JOC The Journal of Organic Chemistry

Note

Oxygenophilic Lewis Acid-Promoted Synthesis of 2-Arylindoles from Anilines and Cyanoepoxides in Alcohol

Chuangchuang Xu, and Jiaxi Xu

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b02203 • Publication Date (Web): 07 Nov 2018

ACS Publications

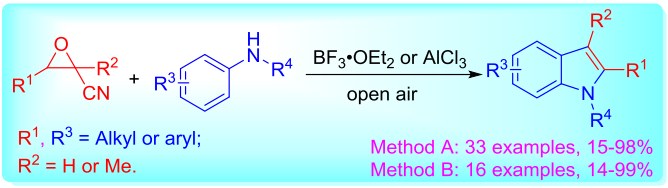
is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Oxygenophilic Lewis Acid-Promoted Synthesis of 2-Arylindoles from Anilines and Cyanoepoxides in Alcohol

Chuangchuang Xu, Jiaxi Xu*

State Key Laboratory of Chemical Resource Engineering, Department of Organic Chemistry, Faculty of Science, Beijing University of Chemical Technology, Beijing 100029, People's Republic of China.

Supporting Information



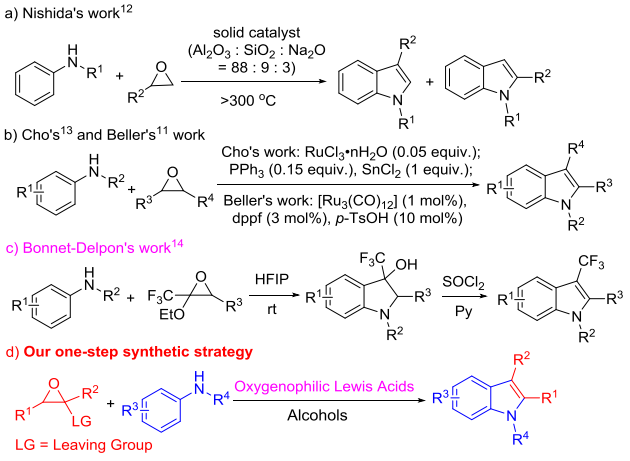
ABSTRACT: A convenient synthetic method to indoles from anilines and cyanoepoxides was developed under the catalysis of BF_3•OEt_2 or $AlCl_3$ in alcohols. The reaction involves a tandem reaction of the regionspecific ring-opening of cyanoepoxides with anilines, elimination of cyanide, intramolecular aromatic electrophilic substitution, and the water elimination. The Lewis acids generated protic acid is efficient catalyst. The method features readily accessible starting materials, wide substrate scope, transition metal-free, and regiospecificity in the ring-opening of cyanoepoxides.

Indoles and their derivatives are one of the most widely existed heterocyclic compounds in nature.[1] Because of their unique biological characteristics and excellent physical properties they have broad application prospects and great values in pharmaceuticals and materials sciences.[2] Therefore, since indole was discovered and characterized by Baeyer in 1866,[3] its derivatives have attracted considerable attention on developing safe and effective synthetic methods. Numerous unique synthetic methods have emerged during the past decades, for example, Fischer,[4] Grandberg,[5] Madelung,[6] Bischler,[7] and other traditional synthetic methods,[8] the recently developed C-H activation methods,[9] and the functionalization of indoles.[10]

By summarizing and understanding the synthetic methods of indoles, the reaction of anilines and epoxides has been considered as an atom-economic model to synthesize indoles and explored.[11] In 1995, Nishida and co-workers first reported the heterogeneous synthesis of indoles from anilines and epoxides through a vapour phase reaction at more than 300 °C with a solid catalyst (Scheme 1a).[12] Besides, Cho and co-workers achieved the regioselective synthesis of 2-substituted indoles from excess anilines (10 equivalents) and epoxides under the catalysis of ruthenium and equivalent cocatalyst $SnCl_2$ in 2003 (Scheme 1b).[13] In 2014, Beller's group realized the ruthenium-catalyzed synthesis of indoles from 7-oxabicyclo[4.1.0]heptane and anilines in the presence of 10 mol% *p*-toluenesulfonic acid (Scheme 1b).[11] They also realized the regioselective synthesis of indoles from more sensitive epoxides in one-pot two steps.

In 2001, Bonnet-Delpon reported a stepwise synthesis of 3-trifluoromethylindoles from anilines and 1-ethoxy-1-trifluoromethylepoxides through a two-stepped tandem reactions, involving the ring opening of epoxides with anilines and

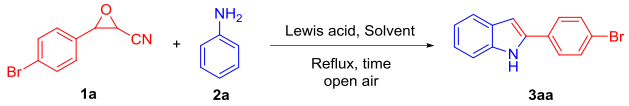
Scheme 1. Synthesis of indoles from anilines and epoxides.



the elimination of the ethoxide group first, followed by an intramolecular aromatic electrophilic substitution, finally chlorination with $SOCl_2$ and base elimination (Scheme 1c).[14] Inspired by this, we designed an oxygenophilic Lewis acid-catalyzed direct conversion of cyanoepoxides and anilines into indoles because acids can not only promote ring-opening of epoxides and intramolecular aromatic electrophilic substitution, but also

elimination of the hydroxyl group, and cyanide is a better leaving group than ethoxide (Scheme 1d). Herein, we present our synthetic strategy to indoles from anilines and cyanoepoxides under the catalysis of oxygenophilic BF_3•OEt_2 or $AlCl_3$ in alcohols. The oxirane-2-carbonitriles (cyanoepoxides) were easily prepared from aldehydes and chloroacetonitrile by the Darzens reaction.

Table 1. Optimization of the reaction conditions[a]

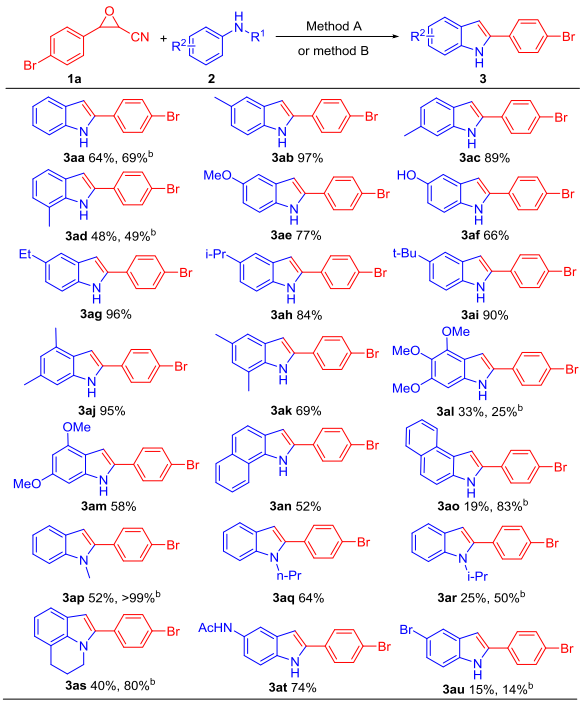


Entry	**2a** equiv.	L.A.[b] equiv.	Solvent EtOH:TFE	Time h	Yield[c] %
1	1.5	0.20 B	3:7	11	30
2	1.5	0.18 B	3:7	11	55
3	1.5	0.16 B	3:7	11	64
4	1.5	0.14 B	3:7	11	51
5	1.5	0.10 B	3:7	11	38
6	1.5	0.16 B	3:7	15	67(64[d])
7	**1.5**	**0.16 B**	**3:7**	**20**	**67(64[d])**
8	1.7	0.16 B	3:7	20	49
9	1.2	0.16 B	3:7	20	46
10	1.0	0.05 Al	0:1	11	19
11	1.0	0.10 Al	0:1	11	35
12	1.0	0.15 Al	0:1	11	23
13	1.5	0.10 Al	0:1	11	39
14	1.9	0.10 Al	0:1	11	74
15	2.3	0.10 Al	0:1	11	50
16	1.9	0.10 Al	0:1	18	77(51[d])
17	**1.9**	**0.10 Al**	**0:1**	**30**	**69[d]**
18	1.9	0.10 Al	0:1	36	69[d]
19	1.9	0.10 Al	3:7	11	35

[a]Reactions were conducted on a 0.5 mmol scale in 5 mL of solvent. [b]L.A. = Lewis acid, B = BF_3•OEt_2, Al = $AlCl_3$. [c]Yield determined by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. [d]Isolated yield. TFE = Trifluoroethanol.

Initially, 3-(4-bromophenyl)oxirane-2-carbonitrile (**1a**) and aniline (**2a**) were employed as the model substrates to optimize reaction conditions. Detailed optimizations on different Lewis acids, solvents, and reaction time, equivalents of substrates and acids are summarized in Table S1 and Table S2 in SI. Detailed optimizations under the catalysis of efficient Lewis acids BF_3•OEt_2 and $AlCl_3$ are present in Table 1. To our delight, **1a** (0.5 mmol) and **2a** (1.5 mmol) were treated with BF_3•OEt_2 (0.20 equiv.) in refluxing EtOH and TFE (3:7, *v*/*v*) for 11 h, affording the desired 2-(4-bromophenyl)-1*H*-indole (**3aa**) in 30% yield (Table 1, entry 1). Evaluation on the equivalent of BF_3•OEt_2 indicated that 0.16 equivalents of BF_3•OEt_2 was good choice (Table 1, entries 1-5). When the reaction time was extended to 15 and 20 hours, the yield was further increased to 67% NMR yield and 64% isolated yield (Table 1, entries 6 and 7). Both increase and decrease of the amount of BF_3•OEt_2 resulted in loss of the yield (Table 1, entries 8 and 9). Thus, the optimal reaction conditions under the catalysis of BF_3 were identified as: **1** (1 equiv.), **2** (1.5 equiv.), and BF_3•OEt_2 (0.16 equiv.) in 5 mL of 3:7 EtOH/TFE refluxing for 20 h (Method A)(Table 1, entry 7). The reaction conditions under the catalysis of $AlCl_3$ were also further optomized (Table 1, entries 10-19). Optimization on the amount of $AlCl_3$ revealed that 0.10 euivalent of $AlCl_3$ was the best case (Table 1, entries 10-12), while screening the amount of aniline showed that 1.9 equivalents of aniline was the best choice (Table 1, entries 13-15). For different reaction times, the best yield was obtained in the reaction under refluxing for 30 hours (Table 1, entries 16-18). The reaction was also conducted in the mixed solvent (EtOH:TFE, 3:7) under the catalysis of $AlCl_3$, but a low yield was obtained (Table 1, entry 19). For the $AlCl_3$-catalyzed reaction, the optimal reaction conditions are as following: **1a** (1 equiv.), **2a** (1.9 equiv.), and $AlCl_3$ (0.1 equiv.) refluxing in 5 mL of commercial TFE for 30 h (Method B), affording **3aa** in 69% isolated yield (Table 1, entry 17).

