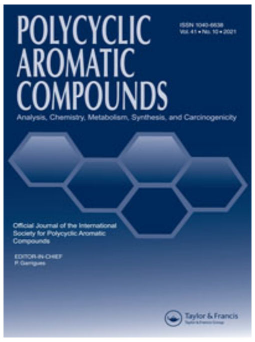

Polycyclic Aromatic Compounds

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Multicomponent Synthesis of Pyrano (3, 2-*c*) Quinolone Fused Spirochromenes

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ABSTRACT

A multicomponent pathway has been described for the synthesis of novel pyrano (3,2-*c*) quinolone fused spirochromenes by piperidine catalyzed reaction between isatins, phenyl (or alkyl) sulfonyl acetonitrile and 4-hydroxy-N-methylquinoline-2-one. Decent yields coupled with easy isolation of the products and avoidance of conventional purification methods are the noteworthy merits of the developed protocol.

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4-hydroxy-N- methylquinolin-2–one; Isatin; phenylsulfonyl acetonitrile; piperidine; multicomponent reactions; spirochromenes

Introduction

The first multicomponent reaction was introduced more than a century ago for the synthesis of a-amino acids.[1] However, with the knowledge about the advantages of multicomponent reactions like reduction in the number of steps, high yields, easy isolation of the product and minimal generation of waste, last two decades have witnessed tremendous advances in this field[2–4] and the current day research in this field has been focused on the design and library synthesis of structurally related molecules with promising biological potential.[5–7] In this context concept of synthesis of hybrid molecules by combination of three or more reactants with individual mode of action, the pharmacophores, is enjoying growing interest.[8–13]

It is well known that, indole (**A**, Figure 1) is the most ubiquitous heterocyclic moiety present in a large number of bioactive natural products and sharing of indole 3-carbon atom in the formation of spiroindoline **(B,** Figure 1**)** highly enhances it's biological activity.[14] The presence of carbonyl group at C-2 in spiroindoline generates spiro-2-oxindole, spirooxindole (**C**, Figure 1) and it serves as an important template in the synthesis of medicinally prevalent organic compounds. Many spirooxindole derivatives are known to exhibit anti-microbial, anti-oxidant, anti-inflammatory, anti-tubercular, anti-cancer, and anti–HIV as well as anti-inflammatory activity.[15–20] Sharing of C-3 in spirooxindoles with another heterocyclic ring generates hetero-annulated spirooxindoles and among the hetero-annulated spirooxindoles, spirochromenes, wherein 4*H*-chromene (tetrahydrobenzo[*b*] pyran) ring is fused to spirooxindole system (**D**, Figure 1) are of particular interest due to their useful biological properties such as spasmolytic, diuretic, anticoagulant, anticancer, and anti-anaphylactic activities.[21,22]

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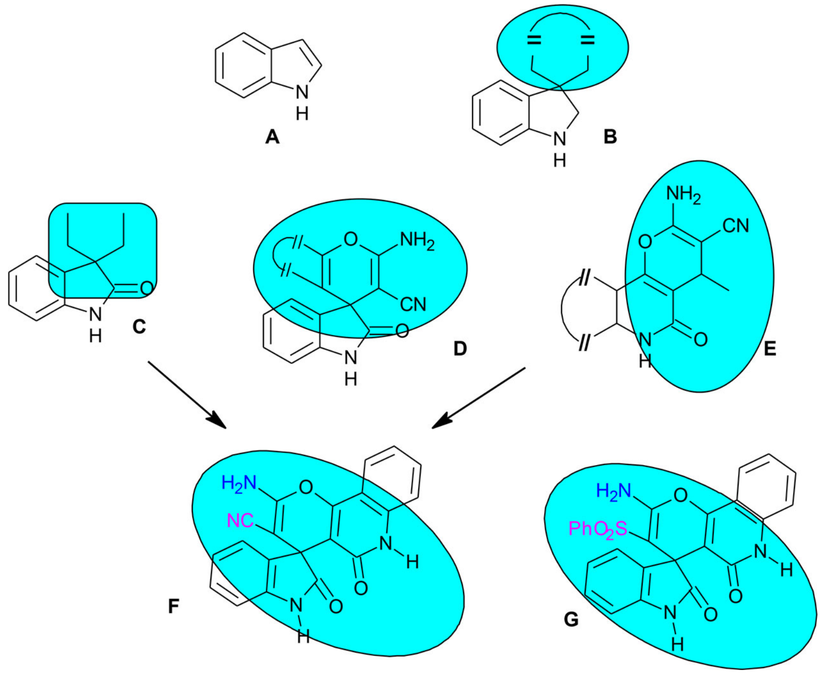


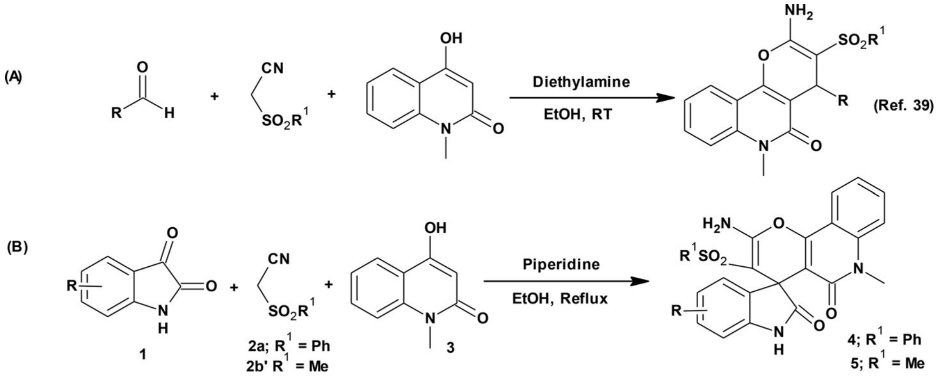
Figure 1. Designing of novel pyrano(3,2-*c*) quinolone fused spirochromenes.

Alike spirochromene, pyrano (3,2-*c*) quinolone moiety (**E**, Figure 1) serves as another important pharmacophore as many compounds of natural as well as synthetic origin containing pyrano(3,2-*c*)quinolone as the structural unit are known to exhibit antidiabetic, anti-proliferative, anti-inflammatory as well as antiallergic activities.[23,24] A few compounds of this class are also known to exhibit calcium channel blocking activities.[25] Taking recourse to the bio-profiles of spirochromenes as well as pyrano(3,2-*c*) quinolones and based upon the hypothesis that, the presence of two different heterocyclic moieties in single molecule can dramatically enhance it’s biological potential,[26,27] it was surmised that, synthesis of pyrano (3,2-*c*) quinolone fused spirochromenes (**F**, Figure 1) serves as an attractive target.

