Synthesis of Novel Methoxy and Hydroxy Derivatives of 2-Phenyl-1*H*-benz[*g*]indoles

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The synthesis of novel methoxy-derivatives of 2-phenyl-1*H*-benz[*g*]indole **3** by condensation of α-naphthylamines **1** with *N*-phenacyl-pyridinium salts **2** is described, as well as their conversion into the corresponding hydroxy-derivatives **5**. Unexpected quinoxaline derivatives **4** were obtained when in the condensation reaction the *N*-nitrophenacylpyridinium salts **2d,e** have been used.

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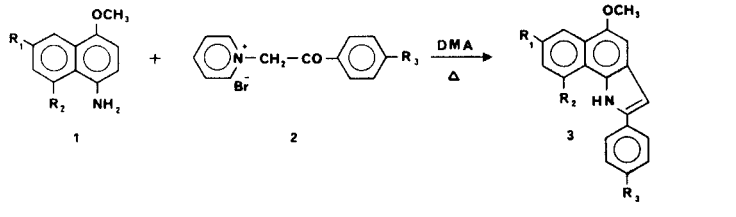
Introduction.

After having reported [1-3] the synthesis of the linearly annulated 4,8-dimethoxy-3*H*-benz[*f*]indoles, we very recently described the synthesis of two new angular benz[*g*]indole dimethoxy-derivatives [4].

In connection with our interest in the field of benzindole derivatives as compounds potentially able to intercalate between two base pairs of the double stranded DNA and, consequently, to exert a cell antiproliferative activity, we now report on the synthesis and properties of a series of new 2-phenyl-1*H*-benz[*g*]indole derivatives, bearing one or more methoxy-groups either in the phenyl ring or in the fused tricyclic structure.

Assuming that the presence of hydroxylic functions could be able to provide a more effective intercalation of the planar heteropolycyclic moiety into DNA, some of the obtained methoxy-derivatives have been converted by demethylation into the corresponding hydroxy-derivatives. For the preparation of the 2-phenyl-1*H*-benz[*g*]indole derivatives the route reported by Bansal and Sharma [5,7]

Scheme 1

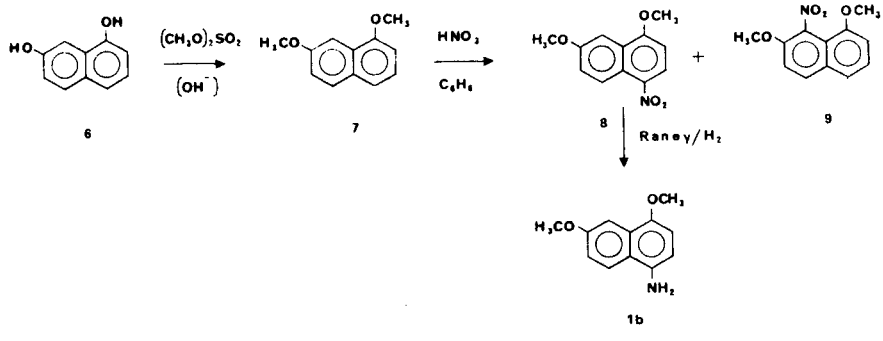


1a: $R_1 = R_2 = H$
1b: $R_1 = OCH_3$; $R_2 = H$
1c: $R_1 = H$; $R_2 = OCH_3$

2a: $R_3 = H$
2b: $R_3 = Cl$
2c: $R_3 = OCH_3$

3a: $R_1 = R_2 = R_3 = H$
3b: $R_1 = OCH_3$; $R_2 = R_3 = H$
3c: $R_1 = R_3 = H$; $R_2 = OCH_3$
3d: $R_1 = H$; $R_2 = R_3 = OCH_3$
3e: $R_2 = OCH_3$; $R_3 = Cl$; $R_1 = H$
3f: $R_1 = OCH_3$; $R_2 = H$; $R_3 = Cl$

