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Stereoselective Synthesis of 1-Methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one Derivatives via Prins Cyclization

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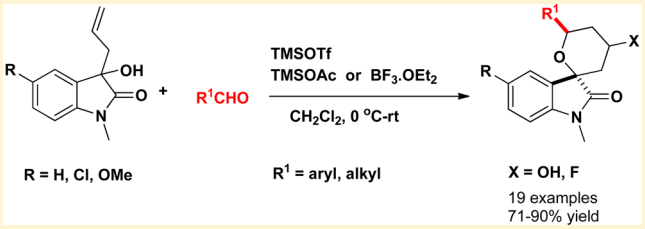
Supporting Information

ABSTRACT: A novel spirocyclization has been developed for the construction of functionalized spirooxindole pyran via Lewis acid promoted Prins cyclization. The reaction proceeds through formation of a single diastereoisomer with high stereoselectivity. This approach can be used to construct biologically important substituted spirooxindole as well as fluorinated pyran scaffolds.



INTRODUCTION

Among the various heterocyclic compounds, spirooxindoles[1−4] are of great interest due to their potential biological activities and their role as key precursors in natural product synthesis.[5,6] For example, spirolactone **1** (Figure 1) has shown cytotoxicity,[2]

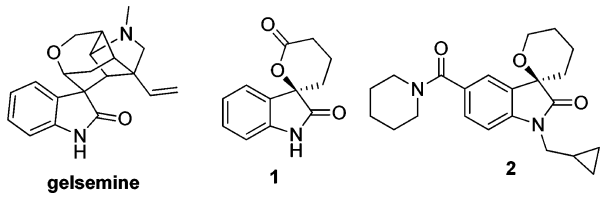


Figure 1. Naturally occurring and biologically active spirocyclic oxindoles.

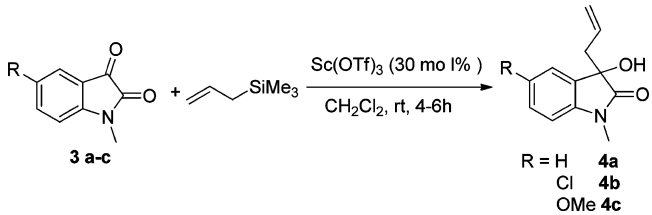
and its analogue (**2**) is capable of binding to the CB2 receptor as an agonist.[7] Similar structures such as gelsemine is a complex alkaloid with anxiolytic activity.[8] Thus, we are interested in the development of new synthetic approaches to spirooxindole.

Recently, Prins cyclization has been used for the construction of tetrahedropyran scaffolds.[9,10] In this context synthesis of spirooxindoles via Prins cyclization allows for the construction of two privileged motifs, the pyrrolidinyl spirooxindole substructure and tetrahydropyranone, with the two rings forming a spiro fusion at the 3-position of the oxindole core. Several elegant processes have been developed for the construction of spirooxindoles. Previous approaches include metal-mediated multistep transformations,[11] oxidative spirocyclization,[12] and *N*-heterocyclic carbene/Lewis acid-mediated synthesis.[13] Past synthetic strategies for spirooxindoles via Prins-type cyclization[14,15] need long reaction time and multistep synthesis for the starting material. In continuation of our interest in developing synthetic methods,[16] herein we report a novel and concise strategy for the stereoselective synthesis of spirooxindoles derivatives through Prins cyclization.

RESULTS AND DISCUSSION

The starting materials **4a−c** for the synthesis of tetrahydrospiro[indoline-3,2′pyran]-2-one derivatives can be made from known compounds 1-methylisatins (**3a−c**)[17] by reacting with allyltrimethylsilane in the presence of 30 mol % of $Sc(OTf)_3$ in dichloromethane at room temperature with good yields. The present method for the synthesis of compound **4a−c** is simple and efficient compared to previously reported literature procedures.[18−21] After successful synthesis of compounds **4a−c** (Scheme 1), we then focused on synthesis of novel spirocyclic compounds.

Scheme 1. Allylation of Substituted 1-Methyl Isatines



In our initial studies, 3-allyl-3-hydroxy-1-methyl indolin-2-one (**4a**) was treated with benzaldehyde (**5a**) in the presence of an acid. To optimize the conditions, the reaction was performed with various acids, and the results are presented in Table 1. It was concluded that $Sc(OTf)_3$ and TFA (Table 1, entries 1 and 2) were ineffective for this transformation. Interestingly, trimthylsilyl triflate (TMSOTf, 4.0 equiv) was

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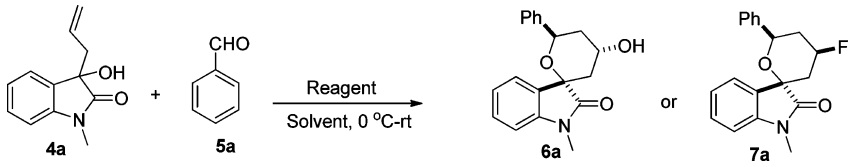
Table 1. Optimization of the Reaction



entry	reagent[a]	solvent	time (h)	products (yield %)[b] 6a	7a
1	20 mol % $Sc(OTf)_3$	CH_2Cl_2	12	NR	
2	1 equiv TFA	CH_2Cl_2	12	NR	
3	1.5 equiv BF_3OEt_2	CH_2Cl_2	4	–	73
4	TMSOTf/TMSOAc AcOH	CH_2Cl_2	2	81[a]	
5	TMSOTf/TMSOAc AcOH	THF	2	45	
6	TMSOTf/TMSOAc AcOH	DCE	2	54	

[a]Reaction conditions (entry 4): **4a** (1.0 equiv), **5a** (1.0 equiv), in CH_2C1_2, TMSOTf (4.0 equiv), TMSOAc (1.2 equiv) and AcOH (4.0 equiv), temperature and time as indicated. **6a** was isolated after the reaction was quenched with sat. $NaHCO_3$ solution. [b]Yields refer to isolated yield; the compounds were characterized by NMR and mass spectrometry

found to be a highly efficient Lewis acid in promoting this cyclization, when the reaction was performed in the presence of 1.2 equiv of trimethylsilyl acetate (TMSOAc) and 4.0 equiv of acetic acid in dichloromethane at 0 °C to room temperature (Table 1, entry 4). After workup, spirocyclic compound **6a** was obtained as a single axial hydroxy isomer in 81% yield. Similar conditions have been used by Willis and co-workers[22] for Prins cyclization in general.

