1.37 (10-CH_3), 2.06 and 2.08 (21-$OCOCH_3$ and 17-$OCOCH_3$), 3.94 (br, 7β-H), 4.77 (21-CH_2), 4.92 (d, J = 3 Hz, 7β-OH), 5.93 (4 H), 6.06 (d of d, J = 10, 2 Hz, 2 H), 7.59 (d, J = 10 Hz, 1 H); mass spectrum, m/z 458 (mol wt found 458.1950, calcd for $C_{25}H_{30}O_8$ 458.1940).

7β,17α-Hydroxy-1,4-pregnadiene-3,20-dione (8). In the manner of the electrochemical conversion of **2** to **7**, 6β,7β-oxy-17α-hydroxy-1,4-pregnadiene-3,20-dione (**3**;[10] 50.7 mg) was converted to a residue of 36.5 mg. Chromatography on 1000-μm silica gel plates (2:1 $CHCl_3$/EtOAc) afforded 17 mg of **8**: UV (MeOH) λ_{max} 243 nm (ε 14 400); ^1H NMR (Me_2SO-d_6) δ 0.566 (13-CH_3), 1.19 (10-CH_3), 2.09 (20-CH_3), 3.12 (br, 7-αH), 4.65 (d, J = 7 Hz, 7β-OH), 5.07 (17α-OH), 5.94 (4 H), 6.08 (d of d, J = 10, 2 Hz, 2 H), 7.16 (J = 10 Hz, 1 H); mass spectrum, m/z 344 (mol wt found 344.1979, calcd for $C_{21}H_{28}O_4$ 344.1987).

Acknowledgment. We thank Mr. P. Bartner, Mr. C. Eckhart, and Dr. M. Puar of the Physical and Analytical Chemistry Department for helpful discussions respectively with mass spectra, circular dichroism, and NMR data.

Registry No. 1, 974-23-2; 2, 79172-19-3; 3, 79172-20-6; 4, 520-88-7; 5, 79253-97-7; 7, 79172-21-7; 8, 79172-22-8.

(10) Prepared by L. Weber of these laboratories from the 1,4,6-triene essentially in the manner of H. Laurent, G. Schulz, and R. Wiechert [*Chem. Ber.*, **102**, 2570 (1969)], using *N*-bromosuccinimide, $HClO_4$, H_2O, dioxane, followed by K_2CO_3 in EtOH, acetone, water, on the 6-hydroxy-7-bromo intermediate; for **3**: UV (MeOH) λ_{max} 246 nm (ε 15 760); $[\alpha]^{26}_D$ −93.6° (dioxane); ^1H NMR (Me_2SO-d_6) δ 3.42 (J = 4 Hz) and 3.71 (J = 4 Hz, 6-αH and 7-αH), 6.13 (d of d, J = 10, 2 Hz, 2 H), 6.5 (d, J = 2 Hz, 4 H), 7.09 (d, J = 10 Hz, 1 H); mass spectrum, m/z 342 (mol wt found 342.1852, calcd for $C_{21}H_{26}O_4$ 342.1831).

