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Synthesis of 3-[(1-Aryl)aminomethyl]indoles

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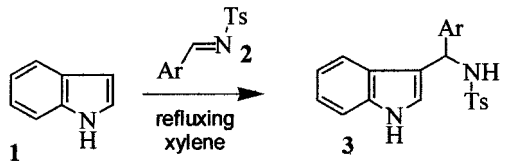
Abstract: We report the novel synthesis of various highly functionalized 3-arylaminomethyl indoles. This synthetic approach makes use of the directing ability of a bulky *tert*-butyldimethylsilyl-protecting group, which directs the condensation of an array of aromatic tosylaldimines specifically into the 3-position of the indole nucleus. The reactions, which occur under relatively mild conditions, afford the desired products in moderate yields. Prior to selective cleavage of the protecting group, the functionalized protected indoles also serve as attractive substrates for many future organic transformations.

There is an increasing interest in indoles possessing substituents in the 3-position due to their numerous biological activities.[1] A variety of methods have been reported for the preparation of 3-substituted indoles.[2] Of these, the Mannich[3] and Vilsmeier−Haack[4] synthesis are used most extensively; however, transforming the resulting adducts into indoles containing functionalized aromatic substituents requires several additional steps. Likewise, the extension of the Vilsmeier−Haack reaction to form long acyl chain derivatives usually proceeds in low yields.[5]

Other less widely used methods for the 3-substitution of indole have also been reported. Treatment of indole with various isocyanates is reported to afford 3-amidoindoles, a method attempted with a limited array of substrates.[6] Reaction of indole with lactams has been reported to generate 3-(iminyl)indoles, which can be hydrolyzed to generate ω-aminoacyl groups.[7] Recently, there have been reports of successful acylation of the 3-position of indole employing weakly activating Lewis acids.[8] Base-promoted substitutions in the 3-position have also been noted; however, the addition of functionalized substrates were not reported.[5,9]

SCHEME 1



Ar = (a) Ph, (b) *p*-MeOPh, (c) *p*-ClPh

Various 3-aminomethylindole derivatives have been synthesized, but those without substituents on the methylene bridge are reported to be intrinsically unstable.[10] Therefore, we sought to find a method for direct synthesis of the aromatic substituted 3-aminomethylindoles. By employing previously synthesized functionalized substituted aromatic *N*-tosylaldimines,[11] a class of compound that should easily condense with the indole, we planned to introduce the desired functionality in one simple step. Direct treatment of indole (**1**) with (**2a**−**c**) in refluxing xylene resulted in the expected 3-substituted product (**3a**−**c**), but in only trace amounts (<8%) (Scheme 1). Unreacted indole, hydrolyzed aldimine, and unidentifiable tars were found in the reaction mixtures upon workup.

Consequently, an examination of indole protecting groups was made. Indoles possessing a sulfonyl protecting group in the 1-position are reported to direct lithiation to the 2-position.[12] Even at −78 °C, 3-lithio-1-phenylsulfonyl indole rearranges to the more stable 2-lithio species as was originally observed by Gribble and Saulnier.[13] This rearrangement was reported to be circumvented by cooling the 3-lithio species to −100 °C, a result that we were unable to reproduce after several attempts.

The use of bulky silyl protecting groups was reported to give good yields when introducing various alkyl and organometallic substituents into the 3-position of the indole ring.[14,15] Rearrangement, as described above, is

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SCHEME 2

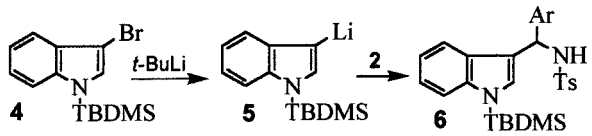
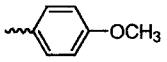
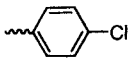
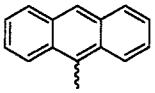
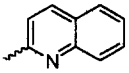
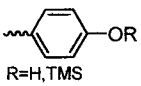


TABLE 1. Yields of Compound 6

entry		(2) Ar =	product	time (h)	yield (%)
1	**a**		**6a**	12	63
2	**b**		**6b**	16	73
3	**c**		**6c**	12	24
4	**d**		**6d**	16	63
5	**e**		**6e**	18	64
6	**f**		**6f**	16	47
7	**g**		**6g**	13	49
8	**h**		**6h**	12	31
9	**i**		**6i**	12	15
10	**j**		**6j**	14	20
11	**k**		**6k**	14	NR

reported to be circumvented through the use of either a *tert*-butyldimethylsilyl (TBDMS) or diisopropylsilyl (TIPS) protecting group. In our laboratory, the 3-bromo-1-TBDMS-indole (**4**) was prepared in an 83% yield using a procedure described by Bosch and co-workers.[15] The 3-lithio-1-TBDMS-indole (**5**) was prepared from **4** (Scheme 2).

