reactions were performed under various conditions as given in Table XI.

Reaction of Ethyl Cyanoacetate with Purified Methylguanidine. Mass spectral analysis of the commercial methylguanidine hydrochloride described above showed that the sets of peaks originated from only methylguanidine but did not the peaks for guanidine and dimethylguanidine as contaminants. Therefore, this commercial one was used for the following reaction. To a methanol solution (6 mL) of methylguanidine hydrochloride (100 mg, 0.91 mmol) were added ethyl cyanoacetate (69 mg, 0.61 mmol) and sodium methoxide (90 mg, 1.64 mmol). The mixture was refluxed for 4 h. The yields of the products of this reaction were determined in the same manner as described above.

Acknowledgment. We are deeply indebted to Dr. Toshifumi Hirata of the Department of Chemistry, Faculty of Science, Hiroshima University, for his assistance with the X-ray crystallography.

Registry No. **2a**, 51093-34-6; **2a**·$^1/_2H_2SO_4$·H_2O, 111291-91-9; **2b**, 111291-90-8; **2b**·$^1/_2H_2SO_4$·H_2O, 111291-93-1; **3**, 89181-81-7; **4**, 56-06-4; **5a**, 111291-89-5; **5b**, 111323-81-0; **6a**, 111291-94-2; **6b**, 111291-95-3; $NCCH_2CO_2CH_2Me$, 105-56-6; $MeNHC(=NH)NH_2$, 471-29-4; $MeNH_2$.HCl, 593-51-1; $H_2NC(=NH)NHCN$, 461-58-5; $H_2NC(=NH)NH_2$, 113-00-8; $Me_2NC(=NH)NH_2$, 3324-71-8.

Supplementary Material Available: Tables VII and VIII, atomic coordinates and bond lengths and angles for **2a** hemisulfate (3 pages). Ordering information is given on any current masthead page.

Conformational Effects on the Oxidative Coupling of Benzyltetrahydroisoquinolines to Morphinane and Aporphine Alkaloids

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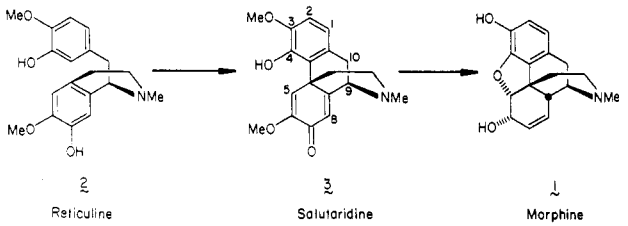
Conformationally rigid 1-benzyltetrahydroisoquinolines **7a** and **7b** were prepared. Oxidation of **7a** with vanadium oxychloride or thallium(III) trifluoroacetate gave structures related to aporphine alkaloids as did oxidation of **7b** with vanadium oxyfluoride. Oxidation of **7a** with (diacetoxyiodo)benzene gave a mixture of structures related to aporphine and morphinane alkaloids.

A great deal of effort has been expended toward developing laboratory syntheses of the alkaloid morphine **1**. Much of this effort has focused on mimicry of the biosynthetic pathway, in particular on the key step in the biosynthesis, the oxidative phenolic coupling of reticuline **2** to salutaridine **3** (Scheme I).[1,2] This oxidative coupling step can, in principle, give salutaridine (**3**), isosalutaridine (**4**), isoboldine (**5**), and corytuberine (**6**) (Figure 1). Reticuline or *N*-acyl-*N*-norreticuline derivatives have been treated with a variety of oxidants to achieve a wide range of yields of these four possible products.[3-6] Several theories have been offered to explain the regiochemical outcome of these studies, including coordination effects,[1b] anion effects,[3b] and steric interactions.[3d] The purpose of this study was to examine conformational effects that may influence the partitioning of benzyltetrahydroisoquinolines between morphinanes and aporphines upon oxidation.

If one examines molecular models, it is evident that reticuline can adopt two conformations, one in which the benzyl side chain is equatorially disposed (**2e**) or one in which it is axially disposed (**2a**) (Scheme II). Conformer **2e** can only lead to aporphines, whereas conformer **2a** can afford both aporphines and morphinanes. Spectroscopic evidence for the conformational equilibrium of benzyltetrahydroisoquinolines has been presented by Cava and Fraenkel.[7] Given that this conformational equilibrium may well be in effect, it was the purpose of this study to determine whether the conformation of reticuline controls the eventual product distribution.[8] Specifically, does conformation **2a** in which the benzyl group is axially disposed lead to morphinanes only, or both morphinanes and aporphines? To answer this question, we decided to prepare compounds **7a**, **7b**, and **11c** in which the benzyl group is axially disposed, and examine their behavior in oxidative phenolic coupling reactions.[9]

Scheme I



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‡ Alfred P. Sloan Foundation Fellow, 1983-1987.

(1) (a) Barton, D. H. R.; Kirby, G. W.; Stelich, W.; Thomas, G. M.; Battersby, A. R.; Dobson, T. A.; Ramuz, H. *J. Chem. Soc.* **1965**, 2423. (b) Barton, D. H. R.; Bhakuni, D. S.; James, R.; Kirby, G. W. *J. Chem. Soc. C* **1967**, 128.

(2) For reviews on oxidative coupling reactions, see: (a) Tobinaga, S. *Bioorganic Chem.* **1975**, *4*, 110. (b) Sainsbury, M. *Tetrahedron* **1980**, *36*, 3327. (c) Kametani, T.; Fukumoto, K.; Satoh, F. *Bioorganic Chem.* **1974**, *3*, 430. (d) Kametani, T.; Fukumoto, K. *Synthesis* **1972**, 657.

(3) Salutaridine, see ref 1b and the following: (a) Schwartz, M. A.; Mami, I. S. *J. Am. Chem. Soc.* **1975**, *97*, 1239. (b) Szántay, C.; Blaskó, G.; Bárczai-Beke, M.; Pechy, P.; Dörnyei, G. *Tetrahedron Lett.* **1980**, *21*, 3509. (c) White, J. D.; Carvatti, G.; Kline, T. B.; Edstrom, E.; Rice, K. C.; Brossi, A. *Tetrahedron* **1983**, *39*, 2393. (d) Vanderlaan, D. G.; Schwartz, M. A. *J. Org. Chem.* **1985**, *50*, 743.

(4) Isosalutaridine: (a) Franck, B.; Dunkelmann, G.; Lubs, H. J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1075. (b) Kametani, T.; Fukumoto, K.; Kozuka, A.; Yagi, H.; Koizumi, M. *J. Chem. Soc. C* **1969**, 2034. (c) Kametani, T.; Sugahara, T.; Yagi, H.; Fukumoto, K. *Tetrahedron* **1969**, *25*, 3667. (d) Kametani, T.; Kozuka, A.; Fukumoto, K. *J. Chem. Soc. C* **1971**, 1021. (e) Bobbitt, J. M.; Noguchi, I.; Ware, R. S.; Chiong, K. N.; Huang, S. J. *J. Org. Chem.* **1975**, *40*, 2924. (f) Blaskó, G.; Dörnyei, G.; Bárczai-Beke, M.; Pechy, P.; Szántay, C. *J. Org. Chem.* **1984**, *49*, 1439.

