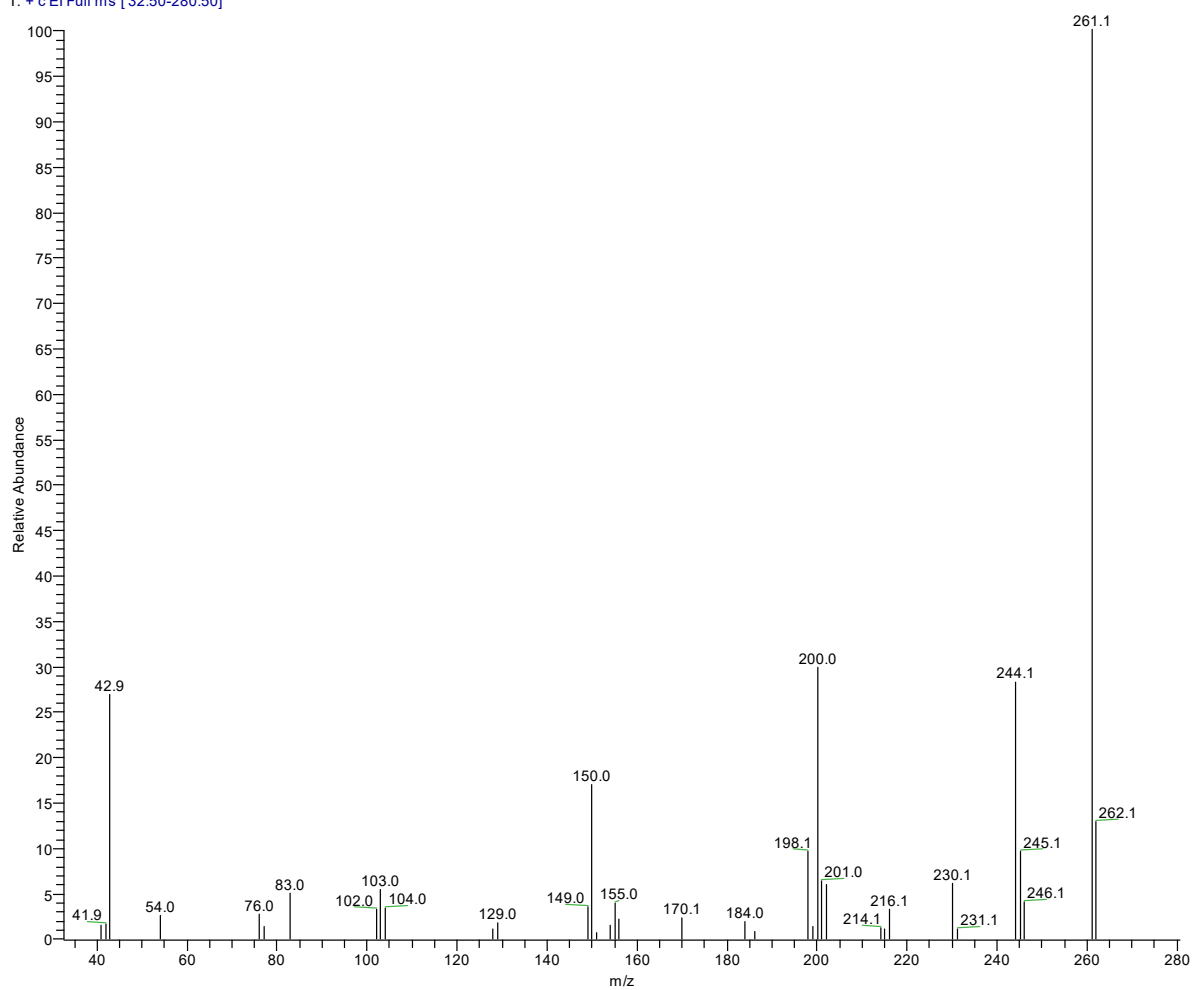


HSQC in DMSO-d<sub>6</sub>:

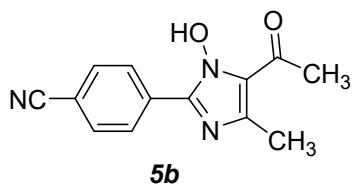


# HRMS (EI):

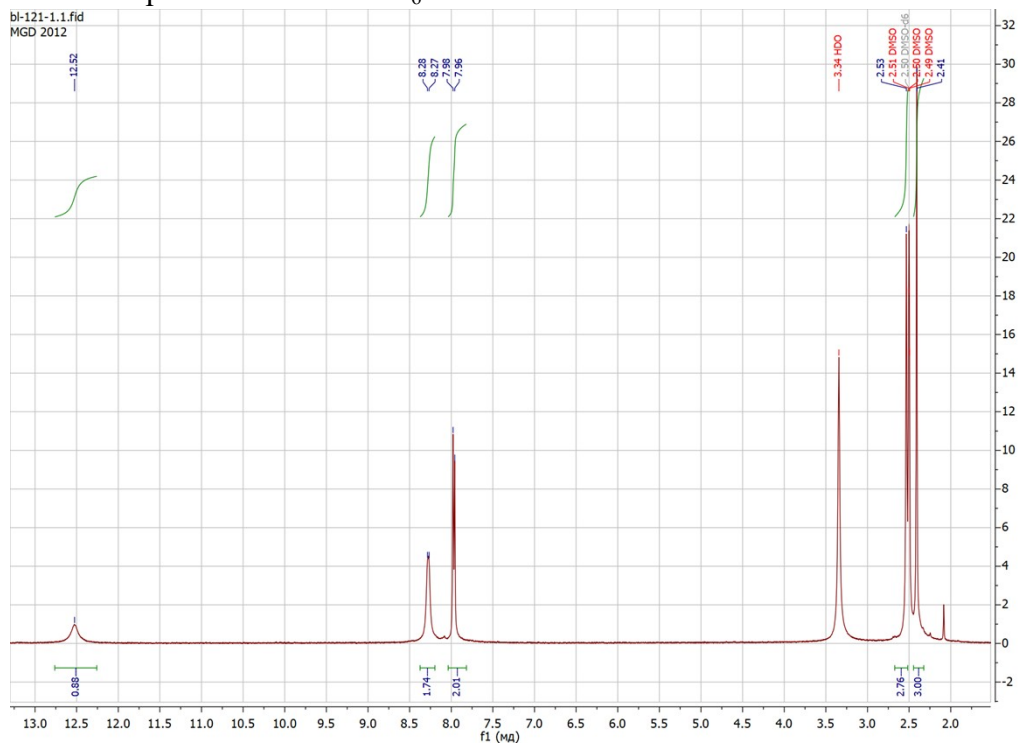
PANI-72 #7 RT: 0.28 AV: 1 NL: 1.38E5  
T: + c EI Full ms [ 32.50-280.50]



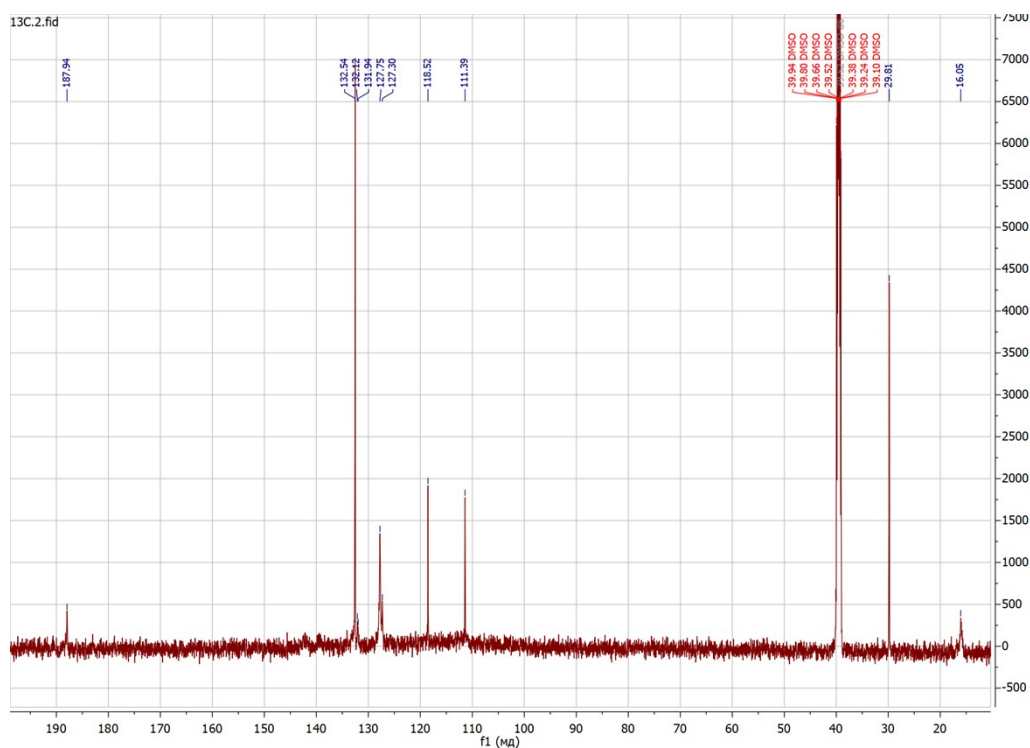
4-(5-Acetyl-1-hydroxy-4-methyl-1H-imidazol-2-yl)benzonitrile (**5b**)



$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :

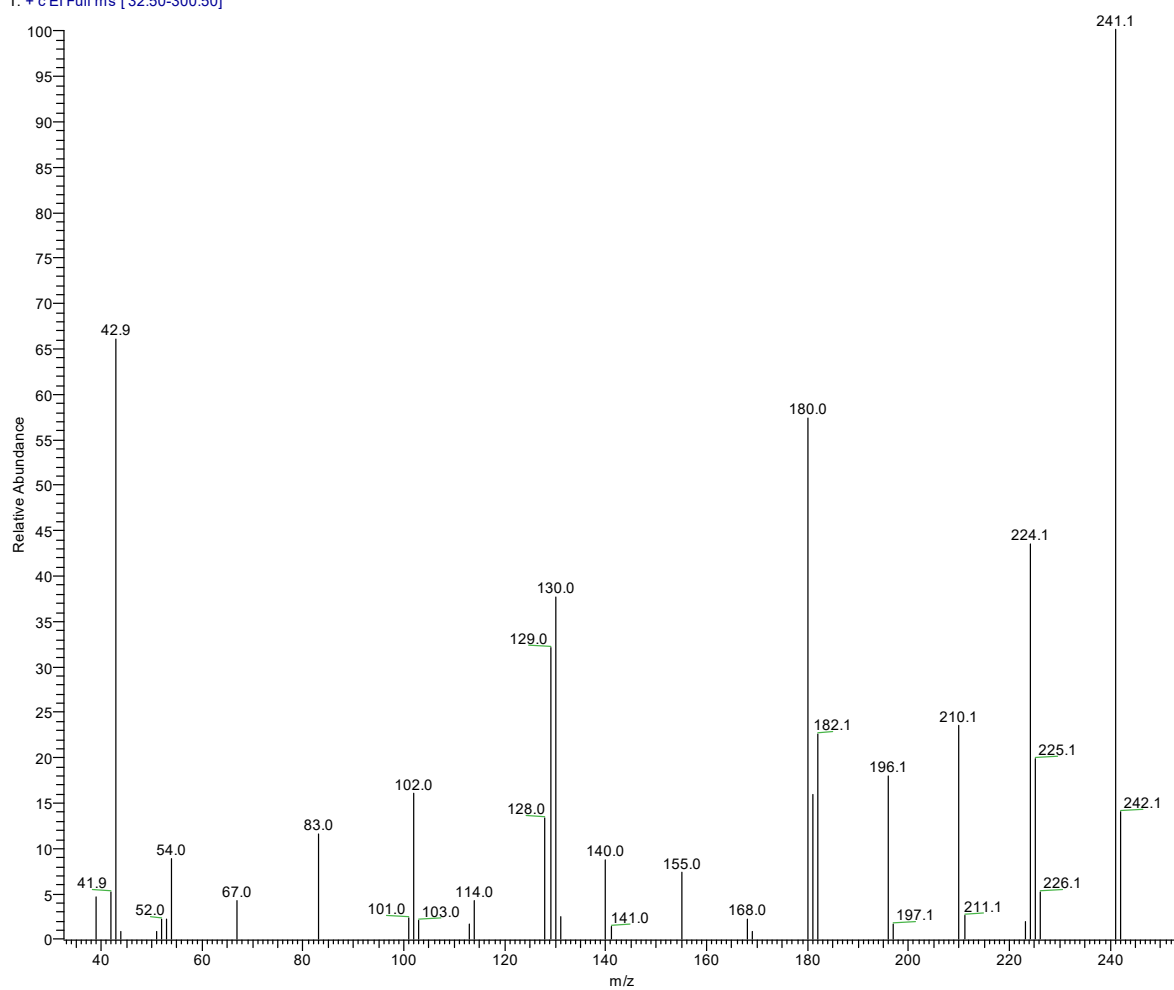


$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :

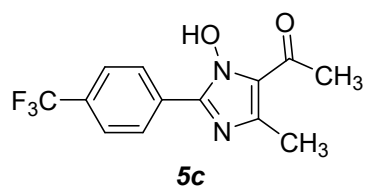


# HRMS (EI):

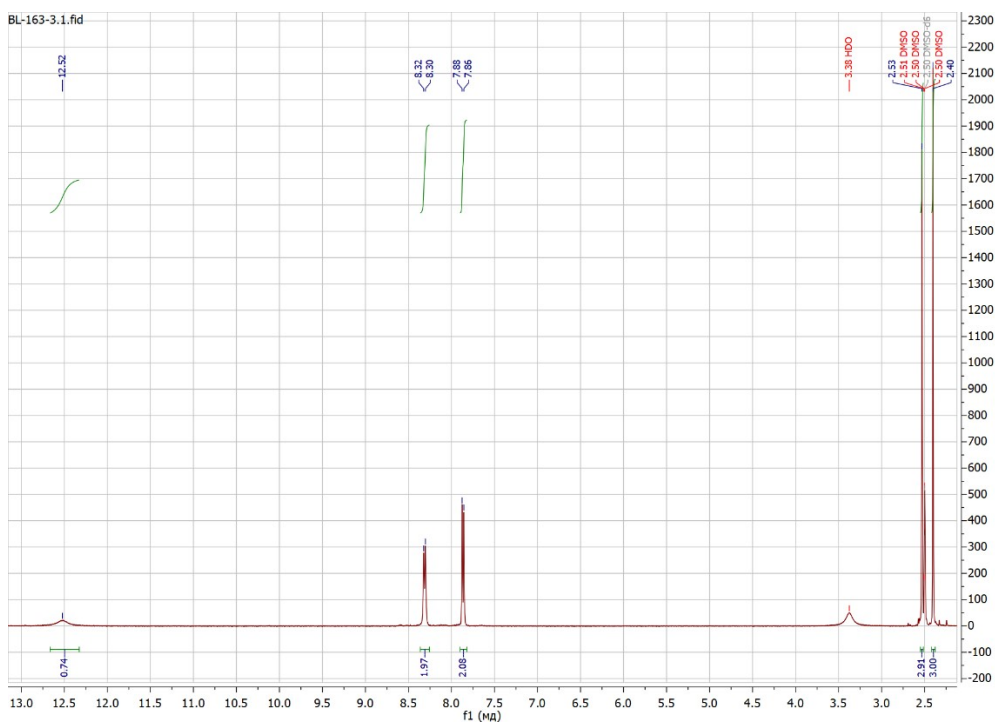
PANI-116\_230807133817 #2 RT: 0.06 AV: 1 NL: 1.15E5  
T: + c EI Full ms [ 32.50-300.50]



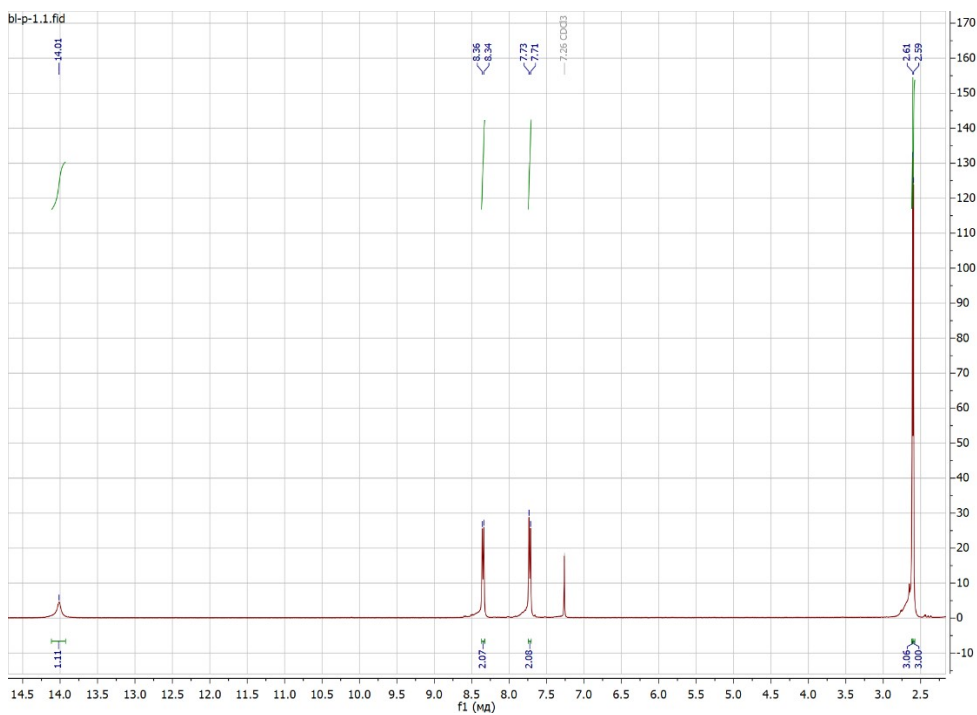
*1-(1-Hydroxy-4-methyl-2-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)ethan-1-one (5c)*



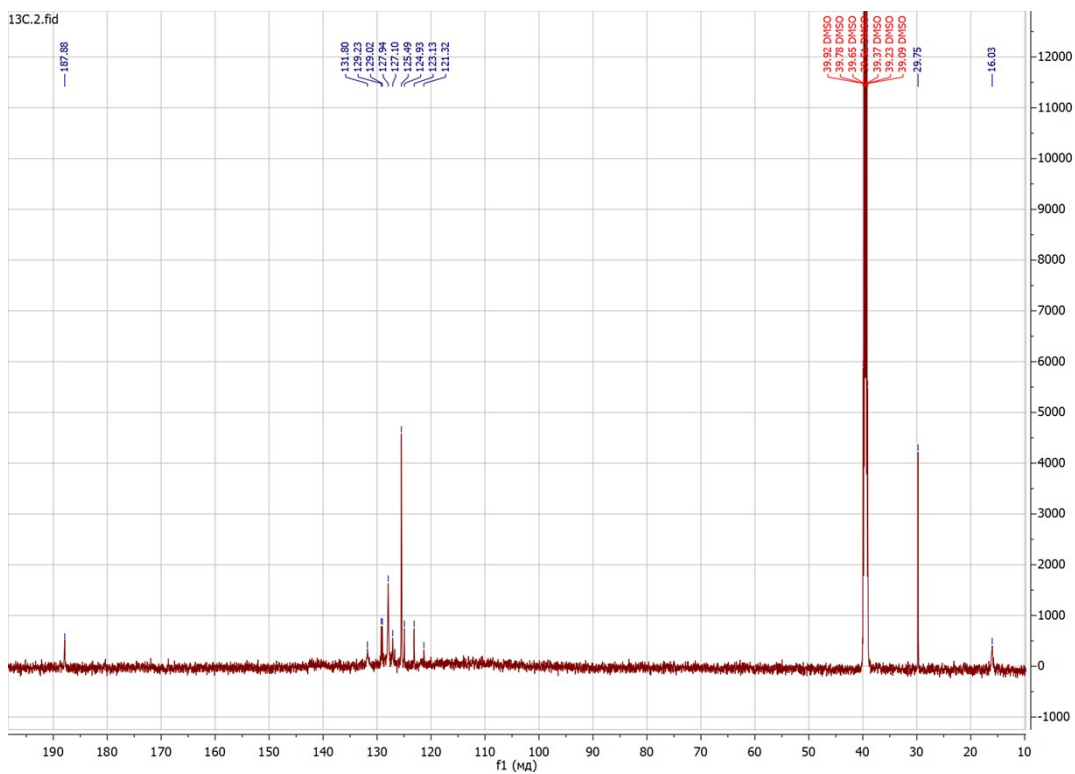
$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



$^1\text{H}$  NMR spectrum in  $\text{CDCl}_3$ :

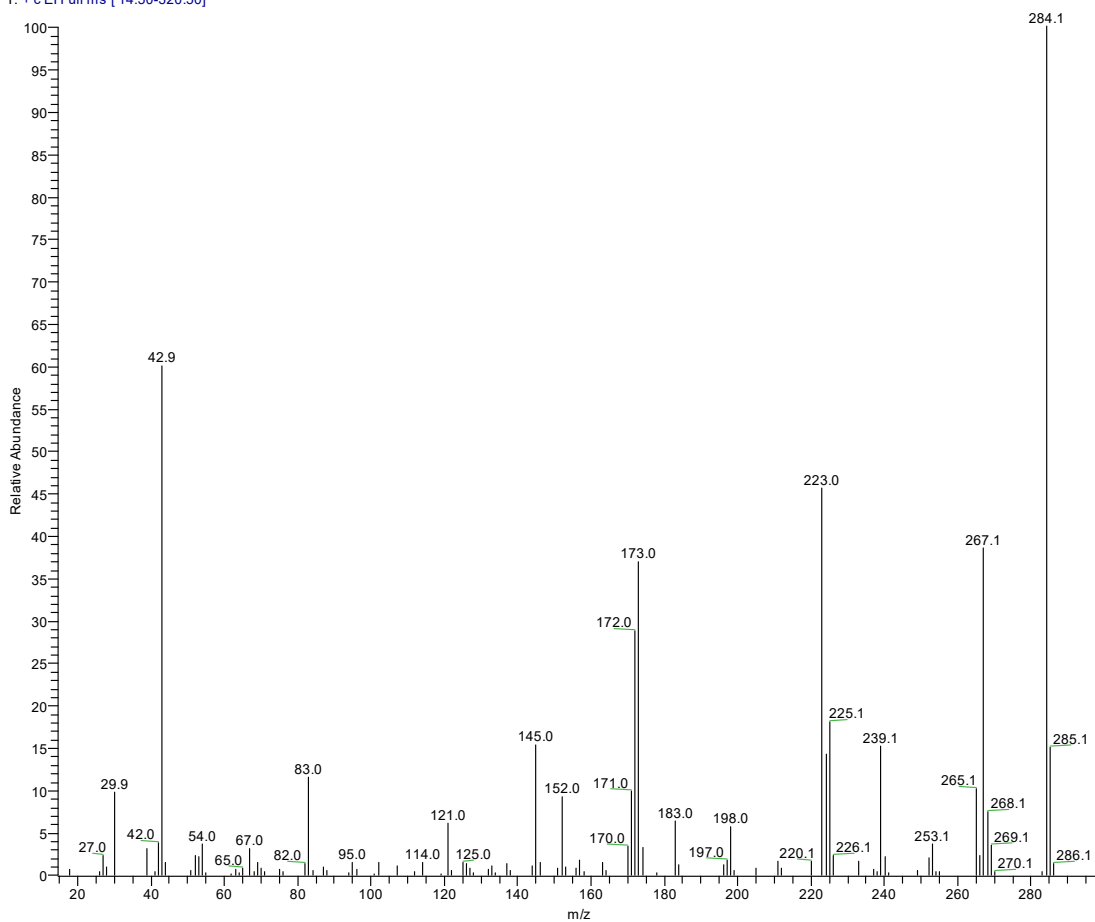


### $^{13}\text{C}$ NMR spectrum in $\text{DMSO-d}_6$ :



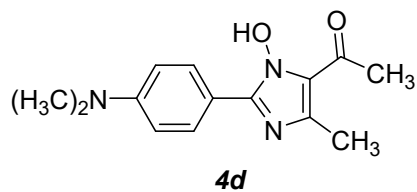
### HRMS (EI):

PANI-114 #6 RT: 0.36 AV: 1 NL: 7.74E5  
T: +c EI Full ms [ 14.50-320.50]

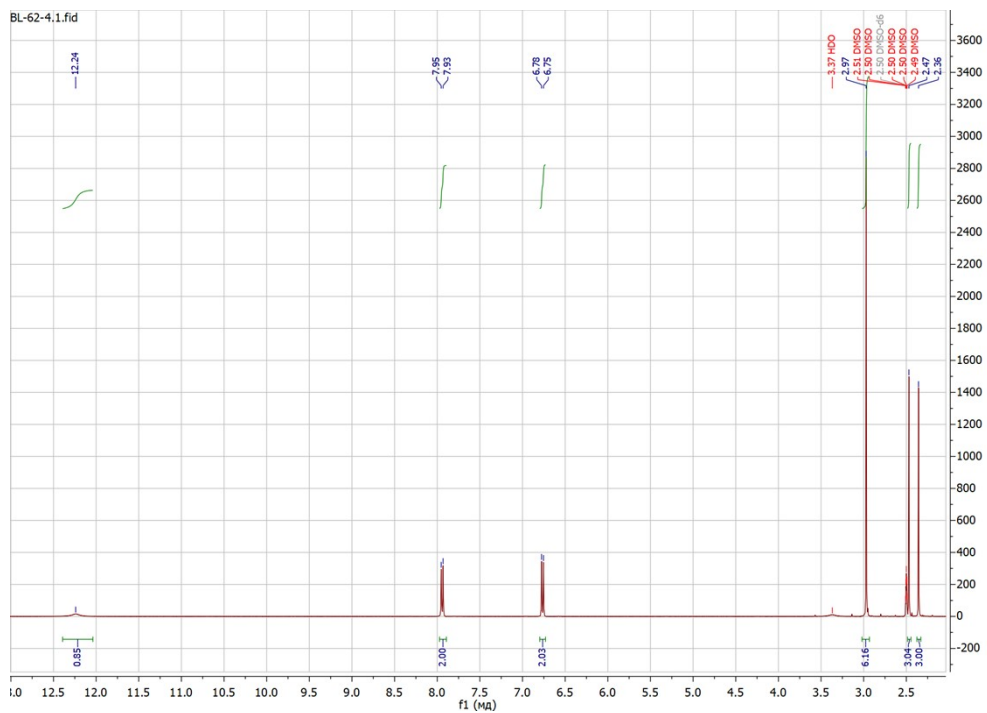




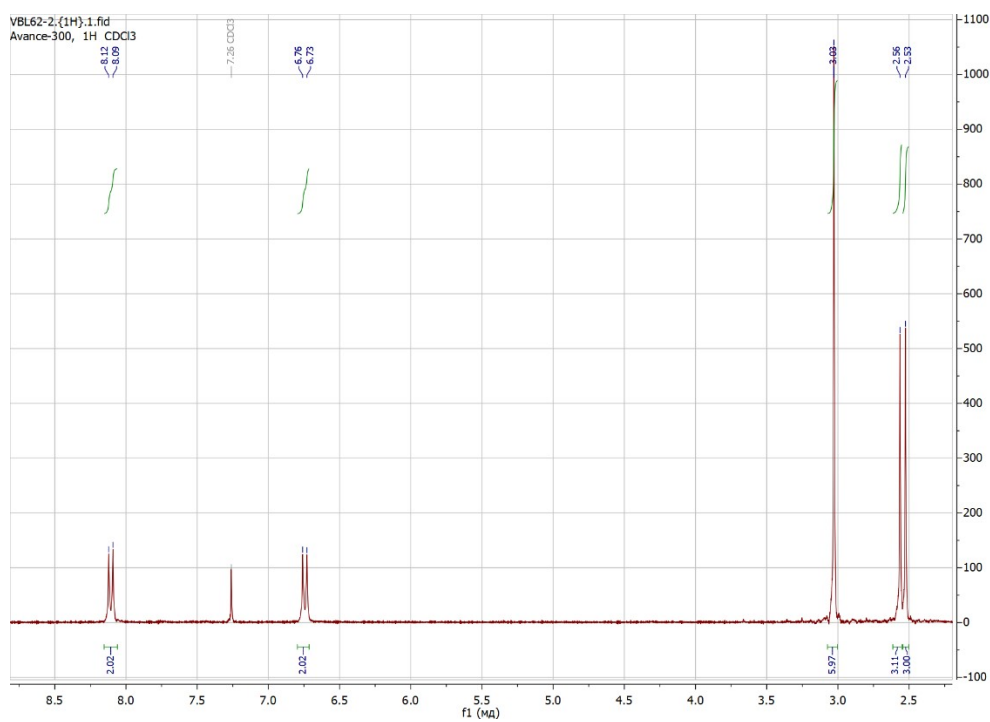
*1-(2-(4-(Dimethylamino)phenyl)-1-hydroxy-4-methyl-1H-imidazol-5-yl)ethan-1-one (5d)*



