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$FeCl_3$ as Lewis acid catalyzed one-pot three-component aza-Friedel–Crafts reactions of indoles, aldehydes, and tertiary aromatic amines

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ABSTRACT

A new strategy for the synthesis of 3-diarylmethyl indoles was developed through $FeCl_3$ as Lewis acid catalyzed three-component aza-Friedel–Crafts reactions of indoles, aldehydes, and tertiary aromatic amines in one-pot. The reactions generated the corresponding 3-diarylmethyl indoles in good yields under mild reaction conditions by using less expensive, readily available, and environmentally benign iron catalyst. It is important to note that the key feature of this reaction is operational simplicity.

1. Introduction

A key goal of modern organic chemistry is to both maximize the efficiency of using readily available materials and minimize the generation of waste, which also is one of the prime principles of green chemistry,[1] and one of the most challenging task in organic synthesis is the efficient preparation of complex molecules starting from easily available raw materials. Especially attractive are one-pot multi-component coupling reactions (MCRs), which introduce several elements of diversity into a molecule in a single step.[2] For a long time, the transition metal-catalyzed multi-component reactions (MCRs) have attracted much interest because of their capability of offering many challenging transformation using one-pot method.[3] Particularly those metal catalysts, which are derived from the group VIII-X metals, display remarkable efficiency for the formation of carbon–carbon and carbon–heteroatom bonds.[4]

Recently, iron salts as effective, alternative, and promising transition-metal catalysts have received much more attention because of their less expensive, readily available, and environmentally benign properties. Since the pioneering research work of Tamura and Kochi,[5] iron-catalyzed oxidation,[6] hydrogenation,[7] hydrosilylation[8] rearrangement,[9] Michael addition,[10] C–C bond[11] and C–heteroatom bond forming reactions,[12] and tandem reactions[13] have been intensively investigated. Because of interest for both the academic as well as the industrial community, it is desirable to expand the application scope of iron catalysts in organic transformations due to their unique and significant advantages.

Indoles are important structural units in many natural products and their derivatives are known to possess various biological properties,[14] such as, antibacterial, antioxidative, and insecticidal activities, and some indole derivatives have been used as antibiotics in pharmaceuticals.[15] Among indole derivatives, bis-indolylalkanes, 3-alkyl indoles, and 3-diarylmethyl indoles are important class of bioactive metabolite, which can be synthesized by Lewis acid (e.g., BBr_3, BF_3, and $Cu(OTf)_2$) or protic acid (e.g., HCl, $HClO_4$ and H_2SO_4) catalysis and much attention has been paid to the synthesis of them for a long while.[3,16] Although the synthesis of 3-alkyl indoles has been studied extensively, the synthesis of other unsymmetrical indole derivatives is still highly desirable in synthetic community due to it need more practical procedures and mild reaction conditions. As part of our ongoing efforts devoted to iron-catalyzed organic reactions,[17] herein we wish to report the first genuinely and highly efficient $FeCl_3$ as Lewis acid catalyzed one-pot three-component aza-Friedel–Crafts reactions of indoles, aldehydes, and tertiary aromatic amines. The reactions generated the corresponding 3-diarylmethyl indole derivatives in good yields under mild reaction conditions (Scheme 1).

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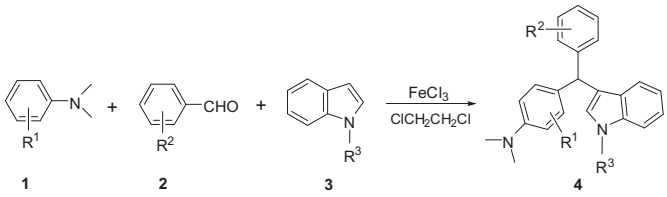
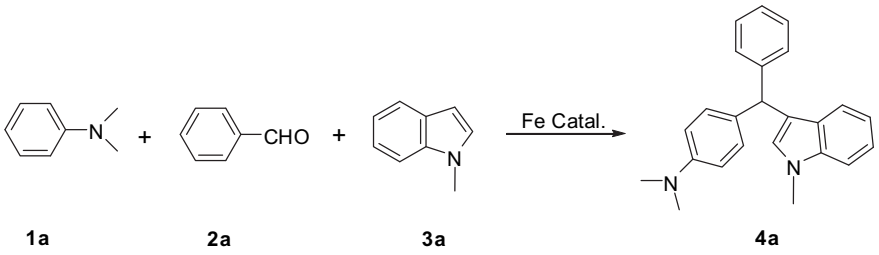


Scheme 1.