(5) Isoboldine, see references 3a, 3d, 4a-4d, and the following: (a) Chan, W. W.-C.; Maitland, P. *J. Chem. Soc. C* **1966**, 753. (b) Schwartz, M. A. *Synth. Commun.* **1973**, *3*, 33.

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(7) (a) Dalton, D. R.; Cava, M. P.; Buck, K. T. *Tetrahedron Lett.* **1965**, 2687. (b) Fraenkel, G.; Cava, M. P.; Dalton, D. R. *J. Am. Chem. Soc.* **1967**, *89*, 329.

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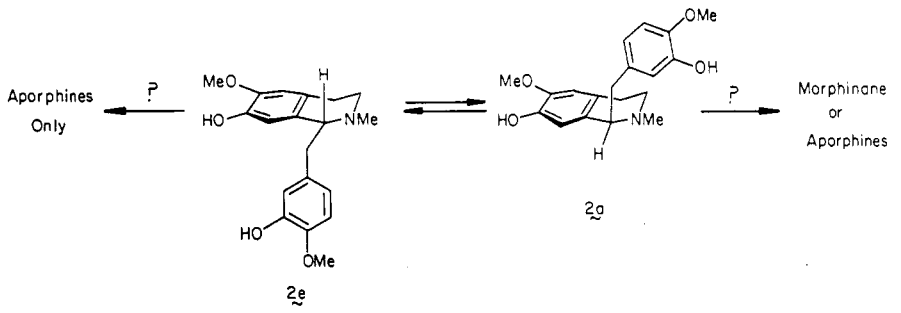
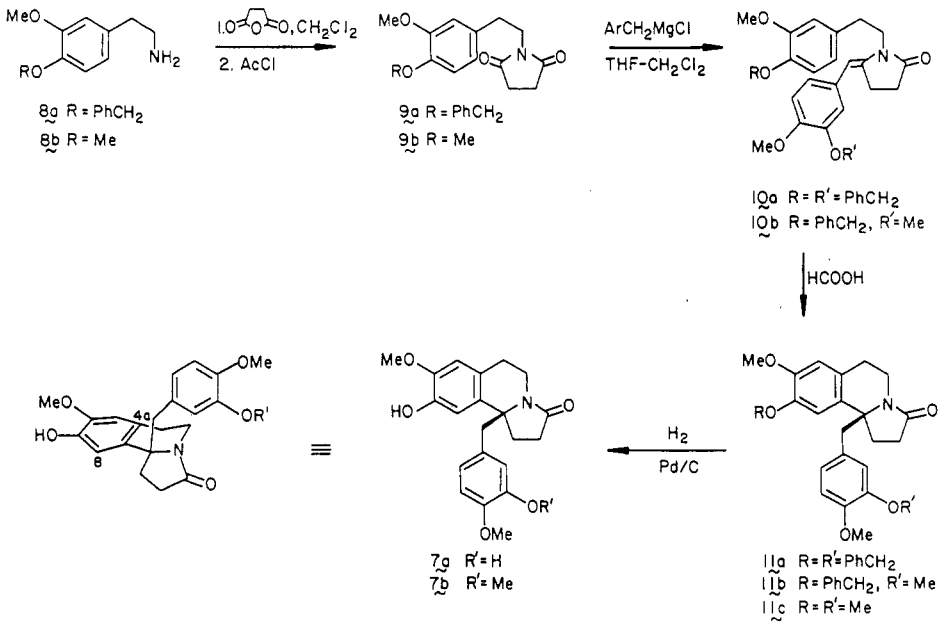
Scheme II



Scheme III



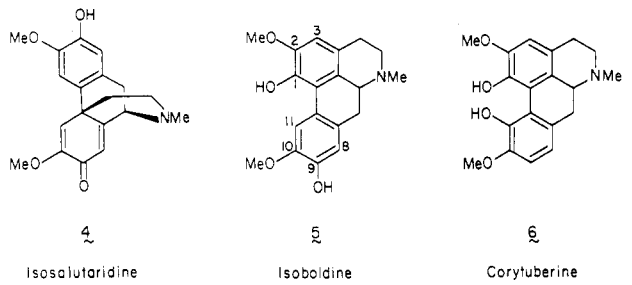


Figure 1.

Preparation of Oxidation Substrates

The preparation of oxidation substrate **7a** was accomplished through the coupling of an *N*-(2-arylethyl)imide and an appropriately substituted benzyl Grignard reagent, followed by intramolecular *N*-acyliminium ion ring closure (Scheme III).[10] Thus, imide **9a** was prepared from the known amine **8a**[11] by sequential treatment with succinic anhydride and acetyl chloride. The addition of an ethereal solution [3-(benzyloxy)-4-methoxybenzyl]magnesium chloride to a dichloromethane solution of imide **9a** gave a 33% yield of enamide **10a** after chromatography.[12] Enamide **10a** was then treated with anhydrous formic acid to give tetrahydroisoquinoline **11a** in 93% yield after purification. By far the most efficient preparation of isoquinoline **11a** was accomplished by treating the crude product of the Grignard reaction with anhydrous formic acid followed by purification of the resulting product. In this way, tetrahydroisoquinoline **11a** could be prepared in 49% overall yield from imide **9a**. Catalytic hydrogenation of **11a** over palladium on charcoal afforded oxidation substrate **7a** in quantitative yield.

To examine the mono- and nonphenolic oxidation of conformationally constrained benzyltetrahydroisoquinolines, we prepared the corresponding mono- and nonphenolic analogues of isoquinoline **7a** by using the same synthetic strategy described above. The phenol **7b** was prepared in three steps from imide **9a** (Scheme III). Thus, imide **9a** was treated with (3,4-dimethoxybenzyl)magnesium chloride in tetrahydrofuran and dichloromethane to give enamide **10b** in 29% yield. Treatment of enamide **10b** with anhydrous formic acid gave tetrahydroisoquinoline **11b**, which was deprotected with hydrogen over palladium on carbon to give the oxidation substrate **7b** in a quantitative yield from **10b**. Once again, the most efficient laboratory procedure involved treating the crude product of the Grignard reaction with formic acid. In this way, tetrahydroisoquinoline **11b** could be prepared in 40% overall yield from imide **9a**.

(8) For relevant discussions of this problem, see: Krejcarek, G. K.; Dominy, B. W.; Lawton, R. G. *J. Chem. Soc. D* **1968**, 1450. Corey, E. J., *Pure Appl. Chem.* **1967**, *14*, 19.

