[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

Cyclizative Condensations. I. 2-Methylindole with Acetone and Methyl Ethyl Ketone[1]

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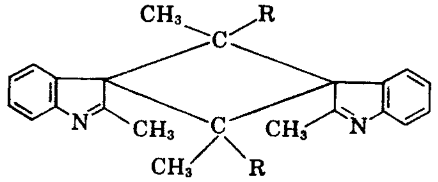
Evidence, both chemical and spectroscopic, has been obtained to indicate that the monobasic 2:2 condensation product from 2-methylindole and acetone, first assigned structure Ia by Scholtz, has structure Va or VIa, the position of the olefinic double bond being uncertain. The same compound was also obtained from reactions of 2-methylindole with: (a) the 1:1 adduct of 2-methylindole and mesityl oxide (IIIa), (b) phorone, and (c) mesityl oxide. Likewise, action of acetic anhydride on the bisindole IIe produced the monobase Va as its monoacetyl derivative, which was also obtained directly by acetylation of the monobase. It has been shown that the acetyl, propionyl, and *n*-butyryl derivatives, previously assigned structures IIa, IIb, and IIc by Scholtz, are, in fact, simple acyl derivatives of the monobase. The presence of both a basic and an acidic NH group in the monobase has been established by stepwise monomethylation (to Vb and Vd), in which the sequence can be reversed, but which leads to the same dimethyl derivative (Vc) in either case. The presence of an olefinic double bond in the monobase is established by hydrogenation to the dihydro derivative VII. A mechanism for formation of the monobase is proposed, involving the intermediates VIII–XI. That indole monobases will also form, however, from cyclic keto monobases is shown by the formation of XII in 70% yield from condensation of 2-methylindole with IVa. An analogy for the proposed mechanism of monobase formation is presented involving formation of the dimer XIVa from the vinylindole XIII. An attempt to prepare a similar product (XIVb) by addition-condensation of 2-methylindole with benzalacetophenone gave 3,3′-benzylidene-2,2′-dimethylbisindole. Condensation of 1,2-dimethylindole with acetone gave only the bisindole IIf, and none of the monobase Vc. 1,2-Dimethylindole and mesityl oxide gave the 1:1 adduct IIIb. Condensation of 2-methylindole with methyl ethyl ketone gave two isomeric monobases (XV).

In 1913 Scholtz[2] described the "unusually easy" condensation of 2-methylindole with acetone in the presence of hydrochloric or hydrobromic acid. The condensation, which was better carried out in ethanolic acid solution at room temperature, was reported to form in quantitative yield a monohydrochloride or monohydrobromide salt of a base, $C_{24}H_{26}N_2$. The colorless free base, m.p. 183°, was liberated by the action of alkali and was shown to have a molecular weight consistent with the formula assigned. The compound was incorrectly assigned the bisindolenine structure Ia. Aside from the improbability of forming a four-membered ring under the reaction conditions employed, structure Ia is untenable for other reasons. For example, the compound should be dibasic rather than monobasic, and the infrared spectrum has two NH bands. The corresponding reaction of 2-methylindole with methyl ethyl ketone was reported to give in unstated yield an analogous colorless monobase, $C_{26}H_{30}N_2$, m.p. 97°, to which structure Ib was incorrectly assigned. It is possible that the reported melting point, which appears at only one point in the paper, may have been a misprint and should have read 197°. Our two isomeric monobasic products from the same reaction have the same empirical formula as the compound described by Scholtz, but have melting points of 197.5–198° (isomer 1) and 197–199° (isomer 2), respectively. Analogous condensations of skatole with methyl ketones were not obtained, nor was diethyl ketone found to react with 2-methylindole.[2]



Ia. $R = CH_3$
b. $R = C_2H_5$

In a later paper Scholtz[3] described the preparation of colorless monoacyl derivatives of the monobasic 2-methylindole:acetone product, specifically the acetyl (m.p. 224°), propionyl (m.p. 194°), *n*-butyryl (m.p. 142°), and isovaleryl (m.p. 190°) derivatives. We have confirmed the report of the preparation of the first three derivatives, which in our hands had melting points of 229–231°, 198–199°, and 183–184°, the latter melting point being 40° higher than that reported. On the basis of what we have found to be erroneous analytical data and his assignment of structure Ia to the monobase, Scholtz incorrectly assigned to these monoacyl derivatives structures IIa–IId, in which a molecular equiva-

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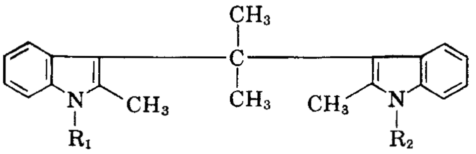
(2) M. Scholtz, *Ber.*, **46**, 1082 (1913).

(3) M. Scholtz, *Arch. Pharm.*, **253**, 629 (1915).

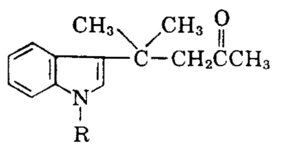
lent of acetone has been lost. In view of the well known instability of *N*-acylindole derivatives toward hydrolysis, and of Scholtz's report that the monoacetyl derivative IIa was unchanged by boiling alcoholic potassium hydroxide, formulations IIa–IId for the monoacyl derivatives must be rejected. Furthermore, we have found that the monoacyl derivatives to which structures IIa–IIc had been assigned have analytical data conforming to the formula of monoacyl derivatives of the original monobase, $C_{24}H_{26}N_2$, and, thus, a molecular equivalent of acetone is not lost in the acylation reactions.



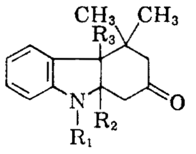
II

IIa. $R_1 = COCH_3$; $R_2 = H$
IIb. $R_1 = COC_2H_5$; $R_2 = H$
IIc. $R_1 = CO(CH_2)_2CH_3$; $R_2 = H$
IId. $R_1 = COCH_2CH(CH_3)_2$; $R_2 = H$
IIe. $R_1 = H$; $R_2 = H$
IIf. $R_1 = CH_3$; $R_2 = CH_3$

2-Methylindole and mesityl oxide (1:5 molar ratio) formed a 1:1 adduct IIIa in 70% yield, which has the ultraviolet spectrum of an indole and an NH and a carbonyl band in the infrared. Compound IIIa forms a mixture of stereoisomeric oximes, but, like a typical 2-methylindole, did not form an *N*-acetyl derivative. For these reasons, its structure was assumed to differ in type from the 1:1 adduct[4] of 1,3-dimethylindole and mesityl oxide, which has been proven to have structure IVa.[5] 1,2-Dimethylindole and mesityl oxide formed a 1:1 adduct IIIb in 5% yield, similar to the adduct (IIIa) from 2-methylindole. Also formed in 1% yield was a solid, m.p. 118–119°, having the same empirical formula, and the ultraviolet spectrum of an indole, but an NH or OH band and no carbonyl band in the infrared. The latter compound may be a tertiary alcohol resulting from cyclizative condensation of the ketone carbonyl with the 2-methyl group of IIIb.