From reterosynthetic view point, pyrano (3,2-*c*) quinolone fused spirochromenes can be synthesized by multicomponent reaction of isatin, 4-hydroxyquinolin-2-one and an active methylene compound containing nitrile function like malononitrile, alkyl cyanoacetate or arylsulfonyl acetonitrile. Focused literature survey in this context revealed that, there are only limited number of protocols reported earlier for the synthesis of pyrano(3,2-*c*) quinolones which make use of malononitrile or alkyl cyanoacetate as an active methylene compound. [23,24,28–31] A more interesting fact in this context was to note that, although many compounds bearing sulfone moiety are known to possess significant biological activities[32–36] there are only two reports on the use of aryl/alkylsulfonyl acetonitrile as an active methylene compound as well as the source of sulfone moiety.[37,38] Based upon this survey and our earlier studies on diversity oriented synthesis of 2-amino-4*H*-chromenes[39–42] we planned to undertake multicomponent synthesis of pyrano (3,2-*c*) quinolone fused spirochromenes containing sulfone group by the reaction between isatin, phenyl (or alkyl) sulfonyl acetonitrile and 4-hydroxy-N-methylquinolin–2-one (Scheme 1A).

Results and discussion

From our laboratory, the diethylamine catalyzed synthesis of 3- (phenylsulfonyl) pyrano [*3,2-c*]-quinolones by the reaction between an aromatic aldehyde, phenylsulfonyl acetonitrile and



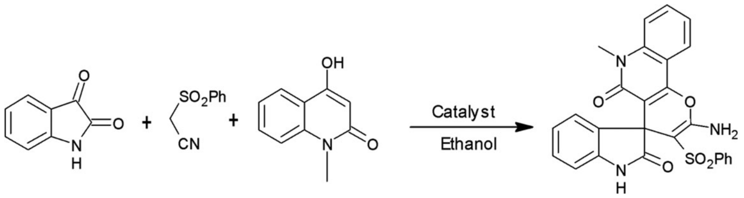
Scheme 1. Multicomponent synthesis of pyrano (3,2-*c*)quinolone fused spirochromenes.

4-hydroxy-N-methylquinoline-2-one (Scheme 1A) has been reported earlier.[39] Taking clues from this report we surmised that, desired synthesis of pyrano (3,2-*c*) quinolone fused spirochromenes can also be achieved by simply replacing aldehyde component from this reaction with isatin (Scheme 1B). Accordingly, a model reaction was carried out using isatin, **1a**, phenylsulfonyl acetonitrile, **2a**, and 4-hydroxy-N-methylquinolin–2-one, **3**, as the substrates (1 mmol, each), diethylamine (30 mol %) as the catalyst and ethanol (4 mL) as the reaction medium. Contrary to our expectation, we did not observe any progress in the reaction even after stirring the reaction mixture overnight **(entry 1,** Table 1). Change in the reaction medium from ethanol to ethyl acetate, acetone, dimethyl formamide as well as dimethyl sulfoxide was also not found to be beneficial in changing the course of the reaction **(entry 2,** Table 1). Hence, the model reaction was carried out under reflux condition. During reflux, formation of a new product was noticed (TLC) however; even after reflux for twelve hours the reaction did not go to completion **(entry 3,** Table 1). The resultant product in moderate yield was isolated, purified and it was characterized by spectral studies. ^{1}H-NMR spectrum **(Spectrum 1)** exhibited a sharp singlet at δ 3.42 for N-methyl group protons and a multiplet between δ 6.31 to 8.15 due to fifteen aromatic and amino group protons. In addition, a characteristic singlet due to highly deshielded N-H proton was also observed at 10.43 ppm. In ^{13}C-NMR spectrum of the same **(Spectrum 2)**, three characteristic signals were observed at δ29.5 (N-methyl group carbon), at δ 49.3 (quaternary carbon $C-3, 4'$) and at δ179.1 (carbonyl group, $C-2$). On the basis of spectral studies it was identified to be the desired spirochromene, **4a**. In high resolution mass spectrum **(Spectrum 3)** the observed exact mass of the compound (486.1117 amu) was in perfect agreement with the calculated value of exact mass of **4a**, $C_{26}H_{19}N_3O_5S$: 486.1118 amu. These spectral details are coherent with those for desired product, 4a. Spectral details are shown in Figure 2.

This encouraging result prompted us to screen other basic catalysts for this reaction. Accordingly, the reaction was repeated using potassium phosphate, potassium carbonate, triethylamine, DBU, DABCO, DMAP as well as piperidine as the catalysts. In the presence most of these catalysts the desired product, **4a**, resulted in moderate but comparable yield **(entries 4-9,** Table 1). On the other hand, in the presence of piperidine as the catalyst desired product, **4a**, was obtained in excellent yield (**entry 10,** Table 1). Subsequent studies on optimization of the reaction conditions revealed that, with the decrease in the amount of the catalyst, the product, **4a,** resulted in lower yields and the increase in the reflux time was not helpful in improvement of yield of the desired product **(entries 11-13,** Table 1).

Having established the optimum reaction conditions, we next turned our attention to establish generality of the reaction conditions. Accordingly, isatins bearing electron-withdrawing or electron-donating group were allowed to react with phenylsulfonyl acetonitrile and 4-hydroxy-N-methylquinolin-2-one. In each case, respective spirochromene, **4 b-g,** was obtained in decent yield

Table 1. Screening of catalyst for multicomponent synthesis of **5a**.[a]



Entry	Catalyst (mol %)	T (°C)	Time (h)	Yield (%)
1	Et_2NH (30)	Rt	24	Trace
2	Et_2NH (30)	Rt	24	Trace$^{b\text{-}e}$
3	Et_2NH (30)	80	12	40
4	K_3PO_4(30)	80	12	30
5	K_2CO_3 (30)	80	12	30
6	Et_3N (30)	80	8	50
7	DABCO (30)	80	8	45
8	DBU (30)	80	8	50
9	DMAP (30)	80	8	50
10	**Piperidine (30)**	80	**3.5**	**92**
11	Piperidine (20)	80	4, 8	65, 77
12	Piperidine (15)	80	4, 8	50, 65
13	Piperidine (10)	80	4, 12	40, 55

[a]:Reaction conditions: isatin, phenylsulfonyl acetonitrile and 4-hydroxy-N-methylquinolin-2-one (1 mmol, each), ethanol (4 mL), catalyst ; b-e: using EtOAc, $(CH_3)_2CO$, DMF and DMSO as the solvent.

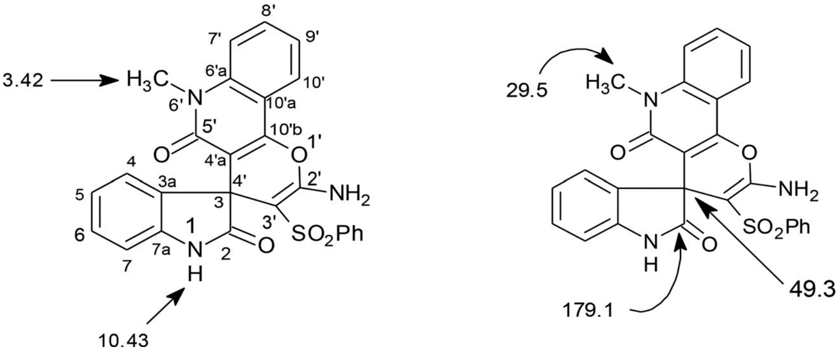
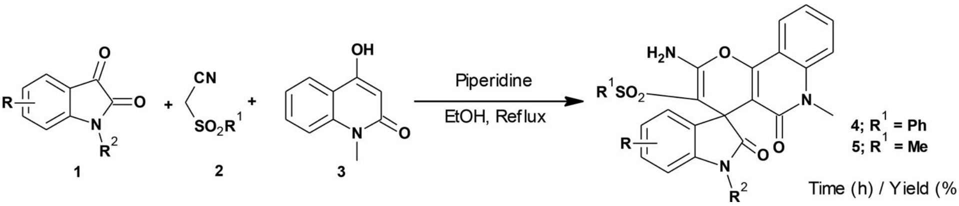


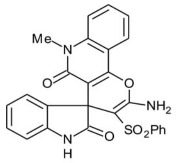
Figure 2. ^{1}H and ^{13}C details of compound **4a**.

