the mixture was allowed to stand at room temperature for 2.5 days, after which it was acidified with 2 N hydrochloric acid till precipitation ceased. The precipitated phthalhydrazide was filtered, the filtrate evaporated in vacuo, and absolute alcohol added to precipitate sodium chloride, which was removed by filtration. Removal of solvent in vacuo gave **4a**·HCl as a hygroscopic solid (40 g, 92.8%): ^{1}H NMR (D_O chemical shifts relative to DSS) identical with that of the product **4a** obtained in section A (above) (lit.[12] reports **4a**·HCl as a deliquescent solid). Treatment of **4a**·HCl with diazomethane in methanol at 0 °C gave N^γ,N^γ-diethyl-L-glutamine methyl ester[17] (**4b**): IR (neat) 3600–3200 (br, NH_2), 1735 (O=$COCH_3$), 1635 [O=$CN(C_2H_5)_2$] cm^{-1}; ^{1}H NMR δ 1.12 and 1.20 (overlapping t, J = 7.5 Hz, 6 H, NCH_2CH_3), 2.15 (m, 6 H, CH_2 and NH_2), 3.33 (m, 5 H, NCH_2 and CH), 3.75 (s, 3 H, OCH_3); high-resolution mass spectrum calcd for $C_{10}H_{20}N_2O_3$ M^+ 216.1470, found 216.1467.

(*S*)-2-Amino-5-(diethylamino)pentanol (6a). A suspension of **4a**·HCl (3.34 g, 14 mmol) in dry tetrahydrofuran (100 mL) was treated at 0 °C with a suspension of lithium aluminum hydride (3.34 g, 88 mmol) in dry tetrahydrofuran (100 mL), and the mixture was then refluxed for 12 h. After decomposition of excess reagent by sodium sulfate decahydrate (6.04 g), 100 mL of alcohol was added, the mixture refluxed for 1 h and filtered, and the filtrate evaporated in vacuo. The residue on distillation gave the alcohol **6a** (1.91 g, 78.5%) as a light yellow oil: bp 100–108 °C (0.18 mm); $[\alpha]^{23}_D$ +5.77° (*c* 10.3, dioxane); $[\alpha]^{33}_D$ +6.91° (*c* 9.24, ethanol); IR (neat) 3200–3600 (OH), 2950 (CH), 1550 (NH_2), 1200 (NH) cm^{-1}; ^{1}H NMR δ 1.02 (t, J = 7.5 Hz, 6 H, CH_3), 1.50 (m, 4 H, CH_2), 2.45 (m, 8 H, $N(CH_2)$, $N(CH_2)_3$ and NH_2), 3.15 (br s, 1 H, OH, exchanged with D_2O), 3.60 (m, 3 H, CH_2OH and CH); ^{1}H NMR (CF_3COOH) δ 1.42 (t, J = 7.5 Hz, 6 H), 2.00 (br s, 4 H, CH_2), 3.25 (m, 7 H, $HN^+(CH_2)_3$), 4.35 (m, 4 H, CH_2OH and CH), 7.35 (br s, 3H, N^+H_3). Anal. Calcd for $C_9H_{22}N_2O$: C, 62.06; H, 12.64; N, 16.09. Found: C, 62.18; H, 12.64; N, 15.87. (Literature[12] reports **6a** as an air-sensitive liquid, no analysis or spectra recorded, prepared from N^γ,N^γ-diethyl-(*S*)-glutamine hydrochloride.)

(*R*)-4-Amino-1-(diethylamino)pentane (6c). A solution of (*S*)-2-amino-5-(diethylamino)pentanol (**6a**) (1.9 g, 11 mmol) in dry ether (100 mL) was treated at 0 °C with 1.75 N ethereal hydrogen chloride (13.0 mL) when a drop of the ether solution indicated a pH of 5 on a wet pH paper. Removal of solvent in vacuo left a residue, which was suspended in dry chloroform (100 mL), treated with thionyl chloride (8.16 g, 5 mL, 68.5 mmol) in chloroform (50 mL), and stirred and refluxed for 12 h. After removal of volatile material in vacuo, the residue was suspended in dry tetrahydrofuran (100 mL) and treated at 0 °C with a suspension of lithium aluminum hydride (2.55 g, 67.2 mmol) in tetrahydrofuran (100 mL). Refluxing for 12 h was followed by cooling to room temperature and addition of sodium sulfate decahydrate (4.5 g) and alcohol (100 mL). Refluxing for 1 h, filtration, and evaporation of the filtrate in vacuo gave a residue, which was taken up in dichloromethane, dried (sodium sulfate), and distilled in a Kugelrohr apparatus to give the diamine **6c** as a colorless liquid (0.36 g, 21% overall yield): bp (airbath) 98 °C (30 mm); $[\alpha]^{23}_D$ +0.30°; $[\alpha]^{23}_{365}$ +2.25° (*c* 10.2, EtOH); IR (neat) 3100–3600 (NH_2), 2950 (CH), 1600, 1475, and 1390 cm^{-1}; ^{1}H NMR δ 1.00 (t, J = 7.0 Hz, 6 H, CH_3), 1.06 (d, J = 6.0 Hz, 3 H, CH_3), 1.47 (m, 4 H, CH_2), 2.90 (q overlapping m, 8 H, CH_2 and NH_2), 3.66 (m, 1 H, CH). Anal. Calcd for $C_9H_{22}N_2$: 158.1783. Found by high-resolution electron-impact mass spectrometry: 158.1777. The compound gave a single peak on gas chromatography, t_R 5.0 min, identical in t_R with a sample of the racemic diamine. Derivatization of **6c** with optically pure (-)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride, $[\alpha]^{23}_D$ -129° (*c* 5.6, CCl_4) (lit.[13] $[\alpha]_D$ -129.0° (*c* 5.2, CCl_4)), was carried out by the method of Dale et al.[13] with one exception: since the derivative contains a tertiary amine functionality, the acid wash must be eliminated. Capillary gas chromatography showed the product to consist of 90.6% of the *R* isomer (t_R 15.09 min) and 9.4% of the *S* isomer (t_R 15.75 min).

(*R*)-(-)-Chloroquine (1). A mixture of 4,7-dichloroquinoline (6 g, 30.3 mmol), phenol (5.72, 60.8 mmol), and (*R*)-4-amino-1-(diethylamino)pentane (**6c**) (4.8 g, 30.4 mmol) was stirred at 120–130 °C for 18 h, cooled to room temperature, and dissolved in chloroform (50 mL). The solution was extracted first with ice-cold 15% NaOH solution and then with 1 N hydrochloric acid (5 × 50 mL). The combined acid layers were washed with ether, basified to pH 11 with saturated sodium carbonate, and extracted with chloroform. The combined chloroform extracts were dried (Na_2SO_4) and evaporated to give (*R*)-(-)-chloroquine (6.24 g, 64%) as white crystals (from hexane): mp and mixed mp 65–67 °C (lit.[3] mp 68–69 °C); $[\alpha]^{20}_D$ -86.2° (*c* 1, EtOH) (lit.[3] $[\alpha]^{22}_D$ -108.0° (*c* 1, EtOH). The diphosphate, prepared by the published method,[15] had mp and mixed mp 202 °C (lit.[3] mp 202 °C) and $[\alpha]^{25}_D$ -68.95° (*c* 2.1, H_2O) (lit.[3] $[\alpha]^{22}_D$ -86.9° (*c* 2.1, H_2O)).

(17) Gas chromatographic analysis of the crude product showed the presence of an impurity (5–10%) identified as the α-N-methylated and α-N,N-dimethylated homologues of **4b** by mass spectrometry. These were readily removed by chromatography on alumina, from which they were eluted first, followed by pure **4b**.

Palladium-Catalyzed Coupling of 2-Bromoanilines with Vinylstannanes. A Regiocontrolled Synthesis of Substituted Indoles

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The palladium-catalyzed cross-coupling reaction of aryl halides and triflates with vinylstannane reagents has been used to produce a variety of substituted indoles. The mild reaction conditions and selectivity inherent in the coupling reaction have been utilized to produce regiochemically pure 4-, 5-, and 6-substituted indoles.

