Lewis Acid-Directed Cyclocondensation of Piperidone Enol Ethers with 2-Methoxy-4-(*N*-phenylsulfonyl)-1,4-benzoquinoneimine: A New Regioselective Synthesis of Oxygenated Carbolines

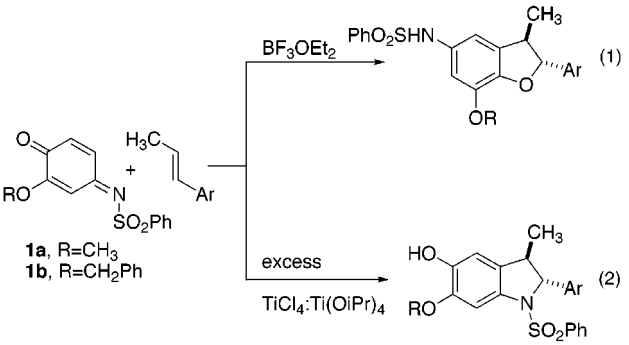
Thomas A. Engler*,† and Jutta Wanner

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

Received October 15, 1999

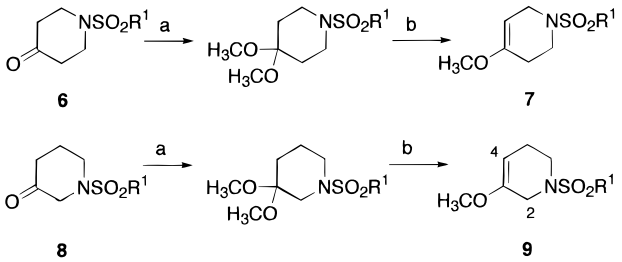
Lewis acid-directed cyclocondensations of piperidone enol ethers with 2-methoxy-4-(*N*-phenylsulfonyl)-1,4-benzoquinoneimine are reported. Benzofurans are obtained with $BF_3{\cdot}OEt_2$ as a promoter, whereas use of excess amounts of $TiCl_4$:$Ti(OiPr)_4$ leads to tetrahydrocarbolines. The latter reactions provide expedient routes to oxygen-substituted tetrahydrocarbolines and carbolines. As applications of this new methodology, the preparations of 1-[3-(dimethylamino)propyl]amino-7-methoxy- and 1-[3-(dimethylamino)propyl]amino-7,8-dimethoxy-5*H*-pyrido[4,3-*b*]indoles are described.

Lewis acid-directed reactions of substituted quinones[1] and imine derivatives[2] with styrenyl systems produce regioisomeric products depending upon the nature of the Lewis acid. For example, $BF_3{\cdot}OEt_2$-promoted reactions of various styrenes with quinone monoimines **1** afford dihydrobenzofurans (eq 1), whereas use of excess Ti(IV) as a promoter produces mainly dihydroindoles (eq 2).[2b]

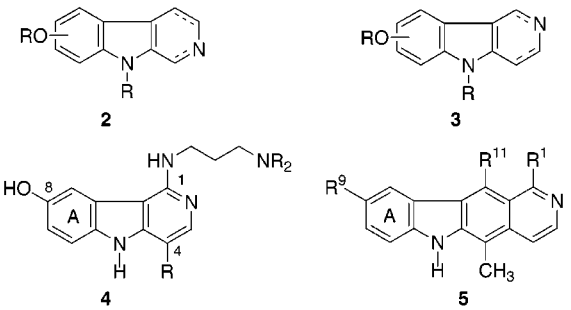


In an effort to extend the lessons learned from these studies to reactions of the quinone imines with alkenyl systems other than styrenes, and to further demonstrate the concept of selective Lewis acid activation of substituted quinones[3,4] and imine derivatives,[5] we have explored reactions of **1** with enol ethers derived from *N*-sulfonyl-3- and -4-piperidones.[6] The choice to use these alkenyl systems was prompted by two considerations. The first was to address the question of whether Lewis acid activation of the quinone imine could be effected in the presence of other entities with mildly basic functionalities and thus significantly extend the synthetic scope of these processes. The second was the expectation that the products would be valuable intermediates to a variety of biologically important alkaloids. For example, numerous β-carbolines **2** possess potent and varied CNS and anticancer activity,[7] and γ-carbolines **3** and **4** have been studied extensively as antitumor agents.[8] The latter are condensed analogues of the ellipticine/olivacine anticancer agents (**5**), and some do indeed display potent activity. In both carboline systems, oxygenation in the A ring often results in more biologically active derivatives.

Scheme 1



For **6**-**9**: **a**, R^1=Ph; **b**, R^1=CH_2Ph; **c**, R^1=2-$NO_2C_6H_4$.
Reagents and Conditions: (a) $(CH_3O)_3CH$, H^+; (b) $AlCl_3/Et_3N$, 59-78% overall.



R^1=R^9=H, R^{11}=CH_3, ellipticine
R^1=H, R^9=OH, R^{11}=CH_3, 9-hydroxyellipticine
R^1=CH_3, R^3=R^{11}=H, olivacine

Piperidone enol ethers **7** and **9** were prepared as shown in Scheme 1.[9] In these syntheses, **9** were formed as the

† Current address: Lilly Corporate Center, Mail Drop 1523, Eli Lilly and Company, Indianapolis, IN 46285. Phone: (317)433-2885. Fax: (317)277-2035. E-mail: ENGLER_THOMAS@Lilly.com.

(1) (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.; Iyengar, R. *J. Org. Chem.* **1998**, *63*, 1929−1934.

(2) (a) Engler, T. A.; Meduna, S. P.; LaTessa, K. O.; Chai, W. *J. Org. Chem.* **1996**, *61*, 8598−8603. (b) Engler, T. A.; Chai, W.; LaTessa, K. O. *J. Org. Chem.* **1996**, *61*, 9297−9308. (c) Engler, T. A.; Chai, W. *Tetrahedron Lett.* **1996** *37*, 6969−6970.

(3) For early studies of Lewis acid-directed Diels−Alder reactions, see: (a) Dickinson, R. A.; Kubela, R.; MacAlpine, G. A.; Stojanac, Z.; Valenta, Z. *Can. J. Chem.* **1972**, *50*, 2377−2380. (b) Stojanac, Z.; Dickinson, R. A.; Stojanac, N.; Woznow, R. J.; Valenta, Z. *Can. J. Chem.* **1975**, *53*, 616−618. (c) Das, J.; Kubela, R.; MacAlpine, G. A.; Stojanac, Z.; Valenta, Z. *Can J. Chem.* **1979**, *57*, 3308−3319. (d) Tou, J. S.; Reusch, W. *J. Org. Chem.* **1980**, *45*, 5012−5014. (e) Hendrickson, J. B.; Singh, V. *J. Chem. Soc., Chem. Commun.* **1983**, 837−838. (f) Hendrickson, J. B.; Haestier, A. M.; Stieglitz, S. G.; Foxman, B. M. *New. J. Chem.* **1990**, *14*, 689−693. (g) Engler, T. A.; Letavic, M. A.; Lynch, K. O., Jr.; Takusagawa, F. *J. Org. Chem.* **1994**, *59*, 1179−1183. For a theoretical discussion of the regioselectivity of these reactions, see: Rozeboom, M. D.; Tegmo-Larson, I.-M.; Houk, K. N. *J. Org. Chem.* **1981**, *46*, 2338−2345.

10.1021/jo9916176 CCC: $19.00
Published on Web 03/23/2000

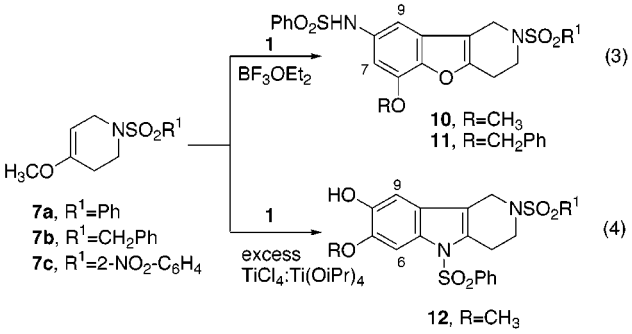
Table 1. BF_3-Promoted Cyclocondensations of Quinone Monoimine 1 with Piperidone Enol Ethers 7/9

entry	quinone imine	enol ether	equiv of BF_3[a]	products (% yield)	
1	**1a**	**7a**	1	**10a** (85)	
2	**1a**	**7a**	2	**10a** (77)	
3	**1a**	**7b**	1	**10b** (65)	
4	**1a**	**7c**	1	**10c** (71)	
5	**1b**	**7a**	1	**11a** (66)	
6	**1a**	**9a**	1	**13a** (68)	
7	**1a**	**9b**	1		**18** (48)[b]
8	**1a**	**9b**	1	**13b** (84)[c]	
9	**1a**	**9c**	1	**13c** (33)	**19** (35)[b]
10	**1a**	**9c**	1	**13c** (80)[c]	
11	**1b**	**9a**	1	**14a** (29)	**20** (31)[b]
12	**1b**	**9a**	2	**14a** (78)[c]	

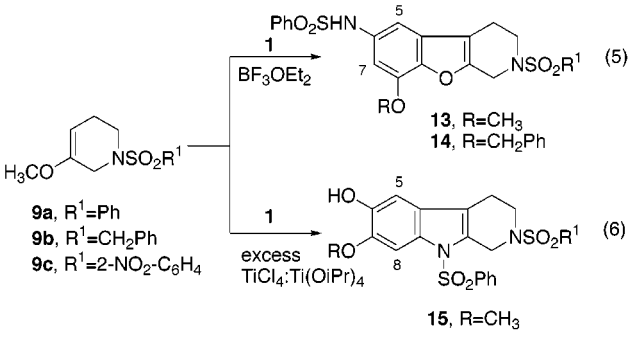
[a] With respect to imine **1**. [b] These reactions were quenched with saturated aqueous NH_4Cl and worked up within 30−60 min. [c] These reactions were quenched with NH_4Cl, and the mixtures were stirred until no dihydrobenzofurans were apparent by TLC, see Experimental Section.

major components of mixtures with their C2−C3 alkenyl isomers (∼4−12:1). These mixtures were used directly in the following reactions, and the minor components did not interfere.

BF_3·OEt_2-promoted reactions of imines **1**[2b] with enol ethers **7** or **9** cleanly afforded benzofurans **10**/**11** and **13**/**14**, respectively (eqs 3 and 5, and Table 1). Distinguishing



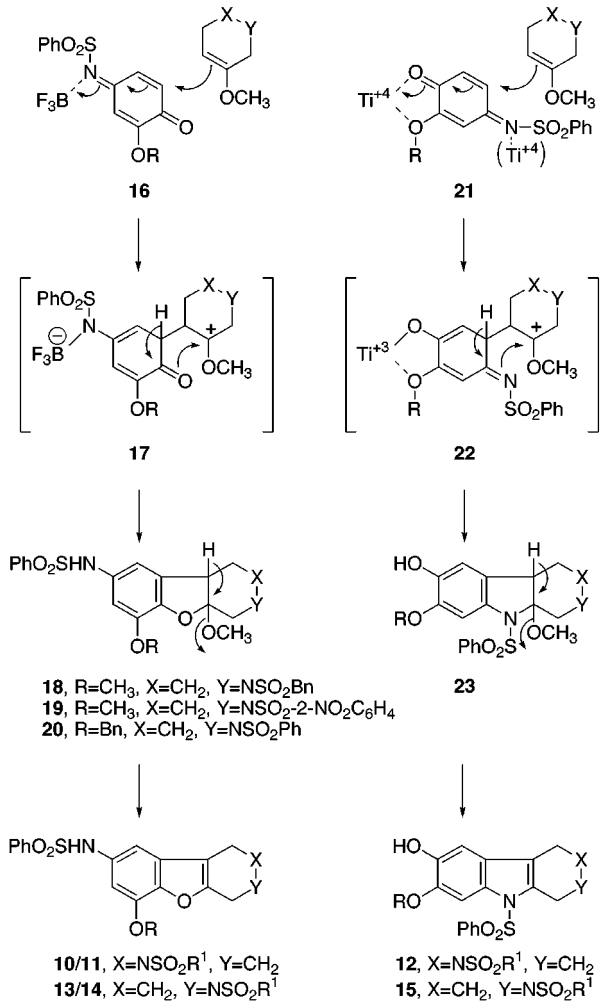
spectral characteristics of these benzofurans included N−H absorbancies at ∼3350 cm^{-1} in their IR spectra and coupled doublets (J ∼ 2 Hz) at ∼6.5−6.6 and ∼6.6−6.8 ppm (H-7/-9 in **10**/**11** and H-5/-7 in **13**/**14**) in their ^1H



For **10-15**: **a**, R^1=Ph; **b**, R^1=CH_2Ph; **c**, R^1=2-NO_2-C_6H_4

NMR spectra. We rationalized that these reactions occurred via intermediates similar to **16**−**20** (Scheme 2). Support for this mechanism was found in some of the reactions of enol ethers **9** in which 2-methoxydihydrobenzofurans **18**−**20** were isolated. Treatment of the latter with protic acid effected elimination to benzofurans **13**/**14**. These reactions imply that the BF_3 activates **1** through binding to the imine moiety, suggesting that it is the most basic site. For the discussion that follows,

Scheme 2



we note that reactions of **1a** with **7a** and of **1b** with **9a** were also studied with 2 equiv of BF_3·OEt_2 as the promoter, and again benzofurans **10a** and **14a**, respectively, were found in good yields (Table 1, entries 2 and 12).

Focus then shifted to Ti(IV)-promoted reactions of 4-piperidone enol ethers **7** with quinone imine **1a**. Guided by our earlier studies involving styrenes,[1,2] we anticipated that reactions employing 1 equiv of Ti(IV) would give mixtures of products. Indeed, initial reactions of **7a**

(4) For other examples of Lewis acid-promoted reactions of quinones with alkenyl systems, see: (a) Engler, T. A.; Agrios, K.; Reddy, J. P.; Iyengar, R. *Tetrahedron Lett.* **1996**, *37*, 327−330. (b) Murphy, W. S.; Neville, D. *Tetrahedron Lett.* **1997**, *38*, 7933−7936. (c) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1977**, 4041−4044. (d) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 2589−2592. (e) Ipaktschi, J.; Heydari, A. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 313−314. (f) Ipaktschi, J.; Heydari, A. *Chem. Ber.* **1992**, *125*, 1513−1515. (g) Naruta, Y. *J. Am. Chem. Soc.* **1980**, *102*, 3774−3783. For reviews, see: (h) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Tetrahedron Organic Chemistry Series Vol. 9; Pergamon: Oxford, 1992; pp 322−330. (i) Finley, K. T. In *The Chemistry of the Quinonoid Compounds*, Vol. 2; Patai, S., Rappaport, Z., Eds.; Wiley: Chichester, 1988; p 537. (j) Nishigaichi, Y.; Takuwa, A.; Naruta, Y. Maruyama, K. *Tetrahedron* **1993**, *49*, 7395−7426. (k) Cintas, P. *Synlett* **1995**, 1087−1109. (l) Fleming, I, Dunogués, J.; Smithers, R. *Org. React.* **1989** *37*, 57−575. (m) Naruta, Y.; Nishigaichi, Y.; Maruyama, K. *Org. Synth.* **1992** *71*, 125−131. (n) Naruta, Y.; Maruyama, K. In *The Chemistry of Quinonoid Compounds*, Vol. 2; Patai, S., Rappoport, Z., Eds.; Wiley-Interscience: Chichester; 1988, Chapter 8. (o) Mukaiyama, T.; Iwasawa, N.; Yura, T.; Clark, R. S. J. *Tetrahedron* **1987**, *43*, 5003−5017. (p) Nucleophilic additions to quinones bearing electron-withdrawing groups are common and are not detailed here; see references cited in the reviews.

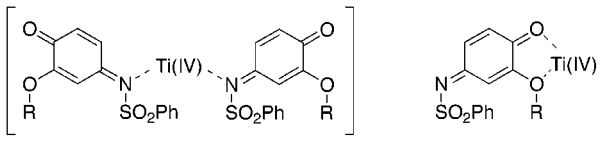


Figure 1. Possible examples of 2:1 and 1:1 complexes of **1** with Ti(IV).[10r] The Ti(IV) is likely octahedral in both, and the other ligands (Cl and OiPr) are not shown for clarity.

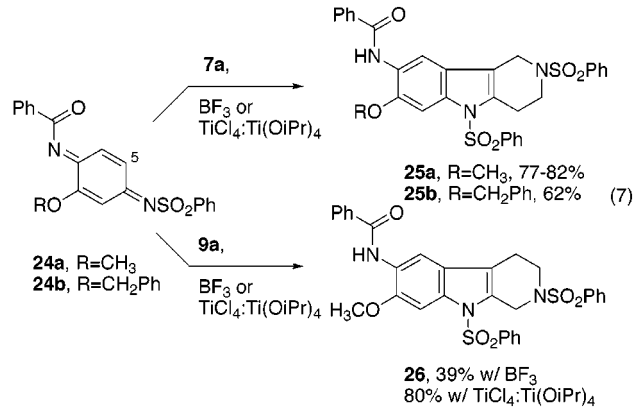
reinforced this bias;[6] however, in subsequent studies we found that these reactions promoted by 1 equiv of Ti(IV), as either $TiCl_4$ or a 1:1 mixture of $TiCl_4$:$Ti(OiPr)_4$, were capricious and inefficient. It was difficult to force them to completion, and mixtures of benzofurans and indoles were usually produced in low yield accompanied by large quantities of the piperidone **6a**. That both benzofuran and indole products were often observed, albeit inconsistently, suggested a competition between activation of the quinone imine **1** via Ti(IV) binding to the C-4 imine moiety and activation via bidentate binding to the C-1/C-2 oxygens (Scheme 2). Inferring that the BF_3·OEt_2-promoted reactions further suggested that the imine moiety is the more basic site in **1**, we postulated that if more than 1 equiv of Ti(IV) was employed, then the first might bind to the imine, leaving the second to bind to the C-1 and C-2 oxygens in a bidentate manner.[10a−j] If so, binding of the second equivalent perhaps would lead to a more reactive complex[10k] such as **21**,[10r] with the second Lewis acid directing the reaction. An alternative hypothesis was that in reactions with 1 equiv of Ti(IV), perhaps considerable amounts of both $[imine]_2$-Ti(IV)[10l−q] and 1:1 complexes (Figure 1)[10r] were present, leading to the product mixtures observed. Use of excess Ti(IV) might then drive the reaction to a 1:1 complex in which the titanium might prefer bidentate binding through the C-1 and C-2 oxygens in order for the metal to attain an octahedral coordination sphere.[10r] Whether either of these postulates are valid remains to be established; however, reactions of **1a** with enol ethers **7** using 5 equiv (with respect to **1**) of Ti(IV), as a 1:1 mixture of $TiCl_4$:$Ti(OiPr)_4$, indeed cleanly produced tetrahydrocarbolines **12**, generally in good yields (eq 4 and Table 2).[11] Similar reactions of enol ethers **9** afforded tetrahydrocarbolines **15** (eq 6). The distinctive spectral features of the tetrahydrocarbolines included IR OH absorbancies at ∼3500 cm^{-1} and singlets at ∼ 6.8 and 7.7 ppm for H-6/-9 in **12** and H-5/-8 in **15** in their ^1H NMR spectra.