Table 2. Scope of anilines[a]



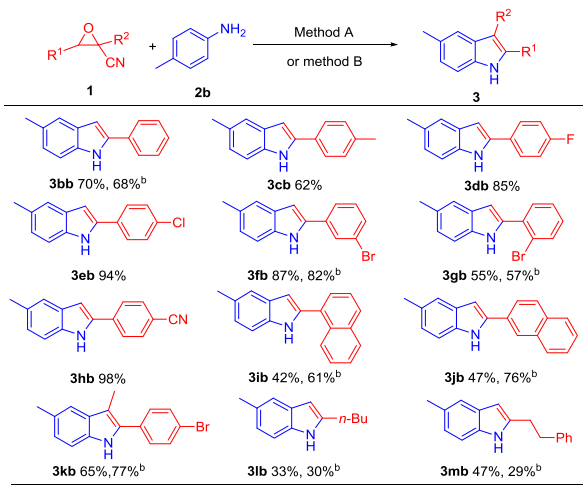
[a]All reactions were performed on a 0.5 mmol scale, yields are isolated yields. Method A: **1** (0.5 mmol), **2** (0.75 mmol), and BF_3•OEt_2 (0.08 mmol) in 5 mL of 3:7 EtOH/TFE mixed solvent were refluxed for 20 h. [b]Method B: **1** (0.5 mmol), **2** (0.95 mmol), and $AlCl_3$ (0.05 mmol) in 5 mL of TFE were refluxed for 30 h.

With the optimized conditions in hand, the scope and generality of the reaction were investigated. Reactions of different anilines with 3-(4-bromophenyl)-oxirane-2-carbonitrile (**1a**) were firstly investigated (Table 2): *p*, *m*, *o*-toluidines (**2b-d**) gave the corresponding products **3ab**, **3ac**, and **3ad** in the yields of 97%, 89%, and 48%, respectively. The yield of the corresponding indoles decreases along with the distance decrease between the methyl and amino groups on the phenyl ring, indicating that the steric hindrance around the nitrogen atom of anilines greatly impacted on the reaction. And it was verified that *m*-toluidine (**2c**) only gave 6-methyindole **3ac**. For other 4-substituted anilines **2e-i**, anilines **2e-i** with electron-donating groups are well suitable to the reaction and gave **3ae-3ai** in 66-96% yields. Moreover, the steric hindrance of *para*-substituents has no obvious effect on the reaction, ethyl, *i*-Pr, and *t*-Bu *p*-substituted anilines **2g-i** provided **3ag-3ai** in 96%, 84%, and 90% yields, respectively. Next, multisubstituted anilines **2j-m** were also investigated, both 3,5-dimethylaniline (**2j**) and 2,4-dimethylaniline (**2k**) were good substrates, giving rise to **3aj** and **3ak** in 95% and 69% yields. While 3,4,5-trimethoxyaniline (**2l**) and 3,5-dimethoxyaniline (**2m**) gave 33% yield of **3al** and 58% yield of **3am**, respectively, possibly due to the steric hindrance and the interaction between the oxygen-containing group and BF_3. Additionally, because of the steric hindrance effect 1-

naphthylamine (**2n**) and 2-naphthylamine (**2o**) gave **3an** and **3ao** in 52% and 19% yields, respectively. Finally, different *N*-substituted anilines **2p-s** were evaluated as well. *N*-Methyl, *N*-propyl, and *N*-isopropylanilines (**2p-r**) were also suitable to the reaction, yielding **3ap-3ar** in 52%, 64%, and 25% yields, respectively. The yields further demonstrate that the steric hindrance around the nitrogen atom of anilines impacts on the reaction. Besides, tetrahydroquinoline (**2s**) also worked well, yielding **3as** in 40% yield. And *N*-(4-aminophenyl)acetamide (**2t**) gave **3at** in 74% yield. As expected, electron-poor 4-bromoaniline (**2u**) generated **3au** only in 15% yield.

Reactions of different 3-substitued oxirane-2-carbonitriles **1b-m** with **2b** were investigated (Table 3). Firstly, for 3-aryloxirane-2-carbonitriles **1b-k**, epoxides with both electron-withdrawing and electron-donating groups on the aryl ring were good substrates, giving **3bb-3hb** in moderate to excellent yields of 55−98%, and epoxides with electron-withdrawing groups gave better yields. Besides, 2-bromophenylepoxide (**1g**) gave **3gb** in a lower yield of 55% than **3ab** owing to the steric hindrance. In addition, naphthalene-1-yl and naphthalene-2-yloxiranes (**1i** and **1j**) worked well and gave **3ib** and **3jb** in 42% and 47% yields, respectively. Trisubstituted 3-(4-bromophenyl)-2-methyloxirane-2-carbonitrile (**1k**) was also compatible, affording **3kb** regiospecifically in 65% yield. Finally, the long-chain *n*-butyl and phenethyl 3-alkyloxiranes (**1l** and **1m**) were suitable substrates and gave **3lb** and **3mb** in 33% and 47% yields, respectively.

Table 3. Scope of epoxides[a]



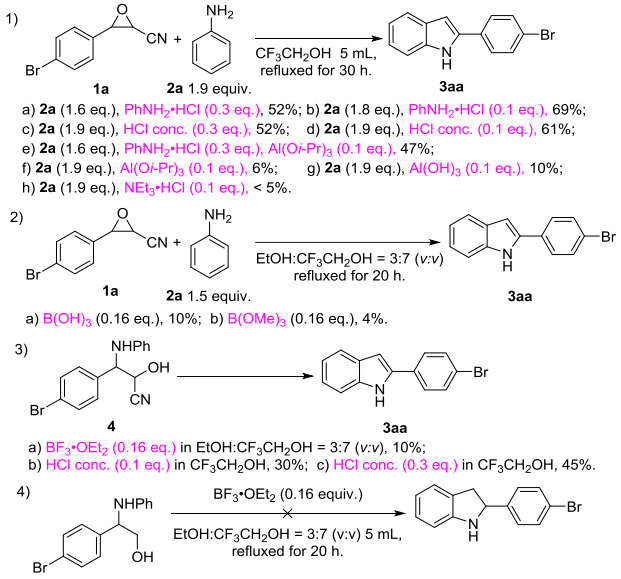
Notes a and b are the same as those in Table 2.

The scope and generality were also simply investigated under Method B conditions. For primary anilines, **3aa** and **3ad** were obtained in 69% and 49% yields, respectively, similar to those in Method A. Interestingly, 2-naphthalenamine (**2o**) gave **3ao** in 83% yield, a higher yield than that in Method A. Similarly, the yields of secondary anilines were also obviously improved. *N*-Methylaniline (**2p**) almost gave **3ap** quantitatively; *N*-isopropylaniline (**2r**) and tetrahydroquinoline (**2s**) gave **3ar** and **3as** in 50% and 80% yields, respectively, which are double to those in Method A. These results indicate that $AlCl_3$ is more powerful than BF_3•OEt_2 for some certain substrates, such as secondary anilines, it can overcome partly the adverse effects of the steric hindrance and the weak nucleophilicity of amines. However, electron-withdrawing 4-bromoaniline (**2u**) did not improve its yield in method B (Table 2).

Additionally, 3-phenyl, 3-(3-bromophenyl), and 3-(2-bromophenyl)oxirane-2-carbonitriles (**1b**, **1f**, and **1g**) also produced **3bb**, **3fb**, and **3gb** in 68%, 82%, and 57% yields, respectively, similar to those in Method A. Naphthalene-1-yl and naphthalene-2-yloxiranes (**1i** and **1j**) gave **3ib** and **3jb** in higher yields of 61% and 76%, respectively, compared with those in Method A. Similarly, 3-(4-bromophenyl)-2-methyloxirane-2-carbonitrile (**1k**) gave **3kb** in a higher yield of 65% as well. Finally, the long-chain *n*-butyl and phenethyl 3-alkyloxiranes (**1l** and **1m**) gave rise to **3lb** and **3mb** in similar yields of 30% and 29% (Table 3).

After comparing and analyzing the yields in Methods A and B, we can summarized that Method B generally gives similar or higher yields, except for 3-alkyloxiranes. Taking into account for the reaction time and economy (the consumption of anilines), method A is ultimately selected as main conditions, and method B as standby conditions for the cases of lower yields obtained in method A. Overall, the results show that this reaction has a wide substrate scope and great advantages for the regiospecific synthesis of 2-arylindoles.

Scheme 2. Control experiments

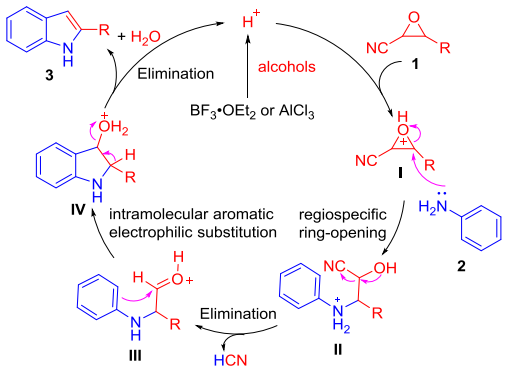


To better understand the reaction mechanism, some control experiments were taken into account (Scheme 2): 1) Inorganic protic acid HCl ($PhNH_2$•HCl and concentrated HCl) were attempted as catalysts in the model reaction, **3aa** was obtained in 52%-69%. $PhNH_2$ • HCl and Al(O*i*-Pr)$_3$ as co-catalysts also gave **3aa** in a slightly lower yield (47%). However, lower yields of **3aa** were obtained when Al(O*i*-Pr)$_3$, $Al(OH)_3$, and Et_3N•HCl in TFE and $B(OH)_3$ and $B(OMe)_3$ in EtOH:TFE (3:7) were applied as catalysts. 2) 3-(4-Bromophenyl)-2-hydroxy-3-(phenylamino)propanenitrile (**4**), the by-product isolated in the optimization process, was reacted under the standard reaction conditions (Method A), giving the desired **3aa** in 10% yield. However, the conversion yield was improved to 30% to 45% under the catalysis of concentrated HClWhen 2-(4-bromophenyl)-2-(phenylamino)ethan-1-ol was performed under the standard reaction conditions, no cyclization product was detected. The results suggest that the cyano group leaves earlier than the hydroxy group in the reaction.

