Lewis Acid-Promoted Reactions of Styrenyl Systems with Benzoquinone Bisimines: New Regioselective Syntheses of Substituted 2-Aryl-2,3-dihydroindoles and 2-Arylindoles

Thomas A. Engler,* Steven P. Meduna, Kenneth O. LaTessa,† and Wenying Chai

Department of Chemistry, University of Kansas, Lawrence, Kansas 66045

Received July 18, 1996⊗

BF_3-promoted reactions of 2-alkoxy-1-(*N*-benzoyl)-4-(*N*-benzenesulfonyl)-1,4-benzoquinone bisimines (**2/3**) with *β*-methylstyrenes yield *trans*-5-(*N*-benzoylamino)-6-alkoxy-2-aryl-3-methyl-2,3-dihydroindoles (**4/5**) or 3-(*N*-benzoylamino)-6-aryl-7-methyl-4,8-dioxobicyclo[3.2.1]oct-2-enes (**6**) regio- and stereoselectively. The former are produced in reactions with styrenes bearing alkoxy substituents, whereas with neutral or electron deficient styrenes, the latter are found. As applications of this new methodology to the synthesis of biologically interesting molecules, reactions of 2*H*-chromenes and 7-methoxy-*N*-toluenesulfonyl-1,2-dihydroquinoline with the bisimines have been developed as routes to substituted aza- and diazapterocarpans. Syntheses of 2-arylindoles via oxidation of the dihydroindoles **4** are also reported.

The presence of highly substituted indole and dihydroindole nuclei in many classes of biologically important materials and synthetic intermediates continues to fuel interest in new syntheses of these substructures.[1] In the context of the present report, compounds incorporating the 2-aryl-1,3-dialkylindole system have attracted attention because of their potent activity as antiestrogens.[2] Such compounds are of interest for the potential development of new treatments for hormone-dependent carcinomas. Over the last few years, we have reported Lewis acid-promoted reactions of 2-alkoxy quinones with various styrenes as efficient and regioselective syntheses of highly substituted 2-aryl-2,3-dihydrobenzofurans.[3] Seeking to extend this methodology to the preparation of dihydroindoles and indoles, we have explored similar reactions of quinone bisimides with styrenyl systems.[4] Herein we report the experimental details of an expanded study designed to explore the generality and limitations of this method and its application to the synthesis of two classes of biologically interesting compounds, 2-arylindoles and azapterocarpans.

Quinone bisimides **2/3** were chosen for the initial studies because the differentially protected imine nitrogens offered the potential for regiocontrol in the reactions and more flexibility in terms of chemoselectivity in future synthetic applications. $BF_3{\cdot}OEt_2$-promoted reactions of electron rich styrenes **1a**−**c**[5] afforded the protected 5-amino-6-alkoxy-2-aryl-2,3-dihydroindoles **4/5** in generally good yields (eq 1, Table 1). The reactions were highly regioselective, and none of the isomeric 7-alkoxydihydroindoles were found. With the more neutral styrene **1d**, reactions of methoxyquinone bisimide **2** gave indole **4d** accompanied by the amino-substituted bicyclo[3.2.1]

† Formerly Kenneth O. Lynch, Jr. Current address: Stephens College, Columbia, MO 65215.

⊗ Abstract published in *Advance ACS Abstracts,* November 1, 1996.

(1) For recent summaries of numerous approaches, see: (a) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 4 (Bird, C. W., Cheeseman, G. W. H., Eds.), Part 3, Chapter 3.06. (b) Bird, C. W.; Cheeseman, G. W. H. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergammon: Oxford, 1984; Vol. 4 (Bird, C. W., Cheeseman, G. W. H., Eds.), Part 3, Chapter 3.03. (c) Gawley, R. E.; Rein, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I. Eds.; Pergammon: Oxford, 1991; Vol. 1 (Schreiber, S. L., Ed.), Chapter 2.1. (d) Knight, D. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3 (Pattenden, G., Ed.), Chapter 2.3. (e) Harding, K. E.; Tiner, T. H. *In Comprehensive Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergammon: Oxford, 1991; Vol. 4 (Semmelhack, M. F., Ed.), Chapter 1.9. (f) Ihara, M.; Fukumoto, K. *Nat. Prod. Rep.* **1995**, 277−301 and previous reviews in this series cited therein. (g) Saxton, J. E. *Ibid.* **1995**, 385−411 and previous reports in this series cited therein. (h) Hugel, H. M.; Kennaway, D. J. *Org. Prep. Proced. Int.* **1995**, *27*, 1−31. (i) Black, D. St. C. *Synlett* **1993**, 246−252. For selected recent approaches: (j) Cacchi, S. *Pure Appl. Chem.* **1996**, *68*, 45−52. (k) Amat, M.; Hadida, S.; Sathyanarayana, S.; Bosch, J. *Tetrahedron Lett.* **1996**, *37*, 3071−3074. (l) Griffen, E. J.; Roe, D. G.; Snieckus, V. *J. Org. Chem.* **1995**, *60*, 1484−1485. (m) Iwao, M.; Motoi, O. *Tetrahedron Lett.* **1995**, *36*, 5929−5932. (n) Prashad, M.; Vecchia, L. L.; Prasad, K.; Repic, O. *Synth. Commun.* **1995**, *25*, 95−100. (o) Katritzky, A. R.; Xie, L.; Cundy, D. *Ibid.* **1995**, *25*, 539−551. (p) Hudkins, R. L.; Diebold, J. L.; Marsh, F. D. *J. Org. Chem.* **1995**, *60*, 6218−6220. (q) Katritzky, A. R.; Li, J.; Stevens, C. V. *Ibid.* **1995**, *60*, 3401−3404. (r) Kihara, M.; Iwai, Y.; Nagao, Y. *Heterocycles* **1995**, *41*, 2279−2287. (s) Bosch, J.; Bennasar, M.-L. *Synlett* **1995**, 587−596. (t) Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215−5229. (u) Fukuyama, T.; Chen, X.; Peng, G. *J. Am. Chem. Soc.* **1994**, *116*, 3127−3128. (v) Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1994**, *35*, 2405−2408. (w) Hwu, J. R.; Patel, H. V.; Lin, R. J.; Gray, M. O. *J. Org. Chem.* **1994**, *59*, 1577−1582. (x) Chen, C.-y.; Lieberman, D. R.; Larsen, R. D.; Reamer, R. A.; Verhoeven, T. R.; Reider, P. J.; Cottrell, I.; Houghton, P. G. *Tetrahedron Lett.* **1994**, *35*, 6981−6984. (y) Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1993**, *34*, 7471−7474. (z) Grigg, R.; Khalil, H.; Levett, P.; Virica, J.; Sridharan, V. *Ibid.* **1994**, *35*, 3197−3200. (aa) Larock, R. C.; Yum, E. K. *J. Am. Chem. Soc.* **1991**, *113*, 6689−6690. (bb) Boger, D. L.; Zarrinmayeh, H. *J. Org. Chem.* **1990**, *55*, 1379−1390. (cc) Boger, D. L.; Coleman, R. S. *J. Am. Chem Soc.* **1988**, *110*, 4796−4807. (dd) Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. I. *J. Am. Chem. Soc.* **1978**, *100*, 5800−5807. (ee) Harrington, P. J.; Hegedus, L. S. *J. Org. Chem.* **1984**, *49*, 2657−2662. (ff) Kasahara, A.; Izumi, T.; Murakami, S.; Yanai, H.; Takatori, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 927−928 and references cited in the above. (gg) For a combinatorial approach: Hutchins, S. M.; Chapman, K. T. *Tetrahedron Lett.* **1996**, *37*, 4869−4872.