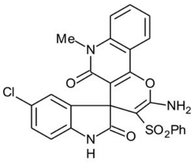
(Table 2). Product, 4e, wherein 5-methylisatin was used as first component, ^{1}H-NMR spectrum **(Spectrum 13)** displayed two singlets at δ 1.76 and 3.41 for aromatic methyl and for N-methyl group protons, respectively. It also exhibited significantly downfield singlet at δ 10.34 for N-H proton. ^{13}C-NMR spectrum **(Spectrum 14)** displayed signals at δ 20.6 and 29.5 for methyl group carbons from indole moiety and N-methyl group form quinolone moiety, respectively. Spiro carbon displayed a signal at 49.2 ppm, while carbonyl carbon form indolone ring was observed at 179.7 ppm. HRMS **(Spectrum 15)** showed a base peak at 500.1274 which also supports the formation of desired product. Spectral details are shown in Figure 3.

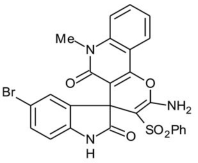
So as to explore the scope of the protocol, phenylsulfonyl acetonitrile in this multicomponent reaction was replaced with methylsulfonyl acetonitrile. With this variation also, the expected spirochromenes, **5a**-**f**, were obtained acceptable yield (Table 2). Happily enough, the resultant solid product in each reaction could be isolated by simple dilution of the reaction mixture with water followed by filtration. Resultant dried solid upon simple washing with chloroform furnished pure products (**4** and **5**).

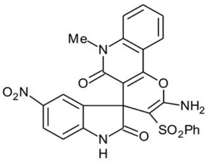
Table 2. Piperidine catalyzed multicomponent synthesis of spirochromenes, **4** / **5**.

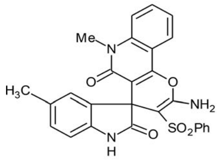


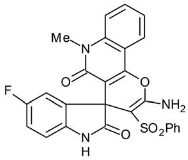

4a; 3.5 / 92

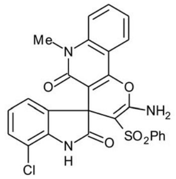

4b; 3.5 / 90

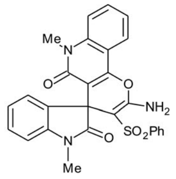

4c; 3.5 / 92

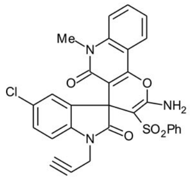

4d; 3 / 92

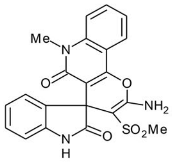

4e; 4 / 90

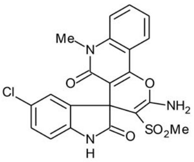

4f; 4 / 89

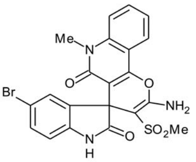

4g; 3.5 / 89

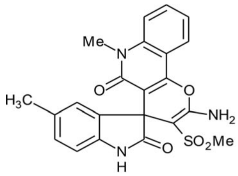

4h; 4 / 87

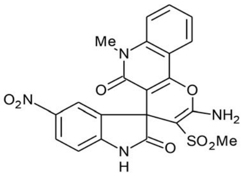

4i; 4 / 92

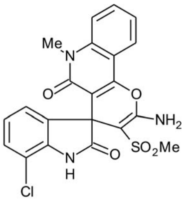

5a; 3 / 87


5b; 4 / 88


5c; 3.5 / 90


5d; 4 / 87


5e; 3.5 / 90


5f; 4 / 90

[a:] Reaction conditions: Isatin, phenyl (or alkyl) sulfonyl acetonitrile and 4-hydroxy-N-methyl quinolin-2-one (1 mmol, each), piperidine (30 mol %), Ethanol (4 mL), reflux.

^{1}H-NMR spectrum of **5a** (**Spectrum 29**) exhibited two sharp singlets at δ 2.75 and 3.45 characteristic for the methyl group attached to sulfonyl group and N-methyl group protons, respectively. Another singlet characteristic for N-H proton from isatin was also observed at δ10.36 ppm. These three signals clearly highlight the formation of **5a**. In ^{13}C-NMR spectrum (**Spectrum 30**) 21 signals were observed due to 21 carbon atoms in **5a**. In HRMS (**Spectrum 31**) the observed mass value of the product, **5a** [424.8963 amu] was in perfect agreement with the calculated mass value of the same [424.4491 amu]. Spectral details are shown in Figure 4.

From mechanistic view point[28] we propose that, isatin initially undergoes base catalyzed Knoevenagel condensation with phenylsulfonyl acetonitrile to yield isatinidinephenylsulfonyl

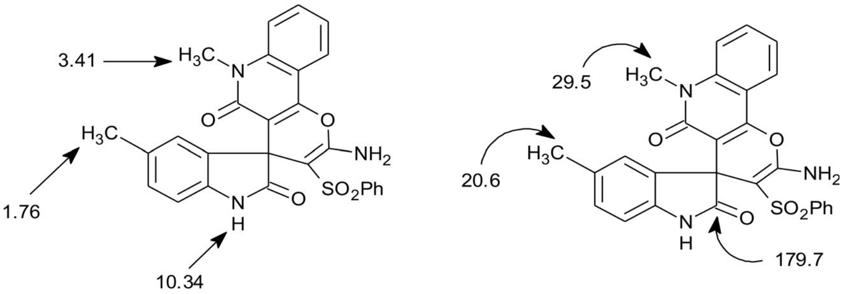


Figure 3. ^1H and ^{13}C details of compound **4e**.

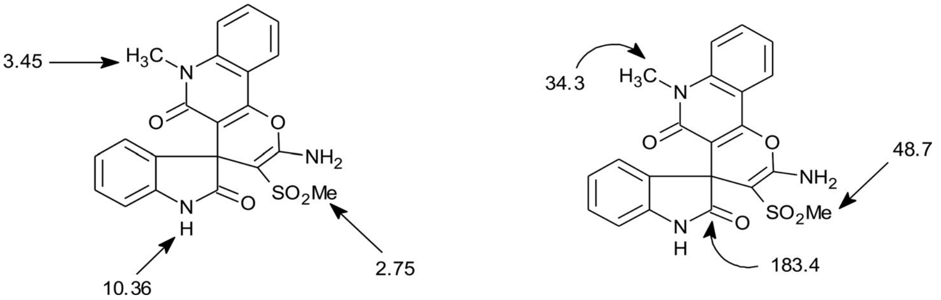


Figure 4. ^1H and ^{13}C details of compound **5a**.

acetonitrile which on subsequent carba-Michael addition with 4-hydroxy-N-methylquinolin-2-one followed by Thorpe–Ziegler type cyclization[43] furnishes the desired spirochromene, **4** (Scheme 2).

