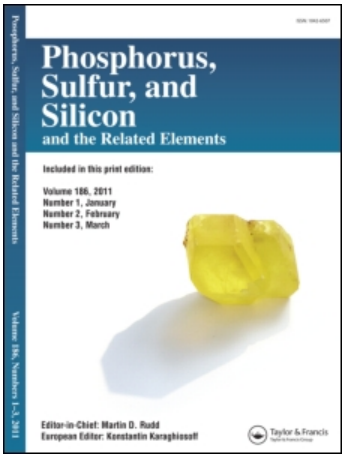

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Novel Fluorinated Spiro [Indole-indazolyl-thiazolidine]-2,4'-diones: Design and Synthesis

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Novel Fluorinated Spiro [Indole-indazolyl-thiazolidine]-2,4′-diones: Design and Synthesis

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*The reaction of indol-2,3-diones (**1a–i**) with 5-aminoindazole (**2**) has resulted in the formation of hitherto unknown 3-(indazol-5-yl)iminoindol-2-ones (**3a–i**) in quantitative yields which, on 1,3-dipolar cyclocondensation with mercaptoacetic acid (**4**), has afforded a series of new spiro heterocycles, 3′-(indazol-5-yl) spiro[3H-indol-3,2′-thiazolidine]-2,4′-diones* (**5a–i**).*

Keywords molecular modification; Schiff's bases; Spiro[indole-indazolyl-thiazolidine]-2,4′-dione

There has been increasing interest in the chemistry of spiro indoles due to their vast physicochemical properties and varied biological activities.[1–4] Of these, spiro[indol-thiazolidines] has attracted our attention because of their antiinflammatory, fungistatic, bacteriostatic, and anticonvulsant activities.[5,6] Thiazolidines themselves are of potential pharmaceutical importance[7–9] as they are known to possess antimicrobial,[10] antiinflammatory,[11] analgesic,[11] and antihistaminic[12] activities. If spiro[indol-thiazolidine] moiety is coupled with other biologically active heterocycles, the resulting system is expected to show

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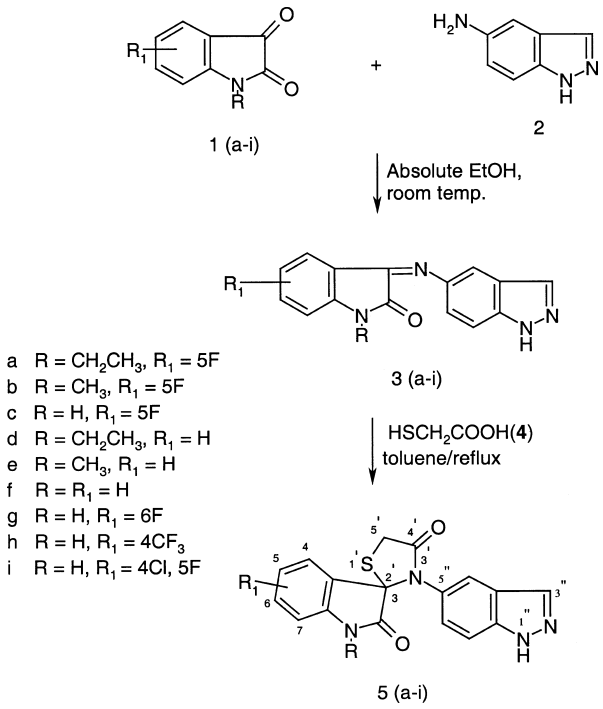
a wide spectrum of biological activities. Keeping this in mind we have earlier designed and synthesised one such system, spiro[indole-pyrazolinyl-thiazolidine]-2,4′-dione, by incorporating the pyrazoline moiety.[13,14] In the present study, we have chosen another biologically active heterocycle, indazole, which is of current interest because of its antimicrobial,[15] antiinflammatory,[16] and anthelmintic[17] activities. The antimicrobial acitvity[18] is found to increase manifold when 5-aminoindazole is used as the core scaffold. Some of the indazolo compounds are found to be more potent antiinflammatory and analgesic agents[19] than even Diclofenac Sodium. A new class of spiro indoles dispiro[oxiindole-hexahydroindazole]pyrrolidines is found to possess antibacterial and antifungal activities[20] against human pathogenic bacteria and fungi. To the best of our knowledge, no report has been cited as yet on the study of spiro-indolines containing thiazolidine and indazole moieties. Even Schiff's bases of indol-2,3-diones with 5-aminoindazole have not been earlier prepared and studied for any kind of biological activities. Besides this, fluorinated analogues of Schiff's bases and spiro compounds could be of interest as incorporation of fluorine often leads to changes in electronic environment, which causes increases in drug persistence as a result of more solubility in lipoid material and fat deposits in the body.[21]