While 4-substituted indoles represent an important class of alkaloids that possess a wide range of biological activity,[1] the synthesis of these compounds is not straightforward. The method of choice, particularly for the 2,3-unsubstituted indoles,[2] relies on the Leimgruber–Batcho procedure[3] starting from the commercially available 2-methyl-3-nitrobenzoic acid, but these procedures generally do not tolerate sensitive functionality.

The synthesis of 4-bromoindoles by a Batcho–Leimgruber procedure from 6-bromo-2-nitroaniline provides an

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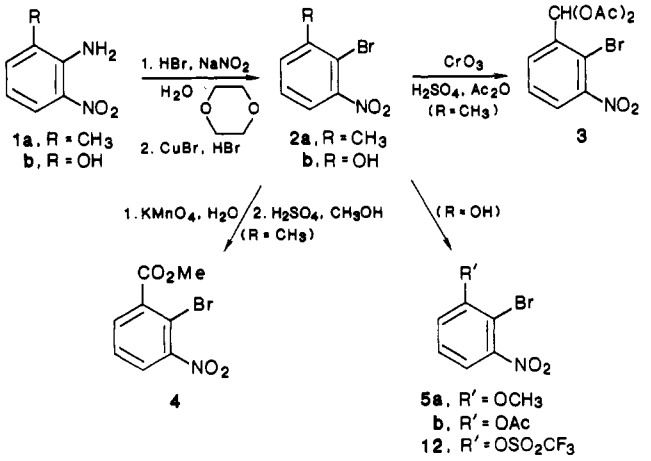
0022-3263/88/1953-1170$01.50/0

Scheme I



entry to 4-substituted indoles.[4] The metal–halogen exchange reaction followed by a reaction with various electrophiles can then be utilized to obtain a variety of regiopure products.

An alternative route to 4-substituted indoles relies on the cyclization of an *o*-vinylaniline, utilizing a palladium catalyst and *p*-benzoquinone as a reoxidant.[5] The routes to *o*-vinylanilines are somewhat difficult, since a number of steps are necessary. In addition to a Wittig olefination procedure[5] for the synthesis of *o*-vinylanilines, the pyrolysis of ethyl- or hydroxyethylaniline in the presence of copper, chromium, or aluminum salts[6] has been utilized, but yields are only 20–40% and high temperatures (400–600 °C) are necessary. Most of the procedures rely on the classical synthesis of *o*-nitrostyrenes followed by reduction. The most direct approach, the palladium-catalyzed arylation of ethylene with *o*-bromoaniline[9] (Heck reaction), proceeds only in moderate yields (~45%).

The palladium-catalyzed cross-coupling reaction of organotin reagents with a variety of organic electrophiles is a mild, high yield method of carbon–carbon bond formation.[10] This reaction has been used to connect a vinyl group to aromatic rings; the utility of the procedure is that a wide variety of substituents, including aldehydes, alcohols, nitro groups, and carboxylic acids, can be tolerated on the coupling partners.[11] Thus this procedure appeared to be ideal for the synthesis of substituted indoles, particularly 4-substituted indoles.

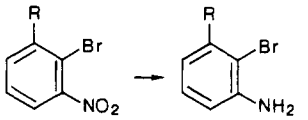
Results and Discussion

The synthesis of the substituted indoles started with substituted 2-bromonitrobenzenes, conversion to the substituted vinylanilines, and cyclization. For the synthesis of 4-substituted indoles, commercially available 2-amino-3-nitrotoluene (**1a**) and 2-amino-3-nitrophenol (**1b**) were converted to the corresponding bromides **2** via a Sandmeyer reaction (Scheme I).[12] Oxidation of **2a** to the acetal **3** or the carbomethoxy derivative **4** was accomplished by using chromium trioxide in acetic anhydride[13] and aqueous potassium permanganate,[14] respectively. Phenol **2b** was protected as the methyl ether,[15] the acetate ester,[16] and the trifluoromethanesulfonic acid ester.

Reduction of the nitro group was accomplished with iron/acetic acid (Table I).

The palladium-catalyzed vinylation of *o*-bromoaniline with vinylstannanes could not be effected under the standard reaction conditions.[11] Because it was possible that the product was forming a strong complex with the catalyst and thereby suppressing its reactivity, the amine was protected as the *p*-toluenesulfonamide. The coupling reaction of tosyl-protected aniline **7** with tributylvinylstannane in refluxing toluene with 2% tetrakis(triphenylphosphine)palladium gave a 70% yield of the *o*-vinylaniline. The 2-bromo-3-substituted anilines were similarly tosylated, as were the commercially available 2-bromo-4-chloroaniline, 2,4-dibromoaniline, and 2,5-dibromoaniline, and the coupling reactions were carried out (Table II). Generally these styrene derivatives were marginally stable, so they were not purified, but cyclized directly.

Table I. Reduction of 2-Bromonitrobenzenes



nitroaromatic	R	yield of 6 (%)
2a	CH_3	**b** 95
2b	OH	**c** 76
3	$CH(OAc)_2$	**d** 44
4	CO_2Me	**e** 86
5a	OCH_3	**f** 88
5b	OAc	**g** 93

Table II. Coupling Reactions of *o*-Bromoanilines[a]

aniline	R	yield (%) of tosylate	yield (%)[a] of *o*-vinylaniline
6a	H	**7a** 73	**8a** 70
6b	3-CH_3	**7b** 84	**8b** 63
6c	3-OH	**7c** 78	**8c** *b*
6d	3-$CH(OAc)_2$	**7d** 94	**8d** 86
6e	3-CO_2Me	**7e** 61	**8e** 60
6f	3-OCH_3	**7f** 72	**8f** 73
6g	3-OAc	**7g** 60	**8g** 57
6h	4-Cl	**7h** 79	**8h** 82
9a	4-Br	**10a** 79	**11a** 52[c]
9b	5-Br	**10b** 84	**11b** 50[c]

[a] Reactions carried out in refluxing toluene with tosylate of tributylvinylstannane and 2 mol % tetrakis(triphenylphosphine)palladium for ~24 h. [b] Only starting material was recovered. [c] 2.25 equiv of tributylvinylstannane gave the bis(ethenyl)-*N*-tosylanilines.

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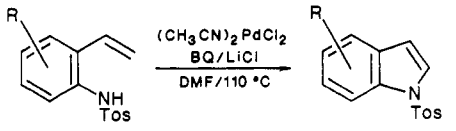
Table III. Cyclization of Vinylanilines to Indoles[a]

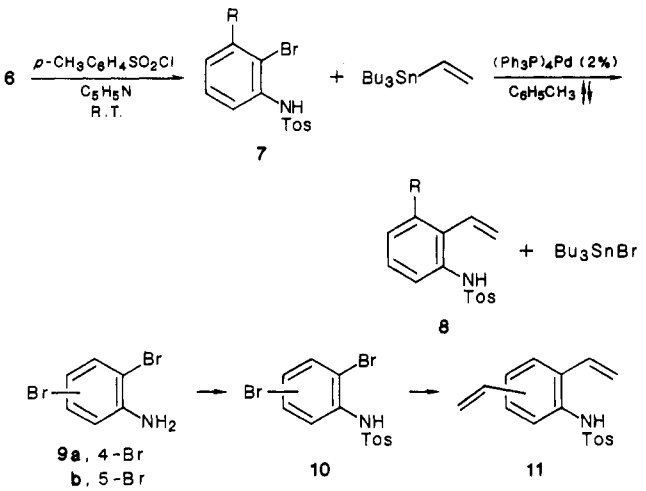


8 16

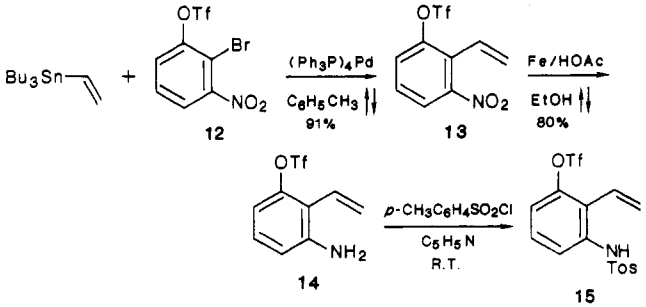
vinylaniline	R (indole 16)	yield (%)
8a	**16a** H	48
8b	**16b** 4-CH_3	87
8d	**16d** 4-$CH(OAc)_2$	60
8e	**16e** 4-CO_2CH_3	49
8f	**16f** 4-OCH_3	68
8g	**16g** 4-OAc	58
8h	**16h** 5-Cl	78
11a	**16i** 5-CH=CH_2	59
11b	**16j** 6-CH=CH_2	47
15	**16k** 4-OSO_2CF_3	88

[a] Reactions were carried out with the vinylaniline, 2 equiv of *p*-benzoquinone and 10 mol % bis(acetonitrile)dichloropalladium(II) and a 10 mol excess of lithium chloride in DMF at 100 °C.

