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Palladium-Catalyzed Reactions in the Synthesis of 3- and 4-Substituted Indoles. Approaches to Ergot Alkaloids

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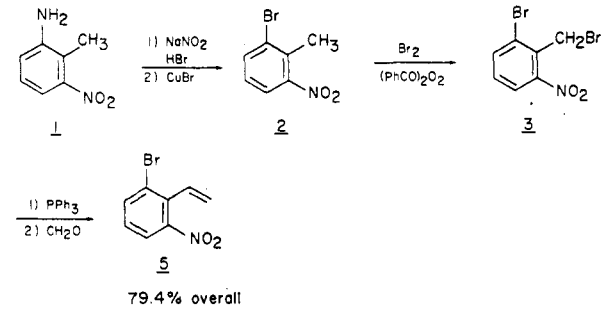
An efficient synthesis of 4-bromo-1-tosylindole (**10**) based on the Pd(II)-catalyzed cyclization of an *o*-ethenylaniline *p*-toluenesulfonamide has been developed. A Pd(0) oxidative addition–olefin insertion–β-hydride elimination cycle converted **10** to a number of 4-substituted 1-tosylindoles. Selective electrophilic substitutions at the 3-position of **10** provided access to the 3-(chloromercurio)- (**18**) and 3-iodo-1-tosylindoles (**22**). Transmetalation to palladium and allyl chloride insertion converted **18** to 3-allyl-4-bromo-1-tosylindole (**20**) which could be cyclized to the benz[*c*,*d*]indoline **21**. A Pd(0) oxidative addition–olefin insertion–β-hydride elimination cycle converted the 3-iodo compound **22** to a number of 4-bromo-3-substituted 1-tosylindoles including **24**, a potential precursor to optically active tryptophans.

The structural diversity, broad spectrum of biological properties, and clear-cut structure–activity relationships make the ergot alkaloids, metabolites of the parasitic fungus *Claviceps*, unique among the plant bases. In addition to the well-known hallucinogen lysergic acid diethylamide (LSD), ergots currently in clinical use are ergonovine and methylergonovine (postpartum hemorrhage), nicergoline (hypertension and poor peripheral and cerebral blood circulation), methysergide (migraine attacks), and 2-bromo-α-ergokryptine and lergotrile (prolactin disorders).[1]

It is apparent from the relative reactivities toward electrophilic substitution of the indole ring positions that the key to the synthesis of the ergoline framework is construction of a 4-substituted indole. This problem has been approached in a variety of ingenious ways[2] with the simplest and most versatile approach perhaps being the synthesis and utilization of indole-4-carboxaldehyde.[3,4]

4-Bromoindole should be useful in ergot synthesis in light of the well-established Pd(0)-catalyzed functionalization of aryl halides by the oxidative addition–olefin insertion–β-hydride elimination process developed by Heck.[5] This methodology is generally applicable to the condensation of aryl and heteroaryl iodides and bromides with a wide variety of olefins.

Scheme I



We have recently developed an indole synthesis based on the Pd(II)-catalyzed cyclization of *o*-aminostyrenes.[6] Herein we report an efficient synthesis of 4-bromoindole and the development of a variety of palladium-catalyzed reactions which functionalize both the 4- and 3-positions.

Results and Discussion

The approach to 3-bromo-2-ethenylaniline (**6**) necessary for a Pd(II)-catalyzed closure is shown in Scheme I. 2-Amino-6-nitrotoluene (**1**) was converted by a Sandmeyer reaction to the 2-bromo compound **2**.[7] Free-radical monobromination produced α,2-dibromo-6-nitrotoluene (**3**). Phosphonium salt formation and Wittig reaction with

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(2) Kozikowski, A. P. *Heterocycles* **1981**, *16*, 267.
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(6) Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. L. *J. Am. Chem. Soc.* **1978**, *100*, 5800.
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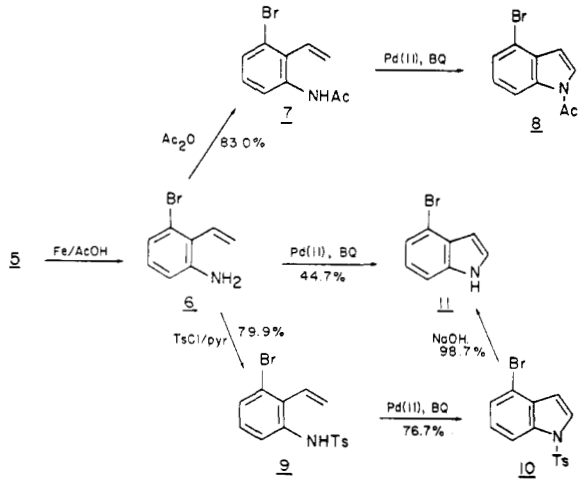
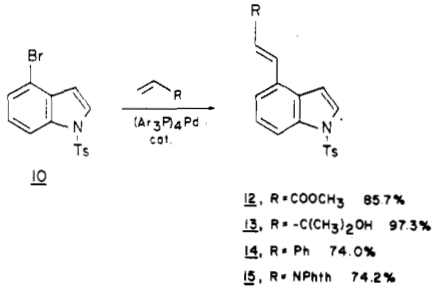
Scheme II



Scheme III



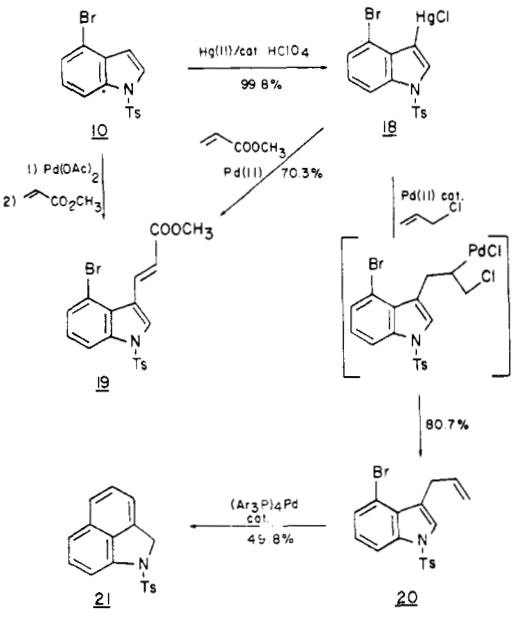
formaldehyde provided the styrene **5**. Reduction with iron in acetic acid produced the requisite aniline **6** contaminated with trace amounts of olefin-reduced material.