(2) (a) von Angerer, E.; Knebel, N.; Kager, M.; Ganss, B. *J. Med. Chem.* **1990**, *33*, 2635−2640. (b) von Angerer, E.; Prekajac, J.; Berger, M. *Eur. J. Cancer Clin. Oncol.* **1985**, *21*, 531−537. (c) von Angerer, E.; Strohmeier, J. *J. Med. Chem.* **1987**, *30*, 131−136. (d) von Angerer, E.; Prekajac, J.; Strohmeier, J. *J. Med. Chem.* **1984**, *27*, 1439−1447. (e) von Angerer, E.; Prekajac, J. *J. Med. Chem.* **1983**, *26*, 113−116.

(3) (a) Engler, T. A.; Combrink, K. D.; Letavic, M. A.; Lynch, K. O., Jr.; Ray, J. E. *J. Org. Chem.* **1994**, *59*, 6567−6587. (b) Engler, T. A.; Wei, D.; Letavic, M. A.; Combrink, K. D.; Reddy, J. P. *J. Org. Chem.* **1994**, *59*, 6588−6599. (c) Engler, T. A.; Gfesser, G. A.; Draney, B. W. *J. Org. Chem.* **1995**, *60*, 3700−3706. (d) Engler, T. A.; Letavic, M. A.; Combrink, K. D.; Takusagawa, F. *J. Org. Chem.* **1990**, *56*, 5810−5812. (e) Engler, T. A.; Letavic, M. A.; Reddy, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 5068−5070. (f) Engler, T. A.; Reddy, J. P.; Combrink, K. D.; Vander Velde, D. *J. Org. Chem.* **1990**, *55*, 1248−1254.

(4) Engler, T. A.; Lynch, K. O., Jr.; Chai, W.; Meduna, S. P. *Tetrahedron Lett.* **1995**, *36*, 2713−2716.

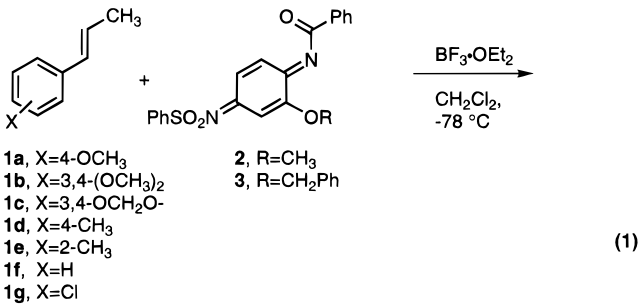
(5) The styrenes were purchased, or made, and used as is; **1a/f** were ∼100% *(E),* whereas the others were 5−15:1 mixtures of *(E)/(Z)*-isomers. The *(Z)*-isomer did not react competitively with the *(E)*-isomer; see ref 3a for a related discussion of the relative rates of reactions of *(E)*- vs *(Z)*-styrenes with quinones.

S0022-3263(96)01359-X CCC: $12.00

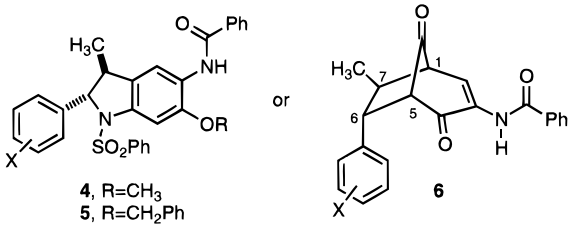
Table 1. BF_3·OEt_2-Promoted Reactions of Styrenes 1 with Quinone Bisimides 2/3[a]

entry	styrene: X[b]	bisimide: R	product(s)[c] (% yield)
1	**1a**: 4-OCH_3	**2**: CH_3	**4a** (75)
2	**1b**: 3,4-$(OCH_3)_2$	**2**: CH_3	**4b** (66)
3	**1b**: 3,4-$(OCH_3)_2$	**3**: CH_2Ph	**5b** (57)
4	**1c**: 3,4-OCH_2O	**2**: CH_3	**4c** (84)
5	**1c**: 3,4-OCH_2O	**3**: CH_2Ph	**5c** (66)
6	**1d**: 4-CH_3	**2**: CH_3	**4d** (23) + **6d** (37)
7	**1d**: 4-CH_3	**3**: CH_2Ph	**5d** (0−12)[d] + **6d** (66−78)
8	**1e**: 2-CH_3	**2**: CH_3	**6e** (54)
9	**1e**: 2-CH_3	**3**: CH_2Ph	**6e** (59)
10	**1f**: H	**2**: CH_3	**6f** (55)
11	**1f**: H	**3**: CH_2Ph	**6f** (76)
12	**1g**: 4-Cl	**2**: CH_3	**6g** (59)
13	**1g**: 4-Cl	**3**: CH_2Ph	**6g** (72)

[a] All reactions were done in CH_2Cl_2 at −78 °C with BF_3·OEt_2 as promoter. [b] Used as (*E*)/(*Z*) mixtures as purchased or prepared (see ref 5). [c] Substituents X and R are the same as in starting materials **1** and **2**/**3**. [d] The isolation of **5d** was not reproducible (see the Experimental Section).



(1)



system **6d**, whereas the latter was usually the only product in the reaction of **1d** with benzyloxy quinone bisimide **3**. Products **6e**−**g** were formed exclusively in reactions of styrenes **1e**−**g** with either bisimide.

The structures of dihydroindoles **4**/**5** are assigned by the presence of an amide N−H stretch at 3425 (CH_2Cl_2) or 3434 (CCl_4) cm^{-1} in their IR spectra and by NOE NMR studies. The signals for H-4 and H-7 appear as sharp singlets at ∼8.28 (due to deshielding by the amide carbonyl) and 7.48 ppm, respectively. In **4b**/**c**, strong $^1H-^1H$ NOE's are observed between the C-3 methyl and both H-2 and H-4 and between the C-6 methoxy and H-7 (Figure 1). The spectra of the other dihydroindoles are very similar to those of **4b**/**c**, and the structures are assigned by analogy.

The structures of the bicyclo[3.2.1] adducts **6** are assigned by comparison of their spectra with those of similar bicyclo[3.2.1]octenediones found in reactions of quinones with styrenes.[3] In particular, the lack of an observable coupling between H-1 and H-7 and a J_{H5-H6} of ∼7 Hz is indicative of an endo C-6 aryl group and an exo C-7 methyl substituent.

The reactions are likely similar mechanistically to the quinone−styrene reactions which have been studied extensively.[3] Thus, regioselective activation[6] of the quinone bisimides by coordination of the Lewis acid to the basic benzoyl nitrogen affords complex **7**, and cycloaddition of the styrenyl C=C bond of **1** gives intermediate **8** which proceeds on to the observed products by dealkylation and hydrolysis of the bridging sulfonyl imine (path a)[7] or fragmentation to **9** followed by C−N bond formation and loss of H^+ (path b). Alternatively, simple

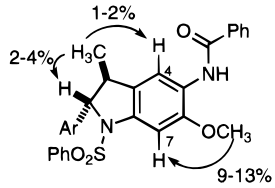
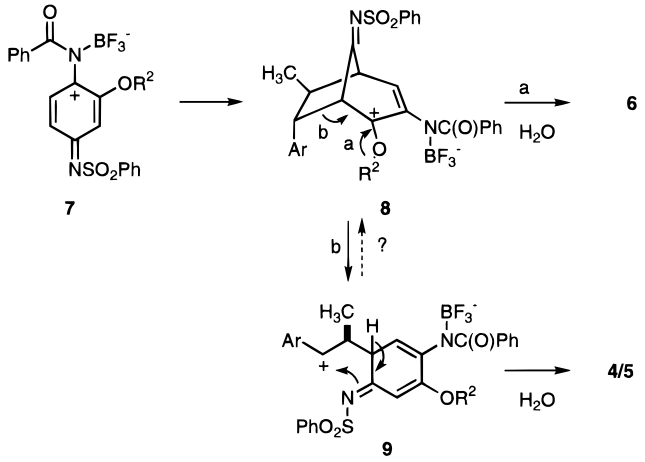