2. Results and discussion

For initial optimization of the reaction conditions, *N*,*N*-dimethylaniline (**1a**), benzaldehyde (**2a**), and 1-methyl-1*H*-indole (**3a**) were chosen as model substrates for the template reaction. The solvent effect was examined for the model reaction by using 10 mol % of $FeCl_3$ as catalyst, and the results were listed in Table 1. Noteworthy is that the choice of $ClCH_2CH_2Cl$ as the solvent was crucial and 65% yield of the desired product was isolated (Table 1, entry 1). Other solvent, such as toluene, DMSO, DMF, $BrCH_2CH_2Br$, or THF was used instead of $ClCH_2CH_2Cl$, desired condensation products were obtained in lower yields (Table 1, entries 2–6). Unfortunately, only trace amount of the desired product was isolated when the reaction was carried out in CH_3OH, CH_2Cl_2, or CH_3NO_2 (Table 2, entries 7–9). A wide range of iron source as catalyst in $ClCH_2CH_2Cl$ at 100 °C was screened and among the Fe^{III} salts tested, $FeCl_3$ was found to be the most suitable one in terms of the isolated product yield in the absence of any ligand and additive (Table 1, entry 1). Other Fe^{III} salt sources, such as $FeCl_3\cdot6H_2O$, $Fe(NO_3)_3\cdot9H_2O$, $Fe(SO_4)_3\cdot7H_2O$, $Fe_2(SO_4)_3$, and $Fe(acac)_3$ were inferior and generated desired products in poor yields (Table 1, entries 10–14). However, only 45% yield of the desired product was obtained when $FeCl_2$ was used as catalyst for the model reaction (Table 1, entry 15). Meanwhile, we also investigated the influence of ligand on the model reaction in the presence of $FeCl_3$ as catalyst in $ClCH_2CH_2Cl$. The result showed that the yield of desired product was slightly decreased when Ph_3P as ligand was added to the reaction system (Table 1, entry 16). When 1,10-phenanthroline (Phen), 2,2,6,6-tetramethyl-3,5-heptanedione (TMHD) or 1,1′-bis (diphenylphosphino)ferrocene (DPPF) as ligand was added to the reaction, the yield of desired product was obtained in the range of 28–38% (Table 1, entries 17–19). Only trace amount of desired product was observed when *N*,*N*′-dimethylethylenediamine (TMEDA) as ligand was added to the model reaction (Table 1, entry 20). We also investigated the influence of peroxide on the model reaction in the presence of $FeCl_2$ as catalyst in $ClCH_2CH_2Cl$. The result showed that the yield of desired product was decreased when *tert*-butyl hydroperoxide (TBHP), di-*tert*-butyl peroxide (DTBP), or dicumyl peroxide (DCP) was added to the reaction (Table 1, entries 21–23). No any desired product was observed and starting materials were recovered when the model reaction was carried out in the absence of iron salt (Table 1, entry 24). With respect to the catalyst loading, 10 mol % of $FeCl_3$ was found to be optimal. When only 5 mol % of $FeCl_3$ was used, the desired product

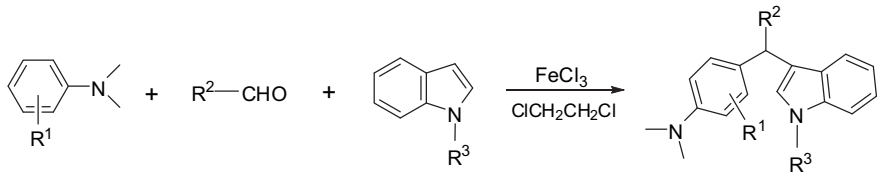
Table 1
Optimization of the reaction conditions[a]



