Synthesis of 3-Indolylarylmethanamides by Samarium Triiodide Catalyzed Friedel–Crafts Amidoalkylation

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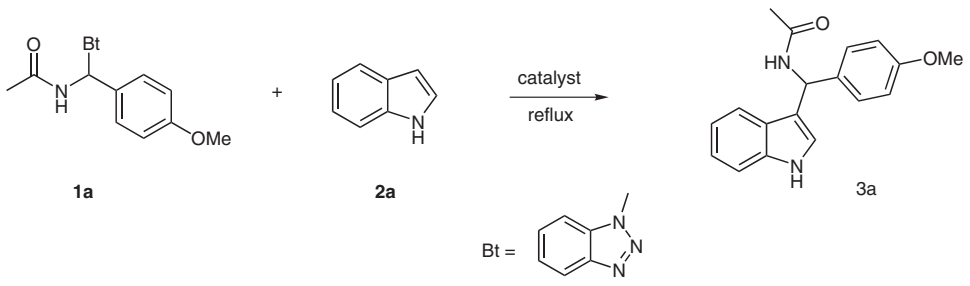
Abstract: The amidoalkylation of indoles with *N*-(α-benzotriazol-1-ylalkyl)amides was smoothly realized with samarium triiodide as a catalyst to give a series of novel 3-indolyl arylmethanamides with good yields and selectivities.

Key words: amidoalkylation, *N*-(α-benzotriazol-1-ylalkyl)amides, indoles, samarium triiodide, catalysis

3-Substituted indoles usually possess numerous biological activities, act as important intermediates for the synthesis of indole-based alkaloids or pharmaceutical compounds, and constitute a key structural unit for many natural products.[1] Among them, the 3-indolyl arylmethanamine derivatives exist in a number of natural and unnatural products with significant biological activities[2] and have attracted the attention of many synthetic chemists in recent years.

The aza-Friedel–Crafts reaction of indole with imines catalyzed by Lewis acids provide straightforward access to 3-indolylarylmethanamines, however, only moderate yields have been obtained[3a,b] and the bisindolylmethanes were always formed as a by-product in significant amounts[3a,b] or even as the sole product.[3c] Very recently, a three-component aza-Friedel–Crafts reaction[3d] of aldehyde, amine, and indole in water was developed, catalyzed by carboxylic acid, which provided the 3-indolylarylmethanamine. Despite the mild reaction conditions and avoidance of the bisindolyl compound formation, the amine was limited only to *o*-anisidine. Good yields of the 3-indolylarylmethanamine derivatives as well as high enantioselectivities could be obtained by an alternative method involving the reaction of indoles with N-protected imines, such as: 1) modification of the imine nitrogen with sulfonyl[4a–4d] using a chiral copper-complex or organic phosphoric acid as the catalyst; 2) introduction of trifluoromethyl[4e,f] to the imino nitrogen, catalyzed by boron trifluoride; 3) employment of *N*-alkoxycarbonyl protected α-imino esters[4g,h] with a copper complex or biphenylphosphine–palladium(II) complex as the catalyst. In addition, treatment of 3-lithio-1-TBDMS-indole with aromatic tosylaldimines offered another approach to the functionalized 3-indolylarylmethanamines.[5] The aldimines may also be transformed into *N*-acyl iminium salts in the presence of acyl chlorides,[6a,b] which has realized the amidoalkylation of indoles smoothly without any catalyst. Although the method seems simple and practical, *N*-acyl iminium salts are generally hygroscopic and sensitive to hydrolysis[6a] and must be prepared under extreme anhydrous conditions, along with the involvement of environmentally toxic media. The aminoalkylbenzotriazoles have been used to alkylate the 3-position of indoles to afford 3-indolylmethyleneamines in the presence of such Lewis acids as $AlCl_3$ or $ZnCl_2$.[6c] Unfortunately, the method was limited to the preparation of compounds without aryl substitution on the methylene. Herein we wish to report the synthesis of 3-indolylarylmethanamides by amidoalkylation of indoles with *N*-(α-benzotriazol-1-ylalkyl)amides.

