

## Recyclization of diethoxymethyl substituted benzimidazo-fused thiazolium salts

Firudin I. Guseinov, Mikhail F. Pistsov, Vladislav M. Malinnikov, Oksana M. Lavrova, Eldar M. Movsumzade and Leonid M. Kustov

### 1. Chemistry

*Synthesis of 3-diethoxymethyl-3-hydroxy-2-R-3,9-dihydro-2H-benz[4,5]imidazo[2,1-b]thiazole hydrochlorides 3a-c from chloro oxiranes 1a-c.* Under stirring with a magnetic stirrer, chloro oxirane **1a-c** (2 g) was dissolved in absolute ethanol (10 ml), then a solution of 2-mercaptobenzimidazole (1 equiv.) in abs. EtOH (10 ml) was added. The mixture was stirred at room temperature for 4 h, the solvent was then evaporated under reduced pressure. The white precipitate was filtered and rinsed with acetone (2×10 ml).

*Synthesis of 3-diethoxymethyl-3-hydroxy-2-R-3,9-dihydro-2H-benz[4,5]imidazo[2,1-b]thiazole hydrochlorides 3a-c from chloro ketones 2a-c.* Under stirring with a magnetic stirrer, chloro ketone **2a-c** (2 g) was dissolved in absolute ethanol (10 ml), then a solution of 2-mercaptobenzimidazole (1 equiv.) in abs. EtOH (10 ml) was added. The mixture was stirred at room temperature for 4 h, the solvent was then evaporated under reduced pressure. The white precipitate was filtered and rinsed with diethyl ether (2×10 ml).

*3-Diethoxymethyl-3-hydroxy-2-methyl-3,9-dihydro-2H-benz[4,5]imidazo[2,1-b]thiazole hydrochloride 3a.* White powder, yield: 2.55 g (86%) from chloro oxirane **1a**, 2.49 g (84%) from chloro ketone **2a**, mp 120-123 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 0.92 (t, 3H, CH<sub>3</sub>, J 5 Hz); 1.17 (t, 3H, CH<sub>3</sub>, J 5 Hz); 1.57-1.63 (d, 3H, CH<sub>3</sub> J 7 Hz); 3.50-3.88 (m, 4H, CH<sub>2</sub>); 4.79-4.84 (q, 1H, CH, J 6.73 Hz); 5.27 (s, 1H, CH); 7.39 (d, 2H, Ar, J 4 Hz); 7.65 (t, 1H, Ar, J 5 Hz); 7.93 (t, 1H, Ar, J 5 Hz). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 15.52; 17.25; 52.89; 65.26; 66.18; 93.95; 103.10; 110.17; 112.86; 115.79; 122.84; 124.02; 124.60. Found (%): C, 52.34; H, 6.25; Cl, 10.55; N, 8.05; O, 13.80; S, 9.21. Calc. for C<sub>15</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>3</sub>S (%): C, 52.24; H, 6.14; Cl, 10.28; N, 8.12; O, 13.92; S, 9.30.

*3-Diethoxymethyl-3-hydroxy-2-phenyl-3,9-dihydro-2H-benz[4,5]imidazo[2,1-b]thiazole hydrochloride 3b.* White powder, yield: 2.9 g (92%) from chloro oxirane **1b**, 2.77 g (88%) from chloro ketone **2b**, mp 134-136 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 0.93 - 1.04 (m, 6H, CH<sub>3</sub>), 3.60 - 3.65 (m, 4H, CH<sub>2</sub>), 5.07 (s, 1H, CH), 5.88 (s, 1H, CH), 7.29-7.95 (m, 9H, Ar). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 15.04 (CH<sub>3</sub>), 55.98, 61.72 (CH<sub>2</sub>), 94.40, 102.61, 113.06, 114.64, 124.18, 125.97, 128.46, 133.99, 138.28, 153.75. Found (%): C, 59.45; H, 5.45; Cl 8.70; N 6.54; O, 11.40; S, 7.95. Calc. for C<sub>20</sub>H<sub>23</sub>ClN<sub>2</sub>O<sub>3</sub>S (%): C, 59.03; H, 5.70; Cl 8.71; N 6.88; O, 11.80; S, 7.88.

*3-Diethoxymethyl-3-hydroxy-2-(4-chlorophenyl)-3,9-dihydro-2H-benz[4,5]imidazo-[2,1-b]thiazole hydrochloride 3c*. White powder, yield: 2.70 g (90%) from chloro oxirane **1c**, 2.73 g (91%) from chloro ketone **2c**, mp 148-150 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 0.93 (t, 3H, CH<sub>3</sub>, J 5 Hz); 1.07 (t, 3H, CH<sub>3</sub>, J 5 Hz); 3.60-3.93 (m, 2H, CH<sub>2</sub>); 5.04 (s, 1H, CH); 5.80 (s, 1H, CH); 7.40-7.96 (m, 8H, Ar). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 20.27; 20.37; 64.12; 70.38; 70.58; 107.99; 117.70; 133.04; 137.82; 138.23; 138.89; 160.90. Found (%): C, 54.52; H, 5.21; Cl, 16.10; N, 6.30; O, 10.78; S, 7.36. Calc. for C<sub>20</sub>H<sub>22</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>S (%): C, 54.42; H, 5.02; Cl, 16.06; N, 6.35; O, 10.87; S, 7.26.