Although the previously reported Pd(II)-catalyzed cyclization of 2-ethenylaniline to indole was efficient (74%),[6] the analogous conversion of 3-bromo-2-ethenylaniline (**6**) to 4-bromoindole (**11**) was slow and inefficient due to indole degradation during the course of the cyclization. To circumvent this problem, N-protected anilines were prepared and subjected to catalytic cyclization (Scheme II).

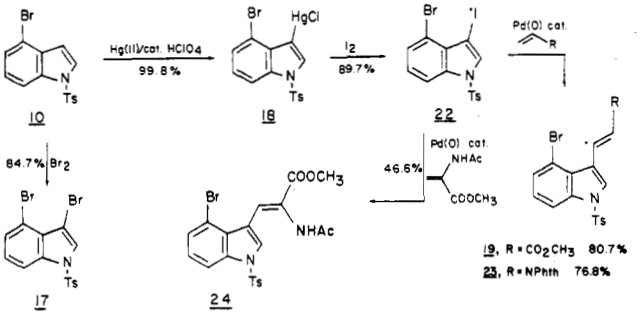
Acetylation of **6** produced the acetanilide **7**. However, the Pd(II)-catalyzed closure to **8** was slow with $Cu(OAc)_2$ and *very* slow with *p*-benzoquinone as reoxidants. Although *p*-toluenesulfonamides are not generally considered to be good nucleophiles, they are effective for attack on Pd(II)-coordinated olefins.[8] Tosylation of **6** produced the *p*-toluenesulfonamide **9**. Closure to 4-bromo-1-tosylindole (**10**) was considerably faster and, accordingly, much more efficient. This product was readily converted to the free indole **11**.

The Pd(0)-catalyzed introduction of carbon substituents at the 4-position was next examined. Since electron-deficient substrates are most efficient in the requisite oxidative addition process, and since both 5-bromoindole and 1-acetyl-3-bromoindole are poor substrates for Heck olefination with methyl acrylate,[9] tosylindole **10** rather than the free indole **11** was used. Efficient olefination with electron-deficient (methyl acrylate), neutral (styrene), and electron-rich (*N*-vinylphthalimide) olefins was observed (Scheme III). Insertion of 2-methyl-3-buten-2-ol produced the clavicipitic acid precursor **13**.[10] Extension of this methodology to more highly substituted olefins is likely

Scheme IV



Scheme V



to be limited since an increase in olefin substitution is accompanied by a decrease in its reactivity toward insertion.[11]

Although indoles themselves are generally reactive toward electrophiles at the 3-position, N-acylation or tosylation results in reduced reactivity. However, a direct stoichiometric palladation of *N*-acetyl- and *N*-benzoylindoles producing an aryl palladium intermediate capable of both carbon monoxide and olefin insertions has been reported.[12,13] The direct palladation–methyl acrylate insertion of **10** produced **19** in low yield but required a stoichiometric amount of $Pd(OAc)_2$. The process could not be made efficiently catalytic in palladium by using bezoquinone or $Cu(OAc)_2$ as reoxidants (Scheme IV).

Direct mercuration offers a synthetically versatile precursor to 3-substituted indoles.[14] Although no reaction was observed between 4-bromo-1-tosylindole (**10**) and mercuric acetate in glacial acetic acid at 25 °C or reflux, mercuration was rapid in the presence of a catalytic amount of 70% $HClO_4$. Stoichiometric transmetalation to palladium(II) followed by acrylate insertion produced **19** in good yield. Small amounts of **10** were also produced, probably by protolytic demercuration.

Aryl mercuric halides undergo Pd(II)-catalyzed insertion of allylic chlorides since β-elimination of PdCl regenerates the requisite Pd(II) species rather than Pd(0), as in ob-

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(11) Holton, R. A.; Kjonaas, R. A. *J. Organomet. Chem.* **1977**, *133*, C5.
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served with simple olefin insertions.[15] Indeed, treatment of 18 with allyl chloride and 3% Li_2PdCl_4 produced **20** in excellent yield.

3-Allyl-4-bromo-1-tosylindole (**20**) was converted via an intramolecular version of the Pd(0)-catalyzed oxidative addition–olefin insertion–β-hydride elimination process to the benz[*cd*]indoline **21**. Although N-acylation or tosylation has been reported to hinder isomerization to the more stable naphthalene, only **21** was observed in this reaction.

Bromination in the dark converted **10** to the 3,4-dibromo compound **17** (Scheme V). However, selective replacement of one bromide was not successful, and this material was not further studied. Analogous conversions of 1-tosylindole using Br_2 or NBS provided 3-bromo-1-tosylindole (**16**). Palladium(0)-catalyzed methyl acrylate insertion with the model compound **16** required much more vigorous conditions (120 °C, 17 h, in DMF, 69%) than for 4-bromo-1-tosylindole (**10**). This is a clear indication of the importance of the electron density of the carbon involved in the Pd(0) oxidative addition.

Alternatively, 4-bromo-3-(chloromercurio)-1-tosylindole (**18**) was converted to the 3-iodo compound **22** with I_2 in $CHCl_3$. Since Pd(0) oxidative addition of aryl iodides does not require the more electron-rich tetrakis(triarylphosphine)palladium catalyst necessary with aryl bromides,[16] selective olefination of the iodide in reaction of a bromoiodo aromatic is possible. The most versatile approach to 4-bromo-3-palladated 1-tosylindoles is based on this selectivity. Despite the electron-rich nature of the 1-tosylindole 3-position, both electron-deficient (methyl acrylate) and electron-rich (*N*-vinylphthalimide) monosubstituted olefins inserted efficiently. Of particular interest was the insertion of α-acetamidoacrylate, which would provide access to optically active tryptophans via the well-established catalytic reduction using a rhodium–chiral phosphine catalyst.[17] The insertion of α-acetamidoacrylate anion was very slow; before even moderate conversions could be achieved, the unstabilized catalyst decomposed.[18] In contrast, insertion of methyl α-acetamidoacrylate was rapid; only one isomer of **24** was observed. Unfortunately, olefin polymerization was competitive under the high concentration conditions employed. Use of a larger excess of olefin did not increase the yield of **24**.

Other organotransition metal mediated conversions of 4-bromo-1-tosylindole (**10**) to 4-substituted 1-tosylindoles and the utilization of these and the methodology reported herein in the synthesis of ergot alkaloids will be reported subsequently.

