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A Convenient Synthesis of 3-Acylindoles via Friedel–Crafts Acylation of 1-(Phenylsulfonyl)indole. A New Route to Pyridocarbazole-5,11-quinones and Ellipticine

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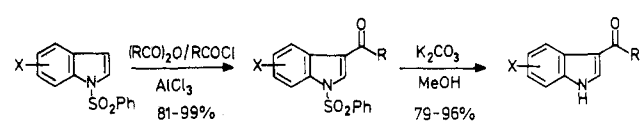
A Friedel–Crafts acylation of 1-(phenylsulfonyl)indoles (**1**) with carboxylic acid anhydrides and acid chlorides in the presence of aluminum chloride gives 3-acyl-1-(phenylsulfonyl)indoles (**2**) in 81–99% yields. Base hydrolysis converts **2** to 3-acylindoles (**3**) in 79–96% yields. The reaction of 1-(phenylsulfonyl)indole (**1a**) with oxalyl chloride gives acid chloride **2h**, which is converted to 3-cyanoindole (**7**) in three steps (75% yield). Although a similar Friedel–Crafts alkylation of **1** was unsuccessful, in some cases the 3-acyl-1-(phenylsulfonyl)indoles **2a,e,f** could be reduced to 3-alkyl-1-(phenylsulfonyl)indoles **8a,b,c** in nearly quantitative yield with sodium borohydride in trifluoroacetic acid. The acid chloride derived from keto acid **9** did not cyclize to the desired pyridocarbazole-5,11-quinone **24** but rather to chloro keto lactam **10**. However, acylation of **1a** with acid chloride **22** followed by strong-base-mediated cyclization gives **24**. Since quinone **24** has been previously converted to the alkaloid ellipticine **26**, this route to **24** represents a new synthesis of ellipticine. Related synthetic schemes give rise to quinones **16** and **20**.

Although the addition of electrophiles to the C-3 (β) position of indole is perhaps the most characteristic reaction of this class of heterocycles,[1] the synthesis of 3-acylindoles is often complicated by the fact that indole can display ambident reactivity leading to competing substitution at nitrogen. For example, acetylation of indole in a refluxing mixture of acetic anhydride and acetic acid affords mainly 1,3-diacetylindole.[2] Other commonly employed routes to 3-acylindoles, such as the use of indole magnesium salts with acid chlorides,[3] or Vilsmeier–Haack conditions involving dialkylamides and phosphorus oxychloride[4] are somewhat limited in scope and usually provide only moderate yields of the desired products. These same shortcomings plague the Friedel–Crafts acylation of simple indoles.[5] Consequently, the need for an efficient and versatile synthesis of 3-acylindoles (A → B) is manifest.

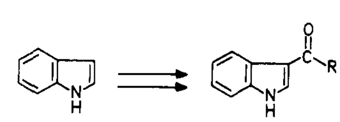
Scheme I



1a, X = H
1b, X = 6-OMe
1c, X = 5-F
1d, X = 5-OMe

2

3



A B

The recently described regioselective 3-acylation of 1-(phenylsulfonyl)pyrrole[6] prompted us to investigate the analogous Friedel–Crafts reaction of 1-(phenylsulfonyl)indole as a possible solution to the problem stated above

(1) (a) Sundberg, R. J. "The Chemistry of Indoles"; Academic Press: New York and London, 1970; p 33. (b) Remers, W. A. "Heterocyclic Compounds, Indole Part 1"; Houlihan, W. J., Ed.; Wiley: New York, 1972; p 111. (c) Remers, W. A. "Heterocyclic Compounds, Indole Part 3"; Houlihan, W. J., Ed.; Wiley: New York, 1979; p 357.

(2) Saxton, J. E. *J. Chem. Soc.* **1952**, 3592.

(3) See: Heacock, R. A.; Kasparek, S. "Advances in Heterocyclic Chemistry"; Katritzky, A. R., Boulton, A. J., Ed.; Academic Press: New York, 1969; Vol. 10, p 43.

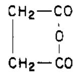
(4) Anthony, W. C. *J. Org. Chem.* **1960**, *25*, 2049.

(5) Olah, G. A. "Friedel-Crafts and Related Reactions"; Interscience: New York, 1964; Vol. I, p 93.

(6) (a) Xu, R. X.; Anderson, H. J.; Gogan, N. J.; Loader, C. E.; McDonald, R. *Tetrahedron Lett.* **1981**, *22*, 4899. (b) Rokach, J.; Hamel, P.; Kakushima, M. *Tetrahedron Lett.* **1981**, *22*, 4901. (c) Hamel, P.; Frenette, R.; Rokach, J. *J. Org. Chem.* **1983**, *48*, 3214. (d) Anderson, H. J.; Loader, C. E.; Xu, R. X.; Le, N.; Gogan, N. J.; McDonald, R.; Edwards, L. G. *Can. J. Chem.* **1985**, *63*, 896.

0022-3263/85/1950-5451$01.50/0

Table I. Synthesis of 3-Acyl-1-(phenylsulfonyl)indoles (2) and 3-Acylindoles (3)

indole (1)	acylating agent	R	isolated product (yield, %) 2	3
1a (X = H)	$(CH_3CO)_2O$	CH_3	**2a** (98)	**3a** (96)
1b (X = 6-OMe)	$(CH_3CO)_2O$	CH_3	**2b** (99)	**3b** (79)
1c (X = 5-F)	$(CH_3CO)_2O$	CH_3	**2c** (99)	**3c** (85)
1d (X = 5-OMe)	$(CH_3CO)_2O$	CH_3	**2d** (85)	**3d** (90)
1a	$(CH_3CH_2CO)_2O$	C_2H_5	**2e** (91)	**3e** (87)
1a	C_6H_5COCl	C_6H_5	**2f** (93)	**3f** (88)
1a		$CH_2CH_2CO_2H$	**2g** (81)	...
1a	$(COCl)_2$	COCl	**2h** (...)	...

and to a synthetic problem in our laboratory. Furthermore, the propensity of these N-protected indoles to undergo regioselective C-2 lithiation[7] allows for the subsequent elaboration of the N-protected 3-acylindoles to molecules of biological interest (vide infra).

Results and Discussion

Synthesis of 3-Acyl-1-(phenylsulfonyl)indoles (2) and 3-Acylindoles (3). We have found that representative 1-(phenylsulfonyl)indoles[8] (**1a–d**) can be acylated with acetic anhydride in the presence of aluminum chloride ($AlCl_3$) in dichloromethane at room temperature to afford the expected 3-acylindole **2** in excellent yields (Scheme I and Table I). Although **1a** (X = H) is acetylated in virtually quantitative yield using only a slight excess (1.1 equiv) of acetic anhydride and $AlCl_3$, optimum results in other cases are achieved by employing larger excesses of both reagents. As expected,[1] acylation occurs regioselectively at C-3 except for **1d** (X = 5-OMe) where acetylation of the benzene ring was observed in addition to C-3 acetylation, affording minor amounts of a diacetyl product. Mild alkaline hydrolysis of the phenylsulfonyl protecting group provides the corresponding 3-acylindoles **3** in good yields as shown in Scheme I and summarized in Table I. Neither reaction requires a chromatography to give relatively pure product.

As shown in Table I, 1-(phenylsulfonyl)indole (**1a**) reacts with several acid chlorides and anhydrides under these conditions to provide a general route to 3-acylindoles. Characteristically, the introduction of one acyl group effectively deactivates the molecule to further electrophilic attack, even when excess acylating agent and catalyst are employed. In fact, both 2- and 3-acetyl-1-(phenylsulfonyl)indole were recovered unchanged after being subjected to acetic anhydride and $AlCl_3$ under the normal reaction conditions.