It is well known that, the molecules containing pyrano (2,3-c) quinolone and spirochromene as the structural motifs do possess anti-cancer activity.[19,25] Based upon this as well as on the philosophy that hybrid molecules synthesized by covalent fusion of these pharmacophores may have enhanced anti-cancer activity, we surmised that, synthesized pyrano (3,2-*c*) quinolone fused spirochromenes, **4** and **5**, will also have pronounced anti-anticancer activity. Thus, all the synthesized compounds were screened for their anti-cancer activity against three different human cancer cells viz. MCF-7 (Breast Carcinoma), HEK (Breast Carcinoma) and HeLa (Cervical Carcinoma) using Doxorubicin as a positive control. IC_{50} values of all the synthesized compounds were obtained. However, contrary to our expectations, the compounds were found to have IC_{50} values greater than 200 (***Pl. see SI***) indicating non-suitability of these compounds for further screening as anti-cancer agents. Hence, the work on biological evaluation of these compounds was discontinued.

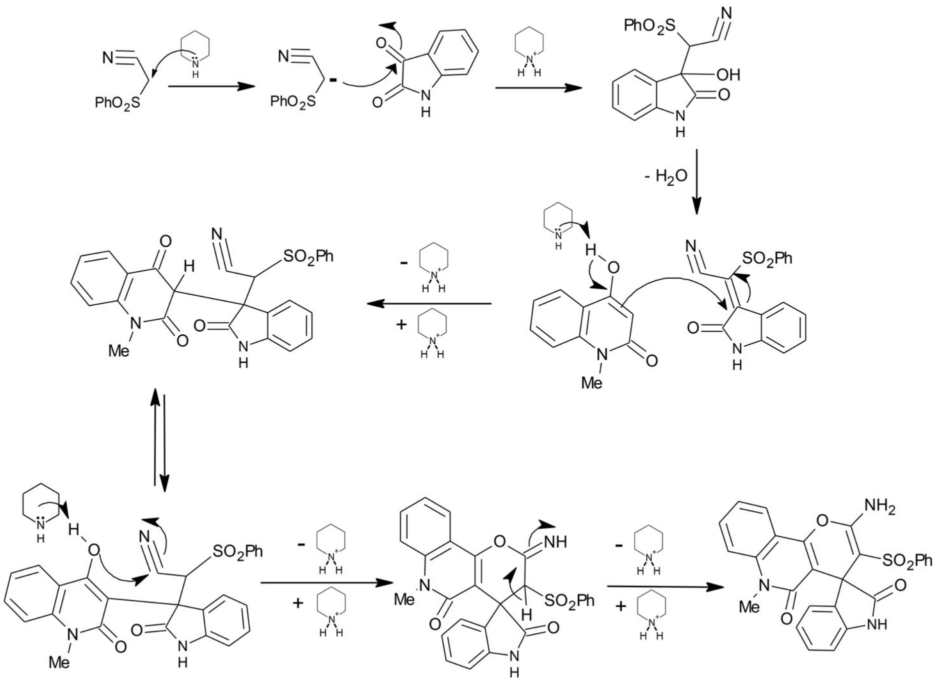
Conclusion

In conclusion, we have developed an efficient protocol for multicomponent synthesis of novel pyrano (3,2-*c*) quinolone-fused spirochromenes by the reaction between isatins, phenyl (or methyl) sulfonyl acetonitrile, and 4-hydroxy-N-methylquinolin–2-one using piperidine as the catalyst. This high yielding protocol is operationally simple and chromatography-free.

Experimental

General

All the chemicals were commercially available and used as received. Melting points were obtained using a Kumar melting point apparatus and were uncorrected. IR spectra were obtained using a



Scheme 2. Plausible mechanism for the formation spirooxindoles, **4**.

Thermo Scientific Nicolet iS10 FT-IR Spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were obtained using a Bruker Avance II spectrometer. High resolution mass spectra (HRMS) were obtained using a Thermo Scientific Q-Exactive, Accela 1250 pump instrument.

Representative procedure for the preparation of spirochromenes 4/5

To a well stirred solution of isatin, phenyl (or methyl) sulfonyl acetonitrile and 4-hydroxy-N-methylquinolin-2-one (1 mmol, each) in ethanol (4 mL) was added piperidine (30 mol %) and the reaction mixture was refluxed on water bath. Upon completion of the reaction (TLC) it was allowed attain room temperature. Cold water (10 mL) was slowly added and magnetic stirring was continued till amorphous solid separates out. It was filtered, washed with water (4 × 5 mL) and dried. The dried solid was then washed with hexane-chloroform mixture (1:1, v/v, 5 × 5 mL) and dried again. Resultant free-flowing solid was pure and did not require any further purification.

Spectral data of all the synthesized compounds

All the synthesized spirochromenes in their IR spectra showed prominent peaks in the range 3400-3360 (amino group), 1330-1345 and 1135- 1150 cm^{-1} (sulfone group) and their melting points were above 300 °C. All these compounds do not show sharp melting point, they form black mass in temperature range 310 – 330 °C.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[indoline-3,4′-pyrano[3,2-c]quinoline]-2,5′(6’H)-dione, 4a, off white powder, yield (446 mg, 0.92 mmol) . **^{1}H-NMR (DMSO-d6, 300 MHz):** δ 3.42 (S, 3H, N-CH_3), 6.31-6.35 (m, 2H), 6.75 (d, 1H, J = 7.5 Hz), 6.99 – 7.04 (m, 1H, ArH), 7.23 – 7.37 (m, 5H), 7.41-7.48 (m, 2H), 7.65 – 7.69 (m, 3H, NH_2 and ArH), 8.15 (d, 1H, J = 8.1 Hz, ArH), 10.43

