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SmI_2 mediated synthesis of 2,3-disubstituted indole derivatives

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Abstract—A novel preparation of 2,3-disubstituted indole derivatives was achieved through SmI_2 induced intramolecular reductive coupling reactions of acylamido carbonyl compounds.

1. Introduction

The substituted indole nucleus is prevalent in natural products[1] and important in medicinal chemistry.[2] Many procedures have been reported for the preparation of indoles,[3] among them, the Fischer indole synthesis is the most commonly used route and has been extensively reviewed.[4] Bischler synthesis[5] and Madelung synthesis[6] are also popular routes for indole synthesis. Recently, Furstner has reported that indoles can also be obtained through low-valent titanium induced intramolecular McMurry type reactions of suitably substituted acylamido carbonyl compounds.[7] However, due to the unavailability of some patterns of indole substitution using classical methods and the need for efficient ways to synthesize more elaborate structures possessing biological activity, the development of novel and convenient methods for the preparation of indole derivatives still remains an active research area.[8]

Since pioneering work by Kagan and following investigation by other scientists, samarium(II) iodide has been shown to be an exceptionally efficient reagent for the promotion of reductive coupling reactions.[9] For instance, pinacol coupling reactions,[10] ketyl-olefin coupling reactions,[11] ketone-nitrile cross-coupling reactions[12] and ketone-ester reductive coupling reactions[13] have been reported using SmI_2 as the reagent. Recently we have also reported that SmI_2 together with metallic samarium can promote the intermolecular deoxygenative coupling reaction of diarylketones and *N*,*N*-disubstituted arylamides to give enamines under reflux conditions.[14] Unfortunately, this process necessitates the use of excessive amounts of metallic samarium and is only suitable for *N*,*N*-disubstituted arylamides and failed with alkylamides.

Herein we wish to report that SmI_2 can efficiently promote the intramolecular reductive coupling reactions of suitably substituted acylamido carbonyl compounds (**1**) to give 2,3-disubstituted indoles (**2**) or 2,3-disubstituted-2,3-dihydro-1H-indole-2,3-diols (**3**) as the main products depending on the starting materials, the reaction temperature and the amount of SmI_2 used (shown in Scheme 1).

2. Results and discussion

2.1. SmI_2 induced intramolecular reductive coupling reactions of 2-arylamidobenzophenone

When 1 equiv. of 2-benzamidobenzophenone (Scheme 2, **1a**) was added to 2 equiv. of SmI_2 as THF solution at room temperature, the deep blue color of the solution turned into yellow immediately. The reaction process was monitored by TLC and it showed that substrate **1a** has been consumed within several minutes. From the reaction mixture, two products were obtained, which were then identified as **2a** and **3a** in a ratio of about 1–3 with an overall yield of 87%. It was not a very exciting result in terms of chemoselectivity. Fortunately, further studies using **1a** as a model substrate showed that the ratio of the two products could be controlled by varying the reaction temperature and the amount of SmI_2 used. The results are listed in Table 1.

From Table 1 it can be seen that the reaction temperature and the amount of SmI_2 used have significant effects on the distribution of the two products. While higher reaction temperature and a larger amount of SmI_2 used are in favor of the formation of **2a**, in fact, it turned out that **2a** was the only product with as high as 85% yield when the reaction was conducted at 65°C with 4 equiv. of SmI_2 for half an hour (Table 1, entry 7). Diol **3a** could also be isolated as the main product with a yield of 72% by treating **1a** with two equiv.

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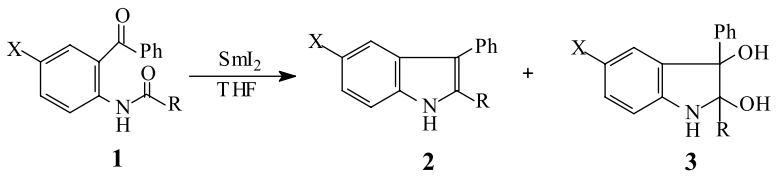
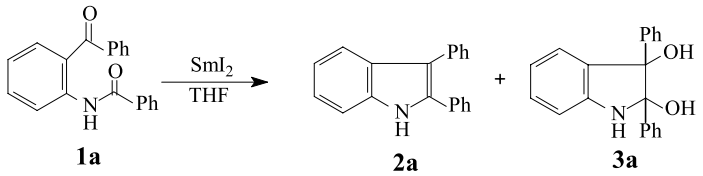


Scheme 1.



Scheme 2.

of SmI_2 at −20°C for 5 min (Table 1, entry 10). That is to say by varying the reaction temperature and the amount of SmI_2, either **2a** or **3a** can be obtained as the main or only product. However, attempts to conduct the process at lower temperature with intention to obtain more amount of **3a** gave us a disappointing result. In fact, neither the ratio of **3a** to **2a** nor the overall yield could be further improved at a lower temperature (Table 1, entry 11).