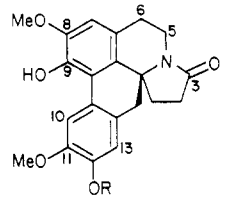
(9) To maintain amide resonance in the pyrrolidinone, the benzylic group in **7a** and **7b** must occupy a pseudoaxial site on the tetrahydroisoquinoline moiety. Rotation around the C(1)-benzylic carbon–carbon bond permits the benzyl group to freely pass over C(4a) and C(8) of the tetrahydroisoquinoline.

(10) Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367.

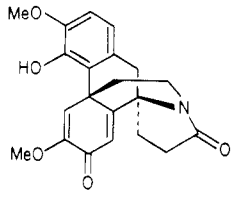
(11) Harmon, R. E.; Jensen, B. L. *J. Heterocycl. Chem.* **1970**, *7*, 1077.

(12) Evans, D. A.; Thomas, E. W.; Cherpeck, R. E. *J. Am. Chem. Soc.* **1982**, *104*, 3695.

Table I. Oxidation of 7a and 7b



12a R=H
12b R=Me



13

entry	substrate	conditions	product (% yield)
1	**7a**	$VOCl_3$, CH_2Cl_2	**12a** (67), **7a** (10)
2	**7a**	$PhI(OAc)_2$, CF_3CO_2H, CH_2Cl_2	**12a** (66), **13**(4), **7a** (25)
3	**7a**	$Tl(OCOCF_3)_3$, CH_2Cl_2	**12a** (15), **7a** (46)
4	**7b**	VOF_3, CF_3CO_2H, $(CF_3CO)_2O$, CH_2Cl_2	**12b** (63), **7b** (14)

Finally, sequential treatment of the known amine **8b**[13] with succinic anhydride and acetyl chloride followed by formic acid cyclization gave the nonphenolic oxidation substrate **11c** in 58% overall yield.

Oxidation Studies

Having the three substrates in hand, we turned our attention to their oxidation chemistry (Table I). We first examined the bisphenol oxidation substrate **7a** with vanadium oxychloride under Schwartz's conditions.[3a] Thus, isoquinoline **7a** was treated with 3.3 equiv of vanadium oxychloride in dry dichloromethane to give a 67% yield of isoboldine analogue **12a** along with 10% of recovered starting material after chromatography. This compound was easily identified by its characteristic proton NMR spectrum. At 500 MHz, each proton was resolved with the resonance at δ 8.11 clearly due to the C(10)-H [corresponding to C-11 of isoboldine (**5**)] exhibiting the deshielding effects of both the aryl ring and the proximate OH. This result is entirely consistent with Schwartz's observations in the corresponding oxidations of reticuline and *N*-(trifluoroacetyl)-*N*-norreticuline.[3a,5b] Since we observed no morphinane products in this reaction, this result was construed as evidence that the axial disposition of the benzyl group does not lead specifically to morphinane products, nor does it necessarily even enhance that reaction pathway.

We next used iodosobenzene diacetate, an oxidant known to give morphinanes in oxidations of reticuline derivatives.[3b,3d] Thus, bisphenol **7a** was oxidized with iodosobenzene diacetate according to the procedure of Vanderlaan and Schwartz[3d] to give a 66% yield of isoboldine analogue **12a** along with 4% of salutaridine derivative **13** and 25% of recovered starting material.[14] Salutaridine derivative **13** was easily identified by its ^1H NMR and IR spectra (1675, 1645, and 1625 cm^{-1}).

These results show that both coupling sites on the isoquinoline moiety are accessible to a benzyl group locked in a pseudoaxial conformation. In fact, in the oxidation of **7a**, a larger percentage of isoboldine-type products was obtained than in Schwartz's studies.[14] This observation may be due to a steric interaction between the benzyl group and the C(5) hydrogens of the isoquinoline moiety, an idea examined by McDonald and Schwartz.[3d,15]

Bisphenol **7a** was also oxidized with thallium tris(trifluoroacetate) in dichloromethane to give 15% of isoboldine analogue **12a** along with 46% of recovered starting material. In contrast to Schwartz's results with *N*-(trifluoroacetyl)-*N*-norreticuline and *N*-(ethoxycarbonyl)-*N*-norreticuline, we did not observe any of the salutaridine derivative **13**.[3a]

The monophenolic oxidation of isoquinoline **7b** was also examined. Thus, monophenol **7b** was treated with 2.5 equiv of vanadium oxyfluoride in the presence of trifluoroacetic acid–trifluoroacetic anhydride (20:1) in dichloromethane at −5 °C for 0.5 h according to the procedure of Kupchan[16] to give 63% of isoboldine analogue **12b** as well as 14% of recovered starting material. In contrast to our results, Kupchan observed a small percentage of morphinane-type products in similar reactions. A possible explanation for our lack of such products may lie in the acid-catalyzed rearrangement of morphinane dienones to aporphines as noted by Kupchan.[17]

Finally, the electrochemical oxidation of nonphenolic substrate **11** was briefly examined. The electrochemical oxidations of **11c** were performed with a 0.1 M solution of lithium perchlorate in acetonitrile. Attempted oxidation of substrate **11c** at +1.30 V vs Ag/AgCl by using a controlled potential electrolysis gave only recovered starting material.[18] Oxidation at +1.56 V, however, gave 3,4-dimethoxybenzyl alcohol (10%) and 3,4-dimethoxybenzaldehyde (36%), in addition to recovered starting material (21%). These products probably arise from oxidation of the benzyl group to a radical cation followed by nitrogen lone pair assisted benzylic cleavage and subsequent oxidation of the resulting benzylic radical. A similar cleavage process was observed by Miller during electrochemical oxidation of *N*-formyllaudanosine.[19,20]

In summary, a variety of conformationally constrained tetrahydroisoquinolines have been prepared, and their oxidation chemistry has been examined. The studies show that the axial–equatorial conformational equilibrium of reticuline derivatives has very little to do with the partitioning of products between the morphinane and aporphine pathways. Thus, both aporphines and morphinanes are obtained when the benzyl moiety is locked in a pseudoaxial conformation.

Experimental Section

All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected as are boiling points. ^1H nuclear magnetic resonance spectra were recorded on Varian Associates EM-390, Varian Associates EM-360, Bruker WP-200, or Bruker WP-500 spectrometers and are reported in parts per million from internal tetramethylsilane on the δ scale. Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, se = septet, m = multiplet), coupling constants in hertz, integration, interpretation]. Infrared spectra were taken with a Perkin-Elmer 457 instrument. Infrared spectra denoted (NaCl) were performed by air-drying a solution of the material on a sodium chloride plate. Mass spectra were recorded on a Kratos MS-30 instrument at an

(13) Kindler, K.; Hedeman, B.; Scharfe, E. *Justus Liebigs Ann. Chem.* **1948**, *560*, 215.