N-[(4-Nitro-1*H*-inden-1-ylidene)methyl]dialkylamines by an Unexpected Reaction

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We have recently prepared 4-substituted indoles from 2-methyl-3-nitrobenzaldehyde by elaboration of the carboxaldehyde function prior to indole-nucleus formation by the Batcho–Leimgruber process.[1] To further assess the scope of this sequence, we investigated the fate of the 2-methoxyethenyl side chain in the reaction of 1-(2-methoxyethenyl)-2-methyl-3-nitrobenzene (**1**) with *N*,*N*-dimethylformamide dimethyl acetal and pyrrolidine in *N*,*N*-dimethylformamide. Of particular interest was the possibility of generating enamine **2** and the preparation of 4-(2-methoxyethenyl)-1*H*-indole by subsequent reductive cyclization. Enamine **2**, however, could not be isolated; instead, a dark magenta, crystalline product with the elemental composition $C_{14}H_{14}N_2O_2$ was the major reaction product. In view of the elevated reaction temperature required for the N,N-disubstituted aminomethylenation, a possible electrocyclic ring closure of the incipient product **2**, yielding a naphthalenoid system, had to be considered. 1-(8-Nitro-2-naphthalenyl)pyrrolidine (**3**), therefore, appeared to be a plausible structural proposal at first. The ^1H NMR spectrum revealed the pyrrolidine moiety, three contiguous benzenoid protons, a singlet at δ 7.78, and an AB pattern at δ 7.28 and 7.58, but J_{AB} was only 5 Hz. As an alternative, 1-[(7-nitro-1*H*-inden-1-ylidene)methyl]-pyrrolidine (**4**), featuring the formally unaltered carbon skeleton of **2** and the AB protons on a five-membered ring, appeared compatible with all spectral data although its genesis was difficult to explain. Roentgen crystallographic analysis revealed yet another isomer as the correct structure; the stereoscopic drawing is shown in Figure 1 and is represented by the two extreme canonical forms **9a** and **9b** (Scheme I). Bond lengths and bond angles of the two independent molecules present in the crystal are listed in Tables I and II, respectively. The pyrrolidine ring approaches planarity and is also nearly coplanar with the indene ring system which, in turn, is nearly coplanar with the nitro group. In the molecule shown in Figure 1 (upper portion, unprimed notation), the nitro group is twisted about 8° out of the indene plane, but deviates only 4° from coplanarity in the molecule shown on the bottom (primed notation).

The bright red color of a solution of **9** points to significant electron delocalization from the pyrrolidine nitrogen

Table I. Bond Lengths (Å) in 9 with Standard Deviations in Parentheses

atoms	unprimed	primed
O1-N2	1.214 (3)	1.220 (3)
O2-N2	1.231 (5)	1.229 (4)
N1-C10	1.316 (3)	1.331 (3)
N1-C12	1.467 (5)	1.472 (3)
N1-C15	1.457 (4)	1.458 (4)
N2-C4	1.456 (5)	1.455 (3)
C1-C2	1.436 (5)	1.439 (4)
C1-C7a	1.450 (3)	1.458 (3)
C1-C10	1.375 (5)	1.366 (3)
C2-C3	1.356 (4)	1.355 (3)
C3-C3a	1.434 (4)	1.436 (4)
C3a-C4	1.394 (3)	1.390 (3)
C3a-C7a	1.424 (5)	1.424 (3)
C4-C5	1.390 (5)	1.386 (4)
C5-C6	1.378 (6)	1.384 (4)
C6-C7	1.384 (4)	1.380 (4)
C7-C7a	1.392 (5)	1.386 (4)
C12-C13	1.457 (5)	1.450 (5)
C13-C14	1.499 (6)	1.440 (5)
C14-C15	1.515 (4)	1.508 (4)

Table II. Bond Angles (Degrees) in 9 with Standard Deviations in Parentheses

atoms	unprimed	primed
C10-N1-C12	122.5 (3)	122.5 (2)
C10-N1-C15	126.1 (3)	125.5 (2)
C12-N1-C15	111.4 (2)	112.0 (2)
O1-N2-O2	121.6 (3)	121.6 (2)
O1-N2-C4	119.8 (3)	120.0 (3)
O2-N2-C4	118.6 (2)	118.3 (2)
C2-C1-C7a	105.2 (3)	105.0 (2)
C2-C1-C10	132.1 (2)	132.8 (2)
C7a-C1-C10	122.7 (3)	122.2 (2)
C1-C2-C3	110.6 (3)	110.7 (2)
C2-C3-C3a	108.9 (3)	109.1 (2)
C3-C3a-C4	135.5 (3)	135.5 (2)
C3-C3a-C7a	107.0 (2)	107.0 (2)
C4-C3a-C7a	117.4 (3)	117.4 (2)
N2-C4-C3a	120.4 (3)	121.4 (2)
N2-C4-C5	117.6 (3)	116.9 (2)
C3a-C4-C5	122.0 (3)	121.7 (2)
C4-C5-C6	119.1 (3)	119.6 (2)
C5-C6-C7	121.2 (3)	120.8 (3)
C6-C7-C7a	119.7 (3)	119.7 (2)
C1-C7a-C3a	108.2 (3)	108.2 (2)
C1-C7a-C7	131.3 (3)	131.0 (2)
C3-C7a-C7	120.5 (2)	120.8 (2)
N1-C10-C1	130.9 (3)	130.6 (3)
N1-C12-C13	105.2 (3)	103.8 (3)
C12-C13-C14	107.3 (3)	111.0 (3)
C13-C14-C15	106.0 (3)	107.0 (3)
N1-C15-C14	104.8 (3)	104.2 (2)

