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Carbon–SO_3H: a novel and recyclable solid acid catalyst for the synthesis of spiro[4*H*-pyran-3,3′-oxindoles]

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ABSTRACT

A bioglycerol derived carbon-sulfonic acid is found to catalyze efficiently the three-component one-pot condensation of isatin, malononitrile, and 1,3-dicarbonyls to afford a wide range of spiro[4H-pyran-3,3′-oxindole]derivatives in good yields and selectivity. The use of a recyclable solid acid catalyst makes this method simple, convenient, and cost-effective.

The spirooxindoles are frequently found in many alkaloids and pharmaceuticals with promising biological activities (Fig. 1).[1–3]

Furthermore, these spirocycles possess anticancer and antimicrobial activity.[4] They are also known to exhibit anticonvulsant, analgesic,[5] herbicidal,[6] fungicidal[7,8], and antibacterial properties.[9] As a result, several synthetic approaches have been developed for the synthesis of multi-stereogenic spirooxindoles.[10] A variety of catalysts such as L-proline,[11] triethylamine,[12] ethylenediamine diacetic acid,[13] piperidine,[14] porcine pancreas lipase,[15] triethanolamine,[16] and 1-*N*-butyl-3-methyl-imidazolium tetrafluoroborate[17] have been reported for the synthesis of spiro[4*H*-pyran-3,3′-oxindole] derivatives.[11–17] Other catalysts such as sodium octadecanoate, TBAF, TPP, and potassium tetrachloroaurate trihydrate have also been reported for this conversion.[18–20] More recently, MgO has been employed as a recyclable heterogeneous catalyst.[21] In recent years, carbon-based solid acid catalysts[22] have attracted significant attention as they are highly efficient, sustainable, and eco-friendly. Of these, bioglycerol- based sulfonic acid functionalized polycyclic aromatic carbon catalyst reported by Prabhavathi et al.[23] has gained lot of attraction due to its high stability, reactivity, recyclability, and also sustainable preparation protocol.[24] The catalyst was prepared from bioglycerol (a by-product of biodiesel) and also from glycerol pitch (waste from fat splitting industry) by in situ partial carbonization and sulfonation in a one-pot operation.

This solid acid catalyst has opened a new avenue in the field of green catalysis by demonstrating its effectiveness for various transformations.[23,25] Therefore, the use of cost-effective solid acids would make the process more practical in view of environmental perception. Following our interest on the catalytic application of solid acid catalysts,[26] we herein report a simple and highly efficient approach for the synthesis of spirooxindoles from isatin, malononitrile, and α-methylenecarbonyl compounds using glycerol-based carbon-sulfonic acid as a recyclable catalyst. The carbon catalyst was fully characterized by CHN analysis, XRD, XPS, IR, ^{13}C NMR, Mass, and Raman spectroscopy to establish its physico-chemical characteristics.[23b,25b] Elemental composition of the catalyst was found to be $CH_{0.74}S_{0.02}O_{0.51}$ with 1.6 mmol/g of acid density and

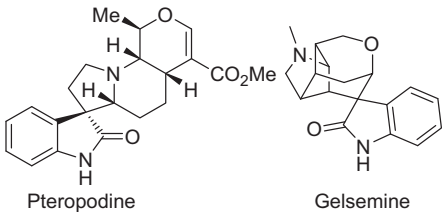

Figure 1. Naturally occurring spirooxindoles.

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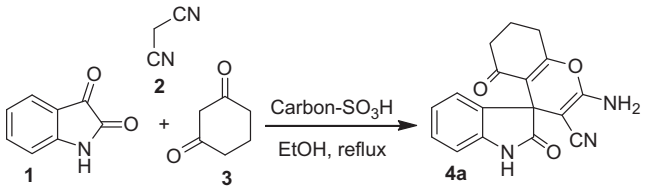


Scheme 1. Three-component reaction for the synthesis of **4a**.

