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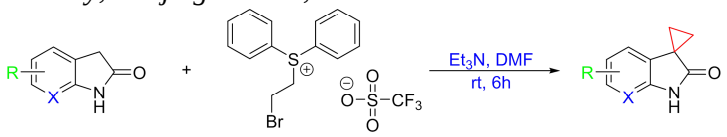

R=H, F, Cl , Br, NO_2
X=C, N

22 examples good yield

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A convenient cyclopropanation process of oxindoles via bromoethylsulfonium salt

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ABSTRACT

A practical convenient conversion of oxindoles into the corresponding spirocyclopropyl oxindoles is achieved efficiently using bromoethylsulfonium salt, which is easily prepared on a large scale and is stable crystalline. This reaction of bromoethylsulfonium salt with different substituted unprotected oxindoles proceeded under mild condition and provided moderate yields.

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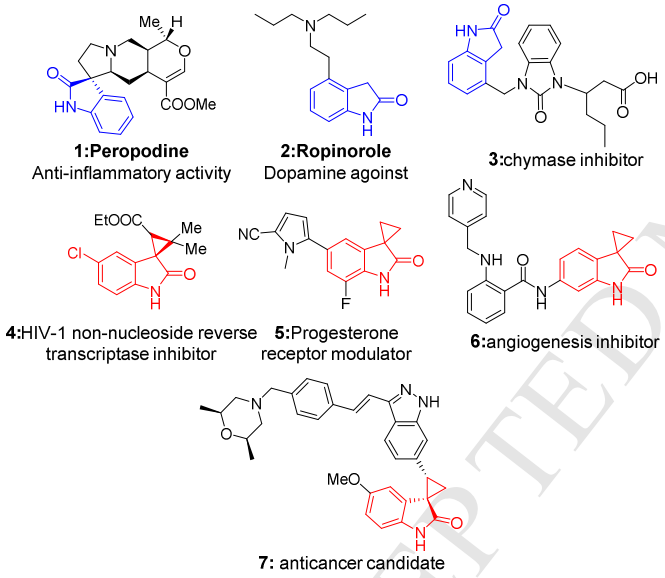
1. Introduction

Oxindole scaffold is prevalent heterocyclic motif in numerous naturally occurring products, marketed pharmaceuticals and agrochemicals, which exhibit all kinds of biological activities, such as anti-inflammatory activity,[1] receptor agonists,[2] protease inhibitors (Scheme 1).[3] Particularly, spirooxindoles are regarded as "privileged structures" owing to their excellent binding ability to many receptors,[4] in which spirocyclopropyl oxindoles (Scheme 1) are significant because such structures in drug discovery and design can introduce potentially favorable conformational rigidity with reasonable addition of molecular weight and lipophilicity. Through the construciton of spiro-ring system, spirocyclopropyl oxindoles integrate two important pharmacophores, quaternary oxindoles[5] and three-membered cyclopropanes,[6] both of which often exist in numerous bioactive compounds showing a broad spectrum of pharmacological activities. As a result, conformational restrained spirocyclopropyl oxindole derivatives usually exhibit remarkable bioactivities.[7] For instance, compound **4** showed nanomolar level biological activity as HIV-1 nonnucleoside reverse transcriptase inhibitors; compound **5** and compound **6** were found to be a progesterone receptor modulator and an angiogenesis inhibitor; in addition, compound of formula **7** displayed an extraordinary anticancer activity in nanomolar level.

