Synthesis of Alkyl-Substituted N-Protected Indoles via Acylation and Reductive Deoxygenation[1]

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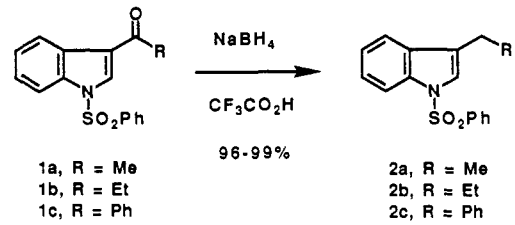
The synthesis of 2-, 3-, and 5-alkyl-1-(phenylsulfonyl)indoles involving Friedel–Crafts acylation followed by reductive deoxygenation is described. The application of this acylation–deoxygenation sequence to 3-acyl-1-(phenylsulfonyl)indoles bearing potentially reducible functionalities was explored using sodium borohydride in trifluoroacetic acid. While halogen atoms attached to the 2-position display a predictable range of lability toward this reducing system, a 5-bromo substituent survives these conditions intact. The 2-acyl-1-(phenylsulfonyl)indoles (**15a–c**) were prepared by Friedel–Crafts acylation of the 2-(trimethylsilyl)-1-(phenylsulfonyl)indoles (**14a,b**). These 2-acyl derivatives were then deoxygenated using borane–*tert*-butylamine complex in the presence of aluminum chloride. The 5-alkyl-1-(phenylsulfonyl)indoles (**20a–c**) were synthesized by the following sequence: (a) C-5 acylation of 1-(phenylsulfonyl)indole (**17**); (b) deoxygenation by one of the above methods; and (c) oxidation using manganese(III) acetate.

In the development of general strategies for the synthesis of indole natural products, one tactic is to effect the selective functionalization of an already extant indole nucleus, thereby avoiding de novo construction of this heterocyclic system. In this regard, early protection of the indole nitrogen can play a pivotal role, because the protecting group can serve to site-direct substitution as well as to modify the reactivity of the indole ring. For example, since the discovery that 1-methylindole could be regioselectively deprotonated at the C-2 position with *n*-butyllithium,[2] 2-lithio species derived from a variety of N-protected indoles have been routinely used to functionalize this position.[3] Additionally, N-protected indoles can also undergo regioselective lithiation at the C-3 position either via halogen–metal exchange of a 3-halo derivative[4] or via a directed-metalation group at the C-2 position.[5] However, although the C-3 position of an N-unprotected indole is susceptible to attack by a wide variety of electrophiles,[6] the presence of an electron-withdrawing substituent on the indole nitrogen substantially attenuates this reactivity, and only a limited number of electrophiles have been found to add to such indole derivatives.[7]

The selective functionalization of the normally unreactive benzene ring of indole remains problematical. Although, in principle, any position of this ring can be functionalized, in fact, C-5 is most easily substituted, but only then if the indole ring is masked as an N-protected indoline (2,3-dihydroindole). Oxidative regeneration of the indole nucleus at a later stage then allows for further elaboration of the 5-substituted N-protected indole at the normal sites of reactivity, i.e., C-2 or C-3. In order to functionalize C-4 or C-7, one must resort to the use of chromium tricarbonyl complexes[8–10] or a sequence involving thallation–palladation.[11] Indeed, the only general method available for the functionalization of carbons 4–7 of the indole nucleus involves halogen–metal exchange of 4-, 5-, 6-, and 7-bromoindoles.[12] However, this method still necessitates the syntheses of the appropriate bromoindoles by de novo ring construction.

Scheme I



1a, R = Me
1b, R = Et
1c, R = Ph

2a, R = Me
2b, R = Et
2c, R = Ph

One commonly employed route to *C*-alkyl-substituted indoles has been the reductive deoxygenation of indolyl carbonyl derivatives which, in general, are more easily accessible than the corresponding alkanes.[13,14] Although

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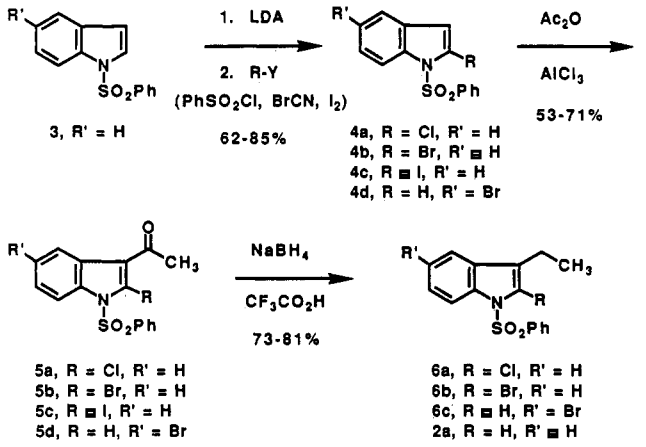
the hydrogenolysis of oxygen-containing functional groups attached to the electron-rich C-3 position of the indole ring was reported as early as 1953 and has been accomplished by using lithium aluminum hydride ($LiAlH_4$),[15] lithium borohydride,[16] or diborane,[17] only diborane is successful in reducing the less activated 2-carbonyl derivatives, and none of these methods have been demonstrated to be effective in the case of an indole bearing a strong electron-withdrawing group substituted on nitrogen. In fact, the $LiAlH_4$ approach is limited to N-unsubstituted 3-indolyl carbonyl derivatives, the ionization of the N–H bond in these vinylogous amides apparently being a necessary requirement for deoxygenation.[18,7c] While in one case the reduction of 1-methyl-3-acetylindole to 1-methyl-3-ethylindole was accomplished using $LiAlH_4$ in the presence of aluminum chloride ($AlCl_3$),[19] this particular combination of reagents has never proven to be of general utility in the realm of indole reductions.

In a previous publication concerning the Friedel–Crafts acylation of 1-(phenylsulfonyl)indoles,[7b] we noted that sodium borohydride ($NaBH_4$) in trifluoroacetic acid (TFA) is capable of reductively deoxygenating several 3-acyl-1-(phenylsulfonyl)indoles (**1a–c**) to the corresponding 3-alkyl derivatives (**2a–c**) in nearly quantitative yields (Scheme I).

In contrast to the well-known tendency of N-unprotected or *N*-alkylindoles to be reduced to indolines by a variety of reducing agents under acidic conditions (e.g., $NaBH_4$ in carboxylic acids,[20] $NaCNBH_3$ in acetic acid[20,21] or TFA,[22] BH_3[22a,23] or BH_3·pyridine in HCl,[24] BH_3·THF[22d,25] or Et_3SiH in TFA[22b,26]), the presence of the electron-withdrawing *N*-phenylsulfonyl group appears to thwart this formal hydrogenation, in that we observed no concomitant reduction of the indole 2,3-double bond in this study.[7b] Moreover, although $NaBH_4$/TFA is known to reduce diaryl ketones[27] and diarylmethanols[28] to diarylmethanes, it is somewhat unusual for monoaryl ketones to be reduced to alkanes under these conditions.[29] The facile deoxygenation achieved in the case of N-protected 3-acylindoles can be rationalized by invoking a resonance-stabilized carbocation (indolenium ion) formed during the suggested deoxygenation sequence: (a) initial reduction of the ketone carbonyl or its conjugate acid by a trifluoroacetoxyborohydride species[29] to produce an indolyl carbinol, (b) acid-catalyzed protonation of the resultant alcohol and loss of water affording an indolenium ion,[30] and (c) transfer of hydride to the indolenium species.

