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Preparation of Substituted Alkylpyrroles via Samarium-Catalyzed Three-Component Coupling Reaction of Aldehydes, Amines, and Nitroalkanes

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Pyrroles were synthesized by three-component coupling reaction of aldehydes, amines, and nitroalkanes in the presence of a catalytic amount of a samarium species under mild conditions. The reaction is considered to involve the coupling of α,*β*-unsaturated imines, which are provided by the samarium-catalyzed aldol-type condensation of imines generated from amines and aldehydes, with nitroalkanes. In the case of the three-component coupling of α,*β*-unsaturated aldehydes (or ketones) with amines and nitroalkanes, alkylpyrroles were obtained by only heating in the absence of any catalyst. For instance, a mixture of butylamine, 2-butylidenecyclohexanone, and nitroethane, allowed to react at 60 °C for 15 h, produced isoindole, **4r**, which is difficult to prepare by conventional methods, in 39% yield.

Introduction

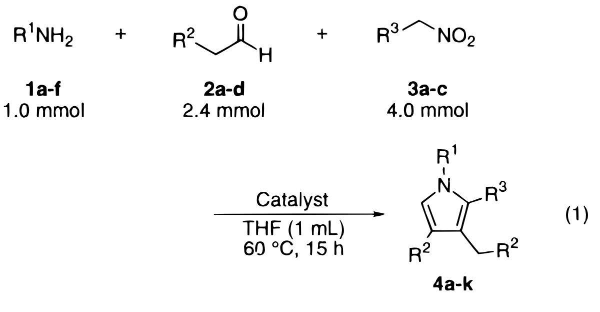
Since the time Kagan has shown a simple preparation method of samarium diiodide (SmI_2) from samarium metal and 1,2-diiodoethane, SmI_2 has been widely used in synthetic organic chemistry.[1] However, there are only a limited number of catalytic reactions using SmI_2 (e.g., the intramolecular Tishchenko reaction,[2] epoxide rearrangement,[3] Michael and aldol reactions,[4] and Diels−Alder reaction[5]).

In a previous paper, we reported that SmI_2 catalyzes the aldol-type condensation of imines under mild conditions to give α,*β*-unsaturated imines in fair to good yields.[6] The condensation was markedly enhanced in the presence of formates or aldehydes which serve as the eliminating reagents of amines from adducts. Furthermore, the reaction of amines with aldehydes in the presence of SmI_2 gave the corresponding α,*β*-unsaturated imines in good yields.[6]

Pyrroles are important compounds. They are a constitutive factor of porphyrin and bile pigment in natural products. Although there are many reports for the synthesis of pyrroles,[7] the Knorr method is extensively used for this purpose.[8] Recently, Pederson et al. have reported that the regioselective synthesis of pyrroles via the coupling of α,*β*-unsaturated imines with esters or *N*,*N*-dimethylformamide is promoted by $NbCl_3$(dme).[9] In the course of our study on the reaction using samarium compounds as catalysts, we found that SmI_2 and $SmCl_3$ catalyze the three-component coupling of amines, aldehydes, and nitroalkanes to give the corresponding pyrroles in fair yields.

Results and Discussion

A mixture of butylamine (**1a**), butyraldehyde (**2a**), and nitroethane (**3a**) in THF was allowed to react in the presence of a catalytic amount of SmI_2 at 60 °C for 15 h to provide *N*-butyl-4-ethyl-2-methyl-3-propylpyrrole (**4a**) in 64% yield (eq 1).



The yield of **4a** using various Lewis acids as catalysts is summarized in Table 1. Among the Lewis acids examined, SmI_2 and $SmCl_3$ were found to be the best catalysts. When the reaction was carried out in the presence of SmI_2 (0.1 mmol) or $SmCl_3$ (0.05 mmol), **4a** was obtained in 64% or 65% yield, respectively (runs 1 and 5). Typical Lewis acids such as $AlCl_3$ and $TiCl_4$ also

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[1] (a) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. (b) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. (c) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.

[2] Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447.

[3] Prandi, J.; Namy, J. L.; Menoret, G.; Kagan, H. B. *J. Organomet. Chem.* **1985**, *285*, 449.

[4] Van de Weghe, P.; Collin, J. *Tetrahedron Lett.* **1993**, *34*, 3881.

[5] Van de Weghe, P.; Collin, J. *Tetrahedron Lett.* **1994**, *35*, 2545.

[6] Shiraishi, H.; Kawasaki, Y.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1996**, *37*, 7291.

[7] (a) Kleinspehn, G. G. *J. Am. Chem. Soc.* **1955**, *77*, 1546. (b) Hendricson, J. B.; Rees, R.; Templeton, J. F. *J. Am. Chem. Soc.* **1964**, *86*, 107. (c) Young, D. M.; Allen, C. F. H. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 219. (d) Roomi, M. W.; MacDonald, S. F. *Can. J. Chem.* **1970**, *48*, 1689. (e) McKinnon, D. M. *Can. J. Chem.* **1965**, *43*, 2628. (f) Trost, B. M.; Keinan, E. *J. Org. Chem.* **1980**, *45*, 2741. (g) Murahashi, S.; Shimamura, T.; Moritani, I. *J. Chem. Soc., Chem. Commun.* **1974**, 931. (h) Schulte, K. E.; Reisch, J.; Walker, H. *Chem. Ber.* **1965**, *98*, 98. (i) Hauptmann, S.; Weissenfels, M.; Scholz, M.; Werner, E.-M.; Koehler, H.-J.; Weisflog, J. *Tetrahedron Lett.* **1968**, *11*, 1317.