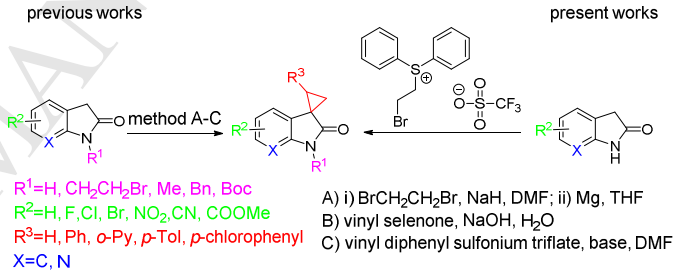


Scheme 1. Bioactive oxindoles and spirocyclopropyl oxindoles

Furthermore, the Carrera's group has developed a new methodology for the synthesis of spiro[pyrrolidin-3,3'-oxindoles] with aldimines via catalytic [3+2] ring-expansion reaction.[4b, 8] The group of Jian Zhou has found that the [3+2] annulation reaction of spirocyclopropyl oxindole to provide spiro[furan-3,3'-indolin]-2-one.[9] As above, the potential of spirocyclopropyl oxindoles in the related reactions would be fully significant. Although different cyclopropanation strategies of oxindole[10] could be provided in the reported literatures, the development of a moderate and convenient method for the direct conversion of unprotected oxindole into the corresponding spirocyclopropyl oxindoles remains to be a significant challenge in organic chemistry. The most notable methods for the preparation of spirocyclopropyl oxindoles directly from indoles are as follows: 1) cyclopropanation of unprotected indoles with 1,2-dibromoethane under strongly alkaline conditions, then deprotection of N-substituted spirocyclopropyl oxindoles with metal Mg (Scheme 2a);[11] 2) N-substituted spirocyclopropyl oxindoles could be synthesized via using vinyl selenone in aqueous basic medium with cetyltrimethyl ammonium bromide (CTAB);[10f] 3) cyclopropanation of indoles with vinyl diphenyl sulfonium triflate catalyzed by zinc triflate in organic alkaline solvents.[10h]

On the other hand, Vinylsulfonium salts[12] are widely used as a cyclization reagent in chemical synthesis. For instance, first vinylsulfonium salts are reported as a cyclopropanation reagent in 1966 from the Gosselck's group;[12a] Lin's team has reported a general access to 1,1-cyclopropane aminoketones via the tandem reaction of a-amino aryl ketones with vinylsulfonium salts in 2012.[12b] In addition, Huang's research group has explored a new strategy for access to hydroindol-5-ones containing a methylthio group via [3+2] annulation of prop-2-ynylsulfonium salts.[13]

As noted above, methods of oxindoles cyclopropanation from reported literatures still have many limitations. For example, the above-mentioned first method usually requires two synthetic steps with an overall poor yield; while application of the second method often need to protect oxindole nitrogen as well as other acidic functional groups, with unprotected oxindoles, over-alkylation on the nitrogen is a common side reaction; despite the third method above, which has been developed and reported by Qian's group in 2017, is highly effective for a series of different substituted oxindoles, it suffers from the need to prepare and isolate the sensitive, oily vinyl sulfonium salt-an especially challenging problem on a large scale.

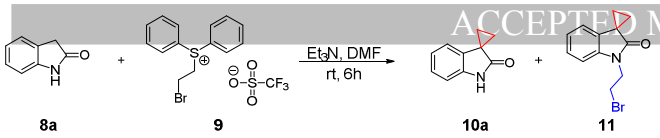


Scheme 2. Different strategies for cyclopropanation of indoles to acquire spirocyclopropyl oxindoles.

Hence, in present work our research team describe that in fact this cyclopropanation chemistry can be conducted without $Zn(OTf)_2$, which is expensive reagent and is easy to pollute the environment, and with the stable crystalline bromoethylsulfonium salt[14] as reaction substrate, which is easily prepared on a large scale. This cyclopropanation reaction is a more convenient and efficient process and has good yields for preparing spirocyclopropyl oxindoles.

2. Results/Discussion

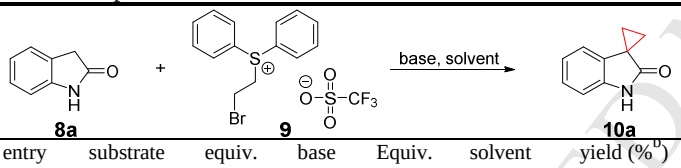
We began our experiment by examining the reaction of oxindole (**8a**) and bromoethylsulfonium salt (**9**) under organic base DBU in DMF solvent. We were pleased to find that the reaction was carried out for stirring 6 h at room temperature under air, the desired product, spiro[cyclopropane-1,3'-indoline]-2'-one (**10a**), was acquired in 57% yield (Table 1, entry 1). The structure of **10a** was confirmed with ^{1}H and ^{13}C NMR spectroscopic analysis, while molecular weight of compound **10a** was deduced via HR-ESI-MS. In addition, by-product, 1'-(2-bromoethyl) spiro[cyclopropane-1,3'-indolune]-2'-one (**11**) was obtained in 35% yield, the structure of which was verified by ^{1}H and ^{13}C NMR spectroscopic analysis and molecular weight of which was determined via HR-ESI-MS.



Scheme 3. Cyclopropanation of unprotected oxindole (**8a**).

