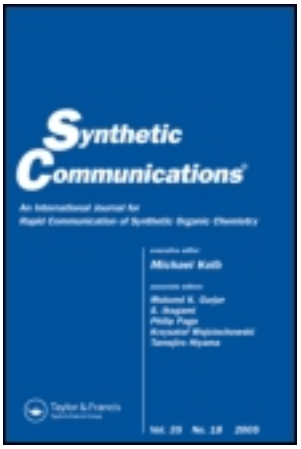

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One-Pot Synthesis of Novel Spiro Pyrano[2,3-d][1,3]thiazolo[3,2-a]pyrimidine Derivatives

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ONE-POT SYNTHESIS OF NOVEL SPIRO PYRANO[2,3-*d*][1,3]THIAZOLO[3,2-*a*]PYRIMIDINE DERIVATIVES

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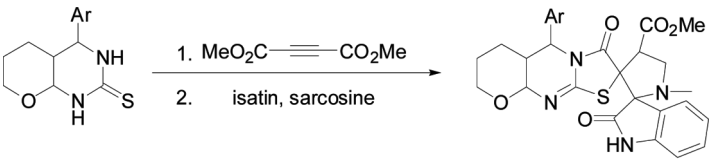
GRAPHICAL ABSTRACT



1a-1i **2a-2i**

Ar: **a**, 4-ClC_6H_4; **b**, 4-$OCH_3C_6H_4$; **c**, 2,4-$Cl_2C_6H_3$; **d**, 3,4,5- $(CH_3O)_3C_6H_2$; **e**, 4-FC_6H_4; **f**, 4-$SCH_3C_6H_4$; **g**, 4-$CH_3C_6H_4$; **h**, 4-$COOCH_3C_6H_4$; **i**, C_6H_5

Abstract *In a one-pot synthesis, 1′-methyl-2,3″-dioxo-5″-aryl-1,2,5a″,7″,8″,9a″-hexahydro-5″H,6″H-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-d][1,3]thiazolo[3,2-a]pyrimidine]-4′-carboxylic acid methyl ester was prepared via the sequential reaction of 4-aryl-octahydro-pyrano[2,3-d]pyrimidine-2-thione, dimethyl acetylenedicarboxylate (DMAD), and a mixture of isatin and sarcosine. All the novel spiro compounds, in moderate yields, were characterized thoroughly by infrared, NMR, mass spectromentry, and elemental analysis together with x-ray crystallographic analysis.*

Keywords Azomethine ylide; 1,3-dipolar cycloaddition; one-pot reaction; pyrano[2,3-*d*]-[1,3]thiazolo[3,2-*a*]pyrimidine; pyrano[2,3-*d*]pyrimidine

INTRODUCTION

One-pot multicomponent reactions are the processes that trigger the conversion of three or more starting materials in a single operation without the need to isolate intermediates. These strategies are used to improve the efficiency of chemical reactions whereby multiple carbon–carbon and carbon–heteroatom and stereocenters are formed.[1–3]

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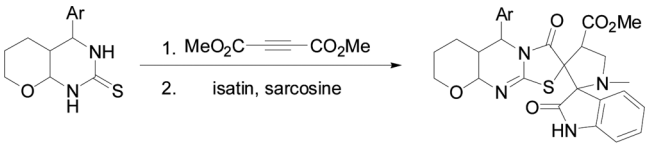


1a-1i 2a-2i

Scheme 1. One-pot synthesis of novel spiro pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine derivatives.

