Condensations with Biaryl Ethers and Carbonyl Groups leading to Spirocycles.

Jeffrey Ferreira, Jacob Hood, and Douglas A. Klumpp*

Department of Chemistry and Biochemistry

Northern Illinois University

DeKalb, Illinois 60115

Abstract

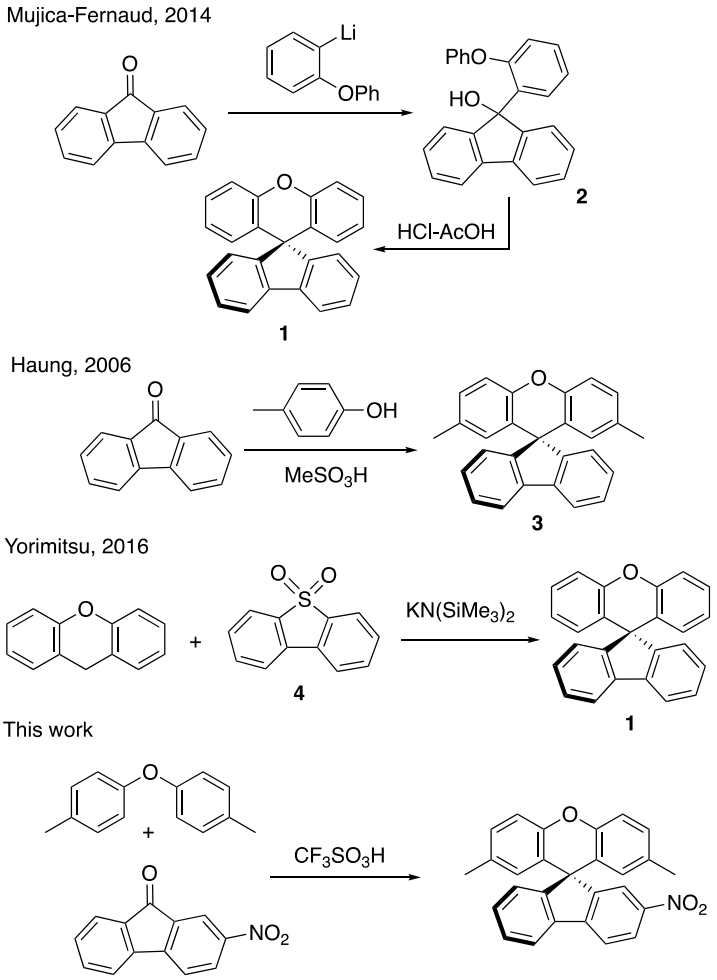
Biaryl ethers condense directly with carbonyl groups on diazafluorenones, acenaphthenequinone, and isatins, to give a variety of spirocyclic compounds. The condensation reactions are promoted by the Brønsted superacid, CF_3SO_3H (triflic acid). This methodology provides a convenient one-pot synthetic route to aromatic spirocycles.

1. Introduction

Aromatic spirocyclic compounds have emerged as some of the most important scaffolds for use in organic based electronics.[1] They are used extensively in the fabrication of organic light emitting diodes (OLEDs), organic field effect transistors, and organic solar cells.[2] Aromatic spirocycles can possess high thermal stabilities, amorphous solid states, and exhibit rigidity that helps control excited state energies. As a scaffold, the aromatic spirocycles are used in design strategies to host hole-transport, electron-carrying, and emissive units.[3] This has driven a considerable amount work to develop new synthetic methods leading spirocycles.

The xanthene-based spirocycles, such as spiro[fluorene-9,9'-xanthene] (**1**), have been utilized in hole-transport layers in dye-sensitized and perovskite solar cells and OLEDs.[4] Their syntheses parallels the methods used to prepare other aromatic spirocycles (Scheme 1). The

Scheme 1. Synthetic route to xanthene-based spirocycles.



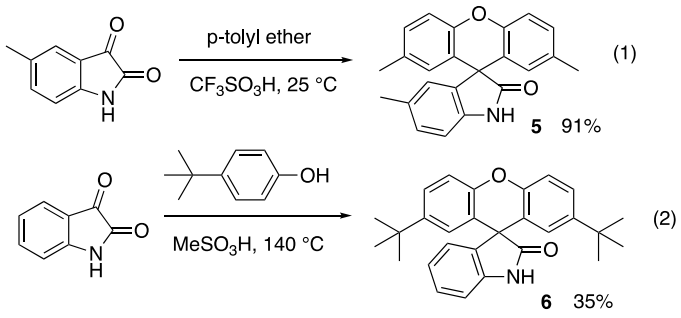
most common method of spirocycle synthesis involves an acid-promoted cyclodehydration of the alcohol **2**, prepared by organometallic chemistry and fluorenone.[5] This methodology has been extensively used in the preparation of 9,9'-spirobifluorenes and related heterocyclic systems.[6]

The cyclization step usually employs AcOH-HCl or AcOH-H_2SO_4 acid promoters. A one-pot synthetic route was described by Haung in which fluorenone is condensed directly with *p*-cresol in the presence of methanesulfonic acid.[7] A similar conversion was described recently involving condensations with diazafluorenones.[8] Yorimitsu reported a method of preparing the fluorene ring by sequential S_NAr reaction steps from the sulfone (**4**).[9] While each of these methods can provide reasonable yields of the spirocyclic products, we describe in this manuscript a new method of spirocyclic ring synthesis - one without the need of organometallic reagents or strong bases. We demonstrate that a variety of aromatic spirocycles may be prepared in one-pot from direct condensations of carbonyl compounds with diarylethers.