*Synthesis of 3,3,4-trihydroxy-2-R-3,4-dihydro-2H-benz[4,5]imidazo[2,1-b][1,3]thiazine hydrochlorides 4a-c*. Compound **3a-c** (0.5 g) was dissolved in a MeCN–H<sub>2</sub>O mixture (20 + 2 ml, respectively). The mixture was boiled for 4 hours, then cooled to room temperature. The crystalline precipitate was filtered and rinsed with MeCN (10 ml).

*3,3,4-Trihydroxy-2-methyl-3,4-dihydro-2H-benz[4,5]imidazo[2,1-b][1,3]thiazine hydrochloride 4a*. White crystals, yield 0.366 g (83%), mp 165-168 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 1.49-1.51 (d, 3H, CH<sub>3</sub>, J 7 Hz); 3.69 (q, 1H, CH, J 6.85 Hz); 5.98 (t, 1H, CH); 7.21-7.25 (m, 1H, Ar); 7.33-7.38 (m, 1H, Ar); 7.76 (d, 1H, Ar, J 9 Hz); 8.17 (d, 1H, Ar, J 8 Hz). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 53.10; 87.87; 91.56; 108.12; 119.95; 123.15; 128.12; 129.12; 133.65; 140.26; 154.18. Found (%): C, 45.62; H, 4.39; Cl, 12.45; N, 9.42; O, 16.53; S, 11.02. Calc. for C<sub>11</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>3</sub>S (%): C, 45.75; H, 4.54; Cl, 12.28; N, 9.70; O, 16.62; S, 11.10.

*3,3,4-Trihydroxy-2-phenyl-3,4-dihydro-2H-benz[4,5]imidazo[2,1-b][1,3]thiazine hydrochloride 4b*. White crystals, yield 0.370 g (85%), mp 150-152 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 5.14 (s, 1H, CH), 5.95 (s, 1H, CH), 7.23-7.92 (m, 8H, Ar). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 46.27, 79.91, 91.38, 111.85, 113.40, 123.21, 125.01, 128.24, 132.64, 133.44, 148.74. Found (%): C, 54.80; H, 4.42; Cl, 10.10; N, 8.12; O, 13.71; S, 9.21. Calc. for C<sub>16</sub>H<sub>15</sub>ClN<sub>2</sub>O<sub>3</sub>S (%): C, 54.78; H, 4.31; Cl, 10.11; N, 7.99; O, 13.68; S, 9.14.

*3,3,4-Trihydroxy-2-(4-chlorophenyl)-3,4-dihydro-2H-benz[4,5]imidazo[2,1-b][1,3]thiazine hydrochloride 4c*. White crystals, yield 0.366 g (83%), mp 163-165 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 5.14 (s, 1H, CH); 5.91 (s, 1H, CH); 7.25-7.98 (m, 8H, Ar). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 53.10; 87.87; 91.56; 108.12; 119.95; 123.25; 128.12; 129.12; 133.65; 134.41; 140.26; 154.18. Found (%): C, 49.72; H, 3.62; Cl, 18.70; N, 7.30; O, 12.35; S, 8.43. Calc. for C<sub>16</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>S (%): C, 49.88; H, 3.66; Cl, 18.40; N, 7.27; O, 12.46; S, 8.32.

*3-Hydroxy-2-phenyl-4-oxo-4H-benz[4,5]imidazo[2,1-b][1,3]thiazine hydrochloride 5'*. Compound **4b** (0.3 g, 0.86 mmol) was dissolved DMSO (2 ml) at room temperature. The solution was incubated within 7 days. The crystalline precipitate formed was filtered and rinsed with acetone (3 ml). Yield 0.175 g (62%), white crystals. mp 266-269 °C. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ: 7.55-7.65 (m, 5H, Ar); 7.72-7.84 (t, 3H, Ar); 8.62-8.74 (d, 2H, Ar); 10.07 (broad s, 1H, OH). <sup>13</sup>C NMR (100.63 MHz, DMSO-*d*<sub>6</sub>) δ: 115.29; 118.12; 123.42; 125.84; 128.75; 128.90; 129.64; 135.79; 142.49. Found (%): C, 58.09; H, 3.35; Cl, 10.72; N, 8.47; O, 9.67; S, 9.69. Calc. for C<sub>16</sub>H<sub>11</sub>ClN<sub>2</sub>O<sub>2</sub>S (%): C, 58.20; H, 3.52; Cl, 10.82; N, 8.33; O, 9.56; S, 9.61.

Figure S1 <sup>1</sup>H NMR spectrum of 3a

Acquisition Time (sec)	0.9961	Date	06 Jul 2018 13:39:12	Date Stamp	06 Jul 2018 13:39:12
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Number of Transients	32	Origin	spect	Original Points Count	8192
Pulse Sequence	zg	Receiver Gain	74.28	SW(cyclical) (Hz)	8223.68
Sweep Width (Hz)	8222.68	Temperature (degree C)	20.135	Solvent	DMSO-d6
				Spectrum Offset (Hz)	3201.4192

