analytical sample as colorless lustrous crystals, m.p. 176–178°; λ_{max} in 95% ethanol, 223 mμ (log ϵ 4.55), 265 (4.25), 282 inflection (3.96), 289 (3.91), 311 (3.53); ν_{NH} 3360 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{30}N_2$ (358.51): C, 83.75; H, 8.43; N, 7.81. Found: C, 83.61; H, 8.41; N, 7.69.

MINNEAPOLIS 14, MINN.

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

Cyclizative Condensations. III. Indole and 1-Methylindole with Methyl Ketones

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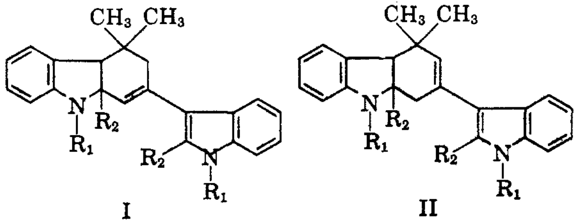
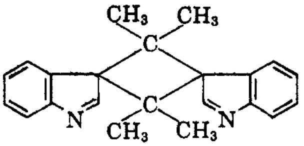
Condensation of indole with acetone in ethanolic hydrochloric acid gave five products, one of which was the easily autoxidizable monobase Ib. Acetylation and methylation of Ib was accompanied by loss of a molecule of hydrogen, giving the diacetyldehydro (IVa) and dimethyldehydro (IVb) derivatives. Condensation of 1-methylindole with acetone gave the same dimethyldehydro derivative (IVb), as well as the bisindole Va in larger yield, while condensation with mesityl oxide gave, depending upon the mole ratio, the 1:1 adduct VIb or the bisindole Va, along with 1-methylindole trimer. Reaction of indole with mesityl oxide gave the 1:1 adduct VIa. Heating of VIb at 140–150° gave a 2:1 condensation and rearrangement product (Vb or IX). Condensation of 1-methylindole with methyl isobutyl ketone gave a 2:2 product, probably XII or XIII, and a 1:2 product, possibly XIV or XV. Attempted cyclization of the 1:1 adduct of indole and methyl vinyl ketone gave two crystalline bimolecular condensation products, a neutral acyclic product (XVIII), and a basic cyclization product which is an indoline derivative, possibly XX.

In Paper I[2] of this series the structure of the monobasic 2:2 condensation product of 2-methylindole and acetone is shown to be Ia (or IIa); two similar cyclization products from 2-methylindole and methyl ethyl ketone are also described. In Paper II[3] cyclizative condensation of 2-methylindole with α,β-unsaturated methyl ketones and with their 1:1 adducts with indoles is shown to be quite general. In 1913 Scholtz[4] reported that the condensation of indole with acetone proceeded less smoothly than the corresponding reaction of 2-methylindole, but yielded, after the action of alkali on the orange-yellow monohydrochloride, a light yellow monobase, $C_{22}H_{22}N_2$, m.p. 170°, to which structure III was incorrectly assigned. We have confirmed the formation of a monobase having this empirical formula, melting point, and color.



I II

Ia or IIa. $R_1 = H$, $R_2 = CH_3$
Ib or IIb. $R_1 = H$, $R_2 = H$
Ic or IIc. $R_1 = CH_3$, $R_2 = H$



III

Condensation of indole with acetone was a very complex reaction, and gave, after chromatography of the products, five compounds, all of which may be products of cyclizative condensation:

(1) "Compound 1," white. m.p. 253–255°, the major product isolated in 9–24% yield, has the empirical formula $C_{25}H_{26}N_2$, corresponding to condensation of two indole and three acetone molecules, with loss of three molecules of water. The compound has a primarily indole type of ultraviolet spectrum, with an additional strong band at 234 mμ. The intensities of the absorption bands indicate that both indole nuclei are participating in the absorption (see Experimental). The two NH bands in the infrared spectrum suggest that both nitrogens of the indole nuclei remain unsubstituted. The compound is very sensitive to autoxidation and easily decomposes autoxidatively when recrystallization is attempted from hot solvents or when the compound is kept in solution for a considerable time. Under such conditions a crystalline autoxidation product, "compound 1 dioxide," $C_{25}H_{26}N_2O_2$,

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[1] It is a pleasure to acknowledge support of most of this research from Research Grant CY-4073 from the National Cancer Institute, U. S. Public Health Service (C.G.R., H.S.D., M.R.V., Oct. 1958–Dec. 1960), and the du Pont Co. (M.R.V., Sept. 1957–Sept. 1958) through a Grant-in-Aid to the Department of Chemistry; postdoctoral fellows: (a) C.G.R., Jan. 1959–June 1960; (b) H.S.D., Sept.–Dec. 1960; (c) M.R.V., Sept. 1957–Dec. 1958. A small part of this work was presented as part of Paper 174 before the Organic Division at the 138th National Meeting of the American Chemical Society, New York, N. Y., Sept. 16, 1960, Abstracts, p. 92P, and as part of Paper 39 by W. E. Noland, M. H. Fischer, D. N. Robinson, and H. Sorger-Domenigg, presented before the Organic Division at the 131st National Meeting of the American Chemical Society, Miami, Fla., April 9, 1957, Abstracts, p. 24–O.

[2] W. E. Noland, M. R. Venkiteswaran, and C. G. Richards, *J. Org. Chem.*, **26**, 4241 (1961).

[3] W. E. Noland, M. R. Venkiteswaran, and R. A. Lovald, *J. Org. Chem.*, **26**, 4249 (1961).