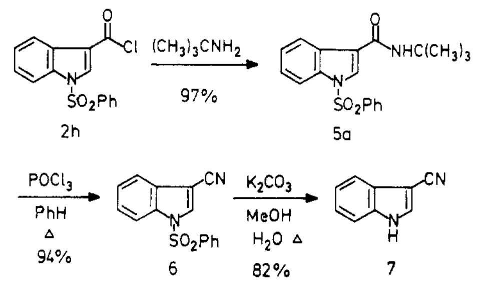
When ethyl chloroformate was used as an acylating agent, we were unable to isolate any of the expected 3-carbethoxy-1-(phenylsulfonyl)indole (**4**) (not shown). However, acylation of **1a** with oxalyl chloride in the presence of $AlCl_3$ proceeds with decarbonylation[9] to produce the acid chloride **2h** as determined by its conversion

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

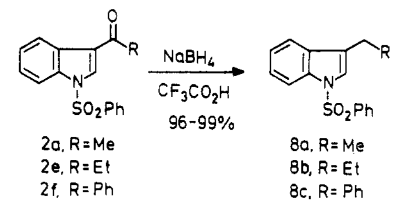
(8) 5-Methoxy- and 5-fluoroindole were prepared according to the procedure of: Batcho, A. D.; Leimgruber, W. *Chem. Abstr.* **1977**, *86*, 29624. The phenylsulfonyl derivatives were prepared according to the procedure described in ref 10.

(9) Oxalyl chloride reacts with indole to give the 3-glyoxalyl chloride derivative: Speeter, M. E.; Anthony, W. C. *J. Am. Chem. Soc.* **1954**, *76*, 6208. For an example of decarbonylation with oxalyl chloride, see: Campbell, T. W. *J. Am. Chem. Soc.* **1960**, *82*, 3126.

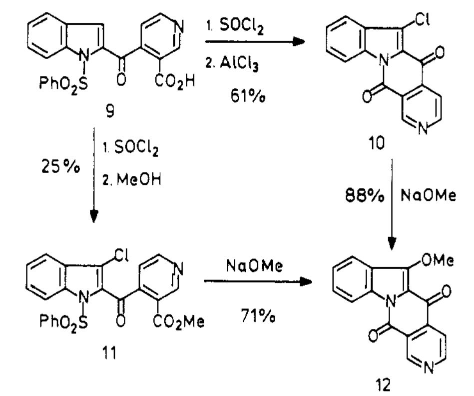
Scheme II



Scheme III



Scheme IV



to the known ester **4**[10] upon treatment of the crude acid chloride with anhydrous ethanol. Furthermore, **2h** can be converted to the corresponding amides **5a,b** when allowed to react with the appropriate amine (cf. Experimental Section). The *tert*-butylamide **5a**, prepared from **2h** in 97% yield, undergoes a von Braun reaction with phosphorus oxychloride[11] to provide 3-cyano-1-(phenylsulfonyl)indole (**6**) in 94% yield. Indeed, following hydrolysis of **6**, this sequence provides a convenient and efficient synthesis of 3-cyanoindole (**7**)[12] (Scheme II).

Attempts to prepare 3-alkyl-1-(phenylsulfonyl)indoles via a similar Friedel–Crafts alkylation met with failure. Thus, neither benzyl bromide nor benzyl alcohol produced the desired 3-benzyl derivative of **1a** in the presence of $AlCl_3$ or trifluoroacetic acid (TFA). However, since we had earlier shown that diaryl ketones[13] and diarylmethanols[14] are efficiently reduced to diarylmethanes with sodium borohydride ($NaBH_4$) in TFA, we anticipated that this methodology could be successfully extended to the present situation. Indeed, the 3-acyl-1-(phenylsulfonyl)indoles **2a,e,f** are converted to the corresponding 3-alkyl derivatives **8a–c** in nearly quantitative yields under these conditions (Scheme III). In no instance was reduction of the indole double bond observed, in contrast to the reaction

(10) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1982**, *47*, 757.

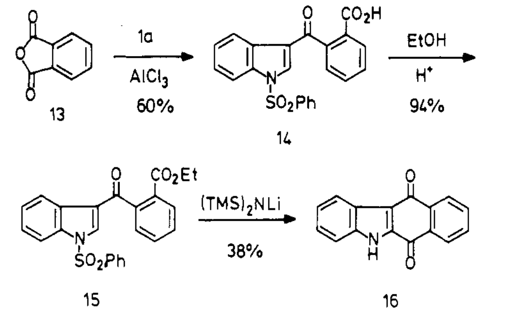
(11) Perni, R. B.; Gribble, G. W. *Org. Prep. Proced. Int.* **1983**, *15*, 297.

(12) For a recent synthesis of 3-cyanoindoles, see: Garcia, J.; Greenhouse, R.; Muchowski, J. M.; Ruiz, J. A. *Tetrahedron Lett.* **1985**, *26*, 1827.

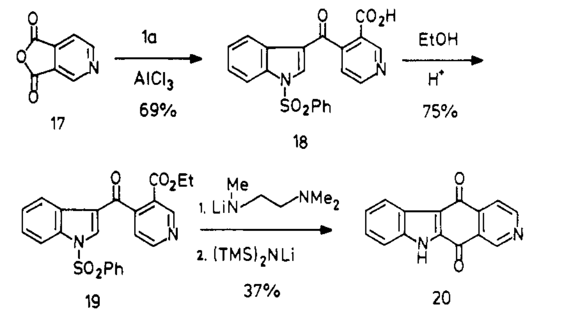
(13) Gribble, G. W.; Kelly, W. J.; Emery, S. E. *Synthesis* **1978**, 763.

(14) Gribble, G. W.; Leese, R. M.; Evans, B. E. *Synthesis* **1977**, 172.

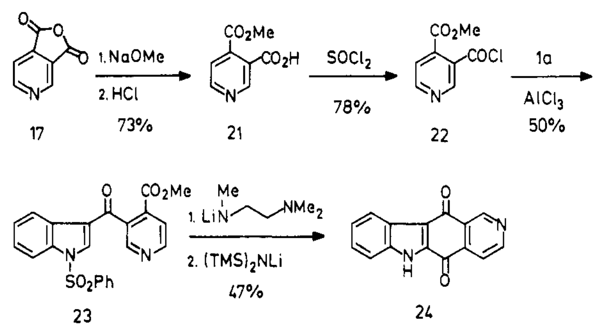
Scheme V



Scheme VI



Scheme VII



of indole with $NaBH_4$ in neat carboxylic acids which produces *N*-alkylindolines[15a] or other products.[15b] In fact, **2f** was recovered unchanged after attempted reduction with $NaBH_4$ in acetic acid (24 h, 25 °C). The apparent generality of the $NaBH_4$/TFA reduction for the preparation of 3-alkyl-1-(phenylsulfonyl)indoles thus constitutes an attractive and efficient alternative to a Friedel–Crafts alkylation.