Table 1. Screening of different reaction temperature and the amount of SmI_2 for the preparation of indole derivatives from oxo amide **1a**

Entry	Reaction temp. (°C)	Molar ratio (SmI_2/1a)	Reaction time (min)	Yield (%)[a]	
				2a	**3a**
1	rt	2	5	22	65
2	rt	3	5	35	47
3	rt	4	5	56	28
4	65	2	5	34	52
5	65	4	5	78	7
6	65	4	10	82	4
7	65	4	30	85	–
8	0	2	5	18	64
9	−10	2	5	12	71
10	−20	2	5	10	72
11	−30	2	5	10	73

[a] Isolated yields based on **1a**.

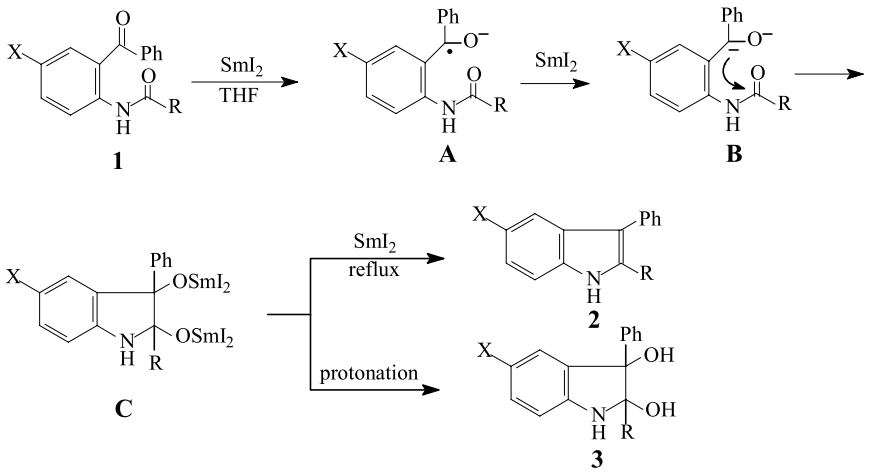
Other substrates derived from 2-aminobenzophenones and various aroyl chlorides have also been investigated, the results are listed in Table 2.

From Table 2, we found that when suitably substituted aryl acylamido carbonyl compounds (**1a**–**g**) were treated with SmI_2 under suitable reaction conditions, the corresponding indole derivatives (**2**) or (**3**) were obtained in fair yields. When the reductive coupling process was conducted at 65°C with 4 equiv. of SmI_2, only **2a**–**g** were obtained in fair yields for all the substrates tested. On the other hand, **3a**–**g** were separated as the main products when the reaction was carried out at −20°C in the presence of 2 equiv. of SmI_2. This reductive coupling process went very rapidly and was completed within several minutes for the preparation of **3**, or less than an hour for the formation of **2**. In addition, the results in Table 2 also show that substrates bearing either electron donating or electron withdrawing groups underwent the reductive coupling smoothly under the same reaction conditions. The absence of observable substituent effects and the chemo-selectivity, in that reducible groups

Table 2. SmI_2 induced preparation of indole derivatives from oxo *N*-aryl amides

Entry	Substrates	X	R	Molar ratio (SmI_2/substrate)	Reaction temp. (°C)	Reaction time (min)	Yield (%)[a]	
							2	**3**
1	**1a**	H	C_6H_5	4	65	30	85	–
				2	−20	5	10	72
2	**1b**	H	4-$CH_3C_6H_4$	4	65	30	84	–
				2	−20	5	10	73
3	**1c**	H	4-ClC_6H_4	4	65	50	88	–
				2	−20	5	8	75
4	**1d**	Cl	C_6H_5	4	65	30	88	–
				2	−20	5	12	71
5	**1e**	Cl	4-$CH_3C_6H_4$	4	65	30	84	–
				2	−20	5	11	70
6	**1f**	Cl	4-ClC_6H_4	4	65	40	87	–
				2	−20	5	9	70
7	**1g**	Cl	4-FC_6H_4	4	65	50	85	–
				2	−20	5	9	74

[a] Isolated yields based on **1**.



Scheme 3.

such as chloro, fluoro groups remain unaffected, suggest that this be a general method for the preparation of 2,3-disubstituted indole derivatives.

Although the detailed mechanism of the above reaction has not been clarified yet, a plausible mechanism (shown in Scheme 3) for the formation of 2,3-disubstituted indoles may be proposed as follows.

