[CONTRIBUTION FROM THE WM. H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

Biindolyls. I. Synthesis of 5,6-Dihydroxy-2,3′-biindolyl Hydroiodide and Some Related Compounds

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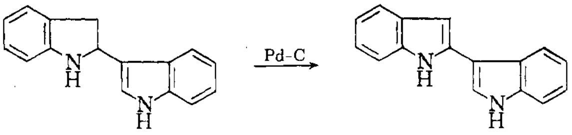
Reductive cyclization of suitably substituted 3-(*o*-nitrophenylacetyl)indoles (Va,b) led to 5,6-dimethoxy-2′-methyl- (VIb) and 5,6-dimethoxy-2,3′-biindolyl (VIa). Demethylation of the last compound with hydriodic acid gave 5,6-dihydroxy-2,3′-biindolyl as a stable hydroiodide (VII). Silver oxide oxidation and autooxidation of this dihydroxy compound in alkaline ethanolic solution proceeded rapidly to give red solutions which showed characteristic absorption maxima at 490 mμ. A convenient synthesis of the parent 2,3′-biindolyl (II), by catalytic dehydrogenation of diindole (I), is also described.

The genesis of mammalian melanin by the enzymic oxidation of tyrosine via the sequence: 3,4-dihydroxyphenylalanine, dopachrome (a red compound believed to be 2-carboxy-2,3-dihydroindole-5,6-quinone), and 5,6-dihydroxyindole to melanin has been well established, and the hypothesis advanced that indole-5,6-quinone may be the first stage in the oxidative polymerization of 5,6-dihydroxyindole to melanin.[1] Further condensation of the indole-5,6-quinone with 5,6-dihydroxyindole (or possibly with itself)[2] yields a deep blue intermediate, termed a "melanochrome",[3] which is considered to be a di- or oligomeric indolequinone similar to the polymeric melanin.[2,3] Various proposals and supporting evidence concerning the mode of self-condensation of indole-5,6-quinone have been reviewed,[4] interpreted on the basis of isotopic tracer experiments,[5] and further discussed elsewhere.[2,6] Spectrophotometric evidence for the formation of an indolylindole-5,6-quinone has been offered by Bu'Lock,[2] who considers such dimeric units to comprise the basic chromophore (λ_{max}, 540 mμ) of the polymeric structure. Although unambiguous assignment of the mode of ring-ring coupling in the melanochrome structure has not been accomplished[2,6] 3-position involvement of the consecutive indole moieties has been consistently supported.[1-6]

In this laboratory we have undertaken a program for the synthesis of 5,6-dihydroxy- and 5,6,5′,6′-tetrahydroxybiindolyls, which have various modes of ring-ring coupling, and which upon oxidation should yield quinonoid compounds whose spectra should provide new criteria for assessing the structure of the true melanochromes. A survey of the literature revealed that present methods of synthesis of biindolyls (2,2′-, 2,3′- and 3,3′-) were inadequate and limited mostly to analogs bearing simple alkyl substituents.[7-10] Biindolyls in which the pyrrole ring of one nucleus is coupled to the benzenoid ring of the second indole moiety have not been reported. In the present work, the first synthesis of 5,6-dihydroxy-2,3′-biindolyl hydroiodide and certain analogs is described, along with a convenient procedure for the preparation of 2,3′-biindolyl.

The parent 2,3′-biindolyl (II) was easily obtained in 86% yield from diindole[11] (I) by catalytic dehydrogenation in refluxing decalin over 10% palladium on carbon. The product was identical with an authentic sample prepared in low yield by the action of ethanolic potassium hydroxide on dinitrosodiindole as reported in the literature.[12]



I II

Since diindole is preparable in 96% yield via acid-catalyzed dimerization of indole,[12] this sequence appeared to be an excellent preparative route. However, repeated attempts to dimerize 5,6-dimethoxyindole[13] in benzene, ethanol, or acetic acid gave deeply colored, poorly defined products, which on dehydrogenation gave some 5,6-dimethoxyindole as the only characterizable product. In view of this result and the apparent complexity of "mixed" dimerizations[14] of even simpler indoles, we

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[1] H. S. Mason, *J. Biol. Chem.*, **172**, 83 (1948).