Based on the control experiments and previously reported work,[15] a plausible mechanism is proposed (Scheme 3): Firstly,

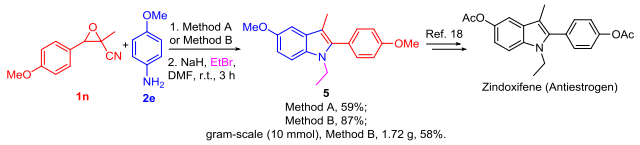
oxygenophilic Lewis acids react with solvent alcohols to generate protic acid, which protonates epoxides **1**, forming intermediates **I**. Anilines **2** nucleophilically attack the protonated epoxy intermediates **I** regiospecifically on the carbon without the cyano group,[16] giving the ring-opening intermediates **II**. Intermediates **II** further undergo an elimination of HCN, generating intermediates **III**. Next, intermediates **III** undergo an intramolecular aromatic electrophilic substitution, yielding intermediates **IV**, which undergo an acid-promoted elimination of water to give rise to the final products **3**. The elimination may undergo a favorable solvent-participating transition-state, similar to the tautomerizations in the Claisen and benzidine rearrangements.[17]

Scheme 3. Proposed mechanism



To demonstrate the synthetic utility of this method, 1-ethyl-5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole (**5**), a precursor compound to synthesize medicine Zindoxifene, was obtained in 59% yield under the Method A conditions and 87% yield under the Method B conditions (Scheme 4). Moreover, a gram-scale reaction was also conducted under the Method B conditions, and gave the product **5** in 58% yield.

Scheme 4. The formal synthesis of Zindoxifene using our method and the gram-scale reaction.



In summary, we developed a novel and convenient method to synthesis of indoles from anilines and cyanoepoxides under the catalysis of BF_3•OEt_2 or $AlCl_3$ in alcohols. The oxygenophilic Lewis acid-generated protic acid promotes not only the regiospecific ring-opening of epoxides, but also intramolecular aromatic electrophilic substitution and elimination of water. The current method features advantages of readily accessible starting materials, wide substrate scope, transition metal-free, and regiospecific synthesis of substituted indoles.

EXPERIMENTAL SECTION

General Information. Melting points were measured on a melting point apparatus and are uncorrected. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a 400 MHz NMR spectrometer. Chemical shifts are reported in ppm and referenced to tetramethylsilane (TMS) or residual solvent peaks as internal standards (for $CDCl_3$, tetramethylsilane 0 ppm for ^{1}H and $CDCl_3$ 77.00 ppm for ^{13}C; for DMSO-d_6, 2.50 ppm for ^{1}H and 39.50 ppm for ^{13}C). IR spectra (KBr pellets, ν [cm^{-1}]) were taken on a FT-IR spectrometer. The high resolution mass spectra were obtained under ESI ionization using an LC/MSD TOF mass spectrometer. Column chromatography was carried out on silica gel (200–300 mesh) with a mixture of petroleum ether (PE, 60 °C–90 °C) and ethyl acetate (EA) as the eluent. All reactions were followed by thin layer chromatography (TLC) where practical, using silica gel 60 F254 fluorescent treated silica gel plates, which were visualized under UV light (254 nm). Commercial grade reagents and solvents were used without further purification unless otherwise noted.

General procedure for the synthesis of compounds 3. *Method A.* A solution of oxirane-2-carbonitrile **1** (0.5 mmol), aniline **2** (0.75 mmol), and BF_3•OEt_2 (11.3 μL, 0.08 mmol) in 5 mL of EtOH/TEF (3:7, *v*/*v*) mixed solvent was refluxed for 20 h under open air conditions. After cooling to room temperature, the crude solution was quenched with water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to afford the corresponding indole **3**.

Method B. A solution of oxirane-2-carbonitrile **1** (0.5 mmol), aniline **2** (0.95 mmol), and $AlCl_3$ (6.7 mg, 0.05 mmol) in 5 mL of TEF was refluxed for 30 h under open air conditions. After cooling to room temperature, the crude solution was quenched with water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to afford the corresponding indole **3**.

2-(4-Bromophenyl)-1H-indole (3aa).[19] Purified by flash column chromatography (PE/EA 30:1, *v*/*v*) on silica gel to give the desired product as beige solid; Method A: 86 mg, 63%; Method B: 94 mg, 69%. M.p. 207–209 °C (Lit.[19] m.p. 212−213 °C). R_F = 0.72, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.0 Hz, 1H), 7.23–7.19 (m, 1H), 7.15–7.11 (m, 1H), 6.82 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 136.9, 136.67, 132.2, 131.3, 129.2, 126.6, 122.7, 121.5, 120.8, 120.5, 110.9, 100.5.

2-(4-Bromophenyl)-5-methyl-1H-indole (3ab).[20] Purified by flash column chromatography (PE/EA 30:1, *v*/*v*) on silica gel to give the desired product as white solid; 139 mg, 97%. M.p. 279–280 °C. R_F = 0.74, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.41 (s, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.74 (s, 1H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 136.7, 135.3, 132.1, 131.5, 129.7, 129.5, 126.5, 124.4, 121.3, 120.4, 110.6, 100.1, 21.4.

2-(4-Bromophenyl)-6-methyl-1H-indole (3ac). Purified by flash column chromatography (PE/EA 30:1, *v*/*v*) on silica gel to give the desired product as beige solid; 127 mg, 89%. M.p. 241–243 °C. R_F = 0.59, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.56–7.48 (m, 5H), 7.18 (s, 1H), 6.96 (dd, J = 8.0, 0.8 Hz, 1H), 6.77 (dd, J = 2.0, 0.8 Hz, 1H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.4, 136.0, 132.7, 132.1, 131.5, 127.0, 126.4, 122.3, 121.2, 120.4, 110.9, 100.4, 21.8. IR (KBr): ν 744, 780, 811, 1005, 1072, 1113, 1231, 1313, 1349, 1412, 1448, 1481, 1529, 1643, 2850, 2920, 3442 cm^{-1}. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd. for $C_{15}H_{13}BrN^+$ 286.0226; Found 286.0226.

2-(4-Bromophenyl)-7-methyl-1H-indole (3ad). Purified by flash column chromatography (PE/EA 30:1, *v*/*v*) on silica gel to give the desired product as beige solid; Method A: 68 mg, 48%; Method B: 70 mg, 49%. M.p. 132–134 °C. R_F = 0.62, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10

(s, 1H), 7.56–7.51 (m, 4H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.07–7.00 (m, 2H), 6.81 (d, *J* = 2.4 Hz, 1H), 2.53 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 136.5, 136.4, 132.1, 131.4, 128.7, 126.6, 123.3, 121.4, 120.7, 120.1, 118.5, 101.1, 16.7. IR (KBr): *v* 743, 799, 826, 1003, 1256, 1304, 1417, 1426, 1479, 1536, 1592, 2913, 2968, 3050, 3446 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{15}H_{13}BrN^+$ 286.0226; Found 286.0227.

2-(4-Bromophenyl)-5-methoxy-1H-indole (3ae).[21] Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as off-white solid; 116 mg, 77%. M.p. 214–215 °C (Lit.[21] m.p. 201−202 °C). R_F = 0.57, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.56–7.54 (m, 2H), 7.50–7.48 (m, 2H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 2.4 Hz, 1H), 6.87 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.74 (d, *J* = 1.2 Hz, 1H), 3.86 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 154.7, 137.4, 132.2, 131.4, 129.7, 126.5, 121.4, 113.1, 111.7, 102.3, 100.4, 55.8.

2-(4-Bromophenyl)-1H-indol-5-ol (3af). Purified by flash column chromatography (PE/EA 8:1, *v/v*) on silica gel to give the desired product as khaki solid; 95 mg, 66%. M.p. 257–258 °C. R_F = 0.26, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.25 (s, 1H), 8.69 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 1H), 6.84 (s, 1H), 6.75 (s, 1H), 6.64 (d, *J* = 8.6 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6) δ 151.0, 136.5, 131.8, 131.7, 129.3, 126.6, 119.9, 112.4, 111.7, 103.8, 98.6. IR (KBr): *v* 788, 845, 1210, 1364, 1423, 1452, 1585, 1624, 3252, 3426 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{14}H_{11}BrNO^+$ 288.0019; Found 288.0015.

2-(4-Bromophenyl)-5-ethyl-1H-indole (3ag). Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as beige solid; 144 mg, 96%. M.p. 239–240 °C. R_F = 0.57, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.57–7.55 (m, 2H), 7.52–7.50 (m, 2H), 7.44 (s, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.07 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.764–6.760 (m, 1H), 2.75 (q, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.6 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 136.8, 136.5, 135.4, 132.1, 131.5, 129.4, 126.5, 123.4, 121.3, 119.1, 110.7, 100.3, 29.0, 16.4. IR (KBr): *v* 789, 810, 828, 1114, 1299, 1418, 1454, 1469, 2850, 2921, 3444 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{15}BrN^+$ 300.0382; Found 300.0381.

2-(4-Bromophenyl)-5-isopropyl-1H-indole (3ah). Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as white solid; 132 mg, 84%. M.p. 196–197 °C. R_F = 0.60, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.46 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.10 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.75 (d, *J* = 1.6 Hz, 1H), 3.00 (hept, *J* = 6.8 Hz, 1H), 1.31 (d, *J* = 6.8 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 141.2, 136.8, 135.5, 132.1, 131.5, 129.3, 126.5, 122.1, 121.3, 117.6, 110.7, 100.4, 34.2, 24.6. IR (KBr): *v* 750, 788, 809, 828, 1004, 1043, 1074, 1240, 1289, 1382, 1420, 1466, 2866, 2923, 3446 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{17}H_{17}BrN^+$ 314.0539; Found 314.0540.

2-(4-Bromophenyl)-5-(tert-butyl)-1H-indole (3ai). Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as white solid; 148 mg, 90%. M.p. 212–214 °C. R_F = 0.8, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.61 (s, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.33–7.28 (m, 2H), 6.77 (d, *J* = 1.6 Hz, 1H), 1.39 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 143.4, 136.8, 135.1, 132.1, 131.5, 129.0, 126.5, 121.3, 121.1, 116.6, 110.4, 100.6, 34.6, 31.9. IR (KBr): *v* 750, 792, 816, 1074, 1114, 1245, 1300, 1361, 1419, 1456, 2865, 2925, 2964, 3425 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{18}H_{19}BrN^+$ 328.0695; Found 328.0698.

2-(4-Bromophenyl)-4,6-dimethyl-1H-indole (3aj). Purified by flash column chromatography (PE/EA 35:1, *v/v*) on silica gel to give the desired product as white solid; 142 mg, 95%. M.p. 111–113 °C. R_F = 0.61, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.01 (s, 1H), 6.79–6.78 (m, 2H), 2.53 (s, 3H), 2.43 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 137.1, 135.4, 132.9, 132.1, 131.6, 130.0, 127.0, 126.3, 122.6, 121.1, 108.4, 99.0, 21.8, 18.7. IR (KBr): *v* 789, 828, 1007, 1071, 1271, 1348, 1375, 1415, 1458, 1481, 1538, 1594, 1619, 2855, 2918, 3008, 3429 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{15}BrN^+$ 300.0382; Found 300.0385.

