Indoles from *o*-Nitrostyrenes. Synthesis and Reactions of 2-Indolyl 4-Piperidylmethyl Ketone[1]

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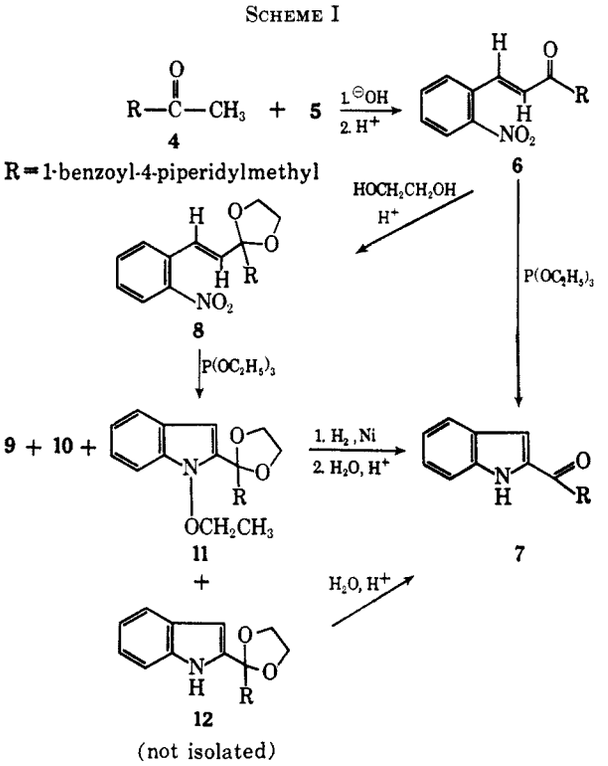
The synthesis of the title compound **1**, a 2-acylindole which is structurally related to the 2-acylindole alkaloids, *via* deoxygenation of the appropriate *o*-nitrostyrene, is reported. Subsequent chemical reactions of **1** include its conversion in three steps to 2-(2-quinuclidinyl)indole. The deoxygenations of two 2-[2-(*o*-nitrophenyl)-vinyl]-1,3-dioxolanes are described. The products of these reactions have been found to include products of fragmentation and rearrangement processes as well as the expected indole derivatives.

Methods for the synthesis of 2-acylindoles have not been widely investigated. Most of the methods[2] developed to date lack generality or are not adaptable to the synthesis of derivatives containing polyfunctional acyl substituents. Recently, considerable interest in 2-acylindoles has developed as the result of the isolation of a number of alkaloids containing this structural unit.[3] In addition, Buchi, Manning, and Monti[4] have demonstrated by their synthesis of voacamine that 2-acylindoles can serve as precursors for the synthesis of the "dimeric" indole alkaloids. We have found[5] that 2-acetylindole and 2-benzoylindole can be prepared by the deoxygenation of 4-(*o*-nitrophenyl)-3-buten-2-one and *o*-nitrochalcone, respectively. The yields in these reactions are rather low (16, 19%, respectively) but, since the appropriate *o*-nitrostyrenes are readily made by condensation of a methyl ketone with *o*-nitrobenzaldehyde, the deoxygenation reaction was felt to merit further attention. In particular, we wished to examine its application to the synthesis of structures related to the vobasine family of 2-acylindole alkaloids.