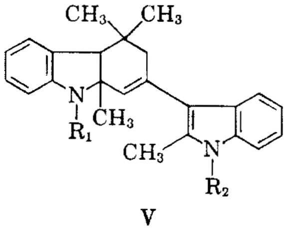
III



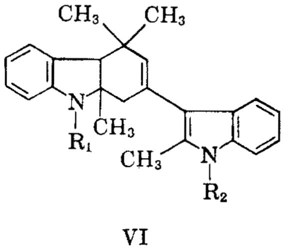
IV

IIIa. R = H. IVa. $R_1 = CH_3$, $R_2 = H$, $R_3 = CH_3$.
IIIb. R = CH_3. IVb. $R_1 = H$, $R_2 = CH_3$, $R_3 = H$.

Condensation of IIIa with 2-methylindole gave a 91% yield of the monobase $C_{24}H_{26}N_2$ (Va) previously reported by Scholtz; Va was also formed directly from 2-methylindole with acetone (82% yield), mesityl oxide (4:3 molar ratio, 67% yield), or phorone (2:1 molar ratio, 88% yield). Interestingly, the bisindole IIe, obtained from condensation of 2-methylindole with acetone in refluxing acetic acid solution[2] in 78% yield, is a suitable acetone (and 2-methylindole) equivalent in acidic solution; IIe, warmed in acetic anhydride solution for two hours and then hydrolyzed with water, gave a 50% yield of the monoacetyl derivative of the monobase $C_{24}H_{26}N_2$, identical by mixed melting point and infrared comparison with the monoacetyl derivative prepared directly in 99% yield by the action of acetic anhydride on the monobase.



V



VI

Va or VIa. $R_1 = H$; $R_2 = H$
Vb or VIb. $R_1 = CH_3$; $R_2 = H$
Vc or VIc. $R_1 = CH_3$; $R_2 = CH_3$
Vd or VId. $R_1 = H$; $R_2 = CH_3$

The presence of a single basic nitrogen in the monobase (Va) is indicated by the formation of a monohydrochloride or monohydrobromide derivative. The presence of a hydrogen on the basic nitrogen is shown by the formation of monoacyl derivatives. That the basic nitrogen is secondary is suggested by the formation of only a monomethyl derivative (Vb), m.p. 182–183°, in 91% yield by action of a seven-fold molar excess of methyl iodide in refluxing acetone solution in the presence of anhydrous potassium carbonate. The monomethylation was accompanied by the disappearance of one of the two NH bands in the infrared spectrum, but there was no radical change in the ultraviolet spectrum. That the NH which remains is acidic is shown by formation of a dimethyl derivative (Vc), m.p. 142°, in 88% yield by monomethylation with sodamide and methyl iodide in liquid ammonia in the manner common for the methylation of the acidic NH of indoles. The dimethyl derivative no longer contains an NH band in the infrared spectrum, showing that both of the nitrogen atoms in the original monobase must have been secondary. The methylation sequence was also reversed; initial monomethylation of the acidic nitrogen with sodamide and methyl iodide in liquid ammonia gave a different monomethyl derivative (Vd), m.p. 148–149°, in 90% yield; subsequent monomethylation of the basic nitrogen with a fifteen-fold molar excess of methyl iodide in

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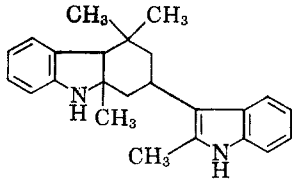
[4] D. A. Cockerill, R. Robinson, and J. E. Saxton, *J. Chem. Soc.*, 4369 (1955).

[5] B. Robinson and G. F. Smith, *J. Chem. Soc.*, 4574 (1960).

the manner described above gave in 88% yield a dimethyl derivative, m.p. 141–142°, identical with the dimethyl derivative (Vc) described previously, as shown by mixed melting point and infrared comparison.

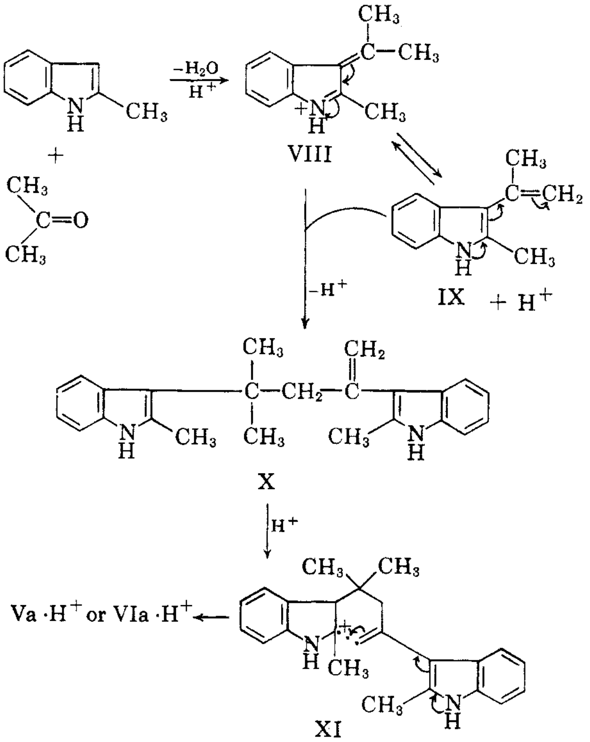
The monobase (Va) and its methylated derivatives (Vb–Vd) have a weak infrared band in the 1644–1660 cm.$^{-1}$ region (see Experimental), which is attributed to an olefinic double bond. Hydrogenation of the monobase at two atmospheres over Raney nickel catalyst gave in 91% yield a dihydro derivative (VII), m.p. 251–253°, which does not have an olefinic band in its infrared spectrum. That this dihydro derivative is also monobasic is shown by the formation in 90% yield of a monoacetyl derivative, m.p. 239–241°.



The monobase (Va), its hydrochloride, its monoacyl derivatives, the dihydro derivative (VII) and its monoacetyl derivative, and its methylated derivatives (Vb–Vd) have the ultraviolet absorption maxima or inflections normally associated with an intact indole nucleus (as in IIe–IIf and III), and an additional maximum or inflection in the 246–265-mμ region, normally associated with an indoline (2,3-dihydroindole) or 1-acylindoline nucleus.[6] An indoline nucleus, which would provide the basic nitrogen in Va, could result from a cyclization, similar to the formation of IVa, involving nucleophilic addition to a protonated 2,3-double bond of an indole nucleus.

The NMR spectrum of the monobase (Va) has been determined in deuterochloroform solution referenced against benzene in an external annulus.[7] The four methyl peaks occur at 9.19, 8.83, 8.66, and 7.57 τ (calculated from the finding with steroids[8] of a separation of 6.38 ppm. between the benzene external and tetramethylsilane internal peaks). The high field peak at 9.19 τ is attributed[7] to the methyl group on the indoline nucleus, the peaks at 8.83 and 8.66 τ to the *gem*-dimethyl groups on opposite sides of the unsymmetrical ring system, and the low field peak at 7.57 τ to the 2-methyl group on the double bond of the still-intact indole nucleus. The data are consistent with either structure Va or VIa containing alternative positions for the olefinic double bond in the monobase, but only a single isomer was isolated from the reaction. For the sake of brevity, only the designations V (rather than VI) have, in general, been used throughout this paper.