[8] Fischer, H. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 202.

[9] Roskamp, E. J.; Dragovich, P. S.; Hartung, J. B., Jr.; Pedersen, S. F. *J. Org. Chem.* **1989**, *54*, 4736.

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Table 1. Three-Component Coupling Reactions Catalyzed by Various Lanthanoide Compounds[a]

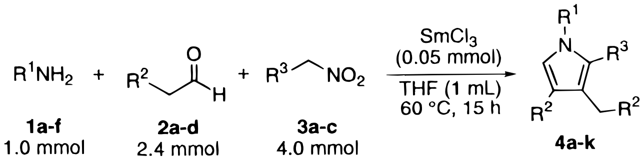
run	catalyst (mmol)	**4a**/yield (%)
1	SmI_2 (0.1)	64
2	SmI_2 (0.05)	60
3	SmI_3 (0.1)	35
4	$SmCl_3$ (0.1)	55
5	$SmCl_3$ (0.05)	65
6	$Sm(OTf)_3$ (0.1)	33
7	$Sc(OTf)_3$ (0.1)	38
8	$AlCl_3$ (0.1)	41
9	$TiCl_4$ (0.1)	39
10		no reaction

[a] Butylamine (**1a**) (1.0 mmol) was allowed to react with butyraldehyde (**2a**) (2.4 mmol) and nitroethane (**3a**) (4.0 mmol) in the presence of a catalytic amount of various Lewis acids in THF (1 mL) at 60 °C for 15 h under Ar.

catalyzed the present reaction (runs 8 and 9), but the catalytic activities of these Lewis acids were low compared with those of SmI_2 and $SmCl_3$. Triflates such as $Sm(OTf)_3$ and $Sc(OTf)_3$, which show high catalytic activity for various aldol-type reactions,[6] were less effective in the present reaction (runs 6 and 7). It is important to mention that no reaction took place in the absence of a catalyst (run 10).

On the basis of these results, the pyrrole synthesis via the three-component coupling of amines (**1a**−**f**), aldehydes (**2a**−**d**), and nitroalkanes (**3a**−**c**) was examined using $SmCl_3$ as the catalyst (Table 2). The coupling reaction using *n*-hexylamine (**1e**) and benzylamine (**1f**) in place of **1a** gave pyrroles **4e** and **4f** in 53% and 48% yields, respectively (runs 5 and 6). The coupling of **2a** and **3a** with bulky amines, such as *sec*-butylamine (**1c**) and *tert*-butylamine (**1d**), afforded the corresponding pyrroles **4c** and **4d** in low yields (runs 3 and 4). The reaction using nitromethane (**3b**) in place of **3a** resulted in a poor yield of pyrrole **4j** (run 10).

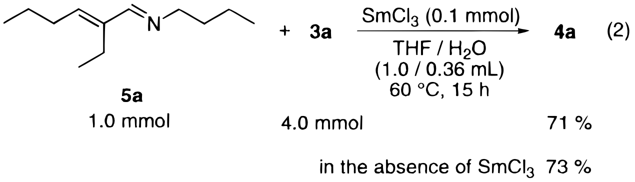
Table 2. Three-Component Coupling Reactions of Amines, Aldehydes, and Nitroalkanes Catalyzed by $SmCl_3$[a]



run	amine R^1	aldehyde R^2	nitroalkane R^3	pyrrole **4a**−**k**	yield (%)[b]
1	*n*-C_4H_9 (**1a**)	C_2H_5 (**2a**)	CH_3 (**3a**)	**4a**	65 (64)
2	*i*-C_4H_9 (**1b**)	**2a**	**3a**	**4b**	48
3	*sec*-C_4H_9 (**1c**)	**2a**	**3a**	**4c**	24 (13)
4	*t*-C_4H_9 (**1d**)	**2a**	**3a**	**4d**	8 (22)
5	*n*-C_6H_{13} (**1e**)	**2a**	**3a**	**4e**	53
6	$PhCH_2$ (**1f**)	**2a**	**3a**	**4f**	48
7	**1a**	CH_3 (**2b**)	**3a**	**4g**	55
8[c]	**1a**	*i*-C_3H_7 (**2c**)	**3a**	**4h**	35 (38)
9	**1a**	*n*-C_6H_{13} (**2d**)	**3a**	**4i**	59 (45)
10	**1a**	**2a**	H (**3b**)	**4j**	12
11[c]	**1a**	**2a**	C_2H_5 (**3c**)	**4k**	42

[a] Amine (1.0 mmol) was allowed to react with aldehyde (2.4 mmol) and nitroalkane (4.0 mmol) in the presence of a catalytic amount of $SmCl_3$ (0.05 mmol) in THF (1 mL) at 60 °C for 15 h under Ar. [b] The number in parenthesis shows the yield using SmI_2 (0.1 mmol). [c] 40 h.