Scheme II



Since our attempts to prepare 3-alkylindoles via a one-step Friedel–Crafts alkylation of 1-(phenylsulfonyl)indoles had been unsuccessful,[7b] this acylation–reductive deoxygenation maneuver appeared to provide an excellent two-step alternative to direct alkylation. We have explored the scope and limitations of this method as a generalized route to *C*-alkylindoles and herein report our results.

Results and Discussion

Synthesis of 3-Alkyl-1-(phenylsulfonyl)indoles. In order to define the chemoselectivity of this deoxygenation process vis-á-vis potentially reducible groups, we first examined the preparation and reduction of 2-halo-3-acetyl-1-(phenylsulfonyl)indoles.[31] To that end, 1-(phenylsulfonyl)indole (**3**)[4a] was treated with lithium diisopropylamide (LDA), and the resulting 2-lithioindole was quenched with the appropriate electrophiles ($PhSO_2Cl$, BrCN, I_2, respectively) to afford 2-chloro-1-(phenylsulfonyl)indole (**4a**), 2-bromo-1-(phenylsulfonyl)indole

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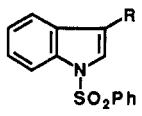
(**4b**), and 2-iodo-1-(phenylsulfonyl)indole (**4c**) (Scheme II). These compounds undergo C-3 acylation under Friedel–Crafts conditions using acetic anhydride in the presence of $AlCl_3$ to provide the requisite 2-halo-3-indolyl ketones **5a–c**. Our attempts to effect deoxygenation with $NaBH_4$/TFA produced mixed results.[32] Thus, although carbonyl deoxygenation was achieved in each instance, only in the case of **5a** was the halogen completely retained, affording 2-chloro-3-ethyl-1-(phenylsulfonyl)indole (**6a**) in 73% yield. Treatment of bromo ketone **5b** with $NaBH_4$/TFA leads to a mixture of **2a** and **6b** (ca. 60:40 by GC/MS), which is one spot on TLC and proved to be inseparable by chromatography. In contrast, iodo ketone **5c** suffers reductive loss of the iodine, in addition to deoxygenation, producing only 3-ethyl-1-(phenylsulfonyl)-indole (**2a**) in 75% yield. On the other hand, 3-acetyl-5-bromo-1-(phenylsulfonyl)indole (**5d**), prepared by acylation of 5-bromo-1-(phenylsulfonyl)indole (**4d**),[33] undergoes reductive deoxygenation using $NaBH_4$/TFA without the loss of bromide[34] to afford 5-bromo-3-ethyl-1-(phenylsulfonyl)indole (**6c**) in 81% yield.

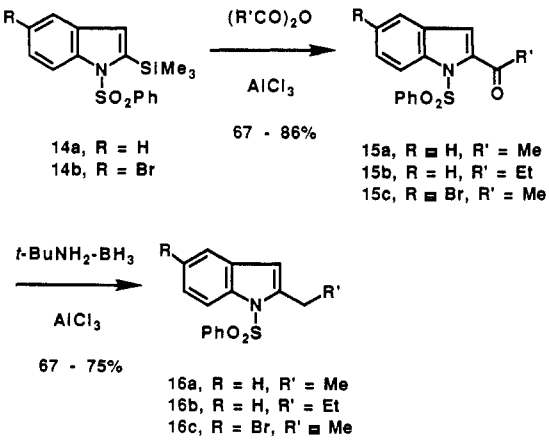
We next examined the deoxygenation of C-3 indolyl ketones bearing oxidized carbon atoms remote from the ketone carbonyl. Thus, when the succinic acid derivatives **7a** and **7b**[7b] are treated with $NaBH_4$/TFA, chemoselective deoxygenation of the ketone moiety occurs to produce **8a** and **8b**, in which the ester and the carboxylic acid functions survive. This selectivity is in marked contrast to the reported reduction of both the keto and the ester functions of methyl 3-indolyl-4-oxobutanoate with diborane.[17b] Additionally, in light of the ability of $LiAlH_4$ to reduce both 3-formylindole and 3-carbethoxyindole to 3-methylindole,[15a] we also examined the reduction of other carbon functionalities at the C-3 position of N-protected indoles using $NaBH_4$/TFA. Whereas both ethyl 1-(phenylsulfonyl)indole-3-carboxylate (**9**)[4a] and 3-cyano-1-(phenylsulfonyl)indole (**10**)[7b] are recovered unchanged after treatment with $NaBH_4$/TFA for 24 h, attempted reduction of 1-(phenylsulfonyl)indole-3-carboxaldehyde (**11**)[4a] leads to a complex mixture of uncharacterized products.[35]



7a, R = $COCH_2CH_2CO_2Et$
7b, R = $COCH_2CH_2CO_2H$
8a, R = $CH_2CH_2CH_2CO_2Et$
8b, R = $CH_2CH_2CH_2CO_2H$
9, R = CO_2Et
10, R = CN
11, R = CHO
12, R = CH_3
13, R = Br

The role of TFA in this reductive deoxygenation process suggested that other acids might perform this function equally well. Indeed, we find this to be true, provided that a sufficiently strong acid and/or an alternative hydride source is employed. For instance, although 3-acetyl-1-(phenylsulfonyl)indole (**1a**) is recovered unchanged after attempted reduction with $NaBH_4$ in acetic acid (24 h, 25 °C),[7b] the use of methanesulfonic acid, neat or in conjunction with acetic acid as cosolvent, leads to the corresponding 3-ethyl derivative **2a** in 90% and 66% yields, respectively.

Scheme III



Especially attractive among those acids under consideration for this purpose was the Lewis acid $AlCl_3$, since the entire sequence of acylation–reductive deoxygenation might then be performed in a single reaction vessel using the same solvent and acid catalyst. However, although we found that **1a** could be deoxygenated in 67% yield using the method of Ono[36] ($NaBH_4/AlCl_3$ in tetrahydrofuran), no reduction was observed when the reaction was attempted using methylene chloride as solvent. This result, undoubtedly attributable to the low solubility of $NaBH_4$ in methylene chloride, cast doubt that the one-pot sequence might be effected using $NaBH_4$ in combination with any of the solvents commonly employed under Friedel–Crafts conditions.