Entry	Iron Source	Additive	Solvent	Temp (°C)	Yield[b] [%]
1	$FeCl_3$	—	$ClCH_2CH_2Cl$	100	65
2	$FeCl_3$	—	Toluene	100	48
3	$FeCl_3$	—	DMSO	100	46
4	$FeCl_3$	—	DMF	100	40
5	$FeCl_3$	—	$BrCH_2CH_2Br$	100	35
6	$FeCl_3$	—	THF	68	24
7	$FeCl_3$	—	CH_3OH	68	Trace
8	$FeCl_3$	—	CH_2Cl_2	40	Trace
9	$FeCl_3$	—	CH_3NO_2	100	Trace
10	$FeCl_3\cdot6H_2O$	—	$ClCH_2CH_2Cl$	100	22
11	$Fe(NO_3)_3\cdot9H_2O$	—	$ClCH_2CH_2Cl$	100	15
12	$Fe(SO_4)_3\cdot7H_2O$	—	$ClCH_2CH_2Cl$	100	18
13	$Fe_2(SO_4)_3$	—	$ClCH_2CH_2Cl$	100	31
14	$Fe(acac)_3$	—	$ClCH_2CH_2Cl$	100	26
15	$FeCl_2$	—	$ClCH_2CH_2Cl$	100	45
16	$FeCl_3$	PPh_3	$ClCH_2CH_2Cl$	100	64
17	$FeCl_3$	Phen[c]	$ClCH_2CH_2Cl$	100	36
18	$FeCl_3$	DPPF[c]	$ClCH_2CH_2Cl$	100	38
19	$FeCl_3$	TMHD[c]	$ClCH_2CH_2Cl$	100	28
20	$FeCl_3$	TMEDA[c]	$ClCH_2CH_2Cl$	100	Trace
21	$FeCl_2$	TBHP[c]	$ClCH_2CH_2Cl$	100	32
22	$FeCl_2$	DTBP[c]	$ClCH_2CH_2Cl$	100	38
23	$FeCl_2$	DCP[c]	$ClCH_2CH_2Cl$	100	29
24	—	—	$ClCH_2CH_2Cl$	100	0

[a] Reaction conditions: *N*,*N*-dimethylaniline (1.1 mmol), benzaldehyde (1.0 mmol), 1-methyl-1*H*-indole (1.0 mmol), Fe source (0.10 mmol), additive (0.20 mmol) if added, solvent (2.0 mL), N_2, 24 h.
[b] Isolated yields.
[c] Phen=1,10-phenanthroline, DPPF=1,1′-bis(diphenylphosphino)ferrocene, TMHD=2,2,6,6-tetramethyl-3,5-heptanedione, TMEDA=*N*,*N*′-dimethylethylenediamine, TBHP=*tert*-butyl hydroperoxide, DTBP=di-*tert*-butyl peroxide, DCP=dicumyl peroxide.

Table 2
$FeCl_3$-catalyzed three-component reactions of indoles, aldehydes, and amines[a]



1 **2** **3** **4**

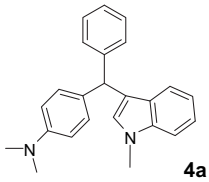
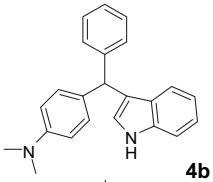
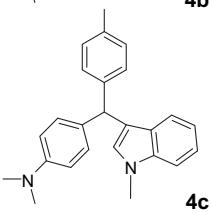
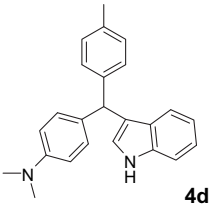
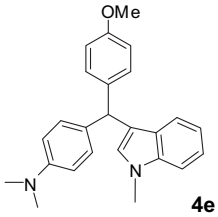
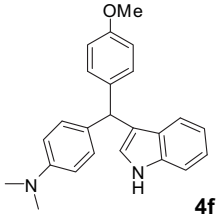
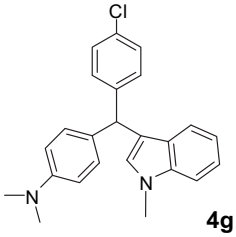
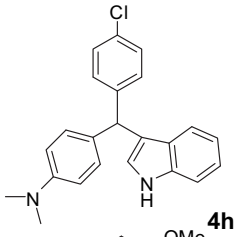
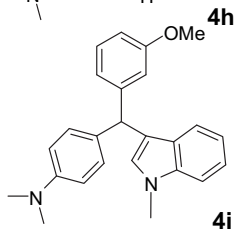
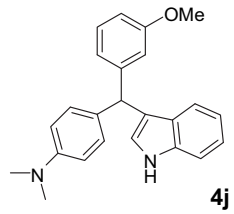
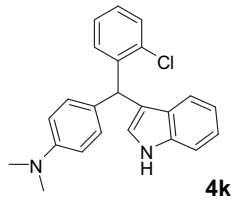
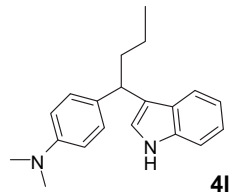
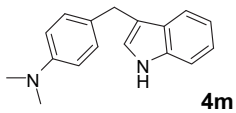
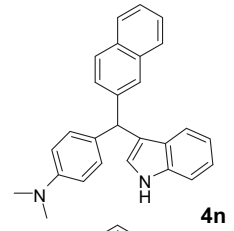
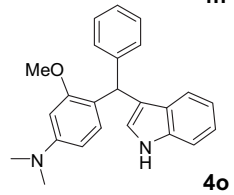
Entry	R^1	R^2	R^3	Product (**4**)	Yield [b] [%]
1	H	C_6H_5	CH_3	 **4a**	65
2	H	C_6H_5	H	 **4b**	71
3	H	4-$CH_3C_6H_4$	CH_3	 **4c**	68
4	H	4-$CH_3C_6H_4$	H	 **4d**	71
5	H	4-$CH_3OC_6H_4$	CH_3	 **4e**	72
6	H	4-$CH_3OC_6H_4$	H	 **4f**	70
7	H	4-ClC_6H_4	CH_3	 **4g**	64

