

## Electronic Supplementary Material file

# New hybrid tetrahydropyrrolo[3,2,1-*ij*]quinolin-1-ylidene-2-thioxothiazolidin-4-ones as New Inhibitors of Factor Xa and Factor XIa: Design, Synthesis, Docking, in silico and experimental evaluation

Nadezhda P. Novichikhina <sup>1</sup>, Alexander S. Shestakov <sup>1</sup>, Svetlana M. Medvedeva <sup>1</sup>, Anna M. Lagutina <sup>1</sup>, Mikhail Yu. Krysin <sup>1</sup>, Nadezhda A. Podoplelova <sup>2,3</sup>, Mikhail A. Panteleev <sup>2,3</sup>, Ivan S. Ilin <sup>4,5</sup>, Alexey V. Sulimov <sup>4,5</sup>, Anna S. Tashchilova <sup>4,5</sup>, Vladimir B. Sulimov <sup>4,5</sup>, Athina Geronikaki <sup>6,\*</sup> and Khidmet S. Shikhaliev <sup>1,\*</sup>

<sup>1</sup> Department of Organic Chemistry, Faculty of Chemistry, Voronezh State University, Universitetskaya pl. 1, 394018 Voronezh, Russia

<sup>2</sup> Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, 117997 Moscow, Russia

<sup>3</sup> Center for Theoretical Problems of Physicochemical Pharmacology, 119991 Moscow, Russia

<sup>4</sup> Dimonta, Ltd., 117186 Moscow, Russia

<sup>5</sup> Research Computing Center, Lomonosov Moscow State University, 119992 Moscow, Russia

<sup>6</sup> School of Pharmacy, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece

\* Correspondence: [geronik@pharm.auth.gr](mailto:geronik@pharm.auth.gr); [shikh1961@yandex.ru](mailto:shikh1961@yandex.ru).

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<sup>1</sup>H, <sup>13</sup>C NMR, IR and data HPLC-HRMS-ESI spectra of 8-bromo-4,4,6-trimethyl-6-phenyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **6**

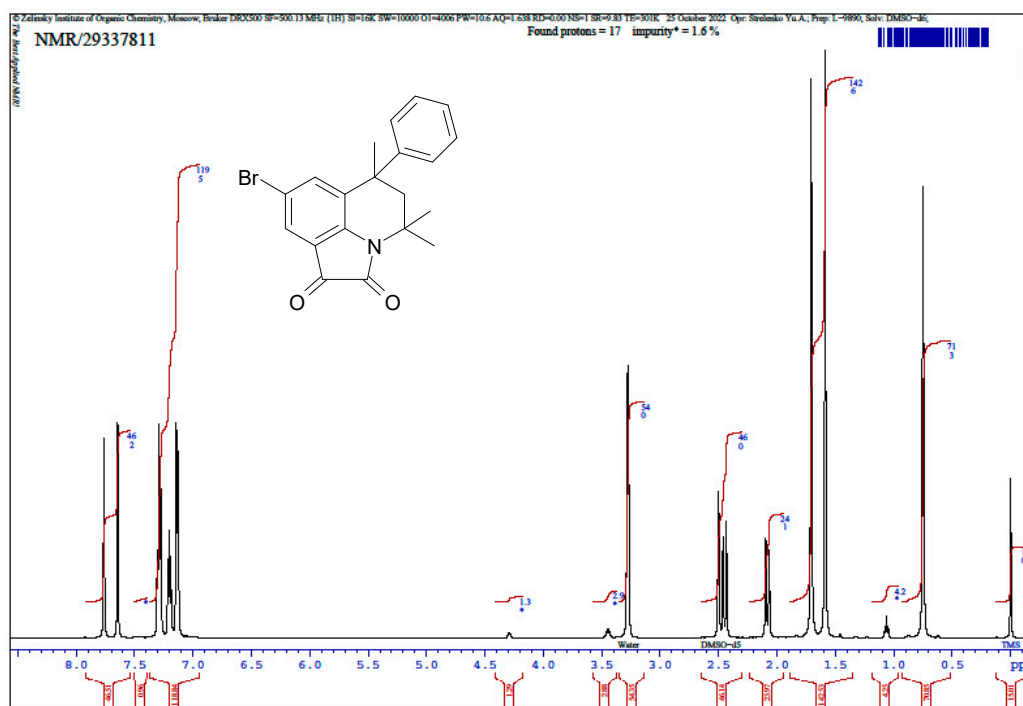


Figure S1. <sup>1</sup>H NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **6**

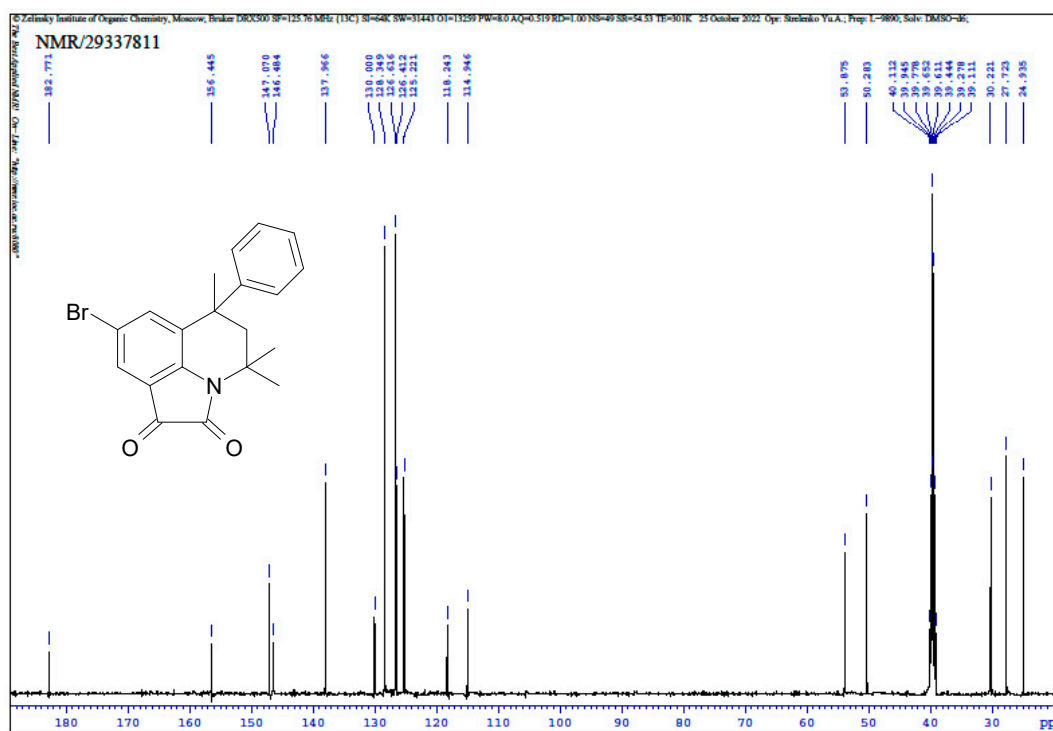
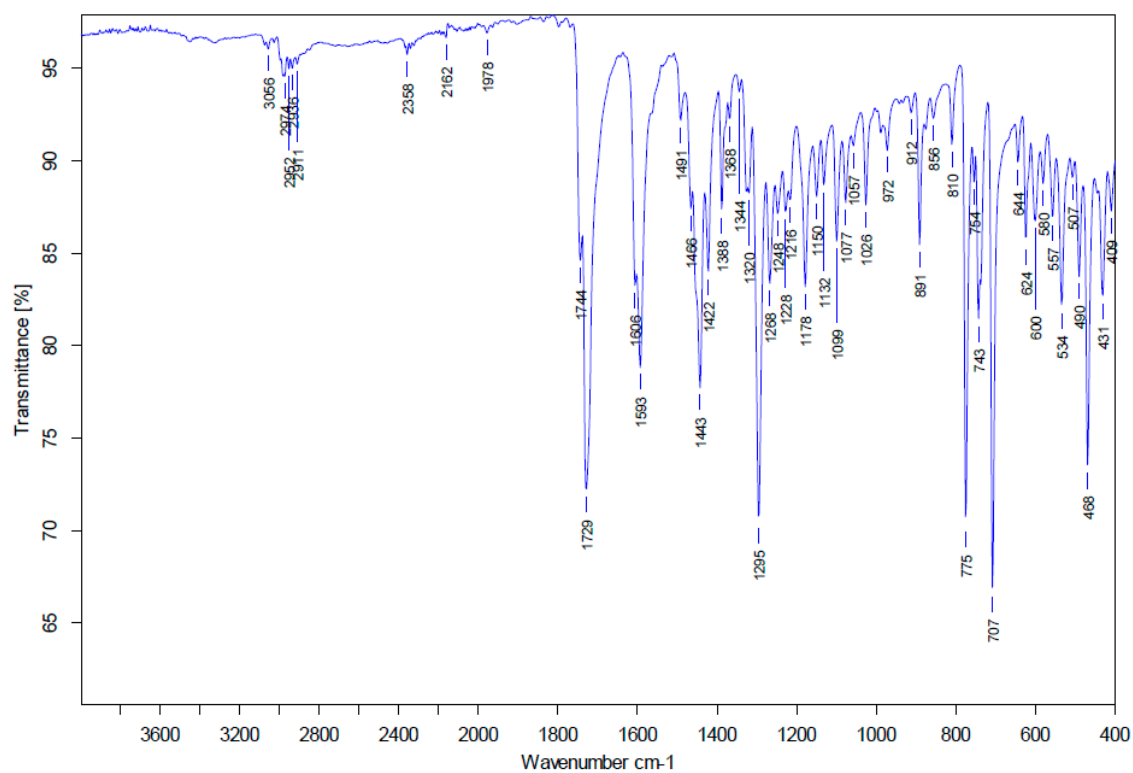
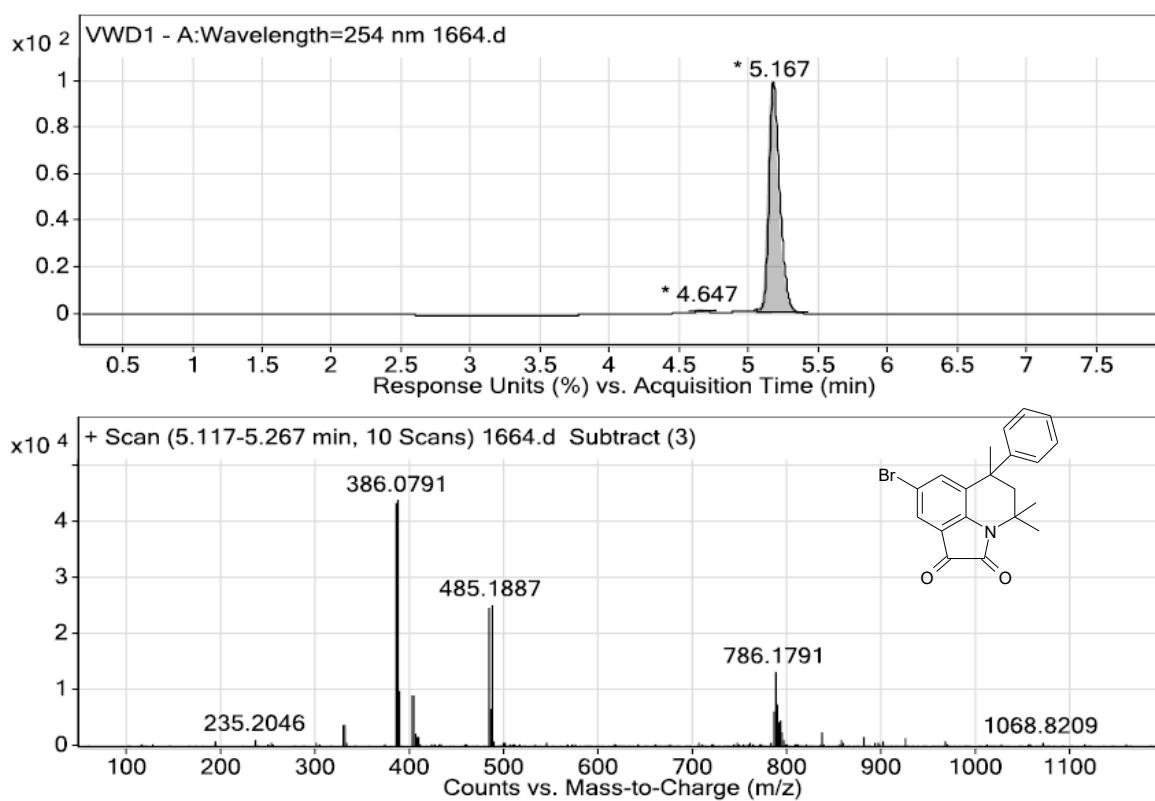


Figure S2. <sup>13</sup>C NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **6**





**Figure S3.** IR spectrum of 5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-1,2-dione **6**



**Figure S4.** Data of HPLC-MS-ESI analysis of **6**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of 6-iodo-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline hydrochloride **8a**

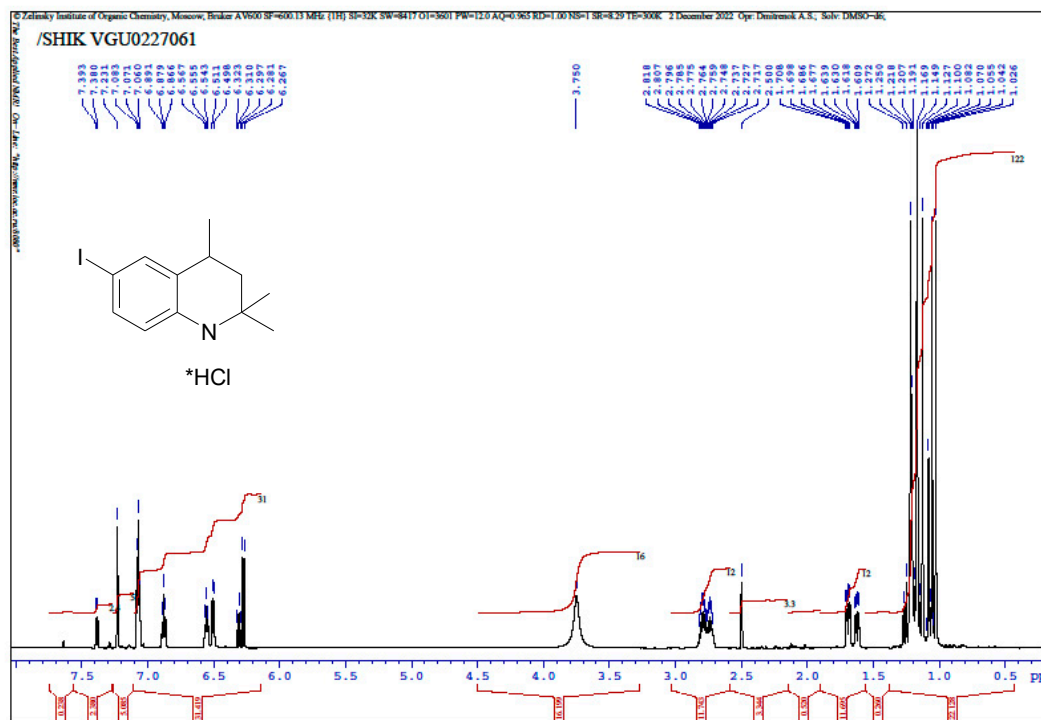


Figure S5.  $^1\text{H}$  NMR spectrum of 6-iodo-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline hydrochloride **8a**

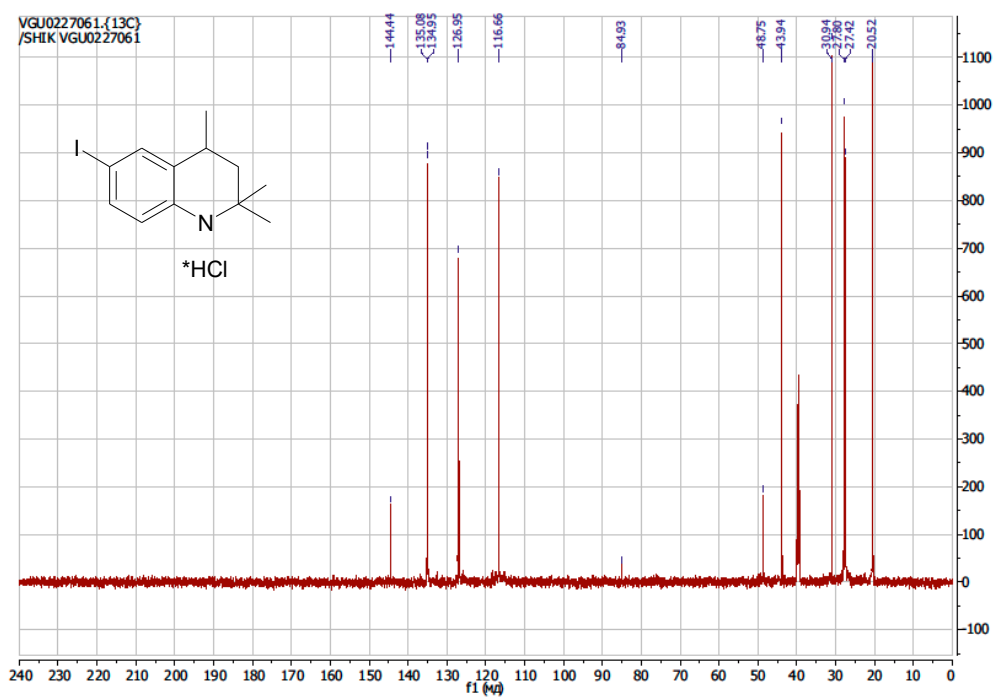


Figure S6.  $^{13}\text{C}$  NMR spectrum of 6-iodo-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline hydrochloride **8a**

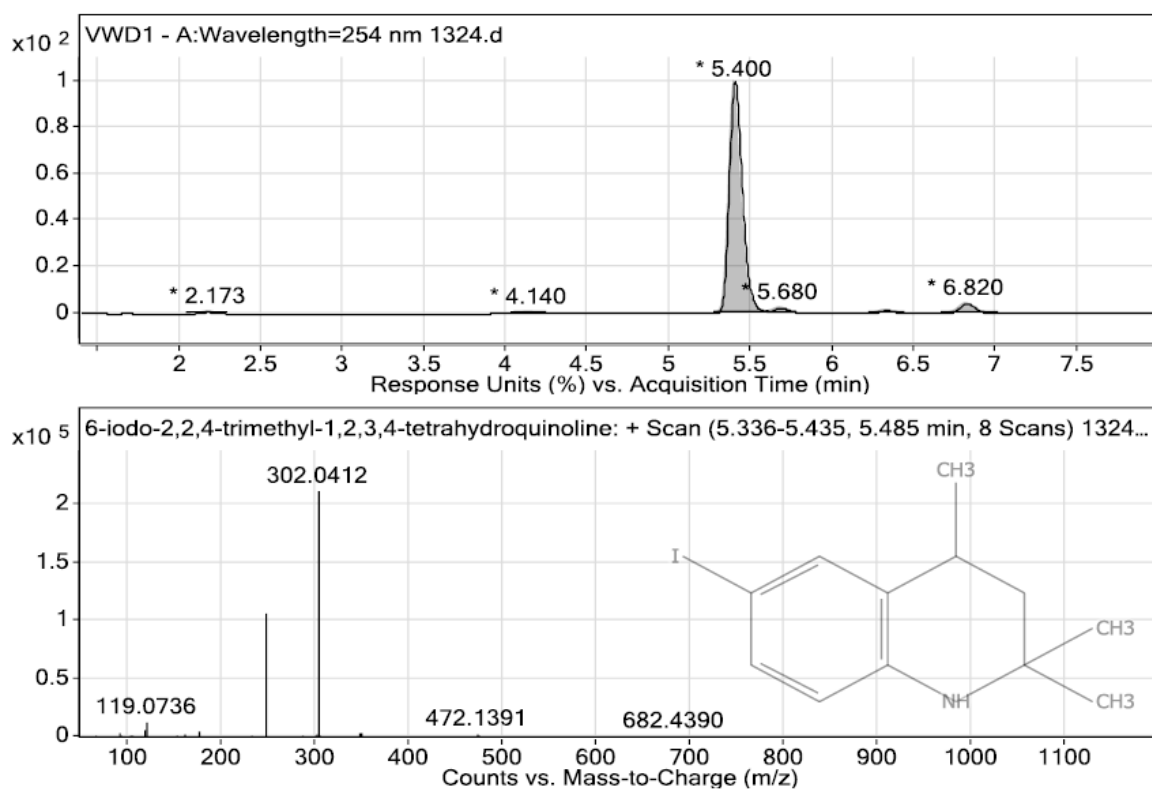


Figure S7. Data of HPLC-MS-ESI analysis of **8a**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of 6-iodo-2,2,4-trimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline hydrochloride **8b**

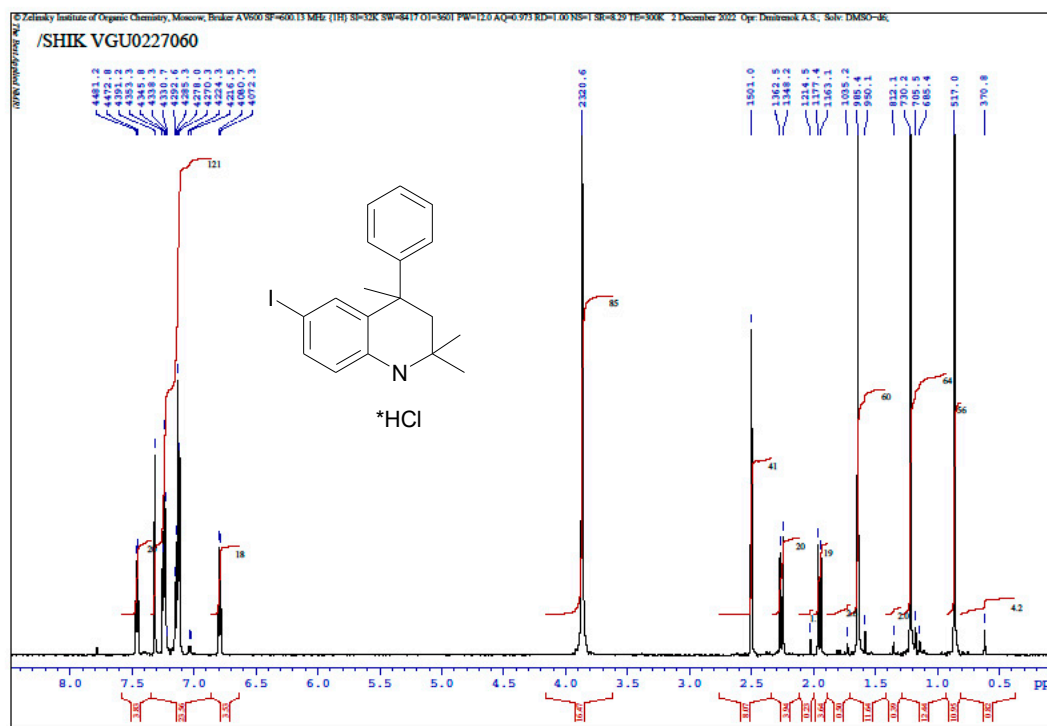


Figure S8.  $^1\text{H}$  NMR spectrum of 6-iodo-2,2,4-trimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline hydrochloride **8b**

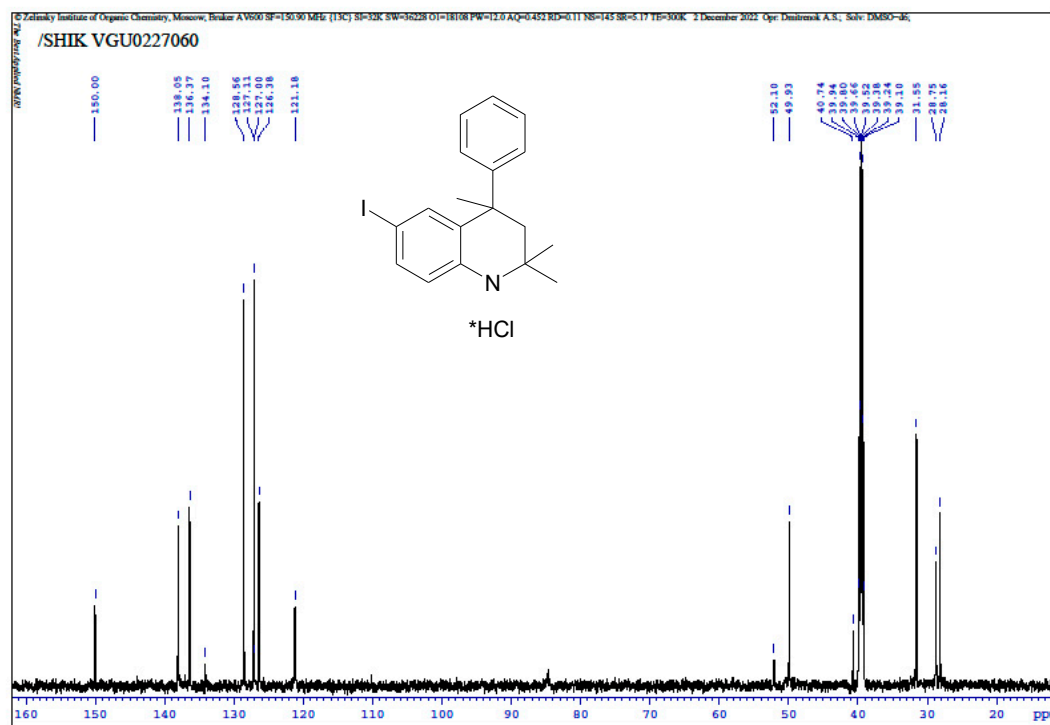


Figure S9.  $^{13}\text{C}$  NMR spectrum of 6-iodo-2,2,4-trimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline hydrochloride

8b

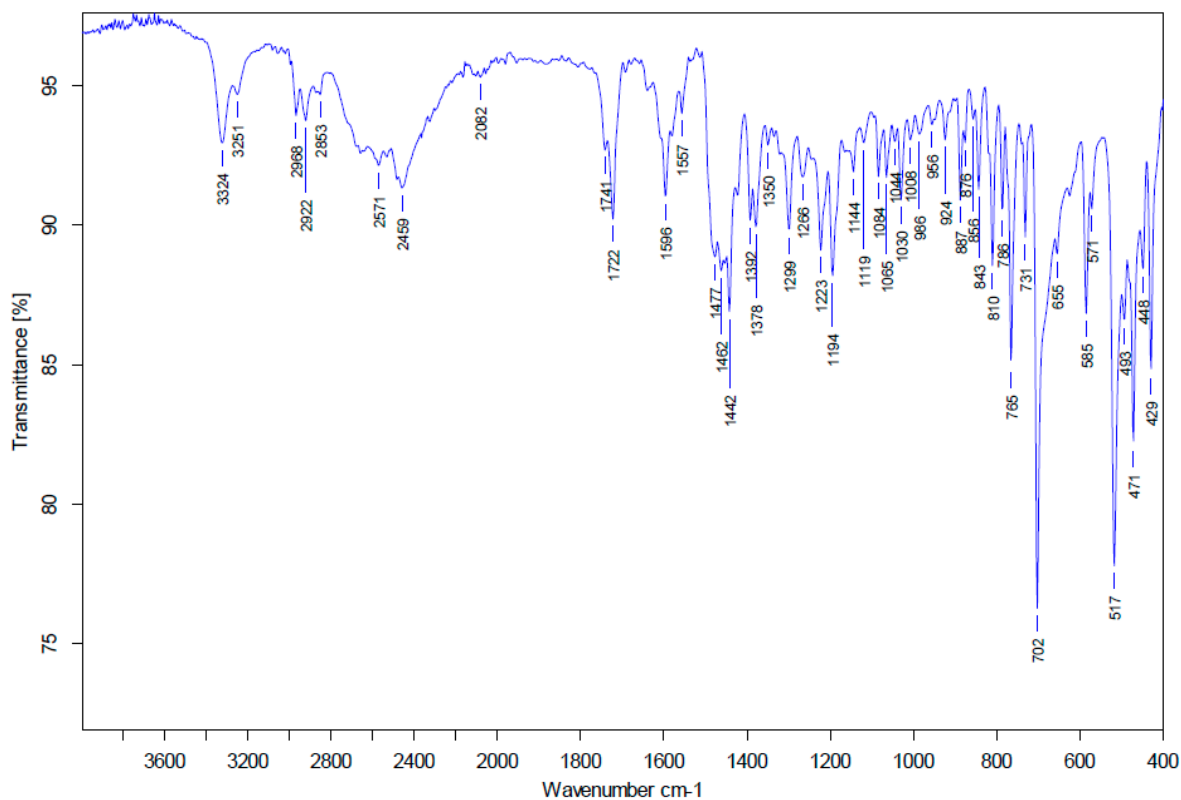


Figure S10. IR spectrum of 8b

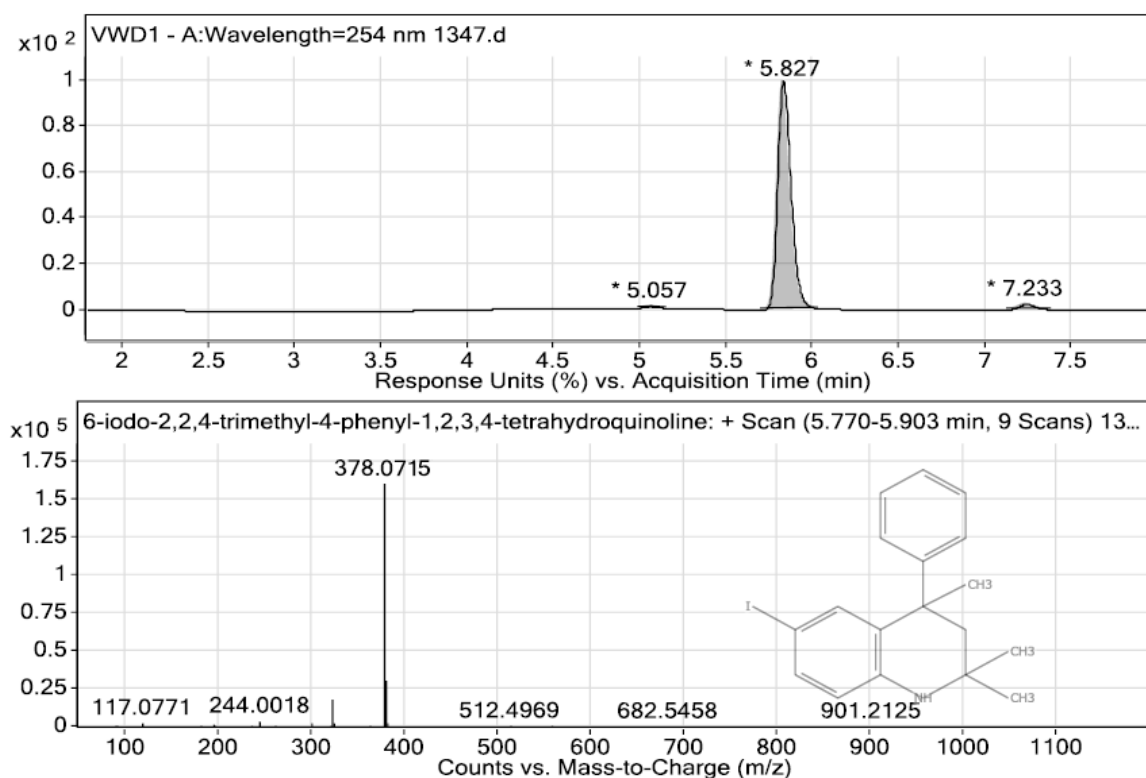


Figure S11. Data of HPLC-MS-ESI analysis of **8b**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of 4-(4-chlorophenyl)-6-iodo-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline hydrochloride **8c**

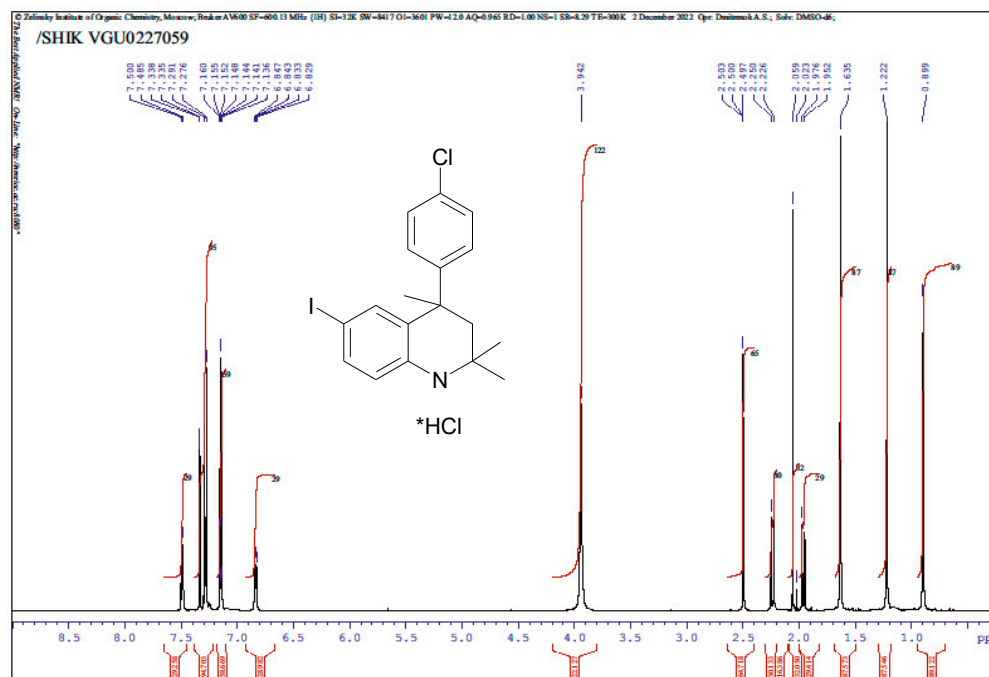
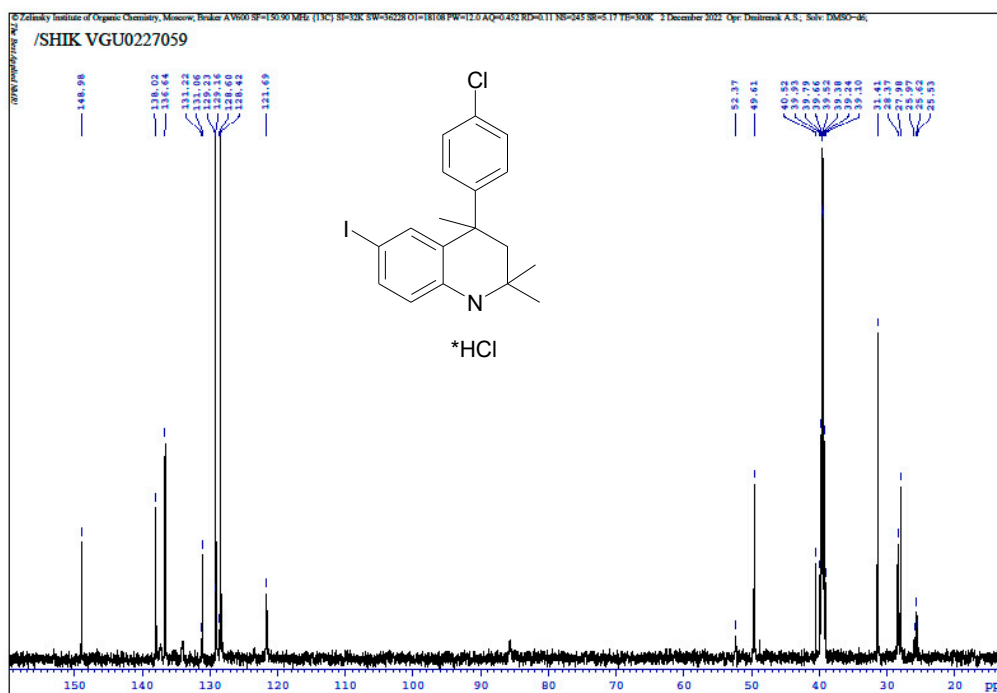
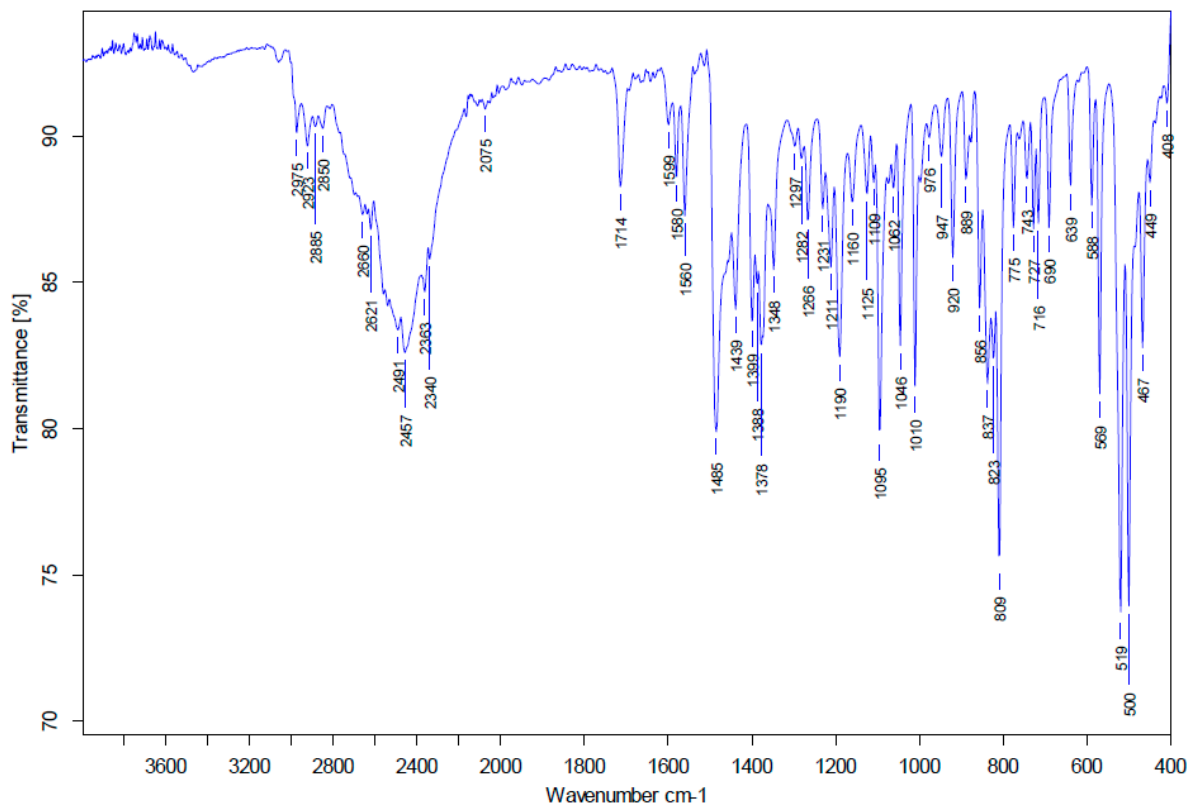