2. Results and Discussion

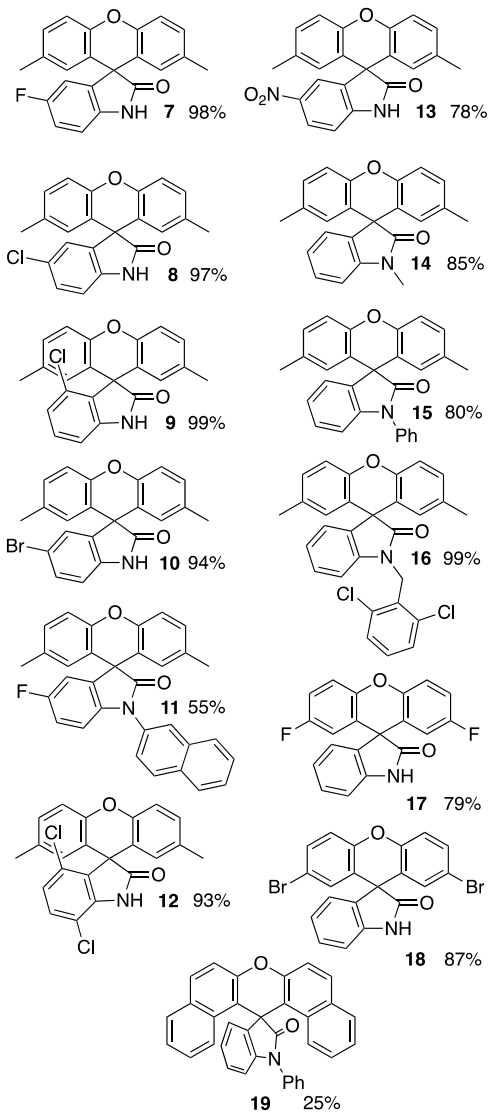
Our research group has carried out numerous studies involving the electrophilic activation of carbonyl groups using superacid catalysis. Some of these reports describe double protonation at dicarbonyl compounds to generate dicationic superelectrophiles.[10] Other reports show that carbonyl protonation along with protonation of a nearby base site can lead to highly reactive dicationic electrophiles.[11] In general, dicationic intermediates react readily with arene nucleophiles and the chemistry can provide high yields of condensation products. We reasoned that similar condensation reactions might be possible with biaryl substrates to give spirocyclic products. To test this hypothesis, we first examined condensations of isatins and diaryl ethers. For our initial investigations, we used *p*-tolyl ether as the arene nucleophile. With the ether oxygen being a strong *ortho/para* director, it was assumed that having the *para* position blocked would inhibit polymerization reactions and electrophilic attack at an *ortho* position would lead to

rapid cyclization to a spirocycle. Thus, 5-methylisatin is reacted with p-tolyl ether to provide the spirocycle **5** in excellent yield (eq 1). The conversion was accomplished using



equimolar amounts of the isatin and diaryl ether with 5 equivalents of triflic acid. A comparable product was reported from the direct condensation of isatin with 4-*tert*-butylphenol (eq 2), however the spirocycle **6** was only isolated in 35% yield (plus 18% yield of dealkylated spirocycle).[12] Following this result, a series of isatins were reacted to provide spirocycles (Table 1). With 4-chloroisatin, a quantitative yield of the spirocycle **9** was formed from a gram-scale synthesis, where 4-chloroisatin (1.0 g, 5.5 mmol) reacts with p-tolyl ether (1.08 g, 5.5 mmol) and TfOH (3 mL, 30.1 mmol) to provide 1.99 g of product **9** (99% yield). Comparable yields of product **9** were obtained using 2 equivalents (98%) and 1.0 equivalent (93%) of TfOH, but 0.5 equivalents provided lower yield (43%). Weaker acids such as H_2SO_4 or CF_3CO_2H gave only trace amounts of product **9** from the condensation reaction. The condensation reactions gave generally good yields from isatins having both N- and C-substituents. Halogen-substituted isatins provide products **7-12** while the *N*-alkyl and *N*-aryl substituted isatins give **11** and **14-15**. With bis(4-fluorophenyl)ether, spirocycle **17** is prepared in good yield from isatin. Likewise, bis(4-bromophenyl)ether gives the spirocycle **18**. A reaction with bis-(2-naphthyl) ether gives the novel spirocycle **19** in low yield.

Table 1. Products and isolated yields from the superacid promoted dehydration reactions of isatins and diaryl ethers. [a,b]

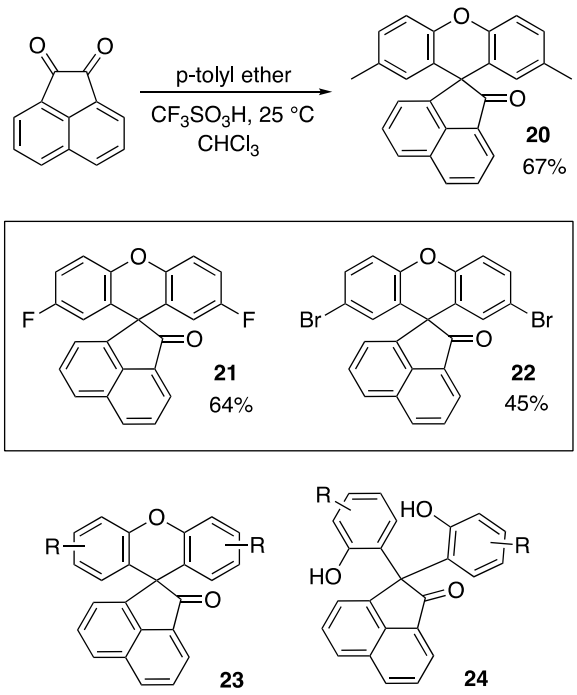


[a]Isolated yields. [b]Reaction conditions: 1 mmol isatin, 1 mmol diaryether, 10 mL $CHCl_3$, and 5 mmol CF_3SO_3H, 25 °C for 20 hrs.

Our group has previously reported condensation reactions of acenaphthenequinone with aromatic nucleophiles.[10b] With p-tolyl ether, acenaphthenequinone gives spirocycle **20** in reasonable yield. Similarly, the halogenated aryl ethers provide spirocycles **21** and **22** in 64%

and 45% yields, respectively. These yields are somewhat lower than those from the condensation reactions involving isatins. This may be a consequence of the poor solubility of acenaphthenequinone in chloroform. Nevertheless, spirocycles **20-22** are obtained directly from the diaryl ethers. This class of spirocycles are not well known. The only literature reference to these substances dates to the 1930s, where acenathpthenequinone is described condensing with naphthols, cresols, and related phenols, in reactions promoted by strong acid.[13] Depending on the conditions, either the spirocycles (**23**) or the 2,2-bi(aryl)-1(*2H*)-acenaphthylenones (**24**) were obtained.[13]

