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Novel Preparation of Hemiaminal Derivatives with BPO and *N,N*-Dimethylamides, and Their Synthetic Use for (Aminomethyl)indoles

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Keywords: BPO / Hemiaminal / Friedel-Crafts Alkylation / Amide / (Aminomethyl)indole

A novel preparation of hemiaminal derivatives bearing both an amide group and a benzoate group was carried out in good yields by the treatment of BPO in *N,N*-dimethylamides under warming condition at 80 °C or irradiation with a mercury lamp. Further treatment of the obtained hemiaminal derivatives with indoles in 1,1,1,3,3,3-hexafluoro-2-propanol generated the corresponding C-C bonded indoles bearing an amide group in good yields. The formed indoles bearing an amide group were transformed into the corresponding indoles bearing an aminomethyl group smoothly.

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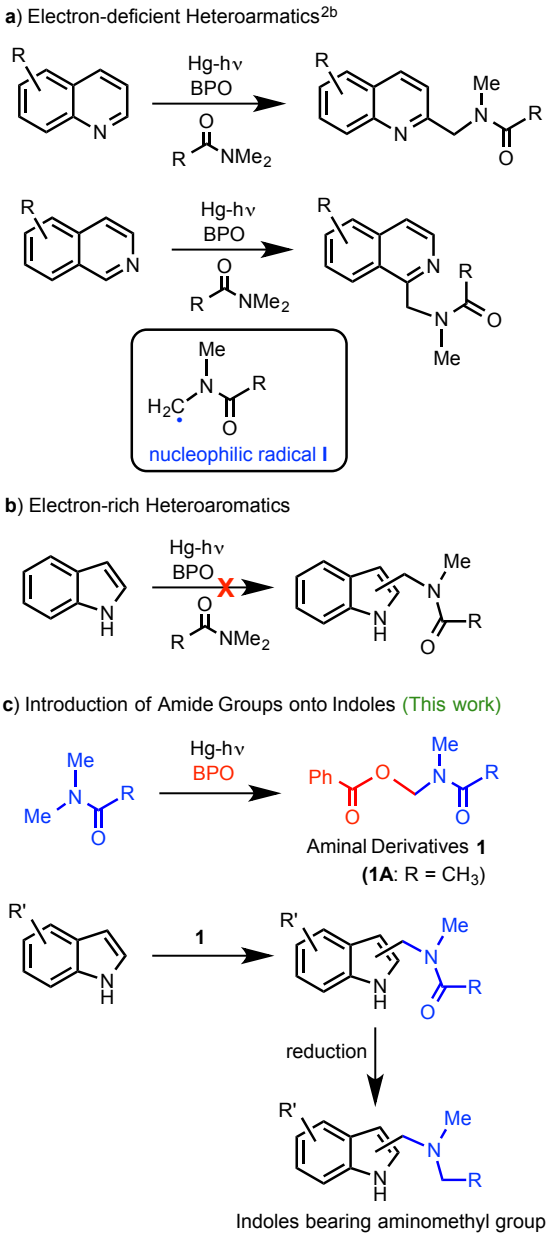
Introduction

Benzoyl peroxide (BPO) is one of the most useful radical initiators and has been used for the bromination of the benzylic position with *N*-bromosuccinimide (NBS), and the reduction and C-C bond formation of alkyl halides, aryl halides, and xanthate esters with Bu_3SnH, $(Me_3Si)_3SiH$, $Ph_4Si_2H_2$, *etc*.[1] Recently, we reported the introduction of ethers, cyclic ethers, and 18-crown-6 onto electron-deficient heteroaromatic bases, such as quinolines, isoquinolines, and pyridines, by using BPO under warming condition at 80 °C or irradiation with a mercury lamp;[2a] the introduction of tertiary amide groups onto quinolines and isoquinolines by using BPO and tertiary amides, such as *N,N*-dimethylacetamide, *N,N*-dimethylpropionamide, and *N*-acetylpyrrolidine, under irradiation with a mercury lamp;[2b] and the introduction of cycloalkyl groups onto quinolines, isoquinolines, and benzothiazole by using BPO and cycloalkanes, such as cyclopentane, cyclohexane, cycloheptane, and cyclooctane, under warming condition (100 °C),[2c] as shown in Scheme 1 (**a**). In those reactions, BPO was used as the radical initiator and the oxidant. Based on those previous studies,[2] we tried to carry out an oxidative introduction of a tertiary amide group onto electron-rich heteroaromatics, such as indole and *N*-methylindole, by using BPO and *N,N*-dimethylacetamide under irradiation with a mercury lamp (Scheme 1, **b**). However, oxidative C-C bonded products were not formed at all because amide radicals **I** had a highly nucleophilic character and a small amount of hemiaminal derivative **1A** (R = CH_3), which was a C-O bonded product of the reaction of BPO and *N,N*-dimethylacetamide, was formed. Then, we attempted to perform the reaction of BPO and *N,N*-dimethylacetamide under irradiation with a mercury lamp and surprisingly, we obtained hemiaminal derivative **1A** in good yield. To the best of our knowledge, the synthetic use of BPO, *i.e*., the introduction of the benzoate group of BPO to the product is quite limited. Recently, the preparation of secondary aromatic amides with diaroyl peroxides and isocyanides in the presence of Bu_4NI,[3a] asymmetric



Scheme 1. Introduction of Amide Groups onto Aromatics

α-benzoyloxylation of aldehydes with BPO,[3b,3c] the preparation of α-aroyloxy chromones with tertiary enaminones and diaroyl peroxides,[3d] and the preparation of α-benzoyloxyketones with tertiary enaminones and BPO in the presence of $Mn(OAc)_2$[3e] were reported. On the other hand, the preparation of hemiaminal derivatives by the reaction of cyclic ethers and $TsNH_2$ in the presence of $Cu(O_3SCF_3)_2$,[4a] the reaction of ethers, diazoles, and ^{t}BuOOH in the presence of $FeCl_3$•$6H_2O$,[4b] the reaction of aromatic α-ketocarboxylic acids, ^{t}BuOOH, and amides, such as *N,N*-dimethylformamide and *N,N*-dimethylacetamide, in the presence of Bu_4NI,[4c] and the reaction of tertiary amides and ^{t}BuOOBu^t in the presence of $FeCl_3$, and their use for C-C bond formation on indoles through the Friedel-Crafts alkylation[4d] were reported.

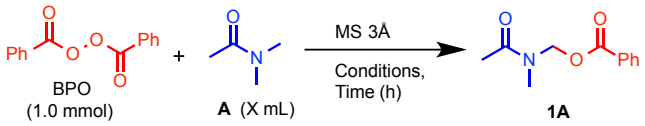
Indoles bearing aminoalkyl groups are quite important because they are found in many natural products isolated from animals and plants and show potent biological activities.[5] In particular, serotonin and melatonin, which are 3-(β-aminoethyl)indoles, are, respectively, a neurotransmitter and a hormone, and both regulate the circadian rhythm.[5c] Recent reports of the preparation of indoles bearing aminoalkyl groups with indoles under transition-metal-free conditions are as follows:[6] the preparation of 3-(α-*N*-*p*-tosylamino)methylindoles with indole, ^{t}BuLi, and aromatic *N*-*p*-tosylaldimines;[6a] the preparation of *N*-acetyl 3-indolyl-α-amino acid esters with indoles and methyl α-(acetylamino)acrylate in the presence of $EtAlCl_2$;[6b] the preparation of 3-(*N,N*-dialkylamino)methylindoles with indoles, formaldehyde, and secondary amines in a mixture of AcOH and water under ultrasonic irradiation (Mannich reaction);[6c] the preparation of α-(indole-3-yl)glycine ester derivatives with indoles, ethyl α-aminoacetate, and *m*CPBA;[6d] the preparation of 4-(2'-amino-1'-arylethyl)-5-hydroxyindoles via the reduction of 4-(1'-aryl-2'-nitroethyl)-5-hydroxyindoles formed from 5-hydroxyindole and β-nitrostyrene (Friedel-Crafts alkylation);[6e] and the preparation of 4-hydroxy-3-[β-(*N,N*-dimethylamino)ethyl]indole by the reaction of 4-acetoxyindole and oxalyl chloride, followed by the reaction with dimethylamine and the reduction with $LiAlH_4$.[6f] Moreover, recent reports of the preparation of indoles bearing aminoalkyl groups using transition metals are as follows:[7] the preparation of 3-(aminoalkyl)indoles with phenylhydrazine and aminoalkenes in the presence of $Rh(acac)(CO)_2$ and XANTPHOS;[7a] the preparation of chiral 3-[(α-aryl)(α-*p*-tosylamino)]methylindoles with indoles and *N*-*p*-tosylaldimines in the presence of $Cu(OTf)_2$ and chiral bisoxazoline;[7b] the preparation of 3-[(*N*-acetyl,*N*-methyl)amino]methylindoles with indoles and *N*-*tert*-butoxymethyl,*N*-methylacetamide in the presence of $FeCl_3$;[7c] the preparation of 3-(α-phenylamino,α-acyl)methylindoles with indoles, α-(phenylamino)acetophenones, and $(NH_4)_2S_2O_8$ in the presence of $Ru(bpy)_3Cl_2$ under blue LED irradiation;[7d] the preparation of 3-β-(*N*-acetylamino)ethylindoles with indoles and β-(*N*-acetylamino)ethanol in the presence of $[Cp^*IrCl_2]_2$;[7e] the preparation of 3-[(*N*-acetyl,*N*-methyl)amino]methylindoles with indoles and ^{t}BuOOBu^t in the presence of $Fe_3O(BDC)_3$;[7f] and the preparation of *N*-heteroaryl-3-(phenylamino)indoles with *N*-(heteroaryl)indoles and α-(phenylamino)acetic acid in the presence of $[RhCp^*Cl_2]_2$ and $AgSbF_6$.[7g]

Here, as synthetic studies of the radical reactions with BPO,[2] we would like to report a novel and simple preparation of hemiaminal derivatives **1** with BPO in *N,N*-dimethylamides, and synthetic use for the introduction of amide groups onto indoles through the Friedel-Crafts alkylation.