[2] J. D. Bu'Lock, *J. Chem. Soc.*, 52 (1961).

[3] R. J. S. Beer, T. Broadhurst, and A. Robertson, *J. Chem. Soc.*, 1947 (1954).

[4] H. S. Mason, in *Advances in Enzymology*, Vol. XVI, F. F. Nord, ed., Interscience, New York, 1955, pp. 110–112, 163–184.

[5] G. A. Swan and D. Wright, *J. Chem. Soc.*, 1549 (1956).

[6] R. I. T. Cromartie and J. Harley-Mason, *Biochem. J.*, **66**, 713 (1957).

[7] O. Schmitz-Dumont, K. Hamann, and K. Geller, *Ann.*, **504**, 1 (1933).

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[9] S. A. Faseeh and J. Harley-Mason, *J. Chem. Soc.*, 4141 (1957).

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[11] Structure I is that assigned to diindole by H. F. Hodson and G. F. Smith, *J. Chem. Soc.*, 3544 (1957).

[12] O. Schmitz-Dumont and B. Nicolojanus, *Ber.*, **63**, 323 (1930).

[13] Prepared by the method of C. F. Huebner, H. A. Troxell, and D. C. Schroeder, *J. Am. Chem. Soc.*, **75**, 5888 (1953).

[14] W. E. Noland and C. F. Hammer, *J. Org. Chem.*, **25**, 1525 (1960).

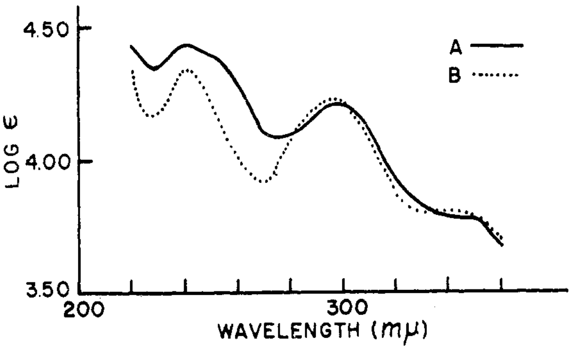
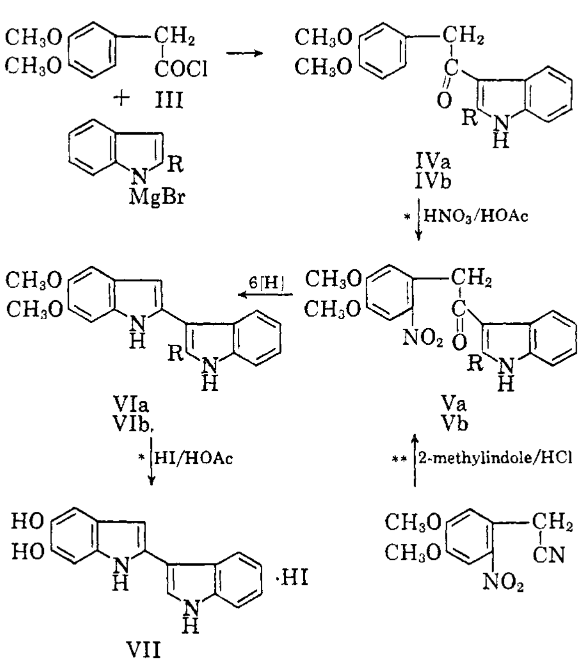


Fig. 1. Ultraviolet absorption spectrum of (A) 3-(4,5-dimethoxy-2-nitrophenylacetyl)indole (Va) in 95% ethanol, and (B) summation of the molar absorbance curves of 3-acetylindole and 4,5-dimethoxy-2-nitrotoluene; both in 95% ethanol.

by-passed this approach to substituted biindolyls, and obtained some examples of the desired class by the following alternative routes.