(14) This result compares with 18% of *N*-carbethoxy-*N*-norisoboldine and 22% of *N*-carbethoxy-*N*-norsalutaridine observed by Schwartz (see ref. 3d).

(15) (a) McDonald, E.; Suksamararn, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 440. (b) McDonald, E.; Suksamararn, A. *Tetrahedron Lett.* **1975**, 4421.

(16) (a) Kupchan, S. M.; Dhingra, O. P.; Kim, C.-K. *J. Org. Chem.* **1978**, *43*, 4076. (b) Kupchan, S. M.; Dhingra, O. P.; Kim, C.-K. *J. Org. Chem.* **1976**, *41*, 4049.

(17) Kupchan, S. M.; Kim, C.-K. *J. Am. Chem. Soc.* **1975**, *97*, 5623.

(18) Cyclic voltammetry of **11c** vs Ag/AgCl with 0.1 M lithium perchlorate in acetonitrile as an electrolyte showed oxidation potentials at 0.96, 1.28, 1.48, and 1.69 V ([**11c**] = 10^{-3} M).

(19) Miller, L. L.; Stewart, R. F.; Gillespie, J. P.; Ramachandran, V.; So, Y. H.; Stermitz, F. R. *J. Org. Chem.* **1978**, *43*, 1580.

(20) Kulnenberg, H.; Schaffer, C.; Schafer, H.-J. *Tetrahedron Lett.* **1982**, *23*, 4581.

ionization energy of 70 eV. Samples on which exact masses were measured exhibited no significant peaks at m/e greater than those of the parent. Combustion analysis were performed by Micro-Analysis, Inc., Wilmington, DE.

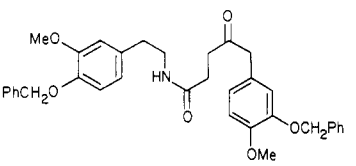
Solvents and reagents were dried and purified prior to use when deemed necessary: tetrahydrofuran, diethyl ether (distilled from Na metal); dichloromethane (passed through activity I alumina). All reaction temperatures refer to those of the reaction mixture. Reactions requiring an inert atmosphere were run under a blanket of nitrogen or argon. Formic acid (97%) was used in all cyclizations. Analytical thin-layer chromatography was performed with EM Laboratories 0.25-mm-thick precoated silica gel 60F-254 plates. Preparative thin-layer chromatography was performed with EM Laboratories 2-mm-thick precoated silica gel 60F-254 plates. Column chromatography was performed over EM Laboratories silica gel (70–230 mesh). Medium-pressure liquid chromatography (MPLC) was performed with EM Laboratories Lobar prepacked silica gel columns. Radial disk chromatography was performed on 1, 2, or 4 mm thick × 7 cm wide silica gel plates.

***N*-[2-(4-(Benzyloxy)-3-methoxyphenyl)ethyl]succinimide (9a).** To a solution of 10.17 g (102 mmol) of succinic anhydride in 190 mL of dry dichloromethane was added 13.05 g (51.0 mmol) of amine **8a**[11] in 96 mL of dry dichloromethane. The mixture was strirred at room temperature for 116 h, 40.0 g (0.51 mol) of acetyl chloride was added, and the mixture was stirred an additional 48.5 h under reflux. The mixture was concentrated in vacuo, and the residue was chromatographed over 300 g of silica gel (eluted with ethyl acetate–hexane, 1:1) to give 6.31 g of imide **9a** (mp 97–99 °C) and 8.48 g of additional imide **9a** (mp 108–112 °C). The lower melting fraction was recrystallized from ethyl acetate–hexane (1:2) to give 5.18 g (79% total) of imide **9a** as clear needles: mp 115–117 °C; IR (NaCl) 1700, 1150 cm^{-1}; NMR ($CDCl_3$) δ 2.60 (s, 4 H, CH_2CO), 2.80 (m, 2 H, $ArCH_2$), 3.70 (m, 2 H, NCH_2), 3.88 (s, 3 H, OCH_3), 5.10 (s, 2 H, OCH_2Ph), 6.35–7.08 (m, 3 H, Ar H), 7.20–7.60 (, 5 H, Ar H); mass spectrum, m/e (relative intensity) 339 (M^+, 27), 91 (100); exact mass calcd for $C_{20}H_{21}NO_4$ m/e 339.1470, found m/e 339.1501. Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24. Found: C, 70.68; H, 6.01.

***N*-[2-[4-(Benzyloxy)-3-methoxyphenyl]ethyl]-5-[(3-(benzyloxy)-4-methoxyphenyl)methylidene]-2-pyrrolidinone (10a).** To a solution of 2.40 g (7.0 mmol) of succinimide **9a** in 18 mL of dry dichloromethane was added 23 mL (7.13 mmol) of [3-(benzyloxy)-4-methoxybenzyl]magnesium chloride (0.31 M) over a period of 5 min via syringe. The mixture was stirred for 10 min at room temperature followed by addition of 95 mL of saturated aqueous ammonium chloride. The organic layer was separated, and the aqueous layer was washed with two 30-mL portions of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give 4.20 g of a tacky yellow oil. The oil was crystallized from ethanol–ethyl acetate–hexane (5:2:1) to give 1.25 g (33%) of enamide **10a** as a white powder: mp 151–153 °C; IR (NaCl) 1708, 1650, 1225 cm^{-1}; NMR ($CDCl_3$) δ 2.44 (m, 2 H, CH_2CO), 2.65 (m, 2 H, $CH_2C{=}C$), 2.82 (t, J = 7, 2 H, $ArCH_2$), 3.78 (t, J = 7, 2 H, NCH_2), 3.88 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.12 (s, 2 H, OCH_2Ph), 5.18 (s, 2 H, OCH_2Ph), 5.5 (s, 1 H, =CH), 6.62–6.95 (m, 6 H, Ar H), 7.20–7.50 (m, 10 H, Ar H); mass spectrum, m/e (relative intensity) 549 (M^+, 9), 91 (100); exact mass calcd for $C_{35}H_{35}NO_5$ m/e 549.2514, found m/e 549.2516. Anal. Calcd for $C_{35}H_{35}NO_5$: C, 76.48; H, 6.42. Found: C, 75.97; H, 6.42.