(S, 1H, NH); **^{13}C-NMR (DMSO-d6, 75 MHz):** δ 29.5, 49.3, 84.3, 108.1, 109.1, 109.2, 112.5, 114.8, 120.9, 122.5, 123.1, 124.3, 126.0, 128.1, 128.6, 132.1, 132.3, 138.9, 144.7, 144.8, 150.7, 157,1,158.0, 179.1 ppm; **HRMS (ESI):** m/z [M + H]$^+$ calcd. for $C_{26}H_{19}N_3O_5S$: 486.1118; found mass: 486.1117.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[5-chloroindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4 b, off white powder, yield (468 mg, 0.90 mmol) . **^{1}H-NMR (DMSO-d6, 300 MHz):** δ 3.41 (s, 3H, N-CH_3), 6.13 (s, 1H), 6.73 (d, 1H, J = 7.8 Hz), 6.92(s, 1H), 7.26-7.41(m, 7H), 7.65 (br s, 3H, NH_2 and ArH), 8.11 (d, 1H, J = 6.6 Hz, ArH), 10.49 (s, 1H, NH): **^{13}C-NMR (DMSO-d6, 75 MHz):** δ 29.5, 49.4, 83.7, 108.4, 110.2, 112.5, 114.4, 122.3, 123.3, 124.6, 125.4, 128.1, 128.4, 132.3, 138.9, 141.0, 143.6, 144.7, 151.0, 157.3, 158.7, 179.1 ppm; **HRMS (ESI):** m/z [M + H]$^+$ calcd. for $C_{26}H_{18}N_3O_5ClS$: 520.0728; found mass: 520.0729.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[5-bromoindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4c, pale yellow powder, yield (518 mg, 0.92 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 3.42 (s, 3H, N-CH_3), 6.29 (s, 1H), 6.70 (s, 1H), 7.08 (s, 1H), 7.27 − 7.44 (m, 7H), 7.62 − 7.71 (m, 3H, NH_2 and ArH), 8.06 (m, 1H, ArH), 10.54 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.5, 49.3, 83.7, 108.4, 110.7, 112.5, 113.1, 114.5, 122.3, 23.3, 125.5, 127.3, 128.5, 130.9, 132.3, 132.4, 133.7, 139.0, 144.1, 144.6, 151.0, 157.2, 158.7, 178.9 ppm; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd. for $C_{26}H_{18}O_5N_3BrS$: 564.0196; found mass: 564.0223.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[5-nitroindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4d, pale yellow powder, yield (488 mg, 0.92 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 3.40 (s, 3H, N-CH_3), 6.86-6.92 (m, 2H), 7.08-7.13 (m, 2H), 7.21-7.30 (m, 5H), 7.57 − 7.65 (m, 3H, NH_2 and ArH), 7.86 (dd, 1H, J = 2.1 Hz, 2.1 Hz), 8.12 (d, 1H, *J* = 7.8 Hz, ArH), 11.01 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.5, 108.8, 112.5, 114.3, 120.1, 122.5, 123.4, 125.0, 125.5, 128.4, 131.9, 132.4, 139.0, 141.9, 144.9, 151.0, 151.4, 157.6, 158.9 ppm; **HRMS (ESI):** m/z [M + H]$^+$ calcd. for $C_{26}H_{18}N_4O_7S$: 531.0968; found: mass 531.0970.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[5-methylindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4e, off white powder, yield (450 mg, 0.90 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 1.76 (s, 3H), 3.41 (s, 3H, N-CH_3), 6.04 (s, 1H), 6.65 (d, 1H, J = 7.5 Hz), 6.82 (d, 1H, J = 7.5 Hz), 7.26 (d, 4H, J = 6 Hz), 7.37 (t, 1H, J = 7.5 Hz), 7.49 (d, 2H, J = 8 4 Hz), 7.66 − 7.74 (m, 3H, NH_2 and ArH), 8.14 (d, 1H, J = 7.8 Hz, ArH), 10.34 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 20.6, 29.5, 49.2, 84.2, 108.9, 109.1, 112.5, 114.5, 122.5, 123.2, 125.2, 125.6, 128.3, 128.7, 130.0, 131.2, 131.8, 132.3, 138.8, 142.0, 144.8, 150.8, 157.1, 188.8, 179.7 ppm; **HRMS (ESI):** m/z [M + H]$^+$ calcd. for $C_{27}H_{21}N_3O_5S$: 500.1275; found mass: 500.1274.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[5-fluoroindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4f, pale gray powder, yield (448 mg, 0.89 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 3.42 (s, 3H, N-CH_3), 6.01 (s, 1H), 6.70-6.75 (m, 2H), 7.23-7.33 (m, 5H), 7.41 (d, 2H, J = 6.3 Hz), 7.61-7.71 (m, 3H, NH_2 and ArH), 8.14 (d, 1H, J = 8.1 Hz, ArH), 10.41 (s, 1H, NH). **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.5, 83.7, 108.5, 109.4, 112.5, 114.2, 114.5, 114.6, 122.4, 123.3, 125.6, 128.5, 132.2, 132.3, 139.0, 144.9, 150.9, 157.2, 158.7, 179.2 ppm; **HRMS (ESI):** m/z [M + H]$^+$ calcd. for $C_{26}H_{18}O_5N_3FS$: 504.1024; found mass: 504.1022.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[7-chlorolindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4 g, off white powder, yield (462 mg, 0.89 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.32 (s, 3H, ArCH_3), 3.42 (s, 3H, N-CH_3), 7.04 (d, 1H, J = 6.6 Hz), 7.30 - 7.49 (m, 7H), 7.69 - 7.72 (m, 3H, NH_2 and ArH), 8.15 (d, 1H, J = 7.8 Hz, ArH), 10.80 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.6, 50.1, 83.9, 108.7, 112.4, 113.5, 114.9, 122.0, 122.6, 122.7, 123.3, 125.9, 128.2, 128.7, 132.3, 132.5, 133.8, 139.0, 142.5, 144.6, 150.8, 157.2, 158.7, 179.0 ppm; **HRMS (ESI):** m/z [M + H]$^+$ calcd. for $C_{26}H_{18}N_3O_5ClS$:520.0728; found mass: 520.0723.

2′-Amino-3′-(phenylsulfonyl)-6′-methylspiro[1-methylindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 4 h, pale gray powder, yield (435 mg, 0.87 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 3.20 (s, 3H, N-CH_3), 3.40 (s, 3H, N-CH_3), 6.42 (d, 2H, J = 6.9 Hz, ArH), 6.91 (d, 1H, J = 7.5 Hz, ArH), 7.13 (t, 1H, J = 7.2 Hz, ArH), 7.27 (br s, 4H, ArH), 7.36 (t, 1H, J = 7.2 Hz, ArH), 7.46 (m, 2H, ArH), 7.68 (br s, 3H, NH_2 and ArH), 8.16 (d, 1H, J = 8.1 Hz, ArH), **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 27.1, 29.6, 48.7, 84.2, 107.8, 108.9, 112.4, 115.0, 121.7, 122.6, 123.2, 124.0, 126.0, 128.4, 128.7, 131.4, 132.2, 132.5, 138.9, 144.5, 146.1, 150.8, 157.1, 158.6, 177.5; **HRMS (ESI):** m/z $[M + H]^+$ calcd. For $C_{27}H_{21}N_3O_5S$: 500.1275; found mass: 500.1270.