Axial selectivity of the nucleophile in Prins cyclization was previously studied by Rychnovsky et al.,[23] where the cyclization proceeds through a chair transition state with an unexpected *syn* addition of nucleophile across the alkene. Such a mechanism is consistent with the formation of a single stereoisomer (Table 2). We were interested in studying the structural aspect with X-ray crystallography using **6b** (Figure 2) as representative cases. The structures of **6b** clearly show a chair conformation with the hydroxyl group in an axial position and being involved in an intramolecular hydrogen bond with the indolinone group (Figure 2). Results from further NOE experiments (see the Supporting Information) are consistent with such findings as well. Interestingly, when the reaction was performed with $BF_3{\bullet}OEt_2$,[24,25] incorporation of F was observed **7a** (Table 1, entry 3), which was confirmed by ^1H and ^{19}F NMR. Next, we screened the reaction using solvents including dichloromethane, dichloroethane (DCE), tetrahydrofuran (THF) and found that dichloromethane gave the best results in terms of yield. By using these optimized conditions, the scope of the reaction was further evaluated using a series of aromatic and aliphatic aldehydes, as well as substituted (5-Cl, 5-OMe) allylisatins **4a–c** (Table 2).

The cyclization reaction was performed with those substrates with halogen (4-F, 4-Br, 4-CF_3) as well as electron-donating (4-Me, 2-OMe) groups on the phenyl ring. The findings showed that the substituents on the aromatic aldehydes had no apparent effect on the stereoselectivity and yields of the products. For instance, *p*-bromo benzaldehyde gave **6b** and **6g** in excellent yields (Table 2, entries 2 and 7). Furthermore, fluoro and trifluoromethyl benzaldehydes also afforded the respective products in good yields (Table 2, entries 4, 6, and 9). Again, the stereochemistry of the tricyclic compound **6b** was determined by X-ray crystallographic analysis[26] (Figure 2).

We next extended the scope of the reaction with aliphatic, α,β-unsaturated aldehydes and acetals. Aliphatic aldehydes such as isobutyraldehyde (entry 13) and methacrolein (entry 12) gave moderate yields. In contrast, aromatic aldehydes gave higher yields (**6g–6k**) than their aliphatic counterparts (**6m**). Encouraged by the results obtained with the carbonyl compounds, we next attempted the Prins spirocyclization with epoxides and acetals. Interestingly, benzaldehyde dimethyl acetal underwent smooth spiro cyclization in the presence of TMSOTf in dichloromethane at 0 °C to room temperature affording desired product **6j** in 88% yield (Table 2 entry **10**). However, styrene oxide failed to give desired product under similar conditions.

Encouraged by the above results we further extended our method to the synthesis of fluorinated spirooxindole pyrans by selective incorporation of fluorine in to pyran ring. When compound **4a** as treated with $BF_3{\bullet}OEt_2$ in dichloromethane at 0 °C to room temperature, fluoride ion from the reagent was incorporated into the product generating a C–F bond (Table 3). It is interesting to note that under similar conditions reported by Willis[22] fluorination did not happen. This was because TMSOAC was used in the literature to trap any fluoride released from BF_3 and to prevent formation of 4-fluoro compound.[27] Thus, there would not be enough fluoride ion available for the substitution reaction.

The Spiro-Prins fluorination reactions were investigated with a variety of aldehydes with compound substituted 3-allyl-3-hydroxy-1-methylindolin-2-one (**4**) to generate 4-fluoropyrans **7a–e** (Table 3). The cyclization reaction can accommodate a variety of substituted aldehydes with moderate yields.

In conclusion, we have developed an approach to construct spirooxindole pyrans with axial selectivity. The reaction is highly diastereoselective and proceeds in good yields in most cases with functional group tolerance. The method is also useful for constructing fluorinated heterocyclic spirocyclic compounds with good diasteroselectivity. This method provides direct access to the synthesis of biologically interesting spirocycles in a single-step process.

EXPERIMENTAL SECTION

All reagents and solvents were of reagent grade or were purified by standard methods before use. Column chromatography was carried out on flash silica gel (230–400 mesh). TLC analysis was conducted on silica gel plates (Silica G UV254). NMR spectra of solutions in $CDCl_3$ were recorded on at ^1H (400 MHz), ^{13}C (100 MHz) and ^{19}F

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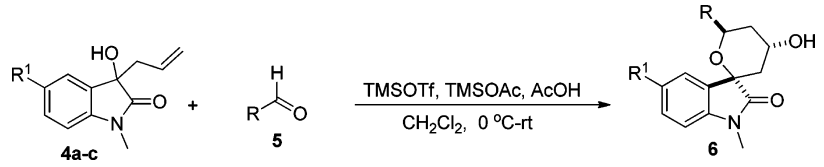
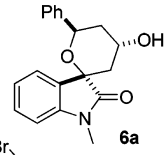
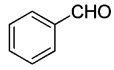
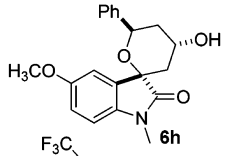
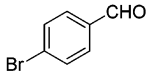
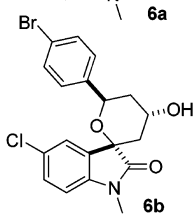
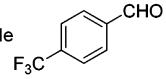
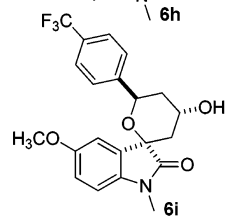
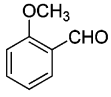
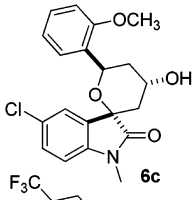
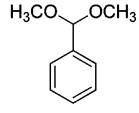
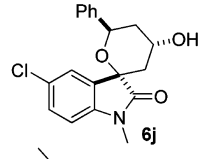
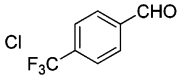
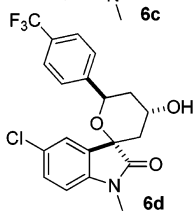
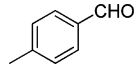
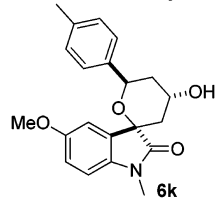
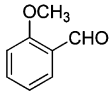
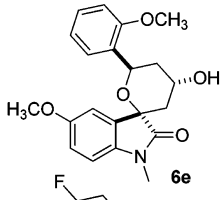
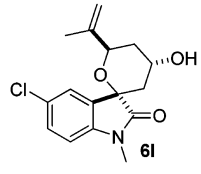
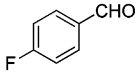
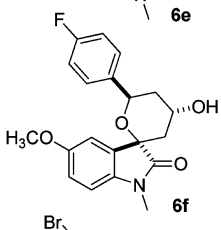
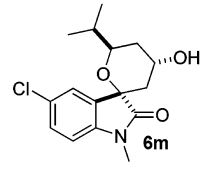
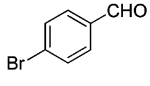
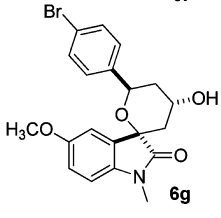
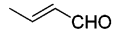
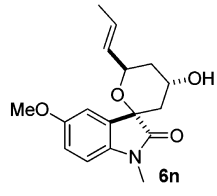
Table 2. Synthesis of Spirooxindole Pyrans