Table 1
Screening of solid acid catalysts in the formation of 4a

Entry	Catalyst	Time (h)	Yield (%)
a	Amberlyst-15	12	20
b	Montmorillonite K10	18	15
c	Phosphomolybdic acid	8	65
d	Cellulose–SO3H	6	50
e	Silica–SO3H	4	60
f	Carbon–SO3H	3	94

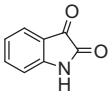
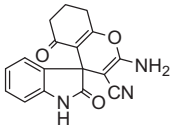
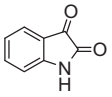
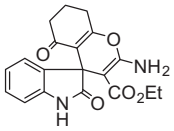
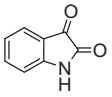
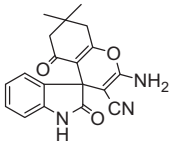
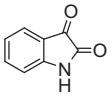
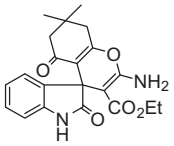
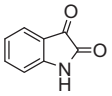
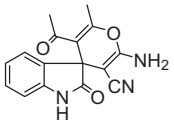
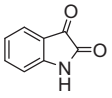
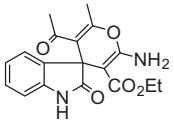
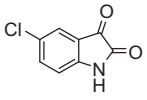
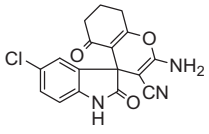
surface area of 0.21 m^2/g. All the physico-chemical characterization studies indicate that the carbon catalyst is a partially crystalline material consisting of polycyclic aromatic carbon sheets with $-SO_3H$, –COOH, and –OH functional groups as reported for other carbon-based catalysts.[22,23]

As a model reaction, we attempted the coupling of isatin (**1**), malononitrile (**2**), and 1,3-cyclohexadione (**3**) in ethanol in the presence of 10 w/w% of carbon acid catalyst at room temperature. Though the reaction was sluggish at 25 °C, it proceeded well at 80 °C to furnish the desired product **4a** in 94% yield (Scheme 1).

To optimize the reaction conditions, the above experiment was performed in various solvents including tetrahydrofuran, acetonitrile, water, 1,4-dioxane, dimethylformamide, ethanol, and chloroform. Of these solvents, ethanol appears to give the best results. Subsequently, the effect of various solid acids such as montmorillonite K10, ion-exchange resin, heteroploy acids, cellulose-sulfonic acid, and silica sulfonic acid was studied. To our surprise, acidic ion-exchange resin and montmorillonite K10 clay afforded the product **4a** in low yields (Table 1, entries a and b). Other solid acids like phosphomolybdic acid, cellulose-sulfonic acid, and silica-sulfonic acid also gave the product **4a** in moderate yields (Table 1, entries c, d, and e). Among them, carbon-sulfonic acid was found to be superior in terms of conversion (Table 1, entry f).

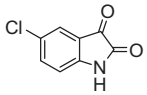
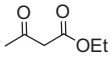
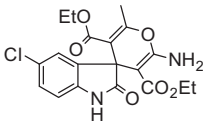
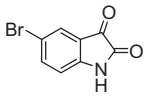
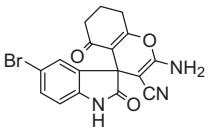
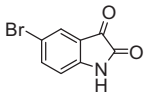
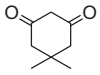
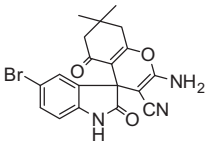
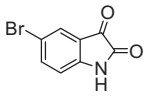
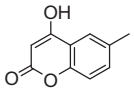
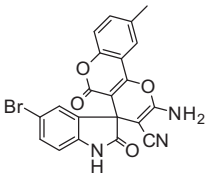
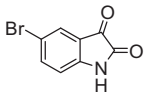
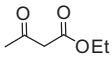
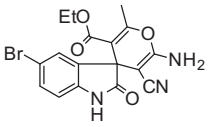
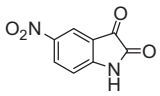
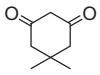
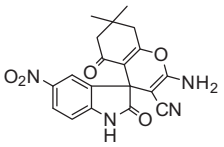
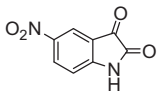
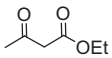
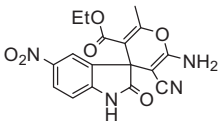
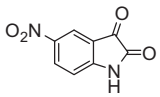
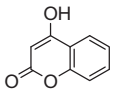
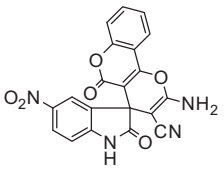
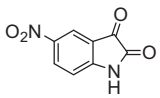
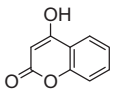
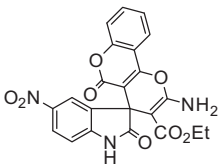
Interestingly, several substituted isatins such as 5-chloro-, 5-bromo-, and 5-nitro- derivatives gave the products in excellent yields under optimized reaction conditions (Table 2). Besides malononitrile,