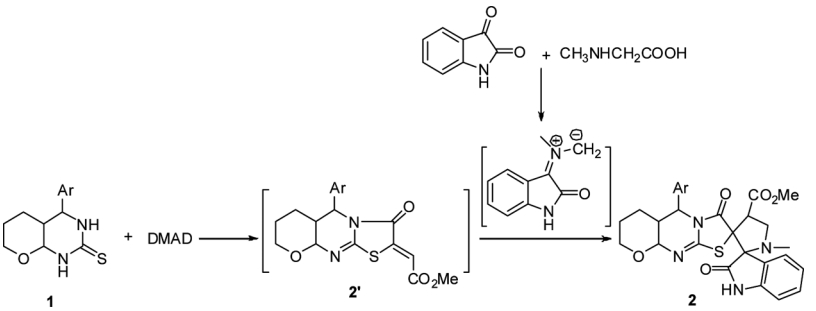
Spiro oxindoles, the main synthetic strategy of which is the 1,3-dipolar cycloaddition of azomethine ylide generated by the decarboxylative condensation of isatin and sarcosine and exocyclic double bond, have become important synthetic targets as these structural frameworks form the core units of many naturally occurring molecules that possess significant biological activities such as antimicrobial, antitumoral, and antibiotic activities and inhibit the human NK-1 receptor.[4–6] The thiazolo[3,2-*a*]pyrimidine moiety represents another common skeleton present in molecules endowed with biological properties such as antiallergic, analgesic, sedative, and calcium antagonistic activities.[7–9] Because of the importance of these two structural frameworks, synthesis of molecular architectures containing both spiro-oxindole and thiazolo[3,2-*a*]pyrimidine could be of great biological interest.

As a part of our ongoing research program in the area of cycloaddtion reactions,[10–12] we herein first report the one-pot synthesis of a series of novel spiro pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine derivatives (Scheme 1).

RESULTS AND DISCUSSION

The condensation reaction of 4-aryl-octahydro-pyrano[2,3-*d*]pyrimidine-2-thione **1**[13] and dimethyl acetylenedicarboxylate (DMAD) afforded intermediates methyl-(3-oxo-5-aryl-5*a*,7,8,9*a*-tetrahydro-5*H*,6*H*-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]-pyrimidine-2(3*H*)-ylidene)acetate **2′**. The 1,3-dipolar cycloaddition of **2′** and azomethine ylide generated in situ from isatin and sarcosine yielded 1′-methyl-2,3″-dioxo-5″-aryl-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine]-4′-carboxylic acid methyl ester **2** in moderate yields (Scheme 2).

The structures of products **2a–2i** were confirmed by different spectroscopic techniques (mass spectrometry [MS], infrared [IR], and NMR) and elemental analysis together with x-ray analysis. The IR spectrum of **2g** exhibited three carbonyl peaks located at 1740.2, 1719.4, and 1652.1 cm^{-1}, which were assigned to the methoxycarbonyl, carbonyl group in the thiazole ring, and the carbonyl group of the pyrrolidine ring, respectively. Further, the mass spectrum of **2g** showed a molecular ion peak at m/z 547 ($[M + H]^+$), which indicates the existence of **2g**. The ^1H NMR spectrum of **2g** revealed three singlets at δ 2.21, 2.30, and 3.71 resulting from N–CH_3(H-13), –CH_3(H-16), and –OCH_3(H-14), respectively. One doublet of doublets at δ 0.96 ($J = 2.5$, 11.5 Hz) and a doublet at δ 4.50 ($J = 11.5$ Hz) were assignable to the proton of CH (H-4) and CH (H-5) in pyrimidine ring. Furthermore, there were a doublet at



Scheme 2. Mechanism of the cycloaddition.

δ 1.32 ($J = 13.5$ Hz) and a multiplet at δ 1.78–1.88 resulting from tetrahydropyran ring for the protons of methylene (H-2), a triplet at δ 3.69 ($J = 11.5$ Hz), and a doublet of doublets at δ 4.10 ($J = 4.5$, 11.5 Hz) corresponding to methylene (H-1) in the tetrahydropyran ring. A doublet at δ 1.32 ($J = 13.5$ Hz) was assignable to the protons of CH_2 (H-3) in the tetrahydropyran ring, and three triplets at δ 3.61 ($J = 8.5$ Hz), 4.03 ($J = 8.5$ Hz), and 4.16 ($J = 8.5$ Hz) resulted from –CH_2(H-10) and –CH (H-11) in the pyrrolidine ring, respectively. The presence of a doublet at δ 4.95 was assignable to the proton of Ar-CH (H-6), and several doublets and triplets in the range of δ 6.76–7.28 were for aromatic protons. The existence of a singlet downfield at δ 8.43 corresponds to NH in indole ring.

