Neospiroenones. Synthesis of 10,11-dimethoxy-1,6,6-trimethyl-5,6,8,12b-tetrahydrobenzo[*d*,*f*]indol-4(3*H*)-one and 10,11-dimethoxy-6,6-dimethyl-1,5,6,12b-tetrahydrobenzo[*d*,*f*]indol-2(8*H*)-one

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The three-component condensation of isobutyraldehyde, 3,4-dimethoxyphenylacetonitrile, and *p*-methylanisole or anisole in the presence of concentrated sulfuric acid affords neospiroenone systems.

Key words: *p*-methylanisole, anisole, isobutyraldehyde, phenylacetonitrile, 3,4-dimethoxyphenylacetonitrile, three-component condensation, neospiroenone, spiro σ-complex, sulfuric acid.

The synthesis of neospiro systems, *viz.*, neospiroenones, neospirodienones, and their structural analogs, has attracted interest in relation to investigation of the biomimetic synthesis of such alkaloids as aporphines, proaporphines, erythrinans, and morphinanodienones, as well as because of the possibility of the preparation of new synthetic analogs of these alkaloids.[1—3] For example, it was shown that the (±)-*N*-methylneospirodienone—BF_3 complex can be transformed into dibenzazonine (eribidine) and the corresponding aporphines.[4]

One of the main approaches to the synthesis of tetracyclic neospiro systems is based on the intramolecular nonphenol oxidative coupling of *N*-substituted 1-benzyl-1,2,3,4-tetrahydroisoquinolines. Such compounds were synthesized[5] by the intramolecular nonphenol oxidative coupling of (±)-laudanosine with vanadium oxytrifluoride in trifluoroacetic acid. More recently,[6] it has been shown that similar transformations can be performed not only for 1-benzyl-1,2,3,4-tetrahydroisoquinolines but also for 1-phenethyl-1,2,3,4-tetrahydroisoquinolines. In further studies, [$IPh(CF_3COO)_2$] (PIFA),[7] PIFA—heteropolyacid,[8,9] and PIFA—$BF_3 \cdot Et_2O$ (see Ref. 10) were used as oxidizing systems for the intramolecular nonphenol oxidative coupling of *N*-substituted 1-benzyl-1,2,3,4-tetrahydroisoquinolines with the aim of preparing neospirodienones. The anodic oxidation of *N*-trifluoroacetyl-1-benzyl-1,2,3,4-tetrahydroisoquinolines in acetonitrile giving the corresponding neospirodienones was also documented.[11]

In most of the above-considered cases, neospiro systems are formed as a result of the intramolecular nonphenol oxidative coupling of *N*-substituted 1-benzyl-1,2,3,4-tetrahydroisoquinolines. An analysis of the possibilities of the formation of such compounds led to the conclusion that tetracyclic neospiro systems can be synthesized without the preliminary synthesis of 1-benzyl-1,2,3,4-tetrahydroisoquinoline.

It is known[12] that the three-component reaction of *p*-methylanisole, isobutyraldehyde, and nitrile affords 1-R-substituted 8-(2´-methoxyphenyl-5´-methyl)-3,3,9-trimethyl-2-azaspiro[4.5]deca-1,7-dien-6-ones. This is attributed to the fact that the spiro σ-complex, which is a precursor of 3,3-dimethyl-2-azaspiro[4.5]dec-8-en-6-one, is a stronger electrophile than the protonated form of isobutyraldehyde, and this complex alkylates unreacted *p*-methylanisole to form the corresponding spiro systems.

It would be expected that in the presence of particular steric and electronic factors, a new C—C bond will be formed *via* intramolecular electrophilic substitution with the involvement of the electron-saturated phenyl moiety and the intermediate spiro σ-complex giving rise to neospiro systems.

The model reaction of *p*-methylanisole, isobutyraldehyde, and phenylacetonitrile in concentrated sulfuric acid (Scheme 1) afforded the only isolated product, *viz.*, 1-benzyl-8-(2´-methoxy-5´-methylphenyl)-3,3,9-trimethyl-2-azaspiro[4.5]deca-1,7-dien-6-one (**1**).