Figure S12.  $^1\text{H}$  NMR spectrum of 4-(4-chlorophenyl)-6-iodo-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline hydrochloride **8c**



**Figure S13.** <sup>1</sup>H NMR spectrum of 4-(4-chlorophenyl)-6-iodo-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline hydrochloride **8c**



**Figure S14.** IR spectrum of **8c**

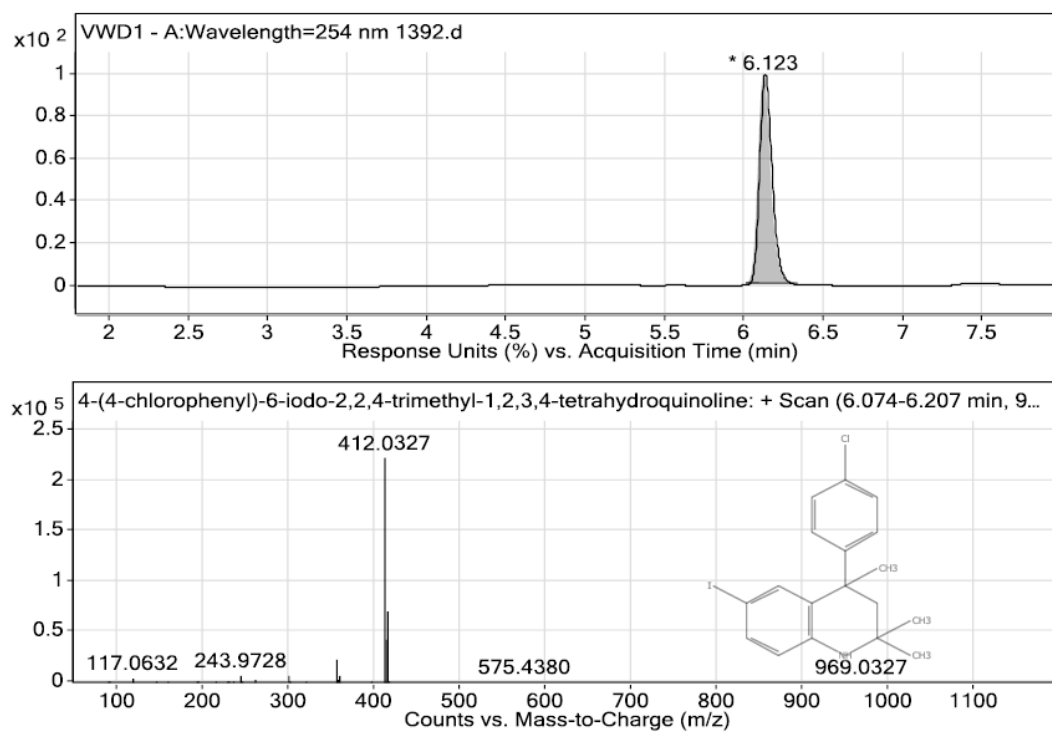


Figure S15. Data of HPLC-MS-ESI analysis of **8c**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of 8-iodo-4,4,6-trimethyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **9a**

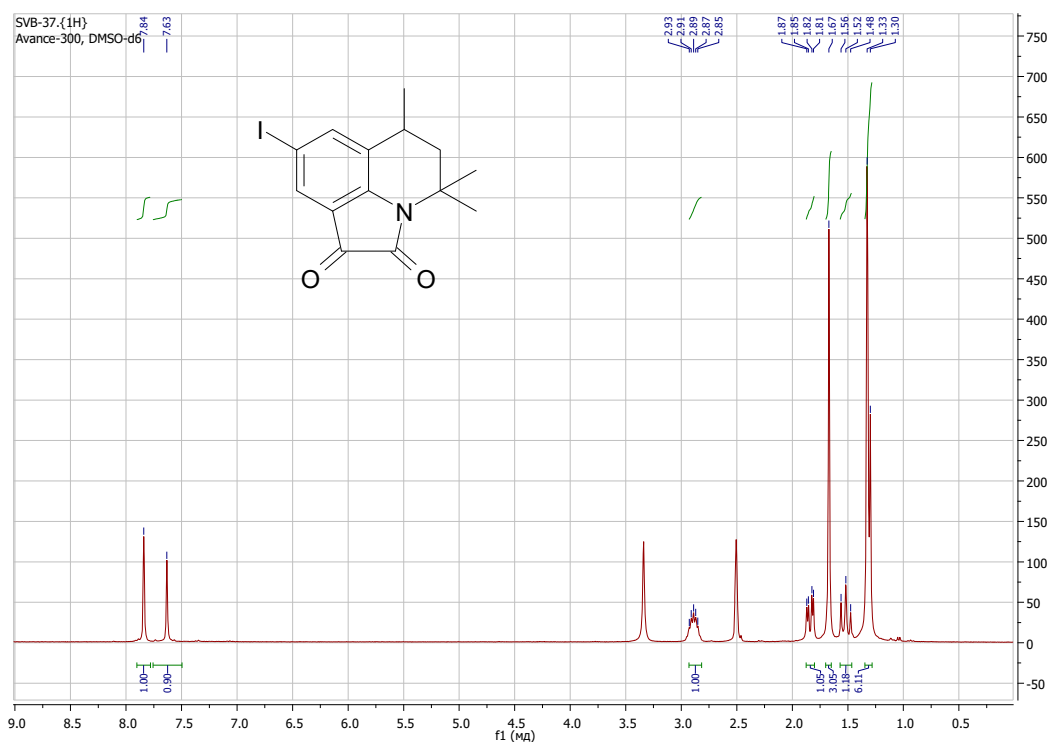
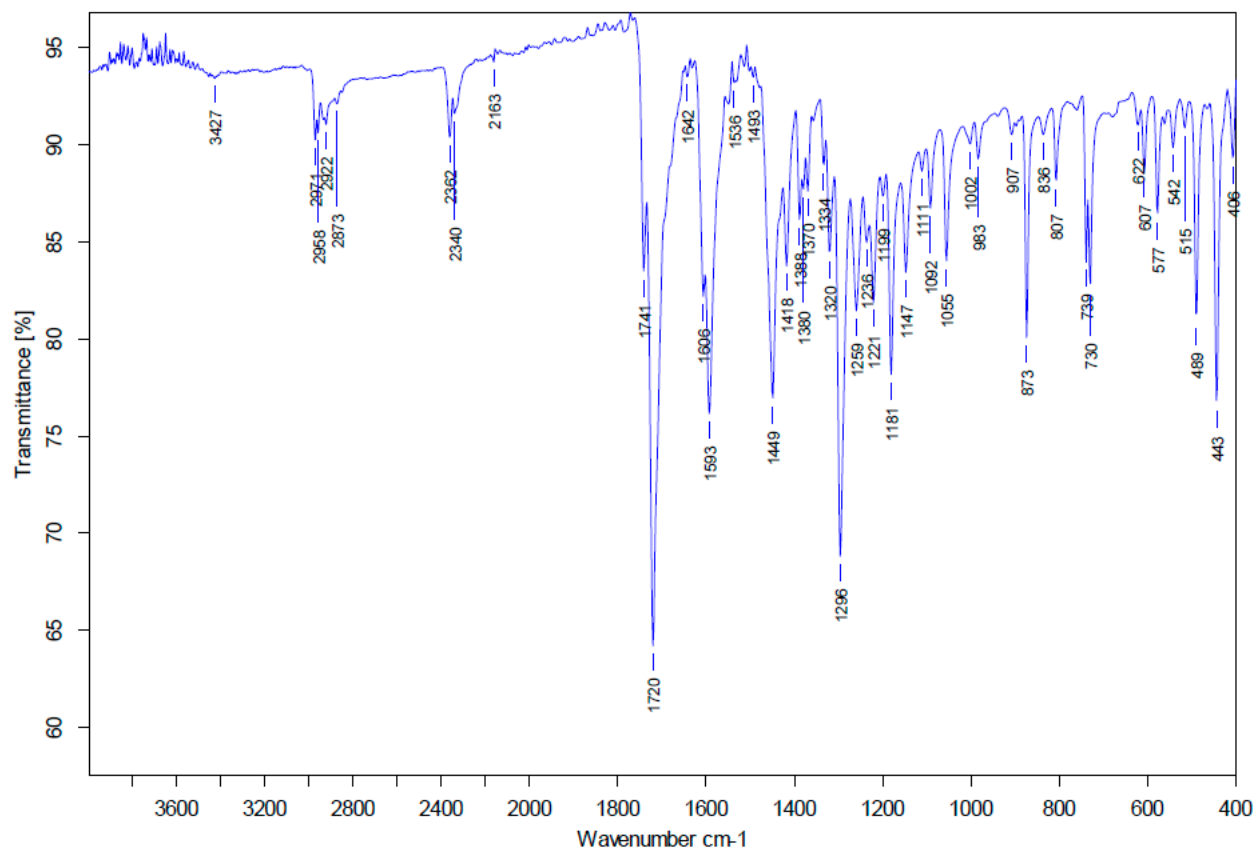
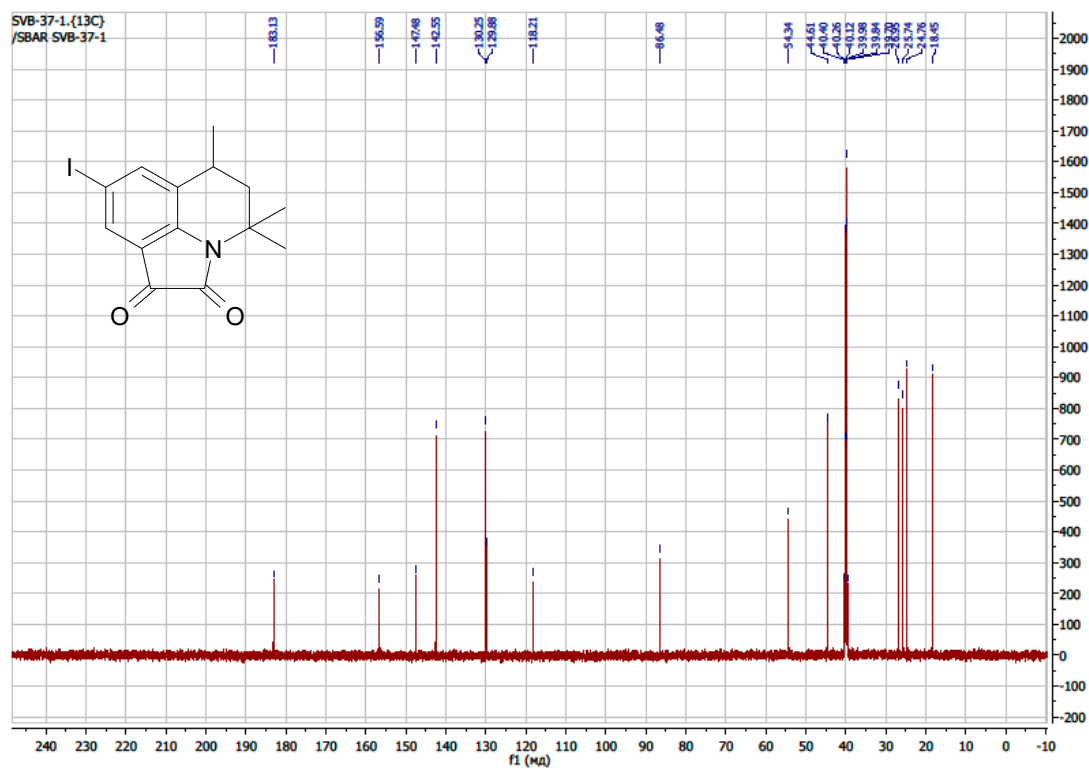
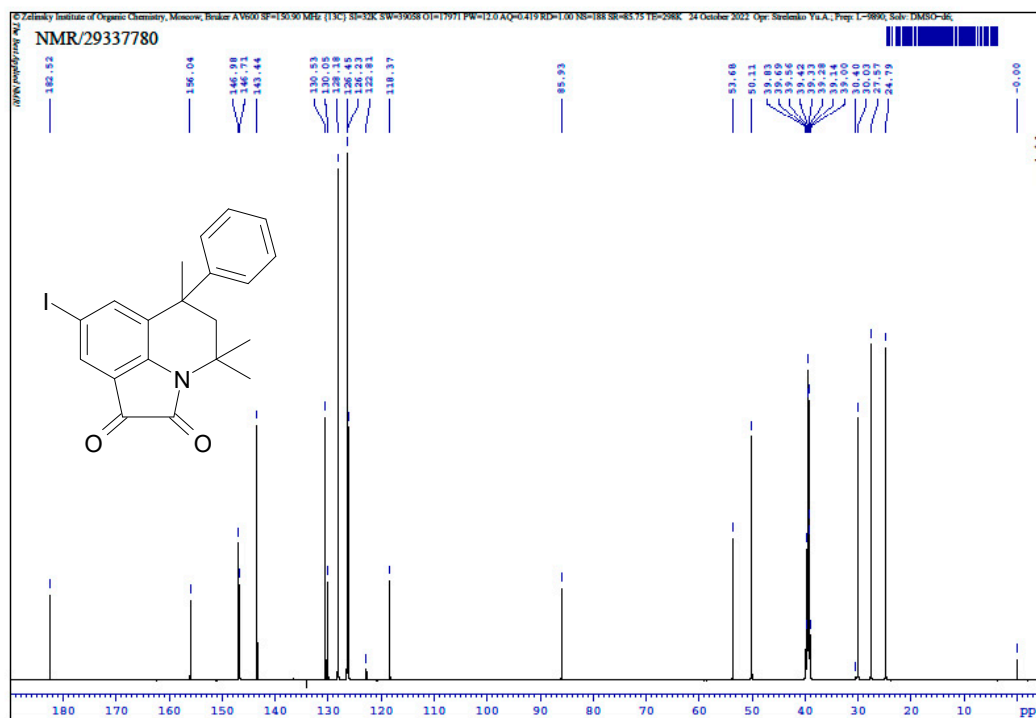


Figure S16.  $^1\text{H}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **9a**

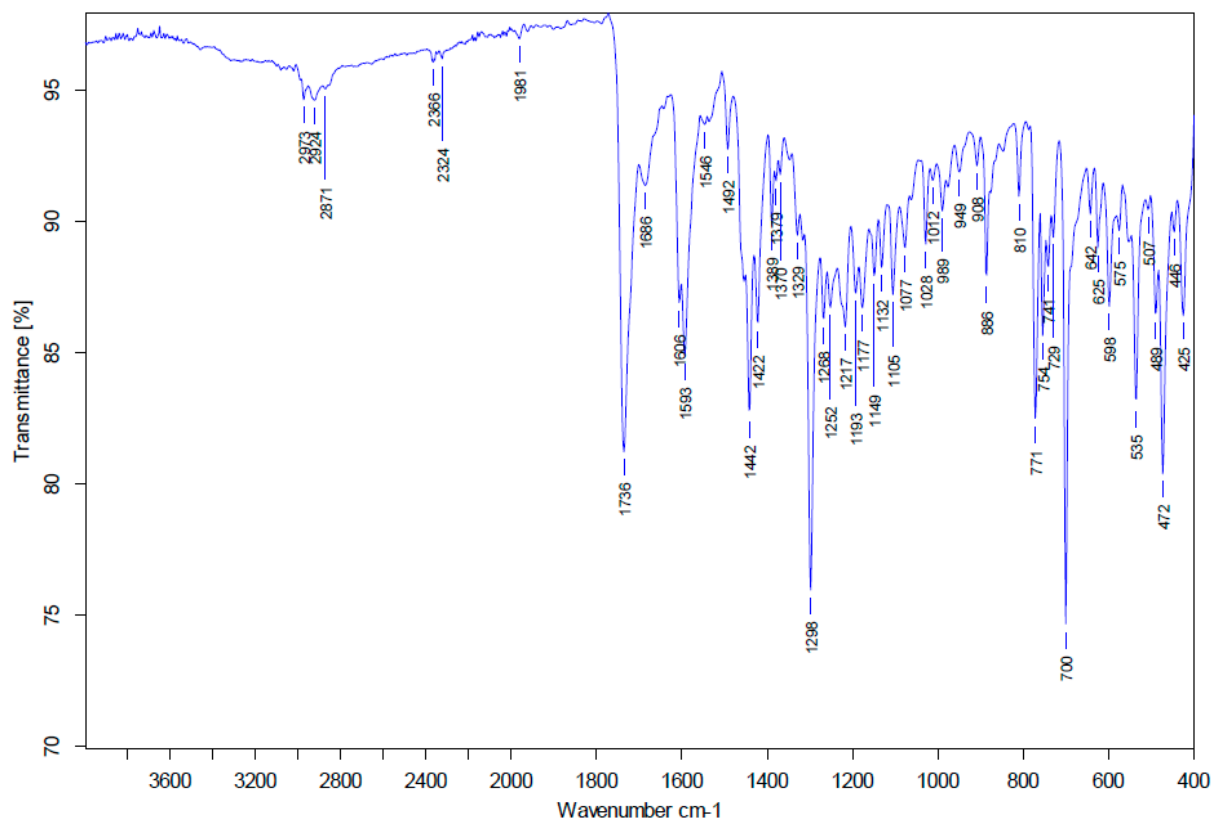








**Figure S21.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **9b**



**Figure S22.** IR spectrum of **9b**



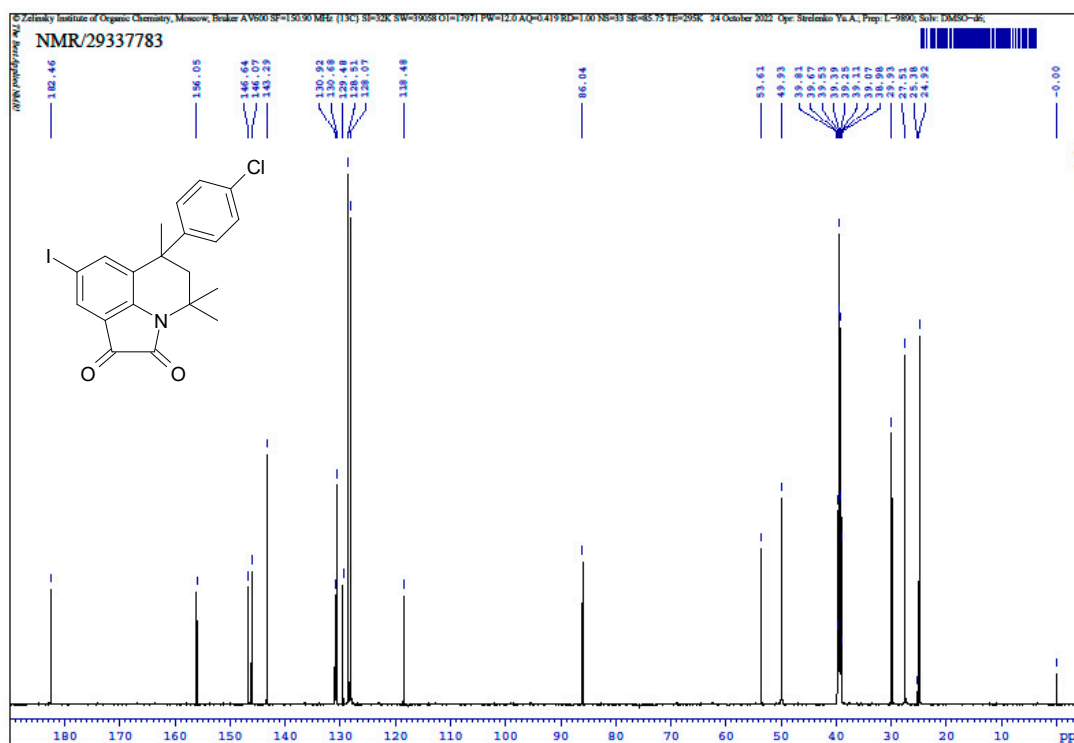


Figure S25.  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-1,2-dione **9c**

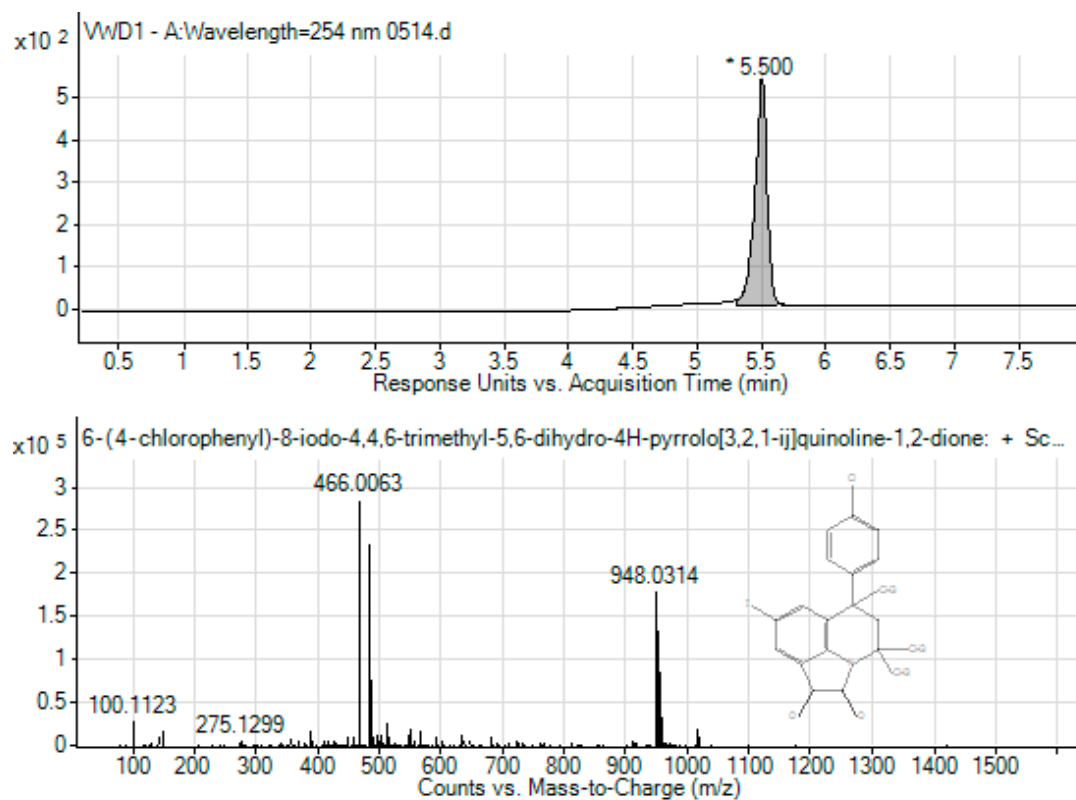
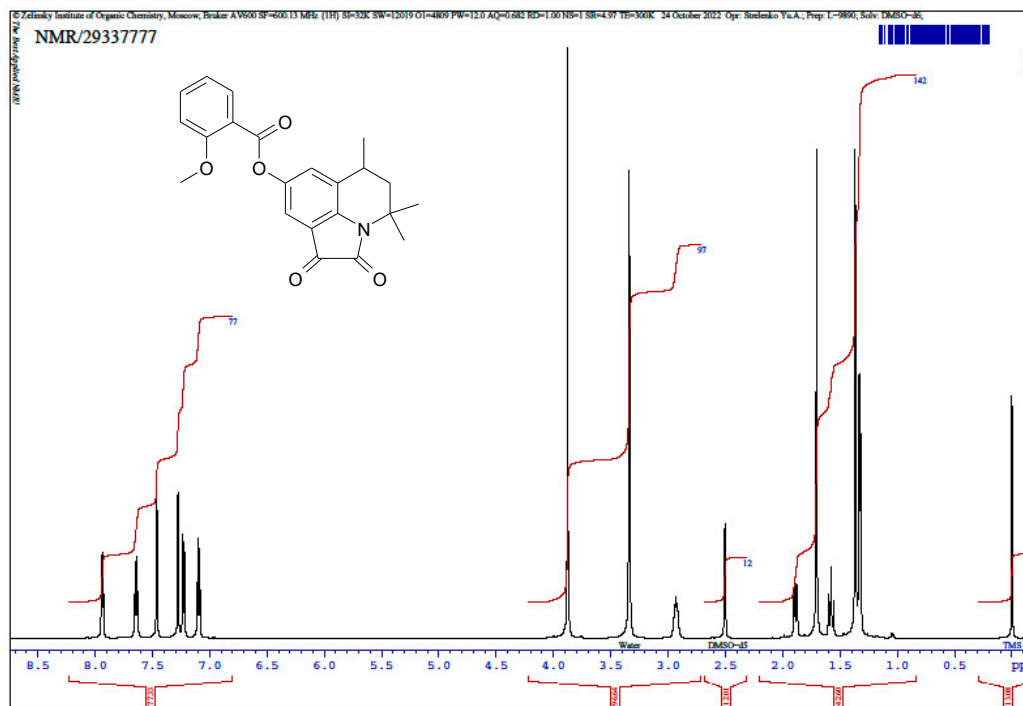
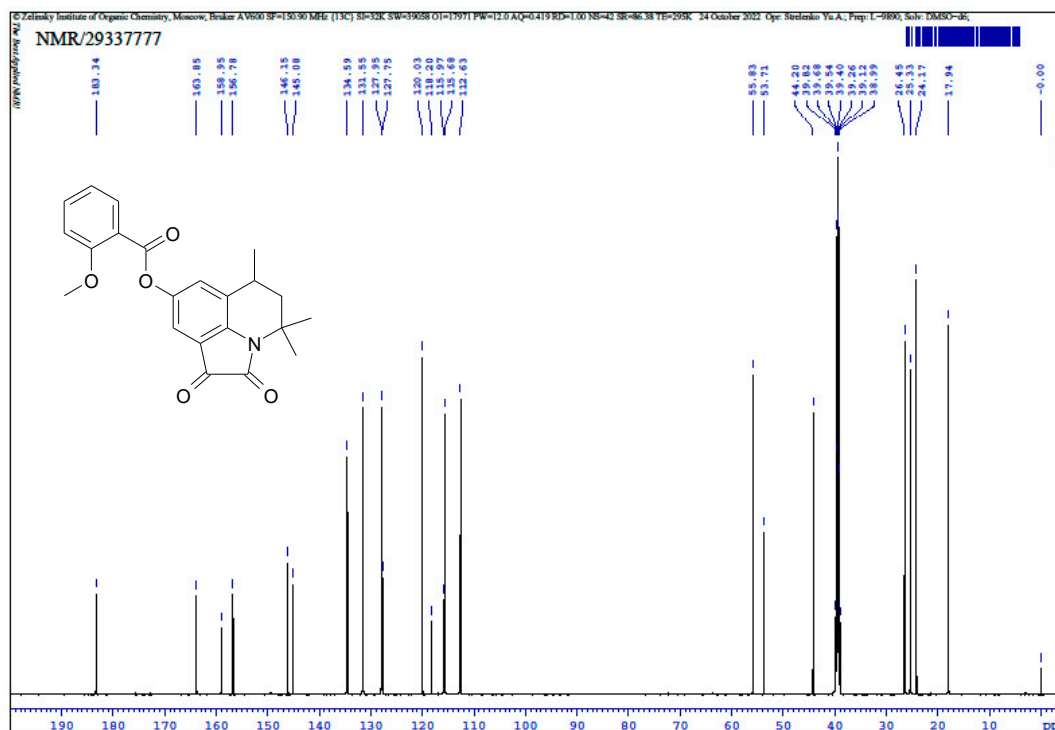


Figure S26. Data of HPLC-MS-ESI analysis of **9c**

**$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of 4,4,6-trimethyl-1,2-dioxo-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-8-yl-2-methoxybenzoate 10c**

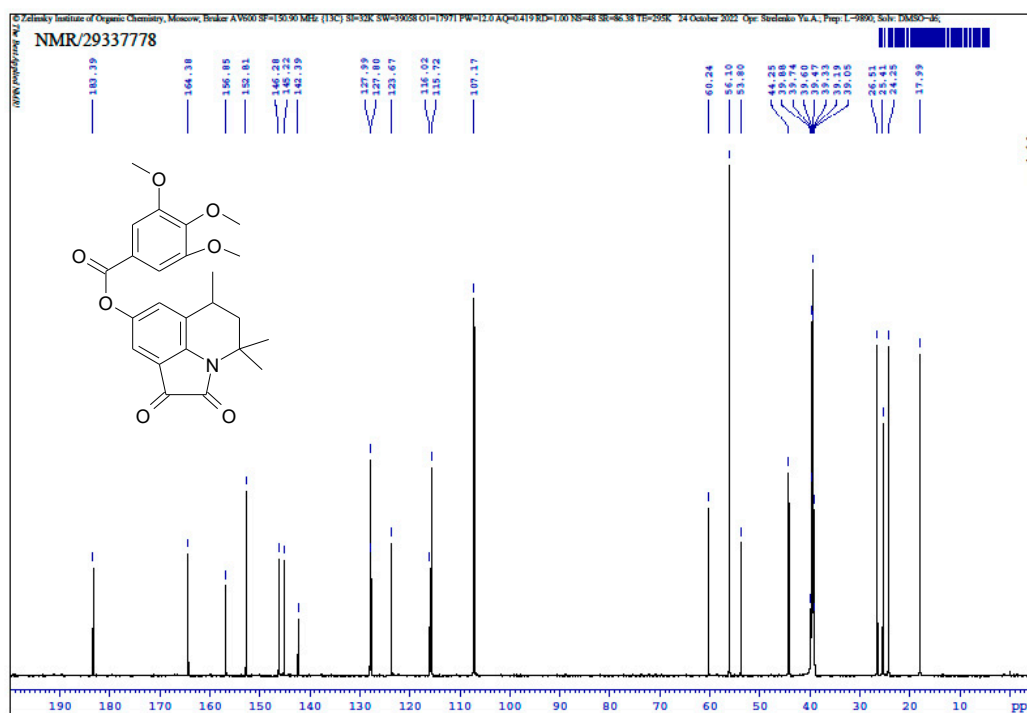


**Figure S27.**  $^1\text{H}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10c

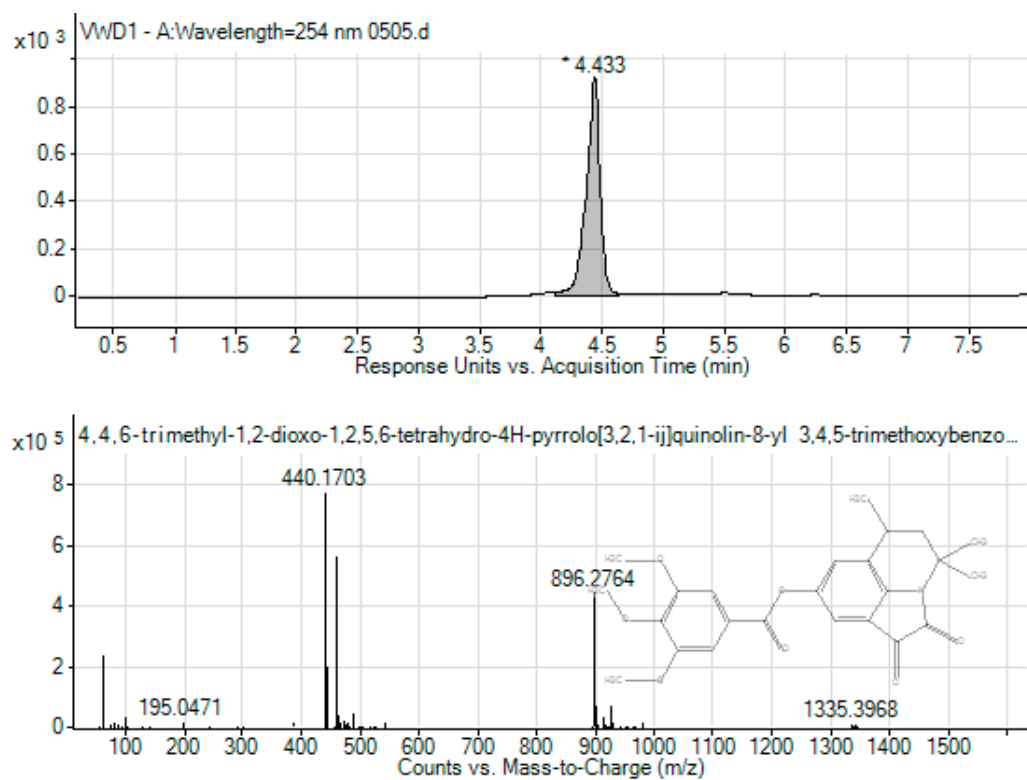


**Figure S28.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10c



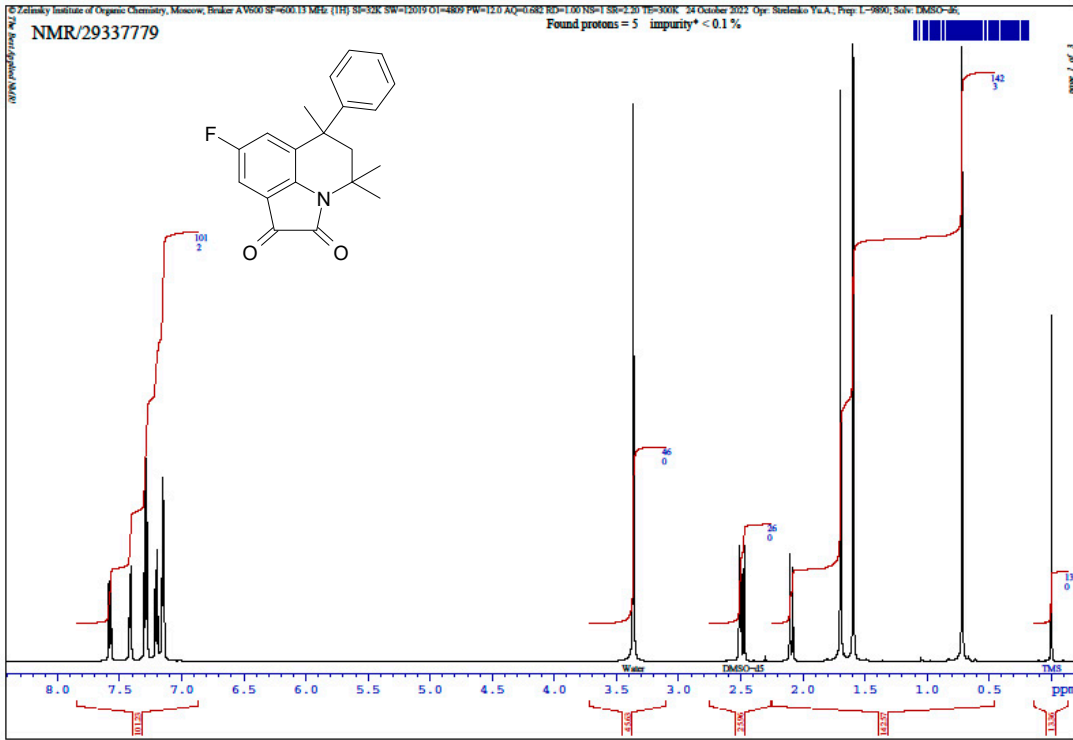


**Figure S31.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10d**

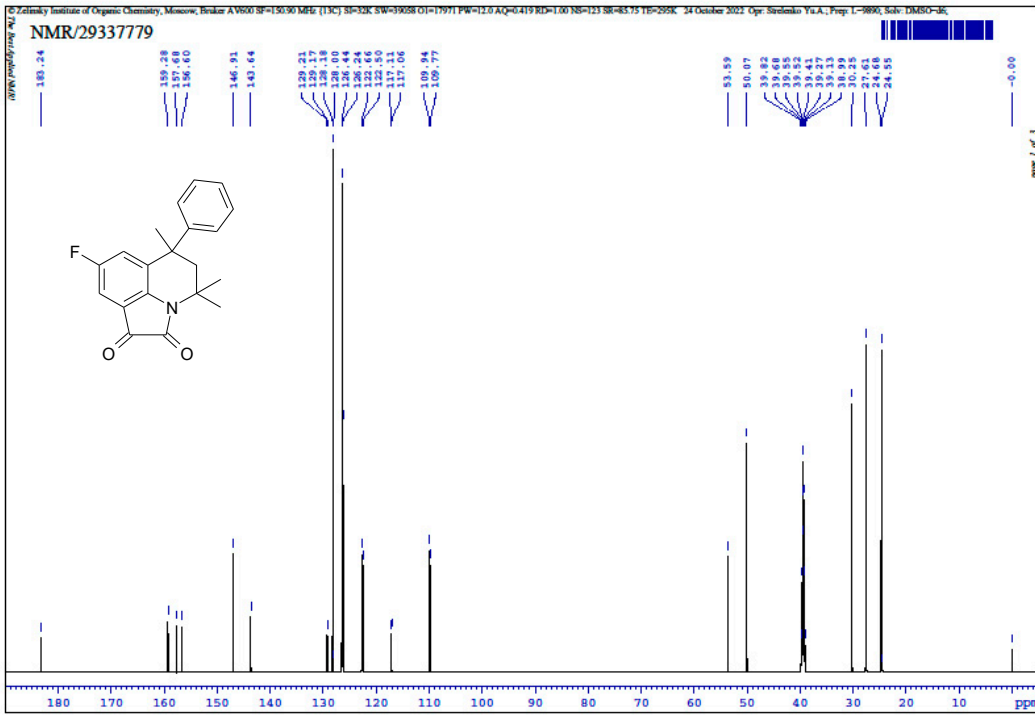


**Figure S32.** Data of HPLC-MS-ESI analysis of **10d**

<sup>1</sup>H, <sup>13</sup>C NMR, IR and data HPLC-HRMS-ESI spectra of 8-fluoro-4,4,6-trimethyl-6-phenyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10f