However, Lau and co-workers[37] have recently introduced a method for the reductive deoxygenation of aryl ketones in organic solvents (methylene chloride or toluene) using the borane–*tert*-butylamine complex (*t*-$BuNH_2{\cdot}BH_3$) and aluminum chloride. This method seemed ideally suited to our requirements for a one-pot reaction. Indeed, acylation of 1-(phenylsulfonyl)indole (**3**) using acetic anhydride and $AlCl_3$ (excess), followed by the addition of borane–*tert*-butylamine led to 3-ethyl-1-(phenylsulfonyl)-indole (**2a**) in 90% isolated yield. Once again, as with $NaBH_4$/TFA, no reduction of the indole 2,3-double bond was observed. Furthermore, whereas reaction of 1-(phenylsulfonyl)indole-3-carboxaldehyde (**11**) with $NaBH_4$/TFA follows an obscure path, reaction of **11** with *t*-$BuNH_2{\cdot}BH_3/AlCl_3$ affords a 44% yield of 3-methyl-1-(phenylsulfonyl)indole (**12**).

Synthesis of 2-Alkyl-1-(phenylsulfonyl)indoles. In order to extend the acylation–deoxygenation methodology to the C-2 position of N-protected indoles, we needed to circumvent the propensity for electrophilic attack at the C-3 position. Therefore, since 1-(phenylsulfonyl)indole (**3**) reacts readily with bromine to afford the 3-bromoindole **13** in very high yield,[4c] we felt that this C-3-blocked derivative would direct Friedel–Crafts acylation to the C-2 position. Subsequent reductive deoxygenation might even proceed with concomitant reductive loss of the 3-bromo protecting group. Instead, however, Friedel–Crafts acylation of **13** using propionic anhydride or acetic anhydride in the presence of $AlCl_3$ results in ipso substitution to afford, after debromination, only the 3-acyl derivatives **1b** and **1a**, respectively, thereby precluding this artifice as a viable route to 2-acyl-1-(phenylsulfonyl)indoles.

(32) The stability of 2-halogenated indoles to reduction seems to vary with reducing agent employed. For the removal of a 2-chloro substituent upon reduction with hydrogen and 10% Pd–C, see: Kubo, A.; Nakai, T. *Synthesis* **1980**, 365. Alternatively, a 2-iodo substituent was found to survive reduction with BH_3: Kline, T. *J. Heterocycl. Chem.* **1985**, *22*, 505.
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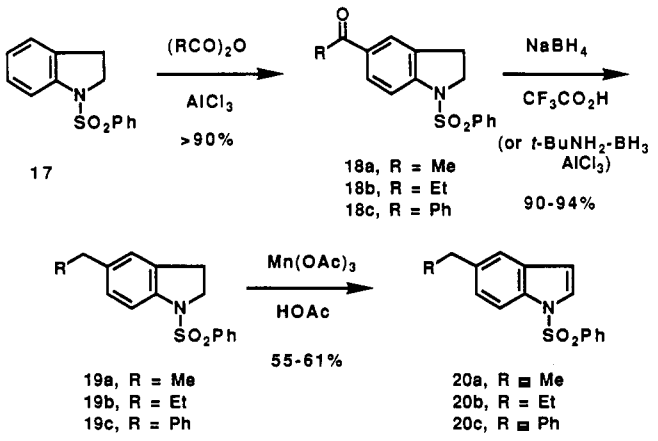
Scheme IV



Thereupon we sought to utilize the well-known ipso directing ability of silicon[38,39] as a potential avenue to the requisite 2-indolyl ketones. To that end, 2-(trimethylsilyl)-1-(phenylsulfonyl)indole (**14a**)[40] was prepared from **3** in 78% yield by C-2 lithiation (LDA, −78 °C) and quenching with trimethylsilyl chloride. Similarly, 5-bromo-2-(trimethylsilyl)-1-(phenylsulfonyl)indole (**14b**) was prepared from **4d** in 82% yield. As expected, Friedel–Crafts acylation of these 2-silyl derivatives with acetic anhydride or propionic anhydride occurs ipso to the silyl substituent to afford the C-2-substituted ketones **15a–c** in good yields (Scheme III). While aliphatic anhydrides efficiently substitute ipso to the trimethylsilyl group under Friedel–Crafts conditions, acid chlorides and aromatic anhydrides are found to react with concomitant desilylation to provide only the C-3 acylated products.[41] Presumably, this is the result of initial desilylation followed by normal acylation at C-3. Why this desilylation is not observed in the case of the two alkyl anhydrides investigated is presently unclear; however, the reactions of **14a** with various other electrophiles are currently under investigation.

The attempted reduction of the 2-indolyl ketone **15a** with $NaBH_4$/TFA produced only a complex mixture of products from which no 2-ethyl derivative could be isolated. Additionally, we observed similar results upon an attempted Clemmensen reduction.[42] We found, however, that these C-2 indolyl ketones **15a–c** can be efficiently reduced to the corresponding 2-alkyl derivatives **16a** (71%), **16b** (75%), and **16c** (67%) using the borane–*tert*-butylamine complex in the presence of $AlCl_3$. Once again, these reactions are clean and no reduction of the indole double bond is observed in any instance, thereby providing a facile route to 2-alkylindoles employing the acylation–reductive deoxygenation methodology.

Synthesis of 5-Alkyl-1-(phenylsulfonyl)indoles. As stated earlier, no methods are available for the direct electrophilic functionalization of the C-5 position of N-protected indoles, due to the inherently higher reactivity of the C-3 and C-2 positions. However, the introduction of electrophiles to the C-5 position of *indolines* is a useful and often exploited synthetic tool.[43] The high reactivity of the C-5 position of indolines toward electrophiles is the expected consequence of the activating effect of the para substituted nitrogen. We, therefore, examined the reductive deoxygenation of 5-acyl-1-(phenylsulfonyl)-indolines as a formal route to 5-alkylindoles.

Friedel–Crafts acylation of 1-(phenylsulfonyl)indoline (**17**)[23] proceeds regioselectively to afford the 5-acyl-1-(phenylsulfonyl)indolines **18a–c** in yields of greater than 90% (Scheme IV). Reductive deoxygenation to the corresponding 5-alkyl-1-(phenylsulfonyl)indolines **19a–c** is achieved in very high yields either $NaBH_4$/TFA or *t*-$BuNH_2$·BH_3/$AlCl_3$. Subsequent oxidation with manganese(III) acetate[33] in acetic acid provides 5-ethyl-1-(phenylsulfonyl)indole (**20a**),[33] 5-propyl-1-(phenylsulfonyl)-indole (**20b**), and 5-benzyl-1-(phenylsulfonyl)indole (**20c**)[33] in good yields.