N-(α-Benzotriazol-1-ylalkyl)amides are readily accessible amidoalkylation reagents, which are prepared from the three-component condensation of a primary (or secondary) amide, benzotriazole and an aldehyde.[7] The reagents have been used for amidoalkylation of many compounds, such as active methylene compounds,[7a,8] alcohols and thiols,[9] active aromatic compounds[10] and amines.[11] In the



Scheme 1

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Table 1 Lewis Acid Catalyzed Friedel–Crafts Amindoalkylation of Indoles with **1a**[a]

Entry	Lewis acid	Catalyst (mol%)	Solvent	Time (h)	Yield (%)[b]
1	$ZnCl_2$	100	THF	20	–[c]
2	$AlCl_3$	100	THF	20	–[c]
3	$FeCl_3$	100	THF	20	–[c]
4	SmI_3	50	THF	16	85
5	SmI_3	20	THF	16	84
6	SmI_3	20	MeCN	16	56
7	SmI_3	20	CH_2Cl_2	16	63
8	SmI_3	20	Toluene	16	34

[a] All reactions were carried out under reflux unless otherwise specified.
[b] Isolated yield.
[c] No reaction.

process of the amidoalkylation reaction, *N*-(α-benzotriazol-1-ylalkyl)amides furnish the azomethine electrophile by acid-promoted elimination of the benzotriazolyl group, which reacts with nucleophiles.[12] In this paper, we present the results of our studies on the reaction between *N*-(α-benzotriazol-1-ylalkyl)amides and indoles catalyzed by samarium triiodide, providing 3-indolylarylmethanamine derivatives in good yields.

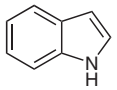
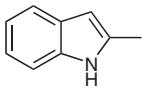
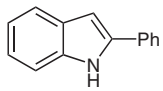
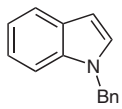
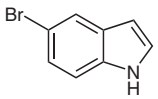
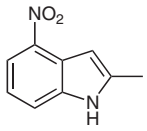
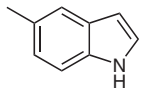
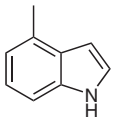
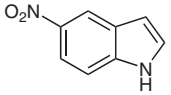
The reaction of *N*-[(α-benzotriazol-1-yl)(4-methoxyphenyl)methyl]acetamide (**1a**) with indole catalyzed by Lewis acids was initially performed in order to optimize the reaction conditions (Scheme 1).

A series of Lewis acids were screened to promote the reaction shown in Scheme 1, and the results are listed in Table 1. Surprisingly, commonly used and less expensive Lewis acids ($ZnCl_2$, $AlCl_3$ and $FeCl_3$) tested in refluxing tetrahydrofuran showed no catalytic activity here; however, the employment of 50 mol% of samarium triiodide (SmI_3) afforded the desired product **3a** in 85% yield (Table 1, entry 4). Reducing the catalyst load to 20 mol% did not decrease the reaction efficiency and afforded a comparable yield in the same period of time (Table 1, entry 5).

The effect of the solvent was also investigated; the reaction of **1a** and **2a** catalyzed by samarium triiodide (20 mol%) was performed in tetrahydrofuran, acetonitrile, dichloromethane and toluene, respectively (Table 1, entries 5–8). Product **3a** could be obtained in 34–84% yields in 16 hours. The reaction carried out in tetrahydrofuran afforded the highest yield (Table 1, entry 5), thus, reflux in THF with 20 mol% of SmI_3 catalyst was established as the optimized reaction conditions.

A variety of indoles and *N*-(α-benzotriazol-1-ylalkyl)amides reacted under the established conditions, demonstrating the generality of the method for the prepa-

Table 2 Samarium Triiodide Catalyzed Friedel–Crafts Amidoalkylation of Indoles with *N*-(α-Benzotriazol-1-ylalkyl)amides

Entry	R^1	R^2	Indole	Product	Time (h)	Yield (%)[a]
1	Me	4-$MeOC_6H_4$	 **2a**	**3a**	16	84
2	Me	Ph	**2a**	**3b**	16	86
3	Ph	Ph	**2a**	**3c**	20	73
4	Ph	4-$O_2NC_6H_4$	**2a**	**3d**	16	87
5	Me	4-$MeOC_6H_4$	 **2b**	**3e**	16	75
6	Me	Ph	**2b**	**3f**	20	80
7	Me	4-$MeOC_6H_4$	 **2c**	**3g**	20	70
8	Me	Ph	**2c**	**3h**	24	76
9	Me	4-$MeOC_6H_4$	 **2d**	**3i**	20	72
10	Me	Ph	**2d**	**3j**	20	75
11	Ph	Ph	 **2e**	**3k**	20	63
12	Me	Ph	**2e**	**3l**	20	65
13	Ph	Ph	 **2f**	–[b]	20	–
14	Ph	4-$O_2NC_6H_4$	 **2g**	**3m**	20	76
15	Me	4-$MeOC_6H_4$	**2g**	**3n**	20	68
16	Me	4-$MeOC_6H_4$	 **2h**	**3o**	16	78
17	Me	4-$MeOC_6H_4$	 **2i**	–[b]	20	–

[a] Yield of pure isolated product.
[b] No reaction.

ration of 3-indolylarylmethanamine derivatives (Scheme 2). The results are listed in Table 2.