The three-component condensation of *p*-methylanisole, isobutyraldehyde, and 3,4-dimethoxyphenylacetonitrile occurs in a different way and gives tetracyclic system **2** (Scheme 2). The structure of heterocyclic compound **2** was confirmed by mass spectrometry, IR spectroscopy, and ^1H and ^{13}C NMR spectroscopy. Thus, the ^1H NMR spectrum of compound **2** in $CDCl_3$ has signals

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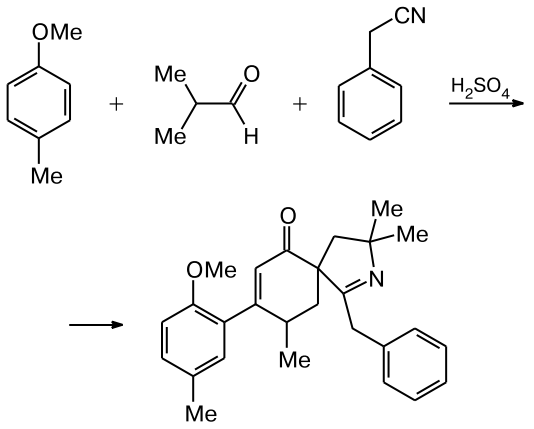
Scheme 1



1

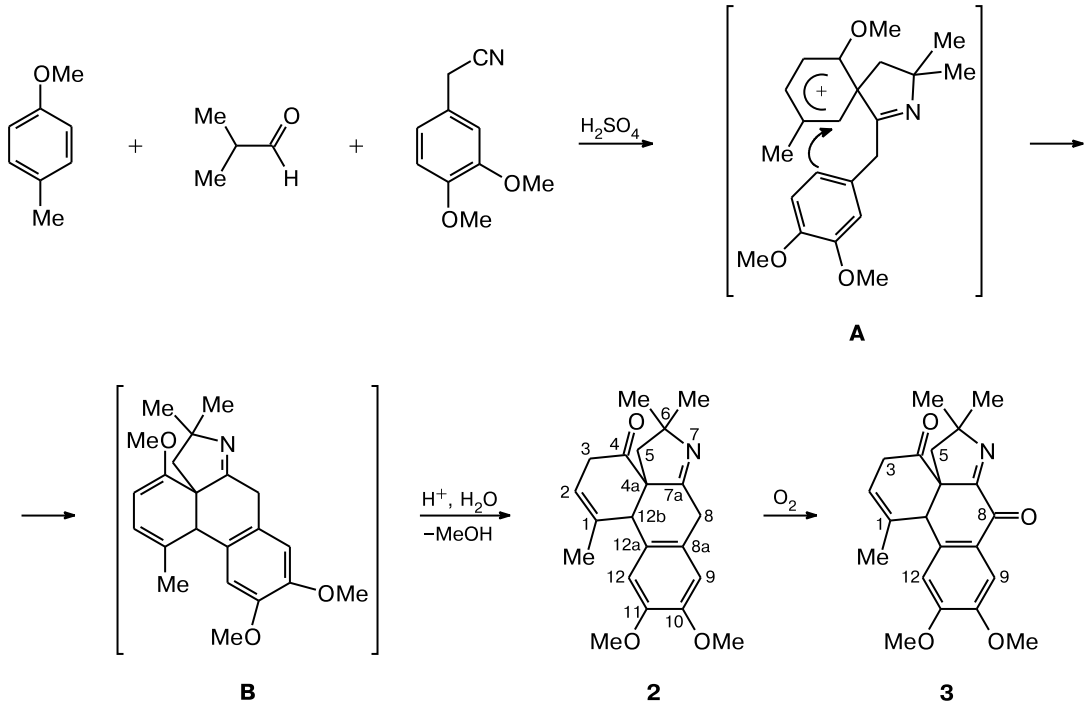
for the aromatic protons H(12) and H(9) as two singlets at δ 6.57 and 6.64 with an integrated intensity of 1 H each. The 2D COSY experiments showed that the signal for the proton H(12b) correlates with the signals for the protons of the methyl group at the C(1) atom and the aromatic proton H(12). The presence of the singlet of the methyl group C(1)Me at δ 2.22 indicates that the double bond in compound **2** is at the C(1) atom. Taking into account the 2D HSQC ^{1}H—^{13}C spectroscopic data, the assignment of the signals for all protonated carbon atoms in compound **2** was made (Table 1). The structure of neospiro compound **2** was finally established based on the 2D ^{1}H—^{13}C HMBC spectrum. The principal HMBC correlations confirming the presence of the bond between the moieties in molecule **2** are as follows (see Table 1): H(12b)/C(12) 3.52/109.27, H(12b)/C(12a) 3.52/124.84, H(12b)/C(1) 3.52/135.61, and H(12b)/C(1)Me 3.52/25.80.