Entry	R^1	Aldehyde **5**	Product **6**	Yield	Entry	R^1	Aldehyde **5**	Product **6**	Yield[a]
1	H	PhCHO	 **6a**	81	8	OMe		 **6h**	89
2	Cl		 **6b**	84	9	OMe		 **6i**	81
3	Cl		 **6c**	79	10	Cl		 **6j**	88
4	Cl		 **6d**	78	11	OMe		 **6k**	82
5	OMe		 **6e**	71	12	Cl		 **6l**	75
6	OMe		 **6f**	82	13	Cl		 **6m**	78
7	OMe		 **6g**	91	14	OMe		 **6n**	83

[a]Yields refer to isolated yield; the compounds were characterized by NMR and mass spectrometry.

(376 MHz) NMR spectrometers. Chemical shifts (δ values) and coupling constants (J values) are given in ppm and hertz, respectively. Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane (TMS) and refer to the solvent signals (δH 7.26 and δC 77.1). Abbreviations for signal couplings are s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectrometry (HRMS) was performed using electrospray ionization (ESI) and time-of-flight (TOF) mass analysis. Infrared spectra were

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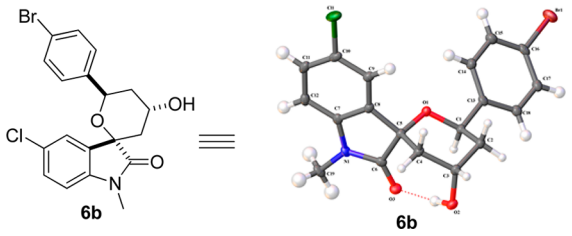
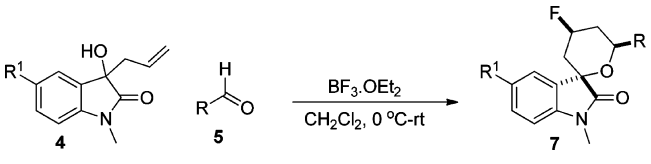
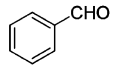
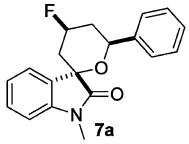
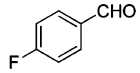
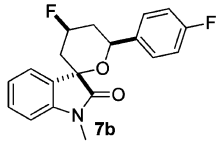
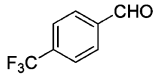
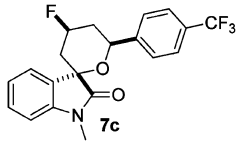
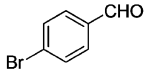
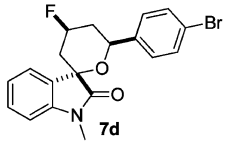
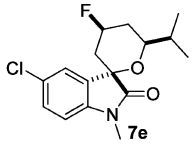


Figure 2. Thermal ellipsoid plot of **6b**, drawn at the 50% probability level.

Table 3. Substrate Scope



Entry	R^1	Aldehyde **5**	Product **7**	Yield[a]
1	H		 **7a**	73
2	H		 **7b**	76
3	H		 **7c**	72
4	H		 **7d**	71
5	Cl		 **7e**	81

[a]Yields refer to isolated yield; the compounds were characterized by NMR and mass spectrometry.

recorded on FT-IR spectrometer, data are represented as follows: frequency of absorption (cm^{-1}).

General Experimental Procedure for Allylation of *N*-Methylisatins. To a mixture of $Sc(OTf)_3$ (30 mol %) in anhydrous dichloromethane (5 mL) was added 1-methylindoline-2,3-dione (**3a**) (1.0 equiv, 0.2 mmol) in anhydrous dichloromethane (2 mL) at room temperature followed by addition of allyltrimethylsilane (3.0 equiv, 0.6 mmol). The resulting mixture was allowed to stir at the same temperature for 4–6 h. After completion of the reaction, the reaction mixture was partitioned between $NaHCO_3$ solution (5 mL) and dichloromethane (2 × 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The resulting crude product was purified by silica gel column chromatography (100–200 mesh) using an ethyl acetate/hexane gradient mixture to afford the pure product **4a**.

3-Allyl-3-hydroxy-1-methylindolin-2-one (4a).[21] (0.22 g, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 1.9 Hz, 1H), 7.33–7.28 (m, 1H), 7.11 (t, J = 1.8 Hz, 1H), 6.83 (d, J = 1.9 Hz, 1H), 5.65–5.55 (m, 1H), 5.10–5.04 (m, 2H), 4.02 (s, 1H), 3.16 (s, 3H), 2.80 (dd, J = 1.6, 3.3 Hz, 1H), 2.66 (d, J = 2.1, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 143.2, 130.6, 129.8, 129.5, 124.1, 123.0, 120.1, 108.3, 76.0, 42.8, 26.1; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{12}H_{13}NO_2$ 204.1017, found 204.1019.