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[5-chloro1-(prop-2-yn-1-yl)indoline-3,4′-pyrano [3,2-c] quinoline]-2,5′(6'H)-dione; 4 l, off white powder, yield (51 mg, 0.92 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 3.13 (s, 3H, SO_2CH_3), 3.41 (s, 3H, N-CH_3), 4.45 (q, 2H, J = 7.5, CH_2), 6.39 (s, 1H, ArH), 7.04 (d, 2H, J = 6.6 Hz, ArH), 7.30‒7.36 (m, 5H), 7.47 (s, 2H, NH_2), 7.68 (s, 1H, ArH), 7.83 (s, 2H, ArH), 8.17 (d, 1H, J = 7.5 Hz, ArH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.7, 30.3, 48.7, 74.7, 77.7, 83.0, 107.8, 109.8, 112.4, 114.9, 122.6, 123.4, 124.6, 125.6, 126.7, 128.3, 128.6, 132.5, 132.6, 139.0, 141.0, 143.3, 144.5, 151.1, 157.2, 158.7, 176.4 ppm; **HRMS (ESI):** m/z $[M + H]^+$ calcd. for $C_{29}H_{20}O_5N_3ClS$: 558.0867; found mass: 558.0876.

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[indoline-3,4′-pyrano[3,2-c]quinoline]-2,5′(6'H)-dione, 5a, off white powder, yield (368 mg, 0.87 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.75 (s, 3H, SO_2CH_3), 3.45 (s, 3H, N-CH_3), 6.73 (d, 1H, *J* = 8.4 Hz, ArH), 6.86 (d, 1H, *J* = 1.8 Hz, ArH), 7.04 (dd, 1H, *J* = 2.1 Hz, 1.8 Hz, ArH), 7.13 (s, 2H, ArH), 7.23‒7.32 (m, 2H, NH_2), 7.59 (s, 1H, ArH), 7.68 (s, 1H, ArH), 8.06 (d, 1H, *J* = 8.1 Hz, ArH), 10.36 (s,1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 34.3, 48.7, 54.3, 88.7, 113.6, 115.4, 117.5, 118.9, 127.1, 128.0, 128.5, 130.9, 133.1, 136.9, 140.6, 143.6, 147.3, 156.1, 161.8, 163.8; HRMS (ESI): m/z $[M + H]^+$ calcd. for $C_{21}H_{17}N_3O_5S$: 424.0905 ppm; found mass: 424.8963.

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[5-chloroindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6'H)-dione, 5 b, off white powder, yield (402 mg, 0.88 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.65 (s, 3H, SO_2CH_3), 3.46 (s, 3H, N-CH_3), 6.73-6.82 (m, 2H, ArH), 7.34 ‒ 7.50 (m, 4H, ArH), 7.67 (d, 1H, J = 6.6 Hz, ArH), 8.16 (d, 1H, J = 7.5 Hz, ArH), 10.41 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.6, 44.1, 49.3, 84.1, 109.5, 112.6, 114.8, 121.1, 122.5, 123.2, 123.9, 128.5, 132.4, 134.0, 183.9, 144.5, 150.9, 156.9, 158.8, 178.8 ppm; HRMS (ESI): m/z $[M + H]^+$ calcd. for $C_{21}H_{16}N_3O_5ClS$:458.8942; found mass: 458.1582.

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[5-bromoindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6'H)-dione, 5c, off white powder, yield (452 mg, 0.90 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.76 (s, 3H, SO_2CH_3), 3.48 (s, 3H, N-CH_3), 6.68 (s, 1H, ArH), 7.16 (s, 1H, ArH), 7.24 (s, 1H, ArH), 7.39 (s, 3H, NH_2 and ArH), 7.49 (s, 1H, ArH), 7.69 (s, 1H, ArH), 8.16 (s, 1H, ArH), 10.59 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.6, 43.9, 49.6, 83.5, 108.8, 111.1, 112.6, 112.7, 114.9, 122.9, 123.4, 126.6, 131.1, 132.5, 136.9, 139.0, 141.0, 144.0, 151.2, 157.0, 158.8, 178.2 ppm; HRMS (ESI): m/z $[M + H]^+$ calcd. for $C_{21}H_{16}N_3O_5BrS$: 502.0067; found mass: 502.0063.

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[5-methylindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6'H)-dione, 5d, pale gray powder, yield (380 mg, 0.87 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.14 (s, 3H, ArCH_3), 2.68 (s, 3H, SO_2CH_3), 3.67 (s, 3H, N-CH_3), 6.62 (d, 1H, J = 9 Hz, ArH), 6.81 (s, 1H, ArH), 6.92 (d, 1H, J = 7.5 Hz, ArHs), 7.36 ‒ 7.44 (m, 3H, NO_2 and ArH), 7.54 (d, 1H, J = 8.4 Hz, ArH), 7.73 (t, 1H, J = 6 Hz, ArH), 8.16 (d, 1H, J = 7.8 Hz, ArH), 10.31 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 20.6, 29.5, 49.2, 84.3, 99.9, 108.9, 109.1, 112.5, 114.5, 122.5, 123.2, 125.2, 125.6, 128.3, 128.7, 129.9, 131.3, 132.3, 138.8, 142.0, 144.8, 150.7, 157.1, 158.8, 179.6 ppm; **HRMS (ESI):** m/z $[M + H]^+$ calcd. For $C_{22}H_{19}N_3O_5S$: 438.1118; found mass: 438.1112.

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[5-nitroindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6'H)-dione, 5e, pale yellow powder, yield (422 mg, 0.90 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.38 (s, 3H, SO_2CH_3), 2.92 (s, 3H, N-CH_3), 6.86 (d, 1H, J = 7.5 Hz), 7.05 (s, 1H, ArH), 7.16 (d, 1H, J = 7.5 Hz, ArH), 7.60 − 7.68 (m, 3H, NO_2 and ArH), 7.79 (d, 1H, J = 8.4 Hz, ArH), 7.95 (t, 1H, J = 7.8 Hz, ArH), 8.41 (d, 1H, J = 7.8 Hz, ArH), 10.56 (s, 1H, NH); **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.7, 43.8, 49.4, 82.9, 108.2, 109.1, 112.6, 114.9, 119.4, 122.6, 123.4, 125.9, 132.5, 135.6, 139.0, 142.1, 151.3, 151.5, 157.3, 158.9, 179.2 ppm; **HRMS (ESI):** m/z $[M+H]^+$ calcd. For $C_{22}H_{18}N_3O_7S$: 469.0878; found mass: 469.0812

2′-Amino-3′-(methylsulfonyl)-6′-methylspiro[7-chlorolindoline-3,4′-pyrano[3,2-c]quinoline]-2,5′ (6’H)-dione, 5f, off white powder, yield (412 mg, 0.90 mmol) . **^{1}H-NMR (DMSO-d^6, 300 MHz):** δ 2.70 (s, 3H, SO_2CH_3), 3.46 (s, 3H, N-CH_3), 6.83 (t, 1H, J = 7.8 Hz, ArH), 7.01 (d, 1H, J = 7.2 Hz, ArH), 7.18 (d,1H, J = 7.8 Hz, ArH), 7.43 (m, 3H,NO_2 and ArH), 7.54 – 7.61(m, 1H, ArH), 7.75 (t, 1H, J = 7.5 Hz, ArH), 8.17 (d, 1H, J = 7.8 Hz, ArH), 10.83 (s, 1H, NH): **^{13}C-NMR (DMSO-d^6, 75 MHz):** δ 29.7, 44.0, 50.2, 83.6, 108.8, 112.4, 113.6, 115.3, 115.5, 122.4, 122.7, 122.9, 123.2, 128.7, 132.9, 135.9, 138.9, 142.5, 150.9, 156.8, 158.8, 178.8 ppm; **HRMS (ESI):** m/z [M + H]+ calcd. for $C_{21}H_{16}N_3O_5ClS$: 458.0547; found mass: 458.0571.