Inspired by this result, we first started to optimize the reaction conditions by screening a series of solvents and bases, containing THF, DCM, triethylamine (Et_3N) and sodium hydride (NaH) (Table 1, entries 2-5). We found that the best results, providing compound **10a** in 75% yield was obtained under organic base Et_3N in DMF solvent (Table 1, entry 3), meanwhile, compound **11** was obtained in 23% yield. In addition, we could separate compound **11** in 28%, 26% and 22% yield under inorganic base NaH in DMF solvent, organic base Et_3N in DCM solvent and organic base Et_3N in THF solvent. In order to improve yield of compound **10a**, the reaction condition was further optimized by adjusting the amount of the Et_3N and bromoethylsulfonium salt, for example, 2.0 equivalents bromoethylsulfonium salt produced **10a** in 77% yield (Table 1, entries 6-9), but there was no significant difference. Based on the above results, it was found that 1.5 equivalents bromoethylsulfonium under 3.0 equivalents Et_3N in DMF solvent was the most suitable reaction condition.

Table 1. Optimization of the reaction conditions with **8a**[a]



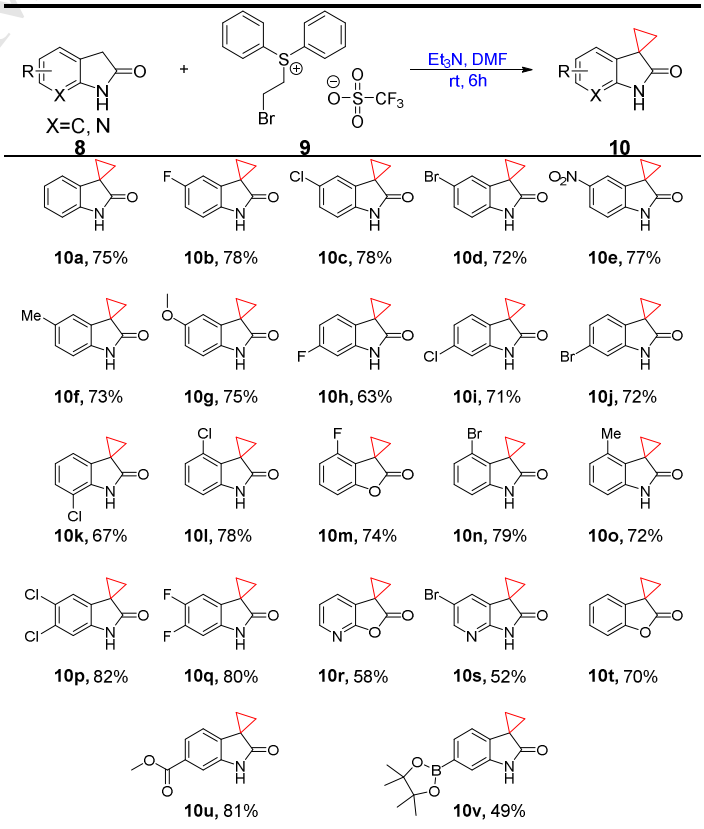
entry	substrate	equiv.	base	Equiv.	solvent	yield (%[b])
1	9	1.5	DBU	3.0	DMF	57
2	9	1.5	NaH	3.0	DMF	41
3	9	1.5	Et_3N	3.0	DMF	75
4	9	1.5	Et_3N	3.0	DCM	36
5	9	1.5	Et_3N	3.0	THF	65
6	9	1.2	Et_3N	3.0	DMF	72
7	9	2.0	Et_3N	3.0	DMF	77
8	9	1.5	Et_3N	1.5	DMF	43
9	9	1.5	Et_3N	6.0	DMF	68

[a] Reaction conditions: 8a (0.2 mmol), with indicated amount of base and additive, 2 mL solvent, at room temperature, under air, stirring for 6 h.

[b] Isolated yields are shown.