Treatment of **5** with a variety of aromatic tosylaldimines (**2a**−**j**), afforded the corresponding 3-substituted 1-TBDMS-indoles (**6a**−**j**), respectively (Table 1). No rearrangement during product formation, to the undesired 2-substituted isomer, was detected. The majority of the

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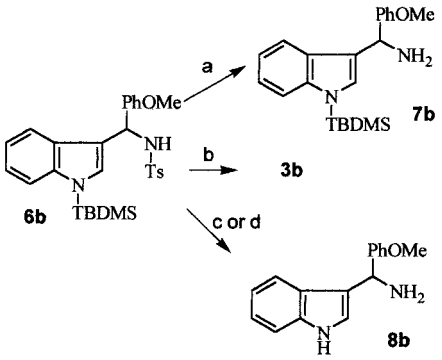
SCHEME 3[a]



[a] Key: (a) 1 equiv of NaOH, THF, cat. Bu_4NBr, rt; (b) 1 equiv of TBAF, THF, rt, 0.5 h; (c) excess NaOH, cat. Bu_4NBr, THF, reflux, 4 h; (d) 6 equiv of TBAF, THF, 100 °C, 6 h.

entries 1−2 and 4−7 afforded moderate yields. The low yield obtained for entry 3 was ascribed to partial lithium halogen exchange, which occurred in competition with the condensation. When **2c** was increased 2-fold, product formation remained constant. Likewise, for entries 8−10, neither increasing the amount of **2h**−**j** nor heating the reaction mixture to reflux for 2 h had a positive effect on product formation.

Since aldimines with acidic protons such as **2k** (R = H) are not expected to react employing this method, a TMS-protected phenol was envisioned **2k** (R = TMS). However, this aldimine was unobtainable because silyl cleavage resulted during its formation. Reaction of the already formed **2k** (R = H) with TMSCl also resulted in no product formation. When other silyl protecting groups were employed, alternative problems resulted that interfered with the selective removal of the silyl-protecting functionalities later in the synthetic scheme.

Selective deprotection methods for compound **6**, which possesses protecting groups on both nitrogens, were developed. Selective cleavage of the protecting groups as shown for **6b** was found to be possible (Scheme 3). The silyl-protecting group was selectively cleaved in quantitative yields using an equimolar solution of TBAF at room temperature to afford **3b**. Selective detosylation of **6b** was achieved through treatment with 1 equiv of NaOH and a catalytic amount of phase-transfer catalyst. Refluxing of **6b** with an excess of sodium hydroxide, under phase-transfer conditions, afforded quantitative cleavage of both the silyl group and the tosyl group to form **8b**. Deprotection of **6b** to afford **8b** also can be achieved by treatment with 6 equiv of TBAF at 100 °C.

In summary, this novel synthetic approach allows for the easy introduction of a variety of aryl-functionalized substituents into the 3-position of indole while allowing one to easily vary the aromatic functionality by a pathway that would normally be attainable only with additional steps. The overall three-step synthesis, as described, generally produces the 3-aminomethyl indoles in approximately 50% yields.

Experimental Section

General Methods. THF was distilled from Na/benzophenone immediately prior to use. CH_2Cl_2 was distilled from calcium hydride under nitrogen. Moisture-sensitive reactions were con-

ducted in oven-dried glassware under a nitrogen atmosphere. Analytical thin-layer chromatography was performed on precoated silica gel sheets, and flash column chromatography was accomplished using silica gel, 60 Å (200−400 mesh). External elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA 30091. All melting points are uncorrected. Unless otherwise noted, ^{1}H and ^{13}C NMR spectra were taken in $CDCl_3$ at 300 and 75 MHz respectively, with a TMS internal standard. Chemical shifts are reported in units downfield from TMS. Coupling constants, *J*, are reported in hertz (Hz).