[4] M. Scholtz, *Ber.*, **46**, 1082 (1913).

white, m.p. 175–178°, having a strong carbonyl infrared band at 1736 cm.$^{-1}$ is formed. Autoxidation of "compound 1" in acetic anhydride solution yielded "monoacetyl compound 1 dioxide," $C_{27}H_{28}N_2O_3$, white, m.p. 230–231°, having a strong carbonyl infrared band at 1699 cm.$^{-1}$

(2) The yellow monobase, $C_{22}H_{22}N_2$, m.p. 170–171°, described by Scholtz,[4] was isolated in 12% yield, or 11% yield without chromatography, in which case it is usually the only crystalline product isolated, as was found previously.[4] The preparation is difficult to reproduce, as the monobase is very easily autoxidized, particularly in the impure state, apparently at least in part to another yellow compound, "compound 2" (see below). Sometimes small amounts of "compound 2," as well as "compound 3," were also isolated without chromatography, but never "compound 1." The ultraviolet spectrum of the yellow monobase contains an indoline band[5] at 261 mμ, and indole-type bands at 226 and 283 mμ. The spectrum is fairly analogous to that of the colorless monobases such as Ia, the yellow color being due to a weak tailing out of ultraviolet absorption into the visible region, not to the appearance of an additional band. The infrared spectrum in Nujol contains three NH bands and a medium strength olefinic band at 1637 cm.$^{-1}$ The monobase is assigned structure Ib or IIb by analogy with the structure of the 2-methylindole product (Ia or IIa), the position of the olefinic double bond being uncertain in both cases. It is easier, however, to account for the ready dehydrogenation of the monobases derived from indole and 1-methylindole (in which case, as discussed below, only the dehydrogenated product, IVb, was isolated) if they are assigned structures of type 1, rather than type II. Consequently, only the designations I have been used throughout the remainder of the paper. In structures I the 2-hydrogen of the indoline nucleus is allylic with respect to a 3-vinylindole system, as well as being tertiary and alpha to an amino nitrogen, all of these being factors which should favor autoxidative attack at the 2-hydrogen. An analogous monobase derived from 1,3-dimethylindole (structure XII in Paper I[2]), which likewise contains a hydrogen in the 2-position of the indoline nucleus, is also notably sensitive to autoxidation, probably in this case to a rosindole, as the compound turns pink and finally reddish in contact with light and air. Additional support for the 2-hydrogen being the point of autoxidative attack is the fact that the analogous monobase (Ia or IIa), containing a 2-methyl group instead of a 2-hydrogen on the indoline nucleus, is not sensitive to autoxidation.

(3) "Compound 2," yellow, m.p. 219–220° (or 230–231° in another form), a minor product isolated in 2–4% yield, has the empirical formula $C_{22}H_{20}N_2O$, corresponding to autoxidation of the monobase, with loss of a molecule of water. The ultraviolet spectrum contains an intense long wave length maximum at 385 mμ (log ε 4.46), which almost certainly indicates the presence of conjugation between the two present or former indole nuclei in the molecule. In this respect the yellow compound resembles the yellow *N,N'*-dimethyldehydro derivative (IVb) of the monobase, which contains a long wave length ultraviolet maximum at 375 mμ (log ε 4.14). The infrared spectrum of "compound 2" shows that the oxygen is not present in a carbonyl group, but may be present in a hydroxyl group or ether linkage. When heated in acetic anhydride solution, "compound 2" yielded a yellow triacetyl derivative, $C_{28}H_{26}N_2O_4$, m.p. 220°. These observations appear at first to be consistent with structure IVc for "compound 2," but this structure is by no means established, particularly in view of the lack of resemblance of the ultraviolet spectra of the triacetyl derivative of "compound 2" and the diacetyldehydro derivative (IVa) of the monobase, which has an ultraviolet chromophore identical with that of structure IVc.

(4) "Compound 3," white, m.p. 260°, a minor product isolated in up to 4% yield, has the empirical formula $C_{25}H_{26}N_2$, the same as "compound 1," of similar melting point. The ultraviolet spectrum of "compound 3," however, is much more conjugated, possibly of the carbazole type, and contains a complex plateau of strong absorption in the 234–254 mμ region, with less intense longer wave length bands at 290, 339, and 353 mμ. The infrared spectrum contains olefinic absorption at 1644 cm.$^{-1}$ and stronger double bond bands at 1624 and 1584 cm.$^{-1}$ The compound forms a diacetyl derivative, $C_{29}H_{30}N_2O_2$, m.p. 226–229°, which, surprisingly, still contains an NH band in the infrared spectrum.

(5) "Compound 4," yellow, m.p. 213–215°, a trace product isolated in less than 0.6% yield, has an infrared spectrum containing NH absorption, a strong carbonyl band at 1679 cm.$^{-1}$, and a strong conjugated double bond band at 1619 cm.$^{-1}$, suggesting the presence of an indole-containing α,β-unsaturated ketone.

Acetylation of the indole-acetone reaction products, followed by chromatography, gave again "compound 1" as the major product, in 21% yield. This was followed by "compound 5," white, m.p. 218–219°, a trace product (1% yield), which has the empirical formula $C_{27}H_{28}N_2O$, corresponding to a monoacetyl derivative of "compound 1" or "compound 3." The final product, white, m.p. 244.5–245.5°, isolated in 12% yield, has the properties to be expected of the monoacetyl derivative of the yellow monobase Ib, as shown by elemental analysis and ultraviolet and infrared spectra.

Direct acetylation of the previously isolated

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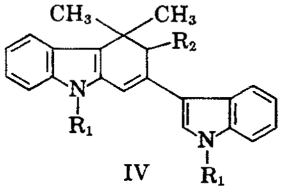
(5) W. E. Noland and C. F. Hammer, *J. Org. Chem.*, 25, 1525 (1960).

yellow monobase (Ib), however, was accompanied by autoxidation, and gave in 82% yield a white diacetyl derivative (IVa), m.p. 210–210.5°, in which a molecule of hydrogen has been lost. The infrared spectrum has no NH band, indicating that both acetyl groups are present as *N*-acetyl groups. The complex carbonyl absorption in Nujol is reduced in chloroform solution to a single strong carbonyl band at 1686 cm.$^{-1}$ The ultraviolet spectrum has the longest wave length inflection at 320 mμ, suggesting that there is only limited conjugative interaction between the indole nuclei, probably because of electron withdrawal from the nitrogen atoms into the amide carbonyl groups. Formation of a diacetyldehydro derivative is interpreted in terms of a prior acetylation of the basic indoline nitrogen, followed by autoxidative dehydrogenation of the acetylated indoline nucleus to an indole. Acetylation of the acidic 3-vinylindolyl nitrogen, whereas in all the preceding cases[2,3] the 2-methyl-3-vinylindolyl nitrogen did not acetylate, has analogy in the fact that acetylation of indole yields 1,3-diacetylindole[6] under conditions under which the more hindered 2-methylindole yields 3-acetyl-2-methylindole, with only small amounts of 1-acetyl-2-methylindole.[7] 1,3-Diacetyl-2-methylindole is, in fact, unknown.



