Synthesis of Tetrahydroindeno[1,2-*b*]indol-10-ones and Their Rearrangement to [2]Benzopyrano[4,3-*b*]indol-5-ones

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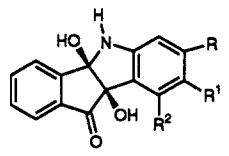
The formation of tetrahydroindeno[1,2-*b*]indol-10-ones **1** by reaction of ninhydrin with substituted anilines is described. The tetrahydroindeno[1,2-*b*]indol-10-ones **1** rearrange to form 5,11-dihydro-[2]benzopyran[4,3-*b*]indol-5-ones **8** when heated under acid conditions. Reaction of ninhydrin with 3-hydroxyaniline gave a benzo[*b*]indeno[2,1-*d*]furan **4**.

Introduction

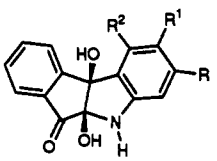
Several examples of tetrahydroindeno[1,2-*b*]indoles have been reported by Sainsbury and co-workers as potent antioxidants.[1,2] These compounds have been prepared by using a Fischer or Wender and Bischler indole synthesis. Our new synthetic approach to this ring system may prove to be beneficial in the preparation of new tetrahydroindeno[1,2-*b*]indoles with antioxidant activity.

A number of articles have been written about the reactions of ninhydrin with aromatic amines.[3-10] To date, no one has reported the formation of tetrahydroindeno-[1,2-*b*]indolones **1** by these reactions. We would like to report the formation of tetrahydroindeno[1,2-*b*]indolones **1**, which subsequently can be rearranged to benzopyranoindoles **8**.

A paper by Shapiro and Chatterjie reported that anilines with an electron-releasing group at the *meta* position react with ninhydrin to give a tetrahydroindeno[2,1-*b*]indolone cyclization product (**2**).[3] This product was presumed to

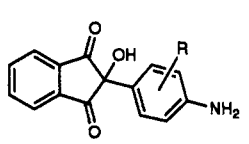


1



2

1a: R = OH, R¹ = OMe, R² = H
1b: R = OMe, R¹ = H, R² = OMe
1c: R = OMe, R¹ = OMe, R² = OMe



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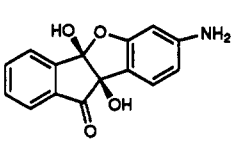
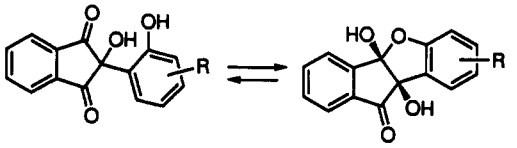


4

3a: R = 3-OMe
3b: R = 2-OMe,5-OMe
3c: R = 2-OMe
3d: R = 2-OH

form via attack of the amine onto the central carbonyl of ninhydrin, followed by ring closure of the *ortho* aromatic carbon onto one of the benzylic carbonyls. Conversely, prior literature has reported that the *para* carbon of

Scheme I



electron-rich anilines reacts with the 2 position of ninhydrin to form 2-(4-aminophenyl)-2-hydroxy-1,3-indanediones **3a** and **3b**.[4,5] Similarly, it has been reported that electron-rich phenols react with the 2-carbonyl of ninhydrin, but demonstrate *ortho* selectivity to form 2-(2-hydroxyphenyl)-2-hydroxy-1,3-indanediones, which are in equilibrium with a cyclized hemiketal structure (Scheme I).[11,12]

On the basis of the phenolic example, one would predict a similar ring closure reaction could occur in anilines if *ortho* selectivity could be achieved. Our findings, which support this hypothesis, prompted us to repeat two previously reported experiments of electron-rich anilines reacting with ninhydrin, for comparison to our results.[3]