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References

1. A. Strecker, “Ueber Die künstlicheBildung Der Milchsäure Und Einenneuen, demGlycocollhomologenKörper, Leibigs,” *Justus Liebigs Annalen Der Chemie* 7 (1850): 27–45.
2. J. Zhu and H. Bienayme, *Multicomponent Reactions*, eds. J. Zhu, and H. Bieayme (Wienheim, Germany: Wiley – VCH, 2005).
3. M. S. Singh, and S. Chowdhury, “Recent Developments in Solvent-Free Multicomponent Reactions: A Perfect Synergy for Eco-Compatible Organic Synthesis,” *RSC Advances* 2, no. 11 (2012): 4547–92.
4. B. H. Rotstein, S. Zaretsky, V. Rai, and A. K. Yudin, “Small Heterocycles in Multicomponent Reactions,” *Chemical Reviews* 114, no. 16 (2014): 8323–59.
5. E. Ruijter, and R. V. Orru, “Multicomponent Reactions - Opportunities for the Pharmaceutical Industry,” *Drug Discovery Today:Technologies* 10 (2013): 15–20.
6. J. E. Biggs-Houck, A. Younai, and J. T. Shaw, “Recent Advances in Multicomponent Reactions for Diversity-Oriented Synthesis,” *Current Opinion in Chemical Biology* 14, no. 3 (2010): 371–82.
7. S. Manohar, U. C. Rajesh, S. I. Khan, B. L. Tekwani, and D. S. Rawat, “Novel 4-Aminoquinoline-Pyrimidine Based Hybrids with Improved in Vitro and in Vivo Antimalarial Activity,” *ACS Medicinal Chemistry Letters* 3, no. 7 (2012): 555–9.
8. C. Viegas Jr., A. Danuello, V. daSilva Bolzani, V. E. J. Barreiro, and C. A. M. Fraga, “Molecular Hybridization: A Useful Tool in the Design of New Drug Prototypes,” *Current Medicinal Chemistry* 14 (2007): 1829–52.
9. I. A. Ibarra, A. Islas-Jacome, and E. González-Zamora, “Synthesis of Polyheterocycles *via* Multicomponent Reactions,” *Organic & Biomolecular Chemistry* 16, no. 9 (2018): 1402–18.
10. N. Sharma, D. Mohanakrishnan, A. Shard, A. Sharma, Saima, A. K. Sinha, and D. Sahal, “Stilbene–Chalcone Hybrids: design, Synthesis, and Evaluation as a New Class of Antimalarial Scaffolds That Trigger Cell Death through Stage Specific Apoptosis,” *Journal of Medicinal Chemistry* 55 (2012): 297–11.
11. F. W. Muregi, and A. Ishih, “Next-Generation Antimalarial Drugs: hybrid Molecules as a New Strategy in Drug Design,” *Drug Development Research* 71, no. 1 (2010): 20–32.
12. M. Decker, “Hybrid Molecules Incorporating Natural Products: applications in Cancer Therapy, Neurodegenerative Disorders and beyond,” *Current Medicinal Chemistry* 18, no. 10 (2011): 1464–75.
13. D. Sunil, and P. R. Kamath, “Multi-Target Directed Indole Based Hybrid Molecules in Cancer Therapy : An Up-To-Date Evidence-Based Review,” *Current Topics in Medicinal Chemistry* 17, no. 9 (2017): 959–85.
14. G. S. Singh, and Z. Y. Desta, “Isatins as Privileged Molecules in Design and Synthesis of Spiro-Fused Cyclic Frameworks,” *Chemical Reviews* 112, no. 11 (2012): 6104–55.
15. A. H. Abdel-Rahman, E. M. Keshk, M. A. Hanna, and S. M. El-Bady, “Synthesis and Evaluation of Some New Spiro Indoline-Based Heterocycles as Potentially Active Antimicrobial Agents,” *Bioorganic & Medicinal Chemistry* 12, no. 9 (2004): 2483–8.