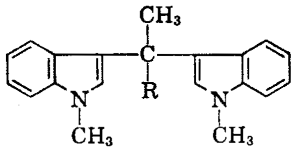
IV

IVa. $R_1 = COCH_3$; $R_2 = H$
IVb. $R_1 = CH_3$; $R_2 = H$
IVc. $R_1 = COCH_3$; $R_2 = OH$

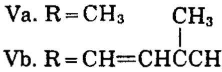
Methylation of the yellow monobase Ib with sodamide and methyl iodide in liquid ammonia was also accompanied by dehydrogenation, giving a yellow dimethyl derivative (IVb), in which a molecule of hydrogen has been lost. Prior dehydrogenation of the indoline nucleus in the reaction medium would make the previously basic nitrogen acidic, and thus account for the dimethylation observed. Absence of an NH band in the infrared spectrum indicates that both entering methyl groups have gone onto the nitrogen atoms. The highly conjugated ultraviolet spectrum, which includes an intense, long wave length maximum at 375 mμ (log ϵ 4.14), seems to require that the vinylindole double bond of IVb is in the conjugated position between the two 1-methylindole nuclei.

Condensation of 1-methylindole with acetone in ethanolic hydrochloric acid gave the corresponding bisindole (Va) in 56% yield. The same bisindole was obtained in 19% yield from condensation of 1-methylindole and acetone in refluxing acetic acid. Chromatography of the remaining products from the condensation in ethanolic hydrochloric acid gave in 14% yield the same yellow dimethyldehydro derivative (IVb) as was obtained from methylation of the indole monobase (Ib), thus establishing a firm relationship between the indole and 1-methylindole cyclizative condensation reactions. In the 1-methylindole case, a molecule of hydrogen must have been lost autoxidatively from the expected monobase Ic either in the ethanolic hydrochloric acid medium used for the condensation, or on the alumina column during chromatography.

Condensation of 1-methylindole with mesityl oxide, employed in 2:1 molar ratio in ethanolic hydrochloric acid gave, without chromatography of the products, the bisindole Va in 36% yield and, in 20% yield, 1-methylindole trimer,[8] identified by comparison with an authentic sample[9] prepared by the hydrochloric acid-catalyzed trimerization of 1-methylindole. Formation of the bisindole Va from mesityl oxide indicates either (a) that mesityl oxide undergoes partial hydrolysis to acetone or its equivalent, an event which is quite probable under the acidic conditions used; or (b) that, under conditions of acidic catalysis, the protonated 1:1 adduct VIb, which may have formed first, undergoes ethylogous fragmentation[10] to 1-methyl-3-isopropylideneindoleninium cation and acetone, an event which has not as yet been demonstrated to occur.



V


Va. $R = CH_3$
Vb. $R = CH{=}CH\overset{\overset{CH_3}{|}}{C}CH_3$

Reaction of equimolar portions of indole and mesityl oxide gave the 1:1 adduct VIa in 6% yield as the only crystalline product. The corresponding reaction of 1-methylindole and mesityl oxide gave the adduct VIb as an oil in 28% yield. The adducts have an indole ultraviolet spectrum and a carbonyl band in the infrared, and an oxime, m.p. 118–118.5°, was prepared from VIb. We had hoped to introduce a methyl group into the 3- position of VIb and thereby induce methylative cyclization, as a very simple synthetic proof of structure of the 1,3-dimethylindole-mesityl oxide adduct (VIII).[11] The methylation sequence (VIb→VII→VIII) was,

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[6] J. E. Saxton, *J. Chem. Soc.*, 3592 (1952).

[7] (a) O. R. Jackson, *Ber.*, 14, 880 (1881); (b) G. Magnanini, *Ber.*, 21, 1936 (1888).

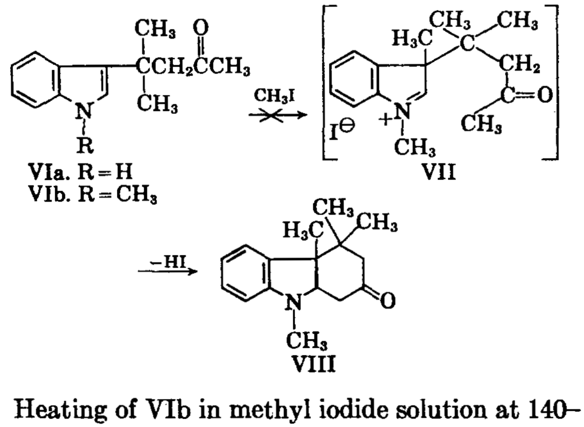
[8] O. Schmitz-Dumont and K. H. Geller, *Ber.*, **66**, 766 (1933).

[9] William C. Kuryla, Ph.D. thesis, University of Minnesota, Sept. 1960, pp. 24, 48.

[10] C. A. Grob, *Experientia*, **13**, 126 (1957).

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

however, unsuccessful. (The proof of structure of VIII has recently been accomplished by another method.[12])

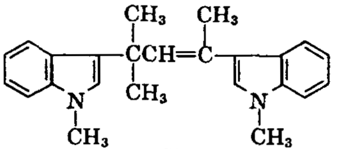


VIa. R = H
VIb. R = CH_3

VII

VIII

Heating of VIb in methyl iodide solution at 140–150° in an autoclave gave, besides unchanged starting material in 46% recovery (after distillation), an 11% yield of a crystalline product, m.p. 177.5–178°, having the composition of a 2:1 condensation product of 1-methylindole and mesityl oxide. Formation of this 2:1 condensation product can be most easily interpreted in terms of a partial dissociation of VIb into its precursors, 1-methylindole and mesityl oxide, followed by condensation of the 1-methylindole with the carbonyl group of unchanged VIb, yielding the 3-vinylindole IX, which is structurally analogous to the dimer of 2-methyl-3-(1-phenylvinyl)indole (structure XIVa in Paper I[2]). Alternatively, 1-methylindole and mesityl oxide, formed by dissociation, could condense to form the bisindole Vb. The typical indole ultraviolet spectrum (see, for example, those of Va and VIb) is consistent with the bisindole structure Vb and possibly with the 3-vinylindole structure IX, but absence in the infrared spectrum of any olefinic double-bond band at higher frequency than the indole double-bond band at 1612 cm.$^{-1}$ tends to favor the 3-vinylindole structure IX for the condensation product. Its failure to tautomerize to the terminal vinylindole and subsequently to cyclize to the corresponding monobase (Ic) can be reconciled with the absence of an acid catalyst in the neutral reaction medium employed.