Table 2
Carbon-sulfonic acid catalyzed synthesis of spiropyrans

Entry	Isatin	Malononitrile (**2**)	1,3-Diketone (**3**)	Product (**4**)[a]	Time (h)	Yield[b]
a					3.0	94
b					3.0	92
c					3.0	81
d					4.0	78
e					3.0	85
f					3.0	87
g					4.5	92

(*continued on next page*)

Table 2 (*continued*)

Entry	Isatin	Malononitrile (**2**)	1,3-Diketone (**3**)	Product (**4**)[a]	Time (h)	Yield[b]
h					3.0	88
i					3.0	85
j					5.0	82
k					5.0	85
l					5.0	89
m					6.0	90
n					6.0	88
o					5.0	86
p					5.0	85

[a] All products were characterized by NMR, IR, and mass spectrometry.
[b] Yield refers to pure products after chromatography.

the reaction was also successful with ethyl cyanoacetate. As shown in Table 2, various cyclic and acyclic 1,3-diketones or β-ketoesters and 4-hydroxycoumarin participated well in this reaction (Table 2).[27]

Inspired by the results obtained with 1,3-diketones, we turned our attention to study the reactivity of acenaphthenequinone (**5**) with malononitrile and ethyl cyanoacetate. The reaction proceeded smoothly under similar conditions affording the corresponding spiro-acenaphthylene derivatives in excellent yields and selectivity (Table 3, entries a–d).

Next we extended our efforts to examine the reactivity of 3-methyl-1*H*-pyrazol-5(4*H*)-ones. As shown in Table 4, numerous spiro[indoline-3,4′-pyrano[2,3-*c*]pyrazole] derivatives (**8**) were prepared by using this approach. To know the catalytic effect of carbon sulfonic acid, the reaction was performed without the catalyst. However, no desired product was obtained in the absence of catalyst even in refluxing ethanol. The use of solid acid catalyst makes this method quite simple and more convenient to prepare a variety of spiropyrans in a single-step process.

A sequence of reactions such as Knoevenagel reaction, Michael reaction followed by Thorpe–Ziegler reaction takes place during the formation of the product. Mechanistically, the reaction was proposed to proceed through the activation of isatin by carbon-