2-(4-Bromophenyl)-5,7-dimethyl-1H-indole (3ak). Purified by flash column chromatography (PE/EA 35:1, *v/v*) on silica gel to give the desired product as beige solid; 103 mg, 69%. M.p. 148–149 °C. R_F = 0.67, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.56–7.54 (m, 2H), 7.53–7.50 (m, 2H), 7.24 (s, 1H), 6.85 (s, 1H), 6.73 (d, *J* = 2.0 Hz, 1H), 2.49 (s, 3H), 2.41 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 136.4, 134.9, 132.1, 131.6, 129.9, 129.0, 126.5, 125.1, 121.2, 119.7, 118.0, 100.7, 21.4, 16.7. IR (KBr): *v* 712, 745, 786, 826, 845, 1003, 1035, 1069, 1104, 1167, 1266, 1300, 1459, 1542, 1579, 1593, 2852, 2918, 3452 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{15}BrN^+$ 300.0382; Found 300.0384.

2-(4-Bromophenyl)-4,5,6-trimethoxy-1H-indole (3al). Purified by flash column chromatography (PE/EA 5:1, *v/v*) on silica gel to give the desired product as off-white solid; Method A: 60 mg, 33%; Method B: 46 mg, 25%. M.p. 194–196 °C. R_F = 0.26, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 1.6 Hz, 1H), 6.63 (s, 1H), 4.12 (s, 3H), 3.884 (s, 3H), 3.880 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 151.7, 145.9, 136.1, 134.9, 134.0, 132.1, 131.3, 126.1, 120.9, 116.6, 98.2, 89.5, 61.5, 60.9, 56.3. IR (KBr): *v* 790, 827, 960, 1007, 1109, 1215, 1299, 1466, 1503, 1538, 1627, 2838, 2933, 3333 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{17}H_{17}BrNO_3^+$ 362.0386; Found 362.0389.

2-(4-Bromophenyl)-4,6-dimethoxy-1H-indole (3am). Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as pale red solid; 96 mg, 58%. M.p. 162–164 °C. R_F = 0.55, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 2.0 Hz, 1H), 6.47 (d, *J* = 0.8 Hz, 1H), 6.23 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 3H), 3.84 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 158.1, 153.8, 138.3, 133.9, 132.0, 131.5, 125.9, 120.6, 114.5, 97.8, 92.1, 86.73, 55.7, 55.4. IR (KBr): *v* 795, 807, 830, 1008, 1035, 1128, 1148, 1198, 1219, 1278, 1306, 1452, 1464, 1513, 1593, 2839, 2932, 3007, 3348 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{15}BrNO_2^+$ 332.0281; Found 332.0280.

2-(4-Bromophenyl)-1H-benzo[g]indole (3an). Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as brick red solid; 84 mg, 52%. M.p. 196–198 °C. R_F = 0.68, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.05 (d, *J* = 8.4 Hz,

1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.60–7.51 (m, 6H), 7.44 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 1.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.0, 132.2, 131.6, 131.4, 130.7, 129.1, 126.4, 125.7, 125.3, 124.2, 121.5, 121.5, 121.2, 120.5, 119.3, 102.2. IR (KBr): *v* 690, 751, 816, 1005, 1074, 1157, 1212, 1302, 1450, 1479, 1537, 1591, 1629, 2853, 2924, 3048, 3445 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{18}H_{13}BrN^+$ 322.0226; Found 322.0229.

2-(4-Bromophenyl)-3H-benzo[e]indole (3ao). Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as brown solid; Method A: 30 mg, 19%; Method B: 134 mg, 83%. M.p. 168–170 °C. R_F = 0.62, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.60–7.57 (m, 5H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.35 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 134.9, 133.4, 132.2, 131.4, 129.4, 128.7, 128.0, 126.3, 126.0, 124.3, 123.8, 123.7, 122.9, 121.1, 112.4, 99.9. IR (KBr): *v* 747, 772, 800, 825, 1006, 1077, 1154, 1246, 1330, 1373, 1393, 1448, 1461, 1592, 1623, 2853, 2924, 3433 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{18}H_{13}BrN^+$ 322.0226; Found 322.0225.

2-(4-Bromophenyl)-1-methyl-1H-indole (3ap).[22] Purified by flash column chromatography (PE/DCM 8:1, *v/v*) on silica gel to give the desired product as white solid; Method A: 75 mg, 52%; Method B: 104 mg, >99%. M.p. 119–120 °C (Lit.[22] 113–114 °C). R_F = 0.76, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.6 Hz, 1H), 7.60–7.57 (m, 2H), 7.38–7.34 (m, 3H), 7.28–7.24 (m, 1H), 7.16–7.12 (m, 1H), 6.55 (d, *J* = 0.8 Hz, 1H), 3.72 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.2, 138.5, 131.7, 130.8, 127.8, 122.1, 122.0, 120.6, 120.0, 109.6, 102.0, 31.2.

2-(4-Bromophenyl)-1-propyl-1H-indole (3aq). Purified by flash column chromatography (PE/DCM 8:1, *v/v*) on silica gel to give the desired product as beige solid; Method A: 100 mg, 64%. M.p. 56–58 °C. R_F = 0.79, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.6 Hz, 1H), 7.62–7.59 (m, 2H), 7.41–7.35 (m, 3H), 7.27–7.23 (m, 1H), 7.17–7.13 (m, 1H), 6.53 (s, 1H), 4.11 (t, *J* = 7.6 Hz, 2H), 1.72 (sext, *J* = 7.6 Hz, 2H), 0.79 (t, *J* = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.1, 137.5, 132.2, 131.7, 130.9, 128.1, 122.2, 121.8, 120.6, 119.9, 110.1, 102.4, 45.6, 23.3, 11.3. IR (KBr): *v* 736, 750, 784, 831, 1009, 1071, 1313, 1346, 1383, 1402, 1459, 1596, 2854, 2873, 2926, 2960 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{17}H_{17}BrN^+$ 314.0539; Found 314.0536.

2-(4-Bromophenyl)-1-isopropyl-1H-indole (3ar). Purified by flash column chromatography (PE/DCM 15:1, *v/v*) on silica gel to give the desired product as white solid; Method A: 40 mg, 25%; Method B: 78 mg, 50%. M.p. 183–184 °C. R_F = 0.60, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.65–7.58 (m, 4H), 7.34–7.31 (m, 2H), 7.23–7.18 (m, 1H), 7.15–7.11 (m, 1H), 6.46 (s, 1H), 4.63 (hept, *J* = 7.2 Hz, 1H), 1.61 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 135.5, 132.6, 131.6, 131.1, 128.9, 122.2, 121.3, 120.9, 119.6, 112.4, 102.5, 48.0, 21.5. IR (KBr): *v* 684, 735, 752, 783, 834, 1002, 1013, 1099, 1172, 1306, 1345, 1358, 1369, 1388, 1406, 1460, 1665, 2852, 2872, 2929, 2971, 3046, 3076 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{17}H_{17}BrN^+$ 314.0539; Found 314.0543.

2-(4-Bromophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-i,j]quinolone (3as). Purified by flash column chromatography (PE/DCM 8:1, *v/v*) on silica gel to give the desired product as white solid; Method A: 62 mg, 40%; Method B: 125 mg, 80%. M.p. 262–264 °C. R_F = 0.59, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 7.4 Hz, 1H), 6.59 (s, 1H), 4.21 (t, *J* = 6.0 Hz, 2H), 2.95 (t, *J* = 6.0 Hz, 2H), 2.11 (quint, *J* = 6.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 138.0, 135.0, 131.7, 131.3, 130.1, 125.3, 122.2, 121.0, 119.7, 118.6, 117.5, 100.4, 43.3, 24.2, 22.7. IR (KBr): *v* 746, 791, 830, 1006, 1070, 1118, 1262, 1328, 1361, 1377, 1408, 1440, 1451, 1477, 2856, 2925, 2956, 3029, 3051 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{17}H_{15}BrN^+$ 312.0382; Found 312.0381.

N-(2-(4-Bromophenyl)-1H-indol-5-yl)acetamide (3at). Purified by flash column chromatography (DCM/MeOH 150:1, *v/v*) on silica gel to give the desired product as beige power; 121 mg, 74%; M.p. 290–291 °C. R_F = 0.56, 33% petroleum ether in ethyl acetate. ^1H NMR (400 MHz, DMSO-d_6) δ 11.48 (s, 1H), 9.75 (s, 1H), 7.89 (s, 1H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 6.90 (s, 1H), 2.04 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 167.6, 136.9, 133.9, 132.0, 131.8, 131.5, 128.4, 126.8, 120.2, 115.7, 111.1, 110.3, 99.4, 23.9. IR (KBr): *v* 746, 791, 830, 1006, 1070, 1118, 1262, 1328, 1361, 1377, 1408, 1440, 1451, 1540, 1680, 2856, 2925, 2956, 3029, 3051, 3300 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{14}BrN_2O^+$ 329.0284; Found 329.0281.

5-Bromo-2-(4-bromophenyl)-1H-indole (3au).[23] Purified by flash column chromatography (PE/EA 15:1, *v/v*) on silica gel to give the desired product as colorless solid; Method A: 27 mg, 15%; Method B: 25 mg, 14%. M.p. 216–218 °C. R_F = 0.46, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.74 (s, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.30–7.25 (m, 2H), 6.74 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.9, 135.5, 132.3, 130.9, 130.8, 126.7, 125.5, 123.2, 122.0, 113.6, 112.3, 100.0.

5-Methyl-2-phenyl-1H-indole (3bb).[24] Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as beige solid; Method A: 72 mg, 70%; Method B: 70 mg, 68%. M.p. 229–230 °C (Lit.[24] m.p. 210−212 °C). R_F = 0.71, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.38 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.30–7.27 (m, 3H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 1.2 Hz, 1H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 137.6, 135.5, 132.3, 128.8, 127.7, 127.2, 124.8, 123.2, 119.6, 112.5, 111.1, 98.2, 21.2.

5-Methyl-2-(p-tolyl)-1H-indole (3cb).[24] Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as white solid; 69 mg, 62%. M.p. 240–242 °C (Lit.[24] m.p. 240 °C). R_F = 0.78, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.40 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 1.6 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.1, 137.5, 135.0, 129.7, 129.7, 129.6, 129.4, 125.0, 123.7, 120.2, 110.4, 99.0, 21.5, 21.2.

2-(4-Fluorophenyl)-5-methyl-1H-indole (3db).[24] Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as white solid; 96 mg, 85%. M.p. 231–233 °C (Lit.[24] m.p. 218−219 °C). R_F = 0.71, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.37 (s, 1H), 7.88 (d, *J* = 5.6 Hz, 1H), 7.86 (d, *J* = 5.6 Hz, 1H),

7.31–7.27 (m, 4H), 6.92 (d, J = 8.4 Hz, 1H), 6.77 (s, 1H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 161.4 (d, $J_{C\text{-}F}$ = 245.4 Hz), 136.7, 135.4, 128.97 (d, $J_{C\text{-}F}$ = 3.0 Hz), 128.9, 127.8, 126.8 (d, $J_{C\text{-}F}$ = 8.1 Hz), 123.2, 119.6, 115.7 (d, $J_{C\text{-}F}$ = 21.2 Hz), 110.9, 98.2, 21.2. ^{19}F NMR (376 MHz, DMSO-d_6) δ -114.88.