Table 2. Ti(IV)-Promoted Cyclocondensations of Quinone Monoimine 1 with Piperidone Enol Ethers 7/9

entry	quinone imine	enol ether	equiv of $TiCl_4$:$Ti(OiPr)_4$[a]	products (% yield)
1	**1a**	**7a**	2.5:2.5	**12a** (82)
2	**1a**	**7b**	2.5:2.5	**12b** (85)
3	**1a**	**7c**	2.5:2.5	**12c** (78)
4	**1a**	**9a**	2.5:2.5	**15a** (71)
5	**1a**	**9b**	2.5:2.5	**15b** (32)
6	**1a**	**9c**	2.5:2.5	**15c** (80)

[a] Equiv of each $TiCl_4$ and $Ti(OiPr)_4$ with respect to imine **1**.

Attempts to develop similar Lewis acid-directed reactions of bisimines **24**,[2a] using either 1 equiv of BF_3·OEt_2 or 5 equiv of Ti(IV), gave only tetrahydrocarboline products **25** and **26** (eq 7).[6] Carboxamide N−H absorbancies at ∼3425 cm^{-1} in their IR spectra and singlets at ∼7.7 and 8.5 ppm in their ^1H NMR spectra were indicative of the structures assigned. These results are consistent with Boger's findings that BF_3·OEt_2-promoted allylations of **24** with allyltributylstannane take place selectively at C-5.[5a]



Reactions of quinone imine **1a** with enol ethers **7**/**9** provide an expedient route to oxygenated carboline platforms, substructures found in a number of biologically active natural products.[7,8] In addition, the adducts incorporate diverse functionality which can be selectively manipulated. For example, the phenolic groups in **12** and **15** are methylated under standard conditions, affording **27** and **30**, respectively, or reductively removed to give **29** via the derived triflates **28** (Scheme 3). These steps remove or alleviate concerns about incompatible functionality in the design of subsequent reactions on tetrahydrocarbolines **12** or **15** and establish the potential utility of the triflates for further transformations. Furthermore, the indole phenylsulfonyl group in **27a** is selectively removed by treatment with either K_2CO_3/MeOH or RedAl to give **31** (Scheme 4). On the other hand, the 2-nitrophenylsulfonyl groups in **27c** and **30c** are selectively cleaved with $HSCH_2CO_2H$/LiOH, affording **32** and **38**, respectively (Schemes 4 and 5).[12] Although

(5) Boger has contrasted the regiochemical course of thermal versus BF_3-promoted nucleophilic additions to quinone diimines, and Mukaiyama has reported a limited number of trityl perchlorate-promoted additions of enol ethers to quinone mono- and diimines. See: (a) Boger, D. L.; Zarrinmayeh, H. *J. Org. Chem.* **1990**, *55*, 1379−1390. (b) Mukaiyama, T.; Sagawa, Y.; Kobayashi, S. *Chem. Lett.* **1987**, 2169−2172. For an early extensive review of reactions of quinone mono- and diimines, see: (c) Adams, R.; Reifschneider, W. *Bull. Chim. Soc. Fr.* **1958**, 23−65.

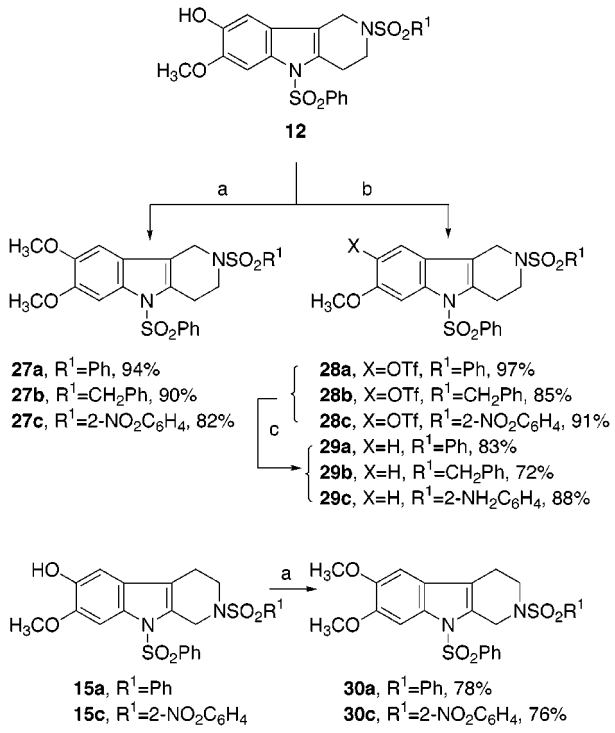
(6) A preliminary communication has appeared: Engler, T. A.; Wanner, J. *Tetrahedron Lett.* **1997**, *38*, 6135−6138.

(7) For reviews, see: (a) Love, B. *Org. Prep Proceed. Int.* **1996** *28*, 1−64. (b) Cox, E. D.; Cook, J. M. *Chem. Rev.* **1995**, *95*, 1797−1842. (c) Baker, B. J. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Pergamon: New York, 1996; Vol. 10. (d) Ohmoto, T.; Koike, K. In *The Alkaloids*; Brossi, A., Ed.; Academic: San Diego, 1989; Vol. 36, pp 135−170. For selected examples, see: (e) Braestrup, C.; Nielson, M.; Olsen, C. E. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 2288−2292. (f) Abou-Gharbia, M.; Patel, R. U.; Moyer, J. A.; Muth, T. A. *J. Med. Chem.* **1987**, *30*, 1100−1105. (g) Abou-Gharbia, M.; Patel, R. U.; Webb, M. B.; Moyer, J. A.; Andree, T. H.; Muth, T. A. *J. Med. Chem.* **1987**, *30*, 1818−1823. (h) Diaz-Arauzo, H.; Evoniuk, G. E.; Skolnick, P.; Cook, J. M. *J. Med. Chem.* **1991**, *34*, 1754−1756. (i) Audia, J. E.; Evrard, D. A.; Murdoch, G. R.; Droste, J. J.; Nissen, J. S.; Schenk, K. W.; Fludzinski, P.; Lucaites, V. L.; Nelson, D. L.; Cohen, M. L. *J. Med. Chem.* **1996**, *39*, 2773−2780. (j) Tsuchiya, H.; Shimizu, H.; Iinuma, M. *Chem. Pharm. Bull.* **1999**, *47*, 440−443. (k) Ishida, J.; Wang, H.-K.; Bastow, K. F.; Hu, C.-Q.; Lee, K.-H. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3319−3324.

(8) For reviews, see: (a) Gribble, G. W. In *The Alkaloids*; Brossi, A., Ed.; Academic: San Diego, 1990; Vol. 39, Chapter 7. (b) Tan, G. T.; Pezzuto, J. M. In *Chemistry and Toxicology of Diverse Classes of Alkaloids*; Blum, M. S., Ed.; Alaken, Inc.: 1996; pp 1−119. For recent reports, see: (c) Nguyen, C. H.; Lavelle, F.; Riou, J.-F.; Bissery, M.-C.; Huel, C.; Bisagni, E. *Anti-Cancer Drug Design* **1992**, *7*, 235−251. (d) Guillonneau, C.; Pierré, A.; Charton, Y.; Guilbaud, N.; Kraus-Berthier, L.; Léonce, S.; Michel, A.; Bisagni, E.; Atassi, G. *J. Med. Chem.* **1999**, *42*, 2191−2203, and references therein.

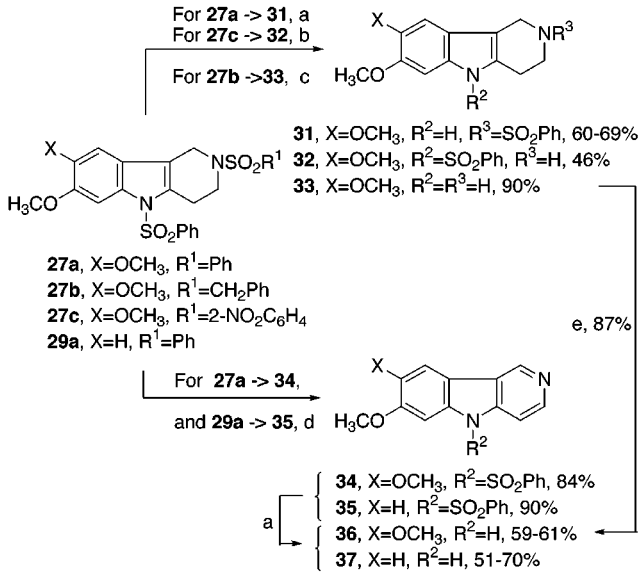
(9) Barbot, F.; Miginiac, P. *Helv. Chim. Acta* **1979**, *62*, 1451−1457.

Scheme 3[a]



[a] Reagents and conditions: a, MeI, K_2CO_3, acetone, reflux; b, Tf_2O, py, −78 °C → warm (see Experimental Section), c, $[Pd(OAc)_2]_3$, 1,1′-bis(diphenylphosphino)ferrocene, Et_3N/HO_2CH, DMF, 90 °C.

Scheme 4[a]

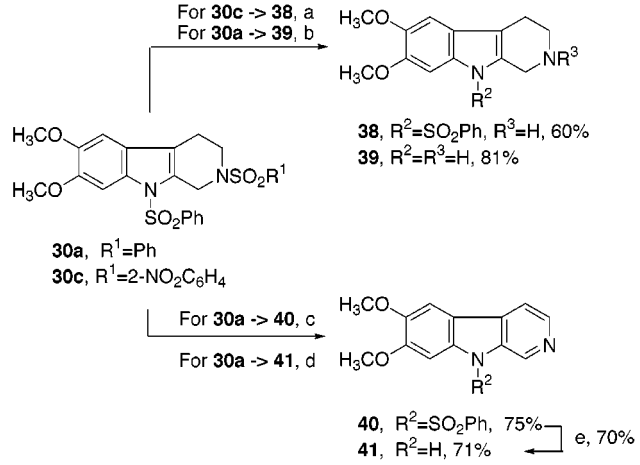


[a] Reagents and conditions: a, K_2CO_3, MeOH/THF, reflux, or RedAl, THF, rt; b, $HSCH_2CO_2H$, LiOH, DMF, rt; c, Na, NH_3; d, SeO_2, dioxane, reflux; e, Pd/C, mesitylene, reflux.

only a few of the possible permutations of these selective desulfonylations have been explored with the various adducts,[13] the reactions presently described do demonstrate the potential for selective manipulation of the different *N*-sulfonyl groups and thus expand the versatility of **27**−**30** as intermediates for specific applications. As expected, removal of both *N*-sulfonyl moieties from **27b** and **30a** occurs with Na/NH_3, producing **33** and **39**, respectively.

A particularly noteworthy transformation found was

Scheme 5[a]



[a] Reagents and conditions: a, $HSCH_2CO_2H$, LiOH, DMF, rt; b, Na, NH_3; c, SeO_2, dioxane, reflux; d, KOtBu (10 equiv), THF, rt; e, K_2CO_3, MeOH/THF.

a direct oxidation/desulfonylation of the tetrahydrocarbolines **27a**/**29a** and **30a** with SeO_2 to produce the carbolines **34**/**35** and **40** in good yields.[14] These reactions are a convenient way to access aromatized carbolines directly from the sulfonylated tetrahydrocarbolines. Desulfonylations of the indole nitrogens in the aromatized products also occur under mild conditions with K_2CO_3/MeOH and afford **36**/**37** and **41**. A double sulfonyl elimination of **30a** to **41** can be effected with excess KOtBu, and dehydrogenation of **33** to **36** also occurs upon heating with Pd/C.

To demonstrate the utility of this new carboline synthesis, we focused on the preparation of compounds

(10) For a general review of Lewis acid complexes with organic substrates, see: (a) Shambayati, S.; Schreiber, S. In *Comprehensive Organic Synthesis*, Vol. 1; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; p 283. For suggestions of carbonyl−(Lewis acid)$_2$ complexes as potential intermediates, see ref 2b and (b) Poll, T.; Metter, J. O.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 112. (c) Schultz, A. G.; Lee, H. *Tetrahedron Lett.* **1992**, *33*, 4397−4400. (d) Majetich, G.; Hull, K.; Casares, A. M.; Khetani, V. *J. Org. Chem.* **1991**, *56*, 3958−3973. (e) Snider, B. B.; Rodini, D. J.; van Straten, J. *J. Am. Chem. Soc.* **1980**, *102*, 5872. (f) Simard, M.; Vaugeois, J.; Wuest, J. D. *J. Am. Chem. Soc.* **1993**, *115*, 370−372. (g) Sharma, V.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1992**, *114*, 7931−7933. (h) Bachand, B.; Wuest, J. D.; *Organometallics* **1991**, *10*, 2015−2025 (and references cited in 10f−h). (i) Springer, J. B.; DeBoard, J.; Corcoran, R. C. *Tetrahedron Lett.* **1995**, *36*, 8733−8736. (j) Sato, M.; Aoyagi, S.; Yago, S.; Kibayashi, C. *Tetrahedron Lett.* **1996**, *37*, 9063−9066. (k) For examples, see 10e and references cited in 10f−h. (l) For selected discussions of $[C{=}O]_2$Lewis acid complexes, see: Turin, E.; Nielson, R. M.; Merbach, A. E. *Inorg. Chim. Acta* **1987**, *134*, 79−85, 67−78. (m) Kiyooka, S.-i.; Nakano, M.; Shiota, F.; Fujiyama, R. *J. Org. Chem.* **1989**, *54*, 5409−5411. (n) Denmark, S. E.; Almstead, N. G. *Tetrahedron* **1992**, *48*, 5565−5578. (o) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1993**, *115*, 3133−3139. (p) Walker, M. A.; Heathcock, C. H. *J. Org. Chem.* **1991**, *56*, 5747−5750. (q) Pellissier, H.; Toupet, L.; Santelli, M. *J. Org. Chem.* **1994**, *59*, 1709−1713 and references cited in 10a and 10i. (r) The complete structures of such complexes are unkown, and they may be mono- or oligomeric.

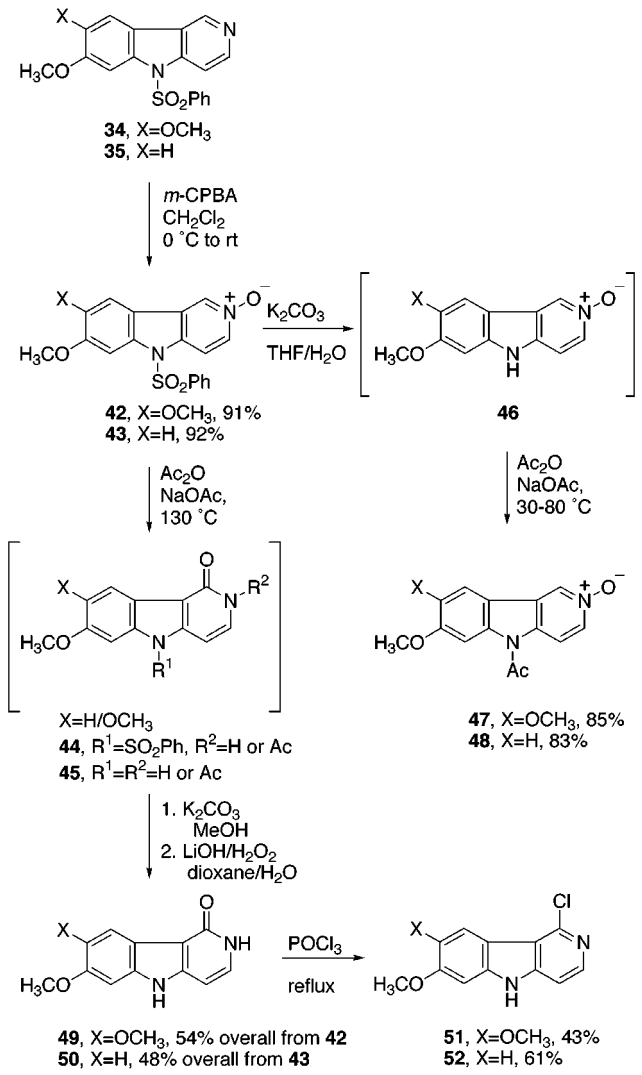
(11) Ti(IV)-promoted reactions of **1b** were not successful; we suspect that debenzylation is a complicating factor leading to degradation.

(12) (a) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373−6374. (b) Fukuyama, T.; Cheung, M.; Jow, C.-K.; Hidai, Y.; Kan, T. *Tetrahedron Lett.* **1997**, *38*, 5831−5834.

(13) For example, benzylsulfonamides have been reported to cleave under mild conditions, see: Larghi, E. L.; Kaufman, T. S. *Tetrahedron Lett.* **1997**, *38*, 3159−3162.

(14) Examples of SeO_2 oxidations of tetrahydrocarbolines to carbolines are known (see references that follow); however, to our knowledge this reaction has not been applied to *N*-sulfonyltetrahydrocarbolines. (a) Gatta, F.; Misiti, D. *J. Heterocycl. Chem.* **1987**, *24*, 1183−1187. (b) Lopez-Rodriguez, M. L.; Morcillo, J.; Gil, P. J.; Rosado, L.; Ventura, P. *Heterocycles* **1994**, *37*, 1053−1068. (c) Maki, Y.; Kimoto, H.; Fujii, S. *J. Fluorine Chem.* **1987**, *35*, 685−688.