The exothermic reaction between 2-methylindole and acetone in ethanolic hydrochloric acid at room temperature probably involves the basic 1:1 condensation product, 3-isopropylidene-2-methylindolenine, in protonated form (VIII), as an intermediate.[9] This could exist in equilibrium with the vinylindole IX, which is, in essence, the enol form (enamine) of the unprotonated form of VIII. In contrast to the situation prevailing in weak (acetic) acid solution, in which the simultaneous presence of free 2-methylindole as a nucleophile leads to formation of the bisindole IIe, in strong (ethanolic hydrochloric) acid it is likely that all the 2-methylindole is rapidly converted to VIII and its transformation products. Hence, the best remaining nucleophiles would be IX or the enol form of acetone. Addition of IX and VIII and loss of a proton would lead to the proposed intermediate X, which is probably in tautomeric equilibrium with the unreactive vinylindole form containing the more highly substituted (and more sterically hindered) double bond.



Alternate pathways leading to IIIa would be the addition of the enol form of acetone to VIII and loss of a proton, a pathway for which we have no direct evidence, and the acid-catalyzed addition of 2-methylindole to the α,β-unsaturation of mesityl oxide, for which we have ample evidence (70%

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[6] W. E. Noland and C. F. Hammer, *J. Org. Chem.*, 25, 1525 (1960).

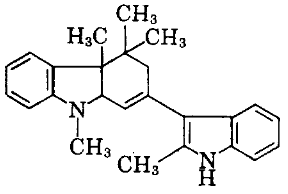
[7] By LeRoy F. Johnson of Varian Associates, Palo Alto, Calif., to whom we are indebted for the analysis and interpretation.

[8] J. S. G. Cox, E. O. Bishop, and R. E. Richards, *J. Chem. Soc.*, 5118 (1960).

[9] W. E. Noland and D. N. Robinson, *J. Org. Chem.*, 22, 1134 (1957).

yield). It seems likely that mesityl oxide would form from acetone (if 2-methylindole does not react with the acetone first) under the acidic conditions[10] employed, since the effectiveness of phorone as a precursor for Va (88% yield) indicates that the reverse sort of process does readily occur under equivalent conditions.

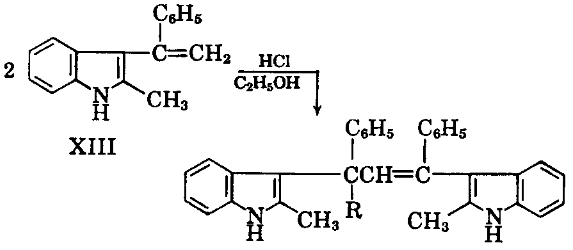
The 1:1 adduct IIIa did not cyclize (to IVb) under the conditions under which it was formed (excess mesityl oxide in ethanolic hydrochloric acid); likewise, under similar conditions in ethanolic hydrochloric acid alone it was recovered unchanged in 64% yield (after distillation and conversion to the oxime). Significantly, none of the monobase Va was formed. These results indicate that the formation of the 1:1 adduct (IIIa) is irreversible under the conditions employed and that prior cyclization to a possible intermediate IVb, before condensation of the second molecule of 2-methylindole, does not occur. That cyclic keto monobases of type IV, once formed, will give indole monobases, however, is shown by condensation of IVa with 2-methylindole to form the monobase XII in 70% yield. In agreement with the spectra of other monobases (Va–Vd, VII), the monobase XII has a weak olefinic band in the infrared at 1667 cm.$^{-1}$, and an indoline band in the ultraviolet at 264 mμ.



XII

It seems likely that the vinylindole X is the key intermediate in the cyclization process leading to the monobase Va. Protonation of the 3-position of the indole nucleus nearest to the *gem*-dimethyl group, followed by nucleophilic attack (XI) by the terminal methylene group of the vinylindole should readily produce cyclization. This process is electronically similar to the intermolecular acid-catalyzed dimerization of 2-methylindole, which does not occur.[4] The intramolecular and six-membered-ring nature of the present process, however, should make the cyclization particularly favorable.

A reaction closely analogous to the mechanism proposed here is the acid-catalyzed dimerization of 2-methyl-3-vinylindoles. In agreement with the proposed mechanism, the vinylindole XIII[11] gave the corresponding dimer XIVa in 27% yield. The dimer is prevented from cyclizing to an indoline by the fact that its vinylindole group is not of the terminal methylene type (like X) necessary for cyclization. An attempt was made to prepare a structurally closely analogous compound (XIVb) by addition-condensation of 2-methylindole with benzalacetophenone under comparable reaction conditions. The reaction gave as the only crystalline product, in 5% yield, 3,3′-benzylidene-2,2′-dimethylbisindole, the bisindole derived from condensation of 2-methylindole with benzaldehyde, suggesting that some hydrolysis of benzalacetophenone may have taken place under the acidic conditions employed.



XIVa. R = CH_3
b. R = H
XIV

The dimer XIVa is not an indoline, as shown by its failure to acetylate. The ultraviolet spectrum contains simple indole absorption but there is also absorption, (no maxima or well defined inflections) in the 236–268-mμ region, which may be attributed to the styrene-type chromophore present in the molecule, as the K-band of styrene appears at 244 mμ in ethanol.[12]

Condensation of 1,2-dimethylindole with acetone, under the conditions used to form Va from 2-methylindole, gave the bisindole IIf in 59% yield as the only product isolated. Failure to isolate the monobase Vc (which has been prepared by the two-step methylation of Va) is attributed to the somewhat lower nucleophilicity (greater difficulty in forming an indolenine cation analogous to VIII) and the greater steric hindrance of 1,2-dimethylindole relative to 2-methylindole.

Condensation of 2-methylindole with methyl ethyl ketone gave, after chromatography of the products, two isomers, m.p. 197.5–198° (isomer 1) and 197–199° (isomer 2), in 15 and 20% yields, respectively. The isomers have different infrared and ultraviolet spectra and give a depression in mixed melting point. The ultraviolet spectra indicate that these products are of the same type as the monobases described previously. The olefinic double-bond band in the infrared spectrum of isomer 1 is either not present or too weak to be discernible. Isomers 1 and 2 form monoacetyl derivatives, m.p. 193–196°, and 216–219°, respectively, analogous to that derived from the monobase IVa. Assignment of structure to Isomers 1 and 2 is complicated by the possibility of positional isomerism of a methyl

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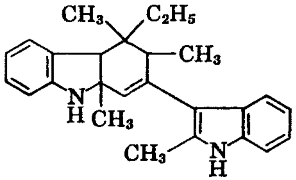
[10] S. Nagakura, A. Minegashi, and K. Stanfield, *J. Am. Chem. Soc.*, 79, 1033 (1957).

[11] W. E. Noland, Mark S. Fawcett, and M. R. Venkiteswaran, unpublished work (to be reported later), 1955, 1958.

[12] A. E. Gillam and E. S. Stern, *Electronic Absorption Spectroscopy*, Edward Arnold Ltd., London, 1954, p. 126.

group and increased possibilities for stereoisomerism. If it is considered (1) as most probable that the two methyl ethyl ketone equivalents condense with themselves in the manner in which they are reported to self-condense in acid (to 3,4-dimethyl-3-hexen-2-one and its β,γ-unsaturated isomer),[13] which would give a terminal methylene group (probably necessary for cyclization) in the intermediate analogous to XI, and (2) that the vinylindole double bond in the cyclization product occupies the position analogous to that shown in Va, then the two isomeric products would have structure XV.



XV

EXPERIMENTAL

The initials of co-authors or names of persons after the heading of each section show who did the experimental work. Melting points were determined on Kofler micro hot stages or on Fisher-Johns hot stages.