Homoveratroyl chloride (III) reacted with indolylmagnesium bromide to form 3-(3,4-dimethoxyphenylacetyl)indole (IVa) in 37.5% yield. The assignment of the 3-acylindole structure to this product was based on the results of similar acylations reported elsewhere[15] and the similarity of the ultraviolet spectrum of this ketone with that of 3-acetylindole.[24] Nitration of this ketone (IVa) at room temperature in glacial acetic acid gave 75.6% yield of 3-(4,5-dimethoxy-2-nitrophenylacetyl)-indole (Va), whose structural assignment was based on the following considerations: a) the similarity of its ultraviolet absorption spectrum with a synthetic curve obtained by addition of the molar absorbance curves of 3-acetylindole and 4,5-dimethoxy-2-nitrotoluene[16] (Fig. 1); b) the similar formation of 4,5-dimethoxy-2-nitrotoluene by nitration of homoveratrole[16]; and c) our observation that 3-acetylindole was not noticeably attacked by an identical nitration medium under similar conditions. Treatment of the nitro ketone (Va) with stannous chloride and hydrochloric acid in boiling glacial acetic acid gave an orange-brown precipitate, which may have been the hexachlorostannate of either the intermediate amino ketone or of the product (VIa). In either case, treatment of this intermediate solid with sodium hydroxide, followed by extraction with ethyl acetate afforded a 28.6% yield of the reductive cyclization product, 5,6-dimethoxy-2,3′-biindolyl (VIa). The structural similarity of this last compound with 2,3′-biindolyl was readily shown by the corresponding similarity of their ultraviolet spectra. Demethylation of the dimethoxy compound was effected by refluxing it with a solution of hydriodic acid in glacial acetic acid. The product, 5,6-dihydroxy-2,3′-biindolyl hydroiodide (VII), crystallized directly from the reaction mixture in 90% yield, provided that the proper proportion of glacial acetic acid had been used (*cf.* Experimental). Silver oxide oxidation of this dihydroxy compound (or autooxidation in alkaline ethanolic solution) proceeded rapidly to give a red solution whose absorption maximum (λ_{max}, 490 mμ) slowly decreased on further aging. Although this absorption is reminiscent of that of other hypothetical indolequinone systems,[2,3,6] the lack of uniformity of solvent and *p*H conditions used for such measurements obviates direct comparison. More detailed studies of this oxidation process, which are currently in progress, are required to provide insight into the nature of the red oxidation product.



Series (a): R is H; series (b); R is CH_3. *Series (a) only. **Series (b) only.

3-(3,4-Dimethoxyphenylacetyl)-2-methylindole (IVb) was also prepared by reaction of homoveratroyl chloride (III) with 2-methylindolylmagnesium bromide (24% yield). However, nitration of this ketone gave only a poor yield of a dinitro compound of undetermined structure. The desired 3-(4,5-dimethoxy-2-nitrophenylacetyl)-2-methylindole (Vb) was obtained in 7.3% yield by reaction of 4,5-dimethoxy-2-nitrophenylacetonitrile[17] with 2-methylindole in the presence of hydrogen chloride after the method of Seka.[18] Reduction of this nitro ketone (Vb) with sodium hydrosulfite in aqueous ethanolic sodium hydroxide produced 5,6-dimethoxy-2′-methyl-2,3′-biindolyl (VIb) in 54% yield. Because of the poor overall yield of this last compound, no attempt was made to demethylate it to the corresponding dihydroxy analog.

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[15] *Cf.* W. C. Sumpter and F. M. Miller, *Heterocyclic Compounds with Indole and Carbazole Systems*, Interscience, New York, 1954, pp. 45, 47.

[16] B. Luff, W. Perkin, and R. Robinson, *J. Chem. Soc.*, 97, 1134 (1910).

[17] G. N. Walker, *J. Am. Chem. Soc.*, **77**, 3844 (1955).

[18] R. Seka, *Ber.*, **56**, 2058 (1923).

The basicity of the 2,3′-biindolyls, as exemplified by isolation of the title compound, is notable. Yellow solutions (λ_{max}, 400–410 mμ) were also formed by the remaining 2,3′-biindolyls in one-tenth molar ethanolic hydrochloric acid. Studies of the basicity of these compounds, and the nature of the chromophoric group, will form the subject of another communication.

EXPERIMENTAL

All melting points are corrected. Ultraviolet-visible spectra were determined in 95% ethanol on a Warren Spectracord; infrared spectra were run in potassium bromide at 1% weight concentration on a Perkin-Elmer Model 21 spectrophotometer.