Table 2 (*continued*)

Entry	R^1	R^2	R^3	Product (**4**)	Yield [b] [%]
8	H	4-ClC_6H_4	H	 **4h**	67
9	H	3-$CH_3OC_6H_4$	CH_3	 **4i**	62
10	H	3-$CH_3OC_6H_4$	H	 **4j**	61
11	H	2-ClC_6H_4	H	 **4k**	53
12	H	*n*-C_3H_7	H	 **4l**	58
13	H	H	H	 **4m**	48
14	H	2-$C_{10}H_7$	H	 **4n**	51
15	3-CH_3O	C_6H_5	CH_3	 **4o**	52

[a] Reaction conditions: *N*,*N*-dimethylaniline (1.1 mmol), aldehyde (1.0 mmol), indole (1.0 mmol), $FeCl_3$ (0.10 mmol), $ClCH_2CH_2Cl$ (2.0 mL), N_2, 100 °C, 24 h.
[b] Isolated yield.

was isolated in 47% yield, and no significant improvement was observed with 20 mol % of $FeCl_3$. During the course of our further optimization of the reaction conditions, the reaction was generally completed within 24 h at 100 °C in $ClCH_2CH_2Cl$ by using 10 mol % of $FeCl_3$.

On the basis of the previously optimized reaction conditions, the scope of this transformation in the direct three-component aza-Friedel–Crafts reactions of indoles, a variety of aldehydes, and substituted tertiary aromatic amines in one-pot was evaluated. The results are listed in Table 2. At the beginning of the search for the aldehydes substrate scope, when *N*,*N*-dimethylaniline was served as tertiary aromatic amine partner, a variety of electron-rich, electron-neutral, and electron-deficient arylaldehydes underwent three-component aza-Friedel–Crafts reactions with either indole or *N*-methylindole smoothly to generate the corresponding 3-diarylmethyl indoles in good yields (Table 2, entries 1–10). Furthermore, sterically demanding *ortho* substituent did not hamper the reaction very much and the corresponding product was obtained in 53% yield (Table 2, entry 11). For aliphatic aldehydes, such as formaldehyde, *n*-butyraldehyde, 48 and 58% yields of the corresponding products were isolated (Table 2, entries 12 and 13). Furthermore, 2-naphthaldehyde also gave the good result (Table 2, entry 14). Fortunately, substituted tertiary aromatic amine, such as *m*-methoxy *N*,*N*-dimethylaniline, also reacted with benzaldehyde and *N*-methylindole to form the corresponding product in 52% yield (Table 2, entry 15).

The plausible mechanism of the reaction was shown in Fig. 1. Tertiary aromatic amine *N*,*N*-dimethylaniline (**1a**) reacted with benzaldehyde (**2a**) in the presence of $FeCl_3$ to form an intermediate **5a**, which on addition of *N*-methylindole (**3a**) gave the desired 3-diarylmethyl *N*-methylindole (**4a**).

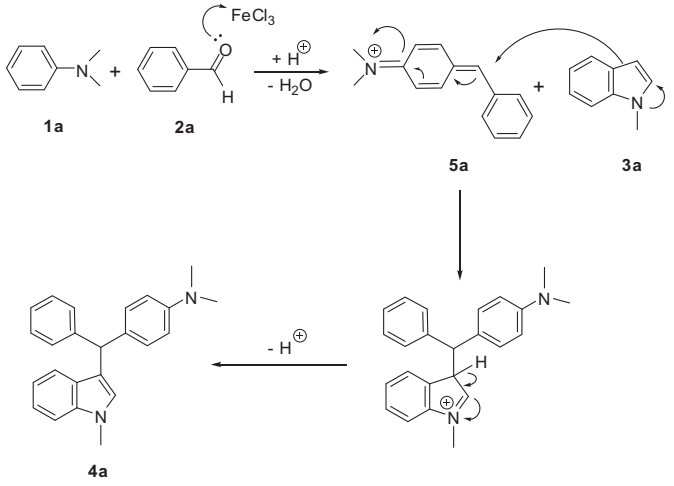


Fig. 1. Plausible mechanism of three-component aza-Friedel–Crafts reactions.