In view of the above and in continuation to our interest in developing new spiro heterocycles of medicinal interest by molecular modification,[13,22–24] we now wish to report a facile and elegant synthesis of novel spiro heterocycles, 3′-(indazol-5-yl) spiro[3*H*-indol-3, 2′-thiazolidine]-2,4′-diones (**5a–i**) via hitherto unknown Schiff's bases, 3-(indazol-5-yl)iminoindol-2-ones (**3a–i**) in 80–95% yield. The Schiff's bases were synthesized by the reaction of indol-2,3-diones (**1a–i**) with 5-aminoindazole (**2**), which on cyclocondensation with mercaptoacetic acid, afforded the respective 3′-(indazol-5-yl)spiro[3*H*-indol-3,2′-thiazolidine]-2,4′-diones—a novel spiro system containing three biodynamic heterocyclic moieties *viz.* indole, thiazolidine, and indazole. All Schiff's bases and spiro compounds have been fully characterized on the basis of their detailed spectral studies (IR, ^{1}H, and ^{13}CNMR, and mass).

RESULTS AND DISCUSSION

We have in all synthesised nine novel 3′-(indazol-5-yl) spiro[3*H*-indol-3,2′-thiazolidine]-2,4′-diones (**5a–i**) via corresponding hitherto unknown Schiff's bases **3a–i** (Scheme 1). However, we have taken 3′-(indazol-5-yl) spiro[3*H*-1-ethyl-5-fluoroindol-3,2′-thiazolidine]-2,4′-dione (**5a**) as the reference compound for our detailed discussion



SCHEME 1

here. The reaction of 1-ethyl-5-fluoroindol-2,3-dione (**1a**) with 5-aminoindazole (**2**) (1:1) in absolute ethanol at room temperature yielded a red-colored solid **3a** which displayed molecular ion peak M^+ at m/z 308 in EIMS, corresponding to the molecular formula $C_{17}H_{13}N_4OF$, thereby indicating that the two moieties have coupled together with the loss of a water molecule. The IR spectrum showed characteristic absorption bands at 3205(>NH, indazole), 1727 (indole carbonyl) and 1648 (C=N) cm^{-1}. Also, its ^1H NMR spectrum displayed signals at δ 7.09 (H-4 & H-6) and 6.33 (H-7) showing the presence of aromatic protons of the indole moiety. A broad singlet at δ 13.12 indicated the presence of –NH proton of the indazole moiety. Further, singlets at δ 8.04 (H-3″) and δ 7.36 (H-4″) integrating for one proton each and doublets at δ 7.67 (H-6″) and δ 6.82 (H-7″) integrating also for one proton each showed the presence of indazole in the resulting compound. The protons of the N-ethyl group appeared at δ 3.88 (q) and δ 1.29 (t). ^{13}C NMR spectrum of **3a** displayed a characteristic carbonyl carbon signal at δ 162.6 (C-2) in addition to a signal at δ 143.9, confirming the presence of (C=N) at C-3 in the molecule. The above spectral studies revealed the formation

of the desired Schiff's base, which was characterised as 3-(indazol-5-yl)imino-1-ethyl-5-fluoroindol-2-one (**3a**).