3-Bromo-1-(*tert*-butyldimethylsilanyl)-1*H*-indole (4). Synthesis was performed according to a modified literature report of Bosch and co-workers.[15] To a solution of indole (4.00 g, 34.00 mmol) in 140 mL of freshly distilled THF at −78 °C was added dropwise a solution of *n*-BuLi (23.4 mL, 37.00 mmol, 1.6 M hexane solution) in a two-neck half-jacketed round-bottomed flask equipped with a stir bar and a positive flow of nitrogen. The temperature was raised to −10 °C over a 15 min period. After being stirred at −10 °C for 30 min, the reaction mixture was cooled to −50 °C and a solution of TBDMSCl (5.80 g, 38 mmol) in 30 mL of freshly distilled THF was added. After the mixture was stirred at −10 °C for 3 h, the temperature was once again lowered to −78 °C, and NBS (6.00 g, 34 mmol) was added to the reaction mixture. The reaction mixture was stirred at −50 °C for 4 h before the temperature was allowed to rise slowly to rt. Hexane (100 mL) and pyridine (1 mL) were added, and the resulting suspension was removed by filtration through a pad of Celite. The filtrate was evaporated *in vacuo*; however, extreme caution was taken not to heat the mixture above ∼65 °C, at which point decomposition occurred. The crude mixture was immediately purified by flash chromatography over silica gel using hexane/CH_2Cl_2 in a 6:1 ratio affording 8.71 g (28.07 mmol) of the desired product, an 83% yield. Spectroscopic data corresponds with that reported in the literature.[15]