Results and Discussion

The following reactions were carried out in water to examine the effects of aromatic substitution on the reaction of anilines with ninhydrin. The products isolated in these reactions differ with the various substituents on the anilines. The reaction of 5-amino-2-methoxyphenol with ninhydrin precipitated a tetrahydroindeno[1,2-*b*]indolone (**1a**). When 3,4,5-trimethoxyaniline was allowed to react with ninhydrin, the product was identified as a 2-(phenylamino)-2-hydroxy-1,3-indanedione (**6**). This reaction did not produce **1c** even after stirring for 88 h. Identification of **6** was done by proton NMR in dry DMSO. A D_2O exchange shifted the equilibrium completely to ninhydrin and 3,4,5-trimethoxyaniline which, because of its reversibility, confirmed that reaction on the aromatic ring had not taken place. When 3,5-dimethoxyaniline and ninhydrin were stirred in water a 2-phenyl-2-hydroxy-1,3-indanedione (**5a**) product formed containing approxi-

(1) Brown, D. W.; Graupner, P. R.; Sainsbury, M.; Shertzer, H. G. *Tetrahedron* **1991**, *47*, 4383.
(2) Graham, J.; Ninan, A.; Reza, K.; Sainsbury, M.; Shertzer, H. G. *Tetrahedron* **1992**, *48*, 167.
(3) Shapiro, R.; Chatterjie, N. *J. Org. Chem.* **1970**, *35*, 447.
(4) Roth, H. J.; Kok; W. *Arch. Pharm.* **1976**, *309*, 81.
(5) Kok, W.; Roth, H. J. *Arch. Pharm.* **1975**, *308*, 301.
(6) Ahmed, M. G.; Ahmed, S. A.; Alam, M. K. *J. Indian Chem. Soc.* **1982**, *59*, 806.
(7) Roth, H. J.; Kok, W. *Arch. Pharm.* **1975**, *308*, 401.
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(9) Ruheman, S. *J. Chem. Soc.* **1910**, *97*, 1438.
(10) Moubasher, R. *J. Chem. Soc.* **1949**, 1038.
(11) Poupelin, J.-P.; Saint-Ruf, G.; Perche, J.-C.; Roussey, J.-C.; Laude, B.; Narcisse, G.; Bakri-Logeais, F.; Hubert, F. *Eur. J. Med. Chem.* **1980**, *15*, 253.
(12) Poupelin, J.-P.; Saint-Ruf, G.; Perche, J.-C.; Lacroix, R.; Uchida-Ernouf, G.; Narcisse, G.; Hubert, F. *Eur. J. Med. Chem.* **1979**, *14*, 171.

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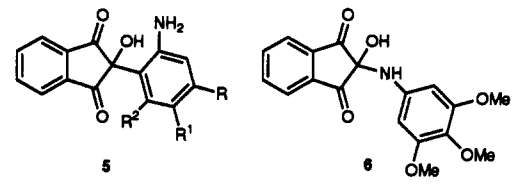
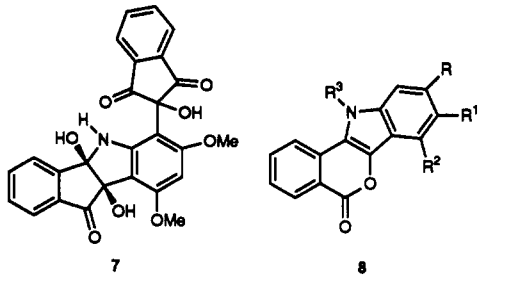


5 6

5a: R = OMe, R¹ = H, R² = OMe



7 8

8a: R = OH, R¹ = OMe, R² = H, R³ = H
8b: R = OMe, R¹ = OMe, R² = OMe, R³ = H
8c: R = OAc, R¹ = OMe, R² = H, R³ = Ac

mately one-third of the cyclized tautomer **1b**, which was observed by NMR. The results of these reactions demonstrate that the product which forms is the first crystalline intermediate which can precipitate and halt the progress to the thermodynamic product.