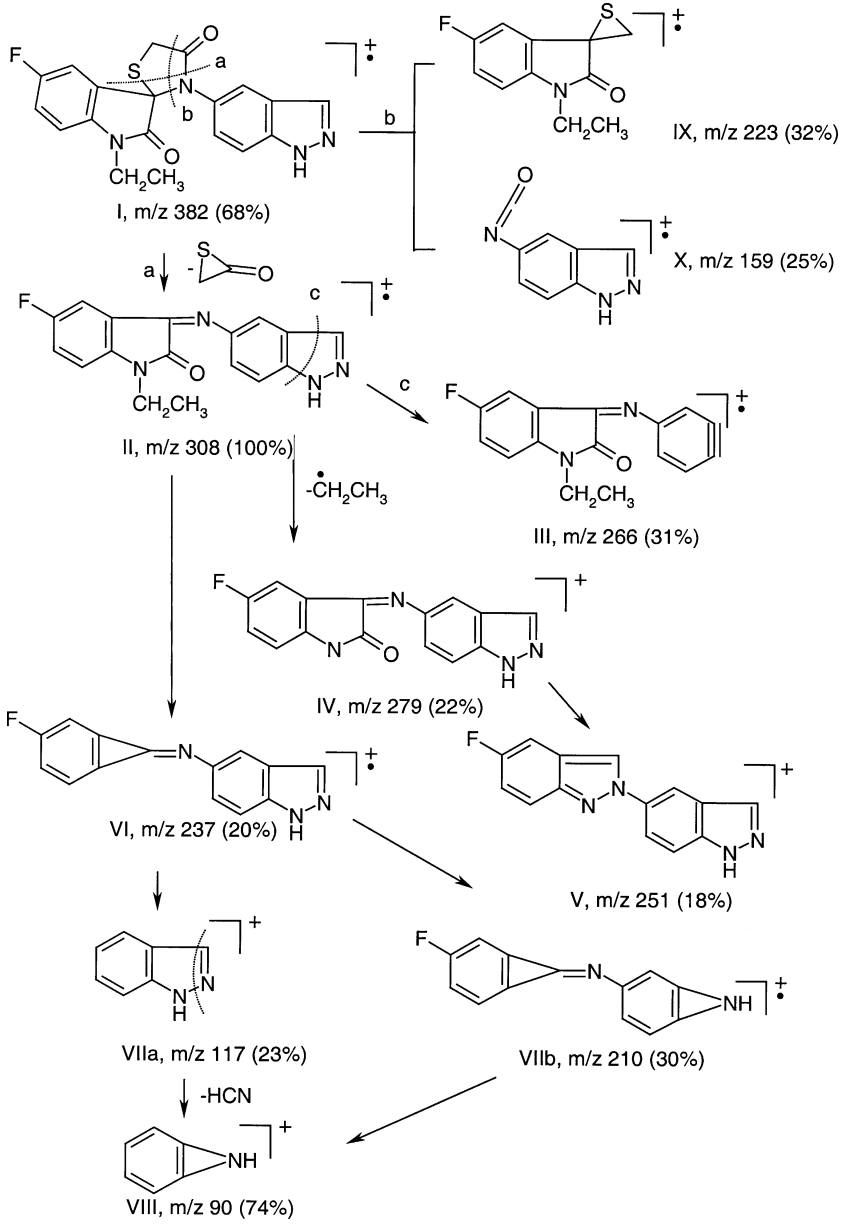
The Schiff's base **3a** on cyclocondensation with mercaptoacetic acid under refluxing conditions using Dean-Stark apparatus afforded a new compound, **5a**, whose molecular mass was found to be 382 by its FAB-MS that corresponded to the molecular formula $C_{19}H_{15}N_4O_2FS$. Its IR spectrum showed the presence of characteristic absorption peaks at 3340 cm^{-1} (>NH, indazole), 1726 (indole carbonyl) and 1708 (thiazolidine carbonyl) cm^{-1}, indicating that cycloaddition has occurred. This was further confirmed by its ^1H and ^{13}C NMR data. In the ^1H NMR spectrum of **5a**, the protons of indole nucleus appeared at δ 7.41 (H-4), δ 7.05 (H-6), and δ 6.88 (H-7) while that of indazole at δ 7.96 (H-3″), δ 7.57 (H-6″), δ 7.41 (H-4″), and δ 7.05 (H-7″). Double doublets, integrating for two geminal protons, appeared at δ 4.20 & 3.99 ($J = 15.0$ Hz each). The protons of N-ethyl group appeared at δ 3.68 (q) and δ 1.00 (t). ^{13}C NMR spectra also displayed all expected characteristic peaks at δ 174.4 (C-4′), 172.0 (C-2), δ 160.5–110.7 (aromatic carbons), δ 73.8 (C-3, spiro carbon), and δ 32.7 (C-5′). The confirmation for the methylene carbon (C-5′) and spiro carbon (C-3) has been done by DEPT-135 experiment also.