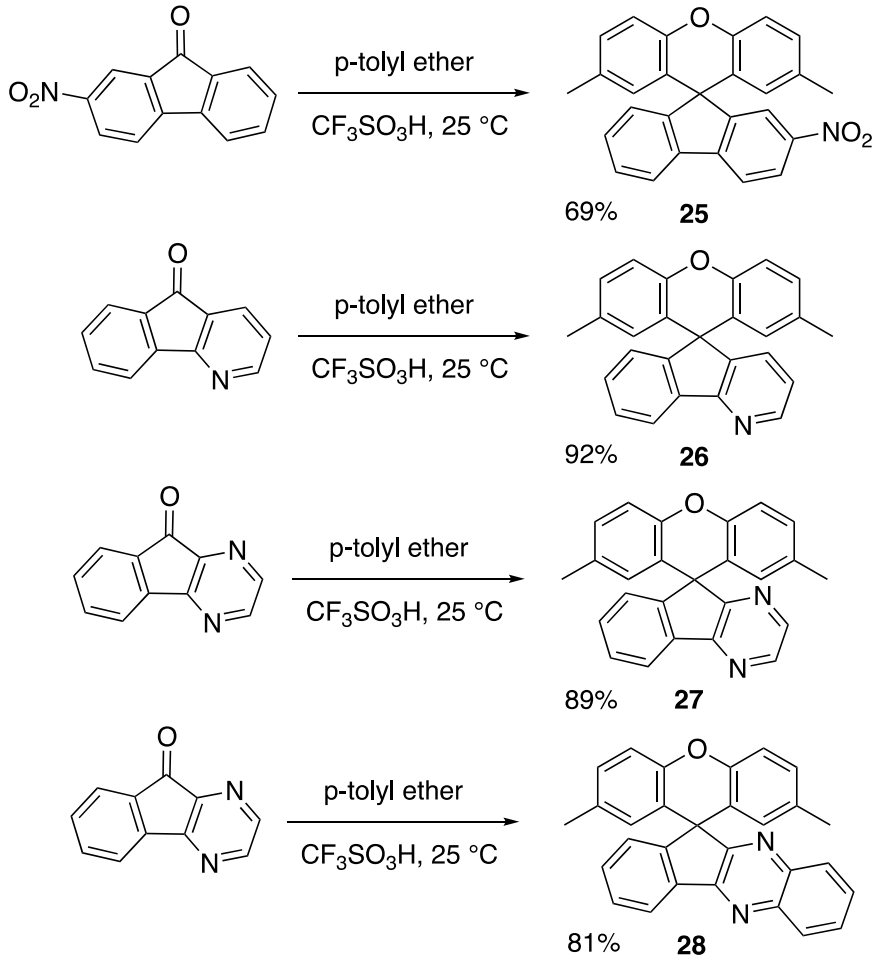
Scheme 1. Condensation products from acenaphthenequinone.



Fluorene-based spirocycles have been particularly useful in OLED devices and other organic electronics. Huang and coworkers described the synthesis of spiro[fluorene-9,9'-

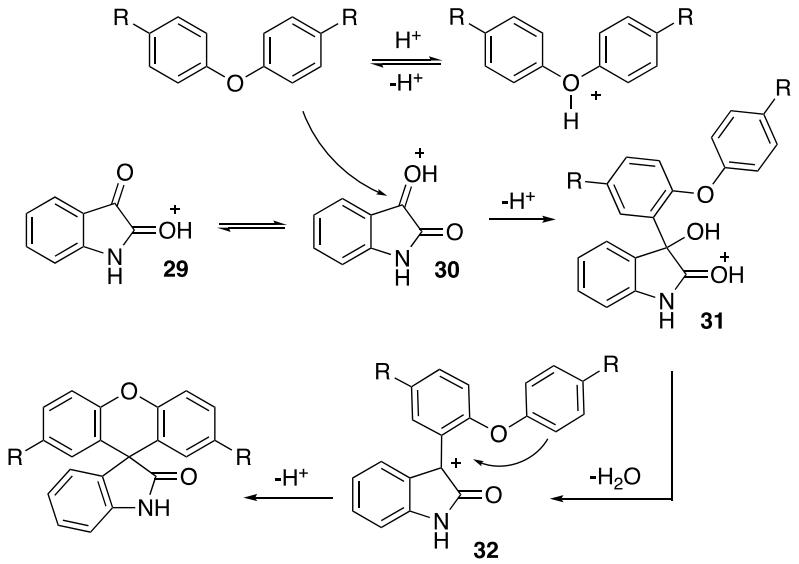
xanthene products from the direct acid-promoted ($MeSO_3H$) condensation of fluorenes with phenol.[8] Despite using several types of acids and reaction conditions, we were unable to form the spirocycle from 9-fluorenone and *p*-tolyl ether. However, 2-nitrofluorenone provides a fair yield of the condensation product **25** with *p*-tolyl ether in a triflic acid-promoted reaction (Scheme 2). Similarly, the 4-aza-9-fluorenone gives an excellent yield of the spirocycle **26** and the pyrazinyl and quinoxalinyl systems give products **27-28**.

Scheme 2. Condensation reactions leading to fluorenyl and azafluorenyl spirocycles.



Regarding the mechanisms of these conversions, condensation reactions at carbonyl groups with arene nucleophiles require formation of the carboxonium ion (protonated carbonyl group). A good yield of the isatin condensation product **9** was obtained with 1.0 equivalent of superacid and this suggests a conversion involving monocationic intermediates. Isatin likely forms an equilibrium between the two monoprotonated isomers (**29** and **30**), the aryl ether reacting with **30** (Scheme 3). Spirocycle formation occurs by ionization to the carbocation **32**

Scheme 3. Proposed mechanism of condensation and presumed electrophilic intermediates.



followed by rapid cyclization. A key aspect of this conversion is the low nucleophilicity of the triflate counter ion, which may allow the electrophilic species (**30** and **32**) to exist as essentially

free ions. In the reactions where excess superacid is used, there is the potential for diprotonated, superelectrophilic species to exist.[14] For the isatins, this would involve diprotonated intermediates such as **34**. A previous report described superacid-promoted condensation reactions with isatins and superelectrophile **34** was proposed as an intermediate.[10d] Similar dicationic electrophiles are plausible (**35** and **36**) for the reactions of acenaphthenequinone and the azafluorenone in excess superacid.

3. Conclusions

In summary, we have found that *p*-tolyl ether provides xanthene-based spirocycles by superacid-promoted condensation reactions at the carbonyl groups of isatins, aceanthrenequinone, as well as with some fluorenones and azafluorenones. In some cases, spirocycle formation may be accomplished with bis-(4-halophenyl)ether.

4. Experimental section

4.1 General Considerations

Condensation reactions were performed with an inert atmosphere using thoroughly dried glassware. Products were isolated by flash chromatography using 60 Å silica gel. ^{1}H and ^{13}C NMR were carried out using either a 300 or 500 MHz spectrometer. Chemical shifts were referenced to NMR solvent signals. High-resolution mass spectra were obtained from a commercial analytical laboratory with a time-of-flight (TOF) mass analyzer used for data collection. Heated reactions were done is thick-walled, glass pressure tube with a Teflon screw cap. Reagents and solvents were purchased from commercial suppliers and used as received. Triflic acid was distilled prior to use and stored under a dry inert atmosphere. SAFETY: triflic acid is highly corrosive – it should

be handled in an efficient fume hood by appropriately trained individuals utilizing personal protective gear.

4.2 General procedure for spirocycle formation

The carbonyl compound (1 mmol) and diarylether (1 mmol) were dissolved in $CHCl_3$ (10 mL) and triflic acid (0.5 mL, 5.7 mmol) was slowly added. The mixture stirred for 24 hrs and then poured over ca. 10 g of ice. The resulting mixture was made basic with saturated $NaHCO_3$ solution, extracted 2x with $CHCl_3$, and the organic extracts washed then brine. The solution was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was purified via silica gel column chromatography to give the final product.