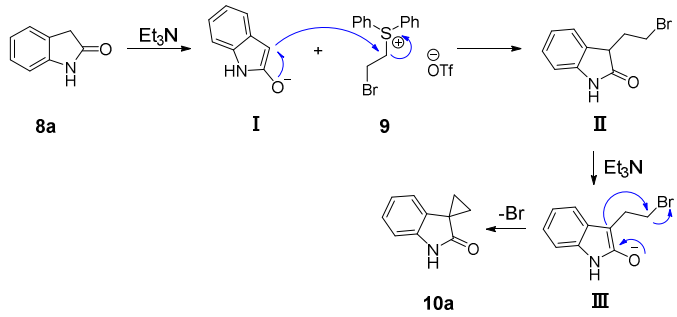
Under the optimized reaction conditions, we went on to explore the scope of the reaction in terms of unprotected indole substrates. As shown in Table 2, the protocol with a variety of unprotected indoles **8** gave the corresponding spirocyclopropyl oxindoles in good yields. Electron-donating as well as electron-withdrawing groups on aromatic rings were tolerated, for example, the yield of desired product **10e** and **10r** was good in 77% and 75% yield respectively. The substitution position of the oxindoles was examined and had minimal influence on the reaction yields either, oxindoles possessing various substitutions underwent cyclopropanation in high yields. Both pyridine **10k** and **10l** were acquired in 58% and 52% yield. 3*H*-Benzofuran-2-one **8m** was also efficiently transformed towards compound 1**0m** in 70% yield. A boronic ester group on C-6 position of oxindole ring provided the corresponding compound **10v** in slightly lower yield. In addition, halogen-substituted oxindoles generally exhibited high reaction activities for over 70% yields.

Table 2. reactions for the synthesis of spirocyclopropyl oxindoles **10**[a]



[a] All the reactions were carried out using 8 (0.2 mmol), 9 (1.5 equiv., 0.3 mmol) and Et3N (3.0 equiv., 0.6 mmol) for stirring 6 h in 2 ml of DMF at room temperature.

We found that reaction system had a common side reaction on the nitrogen of oxindole which provided over-alkylation by-product, which was 1'-(2-bromoethyl) spiro[cyclopropane-1,3'-indolune]-2'-one (**11**) in 35%, 23%, 28%, 26% and 22% yield. Meanwhile, the N-vinyl by-product as previous reported in the literature[10h] was not isolated from reaction solution. Hence, a possible mechanism for cyclopropanation reaction, which was different from mechanism as previous literature reports,[12b, 15] was postulated in Scheme 4. Firstly, enolate **I** is generated from substrate oxindole **8a** in organic base Et_3N. Then, enolate **I** attacks compound **9** to form intermediate **II**, which transform enolate **III** in organic base Et_3N. Finally, an intramolecular nucleophilic substitution of enolate **III** provides the spirocyclopropyl oxindole **10a**.



Scheme 4. Proposed mechanism for cyclopropanation synthesis of oxindoles

3. Conclusion

In conclusion, we have developed a more convenient and efficient method for the synthesis of spirocyclopropyl oxindoles from N-unsubstituted oxindoles using bromoethylsulfonium salt, which is easily commercially available and is stable for a long time, under mild condition. A wide range of functional groups on aromatic rings are well tolerated, and the spirocyclopropyl oxindoles are synthetized in moderate yields. We believe that this synthetic protocol will be adopted to construct spirooxindoles via ring-expansion reaction with aldimines.

4. Experimental Section

4.1. General

All reagents and solvents were of commercial quality and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods.[16] Reactions were carried out using conventional glassware under air atmosphere at room temperature. All reactions were monitored by TLC analysis with silica gel-coated plates with fluorescent indicator UV254. ^1H and ^{13}C NMR spectra were obtained on either a Bruker AV 300 at 300 MHz and 75 MHz, respectively. ^1H and ^{13}C NMR spectra were obtained on either a Bruker AV 300 at 300 MHz and 75 MHz, respectively. Chemical shifts are reported in ppm and coupling constants are reported in Hz with TMS at 0.0 ppm (^1H and ^{13}C) or $CDCl_3$ referenced at 7.26 (^1H) and 77.0 ppm (^{13}C) and DMSO-d_6 referenced at 2.50 (1H) and 39.5 (^{13}C). Mass spectra were measured with an Agilent Q-TOF 6520 mass spectrometer using ESI ionization.

4.2. Preparation of bromoethylsulfonium salt (9)[17]

A solution of 2-bromoethyl trifluoromethanesulfonate[15, 18] (4.12 g, 16.0 mmol) in anhydrous toluene (12 mL) was treated with phenyl sulfide (3.66 g, 19.2 mmol) at room temperature under argon with stirring. The reaction mixture was then heated at 100 °C under argon for 6 h. The solution was allowed to cool to RT and diethyl ether (20 mL) was added to precipitate the product **9** which was isolated by filtration as a white to grey powder (3.22 g, 45%) after washing with Et_2O and used in the next step without further purification.[19] m.p. 85-87 °C (precipitated from toluene/Et_2O) [lit.[15b] 86.5-88 °C (precipitated from Et_2O/CH_2Cl_2)]; R_f (MeOH-CH_2Cl_2, 1:9) 0.53. ^1H NMR (300 MHz, $CDCl_3$): δ 8.06-8.12 (m, 4H), 7.71-7.77 (m, 6H), 4.92 (t, J = 5.9 Hz, 2H), 3.73 (t, J = 5.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.3, 131.9, 131.1, 122.9, 48.2, 23.8. HRMS (ESI-TOF) calcd for $C_{15}H_{14}BrF_3O_3S_2$ [M-CF_3O_3S] $^+$: 292.9994; found: 293.0007.