General Procedure. Preparation 6a−j from 4. To a stirred solution of 3-bromo-1-(*tert*-butyldimethylsilyl)indole (**4**) (0.5 g, 1.6 mmol) in freshly distilled THF (15 mL), cooled to −78 °C, was added a solution of *t*-BuLi (2.1 mL of a 1.7 M solution in pentane, 3.6 mmol). The mixture was allowed to stir for 15 min before the rapid addition of 1.1 equiv of the corresponding tosylaldimine (**2**) (1.7 mmol) in 30 mL of freshly distilled THF. The solution was allowed to stir at rt for 12−18 h. The reaction mixture was quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layer was washed with H_2O (2 × 15 mL) and dried over $MgSO_4$. The resulting organic layer was concentrated with the aid of a rotary evaporator to afford a brown, viscous oil. Purification using flash column chromatography employing silica gel and a solvent system of EtOAc/hexanes (1:4) afforded compounds **6a**−**j**, respectively, in approximately 50% yields.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]phenylmethyl]-4-methylbenzenesulfonamide (6a):** mp = 114−116 °C; IR (neat) 3341, 3240, 2947, 2854, 1451, 1306, 1156, 1093, 984, 907, 839, 813, 787, 741 cm^{-1}; ^{1}H NMR δ 7.82 (d, J = 6, 2H), 7.62 (d, J = 6, 1H), 7.52 (d, J = 6, 1H), 7.41 (d, J = 6, 1H), 7.34 (d, J = 6, 2H), 7.20−7.25 (m, 2H), 7.10−7.19 (m, 3H), 6.62 (d, J = 3, 1H), 6.58 (s, 1H), 4.73 (s, 1H), 2.44 (s, 3H), 0.93 (s, 9H), 0.60 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.66, 140.99, 139.05, 131.33, 130.96, 129.73, 128.29, 126.49, 124.07, 121.98, 120.60, 119.75, 113.86, 110.98, 104.74, 102.66, 52.92, 26.34, 26.27, 21.53, 19.50. Anal. Calcd for $C_{28}H_{34}N_2O_2SSi$: C, 68.53; H, 6.98; N, 5.71. Found: C, 68.22; H, 7.11; N, 5.32.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl](4-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (6b):** mp = 155−156 °C; IR (neat) 3404, 3279, 2947, 2854, 1607, 1509, 1451, 1317, 1254, 1156, 1093, 1029, 965 cm^{-1}; ^{1}H NMR δ 7.56 (d, J = 9, 2H), 7.41 (d, J = 9, 1H), 7.18−7.08 (m, 6H), 6.96 (t, J = 9, 1H), 6.76 (s, 1H), 6.73 (d, J = 9, 2H), 5.79 (d, J = 6, 1H), 4.96 (d, J = 6, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 0.86 (s, 9H), 0.50 (s, 6H). ^{13}C NMR δ 158.88, 141.85, 137.67, 132.60, 130.02, 129.20, 128.61, 128.46 (overlapping peak), 127.16, 121.83, 120.87, 119.83, 119.37, 118.01, 114.04, 113.69, 55.66, 55.08, 26.65, 21.87, 19.77. Anal. Calcd for $C_{29}H_{36}N_2O_3SSi$: C, 66.89; H, 6.97; N, 5.38. Found: C, 66.54; H, 6.67; N, 5.01.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]-(4-chlorophenyl)methyl]-4-methylbenzenesulfonamide (6c):** mp = 135−137 °C; IR (neat) 3269, 3051, 2954, 2928, 2853, 1597, 1493, 1451, 1321, 1259, 1160, 1093, 1041, 1016, 969, 927, 839, 813, 740, 667 cm^{-1}; ^{1}H NMR δ 7.56 (d, J = 6, 2H), 7.41 (d, J = 9, 1H), 7.21 (d, J = 9, 2H), 7.17−7.14 (m, 4H), 7.11 (d, J = 6, 2H), 6.61 (s, 1H), 5.79 (d, J = 9, 1H), 5.08 (d, J = 9, N−H), 2.05 (s, 3H), 0.88 (s, 9H), 0.47 (s, 6H); ^{13}C NMR δ 143.35, 142.02, 139.20, 137.65, 133.36, 130.24, 129.52, 128.89, 128.63, 128.59, 127.36, 122.29, 120.27, 119.33, 117.60, 114.37, 54.67, 26.39, 26.53, 21.68, 19.53. Anal. Calcd for $C_{28}H_{33}ClN_2O_2SSi$: C, 64.04; H, 6.33; N, 5.33. Found: C, 63.81; H, 6.13; N, 5.71.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]pyridin-2-ylmethyl]-4-methylbenzenesulfonamide (6d):** oil; IR (neat) 3466, 3414, 3051, 2958, 2907, 2864, 1618, 1462, 1410, 1394, 1363, 1332, 1265, 1099, 1010, 808, 735, 704 cm^{-1}; ^{1}H NMR δ 8.62 (m, 1H), 7.95 (d, J = 6, 1H), 7.74−7.71 (m, 1H), 7.64 (d, J = 6, 2H), 7.32 (d, J = 6, 3H), 7.21−7.16 (m, 2H), 6.94−6.41 (m, 2H), 6.77 (t, J = 8, 1H), 5.80 (d, J = 4, 1H), 4.72 (bs, 1H), 2.43 (s, 3H), 0.93 (s, 9H), 0.60 (s, 6H); ^{13}C NMR δ 174.44, 153.24, 149.10, 148.30, 144.65, 137.29, 136.95, 135.40, 128.74, 128.60, 127.08, 126.97, 126.47, 123.12, 122.57, 122.21, 119.83, 68.43, 62.04, 54.91, 47.83, 21.68. Anal. Calcd for $C_{27}H_{33}N_3O_2SSi$: C, 65.95; H, 6.76; N, 8.55. Found: C, 65.63; H, 6.92; N, 8.81.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl](2-trifluoromethylphenyl)methyl]-4-methylbenzenesulfonamide (6e):** mp = 199−202 °C; IR (neat) 3436, 3281, 1642, 1599, 1450, 1306, 1258, 1156, 1119, 1093, 1034, 965 cm^{-1}; ^{1}H NMR δ 7.82 (t, J = 9, 1H), 6.70 (d, J = 9, 2H), 7.61 (d, J = 9, 1H), 7.50 (t, J = 9, 1H), 7.38−7.32 (m, 2H), 7.25 (d, J = 9, 2H), 7.12 (t, J = 8.5, 1H), 6.96−6.93 (m, 2H), 6.27 (s, 1H), 6.17 (d, J = 6, 1H), 4.97 (d, J = 6, 1H), 2.43 (s, 3H), 0.77 (s, 9H), 0.41 (s, 6H); ^{13}C NMR δ 143.45, 141.64, 139.41, 136.84, 131.64, 130.83, 129.70, 129.52, 128.99, 128.33, 127.48, 127.21, 126.45, 125.99, 122.13, 120.10, 118.53, 117.85, 114.06, 50.55, 29.69, 26.09, 21.49, 19.23. Anal. Calcd for $C_{29}H_{33}F_3N_2O_2SSi$: C, 62.34; H, 5.95; N, 5.01. Found: C, 62.74; H, 6.12; N, 4.78.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]thiophen-2-ylmethyl]-4-methylbenzenesulfonamide (6f):** mp = 152−154 °C; IR 3259, 3051, 2926, 2854, 1597, 1550, 1451, 1327, 1259, 1156, 1088, 1026, 964, 922, 839, 808, 787, 741, 704, 668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 9, 2H), 7.41 (d, J = 9, 2H), 7.27−7.24 (m, 1H), 7.17−7.14 (m, 1H), 7.12−7.08 (m, 2H), 7.02 (t, J = 6, 1H), 6.86−6.84 (m, 3H), 6.09 (d, J = 9, 1H), 5.11 (d, J = 6, 1NH), 2.35 (s, 3H), 0.87 (s, 9H), 0.52 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.76, 151.80, 145.10, 141.74, 137.53, 129.87, 129.19, 128.34, 127.12, 126.59, 125.28, 121.94, 119.97, 119.31, 117.47, 114.10, 110.97, 51.29, 26.20, 21.77, 19.35. Anal. Calcd for $C_{26}H_{32}N_2O_2S_2Si$: C, 62.86; H, 6.49; N, 5.64. Found: C, 62.97; H, 6.21; N, 5.83.