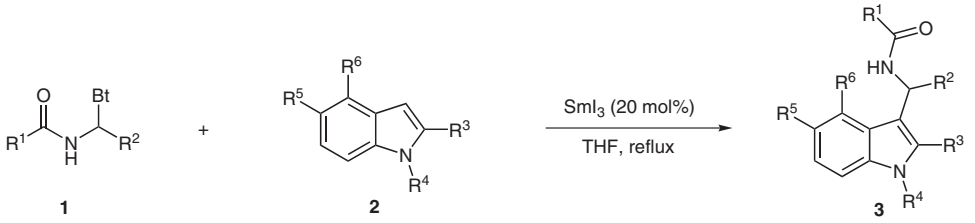
As can be seen, unsubstituted indole **2a** underwent 3-amidoalkylation smoothly to afford **3a**–**d** in 73–87% yields (Table 2, entries 1–4). 2-Methylindole also showed good reactivity, leading to **3e** and **3f** in 75% and 80% yield, respectively, in 16–20 hours (Table 2, entries 5 and 6). However, with a bulky group such as phenyl at the 2-position of the indole, the reaction required longer times to afford satisfactory yields (Table 2, entries 7 and 8). Longer reaction times were also necessary when *N*-benzylindole was used (Table 2, entries 9 and 10). The electronic effect of the substituent on the indole also exerted influence on the amidoalkylation reaction; with electron-donating groups such as methyl, the reaction gave 68–78% yields (Table 2, entries 14, 15 and 16), while with electron-withdrawing groups such as bromo, it afforded lower yields (Table 2, entries 11 and 12). Although the reaction seems general, we did encounter two failures: substrates **2f** and **2i** with a strongly electron-withdrawing nitro group located at the 4- or 5-position of the indole failed to produce the expected amidoalkylation products and no reaction occurred (Table 2, entries 13 and 17). In all the cases, the R^1 group in amidoalkylation reagents **1** could be either methyl or phenyl, and R^2 should be an aryl. When R^2 is an alkyl such as propyl, the amidoalkylation could not occur and the starting materials were recovered almost quantitatively.

To extend the application scope of the reaction, methyl 1-benzotriazol-1-yl phenylmethylcarbamate (**4**) was reacted with indole under the same conditions (Scheme 3). Unfortunately, instead of the desired amidoalkylation product **5**, the bisindole compound **6** was formed (determined by comparison with an authentic sample).

A control experiment in the absence of indole showed that decomposition of **4** took place under the reaction conditions in one hour (benzaldehyde and benzotriazole were detected). Apparently, compound **4** underwent samarium triiodide catalyzed decomposition in preference to amidoalkylation of the indole. It was reported that indoles were prone to dimerization with aldehydes or ketones in the presence of a Lewis acid.[13] Therefore, the formation of **6** could be ascribed to the reaction of indole with the in situ produced benzaldehyde.

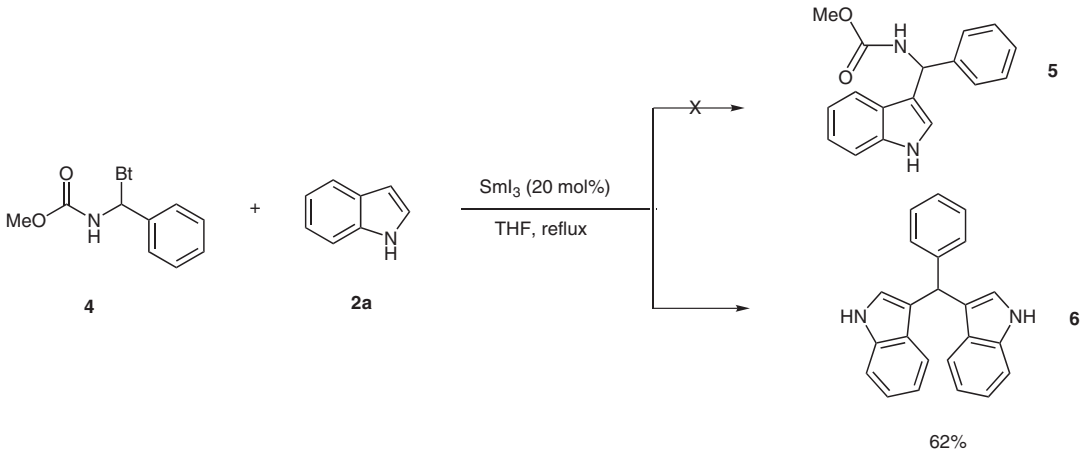
A possible mechanism may also be proposed for the formation of **3**. According to previous reports that, assisted by Lewis acids, benzotriazole adducts could form a benzotriazole anion and the corresponding carbocation that could then react with nucleophiles,[10,14] the samarium triiodide catalyzed amidoalkylation of indoles with *N*-(α-benzotriazol-1-ylalkyl)amides could be described as shown in Scheme 4. It should be mentioned that when R^2 is an aryl group, loss of the benzotriazole anion involves the cleavage of a more active benzylic C–N bond and could facilitate the amidoalkylation process. However, in cases where R^2 is an alkyl group such as propyl, breaking the C–N bond becomes quite difficult even with the assistance of catalyst, therefore no reaction could be observed.