Firstly, ketyl anion **A** may be formed through a SmI_2 induced SET (single electron transfer) process. Then, the formed radical anion **A** can be reduced further to the corresponding dianion (**B**), due to their favorable electrochemical reduction potential.[7,15] Once formed, such highly reactive dianions once formed readily attack the adjacent amide group to form a new C–C bond giving intermediate **C**. Subsequent deoxygenation of **C** in the presence of SmI_2 affords **2** as the final product. On the other hand, if the reaction is conducted at −20°C with only 2 equiv. of SmI_2, the reductive process may mainly stopped at the pinacolates (**C**) stage. Subsequent protonation of intermediate **C** affords **3** as the major product together with little amount of **2**.

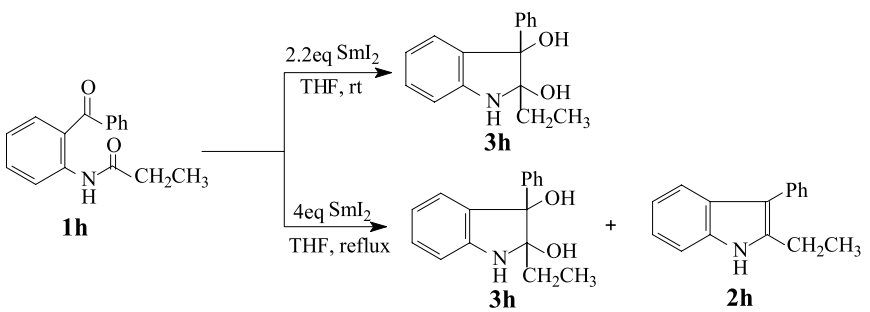
2.2. SmI_2 induced intramolecular reductive coupling reactions of 2-alkylamidobenzophenones

As mentioned above, although SmI_2, together with metallic samarium, can promote the intermolecular deoxygenative coupling reaction of diarylketones and *N*,*N*-disubstituted arylamides to give enamines, this system failed with alkylamides. In fact, on treatment with the SmI_2/Sm system, *N*,*N*-diethylhexanoamide and benzophenone gave a complex mixture rather than the desired enamines.[14] Therefore it is of interest to investigate whether substrates **1** derived from 2-aminobenzophenones and acyl chlorides (such as acetyl chloride and propionyl chloride) can undergo the similar reductive coupling process to give the desired indole derivatives.

Fortunately, when *N*-(2-benzoylphenyl)-propionamide (**1h**, Scheme 4) was treated with 2 equiv. of SmI_2 at room temperature (Table 3, entry 1), it was consumed in a few minutes and only one product was obtained, which was identified as 2-ethyl-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (**3h**) based on its spectra data (IR, ^{1}H NMR, ^{13}C NMR, MS and elemental analysis). This result is different from the results in relation to **1a**–**g** derived from 2-aminobenzophenones and aroyl chlorides, from which both products **2** and **3** were obtained under similar reaction conditions. However, when **1h** was treated with 4 equiv. of SmI_2 under reflux condition for one hour (Table 3, entry 2), both **3h** and **2h** were obtained with yields of 32% and 40%, respectively. Further investigation showed that a greater amount of SmI_2, or prolonged reaction time could not significantly improve the yield of **2h** (Table 3, entries 3 and 4). Substrates derived from 2-aminobenzophenones and other acyl chlorides have also been investigated, the results are listed in Table 3.

3. Conclusion

We have presented a novel process toward 2,3-disubstituted indole derivatives. With its high yields, mild and neutral conditions, the present work may provide a useful



Scheme 4.

Table 3. SmI_2 induced preparation of indole derivatives from oxo *N*-alkyl amides

Entry	Substrates	X	R	Molar ratio (SmI_2/substrates)	Reaction temp. (°C)	Reaction time (min)	Yield (%)[a]	
							2	**3**
1	**1h**	H	CH_2CH_3	2	rt	5	–	78
2	**1h**	H	CH_2CH_3	4	65	60	40	32
3	**1h**	H	CH_2CH_3	4	65	120	42	33
4	**1h**	H	CH_2CH_3	6	65	60	43	31
5	**1i**	H	CH_3	4	65	60	38	35
6	**1i**	H	CH_3	2	rt	5	–	81
7	**1j**	Cl	CH_2CH_3	4	65	60	43	32
8	**1j**	Cl	CH_2CH_3	2	rt	5	–	75
9	**1k**	Cl	CH_3	4	65	60	43	30
10	**1k**	Cl	CH_3	2	rt	5	–	72

[a] Isolated yields based on **1**.

alternative for the construction of the substituted indole nucleus. Further studies to clarify the mechanism of this process and to develop other new uses of SmI_2 in the syntheses of heterocyclic compounds are now in progress in our laboratory.