2,2'-Dimethyl-3,3'-isopropylidenebisindole (IIe) (with Wesley A. Pearson, 1955). Refluxing a solution of 2-methylindole and acetone in glacial acetic acid for 1 hr., according to the method of Scholtz[2] (who did not report the yield), gave a 78% yield, m.p. 185–197°. Recrystallization from ethanol-water gave white crystals having the reported melting point, 197°[2,14]; λ_{max} in 95% ethanol: 229 mμ (log ϵ 4.72), 285 (4.06), 291 (4.04); ν_{NH} 3440 in chloroform, 3380 cm.$^{-1}$ in Nujol.

2-(2-Methyl-3-indolyl)-3,4,4a,9a-tetrahydro-4,4,9a-trimethylcarbazole (Va). (*A*) *From acetone* (M.R.V.). The monobase was obtained in 97% yield as the monohydrochloride and in 82% yield as the free base, m.p. 182–183°, from 2-methylindole and acetone, according to the method of Scholtz[2]; reported: quantitative yield, m.p. 183°: λ_{max} in 95% ethanol: 228 mμ (log ϵ 4.54), 256 (4.23), 282 inflection (4.06), 290 (4.02): ν_{NH} 3450, 3380 in chloroform, 3420 in potassium bromide, 3390, 3350 in Nujol, $\nu_{C=C}$ 1652 in chloroform, 1654 in potassium bromide 1655 cm.$^{-1}$ in Nujol.

An ethanolate or dimorphic form,[15] m.p. 93–94° (not sharp), was sometimes obtained when the monobase was crystallized from absolute ethanol or ethanol-water. This form was converted to the form, m.p. 182–183°, by recrystallization from ethanol, by melting and then cooling, or by drying *in vacuo* at 76°—the manner in which the analytical sample, m.p. 180–183°, described here, was obtained.

Anal. Calcd. for $C_{24}H_{26}N_2$ (342.46): C, 84.17; H, 7.65; N, 8.18. Found: C, 84.01; H, 7.88; N, 7.89.

Ozonolysis of the monobase in ethyl acetate solution gave a brown tar along with 4% of unchanged starting material Similarly, the action of osmium tetroxide on the monobase, followed by periodate cleavage, gave an oil which could not be crystallized.

(*B*) *From mesityl oxide* (with H. S. Desai,[16] 1960). A solution of 2-methylindole (2.62 g., 0.020 mole), mesityl oxide (1.46 g., 0.0149 mole), and concentrated hydrochloric acid (2.5 g.) in 95% ethanol (12 cc.) was kept at room temperature for 20 hr. The dark brown crystalline precipitate was filtered off, dissolved in hot ethanol, and neutralized with ethanolic sodium hydroxide solution. The precipitated sodium chloride was filtered off and the filtrate concentrated, producing more sodium chloride, which was filtered off. Evaporation of the filtrate and solution of the orange sticky residue (3.150 g.) in the minimum amount of ethanol gave two crops of yellowish white solid (2.305 g., 0.00674 mole, 67%), m.p. 182–184°. Recrystallization from ethanol yielded white crystals which had an infrared spectrum in Nujol identical with that of a sample prepared from acetone, and gave no depression in mixed melting point.

Anal. Found:[15] C, 84.33; H, 7.93; N, 8.26.

(*C*) *From phorone* (M.R.V.) A solution of 2-methylindole (2.62 g., 0.020 mole), phorone (1.38 g., 0.010 mole), and concentrated hydrochloric acid (2.5 g.) in 95% ethanol (12 cc.) was kept at room temperature for 12 hr. The color of the solution became deep brown and white crystals precipitated. The crystals were filtered, washed with ether, dried, dissolved in ethanol, and neutralized with ethanolic sodium hydroxide solution. Dilution of the ethanol solution with water gave a white precipitate (3.01 g., 0.0088 mole, 88%). Recrystallization from ethanol yielded white crystals, m.p. 181–182°, mixed melting point with a sample prepared from acetone, 181–183°. Three more recrystallizations from ethanol gave the analytical sample. The infrared spectrum in Nujol was identical with that of a sample prepared from acetone.

Anal. Found: C, 83.83; H, 7.49; N, 8.07.

(*D*) *From 4-Methyl-4-(2-methyl-3-indolyl)-2-pentanone* (M.-R.V.) A solution of 4-methyl-4-(2-methyl-3-indolyl)-2-pentanone (2.29 g., 0.0100 mole), 2-methylindole (1.31 g., 0.0100 mole), and concentrated hydrochloric acid (2.0 g.) in 95% ethanol (10 cc.) was kept at room temperature. After a few minutes a precipitate began to form in the red-brown solution, and after 2 hr. the precipitate was filtered, washed with ether, and dried. Then it was suspended in ethanol, neutralized with ethanolic sodium hydroxide solution, and the solution diluted with water, giving a white precipitate. The precipitate was crystallized from ethanol-water, yielding white crystals (3.12 g., 0.0091 mole, 91%), m.p. 181–182°. The mixed melting point with a sample prepared from acetone was undepressed.

Monohydrochloride of Va (with Wesley A. Pearson, 1955). The compound was obtained from ethanol-water as a white solid, m.p. 172°; reported: from ethanol-ether as colorless needles, m.p. 172°[2]; ν_{NH} 3380, 3340, $\nu_{C=C}$ 1656 cm.$^{-1}$ in Nujol.

Monohydrochloride hemihydrate of Va (with Donald N. Robinson[15]). The hemihydrate was obtained from ethanol-water as colorless plates, m.p. 172–173°; λ_{max} in 95% ethanol: 226 mμ (log ϵ 4.54), 258 (4.14), 280 inflection (4.05), 290 (4.00): ν_{OH} 3460, ν_{NH} 3240, ν_{water} 1635 cm.$^{-1}$ in Nujol. The infrared spectrum in Nujol is quite different from that of the anhydrous form. The analytical sample was dried at 76° *in vacuo.*

Anal. Calcd. for $C_{24}H_{27}N_2Cl \cdot \frac{1}{2}H_2O$ (387.94): C, 74.30; H, 7.28; N, 7.22. Found: C, 74.25; H, 7.40; N, 7.23.

Monoacetyl derivative of Va (W.E.N.). (*A*) *From the monobase.* A mixture of the monobase (1.00 g., 0.00292 mole) and acetic anhydride (5.0 cc.) was warmed on a steam bath for 2 hr. The insoluble white crystals looked different from the insoluble starting material. The mixture was kept at room temperature for several days, water (10 cc.) was added, and the hydrolyzed mixture was kept for several more days. Ether was added and the acetic acid was removed by extraction with aqueous sodium bicarbonate solution. Some of the product remained undissolved at the ether-water interface. This and the residue from evaporation of the ether were white crystals (1.11 g., 0.00289 mole, 99%). Recrystallization from ethanol yielded white needles (1.00 g.), m.p. 228.5–

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(13) A. E. Abbott, G. A. R. Kon, and R. D. Satchell, *J. Chem. Soc.*, 2514 (1928).

(14) B. Oddo and L. Perotti, *Gazz. chim. ital.*, **60**, 13 (1930).

(15) Donald N. Robinson, Ph.D. thesis, University of Minnesota, March 1959, pp. 167, 184–188.

