Preparation of 1-Aryl-β-carbolines

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Owing to their pronounced biological activity, β-carbolines are currently of great interest, particularly in the study of mental illness and alcoholism.[1] The ability of a number of β-carbolines to bind effectively to benzodiazepine receptors[2] has further spurred interest in these compounds and, consequently, methods of their preparation.

Traditional methods of synthesizing β-carbolines such as the Pictet–Spengler reaction[1a,3] and the Bischler–Napieralski cyclization[1a,4] require 2-(3-indolyl)ethylamines as starting materials (typically derived from tryptophan). We sought the development of a more general synthetic route to β-carbolines which would readily accommodate the introduction of substituents at any position on the pyridine ring. The work described herein represents preliminary results we have obtained toward that end.

The general synthetic sequence is outlined in Scheme 1. 1-(Benzenesulfonyl)indole-3-carboxaldehyde (1) was prepared in two steps from indole following literature procedures[5,6] and was obtained in 74% overall yield after recrystallization. Olefination via a Wittig reaction as described by Pindur[7] gave pure 1-(benzenesulfonyl)-3-vinylindole (2) in 62% yield after column chromatography.

On treatment with LDA at −78 °C, indole 2 was lithiated at C-2 in approximately 90% yield, as evidenced by quenching experiments with D_2O. Lithiate 3 was reacted with tosylimines 4[8] to give sulfonamides 5 in good yields (Table 1). Although spectral data for all compounds were completely consistent with the indicated structures, further support for the assigned structure of **5b** was provided by an X-ray crystal structure.[11] This crystal structure also served to prove that the benzenesulfonyl group remained on the indole nitrogen, as removal of this group upon treatment of α-lithiated 1-(benzenesulfonyl)indole with electrophiles has been reported.[12]

Scheme 1

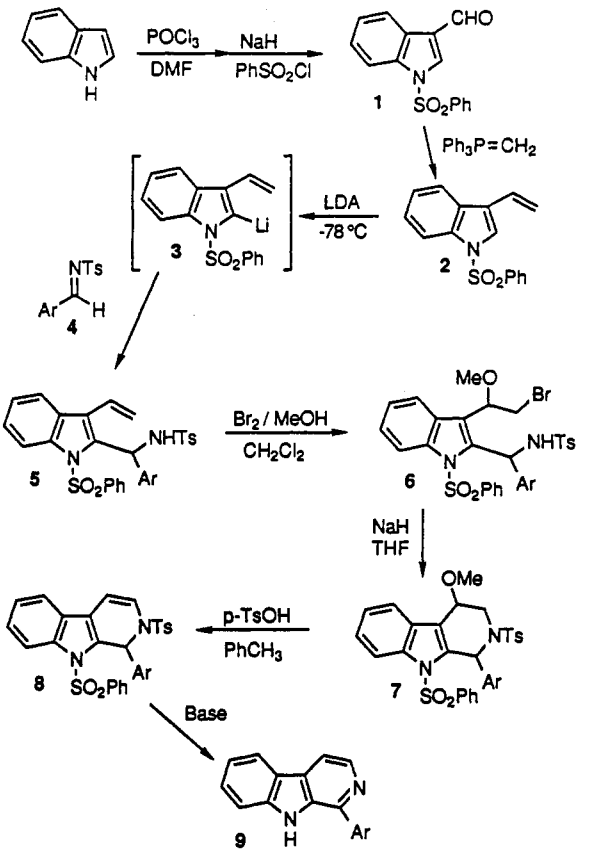

Table 1. Yields[a] of Intermediates in the Synthesis of β-Carbolines 9

	Ar	yield 5	6	7	8
a	Ph	77	98	99	85
b	p-$MeOC_6H_4$	67	97	98	97
c	o-ClC_6H_4	63	85	85	86
d	3,4-$(MeO)_2C_6H_3$	59	96	86	82
e	2-furyl	78	0		

[a] Isolated yield (%) of purified products.

Alkoxybromination of 5 was readily accomplished by treatment with bromine in a methanol/dichloromethane mixture. The addition was completely regiospecific in the formation of **6a** and **6b**, while minor traces of the alternate regioisomer were found to contaminate **6c** and **6d**. The furyl group of **5e** did not survive these conditions, a complex product mixture being obtained.

