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Comparative Evaluation of Substituent Effect on the Photochromic Properties of Spiropyrans and Spirooxazines

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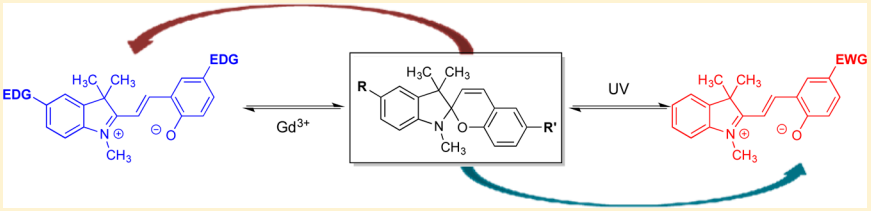
Supporting Information



ABSTRACT: Spiropyrans and spirooxazines represent an important class of photochromic compounds with a wide variety of applications. In order to effectively utilize and design these photoswitches it is desirable to understand how the substituents affect photochromic properties, and how the different structural motifs compare under identical conditions. In this work a small library of photoswitches was synthesized in order to comparatively evaluate the effect of substituent modifications and structure on photochromism. The library was designed to modify positions that were believed to have the greatest effect on C−O bond lability and therefore the photochromic properties. Herein we report a comparative analysis of the UV and visible light responses of 30 spiropyrans, spiroindolinonaphthopyrans, and spirooxazines. The influence of gadolinium(III) binding was also investigated on the library of compounds to determine its effect on photoswitching. Both assays demonstrated different trends in substituent and structural requirements for optimal photochromism.

INTRODUCTION

Photochromic compounds represent a growing area of research as the utility of these compounds begins to be realized. Numerous photochromic compounds have recently been explored for their utility, such as azobenzenes,[1] stilbenes,[2] fulgides,[3] dithienylethenes,[4] and spiropyrans/spirooxazines (Scheme 1),[5] among others.[6] Photochromic compounds have been employed for a myriad of applications including microfluidics,[7] biochemical assays,[8] modulating electric potential,[9] and photopharmacology.[10] Spiropyrans and spirooxazines are two of the most widely studied photochromic compounds due to their reversible activation by a wide range of external stimuli. Examples of light-,[11] thiol-,[12] redox-,[13] metal ion-,[14] and pH-[15] sensitive spiropyrans and spirooxazines have previously been demonstrated. An advantage of spiropyrans and spirooxazines over other photochromic compounds is the dramatic difference in the properties of the two isomers (Scheme 1). In the closed spiro (SP) form, spiropyrans and spirooxazines are pale yellow or colorless in solution, uncharged, hydrophobic, and occupy less volume than the merocyanine (MC) form.[16] The MC-form is intensely colored in solution, zwitterionic, hydrophilic, and has a much higher dipole moment (14−18 D) than the SP-form (~4 D).[5,17]

In many applications, for spiropyran- or spirooxazine-based dynamic materials to be robust and behave reliably they are covalently attached to a surface to prevent leaching,[18] reduce photodegradation,[19] enhance biocompatibility,[20] and otherwise improve performance.[21] Tethered spiropyrans have been used in a wide range of applications including "smart electrodes",[22] photocontrolled enzymatic activity,[23] photocontrolled release of therapeutics,[24] photocontrol of nanoparticle solubility,[25] and modulation of magnetic resonance imaging (MRI) contrast agent efficiency.[26] To aid the development of future spiropyran- and spirooxazine-based systems, knowledge of how these different structural motifs compare under identical experimental conditions is required.

Our goal in this work is 2-fold; first to better understand how substituents affect photoswitching and to identify strong switches under mild irradiation and temperature conditions more amenable to biological applications.[27] We systematically vary substituents with different electron withdrawing or donating power and study them under identical experimental conditions to allow direct comparison for substituent effects on photochromic properties. The results of these studies will help develop a platform for future MRI contrast agent design and development.

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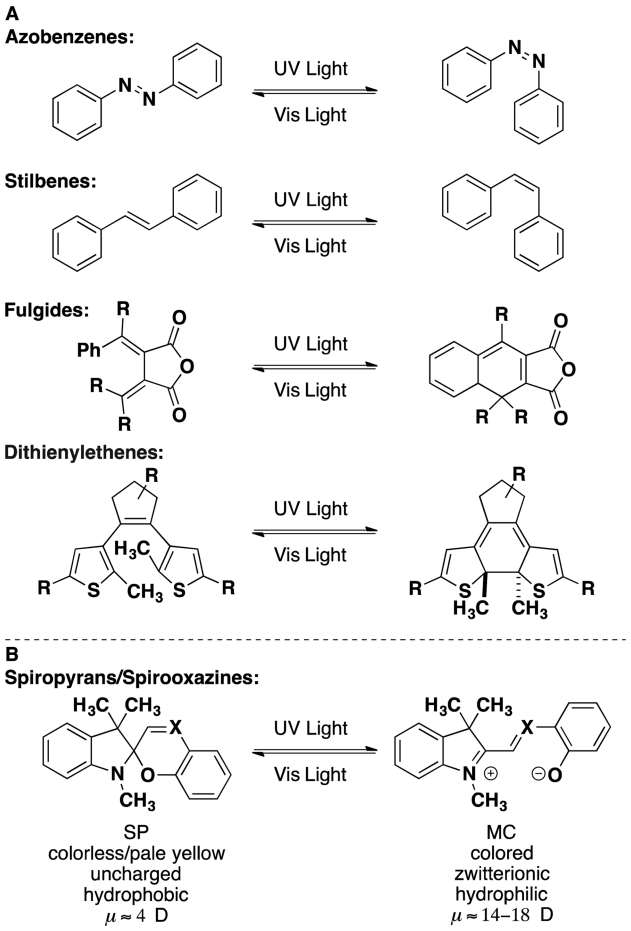
Scheme 1. (A) General Isomerization of Commonly Employed Photoswitching Compounds; (B) General Isomerization of Spiropyrans (X = CH) and Spirooxazines (X = N)



Despite much work in this field, a comparative study between spiropyrans, spiroindolinonaphthopyrans, and spirooxazines with the same substituent patterns has not been conducted (Figure 1). Previous literature reports have demonstrated that electron-withdrawing groups on the chromene ring enhance the UV response of photoswitches.[28] However, little work has been done to understand how these groups affect the visible light response of photochromic compounds. Even less is known how indoline substituents affect photoswitching, and among compounds similar to those reported here, very few have been subjected to identical experimental conditions for direct comparison between substitution patterns.

Herein we report a comparative study on the photochromic properties of different spiropyrans, spiroindolinonaphthopyrans, and spirooxazines, with similar substitution patterns under identical experimental conditions. Also examined was the effect of gadolinium(III) ions on photoswitching in this array of compounds, which is important for applications in contrast agent development and analytical chemistry.[26,29] Based on previous literature, we believed that varying the lability of the C−O bond would have the greatest effect on the photochromic properties of the compounds.[5,30] Therefore, two positions for substitution were selected on either side of the switches that would likely have the most significant effect on the C−O bond lability and consequently their photochromic properties. Initially 36 compounds were chosen as targets for this study

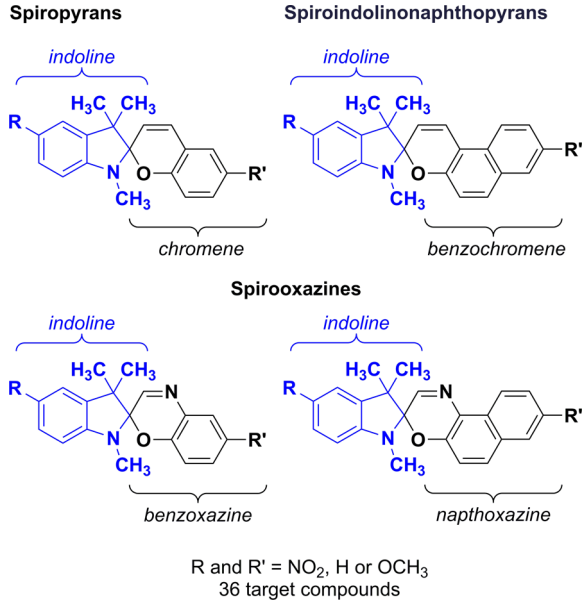


Figure 1. Target compounds for this study.

with varying substituents (NO_2, H, and OCH_3) on either side of the switches (Figure 1).

RESULTS AND DISCUSSION

Synthesis. The commercially available starting materials indoline **1**, salicylaldehydes **2**-**4**, 2-hydroxy-1-naphthaldehyde **5**, and 1-nitroso-2-naphthol **6** were employed. The synthesis of additional starting materials was required in order to generate all of the target compounds (Scheme 2), for full experimental details and compound characterization see Experimental Section.

Indolium iodide synthesis: The 4-methoxy- and 4-nitro-indolium iodides, **7** and **8** respectively, were synthesized in two steps from their respective *p*-hydrazine hydrochlorides. Initially, an interrupted Fischer indole reaction was conducted between the hydrazines and 3-methyl-2-butanone, followed by methylation with iodomethane.[31]

Naphthaldehyde synthesis: 2-Hydroxy-6-methoxynaphthalene-1-carbaldehyde **9** was obtained in three steps from 2,6-dihydroxynaphthalene. 2,6-Dihydroxynaphthalene was initially methylated using NaH and iodomethane to afford 2,6-dimethoxynaphthalene,[32] which was subsequently formylated with *N*-methylformanilide and $POCl_3$.[33] Selective deprotection of the *o*-methoxy group of 2,6-dimethoxy-1-naphthalenecarbaldehyde was achieved by treating it with $MgBr_2$ and NaI in CH_3CN at 150 °C. Nitration of 2-hydroxy-1-naphthaldehyde with concentrated nitric acid afforded the required 2-hydroxy-6-nitro-1-naphthaldehyde **10**.[34]

Nitrosonaphthalenol synthesis: 6-Methoxy-1-nitrosonaphthalen-2-ol **11** was synthesized from 6-methoxynaphthalen-2-ol by nitrosation using $NaNO_2$ in acetic acid and water.[35] The synthesis of 24 of the initial 36 target compounds was achieved in 13−97% yield, through the condensation reaction between the required indoline or indolium salt, and the corresponding salicylaldehydes, 2-hydroxy-1-naphthaldehydes or 1-nitroso-2-naphthols.

The required starting material, 6-nitro-nitroso-2-naphthol, for the synthesis of spirooxazines **SO4**, **SO5** and **SO6**, was neither commercially or synthetically obtainable. In an attempt to install the nitro group on the naphthalene ring system the

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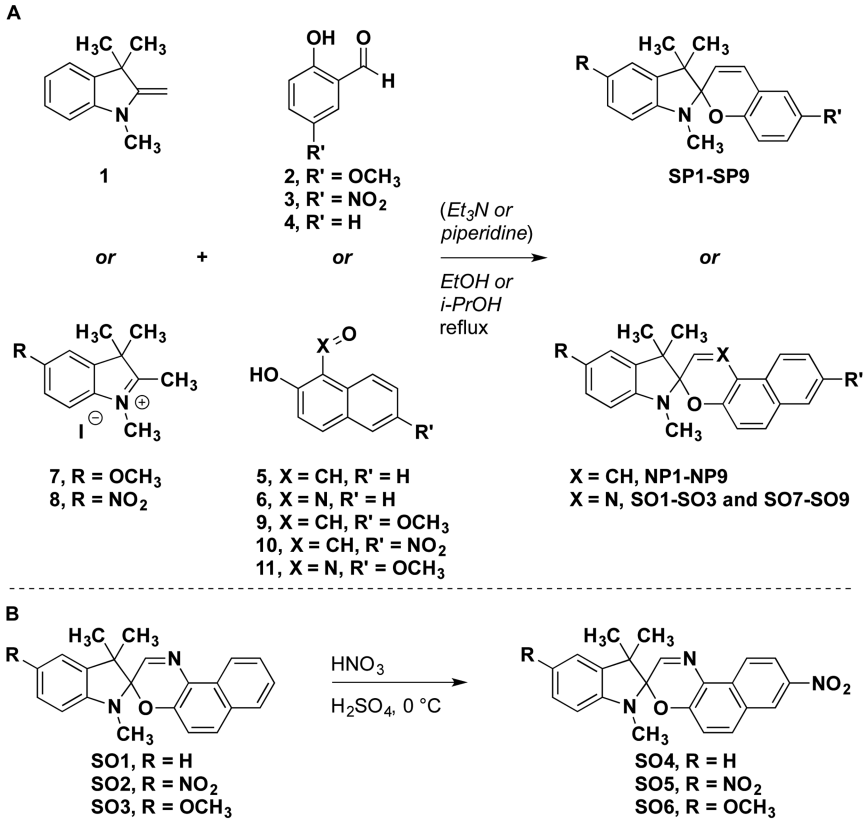
Scheme 2. Synthesis of Target Spiropyrans SP1−SP9, Spiroindolinonaphthopyrans NP1−NP9, and Spirooxazines SO1−SO9[a]



		R'		
		H	NO_2	OCH_3
R	H	**SP1**, 97% **NP1**, 67% **SO1**, 47%	**SP4**, 73% **NP4**, 26% **SO4**, 15%	**SP7**, 86% **NP7**, 40% **SO7**, 38%
	NO_2	**SP2**, 63% **NP2**, 64% **SO2**, 20%	**SP5**, 77% **NP5**, 67% **SO5**, N/A*	**SP8**, 56% **NP8**, 67% **SO8**, 13%
	OCH_3	**SP3**, 44% **NP3**, 73% **SO3**, 45%	**SP6**, 69% **NP6**, 15% **SO6**, N/A*	**SP9**, 93% **NP9**, 50% **SO9**, 15%

[a]*SO5 could not be reproducibly synthesized, and SO6 could not be synthesized.

unfunctionalized spirooxazines **SO1**, **SO2**, and **SO3** were subjected to nitration conditions, employing HNO_3 and H_2SO_4 (Scheme 2, B).[36] Spirooxazine **SO4** was obtained in 15% yield; however, attempts to synthesize spirooxazines **SO5**[27c] and **SO6** were irreproducible and unsuccessful, respectively. We found that for **SO6** there was competing nitration of the indoline ring, resulting in an inseparable mixture of products. In addition, despite spirooxazines originating from *o*-nitrosophenols being known,[37] the required spirooxazines for this study have never been synthesized. *o*-Nitrosophenols are relatively difficult to synthesize, isolate, and handle;[38] and while *o*-nitrosophenols can be accessed through the Baudisch reaction,[39] it was not possible to isolate the required compounds using this methodology. As a result the corresponding nine spirooxazines based on the *o*-nitrosophenols could not be synthesized. Thus, in total 25 of the initial 36 target compounds were obtained and evaluated for their photochromic properties. Of the synthesized compounds (Scheme 2) spiropyrans **SP1**−**SP8**,[27a,31b,40] spiroindolinonaphthopyrans **NP1**−**NP5**,[27a,41] and spirooxazines **SO1**−**SO4**,[27c,41,42] and **SO7**[43] are known in the literature. Spiropyran **SP9**, spiroindolinonaphthopyrans **NP6**−**NP9**, and spirooxazines **SO8** and **SO9** have not previously been reported in the literature.

