[Chem. Pharm. Bull. 27(11)2636—2641(1979)]

*UDC 547.473.04 : 547.233.1.04*

# Heterocycles. VII.[1] Reaction of 12-Hydroxy-5-oxa-6-oxo-5,6-dihydrochrysene with Methylamine

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(Received March 9, 1979)

The lactone (**5**) reacts with methylamine to afford the methylaminophthalide (**6**). On the basis of the reactions of **6** and related compounds, the spiro lactam (**14**) is suggested to be an intermediate in the formation of **6** from **5**.

**Keywords**——molecular rearrangement; indolinone; phthalide; stereoisomer; nuclear magnetic resonance

In the course of our investigations on the benzo[*c*]phenanthridine alkaloids we have found that the arylquinone (**3**) is a useful intermediate for the syntheses of ring C-hydroxylated benzo[*c*]phenanthridines.[4] In this connection, the Bucherer-like reaction of the lactone (**5**) derived from **3** was considered to be attractive. This paper is concerned with the reaction of **5** with methylamine, resulting in a molecular rearrangement, and reports the structural elucidation of the products obtained.

The coupling reaction of 1,4-naphthoquinone (**1**) with *o*-methoxycarbonylbenzenediazonium fluoroborate (**2**) gave the arylquinone (**3**) and diarylquinone (**4**) in 24 and 11% yields, respectively. The structure of **3** is characterized by an infrared (IR) band for the methoxycarbonyl group at 1716 $cm^{-1}$ and a proton magnetic resonance (PMR) signal for the 3-H at $\delta$ 6.91. Hydrogenation of **3** over palladium-carbon afforded the lactone (**5**) (91%), the structure of which was supported by IR bands for the hydroxyl and lactone groups at 3400 and 1680 $cm^{-1}$, respectively.

Stirring of **5** in 40% aqueous methylamine solution at room temperature for 2 hr furnished the methylaminophthalide (**6**) (69%) after preparative thin-layer chromatography (pre. TLC). Its IR spectrum shows bands for the *sec*-amino (3375 $cm^{-1}$), $\gamma$-lactone (1760 $cm^{-1}$) and $\gamma$-lactam (1690 $cm^{-1}$) groups. The PMR spectrum of **6** exhibits a one-proton triplet and a two-proton doublet at $\delta$ 4.12 and 2.75, respectively. Decoupling experiments show these multiplets to be coupled. These spectral properties are in accord with the structure shown for **6**. The carbon-13 magnetic resonance (CMR) spectrum also supports this structure for **6** (Table I). Since each carbon gives a single peak and there are no double peaks, **6** should be an isomer having the (3*RS*, 3'*RS*) or (3*RS*, 3'*SR*) configuration.[5] However, further studies are required on this point. Treatment of **6** with hydrochloric acid provided the methyleneisoindolinone (**7**) (79%), and ozonolysis then gave N-methylphthalimide (**8**) (68%), confirming the presence of a double bond at the 3- and 8'-positions in **7**. The structure of **7** is confirmed on the basis of nuclear Overhauser effect (NOE) data. Irradiation of a methyl signal at $\delta$ 3.19 in **7** caused a 30% enhancement of the 3'-H signal at $\delta$ 5.06, while no enhancement of the 8'-H signal at $\delta$ 5.96 was observed. Also, saturation of a methyl signal at $\delta$ 3.11 gave 9 and 9.5% enhancements of the 3'-H and 8'-H signals, respectively.

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[1] Part VI: M. Onda, Y. Harigaya, and J. Horie, *Chem. Pharm. Bull.* (Tokyo), **26**, 3330 (1978).

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[4] The details will be reported in a subsequent paper.

[5] H. Kagan, "Stereochemistry," Vol. 1, Georg Thieme Publishers, Stuttgart, 1977, pp. 73—77 and references cited therein.

These data lead us to the conclusions that the signals at δ 3.19 and 3.11 are due to the 2-Me and 2′-Me groups, respectively, and that the double bond in **7** is the (*Z*)-configuration.