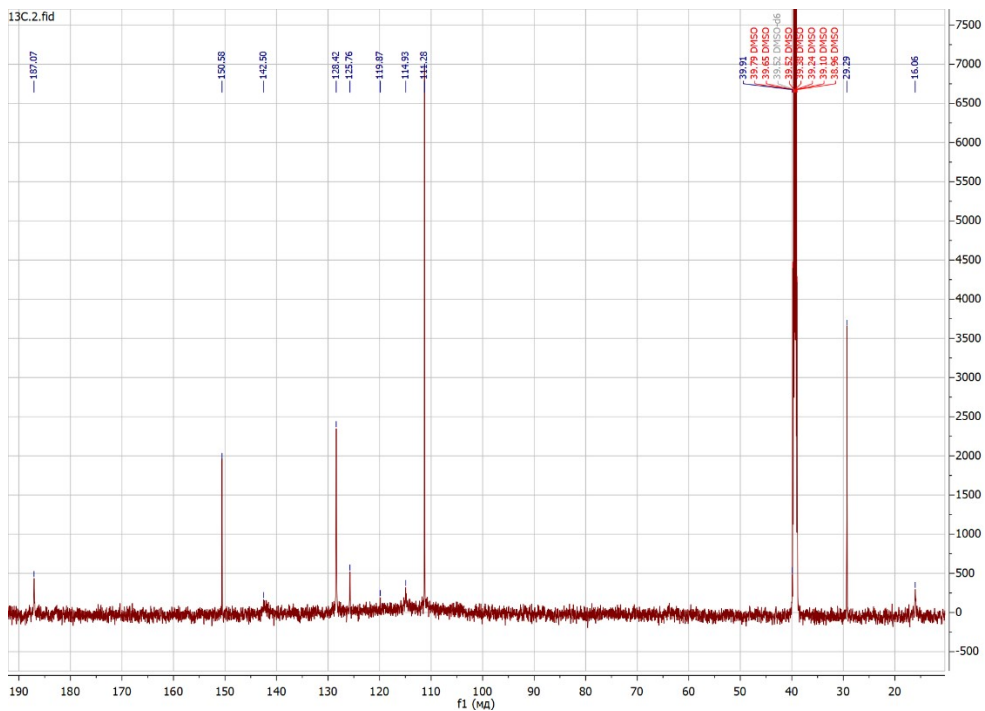
<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:



<sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>:

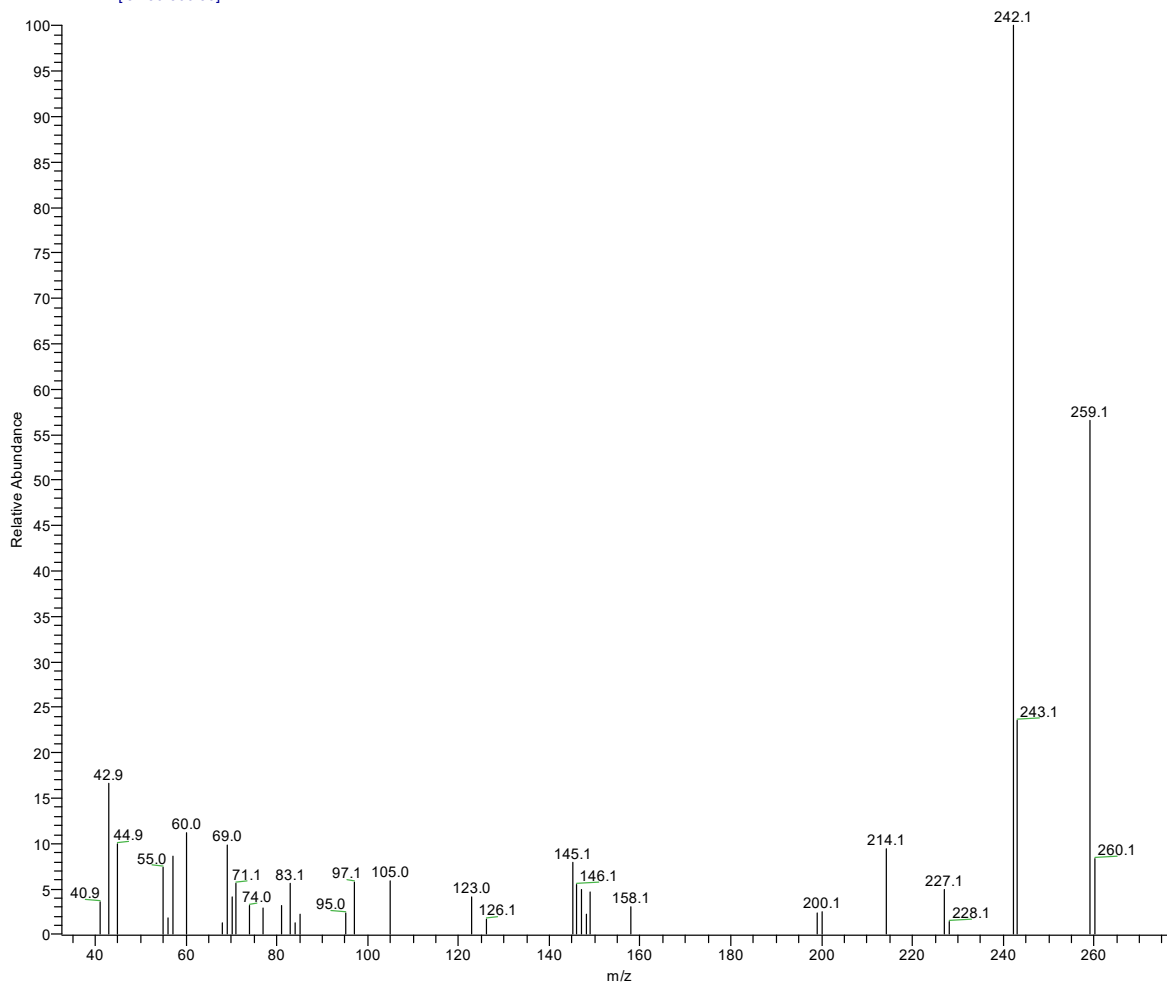


### $^{13}\text{C}$ NMR spectrum in $\text{DMSO-d}_6$ :

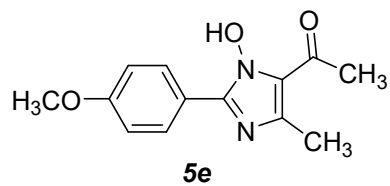


### HRMS (EI):

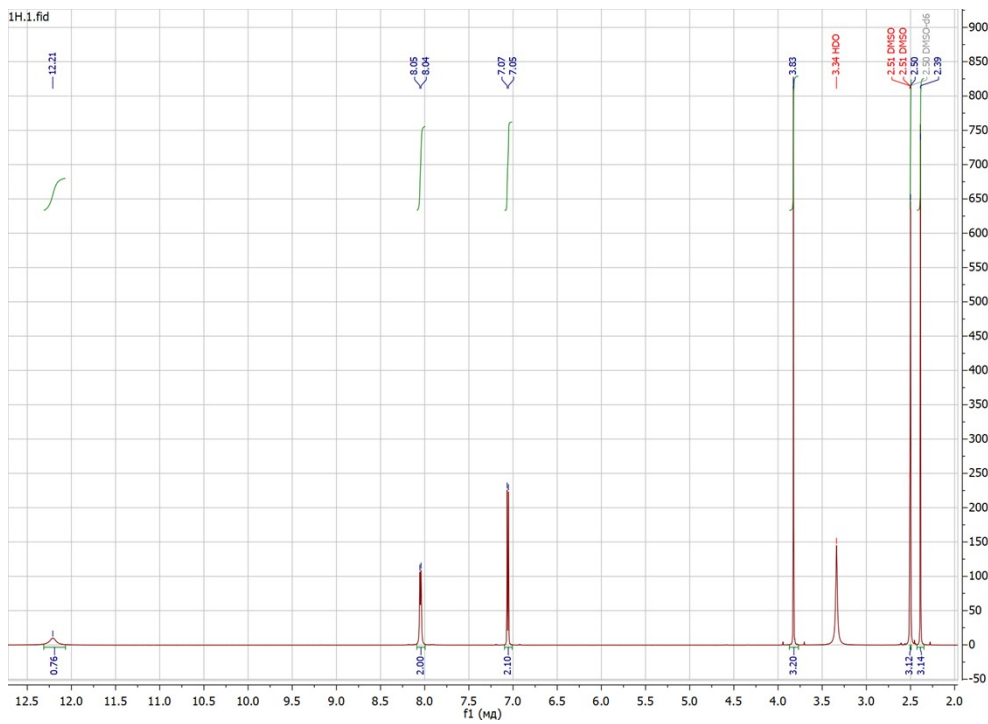
PANI-73 #5 RT: 0.21 AV: 1 NL: 9.08E4  
T: + c EI Full ms [ 32.50-300.50]



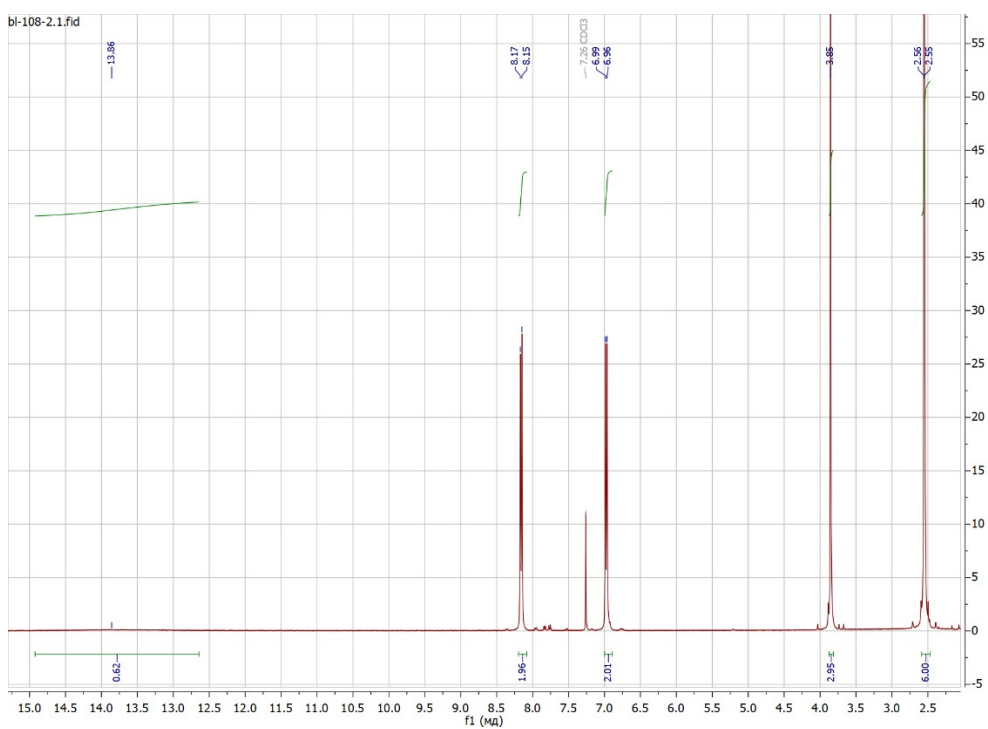
*1-(1-Hydroxy-2-(4-methoxyphenyl)-4-methyl-1H-imidazol-5-yl)ethan-1-one (5e)*



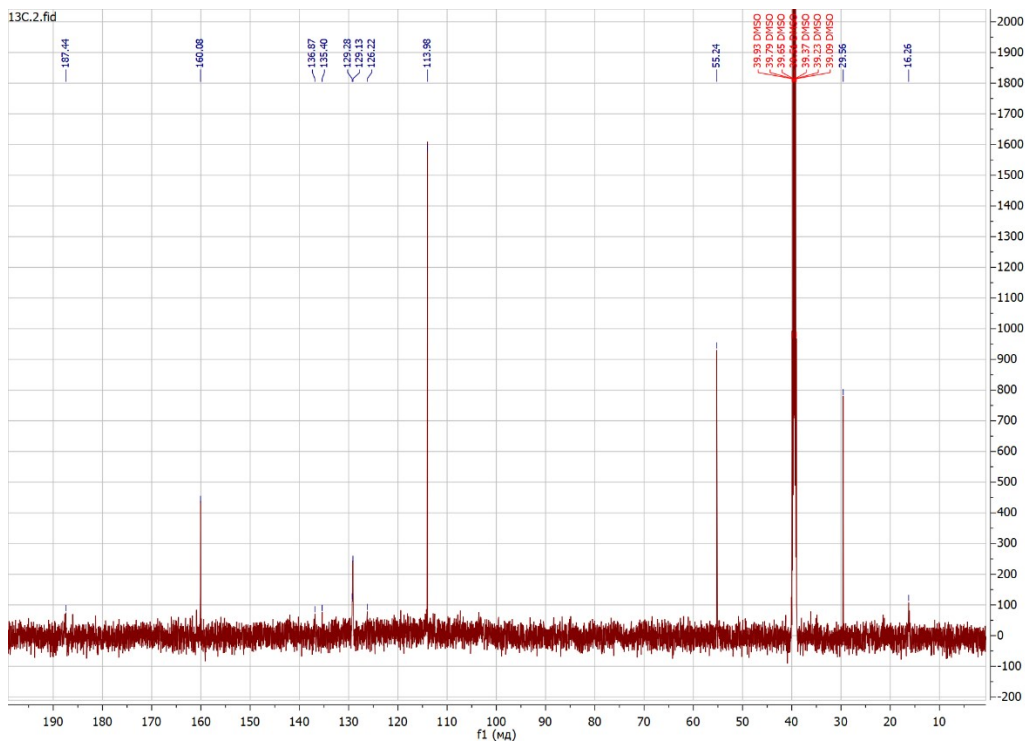
<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:



<sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>:

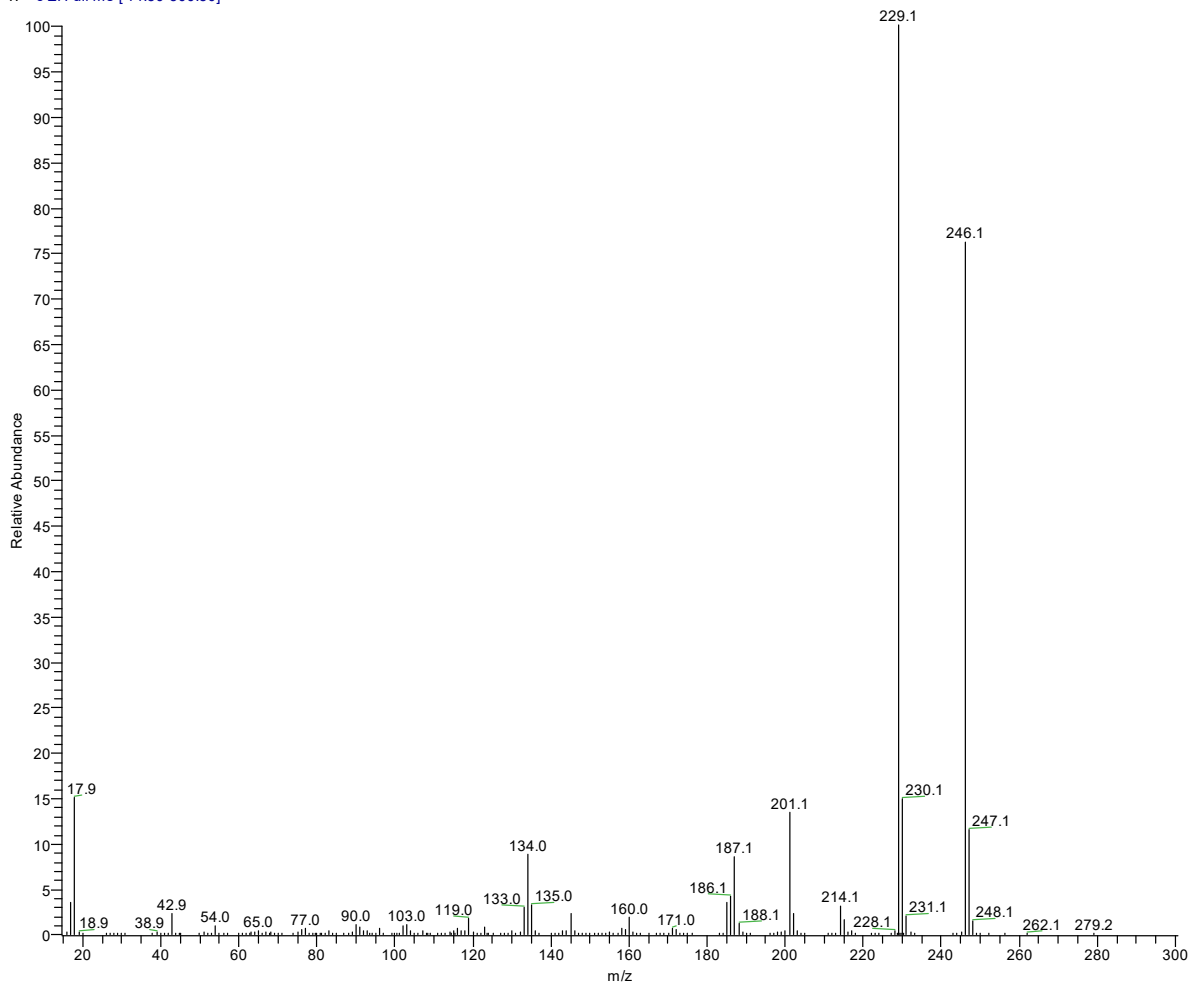


### $^{13}\text{C}$ NMR spectrum in $\text{DMSO-d}_6$ :

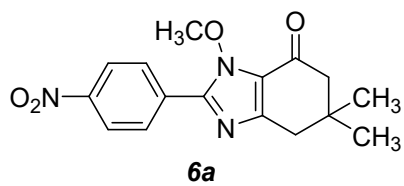


### HRMS (EI):

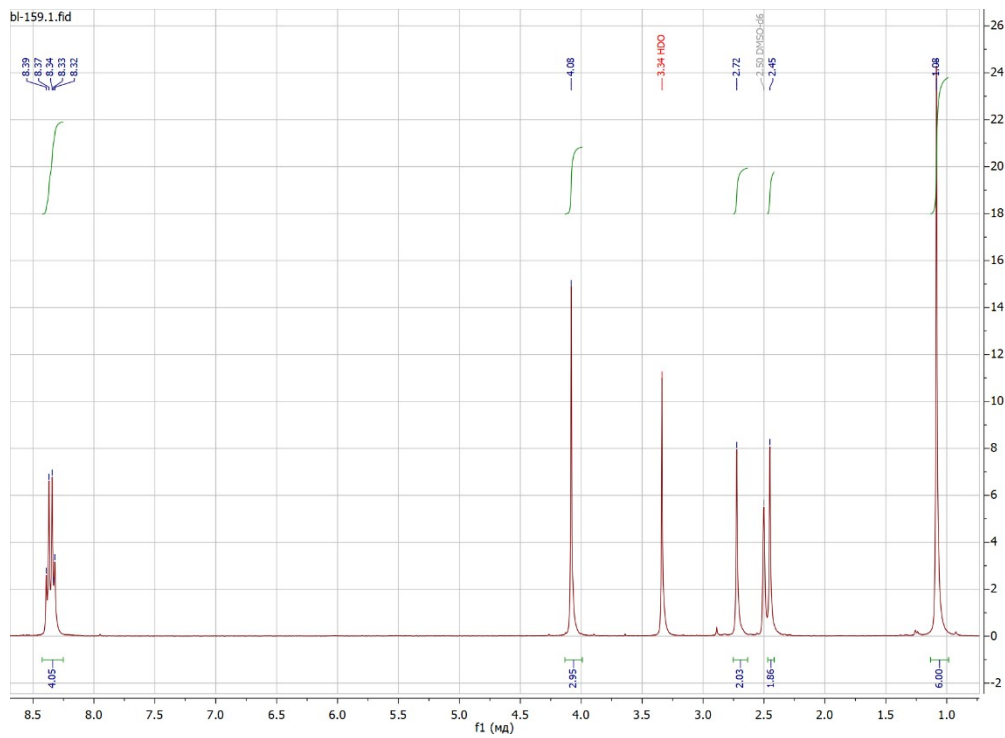
PANI-153 #9 RT: 0.56 AV: 1 NL: 2.14E7  
T: + c EI Full ms [ 14.50-300.50]



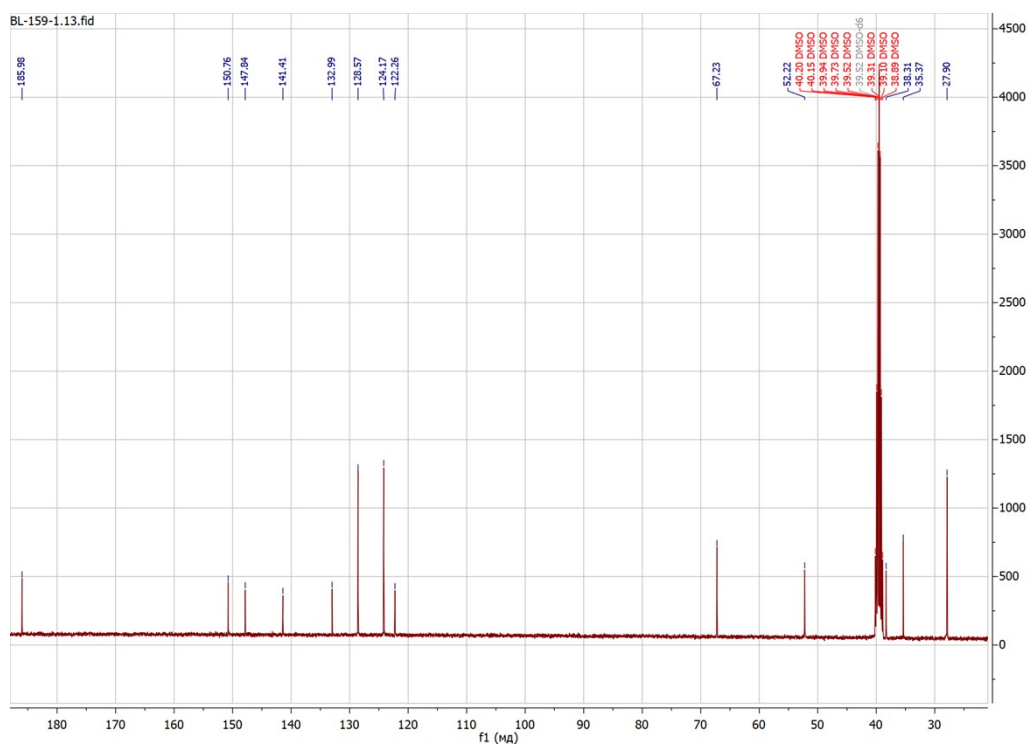
3-Methoxy-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one (**6a**).