On the basis of the results obtained from our assays of the initial targets in the absence and presence of $Gd(NO_3)_3$ (vide infra) five additional novel spiropyrans **SP10**−**SP14** were synthesized to further explore the observed results. The synthesis of spiropyrans **SP10**−**SP13**, containing different electron-withdrawing groups (EWGs) on the chromene portion and the electron-donating methoxy substituent on the

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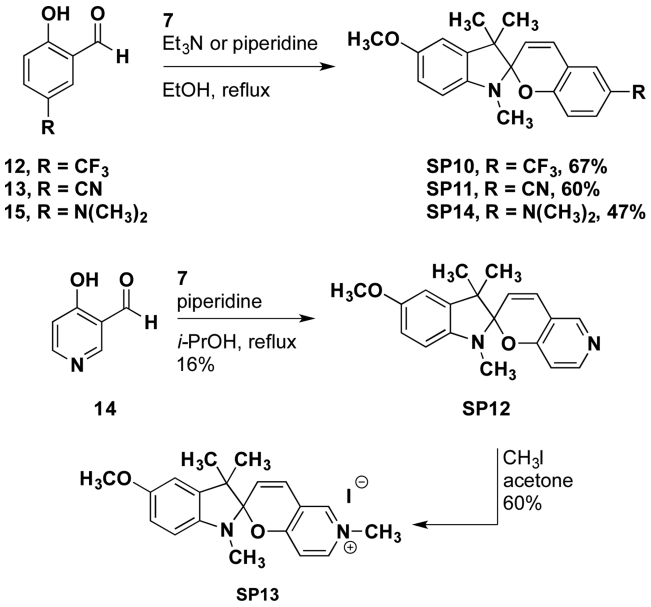
indoline portion, required the synthesis of three salicylaldehyde derivatives **12**−**14**. Both the 4-(trifluoromethyl)- and 4-cyanophenols were formylated with hexamethylenetetramine in TFA, to afford the desired 5-substituted salicylaldehydes, **12** and **13**.[44] 4-Hydroxynicotinaldehyde **14** was synthesized through the hydrolysis of 4-chloronicotinaldehyde with HCl and H_2O_2.[45] The three spiropyrans **SP10**−**SP12** were then synthesized in an analogous fashion to the initial 24 compounds in 16−67% yield, with spiropyran **SP12** methylated with iodomethane to afford the final spiropyran **SP13** in 60% yield (Scheme 3). Spiropyran **SP14** was synthesized, in which an

Scheme 3. Synthesis of Spiropyrans SP10−SP14



alternate electron-donating group (EDG) was incorporated on the chromene ring. The required 5-dimethylamino-2-hydroxybenzaldehyde **15** was obtained by the hydrogenation of 4-nitrophenol in the presence of aqueous formaldehyde.[46] Benzaldehyde **15** was then reacted with 4-methoxyindolium iodide **7** and Et_3N to afford the desired spiropyran **SP14** in 47% yield (Scheme 3).

Photochromic Analysis. Evaluation of response to UV and visible light irradiation was conducted in absolute ethanol at 100 μM for all photoswitches. Samples were irradiated with UV for 15 min using an 8-W UV source; both 365 and 302 nm were tested, with 302 nm light producing the greatest changes in absorbance among spiropyrans and spirooxazines (SI, Figure 103 and Figure 104). For the Job's plot, different volumes of 100 μM solutions of photoswitch and $Gd(NO_3)_3$ in ethanol were mixed together to a constant volume keeping the sum total of photoswitch and $Gd(NO_3)_3$ concentrations equal to 100 μM. Visible light was supplied with 1 min irradiations by a 150-W tungsten halogen lamp. The power output was stable from 500 to 800 nm (SI, Figure 99). All photoswitching solutions were prepared under ambient light conditions and displayed strong absorbance bands between 200 and 400 nm corresponding to the SP-form of the photoswitches. Of the 30 compounds tested, only 10 photoswitches demonstrated an observable shift to the open form upon UV light irradiation (Figure 2A). Five photochromic compounds showed minor photoswitching (<0.1 A.U. SI, Figure 100 and Figure 101). The presence of the electron-withdrawing nitro substituent on the chromene/naphthoxazine rings imparted the greatest UV response among photoswitches with final absorbances of 1.88, and 1.76 A.U. for spiropyran **SP4** (Figure 2A, blue) and spirooxazine **SO4** (Figure 2A, red) respectively. Spiropyrans **SP13** (Figure 2A, light blue) and **SP6** (Figure 2A, green) were the next best at 1.12 and 0.70 A.U. respectively.

Under these assay conditions, none of the spiroindolinonaphthopyrans displayed a UV response; however, previous literature suggests stronger UV sources could induce spiroindolinonaphthopyrans isomerization.[47] In the case of both the spirooxazines and spiropyrans, the presence of the methoxy substituent on the indoline ring reduced the UV response of photoswitches. This was particularly noticeable between spiropyran **SP4**, which had a maximal absorbance of 1.88 A.U. (Figure 2A, blue), and spiropyran **SP6**, which achieved only 0.70 A.U. after 15 min of UV irradiation (Figure 2A, green). Utilizing a stronger electron withdrawing "chromene ring" was capable of restoring some of this UV responsiveness with spiropyrans **SP13** giving a final absorbance of 1.12 A.U., an increase of 0.52 A.U. from spiropyrans **SP6** after 15 min of UV irradiation (Figure 2A, light blue).

All UV-responsive photoswitches shown in Figure 2 could be reverted back to the MC-form, to varying degrees, with visible light irradiation. The application of photoswitches to *in vivo* light sensing requires sensitivity at potentially very low levels of light. Three of the four best photoswitches from Figure 2A were further evaluated for their low light sensitivity. Spiropyrans **SP4**, **SP6** were exposed to decreasing levels of light until no ring closing was observed (SI, Figure 97 and 98). Although spirooxazine **SO4** also had good UV response, spirooxazine photoswitches were not included in this evaluation due to the inherent difficulty in their synthesis. The lower limit of sensitivity for all three switches was 2.29 ± 0.03 mW. The kinetics of these photoswitches was tested at this power level to determine the relative response of photoswitches upon low light irradiation.

Absorbances of photoswitch solutions were tracked every minute for both UV and low power visible light irradiation. Kinetic response times for spiropyrans **SP4**, **SP6**, and **SP13** were determined by fitting the decay curve of their visible light response with an exponential function under the assumption of a first order decay process (eq 1) to find the rate of ring closing. Kinetics assays illustrated that the solutions of spiropyrans **SP4**, **SP6**, and **SP13** were saturated after 10 min of UV irradiation, with a half-maximal time of approximately 2.16, 2.33, and 0.85 min, respectively (Figure 2B−D). Spiropyran **SP4** was the least stable undergoing thermal relaxation of 21% from the maximum absorbance after a 10 min dark incubation, and 30% decrease after 15 min dark incubation (two tailed Student's t test, p = 0.0086) (Figure 2C, green line). In contrast, both spiropyrans **SP6** and **SP13** showed no significant decrease from maximal absorbance after 10 min incubation in the dark (Figure 2B and 2D, green line). Of the three photoswitches, spiropyran **SP6** had the fastest rate at 1.43×10^{-2} s^{-1} (R^2 = 0.9788) with spiropyrans **SP4** and **SP13** an order of magnitude lower at 3.45×10^{-3} s^{-1} (R^2 = 0.9887) and 2.5×10^{-3} s^{-1} (R^2 = 0.9939) respectively (SI, Figures 31−33).

$$A(t) = A(0)e^{-kt} \quad (1)$$

These three compounds highlight the effect that minor variations in substituents can have on photoswitch properties. These results demonstrate again that the absolute absorbance changes are greatest for the 6-Nitro-BIPS (**SP4**), but that

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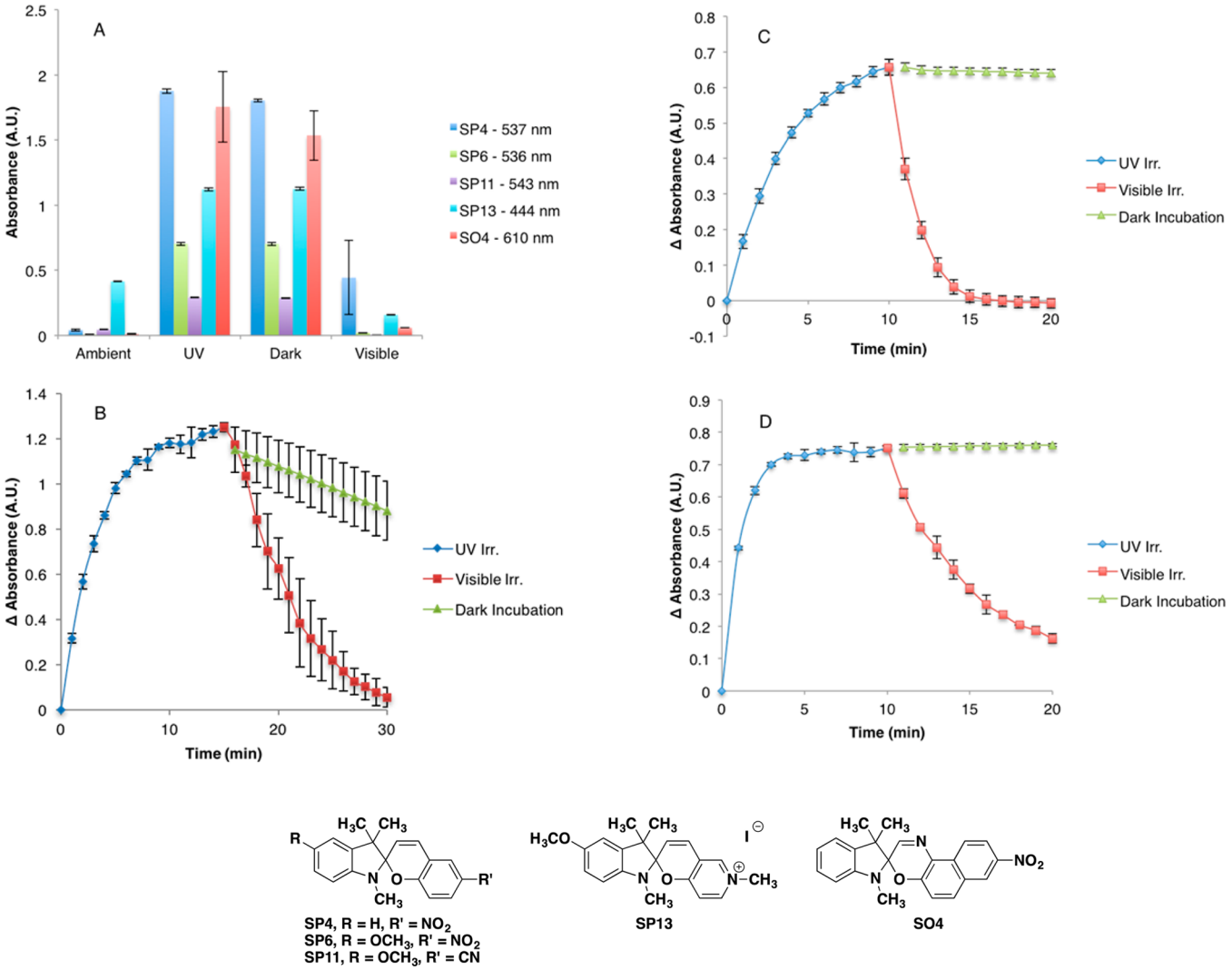


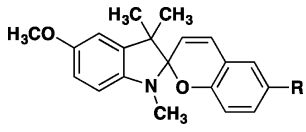
Figure 2. (A) Photochemical properties of photoswitches **SP4** (blue), **SP6** (green), **SP11** (purple), **SP13** (light blue) and **SO4** (red). (B) Kinetics of spiropyran **SP4** at 100 μM in ethanol. (C) Kinetics of spiropyran **SP6** at 100 μM in ethanol. (D) Kinetics of spiropyran **SP13** at 100 μM in ethanol.

addition of an electron donating group speeds up the ring closing of **SP6** by an order of magnitude under low visible light irradiation. These assays also illustrate the importance of a comparative study under identical conditions. While **SP4** has long been considered the best for UV light response, these kinetics assays demonstrate that **SP13** reaches saturation much faster and possesses greater thermal stability.