4. Experimental

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC-400 instrument as $CDCl_3$ solutions using TMS as an internal standard. ^{13}C NMR spectra were recorded on a Bruker AC-100 instrument as $CDCl_3$ solutions using TMS as an internal standard. Chemical shifts (δ) are reported in ppm and coupling constants *J* are given in Hz. IR spectra were taken as KBr discs or thin films with a Bruker Vector-22 infrared spectrometer. Elemental analyses were performed on an EA-1110 instrument. Metallic samarium and all solvents were purchased from commercial sources and were used without further purification. The starting material acylamido carbonyl compounds **1** were prepared according to the literature.[16]

4.1. General procedure for the preparation of 2,3-diaryl-1H-indole (2a–g)

Under anhydrous conditions, a mixture of powdered samarium (0.60 g, 4 mmol) and iodine (1.00 g, 4 mmol) in dry THF (20 mL) was stirred at room temperature until the samarium disappeared. To the resulting dark blue suspension of SmI_2 was added **1** (1 mmol). The mixture was stirred at 65°C for the time shown in Table 2. The reaction mixture was then poured into H_2O (10 mL) and extracted with ethyl acetate (3×15 mL). The combined extracts were washed subsequently with a saturated solution of $Na_2S_2O_3$ (15 mL) and a saturated solution of NaCl (15 mL) and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate–cyclohexane (1:7) as eluent.

4.1.1. 2,3-Diphenylindole (2a). Colorless crystal, yield: 85%, mp 121–123°C (lit.,[7a] 122–124°C); IR (KBr) ν 3410, 1605, 1516, 1486; ^{1}H NMR δ 8.36 (br s, 1H, NH), 7.83 (d, 1H, *J*=8.4 Hz), 7.28–7.68 (m, 13H). MS *m/z* (%): 269 (M^+, 100).

4.1.2. 2-(4-Methylphenyl)-3-phenylindole (2b). Syrup, yield: 84%; IR ν 3409, 1602, 1514, 1487 cm^{-1}; ^{1}H NMR δ 8.44 (br s, 1H, NH), 7.85 (d, 1H, *J*=8.0 Hz), 7.60 (d, 2H, *J*=8.0 Hz), 7.30–7.53 (m, 8H), 7.21 (d, 2H, *J*=8.0 Hz), 2.47 (s, 3H); ^{13}C NMR δ 21.4, 111.1, 114.7, 119.8, 120.6, 122.7, 126.4, 128.3, 128.7, 129.0, 129.9, 130.4, 134.5, 135.5, 136.0, 137.7; MS *m/z* (%): 283 (M^+, 100). Anal. Calcd for $C_{21}H_{17}N$: C, 89.01; H, 6.05; N, 4.94. Found: C, 88.90; H, 6.15; N, 4.88.

4.1.3. 2-(4-Chlorophenyl)-3-phenylindole (2c). Syrup, yield: 88%; IR ν 3408, 1605, 1510, 1480; ^{1}H NMR δ 8.30 (br s, 1H, NH), 7.62 (d, 1H, *J*=8.4 Hz), 7.50–7.25 (m, 10H), 7.11–7.01 (m, 2H); ^{13}C NMR δ 111.2, 115.0, 119.8, 120.6, 122.9, 126.5, 128.5, 128.7, 129.5, 129.9, 130.3, 131.1, 134.5, 135.5, 136.0, 137.7; MS *m/z* (%): 305 (M^++2, 34), 303 (M^+, 100). Anal. Calcd for $C_{20}H_{14}ClN$: C, 79.07; H, 4.65; N, 4.61. Found: C, 79.12; H, 4.68; N, 4.63.

4.1.4. 5-Chloro-2,3-diphenylindole (2d). Colorless crystal, yield: 88%, mp 124–126°C; IR (KBr) ν 3438, 1601, 1505, 1460; ^{1}H NMR δ 8.62 (br s, 1H, NH), 7.61 (d, 1H, *J*=1.5 Hz), 7.34–7.60 (m, 6H), 7.22–7.28 (m, 5H), 7.14–7.16 (m, 1H); ^{13}C NMR δ 111.9, 119.1, 122.9, 126.1, 126.6, 128.0, 128.2, 128.7, 128.8, 129.9, 130.1, 132.3, 134.4, 134.6, 135.6; MS *m/z* (%): 305 (M^++2, 34), 303 (M^+, 100). Anal. Calcd for $C_{20}H_{14}ClN$: C, 79.07; H, 4.65; N, 4.61. Found: C, 79.12; H, 4.68; N, 4.63.