230.5°, mixed melting point with the sample from 2,2'-dimethyl-3,3'-isopropylidenebisindole, 229–231° (undepressed); reported m.p., 224°.[3] The infrared spectra of the two samples in chloroform and Nujol were identical.

(*B*) *From 2,2'-dimethyl-3,3'-isopropylidenebisindole.* A mixture of 2,2'-dimethyl-3,3'-isopropylidenebisindole (1.00 g., 0.00330 mole) and acetic anhydride (5.0 cc.) was warmed on a steam bath for 2 hr., causing part of the crystals to dissolve in the brownish solution. The mixture was kept at room temperature for several days and water (10 cc.) was added, causing the solution to turn dark green. The hydrolyzed mixture was kept for several days, and then ether was added and the acetic acid removed by extraction with aqueous sodium bicarbonate solution. Evaporation of the dark brown ether layer gave a mixture (1.14 g.) of brownish crystals and flocculent brownish material. Recrystallization, with much charcoal, from ethanol-water gave impure brownish crystals (0.59 g., 0.00153 mole, 93%), m.p. 216–227.5°. These were recrystallized from benzene-petroleum ether (b.p. 60–68°), and the flocculent brown precipitate was removed from the denser crystals by decantation. Recrystallization from ethanol and twice from ethanol-water yielded white needles (0.32 g., 0.00083 mole, 50%), m.p. 229–231°; reported m.p. 224° [3]; λ_{max} in 95% ethanol: 228 mμ inflection ($\log \epsilon$ 4.54), 262 (4.36), 281 inflection (4.22), 290 inflection (4.15); ν_{NH} 3420, 3280 in chloroform, 3310 in Nujol, $\nu_{C=O}$ 1637 in chloroform, 1631 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{26}H_{28}N_2O$ (384.50): C, 81.21; H, 7.34; N, 7.29. Found: C, 81.35, 81.51; H, 7.52, 7.36; N, 7.54, 7.32.

The compound was recovered unchanged in 84% yield from attempted hydrogenation at 2 atm. over Raney nickel catalyst in ethanol at room temperature for 3 days.

Monopropionyl derivative of Va (M.R.V.). The compound was obtained in 86% yield from the monobase and propionic anhydride; white crystals from ethanol, m.p. 198–199°; reported[3] m.p. 194°; λ_{max} in 95% ethanol: 228 mμ inflection ($\log \epsilon$ 4.56), 264 (4.37), 284 inflection (4.24), 290 inflection (4.18); ν_{NH} 3460, 3310 in carbon tetrachloride 3320 in Nujol, $\nu_{C=O}$ 1637 in carbon tetrachloride 1629 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{27}H_{30}N_2O$ (398.53): C, 81.37; H, 7.59; N, 7.03. Found: C, 81.16; H, 7.49; N, 7.32.

Mono-n-butyryl derivative of Va (M.R.V.). The compound was obtained in 60% yield from the monobase and *n*-butyric anhydride; white crystals from ethanol, m.p. 183–184°; reported[3] m.p. 142°; λ_{max} in 95% ethanol: 228 mμ inflection ($\log \epsilon$ 4.56), 264 (4.37), 284 inflection (4.23), 290 inflection (4.18); ν_{NH} 3370, $\nu_{C=O}$ 1641 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{28}H_{32}N_2O$ (412.55): C, 81.51; H, 7.82; N, 6.79. Found: C, 81.24; H, 7.71; N, 6.81.

Maleyl derivative of Va (C.G.R.). A solution of the monobase (2.00 g., 0.00584 mole) and maleic anhydride (1.28 g., 0.0131 mole) was refluxed in dry benzene for 2 hr. Evaporation of the benzene gave an oil which, upon trituration with ethanol, left as a residue a solid (2.55 g., 0.00579 mole, 99%). Crystallization from acetone yielded white rhombs, m.p. 193–194°; λ_{max} in 95% ethanol: 228 mμ ($\log \epsilon$ 4.31), 257 (4.50), 290 inflection (4.90), 350 (3.86); $\nu_{NH,\,OH}$ 3390, 3170, $\nu_{C=O}$ 1745, 1690, $\nu_{C=C}$ 1640 inflection, $\nu_{C=C\ conj.}$ 1600 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{28}H_{28}N_2O_3$ (440.52): C, 76.34; H, 6.41; N, 6.36. Found: C, 75.20; H, 7.19; N, 6.51.

Four other attempts to bring the analytical values closer to the calculated values gave erratic results which were even lower in carbon than the result reported.

Isomerization of maleyl derivative of Va. A mixture of the maleyl derivative (2.55 g.), acetone 120 cc.), ethanol (100 cc.), and aqueous potassium hydroxide solution (30%, 300 cc.) was refluxed for 3 hr. The inhomogeneous mixture bumped. Most of the solvent was evaporated, the solid which separated was filtered off, suspended in water, and acidified with hydrochloric acid. The solid product was extracted with ethyl acetate, which upon evaporation gave a brownish glass (0.590 g.). Three recrystallizations from ethyl acetate petroleum ether (b.p. 60–68°) yielded an isomer as tan-tinted whitish crystals (0.060 g., 2%), m.p. 222–225°; λ_{max} in 95% ethanol: 226 mμ ($\log \epsilon$ 4.31), 249 (4.40), 290 inflection (3.64), 350 (3.89); ν_{NH} 3400, 3290, $\nu_{C=O}$ 1740 (weakest), 1722 (strongest), 1705, 1638, $\nu_{C=C}$ 1635 inflection, $\nu_{C=C\ conj.}$ 1601 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{28}H_{28}N_2O_3$ (440.52): C, 76.34; H, 6.41; N, 6.36. Found: C, 76.20; H, 6.32; N, 6.28.

Hydrolysis of maleyl derivative of Va. A solution of the maleyl derivative (1.00 g., 0.00226 mole), potassium hydroxide (5.00 g., 0.089 mole), and water (5.0 cc.) in ethanol (45 cc.) was refluxed for 1 hr. Most of the solvent was then removed and the resulting suspension was poured into water. Extraction with ether and evaporation of the ether gave an oil which crystallized (0.70 g., 0.00204 mole, 90%), m.p. 180–182°. Recrystallization from ethanol yielded the free monobase, melting point and mixed melting point with an authentic sample, 181–182°.

Dihydro derivative: 1,2,3,4,4a,9a-hexahydro-2-(2-methyl-3-indolyl)-4,4,9a-tetramethylcarbazole (VII) (M.R.V., Donald N. Robinson[15]). A solution of the monobase (0.68 g., 0.00199 mole) in absolute ethanol (150 cc.) was hydrogenated at 2 atm. over Raney nickel catalyst at room temperature. Filtration of the catalyst and distillation of most of the ethanol left a residue which formed colorless crystals (0.62 g., 0.00180 mole, 91%), m.p. 245–253°. Three recrystallizations from ethanol-benzene yielded colorless crystals, m.p. 251–253°; λ_{max} in 95% ethanol: 228 mμ ($\log \epsilon$ 4.57), 246 inflection (4.01), 285 (3.95), 292 (3.96); ν_{NH} 3480, 3390 in carbon disulfide, 3470, 3370 in chloroform, 3410 3360 cm.$^{-1}$ in Nujol, $\nu_{C=O\ olefinic}$ none.

Anal. Calcd. for $C_{24}H_{28}N_2$ (344.48): C, 83.67; H, 8.19; N, 8.13. Found: C, 83.38; H, 8.22; N, 8.41.