The methyl ketone required for the synthesis of **1**, 4-piperidyl-2-propanone (**3**), has been prepared from ethyl 4-piperidylacetate in low yield.[6] In this work it was prepared by catalytic hydrogenation of 4-pyridyl-2-propanone[7] (**2**) and isolated as the benzoyl derivative **4** (Scheme I). The ketone **4** reacted readily with *o*-nitrobenzaldehyde (**5**) to give a mixture which, when refluxed in benzene containing *p*-toluenesulfonic acid, gave the crude nitrostyrene **6**. The most significant support for the assigned structure comes from the nmr spectrum, which reveals two doublets (J = 16 cps) centered at δ 6.6 and 8.18 consistent with a *trans* disubstituted olefinic linkage and no signal which could be attributed to a methyl group. These features of the spectrum show that condensation has occurred predominantly at the methyl, rather than the methylene, group of **4**. When the nitrostyrene **6** was heated in excess triethyl phosphite and the crude product mixture separated by chromatography, the crystalline 2-acylindole **7** was isolated in 13% yield. Our earlier work had shown that *o*-nitrostyrenes with β-acyl substituents are cyclized to indoles in much lower yields than β-alkyl-*o*-nitrostyrenes.[5] In the hope of overcoming the deleterious effect of the β-acyl group, compound **6** was converted into its ethylene glycol ketal, which was deoxygenated without extensive purification. The crude product was separated by chromatography and gave indole (**9**, 3%), 1-ethoxyindole (**10**, 5%), the substituted 1-ethoxyindole **11** (4%), and, after hydrolysis, **7** (12% based on **4**). The origins of the by-products are discussed below.

SCHEME I



The structure assigned to **7** is supported by the subsequent chemical transformations which are summarized in Scheme II. Alkaline hydrolysis of the benzoyl group gave the desired 2-indolyl 4-piperidylmethyl ketone (**1**) which had an ultraviolet spectrum

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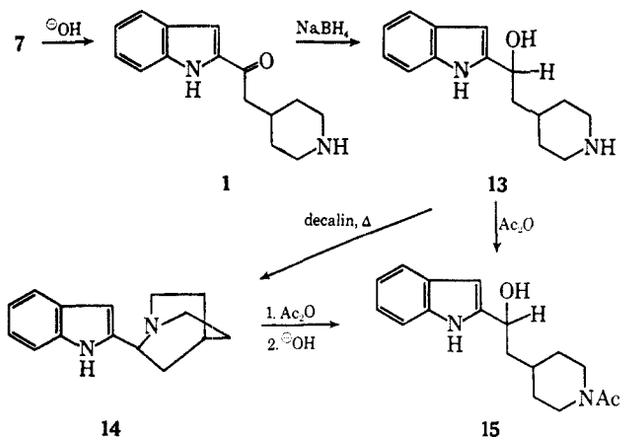
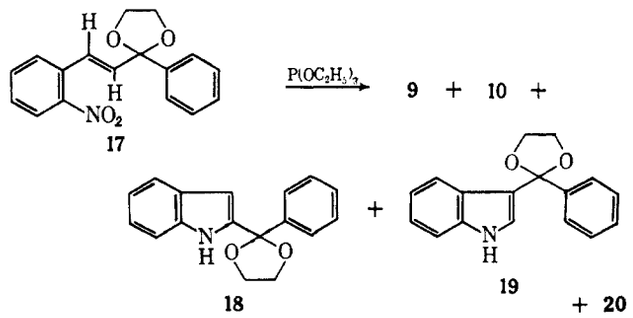
SCHEME II



SCHEME III



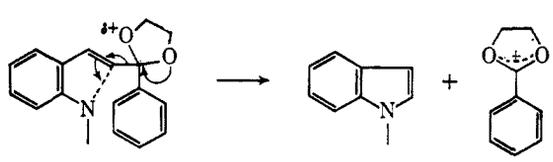
typical of 2-acylindoles.[8] Sodium borohydride gave a dihydro derivative having infrared, nmr, and ultraviolet spectral characteristics in accord with structure **13**.

Extended refluxing of a decalin solution of **13** gave 2-(2-quinuclidinyl)indole (**14**) in 38% yield. The formation of **14** from **13** in hot inert solvent was anticipated on the basis of the cyclization[4] of perivinol under similar conditions. The perivinol cyclization is, however, a transannular process, and it is therefore not surprising that both a higher temperature and longer reaction period were required for the cyclization of **13**. Ultraviolet, infrared, and nmr spectral data support the assigned structure. The nmr of **14** is strikingly different from that of the piperidines **1** and **13**. The signals for the aliphatic protons in the latter compounds are very diffuse multiplets, whereas the high-field multiplets in the spectrum of **14** show well-defined fine structure. The quinuclidine ring of **14** is readily reopened by allowing **14** to react with acetic anhydride under the conditions described by Foster, Harley-Mason, and Waterfield.[9] The amorphous diacetyl derivative obtained in this matter was saponified to give the hydroxyamide **15** which was identical with the N-acetyl derivative of **13**. Both the thermal cyclization of **13** and the ring fission of **14** are examples of the well-documented[4,9,10] facility with which C–O and C–N bonds attached to the 2 position of the indole ring can be broken. The reactions presumably proceed *via* an elimination–addition mechanism.