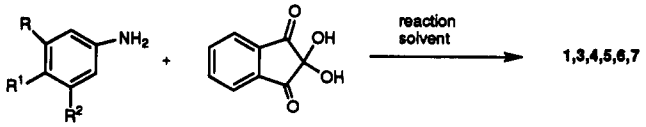
In order to obtain the tetrahydroindeno[1,2-*b*]indolone products, aqueous acetic acid was used in place of water as a solvent. Using this method, only 3,5-dimethoxyaniline did not precipitate the indeno[1,2-*b*]indolone product as a single compound. This reaction gave **1b**, which contained a mixture of the intermediate indanedione **5a** and a byproduct **7**, after the usual 16 h. When the reaction was stirred for an additional 80 h, the final precipitate consisted of a mixture of 80% **1b** and 20% of the byproduct **7**.[13] When the solvent was changed to glacial acetic acid, only the indeno[1,2-*b*]indolone **1b** product was isolated. Using glacial acetic acid as a solvent in the reactions of other aniline substrates did not give a precipitate except for the reaction of 5-amino-2-methoxyphenol, which yielded **1a**.

In order to compare our results with those previously published, we attempted to duplicate the reaction conditions used by Shapiro and Chatterjie. We identified the product of *m*-anisidine with ninhydrin as a 2-phenyl-2-hydroxy-1,3-indanedione (**3c**). The physical data of our product are identical to that reported in the literature for this reaction. The NMR and ^{13}C NMR data show the ninhydrin fragment to be symmetrical around the 1,3-indanedione ring, showing a singlet for the four aromatic protons and only 12 peaks in the carbon spectrum.[14] Irradiation of the methoxy hydrogens shows an NOE only to the proton between the amine and methoxy, which indicates aromatic substitution *para* to the amine. The reaction product of 3-hydroxyaniline gave a similar reaction product **3d** which, because of the presence of the *ortho* phenol, can cyclize to the hemiketal **4**. Compound **4** equilibrates in deuterated DMSO to 15% of the ring-opened indanedione tautomer **3d**. This product is in agreement with publications by Poupelin et al. which show

(13) Compound **7** was prepared in good yield by using 2 equiv of ninhydrin to 1 equiv of aniline. This structure was assigned by NMR, ^{13}C NMR, and the observation of NOEs between the singlet aromatic proton and both methoxy groups.

(14) Chatterjie, N.; Stephani, R. A.; Strom, C. H. *J. Pharm. Sci.* **1980**, *69*, 1431.

Table I



R	R¹	R²	solvent	product	yield, %
OH	OMe	H	H_2O	**1a**	77
OH	OMe	H	1% $AcOH_{(aq)}$	**1a**	85
OH	OMe	H	AcOH	**1a**	83
OMe	H	H	H_2O	**3c**	90
OMe	H	H	1% $AcOH_{(aq)}$	**3c**	94
OH	H	H	H_2O	**4**	89
OH	H	H	1% $AcOH_{(aq)}$	**4**	85
OMe	H	OMe	H_2O	**5a**[a]	91
OMe	H	OMe	1% $AcOH_{(aq)}$	**1b**[b]	96
OMe	H	OMe	AcOH	**1b**	69
OMe	OMe	OMe	H_2O	**6**	91
OMe	OMe	OMe	1% $AcOH_{(aq)}$	**1c**	68

[a] Isolated with 33% **1b**. [b] Isolated with 20% **7**.

that electron-rich phenols can react with ninhydrin and equilibrate to benzo[*b*]indeno[2,1-*d*]furans easily.[11,12] The structure of **4** in the solid state was confirmed to be the tetracyclic product by X-ray crystallography. Both of these aniline reactions were carried out under acid conditions, but show no formation of tetrahydroindeno-[1,2-*b*]indolones **1**. Since these reactions did not result in formation of tetrahydroindeno[1,2-4b]indolones **1**, we did not pursue them any further. The results of all the reactions carried out with ninhydrin are summarized in Table I.