Its EIMS fragmentation pattern further supported the spiro structure for the compound **5a**. The molecular ion at *m/z* 382 can be fragmented by various plausible pathways (Scheme 2). In pathway **a**, it is decomposed by retro 1,3-dipolar addition to a neutral molecule and a radical cation the Schiff's base **3a** (II) at *m/z* 308. II eliminates a neutral molecule to give a cation radical III at *m/z*, 266. Also, II by another pathway eliminates an ethyl radical to give cation IV at *m/z*, 279, which further eliminates a neutral CO molecule to give another cation V at *m/z*, 251. The radical cation II also eliminates a neutral molecule (CH_3CH_2—N═C═O) to give another radical cation VI at *m/z*, 237, which finally gave VIII at *m/z* 90 either via VIIa at *m/z*, 117 or VIIb at *m/z* 210. The peaks observed at *m/z* 223 and *m/z* 159 can be explained if the molecular ion (I) fragments via pathway **b** (Scheme 2).

Thus, on the basis of above spectral studies, the structure of **5a** was confirmed as 3′-(indazol-5-yl) spiro[3*H*-1-ethyl-5-fluoroindol-3,2′-thiazolidine]-2,4′-dione.

EXPERIMENTAL

Melting points were determined in a capillary tube in sulphuric acid bath and are uncorrected. IR spectra were recorded on a Shimadzu model IR-435 spectrophotometer using KBr discs. ^1H NMR spectra were recorded on a Bruker AC (300 MHz) in DMSO-d_6. ^{13}C NMR were



SCHEME 2

TABLE I Spectral Data of Compounds (3a–i)

Compound	Yield (%)	m.p.(°C)	EIMS m/z (major fragments)	^{1}H NMR(δ, DMSO-d_6)	^{13}C NMR (δ, DMSO-d_6)
3a	81	238–240	308 (M^+), 279, 266, 251, 237, 210, 117, 90	13.12 (s, 1H, >NH, indazole), 8.04 (s, 1H, H-3″), 7.67 (d, 1H, $J=8.5$ Hz, H-6″), 7.36 (s, 1H, H-4″), 7.09 (m, 2H, H-4 & H-6), 6.82 (d, 1H, $J=8.5$ Hz, H-7″), 6.33 (d, 1H, $J=8.1$ Hz, H-7), 3.88 (q, 2H, N—**CH**$_2$CH$_3$), 1.29 (t, 3H, N—CH$_2$**CH**$_3$)	162.6 (C-2), 159.1, 156.0, 143.9 (C-3), 142.5, 139.1, 133.9, 122.1, 121.0, 120.7, 118.8, 112.3 112.1, 111.1, 108.3, 35.4 (N—**CH**$_2$CH$_3$), 13.3 (N—CH$_2$**CH**$_3$)
3b	82	174–175	294 (M^+), 279, 252, 251, 237, 177, 163, 117, 90	13.13 (s, 1H, >NH, indazole), 8.05 (s, 1H, H-3″), 7.65 (d, 1H, $J=9.0$ Hz, H-6″), 7.34 (s, 1H, H-4″), 7.05 (m, 2H, H-4 & H-6), 6.78 (d, 1H, $J=9.0$ Hz, H-7″), 6.30 (d, 1H, $J=8.3$ Hz, H-7), 3.32 (s, 3H, N—CH$_3$)	162.9 (C-2), 159.4, 156.3, 144.6 (C-3), 142.2, 139.5, 134.5, 122.5, 121.5, 121.8, 119.1, 112.6, 112.4, 111.6, 108.8, 26.7 (N—CH$_3$)
3c	93	>280	280 (M^+), 279, 251, 237, 117, 90	12.97 (s, 1H, >NH, indazole), 10.84 (s, 1H, >NH, indole), 8.02 (s, 1H, H-3″), 7.62 (d, 1H, $J=8.4$ Hz, H-6″), 7.35 (s, 1H, H-4″), 7.06 (m, 2H, H-4 & H-6), 6.88 (d, 1H, $J=8.4$ Hz, H-7″), 6.32 (d, 1H, $J=7.3$ Hz, H-7)	164.9 (C-2), 159.4, 156.2, 145.1 (C-3), 143.8, 139.1, 134.3, 123.8, 122.6, 121.1, 119.4, 112.9, 112.5, 111.9, 109.0
3d	90	203–205	290 (M^+), 261, 248, 233, 219, 117, 90	12.88 (s, 1H, >NH, indazole), 8.00 (s, 1H, H-3″), 7.60 (d, 1H, $J=9.0$ Hz, H-6″), 7.36 (m, 2H, H-4″ and H-6), 7.08 (d, 1H, $J=8.8$ Hz, H-4), 6.96 (d, 1H, $J=9.0$ Hz, H-7″), 6.70 (m, 2H, H-5 & H-7), 3.86 (q, 2H, N—**CH**$_2$CH$_3$), 1.33 (t, 3H, N—CH$_2$**CH**$_3$)	163.1 (C-2), 154.9, 147.9 (C-3), 143.6, 134.4, 133.9, 126.0, 124.9, 123.8, 123.0, 122.7, 119.5, 111.7, 109.9, 108.8, 35.1 (N—**CH**$_2$CH$_3$), 13.0 (N—CH$_2$**CH**$_3$)

