of white crystals: mp 80–84°; $[\alpha]^{25}D + 1.4 \pm 0.3°$ (*c* 1, $CHCl_3$); uv max (95% EtOH) 282 mμ (ε 22,000); ir (KBr) 5.88 (ester > C=O), 6.09 (amide > C=O), and 6.18 μ (>C=C<); nmr ($CDCl_3$) δ 1.62, 1.70 [s each, 3 each, $C(CH_3)_2$], 3.58 (s, 3, OCH_3), 3.33–4.0 (m, 4, CH_2N and aryl-CH_2), 5.15 [t, 1, J = 7 Hz, $CH=C(CH_3)_2$], 5.50–6.00 (m, 1, C=CNH), and 6.83–7.66 ppm (m, 7, aryl H, =CHN, CONH). *Anal.* ($C_{17}H_{22}N_2O_3$) C, H, N.

Hydrolysis of 28 to Methyl Benzylpenaldate (29) and 3-Methyl-2-butenylamine (30).—To 0.5 g (0.00165 mol) of **28** in 25 ml of warm MeOH was added 0.33 g (0.00165 mol) of 2,4-dinitrophenylhydrazine in 60 ml of warm MeOH and 4 drops of concentrated HCl. The solution was left at 25° overnight. The mixture was cooled to 0°, filtered, and washed with cold MeOH to give 0.5 g (73%) of yellow, matted needles, mp 180–181°; mixture melting point with authentic 2,4-dinitrophenylhydrazone of methyl benzylpenaldate[14] showed no depression.

The MeOH filtrate was evaporated to dryness and the residue partitioned in $CHCl_3$–H_2O. The aqueous phase was separated, washed ($CHCl_3$), and then evaporated *in vacuo* to give a yellowish solid. It was recrystallized from EtOH–Et_2O to afford 0.15 g of shiny leaflets, mp 194.5–198° dec, identical with authentic **30** (ir spectrum, mixture melting point).[15]

***p*-Methoxybenzyl 4,4-Dimethyl-α-(phenylacetamido)-3-thia-1-azabicyclo[3.1.0]hexane-2-acetate (36).**—Compound **5** (1 g, 0.0021 mol) was heated with 0.34 ml (0.0023 mol) of Et_3N and 4 ml of *p*-anisyl alcohol on a steam bath for 3 hr. The yellow solution was diluted ($CHCl_3$) and washed (H_2O, 5% H_3PO_4, H_2O until neutral pH, saturated brine). The dried (Na_2SO_4) filtrate was evaporated and some of the excess *p*-anisyl alcohol distilled at 65–80° and 0.07 mm foil bath temperature 95°). The residual viscous oil was purified by preparative tlc (silica plates, benzene–Et_2O 1:1). Isolation of the band next to the origin afforded 650 mg of a colorless gum: ir ($CHCl_3$) 5.73 (ester > C=O) and 5.97 μ (amide > C=O); nmr ($CDCl_3$) δ 1.4, 1.5 [s each, 3 each, $C(CH_3)_2$], 1.57–1.83 (m, 2, NCH_2), 2.13–2.38 (m, 1, CH_2CHCl), 3.58 (s, 2, aryl-CH_2), 3.73 (s, 3, OCH_3), 4.58–4.75 (m, 2, CHCH), 5.07 (s, 2, aryl-CH_2O), 6.2–6.6 (broad, 1, NH), and 6.7–7.4 ppm (m, 9, aryl H).