Hydrogenation of **7** over palladium-carbon afforded the diisoindolinone (**9**) (73%) which had a symmetrical structure containing two asymmetric centers. Its CMR spectrum shows two sets of carbon resonances for each carbon, suggesting **9** to exist in two forms, namely the *meso* and racemic forms. The PMR spectrum of **9**, which also shows two sets of proton

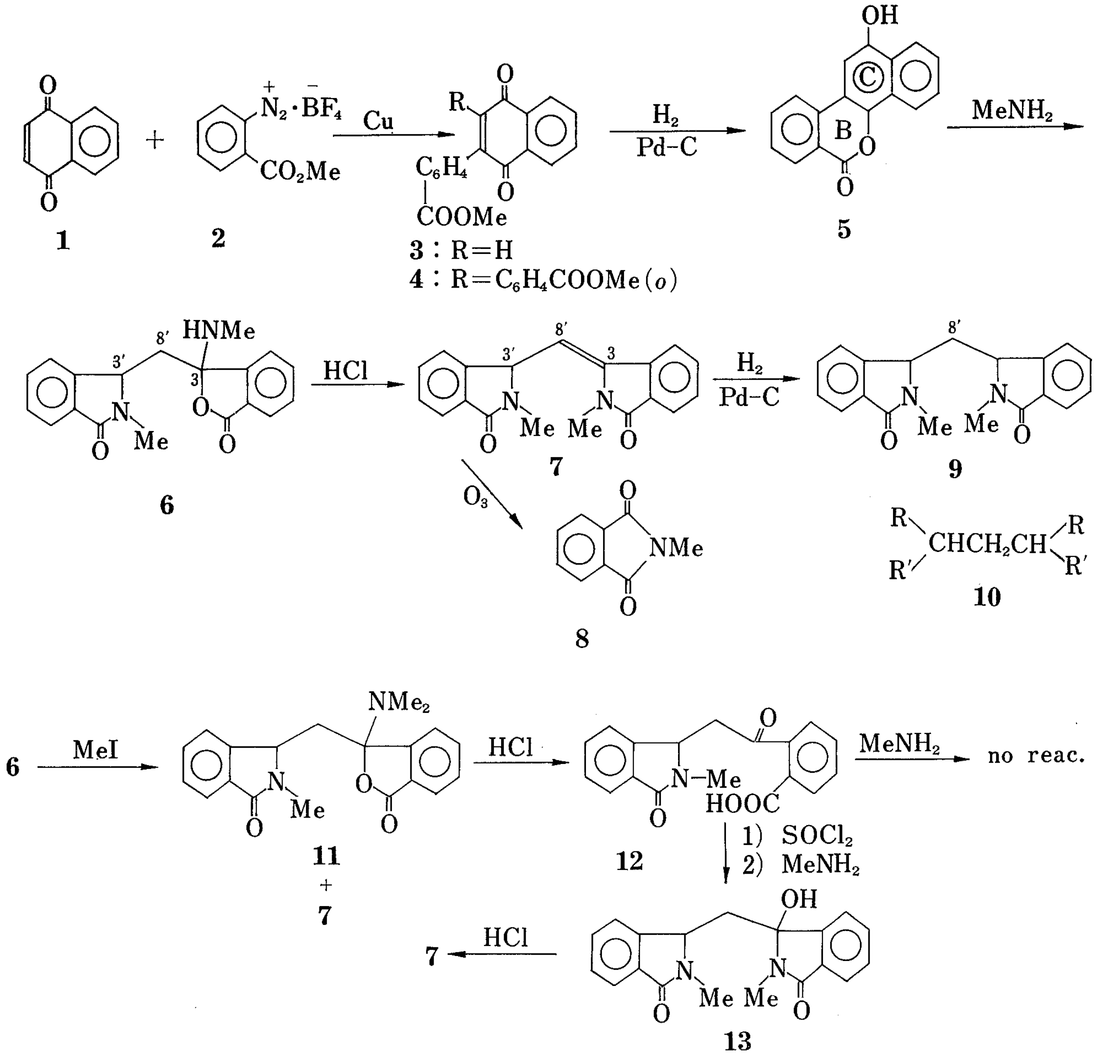

Chart 1

Table I. CMR Data for **6**, **7** and **9**

| | C-1, -1′ | C-3 | C-3′ | C-3a, -3′a | C-4, -4′ | C-5, -5′ | C-6, -6′ | C-7, -7′ | C-7a, -7′a | C-8′ | 2-Me | 2′-Me | 3-NHMe |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **6** | 168.5<br>168.0 | 103.2 | 58.1 | 146.3<br>145.2 | 122.9<br>122.8 | 134.3<br>131.6 | 130.5<br>128.1 | 125.6<br>123.1 | 131.4<br>128.8 | 40.4 | | | 28.2<br>27.4 |
| **7** | 168.0<br>166.1 | 134.6 | 59.0 | 144.1<br>140.6 | 123.0<br>122.9 | 132.4<br>131.8 | 130.0<br>128.9 | 124.0<br>123.7 | 132.1<br>131.2 | 106.7 | 27.7<br>26.1 | | |