Although this route to 5-alkyl-1-(phenylsulfonyl)indoles consists of three separate steps, each individual step proceeds in good to excellent yield. Indeed, this methodology, involving a hydride source in the presence of acid, is especially attractive when compared to previous methods employed for the reductive deoxygenation of 5-acylindolines. For example, 5-ethylindoline is obtained in only 12.5% yield from the Clemmensen reduction of 1,5-diacetylindoline,[44] and catalytic hydrogenation (H_2, 10% Pd/C) of 5-benzoyl-1-methylindoline provides the deoxygenated product in 53% yield.[45]

In summary, we have developed new and concise reaction protocols for the construction of 2-, 3-, and 5-alkyl-1-(phenylsulfonyl)indoles that begin with indole and that feature new acylation and reduction chemistry of the indole ring.

Experimental Section

Melting points were determined in open capillaries with an Electrothermal melting point apparatus and are uncorrected. Elemental analyses were performed by Midwest Microlab, Indianapolis, IN, or, in house, with a Perkin-Elmer 240-B elemental analyzer. Infrared spectra were recorded on a Perkin-Elmer 1330 instrument or with a Nicolet 5DX Fourier transform (FT) instrument. ^1H NMR spectra were obtained on a Varian EM 360 spectrometer and, in certain cases, ^1H and ^{13}C NMR spectra were obtained on an IBM NR/100 FT NMR spectrometer at 100 MHz. Chemical shifts are reported in parts per million downfield from tetramethylsilane as an internal reference. Low-resolution mass spectra were determined with a Finnigan MAT INCOS 50 gas chromatograph–mass spectrometer. Thin-layer chromatography (TLC) was performed on precoated (0.1 mm) silica gel plastic sheets with fluorescent indicator (Eastman Kodak). "Flash chromatography" refers to the technique developed by Still.[46] Tetrahydrofuran was distilled from sodium/benzophenone, and diisopropylamine was distilled over sodium hydride. Sodium borohydride (pellets), *tert*-butylamine–borane complex (pellets), and manganese(III) acetate were purchased from Aldrich Chemical Co. The phrase "usual workup" refers to washing the organic extract with H_2O and then saturated brine, drying over Na_2SO_4 or K_2CO_3, and concentration on a rotary evaporator.

Representative Procedure for the Preparation of 2-Halogenated 1-(Phenylsulfonyl)indoles. 2-Chloro-1-(phe-

(38) For a review of the chemistry of arylsilanes, see: Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: Boston, 1981; Chapter 10.

(39) Cf.: (a) Barrett, A. G. M.; Dauzonne, D.; O'Neil, I. A.; Renaud, A. *J. Org. Chem.* **1984**, *49*, 4409. (b) Majchrzak, M. W.; Simchen, G. *Synthesis* **1986**, 956.

(40) Rubiralta, M.; Casamitjana, N.; Grierson, D. S.; Husson, H.-P. *Tetrahedron* **1988**, *44*, 443.

(41) Homan, D. F. J.; Ketcha, D. M., unpublished results. Note: acetyl chloride, benzoyl chloride, and benzoic anhydride all react with 2-(trimethylsilyl)-1-(phenylsulfonyl)indole in the presence of aluminum chloride to afford only the desilylsilated, 3-acyl derivatives, identical with products reported in ref 7b.

(42) A Clemmensen reduction of a 3-acyl-1-(phenylsulfonyl)pyrrole has been successfully accomplished: Kakushima, M.; Hamel, P.; Frenette, R.; Rokach, J. *J. Org. Chem.* **1983**, *48*, 3214.

(43) For a review on the synthesis of substituted indoles via indolines, see: Preobrazhenskaya, M. N. *Russian Chem. Rev.* (*Engl. Transl.*) **1967**, *36*, 753.

(44) Terent'ev, A. P.; Preobrazhenskaya, M. N.; Sorokina, G. M. *Zh. Obshch. Khim.* **1959**, *29*, 2875 (*Engl. Transl.* **1959**, *29*, 2835).

(45) Hlasta, D. J.; Luttinger, D.; Perrone, M. H.; Silbernagel, M. J.; Ward, S. J.; Haubrich, D. R. *J. Med. Chem.* **1987**, *30*, 1555.

(46) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

nylsulfonyl)indole (4a). To a solution of lithium diisopropylamide (12.1 mmol) prepared from diisopropylamine (12.7 mmol) and *n*-butyllithium (1.56 M in hexane; 12.1 mmol) in dry THF (25 mL) under nitrogen at −78 °C was added dropwise by syringe over 5 min a solution of **3** (3.01 g, 11.7 mmol) in dry THF (30 mL). The mixture was stirred for 1.5 h below −70 °C, allowed to warm to 0 °C over 1 h, recooled to −75 °C, and then treated with benzenesulfonyl chloride (15 mmol), allowed to warm to room temperature overnight, poured into 3% aqueous $NaHCO_3$ (200 mL), and extracted with CH_2Cl_2 (3 × 125 mL). The combined extracts were washed with H_2O (200 mL) and brine (2 × 200 mL), dried (K_2CO_3), and concentrated in vacuo to afford a tan solid. Crystallization from methanol afforded 2.68 g (82%) of **4a** in three crops: mp 63–64 °C; IR (KBr) 1440, 1370, 1210, 1190, 1170, 1110, 1080, 1020, 1000, 810, 755, 745, 720, 680, 660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 10 H), 6.5 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.1, 136.3, 134.0, 129.1, 128.3, 126.7, 124.8, 124.5, 124.0, 120.0, 114.8, 110.2.

Anal. Calcd for $C_{14}H_{10}NO_2SCl$: C, 57.64; H, 3.45; N, 4.80. Found: C, 57.68; H, 3.39; N, 4.86.

2-Bromo-1-(phenylsulfonyl)indole (4b). The same procedure as described above for **4a** but with quenching with cyanogen bromide gave a crude brown solid after workup. Flash chromatography using 1:1 hexanes–CH_2Cl_2 gave **4b** (85%). Crystallization from Et_2O/hexane gave the following: mp 62–64 °C; IR (KBr) 1440, 1380, 1210, 1200, 1185, 1120, 1090, 1015, 995, 810, 750, 725, 685, 655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.1 (m, 10 H), 6.7 (s, 1 H); spectral data matched those reported for this compound.[47]

Anal. Calcd for $C_{14}H_{10}NO_2SBr$: C, 50.02; H, 3.00; N, 4.17. Found: C, 48.89; H, 2.91; N, 4.13.

2-Iodo-1-(phenylsulfonyl)indole (4c). The same procedure as described above for **4a** but with quenching with iodine gave a crude brown solid. Recrystallization from ether–hexane afforded **4c** (62%) after two crops: mp 96–98 °C; IR (KBr) 1440, 1425, 1365, 1210, 1190, 1180, 1120, 1085, 805, 755, 740, 720, 680, 645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.3–7.2 (m, 10 H), 6.9 (s, 1 H).

Anal. Calcd for $C_{14}H_{10}NO_2SI$: C, 43.88; H, 2.63; N, 3.66. Found: C, 43.92; H, 2.77; N, 3.59.