4,4-Dimethyl-α-(phenylacetamido)-3-thia-1-azabicyclo[3.1.0]-hexane-2-acetic Acid (37).—A sample of **36** was treated in the cold with TFAA to give a deep red solution. After 5 min the excess acid was evaporated *in vacuo* at 25°. The residual red mush was dissolved in $CHCl_3$ and washed in the cold with saturated $NaHCO_3$. The basic extracts were combined and acidified in the cold with 10% aqueous H_3PO_4 to pH 3. The gum was extracted with cold $CHCl_3$ and the combined organic fractions washed (H_2O, brine). The dried (Na_2SO_4) filtrate was evaporated *in vacuo* at 25° to afford a colorless, amorphous solid: ir ($CHCl_3$) 3.8–4.1 (broad OH), 5.79 (acid > C=O), and 5.98 μ (amide > C=O); nmr ($CDCl_3$) δ 1.4, 1.5 [s each, 3 each, $C(CH_3)_2$], 1.67–2.0 (m, 2, NCH_2), 2.33–2.67 (m, 1, CH_2CHCl), 3.6 (s, 2, aryl-CH_2), 4.42–5.08 (m, 2, CHCH), 7.0–7.42 (m, 6, aryl H, NH), and 10.6 ppm (s, 1, $COOH$). The carboxylic acid was unstable at room temperature in the amorphous state or in chloroform solution. The change was apparent from the nmr spectra which became diffuse and uninterpretable.

2-Tetrahydropyridylindoles as Histamine and Serotonin Antagonists

ROBERT N. SCHUT, FREDERICK E. WARD, O. J. LORENZETTI,

Therapeutics Research Division, Miles Laboratories, Inc., Elkhart, Indiana

AND ENRIQUE HONG

Instituto Miles de Terapeutica Experimental, Mexico 22, D.F., Mexico

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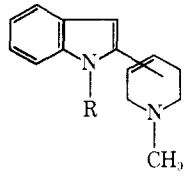
A series of 2-(1-methyl-1,2,5,6-tetrahydro-3(and 4)-pyridyl)indoles was synthesized by borohydride reduction of the corresponding pyridinium compounds. The compounds were tested for antihistaminic and antiserotonin activity.

During an investigation of 2-tetrahydropyridylindoles **1** as intermediates in the synthesis of certain model indole alkaloid systems, it was found that a few of these compounds exhibited antihistaminic and antiserotonon activity. We noticed that those compounds with an indole-*N*-benzyl moiety bore structural resemblance to clemizole (**2**);[1] structural features of the serotonin antagonist benanserin (**3**)[2] are also present.

This paper describes the synthesis and pharmacological action of a small series of such compounds (Table I). Our objective was to obtain a compound which possessed both good antihistaminic and antiserotonin activity.



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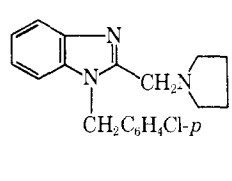

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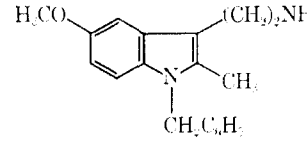

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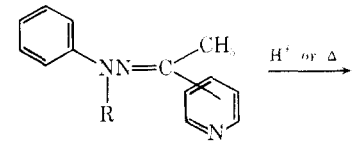
The general synthetic method involves Fischer cyclization of the appropriate hydrazone **4** followed by quaternization and BH_4^- reduction of the pyridylindoles **5**. When R was benzyl or Me thermal indolization was preferred over the usual acid-catalyzed procedure.



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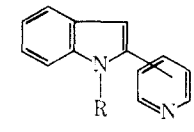

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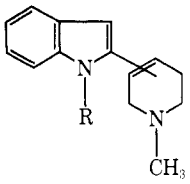
(1) (a) D. Jerchel, H. Fischer, and M. Kracht, *Justus Liebigs Ann. Chem.*, **575**, 173 (1952); (b) H. Muckter, *et al.*, *Arzneim. Forsch.*, **4**, 487 (1954).

(2) (a) E. Shaw, *J. Amer. Chem. Soc.*, **77**, 4319 (1955); (b) D. W. Woolley and E. Shaw, U.S. Patent 2,890,223 (1959).

