Supporting Information

IODINE-PROMOTED CYCLIZATION OF ALKYLIDENE BARBITURATES IN WATER: FACILE SYNTHESIS OF DIHYDROFURYL SPIROBARBITURATES

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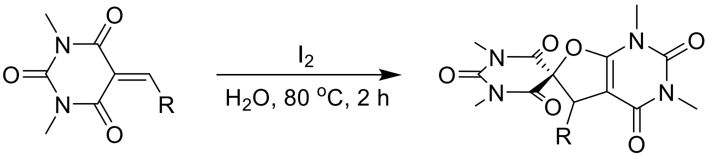
1. General Information

All reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on a 400 MHz NMR spectrometer (400 MHz for ^{1}H NMR; 100 MHz for ^{13}C NMR) or 500 MHz NMR spectrometer (500 MHz for ^{1}H NMR; 125 MHz for ^{13}C NMR). ^{1}H NMR chemical shifts were determined relative to internal TMS at δ 0.0 ppm. ^{13}C NMR chemical shifts were determined relative to $CDCl_3$ at δ 77.16 ppm. Data for ^{1}H NMR and ^{13}C NMR are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet). High-resolution mass spectra (HRMS) were measured with ESI-TOF in a positive mode. All melting points were determined on a XT-4 binocular microscope. IR spectra were recorded on a IRPrestige-21 spectrometer by preparing KBr pellets.

2. Synthetic Procedures and Characterization Data for Products 2

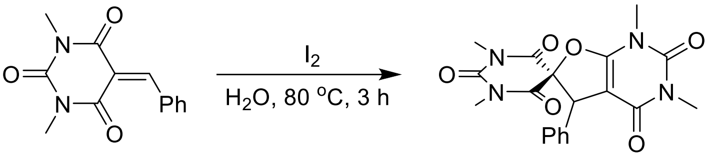
General Procedure for the Synthesis of Dihydrofuryl Spirobarbiturates 2



1 **2**

A mixture of alkylidene barbiturates **1** (0.6 mmol), I_2 (0.6 mmol) and water (4 mL) was introduced into a 25 mL of glass tube. Then the mixture was stirred in an oil bath at 80 °C for 2 h. After completion of the reaction, the reaction mixture was filtered and the resulting precipitate was washed with water to afford crude products. Subsequently, the crude products were further purified by recrystallisation from ethanol to afford pure dihydrofuryl spirobarbiturates **2**.

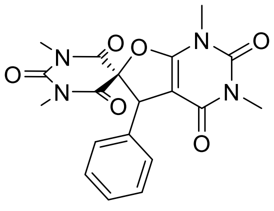
Typical Procedure for the Gram-Scale Synthesis of Dihydrofuryl Spirobarbiturate 2a



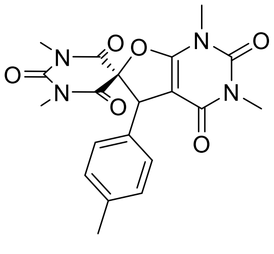
1a (6 mmol) **2a** (86% yield)

A mixture of 5-benzylidene-1,3-dimethyl-pyrimidine-2,4,6-trione **1a** (1.466 g, 6 mmol), I_2 (1.523 g, 6 mmol) and water (40 mL) was introduced into a 100 mL of round bottom flask equipped with a condenser. The flask was first stirred in an oil bath at 80 ºC for 2 h, then the condenser was removed and the opened flask was stirred at 80 ºC for 1 h. After completion of the reaction, the reaction mixture was filtered and the resulting precipitate was washed with water to afford crude products. Subsequently, the crude products were further purified by recrystallisation from ethanol to afford pure dihydrofuryl spirobarbiturate **2a** as a white solid (1.025 g, 86% yield).

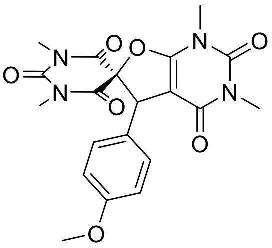
Products **2a**, **2b**, **2c**, **2d**, **2e**, **2h** and **2i** were known compounds, which were characterized by ^{1}H NMR and ^{13}C NMR. Products **2f**, **2g**, **2j**, **2k** and **2l** were unknown compounds, which were characterized by ^{1}H NMR, ^{13}C NMR and HRMS.



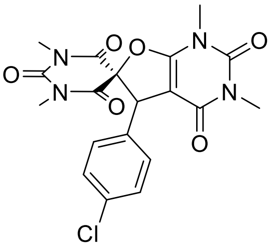
1,1',3,3'-Tetramethyl-5-phenyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2a). The general procedure was followed to afford **2a** as a white solid. Yield: 88% (105.4 mg), mp 257–259 ºC (256–258 ºC[1]); IR (KBr) 1718, 1698, 1675, 1660, 1517, 1436, 1428, 1395, 1374, 1035 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36–7.31 (m, 3H), 7.08–7.04 (m, 2H), 4.93 (s, 1H), 3.53 (s, 3H), 3.43 (s, 3H), 3.31 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.6, 163.1, 162.8, 158.8, 151.3, 149.7, 132.8, 129.6, 129.1 (2C), 128.3 (2C), 90.4, 85.6, 59.4, 30.1, 29.6, 28.5, 28.3.



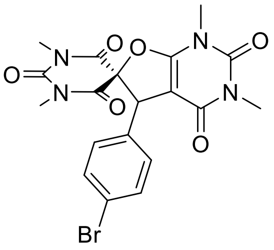
1,1',3,3'-Tetramethyl-5-(*p*-tolyl)-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2b). The general procedure was followed to afford **2b** as a white solid. Yield: 86% (106.3 mg), mp 219–221 °C (219–221 °C[1]); IR (KBr) 1716, 1690, 1685, 1656, 1515, 1401, 1041 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J = 7.9 Hz, 2H), 6.94 (d, J = 7.9 Hz, 2H), 4.89 (s, 1H), 3.52 (s, 3H), 3.42 (s, 3H), 3.30 (s, 3H), 2.59 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 163.2, 162.7, 158.8, 151.3, 149.7, 139.6, 129.73, 129.70 (2C), 128.2 (2C), 90.4, 85.8, 59.1, 30.1, 29.6, 28.5, 28.3, 21.3.



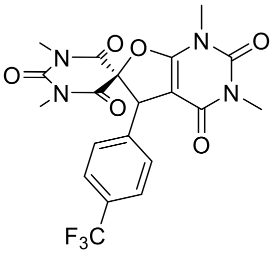
5-(4-Methoxyphenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2c). The general procedure was followed to afford **2c** as a white solid. Yield: 76% (97.9 mg), mp 208–210 °C (206–208 °C[1]); IR (KBr) 1713,1695, 1678, 1662, 1514, 1440, 1427, 1377, 1042 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 4.88 (s, 1H), 3.78 (s, 3H), 3.52 (s, 3H), 3.42 (s, 3H), 3.30 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 163.2, 162.6, 160.5, 158.8, 151.3, 149.8, 129.5 (2C), 124.6, 114.4 (2C), 90.4, 85.8, 58.9, 55.5, 30.1, 29.6, 28.6, 28.3.



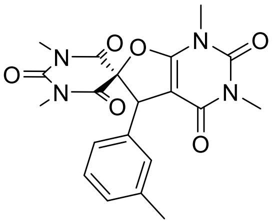
5-(4-Chlorophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2d). The general procedure was followed to afford **2d** as a white solid. Yield: 91% (117.7 mg), mp 260–262 °C (257–259 °C[1]); IR (KBr) 1716, 1698, 1677, 1657, 1516, 1440, 1425, 1394, 1333, 1035 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 4.89 (s, 1H), 3.52 (s, 3H), 3.42 (s, 3H), 3.29 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.4, 162.9, 162.8, 158.7, 151.2, 149.6, 135.6, 131.5, 129.7 (2C), 129.2 (2C), 89.9, 85.4, 58.4, 30.1, 29.7, 28.6, 28.3.



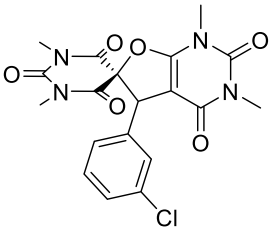
5-(4-Bromophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2e). The general procedure was followed to afford **2e** as a white solid. Yield: 90% (128.8 mg), mp 276–278 °C (267–269 °C[2]); IR (KBr) 1716, 1698, 1676, 1655, 1514, 1428, 1398, 1375, 1032 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (d, J = 8.2 Hz, 2H), 6.95 (d, J = 8.2 Hz, 2H), 4.87 (s, 1H), 3.52 (s, 3H), 3.43 (s, 3H), 3.30 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.4, 162.90, 162.88, 158.7, 151.2, 149.6, 132.2 (2C), 132.0, 130.0 (2C), 123.8, 89.9, 85.4, 58.6, 30.1, 29.7, 28.7, 28.3.



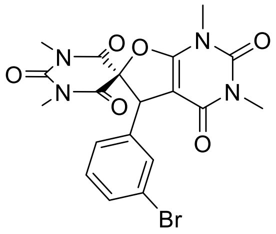
1,1',3,3'-Tetramethyl-5-(4-(trifluoromethyl)phenyl)-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2f). The general procedure was followed to afford **2f** as a white solid. Yield: 87% (121.3 mg), mp 285–287 °C; IR (KBr) 1724, 1709, 1701, 1673, 1520, 1438, 1419, 1389, 1042 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.61 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 4.98 (s, 1H), 3.53 (s, 3H), 3.44 (s, 3H), 3.30 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.2, 163.0, 162.7, 158.7, 151.2, 149.5, 137.1, 131.8 (q, J = 32.9 Hz), 129.0 (2C), 125.9 (q, *J* = 3.6 Hz, 2C), 123.7 (q, *J* = 272.4 Hz), 89.8, 85.2, 58.5, 30.2, 29.7, 28.5, 28.4; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{18}F_3N_4O_6$ [M + H]$^+$ 467.1178, found 467.1182.



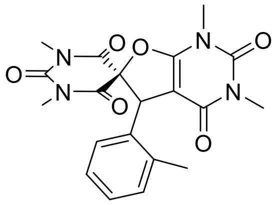
1,1',3,3'-Tetramethyl-5-(*m*-tolyl)-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2g). The general procedure was followed to afford **2g** as a white solid. Yield: 85% (105.0 mg), mp 229–231 °C; IR (KBr) 1712, 1694, 1683, 1666, 1513, 1440, 1426, 1377, 1043 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.8 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 6.84 (s, 1H), 4.88 (s, 1H), 3.53 (s, 3H), 3.43 (s, 3H), 3.31 (s, 3H), 2.57 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 163.1, 162.7, 158.8, 151.4, 149.7, 138.9, 132.8, 130.4, 128.94, 128.88, 125.4, 90.5, 85.7, 59.4, 30.1, 29.6, 28.5, 28.3, 21.4; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{21}N_4O_6$ [M + H]$^+$ 413.1461, found 413.1468.