3-Allyl-5-chloro-3-hydroxy-1-methylindolin-2-one (4b).[28] (0.52 g, 77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.32 (d, J = 2.1 Hz, 1H), 6.77 (d, J = 2.1 Hz, 1H), 5.69–5.58 (m, 1H), 5.15–5.11 (m, 2H), 3.47 (s, 1H), 3.17 (s, 3H), 2.77 (dd, J = 1.5, 3.3 Hz, 1H), 2.64 (dd J = 2.0, 3.3 Hz, 1H,); ^{13}C NMR (100 MHz, $CDCl_3$) δ177.6, 141.7, 131.4, 129.9, 129.4, 128.5, 124.7, 120.7, 76.0, 42.7, 26.2; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{12}H_{12}ClNO_2$ 238.0629, found 238.0632.

3-Allyl-3-hydroxy-5-methoxy-1-methylindolin-2-one (4c).[18] (0.53 g, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, J = 0.6 Hz, 1H), 6.88 (dd, J = 0.6, 2.1 Hz, 1H), 6.76 (d, J = 2.1 Hz, 1H), 5.73–5.62 (m, 1H), 5.16–5.11 (m, 2H), 3.82 (s, 1H), 3.17 (s, 3H), 3.05 (s, 1H), 2.76 (dd, J = 1.6, 3.3 Hz, 1H), 2.63 (dd, J = 2.1, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 156.3, 130.8, 130.4, 120.4, 114.1, 111.3, 108.8, 76.1, 55.8, 43.0, 26.2; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{13}H_{15}NO_3$ 234.1125, found 234.1126.

General Experimental Procedure for Spirocyclization. To a mixture of 3-allyl-3-hydroxy-1-methylindolin-2-one (**4a**) (0.25 mmol) and aldehyde/acetal (0.3 mmol) in anhydrous DCM (5 mL) was added AcOH (4.0 equiv) TMSOAc (1.2 equiv), and TMSOTf (4.0 equiv, dropwise) at 0 °C. The resulting mixture was warmed to room temperature and allowed to stir at the same temperature for 2 h. After completion of the reaction, saturated $NaHCO_3$ solution (5 mL) was added to the reaction mixture and stirred for 10 min at room temperature, which was extracted with dichloromethane (2 × 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The resulting crude product was purified by silica gel column chromatography (100–200 mesh) using an ethyl acetate/hexane gradient mixture to afford the pure product **6a** (Table 2, entry 1).

4′-Hydroxy-1-methyl-6′-phenyl-3′,4′,5′,6′-tetrahydrospiro-[indoline-3,2′-pyran]-2-one (6a). Colorless oil (39 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.35 (m, 3H), 7.33–7.27 (m, 3H), 7.26–7.24 (m, 1H), 7.18–7.14 (m, 1H), 6.83 (d, J = 1.9 Hz, 1H), 5.89 (d, J = 2.9 Hz, 1H), 5.83 (dd, J = 7.0, 3.0 Hz, 1H), 4.38 (dt, J = 7.0, 1.5 Hz, 1H), 3.21 (s, 3H), 2.35 (dd, J = 9.0, 3.7 Hz, 1H), 2.19 (dq, J = 7.0, 1.3 Hz, 1H), 2.06–1.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 143.1, 141.8, 130.0, 129.9, 128.4, 127.7, 126.2, 123.7, 123.2, 108.2, 77.3, 63.4, 43.1, 40.0, 25.8; IR (neat) ν_{max} (neat)/cm^{-1} 3377, 2927, 1715, 1610, 1489, 1364, 1245, 1043, 821, 808; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{19}H_{19}NO_3$ 310.1438, found 310.1437.

6′-(4-Bromophenyl)-5-chloro-4′-hydroxy-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6b). White solid (47 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 2.1 Hz, 2H), 7.37 (d, J = 5.0 Hz, 1H), 7.35 (dd, J = 0.5, 2.1 Hz, 1H), 7.24 (d, J = 2.1 Hz, 2H), 5.75 (dd, J = 0.4, 3.0 Hz, 1H), 5.70 (d, J = 3.0 Hz, 1H), 4.34 (dt, J = 0.8, 1.5 Hz, 1H), 3.20 (s, 3H), 2.27 (dd, 0.8, 3.4 Hz, 1H), 2.18 (dd, J = 0.4, 3.4 Hz, 1H), 2.06–1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 141.3, 140.7, 131.8, 131.5, 130.2, 129.4, 127.8, 124.5, 121.5, 109.8, 68.6, 64.3, 40.7, 35.1, 26.3; IR (neat) ν_{max} (neat)/cm^{-1} 3375, 1715, 1601, 1469, 1354, 1053, 845; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{19}H_{17}BrClNNaO_3$ 443.9994, found 443.9978.

5-Chloro-4′-hydroxy-6′-(2-methoxyphenyl)-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6c). White solid (38 mg, 79%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 1.9 Hz, 1H), 7.40 (s, 1H), 7.33 (d, J = 2.1 Hz, 1H), 7.23 (t, J = 1.9 Hz, 1H), 6.96 (t, J = 1.9 Hz, 1H), 6.86 (d, J = 2.0 Hz, 1H), 6.75 (d, J = 2.0 Hz, 1H), 6.20 (d, J = 2.9 Hz, 1H), 5.70 (d, J = 2.9 Hz, 1H), 4.34 (d, J = 2.9 Hz, 1H), 3.84 (s, 3H), 3.18 (s, 3H), 2.30–2.24 (m, 2H), 2.06 (t, J = 2.9 Hz, 1H), 1.89–1.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ177.8, 155.8, 141.4, 132.2, 130.3, 130.0, 129.2, 128.3, 126.1,

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124.5, 120.6, 110.2, 109.7, 77.3, 64.6, 63.5, 55.3, 39.2, 35.4, 26.3; IR (neat) ν_{max} (neat)/cm^{-1} 3379, 1720, 1618, 1445, 1354, 1203, 1033, 843; HRMS (ESI-TOF) m/z calcd for $[M + Na]^+$ $C_{20}H_{20}ClNNaO_4$ 396.0966, found 396.0979.