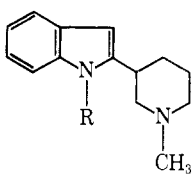
TABLE I



No.	R	Position of substitution	Mp, °C	Formula	Anal
10[a]	H	4	178–179	$C_{14}H_{16}N_2$	C, H, N
			164–166	$C_{14}H_{16}N_2 \cdot (CHCO_2H)_2$	N(total), N(basic)[a]
11	H	3	154–155	$C_{14}H_{16}N_2$	C,[b] H, N
			185–186	$C_{14}H_{16}N_2 \cdot (CHCO_2H)_2$	N(total), N(basic)
12	CH_3	3	240–241	$C_{15}H_{18}N_2 \cdot HCl$	HCl,[c] N
13	$CH_2C_6H_5$	3	106–107	$C_{21}H_{22}N_2$	C, H, N
			161–163	$C_{21}H_{22}N_2 \cdot (CHCO_2H)_2$	N(basic, total)
14	COC_6H_5	3	242–244	$C_{21}H_{20}N_2O \cdot HCl$	HCl, N
15	4-$ClC_6H_4CH_2$	3	172–173	$C_{21}H_{24}ClN_2 \cdot (CHCO_2H)_2$	C, H, N(basic, total)
16	$CH_2C_6H_5$	4	147–148	$C_{21}H_{22}N_2 \cdot (CHCO_2H)_2$	C, H, N(basic, total)
17	$CH_2C_6H_5$	2[d]	192–193	$C_{21}H_{22}N_2 \cdot (CHCO_2H)_2$	C, H, N(basic, total)

[a] Nonaqueous titration in HOAc using standard $HClO_4$ as titrant. [b] Calcd: C, 79.25; found, 78.66. [c] Aqueous titration. [d] 1,2,3,6-Tetrahydro isomer.

The BH_4^- reduction of pyridinium compounds has been extensively investigated by Lyle and coworkers.[3] In the case of the 3- and 4-(2-indolyl)pyridinium salts the reduction proceeded as expected to give tetrahydro derivatives wherein the double bond was conjugated with the indole ring.[4] Conclusive evidence of structure was obtained from nmr and uv spectral data and also by catalytic hydrogenation (1 mol equiv uptake) of **11** and **13** to the 2-(1-methyl-3-piperidyl)-indoles (**6** and **7**).



6, R = H
7, R = $CH_2C_6H_5$

Borohydride reduction of 1-benzyl-2-(1-methyl-2-pyridinium)indole iodide gave as the only isolable product the 1,2,3,6-tetrahydro derivative **17**. The assignment of structure was based on the fact that the 2-proton signal of the tetrahydropyridine ring was split into a quartet by the 2 nonequivalent hydrogens at position 3.[5]

For further structure–activity relationships, **13** was demethylated by the von Braun CNBr method to give **8**. To determine the effect of shifting the tetrahydropyridyl ring to the 3 position of indole, **9** was prepared by Fischer cyclization of the 1-benzyl-1-phenylhydrazone of 3-acetonylpyridine and subsequent BH_4^- reduction of the methiodide.

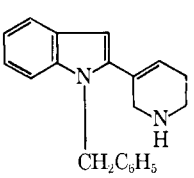
(3) R. E. Lyle and P. S. Anderson, *Advan. Heterocycl. Chem.* **6**, 55 (1966).

(4) While the pharmacology of our compounds was being evaluated, an article by D. Beck and K. Schenker, [*Helv. Chim. Acta*, **51**, 260 (1968)], disclosed the synthesis of **10** by the same method.

(5) This is the argument used by P. S. Anderson and R. E. Lyle [*Tetrahedron Lett.*, 153 (1964)] for the assignment of structure to the product obtained from the BH_4^- reduction of 1,4-dimethyl-2-phenylpyridinium iodide.