***N*-[Anthracen-9-yl-[1-(*tert*-butyldimethylsilanyl)-1*H*-indol-3-yl]methyl]-4-methylbenzenesulfonamide (6g):** mp = 158−161 °C; IR (neat) 3240, 3051, 2947, 2916, 2854, 1659, 1602, 1550, 1519, 1451, 1420, 1259, 1218, 1157, 1088, 1057, 1010, 964, 886, 894, 808, 730, 668 cm^{-1}; ^{1}H NMR δ 8.84 (s, 1H), 8.78 (s, 1H), 8.49 (s, 1H), 8.35 (d, J = 6, 4H), 8.03 (d, J = 6, 4H), 7.80 (d, J = 9, 2H), 7.57−7.48 (m, 6H), 7.31 (d, J = 9, 2H), 7.23 (s, 1H), 7.17, (s, 1H), 6.79 (d, J = 6, 1H), 4.69 (bs, 1H), 2.42, (s, 3H), 0.92 (s, 6H), 0.59 (s, 6H); ^{13}C NMR δ 145.08, 142.67, 142.17, 142.16, 141.57, 137.49, 129.21, 129.04, 129.03, 128.03, 127.93, 127.59, 126.95, 125.88 (overlapping peaks), 124.60, 119.24, 117.38, 113.93, 60.79, 51.11, 26.25, 21.42, 13.53. Anal. Calcd for $C_{36}H_{38}N_2O_2SSi$: C, 73.18; H, 6.48; N, 4.74. Found: C, 72.89; H, 6.47; N, 4.53.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl](2-nitrophenyl)methyl]-4-methylbenzenesulfonamide (6h):** mp = 219−220 °C; IR (neat) 3286, 3259, 2948, 2843, 1524, 1450, 1489, 1348, 1260, 1157, 1090, 1039, 1024, 962, 920, 839, 813, 787 cm^{-1}; ^{1}H NMR δ 8.10 (d, J = 9, 1H), 7.83 (d, J = 9, 1H), 7.74, (d, J = 12, 2H), 7.65 (t, J = 6, 1H), 7.45−7.36 (m, 2H), 7.29 (d, J = 9, 2H), 7.10 (t, J = 6, 1H), 6.91 (t, J = 6, 1H), 6.78 (d, J = 6, 1H), 6.51 (d, J = 6, 1H), 6.45 (s, 1H), 5.15 (d, J = 6, 1H), 2.45 (s, 3H), 0.81 (s, 9H), 0.45 (s, 6H); ^{13}C NMR δ 136.08, 132.93, 130.23, 130.22, 129.76 (overlapping peaks), 128.30, 127.83, 127.47,