| | C-1(1′) | C-3(3′) | C-3a(3′a) | C-4(4′) | C-5(5′) | C-6(6′) | C-7(7′) | C-7a(7′a) | C-8′ | 2(2′)-Me |
|---|---|---|---|---|---|---|---|---|---|---|
| **9** | 168.3<br>168.1 | 59.2<br>58.9 | 144.5<br>144.5 | 122.6<br>122.4 | 131.8<br>131.4 | 128.9<br>128.9 | 123.9<br>123.8 | 132.8<br>132.2 | 34.6<br>33.9 | 28.2<br>27.9 |

resonances for the 3(3')-H and 8'-$H_2$, makes it possible to deduce the ratio of the isomers. One set (A) of signals consists of two triplets for the 3(3')-H at $\delta$ 4.58 and the 8'-$H_2$ at $\delta$ 2.37. The other (B) consists of a double doublet for the 3(3')-H at $\delta$ 4.40 and two double triplets for the 8'-$H_2$ at $\delta$ 2.64 and 2.27. The signals in each set are confirmed to be coupled by means of decoupling experiments. It is known that the methylene protons in the racemic form of the compounds (**10**) are isochronous, whereas in the *meso* form these protons are anisochronous.[5,6] Therefore, the A and B sets mentioned above correspond to the racemic and *meso* forms, respectively. The ratio of the racemic to the *meso* form is deduced to be approximately 1: 2 on the basis of the signal intensities at $\delta$ 4.58 and 4.40.

Methylation of **6** with methyl iodide gave the dimethylaminophthalide (**11**) (44%) and **7** (20%). The PMR spectrum of **11** shows two signals for the 2'-Me group at $\delta$ 3.04 and 2.80 in a ratio of *ca.* 1: 1.3 and two signals for the 3'-H at $\delta$ 4.02 and 3.75 in a ratio of *ca.* 1: 1.4. The dimethylaminophthalide (**11**) may exist as a mixture of two conformers owing to the steric hindrance caused by a bulky substituent, the dimethylamino group, at the C-3. Hydrolysis of **11** with hydrochloric acid furnished the keto acid (**12**) (72%) which did not react with methylamine to give **6**. On the other hand, **12** was recyclized by treatment with thionyl chloride followed by methylamine to give the hydroxyisoindolinone (**13**) (85%), which was further converted into **7** on treatment with hydrochloric acid in 67% yield. The PMR spectrum of **13** exhibits a methyl signal at $\delta$ 2.83 and two methyl signals at $\delta$ 2.93 and 2.85 in a ratio of *ca.* 1: 1.6, suggesting the existence of two conformers as in the case of **11**.