Scheme 6



related to the antitumor agents **4** and **5**. SAR studies on the γ-carboline system **4** and the ellipticines/olivacines (**5**) and have been extensive.[8] These studies have established the importance of ring A oxygenation, particularly at C-8 and C-9, respectively, and also revealed that alkylamino groups at C-1 in both series led to improved DNA binding and antitumor properties. Initially a route to ring A oxygenated/C-1-amino carbolines via pyridones **49**/**50** and chlorocarbolines **51**/**52** was envisioned (Scheme 6). Bisagni has shown that pyridone moieties in similar systems can be converted in this way to the alkylaminopyridine unit found in **4**.[8c,15] Using the successful oxidation of the tetrahydrocarbolines **27a**/**29a** to fully the aromatized carbolines **34**/**35** as a guide, a number of attempts were made to oxidize **27a**, **31**, or **33** under conditions where one of the presumed intermediates might be trapped by water or the oxidant to form the pyridones directly.[16] Unfortunately, either little or no reaction was observed or complex mixtures were obtained with much apparent degradation.[17] However, oxidations of **34** and **35** with MCPBA provided *N*-oxides **42** and **43** cleanly (Scheme 6), and efforts to convert these *N*-oxides to lactams were explored.

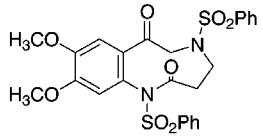
Rearrangement of *N*-oxides **42**/**43** in refluxing acetic anhydride at 130 °C led to the formation of complex mixtures of **44**/**45** which were difficult to separate. In an effort to obtain cleaner reactions, the phenylsulfonyl groups were removed from **42**/**43** with K_2CO_3 in THF/H_2O, affording *N*-oxides **46** as white solids, which rapidly colorized when open to air. Thus, these oxides were prepared and used immediately in subsequent experiments. Reactions with acetic anhydride carried out at 30−80 °C yielded acetylated *N*-oxides **47**/**48** as the sole products. Rearrangement reactions carried out in refluxing acetic anhydride afforded again mixtures of the desired lactams **49**/**50** and their acetylated derivatives **45**. Eventually a reaction protocol was developed that effected deacetylation and desulfonylation of the product(s) as part of the workup. Thus, the crude reaction mixtures from the acetic anhydride rearrangements of **42** and **43** were treated with potassium carbonate/MeOH to remove any remaining *N*-phenylsulfonyl groups, and $LiOH/H_2O_2$[18] was then employed to remove any remaining acetyl groups. Lactams **49**/**50** were obtained in 54% and 48% overall yields, respectively.

Lactams **49**/**50** could be converted to the chlorocarbolines **51**/**52** by treatment with hot $POCl_3$, and **51** did undergo displacement with *N*,*N*-dimethyl-1,3-diaminopropane to afford the desired aminocarboline in 46% yield; however, we sought an overall more efficient route.[19] We found that reactions of the sulfonylated *N*-oxides **42**/**43** with $POCl_3$ produced chlorocarbolines **53**/**54** directly and regioselectively in good yield (Scheme 7).[20] This result suggested a direct synthesis of the desired products **55**/**56** via concomitant chloride displacement and desulfonylation. Thus, treatment of **53**/**54** with *N*,*N*-

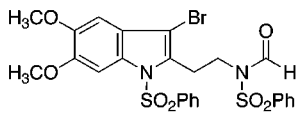
(15) (a) Bisagni, E.; Nguyen, C. H.; Pierré, A.; Pépin, O.; Cointet de, P.; Gros, P. *J. Med. Chem.* **1988**, *31*, 398−405. (b) Nguyen, C. H.; Bisagni, E. *Tetrahedron* **1986**, *42*, 2303−2309. (c) Nguyen, C. H.; Bisagni, E. *Tetrahedron* **1986**, *42*, 2311−2318. (d) Nguyen, C. H.; Bisagni, E. *Tetrahedron* **1987**, *43*, 527−535. See also: (e) Harada, K.; Someya, H.; Zen, S. *Heterocycles* **1994**, *38*, 1867−1880.

(16) Among the oxidants examined for **27a** were $(py)_2CrO_3$, PCC, TPAP/NMO, $Hg(OAc)_2$, $Cr(CO)_6$/tBuOOH,[16a] and $KMnO_4$/18-crown-6[16b] or Et_3NBnCl.[16c] Reaction with aqueous $RuO_2/NaIO_4$[16d] produced small amounts of **A** (by TLC). Attempts to oxidize **33** were made with MnO_2,[16e] $(COCl)_2$/DMSO,[16f] and NaOCl/NaOMe.[16g] One attempt to oxidize **31** with aqueous DDQ[16h] was made without success. For examples of similar oxidations, see: (a) Pearson, A. J.; Chen, Y.-S.; Han, G. R.; Hsu, S.-Y.; Ray, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 267−273. Pearson, A. J.; Han, G. R. *J. Org. Chem.* **1985**, *50*, 2791−2792. (b) Venkov, A. P.; Statkova-Abeghe, S. M. *Tetrahedron* **1996**, *52*, 1451−1460. (c) Markgraf, J. H.; Sangani, P. K.; Finkelstein, M. *Synth. Commun.* **1997**, *27*, 1285−1290. (d) Perrone, R.; Bettoni, G.; Tortella, V. *Synthesis* **1976**, 598−600. (e) Sanmartin, R.; Martinez de Marigorta, E.; Moreno, I.; Dominguez, E. *Heterocycles* **1997**, *45*, 757−763. (f) Keirs, D.; Overton, K. *J. Chem. Soc., Chem. Commun.* **1987**, 1660−1661. (g) Hanquet, G.; Lusinchi, X.; Milliet, P. *Tetrahedron* **1993**, *49*, 423−438. (h) Oikawa, Y.; Yonemitsu, O. *J. Org. Chem.* **1977**, *42*, 1213−1216.

(17) Reactions with CrO_3 (3 equiv)/HOAc in EtOAc[17a] and NBS (1−5 equiv)/AIBN/hν[17b] produced modest quantities of **A**[17c] and **B** (10−20% and 28−36%, respectively). (a) Burnham, J. W.; Duncan, W. P.; Eisenbraun, E. J.; Keen, G. W.; Hamming, M. C. *J. Org. Chem.* **1974**, *39*, 1416−1420. (b) Stanley, A. L.; Stanforth, S. P. *J. Heterocycl. Chem.* **1995**, *32*, 569−571. (c) Similar ring-opening oxidations of indoles are known, see: Witkop, B.; Patrick, J. B. *J. Am. Chem. Soc.* **1950**, *72*, 633−634. Witkop, B.; Patrick, J. B. *J. Am. Chem. Soc.* **1951**, *73*, 2196−2200. Experimental procedures and spectral data for **A**/**B** are included in the Supporting Information.



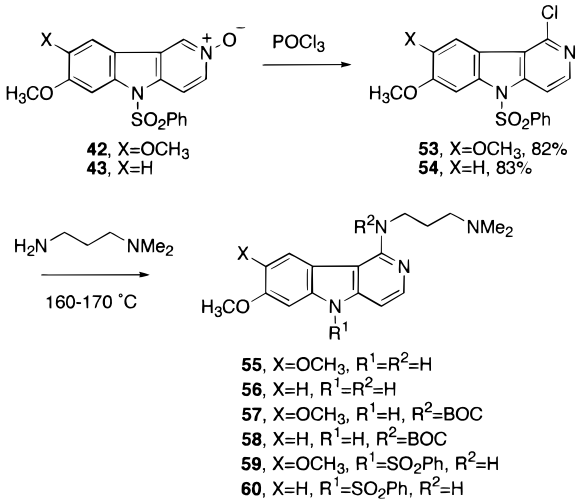
A



B

(18) Evans, D. A.; Britton, T. C.; Ellman, J. A. *Tetrahedron Lett.* **1987**, *28*, 6141−6144.

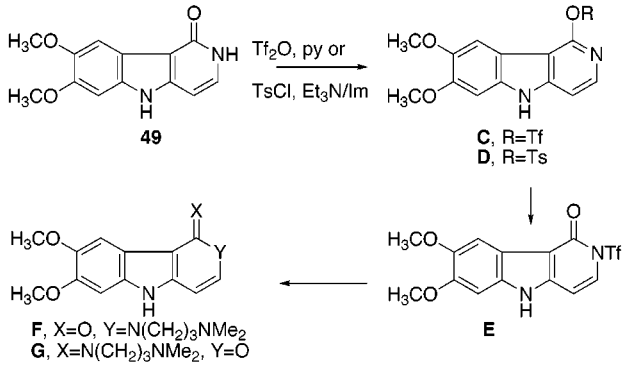
Scheme 7



dimethyl-1,3-propanediamine at 160−170 °C afforded the diamines **55**/**56** of about 70% purity by ^{1}H NMR. Chromatography of these products was difficult, so they were converted to their BOC derivatives **57**/**58**, which were easily chromatographed, and the BOC groups were then removed under mild conditions. Pure **55**/**56** were obtained in 31% and 53% overall yields from **53** and **54**, respectively. Finally it is noted that reactions of the chlorocarbolines **53**/**54** at lower temperatures (130 °C) produced mixtures of **55**/**56**, accompanied by sulfonylated products **59**/**60**.

In summary, a new route to oxygenated carboline platforms is detailed. The process involves a Lewis acid-directed cyclocondensation of piperidone enol ethers with 2-methoxy-4-(*N*-phenylsulfonyl)-1,4-benzoquinoneimine. These reactions demonstrate the versatility of this new indole synthesis and further extend the synthetic scope of Lewis acid-directed reactions of benzoquinones and imine derivatives. In addition, a number of transformations of the cycloadducts are described that lay the groundwork for other specific applications.

(19) Conversion of lactam **49** to triflate **C** was explored in anticipation that displacement of the triflate with amines could be effected under conditions milder than those required for chloride displacement. Triflate **C** was formed upon treatment of **49** with Tf_2O/py; however, it was quite a sensitive species. Upon standing at room temperature, **C** rearranged to a new compound whose spectral data were consistent with those of structure **E**. Treatment of **C** with *N*,*N*-1,3-propanediamine at room temperature produced only original lactam **49**; a result also found with the tosyl derivative **D**. At higher temperatures, reaction of **C** with *N*,*N*-dimethyl-1,3-propanediamine unexpectedly produced a product possessing the molecular formula $C_{18}H_{23}O_3N_3$ rather than the expected $C_{18}H_{23}O_2N_4$. Spectral data for this compound are consistent with either lactam **F** or imino-pyran **G**. We rationalize that the mechanism by which **F**/**G** arises first involves rearrangement of **C** to **E** followed by attack of the diamine on the carbonyl group and collapse of the tetrahedral intermediate to a ring-opened intermediate. Tautomerization followed by ring closure completes the process. Further experiments along these lines were abandoned in favor of the shorter, less laborious route shown in Scheme 7. Experimental details for the preparation of **C**−**F**/**G** and spectral data are included in the Supporting Information.



(20) Lee, C.-S.; Ohta, T.; Shudo, K.; Okamoto, T. *Heterocylces* **1981**, *16*, 1081−1084.

Experimental Section

General. All reactions were done in flame-dried glassware under an atmosphere of argon or nitrogen with magnetic stirring. Thin-layer chromatography (TLC) was done on precoated silica plates (Art. 5715, Merck) containing a 254 nm fluorescent indicator and developed in the indicated solvent systems. Visualization was effected with a UV lamp and/or by staining with either *p*-anisaldehyde/H_2SO_4 or phosphomolybdic acid solutions. Chromatography refers to flash chromatography on silica gel, unless stated otherwise. NMR spectra were recorded at room temperature in deuteriochloroform and referenced to tetramethylsilane (TMS) or residual $CHCl_3$ unless specified otherwise.

Sulfonyl-4-piperidones 6a−c. Benzenesulfonyl chloride (5 mL, 39 mmol) was added to a slurry of K_2CO_3 (8.9 g, 64 mmol) and 4-piperidone monohydrate hydrochloride (3.8 g, 25 mmol) in H_2O (30 mL)/$CHCl_3$ (30 mL). The reaction mixture was stirred at room temperature for 10 h, and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The aqueous layer was separated and extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (EtOAc/hexanes 3/2) afforded **6a** (5.6 g, 95%) as a white solid, mp 117.5−118.5 °C (CH_2Cl_2/hexanes): TLC R_f 0.26 (EtOAc/hexanes 2/3); ^{1}H NMR (400 MHz) 7.82 (br d, 2H, J = 8, <2), 7.65 (br t, 1 H, J = 8, <2), 7.57 (br t, 2H, J = 8, <2), 3.42 (t, 4H, J = 6), 2.55 (t, 4H, J = 6); ^{13}C NMR (100 MHz) 205.2, 136.4, 133.2, 129.3, 127.4, 45.8, 40.6; FABMS *m*/*z* 240 (M + H$^+$); HRMS *m*/*z* 240.0704 (M + H$^+$) (calcd for $C_{11}H_{14}O_3NS$, 240.0694).

Similarly prepared were **6b** and **6c**; **6b** (95%) was isolated by recrystallization of the crude reaction mixture after workup, and **6c** (88%) was obtained by chromatography.

Physical and spectral data for **6b**: a white solid, mp 172−173 °C (CH_2Cl_2/hexanes); TLC R_f 0.21 (EtOAc/hexanes 2/3); ^{1}H NMR (400 MHz) 7.41 (s, 5H), 4.32 (s, 2H), 3.39 (t, 4H, J = 6), 2.42 (t, 4H, J = 6); ^{13}C NMR (100 MHz) 206.3, 130.9, 129.5, 129.4, 129.1, 58.9, 46.1, 42.2; FABMS *m*/*z* 254 (M + H$^+$); HRMS *m*/*z* 254.0878 (M + H$^+$) (calcd for $C_{12}H_{16}O_3NS$, 254.0851).

Physical and spectral data for **6c**: a white solid, mp 121−122 °C (CH_2Cl_2/hexanes); TLC R_f 0.34 (EtOAc/hexanes 3/2); ^{1}H NMR (400 MHz) 8.11−8.08 (m, 1H), 7.78−7.69 (m, 3H), 3.69 (t, 4H, J = 6), 2.60 (t, 4H, J = 6); ^{13}C NMR (100 MHz) 205.8, 148.5, 134.5, 132.5, 132.3, 131.4, 124.8, 45.9, 41.6; FABMS *m*/*z* 285 (M + H$^+$); HRMS *m*/*z* 285.0544 (M + H$^+$) (calcd for $C_{11}H_{13}O_5N_2S$, 285.0545).

Sulfonyl-3-piperidones 8a−c. 2-Nitrobenzenesulfonyl chloride (10.0 g, 45 mmol) was added to a slurry of K_2CO_3 (14.7 g, 0.1 mol) and 3-hydroxypiperidine hydrochloride (5.6 g, 41 mmol) in H_2O (50 mL)/$CHCl_3$ (50 mL). The reaction mixture was stirred at room temperature for 10 h, and then the reaction was quenched by the addition of saturated aqueous sodium $NaHCO_3$. The aqueous layer was separated and extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. The resultant alcohol was dissolved in acetone, and Jones reagent was added until the reaction mixture stayed orange and no alcohol was detectable by TLC analysis. Water was added, and the reaction mixture was extracted with Et_2O (5×). The combined organic extracts were washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Chromatography (EtOAc/hexanes 1/9 to 3/7) afforded **8c** (10.2 g, 88%) as a white solid, mp 86−87.5 °C (CH_2Cl_2/hexanes): TLC R_f 0.25 (EtOAc/hexanes 3/2); ^{1}H NMR (400 MHz) 8.05−8.02 (m, 1H), 7.78−7.66 (m, 3H), 3.89 (s, 2H), 3.60 (t, 2H, J = 6), 2.50 (t, 2H, J = 6), 2.08 (apparent quintet, 2H, J = 6); ^{13}C NMR (100 MHz) 202.2,

147.9, 133.8, 131.5, 131.0, 130.9, 124.1, 54.6, 43.9, 37.6, 22.6; FABMS *m/z* 285 ($M + H^+$); HRMS *m/z* 285.0551 ($M + H^+$) (calcd for $C_{11}H_{13}O_5N_2S$, 285.0545).

Similarly prepared were **8a** (74%) and **8b** (83%); both were isolated by chromatography (EtOAc/hexanes 3/7).

Physical and spectral data for **8a**: a white solid, mp 85−86 °C (CH_2Cl_2/hexanes); TLC R_f 0.40 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 7.80 (d, 2H, $J = 7$), 7.65 (t, 1H, $J = 7$), 7.59 (t, 2H, $J = 7$), 3.64 (s, 2H), 3.33 (t, 2H, $J = 6$), 2.40 (t, 2H, $J = 6$), 2.04 (apparent quintet, 2H, $J = 6$); ^{13}C NMR (100 MHz) 202.9, 136.2, 133.7, 129.8, 128.1, 56.1, 44.9, 38.4, 23.1; FABMS *m/z* 240 ($M + H^+$); HRMS *m/z* 240.0694 ($M + H^+$) (calcd for $C_{11}H_{14}O_3NS$, 240.0694).

Physical and spectral data for **8b**: a white solid, mp 128−129 °C (CH_2Cl_2/hexanes); TLC R_f 0.19 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 7.41 (s, 5H), 4.29 (s, 2H), 3.62 (s, 2H), 3.33 (t, 2H, $J = 6$), 2.42 (t, 2H, $J = 6$), 1.90 (apparent quintet, 2H, $J = 6$); ^{13}C NMR (100 MHz) 203.3, 131.0, 129.5, 129.4, 129.0, 58.2, 55.9, 44.9, 38.4, 23.8; FABMS *m/z* 254 ($M + H^+$); HRMS *m/z* 254.0836 ($M + H^+$) (calcd for $C_{12}H_{16}O_3NS$, 254.0851).

Piperidone Methyl Enol Ethers 7a−c and 9a−c. A solution of ketone **6a** (2.87 g, 12 mmol) was dissolved in trimethyl orthoformate (30 mL), and a small amount of *p*-TsOH·H_2O was added. The reaction mixture was stirred until no starting material was detectable by TLC analysis (∼5 h), and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The aqueous layer was separated and extracted with Et_2O (4×), and the combined organic extracts were dried (Na_2SO_4) and concentrated to yield the crude dimethyl ketal (2.97 g, 87%). This product (2.65 g, 9.5 mmol) was dissolved in Et_2O (80 mL) and added to a slurry of $AlCl_3$ (2.45 g, 18.8 mmol) and Et_3N (5.5 mL, 40 mmol) in Et_2O (20 mL). The reaction mixture was again stirred at room temperature until no dimethyl ketal was detectable by TLC analysis (∼72 h) and then decanted onto 5 N NaOH (100−200 mL). The aqueous layer was separated and extracted with Et_2O (3×), and the combined extracts were dried (Na_2SO_4) and concentrated to give **7a** (1.68 g, 71%) as a white solid, mp 67.5−68 °C (CH_2Cl_2/hexanes): TLC R_f 0.37 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 7.82 (br d, 2H, $J = 8$, <2), 7.61 (br t, 1 H, $J = 8$, <2), 7.55 (br t, 2H, $J = 8$, <2), 4.53 (t, 1H, $J = 3$), 3.68 (m, 2H), 3.50 (s, 3H), 3.28 (t, 2H, $J = 6$), 2.26 (br t, 2H, $J = 6$); ^{13}C NMR (100 MHz) 154.0, 137.1, 133.1, 129.4, 128.0, 89.7, 54.7, 44.1, 43.4, 28.3; FABMS *m/z* 254 ($M + H^+$); HRMS *m/z* 254.0843 ($M + H^+$) (calcd for $C_{12}H_{16}O_3NS$, 254.0851). This material was used in subsequent reactions without further purification.