According to Scheme 2, the reaction occurs as follows: the initially formed spiro σ-complex **A** intramolecularly attacks the C(6) atom of the dimethoxyphenyl moiety to form enol ether **B**, whose hydrolysis affords neospiroenone **2**.

It should be noted that compound **2** in the free-base form is unstable and is readily oxidized at the C(8) atom by atmospheric oxygen, as in the case of 1-benzyl-3,4-dihydroisoquinolines,[13] to form neospiro system **3** (see Scheme 2). In the ^{1}H NMR spectrum of neospiro compound **3**, the signals for the protons H(8A) and H(8B) at δ 4.14 and 4.64, respectively, are absent. In the ^{13}C NMR spectrum, the signal for the C(8) atom is shifted downfield and is observed at δ 181.14 ($\delta_{C(8)}$ 30.66 in the ^{13}C NMR spectrum of compound **2**). Based on these facts, as well as on the elemental analysis, mass spectrometry, and IR spectroscopic data, the structure 10,11-dimethoxy-1,6,6-trimethyl-5,6-dihydrobenzo[*d*,*f*]indole-4,8-(3*H*,12b*H*)-dione was assigned to compound **3**.

Previously, it has been shown[14] that the three-component condensation of anisole, isobutyraldehyde, and α-substituted phenylacetonitriles affords 1-R-substituted 3,3-dimethyl-2-azaspiro[4.5]deca-6,9-dien-8-ones. This reaction, like that with the use of *p*-methylanisole, pro-

Scheme 2



A **B** **2** **3**

Table 1. NMR spectroscopic parameters for compound **2** ($CDCl_3$, δ, *J*/Hz)

Atom, group	^{1}H NMR	^{13}C NMR (DEPT)	HSQC	HMBC
C(1)	—	135.61 (C)	—	—
C(1)Me	2.22 (s, 3 H)	25.80 (Me)	25.80	135.61 (C(1)); 121.32 (C(2)); 51.01 (C(12b))
C(2)H	5.87 (m, 1 H)	121.32 (CH)	121.32	204.35 (C(4)); 51.01 (C(12b)); 36.90 (C(3)); 25.80 (C(1)Me)
C(3)H_2	2.70 (br.d, 1 H, *J* = 23.1); 3.01 (dd, 1 H, *J* = 23.1, *J* = 4.2)	36.90 (CH_2)	36.90	204.35 (C(4)); 121.32 (C(2)); 135.61 (C(1))
C(4)	—	204.35 (C)	—	—
C(4a)	—	65.42 (C)	—	—
C(5)H_2	2.04, 2.26 (both d, 1 H each, *J* = 14.4)	44.04 (CH_2)	44.04	204.35 (C(4)); 65.42 (C(4a)); 70.96 (C(6)); 187.33 (C(7a)); 51.01 (C(12b)); 28.21, 28.78 (C(6)Me_2)
C(6)	—	70.96 (C)	—	—
C(6)Me	1.54, 1.73 (both s, 3 H each)	28.21 (Me); 28.78 (Me)	28.21; 28.78	70.96 (C(6)); 44.04 (C(5))
C(7a)	—	187.33 (C)	—	—
C(8)H_2	4.14, 4.64 (both d, 1 H each, *J* = 23.7)	30.66 (CH_2)	30.66	187.33 (C(7a)); 111.40 (C(9)); 124.84 (C(12a)); 122.17 (C(8a))
C(8a)	—	122.17 (C)	—	—
C(9)H	6.64 (s, 1 H)	111.40 (CH)	111.40	30.66 (C(8)); 124.84 (C(12a)); 148.66 (C(11))
C(10)	—	149.37 (C)	—	—
C(10)OMe	3.84 (s, 3 H)	55.90 (Me)	55.90	149.37 (C(10))
C(11)	—	148.66 (C)	—	—
C(11)OMe	3.82 (s, 3 H)	56.01 (Me)	56.01	148.66 (C(11))
C(12)H	6.57 (s, 1 H)	109.27 (CH)	109.27	51.01 (C(12b)); 122.17 (C(8a)); 149.37 (C(10))
C(12a)H	—	124.84 (C)	—	—
C(12b)H	3.52 (s, 1 H)	51.01 (CH)	51.01	135.61 (C(1)); 121.32 (C(2)); 204.35 (C(4)); 65.42 (C(4a)); 44.04 (C(5)); 187.33 (C(7a)); 124.84 (C(12a)); 109.27 (C(12)); 25.80 (C(1)Me)

* The ^{1}H NMR spectrum of compound **2** isolated as hydrochloride shows also a signal at δ_H 16.54 (br.s, HCl).

ceeds through the formation of the intermediate spiro σ-complex. Consequently, the use of 3,4-dimethoxyphenylacetonitrile as the nitrile component in the reaction with anisole and isobutyraldehyde can lead to the formation of the neospiroenone system.