Figure 1. Summary of selected NOE data on **4b**/**4c**.



alkylation of **7** by the styrene may afford **9** which may proceed on to **4**/**5**[8a] or cyclize to **8** and then undergo dealkylation/hydrolysis to **6**. The cycloaddition route is suggested by similar processes that have been postulated in Lewis acid-promoted reactions of 1,4-benzoquinones with styrenes. With electron rich styrenes **1a**−**c**, the dihydroindoles **4**/**5** are formed because fragmentation of **8** to **9** is faster than dealkylation due to stabilization of the benzylic carbocation in **9** by the aryl ring. With the more neutral styrenyl systems, dealkylation either competes or dominates. Indeed, the generally higher yields of **6** found in reactions of **1d**−**g** with bisimide **3** in comparison to **2** and in reactions of **2** with **1e** compared to those of **1d** are similar to results that have been used to argue in favor of the cycloaddition process in the quinone−styrene reactions.[3a,d,8b] Nevertheless, the data do not rule out the alkylation/cyclization alternative.

As one application of this new methodology, a new synthesis of azapterocarpans was explored. Pterocarpans

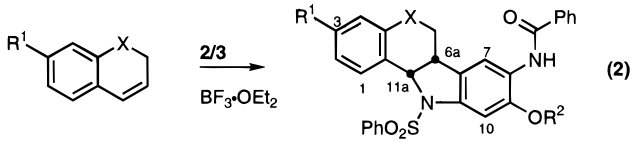
(6) Regioselective Lewis acid activation of quinone bisimides has been described in some detail by Boger and others. See refs 1bb, cc, and (a) Brown, E. R. In *The Chemistry of Quinonoid Compounds*; Patai, S.; Rappoport, Z., Eds.; John Wiley and Sons: New York, 1988; Vol. II, Part 2, Chapter 21. (b) Adams, R.; Reifschneider, W. *Bull. Chim. Soc. Fr.* **1958**, 23−65. (c) Holmes, T. J., Jr.; Lawton, R. G. *J. Org. Chem.* **1983**, *48*, 3146−3150.

(7) This surprisingly facile hydrolysis apparently occurs on workup or chromatography; we have been unable to detect an intermediate or a product with a bridging sulfonyl imine moiety.

(8) (a) For a similar process observed in solvolysis of *N*-acylquinone imine ketals, see: Dalidowicz, P.; Swenton, J. S. *J. Org. Chem.* **1993**, *58*, 4802−4804. (b) The main differences between the reactions reported herein and those of the related quinones are explained by the difference in Lewis acid promoters used. In most of the 2-methoxy quinone reactions, Ti(IV) was used and the major products were dihydrobenzofurans and 2 + 2 adducts resulting from a process analogous to **7** → **8** → **9** → **4**/**5**. In the present report, the milder Lewis acid BF_3 apparently allows the dealkylation process to compete with the fragmentation.

are naturally occurring plant products possessing the fused benzofuranyl−benzopyran ring system. Many are phytoalexins displaying potent antifungal and antibacterial activity.[9] The SAR profiles of the pterocarpan phytoalexins have not been comprehensively examined, particularly regarding potential nitrogen bioisosteres, and there has been recent interest in the synthesis of azapterocarpans.[4,10] In addition, several pterocarpans have been reported to inhibit HIV-1 reverse transcriptase and the cytopathic effect of HIV-1 in cell culture.[11] These novel anti-HIV agents represent new lead structures for potential drug development.

The development of a general synthetic route to substituted aza- and diazapterocarpans via BF_3-promoted reactions of bisimides **2**/**3** with 2*H*-chromenes **10a**/**b** and *N*-toluenesulfonyl-1,2-dihydroquinoline **11a**[11b] was described in our preliminary communication (eq 2).[4] The



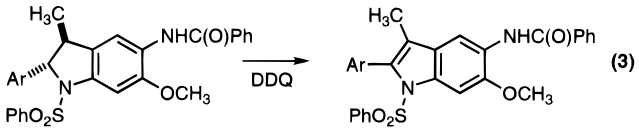
(2)

10a, X=O, R^1=OCH_3
10b, X=O, R^1=H
11a, X=NTs, R^1=OCH_3
11b, X=NTs, R^1=H

12a, X=O, R^1=OCH_3, R^2=CH_3 (63%)
12b, X=O, R^1=OCH_3, R^2=CH_2Ph (62%)
12c, X=O, R^1=H, R^2=CH_2Ph (47%)
13a, X=NTs, R^1=OCH_3, R^2=CH_3 (42%)
13b, X=NTs, R^1=OCH_3, R^2=CH_2Ph (93%)

azapterocarpans **12a**−**c** and diazapterocarpans **13a**/**b** were found in moderate to good yield (reactions of **11b** failed). The full experimental details of these experiments and spectral data for the products appear herein. The structures of **12** are assigned as described previously.[4] Since a number of important spectral characteristics of **12** are similar to those of **13** (e.g., IR absorbances at ∼3427 cm^{-1}, the appearance of H-7 as singlets at ca. 8.15 ppm (H-10 was buried), and NOE enhancements between H-6a and H-11a), the structures of the latter are assigned by analogy.

Application of the reactions reported herein to the synthesis of 2-arylindoles was also examined. Because many of the antiestrogenic 2-arylindoles possess C-3 alkyl substituents and oxygen substitution on both the indole nucleus and the C-2 aryl group, the reactions of styrenes **1a**−**c** with the bisimides appeared well-suited for the preparation of this class of compounds. To demonstrate, oxidation of the products from these reactions with DDQ afforded indoles **14** in excellent yields (eq 3). In addition



(3)

4a-c

14a, Ar=C_6H_4-4-OCH_3 (98%)
14b, Ar=C_6H_3-3,4-$(OCH_3)_2$ (83%)
14c, Ar=C_6H_3-3,4-OCH_2O- (90%)

to the NMR and NOE studies carried out on dihydroindoles **4,** similar experiments on indole **14a** further confirmed the position of the C-6 alkoxy group (Figure 2).

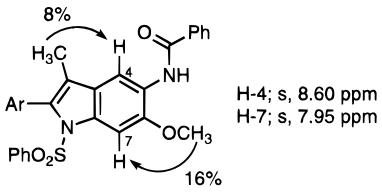


Figure 2. Summary of selected NOE data on **14a**.

We are presently exploring further applications of this new methodology.

Experimental Section[12]

The styrenes,[3a] chromenes,[3f] and dihydroquinoline[4,11b] were purchased (**1a**−**c**,**f**) and used as is[5] or prepared (**1d**,**e**,**f**) by the methods previously reported. Procedures for the preparation of bisimides **2**/**3**[1bb,cc] are given in the Supporting Information.

BF_3·OEt_2-Promoted Reactions of Styrenyl Systems with Quinone Bisimides: Method A. BF_3·OEt_2 was added to a solution of the bisimide in CH_2Cl_2 at −78 °C. The reaction mixture was stirred for 5−10 min and then treated dropwise with the styrene, either neat or as a solution in CH_2Cl_2. After 5−20 min, the reaction was determined to be complete by TLC analysis and the mixture was poured rapidly into saturated, aqueous $NaHCO_3$. The aqueous layer was separated and extracted with CH_2Cl_2, and the combined organic extracts were then washed with brine, dried (Na_2SO_4), and concentrated.