Similarly prepared were **7b** (62%), **7c**, (64%), **9a** (78%), **9b** (59%), and **9c** (62%); in these reactions, the formation of the ketals required ∼10 h, and the elimination reactions took 12−48 h. Physical and spectral properties for these compounds follow.

7b: a white solid, mp 117−118 °C (CH_2Cl_2/hexanes); TLC R_f 0.45 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 7.41−7.37 (m, 5H), 4.52 (t, 1H, $J = 3$), 4.25 (s, 2H), 3.75 (m, 2H), 3.52 (s, 3H), 3.26 (t, 2H, $J = 6$), 2.09 (br t, 2H, $J = 6$); ^{13}C NMR (100 MHz) 154.3, 131.1, 129.4, 129.13, 129.11, 90.4, 57.7, 54.7, 43.9, 43.2, 28.6; FABMS *m/z* 267 (M^+); HRMS *m/z* 268.1003 ($M + H^+$) (calcd for $C_{13}H_{18}O_3NS$, 268.1007).

7c: a white solid, mp 145.5−146.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.36 (EtOAc/hexanes 3/2); ^1H NMR (400 MHz) 8.02−8.00 (m, 1H), 7.73−7.62 (m, 3H), 4.59 (br t, 1H), 3.90 (m, 2H), 3.53 (s, 3H) overlapping with 3.53 (t, 2H, $J = 6$), 2.29 (br t, 2H, $J = 6$); ^{13}C NMR (100 MHz) 154.2, 148.7, 134.0, 132.4, 132.0, 131.2, 124.5, 89.9, 54.8, 43.9, 43.3, 28.4; HRMS *m/z* 298.0626 (M^+) (calcd for $C_{12}H_{14}O_5N_2S$, 298.0623).

9a, as a 4:1 mixture with its 2,3 double bond isomer: TLC R_f 0.51 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 7.81−7.75 (m, 2H), 7.65−7.50 (m, 3H), 4.64 (t, 1H, $J = 4$), 3.52 (m, 2H), 3.49 (s, 3H), 3.14 (t, 2H, $J = 6$), 2.24−2.19 (m, 2H); ^{13}C NMR (125 MHz, 1 aromatic carbon is not apparent) 150.7, 132.8, 129.0, 127.6, 91.2, 54.3, 45.6, 43.2, 23.0; FABMS *m/z* 254 ($M + H^+$); HRMS *m/z* 254.0840 ($M + H^+$) (calcd for $C_{12}H_{16}O_3NS$, 254.0851).

9b, as a 12:1 mixture with its 2,3 double bond isomer: TLC R_f 0.40 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 7.43−7.38 (m, 5H), 4.70 (t, 1H, $J = 4$), 4.28 (s, 2H), 3.60 (m, 2H), 3.53 (s, 3H), 3.18 (t, 2H, $J = 6$), 2.16−2.10 (m, 2H); ^{13}C NMR (125 MHz, 1 aromatic carbon is not apparent) 151.6, 131.1, 129.14, 129.11, 92.0, 57.8, 54.7, 45.8, 43.7, 24.0; FABMS *m/z* 268 ($M + H^+$); HRMS *m/z* 268.0983 ($M + H^+$) (calcd for $C_{13}H_{18}O_3NS$, 268.1007).

9c, as a 4:1 mixture with its 2,3 double bond isomer: TLC R_f 0.48 (EtOAc/hexanes 2/3); ^1H NMR (400 MHz) 8.02−8.00 (m, 1H), 7.74−7.58 (m, 3H), 4.74 (t, 1H, $J = 4$), 3.76 (m, 2H), 3.54 (s, 3H), 3.43 (t, 2H, $J = 6$), 2.29−2.24 (m, 2H); ^{13}C NMR (125 MHz, 1 aromatic carbon is not apparent) 150.7, 147.3, 133.6, 131.5, 130.8, 124.1, 91.5, 54.4, 45.2, 43.2, 23.2; FABMS *m/z* 298 (M^+); HRMS *m/z* 299.0712 ($M + H^+$) (calcd for $C_{12}H_{15}O_5N_2S$, 299.0702).

General Procedure A: BF_3·Et_2O-Promoted Reactions of Enol Ethers 7 and 9 with Mono- and Diimines 1 and 24. BF_3·Et_2O was added to a solution of the imine in CH_2Cl_2 maintained at −78 °C, followed, after 5−10 min, by the enol ether as a solution in CH_2Cl_2. The reaction mixture was allowed to warm to room temperature and stirred until no starting material was detected by TLC (∼10 h), unless specified otherwise, and then the reaction was quenched with saturated aqueous NH_4Cl. In reactions of **7**, the resulting mixture was stirred for 15−30 min, and the aqueous layer was then separated and extracted with CH_2Cl_2 (3×). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated, and the residue was purified by chromatography to give benzofurans as the only products. In reactions with **9**, the elimination of MeOH was slow in some cases, and 2-methoxydihydrobenzofurans could be isolated. To obtain the benzofurans as the sole products, the reaction mixtures after quenching were stirred until no 2-methoxydihydrobenzofuran was detectable by TLC analysis; the aqueous layers were then separated and extracted with CH_2Cl_2 (3×). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated, and the residues were purified by chromatography.

General Procedure B: Ti(IV)-Promoted Reactions of Enol Ethers 7 and 9 with Mono- and Diimines 1 and 24. $TiCl_4$ was added to a solution of $Ti(OiPr)_4$ in CH_2Cl_2 at 0 °C. The resultant solution was stirred for 10−15 min, allowed to warm to room temperature, and then transferred via syringe to a solution of the imine in CH_2Cl_2 maintained at −78 °C. After 5−10 min, the enol ether was added as a solution in CH_2Cl_2. The reaction mixture was allowed to warm to room temperature over ∼10 h, unless specified otherwise, and then the reaction was quenched with saturated aqueous NH_4Cl. The resulting mixture was stirred for 30 min and filtered through Celite. The aqueous layer was separated and extracted with CH_2Cl_2 (3×). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by chromatography and/or recrystallization.

***N*-(2-Benzenesulfonyl-6-methoxy-1,2,3,4-tetrahydrobenzo[4,5]furo[3,2-*c*]pyridin-8-yl)benzenesulfonamide (10a).** According to general procedure A, BF_3·Et_2O (54 μL, 0.44 mmol) was added to a solution of monoimine **1a** (121 mg, 0.44 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7a** (121 mg, 0.44 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **10a** (141 mg, 65%) as a colorless solid, mp 192−192.5 °C (CH_2Cl_2/hexanes): TLC R_f 0.15 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^1H NMR (400 MHz) 7.88−7.86 (m, 2H), 7.77−7.75 (m, 2H), 7.65−7.42 (m, 6H), 6.82 (br s, 1H), 6.71 (d, 1H, $J = 2$), 6.53 (d, 1H, $J = 2$), 4.22 (br s, 2H), 3.87 (s, 3H), 3.55 (t, 2H, $J = 6$), 2.90 (br t, 2H, $J = 6$); ^{13}C NMR (125 MHz) 152.0, 145.0, 141.8, 138.7, 136.8, 133.03, 133.01, 132.1, 129.3, 129.0, 127.6, 127.4, 127.3, 110.1, 105.5, 103.1, 56.2, 43.3, 42.3, 24.1. Anal. Calcd for $C_{24}H_{22}O_6S_2N_2$: C, 57.81; H, 4.45; N, 5.62. Found: C, 57.42; H, 4.80; N, 5.28.

In another experiment according to general procedure A, BF_3·Et_2O (73 μL, 0.59 mmol) was added to a solution of monoimine **1a** (83 mg, 0.30 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7a** (78 mg, 0.31 mmol)

in CH_2Cl_2 (2 mL). After warming to room temperature over 10 h, workup and chromatography (CH_2Cl_2/Et_2O/hexanes 3/3/4) afforded **10a** (115 mg, 77%) as a colorless solid.

***N*-(2-Benzenesulfonylmethyl-6-methoxy-1,2,3,4-tetrahydrobenzo[4,5]furo[3,2-*c*]pyridin-8-yl)benzenesulfonamide (10b).** According to general procedure A, BF_3·Et_2O (65 μL, 0.53 mmol) was added to a solution of monoimine **1a** (139 mg, 0.50 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7b** (136 mg, 0.51 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (EtOAc/hexanes 3/7) afforded **10b** (218 mg, 85%) as a white solid, mp 177−178 °C (CH_2Cl_2/hexanes): TLC R_f 0.37 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 7.77 (d, 2H, J = 7), 7.57 (t, 1H, J = 7), 7.46 (t, 2H, J = 7), 7.38−7.32 (m, 5H), 6.76 (br s, 1H), 6.60 (d, 1H, J = 2), 6.56 (d, 1H, J = 2), 4.32 (s, 2H), 4.23 (br s, 2H), 3.90 (s, 3H), 3.48 (t, 2H, J = 6), 2.69 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 152.3, 145.0, 141.7, 138.8, 133.0, 132.1, 130.5, 129.0, 128.9, 128.8, 128.7, 127.4, 127.3, 110.5, 105.5, 103.1, 58.1, 56.2, 43.2, 42.1, 24.6; HRMS m/z 512.1081 (M^+) (calcd for $C_{25}H_{24}O_6S_2N_2$, 512.1076).

***N*-[6-Methoxy-2-(2-nitrobenzenesulfonyl-1,2,3,4-tetrahydrobenzo[4,5]furo[3,2-*c*]pyridin-8-yl)benzenesulfonamide (10c).** According to general procedure A, BF_3·Et_2O (40 μL, 0.33 mmol) was added to a solution of monoimine **1a** (86 mg, 0.31 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7c** (93 mg, 0.31 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (EtOAc/hexanes 3/7 to 1/1) afforded **10c** (120 mg, 71%) as a white solid: mp 186−188 °C (CH_2Cl_2/hexanes); TLC R_f 0.19 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 8.10−8.07 (m, 1H), 7.77 (d, 2H, J = 7), 7.76−7.71 (m, 2H), 7.66−763 (m, 1H), 7.53 (t, 1H, J = 7), 7.42 (t, 2H, J = 7), 7.32 (s, 1H), 6.75 (d, 1H, J = 2), 6.56 (d, 1H, J = 2), 4.43 (br s, 2H), 3.84 (s, 3H), 3.77 (t, 2H, J = 6), 2.90 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 152.0, 147.9, 144.9, 141.6, 138.5, 133.9, 133.0, 132.3, 132.0, 131.9, 130.8, 129.0, 127.4, 127.2, 124.3, 110.2, 105.3, 102.9, 56.1, 43.2, 42.1, 24.2; HRMS m/z 543.0774 (M^+) (calcd for $C_{24}H_{21}O_8S_2N_3$, 543.0770).

***N*-(2-Benzenesulfonyl-6-benzyloxy-1,2,3,4-tetrahydrobenzo[4,5]furo[3,2-*c*]pyridin-8-yl)benzenesulfonamide (11a).** According to general procedure A, BF_3·Et_2O (32 μL, 0.26 mmol) was added to a solution of monoimine **1b** (92 mg, 0.26 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7a** (67 mg, 0.26 mmol) in CH_2Cl_2 (1 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **11a** (99 mg, 66%) as a white solid: mp 113−114 °C (CH_2Cl_2/hexanes); TLC R_f 0.50 (EtOAc/hexanes 3/2); ^{1}H NMR (400 MHz) 7.86−7.84 (m, 2H), 7.64−7.32 (m, 13H), 6.64 (d, 1H, J = 2), 6.60 (d, 1H, J = 2), 6.50 (br s, 1H), 5.14 (s, 2H), 4.19 (br s, 2H), 3.53 (t, 2H, J = 6), 2.89 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 152.1, 144.0, 142.1, 138.6, 136.9, 136.1, 133.1, 133.0, 132.1, 129.3, 129.0, 128.7, 128.3, 127.9, 127.6, 127.5, 127.2, 110.1, 105.5, 104.7, 71.0, 43.3, 42.3, 24.3. Anal. Calcd for $C_{30}H_{26}O_6S_2N_2$: C, 62.70; H, 4.56; N, 4.88. Found: C, 62.50; H, 4.80; N, 4.70.

2,5-Bis-benzenesulfonyl-8-hydroxy-7-methoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (12a). According to general procedure B, a mixture of $TiCl_4$ (1.19 mL, 10.8 mmol) and $Ti(OiPr)_4$ (3.24 mL, 10.9 mmol) in CH_2Cl_2 (3.5 mL) was added to a solution of monoimine **1a** (1.41 g, 5.1 mmol) in CH_2Cl_2 (5 mL) at −78 °C, followed by a solution of enol ether **7a** (1.28 g, 5.1 mmol) in CH_2Cl_2 (5 mL). Workup and chromatography (EtOAc/hexanes 1/9 to 3/7) afforded **12a** (1.89 g, 82%) as a white solid: mp 187.5−188 °C (CH_2Cl_2/hexanes); TLC R_f 0.19 (EtOAc/hexanes 2/3); ^{1}H NMR (400 MHz) 7.87−7.85 (m, 2H), 7.70 (s, 1H), 7.69−7.41 (m, 8H), 6.79 (s, 1H), 5.62 (s, 1H), 4.16 (br s, 2H), 4.00 (s, 3H), 3.44 (t, 2H, J = 6), 3.15 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 145.2, 143.4, 138.3, 136.3, 133.7, 132.8, 130.8, 129.9, 129.2, 129.0, 127.4, 125.9, 121.0, 114.7, 102.1, 97.8, 56.3, 43.4, 42.4, 25.1. Anal. Calcd for $C_{24}H_{22}O_6S_2N_2$: C, 57.81; H, 4.45; N, 5.62. Found: C, 57.53; H, 4.40; N, 5.38.

5-Benzenesulfonyl-8-hydroxy-7-methoxy-2-phenylmethanesulfonyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (12b). According to general procedure B, a mixture of $TiCl_4$ (1.33 mL, 12.2 mmol) and $Ti(OiPr)_4$ (3.62 mL, 12.2 mmol) in CH_2Cl_2 (10 mL) was added to a solution of monoimine **1a** (1.35 g, 4.87 mmol) in CH_2Cl_2 (10 mL) at −78 °C, followed by a solution of enol ether **7b** (1.30 g, 4.87 mmol) in CH_2Cl_2 (5 mL). Workup and chromatography (EtOAc/hexanes 1/9 to 3/7) afforded **12b** (2.13 g, 85%) as a colorless solid: mp 170−171.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.54 (EtOAc/hexanes 3/2); ^{1}H NMR (400 MHz) 7.71 (s, 1H) 7.69 (d, 2H, J = 8), 7.53 (t, 1H, J = 8), 7.42 (t, 2H, J = 8), 7.34−7.26 (m, 5 H), 6.68 (s, 1H), 5.64 (br s, 1H), 4.24 (s, 2H), 4.15 (br s, 2H), 3.99 (s, 3H), 3.42 (t, 2H, J = 6), 2.97 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 145.4, 143.6, 138.5, 133.9, 131.2, 130.5, 130.0, 129.4, 128.8, 128.77, 128.6, 126.1, 121.1, 115.3, 102.3, 98.0, 57.8, 56.5, 43.4, 42.5, 25.7; HRMS m/z 512.1063 (M^+) (calcd for $C_{25}H_{24}N_2O_6S_2$, 512.1076).

5-Benzenesulfonyl-8-hydroxy-7-methoxy-2-(2-nitrobenzensulfonyl)-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (12c). According to general procedure B, a mixture of $TiCl_4$ (0.28 mL, 2.5 mmol) and $Ti(OiPr)_4$ (0.77 mL, 2.6 mmol) in CH_2Cl_2 (2 mL) was added to a solution of monoimine **1a** (286 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7c** (309 mg, 1.0 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (EtOAc/hexanes 3/7) gave **12c** (436 mg, 78%) as a yellow solid: mp 183−184 °C (CH_2Cl_2/hexanes); TLC R_f 0.22 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 8.08−8.06 (m, 1H), 7.76−7.64 (m, 5H) overlapping with 7.71 (s, 1H), 7.56 (t, 1H, J = 8), 7.44 (t, 2H, J = 8), 6.83 (s, 1H), 5.65 (br s, 1H), 4.41 (br s, 2H), 4.01 (s, 3H), 3.69 (t, 2H, J = 6), 3.19 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 148.2, 145.4, 143.6, 138.4, 133.8, 133.78, 131.9, 131.7, 131.0, 130.9, 130.0, 129.3, 126.1, 124.2, 121.0, 114.9, 102.3, 98.0, 56.4, 43.4, 42.4, 25.3. Anal. Calcd for $C_{24}H_{21}O_8S_2N_3$: C, 53.03; H, 3.89; N, 7.73. Found: C, 52.83; H, 4.21; N, 7.77.

***N*-(2-Benzenesulfonyl-8-methoxy-1,2,3,4-tetrahydrobenzo[4,5]furo[2,3-*c*]pyridin-6-yl)benzenesulfonamide (13a).** According to general procedure A, BF_3·Et_2O (35 μL, 0.28 mmol) was added to a solution of monoimine **1a** (79 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9a** (92 mg, as a 4:1 mixture with its 2,3 double bond isomer, 0.36 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was quenched and stirred for 30 min. Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **13a** (97 mg, 68%) as a colorless solid: mp 178−179 °C (CH_2Cl_2/hexanes); TLC R_f 0.78 (EtOAc/hexanes 3/2); ^{1}H NMR (400 MHz) 7.84−7.82 (m, 2H), 7.71−7.68 (m, 2H), 7.58−7.40 (m, 6H), 6.65 (d, 1H, J = 2), 6.48 (d, 1H, J = 2), 6.34 (br s, 1H) 4.33 (br s, 2H), 3.86 (s, 3H), 3.47 (t, 2H, J = 6), 2.65 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 149.1, 145.1, 142.1, 138.8, 136.9, 133.1, 133.0, 132.0, 129.2, 128.94, 128.89, 127.4, 127.3, 112.1, 106.5, 103.6, 56.2, 43.51, 43.48, 21.0; HRMS m/z 498.0926 (M^+) (calcd for $C_{24}H_{22}O_6S_2N_2$, 498.0919).