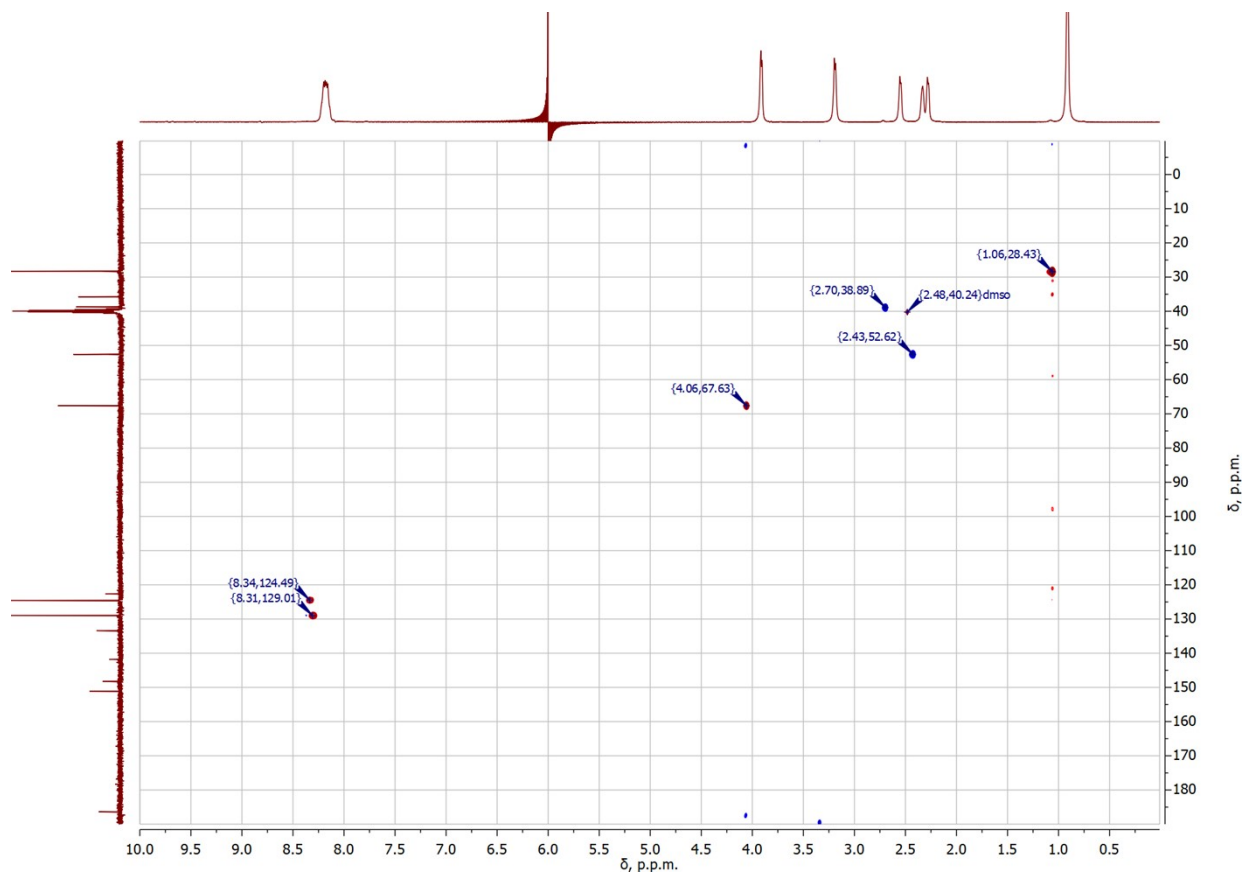
$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



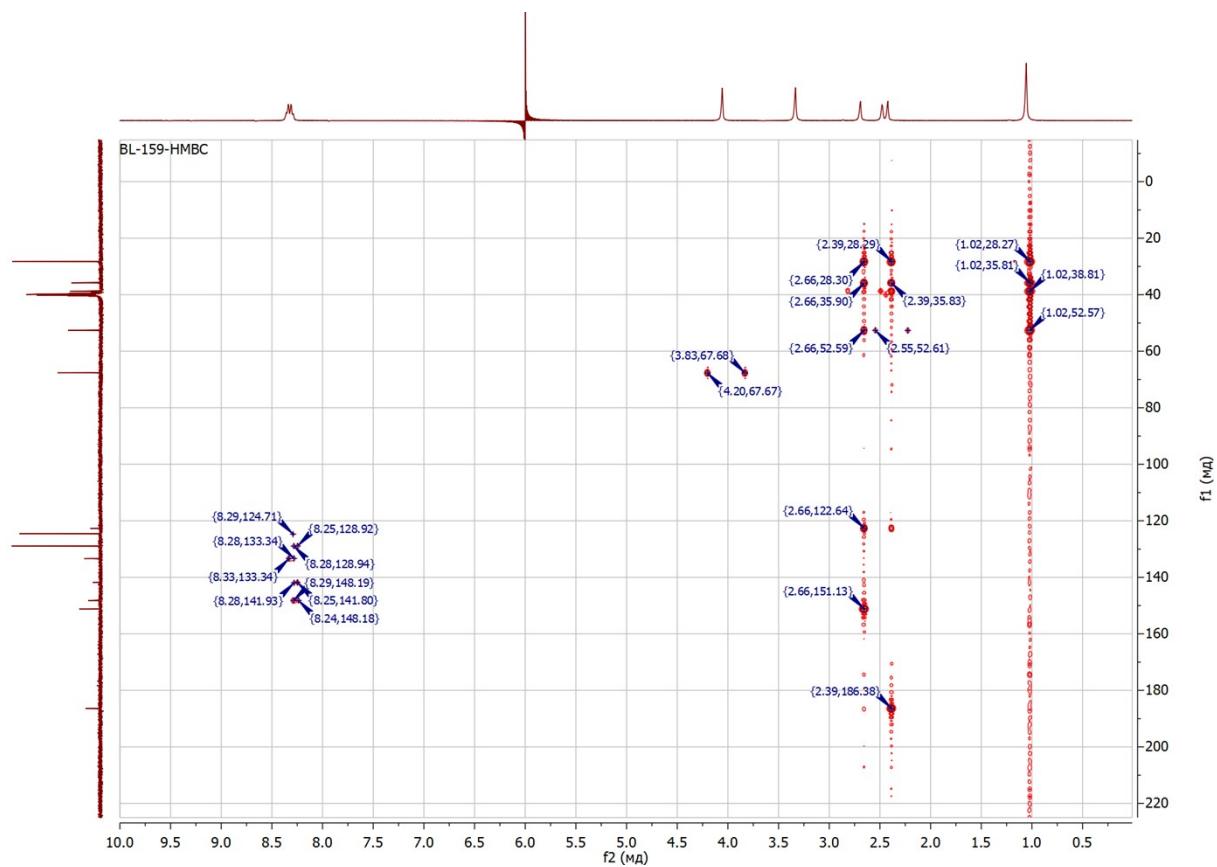
$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



HSQC in DMSO-d<sub>6</sub>:

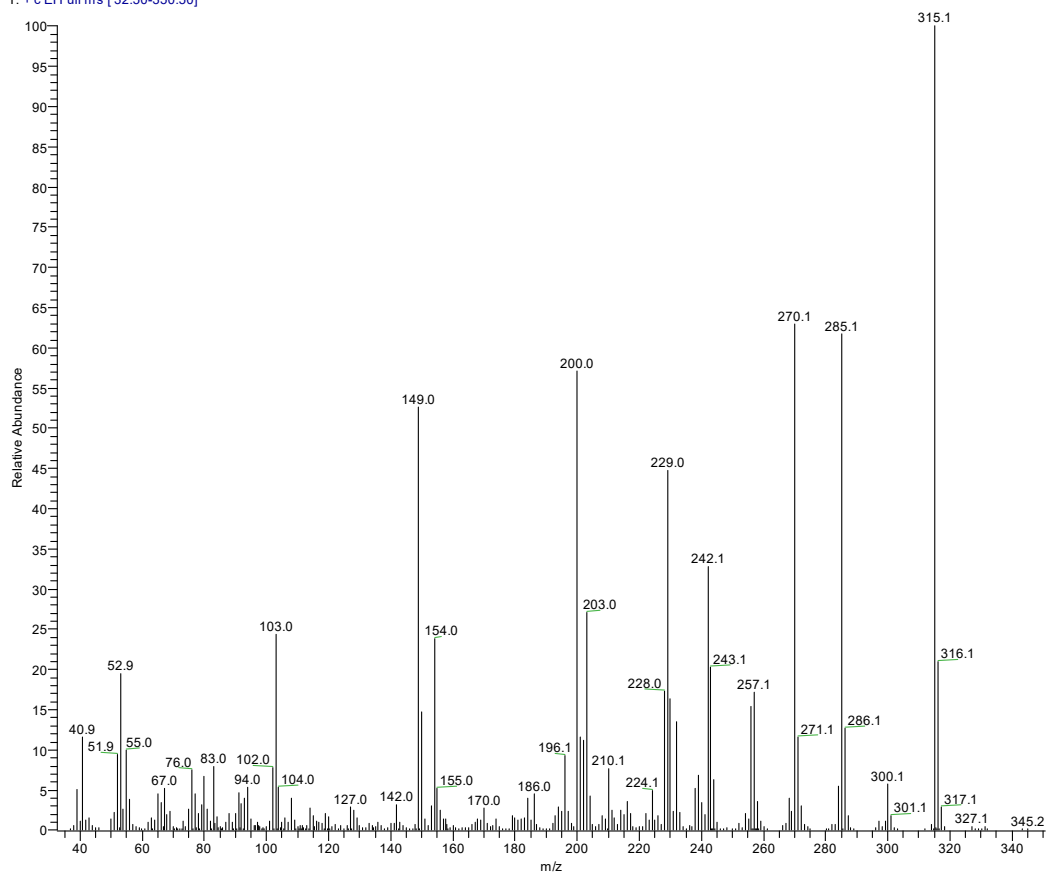


HMBC in DMSO-d<sub>6</sub>:

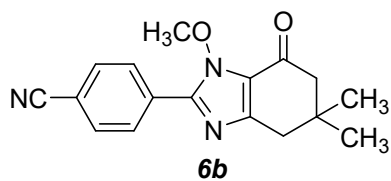


# HRMS (EI):

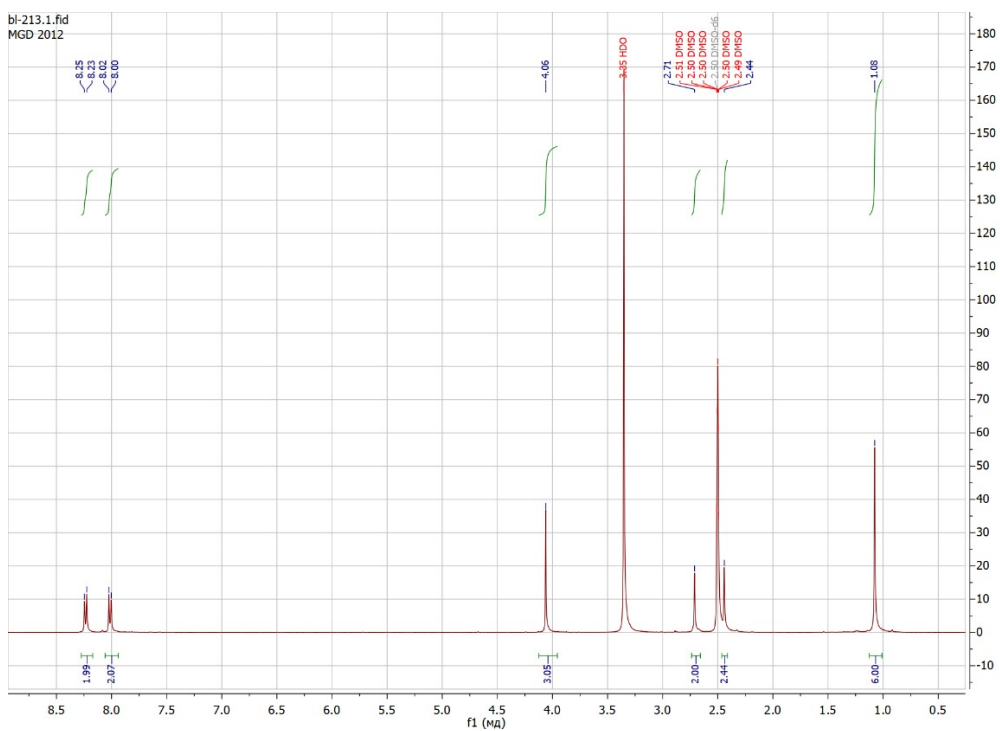
PANI-123 #18 RT: 0.95 AV: 1 NL: 5.86E6  
T: + c EI Full ms [32.50-350.50]



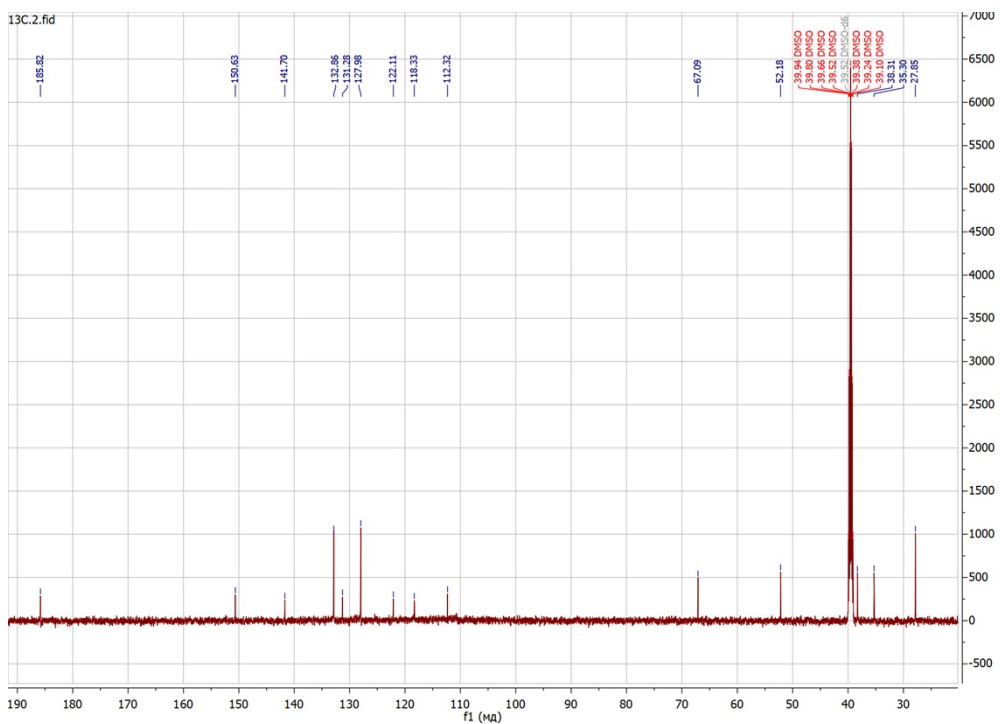
4-(1-Methoxy-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-1H-benzo[d]imidazol-2-yl)benzonitrile (**6b**).



$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



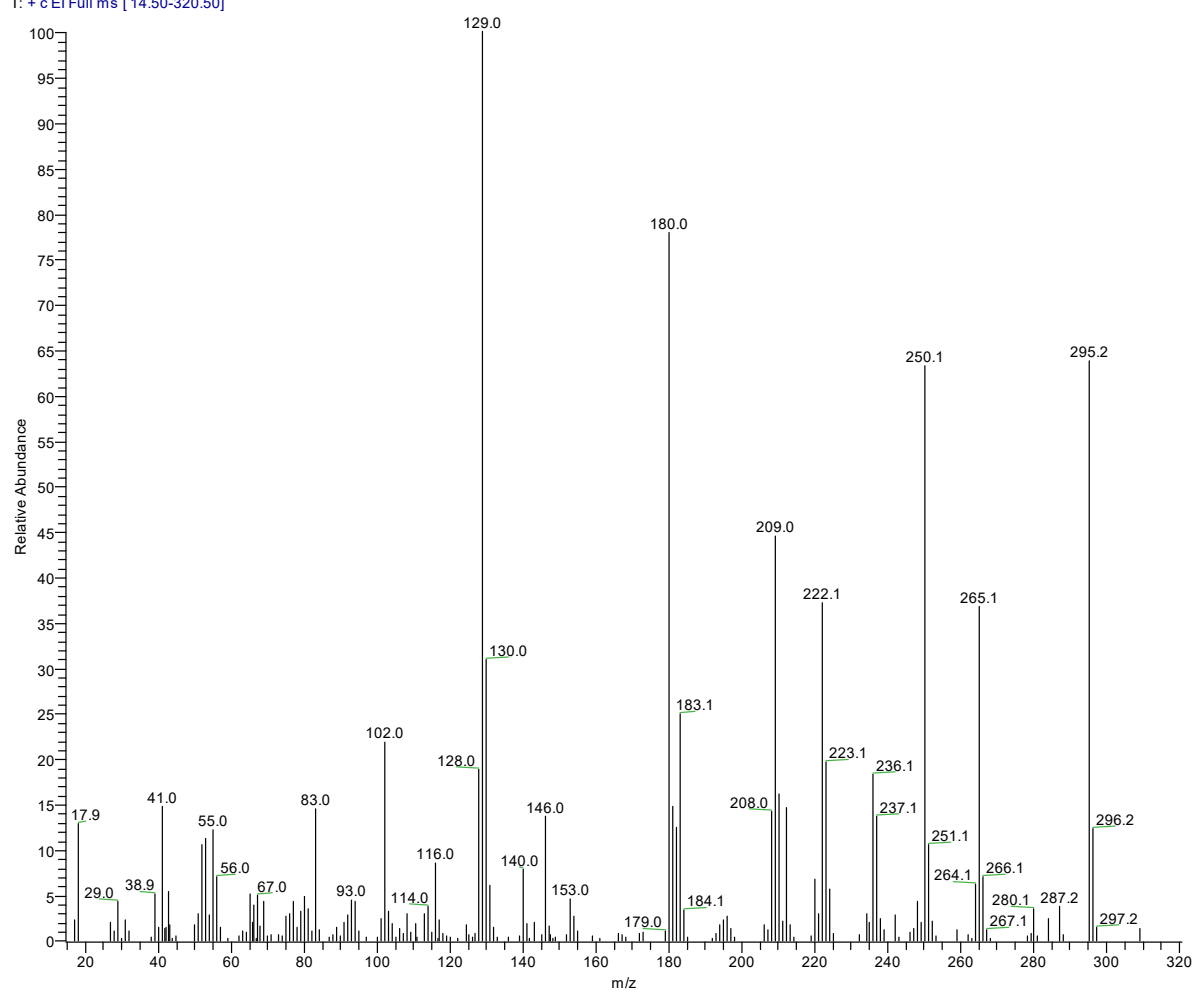
$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



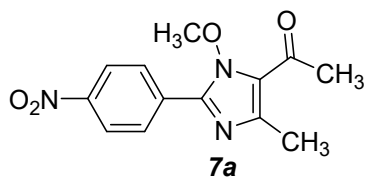


# HRMS (EI):

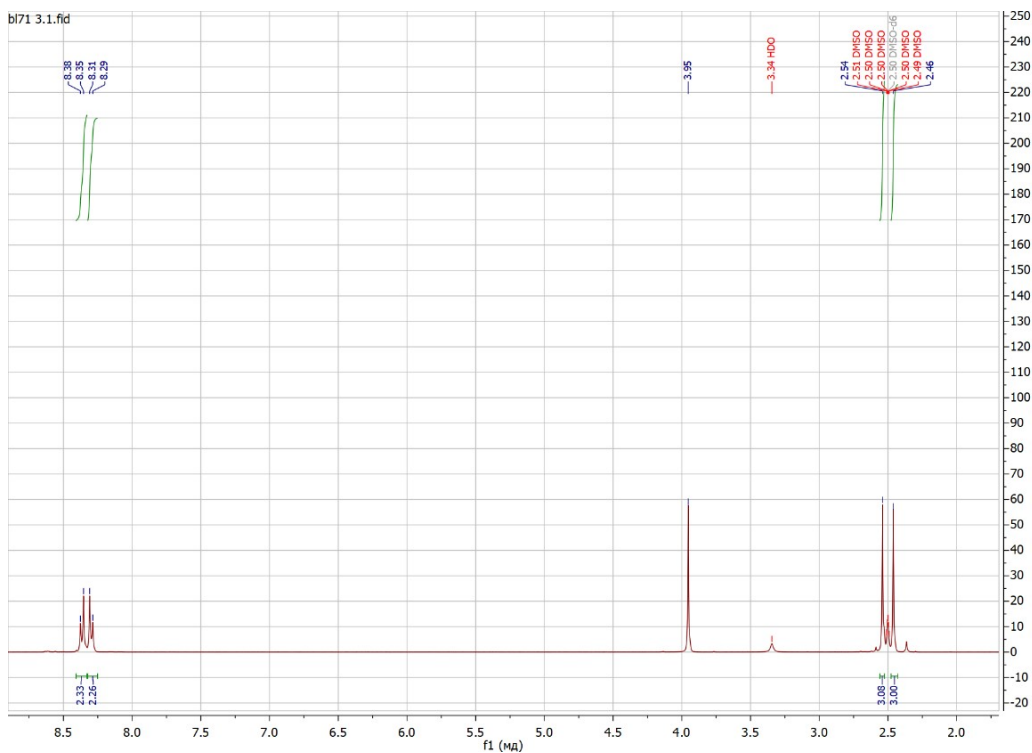
PANI-174 #12 RT: 0.71 AV: 1 NL: 4.72E5  
T: + c EI Full ms [ 14.50-320.50]



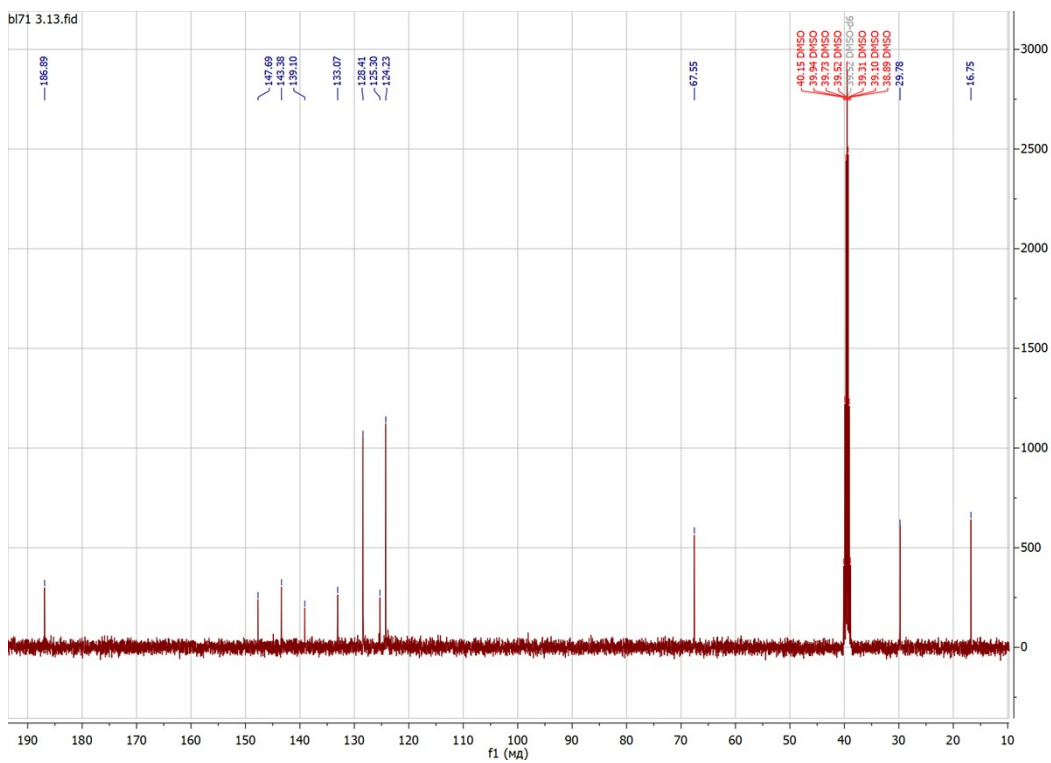
1-(1-Methoxy-4-methyl-2-(4-nitrophenyl)-1H-imidazol-5-yl)ethan-1-one (7a).



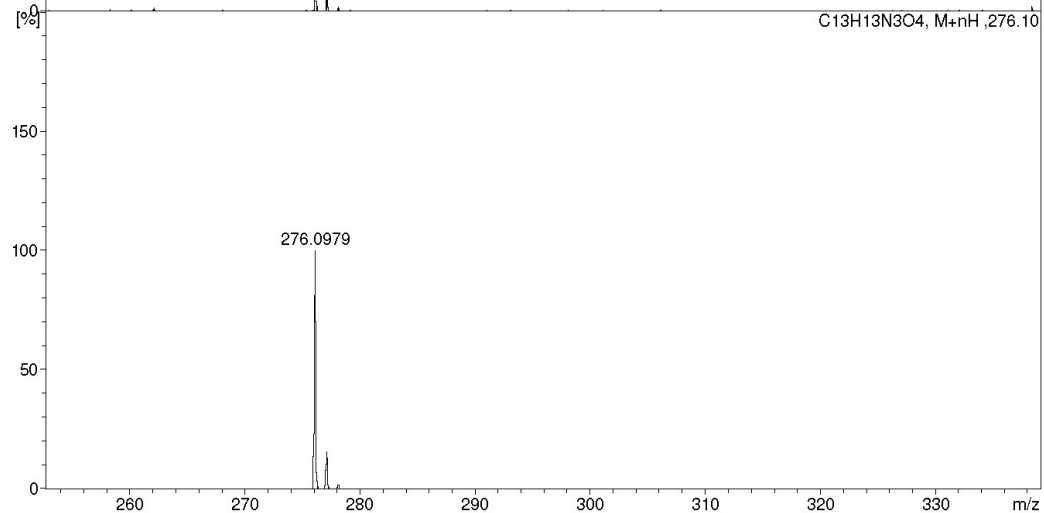
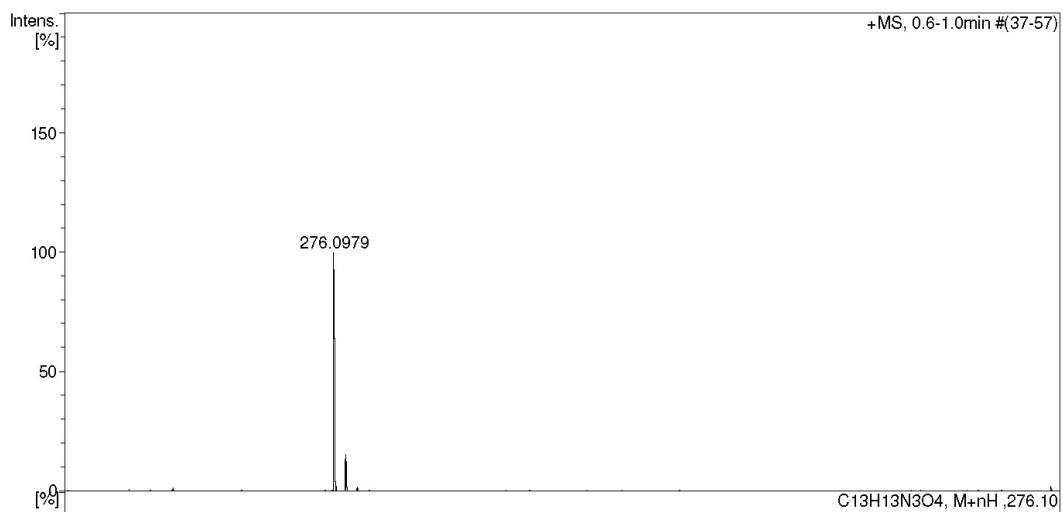
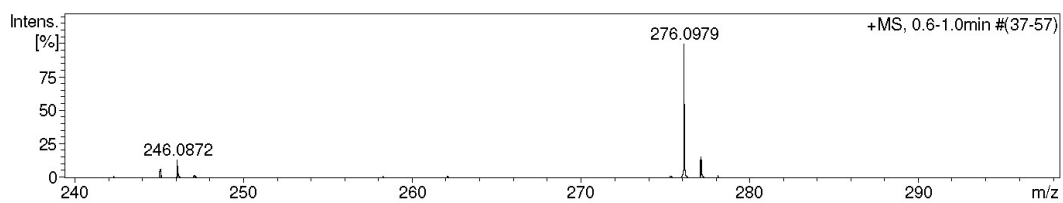
<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:



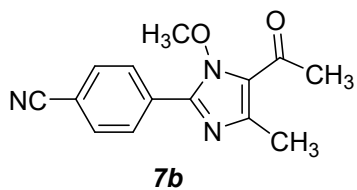
<sup>13</sup>C NMR spectrum in DMSO-d<sub>6</sub>:



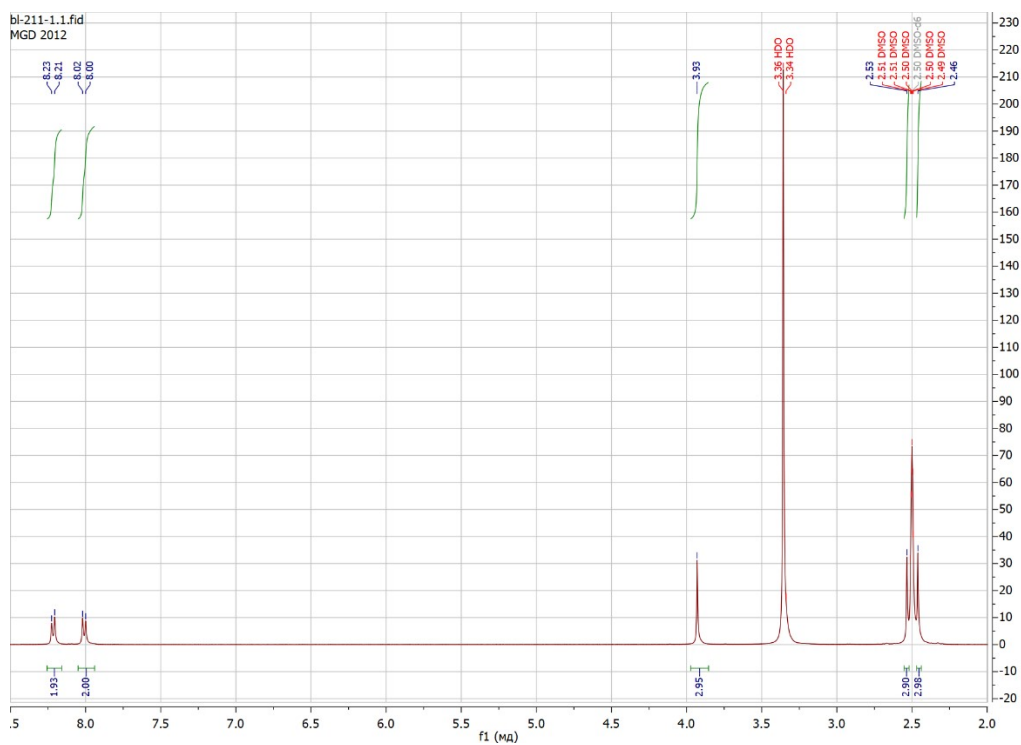
HRMS (ESI):



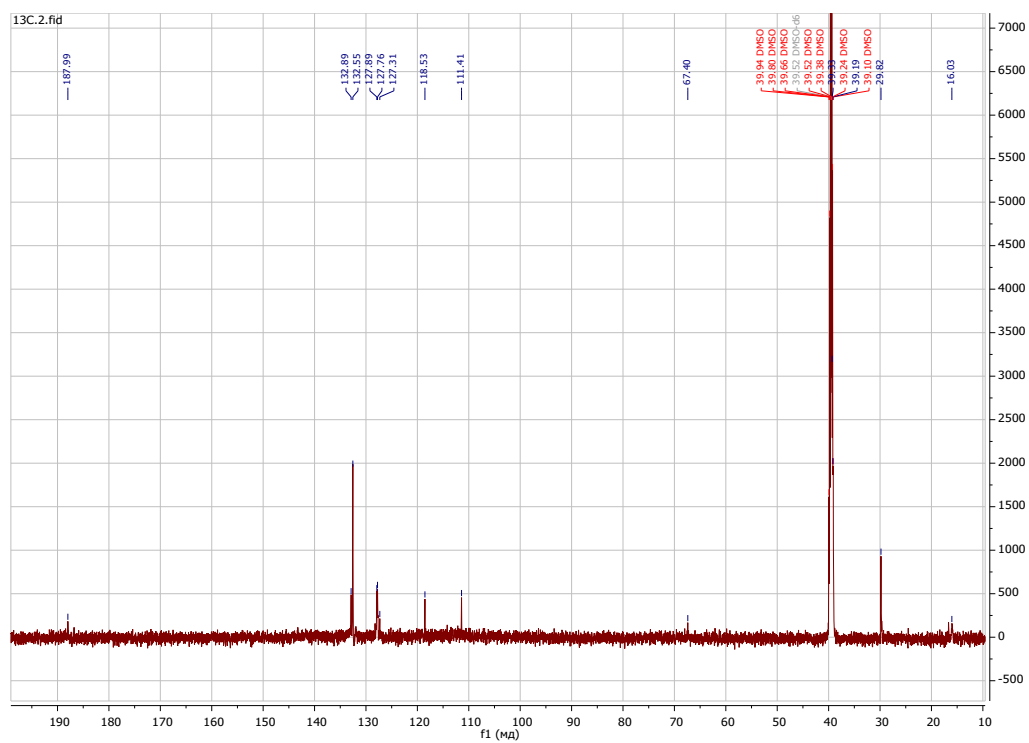
4-(5-Acetyl-1-methoxy-4-methyl-1H-imidazol-2-yl)benzonitrile (**7b**)



<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:

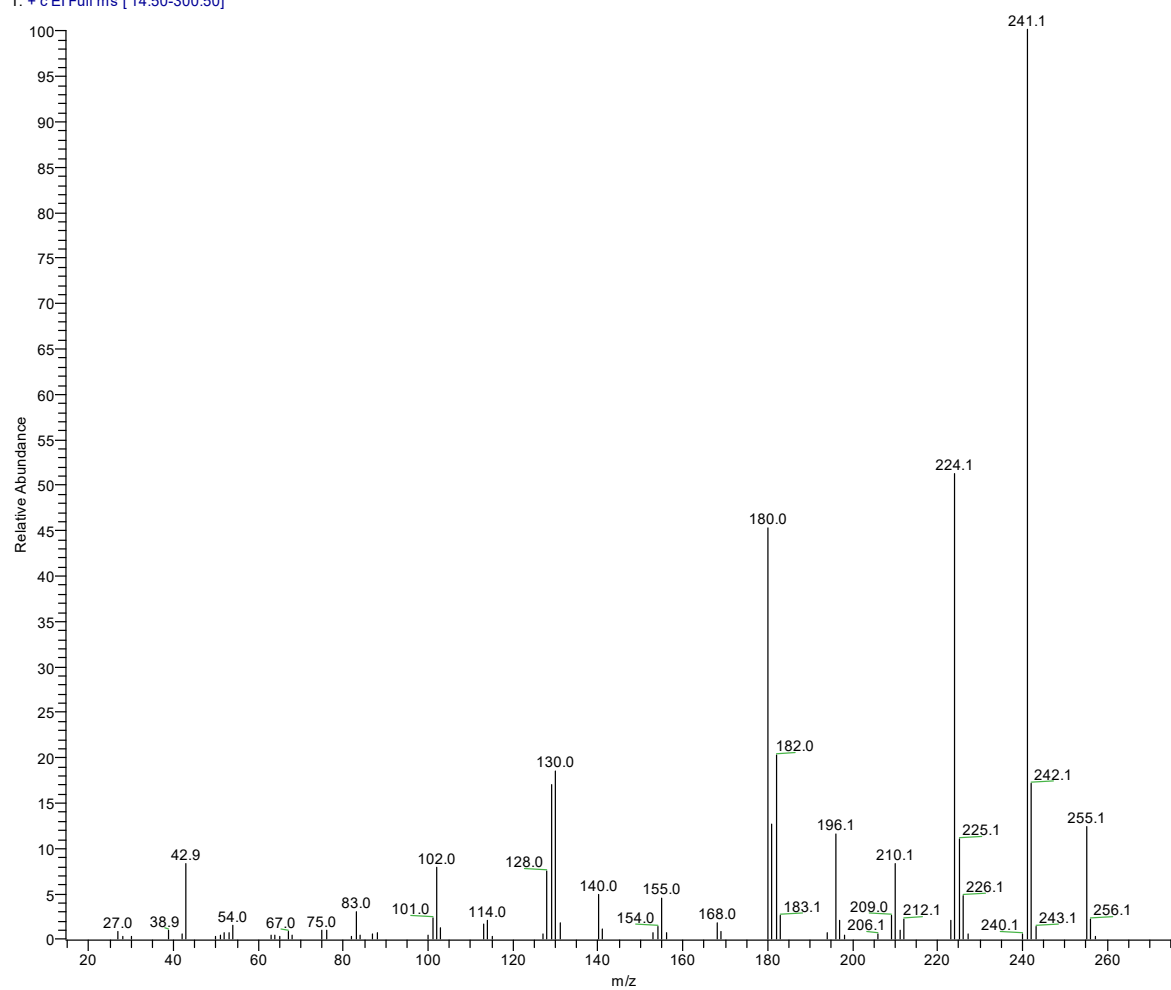


<sup>13</sup>C NMR spectrum in DMSO-d<sub>6</sub>:

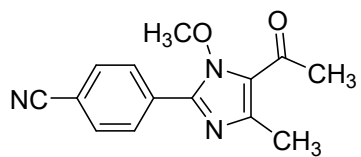


# HRMS (EI):

PANI-172 #1 RT: 0.00 AV: 1 NL: 6.53E5  
T: + c EI Full ms [ 14.50-300.50]

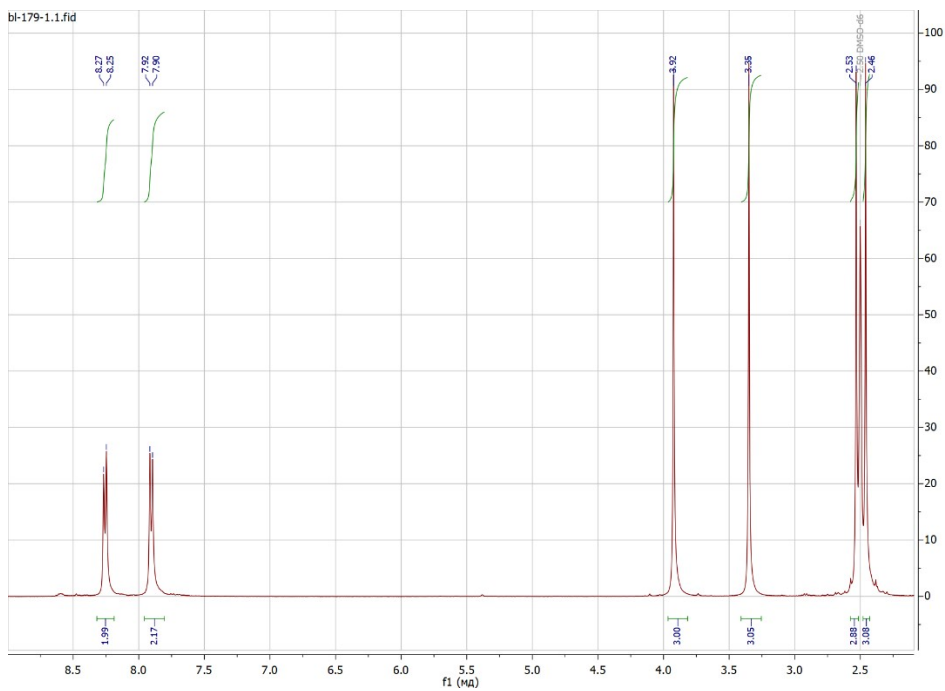


*1-(1-Methoxy-4-methyl-2-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)ethan-1-one (7c)*

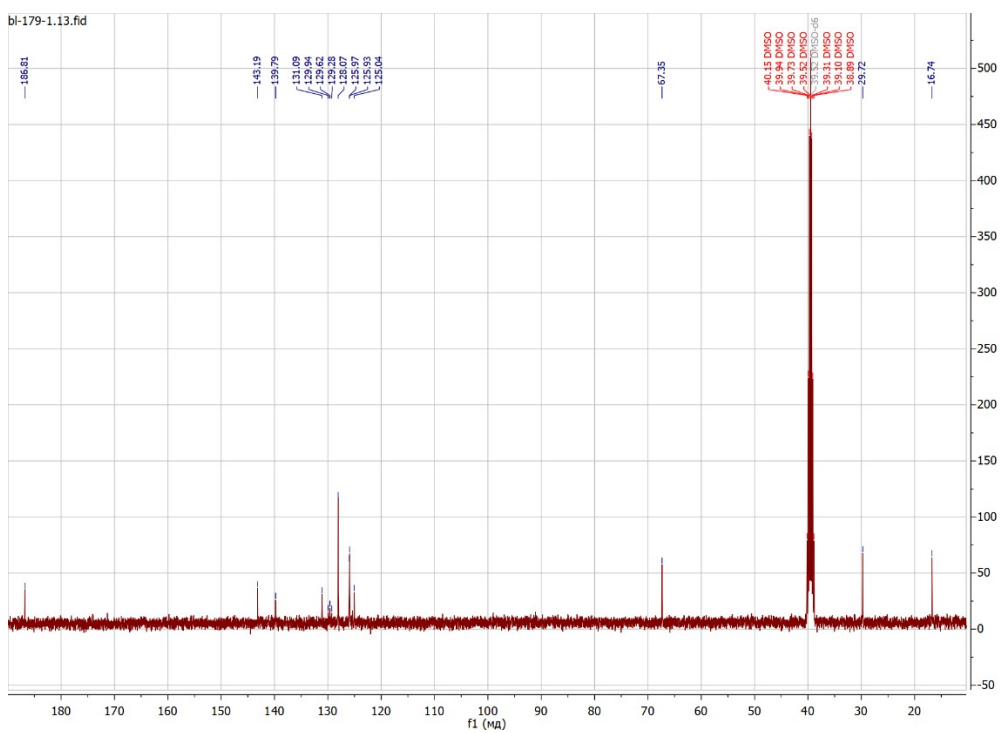


**7c**

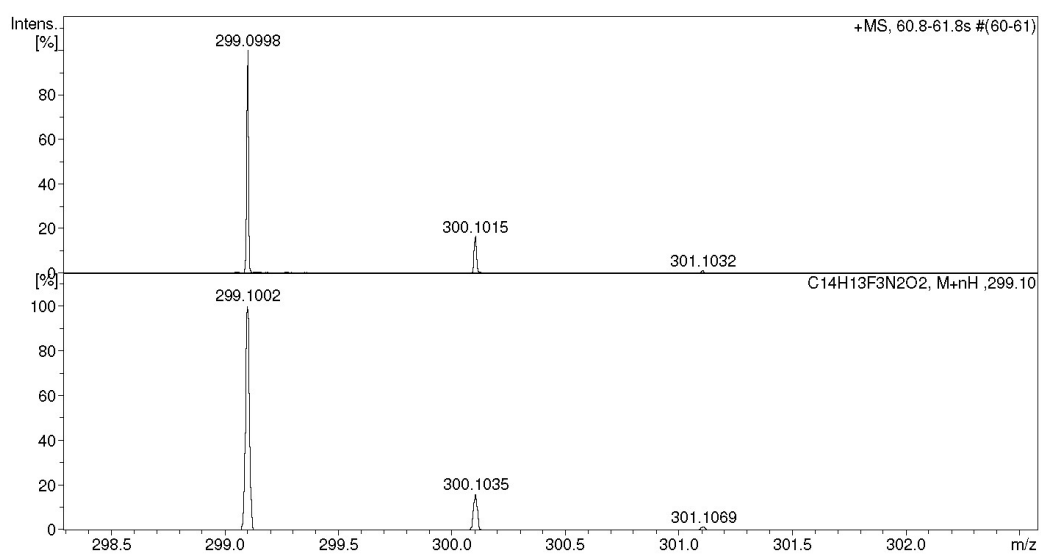
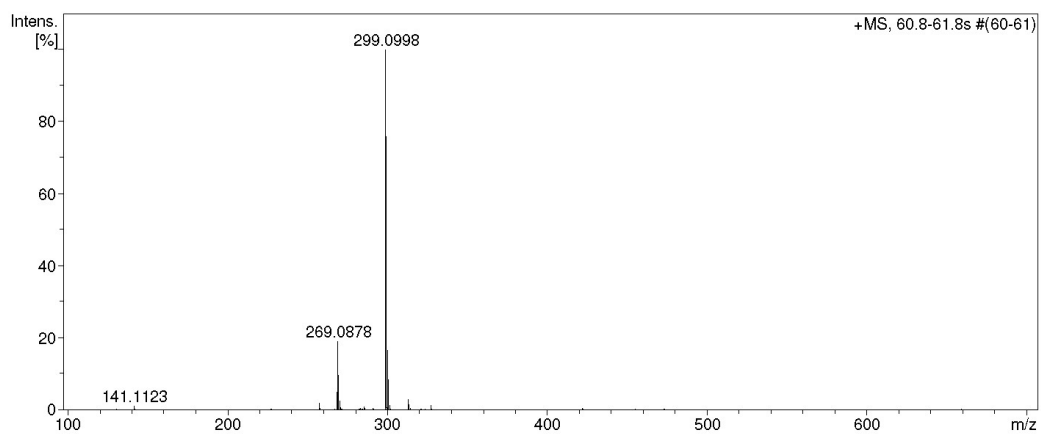
<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:



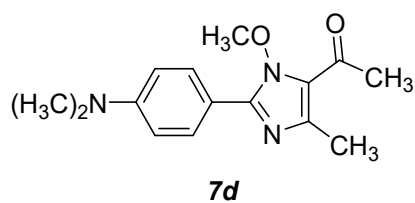
<sup>13</sup>C NMR spectrum in DMSO-d<sub>6</sub>:



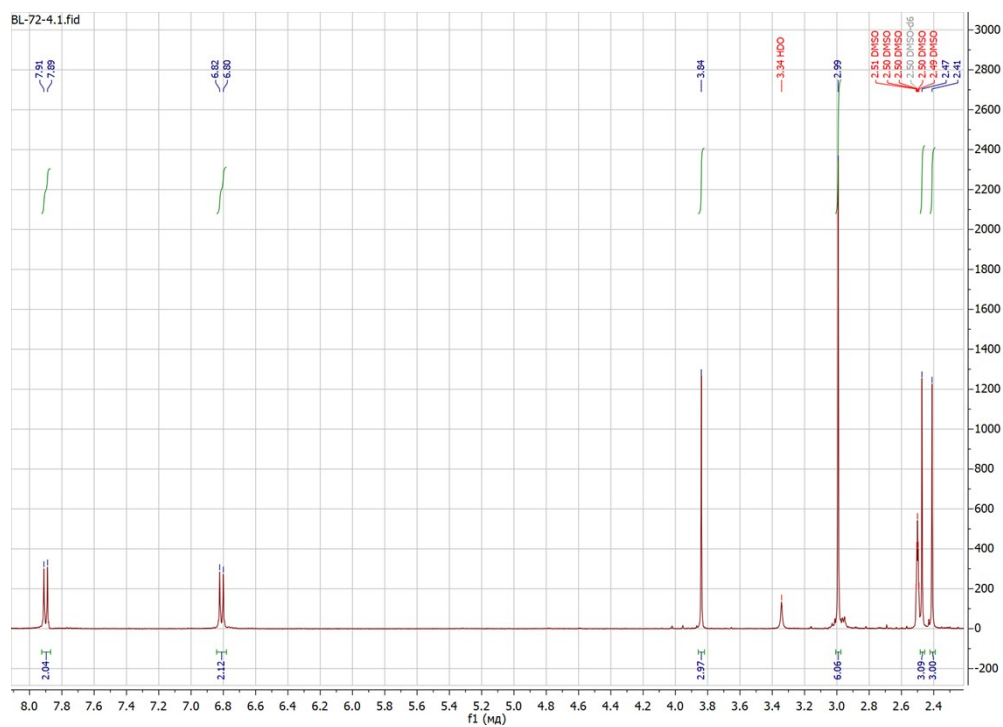
HRMS (ESI):



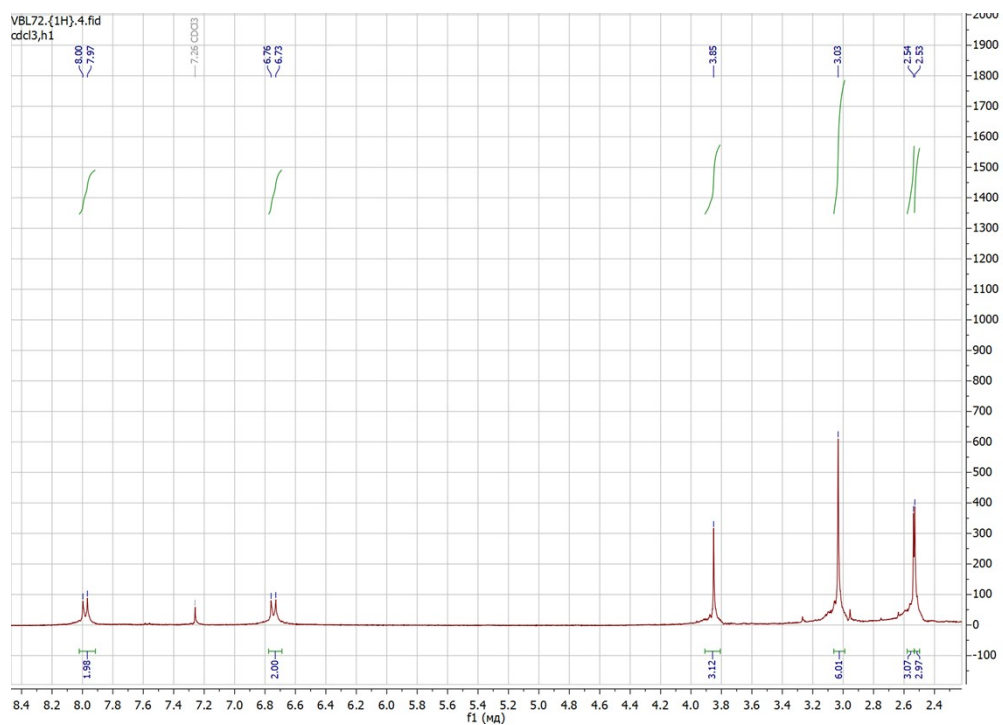
*1-(2-(4-(Dimethylamino)phenyl)-1-methoxy-4-methyl-1H-imidazol-5-yl)ethan-1-one (7d)*



<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:

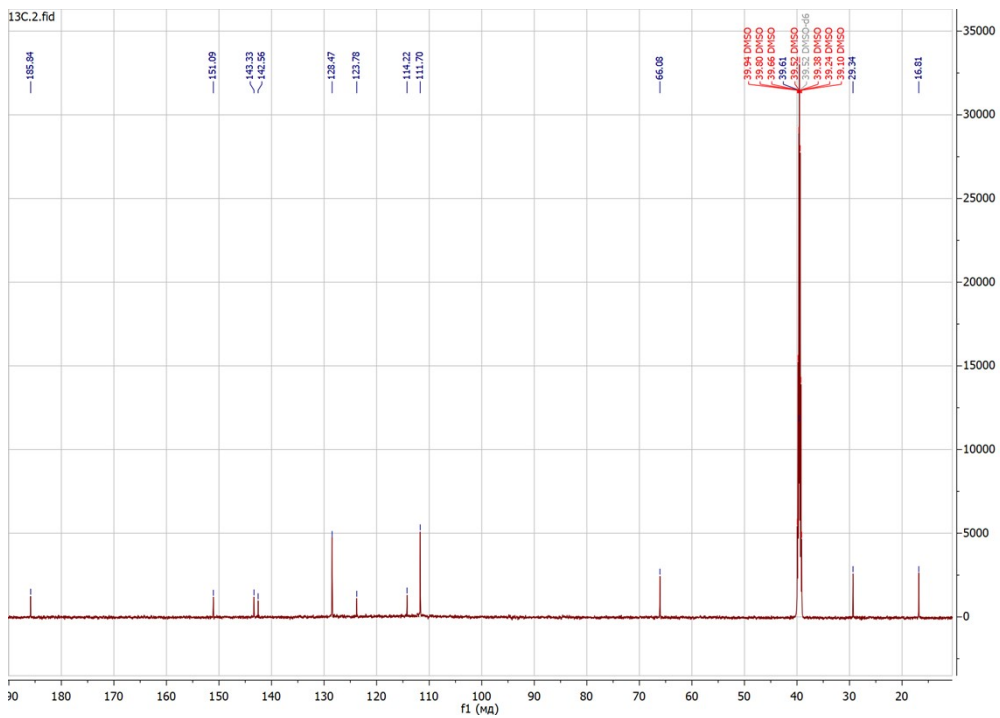


<sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>:



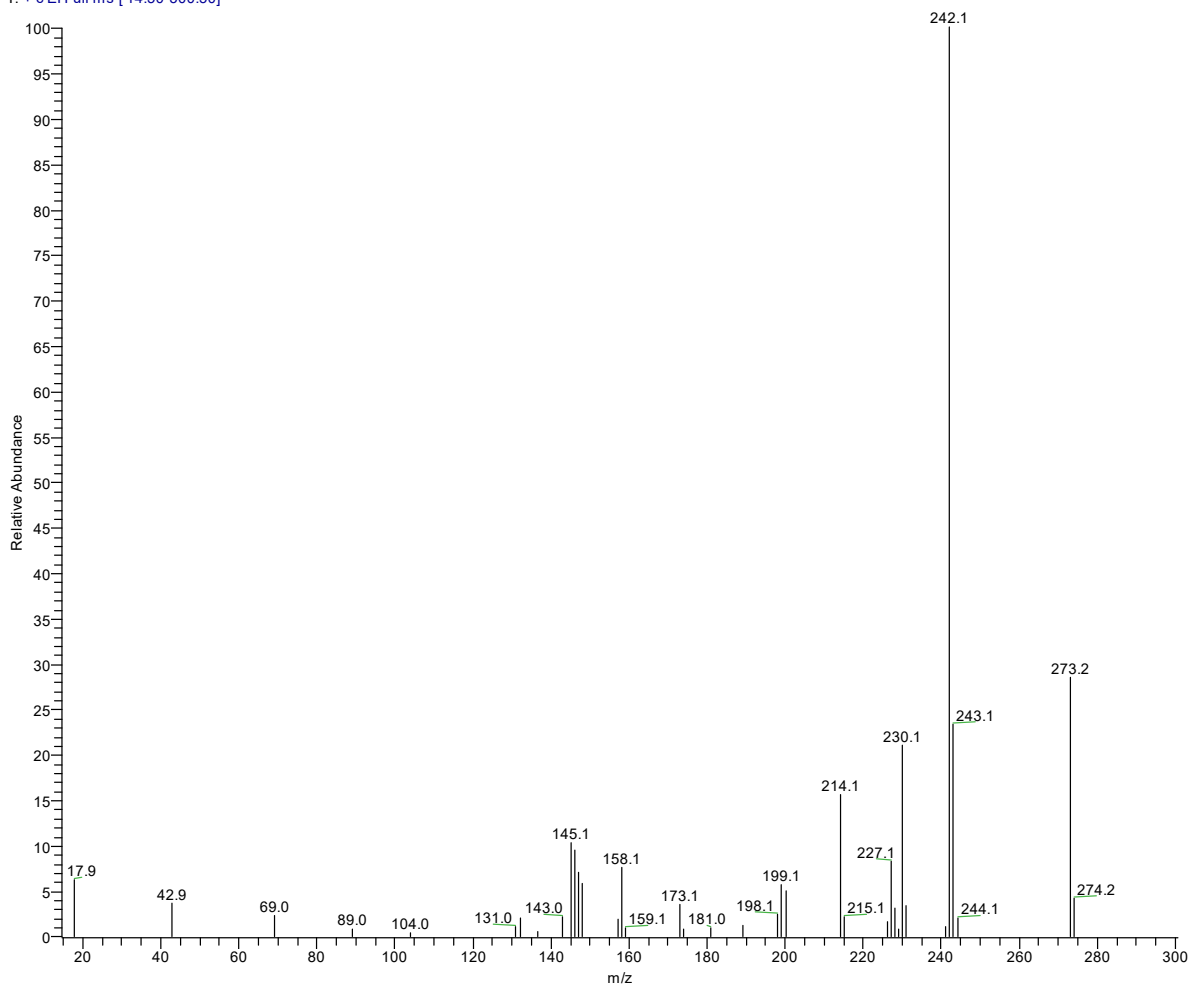


### $^{13}\text{C}$ NMR spectrum in $\text{DMSO-d}_6$ :

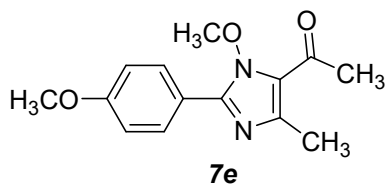


### HRMS (EI):

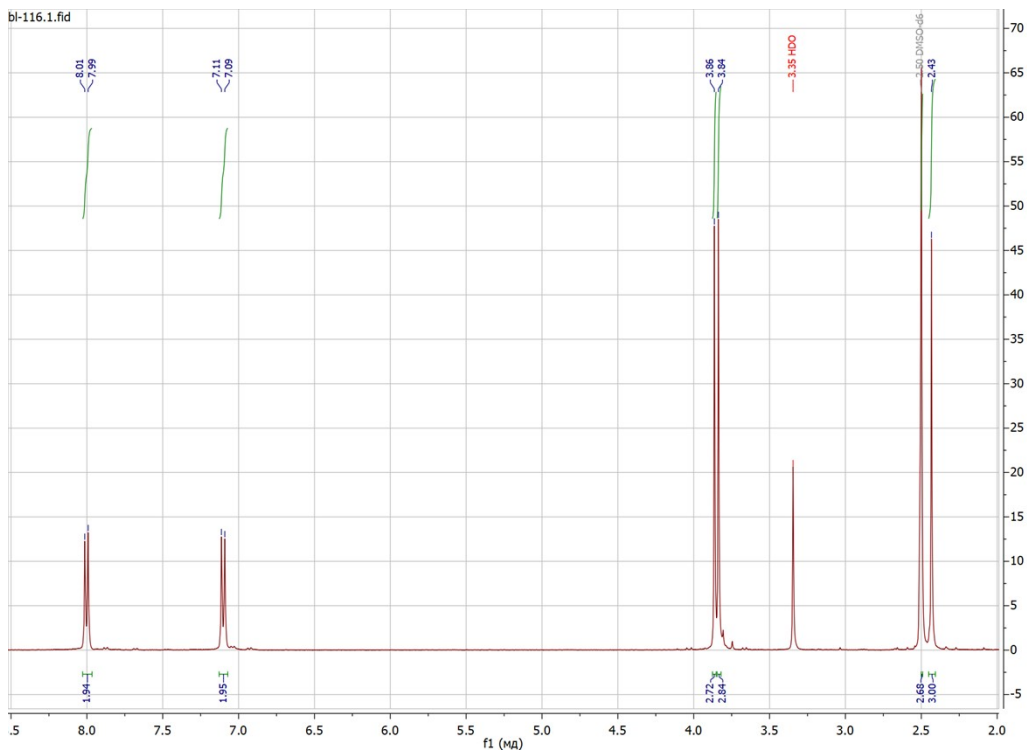
PANI-88 #3 RT: 0.14 AV: 1 NL: 1.82E5  
T: + c EI Full ms [ 14.50-300.50]



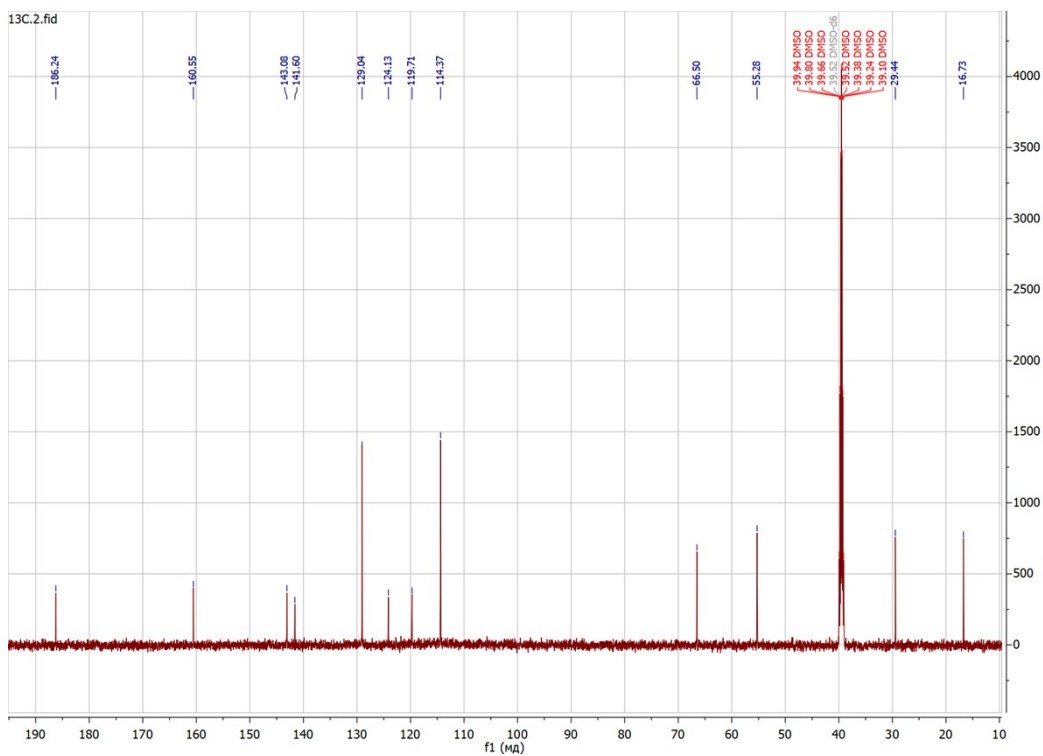
*1-(1-Methoxy-2-(4-methoxyphenyl)-4-methyl-1H-imidazol-5-yl)ethan-1-one (7e)*



<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:

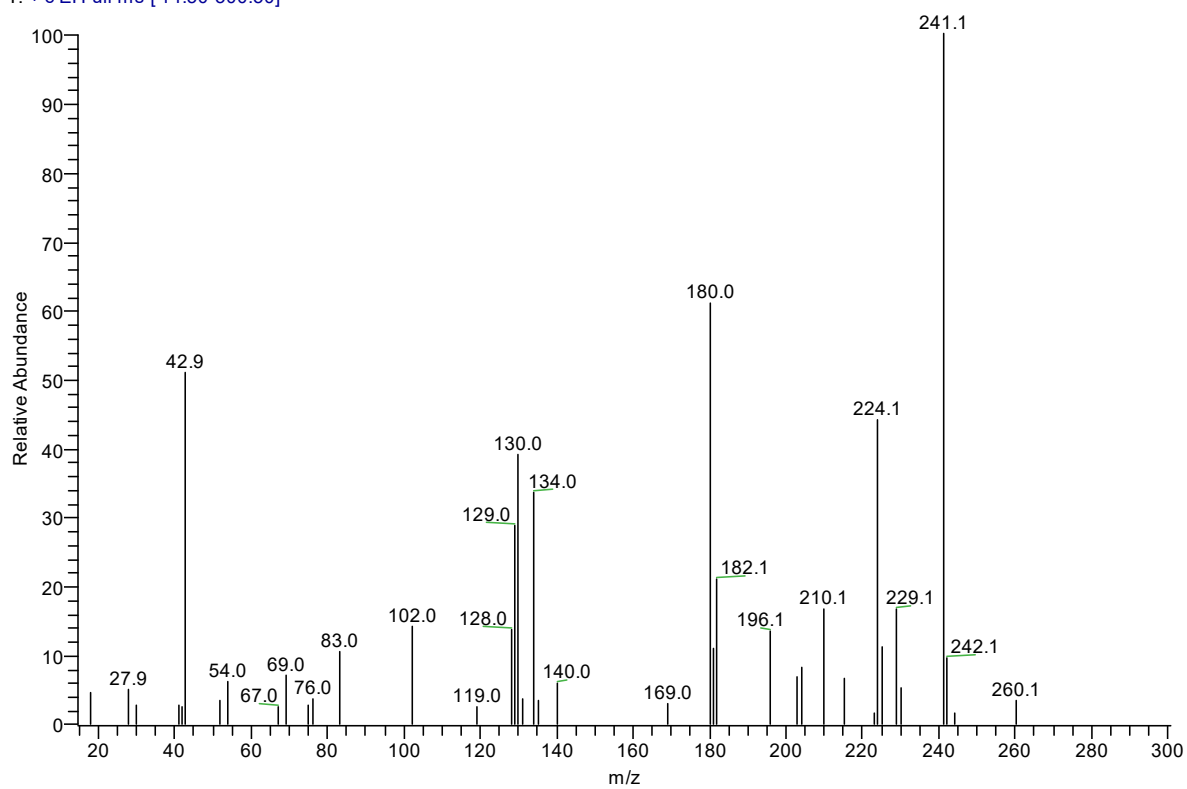


<sup>13</sup>C NMR spectrum in DMSO-d<sub>6</sub>:

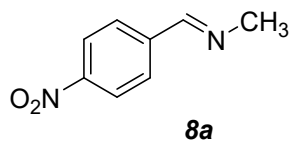


# HRMS (EI):

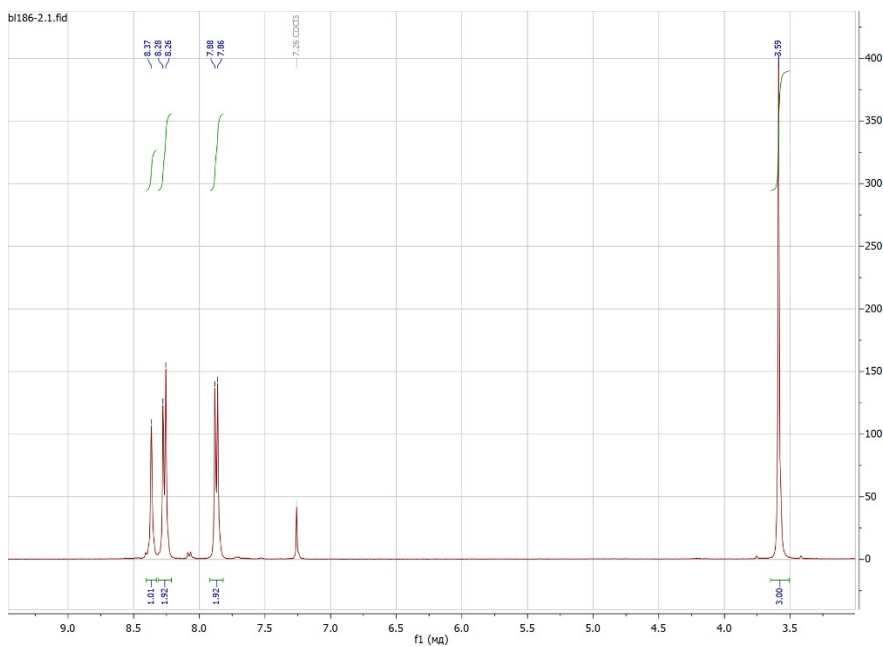
PANI-89 #13 RT: 0.84 AV: 1 NL: 4.87E4  
T: + c EI Full ms [ 14.50-300.50]



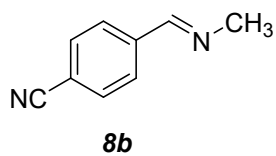
*(E)*-*N*-methyl-1-(4-nitrophenyl)methanimine (**8a**)



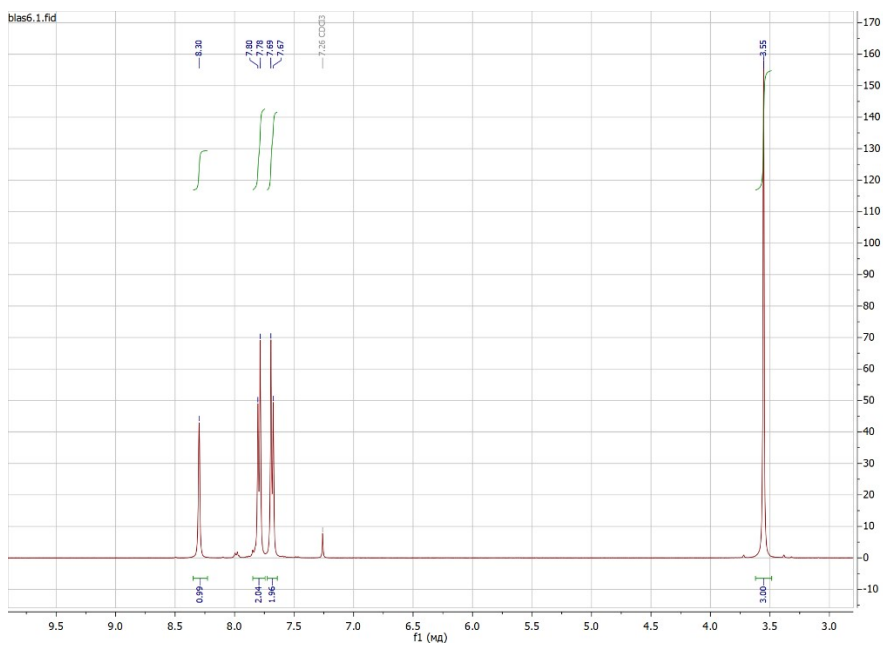
<sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>:



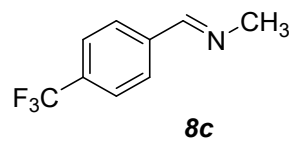
*(E)*-4-((Methylimino)methyl)benzonitrile (**8b**)



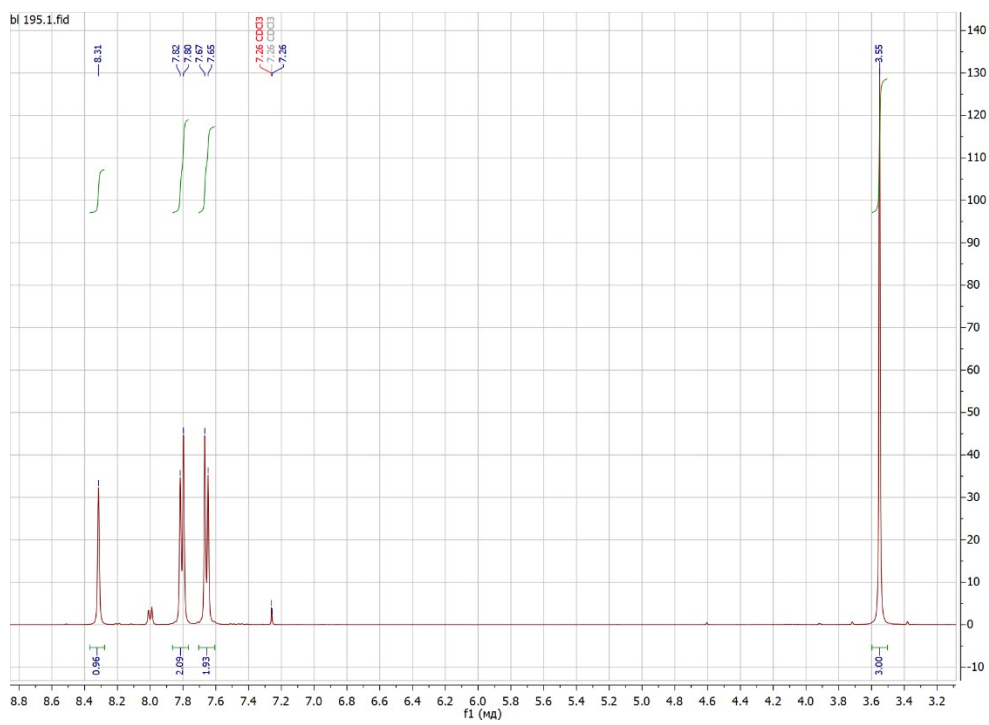
<sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>:



*(E)*-*N*-Methyl-1-(4-(trifluoromethyl)phenyl)methanimine (**8c**).

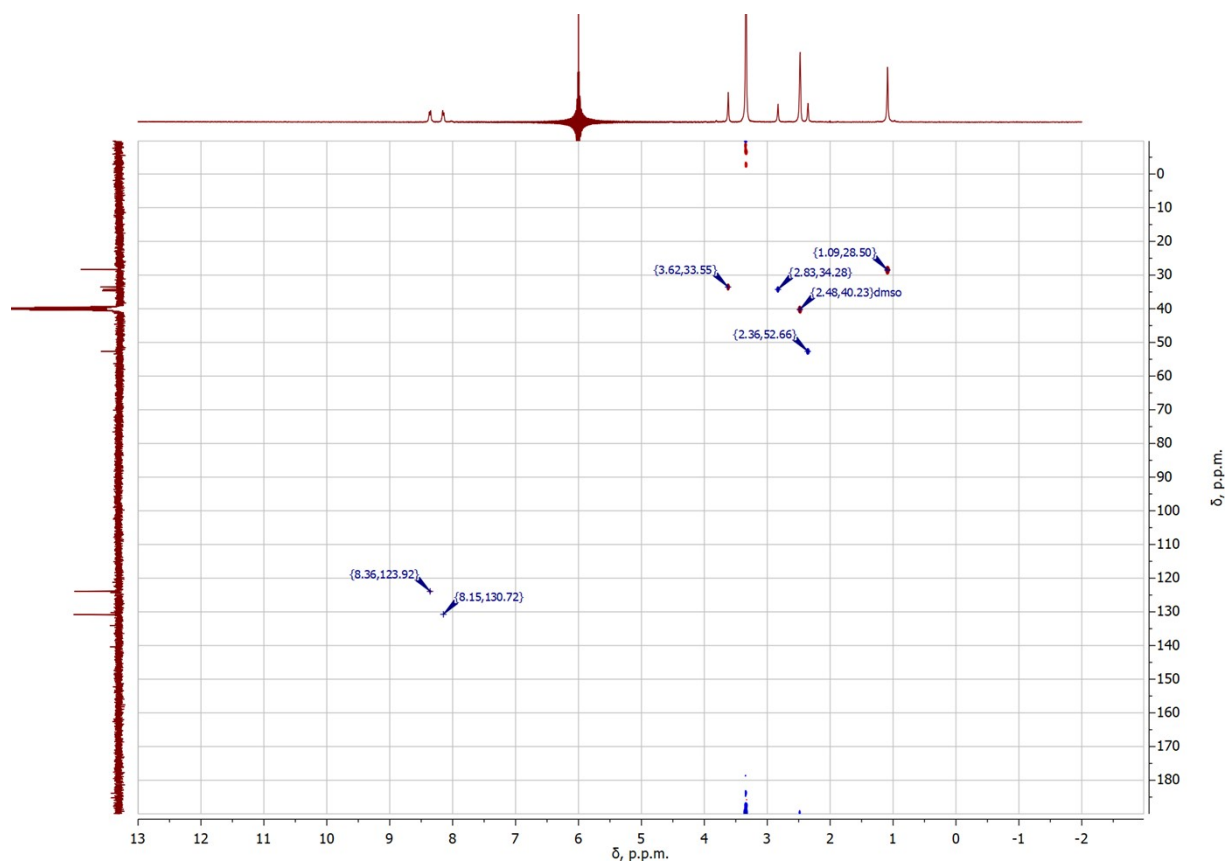


$^1\text{H}$  NMR spectrum in  $\text{CDCl}_3$ :

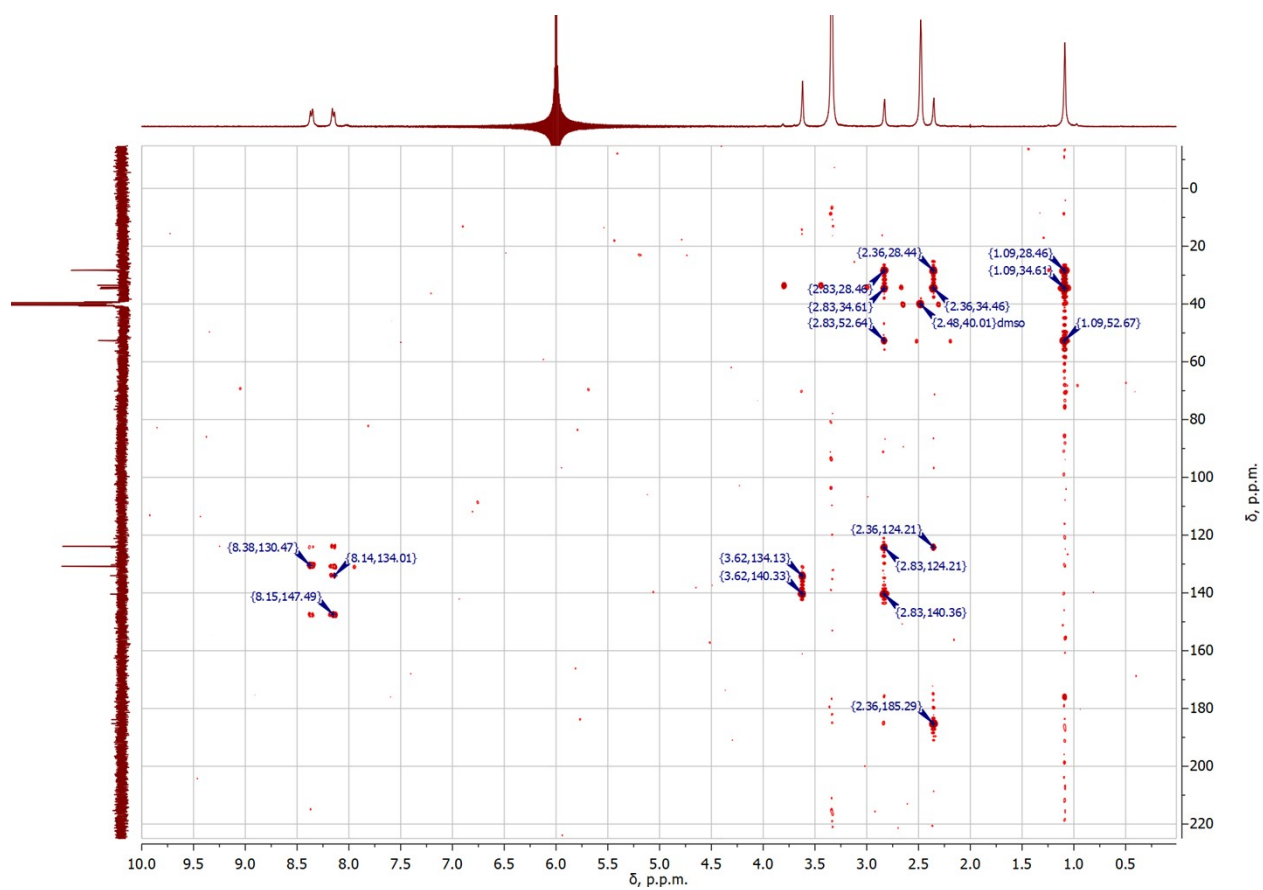




HSQC in DMSO-d<sub>6</sub>:

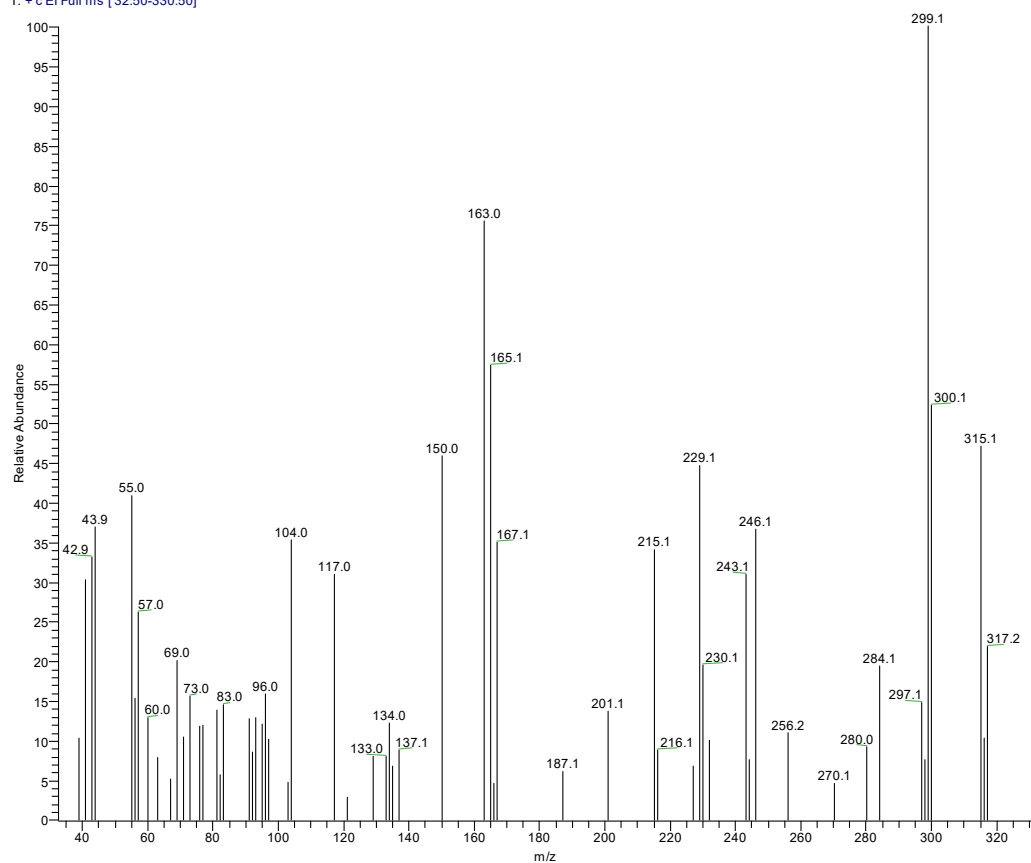


HMBC in DMSO-d<sub>6</sub>:



# HRMS (EI):

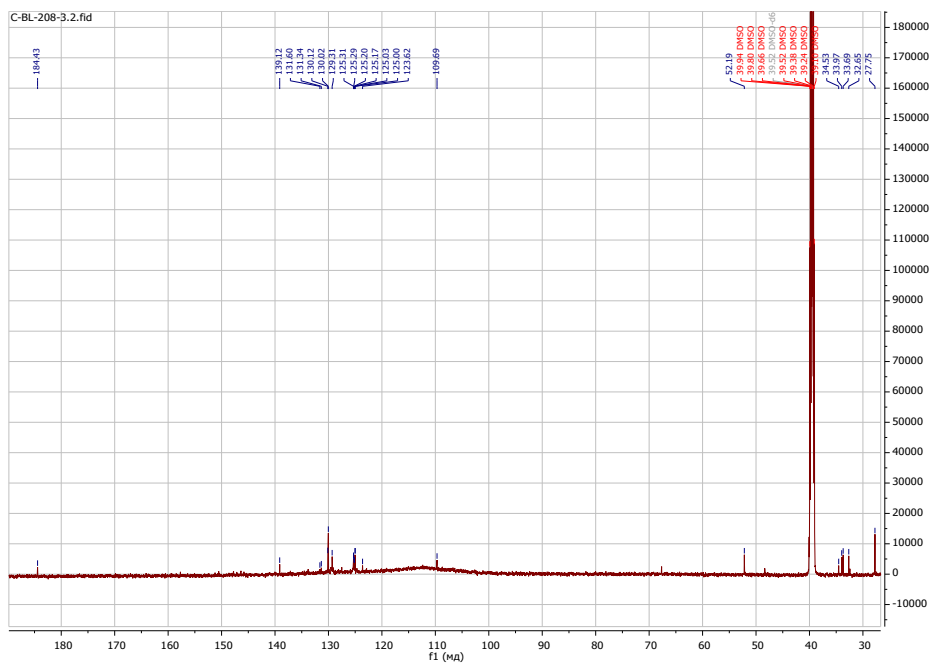
PANI-136 #46 RT: 2.49 AV: 1 NL: 2.01E4  
T: + c EI Full ms [32.50-330.50]





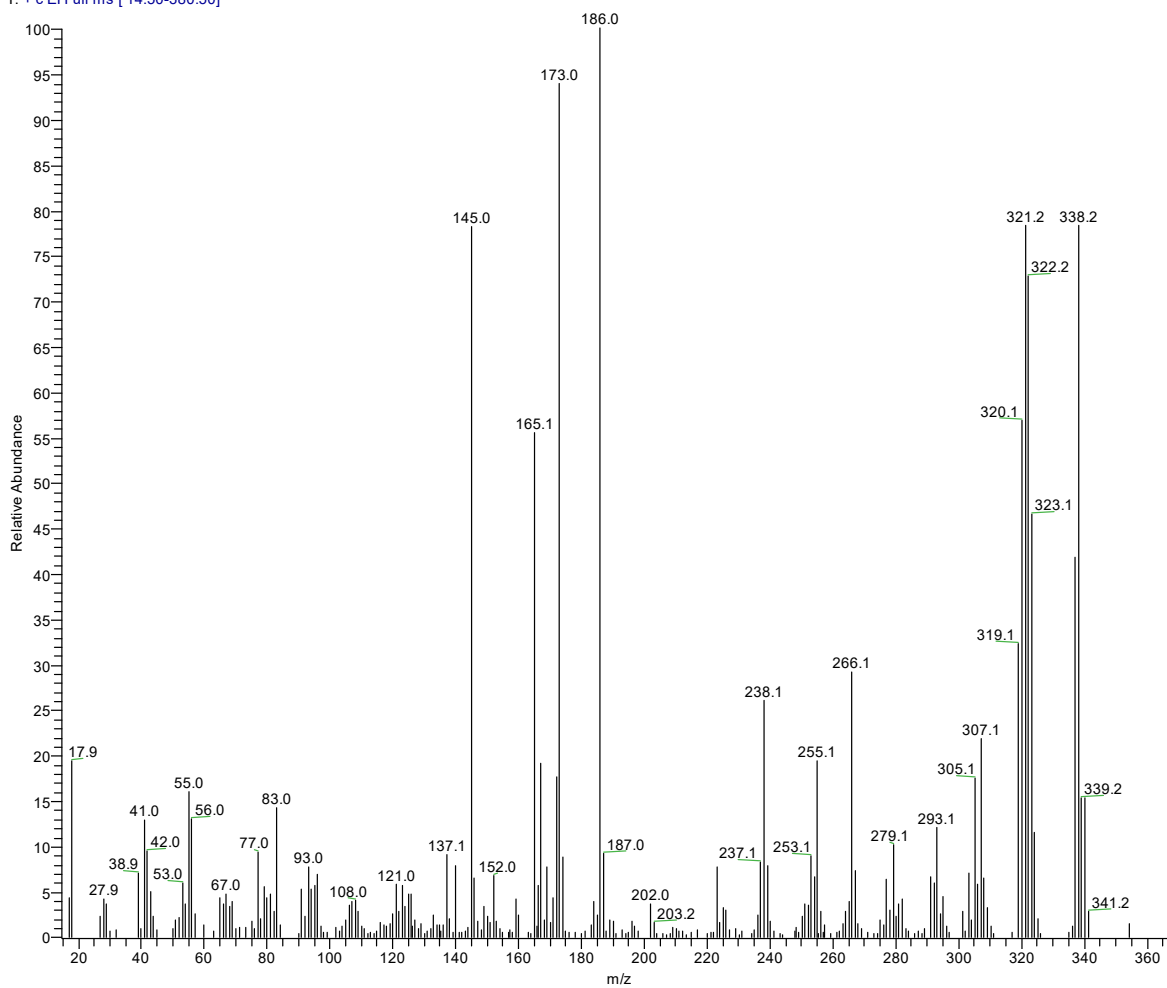


### $^{13}\text{C}$ NMR spectrum in $\text{DMSO-d}_6$ :

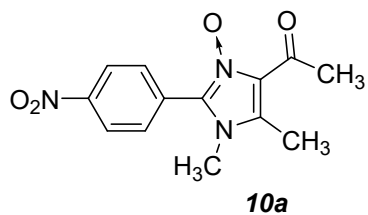


### HRMS (EI):

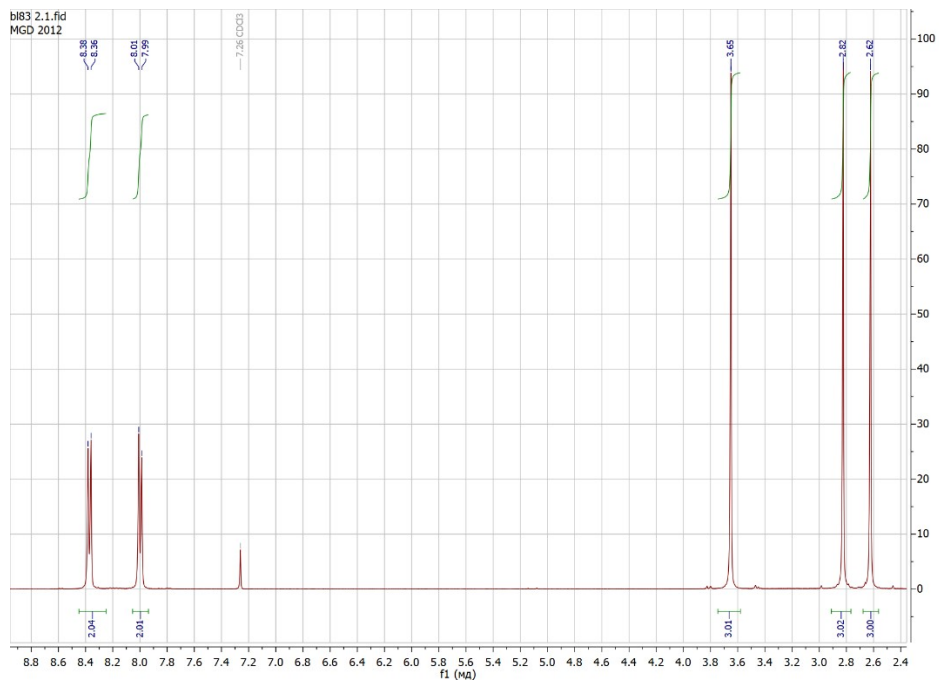
PANI-162 #26 RT: 1.87 AV: 1 NL: 3.30E5  
T: + c EI Full ms [ 14.50-380.50]



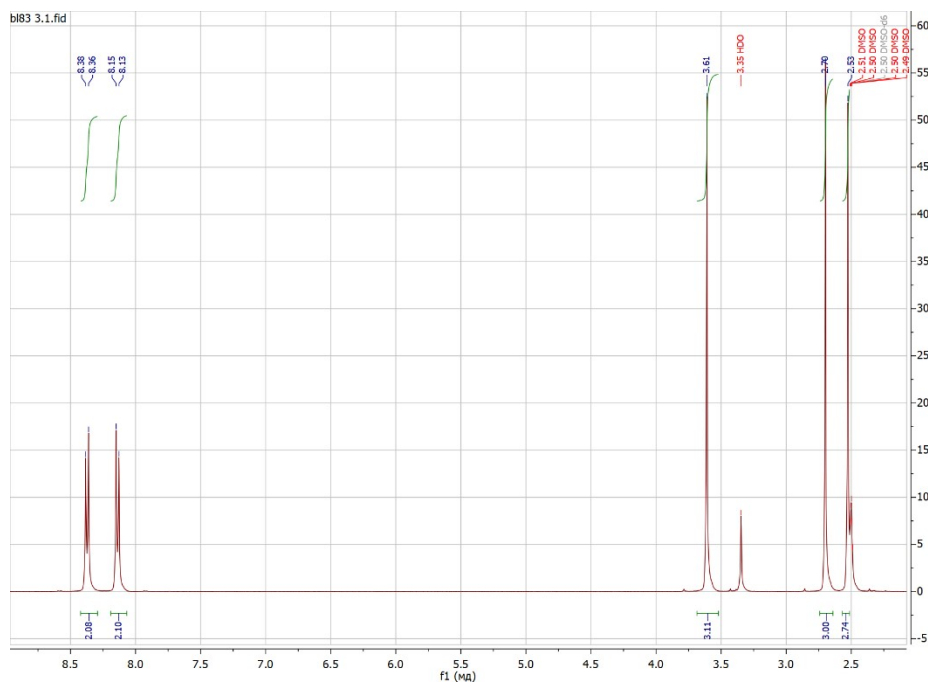
4-Acetyl-1,5-dimethyl-2-(4-nitrophenyl)-1H-imidazole 3-oxide (**10a**)



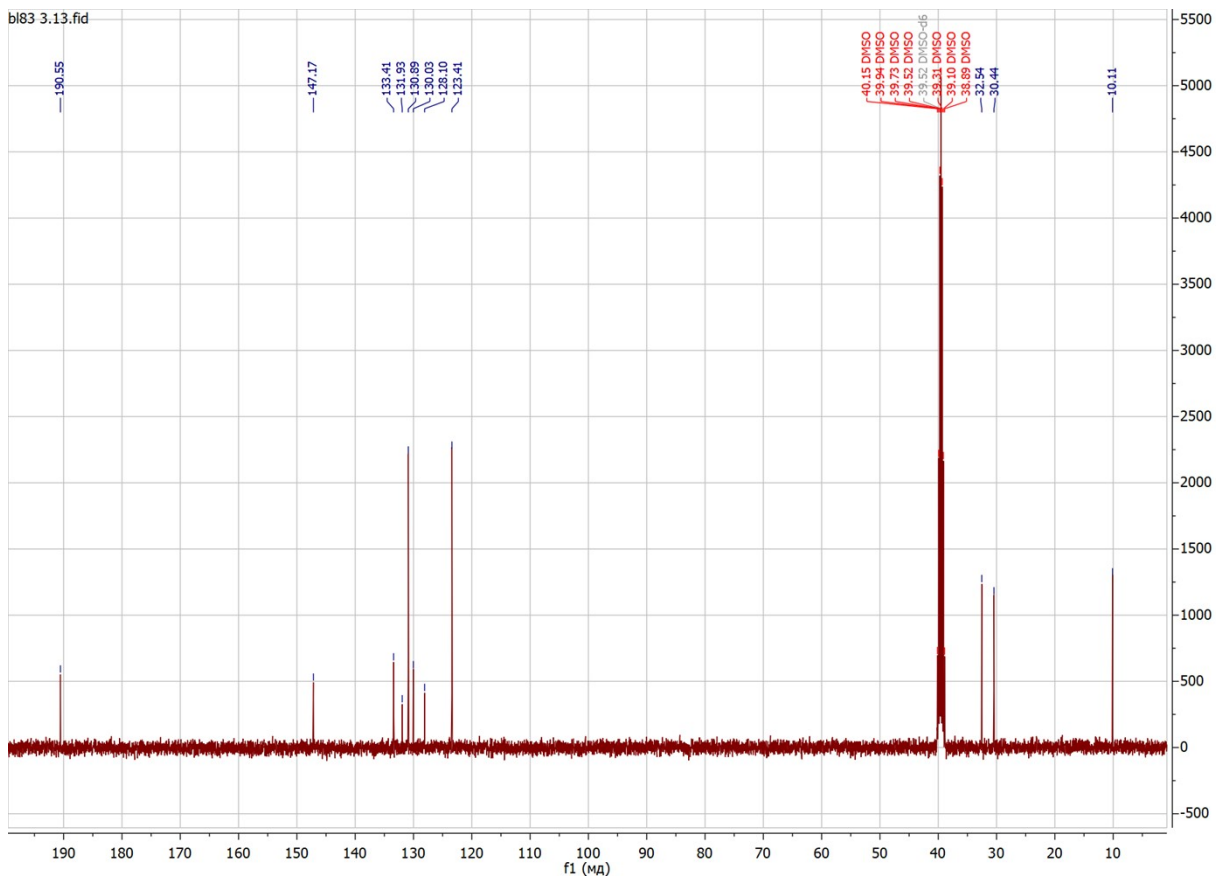
$^1\text{H}$  NMR spectrum in  $\text{CDCl}_3$ :



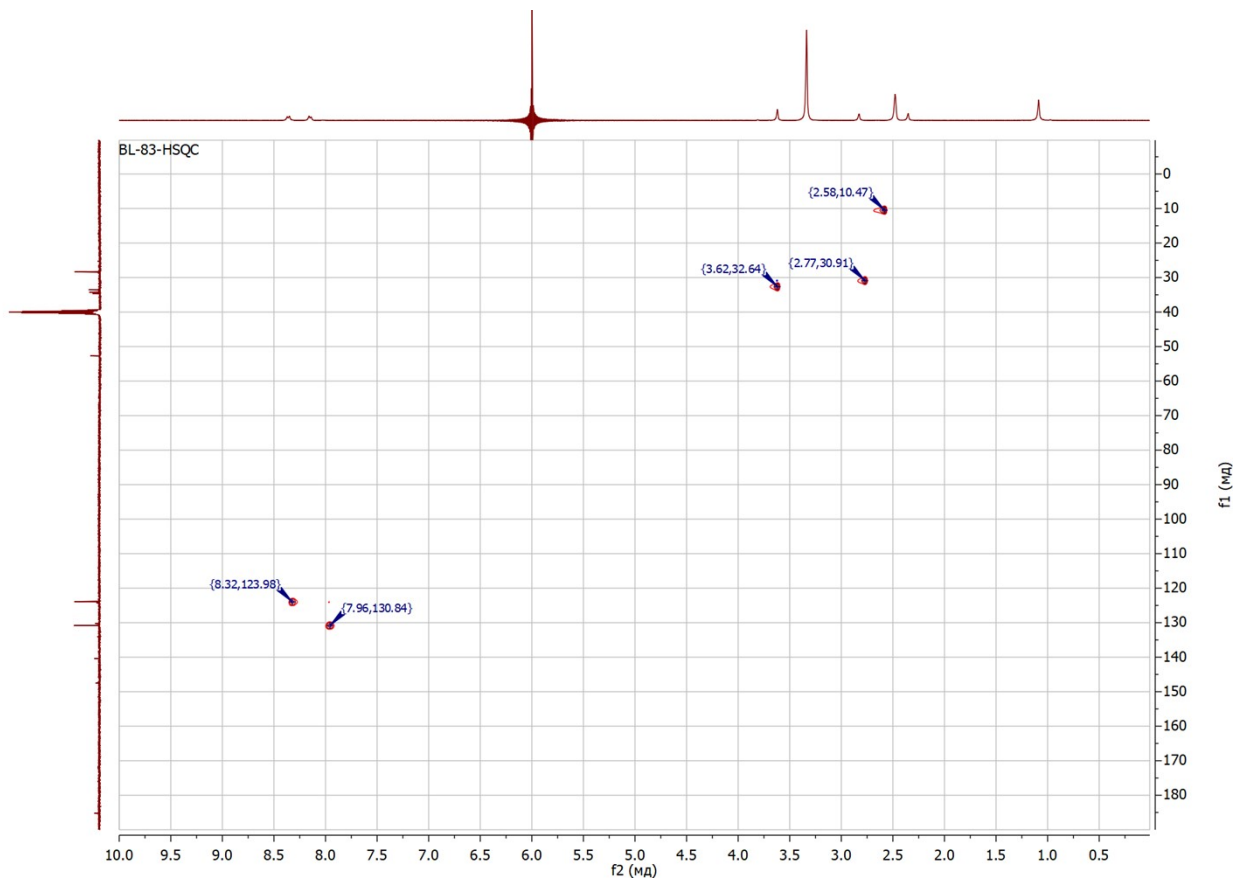
$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



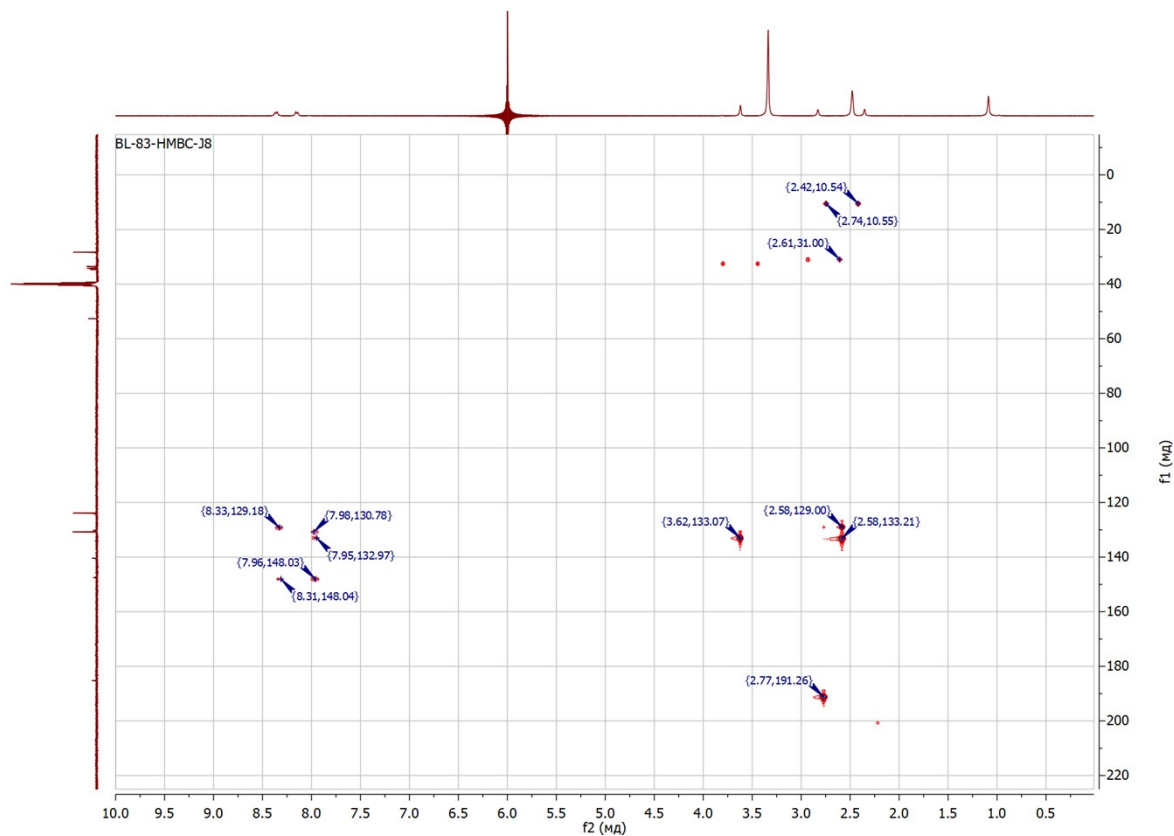
$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



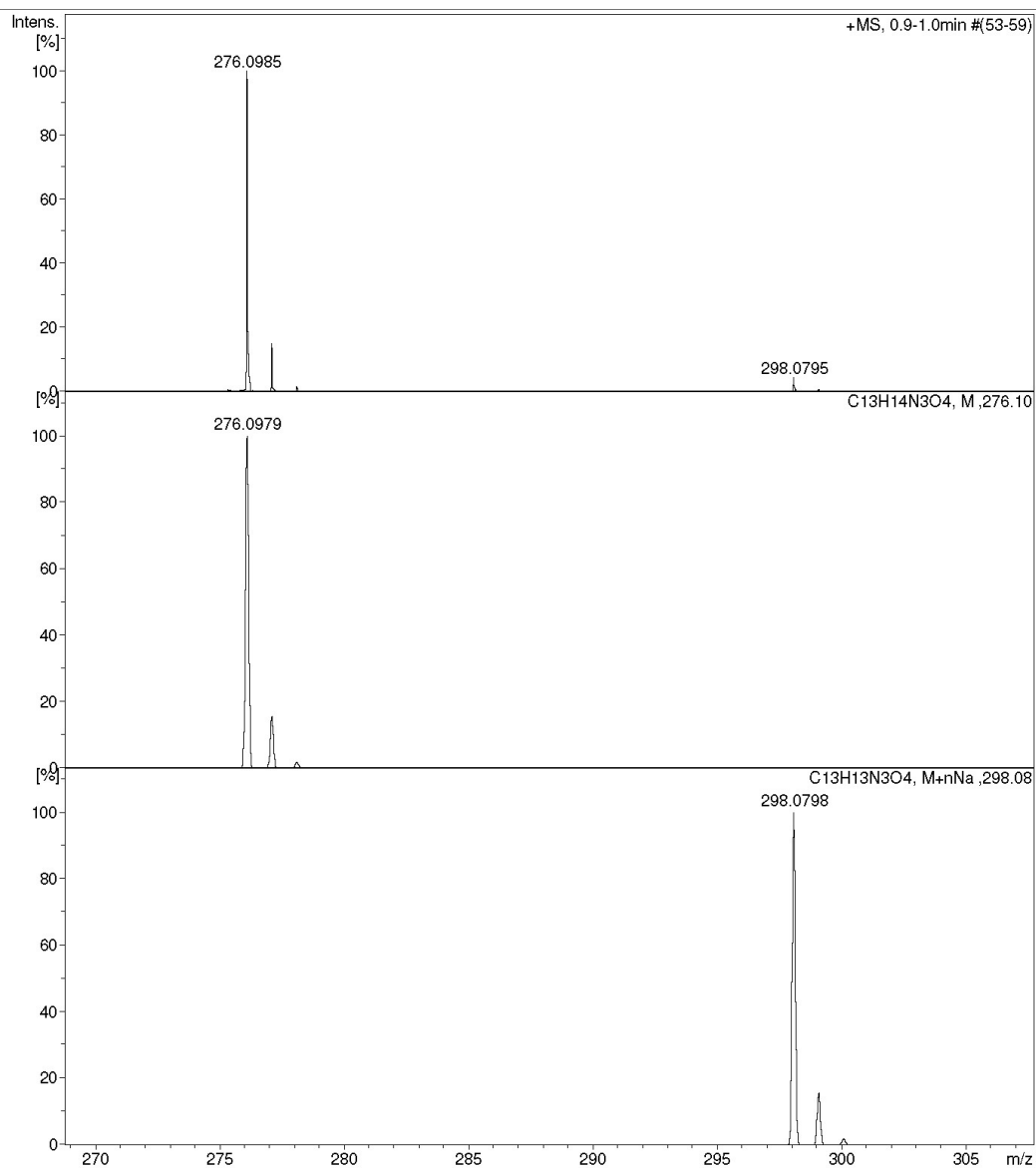
HSQC in  $\text{CDCl}_3$ :



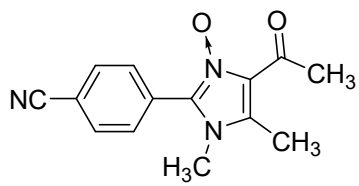
HMBC in CDCl<sub>3</sub>:



HRMS (ESI):

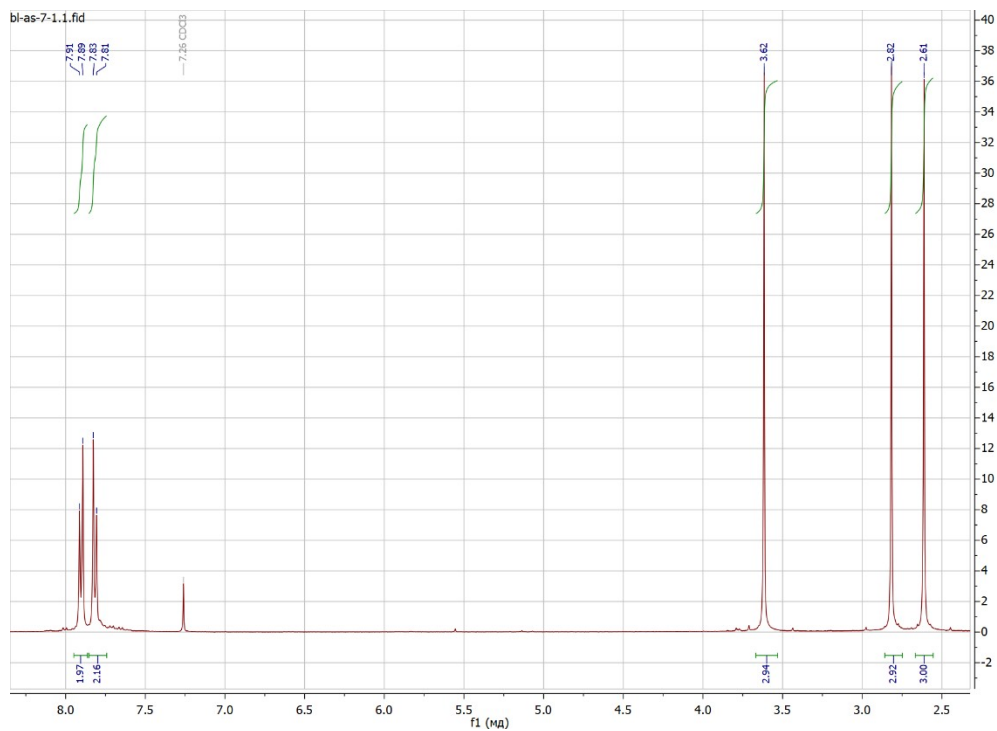


4-Acetyl-2-(4-cyanophenyl)-1,5-dimethyl-1H-imidazole 3-oxide (**10b**)