3. Conclusions

In summary, we have developed a novel, simple, and efficient procedure for the preparation of 3-diarylmethyl indoles derivatives through $FeCl_3$ as Lewis acid catalyzed three-component aza-Friedel–Crafts reactions of indoles, aldehydes, and tertiary aromatic amines in one-pot. The reactions were carried out in the presence of catalytic amounts of $FeCl_3$ in $ClCH_2CH_2Cl$ without any ligand and additive, which generated the corresponding 3-diarylmethyl indoles in good yields under mild reaction conditions using less expensive, readily available, and environmentally benign iron catalyst. Its increased efficiency and enlargement of the substrate scope and further investigation on the application of this kind of catalyst in asymmetric catalysis are being in progress.

4. Experimental

4.1. General methods

All reactions were carried out under nitrogen atmosphere. All reagents were purchased from commercial suppliers and used after further purification. Products were purified by flash chromatography on 230–400 mesh silica gel, SiO_2. All ^1H NMR, ^{13}C NMR spectra were measured on a Bruker Avance NMR spectrometer (400 MHz or 100 MHz, respectively) with $CDCl_3$ as solvent and recorded in parts per million relative to internal tetramethylsilane standard. High resolution mass spectroscopy data of the product were collected on a Waters Micromass GCT instrument.

4.2. Typical procedure for iron-catalyzed one-pot three-component aza-Friedel–Crafts reactions of indoles, aldehydes, and tertiary aromatic amines

A 10 mL of reaction tube was charged with 1-methyl-1*H*-indole (1.0 mmol), benzaldehyde (1.0 mmol), *N*,*N*-dimethylaniline (1.1 mmol), $FeCl_3$ (0.1 mmol), and $ClCH_2CH_2Cl$ (2.0 mL) under nitrogen. The reaction vessel was placed in an oil bath at 100 °C. After the reaction was carried out at this temperature for 24 h, it was cooled to room temperature, diluted with $NaHCO_3$ (aq), extracted twice with CH_2Cl_2 (5.0 mL) and the combined organic layer was dried over anhydrous Na_2SO_4. After filtration, solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel with ethyl acetate/petroleum ether (1:3) as eluent to give the desired product.

4.3. Analytical data for aza-Friedel–Crafts reactions of indoles, aldehydes, and tertiary aromatic amines products

*4.3.1. N,N-Dimethyl-4-((1-methyl-1H-indol-3-yl)(phenyl)methyl) aniline (**4a**)*[16g]. White solid, mp 139–141 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26–7.14 (m, 9H), 7.08 (d, J=8.0 Hz, 2H), 6.95 (t, J=8.2 Hz, 1H), 6.67 (d, J=7.8 Hz, 2H), 6.41 (s, 1H), 6.59 (s, 1H), 3.64 (s, 3H), 2.89 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 144.8, 137.4, 129.5, 128.9, 128.6, 128.5, 128.1, 127.4, 125.9, 121.4, 120.1, 118.9, 118.6, 112.6, 108.9, 47.8, 40.7, 32.6. IR (KBr): 3051, 2923, 2856, 2787, 1803, 1609, 1517, 1475, 1333, 1214, 1123, 1059, 1017, 944, 806, 765, 733, 702, 627, 560, 528 cm^{-1}.

*4.3.2. 4-((1H-Indol-3-yl)(phenyl)methyl)-N,N-dimethylaniline (**4b**).* White solid, mp 161–162 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.32 (d, J=8.2 Hz, 1H), 7.26–7.18 (m, 6H), 7.16–7.12 (m, 2H), 7.09 (d, J=8.0 Hz, 2H), 6.98 (d, J=7.8 Hz, 1H), 6.67 (d, J=8.0 Hz, 2H), 6.56–6.55 (m, 1H), 5.58 (s, 1H), 2.90 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 144.6, 136.6, 132.1, 129.5, 128.9, 128.1, 127.0, 125.9, 123.9, 121.9, 120.6, 120.0, 119.2, 112.5, 110.9, 47.7, 40.7. IR (KBr): 3164, 3054, 2958, 2923, 2853, 2816, 2359, 2341, 732, 1614, 1517, 1491, 1477, 1452, 1336, 1324, 1299, 1222, 1199, 1124, 1074, 1029, 939, 794, 718, 634, 589, 517 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{23}H_{22}N_2$: 326.1783, found: 326.1786.