Experimental Section

General Methods. All melting points are uncorrected. ^1H NMR spectra were measured with Varian EM360A (60 MHz) and Nicolet NTC FT 1180 (360 MHz) spectrometers using Me_4Si as internal standard and are measured in δ. Infrared spectra were measured on a Beckman 4230 spectrophotometer. Analytical TLC was performed on Brinkman 60 F 254 silica gel. Products were visualized by UV light. Analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Materials. Silica gel, Baker-Analyzed reagent grade (60–200 mesh), was purchased from J. T. Baker Chemical Company. Alumina, Alcoa type F-20 chromatographic grade (80–200 mesh) was purchased from MCB Manufacturing Chemists, Inc. 2-Methyl-3-nitroaniline (**1**) was prepared by reduction of 2,6-dinitrotoluene[19] (Aldrich Chemical Company). Pyridine was fractionally distilled from CaH_2 under argon. Acetonitrile was fractionally distilled from CaH_2 under argon. *p*-Benzoquinone was sublimed at 60 °C, 10 mmHg, and then stored in an amber glass bottle at 0 °C under argon. $PdCl_2(CH_3CN)_2$ was prepared by stirring a suspension of $PdCl_2$ (20.00 g) in 400 mL of CH_3CN under argon for 3 days. The precipitate was suction filtered, and dried in vacuo to afford a fluffy yellow solid. Additional material may be obtained by concentration of the mother liquor in vacuo. Tetrahydrofuran was distilled from Na under N_2. *N*-Vinylphthalimide was prepared by the method of Johnson and Wen.[20] 1-Tosylindole was prepared by the method of DeSilva and Snieckus.[21] *N*-Bromosuccinimide was recrystallized from H_2O. Allyl chloride was washed with concentrated HCl and then with Na_2CO_3, dried ($CaCl_2$), and fractionally distilled under argon. Lithium tetrachloropalladate (0.1 M) was prepared by refluxing a suspension of $PdCl_2$ (0.885 g, 5.00 mmol) and LiCl (0.424 g, 10.00 mmol) in 50 mL of CH_3OH under argon for 30 min. Methyl 2-acetamidoacrylate was prepared by the method of Rothstein.[22] Other materials were obtained from commercial suppliers and used without further purification.

2-Bromo-6-nitrotoluene (2). 2-Methyl-3-nitroaniline (**1**) (38.87 g, 0.255 mol) was slurried in 325 mL of H_2O in a 1-L, three-necked flask equipped with a Friedrich condenser, 250-mL dropping funnel, and stopper. The suspension was heated to reflux and 130 mL of 48% HBr was added. The mixture was maintained at reflux for 20 min then cooled to 0 °C. A solution of $NaNO_2$ (17.56 g, 0.255 mol) in 90 mL of H_2O was added with rapid stirring while maintaining the temperature at 0 °C. The resulting diazonium solution was stirred at 0 °C for 15 min and then added dropwise (while kept cold) to a rapidly stirring mixture of CuBr (42.03 g, 0.293 mol) in 86 mL of 48% HBr and 225 mL of H_2O. The thick suspension was stirred at room temperature for 20 min and then heated on a steam bath for an additional 20 min. The suspension was then allowed to stand overnight. Steam distillation afforded 51.95 g (94.3%) of **2** as a colorless solid: mp 36–39 °C (lit[7] mp 42 °C); ^1H NMR ($CDCl_3$) δ 2.55 (s, 3 H, CH_3), 6.96–7.35 (m, 1 H, Ar H meta to nitro), 7.55–7.87 (m, 2 H, Ar H ortho and para to nitro); IR (KBr) 3080, 1525, 1445, 1350, 792, 732, 705 cm^{-1}.

α,2-Dibromo-6-nitrotoluene (3). 2-Bromo-6-nitrotoluene (**2**) (59.75 g, 0.277 mol) was dissolved in 450 mL of CCl_4 in a 1-L, three-necked flask equipped with a Friedrich condenser, 250 mL pressure-equilibrating addition funnel, and stopper. A small amount (750 mg) of benzoyl peroxide was added and the mixture brought to reflux (bath 90 °C). At this point, the solution was irradiated with a 500-W photoflood lamp, and a solution of Br_2 (17.0 mL, 53.1 g, 0.332 mol) in 40 mL of CCl_4 was added dropwise over approximately 2 h. The mixture was refluxed and irradiated for 12 h at which time analysis of an aliquot by NMR revealed complete conversion. The mixture was cooled to room temperature and concentrated in vacuo to afford 80.84 g (~98%) of **3** as a beige solid. Recrystallization from hexanes afforded the analytical sample as small yellow crystals: mp. 65.5–66 °C; ^1H NMR ($CDCl_3$) δ 4.84 (s, 2 H, CH_2), 7.13–7.47 (m, 1 H, Ar H meta to nitro), 7.73–7.96 (m, 2 H, Ar H ortho and para to nitro); IR (KBr) 3075, 3045, 1522, 1350, 805, 747, 703 cm^{-1}.

Anal. Calcd for $C_7H_5Br_2NO_2$: C, 28.51; H, 1.71; N, 4.75. Found: C, 28.68; H, 1.93; N, 4.52.

2-Bromo-6-nitrostyrene (5). The crude α,2-dibromo-6-nitrotoluene (**3**) and triphenylphosphine (71.87 g, 0.274 mol) were dissolved in 400 mL of $CHCl_3$ in a 1-L, one-necked recovery flask and the mixture was refluxed (bath 100 °C) for 10 min. The

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(16) Plevyak, J. E.; Dickerson, J. E.; Heck, R. F. *J. Org. Chem.* **1979**, *44*, 4078.

(17) For examples, see: (a) Ger. Offen. 2 424 543; *Chem. Abstr.* **1975**, *82*, 171186*n*. (b) U.S. Pat 4 137 404; *Chem. Abstr.* **1979**, *90*, 168989*m*. (c) Aviron-Violet, P.; Colleuille, Y.; Varagnat, J. *J. Mol. Catal.* **1979**, *5*, 41 (Fr). (d) Ger. Offen. 2 831 525; *Chem. Abstr.* **1979**, *91*, 20706*s*. (e) Eur. Pat. Appl. EP 36 741; *Chem. Abstr.* **1979**, *96*, 69221*x*. (f) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2567. (g) Hengartner, U.; et al. *J. Org. Chem.* **1979**, *44*, 3741. (h) Riley, D. P.; Shumate, R. E. *Ibid.* **1980**, *45*, 5187.