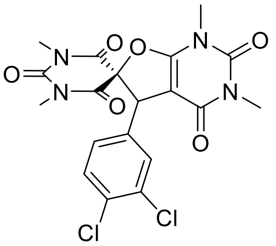
5-(3-Chlorophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2h). The general procedure was followed to afford **2h** as a white solid. Yield: 88% (114.6 mg), mp 226–228 °C (222–224 °C[11]) ; IR (KBr) 1717,1695, 1681, 1654, 1513, 1436, 1428, 1377, 1035 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.32 (m, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 1.9 Hz, 1H), 6.96 (dt, *J* = 7.5, 1.3 Hz, 1H), 4.87 (s, 1H), 3.52 (s, 3H), 3.42 (s, 3H), 3.30 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 162.9, 162.8, 158.7, 151.2, 149.5, 135.14, 135.11, 130.2, 129.8, 128.5, 126.6, 90.0, 85.3, 58.4, 30.1, 29.7, 28.6, 28.3.



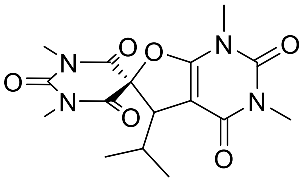
5-(3-Bromophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2i). The general procedure was followed to afford **2i** as a white solid. Yield: 92% (131.9 mg), mp 241–243 ºC (236–238 ºC[1]); IR (KBr) 1718,1694, 1684, 1652, 1515, 1435, 1429, 1383, 1031 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.49 (d, J = 8.2 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.21 (s, 1H), 7.01 (d, J = 7.8 Hz, 1H), 4.86 (s, 1H), 3.52 (s, 3H), 3.43 (s, 3H), 3.31 (s, 3H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.3, 162.9, 162.8, 158.6, 151.2, 149.5, 135.4, 132.7, 131.4, 130.5, 127.1, 123.1, 90.0, 85.2, 58.5, 30.2, 29.7, 28.7, 28.4.



1,1',3,3'-Tetramethyl-5-(*o*-tolyl)-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2j). The general procedure was followed to afford **2j** as a white solid. Yield: 87% (107.3 mg), mp 263–265 ºC; IR (KBr) 1722,1692, 1679, 1658, 1518, 1439, 1425, 1377, 1040 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.22–7.14 (m, 3H), 7.05 (d, J = 7.6 Hz, 1H), 5.30 (s, 1H), 3.53 (s, 3H), 3.38 (s, 3H), 3.29 (s, 3H), 2.60 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.6, 163.5, 162.5, 158.7, 151.4, 149.7, 135.9, 130.9, 130.8, 129.2, 129.0, 126.7, 90.2, 86.9, 54.6, 30.1, 29.5, 28.7, 28.3, 18.9; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{21}N_4O_6$ [M + H]$^+$ 413.1461, found 413.1462.



5-(3,4-Dichlorophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2k). The general procedure was followed to afford **2k** as a white solid. Yield: 91% (127.5 mg), mp 296–298 ºC; IR (KBr) 1715,1694, 1679, 1655, 1522, 1439, 1424, 1378, 1039 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42 (d, J = 8.3 Hz, 1H), 7.17 (s, 1H), 6.93 (d, J = 8.2 Hz, 1H), 4.84 (s, 1H), 3.52 (s, 3H), 3.44 (s, 3H), 3.31 (s, 3H), 2.73 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.2, 163.0, 162.7, 158.6, 151.2, 149.5, 134.0, 133.5, 133.4, 130.9, 130.3, 127.7, 89.7, 85.2, 57.9, 30.2, 29.8, 28.8, 28.4; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{17}Cl_2N_4O_6$ [M + H]$^+$ 467.0525, found 467.0519.



5-Isopropyl-1,1',3,3'-tetramethyl-1,5-dihydro-2*H*,2'*H*-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'*H*,3*H*,3'*H*)-pentaone (2l). The general procedure was followed to afford **2l** as a white solid. Yield: 71% (77.8 mg), mp 171–173 ºC; IR (KBr) 1716,1701, 1670, 1645, 1515, 1443, 1422, 1381, 1039 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.57 (d, J = 2.3 Hz, 1H), 3.46 (s, 3H), 3.39 (s, 3H), 3.34 (s, 3H), 3.33 (s, 3H), 1.84–1.72 (m, 1H), 1.18 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.9, 163.5, 162.4, 159.9, 151.2, 150.1, 90.4, 86.2, 58.7, 31.0, 30.1, 29.8, 29.5, 28.5, 22.9, 18.2; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{21}N_4O_6$ [M + H]$^+$ 365.1461, found 365.1458.

3. References

[1] A. N. Vereshchagin, M. N. Elinson, E. O. Dorofeeva, T. A. Zaimovskaya, N. O. Stepanov, S. V. Gorbunov, P. A. Belyakov, and G. I. Nikishin, *Tetrahedron*, 2012, **68**, 1198.

[2] M. Jalilzadeh and N. N. Pesyan, *Bull. Korean Chem. Soc.*, 2011, **32**, 3382.