Intramolecular cyclization was accomplished by treatment with NaH in THF for 2 h at reflux. Tetrahydro-β-carbolines 7 were obtained in excellent yield, each as mostly one diastereomer. An X-ray crystal structure of **7b** was obtained, which showed a *cis* relationship between the substituents at C-1 and C-4 of the β-carboline ring.[11]

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(7) Pindur, U.; Pfeuffer, L. *Monatsh. Chem.* **1989**, *120*, 157.

(8) *N*-Tosylaldimines were prepared from *p*-toluenesulfonamide and the appropriate aldehyde by either heating the two reagents with tetraethyl orthosilicate[9] or by heating a toluene solution at reflux in the presence of *p*-toluenesulfonic acid and 4-Å molecular sieves in a flask equipped with a Dean–Stark trap.[10]

(9) Love, B. E.; Raje, P. R.; Williams, T. C., unpublished results (manuscript in preparation).

(10) Vishwakarma, L. C.; Stringer, O. D.; Davis, F. A. *Org. Synth.* **1988**, *66*, 203.

(11) The author has deposited atomic coordinates for structures **5b** and **7b** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(12) Sundberg, R. J.; Russel, H. F. *J. Org. Chem.* **1973**, *38*, 3324.

0022-3263/94/1959-3219$04.50/0

Table 2. Yields[a] of Base-Promoted Deprotection/Aromatization of 8

	BuLi/THF	KOH/DMSO	$Bu_4N^+OH^-$(PTC)
a	48	b	47
b	58	66	72
c	b	67	77
d	b	63	73

[a] Isolated yield (%) of purified products. [b] Reaction not attempted.

Conversion of the tetrahydro-β-carbolines 7 to the fully aromatic system was initiated by treatment with *p*-toluenesulfonic acid in toluene to effect elimination of methanol, producing 8 in excellent yield, as shown. Several reagents were then investigated for the simultaneous deprotection and aromatization of 8. Treatment of 8 with *n*-butyllithium in THF effects this transformation, though only in moderate yield.

Alternately, dihydro-β-carbolines 8 could be stirred with excess KOH in DMSO at 50 °C overnight to give the corresponding β-carbolines in somewhat higher yields. The same transformation could also be effected using phase-transfer catalysis. A solution of 8 in toluene was stirred overnight with 50% NaOH in the presence of a catalytic amount of tetrabutylammonium bromide. The crude product was then isolated from the toluene layer. Yields for these procedures are summarized in Table 2.

For all three deprotection/aromatization procedures, 9 was typically purified by passing HCl gas through a solution of the crude product (in either CH_2Cl_2 or toluene) to precipitate the hydrochloride salt. Isolation and neutralization of this salt gave the pure β-carbolines 9.

In summary, a new synthetic route to β-carbolines has been developed, as demonstrated by the synthesis of several 1-aryl-β-carbolines in overall yields ranging from 29% to 44% starting from known 1-(benzenesulfonyl)-3-vinylindole (2). Application of this method to the preparation of more highly substituted β-carbolines is currently under investigation.

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were taken in $CDCl_3$ (unless otherwise noted) at 250 and 62.9 MHz, respectively. Coupling constants are given in hertz. *N*-Tosylaldimines **4a-c** and **4e** are known compounds.[13] Imine **4d** was prepared by heating *p*-toluenesulfonamide with 3,4-dimethoxybenzaldehyde in the presence of tetraethyl orthosilicate.[9,14]