Representative Procedure for the Friedel–Crafts Acylation of 1-(Phenylsulfonyl)indoles.[7b] 3-Acetyl-2-chloro-1-(phenylsulfonyl)indole (5a). To a magnetically stirred suspension of aluminum chloride (4.11 g, 30.9 mmol) in CH_2Cl_2 (30 mL) was added acetic anhydride (1.57 g, 15.4 mmol), and the mixture was stirred for 15 min. A solution of **4a** (1.50 g, 5.10 mmol) in CH_2Cl_2 (30 mL) was added dropwise; the mixture was stirred for 1 h and quenched by the slow addition of crushed ice. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, saturated aqueous $NaHCO_3$, and brine, dried (K_2CO_3), and concentrated in vacuo. Flash chromatography using hexanes–CH_2Cl_2 (60:40) provided 1.23 g (71%) of **5a**: mp 154–155 °C; IR (KBr) 1665, 1525, 1475, 1440, 1365, 1160, 1090, 980, 735, 690, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 9 H), 2.6 (s, 3 H); mass spectrum, *m/z* 333 (M^+), 291 (100), 178, 164, 141, 128, 114, 77.

Anal. Calcd for $C_{16}H_{12}NO_3SCl$: C, 57.57; H, 3.62; N, 4.20. Found: C, 57.70; H, 3.54; N, 4.24.

3-Acetyl-2-bromo-1-(phenylsulfonyl)indole (5b). A similar Friedel–Crafts acylation of **4b** using acetic anhydride in the presence of aluminum chloride gave **5b** (53%) after flash chromatography using hexanes–CH_2Cl_2 (60:40): mp 159–160 °C; IR (KBr) 1665, 1510, 1435, 1380, 1170, 1090, 980, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.3 (m, 9 H), 2.7 (s, 3 H); mass spectrum, *m/z* 379 (M^+, 100), 377, 337, 335, 299, 297, 284, 282, 210, 208, 141, 129, 128, 77.

Anal. Calcd for $C_{16}H_{12}NO_3SBr$: C, 50.81; H, 3.20; N, 3.70. Found: C, 51.03; H, 3.23; N, 3.48.

3-Acetyl-2-iodo-1-(phenylsulfonyl)indole (5c). A similar Friedel–Crafts acylation of **4c** using acetic anhydride in the presence of aluminum chloride gave **5c** (66%) after flash chromatography using hexanes–CH_2Cl_2 (60:40) and recrystallization from Et_2O: mp 132–134 °C; IR (KBr) 1665, 1500, 1440, 1375, 1200, 1170, 1150, 1090, 990, 745, 700, 690, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 9 H), 2.6 (s, 3 H).

(47) Saulnier, M. G.; Gribble, G. W., unpublished results. Saulnier, M. G. Ph.D. Thesis, Dartmouth College, 1982.

Anal. Calcd for $C_{16}H_{12}NO_3SI$: C, 45.19; H, 2.84; N, 3.29. Found: C, 45.60; H, 2.75; N, 3.37.

3-Acetyl-5-bromo-1-(phenylsulfonyl)indole (5d). A similar Friedel–Crafts acylation of **4d** using acetic anhydride in the presence of aluminum chloride gave **5d** (66%), one crop after recrystallization from 95% ethanol: mp 161–163 °C; IR (KBr) 3120, 1660, 1540, 1440, 1380, 1300, 1195, 1170, 1125, 1090, 970, 805, 780, 750, 720, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.8–7.2 (m, 9 H), 2.5 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 192.8, 137.3, 133.6, 132.7, 129.7, 129.1, 128.8, 127.0, 125.9, 121.0, 118.7, 114.4, 27.6; mass spectrum, *m/z* 379, 377 (M^+), 364, 362, 337, 335, 210, 208, 157, 141, 129, 114, 77 (100), 51.

Anal. Calcd for $C_{16}H_{12}NO_3SBr$: C, 50.81; H, 3.20; N, 3.70. Found: C, 50.78; H, 3.24; N, 3.53.

Representative Procedure for Deoxygenation Using $NaBH_4$/TFA.[7b] 3-Ethyl-2-chloro-1-(phenylsulfonyl)indole (6a). To magnetically stirred trifluoroacetic acid (25 mL) at 0 °C was added sodium borohydride (18 mmol, 3 pellets) over 30 min. To this mixture was added dropwise over 30 min a solution of **5a** (0.50 g, 1.50 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred overnight at 25 °C, diluted with H_2O (75 mL), and made basic by the addition of sodium hydroxide pellets at 0 °C. The layers were separated, and the aqueous layer was extracted with additional CH_2Cl_2. The usual workup and flash chromatography using hexanes–CH_2Cl_2 (60:40) afforded 0.35 g (73%) of **6a**: mp 82–83 °C; IR (KBr) 1445, 1385, 1225, 1180, 1090, 980, 755, 680, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 7 H), 2.7 (q, 2 H, J = 7 Hz), 1.1 (t, 3 H, J = 7 Hz); mass spectrum, *m/z* 319 (M^+), 180, 179, 178 (100), 177, 142, 128, 115, 77.

Anal. Calcd for $C_{16}H_{14}NO_2SCl$: C, 60.09; H, 4.41; N, 4.38. Found: C, 60.15; H, 4.43; N, 4.33.

Attempted deoxygenation of **5b** using $NaBH_4$/TFA gave an inseparable mixture of **2a** and **6b** (ca. 60:40 by GC/MS): mass spectrum, *m/z* 365, 363, 224, 222, 204, 143 (100), 128, 115, 101, 77.

Attempted deoxygenation of **5c** using $NaBH_4$/TFA gave only **2a** (75%) after recrystallization from methanol. This sample was identical (IR, ^1H NMR, ^{13}C NMR) with a known sample of **2a**.[7b] The loss of iodine was further confirmed by elemental analysis.

Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.35; H, 5.30; N, 4.91. Found: C, 67.21; H, 5.35; N, 4.92.

5-Bromo-3-ethyl-1-(phenylsulfonyl)indole (6c). A similar reductive deoxygenation of **5d** using $NaBH_4$/TFA afforded **6c** (81%) after crystallization from methanol (one crop): mp 139–141 °C; IR (KBr) 1440, 1370, 1290, 1170, 1115, 990, 810, 725, 690, 635, 610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.0 (m, 9 H), 2.6 (q, 2 H, J = 7.3 Hz), 1.3 (t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 138.0, 134.1, 133.8, 132.8, 129.2, 127.4, 126.6, 124.8, 123.2, 122.3, 116.6, 115.1, 18.0, 13.1; mass spectrum, *m/z* 365, 363 (M^+), 350, 348, 224, 222, 143 (100), 128, 115, 101, 77.

Anal. Calcd for $C_{16}H_{14}NO_2SBr$: C, 52.76; H, 3.87; N, 3.85. Found: C, 52.69; H, 3.85; N, 3.87.

