anhydride and phosphoric acid reagent. The same yield of **2c** was obtained.

Registry No.—1a oxime, 3349-64-2; 1b, 5462-81-7; 1c oxime, 42071-42-1; 2a, 42071-43-2; 2b, 42071-44-3; 2c, 42071-45-4; 3, 781-23-7; *N*-(4-phenanthryl)acetamide, 42071-47-6; γ-(*p*-chlorophenyl)butyric acid, 4619-18-5.

New Reactions of 3-Vinylindoles. II. Synthesis of 1,2-Dimethyl-3-(2-indolylcarbonyl)piperidine

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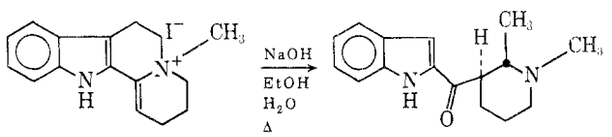
In 1968, we reported[2] that 5-methyl-2,3,4,6,7,12-hexahydroindolo[2,3-*a*]quinolizinium iodide (**1**) is converted on prolonged heating in aqueous ethanolic sodium hydroxide into 1,2-dimethyl-3-(2-indolylcarbonyl)piperidine (**2**), the product of a remarkable structural transformation.



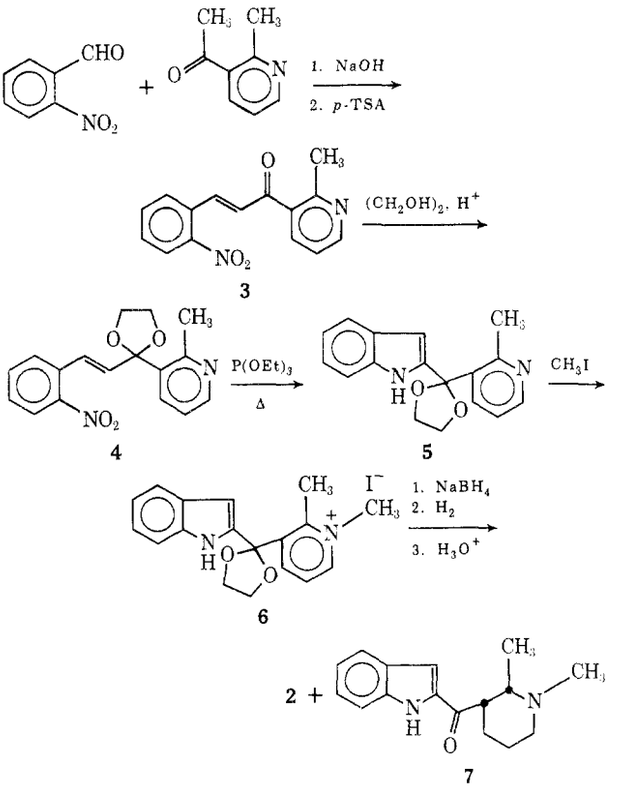
1 **2**

Our original assignment was based on degradative studies, model reactions, and mechanistic considerations.[2] The complexity of the **1** → **2** rearrangement and the potential importance of the observed nucleophilic reactions of the intermediate 3-vinylindoles demanded further investigation of this transformation.

We now wish to describe an independent synthesis of 2-acylindole **2** which confirms the originally proposed structure. Our synthesis of **2** is outlined in Scheme I. An aldol condensation[3] between 2-methyl-3-acetylpyridine[4] and 2-nitrobenzaldehyde gives the unsaturated ketone **3** (17%) after dehydration of the intermediate ketol. Ketalization with ethylene glycol affords the nitrostyrene ketal **4** (97%) which on heating with triethyl phosphite[3] gives indole ketal **5** (52%).[5] Treating **5** with methyl iodide yields pyridinium salt **6** (~100%), which on successive exposure[6] to sodium borohydride, hydrogen, and aqueous acid gives a mixture of 2-acylindoles **2** and **7** (36% from **6**).[7]

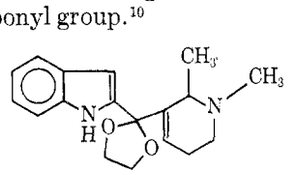
The mixture of 2-acylindoles could be separated by column chromatography into a major (92%) and a minor (8%) compound. The minor 2-acylindole is identical with the 2-acylindole obtained from **1**.