In order to test the feasibility of deoxygenating the β-acyl-*o*-nitrostyrene **6** *via* its ethylene glycol ketal, *o*-nitrochalcone (**16**) was converted into its ketal **17**, which was purified and characterized. When the mixture from the deoxygenation of **17** was subjected to elution chromatography, five products were isolated and identified (Scheme III).

The isolated yields for **9**, **10**, **18**, **19**, and **20** were 9%, trace, 21%, 7%, and 1%, respectively. Indole was identified by infrared and tlc comparison with authentic indole. 1-Ethoxyindole (**10**) was identified by comparison with the sample obtained in the deoxygenation of the ketal **8**. Spectral data and catalytic hydrogenation of **10** over Raney nickel to a mixture of indole and indoline support the assigned structure. Mild acid hydrolysis rapidly converted **18** into the known [2g,5] 2-benzoylindole. The structure of the rearranged indole **19** was deduced from its spectral properties and by hydrolytic conversion into the known[11] 3-benzoylindole **20**. Wolff–Kishner reduction of **20** gave 3-benzylindole.[12]

The formation of the various by-products found in this work is readily accommodated by the mechanism of the *o*-nitrostyrene deoxygenation reaction which we have put forward earlier.[5,13] The formation of the cleavage products indole and 1-ethoxyindole can be regarded as the result of fragmentation processes[14] initiated by the development of electron deficiency at C-3 of the developing indole ring. This fragmentation would be favored by the oxygen atoms of the dioxolane ring and by the phenyl group.



The formation of the rearranged product **19** can also be explained in terms of developing carbonium ion character at C-3. Earlier work in this laboratory[13] showed that one of the substituents on β,β-disubstituted *o*-nitrostyrenes was prone to migrate during deoxygenation, but the present case would be the first case of migration in a monosubstituted styrene. It is possible that **19** arises by recombination of the fragments generated in the cleavage reaction.

Experimental Section

(1-Benzoyl-4-piperidyl)-2-propanone (**4**).—4-Pyridyl-2-propanone (9.5 g, 70 mmoles) was hydrogenated over platinum oxide (0.3 g) in absolute ethanol (80 ml) containing concentrated hydrochloric acid (7 ml) until the theoretical amount of hydrogen had been absorbed (20 hr). The solution was filtered and evaporated to dryness. The crystalline residue was dissolved in a solution of potassium carbonate (45 g) in water (90 ml) and treated with benzoyl chloride (16 g) in chloroform (70 ml). The mixture was stirred vigorously at room temperature for 6 hr. The chloroform layer was washed with 5% aqueous sodium hydroxide, 3% sodium carbonate, and dilute hydrochloric acid and then dried and concentrated. Unreacted benzoyl chloride was removed by treating the residual oil in ethanol with 10% sodium hydroxide solution (8 ml). The product was then iso-

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lated by extracting with chloroform after dilution with water. Distillation gave **4** as a viscous oil (10.0 g, 41 mmoles, 58%): bp 160–170° (0.1 mm); $\nu_{C=O}$ 1720, 1640 cm^{-1} in CCl_4; nmr peaks (CCl_4) at δ 0.8–2.0 (6 H, m), 2.03 (2.5 H, s), 2.3 (1.5 H, d), 2.5–3.1 (2 H, m), 3.9–4.5 (2 H, m), and 7.32 (5 H, s). The oil crystallized to give a white solid, mp 63–65°, when stirred with ether.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.32; H, 7.93.