***N*-(2-Benzenesulfonylmethyl-8-methoxy-1,2,3,4-tetrahydrobenzo[4,5]furo[2,3-*c*]pyridin-6-yl)benzenesulfonamide (13b).** According to general procedure A, BF_3·Et_2O (20 μL, 0.16 mmol) was added to a solution of monoimine **1a** (45 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9b** (44 mg, as a 12.3:1 mixture with its 2,3 double bond isomer, 0.16 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was quenched and stirred for 5−6 h. Workup, chromatography (EtOAc/hexanes 3/7), and recrystallization (CH_2Cl_2/hexanes) afforded **13b** (70 mg, 84%) as a white solid, mp 139.5−140.5 °C (CH_2Cl_2/hexanes): TLC R_f 0.29 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 7.76 (d, 2H, J = 7), 7.55 (t, 1H, J = 7), 7.44 (t, 2H, J = 7), 7.38−7.30 (m, 5H), 6.93 (br s, 1H), 6.71 (d, 1H, J = 2), 6.55 (d, 1H, J = 2), 4.31 (s, 2H), 4.22 (br s, 2H), 3.87 (s, 3H), 3.45 (t, 2H, J = 6), 2.50 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 149.2, 145.1, 141.8, 138.7, 133.0, 132.1, 130.6, 129.0, 128.97, 128.94, 128.8, 128.6, 127.3, 112.4, 106.1, 103.4, 58.4, 56.2, 43.5, 43.47, 21.6; HRMS m/z 512.1079 (M^+) (calcd for $C_{25}H_{24}O_6S_2N_2$, 512.1076).

In another experiment according to general procedure A, BF_3·Et_2O (31 μL, 0.25 mmol) was added to a solution of monoimine **1a** (69 mg, 0.25 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of methyl enol ether **9b** (74 mg, as a 12.3:1 mixture with its 2,3 double bond isomer, 0.27 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was quenched and stirred for 0.5−1 h. Workup and chromatography (EtOAc/

hexanes 3/7) afforded **18** (65 mg, 48%) as a white solid: mp 126−127 °C (CH_2Cl_2/hexanes); TLC R_f 0.22 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 7.72 (d, 2H, J = 7), 7.57 (t, 1H, J = 7), 7.46−7.30 (m, 7H), 6.58 (d, 1H, J = 2), 6.53 (br s, 1H), 6.39 (d, 1H, J = 2), 4.25 (d, 1H, J = 14), 4.10 (d, 1H, J = 14), 3.78 (s, 3H), 3.71 (d, 1H, J = 14), 3.50 (d, 1H, J = 14), 3.38 (s, 3H), 3.28 (t, 1H, J = 6), 3.22−3.17 (m, 1H), 2.85−2.78 (m, 1H), 2.08−2.02 (m, 1H), 1.61−1.51 (m, 1H); ^{13}C NMR (125 MHz) 144.7, 144.2, 138.6, 133.0, 130.7, 130.3, 129.7, 128.9, 128.89, 128.62, 128.6, 127.3, 112.3, 111.5, 109.1, 56.9, 56.2, 49.9, 46.0, 44.2, 41.1, 26.3; HRMS m/z 544.1339 (M^+) (calcd for $C_{26}H_{28}O_7S_2N_2$, 544.1338).

In a related experiment, treatment of a CH_2Cl_2 solution of **18** with p-TsOH·H_2O resulted in the formation of **13b** as observed by TLC.

The stereochemistry of the dihydrobenzofuran moiety was assigned by ^{1}H−^{1}H NOE experiments.

***N*-[8-Methoxy-2-(2-nitrobenzenesulfonyl)-1,2,3,4-tetrahydrobenzo[4,5]furo[2,3-*c*]pyridin-6-yl]benzenesulfonamide (13c).** According to general procedure A, BF_3·Et_2O (13 μL, 0.11 mmol) was added to a solution of monoimine **1a** (28 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9c** (40 mg, as a 3.6:1 mixture with its 2,3 double bond isomer, 0.13 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was quenched and stirred for 5−6 h. Workup and chromatography (EtOAc/hexanes 3/7 to 1/1) afforded **13c** (44 mg, 80%) as a white solid, mp 192−194 °C (CH_2Cl_2/hexanes): TLC R_f 0.21 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 8.10−8.08 (m, 1H), 7.75−7.67 (m, 5H), 7.56 (t, 1H, J = 7), 7.45 (t, 2H, J = 7), 6.72 (d, 1H, J = 2), 6.53 (d, 1H, J = 2) overlapping with 6.53 (s, 1H), 4.57 (br s, 2H), 3.89 (s, 3H), 3.71 (t, 2H, J = 6), 2.74 (br t, 2H, J = 6); ^{13}C NMR (125 MHz, 1 aromatic carbon is not observed) 149.0, 148.1, 145.2, 142.1, 138.8, 133.9, 133.0, 132.3, 132.0, 131.8, 130.9, 129.0, 127.3, 124.4, 112.4, 106.5, 103.7, 56.2, 43.6, 43.4, 21.3; HRMS m/z 543.0767 (M^+) (calcd for $C_{24}H_{21}O_8S_2N_3$, 543.0770).

In another experiment according to general procedure A, BF_3·Et_2O (25 μL, 0.20 mmol) was added to a solution of monoimine **1a** (50 mg, 0.18 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9c** (70 mg, as a 3.6:1 mixture with its 2,3 double bond isomer, 0.23 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was quenched and stirred for 3 h. Workup and chromatography (EtOAc/hexanes 3/7 to 1/1) afforded **13c** (32 mg, 33%) and **19** (36 mg, 35%) as white solids. Physical and spectral properties of **19**: TLC R_f 0.15 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 7.98−7.96 (m, 1H), 7.73−7.60 (m, 5H), 7.56 (t, 1H, J = 7), 7.45 (t, 2H, J = 7), 6.83 (br s, 1H), 6.51 (d, 1H, J = 2), 6.43 (d, 1H, J = 2), 3.80 (d, 1H, J = 14), 3.72 (s, 3H), 3.69 (d, 1H, J = 14), 3.42−3.34 (m, 2H), 3.38 (s, 3H), 3.10−3.04 (m, 1H), 2.20−2.14 (m, 1H), 1.76−1.71 (m, 1H); ^{13}C NMR (125 MHz) 148.1, 144.6, 144.1, 138.5, 133.5, 133.0, 131.9, 131.6, 130.9, 130.3, 129.3, 128.9, 127.3, 124.0, 112.1, 111.4, 109.2, 56.1, 50.0, 45.9, 44.0, 40.9, 25.8; HRMS m/z 575.1055 (M^+) (calcd for $C_{25}H_{25}O_9S_2N_3$, 575.1032).

The stereochemistry in **19** was assigned by analogy to **18**.

***N*-(2-Benzenesulfonyl-8-benzyloxy-9a-methoxy-1,2,3,4,-4a,9a-hexahydrobenzo[4,5]furo[2,3-*c*]pyridin-6-yl)benzenesulfonamide (20) and *N*-(2-Benzenesulfonyl-8-benzyloxy-1,2,3,4-tetrahydrobenzo[4,5]furo[2,3-*c*]pyridin-6-yl)benzenesulfonamide (14a).** According to general procedure A, BF_3·Et_2O (21 μL, 0.17 mmol) was added to a solution of monoimine **1b** (59 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of methyl enol ether **9a** (51 mg, as a 4.7:1 mixture with its 2,3 double bond isomer, 0.20 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was quenched and stirred for 2 h. Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **14a** (28 mg, 29%) and **20** (31 mg, 31%) as white solids. Physical and spectral properties of **14a**: mp 135−136 °C (CH_2Cl_2/hexanes); TLC R_f 0.17 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.89−7.87 (m, 2H), 7.67−7.38 (m, 13H), 6.68 (d, 1H, J = 2), 6.64 (d, 1H, J = 2), 6.44 (br s, 1H), 5.19 (s, 2H), 4.38 (s, 2H), 3.51 (t, 2H, J = 6), 2.70 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 149.2, 144.1, 142.3, 138.7, 136.9, 136.1, 133.1, 132.9, 132.0, 129.2, 129.1, 128.9, 128.7, 128.3, 127.5, 127.46, 127.2, 112.1, 106.3, 105.1, 71.1, 43.6, 43.5, 21.0. Anal. Calcd for $C_{30}H_{26}O_6S_2N_2$: C, 62.70; H, 4.56; N, 4.88. Found: C, 62.40; H, 4.40; N, 4.80.

Physical and spectral properties of **20**: TLC R_f 0.10 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.79−7.77 (m, 2H), 7.60−7.31 (m, 13H), 6.75 (br s, 1H), 6.57 (d, 1H, J = 2), 6.38 (d, 1H, J = 2), 5.05 (s, 2H), 3.65 (d, 1H, J = 13), 3.52 (d, 1H, J = 13), 3.35 (s, 3H), 3.22 (t, 1H, J = 6) overlapping with 3.24−3.15 (m, 1H), 2.95−2.89 (m, 1H), 2.08−2.03 (m, 1H), 1.69−1.58 (m, 1H); ^{13}C NMR (125 MHz) 145.0, 143.0, 138.5, 137.5, 136.5, 132.8, 132.7, 130.3, 130.1, 129.0, 128.8, 128.5, 128.0, 127.4, 127.3, 127.2, 112.2, 111.5, 111.2, 71.2, 50.1, 46.4, 43.9, 41.1, 26.0; HRMS m/z 606.1522 (M^+) (calcd for $C_{31}H_{30}O_7S_2N_2$, 606.1494).

The stereochemistry in **20** was assigned by analogy to **18**.

A similar experiment conducted in the same manner using 2 equiv of BF_3·OEt_2 as promoter gave only **14a** in 78% yield.

2,9-Bis-benzenesulfonyl-7-methoxy-2,3,4,9-tetrahydro-1*H*-β-carbolin-6-ol (15a). According to general procedure B, a mixture of $TiCl_4$ (1.60 mL, 14.6 mmol) and $Ti(OiPr)_4$ (4.35 mL, 14.6 mmol) in CH_2Cl_2 (5 mL) was added to a solution of monoimine **1a** (1.62 g, 5.8 mmol) in CH_2Cl_2 (10 mL) at −78 °C, followed by a solution of enol ether **9a** (1.89 g, as a 3.5:1 mixture with its 2,3 double bond isomer, 7.5 mmol) in CH_2Cl_2 (10 mL). Workup, chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3), and recrystallization afforded **15a** (2.06 g, 71%) as a white solid: mp 221.5−222 °C (CH_2Cl_2/hexanes); TLC R_f 0.22 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.83−7.73 (m, 4H), 7.68 (s, 1H), 7.59−7.44 (m, 6H), 6.80 (s, 1H), 5.62 (s, 1H), 4.64 (br s, 2H), 4.00 (s, 3H), 3.48 (t, 2H, J = 6), 2.63 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 145.5, 143.6, 138.1, 137.6, 133.9, 132.8, 129.8, 129.4, 129.1, 128.3, 127.3, 126.2, 122.9, 117.4, 102.8, 97.7, 56.5, 44.8, 42.8, 21.3. Anal. Calcd for $C_{24}H_{22}O_6S_2N_2$: C, 57.81; H, 4.45; N, 5.62. Found: C, 57.53; H, 4.18; N, 5.60.

9-Benzenesulfonyl-7-methoxy-2-phenylmethanesulfonyl-2,3,4,9-tetrahydro-1*H*-β-carbolin-6-ol (15b). According to general procedure B, a mixture of $TiCl_4$ (107 μL, 0.97 mmol) and $Ti(OiPr)_4$ (290 μL, 0.97 mmol) in CH_2Cl_2 (1.5 mL) was added to a solution of monoimine **1a** (108 mg, 0.39 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9b** (128 mg, as a 4.5:1 mixture with its 2,3 double bond isomer, 0.48 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (EtOAc/hexanes 2/3) afforded **15b** (63 mg, 32%) as a colorless solid: TLC R_f 0.31 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 7.75−7.73 (m, 2H), 7.68 (s, 1H), 7.56−7.52 (m, 1H), 7.46−7.31 (m, 7H), 6.79 (s, 1H), 5.73 (br s, 1H), 4.63 (br s, 2H), 4.26 (s, 2H), 4.00 (s, 3H), 3.34 (t, 2H, J = 6), 2.43 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 145.6, 143.6, 138.0, 134.0, 130.6, 129.7, 129.4, 128.8, 128.77, 128.7, 128.5, 126.2, 123.1, 117.9, 102.9, 97.8, 58.2, 56.5, 44.6, 43.1, 22.0; HRMS m/z 512.1057 (M^+) (calcd for $C_{25}H_{24}N_2O_6S_2$, 512.1076).

9-Benzenesulfonyl-7-methoxy-2-(2-nitrobenzenesulfonyl)-2,3,4,9-tetrahydro-1*H*-β-carbolin-6-ol (15c). According to general procedure B, a mixture of $TiCl_4$ (0.20 mL, 1.8 mmol) and $Ti(OiPr)_4$ (0.54 mL, 1.8 mmol) in CH_2Cl_2 (2 mL) was added to a solution of monoimine **1a** (198 mg, 0.7 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9c** (273 mg, as a 3.6:1 mixture with its 2,3 double bond isomer, 0.9 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 3/3/4) gave **15c** (310 mg, 80%) as a colorless solid: mp 206.5−207 °C (CH_2Cl_2/hexanes); TLC R_f 0.42 (CH_2Cl_2/Et_2O/hexanes 2/2/1); ^{1}H NMR (400 MHz) 8.07−8.05 (m, 1H), 7.79 (d, 2H, J = 7), 7.74−7.69 (m, 3H), 7.68 (s, 1H), 7.57 (t, 1H, J = 7), 7.46 (t, 2H, J = 7), 6.85 (s, 1H), 5.63 (s, 1H), 4.82 (br s, 2H), 4.01 (s, 3H), 3.71 (t, 2H, J = 6), 2.74 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 148.1, 145.6, 143.7, 137.9, 134.0, 133.7, 132.6, 131.8, 130.8, 129.8, 129.4, 128.2, 126.3, 124.3, 123.0, 117.8, 102.9, 97.7, 56.5, 44.7, 43.1, 21.8; HRMS m/z 543.0753 (M^+) (calcd for $C_{24}H_{21}O_8S_2N_3$, 543.0769).

***N*-(2,5-Bis-benzenesulfonyl-7-methoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-b]indol-8-yl)benzamide (25a).** According to general procedure B, a mixture of $TiCl_4$ (85 μL, 0.77 mmol) and $Ti(OiPr)_4$ (0.23 mL, 0.77 mmol) in CH_2Cl_2 (0.75 mL) was added to a solution of diimine **24a** (117 mg, 0.31 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether

7a (77 mg, 0.30 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 3/3/4) gave **25a** (152 mg, 82%) as a colorless solid: mp 216−217 °C (CH_2Cl_2/hexanes); TLC R_f 0.34 (EtOAc/hexanes 2/3); ^{1}H NMR (400 MHz) 8.64 (br s, 1H), 8.51 (s, 1H), 7.91−7.86 (m, 3H), 7.75 (s, 1H), 7.69−7.41 (m, 12H), 4.19 (br s, 2H), 4.03 (s, 3H), 3.43 (t, 2H, J = 6), 3.17 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 165.2, 147.0, 138.4, 136.1, 134.9, 134.0, 133.0, 132.4, 131.8, 131.2, 129.4, 129.2, 128.8, 127.6, 126.9, 126.1, 125.3, 121.0, 115.4, 108.6, 97.2, 56.4, 43.6, 42.8, 25.4. Anal. Calcd for $C_{31}H_{27}O_6S_2N_3$: C, 61.88; H, 4.52; N, 6.99. Found: C, 61.75; H, 4.90; N, 7.11.

In an experiment run according to general procedure A, BF_3·Et_2O (41 μL, 0.33 mmol) was added to a solution of diimine **24a** (127 mg, 0.33 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7a** (88 mg, 0.35 mmol) in CH_2Cl_2 (2 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **25a** (154 mg, 77%) as a white solid.

***N*-(2,5-Bis-benzenesulfonyl-7-benzyloxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indol-8-yl)benzamide (25b).** According to general procedure A, BF_3·Et_2O (40 μL, 0.33 mmol) was added to a solution of diimine **24b** (73 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **7a** (41 mg, 0.16 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred for 40 min at −78 °C, and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. Workup and chromatography (EtOAc/hexanes 1/9 to 25/75) afforded **25b** (67 mg, 62%) as a white solid: mp 203−204 °C (CH_2Cl_2/hexanes); TLC R_f 0.43 (EtOAc/hexanes 2/4); ^{1}H NMR (400 MHz) 8.77 (br s, 1H), 8.53 (s, 1H), 7.90−7.84 (m, 5H), 7.60−7.34 (m, 15 H), 5.34 (s, 2H), 4.20 (br s, 2H), 3.45 (t, 2H, J = 6), 3.21 (br t, 2H, J = 6); ^{13}C (100 MHz) 165.5, 146.2, 138.6, 136.6, 136.5, 135.3, 134.3, 133.4, 132.6, 132.3, 131.8, 129.8, 129.7, 129.3, 129.25, 128.9, 128.1, 127.9, 127.3, 126.5, 126.1, 121.8, 115.9, 109.0, 99.8, 72.0, 44.0, 43.2, 25.9. Anal. Calcd for $C_{37}H_{31}O_6S_2N_3$: C, 65.56; H, 4.61; N, 6.20. Found: C, 65.50; H, 4.50; N, 5.81.

***N*-(2,9-Bis-benzenesulfonyl-7-methoxy-2,3,4,9-tetrahydro-1*H*-*β*-carbolin-6-yl)benzamide (26).** According to general procedure B, a mixture of $TiCl_4$ (0.11 mL, 1.0 mmol) and $Ti(OiPr)_4$ (0.29 mL, 1.0 mmol) in CH_2Cl_2 (0.97 mL) was added to a solution of diimine **24a** (150 mg, 0.39 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9a** (100 mg, as a 4:1 mixture with its 2,3 double bond isomer, 0.39 mmol) in CH_2Cl_2 (1 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) gave **26** (152 mg, 80%) as a white solid: mp 184.5−185.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.53 (EtOAc/hexanes 3/2); ^{1}H NMR (400 MHz) 8.62 (br s, 1H), 8.50 (s, 1H), 7.89 (d, 2H, J = 7), 7.79 (d, 2H, J = 7), 7.73 (d, 2H, J = 7) overlapping with 7.72 (s, 1H), 7.59−7.43 (m, 9H), 4.64 (br s, 2H), 4.03 (s, 3H), 3.47 (t, 2H, J = 6), 2.69 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 165.9, 147.9, 138.6, 137.9, 135.4, 134.5, 133.3, 133.0, 132.3, 129.9, 129.6, 129.2, 128.9, 127.7, 127.4, 126.6, 125.8, 123.1, 118.2, 109.7, 97.5, 56.9, 45.2, 43.3, 21.8. Anal. Calcd for $C_{31}H_{27}O_6S_2N_3$: C, 61.88; H, 4.52; N, 6.99. Found: C, 61.56; H, 4.40; N, 6.90.