SCHEME I



3 **4** **5** **6** **7**

Furthermore, the major 2-acylindole is completely converted into the minor 2-acylindole under the basic reaction conditions. On this basis, we assign the major 2-acylindole to the presumed less stable cis configuration **7** and the minor 2-acylindole to the more stable trans configuration **2**. In our original work[2] we made no attempt to assign stereochemistry to the single 2-acylindole obtained from **1**. If the intermediate tetrahydropyridine from **6** is **8**, as seems likely,[8] then it is reasonable to suppose that catalytic hydrogenation will proceed on the side away from the allylic methyl group to give mainly the cis configuration[9] **7**, after regeneration of the carbonyl group.[10]



8

Experimental Section

Melting points were determined in open capillaries with a MelTemp Laboratory Devices apparatus and are uncorrected. Infrared spectra were measured with Perkin-Elmer 137 or 337 instruments. Nmr spectra were obtained with a Perkin-Elmer R-24 spectrometer. Woelm alumina was used for column chromatography and silica gel G (Merck) was used for thin layer chromatography (tlc). The tlc solvent system generally used was EtOAc–Et_3N (~95:5) and plates were developed with a spray of 3% $Ce(SO_4)_2$–10% H_2SO_4 followed by a brief heat treat-

(1) Recipient of a Public Health Service Research Career Development Award (1 KO4-GM 23756) from the National Institute of General Medical Sciences.

(2) L. J. Dolby and G. W. Gribble, *Tetrahedron*, **24**, 6377 (1968).

(3) R. J. Sundberg, H. F. Russell, W. V. Ligon, Jr., and L.-S. Lin, *J. Org. Chem.*, **37**, 719 (1972).

(4) A. Dornow and W. Schacht, *Chem. Ber.*, **82**, 117 (1949).

(5) Attempts to cyclize **3** with triethyl phosphite give either no reaction or, on prolonged heating, no recognizable products.

(6) Attempts to hydrogenate **6** directly to the piperidine ketal are unsatisfactory.

(7) The crude reaction product also appears to contain the alcohols[2] (14%) corresponding to **2** and **7**, probably resulting from partial deketalization during $NaBH_4$ reduction.

(8) R. E. Lyle and P. S. Anderson, *Advan. Heterocycl. Chem.*, **6**, 45 (1966).

(9) The catalytic hydrogenation of 1,2,3-trimethylpyridinium iodide gives 99% cis product: M. Tsuda and Y. Kawazoe, *Chem. Pharm. Bull.*, **18**, 2499 (1970).

(10) The small amount of **2** obtained probably does not arise by acid-catalyzed epimerization during the deketalization, because treating **7** under acidic conditions (aqueous ethanolic HCl, reflux, 2 hr) does not convert it to **2**.

ment at 110°. Organic solutions were dried with anhydrous granular K_2CO_3 and concentrated *in vacuo* with a Buchler rotary evaporator. Microanalyses were performed by PCR, Inc., Gainesville, Fla., and Micro-Tech Labs Inc., Skokie, Ill. Mass spectra were determined by Mr. J. W. Suggs and Mr. H. E. Ensley at Harvard University.

3-(2-Nitrophenyl)-1-(2-methyl-3-pyridyl)-2-propen-1-one (3).—To a solution of 12 g (0.079 mol) of 2-nitrobenzaldehyde (Aldrich), 3.0 g (0.075 mol) of NaOH, 30 ml of H_2O, 30 ml of EtOH, and 25 ml of Et_2O at 0–5° was added with stirring over 1 hr 10 g (0.074 mol) of 2-methyl-3-acetylpyridine.[4] A yellow precipitate formed during the addition, and near the end of the addition 25 ml of Et_2O was added. The mixture was stirred at 0–5° for 2 hr and then stored in a refrigerator at 5° for 24 hr. The solid was collected by filtration and dissolved in 300 ml of benzene. The benzene solution was washed with water and refluxed with 0.9 g of *p*-toluenesulfonic acid (Dean-Stark trap) for 4 hr. The solution was filtered, washed with aqueous $NaHCO_3$ and then H_2O, dried, and concentrated to give a dark solid. Chromatography over activity III basic alumina gave, with benzene elution, 3.4 g (17%) of **3** as a white solid, mp 133–135°. Recrystallization from MeOH–Et_2O gave colorless needles, mp 140–142°.