The ^{13}C NMR spectrum of the product **2g** exhibits the presence of three methylene carbons that exist in the tetrahydropyran ring at δ 67.97 (C-1), 20.24 (C-2), and 23.55 (C-3); the signals of three methylene carbons of CH in the pyrimidine ring at δ 35.73 (C-4), 58.21 (C-5), and 78.65 (C-6); and the presence of signals at δ 54.60 and 47.64 assignable to the equivalent methylene carbon (C-10) and carbon of CH (C-11) in the pyrrolidine ring. The chemical shifts were as follows: -CH_3 carbon at δ 21.07 (C-16), N-CH_3 carbon at δ 35.70 (C-13), and -OCH_3 carbon at δ 52.28 (C-14). The

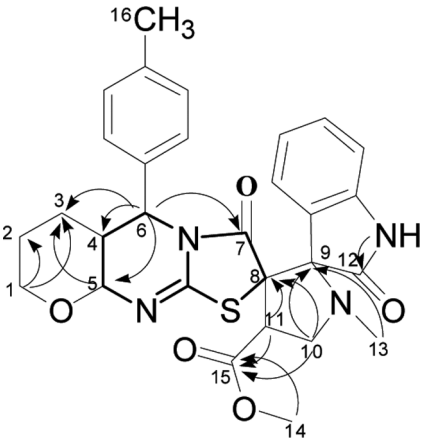


Figure 1. Part HMBC correlations of 2 g.

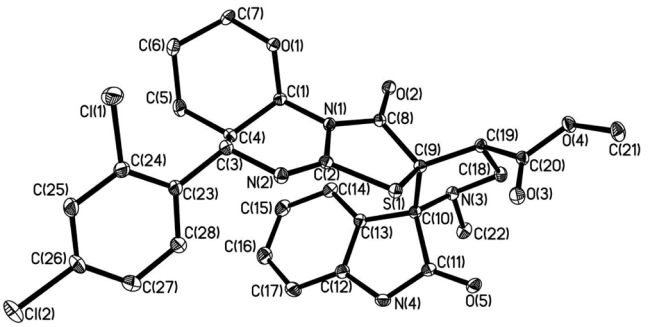


Figure 2. Molecular skeleton structure of compound **2c**.

three carbonyl carbons were at δ 170.23 (C-15), 172.15 (C-7), and 176.20 (C-12). The signals at δ 64.81 and 80.09 are assignable for the two spiro carbons of (C-8) and (C-9) respectively based on ^{1}H-^{13}C heteronuclear multiple-bond correlation (HMBC) (Figure 1). Further, the structure of the product was confirmed by x-ray diffraction analysis of **2c**[14](Fig. 2).

The molecular structure of **2c** contains two spiro junctions, which consist of a planar 2-oxindole ring, a pyrrolidine ring, and a pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine ring. The tetrahydropyrimidine ring and pyrrolidine ring adopt envelope conformations, and the tetrahydropyran ring has a chair conformation.

EXPERIMENTAL

Materials and Instruments

4-Aryl-octahydro-pyrano[2,3-*d*]pyrimidine-2-thione **1**[13] was prepared according to the reported procedures. All NMR spectra were recorded on a Bruker AV-II 500-MHz NMR spectrometer, operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C. Tetramethylsilane (TMS) was used as an internal reference for ^{1}H and ^{13}C chemical shifts. $CDCl_3$ was used as solvent. Elemental analysis was measured by an Elementar Analyzer (Vario EL II). Mass spectra (MS) were measured on a Finnigan LCQ Advantage MAX mass spectrometer; IR spectra were recorded on a Perkin-Elmer spectrometer (Spectrum One). Melting points were measure by a Yanaco MP500 melting-point apparatus and were uncorrected.

Crystal Structure Determination

The white prismatic crystal of **2c** was subjected to x-ray structural analysis and the orthorhombic space group Pbca with $a = 8.9414(18)$ Å, $b = 15.596(3)$ Å, $c = 39.017(8)$ Å, $\alpha = 90.00°$, $\beta = 90.00°$, $\gamma = 90.00°$, $V = 5440.8(19)$ Å^3, $Z = 8$, and $\rho = 1.469$ g/cm^3. Final R and wR (on F^2) were 0.0573 and 0.1477 for 5761 reflections. The crystallographic data is available from the Cambridge Crystallographic Data Centre, CCDC number CCDC 796436.[14]

1′-Methyl-2,3″-dioxo-5″-aryl-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[Indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine]-4′-carboxylic Acid Methyl Ester (2a–2i)

General procedure for the synthesis. A mixture of **1** (1 mmol) and DMAD (1 mmol) in methanol (40 mL) was heated to reflux for 3 h, isatin (1 mmol) and sarcosine (1 mmol) were added, and the resulting solution were further refluxed for 12 h. After completion of the reaction as evident from thin-layer chromatography (TLC), the solvent was evaporated in vacuum. The residue was purified by column chromatography employing petroleum ether/ethyl acetate mixture (4:1, *V*/*V*) as eluent to obtain **2**.

