Synthesis and Demethylation of New 5,6,7,8-Tetrahydro-4,9-dimethoxy-1*H*-benz[*f*]indole

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Received October 5, 1981

The title compound **17** was prepared in good yield starting from 5,6,7,8-tetrahydro-1-naphthol (**9**) by an advantageous synthesis route consisting of eight steps, as indicated in Scheme 2. Demethylation by reflux heating with anhydrous aluminium chloride in dry benzene furnished 4,9-dihydroxy- and 4,9-dioxo-5,6,7,8-tetrahydro-1*H*-benz[*f*]indoles (compounds **18** and **19**, respectively). All new products were identified on the basis of spectral and analytical data.

J. Heterocyclic Chem., **19**, 633 (1982).

Several of our previous reports in the field of potential chemotherapeutic agents have dealt with the chemical synthesis and biological evaluation of heterocyclic derivatives containing a quinazoline or indole system (1-4). A class of compounds which has been studied widely includes alkyl-, aryl- and acyl- derivatives of 4,7-dimethoxyindole and their demethylation and oxidization products (5-9), in order to establish the minimal essential requirements for antimicrobial activity in this series of compounds. A few of these new indole derivatives, in evident structural relationship with the mytomicin antibiotics or other simpler synthetical analogues (10), showed a certain "in vitro" antibacterial potency (11-12).

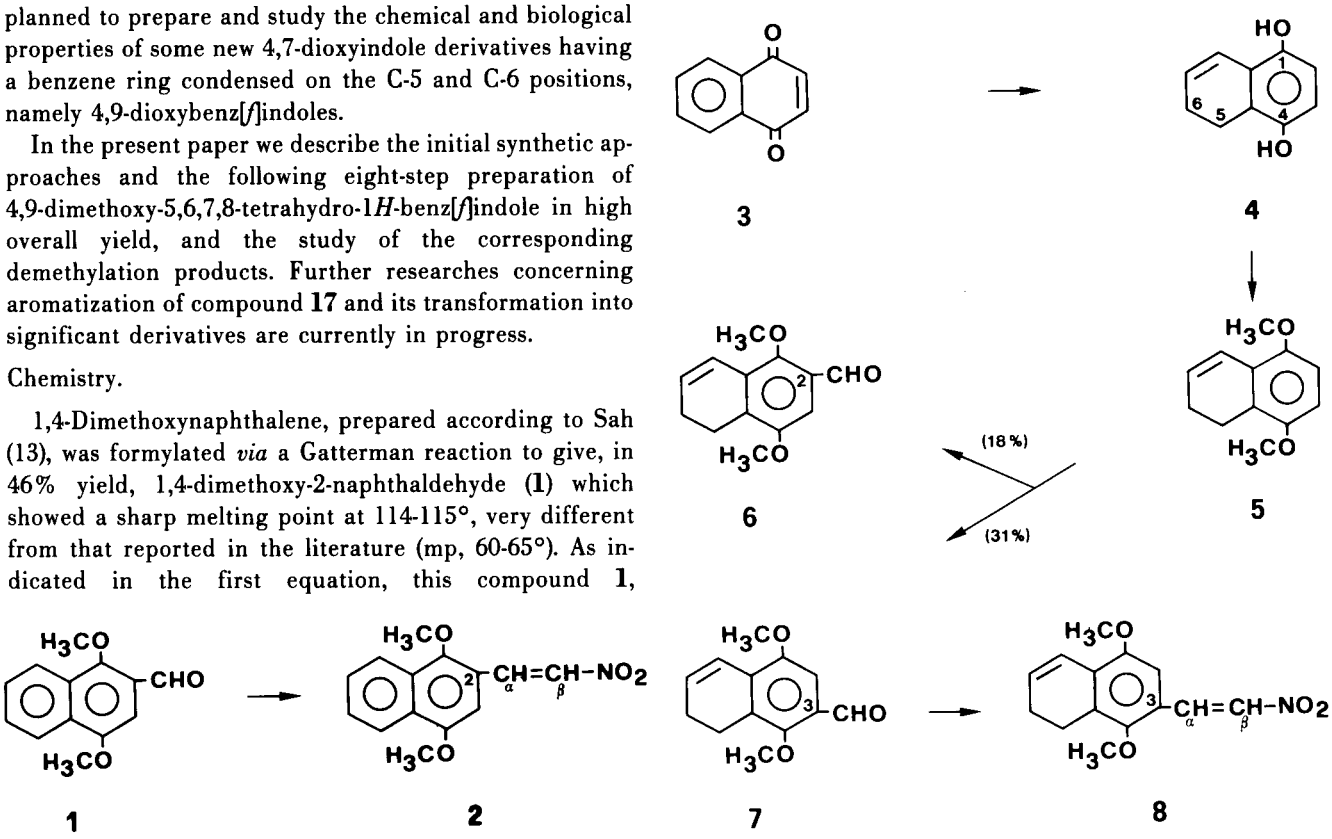
In order to investigate further the relationship between chemical structure and antibacterial activity, we have planned to prepare and study the chemical and biological properties of some new 4,7-dioxyindole derivatives having a benzene ring condensed on the C-5 and C-6 positions, namely 4,9-dioxybenz[*f*]indoles.