1-(1-Benzoyl-4-piperidyl)-4-(2-nitrophenyl)-3-buten-2-one (6).—1-Benzoyl-4-piperidyl-2-propanone (9.8 g, 40 mmoles) and *o*-nitrobenzaldehyde (15.1 g, 0.100 mole) were dissolved in ether (60 ml) at 0° and treated with 12 ml of a solution prepared from 3 ml of 10% sodium hydroxide and 25 ml of ethanol. The reaction solution was kept in an ice bath for 2 hr and then refrigerated overnight. At this point thin layer chromatography indicated that **4** had reacted completely. The reaction mixture was diluted with benzene and washed with dilute sodium bicarbonate and then dilute hydrochloric acid. The solution was dried and concentrated. Unreacted **5** was recovered by chromatographing the crude product on silicic acid. Benzene eluted **5** and 1:1 ether–benzene eluted **6** contaminated by two other more polar components. The crude **6** was dissolved in benzene (200 ml) containing 0.5 g of *p*-toluenesulfonic acid, and the solution was refluxed for 2 hr using a Dean–Stark water trap. The benzene solution was washed with dilute sodium bicarbonate and with dilute hydrochloric acid and then concentrated to give **6** as a very viscous maroon gum (14.3 g, 38 mmoles, 95%). An analytical sample was prepared by rechromatography: $\nu_{C=O}$ 1670, 1635 cm^{-1}; ν_{NO_2} 1530, 1340 cm^{-1}; $\nu_{CH=CH}$ 975 cm^{-1} in CCl_4; nmr peaks ($CDCl_3$) at δ 0.8–2.5 (6 H, m), 2.7 (2 H, d), 2.8–3.4 (2 H, m), 3.4–4.7 (very diffuse signal), 6.6 (1 H, d, J = 16 cps), 7.3–8.2 (10 H, multiplet containing the following prominent features: singlet at 7.42, multiplet at 7.7, 7.8–8.2, doublet at 8.05 (J = 16 cps)).

Anal. Calcd for $C_{22}H_{22}N_2O_4$: C, 69.82; H, 5.86. Found: C, 69.85; H, 6.01.

(1-Benzoyl-4-piperidyl)methyl 2-Indolyl Ketone (7). A. From 1-(1-Benzoyl-4-piperidyl)-4-(2-nitrophenyl)-3-buten-2-one (6).—The nitrostyrene **6** (10.6 g, 28 mmoles) was dissolved in freshly distilled triethyl phosphite (100 ml), and this solution was added dropwise during 1 hr to 175 ml of triethyl phosphite maintained in an oil bath at 125–130°. When the addition was complete, the solution temperature was gradually raised to 145° over 45 min. The solution was cooled and the unreacted triethyl phosphite (bp 42–50° at ~15 mm) was distilled from the mixture. Triethyl phosphate was distilled off by gentle warming at 0.1 mm. The residue was dissolved in hot benzene and washed with dilute sodium carbonate, dilute hydrochloric acid, and water. The benzene layer was dried over sodium sulfate and concentrated. The residue was chromatographed on Florisil. Compound **7** was eluted with 1:2 ether–benzene and crystallized from carbon tetrachloride to yield 1.30 g (3.8 mmoles, 13%): mp 154–156°; ν_{NH} 3240 cm^{-1}; $\nu_{C=O}$ 1650, 1610 cm^{-1} in KBr; nmr peaks ($CDCl_3$) at δ 0.8–2.5 (7 H, m), 2.6–3.3 (5 H, multiplets with a prominent doublet at 2.9), 3.5–5.0 (very diffuse signal), and 7.0–7.9 (11 H, multiplet with a strong singlet at 7.4).

Anal. Calcd for $C_{22}H_{22}N_2O_3$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.48; H, 6.36; N, 7.98.