In an effort to derivatize the indeno[1,2-*b*]indolone products to aid in identification of the structure, attempted dehydration of **1** resulted in rearrangement of the molecules to benzopyranoindoles **8**. Although benzopyranoindoles are known, they have previously been prepared by Fischer indolization of isochroman-1,4-dione.[15,16]

The above rearrangement was accomplished by refluxing the indeno[1,2-*b*]indolone product in glacial acetic acid for 30 min. The structure of these compounds was elucidated by NMR and confirmed by X-ray crystallography of the acetoxy acetyl analog **8c**. Acid rearrangement of α-hydroxy ketones to benzopyranones has been reported in the literature.[17] One possible mechanism may be through formation of a hydroxy epoxide intermediate, which dehydrates to an enamine. The ring expansion can then occur through opening of the epoxide ring to neutralize the positive charge on the nitrogen (Scheme II).

Discussion of NMR Experiments

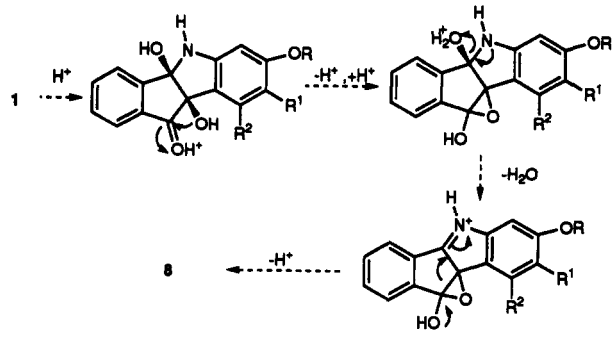
Identification of **1a** was done by NMR, ^{13}C NMR, HETCOR, and COLOC experiments. The most revealing information in the COLOC experiment was the three-bond correlation from the hydroxy proton (OH10a) to the carbonyl (C10) and the aromatic carbon C10b. The position of the carbon (C10a) adjacent to this hydroxy is further delineated by a three-bond coupling to the aromatic hydrogen H1 and to the amine proton (H5). On the basis of these observations, carbon C10a is directly attached to the phenol ring, the carbonyl, and the hydroxy (OH10a).

(15) Buu-Hoi, N. P.; Mangane, M.; Jacquignon, P., *J. Chem. Soc. C* **1966**, 50.

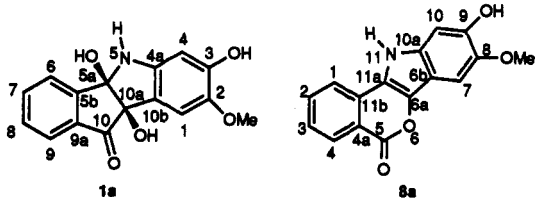
(16) Knott, E. B. *J. Chem. Soc. C* **1963**, 402.

(17) Holland, J. M.; Jones, D. W. *J. Chem. Soc. C* **1970**, 530.

Scheme II



This carbon (C10a) cannot be adjacent to the amine since there is a three-bond distance from this carbon to the amine proton. All of these conditions for carbon C10a are satisfied in **1a**. These connectivities are not possible for **2**, which has an exchangeable hydrogen three bonds away from the carbonyl, which satisfies only one of the correlations described for the hydroxy proton. This exchangeable proton is located four bonds away from the aromatic ring and is adjacent to the amine, which would violate the two other connectivities outlined in the COLOC experiment.



The rest of the three-bond correlations are generic to either structure, but substantiate the identifications of the carbons and hydrogens discussed above. The carbon (C5a) adjacent to the amine is directly attached to the aromatic portion of the indene ring since the neighboring hydroxy proton (OH5a) shows correlations to the aromatic carbon C5b. The aromatic substitution pattern was elucidated by correlations from the phenolic proton to the aromatic carbons C2 and C4, whereas the methoxy hydrogens only couple to the aromatic carbon C2. The aromatic hydrogen H1 shows correlations to the aromatic carbons C3, C4a as well as to the aliphatic carbon C10a, while the aromatic proton H4 correlates to aromatic carbons C2 and C10b. The amine proton H5 shows coupling to the olefinic carbon C10a and to the aromatic carbon C10b to complete the map of the indole ring.