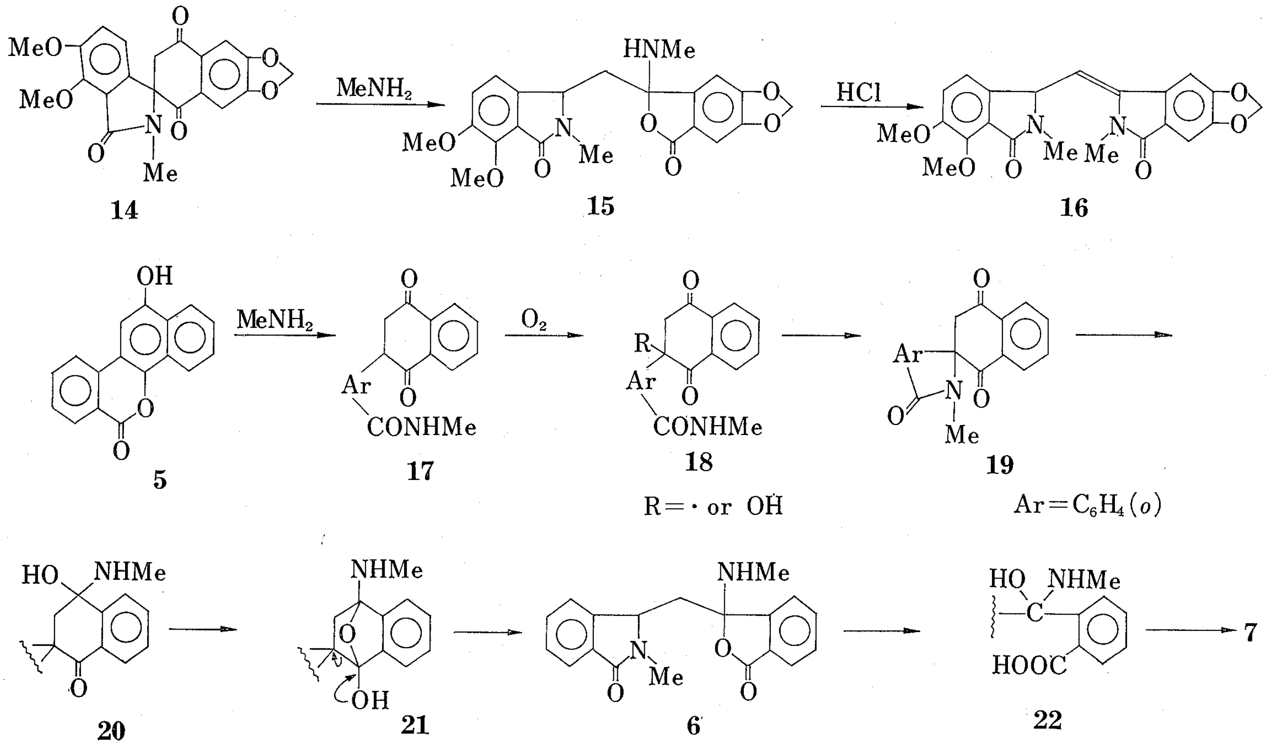

Chart 2

In order to establish a possible pathway of the formation of **6** from **5**, the reaction of the spiro lactam (**14**) with methylamine was examined. The spiro lactam (**14**) (see "Experimental") has been obtained in the course of syntheses of benzo[*c*]phenanthridines from berberinium chloride, and its preparation will be reported in a subsequent paper. The spiro

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6) F.A. Bovey, *Accounts Chem. Res.*, **1**, 175 (1968).

lactam (**14**) reacted with methylamine to give the methylaminophthalide (**15**) quantitatively; the structure of **15** is confirmed by comparison of its PMR spectrum with that of **6**. Treatment of **15** with hydrochloric acid afforded the methyleneisoindolinone (**16**) (76%), the structure of which was confirmed by comparison of its PMR spectrum with that of **7**. These results suggest that the 14-type compound may be an intermediate in the formation of **6** from **5**. Thus, a plausible pathway is as follows. The lactone (**5**) gives the diketo amide (**17**) *via* aminolysis and isomerization. Autoxidation of **17** furnishes the diketo amide (**18**)[7] which cyclizes to afford the spiro lactam (**19**) similar to **14**. Addition of methylamine to the sterically uncrowded ketone group at the C-4 (→**20**), transannular hemiketalization (→**21**) and bond fission then produce **6**. In addition, hydrolysis of **6** (→**22**) under acidic conditions results in the formation of **7**.

Finally, we will comment briefly on some interesting spectral properties of the compounds obtained. The 8'-$H_2$'s in **6** and **15** are exchangeable with deuterium oxide. On addition of deuterium oxide the doublet of 8'-$H_2$ at $\delta$ 2.75 disapeared and the triplet of 3'-H at $\delta$ 4.12 coalesced into a singlet in the PMR spectrum of **6**. Although the change of the 3'-H signal is obscured by overlapping with the 7'-OMe signal, addition of deuterium oxide extinguishes the doublet of 8'-$H_2$ at $\delta$ 2.61 in the PMR spectrum of **15**. The CMR spectrum of **6** taken in methanol-$d_4$ shows no detectable carbon resonance for the C-8'. The mass spectrum (MS) of **6** shows a peak due to loss of $H_2O$ from the molecular ion as the ion of greatest mass, and exhibits fragmentations similar to those of **7**. On the other hand, in the MS of **11** and **13** the normal molecular ions are observed.

## Experimental

Melting points were determined on a micro hot-stage and are not corrected. IR spectra were recorded on a JASCO IR-G spectrometer in chloroform unless otherwise stated. PMR spectra were taken on a JEOL JNM PS-100 (100 MHz) or a Varian T-60 (60 MHz) spectrometer in deuterochloroform unless otherwise stated. NOE data were measured with a JEOL JNM PS-100 (100 MHz) spectrometer in degassed deuterochloroform. CMR spectra were taken on a JEOL JNM PS-100 (25.1 MHz) spectrometer in deuterochloroform. MS were measured with a JEOL JMS-OIS spectrometer.