Results and Discussion

First, treatment of BPO (purity 75% containing 25% water, 1.0 mmol) in *N,N*-dimethylacetamide **A** (0.5 mL, 1.0 mL, 2.0 mL, and 3.0 mL) in the presence of MS 3Å in a 30 mL screw-capped flask under irradiation with a mercury lamp (400 W) for 24 h in the temperature range of 35 °C~38 °C gave hemiaminal derivative **1A** in 72%, 83%, 77%, and 72% yields, respectively, as shown in Table 1 (entries 1~4). The yield of hemiaminal derivative **1A** was slightly decreased to 60%~65% in the absence of MS 3Å because BPO contained water. When BPO (1.0 mmol) in *N,N*-dimethylacetamide **A** (2.0 mL and 3.0 mL) in a 30 mL screw-capped flask was heated at 80 °C for 2 h, hemiaminal derivative **1A** was also obtained in 65% and 75% yields, respectively (entries 5, 6). On the other hand, when a solution of BPO (1.0 mmol) in *N,N*-dimethylacetamide **A** (3.0 mL) was irradiated with a tungsten lamp (300 W) in the temperature range of 35 °C~38 °C for 8 h, the yield of hemiaminal derivative **1A** was decreased to 38% (entry 7). Thus, hemiaminal derivative **1A** was obtained in good yields when the reaction was carried out under irradiation with a mercury lamp for 24 h or under warming condition at 80 °C for 2 h (entries 2 and 6). As gram-scale experiments, treatment of BPO (8.0 mmol) in *N,N*-dimethylacetamide **A** (24.0 mL) in 100 mL screw-capped flasks under the same irradiation and warming conditions gave hemiaminal derivative **1A** in 68% and 79% yields, respectively (entries 8 and 9). When those two reactions were carried out in the presence of 2,6-di-*tert*-butyl-*p*-cresol (BHT, 2.1 equiv.), a hydrogen-atom donor, under the same conditions, hemiaminal derivative **1A** was not obtained at all in both reactions (entries 10 and 11). Thus, the results suggest that those reactions proceed through radical-mediated pathways. In addition, when those two reactions were carried out in the presence of *p*-ethylbenzoic acid (4.0 equiv.), an analog of benzoic acid derived from BPO, under the same conditions, hemiaminal derivative **1A'** was obtained in 2% and 12% yields, together with hemiaminal derivative **1A** in 67% and 34% yields, respectively (entries 12 and 13).

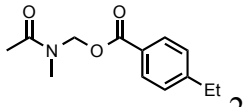
Table 1. Optimization for Formation of Hemiaminal **1A** with BPO in *N,N*-Dimethylacetamide



Entry	X (mL)	Conditions	Time (h)	Yield (%)
1	0.5	Hg-*hν*, 35-38 °C	24	72
2	**1.0**	**Hg-*hν*, 35-38 °C**	**24**	**83**
3	2.0	Hg-*hν*, 35-38 °C	24	77
4	3.0	Hg-*hν*, 35-38 °C	24	72
5	2.0	80 °C	2	65
6	**3.0**	**80 °C**	**2**	**75**
7	3.0	W-*hν*	8	38
8[a]	24.0	Hg-*hν*, 35-38 °C	24	68
9[a]	24.0	80 °C	2	79
10[b]	3.0	Hg-*hν*, 35-38 °C	24	0
11[b]	3.0	80 °C	2	0
12[c]	3.0	Hg-*hν*, 35-38 °C	24	67 (2)[d]
13[c]	3.0	80 °C	2	34 (12)[d]
14[e]	1.0	Hg-*hν*, 35-38 °C	24	3
15[e]	3.0	80 °C	2	0

[a] BPO (8.0 mmol) was used. [b] BHT (2.1 equiv.) was added. [c] 4-Ethylbenzoic Acid (4.0 equiv.) was added. [d] Yield of **1A'**. [e] $PhCO_3Bu^t$ (1.0 mmol) was used instead of BPO.

1A':



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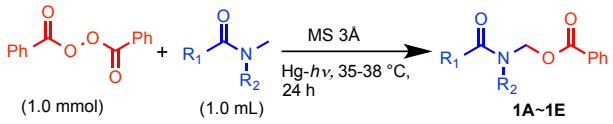
On the other hand, the same treatment of *tert*-butyl peroxybenzoate ($PhCO_3Bu^t$, 1.0 mmol) in *N*,*N*-dimethylacetamide **A** under irradiation with a Hg lamp for 24 h and warming at 80 ° C for 2 h generated hemiaminal **1A** in 3% and 0 % yields, respectively (entries 14 and 15).

Based on those results, solutions of BPO (1.0 mmol) in *N*,*N*-dimethylpropionamide **B** (1.0 mL), *N*,*N*-dimethylbutyramide **C** (3.0 mL), *N*-methylacetamide **D** (3.0 mL), and *N*,*N*-dimethylformamide **E** (3.0 mL) in 30 mL screw-capped flasks were irradiated with a mercury lamp for 24 h to give hemiaminal derivatives **1B**, **1C**, **1D**, and **1E**, in 80%, 84%, 58%, and 59% yields, respectively, as shown in Scheme 2 (entries 2~5). In contrast, the same treatment of BPO in *N*,*N*-diethylacetamide (3.0 mL) and 1-methyl-2-pyrrolidone (3.0 mL) under the irradiation with a mercury lamp did not generate the corresponding hemiaminal derivatives **1F** and **1G** at all (entries 6 and 7).

Scheme 2. Preparation of Hemiaminals **1** with BPO in Dimethylamides

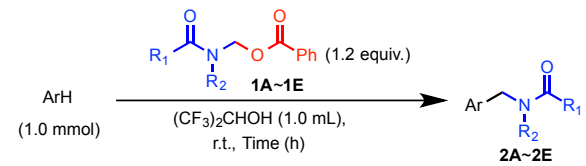


Entry	Amide	Product	Yield (%)
1	(**A**)	**1A**	83
2	(**B**)	**1B**	80
3[a]	(**C**)	**1C**	84
4[a]	(**D**)	**1D**	58
5[a]	(**E**)	**1E**	59
6	(**F**)	**1F**	0
7	(**G**)	**1G**	0

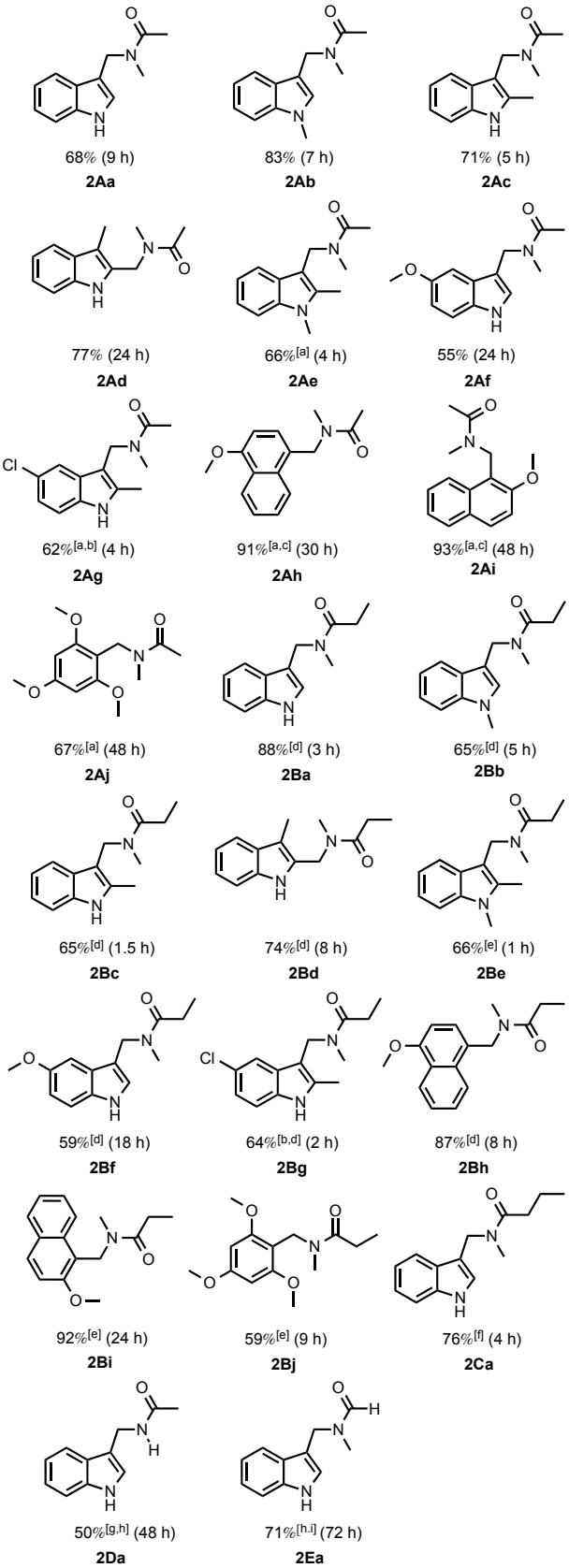
[a] Amide (3.0 mL) was used.