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(20) Johnson, P. Y.; Wen, J. Q. *J. Org. Chem.* **1981**, *46*, 2767.

(21) DeSilva, S. O.; Snieckus, V. *Can. J. Chem.* **1974**, *52*, 1294.

(22) Rothstein, E. *J. Chem. Soc.* **1949**, 1968.

resulting suspension was cooled to room temperature and diluted to 1 L with Et_2O. The precipitate was suction filtered, washed with 200 mL of Et_2O twice, and dried in vacuo to afford the phosphonium salt 4 as a colorless solid. Recrystallization from CH_3CN afforded the analytical sample as pale yellow crystals, mp gradual decomposition above 200 °C.

Anal. Calcd for $C_{25}H_{20}Br_2NO_2P$: C, 53.89; H, 3.62; N, 2.51. Found: C, 53.78; H, 3.76; N, 2.56.

The phosphonium salt 4, Et_3N (138.63 g, 1.37 mol), and 1 L of CH_2Cl_2 were mixed in a 2-L, three-necked flask equipped with a mechanical stirrer and gas inlet tube. Formaldehyde (by pyrolysis of paraformaldehyde) was then bubbled in until the deep blue ylide color changed to yellow. The yellow suspension was stirred at room temperature for 1 h.

The solvent and excess Et_3N were removed in vacuo. The residue was taken up in hexanes and then suction filtered through a fritted glass funnel. This procedure was repeated until the mother liquor showed no product by thin layer chromatography (Et_2O, R_f 0.79). The combined mother liquors were concentrated in vacuo. The residue was chromatographed on alumina (50 g) by using hexanes as eluent. The eluent was concentrated in vacuo to afford 53.74 g (85.1%) of **5** as pale yellow crystals: mp 52–53 °C. Recrystallization from hexanes afforded the analytical sample as shiny colorless plates: mp 52–54 °C; ^1H NMR ($CDCl_3$) δ ABX system δ_A = 5.33, δ_B = 5.50, δ_X = 6.68 (J_{AX} = 17 Hz, J_{BX} = 11 Hz, J_{AB} = 1 Hz, PhC*H*=C*H*$_2$), 7.05–7.32 (m, 1 H, Ar H meta to nitro), 7.49–7.85 (m, 2 H, Ar H ortho and para to nitro); IR (KBr) 1525, 1456, 1365, 947, 806, 743 cm^{-1}.

Anal. Calcd for $C_8H_6BrNO_2$: C, 42.13; H, 2.65; N, 6.14. Found: C, 42.06; H, 2.73; N, 6.01.

3-Bromo-2-ethenylacetanilide (7). A mixture of the crude 3-bromo-2-ethenylaniline (**6**) (0.784 g, 3.96 mmol) and 10 mL of Ac_2O was stirred at room temperature for 1 h. The suspension was diluted to 100 mL with H_2O. The colorless precipitate was suction filtered, washed with H_2O, and dried in vacuo to afford 0.816 g (83.0% from **5**) of **7** as a colorless solid, mp 149 °C. This can be recrystallized from hexanes to afford 0.692 g (70.3% from **5**) of **7** as fine colorless needles, mp 152–154 °C. Recrystallization from hexanes afforded the analytical sample as fine colorless needles: mp 151–152 °C; ^1H NMR (Me_2SO-d_6) δ 2.00 (s, 3 H, CH_3), 5.27–5.57 (m, 2 H, β-styryl H), 6.35–7.55 (m, 4 H, α-styryl H, Ar H), 9.28 (b, 1 H, NH); IR (KBr) 3286–3266, 1658–1650, 1571, 1525, 1443, 1404, 1376, 1288, 926, 775, 745 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}BrNO$: C, 50.02; H, 4.20; N, 5.83. Found: C, 49.95; H, 4.42; N, 5.78.

***N*-Tosyl-3-bromo-2-ethenylaniline (9).** A 1-L, one-necked recovery flask equipped with Friedrich condenser was charged with 2-bromo-6-nitrostyrene (**5**) (5.000 g, 21.93 mmol), iron powder (5.075 g, 0.0909 mol), 125 mL of glacial AcOH, and 125 mL of anhydrous EtOH. The mixture was refluxed (bath 120 °C) for 5 h. The dark suspension was cooled to room temperature, transferred to a 2-L Erlenmeyer flask, diluted with 1 L of H_2O, and neutralized with solid Na_2CO_3. The resulting thick suspension was extracted with 250 mL of Et_2O 3 times. The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to afford 4.193 g (96.6%) of the aniline **6** as a golden oil.

A 50-mL, one-necked recovery flask equipped with magnetic stir bar, reflux condenser, and $CaCl_2$ drying tube was charged with the crude 3-bromo-2-ethenylaniline (**6**), *p*-TsCl (4.036 g, 21.17 mmol), and 25 mL of pyridine. The yellow solution was refluxed (bath 120 °C) for 20 min. The solution was cooled to room temperature and poured into 450 mL of ice water. The precipitate was suction filtered, washed with H_2O, and air-dried to afford 6.791 g of tan solid. Recrystallization from hexanes (charcoal decolorization) afforded 6.170 g (79.9% from **5**) of **9** as colorless needles, mp 126–126.5 °C. Additional recrystallizations from hexanes afforded the analytical sample as long colorless needles: mp 122.5–124.5 °C; ^1H NMR ($CDCl_3$) δ 2.37 (s, 3 H, CH_3), ABX system, δ_A = 5.07, δ_B = 5.50, δ_X = 6.28 (J_{AX} = 18 Hz, J_{BX} = 11 Hz, J_{AB} = 1 Hz, PhC*H*=C*H*$_2$), 6.82–7.73 (m, 8 H, Ar H); IR (KBr) 3260, 1595, 1560, 1490, 1388, 1335, 1163, 925, 782, 737 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}BrNO_2S$: C, 51.15; H, 4.01; N, 3.98. Found: C, 51.26; H, 4.14; N, 3.94.

4-Bromo-1-tosylindole (10). Method A. A 200-mL, one-necked recovery flask equipped with reflux condenser and vacuum adapter with argon baloon was charged with 3-bromo-2-ethenylaniline *p*-toluenesulfonamide (**9**) (6.000 g, 17.03 mmol), *p*-benzoquinone (1.841 g, 17.03 mmol), LiCl (7.219 g, 0.170 mmol), $PdCl_2(CH_3CN)_2$ (0.442 g, 1.70 mmol, 10 mol %), and 85 mL of THF. The orange suspension was refluxed (bath 75 °C) for 18 h.