5″-(4-Chlorophenyl)-1′-methyl-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]-pyrimidine]-4′-carboxylic acid methyl ester (2a). White solid, yield 60%, mp 239–240 °C; IR (KBr) *v*: 1736.2, 1719.9, 1634.2 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.92 (d, $J = 11.0$ Hz, 1H), 1.35 (d, $J = 13.5$ Hz, 1H), 1.46–1.56 (m, 2H), 1.75–1.81 (m, 1H), 2.21 (s, 3H), 3.64 (t, $J = 8.5$ Hz, 1H), 3.70 (t, $J = 11.5$ Hz, 1H), 3.75 (s, 3H), 4.01 (t, $J = 8.5$ Hz, 1H), 4.10–4.16 (m, 2H), 4.53 (d, $J = 11.5$ Hz, 1H), 4.96 (d, $J = 2.0$ Hz, 1H), 6.81 (d, $J = 8.5$ Hz, 2H), 6.91 (d, $J = 8.0$ Hz, 1H), 6.98 (t, $J = 7.5$ Hz, 1H), 7.16 (d, $J = 7.5$ Hz, 1H), 7.24–7.26 (m, 2H), 7.31 (t, $J = 7.5$ Hz, 1H), 8.32 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.23, 23.46, 35.69, 35.89, 47.56, 52.33, 54.62, 57.85, 64.79, 67.99, 78.52, 80.06, 110.28, 122.32, 123.30, 125.74, 128.56, 128.84, 130.62, 133.17, 140.31, 143.35, 148.91, 170.24, 172.07, 176.12; ESI MS *m*/*z*: 567 $[M + H]^+$. Anal. Calcd. for $C_{28}H_{27}ClN_4O_5S$: C, 59.31; H, 4.80; N, 9.88. Found: C, 59.18; H, 5.03; N, 9.72.

5″-(4-Methoxyphenyl)-1′-methyl-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]-pyrimidine]-4′-carboxylic acid methyl ester (2b). White solid, yield 55%, mp 208–209 °C; IR (KBr) *v*: 1730.9, 1719.5, 1651.7 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.95 (dd, $J_1 = 2.0$ Hz, $J_2 = 11.5$ Hz, 1H), 1.33 (d, $J = 8.5$ Hz, 1H), 1.49–1.51 (m, 2H), 1.77–1.81 (m, 1H), 2.21 (s, 3H), 3.61 (t, $J = 8.5$ Hz, 1H), 3.70 (t, $J = 12.0$ Hz, 1H), 3.75 (s, 3H), 3.77 (s, 3H), 4.03 (t, $J = 8.5$ Hz, 1H), 4.09–4.12 (m, 1H), 4.16 (t, $J = 8.5$ Hz, 1H), 4.50 (d, $J = 11.5$ Hz, 1H), 4.95 (d, $J = 2.0$ Hz, 1H), 6.80 (d, $J = 8.5$ Hz, 4H), 6.87 (d, $J = 8.0$ Hz, 1H), 6.97 (t, $J = 7.5$ Hz, 1H), 7.17 (d, $J = 7.5$ Hz, 1H), 7.30 (t, $J = 7.5$ Hz, 1H), 8.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.23, 23.53, 35.69, 35.81, 47.69, 52.27, 54.58, 55.25, 57.87, 64.80, 67.97, 78.68, 80.08, 110.32, 113.80, 122.23, 123.29, 125.68, 128.47, 130.56, 133.82, 143.38, 148.11, 158.86, 170.23, 172.14, 176.20; ESI MS *m*/*z*: 563 $[M + H]^+$. Anal. Calcd. for $C_{29}H_{30}N_4O_6S$: C, 61.91; H, 5.37; N, 9.96. Found: C, 61.64; H, 5.61; N, 10.17.