3-Ethenyl-1-(benzenesulfonyl)-2-[(4-methoxyphenyl)[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (5b). Diisopropylamine (2.45 g, 24.3 mmol) in dry THF (20 mL) was treated with 2.0 M *n*-BuLi in hexanes (12.2 mL, 24.4 mmol) at −78 °C under nitrogen for 30 min to generate a solution of LDA. A solution of **2** (5.3 g, 18.6 mmol) in THF (30 mL) was added dropwise to the LDA solution and allowed to come to 0 °C over 45 min. The solution was then stirred at 25 °C for 3 h, yielding a deep red solution, which was cooled to −78 °C. To this solution was added **4b** (5.64 g, 19.5 mmol) in THF (30 mL) dropwise, followed by 5 min of stirring at −78 °C. The solution was allowed to warm to 0 °C, and then the reaction was quenched with H_2O (60 mL). The solution was extracted with CH_2Cl_2 (3 × 40 mL), the combined extracts were dried ($MgSO_4$), and solvent was removed under reduced pressure. The crude product was dissolved in a minimal amount of EtOAC, and *n*-pentane was added until slight turbidity was observed. The solution was then cooled to 0 °C and the precipitate collected by filtration to give 7.14 g (67%) of **5b**: mp 170–3 °C; ^1H NMR δ 1.97 (s, 3H), 3.81 (s, 3H), 5.61 (d, *J* = 11.8, 1H), 5.72 (d, *J* = 17.3, 1H), 6.37 (br s, 1H), 6.7–7.4 (m, 15H), 7.49 (d, *J* = 6.6, 2H), 7.59 (d, *J* = 7.1, 1H), 8.00 (d, *J* = 7.9, 1H); ^{13}C NMR δ 21.1, 52.5, 113.8, 114.9, 120.1, 120.7, 124.0, 125.5, 126.4, 126.6, 127.0, 127.3, 127.8, 128.7, 130.0, 133.6, 133.9, 136.6, 137.1, 138.0, 142.7, 158.9.

3-Ethenyl-1-(benzenesulfonyl)-2-[phenyl[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (5a): prepared as described for **5b**, mp 176–7 °C; ^1H NMR δ 1.95 (s, 3H), 5.62 (d, *J* = 11.5, 1H), 5.73 (d, *J* = 17.7, 1H), 6.41 (br d, *J* = 10.1, 1H), 6.7–6.9 (m, 6H), 7.06 (t, *J* = 7.8, 2H), 7.2–7.4 (m, 8H), 7.50 (d, *J* = 8.3, 2H), 7.5–7.6 (m, 1H), 7.99 (d, *J* = 8.1, 1H); ^{13}C NMR δ 21.1, 52.9, 114.9, 120.2, 120.7, 124.0, 125.5, 126.1, 126.3, 126.56, 126.58, 126.60, 126.9, 127.2, 127.8, 128.4, 128.68, 128.70, 133.6, 136.5, 137.0, 137.7, 138.0, 142.7.

3-Ethenyl-1-(benzenesulfonyl)-2-[(2-chlorophenyl)[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (5c): prepared as described for **5b**, mp 197 °C; ^1H NMR δ 2.14 (s, 3H), 5.52 (d, *J* = 11.5, 1H), 5.60 (d, *J* = 16.2, 1H), 6.8–7.6 (m, 19H), 8.07 (d, *J* = 8.0, 1H); ^{13}C NMR δ 21.3, 52.5, 115.1, 120.3, 120.6, 123.9, 125.6, 126.3, 126.4, 126.79, 126.86, 128.2, 128.3, 128.9, 129.3, 130.0, 130.3, 132.6, 133.6, 134.0, 134.9, 137.0, 137.1, 138.2, 143.1.

3-Ethenyl-1-(benzenesulfonyl)-2-[3,4-dimethoxyphenyl)-[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (5d): prepared as described for **5b**, mp 185 °C; ^1H NMR δ 1.97 (s, 3H), 3.58 (s, 3H), 3.87 (s, 3H), 5.61 (d, *J* = 11.5, 1H), 5.71 (d, *J* = 17.7, 1H), 6.36 (br s, 1H), 6.6–7.4 (m, 14H), 7.50 (d, *J* = 8.2, 2H), 7.59 (d, *J* = 8.7, 1H), 8.04 (d, *J* = 8.5, 1H); ^{13}C NMR δ 21.1, 52.7, 55.6, 56.0, 110.9, 115.0, 120.1, 120.6, 124.1, 125.6, 126.4, 126.5, 126.8, 127.0, 127.8, 128.6, 128.7, 129.3, 130.5, 133.6, 136.8, 137.0, 138.0, 142.8, 148.3, 148.9.