2,3′-Biindolyl (II). A mixture of 20.0 g. of diindole,[12] 3 g. of 10% palladium on carbon, and 110 ml. of decalin was refluxed (190°) for 57.5 hr. The cooled mixture solidified and was redissolved by addition of 100 ml. of boiling ethyl acetate. The hot solution was filtered to remove the catalyst, and the filtrate was distilled to remove the ethyl acetate. On being cooled to room temperature, the red-tinted residual solution deposited crystals, which were collected on a Büchner funnel with petroleum ether (b.p. 30–40°) as auxiliary wash. The product was powdered in a mortar, washed further with petroleum ether to remove residual decalin, then air dried to give 17.1 g. (86.0%) of tan solid, m.p. 184–192°. Recrystallization from benzene (in which the 2,3′-biindolyl is not very soluble) gave the pure product as a white powder, m.p. 203.5–205° (decomp.); λ_{max}, mμ (log ε): 224- (4.49), 236 shoulder (4.42), 290 shoulder (4.16), 312 (4.34). The literature gives[7] m.p. 206°; ultraviolet spectrum[9] (95% ethanol); λ_{max}, mμ (log ε): 224 (4.52), 312 (4.36). A sample of 2,3′-biindolyl was also prepared as previously reported[7] and found to be identical with this product.

Homoveratroyl chloride (III). This compound was prepared from homoveratric acid[19] and thionyl chloride as already described,[20] and purified by vacuum distillation (b.p. 175.5–178°/20 mm.; lit.[21] b.p. 170°/10 mm.). Redistillation gave a nearly colorless product, b.p. 132–134°/1.2 mm.; $n_D^{20.4°}$ 1.5496.

3-(3,4-Dimethoxyphenylacetyl)indole (IVa). A solution of 13.00 g. (0.111 mole) of indole in 50 ml. of anhydrous benzene was added during 15 minutes to a solution of phenylmagnesium bromide prepared from 2.43 g. (0.100 g.-atom) of magnesium and 17.70 g. (0.113 mole) of bromobenzene in 50 ml. of anhydrous ether. The resulting light yellow solution was then refluxed for 1.5 hr. and finally cooled in an ice bath.

A solution of 21.5 g. (0.100 mole) of homoveratroyl chloride in 125 ml. of anhydrous ether was placed in a 500 ml. three-neck flask equipped with stirrer, condenser (drying tube), and a dropping funnel with a vapor by-pass. The acid chloride solution was stirred vigorously and cooled in ice while the indolylmagnesium bromide solution was added dropwise during 2 hr. The resulting cream colored suspension was stirred for an additional 30 minutes then hydrolyzed by addition of 50 ml. of 10% aqueous ammonium chloride and stirred for another 20 min. The white solid which separated was collected on a Büchner funnel, washed three times with ether, then air dried. The yield was 11.08 g. (37.5%); m.p. 175–181°. Recrystallization from 235 ml. of 95% ethanol gave pure 3-(3,4-dimethoxyphenylacetyl)indole as short white needles, m.p. 183–185°; λ_{max}, mμ (log ε): 240 (4.21), 260 (4.03), 300 (4.12); infrared (cm.$^{-1}$): 3195 (N–H), 1635 (C═O).

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.21; H, 5.80; N, 4.74. Found: C, 73.40; H, 5.89; N, 4.66.

3-(4,5-Dimethoxy-2-nitrophenylacetyl)indole (Va). A solution of 2.80 g. of concentrated nitric acid (sp. g. 1.42, 70% nitric acid, 0.0442 mole) in 50 ml. of glacial acetic acid was added in one portion to a suspension of 9.00 g. (0.0305 mole) of 3-(3,4-dimethoxyphenylacetyl)indole in 200 ml. of glacial acetic acid contained in a 500 ml. Erlenmeyer flask. The mixture was stirred for 3 hours during which the starting material gradually dissolved and the product separated from solution. The crude solid was collected directly on a Büchner funnel, washed four times with glacial acetic acid, then with ether and air dried; it weighed 9.13 g. Recrystallization from 600 ml. of glacial acetic acid gave 7.85 g. (75.6%) of 3-(4,5-dimethoxy-2-nitrophenylacetyl)indole as pale yellow, cotton-like needles, m.p. 234–235° (decomp.); λ_{max}, mμ (log ε): 240 (4.44), 298 (4.22), 346 shoulder (3.79); infrared (cm.$^{-1}$): 3270 (N—H), 1622 (C═O).