4.2.1 **2',5,7'-Trimethylspiro[indoline-3,9'-xanthen]-2-one (5).** Using the general procedure, 5-methylisatin (0.16 g, 1 mmol) and *p*-tolyl ether (0.2 g, 1 mmol) provided compound **5** (0.3 g, 0.91 mmol, 91%) as a white solid. MP > 260°C. R_f = 0.35 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25ºC) δ 8.49 (s, 1H), 7.14-7.06 (m, 6H), 6.92 (d, J = 7.89 Hz, 1H), 6.83 (s, 1H), 6.50 (s, 2H), 2.26 (s, 3H), 2.19 (s, 6H). ^{13}C {^{1}H}NMR (75 MHz, $CDCl_3$, 25ºC) δ 180.5, 149.2, 138.4, 136.7, 133.3, 132.7, 129.9, 129.1, 127.5, 126.2, 120.3, 116.9, 109.8, 53.4, 21.1, 20.7. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{23}H_{20}O_2N$ 342.1489, found 342.1494.

4.2.2 **5-Fluoro-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (7).** Using the general procedure, 5-fluoroisatin (0.12 g, 0.76 mmol) and *p*-tolyl ether (0.15 g, 0.76 mmol) provided compound **7** (0.26 g, 0.75 mmol, 98%) as an orange solid. MP > 260°C. R_f = 0.47 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.15-7.09 (m, 4H), 7.05-6.94 (m, 2H),

6.77 (dd, J = 7.83 Hz, J = 2.43 Hz, 1H), 6.47 (s, 2H), 2.20 (s, 6H). $^{13}C\{^{1}H\}$NMR (75 MHz, $CDCl_3$) δ 180.7, 161.3, 158.1, 149.1, 137.8 (d, J_{C-F} = 7.9 Hz), 136.9 (d, J_{C-F} = 2.7 Hz), 132.9, 130.3, 127.2, 119.4, 117.1, 115.5 (d, J_{C-F} = 23.7 Hz), 113.4 (d, J_{C-F} = 24.6 Hz), 111.0 (d, J_{C-F} = 7.9 Hz), 53.9, 20.7. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{22}H_{16}O_2NFNa$ 368.1057, found 368.1063.

4.2.3 **5-Chloro-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (8).** Using the general procedure, 5-chloroisatin (0.18 g, 1 mmol) and *p*-tolyl ether (0.2 g, 1 mmol) provided compound **8** (0.35 g, 0.97 mmol, 97%) as a white solid. MP > 260°C. R_f = 0.33 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.29-7.27 (m, 2H), 7.15-7.10 (m, 4H), 7.01 (d, J = 2.10 Hz, 1H), 6.95 (d, J = 8.35 Hz, 1H), 6.47 (d, J = 1.6 Hz, 2H), 2.21 (s, 6H). $^{13}C\ \{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 180.2, 149.1, 139.5, 138.0, 133.0, 130.3, 128.9, 127.3, 126.0, 119.3, 117.1, 111.3, 53.5, 20.7. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{22}H_{17}O_2NCl$ 362.0942, found 362.0948.

4.2.4 **4-Chloro-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (9).** Using the general procedure, 4-chloroisatin (0.14 g, 0.76 mmol) and p-tolyl ether (0.15 g, 0.76 mmol) provided compound **9** (0.27 g, 0.76 mmol, 99%) as a yellow solid. MP > 260°C. R_f = 0.39 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.30-7.24 (m, 3H), 7.11 (d, J = 0.81 Hz, 4H), 7.00 (dd, J = 8.16 Hz, J = 0.72, 1H), 6.96 (dd, J = 7.77 Hz, J = 0.75 Hz, 1H), 6.48 (s, 2H), 2.20 (s, 6H). $^{13}C\ \{^{1}H\}$NMR (75 MHz, $CDCl_3$) δ 179.8, 149.3, 142.4, 132.7, 132.6, 131.9, 130.3, 130.1, 126.6, 124.3, 117.6, 117.0, 108.7, 53.6, 20.7. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{22}H_{16}O_2NClNa$ 384.0762, found 384.0767.

4.2.5 **5-Bromo-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (10).** Using the general procedure, 5-bromoisatin (0.17 g, 0.76 mmol) and p-tolyl ether (0.15 g, 0.76 mmol) provided compound **10** (0.29 g, 0.71 mmol, 94%) as a yellow solid. MP > 260°C. R_f = 0.55 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.45 (dd, J = 8.30 Hz, J = 1.90 Hz, 1H), 7.15-7.10 (m, 5H), 6.93 (d, J = 8.3 Hz, 1H), 6.47 (s, 2H), 2.21 (s, 6H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 179.5, 149.1, 139.7, 138.5, 133.0, 131.8, 130.3, 128.9, 127.2, 119.3, 117.2, 116.3, 111.5, 53.4, 20.7. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{22}H_{16}O_2NBrNa$ 428.0257, found 428.0262.

4.2.6 **5-Fluoro-1-(naphthalen-2-yl)-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (11).** Based on a published procedure,[15] 5-fluorisatin (0.10 g, 0.6 mmol), 2-naphthylboronic acid (0.16 g, 0.9 mmol), anhydrous $Cu(OAc)_2$ (0.16 g, 0.9 mmol), and triethylamine (0.25 mL, 1.8 mmol) were dissolved in 15 mL dichloromethane and stirred at room temperature for 3 days. 5-Fluoro-1-(naphthalen-2-yl)indoline-2,3-dione (0.08 g, 0.27 mmol, 45%) was isolated as a red solid from silica gel column chromatography. MP 212-216°C. R_f = 0.24 (hexanes:ethyl acetate. 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 8.70 Hz, 1H), 7.97-7.90 (m, 3H), 7.63-7.59 (m, 2H), 7.51-7.44 (m, 2H), 7.33-7.26 (m, 1H), 6.95 (q, J = 8.70 Hz, J = 3.72 Hz, 1H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 182.6, 160.3, 158.4, 157.4, 148.3, 133.7, 133.0, 131.1, 129.7, 128.0 (d, J = 19.63 Hz), 126.9 (d, J = 8.28 Hz), 125.3, 124.2, 124.0, 118.8 (d, J = 7.14 Hz), 112.7 (d, J = 7.29 Hz), 111.2 (d, J = 24.30 Hz). ^{19}F {^{1}H}NMR (470 MHz, $CDCl_3$) δ -120.8. HRMS calculated for $C_{18}H_{10}O_2NFNa$ $[M+Na]^+$ m/z = 314.0594, found 314.0588. Using the general procedure, 5-fluoro-1-(naphthalen-2-yl)indoline-2,3-dione (0.08 g, 0.27 mmol), p-tolyl ether (0.05 g, 0.27