Actually, the three-component condensation of anisole, isobutyraldehyde, and 3,4-dimethoxyphenylacetonitrile in concentrated sulfuric acid gives compound **4**, whose structure was determined by mass spectrometry, IR spectroscopy, and ^{1}H and ^{13}C NMR spectroscopy (Scheme 3).

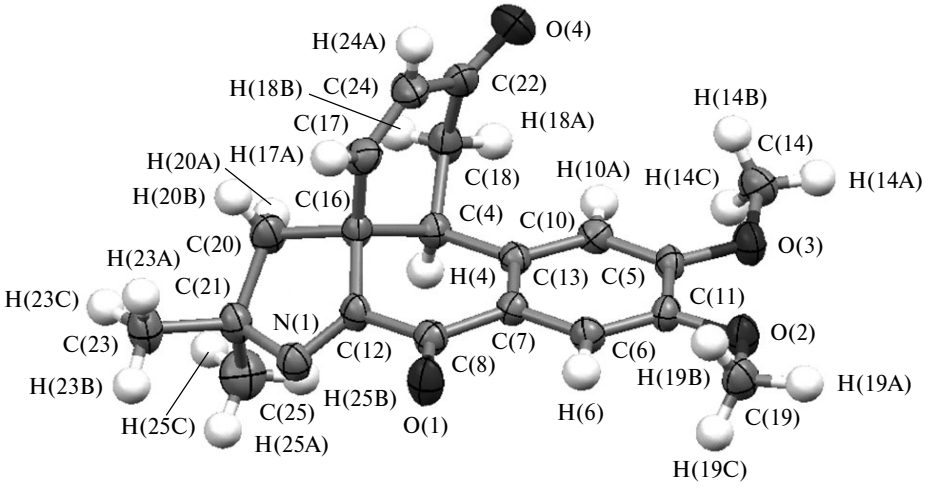
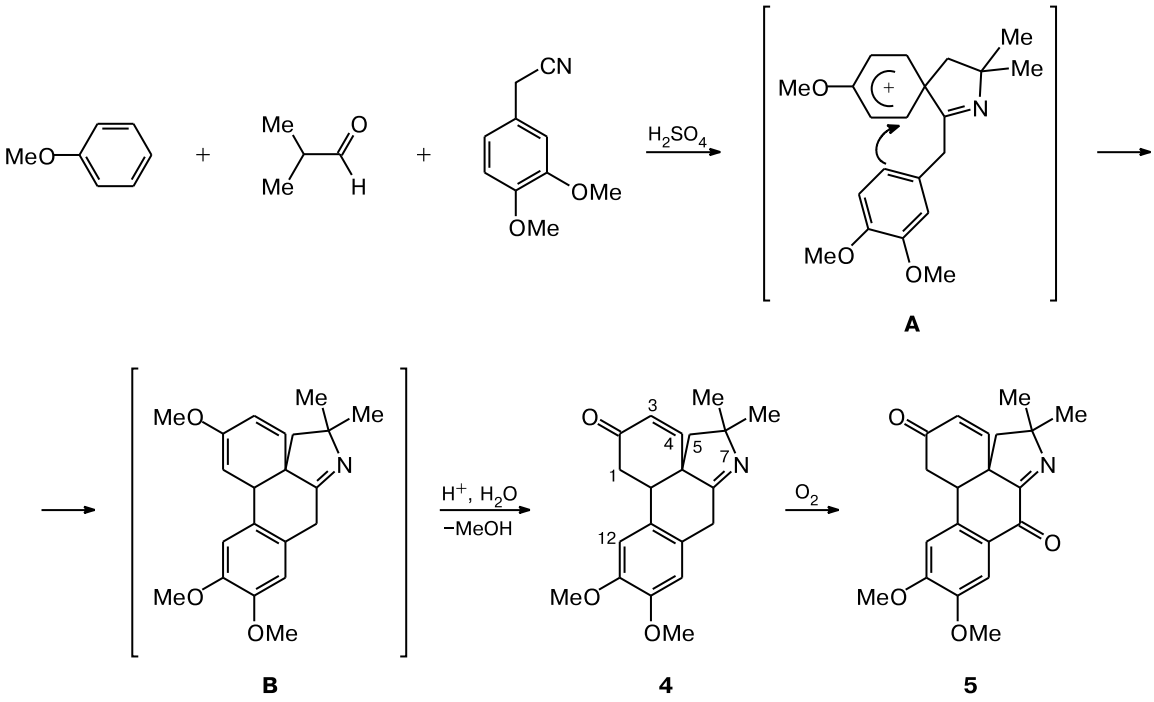


Fig. 1. Molecular structure of compound **5**.