Anal. Calcd. for $C_{18}H_{16}N_2O_5$: C, 63.53; H, 4.74; N, 8.23. Found: C, 63.60; H, 4.91; N, 8.23.

5,6-Dimethoxy-2,3′-biindolyl (VIa). To a boiling solution of 4.48 g. (0.0132 mole) of 3-(4,5-dimethoxy-2-nitrophenylacetyl)indole in 350 ml. of glacial acetic acid, contained in a 1-l. Erlenmeyer flask, was added a solution of 10.5 g. (0.0466 mole) of stannous chloride dihydrate in 15 ml. of concentrated hydrochloric acid during 3 min. There resulted a deep red homogeneous solution, which was kept boiling on the hot plate for 10 minutes during which small crystals separated. The solid was collected by filtration through a sintered glass funnel, washed on the filter with two 10-ml. portions of glacial acetic acid, then with ether and air dried. This orange-brown powder (presumably the hexachlorostannic acid complex) weighed 4.45 g.; it was suspended in 15 ml. of 95% ethanol, and 10% aqueous sodium hydroxide stirred in until a colorless suspension resulted (*p*H about 7). The white powder was collected by filtration, washed once with 95% ethanol, once with ether, then air dried. This material was extracted with six 25-ml. portions of boiling ethyl acetate, the combined extracts concentrated to about 10 ml. and cooled to yield 1.10 g. (28.6%) of crude product, tan crystals, m.p. 229–232° dec. Sublimation of this material at 210–220°/0.5 mm. produced analytically pure 5,6-dimethoxy-2,3′-biindolyl as long, transparent, colorless needles, m.p. 234.5–236° dec.; λ_{max}, mμ (log ε): 224(4.41), 240 shoulder (4.35), 288 (4.03), 325 (4.37). This compound gave an intense blue color with ethanolic Ehrlich's reagent and a green color with ethanolic iodine.

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 74.10; H, 5.85; N, 9.55.

5,6-Dihydroxy-2,3′-biindolyl hydroiodide (VII). A mixture of 0.51 g. of 5,6-dimethoxy-2,3′-biindolyl, 15 ml. of glacial acetic acid, and 5 ml. of 47% hydriodic acid was refluxed for 5.5 hr. By the end of the first hour a homogeneous, light orange solution resulted, and by the end of the second hour orange-yellow crystals began to separate from solution. At the end of the reflux period the mixture was allowed to cool to room temperature, and the product was collected on a sintered glass funnel, washed with glacial acetic acid, then with ether and finally dried over phosphorus pentoxide in a nitrogen atmosphere for 24 hr. This product was then further dried at 100°/0.07 mm. over potassium hydroxide for 1 hr. The yield of 5,6-dihydroxy-2,3′-biindolyl hydroiodide was 0.62 g. (90%); deep yellow needles which blackened at 210–220°, but did not melt up to 360°; λ_{max}, mμ (log ε): 220 (4.57), 242 shoulder (4.35), 280, 292 (4.03), 327 (4.38), 410 (—); the intensity of this last band was strongly *p*H dependent and a true molar extinction coefficient was not calculated; infrared (cm.$^{-1}$): 3496 (O–H).

Anal. Calcd. for $C_{16}H_{13}N_2O_2I$: C, 49.00; H, 3.34; N, 7.14; neut. eq., 392. Found: C, 49.15; H, 3.62; N, 6.94; neut. equiv. 386.[22]

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(19) H. R. Snyder, J. S. Buck, and W. S. Ide, *Org. Syntheses*, Coll. Vol. II, 333 (1943).

(20) R. D. Haworth, W. H. Perkin, and J. Rankin, *J. Chem. Soc.*, **125**, 1694 (1924).