(1) Maehr, H.; Smallheer, J. *J. Org. Chem.* **1981**, *46*, 1752.

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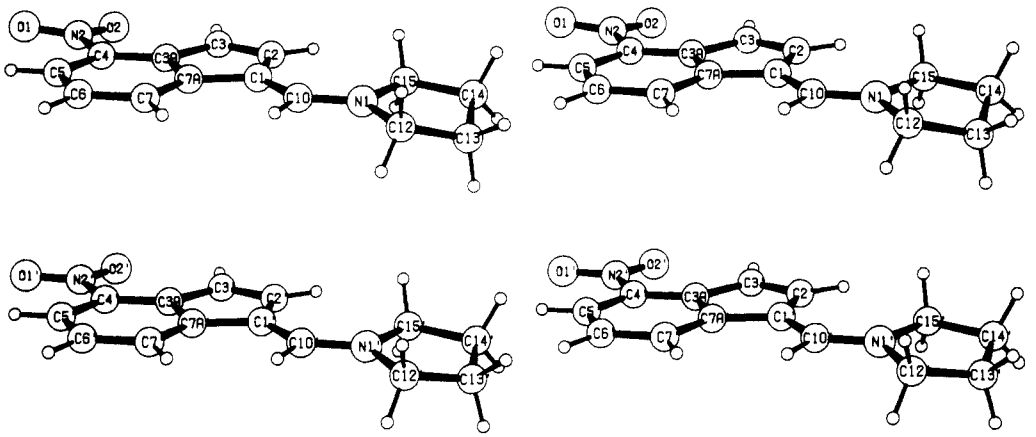
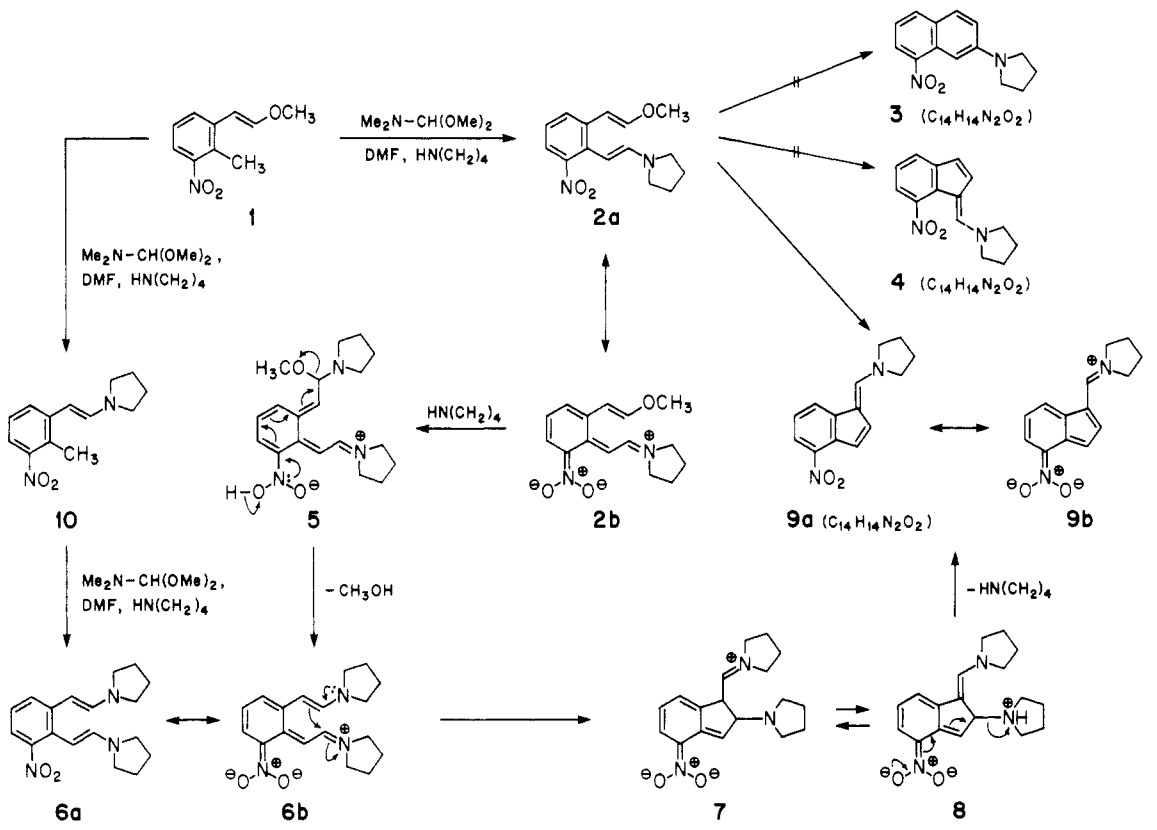