In the case of 2,4-dibromoaniline and 2,5-dibromoaniline (**10**) vinylation took place at both positions; 2.25 equiv of tin reagent produced moderate yields of divinylanilines **11**.



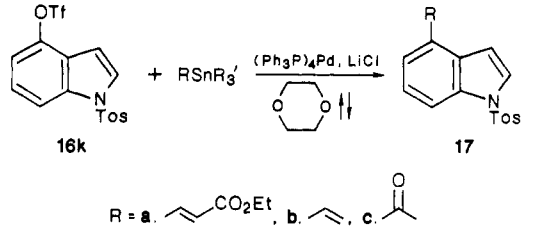
The failure of the vinylation reaction to occur with **6c**, containing the free phenolic group, possibly could be attributed to complexation of the catalyst by the *o*-vinylphenol ligand in the product. The vinylation of the triflate of 2-bromo-3-nitrophenol (**12**) gave an excellent yield of the corresponding triflate of 3-nitro-2-vinylphenol (**13**), which was reduced to the aniline **14** and then protected as the tosylate **15**.



Cyclization reactions of these vinylanilines to the corresponding indoles was carried out with a palladium(II) catalyst in the presence of *p*-benzoquinone as a reoxidant[5] (Table III).

Indole **16k** containing the triflate group proved to be very useful as an entry to a variety of 4-substituted indoles.

Table IV. Coupling Reactions of Indole Triflate 16k[a]



tin reagent		indole 17	yield (%)
R	R′		
CO_2Et	*n*-Bu	**a**	88
	n-Bu	**b**	86
OEt	Me	**c**	44[bc]

[a] Reactions were carried out with ~0.5 mmol of **16k** and tin reagent in the presence of LiCl tetrakis(triphenylphosphine)palladium (catalyst) in refluxing dioxane for 24 h. [b] Starting material (40%) was recovered. [c] The product hydrolyzed on workup to give R = $COCH_3$.

Utilizing a procedure developed for coupling reactions of vinyl triflates[17] and aryl triflates,[18] **16k** was converted to the 4-substituted indoles (**17**, Table IV).

Hydrolysis of the tosyl group could be carried out to yield the free indole in high yield by using sodium hydroxide in refluxing methanol.[19] For example, **16b,f,g,h** were hydrolyzed to the indoles in 96%, 82%, 83%, and 75% yields, respectively. In the case of **16g**, the acetate was also hydrolyzed.

Thus a mild, efficient method for the synthesis of indoles has been developed that utilizes the palladium-catalyzed coupling reaction of organotin reagents. This coupling not only provides a key intermediate in the construction of the indole ring system itself but also allows the introduction of a variety of substituents at the 4-position of the indole ring.

Experimental Section

General. Proton NMR spectra were obtained on a Varian T-60 spectrometer. Infrared spectra were obtained as thin films on sodium chloride plates on a Beckman 4250. Elemental analysis were performed by Atlantic Microlab, Inc., Atlanta, GA. Melting points were determined on a Mel-temp apparatus and are uncorrected.

Toluene, *N,N*-dimethylformamide, and dioxane were distilled from calcium hydride prior to use. Pyridine was distilled prior to use, with approximately 10% forerun being discarded. All reactions were run under an inert atmosphere.

2-Bromo-3-nitrotoluene (2a). 2-Amino-3-nitrotoluene (5.00 g, 32.9 mmol) was dissolved in 30 mL of H_2O and 15 mL of 1,4-dioxane and heated to reflux. Hydrobromic acid (17 mL, 48%) was added dropwise over a 20-min period, after which the mixture was heated at reflux an additional 15 min. The reaction was cooled to 0 °C (ice bath), and sodium nitrite (2.22 g, 32.9 mmol) in 20 mL of H_2O was added dropwise over a 30-min period, followed by stirring 15 min at 0 °C. The mixture was transferred to a jacketed addition funnel at 0 °C and added dropwise to a stirring solution of copper(I) bromide (5.42 g, 37.8 mmol) in 30 mL of H_2O and 17 mL of hydrobromic acid (48%) at 0 °C. The reaction was stirred for 15 min at 0 °C, warmed to 60 °C, stirred for 15 min, then cooled to room temperature, and stirred overnight. The reaction mixture was transferred to a separatory funnel and extracted with three 150-mL portions of diethyl ether. The

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extracts were dried over Na_2SO_4, concentrated in vacuo, and chromatographed on silica gel to yield **2a** (6.90 g, 31.9 mmol, 97%) as a yellow solid: mp 39–40 °C (lit.[20] mp 41–42 °C); NMR ($CDCl_3$) δ 2.55 (s, 3 H), 7.35–7.62 (m, 3 H); IR ($CDCl_3$) cm^{-1} 3080, 2980, 2880, 1590, 1375.

2-Bromo-3-nitrophenol (2b). This compound was prepared from 2-amino-3-nitrophenol by the method described for **2a** on a 162-mmol scale to give 19.6 g (89.9 mmol, 55%) of a product as a white solid: mp 115–116 °C (lit.[21] mp 117–118 °C); NMR ($CDCl_3$) δ 6.10 (s, 1 H), 7.25–7.60 (m, 3 H); IR ($CDCl_3$) cm^{-1} 3400, 3080, 1590.

2-Bromo-3-(diacetoxymethyl)nitrobenzene (3). 2-Bromo-3-nitrotoluene (**2a**) (7.78 g, 36 mmol) was dissolved in 40 mL of acetic anhydride at 0 °C under argon. Concentrated sulfuric acid (8 mL) was added. Chromium trioxide (10.0 g, 100 mmol) was added dropwise as a solution in 50 mL of acetic anhydride. The mixture was stirred at 0–10 °C for 3 h, poured over 30-mL of crushed ice, diluted with 150 mL of water, and allowed to stand overnight. The mixture was extracted with four 150-mL portions of ethyl ether. The extracts were combined, washed with 150 mL each of water and brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatography on silica gel using 3:1 hexane/ethyl acetate as eluent gave 2.1 g (27%) of starting material and 2.26 g (6.81 mmol, 19%) of **3** (26% based on unrecovered starting material) as a solid: mp 73.5–76 °C; NMR ($CDCl_3$) δ 2.20 (s, 6 H), 7.45–7.90 (m, 3 H), 7.97 (s, 1 H); IR ($CDCl_3$) cm^{-1} 3150, 3080, 2990, 1780, 1540. Anal. Calcd for $C_{11}H_{10}BrNO_6$: C, 39.78; H, 3.04. Found: C, 39.85; H, 3.07.

Methyl 2-Bromo-3-nitrobenzoate (4). To a solution of 2-bromo-3-nitrotoluene (**2a**) (4.73 g, 21.9 mmol) dissolved in 110 mL of H_2O was added 10.38 g (65.7 mmol) of potassium permanganate, and the mixture was heated at reflux 5 h. The reaction was cooled, filtered, and digested five times with 100-mL portions of 0.10 N NaOH. The filtrates were combined, acidified to pH 2 with concentrated HCl, and extracted with two 200-mL portions of ethyl ether. The ethereal solution was dried (Na_2SO_4), concentrated in vacuo, dissolved in 50 mL of methanol containing 1.0 mL of concentrated H_2SO_4, and heated at reflux 2 h. Solvent was removed in vacuo, and the residue was chromatographed on silica gel to yield 857 mg (3.3 mmol, 15%) of **4** as a crystalline solid: mp 78–79 °C (lit.[22] mp 78–78.5 °C); NMR ($CDCl_3$) δ 3.98 (s, 3 H), 7.85 (dd, J = 1.7, 7.7 Hz, 1 H), 7.76 (dd, J = 1.8, 7.9 Hz, 1 H), 7.52 (t, J = 7.7, 7.9 Hz, 1 H); IR ($CDCl_3$) cm^{-1} 3060, 2990, 1740, 1720, 1450, 1370.