Pertinent spectral data for **3** are as follows: ir ($CHCl_3$) 2990, 1660, 1520, 1440, 1340, 1290, and 975 cm^{-1}; nmr ($CDCl_3$) δ 2.69 (s, 3), 7.7 (m, 8), and 8.6 ppm (m, 1).

Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.20; H, 4.60; N, 10.34.

2-[2-(2-Nitrophenyl)vinyl]-2-(2-methyl-3-pyridyl)-1,3-dioxolane (4).—A mixture of 6.85 g (0.0255 mol) of ketone **3**, 5.4 g (0.028 mol) of *p*-toluenesulfonic acid, 4.8 ml of ethylene glycol, and 120 ml of benzene was refluxed (Dean-Stark trap) with stirring. After 3 hr, more ethylene glycol (7 ml) and *p*-toluenesulfonic acid (1.7 g) were added and reflux was continued for 23 hr. The solution was allowed to cool and poured into water. The mixture was basified with 2 *N* NaOH and the benzene layer was separated. The aqueous layer was extracted with fresh benzene and the combined benzene extracts were washed with 1 *N* NaOH and then H_2O, dried, and concentrated to give 7.74 g (97%) of **4** as a yellow solid. Recrystallization from Et_2O–hexane gave large, colorless prisms, mp 91–93°.

Pertinent spectral data for **4** are as follows: ir ($CHCl_3$) 2980, 1520, 1440, 1340, 1050, and 969 cm^{-1}; nmr ($CDCl_3$) δ 2.70 (s, 3), 4.05 (m, 4), 6.67 (AB q, 2, J = 15 Hz), 7.4 (m, 4), 7.9 (m, 2), and 8.24 ppm (d of d, 1).

Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.48; H, 5.02; N, 8.89.

2-(2-Indolyl)-2-(2-methyl-3-pyridyl)-1,3-dioxolane (5).—To a refluxing, stirred solution of 30 ml of triethyl phosphite (distilled and passed through activity I basic alumina prior to use) under N_2 was added a solution of 1.57 g (0.00503 mol) of **4** in 40 ml of triethyl phosphite over a period of 3.5 hr. After addition, the mixture was refluxed for 5 hr and then allowed to stand overnight at 25°. The mixture was concentrated to near dryness (vacuum pump) and the residue was dissolved in 100 ml of Et_2O. The solution was stirred and saturated with HCl gas at 0° until the formation of insoluble material was judged complete. The ether was decanted off, and the residue was washed with ether and then treated with $CHCl_3$ and 2 *N* NaOH (ice cooling). Further extraction with $CHCl_3$ gave, after washing, drying, and concentration, a dark oil. Chromatography over activity III basic alumina gave, with benzene elution, 0.73 g (52%) of **5** as oily crystals. Recrystallization from benzene and then $CHCl_3$–hexane gave pure **5** as colorless, fluffy needles, mp 182–183°. A larger run with 7.75 g of **4** gave **5** in 38% yield.

Pertinent spectral data for **5** are as follows: ir ($CHCl_3$) 3495, 2980, 1290, 1170, 1080, and 1430 cm^{-1}; nmr (CDC_3) δ 2.55 (s, 3) 3.85 (m, 4), 6.10 (broad s, 1), 7.1 (m, 5), 7.86 (d of d, 1), and 8.27 ppm (d of d, 1).

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 73.01; H, 5.69; N, 10.11.

1,2-Dimethyl-3-[2-(2-indolyl)-1,3-dioxolan-2-yl]pyridinium Iodide (6).—A mixture of 1.37 g (0.00489 mol) of **5** and 10 ml of methyl iodide in 30 ml of benzene was stirred at 25° for 2 hr and then at 50° for 2 hr. After 3 days at 25°, the precipitate was collected and washed with benzene and then Et_2O to give 2.1 g (~100%) of **6** as a light yellow powder. Recrystallization from MeOH–Et_2O gave pure **6** as tiny, colorless needles, mp 214–216°.