The kinetics results validate previous literature reports that nitro groups on the chromene ring significantly enhance the UV response of photoswitches. These results corroborate previous literature reports that increasing the C−O bond lability enhances photoswitching. We also demonstrated that the UV response could be recovered to a certain degree by increasing the electron-withdrawing nature of the "chromene ring" as shown with spiropyrans **SP6** and **SP13**. The most important aspect of these visible light assays was determining which substituents provided the best visible light response. From these results we found that among compounds with nitro groups on the chromene ring, having an electron donating substituent provided the best light response. In contrast, the additional presence of a nitro group on the indoline ring shut down photoswitching completely as was seen with spiropyrans **SP2**, **SP5**, and **SP8**.

Table 1 presents photoresponse as a function of the electron donating or withdrawing capacity of the chromene substituent when the indoline methoxy is fixed. With the methoxy group at the 5′ on the indoline side, there is a trend toward improved UV response with strong electron withdrawing groups in the 6-position on the chromene side. As seen in Table 1 the UV

Table 1. Comparative Analysis of Different Substituent Combinations on the Absolute Change in Absorbance upon 15 min of UV Irradiation



photoswitch	R	σ	ΔAbs (A.U.)
SP6	NO_2	0.78	0.70
SP11	CN	0.66	0.25
SP10	CF_3	0.54	8.9×10^{-2}
SP3	H	0.00	5.0×10^{-2}
SP9	OCH_3	−0.27	6.7×10^{-4}
SP14	$N(CH3)_2$	−0.83	1.2×10^{-2}

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response seems to improve with the electron-withdrawing capacity on the chromene side, and progressively increases with trifluoromethyl (8.9×10^{-2} A.U.), cyano (0.25 A.U.), and nitro groups (0.70 A.U.), respectively. There is very little photoswitching in the absence of strong electron withdrawing groups on the chromene side, and methoxy, hydrogen and dimethyl amino groups afford little to no improvement in photoresponse. This trend also holds for the switching response in the reverse direction to visible light with trifluoromethyl, cyano, and nitro groups affording increasing visible light response (SI, Figure 105). In contrast, if we fix the nitro group as a strong electron withdrawing group on the chromene side there is no clear trend for photoresponse, UV or visible, against increasing electron-donating ability for 5′ substituents on the indoline side (SI, Figure 106).

Gadolinium(III) Responses. We are interested in photoswitches as vehicles for modulating the behavior of gadolinium-based contrast agents. In the MC-form, spiropyrans and spirooxazines have been previously observed to coordinate to gadolinium(III) to alter the magnetic properties of a gadolinium-chelate.[26] It is currently hypothesized that in the MC-form, the phenoxide of spiropyrans binds gadolinium(III) blocking a coordination site for water, keeping the contrast agent in a low relaxivity state. Upon visible light irradiation the spiropyran closes, removing this coordinated phenoxide and opening a coordination site for water. Before the lengthy synthesis to couple the prepared photoswitches to gadolinium-chelates, we wished to evaluate the capacity for these photoswitches to interact with gadolinium(III). Ideal photoswitches would naturally open in the presence of gadolinium(III) corresponding to a natural tendency to equilibrate to an "off" position when conjugated to a gadolinium-chelate. Thus, all photoswitches were tested for photoresponse in the presence of 1 equiv of gadolinium(III) nitrate ($Gd(NO_3)_3$). A solution of $Gd(NO_3)_3$ was added to photoswitch solutions prior to assays with a final concentration of 1:1 photoswitch to $Gd(NO_3)_3$ (addition volumes were limited to 5 μL so concentration effects could be neglected). These assays were conducted in absolute ethanol with the final concentration of both photoswitch and $Gd(NO_3)_3$ being 100 μM. After addition of $Gd(NO_3)_3$, the solutions were allowed to equilibrate in the dark for 15 min to determine their gadolinium(III) ion response. The solutions were then subjected to UV irradiation for 15 min, dark incubation for 1 min, and visible light irradiation for 1 min with absorbance taken at each time point (Figure 3).

Several of the photoswitches showed sensitivity to the $Gd(NO_3)_3$ alone, isomerizing to the MC-form upon incubation in the dark. The photoswitches with the greatest absorbance after 15 min incubations with $Gd(NO_3)_3$ were photoswitches **SP3** (0.39 A.U., Figure 3A red), **SP9** (0.51 A.U. Figure 3A orange), **NP3** (0.29 A.U. Figure 3B red) **NP9** (0.21 A.U.) (Figure 3B light blue) and, to a lesser degree, **SP1** (0.15 A.U. Figure 3A blue). In addition, the presence of $Gd(NO_3)_3$ induced a UV response for several photoswitches that previously had shown no photoswitching including **SP7** (Figure 3A, light blue), **SP9** (Figure 3A, orange), **SP14** (Figure 3A, navy blue), **NP3** and **NP9** (Figure 3B). Photoswitches that are not shown on Figure 3 had absolute responses of <0.1 A.U. (SI, Figure 101).

The presence of $Gd(NO_3)_3$ diminished the UV response for the photoswitches **SP4** (Figure 3A, light green), and **SP6** (Figure 3A, purple) with final absorbances of 0.26 A.U. for both

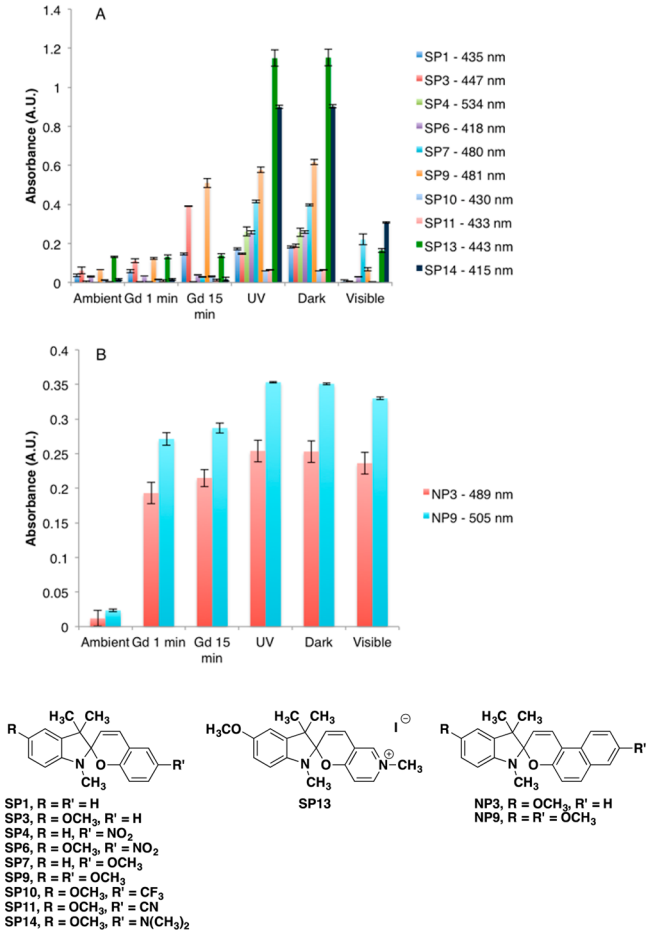

Figure 3. (A) Photophysical properties of spiropyrans with 1 equiv of $Gd(NO_3)_3$ added. (B) Photophysical properties of spiroindolinonaphthopyrans with 1 equiv of $Gd(NO_3)_3$ added.

compounds corresponding to decreases of 1.62 A.U., and 0.44 A.U. from previous assays in the absence of $Gd(NO_3)_3$. To verify that this was not a result of the nitro groups coordinating the gadolinium(III) ion, reducing the free gadolinium(III) ion concentration, spiropyran **SP9** was incubated with *p*-methoxynitrobenzene and $Gd(NO_3)_3$ (1:1:1 mol ratio). The presence of nitrobenzene, or *p*-methoxynitrobenzene had no effect on the $Gd(NO_3)_3$, UV, or visible light response of spiropyran **SP9** (SI, Figure 95).

Spiroindolinonaphthopyrans **NP3**, and **NP9** rapidly isomerized to the open form after 1 min of $Gd(NO_3)_3$ incubation (Figure 3B). There was no significant change from one to 15 min of incubation with gadolinium(III) ions for spiroindolinonaphthopyrans **NP3** and **NP9**. Irradiation with UV light showed some capacity for additional conversion to the MC-form for spiroindolinonaphthopyrans **NP3**, and **NP9**. These results suggest a lack of visible light response for any of these spiroindolinonaphthopyrans in the presence of gadolinium(III) ions. However, utilizing shorter scan times (one second) we were able to demonstrate that spiroindolinonaphthopyrans **NP3** and **NP9** were light-responsive, and after removing the visible light source they rapidly equilibrated back to the MC-form (Figure 4B). For gadolinium(III) ion sensitivity alone, methoxy substitutions on the indoline ring and chromene ring were most effective for spiroindolinonaphthopyrans. However, none of the substitutions tested were able to produce

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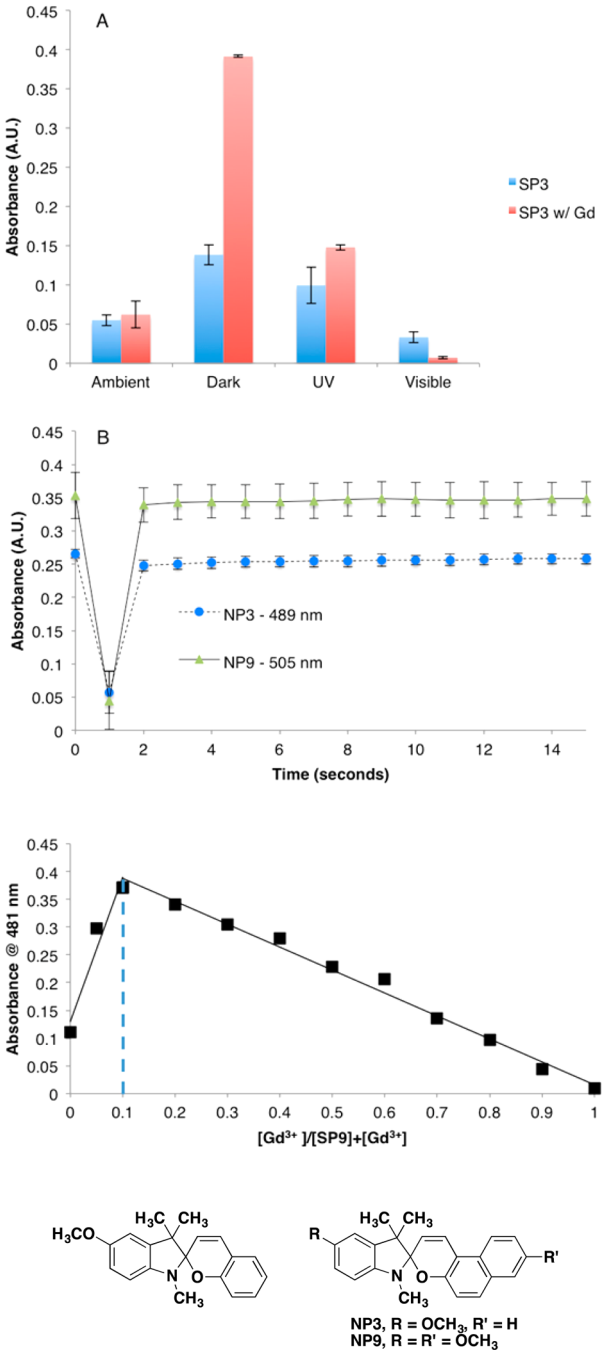

Figure 4. (A) UV response of spiropyran **SP3** in the absence (blue) and presence (red) of 1 equiv of $Gd(NO_3)_3$. (B) Visible light response of spiroindolinonaphthopyrans **NP3** and **NP9**. (C) Job's analysis of **SP9**-Gd^{3+} complex ([**SP9**] + [Gd^{3+}] = 1.0×10^{-4} M).

photoswitching for the spiroindolinonaphthopyrans core in the absence of gadolinium(III) ions.

The photoswitches that were least responsive to $Gd(NO_3)_3$ were the spirooxazines **SO1**–**SO9**, which showed no switching response to the presence of $Gd(NO_3)_3$. The presence of the gadolinium(III) ions did, however, negatively impact UV response of spirooxazine **SO4** and final absorbance going from 1.76 A.U. in the absence of $Gd(NO_3)_3$ to 1.23 A.U. in its presence (SI, Figure 101). The combined results of these $Gd(NO_3)_3$ assays suggest that in the presence of gadolinium(III) ions the electron density of the phenoxide ion is a more important factor for photoswitching than the lability of the spiro C–O bond. The presence of a nitro group on the indoline ring eliminated photoswitching, with spiropyrans **SP2**, **SP5**, and **SP8** showing no UV response in the presence and absence of gadolinium(III) ions. This implies that stabilizing the iminium ion is important for photoswitching both in the presence and absence of gadolinium(III) ions.