(Continued on next page)

TABLE I Spectral Data of Compounds (3a–i) *(Continued)*

Compound	Yield (%)	m.p.(°C)	EIMS m/z (major fragments)	^{1}H NMR(δ, DMSO-d$_6$)	^{13}C NMR (δ, DMSO-d$_6$)
3e	89	146–148	276 (M^+), 261, 233, 219, 117, 90	13.19 (s, 1H, >NH, indazole), 8.08 (s, 1H, H-3″), 7.65 (d, 1H, $J=8.4$ Hz, H-6″), 7.49 (t, 1H, H-6), 7.40 (m, 2H, H-4 & H-4″), 7.09 (d, 1H, $J=8.4$ Hz, H-7″), 6.73 (t, 1H, H-5), 6.50 (d, 1H, $J=7.5$ Hz, H-7), 3.21 (s, 3H, N—CH$_3$)	162.8 (C-2), 154.4, 148.1 (C-3), 143.5, 134.4, 133.9, 124.9, 123.1, 122.5, 122.3, 122.0, 119.1, 111.7, 110.3, 109.6, 26.4 (N—CH$_3$)
3f	80	>280	262 (M^+), 233, 220, 219, 209, 163, 117, 90	12.74 (s, 1H, >NH, indazole), 10.66 (s, 1H, >NH, indole), 8.00 (s, 1H, H-3″), 7.59 (d, 1H, $J=8.7$ Hz, H-6″), 7.34 (s, 1H, H-4″), 7.25 (t, 1H, H-6), 7.07 (d, 1H, $J=8.8$ Hz, H-4), 6.89 (d, 1H, $J=8.7$ Hz, H-7″), 6.65 (m, 2H, H-5 & H-7)	163.4 (C-2), 154.4, 148.3 (C-3), 143.8, 139.8, 135.3, 126.9, 126.3, 124.3, 123.1, 120.5, 120.3, 112.9, 112.6, 109.7
3g	84	>280	280 (M^+), 251, 238, 117, 90	13.09 (s, 1H, >NH, indazole), 11.07 (s, 1H, >NH, indole), 7.98 (s, 1H, H-3″), 7.62 (d, 1H, $J=8.4$ Hz, H-6″), 7.33 (s, 1H, H-4″), 7.05 (d, 1H, $J=8.7$ Hz, H-5), 6.68 (d, 1H, $J=8.4$ Hz, H-7″), 6.57 (m, 1H, H-7), 6.43 (m, 1H, H-4)	167.7 (C-2), 164.8, 154.3, 150.0 (C-3), 143.7, 139.0, 134.4, 128.2, 123.9, 119.4, 113.3, 112.0, 110.3, 108.9, 100.4
3h	89	>280	330 (M^+), 302, 287, 273, 117, 90	13.02 (s, 1H, >NH, indazole), 11.02 (s, 1H, >NH, indole), 8.03 (s, 1H, H-3″), 7.56 (d, 1H, $J=8.4$ Hz, H-6″), 7.47 (s, 1H, H-4″), 7.32 (m, 1H, H-5), 7.17 (d, 1H, $J=8.4$ Hz, H-7″), 7.02 (m, 1H, H-6), 6.72 (m, 1H, H-7)	165.2 (C-2), 159.3, 155.7, 154.9, 152.3, 146.8 (C-3), 139.2, 135.7, 134.8, 128.5, 126.4, 122.1, 115.7, 112.0,113.4, 109.3
3i	93	>280	316 (M^++2), 314 (M^+), 286, 272, 182, 117, 90	13.25 (s, 1H, >NH, indazole), 11.00 (s, 1H, >NH, indole), 8.12 (s, 1H, H-3″), 7.67 (d, 1H, $J=8.7$ Hz, H-6″), 7.43 (s, 1H, H-4″), 7.12 (d, 1H, $J=8.6$ Hz, H-6), 7.06 (d, 1H, $J=8.7$ Hz, H-7″), 6.35 (d, 1H, $J=8.6$ Hz, H-7)	166.2 (C-2), 161.1, 156.2, 155.9, 153.0, 146.5 (C-3), 145.0, 136.8, 136.7, 125.4, 124.7, 121.5, 115.4, 114.6, 111.3