2-Bromo-3-nitroanisole (5a). 2-Bromo-3-nitrophenol (**2b**) (5.00 g, 22.9 mmol) was dissolved in 50 mL of ethanol. Dimethyl sulfate (3.18 g, 2.4 mL, 25.2 mmol) and aqueous sodium hydroxide (2.5 N, 11 mL, 27.5 mmol) were added, and the mixture was stirred at room temperature for 14 h. The resulting precipitate was filtered to yield a tan solid: mp 91–93 °C (lit.[23] mp 93–94 °C); NMR ($CDCl_3$) δ 3.97 (s, 3 H), 6.95–7.22 (m, 3 H); IR ($CDCl_3$) cm^{-1} 3060, 2985, 1600, 1530, 1370.

2-Bromo-3-acetoxynitrobenzene (5b). 2-Bromo-3-nitrophenol (**2b**) (5.00 g, 22.9 mmol) was dissolved in 150 mL of dichloromethane at room temperature under argon. Acetic anhydride (10.8 mL, 115 mmol), triethyl amine (19.2 mL, 138 mmol), and 4-(dimethylamino)pyridine (560 mg, 4.60 mmol) were added. The mixture was stirred for 10 h, quenched with 5 mL of methanol, and diluted with 150 mL of diethyl ether. The ether solution was washed sequentially with 100-mL portions of water, 1 N HCl, saturated $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated in vacuo to yield **5b** (2.66 g, 10.2 mmol, 44%) as a waxy solid: mp 64–68 °C; NMR ($CDCl_3$) δ 2.41 (s, 3 H), 7.12–7.75 (m, 3 H); IR ($CDCl_3$) cm^{-1} 3080, 2920, 1770, 1585, 1365. The compound rapidly decomposed upon exposure to light.

2-Bromo-3-nitrophenyl Trifluoromethanesulfonate (12). 2-Bromo-3-nitrophenol (**2b**) (10.9 g, 50 mmol) and pyridine (4.74 g, 60 mmol) were dissolved in 120 mL of methylene chloride. The mixture was cooled to 0 °C under argon, and triflic anhydride (15.51 g, 55 mmol) was added dropwise. The mixture was slowly warmed to room temperature and stirred for 24 h. The reaction was diluted with 150 mL of methylene chloride, washed with three 100-mL portions of H_2O, dried over Na_2SO_4, and concentrated in vacuo. Chromatography on silica gel using 3:1 hexane/ethyl acetate afforded 9.5 g (27 mmol, 54%) of **12**: NMR ($CDCl_3$) δ 7.52–7.93 (m, 3 H); IR ($CDCl_3$) cm^{-1} 3020, 2980, 1530, 1420, 1350. Anal. Calcd for $C_7H_3BrF_3NO_5S$: C, 24.02; H, 0.86. Found: C, 24.16; H, 0.90.

2-Bromo-3-aminotoluene (6b). 2-Bromo-3-nitrotoluene (**2a**) (2.84 g, 13.1 mmol) was dissolved in 35 mL each of glacial acetic acid and absolute ethanol. Iron powder (3.00 g, 53.7 mmol) was added and the solution was heated at reflux for 3.5 h. The mixture was diluted with 100 mL of H_2O and neutralized with solid Na_2CO_3. The solution was extracted with three 50-mL portions of dichloromethane. The extracts were dried (Na_2SO_4), concentrated in vacuo, and chromatographed on silica gel by using 5:1 hexane/ethyl acetate as eluent to yield **6a** as a pale yellow oil (2.34 g, 12.6 mmol, 95%): NMR ($CDCl_3$) δ 2.33 (s, 3 H), 4.02 (br s, 2 H), 6.61 (m, 2 H), 6.98 (t, 1 H, J = 7 Hz); IR ($CDCl_3$) cm^{-1} 3480, 3390, 3060, 2980, 1620, 1600, 1470. The IR matched the published data.[24]

2-Bromo-3-aminophenol (6c). This compound was prepared from 2-bromo-3-nitrophenol (**2b**) by the method described above on a 6.88-mmol scale in 58% yield: mp 88–89.5 °C; NMR ($CDCl_3$) δ 4.20 (br s, 3 H), 6.35–6.60 (m, 2 H), 7.01 (t, 1 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3530, 3400, 2980, 1640, 1600, 1465.

2-Bromo-3-(diacetoxymethyl)aniline (6d). This compound was prepared from 2-bromo-3-(diacetoxymethyl)nitrobenzene (**3**) by the method described above on a 5.12-mmol scale to yield 44% of **6c** as a pale yellow wax: NMR ($CDCl_3$) δ 2.16 (s, 3 H), 4.25 (br s, 2 H), 6.80 (dd, 1 H, J = 8 Hz, 2 Hz), 6.92 (dd, 1 H, J = 8 Hz, 2 Hz), 7.15 (t, 1 H, J = 8 Hz), 7.98 (s, 1 H); IR ($CDCl_3$) cm^{-1} 3480, 3380, 3040, 2975, 1755, 1615, 1470. Anal. Calcd for $C_{11}H_{12}BrNO_4$: C, 43.73; H, 4.03. Found: C, 43.82; H, 4.04.

Methyl 2-Bromo-3-aminobenzoate (6e). This compound was prepared from methyl 2-bromo-3-nitrobenzoate (**4**) on a 3.85-mmol scale to yield 86% of **6d** as a pale yellow oil: NMR ($CDCl_3$) δ 3.95 (s, 3 H), 4.42 (br s, 2 H), 6.75–7.22 (m, 3 H); IR ($CDCl_3$) cm^{-1} 3480, 3380, 3020, 2950, 1735, 1620, 1565, 1440.

2-Bromo-3-aminoanisole (6f). This compound was prepared by the method described above from 2-bromo-3-nitroanisole (**5a**) on a 2.60-mmol scale to give **6e** in 88% yield: NMR ($CDCl_3$) δ 3.87 (s, 3 H), 4.21 (br s, 2 H), 6.25 (dd, 1 H, J = 8 Hz, 2 Hz), 6.37 (dd, 1 H, J = 8 Hz, 2 Hz), 7.00 (t, 1 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3480, 3380, 3000, 2960, 1615, 1519, 1470, 1435; mp (HCl salt) 198–200 °C (lit.[24] mp 201–202 °C).

2-Bromo-3-acetoxyaniline (6g). This compound was prepared as described above from 2-bromo-3-acetoxynitrobenzene (**5b**) on an 8.65-mmol scale in 93% yield: NMR ($CDCl_3$) δ 2.37 (s, 3 H), 4.22 (br s, 2 H), 6.28–6.59 (m, 2 H), 7.00 (t, 1 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3480, 3380, 3000, 1765, 1670, 1620, 1470.

2-Bromo-*N*-tosylaniline (7a). 2-Bromoaniline (1.72 g, 10.0 mmol) and *p*-toluenesulfonyl chloride (1.91 g, 10.0 mmol) were dissolved in 15 mL of pyridine under argon. The mixture was stirred for 6 h at room temperature, and the solvent was distilled at aspirator pressure. The residue was chromatographed on silica gel by using 3:1 hexane/ethyl acetate as eluent to yield 2.4 g (73%) of **7a** as a white solid: mp 94–95 °C; NMR ($CDCl_3$) δ 2.28 (s, 3 H), 6.85–7.80 (envelope, 9 H); IR ($CDCl_3$) cm^{-1} 3320, 3260, 3100, 2920, 1580, 1475. Anal. Calcd for $C_{13}H_{12}BrNO_2S$: C, 47.86; H, 3.71. Found: C, 47.80; H, 3.75.

2-Vinyl-*N*-tosylaniline (8a). 2-Bromo-*N*-tosylaniline (**7a**) (2.60 g, 7.97 mmol) and tributylvinyltin (2.53 g, 7.97 mmol) were dissolved in 50 mL of toluene under argon. Tetrakis(triphenylphosphine)palladium(0) (184 mg, 2 mol %) was added, and the reaction was heated at reflux for 22 h. The mixture was cooled and concentrated in vacuo, and the residue was partitioned between 25 mL each of acetonitrile and hexane. The acetonitrile layer was removed, concentrated in vacuo, and chromatographed on silica gel to yield 1.52 g (5.57 mmol, 70%) of **8a** as a white solid: mp 121–123 °C; NMR ($CDCl_3$) δ 2.18 (s, 3 H), 5.23 (dd, 1 H, J = 10 Hz, 2 Hz), 5.33 (dd, 1 H, J = 17 Hz, 2 Hz), 6.67 (dd, 1 H, J = 17 Hz, 10 Hz), 7.08–7.46 (envelope, 7 H), 7.65 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3360, 3270, 3060, 2980, 1620, 1595, 1480.