In conclusion, we have developed a samarium triiodide catalyzed amidoalkylation of indoles with *N*-(α-benzotriazol-1-ylalkyl)amides, thus providing a facile and clean synthesis of 3-indolyl arylmethanamides.



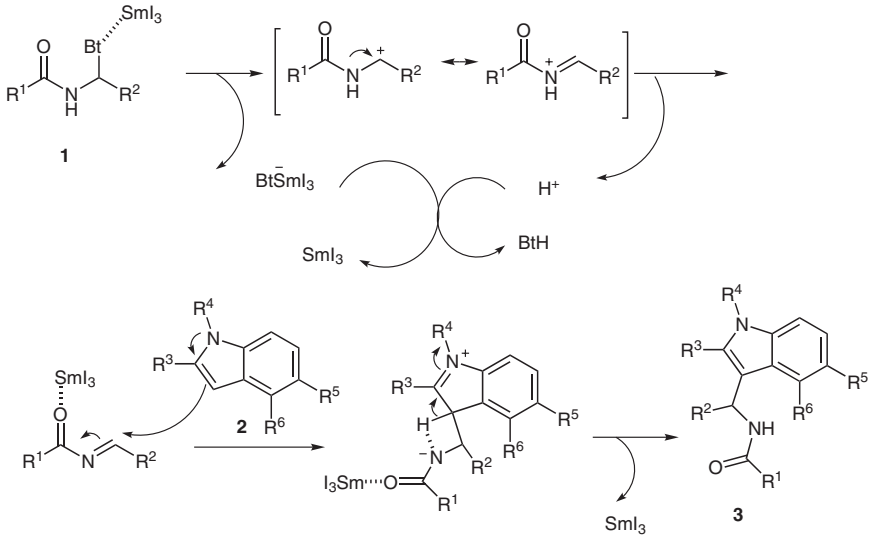
1 **2** **3**

Scheme 2



4 **2a**

Scheme 3



Scheme 4

THF was distilled from sodium-benzophenone immediately prior to use. ^{1}H NMR (400 MHz) spectra were recorded on a Bruker AV400 NMR instrument as DMSO or $CDCl_3$ solutions using TMS as internal standard. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in Hz. IR spectra were recorded as films or using KBr disks with a NEXUS 670 FTIR spectrometer. Mass spectra were performed on a Thermo Finnigan GC-MS instrument (Trace DSQ). Elemental analyses were performed on a Vario-ELIII instrument. *N*-(α-Benzotriazol-1-ylalkyl)amides 1 were easily prepared from benzotriazole, aldehydes and an amide in toluene by a previously described method.[7] Methyl 1-benzotriazol-1-yl phenylmethylcarbamate (4) was prepared according to the general procedure for the preparation of benzyloxycarbonylamino-1-(1-benzotriazolyl)alkanes.[15] Petroleum ether (PE), where used, had a boiling range of 60–90 °C.

Friedel–Crafts Amidoalkylation of Indoles with *N*-(α-Benzotriazol-1-ylalkyl)amides Catalyzed by SmI_3; General Procedure

To samarium powder (0.03 g, 0.2 mmol) in a flask was added anhydrous THF (10 mL) and I_2 (0.076 g, 0.3 mmol) and the mixture was stirred at r.t. for 1 h. To the SmI_3–THF suspension thus prepared was added *N*-(α-benzotriazol-1-ylalkyl)amide **1** (1.0 mmol) and indole **2** (1.0 mmol). The reaction mixture was stirred until the disappearance of **1** was observed, then the reaction was quenched with aq HCl (0.1M, 3 mL) and extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with sat. $Na_2S_2O_3$ (10 mL), sat. Na_2CO_3 (10 mL), then with brine (2 × 10 mL) and were dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by column chromatography (EtOAc–PE, 1:2) to give the desired product **3**.