Identification of **8a** was also done by NMR, ^{13}C NMR, HETCOR, and COLOC experiments. The major observations in these spectra are the ^{13}C NMR chemical shift ranges of carbon C6a and carbon C11a, which suggest that they are olefinic, and also the chemical shift range of carbonyl C5, which implies that it is a lactone. The most revealing observation of the COLOC experiment is the three-bond correlation of the amine proton (H11) to the quaternary carbons C11b, C6a, and C6b, which maps out a 2-phenylindole ring analogous to that discussed for **1a**. The phenol ring substitution is easily identified by the following three-bond couplings. The phenolic proton shows correlations to aromatic carbons C8 and C10, while the methoxy hydrogens couple only to the aromatic carbon C8. The aromatic hydrogen H7 shows correlation to aromatic carbons C9 and C10a and to the olefinic carbon C6a, while the aromatic proton H10 correlates to aromatic carbons C8 and C6b. The olefinic carbon 11a shows a three-bond coupling to the aromatic proton H1 but, because of the overlap of H1 and H2 in the proton NMR, it is difficult to distinguish between other coupling of H1 or H2 in the COLOC experiment. These connections confirm the presence of an indole ring with a phenyl attached at the 2 position. The correlation of the aromatic proton H3 to aromatic carbons C1 and C4a and also the correlation of the aromatic proton H4 to carbon C2 help to identify the protons of the benzopyrano aromatic ring. All of the correlations discussed for **8a** identified the carbon skeleton which was confirmed by X-ray crystallography.[18]

Conclusions

The rate of formation of tetracyclic product **1** from the ring-opened product **5** appears to be related to the substitution pattern of the aniline ring. The examples which have an electron-donating group *para* to the amine cyclize to the tetracyclic product easily. In the case of 3,5-dimethoxyaniline, where neither methoxy group is *para* to the amine, formation of the tetracyclic product is much slower. Anilines having only one electron-donating group located at the *meta* position, react *para* to the amine and therefore cannot close to the tetrahydroindeno[1,2-*b*]-indolone product.

The NMR experiments for the products obtained in the reaction of ninhydrin with anilines strongly support the tetrahydroindeno[1,2-*b*]indolone structure **1** rather than the tetrahydroindeno[2,1-*b*]indolone structure **2**. Ancillary support for formation of tetrahydroindeno[1,2-*b*]indolones comes from the literature reactions of ninhydrin with phenols and anilines described earlier. In the case of 3,5-dimethoxyaniline we isolated the aniline intermediate, which is substituted *ortho* to the amine. Upon further reaction this intermediate converts to the tetracyclic product. If this intermediate was substituted *para* to the amine, as in the case of the literature compounds, no cyclization would occur.

Even though the acid rearrangement of compounds **1a** and **1c** to benzopyranoindoles **8a** and **8b** does not prove the tetrahydroindeno[1,2-*b*]indolone structure, it does lend evidence to existence of these compounds. These findings, combined with the spectral data for these products, brings us to the conclusion that aromatic amines, containing an electron-releasing group at the *meta* position, can undergo electrophilic substitution with the 2-carbonyl of ninhydrin. When this substitution occurs *ortho* to the amine, a cyclization occurs to form tetrahydroindeno[1,2-*b*]indolones **1**.

Experimental Section

^{1}H, ^{13}C, HETCOR, and COLOC experiments were performed on either a 300- or 400-MHz NMR spectrometer.

General Procedure for the Reaction of Aniline with Ninhydrin. A suspension of ninhydrin (5.6 mmol) and aniline (5.6 mmol) was stirred in solvent (100 mL) for 16 h at room temperature. The precipitate was filtered, washed with water, and dried under vacuum to yield product. A small sample was recrystallized to give an analytical sample identical to the initial sample.