B. From 2-(1-Benzoyl-4-piperidylmethyl)-2-[-(2-nitrophenyl)-vinyl]-1,3-dioxolane (8).—1-Benzoyl-4-piperidyl-2-propanone (23.5 g, 96 mmoles) was converted into **6** as described in part A. The crude nitrostyrene was dissolved in benzene (600 ml), and then ethylene glycol (25 ml) and *p*-toluenesulfonic acid (2.0 g) were added. The resulting solution was refluxed for 14 hr in an apparatus equipped with a Dean–Stark water trap. The solution was then cooled and washed with dilute aqueous sodium carbonate and dried over magnesium sulfate. Evaporation of the benzene gave the crude ketal **8** (35.4 g) as a maroon oil. The nmr spectrum showed well-defined peaks at δ 3.95 ($-O-CH_2CH_2-O$) and 5.97 (d, J = 16 cps) as well as the other expected features. The ketal was not further characterized but was directly deoxygenated by dissolving it in 300 ml of freshly distilled triethyl phosphite and adding this solution over a period of 2 hr to refluxing triethyl phosphite (300 ml). Reflux was maintained for 6 hr after completion of the addition. Triethyl phosphite and triethyl phosphate were removed by distillation, and the residue was dissolved in benzene and washed with water and dilute sodium carbonate solution. The benzene solution was concentrated and chromatographed on Florisil. Benzene eluted a mixture (1.7 g) of approximately equal amounts of indole and 1-ethoxyindole (nmr analysis) which was resolved by rechromatography on alumina into indole (0.35 g, 3.3 mmoles, 3%) and 1-ethoxyindole (0.70 g, 4.3 mmoles, 5%): ν_{NH} none; nmr peaks (CCl_4) at δ 1.3 (3 H, t), 4.2 (2 H, q), 6.25 (1 H, d, J = 4 cps), and 6.9–7.7 (5 H, m).

Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.56; H, 6.96; N, 8.76.

Indole was identified by the melting point and comparison of the infrared spectrum with that of an authentic sample.

Ether–benzene mixtures (10–40% ether) eluted first a two-component mixture of **11** and **12** and then **12**.[15] The mixture was resolved by rechromatography to give 2-(1-benzoyl-4-piperidylmethyl)-2-(1-ethoxy-2-indolyl)-1,3-dioxolane (**11**) as an oil which crystallized from benzene–hexane to give crystalline **11**, mp 138–142° (1.60 g, 3.7 mmoles, 4%). An analytical sample was prepared by recrystallization from benzene–hexane: mp 142–144°; ν_{NH} none; $\nu_{C=O}$ 1630 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 220 (log ϵ 4.61), 261 (3.95), 286 (3.82), 297 (3.62); nmr peaks ($CDCl_3$) at δ 1.4 (8 H, triplet superimposed on diffuse multiplet), 2.2 (2 H, d), 2.5–3.0 (2 H, m), 4.0 (4.5 H, s), 4.4 (2.5 H, q), 6.4 (1 H, s), 7.0–7.7 (9 H, singlet at 7.3 superimposed on a multiplet).

Anal. Calcd for $C_{26}H_{30}N_2O_4$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.63; H, 6.88; N, 6.61.

The fractions rich in **12** were combined (12.5 g) and heated for 15 min with a solution of 100 ml of methanol, 30 ml of water, and 2.0 ml of hydrochloric acid. Compound **7** precipitated from the cooled reaction mixture (4.2 g, 12 mmoles, 12%), mp 155–158°.

C. From 2-(1-Benzoyl-4-piperidylmethyl)-2-(1-ethoxy-2-indolyl)-1,3-dioxolane (11).—A solution of **11** (1.0 g, 2.3 mmoles) in absolute ethanol (100 ml) was hydrogenated at 40 psi over Raney nickel for 4 hr. The solution was filtered and evaporated to dryness. The residual foam was dissolved in aqueous methanol, and 2 drops of concentrated hydrochloric acid was added. The solution was heated on a steam bath for 5 min and then allowed to cool. Compound **7** (0.63 g, 1.8 mmoles, 79%), mp 157–158°, crystallized and was identified by comparison of its infrared and nmr spectrum with those of the samples prepared by methods A and B.