In an experiment run according to general procedure A, BF_3·Et_2O (13 μL, 0.11 mmol) was added to a solution of diimine **24a** (41 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by a solution of enol ether **9a** (48 mg, as a 4:1 mixture with its 2,3 double bond isomer, 0.19 mmol) in CH_2Cl_2 (0.8 mL). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **26** (25 mg, 39%) as a white solid.

General Procedure for Methylation of 12a−c and 15a/c. A slurry of the phenol and K_2CO_3 in acetone was treated with CH_3I, and in some cases with Bu_4NI. The reaction mixture was refluxed 24 h, cooled to room temperature, poured into H_2O, and extracted with CH_2Cl_2 (3×). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated.

2,5-Bis-benzenesulfonyl-7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (27a). According to the general procedure, a slurry of phenol **12a** (2.98 g, 6.0 mmol) and K_2CO_3 (1.43 g, 10.3 mmol) in acetone (50 mL) was treated with CH_3I (0.6 mL, 9.6 mmol). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **27a** (2.89 g, 94%) as a white solid: mp 201−202 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f 0.27 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.88−7.86 (m, 2H), 7.72 (s, 1H), 7.70−7.54 (m, 6H), 7.43 (t, 2H, J = 8), 6.71 (s, 1H), 4.22 (br s, 2H), 3.98 (s, 3H), 3.91 (s, 3H), 3.45 (t, 2H, J = 6), 3.18 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 147.9, 147.2, 138.4, 136.4, 133.8, 133.0, 130.6, 130.3, 129.3, 129.2, 127.5, 126.1, 120.4, 114.7, 99.4, 98.6, 56.3, 56.1, 43.5, 42.6, 25.2. Anal. Calcd for $C_{25}H_{24}O_6S_2N_2$: C, 58.58; H, 4.72; N, 5.47. Found: C, 58.37; H, 4.95 N, 5.26.

5-Benzenesulfonyl-7,8-dimethoxy-2-phenylmethanesulfonyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (27b). According to the general procedure, a slurry of phenol **12b** (1.00 g, 1.95 mmol) and K_2CO_3 (3.10 mg, 22.4 mmol) in acetone (30 mL) was treated with CH_3I (0.18 mL, 2.89 mmol). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/6) afforded **27b** (922 mg, 90%) as a white solid: mp 191−192 °C (CH_2Cl_2/hexanes); TLC R_f 0.29 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.77 (s, 1H), 7.73 (d, 2H, J = 8), 7.56 (t, 1H, J = 8), 7.44 (t, 2H, J = 8), 7.35−7.25 (m, 5H), 6.62 (s, 1H), 4.26 (s, 2H), 4.24 (br s, 2H), 4.01 (s, 3H), 3.89 (s, 3H), 3.46 (t, 2H, J = 6), 3.02 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 147.9, 147.3, 138.5, 133.9, 130.9, 130.5, 130.3, 129.4, 128.8, 128.76, 128.6, 126.1, 120.3, 115.3, 99.5, 98.6, 57.9, 56.4, 56.1, 43.4, 42.5, 25.6. Anal. Calcd for $C_{26}H_{26}O_6S_2N_2$: C, 59.30; H, 4.98; N, 5.32. Found: C, 58.97; H, 5.10; N, 5.05.

2-Benzenesulfonyl-7,8-dimethoxy-2-(2-nitrobenzenesulfonyl)-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (27c). According to the general procedure, a slurry of phenol **12c** (100 mg, 0.18 mmol) and K_2CO_3 (327 mg, 2.4 mmol) in acetone (10 mL) was treated with CH_3I (17 μL, 0.27 mmol) and Bu_4NI (7 mg, 0.019 mmol). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/8) afforded **27c** (84 mg, 82%) as a white solid: mp 225−226.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.16 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 8.08−8.06 (m, 1H), 7.72 (s, 1H), 7.71−7.63 (m, 5H), 7.54 (t, 1H, J = 7), 7.42 (t, 2H, J = 7), 6.74 (s, 1H), 4.47 (br s, 2H), 3.98 (s, 3H), 3.90 (s, 3H), 3.67 (t, 2H, J = 6), 3.18 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 148.0, 147.9, 147.2, 138.2, 133.79, 133.77, 131.9, 131.7, 130.7, 130.6, 130.2, 129.3, 126.0, 124.2, 120.2, 114.9, 99.5, 98.5, 56.3, 56.1, 43.3, 42.4, 25.2; HRMS m/z 557.0909 (M^+) (calcd for $C_{25}H_{23}O_8S_2N_3$, 557.0927).

2,9-Bis-benzenesulfonyl-6,7-dimethoxy-2,3,4,9-tetrahydro-1*H*-*β*-carboline (30a). According to the general procedure, a slurry of phenol **15a** (391 mg, 0.78 mmol) and K_2CO_3 (200 mg, 1.4 mmol) in acetone (10 mL) was treated with CH_3I (75 μL, 1.2 mmol). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) gave **30a** (313 mg, 78%) as a white solid: mp 172−173.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.37 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.84 (d, 2H, J = 7), 7.76 (d, 2H, J = 7), 7.70 (s, 1H), 7.61−7.44 (m, 6H), 6.72 (s, 1H), 4.65 (br s, 2H), 4.00 (s, 3H), 3.90 (s, 3H), 3.49 (t, 2H, J = 6), 2.69 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 148.0, 147.3, 138.1, 137.5, 134.0, 132.9, 130.2, 129.5, 129.2, 128.1, 127.4, 126.2, 122.1, 117.3, 100.0, 98.4, 56.4, 56.1, 44.8, 42.9, 21.5. Anal. Calcd for $C_{25}H_{24}O_6S_2N_2$: C, 58.58; H, 4.72; N, 5.47. Found: C, 58.26; H, 4.94; N, 5.29.

9-Benzenesulfonyl-6,7-dimethoxy2-(2-nitrobenzenesulfonyl)-2,3,4,9-tetrahydro-1*H*-*β*-carboline (30c). According to the general procedure, a slurry of phenol **15c** (109 mg, 0.20 mmol) and K_2CO_3 (200 mg, 1.4 mmol) in acetone (10 mL) was treated with CH_3I (18 μL, 0.29 mmol) and Bu_4NI (10 mg, 0.027 mmol). Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/6 to 3/3/4) afforded **30c** (85 mg, 76%) as a white solid: mp 193−194 °C (CH_2Cl_2/hexanes); TLC R_f 0.18 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 8.08−8.06 (m, 1H), 7.80−7.67 (m, 5H) overlapping with 7.70 (s, 1H), 7.55 (t, 1H, J = 7), 7.45 (t, 2H, J = 7), 6.77 (s, 1H), 4.83 (br s, 2H), 4.00 (s, 3H), 3.91 (s, 3H), 3.73 (t, 2H, J = 6), 2.79 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 148.1, 148.05, 147.4, 137.9, 134.0, 133.7, 132.6, 131.8, 130.8, 130.1, 129.4, 127.9, 126.3, 124.3, 122.2, 117.8, 100.1, 98.4, 56.4, 56.1, 44.7, 43.1, 21.9; HRMS m/z 557.0914 (M^+) (calcd for $C_{25}H_{23}O_8S_2N_3$, 557.0927).

General Procedure for Triflation of 12a−c. Pyridine was added to a solution of the phenol in CH_2Cl_2 at −78 °C,

followed after 5 min by trifluoromethanesulfonic anhydride (Tf_2O). The reaction mixture was allowed to warm until no phenol was detectable by TLC analysis, and then the reaction was quenched with water and the solution extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated.

Trifluoromethanesulfonic acid 2,5-Bis-benzenesulfonyl-7-methoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indol-8-yl Ester (28a). According to the general procedure, pyridine (0.56 mL, 6.9 mmol) was added to a solution of phenol **12a** (1.39 g, 2.8 mmol) in CH_2Cl_2 (10 mL) at −78 °C, followed by Tf_2O (0.61 mL, 3.6 mmol). The reaction mixture was allowed to warm to −45 °C over 2 h. Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) gave **28a** (1.7 g, 97%) as a white solid: mp 222−223 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f 0.42 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.89−7.86 (m, 2H) overlapping with 7.87 (s, 1H), 7.76−7.73 (m, 2H), 7.65−7.49 (m, 6H), 7.16 (s, 1H), 4.20 (br s, 2H), 4.01 (s, 3H), 3.46 (t, 2H, J = 6), 3.18 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 149.8, 138.6, 136.8, 136.6, 135.9, 134.9, 133.6, 133.2, 130.1, 129.7, 128.0, 126.7, 120.6, 119.1 (q, J_{C-F} = 319), 114.5, 111.9, 99.9, 57.1, 43.8, 42.7, 25.6. Anal. Calcd for $C_{25}H_{21}O_8S_3N_2F_3$: C, 47.61; H, 3.36; N, 4.44. Found: C, 47.67; H, 3.46; N, 4.17.

Trifluoromethanesulfonic Acid 5-Benzenesulfonyl-7-methoxy-2-phenylmethanesulfonyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indol-8-yl Ester (28b). According to the general procedure, pyridine (0.31 mL, 3.83 mmol) was added to a solution of phenol **12b** (787 mg, 1.54 mmol) in CH_2Cl_2 (5 mL) at −78 °C, followed by Tf_2O (0.39 mL, 2.31 mmol). The reaction mixture was allowed to warm to room temperature over 12 h. Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) gave **28b** (842 mg, 85%) as a white solid: mp 177−178 °C (CH_2Cl_2/hexanes); TLC R_f 0.53 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.91 (s, 1H), 7.77 (d, 2H, J = 8), 7.63 (t, 1H, J = 8), 7.52 (t, 2H, J = 8), 7.33−7.24 (m, 5H), 7.03 (s, 1H), 4.29 (s, 2H), 4.19 (br s, 2H), 4.03 (s, 3H), 3.45 (t, 2H, J = 6), 3.02 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 149.4, 138.3, 136.4, 135.4, 134.5, 132.9, 130.4, 129.7, 128.9, 128.8, 128.4, 126.2, 120.1, 118.7 (q, J_{C-F} = 319), 114.5, 111.5, 99.4, 58.1, 56.7, 43.2, 42.2, 25.5. Anal. Calcd for $C_{26}H_{23}O_8S_3N_2F_3$: C, 48.44; H, 3.60; N, 4.35. Found: C, 48.69; H, 3.39; N, 4.25.

Trifluoromethanesulfonic Acid 5-Benzenesulfonyl-7-methoxy-2-(2-nitrobenzenesulfonyl)-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indol-8-yl Ester (28c). According to the general procedure, pyridine (32 μL, 40 mmol) was added to a solution of phenol **12c** (86 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) at −78 °C, followed by Tf_2O (0.40 μL, 0.24 mmol). The reaction mixture was allowed to warm to −10 °C over 3 h. Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 3/3/4) gave **28c** (97 mg, 91%) as a white solid: mp 189−190.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.45 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 8.12−8.10 (m, 1H), 7.88 (s, 1H), 7.77−7−68 (m, 5H), 7.63 (t, 1H, J = 7), 7.51 (t, 2H, J = 7), 7.18 (s, 1H), 4.44 (br s, 2H), 4.02 (s, 3H), 3.71 (t, 2H, J = 6), 3.21 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 149.5, 148.1, 138.2, 136.5, 135.5, 134.4, 134.0, 132.9, 131.9, 131.88, 131.0, 129.7, 126.3, 124.4, 120.1, 118.7 (q, J_{C-F} = 319), 114.1, 111.6, 99.5, 56.7, 43.2, 42.1, 25.3; HRMS m/z 675.0253 (M^+) (calcd for $C_{25}H_{20}O_{10}S_3N_3F_3$, 675.0263).

2,5-Bis-benzenesulfonyl-7-methoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (29a). To a solution of triflate **28a** (1.72 g, 2.7 mmol) in DMF (10 mL) were added palladium(II) acetate trimer (56 mg, 0.083 mmol), 1,1′-bis(diphenylphosphino)ferrocene (79 mg, 0.14 mmol), triethylamine (8 mL, 57 mmol), and a 90% aqueous formic acid solution (2.2 mL, 53 mmol) in sequence. The mixture was heated to 90 °C for 24 h and then cooled to room temperature. Water was added, and the mixture was poured into EtOAc. The aqueous layer was separated and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$ and H_2O, and the solution was dried (Na_2SO_4) and concentrated. Chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3) afforded **29a** (1.09 g, 83%) as a white solid: mp 144−145 °C (CH_2Cl_2/Et_2O/hexanes); TLC R_f 0.43 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.88−7.85 (m, 2H), 7.74−7.72 (m, 2H), 7.70 (d, 1H, J = 2), 7.62−7.43 (m, 6H), 7.17 (d, 1H, J = 9), 6.88 (dd, 1H, J = 9, 2), 4.22 (br s, 2H), 3.89 (s, 3H), 3.46 (t, 2H, J = 6), 3.19 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 158.4, 138.9, 137.7, 136.9, 134.3, 133.4, 131.3, 129.8, 129.6, 127.9, 126.7, 121.7, 118.7, 114.9, 112.8, 99.8, 56.2, 44.0, 43.0, 25.6. Anal. Calcd for $C_{24}H_{22}O_5S_2N_2$: C, 59.73; H, 4.60; N, 5.81. Found: C, 59.49; H, 4.52; N, 5.69.

Similarly prepared were **29b** (72%) and **29c** (88%).

Physical and spectral properties of **29b**: a white solid, mp 160.5−161.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.56 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz) 7.78−7.76 (m, 2H), 7.74 (d, 1H, J = 2), 7.57 (t, 1H, J = 8), 7.46 (t, 2H, J = 8), 7.35−7.26 (m, 5H), 7.08 (d, 1H, J = 9), 6.88 (dd, 1H, J = 9, 2), 4.27 (s, 2H), 4.23 (br s, 2H), 3.91 (s, 3H), 3.46 (t, 2H, J = 6), 3.02 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 158.0, 138.6, 137.3, 134.0, 131.1, 130.5, 129.4, 128.8, 128.76, 128.6, 126.3, 121.2, 118.3, 114.9, 112.3, 99.4, 57.9, 55.8, 43.4, 42.5, 25.6. Anal. Calcd for $C_{25}H_{24}O_5S_2N_2$: C, 60.46; H, 4.87; N, 5.64. Found: C, 60.07; H, 4.82; N, 5.60.

Physical and spectral characteristics of **29c**: a white solid, mp 171−172 °C (CH_2Cl_2/hexanes); TLC R_f 0.50 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 7.74 (d, 2H, J = 8), 7.70 (d, 1H, J = 2), 7.65 (d, 1H, J = 8), 7.56 (t, 1H, J = 8), 7.44 (t, 2H, J = 8), 7.31−7.28 (m, 1H), 7.18 (d, 1H, J = 9), 6.87 (dd, 1H, J = 9, 2), 6.79−6.72 (m, 2H), 5.12 (br s, 2H), 4.30 (br s, 2H), 3.89 (s, 3H), 3.53 (t, 2H, J = 6), 3.19 (br t, 2H, J = 6); ^{13}C NMR (125 MHz) 157.9, 146.3, 138.5, 137.3, 134.4, 133.8, 131.0, 130.1, 129.4, 126.2, 121.4, 118.3, 118.0, 117.8, 117.4, 114.7, 112.2, 99.4, 55.8, 43.5, 42.4, 25.2; FABMS m/z 498 ($M + H^+$). HRMS m/z 498.1151 ($M + H^+$) (calcd for $C_{24}H_{24}O_5S_2N_3$, 498.1157).

General Procedure C: Desulfonylation of Indole Nitrogens. K_2CO_3 was added to a THF/MeOH/H_2O (10/10/1) solution of the starting material. The reaction mixture was either stirred at room temperature or heated to reflux until no starting material was detectable by TLC and then concentrated to dryness. The residue was dissolved in CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated.

2-Benzenesulfonyl-7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (31). According to general procedure C, K_2CO_3 (406 mg, 2.9 mmol) was added to a solution of **27a** (226 mg, 0.44 mmol) in THF/MeOH/H_2O (10.5 mL), and the reaction mixture was refluxed for 3 d. Workup and chromatography (CH_2Cl_2/Et_2O/hexanes 3/3/4) afforded **31** (98 mg, 60%) as a white solid: mp 212−213 °C (CH_2Cl_2/hexanes); TLC R_f 0.35 (CH_2Cl_2/Et_2O/hexanes 2/2/1); ^{1}H NMR (400 MHz) 7.90−7.88 (m, 2H), 7.76 (br s, 1H), 7.61−7.53 (m, 3H), 6.84 (s, 1H), 6.83 (s, 1H), 4.38 (br s, 2H), 3.93 (s, 3H), 3.89 (s, 3H), 3.53 (t, 2H, J = 6), 2.85 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 147.1, 145.3, 137.6, 133.2, 130.5, 129.6, 129.5, 127.9, 118.5, 106.2, 100.0, 95.2, 56.7, 56.6, 44.0, 43.6, 24.1; HRMS m/z 372.1146 (M^+) (calcd for $C_{19}H_{20}O_4SN_2$, 372.1144).

Alternative Method. Red-Al (65+ wt % in toluene, 0.22 mL, 0.73 mmol) was added to a solution of **27a** (142 mg, 0.28 mmol) in THF (5 mL), and the reaction mixture was stirred at room temperature for 4 d. The mixture was quenched by the addition of H_2O with ice cooling. The aqueous layer was extracted with EtOAc (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (CH_2Cl_2/Et_2O/hexanes2/2/1) gave **31** (71 mg, 69%) as a white solid.