Synthesis of Pyridocarbazole-5,11-quinones. Although 2-acetyl-1-(phenylsulfonyl)indole is resistant to further acylation,[16] we felt that C-3 acylation of a 2-acylindole might be feasible if the reaction was intramolecular. It was envisioned that such a cyclization would provide a simple approach to quinones related to the anticancer alkaloid ellipticine.[17] Accordingly, this reaction was attempted by using the keto acid **9**, an intermediate in our previously published synthesis of ellipticine.[18] However, when **9** was treated with neat thionyl chloride and the resulting crude acid chloride (IR 1790 cm^{-1}) subjected to $AlCl_3$ under the usual conditions, the 3-chloro keto lactam **10** was unexpectedly produced (Scheme IV). The structure of this material is supported by the absence of a C-3 proton[18] in the 300-MHz ^1H NMR spectrum. Apparently, formation of the desired acid chloride was accompanied by chlorination at C-3. A reexamination of the thionyl chloride reaction confirmed this hypothesis since addition of methanol to the crude acid chloride gave the 3-chloro keto ester **11**. The observed proclivity for N vs. C-3 acylation in these systems is further exemplified by the fact that **11** was converted to the 3-methoxy keto lactam **12** upon treatment with sodium methoxide or magnesium methoxide, a result which also serves to demonstrate the facile displacement of the chlorine atom at C-3. As expected from the work of Joule,[19] the 3-chloro keto lactam **10** was also converted to **12** with sodium methoxide at 0 °C.

The synthesis of quinones related to ellipticine was, however, accomplished via a sequence involving initial Friedel–Crafts C-3 acylation of 1-(phenylsulfonyl)indole with an appropriate dicarboxylic acid anhydride (or derivative thereof) followed by a base induced cyclization[20] to C-2. Thus, as shown in Scheme V, the reaction of **1a** with phthalic anhydride (**13**) in the presence of $AlCl_3$ produced the 3-keto acid **14** in 60% yield after recrystallization. The ester **15** was prepared in 94% yield and when treated with lithium bis(trimethylsilyl)amide (−75 °C, THF), cyclized to the known[17a] 5*H*-benzo[*b*]carbazole-6,11-quinone (**16**) in 38% yield after chromatography. As we previously observed with related systems,[20] the phenylsulfonyl group is apparently removed during the reaction, probably by the ethoxide generated therein.

Similarly, the reaction of **1a** with 3,4-pyridinedicarboxylic anhydride (**17**) and $AlCl_3$ produced the keto acid **18** with apparent complete regioselectivity (Scheme VI). This result is in concert with our earlier observations on the ring opening of **17** with both 2- and 3-lithio-1-(phenylsulfonyl)indole, wherein attack at the C-4 carbonyl group of **17** is the predominant[18] or exclusive[20] pathway. The ethyl ester **19** was prepared in 75% yield by Fischer esterification and allowed to react with lithium diisopropylamide (LDA) (2.2 equiv, 0 °C) to afford the "isoellipticine" quinone **20** in 25% yield. A slight improvement in the cyclization step was realized by using the methodology recently developed by Comins.[21] Thus, addition of the anion derived from *N,N,N'*-trimethylethylenediamine (1 equiv, −75 ° → 0 °C, THF) to **19** presumably generates an α-amino alkoxide intermediate which upon treatment with lithium bis(trimethylsilyl)amide (−75 °C) cyclizes to **20** in 37% yield.

The synthesis of ellipticine quinone **24** requires a reversal of the normal reactivity associated with the 3,4-pyridinedicarboxylic acid moiety. As summarized in Scheme VII, this was accomplished by blocking the C-4 carboxylic acid function as the monomethyl ester **21** by treatment of the anhydride **17** with sodium methoxide to give acid ester **21**. The requisite acid chloride **22** was prepared from **21** by using thionyl chloride, and **22** underwent Friedel–Crafts acylation of **1a** to afford the keto ester **23** in 50% yield. Again, in this case, cyclization was best effected employing Comins' methodology and lithium

(15) (a) Gribble, G. W.; Lord, P. D.; Skotnicki, J.; Dietz, S. E.; Eaton, J. T.; Johnson, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 7812. (b) Gribble, G. W.; Wright, S. W. *Heterocycles* **1982**, *19*, 229. (c) Gribble, G. W.; Nutaitis, C. F.; Leese, R. M. *Ibid.* **1984**, *22*, 379.

(16) Ketcha, D. M.; Gribble, G. W., unpublished results.

(17) Ellipticine quinones have served as precursors in the synthesis of various ellipticine derivatives: (a) Taylor, D. A.; Baradarani, M. M.; Martinez, S. J.; Joule, J. A. *J. Chem. Res., Synop.* **1979**, 387; *J. Chem. Res., Miniprint* **1979**, 4801. (b) Taylor, D. A.; Joule, J. A. *J. Chem. Soc., Chem. Commun.* **1979**, 642. (c) Watanabe, M.; Snieckus, V. *J. Am. Chem. Soc.* **1980**, *102*, 1457. (d) Robaut, C.; Rivalle, C.; Rautureau, M.; Lhoste, J.-M.; Bisagni, E. *Tetrahedron* **1985**, *41*, 1945. (e) Reference 20.

(18) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1982**, *47*, 2810.

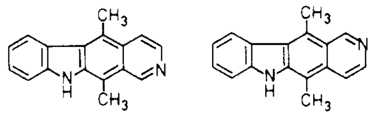
(19) This reaction presumably occurs via an addition elimination sequence. For other examples of indole β-nucleophilic substitution see: Ashcroft, W. R.; Dalton, L.; Beal, M. G.; Humphrey, G. L.; Joule, J. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2409.

(20) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1983**, *48*, 2690.

(21) Comins, D. L.; Brown, J. D. *J. Org. Chem.* **1984**, *49*, 1078.

bis(trimethylsilyl)amide to produce ellipticine quinone **24** in 47% yield.

Since quinones **20** and **24** have been previously converted to "isoellipticine" (**25**) and ellipticine (**26**),[17,20] respectively, this work represents formal syntheses of these alkaloids.



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Experimental Section

Melting points were determined in open capillaries with a Büchi 510 melting point apparatus and are uncorrected. High-resolution mass spectra were taken on a VG 7070 mass spectrometer at the University of Pennsylvania Mass Spectrometry Center, John Dykins, Director. General techniques and the instruments used in this research have been described.[20]

The phrase "usual workup" refers to washing the organic extract with water and then brine, drying over Na_2SO_4 or K_2CO_3, and concentration on a rotary evaporator.

6-Methoxy-1-(phenylsulfonyl)indole (1b). To a solution of 2-(3-methoxyanilino)acetaldehyde diethyl acetal[22] (9.56 g, 40 mmol) in CH_2Cl_2 (100 mL) and pyridine (25 mL) under N_2 at 0 °C was added dropwise benzenesulfonyl chloride (7.66 mL, 60 mmol). The mixture was stirred at 0 °C for 1 h and then overnight at 25 °C. It was poured into saturated aqueous $NaHCO_3$ (150 mL) and extracted with CH_2Cl_2 (200 mL). The organic extract was washed with 5% HCl, dried (K_2CO_3), and evaporated in vacuo to afford the corresponding *N*-phenylsulfonyl derivative as an amber oil: 15.16 g (100%); IR (neat) 1605, 1485, 1450, 1350, 1285, 1260, 1205, 1170, 1060, 955, 705, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.8–6.4 (m, 9 H), 4.5 (t, 1 H), 3.9–2.8 (m, 9 H), 1.5–0.7 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 159.7, 141.1, 138.0, 132.6, 129.3, 128.6, 127.5, 120.6, 114.5, 113.7, 100.8, 62.1, 55.1, 53.1, 15.1.