Scheme 3



Thus, the ^{1}H NMR spectrum of compound **4** in $CDCl_3$ has signals for the aromatic protons H(9) and H(12) as two singlets at δ 6.66 and 6.62 with an integrated intensity of 1 H each, which partially overlap with the signal for the proton H(4). The 2D COSY experiment showed that the signal for the proton H(12b) correlates with the signals for the protons H(1A) and H(1B), as well as with the signal for the proton H(12).

Like compound **2**, 10,11-dimethoxy-6,6-dimethyl-1,5,6,12b-tetrahydrobenzo[*d*,*f*]indol-2(8*H*)-one (**4**) in the free-base form is unstable in air and is readily oxidized at the C(8) atom to form neospiro system **5** (see Scheme 3). The structure of compound **5** was unambiguously established by X-ray diffraction (Fig. 1).

Although the stereochemistry of neospiroenones **2**—**5** remains unknown, the ^{1}H NMR spectra of compounds **2**—**5** have one set of signals. This is evidence that one of the possible diastereomers was isolated. It should be noted that the GC-mass spectra of the reaction mixtures in the case of compounds **4** and **5** have exclusively peaks at masses corresponding to the neospiro systems. For compounds **2** and **3**, the GC-mass spectra of the reaction mixtures show major peaks at masses 339 and 353, respectively, and minor peaks (<5%) at the same masses.

Therefore, the above-described method can be used to synthesize polyfunctional derivatives of neospiro systems, four new covalent bonds being formed in the course of the reaction.

Experimental

The ^{1}H and ^{13}C (DEPT) NMR spectra were recorded on a Varian Mercury Plus spectrometer (300.06 MHz for ^{1}H and 75.46 MHz for ^{13}C) with HMDS as the internal standard in $CDCl_3$. The electron impact mass spectra (200 °C, 70 eV) were obtained on an Agilent Technologies 6890N/5975B GC-mass spectrometer equipped with an HP-5ms column (30×0.25 mm, 0.25 μm) using helium as the carrier gas. The elemental analysis was carried out on a CHNS-932 Leco Corporation analyzer. The IR spectra were recorded on a UR-20 instrument in Nujol mulls. The course of the reactions was monitored and the purity of the reaction products was checked by TLC on Silufol plates; the spots were visualized with the use of a 0.5% chloranil solution in toluene. The column chromatography was performed on silica gel (0.06—0.20 mm, 70—230 mesh, Lancaster). The melting points were measured on a PTP instrument and are uncorrected.

1-Benzyl-8-(2′-methoxyphenyl-5′-methyl)-3,3,9-trimethyl-2-azaspiro[4.5]deca-1,7-dien-6-one hydrochloride (1). A mixture of *p*-methylanisole (0.48 g, 4 mmol), isobutyraldehyde (0.14 g, 2 mmol), and phenylacetonitrile (0.24 g, 2 mmol) in dichloromethane (2 mL) was added dropwise with stirring and cooling with ice water to concentrated H_2SO_4 (10 mL). The reaction mixture was poured into crushed ice (50 g) and extracted with hexane (20 mL). The aqueous layer was adjusted with aqueous ammonia to pH 7—8. The resulting oil was extracted with hexane (2×10 mL), dried with $MgSO_4$, and filtered. Dry HCl was bubbled through the filtrate until the solution became completely transparent. The precipitate that formed was separated and crystallized from ethyl acetate. Compound **1**, m.p. 187—191 °C, was obtained in a yield of 0.18 g (21%). Found (%):