5″-(2,4-Dichlorophenyl)-1′-methyl-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]-pyrimidine]-4′-carboxylic acid methyl ester (2c). White solid, yield 62%, mp 233–234 °C; IR (KBr) *v*: 1740.3, 1719.5, 1648.9 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.96 (d, $J = 9.0$ Hz, 1H), 1.40 (d, $J = 13.5$ Hz, 2H), 1.51–1.57 (m, 1H), 2.00 (s, 1H), 2.19 (s, 3H), 3.67 (d, $J = 11.0$ Hz, 2H), 3.75 (s, 3H), 4.00 (t, $J = 8.5$ Hz, 1H), 4.09–4.17 (m, 2H), 4.96 (s, 1H), 5.09 (d, $J = 11.0$ Hz, 1H), 6.37 (d, $J = 8.0$ Hz,

1H), 6.98 (t, $J = 7.5$ Hz, 2H), 7.15 (d, $J = 7.5$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 8.67 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.92, 23.37, 35.76, 36.63, 47.34, 52.40, 54.32, 54.67, 64.73, 67.98, 78.43, 80.15, 110.44, 122.38, 13.38, 125.73, 127.78, 128.62, 130.24, 130.67, 133.58, 134.10, 170.34, 172.05, 176.38; ESI MS m/z: 601 $[M + H]^+$. Anal. Calcd. for $C_{28}H_{26}Cl_2N_4O_5S$: C, 55.91; H, 4.36; N, 9.31. Found: C, 55.80; H, 4.49; N, 9.19.

1′-Methyl-2,3″-dioxo-5″-(3,4,5-trimethoxyphenyl)-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine]-4′-carboxylic acid methyl ester (2d). White solid, yield 58%, mp 209–210 °C; IR (KBr) ν: 1740.2, 1719.4, 1652.1 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.01 (d, $J = 11.5$ Hz, 1H), 1.35 (d, $J = 13.0$ Hz, 1H), 1.53–1.56 (m, 2H), 1.76–1.80 (m, 1H), 2.21 (s, 3H), 3.64 (t, $J = 9.0$ Hz, 1H), 3.67–3.72 (m, 1H), 3.75 (s, 3H), 3.79 (s, 3H), 3.83 (s, 6H), 3.99 (t, $J = 8.5$ Hz, 1H), 4.11–4.16 (m, 2H), 4.48 (d, $J = 11.5$ Hz, 1H), 4.98 (d, $J = 2.0$ Hz, 1H), 6.13 (s, 2H), 6.83 (d, $J = 7.5$ Hz, 1H), 7.01 (t, $J = 7.5$ Hz, 1H), 7.19 (d, $J = 7.5$ Hz, 1H), 7.28 (t, $J = 7.5$ Hz, 1H), 8.58 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.25, 23.60, 35.28, 35.66, 47.51, 52.28, 54.59, 56.08, 58.73, 60.74, 64.58, 67.95, 78.75, 80.01, 104.41, 110.03, 122.23, 123.36, 125.72, 130.40, 137.21, 137.25, 143.56, 148.49, 153.17, 170.23, 172.16, 176.14; ESI MS m/z: 623 $[M + H]^+$. Anal. calcd. for $C_{31}H_{34}N_4O_8S$: C, 59.79; H, 5.50; N, 9.00. Found: C, 59.88; H, 5.30; N, 9.12.