2-(4-Chlorophenyl)-5-methyl-1H-indole (3eb).[25] Purified by flash column chromatography (PE/EA 30:1, *v/v*) on silica gel to give the desired product as white solid; 114 mg, 94%. M.p. 263–266 °C. R_F = 0.71, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.43 (s, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.30 (s, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.93 (dd, J = 8.4, 1.2 Hz, 1H), 6.83 (d, J = 1.2 Hz, 1H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 136.3, 135.6, 131.6, 131.2, 128.9, 128.8, 127.9, 126.5, 123.5, 119.7, 111.0, 98.8, 21.2.

2-(3-Bromophenyl)-5-methyl-1H-indole (3fb).[26] Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as white solid; Method A: 125 mg, 87%; Method B: 117 mg, 82%. M.p. 196–197 °C (Lit.[26] m.p. 189−190 °C). R_F = 0.73, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.79–7.78 (m, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.44–7.42 (m, 2H), 7.31–7.28 (m, 2H), 7.05 (dd, J = 8.0, 1.0 Hz, 1H), 6.76 (d, J = 1.2 Hz, 1H), 2.46 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 136.2, 135.3, 134.6, 130.5, 130.3, 129.8, 129.3, 128.0, 124.5, 123.5, 123.1, 120.5, 110.6, 100.6, 21.4.

2-(2-Bromophenyl)-5-methyl-1H-indole (3gb).[27] Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as beige solid; Method A: 79 mg, 55%; Method B: 82 mg, 57%. M.p. 125–127 °C. R_F = 0.71, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.69 (dd, J = 8.0, 1.2 Hz, 1H), 7.61 (dd, J = 7.6, 2.0 Hz, 1H), 7.46 (d, J = 0.8 Hz, 1H), 7.38 (td, J = 7.6, 1.2 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 7.1 (ddd, J = 8.0, 7.6, 1.2 Hz, 1H), 7.07 (dd, J = 8.4, 1.2 Hz, 1H), 6.75 (dd, J = 2.0, 0.8 Hz, 1H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 136.3, 134.6, 134.0, 133.6, 131.3, 129.4, 129.0, 128.4, 127.6, 124.3, 121.2, 120.3, 110.7, 103.2, 21.5.

4-(5-Methyl-1H-indol-2-yl)benzonitrile (3hb). Purified by flash column chromatography (PE/EA 25:1, *v/v*) on silica gel to give the desired product as beige solid; 114 mg, 98%. M.p. 218–220 °C. R_F = 0.58, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.61 (s, 1H), 8.01 (d, J = 8.0, 2H), 7.89 (d, J = 8.0, 2H), 7.34 (s, 1H), 7.31 (d, J = 8.4, 1H), 7.03 (s, 1H), 6.98 (d, J = 8.4, 1H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 136.6, 136.1, 135.5, 132.8, 128.6, 128.3, 125.2, 124.5, 120.1, 119.0, 111.3, 108.9, 101.1, 21.1. IR (KBr): v 792, 838, 1179, 1320, 1425, 1444, 1542, 1604, 2226, 2852, 2920, 3344 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd. for $C_{16}H_{13}N_2^+$ 233.1073; Found 233.1072.

5-Methyl-2-(naphthalen-1-yl)-1H-indole (3ib). Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as beige solid; Method A: 54 mg, 42%; Method B: 78 mg, 61%. M.p. 106–108 °C. R_F = 0.73, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.42 (s, 1H), 8.33–8.31 (m, 1H), 8.03–8.01 (m, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 6.8 Hz, 1H), 7.63–7.57 (m, 3H), 7.40 (s, 1H), 7.33 (d, J = 8.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.64 (s, 1H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 136.4, 135.0, 133.5, 131.0, 130.7, 128.6, 128.4, 128.0, 127.6, 127.1, 126.6, 126.0, 125.5, 125.4, 123.0, 119.5, 111.0, 102.0, 21.2. IR (KBr): v 686, 776, 792, 1009, 1023, 1110, 1308, 1325, 1394, 1455, 1508, 1588, 1593, 2855, 2924, 3014, 3045, 3398 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd. for $C_{19}H_{16}N^+$ 258.1277; Found 258.1279.

5-Methyl-2-(naphthalen-2-yl)-1H-indole (3jb). Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as beige solid; Method A: 61 mg, 47%; Method B: 98 mg, 76%. M.p. 210–212 °C. R_F = 0.68, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 8.35 (s, 1H), 8.01 (dd, J = 8.8, 1.2 Hz, 1H), 7.97 (d, J = 8.8 Hz, 1H), 7.93 (d, J = 3.2 Hz, 1H), 7.91 (d, J = 2.8 Hz, 1H), 7.55 (td, J = 7.2 Hz, J = 1.2 Hz, 1H), 7.50 (td, J = 7.2 Hz, J = 0.8 Hz, 1H), 7.34 (s, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.96–6.94 (m, 2H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 137.5, 135.7, 133.2, 132.2, 129.8, 128.9, 128.3, 127.8, 127.8, 127.6, 126.6, 125.9, 123.7, 123.4, 122.6, 119.7, 111.0, 99.1, 21.2. IR (KBr): v 749, 794, 823, 854, 1037, 1136, 1236, 1385, 1407, 1453, 1509, 1597, 1644, 2849, 2920, 2953, 3439 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd. for $C_{19}H_{16}N^+$ 258.1277; Found 258.1277.

2-(4-Bromophenyl)-3,5-dimethyl-1H-indole (3kb). The product was obtained by recrystallization from EA-PE as pink solid; Method A: 97 mg, 65%; Method B: 116 mg, 77%. M.p. 237–238 °C. R_F = 0.76, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, DMSO-d_6) δ 11.06 (s, 1H), 7.69 (d, J = 8.4, 2H), 7.60 (d, J = 8.4, 2H), 7.31 (s, 1H), 7.24 (d, J = 8.2, 1H), 6.94 (d, J = 8.2, 1H), 2.39 (s, 3H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 134.4, 132.5, 132.3, 131.6, 129.5, 129.2, 127.1, 123.5, 119.9, 118.1, 110.8, 107.0, 21.3, 9.8. IR (KBr): v 800, 1003, 1245, 1391, 1455, 1475, 1645, 3413 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd. for $C_{16}H_{15}BrN^+$ 300.0382; Found 300.0378.

2-Butyl-5-methyl-1H-indole (3lb).[28] Purified by flash column chromatography (PE/EA 50:1, *v/v*) on silica gel to give the desired product as colorless solid; Method A: 31 mg, 33%; Method B: 28 mg, 30%. M.p. 67–70 °C. R_F = 0.68, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.34 (s, 1H), 7.19 (d, J = 8.2 Hz, 1H), 6.96 (d, J = 8.2 Hz, 1H), 6.18 (d, J = 0.8 Hz, 1H), 2.74 (t, J = 7.8 Hz, 2H), 2.46 (s, 3H), 1.71 (quint, J = 7.8 Hz, 2H), 1.44 (sext, J = 7.8 Hz, 2H), 0.98 (t, J = 7.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.1, 134.1, 129.1, 128.7, 122.3, 119.5, 109.9, 99.0, 31.3, 28.0, 22.4, 21.4, 13.8.

5-Methyl-2-phenethyl-1H-indole (3mb). Purified by flash column chromatography (PE/DCM 50:1, *v/v*) on silica gel to give the desired product as colorless solid; Method A: 55 mg, 47%; Method B: 34 mg, 29%. M.p. 115–118 °C. R_F = 0.82, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.33–7.30 (m, 3H), 7.26–7.21 (m, 3H), 7.15 (d, J = 8.0, 1H), 6.94 (dd, J=8.4, 1.2, 1H), 6.20 (d, J=0.8, 1H), 3.09–3.01 (m, 4H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.2, 139.1, 134.1, 129.0, 128.8, 128.5, 128.4, 126.2, 122.6, 119.6, 109.9, 99.4, 35.7, 30.2, 21.4. IR (KBr): v 701, 779, 797, 1056, 1245, 1455, 2929, 2995, 3391 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd. for $C_{17}H_{18}N^+$ 236.1434; Found 236.1438.

Procedure for the synthesis of 3-(4-bromophenyl)-2-hydroxy-3-(phenylamino)propanenitrile (4). A solution of 3-(4-bromophenyl)oxirane-2-carbonitrile **1a** (112 mg, 0.5 mmol), aniline **2a** (69.8 mg, 0.75 mmol) and BF_3•OEt_2 (17.7 µL, 0.125 mmol) in 5 mL of EtOH was refluxed for 11 h under open air conditions. After cooling to room temperature, the crude solution was quenched with water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was dried over

Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (PE/EA 8:1, *v/v*) to afford the corresponding 3-(4-bromophenyl)-2-hydroxy-3-(phenylamino)propanenitrile (**4**) 87 mg, 55% yield. R_F = 0.82, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.2, 2H), 7.21 (d, *J* = 8.2, 2H), 7.05 (t, *J* = 7.8, 2H), 6.69 (t, *J* = 7.2, 1H), 6.51 (d, *J* = 8.0, 2H), 4.57 (d, *J* = 6.0, 1H), 4.54 (d, *J* = 6.0, 1H), 4.01 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.3, 135.7, 132.3, 129.4, 129.1, 123.0, 119.5, 117.8, 114.6, 65.1, 60.6. IR (KBr): *v* 692, 754, 829, 1010, 1070, 1263, 1315, 1403, 1434, 1504, 1602, 2247 (CN), 2929, 3052, 3388 (br s, OH, NH) cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{15}H_{12}BrN_2O^+$ 317.0284; Found 317.0291.

Procedure for the synthesis of 1-ethyl-5-methoxy-2-(4-methoxyphenyl)-3-methyl-*1*H-indole (5).