Here, obtained hemiaminals **1A**~**1E** bearing an amide group are mixtures of *anti* and *syn* forms. Then, as the synthetic use of hemiaminal derivatives **1A**~**1E**, they were subjected to the Friedel-Crafts alkylation of indoles because indoles bearing aminoalkyl groups have potent biological activities, as mentioned previously. Thus, treatment of hemiaminal **1A** (1.2 equiv.) and 3-methylindole **d** (1.0 mmol) in the presence of $ZnCl_2$ (1.0 equiv.), BF_3•Et_2O (1.0 equiv.), and $FeCl_3$ (1.0 equiv.) in CH_2Cl_2 (2.0 mL) at room temperature for 1 h provided 2-(*N*-acetyl,*N*-methylamino)methyl-3-methylindole (**2Ad**) in 64%, 73%, and 29% yields, respectively. When the same reaction of **1A** and 3-methylindole **d** was carried out in nitromethane (1.0 mL), 2,2,2-trifluoroethanol (1.0 mL), and 1,1,1,3,3,3-hexafluoro-2-propanol (1.0 mL) at room temperature for 24 h without Lewis acids, 2-(*N*-acetyl,*N*-methylamino)methyl-3-methylindole (**2Ad**) was obtained in 0%, 48% and 77% yields,

Scheme 3. Transformation of Hemiaminals **1** into Amides **2**



Product, Yield, (Time)

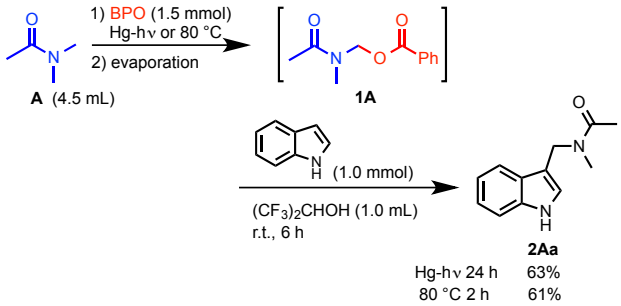


[a] **1A** (2.0 equiv.) was used. [b] 1,1,1,3,3,3-Hexafluoro-2-propanol (1.0 mL) and CH_2Cl_2 (1.0 mL) were used. [c] Reaction was carried out at 35 °C. [d] **1B** (1.5 equiv.) was used. [e] 1**B** (2.0 equiv.) was used. [f] 1**C** (1.5 equiv.) was used. [g] 1**D** (1.2 equiv.) was used. [h] Reaction was carried out at 40 °C. [i] 1**E** (1.5 equiv.) was used.

together with the recovery of 3-methylindole in 93%, 40%, and 0% yields, respectively. Recently, it was shown that 1,1,1,3,3,3-hexafluoro-2-propanol promotes the Friedel-Crafts alkylation and acylation reactions through hydrogen bonding.[8] Thus, treatment of hemiaminal derivative **1A** and 3-methylindole **d** in 1,1,1,3,3,3-hexafluoro-2-propanol at room temperature was the best choice, forming 2-(*N*-acetyl,*N*-methylamino)methyl-3-methylindole **2Ad** in the highest yield.

Based on those results, hemiaminal derivative **1A** (1.2 equiv.) was treated with indoles (1.0 mmol), such as indole (**a**), 1-methylindole (**b**), 2-methylindole (**c**), 3-methylindole (**d**), 1,2-dimethylindole (**e**), 5-methoxyindole (**f**), and 5-chloro-2-methylindole (**g**), in 1,1,1,3,3,3-hexafluoro-2-propanol (1.0 mL) at room temperature to give the corresponding indoles **2Aa**~**2Ag** bearing a (*N*-acetyl,*N*-methylamino)methyl group in good to moderate yields, as shown in Scheme 3. The same treatment of electron-rich aromatics, such as 1-methoxynaphthalene (**h**), 2-methoxynaphthalene (**i**), and 1,3,5-trimethoxybenzene (**j**), with hemiaminal derivative **1A** gave also the corresponding aromatics **2Ah**~**2Aj** bearing a (*N*-acetyl,*N*-methylamino)methyl group in good yields, respectively. Treatment of hemiaminal derivative **1B** with indoles (**a**)~(**g**) also gave the corresponding indoles **2Ba**~**2Bg** bearing a (*N*-methyl,*N*-propionylamino)methyl group in good to moderate yields, respectively. 1-Methoxynaphthalene (**h**), 2-methoxynaphthalene (**i**), and 1,3,5-trimethoxybenzene (**j**) also reacted with hemiaminal derivative **1B** to form the corresponding aromatics **2Bh**~**2Bj** bearing a (*N*-methyl,*N*-propionylamino)methyl group in good to moderate yields, respectively. In addition, indole (**a**) reacted with hemiaminal derivatives **1C**, **1D**, and **1E** to give indoles **2Ca** bearing a (*N*-butyryl,*N*-methylamino)methyl group, **2Da** bearing a (*N*-acetylamino)methyl group, and **2Ea** bearing a (*N*-formyl,*N*-methylamino)methyl group in good to moderate yields, respectively.

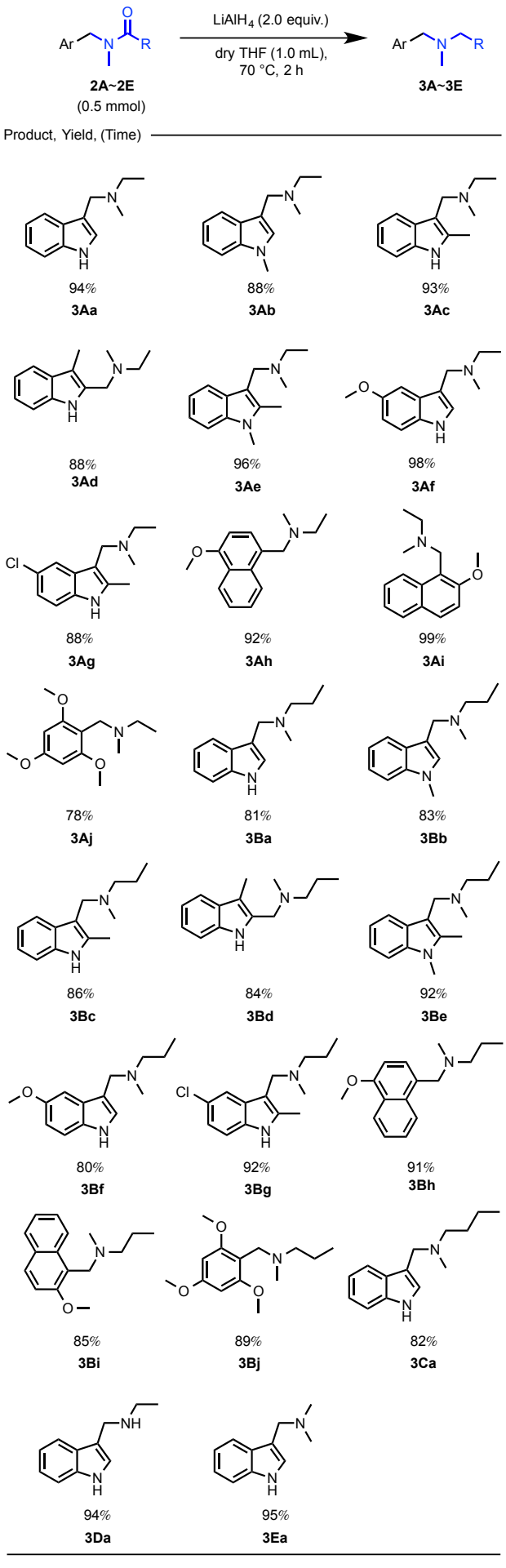
Scheme 4. One-pot preparation of 3-(*N*-Acetyl,*N*-methylamino)methylindole **2Aa**



Treatment of BPO in *N*,*N*-dimethylacetamide **A** under irradiation with a Hg lamp for 24 h and warming at 80 °C for 2 h, followed by evaporation, and then reaction with indole (**a**) in 1,1,1,3,3,3-hexafluoro-2-propanpl gave 3-(*N*-acetyl,*N*-methylamino)methylindole **2Aa** in one pot in 63% and 61% yields, respectively, as shown in Scheme 4. Thus, one-pot preparation of indoles **2A** bearing an amide group without isolation of hemiaminal **1A** can be carried out.

Here, all obtained amides **2** are mixtures of *anti* and *syn* forms. Then, the reduction of amides **2** was carried out to furnish indoles **3** bearing an aminomethyl group. Treatment of indoles **2Aa**~**2Ag**

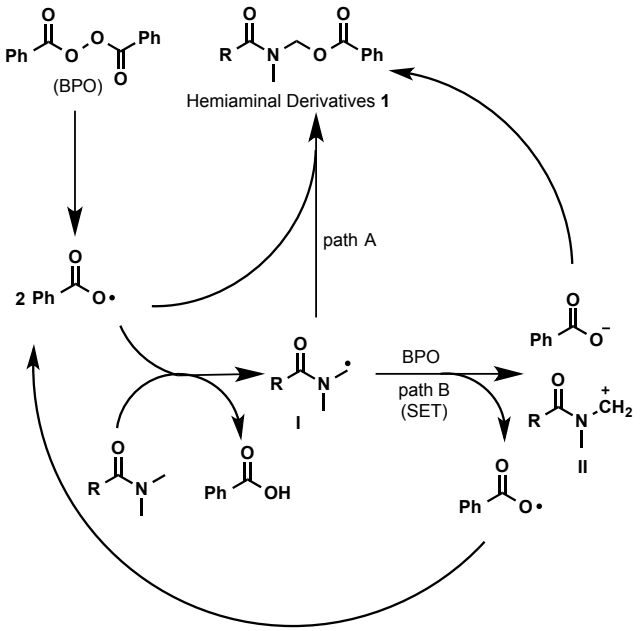
Scheme 5. Transformation of Amides 2 into Amines 3



(0.5 mmol) bearing a (*N*-acetyl,*N*-methylamino)methyl group with $LiAlH_4$ (2.0 equiv.) in THF (1.0 mL) at 70 °C for 2 h gave the corresponding indoles **3Aa**~**3Ag** bearing a (*N*-ethyl,*N*-methylamino)methyl group in good yields, respectively, as shown in Scheme 5. The same reduction of indoles **2Ba**~**2Bg** bearing a (*N*-methyl,*N*-propionylamino)methyl group with $LiAlH_4$ also generated the corresponding indoles **3Ba**~**3Bg** bearing a (*N*-methyl,*N*-propylamino)methyl group in good yields, respectively. In addition, the same reduction of 3-(*N*-butyryl,*N*-methylamino)methylindole **2Ca**, 3-(*N*-acetylamino)methylindole **2Da**, and 3-(*N*-formyl,*N*-methylamino)methylindole **2Ea** produced 3-(*N*-butyl,*N*-methylamino)methylindole **3Ca**, 3-(*N*-ethylamino)methylindole **3Da**, and 3-(*N,N*-dimethylamino)methylindole **3Ea** in good yields, respectively. 1-Methoxynaphthalenes **2Ah** and **2Bh**, 2-methoxynaphthalenes **2Ai** and **2Bi**, and 1,3,5-trimethoxybenzenes **2Aj** and **2Bj** bearing a (*N*-acetyl,*N*-methylamino)methyl group or a (*N*-methyl,*N*-propionylamino)methyl group were also reduced to the corresponding tertiary amines **3Ah**~**3Aj** and **3Bh**~**3Bj** in good yields, respectively.