4.1.5. 5-Chloro-2-(4-methylphenyl)-3-phenylindole (2e). Colorless crystal, yield: 84%, mp 140–142°C; IR ν 3411, 1602, 1514, 1489; ^{1}H NMR δ 8.14 (br s, 1H, NH), 7.58 (d, 1H, *J*=1.4 Hz), 7.27–7.37 (m, 10H), 7.16–7.19 (m, 1H), 2.36 (s, 3H); ^{13}C NMR δ 21.6, 111.6, 114.6, 119.2, 122.8, 126.1, 126.5, 128.0, 128.3, 128.6, 128.8, 129.8, 130.1, 132.5, 134.6, 134.8, 135.3; MS *m/z* (%): 319 (M^++2, 34), 317 (M^+, 100). Anal. Calcd for $C_{21}H_{16}ClN$: C, 79.36; H, 5.07; N, 4.41. Found: C, 79.32; H, 5.14; N, 4.48.

4.1.6. 5-Chloro-2-(4-chlorophenyl)-3-phenylindole (2f). Colorless crystal, yield: 87%, mp 161–162°C; IR (KBr) ν 3410, 1602, 1525, 1499; ^{1}H NMR δ 8.23 (br s, 1H, NH), 7.60 (d, 1H, *J*=1.4 Hz), 7.28–7.41 (m, 10H), 7.18–7.20 (m, 1H); ^{13}C NMR δ 112.1, 119.3, 123.3, 126.4, 126.9, 128.8,

129.1, 129.4, 129.9, 130.0, 130.7, 134.0, 134.1, 135.6, 136.0; MS *m/z* (%): 339 (M^++2, 66), 337 (M^+, 100). Anal. Calcd for $C_{20}H_{13}Cl_2N$: C, 71.02; H, 3.87; N, 4.14. Found: C, 71.20; H, 3.75; N, 4.20.

4.1.7. 5-Chloro-2-(4-fluorophenyl)-3-phenylindole (2g). Colorless crystal, yield: 85%, mp 146–148°C; IR (KBr) ν 3416, 1602, 1516, 1497; ^{1}H NMR δ 8.17 (br s, 1H, NH), 7.62 (s, 1H), 7.28–7.41 (m, 8H), 7.18–7.20 (m, 1H), 6.99–7.03 (m, 2H); ^{13}C NMR δ 111.9, 114.8, 115.8, 116.0, 119.2, 123.1, 126.3, 126.7, 128.3, 128.4, 128.8, 129.8, 129.9, 130.0, 134.2, 134.3, 134.5, 161.3, 163.7; MS *m/z* (%): 323 (M^++2, 34), 321 (M^+, 100). Anal. Calcd for $C_{20}H_{13}ClFN$: C, 74.65; H, 4.07; N, 4.35. Found: C, 74.52; H, 4.21; N, 4.26.

4.2. General procedure for the preparation of 2,3-diaryl-2,3-dihydro-1H-indole-2,3-diol (3a–g)

To a dark blue suspension of SmI_2 (2 mmol) in THF (cooled to −20°C) was added **1** (1 mmol). The mixture was stirred at this temperature for 5 min. The reaction mixture was then poured into H_2O (15 mL) and extracted with diethyl ether (3×30 mL). The combined extracts were washed subsequently with a saturated solution of $Na_2S_2O_3$ (15 mL) and a saturated solution of NaCl (15 mL) and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate–cyclohexane (1:3) as eluent.

4.2.1. 2,3-Diphenyl-2,3-dihydro-1H-indole-2,3-diol (3a). Colorless crystal, yield: 72%, mp 152–154°C; IR ν 3395, 3315, 1658, 1580 cm^{-1}; ^{1}H NMR δ 9.78 (br s, 1H, NH), 8.20 (d, 1H, *J*=8.0 Hz), 7.62 (d, 2H, *J*=7.8 Hz), 7.42 (d, 1H, *J*=7.2 Hz), 7.26–7.32 (m, 8H), 7.01–7.20 (m, 2H), 5.86 (s, 1H), 4.83 (s, 1H); ^{13}C NMR δ 72.6, 126.0, 126.7, 127.5, 127.7, 127.9, 128.1, 128.6, 129.1, 129.2, 132.4, 134.7, 135.6, 138.7, 143.4, 165.1; MS *m/z* (%): 303 (M^+, 9), 286 (2), 198 (41), 182 (42), 180 (30), 105 (100), 77 (88). Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.23; H, 5.68; N, 4.58.

4.2.2. 2-(4-Methylphenyl)-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3b). Colorless crystal, yield: 73%, mp 168–170°C; IR ν 3410, 3320, 1656, 1580 cm^{-1}; ^{1}H NMR δ 9.92 (br s, 1H, NH), 7.98 (d, 1H, *J*=8.8 Hz), 7.64 (d, 2H, *J*=7.8 Hz), 7.28–7.45 (m, 8H), 7.15–7.20 (m, 2H), 6.66 (s, 1H), 5.70 (s, 1H), 2.37 (s, 3H); ^{13}C NMR δ 23.6, 73.8, 126.1, 126.9, 127.5, 127.7, 128.0, 128.2, 128.9, 129.4, 129.8, 132.4, 135.2, 136.3, 139.9, 145.1, 165.6; MS *m/z* (%): 317 (M^+, 7), 300 (2), 198 (20), 182 (22), 180 (15), 119 (100), 91 (85). Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.31; H, 5.96; N, 4.44.