Table 3
Carbon-sulfonic acid catalyzed synthesis of spiroacenaphthylenes

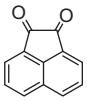
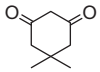
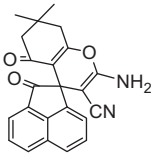
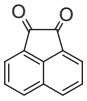
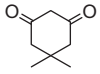
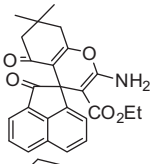
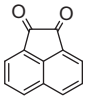
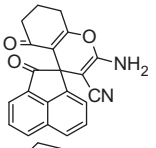
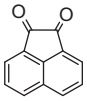
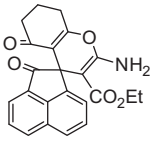
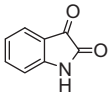
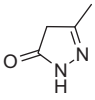
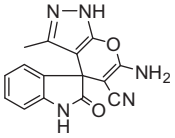
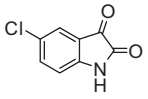
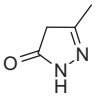
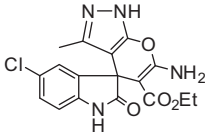
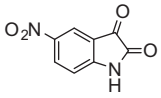
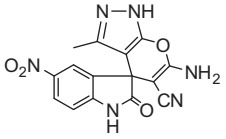
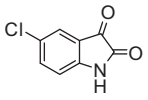
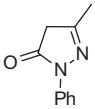
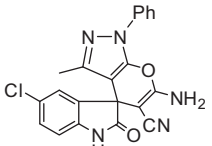
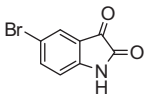
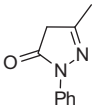
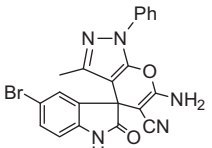
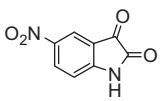
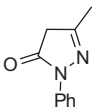
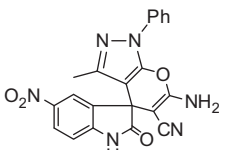
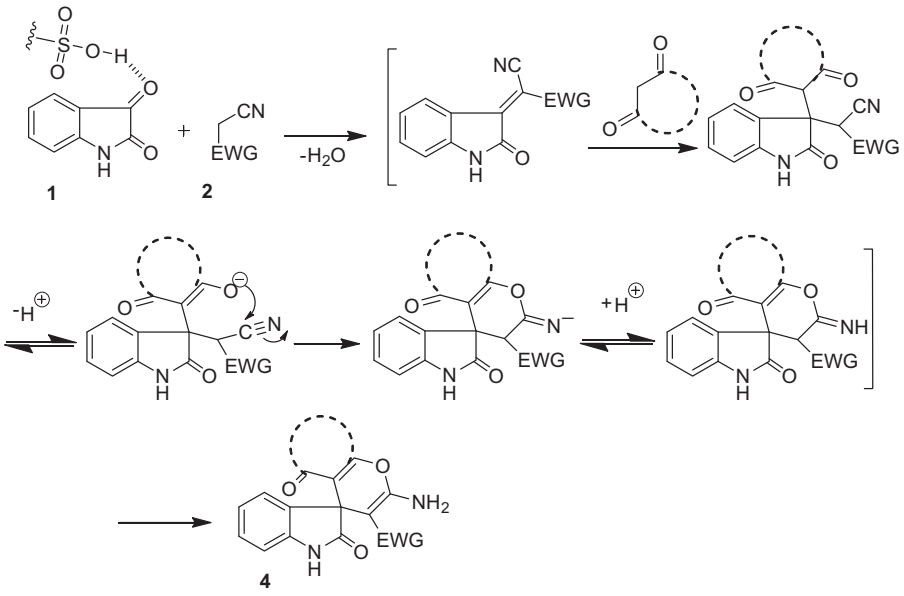
Entry	Acenaphthe quinone (**5**)	Malononitrile (**2**)	1,3-Diketone (**3**)	Product (**6**)	Time (h)	Yield (%)
a					3.0	91
b					3.5	90
c					3.0	93
d					3.0	92

Table 4
Carbon-sulfonic acid catalyzed synthesis of spiropyrans with pyrazoles

Entry	Isatin(1)	Malonoitrile(2)	1,3-Diketone(7)	Product (**8**)	Time (h)	Yield (%)
a					5.0	90
b					5.0	92
c					5.0	92
d					5.0	94
e					5.0	95
f					5.0	94



Scheme 2. A plausible reaction mechanism.

sulfonic acid to generate α,β-unsaturated dicyano adduct. Subsequent 1,4-addition of 1,3-dione on α,β-unsaturated dicyano adduct followed by an intramolecular cyclization of the adduct through [1,3]-sigmatropic proton shift of the iminopyrans led to the formation of a stable 2-amino-4*H*-pyran ring system. In the presence of both nitrile and ester groups, the nucleophilic addition of enolic oxygen occurs predominantly to nitrile rather than to the ester group affording the desired 2-amino-4*H*-pyran. This predominance can be explained by the higher electrophilicity and lower steric hindrance of the nitrile group toward nucleophilic addition compared to ester functionality. Thus the formation of 2-amino-4*H*-pyran ring is highly regioselective (Scheme 2).[12]

Finally, the reusability of the carbon acid catalyst was checked by performing the reaction of isatin, malononitrile, and 1,3-cyclohexadione using the recovered catalyst. The desired product **3a** was isolated in 94%, 93%, 90%, 89%, and 85% yields over five cycles with a gradual decrease of activity.

In summary, bioglycerol derived carbon-sulfonic acid has proved to be a highly efficient solid acid catalyst for the synthesis of spiro[4*H*-pyran-3,3′-oxindole] derivatives by means of the Knoevenagel/Michael/cyclization reaction. The major advantages of the present method are high conversions, low cost, and recyclability of the catalyst, which makes this method more attractive.