Method B. BF_3·Et_2O was added to a solution of the styrene and the bisimide in CH_2Cl_2 at −78 °C. After 5−20 min, the mixture was worked up as described in method A.

***N*-[(2*R**,3*R**)-1-Benzenesulfonyl-6-methoxy-2-(4-methoxyphenyl)-3-methyl-2,3-dihydro-1*H*-indol-5-yl]benzamide (4a).** According to method A, BF_3·OEt_2 (33 μL, 0.36 mmol) was added to a solution of bisimide **2** (105 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) at −78 °C followed by *trans*-anethole (50 μL, 0.33 mmol). Workup and chromatography (2:2:6 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded **4a** (146 mg, 75%) as a white crystalline solid: mp 174−175 °C (Et_2O/hexanes); ^1H NMR (500 MHz) 0.77 (d, *J* = 7.0, 3H), 3.07 (dq, *J* = 3.0, 7.0, 1H), 3.78 (s, 3H), 4.03 (s, 3H), 4.61 (d, *J* = 3.0, 1H), 6.83 (d, *J* = 8.5, 2H), 7.23 (d, *J* = 8.5, 2H), 7.42−7.57 (m, 7H), 7.74 (d, *J* = 7.6, 2H), 7.87 (d, *J* = 7.5, 2H), 8.28 (s, 1H), 8.53 (s, 1H); ^{13}C NMR (125 MHz) 21.9, 45.8, 55.2, 56.4, 73.0, 99.3, 114.0, 115.6, 124.9, 126.9, 127.0, 127.2, 128.0, 128.8, 128.9, 131.7, 133.1, 134.7, 135.1, 136.9, 137.5, 148.4, 159.1, 165.1. Anal. Calcd for $C_{30}H_{28}N_2O_5S$: C, 68.16; H, 5.34; N, 5.30. Found: C, 68.00; H, 5.50; N, 5.20.

***N*-[(2*R**,3*R**)-2,3-Dihydro-6-methoxy-2-(3,4-dimethoxyphenyl)-3-methyl-1-(benzenesulfonyl)-1*H*-indol-5-yl]-benzamide (4b).** According to method A, BF_3·OEt_2 (140 μL, 1.14 mmol) was added to a solution of bisimide **2** (0.384 g, 1.01 mmol) in CH_2Cl_2 (6 mL) at −78 °C followed by (*E*)-1,2-dimethoxy-4-propenylbenzene (180 μL, 1.06 mmol). Workup and chromatography (2:3:5 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded the title compound (0.374 g, 66%) as a white crystalline solid: mp 193−194 °C (EtOAc/hexanes); TLC R_f = 0.24

(9) For reviews see: Donnelly, D. M. X.; Boland, G. M. *Nat. Prod. Rep.* **1995**, 321−338 and previous reviews cited therein. See also references cited in ref 3f.

(10) Tökés, A. L.; Antus, S. *Liebigs Ann. Chem.* **1994**, 911−915.

(11) (a) Engler, T. A.; Lynch, K. O., Jr.; Reddy, J. P.; Gregory, G. S. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 1229−1232. (b) Engler, T. A.; Lynch, K. O., Jr.; Iyengar, R.; Chai, W.; Agrios, K. *Bioorg. Med. Chem.*, in press.

(12) All compounds were prepared as racemic mixtures. All reactions were done in oven- or flame-dried glassware under a nitrogen atmosphere with magnetic stirring. CH_2Cl_2 and BF_3·OEt_2 were distilled under nitrogen from CaH_2 immediately before use. Brine refers to saturated aqueous sodium chloride. NMR spectra were recorded on samples dissolved in $CDCl_3$, unless otherwise noted, and chemical shifts are reported in δ (ppm) relative to Me_4Si or residual $CHCl_3$. Coupling constants (*J*) are reported in Hertz. Reactions were monitored by thin-layer chromatography on precoated 0.25 mm silica gel plates with a fluorescent indicator (Merck Kieselgel 60_{F254}); visualization was effected with a UV lamp or by staining with solutions of *p*-anisaldehyde/H_2SO_4 or phosphomolybdic acid. Chromatography refers to flash chromatography on silica gel [EM-Kieselgel 60 (0.04−0.063 mm mesh) or Selectro Scientific (0.032−0.063 mm mesh)] with the indicated eluent. Melting points are uncorrected.

(2:4:4 CH_2Cl_2/Et_2O/hexanes); ^{1}H NMR (500 MHz) 0.80 (d, J = 7.0, 3H), 3.10 (dq, J = 3.3, 7.0, 1H), 3.82 (s, 3H), 3.85 (s, 3H), 4.04 (s, 3H), 4.60 (d, J = 3.3, 1H), 6.78−6.80 (m, 2H), 6.87 (dd, J = 1.9, 8.3, 1H), 7.42−7.56 (m, 7H), 7.73 (d, J = 7.9, 2H), 7.87 (d, J = 7.9, 2H), 8.28 (s, 1H), 8.53 (s, 1H); ^{13}C NMR (125 MHz) 21.9, 45.7, 55.89, 55.90, 56.4, 73.3, 99.2, 109.1, 111.1, 115.6, 118.2, 124.9, 126.9, 127.2, 127.9, 128.8, 128.9, 131.8, 133.2, 134.9, 135.1, 136.9, 137.5, 148.4, 148.6, 149.1, 165.1. Anal. Calcd for $C_{31}H_{30}N_2O_6S$: C, 66.65; H, 5.41; N, 5.01. Found: C, 66.49; H, 5.25; N, 5.00.

***N*-[(2*R**,3*R**)-1-Benzenesulfonyl-2-[1,3]benzodioxolyl-6-methoxy-3-methyl-2,3-dihydro-1*H*-indol-5-yl]benzamide (4c).** According to method A, BF_3·OEt_2 (40 μL, 0.33 mmol) was added to a solution of bisimide **2** (95.6 mg, 0.25 mmol) in CH_2Cl_2 (2 mL) at −78 °C followed by isosafrole (43 μL, 0.30 mmol). Workup and chromatography (2:2:6 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded **4c** (114 mg, 84%) as a white crystalline solid: mp 171−173.5 °C (CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz) 0.76 (d, J = 7.0, 3H), 3.04 (dq, J = 3.0, 7.0, 1H), 4.04 (s, 3H), 4.55 (d, J = 3.0, 1H), 5.92 (s, 2H), 6.73−6.85 (m, 3H), 7.43−7.57 (m, 7H), 7.65 (d, J = 7.6, 2H), 7.87 (d, J = 7.3, 2H), 8.27 (s, 1H), 8.53 (s, 1H); ^{13}C NMR (125 MHz) 21.9, 45.9, 56.4, 73.2, 99.3, 101.0, 106.3, 108.2, 115.6, 119.2, 125.0, 126.9, 127.2, 127.8, 128.8, 129.0, 131.7, 133.2, 135.1, 136.5, 136.8, 137.4, 147.1, 147.9, 148.4, 165.1. Anal. Calcd for $C_{30}H_{26}N_2O_6S$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.18; H, 4.80; N, 4.98.

