to be produced in substantial amounts under comparable aquatic conditions.

Experimental Section

(-)-*cis*-(5-Vinyl-2-cyclopentenyl)acetic Acid (2). Various mother liquor fractions obtained from resolution of the racemic acid with *endo*-bornylamine[8] were acidified with 10% hydrochloric acid and extracted with ether (3 × 50 mL). The combined organic layers were washed with brine, dried, and evaporated to provide 4.56 g of **2**, $[\alpha]^{25}_D$ -47.1° (*c* 0.035, C_2H_5OH), which was directly reduced without further purification.

(-)-*cis*-(5-Vinyl-2-cyclopentenyl)acetaldehyde (4). A slurry of (-)-**2** (4.56 g, 30.0 mmol) and lithium aluminum hydride (2.0 g, 52.6 mmol) in anhydrous ether (100 mL) was stirred at the reflux temperature for 1 h. The reaction mixture was cooled in an ice bath while treated dropwise sequentially with water (2 mL), 15% sodium hydroxide solution (2 mL), and again with water (6 mL). The solids were separated by filtration and rinsed well with ether. The combined filtrates were evaporated to give 3.24 g (78%) of alcohol: $[\alpha]^{25}_D$ -40.1° (*c* 0.041, C_2H_5OH); ^1H NMR (300 MHz, $CDCl_3$) δ 5.85-5.76 (m, 1 H), 5.70 (s, 2 H), 5.03-4.93 (m, 2 H), 3.60 (t, J = 6.1 Hz, 2 H), 2.88-2.72 (m, 2 H), 2.41-2.13 (AB of ABMX, J_{AB} = 14 Hz, 2 H), 1.66-1.39 (m, 2 H); ^{13}C NMR ($CDCl_3$) ppm 139.8, 134.4, 129.8, 114.7, 61.9, 46.1, 44.9, 37.5, 33.8; *m/z* calcd (M^+) 138.1044, obsd 138.1034.

A cold (-78 °C) solution of oxalyl chloride (0.40 mL, 4.58 mmol) in dichloromethane (5 mL) was treated dropwise with a solution of dimethyl sulfoxide (0.71 mL, 10.0 mmol) in the same medium (2 mL). After 10 min, the above alcohol (248 mg, 1.79 mmol) in dichloromethane (5 mL) was introduced and the reaction mixture was stirred at -78 °C for 30 min. Following the addition of triethylamine (3 mL, 21.5 mmol), the solution was allowed to warm to room temperature during 1 h and treated with water (10 mL). The aqueous phase was extracted with dichloromethane and the combined organic phases were washed with brine, dried, and evaporated. MPLC purification of the residue (silica gel, elution with 5% ethyl acetate in petroleum ether) afforded 130 mg (50%) of **4**, $[\alpha]^{25}_D$ -34.4° (*c* 0.036, C_2H_5OH), identical in all respects with the known racemic material.

Enamine 5. A mixture of (-)-**4** (500 mg, 3.68 mmol), freshly distilled piperidine (2.0 mL, 20.2 mmol), and activated 3-Å molecular sieves (2.0 g) in dry benzene was stirred at 25 °C for 14 h. The reaction mixture was filtered, and the filtrate was evaporated to provide 733 mg (99%) of **5** which was used directly without further purification: ^1H NMR (300 MHz, $CDCl_3$) δ 6.20-5.80 (m, 1 H), 5.76 (s, 2 H), 5.10 (m, 2 H), 4.85 (m, 2 H), 4.20 (m, 2 H), 2.80 (m, 4 H), 2.2-2.0 (m, 2 H), 1.60 (br s, 6 H).

Phenylselenation of 5. A solution of **5** (733 mg, 3.64 mmol) in dry tetrahydrofuran (15 mL) was cooled to -115 °C under an argon atmosphere prior to dropwise addition of phenylselenenyl chloride (740 mg, 3.86 mmol) in 5 mL of the same solvent. The reaction mixture was stirred at -110 °C for 5 min, warmed to -78 °C during 15 min, treated with water (20 mL) and ether (80 mL), and stirred vigorously at room temperature for 4 h. The separated organic layer was dried and evaporated to leave a residue which was purified by MPLC on silical gel. Elution with 3% ethyl acetate in petroleum ether provided 500 mg (47%) of **6a** and **6b** as a 9:1 mixture (^1H NMR analysis); $[\alpha]^{25}_D$ -56.3° (*c* 0.010, C_2H_5OH). The spectral properties of this mixture were identical with those reported earlier.[5]

Epoxide 7. Reaction of (-)-**6** (500 mg, 1.72 mmol) with ethylmagnesium bromide [prepared from freshly distilled ethyl bromide (0.30 mL, 4.02 mmol) and magnesium turnings (100 mg, 4.17 mmol)] in ether (25 mL) at -116 °C to -78 °C as outlined previsouly[5] returned 70 mg of unreacted **6** and gave 353 mg (74% based on recovered **6**) of selenyl alcohol, $[\alpha]^{25}_D$ -39.1° (*c* 0.011, C_2H_5OH).

A solution of this substance (350 mg, 1.09 mmol) in dry dimethoxyethane (10 mL) was stirred at 25 °C under nitrogen in a drybox as freshly prepared triethyloxonium tetrafluoroborate (277 mg, 1.44 mmol) was added in portions over a few minutes. After 2 h, the reaction mixture was transferred via syringe to a slurry of sodium hydride (3.54 mmol) in dry dimethoxyethane (5 mL), stirred for 30 min, and poured into brine. Following the predescribed workup[5] and MPLC on silica gel (elution with 5% ethyl acetate in petroleum ether), there was isolated 100 mg (56%) of (-)-**7**, $[\alpha]^{25}_D$ -47.5° (*c* 0.0305, C_2H_5OH). The spectral properties of this substance were identical with those reported earlier.[5]

(-)-Multifidene (1). A solution of diphenylphosphine (70 μL, 0.402 mmol) in anhydrous tetrahydrofuran (0.5 mL) was stirred at 0 °C as *n*-butyllithium in hexane (0.25 mL of 1.6 M) was added via syringe. A solution of (-)-**7** (32.3 mg, 0.196 mmol) in anhydrous tetrahydrofuran (1.5 mL) was then introduced and the reaction mixture was stirred at 25 °C for 14 h. Following recooling to 0 °C, acetic acid (0.25 mL) and 30% hydrogen peroxide (0.25 mL) were sequentially added. The solution was stirred at 0 °C for 4 h and diluted with dichloromethane (25 mL). The separated organic phase was washed with saturated sodium bicarbonate solution (10 mL) and brine (10 mL), dried, and evaporated to leave 92 mg of crude hydroxy phosphine oxide.