5-Benzenesulfonyl-7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (32). Compound **27c** (49 mg, 0.088 mmol) was dissolved in DMF (2 mL), and LiOH (17 mg, 0.74 mmol) and $HSCH_2COOH$ (12.1 μL, 0.18 mmol) were added. The reaction mixture was stirred at room temperature until no starting material was detectable by TLC (∼10 h), and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (MeOH/EtOAc 3/7) gave **32** (15 mg, 46%) as a white solid: mp 176−177 °C (CH_2Cl_2/hexanes); TLC R_f 0.14 (MeOH/EtOAc 3/7); ^{1}H NMR (400 MHz) 7.79 (s, 1H), 7.76−7.74 (m, 2H), 7.55 (t, 1H, J = 8), 7.43 (t, 2H, J = 8), 6.73 (s, 1H), 4.00 (s, 3H), 3.91 (s, 3H) overlapping with 3.91 (br s, 2H), 3.17 (t, 2H, J = 6), 3.02 (br t, 2H, J = 6),

(the N−H is not visible); ^{13}C NMR (125 MHz) 147.5, 147.1, 138.9, 133.6, 132.3, 130.1, 129.2, 126.2, 121.5, 118.3, 99.8, 98.8, 56.4, 56.1, 43.6, 42.1, 26.2; HRMS *m/z* 373.1229 (M + H$^+$) (calcd for $C_{19}H_{21}O_4SN_2$, 373.1222).

Compound **30c** was converted into **38** in a similar manner. Thus, a solution of **30c** (21 mg, 0.038 mmol) in DMF (1 mL) was treated with LiOH (9 mg, 0.39 mmol) and $HSCH_2COOH$ (5.3 μL, 0.076 mmol) and stirred for 3 h. Workup and chromatography (MeOH/EtOAc 3/7) gave **38** (8.5 mg, 60%) as a white solid: mp 188.5−190 °C (CH_2Cl_2/hexanes); TLC R_f 0.25 (MeOH/EtOAc 3/7); ^{1}H NMR (400 MHz) 7.76−7.74 (m, 2H) overlapping with 7.75 (s, 1H), 7.55 (t, 1H, *J* = 8), 7.43 (t, 2H, *J* = 8), 6.80 (s, 1H), 4.25 (br s, 2H), 4.00 (s, 3H), 3.92 (s, 3H), 3.12 (t, 2H, *J* = 6), 2.62 (br t, 2H, *J* = 6), (the N−H is not visible); ^{13}C NMR (125 MHz) 147.6, 147.1, 138.6, 133.6, 132.3, 129.9, 129.2, 126.1, 123.1, 117.7, 100.0, 98.5, 56.4, 56.1, 44.5, 42.6, 22.6; HRMS *m/z* 373.1248 (M + H$^+$) (calcd for $C_{19}H_{21}O_4SN_2$, 373.1222).

7,8-Dimethoxy-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (33). A solution of **27b** (532 mg, 1.0 mmol) in THF (30 mL) was added to liquid NH_3 (30 mL), followed by Na until a blue color persisted for 5 min (105 mg, 4.6 mmol). The reaction was then quenched by the addition of solid NH_4Cl. The NH_3 was allowed to evaporate, H_2O was added to the residue, and the pH was adjusted to 9−10 by the addition of solid NaOH. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated to give crude **33** (234 mg, 100%) as a yellowish solid which was ∼90% pure by NMR: ^{1}H NMR (400 MHz) 7.88 (br s, 1H), 6.88 (s, 1H), 6.84 (s, 1H), 4.05 (br s, 2H), 3.93 (s, 3H), 3.89 (s, 3H), 3.23 (t, 2H, *J* = 6), 2.75 (br t, 2H, *J* = 6); ^{13}C NMR (100 MHz) 146.7, 145.1, 131.1, 130.1, 119.1, 109.4, 100.5, 95.3, 56.8, 56.7, 43.7, 42.7, 24.7; HRMS *m/z* 233.1294 (M + H$^+$) (calcd for $C_{13}H_{17}O_2N_2$, 233.1290).

This material was further purified by formation of its BOC derivative. Thus, EtN(iPr)$_2$ (18 μL) was added to a solution of crude **33** (21 mg, 0.091 mmol) in THF (2 mL), followed by $(BOC)_2O$ (22 μL, 0.096 mmol). The reaction mixture was stirred for 4 h at room temperature, and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (CH_2Cl_2/Et_2O/hexanes 1/1/3 to 3/3/4) afforded the BOC derivative of **33** (15 mg, 50%) as a white solid: mp 189.5−191.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.21 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (500 MHz, *T* = 323 K) 7.73 (br s, 1H), 6.92 (s, 1H), 6.87 (s, 1H), 4.61 (br s, 2H), 3.93 (s, 3H), 3.91 (s, 3H), 3.82 (t, 2H, *J* = 6), 2.80 (t, 2H, *J* = 6), 1.54 (s, 9H); ^{13}C NMR (125 MHz, *T* = 323 K, 1 aromatic carbon is not observed) 155.3, 146.9, 145.3, 130.4, 118.8, 107.7, 100.7, 95.5, 79.8, 56.7, 56.6, 41.3 (2 carbons), 28.6, 23.7; EIMS (relative intensity) *m/z* 332 (M$^+$, 6), 275 (24), 203 (16), 86 (31), 84 (48), 57 (12), 51 (32), 49 (100), 44 (17): HRMS *m/z* 332.1748 (M$^+$) (calcd for $C_{18}H_{24}O_4N_2$, 332.1736).

SeO_2 Oxidations of 27a, 29a, and 30a. 5-Benzenesulfonyl-7-methoxy-5*H*-pyrido[4,3-*b*]indole (35). A solution of **29a** (1.09 g, 2.26 mmol) and SeO_2 (1.28 g, 11.5 mmol) in dioxane (20 mL) was refluxed for 24−48 h (until no starting material was detectable by TLC). The reaction mixture was cooled to room temperature and stirred with anhydrous $NaHCO_3$ powder and anhydrous $MgSO_4$.[21] The slurry was filtered through a thin pad of a 1:1 mixture of Florisil and Celite, rinsed with $CHCl_3$, dried (Na_2SO_4), and concentrated. Chromatography (EtOAc/hexanes 3/7 to 1/1 to 4/1) gave **35** (685 mg, 90%) as a white solid: mp 191−192 °C (EtOAc/hexanes); TLC R_f 0.44 (EtOAc/hexanes 4/1); ^{1}H NMR (400 MHz) 9.17 (s, 1H), 8.62 (d, 1H, *J* = 6), 8.31 (d, 1H, *J* = 6), 7.94−7.90 (m, 3H), 7.88 (d, 1H, *J* = 2), 7.60 (t, 1H, *J* = 8), 7.46 (t, 2H, *J* = 8), 7.09 (dd, 1H, *J* = 9, 2), 4.00 (s, 3H); ^{13}C NMR (125 MHz) 160.5, 146.2, 143.4, 141.9, 139.4, 137.6, 134.4, 129.4, 126.5, 122.4, 121.1, 117.1, 112.7, 109.5, 99.6, 55.9; HRMS *m/z* 339.0795 (M + H$^+$) (calcd for $C_{18}H_{15}O_3SN_2$, 339.0803).

(21) Ren, R. X.-F.; Nakanishi, K. *Aldrichimica Acta* **1997**, *30*, 106.

Similarly prepared were **34** (84%) and **40** (75%).

Physical and spectral properties of **34**: a white solid, mp 233.5−234.5 °C (dec) (CH_2Cl_2/hexanes); TLC R_f 0.17 (EtOAc/hexanes 4/1); ^{1}H NMR (400 MHz) 9.13 (s, 1H), 8.60 (d, 1H, *J* = 6), 8.17 (d, 1H, *J* = 6), 7.89 (s, 1H), 7.82 (d, 2H, *J* = 8), 7.54 (t, 1H, *J* = 8), 7.40 (t, 2H, *J* = 8) overlapping with 7.40 (s, 1H), 4.08 (s, 3H), 4.01 (s, 3H); ^{13}C NMR (125 MHz) 150.6, 147.8, 145.2, 143.3, 141.3, 137.4, 134.4, 132.5, 129.3, 126.4, 122.9, 116.1, 109.8, 101.8, 98.4, 56.4, 56.3. Anal. Calcd for $C_{19}H_{16}O_4SN_2$, C, 61.94; H, 4.38; N, 7.61. Found: C, 61.68; H, 4.35; N, 7.37.

Physical and spectral properties of **40**: a white solid, mp 241−242 °C (dec) (EtOAc/hexanes); TLC R_f 0.36 (EtOAc/hexanes 4/1); ^{1}H NMR (400 MHz) 9.55 (s, 1H), 8.55 (d, 1H, *J* = 5), 7.92 (s, 1H), 7.81−7.79 (m, 2H), 7.68 (d, 1H, *J* = 5), 7.50 (t, 1H, *J* = 8), 7.35 (t, 2H, *J* = 8) overlapping with 7.33 (s, 1H), 4.11 (s, 3H), 4.00 (s, 3H); ^{13}C NMR (125 MHz) 151.9, 147.7, 143.8, 137.14, 137.1, 134.7, 134.1, 133.8, 133.1, 129.2, 126.4, 116.7, 113.4, 102.3, 98.4, 56.5, 56.3; HRMS *m/z* 369.0909 (M + H$^+$) (calcd for $C_{19}H_{17}O_4SN_2$, 369.0909).

7,8-Dimethoxy-5*H*-pyrido[4,3-*b*]indole (36). According to general procedure C, K_2CO_3 (100 mg, 0.72 mmol) was added to a solution of **34** (71 mg, 0.19 mmol) in THF/MeOH/H_2O (4.2 mL), and the reaction mixture was refluxed overnight. Workup and chromatography (EtOAc/MeOH 19/1 to 7/3) afforded **36** (27 mg, 61%) as a white solid: mp 206−207 °C (EtOAc/MeOH); TLC R_f 0.26 (EtOAc/MeOH 7/3); ^{1}H NMR (400 MHz) 9.24 (s, 1H), 8.83 (bs, 1H), 8.46 (d, 1H, *J* = 6), 7.58 (s, 1H), 7.34 (d, 1H, *J* = 6), 7.02 (s, 1H), 4.04 (s, 3H), 4.00 (s, 3H); ^{13}C NMR (125 MHz) 150.2, 145.4, 143.5, 143.0, 141.5, 134.0, 120.7, 113.3, 106.0, 102.6, 94.5, 56.5, 56.2; HRMS *m/z* 229.0979 (M + H$^+$) (calcd for $C_{13}H_{13}O_2N_2$, 229.0977).

Alternative Method. Red-Al (65+ wt % in toluene, 0.72 mL, 2.40 mmol) was added to a solution of **34** (289 mg, 0.79 mmol) in THF (15 mL). The reaction mixture was stirred at room temperature for 2 d, and then the reaction was quenched by the addition of water with ice cooling. The aqueous layer was extracted with EtOAc (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (EtOAc/MeOH 19/1) gave **36** (106 mg, 59%) as a white solid.

Alternative Method. 10% Pd/C (10 mg) was added to a solution of crude **33** (27 mg, 0.12 mmol) in mesitylene, and the reaction mixture was heated to 150−160 °C overnight. After cooling to room temperature, the reaction mixture was filtered through Celite, the Celite rinsed with CH_2Cl_2, and the filtrate was washed with 10% aqueous HCl. The aqueous layer was treated with solid NaOH until pH 8 was reached, the solution was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (EtOAc/MeOH 7/3) gave **36** (23 mg, 87%) as a white solid.

7-Methoxy-5*H*-pyrido[4,3-*b*]indole (37). According to general procedure C, K_2CO_3 (104 mg, 0.75 mmol) was added to a solution of **35** (98 mg, 0.29 mmol) in THF/MeOH/H_2O (5.3 mL), and the reaction mixture was refluxed overnight. Workup and chromatography (EtOAc/MeOH 9/1) afforded **37** (29 mg, 51%) as a white solid: mp 172−173 °C (CH_2Cl_2/hexanes); TLC R_f 0.43 (EtOAc/MeOH 7/3); ^{1}H NMR (400 MHz) 9.24 (s, 1H), 8.94 (br s, 1H), 8.48 (d, 1H, *J* = 6), 8.02 (d, 1H, *J* = 9), 7.34 (d, 1H, *J* = 6), 6.99 (d, 1H, *J* = 2), 6.96 (dd, 1H, *J* = 9, 2), 3.93 (s, 3H); ^{13}C NMR (125 MHz) 159.8, 143.9, 143.8, 141.7, 140.7, 121.4, 120.4, 115.1, 109.5, 105.8, 95.2, 55.7; HRMS *m/z* 199.0872 (M + H$^+$) (calcd for $C_{12}H_{11}ON_2$, 199.0871).

Alternative Method. Red-Al (65+ wt % in toluene, 0.11 mL, 0.37 mmol) was added to a solution of **35** (34 mg, 0.10 mmol) in THF (4 mL). The reaction mixture was stirred at room temperature for 1 d, and then the reaction was quenched by the addition of water with ice cooling. The aqueous layer was extracted with EtOAc (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (EtOAc/MeOH 9/1) gave **37** (14 mg, 70%) as a white solid.

6,7-Dimethoxy-2,3,4,9-tetrahydro-1*H*-β-carboline (39). A solution of **30a** (228 mg, 0.45 mmol) in THF (20 mL) was

added to liquid NH_3 (30 mL), followed by Na (46 mg, 2.0 mmol), until a blue color persisted for 5 min. The reaction was then quenched by the addition of solid NH_4Cl. The ammonia was allowed to evaporate, H_2O was added to the residue, and the pH was adjusted to 9−10 by the addition of solid NaOH. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated to give crude **39** (93 mg, 90%) as a yellowish solid which was ∼90% pure by NMR: ^{1}H NMR (400 MHz) 7.80 (br s, 1H), 6.94 (s, 1H), 6.85 (s, 1H), 4.00 (br s, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 3.19 (t, 2H, J = 6), 2.73 (br t, 2H, J = 6); ^{13}C NMR (100 MHz) 146.8, 145.1, 131.7, 130.1, 120.7, 108.8, 100.5, 95.2, 56.8, 56.7, 44.3, 43.7, 23.0; HRMS m/z 233.1277 (M + H$^+$) (calcd for $C_{13}H_{17}O_2N_2$, 233.1290).

This material was further purified by conversion to its BOC derivative. Thus, EtN(iPr)$_2$ (15 μL) was added to a solution of crude **39** (18 mg, 0.078 mmol) in THF (2 mL), followed by $(BOC)_2O$ (20 μL, 0.087 mmol). The reaction mixture was stirred for 4 h at room temperature, and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (CH_2Cl_2/Et$_2$O/hexanes 1/1/3 to 3/3/4) afforded the BOC derivative of **39** (14 mg, 54%) as a white solid: mp 166−167 °C (CH_2Cl_2/hexanes); TLC R_f 0.20 (CH_2Cl_2/Et$_2$O/hexanes 3/3/4); ^{1}H NMR (500 MHz, T = 323 K) 7.77 (br s, 1H), 6.95 (s, 1H), 6.88 (s, 1H), 4.62 (br s, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.78 (t, 2H, J = 6), 2.77 (t, 2H, J = 6), 1.52 (s, 9H); ^{13}C NMR (125 MHz, T = 323 K, 1 aromatic carbon is not observed) 155.2, 147.1, 145.3, 130.7, 129.3, 120.2, 101.0, 95.5, 80.0, 56.7, 56.6, 42.0 (2 carbons), 28.5, 21.5; HRMS m/z 332.1715 (M$^+$) (calcd for $C_{18}H_{24}O_4N_2$, 332.1736).

6,7-Dimethoxy-9*H*-*β*-carboline (41). According to general procedure C, K_2CO_3 (25 mg, 0.18 mmol) was added to a solution of **40** (23 mg, 0.063 mmol) in THF/MeOH/H_2O (2.1 mL), and the reaction mixture was stirred at room temperature for 5 d. Workup and chromatography (EtOAc/MeOH 9/1) afforded **41** (10 mg, 70%) as a yellowish solid: mp 216.5−218 °C (CH_2Cl_2/hexanes); TLC R_f 0.33 (EtOAc/MeOH 7/3); ^{1}H NMR (400 MHz) 9.44 (br s, 1H), 8.88 (d, 1H, J = 1), 8.44 (d, 1H, J = 5), 7.88 (dd, 1H, J = 5, 1), 7.54 (s, 1H), 7.01 (s, 1H), 4.03 (s, 3H), 4.00 (s, 3H); ^{13}C NMR (125 MHz) 151.7, 145.0, 138.5, 136.1, 136.0, 133.1, 129.2, 113.8, 113.3, 102.9, 94.3, 56.5, 56.1; HRMS m/z 229.0996 (M + H$^+$) (calcd for $C_{13}H_{13}O_2N_2$, 229.0977).

Alternative Method. KOtBu (83 mg, 0.74 mmol) was added to a solution of **30a** (38 mg, 0.074 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 4 h, and then the reaction was quenched by the addition of H_2O. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (EtOAc/MeOH 9/1) afforded **41** (12 mg, 71%).

5-Benzenesulfonyl-7,8-dimethoxy-5*H*-pyrido[4,3-*b*]indole 2-Oxide (42). Carboline **34** (238 mg, 0.65 mmol) was dissolved in CH_2Cl_2 (10 mL), and *m*-CPBA (250 mg, 1.45 mmol) was added. The reaction mixture was allowed to warm to room temperature, stirred for 15 h, and then transferred directly to a silica gel column. Chromatography (EtOAc/hexanes 4/1, to remove excess *m*-CPBA, and then MeOH/EtOAc 1/9 to 3/7) gave **42** (227 mg, 91%) as a white solid: mp 218.5−220 °C (dec) (EtOAc/MeOH/hexanes); TLC R_f 0.45 (MeOH/EtOAc 3/7); ^{1}H NMR (400 MHz) 8.78 (d, 1H, J = 1), 8.24 (dd, 1H, J = 7, 1), 8.12 (d, 1H, J = 7), 7.79 (s, 1H), 7.76 (d, 2H, J = 8), 7.57 (t, 1H, J = 8), 7.41 (t, 2H, J = 8), 7.24 (s, 1H), 4.08 (s, 3H), 3.99 (s, 3H); ^{13}C NMR (100 MHz) 152.2, 148.6, 137.2, 136.6, 135.4, 135.2, 134.7, 131.3, 129.9, 126.8, 125.8, 114.8, 112.2, 102.3, 98.7, 56.9, 56.8. Anal. Calcd for $C_{19}H_{16}O_5SN_2$: C, 59.36; H, 4.20; N, 7.29. Found: C, 59.15; H, 4.52; N, 7.11.