The solvent was removed in vacuo. The residual brown, slightly gummy solid was transferred to a Soxhlet thimble and extracted with 250 mL of hexanes for 4 h. The resulting pot solution was treated with 0.5 g of charcoal and hot-gravity filtered. After cooling to room temperature, the hexanes were removed in vacuo. The residual beige, slightly gummy solid was transferred to the top of a silica gel (10 g) column and dissolved—eluted with hexanes. Concentration of the eluent in vacuo afforded 4.704 g (78.8%) of **10** as a colorless solid, mp 119–121 °C. This material may be recrystallized from hexanes to afford 4.577 g (76.7%) of **10** as shiny colorless crystals, mp 119–121 °C.

Method B. A 12-oz pressure bottle was charged with 3-bromo-2-ethenylaniline *p*-toluenesulfonamide (**9**) (6.000 g, 17.03 mmol), *p*-benzoquinone (1.841 g, 17.03 mmol), LiCl (7.219 g, 0.170 mol), $PdCl_2(CH_3CN)_2$ (0.221 g, 0.850 mmol, 5 mol %), and 50 mL of THF. The orange suspension was flushed with argon and then heated at 125 °C for 75 min. An identical workup afforded 4.633 g (77.7%) of **10** as a colorless solid, mp 118–121 °C. This material may be recrystallized from hexanes to afford 4.553 g (76.3%) of **10** as shiny colorless crystals, mp 120–122 °C. Additional recrystallizations from hexanes afforded the analytical sample as shiny colorless crystals: mp 117–122 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.35 (s, 3 H, CH_3), 6.73 (d, J = 4 Hz, 1 H, indole 3 H), 7.17 (t, J = 8 Hz, 1 H, indole 6 H), 7.24 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.39 (d, J = 8 Hz, 1 H, indole 5 H), 7.62 (d, J = 4 Hz, 1 H, indole 2 H); 7.76 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl); 7.95 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1598, 1568, 1472, 1374, 1358, 1170, 1132, 751, 673 cm^{-1}.

Anal. Calcd for $C_{15}H_{12}BrNO_2S$: C, 51.44; H, 3.45; N, 4.00. Found: C, 51.41; H, 3.50; N, 3.94.

4-Bromoindole (11). Method A. A mixture of crude 3-bromo-2-ethenylaniline (**6**) (0.606 g, 3.06 mmol), *p*-benzoquinone (0.496 g, 4.59 mmol), LiCl (0.616 g, 15.0 mmol), $PdCl_2(CH_3CN)_2$ (39 mg, 0.15 mmol), and 15 mL of THF was purged with argon and then heated in a sealed tube at 100 °C for 22 h. After cooling to room temperature, the solvent was removed in vacuo.

The residue was chromatographed on silica gel (5 g) by using hexanes as eluent. The eluent was concentrated in vacuo to afford 0.277 g (46.3%) of **11** as a yellow oil.

Method B. A mixture of 4-bromo-1-tosylindole (**10**) (2.100 g, 6.00 mmol), 30 mL of CH_3OH, and 30 mL of 20% aqueous NaOH was refluxed (bath 100 °C) for 12 h (argon). The pale pink solution was cooled to room temperature and concentrated in vacuo until the solution became cloudy. The suspension was neutralized with 1 N HCl and then extracted with 100 mL of Et_2O 3 times. The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to afford 1.153 g (98.0%) of **11** as a yellow oil; 360-MHz ^1H NMR ($CDCl_3$) δ 6.63 (m, 1 H, indole 3 H), 7.06 (t, J = 8 Hz, 1 H, indole 6 H), 7.27 (d, J = 5 Hz, 1 H, indole 2 H), 7.31 (d, J = 8 Hz, 1 H, indole 5 H), 7.36 (d, J = 8 Hz, 1 H, indole 7 H), 8.2–8.4 (br, 1 H, NH); IR (neat) 3460–3440, 1572, 1437, 1338, 1183, 893, 750 cm^{-1}.

4-(2-Carbomethoxyethen-1-yl)-1-tosylindole (12). A mixture of 4-bromo-1-tosylindole (**10**) (0.350 g, 1.00 mmol), methyl acrylate (0.108 g, 1.25 mmol), Et_3N (0.127 g, 1.25 mmol), $Pd(OAc)_2$ (11 mg, 0.050 mmol), and tri-*o*-tolylphosphine (61 mg, 0.20 mmol) was flushed with argon and then heated in a sealed tube at 100 °C for 1 h. After cooling to room temperature, the residue was taken up in 100 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo to afford a yellow solid. Recrystallization from hexanes–benzene afforded 0.304 g (85.7%) of **12** as shiny beige crystals. Recrystallization from benzene afforded the analytical sample as shiny colorless crystals: mp 192–194 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.34 (s, 3 H, CH_3), 3.81 (s, 3 H, $COOCH_3$), 6.52 (d, J = 16 Hz, 1 H, olefin H adjacent to ring), 6.93 (d, J = 4 Hz, 1 H, indole 3 H), 7.24 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.33 (t, J = 8 Hz, 1 H, indole 6 H), 7.48 (d, J = 8 Hz, 1 H, indole 5 H), 7.67 (d, J = 4 Hz, 1 H, indole 2 H), 7.78 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.97 (d, J = 16 Hz, 1 H, olefin H adjacent to ester), 8.02 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1716, 1635, 1592, 1370, 1357,

1262, 1188–1178, 1157, 1130, 751, 666 cm^{-1}.

Anal. Calcd for $C_{19}H_{17}NO_4S$: C, 64.21; H, 4.82; N, 3.94. Found: C, 64.49; H, 4.89; N, 3.92.