The (*N*-(phenylsulfonyl)anilino)acetaldehyde diethyl acetal (16.60 g, 43.8 mmol) was dissolved in CH_2Cl_2 (350 mL) at 0 °C and treated dropwise with boron trifluoride etherate (9.32 g, 65.7 mmol). The mixture was stirred at 0 °C for 1.5 h and poured into saturated aqueous $NaHCO_3$ (250 mL). The usual workup gave a solid which was recrystallized from ether to afford 10.12 g (81%) of **1b**, apparently as a single regioisomer; mp 137–139 °C (lit.[23] mp 140–142 °C). The use of titanium tetrachloride[24] as the Lewis acid catalyst produced an inseparable mixture of **1b** and the 4-methoxy isomer (94%), from which 6-methoxyindole and 4-methoxyindole could be obtained after cleavage of the phenylsulfonyl protecting group and chromatography. Reprotection of the 6-methoxy derivative, thus obtained, with benzenesulfonyl chloride[10] gave a product identical (IR, UV, NMR) with the sample of **1b** prepared above.

Representative Procedure for the Acylation of 1-(Phenylsulfonyl)indoles. 3-Acetyl-1-(phenylsulfonyl)indole (2a). To a magnetically stirred suspension of $AlCl_3$ (20.00 g, 0.15 mol) in CH_2Cl_2 (250 mL) at 25 °C was added acetic anhydride (7.60 g, 0.075 mol), and the mixture was stirred for 15 min at which time a clear solution resulted. A solution of **1a**[10] (6.43 g, 0.025 mol) in CH_2Cl_2 (50 mL) was added dropwise; the mixture was stirred at 25 °C for 2 h and poured onto crushed ice (400 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), and the organic extract was washed with brine (100 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL), dried (K_2CO_3), and concentrated in vacuo to give 7.39 g (98%) of **2a** as colorless crystals: mp 155–157 °C. Crystallization from MeOH gave the analytical sample: mp 159–160 °C; IR (KBr) 1675, 1550, 1445, 1390, 1370, 1190, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4–7.2 (m, 10 H), 2.55 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 193.4, 137.5, 134.9, 134.6, 132.1, 129.6, 127.5, 127.0, 125.8, 124.9, 123.1, 121.7, 113.0, 27.8; mass spectrum, *m/e* 299 (M^+), 284, 257, 141, 130, 115, 103, 77 (100); UV (95% EtOH) λ_{max} 231 nm, 270 (sh), 277, 288.

Anal. Calcd for $C_{16}H_{13}NO_3S$: C, 64.19; H, 4.38; N, 4.70. Found: C, 63.95; H, 4.55; N, 4.70.

3-Acetyl-6-methoxy-1-(phenylsulfonyl)indole (2b). The same procedure as described above but using **1b** gave **2b** (99%). Flash chromatography using CH_2Cl_2 gave analytically pure **2b**: mp 160–161 °C; IR (KBr) 1670, 1615, 1550, 1365, 1170, 720 cm^{-1}; UV (95% EtOH) λ_{max} 212 nm, 228, 260, 269, 295; ^1H NMR ($CDCl_3$) δ 8.3–6.8 (m, 9 H), 3.82 (s, 3 H), 2.50 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 193.5, 158.5, 137.5, 136.0, 134.5, 131.0, 129.6, 126.9, 123.7, 121.8, 121.1, 113.6, 97.3, 55.7, 27.6.

Anal. Calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25; S, 9.73. Found: C, 61.94; H, 4.63; N, 4.25, S, 9.71.

3-Acetyl-5-fluoro-1-(phenylsulfonyl)indole (2c). The same procedure as described above but using **1c** gave **2c** (99%). Recrystallization from MeOH gave analytically pure **2c**: mp 169–170 °C; IR (KBr) 1674, 1445, 1375, 860 cm^{-1}; UV (95% EtOH) λ_{max} 211 nm, 225, 262 (sh), 270 (sh), 275, 290; ^1H NMR ($CDCl_3$) δ 8.4–6.8 (m, 9 H), 2.45 (s, 3 H).

Anal. Calcd for $C_{16}H_{12}FNO_3S$: C, 60.56; H, 3.81; N, 4.41; S, 10.10. Found: C, 60.60; H, 3.86, N, 4.41; S, 10.12.

3-Acetyl-5-methoxy-1-(phenylsulfonyl)indole (2d). The same procedure as described above but using **1d** gave crude **2d**. Flash chromatography using 1:1 hexane/CH_2Cl_2 gave 85% of **2d**: mp 200–202 °C; IR (KBr) 1670, 1545, 1485, 1455, 1385, 1155, 1035, 985, 860, 740, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.1–6.9 (m, 9 H), 3.85 (s, 3 H), 2.55 (s, 3 H); UV (95% EtOH) λ_{max} 221 nm, 268 (sh), 276, 285 (sh); mass spectrum, *m/e* 329 (M^+, 100), 314, 287, 188, 173, 160, 145, 117, 77.

Anal. Calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25; S, 9.74. Found: C, 61.82; H, 4.61; N, 4.18; S, 9.74.

Further elution with ethyl acetate afforded what we tentatively assign as 3,4-diacetyl-5-methoxy-1-(phenylsulfonyl)indole: mp 182–184 °C; IR (KBr) 1665, 1536, 1160, 1100, 1020, 865, 730, 615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.3–7.2 (m, 8 H), 3.90 (s, 3 H), 2.60 (s, 3 H), 2.40 (s, 3 H); UV (95% EtOH) λ_{max} 224 nm, 261 (sh), 269, 300 (sh); mass spectrum, *m/e* 371 (M^+), 356, 314, 215, 200, 187, 174.

Anal. Calcd for $C_{19}H_{17}NO_5S$: C, 61.44; H, 4.61; N, 3.77. Found: C, 61.31; H, 4.62; N, 3.75.

3-Propionyl-1-(phenylsulfonyl)indole (2e). The same procedure as described above but using **1a** and propionic anhydride gave **2e** (91%). Recrystallization from 95% ethanol gave analytically pure **2e** as white flakes: mp 143–144 °C; IR (KBr) 1660, 1615, 1530, 1160, 1100, 1020, 865, 730, 615 cm^{-1}; mass spectrum, *m/e* 313 (M^+), 284, 141, 115, 77.

Anal. Calcd for $C_{17}H_{15}NO_3S$: C, 65.16; H, 4.82; N, 4.47; S, 10.23. Found: C, 65.24; H, 4.86; N, 4.47; S, 10.16.

3-Benzoyl-1-(phenylsulfonyl)indole (2f). The same procedure as described above but using **1a** and benzoyl chloride gave **2f** (93%). Recrystallization from ether gave material, mp 111–112 °C (lit.[10] mp 109.5–111 °C), which was identical (IR, UV) with a known sample prepared earlier in our laboratory.[10]

4-[1-(Phenylsulfonyl)-3-indolyl]-4-oxobutyric Acid (2g). The same procedure as described above but using **1a** and succinic anhydride gave **2g** (81%). Recrystallization from EtOH gave analytically pure **2g**: mp 186.5–188 °C dec; IR (KBr) 3420, 1725, 1670, 1540, 1405, 1400, 1195, 1175, 1142, 1000, 760 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.32 (s, 1 H), 8.1–6.9 (m, 9 H), 3.05 (t, 2 H, J = 6 Hz), 2.38 (t, 2 H, J = 6 Hz); ^{13}C NMR (acetone-d_6) δ 194.2, 173.5, 137.8, 135.1, 133.0, 130.1, 128.0, 127.5, 125.8, 124.9, 123.0, 121.2, 34.6, 27.6; UV (95% EtOH) λ_{max} 225 nm, 290; mass spectrum, *m/e* 357 (M^+), 284, 191, 141, 115, 77 (100).