One of the more surprising results for the spiropyrans was the inversion in UV sensitivity of spiropyran **SP3** in the presence of $Gd(NO_3)_3$ (Figures 4A, red). Without $Gd(NO_3)_3$, spiropyran **SP3** followed showed no significant decrease in absorbance after UV irradiation ($p > 0.05$). However, addition of $Gd(NO_3)_3$ to spiropyran **SP3** induces a significant shift to the MC-form (0.40–0.48 A.U.) and upon UV irradiation instead of an increase in the MC-form, as expected, the compound reverted back to the SP-form (0.15 A.U., Figure 4A, red) ($p = 0.0001$). While we currently do not have an explanation for this change in photochromic properties, this will be explored further with additional metal ion salts and computational studies. Spiropyran **SP3** however, still follows full conversion to the SP-form under visible light (0.07 A.U.) (Figure 4A) as normally expected and was slightly more responsive to visible light irradiation ($k = 0.6909\ M^{-1}\ s^{-1}$) than **SP9** ($k = 0.6909\ M^{-1}\ s^{-1}$) (SI, Figures 109 and 110). Both **SP3** and **SP9** based on their low light responses and gadolinium(III) interactions are ideal candidates for gadolinium-chelate conjugation and contrast evaluation.

The nature of the complex between spiropyran **SP9** and $Gd(NO_3)_3$ was investigated by the continuous variations method, Job's plot analysis (Figure 4C). The absorption values were taken at the absorbance maximum (481 nm) and plotted against $Gd(NO_3)_3$ concentration under the condition of an invariant total concentration. From this plot the maximum molar fraction of 0.1 indicates a 1:9 stoichiometry of $Gd(NO_3)_3$ to **SP9** in the complex. This observation is quite unique to the stoichiometric ratio for the metal ion/SP derivatives (2:1 and 1:1) reported previously,[48] but this stoichiometric ratio does match the known coordination chemistry of gadolinium(III), which is nine coordinate.[49]

In contrast to our initial assays in the absence of the lanthanide, the $Gd(NO_3)_3$ assays suggest EDGs on both ring systems would provide better photochromic properties when conjugated to a gadolinium-based MRI contrast agent. The $Gd(NO_3)_3$ assays also suggest that analyzing the photochromic behavior of switches alone in solution are not indicative of the best possible photochromic properties when coordinated to a contrast agent.

CONCLUSION

In summary, we have synthesized 30 spiropyrans, spiroindolinonaphthopyrans, and spirooxazines and identified 10 compounds that demonstrate reversible response to UV–visible irradiation under our experimental setup. As expected, the magnitude of response to UV irradiation was found to be greater for spiropyrans and spirooxazines containing nitro groups on the chromene and naphthoxazine rings, respectively. However, we were intrigued to find that increasing the electron donating character at the 6-position of the indoline ring improved the rate of UV and visible light responses. The addition of an electron donating methoxy to the indoline side significantly improved rate of visible light response, but there was no clear trend for degree of electron donating capacity on the indoline side and the amplitude of the photoresponse.

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However, in the presence of $Gd(NO_3)_3$ the behavior of photoswitches was significantly altered, where compounds with EDGs on both ring systems showed greatest photochemical responses. Interestingly, the direction of switching was reversed for spiropyran **SP3** with a methoxy substituent on the indoline ring. These results suggest that the behavior of photoswitches in the absence of gadolinium(III) ions are not absolutely predictive for their performance in the presence of gadolinium(III) ions, such as might be found when coupled to a gadolinium-chelate. Overall, EDGs tend to improve the thermal conversion to MC-form in the presence of gadolinium(III) ions while maintaining the ability to isomerize to the SP-form under visible light irradiation. From these gadolinium(III) assays two lead spiropyrans, **SP3** and **SP9**, were identified as ideal candidates for light activated contrast agent development.

This study highlights the importance of taking a comparative approach to evaluating photoswitches. While several compounds in our studies exhibited no photochromic activity, these compounds can be found in the literature demonstrating photochromism. However, these results were obtained using extreme conditions of high temperature[27a] or exceptionally high intensity light sources[27b−d] to observe photochromism. Unlike these previous literature reports, we utilized irradiation sources and temperatures closer to what one might use for biological systems.[27] These results can be used to intelligently design photoswitches for various applications through the optimization of UV and visible light characteristics in the absence and/or presence of a metal. Future work will focus on exploring the effect of various metal salts on the photochromic properties of this library of spiropyrans, spiroindolinonaphthopyrans and spirooxazines in order to utilize the results to develop novel, light sensitive contrast agents.

EXPERIMENTAL SECTION

General Experimental Methods. All reagents were purchased from commercial sources and used without further purification unless stated otherwise. Solvents were dried over an activated alumina solvent system or purchased anhydrous where required. Reactions requiring anhydrous conditions were performed under argon; glassware was flame-dried under vacuum immediately prior to use and allowed to cool under reduced pressure; liquid reagents, solutions or solvents were added via syringe through rubber septa; solid reagents were added under a flow of argon. Reactions were monitored by TLC on Silica Gel 60 F254, and detected by examination under UV light (254 and 365 nm). Flash column chromatography was performed using silica gel [230−400 mesh (40−63 μm)], unless otherwise stated. Microwave reactions were conducted in a Biotage Initiator Classic microwave reactor, using 2.45 GHz microwaves with temperatures measured with an integrated IR sensor. Accurate mass measurements were recorded on positive ESI mode in CH_3OH or CH_3CN. Extracts were concentrated in vacuo using both a rotary evaporator at a pressure of 15 mmHg (diaphragm pump), and a high vacuum line at a pressure of 0.1 mmHg (oil pump) at room temperature. ^1H and ^{13}C spectra were measured in the solvent stated at 400 or 600 MHz, and 101 or 151 MHz, respectively. ^1H and ^{13}C NMR chemical shifts are quoted in parts per million (ppm) and referenced to the residual solvent peak ($CDCl_3$: ^1H = 7.26 ppm and ^{13}C = 77.2 ppm, DMSO-d_6: ^1H = 2.50 ppm and ^{13}C = 39.5 ppm, CD_3CN: ^1H = 1.94 ppm and ^{13}C = 1.3 ppm, CD_3OD: ^1H = 3.31 ppm and ^{13}C = 49.0 ppm), coupling constants (J) are given in Hertz (Hz). Multiplicities are abbreviated as br (broad), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet) or combinations thereof. UV irradiation (302 nm) was achieved with a UV viewing cabinet with 8-W UV Lamp. Visible light irradiation was provided by a 150W tungsten halogen lamp. Absorption spectra were recorded in 1.0 cm path length 0.7 mL quartz cuvettes on a UV−vis spectrophotometer. Light power was determined using a hand-held power meter with photodiode sensor. All lamps and spectrometers were allowed to warm for 15 min prior to use to ensure consistent spectral output.

*5-Methoxy-1,2,3,3-tetramethyl-3H-indol-1-ium iodide (**7**).*[31b] Following the literature procedure,[50] to a solution containing 3-methylbutan-2-one (5.90 mL, 55.2 mmol) in glacial acetic acid (88 mL) was added 4-methoxyphenylhydrazine hydrochloride (4.815 g, 27.57 mmol). The solution was stirred at reflux for 5.5 h. The solution was allowed to cool to room temperature and neutralized with KOH pellets. The crude material was extracted with Et_2O (3 × 100 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (70:30, hexanes:EtOAc) to afford 2,3,3-trimethyl-5-methoxy-3*H*-indole as a red amorphous solid (5.149 g, 99%). ^1H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, J = 8.3 Hz, 1H), 6.84−6.80 (m, 2H), 3.82 (s, 3H), 2.24 (s, 3H), 1.28 (s, 6H). ^1H NMR spectrum is consistent with published data.[51] Following the literature procedure,[31b] to a solution of 2,3,3-trimethyl-5-methoxy-3*H*-indole (0.133 g, 0.716 mmol) in anhydrous CH_3CN (14.3 mL) was added iodomethane (0.048 mL, 0.76 mmol). The solution was stirred at reflux for 21 h. The solution was allowed to cool to room temperature, concentrated in vacuo, and suspended in $CHCl_3$ (2.5 mL) and hexanes (20 mL). The suspension was sonicated for 30 min and filtered to afford indolium **7** as a pink amorphous solid (0.117 g, 49%). ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.7 Hz, 1H), 7.07−7.01 (m, 2H), 4.23 (s, 3H), 3.90 (s, 3H), 3.04 (s, 3H), 1.65 (s, 6H). ^1H NMR spectrum is consistent with published data.[31b]

*1,2,3,3-Tetramethyl-5-nitro-3H-indolium iodide (**8**).*[52] Following a modified literature procedure,[31a] to a solution containing 3-methylbutan-2-one (10.16 mL, 94.91 mmol) in glacial acetic acid (68 mL) were added 4-nitrophenylhydrazine (9.002 g, 47.50 mmol) and concentrated H_2SO_4 (6.9 mL). The solution was stirred at reflux for 23 h, allowed to cool to room temperature and then concentrated in vacuo. The crude material was purified by flash column chromatography (60:40, hexanes:EtOAc) to afford 2,3,3-trimethyl-5-nitro-3*H*-indole as a light brown amorphous solid (4.515 g, 47%). ^1H NMR (600 MHz, $CDCl_3$) δ 8.26 (dd, J = 8.5, 2.3 Hz 1H), 8.17 (d, J = 2.2 Hz, 1H), 7.62 (d, J = 8.5 Hz, 1H), 2.36 (s, 3H), 1.38 (s, 6H). ^1H NMR spectrum is consistent with published data.[31a] Following a modified literature procedure,[31b] to a solution of 2,3,3-trimethyl-5-nitro-3*H*-indole (2.04 g, 10.0 mmol) in anhydrous CH_3CN (50 mL) was added iodomethane (1.25 mL, 20.1 mmol). The reaction mixture was stirred at reflux for 24 h. The solution was concentrated in vacuo, dissolved in $CHCl_3$ (15 mL) and hexanes (30 mL), and sonicated for 30 min. After filtration, indolium **8** was afforded as a light brown amorphous solid (3.27 g, 95%). ^1H NMR (400 MHz, CD_3CN) δ 8.59 (d, J = 2.3 Hz, 1H), 8.50 (dd, J = 8.8, 2.2 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 3.98 (s, 3H), 2.78 (s, 3H), 1.62 (s, 6H). ^1H NMR was consistent with that reported in the literature.[52b]

*2-Hydroxy-6-methoxynaphthalene-1-carbaldehyde (**9**).*[53] Following a literature procedure,[32] a solution of 2,6-dihydroxynapthalene (4.20 g, 26.2 mmol) in DMF (200 mL) was cooled to 0 °C and NaH (60% in mineral oil, 2.63 g, 65.8 mmol) was added in 5 portions. The solution was allowed to warm to room temperature and stirred for 30 min, then cooled back to 0 °C and iodomethane (4.1 mL, 66 mmol) was added dropwise. The reaction mixture was allowed to slowly warm to room temperature and stirred for 16 h. The reaction mixture was quenched with CH_3OH (1.0 mL), concentrated in vacuo, and purified by flash column chromatography (95:5, hexanes:EtOAc) to afford 2,6-dimethoxynapthalene as a white amorphous solid (3.91 g, 80%). ^1H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, J = 8.9 Hz, 2H), 7.17−7.08 (m, 4H), 3.91 (s, 6H). ^1H NMR was consistent with that reported in the literature.[54] Following a literature procedure,[33] a solution of *N*-methylformanilide (3.2 mL, 26 mmol), 2,6-dimethoxynapthalene (4.40 g, 23.4 mmol) and $POCl_3$ (2.4 mL, 26 mmol) was stirred at 100 °C for 18 h. The solution was added to DMF (50 mL) and the resulting solution was added to cold 1 M HCl (200 mL), with vigorous stirring. The resulting precipitate was filtered and purified by flash column chromatography (50:50 to 30:70, hexanes:CH_2Cl_2) afforded 2,6-dimethoxy-1-naphthalenecarbaldehyde as a yellow amorphous solid (3.25 g, 64%). ^1H NMR (600 MHz, $CDCl_3$) δ 10.88 (s, 1H), 9.22 (d, J

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= 9.4 Hz, 1H), 7.95 (d, J = 9.1 Hz, 1H), 7.31 (dd, J = 9.4, 2.8 Hz, 1H), 7.27 (d, J = 9.1 Hz, 1H), 7.09 (d, J = 2.8 Hz, 1H), 4.03 (s, 3H), 3.92 (s, 3H). ^{1}H NMR was consistent with that reported in the literature.[33] 2,6-Dimethoxy-1-naphthalenecarbaldehyde (3.24 g, 15.0 mmol), $MgBr_2$ (5.52 g, 30.0 mmol), NaI (4.49 g, 30.0 mmol), and CH_3CN (100 mL) were added to a reaction vessel that was sealed and the stirred at 150 °C for 2 h. The resulting solution was added to CH_2Cl_2 (60 mL), washed with 1 M HCl (20 mL), H_2O (60 mL), dried over Na_2SO_4, and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (60:40, hexanes:CH_2Cl_2) to afford the desired carbaldehyde **9** as a yellow amorphous solid (2.91 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.79 (s, 1H), 10.78 (s, 1H), 8.27 (d, J = 9.2 Hz, 1H), 7.90 (d, J = 9.0 Hz, 1H), 7.29 (dd, J = 9.2, 2.4 Hz, 1H), 7.16−7.12 (m, 2H), 3.92 (s, 3H). ^{1}H NMR was consistent with that reported in the literature.[53]