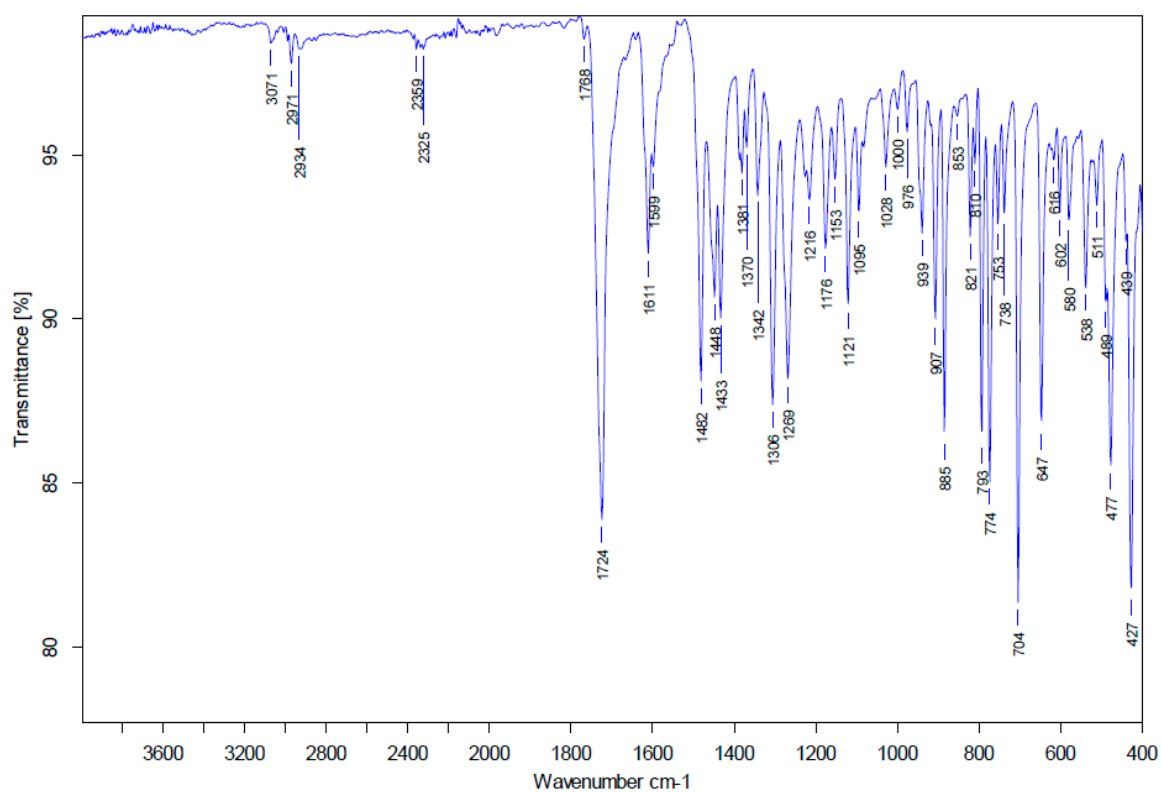


**Figure S33.** <sup>1</sup>H NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10f**

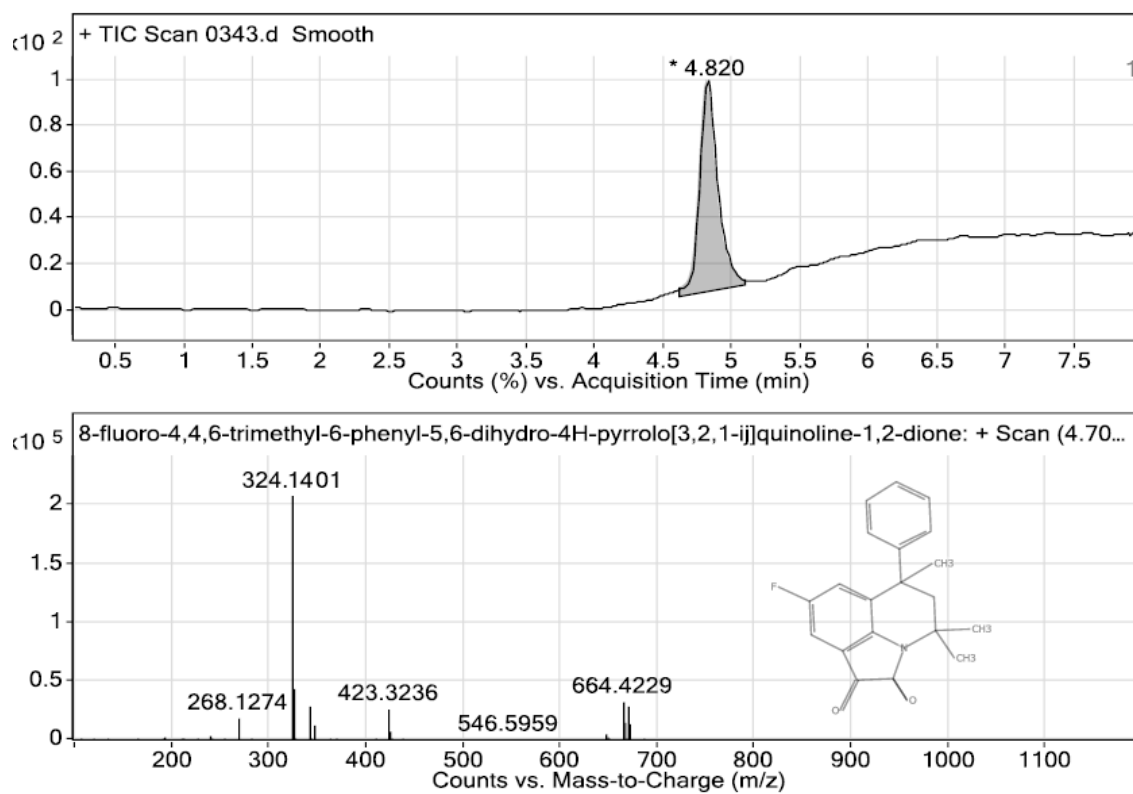


**Figure S34.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10f**



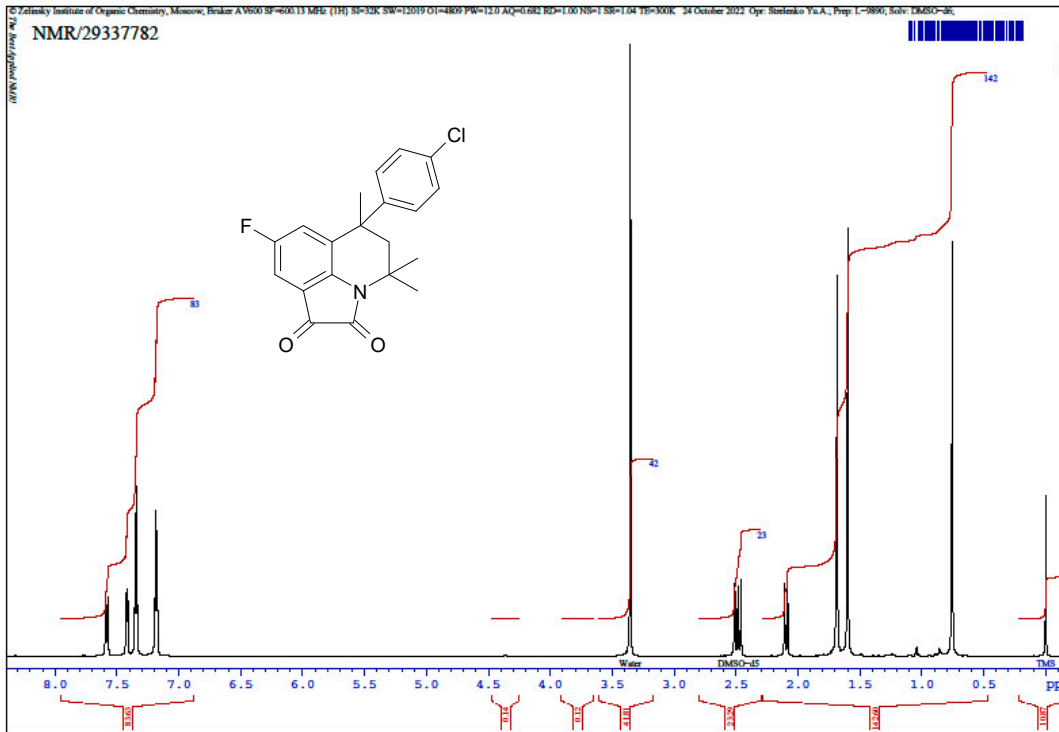


**Figure S35.** IR spectrum of **10f**

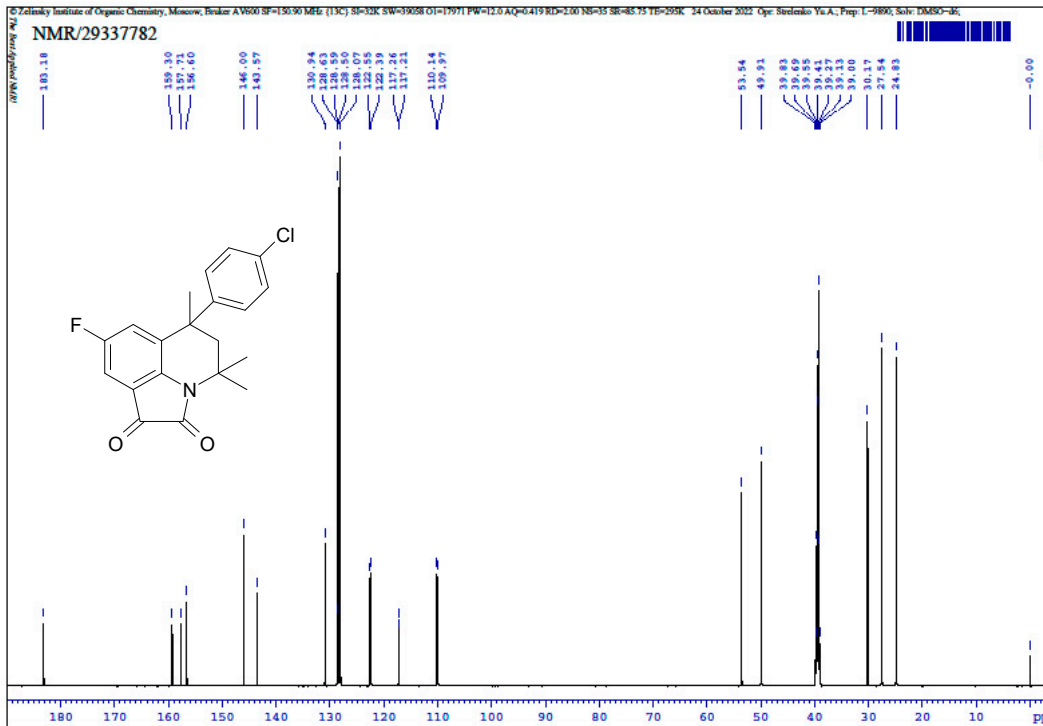


**Figure S36.** Data of HPLC-MS-ESI analysis of **10f**

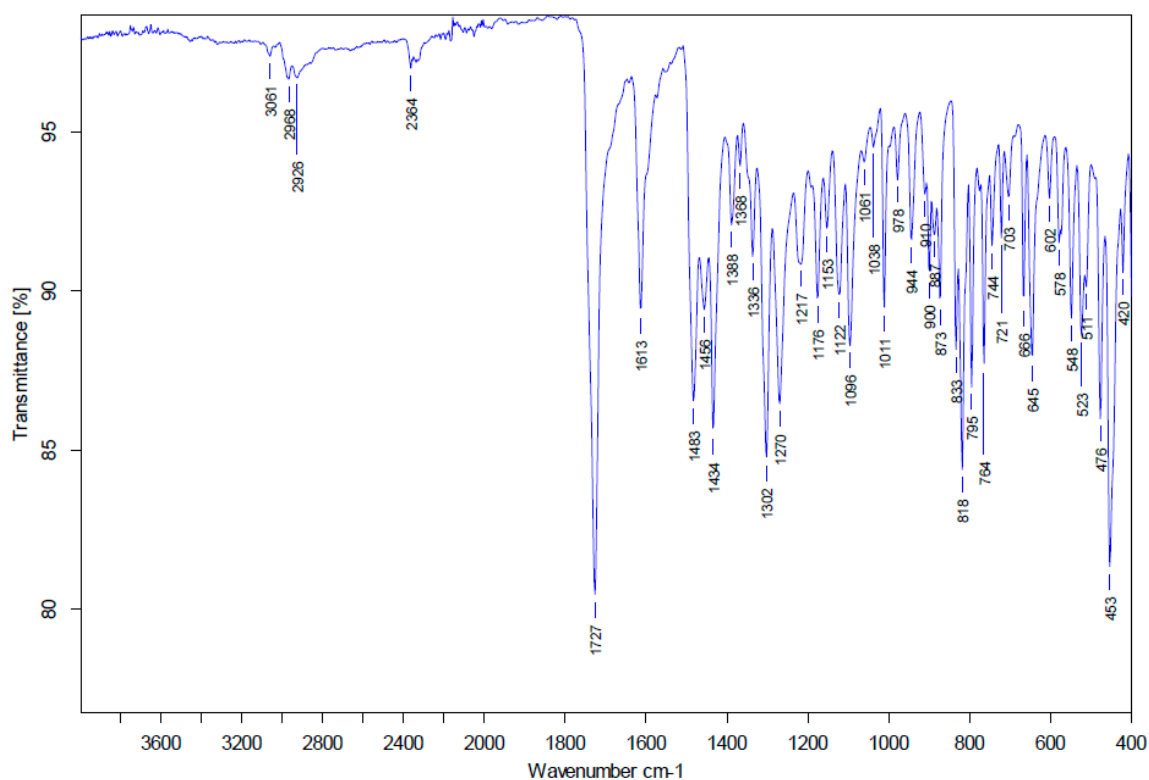
**5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10g**



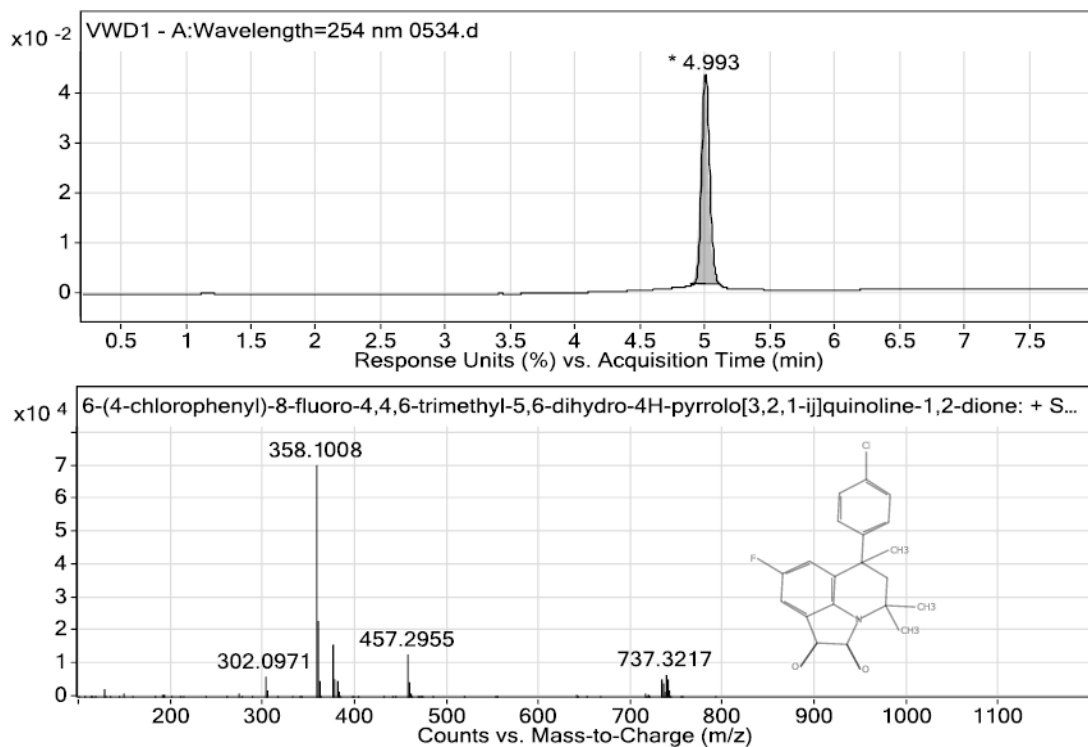
**Figure S37.** <sup>1</sup>H NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10g**



**Figure S38.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10g**

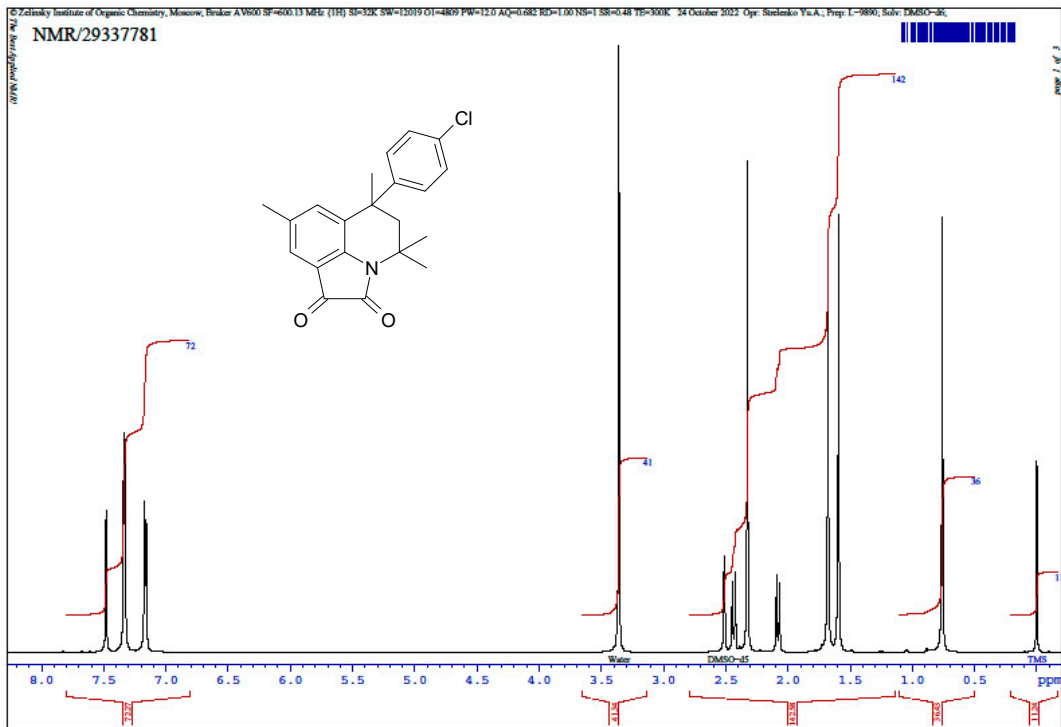


**Figure S39.** IR spectrum of **10g**

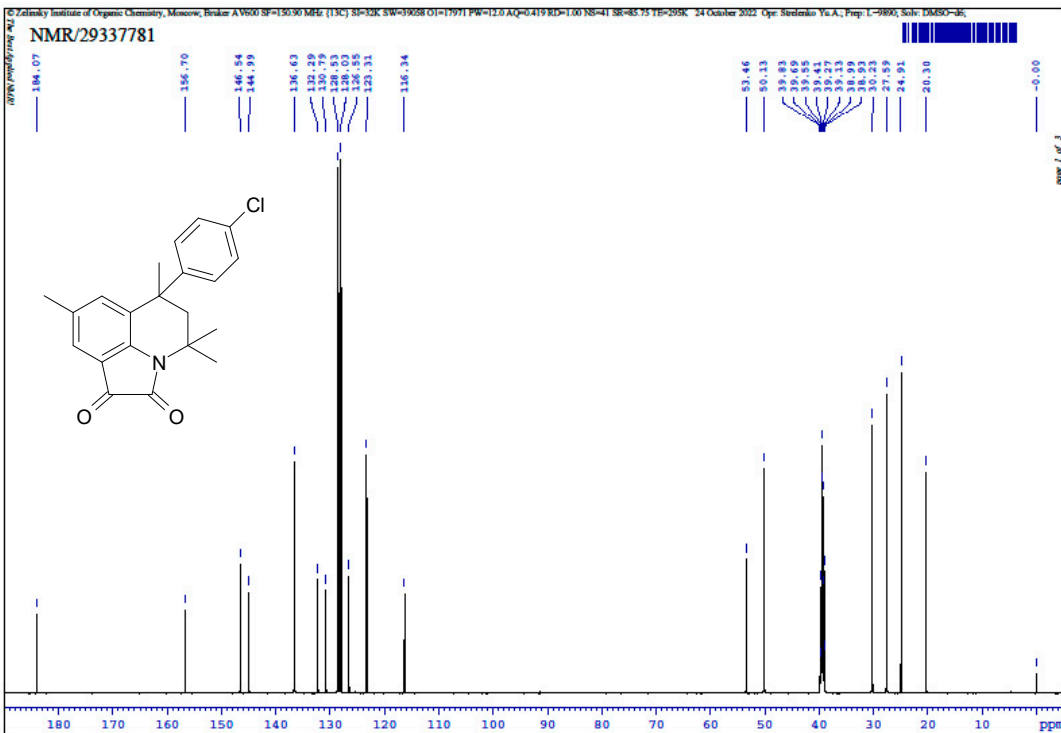


**Figure S40.** Data of HPLC-MS-ESI analysis of **10g**

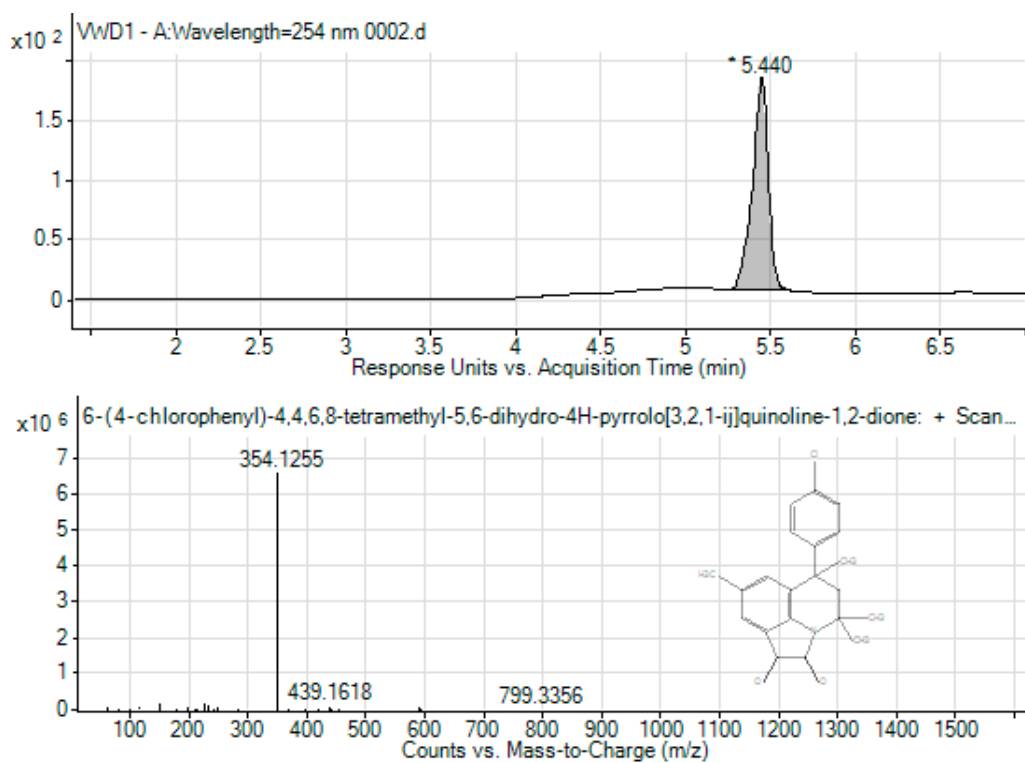
**<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of 6-(4-chlorophenyl)-4,4,6,8-tetramethyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10l**



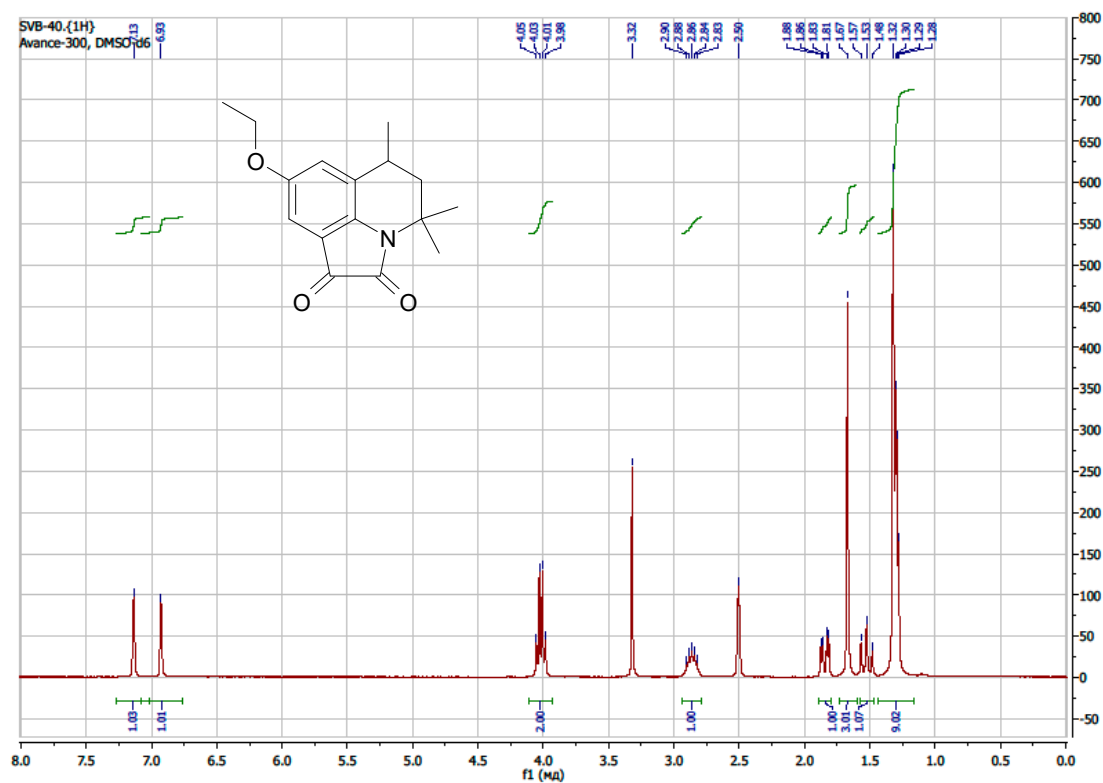
**Figure S41.** <sup>1</sup>H NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2-*l*-*ij*]quinoline-1,2-dione **10l**



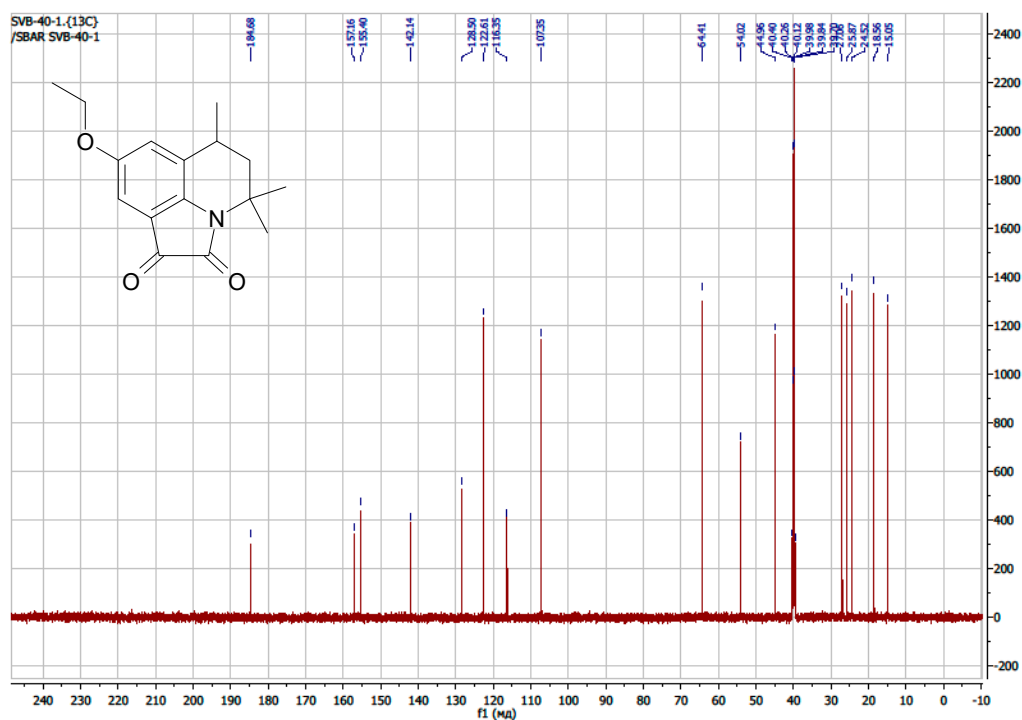
**Figure S42.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10l**



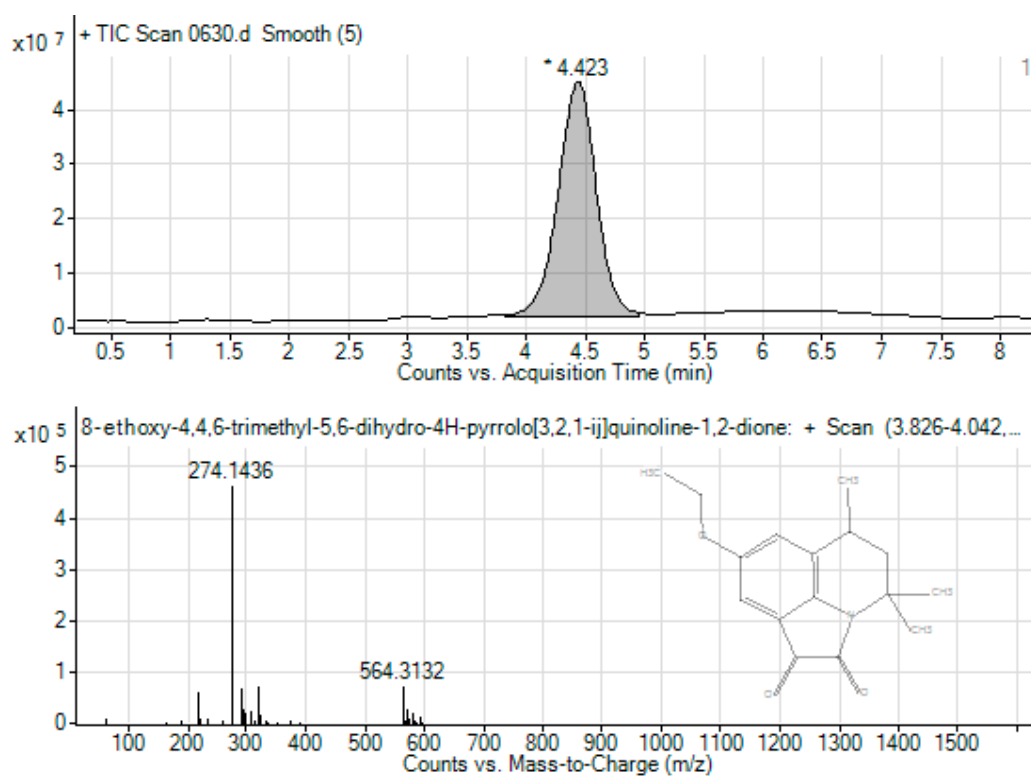
<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of 8-ethoxy-4,4,6-trimethyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10m