**2-(*o*-Methoxycarbonylphenyl)-1,4-naphthoquinone** (3) **and 2,3-Bis(*o*-methoxycarbonylphenyl)-1,4-naphthoquinone** (4)——A solution of $NaNO_2$ (3.5 g) in water (5 ml) was added dropwise to a stirred suspension of methyl anthranilate (5.0 g) in conc. HCl (6 ml) and water (7 ml) with cooling in ice-water. After stirring for 30 min, a suspension of $NaBF_4$ (6 g) in water (5 ml) was added dropwise with cooling. Stirring was continued for 30 min to obtain a solution of **2**.

The solution of **2** obtained above was added dropwise to a stirred suspension of **1** (5.0 g) in acetic acid (80 ml) at 40° and then Cu powder (1.7 g) was added over 6 hr. Addition of **2** and Cu powder (0.3 g) was repeated twice in the same way. After concentration *in vacuo*, the residue was dissolved in benzene and filter. The residue obtained from the benzene solution was purified three times by almina column chromatography (neutral, grade III, 50 g) using benzene/hexane (1/2, v/v) as an eluant, followed by recrystallization from ethanol to give **3** (1.36 g). The residue obtained from the ethanol mother liquor was chromatographed on neutral alumina (grade III, 200 g) using benzene/hexane (1/2, v/v) as an eluant to give additional **3** (0.87 g) and **4** (1.46 g, 11%). The total yield of **3** was 24%.

The Aryquinone (**3**): Yellow prisms of mp 157—158° (from EtOH). IR $\nu_{max}$ cm$^{-1}$: 1716 (OC=O), 1663 (C=O). PMR (100 MHz) $\delta$: 8.19—8.05 (3H, m, aromatic H's), 7.84—7.30 (5H, m, aromatic H's), 6.91 (1H, s, 3-H), 3.73 (3H, s, *o*-COOMe). *Anal.* Calcd. for $C_{18}H_{12}O_4 \cdot 1/3H_2O$: C, 72.48; H, 4.28. Found: C, 72.17; H, 3.92. MS *m/e*: $M^+$, 292.076 (M, 292.074).

The Diarylquinone (**4**): Yellow prisms of mp 244.5—247° (from EtOH). IR $\nu_{max}$ cm$^{-1}$: 1715 (OC=O), 1665 (C=O). PMR (60 MHz) $\delta$: 8.23—7.65 (6H, m, aromatic H's), 7.42—6.95 (6H, m, aromatic H's), 3.84 (6H, s, 2 × *o*-COOMe). *Anal.* Calcd. for $C_{26}H_{18}O_6 \cdot 1/10H_2O$: C, 72.92; H, 4.28. Found: C, 72.84; H, 4.21. MS *m/e*: $M^+$, 426.110 (M, 426.100).

**12-Hydroxy-5-oxa-6-oxo-5,6-dihydrochrysene** (5)——A solution of **3** (199 mg) in a mixture (50 ml) of ethyl acetate/methanol (1/1, v/v) was shaken with $H_2$ over 10% Pd-C (40 mg) for 3 hr. The reaction mixture was filtered and concentrated *in vacuo* to afford **5** (162 mg, 91%) as colorless needles of mp over 300° (from EtOH). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400 (OH), 1680 (OC=O). PMR (100 MHz, $Me_2SO$-$d_6$) $\delta$: 10.42 (1H, s, 12-OH),[8]

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[7] Autoxidation of this type of compound under alkaline conditions is known to occur.[1]

[8] On addition of $D_2O$ this signal disappeared.

8.36—8.14 (4H, m, aromatic H's), 7.99 (1H, dt, *J* 8 and 2 Hz, 7-H), 7.76—7.60 (3H, m, aromatic H's), 7.50 (1H, s, 11-H). *Anal.* Calcd. for $C_{17}H_{10}O_3\cdot1/5H_2O$: C, 76.80; H, 3.94. Found: C, 76.71; H, 3.85. MS *m/e*: $M^+$, 262.060 (M, 262.063).