TABLE II Spectral Data of Compounds (5a–i)

Compound	Yield (%)	m.p.(°C)	EIMS m/z (major fragments)	^{1}H NMR(δ, DMSO-d$_6$)	^{13}C NMR (δ, DMSO-d$_6$)
5a	83	246–248	382 (M^+), 308, 279, 266, 251, 237, 223, 159, 117, 90	13.06 (s, 1H, >NH, indazole), 7.96 (s, 1H, H-3″), 7.57 (d, 1H, $J=7.7$ Hz, H-6″), 7.41 (m, 2H, H-4 & H-4″), 7.05 (m, 2H, H-6 & H-7″), 6.88 (m, 1H, H-7), 4.20 and 3.99 (d, 2H, $J=15.0$ Hz each, 2xH-5′), 3.68 (q, 2H, N—**CH**$_2$CH$_3$), 1.00 (t, 3H, N—CH$_2$**CH**$_3$)	174.4 (C-4′), 172.0 (C-2), 160.5, 157.3, 139.2, 138.3, 135.4, 133.9, 128.4, 126.6, 123.0, 120.9, 117.7, 114.5, 110.7, 73.8 (C-3), 35.0 (N—**CH**$_2$CH$_3$), 32.7 (C-5′), 12.1 (N—CH$_2$**CH**$_3$)
5b	90	>280	368 (M^+), 340, 294, 266, 209, 159, 117, 90	12.95 (s, 1H, >NH, indazole), 7.97 (s, 1H, H-3″), 7.58 (d, 1H, $J=7.2$ Hz, H-6″), 7.43 (m, 2H, H-4 & H-4″), 7.06 (m, 2H, H-6 & H-7″), 6.86 (m, 1H, H-7), 4.22 and 3.99 (d, 2H, $J=15.3$ Hz each, 2xH-5′), 3.10 (s, 3H, N—CH$_3$)	174.5 (C-4′), 171.9 (C-2), 160.4, 157.2, 139.1, 136.0, 133.7, 128.3, 126.4, 122.9, 120.8, 117.7, 114.1, 110.9, 110.5, 69.6 (C-3), 32.4 (C-5′), 26.6 (N—CH$_3$)
5c	88	>280	354 (M^+), 335, 280, 251, 238, 195, 159, 117, 90	13.02 (s, 1H, >NH, indazole), 10.60 (s, 1H, >NH indole), 8.08 (s, 1H, H-3″), 7.45 (s, 1H, H-4″), 7.41 (m, 2H, H-4 & H-6″), 7.04 (d, 1H, $J=7.5$ Hz, H-7″), 6.93 (m, 1H, H-6), 6.68 (m, 1H, H-7), 4.20 and 3.93 (d, 2H, $J=15.0$ Hz each, 2xH-5′)	176.5 (C-4′), 172.1 (C-2), 160.1, 156.9, 139.3, 138.0, 133.9, 128.6, 126.6, 123.0, 120.9, 117.8, 114.2, 111.8, 110.9, 70.1 (C-3), 32.6 (C-5′)
5d	91	>280	364 (M^+), 336, 290, 248, 233, 219, 205, 159, 131, 117, 90	13.25 (s, 1H, >NH, indazole), 7.89 (s, 1H, H-3″), 7.58 (d, 1H, $J=7.3$ Hz, H-6″), 7.36 (m, 2H, H-4 and H-4″), 7.24 (t,1H, H-6), 7.06 (t, 1H, H-5), 6.94 (d, 1H, $J=9.0$ Hz, H-7), 6.80 (d, 1H,$J=7.3$ Hz, H-7″), 4.24 and 3.93 (d, 2H, $J=15.3$ Hz each, 2xH-5′), 3.77 (q, 2H, N—**CH**$_2$CH$_3$), 1.05 (t, 3H, N—CH$_2$**CH**$_3$)	174.6 (C-4′), 172.1 (C-2), 142.3, 139.2, 133.7, 131.2, 128.5, 126.6, 126.5, 124.8, 123.2, 122.9, 120.8, 110.8, 109.3, 70.2 (C-3), 34.8 (N—**CH**$_2$CH$_3$), 32.7 (C-5′), 12.1 (N—CH$_2$**CH**$_3$)