C, 73.89; H, 7.33; N, 3.24. $C_{27}H_{31}NO_2 \cdot HCl$. Calculated (%): C, 74.04; H, 7.36; N, 3.20. IR, ν/cm^{-1}: 1590, 1660. ^{1}H NMR, δ: 1.01 (d, 3 H, C(9)Me, J = 7.2 Hz); 1.70 and 1.75 (both s, 3 H each, C(3)Me, C(3)Me); 1.82 (m, 1 H, H(10A)); 2.01 (d, 1 H, H(4A), J = 13.7 Hz); 2.29 (s, 3 H, C(5′)Me); 2.66 (m, 2 H, H(10B), H(4B)); 3.47 (m, 1 H, H(9)); 3.83 (s, 3 H, OMe); 4.25 and 4.39 (both d, 1 H each, CH(A)Ph, CH(B)Ph, J = 13.8 Hz); 5.98 (d, 1 H, H(7), J = 1.2 Hz); 6.86 (m, 2 H, H(Ar)); 7.26 (m, 6 H, H(Ar)); 16.68 (br.s, 1 H, HCl). ^{13}C NMR, δ: 20.18, 20.45 (C(9)Me, C(5′)Me); 27.87, 29.31 (C(3)Me_2); 31.01 (C(9)); 35.83 (CH_2Ph); 40.12 (C(10)); 47.60 (C(4)); 55.51 (OMe); 62.89, 69.86 (C(3), C(5)); 110.91, 125.89, 126.93, 128.05, 129.03, 129.44, 129.51, 130.20, 130.76, 131.35, 153.87, 167.89 (C(7), C(8), C(Ar)); 186.32 (C(1)); 193.04 (C(6)). MS, m/z (I_{rel} (%)): 401 $[M - HCl]^+$ (72), 386 $[M - HCl - Me]^+$ (6), 284 (100), 269 (18), 241 (14), 228 (13), 213 (8), 200 (8), 184 (6), 173 (15), 159 (20), 145 (10), 135 (11), 128 (10), 115 (9), 91 (31), 77 (6), 41 (5).

10,11-Dimethoxy-1,6,6-trimethyl-5,6,8,12b-tetrahydrobenzo-[*d*,*f*]indol-4(3*H*)-one hydrochloride (2). A mixture of *p*-methylanisole (0.24 g, 2 mmol), isobutyraldehyde (0.14 g, 2 mmol), and 3,4-dimethoxyphenylacetonitrile (0.35 g, 2 mmol) in dichloromethane (2 mL) was added dropwise with stirring and cooling with ice water to concentrated H_2SO_4 (10 mL). The reaction mixture was stirred for 10 min, poured into crushed ice (50 g), adjusted with aqueous ammonia to pH 7—8, and extracted with dichloromethane (3×15 mL). After the extraction, the dichloromethane solution was separated from the aqueous layer, and dry HCl was bubbled through the dichloromethane solution. Then ethyl acetate (20 mL) was added to the solution, and dichloromethane was evaporated. The crystals that formed were separated. Compound **2**, m.p. 212 °C (with decomp.), was obtained in a yield of 0.42 g (56%). Found (%): C, 67.15; H, 7.04; N, 3.76. $C_{21}H_{25}NO_3 \cdot HCl$. Calculated (%): C, 67.10; H, 6.97; N, 3.73. IR, ν/cm^{-1}: 1520, 1612, 1708. MS, m/z (I_{rel} (%)): 339 $[M - HCl]^+$ (100), 324 $[M - HCl - Me]^+$ (70), 296 $[M - HCl - Me - CO]^+$ (23), 280 (3), 265 (3), 242 (4), 209 (3), 177 (5), 151 (5), 115 (4), 77 (3), 41 (2).