A possible reaction pathway for the formation of hemiaminal derivatives **1** is shown in Scheme 6. Homolytic bond cleavage of the O-O bond in BPO under irradiation with a mercury lamp or warming condition would occur to form a benzoyloxyl radical. The benzoyloxyl radical would abstract a hydrogen atom from the *N*-methyl group of *N,N*-dimethylamide to form nucleophilic radical **I** and benzoic acid. Nucleophilic radical **I** would react with benzoyloxyl radical to form hemiaminal derivatives **1** (path A). However, generally, the concentration of radical species is quite low and therefore, the radical coupling reaction is not efficient. Thus, nucleophilic radical **I** would be oxidized by BPO via SET to form electrophilic cation **II**, together with the generation of benzoyloxyl radical and benzoate anion. Once electrophilic cation **II** is formed, it would smoothly react with benzoate anion to form hemiaminal derivative **1** (path B). Practically, when the present reaction was carried out in the presence of *p*-ethylbenzoic acid (4.0 equiv.), hemiaminal derivative **1A'** was obtained in 12% yield, as shown in Table 1. In addition, benzoic acid was obtained quantitatively as a co-product.

Scheme 6. Possible Reaction Pathway for Hemiaminal Derivatives **1**



Conclusions

A novel preparation of hemiaminal derivatives **1** bearing an amide group and a benzoate group with BPO in *N,N*-dimethylamides under irradiation with a mercury lamp or warming condition could be simply carried out. Treatment of formed hemiaminal derivatives **1** with indoles in 1,1,1,3,3,3-hexafluoro-2-propanol gave the corresponding indoles **2** bearing a (*N*-acyl,*N*-methylamino)methyl group through the Friedel-Crafts alkylation. Reduction of indoles **2** bearing a (*N*-acyl,*N*-methylamino)methyl group gave indoles bearing a (*N*-alkyl,*N*-methylamino)methyl group. We believe the present method for the preparation of hemiaminal derivatives **1** would be useful because hemiaminal derivatives **1** could be obtained in good yields from easily available BPO and *N,N*-dimethylamides, and the formed hemiaminal derivatives **1** could be used for the introduction of (*N*-acyl,*N*-methylamino)methyl groups onto electron-rich aromatics, such as indoles, via the Friedel-Crafts alkylation.

Experimental Section

General. : ^{1}H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-ECX400 and JEOL-JNM-ECS400 spectrometers. Chemical shifts were recorded as follows: chemical shift in ppm from internal tetramethylsilane (TMS) on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; b = broad), coupling constant (Hz) and integration. High-resolution mass spectra (HRMS) were recorded by a Thermo Fisher Scientific Exactive Orbitrap mass spectrometer. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel $60F_{254}$ (Merck) was used for TLC and Silica gel 60N (63~210 mesh, Kanto Kagaku Co.) was used for short column chromatography.

Typical Procedure for Preparation of Hemiaminals 1A: To a solution of BPO (purity 75% containing 25% water, 1.0 mmol, 323.0 mg) in *N,N*-dimethylacetamide (1.0 mL) in a 30 mL screw-capped flask was added 3 Å molecular sieves (Ca. 1.0 g). The flask was flashed by argon gas, and then, the mixture was stirred in the temperature range of 35 °C~38 °C for 24 h under irradiation with a high-pressure mercury lamp (Hg-lamp, 400 W: AHH400S, 1.7 mW/cm^2). Sat. $NaHCO_3$ aq. solution (10.0 mL) was added to the reaction mixture and the product was extracted with $CHCl_3$ (15.0 mL × 3). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane/EtOAc = 1:1) to give *N*-(benzoyloxy)methyl,*N*-methylacetamide **1A** (171.7 mg, 83% (*anti*/*syn* mixture = 59/24)).

***N*-(Benzoyloxy)methyl,*N*-methylacetamide 1A**: Yield: 171.7 mg (83%, *anti*/*syn* mixture = 59/24); colorless oil; IR (neat): 1716, 1601, 1176 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.17 and 2.30 (s, 3H), 3.10 and 3.20 (s, 3H), 5.63 and 5.69 (s, 2H), 7.42-7.49 (m, 2H), 7.55-7.63 (m, 1H), 8.03-8.10 (m, 2H); HRMS (ESI): Calcd for $C_{11}H_{14}O_3N$ $[M+H]^+$ = 208.0968, Found = 208.0971.

***N*-(Benzoyloxy)methyl,*N*-methylpropionamide 1B**: Yield: 177.2 mg (80%, *anti*/*syn* mixture = 54 /26); colorless oil; IR (neat): 1715, 1602, 1176 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.16-1.22 (m, 3H), 2.41 and 2.58 (q, 2H, *J* = 7.5 Hz), 3.11-3.18 (bs, 3H), 5.65 and 5.70 (s, 2H), 7.42-7.49 (m, 2H), 7.55-7.63 (m, 1H), 8.02-8.10 (m, 2H); HRMS (ESI): Calcd for $C_{12}H_{16}O_3N$ $[M+H]^+$ = 222.1125, Found = 222.1126.

***N*-(Benzoyloxy)methyl,*N*-methylbutyramide 1C**: Yield: 197.4 mg (84%, *anti*/*syn* mixture = 58/26); colorless oil; IR (neat): 1714, 1601, 1176 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, 3H, *J* = 7.3 Hz), 1.67-1.77 (m, 2H), 2.36 and 2.52 (t, 2H, *J* = 7.7 Hz), 3.11 and 3.18 (s, 3H), 5.65 and 5.70 (s, 2H), 7.42-7.49 (m, 2H), 7.55-

7.62 (m, 1H), 8.02-8.11 (m, 2H) ; HRMS (ESI): Calcd for $C_{13}H_{18}O_3N$ $[M+H]^+$ = 236.1281, Found = 236.1279.

***N*-(Benzoyloxy)methylacetamide 1D**: Yield: 111.2 mg (58%, *anti*/*syn* mixture = 56/2); colorless oil; IR (neat): 3065, 1709, 1601, 1584, 1541 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.04 and 2.24 (s, 3H), 5.45 and 5.49 (d, 2H, *J* = 7.4 Hz), 6.79 (bs, 1H), 7.43-7.47 (m, 2H), 7.56-7.61 (m, 1H), 8.04-8.07 (m, 2H); HRMS (ESI): Calcd for $C_{10}H_{12}O_3N$ $[M+H]^+$ = 194.0812, Found = 194.0811.

***N*-(Benzoyloxy)methy,*N*-methylformamide 1E**: Yield: 113.9 mg (59%, *anti*/*syn* mixture = 52/7); colorless oil; IR (neat): 2975, 2881, 1718, 1601, 617 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.04 and 3.14 (s, 3H), 5.56 and 5.66 (s, 2H), 7.43-7.49 (m, 2H), 7.57-7.63 (m, 1H), 8.02-8.12 (m, 2H), 8.18 and 8.44 (s, 1H); HRMS (ESI): Calcd for $C_{10}H_{12}O_3N$ $[M+H]^+$ = 194.0812, Found = 194.0812.

Typical Procedure for Preparation of Amides 2Aa~2Ea: To a solution of *N*-(benzoyloxy)methyl,*N*-methylacetamide **1A** (1.2 mmol, 248.7 mg) in 1,1,1,3,3,3-hexafluoro-2-propanol (1.0 mL) was added indole **a** (1.0 mmol 117.2 mg) at room temperature. The mixture was stirred at room temperature for 9 h under argon atmosphere. Sat. $NaHCO_3$ aq. solution (10.0 mL) was added to the reaction mixture and the product was extracted with $CHCl_3$ (15.0 mL × 3). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (eluent: EtOAc) to give 3-(*N*-acetyl,*N*-methylamino)methylindole **2Aa** (138.2 mg, 68% (*anti*/*syn* mixture = 44/24)).

3-(*N*-Acetyl,*N*-methylamino)methylindole 2Aa: Yield: 138.2 mg (68%, *anti*/*syn* mixture = 44/24); reddish brown solid; mp: 86-95 °C; IR (neat): 1616, 1541, 1507, 1457 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.12 and 2.26 (s, 3H), 2.91 and 2.99 (s, 3H), 4.69 and 4.76 (s, 2H), 7.06-7.25 (m, 3H), 7.38 and 7.41 (d, 1H, *J* = 8.2 Hz), 7.53 and 7.72 (d, 1H, *J* = 8.0 Hz), 8.09 and 8.17 (bs, 1H) ; HRMS (ESI): Calcd for $C_{12}H_{15}ON_2$ $[M+H]^+$ = 203.1179, Found = 203.1182.

3-(*N*-Acetyl,*N*-methylamino)methyl-1-methylindole 2Ab: Yield: 179.3 mg (83%, *anti*/*syn* mixture = 54/29); red oil; IR (neat): 1627, 1614, 1551 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.11 and 2.26 (s, 3H), 2.91 and 2.98 (s, 3H), 3.76 and 3.78 (s, 3H), 4.67 and 4.73 (s, 2H), 6.91 and 7.04 (s, 1H), 7.10- 7.16 (m, 1H), 7.22-7.27 (m, 1H), 7.29-7.34 (m, 1H), 7.52 and 7.70 (d, 1H, *J* = 7.9 Hz); HRMS (ESI): Calcd for $C_{13}H_{17}ON_2$ $[M+H]^+$ = 217.1335, Found = 217.1335.

3-(*N*-Acetyl,*N*-methylamino)methyl-2-methylindole 2Ac: Yield: 154.1 mg (71%, *anti*/*syn* mixture = 56/15); reddish brown solid; mp: 99-101 °C; IR (neat): 1647, 1558, 1542 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.11 and 2.36 (s, 3H), 2.42 and 2.46 (s, 3H), 2.80 and 2.84 (s, 3H), 4.64 and 4.75 (s, 2H), 7.07-7.11 (m, 1H), 7.11-7.15 (m, 1H), 7.27-7.32 (m, 1H), 7.41 and 7.61 (d, 1H, *J* = 7.7 Hz), 7.97 and 8.06 (bs, 1H); HRMS (ESI): Calcd for $C_{13}H_{17}ON_2$ $[M+H]^+$ = 217.1335, Found = 217.1337.