Scheme 2



utilizing naphthylamines as starting materials and condensing them with *N*-phenacylpyridinium bromides appeared more attractive than the three step sequence recently utilized by us to obtain the two analogous compounds [4]. With the aim to obtain hydroxylic derivatives as final products, it appeared suitable to start from methoxynaphthylamines and then to subject the new mono-, di- or trimethoxy-2-phenyl-1*H*-benz[*g*]indoles to a suitable demethylating procedure. Benzindoles **3** were obtained *via* the reaction of some methoxy-α-naphthylamines **1a-c** with various *N*-phenacylpyridinium bromides **2a-c** (see Scheme 1). Some of the starting compounds, **1a** and **1c**, were already known and have been prepared following described procedures [8,12,13].

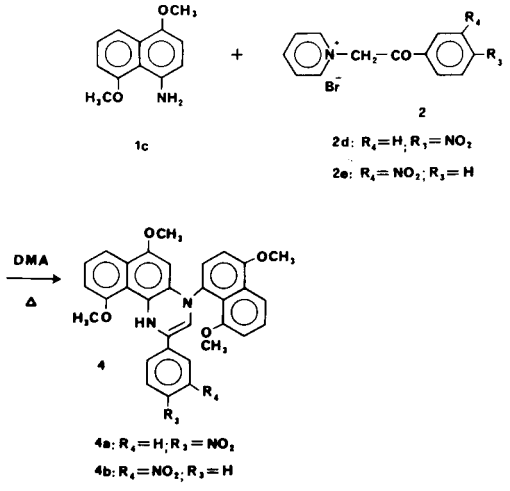
In the Scheme 2 the preparation of **1b**, not already known, is reported: 1,7-dihydroxynaphthalene **(6)** was alkylated by modifying the reported procedure [9] obtaining a yield of 96% of almost pure **7**.

By treating a benzene solution of the thus prepared 1,7-dimethoxynaphthalene with 20% nitric acid at room temperature, we obtained a mixture of two mononitro compounds which were separated by fractional crystallisation from absolute methyl alcohol. The identification of the two isomers was based on their physico-chemical properties (one of them was already known) and on ^{1}H-nmr data (see Experimental). 1,7-Dimethoxy-4-nitronaphthalene **(8)** [10] was then reduced to the corresponding amine derivative **1b** under hydrogen pressure and in the presence of Ni-Raney catalyst.

As shown in Scheme 1, α-naphthylamines **1a-c** when condensed with *N*-phenacylpyridinium salts **2a-c** in the stoichiometric ratio of 3:1 gave the expected 2-phenyl-1*H*-benz[*g*]indoles **3a-f**.

A different behaviour was observed in the case of the condensation reaction between the 1,5-dimethoxy-4-aminonaphthalene **(1c)** and *N*-nitrophenacylpyridinium salts **2de** (Scheme 3).

Scheme 3



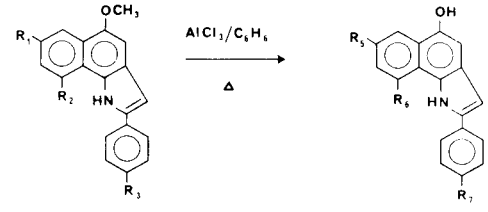
Quinoxaline derivatives **4** were isolated as reaction products using both *meta*- and *ortho*-nitrophenacylpyridinium salts also adopting different condensation conditions. Quinoxaline structures were established by ^{1}H-nmr and mass spectrometry (see Experimental).

The electron-withdrawing effect of the nitro group is most probably responsible for the change of the reaction mechanism, but at this stage of the work, we are not able to provide a certain explanation of such a different behaviour.

The fact that both *meta* and *para*-nitro-substituted derivatives apparently exert the same effect may suggest an electron-transfer mechanism between the electron-rich methoxynaphthylamine **(1c)** and the electron-poor nitro derivatives **2de.**

Scheme 4 shows the demethylation reaction to hydroxy-2-phenyl-1*H*-benz[*g*]indoles **5a-d** obtained by treating **3a-d** with anhydrous aluminum chloride in dry boiling benzene.