Anal. Calcd for $C_{18}H_{19}N_2O_2I$: C, 51.20; H, 4.54; N, 6.63. Found: C, 51.02; H, 4.56; N, 6.48.

***cis*- and *trans*-1,2-Dimethyl-3-(2-indolylcarbonyl)piperidine (2 and 7).**—To a stirred solution of 0.5 g of $NaBH_4$ in 30 ml of 70% aqueous EtOH at 0–5° was added 0.56 g (0.0013 mol) of **6** over 1 min. After addition, more EtOH (5 ml) was added and the mixture was stirred at 0–5° for 1 hr and then at 25°. An additional 0.5 g of $NaBH_4$ and 15 ml of 50% EtOH were added after 4 hr at 25°. After stirring for 22 hr, the mixture was extracted with CH_2Cl_2. The extract was washed, dried, and concentrated to give 0.42 g of a yellow foam. The yellow foam was hydrogenated in 30 ml of EtOH with 0.15 g of 10% Pd/C at 25° (1 atm). Filtration and concentration gave 0.42 g of an amber oil. The amber oil was refluxed for 1 hr with 20 ml of 80% aqueous ethanol and 10 drops of concentrated HCl. The mixture was basified with 2 *N* NaOH, concentrated to near dryness, and extracted with CH_2Cl_2. The extract was washed, dried, and concentrated to give 0.30 g (88% crude from **6**) of a yellow-brown solid. Chromatography over activity III basic alumina gave, with benzene elution, 0.009 g (3%) of **2** as a yellow solid and 0.114 g (33%) of **7** as a white solid. Further elution with benzene and benzene–$CHCl_3$ gave 0.046 g of an amber gum which appeared to be a mixture of the alcohols derived from **2** and **7**.

Recrystallization from MeOH–Et_2O–hexane gave pure **2** as tiny prisms, mp 169–170° (lit.[2] mp 167–168°). This synthetic material was completely identical (tlc, infrared, mass spectrum) with a freshly recrystallized sample (mp 172–174°) of **2** as obtained[2] from **1**.

Recrystallization from MeOH–Et_2O–hexane gave pure **7** as tiny cubes of fluffy needles, mp 184–185°. This material was distinguishable from **2** in the fingerprint region of the infrared spectrum, and **7** exhibited a higher R_f (0.73) and a lighter brown-colored spot on tlc than did **2** (R_f 0.69). **7** showed nearly the same mass spectrum as **2**.

Pertinent spectral data for **7** are as follows: ir ($CHCl_3$) 3520, 3370, 2970, 1650, 1520, 1340, 1130, and 1110 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, 3, J = 6 Hz), 2.38 (s, 3), 7.3 ppm (m, 5). A mixture nmr spectrum of **2** and **7** clearly showed separate methyl resonances for the two epimers.

Anal. (**7**) Calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.93; H, 7.92; N, 10.97.

Conversion of 7 into 2.—A mixture of 15 mg of a mixture of **2** and **7** (~50:50 by tlc) was refluxed under N_2 with 1.2 ml of 10% aqueous NaOH and 1.5 ml of 50% aqueous EtOH for 5 hr. Extraction with CH_2Cl_2 gave, after the usual work-up, 15 mg of a yellow solid showing only **2** by tlc, mp 167–169°. Recrystallization from MeOH–Et_2O–hexane gave pure **2** (tlc, infrared). A similar reaction with 44 mg of pure **7** gave 37 mg (84%) of **2**. The epimerization appears to be complete in 30 min by tlc and no **7** can be detected by tlc or nmr.

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Registry No.—**2**, 42031-20-9; **3**, 42031-21-0; **4**, 42031-22-1; **5**, 42031-23-2; **6**, 42031-24-3; **7**, 42031-25-4; *o*-nitrobenzaldehyde, 552-89-6; 2-methyl-3-acetylpyridine, 1721-12-6.

Secondary Orbital Interactions Determining Regioselectivity in the Diels–Alder Reaction

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Recently, there has been considerable interest in the prediction of the preferred regioisomers of the Diels–