5-Chloro-4′-hydroxy-1-methyl-6′-(4-(trifluoromethyl)-phenyl)-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6d). White solid (51 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 2.0 Hz, 2H), 7.51 (d, J = 2.0 Hz, 2H), 7.39 (d, J = 5.0 Hz, 1H), 7.36 (dd, J = 5.0, 2.0 Hz, 1H), 6.78 (d, J = 2.1 Hz, 1H), 5.86 (d, J = 3.0 Hz, 1H), 5.72 (d, 2.9 Hz, 1H), 4.37 (dt, J = 0.7, 1.5 Hz, 1H), 3.21 (s, 3H), 2.30 (dd, J = 1.0, 3.5 Hz, 1H), 2.23 (dd, J = 0.7, 3.5 Hz, 1H), 2.07−2.03 (m, 1H), 1.99−1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 145.7, 141.4, 131.7, 130.3, 130.0, 129.4, 126.3, 125.4, 125.5, 109.9, 68.7, 642, 40.7, 35.1, 26.4; IR (neat) ν_{max} (neat)/cm^{-1} 3367, 1710, 1611, 1377, 1235, 1033, 990; HRMS (ESI-TOF) m/z calcd for $[M + Na]^+$ $C_{20}H_{17}ClF_3NNaO_3$ 434.0736, found 434.0747.

4′-Hydroxy-5-methoxy-6′-(2-methoxyphenyl)-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6e). Colorless oil (38 mg, 71%): IR (neat) ν_{max} (neat)/cm^{-1} 3365, 2929, 1725, 1489, 1354, 1245, 912; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 0.4, 1.9 Hz, 1H), 7.24−7.19 (m, 1H), 7.03 (d, J = 0.6 Hz, 1H), 6.94 (t, J = 1.9 Hz, 1H), 6.87−6.83 (m, 2H), 6.73 (d, J = 2.1 Hz, 1H), 6.22 (dd, J = 0.4, 2.9 Hz, 1H), 5.93 (d, J = 2.9 Hz, 1H), 4.32 (dt, J = 0.7, 1.5, 2.9 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.18 (s, 3H), 2.31−2.24 (m, 2H), 2.04−1.999 (m, 1H), 1.88−1.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 156.9, 155.9, 136.2, 132.0, 130.7, 128.1, 126.2, 120.5, 114.0, 111.4, 110.2, 109.0, 77.6, 77.2, 64.7, 63.4, 55.9, 55.3, 39.4, 35.6, 26.2.; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{23}NNaO_5$ 392.1478, found 392.1474.

6′-(4-Fluorophenyl)-4′-hydroxy-5-methoxy-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6f). Colorless oil (39 mg, 82%): IR (neat) ν_{max} (neat)/cm^{-1} 3365, 2929, 1716, 1610, 1489, 1364, 1245, 1043; ^{1}H NMR ($CDCl_3$) δ 7.38−7.34 (m, 2H), 7.03−6.99 (m, 3H), 6.87 (dd, J = 0.6, 2.1 Hz, 1H), 6.74 (d, J = 2.2 Hz, 1H), 5.94 (d, J = 2.8 Hz, 1H), 5.80 (d, J = 2.8 Hz, 1H), 4.35 (dt, J = 0.7, 1.5, 2.8 Hz, 1H), 3.84 (s, 3H), 3.19 (s, 3H), 2.28 (dd, J = 0.9, 3.5 Hz, 1H), 2.18 (dd, J = 0.6, 3.5 Hz, 1H), 2.04−1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 157.0, 137.8, 136.1, 131.5, 127.9, 115.3, 115.1, 114.2, 111.5, 109.2, 77.3, 68.6, 64.4, 55.9, 40.9, 35.4, 26.3; HRMS (ESI-TOF) m/z calcd for $[M + Na]^+$ $C_{20}H_{20}FNNaO_4$ 380.1261, found 380.1274.

6′-(4-Bromophenyl)-4′-hydroxy-5-methoxy-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6g). White solid (52 mg, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 2.1 Hz, 2H), 7.25 (d, J = 2.1 Hz, 2H), 6.99 (d, J = 0.7 Hz, 1H), 6.88 (dd, J = 0.6, 2.1 Hz, 1H), 6.75 (d, J = 2.1 Hz, 1H), 5.94 (d, J = 2.9 Hz, 1H), 5.79 (dd, J = 0.4, 2.9 Hz, 1H), 4.36 (dt, J = 0.6, 1.5, 2.9 Hz, 1H), 3.84 (s, 3H), 3.19 (s, 3H), 2.27 (dd, J = 0.9, 3.5 Hz, 1H), 2.18 (dd, J = 0.6, 3.7 Hz, 1H), 2.04−1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 157.0, 141.1, 136.1, 131.5, 127.8, 121.3, 114.2, 111.5, 109.2, 77.6, 68.5, 64.4, 55.9, 40.8, 35.3, 26.3; IR (neat) ν_{max} (neat)/cm^{-1} 3362,, 1714, 1609, 1479, 1354, 1246; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{20}BrNO_4$ 418.0648, found 418.0649.

4′-Hydroxy-5-methoxy-1-methyl-6′-phenyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6h). White solid (41 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 1.8 Hz, 2H), 7.35 (t, J = 1.8 Hz, 2H), 7.25 (d, J = 1.8 Hz, 1H), 7.01 (d, J = 0.6 Hz, 1H), 6.86 (dd, J = 0.6, 2.1 Hz, 1H), 6.73 (d, J = 2.1 Hz, 1H), 5.96 (d, J = 2.9 Hz, 1H), 5.82 (dd, J = 0.5, 2.9 Hz), 4.35 (dt, J = 0.8, 1.6, 2.9 Hz, 1H), 3.84 (s, 3H), 3.18 (s, 3H), 2.29 (dd, 1.0, 3.4 Hz, 1H), 2.21 (dd, J = 0.5, 3.4 Hz, 1H), 2.06−1.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 156.9, 142.0, 136.1, 131.7, 128.4, 127.6, 126.1, 114.1, 111.5, 109.1, 77.3, 69.1, 64.5, 55.9, 40.9, 35.4, 26.2; IR (neat) ν_{max} (neat)/cm^{-1} 3367, 1721, 1609, 1494, 1255, 1043 HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{21}NNaO_4$ 362.1368, found 362.1368.