4. Copies of NMR Spectra for Products 2

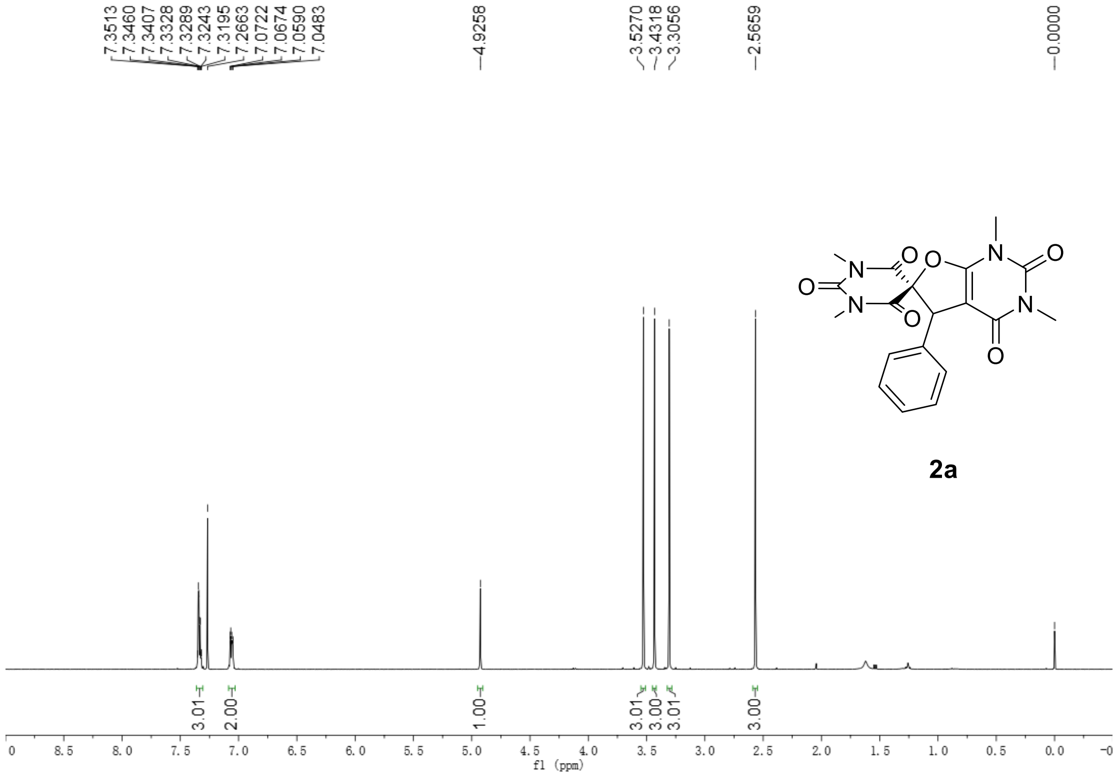


Figure S1. ^{1}H NMR (400 MHz, CDCl$_3$) of compound 2a

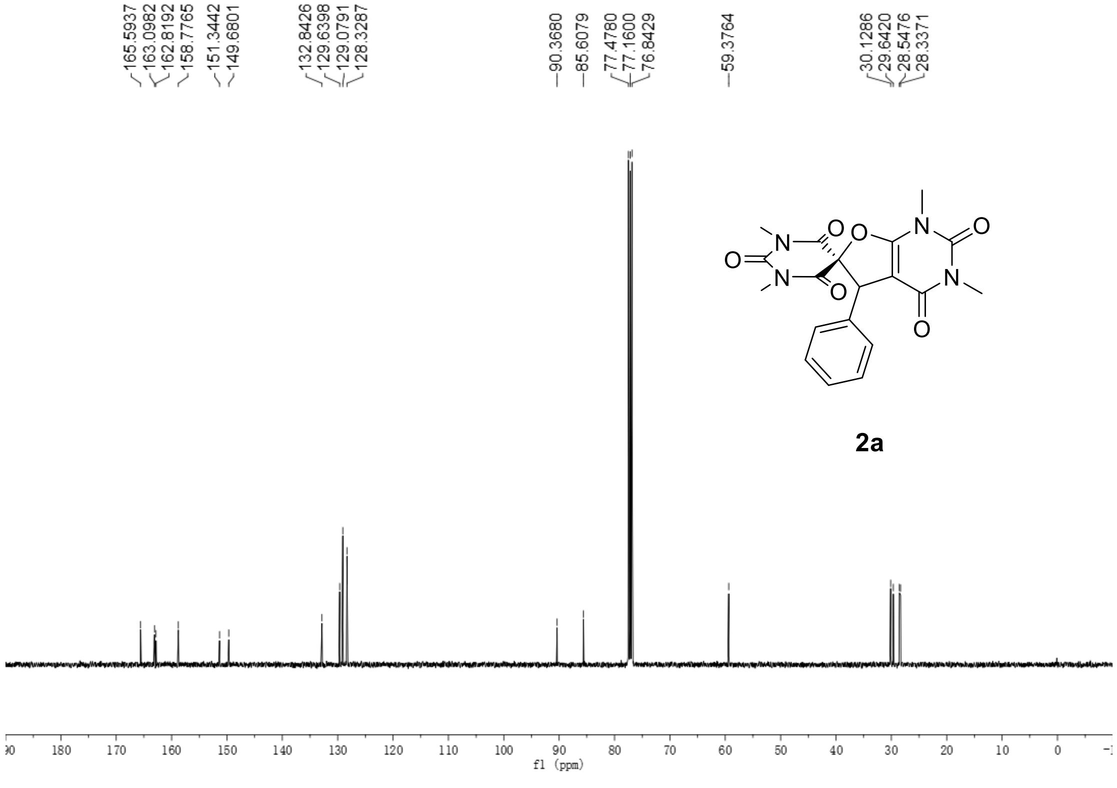


Figure S2. ^{13}C NMR (100 MHz, CDCl$_3$) of compound 2a

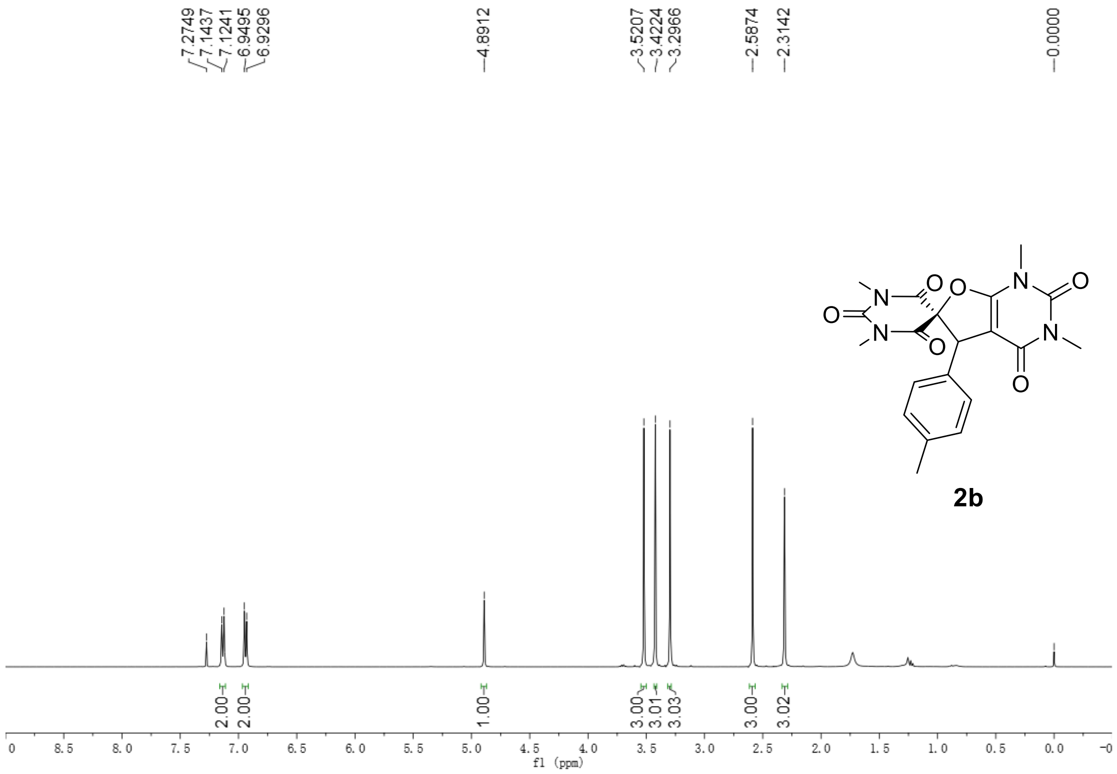


Figure S3. ^{1}H NMR (400 MHz, $CDCl_3$) of compound 2b

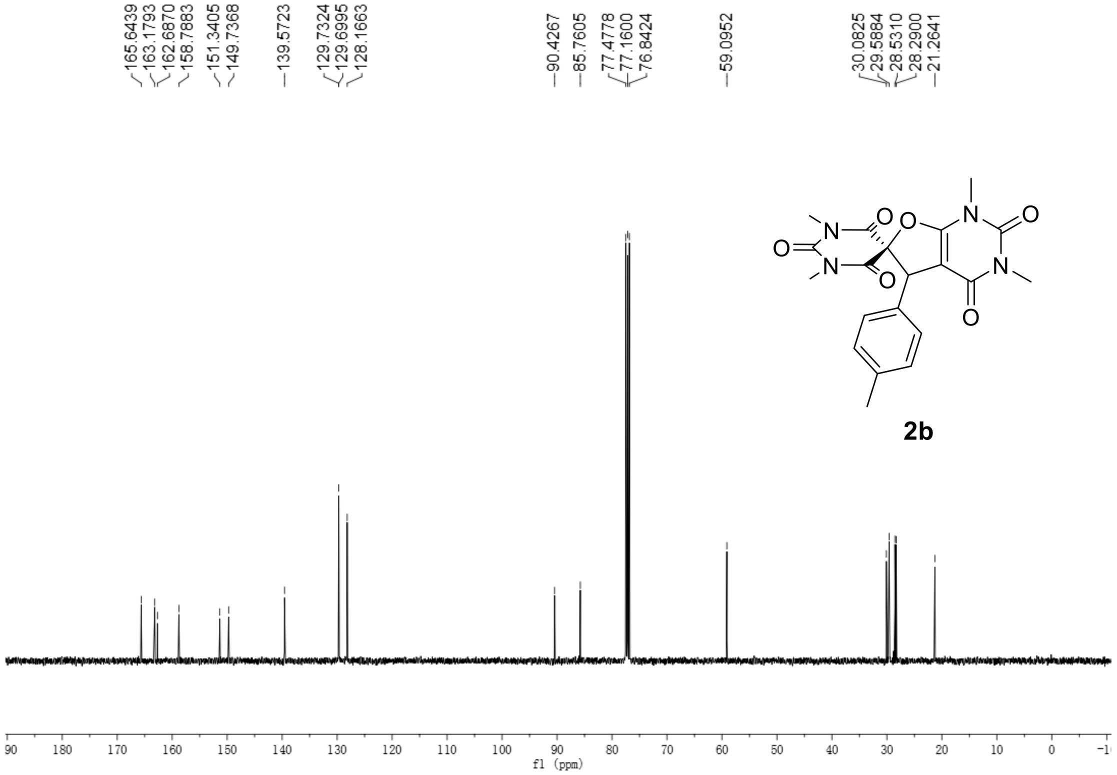


Figure S4. ^{13}C NMR (100 MHz, $CDCl_3$) of compound 2b