TABLE II
ANTIHISTAMINIC AND ANTISEROTONIN ACTION OF 2-TETRAHYDROPYRIDYLINDOLES

	Histamine antagonism		Serotonin antagonism	
Compd	Guinea pig ileum ED_{50} (μg/ml)	Konzett–Rössler preparation ED_{50} (mg/kg)	Rat uterine segment EC_{50} (μg/ml)	Konzett–Rössler preparation ED_{50} (mg/kg)
7	0.46	0.295	0.126	>1.0
8	0.05	>1.0	0.114	>1.0
9	1.99	>1.0	0.118	>1.0
10	0.03	>1.0	0.140	0.355
11	0.21	>1.0	0.017	>1.0
12	0.13	>1.0	1.95	>1.0
13	0.0085	0.1	0.0057	0.191
14	0.24	>1.0	0.290	>1.0
15	0.0457	0.275	0.162	>1.0
16	0.0447	0.316	0.022	0.302
17	0.219	>1.0	0.235	0.479



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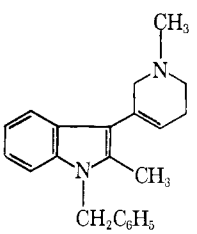

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Pharmacology.—All compounds of this series antagonized responses to histamine in the guinea pig ileum, and to serotonin in the rat uterine segment. However, when 2-tetrahydropyridylindoles were tested in an *in vivo* preparation (Konzett–Rössler[6]), only a few antagonized significantly the bronchoconstrictor action of histamine (**7**, **13**, **15**, and **16** and of serotonin (**10**, **13**, **16**, and **17**). Only **13** and **16** produced nearly equipotent antihistaminic and antiserotonon actions, **13** being the most potent (Table II). Therefore, **13** was selected for further pharmacological studies in

(6) H. Konzett and R. Rössler, *Arch. Exp. Pathol. Pharmacol.*, **195**, 71 (1940).

Table III
Comparative Actions of **13**, Diphenhydramine, and Cyproheptadine. Values Correspond to Either LD_{50}, EC_{50}, or ED_{50}

Parameter	**13**	Diphenhydramine	Cyproheptadine
LD_0 (mice, mg/kg, i.p.)	521.0	60.7	56.2
Histamine antagonism			
Ileum segment (guinea pig, μg/ml)	0.0085	0.057	0.00135
Tracheal chain (guinea pig, μg/ml)	0.052	0.098	0.01
Konzett–Rössler preparation (guinea pig, mg/kg, i.v.)	0.1	0.052	0.0126
Histamine aerosol (guinea pig, mg/kg, p.o.)	20.7	26.5	0.67
Serotonin antagonism			
Konzett–Rössler preparation (guinea pig, mg/kg, i.v.)	0.191		0.005
Serotonin aerosol (guinea pig, mg/kg, p.o.)	1.85		0.18
CNS actions			
Rotarod test (coordinated motor activity) (rat, mg/kg, i.p.)	130.0	29.0	41.4
Spontaneous motor activity (rat, mg/kg, i.p.)	60.9	53.9	40.2
CMA/SMA	2.14	0.54	1.03
Antiemetic activity (dog, mg/kg, p.o.)	37.2	56.2	
Anticholinergic action			
Ileum segment (guinea pig, μg/ml)	2.82	0.645	0.025
Vagal stimulation blockade (cat, mg/kg, i.v.)	13.8	3.64	0.113

which diphenhydramine and cyproheptadine were included as reference compounds (Table III).

Antihistaminic activity was assessed in the guinea pig ileum, the guinea pig tracheal chain,[7] the Konzett-Rössler preparation, and in the guinea pig bronchospasm induced by histamine aerosol. Antiserotonin activity was evaluated in the Konzett-Rössler preparation and in the guinea pig bronchospasm induced by serotonin aerosol.[8] CNS depression was studied in rats by the rotarod test[9] and by means of an activity cage. Antiemetic activity was evaluated by the protection to emesis induced by apomorphine in dogs.[10] Anticholinergic activity was studied by guinea pig ileum responses to acetylcholine and blockade of heart rate responses of cats to vagal stimulation. The LD_{50} was calculated by the method of Litchfield and Wilcoxon,[11] and the EC_{50} and ED_{50} were determined both by the same method and graphically.

Compound **13** had an antihistaminic potency of the order of diphenhydramine; however, it was clearly less potent than cyproheptadine in antagonizing the actions of both histamine and serotonin. On the other hand, **13** was less toxic and produced less depression of coordinated motor activity and less anticholinergic effects than the two reference compounds. These results suggest that **13** might produce less side effects than diphenhydramine and cyproheptadine.