Figure 1. Stereoscopic drawing of the two independent molecules of **9** found in the crystal. The two molecules are shown in similar orientations for comparison. Their relative orientation in the crystal is different.

Scheme I



(N1) toward the nitro group. The resulting sp^2 hybridization of N1 is in agreement with the N1–C10 bond length and the bond angles around N1 observed in the crystal.

To explain the formation of **9**, we envision the intermediacy of 1,2-bis[2-(1-pyrrolidinyl)ethenyl]-3-nitrobenzene (**6a**). The nitro group imposes imminium ion character specifically upon the enamine side chain in the ortho position (**6b**), so that ring closure leads to the 1-[[(1,2-dihydro-4-*aci*-nitro-2-(1-pyrrolidinyl)-4*H*-inden-1-yl]methylene]pyrrolidinium hydroxide inner salt (**7**). Loss of pyrrolidine can readily occur from its tautomeric form **8**, generating the observed product **9**.

Two pathways for the generation of **6** can be considered. Initial enamine formation could convert **1** to **2**, which then could add pyrrolidine, presumably in the mesomeric form **2b**. The resulting pyrrolidine adduct **5** could give **6** upon elimination of methanol. Alternatively, an addition–elimination reaction of **1** effecting a methanol–pyrrolidine exchange could be the first step in this conversion. A precedent for a similar addition reaction with (*E*)-[2-(2-methyl-3-nitrophenyl)ethenyl]carbamate as the substrate is already known.[1] The resulting 1-[2-[(2-methyl-3-nitrophenyl)ethenyl]]pyrrolidine (**10**) could subsequently be converted to **6**.

Amine analogues of **9** are readily accessible by substituting other secondary amines for pyrrolidine in the condensation reaction of **1** with *N,N*-dimethylformamide dimethyl acetal. With morpholine, for example, 4-[(4-nitro-1*H*-inden-1-ylidene)methyl]morpholine was produced. Each amine requires different reaction temperatures and times for best yields, neither of which was optimized in this study. Without added amine the dimethylamine analogue of **9** is obtained as expected, although in low yield.

Experimental Section

UV (Cary 14) and ^1H NMR spectra (Varian XL-100) were recorded with the indicated solvents. Crystallographic data were

collected with a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ-2θ scans, pulse-height discrimination) and mass spectra with a Varian MAT CH5 instrument (70 eV, 250 °C ion source temperature). Melting points (Thermopan hot stage, Reichert) are uncorrected. TLC was performed on silica gel 60 F-254 plates (Merck) with dichloromethane as the mobile phase.