**Figure S44.** <sup>1</sup>H NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10m**.

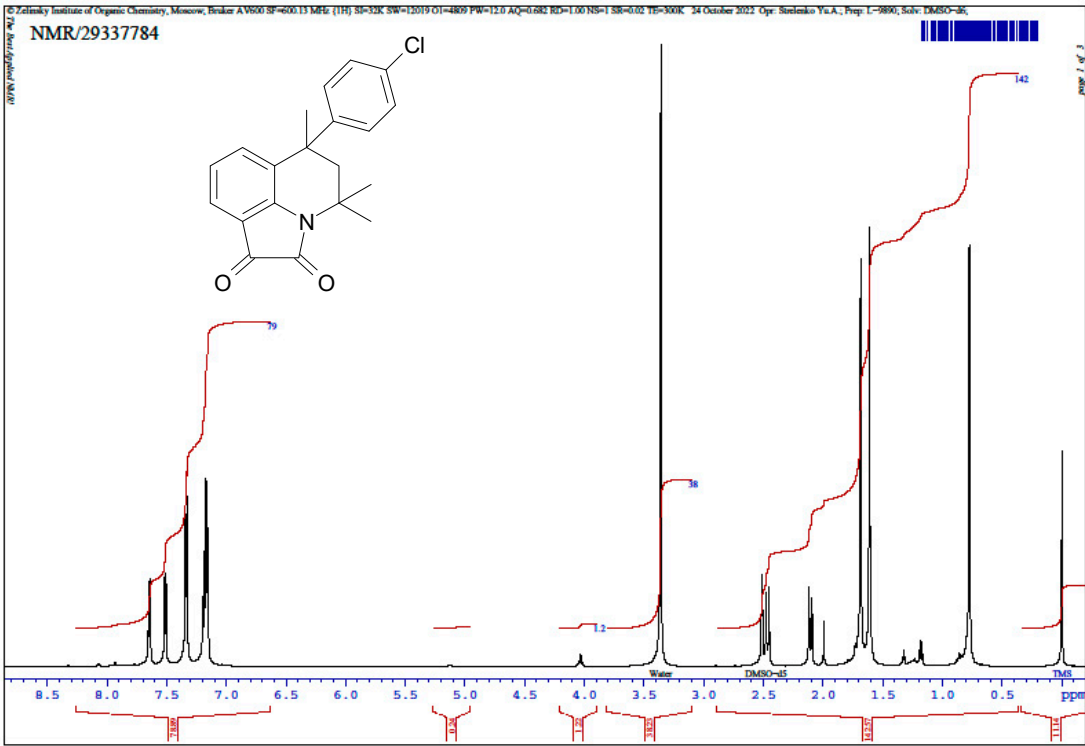


**Figure S45.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-1,2-dione **10m**

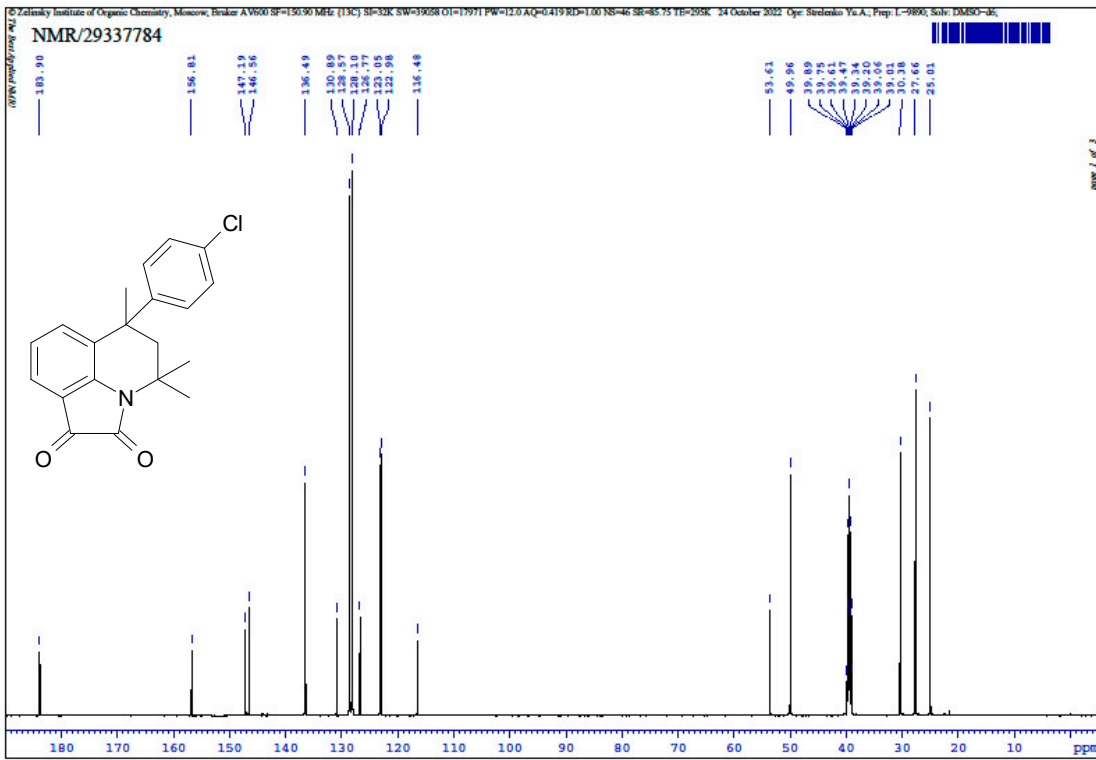


**Figure S46.** Data of HPLC-MS-ESI analysis of **10m**

### 4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione 10o



**Figure S47.** <sup>1</sup>H NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10o**



**Figure S48.**  $^{13}\text{C}$  NMR spectrum of 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-dione **10o**





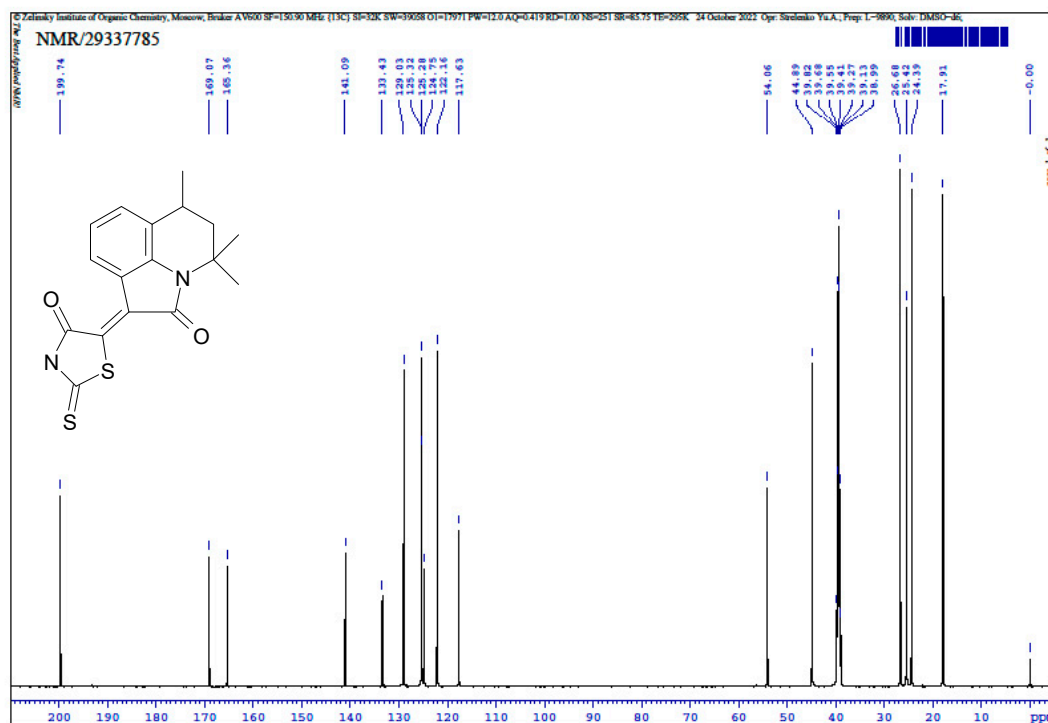


Figure S51.  $^{13}\text{C}$  NMR spectrum of compound 12a

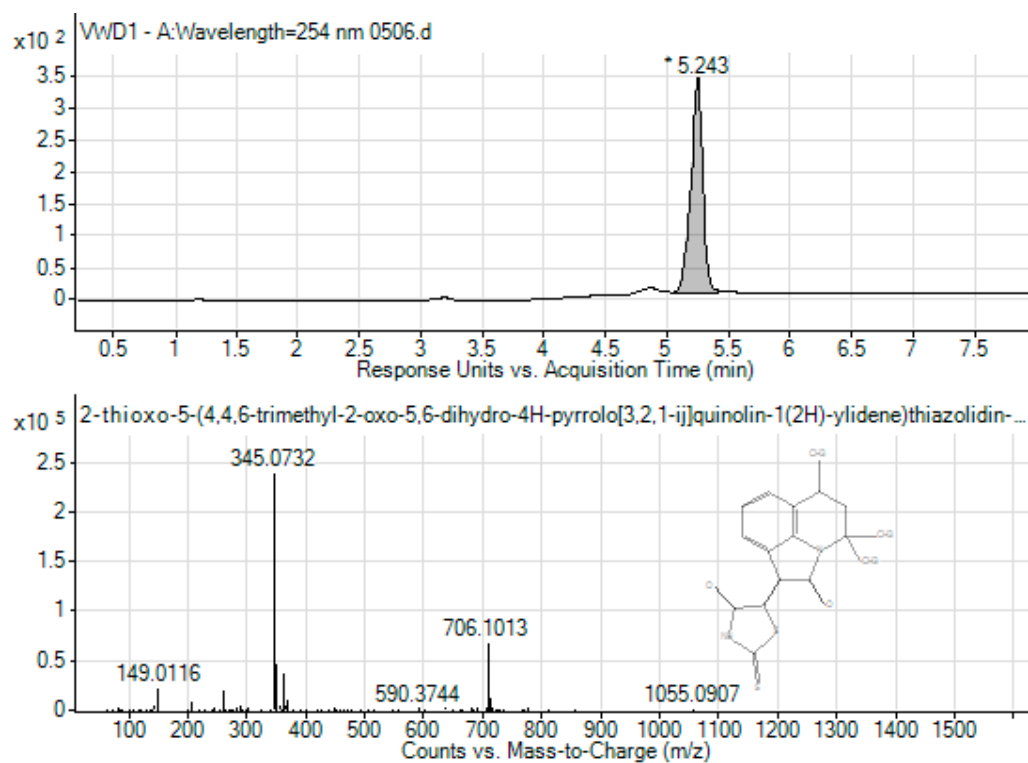
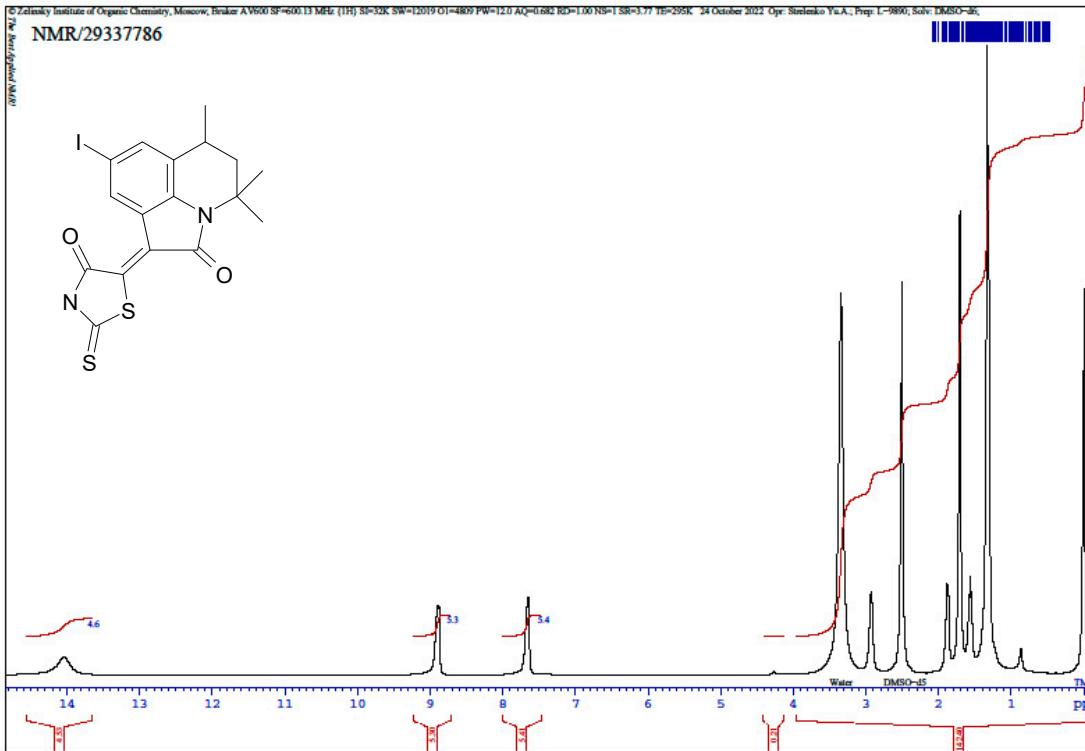
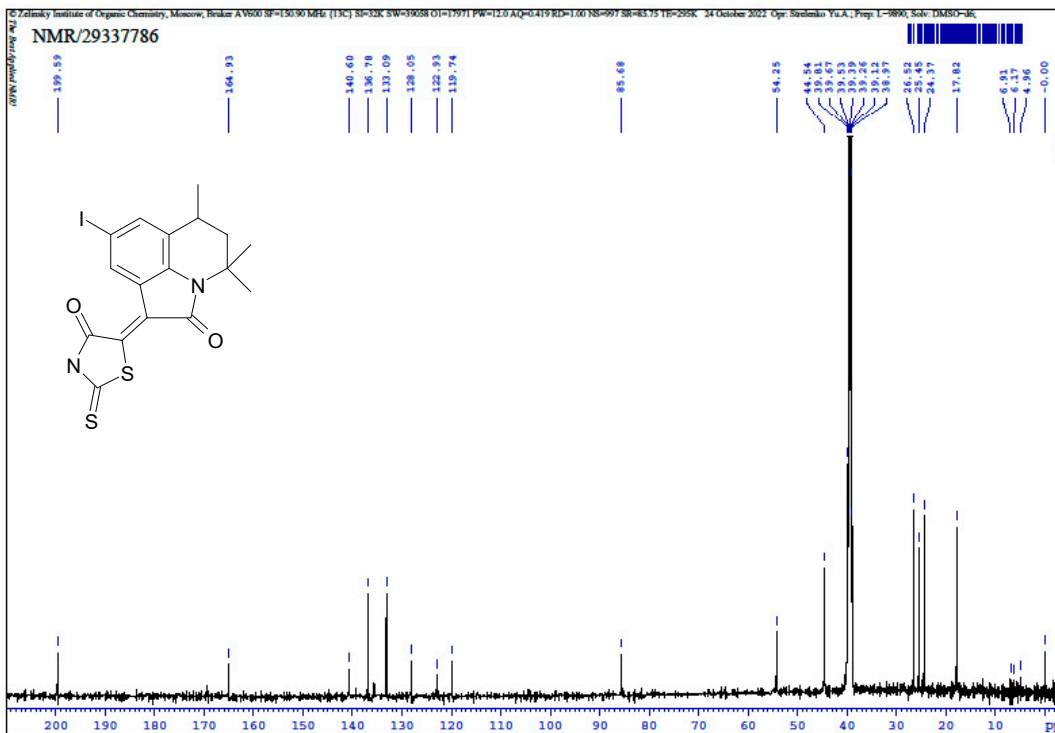


Figure S52. Data of HPLC-MS-ESI analysis of compound 12a

**<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(8-iodo-4,4,6-trimethyl-2-oxo-5,6-dihydro-4H-pyrrolo[3,2,1-*ij*]quinolin-1(2H)-ylidene)-2-thioxothiazolidin-4-one 12b**



**Figure S53.**  $^1\text{H}$  NMR spectrum of compound **12b**



**Figure S54.**  $^{13}\text{C}$  NMR spectrum of compound **12b**

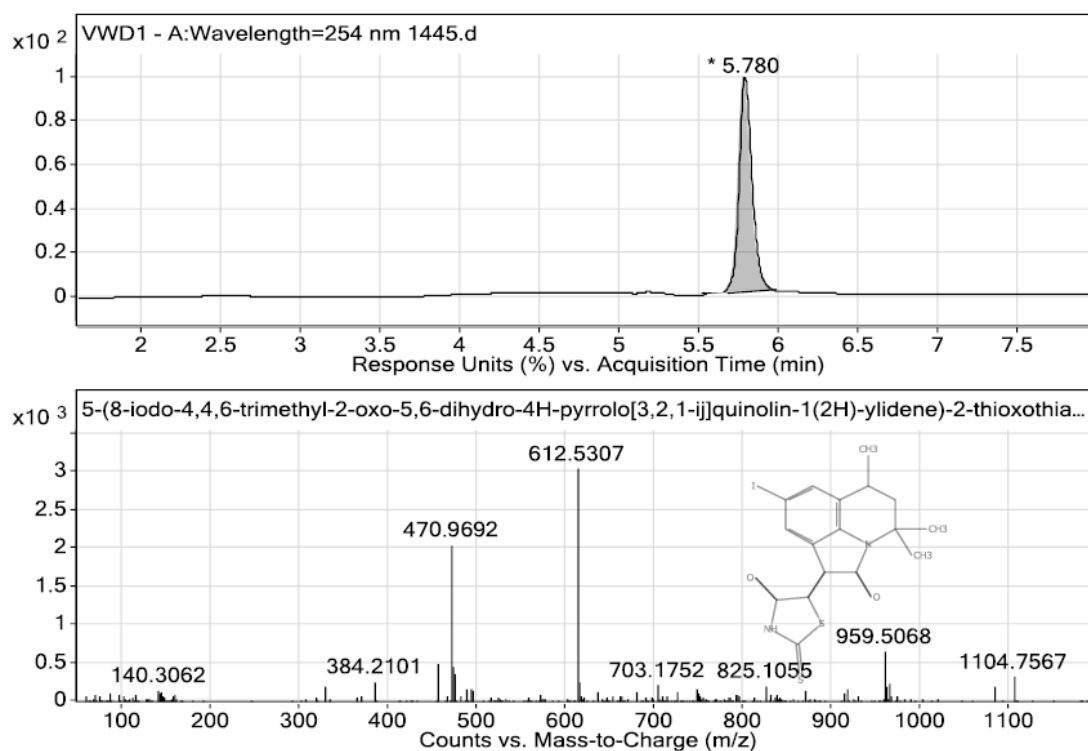


Figure S55. Data of HPLC-MS-ESI analysis of compound **12b**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-4,4,6-trimethyl-2-oxo-1-(4-oxo-2-thioxothiazolidin-5-ylidene)-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-*ij*]quinolin-8-yl benzoate **12c**

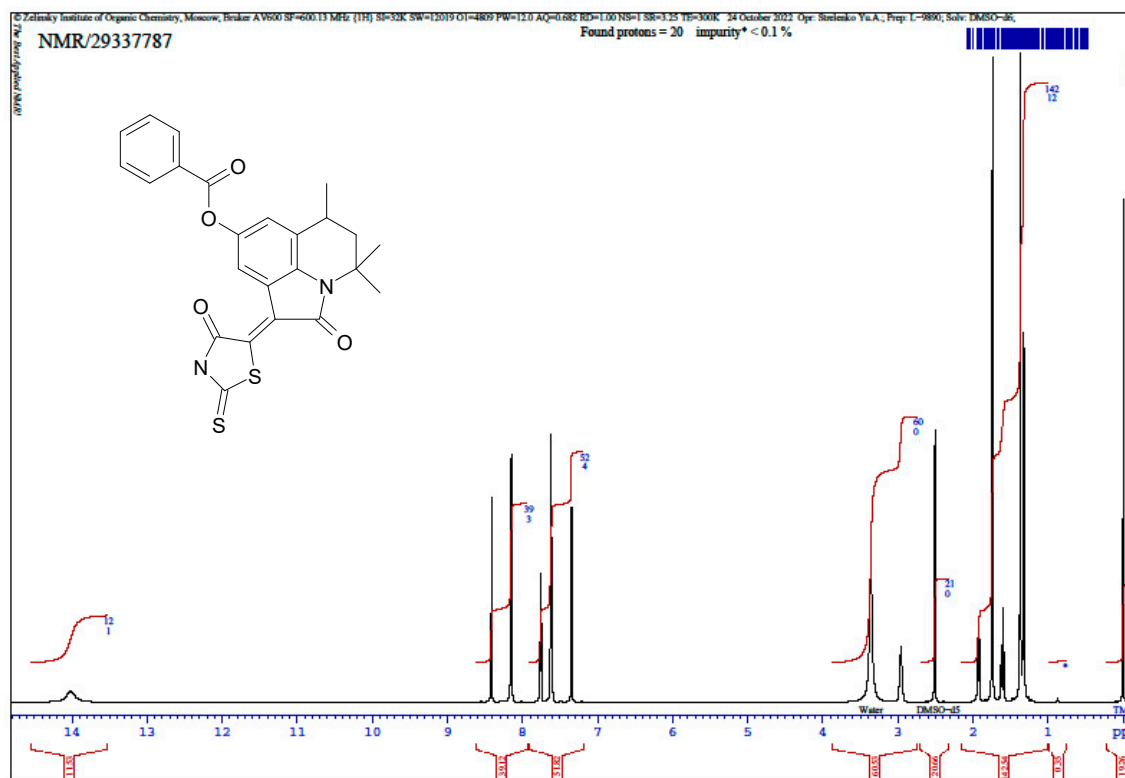


Figure S56.  $^1\text{H}$  NMR spectrum of compound **12c**

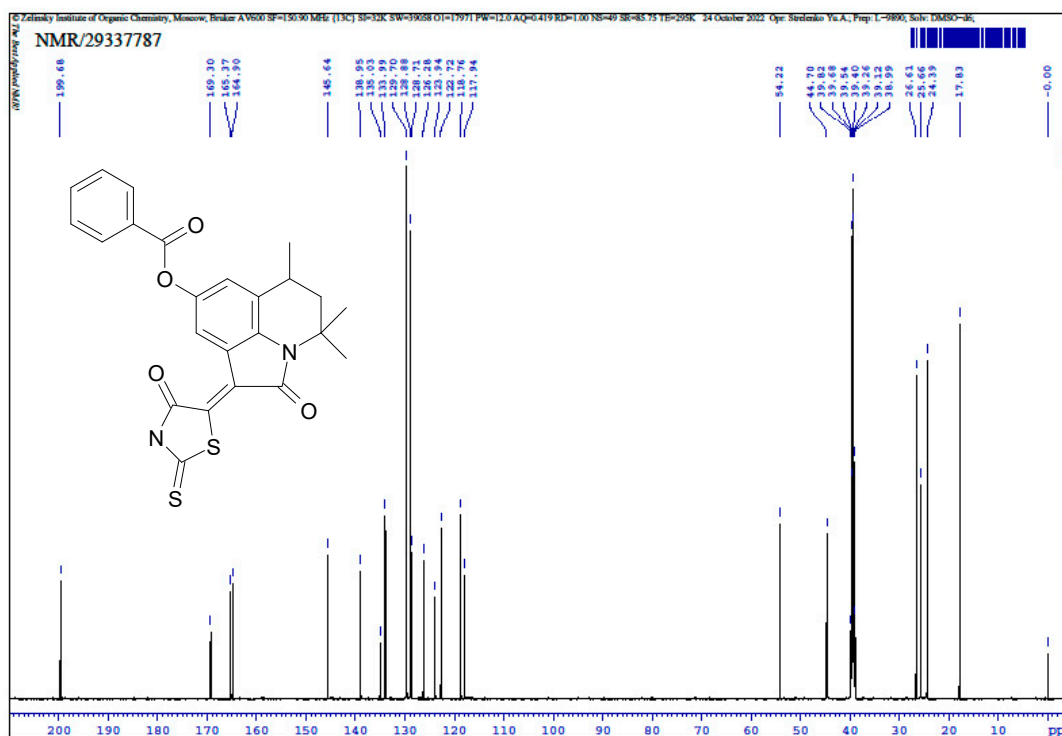


Figure S57.  $^{13}\text{C}$  NMR spectrum of compound **12c**

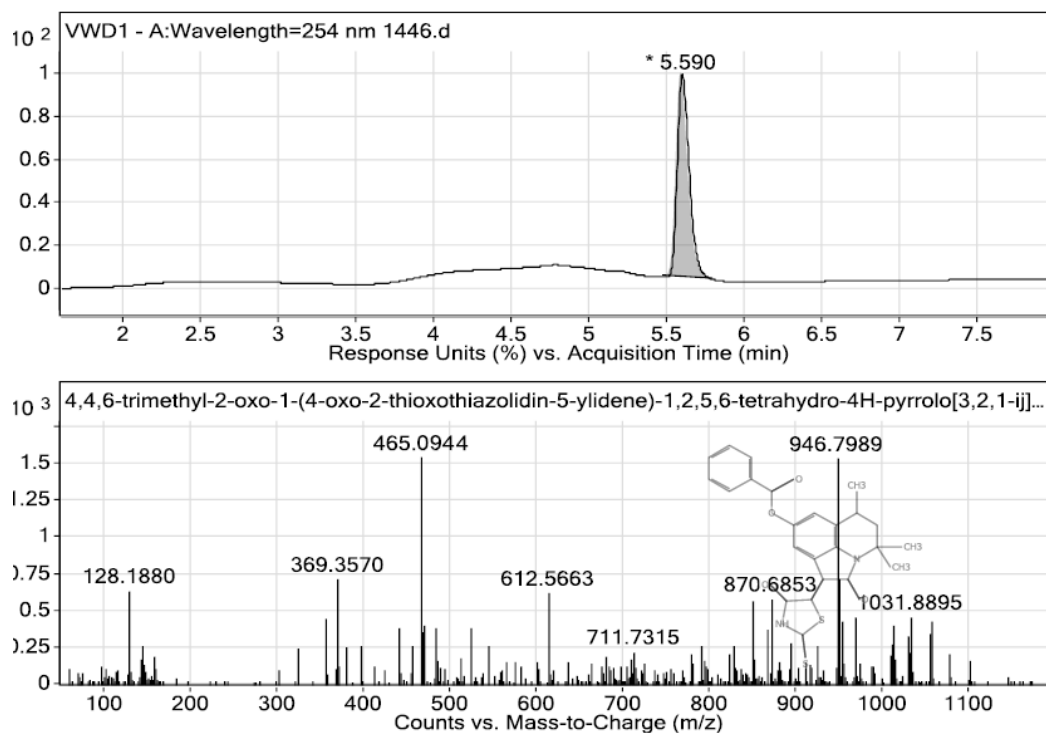


Figure S58. Data of HPLC-MS-ESI analysis of compound **12c**

<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of (Z)-4,4,6-trimethyl-2-oxo-1-(4-oxo-2-thioxothiazolidin-5-ylidene)-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-8-yl 2-methoxybenzoate  
12d

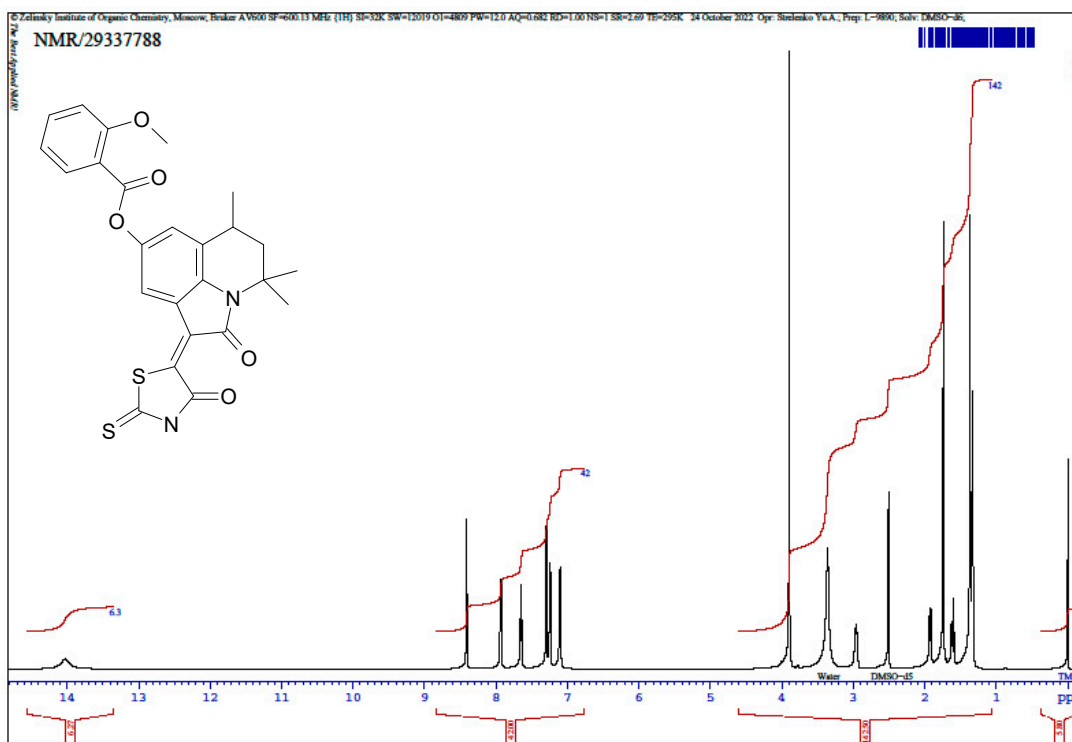


Figure S59. <sup>1</sup>H NMR spectrum of compound 12d

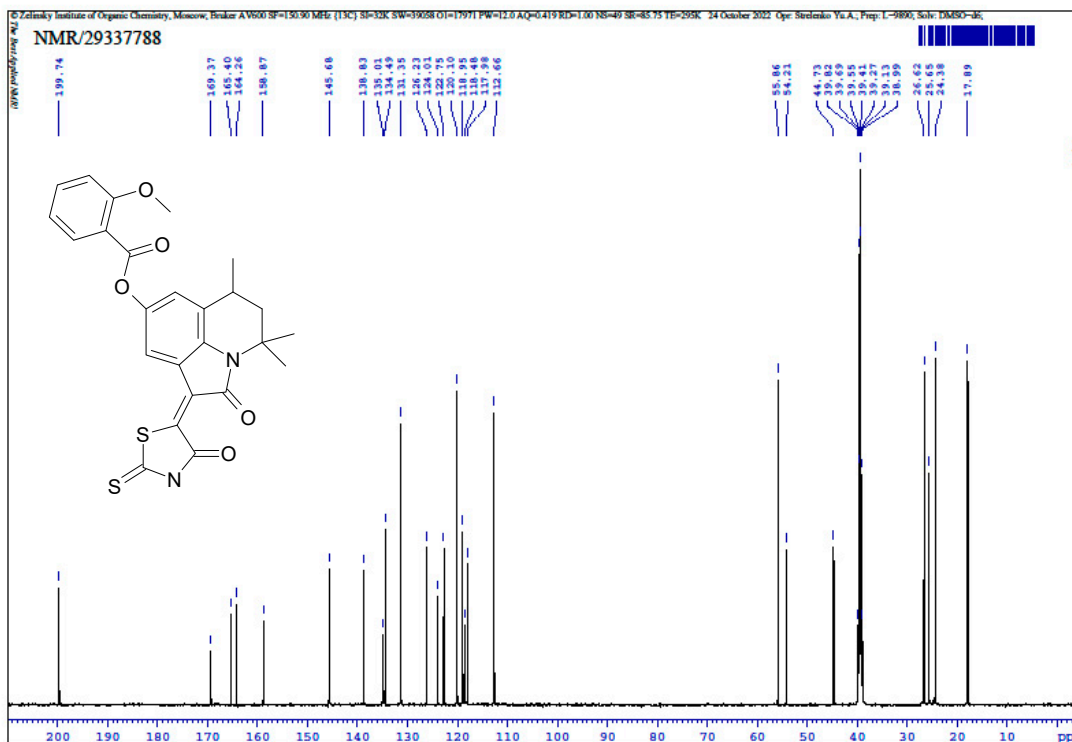


Figure S60. <sup>13</sup>C NMR spectrum of compound 12d

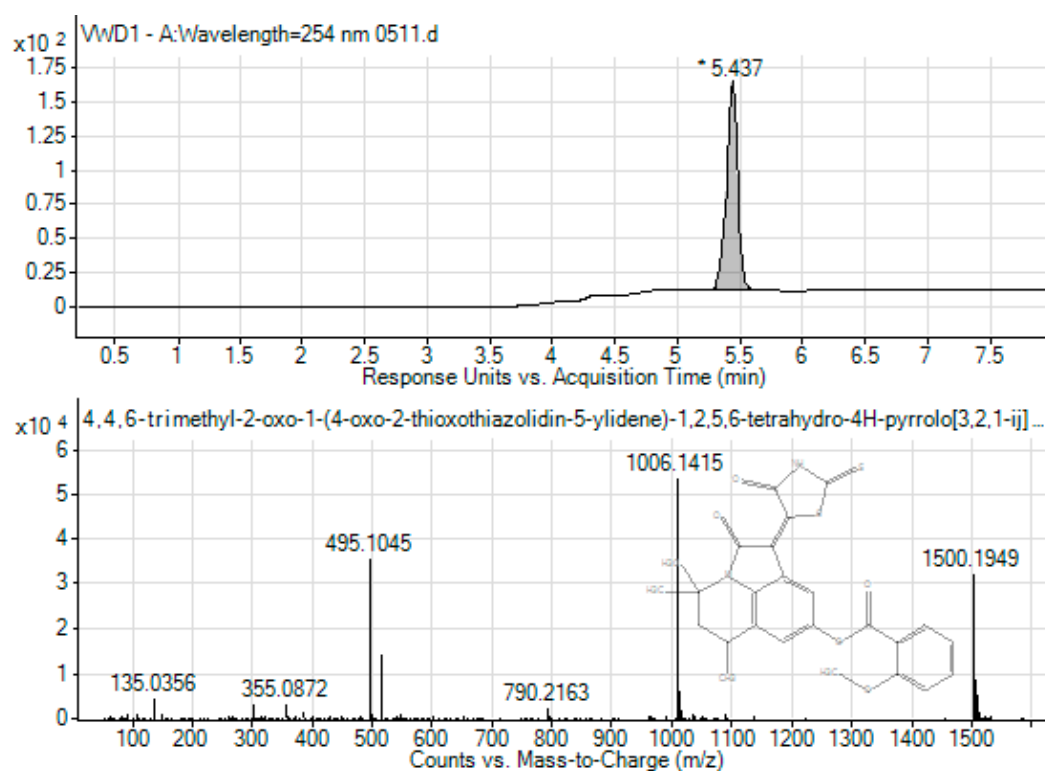


Figure S61. Data of HPLC-MS-ESI analysis of compound **12d**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of (Z)-4,4,6-trimethyl-2-oxo-1-(4-oxo-2-thioxothiazolidin-5-ylidene)-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-8-yl 3,4,5-trimethoxybenzoate **12e**

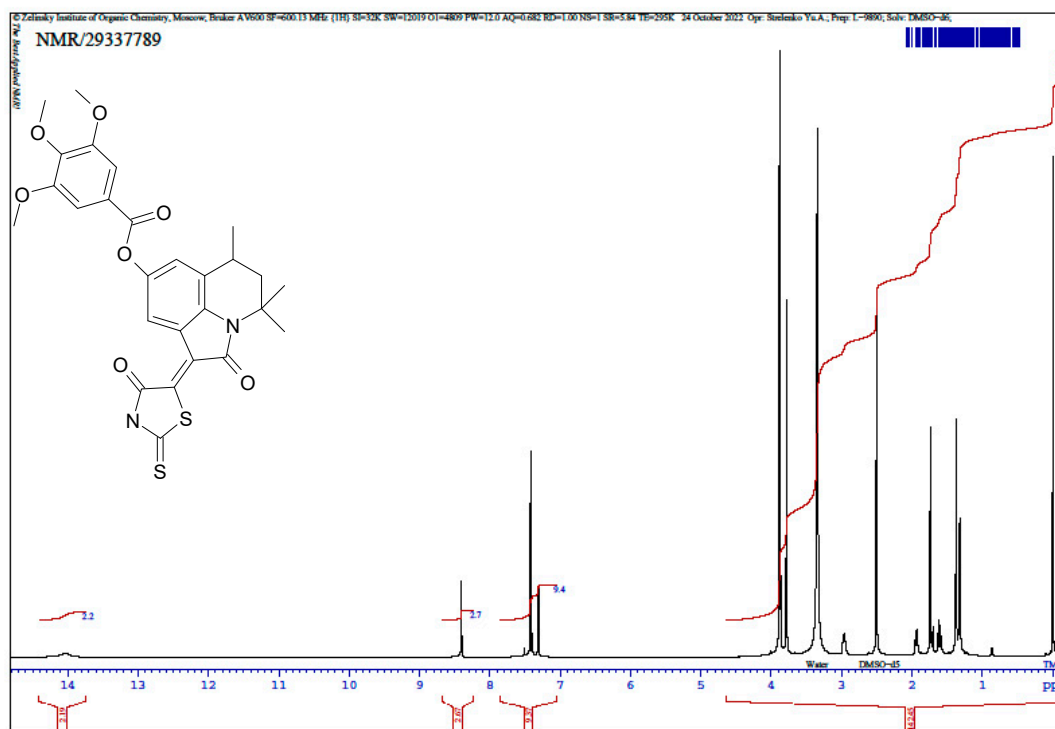
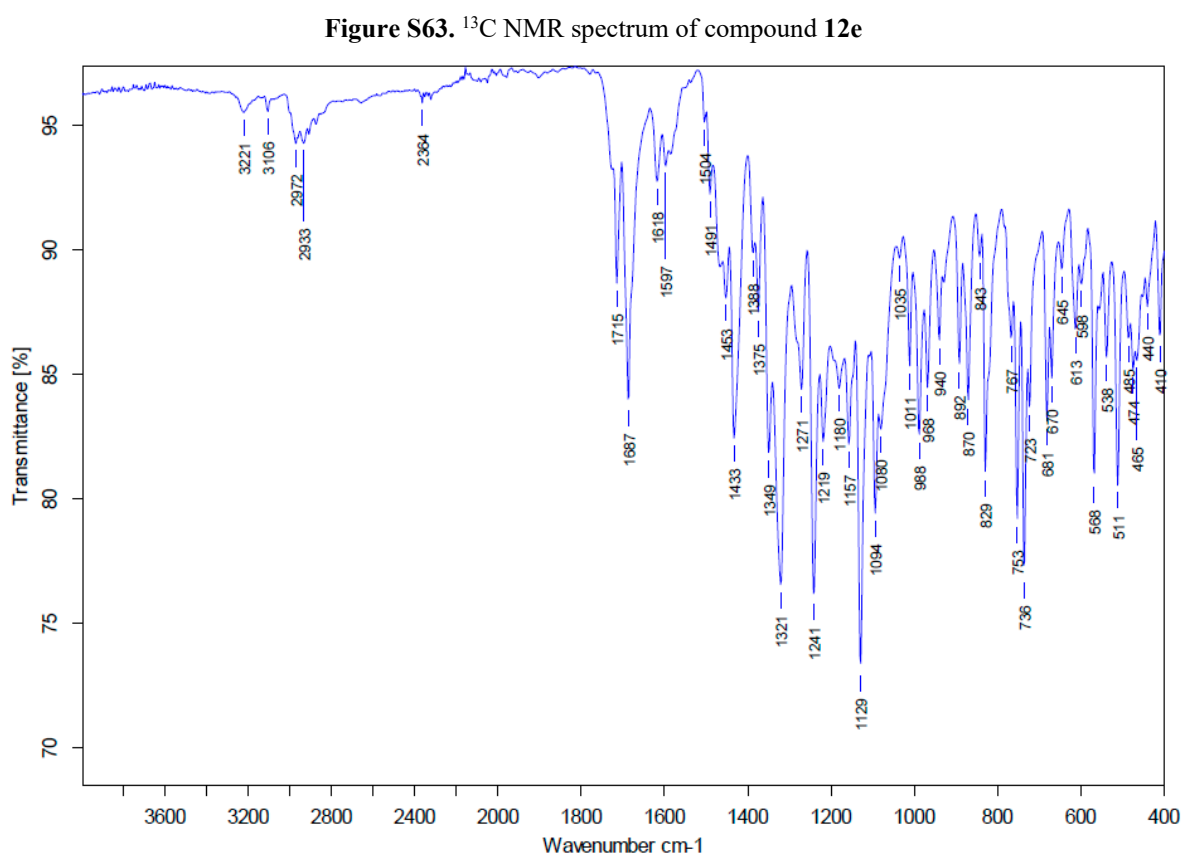
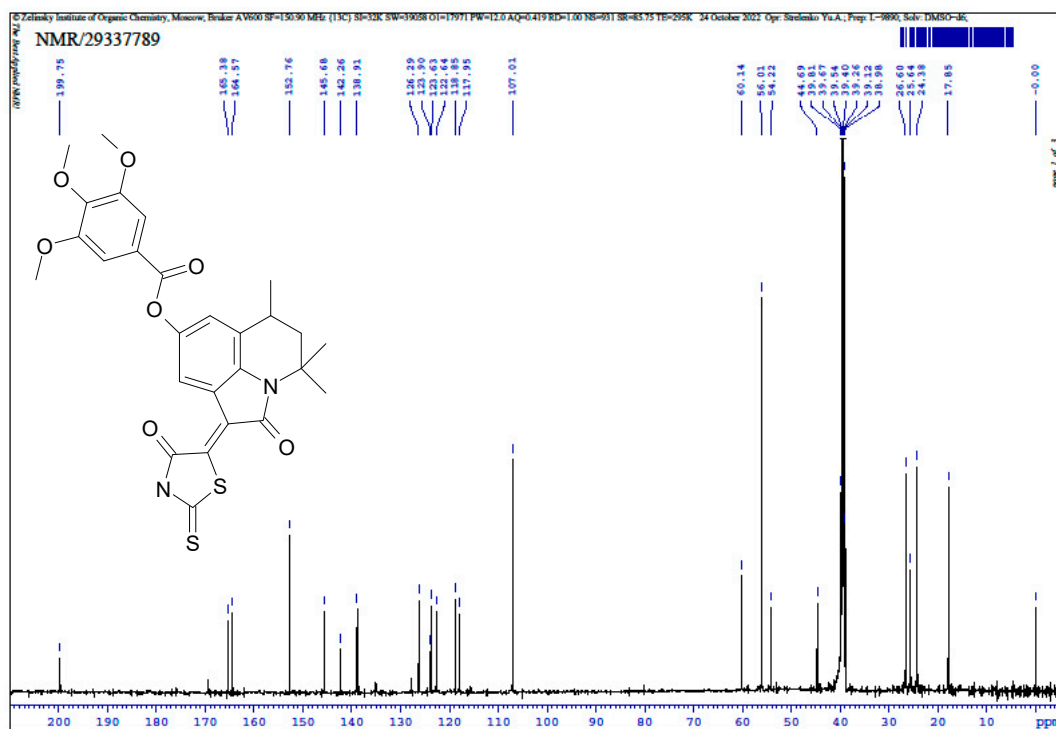