Experimental Section[12]

2-(1-Methyl-1,2,5,6-tetrahydro-3-pyridyl)indole (11).—A 33.6-g sample of 3-(2-indolyl)-1-methylpyridinium iodide[13] was suspended in 500 ml of 50% aqueous EtOH and then 8 g of $NaBH_4$ was slowly added. The solid gradually dissolved during the addition. When the vigorous reaction had subsided, the soln was heated under reflux for 1 hr. EtOH was distilled *in vacuo* and the residue stirred with NaOH soln. Extraction with $CHCl_3$, drying the extract, and concentration *in vacuo* gave 17.3 g (82%) of material, mp 145–147°. Crystallization from C_6H_6–Et_2O followed by recrystallization (Et_2O) gave the analytical sample: uv max (MeOH) 218 mμ (ε 20,100), 301 (20,700); nmr ($CDCl_3$, 10%) τ 6.63 (d, 2, $NCH_2C{=}CH$), 3.93 (m, 1, olefinic), 3.58 (d, 1, $J_{1,3}$ = 4.0 cps, indole-C$_3$**H**).

Maleate.—A soln of 5.00 g of the base in 200 ml of EtOAc containing a little MeOH was treated with 2.5 g of maleic acid in 30 ml of MeOH–EtOAc; the salt was collected and recrystallized from MeOH–EtOAc; yield 4.83 g.

1-Benzyl-2-(3-pyridyl)indole.—A soln of 7.0 g (0.06 mol) of 3-acetylpyridine, 11.5 g (0.06 mol) of 1-benzyl-1-phenylhydrazine, and 0.2 g of *p*-TsOH in 100 ml of dry toluene was heated under reflux for 16 hr while the H_2O liberated was collected in a Dean–Stark trap. PhMe was distilled *in vacuo* and the residue (17 g) was dissolved in 100 ml of $HOCH_2CH_2OH$. The soln was heated under reflux for 20 hr, then poured into 500 ml of H_2O. The organic material was extracted into $CHCl_3$ and the extract was dried and concentrated *in vacuo*. The resulting oil was dissolved in boiling Et_2O and the solution clarified and cooled; yield 5.0 g, mp 120–121°. *Anal.* ($C_{20}H_{16}N_2$) N (basic).

3-(1-Benzyl-2-indolyl)-1-methylpyridinium Iodide.—To 6 g of 1-benzyl-2-(3-pyridyl)indole in 100 ml of Me_2CO was added 8 ml of MeI. The mixture was heated under reflux for 30 min. The salt was filtered and washed with Me_2CO to give 9.4 g of product, mp 146–147°. *Anal.* ($C_{21}H_{19}IN_2$) N.

3-[2-(1-Benzyl)indolyl]-1-methyl-1,2,5,6-tetrahydropyridine.—To 9.4 g of 3-(1-benzyl-2-indolyl)-1-methylpyridinium iodide in 200 ml of MeOH was slowly added 6 g of $NaBH_4$. The mixture was heated under reflux for 2 hr. After removal of solvent the residue was made basic with 20% NaOH and extracted with $CHCl_3$. Concentration of solvent gave 6.5 g of syrupy material which was chromatographed over 150 g of Florisil. Elution with C_6H_6–Et_2O (1:1) gave 3 g of solid, mp 100–101°. The base was dissolved in 2-PrOH, excess maleic acid was added and the salt which formed was recrystallized twice from *i*-PrOH; yield 2.6 g.