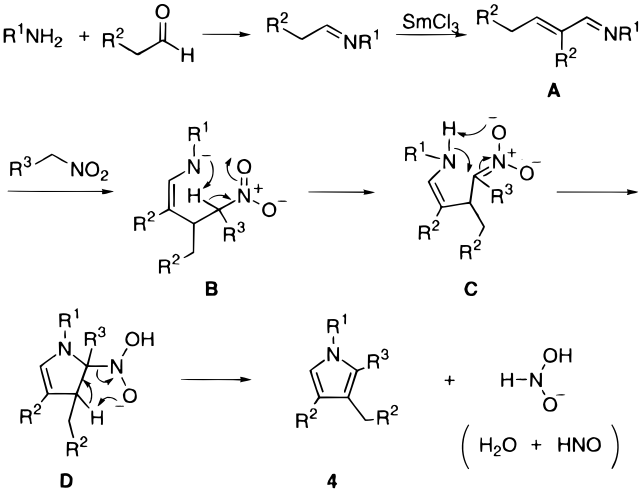
To gain information on the reaction path for the formation of pyrrole **4a**, the α,β-unsaturated imine **5a**, which is thought to be a key intermediate of **4a**, was allowed to react with **3a**. Actually, the reaction of *N*-(2-ethyl-2-hexenilidene)butylamine (**5a**), prepared independently from **1a** and **2a**, with **3a** in THF/H_2O (1.0/0.36) in the presence or absence of $SmCl_3$ at 60 °C for 15 h produced **4a** in 71% and 73% yield, respectively (eq 2).



It is interesting to note that the coupling of α,β-unsaturated imine **5a** with **3a** takes place in the absence of any catalyst. This shows that **5a** easily couples with **3a** to form the pyrrole **4a** by only heating.

On the basis of these results, a plausible reaction path for the present coupling reaction is shown in Scheme 1.

Scheme 1. A Plausible Reaction Path for the Formation of Pyrrole



We previously showed that the aldol-type condensation of the imine derived from amine and aldehyde in the presence of a samarium catalyst provides an α,β-unsaturated imine (**A**). Therefore, the most important step in the present three-component coupling reaction is considered to be the formation of α,β-unsaturated imine, **A**, resulting from the condensation of imine which is catalyzed by $SmCl_3$.[6] The thus-generated **A** couples with nitroalkane to give an intermediate (**B**). Proton transfer and successive intramolecular cyclization of the **B** to **D** followed by elimination of H_2O and HNO from the intermediate **D** lead to pyrrole **4**. A similar reaction path is demonstrated by Gómez-Sánchez[10] and Tamura.[11]

By the three-component coupling of amines with aldehydes and nitroalkanes, 1,2,3,4-tetraalkyl-substituted pyrroles were selectively obtained. If the coupling proceeds according to Scheme 1, it was expected that the reaction of α,β-unsaturated aldehydes, amines, and nitroalkanes would provide 1,2,3,5-tetraalkyl-substituted pyrroles. Thus, we next tried the introduction of an alkyl substituent at the 5-position of the pyrrole ring. The reaction was carried out using of α,β-unsaturated ketones and aldehydes instead of aldehydes (eqs 3 and 4).

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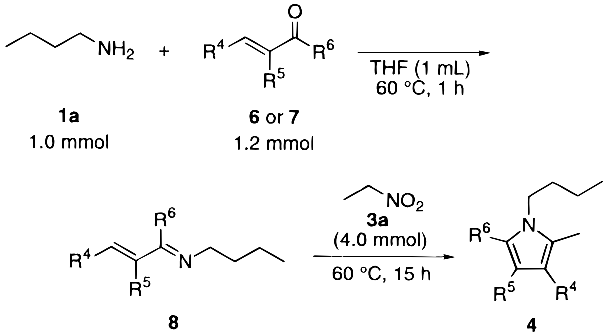
(10) Escribano, F. C.; Alcántara, M. P. D.; Gómez-Sánchez, A. *Tetrahedron Lett.* **1988**, *29*, 6001.

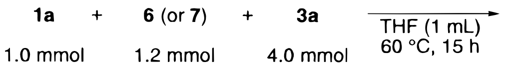
(11) Tamura, R.; Kamimura, A.; Ono, N. *Synthesis* **1991**, 423.

Method A



(3)

Method B



$$\underset{1.0\ \text{mmol}}{\mathbf{1a}} + \underset{1.2\ \text{mmol}}{\mathbf{6}\ (\text{or}\ \mathbf{7})} + \underset{4.0\ \text{mmol}}{\mathbf{3a}} \xrightarrow[60\ ^\circ\text{C},\ 15\ \text{h}]{\text{THF (1 mL)}} \mathbf{4} \quad (4)$$

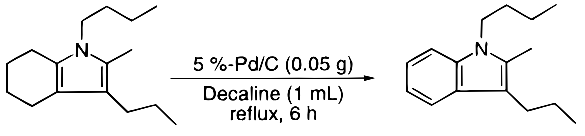
The reaction of **1a** with **3a** in the presence of various α,*β*-unsaturated ketones is shown in Table 3.