3-Ethenyl-1-(benzenesulfonyl)-2-[(2-furyl)[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (5e): prepared as described for **5b**, mp 195 °C; ^1H NMR δ 1.99 (s, 3H), 5.63 (d, *J* = 11.4, 1H), 5.76 (d, *J* = 17.6, 1H), 6.3–6.5 (m, 3H), 6.7–6.9 (m, 4H), 7.1–7.6 (m, 9H), 7.49 (d, *J* = 8.4, 2H), 7.92 (d, *J* = 7.7, 1H); ^{13}C NMR δ 21.1, 49.5, 111.0, 114.8, 120.0, 121.6, 124.0, 125.6, 126.4, 126.6, 128.0, 128.71, 128.79, 128.82, 128.83, 128.85, 128.86, 133.7, 136.3, 136.7, 137.5, 141.6, 142.9, 150.9.

3-(2-Bromo-1-methoxyethyl)-1-(benzenesulfonyl)-2-[(4-methoxyphenyl)[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (6b). To **5b** (2.35 g, 4.1 mmol) in CH_2Cl_2 (25 mL) was added MeOH until slight turbidity was observed (*ca.* 60 mL). The solution was made clear with the addition of a few drops of CH_2Cl_2, and a 0.72 M solution of Br_2 in CCl_4 (20 mL, 14.4 mmol) was added dropwise over 30 min. The solution was stirred at 25 °C for 3 h, treated with 0.1 M $Na_2S_2O_3$ (30 mL), and extracted with CH_2Cl_2 (3 × 35 mL). The combined extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure to give 2.72 g (97%) of **6b**, mp 85–8 °C: ^1H NMR δ 2.38 (s, 3H), 3.28 (s, 3H), 3.2–3.4 (m, 1H), 3.74 (s, 3H), 3.6–3.9 (m, 1H), 4.89 (br d, *J* = 8.3, 1H), 6.38 (br s, 1H), 6.5–6.7 (m, 1H), 6.65 (d, *J* = 8.9, 2H), 6.86 (d, *J* = 8.6, 2H), 7.2–7.5 (m, 9H), 7.7–7.9 (m, 1H), 7.79 (d, *J* = 8.3, 2H), 8.01 (d, *J* = 7.9, 1H); ^{13}C NMR δ 21.5, 34.7, 52.2, 55.2, 58.0, 78.3, 113.8, 114.9, 124.0, 125.7, 126.5, 126.6, 126.86, 126.93, 127.0, 129.02, 129.05, 129.75, 129.77, 129.79, 133.8, 136.5, 137.7, 138.3, 143.6, 158.9.

3-(2-Bromo-1-methoxyethyl)-1-(benzenesulfonyl)-2-[phenyl[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (6a): prepared as described for **6b**, mp 150 °C; ^1H NMR δ 2.37 (s, 3H), 3.28 (s, 3H), 3.7–3.9 (m, 2H), 4.8–4.9 (m, 1H), 6.44 (br d, 1H), 6.38 (br s, 1H), 6.76 (d, *J* = 9.9, 1H), 6.98 (m, 2H), 7.0–7.5 (m, 12H), 7.7–7.9 (m, 3H), 7.98 (d, *J* = 7.3, 1H); ^{13}C NMR δ 21.5, 34.7, 52.5, 58.0, 78.3, 114.9, 125.8, 126.0, 126.4, 126.5, 126.6, 126.8, 126.9, 127.4, 128.4, 128.5, 129.0, 129.1, 129.7, 129.8, 133.8, 136.4, 137.6, 138.3, 143.6.

3-(2-Bromo-1-methoxyethyl)-1-(benzenesulfonyl)-2-[(2-chlorophenyl)[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (6c): prepared as described for **6b**, mp 108–9 °C; ^1H NMR δ 2.38 (s, 3H), 3.46 (s, 3H), 3.63 (dd, *J* = 3.1, 11.0, 1H), 3.90 (dd,

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(14) Data for **4d**: mp 103 °C; ^1H NMR δ 2.43 (s, 3H), 3.91 (s, 3H), 3.96 (s, 3H), 6.94 (d, *J* = 8.3, 1H), 7.34 (d, *J* = 8.3, 2H), 7.43 (dd, *J* = 8.3, 1.9, 1H), 7.51 (d, *J* = 1.9, 1H), 7.88 (d, *J* = 8.3, 2H), 8.91 (s, 1H); ^{13}C NMR δ 21.6, 56.0, 56.1, 110.2, 110.6, 125.4, 127.9, 129.1, 129.7, 135.6, 144.2, 149.6, 155.2, 169.4; HRMS calcd for $C_{16}H_{17}NO_4S$ 319.0878, found 319.0877.