*2-Hydroxy-6-nitro-1-naphthaldehyde (**10**).*[34] Following a modified literature procedure,[34] to an aqueous solution of 85% nitric acid (10 mL) at −5 °C, 2-hydroxy-1-naphthaldehyde (0.994 g, 5.77 mmol) was added in small portions over 10 min. The mixture was stirred for another 10 min at −5 °C before being poured over ice (20 g). The precipitate was filtered, washed with water and dried, followed by recrystallization from hexanes:EtOAc (10:1) to afford the desired naphthaldehyde **10** as a pale yellow powder (0.459 g, 37%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.30 (s, 1H), 10.74 (s, 1H), 9.14 (d, J = 9.7 Hz, 1H), 8.88 (d, J = 2.0 Hz, 1H), 8.40 (d, J = 9.3 Hz, 1H), 8.30 (dd, J = 9.5, 2.4 Hz, 1H), 7.41 (d, J = 9.0 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 191.8, 166.5, 143.2, 139.5, 135.0, 126.4, 125.0, 124.4, 122.3, 121.1, 113.0. ^{1}H NMR was consistent with that reported in the literature.[34]

*6-Methoxy-1-nitrosonaphthalen-2-ol (**11**).*[35] Following the reported literature,[35] 6-methoxy-2-naphthol (1.125 g, 6.458 mmol) was dissolved in a mixture of AcOH (5.0 mL) and water (10 mL) before being cooled to 0 °C. $NaNO_2$ (0.453 g, 6.57 mmol) was added as a amorphous solid and stirred for 15 min at 0 °C before the solution was filtered and washed with cold water. The product was dried in vacuo to afford the desired nitrosonaphthalenol **11** as a dark brown amorphous solid (0.664 g, 51%, ∼80% purity). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 9.8 Hz, 1H), 7.09 (dd, J = 8.8, 2.6 Hz, 1H), 6.93 (d, J = 2.6 Hz, 1H), 6.57 (d, J = 9.8 Hz, 1H), 3.89 (s, 3H) (hydroxyl proton not observed); ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.2, 160.8, 147.7, 144.7, 130.0, 126.5, 125.1, 123.7, 117.9, 113.4, 55.7 (^{13}C NMR has been tentatively assigned due to a purity of ∼80%. The compound could not be purified further as it is known to readily degrade under recrystallization conditions.);[35] HRMS (ESI) m/z calcd for $C_{11}H_{10}NO_3^+$ $(M + H)^+$ 204.0655, found 204.0662.

*2-Hydroxy-5-(trifluoromethyl)benzaldehyde (**12**).*[44b] Following a modified literature procedure,[55] to a solution of p-trifluoromethylphenol (0.069 g, 5.4 mmol) in TFA (10.7 mL), was added hexamethylenetetramine (0.751 g, 5.36 mmol) under argon. The reaction mixture was stirred at reflux under argon for 15 h. The solution was allowed to cool to room temperature and the solvent was removed in vacuo. The crude mixture was dissolved in CH_2Cl_2 (5.0 mL) and was diluted with water (5.0 mL). The aqueous phase was acidified with concentrated HCl (1.2 mL) and extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were washed with 3.5 M HCl (10.0 mL), saturated aqueous $NaHCO_3$ (10.0 mL) and water (10.0 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude amorphous solid was purified by flash column chromatography (98:2, hexanes:EtOAc) to afford the desired benzaldehyde **12** as a white amorphous solid (0.311 g, 31%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.31 (s, 1H), 9.96 (s, 1H), 7.87 (d, J = 1.6 Hz, 1H), 7.76 (d, J = 8.8, 1.6 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H). ^{1}H NMR spectrum is consistent with published data.[44b]

*3-Formyl-4-hydroxybenzonitrile (**13**).*[44a] Following a modified literature procedure,[55] to a solution of 4-cyanophenol (0.200 g, 1.68 mmol) in TFA (1.7 mL), was added hexamethylenetetramine (0.471 g, 3.36 mmol) under argon. The reaction mixture was stirred at reflux for 5 h. The solution was cooled to 0 °C, followed by the addition of 1 M HCl (11 mL) and stirred for 30 min. The aqueous solution was extracted with of CH_2Cl_2 (3 × 25 mL) and the organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude amorphous solid was purified by flash column chromatography (85:15, hexanes:EtOAc) to afford the desired benzonitrile **13** as a white amorphous solid (0.016 g, 17%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.45 (s, 1H), 9.93 (s, 1H), 7.94 (d, J = 1.8 Hz, 1H), 7.78 (dd, J = 8.7, 1.9 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H). ^{1}H NMR spectrum is consistent with published data.[44a]

*4-Hydroxynicotinaldehyde (**14**).*[45] Following the literature procedure,[45] to a round-bottom flask containing 4-chloronicotinaldehyde (0.092 g, 0.70 mmol) was added 3 M HCl (1.0 mL) and two drops of 30% H_2O_2. The reaction mixture was stirred at reflux for 17.5 h before being allowed to cool to room temperature, neutralized with Na_2CO_3, and concentrated in vacuo. The crude product mixture was suspended in EtOH (10.0 mL) and filtered. The filtrate was concentrated in vacuo and purified by flash column chromatography (9:1, CH_2Cl_2:CH_3OH) to afford the desired nicotinaldehyde **14** as a white amorphous solid (0.083 g, 96%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 10.09 (s, 1H), 8.15 (d, J = 1.1 Hz, 1H), 7.70 (dd, J = 7.6, 1.1 Hz, 1H), 6.36 (d, J = 7.5 Hz, 1H). ^{1}H NMR spectrum is consistent with published data.[45]

*5-Dimethylamino-2-hydroxy-benzaldehyde (**15**).*[46] Following the reported literature procedure,[46] EtOH (30 mL) and aqueous formaldehyde solution (37%, 3.8 mL) were added to a flask containing 2-hydroxy-5-nitrobenzaldehyde (0.160 g, 0.957 mmol) and Pd/C (20 wt %, 0.098 g). The solution was purged with argon and then H_2. The mixture was then stirred under a balloon of H_2 for 18 h at room temperature. Additional aqueous formaldehyde solution (37%, 2.0 mL) was added, and the mixture was again purged with argon and H_2, and then stirred for an additional 24 h under a balloon of H_2. The mixture was filtered through Celite and the filtrate was acidified with 1 M HCl (15 mL) and concentrated in vacuo. The residue was neutralized with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 35 mL). The combined organic extracts were dried over Na_2SO_4 concentrated in vacuo. Purification by flash chromatography (8:2, hexanes:EtOAc) afforded aldehyde **15** as a red oil (0.117 g, 74%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.45 (s, 1H), 9.86 (s, 1H), 7.08 (dd, J = 9.0, 3.1 Hz, 1H), 6.91 (d, J = 9.0 Hz, 1H), 6.85 (d, J = 3.0 Hz, 1H), 2.91 (s, 6H). ^{1}H NMR was consistent with that reported in the literature.[46]

General Procedures for Spiropyran, Spiroindolinonaphthopyrans, and Spirooxazine Synthesis. *General Procedure A.* To a solution of 5-substituted indolium iodide (1 equiv) in either EtOH or *i*-PrOH, were added the substituted salicylaldehyde, naphthaldehyde, or nitrosonaphthalenol (1 equiv), and piperidine or Et_3N (>1 equiv). The reaction mixture was stirred at reflux for the time stated, allowed to cool to room temperature, and concentrated in vacuo. The crude reaction mixture was purified by flash column chromatography to afford the desired product.

General Procedure B. To a solution of 1,3,3-trimethyl-2-methyleneindoline **1** (1 equiv) in EtOH or *i*-PrOH, was added the substituted salicylaldehyde, naphthaldehyde, or nitrosonaphthalenol (1 equiv). The reaction mixture was stirred at reflux for the time stated, allowed to cool to room temperature, and concentrated in vacuo. The crude reaction mixture was purified by flash column chromatography to afford the desired product.

*1′,3′,3′-Trimethylspiro[chromene-2,2′-indoline] (**SP1**).*[40d] The title compound was prepared according to general procedure B using indoline **1** (0.288 mL, 1.63 mmol) and salicylaldehyde (0.173 mL, 1.63 mmol) in EtOH (16.3 mL). The solution was refluxed for 5 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (98:2, hexanes:EtOAc) to afford the desired spiropyran **SP1** as a red amorphous solid (0.449 g, 97%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (td, J = 7.6, 1.2 Hz, 1H), 7.12−7.08 (m, 2H), 7.06 (dd, J = 7.5, 1.6 Hz, 1H), 6.88−6.82 (m, 3H), 6.73 (d, J = 7.7 Hz, 1H), 6.55 (d, J = 7.7 Hz, 1H), 5.67 (d, J = 10.2 Hz, 1H), 2.73 (s, 3H), 1.31 (s, 3H), 1.16 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[40d]

*1′,3′,3′-Trimethyl-5′-nitrospiro[chromene-2,2′-indoline] (**SP2**).*[40b] The title compound was prepared according to general procedure A using indolium **8** (0.241 g, 0.693 mmol), salicylaldehyde (0.074 mL,

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0.70 mmol), and piperidine (0.080 mL, 0.73 mmol) in EtOH (2.8 mL). The solution was refluxed for 19 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (98:2, hexanes:EtOAc) to afford the desired spiropyran **SP2** as a red amorphous solid (0.140 g, 63%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (dd, J = 8.6, 2.3 Hz, 1H), 7.94 (d, J = 2.3 Hz, 1H), 7.13 (td, J = 7.8, 1.6 Hz, 1H), 7.08 (dd, J = 7.5, 1.6 Hz, 1H), 6.92 (d, J = 10.2 Hz, 1H), 6.87 (td, J = 7.5, 1.0 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 6.48 (d, J = 8.7 Hz, 1H), 5.65 (d, J = 10.2 Hz, 1H), 2.85 (s, 3H), 1.35 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.6, 153.3, 140.3, 137.5, 130.3, 130.2, 127.0, 126.2, 120.8, 188.3, 117.6, 114.9, 105.2, 104.1, 51.2, 29.7, 28.8, 25.7, 20.0; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_2O_3^+$ $(M + H)^+$ 323.1390, found 323.1382. ^{1}H NMR spectrum is consistent with published data.[40b]

*5′-Methoxy-1′,3′,3′-trimethylspiro[chromene-2,2′-indoline] (**SP3**).*[27a] The title compound was prepared according to general procedure A using indolium **7** (0.117 g, 0.353 mmol), salicylaldehyde (0.038 mL, 0.35 mmol), and piperidine (0.037 mL, 0.38 mmol) in EtOH (3.5 mL). The solution was refluxed for 19 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (99:1, hexanes:EtOAc) to afford the desired spiropyran **SP3** as a red amorphous solid (0.043 g, 44%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (td, J = 7.8, 1.6 Hz, 1H), 7.05 (dd, J = 7.5, 1.6 Hz, 1H), 6.87−6.80 (m, 2H), 6.75−6.68 (m, 3H), 6.44 (d, J = 8.2 Hz, 1H), 5.68 (d, J = 10.2 Hz, 1H), 3.80 (s, 3H), 2.69 (s, 3H), 1.30 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.3, 153.5, 142.4. 138.2, 129.5, 129.4, 126.5, 119.7, 119.1, 118.6, 114.8, 111.0, 109.4, 106.7, 104.4, 55.7, 51.7, 29.1, 25.6, 19.9; HRMS (ESI) m/z calcd for $C_{20}H_{22}NO_2^+$ $(M + H)^+$ 308.1645, found 308.1641.