Scheme 4



3a: $R_1 = R_2 = R_3 = H$ — 5a: $R_5 = R_6 = R_7 = H$

3b: $R_1 = OCH_3$; $R_2 = R_3 = H$ — 5b: $R_5 = OH$; $R_6 = R_7 = H$

3c: $R_2 = OCH_3$; $R_1 = R_3 = H$ — 5c: $R_6 = OH$; $R_5 = R_7 = H$

3d: $R_2 = OCH_3$; $R_3 = Cl$; $R_1 = H$ — 5d: $R_6 = OH$; $R_7 = Cl$; $R_5 = H$

EXPERIMENTAL

Melting points were determined with a Büchi-Tottoli S.MP-20 capillary melting point apparatus, and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer 437 spectrophotometer as potassium bromide pressed disks; values are expressed in cm^{-1}. Proton nmr spectra were recorded with a Varian FT-80A instrument using the indicated solvents; chemical shifts are reported in (ppm) downfield from tetramethylsilane as internal reference. J values are given in Herz; abbreviations s, d, dd, m and b refer to singlet, doublet, doublet of doublets, multiplet and broadened, respectively. In the case of multiplets, the chemical shift quoted was measured from the approximate center. Integrals corresponded satisfactory to those expected on the basis of the structure of the compounds. Mass spectra were run on a YG ZAB 2F instrument operating at 70 eV (200 μA); the samples were introduced in DEI conditions [11]. Catalytic reductions were carried out in a Prolabo Mecabar autoclave, equipped with an automatic thermostatic apparatus. Elemental Analysis were performed in the Microanalytical Laboratory of the Dipartimento di Scienze Farmaceutiche, Università di Padova, using a Perkin-Elmer Elemental Analyser Model 240B. Column Chromatography was carried out on Merck silica gel 60 (70-230 mesh ASTM) and thin-layer chromatography (tlc) was performed on silica gel F_{254} plates. Solutions were concentrated in a rotary evaporator under reduced

pressure. Starting materials were purchased from Janssen Chimica. The following compounds were obtained according to literature procedures: 4-methoxy-1-naphthylamine (**1a**) [12]; 4,9-dimethoxy-1-naphthylamine (**1c**) [13].

N-Phenacylpyridinium Salts **2**.

The employed *N*-phenacylpyridinium salts were synthesized by the action of pyridine on the appropriate phenacyl bromides in benzene [14].

N-Phenacylpyridinium Bromide (**2a**).

This compound had mp 197-198° [lit 194.5-197°] [14].

N-(*p*-Chlorophenacyl)pyridinium Bromide (**2b**).

This compound had mp 210-212°, 84% yield; ^{1}H-nmr (deuterioacetone): δ 6.65 (2H, bs, CH_2-1), 7.75 (2H, dd, J = 8.7 and 2.1 Hz, HC-4 and HC-8), 8.10 (2H, dd, J = 8.7 and 2.1 Hz, HC-5 and HC-7), 8.29 (2H, dd, J = 8.5 and 1.5 Hz, HC-3′ and HC-5′), 8.72 (1H, dd, J = 7.8 and 1.4 Hz, HC-4′), 9.06 (2H, m, HC-2′ and HC-6′).

Anal. Calcd. for $C_{13}H_{11}BrClNO$: C, 49.94; H, 3.55; N, 4.48. Found: C, 49.71; H, 3.43; N, 4.59.

N-(*p*-Methoxyphenacyl)pyridinium Bromide (**2c**).

This compound had mp 211° [lit 208-210°] [14].

N-(*p*-Nitrophenacyl)pyridinium Bromide (**2d**).

This compound had mp 257°, 83% yield [lit mp 255-257°, 65% yield] [14].

N-(*m*-Nitrophenacyl)pyridinium Bromide (**2e**).