J = 8.9, 11.0, 1H), 5.30 (dd, J = 3.1, 8.9, 1H), 6.46 (d, J = 8.9, 1H), 6.74 (d, J = 9.0, 1H), 6.9–8.1 (m, 17H); ^{13}C NMR δ 21.4, 35.3, 52.3, 59.0, 78.3, 115.4, 121.5, 124.2, 125.7, 126.27, 126.30, 127.3, 128.2, 128.9, 129.0, 129.2, 129.36, 129.42, 129.8, 133.3, 133.7, 135.0, 135.4, 137.0, 137.6, 137.8, 143.5.

3-(2-Bromo-1-methoxyethyl)-1-(benzenesulfonyl)-2-[(3,4-dimethoxyphenyl)[*N*-(*p*-toluenesulfonyl)amino]methyl]indole (6d): prepared as described for **6b**, mp 162–3 °C; ^{1}H NMR δ 2.37 (s, 3H), 3.29 (s, 3H), 3.46 (s, 3H), 3.4–3.5 (m, 1H), 3.81 (s, 3H), 3.7–3.9 (m, 1H), 4.90 (br d, J = 8.3, 1H) 6.3–6.5 (m, 3H), 6.59 (d, J = 8.4, 1H), 6.73 (br d, J = 9.8, 1H), 7.2–7.5 (m, 9H), 7.7–7.9 (m, 1H), 7.80 (d, J = 8.3, 2H), 8.04 (d, J = 7.7, 1H); ^{13}C NMR δ 21.4, 34.6, 52.2, 55.3, 55.8, 57.9, 78.2, 109.1, 110.8, 114.9, 115.4, 118.2, 124.0, 125.7, 126.0, 126.4, 126.8, 127.2, 128.8, 128.87, 128.90, 129.7, 133.7, 135.5, 137.8, 138.2, 143.5, 148.3, 148.8.

1-(*p*-Methoxyphenyl)-2-(*p*-toluenesulfonyl)-4-methoxy-9-(benzenesulfonyl)-1,2,3,4-tetrahydro-β-carboline (7b). To **6b** (1.64 g, 2.4 mmol) in THF (25 mL) at 0 °C under nitrogen was added slowly via power addition funnel NaH (60% in mineral oil, 0.11 g, 2.6 mmol). The mixture was stirred at 0 °C for 10 min, allowed to come to 25 °C for 10 min, and then heated at reflux for 2 h. The solution was cooled, diluted with 40 mL of H_2O, and extracted with CH_2Cl_2 (2 × 35 mL). The combined extracts were dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was washed with n-pentane to remove mineral oil, yielding 1.41 g (98%) of **7b**, mp 177–9 °C: ^{1}H NMR δ 2.26 (s, 3H), 3.04 (dd, J = 9.7, 14.3, 1H), 3.45 (s, 3H), 3.76 (s, 3H), 4.14 (dd, J = 6.7, 14.3, 1H), 4.58 (dd, J = 6.7, 9.7, 1H), 6.68 (d, J = 8.8, 2H), 6.85 (s, 1H), 6.96 (d, J = 8.7, 2H), 7.10 (d, J = 8.0, 2H), 7.2–7.6 (m, 10H), 8.12 (d, J = 8.1, 1H); ^{13}C NMR δ 21.3, 41.4, 55.2, 55.4, 56.5, 70.5, 113.6, 113.8, 114.3, 119.1, 120.4, 123.8, 125.1, 126.7, 127.0, 129.0, 129.5, 129.6, 130.0, 133.6, 134.1, 136.3, 137.2, 138.3, 143.6, 159.5.