1,5,6,10b-Tetrahydro-8-methoxy-10b-[[4-methoxy-3-(phenylmethoxy)phenyl]methyl]-9-(phenylmethoxy)pyrrolo-[2,1-*a*]isoquinolin-3(2*H*)-one (11a). From 10a. A solution of 1.50 g (2.79 mmol) of enamide **10a** in 14 mL of anhydrous formic acid was stirred for approximately 3 min at room temperature. The formic acid was then removed in vacuo, and the residue was dissolved in 40 mL of dichloromethane. The resulting solution was washed with 30 mL of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo to give 1.49 g (99.5%) of crude **11a**. Radial disk chromatography (silica gel; 2 mm × 7 cm; eluted with ethyl acetate–hexane, 5:1) gave 1.38 g (93%) of dibenzyl ether **11a** as a white solid: mp 119.0–120.5 °C; IR (NaCl) 1680, 1260, 1140 cm^{-1}; NMR ($CDCl_3$) δ 1.54–2.14 (m, 4 H, CH_2CH_2CO), 2.54–3.00 (m with AB q at 2.61 and 2.96, J_{AB} = 13.7, 5 H, $ArCH_2$, $ArCH_2CHN$), 3.87 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.21–4.36 (m, 1 H, CHN), 4.99 and 5.11 (AB q, J_{AB} = 12.7, 2 H, OCH_2Ph), 5.12 (s, 2 H, OCH_2Ph), 6.45 (d, J = 2.4, 1 H, Ar H), 6.51 (s, 1 H, Ar H), 6.53 (dd, J = 2.4, 8.5, 1 H, Ar H), 6.58 (s, 1 H, Ar H), 6.78 (d, J = 8.5, 1 H, Ar H), 7.28–7.50 (m, 10 H, Ph); mass spectrum, m/e (relative intensity) 322 (100), 232 (13), 231 (13), 217 (2), 137 (2), 91 (13), 77 (2), 65 (3). Anal. Calcd for $C_{35}H_{35}NO_5$: C, 76.48; H, 6.42. Found: C, 76.68; H, 6.86.

From Imide 9a: To a solution of 7.71 g (22.7 mmol) of imide **9a** in 76 mL of dry dichloromethane under argon was added 119.5 mL (22.7 mmol) of a 0.19 M solution of [3-(benzyloxy)-4-methoxybenzyl]magnesium chloride in tetrahydrofuran. The mixture was stirred for 3 h and quenched with 80 mL of saturated ammonium chloride. The aqueous layer was extracted with two 40-mL portions of dichloromethane, and the combined organic layers were filtered through sodium sulfate and dried ($MgSO_4$). The mixture was concentrated in vacuo to give 16.0 g of a tacky yellow oil. This oil was dissolved in 37 mL of anhydrous formic acid for 15 min. The acid was removed in vacuo, and the residue was dissolved in 100 mL of dichloromethane. The solution was washed with two 30-mL portions of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo to give a red-brown oil. This oil was chromatographed over 150 g of silica gel (eluted with ethyl acetate–hexane, 2:1, progressing to ethyl acetate) to give 13.6 g of a mixture of products as a red oil. This oil was subjected to radial disk chromatography over silica gel (4-mm thickness, eluted with ethyl acetate–hexane, 2:1, progressing to ethyl acetate) to give 1.79 g (14%) of ring-opened amide **i** as a white solid: mp 93–98 °C; IR ($CHCl_3$) 3340, 1705, 1660, 1505 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30 (t, J = 6.5, 2 H, NCH_2CH_2), 2.70 (t, J = 6.5, 4 H, $C(O)CH_2CH_2$), 3.44 (q, J = 6.5, 2 H, CH_2N), 3.59 (s, 2 H, $ArCH_2C(O)$), 3.86 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 5.12 (s, 4 H, CH_2Ph), 5.59 (br s, 1 H, NH), 6.62–6.86 (m, 6 H, Ar H), 7.28–7.47 (m, 10 H, Ar H); mass spectrum, m/e (relative intensity) 567 (M^+, 5), 91 (100); exact mass calcd for $C_{35}H_{37}NO_6$ m/e 567.2621, found m/e 567.2607. Further elution gave 6.11 g (49%) of tetrahydroisoquinoline **11a** as a white solid (mp 116.5–117.5 °C).



1,5,6,10b-Tetrahydro-9-hydroxy-10b-[(3-hydroxy-4-methoxyphenyl)methyl]-8-methoxypyrrolo[2,1-*a*]isoquinolin-3-(2*H*)-one (7a). A mixture of 0.45 g of 5% palladium on charcoal, 4.60 g (8.38 mmol) of dibenzyl ether **11a**, and 210 mL of ethanol–ethyl acetate (2:1) was hydrogenated at 60 psi of H_2 for 56 h with a Parr apparatus. The mixture was filtered through Celite and concentrated in vacuo to give 3.09 g (100%) of bisphenol **7a** as an off-white powder: mp 203–204 °C dec; IR (NaCl) 3300 (br), 1660, 1250, 1040 cm^{-1}; NMR ($CDCl_3$) δ 1.49–1.60 (m, 1 H), 1.8–2.1 (m, 2 H), 2.40–3.16 (m with AB q at 2.79 and 3.10, J_{AB} = 13, 6 H, $ArCH_2$, $NCHH$, $ArCH_2CH_2$), 3.85 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.26–4.41 (m, 1 H, $NCHH$), 5.65 (s, 1 H, OH), 5.67 (s, 1 H, OH), 6.48–6.80 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 232 (100), 217 (9), 137 (5). Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28. Found: C, 68.09; H, 6.15.

***N*-[2-[4-(Benzyloxy)-3-methoxyphenyl]ethyl]-5-[(3,4-dimethoxyphenyl)methylidene]-2-pyrrolidinone (10b).** To a solution of 500 mg (1.50 mmol) of succinimide **9a** in 5 mL of freshly dried dichloromethane was added 5.2 mL (1.71 mmol) of (3,4-dimethoxybenzyl)magnesium chloride (0.33 M) via a syringe under an argon atmosphere. The reaction was stirred at room temperature for 45 min followed by addition of 20 mL of saturated aqueous ammonium chloride. The aqueous layer was extracted with two 15-mL portions of dichloromethane. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to give 0.86 g of a yellow oil. The oil was passed over 3 g of silica gel (eluted with ethyl acetate) and subjected to radial disk chromatography over silica (4-mm thickness, eluted with ethyl acetate–hexane, 3:1). Isolation of the most intense band gave a yellow oil, which was triturated with ether to give 247 mg (mp 84–89 °C) of a solid. Two recrystallizations from ethanol gave

207 mg (29%) of lactam **10b** as a yellow fluffy solid: mp 119–121 °C; IR ($CHCl_3$) 1710, 1650, 1260 cm^{-1}; NMR ($CDCl_3$) δ 2.47–2.63 (m, 2 H, $ArCH_2CH_2N$), 2.82–2.97 (m, 4 H, CH_2CH_2CO), 3.78–3.85 (m, 2 H, NCH_2), 3.88 (s, 3 H, OCH_3), 3.89 (s, 6 H, OCH_3), 5.12 (s, 2 H, OCH_2Ph), 5.73 (s, 1 H, =CH), 6.70–6.87 (m, 6 H, Ar H), 7.27–7.45 (m, 5 H, Ar H); mass spectrum, *m/e* (relative intensity) 473 (M^+, 15), 91 (100); exact mass calcd for $C_{29}H_{31}NO_5$ *m/e* 473.2202, found *m/e* 473.2162.