***N*-[(2*R**,3*R**)-1-Benzenesulfonyl-6-(benzyloxy)-2-(3,4-dimethoxyphenyl)-3-methyl-2,3-dihydro-1*H*-indol-5-yl]-benzamide (5b).** According to method A, BF_3·OEt_2 (36 μL, 0.40 mmol) was added to a solution of bisimide **3** (140 mg, 0.31 mmol) in CH_2Cl_2 (2 mL) at −78 °C followed by 1,2-dimethoxy-4-propenylbenzene (62 μL, 0.37 mmol). Workup and chromatography (2:2:6 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded **5b** (111 mg, 57%) as a white crystalline solid: mp 144−146.5 °C (CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz) 0.80 (d, J = 7.0, 3H), 3.10 (dq, J = 3.3, 6.7, 1H), 3.81 (s, 3H), 3.86 (s, 3H), 4.58 (d, J = 3.3, 1H), 5.34 (s, 2H), 6.78−6.80 (m, 2H), 6.87 (d, J = 8.2, 1H), 7.33−7.55 (m, 14H), 7.82 (d, J = 7.7, 2H), 8.29 (s, 1H), 8.64 (s, 1H); ^{13}C NMR (125 MHz) 21.8, 45.8, 55.87, 55.90, 71.2, 73.4, 101.0, 109.0, 111.0, 115.7, 118.2, 125.3, 126.9, 127.1, 127.6, 128.3, 128.4, 128.8, 128.87, 128.89, 131.8, 133.1, 134.9, 135.0, 136.3, 136.8, 137.3, 147.1, 148.6, 149.1, 164.9. Anal. Calcd for $C_{37}H_{34}N_2O_6S$: C, 69.54; H, 5.40; N, 4.41. Found: C, 69.78; H, 5.10; N, 4.24.

***N*-[(2*R**,3*R**)-1-Benzenesulfonyl-2-[1,3]benzodioxolyl-6-benzyloxy-3-methyl-2,3-dihydro-1*H*-indol-5-yl]benzamide (5c).** According to method A, BF_3·OEt_2 (50 μL, 0.55 mmol) was added to a solution of bisimide **3** (192 mg, 0.42 mmol) in CH_2Cl_2 (3 mL) at −78 °C followed by isosafrole (73 μL, 0.51 mmol). Workup and chromatography (2:2:6 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded **5c** (172 mg, 66%) as a white crystalline solid: mp 178−178.5 °C (CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz) 0.77 (d, J = 7.0, 3H), 3.04 (dq, J = 3.3, 7.0, 1H), 4.54 (d, J = 3.3, 1H), 5.34 (s, 2H), 5.91 (s, 2H), 6.73−6.81 (m, 3H), 7.34−7.62 (m, 14H), 7.83 (d, J = 7.5, 2H), 8.29 (s, 1H), 8.65 (s, 1H); ^{13}C NMR (125 MHz) 21.9, 45.9, 71.2, 73.3, 101.0, 101.1, 106.3, 108.1, 115.6, 119.2, 125.3, 126.8, 127.1, 127.6, 128.1, 128.4, 128.85, 128.86, 128.9, 131.7, 133.0, 134.9, 136.2, 136.5, 136.7, 137.1, 147.1, 147.2, 147.9, 164.9. Anal. Calcd for $C_{36}H_{30}N_2O_6S$: C, 69.89; H, 4.89; N, 4.53. Found: C, 69.55; H, 4.63; N, 4.50.

***N*-[(2*R**,3*R**)-1-Benzenesulfonyl-6-methoxy-3-methyl-2-(4-methylphenyl)-2,3-dihydro-1*H*-indol-5-yl]benzamide (4d) and *N*-[(1*R**,5*R**,6*R**,7*R**)-7-Methyl-4,8-dioxo-6-(4-methylphenyl)bicyclo[3.2.1]oct-2-en-3-yl]benzamide (6d).** According to method A, BF_3·OEt_2 (34 μL, 0.37 mmol) and (*E*)-1-methyl-4-(1-propenyl)benzene (46 μL, 34 mmol) were added sequentially to a solution of bisimide **2** (109 mg, 0.29 mmol) in CH_2Cl_2 (2 mL) at −78 °C. Workup and chromatography (2:2:6 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded **4d** (34 mg, 23%) as a white crystalline solid and **6d** (38 mg, 37%) as a light yellow foam.

Physical and spectral data for **4d**: mp 182−184 °C (CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz) 0.78 (d, J = 7.0, 3H), 2.32 (s, 3H), 3.07 (dq, J = 3.3, 7.0, 1H), 4.04 (s, 3H), 4.61 (d, J = 3.3, 1H), 7.11 (d, J = 8.0, 2H), 7.20 (d, J = 8.0, 2H), 7.42−7.57 (m, 7H), 7.74 (d, J = 7.9, 2H), 7.87 (d, J = 7.8, 2H), 8.27 (s, 1H), 8.53 (s, 1H); ^{13}C NMR (125 MHz) 21.1, 22.0, 45.9, 56.4, 73.3, 99.3, 115.6, 124.9, 125.7, 126.9, 127.2, 128.0, 128.8, 129.0, 129.3, 131.7, 133.2, 135.1, 137.0, 137.35, 137.42, 139.5, 148.4, 165.1. Anal. Calcd for $C_{30}H_{28}N_2O_4S$: C, 70.29; H, 5.50; N, 5.46. Found: C, 69.88; H, 5.48; N, 5.28.

Physical and spectral data for **6d**: mp 70−75 °C; ^{1}H NMR (500 MHz) 1.30 (d, J = 7.0, 3H), 2.28 (s, 3H), 2.70 (dq, J = 7.0, 7.0, 1H), 3.22 (dd, J = 1.8, 8.6, 1H), 3.25 (dd, J = 7.0, 7.0, 1H), 3.89 (dd, J = 1.8, 7.0, 1H), 6.97 (d, J = 8.0, 2H), 7.08 (d, J = 8.0, 2H), 7.48 (t, J = 7.5, 2H), 7.56 (t, J = 7.5, 1H), 7.83 (d, J = 7.5, 2H), 8.45 (s, 1H), 8.62 (d, J = 8.6, 1H); ^{13}C NMR (125 MHz) 20.9, 21.4, 42.1, 48.9, 55.2, 70.4, 127.1, 128.1, 128.8, 129.5, 130.8, 132.3, 133.6, 134.5, 134.6, 137.3, 165.7, 191.6, 199.4. Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.89. Found: C, 76.38; H, 5.98; N, 3.73.

In another experiment according to method B, (*E*)-1-methyl-4-(1-propenyl)benzene (46 μL, 0.34 mmol) was added to a solution of bisimide **3** (123 mg, 0.27 mmol) in CH_2Cl_2 (2 mL) at −78 °C followed by BF_3·Et_2O (32 μL, 0.35 mmol). Workup and chromatography gave **6d** (76 mg, 78%) as a light yellow oil, which crystallized from hexanes to afford a white solid.

In yet another experiment according to method A, a BF_3·OEt_2 (70 μL, 0.77 mmol) promoted reaction of bisimide **3** (269 mg, 0.59 mmol) with (*E*)-1-methyl-4-(1-propenyl)benzene (93 μL, 0.71 mmol) afforded **6d** (143 mg, 67%) and **5d** (39 mg, 11%) as a white solid, mp 169−172 °C.[13] Spectral data for **5d**: ^{1}H NMR (500 MHz) 0.77 (d, J = 7.0, 3H), 2.32 (s, 3H), 3.06 (dq, J = 3.3, 7.0, 1H), 4.57 (d, J = 3.3, 1H), 5.33 (s, 2H), 7.10−7.55 (m, 18H), 7.81 (d, J = 7.1, 2H), 8.26 (s, 1H), 8.63 (s, 1H); ^{13}C NMR (125 MHz) 21.1, 21.9, 45.9, 71.3, 73.4, 101.1, 115.7, 125.3, 125.8, 126.9, 127.2, 127.6, 128.4, 128.5, 128.6, 128.8, 128.9, 129.3, 131.8, 133.1, 135.0, 136.3, 136.9, 137.2, 137.4, 139.5, 147.2, 164.9; HRMS m/z 589.2159 (M^+ + 1) (calcd for $C_{36}H_{33}N_2O_4S$ 589.2161).