5″-(4-Fluorophenyl)-1′-methyl-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]-pyrimidine]-4′-carboxylic acid methyl ester (2e). White solid, yield 67%, mp 225–226 °C; IR (KBr) ν: 1741.1, 1719.1, 1651.7 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.94 (d, $J = 11.5$ Hz, 1H), 1.35 (d, $J = 13.5$ Hz, 1H), 1.45–1.56 (m, 2H), 1.75–1.81 (m, 1H), 2.21 (s, 3H), 3.63 (t, $J = 9.0$ Hz, 1H), 3.71 (t, $J = 11.0$ Hz, 1H), 3.75 (s, 3H), 4.01 (t, $J = 8.5$ Hz, 1H), 4.01–4.17 (m, 2H), 4.54 (d, $J = 11.5$ Hz, 1H), 4.96 (d, $J = 2.0$ Hz, 1H), 6.85 (dd, $J_1 = 5.5$ Hz, $J_2 = 8.5$ Hz, 2H), 6.91–7.00 (m, 4H), 7.17 (d, $J = 7.5$ Hz, 1H), 7.30 (t, $J = 7.5$ Hz, 1H), 8.47 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.21, 23.46, 35.68, 35.94, 47.61, 52.31, 54.59, 57.77, 64.77, 67.97, 78.58, 80.05, 110.33, 115.18, 115.35, 122.28, 123.27, 125.70, 128.97, 129.03, 130.60, 137.49, 137.51, 143.40, 148.72, 161.07, 163.03, 170.25, 172.09, 176.18; ESI MS m/z: 551 $[M + H]^+$. Anal. calcd. for $C_{28}H_{27}FN_4O_5S$: C, 61.08; H, 4.94; N, 10.18. Found: C, 61.00; H, 4.83; N, 10.40.

1′-Methyl-5″-[4-(methylthio)phenyl]-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine]-4′-carboxylic acid methyl ester (2f). White solid, yield 65%, mp 207–208 °C; IR (KBr) ν: 1732.1, 1727.4, 1652.0 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.94 (dd, $J_1 = 2.0$ Hz, $J_2 = 11.0$ Hz, 1H), 1.34 (d, $J = 13.5$ Hz, 1H), 1.50 (d, $J = 4.0$ Hz, 2H), 1.77–1.82 (m, 1H), 2.21 (s, 3H), 2.45 (s, 3H), 3.62 (t, $J = 9.0$ Hz, 1H), 3.70 (t, $J = 11.5$ Hz, 1H), 3.75 (s, 3H), 4.02 (t, $J = 8.5$ Hz, 1H), 4.09–4.12 (m, 2H), 4.50 (d, $J = 11.5$ Hz, 1H), 4.95 (d, $J = 2.0$ Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 2H), 6.88 (d, $J = 8.0$ Hz, 1H), 6.97 (t, $J = 7.5$ Hz, 1H), 7.17 (d, $J = 8.0$ Hz, Hz, 3H), 7.30 (t, $J = 7.5$ Hz, 1H), 8.38 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 15.97, 20.23, 23.50, 35.68, 35.74, 47.57, 52.30, 54.60, 58.03, 64.79, 67.97, 78.58, 80.07,

110.29, 122.27, 123.28, 125.68, 126.76, 127.94, 130.60, 137.47, 138.66, 143.34, 148.51, 170.22, 172.10, 176.15; ESI MS m/z: 579 $[M+H]^+$. Anal. calcd. for $C_{29}H_{30}N_4O_5S_2$: C, 60.19; H, 5.23; N, 9.68. Found: C, 60.01; H, 4.99; N, 9.78.

1′-Methyl-5″-(4-methylphenyl)-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]-pyrimidine]-4′-carboxylic acid methyl ester (2g). White solid, yield 70%, mp 227–228 °C; IR (KBr) v: 1740.2, 1719.4, 1652.1 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.96 (dd, $J_1=2.5$ Hz, $J_2=11.5$ Hz, 1H), 1.32 (d, $J=13.5$ Hz, 1H), 1.50 (d, $J=4.0$ Hz, 2H), 1.78–1.88 (m, 1H), 2.21 (s, 3H), 2.30 (s, 3H), 3.61 (t, $J=8.5$ Hz, 1H), 3.69 (t, $J=11.5$ Hz, 1H), 3.71 (s, 3H), 4.03 (t, $J=8.5$ Hz, 1H), 4.10 (dd, $J_1=4.5$ Hz, $J_2=11.5$ Hz, 1H), 4.16 (t, $J=8.5$ Hz, 1H), 4.50 (d, $J=11.5$ Hz, 1H), 4.95 (d, $J=2.0$ Hz, 1H), 6.76 (d, $J=8.0$ Hz, 2H), 6.85 (d, $J=7.5$ Hz, 1H), 6.96 (t, $J=7.5$ Hz, 1H), 7.08 (d, $J=7.5$ Hz, 2H), 7.16 (d, $J=7.5$ Hz, 1H), 7.28 (d, $J=9.0$ Hz, 1H), 8.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.24, 21.07, 23.55, 35.70, 35.73, 47.64, 52.28, 54.60, 58.21, 64.81, 67.97, 78.65, 80.09, 110.32, 122.22, 123.29, 125.65, 127.33, 129.06, 130.55, 137.03, 138.68, 143.37, 148.15, 170.23, 172.15, 176.20; ESI MS m/z: 547 $[M+H]^+$. Anal. calcd. for $C_{29}H_{30}N_4O_5S$: C, 63.72; H, 5.53; N, 10.25. Found: C, 63.61; H, 5.40; N, 10.47.