1-Phenyl-2-(*p*-toluenesulfonyl)-4-methoxy-9-(benzenesulfonyl)-1,2,3,4-tetrahydro-β-carboline (7a): prepared as described for **7b**, mp 177–8 °C; ^{1}H NMR δ 2.26 (s, 3H), 3.03 (dd, J = 9.7, 14.4, 1H), 3.45 (s, 3H), 4.14 (dd, J = 6.7, 14.4, 1H), 4.59 (dd, J = 6.7, 9.7, 1H), 6.90 (s, 1H), 7.0–7.6 (m, 17H), 8.12 (d, J = 8.1, 1H); ^{13}C NMR δ 21.4, 41.5, 55.9, 56.5, 70.5, 114.3, 119.3, 120.4, 123.9, 125.2, 126.6, 127.1, 128.2, 128.4, 128.5, 128.8, 129.05, 129.09, 129.6, 133.7, 136.4, 137.5, 138.1, 143.7.

1-(2-Chlorophenyl)-2-(*p*-toluenesulfonyl)-4-methoxy-9-(benzenesulfonyl)-1,2,3,4-tetrahydro-β-carboline (7c): prepared as described for **7b**, mp 184–5 °C; ^{1}H NMR δ 2.29 (s, 3H), 3.04 (dd, J = 9.3, 14.7, 1H), 3.50 (s, 3H), 3.93 (dd, J = 6.7, 14.7, 1H), 4.81 (dd, J = 6.7, 9.3, 1H), 6.8–7.7 (m, 15H), 7.80 (d, J = 7.7, 2H), 8.12 (d, J = 8.2, 1H); ^{13}C NMR δ 21.3, 42.2, 53.1, 57.1, 70.7, 114.3, 120.2, 120.3, 123.9, 125.3, 126.3, 126.8, 127.6, 128.0, 129.2, 129.3, 129.7, 130.46, 130.55, 133.5, 133.9, 134.9, 135.0, 136.1, 136.6, 137.9, 143.8.

1-(3,4-Dimethoxyphenyl)-2-(*p*-toluenesulfonyl)-4-methoxy-9-(benzenesulfonyl)-1,2,3,4-tetrahydro-β-carboline (7d): prepared as described for **7b**, mp 162–3 °C; ^{1}H NMR δ 2.25 (s, 3H), 3.08 (dd, J = 9.7, 14.3, 1H), 3.46 (s, 3H), 3.67 (s, 3H), 3.82 (s, 3H), 4.18 (dd, J = 7.0, 14.3, 1H), 4.61 (dd, J = 7.0, 9.7, 1H), 6.43 (dd, J = 2.0, 8.3, 1H), 6.55 (d, J = 8.3, 1H), 6.65 (d, J = 2.0, 1H), 6.82 (s, 1H), 7.12 (d, J = 8.1, 2H), 7.66 (d, J = 8.3, 2H), 8.13 (d, J = 8.2, 1H); ^{13}C NMR δ 21.2, 41.5, 55.6, 55.7, 55.8, 56.4, 70.5, 110.3, 111.9, 114.2, 119.1, 120.3, 121.1, 123.8, 125.1, 126.6, 127.0, 127.4, 127.9, 128.9, 129.5, 129.9, 133.6, 134.0, 136.1, 137.2, 138.2, 143.6, 149.0.

1-(*p*-Methoxyphenyl)-2-(*p*-toluenesulfonyl)-1,2-dihydro-β-carboline (8b). To **7b** (2.90 g, 4.8 mmol) in toluene (60 mL) were added 4-Å molecular sieves (2 g) and a catalytic amount of *p*-TsOH. The mixture was heated at reflux 4 h, cooled, and filtered. Solvent was removed from the filtrate under reduced pressure to give the crude product, which was dissolved in CH_2Cl_2 (50 mL) and washed with 0.1 M NaOH (25 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure to give 2.66 g (97%) of **8b**: ^{1}H NMR δ 2.23 (s, 3H), 3.77 (s, 3H), 6.24 (d, J = 7.3, 1H), 6.58 (d, J = 7.3, 1H), 6.69 (d, J = 8.8, 2H), 7.0–7.5 (m, 13H), 7.62 (d, J = 8.3, 2H), 8.06 (d, J = 7.8, 1H); ^{13}C NMR δ 21.4, 55.3, 56.3, 105.6, 113.8, 115.3, 118.7, 122.7, 123.8, 125.0, 125.6, 126.56, 126.64, 128.2, 128.4, 128.9, 129.5, 129.6, 130.3,133.6, 136.1, 136.3, 137.8, 143.7, 159.8.