2-Indolyl 4-Piperidylmethyl Ketone (1).—(1-Benzoyl-4-piperidyl)methyl 2-indolyl ketone (4.1 g, 1.2 mmoles) was heated under reflux for 20 hr with a solution of potassium hydroxide (7.5 g) in methanol (120 ml) and water (30 ml). The cooled reaction mixture was diluted with water and extracted thoroughly with chloroform. The extract was dried over sodium sulfate and evaporated to dryness. The crystalline residue was crystallized from benzene–hexane giving **1** in two crops (2.3 g, 0.95 mmole, 78%), mp 167–169°. The analytical sample was prepared by recrystallization from benzene: mp 173–174°; ν_{NH} 3330, 3000–3500 (very broad); $\nu_{C=O}$ 1660 cm^{-1} in KBr; $\lambda_{max}^{95\%\ EtOH}$ 309 (log ϵ 4.35), 227 (4.96); nmr peaks ($CDCl_3$) at δ 0.5–3.5 (12 H, multiplets with a prominent doublet at 2.85) and 7.0–7.8 (6 H, multiplets, prominent peak at 7.22).

Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.10; H, 7.54; N, 11.74.

2-[1-Hydroxy-2-(4-piperidyl)ethyl]indole (13).—2-Indolyl 4-piperidylmethyl ketone (730 mg, 3.00 mmoles) was dissolved in methanol (60 ml) and during 3 hr a total of 600 mg of sodium borohydride was added in small portions. The solution was stirred at room temperature for 0.5 hr and then concentrated to about 10 ml on a rotary evaporator. The suspension was diluted with water and thoroughly extracted with chloroform. The extract was dried over sodium sulfate and evaporated to dryness. The residue was crystallized from methanol–water giving crystalline **13** (640 mg, 2.62 mmoles, 88%), mp 185°. Recrystallization gave the analytical sample: mp 184–185°; $\nu_{OH,NH}$ 3200 cm^{-1} in KBr; $\lambda_{max}^{95\%\ EtOH}$ 290 (log ϵ 3.76), 282 (3.87), 282 (3.87), 273 (3.87), 220 (4.57); nmr peaks (DMSO-d_6) at δ 0.8–2.0 (9 H, m), 2.1–3.3 (4.5 H, m), 4.0–4.5 (2 H, m), 4.8 (1 H, t), 6.25 (1 H, s), and 6.7–7.7 (4.5 H, m).

Anal. Calcd for $C_{15}H_{20}N_2O$: C, 73.73; H, 8.25; N, 11.47. Found: C, 73.58; H, 8.40; N, 11.53.

The N-acetyl derivative was prepared by stirring **13** in acetic anhydride containing sodium acetate for 5 hr. The product was isolated by chloroform extraction after hydrolysis of the acetic anhydride. The analytical sample was prepared by recrystalliza-

(15) The infrared spectrum indicated contamination with triethyl phosphate.

tion from benzene: mp 152–153°; $\nu_{NH,OH}$ 3400, 3250 cm^{-1}; $\nu_{C=O}$ 1600, 1620 cm^{-1} in KBr; nmr peaks (DMSO-d_6) at δ 0.8–1.8 (7 H, m), 2.0 (3 H, s), 2.2–4.6 (6 H, m), 4.8 (1 H, t), 6.3 (1 H, s), 6.8–7.4 (4 H, m), and 10.8 (1 H, s).

Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.55; H, 7.66; N, 9.47.

2-(2-Quinuclidinyl)indole (14).—2-[1-Hydroxy-2-(4-piperidyl)-ethyl]indole (1.50 g, 10.4 mmoles) was refluxed for 60 hr in freshly distilled decalin in a nitrogen atmosphere. An amorphous solid was removed from the reaction mixture by filtration. The filtrate was evaporated to dryness by careful vacuum distillation. The residue was crystallized from hexane–ether giving **14** (0.50 g, 4.0 mmoles, 38%), mp 150–156°. An analytical sample was prepared by vacuum sublimation (120°, 0.1 mm) followed by recrystallization from hexane: mp 155–156°; ν_{NH} 3450 cm^{-1} in $CHCl_3$; $\lambda_{max}^{95\% EtOH}$ 209 (log ϵ 4.44), 272 (3.94), 283 (3.91), 291 (3.79); nmr peaks ($CDCl_3$) at δ 1.0–2.2 (8 H, multiplet), 2.4–3.4 (4 H, multiplet), 4.2 (1 H, distorted triplet), 6.4 (1 H, singlet), 7.0–7.4 (3 H, multiplet), 7.4–7.8 (1 H, multiplet), 9.8 and (1 H, singlet, exchanged by D_2O).