4′-Hydroxy-5-methoxy-1-methyl-6′-(4-(trifluorom-ethyl)-phenyl)-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6i). White solid (39 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 2.0 Hz, 2H), 7.51 (d, J = 2.0 Hz, 2H), 7.01 (d, J = 0.6 Hz, 1H), 6.88 (dd, J = 0.6, 2.0 Hz, 1H), 6.76 (d, J = 2.1 Hz, 1H), 5.96 (d, J = 2.9 Hz, 1H), 5.89 (d, J = 2.9 Hz, 1H), 4.37 (dt, J = 0.8, 1.6, 2.9 Hz, 1H), 3.85 (s, 3H), 3.20 (s, 3H), 2.31 (dd, J = 1.0, 3.5 Hz, 1H), 2.23 (dd, J = 0.5, 3.5 Hz, 1H), 2.03−1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 168.1, 157.0, 146.0, 136.1, 131.4, 126.3, 125.3, 114.2, 111.5, 109.3, 77.3, 68.6, 64.3, 55.9, 40.9, 35.3, 26.3; IR (neat) ν_{max} (neat)/cm^{-1} 3355, 2919, 1716, 1610, 1479, 1235, 1043; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{20}F_3NNaO_4$ 430.1229, found 430.1231.

5-Chloro-4′-hydroxy-1-methyl-6′-phenyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6j). White solid (31 mg, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.27 (m, 7H), 6.76 (d, J = 2.1 Hz, 1H), 5.80 (dd, J = 0.5, 2.9 Hz, 1H), 5.73 (d, J = 2.9 Hz, 1H), 4.37 (dt, J = 0.8, 1.6, 2.9 Hz, 1H), 3.20 (s, 3H), 2.30 (dd, J = 1.0, 3.7 Hz, 1H), 2.22−2.17 (m, 1H), 2.07−2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 141.6, 141.4, 132.0, 130.1, 129.3, 128.5, 127.8, 126.1, 124.6, 109.7, 69.2, 64.4, 40.7, 35.2, 26.3; IR (neat) ν_{max} (neat)/cm^{-1} 3365, 2929, 1716, 1610, 1489, 1364, 1245, 1043; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{19}H_{18}ClNO_3$ 344.1046, found 344.1048.

4′-Hydroxy-5-methoxy-1-methyl-6′-(p-tolyl)-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6k). Yellow solid (39 mg, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 1.9 Hz, 2H), 7.15 (d, J = 1.9 Hz, 2H), 7.00 (d, J = 0.6 Hz, 1H), 6.86 (dd, J = 0.6, 2.1 Hz, 1H), 6.73 (d, J = 2.1 H, 1H z), 5.98 (d, J = 2.9 Hz, 1H), 5.78 (dd, 1H, J = 0.2, 3.0 Hz), 4.36 (dd, J = 0.7, 2.0 Hz, 1H), 3.84 (s, 3H), 3.18 (s, 3H), 2.44 (s, 3H), 2.32 (dd, J = 0.2, 3.6 Hz, 1H), 2.19−2.15 (m, 1H), 2.04−2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 156.9, 139.0, 137.3, 136.1, 131.8, 129.0, 126.1, 114.1, 111.4, 109.1, 77.6, 69.0, 64.6, 55.9, 40.8, 35.4, 26.2, 21.1; IR (neat) ν_{max} (neat)/cm^{-1} 3366, 2931, 1721, 1609, 1364, 1043; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{23}NO_4$ 354.1700. Found 354.1702.

5-Chloro-4′-hydroxy-1-methyl-6′-(prop-1-en-2-yl)-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6l). White solid (32 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 5.0 Hz, 0.5H), 7.29 (d, J = 5.0 Hz, 0.5H), 7.28 (d, J = 5.0 Hz, 1H), 7.26 (s, 1H), 6.72 (d, J = 2.1 Hz, 1H), 5.56 (d, J = 2.9 Hz, 1H), 5.14 (d, J = 2.6 Hz, 1H), 5.01 (t, J = 4.0 Hz, 1H), 4.86 (t, J = 4.0 Hz, 1H), 4.29 (dt, J = 8.0, 16.0 Hz, 1H), 3.17 (s, 3H), 2.15 (dd, J = 9.0, 3.7 Hz, 1H), 2.01 (dq, J = 6.0, 14.0 Hz, 1H), 1.95 (dt, J = 6.0, 3.7 Hz, 1H), 1.85−1.77 (m, 1H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 144.7, 141.3, 132.1, 130.0, 129.2, 124.5, 111.8, 109.7, 77.2, 70.1, 64.2, 37.0, 35.4, 26.3, 18.2; IR (neat) ν_{max} (neat)/cm^{-1} 3366, 2929, 1719, 1601, 1245, 1043; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{16}H_{18}ClNO_3$ 308.1048, found 308.1049.

(2′*S*,4′*S*,6′*R*)-5-Chloro-4′-hydroxy-6′-isopropyl-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6m). White solid (31 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) 7.32 (dd, J = 0.6, 2.1 Hz, 1H), 7.25 (d, J = 0.6 Hz, 1H), 6.76 (d, J = 2.1 Hz, 1H), 5.46 (d, J = 2.9 Hz, 1H), 4.49−4.44 (m, 1H), 4.29 (m, 1H), 3.19 (s, 3H), 2.11 (dd, J = 1.0, 3.8 Hz, 1H), 1.95−1.88 (m, 2H), 1.76−1.65 (m, 2H), 0.92 (dd, J = 0.3, 1.7 Hz, 6H); ^{3}C NMR (100 MHz, $CDCl_3$) δ 178.2, 141.2, 132.6, 129.8, 129.1, 124.4, 109.6, 76.8, 71.0, 64.2, 35.8, 33.9, 32.6, 26.3, 18.2, 17.4.; IR (neat) ν_{max} (neat)/cm^{-1} 3350, 2931, 1721, 1609, 1365, 1255, 1043; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{16}H_{20}ClNO_3$ 310.1204, found 310.1196.