4-(3-Hydroxy-3-methyl-1-buten-1-yl)-1-tosylindole (13). A mixture of 4-bromo-1-tosylindole (**10**) (0.350 g, 1.00 mmol), 2-methyl-3-buten-2-ol (0.108 g, 1.25 mmol), Et_3N (0.127 g, 1.25 mmol), $Pd(OAc)_2$ (11 mg, 0.050 mmol), and tri-*o*-tolylphosphine (61 mg, 0.20 mmol) was flushed with argon and then heated in a sealed tube at 100 °C for 5 h. After cooling to room temperature, the residue was taken up in 100 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residue was chromatographed on silica gel (10 g) by using hexanes–benzene (1:1) to elute impurities and benzene to elute the product. The benzene eluent was concentrated in vacuo to afford 0.345 g (97.3%) of **13** as a colorless foam: 360-MHz ^1H NMR ($CDCl_3$) δ 1.44 (s, 6 H, geminol CH_3), 2.33 (s, 3 H, CH_3), 6.43 (d, J = 16 Hz, 1 H, olefin H adjacent to aliphatic), 6.85, 6.87 (pair of d, J = 3 Hz, J = 16 Hz, 2 H, olefin H and indole 3 H), 7.22 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.26–7.34 (m, 2 H, indole 6 and 5 H), 7.59 (d, J = 3 Hz, 1 H, indole 2 H), 7.72 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.89 (d, J = 8 Hz, 1 H, indole 7 H); IR (CCl_4) 3640–3160, 1420, 1377, 1362, 1188, 1180, 1165, 1136, 967 cm^{-1}.

Anal. Calcd for $C_{20}H_{21}NO_3S$: C, 67.58; H, 5.96; N, 3.94. Found: C, 67.64; H, 6.09; N, 3.73.

4-(2-Phenylethen-1-yl)-1-tosylindole (14). A mixture of 4-bromo-1-tosylindole (**10**) (0.350 g, 1.00 mmol), styrene (0.130 g, 1.25 mmol), Et_3N (0.127 g, 1.25 mmol), $Pd(OAc)_2$ (11 mg, 0.050 mmol), and tri-*o*-tolylphosphine (61 mg, 0.20 mmol) was flushed with argon and then heated in a sealed tube at 100 °C for 7 H. After cooling to room temperature, the residue was taken up in 100 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo to afford a colorless solid. Recrystallization from CH_3OH afforded 0.276 g (74.0%) of **14** as beige crystals. Additional recrystallization from CH_3OH afforded the analytical sample as colorless crystals: mp 129–130 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.33 (s, 3 H, CH_3), 6.93 (d, J = 4 Hz, 1 H, indole 3 H), 7.16–7.54 (m, 11 H, Ar H), 7.63 (d, J = 4 Hz, 1 H, indole 2 H), 7.78 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.92 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1592, 1371, 1185, 1177, 1164, 1132, 743, 673 cm^{-1}.

Anal. Calcd for $C_{23}H_{19}NO_2S$: C, 73.97; H. 5.13; N, 3.75. Found: C, 73.84; H, 5.14; N, 3.67.

4-(2-Phthalimidoethen-1-yl)-1-tosylindole (15). A mixture of 4-bromo-1-tosylindole (**10**) (0.350 g, 1.00 mmol), *N*-vinylphthalimide (0.190 g, 1.10 mmol), Et_3N (0.127 g, 1.25 mmol), $Pd(OAc)_2$ (11 mg, 0.050 mmol), tri-*o*-tolylphosphine (61 mg, 0.20 mmol), and 0.5 mL of CH_3CN was flushed with argon and then heated in a sealed tube at 100 °C for 24 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residue was chromatographed on silica gel (10 g) by using hexane to elute tri-*o*-tolylphosphine, 20% benzene in hexane to elute **10**, 30% benzene in hexane to elute *N*-vinylphthalimide, and 10% Et_2O in benzene to elute product. The 10% Et_2O in benzene eluent was concentrated in vacuo to afford 0.328 g (74.2%) of **15** as a light yellow solid. Recrystallization from CH_3CN afforded the analytical sample as a yellow solid: mp 220–221 °C; 360–MHz ^1H NMR ($CDCl_3$) δ 2.33 (s, 3 H, CH_3), 6.91 (d, J = 4 Hz, 1 H, indole 3 H), 7.22 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.30 (t, J = 8 Hz, 1 H, indole 6 H), 7.43 (d, J = 8 Hz, 1 H, indole 5 H), 7.41 (d, J = 15 Hz, 1 H, olefin H adjacent to indole), 7.63 (d, J = 4 Hz, 1 H, indole 2 H), 7.75–7.78 (m, 4 H, tosyl H adjacent to sulfonyl, phthalimide H meta to carbonyl), 7.88–7.94 (m, 4 H, phthalimide H ortho to carbonyl, olefin H adjacent to nitrogen, indole 7 H); IR (KBr) 1731, 1648, 1383, 1179, 1164, 1124, 702, 672 cm^{-1}.

Anal. Calcd for $C_{25}H_{18}N_2O_4S$: C, 67.86; H, 4.10; N, 6.33. Found: C, 68.40; H, 4.46; N, 6.27.

3-Bromo-1-tosylindole (16). Method A. A mixture of 1-tosylindole (1.085 g, 4.00 mmol), *N*-bromosuccinimide (0.748 g, 4.20 mmol), and 25 mL of CCl_4 was refluxed (bath 90 °C) *in the dark* for 23.5 h. The suspension was cooled to room temperature and suction filtered. The precipitate was washed with fresh CCl_4. The mother liquor was concentrated in vacuo to afford 1.422 g of beige solid. This was recrystallized from hexanes (charcoal decolorization) to afford 1.251 g (89.3%) of **16** as colorless crystals, mp 120–123 °C.

Method B. Bromine (4.56 g, 28.6 mmol) in 20 mL of CCl_4 was added to a solution of 1-tosylindole (7.38 g, 27.2 mmol) in 30 mL of CCl_4 at reflux (bath 90 °C) over 30 min. The solution was then refluxed for 4.5 h. After being cooled to room temperature, the solvent was removed in vacuo. The residual solid was recrystallized from hexanes (charcoal decolorization) to afford 8.85 g (92.9%) of **16** as colorless crystals; mp 122–126 °C. Recrystallization from hexanes afforded the analytical sample as colorless crystals: mp 122–125 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.35 (s, 3 H, CH_3), 7.25 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.29–7.40 (m, 2 H, indole 5 and 6 H), 7.50 (d, J = 8 Hz, 1 H, indole 4 H), 7.62 (s, 1 H, indole 2 H), 7.78 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 8.00 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1600, 1580, 1494, 1448, 1364, 1170 cm^{-1}.

Anal. Calcd for $C_{15}H_{12}BrNO_2S$: C, 51.44; H, 3.45; N, 4.00. Found: C, 51.20; H, 3.42; N, 4.07.