**3-(2′-Methyl-3′-isoindolinonyl)methyl-3-methylaminophthalide (6)**——A suspension of **5** (99 mg) in 40% aq. methylamine solution (1 ml) was stirred at room temperature for 2 hr until the solution became clear. After concentration *in vacuo*, the residue was purified by pre. TLC (silica gel plates; $CHCl_3$/MeOH=10/1, v/v) to give **6** (84 mg, 69%), *Rf* 0.40, as a light yellow oil. IR $\nu_{max}$ $cm^{-1}$: 3375 (NH), 1760 (OC=O), 1690 (NC=O). PMR (100 MHz) $\delta$: 7.81 (1H, dd, *J* 8 and 2 Hz, 7- or 7′-H), 7.66—7.32 (7H, m, aromatic H's), 4.12 (1H, t, *J* 4 Hz, 3′-H),[9] 2.89 (4H, s, 2′-Me and 3-N$\underline{H}$Me),[8] 2.75 (2H, d, *J* 4 Hz, 8′-H),[8] 2.14 (3H, s, 3-NH$\underline{Me}$). CMR (Table I). MS *m/e*: 322 ($C_{19}H_{18}N_2O_3$, 0%), 304 ($C_{19}H_{16}N_2O_2$, 100%), 158 ($C_{10}H_8NO$, 42%), 146 ($C_9H_8NO$, 87%), 117 ($C_8H_7N$, 80%).

**2-Methyl-3-(2′-methyl-3-isoindolinonyl)methyleneisoindolinone (7)**——1) A suspension of **5** (138 mg) in 40% aq methylamine solution (5 ml) was treated by the procedure described above to give **6**, which was heated in 10% HCl (10 ml) on a boiling water-bath for 3 hr. The reaction mixture was extracted with chloroform to afford **7** (124 mg, 75%) as colorless prisms of mp 248—249° (from EtOH). IR $\nu_{max}$ $cm^{-1}$: 1705 and 1690 (NC=O), 1650 (C=C). PMR (100 MHz) $\delta$: 8.04, 7.94 and 7.82 (1H each, dd, *J* 8 and 2 Hz, 4-, 7- and 7′-H's),[10] 7.74—7.28 (5H, m, aromatic H's), 5.96 (1H, d, *J* 10 Hz, 8′-H), 5.06 (1H, d, *J* 10 Hz, 3′-H), 3.19 (3H, s, 2-Me), 3.11 (3H, s, 2′-Me). CMR (Table I). *Anal.* Calcd. for $C_{19}H_{16}N_2O_2\cdot1/4H_2O$: C, 74.14; H, 5.37; N, 9.11. Found: C, 74.07; H, 5.33; N, 9.05. MS *m/e*: $M^+$, 304.122 (M, 304.121).

2) A solution of **6** (6.0 mg) in 10% HCl (0.5 ml) was heated on a boiling water-bath for 1 hr. The precipitate was collected by filtration and dried to give **7** (4.5 mg, 79%), mp 244—245°.

**N-Methylphthalimide (8)**——A stream of $O_3$ was passed through a solution of **7** (100 mg) in methylene chloride (20 ml) at −70° for 3 hr. After addition of acetic acid (0.2 ml), the reaction mixture was allowed to warm to room temperature and saturated aq. KI solution was added with vigorous shaking. After standing at room temperature for 15 min, the separated water layer was removed. This procedure was repeated three times and then the reaction mixture was shaken with saturated aq. $Na_2S_2O_3$ solution until the orange-brown color ($I_2$) disappeared. Work-up afforded a syrup, and pre. TLC (silica gel plates; benzene/ethyl acetate=10/1, v/v) gave **8** (36 mg, 68%), *Rf* 0.75, as colorless needles of mp 135.5° (from ether/hexane). IR $\nu_{max}$ $cm^{-1}$: 1770 and 1710 (NC=O). PMR (60 MHz) $\delta$: 7.86—7.53 (4H, m, aromatic H's), 3.15 (3H, s, N–Me). MS Calcd. for $C_9H_7NO_2$: M, 161.048. Found: *m/e*: $M^+$, 161.047. This compound was identical with an authentic sample prepared from phthalic anhydride and methylamine on the basis of the spectral data and mixed melting point determination.