***N*-[(1*H*-Indol-3-yl)(4-methoxyphenyl)methyl]acetamide (3a)**

White powder; mp 162–165 °C.

IR (KBr): 3370, 3300, 1642, 1513, 1400, 743 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.03 (s, 3 H), 3.80 (s, 3 H), 6.12 (d, *J* = 8.0 Hz, 1 H), 6.46 (d, *J* = 8.0 Hz, 1 H), 6.77 (s, 1 H), 6.86 (d, *J* = 8.0 Hz, 2 H), 7.07 (t, *J* = 8.0 Hz, 1 H), 7.19 (t, *J* = 8.0 Hz, 1 H), 7.25–7.29 (m, 1 H), 7.34 (d, *J* = 8.0 Hz, 1 H), 7.44 (d, *J* = 8.0 Hz, 1 H), 8.24 (br s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 23.1, 49.0, 55.5, 112.0, 114.0, 117.4, 119.0, 119.4, 121.7, 123.8, 126.4, 128.7, 135.5, 137.1, 158.5, 168.6.

MS (EI, 70 eV): *m*/*z* (%) = 295 (5.4) [M + H]$^+$, 177 (99.2) [M – indole]$^+$, 162 (100) [177 – CH_3]$^+$, 134 (99.5), 107 (29.7), 92 (46.3), 77 (57.1).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.63; H, 5.90; N, 9.63.

***N*-[(1*H*-Indol-3-yl)(phenyl)methyl]acetamide (3b)**

White powder; mp 176–179 °C.

IR (KBr): 3407, 3381, 3305, 1646, 1538, 742 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.01 (s, 3 H), 6.13–6.22 (m, 2 H), 6.52–6.71 (m, 1 H), 6.69 (s, 1 H), 7.07–7.11 (m, 1 H), 7.19–7.34 (m, 5 H), 7.44 (m, 1 H), 8.41 (s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 23.4, 50.4, 111.5, 117.2, 119.3, 119.9, 122.5, 123.6, 125.9, 127.0, 127.2, 128.5, 136.7, 141.3, 169.2.

MS (EI, 70 eV): *m*/*z* (%) = 265 (75.1) [M + H]$^+$, 264 (100) [M]$^+$, 222 (98.9) [M + H – CH_3CO]$^+$, 205 (99.1), 145 (52.5), 118 (98.3), 104 (90.7), 77 (30.0).

Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.47; H, 5.87; N, 10.43.

***N*-[(1*H*-Indol-3-yl)(phenyl)methyl]benzamide (3c)**

White powder; mp 178–180 °C.

IR (KBr): 3410, 3299, 3309, 1642, 1524, 701 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 6.63 (d, *J* = 8.0 Hz, 1 H), 6.88 (s, 1 H), 6.97 (d, *J* = 8.0 Hz, 1 H), 7.07–7.10 (t, *J* = 8.0 Hz, 1 H), 7.28–7.53 (m, 10 H), 7.93 (d, *J* = 8.0 Hz, 2 H), 9.19 (d, *J* = 8.0 Hz, 1 H), 11.0 (s, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 50.3, 112.1, 116.9, 119.2, 121.7, 124.4, 126.6, 127.3, 127.8, 128.0, 128.1, 128.6, 128.8, 131.6, 135.1, 137.0, 143.3, 166.2.

MS (EI, 70 eV): *m*/*z* (%) = 207 (16.3) [M – indolyl]$^+$, 206 (100) [M – PhCONH]$^+$, 105 (32.0), 91 (38.2).

Anal. Calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 81.25; H, 5.68; N, 8.66.

***N*-[(1*H*-Indol-3-yl)(4-nitrophenyl)methyl]benzamide (3d)**

White powder; mp 107–110 °C.

IR (KBr): 3415, 3299, 1642, 1520, 744 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 6.68–6.73 (m, 1 H), 6.91–6.98 (m, 2 H), 7.06–7.10 (m, 1 H), 7.43–7.51 (m, 4 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 7.90 (d, *J* = 8.0 Hz, 2 H), 8.22 (d, *J* = 8.0 Hz, 2 H), 9.33 (d, *J* = 8.0 Hz, 1 H), 11.00 (s, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 50.2, 112.2, 115.5, 119.0, 119.4, 122.0, 124.0, 124.7, 126.4, 128.1, 128.7, 129.0, 131.8, 134.7, 137.0, 147.0, 151.1, 166.5.