The above product was dissolved in dry dimethylformamide (1.5 mL) and slowly added to a stirred slurry of sodium hydride (2.5 mmol) in the same solvent (0.5 mL). After 16 h at 25 °C, the reaction mixture was quenched with water and extracted with petroleum ether (3 × 15 mL). The combined extracts were dried and carefully evaporated to provide 20 mg (69%) of (-)-**1**, $[\alpha]^{25}_D$ -80° (*c* 0.0005, CCl_4), whose spectra (MS, ^1H NMR) were identical with those of the natural product.

Acknowledgment. The financial support of the National Institutes of Health (Grant GM 30827) is gratefully acknowledged.

Synthesis and Diels-Alder Reactions of 1,3-Dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole. A New Annulation Strategy for the Construction of Ellipticine and Isoellipticine

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The novel fused heterocycle 1,3-dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (**4**) is synthesized from 3-ethylindole (**6**) in six steps (46% yield) or from indole-3-carboxaldehyde (**12**) in four steps (21% yield). Furoindole **4** undergoes Diels-Alder reactions with dimethyl acetylenedicarboxylate, *N*-phenylmaleimide, benzyne, and 3,4-pyridyne (**5**) to give the expected adducts **17**, **18a,b**, **19**, and **23a,b**, respectively. Deoxygenation and desulfonylation of **19** and **23a,b**, respectively, give benzocarbazole **22** and a readily separable mixture of the pyridocarbazole alkaloids ellipticine (**1a**) and isoellipticine (**2a**).

The 6*H*-pyrido[4,3-*b*]carbazole alkaloids ellipticine (**1a**) and 9-methoxyellipticine (**1b**) exhibit pronounced anticancer activity toward several experimental[1] and human[2] tumor systems, and 2-methyl-9-hydroxyellipticinium ace-

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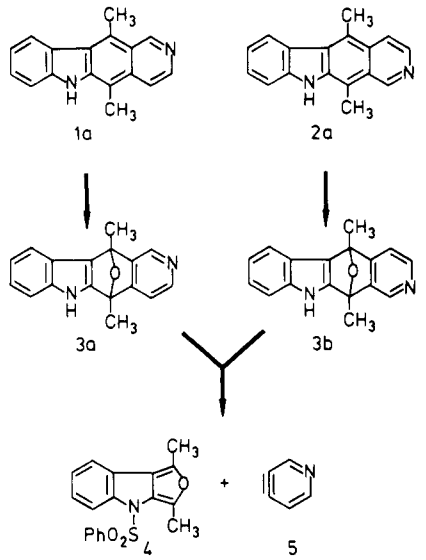
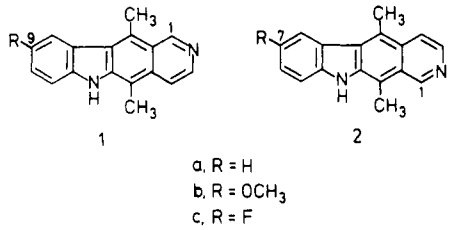
Scheme I



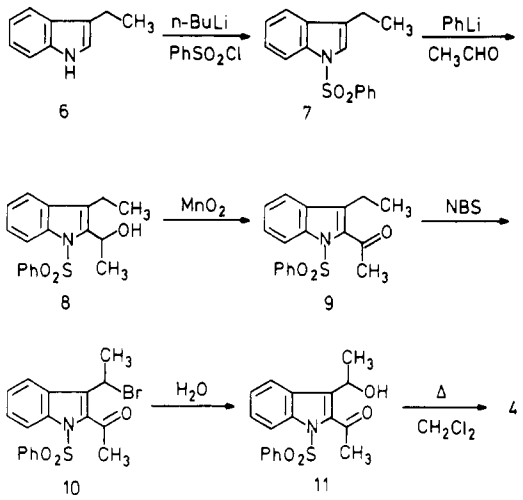
tate is currently in clinical use in France.[3] Not surprisingly, these alkaloids have been the target of many synthetic efforts,[4] and our own work in this area[5]—involving the regioselective acylation of lithiated indoles with 3,4-pyridinedicarboxylic acid anhydride—has led to efficient syntheses of **1a**,[5a] **1b**,[5b] **1c**,[5b] the isomeric 10*H*-pyrido[3,4-*b*]carbazoles **2a**[5c] ("isoellipticine") and **2b**,[5c] and the *Strychnos* alkaloid 17-oxoellipticine.[5d]



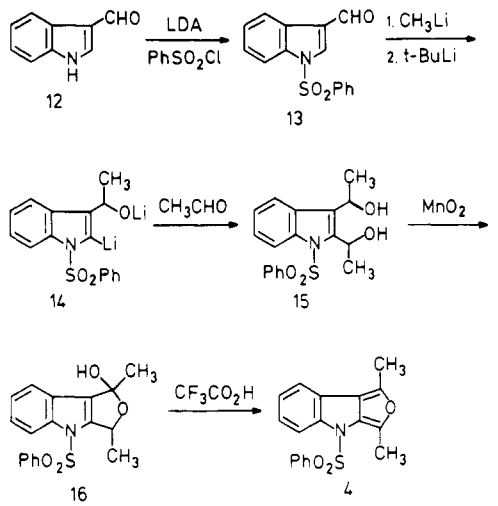
a, R = H
b, R = OCH_3
c, R = F

We now report a new annulation strategy for the construction of the pyridocarbazole ring system and its application to the synthesis of ellipticine (**1a**) and isoellipticine (**2a**). Our approach is illustrated retrosynthetically in Scheme I and utilizes a Diels–Alder reaction between 3,4-pyridyne (**5**) and 1,3-dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (**4**),[6] followed by extrusion of the oxygen bridge from **3a** and **3b** to give **1a** and **2a**, respectively.