Anal. Calcd for $C_{18}H_{15}NO_5S$: C, 60.39; H, 4.26; N, 3.91; S, 9.05. Found: C, 60.48; H, 4.23; N, 3.94; S, 8.97.

Representative Procedure for the Hydrolysis of 2 to 3. 3-Acetylindole (3a). A magnetically stirred solution of **2a** (7.39 g, 0.024 mol), K_2CO_3 (8.30 g, 0.06 mol), MeOH (400 mL), and H_2O (100 mL) was refluxed under N_2 for 2 h. The methanol was evaporated in vacuo, and the aqueous residue was thoroughly extracted with CH_2Cl_2. The organic extract was washed with brine, dried (K_2CO_3), and concentrated in vacuo to give 3.80 g (96%) of **3a** as a white solid: mp 190–191 °C (lit.[4] mp 191–193 °C); IR (KBr) 3180, 1630, 1450, 1250, 1190, 945, 760 cm^{-1}; ^1H NMR (acetone-d_6) δ 8.7–7.0 (m, 5 H), 2.4 (s, 3 H); UV (95% EtOH) λ_{max} 219 nm, 241, 260 (sh), 296.

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6-Methoxy-3-acetylindole (3b). The same procedure as described above but with **2b** gave **3b** (79%). Recrystallization from MeOH gave analytically pure **3b**: mp 212–214 °C; IR (KBr) 3180, 1620, 1525, 1445, 1415, 1280, 1235, 1150, 945, 825, 810 cm^{-1}; UV (95% EtOH) λ_{max} 219 nm, 238, 281, 305; mass spectrum, *m/e* 189 (M^+), 164, 149, 131, 119, 100, 71, 57, 44, 40 (100).

Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.62; H, 5.91; N, 7.32.

5-Fluoro-3-acetylindole (3c). The same procedure as described above but with **2c** gave **3c** (85%). Recrystallization from ether gave analytically pure **3c**: mp 200–201.5 °C; IR (KBr) 3180, 1620, 1525, 1470, 1430, 1190, 1050, 1030, 960, 815, 790 cm^{-1}; UV (95% EtOH) λ_{max} 213 nm, 244, 257, 293; mass spectrum, *m/e* 177 (M^+), 162 (100), 148, 134, 107, 101, 75, 57.

Anal. Calcd for $C_{10}H_8FNO$: C, 67.79; H, 4.55; N, 7.91. Found: C, 67.60; H, 4.60; N, 7.81.

5-Methoxy-3-acetylindole (3d). The same procedure as described above but with **2d** gave **3d** (90%). Recrystallization from MeOH gave analytically pure **3d**: mp 208–209 °C; IR (KBr) 3150, 1610, 1420, 1210, 1030, 805, 650 cm^{-1}; UV (95% EtOH) λ_{max} 217 nm, 250, 268, 299; mass spectrum, *m/e* 189 (M^+), 174, 159, 149, 131, 85, 71, 57, 44, 40 (100).

Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.62; H, 5.93; N, 7.41.

3-Propionylindole (3e). The same procedure as described above but with **2e** gave **3e** (87%). Recrystallization from MeOH gave white crystals: mp 170–172 °C (lit.[4] mp 171–173 °C).

3-Benzoylindole (3f). The same procedure as described above but with **2f** gave **3f** (88%). Recrystallization from MeOH gave white crystals: mp 242–245 °C (lit.[4] mp 241–243.5 °C).

1-(Phenylsulfonyl)-*N*-(1,1-dimethylethyl)indole-3-carboxamide (5a). To a magnetically stirred suspension of $AlCl_3$ (6.66 g, 50 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added dropwise oxalyl chloride (4.40 mL, 50 mmol). After 30 min at 0 °C, a solution of **1a** (2.58 g, 10 mmol) in CH_2Cl_2 (50 mL) was added and the resulting mixture was allowed to warm to 25 °C. After an additional 2 h crushed ice (100 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL). the usual workup gave **2h** as a brown oil (IR (neat) 1750 cm^{-1}). This crude oil was taken up in CH_2Cl_2 (100 mL) and stirred overnight under N_2 with excess *tert*-butylamine. The reaction mixture was washed with 10% aqueous HCl (2 × 100 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL), dried (K_2CO_3), and evaporated in vacuo to give a white solid. Recrystallization from ether gave 2.23 g (three crops) of pure **5a** and flash chromatography of the mother liquor using CH_2Cl_2 afforded an additional 1.22 g (97%) of **5a**: mp 209–210 °C; IR (KBr) 3260, 1640, 1560, 1455, 1385, 1180, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.2 (m, 10 H); 1.5 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 162.8, 137.6, 134.9, 134.3, 129.5, 127.9, 126.9, 126.9, 125.4, 124.2, 121.5, 118.9, 113.4, 51.8, 29.0; mass spectrum, *m/e* 356 (M^+), 341, 300, 284, 215, 143, 77 (100); UV (95% EtOH) λ_{max} 217 nm, 261, 268 (sh), 276 (sh), 284 (sh), 291 (sh).

Anal. Calcd for $C_{19}H_{20}N_2SO_3$: C, 64.02; H, 5.65; N, 7.86; S, 9.00. Found: C, 63.82; H, 5.62; N, 7.70; S, 9.37.

1-(Phenylsulfonyl)-*N*,*N*-diethylindole-3-carboxamide (5b). This was prepared from **2h** and diethylamine in a similar fashion in 80% yield after flash chromatography with CH_2Cl_2: mp 132–133 °C; IR (KBr) 1615, 1445, 1370, 1180, 740, 690, 650, 600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.0 (m, 10 H), 3.5 (q, 4 H, J = 6 Hz), 1.3 (t, 6 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 164.5, 137.7, 134.3, 134.2, 129.4, 128.8, 126.8, 125.4, 124.1, 123.9, 121.0, 118.1, 113.3; UV (95% EtOH) λ_{max} 215 nm, 252, 282, 293; mass spectrum, *m/e* 356 (M^+), 284, 215, 187, 141, 116, 77 (100).

Anal. Calcd for $C_{19}H_{20}N_2O_3S$: C, 64.02; H, 5.65; N, 7.86. Found: C, 64.19; H, 5.50; N, 7.83.

3-Cyano-1-(phenylsulfonyl)indole (6). A magnetically stirred suspension of the *tert*-butylamide **5a** (0.505 g, 1.42 mmol) in benzene (25 mL) at room temperature was treated with phosphorus oxychloride (1.5 mL, 15 mmol). The mixture was refluxed for 7 h and concentrated in vacuo. Dichloromethane (50 mL) and saturated aqueous $NaHCO_3$ (50 mL) were added to the residue, and the mixture was stirred overnight. The usual workup and flash chromatography (CH_2Cl_2) of the residue gave 0.378 g (94%) of nitrile **6**: mp 151–152 °C; IR (KBr) 2250, 1545, 1450, 1380, 1180, 970 cm^{-1}; ^{13}C NMR δ 137.1, 134.9, 133.6, 133.1, 129.8, 128.3, 127.1, 126.6, 124.9, 120.3, 113.7, 113.4, 93.9; mass spectrum, *m/e* 282 (M^+), 141, 77 (100); UV (95% EtOH) λ_{max} 216 nm, 262, 267, 283 (sh), 290 (sh).

Anal. Calcd for $C_{15}H_{10}N_2O_2S$: C, 63.81; H, 3.57; N, 9.93; S, 11.36. Found: C, 63.58; H, 3.39; N, 9.81; S, 11.46.