Since α,*β*-unsaturated imine (**8**) is expected to be formed by the condensation of an amine with an α,*β*-unsaturated aldehyde or ketone, a mixture of **1a** (1.0 mmol) and 3-nonen-2-one (**6a**) (1.2 mmol) was stirred in THF (1 mL) at 60 °C for 1 h, and then **3a** (4.0 mmol) was added to the reaction mixture (Method A). Stirring at 60 °C for 15 h gave the corresponding 1,2,3,5-tetra-alkyl-substituted pyrrole (**4m**) in 78% yield (Table 3, run 1). If the above reaction takes place successively, it is assumed that stirring of a mixture of **1a**, **6a**, and **3a** should produce **4m** (Method B). As expected, the reaction gave almost the same yield of **4m** as that obtained by Method A (Table 3, run 2). Furthermore, when 1-acetyl-1-cyclohexene (**6d**) and 2-butylidenecyclohexanone (**6e**)[12] were used instead of **6a**, tetrahydroisoindole derivative (**4q**) and tetrahydroindole derivative (**4r**) were respectively obtained in fair yields by both methods (Table 3, runs 7−10).

These reactions in the presence of $SmCl_3$ gave almost the same results as those in the absence of a catalyst. It is interesting to note that these couplings take place under relatively mild conditions in the absence of a catalyst. The reaction of **1a** with **3a** and various α,*β*-unsaturated aldehydes is summarized in Table 4.

The reaction of **1a** with 2-methyl-2-pentenal (**7a**) followed by **3a** without a catalyst at 60 °C for 15 h resulted in pyrrole **4g** in 76% yield (Table 4, run 1). However, the direct reaction of **1a**, **7a**, and **3a** under these conditions afforded **4g** in somewhat lower yield (52%) (Table 4, run 2). When (1*R*)-(−)-myrtenal (**7d**) was used instead of **7a**, the corresponding tetrahydroisoindole derivative (**4u**) was formed although the yield was low (Table 4, runs 7 and 8).

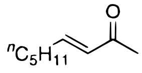
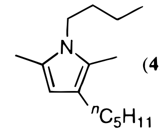
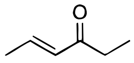
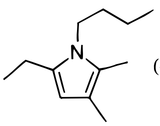
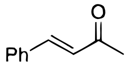
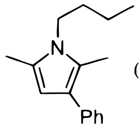
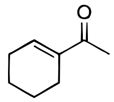
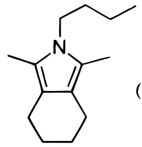
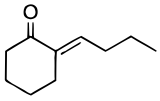
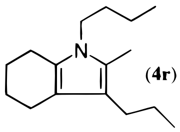
The dehydrogenation of *N*-butyl-2-methyl-3-propyl-4,5,6,7-tetrahydroindole (**4r**) catalyzed by palladium on carbon in Decalin under reflux formed *N*-butyl-2-methyl-3-propylindole (**9**) in good yield (eq 5).



(5)

4r **9** (>99%)

Table 3. Three-Component Coupling Reactions of Butylamine (1a), α,*β*-Unsaturated Ketones (6), and Nitroethane (3a)[a]

Run	Substrate	Product	Method	Yield (%)
1	 (**6a**)	 (**4m**)	A	78
2			B	80
3	 (**6b**)	 (**4n**)	A	49
4			B	47
5	 (**6c**)	 (**4p**)	A	40
6			B	39
7[b][c]	 (**6d**)	 (**4q**)	A	52
8[b]			B	34
9[b][c]	 (**6e**)	 (**4r**)	A	22
10[b][c]			B	39

[a] Method A: Butylamine (**1a**) (1.0 mmol) was allowed to react with α,*β*-unsaturated ketone (**6**) (1.2 mmol) in THF (1 mL) at 60 °C for 1 h under Ar, and then nitroethane (**3a**) (4.0 mmol) was added to the reaction mixture and stirred at 60 °C for 15 h. Method B: **1a** (1.0 mmol) was allowed to react with **6** (1.2 mmol) and **3a** (4.0 mmol) in THF (1 mL) at 60 °C for 15 h under Ar. [b] The reaction was carried out using toluene (1 mL) in place of THF at 100 °C. [c] **6** (2.0 mmol) was used.

In conclusion, it was found that pyrroles can be prepared with ease via the three-component coupling of amines, aldehydes, and nitroalkanes in the presence of a catalytic amount of a samarium species. The three-component coupling of α,*β*-unsaturated aldehydes or ketones with amines and nitroalkanes was achieved by only heating in the absence of catalyst to form the corresponding pyrroles in fair yields. The present reaction provides a new straightforward access to isoindoles and indoles which are an important class of compounds in pharmaceutical chemistry, although the optimum reaction conditions have not been established.

Experimental Section

General Procedures. ^1H and ^{13}C NMR were measured at 270 and 67.5 MHz, respectively, in $CDCl_3$ with TMS as the internal standard. IR spectra were measured as thin films on NaCl plate. GLC analysis was performed with flame ionization detector using 1 mm × 30 m capillary column (OV-1). Mass spectra were determined at an ionizing voltage of 70 eV.