1-Phenyl-2-(*p*-toluenesulfonyl)-1,2-dihydro-β-carboline (8a): prepared as described for **8b**; ^{1}H NMR δ 2.22 (s, 3H), 6.25 (d, J = 7.6, 1H), 6.58 (d, J = 7.6, 1H), 7.0–7.5 (m, 16H), 7.63 (d, J = 8.4, 2H), 8.06 (d, J = 7.2, 1H); ^{13}C NMR δ 21.4, 55.9, 105.9, 114.6, 115.5, 118.7, 122.8, 123.8, 125.1, 125.3, 126.6, 126.7, 128.2, 128.4, 128.5, 128.9, 129.1, 129.5, 133.6, 136.0, 136.4, 137.8, 137.9, 143.8.

1-(2-Chlorophenyl)-2-(*p*-toluenesulfonyl)-1,2-dihydro-β-carboline (8c): prepared as described for **8b**, except the solution was heated for 6 h at reflux; mp 205–6 °C; ^{1}H NMR δ 1.97 (s, 3H), 6.35 (d, J = 7.0, 1H), 6.44 (d, J = 7.0, 1H), 6.62 (dd, J = 1.6, 7.9, 1H), 6.8–6.9 (m, 3H), 7.1–7.5 (m, 12H), 7.68 (s, 1H), 8.12 (d, J = 7.9, 1H); ^{13}C NMR δ 21.0, 52.3, 111.6, 114.4, 115.9, 118.4, 123.4, 123.8, 125.16, 125.22, 126.3, 126.6, 126.9, 128.1, 129.0, 129.7, 130.5, 130.7, 133.2, 133.6, 133.8, 134.2, 136.2, 137.9, 143.7.

1-(3,4-Dimethoxyphenyl)-2-(*p*-toluenesulfonyl)-1,2-dihydro-β-carboline (8d): prepared as described for **8b**, except the solution was heated for 9 h at reflux; ^{1}H NMR δ 2.21 (s, 3H), 3.73 (s, 3H), 3.82 (s, 3H), 6.24 (d, J = 7.2, 1H), 6.57–6.61 (m, 3H), 6.91 (s, 1H), 7.0–7.5 (m, 12H), 7.63 (d, J = 6.5, 2H), 8.09 (d, J = 7.3, 1H); ^{13}C NMR δ 21.3, 55.7, 55.8, 55.9, 105.6, 110.7, 111.5, 114.6, 115.3, 118.7, 120.7, 122.8, 123.8, 125.1, 125.6, 126.5, 126.6, 128.2, 128.8, 129.4, 130.5, 133.6, 136.1, 136.4, 137.9, 143.8, 149.0, 149.3.

1-(*p*-Methoxyphenyl)-β-carboline (9b) (Using BuLi). To **8b** (0.14 g, 0.25 mmol) in THF (20 mL) at 0 °C under nitrogen was added 2.0 M n-BuLi in hexanes (0.13 mL, 0.26 mmol) dropwise. The solution was stirred at 0 °C for 10 min, allowed to come to 25 °C, and then heated at reflux for 3 h. The solution was then cooled, diluted with H_2O (30 mL), and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and then HCl gas was bubbled through the solution, resulting in the formation of a precipitate. The precipitate was collected by filtration, dissolved in MeOH (15 mL), and treated with 0.5 M NaOH (15 mL). The solution was extracted with CH_2Cl_2 (2 × 15 mL), the combined extracts were dried ($MgSO_4$), and the solvent was removed under reduced pressure to give 0.04 g (58%) of **9b**: mp 159–60 °C; ^{1}H NMR δ 3.89 (s, 3H), 7.10 (d, J = 8.9, 2H), 7.2–7.3 (m, 1H), 7.5–7.6 (m, 2H), 7.9–8.0 (m, 3H), 8.15 (d, J = 7.9, 1H), 8.54 (d, J = 5.3, 1H), 8.68 (br s, 1H); ^{13}C NMR ($CDCl_3$/DMSO-d_6) δ 54.2, 111.8, 113.5, 113.8, 118.5, 120.1, 121.4, 127.8, 129.8, 129.9, 130.9, 132.4, 136.2, 143.0, 160.7; HRMS calcd for $C_{18}H_{14}N_2O$ 274.1106, found 274.1110.