(Continued on next page)

TABLE II Spectral Data of Compounds (5a–i) *(Continued)*

Compound	Yield (%)	m.p.(°C)	EIMS m/z (major fragments)	^{1}H NMR(δ, DMSO-d_6)	^{13}C NMR (δ, DMSO-d_6)
5e	96	>280	350 (M^+), 276, 219, 233, 191, 159, 117, 90	13.17 (s, 1H, >NH, indazole), 7.91 (s, 1H, H-3″), 7.59 (d, 1H, J = 7.3 Hz, H-6″), 7.37 (m, 2H, H-4 & H-4″), 7.25 (t, 1H, H-6), 7.07 (t, 1H, H-5), 6.95 (d, 1H, J = 9.1 Hz, H-7), 6.80 (d, 1H, J = 7.3 Hz, H-7″), 4.25 and 3.92 (d, 2H, J = 15.3 Hz each, 2xH-5′), 3.11 (s, 3H, N—CH_3)	174.5 (C-4′), 171.9 (C-2), 143.0, 139.0, 133.5, 130.9, 128.3, 126.2, 126.0, 124.2, 123.0, 122.7, 120.5, 110.6, 109.0, 69.6 (C-3), 32.4 (C-5′), 26.3 (N—CH_3)
5f	90	>280	336 (M^+), 308, 262, 234, 219, 177, 159, 117, 90	12.88 (s, 1H, >NH, indazole), 10.47 (s, 1H, >NH, indole), 7.88 (s, 1H, H-3″), 7.49 (d, 1H, J = 7.3 Hz, H-6″), 7.41 (s, 1H, H-4″), 7.37 (d, 1H, J = 8.9 Hz, H-4), 7.14 (t, 1H, H-6), 6.99 (m, 2H, H-5 & H-7), 6.68 (d, 1H, J = 7.3 Hz, H-7″), 4.25 and 3.87 (d, 2H, J = 15.3 Hz each, 2xH-5′)	174.8 (C-4′), 172.4 (C-2), 142.5, 139.4, 133.9, 131.5, 128.9, 126.7, 126.6, 125.0, 123.6, 123.0, 121.0, 111.0, 109.8, 69.7 (C-3), 32.8 (C-5′)
5g	87	>280	354 (M^+), 335, 280, 237, 195, 159, 117, 90	12.98 (s, 1H, >NH, indazole), 10.69 (s, 1H, >NH indole), 7.93 (s, 1H, H-3″), 7.48 (m, 3H, H-5, H-4″ & H-6″), 6.99 (d, 1H, J = 7.5 Hz, H-7″), 6.73 (m, 1H, H-7), 6.47 (d, 1H, J = 8.8 Hz, H-4), 4.19 & 3.94 (d, 2H, J = 15.2 Hz, 2xH-5′)	175.9 (C-4′), 171.7 (C-2), 160.3, 156.5, 139.1, 137.6, 133.5, 128.1, 126.0, 123.4, 120.2, 117.2, 114.0, 111.2, 110.5, 71.2 (C-3), 32.1 (C-5′)
5h	78	>280	404 (M^+), 330, 301, 273, 117, 90	12.90 (s, 1H, >NH, indazole), 10.81 (s, 1H, >NH indole), 8.17 (s, 1H, H-3″), 7.51 (d, 1H, J = 7.4 Hz, H-6″), 7.43 (s, 1H, H-4″), 7.23 (m, 1H, H-6), 7.07 (d, 1H, J = 7.4 Hz, H-7″), 6.81 (m, 2H, H-5 & H-7), 4.21 & 3.96 (d, 2H, J = 15.3 Hz, 2xH-5′)	174.9 (C-4′), 172.3 (C-2), 159.9, 155.8, 139.4, 138.9, 134.1, 127.7, 126.4, 121.1, 120.4, 117.5, 115.8, 114.8, 110.9, 110.2, 69.4 (C-3), 32.7 (C-5′)
5i	91	>280	390 (M^++2), 388 (M^+), 358, 314, 272, 230, 182, 159, 117, 90	13.08 (s, 1H, >NH, indazole), 10.70 (s, 1H, >NH, indole), 7.95 (s, 1H, H-3″), 7.56 (d, 1H, J = 8.0 Hz, H-6″), 7.43 (m, 2H, H-4″ & H-6), 7.03 (d, 1H, J = 8.0 Hz, H-7″), 6.76 (d, 1H, J = 7.1 Hz, H-7), 4.20 and 3.94 (d, 2H, J = 15.0 Hz, 2xH-5′)	175.8 (C-4′), 171.6 (C-2), 159.4, 155.1, 151.1, 138.9, 138.1, 133.4, 128.0, 126.1, 122.6, 120.5, 114.6, 112.0, 110.7, 69.7 (C-3), 32.2 (C-5′)