*4.3.3. N,N-Dimethyl-4-((1-methyl-1H-indol-3-yl)(p-tolyl)methyl) aniline (**4c**).* White solid, mp 130–131 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J=8.0 Hz, 2H), 7.20–7.16 (m, 2H), 7.13–7.04 (m, 5H), 6.96 (d, J=7.8 Hz, 2H), 6.66 (d, J=8.0 Hz, 2H), 6.42 (s, 1H), 5.53 (s, 1H), 3.65 (s, 3H), 2.89 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 141.9, 137.4, 135.2, 132.6, 129.4, 128.8, 128.7, 128.6, 127.5, 121.4, 120.1, 119.1, 118.6, 112.5, 108.9, 47.3, 40.7, 32.6, 29.7. IR (KBr): 2922, 2854, 2795, 1610, 1514, 1470, 1335, 1216, 1120, 1055,

1014, 944, 805, 735, 563, 497 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{25}H_{26}N_2$: 354.2096, found: 354.2097.

*4.3.4. 4-((1H-Indol-3-yl)(p-tolyl)methyl)-N,N-dimethylaniline (**4d**).* White solid, mp 164–165 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.30–7.22 (m, 2H), 7.13–7.05 (m, 6H), 6.97 (d, *J*=7.8 Hz, 2H), 6.66 (d, *J*=8.0 Hz, 2H), 6.53 (s, 1H), 5.54 (s, 1H), 2.89 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 141.6, 136.6, 135.3, 132.4, 129.4, 128.8, 128.7, 127.0, 123.9, 121.8, 120.7, 120.0, 119.2, 112.6, 110.9, 47.3, 40.8, 29.7. IR (KBr): 3735, 3587, 3397, 3186, 3047, 2890, 2858, 2814, 2360, 2341, 1615, 1518, 1457, 1418, 1355, 1338, 1162, 1093, 1022, 943, 802, 761, 668, 631, 574, 532 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{24}H_{24}N_2$: 340.1939, found: 340.1937.

*4.3.5. 4-((4-Methoxyphenyl)(1-methyl-1H-indol-3-yl)methyl)-N,N-dimethylaniline (**4e**).* White solid, mp 155–156 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26–7.12 (m, 5H), 7.08 (d, *J*=8.2 Hz, 2H), 6.95 (t, *J*=7.8 Hz, 1H), 6.79 (d, *J*=8.4 Hz, 2H), 6.67 (d, *J*=8.0 Hz, 2H), 6.40 (s, 1H), 5.52 (s, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 2.90 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 148.8, 137.4, 137.0, 129.7, 129.4, 128.5, 127.4, 121.4, 120.1, 119.2, 118.6, 113.4, 112.6, 108.9, 55.1, 46.9, 40.8, 32.6. IR (KBr): 3042, 2924, 2813, 1694, 1608, 1467, 1338, 1246, 1167, 1119, 1029, 944, 807, 740, 568, 522 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{25}H_{26}N_2O$: 370.2050, found: 370.2050.

*4.3.6. 4-((1H-Indol-3-yl)(4-methoxyphenyl)methyl)-N,N-dimethylaniline (**4f**).* White solid, mp 162–164 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.33 (d, *J*=8.4 Hz, 1H), 7.26–7.24 (m, 1H), 7.17–7.13 (m, 3H), 7.08 (d, *J*=8.0 Hz, 2H), 6.97 (t, *J*=8.2 Hz, 1H), 6.80 (d, *J*=7.8 Hz, 2H), 6.67 (d, *J*=8.0 Hz, 2H), 6.56 (s, 1H), 5.53 (s, 1H), 3.77 (s, 3H), 2.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 148.9, 136.9, 136.6, 132.5, 129.8, 129.4, 127.0, 123.9, 121.8, 120.8, 120.0, 119.1, 113.4, 112.6, 110.9, 55.2, 46.9, 40.7. IR (KBr): 3411, 3171, 3059, 3029, 2958, 2890, 2854, 2833, 2360, 1610, 1508, 1473, 1338, 1314, 1244, 1218, 1201, 1134, 1031, 1007, 942, 839, 773, 577, 518 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{24}H_{24}N_2O$: 356.1889, found: 356.1886.

*4.3.7. 4-((4-Chlorophenyl)(1-methyl-1H-indol-3-yl)methyl)-N,N-dimethylaniline (**4g**).* White solid, mp 157–158 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, *J*=8.0 Hz, 1H), 7.22–7.19 (m, 4H), 7.15 (d, *J*=8.8 Hz, 2H), 7.05 (d, *J*=8.2 Hz, 2H), 6.96 (t, *J*=7.8 Hz, 1H), 6.66 (d, *J*=8.0 Hz, 2H), 6.39 (s, 1H), 5.53 (s, 1H), 3.66 (s, 3H), 2.90 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 143.4, 137.4, 131.6, 131.5, 130.2, 129.4, 128.6, 128.2, 127.2, 121.6, 119.9, 118.7, 118.4, 112.5, 109.1, 47.1, 40.6, 32.6. IR (KBr): 3048, 2920, 2804, 1610, 1518, 1477, 1340, 1230, 1160, 1124, 1086, 1010, 940, 851, 800, 736, 708, 563, 530 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{24}H_{23}ClN_2$: 374.1550, found: 374.1549.