MS (EI, 70 eV): *m*/*z* (%) = 207 (100) [M + H – NO_2 – $PhCONH_2$]$^+$, 178 (16.5), 129 (26.4), 117 (99.2), 91 (96.3), 77 (61.1).

Anal. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31. Found: C, 70.99; H, 4.46; N, 11.15.

N-[(4-Methoxyphenyl)(2-methyl-1*H*-indol-3-yl)methyl]acetamide (3e)
White powder; mp 160–163 °C.

IR (KBr): 3405, 3268, 3058, 1630, 1544, 696 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 1.92 (s, 3 H), 2.34 (s, 3 H), 3.35 (s, 3 H), 6.33 (d, *J* = 8.0 Hz, 1 H), 6.85–6.93 (m, 2 H), 7.18–7.37 (m, 6 H), 8.63 (s, 1 H), 10.80 (s, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 21.8, 23.1, 40.0, 49.6, 111.7, 116.5, 118.8, 123.3, 124.0, 126.6, 127.1, 127.5, 128.5, 135.4, 143.6, 168.7.

MS (EI, 70 eV): *m*/*z* (%) = 218 (30.1) [M – H – OCH_3 – $NHCOCH_3$]$^+$, 207 (78.9), 117 (96.3), 91 (100) [$PhCH_2$]$^+$, 77 (22.6).

Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.13; H, 6.40; N, 9.17.

N-[(2-Methyl-1*H*-indol-3-yl)(phenyl)methyl]acetamide (3f)
White powder; mp 160–163 °C.

IR (KBr): 3382, 3324, 3057, 1639, 1536, 744 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.05 (s, 3 H), 2.37 (s, 3 H), 6.25 (d, *J* = 8.0 Hz, 1 H), 6.54 (d, *J* = 8.0 Hz, 1 H), 6.92–6.96 (m, 1 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 7.21–7.30 (m, 5 H), 8.23 (s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 12.0, 23.4, 49.2, 110.7, 111.5, 118.5, 119.6, 121.3, 126.6, 126.9, 128.4, 129.1, 133.3, 135.5, 141.2, 169.5.

MS (EI, 70 eV): *m*/*z* (%) = 279 (30.6) [M + H]$^+$, 278 (100) [M]$^+$, 235 (40.5), 220 (95.2), 204 (31.7), 148 (99.3), 132 (45.0), 106 (94.3).

Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.48; H, 6.64; N, 9.89.

N-[(4-Methoxyphenyl)(2-phenyl-1*H*-indol-3-yl)methyl]acetamide (3g)
White powder; mp 200–202 °C.

IR (KBr): 3421, 3270, 1662, 1510, 747 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.03 (s, 3 H), 3.77 (s, 3 H), 6.30 (d, *J* = 8.0 Hz, 1 H), 6.65 (d, *J* = 8.0 Hz, 1 H), 6.80 (d, *J* = 8.0 Hz, 2 H), 7.02 (t, *J* = 8.0 Hz, 1 H), 7.18–7.26 (m, 3 H), 7.38–7.46 (m, 4 H), 7.57 (d, *J* = 8.0 Hz, 2 H), 8.30 (s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 23.4, 49.3, 55.3, 111.4, 112.0, 113.8, 119.7, 120.1, 122.5, 126.9, 128.0, 128.48, 128.53, 129.1, 132.2, 133.6, 136.2, 136.5, 158.5, 169.4.

MS (EI, 70 eV): *m*/*z* (%) = 193 (99.5) [2-phenyl-3-indolyl]$^+$, 163 (68.8), 115 (26.4), 92 (98.9), 77 (29.7), 71 (69.3).

Anal. Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.65; H, 6.12; N, 7.38.

N-[Phenyl(2-phenyl-1*H*-indol-3-yl)methyl]acetamide (3h)
White powder; mp 250 °C (dec.).

IR (KBr): 3418, 3269, 3060, 1657, 1495, 743 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.07 (s, 3 H), 6.30 (s, 1 H), 6.70 (d, *J* = 8.0 Hz, 1 H), 7.01 (t, *J* = 8.0 Hz, 1 H), 7.19–7.31 (m, 6 H), 7.40–7.49 (m, 4 H), 7.59 (d, *J* = 8.0 Hz, 2 H), 8.25 (s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 22.9, 49.3, 111.8, 112.6, 119.2, 120.9, 121.9, 126.9, 127.1, 127.2, 128.3, 128.6, 129.0, 129.2, 132.9, 136.3, 136.8, 142.9, 169.2.

MS (EI, 70 eV): *m*/*z* (%) = 220 (100) [M – Ph – $COCH_3$]$^+$, 205 (99.8), 177 (95.3), 145 (98.3), 105 (66.8), 57 (99.7).

Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 80.96; H, 6.07; N, 8.32.

N-[(1-Benzyl-1*H*-indol-3-yl)(4-methoxyphenyl)methyl]acetamide (3i)
White powder; mp 174–176 °C.

IR (KBr): 3327, 3131, 1693, 1543, 753 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 1.87 (s, 3 H), 3.72 (s, 3 H), 5.34 (s, 2 H), 6.29 (d, *J* = 8.0 Hz, 1 H), 7.39–6.87 (m, 14 H), 8.62 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 23.1, 48.9, 49.4, 55.5, 110.7, 114.0, 117.3, 119.4, 119.7, 122.0, 127.0, 127.4, 127.6, 127.8, 128.7, 129.0, 135.2, 136.9, 138.8, 158.5, 168.6.

MS (EI, 70 eV): *m*/*z* (%) = 327 (3.1) [M + H – $NHCOCH_3$]$^+$, 221 (98.3), 205 (100) [M + H – $PhCH_2$ – OCH_3 – CH_3CONH]$^+$, 177 (66.4), 145 (75.9), 119 (99.1), 91 (99.7), 64 (99.5).

Anal. Calcd for $C_{25}H_{24}N_2O_2$: C, 78.10; H, 6.29; N, 7.29. Found: C, 78.32; H, 6.16; N, 7.17.

N-[(1-Benzyl-1*H*-indol-3-yl)(phenyl)methyl]acetamide (3j)
White powder; mp 181–184 °C.

IR (KBr): 3300, 3059, 1641, 1538, 741 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.05 (s, 3 H), 5.23 (s, 2 H), 6.10 (d, *J* = 8.0 Hz, 1 H), 6.54 (d, *J* = 8.0 Hz, 1 H), 6.74 (s, 1 H), 7.08 (t, *J* = 6.8 Hz, 3 H), 7.19 (s, 1 H), 7.25–7.29 (m, 5 H), 7.32–7.40 (m, 4 H), 7.48 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 23.4, 50.1, 50.3, 110.1, 116.5, 119.6, 119.8, 122.4, 126.7, 127.0, 127.3, 127.55, 127.59, 127.7, 128.5, 128.8, 137.1, 137.3, 141.3, 169.2.

MS (EI, 70 eV): *m*/*z* (%) = 341 (100) [M + 2H – CH_3]$^+$, 298 (51.3), 204 (73.1), 117 (34.6), 104 (70.9), 91 (18.3).

Anal. Calcd for $C_{24}H_{22}N_2O$: C, 81.33; H, 6.26; N, 7.90. Found: C, 81.54; H, 6.32; N, 7.79.

N-[(5-Bromo-1*H*-indol-3-yl)(phenyl)methyl]benzamide (3k)
White powder; mp 179–181 °C.

IR (KBr): 3310, 3127, 1656, 1510, 826 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 6.64 (d, *J* = 8.0 Hz, 1 H), 6.73 (d, *J* = 7.6 Hz, 1 H), 6.81 (s, 1 H), 7.21–7.52 (m, 8 H), 7.62 (s, 1 H), 7.79–7.84 (m, 3 H), 8.36 (s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 50.8, 112.9, 113.3, 116.9, 121.9, 124.9, 125.5, 125.9, 127.0, 127.1, 127.2, 127.6, 128.7, 131.7, 134.2, 135.4, 140.8, 166.7.

MS (EI, 70 eV): *m*/*z* (%) = 220 (67.4), 205 (100) [M – Br – Ph-CONH]$^+$, 177 (30.7), 145 (32.0), 115 (15.8), 105 (21.1), 81 (21.1).

Anal. Calcd for $C_{22}H_{17}BrN_2O$: C, 65.20; H, 4.23; N, 6.91. Found: C, 65.53; H, 4.21; N, 6.81.

N-[(5-Bromo-1*H*-indol-3-yl)(phenyl)methyl]acetamide (3l)
White powder; mp 140–143 °C.

IR (KBr): 3298, 3122, 1668, 1517, 1401, 750 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 1.90 (s, 3 H), 6.32 (d, *J* = 8.0 Hz, 1 H), 7.00 (s, 1 H), 7.17–7.27 (m, 2 H), 7.34–7.36 (m, 5 H), 7.49 (s, 1 H), 8.68 (d, *J* = 8.0 Hz, 1 H), 11.2 (s, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 23.0, 49.3, 111.7, 114.1, 116.8, 121.6, 124.2, 125.7, 127.2, 127.5, 128.1, 128.7, 135.7, 143.0, 168.8.