General Procedure for the Three-Component Coupling of Amine (1), Aldehyde (2), and Nitroalkane (3) Catalyzed by Samarium Compounds. To a solution of samarium(II) diiodide or samarium(III) trichloride (0.1 mmol) in THF (1 mL) were added amines (**1**) (1.0 mmol), aldehydes (**2**) (2.4 mmol), and nitroalkanes (**3**) (4.0 mmol), and the

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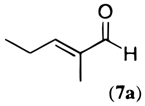
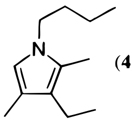
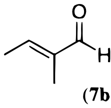
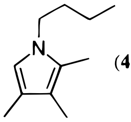
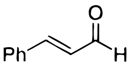
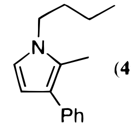
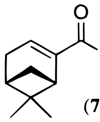
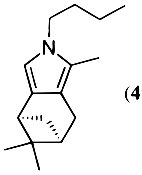
[12] Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503.

Table 4. Three-Component Coupling Reactions of Butylamine (1a), α,β-Unsaturated Aldehydes (7), and Nitroethane (3a)[a]

Run	Substrate	Product	Method	Yield (%)
1	 (**7a**)	 (**4g**)	A	76
2			B	52
3[b)]	 (**7b**)	 (**4s**)	A	69
4[b)]			B	60
5[c)]	 (**7c**)	 (**4t**)	A	32
6[c)]			B	30
7[d)]	 (**7d**)	 (**4u**)	A	25
8[d)]			B	19

[a] Method A: Butylamine (**1a**) (1.0 mmol) was allowed to react with α,β-unsaturated aldehyde (**7**) (1.2 mmol) in THF (1 mL) at 60 °C for 1 h under Ar, and then nitroethane (**3a**) (4.0 mmol) was added to the reaction mixture and stirred at 60 °C for 15 h. Method B: **1a** (1.0 mmol) was allowed to react with **7** (1.2 mmol) and **3a** (4.0 mmol) in THF (1 mL) at 60 °C for 15 h under Ar. [b] **7** (2.0 mmol) was used. [c] Reaction time is 40 h. [d] The reaction was carried out using toluene (1 mL) in place of THF at 100 °C.

reaction mixture was stirred at 60 °C for 15 h. After removal of the catalyst by filtration, products were isolated by column chromatography (silica gel, ethyl acetate/hexane = 1/10 eluent).

General Procedure for the Three-Component Coupling of α,β-Unsaturated Ketone (6) or Aldehyde (7), Amine (1), and Nitroalkane (3). Method A: A solution of butylamine (**1a**) (1.0 mmol) and α,β-unsaturated compounds (**6** or **7**) (1.2 mmol) in THF (1 mL) was allowed to react under stirring at 60 °C for 1 h, and then nitroalkane (**3**) (4.0 mmol) was added to the solution and the mixture was stirred at that temperature for 15 h. Method B: A solution of **1a** (1.0 mmol), α,β-unsaturated compounds (**6** or **7**) (1.2 mmol), and **3a** (4.0 mmol) in THF (1 mL) was allowed to react under stirring at 60 °C for 15 h. After removal of the solvent under reduced pressure, products were isolated by column chromatography (silica gel, ethyl acetate/hexane = 1/10 eluent).

General Procedure for the Pd/C-Catalyzed Dehydrogenation of *N*-Butyl-2-methyl-3-propyl-4,5,6,7-tetrahydroindole (4r) to *N*-Butyl-2-methyl-3-propylindole (9). A mixture of *N*-butyl-2-methyl-3-propyl-4,5,6,7-tetrahydroindole (**4r**) (0.04 mmol), 5% palladium on carbon (0.05 g), and Decalin (1 mL) was allowed to react under reflux for 6 h. After removal of the Pd/C by filtration, *N*-Butyl-2-methyl-3-propylindole (**9**) was isolated by column chromatography (silica gel, ethyl acetate/hexane = 1/10 eluent).

***N*-Butyl-4-ethyl-2-methyl-3-propylpyrrole (4a):** ^{1}H NMR δ 6.31 (s, 1H), 3.70 (t, $J = 7.4$ Hz, 2H), 2.38 (q, $J = 7.6$ Hz, 2H), 2.32 (t, $J = 7.8$ Hz, 2H), 2.10 (s, 3H), 1.70−1.58 (m, 2H), 1.53−1.24 (m, 4H), 1.17 (t, $J = 7.4$ Hz, 3H), 0.93 (t, $J = 7.4$ Hz, 3H), 0.92 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR δ 124.3, 123.3, 118.3, 115.2, 46.3, 33.6, 26.9, 24.7, 20.1, 18.5, 14.7, 14.3, 13.8, 9.7; IR (neat) 2960, 1549, 1463, 1386, 1261, 1098, 804 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 207 (26), 178 (100), 136 (18).