Anal. Calcd for $C_{15}H_{16}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.67; H, 8.30; N, 12.04.

2-[1-Hydroxy-2-(1-acetyl-4-piperidyl)ethyl]indole (15).—2-(2-Quinuclidinyl)indole (0.100 g, 0.44 mmole) was dissolved in freshly distilled acetic anhydride (25 ml) and the solution was kept in a refrigerator for 48 hr and then at room temperature for 2 hr. The acetic anhydride was removed by vacuum distillation and the residue was treated with water giving a gum. The water layer was extracted with chloroform and the extract was added to the residual gum. The resulting solution was washed with dilute aqueous sodium bicarbonate, dried, and evaporated to an oil with infrared bands at $\nu_{C=O}$ 1720, 1620 cm^{-1} in $CHCl_3$. The oil was stirred at room temperature for 6 hr with a solution of sodium hydroxide (0.5 g) in 50% aqueous methanol (10 ml). The methanol was then removed using a rotary evaporator and water was added to the residue. This mixture was extracted with chloroform and the extract was dried and evaporated to give a gum. The gum partially dissolved in hot benzene and the resulting solution on cooling gave **15** (0.033 g, 26%), mp 148–152°. The identity of the product was established by tlc and infrared comparison with the sample prepared by acetylation of **13**.

2-[2-(*o*-Nitrophenyl)vinyl]-2-phenyl-1,3-dioxolane (17).—2-Nitrochalcone[16] (2.9 g, 11 mmoles) and ethylene glycol (2 ml) were dissolved in benzene (50 ml) and *p*-toluenesulfonic acid (0.05 g) was added. After 3 hr of reflux additional ethylene glycol (3 ml) and *p*-toluenesulfonic acid (0.05 g) were added. The solution was refluxed for 14 hr, cooled, washed with 10% sodium carbonate solution, dried over sodium sulfate, and concentrated. The residual green oil was washed through a short Florosil column with benzene, giving a clear yellow oil which crystallized readily (2.78 g, 9.3 mmoles, 84%). The analytical sample, mp 78–79°, was prepared by recrystallization from benzene–hexane: ν_{NO_2} 1510, 1340 cm^{-1} in KBr; nmr peaks ($CDCl_3$) at δ 4.0–4.2 (m, 4 H), 6.3 (1 H, d, J = 16 cps), and 7.1–8.1 (10 H, m).

Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.67; H, 5.08. Found: C, 68.71; H, 5.12.

Deoxygenation of 2-[2-(*o*-Nitrophenyl)vinyl]-2-phenyl-1,3-dioxolane.—The ketal **17** (8.30 g, 27.9 mmoles) was dissolved freshly distilled triethyl phosphite (100 ml) and the solution was added over 2 hr to refluxing triethyl phosphite (nitrogen atmosphere). Heating was continued for 4 hr after completion of the addition, and the reaction mixture was then cooled to room temperature. The triethyl phosphite and triethyl phosphate were removed in the usual manner, and the residue was dissolved in benzene and washed with sodium carbonate solution and water. Five pure products were obtained by chromatography of the crude product on Florisil.

Benzene eluted first a mixture of 1-ethoxyindole and indole, which was separated by rechromatography. The ethoxyindole was present in only trace amounts but was identified by tlc and infrared spectral comparison with a previously isolated sample. The indole (0.26 g, 2.4 mmoles, 9%), mp 50–52°, was identified by its infrared spectrum.