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Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53. Found: C, 65.80; H, 5.56.

2-Bromo-3-methyl-*N*-tosylaniline (7b). This compound was prepared from 2-bromo-3-methylaniline (**6b**) by the method described for 2-bromo-*N*-tosylaniline (**7a**) on a 12.6-mmol scale in 84%. The product was a white crystalline solid: mp 106–108 °C; NMR ($CDCl_3$) δ 2.27 (s, 3 H), 2.32 (s, 3 H), 6.96–7.38 (envelope, 5 H), 7.41 (d, 1 H, J = 2 Hz); IR ($CDCl_3$) cm^{-1} 3340, 3060, 2980, 1590, 1460. Anal. Calcd for $C_{14}H_{14}BrNO_2S$: C, 49.42; H, 4.15. Found: C, 49.34; H, 4.20.

2-Bromo-3-hydroxy-*N*-tosylaniline (7c). This compound was prepared from 2-bromo-3-hydroxyaniline (**6c**) by the method described above on a 3.2-mmol scale in 78% yield. The product was a white crystalline solid: 114–116 °C; NMR ($CDCl_3$) δ 2.40 (s, 3 H), 6.41 (dd, 1 H, J = 9 Hz, 2 Hz), 6.72 (dd, 1 H, J = 6 Hz, 3 Hz), 6.87 (dd, 1 H, J = 9 Hz, 2 Hz), 7.18 (m, 2 H), 7.21 (d, 2 H, J = 8 Hz), 7.67 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3400, 2980, 1740, 1700, 1620, 1575, 1490, 1465. Anal. Calcd for $C_{13}H_{12}BrNO_3S$: C, 45.62; H, 3.53. Found: C, 45.58; N, 3.57.

2-Bromo-3-(diacetoxymethyl)-*N*-tosylaniline (7d). This compound was prepared as described above from 2-bromo-3-(diacetoxymethyl)aniline (**6d**) on a 2.25-mmol scale in 94% yield. The compound was a tan solid: mp 110–113 °C; NMR ($CDCl_3$) δ 2.09 (s, 6 H), 2.37 (s, 3 H), 7.10–7.35 (envelope, 5 H), 7.55–7.82 (envelope, 3 H), 7.78 (s, 1 H); IR ($CDCl_3$) cm^{-1} 3330, 3260, 2980, 1765, 1620, 1600, 1460, 1370. Anal. Calcd for $C_{13}H_{12}BrNO_3S$: C, 45.62; H, 3.53. Found: C, 46.08; H, 3.67. Anal. Calcd for $C_{18}H_{18}BrNO_6S$: C, 47.38; H, 3.98. Found: C, 47.75; H, 3.92.

2-Bromo-3-carbomethoxy-*N*-tosylaniline (7e). This compound was prepared as described above from methyl 2-bromo-3-aminobenzoate (**6e**) on a 7.50-mmol scale in 61% yield. The product was a white crystalline solid: mp 115–117 °C; NMR ($CDCl_3$) δ 2.37 (s, 3 H), 3.86 (s, 3 H), 7.10 (br s, 1 H), 7.28 (d, 2 H, J = 8 Hz), 7.32 (m, 2 H), 7.65 (d, 2 H, J = 8 Hz), 7.75 (dd, 1 H, J = 6 Hz, 2 Hz); IR ($CDCl_3$) cm^{-1} 3320, 3260, 3020, 2950, 1730, 1595, 1570, 1450. Anal. Calcd for $C_{15}H_{14}BrNO_4S$: C, 46.89; H, 3.67. Found: C, 47.04; H, 3.76.

2-Bromo-3-methoxy-*N*-tosylaniline (7f). This compound was prepared as described above from 2-bromo-3-methoxyaniline (**6f**) on an 8.65-mmol scale in 72% yield. The product was a white crystalline solid: mp 110–112 °C; NMR ($CDCl_3$) δ 2.38 (s, 3 H), 3.80 (s, 3 H), 6.48 (dd, 1 H, J = 6 Hz, 3 Hz), 6.99–7.38 (envelope, 5 H), 7.66 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3330, 3005, 2950, 1590, 1575, 1470. Anal. Calcd for $C_{14}H_{14}BrNO_3S$: C, 47.20; H, 3.96. Found: C, 47.30; H, 4.00.

2-Bromo-3-acetoxy-*N*-tosylaniline (7g). This compound was prepared from 2-bromo-3-acetoxyaniline (**6g**) on an 8.04-mmol scale in 60% yield. The product was a white solid: mp 101–103 °C; NMR ($CDCl_3$) δ 2.36 (s, 3 H), 2.41 (s, 3 H), 6.82 dd, 1 H, J = 8 Hz, 2 Hz), 7.02–7.56 (envelope, 5 H), 7.62 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3350, 3040, 3020, 2950, 1770, 1595, 1460. Anal. Calcd for $C_{15}H_{14}BrNO_4S$: C, 46.89; H, 3.67; N, 3.65. Found: C, 46.87; H, 3.68; N, 3.62.

2-Bromo-4-chloro-*N*-tosylaniline (7h). This compound was prepared as described above from 2-bromo-4-chloroaniline (**6h**) on a 20-mmol scale in 83% yield. The product was a white crystalline solid: mp 120–122 °C; NMR ($CDCl_3$) δ 2.42 (s, 3 H), 6.93–7.81 (envelope, 8 H); IR ($CDCl_3$) cm^{-1} 3340, 3000, 2920, 1610, 1595, 1475. Anal. Calcd for $C_{13}H_{11}BrClNO_2S$: C, 43.29; H, 3.07. Found: C, 43.53; H, 2.99.

2,4-Dibromo-*N*-tosylaniline (10a). This compound was prepared as described above from 2,4-dibromoaniline (**9a**) on a 10-mmol scale to yield 79% of **10a** as a white crystalline solid: mp 107–109 °C; NMR ($CDCl_3$) δ 2.02 (s, 3 H), 6.55–7.35 (envelope, 8 H); IR ($CDCl_3$) cm^{-1} 3340, 2940, 1580, 1470. Anal. Calcd for $C_{13}H_{11}Br_2NO_2S$: C, 38.54; H, 2.74. Found: C, 38.49; H, 2.75.

2,5-Dibromo-*N*-tosylaniline (10b). This compound was prepared as described above from 2,5-dibromoaniline (**9b**) on a 9.12-mmol scale to give 84% of **10b** as an off-white solid: mp 101–103 °C; NMR ($CDCl_3$) δ 2.43 (s, 3 H), 6.81–7.46 (envelope, 5 H), 7.66 (d, 2 H, J = 8 Hz), 7.80 (d, 1 H, J = 2 Hz); IR ($CDCl_3$) cm^{-1} 3330, 2940, 2920, 1590, 1570, 1465. Anal. Calcd for $C_{13}H_{11}Br_2NO_2S$: C, 38.54; H, 2.74. Found: C, 38.39; H, 2.77.

2-Vinyl-3-methyl-*N*-tosylaniline (8b). 2-Bromo-3-methyl-*N*-tosylaniline (**7b**) (1.00 g, 2.94 mmol) and tributylvinyltin (929 mg, 2.94 mmol) were dissolved in 30 mL of toluene under argon. Tetrakis(triphenylphosphine)palladium(0) (70 mg, 0.06 mmol) was added and the reaction was heated at reflux for 36 h. The mixture was cooled and concentrated in vacuo, and the residue was partitioned between 25 mL each of hexane and acetonitrile. The acetonitrile layer was removed, filtered through 2 g of silica gel to remove palladium, and concentrated in vacuo to yield **8b** as a yellow oil, which was carried on without further purification to 4-methyl-*N*-tosylindole (**16b**): NMR ($CDCl_3$) δ 2.12 (s, 3 H), 2.39 (s, 3 H), 5.08 (dd, 1 H, J = 17 Hz, 2 Hz), 5.60 (dd, 1 H, J = 11 Hz, 2 Hz), 6.36 (dd, 1 H, J = 17 Hz, 11 Hz), 6.98–7.43 (envelope, 6 H), 7.68 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3360, 2980, 1600, 1580, 1430, 1385.