(*E*)-5-Chloro-4′-hydroxy-1-methyl-6′-(prop-1-en-1-yl)-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (6n). Pale yellow oil (36 mg, 83%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 5.0 Hz, 1H), 7.29 (d, J = 5.0 Hz, 1H), 6.74−6.72 (m, 1H), 5.82−5.73 (m, 1H), 5.60 (d, J = 2.9 Hz, 1H), 5.49−5.43 (m, 1H), 5.16 (dd, J = 1.9, 2.5 Hz, 1H), 4.27 (dd, J = 0.8, 2.4 Hz, 1H), 3.18 (s, 3H), 2.16 (dd, J = 1.0, 36.0 Hz, 1H), 2.01 (dq, J = 0.6, 1.4, 37.0 Hz, 1H), 1.94 (dt, J = 0.6, 1.1, 37.0 Hz, 1H), 1.82−1.75 (m, 1H), 1.69 (dd, J = 0.3, 1.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 141.3, 132.0, 130.9, 130.0, 129.3, 129.1, 124.6, 109.7, 77.0, 68.2, 64.1, 38.4, 35.1, 26.3, 17.8; IR (neat) ν_{max} (neat)/cm^{-1} 3365, 2895, 1719, 1607, 1489, 1364, 1245, 1073; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{16}H_{18}ClNO_3$ 308.1046, found 308.1048.

General Experimental Procedure for Fluoro Pyran. To a mixture of 3-allyl-3-hydroxy-1-methylindolin-2-one (**4a**) (0.25 mmol) and benzaldehyde (0.3 mmol) in anhydrous DCM (5 mL) was added $BF_3{\bullet}OEt_2$ (1.5 equiv) at 0 °C. The resulting mixture was warmed to

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room temperature and allowed to stir at the same temperature for 4 h. After completion of the reaction, the reaction mixture was partitioned between sat. $NaHCO_3$ solution (5 mL) and dichloromethane (2 × 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The resulting crude product was purified by silica gel column chromatography (100−200 mesh) using an ethyl acetate/hexane gradient mixture to afford the pure product **7a** (Table 3, entry 1).

4′-Fluoro-1-methyl-6′-phenyl-3′,4′,5′,6′-tetrahydrospiro-[indoline-3,2′-pyran]-2-one (7a). Colorless oil (28 mg, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.40 (m, 3H), 7.36−7.33 (m, 3H), 7.30 (d, J = 2.0 Hz, 1H), 7.16 (t, J = 1.9 Hz, 1H), 6.82 (d, J = 2.0 Hz, 1H), 5.87−5.79 (m, 0.5H), 5.74−5.66 (m, 1.5H), 3.17 (s, 3H), 2.57−2.52 (m, 1H), 2.33−2.30 (m, 1H), 2.19−2.10 (m, 1H), 1.99−1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 143.1, 141.9, 130.2, 129.4, 128.4, 127.9, 126.2, 123.8, 123.3, 108.4, 86.4, 84.7, 77.6, 72.8, 72.6, 40.5, 40.3, 37.4, 37.2, 25.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.3; IR (neat) ν_{max} (neat)/cm^{-1} 3050, 2913, 1719, 1615, 1471, 1369, 985, 750; HRMS (ESI-TOF) m/z [M + H]$^+$calcd for $C_{19}H_{18}FNO_2$ 312.1394, found 312.1392.

4′-Fluoro-6′-(4-fluorophenyl)-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (7b). Colorless oil (42 mg, 76%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 1.7 Hz, 1H), 7.41−7.33 (m, 3H), 7.16−7.13 (m, 1H), 7.05−7.00 (m, 2H), 6.82 (d, J = 2.0 Hz, 1H), 5.84−5.76 (m, 0.5H), 5.70−5.65 (m, 1.5H), 3.18 (s, 3H), 2.54−2.48 (m, 1H), 2.33−2.28 (m,1H), 2.28−2.06 (m, 1H), 1.94−1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 143.1, 137.0, 130.2, 129.2, 128.0, 127.9, 123.7, 123.4, 115.4, 115.2, 108.4, 86.3, 84.5, 77.6, 72.1, 72.0, 53.4, 40.5, 40.3, 37.4, 37.2, 25.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.3, −173.4; IR (neat) ν_{max} (neat)/cm^{-1} 3031, 2961, 1710, 1608, 1478, 1345, 1135; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{19}H_{17}F_2NO_2$ 330.1301, found 330.1300.

4′-Fluoro-1-methyl-6′-(4-(trifluoromethyl)phenyl)-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (7c). Colorless oil (38 mg, 73%). 2923, 1720, 1476, 1345, 1075, 754; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 2.1 Hz, 2H), 7.53 (d, J = 2.1 Hz, 2H), 7.45−7.43 (m, 1H), 7.40−7.35 (m, 1H), 7.18−7.14 (m, 1H), 6.84 (d, J = 2.0 Hz, 1H), 5.87−5.77 (m, 1.5H), 5.75−5.71 (m, 0.5H), 3.18 (s, 3H), 2.59−2.54 (m, 1H), 2.35−2.31 (m, 1H), 2.20−2.11 (m, 1H), 1.90−1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 145.1, 143.1, 130.3, 129.0, 126.4, 125.4, 123.7, 123.4, 108.5, 86.1, 84.4, 77.6, 72.0, 71.9, 50.3, 40.2, 37.3, 37.2, 25.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.58, 173.6; ; IR (neat) ν_{max} (neat)/cm^{-1} 2923, 1720, 1476, 1345, 1075, 754; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{20}H_{17}F_4NO_2$ 379.1179, found 379.1181.

6′-(4-Bromophenyl)-4′-fluoro-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (7d). Colorless oil (42 mg, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.41 (m, 3H), 7.38−7.34 (m, 1H), 7.28 (d, J = 0.7 Hz, 2H), 7.26−7.13 (m, 1H), 6.83 (d, J = 1.9 Hz, 1H), 5.84−5.76 (m, 0.5H), 5.72−5.64 (m, 1.5H), 3.18 (s, 3H), 2.54−2.49 (m, 1H), 2.33−2.27 (m, 1H), 2.17−2.06 (m, 1H), 1.91−1.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 143.1, 140.2, 131.5, 130.3, 129.1, 127.9, 123.7, 123.4, 121.7, 108.4, 86.2, 84.4, 77.6, 72.0, 71.9, 40.4, 40.2, 37.4, 37.2, 25.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.5; IR (neat) ν_{max} (neat)/cm^{-1} 3032, 2964, 1715, 1620, 1461, 1366, 751; HRMS (ESI-TOF) m/z [M +H]$^+$ calcd for $C_{19}H_{17}BrFNO_2$ 390.0419, found 390.0421.