Scheme II



Scheme III



Results and Discussion

Synthesis of 1,3-Dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (4). At the outset of this research, the ring system represented by **4** was new,[6,7] although a few examples of pyrrolo-,[8] thieno-,[9] and selenolo[3,4-*b*]indoles[9] had been reported. Our target molecule for the synthesis of **4** was hydroxy ketone **11**, which we reasoned would undergo facile cyclodehydration to yield **4**.[10] The preparation of **11** and its conversion to **4** were readily accomplished as follows (Scheme II). Treatment of 3-ethylindole (**6**)[11] with *n*-butyllithium in tetrahydrofuran (THF) followed by the addition of benzenesulfonyl chloride at −78 °C[12] gave the known[13] protected indole **7** in 74% purified yield. Regioselective C-2 lithiation of **7** was achieved with

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(4) For reviews, see: (a) Sainsbury, M. *Synthesis* **1977**, 437. (b) Barone, R.; Chanon, M. *Heterocycles* **1981**, *16*, 1357. (c) Gribble, G. W.; Saulnier, M. G. *Heterocycles*, submitted for publication. For post 1980 syntheses, see the references cited in ref 5.

(5) (a) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1982**, *47*, 2810. (b) Unpublished results. (c) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1983**, *48*, 2690. (d) Saulnier, M. G.; Gribble, G. W. *Tetrahedron Lett.* **1983**, *24*, 3831.

(6) For a preliminary communication describing one synthesis of the 4*H*-furo[3,4-*b*]indole ring system, see: Saulnier, M. G.; Gribble, G. W. *Tetrahedron Lett.* **1983**, *24*, 5435.

(7) See Gribble and Saulnier (Gribble, G. W.; Saulnier, M. G. *J. Chem. Soc., Chem. Commun.* **1984**, 168) for another example of the 4*H*-furo[3,4-*b*]indole ring system.

(8) Welch, W. M. *J. Org. Chem.* **1976**, *41*, 2031.

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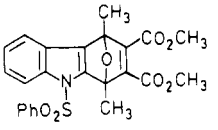
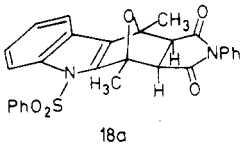
phenyllithium[14] (THF, −78 °C), and, after quenching with excess acetaldehyde, the desired alcohol **8** was isolated in 73% yield following flash chromatography. This alcohol was smoothly transformed into the target hydroxy ketone **11** in 86% yield by a sequence of oxidation (MnO_2;[15] CH_2Cl_2, reflux), bromination (*N*-bromosuccinimide, CCl_4, reflux), and solvolysis (aqueous $NaHCO_3$, THF, 25 °C). Although **11** could be purified by flash chromatography, it conveniently cyclized to **4** in essentially quantitative yield during attempted recrystallization from dichloromethane. This exceedingly facile transformation, **11** → **4**, is complete within 10 min in refluxing dichloromethane and provides analytically pure material. The overall yield of **4** from **6** is 46%. Furoindole **4** is an air-stable, colorless solid, mp 167–170 °C(dec), but slowly decomposes in solution when exposed to air over several days. Its structure is supported by analytical and spectral data (cf. Experimental Section) and by subsequent reactions (vide infra).

As described earlier in preliminary form,[6] we have also synthesized **4** from indole-3-carboxaldehyde (**12**), as shown in Scheme III. Thus, **12** was converted to the *N*-phenylsulfonyl derivative **13** in 86% yield (LDA, $PhSO_2Cl$, THF, −70 °C), which upon sequential treatment with methyllithium, *tert*-butyllithium, and acetaldehyde gave diol **15** as a mixture of diastereomers in 81% yield. Oxidation of **15** with activated manganese dioxide[15] ($CHCl_3$, reflux, 25 h) gave lactol **16**, which was directly converted to **4** with a catalytic amount of trifluoroacetic acid (TFA) in refluxing dichloromethane, in 30% yield from **15**. This material was identical with that prepared as described in Scheme II. The overall yield of **4** from **12**, without purification of intermediates **15** and **16**, is 21%.

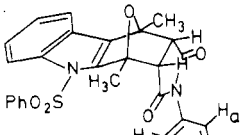
Diels–Alder Reactions of 4. Prior to pursuing the synthesis of pyridocarbazoles from **4**, we examined several model Diels–Alder reactions of **4**. Thus, a benzene solution of **4** and dimethyl acetylenedicarboxylate (DMAD), when refluxed for 5 h, gave the expected adduct **17** in quantitative yield. This material is somewhat unstable on silica gel but an analytical sample was obtained following flash chromatography. Reaction of **4** with *N*-phenylmaleimide was more rapid than that with DMAD and afforded a mixture of exo–endo adducts **18** in quantitative yield after 30 min (benzene, reflux).



17



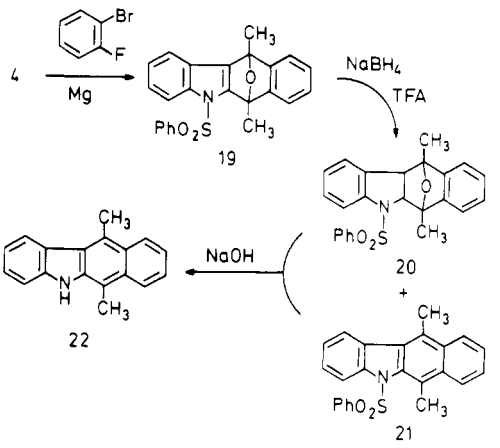
18a



18b

The 300-MHz ^1H NMR spectrum of the mixture of adducts **18** suggested that the major isomer (ca. 63% by integration) was the exo adduct **18a** and the minor isomer (ca. 37%) was the endo adduct **18b**. This assignment is based on the chemical shifts of the methine protons. Thus, the major component **18a** displays the methine protons as an AX pattern at relatively high field (δ 2.86 and 3.03, ^3J = 6.6 Hz), characteristic of endo protons in similar bicyclo[2.2.1]heptane systems.[16] In contrast, the minor isomer **18b** displays the methine protons as an AB quartet (δ 3.60 and 3.66, ^3J = 7.6 Hz). The somewhat larger syn vicinal coupling between exo protons than between endo protons is not unexpected.[17] Moreover, it is interesting to note that the aromatic protons Ha in the minor isomer (**18b**) are shielded by the indole ring and resonate at relatively high field: δ 6.07 (dd, J_{app} = 1.4 and 8.1 Hz). Similar shielding of these two aromatic protons has been observed for other *endo*-*N*-phenylmaleimide cycloadducts.[18] The fact that the exo adduct **18a** is the major isomer formed in this cycloaddition reaction is perhaps not surprising since several examples of high exo stereoselectivity in Diels–Alder reactions with N-substituted maleimides have been reported.[16b,18a,19]