MS (EI, 70 eV): *m*/*z* (%) = 342 (2.3), 220 (64.1), 205 (100) [M – Br – PhCONH]$^+$, 177 (20.9), 145 (25.0), 115 (8.1), 105 (15.5), 81 (16.7), 57 (42.8).

Anal. Calcd for $C_{17}H_{15}BrN_2O$: C, 59.49; H, 4.41; N, 8.16. Found: C, 59.28; H, 4.52; N, 8.02.

_N_-[(5-Methyl-1_H_-indol-3-yl)(4-nitrophenyl)methyl]benzamide (3m)

Red powder; mp 205–209 °C.

IR (KBr): 3419, 3098, 1641, 1521, 720 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 2.30 (s, 3 H), 6.69 (d, *J* = 8.0 Hz, 1 H), 6.90 (m, 2 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 7.43–7.57 (m, 3 H), 7.75 (d, *J* = 8.0 Hz, 2 H), 7.90–7.96 (m, 2 H), 8.22 (d, *J* = 8.0 Hz, 2 H), 9.29 (d, *J* = 8.0 Hz, 1 H), 10.93 (s, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 21.8, 50.1, 111.9, 114.9, 118.5, 124.0, 124.8, 126.3, 126.7, 127.9, 128.1, 128.7, 128.9, 131.8, 134.7, 135.3, 146.9, 151.2, 166.5.

MS (EI, 70 eV): *m*/*z* (%) = 340 (3.8) [M + H – NO_2]$^+$, 250 (100) [M – CH_3 – PhCONH]$^+$, 235 (98.2), 220 (98.5), 143 (70.6), 134 (99.1), 117 (99.4).

Anal. Calcd for $C_{23}H_{19}N_3O_3$: C, 71.67; H, 4.97; N, 10.90. Found: C, 71.78; H, 5.06; N, 10.78.

_N_-[(4-Methoxyphenyl)(5-methyl-1_H_-indol-3-yl)methyl]acetamide (3n)

White powder; mp 194–197 °C.

IR (KBr): 3399, 3285, 2650, 1648, 1511, 745 cm^{-1}.

^{1}H NMR (400 Hz, DMSO-d_6): δ = 1.89 (s, 3 H), 2.67 (s, 3 H), 3.69 (s, 3 H), 6.29 (d, *J* = 8.0 Hz, 1 H), 6.77–6.84 (m, 3 H), 6.93 (d, *J* = 8.0 Hz, 1 H), 7.14–7.22 (m, 4 H), 8.48 (d, *J* = 8.0 Hz, 1 H), 10.83 (s, 1 H).

^{13}C NMR (100 Hz, DMSO-d_6): δ = 12.2, 23.0, 48.1, 55.5, 110.9, 111.9, 113.8, 118.6, 119.1, 120.4, 127.3, 128.1, 133.2, 135.0, 135.6, 158.3, 168.8.

MS (EI, 70 eV): *m*/*z* (%) = 310 (3.2) [M + 2H], 220 (99.3), 205 (100) [M + H – CH_3 – CH_3O – CH_3CONH]$^+$, 177 (44.7), 161 (16.1), 145 (52.5), 115 (9.8), 105 (32.6), 57 (98.9).

Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.26; H, 6.65; N, 8.86.

_N_-[(4-Methoxyphenyl)(4-methyl-1_H_-indol-3-yl)methyl]acetamide (3o)

White powder; mp 199–202 °C.

IR (KBr): 3401, 3380, 3003, 2955, 2838, 1652, 1511, 1253, 748 cm^{-1}.

^{1}H NMR (400 Hz, $CDCl_3$): δ = 2.02 (s, 3 H), 2.58 (s, 3 H), 3.79 (s, 3 H), 6.09 (d, *J* = 8.0 Hz, 1 H), 6.59 (d, *J* = 6.8 Hz, 2 H), 6.85–6.88 (m, 3 H), 7.07–7.11 (m, 1 H), 7.18 (d, *J* = 8.0 Hz, 1 H), 7.25 (d, *J* = 6.8 Hz, 2 H), 8.24 (s, 1 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 20.1, 23.4, 50.8, 55.3, 109.2, 113.8, 118.4, 121.7, 122.6, 124.3, 124.9, 128.1, 130.9, 134.4, 137.2, 158.7, 168.6.

MS (EI, 70 eV): *m*/*z* (%) = 220 (91.8), 205 (100) [M + H – CH_3 – CH_3O – CH_3CONH]$^+$, 177 (51.2), 145 (36.6), 117 (20.0), 57 (96.3).

Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.19; H, 6.37; N, 9.15.

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