(2′*R*,4′*S*,6′*S*)-5-Chloro-4′-fluoro-6′-isopropyl-1-methyl-3′,4′,5′,6′-tetrahydrospiro[indoline-3,2′-pyran]-2-one (7e). White solid (38 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.28 (m, 2H), 6.74 (d, J = 2.0 Hz, 1H), 5.64−5.55 (m, 0.5H), 5.51−5.43 (m, 0.5H), 4.41 (dd, J = 1.4, 2.9 Hz, 1H), 3.15 (s, 3H), 2.30−2.25 (m, 1H), 2.19−2.15 (m, 1H), 1.95−1.86 (m, 1H), 1.80−1.74 (m, 1H), 1.60−1.52 (m, 1H), 0.92 (t, J = 1.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 141.5, 131.4, 129.8, 128.6, 124.3, 109.3, 86.8, 85.1, 75.3, 37.8, 37.6, 34.1, 34.0, 32.5, 25.9, 18.2, 17.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.0; IR (neat) ν_{max} (neat)/cm^{-1} 2930, 1710, 1615, 1461, 1325, 1092, 751; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{16}H_{19}ClFNO_2$ 312.1161, found 312.1160.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra and crystallographic information on compounds **6b** and **6g**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00249.

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Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Wang, Q.; Lian, Z.; Xu, Q.; Shi, M. *Adv. Synth. Catal.* **2013**, *355*, 3344.

(2) Zhu, B.; Zhang, W.; Lee, R.; Han, Z.; Yang, W.; Tan, D.; Huang, K.-W.; Jiang, Z. *Angew. Chem., Int. Ed.* **2013**, *52*, 6666.

(3) Hanhan, N. V.; Ball-Jones, N. R.; Tran, N. T.; Franz, A. K. *Angew. Chem., Int. Ed.* **2012**, *51*, 989.

(4) Cheng, D.; Ishihara, Y.; Tan, B.; Barbas, C. F. *ACS Catal.* **2014**, *4*, 743.

(5) Lin, H.; Danishefsky, S. J. *Angew. Chem.* **2003**, *115*, 38.

(6) Ding, K.; Lu, Y.; Nikolovska-Coleska, Z.; Qiu, S.; Ding, Y.; Gao, W.; Stuckey, J.; Krajewski, K.; Roller, P. P.; Tomita, Y.; Parrish, D. A.; Deschamps, J. R.; Wang, S. *J. Am. Chem. Soc.* **2005**, *127*, 10130.

(7) Dollings, P. J. D., Donnell A. F.; Gilbert, A. M.; Zhang, M.; Harrison, B. L.; Stanton, C. J.; O'Neil, S. V.; Havran, L. M.; Chong, D. C. 2010, WO2010077839.

(8) Liu, Z.; Lu, R. In *The Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, 1988; Vol. 33, pp 83.

(9) M. Pastor, I.; Yus, M. *Curr. Org. Chem.* **2012**, *16*, 1277.

(10) Olier, C.; Kaafarani, M.; Gastaldi, S.; Bertrand, M. P. *Tetrahedron* **2010**, *66*, 413.

(11) Hojo, D.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 5820.

(12) Wang, H.; Guo, L.-N.; Duan, X.-H. *Org. Lett.* **2013**, *15*, 5254.

(13) Xiao, Z.; Yu, C.; Li, T.; Wang, X.-S.; Yao, C. *Org. Lett.* **2014**, *16*, 3632.

(14) Wang, J.; Crane, E. A.; Scheidt, K. A. *Org. Lett.* **2011**, *13*, 3086.

(15) Castaldi, M. P.; Troast, D. M.; Porco, J. A. *Org. Lett.* **2009**, *11*, 3362.

(16) Damera, K.; Ke, B.; Wang, K.; Dai, C.; Wang, L.; Wang, B. *RSC Adv.* **2012**, *2*, 9403.

(17) Trost, B. M.; Zhang, Y. *J. Am. Chem. Soc.* **2007**, *129*, 14548.

(18) Cao, Z.-Y.; Zhang, Y.; Ji, C.-B.; Zhou, J. *Org. Lett.* **2011**, *13*, 6398.

(19) Wang, T.; Hao, X.-Q.; Huang, J.-J.; Wang, K.; Gong, J.-F.; Song, M.-P. *Organometallics* **2013**, *33*, 194.

(20) Meshram, H. M.; Ramesh, P.; Reddy, B. C.; Kumar, G. S. *Chem. Lett.* **2011**, *40*, 357.

(21) Hanhan, N. V.; Tang, Y. C.; Tran, N. T.; Franz, A. K. *Org. Lett.* **2012**, *14*, 2218.

(22) Crosby, S. R.; Harding, J. R.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2002**, *4*, 577.

(23) Jasti, R.; Vitale, J.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2004**, *126*, 9904.

(24) Launay, G. G.; Slawin, A. M. Z.; O'Hagan, D. *Beilstein J. Org. Chem.* **2010**, *6*, 41.

(25) Jaber, J. J.; Mitsui, K.; Rychnovsky, S. D. *J. Org. Chem.* **2001**, *66*, 4679.

(26) Supplementary crystallographic data (CIF file) and ORTEP diagram for compound **6b** and **6g** are provided in the Supporting Information.

DOI: 10.1021/acs.joc.5b00249
J. Org. Chem. 2015, 80, 5457−5463

(27) Al-Mutairi, E. H.; Crosby, S. R.; Darzi, J.; Harding, J. R.; Hughes, R. A.; King, C. D.; Simpson, T. J.; Smith, R. W.; Willis, C. L. *Chem. Commun.* **2001**, 835.
(28) Qiao, X.-C.; Zhu, S.-F.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2009**, *20*, 1254.

DOI: 10.1021/acs.joc.5b00249
J. Org. Chem. 2015, 80, 5457−5463