recorded on Bruker AC (75.47 MHz) in DMSO-d_6. Mass spectra were recorded on Jeol-JMS-DX 303 mass spectrometer. Substituted indol-2,3-diones were prepared by literature procedures starting from the corresponding anilines.[13]

General Procedure for the Synthesis of 3-(Indazol-5-yl) Imino-1-ethyl-5-fluoroindol-2-one (3a)

A mixture of 1-ethyl-5-fluoroindol-2,3-dione (**1a**) (193 mg, 1 mmol) and 5-aminoindazole (**2**) (133 mg, 1 mmol) in absolute ethanol (20 mL) was stirred at room temperature. A red-colored solid that separated after 4 h was filtered, dried, and recrystallized from ethanol to give Schiff's base **3a** as red crystals. Compounds **3b–i** were also synthesised by following this procedure. The spectral data recorded for compounds **3a–i** is listed in Table I.

General Procedure for the Synthesis of 3′-(Indazol-5-yl) Spiro[3*H*-1-ethyl-5-fluoroindol-3,2′-thiazolidine]-2,4′-dione (5a)

A mixture of 3-indolylimine (**3a**) (154 mg, 0.5 mmol) and mercaptoacetic acid (**4**) (55 mg, 0.6 mmol) was refluxed in dry toluene for 8 h with simultaneous removal of water azeotropically using Dean-Stark apparatus. Solution turned light yellow after 1 h and a sticky yellow solid was formed. The solvent was removed under reduced pressure and the residue left was treated with a saturated solution of sodium bicarbonate to remove the unreacted acid. The solid left was filtered, washed, dried, and then crystallized from methanol-chloroform mixture to obtain **5a** as colorless crystals. Compounds **5b–i** were also synthesised by following the similar procedure as above. The spectral data for compounds **5a–i** is recorded as in Table II.

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