2-(*N*-Acetyl,*N*-methylamino)methyl-3-methylindole 2Ad: Yield: 155.4 mg (77%, *anti*/*syn* mixture = 76/1); yellow solid; mp: 171-173 °C; IR (neat): 1699, 1558, 1541, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.11 and 2.26 (s, 3H), 2.29 and 2.34 (s, 3H), 2.92 and 3.01 (s, 3H), 4.57 and 4.65 (s, 2H), 7.07-7.11 (m, 1H), 7.14-7.18 (m, 1H), 7.28 (d, 1H, *J* = 7.9 Hz), 7.52 (d, 1H, *J* = 7.9 Hz), 8.77 (bs, 1H); HRMS (ESI): Calcd for $C_{13}H_{17}ON_2$ $[M+H]^+$ = 217.1335, Found = 217.1332.

3-(*N*-Acetyl,*N*-methylamino)methyl-1,2-dimethylindole 2Ae: Yield: 153.1 mg (66%, *anti*/*syn* = 53/13); pale yellow solid; mp: 92-98 °C; IR (neat): 1616, 1558, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.10 and 2.36 (s, 3H), 2.39 and 2.44 (s, 3H), 2.76 and 2.83 (s, 3H), 3.67 and 3.69 (s, 3H), 4.66 and 4.77 (s, 2H), 7.07-7.11 (m, 1H), 7.16-7.22 (m,1H), 7.26 and 7.29 (d, 1H, *J* = 8.2 Hz), 7.43 and 7.62 (d, 1H, *J* = 7.9 Hz); HRMS (ESI): Calcd for $C_{14}H_{19}ON_2$ $[M+H]^+$ = 231.1492, Found = 231.1493.

3-(*N*-Acetyl,*N*-methylamino)methyl-5-methoxyindole 2Af: Yield: 127.5 mg (55%, *anti*/*syn* mixture = 37/18); brown solid; mp: 113-116 °C; IR (neat): 1616, 1558, 1541, 1211, 1065 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.12 and 2.26 (s, 3H), 2.90 and 2.99 (s, 3H), 3.85 and 3.86 (s, 3H), 4.66 and 4.72 (s, 2H), 6.87 and 6.90 (dd, 1H, *J* = 8.7, 2.3 Hz), 6.94-7.04 (m, 1H), 7.15 and 7.21 (d, 1H, *J* = 2.5 Hz), 7.24-7.26 and 7.29-7.31 (m, 1H), 7.98 and 8.07 (bs, 1H); HRMS (ESI): Calcd for $C_{13}H_{17}O_2N_2$ $[M+H]^+$ = 233.1285, Found = 233.1282.

3-(*N*-Acetyl,*N*-methylamino)methyl-5-chloro-2-methylindole 2Ag: Yield: 154.7 mg (62%, *anti*/*syn* mixture = 51/11); pale purple solid; mp: 171-175 °C; IR (neat): 1653, 1558, 1541 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.12 and 2.34 (s, 3H), 2.42 and 2.46 (s, 3H), 2.78 and 2.85 (s, 3H), 4.59 and 4.69 (s, 2H), 7.06-7.12 (m, 1H), 7.19 and 7.22 (d, 1H, *J* = 8.7 Hz), 7.36-7.55 (m, 1H), 7.97 and 8.06 (bs, 1H) ; HRMS (ESI): Calcd for $C_{13}H_{16}ON_2{}^{35}Cl$ $[M+H]^+$ = 251.0946, Found = 251.0943.

4-(*N*-Acetyl,*N*-methylamino)methyl-1-methoxynaphthalene 2Ah: Yield: 220.6 mg (91%, *anti*/*syn* mixture = 58/33); colorless solid; mp: 111-114 °C; IR (neat): 1637, 1584, 1514 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.15 and 2.16 (s, 3H), 2.80 and 3.04 (s, 3H), 4.00 and 4.01 (s, 3H), 4.91 and 4.98 (s, 2H), 6.75 and 6.79 (d, 1H, *J* = 7.9 Hz), 7.12 and 7.26 (d, 1H, *J* = 7.9 Hz), 7.47-7.60 (m, 2H), 7.79 and 8.05 (d, 1H, *J* = 7.7 Hz), 8.29-8.31 and 8.34-8.37 (m, 1H); HRMS (ESI): Calcd for $C_{15}H_{18}O_2N$ $[M+H]^+$ = 244.1332, Found = 244.1331.

1-(*N*-Acetyl,*N*-methylamino)methyl-2-methoxynaphthalene 2Ai: Yield: 226.4 mg (93%, *anti*/*syn* mixture = 77/16); colorless solid; mp: 103-105 °C; IR (neat): 1648, 1558, 1542 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.11 and 2.43 (s, 3H), 2.63 and 2.74 (s, 3H), 3.97 and 3.98 (s, 3H), 4.97 and 5.17 (s, 2H), 7.30 and 7.31 (d, 1H, *J* = 9.1 Hz), 7.34-7.38 (m, 1H), 7.49-7.53 (m, 1H), 7.78-7.89 (m, 2H), 7.93 and 8.11 (d, 1H, *J* = 8.5 Hz); HRMS (ESI): Calcd for $C_{15}H_{18}O_2N$ $[M+H]^+$ = 244.1332, Found = 244.1330.

2-(*N*-Acetyl,*N*-methylamino)methyl-1,3,5-trimethoxybenzene 2Aj: Yield: 169.5 mg (67%, *anti*/*syn* mixture = 55/12); colorless solid; mp: 80-82 °C; IR (neat): 1647, 1558, 1542 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.07 and 2.29 (s, 3H), 2.71 (s, 3H), 3.79 and 3.80 (s, 6H), 3.83 (s, 3H), 4.45 and 4.63 (s, 2H), 6.12 (s, 2H); HRMS (ESI): Calcd for $C_{13}H_{20}O_4N$ $[M+H]^+$ = 254.1387, Found =254.1384.

3-[(*N*-Methyl,*N*-propionylamino)methyl]indole 2Ba: Yield: 190.5 mg (88%, *anti*/*syn* mixture = 59/29); brown solid; mp: 84-93 °C; IR (neat): 1617, 1558, 1541 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.17-1.22 (m, 3H), 2.36 and 2.53 (q, 2H, *J* = 7.4 Hz), 2.90 and 3.00 (s, 3H), 4.70 and 4.78 (s, 2H), 7.03-7.24 (m, 3H), 7.37 and 7.41 (d, 1H, *J* = 8.1 Hz), 7.52 and 7.71 (d, 1H, *J* = 7.8 Hz), 8.24 and 8.36 (bs, 1H); HRMS (ESI): Calcd for $C_{13}H_{17}ON_2$ $[M+H]^+$ = 217.1335, Found = 217.1333.

1-Methyl-3-(*N*-methyl,*N*-propionylamino)methylindole 2Bb: Yield: 139.9 mg (65%, *anti*/*syn* mixture = 44/21); brown solid; mp: 111-116 °C; IR (neat): 1653, 1558, 1541 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.16-1.22 (m, 3H), 2.34 and 2.53 (q, 2H, *J* = 7.4 Hz), 2.91 and 2.99 (s, 3H), 3.77 and 3.77 (s, 3H), 4.68 and 4.74 (s, 2H), 6.88 and 7.05 (s, 1H), 7.10-7.15 (m, 1H), 7.21-7.34 (m, 2H), 7.51 and 7.69 (d, 1H, *J* = 7.9 Hz); HRMS (ESI): Calcd for $C_{14}H_{19}ON_2$ $[M+H]^+$ = 231.1492, Found = 231.1492.

2-Methyl-3-(*N*-methyl,*N*-propionylamino)methylindole 2Bc: Yield: 149.0 mg (65%, *anti*/*syn* mixture = 52/13); yellowish brown solid; mp: 111-115 °C; IR (neat): 1653, 1558, 1541 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.19 and 1.26 (t, 3H, *J* = 7.5 Hz), 2.35 and 2.65 (q, 2H, *J* = 7.5 Hz), 2.40 and 2.44 (s, 3H), 2.82 (s, 3H), 4.64 and 4.77 (s, 2H), 7.05-7.15 (m, 2H), 7.26-7.31 (m, 1H), 7.39 and 7.59 (d, 1H, *J* = 7.7 Hz), 8.27 and 8.46 (bs, 1H); HRMS (ESI): Calcd for $C_{14}H_{19}ON_2$ $[M+H]^+$ = 231.1492, Found = 231.1492.

3-Methyl-2-(*N*-methyl,*N*-propionylamino)methylindole 2Bd: Yield: 169.6 mg (74%, *anti*/*syn* mixture = 73/1); colorless solid; mp: 124-127 °C; IR (neat): 1627, 1541, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, 3H, *J* = 7.5 Hz), 2.32-2.37 (m, 5H), 2.94 and 3.00 (s, 3H), 4.57 and 4.65 (s, 2H), 7.06-7.10 (m, 1H), 7.14-7.18 (m, 1H), 7.28-7.30 (m, 1H), 7.50-7.52 (m, 1H), 8.78 (bs, 1H); HRMS (APCI): Calcd for $C_{14}H_{17}ON_2$ $[M-H]^+$ = 229.1335, Found = 229.1334.

1,2-Dimethyl-3-(*N*-methyl,*N*-propionylamino)methylindole 2Be: Yield: 161.3 mg (66%, *anti*/*syn* mixture = 56/10); brown

solid; mp: 91-95 °C; IR (neat): 1621, 1558, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ =1.18 and 1.26 (t, 3H, *J* = 7.4 Hz), 2.34 and 2.65 (q, 2H, *J* = 7.4 Hz), 2.39 and 2.44 (s, 3H), 2.77 and 2.82 (s, 3H), 3.67 and 3.69 (s, 3H), 4.66 and 4.78 (s, 2H), 7.07-7.11 (m, 1H), 7.15-7.19 (m, 1H), 7.25-7.30 (m, 1H), 7.41 and 7.61 (d, 1H, *J* = 7.6 Hz); HRMS (ESI): Calcd for $C_{15}H_{21}ON_2$ $[M+H]^+$ = 245.1648, Found = 245.1647.

5-Methoxy-3-(*N*-methyl,*N*-propionylamino)methylindole 2Bf: Yield: 145.8 mg (59%, *anti*/*syn* mixture = 42/17); reddish brown solid; mp: 118-125 °C; IR (neat): 1653, 1558, 1541, 1049 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.19 and 1.20 (t, 3H, *J* = 7.5 Hz), 2.36 and 2.54 (q, 2H, *J* = 7.5 Hz), 2.88 and 3.00 (s, 3H), 3.83 and 3.85 (s, 3H), 4.66 and 4.74 (s, 2H), 6.85 and 6.89 (dd, 1H, *J* = 8.6, 2.5 Hz), 6.94 and 7.13 (d, 1H, *J* = 2.3 Hz), 6.99 and 7.19 (d, 1H, *J* = 2.3 Hz), 7.25 and 7.29 (d, 1H, *J* = 8.6 Hz), 8.27 and 8.44 (bs, 1H); HRMS (ESI): Calcd for $C_{14}H_{19}O_2N_2$ $[M+H]^+$ = 247.1441, Found = 247.1441.