(21) C. Mannich and M. Falber, *Arch. Pharm.*, **267**, 606 (1929); *cf. Chem. Cent.*, **1930**, I, 77.

This deep yellow hydroiodide could not easily be crystallized from any solvent other than the reducing medium in which it was prepared because of its sensitivity to oxidation. The solid could, however, be stored in vials without special precautions for periods up to six months with only slight darkening, and with no noticeable change in absorption spectrum of a freshly prepared ethanolic solution. When allowed to stand exposed to air, such solutions turned dark green within one-half day.

A sample of the hydroiodide was dissolved in water and neutralized with dilute sodium bicarbonate solution to give a colorless solid, which was washed with water and dried in a nitrogen atmosphere over phosphorus pentoxide. This compound, presumably the free base, blackened at 165–170°, but did not melt up to 260°. The material was dark brown after a few hours exposure to air, and was not obtained in satisfactory analytical purity. Dissolution of either this free base or the hydroiodide in 0.1 *M* sodium hydroxide, which had been refluxed and cooled to room temperature under nitrogen, gave a colorless solution. Displacement of the protective nitrogen atmosphere with air caused an immediate change to a deep red color. Similar red solutions (λ_{max}, 324, 490 mμ) were formed in 95% ethanolic solutions of the hydroiodide, 1.2×10^{-4} *M*, which had either been shaken for one minute with silver oxide or allowed to autooxidize for one-half hour in the presence of 1.2×10^{-4} *M* sodium hydroxide.

3-(3,4-Dimethoxyphenylacetyl)-2-methylindole (IVb). A solution of ethylmagnesium bromide was prepared in 50 ml. of anhydrous ether from 0.69 g. (0.028 g.-atom) of magnesium turnings and 3.50 g. (0.032 mole) of ethyl bromide in a 250 ml. three-neck flask equipped with stirrer, condenser protected with a calcium chloride tube, and a vapor-by-pass dropping funnel. To the well-stirred Grignard reagent was added a solution of 4.00 g. (0.037 mole) of 2-methylindole in 15 ml. of anhydrous ether during 10 min. The resulting two-phase liquid mixture was refluxed for 30 minutes then allowed to stand at ambient conditions for 1 hr. This mixture was stirred vigorously while a solution of 6.07 g. (0.0283 mole) of homoveratroyl chloride in 20 ml. of anhydrous ether was added dropwise during 30 min. A canary-yellow suspension formed; it was stirred for another 30 min. then hydrolyzed by addition of 30 ml. of 10% aqueous ammonium chloride. The resulting mixture consisted of a nearly colorless aqueous phase, a red ethereal phase, and a solid at the interface. The solid was collected by filtration, washed on the filter with water, then with ether, and air dried overnight. The yield of pink-tinted white crystals was 2.40 g. (24%), m.p. 150–154°. Recrystallization from 25 ml. of 95% ethanol gave 1.57 g. (and a second crop of 0.14 g. by subsequent concentration to 7 ml.) of white crystals of 3-(3,4-dimethoxyphenylacetyl)-2-methylindole, m.p. 155–157.5°; λ_{max} mμ (log ϵ): 220 (4.41), 238 shoulder (4.15), 270 (4.08), 304 (4.10); infrared (cm.$^{-1}$): 3330 (N—H), 1653 (C=O).

Anal. Calcd. for $C_{19}H_{19}NO_3$: C, 73.75; H, 6.19; N, 4.53. Found: C, 73.90; H, 6.31; N, 4.50.

This compound (0.74 g.) was nitrated in 10 ml. of glacial acetic acid containing 0.24 g. of concentrated nitric acid for one-half hour. Dilution of the reaction mixture with water and repeated recrystallization of the crude solid (m.p. less than 100°) from 95% ethanol gave 0.07 g. of fine yellow needles, m.p. 233.5–235.5° (decomp.), m.m.p. with (Vb) was 187–206°. This product appeared to be a dinitro derivative.

Anal. Calcd. for $C_{19}H_{17}N_3O_7$: N, 10.52. Found: N, 10.40.