In the present paper we describe the initial synthetic approaches and the following eight-step preparation of 4,9-dimethoxy-5,6,7,8-tetrahydro-1*H*-benz[*f*]indole in high overall yield, and the study of the corresponding demethylation products. Further researches concerning aromatization of compound **17** and its transformation into significant derivatives are currently in progress.

Chemistry.

1,4-Dimethoxynaphthalene, prepared according to Sah (13), was formylated *via* a Gatterman reaction to give, in 46% yield, 1,4-dimethoxy-2-naphthaldehyde (**1**) which showed a sharp melting point at 114-115°, very different from that reported in the literature (mp, 60-65°). As indicated in the first equation, this compound **1**, characterized by ir and nmr spectroscopy, was condensed with nitromethane in alkali, yielding an alcoholic intermediate, which was dehydrated to 1,4-dimethoxy-2-(β-nitrovinyl)naphthalene (**2**). This product (40% yield), subjected to nitration under mild conditions (cold 65% nitric acid in an ice-bath), instead of yielding a nitro derivative (which in any case would be probably not the required 3-nitro compound, because of the involved β-position of the activated ring in the naphthalene system), underwent loss of one of the methoxyl groups. Therefore, the preparation of compounds **1** and **2** proved useful in correctly interpreting the structures of the following derivatives (see below) by comparison with the cor-

Scheme 1



responding spectral data.

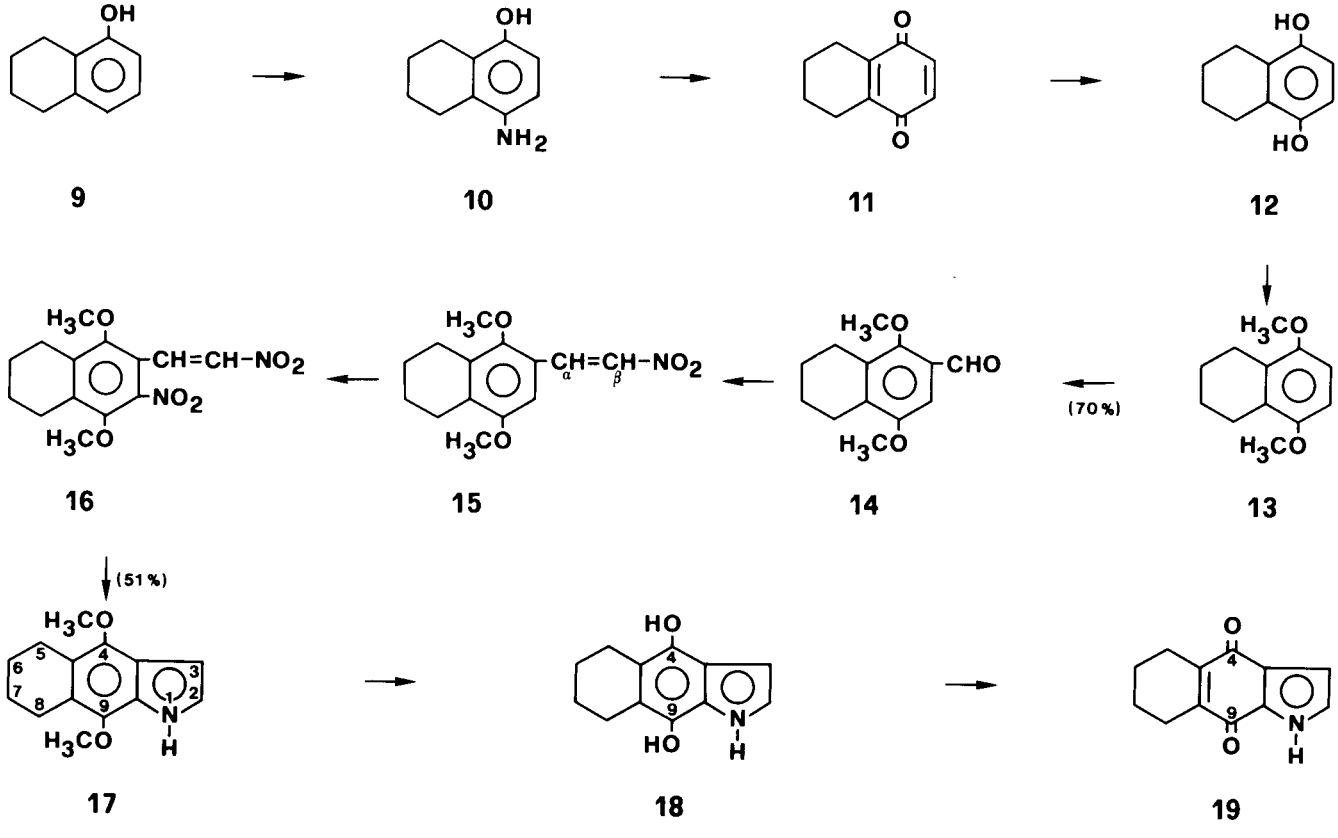
In order to synthesize the desired benzindole, we then attempted to reduce catalytically the starting available 1,4-naphthoquinone, according to the procedure of Cardani (14), with the aim of hydrogenating not only the quinonoid structure but also saturating two double bonds of the unsubstituted condensed benzene ring, thus reducing the naphthalene character of the fused system. Contrary to expectations, although the reductive procedures were strengthened, it was always possible to separate a crystalline compound, the structure of which was identified as 1,4-dihydroxy-5,6-dihydronaphthalene (**4**). This partly dearomatized compound also seemed to be interesting because the unsubstituted ring appeared to have, in practice, only two electrons (butene system) (15).