10,11-Dimethoxy-1,6,6-trimethyl-5,6-dihydrobenzo[*d*,*f*]-indole-4,8-(3*H*,12b*H*)-dione (3). A mixture of *p*-methylanisole (0.24 g, 2 mmol), isobutyraldehyde (0.14 g, 2 mmol), and 3,4-dimethoxyphenylacetonitrile (0.35 g, 2 mmol) in dichloromethane (2 mL) was added dropwise with stirring and cooling with ice water to concentrated H_2SO_4 (10 mL). The reaction mixture was stirred for 10 min, poured into crushed ice (50 g), and adjusted with aqueous ammonia to pH 7—8. The precipitate that formed after the neutralization was filtered off and kept in ethyl acetate for 24 h in air. Then the product was filtered off, dried, and purified by chromatography (chloroform—acetone, 35 : 1, as the eluent). Compound **3**, m.p. 248 °C (with decomp.), was obtained in a yield of 0.15 g (21%). Found (%): C, 71.42; H, 6.48; N, 3.89. $C_{21}H_{23}NO_4$. Calculated (%): C, 71.37; H, 6.56; N, 3.96. IR, ν/cm^{-1}: 1514, 1568, 1592, 1632, 1676, 1708. ^{1}H NMR, δ: 1.26 and 1.52 (both s, 3 H each, C(6)Me, C(6)Me); 1.92 and 2.17 (both d, 1 H each, H(5A), H(5B), J = 13.5 Hz); 2.00 (s, 3 H, C(1)Me); 2.66 (br.d, 1 H, H(3A), J = 22.7 Hz); 2.99 (dd, 1 H, H(3B), J = 22.7 Hz, J = 1.3 Hz); 3.67 (s, 1 H, H(12b)); 3.91 and 3.92 (both s, 3 H each, C(10)OMe, C(11)OMe); 5.85 (m, 1 H, H(2)); 6.65 and 7.63 (both s, 1 H each, H(9), H(12)). ^{13}C NMR, δ: 25.52 (C(1)Me); 28.24, 30.76 (C(6)Me_2); 37.48 (C(3)); 46.44 (C(5)); 52.00 (C(12b)); 55.95, 56.06 (C(10)OMe, C(11)OMe); 70.09, 73.65 (C(4a), C(6)); 108.23 (C(12)); 110.15 (C(9)); 121.99 (C(2)); 127.48, 136.03, 137.26 (C(1), C(8a), C(12a)); 148.14, 154.45 (C(10), C(11)); 165.81 (C(7a)); 181.14 (C(8)); 208.16 (C(4)). MS, m/z (I_{rel} (%)): 353 $[M]^+$ (100), 338 $[M - Me]^+$ (18), 324 (5), 310 $[M - Me - CO]^+$ (37), 296 (10), 282 (6), 268 (30), 258 (17), 241 (5), 225 (5), 210 (6), 164 (9), 115 (7), 77 (4), 41 (4).

10,11-Dimethoxy-6,6-dimethyl-1,5,6,12b-tetrahydrobenzo-[*d*,*f*]indol-2(8*H*)-one hydrochloride (4). A mixture of anisole (0.22 g, 2 mmol), isobutyraldehyde (0.14 g, 2 mmol), and 3,4-dimethoxyphenylacetonitrile (0.35 g, 2 mmol) in dichloromethane (2 mL) was added dropwise with stirring and cooling with ice water to concentrated H_2SO_4 (10 mL). The reaction mixture was stirred for 10 min, poured into crushed ice (50 g), adjusted with aqueous ammonia to pH 7—8, and extracted with dichloromethane (3×15 mL). Dry HCl was bubbled through the extract. Then ethyl acetate (20 mL) was added to the solution, and dichloromethane was evaporated. The crystals that formed were separated and recrystallized from ethanol. Compound **4**, m.p. 220 °C (with decomp.), was obtained in a yield of 0.08 g (11%). Found (%): C, 66.32; H, 6.73; N, 3.90. $C_{20}H_{23}NO_3 \cdot HCl$. Calculated (%): C, 66.38; H, 6.69; N, 3.87. IR, ν/cm^{-1}: 1524, 1612, 1684. ^{1}H NMR, δ: 1.75 and 1.76 (both s, 3 H each, C(6)Me, C(6)Me); 2.42 and 2.59 (both d, 1 H each, H(5A), H(5B), J = 14 Hz); 2.93 (dd, 1 H, H(1A), J = 17.6 Hz, J = 4.1 Hz); 3.39 (br.d, 1 H, H(1B), J = 17.6 Hz); 3.60 (br.s, 1 H, H(12b)); 3.83 and 3.84 (both s, 3 H each, C(10)OMe, C(11)OMe); 4.10 and 4.74 (both d, 1 H each, H(8A), H(8B), J = 21.5 Hz); 6.03 (d, 1 H, H(3), J = 11 Hz); 6.62 (s, 1 H, H(12)); 6.66 (s, 1 H, H(9)); 6.64 (d, 1 H, H(4), J = 11 Hz); 16.85 (br.s, 1 H, HCl). ^{13}C NMR, δ: 29.08, 29.36 (C(6)Me_2); 31.36 (C(8)); 38.26, 46.38 (C(1), C(5)); 46.61 (C(12b)); 56.01, 56.09 (C(10)OMe, C(11)OMe); 54.65, 70.91 (C(4a), C(6)); 109.14, 111.58 (C(9), C(12)); 120.92, 124.48 (C(8a), C(12a)); 131.29, 143.18 (C(3), C(4)); 148.95, 149.34 (C(10), C(11)); 187.80 (C(7a)); 193.67(C(2)). MS, m/z (I_{rel} (%)): 325 $[M - HCl]^+$ (100), 310 $[M - HCl - Me]^+$ (36), 282 $[M - HCl - Me - CO]^+$ (9), 268 (5), 242 (6), 218 (10), 196 (2), 176 (10), 152 (3), 114 (4), 76 (3), 41 (2).