4.3. General Procedure for cyclopropanation of compound 10

To a 25 mL round bottomed flask was added different substituted oxindoles **8** (0.2 mmol, 1.0 equiv.) and bromoethylsulfonium salt **9** (132.99 mg, 0.3 mmol, 1.5 equiv.), DMF (2 mL). The mixture was stirred at room temperature for 5 min and Et_3N (61.88 mg, 0.6 mmol, 3.0 equiv.) was added into reaction system. The mixture was stirred for 6 hours at room temperature until the reaction completed, quenched with saturated ammonium chloride solution (5 mL), and was extracted with EtOAc (3 x 30 mL). The combined organic layer washed with H_2O (2 x 10 mL), dried with anhydrous sodium sulfate. After concentration, product was purified using column chromatography on silica gel with suitable eluent.

*4.3.1. spiro[cyclopropane-1,3'-indoline]-2'-one **(10a)***

Colorless crystalline (24 mg, 75% yield). mp 177-180 °C. Analytical data for **10a** was consistent with that previously reported.[10h] ^1H NMR (300 MHz, $CDCl_3$): δ 8.94 (s, 1H), 7.16-7.26 (m, 1H), 6.97-7.00 (m, 2H), 6.84 (d, J = 7.4 Hz, 1H), 1.75-1.79 (m, 2H), 1.52-1.56 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.8, 140.8, 131.3, 126.8, 122.0, 118.6, 109.9, 27.6, 19.5. HRMS (ESI-TOF) calcd for $C_{10}H_{10}NO$ [M+H] $^+$: 160.0757; found: 160.0757.

*4.3.2. 5'-fluorospiro[cyclopropane-1,3'-indoline]-2'-one **(10b)***

Colorless crystalline (28 mg, 78% yield). mp 215-218 °C. Analytical data for **10b** was consistent with that previously reported.[10h] ^1H NMR (300 MHz, DMSO-d_6): δ 10.54 (s, 1H), 6.92-6.99 (m, 2H), 6.84-6.87 (m, 1H), 1.59 (m, 2H), 1.49 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.1, 156.9-160.0 (d, J_{C-F} = 233.9 Hz), 138.3, 133.4-133.5 (d, J_{C-F} = 9.3 Hz), 112.9-133.3 (d, J_{C-F} = 23.3 Hz), 110.2-110.3 (d, J_{C-F} = 8.3 Hz), 107.6-108.0 (d, J_{C-F} = 25.3 Hz), 28.1, 19.2. HRMS (ESI-TOF) calcd for $C_{10}H_9NFO$ [M+H] $^+$: 178.0663; found: 178.0663.

*4.3.3. 5'-chlorospiro[cyclopropane-1,3'-indoline]-2'-one **(10c)***

Pale yellow solid (31 mg, 78% yield). mp 212-215 °C. ^1H NMR (300 MHz, DMSO-d_6): δ 10.67 (s, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.10 (s, 1H), 6.87 (d, J = 8.2 Hz, 1H), 1.63 (m, 2H), 1.48 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.9, 141.0, 133.7, 126.7, 125.8, 120.1, 110.9, 27.7, 19.3. HRMS (ESI-TOF) calcd for $C_{10}H_9NClO$ [M+H] $^+$: 194.0367; found: 194.0371.

*4.3.4. 5'-bromospiro[cyclopropane-1,3'-indoline]-2'-one **(10d)***

Colorless crystalline (35 mg, 72% yield). mp 207-209 °C. ^1H NMR (300 MHz, DMSO-d_6): δ 10.67 (s, 1H), 7.32 (d, J = 8.2 Hz, 1H), 7.21 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 1.64 (m, 2H), 1.48 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.3, 140.9, 133.6, 129.1, 122.3, 113.0, 111.0, 27.1, 18.8. HRMS (ESI-TOF) calcd for $C_{10}H_9NBrO$ [M+H] $^+$: 237.9862; found: 237.9859.