***N*-Isobutyl-4-ethyl-2-methyl-3-propylpyrrole (4b):** ^{1}H NMR δ 6.27 (s, 1H), 3.51−3.50 (d, $J = 7.0$ Hz, 2H), 2.41 (q, $J = 7.5$ Hz, 2H), 2.33 (t, $J = 7.6$ Hz, 2H), 2.09 (s, 3H), 2.01−1.85 (m, $J = 6.9$ Hz, 2H), 1.51−1.40 (m, 2H), 1.17 (t, $J = 7.7$ Hz, 3H), 0.91 (t, $J = 7.6$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR δ 124.4, 123.1, 118.2, 116.1, 54.2, 30.4, 26.9, 24.7, 20.2, 18.5, 14.8, 14.2, 9.9; IR (neat) 2958, 1548, 1465, 1387, 1196, 723 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 207 (19), 178 (100), 136 (12).

***N*-*sec*-Butyl-4-ethyl-2-methyl-3-propylpyrrole (4c):** ^{1}H NMR δ 6.27 (s, 1H), 3.86−3.78 (m, 2H), 2.36 (q, $J = 7.5$ Hz, 2H), 2.27 (t, $J = 7.6$ Hz, 2H), 2.03 (s, 3H), 1.68−1.50 (m, 2H), 1.41−1.34 (m, 2H), 1.28 (d, $J = 6.8$ Hz, 3H), 1.10 (t, $J = 7.8$ Hz, 3H), 0.83 (t, $J = 7.3$ Hz, 3H), 0.74 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR δ 124.3, 123.5, 117.6, 110.8, 52.4, 31.0, 26.8, 24.7, 21.3, 18.7, 14,6, 14.1, 11.0, 9.9; IR (neat) 2962, 1528, 1461, 1374, 1312, 1195, 720 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 207 (22), 178 (100), 136 (16).

***N*-*tert*-Butyl-4-ethyl-2-methyl-3-propylpyrrole (4d):** ^{1}H NMR δ 6.43 (s, 1H), 2.35 (q, $J = 7.6$ Hz, 2H), 2.24 (t, $J = 8.0$ Hz, 2H), 2.24 (s, 3H), 1.49 (s, 9H), 1.44−1.30 (m, 2H), 1.11 (t, $J = 7.6$ Hz, 3H), 0.86 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR δ 124.8, 121.6, 120.9, 113.2, 55.3, 30.8, 27.0, 24.5, 18.6, 14.4, 14.3, 13.4; IR (neat) 2961, 1526, 1463, 1367, 1216, 912 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 207 (26), 178 (100), 136 (19).

4-Ethyl-*N*-hexyl-2-methyl-3-propylpyrrole (4e): ^{1}H NMR δ 6.24 (s, 1H), 3.61 (t, $J = 7.0$ Hz, 2H), 2.34 (q, $J = 7.5$ Hz, 2H), 2.26 (t, $J = 7.7$ Hz, 2H), 2.03 (s, 3H), 1.61−1.53 (m, 2H), 1.42−1.30 (m, 2H), 1.29−1.20 (m, 6H), 1.10 (t, $J = 7.3$ Hz, 3H), 0.84 (t, $J = 7.3$ Hz, 3H), 0.81 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR δ 124.2, 123.3, 118.3, 115.2, 46.6, 31.5, 26.9, 26.6, 24.7, 22.5, 18.6, 14.7, 14.2, 14.0, 9.6; IR (neat) 2958, 1548, 1463, 1386, 1184, 722 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 235 (30), 206 (100), 164 (22).

***N*-Benzyl-4-ethyl-2-methyl-3-propylpyrrole (4f):** ^{1}H NMR δ 7.24−7.14 (m, 3H), 6.91−6.88 (m, 2H), 6.29 (s, 1H), 4.87 (s, 2H), 2.36 (q, $J = 7.5$ Hz, 2H), 2.27 (t, $J = 7.4$ Hz, 2H), 1.95 (s, 3H), 1.48−1.21 (m, 2H), 1.11 (t, $J = 7.6$ Hz, 3H), 0.84 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR δ 139.0, 128.6, 127.0, 126.3, 124.8, 123.9, 119.1, 116.2, 50.2, 26.9, 24.7, 18.5, 14.7, 14.1, 9.7; IR (neat) 2960, 1694, 1454, 1389, 731 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 241 (22), 212 (100), 77 (38).

***N*-Butyl-3-ethyl-2,4-dimethylpyrrole (4g):** ^{1}H NMR δ 6.30 (s, 1H), 3.68 (t, $J = 7.4$ Hz, 2H), 2.38 (q, $J = 7.5$ Hz, 2H), 2.11 (s, 3H), 2.02 (s, 3H), 1.69−1.58 (m, 2H), 1.41−1.13 (m, 2H), 1.06 (t, $J = 7.7$ Hz, 3H), 0.93 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR δ 123.8, 120.6, 116.5, 115.7, 46.2, 33.6, 20.1, 17.9, 15.9, 13.8, 10.1, 9.5; IR (neat) 2959, 1460, 1392, 1188, 720 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 179 (60), 164 (100), 137 (70).