4.2.3. 2-(4-Chlorophenyl)-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3c). Colorless crystal, yield: 75%, mp 185–186°C; IR ν 3425, 3310, 1660, 1580 cm^{-1}; ^{1}H NMR δ 10.06 (br s, 1H, NH), 8.15 (d, 1H, *J*=8.4 Hz), 7.68–7.75 (m, 2H), 7.28–7.38 (m, 7H), 7.16–7.20 (m, 3H), 6.65 (s, 1H), 5.86 (s, 1H); ^{13}C NMR δ 73.2, 125.8, 126.8, 127.2, 127.8, 128.1, 128.9, 129.9, 130.4, 134.0, 135.5, 135.9, 140.6, 144.6, 168.2; MS *m/z* (%): 339 (M^++2, 3), 337 (M^+, 9), 198 (23), 182 (20), 180 (18), 139 (100), 111(78). Anal. Calcd for $C_{20}H_{16}ClNO_2$: C, 71.11; H, 4.77; N, 4.15. Found: C, 71.26; H, 4.59; N, 4.06.

4.2.4. 5-Chloro-2,3-diphenyl-2,3-dihydro-1H-indole-2,3-diol (3d). Colorless crystal, yield: 73%, mp 152–154°C; IR ν 3403, 3317, 1653, 1578 cm^{-1}; ^{1}H NMR δ 10.26 (br s, 1H, NH), 7.90 (d, 1H, *J*=8.4 Hz), 7.79 (d, 2H, *J*=7.8 Hz), 7.60–7.51 (m, 4H), 7.40–7.20 (m, 6H), 6.78 (s, 1H), 6.01 (s, 1H); ^{13}C NMR δ 72.6, 126.0, 126.7, 127.5, 127.7, 127.9, 128.1, 128.6, 129.1, 129.2, 132.4, 134.7, 135.6, 138.7, 143.4, 165.1; MS *m/z* (%): 339 (M^++2, 2), 337 (M^+, 5), 232 (15), 216 (32), 214 (15), 105 (100), 77 (98). Anal. Calcd for $C_{20}H_{16}ClNO_2$: C, 71.11; H, 4.77; N, 4.15. Found: C, 71.15; H, 4.78; N, 4.13.

4.2.5. 5-Chloro-2-(4-methylphenyl)-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3e). Colorless crystal, yield: 70%, mp 174–176°C; IR ν 3406 3310, 1655, 1575 cm^{-1}; ^{1}H NMR δ 10.21 (br s, 1H, NH), 7.92 (d, 1H, *J*=8.8 Hz), 7.70 (d, 2H, *J*=7.8 Hz), 7.50 (s, 1H), 7.32–7.38 (m, 3H), 7.19–7.26 (m, 5H), 6.81 (s, 1H), 5.99 (s, 1H), 2.38 (s, 3H); ^{13}C NMR δ 23.8, 72.5, 126.2, 126.8, 127.6, 127.7, 127.9, 128.4, 128.9, 129.5, 129.7, 133.2, 135.2, 136.4, 138.9, 143.4, 165.6; MS *m/z* (%): 351 (M^+, 4), 232 (14), 216 (7), 214 (13), 119 (100), 91 (65). Anal. Calcd for $C_{21}H_{18}ClNO_2$: C, 71.69; H, 5.16; N, 3.98. Found: C, 71.63; H, 5.25; N, 4.14.

4.2.6. 5-Chloro-2-(4-chlorophenyl)-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3f). Colorless crystal, yield: 70%, mp 174–176°C; IR ν 3386, 1651, 1584 cm^{-1}; ^{1}H NMR δ 10.24 (br s, 1H, NH), 7.81–7.19 (m, 12H), 6.68 (s, 1H), 6.00 (s, 1H); ^{13}C NMR δ 72.3, 126.6, 126.7, 127.7, 127.8, 127.9, 128.7, 129.2, 129.5, 129.6, 133.4, 136.1, 137.3, 139.6, 143.4, 164.3; MS *m/z* (%): 373 (M^++2, 1), 371 (M^+, 2), 232 (18), 216 (39), 214 (18), 139 (100), 111 (58). Anal. Calcd for $C_{20}H_{15}Cl_2NO_2$: C, 64.53; H, 4.25; N, 3.94. Found: C, 64.28; H, 4.28; N, 3.88.