IX

Condensation of 1-methylindole with methyl isobutyl ketone in ethanolic hydrochloric acid gave markedly different results from those obtained with 2-methylindole.[8] In contrast to the monobasic 2:1 product obtained from 2-methylindole and methyl isobutyl ketone, 1-methylindole and methyl isobutyl ketone gave two products, a 2:2 and a 1:2 condensation product. The first product, isolated in 25% yield, corresponds in composition to the simple 3-vinylindole 1:1 condensation product X, but the fact that it is a crystalline solid, m.p. 148–150°, rather than an oil like VIb, an open-chain compound of slightly higher molecular weight, suggests strongly that it is a dimer of X. Many possibilities for structural isomerism exist in such a dimer, but structures XII and XIII are proposed as most probable, as they are easily derived from acid-catalyzed self-addition of X or the reactive tautomeric form XI. Dimer structure XII is analogous to the indolo-[3,2,-b]carbazole structure proposed for the dimer of 3-(1-phenylvinyl)indole (see Paper IV[13]). Dimer structure XIII is analogous to the 3-vinylindole IX or to the dimer of 2-methyl-3-(1-phenylvinyl)-indole (structure XIVa in Paper I[2]). The typical indole ultraviolet spectrum, with no evidence of indoline bands, and the absence in the infrared spectrum of an olefinic band at higher frequency than the indole double-bond band at 1611 cm.$^{-1}$, are consistent with the indolo[3,2-b]carbazole structure XII and possibly with the 3-vinylindole structure XIII.

The other product, an oil formed in 21–75% yield, is a condensation product of 1-methylindole and methyl isobutyl ketone in a 1:2 molar ratio. It forms a crystalline 1,3,5-trinitrobenzene derivative, m.p. 105.5–106°. The ultraviolet spectrum is considerably more conjugated than a simple indole, and has the strongest bands at 225 (4.28), 250 (4.12) and 316 (4.09), with the longest wave length band at 329 mμ (log ε 3.89). The infrared spectrum of the oil contains double-bond bands at 1649 and 1610 cm.$^{-1}$ It appears likely that the condensation product may contain a 1-methylindole nucleus conjugated with a 1,3-butadiene system. Among the various possible isomeric structural formulas, XIV and XV have the advantage that they are derivable from a common intermediate (XI, already proposed in the formation of XIII), by acid-catalyzed addition of the reactive vinylindole group of XI to the carbonyl group of methyl isobutyl ketone, with subsequent dehydration. The presence of two conjugated double bonds is indicated by formation of a maleic anhydride adduct, which was isolated as the diacid. The ultraviolet spectrum of the adduct contains bands at 247 mμ (log ε 3.93) and 298 mμ (log ε 3.44), indicating the presence in the adduct of more conjugation than would be present in a simple 1,3-dialkylindole derivative (see, for example, the ultraviolet data for Va and VIb), such as would be found in the chromophore of the adduct of XIV. The data tend to favor a structure such as XV, which would

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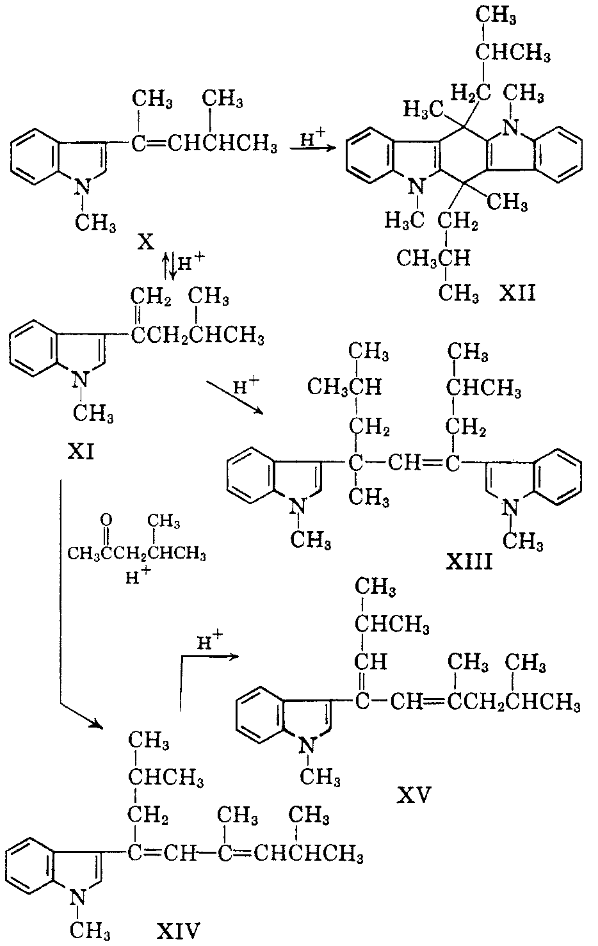
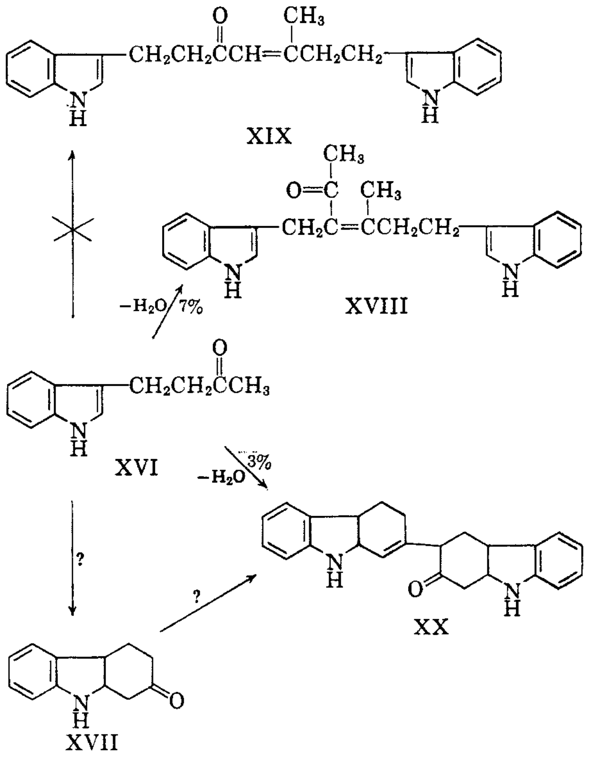
[12] B. Robinson and G. F. Smith, *J. Chem. Soc.*, 4574 (1960).