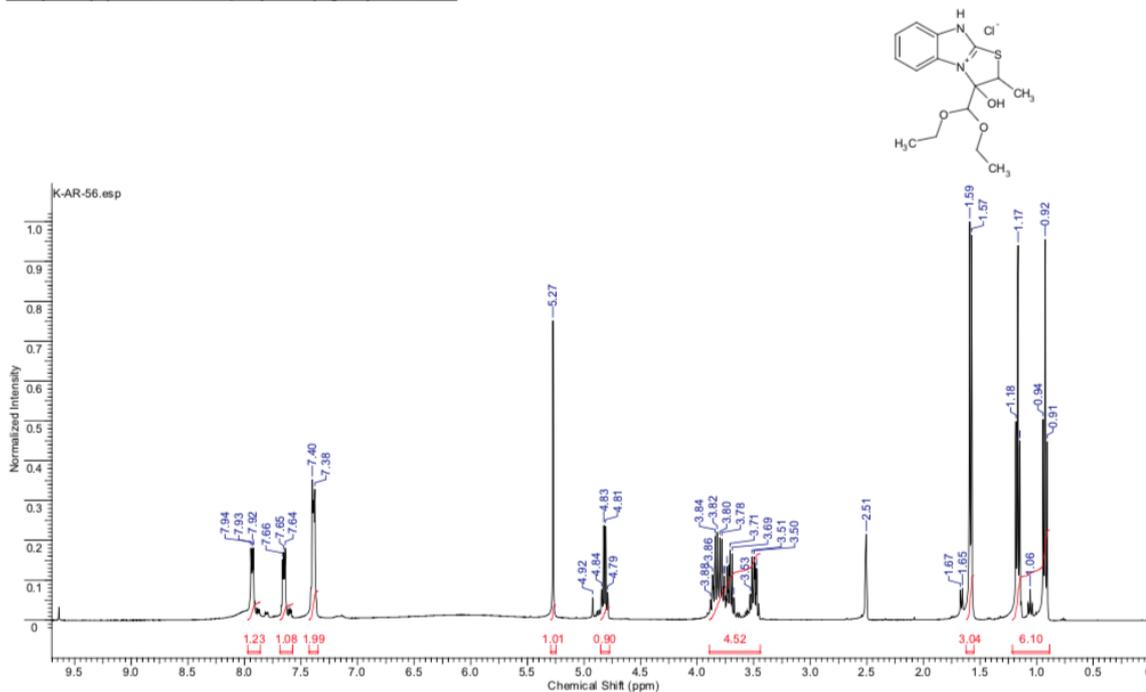
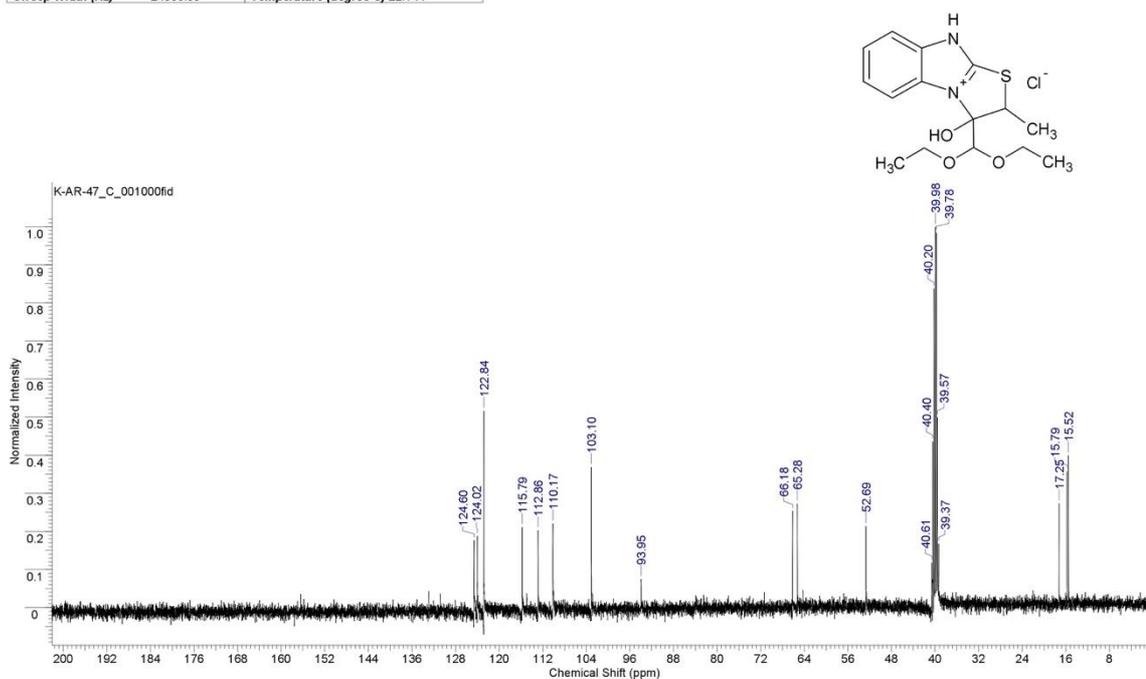