4.2.7. 5-Chloro-2-(4-fluorophenyl)-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3g). Colorless crystal, yield: 74%, mp 139–141°C; IR ν 3390, 1648, 1580 cm^{-1}; ^{1}H NMR δ 9.60 (br s, 1H, NH), 8.17 (d, 1H, *J*=8.4 Hz), 7.60–7.10 (m, 11H), 6.68 (s, 1H), 5.83 (s, 1H); ^{13}C NMR δ 72.3, 115.9, 116.2, 126.4, 126.5, 126.7, 127.5, 127.7, 127.8, 128.7, 129.4, 130.2, 130.3, 131.1, 131.2, 136.2, 136.3, 139.4, 143.4, 163.4, 164.1, 165.9; MS *m/z* (%): 357 (M^++2, 1), 355 (M^+, 3), 232 (11), 216 (28), 214 (16), 123 (100), 105 (32), 95 (63), 57 (55). Anal. Calcd for $C_{20}H_{15}ClFNO_2$: C, 67.52; H, 4.25; N, 3.94. Found: C, 67.38; H, 4.36; N, 4.05.

4.3. General procedure for the preparation of 2-alkyl-3-aryl-2,3-dihydro-1H-indole-2,3-diol (3h–3k)

To a dark blue suspension of SmI_2 (2 mmol) in THF was added **1** (1 mmol). The mixture was stirred at room temperature for 5 min. At completion, the reaction mixture was poured into H_2O (15 mL) and extracted with diethyl ether (3×15 mL). The combined extracts were washed subsequently with a saturated solution of $Na_2S_2O_3$ (15 mL) and a saturated solution of NaCl (15 mL) and dried over anhydrous Na_2SO_4. After evaporating the solvent under

reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate–cyclohexane (1:3) as eluent.

4.3.1. 2-Ethyl-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3h). Colorless crystal, yield: 78%, mp 106–108°C; IR ν 3414, 3055, 2970, 1600 cm^{-1}; ^1H NMR δ 8.52 (br s, 1H, NH), 7.99 (d, 1H, J=8.4 Hz), 7.23–7.32 (m, 6H), 7.04–7.10 (m, 2H), 5.82 (s, 1H), 3.62 (s, 1H), 2.12 (q, 2H, J=7.2 Hz), 1.00 (t, 3H, J=7.2 Hz); ^{13}C NMR δ 9.5, 30.7, 75.3, 123.2, 124.1, 126.1, 127.5, 128.7, 128.9, 132.5, 132.6, 136.6, 141.7, 172.6; MS m/z (%): 255 (M^+, 15), 238 (9), 198 (48), 182 (73), 180 (100), 105 (57), 57 (56). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.38; H, 6.66; N, 5.37.

4.3.2. 2-Methyl-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3i). Colorless crystal, yield: 81%, mp 96–98°C; IR ν 3332, 3064, 2958, 1589 cm^{-1}; ^1H NMR δ 8.81 (br s, 1H), 7.83 (d, 1H, J=8.4 Hz), 7.20–7.29 (m, 6H), 7.03–7.06 (m, 2H), 5.76 (s, 1H), 3.58 (s, 1H), 1.79 (s, 3H); ^{13}C NMR δ 23.8, 74.1, 123.8, 125.1, 126.3, 127.8, 128.9, 130.1, 132.9, 132.5, 135.6, 140.2, 169.1; MS m/z (%): 241 (M^+, 14), 224 (5), 198 (34), 182 (68), 180 (82), 105 (56), 43 (100). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.49; H, 6.38; N, 5.69.

4.3.3. 5-Chloro-2-ethyl-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3j). Colorless crystal, yield: 75%, mp 120–122°C; IR ν 3418, 3057, 2971, 1602 cm^{-1}; ^1H NMR δ 8.48 (br s, 1H, NH), 7.98 (d, 1H, J=8.4 Hz), 7.36–7.10 (m, 7H), 5.80 (s, 1H), 3.72 (s, 1H), 2.14 (q, 2H, J=7.8 Hz), 1.02 (t, 3H, J=7.8 Hz); ^{13}C NMR δ 9.4, 30.8, 74.9, 124.5, 126.1, 128.0, 128.6, 128.8, 129.2, 133.9, 135.2, 140.7, 172.4; MS m/z (%): 291 (M^++2, 9), 289 (M^+, 25), 272 (10), 232 (13), 216 (69), 214 (100), 105 (51), 57 (74). Anal. Calcd for $C_{16}H_{16}ClNO_2$: C, 66.32; H, 5.57; N, 4.83. Found: C, 66.16; H, 5.72; N, 4.71.