3-(4,5-Dimethoxy-2-nitrophenylacetyl)-2-methylindole (Vb). A solution of 2.22 g. (0.010 mole) of 4,5-dimethoxy-2-nitrophenylacetonitrile[17] in 25 ml. of chloroform was added to a solution of 1.20 g. (0.0107 mole) of 2-methylindole in 150 ml. of anhydrous ether. The resulting solution was placed in a 250 ml. Erlenmeyer flask equipped with a magnetic stirrer, a gas delivery tube leading beneath the surface of the liquid, and an exhaust vent protected from atmospheric moisture by a calcium chloride tube. The solution was stirred vigorously while anhydrous hydrogen chloride was bubbled in for 24 hr. Initially some precipitation of solid occurred, but by the end of three hours the mixture consisted of amber oil droplets suspended in the bulk phase. By the end of 5 hr. most of the oil droplets had redissolved and a new solid phase appeared. At the end of the reaction period the solid product, presumably the ketimine hydrochloride, was collected by filtration, washed twice with ether, air dried briefly then dissolved in 50 ml. of water. The aqueous solution was filtered then boiled for 15 min. during which a light yellow solid formed. The crude product was collected by filtration, washed with water, and air dried; it weighed 0.26 g. (7.3% yield) and had m.p. 212–215°. Two recrystallizations from 95% ethanol gave small yellow prisms of 3-(4,5-dimethoxy-2-nitrophenylacetyl)-2-methylindole, m.p. 220.5–222°; λ_{max}, mμ (log ϵ): 242(4.34), 268 (4.18), 302 (4.25), 340 shoulder (3.90); infrared (cm.$^{-1}$): 3380 (N—H), 1613 (C=O).

Anal. Calcd. for $C_{19}H_{18}N_2O_5$: C, 64.39; H, 5.12; N, 7.91. Found: C, 64.60; H, 5.37; N, 8.04.

5,6-Dimethoxy-2′-methyl-2,3′-biindolyl (VIb). To a boiling solution of 0.24 g. (0.00067 mole) of 3-(4,5-dimethoxy-2-nitrophenylacetyl)-2-methylindole in 50 ml. of 95% ethanol was added a solution of 1.00 g. (0.00476 mole) of sodium hydrosulfite dihydrate and 5 ml. of 1 N sodium hydroxide diluted to 10 ml. with water. There was a fleeting dark color as the solutions were mixed, and a light yellow suspension resulted. Boiling was continued and five 5 ml.-portions of water were added during 10 min. The hot solution was filtered free of a little water-soluble white solid, and the filtrate diluted with 200 ml. of water to give a colloidal suspension, which was then distilled to remove 210 ml. of distillate. A solid separated from the residual solution; it was collected by filtration and air dried to give 0.11 g. (54%) of crude product, m.p. 225–227°. Sublimation at 210°/0.07 mm. gave pure 5,6-dimethoxy-2′-methyl-2,3′-biindolyl as a dull white powder, m.p. 227–229° (dec.); λ_{max}, mμ (log ϵ): 224 (4.47), 284 (4.07), 318 (4.32). The compound gave a deep blue color with ethanolic Ehrlich's reagent and a deep green color with ethanolic iodine.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.47; H, 5.92; N, 9.14. Found: C, 74.70; H, 6.04; N, 9.10.

Effect of nitric acid/acetic acid on 3-acetylindole. A mixture of 0.80 g. of 3-acetylindole,[23] 20 ml. of glacial acetic acid, and 0.55 g. of concentrated nitric acid (71% nitric acid) was stirred for 4 hr. at room temperature. The resulting solution was poured into 200 ml. of cold water, and the fine white needles which separated were collected, washed with water, and air dried; weight 0.57 g. (71% recovery) of 3-acetylindole, m.p. 188–190°; m.m.p. with pure starting material (m.p. 190–192°) was 189.5–192°, and the compounds showed identical absorption spectra: λ_{max}, mμ (log ϵ): 240 (4.09), 256 shoulder (3.93), 296 (4.08); lit.[24] gives; 241 (4.10), 259 (3.94), 297 (4.09), also in 95% ethanol.

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(22) Reagents for this determination must be completely air free. Titration with standard sodium hydroxide was conducted under a nitrogen atmosphere with phenolphthalein indicator.

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