Figure S62.  $^1\text{H}$  NMR spectrum of compound **12e**







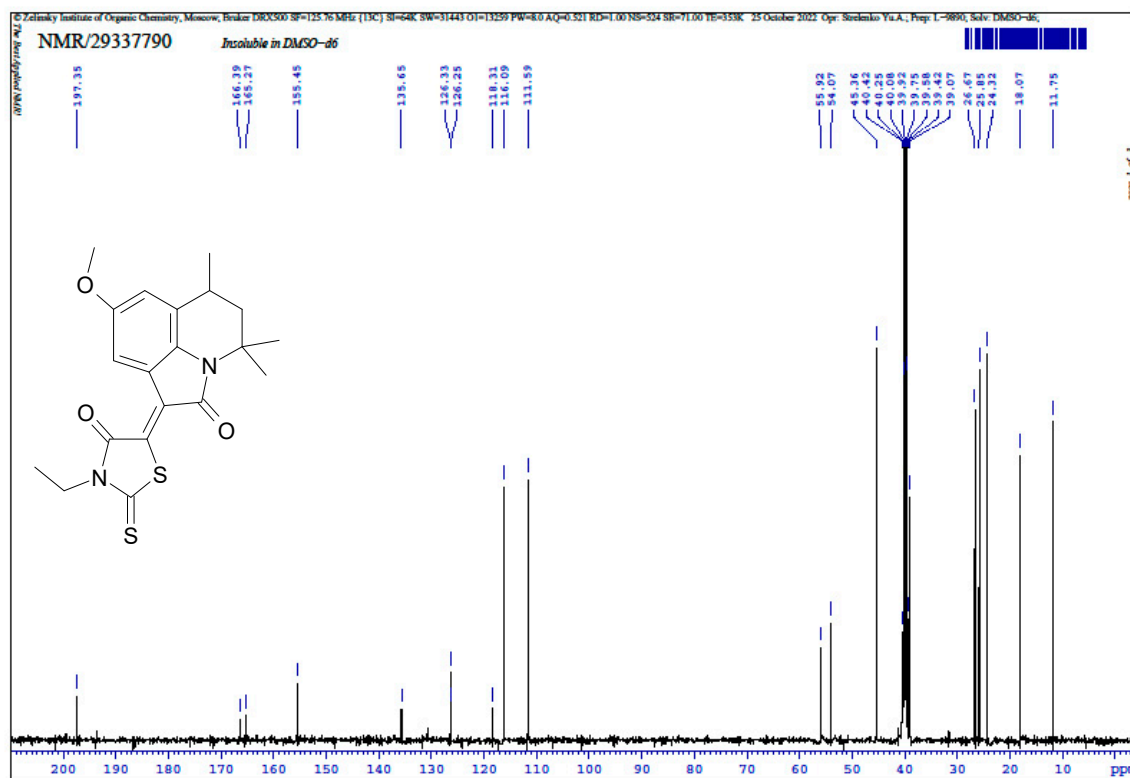


Figure S67.  $^{13}\text{C}$  NMR spectrum of compound 12f

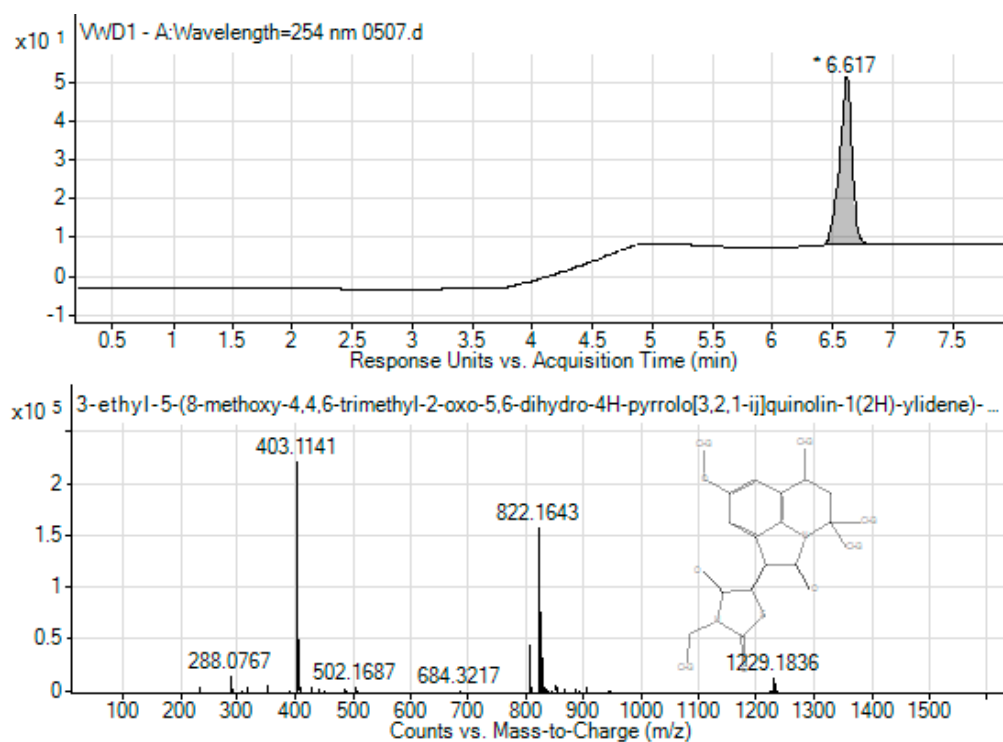
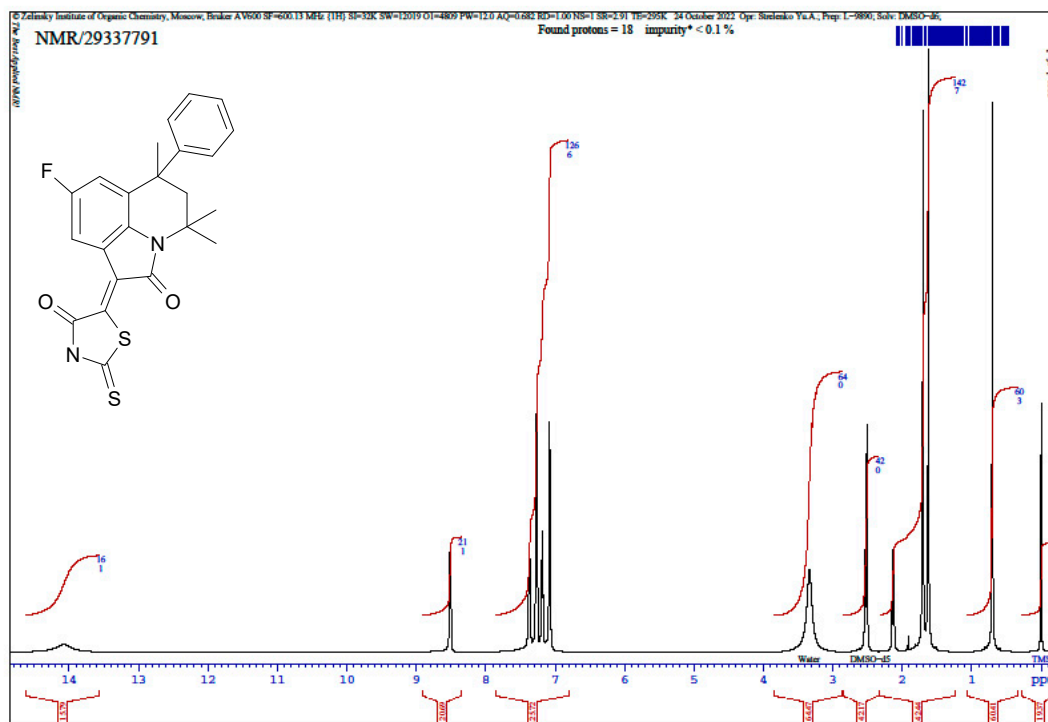
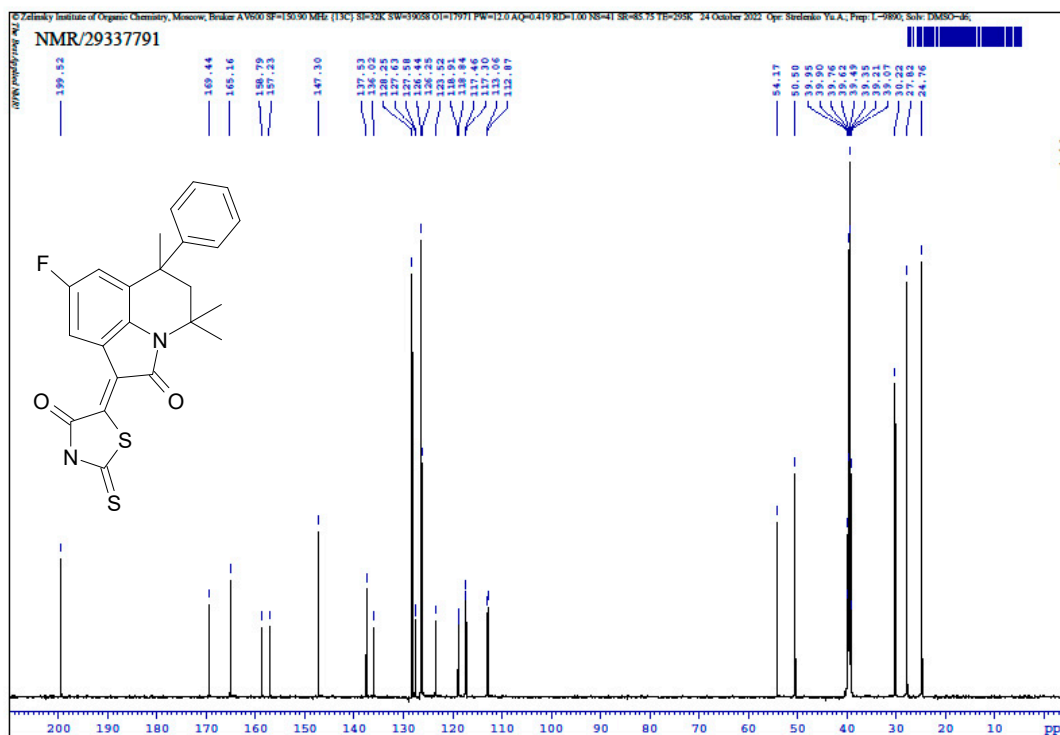


Figure S68. Data of HPLC-MS-ESI analysis of compound 12f

**$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(8-fluoro-4,4,6-trimethyl-2-oxo-6-phenyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-1(2*H*)-ylidene)-2-thioxothiazolidin-4-one 12g**



**Figure S69.**  $^1\text{H}$  NMR spectrum of compound 12g



**Figure S70.**  $^{13}\text{C}$  NMR spectrum of compound 12g



77.261 MHz (1H) 293.15 K SWH=10000.01=4006.006 FWH=10.6 AQ=1.238 RD=0.00 NS=1 SR=0.05 TH=301.8 23 October 2022 Opr: Sireniko Yu. A.; Prep: L-9880; Solv: DMSO-d6;

**NMR/29337812**

Found protons = 21    impurity\* = 1.8 %

Chemical Shift (ppm)	Integration
~13.5	1.00
~9.0	1.00
~7.5	1.00
~7.2	1.00
~7.0	1.00
~3.0	1.00
~2.5	1.00
~2.2	1.00
~1.8	1.00
~1.5	1.00
~1.2	1.00
~0.8	1.00

**Figure S72.**  $^1\text{H}$  NMR spectrum of compound **12h**

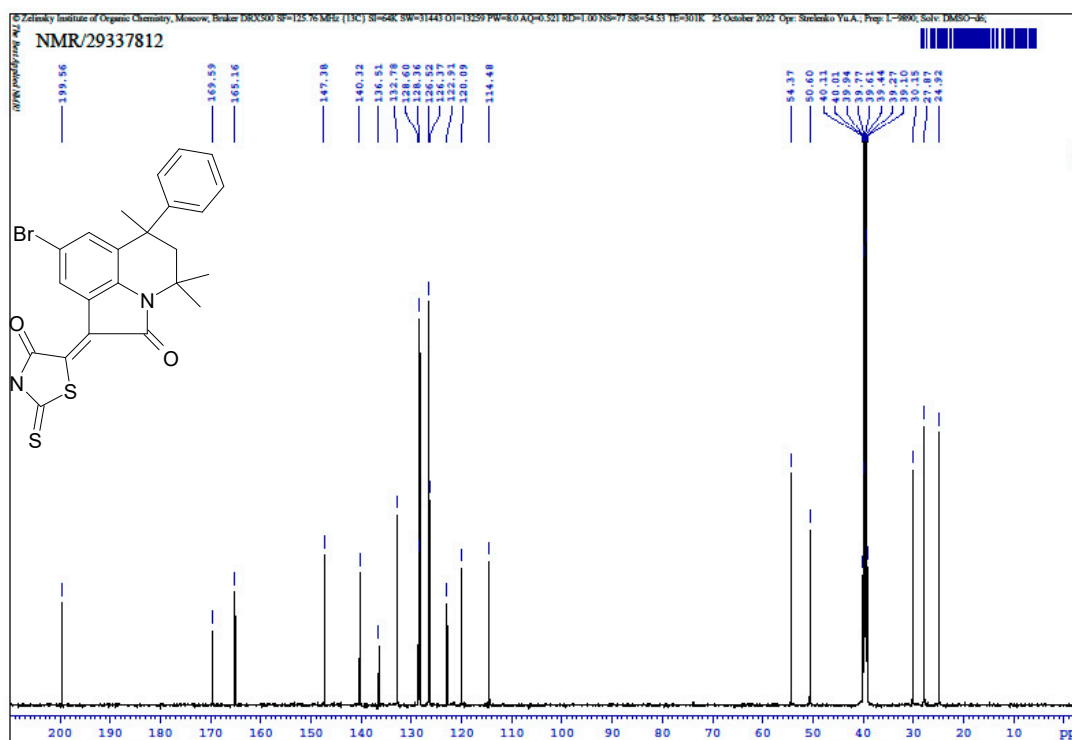


Figure S73.  $^{13}\text{C}$  NMR spectrum of compound 12h

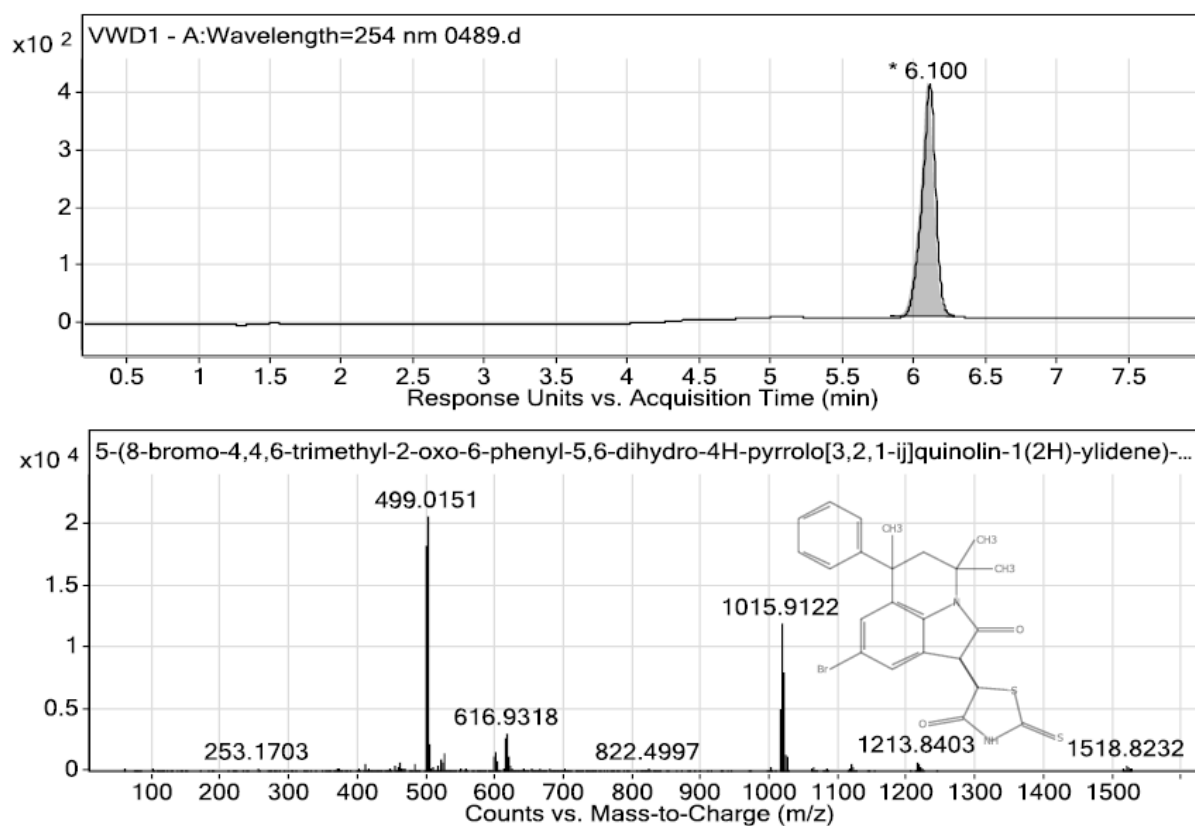
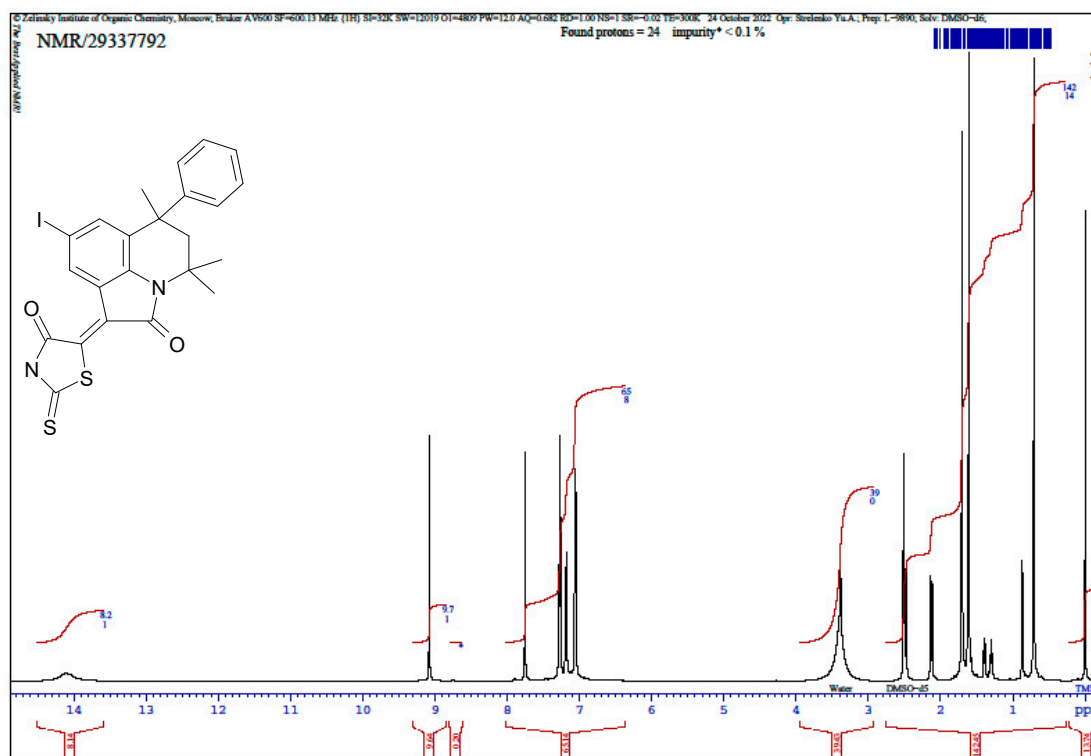
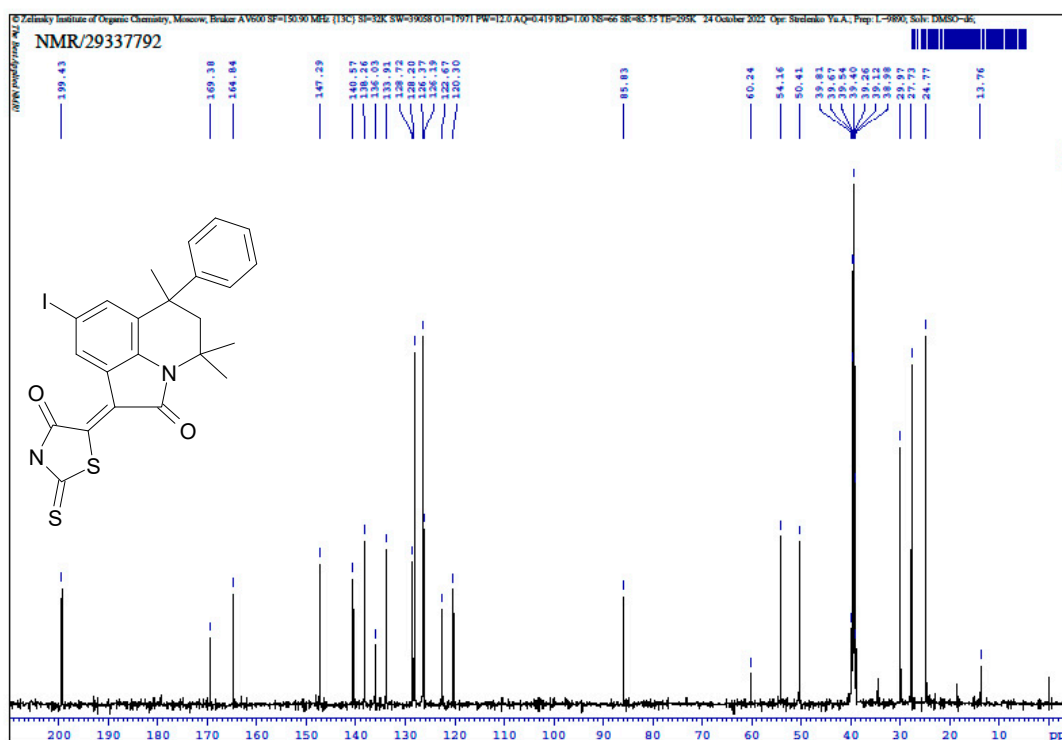


Figure S74. Data of HPLC-MS-ESI analysis of compound 12h

**$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(8-iodo-4,4,6-trimethyl-2-oxo-6-phenyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1(2H)-ylidene)-2-thioxothiazolidin-4-one 12i**



**Figure S75.**  $^1\text{H}$  NMR spectrum of compound 12i



**Figure S76.**  $^{13}\text{C}$  NMR spectrum of compound 12i

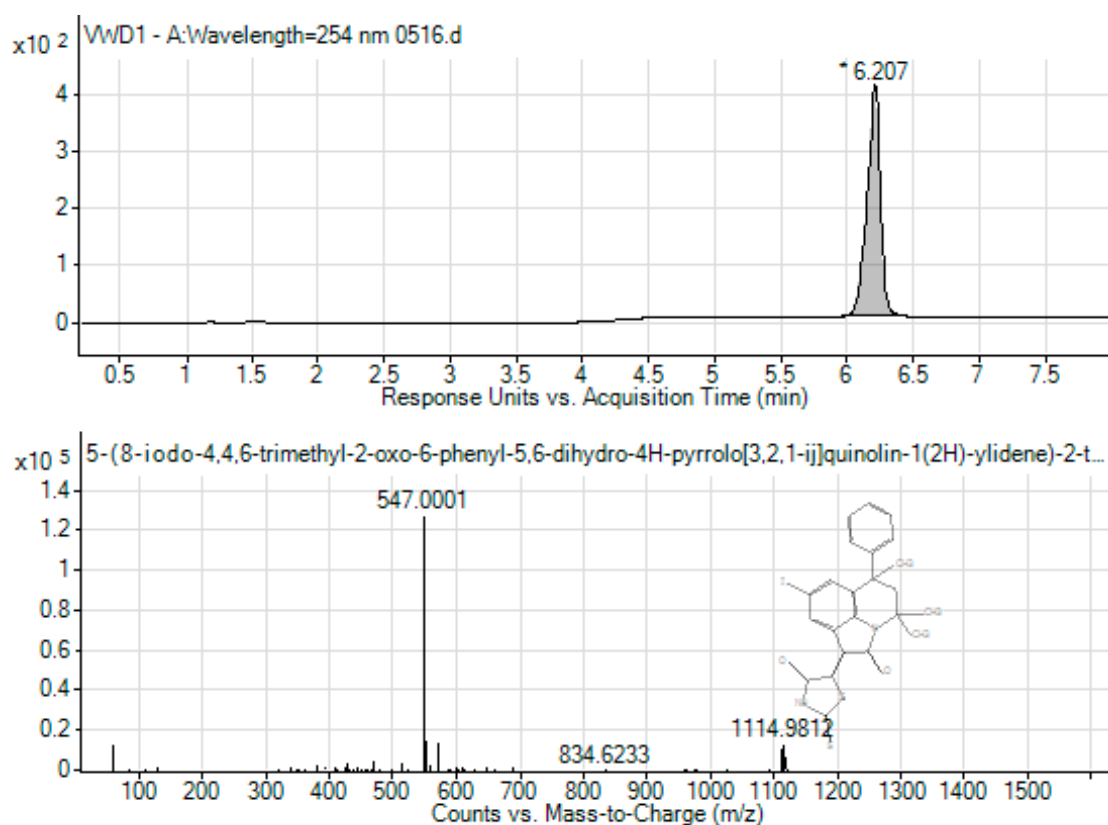


Figure S77. Data of HPLC-MS-ESI analysis of compound **12i**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-3-ethyl-2-thioxo-5-(4,4,6-trimethyl-2-oxo-6-phenyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1(2H)-ylidene)thiazolidin-4-one **12j**

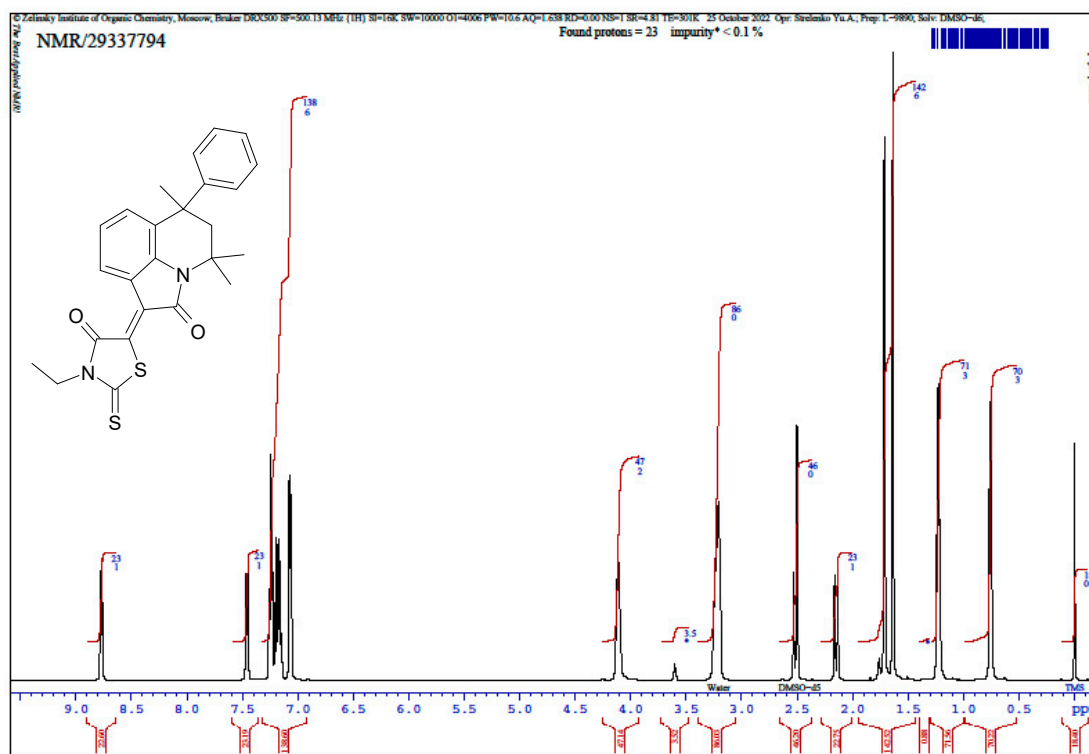


Figure S78.  $^1\text{H}$  NMR spectrum of compound **12j**

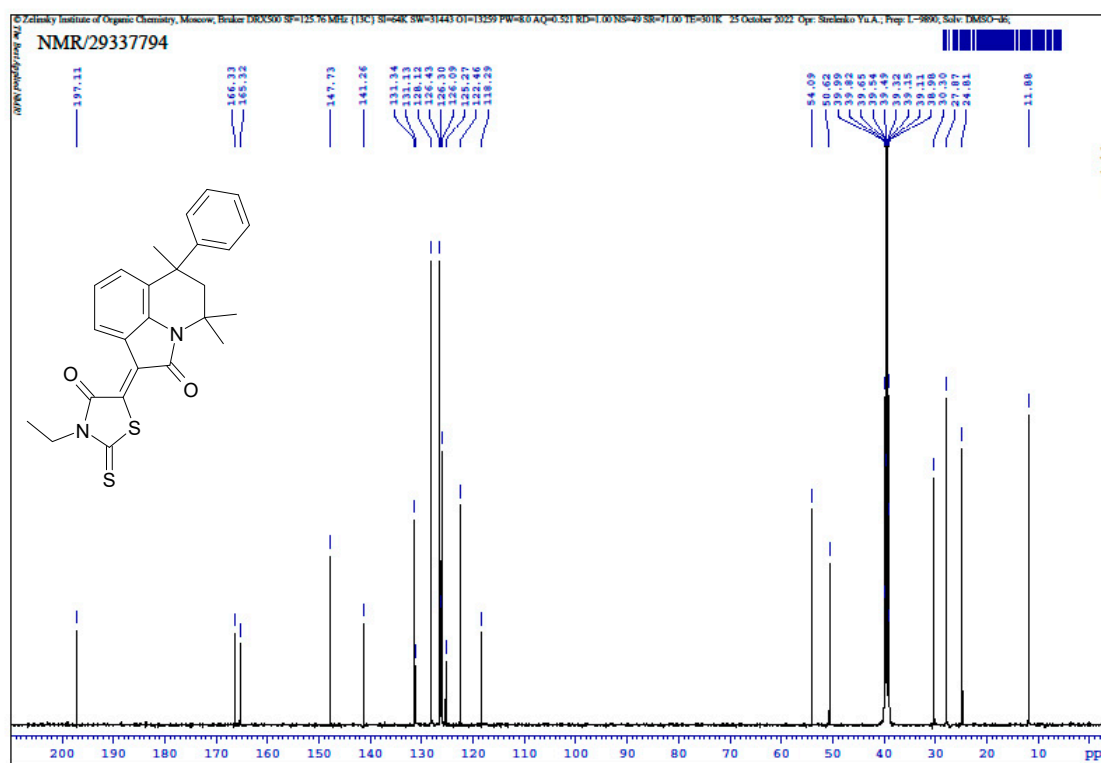


Figure S79.  $^{13}\text{C}$  NMR spectrum of compound 12j

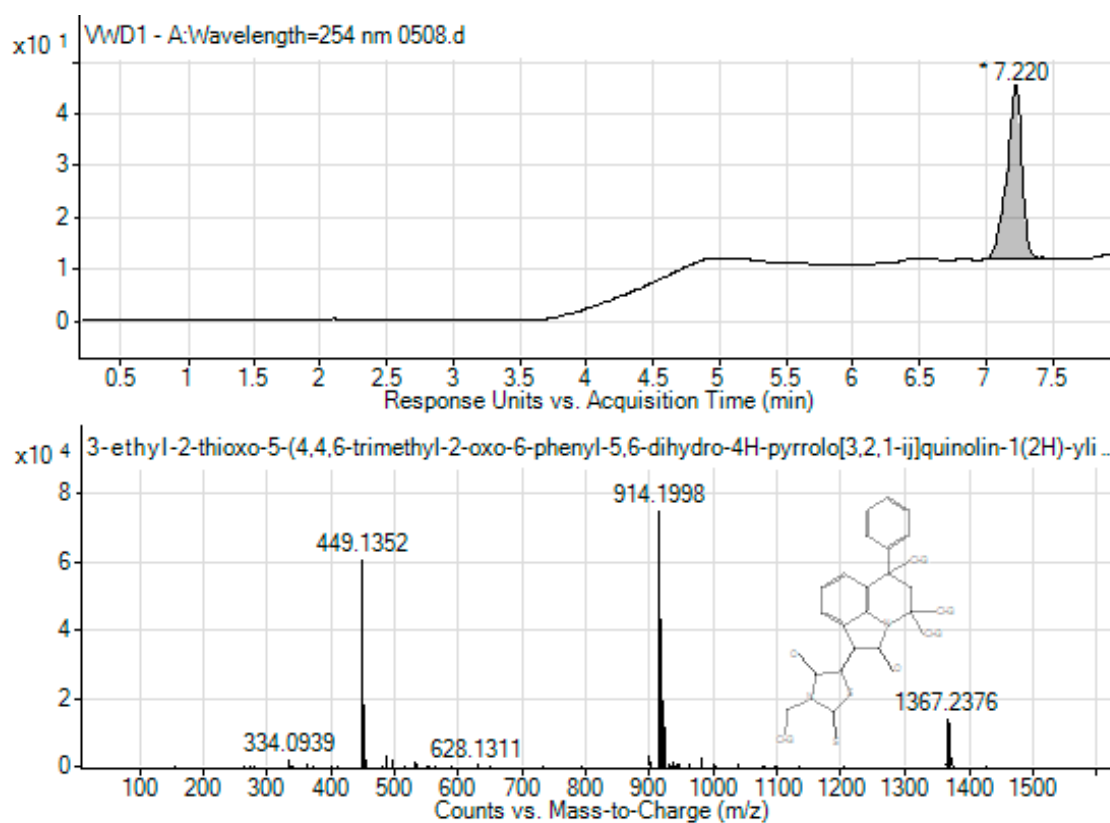
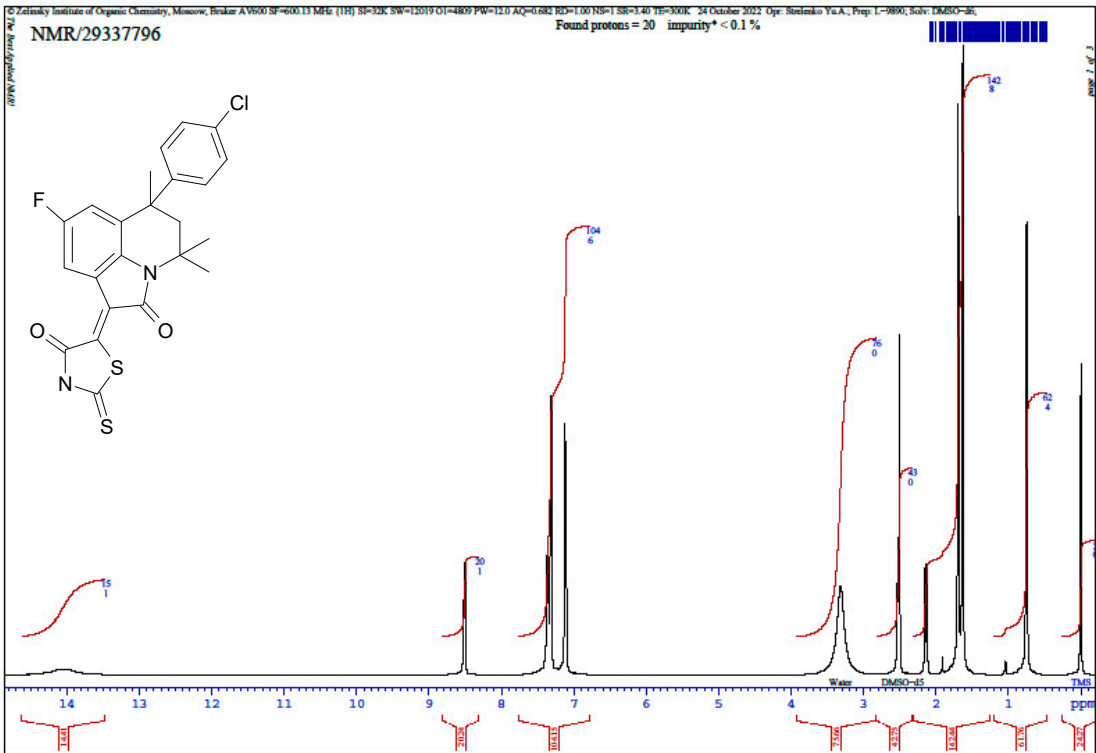
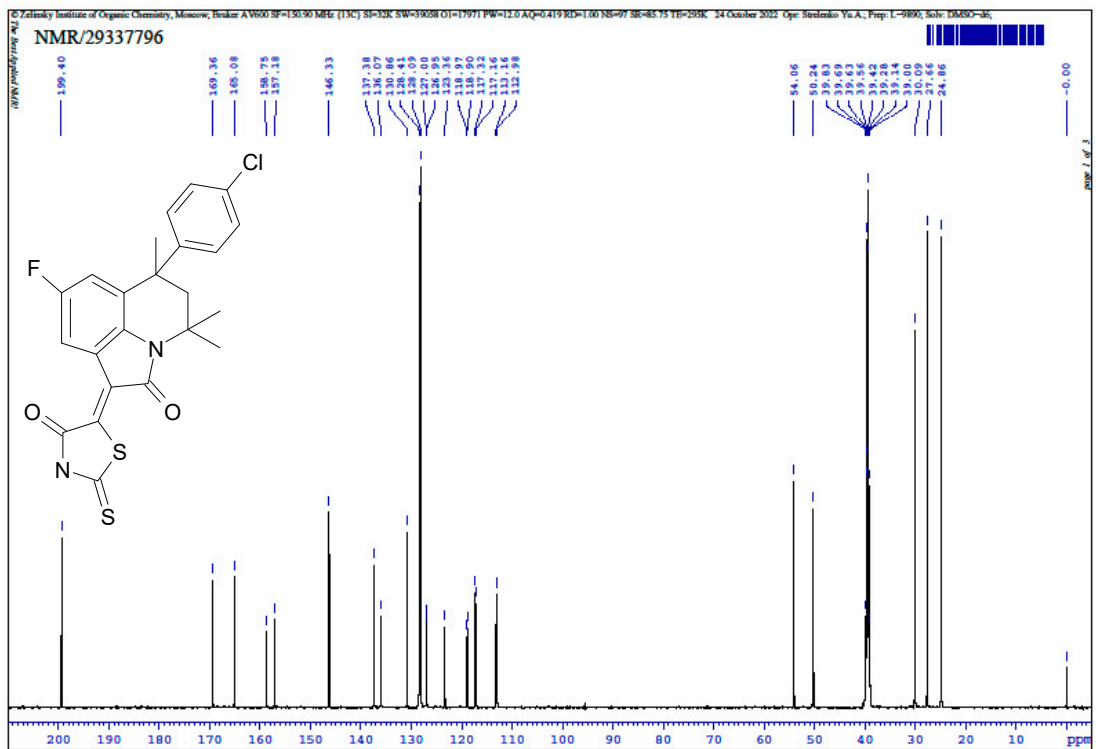


Figure S80. Data of HPLC-MS-ESI analysis of compound 12j

<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(6-(4-chlorophenyl)-8-fluoro-4,4,6-trimethyl-2-oxo-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1(2H)-ylidene)-2-thioxothiazolidin-4-one 12k

**Figure S81.**  $^1\text{H}$  NMR spectrum of compound **12k**



**Figure S82.**  $^{13}\text{C}$  NMR spectrum of compound **12k**



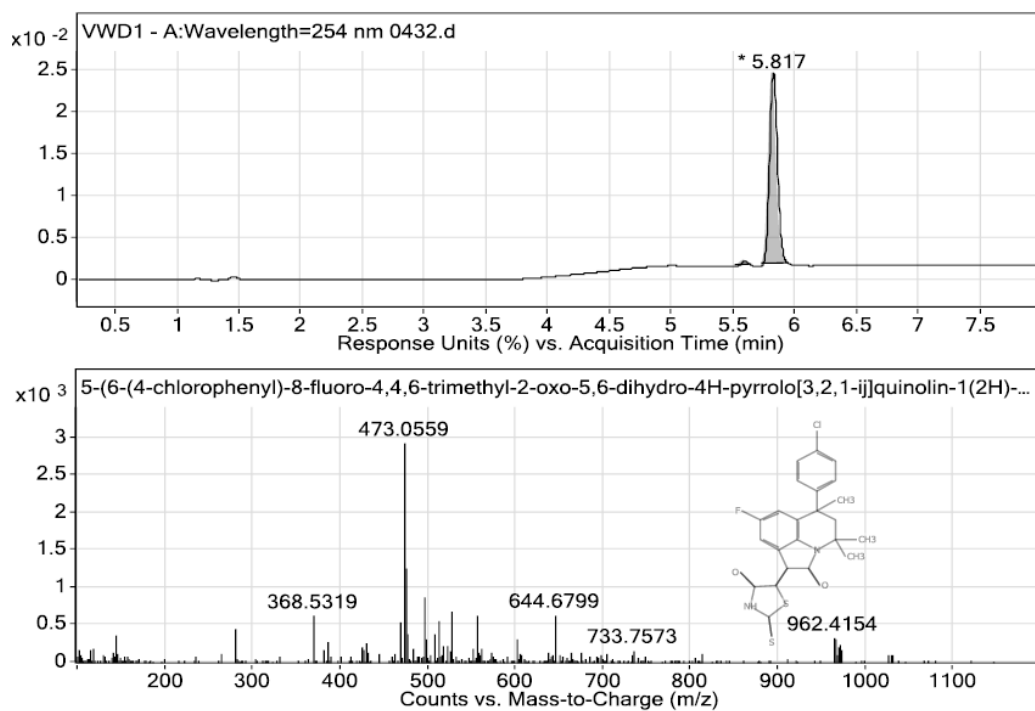


Figure S83. Data of HPLC-MS-ESI analysis of compound **12k**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(6-(4-chlorophenyl)-8-iodo-4,4,6-trimethyl-2-oxo-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1(2H)-ylidene)-2-thioxothiazolidin-4-one **12l**