This compound had mp 254-256°, 76% yield [lit 238°] [5]; ^{1}H-nmr (DMSO-d_6): δ 6.78 (1H, s, CH-1), 8.10 (1H, t, J = 8.1 Hz, HC-7), 9.18 (2H, dd, J = 6.7 and 1.3 Hz, HC-2′ and 6′), 8.33-9.00 (6H, m, aromatic).

Anal. Calcd. for $C_{13}H_{11}BrN_2O_3$: C, 48.32; H, 3.43; N, 8.53. Found: C, 48.09; H, 3.39; N, 8.53.

1,7-Dimethoxynaphthalene (**7**).

Twenty g of 1,7-dihydroxynaphthalene (**6**) (125 mmoles) was suspended into 60 ml of dimethyl sulfate and purged with nitrogen. To the resulting vigorously stirred suspension a 50% potassium hydroxide (100 ml) was carefully added dropwise. The reaction mixture was kept in an ice bath for 5 hours. Then the mixture was poured into 500 ml of stirred water and after 1 hour the separated oily product was extracted with ether and the aqueous alkaline layer repeatedly extracted with the same solvent. The combined ether layers were washed with water, dried with anhydrous sodium sulfate, filtered and evaporated to give 23.3 g (98%) of an oily green almost pure residue which was used in the following reaction without any further purification.

Distillation of a sample yielded analytically pure **7**, bp 102-105°/0.2 mm Hg [lit 123-130°/0.4 mm Hg] [9]; ^{1}H-nmr (deuterioacetone): δ 3.85 (3H, s, OCH_3, at C-1), 3.92 (3H, s, OCH_3, at C-5), 6.82 (1H, dd, J = 7.1 and 1.6 Hz, HC-2), 7.12 (1H, dd, J = 8.8 and 2.9 Hz, HC-6), 7.21 (1H, dd, J = 8.8 and 7.1 Hz, HC-3), 7.38 (1H, dd, J = 8.2 and 1.7 Hz, HC-4), 7.57 (1H, d, J = 2.6 Hz, HC-8), 7.71 (1H, d, J = 8.9 Hz, HC-5).

1,7-Dimethoxy-4-nitronaphthalene (**8**).

Nitric acid (20%, 83 ml) was added in equal parts to a solution of 10 g of 1,7-dimethoxynaphthalene (53 mmoles) in 100 ml of benzene. The red reaction mixture was vigorously stirred at room temperature for 5 hours. Then the two phases were separated and the aqueous one was repeatedly extracted with chloroform. The combined extracts were washed with water, dried and evaporated under reduced pressure to give 12.2 g of a crude dark red solid residue consisting of a mixture of two mononitroderivatives. They have been separated by crystallisation from a large amount of hot methanol. The first crystallisation gave a 60% average yield of **8**, mp 128-129° [lit 127-128°] [10]. After concentration of the methanolic solution to a small volume it was possible to isolate a minor amount of the other mononitro isomer, identified as 1,7-dimethoxy-8-nitronaphthalene (**9**).

1,7-Dimethoxy-8-nitronaphthalene (**9**).

This compound had mp 152-153° from methanol; ^{1}H-nmr (deuterioacetone): δ 3.87 (3H, s, OCH_3 at C-1), 4.01 (3H, s, OCH_3 at C-7), 7.09 (1H, dd, J = 7.6 and 1 Hz, HC-2), 7.40 (1H, t, J = 7.6 Hz, HC-3), 7.55 (1H, dd, J = 7.6 and 1 Hz, HC-4), 7.62 (1H, d, J = 9.2 Hz, HC-6), 8.07 (1H, d, J = 9.2 Hz, HC-5).

Anal. Calcd. for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 5.91. Found: C, 61.68; H, 4.69; N, 5.83.

1,7-Dimethoxy-4-aminonaphthalene (**1b**).

The compound **1b** was obtained by the following two different procedures with high yields in both cases.

Method A.