**Bis(2-methyl-3-isoindolinonyl)methane (9)**——A solution of 7 (19 mg) in ethyl acetate (30 ml) was shaken with $H_2$ over 10% Pd–C (10 mg) for 4 hr. Work-up gave an oil which was crystallized from ether to give **9** (14 mg, 73%) as colorless prisms of mp 146—166°. IR $\nu_{max}$ $cm^{-1}$: 1685 (NC=O). PMR (100 MHz) $\delta$: 7.62—7.20 (6H, m. aromatic H's), 4.58 (t, *J* 6 Hz, 3(3′)-H), 4.40 (dd, *J* 7 and 4 Hz, 3(3′)-H), 2.64 (dt, *J* 15 and 4 Hz, 8′-H), 2.37 (t, *J* 6 Hz, 8′-$H_2$), 2.27 (dt, *J* 15 and 7 Hz, 8′-H), 3.07 (6H, s, 2(2′)-Me). CMR (Table I). *Anal.* Calcd. for $C_{19}H_{18}N_2O_2\cdot1/5H_2O$: C, 73.62; H, 5.98; N, 9.04. Found: C, 73.79; H, 5.93; N, 8.92.

**3-Dimethylamino-3-(2′-methyl-3′-isoindolinonyl)methylphthalide (11)**——A mixture of **6** (100 mg), methyl iodide (0.4 ml) and $K_2CO_3$ (200 mg) in chloroform (3 ml) was stirred at room temperature for 40 hr. The reaction mixture was filtered and evaporated down *in vacuo*. The residue was purified by pre. TLC (silica gel plates; $CHCl_3$/MeOH=10/1, v/v) to give **11** (46 mg, 44%), *Rf* 0.44, as a colorless oil and **7** (19 mg, 20%), *Rf* 0.73, as colorless prisms of mp 248—249° (from EtOH).

Spectral data for **11**: IR $\nu_{max}$ $cm^{-1}$: 1753 (OC=O), 1687 (NC=O). PMR (100 MHz) $\delta$: 7.84—7.11 (8H, m, aromatic H's), 4.02 (t, *J* 4 Hz, 3′-H), 3.75 (dd, *J* 7 and 1 Hz, 3′-H), 3.19—2.56 (2H, m, 8′-$H_2$), 3.04 and 2.80 (3H, s each, 2′-Me), 2.32 (6H, s, 3-$NMe_2$). MS Calcd. for $C_{20}H_{20}N_2O_3$: M, 336.147. Found: *m/e*: $M^+$, 336.147.

***o*-(2′-Methyl-3′-isoindolinonyl)acetylbenzoic Acid (12)**——A solution of **11** (45 mg) in 10% HCl (10 ml) was heated on a boiling water-bath for 8 hr, then extracted with ethyl acetate. The ethyl acetate layer was shaken with 5% aq. KOH solution, then the water layer was acidified with 10% HCl for extraction with ethyl acetate. Removal of the solvent *in vacuo* and subsequent pre. TLC (silica gel plates; $CHCl_3$/MeOH=5/1, v/v) gave **12** (30 mg, 72%), *Rf* 0.36, as a light yellow oil. IR $\nu_{max}$ $cm^{-1}$: 1685 (OC=O and C=O). PMR (60 MHz) $\delta$: 8.09 (1H, s, 1-COOH),[8] 7.93—7.30 (8H, m, aromatic H's), 4.96 (1H, t, *J* 5.5 Hz, 3′-H), 3.09 (5H, s, 2′-Me and 8′-$H_2$). MS Calcd. for $C_{18}H_{15}NO_4$: M, 309.100. Found: *m/e*: $M^+$, 309.102.

**2,2′-Dimethyl-3-hydroxy-3,3′-methylenediisoindolinone (13)**——$SOCl_2$ (0.1 ml) was added to a solution of **12** (19 mg) in a mixture of anhyd. benzene (1 ml) and anhyd. chloroform (1 ml), and stirring was continued at room temperature for 30 min. After concentration *in vacuo*, the residue was dissolved in anhyd. benzene (2 ml) and a stream of methylamine was passed at room temperature until the solution was saturated with methylamine. After standing at room temperature for 1 hr, the reaction mixture was evaporated down

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[9] On addition of $D_2O$ this multiplet coalesced into a singlet.

[10] These protons could not be assigned.

*in vacuo* and the residue was extracted with chloroform. The chloroform residue was purified by pre. TLC (silica gel plates; $CHCl_3$/MeOH=15/1, v/v) to furnish **13** (17 mg, 85%), *Rf* 0.40, as a colorless oil. IR $\nu_{max}$ $cm^{-1}$: 3570 and 3320 (OH), 1686 (NC=O). PMR (60 MHz) $\delta$: 7.68—6.85 (8H, m, aromatic H's), 5.10 (1H, s, 3-OH),[8] 4.50—4.17 (1H, m, 3′-H), 2.65—2.02 (2H, m, 8′-$H_2$), 2.93 and 2.85 (3H each, s, 3- and 3′-Me's).[10] MS Calcd. for $C_{19}H_{18}N_2O_3$: M, 322.132. Found: *m/e*: $M^+$, 322.134.