3-Cyanoindole (7). A magnetically stirred solution of **6** (0.378 g, 1.34 mmol), K_2CO_3 (0.55 g, 4.0 mmol), MeOH (25 mL), and H_2O (10 mL) was refluxed under N_2 for 2 h. The MeOH was evaporated in vacuo, and the aqueous residue was extracted with CH_2Cl_2. The usual workup and flash chromatography (CH_2Cl_2) gave 0.156 g (82%) of **7**: mp 181–182 °C (lit.[25] mp 178–180.5 °C); IR (KBr) 3260, 2230, 1525, 1435, 1240, 750, 740 cm^{-1}; UV (95% EtOH) λ_{max} 217 nm, 270, 278, 285; mass spectrum, *m/e* 142 (M^+, 100), 115, 100, 88, 71.

Representative Procedure for the Reduction of 2. 3-Ethyl-1-(phenylsulfonyl)indole (8a). To magnetically stirred trifluoroacetic acid (25 mL) at 0 °C under N_2 was added sodium borohydride (30 mmol, five pellets) over 30 min. To this mixture at 15 °C was added dropwise over 30 min a solution of **2a** (0.50 g, 1.67 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred overnight at 25 °C, diluted with water (75 mL), and made basic by the addition of sodium hydroxide pellets at 0 °C. The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the usual workup gave 0.47 g (99%) of **8a** as a white solid: mp 121–122 °C. Recrystallization from ether/hexane gave crystals, mp 123.5–124.5 °C (lit.[26] mp 125–125.5 °C), identical (IR, UV) with a sample previously prepared in this laboratory.[27]

3-Propyl-1-(phenylsulfonyl)indole (8b). The same procedure as described above but with **2e** gave **8b** in 96% yield: mp 95–96 °C; IR (KBr) 1445, 1360, 1275, 1165, 975, 750, 720, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–7.2 (m, 10 H), 2.65 (t, 2 H, J = 7 Hz), 1.75 (m, 2 H), 1.0 (t, 3 H, J = 7 Hz); UV (95% EtOH) λ_{max} 217 nm, 255, 292; mass spectrum, *m/e* 299 (M^+), 270, 158, 143, 130, 116, 102, 77 (100).

Anal. Calcd for $C_{17}H_{17}NSO_2$: C, 68.20; H, 5.72; N, 4.68; S, 10.71. Found: C, 68.03; H, 5.70; N, 4.53; S, 11.17.

3-Benzyl-1-(phenylsulfonyl)indole (8c). The same procedure as described above but with **2f** gave **8c** in 99% yield: mp 84–85 °C; IR (KBr) 1450, 1360, 1175, 975, 800, 765, 755, 735, 720, 700, 685, 650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0–6.9 (m, 15 H), 3.8 (s, 3 H); UV (95% EtOH) λ_{max} 217 nm, 254, 292; mass spectrum, *m/e* 77.

Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03; S, 9.23. Found: C, 72.50; H, 4.96; N, 4.00; S, 9.17.

5-Chloroindolo[1,2-*b*][2,7]naphthyridine-6,11-quinone (10). Keto acid **9**[18] (0.30 g, 0.64 mmol) was added slowly to thionyl chloride (15 mL) at 25 °C, and the mixture was stirred overnight under N_2. Removal of the excess thionyl chloride in vacuo gave a yellowish oil (IR (neat) 1790 cm^{-1}) which was taken up in CH_2Cl_2 (20 mL) and added dropwise to a stirred suspension of $AlCl_3$ (0.30 g, 2.3 mmol) in CH_2Cl_2 (20 mL). The resulting red mixture was stirred at 25 °C for 1 h, quenched with ice, and worked up as usual. Flash chromatography of the crude residue using 1:1 hexane/CH_2Cl_2 afforded 0.11 g (61%) of **10** as a bronze solid: mp 219–220 °C dec; IR (KBr) 1690, 1670, 1535, 1365, 1330, 1260, 1240, 765, 750, 725, 690 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 173.4, 157.6, 155.5, 151.4, 139.0, 135.1, 132.0, 127.4, 126.8, 126.2, 124.8, 123.7, 121.3, 118.6, 117.4; mass spectrum, *m/e* 282 (M^+, 100), 254, 226, 191, 164, 149, 141, 114, exact mass calcd for $C_{15}H_7ClN_2O_2$ 282.0196, found 282.0131; UV (95% EtOH) λ_{max} 214 nm, 241, 391, with added base 223 nm, 247, 343.

Anal. Calcd for $C_{15}H_7ClN_2O_2$: C, 63.73; H, 2.50; N, 9.91; Cl, 12.54. Found: C, 62.21; H, 2.83; N, 9.07; Cl, 11.54.

5-Methoxyindolo[1,2-*b*][2,7]naphthyridine-6,11-quinone (12). The chloro keto lactam **10** was dissolved in a 2:1 mixture of THF/MeOH (30 mL) and added dropwise to a solution of sodium methoxide (3 equiv) in methanol at 0 °C. The mixture was allowed to warm to 25 °C over a period of 2 h, the solvent was removed in vacuo, and the solid residue was suspended in

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water (25 mL) and extracted with ethyl acetate (5 × 50 mL). The usual workup gave 0.041 g (88%) of **12**: mp 214–219 °C dec; IR (KBr) 1690, 1650, 1545, 1460, 1365, 1330, 1245, 1015, 995, 745, 720, 690 cm^{-1}; mass spectrum, *m/e* 278 (M$^+$), 249 (100), 235, 207, 152, 130, 102, 76; UV (95% EtOH) λ_{max} 209 nm, 244, 404, with added base 219, 246 (sh) 404.

Anal. Calcd for $C_{16}H_{10}N_2O_3$: C, 69.06; H, 3.62; N, 10.07. Found: C, 68.84; H, 3.69; N, 9.97.

1-(Phenylsulfonyl)-3-chloroindol-2-yl 3-Carbomethoxy-4-pyridyl Ketone (11). Keto acid **9**[18] (2.02 g, 4.35 mmol) was added slowly to thionyl chloride (50 mL) at 25 °C, and the mixture was stirred overnight under N_2. The excess thionyl chloride was removed in vacuo, MeOH (25 mL) was added to the residue, and the mixture was refluxed for 1 h under N_2. The solvent was removed in vacuo, and the residue was taken up in ethyl acetate. Washing with saturated aqueous $NaHCO_3$, and the usual workup gave 2.06 g of a crude solid. Flash chromatography (CH_2Cl_2) and recrystallization from ether afforded 0.50 g (25%) of **11**: mp 153–154 °C; IR (KBr) 1745, 1675, 1355, 1280, 1210, 1180, 1160, 760, 740, 590, 580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.0 (s, 1 H), 8.8–8.7 (d, 1 H), 8.1–7.2 (m, 10 H), 3.6 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 183.8, 165.6, 153.0, 150.8, 146.3, 137.5, 137.0, 134.2, 131.8, 129.4, 129.1, 127.4, 127.3, 125.3, 125.1, 123.5, 122.3, 120.8, 115.7, 52.8; UV (95% EtOH) λ_{max} 219 nm, 310; mass spectrum, *m/e* 454 (M$^+$), 297, 282, 249, 164, 141, 114, 77 (100).

Anal. Calcd for $C_{22}H_{15}ClN_2O_5S$: C, 58.09; H, 3.32; N, 6.16; S, 7.05. Found: C, 58.03; H, 3.36; N, 6.13; S, 7.01.