Benzene next eluted 2-(2-indolyl)-2-phenyl-1,3-dioxolane (1.55 g, 5.9 mmoles, 21%), mp 145–157°. An analytical sample was prepared by recrystallization from benzene–hexane: ν_{NH} 3340 cm^{-1} in KBr; $\lambda_{max}^{95\% EtOH}$ 291 (log ϵ 3.81), 283 (3.96), 275 (3.98); nmr peaks ($CDCl_3$) at δ 4.1 (singlet, 4 H), 6.4 (singlet, 1 H), and 7.0–7.8 (multiplet, 10 H).

Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.77; H, 5.75; N, 5.14.

Benzene next eluted 2-(3-indolyl)-2-phenyl-1,3-dioxolane (0.50 g, 1.9 mmoles, 7%), mp 174–178°. The analytical sample was prepared by recrystallization from benzene–hexane: mp 175–177°; ν_{NH} 3350 cm^{-1}; $\lambda_{max}^{95\% EtOH}$ 205 (log ϵ 4.85), 271 (4.09), 279 (4.08), 288 (3.98); nmr peaks at δ 4.0 (8 H, doublet), 6.6–7.8 (18 H, multiplet), and 11.0 (2 H, singlet); osmometric mol wt 280 (calcd 265).

Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.20; H, 5.45; N, 5.14.

Finally ether–benzene (1:9) eluted 3-indolyl phenyl ketone (0.10 g, 0.45 mmole, 15%), mp 239–242°. An analytical sample was prepared by recrystallization from ethanol: mp 242–243° (lit.[11,17] mp 241–243.5°, 245–247°); ν_{NH} 3150 cm^{-1}; $\nu_{C=O}$ 1590 cm^{-1} in KBr; $\lambda_{max}^{95\% EtOH}$ 248 (log ϵ 4.51), 268 (4.35), 315 (4.41); nmr peaks (DMSO-d_6) at δ 7.2–8.6 (20 H, m) and 12.2 (2 H, s).

Anal. Calcd for $C_{15}H_{11}NO$: C, 81.42; H, 5.01; N, 6.33. Found: C, 81.69; H, 4.90; N, 6.07.

The infrared spectrum of **20** was identical with that of authentic 3-benzoylindole.[11]

Wolff–Kischner Reduction of 3-Indolyl Phenyl Ketone.—A solution of the ketone **20** (0.100 g, 0.45 mmole), 0.2 ml of hydrazine hydrate, 0.2 g of potassium hydroxide, and 2.0 ml of diethylene glycol was refluxed for 2 hr (145°) and the distillate was collected until the solution temperature reached 190°. Reflux was then continued (200–210°) for 4 hr. The solution was kept overnight and diluted with water and extracted with ether. The extract was dried, filtered, and concentrated. Recrystallization of the residue from ethanol–water gave 3-benzylindole (0.055 g, 0.27 mmole, 60%), mp 108–109° (lit.[12] mp 106.5–107°).

Catalytic Hydrogenation of 1-Ethoxyindole.—A solution of 1-ethoxyindole (0.42 g) in ethanol (20 ml) was hydrogenated at 45 psi over Raney nickel for 4 hr. The filtered solution showed two spots on tlc, one of which was indole. The solvent was removed at reduced pressure, and the residue was dissolved in ether. One of the components was extracted into dilute hydrochloric acid. This component was isolated as an oil by making the acidic extract alkaline and extracting with ether. The nmr and infrared spectrum of the oil suggested that the basic product was indoline. The oil formed a picrate, mp 177–178° (indoline picrate lit.[18] mp 174°).

The neutral component was identified as indole by its infrared spectrum.

Registry No.—**1**, 15224-16-5; **4**, 15224-17-6; **6**, 15224-18-7; **7**, 15224-19-8; **8**, 15224-26-7; 1-ethoxyindole, 15224-27-8; **11**, 15224-20-1; **13**, 15224-21-2; **14**, 15224-31-4; **15**, 15224-32-5; **17**, 15224-22-3; **18**, 15224-23-4; **19**, 15224-24-5; **20**, 15224-25-6.

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