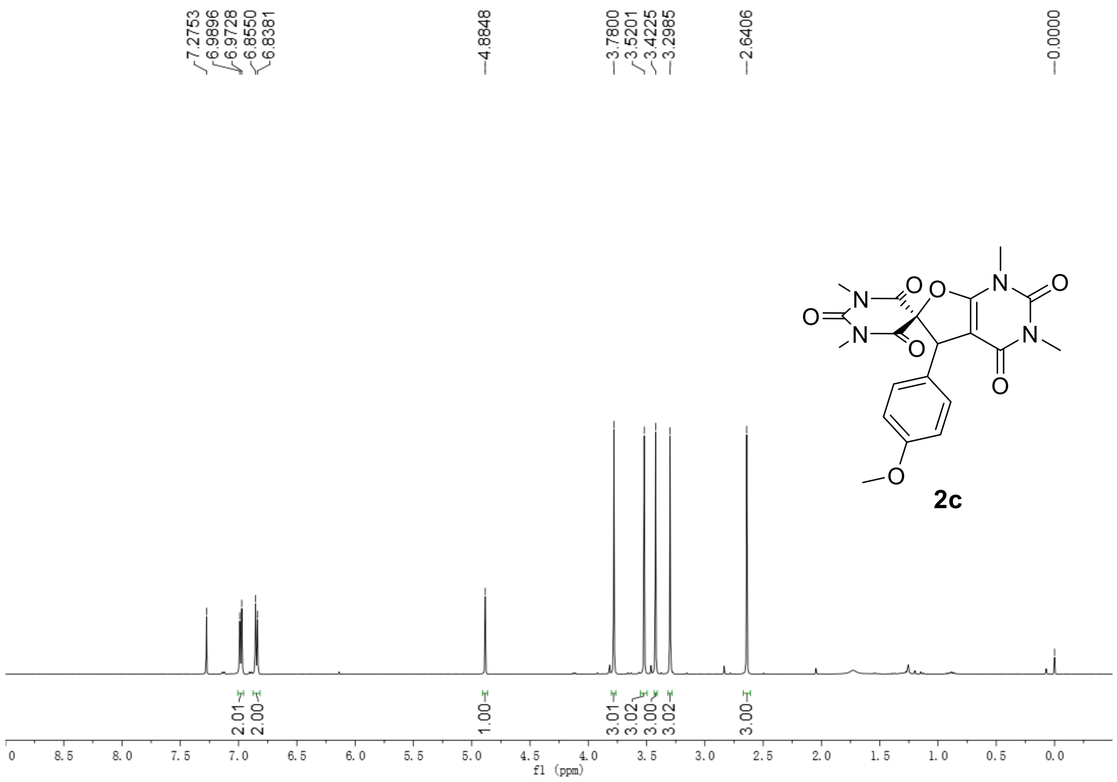


Figure S5. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 2c

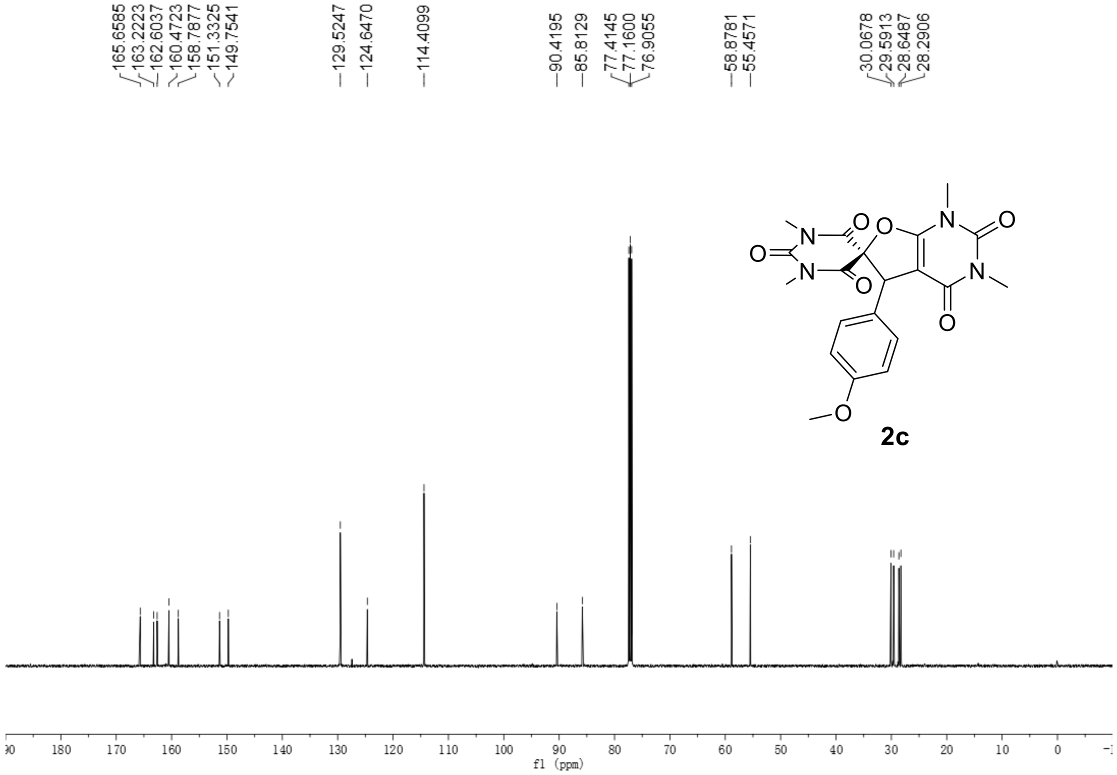


Figure S6. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 2c

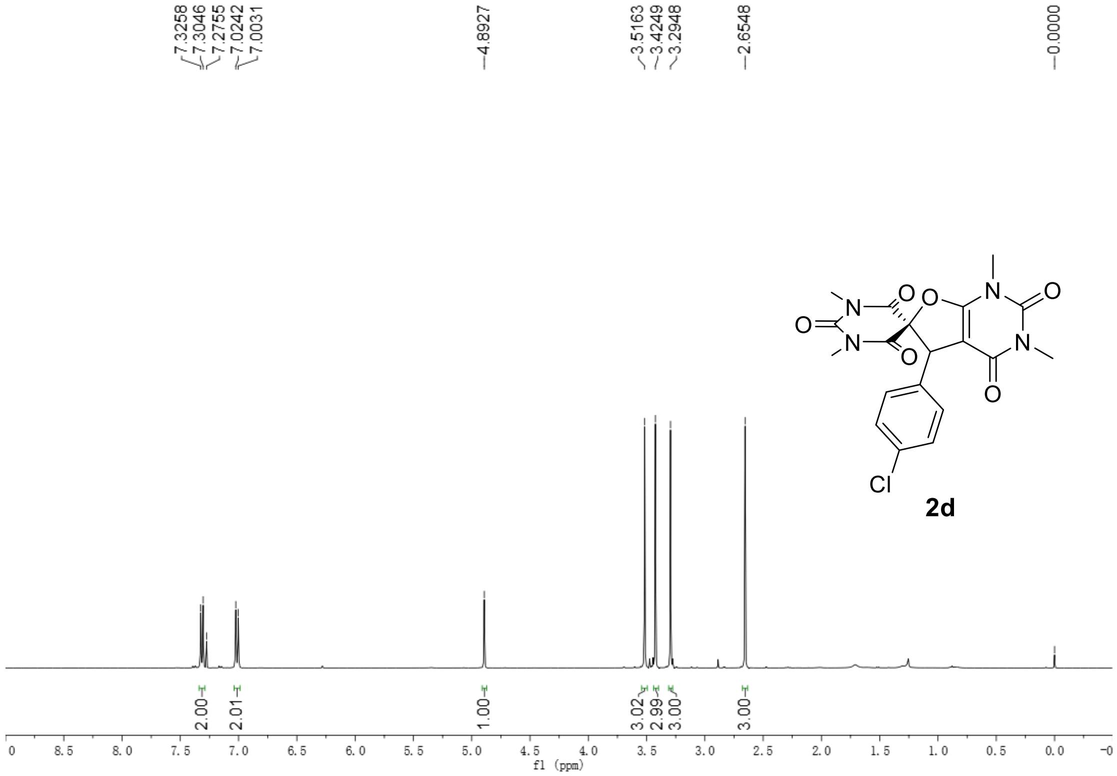


Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$) of compound 2d

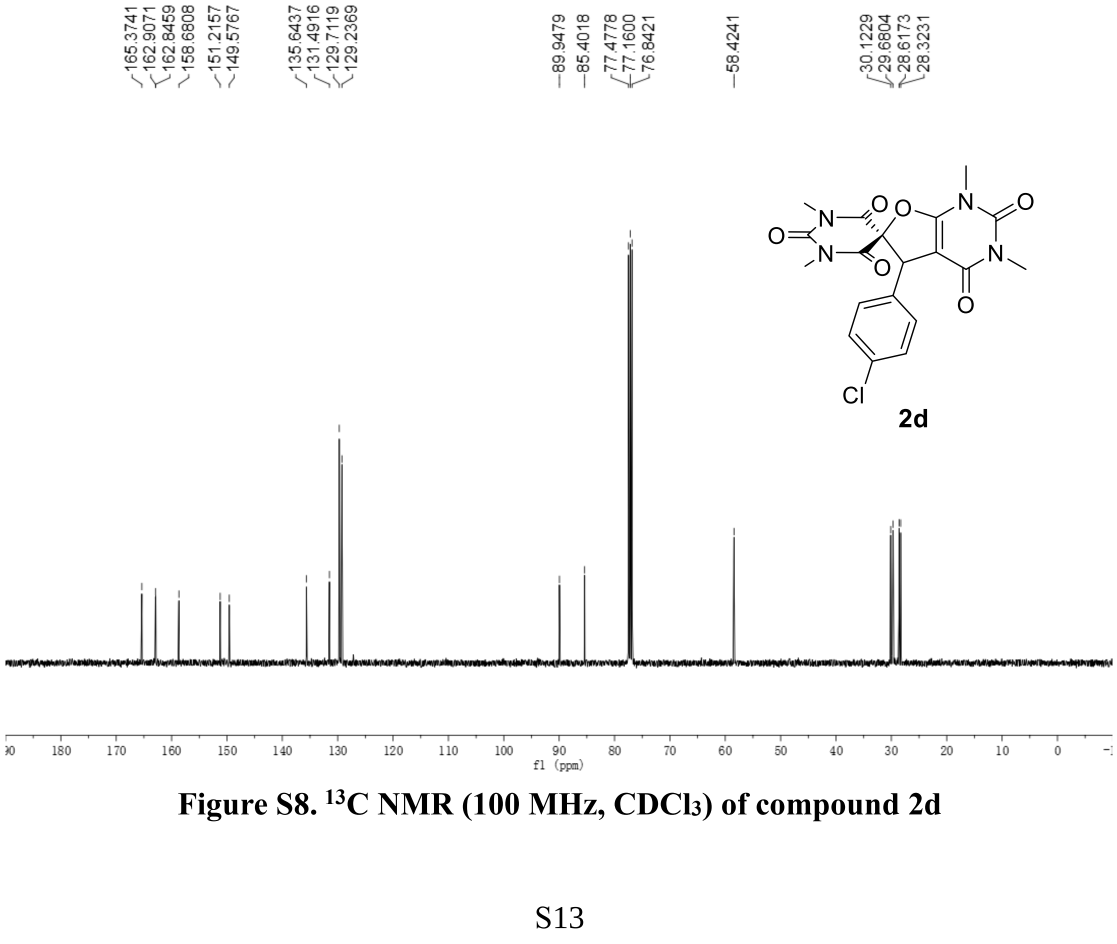