***N*-[(1*R**,5*R**,6*R**,7*R**)-7-Methyl-4,8-dioxo-6-(2-methylphenyl)bicyclo[3.2.1]oct-2-en-3-yl]benzamide (6e).** According to method A, BF_3·Et_2O (30 μL, 0.32 mmol) and (*E*)-2-methyl-4-propenylbenzene (42 μL, 0.29 mmol) were added sequentially to a solution of bisimide **3** (110 mg, 0.24 mmol) in CH_2Cl_2 (2 mL) at −78 °C. Workup and chromatography (9:1 CH_2Cl_2/hexanes as the eluent) gave **6e** (87 mg, 59%) as a clear colorless oil, which crystallized from hexanes as a white solid: mp 136−138 °C; ^{1}H NMR (500 MHz) 1.29 (d, J = 7.0, 3H), 2.41 (s, 3H), 2.85 (dq, J = 7.0, 6.0, 1H), 3.24 (dd, J = 1.8, 8.5, 1H), 3.50 (dd, J = 6.0, 7.0, 1H), 3.92 (dd, J = 1.8, 7.0, 1H), 6.89 (d, J = 7.5, 1H), 7.06 (t, J = 7.5, 1H), 7.12 (t, J = 7.5, 1H), 7.17 (d, J = 7.5, 1H), 7.47 (t, J = 7.9, 2H), 7.55 (t, J = 7.9, 1H), 7.80 (d, J = 7.9, 2H), 8.37 (s, 1H), 8.60 (d, J = 8.5, 1H); ^{13}C NMR (125 MHz) 20.0, 21.7, 41.3, 45.2, 55.2, 68.0, 126.4, 126.6, 127.1, 127.4, 128.8, 130.1, 130.7, 132.3, 133.6, 134.9, 136.0, 137.1, 165.8, 191.5, 199.7. Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.88; N, 3.89. Found: C, 76.95; H, 5.87; N, 3.50.

In a similar manner, a BF_3·Et_2O (35 μL, 0.38 mmol) promoted reaction of bisimide **2** (112 mg, 0.30 mmol) with 2-methyl-4-propenylbenzene (52 μL, 0.35 mmol) afforded **6e** (57 mg, 54%).

***N*-[(1*R**,5*R**,6*R**,7*R**)-7-Methyl-4,8-dioxo-6-phenylbicyclo[3.2.1]oct-2-en-3-yl]benzamide (6f).** According to method A, BF_3·Et_2O (30 μL, 0.32 mmol) was added to a solution of bisimide **3** (113 mg, 0.25 mmol) in CH_2Cl_2 (2 mL) at −78 °C followed by *trans*-β-methylstyrene (39 μL, 0.30 mmol). Workup and chromatography (2:2:6 Et_2O/CH_2Cl_2/hexanes as the eluent) gave **6f** (65 mg, 76%) as a light yellow oil, which crystallized from hexanes as a white solid: mp 152.2−153 °C; ^{1}H NMR (500 MHz) 1.31 (d, J = 7.0, 3H), 2.73 (dq, J = 7.0, 7.0, 1H), 3.23 (dd, J = 1.8, 8.6, 1H), 3.29 (dd, J = 7.0, 7.0, 1H), 3.92 (dd, J = 1.8, 7.0, 1H), 7.08 (d, J = 7.3, 2H), 7.23 (t, J = 7.3, 1H), 7.28 (t, J = 7.3, 2H), 7.48 (t, J = 7.9, 2H), 7.56 (t, J = 7.9, 1H), 7.82 (d, J = 7.9, 2H), 8.44 (s, 1H), 8.62 (d, J = 8.6, 1H); ^{13}C NMR (125 MHz) 21.5, 42.0, 49.3,

(13) The isolation of **5d** was not consistently reproducible and thus was not fully characterized.

55.2, 70.3, 127.1, 127.7, 128.3, 128.8, 128.9, 130.8, 132.4, 133.6, 134.6, 137.6, 165.7, 191.5, 199.2; HRMS *m/z* 346.1430 ($M^+ + 1$) (calcd for $C_{22}H_{19}NO_3$ 346.1443). Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.00; H, 5.70; N, 4.46.

In a similar manner, a $BF_3{\cdot}Et_2O$ (43 μL, 0.35 mmol) promoted reaction of bisimide **2** (100 mg, 0.27 mmol) with *trans*-β-methylstyrene (24 μL, 0.32 mmol) afforded **6f** (50 mg, 55%).

***N*-[(1*R**,5*R**,6*R**,7*R**)-6-(4-Chlorophenyl)-7-methyl-4,8-dioxobicyclo[3.2.1]oct-2-en-3-yl]benzamide (6g).** According to method A, $BF_3{\cdot}Et_2O$ (33 μL, 0.37 mmol) was added to a solution of bisimide **3** (130 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) at −78 °C followed by (*E*)-1-chloro-4-(1-propenyl)benzene (43 μL, 0.34 mmol). Workup and chromatography (2:2:6 Et_2O/CH_2Cl_2/hexanes as the eluent) gave **6g** (78.4 mg, 72%) as a light yellow oil, which crystallized from hexanes as a white solid: mp 97−99 °C; ^{1}H NMR (300 MHz) 1.31 (d, J = 7, 3H), 2.67 (dq, J = 6, 7, 1H), 3.21−3.29 (m, 2H), 3.90 (dd, J = 2, 7, 1H), 7.02 (d, J = 8, 2H), 7.25 (d, J = 8, 2H), 7.46−7.60 (m, 3H), 7.82 (d, J = 7, 2H), 8.42 (bs, 1H), 8.62 (d, J = 9, 1H); ^{13}C (75 MHz) 198.8, 191.4, 165.8, 136.2, 134.6, 133.7, 133.5, 132.5, 130.9, 129.6, 129.1, 128.9, 127.1, 70.1, 55.2, 48.6, 42.2, 21.5. Anal. Calcd for $C_{22}H_{18}NO_3Cl$: C, 69.57; H, 4.78; N, 3.69. Found: C, 69.28; H, 4.99; N, 3.59.

In a similar manner, a $BF_3{\cdot}Et_2O$ (32 μL, 0.34 mmol) promoted reaction of bisimide **2** (101 mg, 0.26 mmol) with (*E*)-1-chloro-4-(1-propenyl)benzene (40 μL, 0.32 mmol) afforded **6g** (59 mg, 59%).

***N*-[(6a*S*,*11a*S**)-6,6a,11,11a-Tetrahydro-3,9-dimethoxy-11-(benzenesulfonyl)[1]benzopyrano[4,3-*b*]indol-8-yl]-benzamide (12a).** According to method A, $BF_3{\cdot}OEt_2$ (140 μL, 1.14 mmol) was added to a solution of bisimide **2** (0.368 g, 0.967 mmol) in CH_2Cl_2 (5 mL) at −78 °C followed by 7-methoxy-2*H*-chromene (0.163 g, 1.00 mmol). Workup and chromatography (2:2:6 and then 2:3:5 CH_2Cl_2/Et_2O/hexanes as the eluents) afforded **12a** (0.332 g, 63%) as a white solid: mp 245−250 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.34 (2:3:5 CH_2Cl_2/Et_2O/hexanes); ^{1}H NMR (500 MHz) 8.55 (s, 1H), 8.42 (s, 1H), 7.86 (d, J = 7.1, 2H), 7.74 (d, J = 8.7, 1H), 7.64 (d, J = 7.4, 2H), 7.57−7.54 (m, 2H), 7.49 (apparent t, J = 7.7, 7.1, 2H), 7.40 (apparent t, J = 7.9, 7.8, 2H), 7.24 (s, 1H), 6.61 (dd, J = 2.5, 8.7, 1H), 6.21 (d, J = 2.5, 1H), 5.41 (d, J = 8.4, 1H), 4.48 (dd, J = 1.6, 12, 1H), 4.05 (dd, J = 2.4, 12, 1H), 3.93 (s, 3H), 3.69 (s, 3H), 2.95 (bd, J = 8.4, 1H); ^{13}C NMR (125 MHz) 165.2, 160.2, 156.7, 148.5, 138.1, 137.3, 135.0, 133.2, 131.9, 131.8, 129.2, 128.8, 126.9 (2C), 126.1, 125.2, 114.4, 113.2, 109.5, 103.0, 101.2, 64.2, 60.3, 56.3, 55.2, 40.3; HRMS *m/z* 542.1513 (calcd for $C_{30}H_{26}N_2O_6S$ 542.1512). Anal. Calcd for $C_{30}H_{26}N_2O_6S$: C, 66.40; H, 4.84; N, 5.16. Found: C, 65.83; H, 4.70; N, 5.23.