Method A. A solution of 3-(4-methoxyphenyl)-2-methyloxirane-2-carbonitrile (**1n)** (94.6 mg, 0.5 mmol), 4-methoxyaniline (**2e)** (92.3 mg, 0.75 mmol) and BF_3•OEt_2 (11.3 μL, 0.08 mmol) in 5 mL of EtOH/TEF (3:7 *v/v*) mixed solvent was refluxed for 20 h under open air conditions. After cooling to room temperature, the crude solution was concentrated *in vacuo* and then purified by flash column chromatography on silica gel using dichloromethane (DCM) as eluent to afford the crude 5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole (**3ne**). **3ne** was dissolved in 3 mL of anhydrous DMF. The solution was cooled to 0 ºC. 36 mg (0.75 mmol) of NaH (50% oil suspension) was added. After stirring for 30 min a solution of 65 mg (0.6 mmol) of ethyl bromide in 2 mL of anhydrous DMF was added. After the reaction mixture was stirred at room temperature for 3 h, the mixture was quenched with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layer was washed with brine (3 × 20 mL), and then dried over Na_2SO_4. The resulting mixture was concentrated *in vacuo* and purified by flash column chromatography on silica gel (PE/EA 50:1, *v/v*) to afford the white solid 1-ethyl-5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole (**5**) as colorless solid 87 mg, 59% yield.

Method B. A solution of 3-(4-methoxyphenyl)-2-methyloxirane-2-carbonitrile (**1n)** (94.6 mg, 0.5 mmol), 4-methoxyaniline (**2e)** (117 mg, 0.95 mmol), and $AlCl_3$ (6.7 mg, 0.05 mmol) in 5 mL of TFE was refluxed for 30 h under open air conditions. After cooling to room temperature, the crude solution was concentrated *in vacuo* and then purified by flash column chromatography on silica gel using dichloromethane (DCM) as eluent to afford the crude 5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole (**3ne**). **3ne** was dissolved in 3 mL of anhydrous DMF. The solution was cooled to 0 ºC. 36 mg (0.75 mmol) of NaH (50% oil suspension) was added. After stirring for 30 min a solution of 65 mg (0.6 mmol) of ethyl bromide in 2 mL of anhydrous DMF was added. The reaction was stirred at room temperature for 3 h. Then the mixture was quenched with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layer was washed with brine (3 × 20 mL), and then dried over Na_2SO_4. The resulting mixture was concentrated *in vacuo* and purified by flash column chromatography on silica gel using ethyl acetate/petroleum ether (1/50, *v/v*) as eluent to afford white solid 1-ethyl-5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole (**5**) as colorless solid 128 mg, 87% yield.

Gram-scale reaction was conducted on a 10 mmol scales reaction in 50 mL solvent, affording 1.72 g, 58% yield. M.p. 124–125 ºC (Lit.[29] m.p. 124−126 ºC). R_F = 0.71, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6, 2H), 7.24 (d, *J* = 8.8, 1H), 7.03 (d, *J* = 2.4, 1H), 7.01 (d, *J* = 8.6, 2H), 6.88 (dd, *J* = 8.8, 2.4, 1H), 4.01 (q, *J* = 7.2, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 2.19 (s, 3H), 1.18 (t, *J* = 7.2, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.2, 153.9, 137.8, 131.6, 131.2, 128.9, 124.8, 113.8, 111.4, 110.1, 108.1, 100.8, 56.1, 55.3, 38.6, 15.4, 9.3.

General procedure for the synthesis of compounds 1. All oxirane-2-carbonitriles **1** were prepared with the literature reported method.[30] A solution of chloroacetonitrile (1.81 g, 24 mmol) or 2-chloropropanenitrile (2.15 g, 24 mmol), KOH (1.35 g, 24 mmol) in 75 mL of THF was added an aldehyde (20 mmol) in one jet. The reaction mixture was stirred at room temperature for 24 h. After the mixture solution was concentrated *in vacuo*, extracted with ethyl acetate-water, the combined organic phase was dried over anhydrous Na_2SO_4. After filtered and concentrated *in vacuo* the residue was purified by flash column chromatography on silica gel (PE/EA 30:1, *v/v*) to afford the corresponding oxirane-2-carbonitrile **1**.

cis-3-(4-Bromophenyl)oxirane-2-carbonitrile (1a).[31] Colorless crystals, 1.542 g, 34%. M.p. 105−106 ºC (Lit.[31] 96–97 ºC). R_F = 0.50, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.22 (d, *J* = 3.6 Hz, 1H), 3.79 (d, *J* = 3.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 131.9, 130.4, 127.9, 124.0, 114.7, 57.2, 45.0.

cis-3-Phenyloxirane-2-carbonitrile (1b).[32] Colorless crystals, 0.934 g, 32%. M.p. 60−61 ºC (Lit.[32] 55–56 ºC). R_F = 0.62, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 5H), 4.25 (d, *J* = 3.6 Hz, 1H), 3.78 (d, *J* = 3.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 131.3, 129.7, 128.6, 126.3, 115.0, 57.7, 45.1.

cis-3-(p-Tolyl)oxirane-2-carbonitrile (1c).[32] Colorless crystals, 509 mg, 16%. M.p. 56−58 ºC. R_F = 0.68, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.22 (d, *J* = 3.8 Hz, 1H), 3.76 (d, *J* = 3.8 Hz, 1H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 139.7, 129.4, 128.3, 126.2, 115.1, 57.7, 45.1, 21.3.

trans-3-(4-Fluorophenyl)oxirane-2-carbonitrile (1d). Colorless crystals, 1.14 g, 35%. M.p. 62−63 ºC. R_F = 0.78, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H), 7.12–7.06 (m, 2H), 4.28 (d, *J* = 1.6 Hz, 1H), 3.39 (d, *J* = 1.8 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.5 (d, $J_{C\text{-}F}$ = 250.5 Hz), 128.5 (d, $J_{C\text{-}F}$ = 3.0 Hz), 127.5 (d, $J_{C\text{-}F}$ = 9.1 Hz), 116.1 (d, $J_{C\text{-}F}$ = 22.2 Hz), 115.7, 57.9, 44.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.73. IR (KBr): *v* 1102, 1120, 1246, 1442, 1518, 1610, 2244, 3033 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_9H_7FNO^+$ 164.0506; Found 164.0510.

cis-3-(4-Chlorophenyl)oxirane-2-carbonitrile (1e).[33] Colorless crystals, 790 mg, 22%. M.p. 87−88 ºC (Lit.[34] 79–81 ºC). R_F = 0.6, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 4.23 (d, *J* = 3.8 Hz, 1H), 3.79 (d, *J* = 3.8 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 135.8, 129.9, 129.0, 127.7, 114.7, 57.1, 45.0.

trans-3-(3-Bromophenyl)oxirane-2-carbonitrile (1f). Colorless crystals, 1.1 g, 25%. M.p. 60−61 ºC. R_F = 0.53, 33% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.54 (m, 2H), 7.35–7.26 (m, 2H), 4.21 (s, 1H), 3.78 (d, *J* = 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 133.7, 132.8,

130.3, 129.5, 124.7, 122.7, 114.5, 56.8, 44.9. IR (KBr): *v* 1050, 1070, 1116, 1187, 1241, 1258, 1433, 1475, 1570, 1599, 2249, 2925, 3030 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_9H_7BrNO^+$ 223.9706; Found 223.9704.

***cis/trans*-3-(2-Bromophenyl)oxirane-2-carbonitrile (1g).** Colorless oil, 3.58 g, 80%. R_F = 0.73, 33% ethyl acetate in petroleum ether. *cis:trans* = 44:56; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62–7.58 (m, 1H), 7.42–7.24 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 4.56 (d, *J* = 1.4 Hz, 1H) (*trans*-isomer), 4.46 (d, *J* = 3.6 Hz, 1H) (*cis*-isomer), 3.86 (d, *J* = 3.6 Hz, 1H) (*cis*-isomer), 3.31 (d, *J* = 1.4 Hz, 1H) (*trans*-isomer). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 132.8, 132.7, 132.6, 131.5, 130.9, 130.8, 127.9, 127.7, 127.4, 126.1, 122.7, 122.5, 115.7, 114.6, 58.3, 57.7, 44.5, 44.0. IR (KBr): *v* 752, 800, 1027, 1101, 1160, 1192, 1237, 1442, 1474, 1570, 1593, 2248, 2853, 2924 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_9H_7BrNO^+$ 223.9706; Found 223.9711.

***cis*-3-(4-Cyanophenyl)oxirane-2-carbonitrile (1h).**[35] Colorless crystals, 578 mg, 17%. M.p. 113−115 °C. R_F = 0.30, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 4.31 (d, *J* = 3.8 Hz, 1H), 3.86 (d, *J* = 3.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 136.6, 132.5, 127.1, 118.1, 114.3, 113.7, 56.8, 45.0.

***cis*-3-(Naphthalen-1-yl)oxirane-2-carbonitrile (1i).** Colorless crystals, 312 mg, 8%. M.p. 76−77 °C. R_F = 0.63, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 8.00–7.98 (m, 1H), 7.96–7.91 (m, 2H), 7.63–7.52 (m, 4H), 4.84 (d, *J* = 3.6 Hz, 1H), 3.99 (d, *J* = 3.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 133.3, 130.9, 129.8, 129.1, 127.4, 127.0, 126.3, 125.3, 123.7, 121.9, 114.9, 56.1, 44.8. IR (KBr): *v* 796, 886, 1028, 1056, 1123, 1160, 1216, 1256, 1459, 1512, 1597, 2248, 2924, 2955 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{13}H_{10}NO^+$ 196.0757; Found 176.0754.

***cis*-3-(Naphthalen-2-yl)oxirane-2-carbonitrile (1j).**[33] colorless crystals, 741 mg, 19%. M.p. 137−139 °C. R_F = 0.58, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93–7.86 (m, 4H), 7.56–7.52 (m, 2H), 7.49 (dd, *J* = 8.4, 1.6 Hz, 1H), 4.42 (d, *J* = 3.8 Hz, 1H), 3.86 (d, *J* = 3.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 133.9, 132.9, 128.8, 128.7, 128.1, 127.9, 126.9, 126.7, 126.3, 123.0, 115.0, 57.9, 45.2.

***3*-(4-Bromophenyl)-2-methyloxirane-2-carbonitrile (1k).** Colorless crystals, 1.05 g, 22%. M.p. 88−89 °C. R_F = 0.60, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.6, 2H), 7.27 (d, *J* = 8.6, 2H), 3.96 (s, 1H), 1.78 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 131.8, 131.2, 127.9, 123.7, 116.8, 63.5, 53.4, 20.7. IR (KBr): *v* 1010, 1067, 1420, 1451, 1490, 1594, 2244, 2938, 2996 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{10}H_9BrNO^+$ 237.9862; Found 237.9857.

***cis/trans*-3-Butyloxirane-2-carbonitrile (1l).** Colorless oil, 1.16 g, 31%. B.p. 192−195 °C. *cis:trans* = 23:77; ^1H NMR (400 MHz, $CDCl_3$) δ 3.45 (d, *J* = 3.6 Hz) & 3.33 (d, *J* = 2.0 Hz, 1H), 3.20–3.15 (m, 1H), 1.66–1.51 (m, 2H), 1.49–1.33 (m, 4H), 0.97–0.90 (m, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 116.7 &115.9, 59.1 & 57.4, 41.7 & 40.9, 30.7 & 29.4, 27.8 & 27.3, 22.3 & 22.2, 13.8. IR (KBr): *v* 800, 860, 1056, 1096, 1244, 1381, 1466, 2248, 2931, 2960 cm^{-1}. HR-MS (ESI) *m/z*, calcd. for $C_7H_{12}NO^+$ ($[M + H]^+$): 126.0913; Found: 126.0912.