[13] W. E. Noland and M. R. Venkiteswaran, *J. Org. Chem.*, 26, 4263 (1961).



give an adduct containing the 3-vinylindole chromophore, in which there is unsaturation still conjugated with the indole nucleus.

Because of a possible relationship to the mechanism of formation of monobases like Ia or Ib, the tendency of the 1:1 adduct of indole and methyl vinyl ketone (XVI)[14,15] to cyclize in ethanolic hydrochloric acid was examined. It was hoped by this means to prepare the cyclic ketone XVII, and, in turn, to examine its reaction behavior toward indoles as a model for a possible step in the mechanism of formation of monobases of type I. The results with the 1:1 adduct (XVI) were more complex than had been desired. After chromatography of the neutral and basic reaction products, two colorless crystalline products were isolated, one from each fraction. The neutral product (XVIII), m.p. 241.5–242.5°, isolated in 7% yield, results from a bimolecular aldol condensation of the ketone side chain of XVI. The infrared spectrum indicates the presence of an α,β-unsaturated ketone. The ultraviolet spectrum in 95% ethanol contains typical indole absorption and, in addition, a band at 250 (4.11) and an inflection at 309 mμ (log ϵ 3.60), attributed to the K and R bands of an α,β-unsaturated ketone.[16] The observed wave length of the K band (250 mμ) is in excellent agreement with that calculated (247 ± 5 mμ) for the structure proposed for the neutral product (XVIII) according to Woodward's rules for a trisubstituted α,β-unsaturated ketone, and with that observed (249 mμ, log ϵ > 3.60) for the model compound, 3,4-dimethyl-3-buten-2-one. The orientation of condensation in XVIII is in accord with that observed in acid for the related compound, methyl ethyl ketone, which yields 3,4-dimethyl-3-hexen-2-one and its β,γ-unsaturated isomer.[17] The observed wave length of the K band (250 mμ) in XVIII rules out the possibility that the neutral product could have the alternative structure (XIX) involving condensation at the methyl group of the ketone, because the wave length calculated for the disubstituted α,β-unsaturated ketone which would result is 235 ± 5 mμ.



The basic product, m.p. 246–249°, isolated in 3% yield, has the same empirical formula as the neutral product and, like it, appears to be an aldol condensation product. The simple ultraviolet spectrum, however, has only two maxima, at 238 (4.12) and 283 mμ (log ϵ 3.82), characteristic of indolines,[5] but the intensities are twice those of simple indolines, indicating the presence of two indoline nuclei in the molecule. The infrared spec-

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[14] J. Szmuszkovicz, *J. Am. Chem. Soc.*, **79**, 2819 (1957).

[15] Ronald F. Lange, Ph.D. thesis, University of Minnesota, June 1958, pp. 77–78.

[16] A. E. Gillam and E. S. Stern, *Electronic Absorption Spectroscopy*, Edward Arnold Ltd., London, England, 1954, pp. 94–95.

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

trum indicates the presence of a ketone carbonyl and of olefinic unsaturation. The results indicate that, at least to a limited extent, the desired cyclization has taken place, but that complications resulting from aldol condensation have carried the reaction farther than had been desired. The structure of the basic product appears to be of the type illustrated by formula XX.

EXPERIMENTAL

The initials of coauthors 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.

Condensation of indole and acetone in ethanolic hydrochloric acid. (A) Without chromatography of products (M.R.V.). A solution of indole (5.00 g., 0.0426 mole), acetone (10.0 g., 0.172 mole), and concentrated hydrochloric acid (5.0 g.) in 95% ethanol (20 g.) was kept at room temperature for 5 days. The deep brown solution was neutralized with aqueous ethanolic sodium hydroxide solution and the resulting mixture extracted with ether, and the ether extract washed with water, dried, and the ether evaporated. The residual brown oil was dissolved in ethanol, treated with charcoal, and concentrated, producing pale yellow crystals (0.75 g., 0.00238 mole, 11%). Three recrystallizations from ethanol yielded *4,4-dimethyl-2-(3-indolyl)-3,4,4a,9a-tetrahydrocarbazole* (Ib) as pale yellow rectangular prisms, m.p. 170–171°; reported: no yield given, m.p. 170°[4]; λ_{max} in 95% ethanol: 226 mμ (log ϵ 4.43), 261 (4.33), 283 (4.06); ν_{NH} 3370s, 3300w, 3100s, $\nu_{C=C}$ 1637 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{22}H_{22}N_2$ (314.41): C, 84.04; H, 7.05; N, 8.91. Found: C, 84.14; H, 6.91; N, 9.12.

(B) With direct chromatography of products (C.G.R., H.S.D.). The reaction was carried out and worked up as described in part A except that 20 cc. of ethanol was used (instead of 20 g.) and the reaction solution was kept for 24 hr. (instead of 5 days). The residual brown, viscous oil was dissolved in benzene–petroleum ether (b.p. 60–68°) and chromatographed on alumina (350 g.). Elution with the same solvent gave first a pale yellowish oil which crystallized to colorless prisms (2.00 g., 0.00517 mole, 24%), m.p. 245–248°. The compound was recrystallized three times *at room temperature* by dissolving it in methylene chloride, then adding petroleum ether (b.p. 60–68°), and promptly removing the methylene chloride under reduced pressure, yielding "*compound 1*" as white crystals, m.p. 253–255°; λ_{max} in 95% ethanol: 226 mμ inflection (log ϵ 4.79), 234 (4.85), 285 (4.29), 291 inflection (4.26); ν_{NH} 3430, 3390 cm.$^{-1}$ in Nujol. The infrared spectrum of the analytical sample was the same as that of the crude sample.

Anal. Calcd. for $C_{25}H_{26}N_2$ (354.47): C, 84.70; H, 7.39; N, 7.90. Found: C, 84.88; H, 7.28; N, 7.99.