***N*-[(6a*S*,*11a*S**)-9-(Benzyloxy)-6,6a,11,11a-tetrahydro-3-methoxy-11-(benzenesulfonyl)[1]benzopyrano[4,3-*b*]indol-8-yl]benzamide (12b).** According to method A, $BF_3{\cdot}OEt_2$ (140 μL, 1.14 mmol) was added dropwise to a solution of bisimide **3** (0.456 g, 0.999 mmol) in CH_2Cl_2 (4 mL) followed by a solution of 7-methoxy-2*H*-chromene (0.192 g, 1.18 mmol) in CH_2Cl_2 (1 mL). Workup and chromatography (2:3:5 CH_2Cl_2/Et_2O/hexanes as the eluent) gave **12b** (0.383, 62%) as a white solid: mp 196−197 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.20 (2:3:5 CH_2Cl_2/Et_2O/hexanes); ^{1}H NMR (500 MHz) 8.64 (s, 1H), 8.43 (s, 1H), 7.78 (d, J = 7.2, 2H), 7.74 (d, J = 8.7, 1H), 7.55−7.34 (m, 14H), 6.62 (dd, J = 2.5, 8.7, 1H), 6.21 (d, J = 2.5, 1H), 5.43 (d, J = 8.5, 1H), 5.20 (ABq, J = 12, $\Delta\nu$ = 35 Hz, 2H), 4.50 (dd, J = 1.9, 12, 1H), 4.07 (dd, J = 2.5, 12, 1H), 3.70 (s, 3H), 2.97 (bd, J = 8.4, 1H); ^{13}C NMR (125 MHz) 165.0, 160.2, 156.7, 147.4, 138.1, 137.2, 136.0, 134.8, 133.2, 132.0, 131.8, 129.2, 128.8 (2C), 128.5, 127.7, 126.9, 126.8, 126.6, 125.6, 114.5, 133.3, 109.6, 104.7, 101.2, 71.3, 64.2, 60.3, 55.2, 40.4; HRMS *m/z* 618.1825 (calcd for $C_{36}H_{30}N_2O_6S$ 618.1813).

***N*-[(6a*S*,*11a*S**)-9-(Benzyloxy)-6,6a,11,11a-tetrahydro-11-(benzenesulfonyl)[1]benzopyrano[4,3-*b*]indol-8-yl]-benzamide (12c).** According to method A, $BF_3{\cdot}OEt_2$ (60 μL, 0.49 mmol) was added to a solution of bisimide **3** (110 mg, 0.241 mmol) in CH_2Cl_2 (3 mL) at −78 °C followed by 2*H*-chromene (63 mg, 0.48 mmol). Workup and chromatography (2:3:5 CH_2Cl_2/Et_2O/hexanes as the eluent) yielded **12c** (67 mg, 47%) as a white solid: mp 260−265 °C dec (THF/hexanes); TLC R_f = 0.30 (2:3:5 CH_2Cl_2/Et_2O/hexanes); ^{1}H NMR (500 MHz) 8.64 (s, 1H), 8.44 (s, 1H), 7.87 (dd, J = 1.0, 7.8, 1H), 7.78 (d, J = 8.5, 2H), 7.56−7.35 (m, 13H), 7.34 (s, 1H), 7.13 (ddd, J = 1.1, 7.8, 7.85, 1H), 7.03 (ddd, J = 1.0, 7.8, 8.1, 1H), 6.69 (dd, J = 1.1, 8.1, 1H), 5.47 (d, J = 8.5, 1H), 5.21 (ABq, J = 12, $\Delta\nu$ = 35 Hz, 2H), 4.51 (dd, J = 2.0, 12, 1H), 4.09 (dd, J = 2.5, 12, 1H), 2.99 (bd, J = 8.5, 1H); ^{13}C NMR (125 MHz) 165.0, 155.7, 147.4, 137.9, 137.2, 136.0, 134.8, 133.2, 131.9, 131.2, 129.2, 129.1, 128.8, 128.5, 128.4, 127.7, 126.9, 126.8, 126.7, 125.6, 122.1, 121.3, 117.1, 114.5, 104.7, 71.4, 64.1, 60.4, 40.6. Anal. Calcd for $C_{35}H_{28}N_2O_5$: C, 71.40; H, 4.80; N, 4.76. Found: C, 71.48; H, 4.77; N, 4.60.

***N*-[(6a*S**,11a*S**)-11-Benzenesulfonyl-3,9-dimethoxy-5-toluenesulfonyl-5,6,6a,11a-tetrahydroindolo[3,2-*c*][1]-quinoline-8-yl]benzamide (13a).** According to method A, $BF_3{\cdot}Et_2O$ (33 μL, 0.26 mmol) was added to a solution of bisimide **2** (78 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) at −78 °C followed by a 3.4:1 mixture of dihydroquinoline **11a** and its 5-methoxy isomer[4,11b] (89 mg, 0.28 mmol) in CH_2Cl_2 (2 mL). [Note: the 5-methoxy isomer did not react in these experiments and could be recovered cleanly.] Workup and chromatography (1:1:8 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded the 5-methoxy isomer of the starting quinoline,[11b] R_f = 0.30 (20% EtOAc/hexanes), and **13a** (60 mg, 42%) as a white solid: mp 202−204 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.07 (20% EtOAc/hexanes); ^{1}H NMR (500 MHz) 8.45 (s, 1H), 8.14 (s, 1H), 7.85 (d, J = 8.0, 2H), 7.80 (d, J = 8.5, 1H), 7.56−7.47 (m, 6H), 7.36−7.24 (m, 7H), 7.08 (d, J = 2.5, 1H), 6.86 (dd, J = 2.5, 8.5, 1H), 4.41−4.37 (m, 2H), 3.96 (s, 3H), 3.78 (s, 3H), 3.38−3.30 (m, 2H), 2.49 (s, 3H); ^{13}C NMR (125 MHz) 165.0, 159.3, 148.4, 143.6, 138.1, 137.3, 136.9, 136.7, 134.8, 133.4, 131.9, 129.8, 129.7, 128.9, 128.8, 127.2, 127.1, 127.1, 127.0, 126.1, 122.2, 115.2, 113.3, 103.9, 102.0, 60.7, 56.4, 55.5, 47.8, 42.2, 21.7. Anal. Calcd for $C_{37}H_{33}N_3O_7S_2$: C, 63.87; H, 4.78; N, 6.04. Found: C, 63.71; H, 4.44; N, 5.99.