Three g of the 4-nitro-derivative **8** (13 mmoles) dissolved in 130 ml of absolute ethanol was hydrogenated in the presence of Raney-Nickel catalyst (15 hours at 100° and 80 bars). After cooling, the alcoholic solution was filtered and then evaporated under reduced pressure to give a semisolid almost pure residue of 2.57 g (99%).

Method B.

To a solution of 2.5 g of the 4-nitro-derivative (11 mmoles) in 150 ml of ethanol, 8 g of mossy tin and 5 g of stannous chloride dihydrate was added. Then 25 ml of concentrated hydrochloric acid was added slowly to the mixture under magnetic stirring and the stirring was continued for 6 hours at room temperature. At the end the reaction mixture was poured into water, basified with sodium hydroxide solution and extracted with ether. The organic layer was washed repeatedly with water, dried over anhydrous sodium sulfate and evaporated in vacuum to give 2.05 g of a sufficiently pure product (94%) to be used in reactions; ^{1}H-nmr (deuterioacetone): δ 3.88 (6H, s, 2OCH_3 at C-1 and C-7), 4.59 (1H, bs, NH_2), 6.54 (1H, d, J = 8.1 Hz, HC-3), 6.72 (1H, d, J = 8.1 Hz, HC-2), 7.07 (1H, dd, J = 9.2 and 2.7 Hz, HC-6), 7.49 (1H, d, J = 2.7 Hz, HC-8), 7.91 (1H, d, J = 9.2 Hz, HC-5).

General Procedure for Preparation of Methoxy-substituted 2-Phenyl-1*H*-benz[*g*]indoles **3**. Reaction of *N*-Phenacylpyridinium Bromides **2** with α-Naphthylamines **1**.

A mixture of *N*-phenacylpyridinium bromide (**2**) (10 mmoles) and naphthylamine (**1**) (30 mmoles) was refluxed in *N,N*-dimethylaniline (50 ml) for three hours. The reaction mixture was cooled at room temperature, water (50 ml) was added and then the resulting solution was extracted repeatedly with diethyl ether. The organic layer was washed with 4% hydrochloric acid and water and dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure and the yielded crude product was purified by column chromatography on silica gel 60 using benzene as eluant. The obtained compounds always needed further suitable purification in order to obtain analytical pure samples.

5-Methoxy-2-phenyl-1*H*-benz[*g*]indole (**3a**).

The product obtained from the chromatographic separation was further purified by sublimating it at 100° and 10^{-2} torr to give compound **3a** in a yield of 21%, mp 124-126°; ^{1}H-nmr (deuterioacetone): δ 64.02 (1H, s, OCH_3), 6.96 (1H, d, J = 2.3 Hz, HC-4), 7.11 (1H, s, HC-3), 7.37 (2H, m, HC-7 and HC-8), 7.47 (2H, dd, J = 8.1 and 1.4 Hz, HC-3′ and HC-5′), 7.90 (2H, dd, J = 8.1 and 1.4 Hz, HC-6′ and HC-2′), 8.34 (2H, m, HC-6 and HC-9), 11.07 (1H, bs, NH).

Anal. Calcd. for $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.12. Found: C, 83.34; H, 5.49; N, 5.08.

5,7-Dimethoxy-2-phenyl-1*H*-benz[*g*]indole (**3b**).

The product obtained from silica gel chromatography not yet analytically pure, was further purified by sublimating it at 100° and 10^{-2} torr, to give tlc-pure **3b** (25%). It becomes soft at 147° and decomposes at 182°; ^{1}H-nmr (deuterioacetone): δ 3.90 (3H, s, OCH_3 at C-5), 4.00 (3H, s, OCH_3 at C-7), 6.91 (1H, d, J = 2.2 Hz, HC-6), 7.09 (1H, s, HC-4), 7.19 (1H, dd, J = 8.9 and 2.6 Hz, HC-8), 7.67 (1H, s, HC-3), 7.6 (5H, m, phenyl

at C-2), 8.35 (1H, d, J = 9.0 Hz, HC-9), 10.9 (1H, bs, NH).