Monoacetyl dihydro derivative (*monoacetyl derivative of* VII) (M.R.V.). A mixture of the dihydro derivative (1.72 g., 0.0050 mole) and acetic anhydride (6 cc.) was refluxed for 1.5 hr. and then poured on crushed ice and the mixture kept overnight. The resulting precipitate was crystallized from ethanol, giving crystals (1.74 g., 0.00450 mole, 90%). Three recrystallizations from ethanol yielded white plates, m.p. 239–241°; λ_{max} in 95% ethanol: 226 mμ ($\log \epsilon$ 4.58), 259 (4.17), 284 (4.06), 291 (4.03); ν_{NH} 3480, 3330 in chloroform, 3310 in Nujol, $\nu_{C=O}$ 1646 in chloroform, 1628 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{26}H_{30}N_2O$ (386.52): C, 80.79; H, 7.82; N, 7.25. Found: C, 80.77; H, 7.88; N, 7.55.

The compound was recovered unchanged in 71% yield from an attempted catalytic hydrogenation at 2 atm. in ethanol over Raney nickel at room temperature (R.A.L.).

N-(Indoline)-methyl derivative (Vb) (M.R.V.) A solution of 2-(2-methyl-3-indolyl)-3,4,4a,9a-tetrahydro-4,4,-9a-tetrahydrocarbazole (1.50 g., 0.00438 mole) and methyl iodide (5.0 g., 0.035 mole) in dry acetone (50 cc.) over anhydrous potassium carbonate (5 g.) was refluxed for 6 hr. and kept at room temperature overnight. The acetone was evaporated and the residue extracted twice with cold water to remove potassium carbonate. The dried residue, m.p. 173–175°, was crystallized from ethanol, with charcoal, giving solid (1.42 g., 0.00398 mole, 91%). Three recrystallizations from ethanol yielded white plates, m.p. 182–183°; λ_{max} in 95% ethanol: 226 mμ ($\log \epsilon$ 4.52), 265 (4.34), 290 inflection (3.99); ν_{NH} 3340, $\nu_{C=C}$ 1644 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{28}N_2$ (356.49): C, 84.22; H, 7.93; N, 7.86. Found: C, 84.66; H, 7.92; N, 7.83.

The mixed melting point with starting material of m.p. 182–183° was depressed, 171–172°.

N-(Indole)-methyl derivative (Vd) (C.G.R.). A solution of 2-(2-methyl-3-indolyl)-3,4,4a,9a-tetrahydro-4,4,9a-trimethylcarbazole (0.500 g., 0.00146 mole) in dry tetrahydrofuran (25 cc.) was added to a solution of sodamide [from sodium (0.067 g., 0.00291 g.-atom) and ferric nitrate nonahydrate (one crystal)] in liquid ammonia (200 cc.). The mixture was stirred for 15 min. and methyl iodide (0.18 cc., 0.0029 mole) was added. As the sodium salt appeared insoluble, more dry tetrahydrofuran (25 cc.) and methyl iodide (1.00 cc., 0.016 mole) were added after 10 min. and stirring was continued for 1 hr. The ammonia was allowed to evaporate, water was added, and the product was extracted with ether. The oily product was crystallized from ethanol, yielding white crystals (0.470 mg., 0.00132 mole, 90%), m.p. 148–149°, analytical sample, m.p. 149–149.5°; λ_{max} in 95% ethanol: 230 mμ (log ϵ 4.53), 251 inflection (4.20), 284 (4.00), 293 (4.00); ν_{NH} 3350, $\nu_{C=C}$ 1660 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{28}N_2$ (356.49): C, 84.22; H, 7.93; N, 7.86. Found: C, 84.41; H, 8.07; N, 7.64.

N,N'-Dimethyl derivative (Vc) (C.G.R.). (*A*) *By methylation of the N-(indole)-methyl derivative.* A solution of the N-(indole)-methyl derivative (0.350 g., 0.000981 mole) and methyl iodide (1 cc., 0.016 mole) in dry acetone (25 cc.) over anhydrous potassium carbonate (1.5 g.) was refluxed for 13 hr. The acetone was evaporated, water was added and, the product was extracted with ether, giving a white solid (0.320 g., 0.000864 mole, 88%). Crystallization from ethanol yielded white crystals, m.p. 141–142°; λ_{max} in 95% ethanol: 229 mμ (log ϵ 4.60), 263 (4.38), 284 inflection (4.07), 293 (4.05); ν_{NH} none, $\nu_{C=C}$ 1646 cm.$^{-1}$ in Nujol. The infrared spectrum in Nujol was identical with that of the sample prepared from the *N*-(indoline)-methyl derivative, and the mixed melting point was undepressed.

Anal. Calcd. for $C_{26}H_{30}N_2$ (370.52): C, 84.28; H, 8.16; N, 7.56. Found: C, 84.45; H, 8.17; N, 7.85.

(*B*) *By methylation of the N-(indoline)-methyl derivative.* A solution of the *N*-(indoline)-methyl derivative (0.480 g., 0.00135 mole) in dry tetrahydrofuran (10 cc.) was added in portions to a solution of sodamide [from sodium (0.032 g., 0.00139 g.-atom) and ferric nitrate nonahydrate (one crystal)] in liquid ammonia (50 cc.). The solution was stirred for 15 min., methyl iodide (0.284 g., 0.00200 mole) was added, and stirring was continued for an additional 15 min. The ammonia was allowed to evaporate, water was added, and the product was extracted with ether. The oily product was triturated with a little warm ethanol, giving white crystals (0.440 g., 0.00119 mole, 88%), m.p. 142°. The infrared spectrum in Nujol was identical with that of the sample prepared from the *N*-(indole)-methyl derivative, and the mixed melting point was undepressed.

4-Methyl-4-(2-methyl-3-indolyl)-2-pentanone (IIIa) (M.-R.V.). A solution of 2-methylindole (5.24 g., 0.040 mole), mesityl oxide (20 g., 0.20 mole), and concentrated hydrochloric acid (5 cc.) in 95% ethanol (10 cc.) was kept for 15 hr. The dark brown solution was neutralized with ethanolic sodium hydroxide solution, the precipitated sodium chloride filtered, and the orange filtrate distilled under aspirator pressure on a steam bath to remove the ethanol and most of the mesityl oxide. The residual brownish oil was transferred with ether to a bulb tube. The ether was evaporated and the residue distilled. The forerun, containing mainly mesityl oxide, was discarded and the main fraction collected as a pale yellow oil (6.42 g., 0.0280 mole, 70%), b.p. 160–161° (bath temperature; 0.5–1.0 mm.). Two more distillations yielded the analytical sample as a pale yellow oil, b.p. 160–165° (1 mm.), which solidified after being kept for a time, m.p. 41–45°; λ_{max} in 95% ethanol: 225 mμ (log ϵ 4.47), 283 (3.79), 291 (3.78); ν_{NH} 3380 on the liquid, 3460, 3380 in chloroform, 3420 in Nujol, $\nu_{C=O}$ 1698 on the liquid, 1692 in chloroform, 1714 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{15}H_{19}NO$ (229.31): C, 78.56; H, 8.35; N, 6.11. Found: C, 79.09; H, 8.37; N, 6.65.