Figure S2 <sup>13</sup>C NMR spectrum of 3a

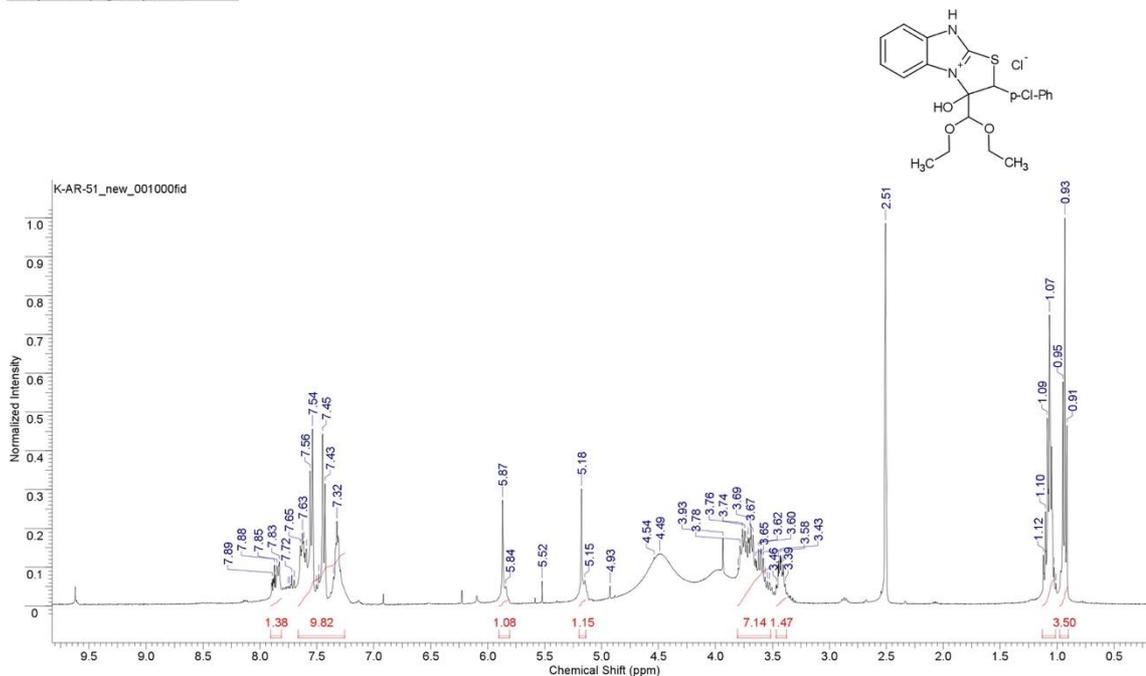
Acquisition Time (sec)	0.6816	Date	29 Jun 2018 14:51:44	Date Stamp	29 Jun 2018 14:51:44
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Number of Transients	800	Origin	spect	Original Points Count	16384
Pulse Sequence	zgpg	Receiver Gain	189.90	SW(cyclical) (Hz)	24038.46
Sweep Width (Hz)	24036.99	Temperature (degree C)	22.144	Solvent	DMSO-d6
				Spectrum Offset (Hz)	11574.3340





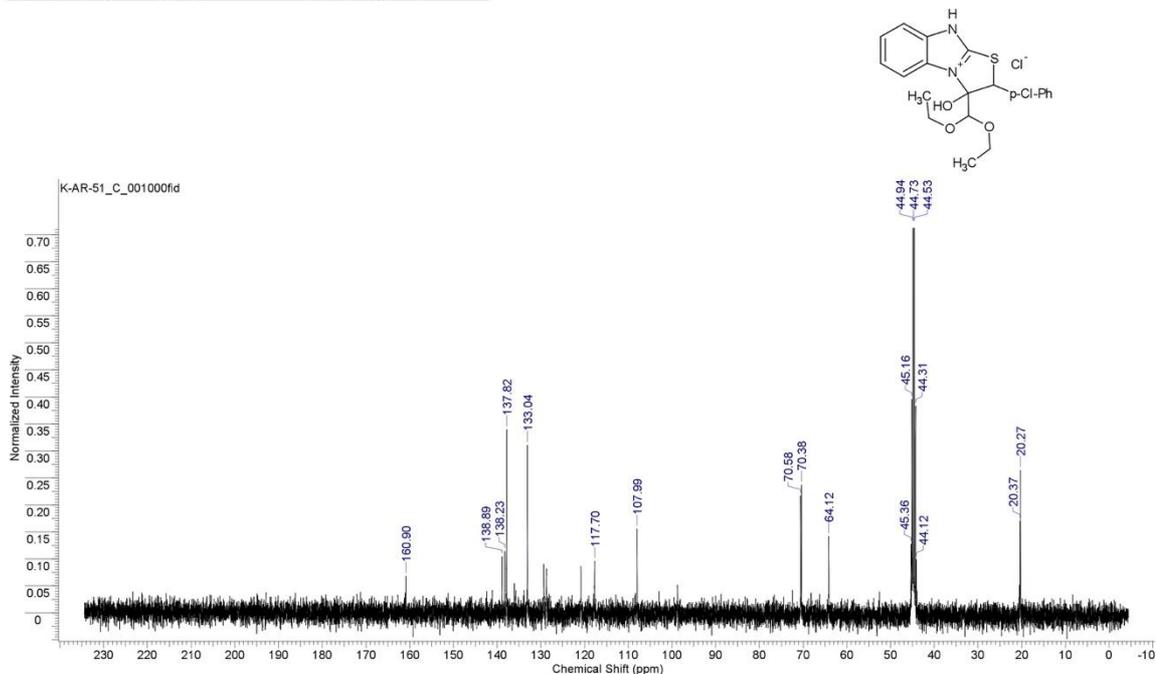
**Figure S5**  $^1\text{H}$  NMR spectrum of **3c**