1-[(4-Nitro-1*H*-inden-1-ylidene)methyl]pyrrolidine (9). A solution of 1[1] (450 mg, 2.33 mmol) in *N,N*-dimethylformamide (3 mL), *N,N*-dimethylformamide dimethyl acetal (0.375 mL, 2.82 mmol), and pyrrolidine (0.225 mL, 2.70 mmol) was heated under a nitrogen blanket in an oil bath (125 °C) for 18 h. The mixture was concentrated in a rotary evaporator at a bath temperature of 90 °C under aspirator vacuum and the resulting residue chromatographed on a column of silica gel (LiChroprep Si 60; E. Merck) with dichloromethane as the mobile phase. The dark red solids which were obtained after solvent evaporation were recrystallized from dichloromethane/methanol to give dark magenta prisms: 240 mg (42.5%); mp 151-152 °C; TLC R_f 0.75; UV (EtOH) λ_{max} 209 nm (ϵ 34 200), 240 (sh, 9500), 276 (5900), 352 (31 500), 369 (sh, 21 700), 448 (9000); NMR ($CDCl_3$) δ 2.04 (s, CH_2CH_2), 3.63 (s, CH_2NCH_2), 7.12 (t, H6, $J_{5,6} = J_{6,7} = 8$ Hz), 7.21, 7.54 (AB, H2 and H3, $J_{2,3} = 5$ Hz),[2] 7.70 (s, CH), 7.79 (d, H7, $J_{6,7} = 8$ Hz), 8.06 (d, H5, $J_{5,6} = 8$ Hz); EI mass spectrum, m/z (relative intensity) 242 ($M^{+\cdot}$, 100), 225 (M - OH, 14), 195 (M - HO - NO, 45).

Anal. Calcd for $C_{14}H_{14}N_2O_2$ (mol wt 242.27): C, 69.41; H, 5.82; N, 11.56. Found: C, 69.63; H, 6.04; N, 11.44.

Crystallographic Analysis. The crystal was of space group $P\bar{1}$ with unit cell dimensions a = 9.262 (2) Å, b = 11.056 (3) Å, c = 12.980 (3) Å, α = 66.66 (2)°, β = 80.73 (2)°, and γ = 82.74 (2)°, and d_{calcd} = 1.339 g cm^{-3} for $Z = 4$.

A crystal of the approximate dimensions 0.10 × 0.12 × 0.30 mm served for the collection of data which were not corrected for absorption [μ(Cu Kα) = 7.5 cm^{-1}]. Of the 3222 independent reflections for $\theta < 57°$, 2513 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[3] and was refined by full-matrix least-squares methods. In the final refinement, anisotropic thermal parameters were used for the nonhydrogen atoms and isotropic temperature factors for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are R = 0.047 and R_w = 0.054 for the 2513 observed reflections. The final difference map has no peaks greater than ±0.2 e Å^{-3}.

1-[(4-Nitro-1*H*-inden-1-ylidene)methyl]morpholine. The procedure used for the synthesis of **9** was followed, but morpholine was substituted for pyrrolidine. TLC indicated only a little product after 18 h at 125 °C. Thus, the bath temperature was increased to 150 °C and the mixture again heated overnight. Although an appreciable amount of starting material still remained, additional product was formed. The mixture was worked up as described to furnish the title compound in 25% yield as dark magenta prisms: mp >204 °C dec; TLC R_f 0.35; NMR ($CDCl_3$) δ 3.76 and 3.90 (2 m, $N(CH_2CH_2)_2O$), 7.21 (t, H6, $J_{5,6} = J_{6,7} = 8$ Hz), 7.29, 7.63 (AB, H2 and H3, $J_{2,3} = 5.5$ Hz),[2] 7.46 (s, CH), 7.83 (d, H5, $J_{5,6} = 8$ Hz), 8.09 (d, H7, $J_{6,7} = 8$ Hz); EI mass spectrum, m/z (relative intensity) 258 ($M^{+\cdot}$, 100), 241 (M - OH, 14), 228 (M - NO, 6), 212 (M - NO_2, 16), 211 (M - OH - NO, 23).