Ethyl 4-[1-(Phenylsulfonyl)-3-indolyl]-4-oxobutanoate (7a). Friedel–Crafts acylation of **3** with ethyl succinyl chloride and aluminum chloride gave **7a** (49%) as a colorless oil after flash chromatography using 1:1 hexanes–CH_2Cl_2: IR (KBr) 1725, 1670, 1535, 1450, 1375, 1190, 1170, 1135, 1085, 990, 750, 725, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.3 (s, 1 H), 8.0–7.2 (m, 9 H), 4.2 (q, 2 H, J = 7 Hz), 3.2 (t, 2 H, J = 6 Hz), 2.8 (t, 2 H, J = 6 Hz), 1.2 (t, 3 H, J = 7 Hz); mass spectrum, *m/z* 385 (M^+), 340, 312, 284 (100), 143, 141, 115, 77. Attempts to obtain material that gave a correct elemental analysis were unsuccessful.

Ethyl 4-[1-(Phenylsulfonyl)-3-indolyl]butanoate (8a). Reductive deoxygenation of **7a** using $NaBH_4$/TFA gave **8a** (85%) as a colorless oil after flash chromatography using 1:1 hexanes–CH_2Cl_2. Crystallization from methanol gave the analytical sample: mp 53–54 °C; IR (KBr) 2970, 2960, 1735, 1445, 1380, 1180, 1140, 1080, 980, 850, 750, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 10 H), 4.2 (q, 2 H, J = 7.5 Hz), 3.4 (t, 2 H, J = 7 Hz), 2.8 (t, 2 H, J = 7 Hz), 2.5–2.2 (m, 2 H), 1.3 (t, 3 H, J = 7.5 Hz); mass spectrum, *m/z* 371 (M^+), 283, 270, 230, 184, 156 (100), 142, 129.

Anal. Calcd for $C_{20}H_{21}NO_4S$: C, 64.67; H, 5.70; N, 3.77. Found: C, 64.65; H, 5.68; N, 3.75.

4-[1-(Phenylsulfonyl)-3-indolyl]butanoic Acid (8b). Reductive deoxygenation of **7b** using $NaBH_4$/TFA gave **8b** (65%) in two crops after crystallization from ether: mp 155–156 °C; IR (KBr) 1690, 1445, 1360, 1180, 1120, 1090, 975, 765, 750, 720, 680, 640, 600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.3–7.2 (m, 10 H), 2.8–1.9 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 178.8, 138.4, 135.7, 133.6, 130.9, 129.2, 126.7, 124.8, 123.2, 123.0, 122.3, 119.5, 113.9, 33.2, 24.1, 23.9; mass spectrum, m/z 343 (M^+), 283, 270, 202, 156, 142, 129, 115, 77 (100).

Anal. Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08. Found: C, 63.23; H, 5.06; N, 4.18.

Reductive Deoxygenation of 3-Acetyl-1-(phenylsulfonyl)indole (1a) Using $NaBH_4$/Methanesulfonic Acid. To a magnetically stirred mixture of **1a** (0.50 g, 1.67 mmol) in methanesulfonic acid (10 mL) at 25 °C was added sodium borohydride (18 mmol, 3 pellets), and the reaction was stirred overnight. H_2O (75 mL) was added, and the mixture was made basic by the slow addition of sodium hydroxide pellets. The layers were separated, and the aqueous layer was extracted with additional CH_2Cl_2. The usual workup afforded light tan crystals, which were recrystallized from methanol to afford 0.43 g (90%) of **2a** after three crops: mp 118–119 °C (lit.[7b] mp 121–122 °C), which was identical (IR, ^1H NMR) with a sample previously prepared in these laboratories.

Reductive Deoxygenation of 3-Acetyl-1-(phenylsulfonyl)indole (1a) Using $NaBH_4$/Methanesulfonic Acid/Acetic Acid. To a magnetically stirred mixture of acetic acid (20 mL) and methanesulfonic acid (5 mL) at 25 °C was added sodium borohydride (18 mmol, 3 pellets) over 30 min. To this mixture was added dropwise over 30 min a solution of **1a** (0.40 g, 1.34 mmol) in acetic acid (15 mL). The mixture was stirred overnight at 25 °C, diluted with H_2O (75 mL), and made basic by the addition of sodium hydroxide pellets at 0 °C. The layers were separated, and the aqueous layer was extracted with additional CH_2Cl_2. The usual workup and flash chromatography using hexanes–CH_2Cl_2 (60:40) afforded 0.36 g (66%) of **2a**: mp 118–119 °C (lit.[7b] mp 121–122 °C), identical (IR, ^1H NMR) with a known sample.

Reductive Deoxygenation of 3-Acetyl-1-(phenylsulfonyl)indole (1a) Using $NaBH_4$/$AlCl_3$.[36] To a magnetically stirred mixture of $NaBH_4$ (2 pellets, 12 mmol) and $AlCl_3$ (1.33 g, 10.0 mmol) in THF (250 mL) was added a solution of **1a** (0.50 g, 1.67 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred overnight, H_2O (50 mL) was added, and the solution was extracted with EtOAc. The combined organic layers were washed with brine, dried (K_2CO_3), and evaporated. Flash chromatography of the residue with 4:1 hexane–CH_2Cl_2 afforded 0.32 g (67%) of **2a**: mp 121–122 °C (lit.[7b] mp 121–122 °C), identical (IR, ^1H NMR) with a known sample.

One-Pot Synthesis of 3-Ethyl-1-(phenylsulfonyl)indole (2a) from 1-(Phenylsulfonyl)indole (3). To a magnetically stirred suspension of $AlCl_3$ (3.10 g, 23.0 mmol) in CH_2Cl_2 (100 mL) at 25 °C was added acetic anhydride (1.1 mL, 12 mmol), and the mixture was stirred for 15 min. A solution of **3** (1.00 g, 3.90 mmol) in CH_2Cl_2 (50 mL) was added, and the mixture was stirred for 2 h at 25 °C. Borane–*tert*-butylamine complex (1.00 g, 11.7 mmol) was added, and the mixture was allowed to stir overnight. The reaction was then quenched by the slow addition of crushed ice and made basic by the addition of sodium hydroxide pellets. The aqueous layer was extracted with additional CH_2Cl_2, and the combined organic layers were washed with brine, dried (K_2CO_3), and evaporated. Crystallization from methanol afforded 1.00 g (90%) of **2a** after two crops, identical with a known sample by spectral analysis.

Representative Procedure for Reductive Deoxygenation Using Borane–*tert*-Butylamine Complex and Aluminum Chloride.[37] 3-Methyl-1-(phenylsulfonyl)indole (12). To a magnetically stirred mixture of $AlCl_3$ (1.40 g, 10.5 mmol) and borane–*tert*-butylamine complex (0.91 g, 10.5 mmol) in CH_2Cl_2 (50 mL) was added a solution of 3-formyl-1-(phenylsulfonyl)indole (**11**) (1.00 g, 3.5 mmol) in CH_2Cl_2 (30 mL). The mixture was stirred overnight, crushed ice was added, and the aqueous layer was made basic by the addition of sodium hydroxide pellets. The usual workup afforded a crude residue, which was submitted to flash chromatography using hexanes–CH_2Cl_2 (60:40) to afford 0.42 g (44%) of **12**: mp 119–121 °C (lit.[4a] mp 117–118.5 °C); IR (KBr) 3315, 1605, 1580, 1450, 1375, 1270, 1170, 1115, 1060, 970, 765, 666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.2 (m, 10 H), 3.3 (s, 3 H); mass spectrum, m/z 271 (M^+), 141, 130, 103, 102, 77 (100), 63, 51.

Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16. Found: C, 66.48; H, 4.80; N, 5.03.

Friedel–Crafts Acylation of 3-Bromo-1-(phenylsulfonyl)indole (13). Friedel–Crafts acylation of **13** using propionic anhydride in the presence of aluminum chloride gave **1b** (66%) after treatment with charcoal and recrystallization from ether/hexanes (two crops): mp 136–138 °C (lit.[7b] mp 143–144 °C). This sample was identical (IR, MS, ^1H NMR) with a known sample.

Similarly, acylation of **13** with acetic anhydride provided **1a** (24%) after treatment with charcoal and recrystallization from methanol (one crop): mp 133–135 °C (lit.[7b] mp 159–160 °C). This sample was identical (IR, ^1H NMR) with a known sample.

1-(Phenylsulfonyl)-2-(trimethylsilyl)indole (14a). Use of the same procedure as described earlier for the LDA-promoted deprotonation of **3**, but by quenching with trimethylsilyl chloride, gave a colorless oil. Crystallization from methanol afforded **14** (78%) after four crops: mp 76–78 °C (lit.[40] mp 65–67 °C); IR (KBr) 3050, 2940, 2890, 1360, 1245, 1225, 1170, 1130, 900, 845, 825, 750, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0–7.0 (m, 10 H), 6.8 (s, 1 H), 0.5 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 142.9, 139.2, 138.6, 133.3, 130.7, 129.0, 126.2, 124.9, 123.2, 121.8, 121.0, 114.0, 0.5; mass spectrum, m/z 329 (M^+), 314 (100), 250, 189, 173, 158, 130, 115, 77.

Anal. Calcd for $C_{17}H_{19}NO_2SSi$: C, 61.97; H, 5.81; N, 4.25. Found: C, 61.98; H, 5.88; N, 4.17.

5-Bromo-2-(trimethylsilyl)-1-(phenylsulfonyl)indole (14b). Deprotonation of **4d** with LDA as described earlier, followed by quenching with trimethylsilyl chloride, afforded **14b** (82%) as a colorless semisolid: IR (KBr) 2940, 2890, 1500, 1445, 1435, 1365, 1245, 1225, 1190, 1165, 1135, 1115, 1090, 1040, 850, 755, 725, 695, 670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.9–7.2 (m, 9 H), 6.8 (s, 1 H), 0.5 (s, 9 H); mass spectrum, m/z 409, 407 (M^+), 394, 392 (100), 301, 299, 267, 187, 167, 77.

Anal. Calcd for $C_{17}H_{18}NO_2SSiBr$: C, 50.00; H, 4.44; N, 3.43. Found: C, 50.10; H, 4.60; N, 3.45.

2-Acetyl-1-(phenylsulfonyl)indole (15a). Use of the same procedure as described earlier for a Friedel–Crafts acylation but with **14a** and acetic anhydride gave a light tan solid, which upon crystallization from methanol afforded **15a** (86%) after three crops: mp 89–90 °C (lit.[5c] mp 89–90 °C); IR (KBr) 1675, 1530, 1440, 1360, 1260, 1180, 1170, 830, 750, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.3 (m, 9 H), 7.1 (s, 1 H), 2.6 (s, 3 H); mass spectrum, m/z 299 (M^+), 284, 235, 220, 158, 141, 130, 115, 77 (100).

Anal. Calcd for $C_{16}H_{13}NO_3S$: C, 64.20; H, 4.38; N, 4.68. Found: C, 64.45; H, 4.32; N, 4.72.

2-Propionyl-1-(phenylsulfonyl)indole (15b). Use of the same procedure as described earlier for a Friedel–Crafts acylation but with **14a** and propionic anhydride gave a colorless solid, which upon crystallization from methanol afforded **15b** (70%) (two crops): mp 135–137 °C; IR (KBr) 1680, 1380, 1170, 1090, 730, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.1 (m, 10 H), 7.0 (s, 1 H), 3.0 (q, 2 H, J = 7 Hz), 1.2 (t, 3 H, J = 7 Hz); mass spectrum, m/z 313 (M^+), 284 (100), 220, 144, 115, 89, 77, 51.

Anal. Calcd for $C_{17}H_{15}NO_3S$: C, 65.16; H, 4.82; N, 4.47. Found: C, 65.16; H, 4.72; N, 4.46.

2-Acetyl-5-bromo-1-(phenylsulfonyl)indole (15c). Use of the same procedure as described earlier for Friedel–Crafts acylation but with **14b** gave a tan solid, which upon crystallization from methanol afforded **15c** (67%) (one crop): mp 157–158 °C; IR (KBr) 1665, 1530, 1445, 1365, 1330, 1265, 1225, 1190, 1090, 790, 755, 725, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.1–7.2 (m, 8 H), 7.0 (s, 1 H), 2.6 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 191.3, 140.8, 138.1, 137.4, 134.0, 130.4, 130.1, 128.9, 127.3, 125.2, 117.7, 117.2, 115.6, 29.7; mass spectrum, m/z 379, 377 (M^+), 337, 335, 315, 313, 300, 298, 223, 221, 210, 208, 141, 129, 114, 77 (100), 51.

Anal. Calcd for $C_{16}H_{12}NO_3SBr$: C, 50.81; H, 3.20; N, 3.70. Found: C, 50.49; H, 3.19; N, 3.69.

2-Ethyl-1-(phenylsulfonyl)indole (16a). The same procedure as described earlier for deoxygenation using borane–*tert*-butylamine complex and $AlCl_3$ with **15a** gave **16a** (71%) after recrystallization from methanol (two crops): mp 78–80 °C; IR (KBr) 2970, 1450, 1370, 1225, 1170, 1145, 1095, 820, 780, 725, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 10 H), 6.4 (s, 1 H), 3.0 (q, 2 H,

J = 7 Hz), 1.4 (t, 3 H, J = 7 Hz); mass spectrum, m/z 285 (M^+), 206, 160, 143 (100), 128, 115, 102, 89, 77.

Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.35; H, 5.30; N, 4.91. Found: C, 67.34; H, 5.40; N, 4.84.