(18) The author has deposited atomic coordinates for **4e** and **8f** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

5,5a,10,10a-Tetrahydro-3,5a,10a-trihydroxy-2-methoxyindeno[1,2-*b*]indol-10-one (1a). The general method was followed, with water as the solvent and a 30-min reaction time. Recrystallized from ethyl acetate: mp 186–189 °C;^{1}H NMR (DMSO-d_6) δ 3.63 (s, 3H), 5.90 (s, 1H), 5.96 (s, 1H), 6.78 (s, 1H), 6.93 (s, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.82 (t, J = 7.5 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 8.91 (s, 1H); ^{13}C NMR (DMSO-d_6) 56.75, 92.55, 96.92, 83.90, 110.54, 114.28, 122.35, 124.94, 129.30, 133.94, 135.75, 140.68, 142.87, 149.8, 152.52, 200.71. Anal. Calcd for $C_{16}H_{13}NO_5$: C, 64.21; H, 4.38; N, 4.68. Found: C, 64.17; H, 4.40; N, 4.36.

5,5a,10,10a-Tetrahydro-5a,10a-dihydroxy-1,3-dimethoxyindeno[1,2-*b*]indol-10-one (1b). The general method was followed, with AcOH (50 mL) as the solvent and a 1-h reaction time. A small sample was recrystallized from methanol to give yellow crystals which upon standing slowly hydrated to the monohydrate as observed by elemental analysis: mp 212–213 °C; ^{1}H NMR (DMSO-d_6) δ 3.62 (s, 3H), 3.66 (s, 3H), 5.64 (s 1H), 5.66 (d, J = 2.0 Hz, 1H), 5.75 (d, J = 2.0 Hz, 1H), 6.00 (s, 1H), 7.42 (s, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.77 (t, J = 7.5 Hz, 1H), 7.85 (d, J = 7.7 Hz, 1H); ^{13}C NMR (DMSO-d_6) 56.72, 85.82, 88.45, 90.27, 94.35, 105.33, 124.05, 126.45, 131.14, 136.21, 137.06, 152.07, 152.80, 160.73, 164.86, 200.71. Anal. Calcd for $C_{17}H_{15}NO_5$: C, 61.63; H, 5.17; N, 4.23. Found: C, 61.93; H, 5.09; N, 3.84.

5,5a,10,10a-Tetrahydro-5a,10a-dihydroxy-1,2,3-trimethoxyindeno[1,2-*b*]indol-10-one (1c). The general method was followed, with water (99 mL) and AcOH (1 mL) as the solvent. Recrystallized from ethyl acetate: mp 263–264 °C, ^{1}H NMR (DMSO-d_6) δ 3.55 (s, 3H), 3.65 (s, 3H), 3.82 (s, 3H), 5.82 (s, 1H), 5.88 (s, 1H), 6.04 (s, 1H), 7.26 (s, 1H), 7.50 (t, J = 7.2 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.78 (t, J = 7.2 Hz, 1H), 7.88 (d, J = 7.7 Hz, 1H); ^{13}C NMR (DMSO-d_6) 57.31, 62.24, 62.71, 86.38, 90.54, 94.32, 110.36, 124.09, 126.53, 131.22, 135.31, 136.20, 137.26, 146.83, 153.03, 154.09, 157.64, 201.03. Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 63.01; H, 4.90; N, 4.05.

2-(2-Methoxy-4-aminophenyl)-2-hydroxy-1,3-indanedione (3c). The general method was followed, with water (99 mL) and AcOH (1 mL) as the solvent. Recrystallized from acetonitrile: mp 211–212 °C; ^{1}H NMR (DMSO-d_6) δ 3.32 (s, 3H), 5.15 (br, 2H), 6.04 (s, 1H), 6.23 (d, J = 8.2 Hz, 1H), 6.78 (s, 1H), 7.30 (d, J = 8.2 Hz, 1H), 8.01 (s, 4H); ^{13}C NMR (DMSO-d_6) 56.27, 77.07, 98.52, 107.54, 115.21, 124.70 (2C), 129.95, 137.74 (2C), 141.44 (2C), 151.81, 157.19, 202.26 (2C). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.44; H, 4.71; N, 5.16.