A similar procedure starting with carboline **35** (125 mg) afforded **43** (120 mg, 92%), a white solid: mp 209.5−210.5 °C (dec) (MeOH/EtOAc); TLC R_f 0.29 (MeOH/EtOAc 3/7); ^{1}H NMR (400 MHz) 8.71 (s, 1H), 8.26 (dd, 1H, J = 7, 1), 8.15 (d, 1H, J = 7), 7.85−7.83 (m, 2H) overlapping with 7.82 (d, 1H, J = 2), 7.74 (d, 1H, J = 9), 7.60 (t, 1H, J = 8), 7.45 (t, 2H, J = 8), 7.05 (dd, 1H, J = 9, 2), 3.99 (s, 3H); ^{13}C NMR (125 MHz) 161.6, 141.1, 137.0, 136.5, 135.0, 134.8, 130.9, 129.6, 126.5, 125.1, 121.8, 115.2, 113.5, 111.6, 99.7, 56.0; HRMS m/z 355.0735 (M + H$^+$) (calcd for $C_{18}H_{15}O_4SN_2$, 355.0753).

1-(7-Methoxy-2-oxypyrido[4,3-*b*]indol-5-yl)ethanone (48). A mixture of K_2CO_3 (25 mg, 0.18 mmol) and **43** (24 mg, 0.068 mmol) in THF (5 mL)/H_2O (1 mL) was refluxed for 4 d. The reaction mixture was allowed to cool to room temperature and concentrated to dryness. The residue was dissolved in CH_2Cl_2 and transferred to a short plug of silica gel and eluted with MeOH/EtOAc 3/7. Concentration of the eluent afforded the deprotected *N*-oxide (15 mg, 100%). This material was dissolved in Ac_2O (5 mL)/THF (0.5), sodium acetate (13 mg, 0.16 mmol) was added, and the reaction mixture was stirred at room temperature for 10 h. The excess Ac_2O was coevaporated with toluene, and the residue was dissolved in CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Chromatography (MeOH/EtOAc 3/7) gave **48** (13 mg, 83%) as a white solid: TLC R_f 0.19 (MeOH/EtOAc 3/7); ^{1}H NMR (400 MHz) 8.78 (d, 1H, J = 2), 8.25 (dd, 1H, J = 7, 2), 8.15 (d, 1H, J = 7), 7.84 (d, 1H, J = 9), 7.63 (d, 1H, J = 2), 7.07 (dd, 1H, J = 9, 2), 3.96 (s, 3H), 2.89 (s, 3H); ^{13}C NMR (125 MHz) 169.3, 161.4, 140.9, 136.3, 135.3, 130.4, 124.8, 121.6, 115.4, 113.1, 111.9, 101.7, 55.9, 27.3; HRMS m/z 257.0948 (M + H$^+$) (calcd for $C_{14}H_{13}O_3N_2$, 257.0926).

A similar procedure was followed for *N*-oxide **42** (16 mg), except that the rearrangement reaction with Ac_2O was carried out at 80 °C for 4 h, and gave **47** (10 mg, 85%) as a white solid: mp 225−226 °C (dec) (MeOH/EtOAc); TLC R_f 0.15 (MeOH/EtOAc 3/7); ^{1}H NMR (400 MHz) 8.77 (d, 1H, J = 2), 8.25 (dd, 1H, J = 7, 2), 7.98 (d, 1H, J = 7), 7.82 (s, 1H), 7.29 (s, 1H), 4.04 (s, 3H), 4.036 (s, 3H), 2.90 (s, 3H); ^{13}C NMR (125 MHz) 168.9, 151.4, 147.7, 135.9, 134.63, 134.61, 130.4, 125.2, 114.3, 112.5, 101.6, 100.2, 56.4, 56.38, 27.2; EIMS (relative intensity) m/z 286 (M$^+$, 2), 270 (57), 228 (100), 213 (65), 185 (42), 170 (18), 155 (11), 84 (35), 75 (12).

7,8-Dimethoxy-2,5-dihydropyrido[4,3-*b*]indol-1-one (49). A mixture of *N*-oxide **42** (240 mg, 0.63 mmol) and NaOAc (164 mg, 2.0 mmol) was refluxed in Ac_2O (10 mL) for 24 h. The mixture was allowed to cool to room temperature, and the excess Ac_2O was coevaporated with toluene. The residue was dissolved in CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated to afford a brown residue which was dissolved in MeOH (10 mL), and K_2CO_3 (190 mg, 1.4 mmol) was added. The reaction mixture was stirred for 1−2 h and then concentrated to dryness. The residue was dissolved in dioxane/H_2O (10 mL/0.7 mL) and cooled to 0 °C, and aqueous H_2O_2 (30%, 0.26 mL) was added, followed by aqueous LiOH (0.8 M, 1.2 mL). The reaction mixture was allowed to warm to room temperature over 4 h, and then the reaction was quenched by the addition of saturated aqueous $NaHSO_3$. The solvent was evaporated, and chromatography of the residue (EtOAc/hexanes 2/3 to 4/1 then MeOH/EtOAc 1/9) afforded **49** (83 mg, 54%) as a white solid: mp 270−272.5 °C (dec) (H_2O); TLC R_f 0.33 (MeOH/EtOAc 1/9); ^{1}H NMR (400 MHz, DMSO-d_6) 11.44 (br s, 1H), 11.00 (br s, 1H), 7.57 (s, 1H), 7.17 (d, 1H, J = 7), 7.04 (s, 1H), 6.47 (d, 1H, J = 7), 3.83 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) 159.8, 147.5, 145.0, 143.7, 131.7, 130.2, 116.5, 107.4, 102.7, 95.2, 94.6, 55.8, 55.7; HRMS m/z 245.0939 (M + H$^+$) (calcd for $C_{13}H_{13}O_3N_2$, 245.0926).

A similar procedure starting with *N*-oxide **43** (148 mg) gave **50** (43 mg, 48%) as a white solid: mp 286−287.5 °C (dec) (H_2O); TLC R_f 0.43 (MeOH/EtOAc 1/9); ^{1}H NMR (500 MHz, DMSO-d_6) 11.55 (br s, 1H), 11.04 (br s, 1H), 7.93 (d, 1H, J = 9), 7.21 (d, 1H, J = 7), 6.97 (d, 1H, J = 1), 6.81 (dd, 1H, J = 9, 1), 6.46 (d, 1H, J = 7), 3.80 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) 159.6, 157.0, 144.5, 138.5, 130.9, 121.0, 117.8, 109.6, 107.2, 95.0, 94.4, 55.3; HRMS m/z 214.0721 (M$^+$) (calcd for $C_{12}H_{10}O_2N_2$, 214.0747).

General Procedure D: Formation of Chlorocarbolines 51−54. The starting material was refluxed in $POCl_3$ for 40−41 h. The mixture was cooled to room temperature, the excess $POCl_3$ was removed under vacuum, and 10% aqueous HCl was added to the residue with ice cooling. The resultant slurry was refluxed for 2 h in the case of **51**/**52** and for 30 min in the case

of **53**/**54**. After cooling, the mixture was transferred to a beaker, and solid $NaHCO_3$ was added until a pH of 7−8 was reached. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated.

1-Chloro-7,8-dimethoxy-5*H*-pyrido[4,3-*b*]indole (51). According to general procedure D, lactam **49** (50 mg, 0.20 mmol) gave, after workup and chromatography (MeOH/EtOAc 1/19 to 1/9), **51** (23 mg, 43%) as a white solid: mp 257−258 °C (CH_2Cl_2/hexanes); TLC R_f 0.64 (MeOH/EtOAc 1/9); ^{1}H NMR (400 MHz, DMSO-d_6) 11.96 (br s, 1H), 8.11 (d, 1H, J = 6), 7.79 (s, 1H), 7.47 (d, 1H, J = 6), 7.17 (s, 1H), 3.90 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) 150.3, 144.9, 144.8, 142.3, 141.9, 134.7, 116.6, 111.2, 106.3, 104.1, 95.0, 56.1, 55.7; HRMS m/z 263.0596 (M + H$^+$) (calcd for $C_{13}H_{12}O_2N_2{}^{35}Cl$, 263.0587).

1-Chloro-7-methoxy-5*H*-pyrido[4,3-*b*]indole (52). According to general procedure D, lactam **50** (21 mg, 0.098 mmol) gave, after workup and chromatography (CH_2Cl_2/Et_2O/hexanes 3/3/4), **52** (14 mg, 61%) as a white solid: mp 256−266 °C (CH_2Cl_2/hexanes); TLC R_f 0.11 (CH_2Cl_2/Et_2O/hexanes 3/3/4); ^{1}H NMR (400 MHz, DMSO-d_6) 12.04 (br s, 1H), 8.21 (d, 1H, J = 9), 8.16 (d, 1H, J = 5), 7.49 (d, 1H, J = 5), 7.12 (d, 1H, J = 2), 6.97 (dd, 1H, J = 9, 2), 3.88 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) 159.5, 145.6, 142.7, 142.4, 141.3, 122.7, 116.5, 113.0, 110.0, 106.2, 95.2, 55.4; HRMS m/z 233.0467 (M + H$^+$) (calcd for $C_{12}H_{10}ON_2{}^{35}Cl$, 233.0482).

5-Benzenesulfonyl-1-chloro-7,8-dimethoxy-5*H*-pyrido[4,3-*b*]indole (53). According to general procedure D, *N*-oxide **42** (78 mg, 0.20 mmol) gave, after workup and chromatography (EtOAc/hexanes 2/3) **53** (67 mg, 82%) as a white solid: mp 254.5−255.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.30 (EtOAc/hexanes 2/3); ^{1}H NMR (400 MHz) 8.35 (d, 1H, J = 6), 8.15 (d, 1H, J = 6), 7.92 (s, 1H), 7.88 (s, 1H), 7.82 (d, 2H, J = 8), 7.56 (t, 1H, J = 8), 7.41 (t, 2H, J = 8), 4.10 (s, 3H), 4.02 (s, 3H); ^{13}C NMR (125 MHz) 150.8, 147.6, 144.7, 144.68, 144.0, 137.3, 134.6, 132.7, 129.4, 126.4, 120.5, 115.4, 109.0, 104.2, 97.9, 56.4, 56.3; FABMS m/z 403 (M + H$^+$); HRMS m/z 403.0530 (M + H$^+$) (calcd for $C_{19}H_{16}O_4SN_2{}^{35}Cl$, 403.0519).

5-Benzenesulfonyl-1-chloro-7-methoxy-5*H*-pyrido[4,3-*b*]indole (54). According to general procedure D, *N*-oxide **43** (106 mg, 0.30 mmol) gave, after workup and chromatography (EtOAc/hexanes 1/1), **54** (92 mg, 83%) and **52** (2 mg, 3%) as white solids. Physical and spectral properties of **54**: mp 208−209 °C (CH_2Cl_2/hexanes); TLC R_f 0.51 (EtOAc/hexanes 1/1); ^{1}H NMR (400 MHz) 8.37 (d, 1H, J = 6), 8.32 (d, 1H, J = 9), 8.17 (d, 1H, J = 6), 7.87 (d, 2H, J = 8) overlapping with 7.88 (d, 1H, J = 2), 7.57 (t, 1H, J = 8), 7.43 (t, 2H, J = 8), 7.07 (dd, 1H, J = 9, 2), 3.98 (s, 3H); ^{13}C NMR (100 MHz) 160.8, 144.96, 144.95, 144.2, 139.6, 137.4, 134.7, 129.5, 126.6, 123.8, 120.2, 116.1, 112.8, 108.8, 99.2, 55.9; FABMS m/z 373 (M + H$^+$); HRMS m/z 373.0396 (M + H$^+$) (calcd for $C_{18}H_{14}O_3SN_2{}^{35}Cl$, 373.0414).

***N*-(7,8-Dimethoxy-5*H*-pyrido[4,3-*b*]indol-1-yl)-*N*′,*N*′-dimethylpropane-1,3-diamine (55) and (7,8-Dimethoxy-5*H*-pyrido[4,3-*b*]indol-1-yl)-1,3-(dimethylamino)propyl)carbamic Acid *tert*-Butyl Ester (57).** A solution of **53** (50 mg, 0.12 mmol) in *N*,*N*-dimethyl-1,3-propanediamine (5 mL) was heated to 170 °C for 12 d. The reaction mixture was allowed to cool to room temperature, and the excess amine was removed under reduced pressure. The residue was dissolved in 10% aqueous NaOH and extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (MeOH/EtOAc/Et_3N 4.5/85.5/10) gave **55** as a yellowish solid which was ∼70% pure by NMR. The compound was dissolved in CH_2Cl_2 (3 mL), and DMAP (9 mg, 0.07 mmol) was added followed by $(BOC)_2O$ (37 μL, 0.16 mmol). The reaction mixture was stirred for 30 min, and then the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (MeOH/EtOAc/Et_3N 4.5/85.5/10) afforded BOC derivative **57** (19 mg, 37%) as a white solid: TLC R_f 0.23 (MeOH/EtOAc/Et_3N 4.5/85.5/10); ^{1}H NMR (400 MHz) 8.12 (d, 1H, J = 6), 8.08 (s, 1H), 7.48 (d, 1H, J = 6) overlapping with 7.48 (s, 1H), 6.43 (br s, 1H), 4.03 (s, 3H), 4.02 (s, 3H), 3.80 (br t, 2H, J = 6), 2.56 (t, 2H, J = 6), 2.32 (s, 6H), 1.93 (apparent quintet, 2H, J = 6), 1.77 (s, 9H); ^{13}C NMR (125 MHz) 153.7, 150.7, 149.0, 146.3, 144.4, 144.1, 132.7, 116.7, 106.4, 105.7, 102.0, 100.3, 84.4, 59.7, 58.2, 56.1, 45.8, 42.3, 28.3, 26.1; FABMS m/z 429 (M + H$^+$); HRMS m/z 429.2481 (M + H$^+$) (calcd for $C_{23}H_{33}O_4N_4$, 429.2502).

The BOC derivative **57** (14 mg, 0.033 mmol) was dissolved in EtOAc (4 mL), and concentrated aqueous HCl (1 mL) was added. The reaction mixture was stirred for 48 h and then concentrated to dryness. The residue was dissolved in water, and the pH of the solution was adjusted to 7−8 by the addition of solid $KHCO_3$. The free diamine was extracted with CH_2Cl_2 (3×), and the combined organic extracts were dried (Na_2SO_4) and concentrated. Chromatography (MeOH/EtOAc/Et_3N 4.5/85.5/10) afforded **55** (9 mg, 84%) as a white solid: mp 170−171.5 °C (CH_2Cl_2/hexanes); TLC R_f 0.18 (MeOH/EtOAc/Et_3N 4.5/85.5/10); ^{1}H NMR (400 MHz) 9.17 (br s, 1H), 7.96 (d, 1H, J = 6), 7.54 (s, 1H), 6.96 (s, 1H), 6.73 (d, 1H, J = 6), 6.53 (br s, 1H), 4.02 (s, 3H), 3.93 (s, 3H), 3.83 (t, 2H, J = 6), 2.55 (t, 2H, J = 6), 2.34 (s, 6H), 1.93 (apparent quintet, 2H, J = 6); ^{13}C NMR (125 MHz) 153.6, 149.0, 144.8, 144.4, 141.7, 133.5, 114.1, 106.0, 104.5, 98.0, 94.6, 59.4, 58.4, 56.1, 45.7, 42.1, 26.2; FABMS m/z 329 (M + H$^+$); HRMS m/z 329.1988 (M + H$^+$) (calcd for $C_{18}H_{25}O_2N_4$, 329.1977).

In a similar manner, chlorocarboline **54** (60 mg, 0.16 mmol) gave, after workup and chromatography (MeOH/EtOAc/Et_3N 4.5/85.5/10), **56** as a yellowish solid which was ∼70% pure by NMR. This compound was converted as described above to BOC derivative **58** (37 mg, 58%), a white solid: TLC R_f 0.28 (MeOH/EtOAc/Et_3N 4.5/85.5/10); ^{1}H NMR (400 MHz) 8.12 (d, 1H, J = 6), 7.99 (d, 1H, J = 2), 7.87 (d, 1H, J = 9), 7.48 (d, 1H, J = 6), 7.06 (br s, 1H), 6.99 (dd, 1H, J = 9, 2), 3.94 (s, 3H), 3.79 (br t, 2H, J = 6), 2.62 (t, 2H, J = 6), 2.38 (s, 6H), 1.94 (apparent quintet, 2H, J = 6), 1.77 (s, 9H); ^{13}C NMR (125 MHz) 158.3, 153.6, 150.7, 144.5, 144.3, 138.7, 119.9, 117.8, 111.3, 106.0, 101.6, 100.9, 84.4, 59.8, 55.6, 45.7, 42.7, 28.3, 25.4; FABMS m/z 399 (M + H$^+$); HRMS m/z 399.2411 (M + H$^+$) (calcd for $C_{22}H_{31}O_3N_4$, 399.2396).

The BOC derivative **58** (16 mg, 0.040 mmol) was deprotected as described above, and chromatography (MeOH/EtOAc/Et_3N 4.5/85.5/10) afforded **56** (11 mg, 92%) as a white solid: mp 169.5−170.0 °C (CH_2Cl_2/hexanes); TLC R_f 0.19 (MeOH/EtOAc/Et_3N 4.5/85.5/10); ^{1}H NMR (400 MHz) 9.01 (br s, 1H), 8.00 (d, 1H, J = 6), 7.88 (d, 1H, J = 9), 7.09 (br s, 1H), 6.97 (d, 1H, J = 2), 6.91 (dd, 1H, J = 9, 2), 6.72 (d, 1H, J = 6), 3.89 (s, 3H), 3.83 (t, 2H, J = 6), 2.60 (t, 2H, J = 6), 2.38 (s, 6H), 1.93 (apparent quintet, 2H, J = 6); ^{13}C NMR (125 MHz) 157.8, 153.5, 144.7, 142.2, 139.4, 120.4, 115.8, 108.8, 104.0, 97.6, 95.2, 59.7, 55.6, 45.7, 42.7, 25.6; FABMS m/z 299 (M + H$^+$); HRMS m/z 299.1890 (M + H$^+$) (calcd for $C_{18}H_{25}O_2N_4$, 299.1872).

Acknowledgments. Financial support from the Department of Chemistry at the University of Kansas and the National Science Foundation is gratefully acknowledged. We thank Professors Paul Hanson and Robert Carlson for helpful discussions and guidance during the later stages of this work.

Supporting Information Available: Experimental procedures and spectral data for **A**−**F**/**G** and **59**/**60** and IR and mass spectral data and NMR spectra for all compounds lacking CHN analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9916176