Methoxy Keto Lactam 12. Keto ester **11** (0.30 g, 0.71 mmol) was added dropwise in methanol (20 mL) to a solution of sodium methoxide (4.28 mmol) in methanol (50 mL) at 0 °C. After being stirred at 0 °C for 1 h, the mixture was then refluxed for an additional 1 h. The solvent was removed in vacuo, water (50 mL) was added, and the aqueous layer was extracted with ethyl acetate (5 × 50 mL). The usual workup and recrystallization from acetone gave 0.13 g (71%) of **12**. Similar results were obtained upon treatment of **11** with magnesium methoxide.

1-(Phenylsulfonyl)indol-3-yl 2-Carboxy-1-phenyl Ketone (14). To a magnetically stirred suspension of $AlCl_3$ (3.1 g, 23.3 mmol) in CH_2Cl_2 (100 mL) was added freshly sublimed phthalic anhydride (2.00 g, 13.4 mmol), and the mixture was stirred for 1 h at 25 °C. A solution of **1a** (3.00 g, 11.67 mmol) in CH_2Cl_2 (50 mL) was added, and the mixture was stirred for 18 h at 25 °C. The reaction was quenched with ice and water (200 mL), and the usual workup with CH_2Cl_2 (200 mL) gave 4.77 g of an off white solid was obtained. Recrystallization from acetone gave 2.85 g (60%) of **14** in three crops: mp 205–207 °C; IR (KBr) 1690, 1660, 1375, 1290, 1185, 975, 735, 595 cm^{-1}; ^{13}C NMR (Me_2SO-d_6) δ 191.4, 167.5, 141.4, 136.3, 135.5, 134.3, 133.3, 132.4, 130.6, 130.5, 129.9, 127.8, 127.5, 127.4, 126.2, 125.1, 122.5, 121.7, 113.2: UV (95% EtOH) λ_{max} 215 nm, 268, 275, 292; mass spectrum, *m/e* 405 (M$^+$), 361, 284, 247, 220, 144, 115, 77 (100).

Anal. Calcd for $C_{22}H_{15}NO_5S$: C, 65.17; H, 3.73; N, 3.46; S, 7.91. Found: C, 64.21; H, 3.80; N, 3.38; S, 7.80.

1-(Phenylsulfonyl)indol-3-yl 2-Carbethoxy-1-phenyl Ketone (15). A mixture of keto acid **14** (1.50 g, 3.70 mmol), absolute EtOH (100 mL), benzene (100 mL), and *p*-toluenesulfonic acid (1.70 g) was refluxed for 8 days with azeotropic removal of water. The solvent was removed in vacuo and CH_2Cl_2 (300 mL) was added. The solution was washed with 10% aqueous sodium bicarbonate (3 × 150 mL), and the usual workup gave a brown oil. Flash chromatography with CH_2Cl_2 gave 1.50 g (94%) of **15** as a colorless foam. Recrystallization from ether/hexane gave the analytical sample: mp 104–105 °C; IR (KBr) 1715, 1660, 1540, 1445, 1370, 1275, 1175, 970, 850, 735, 680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.5–7.2 (m, 14 H), 3.95 (q, 2 H, J = 6 Hz), 0.85 (t, 3 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 191.6, 166.1, 141.5, 137.3, 135.0, 134.9, 133.4, 132.3, 130.4, 130.3, 129.9, 129.6, 127.6, 127.5, 127.0, 126.0, 125.0, 123.0, 122.3, 113.1, 61.3, 13.5; UV (95% EtOH) λ_{max} 214 nm, 267 (sh), 276 (sh), 293; mass spectrum, *m/e* 433 (M$^+$), 284, 264, 248, 236, 220, 208, 165, 141, 115, 105, 77 (100).

Anal. Calcd for $C_{24}H_{19}NO_5S$: C, 66.50; H, 4.42; N, 3.23; S, 7.40. Found: C, 66.46; H, 4.32; N, 3.13; S, 7.66.

***5H*-Benzo[*b*]carbazole-6,11-quinone (16).** A solution of the keto ester **15** (0.699 g, 1.62 mmol) in dry THF (50 mL) was added slowly at −75 °C to a magnetically stirred solution of lithium bis(trimethylsilyl)amide (4 mmol) prepared from 1,1,1,3,3,3-hexamethylsilazane (0.78 g, 4.8 mmol) and *n*-butyllithium (1.46 M in hexane; 2.7 mL, 4 mmol) in dry THF (50 mL) under N_2. The mixture was allowed to warm to room temperature overnight and adsorbed directly onto silica gel in vacuo. Flash chromatography using 8:2 hexane/methylene chloride afforded 0.153 g (38%) of **16**, mp 315–316 °C dec (lit.[17a] mp 307–310 °C). The spectra (IR, UV, mass) of **16** are in excellent agreement with those reported.[17a]

1-(Phenylsulfonyl)indol-3-yl 3-Carboxy-4-pyridyl Ketone (18). To a magnetically stirred suspension of $AlCl_3$ (9.30 g, 70.0 mmol) in CH_2Cl_2 (200 mL) was added pyridine-3,4-dicarboxylic acid anhydride (5.32 g, 35 mmol), and the mixture was stirred for 30 min at 25 °C. A solution of **1a** (2.50 g, 9.70 mmol) in CH_2Cl_2 (40 mL) was added dropwise, and the mixture was stirred for 2 h at 25 °C. The reaction was quenched with ice, and the resulting solids were collected and dried. This material was refluxed in acetone (400 mL) for 1 h. Hot gravity filtration and concentration of the filtrate to half volume gave white crystals which were collected (in three crops) affording 2.71 g (69%) of **18**, mp 226–228 °C dec. (lit.[20] mp 228–229 °C dec).

1-(Phenylsulfonyl)indol-3-yl 3-Carbethoxy-4-pyridyl Ketone (19). A mixture of the keto acid **18** (2.05 g, 5.05 mmol), absolute EtOH (75 mL), benzene (250 mL), and *p*-toluenesulfonic acid (1.53 g, 8.04 mmol) was refluxed for 3 days with azeotropic removal of water. The solvents were removed in vacuo, ethyl acetate (200 mL) was added, and the mixture was washed with 10% aqueous $NaHCO_3$ (3 × 150 mL). The usual workup gave 1.66 g (75%) of **19**: mp 155–157 °C (lit.[20] mp 163–165 °C). This material was identical (TLC, IR, ^{1}H NMR) with a sample prepared earlier in our laboratory.[20]

***10H*-Pyrido[3,4-*b*]carbazole-5,11-quinone (20).** To a magnetically stirred solution of the keto ester **19** (0.338 g, 0.77 mmol) in dry THF (50 mL) at −75 °C was slowly added via cannula a solution of the lithium salt of *N,N,N'*-trimethylethylenediamine (0.77 mmol) prepared from the diamine (0.09 g, 0.85 mmol) and *n*-butyllithium (1.31 M in hexane; 0.6 mL, 0.77 mmol) in dry THF (20 mL) at −75 °C. The resulting yellow solution was stirred at −75 °C for 2 h. To this was added slowly via cannula a solution of lithium bis(trimethylsilyl)amide (0.85 mmol) (prepared in dry THF (25 mL) from 1,1,1,3,3,3-hexamethyldisilazane (0.19 g, 1.17 mmol) and *n*-butyllithium (0.62 mL, 0.85 mmol)), and the mixture was allowed to warm to room temperature overnight under N_2. The reaction mixture was treated with 10% aqueous ammonium chloride (40 mL) and extracted with ethyl acetate (3 × 100 mL). The organic extract was washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried (K_2CO_3), and evaporated in vacuo onto silica gel. Flash chromatography with 1:1 methylene chloride/ethyl acetate provided 0.071 g (37%) of **20**: mp 317–320 °C dec (lit.[19] mp 317–320 °C). This sample was identical (TLC, IR, mmp) with a sample kindly provided by Professor J. A. Joule and with material previously prepared in this laboratory.[20]