***cis*-3-Phenethyloxirane-2-carbonitrile (1m).** Colorless oil, 0.97 g, 28%. R_F = 0.56, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.2 Hz, 2H), 7.25–7.22 (m, 3H), 3.43 (d, *J* = 3.6 Hz, 1H), 3.21–3.18 (m, 1H), 2.95–2.82 (m, 2H), 2.13–2.07 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.8, 128.7, 128.4, 126.5, 115.7, 56.7, 41.9, 31.9, 31.4. IR (KBr): *v* 751, 792, 1010, 1029, 1251, 1383, 1421, 1455, 1515, 1603, 2246, 2925, 2953, 3028 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{11}H_{12}NO^+$ 174.0913; Found 174.0922.

***3*-(4-Methoxyphenyl)-2-methyloxirane-2-carbonitrile (1n).** colorless oil, 2.21 g, 58%. R_F = 0.71, 33% ethyl acetate in petroleum ether. ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J*=8.8, 2H), 6.92 (d, *J*=8.8, 2H), 4.42 (s, 1H), 3.82 (s, 3H), 1.39 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.2, 128.0, 123.1, 119.3, 114.0, 62.8, 55.3, 50.0, 15.1. IR (KBr): *v* 776, 812, 1031, 1077, 1112, 1173, 1248, 1384, 1443, 1460, 1514, 1584, 1613, 2241, 2934, 2961 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{11}H_{12}NO_2^+$ 190.0863; Found 190.0869.

Synthesis of compound 6.[36a] 2-(4-Bromophenyl)-2-(phenylamino)ethan-1-ol (**6**) was prepared on a 10 mmol scale reaction according to the literature reported method,[36b] giving the product 331 mg, 11% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4, 2H), 7.24 (d, *J* = 8.4, 2H), 7.10 (t, *J* = 7.6, 2H), 6.69 (t, *J* = 7.6, 2H), 6.52 (d, *J* = 7.6, 1H), 4.50 (s, 1H), 4.43 (dd, *J* = 6.8, 4.0, 1H), 3.90 (dd, *J* = 11.2, 4.0, 1H), 3.70 (dd, *J* = 11.2, 6.8, 1H), 1.84 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.9, 139.3, 131.9, 129.2, 128.5, 121.4, 118.1, 113.8, 67.1, 59.4.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Table S1 and Table S2 on optimizations of reaction conditions, copies of ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra for all isolated compounds (PDF)

AUTHOR INFORMATION

Corresponding Author

* E-mail: jxxu@mail.buct.edu.cn.

ORCID

Jiaxi Xu: 0000-0002-9039-4933;
Chuangchuang Xu: 0000-0002-7383-2313.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was supported by the National Natural Science Foundation of China (Nos. 21572017 and 21372025).

REFERENCES

1. (a) Tanner, M. E. Mechanistic Studies on the Indole Prenyltransferases. *Nat. Prod. Rep.* **2015**, *32*, 88-101. (b) Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S. Simple Indole Alkaloids and Those with a Non-rearranged Monoterpenoid Unit. *Nat. Prod. Rep.* **2015**, *32*, 1389-1471. (c) Xu, W.; Gavia, D. J.; Tang, Y. Biosynthesis of Fungal Indole Alkaloids. *Nat. Prod. Rep.* **2014**, *31*, 1474-1487. (d) Ishikura, M.; Yamada, K.; Abe, T. Simple Indole Alkaloids and Those with a Nonrearranged Monoterpenoid Unit. *Nat. Prod. Rep.* **2010**, *27*, 1630-1680.

2. For recent reviews see: (a) Konopelski, P.; Ufnal, M. Meet Our Editorial Board Member. *Curr. Drug. Metab.* **2018**, *19*, 1-8. (b) Sravanthi, T. V.; Manju, S. L. Indoles-A Promising Scaffold for Drug Development. *Eur. J. Pharm. Sci.* **2016**, *91*, 1-10. (c) Kaushik, N. K.; Kaushik, N.; Attri, P.; Kumar, N.; Kim, C. H.; Verma, A. K.; Choi, E. H. Biomedical Importance of Indoles. *Molecules* **2013**, *18*, 6620-6662. (d) Kochanowska-Karamyan, A. J.; Hamann, M. T. Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and

Anxiety. *Chem. Rev.* **2010**, *110*, 4489-4497. (e) Liu, Y.; Ai, K.; Lu, L. Polydopamine and Its Derivative Materials: Synthesis and Promising Applications in Energy, Environmental, and Biomedical Fields. *Chem. Rev.* **2014**, *114*, 5057-5115. (f) Ates-Alagoz, Z. Antioxidant Activities of Retinoidal Benzimidazole or Indole Derivatives in In Vitro Model Systems. *Curr. Med. Chem.* **2013**, *20*, 4633-4639. For selected examples see: (g) Kaufmann, D.; Pojarova, M.; Vogel, S.; Liebl, R.; Gastpar, R.; Gross, D.; Nishino, T.; Pfaller, T.; von Angerer, E. Antimitotic Activities of 2-Phenylindole-3-carbaldehydes in Human Breast Cancer Cells. *Bioorg. Med. Chem.* **2007**, *15*, 5122-5136. (h) Von Angerer, E.; Prekajac J.; Berger M. The Inhibitory Effect of 5-Acetoxy-2-(4-acetoxyphenyl)-1-ethyl-3-methylindole (D 16726) on Estrogen-Dependent Mammary Tumors. *Eur. J. Cancer. Clin. Oncol.* **1985**, *21*, 531-537. (i) Von Angerer, E.; Prekajac, J.; Strohmeier, J. 2-Phenylindoles. Relationship Between Structure, Estrogen Receptor Affinity, and Mammary Tumor Inhibiting Activity in the Rat. *J. Med. Chem.* **1984**, *27*, 1439-1447.

3. Baeyer, A. Ueber die Reduction aromatischer Verbindungen mittelst Zinkstaub. *Ann. Chem. Pharm.* **1866**, *140*, 295-296.

4. Fischer, E. J., F. Ueber die Hydrazine der Brenztraubensäure. *Ber. Dtsch. Chem. Ges.***1883**, *16*, 2241−2245.

5. Street, L. J.; Baker, R.; Castro, J. L.; Chambers, M. S.; Guiblin, A. R.; Hobbs, S. C.; Matassa, V. G.; Reeve, A. J.; Beer, M. S. Synthesis and Serotonergic Activity of 5-(Oxadiazolyl)tryptamines: Potent Agonists for 5-HT1D Receptors. *J. Med. Chem.* **1993**, *36*, 1529-1538.

6. Houlihan, W. J.; Parrino, V. A.; Uike, Y. Lithiation of *N*-(2-alkylphenyl)alkanamides and Related Compounds. A Modified Madelung Indole Synthesis. *J. Org. Chem.* **1981**, *46*, 4511-4515.

7. Nordlander, J. E.; Catalane, D. B.; Kotian, K. D.; Stevens, R. M.; Haky, J. E. Synthesis of Indoles from *N*-(trifluoroacetyl)-2-anilino acetals. *J. Org. Chem.* **1981**, *46*, 778-782.

8. For reviews see: (a) Taber, D. F.; Tirunahari, P. K. Indole Synthesis: A Review and Proposed Classification. *Tetrahedron* **2011**, *67*, 7195-7210. (b) Inman, M.; Moody, C. J. Indole Synthesis-Something Old, Something New. *Chem. Sci.* **2013**, 4, 29. For selected examples see: (c) Fürstner, A.; Ernst, A. Syntheses of Camalexin, Indolopyridocoline and Flavopereirine. *Tetrahedron* **1995**, *51*, 773-786. (d) Fukuyama, T.; Chen, X.; Peng, G. A Novel Tin-Mediated Indole Synthesis. *J. Am. Chem. Soc.* **1994**, *116*, 3127-3128. (e) Bartoli, G.; Palmieri, G.; Bosco, M.; Dalpozzo, R. The Reaction of Vinyl Grignard Reagents with 2-Substituted Nitroarenes: A New Approach to the Synthesis of 7-Substituted Indoles. *Tetrahedron Lett.* **1989**, *30*, 2129-2132. (f) Gassman, P. G.; Roos, J. J.; Lee, S. J. Use of [2,3]-Sigmatropic Rearrangements in A One-step Conversion of Tetrahydroquinoline to Substituted 1,2,5,6-Eetrahydro-4*N*-pyrrolo[3,2,1-ij]quinolin-2-one and 5,6-Dihydro-4*H*-pyrrolo[3,2,1-ij]quinoline. *J. Org. Chem.* **1984**, *49*, 717-718.

9. (a) Xu, F.; Li, Y.-J.; Huang, C.; Xu, H.-C. Ruthenium-Catalyzed Electrochemical Dehydrogenative Alkyne Annulation. *ACS Catal.* **2018**, *8*, 3820-3824. (b) Fan, Z.; Lu, H.; Li, W.; Geng, K.; Zhang, A. Rhodium-Catalyzed Redox-Neutral Coupling of Phenidones with Alkynes. *Org. Biomol. Chem.* **2017**, *15*, 5701-5708. (c) Fan, Z.; Song, S.; Li, W.; Geng, K.; Xu, Y.; Miao, Z. H.; Zhang, A. Rh^{III}-Catalyzed Redox-Neutral C–H Activation of Pyrazolones: An Economical Approach for the Synthesis of *N*-Substituted Indoles. *Org. Lett.* **2015**, *17*, 310-313. (d) Stuart, D. R.; Bertrand-Laperle, M.; Burgess, K. M. N.; Fagnou, K. Indole Synthesis via Rhodium Catalyzed Oxidative Coupling of Acetanilides and Internal Alkynes. *J. Am. Chem. Soc.* **2008**, *130*, 16474-16475.