5-Chloro-2-methyl-3-(*N*-methyl,*N*-propionylamino)methylindole 2Bg: Yield: 168.2 mg (64%, *anti*/*syn* mixture = 54/10); purple solid; mp: 124-130 °C; IR (neat): 1615, 1541, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.19 and 1.26 (t, 3H, *J* = 7.5 Hz), 2.36 and 2.62 (q, 2H, *J* = 7.5 Hz), 2.40 and 2.45 (s, 3H), 2.79 and 2.83 (s, 3H), 4.59 and 4.71 (s, 2H), 7.06-7.10 (m, 1H), 7.17-7.22 (m, 1H), 7.34 and 7.53 (s, 1H), 8.02 and 8.14 (bs, 1H); HRMS (ESI): Calcd for $C_{14}H_{18}ON_2{}^{35}Cl$ $[M+H]^+$ = 265.1102, Found = 265.1099.

1-Methoxy-4-(*N*-methyl,*N*-propionylamino)methylnaphthalene 2Bh: Yield: 224.3 mg (87%, *anti*/*syn* mixture = 57/30); colorless solid; mp: 117-121 °C; IR (neat): 1635, 1541, 1508 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.16 and 1.21 (t, 3H, *J* = 7.5 Hz), 2.36-2.42 (m, 2H), 2.79 and 3.05 (s, 3H), 4.01 (s, 3H), 4.92 and 5.00 (s, 2H), 6.75 and 6.78 (d, 1H, *J* = 7.8 Hz), 7.10 and 7.26 (d, 1H, *J* = 7.8 Hz), 7.47-7.60 (m, 2H), 7.80 and 8.04 (d, 1H, *J* = 7.9 Hz), 8.29-8.31 and 8.34-8.36 (m, 1H); HRMS (ESI): Calcd for $C_{16}H_{20}O_2N$ $[M+H]^+$ = 258.1489, Found = 258.1486.

2-Methoxy-1-(*N*-methyl,*N*-propionylamino)methylnaphthalene 2Bi: Yield: 236.6 mg (92%, *anti*/*syn* mixture = 79/13); colorless solid; mp: 78-84°C; IR (neat): 1653, 1558, 1541 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.19 and 1.29 (t, 3H, *J* = 7.4 Hz), 2.35 (q, 2H, *J* = 7.4 Hz), 2.63 and 2.72 (s, 3H), 3.96 and 3.97 (s, 3H), 4.97 and 5.19 (s, 2H), 7.29 and 7.30 (d, 1H, *J* = 9.2 Hz), 7.37-7.38 (m, 1H), 7.48-7.52 (m, 1H), 7.78 and 7.82 (d, 1H, *J* = 8.1 Hz), 7.83 and 7.87 (d, 1H, *J* = 9.2 Hz), 7.91 and 8.10 (d, 1H, *J* = 8.1 Hz); HRMS (ESI): Calcd for $C_{16}H_{20}O_2N$ $[M+H]^+$ = 258.1489, Found = 258.1488.

2-(*N*-Methyl,*N*-propionylamino)methyl-1,3,5-trimethoxybenzene 2Bj: Yield: 156.5 mg (59%, *anti*/*syn* mixture = 45/14); colorless solid; mp: 61-73 °C; IR (neat): 1698, 1558, 1541, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.16 and 1.19 (t, 3H, *J* = 7.5 Hz), 2.31 and 2.62 (q, 2H, *J* = 7.5 Hz), 2.70 and 2.71 (s, 3H), 3.78 and 3.79 (s, 6H), 3.82 (s, 3H), 4.46 and 4.64 (s, 2H), 6.12 (s, 2H); HRMS (ESI): Calcd for $C_{14}H_{22}O_4N$ $[M+H]^+$ = 268.1543, Found = 268.1543.

3-(*N*-Butyryl,*N*-methylamino)methylindole 2Ca: Yield: 174.1 mg (76%, *anti*/*syn* mixture = 52/24); reddish brown solid; mp: 61-68 °C ; IR (neat): 1653, 1558, 1541, 1507 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.95-1.00 (m, 3H), 1.72 (sext, 2H, *J* = 7.6 Hz), 2.32 and 2.48 (t, 2H, *J* = 7.6 Hz), 2.90 and 2.99 (s, 3H), 4.71 and 4.77 (s, 2H), 7.03-7.24 (m, 3H), 7.37 and 7.41 (d, 1H, *J* = 8.1 Hz), 7.53 and 7.71 (d, 1H, *J* = 7.6 Hz), 8.16 and 8.26 (bs, 1H); HRMS (ESI): Calcd for $C_{14}H_{19}ON_2$ $[M+H]^+$ = 231.1492, Found = 231.1490.

3-(*N*-Acetylamino)methylindole 2Da: Yield: 94.1 mg (50%, *anti*/*syn* mixture = 49/1); red solid; mp: 120-126 °C; IR (neat): 3321, 1611, 1542 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.99 and 2.16 (s, 3H), 4.57 and 4.62 (d, 2H, *J* = 5.2 Hz), 5.63 (bs, 1H), 7.14-7.19 (m, 2H), 7.22-7.26 (m, 1H), 7.39-7.41 (m, 1H), 7.65 (d, 1H, *J* = 7.9 Hz), 8.18 (bs, 1H); HRMS (ESI): Calcd for $C_{11}H_{13}ON_2$ $[M+H]^+$ = 189.1022, Found = 189.1023.

3-(*N*-Formyl,*N*-methylamino)methylindole 2Ea: Yield: 134.2 mg (71%, *anti*/*syn* mixture = 39/32); pale yellow solid; mp: 132-139 °C; IR (neat): 3675, 2901, 1653, 878, 687 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.82 and 2.83 (s, 3H), 4.60 and 4.71 (s, 2H), 7.12-7.17 (m, 1H), 7.20-7.25 (m, 1H), 7.37- 7.42 (m, 1H), 7.53-7.55 (m, 1H), 7.71-7.73 (m, 1H), 8.13 and 8.43 (s, 1H), 8.17 and 8.25 (bs, 1H); HRMS (ESI): Calcd for $C_{11}H_{13}ON_2$ $[M+H]^+$ = 189.1022, Found = 189.1024.

Typical Procedure for Preparation of Amines 3Aa~3Ea: To a solution of 3-(*N*-acetyl,*N*-methylamino)methylindole **2Aa** (0.5 mmol, 101.1 mg) in THF (1.0 mL) was added $LiAlH_4$ (1.0 mmol, 41.3 mg) at room temperature. The mixture was stirred at 70 °C for 2 h under argon atmosphere. Ice water (10.0 mL) was added to the reaction mixture. The quenched mixture was filtrated, and then the product was extracted with $CHCl_3$ (15.0 mL × 3). The organic layer was dried over Na_2SO_4. Filtration and removal of the solvent under reduced pressure gave 3-(*N*-ethyl,*N*-methylamino)methylindole **3Aa** (88.4 mg, 94%).

3-(*N*-Ethyl,*N*-methylamino)methylindole 3Aa: Yield: 88.4 mg (94%); brown solid; mp: 93-94 °C; IR (neat): 1233, 1209, 1171, 1129, 1093 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.13 (t, 3H, *J* = 7.2 Hz), 2.25 (s, 3H), 2.49 (q, 2H, *J* = 7.2 Hz), 3.71 (s, 2H), 7.10-7.14 (m, 2H), 7.19 (td, 1H, *J* = 7.0, 1.1 Hz), 7.37 (d, 1H, *J* = 8.1 Hz), 7.72 (d, 1H, *J* = 7.9 Hz), 8.07 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.6, 41.7, 51.0, 52.1, 111.0, 112.9, 119.2, 119.3, 121.8, 123.7, 128.0, 136.1; HRMS (ESI): Calcd for $C_{12}H_{17}N_2$ $[M+H]^+$ = 189.1386, Found = 189.1385.

3-(*N*-Ethyl,*N*-methylamino)methyl-1-methylindole 3Ab: Yield: 88.9 mg (88%); red oil; IR (neat): 1245, 1199, 1173, 1126, 1061, 1038 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.13 (t, 3H, *J* = 7.2 Hz), 2.24 (s, 3H), 2.48 (q, 2H, *J* = 7.2 Hz), 3.69 (s, 2H), 3.77 (s, 3H), 7.00 (s, 1H), 7.09-7.13 (m, 1H), 7.20-7.24 (m, 1H), 7.30 (d, 1H, *J* = 8.1 Hz), 7.70 (d, 1H, *J* = 7.9 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.6, 32.5, 41.5, 50.9, 51.9, 109.0, 111.2, 118.9, 119.3, 121.3, 128.3, 128.4, 136.8; HRMS (ESI): Calcd for $C_{13}H_{19}N_2$ $[M+H]^+$ = 203.1543, Found = 203.1541.

3-(*N*-Ethyl,*N*-methylamino)methyl-2-methylindole 3Ac : Yield: 93.8 mg (93%); reddish brown oil; IR (neat): 1239, 1147, 1056, 1014 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, 3H, *J* = 7.2 Hz), 2.20 (s, 3H), 2.41 (s, 3H), 2.49 (q, 2H, *J* = 7.2 Hz), 3.59 (s, 2H), 7.05-7.12 (m, 2H), 7.24-7.26 (m, 1H), 7.61-7.63 (m, 1H), 7.84 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 8.4, 12.3, 41.6, 51.4, 52.7, 108.5, 110.5, 118.3, 118.7, 121.3, 129.1, 132.1, 135.4; HRMS (ESI): Calcd for $C_{13}H_{19}N_2$ $[M+H]^+$ = 203.1543, Found = 203.1543.