Figure S8. ^{13}C NMR (100 MHz, $CDCl_3$) of compound 2d

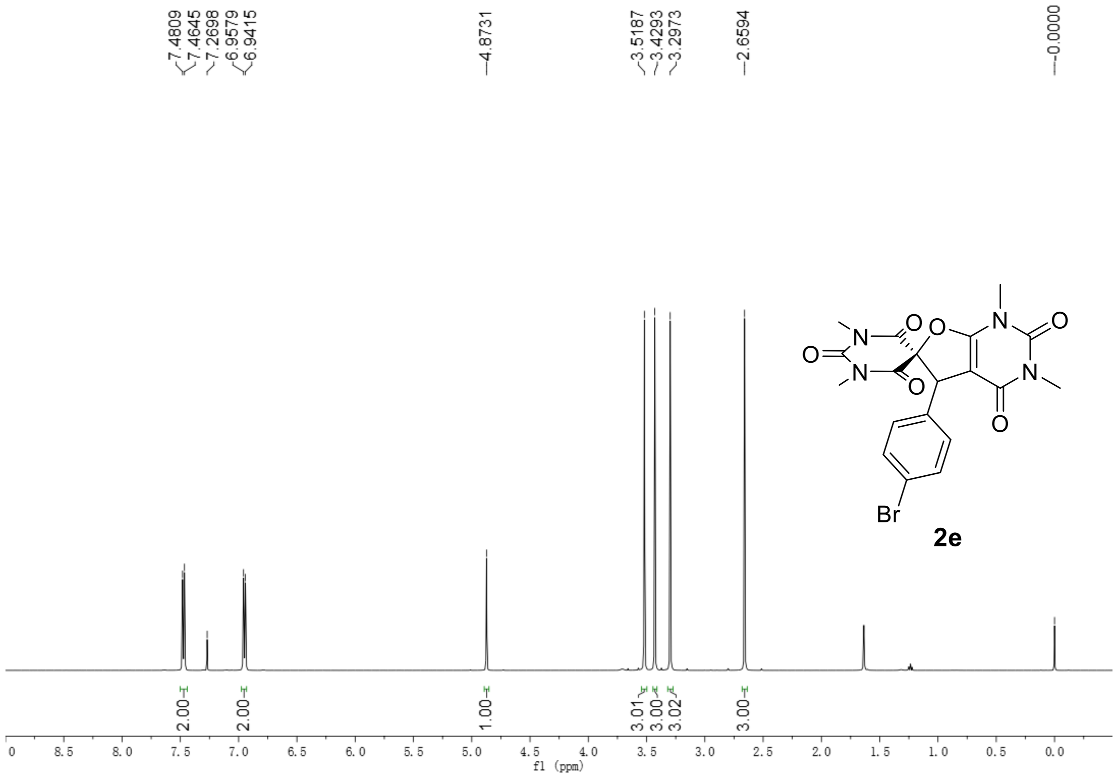


Figure S9. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 2e

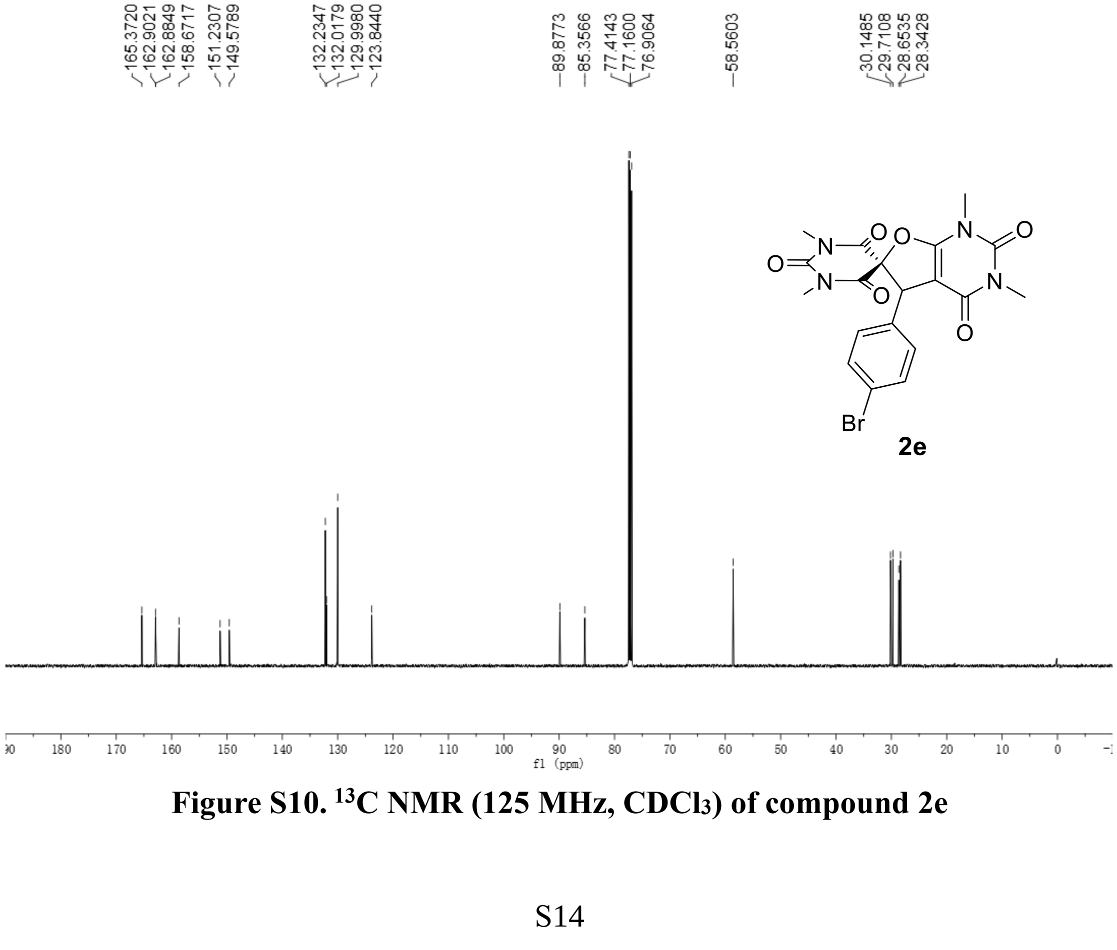


Figure S10. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 2e

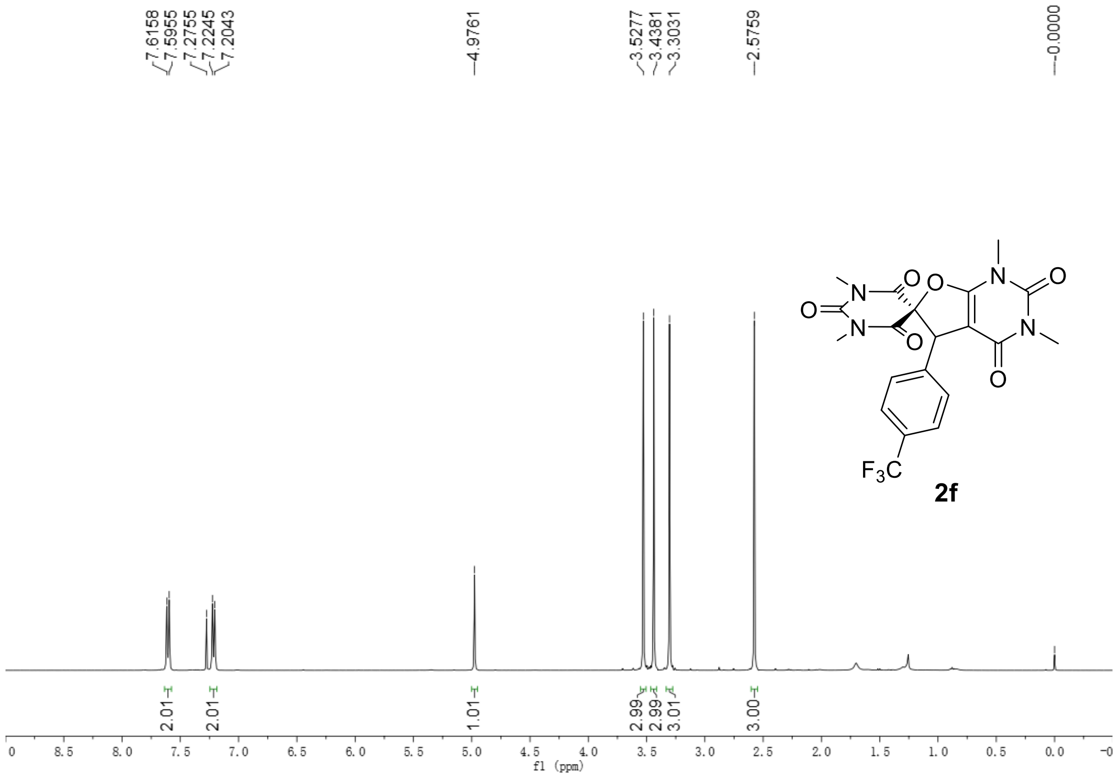


Figure S11. ^{1}H NMR (400 MHz, CDCl$_3$) of compound 2f

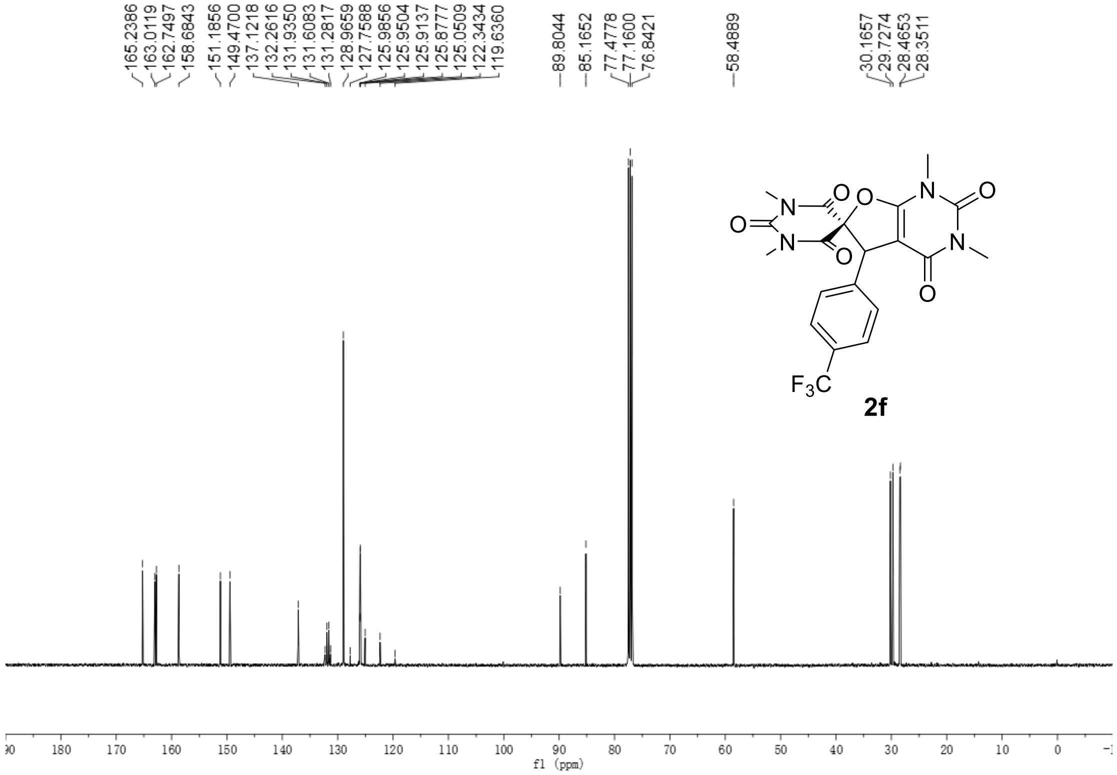