2-Vinyl-3-(diacetoxymethyl)-*N*-tosylaniline (8d). This compound was prepared as described above from 2-bromo-3-(diacetoxymethyl)-*N*-tosylaniline (**7d**) on a 1.76-mmol scale in 86% yield: NMR ($CDCl_3$) δ 2.06 (s, 6 H), 2.40 (s, 3 H), 5.12 (dd, 1 H, J = 17 Hz, 2 Hz), 5.63 (dd, 1 H, J = 11 Hz, 2 Hz), 6.38 (dd, 1 H, J = 17 Hz, 11 Hz), 6.95–7.38 (envelope, 4 H), 7.36 (s, 1 H), 7.55–7.82 (m, 3 H), 7.62 (s, 1 H); IR ($CDCl_3$) cm^{-1} 3350, 3280, 3020, 1765, 1615, 1595, 1460.

2-Vinyl-3-carbomethoxy-*N*-tosylaniline (8e). This compound was prepared as described above from 2-bromo-3-carbomethoxy-*N*-tosylaniline (**7e**) on a 1.77-mmol scale in 60% crude yield: NMR ($CDCl_3$) δ 2.35 (s, 3 H), 3.93 (s, 3 H), 4.88 (dd, 1 H, J = 18 Hz, 2 Hz), 5.40 (dd, 1 H, J = 11 Hz, 2 Hz), 6.45 (dd, 1 H, J = 18 Hz, 11 Hz), 7.01–7.85 (envelope, 8 H); IR ($CDCl_3$) cm^{-1} 3260, 3080, 2950, 1725, 1630, 1595, 1475.

2-Vinyl-3-methoxy-*N*-tosylaniline (8f). This compound was prepared as described above from 2-bromo-3-methoxy-*N*-tosylaniline (**7f**) on a 2.44-mmol scale to give 73% of crude product as a yellow oil: NMR ($CDCl_3$) δ 2.38 (s, 3 H), 3.71 (s, 3 H), 5.25 (dd, 1 H, J = 18 Hz, 2 Hz), 5.42 (dd, 1 H, J = 9 Hz, 2 Hz), 6.15–6.68 (envelope, 2 H), 6.98–7.35 (envelope, 5 H), 7.82 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3340, 3005, 2960, 2840, 1600, 1585, 1470.

2-Vinyl-3-acetoxy-*N*-tosylaniline (8g). This compound was prepared as described above from 2-bromo-3-acetoxy-*N*-tosylaniline (**7g**) on a 1.50-mmol scale to give 57% of crude product as a viscous yellow-brown oil: NMR ($CDCl_3$) δ 2.23 (s, 3 H), 2.42 (s, 3 H), 5.22 (dd, 1 H, J = 17 Hz, 2 Hz), 5.44 (dd, 1 H, J = 10 Hz, 2 Hz), 6.18 (dd, 1 H, J = 17 Hz, 10 Hz), 6.65–7.40 (envelope, 6 H), 7.59 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3460, 3270, 3050, 1765, 1615, 1590, 1455.

2-Vinyl-4-chloro-*N*-tosylaniline (8h). This compound was prepared from 2-bromo-4-chloro-*N*-tosylaniline (**7h**) on a 1.00-mmol scale to give 82% of product as a pale yellow oil: NMR ($CDCl_3$) δ 2.43 (s, 3 H), 5.30 (dd, 1 H, J = 11 Hz, 2 Hz), 5.52 (dd, 1 H, J = 17 Hz, 2 Hz), 6.62 (dd, 1 H, J = 17 Hz, 11 Hz), 6.85 (br s, 1 H), 7.19–7.50 (envelope, 5 H), 7.68 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3360, 3260, 2980, 1595, 1475.

2,4-Divinyl-*N*-tosylaniline (11a). This compound was prepared as described above from 2,4-dibromo-*N*-tosylaniline (**10a**) and 2.25 equiv of tributylvinyltin on a 4.00-mmol scale in 52% crude yield. The compound was a pale yellow oil: NMR ($CDCl_3$) δ 2.35 (s, 3 H), 5.10–5.82 (envelope, 4 H), 6.32–6.95 (envelope, 2 H), 6.88 (br s, 1 H), 7.05–7.42 (envelope, 5 H), 7.63 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3360, 2940, 1620, 1590, 1370.

2,5-Divinyl-*N*-tosylaniline (11b). This compound was prepared as described above from 2,5-dibromo-*N*-tosylaniline (**10b**) and 2.25 equiv of tributylvinyltin on a 2.81-mmol scale in 50% crude yield: NMR ($CDCl_3$) δ 2.41 (s, 3 H), 5.08–5.82 (envelope, 4 H), 6.25–6.83 (envelope, 3 H), 6.90–7.35 (envelope, 5 H), 7.62 (d, 2 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3355, 3250, 2985, 1615, 1590, 1485, 1405.

2-Vinyl-3-nitrophenyl Trifluoromethanesulfonate (13). To a solution of 2-bromo-3-nitrophenyl trifluoromethanesulfonate (**12**) (3.50 g, 10.0 mmol) and tributylvinyltin (3.17 g, 10.0 mmol) in 50 mL of toluene under argon was added tetrakis(triphenylphosphine)palladium(0) (25 mg, 0.02 mmol), and the reaction was heated at reflux for 48 h. The residue was concentrated in vacuo, partitioned between 50 mL each of hexane and acetonitrile, and the acetonitrile layer was concentrated in vacuo. Chromatography on silica gel using 4:1 hexane/ethylacetate as eluent afforded 2.7 g (9.1 mmol, 91%) of **13** as a waxy solid: NMR ($CDCl_3$) δ 5.57 (dd, 1 H, J = 17 Hz, 1.5 Hz), 5.78 (dd, 1 H, J = 5 Hz, 1.5 Hz), 6.79 (dd, 1 H, J = 17 Hz, 5 Hz), 7.42–7.75 (envelope, 2 H), 7.92 (dd, 1 H, J = 5 Hz, 2 Hz); IR ($CDCl_3$) cm^{-1} 3040, 2980, 1580, 1530,

1420, 1350. Anal. Calcd for $C_9H_6F_3NO_5S$: C, 36.36; H, 2.02. Found: C, 35.64; H, 2.27.

2-Vinyl-3-aminophenyl Trifluoromethanesulfonate (14). This compound was prepared from 2-vinyl-3-nitrophenyl trifluoromethanesulfonate (**13**) by the method described for 2-bromo-3-aminotoluene (**6b**) on an 8.4-mmol scale in 80% yield. The crude yellow oil was carried directly on without purification.

2-Vinyl-3-(tosylamino)phenyl Trifluoromethanesulfonate (15). This compound was prepared from 2-vinyl-3-aminophenyl trifluoromethanesulfonate (**14**) by the method developed for 2-bromo-*N*-tosylaniline (**7a**) on a 6.37-mmol scale in 65% yield. The product was a slightly waxy solid: mp 72–74 °C; NMR ($CDCl_3$) δ 2.43 (s, 3 H), 5.40 (dd, 1 H, J = 17 Hz, 2 Hz), 5.82 (dd, 1 H, J = 11 Hz, 2 Hz), 6.27 (dd, 1 H, J = 17 Hz, 11 Hz), 6.93–7.98 (envelope, 8 H); IR ($CDCl_3$) cm^{-1} 3270, 2960, 1610, 1595, 1460. Anal. Calcd for $C_{16}H_{14}F_3NO_5S_2$: C, 45.60; H, 3.35; N, 3.32. Found: C, 45.65; H, 3.37; N, 3.32.