Scheme IV



That furoindole **4** is indeed a reactive diene was further exemplified by its cycloaddition reaction with benzyne. Thus, when an equimolar solution of 2-fluorobromobenzene (THF) was slowly added to a refluxing solution of **4** in dry THF in the presence of magnesium,[20] the generated benzyne was very efficiently trapped by **4** to afford the epoxy adduct **19** in 93% yield after flash chromatography (Scheme IV). This was smoothly converted to the known[21] 5,11-dimethyl-6*H*-benzo[*b*]carbazole (**22**) as follows. Reduction of **19** with sodium borohydride/trifluoroacetic acid[22] gave indoline **20** along with some **21**. This crude mixture was treated with base (aqueous NaOH, MeOH–THF, reflux, 48 h) to give **22**, mp 208–209 °C, in 98% yield from **19**.

Synthesis of Ellipticine (1a) and Isoellipticine (2a). In order to fashion the pyridocarbazole ring system from furoindole **4** (Scheme I), we needed an efficient procedure for the generation of 3,4-pyridyne (**5**). We previously

(14) Deprotonation at C-2 could also be accomplished with lithium diisopropylamide (LDA), but after the ensuing reaction with acetaldehyde we could only isolate **7**, presumably as a result of diisopropylamine-mediated enolization of acetaldehyde.

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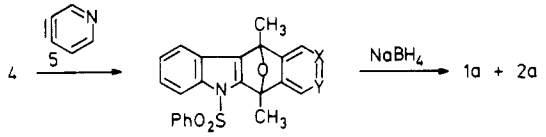
generated[23] **5** from 3-chloro-4-iodopyridine and alkyllithium reagents and, therefore, examined this methodology first. Indeed, when a solution of 3-chloro-4-iodopyridine in dry THF was treated with 2 equiv[24] of *tert*-butyllithium at −100 °C, followed after 10 min by the addition of **4**, there was obtained a mixture of the isomeric Diels–Alder adducts **23** in 15% yield (34% based on unrecovered **4**) following flash chromatography.



23a X = N, Y = CH
23b X = CH, Y = N

The yield of **23** was substantially improved by using 1-aminotriazolo[4,5-*c*]pyridine[25] and its reaction with lead tetraacetate to generate[26] **5**. This procedure afforded the mixture of **23a,b** in 38% yield after flash chromatography. Since initial attempts to separate this mixture, including using high-pressure liquid chromatography, were unsuccessful, we carried it on to the next step. Simply treating **23a,b** with sodium borohydride (NaOH, MeOH, reflux) effected oxygen-bridge extrusion as well as desulfonylation to give, after flash chromatography, ellipticine (**1a**) and isoellipticine (**2a**) in 23% and 29% yield, respectively. These compounds were identical with samples previously prepared in our laboratory.

In summary, we have described two synthetic routes to the novel fused heterocycle 1,3-dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (**4**) and have demonstrated its utility as a diene in Diels–Alder reactions. In particular, utilizing 3,4-pyridyne (**5**) as the dienophile, this methodology provides for a short synthesis of the pyridocarbazole alkaloid ellipticine (**1a**) and its isomer isoellipticine (**2a**).

Experimental Section

General techniques and instruments have been described earlier.[5c]

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.

1-(Phenylsulfonyl)-3-ethylindole (7). To a solution of 3-ethylindole (**6**)[11] (16.3 g, 112 mmol) in dry THF (200 mL) under nitrogen at −78 °C was added dropwise via syringe *n*-butyllithium (1.60 M in hexane; 70.3 mL, 113 mmol). The cooling bath was removed and the solution was stirred for 1 h while warming to 0 °C. The mixture was recooled to −78 °C and treated via syringe with benzenesulfonyl chloride (24.7 g, 140 mmol), keeping the internal temperature below −60 °C. The reaction mixture was allowed to warm to room temperature overnight, poured into saturated aqueous sodium bicarbonate, and extracted thoroughly with Et_2O. The usual workup gave a viscous oil which was crystallized from ethanol to afford 23.6 g (74%) of pure **7** as colorless needles, mp 123–124 °C (lit.[13] mp 125–125.5 °C).

1-[1-(Phenylsulfonyl)-3-ethylindol-2-yl]ethanol (8). A magnetically stirred solution of **7** (10.0 g, 35.0 mmol) in dry THF (125 mL) at −78 °C under argon was treated via syringe with phenyllithium (1.70 M in cyclohexane, 20.5 mL, 34.9 mmol). The mixture was stirred at −78 °C for 15 min, allowed to warm to room temperature over 45 min, and then kept at room temperature for an additional 2 h. The resulting dark red mixture was recooled to −78 °C, treated rapidly via syringe with freshly distilled excess acetaldehyde (15 mL), and then allowed to warm slowly to room temperature overnight. The mixture was poured into 5% aqueous sodium bicarbonate and extracted with methylene chloride. The usual workup followed by flash chromatography over silica gel with methylene chloride elution provided 8.4 g (73%) of analytically pure **8** as an amber, very viscous oil: IR ($CHCl_3$) 3540, 1448, 1355, 1168, 1008, 900, 585 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.22–6.93 (m, 9 H), 5.95–5.45 (m, 1 H), 3.72 (d, 1 H, J = 9 Hz), 2.78 (q, 2 H, J = 7.5 Hz), 1.68 (d, 3 H, J = 7 Hz), 1.13 (t, 3 H, J = 7.5 H); ^{13}C NMR ($CDCl_3$) δ 138.6, 137.7, 136.8, 133.4, 130.2, 128.7, 126.2, 125.9, 124.9, 123.6, 119.1, 115.2, 63.2, 23.8, 17.7, 14.7; UV (95% EtOH) λ_{max} 224, 258 nm; mass spectrum, m/e 329 (M^+), 314, 312, 311, 286, 187, 170, 144 (100), 115, 77; m/e 329.1112 (calcd for $C_{18}H_{19}NO_3S$, 329.1086).

Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25; S, 9.73. Found: C, 65.82; H, 5.84; N, 4.20; S, 9.78.

1-(Phenylsulfonyl)-3-ethyl-2-indolyl Methyl Ketone (9). A magnetically stirred solution of **8** (7.40 g, 22.5 mmol) in CH_2Cl_2 (200 mL) was treated under N_2 with activated MnO_2[15] (27 g) and then refluxed for 16 h. The mixture was cooled and the solids were filtered and thoroughly extracted with CH_2Cl_2. The usual workup gave 6.60 g (90%) of **9** as an off-white solid, mp 113–117 °C. Recrystallization from Et_2O–hexane gave the analytical sample as colorless prisms: mp 119–120 °C; IR (KBr) 1687, 1560, 1448, 1362, 1180, 1134, 963, 805, 756, 592 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21–7.96 (m, 1 H), 7.80–7.02 (m, 8 H), 2.69 (s, 3 H), 2.66 (q, 2 H, J = 8 Hz), 1.13 (t, 3 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 195.2, 137.6, 136.1, 135.0, 133.6, 133.2, 130.9, 128.3, 127.2, 127.0, 124.8, 120.7, 116.4, 32.1, 17.6, 14.6; UV (95% EtOH) λ_{max} 245, 269 (sh), 274, 288 nm.

Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.27; S, 9.79. Found: C, 66.12; H, 5.25; N, 4.28; S, 9.80.

1-(Phenylsulfonyl)-3-(1-bromoethyl)-2-indolyl Methyl Ketone (10). A magnetically stirred solution of ketone **9** (3.12 g, 9.53 mmol), *N*-bromosuccinimide (1.70 g, 9.55 mmol), and benzoyl peroxide (50 mg) in CCl_4 (110 mL) was refluxed under argon for 2.5 h. The reaction mixture was cooled to room temperature and filtered to remove the insoluble succinimide. The solids were washed with CCl_4 and the combined filtrates were concentrated in vacuo and then further dried at 1 torr to provide 3.93 g (100%) of **10** as a light tan solid, mp 113–118 °C dec. The ^1H NMR spectrum and TLC showed no impurities, and this crude bromo ketone was utilized directly in the next reaction. Recrystallization from Et_2O–hexane gave the analytical sample as colorless crystals: mp 129–131 °C dec; IR (KBr) 1698, 1557, 1452, 1366, 1180, 945, 769, 745, 681, 569 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28–7.00 (m, 9 H), 5.41 (q, 1 H, J = 7 Hz), 2.72 (s, 3 H), 1.99 (d, 3 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 195.5, 137.3, 135.1, 134.0, 129.5, 128.9, 128.6, 128.2, 127.2, 127.0, 124.6, 122.6, 116.1, 38.7, 32.3, 26.0; UV (95% EtOH) λ_{max} 241, 269 (sh), 274, 287 nm.

Anal. Calcd for $C_{18}H_{16}NO_3SBr$: C, 53.21; H, 3.97; N, 3.45; S, 7.89; Br, 19.67. Found: C, 53.18; H, 4.00; N, 3.47; S, 7.84; Br, 19.70.

1-[1-(Phenylsulfonyl)-2-acetylindol-3-yl]ethanol (11). The crude bromo ketone **10** (3.36 g, 8.27 mmol) was dissolved in THF (100 mL) and treated sequentially with sodium bicarbonate (0.84 g, 9.98 mmol) and H_2O (20 mL). This mixture was magnetically stirred under N_2 for 22.5 h. The solvent was partially removed in vacuo and the residue was treated with CH_2Cl_2 and saturated aqueous sodium bicarbonate. The phases were separated and the aqueous portion was further extracted with CH_2Cl_2. The usual workup gave 2.73 g (96%) of **11** which was used directly as described below: mp 152–154 °C dec; ^1H NMR ($CDCl_3$) δ 8.17–6.90 (m, 9 H), 5.07 (q, 1 H, J = 7 Hz), 3.12 (br s, 1 H), 2.70 (s, 3 H), 1.45 (d, 3 H, J = 7 Hz); mass spectrum, m/e 343 (M^+), 325, 300, 286, 202, 184, 77, 43 (100).

1,3-Dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (4). The crude alcohol **11** (2.73 g, 7.95 mmol) was dissolved in CH_2Cl_2 (40 mL), heated to boiling at atmospheric pressure, and concentrated over 45 min to a volume of 25 mL while slowly adding hexane (ca. 5 mL). After cooling to room temperature over 1 h, and then further at 5 °C overnight, the product was collected by filtration and washed with hexane to provide 1.64 g (61%) of analytically pure **4** as colorless prisms, mp 167–170 °C dec. An additional 0.92 g (38%) of **4** was obtained from the filtrate: IR (KBr) 1458, 1368, 1182, 1000, 785, 770, 752, 728, 686, 669, 602, 583, 567 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28–8.03 (m, 1 H), 7.90–7.15 (m, 8 H), 2.69 (s, 3 H), 2.42 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 144.8,

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138.0, 136.6, 133.3, 132.4, 128.6, 127.8, 126.9, 126.2, 124.5, 123.5, 120.9, 118.4, 116.5, 13.3, 12.8; mass spectrum, *m/e* 325 (M^+), 184, 142, 115, 77, 43 (100); UV (EtOH) λ_{max} 240 (sh), 266 (sh), 305 nm (log ϵ 4.21, 3.82, 3.81).

Anal. Calcd for $C_{18}H_{15}NO_3S$: C, 66.45; H, 4.65; N, 4.30; S, 9.85. Found: C, 66.41; H, 4.69; N, 4.22; S, 9.75.