3,4-Dibromo-1-tosylindole (17). A solution of Br_2 (0.504 g, 3.15 mmol) in 30 mL of CCl_4 was added dropwise *in the dark* to a solution of 4-bromo-1-tosylindole (**10**) (1.051 g, 3.00 mmol) in 30 mL of CCl_4 at reflux (bath 100 °C) over 30 min. The resulting solution was refluxed for 17 h. After being cooled to room temperature, the solvent and excess Br_2 were removed in vacuo. The residual oil was easily triturated with cold petroleum ether to afford a colorless solid. Recrystallization from hexanes afforded 1.090 g (84.7%) of **17** as colorless crystals. Additional recrystallizations from hexanes afforded the analytical sample as colorless crystals: mp 100.5–102.5 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.37 (s, 3 H, CH_3), 7.17 (t, J = 8 Hz, 1 H, indole 6 H), 7.27 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.45 (d, J = 8 Hz, 1 H, indole 5 H), 7.70 (s, 1 H, indole 2 H), 7.77 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 8.01 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1593, 1369, 1175, 1161, 1085, 1034 cm^{-1}.

Anal. Calcd for $C_{15}H_{11}Br_2NO_2S$: C, 41.98; H, 2.58; N, 3.26. Found: C, 42.13; H, 2.63; N, 3.24.

4-Bromo-3-(chloromercurio)-1-tosylindole (18). A mixture of 4-bromo-1-tosylindole (**10**) (0.350 g, 1.00 mmol), mercuric acetate (0.318 g, 1.00 mmol), 20 mL of glacial AcOH, and 1 drop of 70% $HClO_4$ was stirred at room temperature for 24 h. The suspension was poured into a solution of NaCl (10 g) in 100 mL of H_2O. The resulting suspension was stirred 5 min at room temperature. The precipitate was suction filtered, washed with H_2O, and air-dried to afford 0.584 g (99.8%) of the mercuric salt **18** as a colorless solid.

4-Bromo-3-(2-carbomethoxyethen-1-yl)-1-tosylindole (19). Method A. Palladium acetate (0.219 g, 0.977 mmol) was added to a suspension of 4-bromo-3-(chloromercurio)-1-tosylindole (**18**) (0.572 g, 0.977 mmol), 0.5 mL of methyl acrylate, and 3 mL of CH_3CN at 0 °C. The suspension was stirred at 0 °C for 0.5 h and at room temperature for 12 h. After dilution to 10 mL with CH_3CN, the black suspension was suction filtered through Celite. The Celite was washed with fresh CH_3CN. The mother liquor was concentrated in vacuo.

The residue was chromatographed on silica gel (10 g) by using 20% benzene in hexanes to elute impurities and benzene to elute the product. The benzene eluent was concentrated in vacuo to afford 0.358 g of pale yellow solid. Recrystallization from hexanes afforded 0.298 g (70.3%) of **19** as shiny colorless crystals.

Method B. A mixture of 4-bromo-3-iodo-1-tosylindole (**22**) (0.476 g, 1.00 mmol), methyl acrylate (0.108 g, 1.25 mmol), Et_3N (0.127 g, 1.25 mmol), and $Pd(OAc)_2$ (11 mg, 0.050 mmol) was flushed with argon and then heated in a sealed tube at 100 °C for 1 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residual beige oil–solid was chromatographed on silica gel (10 g) by using 20% benzene in hexanes to elute impurities and 25% hexanes in benzene to elute the product. Concentration of the 25% hexanes in benzene eluent in vacuo afforded 0.350 g (80.7%) of **19** as a pale yellow solid. Recrystallization from hexanes afforded the analytical sample as shiny colorless needles: mp 128–132 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.37 (s, 3 H, CH_3), 3.82 (s, 3 H, $COOCH_3$), 6.31 (d, J = 16 Hz, 1 H, olefin H adjacent to ester), 7.17 (t, J = 8 Hz, 1 H, indole 6 H), 7.28 (d, J = 8 Hz,

2 H, tosyl H adjacent to methyl), 7.45 (d, J = 8 Hz, 1 H, indole 5 H), 7.79 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.91 (s, 1 H, indole 2 H), 7.97 (d, J = 8 Hz, 1 H, indole 7 H), 8.54 (d, J = 16 Hz, 1 H, olefin H adjacent to ring); IR (KBr) 1708, 1634, 1385, 1354, 1275, 1168, 1154, 981 cm^{-1}.

Anal. Calcd for $C_{19}H_{16}BrNO_4S$: C, 52.55; H, 3.71; N, 3.23. Found: C, 52.59; H, 3.80; N, 3.13.

3-Allyl-4-bromo-1-tosylindole (20). Lithium tetrachloropalladate (0.9 mL of 0.1 M Li_2PdCl_4 in CH_3OH) was added to a suspension of 4-bromo-3-(chloromercurio)-1-tosylindole (18) (1.755 g, 3.00 mmol) and 3 mL of allyl chloride in 30 mL of CH_3OH. The suspension was stirred at room temperature for 24 h. The resulting black suspension was suction filtered through Celite. The Celite was washed with fresh CH_3OH. The mother liquor was concentrated in vacuo.

The residue was chromatographed on silica gel (20 g) by using 10% benzene in hexanes as eluent. Concentration of the eluent in vacuo afforded 0.946 g (80.7%) of **20** as a colorless solid. Recrystallization from hexanes afforded the analytical sample as colorless crystals: mp 90–92 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.35 (s, 3 H, CH_3), 3.74 (t, J = 8 Hz, 2 H, CH_2), 5.04–5.16 (m, 2 H, $=CH_2$), 6.03–6.14 (m, 1 H, $=CH$), 7.11 (t, J = 8 Hz, 1 H, indole 6 H), 7.24 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.37 (d, J = 8 Hz, 1 H, indole 5 H), 7.38 (s, 1 H, indole 2 H), 7.74 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.96 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1646, 1370, 1188, 1173, 1152, 1090, 982 cm^{-1}.

Anal. Calcd for $C_{18}H_{16}BrNO_2S$: C, 55.39; H, 4.13; N, 3.59. Found: C, 55.36; H, 4.38; N, 3.50.