125.01, 123.32, 122.15, 120.15, 118.42 (overlapping peaks), 51.25, 30.94, 26.14, 21.55, 19.27. Anal. Calcd for $C_{28}H_{33}N_3O_4SSi$: C, 62.77; H, 6.21; N, 7.84. Found: C, 62.54; H, 5.87; N, 8.02.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]furan-2-ylmethyl]-4-methylbenzenesulfonamide (6i):** semisolid; IR (neat) 3259, 2916, 2843, 1446, 1327, 1259, 1161, 1155, 1088, 1021, 964, 839, 808, 787, 741 cm^{-1}; ^1H NMR δ 7.94 (s, 1H), 7.73, (d, J = 9, 1H), 7.45 (d, J = 9, 2H), 7.33−7.25 (m, 2H), 7.16−7.08 (m, 2H), 7.00 (t, J = 6, 2H), 6.91 (s, 1H), 6.85 (d, J = 3, 1H), 6.27 (q, J = 3, 1H), 6.03 (d, J = 3, 1H), 5.91 (s, 1H), 5.33 (d, J = 6, 1H), 2.32 (s, 3H), 1.39 (s, 9H), 0.88 (s, 6H); ^{13}C NMR δ 157.05, 141.22, 136.53, 129.41, 126.78, 122.99, 121.96 (overlapping peaks), 119.36, 117.25, 111.07, 110.11 (overlapping peaks), 106.59, 53.92, 34.10, 29.68, 29.60, 22.68, 15.31. Anal. Calcd for $C_{26}H_{32}N_2O_3SSi$: C, 64.96; H, 6.71; N, 5.83. Found: C, 65.21; H, 6.58; N, 5.78.

***N*-[[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]quinolin-2-ylmethyl]-4-methylbenzenesulfonamide (6j):** oil; IR (neat) 3414, 2958, 2903, 2854, 1638, 1514, 1446, 1259, 1140, 1099, 1021, 803, 741 cm^{-1}; ^1H NMR δ 8.30 (s, 1H), 7.63 (d, J = 9, 2H), 7.44 (d, J = 12, 1H), 7.36 (d, J = 6, 2H), 7.23−7.08 (m, 8H), 6.62 (d, J = 3, 1H), 6.53 (d, J = 3, 1H), 2.38 (s, 3H), 0.93 (s, 9H), 0.59 (s, 6H); ^{13}C NMR δ 156.20, 146.81, 136.94, 136.87, 130.40, 130.24, 129.81, 129.64, 129.40, 129.21, 128.53, 127.93, 127.74, 127.59, 126.59, 126.40, 126.24, 123.72, 122.91, 120.25, 111.24, 34.51, 31.91, 29.68, 22.68; 14.11. Anal. Calcd for $C_{31}H_{35}N_3O_2SSi$: C, 68.72; H, 6.51; N, 7.76. Found: C, 69.03; H, 6.57; N, 7.94.

***N*-[(1*H*-Indol-3-yl)(4-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (3b) from (6b).** Compound **6b** (0.30 g, 0.58 mmol) was dissolved in 15 mL of freshly distilled THF in a 50 mL round-bottomed flask. To this stirred solution was added TBAF (0.18 g, 0.58 mmol). The resulting solution was allowed to stir for 20 min at rt, quenched with 15 mL of H_2O, extracted with CH_2Cl_2 (3 × 15 mL), and washed with H_2O (2 × 10 mL). The organic layer was dried over $MgSO_4$ and the solvent evaporated under reduced pressure to afford a yellow powder as the desired product in a 92% yield (0.22 g, 0.53 mmol): mp = 123−125 °C; IR (HATR) 1578, 1563, 1513, 1432, 1278, 1265, 1253, 1175, 1101, 1031, 896, 858, 826, 719 cm^{-1}; ^1H NMR δ 8.01 (bs, 1NH), 7.57 (d, J = 9, 2H), 7.30 (t, J = 6, 1H), 7.22−7.13 (m, 6H), 6.99 (t, J = 9, 1H), 6.75−6.73 (m, 3H), 5.80 (d, J = 6, 1H), 4.94 (d, J = 6, 1H), 3.77 (s, 3H), 2.38 (s, 3H); ^{13}C NMR δ 149.90, 143.65, 142.93, 139.05, 132.49, 129.73, 129.22, 128.42, 127.22, 126.49, 123.62, 119.94, 113.71, 111.19, 77.42, 55.25, 21.51. Anal. Calcd for $C_{23}H_{22}N_2O_3S$: C, 67.96; H, 5.46; N, 6.89. Found: C, 68.32; H, 5.65; N, 6.52.