2-(*N*-Ethyl,*N*-methylamino)methyl-3-methylindole 3Ad : Yield: 89.1 mg (88%); white solid; mp: 63-66 °C; IR (neat): 1256, 1232, 1206, 1151, 1125, 1008 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.09 (t, 3H, *J* = 7.0 Hz), 2.21 (s, 3H), 2.26 (s, 3H), 2.47 (q, 2H, *J* = 7.0 Hz), 3.61 (s, 2H), 7.06-7.10 (m, 1H), 7.12-7.16 (m, 1H), 7.29 (d, 1H, *J* = 7.7 Hz), 7.51 (d, 1H, *J* = 7.7 Hz), 8.31 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 8.4, 12.3, 41.6, 51.4, 52.7, 108.5, 110.5, 118.3, 118.7, 121.3, 129.1, 132.1, 135.4; HRMS (ESI): Calcd for $C_{13}H_{19}N_2$ $[M+H]^+$ = 203.1543, Found = 203.1538.

1,2-Dimethyl-3-(*N*-ethyl,*N*-methylamino)methylindole 3Ae: Yield: 104.3 mg (96%); yellow oil; IR (neat): 1245, 1217, 1135, 1059 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, 3H, *J* = 7.0 Hz), 2.20 (s, 3H), 2.41 (s, 3H), 2.49 (q, 2H, *J* = 7.0 Hz), 3.62 (s, 2H), 3.67 (s, 3H), 7.06-7.10 (m, 1H), 7.13-7.17 (m, 1H), 7.25 (d, 1H, *J* = 8.4 Hz), 7.62 (d, 1H, *J* = 7.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 10.5, 12.8, 29.4, 41.7, 51.3, 51.4, 108.0, 108.4, 118.4, 118.9, 120.4, 128.5, 135.2, 136.4; HRMS (ESI): Calcd for $C_{14}H_{21}N_2$ $[M+H]^+$ = 217.1699, Found = 217.1700.

3-(*N*-Ethyl,*N*-methylamino)methyl-5-methoxyindole 3Af: Yield: 107.0 mg (98%); brown solid; mp: 103-106 °C; IR (neat): 1245, 1213, 1172, 1027 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, 3H, *J* = 7.2 Hz), 2.25 (s, 3H), 2.50 (q, 2H, *J* = 7.2 Hz), 3.67 (s, 2H), 3.87 (s, 3H), 6.85 (dd, 1H, *J* = 8.8, 2.5 Hz), 7.10 (d, 1H, *J* = 2.2 Hz), 7.16 (d, 1H, *J* = 2.5 Hz), 7.24 (d, 1H, *J* = 8.8 Hz), 8.03 (bs,

1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.7, 41.7, 51.0, 52.2, 55.8, 101.1, 111.7, 111.9, 112.8, 124.4, 128.4, 131.3, 153.9; HRMS (ESI): Calcd for $C_{13}H_{19}ON_2$ $[M+H]^+$ = 219.1492, Found = 219.1490.

5-Chloro-3-(*N*-ethyl,*N*-methylamino)methyl-2-methylindole 3Ag: Yield: 104.5 mg (88%); pale yellow solid; mp: 135-141 °C; IR (neat): 1236, 1170, 1150, 1065, 1036, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, 3H, *J* = 7.3 Hz), 2.18 (s, 3H), 2.40 (s, 3H), 2.47 (q, 2H, *J* = 7.3 Hz), 3.52 (s, 2H), 7.04 (dd, 1H, *J* = 8.4, 2.0, Hz), 7.15 (d, 1H, *J* = 8.6 Hz), 7.59 (d, 1H, *J* = 1.8 Hz), 7.85 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 11.8, 12.7, 41.7, 51.1, 51.5, 109.0, 110.9, 118.1, 121.0, 125.0, 130.5, 133.4, 134.8 ; HRMS (ESI): Calcd for $C_{13}H_{18}N_2{}^{35}Cl$ $[M+H]^+$ = 237.1153, Found = 237.1150.

4-(*N*-Ethyl,*N*-methylamino)methyl-1-methoxynaphthalene 3Ah: Yield: 105.4 mg (92%); colorless oil; IR (neat): 1240, 1223, 1158, 1052, 1025 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, 3H, *J* = 7.2 Hz), 2.19 (s, 3H), 2.53 (q, 2H, *J* = 7.2 Hz), 3.79 (s, 2H), 3.99 (s, 3H), 6.73 (d, 1H, *J* = 7.9 Hz), 7.30 (d, 1H, *J* = 7.9 Hz), 7.45-7.49 (m, 1H), 7.51-7.55 (m, 1H), 8.23 (d, 1H, *J* = 8.1 Hz), 8.26-8.29 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.4, 41.7, 51.7, 55.4, 60.0, 102.7, 122.2, 124.4, 124.8, 125.8, 126.4, 126.9, 127.4, 133.3, 155.0; HRMS (ESI): Calcd for $C_{15}H_{20}ON$ $[M+H]^+$ = 230.1539, Found = 230.1535.

1-(*N*-Ethyl,*N*-methylamino)methyl-2-methoxynaphthalene 3Ai: Yield: 114.5 mg (99%); colorless oil; IR (neat): 1247, 1177, 1086, 1058, 1023 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, 3H, *J* = 7.0 Hz), 2.21 (s, 3H), 2.58 (q, 2H, *J* = 7.3 Hz), 3.93 (s, 2H), 3.94 (s, 3H), 7.27 (d, 1H, *J* = 8.6 Hz), 7.31-7.35 (m, 1H), 7.46-7.50 (m, 1H), 7.76 (d, 1H, *J* = 7.5 Hz), 7.78 (d, 1H, *J* = 9.1 Hz), 8.20 (d, 1H, *J* = 8.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.4, 41.5, 50.4, 51.9, 56.5, 113.2, 120.0, 123.3, 124.3, 126.4, 128.1, 129.0, 129.1, 134.1, 155.5; HRMS (ESI): Calcd for $C_{15}H_{20}ON$ $[M+H]^+$ = 230.1539, Found = 230.1535.

2-(*N*-Ethyl,*N*-methylamino)methyl-1,3,5-trimethoxybenzene 3Aj: Yield: 93.1 mg (78%); colorless oil; IR (neat): 1227, 1185, 1060, 1038, cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.12 (t, 3H, *J* = 7.3 Hz), 2.18 (s, 3H), 2.48 (q, 2H, *J* = 7.3 Hz), 3.48 (s, 2H), 3.79 (s, 6H), 3.81 (s, 3H), 6.12 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.3, 41.7, 47.5, 51.4, 55.2, 55.6 (2C), 90.2 (2C), 107.7 159.9 (2C), 160.3; HRMS (ESI): Calcd for $C_{13}H_{22}O_3N$ $[M+H]^+$ = 240.1594, Found = 240.1592.

3-(*N*-Methyl,*N*-propylamino)methylindole 3Ba : Yield: 81.9 mg (81%); pale yellow solid; mp: 75-78 °C; IR (neat): 1231, 1066, 1004 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.3 Hz), 1.58 (sext, 2H, *J* = 7.5 Hz), 2.23 (s, 3H), 2.38 (t, 2H, *J* = 6.6 Hz), 3.70 (s, 2H), 7.10-7.14 (m, 2H), 7.19 (td, 1H, *J* = 7.0, 1.1 Hz), 7.4 (d, 1H, *J* = 8.2 Hz), 7.73 (d, 1H, *J* = 7.7 Hz), 8.11 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.0, 20.7, 42.2, 52.5, 59.5, 111.0, 113.0, 119.3 (2C), 121.7, 123.6, 128.0, 136.1; HRMS (ESI): Calcd for $C_{13}H_{19}N_2$ $[M+H]^+$ = 203.1543, Found = 203.1541.

1-Methyl-3-(*N*-methyl,*N*-propylamino)methylindole 3Bb: Yield: 89.5mg (83%); pale yellow oil; IR (neat): 1244, 1197, 1157, 1126, 1063, 1010 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.3 Hz), 1.57 (sext, 2H, *J* = 7.7 Hz), 2.22 (s, 3H), 2.37 (t, 2H, *J* = 7.7 Hz), 3.68 (s, 2H), 3.77 (s, 3H), 6.98 (s, 1H), 7.09-7.13 (m, 1H), 7.20-7.24 (m, 1H), 7.29 (td, 1H, *J* = 8.4, 0.9 Hz), 7.70 (td, 1H, *J* = 7.9, 0.9 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.0, 20.7, 32.6, 42.2, 52.5, 59.4, 109.0, 111.8, 118.8, 119.5, 121.3, 128.2, 128.4, 136.9; HRMS (ESI): Calcd for $C_{14}H_{21}N_2$ $[M+H]^+$ = 217.1699, Found = 217.1697.

2-Methyl-3-(*N*-methyl,*N*-propylamino)methylindole 3Bc: Yield: 100.0 mg (86%); colorless solid; mp: 94-96 °C; IR (neat): 1241, 1065, 1057, cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.2 Hz), 1.58 (sext, 2H, *J* = 7.6 Hz), 2.17 (s, 3H), 2.37 (t, 2H, *J* = 7.6 Hz), 2.42 (s, 3H), 3.58 (s, 2H), 7.05-7.12 (m, 2H), 7.25-7.27 (m, 1H), 7.62-7.64 (m, 1H), 7.80 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 11.9, 12.0, 20.8, 42.2, 51.6, 59.9, 109.2, 109.9, 118.7, 119.3, 120.8, 129.4, 133.1, 135.0; HRMS (ESI): Calcd for $C_{14}H_{21}N_2$ $[M+H]^+$ = 217.1699, Found = 217.1697.

3-Methyl-2-(*N*-methyl,*N*-propylamino)methylindole 3Bd: Yield: 91.0 mg (84%); pale yellow oil; IR (neat): 1167, 1040, 1007 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.3 Hz), 1.53 (sext, 2H, *J* = 7.5 Hz), 2.21 (s, 3H), 2.25 (s, 3H), 2.35 (t, 2H, *J* = 7.5 Hz), 3.60 (s, 2H), 7.06-7.10 (m, 1H), 7.12-7.16 (m, 1H), 7.29 (td, 1H, *J* = 7.7, 1.1 Hz), 7.50-7.52 (m, 1H), 8.27 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 8.4, 11.8, 20.5, 42.2, 53.1, 59.6, 108.4, 110.4, 118.2, 118.7, 121.3, 129.2, 132.2, 135.3; HRMS (ESI): Calcd for $C_{14}H_{21}N_2$ $[M+H]^+$ = 217.1699, Found = 217.1699.