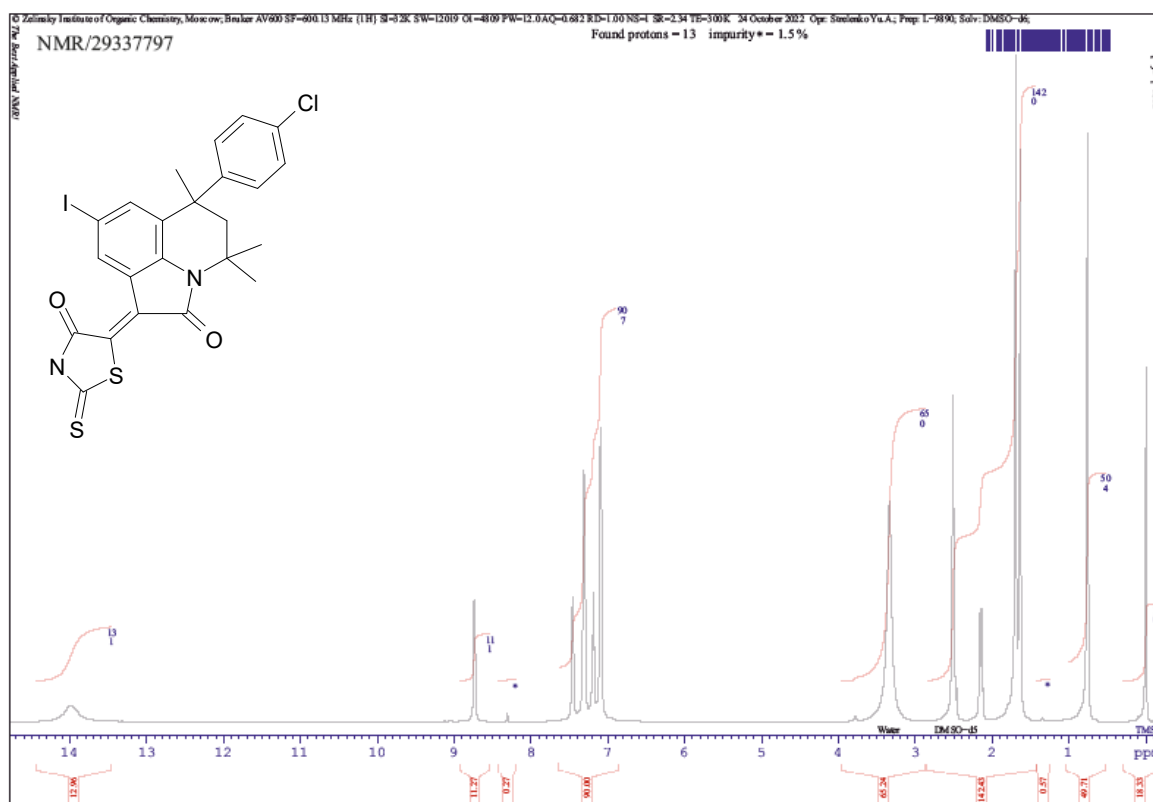


Figure S84.  $^1\text{H}$  NMR spectrum of compound **12l**

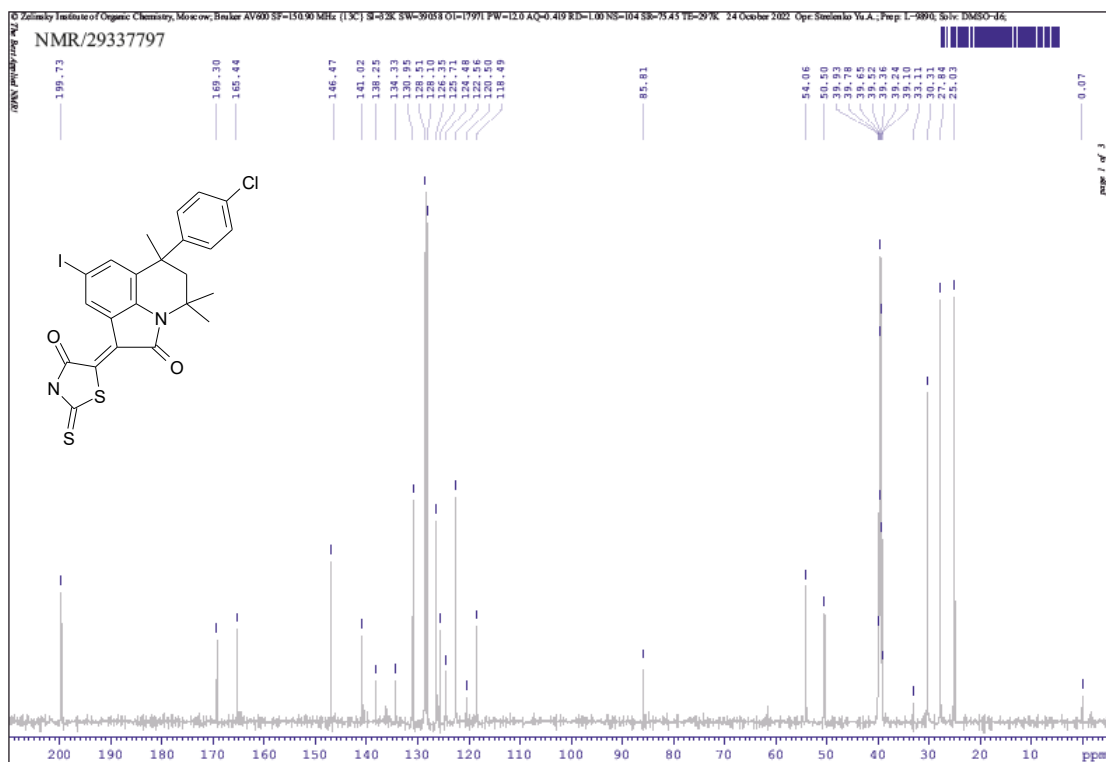


Figure S85.  $^{13}\text{C}$  NMR spectrum of compound 121

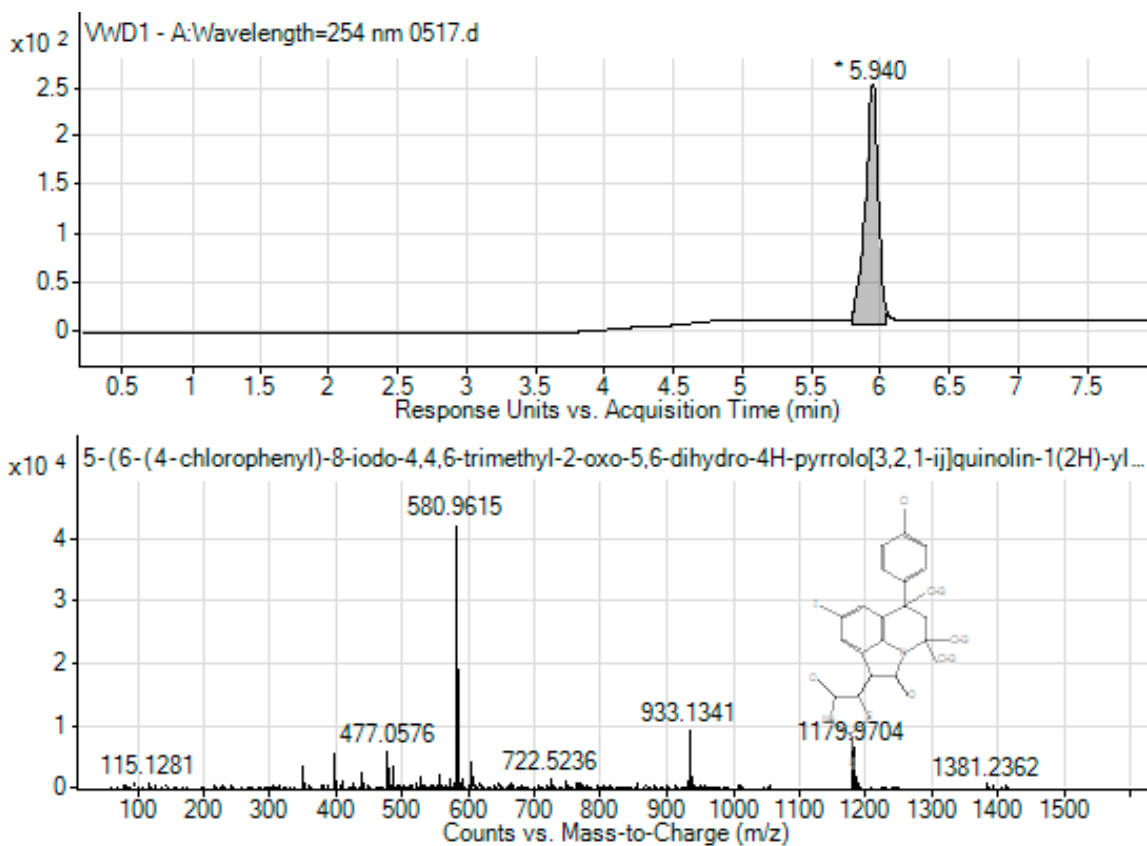


Figure S86. Data of HPLC-MS-ESI analysis of compound 121

<sup>1</sup>H, <sup>13</sup>C NMR, IR and data HPLC-HRMS-ESI spectra of (Z)-5-(6-(4-chlorophenyl)-8-fluoro-4,4,6-trimethyl-2-oxo-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1(2H)-ylidene)-3-ethyl-2-thioxothiazolidin-4-one 12m

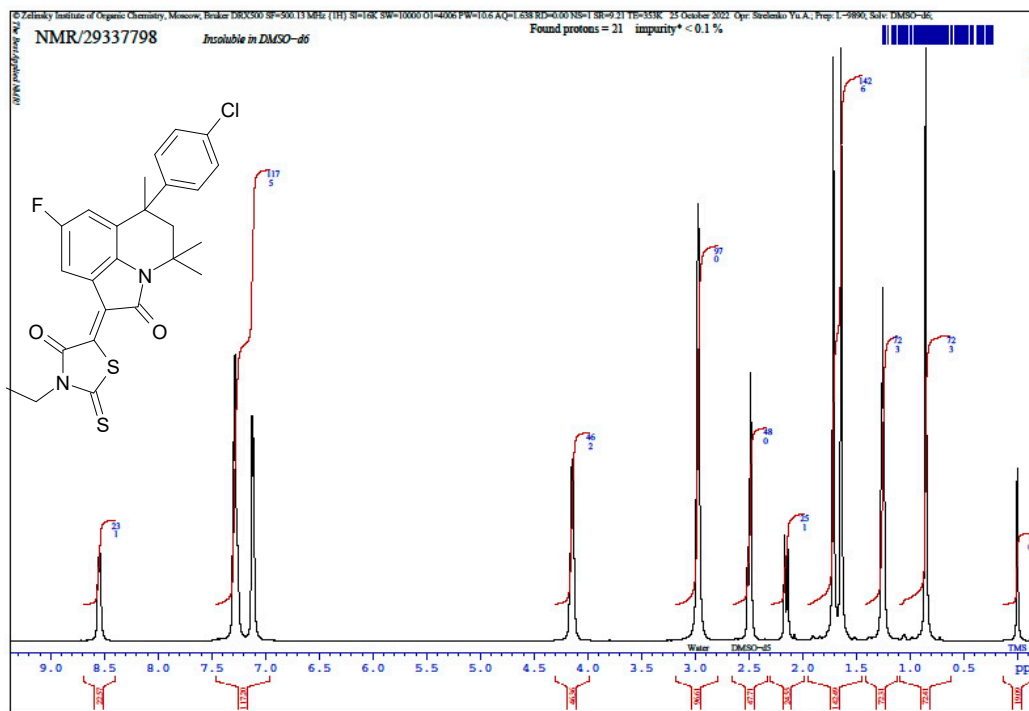


Figure S87. <sup>1</sup>H NMR spectrum of compound 12m

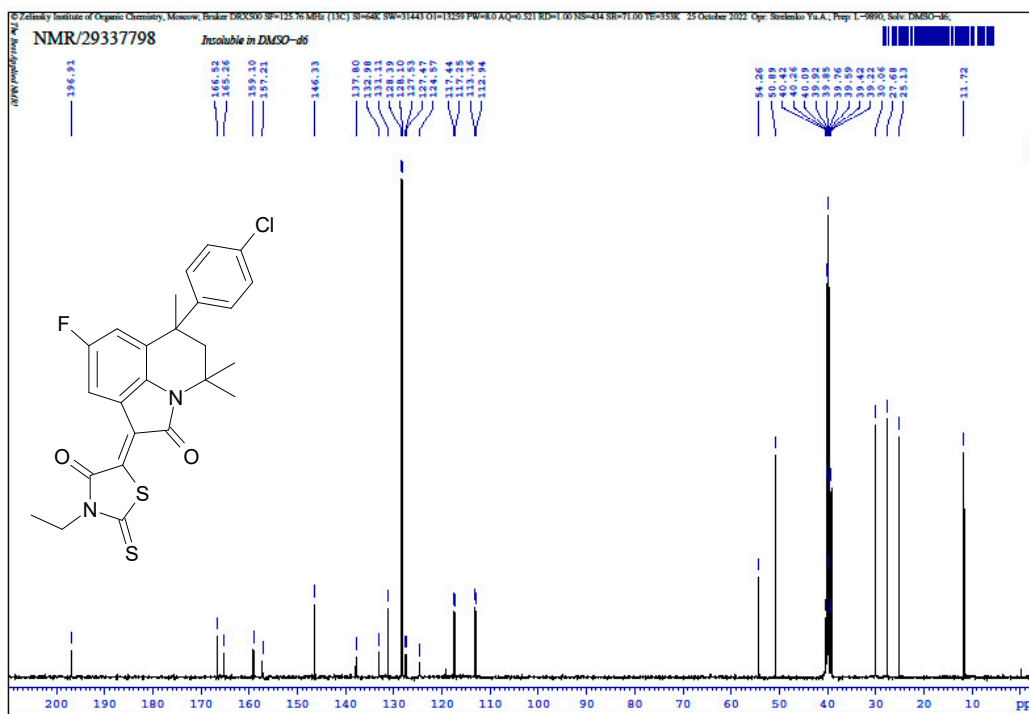
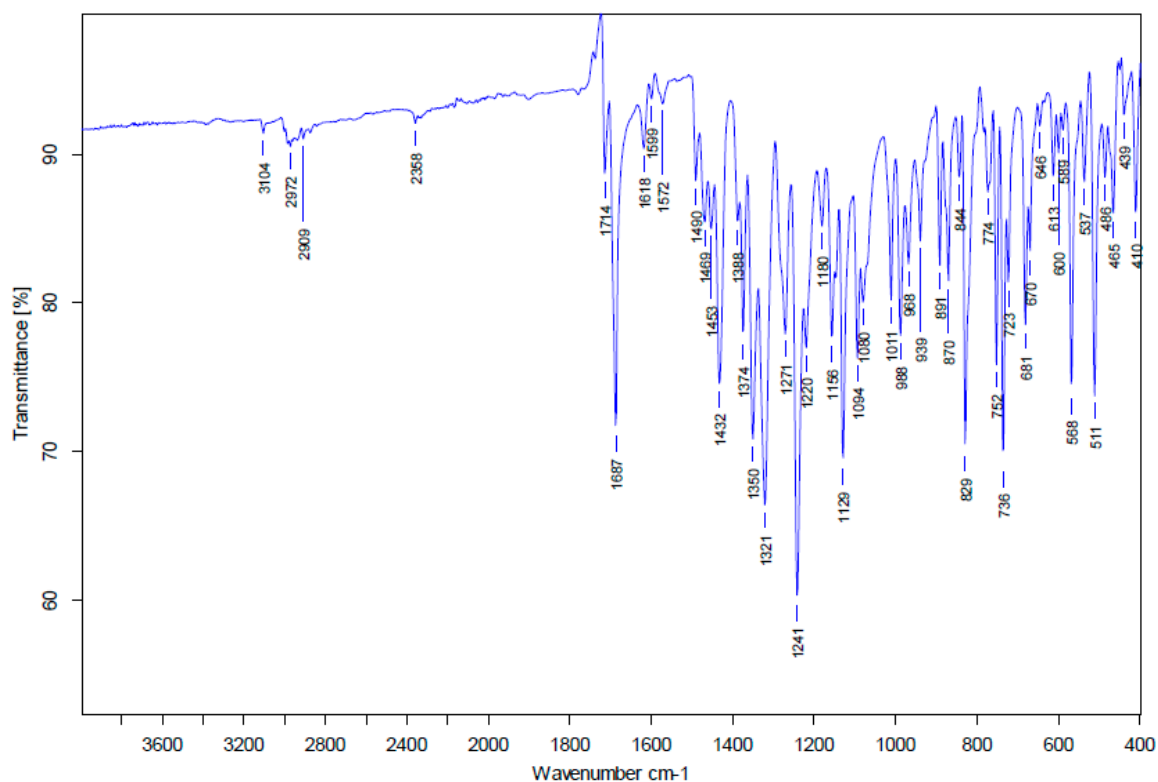
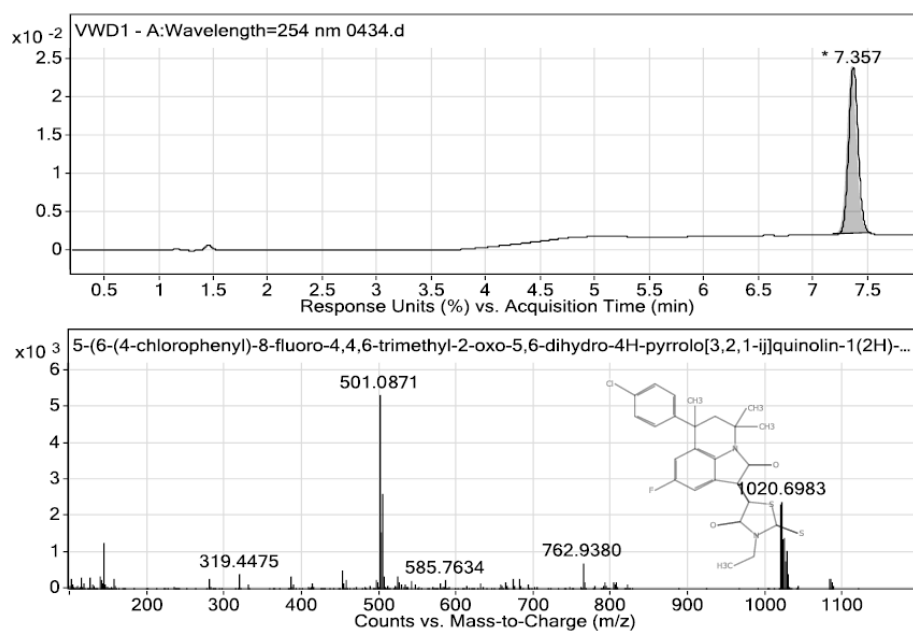


Figure S88. <sup>13</sup>C NMR spectrum of compound 12m



**Figure S89.** IR spectrum of compound **12m**



**Figure S90.** Data of HPLC-MS-ESI analysis of compound **12m**

<sup>1</sup>H, <sup>13</sup>C NMR, IR and data HPLC-HRMS-ESI spectra of (Z)-5-(6',6'-dimethyl-2'-oxo-5',6'-dihydrospiro[cyclohexane-1,4'-pyrrolo[3,2,1-*ij*]quinolin]-1'(2'*H*)-ylidene)-2-thioxothiazolidin-4-one 12n

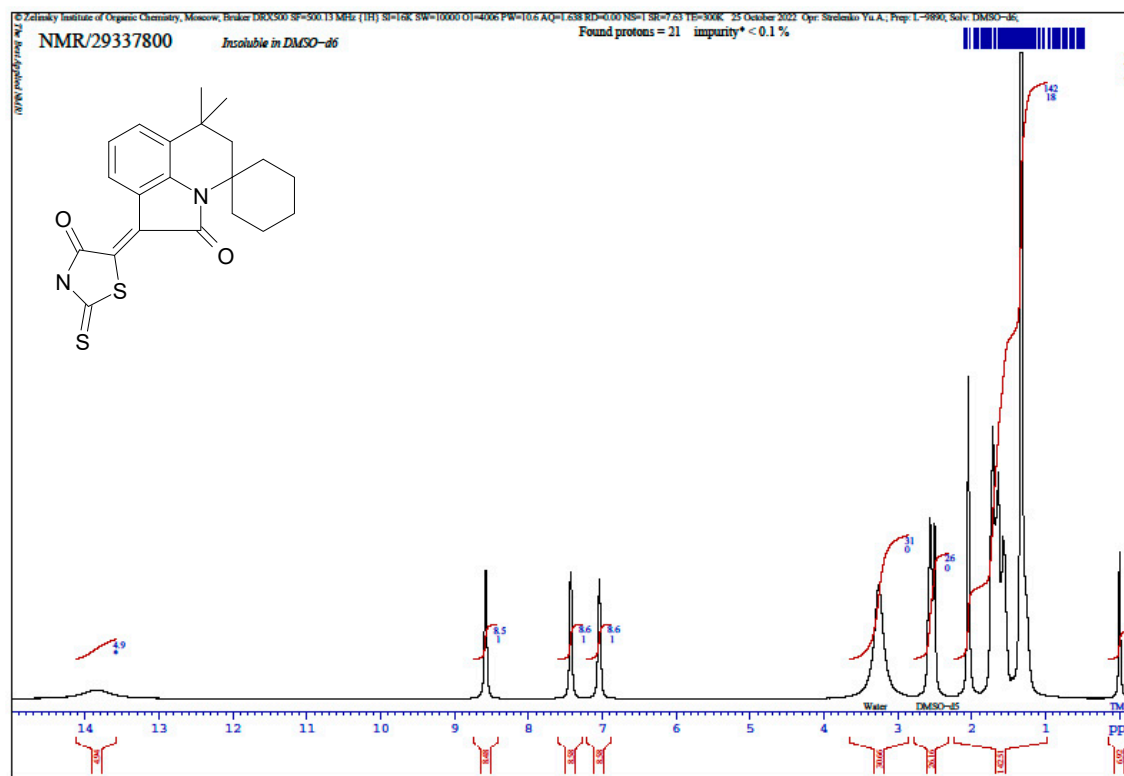


Figure S91. <sup>1</sup>H NMR spectrum of compound 12n

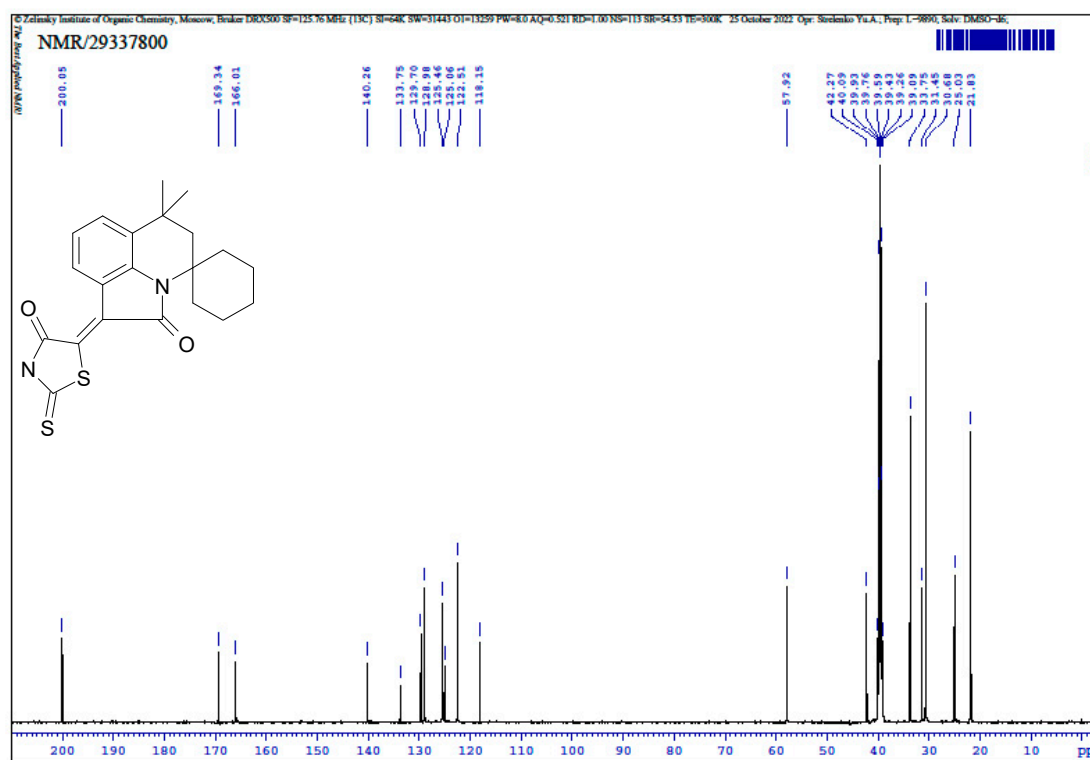
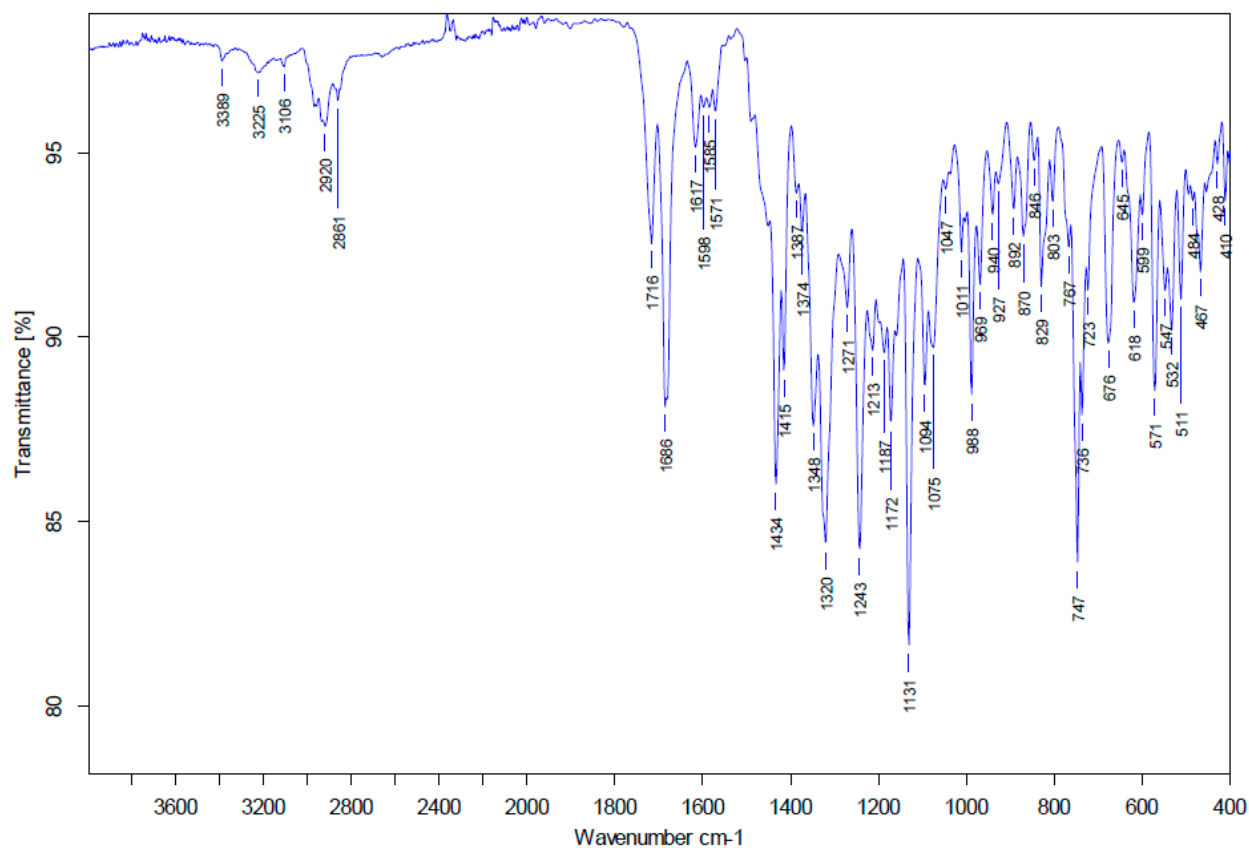
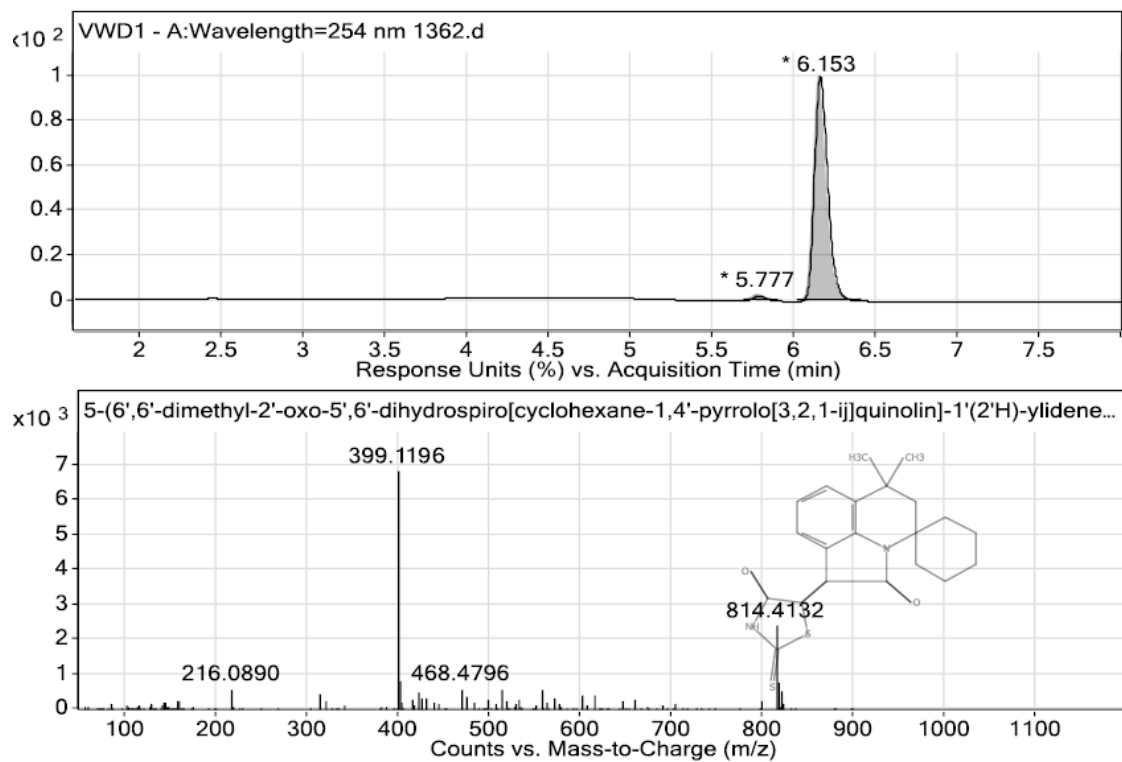


Figure S92. <sup>13</sup>C NMR spectrum of compound 12n



**Figure S93.** IR spectrum of compound **12n**



**Figure S94.** Data of HPLC-MS-ESI analysis of compound **12n**

<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(6',8'-dimethyl-2'-oxo-5',6'-dihydrospiro[cyclohexane-1,4'-pyrrolo[3,2,1-ij]quinolin]-1'(2'H)-ylidene)-2-thioxothiazolidin-4-one 12o

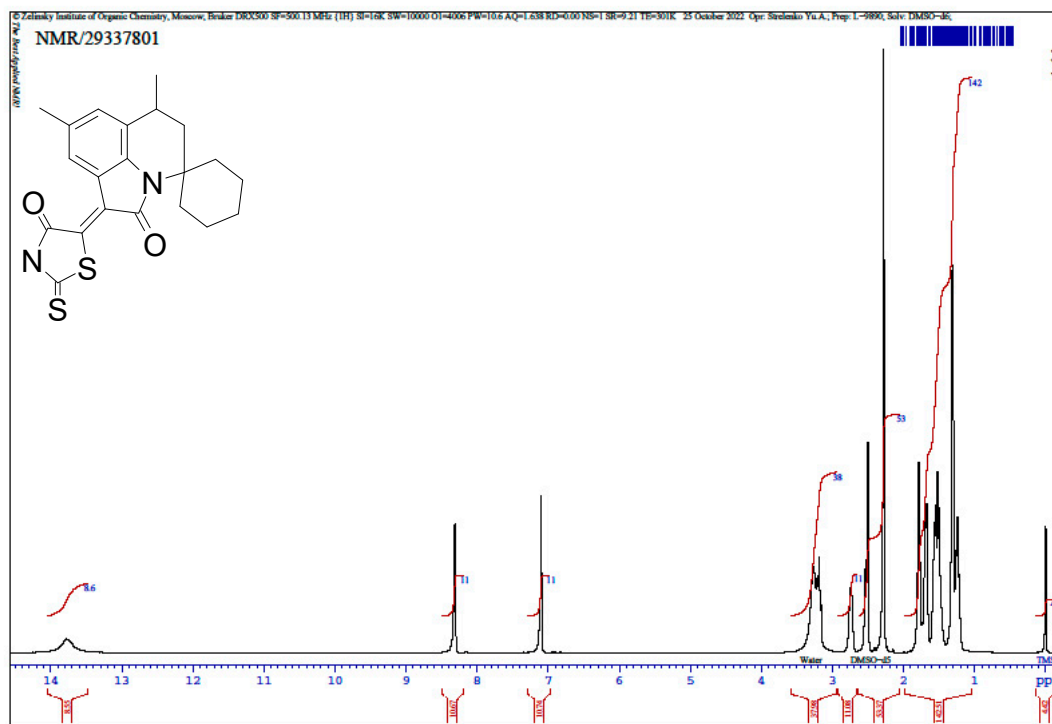


Figure S95. <sup>1</sup>H NMR spectrum of compound 12o

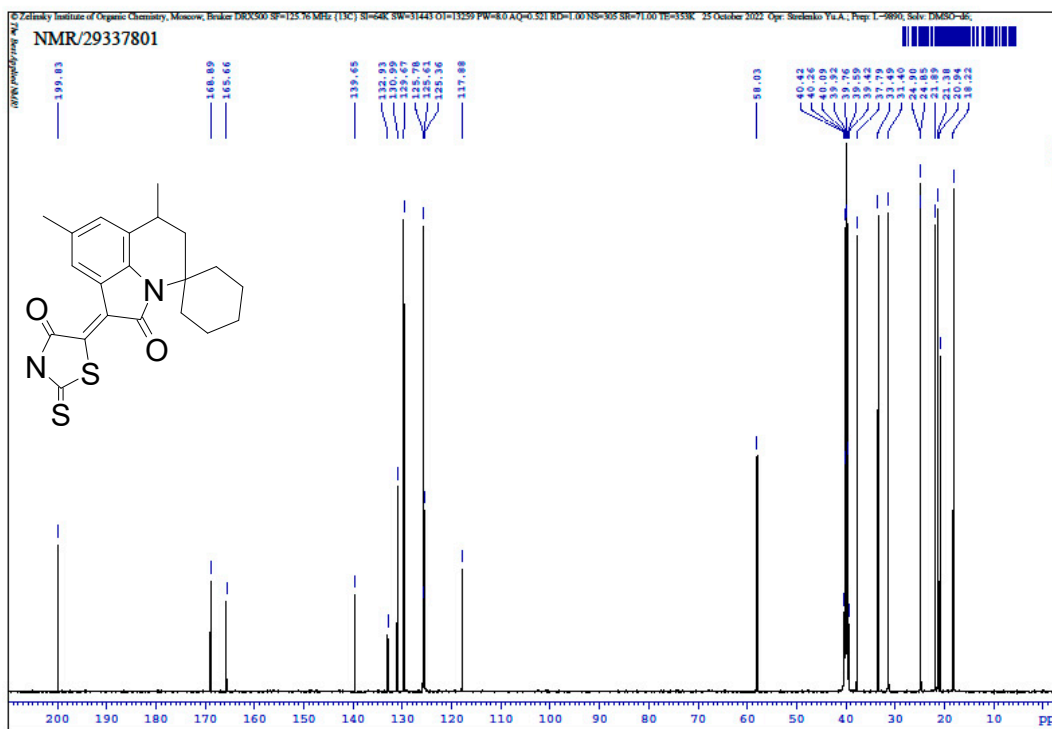


Figure S96. <sup>13</sup>C NMR spectrum of compound 12o

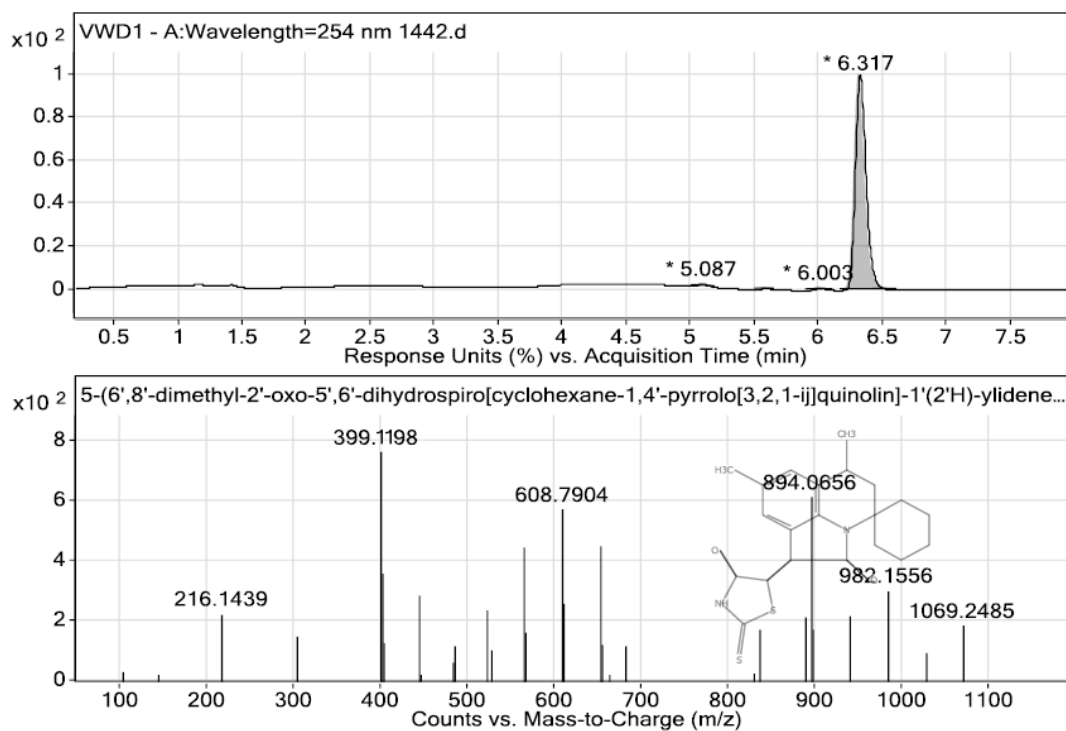


Figure S97. Data of HPLC-MS-ESI analysis of compound **12o**

<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of (Z)-5-(8'-fluoro-6'-methyl-2'-oxo-5',6'-dihydrospiro[cyclopentane-1,4'-pyrrolo[3,2,1-ij]quinolin]-1'(2'H)-ylidene)-2-thioxothiazolidin-4-one **12p**