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hot water until the washings indicated a neutral pH. The partially crystalline product was filtered and dried till it was moisture-free to afford bioglycerol based carbon catalyst (4 g).

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27. *General procedure for the preparation of spiro[4H-pyran-3,3′-oxindole]derivatives*: A mixture of isatin (1 mmol), malononitrile or cyanoacetic esters (1 mmol), 1,3-dicarbonyl compounds (1 mmol), and the catalyst (10 wt %) in ethanol (3 ml) was stirred at 80 °C for a specified time (see Table 2). After complete conversion, as indicated by TLC, the reaction mixture was cooled to room temperature. The resulting solid precipitate was filtered and dried along with the catalyst. Further purification of the product was performed by recrystallization using ethanol and the catalyst was recovered by filtration.
(**4a**)*2-Amino-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chro-mene-4,3′-indoline]-3-carbonitrile*: Solid, mp 278–280 °C (dec). IR (KB**r**): ν_{max} 3370, 3286, 3132, 2191, 1709, 1680, 1655, 1630, 1471, 1351, 1211, 1076, 1011 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.92 (t, J = 6.4 Hz, 2H), 2.27–2.16 (m, 2H, CH_2), 2.66 (t, J = 6.2 Hz, 2H, CH_2), 6.80 (d, J = 7.5 Hz, 1H, ArH), 6.90 (t, J = 7.6 Hz, 1H, ArH), 7.05 (d, J = 7.2 Hz, 1H, ArH), 7.14 (t, J = 7.6 Hz, 1H, ArH), 7.23 (s, 2H), 10.42 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 20.3, 27.4, 37.0, 47.5, 58.2, 109.8, 112.5, 118.0, 122.3, 123.8, 128.8, 135.2, 142.5, 158.9, 166.7, 178.8, 195.7, 37.8, 41.3, 71.4, 72.7, 74.4, 75.7, 125.9, 127.5, 128.3, 128.4, 130.1, 133.6; ESI-MS: m/z 307.
(**4g**) *2-Amino-5′-chloro-2′,5-dioxo-5,6,7,8-tetrahydro-spiro[chromene-4,3′-indoline]-3-carbonitrile:* Solid, mp 294–296 °C (dec). IR (KBr): ν_{max} 3364, 3247, 3175, 2193, 1719, 1681, 1477, 1350, 1219, 1079, 1011 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.90–2.01 (m, 2H, CH_2), 2.23 (t, J = 6.8 Hz, 2H, CH_2), 2.66 (t, J = 6.4 Hz, 2H, CH_2), 6.80 (d, J = 8.4 Hz, 1H, ArH), 7.16 (d, J = 2.0 Hz, 1H, ArH), 7.26 (dd, J = 2.0, 8.0 Hz, 1H, ArH), 7.33(s, 2H), 10.55 (s, 1H, NH). ESI-MS: m/z 341.
(**4d**) *Ethyl 2-amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahy-drospiro[chromene-4,3′-indoline]-3-carboxylate*: Solid, mp 258–260 °C; IR (KBr): ν_{max} 3370, 3236, 3180, 2957, 1715, 1690, 1670, 1648, 1615, 1525, 1470, 1344, 1316, 1289, 1220, 11664, 1055, 905, 785, 745 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 0.81 (t, J = 7.2 Hz, 3H, CH_3), 0.95 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.98–2.15 (m, 2H, CH_2), 2.45–2.62 (m, 2H, CH_2), 3.63–3.73 (m, 2H, CH_2O), 6.67 (d, J = 7.6 Hz, 1H, ArH), 6.76 (t, J = 7.2 Hz, 1H, ArH), 6.84 (d, J = 7.2, Hz, 1H, ArH), 7.03–7.07 (m, 1H, ArH), 7.87 (s, 2H, NH_2), 10.15 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 13.7, 27.3, 28.4, 32.2, 47.2, 51.3, 59.5, 76.9, 108.8, 113.7, 121.2, 122.9, 127.8, 136.6, 144.7, 159.7, 160.8, 163.0, 168.3, 180.4, 195.3; ESI-MS: m/z 405.