1-(Phenylsulfonyl)indole-3-carboxaldehyde (13). To a magnetically stirred solution of lithium diisopropylamide (LDA) prepared from diisopropylamine (5.91 g, 58.4 mmol) and *n*-butyllithium (1.75 M in hexane; 33.1 mL, 57.9 mmol) in dry THF (65 mL) under argon at −70 °C was added a suspension of **12** (Alfa Chemical Co.) (7.90 g, 54.5 mmol) in dry THF (150 mL). The mixture was allowed to warm to room temperature and stirred for 1.5 h. After recooling to −70 °C, benzenesulfonyl chloride (10.8 g, 61.1 mmol) was added neat via syringe, and the reaction mixture was allowed to slowly warm to room temperature overnight. The solvent was removed in vacuo to afford a tan solid which was digested with CH_2Cl_2 (300 mL). The combined digests were washed with 5% aqueous sodium bicarbonate, and the aqueous phase was then back-extracted with fresh CH_2Cl_2. The usual workup gave a yellow solid. Recrystallization from 5:1 methylene chloride–cyclohexane afforded 10.1 g (65%) of **13** as an off-white solid, mp 157.5–158.5 °C (lit.[12] mp 158–158.5 °C). An additional 3.32 g (21%) of **13** was obtained after chromatography of the mother liquor on Florisil with Et_2O elution. Recrystallization from ether–hexane–methylene chloride gave the analytical sample as very fine fluffy needles: mp 158–158.5 °C; IR (KBr) 1683, 1609, 1543, 1482, 1446, 1380, 1273, 1230, 1180, 1123, 1020, 970, 824, 783, 750, 682, 594, 577, 555, 520 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.09 (s, 1 H), 8.38–8.15 (m, 2 H), 8.12–7.80 (m, 3 H), 7.68–7.20 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 185.0, 137.4, 135.9, 135.2, 134.6, 129.6, 127.0, 126.2, 125.0, 122.5, 113.1,; UV (95% EtOH) λ_{max} 225 and 287 nm.

Anal. Calcd for $C_{15}H_{11}NO_3S$: C, 63.14; H, 3.89; N, 4.91; S, 11.24. Found: C, 63.10; H, 3.93; N, 4.87; S, 11.20.

1,3-Dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (4). To a magnetically stirred solution of aldehyde **13** (2.50 g, 8.76 mmol) in dry THF (120 mL) cooled to −75 °C under argon was added methyllithium (1.45 M in Et_2O; 6.23 mL, 9.03 mmol). The mixture was stirred at −60 to −70 °C for 2 h and then warmed to −40 °C over 30 min and treated via syringe with *tert*-butyllithium (1.70 M in pentane, 5.41 mL, 9.20 mmol). The reaction mixture was warmed to 20 °C over 40 min, stirred for 2 h, and warmed to 35 °C for 5 min. The resulting bright red solution was rapidly cooled to −40 °C, treated via syringe with TMEDA (2.76 mL, 18.3 mmol), and stirred for 15 min. Freshly distilled acetaldehyde (5.2 mL, 93 mmol) was rapidly added via syringe at −35 °C. The reaction contents were stirred for 1 h at ca. −30 °C and warmed to −5 °C over 20 min. The reaction was quenched with 5% aqueous ammonium chloride (50 mL), then poured into a mixture of additional ammonium chloride (200 mL) and brine (50 mL), and extracted with CH_2Cl_2. The usual workup gave 5.3 g of an amber viscous oil. Flash chromatography over silica gel with 1:1 ethyl acetate–methylene chloride gave 81% of diol **15** as a syrup (two spots on TLC). Generally, the crude diol was immediately dissolved in $CHCl_3$ (425 mL), treated with brown MnO_2 (37 g) (Aldrich or activated[15]), and refluxed for 26 h, at the end of which time TLC indicated complete disappearance of diol **15** with formation of a higher R_f material (EtOAc). The reaction mixture was cooled and filtered through Celite. The solids were extracted with $CHCl_3$. The usual workup and flash chromatography over silica gel with 1:9 ethyl acetate–methylene chloride gave lactol **16** as a colorless solid. Generally, the crude lactol was dissolved in CH_2Cl_2 (250 mL), treated with anhydrous Na_2SO_4 (11 g), and refluxed under N_2 with magnetic stirring. Trifluoroacetic acid (ca. 0.5 mL) was added dropwise and the reaction mixture was refluxed for 55 min. The mixture was cooled to 0 °C and poured into cold saturated aqueous sodium bicarbonate. The phases were separated and the aqueous portion was further extracted with CH_2Cl_2. The usual workup and chromatography over Florisil with 1:1 pentane–methylene chloride gave 0.70 g of pure furo[3,4-*b*]indole **4**, mp 166–168 °C. The overall yield of **4** from **13** was 24%.

Pertinent spectral data for **15** and **16**. For **15**: IR (neat film) 3380, 1365, 1170 cm^{-1}; partial ^1H NMR ($CDCl_3$) δ 8.2–7.0 (m, 9 H), 1.8–1.0 (m, 6 H); partial ^{13}C NMR ($CDCl_3$) δ 64.9, 64.2, 63.2, 61.7, 25.1, 24.3, 23.8, 23.4; mass spectrum, *m/e* 345 (M^+) 312, 284, 203, 186, 185, 144 (100); M^+ 345.1049 ($C_{18}H_{19}NO_4S$ requires 345.1035). For **16**: IR (KBr) 3425, 1370, 1180 cm^{-1}; partial ^1H NMR ($CDCl_3$) δ 8.0–6.9 (m, 9 H), 2.66 (s, 3 H), 1.38 (d, 3 H); ^{13}C NMR ($CDCl_3$) δ 137.4, 135.4, 135.0, 134.4, 133.9, 128.9, 128.5, 127.3, 127.0, 124.9, 122.1, 116.2, 63.6, 32.5, 23.8; mass spectrum, *m/e* 343 (M^+), 286, 202, 184, 160, 77, 43 (100); M^+ 343.0898 ($C_{18}H_{17}NO_4S$ requires 343.0878).