According to the sequence of steps outlined in Scheme 1, compound **4** was methylated to 1,4-dimethoxy-5,6-dihydronaphthalene (**5**) and then formylated by the procedure previously reported to produce in a 49% total yield, a mixture of two isomers, which was resolved by means of a fractionated sublimation in vacuum, thus obtaining 1,4-dimethoxy-5,6-dihydro-2-naphthaldehyde (**6**) as a minor product (17.6%) together, with a major amount (31.3%) of 1,4-dimethoxy-5,6-dihydro-3-naphthaldehyde (**7**), whose structures were assigned on the basis of their nmr and ir spectra. As previously indicated, this latter compound **7** was easily transformed into 1,4-dimethoxy-5,6-dihydro-3-(β-nitrovinyl)naphthalene (**8**). This compound **8**, however, also proved incapable of undergoing nitration at C-2 position, *i.e.*, the indispensable structural requirement for achieving the subsequent reductive cyclization to the benzindole system.

More promising results were expected by using the commercial 5,6,7,8-tetrahydro-1-naphthol (**9**), which, by virtue of its tetrasaturated ring, appeared to be ideal starting material for the synthesis. We also decided to accomplish its complete transformation into a benzindole derivative, proceeding through the sequence outlined in Scheme 2, as described in the Experimental.

Starting material **9** was coupled first with an appropriate diazonium salt to produce an azonaphthol intermediate, which was then hydrogenated to 4-amino-5,6,7,8-tetrahydro-1-naphthol (**10**). This amino derivative was used directly in the next oxidization step without further purification, yielding 5,6,7,8-tetrahydronaphtho-1,4-dione (**11**). An easy reduction with sodium hydrosulfite in ether produced the corresponding dihydroxy derivative (**12**), which was methylated with dimethyl sulfate in alkaline medium to give 1,4-dimethoxy-5,6,7,8-tetrahydronaphthalene (**13**). A 23% total yield was obtained in these four

Scheme 2



steps just described. In this case too, a formylation with zinc cyanide and dry hydrogen chloride gas furnished the crystalline 1,4-dimethoxy-5,6,7,8-tetrahydro-2-naphthaldehyde (**14**) in good yield (over 70%). The subsequent step, carried out in the manner previously reported, gave compound **15** [1,4-dimethoxy-5,6,7,8-tetrahydro-2-(β-nitrovinyl)naphthalene], in a 47% yield. Nitration of **15** under mild conditions afforded in satisfactory yield (62%) the required 1,4-dimethoxy-5,6,7,8-tetrahydro-2-(β-nitrovinyl)-3-nitronaphthalene (**16**). Reduction of this product, accompanied by spontaneous cyclization, produced the expected 4,9-dimethoxy-5,6,7,8-tetrahydro-1*H*-benz[*f*]indole (**17**) as a white crystalline compound, easily sublimable in vacuum, in 51% yield. Demethylation of the benzindole derivative **17** by reflux-heating in dry benzene solution with anhydrous aluminum chloride followed by extraction with ether and concentration in a water bath under a nitrogen stream, furnished a crude residue, from which two demethylated compounds were separated. By dissolving first the residue in boiling ethyl acetate and, after concentration to a small volume by adding petroleum ether, a crystalline product was collected, sublimable in vacuum, which turned out to be 5,6,7,8-tetrahydro-1*H*-benz[*f*]-indole-4,9-dione (**19**). By evaporation to dryness of the solvents of crystallization, a new residue was obtained, from which under fractionated sublimation the 4,9-dihydroxy-5,6,7,8-tetrahydro-1*H*-benz[*f*]indole (**18**) was separated as a crystalline red sublimate.