*4.3.8. 4-((4-Chlorophenyl)(1H-indol-3-yl)methyl)-N,N-dimethylaniline (**4h**).* White solid, mp 130–132 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.29 (d, *J*=8.0 Hz, 1H), 7.23–7.20 (m, 3H), 7.16–7.13 (m, 3H), 7.05 (d, *J*=8.4 Hz, 2H), 6.98 (t, *J*=8.2 Hz, 1H), 6.66 (d, *J*=7.8 Hz, 2H), 6.50 (s, 1H), 5.53 (s, 1H), 2.90 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 143.2, 136.6, 131.6, 131.5, 130.2, 129.4, 128.2, 126.8, 123.9, 122.0, 120.0, 119.9, 119.3, 112.5, 111.0, 47.1, 40.6. IR (KBr): 3646, 3626, 3606, 3592, 3585, 3565, 3411, 2919, 2848, 2358, 1614, 1518, 1487, 1455, 1384, 1338, 1212, 1161, 1091, 1016, 940, 858, 799, 765, 690, 621, 581, 554 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{23}H_{21}ClN_2$: 360.1388, found: 360.1388.

*4.3.9. 4-((3-Methoxyphenyl)(1-methyl-1H-indol-3-yl)methyl)-N,N-dimethylaniline (**4i**).* White solid, mp 171–173 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J*=7.8 Hz, 2H), 7.19–7.15 (m, 2H), 7.09 (d, *J*=8.0 Hz, 2H), 6.97–6.93 (m, 1H), 6.84–6.80 (m, 2H), 6.75–6.71 (m, 1H), 6.66 (d, *J*=8.2 Hz, 2H), 6.43 (s, 1H), 5.54 (s, 1H), 3.70 (s, 3H), 3.64 (s, 3H), 2.89 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 148.9, 146.5, 137.3, 132.1, 129.8, 129.4, 129.0, 128.5, 127.3, 121.4, 120.0, 118.6, 114.8, 112.5, 110.8, 108.9, 55.0, 47.7, 40.7, 32.6. IR (KBr): 3044, 2928, 1728, 1605, 1475, 1365, 1332, 1257, 1129, 1049, 1006, 870, 779, 738, 695, 567 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{25}H_{26}N_2O$: 370.2045, found: 370.2047.

*4.3.10. 4-((1H-Indol-3-yl)(3-methoxyphenyl)methyl)-N,N-dimethylaniline (**4j**).* White solid, mp 151–153 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.32 (d, *J*=8.0 Hz, 1H), 7.25 (d, *J*=8.2 Hz, 1H), 7.18–7.14 (m, 2H), 7.10–7.08 (m, 2H), 6.97 (t, *J*=8.4 Hz, 1H), 6.83–6.80 (m, 2H), 6.74 (d, *J*=7.8 Hz, 1H), 6.67 (d, *J*=8.0 Hz, 2H), 6.60–6.59 (m, 1H), 5.55 (s, 1H), 3.72 (s, 3H), 2.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 146.4, 136.6, 129.5, 129.0, 127.0, 123.9, 121.9, 121.5, 120.3, 120.0, 119.2, 114.9, 112.6, 111.0, 110.9, 55.0, 47.8, 40.8. IR (KBr): 3223, 3042, 2921, 2858, 1609, 1516, 1449, 1328, 1271, 1216, 1133, 1092, 1048, 934, 809, 765, 733, 692, 594, 531 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{24}H_{24}N_2O$: 356.1889, found: 356.1888.

*4.3.11. 4-((2-Chlorophenyl)(1H-indol-3-yl)methyl)-N,N-dimethylaniline (**4k**).* White solid, mp 152–153 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.37 (d, *J*=8.0 Hz, 1H), 7.33 (d, *J*=8.0 Hz, 1H), 7.22 (d, *J*=8.2 Hz, 1H), 7.17–7.12 (m, 2H), 7.11–7.05 (m, 4H), 6.98 (t, *J*=7.8 Hz, 1H), 6.72 (d, *J*=8.4 Hz, 2H), 6.54 (s, 1H), 6.00 (s, 1H), 2.92 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 141.9, 136.7, 134.0, 130.5, 130.3, 129.7, 129.4, 127.3, 126.9, 126.5, 122.0, 119.8, 119.6, 119.3, 112.4, 110.9, 44.1, 40.6. IR (KBr): 3254, 2936, 2856, 1606, 1561, 1514, 1460, 1324, 1208, 1129, 1042, 937, 806, 751, 603, 560 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{23}H_{21}ClN_2$: 360.1388, found: 360.1390.