*1′,3′,3′-Trimethyl-6-nitrospiro[chromene-2,2′-indoline] (**SP4**).*[40c] The title compound was prepared according to general procedure B using indoline **1** (0.058 mL, 0.32 mmol) and 5-nitrosalicylaldehyde (0.049 g, 0.29 mmol) in EtOH (3.3 mL). The solution was refluxed for 3 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (97:3, hexanes:EtOAc) to afford the desired spiropyran **SP4** as red amorphous solid (0.070 g, 73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04−8.00 (m, 2H), 7.17 (td, J = 7.6, 1.2 Hz, 1H), 7.10 (dd, J = 7.2, 1.1 Hz, 1H), 6.94 (d, J = 10.4 Hz, 1H), 6.90 (td, J = 7.5, 0.9 Hz, 1H), 6.77 (d, J = 8.8, Hz, 1H), 6.57 (d, J = 7.7, 1H), 5.87 (d, J = 10.3 Hz, 1H), 2.76 (s, 3H), 1.33 (s, 3H), 1.20 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[40c]

*1′,3′,3′-Trimethyl-5′,6-dinitrospiro[chromene-2,2′-indoline] (**SP5**).*[40b] The title compound was prepared according to general procedure A using indolium **8** (0.240 g, 0.693 mmol), 5-nitrosalicylaldehyde (0.122 g, 0.728 mmol), and piperidine (0.072 mL, 0.73 mmol) in EtOH (2.8 mL). The solution was refluxed for 5 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (90:10, hexanes:EtOAc) to afford the desired spiropyran **SP5** as a red amorphous solid (0.195 g, 77%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (dd, J = 8.6, 2.3 Hz, 1H), 8.05 (dd, J = 8.8, 2.6 Hz, 1H), 8.06 (d, J = 2.6 Hz, 1H), 7.96 (d, J = 2.3 Hz, 1H), 7.01 (d, J = 10.4 Hz, 1H), 6.80 (d, J = 9.0 Hz, 1H), 6.55 (d, J = 8.7 Hz, 1H), 5.86 (d, J = 10.3 Hz, 1H), 2.88 (s, 3H), 1.35 (s, 3H), 1.23 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[40b]

*5′-Methoxy-1′,3′,3′-trimethyl-6-nitrospiro[chromene-2,2′-indoline] (**SP6**).*[31b] The title compound was prepared according to general procedure A using indolium **7** (0.094 g, 0.28 mmol), 5-nitrosalicylaldehyde (0.046 g, 0.26 mmol), and piperidine (0.029 mL, 0.30 mmol) in EtOH (2.8 mL). The solution was refluxed for 18 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (99:1, hexanes:EtOAc) to afford the desired spiropyran **SP6** as a red amorphous solid (0.062 g, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03−7.98 (m, 2H), 6.91 (d, J = 10.3 Hz, 1H), 6.77 (d, J = 8.7 Hz, 1H), 6.77−6.71 (m, 2H), 6.46 (d, J = 9.0 Hz, 1H), 5.85 (d, J = 10.4 Hz, 1H), 3.79 (s, 3H), 2.69 (s, 3H), 1.28 (s, 3H), 1.19 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[31b]

*6-Methoxy-1′,3′,3′-trimethylspiro[chromene-2,2′-indoline] (**SP7**).*[40d] The title compound was prepared according to general procedure B using indoline **1** (0.058 mL, 0.32 mmol) and 5-methoxysalicylaldehyde (0.041 mL, 0.32 mmol) in EtOH (3.3 mL). The solution was refluxed for 5 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (99:1, hexanes:EtOAc) to afford the desired spiropyran **SP7** as an orange oil (0.082 g, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 (td, J = 7.7, 1.3 Hz, 1H), 7.06 (dd, J = 7.3, 1.1 Hz, 1H), 6.83, (td, J = 7.4, 0.9 Hz, 1H), 6.80 (d, J = 10.2 Hz, 1H), 6.67−6.63 (m, 2H), 6.60 (d, J = 2.9 Hz, 1H), 6.51 (d, J = 7.7 Hz, 1H), 5.70 (d, J = 10.1 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 1.30 (s, 3H), 1.16 (s, 3H). ^{1}H NMR spectrum is consistent with published data.[40d]

*6-Methoxy-1′,3′,3′-trimethyl-5′-nitrospiro[chromene-2,2′-indoline] (**SP8**).*[27b] The title compound was prepared according to general procedure A using indolium **8** (0.174 g, 0.494 mmol), 2-hydroxy-5-methoxybenzaldehyde (0.09 mL, 0.7 mmol) and piperidine (0.06 mL, 0.6 mmol) in *i*-PrOH (2.5 mL). The solution was refluxed for 18 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (2:8 to 1:9, hexanes:toluene). Further purification by flash column chromatography (95:5, hexanes:EtOAc) afforded the spiropyran **SP8** as a yellow amorphous solid (0.099 g, 56%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (dd, J = 8.7, 2.3 Hz, 1H), 7.93 (d, J = 2.3 Hz, 1H), 6.87 (d, J = 10.2 Hz, 1H), 6.71 (dd, J = 8.8, 3.0 Hz, 1H), 6.61−6.67 (m, 2H), 6.47 (d, J = 8.7 Hz, 1H), 5.67 (d, J = 10.1 Hz, 1H), 3.76 (s, 3H), 2.84 (s, 3H), 1.34 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.7, 153.4, 147.8, 140.4, 137.6, 130.3, 126.4, 118.7, 118.4, 115.8, 115.7, 111.8, 110.2, 105.3, 104.0, 55.9, 51.3, 29.0, 25.9, 20.2; HRMS (ESI) m/z calcd for $C_{20}H_{21}N_2O_4^+$ $(M + H)^+$ 353.1496, found 353.1485.

*5′,6-Dimethoxy-1′,3′,3′-trimethylspiro[chromene-2,2′-indoline] (**SP9**).* The title compound was prepared according to general procedure A using indolium **7** (0.166 g, 0.492 mmol), 2-hydroxy-5-methoxybenzaldehyde (0.06 mL, 0.5 mmol) and piperidine (0.06 mL, 0.6 mmol) in *i*-PrOH (2.5 mL). The solution was refluxed for 2 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (97.5:2.5 to 92:8, hexanes:EtOAc) to afford spiropyran **SP9** as a pink amorphous solid (0.157 g, 93%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.80 (d, J = 10.2 Hz, 1H), 6.59−6.75 (m, 5H), 6.42 (d, J = 8.1 Hz, 1H), 5.70 (d, J = 10.2 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 2.68 (s, 3H), 1.29 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.8, 153.2, 148.8, 142.7, 138.6, 129.4, 120.4, 119.2, 115.4, 111.6, 111.3, 109.7, 107.0, 104.3, 56.1, 55.9, 52.9, 51.9, 29.5, 25.9, 20.3; HRMS (ESI) m/z calcd for $C_{21}H_{24}NO_3^+$ $(M + H)^+$ 338.1751, found 338.1747.

*5′-Methoxy-1′,3′,3′-trimethyl-6-(trifluoromethyl)spiro[chromene-2,2′-indoline] (**SP10**).* The title compound was prepared according to general procedure A using indolium **7** (0.087 g, 0.26 mmol), salicylaldehyde **12** (0.050 g, 0.26 mmol), and piperidine (0.027 mL, 0.28 mmol) in EtOH (2.6 mL). The solution was refluxed for 6 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (98:2, hexanes:EtOAc) to afford the desired spiropyran **SP10** as a colorless oil (0.066 g, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, J = 8.5 Hz, 1H), 7.31 (s, 1H), 6.87 (d, J = 10.3 Hz, 1H), 6.79 (d, J = 8.5 Hz, 1H), 6.75−6.70 (m, 2H), 6.45 (d, J = 7.7 Hz, 1H), 5.78 (d, J = 10.3 Hz, 1H), 3.80 (s, 3H), 2.69 (s, 3H), 1.29 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.1, 154.1, 142.4, 138.2, 128.7, 126.9 (q, $^3J_{C-F}$ = 3.8 Hz), 124.5 (q, $^1J_{C-F}$ = 270.9 Hz), 124.0 (q, $^3J_{C-F}$ = 3.8 Hz), 122.3 (q, $^2J_{C-F}$ = 32.7 Hz), 120.9, 118.9, 115.4, 111.5, 109.7, 107.2, 105.7, 56.0, 52.3, 29.4, 25.9, 20.1; HRMS (ESI) m/z calcd for $C_{21}H_{21}F_3NO_2^+$ $(M + H)^+$ 376.1519, found 376.1511.

*5′-Methoxy-1′,3′,3′-trimethylspiro[chromene-2,2′-indoline]-6-carbonitrile (**SP11**).* The title compound was prepared according to general procedure A using indolium **7** (0.093 g, 0.28 mmol), salicylaldehyde **13** (0.041 g, 0.28 mmol), and piperidine (0.029 mL, 0.29 mmol) in EtOH (2.9 mL). The solution was refluxed for 19 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (95:5, hexanes:EtOAc) to afford the desired **SP11** as an orange amorphous solid (0.054 g, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.35 (m, 2H), 6.84 (d, J = 10.3 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 6.73−6.72 (m, 2H), 6.46 (d, J = 9.1 Hz, 1H), 5.81 (d, J = 10.3 Hz, 1H), 3.80 (s, 3H), 2.68 (s, 3H), 1.28 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.0, 154.1, 142.0, 137.8,

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133.8, 130.7, 127.9, 121.3, 119.6, 119.17, 116.1, 111.4, 109.5, 107.1, 106.2, 103.1, 55.9, 52.3, 29.2, 25.8, 19.9; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_2O_2^+$ $(M + H)^+$ 333.1598, found 333.1601.

*5-Methoxy-1,3,3-trimethylspiro[indoline-2,2′-pyrano[3,2-c]-pyridine] (**SP12**).* The title compound was prepared according to general procedure A using indolium **7** (0.093 g, 0.28 mmol), salicylaldehyde **14** (0.034 g, 0.28 mmol), and piperidine (0.029 mL, 0.29 mmol) in EtOH (2.8 mL). The solution was refluxed for 7 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (25:75, hexanes:EtOAc) to afford the desired spiropyran **SP12** as a yellow oil (0.014 g, 16%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.21 (d, J = 5.5 Hz, 1H), 6.89 (d, J = 10.3 Hz, 1H), 6.72−6.71 (m, 2H), 6.63 (d, J = 5.5 Hz, 1H), 6.45 (d, J = 9.1 Hz, 1H), 5.76 (d, J = 10.3 Hz, 1H), 3.79 (s, 3H), 2.68 (s, 3H), 1.27 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 154.2, 151.2, 147.7, 142.2, 138.0, 126.5, 120.7, 115.8, 111.5, 110.6, 109.7, 107.3, 106.4, 56.0, 52.4, 29.3, 25.9, 19.9; HRMS (ESI) m/z calcd for $C_{19}H_{21}N_2O_2^+$ $(M + H)^+$ 309.1598, found 309.1607.

*5-Methoxy-1,3,3,6′-tetramethylspiro[indoline-2,2′-pyrano[3,2-c]-pyridin]-6′-ium iodide (**SP13**).* To a solution of **SP12** (0.020 g, 0.066 mmol) in acetone (1.0 mL) was added iodomethane (0.006 mL, 0.1 mmol). The solution was stirred for 16 h at reflux and was then allowed to cool to room temperature. The reaction mixture was filtered to afford the desired spiropyran **SP13** as a red amorphous solid (0.014 g, 60%). ^{1}H NMR (800 MHz, DMSO-d_6) δ 8.64 (d, J = 1.9 Hz, 1H), 8.24 (dd, J = 7.2, 2.0 Hz, 1H), 7.16 (d, J = 11.5 Hz, 1H), 7.07 (d, J = 2.6 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.95 (d, J = 7.9, 1H), 6.97 (dd, J = 8.6, 2.5 Hz, 1H), 6.38 (d, J = 11.4 Hz, 1H), 3.97 (s, 3H), 3.77 (s, 3H), 2.88 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 156.5, 144.9, 144.5, 139.5, 138.8, 129.5, 119.3, 119.2, 114.9, 112.7, 110.8, 109.2, 55.8, 52.9, 45.3, 31.1, 29.2; HRMS (ESI) m/z calcd for $C_{20}H_{23}N_2O_2^+$ $(M - I)^+$ 323.1754, found 323.1746.

*5′-Methoxy-N,N,1′,3′,3′-pentamethylspiro[chromene-2,2′-indolin]-6-amine (**SP14**).* The title compound was prepared according to general procedure A using indolium **7** (0.223 g, 0.707 mmol), salicylaldehyde **15** (0.117 g, 0.708 mmol), and Et_3N (0.20 mL, 1.4 mmol) in EtOH (5.0 mL). The solution was refluxed for 4 h before being concentrated in vacuo. Purification by column chromatography (85:15 to 80:20, hexanes:EtOAc) afforded the desired spiropyran **SP14** as a red amorphous solid (0.118 g, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.81 (d, J = 10.1 Hz, 1H), 6.73 (d, J = 2.5 Hz, 1H), 6.71 (dd, J = 8.2, 2.5 Hz, 1H), 6.66 (d, J = 8.8 Hz, 1H), 6.61 (dd, J = 8.8, 2.9 Hz, 1H), 6.51 (d, J = 2.9 Hz, 1H), 6.43 (d, J = 8.2 Hz, 1H), 5.68 (d, J = 10.1 Hz, 1H), 3.80 (s, 3H), 2.86 (s, 6H), 2.69 (s, 3H), 1.30 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.7, 147.1, 145.2, 142.8, 138.8, 129.9, 120.0, 119.0, 115.7, 115.4, 112.1, 111.3, 109.7, 106.9, 104.1, 56.0, 51.8, 42.0, 29.5, 25.9, 20.3; HRMS (ESI) m/z calcd for $C_{22}H_{27}N_2O_2^+$ $(M + H)^+$ 351.2067, found 351.2073.