The compound showed a marked tendency to decompose autoxidatively upon attempted recrystallization from boiling benzene, petroleum ether, methylene chloride, acetone, or ethanol, as the solutions tended to turn brown and deposit varying amounts of white crystals, m.p. 175–178°. This autoxidative decomposition even occurred after a time in solution at room temperature. For example, when the compound was dissolved in methylene chloride–petroleum ether (b.p. 60–68°) and allowed to evaporate slowly at room temperature, the colorless solution turned brown and after 2 days deposited "*compound 1 dioxide*" as white crystals, m.p. 175–178°, λ_{max} in 95% ethanol: 230 mμ (log ϵ 4.65), 284 (4.06) 291 inflection (4.02); $\nu_{OH,\ NH}$ 3500m, 3350s, 3300w inflection, $\nu_{C=O}$ 1736s, $\nu_{C=C}$ 1612s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{26}N_2O_2$ (386.47): C, 77.69; H, 6.78; N, 7.25. Found: C, 77.15; H, 7.07; N, 7.28.

"*Monoacetyl compound 1 dioxide*" (H.S.D.). A solution of "compound 1" (m.p. 248–250°, 1.00 g., 0.00282 mole) in acetic anhydride (6 cc.) was kept at room temperature for 1 day, then heated at 98° in a water bath for 2 hr., and again kept at room temperature for 1 day. The solution was poured on crushed ice and the resulting mixture kept overnight. The brownish precipitate (0.330 g., 27%), m.p. 198–235°, was crystallized from benzene, giving a sample (0.230 g., 0.000537 mole, 19%), m.p. 230–231°. Two recrystallizations from benzene yielded small whitish needles, m.p. 230–231°; λ_{max} in 95% ethanol: 225 mμ (log ϵ 4.69), 247 inflection (3.76), 254 (3.74), 260 (3.80), 275 (3.95), 290 (3.83); ν_{NH} 3420m, $\nu_{C=O}$ 1714w, 1699s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{27}H_{28}N_2O_3$ (428.51): C, 75.67; H, 6.59; N, 6.54. Found: C, 75.85; H, 6.56; N, 6.66.

Further elution with benzene–petroleum ether (b.p. 60–68°) gave a yellow oil (1.44 g.), which partially crystallized. Crystallization from benzene–petroleum ether (b.p. 60–68°) gave a yellow solid (0.80 g., 0.00254 mole, 12%), m.p. 156–158°. The solid is difficult to crystallize, as it tends to autoxidize to an amorphous, yellowish brown mixture. Recrystallization from benzene–petroleum ether (b.p. 60–68°) yielded *4,4-dimethyl-2-(3-indolyl-3,4,4a,9a-tetrahydrocarbazole* (Ib) as a yellow solid, m.p. 170–171°. The infrared spectrum in Nujol was the same as that of the sample described in part A.

Anal. Found: C, 84.34; H, 6.98; N, 9.21.

Further elution, with ether, gave an oily yellow solid. Washing with acetone gave yellow solid (0.110 g., 0.00034 mole, 2%), m.p. 212–217°. Two recrystallizations from benzene yielded "*compound 2*"[18] as bright yellow flakes, m.p. 219–220°; λ_{max} in 95% ethanol: 225 mμ (log ϵ 4.33), 251 (4.10), 279 (3.85), 385 (4.47;) $\nu_{OH,\ NH}$ 3390w, 3170ms. $\nu_{C=O}$ none, $\nu_{C=C}$ 1614mw, 1589s. 1574s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{22}H_{20}N_2O$ (328.40): C, 80.46; H, 6.14; N, 8.53. Found: C, 80.48; H, 6.31; N, 8.42.

The compound was obtained in another form, after three recrystallizations from ethanol, as yellow flakes, m.p. 230–231°. The infrared spectrum in Nujol and the ultraviolet spectrum in 95% ethanol were identical with those of the lower-melting sample described above.

Anal. Found: C, 80.63; H, 6.40; N, 8.41.

"Compound 2" in suspension in dry tetrahydrofuran (in which it did not dissolve) was recovered unchanged in 78% yield from attempted methylation with methyl iodide and sodamide in liquid ammonia.

Triacetyl derivative of "compound 2" (H.S.D.). A mixture of "compound 2" (m.p. 218–220°, 0.300 g., 0.000913 mole) and acetic anhydride (12 cc.) was kept overnight and then heated to 100° to form a homogeneous solution. The solution was heated at 100° for 2 hr. and kept overnight again at room temperature. The pale lemon yellow crystals (0.116 g., 0.000256 mole, 28%), m.p. 215–220°, which separated, were recrystallized twice from ethanol-benzene, yielding pale lemon yellow plates, m.p. 220°; λ_{max} in 95% ethanol: 218 mμ (log ϵ 4.56), 276 (4.03), 309 inflection (4.01), 373 (4.47); $\nu_{OH,\ NH}$ none, $\nu_{C=O}$ 3390 (faint overtone), 1727ms, 1701s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{28}H_{26}N_2O_4$ (454.51): C, 73.99; H, 5.77; N, 6.16. Found: C, 74.07; H, 5.73; N, 6.17.

When the reaction of indole and acetone was carried out on a scale fifteen times that described above, and the mildly exothermic reaction solution was kept for 48 hr. at room temperature, in addition to compound 1 (isolated in 9% yield) and compound 2 (isolated in 4% yield), two new compounds were isolated. After the deep brown reaction solution had been neutralized with aqueous potassium hydroxide solution and extracted with ether and benzene, there remained an amorphous white residue (4.45 g., 0.0126 mole, 4%), m.p. 240–248°, along with some sticky polymeric material (2.15 g.) which was separated by trituration with ether. The white residue decomposed slowly in hot acetone or ethanol solutions, as indicated by gradual appearance of a brown color,

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[18] First described by Donald N. Robinson, Ph.D. thesis, University of Minnesota, March 1959, pp. 188–190.

but purification was successfully accomplished by three recrystallizations from hot benzene, yielding *"compound 3"* as white needles, m.p. 260° (turns brown ~210°); λ_{max} in 95% ethanol: 234 mμ inflection (log ε 4.47), 238 (4.48), 245 (4.48), 254 (4.47), 261 inflection (4.42), 290 (3.82), 325 inflection (3.48), 339 (3.68), 353 (3.67); ν_{NH} 3430mw, 3330m, 3210ms, $\nu_{C=C}$ 1644ms, 1624s, 1603w, 1584s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{26}N_2$ (354.47): C, 84.70; H, 7.39; N, 7.90. Found: C, 84.70; H, 7.41; N, 7.93.

During the chromatography an additional small amount of "compound 3" (0.20 g.), m.p. 240–248°, was eluted with ether just after "compound 4" and before the bulk of "compound 2." Two recrystallizations from benzene gave colorless needles, m.p. 260°, having an infrared spectrum in Nujol identical with that of the sample described above.