1-(*p*-Methoxyphenyl)-β-carboline (9b) (Using KOH). To **8b** (0.36 g, 0.63 mmol) in DMSO (25 mL) was added two powdered KOH pellets. The solution was heated at 50 °C for 14 h, cooled, diluted with H_2O (30 mL), and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were washed with H_2O (3 × 15 mL), dried ($MgSO_4$), and treated as described above to afford 0.11 g (66%) of **9b**.

1-(*p*-Methoxyphenyl)-β-carboline (9b) (Using Phase-Transfer Catalysis). To **8b** (0.33 g, 0.58 mmol) in toluene (20 mL) were added a catalytic amount of $Bu_4N^+Br^-$ and 50% NaOH (15 mL). The mixture was heated at reflux for 16 h, cooled, and diluted with H_2O (25 mL). The organic phase was treated with HCl gas to yield a precipitate, which was treated as described above to yield 0.11 g (72%) of **9b**.

1-Phenyl-β-carboline (9a): prepared as described for **9b**; mp 240–3 °C (lit.[15] mp 246–7 °C); ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 7.25 (t, J = 7.5, 1H), 7.4–7.7 (m, 5H), 7.95 (d, J = 4.6, 1H), 8.04 (d, J = 7.5, 2H), 8.14 (d, J = 8.1, 1H), 8.49 (d, J = 5.2, 1H), 11.07 (br s, 1H); ^{13}C NMR ($CDCl_3$/DMSO-d_6) δ 111.4, 112.6, 118.5, 120.25, 120.30, 127.1, 127.4, 127.6, 127.8, 128.6, 132.6, 137.5, 137.8, 140.4, 141.8; HRMS calcd for $C_{17}H_{12}N_2$ 244.1000, found 244.0997.

1-(2-Chlorophenyl)-β-carboline (9c): prepared as described for **9b**, mp 209–10 °C; ^{1}H NMR δ 7.2–7.7 (m, 7H), 7.99 (d, J = 5.3, 1H), 8.16 (d, J = 7.9, 1H), 8.46 (br s, 1H), 8.55 (d, J = 5.3, 1H); ^{13}C NMR δ 111.5, 114.3, 120.2, 121.7, 127.3, 128.6, 129.4, 130.07, 130.12, 131.9, 132.8, 134.1, 137.0, 139.1, 140.4, 141.4; HRMS calcd for $C_{17}H_{11}N_2Cl$ 278.0611, found 278.0613.

1-(3,4-Dimethoxyphenyl)-β-carboline (9d): prepared as described for **9b**; mp 105–8 °C (lit.[16] mp 90–2 °C); ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 3.99 (s, 3H), 4.04 (s, 3H), 7.27 (d, J = 8.5,

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1H), 7.44 (t, J = 6.9, 1H), 7.65 (s, 1H), 7.6–7.9 (m, 3H), 8.42 (d, J = 8.1, 1H), 8.47 (d, J = 6.2, 1H), 8.59 (d, J = 6.2, 1H), 12.66 (br s, 1H); ^{13}C NMR ($CDCl_3$/DMSO-d_6) δ 54.38, 54.41, 110.3, 111.0, 111.7, 113.7, 118.3, 119.9, 120.0, 121.28, 121.34, 127.5, 129.7, 130.7, 132.2, 136.0, 142.8, 147.8, 150.2; HRMS calcd for $C_{19}H_{16}N_2O_2$ 304.1212, found 304.1215.

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Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra of **2**, **4d**, **5a–e**, **6a–d**, **7a–d**, **8a–d**, and **9a–d** (46 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.