16. A. Dandia, D. Saini, S. Bhaskaran, and D. K. Saini, "Ultrasound Promoted Green Synthesis of Spiro [Pyrano(2, 3- c) Pyrazoles] as Antioxidant Agents," *Medicinal Chemistry Research* 23, no. 2 (2014): 725–34.
17. J. Liu, Y. Song, X. Zhang, X. Liang, Y. Wu, Y. Wang, and X. Jiang, "Spirooxindoles, a Potential Class of anti-Inflammatory Agents," *Inflammation and Cell Signaling* 1 (2014): 374–8.
18. V. V. Vintonyak, K. Warburg, H. Kruse, S. Grimme, K. Hubel, D. Rauh, and H. Waldmann, "Identification of Thiazolidinones Spiro-Fused to Indolin-2-Ones as Potent and Selective Inhibitors of the Mycobacterium tuberculosis Protein Tyrosine Phosphatase B," *Angewandte Chemie (International ed. in English)* 49, no. 34 (2010): 5902–5.
19. B. Yu, D. Q. Yu, and H. M. Liu, "Spirooxindoles: Promising Scaffolds for Anticancer Agents," *European Journal of Medicinal Chemistry* 97 (2015): 673–98.
20. B. E. Evans, K. E. Rittle, M. G. Bock, R. M. DiPardo, R. M. Freidinger, W. L. Whitter, G. F. Lundell, D. F. Veber, P. S. Andersons andR, and S. Chang, "Rhodium(II) Acetate-Catalyzed Stereoselective Synthesis, SAR and anti-HIV Activity of Novel Oxindoles Bearing Cyclopropane Ring," *European Journal of Medicinal Chemistry* 46 (2011): 1181–8.
21. Tetyana L. Pavlovska, Ruslan Gr Redkin, Victoria V. Lipson, and Dmytro V. Atamanuk, "Molecular Diversity of Spirooxindoles. Synthesis and Biological Activity," *Molecular Diversity* 20, no. 1 (2016): 299–44.
22. M. M. M. Santos, "Recent Advances in the Synthesis of Biologically Active Spirooxindoles," *Tetrahedron* 70, no. 52 (2014): 9735–57. *and references cited therein.*
23. S. Zhu, J. Wang, Z. Xu, and J. Li, "An Efficient One-Pot Synthesis of Pyrano[3,2-*c*]Quinolin-2,5-Dione Derivatives Catalyzed by L-Proline," *Molecules (Basel, Switzerland)* 17, no. 12 (2012): 13856–63.
24. M.-J. Yao, Z. Guan, and Y.-H. He, "Simple, Catalyst-Free, One-Pot Procedure for the Synthesis of 2-Amino-3-Cyano-1,4,5,6-Tetrahydropyrano[3,2-*c*]Quinolin-5-One Derivatives," *Synthetic Communications* 43, no. 15 (2013): 2073–8.
25. I. V. Magedov, M. Manpadi, M. A. Ogasawara, A. S. Dhawan, S. Rogelj, S. Van Slambrouck, W. F. A. Steelant, N. M. Evdokimov, P. Y. Uglinskii, E. M. Elias, et al. "Structural Simplification of Bioactive Natural Products with Multicomponent Synthesis. 2. Antiproliferative and Antitubulin Activities of pyrano[3,2-c]pyridones and pyrano[3,2-c]quinolones," *Journal of Medicinal Chemistry* 51, no. 8 (2008): 2561–70.
26. K. S. Atwal, J. R. McCullough, A. Hedberg, M. L. Conder, S. Z. Ahmed, G. Cucinotta, and D. E. Normandin, "The Discovery of a Novel Calcium Channel Blocker Related to the Structure of Potassium Channel Opener Cromakalim," *Bioorganic & Medicinal Chemistry Letters* 2, no. 12 (1992): 1475–8.
27. S. T. Hilton, T. C. T. Ho, G. Pljevaljcic, and K. Jones, "A New Route to Spirooxindoles," *Organic Letters* 2, no. 17 (2000): 2639–41.
28. A. A. Aly, E. M. El-Sheref, A.-F E. Mourad, A. B. Brown, S. Brase, M. E. M. Bakheet, and M. Nieger, "Synthesis of Spiro[Indoline-3,4′-Pyrano[3,2-*c*]Quinolone]-3′-Carbonitriles," *Monatshefte Für Chemie - Chemical Monthly* 149, no. 3 (2018): 635–44. 149,
29. M. A. Nasseri, and S. M. Sadeghzadeh, "A Highly Active $FeNi_3$-SiO_2 Magnetic Nanoparticles Catalyst for the Preparation of 4H-Benzo[*b*]Pyrans and Spirooxindoles under Mild Conditions," *Journal of the Iranian Chemical Society* 10, no. 5 (2013): 1047–56.
30. S. S. Khot, P. V. Anbhule, U. V. Desai, and P. P. Wadgaonkar, "Tris-Hydroxymethyl-Aminomethane (THAM) as an Efficient Organocatalyst in Diversity Oriented and Environmentally Benign Synthesis of Spirochromenes," *Comptes Rendus Chimie* 21, no. 9 (2018): 814–21.
31. L. Han, X. Hu, and Z. Zhou, "Diammonium Hydrogen Phosphate as a Recyclable Catalyst for the Rapid and Green Synthesis of 2-Amino-1,4,5,6-Tetrahydropyrano[3,2-*c*]-Quinolin-5-One Derivatives," *Polycyclic Aromatic Compounds* 37, no. 1 (2017): 73–80.
32. R. L. L. de Compadre, R. A. Pearlstein, A. J. Hopfinger, and J. K. Seyde, "A Quantitative Structure-Activity Relationship Analysis of Some 4-Aminodiphenyl Sulfone Antibacterial Agents Using Linear Free Energy and Molecular Modeling Methods," *Journal of Medicinal Chemistry* 30, no. 5 (1987): 900–6.
33. Z. Y. Sun, E. Botros, A. D. Su, Y. Kim, E. Wang, N. Z. Baturay, and C. H. Kwon, " Sulfoxide-Containing Aromatic Nitrogen Mustards as Hypoxia-Directed Bioreductive Cytotoxins ," *Journal of Medicinal Chemistry* 43, no. 22 (2000): 4160–8.
34. M. Artico, R. Silvestri, E. Pagnozzi, B. Bruno, E. Novellino, G. Greco, S. Massa, A. Ettorre, A. G. Loi, F. Scintu, et al. "Structure-Based Design, Synthesis, and Biological Evaluation of Novel Pyrrolyl Aryl Sulfones: HIV-1 Non-Nucleoside Reverse Transcriptase Inhibitors Active at Nanomolar Concentrations," *Journal of Medicinal Chemistry* 43, no. 9 (2000): 1886–91.
35. M. Teall, P. Oakley, T. Harrison, D. Shaw, E. Kay, J. Elliott, U. Gerhard, J. L. Castro, M. Shearman, R. G. Ball, et al. "Aryl Sulfones: A New Class of Gamma-Secretase Inhibitors," *Bioorganic & Medicinal Chemistry Letters* 15, no. 10 (2005): 2685–92.
36. D. C. Meadows, T. Sanchez, N. Neamati, T. W. North, and J. Gervay-Hague, "Ring Substituent Effects on Biological Activity of Vinyl Sulfones as Inhibitors of HIV-1," *Bioorganic & Medicinal Chemistry* 15, no. 2 (2007): 1127–37.

37. S. S. Jin, H. Wang, and H. Y. Guo, “Ionic Liquid Catalyzed One-Pot Synthesis of Novel Spiro-2-Amino-3-Phenylsulfonyl-4*H*-Pyran Derivatives,” *Tetrahedron Letters* 54, no. 19 (2013): 2353–6.
38. A. S. Al-Bogami, “One-Pot, Three Component Synthesis of Novel Pyrano [3 2-*c*] Coumarins Containing Sulfone Moiety Utilizing Ultrasonic Irradiation as Eco-Friendly Energy Source,” *Research on Chemical Intermediates* 41, no. 1 (2015): 93–104.
39. K. S. Pandit, R. V. Kupwade, P. V. Chavan, U. V. Desai, P. P. Wadgaonkar, and K. M. Kodam, “Problem Solving and Environmentally Benign Approach toward Diversity Oriented Synthesis of Novel 2-Amino-3-Phenyl (or Alkyl) Sulfonyl-4*H*-Chromenes at Ambient Temperature,” *ACS Sustainable Chemistry & Engineering* 4, no. 6 (2016): 3450–64.
40. K. S. Pandit, P. V. Chavan, M. A. Kulkarni, U. V. Desai, and P. P. Wadgaonkar, “Tris-Hydroxymethylaminomethane (THAM): a Novel Organocatalyst for a Environmentally Benign Synthesis of Medicinally Important Tetrahydrobenzo[*b*]Pyrans and Pyran-Annulated Heterocycles,” *New Journal of Chemistry* 39, no. 6 (2015): 4452–68.
41. M. A. Kulkarni, V. R. Pandurangi, U. V. Desai, and P. P. Wadgaonkar, “A Practical and Highly Efficient Protocol for Multicomponent Synthesis of *β*-Phosphonomalononitriles and 2-Amino-4*H*-Chromen-4-yl-Phosphonates Using Diethylamine as a Novel Organocatalyst,” *Comptes Rendus Chimie* 15, no. 9 (2012): 745–52.
42. M. A. Kulkarni, K. S. Pandit, U. V. Desai, U. P. Lad, and P. P. Wadgaonkar, “Diethylamine: A Smart Organocatalyst in Eco-Safe and Diastereoselective Synthesis of Medicinally Privileged 2-Amino-4H-Chromenes at Ambient Temperature,” *Comptes Rendus Chimie* 16, no. 8 (2013): 689–95.
43. J. J. Li, *Name Reactions for Carbocyclic Ring Formation* (Hoboken, New Jersey: John Wiley & Sons, 2010), ISBN: 9780470085066.