Acquisition Time (sec)	0.9961	Date	05 Jul 2018 13:17:52	Date Stamp	05 Jul 2018 13:17:52
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Nucleus	$^1\text{H}$	Number of Transients	32	Origin	spect
Owner	nmr	Points Count	8192	Pulse Sequence	zg
SW(cyclical) (Hz)	8223.68	Solvent	DMSO-d6	Spectrum Offset (Hz)	3201.4192
Temperature (degree C)	20.027			Receiver Gain	106.79
				Sweep Width (Hz)	8222.68



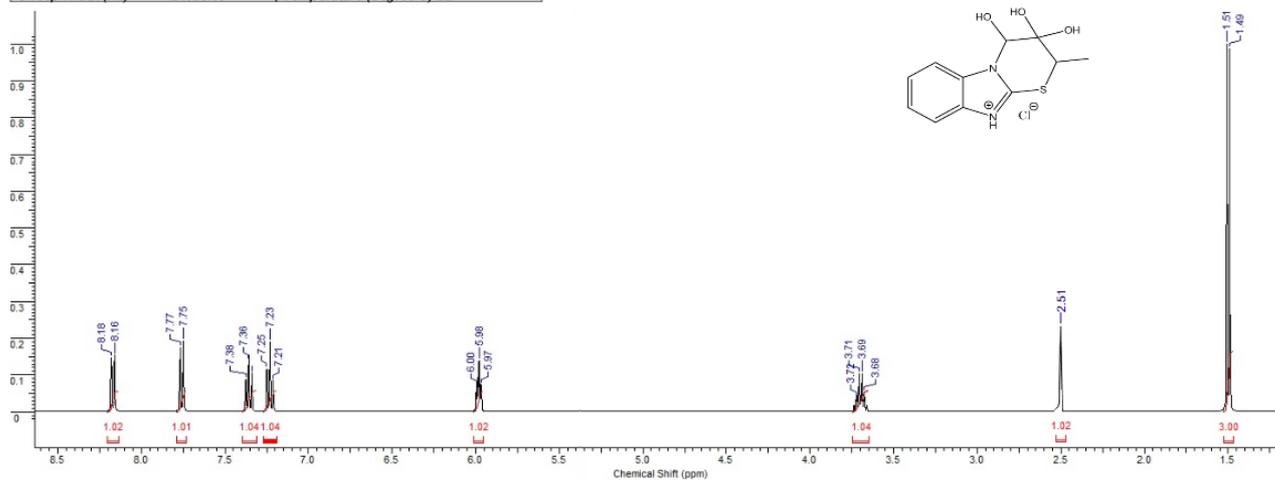
**Figure S6**  $^{13}\text{C}$  NMR spectrum of **3c**

Acquisition Time (sec)	0.6816	Date	30 Jun 2018 12:18:08	Date Stamp	30 Jun 2018 12:18:08
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Nucleus	$^{13}\text{C}$	Number of Transients	300	Origin	spect
Owner	nmr	Points Count	16384	Pulse Sequence	zgpg
SW(cyclical) (Hz)	24038.46	Solvent	CHLOROFORM-d	Receiver Gain	189.90
Sweep Width (Hz)	24036.99	Temperature (degree C)	22.199	Spectrum Offset (Hz)	11574.3340



**Figure S7**  $^1\text{H}$  NMR spectrum of **4a**

Acquisition Time (sec)	0.6816	Date	2. Jun 2018 14:51:44	Date Stamp	2. Jun 2018 14:51:44
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Frequency (MHz)	400	Nucleus	$^1\text{H}$	Number of Transients	800
Original Points Count	16384	Owner	nmr	Points Count	16384
Receiver Gain	189.90	SW(cyclical) (Hz)	24038.46	Solvent	DMSO-d6
Sweep Width (Hz)	24036.99	Temperature (degree C)	22.144	Pulse Sequence	zgpg
				Spectrum Offset (Hz)	11574.3340



**Figure S8**  $^{13}\text{C}$  NMR spectrum of **4a**

Acquisition Time (sec)	0.6816	Comment	5 mm PABBO BB-1H/D Z-GRD Z108618/0403	Date	08 May 2019 15:13:04
Date Stamp	08 May 2019 15:13:04				
Frequency (MHz)	100.63	Nucleus	$^{13}\text{C}$	File Name	C:\Users\Space\Desktop\Спектры\210519\спрецик\nmr\K-AR-5_1\K-AR-5_1_001000.fid
Original Points Count	16384	Owner	nmr	Number of Transients	759
Receiver Gain	32.27	SW(cyclical) (Hz)	24038.46	Points Count	16384
Sweep Width (Hz)	24036.99	Temperature (degree C)	19.178	Solvent	DMSO-d6
				Pulse Sequence	zgpg
				Spectrum Offset (Hz)	11574.3340