*4.3.12. 4-(1-(1H-Indol-3-yl)butyl)-N,N-dimethylaniline (**4l**).* Light yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.47 (d, *J*=8.4 Hz, 1H), 7.27 (d, *J*=8.0 Hz, 1H), 7.17–7.09 (m, 3H), 7.02–6.95 (m, 2H), 6.67 (d, *J*=8.2 Hz, 2H), 4.08 (t, *J*=8.0 Hz, 1H), 2.88 (s, 6H), 2.12–2.09 (m, 1H), 1.97–1.95 (m, 1H), 1.35–1.33 (m, 2H), 0.92 (t, *J*=6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8, 136.4, 133.8, 128.4, 127.1, 121.7, 121.3, 120.7, 119.6, 118.9, 112.7, 110.9, 41.4, 40.8, 38.5, 21.2, 14.2. IR (KBr): 3130, 2752, 2460, 1861, 1616, 1501, 1432, 1302, 1246, 1048, 930, 781, 711, 647, 542 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{20}H_{24}N_2$: 292.1939, found: 292.1936.

*4.3.13. 4-((1H-Indol-3-yl)methyl)-N,N-dimethylaniline (**4m**)*[3]. Light yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.54 (d, *J*=8.2 Hz, 1H), 7.30 (d, *J*=8.0 Hz, 1H), 7.21–7.14 (m, 3H), 7.06 (t, *J*=8.4 Hz, 1H), 6.83 (s, 1H), 6.70–6.68 (m, 2H), 4.02 (s, 2H), 2.89 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 136.4, 129.4, 129.2, 127.4, 122.1, 121.8, 119.2, 116.6, 113.0, 110.9, 40.9, 30.4. IR (KBr): 3240, 2864, 2641, 1826, 1716, 1623, 1512, 1452, 1232, 1234, 1046, 932, 803, 783, 734, 712, 657, 603, 534 cm^{-1}.

*4.3.14. 4-((1H-Indol-3-yl)(naphthalen-2-yl)methyl)-N,N-dimethylaniline (**4n**).* White solid, mp 151–152 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.80–7.69 (m, 3H), 7.61 (s, 1H), 7.43–7.40 (m, 3H), 7.35 (d, *J*=8.0 Hz, 1H), 7.28 (d, *J*=8.4 Hz, 1H), 7.14–7.11 (m, 3H), 6.96 (t, *J*=8.2 Hz, 1H), 6.68 (d, *J*=8.0 Hz, 2H), 6.59 (s, 1H), 5.75 (s, 1H), 2.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 142.3, 136.6, 132.1, 131.9, 129.6, 128.0, 127.9, 127.6, 127.5, 127.0, 126.9, 125.6, 125.2, 121.9, 120.4, 120.0, 119.3, 112.5, 110.9, 40.7, 29.7. IR (KBr): 3410, 3048, 2920, 2848, 1605, 1515, 1452, 1417, 1343, 1216, 1132, 1091, 1009, 950, 803, 744, 580 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{27}H_{24}N_2$: 376.1939, found: 376.1942.

*4.3.15. 3-Methoxy-N,N-dimethyl-4-((1-methyl-1H-indol-3-yl)(phenyl)methyl)aniline (**4o**).* White solid, mp 153–155 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26–7.22 (m, 6H), 7.16–7.14 (m, 2H), 6.96–6.94 (m, 1H), 6.86–6.83 (m, 1H), 6.38 (s, 1H), 6.29 (s, 1H), 6.19 (d, *J*=8.4 Hz, 1H), 5.96 (s, 1H), 3.73 (s, 3H), 3.61 (s, 3H), 2.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 150.2, 144.9, 137.3, 130.2, 128.8, 128.6, 127.8, 127.5,

125.5, 121.2, 120.9, 120.1, 118.6, 118.4, 108.8, 104.4, 96.2, 55.5, 40.7, 40.3, 32.5. IR (KBr): 3021, 2923, 2358, 1610, 1564, 1510, 1475, 1358, 1238, 1190, 1113, 1027, 977, 807, 741, 699, 643, 572 cm^{-1}. HRMS (ESI) ($[M]^+$) calcd for $C_{25}H_{26}N_2O$: 370.2052, found: 370.2049.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.03.050.

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