Similar results were obtained when dry hydrogen chloride was passed into the ethanol solution, instead of using concentrated hydrochloric acid.

The compound was recovered unchanged in 75% yield (after distillation) from attempted acetylation after refluxing for 4 hr. in acetic anhydride solution. The infrared spectrum of the recovered liquid was identical with that of the starting material.

Oxime of IIIa (*mixture of syn and anti forms*). A mixture of the compound (1.00 g., 0.00435 mole), hydroxylamine hydrochloride (1.00 g., 0.0144 mole), sodium hydroxide (4 g.), and ethanol (25 cc.) was refluxed for 3 hr. The cooled mixture, containing precipitated sodium chloride, was diluted with water (400 cc.). The resulting pale yellow brown precipitate was crystallized from ethanol-water. The product (0.92 g., 0.00376 mole, 86%) was recrystallized three times from ethanol-water to obtain the oxime as white crystals, m.p. 147–155°; λ_{max} in 95% ethanol: 227 mμ (log ϵ 4.54), 284 (3.83), 291 (3.82); ν_{NH} 3460, 3260 (broad) in chloroform, 3400, 3310 (broad) in Nujol, $\nu_{C=N}$ 1663 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{15}H_{20}N_2O$ (244.33): C, 73.73; H, 8.25; N, 11.47. Found: C, 73.76; H, 8.40; N, 11.59.

4-Methyl-4-(1,2-dimethyl-2-indolyl)-2-pentanone (IIIb) (with Gerald R. Simon, 1961).[16] Concentrated hydrochloric acid (2.08 g.) was added, with shaking, to a solution of 1,2-dimethylindole (free of NH in the infrared spectrum, 2.4 g., 0.0165 mole) and mesityl oxide (n_D^{25} 1.4415, 1.63 g., 0.0166 mole) in 95% ethanol (6.58 g.), causing the solution to turn brown and an oil to settle out. The mixture was kept for 24 hr., at the end of which time the oil had dissolved. The solution was poured into water (200 cc.), producing a green color. The mixture was neutralized with sodium bicarbonate and extracted with ether. Evaporation of the ether left a yellow oil, which was mixed with petroleum ether (b.p. 60–68°) and chromatographed on a column containing alumina (2.3 × 50.0 cm.). Elution with petroleum ether (b.p. 60–68°) for 2.75 hr. developed the column and elution with petroleum ether-benzene removed a solid (0.20 g., 0.00082 mole, 5%). Four recrystallizations from methanol-water yielded white crystals (0.10 g., 2%), m.p. 79–80°; λ_{max} in 95% ethanol: 229 mμ (log ϵ 4.50), 289 (3.81), 293 inflection (3.80); $\nu_{C=O}$ 1702 in carbon tetrachloride, 1692 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{16}H_{21}NO$ (243.35): C, 78.97; H, 8.70; N, 5.76. Found: C, 79.17; H, 8.90; N, 5.75.

Elution with benzene and ether removed a small amount of solid having the same elemental composition. Four recrystallizations from methanol-water yielded white needles (0.04 g., 0.00016 mole, 1%), m.p. 118–119°; λ_{max} in 95% ethanol: 230 mμ (log ϵ 4.56), 286 (3.84), 293 (3.82); $\nu_{NH\text{ or }OH}$ 3320 (sharp) cm.$^{-1}$ in Nujol, $\nu_{C=O}$ none.

Anal. Calcd. for $C_{16}H_{21}NO$ (243.35): C, 78.97; H, 8.70; N, 5.76. Found: C, 78.92; H, 8.68; N, 5.97.

When a similar reaction was carried out for 48 instead of 24 hr., and then worked up in the manner described here, no crystalline product was obtained.

1,2,3,4,4a,9a-Hexahydro-2-oxo-4,4,4a,9-tetramethylcarbazole (IVa) (C.G.R.). The compound was prepared by the action of hydrochloric acid on 1,3-dimethylindole and mesityl oxide, as described[4]; λ_{max} in 95% ethanol: 251 mμ (log ϵ 3.88), 298 (3.51); $\nu_{C=O}$ 1708 cm.$^{-1}$ in Nujol.

2-(2-Methyl-3-indolyl)-3,4,4a,9a-tetrahydro-4,4,4a,9-tetramethylcarbazole (XII) (with H. S. Desai,[1c] 1960). 1,2,3,4,4a,-9a-Hexahydro-2-oxo-4,4,4a,9-tetramethylcarbazole (0.80 g., 0.00329 mole) was suspended in 95% ethanol (5 cc.) and concentrated hydrochloric acid (1.0 g.) was added, causing the suspension to become a clear solution. 2-Methylindole (0.44 g., 0.00335 mole) and additional 95% ethanol (1 cc.) were added and the solution was kept at room temperature for 18 hr. The reddish brown solution was decanted and the precipitated pale orange crystalline hydrochloride was mixed with ethanol (in which part of it dissolved) and neutralized with ethanolic sodium hydroxide solution, causing precipitation of sodium chloride. The mixture was kept, with occasional shaking, for 2 hr. and then diluted with water (100 cc.). The resulting brown precipitate (1.200 g.), m.p. 184–195°, was recrystallized from 1:1 benzene–petroleum ether (b.p. 60–68°), giving two crops of pinkish brown plates (0.817 g., 0.00229 mole, 70%), m.p. 192–195°. Four recrystallizations from benzene–petroleum

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[16] Section added to manuscript, May 1, 1961.

ether (b.p. 60–68°) yielded pinkish plates, m.p. 194–195°. The compound is sensitive to light and air and readily turns pink and finally reddish; λ_{max} in 95% ethanol: 226 mμ (log ϵ 4.54), 264 (4.29), 290 (4.00); ν_{NH} 3200, $\nu_{C=C}$ 1667, 1605 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{28}N_2$ (356.49): C, 84.22; H, 7.93; N, 7.86. Found: C, 84.14; H, 7.86; N, 7.83.

The compound was also obtained in another form from benzene–petroleum ether (b.p. 60–68°) as white micro needles, m.p. 203–205°, having an ultraviolet spectrum identical with that of the preceding sample. The infrared spectrum in Nujol differed only at two points: There was an additional NH band at 3320, and the band at 1305 cm.$^{-1}$ was relatively more intense.

Anal. Found: C, 84.25; H, 7.93; N, 7.78.

1,3-Bis-(2-methyl-3-indolyl)-1,3-diphenyl-1-butene (XIVa) (with Roger A. Lovald,[1d] 1960). 2-Methyl-3-(1-phenylvinyl)-indole[11] (m.p. 105.5–106°, 2.21 g., 0.00947 mole) was dissolved in hot 95% ethanol (5 cc.) and the solution cooled to room temperature. Concentrated hydrochloric acid (1.0 g.) was added and the solution kept at room temperature for 24 hr. The black solution was neutralized with ethanolic sodium hydroxide solution. The precipitated sodium chloride was filtered, and the filtrate evaporated. The residual oil and solid were dissolved in a little methanol and a small amount of ether added, causing precipitation of a white solid (0.60 g., 0.00128 mole, 27%), m.p. 224–230°. Three recrystallizations from ethanol-water yielded white crystals, m.p. 234–236°; λ_{max} in 95% ethanol: 224 mμ inflection (log ϵ 4.64), ~ 236–268 (broad region of inflection), 283 (4.05), 291 (4.02); ν_{NH} 3260 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{34}H_{30}N_2$ (466.60): C, 87.51; H, 6.48; N, 6.00. Found: C, 87.29; H, 6.65; N, 5.79.