1,5,6,10b-Tetrahydro-8-methoxy-10b-[(3,4-dimethoxyphenyl)methyl]-9-(phenylmethoxy)pyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (11b). From 10b. A solution of 36 mg (0.076 mmol) of enamide **10b** in 3 mL of anhydrous formic acid was stirred at room temperature for 10 min. The formic acid was then removed in vacuo, and the residue was dissolved in 5 mL of dichloromethane. The resulting solution was washed with 5 mL of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo to give 36 mg (100%) of lactam **11b** as an off-white powder: mp 152.0–153.0 °C; IR (NaCl) 1680, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68–2.46 (m, 4 H, CH_2CH_2CO), 2.53–3.12 (m with AB q at 2.72 and 3.05, J_{AB} = 13.3, 5 H, $ArCH_2$, $ArCH_2CHN$), 3.78 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.10–4.38 (m, 1 H, CHN), 5.13 (s, 2 H, OCH_2Ph), 6.37–6.82 (m, 5 H, Ar H), 7.30–7.51 (m, 5 H, Ar H); mass spectrum, *m/e* (relative intensity) 322 (100), 232 (21), 231 (36), 202 (31), 151 (13), 91 (42), 77 (7), 65 (16), 51 (6), 39 (11). Anal. Calcd for $C_{29}H_{31}NO_5$: C, 73.55; H, 6.60. Found: C, 72.75; H, 6.46.

From Imide 9a. To a solution of 11.52 g (34 mmol) of imide **9a** in 113 mL of dry dichloromethane under argon was added 130 mL (34 mmol) of a 0.26 M solution of (3,4-dimethoxybenzyl)-magnesium chloride in tetrahydrofuran. The mixture was stirred at room temperature for 7 h and quenched with 100 mL of saturated ammonium chloride. The aqueous layer was extracted with two 50-mL portions of dichloromethane, and the combined organic layers were filtered through sodium sulfate and dried ($MgSO_4$). The mixture was concentrated in vacuo to give 16.6 g of a dark yellow oil. This oil was dissolved in 39 mL of anhydrous formic acid for 15 min. The acid was removed in vacuo, and the residue was dissolved in 100 mL of dichloromethane. The solution was washed with two 50-mL portions of saturated aqueous sodium bicarbonate solution, dried ($MgSO_4$), and concentrated in vacuo to give 14.9 g of a dark green oil. This oil was chromatographed over 150 g of silica gel (eluted with ethyl acetate–hexane, 4:1, progressing to ethyl acetate) to give 7.65 g (48%) of tetrahydroisoquinoline **11b** as a white solid (mp 152.0–153.0 °C).

1,5,6,10b-Tetrahydro-9-hydroxy-10b-[(3,4-dimethoxyphenyl)methyl]-8-methoxypyrrolo[2,1-*a*]isoquinolin-3-(2*H*)-one (7b). A mixture of 400 mg of 5% palladium on charcoal, 2.00 g (4.2 mmol) of benzyl ether **11b**, and 200 mL of ethanol–ethyl acetate (1:1) was hydrogenated at 60 psi of H_2 on a Parr hydrogenation apparatus for 12 h. The mixture was filtered through Celite and concentrated in vacuo to give an opaque gray oil. This oil was filtered through 10 g of silica gel (eluted with ethyl acetate) to give 1.60 g (100%) of hydroxy lactam **7b** as a white foamy solid: mp 166.5–167.0 °C; IR (KBr) 3450, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65 (dt, *J* = 16, 10, 1 H), 2.0 (m, 1 H), 2.08 (m, 1 H), 2.45 (dd, *J* = 12, 8, 1 H), 2.60 (dd, *J* = 16, 6, 1 H, ArCH), 2.83 (d, *J* = 14, 1 H, ArCH), 2.85 (m, 1 H), 2.97 (td, *J* = 13, 4.5, 1 H), 3.14 (d, *J* = 14.0, 1 H, ArCH), 3.78 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.87 (s, 3 H, OMe), 4.30 (ddd, *J* = 13, 6, 2, 1 H, CHN), 5.66 (s, 1 H, OH), 6.48 (d, *J* = 2, 1 H, Ar H), 6.54 (s, 1 H, Ar H), 6.62 (dd, *J* = 6, 2, 1 H, Ar H), 6.76 (d, *J* = 6, 1 H, Ar H), 6.77 (s, 1 H, Ar H); mass spectrum, *m/e* (relative intensity 233 (17), 232 (100), 217 (14), 189 (6), 119 (5), 107 (5), 70 (7). Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.91; H, 6.57. Found: C, 68.62; H, 6.74.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]succinimide (9b).** To a solution of 3.0 g (30 mmol) of succinic anhydride in 66 mL of dry dichloromethane was added 2.80 g (15 mmol) of amine **8b**[13] in 20 mL of dry dichloromethane. The mixture was stirred at room temperature for 19.5 h, 11.8 g (0.15 mol) of acetyl chloride was added, and the mixture was stirred an additional 90 h at room temperature. The mixture was concentrated in vacuo, and the residue was chromatographed over 150 g of silica gel (eluted with ethyl acetate) to give 2.58 g (65%) of succinimide **9b** as a blue green solid. This material was recrystallized from ethyl acetate–hexane (1:1) to give 1.37 g of imide **9b** (mp 126.5–127.5 °C) and 1.10 g of imide **9b** (mp 122.0–126.0 °C): IR ($CHCl_3$) 1770, 1700, 1150 cm^{-1}; NMR ($CDCl_3$) δ 2.58 (s, 4 H, $COCH_2CH_2CO$), 2.80 (m, 2 H, $ArCH_2$), 3.62 (m, 2 H, NCH_2), 3.81 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 6.68 (br s, 3 H, Ar H); mass spectrum, *m/e* (relative intensity) 263 (M^+, 23), 164 (100), 151 (52); exact mass calcd for $C_{14}H_{17}NO_4$ *m/e* 263.1157, found *m/e* 263.1181. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.85; H, 6.51. Found: C, 63.56; H, 6.39.