Anal. Calcd. for $C_{20}H_{17}NO_2$: C, 79.18; H, 5.65; N, 4.62. Found: C, 78.82; H, 5.60; N, 4.68.

5,9-Dimethoxy-2-phenyl-1*H*-benz[*g*]indole (**3c**).

By the same purifying procedures the title compound **3c** was prepared in 26% yield, mp 151-152°; ^{1}H-nmr (deuterioacetone): δ 4.01 (3H, s, OCH_3 at C-9), 4.09 (3H, s, OCH_3 at C-5), 7.05 (1H, dd, J = 1.2 and 7.8 Hz, HC-8), 7.30 (2H, dd, J = 1.4 and 8.2 Hz, HC-3′ and HC-5′), 7.32 (1H, 2d, J = 7.8 and 8.3 Hz, HC-7), 7.45 (1H, s, HC-4), 7.47 (1H, s, HC-3), 7.48 (1H, dd, J = 1.4 and 7.4 Hz, HC-4′), 7.74 (2H, dd, J = 1.4 and 8.2 Hz, HC-2′ and HC-6′), 7.91 (1H, dd, J = 1.3 and 8.2 Hz, HC-6), 10.96 (1H, bs, NH); ir (potassium bromide): 3442 (NH), 3060 (OCH_3 at C-9), 2825 cm^{-1} (OCH_3 at C-5).

Anal. Calcd. for $C_{20}H_{17}NO_2$: C, 79.18; H, 5.65; N, 4.62. Found: C, 79.12; H, 5.77; N, 4.35.

5,9-Dimethoxy-2-(4′-methoxyphenyl)-1*H*-benz[*g*]indole (**3d**).

Chromatography (benzene) yielded tlc-pure crystals of compound **3d** with mp 180-181° (26%); ^{1}H-nmr (deuterioacetone): δ 3.81 (3H, s, OCH_3 at C-4′), 4.01 (3H, s, OCH_3 at C-9), 4.11 (3H, s, OCH_3 at C-5), 7.01 (2H, dd, J = 2.2 and 6.6 Hz, HC-3′ and HC-5′), 7.07 (1H, dd, J = 1.2 and 7.8 Hz, HC-8), 7.34 (1H, 2d, J = 7.7 and 8.2 Hz, HC-7), 7.39 (1H, s, HC-4), 7.43 (1H, s, HC-3), 7.63 (2H, dd, J = 2.2 and 6.6 Hz, HC-2′ and HC-6′), 7.90 (1H, dd, J = 1.3 and 8.3 Hz, HC-6), 10.88 (1H, bs, NH).

Anal. Calcd. for $C_{21}H_{19}NO_3$: C, 75.65; H, 5.74; N, 4.20. Found: C, 75.14; H, 6.15; N, 4.57.

5,9-Dimethoxy-2-(4′-chlorophenyl)-1*H*-benz[*g*]indole (**3e**).

The title compound **3e** was obtained as tlc-pure crystals by sublimation at 200° and 10^{-2} torr with a yield of 26%, mp 188-190°; ^{1}H-nmr (deuteriochloroform): δ 4.00 (3H, s, OCH_3 at C-9), 4.10 (3H, s, OCH_3 at C-5), 6.83 (1H, d, HC-4), 6.98 (1H, dd, J = 7.8 and 0.9 Hz, HC-8), 7.95 (1H, dd, J = 8.3 and 1.2 Hz, HC-6), 7.23-7.66 (7H, m), 9.97 (1H, bs, NH).

Anal. Calcd. for $C_{20}H_{16}ClNO_2$: C, 71.11; H, 4.77; N, 4.14; Cl, 10.49. Found: C, 71.22; H, 4.70; N, 4.33; Cl, 10.63.

5,7-Dimethoxy-2-(4′-chlorophenyl)-1*H*-benz[*g*]indole (**3f**).