10. For recent reviews see: (a) Yang, Y.; Shi, Z. Regioselective Direct Arylation of Indoles on The Benzenoid Moiety. *Chem. Commun.* **2018**, *54*, 1676-1685. (b) Pirovano, V. Gold-Catalyzed Functionalization Reactions of Indole. *Eur. J. Org. Chem.* **2018**, *17*, 1925-1945. (c) Leitch, J. A.; Bhonoah, Y.; Frost, C. G. Beyond C2 and C3: Transition-Metal-Catalyzed C–H Functionalization of Indole. *ACS Catal.* **2017**, *7*, 5618-5627. For selected examples see: (d) Zhou, L.; Zhu, C.; Loh, T. P.; Feng, C. Rh-Catalyzed C–H Bond Alkylation of Indoles with α,α-Difluorovinyl Tosylate *via* Indolyl Group Migration. *Chem. Commun.* **2018**, *54*, 5618-5621. (e) Nareddy, P.; Jordan, F.; Szostak, M. Ruthenium(II)-Catalyzed Direct C–H Arylation of Indoles with Arylsilanes in Water. *Org. Lett.* **2018**, *20*, 341-344. (f) Guo, T.; Huang, F.; Yu, L.; Yu, Z. Indole Synthesis Through Transition Metal-Catalyzed C–H Activation. *Tetrahedron Lett.* **2015**, *56*, 296-302.

11. Pena-Lopez, M.; Neumann, H.; Beller, M. Ruthenium−Catalyzed Synthesis of Indoles from Anilines and Epoxides. *Chem.-Eur. J.* **2014**, *20*, 1818-1824.

12. Nishida, T.; Tokuda, Y.; Tsuchiya, M. Synthesis of 1-Substituted Indoles by The Vapour Phase Reaction of *N*-substituted Anilines with Glycols and Epoxides over A Solid Catalyst and A Vapour Phase Dealkylation of 1-Alkylindole. *J. Chem. Soc., Perkin Trans. 2*, **1995**, *4*, 823-830.

13. Cho, C. S.; Kim, J. H.; Choi, H.-J.; Kim, T.-J.; Shim, S. C. Ruthenium-Catalyzed Regioselective Synthesis of 2-Substituted Indoles via Ring-opening of Epoxides by Anilines. *Tetrahedron Lett.* **2003**, *44*, 2975-2977.

14. Rodrigues, I.; Bonnet-Delpon, D.; Bégué, J.-P. 1-Trifluoromethyl Epoxy Ethers. Effect of Hexafluoro-2-propanol on Reactions with Secondary Aromatic Amines: Synthesis of 3-Trifluoromethyl Indole Derivatives. *J. Org. Chem.* **2001**, *66*, 2098-2103.

15. (a) Kumar, M. P.; Liu, R. S. $Zn(OTf)_2$-Catalyzed Cyclization of Proparyl Alcohols with Anilines, Phenols, and Amides for Synthesis of Indoles, Benzofurans, and Oxazoles through Different Annulation Mechanisms. *J. Org. Chem.* **2006**, *71*, 4951-4955. (b) Campanati, M.; Franceschini, S.; Piccolo, O.; Vaccari, A. Reaction Pathway in the Vapour-Phase Synthesis of Indole and Alkylindoles. *J. Catal.* **2005**, *232*, 1-9.

16. For a review, see: (a) Zhou, C.; Xu, J. X. Regioselective Nucleophilic Ring Opening Reactions of Unsymmetric Oxiranes. *Prog. Chem.* **2011**, *23*, 174–189. For examples, see: (b) Li, X. Y.; Yang, Z. Y.; Xu, J. X. Comprehensive Theoretical Investigation on the Regioselectivity in the Nucleophilic Ring Opening of Epoxides. *Curr. Org. Synth.* **2013**, *10*, 169–177. (c) Li, X. Y.; Xu, J. X. Theoretical Calculational Investigation on the Regioselectivity of the Ring Opening of Thiiranes with Ammonia and Amines. *Tetrahedron* **2011**, *67*, 1681–1688. (d) Yu, H.; Cao, S. L.; Zhang, L. L.; Liu, G.; Xu, J. X. Synthesis of α-Aliphatic and β-Aromatic Substituted Taurines via Regioselective Ring Opening of Thiiranes with Ammonia. *Synthesis* **2009**, *(13)*, 2205–2209.

17. (a) Hou, S. L.; Li, X. Y., Xu, J. X. Mechanistic Insight into the Formal [1,3]-Migration in the Thermal Claisen Rearrangement. *J. Org. Chem.* **2012**, *77*, 10856–10869. (b) Hou, S. L.; Li, X. Y.; Xu, J. X. *N*[1,3]-Sigmatropic Shift in the Benzidine Rearrangement: Experimental and Theoretical Investigation. *Org. Biomol. Chem.* **2014**, *12*, 4952–4963. (c) Yang, Z. H.; Hou, S. L.; He, W., Cheng, B. X.; Jiao, P.; Xu, J. X. Regioselectivity of the *ortho*- and *para*-Semidine, and Diphenyline Rearrangements. *Tetrahedron* **2016**, *72*, 2186–2195. (d) Xu, J. X. Diversity and Chemoselectivity in the Acid-Catalyzed Rearrangements of *N*, *N'*-Diarylhydrazines. *Curr. Org. Synth.* **2017**, *14*, 511–530.

18. Von Angerer, E.; Prekajac, J.; Strohmeier, J. 2-Phenylindoles. Relationship Between Structure, Estrogen Receptor Affinity, and Mammary Tumor Inhibiting Activity in the Rat. *J. Med. Chem.* **1984**, *27*, 1439-1447.

19. Joucla, L.; Batail, N.; Djakovitch, L. "On Water" Direct and Site-Selective Pd-Catalysed C-H Arylation of (NH)-Indoles. *Adv. Synth. Cat.* **2010**, *352*, 2929-2936.

20. Wang, X.; Gribkov, D. V.; Sames, D. Phosphine-free Palladium-Catalyzed C-H Bond Arylation of Free (N-H)-Indoles and Pyrroles. *J. Org. Chem.* **2007**, *72*, 1476-1479.

21. Wei, Y.; Deb, I.; Yoshikai, N. Palladium-Catalyzed Aerobic Oxidative Cyclization of *N*-Aryl Imines: Indole Synthesis from Anilines and Ketones. *J. Am. Chem. Soc.* **2012**, *134*, 9098-9101.

22. Lebrasseur, N.; Larrosa, I. Room Temperature and Phosphine Free Palladium Catalyzed Direct C-2 Arylation of Indoles. *J. Am. Chem. Soc.* **2008**, *130*, 2926-2927.

23. Yu, S.; Qi, L.; Hu, K.; Gong, J.; Cheng, T.; Wang, Q.; Chen, J.; Wu, H. The Development of a Palladium-Catalyzed Tandem Addition/Cyclization for the Construction of Indole Skeletons. *J. Org. Chem.* **2017**, *82*, 3631-3638.

24. Jin, Z.; Guo, S.-X.; Qiu, L.-L.; Wu, G.-P.; Fang, J.-X. Well-defined NHC-Pd Complex-Mediated Intermolecular Direct Annulations

for Synthesis of Functionalized Indoles (NHC = *N*-hetero-cyclliccarbene). *Appl. Organometal. Chem.* **2011**, *25*, 502-507.
25. Pena-Lopez, M.; Neumann, H.; Beller, M. Ruthenium-Catalyzed Synthesis of Indoles from Anilines and Epoxides. *Chem.-Eur. J.* **2014**, *20*, 1818-1824.
26. Alverez, C.; Arkin, M. R.; Bulfer, S. L.; Colombo, R.; Kovaliov, M.; LaPorte, M. G.; Lim, C.; Liang, M.; Moore, W. J.; Neitz, R. J.; Yan, Y.; Yue, Z.; Huryn, D. M.; Wipf, P. Structure–Activity Study of Bioisosteric Trifluoromethyl and Pentafluorosulfanyl Indole Inhibitors of the AAA ATPase p97. *ACS Med. Chem. Lett.* **2015**, *6*, 1225-1230.
27. Sang, P.; Xie, Y.; Zou, J.; Zhang, Y. Copper-Catalyzed Sequential Ullmann *N*-Arylation and Aerobic Oxidative C–H Amination: A Convenient Route to Indolo[1,2-*c*]quinazoline Derivatives. *Org. Lett.* **2012**, *14*, 3894-3897.
28. Lai, R.-Y.; Surekha, K.; Hayashi, A.; Ozawa, F.; Liu, Y.-H.; Peng, S.-M.; Liu, S.-T. Intra- and Intermolecular Hydroamination of Alkynes Catalyzed by *ortho*-Metalated Iridium Complexes**.** *Organometallics* **2007**, *26*, 1062-1068.
29. Anna Kaczor, A.; Kronbach, C.; Unverferth, K.; Pihlaja, K.; Wiinamaki, K.; Sinkkonen, J.; Kijkowska-Murak, U.; Wrobel, T.; Stachal, T.; Matosiuk, D. Novel Non-Competitive Antagonists of Kainate GluK1/GluK2 Receptors. *Lett. Drug Des. Disc.* **2012**, *9*, 891-898.
30. Mhamdi, L.; Bohli, H.; Moussaoui, Y.; Salem, R. b. Phase Transfer Catalysis of Henry and Darzens Reaction. *Int. J. Org. Chem.* **2011**, *1*, 119-124.
31. Zagozda, M.; Plenkiewicz, J. Biotransformations of 2,3-Epoxy-3-arylpropanenitriles by *Debaryomyces hansenii* and *Mortierella isabellina* Cells. *Tetrahedron: Asymmetry* **2008**, *19*, 1455-1460.
32. Annese, C.; D'Accolti, L.; Dinoi, A.; Fusco, C.; Gandolfi, R.; Curci, R. Concerning the Reactivity of Dioxiranes. Observations from Experiments and Theory. *J. Am. Chem. Soc.* **2008**, *130*, 1197-1204.
33. Quinodoz, P.; Lo, C.; Kletskii, M.; Burov, O.; Marrot, J.; Couty, F. Regio- and Stereoselective Synthesis of α-Hydroxy-β-azido Tetrazoles. *Org. Chem. Front.* **2015**, *2*, 492-496.
34. Svoboda, J.; Kocfeldová, Z.; Paleček, J. Reaction of 4-Substituted Benzaldehydes and Acetophenones with Chloroacetonitrile. *Collect. Czech. Chem. Commun.* **1988**, *53*, 822-832.
35. Jonczyk, A. Gadaj, A. Expedient Synthesis of Glycidonitriles by Darzens Condensation of α-Halo Nitriles with Aldehydes and Ketones. *Polish J. Chem.* **2007**, *81*, 1595-1610.
36. (a) Mukherjee, A.; Dateer, R. B.; Chaudhuri, R.; Bhunia, S.; Karad, S. N.; Liu, R. S. Gold-Catalyzed 1,2-Difunctionalizations of Aminoalkynes Using Only *N*- and *O*-Containing Oxidants**.** *J. Am. Chem. Soc.* **2011**, *133*, 15372-15375. (b) Bansal, S.; Kumar, Y.; Pippal, P.; Das, D. K.; Pramanik, P.; Singh, P. P. An Efficient Method for Regioselective Ring Opening of Epoxides by Amines under Microwave Irradiation using $Bi(NO_3)_3{\cdot}5H_2O$ as A Catalyst. *New J. Chem.* **2017**, *41*, 2668-2671.