1,5,6,10b-Tetrahydro-8,9-dimethoxy-10b-[(3,4-dimethoxyphenyl)methyl]pyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one (11c). To a mixture of 5.45 g (21 mmol) of imide **9b** in 69 mL of dry dichloromethane under argon was added 101 mL (21 mmol) of a 0.205 M tetrahydrofuran solution of (3,4-dimethoxybenzyl)-magnesium chloride, and the mixture was stirred for 3 h at room temperature. The reaction was quenched with 100 mL of saturated aqueous ammonium chloride, and the aqueous layer was extracted with two 50-mL portions of dichloromethane. The combined organic layers were filtered through Na_2SO_4, dried ($MgSO_4$), and concentrated in vacuo to give 10.5 g of a dark yellow oil. The oil was dissolved in 100 mL of anhydrous formic acid and stirred for 30 min. The acid was removed in vacuo, and the residue was dissolved in 100 mL of dichloromethane. The solution was washed with two 50-mL portions of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo to give 9.41 g of a brown oil. The oil was chromatographed over 300 g of silica gel (eluted with ethyl acetate) to give 4.68 g (58%) of lactam **11c** as a light pale green solid: mp 130.0–130.5 °C; IR ($CDCl_3$) 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.73 (dt, *J* = 16.4, 9.7, 1 H), 2.02 (dt, *J* = 12.5, 10.7, 1 H), 2.14 (ddd, *J* = 16.4, 9.8, 1.0, 1 H), 2.50 (ddd, *J* = 12, 9, 1, 1 H), 2.64 (dd, *J* = 16.0, 3.5, 1 H), 2.86 (d, *J* = 13.9, 1 H, ArCH), 2.87 (m, 1 H), 3.00 (td, *J* = 11.9, 4.8, 1 H), 3.15 (d, *J* = 13.9, 1 H, ArCH), 3.78 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.31 (ddd, *J* = 13.2, 6.7, 0.5, 1 H, CHN), 6.48 (d, *J* = 1.9, 1 H, Ar H), 6.57 (s, 1 H, Ar H), 6.58 (s, 1 H, Ar H), 6.63 (dd, *J* = 8.1, 1.9, 1 H, Ar H), 6.78 (d, *J* = 8.1 1 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 27.84 (t), 30.69 (t), 32.60 (t), 34.29 (t), 45.83 (t), 55.66 (q), 55.72 (q, 2 C), 56.06 (q), 64.25 (s), 108.76 (d), 111.22 (d), 111.60 (d), 113.46 (d), 122.37 (d), 125.16 (s), 128.60 (s), 133.91 (s), 148.01 (s, 2 C), 148.23 (s), 148.72 (s), 173.11 (s); mass spectrum, *m/e* (relative intensity) 246 (100), 231 (7), 230 (8), 202 (6). Anal. Calcd for $C_{23}H_{27}NO_5$: C, 69.50; H, 6.85. Found: C, 69.22; H, 7.03.

Vanadium Oxychloride Oxidation of Bisphenol 7a: 1,2,5,6-Tetrahydro-9,12-dihydroxy-8,11-dimethoxy-3*H*,14*H*-dibenzo[*de*,*g*]pyrrolo[2,1-*j*]quinolin-3-one (12a). To a solution of 48 mg (0.13 mmol) of bisphenol **7a** in 75 mL of dry, degassed dichloromethane cooled to −78 °C under argon was added 41 μL (75 mg, 0.43 mmol) of vanadium oxychloride.[3d] The resulting blue mixture was allowed to warm to room temperature and then stirred for 1.5 h. The mixture was heated under reflux for 7 h, diluted with 30 mL of dichloromethane, and washed with 35 mL of saturated aqueous sodium bicarbonate. The organic layer was dried (Na_2SO_4) and concentrated in vacuo to give a greenish oily solid. This material was chromatographed over 10 g of silica gel (eluted with ethyl acetate) to give 5 mg (10%) of biaryl **12a** as a colorless oil, 32 mg of a mixture of **7a** and biaryl **12a**, and 5 mg (10%) of recovered **7a**. The mixture was further purified by radial disk chromatography over silica gel (2-mm thick, eluted with ethyl acetate) to give 27 mg (57%, 67% total) of biaryl **12a** as a white crystalline solid: mp 235–237 °C dec; IR (KBr) 3410, 1665, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (dd, *J* = 11, 8, 1 H), 2.23 (dd, *J* = 14.7, 8, 1 H), 2.26 (dd, *J* = 12.2, 8, 1 H), 2.54 (m, 1 H), 2.58 (d, *J* = 15.4, 1 H), 2.66 (d, *J* = 14.5, 1 H, ArCH), 2.80 (td, *J* = 12, 4.5, 1 H), 2.88 (br t, *J* = 12, 1 H), 3.12 (d, *J* = 14.5, 1 H, ArCH), 3.92 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 4.41 (dd, *J* = 12.2, 3.6, 1 H, CH*H*N), 5.75 (s, 1 H, OH), 6.18 (s, 1 H, OH), 6.57 (s, 1 H, Ar H), 6.78 (s, 1 H, Ar H), 8.11 (s, 1 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 30.40, 30.56, 31.16, 36.52, 38.27, 56.15, 56.37, 62.00, 109.67, 112.30, 114.98, 119.79, 124.16 (2 C), 129.74, 129.85, 141.55, 145.05 (2 C), 146.03, 174.51; mass spectrum, *m/e* (relative intensity) 367 (M^+, 48), 352 (100), 320 (21), 243 (36), 232 (37), 165 (34), 111 (49), 97 (79), 83 (87), 74 (61), 71 (64); exact mass calcd for $C_{21}H_{21}NO_5$ *m/e* 367.1420, found *m/e* 367.1419. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76. Found: C, 68.99; H, 5.59.

(Diacetoxyiodo)benzene Oxidation of Bisphenol 7a: Aporphine 12a and 1,2,5,6-Tetrahydro-14-hydroxy-8,15-dimethoxy-3*H*,9*H*-6a,10b-([1,2]benzenomethano)pyrrolo[2,1-*a*]isoquinoline-3,9-dione (13). To a solution of 200 mg (0.54