Anal. Found: C, 84.66; H, 7.40; N, 7.87.

Diacetyl derivative of "compound 3" (H.S.D.). A solution of "compound 3" m.p. 260°, 0.100 g., 0.00028 mole) in acetic anhydride (3 cc.) was kept at room temperature for 1 day, then heated at 100° for 2 hr. and kept at room temperature for another day. The solution was poured on crushed ice and the mixture left for 10 hr., with occasional shaking. The white precipitate (0.031 g., 0.00071 mole, 25%), m.p. 222–226°, oiled out when crystallization was attempted from ethanol or acetone, but crystallization of the oil from benzene–light petroleum (b.p. 60–68°) gave a white amorphous powder, which was washed several times with petroleum ether (b.p. 60–68°) yielding a sample, m.p. 226–229°; λ_{max} in 95% ethanol: 238 mμ (log ε 4.56), 246 inflection (4.54), 253 inflection (4.50), 262 inflection (4.40), 287 inflection (3.71), 299 (3.68), 309 inflection (3.56), 323 inflection (3.56), 339 (3.73), 353 (3.71); ν_{NH} 3300m, $\nu_{C=O}$ 1683w, 1665s, $\nu_{C=C}$ 1636m, 1589ms, 1541s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{29}H_{30}N_2O_2$ (438.55): C, 79.42; H, 6.90; N, 6.39. Found: C, 79.28; H, 7.23; N, 6.58.

The earliest fraction of the ether eluate of "compound 3" was contaminated with a trace product, in the form of yellow needles (<0.585 g., <0.6%), which was separated by hand and by fractional crystallization. Four recrystallizations from benzene yielded *"compound 4"* as yellow needles, m.p. 213–215°; ν_{NH} 3380m, 3310m, $\nu_{C=O}$ 1679s, $\nu_{C=C}$ conj. 1619s cm.$^{-1}$ in Nujol.

Anal. Found: C, 81.42; H, 6.44.

(C) With acetylation before chromatography of products (C.G.R.). A solution of indole (2.00 g., 0.0170 mole), acetone (4.0 g., 0.066 mole), and concentrated hydrochloric acid (2.0 g.) in 95% ethanol (10 cc.) was cooled in ice for 0.5 hr. and then kept at room temperature for 4 days. The solution was neutralized with aqueous potassium hydroxide solution, extracted with ether, and the ether evaporated. The residual oil was dissolved in acetic anhydride (50 cc.), refluxed for 1.5 hr., and then kept overnight. The solution was poured on ice and the oily product, which solidified (3.55 g.), was dissolved in benzene and chromatographed on alumina (200 g.). Elution with benzene–petroleum ether (b.p. 60–68°) gave "compound 1" (0.700 g., 0.00181 mole, 21%), m.p. 243–245°, mixed melting point with the sample obtained by direct chromatography, 250–252°.

Further elution with benzene–petroleum ether (b.p. 60–68°) gave a light tan solid (0.035 g., 0.000088 mole, 1%), m.p. 201–206°. Four recrystallizations from methanol-water yielded *"compound 5"* (possibly a monoacetyl derivative of "compound 1" or "compound 3") as a white solid, m.p. 218–219°.

Anal. Calcd. for $C_{27}H_{28}N_2O$ (396.51): C, 81.78; H, 7.12; N, 7.07. Found: C, 81.42; H, 7.37; N, 7.19.

Further elution, with benzene, gave a solid which upon crystallization from ethanol gave a light tan solid (0.350 g., 0.00098 mole, 12%), m.p. 220–226°. Two or three recrystallizations from ethanol-benzene yielded *9-acetyl-4,4-dimethyl-2-(3-indolyl)-3,4,4a,9a-tetrahydrocarbazole (monoacetyl derivative of* Ib) as white crystals, m.p. 244.5–245.5°; λ_{max} in 95% ethanol: 223 mμ inflection (log ε 4.45), 261 (4.39), 281 (4.15), 288 inflection (4.10); ν_{NH} 3190, $\nu_{C=O}$ 1639 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{24}H_{24}N_2O$ (356.45): C, 80.86; H, 6.79; N, 7.86. Found: C, 80.91, 81.40; H, 6.91, 6.97; N, 8.51, 8.02.

Diacetyldehydro derivative of Ib:9-acetyl-2-(1-acetyl-3-indolyl)-3,4-dihydro-4,4-dimethylcarbazole (IVa) (M.R.V.). A solution of 4,4-dimethyl-2-(3-indolyl)-3,4,4a,9a-tetrahydrocarbazole (0.30 g., 0.00095 mole) in acetic anhydride (5 cc., 0.053 mole) was refluxed for 1 hr. The cooled solution was poured on ice, giving a pale yellow precipitate (0.31 g., 0.00078 mole, 82%). Four crystallizations, once with charcoal, from ethanol containing a little benzene yielded white needles, m.p. 210–210.5°; λ_{max} in 95% ethanol 232 mμ (log ε 4.74), 265 (4.40), 291 (4.43), 301 inflection (4.38), 320 inflection (4.12); ν_{NH} none, $\nu_{C=O}$ 1686 in chloroform, 1710, 1691, 1677 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{26}H_{24}N_2O_2$ (396.47): C, 78.76; H, 6.10; N, 7.07. Found: C, 78.64; H, 5.94; N, 7.10.

N,N'-Dimethyldehydro derivative of Ib: *3,4-dihydro-2-(1-methyl-3-indolyl)-4,4,9-trimethylcarbazole* (IVb) (C.G.R.). A solution of 4,4-dimethyl-2-(3-indolyl)-3,4,4a,9a-tetrahydrocarbazole (0.420 g., 0.00133 mole) in dry tetrahydrofuran (20 cc.) was added 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 (0.087 cc., 0.00140 mole) was added, and stirring was continued for an additional 30 min. The ammonia was allowed to evaporate, water was added, the product was extracted with ether, and the ether evaporated. The residual yellow oil was triturated with ethanol, leaving a residue of yellow prisms (0.100 g., 0.000293 mole, 22%), m.p. 205–207°. Two crystallizations from acetone-ethanol yielded yellow crystals, m.p. 221–223°, mixed melting point with the sample prepared from 1-methylindole, 223–224°. The infrared spectra of the two samples in potassium bromide pellets were identical; ν_{NH} none.