(7) R. W. Foster, *J. Pharm. Pharmacol.*, **12**, 189 (1960).
(8) H. Herxheimer, *Arch. Int. Pharmacodyn.*, **106**, 371 (1956).
(9) N. W. Dunham and T. S. Miya, *J. Amer. Pharm. Assoc. Sci. Ed.*, **46**, 208 (1957).
(10) C. D. Schmidt, E. Sata, K. R. Brizzee, and H. L. Borison, *Proc. Soc. Exp. Biol. Med.*, **82**, 441 (1953).
(11) J. T. Litchfield and F. Wilcoxon, *J. Pharmacol. Exp. Ther.*, **96**, 99–113 (1949).
(12) Melting points were taken on a Büchi melting point determination apparatus and are uncorrected. Uv spectra were recorded on a Perkin-Elmer Model 202 or Beckmann DB-G spectrophotometer. Nmr spectra were obtained with a Varian Model A-60 spectrometer (resonance peaks in τ units, relative to Me_4Si at τ 10). Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values.
(13) A. P. Gray and W. L. Archer, *J. Amer. Chem. Soc.*, **79**, 3554 (1957).

The base was regenerated from the maleate with Na_2CO_3 and recrystallized from pentane to give analytical material: ir max ($CHCl_3$) no indole NH; uv max (MeOH) 295 mμ (ε 13,500).

1-Benzoyl-2-(1-methyl-1,2,5,6-tetrahydro-3-pyridyl)indole (14).—A soln of C_6H_5MgBr in 50 ml of THF was prepared using 4.45 g (0.0283 mol) of C_6H_5Br and 0.680 g (0.0283 g-atoms) of Mg turnings under N_2. A soln of 6.00 g (0.0283 mol) of **11** in THF was added to the Grignard reagent with stirring. After 0.5 hr, the reaction mixture was cooled to 0° and 3.98 g (0.0283 mol) of C_6H_5COCl was added over a 15-min period at this temperature. After stirring for 12 hr at room temperature, the mixture was hydrolyzed with cold saturated NH_4Cl soln. The THF layer was separated, dried, and evaporated, and the residue chromatographed on Florisil using C_6H_6 as eluent. An oily base (3.0 g) was obtained; ir max ($CHCl_3$) no indole NH in the 3400–3500 cm^{-1} region.

Hydrochloride.—An Et_2O solution of 3.0 g of the above base was treated with a slight excess of HCl in *i*-PrOH; yield 2.0 g; ir max (KCl) 1690 (indole-NC=O) cm^{-1}.

1-Benzyl-2-(1-methyl-3-piperidyl)indole (7).—A soln of 5.1 g of 1-benzyl-2-(1-methyl-1,2,5,6-tetrahydro-3-pyridyl)indole in HOAc containing 0.2 g of PtO_2 was hydrogenated at 3.5 kg/cm^2 (room temperature). After 1 hr, 1 mol equiv of H_2 had been absorbed and no further uptake was observed. The catalyst was removed and the filtrate concentrated *in vacuo*. The residual oil was stirred with $NaHCO_3$ soln and the organic material was extracted into $CHCl_3$. Drying and concentration *in vacuo* gave 5.1 g of thick oil; ir max ($CHCl_3$) no indole NH absorption; uv max (MeOH) 281–282 mμ (ε 5950).

The base was converted into the maleate in Me_2CO–Et_2O; mp 150–151°. *Anal.* [$C_{21}H_{24}N_2 \cdot (CHCO_2H)_2$] C, H, N.

Compound **11** was converted into the known 2-(1-methyl-3-piperidyl)indole[13] in the same way.

1-Benzyl-2-(1-methyl-1,2,3,6-tetrahydro-2-pyridyl)indole (17).—$NaBH_4$ (7.6 g, 0.20 mol) was added in small portions to a MeOH soln of 19.2 g (0.045 mol) of 1-benzyl-2-(2-pyridyl)indole methiodide (mp 169–171°, prepared by thermal indolization and subsequent quaternization). The mixture was stirred under reflux for 3 hr, then worked up in the usual way. A C_6H_6 soln of the crude base was chromatographed on a silicic acid column. The material obtained by elution with EtOAc was recrystallized twice from pentane to give 4.0 g of product: mp 92–94°; nmr ($CDCl_3$, 10%) τ 7.52 (m, 2, tetrahydropyridine-C_3**H**), 6.20 (q, 1, tetrahydropyridine-C_2**H**); 4.20 (m, 2, olefinic), 3.34 (s, 1, indole-C_3**H**), 2.30 (1, indole-C_7**H**); uv vax (MeOH) no absorption in the 300-mμ region.