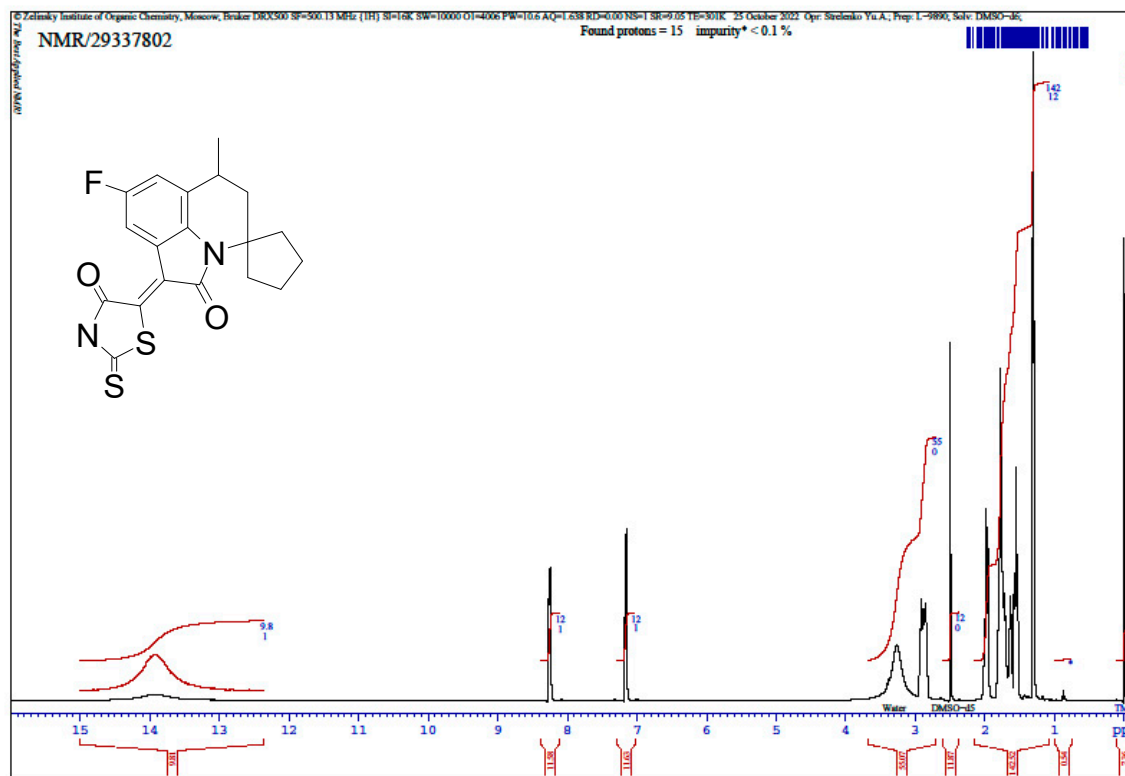
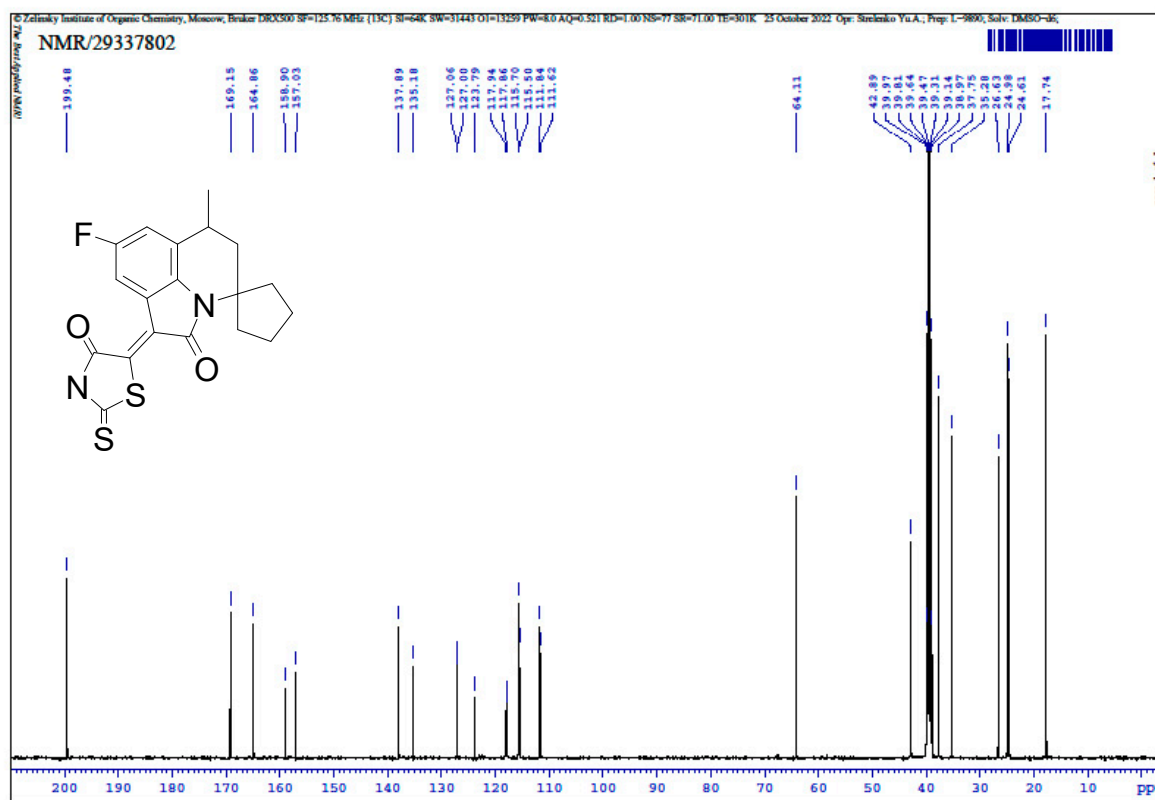
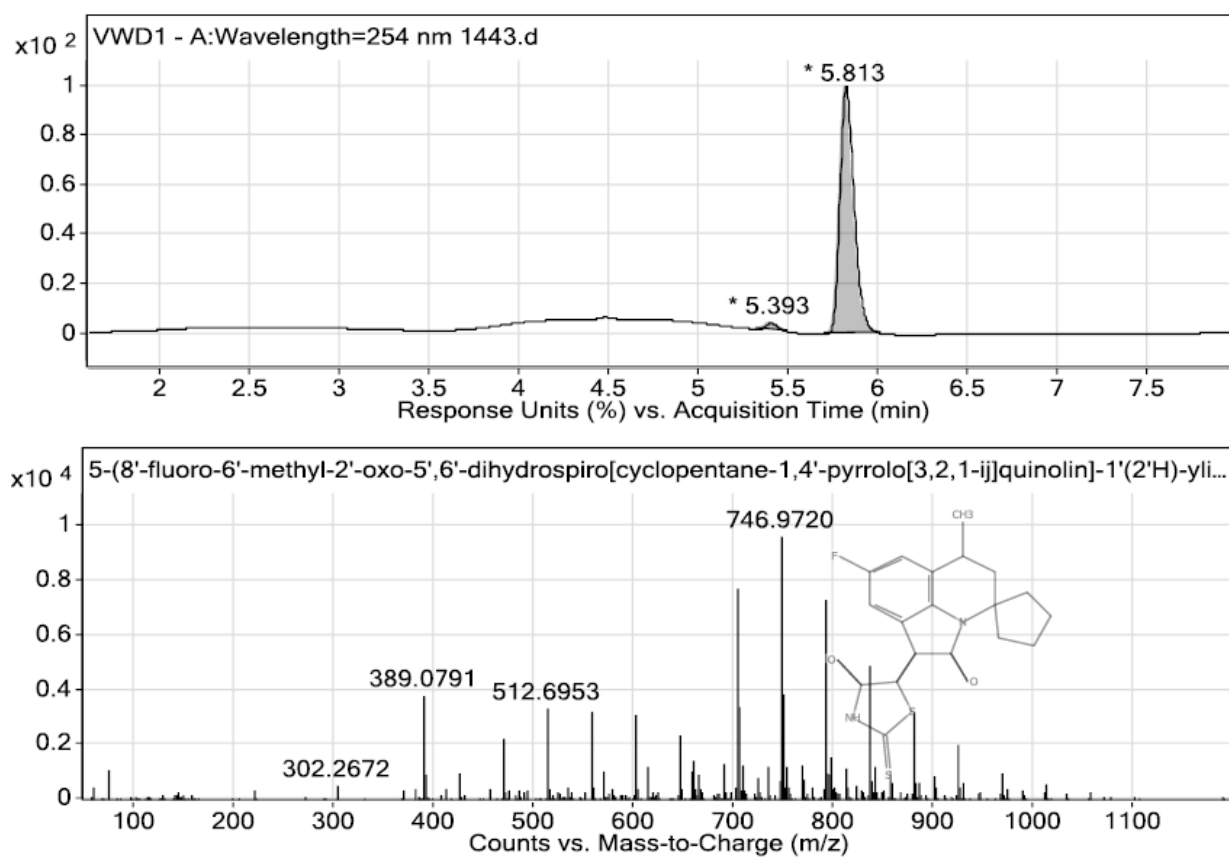


Figure S98. <sup>1</sup>H NMR spectrum of compound **12p**





**Figure S99.**  $^{13}\text{C}$  NMR spectrum of compound **12p**



**Figure S100.** Data of HPLC-MS-ESI analysis of compound **12p**



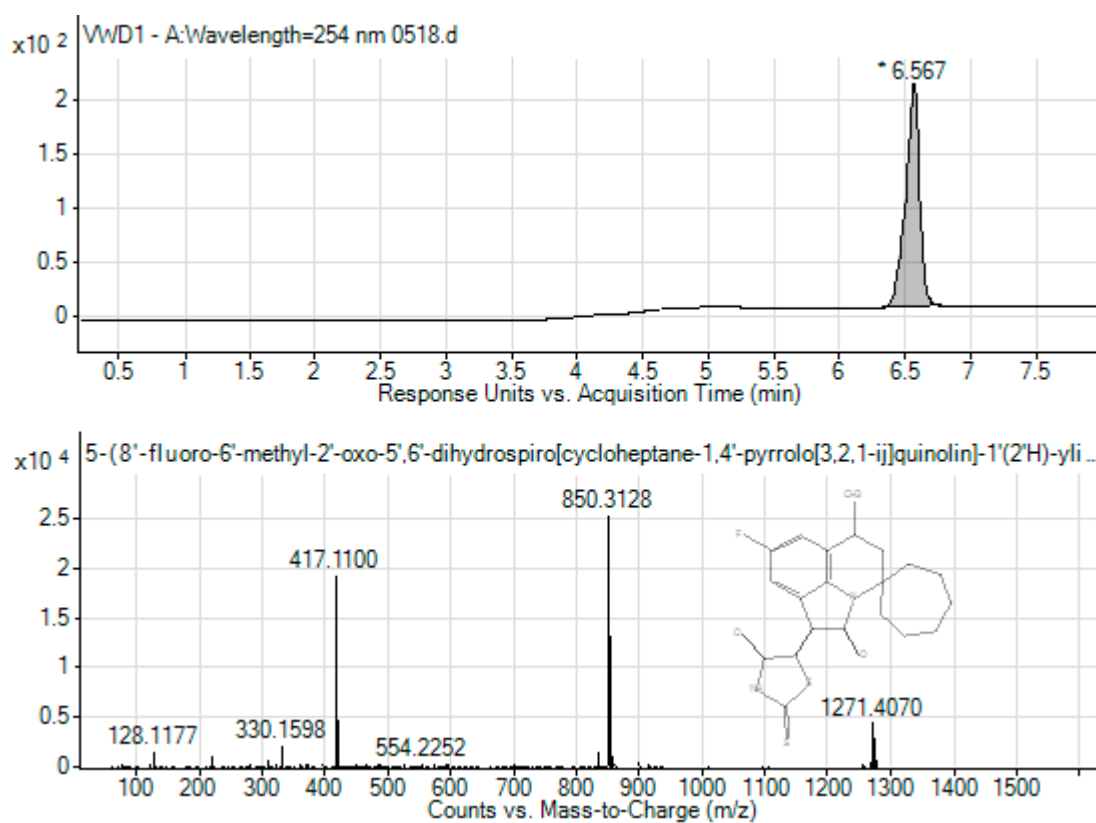


Figure S103. Data of HPLC-MS-ESI analysis of compound 12q

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of (Z)-5-(8-fluoro-4,4,6-trimethyl-2-oxo-6-phenyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1(2H)-ylidene)-3-(prop-2-yn-1-yl)-2-thioxothiazolidin-4-one 14a

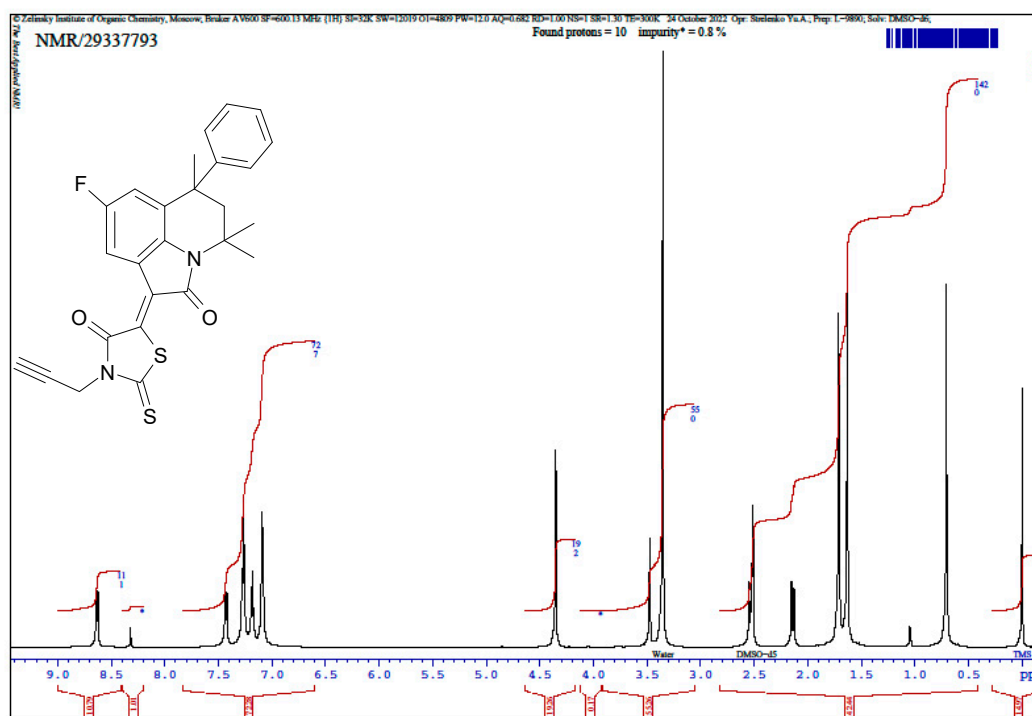


Figure S104.  $^1\text{H}$  NMR spectrum of compound 14a

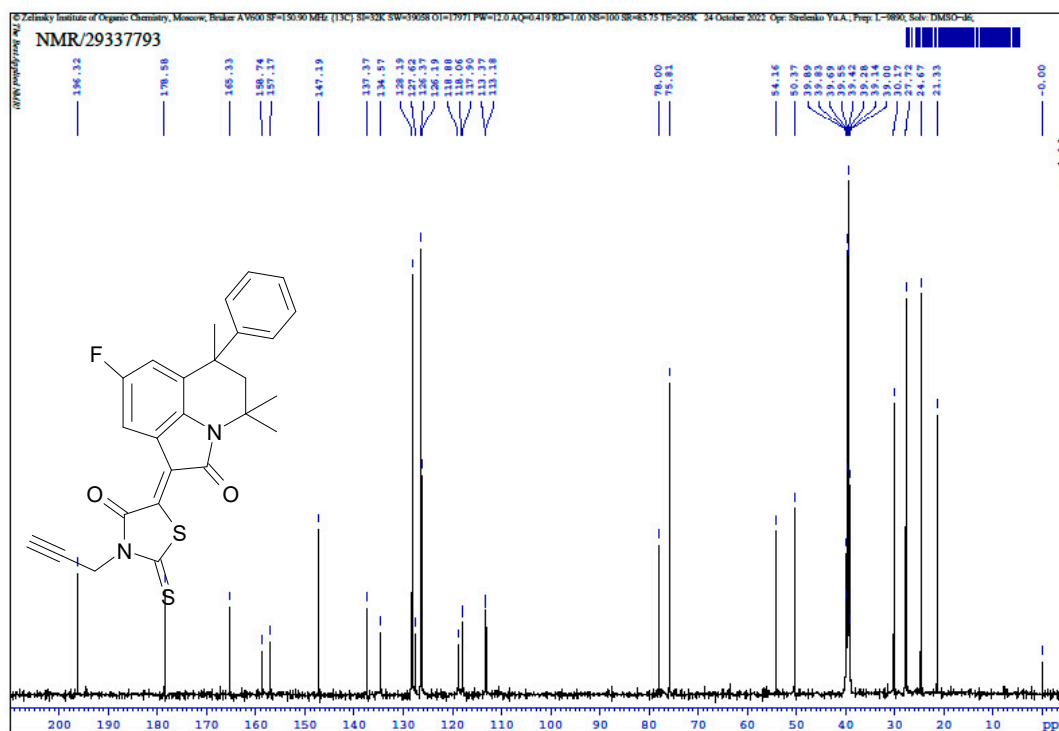


Figure S105. <sup>13</sup>C NMR spectrum of compound 14a

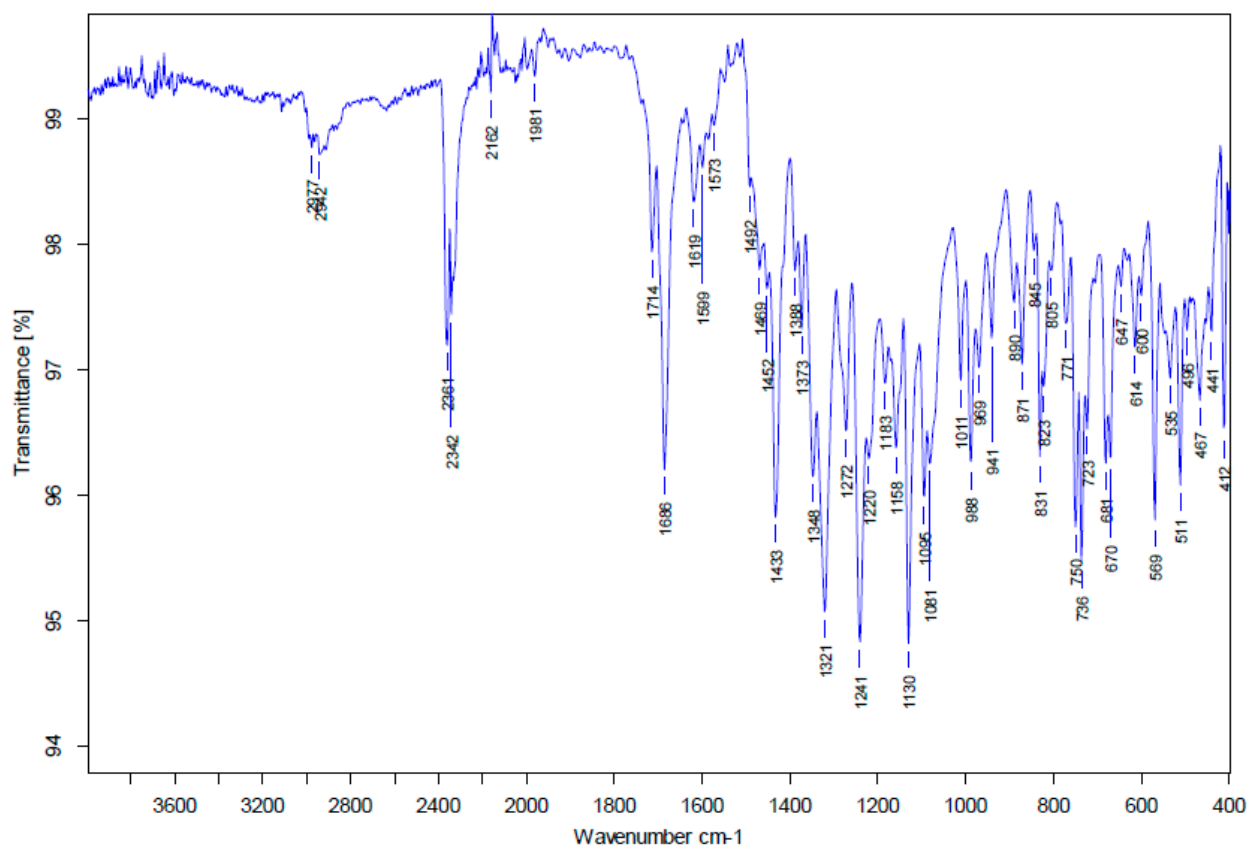
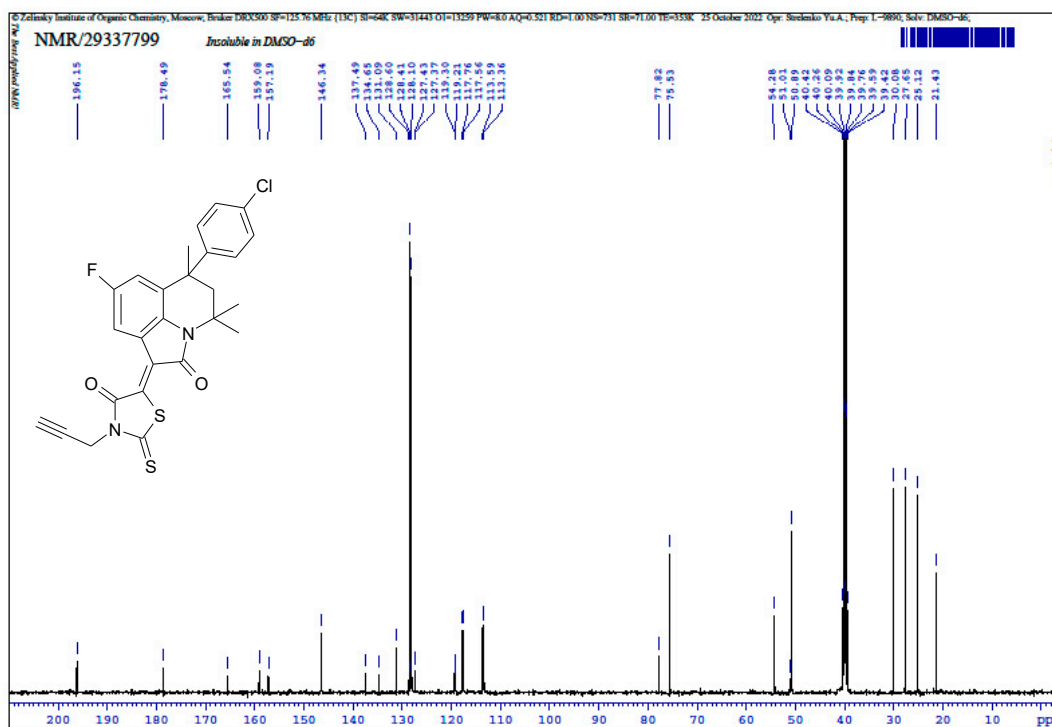
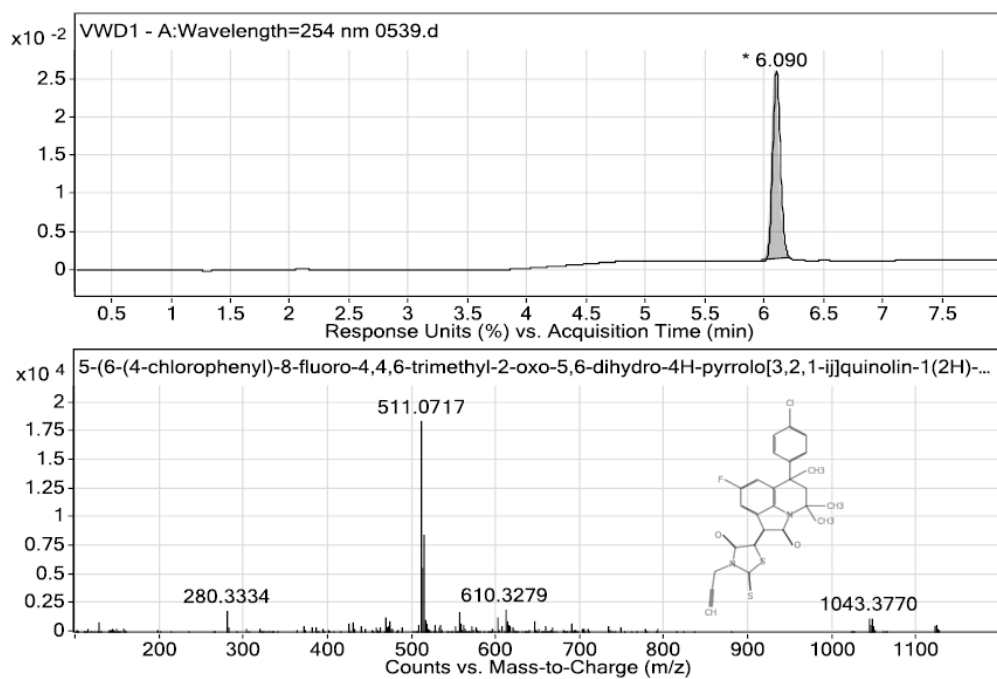


Figure S106. IR spectrum of compound 14a





**Figure S109.** <sup>13</sup>C NMR spectrum of compound **14b**



**Figure S110.** Data of HPLC-MS-ESI analysis of compound **14b**

<sup>1</sup>H, <sup>13</sup>C NMR and data HPLC-HRMS-ESI spectra of (Z)-8-ethoxy-4,4,6-trimethyl-1-(5-oxo-2-thioxoimidazolidin-4-ylidene)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2(1H)-one 16a

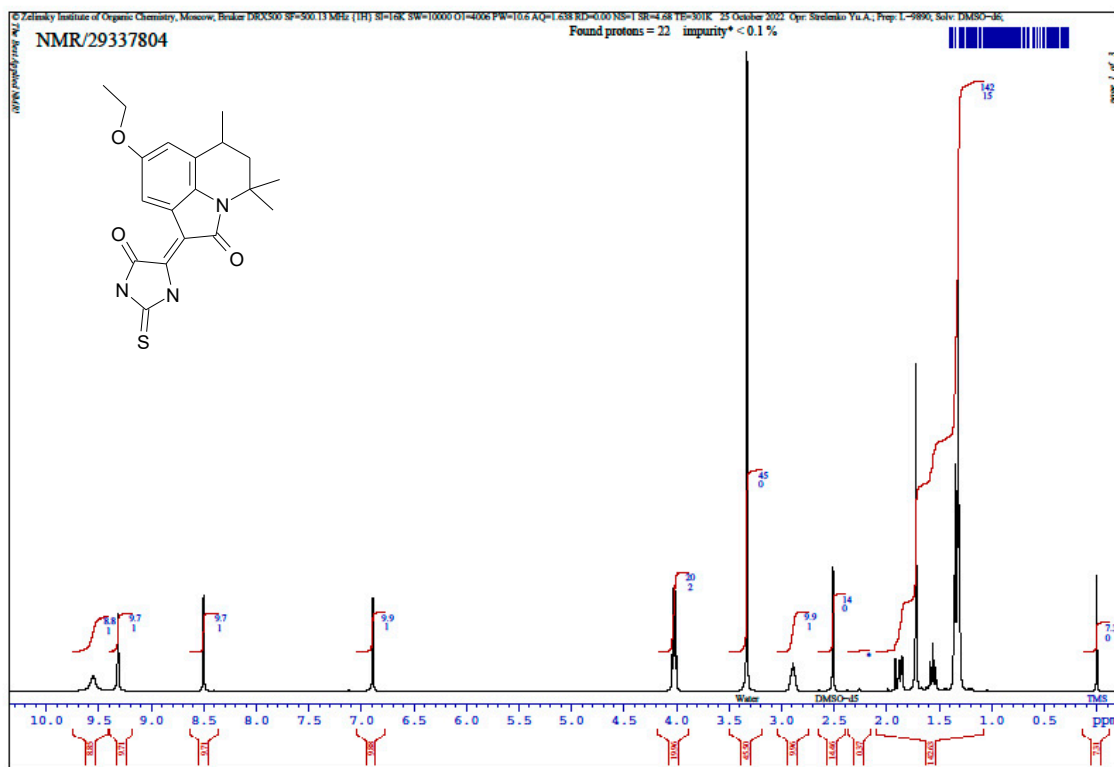


Figure S111. <sup>1</sup>H NMR spectrum of compound 16a

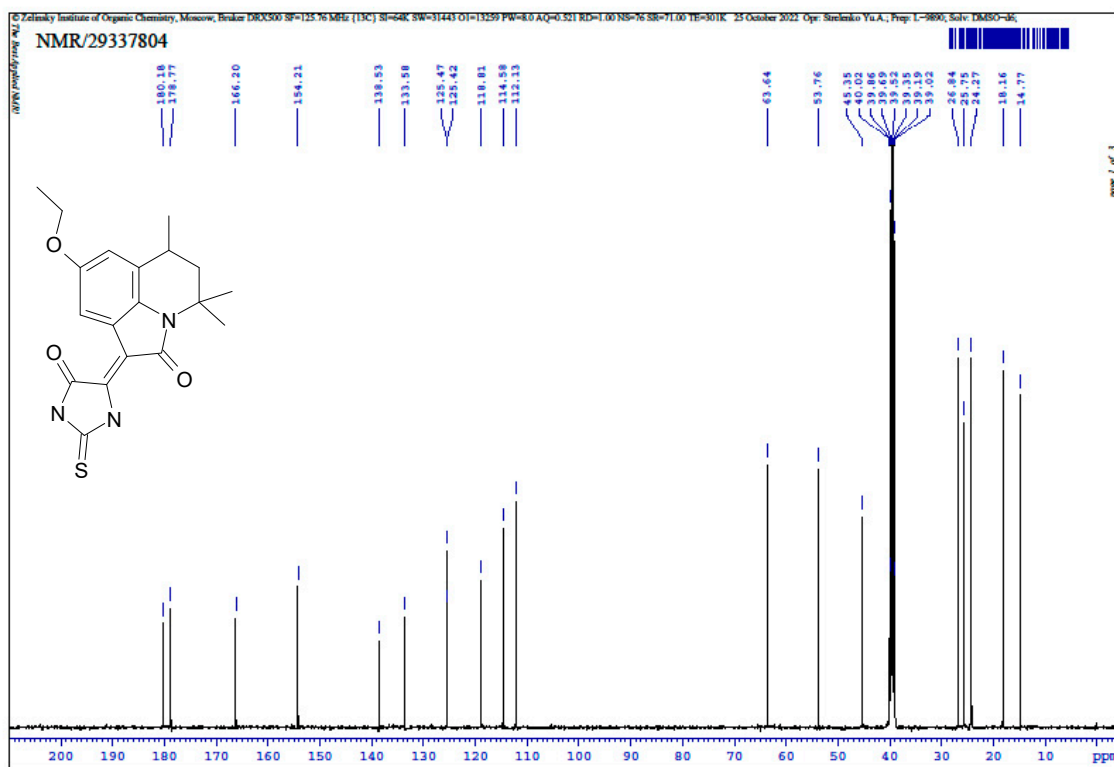


Figure S112. <sup>13</sup>C NMR spectrum of compound 16a

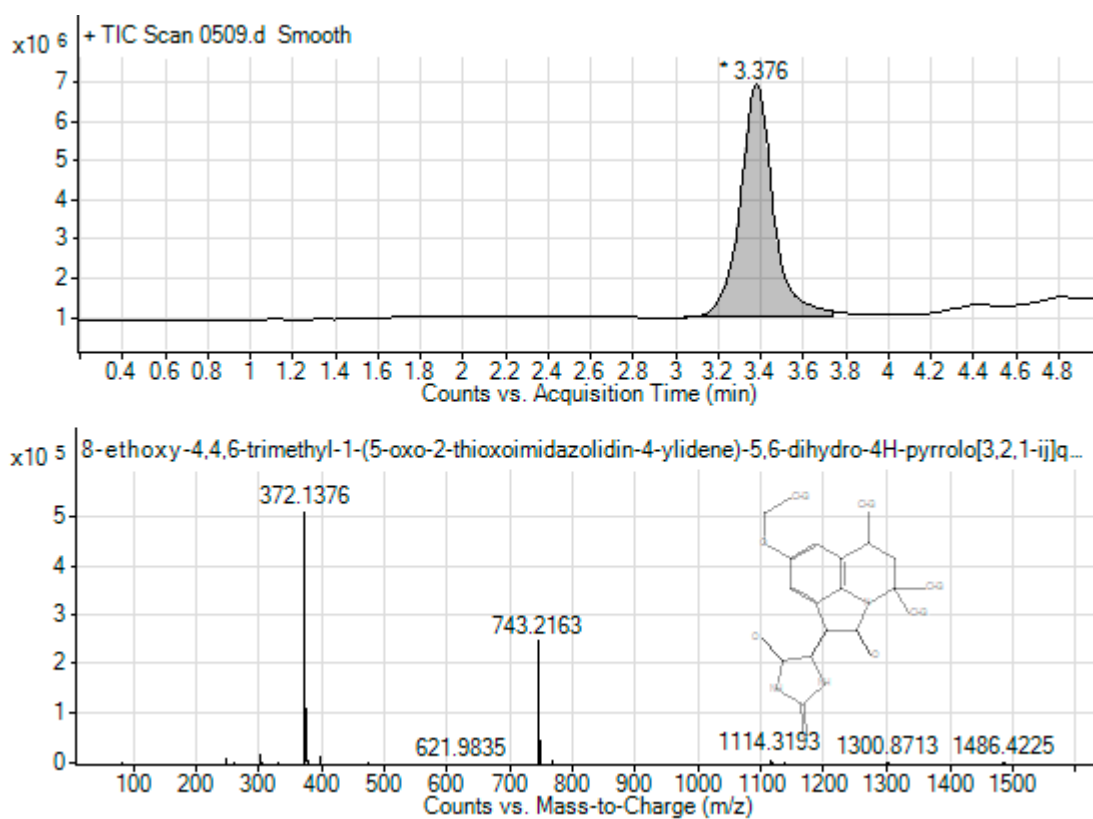


Figure S113. Data of HPLC-MS-ESI analysis of compound 16a

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of (Z)-4,4,6,8-tetramethyl-1-(5-oxo-2-thioxoimidazolidin-4-ylidene)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2(1H)-one 16b