Dimethyl 1,4-Epoxy-1,4-dimethyl-1,4-dihydro-5-(phenylsulfonyl)-2,3-carbazoledicarboxylate (17). A magnetically stirred solution of dimethyl acetylenedicarboxylate (44.8 mg, 0.315 mmol) in dry benzene (1 mL) was treated under nitrogen with a warm solution of the furo[3,4-*b*]indole **4** (102.6 mg, 0.3152 mmol) in benzene (2.5 mL). The reaction mixture was stirred at room temperature for 1 h and then refluxed for 5 h. The benzene was removed under a stream of argon and the product was dried at 30 °C (0.5 torr) to give 148.0 mg (100%) of **17** as a colorless solid. Flash chromatography on silica gel with methylene chloride resulted in considerable decomposition to give a bright yellow band which could not be eluted from the column. However, 45.8 mg of analytically pure **17** was obtained as a colorless solid: mp 159–165 °C; IR (KBr) 1727, 1442, 1380, 1270, 1190, 1024, 970, 750, 726, 685, 580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21–7.75 (m, 3 H), 7.68–7.13 (m, 6 H), 3.80 (s, 3 H), 3.71 (s, 3 H), 2.20 (s, 3 H), 2.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.6, 163.5, 156.8, 156.1, 154.4, 144.7, 140.7, 138.0, 133.8, 129.1, 126.6, 125.1, 124.2, 124.1, 119.5, 115.3, 92.8, 90.3, 52.2, 52.0, 16.3, 15.4; UV (95% EtOH) λ_{max} 220, 245 (sh), 295 (sh) nm; mass spectrum, *m/e* 467 (M^+), 393, 326, 325, 252, 184, 142, 115, 77; *m/e* 467.1033 (calcd for $C_{24}H_{21}NO_7S$, 467.1039).

Anal. Calcd for $C_{24}H_{21}NO_7S$: C, 61.66; H, 4.53; N, 3.00; S, 6.86. Found: C, 61.57; H, 4.58; N, 2.99; S, 6.89.

***N*-Phenyl-1,4-epoxy-1,4-dimethyl-1,2,3,4-tetrahydro-5-(phenylsulfonyl)-2,3-carbazoledicarboximides (18a,b).** A magnetically stirred solution of *N*-phenylmaleimide (65.9 mg, 0.381 mmol) in dry benzene (1 mL) was treated under nitrogen with a solution of furo[3,4-*b*]indole **4** (114.0 mg, 0.3503 mmol) in benzene (2.25 mL). The reaction mixture was stirred at room temperature for 15 min and then refluxed for 0.5 h. The benzene was removed in vacuo and the product was dried at 45 °C (0.5 torr) to give **18** as a colorless, foamy solid in quantitative yield. The 300-MHz ^1H NMR spectrum suggested a 63:37 mixture of exo–endo adducts and the TLC showed two spots (R_f 0.05, 0.15, CH_2Cl_2). Recrystallization from 2:2:1 methylene chloride–cyclohexane–ether gave the analytical sample as a mixture of adducts, mp 145–169 °C. The mass spectrum exhibited a very intense retro-Diels–Alder fragmentation (*m/e* 325, 173); IR (KBr) 1784, 1723, 1506, 1453, 1379, 1191, 974, 870, 832, 750, 599 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 8.20–7.70 (m), 7.64–6.80 (m), 6.07 (dd, 2 H for endo isomer **18b**, J = 8.1 and 1.4 Hz), 3.66, 3.60 (AB q, 2 H for endo isomer **18b**, J = 7.6 Hz), 3.03, 2.86 (AX q, 2 H for exo isomer **18a**, J = 6.6 Hz), 2.35 (s, 3 H for endo isomer **18b**), 2.18, (s, 3 H for exo ixomer **18a**), 2.10 (s, 3 H for exo isomer **18a**), 1.56 (s, 3 H for endo isomer **18b**); UV (95% EtOH) λ_{max} 220, 265 nm; mass spectrum, *m/e* 325.0811 (calcd for $C_{18}H_{15}NO_3S$, 325.0773), 173.0464 (calcd for $C_{10}H_7NO_2$, 173.0477).

Anal. Calcd for $C_{28}H_{22}N_2O_5S$: C, 67.46; H, 4.45; N, 5.62; S, 6.43. Found: C, 67.69; H, 4.80; N, 5.38; S, 6.30.

5-(Phenylsulfonyl)-6,11-epoxy-6,11-dimethyl-6,11-dihydrobenzo[*b*]carbazole (19). A solution of 2-bromofluorobenzene (75.2 mg, 0.430 mmol) in dry THF (4 mL) was added dropwise over 15 min to a refluxing, magnetically stirred mixture of magnesium metal (32.7 mg, 1.35 mmol) and furoindole **4** (131.2 mg, 0.4032 mmol) in dry THF (4 mL) under argon. Reflux was maintained for 4.5 h, and the resulting red reaction mixture was then cooled, treated with 5% aqueous ammonium chloride (1 mL), and poured into additional 5% ammonium chloride (100 mL). Extraction with CH_2Cl_2 and the usual workup gave 160.7 mg (99%) of **19** as a light tan solid, mp 123–126 °C. Flash chromatography over silica gel with 1:1 hexane–methylene chloride elution afforded 143.8 mg (93%) of **19**: mp 127–129 °C; IR (KBr) 1450, 1380, 1184, 1110, 980, 918, 850, 749, 689, 576 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15–7.66 (m, 3 H), 7.66–6.75 (m, 10 H), 2.31 (s, 3 H), 2.20 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 156.6, 152.2, 152.1, 151.3, 143.6, 140.8, 138.3, 133.7, 129.1, 126.4, 125.3, 125.1, 124.7, 124.0, 123.8, 119.1, 118.0, 115.3, 89.5, 86.7, 16.1, 15.1; UV (95% EtOH) λ_{max} 233, 274 (sh), 284 (sh), 297 (sh) nm; mass spectrum, *m/e* 401 (M^+),

386, 358, 260, 245, 218, 217, 84, 77 (100%); *m/e* 401.1098 (calcd for $C_{24}H_{19}NO_3S$, 401.1086).