mmol), and triflic acid (1 mL, 11.6 mmol) provided compound **11** (0.07 g, 0.15 mmol, 55%) as a yellow solid from silica gel column chromatography. MP 246-250°C. R_f = 0.61 (hexanes:ethyl acetate, 9:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (q, J = 5.1 Hz, J = 3.2 Hz, 2H), 7.95-7.91 (m, 2H), 7.63-7.58 (m, 3H), 7.18-7.13 (m, 4H), 7.05 (q, J = 7.45 Hz, J = 1.95 Hz, 2H), 6.93-6.91 (m, 1H), 6.63 (s, 2H), 2.27 (s, 6H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 177.2, 161.0, 159.1, 149.3, 139.7 (d, J = 1.73 Hz), 137.1 (d, J = 7.65 Hz), 133.7, 133.0, 132.7, 131.8, 130.2, 129.7, 127.9 (d, J = 10.90 Hz), 127.1, 126.8 (d, J = 5.33 Hz), 125.3, 124.0, 120.1, 117.2, 115.3 (d, J = 23.46 Hz), 113.5 (d, J = 24.59 Hz), 110.5 (d, J = 7.94 Hz), 53.4, 20.8. ^{19}F {^{1}H}NMR (470 MHz, $CDCl_3$) δ -118.1. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{32}H_{22}O_2NFNa$ 494.1533, found 494.1527.

4.2.7 **4,7-Dichloro-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (12).** Using the general procedure, 4,7-dichloroisatin (0.16 g, 0.76 mmol) and p-tolyl ether (0.15 g, 0.76 mmol) provided compound **12** (0.28 g, 0.71 mmol, 93%) as a white solid from silica gel column chromatography. MP > 260°C. R_f = 0.68 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.30 (d, J = 8.65 Hz, 1H), 7.15-7.07 (m, 4H), 6.96 (d, J = 8.70 Hz, 1H), 6.50 (s, 2H), 2.22 (s, 6H); ^{13}C {^{1}H} NMR (75 MHz, d_6-DMSO) δ 178.5, 149.0, 142.5 133.6, 133.2, 131.3, 130.8, 129.2, 126.3, 124.6 118.1, 117.1, 113.9, 54.2, 20.6. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{22}H_{15}O_2NCl_2$ 418.0372, found 418.0378.

4.2.8 **5-Nitro-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (13).** Using the general procedure, 5-nitroisatin (0.19 g, 1 mmol) and p-tolyl ether (0.2 g, 1 mmol) provided compound **13** (0.29 g, 0.78 mmol, 78%) as a white solid from silica gel column chromatography. MP > 260°C. R_f = 0.38 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.29 (dd, J = 8.64 Hz, J = 2.28 Hz, 1H), 7.93 (d, J = 2.19 Hz, 1H), 7.20-7.12 (m, 5H), 6.40 (s, 2H),

2.20 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, DMSO) δ 179.4, 149.3, 148.9, 143.6, 137.3, 133.5, 130.8, 127.3, 126.9, 120.0, 119.7, 117.3, 111.2, 53.0, 20.6. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{22}H_{17}O_4N_2$ 373.1183, found 373.1189.

4.2.9 **1,2',7'-Trimethylspiro[indoline-3,9'-xanthen]-2-one (14).** Using the general procedure, *N*-methylisatin (0.12 g, 0.76 mmol) and p-tolyl ether (0.15 g, 0.76 mmol) provided compound **14** (0.23 g, 0.65 mmol, 85%) as a white solid after silica gel column chromatography. MP 208-210 °C. R_f = 0.53 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25ºC) δ 7.44-7.39 (m, 1H), 7.13-7.02 (m, 7H), 6.38 (d, J = 1.17 Hz, 2H), 3.34 (s, 3H), 2.17 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$, 25ºC) δ 178.2, 149.4, 143.9, 135.8, 132.6 129.8, 128.8, 127.1, 125.4 123.8, 120.5, 116.7, 108.3, 53.0, 26.8, 20.7. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{23}H_{20}O_2N$ 342.1489, found 342.1494.

4.2.10 **1-Phenyl-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (15).** Using the general procedure, *N*-phenylisatin (0.22 g, 1 mmol) and p-tolyl ether (0.2 g, 1 mmol) provided compound **15** (0.32 g, 0.80 mmol, 80%) as a yellow solid from silica gel column chromatography. MP 201-203°C. R_f = 0.83 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58-7.53 (m, 4H), 7.45-7.42 (m, 1H), 7.35-7.32 (m, 1H), 7.15-7.08 (m, 6H), 7.04 (d, J = 7.90 Hz, 1H), 6.57 (d, J = 1.4 Hz, 2H), 2.22 (s, 6H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 177.2, 149.4, 143.6, 135.7, 134.5, 132.7, 129.9, 129.6, 128.6, 128.1, 127.2, 126.5, 125.8, 124.2, 120.7, 117.0, 109.6, 53.1, 20.7. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{28}H_{22}O_2N$ 404.1645, found 404.1651.

4.2.11 **1-(2,6-Dichlorobenzyl)-2',7'-dimethylspiro[indoline-3,9'-xanthen]-2-one (16).** Using the general procedure, *N*-(2,6-dichlorobenzyl)isatin (0.1 g, 0.33 mmol), p-tolyl ether (0.07 g, 0.33 mmol), and triflic acid (1 mL, 34 equiv) provided compound **16** (0.16 g, 0.33 mmol, 99%) as a pure yellow solid. MP 213-216°C. R_f = 0.73 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.39 (s, 1H), 7.28-7.25 (m, 2H), 7.13-7.06 (m, 6H), 6.92 (d, J = 7.89 Hz, 1H), 6.45 (s, 2H), 5.29 (s, 2H), 2.18 (s, 6H). ^{13}C {^{1}H}NMR (75 MHz, $CDCl_3$) δ 177.3, 149.3, 143.3, 136.5, 135.5, 132.4, 130.5, 130.0, 129.9, 129.0, 128.8, 127.8, 125.7, 123.6, 120.3, 116.9, 109,2, 52.7, 40.7, 20.7. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{29}H_{22}O_2NCl_2$ 486.1022, found 486.1020.

4.2.12 **2',7'-Difluorospiro[indoline-3,9'-xanthen]-2-one (17).** Using the general procedure, isatin (0.10 g, 0.68 mmol) and di-(p-fluorophenyl) ether (0.23 mL, 1.36 mmol) provided compound **17** (0.18 g, 0.54 mmol, 79%) as a yellow solid from silica gel column chromatography. MP >260°C. R_f = 0.40 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.37 (td, J = 7.75 Hz, J = 1.25 Hz, 1H), 7.22 (dd, J = 9.05 Hz, J = 4.70 Hz, 2H), 7.13 (td, J = 7.50 Hz, J = 0.70 Hz, 1H), 7.08-7.01 (m, 4H), 6.40 (dd, J = 8.80 Hz, J = 2.95 Hz, 2H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 178.9, 159.5, 157.6, 147.6, 141.2, 133.9, 129.7, 125.8, 124.1, 121.1 (d, J = 7.68 Hz), 118.6 (d, J = 8.23 Hz), 116.5 (d, J = 23.59 Hz), 113.4 (d, J = 24.28 Hz), 110.6, 53.8. ^{19}F {^{1}H}NMR (470 MHz, $CDCl_3$) δ -119.1. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{20}H_{12}O_2NF_2$ 336.0831, found 336.0824.