***C*-[1-(*tert*-Butyldimethylsilanyl)-1*H*-indol-3-yl]-*C*-(4-methoxyphenyl)methylamine (7b)**. Compound **6b** (0.30 g, 0.58 mmol) was dissolved in 30 mL of freshly distilled THF in a 50 mL round-bottomed flask. To this stirred solution were added tetra-*n*-butylammonium bromide (0.02 g, 0.06 mmol) and solid sodium hydroxide pellet (0.024 g, 0.60 mmol). The resulting solution was allowed to stir at rt for 6 h and quenched with 15 mL of H_2O. The mixture was extracted with CH_2Cl_2 (3 × 25 mL) and washed with H_2O (3 × 20 mL). The organic layer was dried over $MgSO_4$ and the solvent evaporated under reduced pressure. The final traces of solvent were removed under vacuum overnight. The desired selective detosylated compound was afforded in a 62% yield (0.09 g, 0.36 mmol): mp = 155−156 °C; IR 2947, 2854, 1607, 1509, 1451, 1317, 1254, 1156, 1093, 1029, 965 cm^{-1}; ^1H NMR δ 7.56 (d, J = 9, 2H), 7.41 (d, J = 9, 1H), 7.18−7.08 (m, 4H), 6.96 (t, J = 9, 1H), 6.76 (s, 1H), 6.73 (d, J = 9, 2H), 5.79 (d, J = 6, 1H), 4.96 (d, J = 6, 1H), 3.77 (s, 3H), 0.86 (s, 9H), 0.50 (s, 6H); ^{13}C NMR δ 158.88, 141.85, 137.67, 132.60, 130.02, 129.20, 128.61, 127.16, 121.83, 120.87, 119.83, 118.01, 113.69, 55.66, 26.65, 21.87, 19.77. Anal. Calcd for $C_{22}H_{30}N_2OSi$: C, 72.08; H, 8.25; N, 7.64. Found: C, 71.75; H, 8.09; N, 7.87.

***C*-(1*H*-Indol-3-yl)-*C*-(4-methoxyphenyl)methylamine (8b).** Compound **6b** (0.29 g, 0.56 mmol) was dissolved in 15 mL of CH_2Cl_2 in a 25 mL round-bottomed flask equipped with a magnetic stir bar and a reflux condenser. To this were added NaOH pellets (0.09 g, 2.22 mmol) and 0.20 g of tetra-*n*-butylammonium bromide (0.06 mmol). The resulting solution was allowed to reflux with rapid stirring for 4 h. After being allowed to stir and cool to rt, the reaction mixture was diluted with an additional 25 mL of CH_2Cl_2 and quenched with (15 mL) water. The organic layer was removed and washed with H_2O (3 × 25 mL). The resulting organic layer was dried over $MgSO_4$ and the solvent removed under reduced pressure. Upon removal of the last traces of solvent under vacuum, 0.04 g of the desired viscous oily product (0.17 mmol) in a 31% yield was isolated: IR 3252, 1618, 1516, 1462, 1453, 1327, 1249, 1151, 1083, 1041, 951, 926 cm^{-1}; ^1H NMR δ 7.93 (bs, 1NH), 7.51 (d, J = 9, 1H), 7.33 (d, J = 9, 1H), 7.21−7.15 (m, 4H), 7.07 (t, J = 6, 1H), 6.88 (s, 1H), 6.81 (d, J = 9, 2H), 4.05 (s, NH_2), 3.77 (s, 3H); ^{13}C NMR δ 142.4, 140.9, 136.5, 131.6, 129.5, 128.3, 127.1, 126.5, 122.8, 121.7, 120.5, 112.1, 111.3, 56.2. Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 75.81; H, 6.54; N, 10.83.

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