By silica gel chromatography (benzene) the title compound **3f** was obtained in a yield of 21%, mp 193-194°; ^{1}H-nmr (deuterioacetone): δ 3.91 (3H, s, OCH_3 at C-5), 4.01 (3H, s, OCH_3 at C-7), 6.95 (1H, d, J = 2.3 Hz, HC-6), 7.09 (1H, s, HC-4), 7.21 (1H, dd, J = 9.0 and 2.7 Hz, HC-8), 7.42 (2H, dd, J = 8.7 and 2.3 Hz, HC-2′ and HC-6′), 7.87 (2H, dd, J = 6.7 and 2.1 Hz, HC-3′ and HC-5′), 8.33 (1H, d, J = 9.1 Hz, HC-9), 11.09 (1H, bs, NH).

Anal. Calcd. for $C_{20}H_{16}ClNO_2$: C, 71.11; H, 4.77; N, 4.14. Found: C, 71.41; H, 4.87; N, 4.06.

Reaction of **2d** and **2c** with 4,8-Dimethoxy-α-naphthylamine (**1c**).

Applying the same general procedure described above we were not able in these cases to obtain the corresponding 2-nitrophenyl-1*H*-benz[*g*]indoles, but only the quinoxaline derivatives **4**.

The condensation reaction was also carried out by adopting another stoichiometric ratio (1:1) between *N*-phenacylpyridinium bromides and 4,8-dimethoxy-α-naphthylamine (**1c**). In all cases, however, it was possible to isolate from crude product by silica gel chromatography only the quinoxaline derivatives in good yields.

2-(*p*-Nitrophenyl)-4-(4′,8′-dimethoxynaphthyl)-6,10-dimethoxy-1,4-dihydrobenz[*h*]quinoxaline (**4a**).

Crystallization from ethanol gave compound **4a**, red crystals, mp 255°; ^{1}H-nmr (deuteriochloroform): δ 3.85 (6H, s, OCH_3 at C-6 and OCH_3 at C-4′), 4.03 (3H, s, OCH_3 at C-8′), 4.21 (3H, s, OCH_3 at C-10), 6.38 (1H, d, J = 8.5 Hz, HC-3′), 6.60 (1H, d, J = 8.2 Hz, HC=2′), 6.81 (1H, s, HC-5), 6.93 (1H, dd, J = 9.8 and 1.1 Hz, HC-7′), 7.03 (1H, dd, J = 9.8 and 1.1 Hz, HC-9), 7.37 (1H, dd, J = 8.5 and 1.0 Hz, HC-5′), 7.46 (1H, dd, J = 8.5 and 1.0 Hz, HC-7), 7.93 (4H, 2dd, *p*-nitrophenyl at C-2), 8.14 (1H, s, HC-3), 8.25 (2H, 2d, J = 6.8 Hz, HC-8 and HC-6′), 9.93 (1H, bs, NH); ms: m/e 549 (M^+, 100), 534 (37), 519 (14), 504 (7), 355 (10).

Anal. Calcd. for $C_{32}H_{27}N_3O_6$: C, 69.93; H, 4.95; N, 7.65. Found: C, 70.06; H, 5.12; N, 8.08.

2-(*m*-Nitrophenyl)-4-(4′,8′-dimethoxynaphthyl)-6,10-dimethoxy-1,4-dihydrobenz[*h*]quinoxaline (**4b**).

The chromatographed product was analytically pure and was identified as compound **4b**, mp 220-222°; ^{1}H-nmr (deuteriochloroform): δ 3.83 (3H, s, OCH_3 at C-4′), 3.85 (3H, s, OCH_3 at C-6), 4.03 (3H, s, OCH_3 at C-8′), 4.18 (3H, s, OCH_3 at C-10), 6.35 (1H, d, J = 8.5 Hz, HC-3′), 6.57 (1H, d, J = 8.5 Hz, HC-2′), 6.84 (1H, s, HC-5), 7.00 (1H, dd, J = 8.8 and 1 Hz, HC-7′), 7.22-7.49 (4H, m, aromatic), 7.90-8.19 (4H, m, aromatic), 8.33 (1H, s, HC-3), 8.63 (1H, t, HC-8), 9.9 (1H, bs, NH).