4-Carbomethoxynicotinic Acid (21). To a suspension of pyridine-3,4-dicarboxylic acid anhydride (**17**) (18.85 g, 0.13 mol) in dry THF (200 mL) at −70 °C under argon was added a solution of sodium methoxide (8.10 g, 0.15 mol) in dry MeOH (25 mL). The mixture was allowed to warm to 25 °C overnight. The solvents were removed in vacuo to afford 26.11 g (99%) of the sodium salt of **21**. This salt (10.00 g, 48.3 mmol) was dissolved in 100 mL of H_2O at 0 °C and was acidified to pH 2–3 by the slow dropwise addition of concentrated HCl with vigorous stirring. The resulting white solid was collected by filtration and recrystallized from acetone (200 mL) to give 6.42 g (73%) of the mixed acid ester **21**: mp 172–174 °C (lit.[28] mp 172 °C); ^{1}H NMR (Me_2SO-d_6) δ 9.13 (s, 1 H), 8.94 (d, 1 H, J = 5.5 Hz), 8.70 (br, 1 H), 7.65 (d, 1 H, J = 5.5 Hz), 3.93 (s, 3 H); ^{13}C NMR (Me_2SO-d_6) δ 166.6, 165.9, 153.0, 140.3, 125.2, 121.6, 52.8.

4-Carbomethoxynicotinoyl Chloride (22). The acid ester **21** (2.10 g, 11.6 mmol) was suspended in benzene (75 mL), and thionyl chloride (25 mL) was added dropwise with stirring. The mixture was refluxed overnight under N_2, and the solvents were removed under reduced pressure. Vacuum distillation of the residue afforded 1.82 g (78%) of **22**: bp 95–100 °C (0.6 torr); IR

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(neat) 1769, 1741, 1585, 1434, 1295, 1201, 1100, 1050, 954, 868, 824, 696, 664 cm^{-1}; ^1H NMR (acetone-d_6) δ 9.14 (s, 1 H), 9.01 (d, 1 H, J = 5 Hz), 7.79 (d, 1 H, J = 5 Hz), 3.97 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.1, 164.9, 152.9, 149.7, 138.0, 130.2, 122.3, 53.4.

1-(Phenylsulfonyl)indol-3-yl 4-Carbomethoxy-3-pyridyl Ketone (23). To a magnetically stirred suspension of $AlCl_3$ (4.85 g, 36.4 mmol) in CH_2Cl_2 (100 mL) at 25 °C was added the acid chloride **22** (3.59 g, 18 mmol) in 25 mL of CH_2Cl_2, and the mixture was stirred for 10 min. A solution of **1a** (2.34 g, 9.1 mmol) in CH_2Cl_2 (25 mL) was added dropwise, and the mixture was stirred overnight at 25 °C and quenched with ice. The usual workup and flash chromatography with 1:1 hexane/CH_2Cl_2 gave 1.93 g (50%) of **23** as an amber oil. Crystallization from ether gave the analytical sample as light yellow crystals: mp 146–149 °C; IR (KBr) 1740, 1670, 1545, 1445, 1380, 1290, 1180, 975, 865, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.9–7.0 (m, 13 H), 3.4 (s, 3 H); ^{13}C NMR 188.8, 165.2, 151.8, 148.6, 137.0, 136.9, 135.0, 134.9, 134.6, 133.6, 129.6, 127.2, 127.0, 126.2, 125.1, 123.1, 122.9, 121.7, 113.0, 52.8; mass spectrum, m/e 420, 284, 236, 220, 164, 141, 115, 77 (100); UV (95% EtOH) λ_{max} 222 nm, 263 (sh), 268 (sh), 277 (sh), 280.

Anal. Calcd for $C_{22}H_{16}N_2O_5S$: C, 62.85; H, 3.84; N, 6.66; S, 7.63. Found: C, 62.79; H, 3.86; N, 6.65; S, 7.55.

6*H*-Pyrido[4,3-*b*]carbazole-5,11-quinone (24). To a magnetically stirred solution of the keto ester **23** (0.461 g, 1.1 mmol) in dry THF (50 mL) at −75 °C was slowly added via cannula a solution of the lithium salt of *N,N,N'*-trimethylethylenediamine (1.2 mmol) prepared as described earlier in 25 mL of dry THF. The resulting light orange solution was stirred at −75 °C for 2 h, and a solution of lithium bis(trimethylsilyl)amide (1.25 mmol) in THF (50 mL) was added via cannula and the mixture was stirred overnight under N_2. The solvent was removed in vacuo, saturated aqueous $NaHCO_3$ (100 mL) was added, and the mixture was extracted with ethyl acetate. The usual workup and flash chromatography using initially 1:1 hexane/CH_2Cl_2 and then 1:1 hexane/ethyl acetate gave 0.129 (47%) of **24**: mp 345–347 °C dec (lit.[19] mp 317–320 °C). This sample was identical (TLC, IR, mass spectrum) with a sample kindly provided by Professor J. A. Joule.

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Photocyclization of *o*-Halostilbenes

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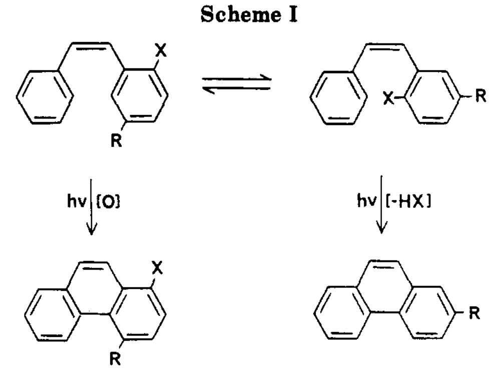
The photocyclization reactions of several ortho-halogenated stilbene derivatives were examined under both oxidative conditions (iodine/cyclohexane) and basic conditions (sodium methoxide/methanol). The major products were those anticipated from photodehydrogenation and photodehydrohalogenation, respectively. In some cases photodebromination of the product occurred. Some regiochemical control in phenanthrene synthesis can be achieved as is illustrated by a synthesis of dehydroorchinol acetate.

Since its discovery more than three decades ago[1] the photocyclization of stilbene derivatives has become a standard method for the preparation of phenanthrenes.[2,3] The yields are generally good and the preparation of the necessary stilbenes is typically straightforward. While the reaction is usually carried out under oxidative conditions, some interesting variations are known, including the photolysis of stilbenes with halogen in an ortho position. These substituents have been used as blocking groups in oxidative photolyses[4] and have been removed in photodehydrohalogenations[5] (Scheme I).

This scheme offers the potential for regiochemical control in the photolysis of stilbenes with meta substituents (Scheme I, R ≠ H). These generally photocyclize with little selectivity giving mixtures of 2- and 4-substituted phenanthrenes.[6] To date, no comparative study has been published in which the photochemistry of *o*-halostilbenes is examined under both oxidative and nonoxidative (i.e., basic) conditions. We wish to report the results of such a study.

Scheme I



Results

Stilbenes **1a–d** and the naphthyl compounds **4a** and **4b** were prepared by Wittig reactions (Experimental Section),

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