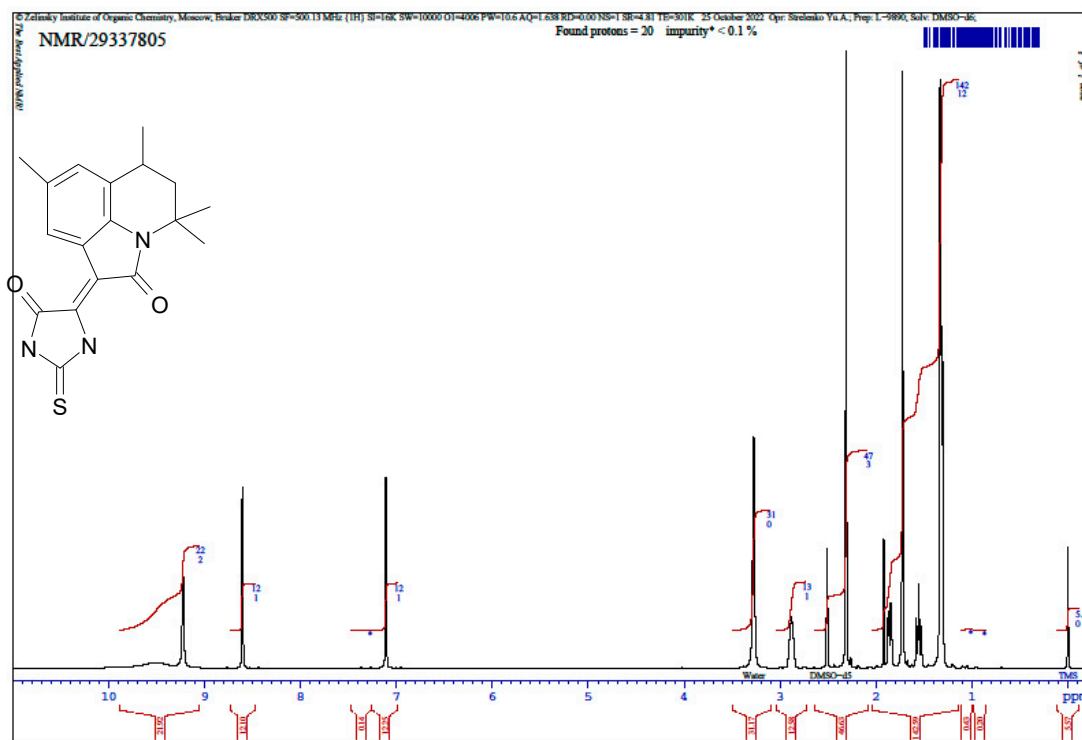


Figure S114.  $^1\text{H}$  NMR spectrum of compound 16b



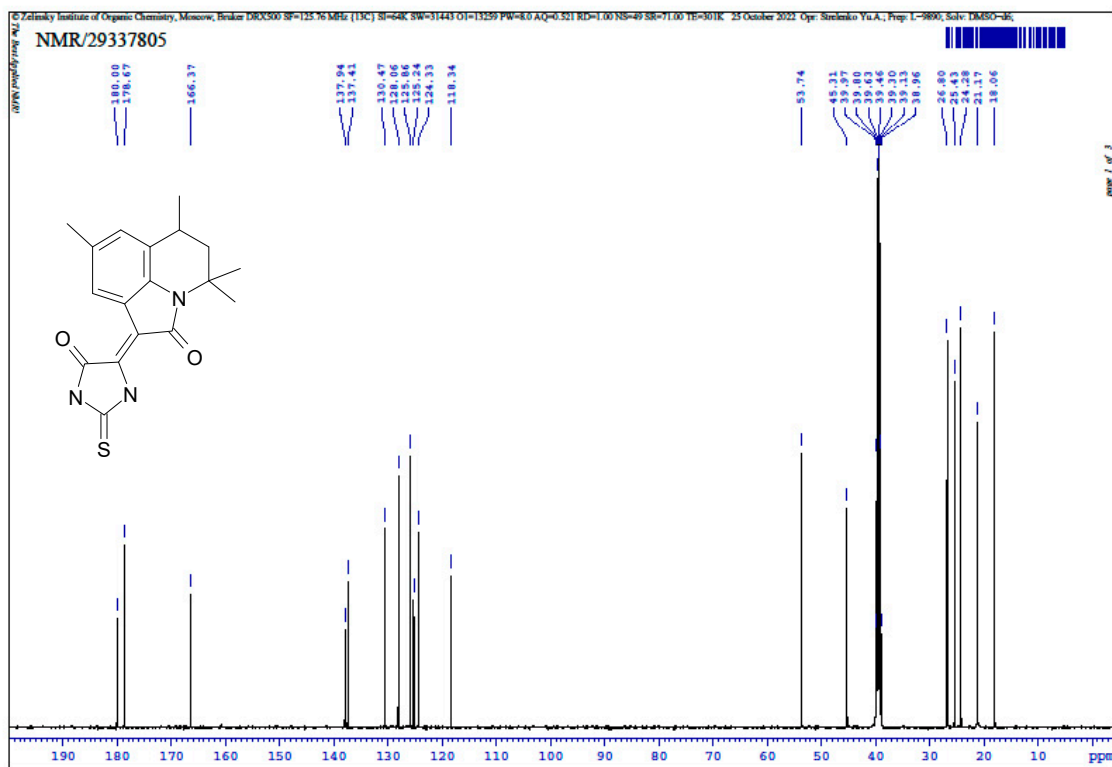


Figure S115.  $^{13}\text{C}$  NMR spectrum of compound 16b

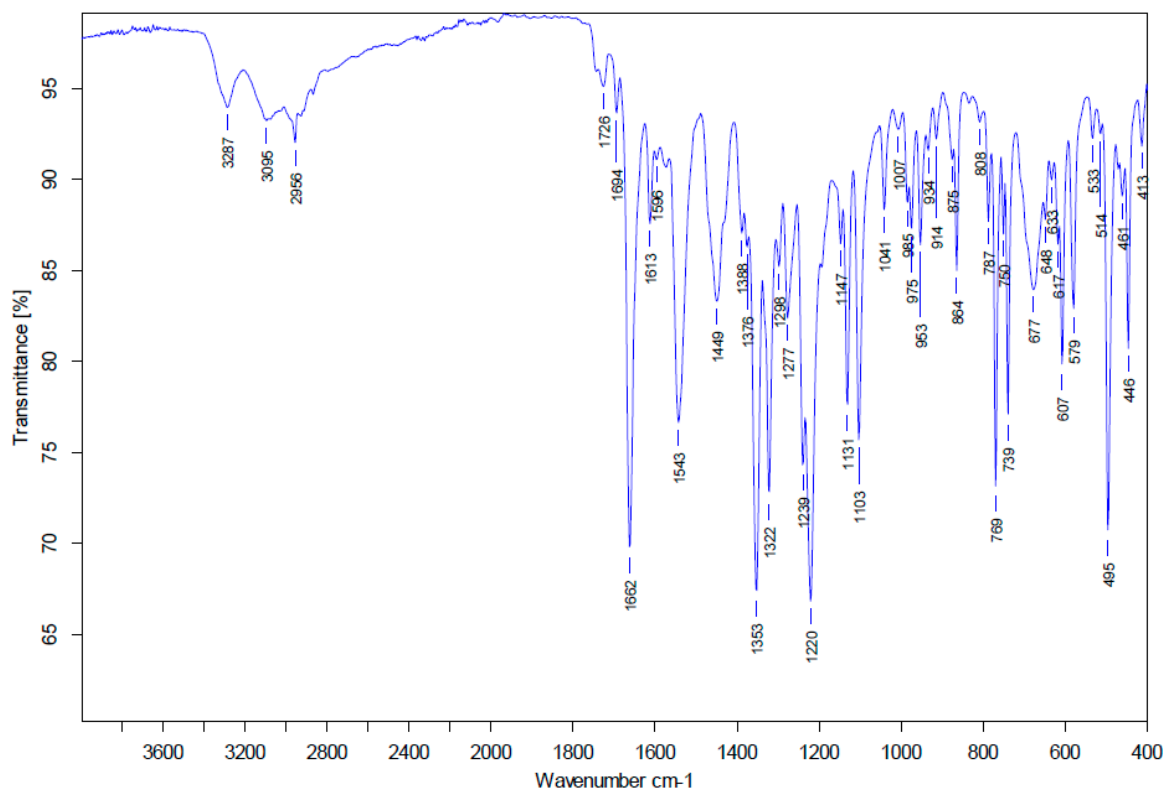


Figure S116. IR spectrum of compound 16b

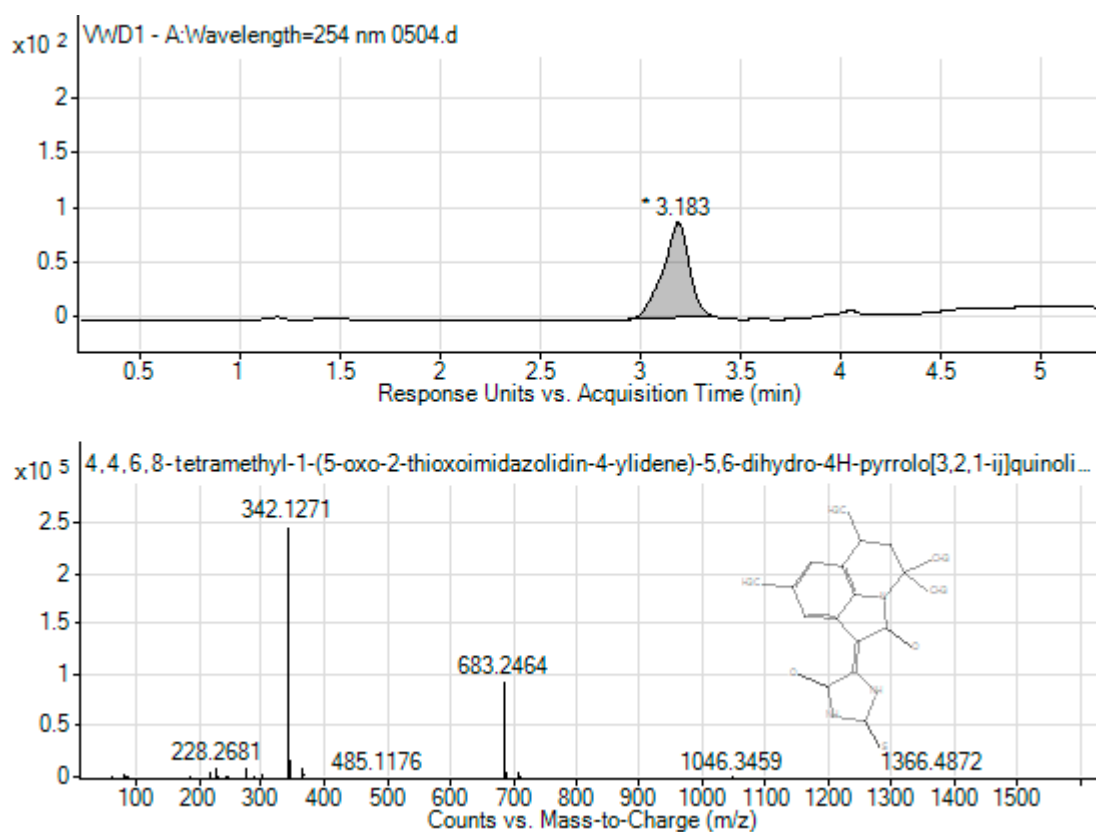


Figure S117. Data of HPLC-MS-ESI analysis of compound **16b**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-4,4,6-trimethyl-1-(5-oxo-2-thioxoimidazolidin-4-ylidene)-6-phenyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2(1H)-one **16c**

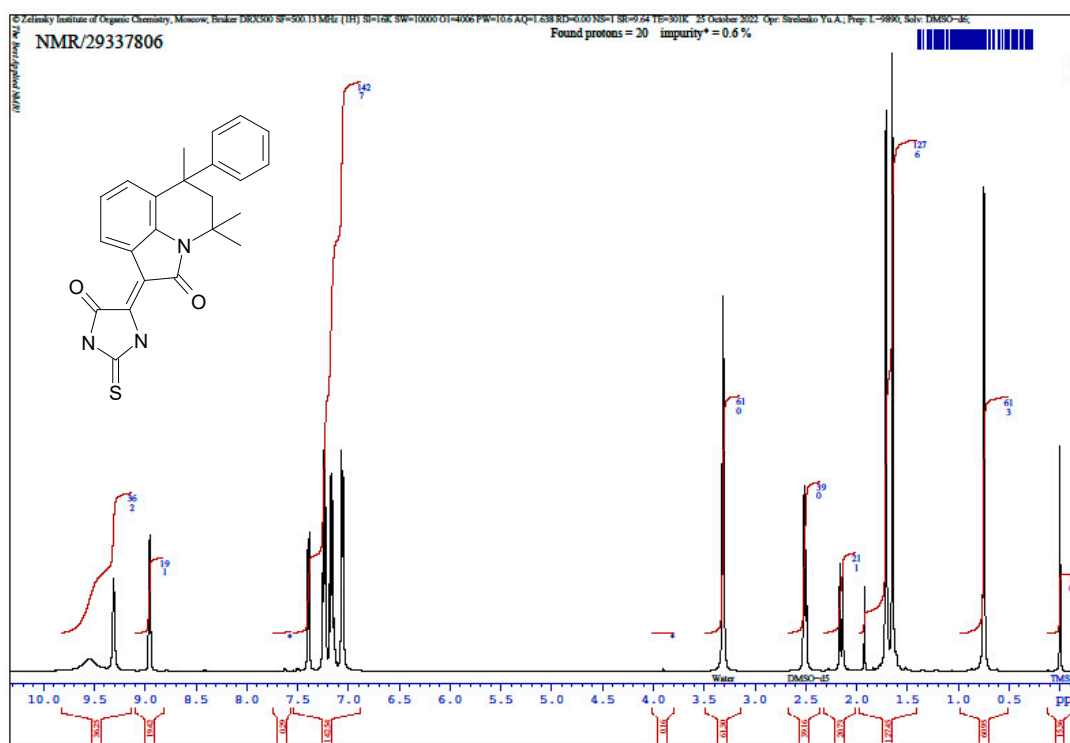
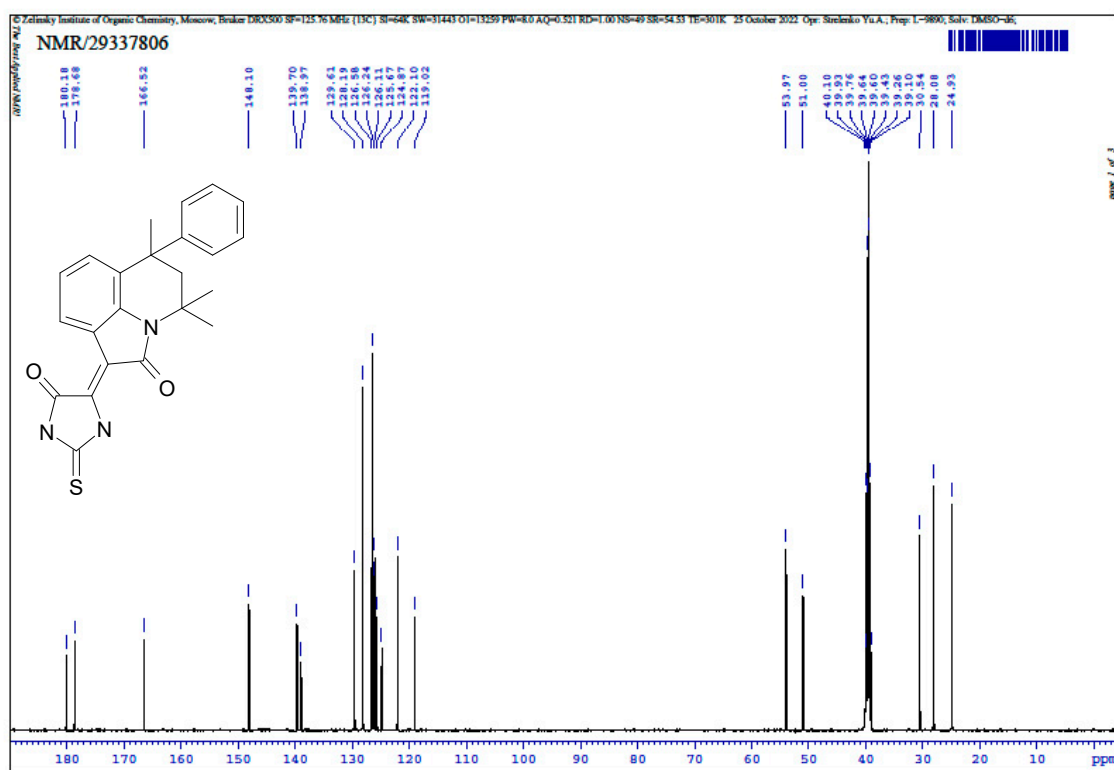
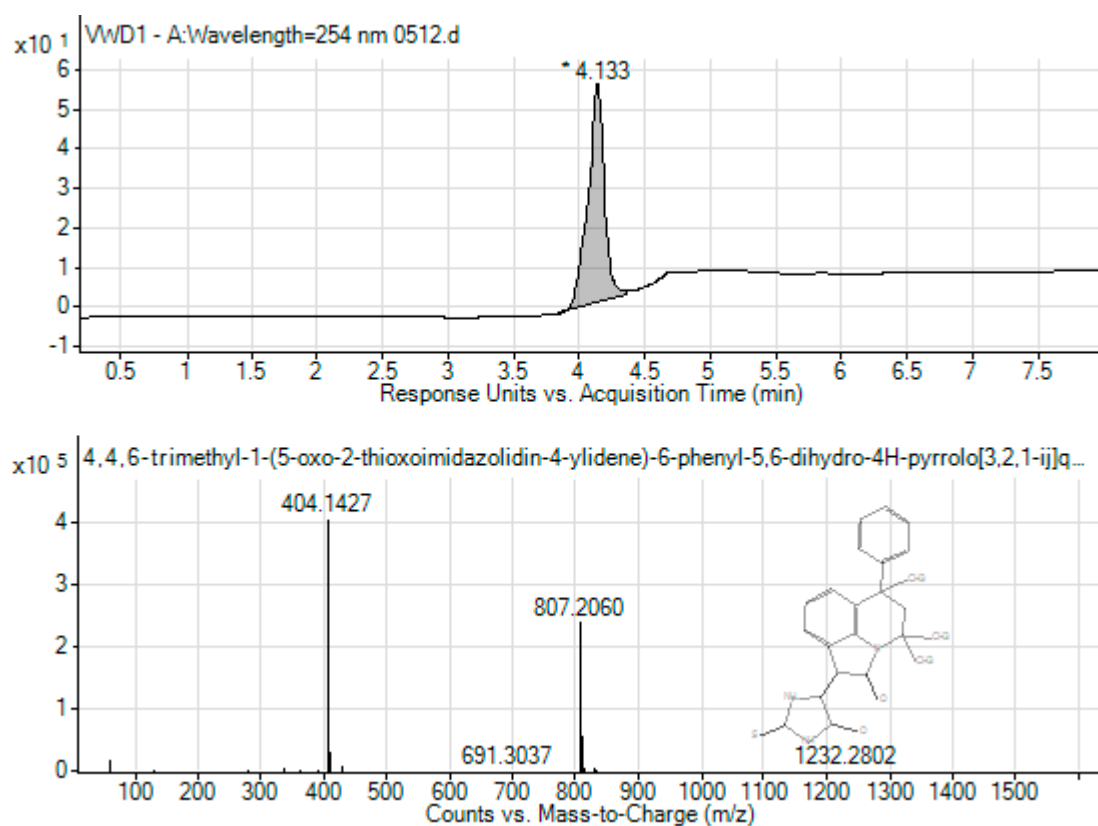


Figure S118.  $^1\text{H}$  NMR spectrum of compound **16c**



**Figure S119.**  $^{13}\text{C}$  NMR spectrum of compound **16c**



**Figure S120.** Data of HPLC-MS-ESI analysis of compound **16c**

$^1\text{H}$ ,  $^{13}\text{C}$  NMR, IR and data HPLC-HRMS-ESI spectra of (Z)-8-fluoro-4,4,6-trimethyl-1-(5-oxo-2-thioxoimidazolidin-4-ylidene)-6-phenyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2(1H)-one **16d**

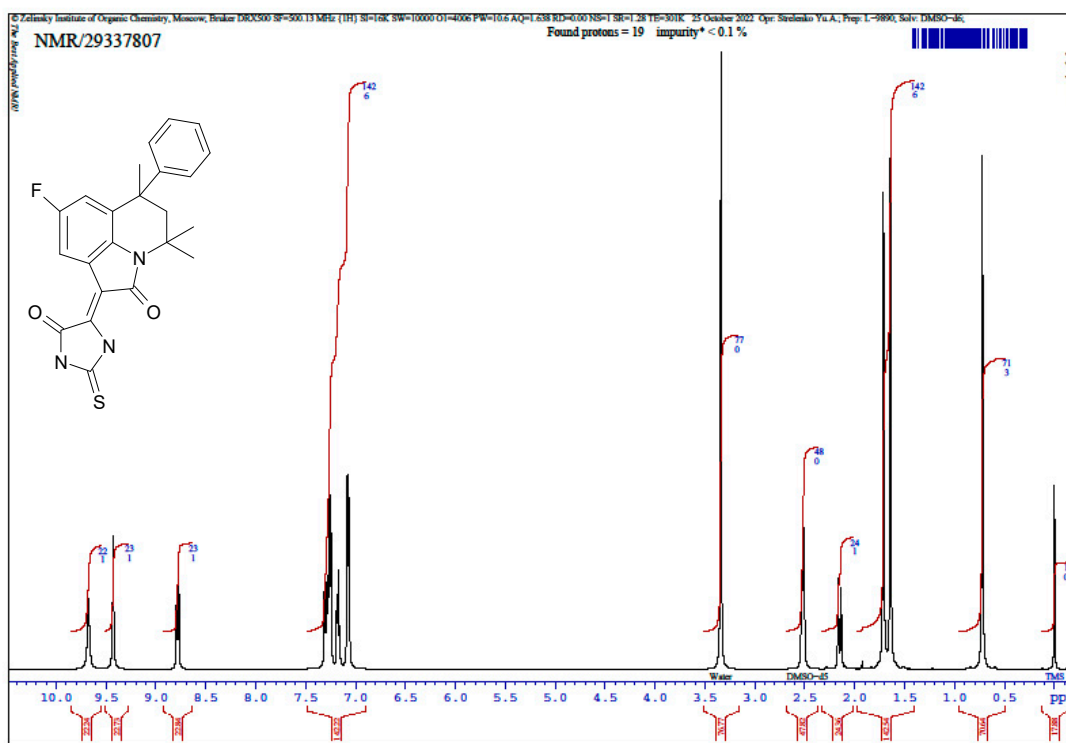


Figure S121.  $^1\text{H}$  NMR spectrum of compound **16d**

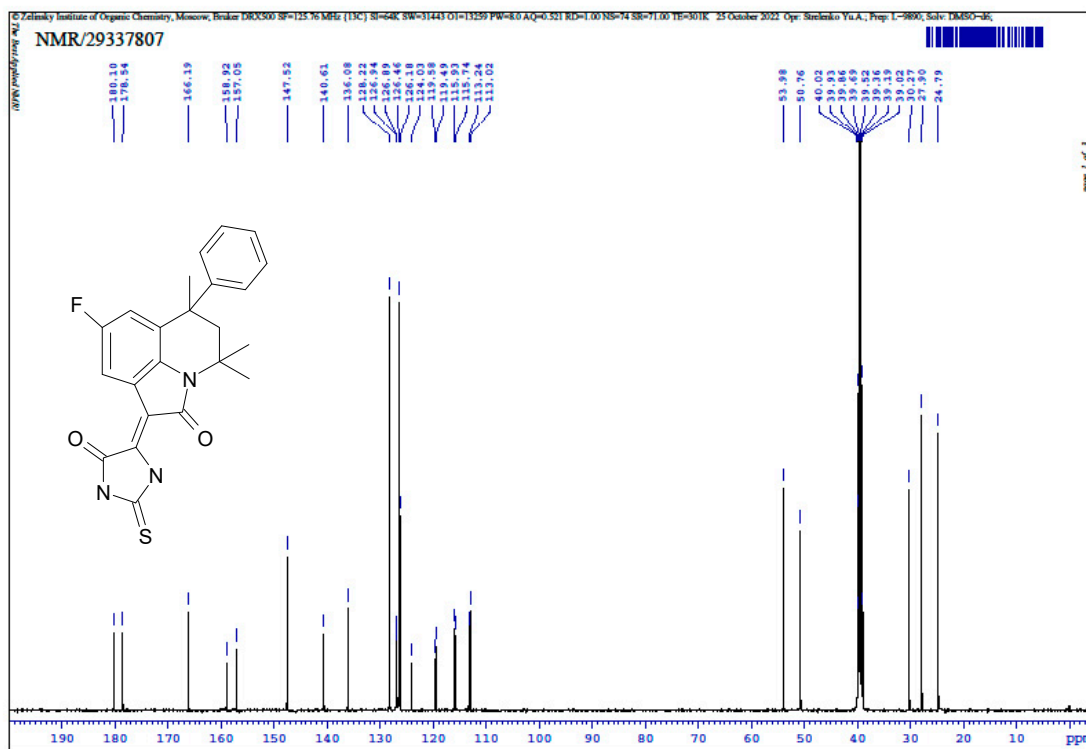
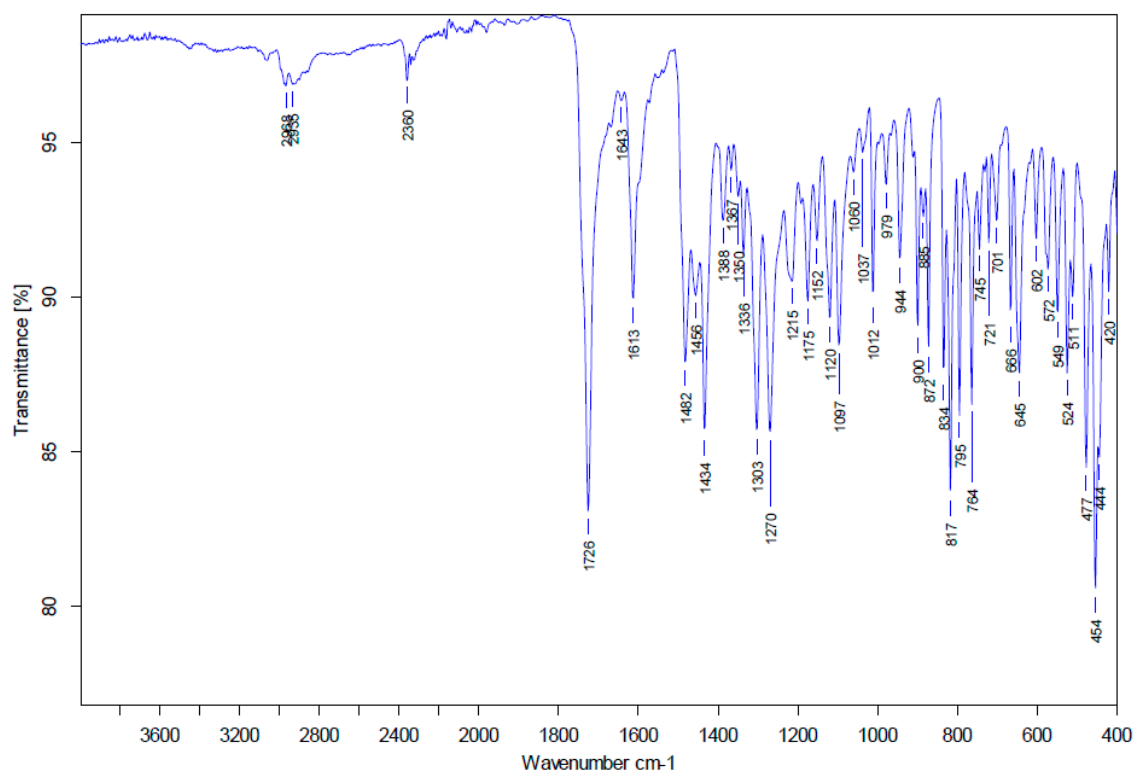
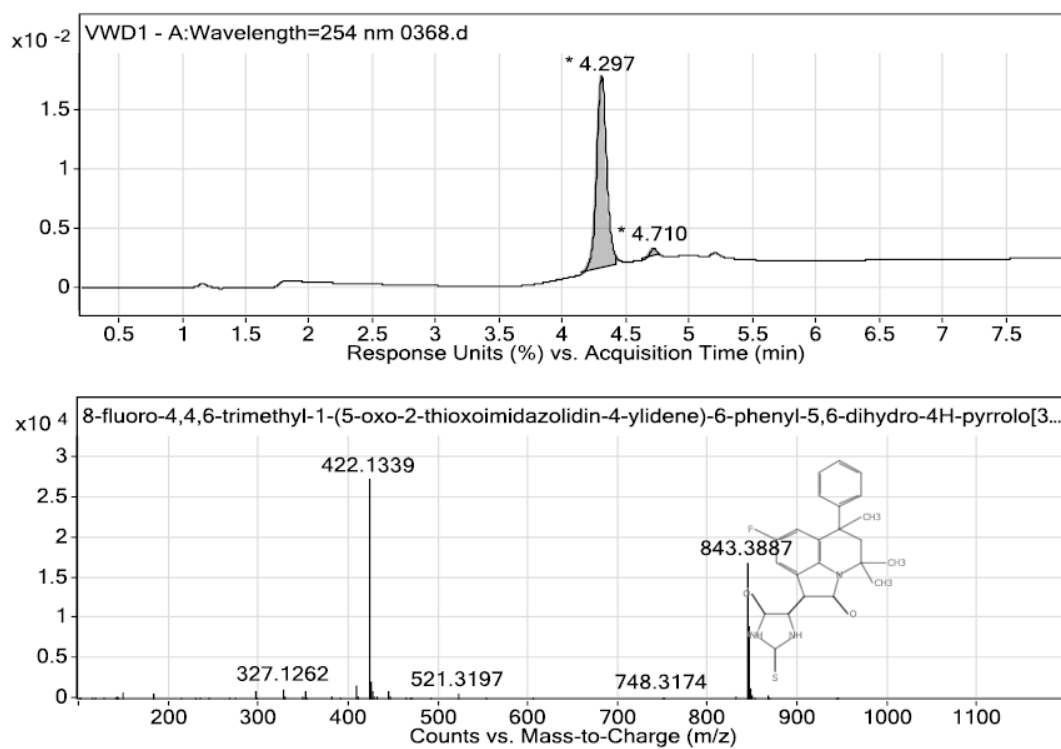


Figure S122.  $^{13}\text{C}$  NMR spectrum of compound **16d**

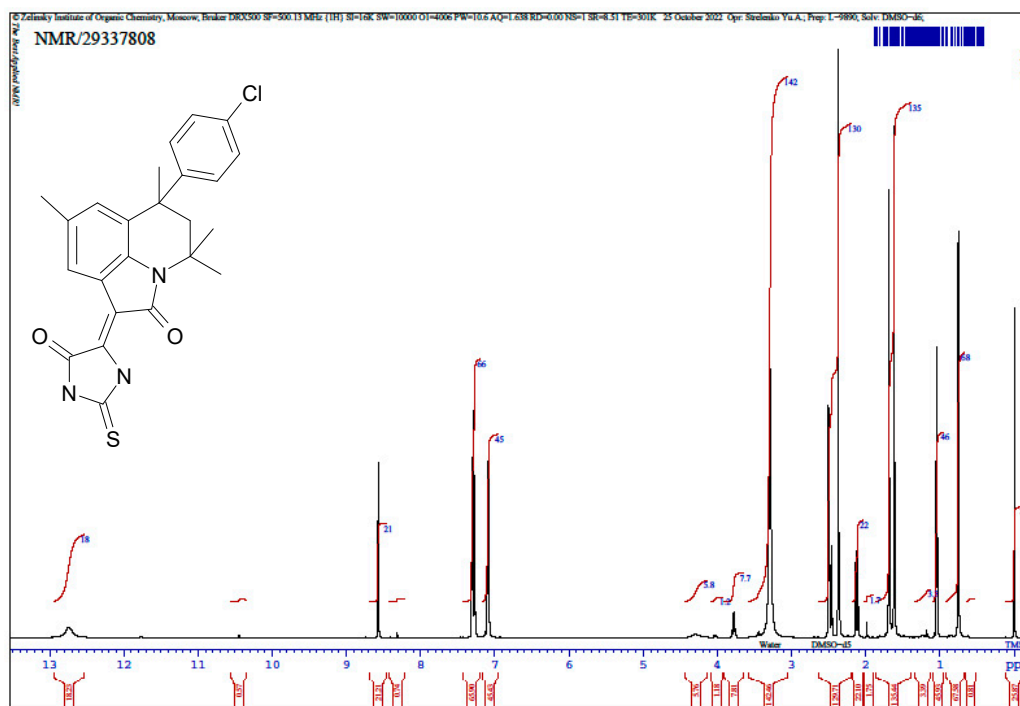


**Figure S123.** IR spectrum of compound **16b**

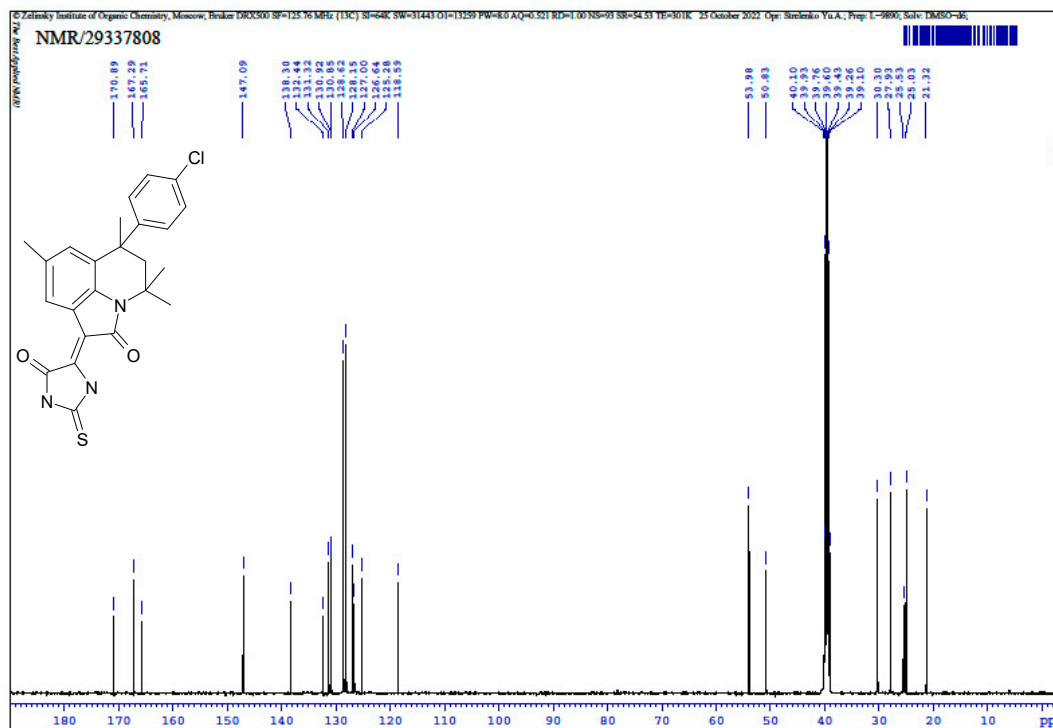


**Figure S124.** Data of HPLC-MS-ESI analysis of compound **16d**

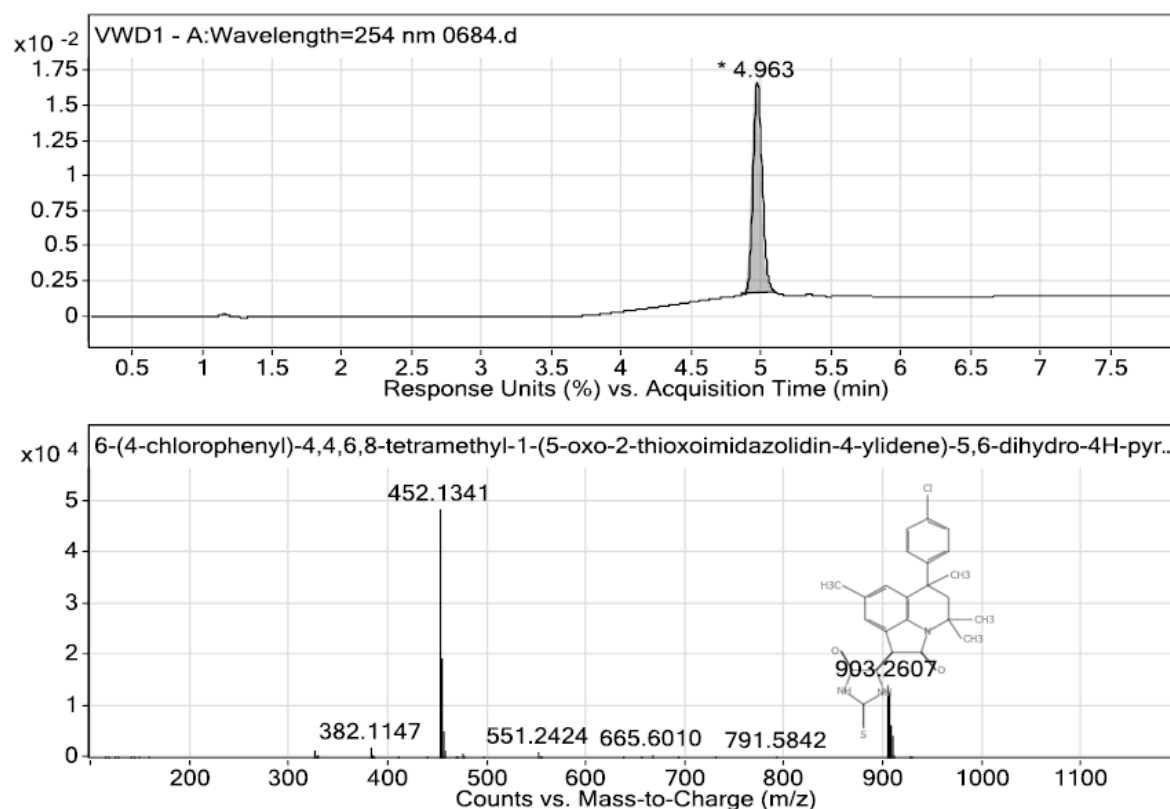
**$^1\text{H}$ ,  $^{13}\text{C}$  NMR and data HPLC-HRMS-ESI spectra of (Z)-6-(4-chlorophenyl)-4,4,6,8-tetramethyl-1-(5-oxo-2-thioxoimidazolidin-4-ylidene)-5,6-dihydro-4H-pyrrolo[3,2,1-*ij*]quinolin-2(1H)-one 16e**



**Figure S125.**  $^1\text{H}$  NMR spectrum of compound 16e



**Figure S126.**  $^{13}\text{C}$  NMR spectrum of compound 16e



**Figure S127.** Data of HPLC-MS-ESI analysis of compound **16e**

**Table S1.** Residues participating in interaction with each of 24 tested compounds after docking into factor Xa and factor XIa active sites.

No	Interaction residues in factor Xa	Interaction residues in factor XIa
12a	Gly-216, Glu-217	Ser-195, Ser-214
12b	Gly-216	Lys-192, Gly-193, Ser-195
12c	Gly-216	Gly-216
12d	Gln-61, Gly-216	His-57
12e	Gly-216	Met-96
12f	Ala-190	His-57, Met-96, Glu-98
12g	Glu-217	His-57, Tyr-59
12h	Arg-222	Lys-192
12i	Glu-217	Tyr-59, Val-227
12j	Glu-217	Tyr-59
12k	Glu-217, Arg-222	His-57, Tyr-59
12l	Gly-216, Arg-222	Cys-40, Tyr-59
12m	Ala-190, Gln-192, Trp-215	Met-96, Glu-98
12n	Tyr-99	Arg-37, Cys-40, Ala-190
12o	Trp-215	-
12p	Gly-216	Lys-192
12q	Glu-217	His-57, Trp-215
14a	Glu-217	His-57, Trp-215
14b	Gly-216	Lys-192, Gly-193, Ser-195
16a	Tyr-99, Glu-217, Arg-222	His-57, Met-96, Ala-190, Ser-195
16b	Arg-222	Met-96, Glu-98
16c	Gly-216	Ser-195
16d	Phe-174	Cys-191, Gly-193
16e	Tyr-99	His-57, Tyr-59, Cys-191

**Table S2.** Crystal complexes with actives used in validation of docking protocol for factor Xa and factor XIa.

Factor Xa				Factor XIa			
PDB ID	Ligand ID	SOL score, kcal/mol	IC <sub>50</sub> , nM	PDB ID	Ligand ID	SOL score, kcal/mol	IC <sub>50</sub> , nM (Ki, nM)
2P3T	993	-6.89	0.06	4CRA	XJ8	-5.10	(60)
2P94	ME4	-7.39	0.67	4CRB	7P0	-3.70	(1.6)
2VH6	GSV	-6.78	0.2	4CRG	J4X	-5.98	<140
2VVC	LZF	-6.42	3	4CRE	MVN	-4.89	>1.1 · 10 <sup>5</sup>
2W26	RIV	-6.87	0.4	-	BMS-654457 [1]	-6.04	(0.2)
2Y7X	MZA	-7.17	1.3	-	BMS-962212 [2]	-6.0	(0.7)
3IIT	D14	-6.64	9.5	-	3 [3]	-5.76	1.0
3TK6	D46	-6.95	1.7	-	4a [4]	-6.52	(0.31)
4ZH8	4O4	-7.09	-	-	6b [5]	-5.35	(3.7)
4ZHA	4O5	-5.77	-	-	8 [6]	-5.85	(2.0)

Structures of factor XIa inhibitors 3, 4a, 6b, and 8 can be found in Table 3 in ref. [7]; references to the original articles about these factor XIa inhibitors are presented in column “Ligand ID”. For all cases of factor Xa presented in Table S2, and for PDB complexes of factor XIa 4CRA, 4CRB, 4CRG, 4CRE, and for the PDB complex 4CRC, the root-mean-square deviation, RMSD, between all atoms of the crystallized native ligand pose and the docked ligand pose corresponding to the lowest energy of the pro-teín-ligand complex, is less than 2.0 Å.

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