4.2.13 **2',7'-Dibromospiro[indoline-3,9'-xanthen]-2-one (18).** Using the general procedure, isatin (0.10 g, 0.68 mmol) and di-(p-bromophenyl) ether (0.44 g, 1.36 mmol) provided compound **18** (0.27 g, 0.59 mmol, 87%) as a white solid from silica gel column chromatography.

MP > 260°C; R_f = 0.50 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.42 (dd, J = 8.75 Hz, J = 2.30 Hz, 2H), 7.38 (td, J = 15.45 Hz, J = 7.75 Hz, J = 1.05 Hz, 1H), 7.14 (m, 3H), 7.05 (dd, J = 11.1 Hz, J = 7.75 Hz, 2H), 6.79 (d, J = 2.3 Hz, 2H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 178.5, 150.2, 141.1, 133.8, 132.5, 129.9, 129.8, 125.8, 124.3, 122.4, 119.1, 116.1, 110.6, 53.1. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{20}H_{12}O_2NBr_2$ 455.9229, found 455.9219.

4.2.14 **1'-Phenylspiro[dibenzo[*a,j*]xanthene-14,3'-indol]-2'-one (19).** Using the general procedure (2.5 mL, 27 mmol, triflic acid used), *N*-phenylisatin (0.2 g, 0.9 mmol) and 2-dinaphthyl ether (0.24 g, 0.9 mmol) provided compound **19** (0.11 g, 0.23 mmol, 25%) as a yellow solid from silica gel column chromatography. MP > 260 °C. R_f = 0.32 (hexanes:ethyl acetate, 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12-8.09 (m, 2H), 7.87 (s, 1H), 7.84-7.80 (m, 5H), 7.69 (t, J = 7.53 Hz, 2H), 7.54 (t, J = 7.41 Hz, 1H), 7.47 (s, 1H), 7.44 (s, 1H), 7.38-7.32 (m, 5H), 7.29-7.24 (m, 1H), 7.17 (d, J = 7.05 Hz, 1H), 6.98 (td, J = 7.32 Hz, J = 1.17 Hz, 1H). ^{13}C {^{1}H}NMR (75 MHz, $CDCl_3$) δ 177.6, 148.5, 143.3, 135.4, 134.6, 131.8, 131.7, 131.4, 130.0, 129.7, 129.0, 128.5, 127.1, 126.4, 125.8, 125.0, 124.0, 122.8, 118.5, 112.2, 109.7, 53.4. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{34}H_{21}NO_2$ Na 498.1470 found 498.1465.

4.2.15 **2',7'-Dimethyl-2H-spiro[acenaphthylene-1,9'-xanthen]-2-one (20).** Using the general procedure, acenaphthenequinone (0.14 g, 0.76 mmol) and *p*-tolyl ether (0.15 g, 0.76 mmol) provided compound **30** (0.18 g, 0.51 mmol, 67%) as a yellow solid from silica gel column chromatography. MP 170-172°C. R_f = 0.68 (hexanes:ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 8.10 Hz, 1H), 8.13 (d, J = 6.96 Hz, 1H), 8.01 (d, J = 8.34 Hz, 1H), 7.88 (dd, J = 8.01, J = 7.23, 1H), 7.74 (dd, J = 8.22 Hz, J = 7.02 Hz, 1H), 7.38 (d, J = 6.93 Hz, 1H),

7.18 (d, J = 8.34 Hz, 2H), 7.06 (dd, J = 8.34 Hz, J = 1.80 Hz, 2H), 6.20 (d, J = 1.05 Hz, 2H), 2.07 (s, 6H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 203.0, 149.4, 144.1, 143.2, 132.4, 131.9, 131.4, 130.5, 130.2, 129.8, 129.6, 129.0, 127.7, 124.8, 124.0, 122.3, 121.8, 118.6, 116.9, 58.0, 20.6. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{26}H_{18}O_2Na$ 385.1199, found 385.1205.

4.2.16 **2',7'-Diflouro-2H-spiro[acenaphthylene-1,9'-xanthen]-2-one (21).** Using the general procedure, acenaphthenequinone (0.12 g, 0.68 mmol) and di-(p-fluorophenyl) ether (0.23 mL, 1.36 mmol) provides compound **21** (0.16 g, 0.44 mmol, 64%) as a yellow solid from silica gel column chromatography. MP 185-188°C. R_f = 0.52 (hexanes:ethyl acetate, 9:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 8.15 Hz, 1H), 8.08 (dd, J = 23.55, J = 6.95 Hz, 2H), 7.89 (t, J = 15.15 Hz, J = 7.5 Hz, 1H), 7.78 (t, J = 15.30 Hz, J = 7.25 Hz, 1H), 7.40 (d, J = 6.90 Hz, 1H), 7.24 (q, J = 4.75 Hz, 2H), 6.99 (m, 2H), 6.09 (dd, J = 8.85 Hz, J = 2.80 Hz, 2H). ^{13}C {^{1}H}NMR (125 MHz, $CDCl_3$) δ 201.2, 159.4, 157.5, 147.6 (d, J = 1.68 Hz), 143.2, 141.9, 132.3, 130.5, 130.1, 129.7, 129.3, 125.6, 124.6, 122.5 (d, J = 5.76 Hz), 118.4 (d, J = 8.18 Hz), 116.1 (d, J = 23.49 Hz), 113.5 (d, J = 24.28 Hz), 58.4. ^{19}F {^{1}H}NMR (470 MHz, $CDCl_3$) δ -119.7. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{24}H_{12}O_2F_2Na$ 393.0698, found 393.0689.

4.2.17 **2',7'-Dibromo-2H-spiro[acenaphthylene-1,9'-xanthen]-2-one (22).** Using the general procedure, acenaphthenequinone (0.12 g, 0.68 mmol) and di-(p-bromophenyl) ether (0.44 g, 1.36 mmol) provides compound **22** (0.15 g, 0.31 mmol, 45%) as a yellow solid from silica gel column chromatography. MP 217-219°C. R_f = 0.41 (hexanes:ethyl acetate, 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, J = 8.16 Hz, 1H), 8.09 (dd, J = 9.54 Hz, J = 7.05 Hz, 2H), 7.91 (dd, J = 8.04 Hz, J = 7.14 Hz, 1H), 7.79 (dd, J = 8.31 Hz, J = 7.02 Hz, 1H), 7.41-7.36 (m, 3H), 7.18 (s, 1H), 7.15 (s, 1H), 6.46 (d, J = 2.34 Hz, 2H). ^{13}C {^{1}H}NMR (75 MHz, $CDCl_3$) δ 201.0, 150.3, 143.3,

141.7, 132.4, 132.1, 130.6, 130.0, 129.9, 129.8, 129.4, 125.7, 124.9, 123.8, 122.6, 119.0, 115.8, 57.7. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{24}H_{12}O_2Br_2Na$ 512.9096, found 512.9088.