***N*-Butyl-3-isobutyl-2-methyl-4-isopropylpyrrole (4h):** ^{1}H NMR δ 6.31 (s, 1H), 3.70 (t, $J = 7.6$ Hz, 2H), 2.81−2.70 (m, 1H), 2.24 (d, $J = 7.3$ Hz, 2H), 2.08 (s, 1H), 1.75−1.59 (m, 3H), 1.39−1.22 (m, 2H), 1.16 (d, $J = 6.8$ Hz, 6H), 0.92 (t, $J = 7.3$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR δ 129.1, 124.3, 117.0, 113.9, 46.4, 34.1, 33.5, 30.6, 25.0, 24.8, 22.7, 20.1, 13.8, 10.1; IR (neat) 2955, 1463, 1372, 1193, 735; MS (70 eV) *m*/*e* = M^{+} 221 (22), 178 (100), 136 (30).

***N*-Butyl-3-heptyl-4-hexyl-2-methylpyrrole (4i):** ^{1}H NMR δ 6.29 (s, 1H), 3.69 (t, $J = 7.4$ Hz, 2H), 2.34 (q, $J = 8.2$ Hz, 4H), 2.10 (s, 3H), 1.72−1.22 (m, 22H), 0.95−0.82 (m, 9H); ^{13}C NMR δ 124.0, 121.6, 118.7, 115.7, 46.3, 33.6, 32.0, 31.9, 31.8, 30.7, 29.8, 29.6, 29.3, 25.5, 24.8, 22.7, 20.1, 14.1, 13.8, 9.7. IR (neat) 2925, 1654, 1551, 1465, 723; MS (70 eV) *m*/*e* = M^{+} 263 (21), 178 (100), 136 (24).

***N*-Butyl-4-ethyl-3-propylpyrrole (4j):** ^{1}H NMR δ 6.35 (s, 2H), 3.74 (t, $J = 7.3$ Hz, 2H), 2.42 (q, $J = 7.5$ Hz, 2H), 2.36 (t, $J = 7.8$ Hz, 2H), 1.76−1.61 (m, 2H), 1.61−1.45 (m, 2H), 1.39−1.21 (m, 2H), 1.17 (t, $J = 7.4$ Hz, 3H), 0.96 (t, $J = 7.4$ Hz, 3H), 0.92 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR δ 124.1, 122.2, 117.8, 117.1, 49.1, 33.7, 27.6, 23.7, 20.1, 18.5, 14.6, 14.3, 13.7; IR (neat) 2859, 1532, 1463, 1372, 1159, 767 cm^{-1}; MS (70 eV) *m*/*e* = M^{+} 193 (30), 164 (100), 122 (69).

***N*-Butyl-2,4-diethyl-3-propylpyrrole (4k):** ^{1}H NMR δ 6.23 (s, 1H), 3.63 (t, $J = 7.8$ Hz, 2H), 2.45 (q, $J = 7.6$ Hz, 2H), 2.35 (q, $J = 7.6$ Hz, 2H), 2.25 (t, $J = 8.0$ Hz, 2H), 1.68−1.57 (m, 2H), 1.44−1.35 (m, 2H), 1.33−1.24 (m, 2H), 1.10 (t, $J = 7.8$ Hz, 3H), 1.04 (t, $J = 7.4$ Hz, 3H), 0.87 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR δ 130.4, 123.4, 117.8, 115.0, 46.0, 33.9, 27.1, 25.2, 20.2, 18.5, 17.4, 15.5, 14.5, 14.3, 13.8; IR (neat) 2960, 1707, 1525, 1463, 1385, 1190, 725 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 221 (20), 192 (100), 150 (18).

***N*-Butyl-2,5-dimethyl-3-pentylpyrrole (4m):** ^{1}H NMR δ 5.67 (s, 1H), 3.68 (t, J = 7.2 Hz, 2H), 2.33 (t, J = 7.6 Hz, 2H), 2.19 (s, 3H), 2.11 (s, 3H), 1.61−1.24 (m, 10H), 0.94 (t, J = 7.2 Hz, 3H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 125.8, 122.7, 118.8, 105.6, 43.3, 33.3, 31.9, 31.3, 26.2, 22.6, 20.2, 14.1, 13.8, 12.2, 9.8; IR (neat) 2927, 1547, 1463, 1356, 774 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 221 (35), 164 (100), 122 (32).

***N*-Butyl-2-ethyl-4,5-dimethylpyrrole (4n):** ^{1}H NMR δ 5.68 (s, 1H), 3.68 (t, J = 7.7 Hz, 2H), 2.52 (q, J = 7.5 Hz, 2H), 2.11 (s, 3H), 2.00 (s, 3H), 1.61−1.48 (m, 2H), 1.42−1.31 (m, 2H), 1.23 (t, J = 7.4 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 132.4, 123.1, 113.0, 104.8, 43.3, 33.4, 20.2, 19.5, 13.8, 13.0, 11.1, 9.7; IR (neat) 2962, 1462, 1372, 1344, 766 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 179 (65), 164 (100), 122 (61).