5,11-Dimethyl-6*H*-benzo[*b*]carbazole (22). To a magnetically stirred mixture of **19** (110 mg, 0.274 mmol) and sodium borohydride powder (34 mg, 0.90 mmol) in dry THF (5 mL) at 0–5 °C under N_2 was slowly added dropwise over 1.5 h a solution of trifluoroacetic acid (2.10 g) in dry THF (5 mL). The mixture was stirred at room temperature for 24 h. The reaction mixture was poured into H_2O and extracted with CH_2Cl_2. The aqueous layer was treated with saturated aqueous sodium bicarbonate (100 mL) and further extracted with CH_2Cl_2. The combined organic portions were washed with 5% bicarbonate and worked up to give a tan residue. The mass spectrum of this crude material exhibited *m/e* 403 and 385, which were assigned as M^+ for **20** and **21**, respectively. This crude mixture was dissolved in THF (5 mL) and methanol (15 mL) and treated under N_2 with 2 N sodium hydroxide (5 mL). The mixture was refluxed for 6 h, treated with 50% aqueous sodium hydroxide (1 mL), and refluxed for another 24 h. The reaction mixture was cooled, treated with concentrated hydrochloric acid to pH 2, and stirred for 1.5 h at room temperature. The mixture was partitioned between saturated aqueous sodium bicarbonate and $CHCl_3$, and the aqueous portion was then further extracted with $CHCl_3$. The usual workup gave 66 mg (98%) of **22**, mp 190–192 °C, which showed one spot on TLC. Flash chromatography over silica gel with 1:2 cyclohexane–methylene chloride afforded 52 mg of pure **22** as a pale yellow solid: mp 208–209 °C (lit.[21] mp 211–213 °C); mass spectrum, *m/e* 245 (M^+, 100), 230, 215, 202, 149, 123; *m/e* 245.1192 (calcd for $C_{18}H_{15}N$, 245.1204).

6-(Phenylsulfonyl)-5,11-epoxy-5,11-dimethyl-5,11-dihydropyrido[4,3-*b*]carbazole (23a) and 10-(Phenylsulfonyl)-5,11-epoxy-5,11-dimethyl-5,11-dihydropyrido[3,4-*b*]carbazole (23b). To a magnetically stirred solution of **4** (1.00 g, 3.08 mmol) and 1-aminotriazolo[4,5-*c*]pyridine[25] (0.417 g, 3.09 mmol) in dry THF (30 mL) at 20 °C was added over 5 min via a solid addition funnel freshly recrystallized (HOAc) lead tetraacetate (1.37 g, 3.10 mmol). After 10 min, a second equivalent of lead tetraacetate (1.42 g, 3.20 mmol) was added in the same manner. The reaction was stirred at 20 °C for 3 h, the lead salts were removed by filtration, and the filtrate was concentrated in vacuo to give an amorphous solid. Flash chromatography with 1:4 ethyl acetate–methylene chloride gave 0.465 g (38%) of a mixture of **23a** and **23b** as an amorphous solid which was one spot by TLC (R_f 0.55, THF): UV (95% EtOH) λ_{max} 239, 221 nm; mass spectrum, *m/e* 402.1048 (M^+, calcd 402.1038).

Ellipticine (1a) and Isoellipticine (2a). A magnetically stirred solution of **23a** and **23b** (465 mg, 1.43 mmol) in THF (5 mL) was treated with methanol (15 mL), 50% sodium hydroxide (3 mL), H_2O (3 mL), and sodium borohydride (1 pellet, 0.3 g, 8 mmol) and was refluxed. After 1 h at reflux, more sodium borohydride (1 pellet, 0.3 g, 8 mmol) was added and the reaction was refluxed for an additional 16 h. The resulting yellow-orange fluorescent mixture was allowed to cool, poured into saturated sodium bicarbonate solution (100 mL), and extracted with $CHCl_3$ until the aqueous layer was not fluorescent. The usual workup gave 250 mg of a yellow solid. Flash chromatography with methylene chloride and then ethyl acetate gave 147 mg (52%) of a mixture of **1a** and **2a** as a yellow solid. Flash chromatography of the pure ellipticine–isoellipticine mixture with 9:1 ethyl acetate–triethyl amine afforded clean separation of **1a** and **2a** in a 45:55 ratio. Both were identical (IR, UV, TLC, mp) with authentic samples.

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Registry No. **1a**, 519-23-3; **2a**, 13799-49-0; **4**, 89241-38-3; **6**, 1484-19-1; **7**, 77507-52-9; **8**, 92399-33-2; **9**, 92399-34-3; **10**, 92399-35-4; **11**, 92399-36-5; **12**, 487-89-8; **13**, 80360-20-9; **15**, 92399-37-6; **16**, 89241-39-4; **17**, 92399-38-7; **18a**, 92399-39-8; **18b**, 92470-57-0; **19**, 92399-40-1; **20**, 92399-41-2; **21**, 92399-42-3; **22**, 73326-97-3; **23a**, 92399-43-4; **23b**, 92399-44-5; benzenesulfonyl chloride, 98-09-9; acetaldehyde, 75-07-0; dimethyl acetylenedicarboxylate, 762-42-5; *N*-phenylmaleimide, 941-69-5; 2-bromofluorobenzene, 1072-85-1; 1-aminotriazolo[4,5-*c*]pyridine, 23589-45-9.

Photoisomerization of 4-Hydroxypyrylium Cations in Concentrated Sulfuric Acid

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Irradiation of di-, tri-, and tetraalkyl-4-hydroxypyrylium cations in concentrated sulfuric acid leads to the formation of 2-hydroxypyrylium cations as phototransposition products and, in certain cases, to furyl cations by a photo-ring-contraction reaction. Product analysis by spectroscopic techniques, deuterium labeling, and unambiguous synthesis reveals that 2-hydroxypyrylium cations are formed by two distinct transposition patterns and accordingly, by two distinct mechanistic pathways. The bond-forming and -breaking requirements of the major transposition pattern, which constitutes approximately 95% of the reaction, are consistent with a mechanism initiated by 2,6-bridging in the first excited state of the 4-hydroxypyrylium cation. Similarly, the bond-formation and -breaking requirements of the minor pattern are consistent with a mechanism involving 2,5-bridging in the first excited state of the starting cation.

The photoisomerization of 2,6-dimethyl-4-hydroxypyrylium cation ($1H^+$) in concentrated sulfuric acid to yield 4,5-dimethyl-2-hydroxypyrylium cation ($2H^+$) was the first reported example of a 4-hydroxypyrylium cation photorearrangement.[1] The initially formed 2-hydroxypyrylium cation $2H^+$ was also observed to be in photoequilibrium with 5,6-dimethyl-2-hydroxypyrylium cation ($3H^+$). Thus,

(1) Pavlik, J. W.; Clennan, E. L. *J. Am. Chem. Soc.* **1973**, *95*, 1697.

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