*1′,3′,3′-Trimethylspiro[benzo[f]chromene-3,2′-indoline] (**NP1**).*[41] The title compound was prepared according to general procedure B using indoline **1** (0.095 mL, 0.54 mmol) and 2-hydroxy-1-naphthaldehyde (0.093 g, 0.54 mmol) in EtOH (10.0 mL). The solution was refluxed for 5 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (95:5, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP1** as a pale white amorphous solid (0.134 g, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.62 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 10.5 Hz, 1H), 7.51 (t, J = 7.9 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 7.2 (t, J = 7.9 Hz, 1H), 7.10 (d, J = 7.2 Hz, 1H), 6.99 (d, J = 9.1 Hz, 1H), 6.87 (d, J = 7.3 Hz, 1H), 6.54 (d, J = 7.6 Hz, 1H), 5.80 (d, J = 10.7 Hz, 1H), 2.74 (s, 3H), 1.34 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.7, 148.1, 136.8, 130.8, 129.8, 128.7, 128.6, 127.6, 126.7, 124.9, 123.3, 121.6, 119.2, 117.8, 117.5, 110.6, 106.8, 104.3, 51.6, 29.0, 25.8, 20.3. ^{1}H NMR was consistent with that reported in the literature.[41]

*1′,3′,3′-Trimethyl-5′-nitrospiro[benzo[f]chromene-3,2′-indoline] (**NP2**).*[41] The title compound was prepared according to general procedure A using indolium **8** (0.174 g, 0.503 mmol), 2-hydroxy-1-naphthaldehyde (0.098 g, 0.57 mmol), and Et_3N (0.073 mL, 0.52 mmol) in EtOH (25 mL). The solution was refluxed for 22 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (93:7, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP2** as a pale yellow amorphous solid (0.116 g, 64%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (dd, J = 8.6, 2.0 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.97 (d, J = 2.1 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.68 (s, 1H), 7.66 (d, J = 2.2 Hz, 1H), 7.54 (t, J = 7.7 Hz, 1H), 7.37 (d, J = 7.7 Hz, 1H), 6.97 (d, J = 9.0 Hz, 1H), 6.50 (d, J = 8.7 Hz, 1H), 5.77 (d, J = 10.4 Hz, 1H), 2.86 (s, 3H), 1.38 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.3, 152.0, 140.6, 137.5, 130.7, 129.8, 129.1, 128.8, 127.2, 126.4, 126.0, 123.9, 120.8, 118.5, 117.1, 116.2, 110.5, 105.4, 104.3, 51.2, 28.9, 25.8, 20.2; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_2NaO_3^+$ $(M + Na)^+$ 395.1366, found 395.1372. ^{1}H NMR was consistent with that reported in the literature.[41]

*5′-Methoxy-1′,3′,3′-trimethylspiro[benzo[f]chromene-3,2′-indoline] (**NP3**).*[27a] The title compound was prepared according to general procedure A using indolium **7** (0.172 g, 0.519 mmol), 2-hydroxy-1-naphthaldehyde (0.086 g, 0.50 mmol), and Et_3N (0.073 mL, 0.52 mmol) in EtOH (25 mL). The solution was refluxed for 23 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (95:5, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP3** as a pale white amorphous solid (0.135 g, 73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.0 Hz, 1H), 7.59 (d, J = 10.5 Hz, 1H), 7.50 (t, J = 7.8 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 6.75 (s, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.44 (d, J = 8.5 Hz, 1H), 5.79 (d, J = 10.7 Hz, 1H), 3.81 (s, 3H), 2.69 (s, 3H), 1.32 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.9, 152.8, 142.5, 138.5, 130.1, 129.9, 128.8, 128.7, 126.8, 124.9, 123.4, 120.8, 117.8, 117.6, 111.3, 110.7, 109.7, 107.0, 104.8, 56.1, 51.8, 29.4, 25.8, 20.3; HRMS (ESI) m/z calcd for $C_{24}H_{23}NNaO_2^+$ $(M + Na)^+$ 380.1621, found 380.1634.

*1′,3′,3′-Trimethyl-8-nitrospiro[benzo[f]chromene-3,2′-indoline] (**NP4**).*[41] The title compound was prepared according to general procedure B using indoline **1** (0.070 mL, 0.39 mmol) and naphthaldehyde **10** (0.081 g, 0.37 mmol) in EtOH (20 mL). The solution was refluxed for 8 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (95:5, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP4** as a yellow powder (0.036 g, 26%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (d, J = 2.2 Hz, 1H), 8.26 (dd, J = 9.3, 2.4 Hz, 1H), 8.10 (d, J = 9.3 Hz, 1H), 7.79 (d, J = 8.9 Hz, 1H), 7.58 (d, J = 10.5 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.13 (dd, J = 8.7, 5.7 Hz, 1H), 7.12 (d, J = 5.7 Hz, 1H), 6.90 (d, J = 7.5 Hz, 1H), 6.57 (d, J = 7.8 Hz, 1H), 5.90 (d, J = 10.4 Hz, 1H), 2.76 (s, 3H), 1.34 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.9, 147.8, 143.5, 136.3, 132.7, 132.2, 127.8, 127.0, 125.5, 124.3, 122.1, 121.6, 120.2, 119.6, 119.2, 111.2, 107.0, 105.3, 51.9, 28.9, 25.8, 20.2; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_2NaO_3^+$ $(M + Na)^+$ 395.1366, found 395.1372. ^{1}H NMR was consistent with that reported in the literature.[41]

*1′,3′,3′-Trimethyl-5′,8-dinitrospiro[benzo[f]chromene-3,2′-indoline] (**NP5**).*[41] The title compound was prepared according to general procedure A using indolium **8** (0.150 g, 0.433 mmol), naphthaldehyde **10** (0.093 g, 0.43 mmol), and Et_3N (0.060 mL, 0.43 mmol) in *i*-PrOH (25 mL). The solution was refluxed for 28 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (80:20, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP5** as a reddish brown amorphous solid (0.120 g, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (d, J = 2.3 Hz, 1H), 8.30 (dd, J = 9.2, 2.4 Hz, 1H), 8.21 (dd, J = 8.7, 2.4 Hz, 1H), 8.12 (d, J = 9.3 Hz, 1H), 7.98 (d, J = 2.3 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.65 (t, J = 10.3 Hz, 1H), 7.12 (d, J = 8.9 Hz, 1H), 6.54 (d, J = 8.7 Hz, 1H), 5.88 (d, J = 10.2 Hz, 1H), 2.88 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.1, 153.0, 143.9, 140.9, 137.2, 132.8, 132.7, 127.5, 126.4, 125.3, 122.3, 120.6, 119.5, 118.5, 117.7, 111.1, 105.7, 105.1, 51.6, 29.0, 25.7, 20.1; HRMS (ESI) m/z calcd for $C_{23}H_{19}N_3NaO_5^+$ $(M + Na)^+$ 440.1217, found 440.1223. ^{1}H NMR was consistent with that reported in the literature.[41]

*5′-Methoxy-1′,3′,3′-trimethyl-8-nitrospiro[benzo[f]chromene-3,2′-indoline] (**NP6**).* The title compound was prepared according to

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general procedure A using indolium **7** (0.206 g, 0.622 mmol), naphthaldehyde **10** (0.129 g, 0.594 mmol), and Et_3N (0.10 mL, 0.72 mmol) in EtOH (5.0 mL). The solution was refluxed for 7 h before being concentrated in vacuo. Purification by column chromatography on neutral alumina (95:5 to 80:20, hexanes:EtOAc) afforded the desired spiropyran **NP6** as a yellow amorphous solid (0.092 g, 38%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (d, J = 2.0 Hz, 1H), 8.26 (dd, J = 9.3, 2.1 Hz, 1H), 8.09 (d, J = 9.5 Hz, 1H), 7.79 (d, J = 8.9 Hz, 1H), 7.57 (d, J = 10.5 Hz, 1H), 7.13 (d, J = 8.9 Hz, 1H), 6.77−6.72 (m, 2H), 6.47 (d, J = 8.2 Hz, 1H), 5.89 (d, J = 10.5 Hz, 1H), 3.81 (s, 3H), 2.71 (s, 3H), 1.32 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.0, 154.2, 143.6, 142.2, 138.1, 132.8, 132.2, 127.1, 125.5, 124.3, 122.1, 120.3, 119.9, 119.2, 111.5, 111.4, 109.7, 107.2, 105.8, 56.1, 52.2, 29.4, 25.8, 20.2; HRMS (ESI) m/z calcd for $C_{24}H_{23}N_2O_4^+$ $(M + H)^+$ 403.1652, found 403.1648.

*8-Methoxy-1′,3′,3′-trimethylspiro[benzo[f]chromene-3,2′-indoline] (**NP7**).* The title compound was prepared according to general procedure B using indoline **1** (0.036 mL, 0.20 mmol) and naphthaldehyde **9** (0.041 g, 0.20 mmol) in EtOH (2.0 mL). The solution was refluxed for 22 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (90:10, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP7** as a light yellow amorphous solid (0.020 g, 40%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, J = 9.1 Hz, 1H), 7.55 (d, J = 10.4 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.22−7.17 (m, 2H), 7.09 (d, J = 7.2 Hz, 1H), 7.06 (d, J = 2.2 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H), 6.85 (t, J = 7.4 Hz, 1H), 6.53 (d, J = 7.6 Hz, 1H), 5.79 (d, J = 10.3 Hz, 1H), 3.90 (s, 3H), 2.74 (s, 3H), 1.34 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.9, 151.2, 148.3, 136.9, 129.7, 128.8, 127.7, 125.1, 122.4, 121.7, 119.22, 119.18, 118.2, 117.9, 111.1, 107.1, 106.9, 104.1, 55.5, 51.6, 29.9, 29.1, 25.9, 20.4; HRMS (ESI) m/z calcd for $C_{24}H_{24}NO_2^+$ $(M + H)^+$ 358.1802, found 358.1810.

*8-Methoxy-1′,3′,3′-trimethyl-5′-nitrospiro[benzo[f]chromene-3,2′-indoline] (**NP8**).* The title compound was prepared according to general procedure A using indolium **8** (0.069 g, 0.20 mmol), naphthaldehyde **9** (0.040 g, 0.19 mmol), and piperidine (0.021 mL, 0.20 mmol) in EtOH (1.9 mL). The solution was refluxed for 24 h before being concentrated in vacuo. The crude product was purified by flash column chromatography (90:10, hexanes:EtOAc) to afford the desired spiroindolinonaphthopyran **NP8** as a light yellow amorphous solid (0.054 g, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (dd, J = 8.6, 2.0 Hz, 1H), 7.96 (d, J = 1.9 Hz, 1H), 7.94 (d, J = 9.2 Hz, 1H), 7.61 (d, J = 10.4 Hz, 1H), 7.56 (d, J = 8.9 Hz, 1H), 7.22 (dd, J = 9.1, 2.4 Hz, 1H), 7.08 (d, J = 2.3 Hz, 1H), 6.94 (d, J = 8.8 Hz, 1H), 6.49 (d, J = 8.7 Hz, 1H), 5.76 (d, J = 10.4 Hz, 1H), 3.91 (s, 3H), 2.85 (s, 3H), 1.37 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.2, 153.3, 150.4, 140.5, 137.6, 131.1, 129.3, 126.4, 124.9 126.0, 122.3, 119.6, 118.5, 117.5, 116.5, 110.8, 107.1, 105.3, 104.1, 55.5, 51.2, 28.9, 25.8, 20.3; HRMS (ESI) m/z calcd for $C_{24}H_{23}N_2O_4^+$ $(M + H)^+$ 403.1652, found 403.1657.

*5′,8-Dimethoxy-1′,3′,3′-trimethyl-spiro[benzo[f]chromene-3,2′-indole] (**NP9**).* The title compound was prepared according to general procedure A using indolium **7** (0.066 g, 0.20 mmol), naphthaldehyde **9** (0.040 g, 0.20 mmol), and piperidine (0.02 mL, 0.2 mmol) in *i*-PrOH (2.5 mL). The solution was refluxed for 2 h before being concentrated in vacuo. The obtained residue was purified by flash column chromatography (97:3 to 95:5, hexanes:EtOAc) to afford napthopyran **NP9** as a white amorphous solid (0.038 g, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, J = 9.2 Hz, 1H), 7.53 (d, J = 9.6 Hz, 1H), 7.51 (d, J = 9.6 Hz, 1H), 7.19 (dd, J = 9.0, 2.5 Hz, 1H), 7.06 (d, J = 2.6 Hz, 1H), 6.97 (d, J = 8.9 Hz, 1H), 6.83−6.68 (m, 2H), 6.44 (d, J = 8.2 Hz, 1H), 5.78 (d, J = 10.4 Hz, 1H), 3.90 (s, 3H), 3.80 (s, 3H), 2.68 (s, 3H), 1.31 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.9, 153.9, 151.2, 142.6, 138.5, 129.7, 128.7, 125.1, 125.0, 122.3, 119.1, 118.1, 117.9, 111.3, 111.1, 109.7, 107.1, 107.0, 104.4, 56.0, 55.4, 51.8, 29.4, 25.8, 20.3; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_3^+$ $(M + H)^+$ 388.1907, found 388.1897.