1-Tosylbenz[*cd*]indoline (21). A mixture of 3-allyl-4-bromo-1-tosylindole (**20**) (0.390 g, 1.00 mmol), Et_3N (0.127 g, 1.25 mmol), $Pd(OAc)_2$ (11 mg, 0.050 mmol), tri-*o*-tolylphosphine (61 mg, 0.20 mmol), and 1 mL of CH_3CN was flushed with argon and then heated in a sealed tube at 100 °C for 22 h. After being cooled to room temperature, the mixture was taken up in 50 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residual orange-brown oil was chromatographed on silica gel (10 g) by using 10% benzene in hexanes to elute impurities and 25% benzene in hexanes to elute the product. The 25% benzene in hexanes eluent was concentrated in vacuo to afford 0.154 g (49.8%) of the naphthalene **21** as a colorless solid. Recrystallization from hexanes afforded the analytical sample as colorless crystals: mp 149.5–150.5 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.32 (s, 3 H, CH_3), 5.18 (s, 2 H, CH_2), 7.18 (d, J = 8 Hz, 1 H, Ar H), 7.22 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.34 (d, J = 8 Hz, 1 H, Ar H), 7.39–7.48 (m, 3 H, Ar H), 7.58 (d, J = 8 Hz, 1 H, Ar H), 7.80 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl); IR (KBr) 1598, 1495, 1467, 1381, 1343, 1194, 1177, 1161, 1118, 1087, 1063, 796, 653 cm^{-1}.

Anal. Calcd for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53. Found: C, 70.08; H, 4.95; N, 4.48.

4-Bromo-3-iodo-1-tosylindole (22). A mixture of 4-bromo-3-(chloromercurio)-1-tosylindole (18) (1.755 g, 3.00 mmol), iodine (0.761 g, 3.00 mmol), and 30 mL of $CHCl_3$ was stirred at room temperature for 5 h. The resulting suspension was suction filtered through Celite. The Celite was washed with fresh $CHCl_3$. The mother liquor was washed with 3 M sodium thiosulfate and with H_2O, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residual yellow oil was chromatographed on silica gel (20 g) by using 20% benzene in hexanes as eluent. The eluent was concentrated in vacuo to afford 1.281 g (89.7%) of **22** as a colorless solid. Recrystallization from hexanes afforded the analytical sample as colorless crystals: mp 107–109 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.36 (s, 3 H, CH_3), 7.15 (t, J = 8 Hz, 1 H, indole 6 H), 7.27 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.43 (d, J = 8 Hz, 1 H, indole 5 H), 7.77 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.81 (s, 1 H, indole 2 H), 8.02 (d, J = 8 Hz, 1 H, indole 7 H); IR (KBr) 1593, 1405, 1367, 1172, 1155–1145, 1025, 678 cm^{-1}.

Anal. Calcd for $C_{15}H_{11}BrINO_2S$: C, 37.84; H, 2.33; N, 2.94. Found: C, 37.90; H, 2.54; N, 2.90.

4-Bromo-3-(2-phthalimidoethen-1-yl)-1-tosylindole (23). A mixture of 4-bromo-3-iodo-1-tosylindole (**22**) (0.476 g, 1.00 mmol), *N*-vinylphthalimide (0.216 g, 1.25 mmol), Et_3N (0.127 g, 1.25 mmol), and $Pd(OAc)_2$ (11 mg, 0.050 mmol) was flushed with argon and then heated in a sealed tube at 100 °C for 13 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residue was chromatographed on silica gel (10 g) by using 30% benzene in hexanes to elute impurities and unreacted *N*-vinylphthalimide and 10% Et_2O in benzene to elute product. The 10% Et_2O in benzene eluent was concentrated in vacuo to afford 0.400 g (76.8%) of **23** as a yellow solid. Recrystallization from CH_3CN afforded the analytical sample as yellow needles: mp 255–262 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.36 (s, 3 H, CH_3), 7.15 (d, J = 15 Hz, 1 H, olefin H adjacent to indole), 7.17 (t, J = 8 Hz, 1 H, indole 6 H), 7.27 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.42 (d, J = 7 Hz, 1 H, indole 5 H), 7.76–7.80 (m, 5 H, indole 2 H, tosyl H adjacent to sulfonyl, phthalimide H meta to carbonyl), 7.90–7.92 (m, 2 H, phthalimide H ortho to carbonyl), 7.99 (d, J = 7 Hz, 1 H, indole 7 H), 8.33 (d, J = 15 Hz, 1 H, olefin H adjacent to nitrogen); IR (KBr) 1727, 1387, 1362, 1172, 1145, 1097, 988, 668 cm^{-1}.

Anal. Calcd for $C_{25}H_{17}BrN_2O_4S$: C, 57.59; H, 3.29; N, 5.37. Found: C, 57.64; H, 3.42; N, 5.39.

4-Bromo-3-(2-acetamido-2-carbomethoxyethen-1-yl)-1-tosylindole (24). A mixture of 4-bromo-3-iodo-1-tosylindole (**22**) (0.476 g, 1.00 mmol), methyl 2-acetamidoacrylate (0.158 g, 1.10 mmol), Et_3N (0.127 g, 1.25 mmol), and $Pd(OAc)_2$ (11 mg, 0.050 mmol) was flushed with argon and then heated in a sealed tube at 100 °C for 2.5 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with H_2O 3 times, dried (Na_2SO_4), filtered, and concentrated in vacuo.

The residual orange solid was chromatographed on silica gel (10 g) by using benzene to elute first 4-bromo-1-tosylindole (**10**) and then unreacted **22** and then 10% Et_2O in benzene to elute the product. The initial benzene fractions were concentrated in vacuo to afford 54 mg of **10** as a colorless solid. The remaining benzene fractions were concentrated in vacuo to afford 0.135 g of **22** as a colorless solid. The 10% Et_2O in benzene eluent was concentrated in vacuo to afford 0.164 g (46.6%) of **24** as a colorless solid. Recrystallization from EtOH–H_2O afforded the analytical sample as a pale yellow solid: mp 199–202 °C; 360-MHz ^1H NMR ($CDCl_3$) δ 2.23 (s, 3 H, CH_3CON), 2.35 (s, 3 H, CH_3Ar), 3.87 (s, 3 H, CH_3O), 7.10 (s, 1 H, olefinic H), 7.15 (t, J = 8 Hz, 1 H, indole 6 H), 7.28 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.44 (d, J = 8 Hz, 1 H, indole 5 H), 7.78 (d, J = 8 Hz, 2 H, tosyl H adjacent to sulfonyl), 7.81 (s, 1 H, indole 2 H), 7.94 (d, J = 8 Hz, 1 H, indole 7 H), 8.43 (s, 1 H, NH); IR (KBr) 3280, 1730, 1665–1658, 1640, 1380–1370, 1263, 1235, 1167, 987, 662 cm^{-1}.

Anal. Calcd for $C_{21}H_{19}BrN_2O_5S$: C, 51.33; H, 3.90; N, 5.70. Found: C, 51.47; H, 3.99; 5.64.

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