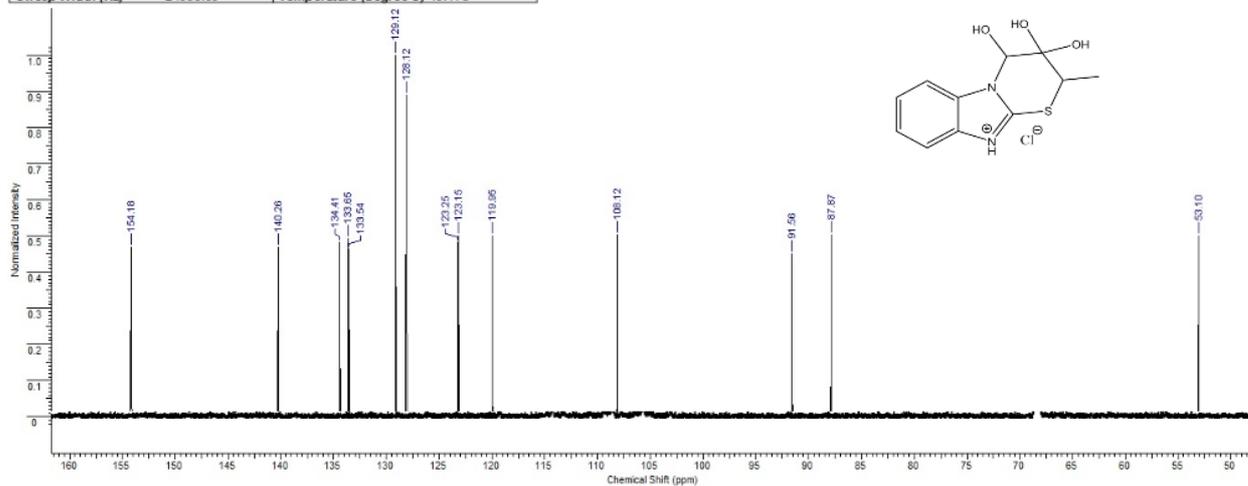


Figure S9 <sup>1</sup>H NMR spectrum of **4b**

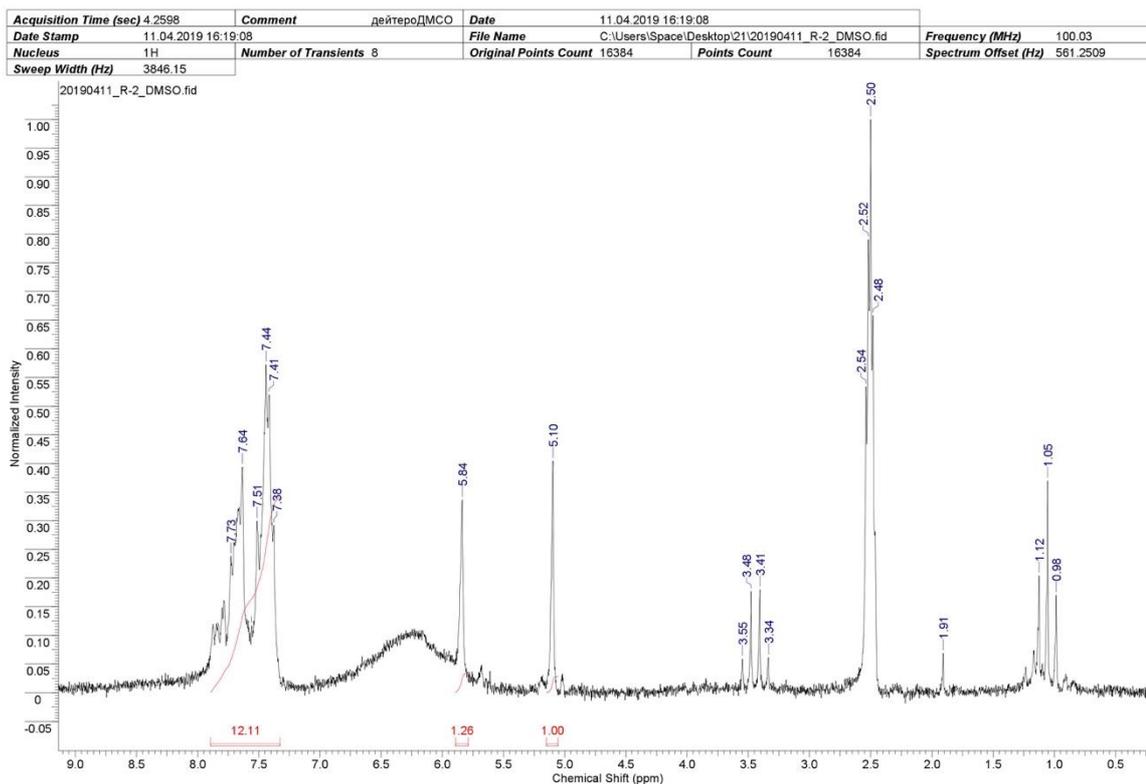


Figure S10 <sup>13</sup>C NMR spectrum of **4b**

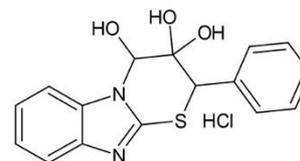
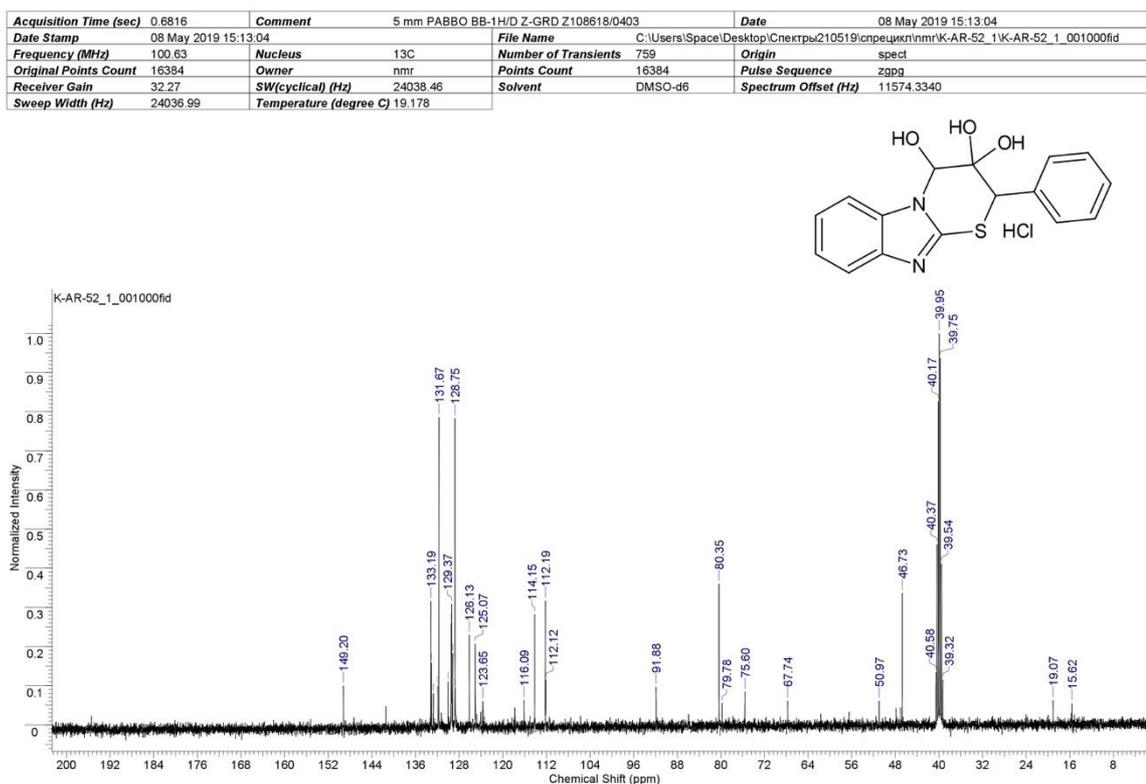


Figure S11 <sup>1</sup>H NMR spectrum of **4c**

Acquisition Time (sec)	0.9961	Date	06 Jul 2018 13:43:28	Date Stamp	06 Jul 2018 13:43:28
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Number of Transients	32	Origin	spect	Owner	nmr
Pulse Sequence	zg	Receiver Gain	106.79	SW(cyclical) (Hz)	8223.68
Sweep Width (Hz)	8222.68	Temperature (degree C)	20.146	Solvent	DMSO-d6
				Spectrum Offset (Hz)	3201.4192