2',7'-dimethyl-2-nitrospiro[fluorene-9,9'-xanthene] (25). Using the general procedure , 2-nitro-9H-fluoren-9-one (112 mg, 0.5 mmol) and *p*-tolyl ether (99 mg, 0.5 mmol) produced compound **25** (140 mg, 0.35 mmol, 69%) as a white solid from silica gel chromatography. MP>250 ºC. R_f=0.56 (hexanes;ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (dd, J= 6.3, 2.1, 1H), 8.00 (d, J= 2.1, 1H), 7.95-7.92 (m, 2H), 7.50 (td, J=6.4 ,1.1, 1H), 7.39 (td, J= 6.3 ,1.1, 1H), 7.27-7.24 (m, 1H), 7.16 (d, J= 8.3, 2H), 7.04 (dd, J= 6.5, 1.9, 2H), 6.10 (d, J=1.4, 2H), 2.05 (s, 6H). ^{13}C {^{1}H}NMR (75 MHz, $CDCl_3$) δ 156.4, 156.3, 149.4, 147.9, 137.4, 132.6, 130.6, 129.6, 128.4, 127.4, 124.0, 122.4, 121.30, 121.27, 120.2, 117.0, 54.5, 20.6. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{27}H_{20}NO_3$ 406.1438, found 406.1440.

4.2.18 **2',7'-dimethylspiro[indeno[1,2-b]pyridine-5,9'-xanthene] (26).** Using the general procedure, 5H-indeno[1,2-b]pyridin-5-one (90 mg, 0.5 mmol) and *p*-tolyl ether (99 mg, 0.5 mmol) produced compound **26** (166 mg, 0.46 mmol, 92%) as a white solid from silica gel chromatography. R_f=0.21 (hexanes:ethyl acetate, 2:1). MP>250 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (dd, J= 4.9, 1.5, 1H), 8.17 (d, J= 7.6, 1H), 7.54-7.46 (m, 2H), 7.38 (td, J=7.5, 1.1, 1H), 7.26 (t, J= 6.6, 1H), 7.15-7.10 (m, 3H), 7.02 (dd, J= 8.4, 1.9, 2H), 6.18 (d, J= 1.5, 2H), 2.05 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.7, 155.2, 149.5, 149.2, 149.0, 139.1, 133.1, 130.5, 129.3, 128.4, 127.6, 125.8, 123.1, 122.7, 120.8, 116.6, 52.4, 20.62, 20.59. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{26}H_{20}NO$ 362.1539, found 362.1542.

4.2.19 **2',7'-dimethylspiro[indeno[1,2-b]pyrazine-9,9'-xanthene] (27).** A solution of ninhydrin (356 mg, 2 mmol) in EtOH (10 mL) is added to ethylenediamine (0.13 ml, 2 mmol)

and acetic acid (0.5 mL).[16] The mixture is stirred at 60 °C for 4 h (open to the air). After cooling to room temperature, the solvent is removed under reduced pressure and the residue is purified from silica gel column chromatography to afford 9H-indeno[1,2-b]pyrazin-9-one (138 mg, 0.76 mmol, 38%) as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.55-8.51 (m, 2H), 7.90 (d, J= 7.4, 1H), 7.83 (d, J=7.4, 1H), 7.70 (td, J=6.5, 1.1, 1H), 7.56 (td, J=6.6, 0.9, 1H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 190.3, 160.5, 148.1, 146.6, 144.5, 140.6, 136.3, 133.7, 132.0, 124.7, 121.8. Using a modified general procedure, 9H-indeno[1,2-b]pyrazin-9-one (91mg, 0.5 mmol), *p*-tolyl ether (99 mg, 0.5 mmol), and triflic acid (0.44 ml, 5 mmol) where heated to 50ºC for 20 hours, which produced compound **27** (161 mg, 0.44 mmol, 89%) as a white solid from silica gel chromatography. R_f=0.43 (hexanes:ethyl acetate, 2:1). MP>250 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.48 (d, J= 2.8, 1H), 8.29 (d, J= 2.8, 1H), 8.19 (d, J= 7.2, 1H), 7.59 (td, J=7.4, 1.2, 1H), 7.52 (td, J= 7.4, 1.2, 1H), 7.36 (d, J= 7.5, 1H), 7.18 (s, 1H), 7.16 (s, 1H), 7.05 (d, J=1.8 1H), 7.02 (d, J=1.8, 1H, 6.11 (d, J=1.5 1H), 2.06 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 167.6, 153.1, 152.7, 149.9, 143.5, 142.8, 137.4, 132.5, 131.7, 129.6, 128.9, 127.2, 126.4, 121.5, 121.3, 117.0, 52.9, 20.6. High-resolution MS $(M+Na)^+$ (ESI): calcd for $C_{25}H_{19}N_2O$ 385.1311 found 385.1319.

4.2.20 **2',7'-dimethylspiro[indeno[1,2-b]quinoxaline-11,9'-xanthene] (28).** A solution of ninhydrin (356 mg, 2 mmol) in EtOH (10 mL) is added to 1,2-diaminobenzene (216 mg, 2 mmol) and acetic acid (0.5 mL).[16] This provided 1H-indeno[1,2-b]quinoxalin-11-one (246 mg, 1.1 mmol, 53%) as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (dd, J= 6.8, 1.5, 1H), 8.11-8.07 (m, 2H), 7.91 (d, J= 7.5, 1H), 8.84-7.72 (m, 3H), 7.59 (td, J=6.7, 0.8, 1H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.9, 156.6, 149.2, 143.1, 142.6, 141.5, 136.8, 136.6, 132.5, 131.4, 130.3, 129.6, 124.7, 122.5. Using a modified general procedure, 1H-indeno[1,2-b]quinoxalin-11-

one (121 mg, 0.5 mmol) and *p*-tolyl ether (99 mg, 0.5 mmol) where heated to 50 °C for 20 hours, which produced compound **28** (167 mg, 0.41 mmol, 81%) as a white solid from silica gel chromatography. R_f=0.33 (hexanes:ethyl acetate, 2:1). MP>250 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36 (d, J=7.4, 1H), 8.20 (d, J= 8.2, 1H), 8.00 (d, J= 8.3 1H), 7.75 (t, J= 7.1, 1H), 7.67-7.52 (m, 3H), 7.36 (d, J= 7.6, 1H), 7.19 (d, J= 8.3, 2H), 7.03 (d, J= 8.2, 2H), 6.13 (s, 2H), 2.02 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 167.4, 154.6, 153.8, 149.6, 142.6, 142.1, 136.7, 132.8, 132.4, 129.9, 129.6, 129.5, 129.0, 128.9, 128.8, 127.8, 126.6, 122.4, 122.1, 116.9, 52.7, 20.6. High-resolution MS $(M+H)^+$ (ESI): calcd for $C_{29}H_{21}N_2O$ 413.1648, found 413.1648.