Anal. Calcd. for $C_{32}H_{27}N_3O_6$: C, 69.93; H, 4.49; N, 7.65. Found: C, 69.21; H, 4.99; N, 7.26.

General Procedure for Demethylation of the Polymethoxy-2-phenyl-1*H*-benz[*g*]indoles (**3**).

Demethylation of compounds **3** was carried out by refluxing them in a suitable volume of dry benzene solution containing an excess of anhydrous aluminum chloride for several hours in a water bath. The reaction flask was 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 with water, dried with sodium sulfate and evaporated to dryness under vacuum to give the crude residue. The last one was worked up as indicated below in order to obtain pure compounds **5**.

5-Hydroxy-2-phenyl-1*H*-benz[*g*]indole (**5a**).

The crude green demethylate residue (see above) was purified by sublimation in vacuum at 170°. The crystalline product, obtained in a 40% yield, mp 130°, confirmed as **5a** by means of ^{1}H-nmr and ir (potassium bromide) spectroscopy as well as elemental analysis data; ^{1}H-nmr (deuterioacetone): δ 8.36 (1H, bs, OH exchangeable with deuterium oxide), 11.08 (1H, bs, NH), 6.86-7.95 (m, 11H); ir (potassium bromide) broad absorption from 3580 to 3100 cm^{-1} (OH and NH).

Anal. Calcd. for $C_{18}H_{13}NO$: C, 83.37; H, 5.05; N, 5.40. Found: C, 83.36; H, 5.03; N, 5.15.

5,7-Dihydroxy-2-phenyl-1*H*-benz[*g*]indole (**5b**).

The crude product was purified by sublimating it twice in vacuum at 250° to give compound **5b** in 53% yield, mp 157°. The ^{1}H-nmr and ir (potassium bromide) data confirm that demethylation occurred as they lack the absorptions due to the two methoxyl groups; ^{1}H-nmr (deuterioacetone): δ 6.82 (1H, d, J = 2.3 Hz, HC-6), 7.04 (1H, s, HC-4), 7.07-8.35 (10H, m), 10.82 (1H, bs, NH); ir (potassium bromide) broad absorption from 3560 to 3000 cm^{-1} (OH and NH).

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.64; H, 4.94; N, 4.85.

5,9-Dihydroxy-2-phenyl-1*H*-benz[*g*]indole (**5c**).

The crude demethylated residue was crystallized from toluene. Crystals of the title compound **5c** were obtained in 28% yield, dec at 170°. The ^{1}H-nmr, ir and elemental analysis data permitted us to identify **5c**; ^{1}H-nmr (deuterioacetone): δ 8.28 (1H, bs, OH at C-9), 9.59 (1H, bs, OH at C-5), 6.86-7.92 (m, 10H), 10.49 (1H, bs, NH); ir (potassium bromide): broad absorption from 3600 to 3090 cm^{-1} (OH and NH).

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 79.03; H, 5.13; N, 4.78.

5,9-Dihydroxy-2-(4′-chlorophenyl)-1*H*-benz[*g*]indole (**5d**).

The title compound **5d** was obtained as pure crystals by subliming the crude residue in vacuum and then by washing the sublimed product with petroleum ether (40-60°) twice, 40% yield, mp 230°. The ^{1}H-nmr splitting pattern shows the demethylated 2-(4′-chlorophenyl)-1*H*-benz[*g*]-

indole, as the absorptions of two methoxy groups are lacking; ^{1}H-nmr (deuterioacetone): δ 6.88-7.91 (9H, m), 8.30 (1H, bs, OH at C-5), 9.48 (1H, bs, OH at C-9), 10.7 (1H, bs, NH).

Anal. Calcd. for $C_{18}H_{12}ClNO_2$: C, 69.79; H, 3.90; N, 4.52; Cl, 11.44. Found: C, 70.18; H, 3.95; N, 4.41; Cl, 11.15.

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