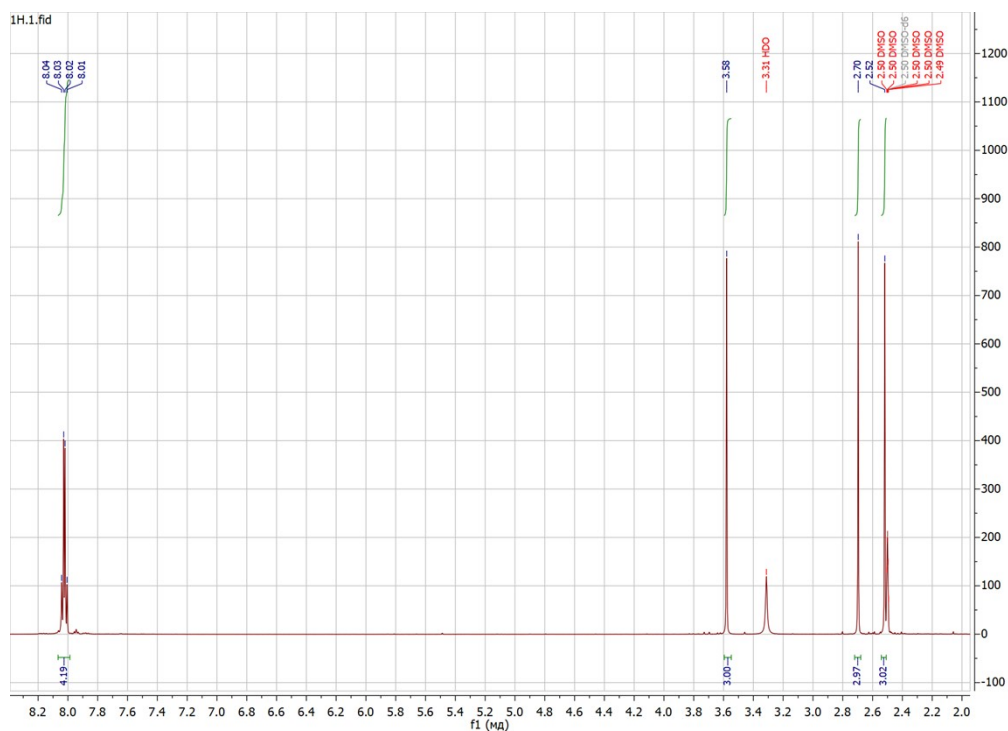


**10b**

<sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>:



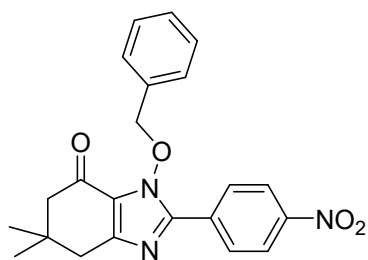
<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:





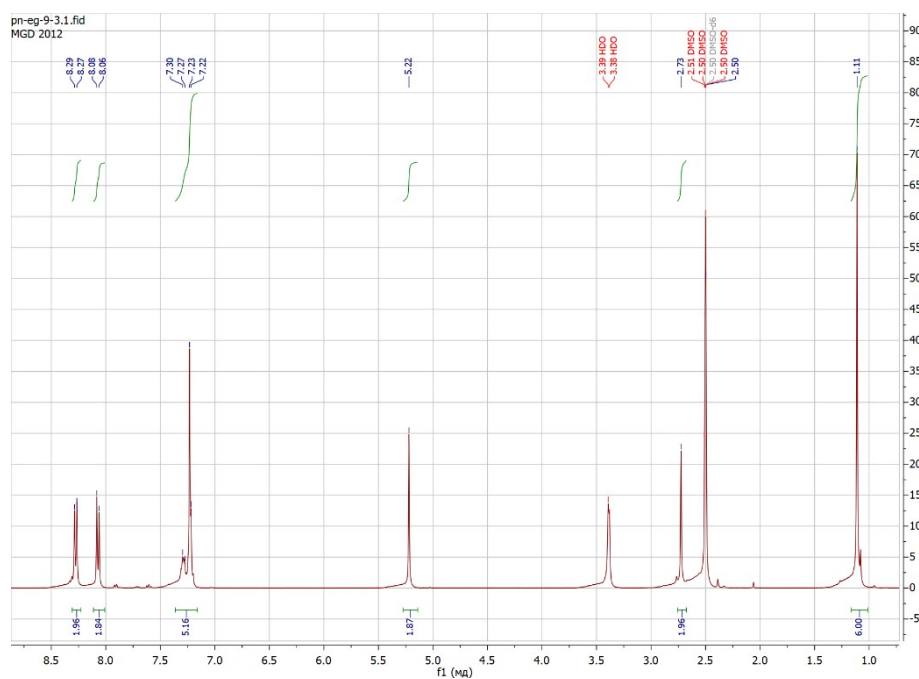


3-(Benzyloxy)-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one  
(11a)

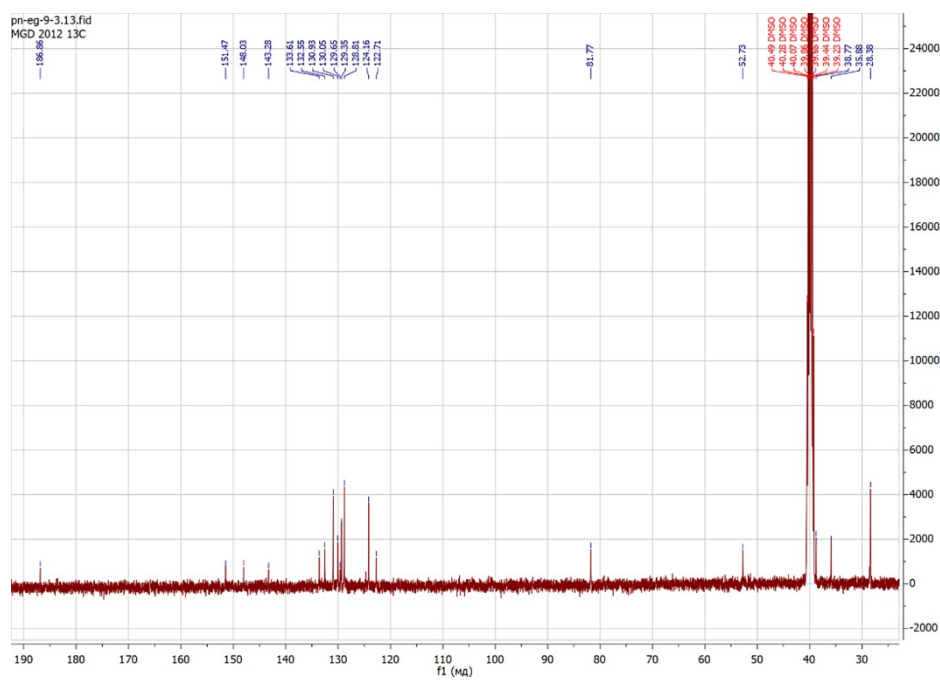


11a

$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :

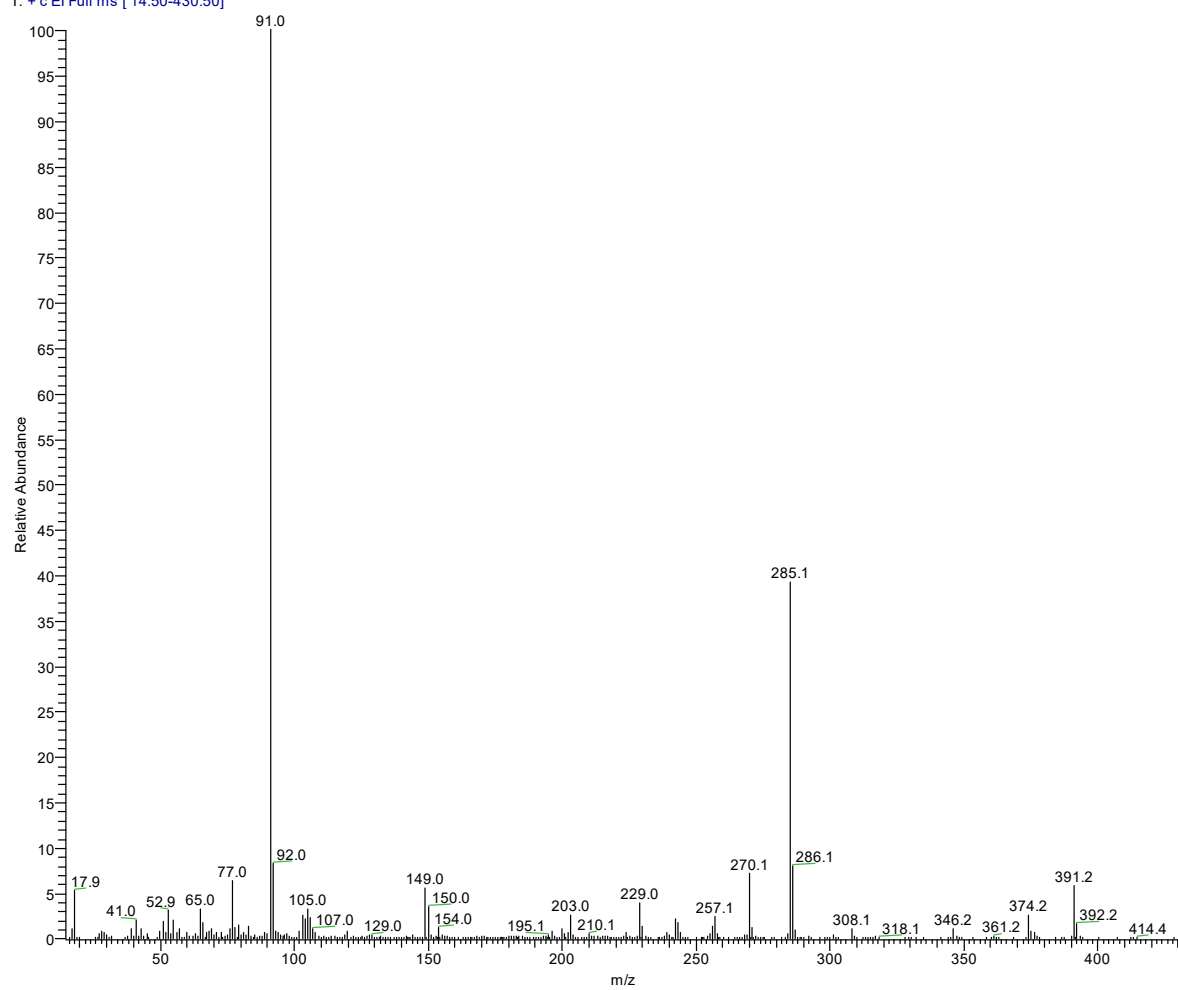


$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :

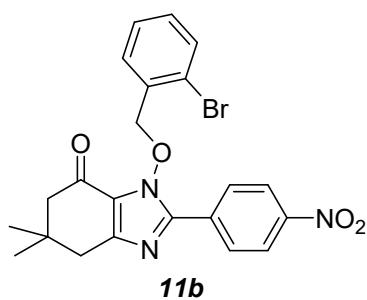


# HRMS (EI):

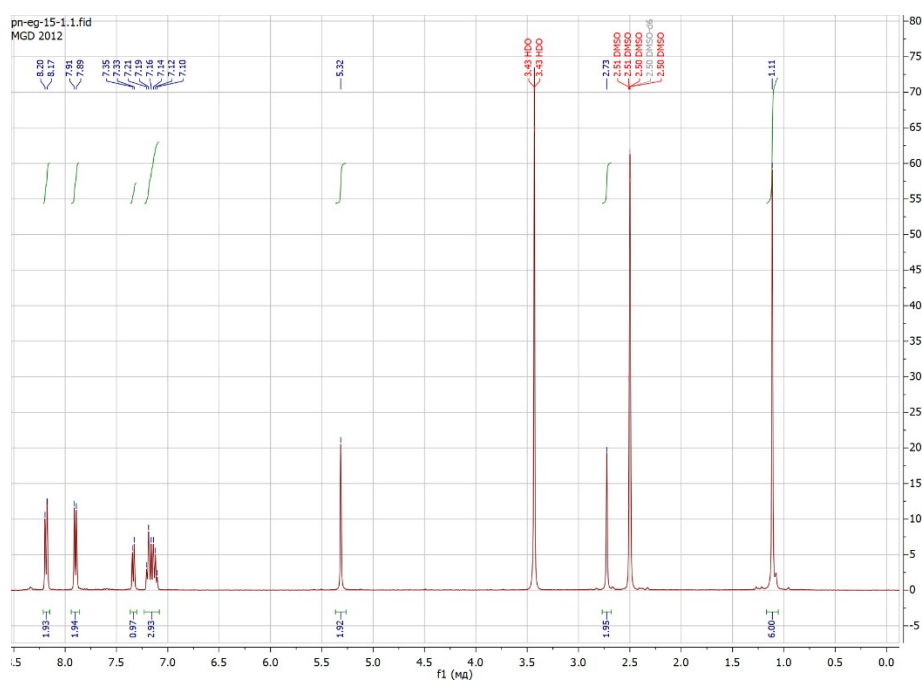
PANI-188 #6 RT: 0.46 AV: 1 NL: 1.18E7  
T: + c EI Full ms [ 14.50-430.50]



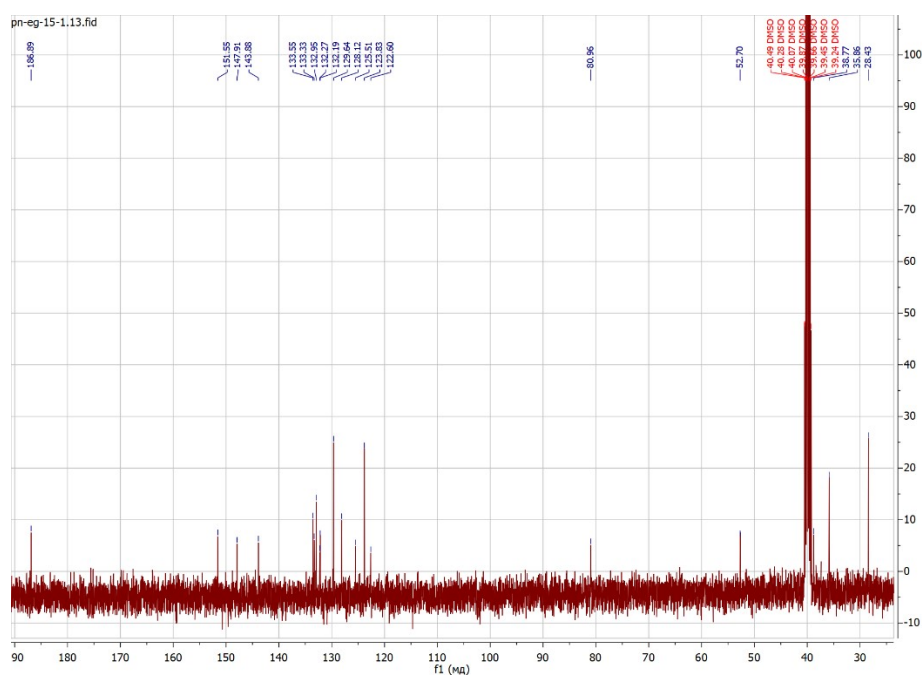
3-((2-Bromobenzyl)oxy)-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one (**11b**)



$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :

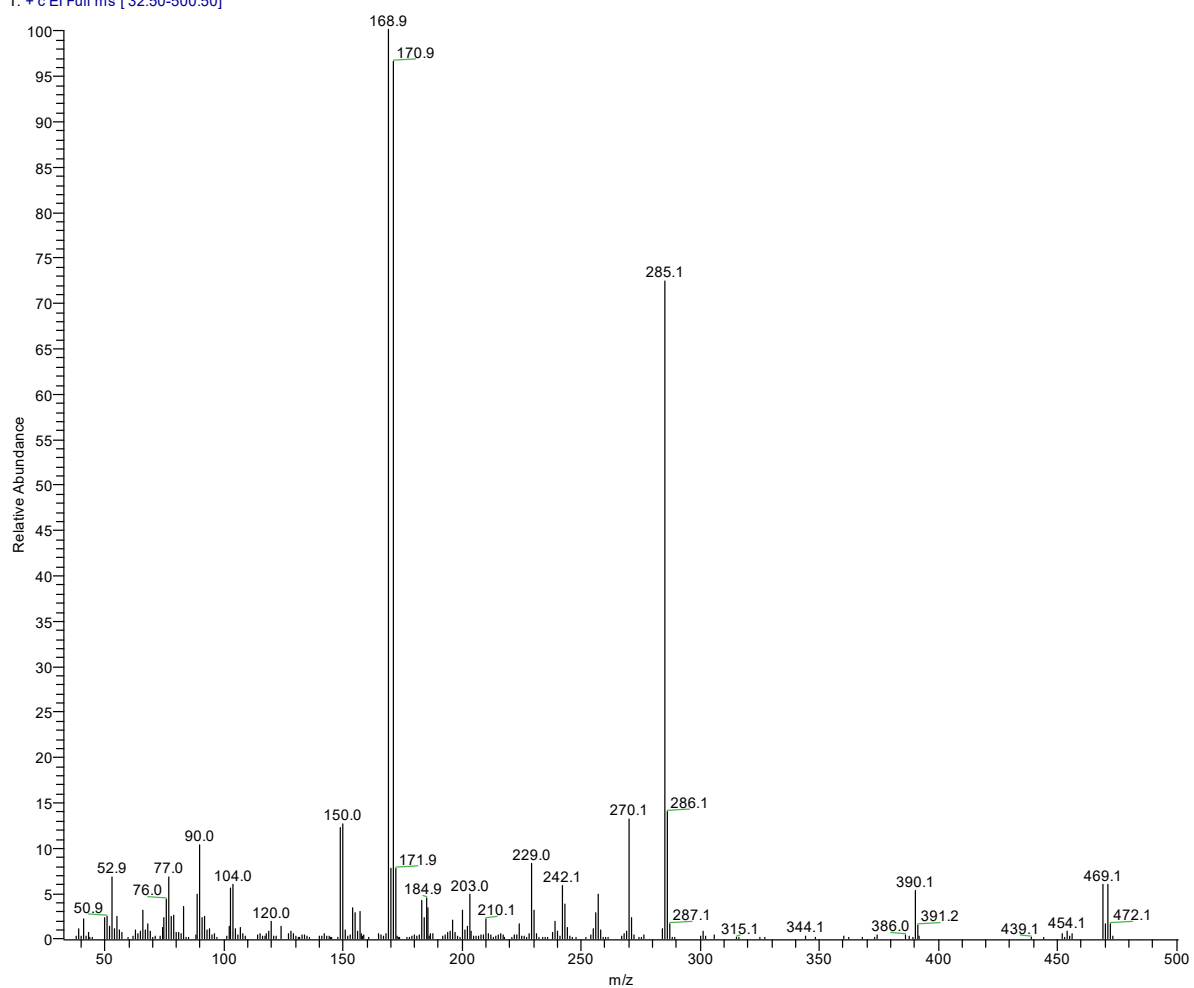


$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :

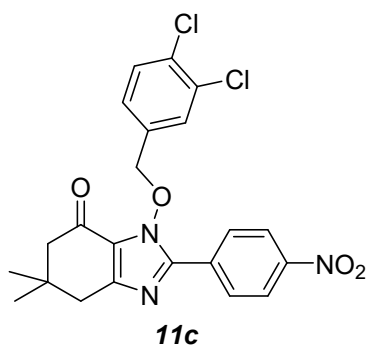


# HRMS (EI):

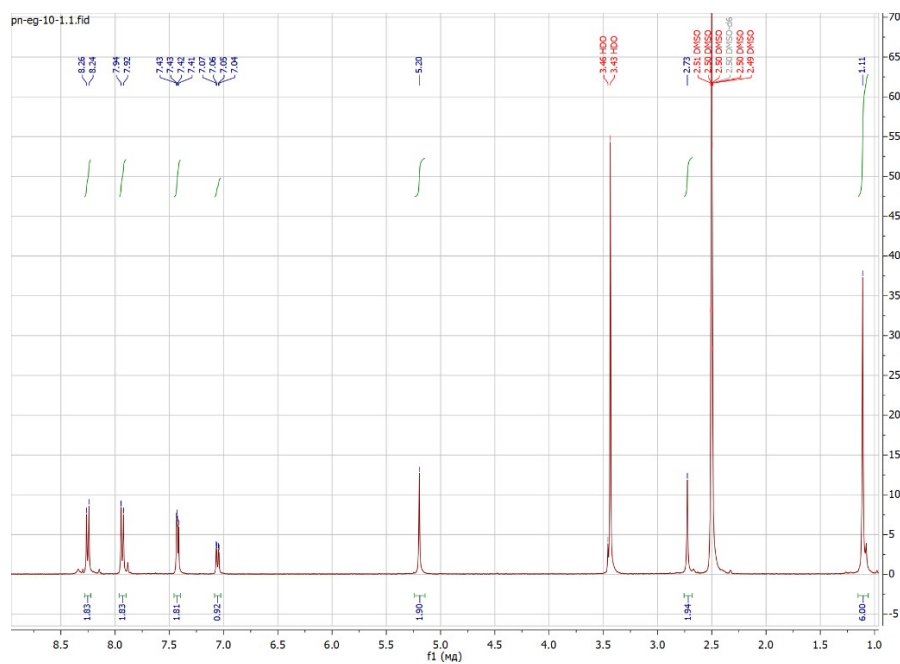
PANI-189 #2 RT: 0.07 AV: 1 NL: 1.50E6  
T: + c EI Full ms [ 32.50-500.50]



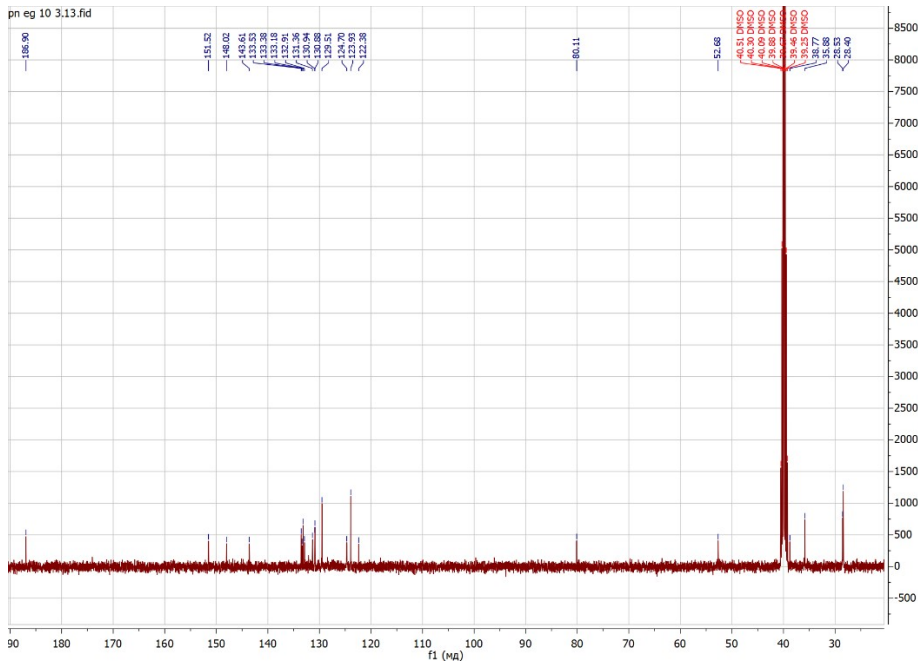
3-((3,4-Dichlorobenzyl)oxy)-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one (**11c**)



$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :

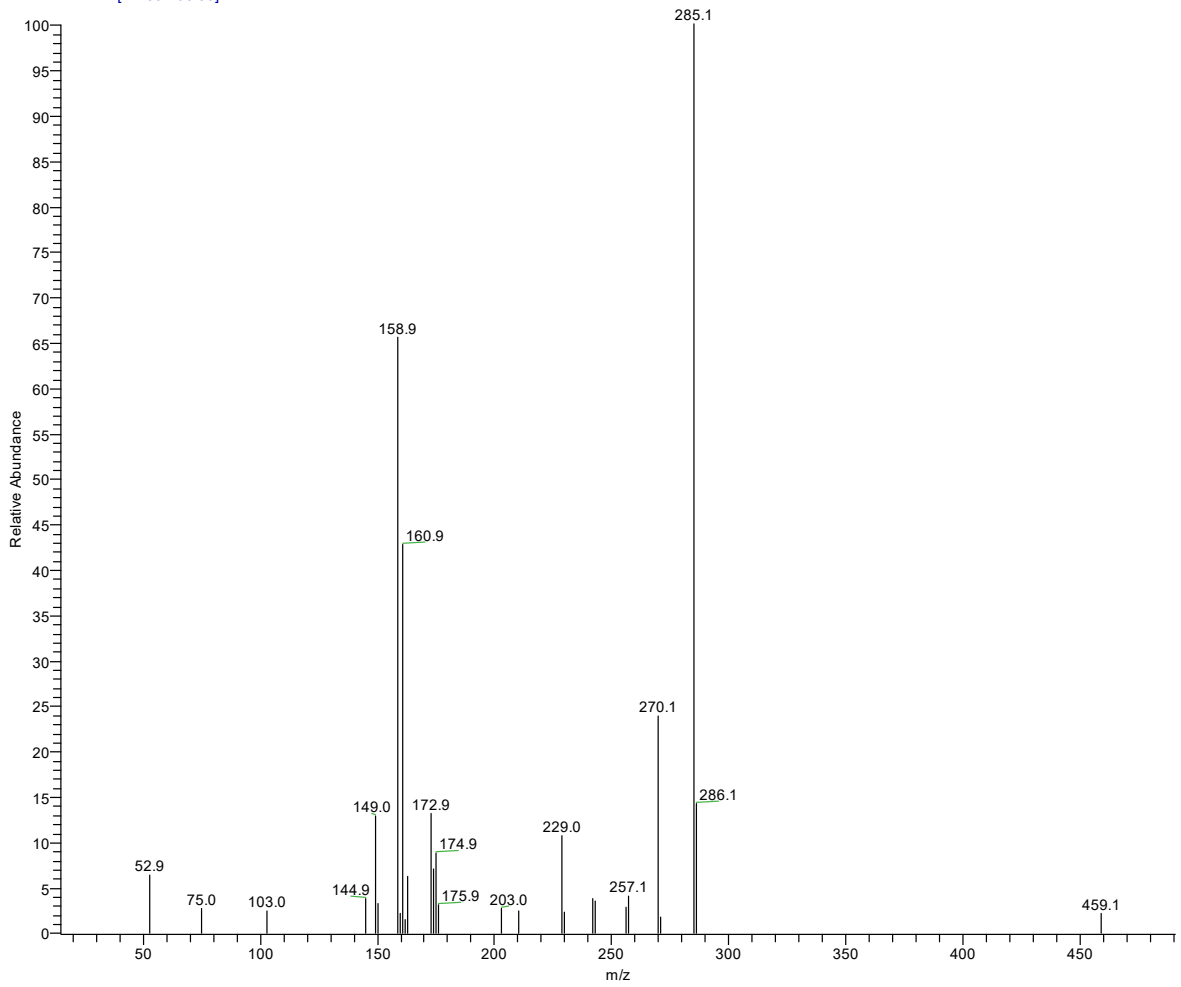


$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :

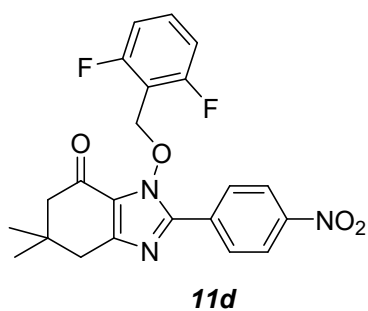


HRMS (EI):

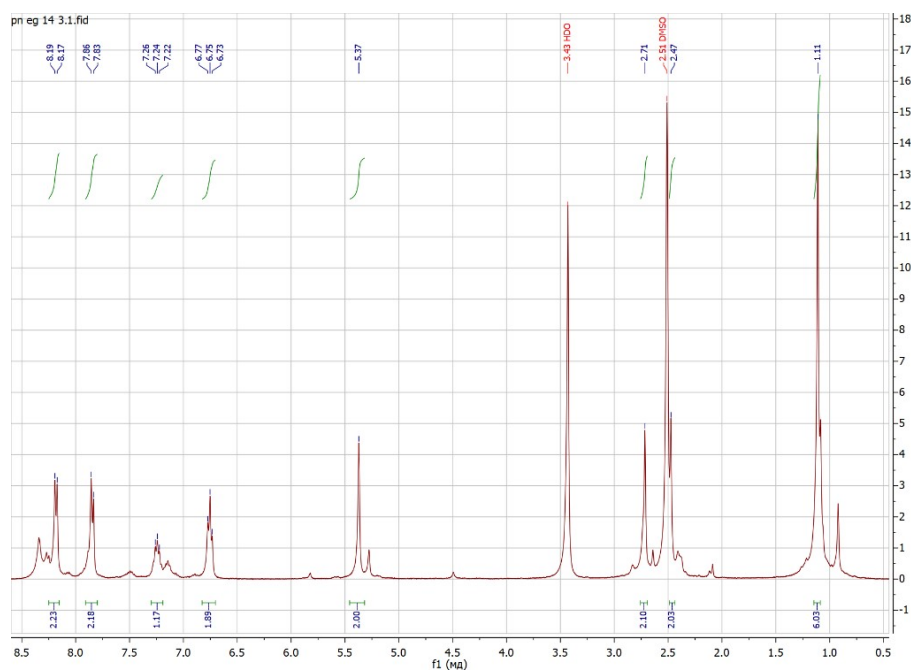
PANI-191 #1 RT: 0.00 AV: 1 NL: 4.75E4  
 T: + c EI Full ms [ 14.50-490.50]



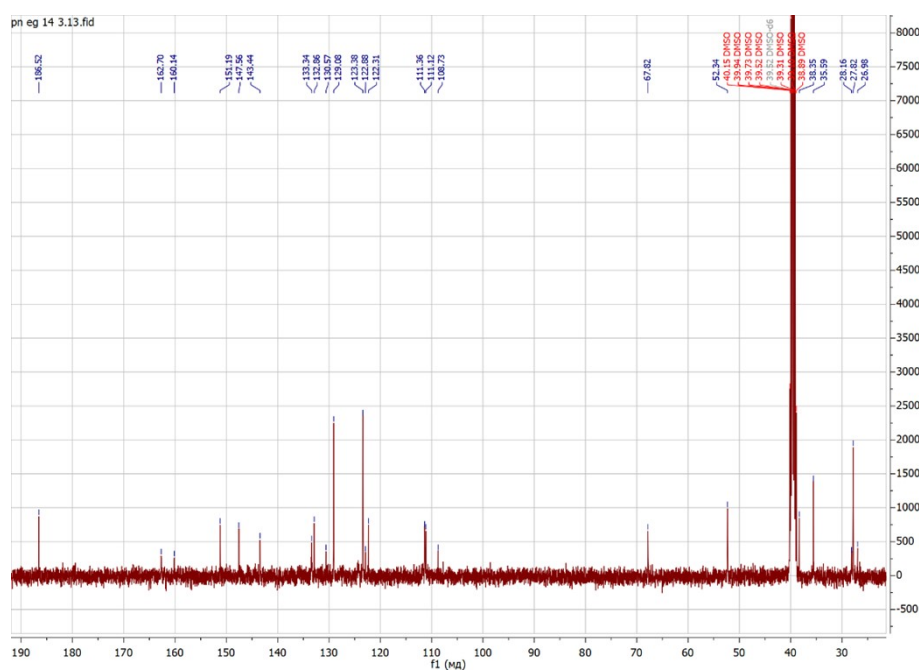
3-((2,6-Difluorobenzyl)oxy)-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one (**11d**)



$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :

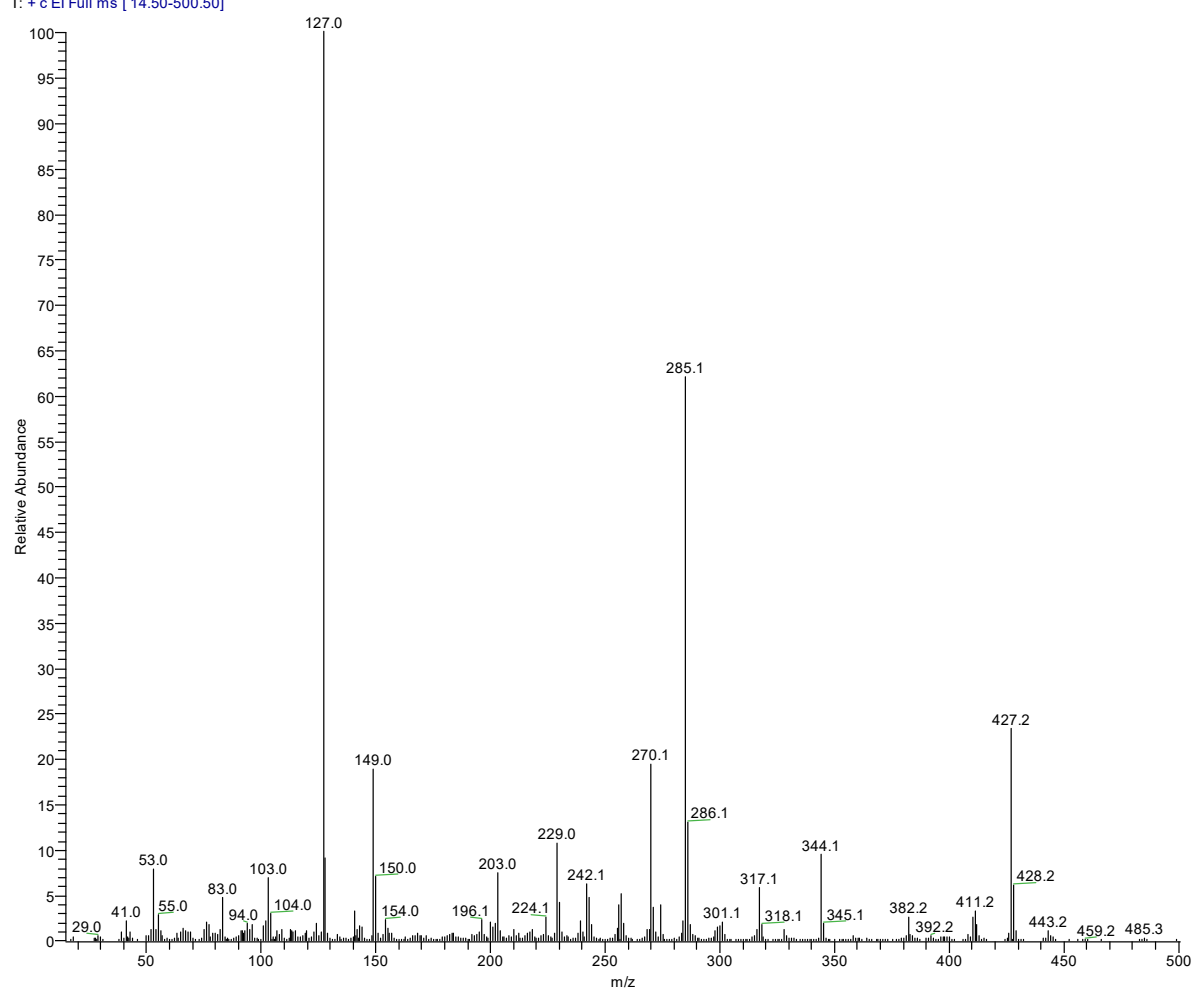


$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



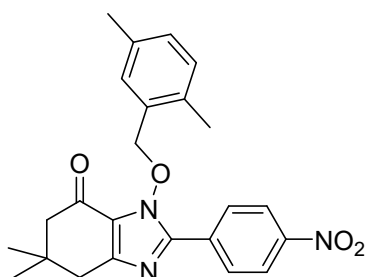
# HRMS (EI):

PANI-192 #17 RT: 1.01 AV: 1 NL: 4.83E6  
T: + c EI Full ms [ 14.50-500.50]



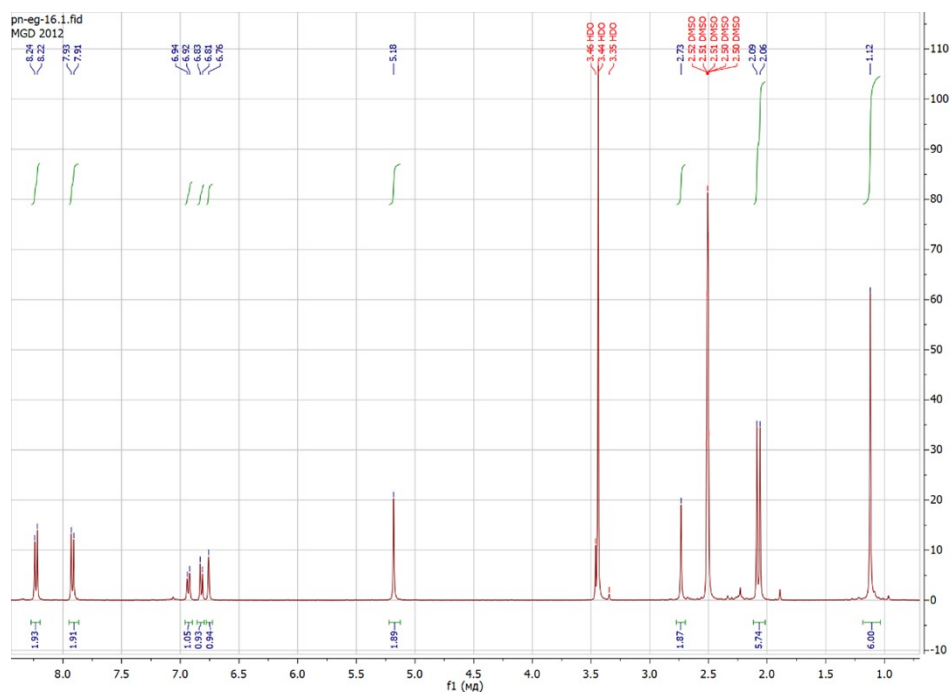


3-((2,5-Dimethylbenzyl)oxy)-6,6-dimethyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-4H-benzo[d]imidazol-4-one (**11e**)

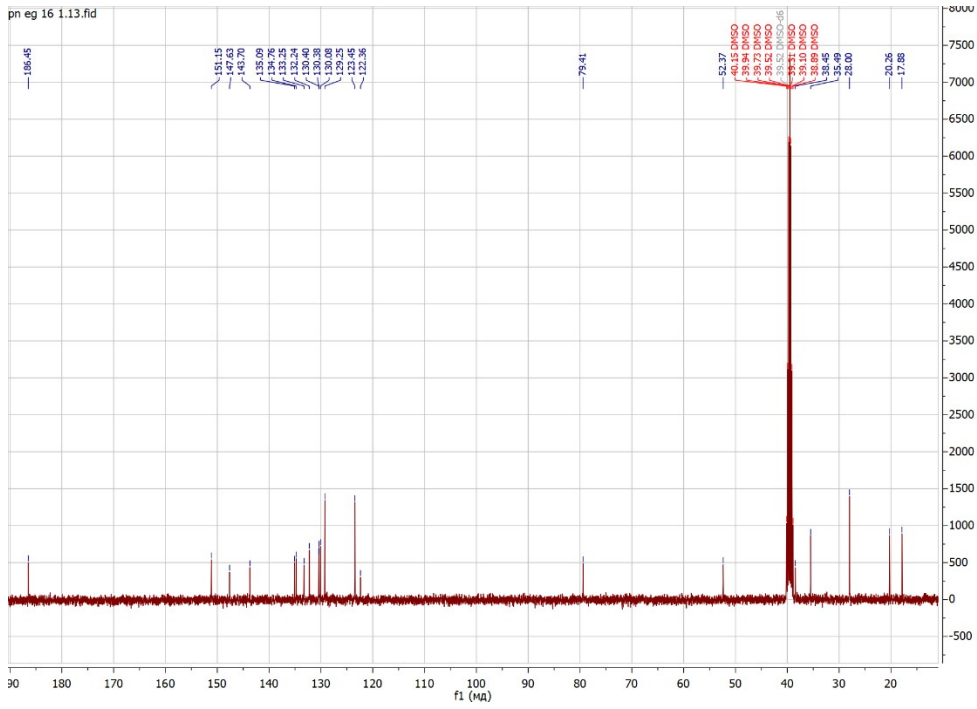


**11e**

$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :

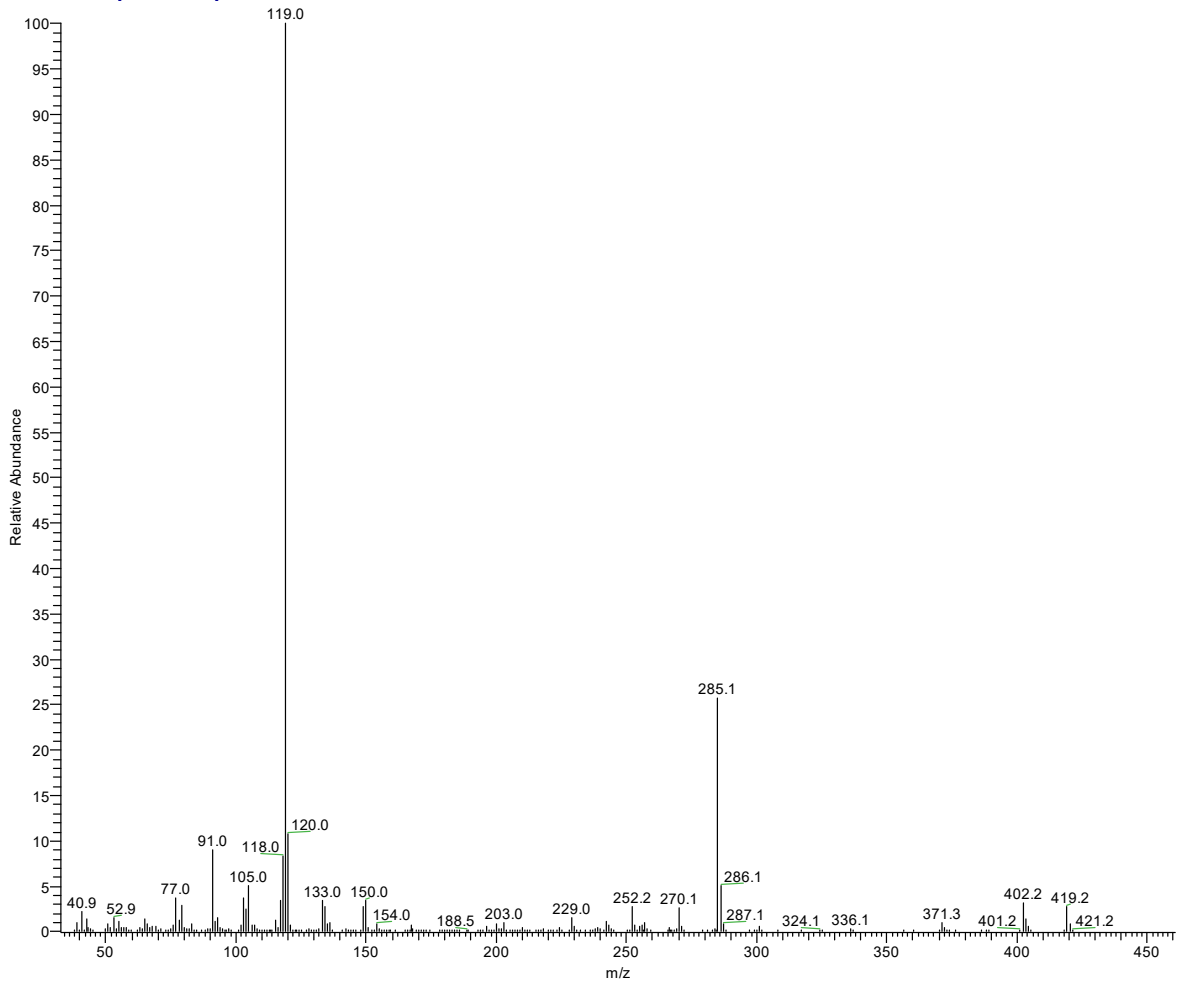


$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :

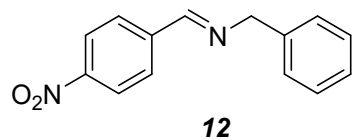


HRMS (EI):

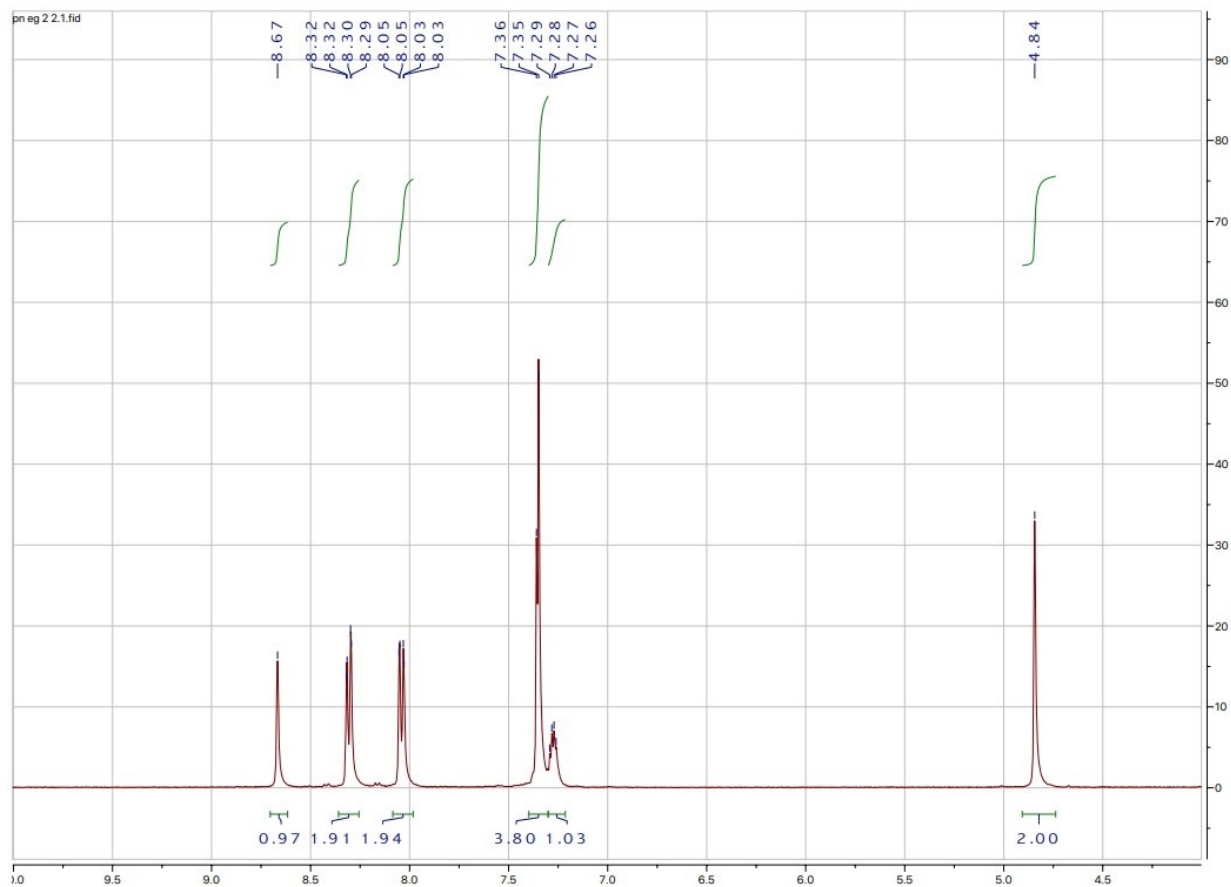
PANI-190 #4 RT: 0.19 AV: 1 NL: 6.77E6  
 T: + c EI Full ms [ 32.50-460.50]



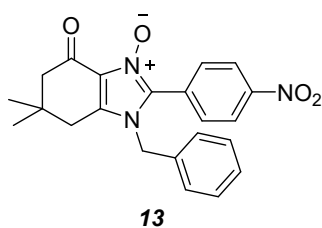
*(E)*-*N*-benzyl-1-(4-nitrophenyl)methanimine (**12**)



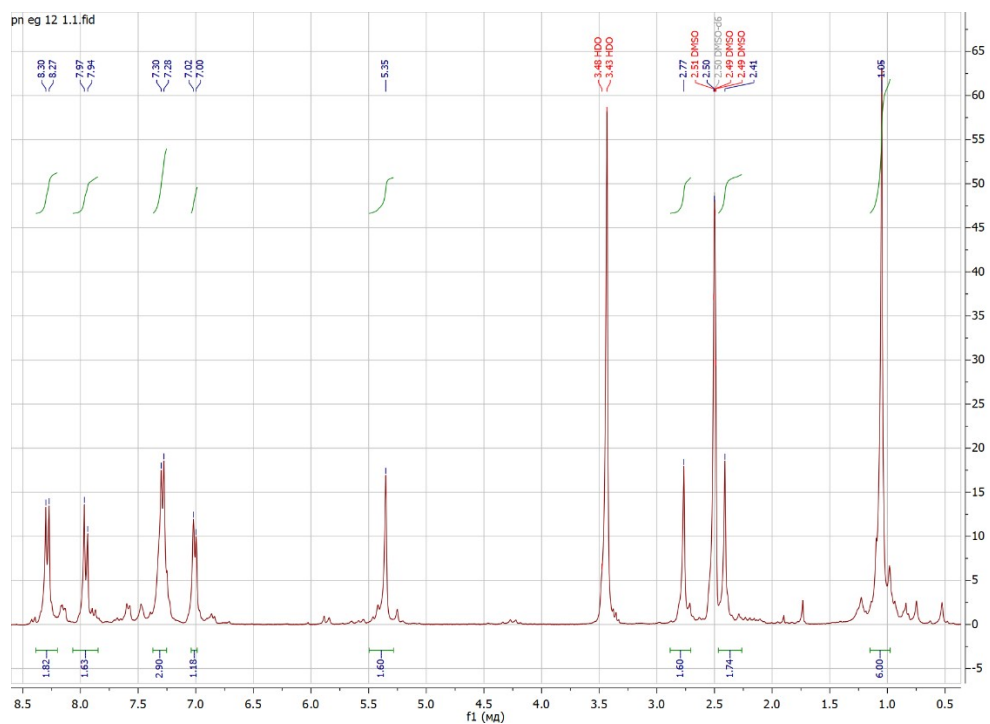
<sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub>:



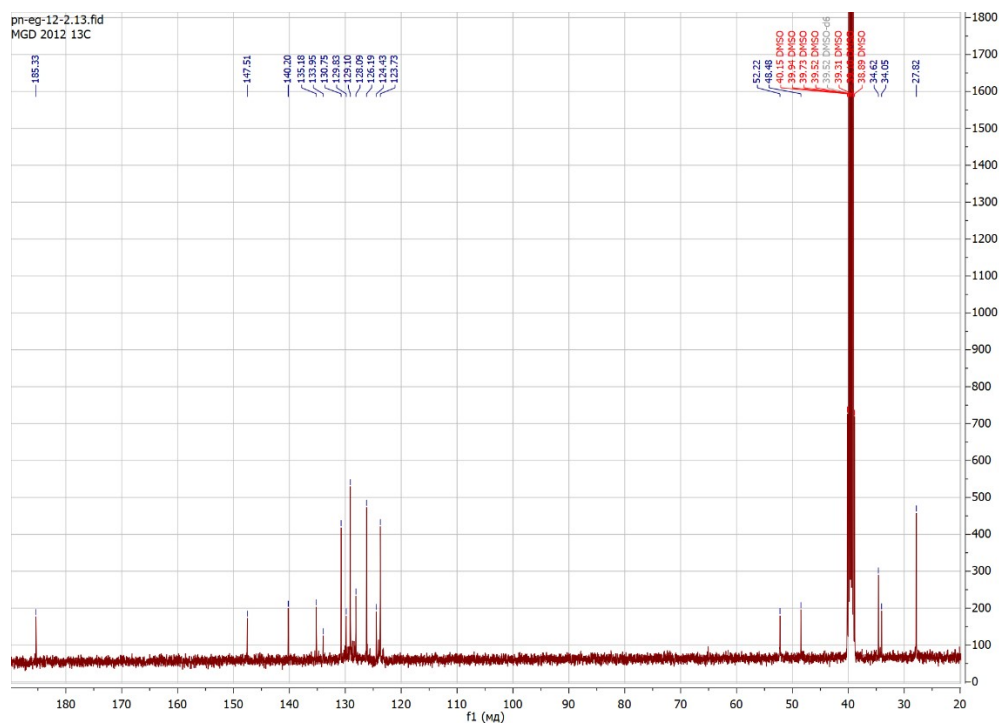
1-Benzyl-6,6-dimethyl-2-(4-nitrophenyl)-4-oxo-4,5,6,7-tetrahydro-1H-benzo[d]imidazole 3-oxide (13)



$^1\text{H}$  NMR spectrum in  $\text{DMSO-d}_6$ :



$^{13}\text{C}$  NMR spectrum in  $\text{DMSO-d}_6$ :



# HRMS (EI):

PANI-187 #1 RT: 0.00 AV: 1 NL: 3.59E5  
T: + c EI Full ms [ 14.50-430.50]