*1,3,3-Trimethylspiro[indoline-2,3′-naphtho[2,1-b][1,4]oxazine] (**SO1**).*[41] The title compound was prepared according to general procedure B using indoline **1** (0.940 mL, 5.31 mmol) and nitrosonaphthol **6** (0.916 g, 5.29 mmol) in EtOH (50 mL). The solution was refluxed for 24 h before being concentrated in vacuo. Purification by column chromatography (95:5, hexanes:EtOAc) afforded the desired spiropyran **SO1** as a yellow amorphous solid (0.818 g, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, J = 8.4 Hz, 1H), 7.76−7.74 (m, 2H), 7.67 (d, J = 8.9 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.40 (d, 8.1 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.3 Hz, 1H), 7.02 (d, J = 8.9 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 2.76 (s, 3H), 1.36 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.8, 147.6, 144.1, 135.9, 130.9, 130.3, 129.3, 128.1, 127.8, 127.2, 124.2, 123.0, 121.6, 121.5, 119.9, 116.8, 107.2, 98.6, 51.8, 29.6, 25.4, 20.8; HRMS (ESI) m/z calcd for $C_{22}H_{21}N_2O^+$ $(M + H)^+$ 329.1648, found 329.1655. ^{1}H NMR was consistent with that reported in the literature.[41]

*1,3,3-Trimethyl-5-nitrospiro[indoline-2,3′-naphtho[2,1-b][1,4]-oxazine] (**SO2**).*[41] The title compound was prepared according to general procedure A using indolium **8** (0.174 g, 0.503 mmol), nitrosonaphthol **6** (0.089 g, 0.51 mmol), and Et_3N (0.07 mL, 0.5 mmol) in EtOH (0.5 mL). The mixture was heated at 150 °C under microwave conditions for 45 min before being concentrated in vacuo. Purification by column chromatography (80:20, pentane:Et_2O) afforded the desired spiropyran **SO2** as a light brown amorphous solid (0.037 g, 20%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, J = 8.5 Hz, 1H), 8.22 (dd, J = 8.6, 1.9 Hz, 1H), 7.96 (d, J = 1.9 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.73 (s, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.61 (br t, J = 7.8 Hz, 1H), 7.43 (br t, J = 7.6 Hz, 1H), 7.02 (d, J = 8.9 Hz, 1H), 6.56 (d, J = 8.7 Hz, 1H), 2.89 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.9, 149.1, 143.4, 141.2, 136.8, 130.9, 130.8, 129.7, 128.0, 127.6, 126.5, 124.7, 122.9, 121.6, 118.4, 116.5, 105.9, 98.5, 51.3, 29.7, 25.4, 21.0; HRMS (ESI) m/z calcd for $C_{22}H_{20}N_3O_3^+$ $(M + H)^+$ 374.1499, found 374.1501. ^{1}H NMR was consistent with that reported in the literature.[41]

*5-Methoxy-1,3,3-trimethylspiro[indoline-2,3′-naphtho[2,1-b]-[1,4]oxazine] (**SO3**).*[41] The title compound was prepared according to general procedure A using indolium **7** (1.660 g, 5.012 mmol), nitrosonaphthol **8** (0.880 g, 5.08 mmol), and Et_3N (0.70 mL, 5.0 mmol) in *i*-PrOH (50 mL). The solution was refluxed for 14 h before being concentrated in vacuo. Purification by column chromatography (95:5, hexanes:EtOAc) afforded the desired spiropyran **SO3** as a light brown amorphous solid (0.820 g, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d J = 8.6 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.74 (s, 1H), 7.66 (d, J = 8.9 Hz, 1H), 7.58 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 7.39 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H), 7.02 (d, J = 8.9 Hz, 1H), 6.73 (dd, J = 8.3, 2.6 Hz, 1H), 6.72 (d, J = 2.5 Hz, 1H), 6.48 (d, J = 8.3 Hz, 1H), 3.80 (s, 3H), 2.71 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.4, 150.8, 144.3, 141.9, 137.6, 131.0, 130.3, 129.3, 127.9, 127.2, 124.3, 123.0, 121.6, 116.9, 111.8, 109.5, 107.5, 99.1, 56.1, 52.0, 30.1, 25.5, 20.8; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_2O_2^+$ $(M + H)^+$ 359.1754, found 359.1750. ^{1}H NMR was consistent with that reported in the literature.[41]

*1,3,3-Trimethyl-8′-nitrospiro[indoline-2,3′-naphtho[2,1-b][1,4]-oxazine] (**SO4**).*[42] Following the reported procedure,[36] spirooxazine **SO1** (0.100 g, 0.304 mmol) was slowly added to H_2SO_4 (3.0 mL) and cooled to 0 °C. HNO_3 (30%, 0.025 mL) was added dropwise, followed by stirring at 0 °C for 1.5 h. The mixture was poured onto ice and then added to CH_2Cl_2 (50 mL) and saturated aqueous $NaHCO_3$ (50 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 25 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude residue by column chromatography (95:5, hexanes:EtOAc) afforded the desired spiropyran **SO4** as a yellow amorphous solid (0.017 g, 15%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (d, J = 2.2 Hz, 1H), 8.68 (d, J = 9.3 Hz, 1H), 8.32 (dd, J = 9.3, 2.2 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.81 (s, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 7.11 (d, J = 7.3 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 6.61 (d, J = 7.8 Hz, 1H), 2.78 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.1, 147.5, 147.4, 144.5, 135.6, 133.9, 132.3, 128.3, 127.6, 124.8, 123.4, 123.2, 121.7, 120.6, 120.4, 119.4, 107.4, 99.5, 52.3, 29.8, 25.6, 20.8; HRMS (ESI) m/z calcd for $C_{22}H_{20}N_3O_3^+$ $(M + H)^+$ 374.1499, found 374.1506. ^{1}H NMR was consistent with that reported in the literature.[42]

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*8′-Methoxy-1,3,3-trimethylspiro[indoline-2,3′-naphtho[2,1-b]-[1,4]oxazine] (**SO7**).*[43] The title compound was prepared according to general procedure B using indoline **1** (0.090 mL, 0.50 mmol) and nitrosonaphthalenol **11** (~80% purity, 0.136 g, 0.536 mmol) in EtOH (5.0 mL). The solution was refluxed for 3 h before being concentrated in vacuo. Purification by column chromatography (95:5, hexanes:EtOAc) afforded the desired spiropyran **SO7** as a yellow amorphous solid (0.068 g, 38%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, J = 9.2 Hz, 1H), 7.75 (s, 1H), 7.56 (d, J = 8.9 Hz, 1H), 7.27 (dd, J = 9.3, 1.7 Hz, 1H), 7.23 (t, J = 7.7 Hz, 1H), 7.12−7.07 (m, 2 H), 7.00 (d, J = 8.8 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.58 (d, J = 7.7 Hz, 1H), 3.94 (s, 3H), 2.77 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.7, 151.3, 147.8, 142.6, 136.0, 130.3, 128.9, 128.1, 126.2, 123.4, 123.3, 121.6, 119.9, 119.6, 117.3, 107.2, 106.3, 98.5, 55.5, 51.9, 29.8, 25.6, 21.0; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_2O_2^+$ $(M + H)^+$ 359.1754, found 359.1760.

*8′-Methoxy-1,3,3-trimethyl-5-nitrospiro[indoline-2,3′-naphtho-[2,1-b][1,4]oxazine] (**SO8**).* The title compound was prepared according to general procedure A using indolium **8** (0.175 g, 0.506 mmol), nitrosonaphthalenol **11** (~80% purity, 0.137 g, 0.541 mmol), and Et_3N (0.070 mL, 0.044 mmol) in EtOH (0.5 mL). The mixture was heated at 150 °C under microwave conditions for 15 min before being concentrated in vacuo. Purification by column chromatography (80:20, pentane:Et_2O) afforded the desired spiropyran **SO8** as a light brown amorphous solid (0.027 g, 13%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, J = 9.1 Hz, 1H), 8.21 (dd, J = 8.7, 2.1 Hz, 1H), 7.95 (d, J = 2.1 Hz, 1H), 7.71 (s, 1H), 7.60 (d, J = 8.9 Hz, 1H), 7.27 (dd, J = 9.2, 2.1 Hz, 1H), 7.09 (d, J = 1.9 Hz, 1H), 6.98 (d, J = 8.8 Hz, 1H), 6.55 (d, J = 8.6 Hz, 1H), 3.92 (s, 3H), 2.89 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.0, 152.9, 149.4, 141.8, 141.1, 136.9, 130.7, 129.5, 126.5, 126.0, 123.3, 123.3, 120.0, 118.4, 116.9, 106.3, 105.8, 98.4, 55.5, 51.3, 29.7, 25.4, 21.0; HRMS (ESI) m/z calcd for $C_{23}H_{22}N_3O_4^+$ $(M + H)^+$ 404.1605, found 404.1615.

*5,8′-Dimethoxy-1,3,3-trimethylspiro[indoline-2,3′-naphtho[2,1-b][1,4]oxazine] (**SO9**).* The title compound was prepared according to general procedure A using indolium **7** (0.245 g, 1.06 mmol), nitrosonaphthalenol **11** (~80% purity, 0.349 g, 1.37 mmol), and Et_3N (0.16 mL, 1.1 mmol) in EtOH (5.0 mL). The mixture was heated at reflux for 18 h before being concentrated in vacuo. Purification by column chromatography (100:0 to 97:3, toluene:EtOAc) afforded the desired spiropyran **SO9** as a dark yellow amorphous solid (0.063 g, 15%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, J = 9.1 Hz, 1H), 7.74 (s, 1H), 7.56 (d, J = 8.9 Hz, 1H), 7.26 (dd, J = 9.1, 2.5 Hz, 1H), 7.08 (d, J = 2.5 Hz, 1H), 7.00 (d, J = 8.9 Hz, 1H), 6.75 (dd, J = 8.3, 2.6 Hz, 1H), 6.73 (d, J = 2.5 Hz, 1H), 6.48 (d, J = 8.3 Hz, 1H), 3.92 (s, 3H), 3.81 (s, 3H), 2.71 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.7, 154.3, 151.2, 142.7, 141.9, 137.7, 130.3, 128.9, 126.2, 123.4, 123.3, 119.6, 117.3, 111.8, 109.5, 107.4, 106.3, 98.9, 56.1, 55.5, 52.0, 30.2, 25.5, 20.8; HRMS (ESI) m/z calcd for $C_{24}H_{25}N_2O_3^+$ $(M + H)^+$ 389.1860, found 389.1869.

General Procedure for Absorbance Assays of Spiropyrans, Spiroindolinonaphthopyrans, and Spirooxazines. *Preparation of Spiropyran Solutions.* 1 ×10^{-3} M stock solutions of photoswitches were prepared by first dissolving 2.5 × 10^{-5} moles into 25 mL of absolute ethanol. Second, a 1 mL aliquot from the 1 × 10^{-3} M stock solution was diluted to 10 mL with absolute ethanol yielding a 1 × 10^{-4} M solution for testing.

General Procedure for Gadolinium Nitrate Solutions. A 1.4 × 10^{-2} M solution of gadolinium nitrate was prepared by dissolving 3.5 × 10^{-4} moles (0.1579 g) of gadolinium nitrate in 25 mL of absolute ethanol.

General Light Response Assay. To a quartz cuvette was added 0.7 mL of a 1 × 10^{-4} M solution of photoswitch in ethanol. These solutions, prepared under ambient light conditions, were then tested for their absorbance profile. After taking the initial absorbance the cuvette was irradiated with UV light for 15 min. Absorbance was recorded again and the cuvette was allowed to incubate for 1 min under completely dark conditions before taking another absorbance measurement. The cuvette was then irradiated with visible light for 1 min before taking the final absorbance.

General Gadolinium Nitrate Assay Procedure. To a quartz cuvette was added 0.7 mL of a 1 × 10^{-4} M solution of photoswitch in ethanol. These solutions, prepared under ambient light conditions, were then tested for their absorbance profile. To the cuvette was then added 1 equiv of gadolinium nitrate (5 μL of a 1.4 × 10^{-2} M solution of gadolinium nitrate in absolute ethanol), mixed with a Pasteur pipet and incubated under completely dark conditions before taking absorbance measurements at 1 and 15 min. After gadolinium nitrate incubation this solution was irradiated with UV light for 15 min and absorbance was measured again. The solution was then incubated under completely dark conditions for 1 min, absorbance recorded, and the cuvette was irradiated with visible light for 1 min before taking the final absorbance.

General Kinetics Assay. To a quartz cuvette was added 0.7 mL of a 1 × 10^{-4} M solution of photoswitch in ethanol. These solutions, prepared under ambient light conditions, were then tested for their absorbance profile. After taking the initial absorbance the cuvette was irradiated with UV light at 1 min intervals. After saturation of the UV response, the solutions were irradiated with visible light at 2.29 ± 0.03 mW for 1 min intervals until the visible light response was saturated. For dark incubation, the photoswitching solution was saturated with UV light and then absorbance was taken every minute while the cuvette remained in the UV−vis spectrophotometer.

Evaluating UV and Visible Response for SP3 in the Presence of Gd^{3+} Ions. To a quartz cuvette was added 0.7 mL of a 1 × 10^{-4} M solution of photoswitch in ethanol. These solutions, prepared under ambient light conditions, were then tested for their absorbance profile. To the cuvette was then added 1 equiv of gadolinium nitrate (5 μL of a 1.4 × 10^{-2} M solution of gadolinium nitrate in absolute ethanol), mixed with a Pasteur pipet and incubated under dark taking absorbance measurements every minute. After gadolinium nitrate incubation this solution was irradiated with UV light for 10 min taking absorbance measurements every minutes. After 10 min of UV irradiation the solution was irradiated with visible light for 5 min, taking absorbance measurements every minute.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01193.

^{1}H NMR spectra for compounds **8**, **9**, **10**, **11**, **12**, **13**, **SP2**, **SP3**, **SP8**−**SP14**, **NP1**−**NP9**, **SO1**−**SO4**, and **SO7**−**SO9**; ^{13}C NMR spectra for compounds **10**, **11**, **SP2**, **SP3**, **SP8**−**SP14**, **NP1**−**NP9**, **SO1**−**SO4**, and **SO7**−**SO9**; UV−vis spectra for all spiropyrans, spiroindolinonaphthopyrans, and spirooxazines (PDF)

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Notes

The authors declare no competing financial interest.

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