5″-[4-(Methoxycarbonyl)phenyl]-1′-methyl-2,3″-dioxo-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]-thiazolo[3,2-*a*]pyrimidine]-4′-carboxylic acid methyl ester (2h). White solid, yield 58%, mp 224–225 °C; IR (KBr) v: 1725.1, 1719.8, 1654.6 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.96 (d, $J=11.0$ Hz, 1H), 1.39 (d, $J=13.5$ Hz, 1H), 1.45–1.57 (m, 2H), 1.83–1.85 (m, 1H), 2.24 (s, 3H), 3.67 (t, $J=9.0$ Hz, 1H), 3.73 (s, 1H), 3.78 (s, 3H), 3.92 (s, 3H), 4.02 (t, $J=8.5$ Hz, 1H), 4.14–4.18 (m, 2H), 4.62 (d, $J=11.5$ Hz, 1H), 4.98 (d, $J=2.0$ Hz, 1H), 6.94–7.01 (m, 4H), 7.18 (d, $J=7.5$ Hz, 1H), 7.34 (t, $J=7.5$ Hz, 1H), 7.97 (d, $J=8.0$ Hz, 2H), 8.05 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.25, 23.45, 35.69, 35.89, 47.37, 52.13, 52.35, 54.69, 58.24, 64.77, 68.02, 78.47, 80.06, 110.25, 122.35, 123.32, 125.74, 127.56, 129.30, 129.76, 130.20, 143.27, 147.04, 149.12, 166.83, 170.25, 172.04, 175.93; ESI MS m/z: 591 $[M+H]^+$. Anal. calcd. for $C_{30}H_{30}N_4O_7S$: C, 61.00; H, 5.12; N, 9.49. Found: C, 60.93; H, 5.29; N, 9.25.

1′-Methyl-2,3″-dioxo-5″-phenyl-1,2,5*a*″,7″,8″,9*a*″-hexahydro-5″*H*,6″*H*-dispiro[indole-3,2′-pyrrolidine-3′,2″-pyrano[2,3-*d*][1,3]thiazolo[3,2-*a*]pyrimidine]-4′-carboxylic acid methyl ester (2i). White solid, yield 65%, mp 208–209 °C; IR (KBr) v: 1748.0, 1727.8, 1715.4, 1643.2 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.97 (d, $J=10.0$ Hz, 1H), 1.34 (d, $J=13.5$ Hz, 1H), 1.50 (d, $J=4.0$ Hz, 2H), 1.80–1.82 (m, 1H), 2.22 (s, 3H), 3.63 (t, $J=8.5$ Hz, 1H), 3.72 (t, $J=7.5$ Hz, 1H), 3.75 (s, 3H), 4.02 (t, $J=9.0$ Hz, 1H), 4.10–4.17 (m, 2H), 4.54 (d, $J=11.0$ Hz, 1H), 4.96 (d, $J=2.0$ Hz, 1H), 6.87 (d, $J=6.5$ Hz, 3H), 6.97 (t, $J=7.5$ Hz, 1H), 7.17 (d, $J=7.5$ Hz, 1H), 7.16–7.24 (m, 1H), 7.28–7.31 (m, 3H), 8.20 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.32, 23.57, 35.75, 35.85, 47.67, 52.34, 54.67, 58.56, 64.87, 68.04, 78.71, 80.15, 110.40, 122.27, 123.32, 125.69, 127.52, 128.47, 130.66, 141.73, 143.47, 148.51, 170.31, 172.20, 176.24; ESI MS m/z: 533 $[M+H]^+$. Anal. Calcd. for $C_{28}H_{28}N_4O_5S$: C, 63.14; H, 5.30; N, 10.52. Found: C, 63.29; H, 5.16; N, 10.88.

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14. CCDC 796436 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.