The compound was recovered unchanged in 75% yield from attempted acetylation by warming for 15 min. in acetic anhydride solution.

Reaction of 2-methylindole with benzalacetophenone (M.R.V.). A solution of 2-methylindole (2.62 g., 0.20 mole), benzalacetophenone (2.08 g., 0.010 mole), and concentrated hydrobromic acid (2.5 g.) in 95% ethanol (18 g.) was kept at room temperature overnight. The red solution was neutralized with ethanolic sodium hydroxide solution, the precipitated sodium bromide was filtered off, and the filtrate was diluted with water, producing an oil. The oil was separated by decantation, dissolved in the minimum amount of hot ethanol, cooled to room temperature, and then kept in an ice-box. The white crystals (0.180 g., 5.1 × 10^{-4} mole, 5%) which precipitated were recrystallized three times from ethanol, yielding 3,3′-benzylidene-2,2′-dimethylbisindole, m.p. 248–249°; reported[17] m.p. 246–247°; λ_{max} in 95% ethanol: 227 mμ (log ϵ 4.78), 277 inflection (4.11), 283 (4.14), 291 (4.10); ν_{NH} 3390 cm.$^{-1}$ in Nujol. The infrared spectrum in Nujol was identical with that of an authentic sample, m.p. 252–255°,[15] prepared from benzaldehyde.[17]

Anal. Calcd. for $C_{25}H_{22}N_2$ (350.44): C, 85.68; H, 6.33; N, 7.99. Found: C, 85.72; H, 6.40; N, 8.03.

Passing dry hydrogen chloride into an equimolar solution of 2-methylindole and benzalacetophenone in anhydrous ether produced only a deep purple amorphous solid.[18]

3,3′-Isopropylidene-1,1′,2,2′-tetramethylbisindole (IIf) (with George J. Schroepfer, Jr.[19]). A solution of acetone (5.0 g., 0.086 mole) in concentrated hydrochloric acid (5.0 g.) was added to a solution of 1,2-dimethylindole (5.525 g., 0.0380 mole) in absolute ethanol (40 cc.), producing a brilliant red color. The solution was stirred briefly and then cooled in an ice bath for 30 min. The resulting yellowish white precipitate (3.690 g., 0.00112 mole, 59%), m.p. 167–178°, after being filtered off and dried, was partitioned between ether (180 cc.), ethanol (40 cc.), and aqueous 10% potassium hydroxide solution (40 cc.). The ethereal layer was separated and the aqueous layer extracted with ether (160 cc.). The combined ethereal extracts were dried over anhydrous magnesium sulfate and evaporated. The residual white solid was recrystallized from absolute ethanol, yielding colorless needles (1.064 g.), m.p. 195–197°; λ_{max} in 95% ethanol: 233 mμ (log ϵ 4.78), 289 (4.09), 293 (4.09).

Anal. Calcd. for $C_{23}H_{26}N_2$ (330.45): C, 83.59; H, 7.93; N, 8.48. Found: C, 83.48; H, 7.90; N, 8.51.

An attempt[20] to prepare the compound by refluxing a solution of 1,2-dimethylindole and acetone in glacial acetic acid for 3.5 hr. gave only an oil.

4-Ethyl-2-(2-methyl-3-indolyl)-3,4,4a,9a-tetrahydro-3,4,9a-trimethylcarbazole (XV, *isomers 1 and 2*) (C.G.R.). A solution of 2-methylindole (2.00 g., 0.0152 mole), methyl ethyl ketone (5.00 g., 0.0693 mole), and concentrated hydrochloric acid (3 g.) in 95% ethanol (10 cc.) was kept at room temperature for 24 hr. The solution was made basic with aqueous sodium hydroxide solution and the products were extracted with ether. The resulting pale yellow oil was dissolved in 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°) and chromatographed on alumina (350 g.). Elution with the same solvent gave first pale yellow semicrystalline oils (0.510 g.), which upon trituration with methanol left behind a white solid (0.430 g., 0.00116 mole, 15%), m.p. 192–197°. Crystallization from ethanol yielded isomer 1 as whitish crystals, m.p. 197.5–198°; λ_{max} in 95% ethanol: 226 mμ (log ϵ 4.55), 246 inflection (4.14), 284 (3.96), 291 (3.95): ν_{NH} 3320, $\nu_{C=C}$ 1607 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{26}H_{30}N_2$ (370.52): C, 84.28; H, 8.16; N, 7.56. Found: C, 84.41; H, 8.23; N, 7.87.

The mixed melting point with isomer 2 was depressed, 167.5–169.5°.

Further elution with 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°) gave a semicrystalline oil (0.740 g.), which upon trituration with methanol left behind a white solid (0.570 g., 0.00154 mole, 20%), m.p. 183–185°. Three recrystallizations from methanol yielded isomer 2 as white crystals, m.p. 197–199°; λ_{max} in 95% ethanol: 227 mμ (log ϵ 4.55), 254 (4.18), 283 (3.99), 291 (3.97); ν_{NH} 3310, 3240, $\nu_{C=C}$ 1665, 1605 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{26}H_{30}N_2$ (370.52): C, 84.28; H, 8.16; N, 7.56. Found: C, 84.14; H, 8.26; N, 7.89.

The mixed melting point with isomer 1 was depressed, 167.5–169.5°.

From another run, a sample of isomer 2 recrystallized from ethanol was found to have a lower melting point, 180–181°, but the infrared spectrum in Nujol was identical with that of the sample of Isomer 2 recrystallized from methanol, suggesting the presence of dimorphic forms.

Anal. Found: C, 84.21; H, 8.17.

Monoacetyl derivative of isomer 1 (*of* XV) (with H. S. Desai,[1e] 1960). The compound was obtained in 21% yield from isomer 1 of the monobase and acetic anhydride; white cubic crystals from methanol, m.p. 193–196°; λ_{max} in 95% ethanol; 217 mμ (log ϵ 4.64), 258 (4.26), 284 (4.11), 291 (4.07); ν_{NH} 3310, $\nu_{C=O}$ 1630 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{28}H_{32}N_2O$ (412.55): C, 81.51; H, 7.82; N, 6.79. Found: C, 81.30; H, 7.86; N, 6.91.

Monoacetyl derivative of isomer 2 (*of* XV) (with H. S. Desai,[1e] 1961).[16] The compound was obtained in 31% yield from isomer 2 of the monobase and acetic anhydride; pale yellowish white crystals from ethanol, m.p. 216–219°; λ_{max} in 95% ethanol: 215 mμ (log ϵ 4.64), 227 inflection (4.57), 262 (4.32), 283 inflection (4.17), 290 inflection (4.12); ν_{NH} 3360, $\nu_{C=O}$ 1649 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{28}H_{32}N_2O$ (412.55): C, 81.51; H, 7.82; N, 6.79. Found: C, 81.11; H, 8.14; N, 6.90.

MINNEAPOLIS 14, MINN.

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(17) E. Fischer, *Ber.*, 19, 2988 (1886).

(18) Experiment performed by Allan M. Huffman, 1959.

(19) Postdoctoral Research Fellow of the National Heart Institute, U. S. Public Health Service, 1959.

(20) By Joel G. Malmberg, 1958.