EXPERIMENTAL

Melting points were determined on a Büchi-Tottoli SPM-20 apparatus in open capillaries and are uncorrected. Infrared spectra were measured on a Perkin-Elmer 437 spectrometer as potassium bromide pressed discs, unless otherwise stated; the absorptions are given in cm^{-1}. Proton nmr spectra were recorded in the indicated solvent on a Varian FT-80A instrument, and chemical shifts are reported in δ units, downfield from tetramethylsilane; the abbreviations s, d, t, q, m, br, refer to singlet, doublet, triplet, quartet, multiplet and broad, respectively; in the case of multiplets, chemical shifts quoted were measured from the approximate center. Integrals correspond satisfactorily to the chemical formula. Elemental analyses were performed by the Microanalytical Laboratory of the Institute of Pharmaceutical Chemistry of the University of Padua. All distillative concentration of solvents (dried over anhydrous reagent-grade sodium sulfate) was done with a rotary evaporator under reduced pressure. "Dry" solvents were distilled shortly before use from appropriate classical drying reagents. Optimization of product yields was not attempted.

Starting materials **3** and **9** were purchased from Aldrich-Europe Division. 1,4-Dimethoxynaphthalene was prepared as described by Sah (13), mp 85°; nmr (deuterioacetone): δ 3.93 (6H, s, 2 × OCH_3), 6.77 (2H, s, HC_2 and HC_3), 7.47 (2H, m, HC_6 and HC_7), 8.16 (2H, m, HC_5 and HC_8).

1,4-Dihydroxy-5,6-dihydronaphthalene (**4**).

1,4-Naphthoquinone (**3**) (22 g) was dissolved in 300 ml of ethanol and hydrogenated at 70° and 100 atmospheres with 5 g of active Raney nickel, freshly produced according to Pavlic and Adkins (16), in a classical apparatus for catalytic hydrogenation. After 4 hours, the catalyst was filtered and the solution concentrated to *ca.* 30 ml, before steam-distilling. From the aqueous distillate a crystalline translucent product (8.6 g) was separated by suction and purified by sublimation in vacuum (100° at 0.5 × 10^{-1} torr), to give a crystalline pale violet product, mp 173-174°; ir (potassium bromide): 3218 (broad OH), 2924-2906 (CH and C=C) cm^{-1}; nmr (deuterioacetone): δ 1.71 (2H, m, CH_2 at C_6), 2.62 (2H, m, CH_2 at C_5), 3.18-3.85 (2H, 2s br, 2 × OH), 6.47 (1H, s, HC_3), 6.72 (1H, s, HC_2), 7.44 (1H, m, HC_7), 8.18 (1H, m, HC_8).

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.19; H, 6.11.

1,4-Dimethoxy-5,6-dihydronaphthalene (**5**).

To a stirred solution of 3.9 g of compound **4** in 10 ml of aqueous 5*N* sodium hydroxide in a three-necked flask equipped with a dropping funnel and a reflux water-condenser under a continuous current of nitrogen, 4.8 ml of dimethyl sulfate was added dropwise, and the mixture was stirred at room temperature for 2 hours. An additional 2 ml of dimethyl sulfate was introduced and the reaction continued for 2 hours. The solid, collected by suction filtration, was washed with aqueous sodium hydroxide, then with water and subjected to sublimation in vacuum at 60°/0.4 × 10^{-1} torr. The white sublimate melted at 49-50° [lit (17), mp 54°]; ir (potassium bromide): 2924 (CH and C=C), 2824 (OCH_3) cm^{-1}; nmr (deuterioacetone): δ 1.68 (2H, m, CH_2 at C_6), 2.58 (2H, m, CH_2 at C_5), 3.71 (3H, s, OCH_3 at C_4), 3.92 (3H, s, OCH_3 at C_1), 6.61 (1H, s, HC_3), 6.77 (1H, s, HC_2), 7.48 (1H, m, HC_7), 8.17 (1H, m, HC_8).

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 76.05; H, 7.42.

4-Amino-5,6,7,8-tetrahydro-1-naphthol (**10**).