***N*-Tosylindole (16a).** 2-Vinyl-*N*-tosylaniline (**8a**) (273 mg, 1.00 mmol) was dissolved in 5 mL of *N*,*N*-dimethylformamide. The system was flushed with argon, and 26 mg (0.10 mmol) bis(acetonitrile)palladium dichloride, 216 mg (2.00 mmol) *p*-benzoquinone, and 445 mg (10 mmol) of lithium chloride were added. The mixture was heated at 100–110 °C for 28 h, cooled, diluted with 25 mL each of diethyl ether and water, and filtered through Florisil. The Florisil was washed with 100 mL of diethyl ether and the combined filtrates were washed with 50 mL each of water and brine. After drying (Na_2SO_4), the solution was concentrated in vacuo and the residue was chromatographed on silica gel to yield **16a** as a colorless solid that rapidly decomposed upon exposure to air to a red oil: NMR ($CDCl_3$) δ 2.35 (s, 3 H), 6.58 (d, 1 H, J = 4 Hz), 7.27 (d, 2 H, J = 9 Hz), 7.29 (d, 1 H, J = 9 Hz), 7.50 (d, 1 H, J = 2 Hz), 7.58 (d, 1 H, J = 4 Hz), 7.78 (d, 2 H, J = 9 Hz), 7.95 (br d, 1 H, J = 9 Hz); IR ($CDCl_3$) cm^{-1} 3010, 2960, 1585, 1435, 1370. The spectra match published data.[25]

4-Methyl-*N*-tosylindole (16b). This compound was prepared from 2-vinyl-3-methyl-*N*-tosylaniline (**8b**) by the method described above on a 0.73-mmol scale in 87% yield. The product was a white solid: mp 97–99 °C; NMR ($CDCl_3$) δ 2.35 (s, 3 H), 2.52 (s, 3 H), 6.74 (d, 1 H, J = 4 Hz), 7.22 (br d, 4 H, J = 8 Hz), 7.53–8.01 (envelope, 4 H); IR ($CDCl_3$) cm^{-1} 3020, 2920, 1595, 1520, 1480. Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.35; H, 5.30; N, 4.91. Found: C, 67.38; H, 5.34; N, 4.90.

4-(Diacetoxymethyl)-*N*-tosylindole (16d). This compound was prepared as described above from 2-vinyl-3-(diacetoxymethyl)-*N*-tosylaniline (**8d**) on a 1.37-mmol scale in 60% yield. The product was a white solid: mp 110–113 °C; NMR ($CDCl_3$) δ 2.18 (s, 6 H), 2.43 (s, 3 H), 7.03 (d, 1 H, J = 4 Hz), 7.18–7.56 (envelope, 4 H), 7.78 (m, 3 H), 8.03 (m, 1 H), 8.06 (m, 1 H); IR ($CDCl_3$) cm^{-1} 3010, 2920, 1765, 1595, 1430, 1370. Anal. Calcd for $C_{20}H_{19}NO_6S$: C, 59.85; H, 4.77. Found: C, 59.79; H, 4.82.

4-Carbomethoxy-*N*-tosylindole (16e). This compound was prepared as described above from 2-vinyl-3-carbomethoxy-*N*-tosylaniline (**8e**) on a 1.00-mmol scale in 49% yield. The compound was a white solid: mp 144–145.5 °C; NMR ($CDCl_3$) δ 2.28 (s, 3 H), 3.96 (s, 3 H), 7.06–7.33 (envelope, 4 H), 7.72 (m, 3 H), 7.94 (d, 1 H, J = 7 Hz), 8.23 (d, 1 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3130, 2950, 1715, 1600, 1440, 1420, 1375. Anal. Calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59. Found: C, 62.07; H, 4.82.

4-Methoxy-*N*-tosylindole (16f). This compound was prepared by the method described above from 2-vinyl-3-methoxy-*N*-tosylaniline (**8f**) on a 1.65-mmol scale in 68% yield. The product was a white solid: mp 123–124 °C; NMR ($CDCl_3$) δ 2.33 (s, 3 H), 3.88 (s, 3 H), 6.63 (d, 1 H, J = 8 Hz), 6.75 (d, 1 H, J = 3.5 Hz), 7.19–7.32 (envelope, 3 H), 7.46 (d, 1 H, J = 3.5 Hz), 7.57 (d, 1 H, J = 8.0 Hz), 7.74 (d, 2 H, J = 7.9 Hz); IR ($CDCl_3$) cm^{-1} 3410, 3000, 2950, 1600, 1590, 1460, 1370. Cyclization resulted in an impure product, which was hydrolyzed to yield 4-methoxyindole. Anal. Calcd for $C_{16}H_{15}NO_3S$: C, 63.77; H, 5.02. Found: C, 64.57; H, 5.26.

4-Acetoxy-*N*-tosylindole (16g). This compound was prepared as described above from 2-vinyl-3-acetoxy-*N*-tosylaniline (**8g**) on a 0.76-mmol scale in 58% yield. The product was a viscous tan oil that rapidly darkened upon exposure to air: NMR ($CDCl_3$) δ 2.25 (s, 3 H), 2.40 (s, 3 H), 6.52 (d, 1 H, J = 4 Hz), 6.96–7.38 (envelope, 4 H), 7.43–7.96 (envelope, 4 H); IR ($CDCl_3$) cm^{-1} 3140, 2950, 1765, 1595, 1480, 1425, 1370. Anal. Calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.63. Found: C, 61.95; H, 4.63.

5-Chloro-*N*-tosylindole (16h). This compound was prepared by the method described above from 2-vinyl-4-chloro-*N*-tosylaniline (**8h**) on a 0.50-mmol scale in 78% yield. The product was a yellow wax that rapidly darkened upon exposure to air: NMR ($CDCl_3$) δ 2.35 (s, 3 H), 6.58 (d, 1 H, J = 4 Hz), 7.27 (d, 2 H, J = 9 Hz), 7.29 (d, 1 H, J = 9 Hz), 7.50 (d, 1 H, J = 2 Hz), 7.58 (d, 1 H, J = 4 Hz), 7.78 (d, 2 H, J = 9 Hz), 7.95 (br d, 1 H, J = 9 Hz); IR ($CDCl_3$) cm^{-1} 3010, 2960, 1585, 1435, 1370.

5-Vinyl-*N*-tosylindole (16i). This compound was prepared from 2,4-divinyl-*N*-tosylaniline (**11a**) as described above on a 1.00-mmol scale to give 59% of product as a pale yellow oil: NMR ($CDCl_3$) δ 2.36 (s, 3 H), 5.23 (dd, 1 H, J = 10 Hz, 2 Hz), 5.75 (dd, 1 H, J = 17 Hz, 2 Hz), 6.62 (d, 1 H, J = 3 Hz), 6.69 (dd, 1 H, J = 17 Hz, 10 Hz), 7.04–8.16 (envelope, 8 H); IR ($CDCl_3$) cm^{-1} 3160, 2920, 1605, 1485, 1410, 1360. Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08. Found: C, 68.94, 5.11.

6-Vinyl-*N*-tosylindole (16j). This compound was prepared from 2,5-divinyl-*N*-tosylaniline (**11b**) as described above on a 0.57-mmol scale in 47% yield. The product was a yellow oil: NMR ($CDCl_3$) δ 2.32 (s, 3 H), 5.25 (dd, 1 H, J = 10 Hz, 2 Hz), 5.72 (dd, 1 H, J = 18 Hz, 2 Hz), 6.53 (d, 1 H, J = 4 Hz), 6.81 (dd, 1 H, J = 18 Hz, 10 Hz), 7.18 (d, 2 H, J = 8 Hz), 7.35–7.65 (envelope, 3 H), 7.72 (d, 2 H, J = 8 Hz), 7.96 (br s, 1 H); IR ($CDCl_3$) cm^{-1} 3140, 3050, 2940, 1620, 1595, 1470, 1420, 1370. Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08. Found: C, 68.87; H, 5.14.

4-[[(Trifluoromethyl)sulfonyl]oxy]-*N*-tosylindole (16k). This compound was prepared as described above from 2-vinyl-3-(tosylamino)phenyl trifluoromethanesulfonate (**15**) on a 1.66-mmol scale in 88% yield. The product was a pale yellow oil: NMR ($CDCl_3$) δ 2.37 (s, 3 H), 6.75 (d, 1 H, J = 4 Hz), 7.03–7.38 (envelope, 4 H), 7.63 (d, 1 H, J = 3 Hz), 7.78 (d, 2 H, J = 8 Hz), 8.02 (br d, 1 H, J = 7 Hz); IR ($CDCl_3$) cm^{-1} 3150, 2960, 1625, 1595, 1480, 1420, 1375. Anal. Calcd for $C_{16}H_{12}F_3NO_5S_2$: C, 45.82; H, 2.88. Found: C, 45.80; H, 2.90.