***N*-Butyl-2,5-dimethyl-3-phenylpyrrole (4p):** ^{1}H NMR δ 7.38−7.30 (m, 4H), 7.21−7.13 (m, 1H), 5.99 (s, 1H), 3.76 (t, J = 7.7 Hz, 2H), 2.34 (s, 3H), 2.26 (s, 3H), 1.67−1.59 (m, 2H), 1.44−1.36 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 137.7, 128.2, 128.0, 127.1, 124.7, 123.6, 120.6, 105.9, 43.6, 33.1, 20.2, 13.8, 12.3, 11.1; IR (neat) 2959, 1602, 1529, 1491, 1420, 1353, 1185, 762, 700 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 227 (48), 184 (100), 170 (45).

***N*-Butyl-1,3-dimethyl-4,5,6,7-tetrahydroisoindole (4q):** ^{1}H NMR δ 3.77 (t, J = 8.0 Hz, 2H), 2.58−2.48 (m, 4H), 2.19 (s, 6H), 1.84−1.79 (m, 4H), 1.74−1.62 (m, 2H), 1.54−1.43 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR δ 112.9, 118.8, 47.5, 37.8, 28.6, 26.0, 24.5, 18.1, 13.9; IR (neat) 2925, 1443, 1384, 1326 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 205 (48), 162 (100), 148 (47).

***N*-Butyl-2-methyl-3-propyl-4,5,6,7-tetrahydroindole (4r):** ^{1}H NMR δ 3.64 (t, J = 7.7 Hz, 2H), 2.54−2.28 (m, 6H), 2.19 (s, 6H), 1.84−1.22 (m, 10H), 0.96−0.89 (m, 6H); ^{13}C NMR δ 125.2, 122.3, 116.9, 115.2, 43.1, 33.5, 26.9, 24.6, 23.8, 23.6, 22.0, 21.7, 20.2, 14.3, 13.8, 9.6; IR (neat) 2960, 1465, 1362, 736 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 233 (20), 191 (100), 177 (18).

***N*-Butyl-2,3,4-trimethylpyrrole (4s):** ^{1}H NMR δ 6.31 (s, 1H), 3.68 (t, J = 7.3 Hz, 2H), 2.10 (s, 3H), 1.99 (s, 3H), 1.93 (s, 3H), 1.69−1.58 (m, 2H), 1.41−1.29 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 124.2, 116.4, 116.3, 113.7, 46.2, 33.7, 20.2, 13.7, 10.2, 9.6, 9.2; IR (neat) 3340, 2928, 1699, 1533, 1442, 1396, 1187, 718 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 193 (21), 178 (100), 136 (12).

***N*-Butyl-2-methyl-3-phenylpyrrole (4t):** ^{1}H NMR δ 7.40−7.18 (m, 5H), 6.62 (d, J = 3.0 Hz, 1H), 6.25 (d, J = 2.4 Hz, 1H), 3.83 (t, J = 7.4 Hz, 2H), 2.34 (s, 3H), 1.76−1.67 (m, 2H), 1.43−1.34 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 137.7, 128.2, 128.0, 125.0, 124.6, 121.9, 119.6, 107.6, 46.8, 33.4, 20.1, 13.8, 10.8; IR (neat) 2958, 1602, 1501, 1350, 702 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 213 (64), 170 (100), 156 (20), 128 (18).

***N*-Butyl-1,5,5-trimethyl-4,5,6,7-tetrahydro-4,6-methanoisoindole (4u):** ^{1}H NMR δ 6.17 (s, 1H), 3.67 (t, J = 7.7 Hz, 2H), 2.65−2.59 (m, 3H), 2.21−2.17 (m, 1H), 2.07 (s, 3H), 1.68−1.57 (m, 2H), 1.33 (s, 3H), 1.31−1.26 (m, 4H), 0.92 (t, J = 7.3 Hz, 3H), 0.67 (s, 3H); ^{13}C NMR δ 128.6, 122.8, 113.4, 112.0, 46.1, 41.5, 41.2, 40.8, 34.1, 33.7, 26.7, 25.9, 21.6, 20.0, 13.8, 9.9; IR (neat) 2929, 1466, 1378, 1326, 1259, 730 cm^{-1}; MS (70 eV) *m*/*e* = M$^+$ 231 (58), 216 (73), 88 (100), 121 (34).

***N*-Butyl-2-methyl-3-propylindole (9):** ^{1}H NMR δ 7.43 (d, J = 7.3 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.05−6.95 (m, 2H), 3.92 (t, J = 7.6 Hz, 2H), 2.61 (t, J = 7.3 Hz, 2H), 2.57 (s, 3H), 1.63−1.51 (m, 4H), 1.31−1.22 (m, 2H), 0.87−0.80 (m, 6H). ^{13}C NMR ($CDCl_3$/TMS) δ 135.9, 132.1, 128.0, 120.1, 118.3, 118.1, 111.5, 108.7, 42.9, 32.5, 26.5, 24.2, 20.3, 14.1, 13.9, 10.2; IR (neat) 3050, 2958, 1613, 1468, 1362, 1183, 737 cm^{-1}.

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Supporting Information Available: Copies of ^{13}C NMR, ^{1}H NMR, and IR spectra for the compounds **4a**−**u**, **6e**, and **9** (62 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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