This compound was prepared from 5,6,7,8-tetrahydro-1-naphthol by a procedure similar to that described by Smith and Austin (18). Sulfanilic acid (57.5 g) was diazotized with 23 g of sodium nitrite in the presence of 17.6 g of sodium carbonate by means of acidification with a solution of 36% hydrochloric acid (69 ml) in 200 ml of water. The cold mixture of the diazonium salt was slowly stirred into a cooled solution of sodium hydroxide (37.5 g) in 150 ml of water containing 37 g of 5,6,7,8-tetrahydro-1-naphthol. The mixture was allowed to stand overnight, then cooled to 5° before slowly adding 110 g of sodium hydrosulfite to produce a complete reduction. After 5 hours of stirring at room temperature, the title aminonaphthol was filtered by suction, washed with cold water and dried, giving a resinous crude product which was subjected directly to oxidization (see next paragraph). An analytical sample was obtained by sublimation at 100° and 0.3 × 10^{-2} torr, white crystalline product, mp 144°; ir (potassium bromide): 3364-3018 (NH_2, OH), 2918-2860 (CH_2-CH_2), 1276-1262 ($ArNH_2$) cm^{-1}; nmr (deuterioacetone): δ 1.72 (4H, m, CH_2 at C_6 and C_7), 2.06 (2H, s br, NH_2), 2.33 (2H, m, CH_2 at C_5), 2.63 (2H, m, CH_2 at C_8); 6.26 (1H, t, HC_3), 6.54 (1H, t, HC_2).

Anal. Calcd. for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.21; H, 8.02; N, 8.32.

5,6,7,8-Tetrahydronaphtho-1,4-dione (**11**).

This compound was prepared by the oxidative method of Arnold and Zaugg (19). Crude 4-amino-5,6,7,8-tetrahydronaphthol (**10**) (see previous paragraph) was dissolved by warming in 1000 ml of water containing 60 ml of concentrated sulfuric acid. This solution was oxidized by its dropwise addition to a suspension of 280 g of manganese dioxide in 1000 ml of water containing 30 ml of 95% sulfuric acid, with continuous removal of the product by steam distillation. The distillate was cooled and the crude naphthoquinone in the distillate filtered by water suction. The filtrate was extracted with ether until colourless, the solvent was evaporated and the crystalline residue was added to the previous compound giving 6.8 g of a yellow crystalline product, mp 55-56°; ir (potassium bromide): 2932-2867 (CH_2-CH_2), 1610-1588-1557 (C=O) cm^{-1}; nmr (deuterioacetone): δ 1.68 (4H, m, CH_2 at C_6 and C_7), 2.37 (4H, m, CH_2 at C_5 and C_8), 6.72 (2H, s, HC_2 and HC_3).

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 73.90; H, 6.13.

5,6,7,8-Tetrahydro-1,4-dihydroxynaphthalene (**12**).

The title compound was obtained in 96% yield by shaking an ethereal solution of compound **11** (6.5 g in 250 ml) at room temperature with an excess of aqueous solution of sodium hydrosulfite (48 g in 250 ml) until decoloration. The ethereal layer was separated and the aqueous phase ex-

tracted with ether. The total extracts were combined and dried. Removal of the solvent yielded 6.34 g of a white crystalline product, sublimable in vacuum (140° at 0.2 × 10^{-1} torr), mp 178°; ir (potassium bromide): 3245-3178 (OH), 2916-2850 (CH_2-CH_2), cm^{-1}; nmr (deuterioacetone): δ 1.71 (4H, m, CH_2 at C_6 and C_7), 2.60 (4H, m, CH_2 at C_5 and C_8), 2.57-7.40 (2H, 2s br, 2 × OH), 6.46 (2H, s, HC_2 and HC_3).

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.86; H, 7.41.

5,6,7,8-Tetrahydro-1,4-dimethoxynaphthalene (**13**).

By the procedure of Cardani (14), to a stirred solution of compound **12** (25 g) in 62 ml of 5*N* sodium hydroxide in a three-necked flask equipped with a dropping-funnel and a nitrogen stream, 35 ml of dimethyl sulfate was added slowly. After 4 hours the reaction mixture was diluted with water and, after a vigorous shaking, the crude solid product was filtered by suction and washed first with 2*N* sodium hydroxide then repeatedly with water, 24.4 g (83.4%) of crystalline colourless needles, mp 42-43°. An analytical sample was purified by vacuum sublimation (0.4 × 10^{-1} torr at 40°, white crystals, mp 45° (lit (14), mp 43-44°); ir (potassium bromide): 2980-2919-2822 (CH_2-CH_2 and CH_3), cm^{-1}; nmr (deuterioacetone): δ 1.68 (4H, m, CH_2 at C_6 and C_7), 2.58 (4H, m, CH_2 at C_5 and C_8), 3.71 (6H, s, 2 × OCH_3), 6.61 (2H, s, HC_2 and HC_3).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.76; H, 8.31.

General Procedure for Preparation of 1,4-Dimethoxynaphthaldehydes.