Maleate.—The base described above was dissolved in Et_2O and maleic acid (2.3 g) in Me_2CO was added. The salt was recrystallized from Me_2CO–Et_2O, yield 4.0 g.

1-Benzyl-2-(1-cyano-1,2,5,6-tetrahydro-3-pyridyl)indole.—A C_6H_6 soln of 1.50 g (0.005 mol) of **13** was added dropwise to a C_6H_6 soln of 0.64 g (0.006 mol) of CNBr over a 1-hr period. The mixture was stirred overnight, a small amount of insoluble material was filtered and the filtrate concentrated *in vacuo*. Crystallization from MeOH–H_2O yielded 1.0 g of product: mp 97–99°; ir 2225 (C≡N) cm^{-1}; nmr ($CDCl_3$, 20%) τ 4.59 (s, 2, benzylic), 4.02 (m, 1, olefinic); absence of NMe signal at 7.87. *Anal.* ($C_{21}H_{19}N_3$) N.

1-Benzyl-2-(1,2,5,6-tetrahydro-3-pyridyl)indole (8).—The above intermediate (1.0 g) in 50 ml of MeOH–20% aq NaOH (1:1) was heated under reflux overnight. MeOH was distilled and the oil extracted into $CHCl_3$. The extract was dried and concentrated *in vacuo* to give 0.82 g of material, ir ($CHCl_3$) absence of C≡N absorption band at 2225 cm^{-1}.

Maleate.—The base was converted into the maleate in Me_2CO–MeOH to give 0.80 g of product, mp 185–186°. *Anal.* [$C_{20}H_{20}N_2 \cdot (CHCO_2H)_2$] C, H, N.

1-Benzyl-2-methyl-3-(3-pyridyl)indole.—A mixture of 14.6 g (0.11 mol) of 3-pyridylacetone[14] and 21.0 g (0.11 mol) of 1-benzyl-1-phenylhydrazine in 200 ml of PhMe was heated under reflux for 2 hr while collecting the water in a Dean–Stark trap. After removal of solvent the residue was dissolved in 300 ml of AcOH and the solution heated at 90° for 3 hr. The AcOH was distilled *in vacuo*, the residue treated with $NaHCO_3$ soln, and then extracted into $CHCl_3$. Drying of the extract and concentration *in vacuo* gave 26 g of material whose ir spectrum ($CHCl_3$) showed complete removal of the NN=C band at 1635 cm^{-1}.

Methiodide.—The crude indole was dissolved in 200 ml of Me_2CO and 40 ml of MeI. The mixture was heated under reflux for 16 hr, then the solvent and excess MeI were removed *in vacuo*. Stirring with a little Me_2CO gave 23 g of product, mp 194–196°. An analytical sample was prepared by recrystallization from a small amount of MeOH, mp 196–198°. *Anal.* ($C_{22}H_{21}IN_2$) N (basic).[15]

1-Benzyl-2-methyl-3-(1-methyl-1,2,5,6-tetrahydro-3-pyridyl)-indole (9).—A 33-g sample of the above methiodide was reduced with 14 g of $NaBH_4$ in the usual way. The free base obtained (12 g) failed to crystallize, but was characterized by its nmr spectrum ($CDCl_3$, 10%); τ 7.54 (s, 3, NMe), 7.42 (s, 3, indole-C_2Me), 4.1 (m, 1, olefinic); absence of indole-C_3H signal in the τ 3.5 region.

Oxalate.—The base was converted into the oxalate in *i*-PrOH. Recrystallization from MeOH–*i*-PrOH gave the analytical sample, mp 195–197°. *Anal.* [$C_{22}H_{24}N_2.(CO_2H)_2$] N.

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(14) A. Burger and C. R. Walter, Jr., *J. Amer. Chem. Soc.*, **72**, 1988 (1950).

(15) Titration in AcOH containing $Hg(OAc)_2$, using standard $HClO_4$ as titrant.