(**4n**) *(Ethyl 2′-amino-3′-cyano-6′-methyl-5-nitro-2-oxosp-iro[indoline-3,4′-pyran]-5′-carboxylate*: mp 244–246 °C. IR (KBr)): ν_{max} 3405, 3300, 3200, 2200, 1725, 1668, 1632, 1579, 1475, 1382, 1355, 1283, 1223, 1083 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 0.84 (t, J = 7.2 Hz, 3H, CH_3), 3.38 (s, 3H, CH_3), 3.88–3.76 (m, 2H, CH_2), 7.05 (d, J = 8.3 Hz, 1H, ArH), 7.41 (s, 1H, NH_2), 8.08 (s, 1H, ArH), 8.18 (dd, J = 2.4, 7.2 Hz, 1H, ArH), 11.35 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.5, 19.5, 49.4, 49.5, 55.5, 61.0, 103.3, 110.0, 117.6, 119.5, 126.4, 136.3, 142.8, 148.8, 159.3, 160.7, 164.6, 179.4; ESI-MS: m/z 405.
(**4i**) *2-Amino-5′-bromo-2′,5-dioxo-5,6,7,8-tetrahydro-spiro[chromene-4,3′-indoline]-3-carbonitrile*: mp 278–280 °C (dec). IR (KBr): ν_{max} 3357, 3289, 3147, 2494, 1726, 1659, 1603, 1474, 1352, 1215, 1077, 1009 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.92–1.97 (m, 2H, CH_2), 2.23–2.26 (m, 2H, CH_2), 2.72 (t, J = 6.4 Hz, 2H, CH_2), 6.75 (d, J = 8.0 Hz, 1H, ArH), 7.22–7.26 (m, 1H, ArH), 7.32 (s, 1H, ArH), 7.33 (s, 2H, NH_2), 10.55 (s, 1H, NH). ESI-MS: m/z 385.
(**4l**) *Ethyl 2′-amino-5-bromo-3′-cyano-6′-methyl-2-oxo-spiro[indoline-3,4′-pyran]-5′-carboxylate*: mp 260–262 °C. IR (KBr): ν_{max} 3384, 3314, 3190, 2207, 1716, 1661, 1596, 1476, 1417, 1380, 1282, 1221, 1073 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 0.85 (t, J = 6.8 Hz, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.80–3.84 (m, 2H, CH_2), 6.77 (d, J = 8.0 Hz, 1H, ArH), 7.23 (s, 2H, NH_2), 7.29 (s, 1H, ArH), 7.36 (d, J = 8.4 Hz, 1H, ArH), 10.55 (s, 1H, NH); ESI-MS: m/z 403.
(**6a**) *2′-Aminno-7′,7′-dimethyl-2,5′,6′,7′,8′,-tetrahydro-2H-spiro[acenaphthylene-1,4′-chromene]-3′-carboni-tirle*: Solid, mp 266–268 °C. IR (KBr): ν_{max} 3368, 3295, 2956, 2190, 1717, 1664, 1599 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 0.98 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.11 (d, J = 16.0 Hz, 1H), 2.13 (d, J = 16.0 Hz, 1H), 2.70 (s, 2H, CH_2), 7.32 (s, 2H, NH_2), 7.39–8.28 (m, 6H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 28.1, 28.3, 32.8, 50.6, 51.5, 58.8, 64.6, 112.8, 118.4, 120.7, 122.2, 125.5, 129.1, 129.7, 130.7, 132.3, 133.3, 142.2, 145.1, 160.4, 164.9, 191.3, 206.3; ESI-MS: m/z 370.
(**6b**) *Ethyl 2′-amino-7′,7′-dimethyl-2,5′-dioxo-5′,6′,7′,8′-tetrahydro-2H-spiro[acenaphthylene-1,4′-chromene]-3′-carboxylate*: Solid, mp 257–259 °C. IR (KBr): ν_{max} 3379, 3269, 2958, 1718, 1685, 1520 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 0.42 (t, J = 7.0 Hz, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.99 (d, J = 16.0 Hz, 1H), 2.12 (d, J = 16.0 Hz, 1H), 2.61 (d, J = 17.6 Hz, 1H), 2.71 (d, J = 17.6 Hz, 1H), 3.36 (q, J = 7.3 Hz, 2H), 8.01 (s, 2H, NH_2), 8.16-7.30 (m, 6H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.1, 27.6, 28.6, 32.4, 50.1, 51.6, 59.3, 68.6, 78.1, 115.7, 119.8, 120.1, 124.5, 128.6, 129.1, 130.1, 130.3, 136.9, 142.2, 146.1, 160.3, 163.6, 168.3, 196.1, 206.1; ESI-MS: m/z 417.