According to the methods previously described (20-21), the three dimethyl ethers of naphthohydroquinones, *i.e.*, the completely aromatized 1,4-dimethoxynaphthalene [prepared, as mentioned, using the procedure of Sah (13)], and the dihydro compound **5** and tetrahydro compound **13**, were formylated *via* the Gatterman reaction, in this general manner: 0.05 mole of each dimethyl ether were dissolved in dry tetrachloroethane (70 ml). Oven-dried zinc cyanide (13.5 g) was added and the mixture stirred vigorously at room temperature while a continuous stream of dry hydrogen chloride was introduced. After 1 hour, the mixture was thoroughly cooled at 0° and 12 g of anhydrous aluminium chloride was added. Hydrogen chloride was passed into the mixture for an additional 2 hours, maintaining the temperature at 65-70°. Additional dry zinc cyanide (6.8 g) was then added, while continuing introduction of the dry gas for an additional 2 hours. Further zinc cyanide (6.8 g) was again added and introduction of the gas was continued for an additional 4 hours. 90 Ml of 2.5 *N* sulfuric acid was added slowly to the cooled mixture, which was then allowed to stand overnight at room temperature. The mixture was slowly heated to boiling point and then steam distilled. The organic solvent came over first and was collected separately; this was followed by the aldehyde, partly in a solid state, which was filtered off by suction, and partly dissolved in the aqueous distillate, which was extracted with ether. Removal of the solvent yielded the corresponding aldehyde, which was combined with the solid already collected.

1,4-Dimethoxy-2-naphthaldehyde (**1**).

1,4-Dimethoxynaphthalene (9.41 g) mp 85°, produced 4.93 g (45.6%) of a yellowish crystalline product, mp 114-115° (lit (13), 60-65°, no sharp melting point); ir (potassium bromide): 2963-2924-2862 (CH_3), 1640-1586 (CHO) cm^{-1}; nmr (deuterioacetone): δ 4.03-4.11 (6H, 2s, 2 × OCH_3), 7.09 (1H, s, HC_3), 7.67 (2H, m, HC_6 and HC_7), 8.24 (2H, m, HC_5 and HC_8), 10.54 (1H, s, CHO).

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.11; H, 5.72.

1,4-Dimethoxy-5,6-dihydronaphthaldehydes.

1,4-Dimethoxy-5,6-dihydronaphthalene (**5**) (9.51 g) furnished 5.34 g (49% total yield) of a mixture of two isomers, which was resolved by means of a fractionated sublimation.

a) 1,4-Dimethoxy-5,6-dihydro-2-naphthaldehyde (**6**).

The title compound, collected at 50° and 0.5 × 10^{-2} torr, was crystallized from benzene-petroleum ether giving 1.92 g (17.6%) of whitish product, mp 98°; ir (potassium bromide): 2972-2860 (CH_3 and CH_2-CH_2), 1612-1580 (CHO) cm^{-1}; nmr (deuterioacetone): δ 1.74 (2H, m, CH_2 at C_6), 2.74 (2H, m, CH_2 at C_5), 4.04-4.12 (6H, 2s, 2 × OCH_3), 7.10 (1H, s, HC_3), 7.68 (1H, m, HC_7), 8.25 (1H, m, HC_8), 10.54 (1H, s, CHO).

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.63; H, 6.38.

b) 1,4-Dimethoxy-5,6-dihydro-3-naphthaldehyde (**7**).

In continuing the sublimation at 60-65° and 0.2 × 10^{-2} torr, a crystalline sublimate was obtained which, by crystallization from toluene, produced 3.42 g (31.4%) of a light yellow substance, mp 113-114°; ir (potassium bromide): 2938-2843 (CH_3 and CH_2-CH_2), 1652-1575 (CHO) cm^{-1}; nmr (deuterioacetone): δ 1.74 (2H, m, CH_2 at C_6), 2.63 (2H, m, CH_2 at C_5), 3.83 (6H, s, 2 × OCH_3), 7.03 (1H, s, HC_2), 7.68 (1H, m, HC_7), 8.25 (1H, m, HC_8), 10.28 (1H, s, CHO).

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.39; H, 6.28.

1,4-Dimethoxy-5,6,7,8-tetrahydro-2-naphthaldehyde (**14**).

1,4-Dimethoxy-5,6,7,8-tetrahydronaphthalene (**13**) (9.61 g) yielded 7.72 g (70.2%) of translucent macrocrystals, mp 68-69°; ir (potassium bromide): 2920-2836 (CH_3 and CH_2-CH_2), 1657-1575 (CHO) cm^{-1}; nmr (deuterioacetone): δ 1.72 (4H, m, CH_2 at C_6 and C_7), 2.62 (4H, m, CH_2 at C_5 and C_8), 3.82 (6H, s, 2 × OCH_3), 7.02 (1H, s, HC_3), 10.26 (1H, s, CHO).