4.3.5. 5'-nitrospiro[cyclopropane-1,3'-indoline]-2'-one ***(10e)***

White solid (32 mg, 77% yield). mp 241-244 °C. Analytical data for **10e** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.28 (s, 1H), 8.17 (d, J = 4.9 Hz, 1H), 7.99 (s, 1H), 7.12 (d, J = 7.1 Hz, 1H), 1.86 (m, 2H), 1.61 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.5, 148.5, 142.4, 132.6, 124.4, 115.8, 109.6, 27.8, 20.0. HRMS (ESI-TOF) calcd for $C_{10}H_9N_2O_3$ [M+H] $^+$: 205.0608; found: 205.0744.

4.3.6. 5'-methylspiro[cyclopropane-1,3'-indoline]-2'-one ***(10f)***

Pale yellow crystalline (26 mg, 73% yield). mp 195-198 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.43 (s, 1H), 6.96 (dd, J = 0.9, 7.8 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.77 (br s, 1H), 2.23 (s, 3H), 1.50 (m, 2H), 1.44 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.4, 139.9, 131.6, 130.5, 127.4, 120.4, 109.6, 27.5, 21.4, 18.8. HRMS (ESI-TOF) calcd for $C_{11}H_{12}NO$ [M+H] $^+$: 174.0913; found: 174.0912.

4.3.7. 5'-methoxyspiro[cyclopropane-1,3'-indoline]-2'-one ***(10g)***

Colorless crystalline (29 mg, 75% yield). mp 158-160 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.33 (s, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.68-6.75 (m, 1H), 6.64 (d, J = 2.2 Hz, 1H), 3.69 (s, 3H), 1.51-1.55 (m, 2H), 1.41-1.49 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.3, 155.3, 135.6, 132.9, 112.0, 110.1, 106.9, 56.0, 28.0, 18.9. HRMS (ESI-TOF) calcd for $C_{11}H_{12}NO_2$ [M+H] $^+$: 190.0863; found: 190.0864.

4.3.8. 6'-fluorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10h)***

Pale yellow solid (23 mg, 63% yield). mp 173-175 °C. Analytical data for **10h** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.67 (s, 1H), 6.95-6.97 (m, 1H), 6.70-6.73 (m, 1H), 1.54 (m, 2H), 1.45 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.6, 160.3-163.5 (d, J_{C-F} = 238.1 Hz), 143.3-143.5 (d, J_{C-F} = 12.2 Hz), 127.0-127.1 (d, J_{C-F} = 2.3 Hz), 120.7-120.8 (d, J_{C-F} = 9.6 Hz), 107.4-107.7 (d, J_{C-F} = 22.3 Hz), 97.8-98.2 (d, J_{C-F} = 27.0 Hz), 27.1, 18.7. HRMS (ESI-TOF) calcd for $C_{10}H_9NFO$ [M+H] $^+$: 178.0663; found: 178.0659.

4.3.9. 6'-chlorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10i)***

Colorless crystalline (27 mg, 71% yield). mp 225-228 °C. Analytical data for **10i** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.73 (s, 1H), 7.02 (br s, 2H), 6.95 (br s, 1H), 1.62 (m, 2H), 1.53 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.1, 143.5, 131.2, 130.3, 121.2, 121.1, 109.8, 27.3, 19.1. HRMS (ESI-TOF) calcd for $C_{10}H_9NClO$ [M+H] $^+$: 194.0367; found: 194.0363.

4.3.10. 6'-bromospiro[cyclopropane-1,3'-indoline]-2'-one ***(10j)***

White solid (35 mg, 72% yield). mp 243-246 °C. Analytical data for **10j** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.68 (s, 1H), 7.12 (d, J = 7.6 Hz, 1H), 7.04 (s, 1H), 6.94 (d, J = 5.8 Hz, 1H), 1.58 (m, 2H), 1.49 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.0, 143.8, 130.8, 124.0, 121.5, 119.3, 112.5, 27.1, 18.8. HRMS (ESI-TOF) calcd for $C_{10}H_9NBrO$ [M+H] $^+$: 237.9862; found: 237.9860.

4.3.11. 7'-chlorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10k)***

Pale yellow crystalline (26 mg, 67% yield). mp 163-165 °C. Analytical data for **10k** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.03 (s, 1H), 7.25 (m, 2H), 6.99-7.00 (m, 2H), 1.66 (m, 2H), 1.58 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.1, 139.6, 133.4, 127.0, 122.9, 118.3, 114.1, 28.2, 19.5. HRMS (ESI-TOF) calcd for $C_{10}H_9NClO$ [M+H] $^+$: 194.0367; found: 194.0380.