3-Amino-5a,10a-dihydroxybenzo[*b*]indeno[2,1-*d*]furan-10-one (4). The general method was followed, with water as a solvent. Recrystallized from acetonitrile: mp >340 °C. ^{1}H NMR (C_6D_5N) δ 5.8 (br, 2H), 6.55 (dd, 7.7 Hz, 2.0 Hz, 1H), 6.56 (s, 1H), 7.37 (dt, J = 7.5, 0.9 Hz, 1H), 7.66 (dt J = 7.6, 1.0 Hz, 1H), 7.73 (t, J = 7.7, Hz, 1H), 7.85 (d, J = 7.7 Hz, 1H), 8.29 (d, J = 7.7 Hz, 1H), 9.5 (br, 1H), 10.5 (br, 1H); ^{13}C NMR (C_6D_5N) 84.07, 96.22, 108.90, 112.63, 115.03, 123.37, 125.67, 127.12, 130.82, 135.56, 136.23, 150.61, 153.27, 159.78, 201.42. Anal. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.51; H, 3.87; N, 5.10.

2-(2-Amino-4,6-dimethoxyphenyl)-2-hydroxy-1,3-indanedione (5a). The general method was followed, with water as a solvent and stirring for 1 h. Recrystallized from ethyl acetate: mp 170–171 °C. ^{1}H NMR (DMSO-d_6) δ 3.45 (s, 6H), 5.38 (s, 2H), 5.89 (s, 2H), 6.67 (s, 1H), 7.99–8.00 (s, 4H); ^{13}C NMR (DMSO-d_6) 57.26 (2C), 79.08, 93.25, 100.93, 125.08, 137.94 (2C), 141.07 (2C), 152.45, 160.72, 200.75 (2C). Anal. Calcd for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 64.82; H, 4.65; N, 4.44.

2-[(3,4,5-Trimethoxyphenyl)amino]-2-hydroxy-1,3-indanedione (6). The general method was followed, with water as a solvent. Recrystallized from ether: mp 116–120 °C dec; ^{1}H NMR (DMSO-d_6) δ 3.13 (s, 3H), 3.68 (s, 3H), 5.86 (s, 1H), 6.45 (s, 2H), 7.04 (s, 1H), 8.04 (s, 5H). Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 62.85; H, 4.88; N, 4.08.

5,5a,10,10a-Tetrahydro-5a,10a-dihydroxy-4-(2-hydroxy-1,3-dioxoindanyl)-1,3-dimethoxyindeno[1,2-*b*]indol-10-one (7). A suspension of ninhydrin (1.00 g, 5.6 mmol) and 3,5-dimethoxyaniline (0.43 g, 2.8 mmol) was stirred in water (99 mL) and AcOH (1 mL) for 16 h. The yellow precipitate was filtered, washed with water, and air-dried under vacuum to yield 1.3 g (98%) of 7. A small sample was recrystallized from acetonitrile to give an analytical sample identical to the initial sample: mp 234–236 °C; ^{1}H NMR (DMSO-d_6) δ 3.13 (s, 3H), 3.67 (s, 3H), 5.78 (s, 1H), 5.80 (s, 1H), 6.26 (s, 1H), 7.07 (s, 1H), 7.16 (s, 1H), 7.53 (dd, J = 7.1, 7.6 Hz 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.77 (dd, J = 7.1, 7.6 Hz, 1H), 7.92–7.99 (m, 5H); ^{13}C NMR (DMSO-d_6) 57.071 (2C), 78.87, 84.71, 88.24, 93.98, 124.18, 124.84, 124.97, 126.22, 131.31, 136.16, 137.43, 137.92, 141.06, 141.46, 151.05, 152.95, 160.19, 160.55, 200.52, 200.89, 201.06. Anal. Calcd for $C_{26}H_{19}NO_8$: C, 65.96; H, 4.05; N, 2.96. Found: C, 65.94; H, 4.00; N, 3.08.