Declaration of competing interest. The authors declare no conflict of interest.

Acknowledgements. The support of the NSF (award no. 1955584) is gratefully acknowledged. We also acknowledge the generous support from the NSF MRI program (award no. CHE-1726931) for the purchase of a high-resolution mass spectrometer and (award no. CHE-2117776) an NMR spectrometer used in this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at

References

(1) Liu, S., Xia, D., Baumgarten, M. Rigidly Fused Spiro-Conjugated π-Systems *ChemPlusChem* 86, (2021) 36-48.

(2) Saragi, T. P. I.; Spehr, T.; Siebert, A.; Fuhrmann-Lieker, T.; Salbeck, J. Spiro Compounds for Organo Optoelectronics. *Chem. Rev.* 107, (2007) 1011-1065.

(3) Qu., Y.-K., Zheng, Q., Fan, J., Liao, L.-S., Jiang, Z.-Q. Spirocycles for organic light-emitting diodes. *Accts. Mat. Res.* 2, (2021) 1261-1271.

(4) a) Xu, B.; Bi, D.; Hua, Y.; Liu, P.; Cheng, M.; Graetzel, M.; Kloo, L.; Hagfeldt, A.; Sun, L. A low-cost spiro[fluorene-9,9'-xanthene]-based hole transport material for highly efficient solid-state dye-sensitized solar cells and perovskite solar cells. *Energy Envr. Sci.* 9, (2016) 873-877. b) Maciejczyk, M.; Ivaturi, A.; Robertson, N. SFX as a low-cost 'spiro' hole-transport material for efficient perovskite solar cells. *J. Mat. Chem. A* 4, (2016) 4855-4863.

(5) a) Mujica-Fernaud, T., Montenegro, E., Voges, F., Kroeber, J. V., Stoessel, P. Heterocyclic materials and their preparation and use in organic electronic devices and the devices. World Patent WO2014072017 A1 (2014). b) Kreuder, W., Spreitzer, H. Polymers containing spiro atoms and methods of using the same as electroluminescence materials. U.S. Patent US5763636 (1998).

(6) a) Poriel, C., Rault-Berthelot, J. Designing Host Materials for the Emissive Layer of Single-Layer Phosphorescent Organic Light-Emitting Diodes: Toward Simplified Organic Devices. *Adv. Funct. Mater.* 31, (2021) 2010547. b) Bera, M. K., Pal, P., Malik, S. Solid-state emissive organic chromophores: design, strategy and building blocks. *J. Mat. Chem. C* 8, (2020) 788-802.

(7) Xie, L.-H.; Liu, F.; Tang, C.; Hou, X.-Y.; Hua, Y.-R.; Fan, Q.-L.; Huang, W. Unexpected one-pot method to synthesize spiro[fluorene-9,9'-xanthene] building blocks for blue-light-emitting materials. *Org. Lett.* 8, (2006) 2787-2790.

(8) Lin, D.; Wei, Y.; Ou, C.; Huang, H.; Xie, L.; Tang, L.; Huang, W. Carbon cationic relay via superelectrophiles: synthesis of spiro-diazafluorenes. *Org. Lett.* 18, (2016) 6220-6223.

(9) Bhanuchandra, M.; Yorimitsu, H.; Osuka, A. Synthesis of spirocyclic diarylfluorenes by one-pot twofold S_NAr reactions of diaryl sulfones with diarylmethanes. *Org. Lett.* 18, (2016) 384-387.

(10) a) Sai, K. K. S.; Esteves, P. M.; Tanoue da Penha, E. T.; Klumpp, D. A. Superacid-Promoted Reactions of α-Keto Amides and Related Systems. *J. Org. Chem.* 73, (2008) 6506-6512. b) Klumpp, D. A.; Zhang, Y.; Do, D.; Kartika, R. Reactions of acenaphthenequinone and aceanthrenequinone with arenes in superacid. *Appl. Cat. A: Gen.* 336, (2008) 128-132. c) Klumpp, D. A.; Garza, M.; Lau, S.; Shick, B.; Kantardjieff, K. Electrophilic Chemistry of Biologically Important α-Keto Acids. *J. Org. Chem.* 64, (1999) 7635-7637. d) Klumpp, D. A.; Yeung, K. Y.; Prakash, G. K. S.; Olah, G. A. Preparation of 3,3-Diaryloxindoles by Superacid-Induced Condesations of Isatins and Aromatics with a Combinatorial Approach. *J. Org. Chem.* 63, (1998) 4481-4484.

(11) Klumpp, D. A.; Anokhin, M. V. Superelectrophiles: Recent Advances. *Molecules* 25 (14), (2020) 3281.

(12) Yang, H.; Takrouri, K.; Chorev, M. Insight into acid driven formation of spiro-[oxindole]xanthene from isatins and phenols. *Curr. Org. Chem.* 16, (2012) 1581-1593.

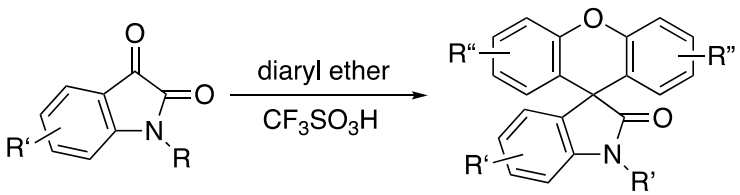
(13) Bogdan, H. The condensation of acenaphthenequinone with monohydric phenols; cyclic pinacols; reduction and autoxidation products. *Ann. Sci. Univ. Jassy, Pt. 1 1:25*, (1939) 645-679.

(14) Olah, G. A., Klumpp, D. A. *Superelectrophiles and Their Chemistry*. Wiley & Sons: New York, (2008), pp 1-301

(15) Bain, Z.-L., Lv, X.-X., Li, Y.-L., Sun, W.-W., Liu, J.-K., Wu, B. Acid-promoted synthesis and photophysical properties of substituted acridine derivatives. *Org. Biomol. Chem.*, 61, (2020) 8141-8146.

(16) Wu X.; Li X.; Li Z.; Yu Y.; You Q.; Zhang X. Discovery of Nonquinone Substrates for NAD(P)H: Quinone Oxidoreductase 1 (NQO1) as Effective Intracellular ROS Generators for the Treatment of Drug-Resistant Non-Small-Cell Lung Cancer. *J. Med. Chem.* 61, (2018) 11280–11297.

Graphical Abstract



Carbonyl electrophiles:
isatins, acenapthenequinone,
and azafluorenones

Yields:
25-98%
20 examples