**The Methyleneisoindolinone (7) from 13**——Conc. HCl (0.1 ml) was added to a solution of **13** (16 mg) in methanol (0.5 ml) and the mixture was refluxed for 2 hr. After concentration *in vacuo*, the residue was purified by pre. TLC (silica gel plates; benzene/ethyl acetate=1/2. v/v) to give **7** (10 mg, 67%), *Rf* 0.38, as colorless prisms of mp 245—247° (from EtOH).

**1,4-Dioxo-6,7-methylenedioxy-1,2,3,4-tetrahydronaphthbalene-2-spiro-3′-(6′,7′-dimethoxy-2′-methyl)-isoindolinone (14)**——Light yellow needles of mp 128—129° (from benzene). IR $\nu_{max}$ $cm^{-1}$: 1700 (C=O and NC=O). PMR (100 MHz) $\delta$: 7.59 and 7.46 (1H each, s, 5- and 8-H's),[10] 6.83 and 6.53 (1H, each, d, *J* 8 Hz, 4′- and 5′-H's),[10] 620 (2H, s, 6,7-$OCH_2O$), 4.07 (3H, s, 7′-OMe), 3.80 (3H, s, 6′-OMe), 3.63 (1H, d, *J* 16 Hz, 3-H), 3.07 (3H, s, 2′-Me), 2.91 (1H, d, *J* 16 Hz, 3-H). MS Calcd. for $C_{21}H_{18}NO_7$: M, 395.101. Found: *m/e*: $M^+$, 395.101.

**3-(6′,7′-Dimethoxy-2′-methyl-3′-isoindolinonyl)methyl-3-methylamino-5,6-methylenedioxyphthalide (15)**——A suspension of **14** (28 mg) in 40% aq. methylamine solution (2 ml) was stirred at room temperature for 30 min. Work-up afforded **15** (30 mg, quantitative yield) as a light yellow oil. IR $\nu_{max}$ $cm^{-1}$: 3380 (NH), 1753 (OC=O), 1686 (NC=O). PMR (60 MHz) $\delta$: 7.25 (2H, s, 4′- and 5′-H's), 7.18 (1H, s, 7-H), 7.00 (1H, s, 4-H), 6.04 (2H, s, 5,6-$OCH_2O$), *ca.* 4.00 (1H, 3′-H, overlapping with the 7′-OMe signal), 3.95 (3H, s, 7′-OMe), 3.82 (3H, s, 6′-OMe), 2.90 (3H, s, 2′-Me), 2.61 (2H, d, *J* 4 Hz, 8′-$H_2$),[8] 2.41 (1H, s, 3-N$\underline{\text{H}}$Me),[8] 2.10 (3H, s, 3-NH$\underline{\text{Me}}$).

**3-(6′,7′-Dimethoxy-2′-methyl-3′-isoindolinonyl)methylene-2-methyl-5,6-methylenedioxyisoindolinone (16)**——A solution of **15** (30 mg) in 10% HCl (2 ml) was heated on a boiling water-bath for 1 hr. The precipitate was collected by filtration and purified by pre. TLC (silica gel plates; $CHCl_3$/MeOH=20/1, v/v) to give **16** (22 mg, 76%), *Rf* 0.50, as colorless prisms of mp 288—290° (from $CHCl_3$/EtOH). IR $\nu_{max}$ $cm^{-1}$: 1691 (NC=O). PMR (100 MHz) $\delta$: 7.41 (1H, s, 7-H), 7.31 (1H, s, 4-H), 7.04 (1H, d, *J* 8 Hz, 4′-H), 6.99 (1H, d, *J* 8 Hz, 5′-H), 6.12 (2H, s, 5,6-$OCH_2O$), 5.69 (1H, d, *J* 10 Hz, 8′-H), 4.95 (1H, d, *J* 10 Hz, 3′-H), 4.09 (3H, s, 7′-OMe), 3.86 (3H, s, 6′-OMe), 3.17 (3H, s, 2-Me), 3.08 (3H, s, 2′-Me). *Anal.* Calcd. for $C_{22}H_{20}N_2O_6 \cdot 1/3H_2O$: C, 63.76; H, 5.03; N, 6.76. Found: C, 63.81; H, 4.94; N, 6.56.