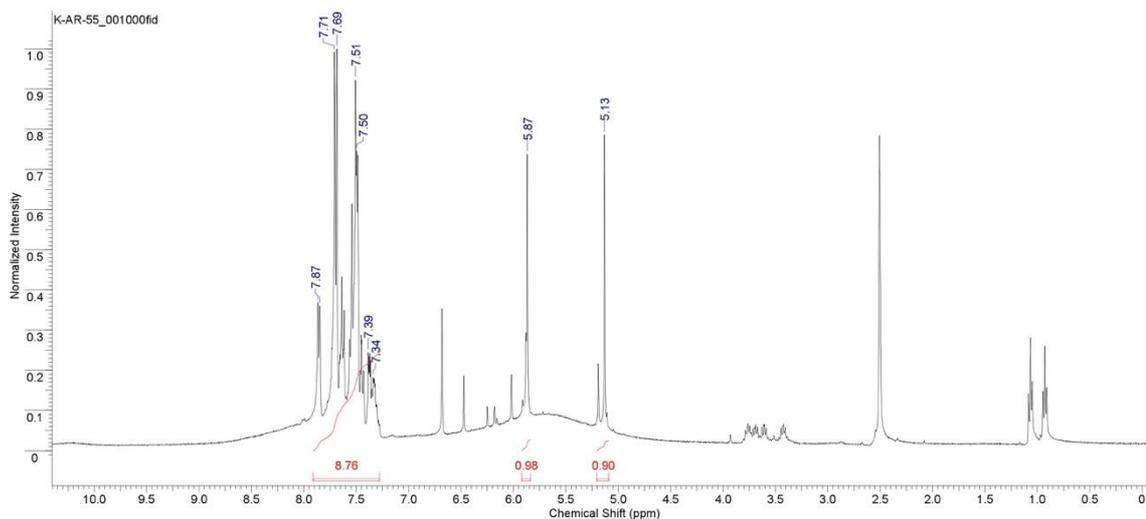
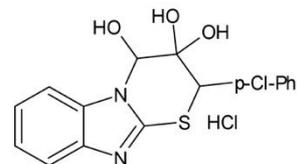
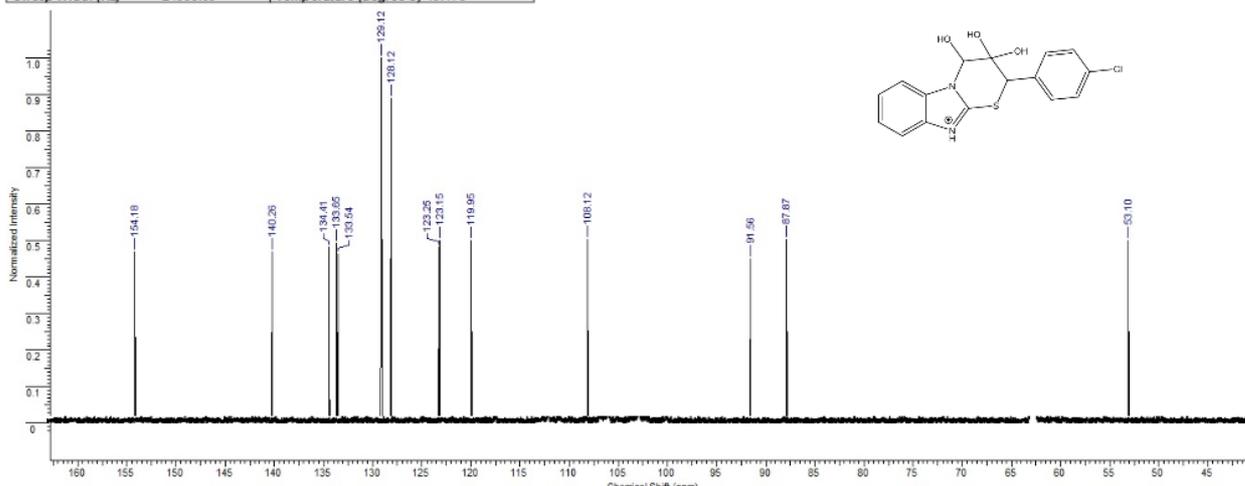
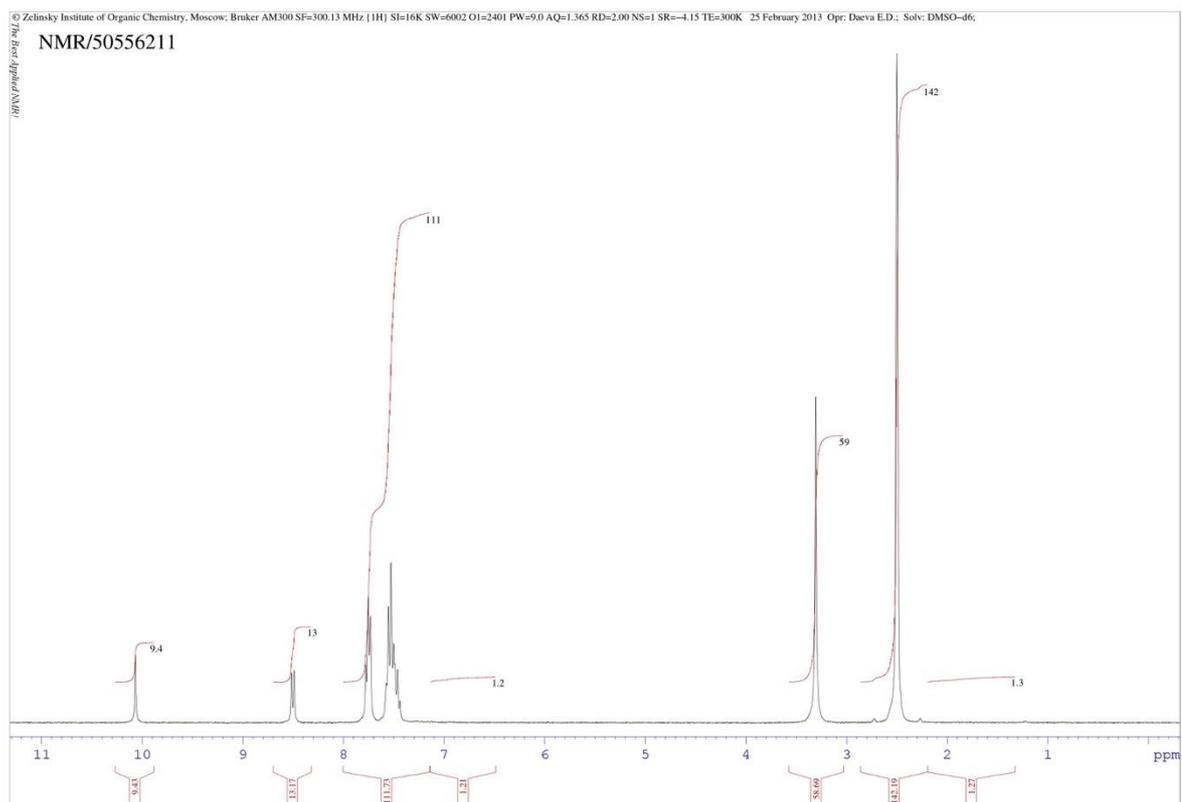


Figure S12 <sup>13</sup>C NMR spectrum of **4c**

Acquisition Time (sec)	0.6816	Comment	5 mm PABBO BB-1H/D Z-GRD Z108618/0403	Date	08 May 2019 15:13:04
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Frequency (MHz)	100.63	Nucleus	<sup>13</sup> C	Number of Transients	759
Original Points Count	16384	Owner	nmr	Points Count	16384
Receiver Gain	32.27	SW(cyclical) (Hz)	24038.46	Solvent	DMSO-d6
Sweep Width (Hz)	24036.99	Temperature (degree C)	19.178	Spectrum Offset (Hz)	11574.3340



**Figure S13**  $^1\text{H}$  NMR spectrum of **5'**



**Figure S14**  $^{13}\text{C}$  NMR spectrum of **5'**

