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 $\delta$ 0.0 ppm. $^{13}$C NMR chemical shifts were determined relative to CDCl$_3$ at $\delta$ 77.16 ppm. Data for $^1$H NMR and $^{13}$C NMR are reported as follows: chemical shift ($\delta$, 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

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 $^o$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) $\xrightarrow{I_2, H_2O, 80 ^\circ C, 3 h}$ 2a (86% yield)
A mixture of 5-benzylidene-1,3-dimethyl-pyrimidine-2,4,6-trione 1a (1.466 g, 6 mmol), I₂ (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 °C for 2 h, then the condenser was removed and the opened flask was stirred at 80 °C 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 ¹H NMR and ¹³C NMR. Products 2f, 2g, 2j, 2k and 2l were unknown compounds, which were characterized by ¹H NMR, ¹³C NMR and HRMS.

1,1',3,3'-Tetramethyl-5-phenyl-1,5-dihydro-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,3'H)-pentaone (2a). The general procedure was followed to afford 2a as a white solid. Yield: 88% (105.4 mg), mp 257–259 °C (256–258 °C[1]); IR (KBr) 1718, 1698, 1675, 1660, 1517, 1436, 1428, 1395, 1374, 1035 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 165.6, 163.2, 162.7, 158.5, 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-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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\textsubscript{20}H\textsubscript{18}F\textsubscript{3}N\textsubscript{4}O\textsubscript{6} [M + H]\textsuperscript{+} 467.1178, found 467.1182.

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**1,1',3,3'-Tetramethyl-5-(m-tolyl)-1,5-dihydro-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 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); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 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\textsubscript{20}H\textsubscript{21}N\textsubscript{4}O\textsubscript{6} [M + H]\textsuperscript{+} 413.1461, found 413.1468.

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**5-(3-Chlorophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,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\textsuperscript{[1]}); IR (KBr) 1717,1695, 1681, 1654, 1513, 1436, 1428, 1377, 1035 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 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); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 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-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,3'H)-pentaone (2i). The general procedure was followed to afford 2i as a white solid. Yield: 92% (131.9 mg), mp 241–243 °C (236–238 °C[1]); IR (KBr) 1718, 1694, 1684, 1652, 1345, 1429, 1383, 1031 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.49 (d, J = 8.2 Hz, 1H), 7.2 (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); ¹³C NMR (100 MHz, CDCl₃) 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, 50.5, 28.7, 28.4.

1,1',3,3'-Tetramethyl-5-(o-tolyl)-1,5-dihydro-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,3'H)-pentaone (2j). The general procedure was followed to afford 2j as a white solid. Yield: 87% (107.3 mg), mp 263–265 °C; IR (KBr) 1722, 1692, 1679, 1658, 1518, 1439, 1425, 1377, 1040 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₂₀H₂₁N₄O₆ [M + H]⁺ 413.1461, found 413.1462.
5-(3,4-Dichlorophenyl)-1,1',3,3'-tetramethyl-1,5-dihydro-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,3'H)-pentaone (2k). The general procedure was followed to afford 2k as a white solid. Yield: 91% (127.5 mg), mp 296–298 °C; IR (KBr) 1715, 1694, 1679, 1655, 1522, 1439, 1424, 1378, 1039 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₉H₁₇Cl₂N₄O₆ [M + H]⁺ 467.0525, found 467.0519.

5-Isopropyl-1,1',3,3'-tetramethyl-1,5-dihydro-2H,2'H-spiro[furo[2,3-d]pyrimidine-6,5'-pyrimidine]-2,2',4,4',6'(1'H,3H,3'H)-pentaone (2l). The general procedure was followed to afford 2l as a white solid. Yield: 71% (77.8 mg), mp 171–173 °C; IR (KBr) 1716, 1701, 1670, 1645, 1515, 1443, 1422, 1381, 1039 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.57 (d, J = 2.3 Hz, 1H), 3.46 (s, 3H), 3.39 (s, 3H), 3.34 (s, 3H), 1.84–1.72 (m, 1H), 1.18 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 6.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₆H₂₁N₄O₆ [M + H]⁺ 365.1461, found 365.1458.
3. References


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. $^1$H NMR (400 MHz, CDCl$_3$) of compound 2i

Figure S18. $^{13}$C NMR (100 MHz, CDCl$_3$) of compound 2i
Figure S19. $^1$H NMR (500 MHz, CDCl$_3$) of compound 2j

Figure S20. $^{13}$C NMR (125 MHz, CDCl$_3$) of compound 2j
Figure S21. $^1$H 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