Figure S12. ^{13}C NMR (100 MHz, CDCl$_3$) of compound 2f

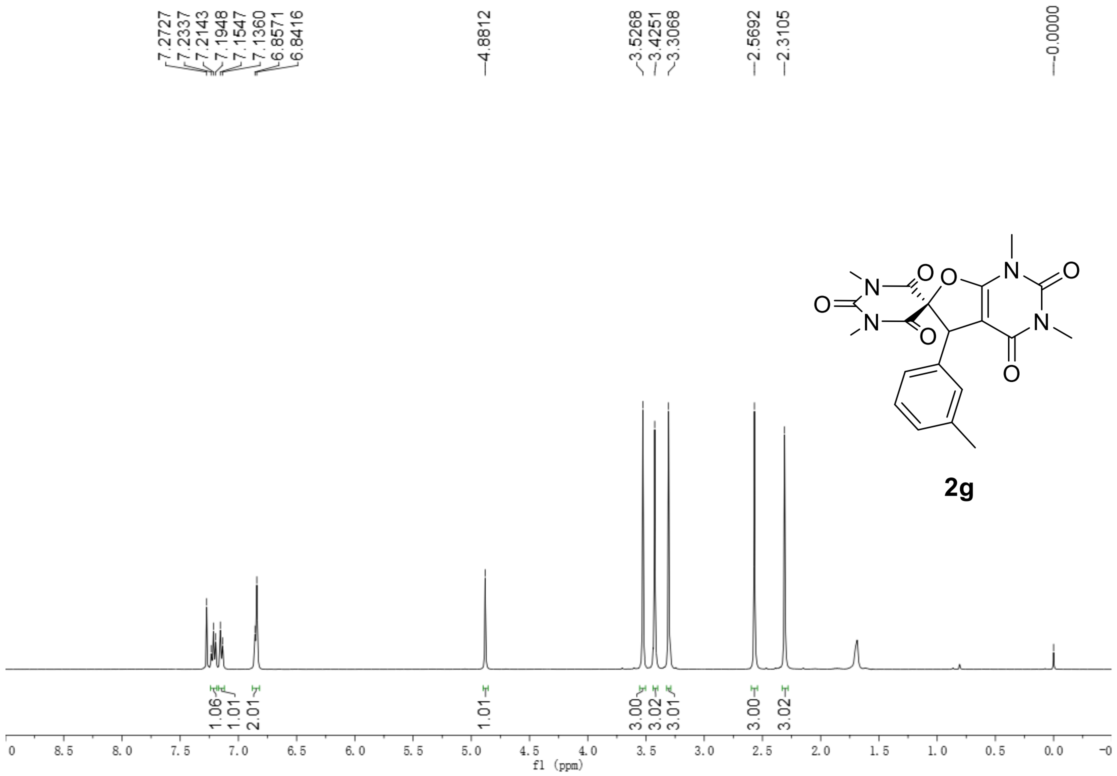


Figure S13. ^{1}H NMR (400 MHz, CDCl$_3$) of compound 2g

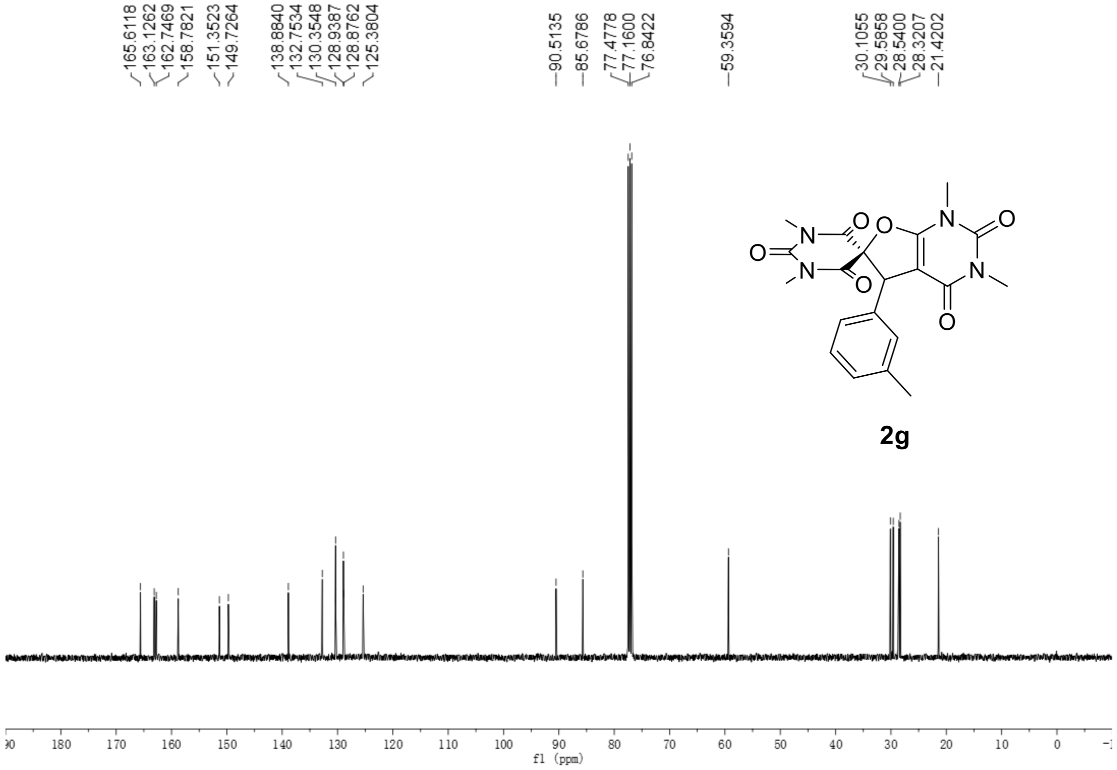


Figure S14. ^{13}C NMR (100 MHz, CDCl$_3$) of compound 2g

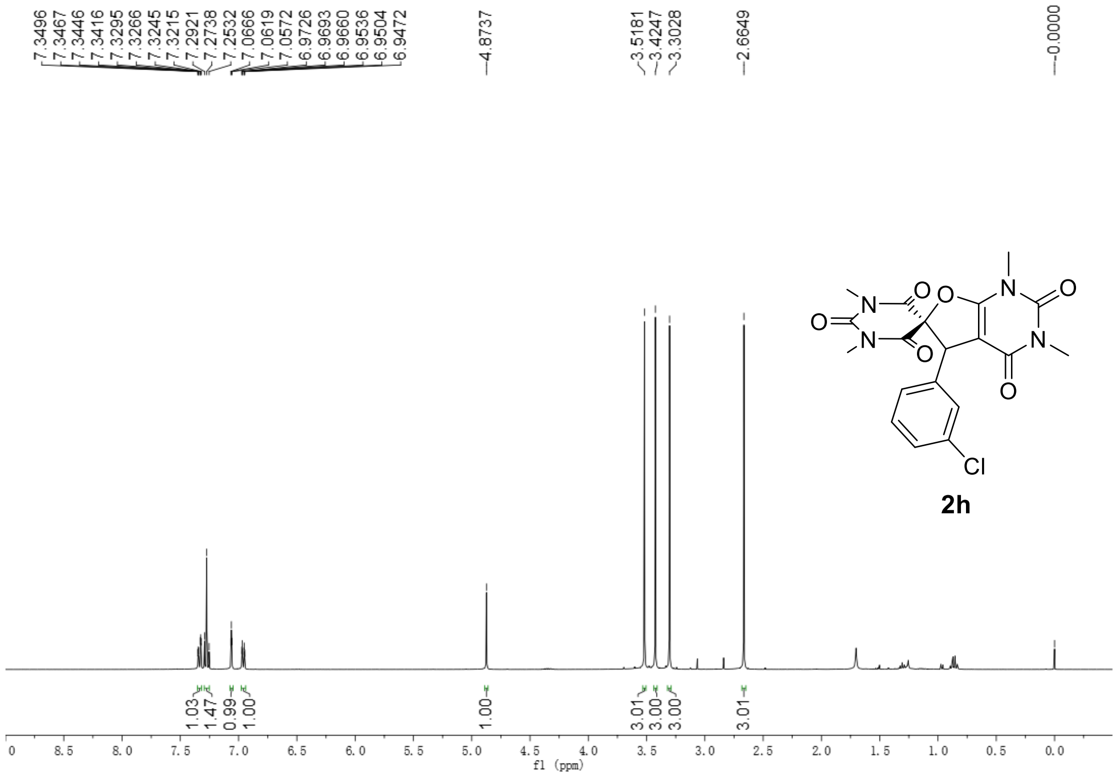


Figure S15. ^{1}H NMR (400 MHz, CDCl$_3$) of compound 2h

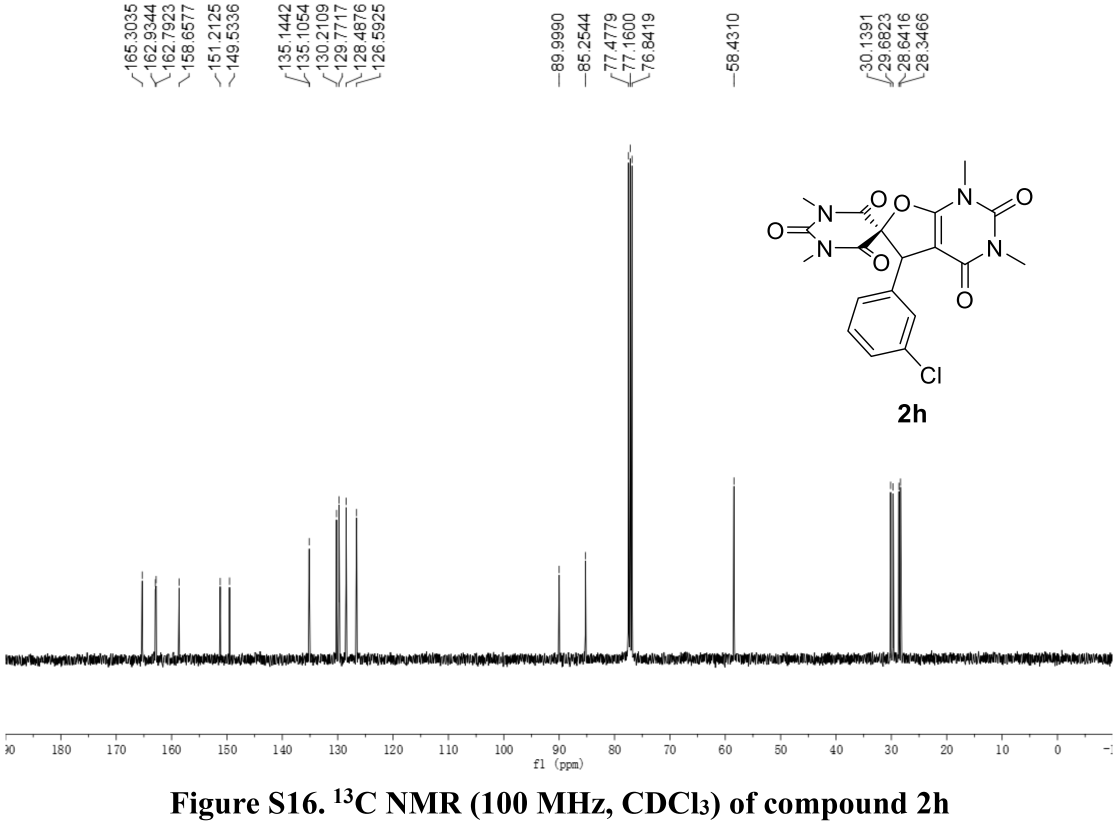


Figure S16. ^{13}C NMR (100 MHz, CDCl$_3$) of compound 2h