***N,N*-Dimethyl(4-nitro-1*H*-inden-1-ylidene)methanamine.** The described procedure leading to **9** was repeated without pyrrolidine, yielding the title compound as dark magenta crystals: 5% yield; mp > 173 °C dec; TLC R_f 0.72; NMR ($CDCl_3$) δ 3.34 (s, $N(CH_3)_2$), 7.16 (t, H6, $J_{5,6} = J_{6,7} = 8$ Hz), 7.32, 7.58 (AB, H2 and H3, $J_{2,3} = 5.5$ Hz), 7.53 (s, CH), 7.82 (d, H7, $J_{6,7} = 8$ Hz), 8.07 (d, H5, $J_{5,6} = 8$ Hz); EI mass spectrum, m/z (relative intensity) 216 ($M^{+\cdot}$, 100), 199 (M - OH, 6), 186 (M - NO, 6), 170 (M - NO_2, 23), 169 (M - OH - NO, 19).

Registry No. 1, 79172-35-3; 9, 79172-36-4; pyrrolidine, 123-75-1; 1-[(4-nitro-1*H*-inden-1-ylidene)methyl]morpholine, 79172-37-5; morpholine, 110-91-8; *N,N*-dimethyl(4-nitro-1*H*-inden-1-ylidene)-methanamine, 79172-38-6.

(2) The assignment of H2 and H3 is unambiguously established by Eu(fod)$_3$-induced shifts.

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Supplementary Material Available: Tables containing atomic coordinates and anisotropic thermal parameters for **9** (3 pages). Ordering information is given on any current masthead page.

An Efficient Synthesis of 3,5-Dihydroxy-4-methylbenzoic Acid

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In connection with our synthesis and elucidation of molecular mechanism of serotonin neurotoxins[1] we needed access to 3,5-dihydroxy-4-methylbenzoic acid (1). This benzoic acid, in various modified forms, is a component of a number of natural products including long-chain phenols[2] (of cashew nutshell liquid), fungal[3,4] and lichen[5,6] metabolites (e.g., depsidones), and the antitumor antibiotic sibiromycin.[7] This compound has been used as a starting material, for example, in the synthesis of sclerotiorin group of fungal metabolites and their numerous degradation products,[8] long-chain resorcinols,[2] and in the total synthesis efforts toward sibiromycin.[9] However, this relatively simple benzoic acid is not available commercially and is extremely inaccessible by the procedures described in early literature.[10-12] More recently, a relatively simple five-step synthesis of 1 from 3,4,5-trimethoxybenzoic acid was described,[13] although the overall yield was low. We now report an operationally simple and high yielding three-step synthesis of 1 from readily available starting material, 3,5-dihydroxybenzoic acid (2).

Our approach involved selective protection of C-2 and C-6 of 2 followed by introduction of a methyl group equivalent on C-4 and finally removal of the protecting groups and generation of the methyl function both in one step.[14] Thus, addition of bromine (in slight excess of 2

(1) Borchardt, R. T.; Sinhababu, A. K. manuscripts in preparation; for example, synthesis of 6-methyl-5,7-dihydroxytryptamine from 1; for a review on serotonin neurotoxins, see: "Serotonin Neurotoxins"; Jacoby, J. H.; Lytle, L. D., Eds., *Ann. N.Y. Acad. Sci.* **1978**, *305*, 1-702.

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(8) Gray, R. W.; Whalley, W. B. *J. Chem. Soc. C* **1971**, 3575-3577 and references cited therein.

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(12) Wessely, F.; Swoboda, J.; Guth, V. *Monatsh. Chem.* **1964**, *95*, 649-670.

(13) Briggs, D. R.; Whalley, W. B. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1382-1384. A slightly modified version of this procedure appeared in literature (see ref 9) after we had completed the present work.

(14) Reference 9 described failure to introduce a methyl group on C-4 by way of iodination or formylation of 2 or its methyl ester, respectively.

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