4.3.4. 5-Chloro-2-methyl-3-phenyl-2,3-dihydro-1H-indole-2,3-diol (3k). Colorless crystal, yield: 72%, mp 140–142°C; IR ν 3355, 3015, 2966, 1590 cm^{-1}; ^1H NMR δ 8.46 (br s, 1H, NH), 7.92 (d, 1H, J=8.4 Hz), 7.38–7.11 (m, 7H), 5.81 (s, 1H), 3.66 (s, 1H), 1.82 (s, 3H); ^{13}C NMR δ 24.3, 74.9, 124.7, 126.1, 128.1, 128.7, 128.8, 129.5, 134.3, 136.1, 140.7, 168.8; MS m/z (%): 277 (M^++2, 2), 275 (M^+, 5), 258 (3), 232 (11), 216 (56), 214 (44), 105 (53), 43 (100). Anal. Calcd for $C_{15}H_{14}ClNO_2$: C, 66.32; H, 5.57; N, 4.83. Found: C, 66.16; H, 5.72; N, 4.86.

4.4. General procedure for the preparation of 2-alkyl-3-aryl-1H-indole (2h–2k)

To a dark blue suspension of SmI_2 (4 mmol) in THF was added **1** (1 mmol). The mixture was stirred under reflux for 1 h. At completion, the reaction mixture was poured into H_2O (15 mL) and extracted with diethyl ether (3×30 mL). The combined extracts were washed subsequently with a saturated solution of $Na_2S_2O_3$ (15 mL) and a saturated solution of NaCl (15 mL) and dried over anhydrous Na_2SO_4. After evaporating the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate–cyclohexane (1: 4) as eluent.

4.4.1. 2-Ethyl-3-phenylindole (2h). Syrup, yield: 32%; IR ν 3413, 3060, 2971, 1603, 1495; ^1H NMR, 7.93 (br s, 1H, NH), 7.76 (d, 1H, J=8.0 Hz), 7.53–7.61 (m, 4H), 7.36–7.42 (m, 2H), 7.18–7.29 (m, 2H), 2.92 (q, 2H, J=7.6 Hz), 1.35 (t, 3H, J=7.6 Hz); ^{13}C NMR δ 14.5, 19.8, 110.7, 113.9, 119.1, 120.1, 121.7, 126.1, 128.1, 128.7, 129.7, 135.4, 135.6, 137.5; MS m/z (%): 221 (M^+, 100). Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.64; H, 6.95; N, 6.21.

4.4.2. 2-Methyl-3-phenylindole (2i). Colorless crystal, yield: 35%, mp 56–57°C (lit.,[7a] 58–61°C); IR (KBr) ν 3405, 3038, 2965, 1603, 1556, 1489; ^1H NMR, 7.96 (br s, 1H, NH), 7.78 (d, 1H, J=8.0 Hz), 7.57–7.64 (m, 4H), 7.44–7.22 (m, 4H), 2.52 (s, 3H); MS m/z (%): 207 (M^+, 100).

4.4.3. 5-Chloro-2-ethyl-3-phenylindole (2j). Syrup, yield: 32%, IR ν 3418, 3057, 2971, 1617, 1485; ^1H NMR, 7.99 (br s, 1H, NH), 7.68 (d, 1H, J=1.6 Hz), 7.50–7.54 (m, 4H), 7.37–7.41 (m, 1H), 7.16–7.21 (m, 2H), 2.86 (q, 2H, J=8.0 Hz), 1.32 (t, 3H, J=8.0 Hz); ^{13}C NMR δ 14.1, 18.7, 110.5, 113.4, 118.8, 120.5, 125.9, 127.6, 128.5, 128.9, 129.1, 134.3, 134.7, 136.8; MS m/z (%): 257 (M^++2, 34), 255 (M^+, 100). Anal. Calcd for $C_{16}H_{14}ClN$: C, 75.14; H, 5.52; N, 5.48. Found: C, 75.30; H, 5.40; N, 5.58.

4.4.4. 5-Chloro-2-methyl-3-phenylindole (2k). Syrup, yield: 30%, IR ν 3415, 3026, 2965, 1604, 1497; ^1H NMR, 7.86 (br s, 1H, NH), 7.68 (d, 1H, J=1.5 Hz), 7.50–7.52 (m, 4H), 7.36–7.39 (m, 1H), 7.19–7.13 (m, 2H), 2.45 (s, 3H); ^{13}C NMR δ 12.5, 111.5, 114.4, 118.3, 121.7, 125.7, 126.3, 128.8, 129.1, 129.4, 133.3, 133.7, 134.8; MS m/z (%): 243 (M^++2, 32), 241 (M^+, 100). Anal. Calcd for $C_{15}H_{12}ClN$: C, 74.53; H, 5.00; N, 5.79. Found: C, 74.35; H, 5.16; N, 5.82.

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