mmol) of bisphenol **7a** and 48 mL (0.62 mmol) of trifluoroacetic acid in 215 mL of dry, degassed dichloromethane under argon at room temperature was added 195 mg (0.61 mmol) of (diacetoxyiodo)benzene.[3d] The mixture was stirred for 1.25 h at room temperature, washed with 75 mL of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo to give a deep red oil. The oil was flash chromatographed over 20 g of silica gel (eluted with ethyl acetate–hexane, 4:1, and then ethyl acetate followed by ethyl acetate–methanol, 96:4) to give 106 mg of crude aporphine **12a**, 124 mg of a mixture of **7a**, **12a**, and **13**, and 32 mg of crude morphinane **13** as an off-white solid. The crude **12a** was dissolved in 40 mL of dichloromethane, washed with 15 mL of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo. The residue was filtered through 5 g of silica gel (eluted as above), appropriate fractions were concentrated, and the resulting solid was recrystallized from ethyl acetate–hexane to give 58 mg of **12a** as a white solid. The crude **13** was subjected to identical treatment to afford 8 mg (4%) of **13** (mp 263–263.5 °C) as a white solid after two recrystallizations from ethyl acetate–hexane (4:1). The mixture of **7a**, **12a**, and **13** were combined with the mother liquors obtained above and chromatographed over 50 g of silica gel (eluted as above) to give an additional 74 mg (66% total) of **12a**, 52 mg (25%) of impure starting bisphenol **7a**, and 11 mg of slightly impure dienone **13**. Dienone **13**: IR ($CHCl_3$) 3500, 1675, 1645, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5 (m, 1 H), 2.07 (m, 1 H), 2.45 (m, 2 H), 2.60 (m, 2 H), 2.67 (m, 1 H, CHN), 3.10 (d, J = 16.6, 1 H, ArCH), 3.23 (d, J = 16.6, 1 H, ArCH), 3.76 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 3.99 (ddd, J = 13.5, 5.3, 1.2, 1 H, C*H*N), 6.27 (s, 1 H, OH), 6.32 (s, 1 H, =CHCO), 6.62 (d, J = 8.3, 1 H, Ar H), 6.78 (d, J = 8.3, 1 H, Ar H), 7.55 (s, 1 H, =CH); ^{13}C NMR ($CDCl_3$) δ 29.1, 29.5, 36.4, 36.5, 45.4, 45.5 (s), 54.9, 56.3, 62.6 (s), 109.9, 119.5, 119.7, 119.9, 123.0 (s), 127.7 (s), 143.5 (s), 145.9 (s), 151.1 (s), 160.7 (s), 172.7 (s), 180.9 (s); mass spectrum, m/e (relative intensity) 367 (M^+, 100), 352 (55), 339 (32), 324 (43), 307 (29), 262 (28), 233 (26), 230 (50), 137 (16); exact mass calcd for $C_{21}H_{21}NO_5$ m/e 367.1420, found m/e 367.1423.

Thallium Tris(trifluoroacetate) Oxidation of Bisphenol 7a. To a solution of 0.31 g (0.55 mmol) of thallium tris(trifluoroacetate) in 46 mL of dry, degassed dichloromethane prepared in a dry box under argon, cooled in a dry ice–acetone bath was added a solution of 185 mg (0.50 mmol) of bisphenol **7a** in 75 mL of dry, degassed dichloromethane.[3a] The mixture was stirred at −78 °C for 3 h, allowed to warm to −20 °C, and stirred at −20 °C for 19 h. The mixture was concentrated in vacuo, and the residue was chromatographed over 30 g of silica gel (eluted with chloroform–methanol, 98:2) to give 195 mg of a brown oil. This oil was purified by preparative thin-layer chromatography (eluted with ethyl acetate–methanol, 98:2, 4 elutions) to give 27 mg (15%) of aporphine **12a** as a white solid and 85 mg (46%) of starting bisphenol **7a** as a light yellow oil. Aporphine **12a** prepared in this manner was identical in all respects with the material described above.

Vanadium Oxyfluoride Oxidation of Monophenol 7b: 1,2,5,6-Tetrahydro-9-hydroxy-8,12,13-trimethoxy-3*H*,14*H*-dibenzo[*de*,*g*]pyrrolo[2,1-*j*]quinolin-3-one (12b). To a solution of 192 mg (0.50 mmol) of monophenol **7b** in 10 mL of a 20% trifluoroacetic acid–trifluoroacetic anhydride (20:1) solution in dichloromethane cooled to −5 °C in an ice–salt bath under argon was added 0.15 g (1.3 mmol) of vanadium oxyfluoride in 1.5 mL (minimum) of a 1:1 solution of ethyl acetate–TFA/TFAA (20:1), and the mixture was stirred for 30 min.[17] The reaction was quenched with 6 mL of 10% aqueous citric acid. The solution was adjusted to pH 7.5 with concentrated (58%) ammonium hydroxide, and the mixture was extracted with two 30-mL portions of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give 212 mg of a dark blue oil. This oil was chromatographed over 25 g of flash silica gel (eluted with chloroform, progressing to chloroform–methanol, 95:5) to give 119 mg (63%) of aporphine **12b** as a white solid: mp 190.0–191.0 °C (dec; IR ($CHCl_3$) 3570, 1675, 870 cm^{-1}; ,1H NMR ($CDCl_3$) δ 1.50 (m, 1 H), 2.26 (m, 2 H), 2.54–2.62 (m, 2 H), 2.68 (d, J = 14.5, 1 H, ArCH), 2.81 (td, J = 14.7, 4.6, 1 H), 2.90 (td, J = 12.3, 2.3, 1 H), 3.17 (d, J = 14.5, 1 H, ArCH), 3.92 (s, 6 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.42 (ddd, J = 12.3, 3.8, 1.9, 1 H, CHN), 6.18 (s, 1 H, OH), 6.57 (s, 1 H, Ar H), 6.72 (s, 1 H, Ar H), 8.14 (s, 1 H, Ar H); mass spectrum, m/e (relative intensity) 381 (M^+, 63), (100), 335 (38); exact mass calcd for $C_{22}H_{23}NO_5$ m/e 381.1576, found m/e 381.1605.

Electrochemical Oxidation of 11c. To a solution of 101 mg (0.25 mmol) of isoquinoline **11c** in 35 mL of degassed 0.1 N lithium perchlorate in acetonitrile containing 0.5% water was added 1.0 g of sodium bicarbonate. The mixture was electrolyzed at +1.56 V vs Ag/AgCl by using a platinum anode, a carbon rod cathode, and a Ag/AgCl reference electrode in a two-compartment cell with a PAR (Princeton Applied Research) potentiostat. After 2 h, the mixture was concentrated in vacuo and partitioned between 60 mL of water and 40 mL of dichloromethane. The aqueous layer was extracted with 40 mL of dichloromethane, and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give 70 mg of a dark green oil. The oil was chromatographed over 20 g of silica gel to give 15 mg (36%) of 3,4-dimethoxybenzaldehyde, 4 mg (10%) of 3,4-dimethoxybenzyl alcohol, and 21 mg (21%) of recovered **11c** as a gray oil.

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Registry No. **7a**, 110698-44-7; **7b**, 110698-47-0; **8a**, 22231-61-4; **8b**, 120-20-7; **9a**, 110698-41-4; **9b**, 39662-45-8; **10a**, 110698-42-5; **10b**, 110698-45-8; **11a**, 110698-43-6; **11b**, 110698-46-9; **11c**, 110698-48-1; **12a**, 110717-92-5; **12b**, 110698-49-2; **13**, 110717-22-1; i, 110698-50-5; [3-(benzyloxy)-4-methoxybenzyl]magnesium chloride, 88185-18-6; (3,4-dimethoxybenzyl)magnesium chloride, 108071-30-3; 3,4-dimethoxybenzaldehyde, 120-14-9; 3,4-dimethoxybenzyl alcohol, 93-03-8.