2-Propyl-1-(phenylsulfonyl)indole (16b). The same procedure as described earlier for deoxygenation using borane–*tert*-butylamine complex and $AlCl_3$ with **15b** gave **16b** (75%) after recrystallization from methanol (two crops): mp 111–113 °C; IR (KBr) 1595, 1450, 1360, 1160, 810, 760, 730, 680, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.3–7.1 (m, 10 H), 6.4 (s, 1 H), 3.0 (t, 2 H, J = 7 Hz), 2.0–1.5 (m, 2 H), 1.1 (t, 3 H, J = Hz); mass spectrum, m/z 299 (M^+), 270, 206, 157, 143, 130 (100), 117, 103, 89, 77.

Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.18; H, 5.66; N, 4.66.

5-Bromo-2-ethyl-1-(phenylsulfonyl)indole (16c). One-Pot Procedure from 14b. The same procedure as described earlier for acylation–reductive deoxygenation using borane–*tert*-butylamine complex and $AlCl_3$ with **14b** gave **16c** (67%) after flash chromatography using hexanes–CH_2Cl_2 (60:40): mp 115–117 °C; IR (KBr) 1445, 1370, 1225, 1200, 1170, 1145, 1095, 1060, 870, 850, 805, 730, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.1 (m, 8 H), 6.4 (s, 1 H), 3.0 (q, 2 H, J = 7 Hz), 1.4 (t, 3 H, J = 7 Hz).

Anal. Calcd for $C_{16}H_{14}NO_2SBr$: C, 52.76; H, 3.87; N, 3.85. Found: C, 52.64; H, 3.78; N, 3.88.

5-Propionyl-1-(phenylsulfonyl)indoline (18b). The same procedure as described earlier for Friedel–Crafts acylation but with **17** and propionic anhydride gave **18b** (60%) after recrystallization from methanol (two crops): mp 115–120 °C; IR (KBr) 1670, 1360, 1240, 1170, 1105, 980, 745, 690, 605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.8–7.2 (m, 8 H), 4.0 (t, 2 H, J = 7.5 Hz), 3.0 (t, 4 H, J = 7.5 Hz, two CH_2 groups superimposed), 1.2 (t, 3 H, J = 7.5 Hz); mass spectrum, m/z 315 (M^+), 286 (100), 174, 145, 117, 89, 77.

Anal. Calcd for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44. Found: C, 64.92; H, 5.44; N, 4.49.

5-Ethyl-1-(phenylsulfonyl)indoline (19a). The same procedure as described earlier for deoxygenation using borane–*tert*-butylamine complex and $AlCl_3$ with **18a** gave **19a** (94%): mp 70–71 °C (lit.[33] mp 70–71 °C); IR (KBr) 1485, 1445, 1350, 1165, 980, 840, 690, 620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.8–6.9 (m, 8 H), 3.9 (t, 2 H, J = 8 Hz), 2.8 (t, 2 H, J = 8 Hz), 2.5 (q, 2 H, J = 7.5 Hz), 1.2 (t, 2 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 140.0, 139.6, 137.0, 132.9, 131.9, 128.7, 127.2, 127.0, 124.5, 114.9, 50.1, 28.2, 27.8, 15.6; mass spectrum, m/z 287 (M^+), 272, 146 (100), 141, 130, 118, 103, 91, 77. This sample was identical (mp, IR, ^1H NMR) with a sample previously prepared from **18a** and $NaBH_4$/TFA.

Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.95; H, 6.09; N, 4.90.

5-Propyl-1-(phenylsulfonyl)indoline (19b). The same procedure as described earlier for deoxygenation using borane–*tert*-butylamine complex and $AlCl_3$ with **18b** gave **19b** (90%). Recrystallization from methanol afforded the analytical sample: mp 72–74 °C; IR (KBr) 2960, 1490, 1350, 1160, 1090, 1050, 975, 820, 670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.9–6.9 (m, 8 H), 3.9 (t, 2 H, J = 8 Hz), 3.0–2.2 (m, 4 H), 1.8–1.4 (m, 2 H), 0.9 (t, 3 H, J = 7 Hz); mass spectrum, m/z 301 (M^+), 272, 160, 130, 118 (100), 105, 91, 77.

Anal. Calcd for $C_{17}H_{19}NO_2S$: C, 67.75; H, 6.35; N, 4.65. Found: C, 67.71; H, 6.23; N, 4.63.

5-Propyl-1-(phenylsulfonyl)indole (20b). To a magnetically stirred suspension of manganese(III) acetate dihydrate (0.60 g, 2.2 mmol) in acetic acid (10 mL) at 110 °C was added **19b** (0.17 g, 0.56 mmol). The mixture was stirred for 6 h, allowed to cool to room temperature, and filtered. The solid precipitate (presumably Mn(II) acetate) was washed with acetone, and the combined filtrate and washings were evaporated in vacuo and submitted to flash chromatography using hexanes–CH_2Cl_2 (60:40) to afford 0.10 g (60%) of **20b** as a colorless oil: IR (neat) 2960, 2930, 2870, 1560, 1462, 1390, 1265, 1225, 1095, 995, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0–7.0 (m, 10 H), 6.7 (d, 1 H, J = 3 Hz), 2.7 (t, 2 H, J = 7 Hz), 1.6 (m, 2 H), 0.9 (t, 3 H, J = 7 Hz); mass spectrum, m/z 299 (M^+), 270, 158, 143, 129, 116, 102, 77 (100).

Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.28; H, 5.63; N, 4.61.

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Substituent-Dependent Competition between 1,5- and 1,5′-Cyclization of Vinyl Azides. 1,2,3-Triazoles and 4,5-Dihydro-1*H*-tetrazol-5-ylidenes from Methyl 3,3-Diazido-2-cyanoacrylate with Amines[1]

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Reaction of methyl 3,3-diazido-2-cyanoacrylate (1) with amines **2** leads to vinyl azides **4a–g**, with **4a–d** being remarkably stable. Among these, the *di*alkylamino-substituted vinyl azides **4a,b** undergo 1,5 ring closure and give via 4*H*-1,2,3-triazoles **5a,b** 2-(methoxycarbonyl)-1,2,3-triazoles **6a,b**. On the contrary, vinyl azides **4c,d** with *mono*alkylamino substituents in the 4-position in the presence of equivalent amounts of triethylamine undergo 1,5′ ring closure to afford tetrazolyl triethylammonium salts **7c,d**. Treatment of **7c,d** with hydrochloric acid yields 4,5-dihydro-1*H*-tetrazol-5-ylidenes **8c,d**. The vinyl azides **4e–g** in situ generated from 1 and primary/tertiary diamines **2e–g** undergo self-induced 1,5′ ring closure to give tetrazolyl ammonium betaines **9e–g**. Reaction of vinyl diazide 1 with bis primary 1,ω-diamines **10** yields crystalline bis vinyl azides **11**. Triethylamine-induced 1,5′ ring closure of **11** produces the bis tetrazolyl ammonium salts **12**.

Acyl azides exist exclusively in the open-chain azide form,[2,3] whereas thioacyl azides cyclize to give 1,2,3,4-thiatriazoles.[2,4]

In the case of imino azides, electron-accepting substit-

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