4.3.12. 4'-chlorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10l)***

Pale yellow solid (31 mg, 78% yield). mp 203-205 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.82 (s, 1H), 7.15-7.20 (m, 1H), 6.89-6.94 (m, 2H), 2.05-2.08 (m, 2H), 1.37-1.41 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.2, 144.3, 128.7, 126.6, 126.1, 122.3, 109.1, 28.2, 15.2. HRMS (ESI-TOF) calcd for $C_{10}H_9NClO$ [M+H] $^+$: 194.0367; found: 194.0362.

4.3.13. 4'-fluorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10m)***

Colorless crystalline (27 mg, 74% yield). mp 168-170 °C. Analytical data for **10m** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.78 (s, 1H), 7.18 (td, J = 8.1, 5.8 Hz, 1H), 6.75 (dd, J = 16.7, 8.2 Hz, 2H), 1.76 (td, J = 7.6, 3.8 Hz, 2H), 1.45 (td, J = 7.6, 3.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.5, 158.6, 144.5-144.6 (d, J_{C-F} = 9.3 Hz), 128.7-128.8 (d, J_{C-F} = 8.3 Hz), 116.1-116.4 (d, J_{C-F} = 17.9 Hz), 108.6-108.8 (d, J_{C-F} = 19.7 Hz), 106.7, 26.4, 16.5. HRMS (ESI-TOF) calcd for $C_{10}H_9NFO$ [M+H] $^+$: 178.0663; found: 178.0662.

4.3.14. 4'-bromospiro[cyclopropane-1,3'-indoline]-2'-one ***(10n)***

White solid (38 mg, 79% yield). mp 195-198 °C. Analytical data for **10n** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.85 (s, 1H), 7.14-7.17 (m, 2H), 6.98-7.00 (m, 1H), 2.17 (m, 2H), 1.40 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.2, 144.6, 129.0, 127.4, 125.5, 114.8, 109.5, 28.9, 15.0. HRMS (ESI-TOF) calcd for $C_{10}H_9NBrO$ [M+H] $^+$: 237.9862; found: 237.9863.

4.3.15. 4'-methylspiro[cyclopropane-1,3'-indoline]-2'-one ***(10o)***

Colorless crystalline (25 mg, 72% yield). mp 170-172 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.52 (s, 1H), 7.03 (t, J = 7.7 Hz, 1H), 6.68-6.76 (m, 2H), 2.12 (s, 3H), 1.93 (m, 2H), 1.29 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.1, 142.5, 132.0, 126.9, 126.8, 124.0, 107.8, 28.1, 16.8, 14.7. HRMS (ESI-TOF) calcd for $C_{11}H_{12}NO$ [M+H] $^+$: 174.0913; found: 174.0911.

4.3.16. 5',6'-dichlorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10p)***

Colorless crystalline (38 mg, 82% yield). mp 245-247 °C. Analytical data for **10p** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.78 (s, 1H), 7.31 (s, 1H), 7.06 (s, 1H), 1.66-1.70 (m, 2H), 1.49-1.53 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.8, 142.2, 132.6, 129.0, 123.6, 121.9, 111.2, 27.6, 19.6. HRMS (ESI-TOF) calcd for $C_{10}H_8Cl_2NO$ [M+H] $^+$: 227.9977; found: 227.9975.

4.3.17. 5',6'-difluorospiro[cyclopropane-1,3'-indoline]-2'-one ***(10q)***

Colorless crystalline (31 mg, 80% yield). mp 248-250 °C. Analytical data for **10q** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.70 (s, 1H), 7.21 (dd, J_{H-F} = 8.1, 10.2 Hz, 1H), 6.94 (dd, J_{H-F} = 6.8, 10.6 Hz, 1H), 1.63-1.65 (m, 2H), 1.51-1.53 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.3, 150.4-150.6 (d, J_{C-F} = 14.0 Hz), 147.2-147.4 (d, J_{C-F} = 13.9 Hz), 138.3-138.4 (d, J_{C-F} = 10.2 Hz), 127.5-127.6 (d, J_{C-F} = 7.5 Hz), 109.5-109.8 (d, J_{C-F} = 20.6 Hz), 99.4-99.7 (d, J_{C-F} = 22.5 Hz), 27.6, 19.2. HRMS (ESI-TOF) calcd for $C_{10}H_8F_2NO$ [M+H] $^+$: 196.0568; found: 196.0565.