***N*-[(6a*S**,11a*S**)-11-Benzenesulfonyl-9-(benzyloxy)-3-methoxy-5-toluenesulfonyl-5,6,6a,11a-tetrahydroindolo-[3,2-*c*][1]quinoline-8-yl]benzamide (13b).** According to method A, $BF_3{\cdot}Et_2O$ (16 μL, 0.13 mmol) was added to bisimide **3** (50 mg, 0.11 mmol) in CH_2Cl_2 (10 mL) at −78 °C followed by a 2:3 mixture of dihydroquinoline **11a** and its 5-methoxy isomer[4,11b] (95 mg, 0.30 mmol) in CH_2Cl_2 (2 mL). [Note: the 5-methoxy isomer did not react in these experiments and could be recovered cleanly.] Workup and chromatography (1:1:8 CH_2Cl_2/Et_2O/hexanes as the eluent) afforded the 5-methoxy isomer of the starting quinoline,[11b] R_f = 0.30 (20% EtOAc/hexanes), and **13b** (78 mg, 93%) as a white solid: mp 213−215 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f = 0.11 (20% EtOAc/hexanes); ^{1}H NMR (500 MHz) 8.59 (s, 1H), 8.16 (s, 1H), 7.79 (m, 3H), 7.53−7.09 (m, 19H), 6.86 (dd, J = 2.4, 8.7, 1H), 5.25 (s, 2H), 4.38 (dd, J = 7.2, 13.8, 1H), 4.36 (d, J = 9.7, 1H), 3.80 (s, 3H), 3.39 (m, 1H), 3.33 (dd, J = 13.8, 8.9, 1H), 2.50 (s, 3H); ^{13}C NMR (125 MHz) 164.9, 159.3, 147.2, 143.6, 138.1, 137.3, 136.9, 136.5, 135.9, 134.7, 133.3, 131.9, 129.8, 129.7, 128.9, 128.8, 128.6, 127.6, 127.5, 127.2, 127.0, 126.9, 126.6, 122.3, 115.3, 113.4, 110.0, 103.8, 71.3, 60.7, 55.5, 47.9, 42.2, 21.6 (one sp^2-C signal is not visible). Anal. Calcd for $C_{43}H_{37}N_3O_7S_2$: C, 66.91; H, 4.83; N, 5.44. Found: C, 66.77; H, 4.68; N, 5.30.

***N*-(1-Benzenesulfonyl-6-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indol-5-yl)benzamide (14a).** DDQ (59 mg, 0.26 mmol) was added to a solution of dihydroindole **4a** (106 mg, 0.070 mmol) in benzene (12 mL) at 23 °C. After 1.5 h, the mixture was treated with 10% aqueous NaOH (3 mL) and acetone (2 mL). Concentration of the mixture *in vacuo* produced a white precipitate which was collected by filtration and washed with H_2O. This white solid was passed through a small plug of silica gel with 2:2:6 CH_2Cl_2/Et_2O/hexanes as the eluent to afford **14a** (106 mg, 98%) as a white solid: decomposition starts at 237 °C without melting (CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz) 2.03 (s, 3H), 3.89 (s, 3H), 4.09 (s, 3H), 6.95 (d, J = 8.7, 2H), 7.21−7.29 (m, 4H), 7.33 (dd, J = 1.0, 8.2, 2H), 7.43−7.58 (m, 4H), 7.93 (d, J = 6.8, 2H), 7.95 (s, 1H), 8.60 (s, 1H), 8.70 (s, 1H); ^{13}C NMR (125 MHz) 9.6, 55.2, 56.5, 99.0, 109.7, 112.8, 120.2, 123.6, 125.5, 125.6, 126.6, 127.0,

128.5, 128.8, 131.7, 132.6, 133.37, 133.38, 135.2, 135.6, 137.8, 147.0, 159.5, 165.2. Anal. Calcd for $C_{30}H_{26}N_2O_5S$: C, 68.56; H, 4.80; N, 5.33. Found: C, 68.40; H, 5.00; N, 4.99.

***N*-[1-Benzenesulfonyl-2-(3,4-dimethoxyphenyl)-6-methoxy-3-methyl-1*H*-indol-5-yl]benzamide (14b).** DDQ (18.2 mg, 0.080 mmol) was added to a solution of dihydroindole **4b** (34.5 mg, 0.060 mmol) in benzene (4 mL) at 23 °C. After 3 h, the mixture was treated with 10% aqueous NaOH (5 mL) and acetone (5 mL). Concentration of the mixture *in vacuo* produced a white precipitate. The mixture was filtered, and the precipitate was washed with H_2O. Chromatography of the white solid with 30% Et_2O/hexanes as the eluent afforded **14b** (28.6 mg, 83%) as a white solid: mp 223 °C dec (CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz) 2.05 (s, 3H), 3.86 (s, 3H), 3.96 (s, 3H), 4.09 (s, 3H), 6.80−6.82 (m, 2H), 6.9 (d, J = 8.2, 1H), 7.28 (d, J = 7.5, 2H), 7.34 (dd, J = 1.2, 8.2, 2H), 7.44−7.58 (m, 4H), 7.93 (d, J = 7.1, 2H), 7.97 (s, 1H), 8.62 (s, 1H), 8.71 (s, 1H); ^{13}C NMR (125 MHz) 9.7, 55.8, 55.9, 56.5, 98.9, 109.7, 109.9, 115.0, 120.2, 123.7, 124.0, 125.4, 125.5, 126.6, 127.0, 128.5, 128.8, 131.8, 133.39, 133.43, 135.2, 135.7, 137.9, 147.1, 147.8, 149.1, 165.2. Anal. Calcd for $C_{31}H_{28}N_2O_6S$: C, 66.89; H, 5.07; N, 5.03. Found: C, 66.49; H, 5.30; N, 4.89.

***N*-(1-Benzenesulfonyl-2-[1,3]benzodioxolyl-6-methoxy-3-methyl-1*H*-indol-5-yl)benzamide (14c).** DDQ (14.5 mg, 0.060 mmol) was added to a solution of dihydroindole **4c** (32.5 mg, 0.060 mmol) in benzene (4 mL) at 23 °C. After 1.5 h, the mixture was filtered with an ether wash. The filtrate was treated with 10% aqueous NaOH (5 mL), and the organic layer was separated, dried (Na_2SO_4), and concentrated. Chromatography of the resultant tan residue with 2:3:5 CH_2Cl_2/Et_2O/hexanes as the eluent afforded **14c** (29.3 mg, 90%) as a white solid: mp 223 °C dec; ^{1}H NMR (300 MHz) 2.05 (s, 3H), 4.09 (s, 3H), 6.05 (s, 2H), 6.72 (dd, J = 1.7, 8.0, 1H), 6.82 (d, J = 1.7, 1H), 6.85 (d, J = 8.0, 1H), 7.29−7.58 (m, 8H), 7.91−7.94 (m, 3H), 8.60 (s, 1H), 8.69 (s, 1H); ^{13}C NMR (75 MHz) 9.7, 56.6, 99.0, 101.3, 107.4, 109.8, 112.0, 120.7, 125.07, 125.14, 125.5, 125.6, 126.6, 127.0, 128.6, 128.8, 131.8, 133.4, 133.5, 135.2, 135.5, 137.7, 146.9, 147.2, 147.7, 165.3. Anal. Calcd for $C_{30}H_{24}N_2O_6S$: C, 66.78; H, 4.30; N, 5.19. Found: C, 66.43; H, 4.68; N, 5.40.

Acknowledgment. Financial support for this research was provided by the National Science Foundation (CHE-9116576, OSR-9255223, and OSR-9550487) and the University of Kansas General Research Fund. T.A.E. gratefully acknowledges a fellowship from the Alfred P. Sloan Foundation. We thank Ms. Deborah Pierson for initial experiments with **1a**.

Supporting Information Available: Full experimental procedures for preparation of bisimides **2/3** and spectra of all intermediates; IR and mass spectral data for all new products; ^{1}H and ^{13}C NMR spectra of new compounds lacking combustion analysis (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9613592