10,11-Dimethoxy-6,6-dimethyl-1,5,6,12b-tetrahydrobenzo-[*d*,*f*]indole-2,8-dione (5). A mixture of anisole (0.22 g, 2 mmol), isobutyraldehyde (0.14 g, 2 mmol), and 3,4-dimethoxyphenylacetonitrile (0.35 g, 2 mmol) in dichloromethane (2 mL) was added dropwise with stirring and cooling with ice water to concentrated H_2SO_4 (10 mL). The reaction mixture was stirred for 10 min, poured into crushed ice (50 g), adjusted with aqueous ammonia to pH 7—8, and extracted with dichloromethane (3×15 mL). After the extraction, dichloromethane was dried with anhydrous $MgSO_4$. Then the solution was filtered, dichloromethane was distilled off, and the residue was crystallized from ethyl acetate. Compound **5** was obtained in a yield of 0.16 g (24%), m.p. 244—247 °C. Found (%): C, 70.72; H, 6.20; N, 4.17. $C_{20}H_{21}NO_4$. Calculated (%): C, 70.78; H, 6.24; N, 4.13. IR, ν/cm^{-1}: 1516, 1568, 1596, 1672, 1688. ^{1}H NMR, δ: 1.46 and 1.55 (both s, 3 H each, C(6)Me, C(6)Me); 2.35 and 2.44 (both d, 1 H each, H(5A), H(5B), J = 13.4 Hz); 2.95 and 3.29 (both dd, 1 H each, H(1A), H(1B), J = 16.8 Hz, J = 3.9 Hz, J = 2.4 Hz); 3.64 (br.s, 1 H, H(12b)); 3.93 and 3.94 (both s, 3 H each, C(10)OMe, C(11)OMe); 5.84 (d, 1 H, H(3), J = 10.1 Hz); 6.66 (dd, 1 H, H(4), J = 10.1 Hz, J = 2.1 Hz); 6.75 and 7.66 (both s, 1 H each, H(9), H(12)). ^{13}C NMR, δ: 29.21, 30.88 (C(6)Me_2); 39.08, 49.45 (C(1), C(5)); 45.72 (C(12b)); 56.05, 56.14 (C(10)OMe, C(11)OMe); 60.12, 73.38 (C(4a), C(6)); 108.65,

Table 2. Crystallographic parameters and the X-ray data collection and structure refinement statistics for compound **5**

Parameter	Characteristics
Molecular formula	$C_{20}H_{21}NO_4$
Molecular weight	339.15
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell parameters	
a/Å	12.036 (2)
b/Å	10.0103 (17)
c/Å	14.243 (2)
α/deg	90.00
β/deg	95.41(1)
γ/deg	90.00
V/Å^3	1708.41(216)
Z	4
d_{calc}/g cm^{-3}	1.319
μ/mm^{-1}	0.092
θ-scan range/deg	2.87—31.80
Total number of reflections	27365
Number of independent reflections	5377
Number of refined parameters, N	264
R_{int}	0.0867
R_1 factor (%)	4.71
R factors based on reflections with $I > 2(I)$	
R_1	0.0471
wR_2	0.0689
R factors based on all reflections	
R_1	0.1744
wR_2	0.0747

109.89 (C(9), C(12)); 128.87, 149.86 (C(3), C(4)); 127.68 (C(12a)); 137.77, 148.64, 154.85 (C(8a), C(10), C(11)); 167.50 (C(7a)); 181.18 (C(8)); 194.83 (C(2)). MS, m/z (I_{rel} (%)): 339 $[M]^+$ (100), 324 $[M - Me]^+$ (19), 296 $[M - Me - CO]^+$ (23), 282 (2), 271 (17), 256 (31), 229 (12), 213 (7), 201 (7), 184 (3), 157 (4), 141 (4), 128 (4), 115 (5), 91 (2), 77 (6), 41 (4).

X-ray diffraction study of compound 5. Single crystals of compound **5** were obtained by the crystallization from ethyl acetate. The X-ray diffraction data were collected on a Xcalibur-3 diffractometer equipped with a CCD area detector at 295(2) K (λ(Mo-Kα), graphite monochromator, φ- and ω-scanning mode). The structure of compound **5** was solved by direct methods with the use of the SHELXS-97 program packages and refined anisotropically (isotropically for hydrogen atoms) with the use of the SHELXL-97 program package. Principal crystallographic parameters and the X-ray data collection and structure refinement statistics for compound **5** are given in Table 2.

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