(**8a**) *6′-Amino-3′-methyl-2-oxo-1′H-spiro[indoline-3,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile*: Solid, mp 284–286 °C (dec). IR (KBr): ν_{max} 3420, 3389, 3338, 3134, 2182, 2183, 1711, 1640, 1572, 1514, 1407, 1311, 1209, 1149, 1055, 939 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.54 (s, 3H, CH_3), 6.91 (s, 1H, ArH), 7.02 (s, 2H, NH_2), 7.22 (s, 1H, ArH), 10.51 (s, 1H, NH), 12.2 (s, 1H, NH). ESI-MS: m/z 293.
(**8b**) *6′-Amino-5-chloro-3′methyl-2-oxo-1′H-spiro[indoline-3,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile*: Solid, mp 295–297 °C (dec). IR (KBr): ν_{max} 3390, 3346, 3136, 2967, 2179, 1713, 1642, 1580, 1497, 1414, 1298, 1157, 1055, 823, 697 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 1.06 (s, 3H, CH_3), 6.92 (d, J = 8.4 Hz, 1H, ArH), 7.12 (s, 1H, ArH), 7.27 (s, 2H, NH_2), 7.29–7.31 (m, 1H, ArH), 10.73 (s, 1H), 12.32 (s, 1H). ESI-MS: m/z 327.
(**8d**) *6′-Amino-5-chloro-3′-methyl-2-oxo-1′-phenyl-1′H-spiro[indoline-3,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile*: Solid, mp 232–234 °C. IR (KBr): ν_{max} 3440, 3264, 3172, 2196, 1698, 1653, 1577, 1175 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.54 (s, 3H, CH_3), 6.95 (d, J = 8.4 Hz, 1H), 7.34–7.42 (m, 3H), 7.52 (t, J = 8.2 Hz, 2H), 7.62 (s, 2H, NH_2), 7.78 (d, J = 8.0 Hz, 2H), 10.88 (s, 1H); ^{13}C NMR (300 MHz, DMSO-d_6): δ 11.8, 47.8, 56.4, 95.5, 109.8, 118.0, 120.2, 125.5, 126.5, 129.5, 129.6, 131.7, 132.2, 137.3, 139.2, 144.1, 145.1, 161.1, 177.5; ESI-MS: m/z 404.
(**8e**) *6′-Amino-5-bromo-3′-methyl-2-oxo-1′-phenyl-1′H-spiro[indoline-3,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile*: Solid, mp 232–234 °C. IR (KBr): ν_{max} 3436, 3268, 3168, 2198, 1705, 1650, 1576, 1168 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 1.57 (s, 3H, CH_3), 6.91 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.9 Hz, 1H), 7.43–7.52 (m, 4H), 7.64 (s, 2H, NH_2), 7.78 (d, J = 7.8 Hz, 2H), 10.9 (s, 1H); ^{13}C NMR (300 MHz, DMSO-d_6): δ 12.1, 47.9, 56.5, 96.6, 110.2, 118.2, 120.8, 125.5, 126.6, 129.5, 129.6, 131.6, 132.3, 137.2, 139.2, 144.1, 145.0, 161.0, 178.8; ESI-MS: m/z 448.
(**8f**) *6′-Amino-3′-methyl-5-nitro-2-oxo-1′-phenyl-1′H-spiro[indoline-3,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile*: Solid, mp 228–230 °C (dec). IR (KBr): ν_{max} 3268, 3175, 2209, 1710, 1650, 1576, 1178 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.57(s, 3H, CH_3), 7.12 (d, J = 8.4 Hz, 1H), 7.38–7.54 (m, 3H), 7.67 (s, 2H, NH_2), 7.78 (m, 2H), 7.98 (d, J = 6.8 Hz, 2H), 11.45 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 12.3, 47.8, 56.5, 96.5, 109.5, 118.1, 120.1, 125.6, 126.6, 132.0, 132.6, 131.7, 134.3, 137.6, 139.2, 144.9, 145.0, 161.2, 178.8; ESI-MS: m/z 415.