4-[(*E*)-2-Carbethoxyvinyl]-*N*-tosylindole (17a). 4-[[(Trifluoromethyl)sulfonyl]oxy]-*N*-tosylindole (**16k**) (195 mg, 0.46 mmol) was combined with ((*E*)-2-carbethoxyvinyl)tributyltin (195 mg, 0.50 mmol) and dissolved in 10 mL of dioxane. Tetrakis(triphenylphosphine)palladium(0) and lithium chloride (67 mg, 1.50 mmol) were added, and the mixture was heated at reflux for 24 h. The mixture was cooled, diluted with 50 mL of diethyl ether, and washed sequentially with 25-mL portions of water (3×), 10% saturated NaOH, and brine. The organic layer was dried (Na_2SO_4), concentrated in vacuo, and chromatographed on silica gel by using 3:1 hexane/ethylacetate as eluent to give 150 mg (0.41 mmol, 88%) of **17a** as a white solid: mp 125–126 °C; NMR ($CDCl_3$) δ 1.22 (t, 3 H, J = 7 Hz), 2.37 (s, 3 H), 4.35 (q, 2 H, J = 7 Hz), 6.46 (d, 1 H, J = 16 Hz), 6.85 (d, 1 H, J = 4 Hz), 7.05–8.10 (envelope, 9 H); IR ($CDCl_3$) cm^{-1} 3140, 2970, 1705, 1630, 1590, 1470, 1415, 1305. Anal. Calcd for $C_{20}H_{19}NO_4S$: C, 63.98; H, 5.10. Found: C, 64.15; H, 5.45.

4-Vinyl-*N*-tosylindole (17b). This compound was prepared as described above from 4-[[(trifluoromethyl)sulfonyl]oxy]-*N*-tosylindole (**16k**) and tributylvinyltin on a 1.1-mmol scale in 86% yield: NMR ($CDCl_3$) δ 2.24 (s, 3 H), 5.23 (dd, 1 H, J = 11 Hz, 2 Hz), 5.73 (dd, 1 H, J = 17 Hz, 2 Hz), 6.68 (d, 1 H, J = 4 Hz), 6.80 (dd, 1 H, J = 17 Hz, 11 Hz), 6.85–9.90 (envelope, 8 H); IR ($CDCl_3$) cm^{-1} 3120, 3050, 2940, 1620, 1595, 1470, 1370. The spectra match published data.[26]

4-Acetyl-*N*-tosylindole (17c). This compound was prepared as described above from 4-[[(trifluoromethyl)sulfonyl]oxy]-*N*-tosylindole (**16k**) and (ethoxyvinyl)trimethyltin, to give, upon hydrolytic workup, a 44% yield of product on a 0.69-mmol scale: mp 141–143 °C; NMR ($CDCl_3$) δ 2.42 (s, 3 H), 2.70 (s, 3 H), 7.06–7.90 (envelope, 8 H), 8.22 (d, 1 H, J = 8 Hz); IR ($CDCl_3$) cm^{-1} 3140, 2920, 1680, 1595, 1575, 1420, 1370. Anal. Calcd for $C_{17}H_{15}NO_3S$: C, 65.16; H, 4.82. Found: C, 65.01; H, 4.74.

4-Methylindole. 4-Methyl-*N*-tosylindole was dissolved in 5 mL each of 20% aqueous NaOH and methanol and heated at

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reflux 12 h. The methanol was removed in vacuo and the mixture was diluted with 25 mL of H_2O and extracted with three 25-mL portions of diethyl ether. The etherial extracts were concentrated to give 27 mg (0.21 mmol, 82%) of 4-methylindole: NMR ($CDCl_3$) δ 2.44 (s, 3 H), 6.43 (m, 1 H), 6.62–7.05 (envelope, 4 H), 7.3 (br s, 1 H); IR ($CDCl_3$) cm^{-1} 3480, 3410, 2940, 1590, 1510, 1465. Spectra match that of an authentic sample (Aldrich).

4-Methoxyindole. This compound was prepared as described above from 4-methoxy-*N*-tosylindole on a 0.43-mmol scale in 96% yield: NMR ($CDCl_3$) δ 3.85 (s, 3 H), 6.52 (m, 2 H), 6.71–7.20 (envelope, 3 H), 7.75 (br s, 1 H); IR ($CDCl_3$) cm^{-1} 3460, 3390, 2990, 1585, 1470. Spectra match that of an authentic sample (Aldrich).

4-Hydroxyindole. This compound was prepared as described above from 4-acetoxy-*N*-tosylindole on a 0.36-mmol scale in 83%: NMR ($CDCl_3$) δ 6.50 (m, 2 H), 6.65–7.25 (envelope, 3 H), 10.6 (br s, 2 H); IR ($CDCl_3$) cm^{-1} 3620, 3380, 1590, 1460. Spectra match literature data.[27]

5-Chloroindole. This compound was prepared as described above from 5-chloro-*N*-tosylindole on a 0.28-mmol scale in 75% yield: NMR ($CDCl_3$) δ 6.55 (m, 1 H), 6.95–7.25 (envelope, 3 H), 7.58 (br s, 1 H); IR ($CDCl_3$) cm^{-1} 3370, 1590, 1470, 1370. Spectra match that of an authentic sample (Aldrich).

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Lead Tetraacetate Mediated Oxidation of the Enamides Derived from 1-Benzyl-3,4-dihydroisoquinolines

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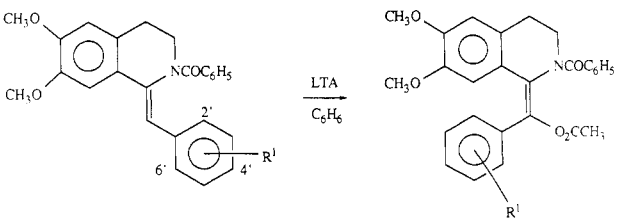
The products obtained from the lead tetraacetate (LTA) oxidation of *N*-acylbenzylidene isoquinoline enamides are a function of the type of carbonyl function in the enamide, the solvent, and the type of substitution on the benzylidene aromatic ring. The benzoyl enamides yield *Z*-β-acetoxy-substituted enamides. The ethoxycarbonyl enamides, containing electron-releasing substituents on the benzylidene ring, efficiently form oxazolones when oxidized with LTA in acetic acid. In the absence of electron-releasing substituents, ring opening occurs to form benzoin esters. When the same oxidation is conducted in benzene, the enamide double bond is converted into its diacetoxy derivative, which can undergo a variety of reactions. LTA oxidation of acetyl enamides results in cleavage of the acetyl group with ultimate formation of 1-benzoyl-3,4-dihydroisoquinolines and isoquinolines. Oxidation of the formyl enamide with LTA results in cleavage of the formyl group with formation of a variety of products. Most of these have an acetyl group in place of the original formyl and are the result of either cleavage of the benzylidene ring at the double bond, oxidation, and subsequent ring opening to a benzil or various other oxidative and rearrangement processes.

The photochemical reactions of enamides (acyl enamines) have been well studied and extensively employed in the total synthesis of various classes of alkaloids.[1,2] On the other hand, with the obvious exception of the Diels–Alder cycloadditions of enamides and dienamides,[2,3] the nonphotochemical reactivity of this grouping has been less thoroughly investigated. There are several reports on the oxidation of the enamide double bond, usually isolated instances in connection with a natural product synthesis. The enamide double bond has been oxyaminated,[4] oxidized to a variety of products with benzeneseleninic anhydride,[5] and oxidized to diketones with chromium trioxide.[6] Attempted epoxidation with peracids usually results in bond cleavage,[7] while thallium(III) oxidation can result in oxidative ring expansion.[8] Osmium tetraoxide results in formation of the glycol,[9] which can, in some instances, readily open to the hydroxy ketone.[10] Lead(IV) acetate has been reported to introduce a β-acetoxy group in steroidal enamides,[11] with the reaction occurring through the diacetoxy derivative.[9] This lead tetraacetate oxidation has been used to convert oxyprotoberberines to their acetoxy derivatives which were subsequently converted to the benzylisoquinoline alkaloids ophiocarpine and chile-

Table I



enamide	R^1	acetoxy enamide	yield, %
1	3′,4′-$(OCH_3)_2$	2	80
3	H	4	56[a]
5	4′-Cl	6	55[b]

[a] 16% recovered 3. [b] 15% recovered 5.

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