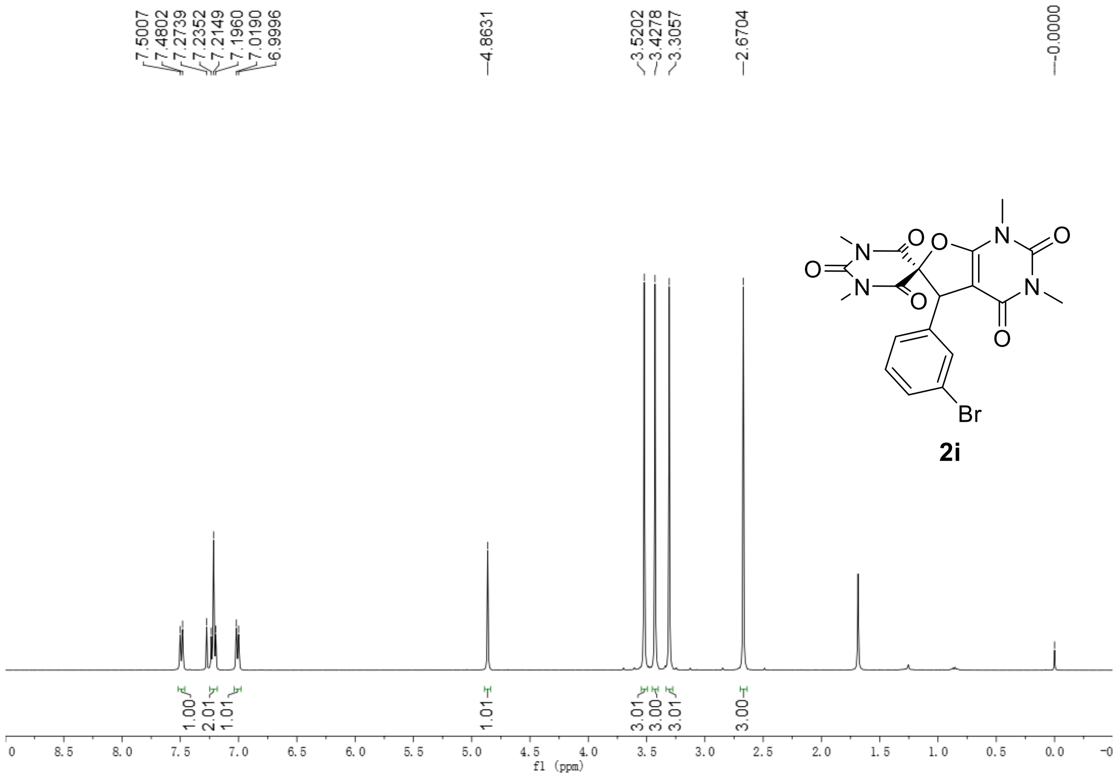


Figure S17. ^1H NMR (400 MHz, $CDCl_3$) of compound 2i

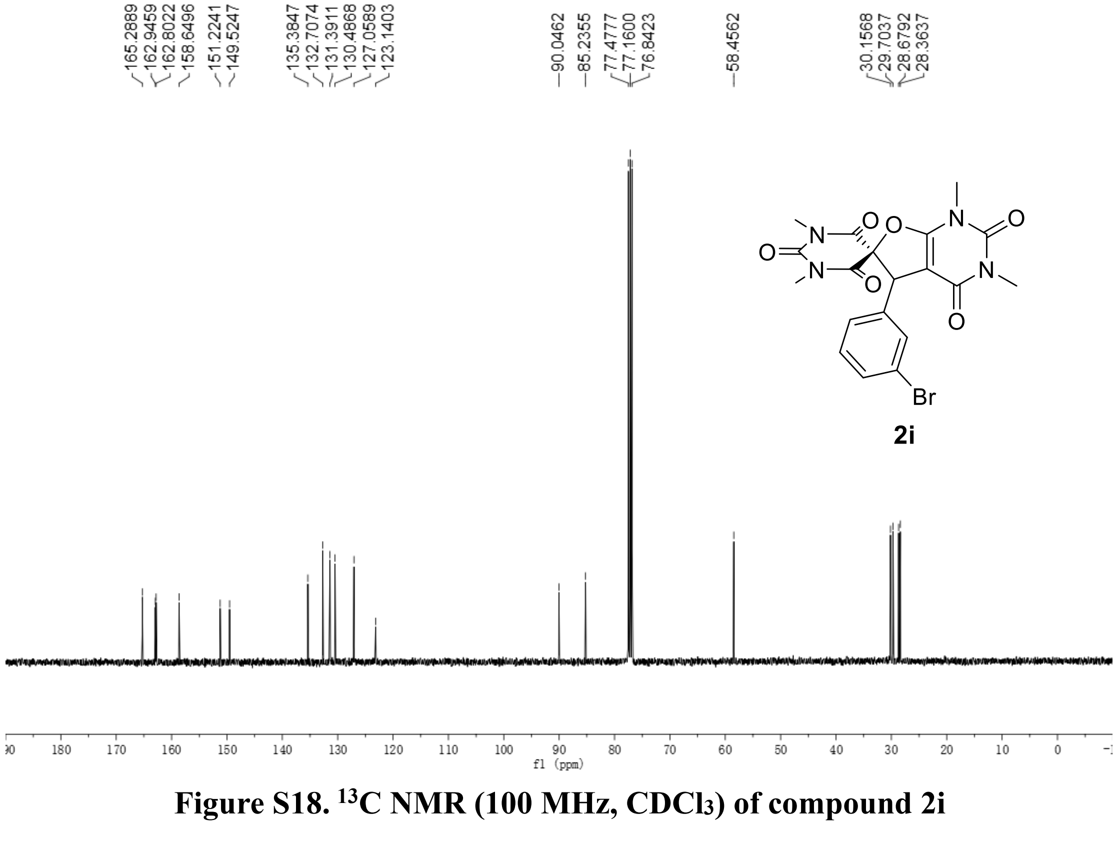


Figure S18. ^{13}C NMR (100 MHz, $CDCl_3$) of compound 2i

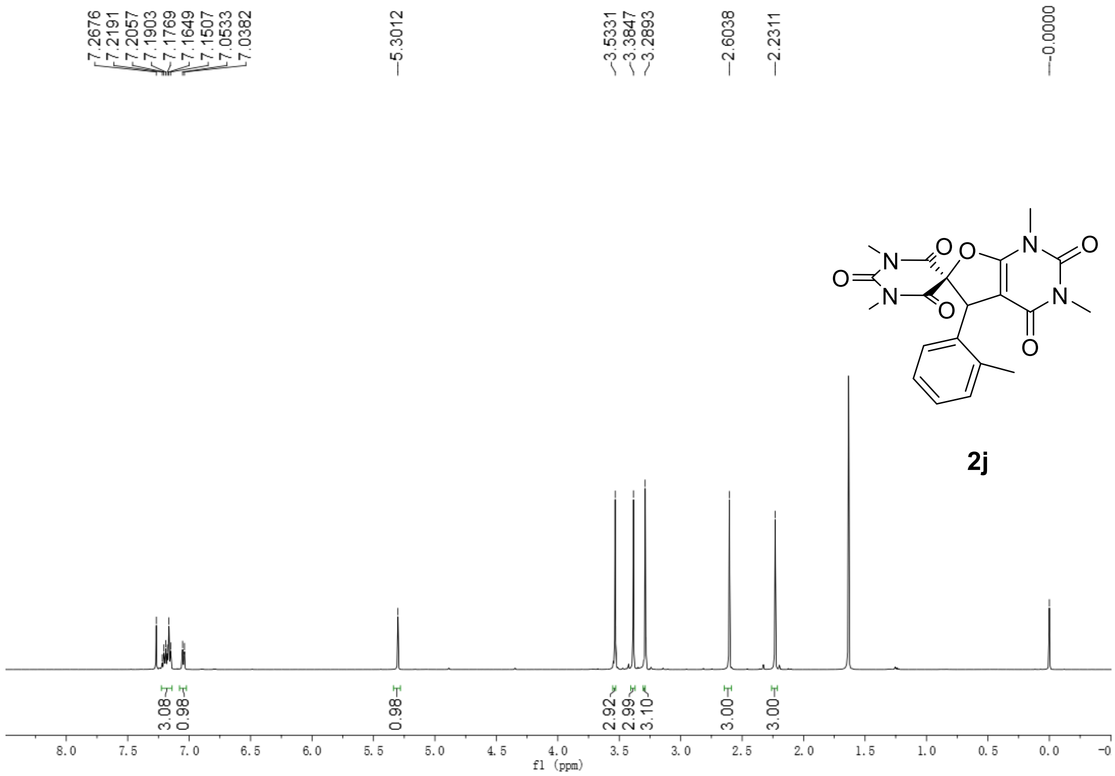


Figure S19. ^1H NMR (500 MHz, $CDCl_3$) of compound 2j

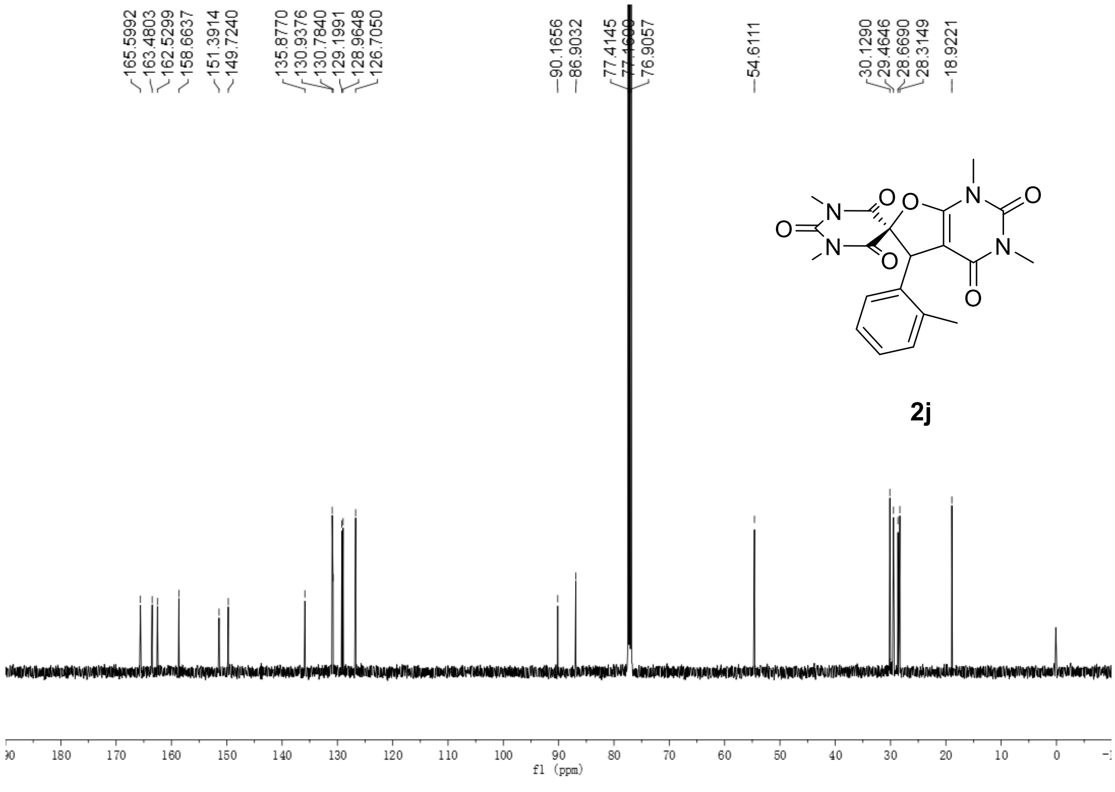


Figure S20. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 2j