5,11-Dihydro-9-hydroxy-8-methoxy[2]benzopyrano[4,3-*b*]indol-5-one (8a). A suspension of **1a** (0.40 g, 13 mmol) in acetic acid (40 mL) was refluxed for 30 min. After cooling to 25 °C, the precipitate was poured into water and filtered, washed with water, and air-dried (0.2 g, 55%). A small sample was recrystallized from ethanol to give an analytical sample identical to the initial sample: mp 350–353 °C; ^{1}H NMR (DMSO-d_6) δ 3.86 (s, 3H), 6.91 (s, 1H), 7.16 (s, 1H), 7.48 (m, 1H), 7.91 (m, 2H), 8.22 (d, J = 7.8 Hz, 1H), 9.22 (s, 1H), 11.47 (s, 1H); ^{13}C NMR (DMSO-d_6) 55.89, 97.76, 98.53, 108.12, 117.49, 115.01, 119.85, 126.08, 130.82, 130.96, 130.96, 134.38, 135.31, 144.66, 146.70, 161.64. Anal. Calcd for $C_{16}H_{11}NO_4$: C, 68.32; H, 3.94; N, 4.98. Found: C, 68.72; H, 3.82; N, 4.79.

5,11-Dihydro-7,8,9-trimethoxy[2]benzopyrano[4,3-*b*]indol-5-one (8b). The same procedure was used as described for **8a**. Recrystallized from MeOH: mp 277–278 °C; ^{1}H NMR (DMSO-d_6) δ 3.75 (s, 3H), 3.88 (s, 3H), 4.02 (s, 3H), 6.76 (s, 1H), 7.53 (m, 1H), 7.95 (m, 2H), 8.23 (d, J = 7.8 Hz, 1H), 11.82 (s, 1H); ^{13}C NMR (DMSO-d_6) 57.95, 62.83, 63.27, 92.17, 105.86, 117.21, 119.38, 121.92, 128.38, 132.21, 132.51, 134.35, 135.20, 137.10, 137.79, 146.56, 154.52, 163.35. Anal. Calcd for $C_{18}H_{15}NO_5$: C, 66.47; H, 4.65; N, 4.30. Found: C, 66.17; H, 4.59; N, 4.20.

9-Acetoxy-11-acetyl-5,11-dihydro-8-methoxy[2]benzopyrano[4,3-*b*]indol-5-one (8c). A suspension of **8a** (0.5 g, 0.0018 mol) and Et_3N (1 mL) in acetic anhydride (20 mL) was refluxed for 1 h. After cooling to 25 °C, the solution was poured into water and the resulting precipitate was filtered and washed with water (5.3 g, 81% yield). A small sample was recrystallized from ethyl acetate to give an analytical sample identical to the initial sample: mp 232–234 °C; ^{1}H NMR ($CDCl_3$ δ 2.38 (s, 3H), 2.78 (s, 3H), 3.93 (s, 3H), 7.35 (s, 1H), 7.52 (m, 1H), 7.63 (s, 2H), 7.79 (m, 1H), 8.41 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) 20.52, 27.07, 56.15, 100.40, 109.39, 117.94, 118.03, 119.14, 123.72, 127.37, 130.21, 130.91, 131.27, 134.39, 140.24, 141.24, 148.85, 161.23, 168.94, 169.91. Anal. Calcd for $C_{20}H_{15}NO_6$: C, 65.75; H, 4.14; N, 3.83. Found: C, 65.45; H, 4.13; N, 3.69.

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Supplementary Material Available: Copies of the ^{1}H, ^{13}C, and ^{1}H-^{13}C 2D spectra of **1a**, **4**, and **8a** and ORTEP diagrams of **8c** and **4** (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.