1,2-Dimethyl-3-(*N*-methyl,*N*-propylamino)methylindole 3Be: Yield: 105.6 mg (92%); yellow oil; IR (neat): 1245, 1211, 1170, 1128 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.5 Hz), 1.58 (sext, 2H, *J* = 7.5 Hz), 2.16 (s, 3H), 2.37 (t, 2H, *J* = 7.5 Hz), 7.41 (s, 3H), 3.60 (s, 2H), 3.66 (s, 3H), 7.05-7.09 (m, 1H), 7.12-7.16 (m, 1H), 7.23-7.25 (m, 1H), 7.63 (d, 1H, *J* = 7.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 10.4, 12.0, 20.8, 29.3, 42.2, 51.9, 59.9, 108.3 (2C), 118.4, 118.8, 120.3, 128.5, 135.0, 136.3; HRMS (ESI): Calcd for $C_{15}H_{23}N_2$ $[M+H]^+$ = 231.1856, Found = 231.1854.

5-Methoxy-3-(*N*-methyl,*N*-propylamino)methylindole 3Bf: Yield: 92.6 mg (80%); brown solid; mp: 91-96 °C; IR (neat): 1212, 1176, 1087, 1047 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, 3H, *J* = 7.3 Hz), 1.58 (sext, 2H, *J* = 7.5 Hz), 2.22 (s, 3H), 2.38 (t, 2H, *J* = 7.3 Hz), 3.65 (s, 2H), 3.86 (s, 3H), 6.85 (dd, 1H, *J* = 8.8, 2.5 Hz), 7.09 (d, 1H, *J* = 2.5 Hz), 7.18 (d, 1H, *J* = 2.5 Hz), 7.25 (d, 1H, *J* = 8.8 Hz), 7.94 (bs,1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.0, 20.7, 42.2, 52.8, 55.8, 59.5, 101.3, 111.7, 112.0, 113.1, 124.3, 128.4, 131.4, 153.9; HRMS (ESI): Calcd for $C_{14}H_{21}ON_2$ $[M+H]^+$ = 233.1648, Found = 233.1646.

5-Chloro-2-methyl-3-(*N*-methyl,*N*-propylamino)methylindole 3Bg: Yield: 115.0 mg (92%); pale yellow solid; mp: 109-111 °C; IR (neat): 1242, 1216, 1057 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, 3H, *J* = 7.0 Hz), 1.57 (sext, 2H, *J* = 7.5 Hz), 2.15 (s, 3H), 2.36 (t, 2H, *J* = 7.3 Hz), 2.41 (s, 3H), 3.52 (s, 2H), 7.05 (dd, 1H, *J* = 8.6, 2.0 Hz), 7.15-7.17 (m, 1H), 7.59 (d, 1H, *J* = 2.0 Hz), 7.81 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 11.9, 12.0, 20.7, 42.1, 51.6, 60.0, 109.3, 110.9, 118.2, 121.0, 125.0, 130.5, 133.4, 134.6; HRMS (ESI): Calcd for $C_{14}H_{20}N_2{}^{35}Cl$ $[M+H]^+$ = 251.1310, Found = 251.1307.

1-Methoxy-4-(*N*-methyl,*N*-propylamino)methylnaphthalene 3Bh: Yield: 110.6 mg (91%); pale yellow oil; IR (neat): 1240, 1225, 1158, 1054, 1023 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.5 Hz), 1.59 (sext, 2H, *J* = 7.5 Hz), 2.17 (s, 3H), 2.41 (t, 2H, *J* = 7.3 Hz), 3.79 (s, 2H), 4.00 (s, 3H), 6.73 (d, 1H, *J* = 7.9 Hz), 7.29 (d, 1H, *J* = 7.7 Hz), 7.44-7.48 (m, 1H), 7.50-7.54 (m, 1H), 8.24-8.28 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.0, 20.5, 42.1, 55.4, 60.1, 60.7, 102.7, 122.1, 124.6, 124.9, 125.8, 126.3, 127.1, 127.4, 133.3, 155.0; HRMS (ESI): Calcd for $C_{16}H_{22}ON$ $[M+H]^+$ = 244.1696, Found = 244.1693.

2-Methoxy-1-(*N*-methyl,*N*-propylamino)methylnaphthalene 3Bi: Yield: 103.4 mg (85%); yellow oil; IR (neat): 1147, 1085, 1057, 1023 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.3 Hz), 1.61 (sext, 2H, *J* = 7.5 Hz), 2.19 (s, 3H), 2.47 (t, 2H, *J* = 7.3 Hz), 3.92 (s, 2H), 3.94 (s, 3H), 7.27 (d, 1H, *J* = 7.9 Hz), 7.31-7.35 (m, 1H), 7.46-7.50 (m, 1H), 7.76 (d, 1H, *J* = 7.7 Hz), 7.78 (d, 1H, *J* = 8.8 Hz), 8.21 (d, 1H, *J* = 8.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.0, 20.4, 41.9, 51.0, 56.6, 60.4, 113.3, 123.3 (2C), 124.4, 126.4, 128.0, 129.1 (2C), 134.1, 155.6; HRMS (ESI): Calcd for $C_{16}H_{22}ON$ $[M+H]^+$ = 244.1696, Found = 244.1693.

2-(*N*-Methyl,*N*-propylamino)methyl-1,3,5-trimethoxybenzene 3Bj: Yield: 112.3mg (89%); colorless oil; IR (neat): 1227, 1203, 1042, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3H, *J* = 7.5 Hz), 1.58 (sext, 2H, *J* = 7.7 Hz), 2.18 (s, 3H), 2.37 (t, 2H, *J* = 7.7 Hz), 3.47 (s, 2H), 3.79 (s, 6H), 3.81 (s, 3H), 6.12 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.0, 20.3, 42.3, 47.7, 55.2, 55.6 (2C), 60.1, 90.2 (2C), 107.8, 159.9 (2C), 160.3; HRMS (ESI): Calcd for $C_{14}H_{24}O_3N$ $[M+H]^+$ = 254.1751, Found = 254.1746.

3-(*N*-Butyl,*N*-methylamino)methylindole 3Ca: Yield: 89.0 mg (82%); pale yellow solid; mp: 58-65 °C; IR (neat): 1236, 1194, 1107, 1072, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, 3H, *J* = 7.3 Hz), 1.34 (sext, 2H, *J* = 7.3 Hz), 1.50-1.58 (m, 2H),

2.23 (s, 3H), 2.42 (t, 2H, J = 7.3 Hz), 3.70 (s, 2H), 7.10-7.11 (m, 1H), 7.12-7.14 (m, 1H), 7.17-7.21 (m, 1H), 7.35 (d, 1H, J = 8.2 Hz), 7.72 (d, 1H, J = 7.9 Hz), 8.12 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.1, 20.7, 29.7, 42.3, 52.6, 57.3, 111.0, 113.2, 119.4 (2C), 121.8, 123.5, 128.0, 136.1; HRMS (ESI): Calcd for $C_{14}H_{21}N_2$ $[M+H]^+$ = 217.1699, Found = 217.1696.

3-(*N*-Ethylamino)methylindole 3Da: Yield: 81.6 mg (94%); colorless oil; IR (neat): 3409, 1645, 1620, 1549 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, 3H, J = 7.3 Hz), 1.44 (bs, 1H), 2.77 (q, 2H, J = 7.3 Hz), 4.00 (d, 2H, J = 0.45 Hz), 7.11-7.16 (m, 2H), 7.19-7.23 (m, 1H), 7.37 (d, 1H, J = 8.2 Hz), 7.67 (d, 1H, J = 7.9 Hz), 8.07 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 15.2, 43.8, 44.5, 111.2, 114.7, 118.5, 119.3, 121.9, 122.6, 127.0, 136.3; HRMS (ESI): Calcd for $C_{11}H_{15}N_2$ $[M+H]^+$ = 175.1230, Found = 175.1228.

3-(*N*,*N*-Dimethylamino)methylindole 3Ea: Yield: 83.1 mg (95%); pale yellow solid; mp: 123-128 °C; IR (neat): 1250, 1065, 1057 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 6H), 3.63 (s, 2H), 7.11-7.15 (m, 2H), 7.18-7.22 (m, 1H), 7.37 (td, 1H, J = 8.1, 0.9 Hz), 7.70-7.72 (m, 1H), 8.10 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 45.3 (2C), 54.4, 111.1, 112.9, 119.1, 119.4, 121.8, 123.8, 127.8, 136.1; HRMS (ESI): Calcd for $C_{11}H_{15}N_2$ $[M+H]^+$ = 175.1230, Found = 175.1227.

Supporting Information (see footnote on the first page of this article): … . Copies of ^{1}H NMR spectra of all hemiaminal derivatives **1A**~**1E** and amides **2Aa**~**2Ea**, and ^{1}H NMR and ^{13}C NMR spectra of all amines **3Aa**~**3Ea**.

Acknowledgments

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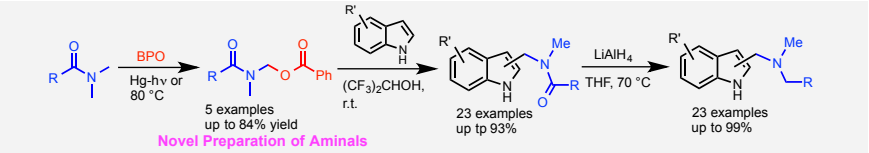
Layout 2:

(Aminals and Indoles bearing Amino Group)



Hemiaminal derivatives could be obtained in good yields by the reaction of BPO and *N*,*N*-dimethylamides under irradiation or warming condition. By using the hemiaminal derivatives, indoles bearing a (*N*-alkyl,*N*-methylamino)methyl group could be smoothly obtained by the reduction of the indoles bearing a (*N*-acyl,*N*-methylamino)methyl group that were obtained through the Friedel-Crafts alkylation reaction of indoles and the hemiaminal derivatives.

Kohei Nakamura, Hideo Togo*…….....
Page No. – Page No.

Nobel Preparation of Hemiaminal Derivatives with BPO and *N*,*N*-Dimethylamides, and Their Synthetic Use for (Aminomethyl)indoles

Keywords: (BPO / Hemiaminal / Friedel-Crafts Alkylation / Amide / (Aminomethyl)indole)

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Supporting Information

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