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.16; H, 7.44.

General Procedure for Preparation of 1,4-Dimethoxy-(β-nitrovinyl)-naphthalenes.

Each 1,4-dimethoxynaphthaldehyde (compounds **1**, **7** and **14**, respectively) (0.021 mole) was dissolved by heating in 50 ml of ethanol. To the cold solution, 2.56 g (0.042 mole) of nitromethane in 50 ml of ethanol was added slowly. An aqueous cold solution of potassium hydroxide [2.7 g (0.048 mole) in 7 ml of water] was introduced dropwise and the mixture allowed to stand at 5° for 24 hours. The suspension was then diluted with 200 ml of ice-water and acidified with concentrated hydrochloric acid. The mixture was extracted exhaustively with ether. The combined extracts were washed first with a saturated aqueous solution of sodium bisulfite, then with water, and dried. Removal of the ether left the crude residue, which was dealcoholized by refluxing with 18 ml of acetic anhydride and 3.5 g of fused sodium acetate. After 20 minutes, each mixture was cooled, diluted with 80 ml of ice-water and stirred vigorously. The crude material which separated was collected, washed repeatedly with water and crystallized in all cases from dioxane.

1,4-Dimethoxy-2-(β-nitrovinyl)naphthalene (**2**).

Starting from 4.54 g of 1,4-dimethoxy-2-naphthaldehyde (**1**), after crystallization from 10 ml of dioxane, 2.18 g (40%) of crude product was collected, which was recrystallized from absolute ethanol to separate a brown crystalline product, mp 143-144°; ir (potassium bromide): 1608 (CH=CH), 1332 (NO_2) cm^{-1}; nmr (deuterioacetone): δ 4.01-4.09 (6H, 2s, 2 × OCH_3), 7.23 (1H, s, HC_3), 7.65 (2H, m, HC_6 and HC_7), 8.25 (2H, m, HC_5 and HC_8), 8.16-8.42 (2H, 2d, HC_β and HC_α).

Anal. Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.82; H, 5.10; N, 5.67.

1,4-Dimethoxy-5,6-dihydro-3-(β-nitrovinyl)naphthalene (**8**).

The crude product obtained from 4.58 g of **7** was a crystalline solid, 2.58 g (47.1%) mp 137° (dioxane). This compound was recrystallized from toluene to yield light yellow crystals, mp 139-140°; ir (potassium bromide): 1584 (CH=CH), 1328 (NO_2) cm^{-1}; nmr (deuterioacetone): δ 1.75 (2H, m, CH_2 at C_6), 2.75 (2H, m, CH_2 at C_5), 3.76-3.87 (6H, 2s, 2 × OCH_3), 7.17 (1H, s, HC_2), 7.65 (1H, m, HC_7), 8.10 (1H, m, HC_8), 8.02 (1H, d, HC_β), 8.19 (1H, d, HC_α).

Anal. Calcd. for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.07; H, 5.89; N, 5.39.

1,4-Dimethoxy-5,6,7,8-tetrahydro-2-(β-nitrovinyl)naphthalene (**15**).

As above, 4.63 g of **14** produced 2.60 g (47%) of crude crystalline product, mp 149° (dioxane). One crystallization from absolute ethanol gave yellow needles, mp 153-154°; ir (potassium bromide): 3102 (=C-H), 2938-2853 (C-H), 1612-1590-1568 (C=C) cm^{-1}; nmr (deuterioacetone): δ 1.73 (4H, m, CH_2 at C_6 and C_7), 2.63 (4H, m, CH_2 at C_5 and C_8), 3.74-3.85

(6H, 2s, 2 × OCH_3), 7.13 (1H, s, HC_3), 7.98 (1H, d, HC_β), 8.17 (1H, d, HC_α).

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32. Found: C, 63.91; H, 6.42; N, 5.16.

1,4-Dimethoxy-5,6,7,8-tetrahydro-2-(β-nitrovinyl)-3-nitronaphthalene (**16**).

The nitration was carried out with 65% nitric acid at 0° on slightly stirred aliquots of compound **15**. The reaction flask, containing 2.5 g of 1,4-dimethoxy-5,6,7,8-tetrahydro-2-(β-nitrovinyl)naphthalene, was cooled in an ice-bath while 9 ml of nitrating reactive was slowly added under mixing and crushing. After 15 minutes, 20 g of minced ice was added to the mixture, waiting for its total melting at room temperature. The crude product was collected by suction, thoroughly washed with water, crystallized from 20 ml of absolute ethanol and air dried to give 1.82 g (62.3%) of brownish-yellow crystals, mp 116°. A sample for analysis was obtained by recrystallization from the same solvent, mp 118°; ir (potassium bromide): 3127 (=C-H), 2938-2860 (C-H), 1510-1328 (NO_2) cm^{-1}; nmr (deuteriodimethylsulfoxide): δ 1.75 (4H, m, CH_2 at C_6 and C_7), 2.78 (4H, m, CH_2 at C_5 and C_8), 3.73-3.79 (6H, 2s, 2 × OCH_3), 7.67 (1H, d, HC_β), 7.82 (1H, d, HC_α).