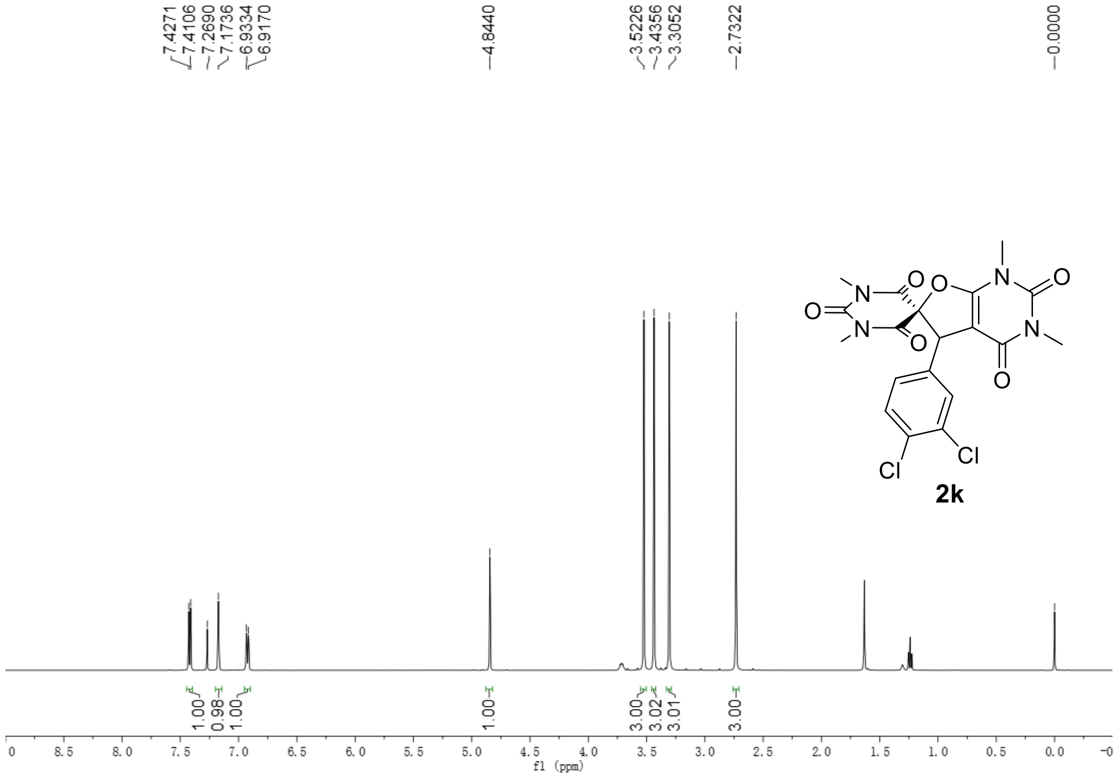


Figure S21. ^1H NMR (500 MHz, $CDCl_3$) of compound 2k

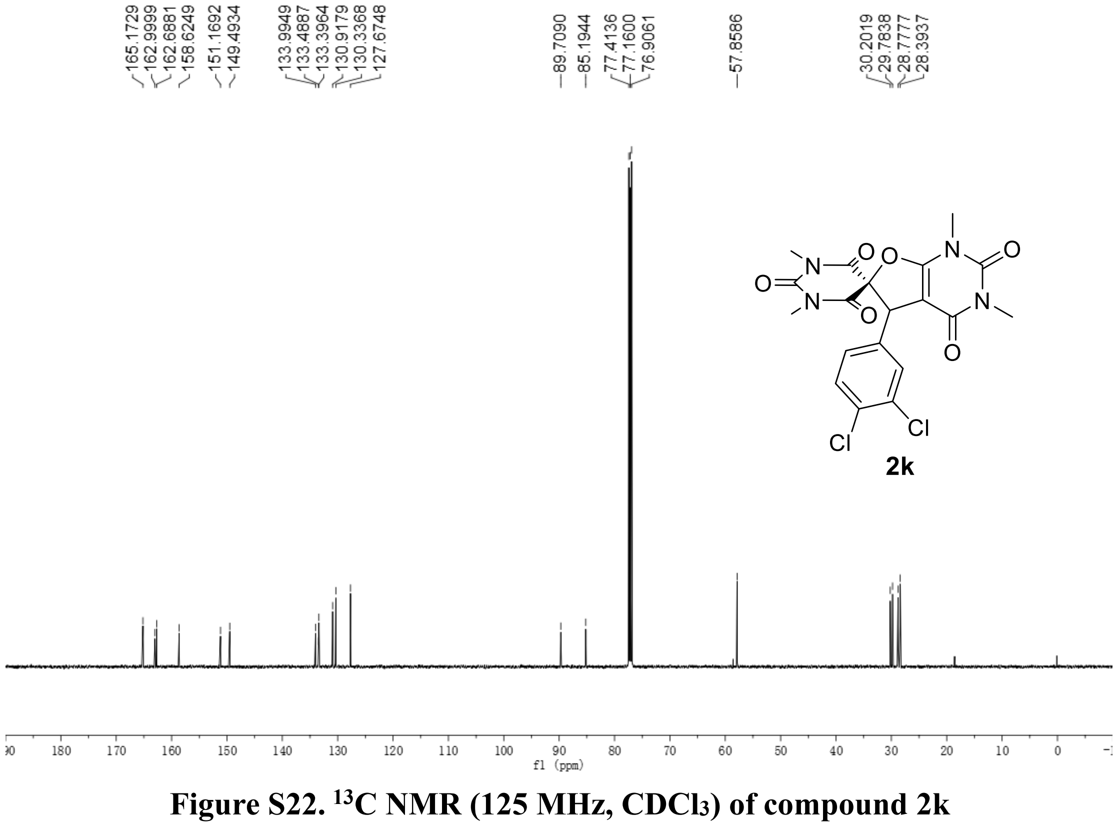


Figure S22. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 2k

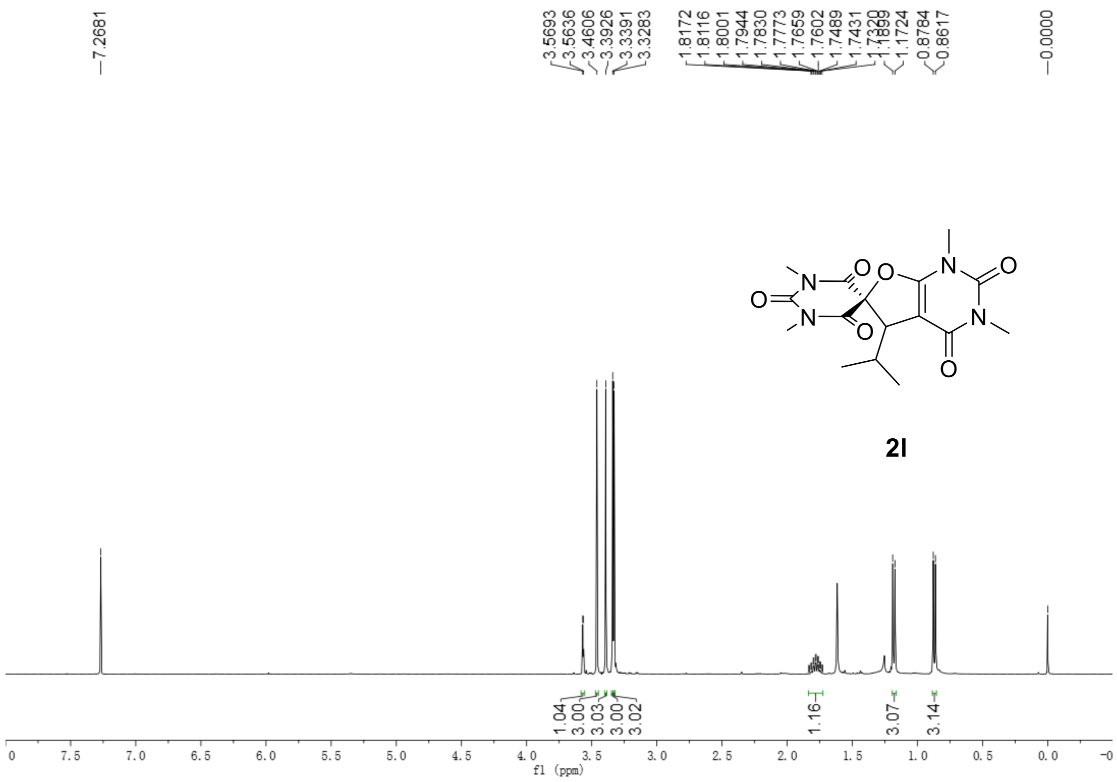


Figure S23. ^{1}H NMR (400 MHz, $CDCl_3$) of compound 2l

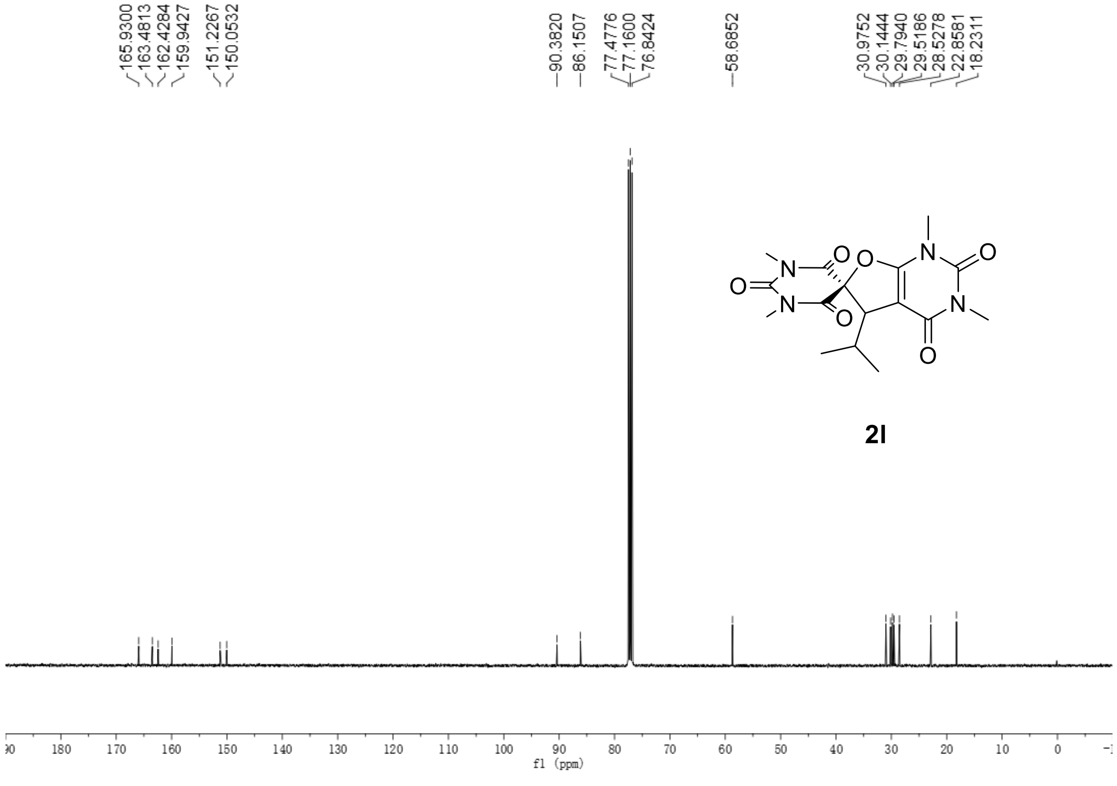


Figure S24. ^{13}C NMR (100 MHz, $CDCl_3$) of compound 2l