4.3.18. spiro[1H-pyrrolo[2,3-b]pyridine-3,1'-cyclopropane]-2-one ***(10r)***

Pale Yellow crystalline. (19 mg, 58% yield). mp 170-173 °C. Analytical data for **10r** was consistent with that previously reported.[10h] ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.14 (s, 1H), 8.04 (br s, 1H), 7.33-7.36 (m, 1H), 6.92 (br s, 1H), 1.63 (m, 2H), 1.52 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.9, 156.8, 145.7, 127.2, 125.7, 117.6, 27.0, 18.7. HRMS (ESI-TOF) calcd for $C_9H_9N_2O$ [M+H] $^+$: 161.0709; found: 161.0708.

4.3.19. 5-bromospiro[1H-pyrrolo[2,3-b]pyridine-3,1'-cyclopropane]-2-one ***(10s)***

Red crystalline. (25 mg, 52% yield). mp 238-240 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.35 (s, 1H), 8.15 (d, J = 2.2 Hz, 1H), 7.66 (d, J = 1.9 Hz, 1H), 1.73-1.76 (m, 2H), 1.55-1.57 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.6, 155.8, 145.9, 130.1, 128.3, 112.6, 27.3, 19.4. HRMS (ESI-TOF) calcd for $C_9H_8BrN_2O$ [M+H] $^+$: 238.9815; found: 238.9814.

4.3.20. Spiro[benzofuran-3,1'-cyclopropan]-2-one ***(10t)***

Yellow crystalline (23 mg, 70% yield). mp 83-85 °C. Analytical data for **10t** was consistent with that previously reported[20]. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.35 (s, 1H), 8.15 (d, J = 2.2 Hz, 1H), 7.66 (d, J = 1.9 Hz, 1H), 1.73-1.76 (m, 2H), 1.55-1.57 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.9, 153.6, 129.2, 127.8, 124.2, 119.1, 110.8, 25.1, 21.2. HRMS (ESI-TOF) calcd for $C_{10}H_9IO_2$ [M+H] $^+$: 161.0597; found: 161.0597.

4.3.21. Methyl 2'-oxospiro[cyclopropane-1,3'-indoline]-6'-carboxylate ***(10u)***

Colorless crystalline (36 mg, 81% yield). mp 226-230 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.76 (s, 1H), 7.57 (dd, J = 1.5, 7.8 Hz, 1H), 7.43 (d, J = 1.1 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 3.84 (s, 3H), 1.66-1.68 (m, 2H), 1.55-1.58 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.9, 166.7, 142.5, 137.3, 128.4, 123.1, 119.7,109.6, 52.6, 27.9, 19.8. HRMS (ESI-TOF) calcd for $C_{12}H_{12}NO_3$ [M+H] $^+$: 218.0812; found: 218.0811.

4.3.22. 6'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[cyclopropane-1,3'-indoline]-6'-carboxylate ***(10v)***

Colorless crystalline (29 mg, 49% yield). mp 252-254 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.59 (s, 1H), 7.26 (d, J = 7.4 Hz, 1H), 7.17 (s, 1H), 6.97 (d, J = 7.4 Hz, 1H), 1.57-1.60 (m, 2H), 1.48-1.52 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.0, 141.9, 135.2, 128.1, 119.2, 114.8, 84.0, 27.8, 25.1, 19.2. HRMS (ESI-TOF) calcd for $C_{16}H_{21}BNO_3$ [M+H] $^+$: 286.1612; found: 286.1617.

4.3.23. 1'-(2-bromoethyl) spiro[cyclopropane-1,3'-indolin]-2'-one ***(11)***

Yellow oil. (19 mg, 35% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.31 (m, 1H), 7.00-7.09 (m, 2H), 6.97 (d, J = 7.3 Hz, 1H), 4.21 (t, J = 7.2 Hz, 2H), 3.61 (t, J = 7.2 Hz, 2H), 1.78-1.81 (m, 2H), 1.56-1.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.0, 142.2, 130.7, 126.8, 122.3, 118.6, 108.2, 42.1, 27.6, 27.0, 18.7. HRMS (ESI-TOF) calcd for $C_{12}H_{13}BrNO$ [M+H] $^+$: 266.0175; found: 266.0181.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at DOI:

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