Anal. Calcd. for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.23; N, 9.09. Found: C, 54.87; H, 5.20; N, 8.92.

4,9-Dimethoxy-5,6,7,8-tetrahydro-1*H*-benz[*f*]indole (**17**).

To a solution of 4.82 g of 1,4-dimethoxy-5,6,7,8-tetrahydro-2-(β-nitrovinyl)-3-nitronaphthalene (**16**) in 150 ml of ethanol, 25 g of reduced iron powder and 120 ml of acetic acid were added. After heating under reflux for 30 minutes, the mixture was cooled and the iron filtered by suction and washed several times with warm ethanol. The combined filtrates, diluted with 300 ml of water and neutralized with sodium hydrogen carbonate were then extracted with ether. Removal of solvents under reduced pressure afforded a resinous crude residue (4.13 g), which was sublimed at 80-85° (0.3 × 10^{-1} torr) to give the title compound as white plates, 1.84 g (50.9%), mp 99-100°; ir (potassium bromide): 3282 (NH), 2918-2830 (C-H), 2848 (OCH_3) cm^{-1}; nmr (deuterioacetone): δ 1.73 (4H, m, CH_2 at C_6 and C_7), 2.82 (4H, m, CH_2 at C_5 and C_8), 3.79-3.89 (6H, 2s, 2 × OCH_3), 6.48 (1H, d, HC_3), 7.15 (1H, d, HC_2), 10.07 (1H, s br, NH).

Anal. Calcd. for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06; O, 13.84. Found: C, 72.62; H, 7.30; N, 6.05; O, 13.98.

Demethylation of 4,9-Dimethoxy-5,6,7,8-tetrahydro-1*H*-benz[*f*]indole.

Demethylation of compound **17** (0.51 g) was carried out by refluxing it in 50 ml of dry benzene solution containing 5 g of anhydrous aluminium chloride for 6 hours over a water bath in a flask equipped with a water reflux condenser protected from moisture with a calcium chloride drying tube. After cooling, the solid mass was broken up and treated with 100 ml of ice-cold water. The organic layer was then separated and the aqueous layer extracted with diethyl ether. The combined extracts were washed first with a concentrated solution of sodium hydrosulfite, then with water, dried and evaporated to dryness under a positive atmosphere of dry nitrogen to give 0.49 g of crude brown residue.

a) 5,6,7,8-Tetrahydro-1*H*-benz[*f*]indole-4,9-dione (**19**).

The crude demethylated residue (see above) was dissolved in 30 ml of boiling ethyl acetate and the solution filtered, concentrated to *ca.* 6 ml and mixed with 3 ml of petroleum ether. After being cooled overnight at −10°, 127 mg of a crystalline product separated, which was purified by sublimation in vacuum (0.2 × 10^{-1} torr at 100°). The yellow sublimate melted at 203-204°. Recrystallization from toluene did not change the melting point; ir (potassium bromide): 3207 (NH), 2935-2860 (C-H), 1591 (C=O) cm^{-1}; nmr (deuterioacetone): δ 1.67 (4H, m, CH_2 at C_6 and C_7), 2.43 (4H, m, CH_2 at C_5 and C_8), 6.51 (1H, d, HC_3), 7.16 (1H, d, HC_2).

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.49; H, 5.42; N, 6.95.

b) 4,9-Dihydroxy-5,6,7,8-tetrahydro-1*H*-benz[*f*]indole (**18**).

By evaporation to dryness of the ethyl acetate-petroleum ether solution from which compound **19** was collected, a crude residue was obtained, which was fractionally sublimated first at 100-110° (0.2 × 10^{-1} torr) in order to separate the yellow crystalline product still present, then at 150-160° under the same vacuum. Red crystalline sublimate, melting around 227° dec. (with no sharp mp). Repeated attempts to crystallize the product were unsuccessful; ir (potassium bromide): broad absorption from 3368 and 3021 (OH and NH), 2920-2844 (C-H) cm^{-1}; nmr (deuteriodimethylsulfoxide): δ 1.60 (4H, m, CH_2 at C_6 and C_7), 2.36 (4H, m, CH_2 at C_5 and C_8), 6.45 (1H, d, HC_3), 7.13 (1H, d, HC_2), 3.29-7.35 (2H, 2s, 2 × OH), 12.50 (1H, s br, NH).

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.53; H, 6.30; N, 6.87.

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