Anal. Calcd. for $C_{24}H_{24}N_2$ (340.45): C, 84.66; H, 7.11; N, 8.23. Found: C, 84.34; H, 7.18; N, 8.34.

Condensation of 1-methylindole with acetone in ethanolic hydrochloric acid (C.G.R.). Concentrated hydrochloric acid (2.1 cc.) was added to a solution of 1-methylindole (2.50 g., 0.0190 mole) and acetone (5.0 g., 0.086 mole) in ethanol (10 cc.), causing the solution to become hot and cloudy. Additional ethanol was added and, after the mixture was shaken, a solid precipitated. The mixture was kept at room temperature for 16 hr. and then the yellow precipitate was filtered off (1.60 g., 0.00529 mole, 56%). Crystallization from benzene–petroleum ether (b.p. 60–68°) yield *1,1'-dimethyl-3,3'-isopropylidenebisindole* (Va), m.p. 153–155°, mixed melting point with the sample prepared from mesityl oxide, 155–156° (undepressed).

The filtrate was neutralized with aqueous sodium hydroxide solution, extracted with ether, and the ether evaporated. The residual oil was dissolved in 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°) and chromatographed on alumina (50 g.). Elution with the same solvent and with benzene gave an oil which, upon trituration with hot ethanol, left a residue of yellow crystals (0.440 g., 0.00129 mole, 14%). Three recrystallizations from acetone yielded *3,4-dihydro-2-(1-methyl-3-indolyl)-4,4,9-trimethylcarbazole* (IVb) as yellow crystals, m.p. 223–224°; λ_{max} in 95% ethanol: 238 mμ (log ε 4.34), 280 (4.06), 342 inflection (4.21), 375 (4.14). The infrared spectrum in a potassium bromide pellet was identical with that of the sample prepared by methylation (with dehydrogenation) of the indole product, 4,4-dimethyl-2-(3-indolyl)-3,4,4a,9a-tetrahydrocarbazole. The mixed melting point was undepressed.

Anal. Calcd. for $C_{24}H_{24}N_2$ (340.45): C, 84.66; H, 7.11; N, 8.23. Found: C, 84.43; H, 7.31; N, 8.16.

1,1'-Dimethyl-3,3'-isopropylidenebisindole (*Va*). (*A*) *From 1-methylindole and mesityl oxide in ethanolic hydrochloric acid* (M.R.V.). A solution of 1-methylindole (2.62 g., 0.020 mole), mesityl oxide (1.0 g., 0.010 mole), and concentrated hydrochloric acid (2.0 g.) in 95% ethanol (15 cc.) was kept at room temperature for 8 hr. The brown solution was carefully decanted from the brown oil which had separated. The brown oil was dissolved in ethanol, made faintly alkaline by addition of a few drops of ethanolic sodium hydroxide solution, treated with charcoal, and cooled in a refrigerator, yielding white plates (1.1 g., 0.0036 mole, 36%), m.p. 156–157°. Three recrystallizations from ethanol gave the analytical sample; λ_{max} in 95% ethanol: 226 mμ (log ϵ 4.70), 291 (3.94). The mixed m.p., 156–158°, with the sample prepared from acetone was undepressed.

Anal. Calcd. for $C_{21}H_{22}N_2$ (302.40): C, 83.40; H, 7.33; N, 9.26. Found: C, 83.02; H, 7.47; N, 9.46.

The decanted brown solution was neutralized with ethanolic sodium hydroxide solution, the precipitated sodium chloride filtered, and the filtrate cooled. The copious white precipitate (0.52 g., 0.00132 mole, 20%) was crystallized three times from ethanol, giving white needles, and once from methanol,[19] yielding *1-methylindole trimer* as white platelets, m.p. 173–174°, mixed melting point with a sample of m.p. 173–174° prepared[8,9] from 1-methylindole, 173–174°. The infrared spectra of the two samples in Nujol were identical.

(B) *From 1-methylindole and acetone in refluxing acetic acid* (with Heinz Sorger-Domenigg, 1955). A solution of 1-methylindole (10.70 g., 0.0815 mole) and acetone (67 g., 1.15 mole) in glacial acetic acid (100 g.) was refluxed for 11 hr. The orange solution was cooled and diluted with water (400 cc.), causing separation of a yellow oil, which partially emulsified. The mixture was neutralized with sodium carbonate, extracted with ether, and the ether and acetone evaporated. The residual dark orange oil was triturated with 95% ethanol, causing immediate separation of crystals. Three recrystallizations from absolute ethanol yielded colorless prisms (2.40 g., 0.00794 mole, 19%), m.p. 151–152°. The infrared spectra in chloroform and Nujol were identical with those of the sample prepared from mesityl oxide.

Anal. Found: C, 83.51; H, 7.44; N, 9.46.

4-Methyl-4-(3-indolyl)-2-pentanone (VIa). (with Albert W. Morgan, 1961).[20] Concentrated hydrochloric acid (6 g.) was added to a solution of indole (5.86 g., 0.0500 mole) and freshly distilled mesityl oxide (4.91 g., 0.0500 mole) in 95% ethanol (25 cc.), causing immediate formation of a dark brown color. After 1 hr. the solution turned dark red and after 10 hr. it had become black. After 48 hr. the black oil was poured into water and sodium hydroxide was added until the mixture remained alkaline to litmus. The mixture was extracted with ether, the ether was distilled, and the residue was dissolved in benzene and chromatographed on alumina which had been packed wet with petroleum ether (b.p. 60–68°). Elution with petroleum ether and with benzene removed tars; elution with benzene-chloroform removed a red oil, which became a black tar upon attempted recrystallization from methanol. Elution with chloroform removed colorless oils which crystallized upon being cooled in an ice bath. The crystals (0.650 g., 6%), m.p. 75–100°, were recrystallized several times from methanol-water, giving a sample (0.212 g., 0.00099 mole, 2%), m.p. 86–88° (sublimes > 90°). The colorless analytical sample had a m.p. of 88–89°; λ_{max} in 95% ethanol: 221 mμ (log ϵ 4.54), 276 inflection (3.73), 282 (3.77), 290 (3.71); ν_{NH} 3340, $\nu_{C=O}$ 1700 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{14}H_{17}NO$ (215.28): C, 78.10; H, 7.96; N, 6.51. Found: C, 78.13; H, 8.08; N, 6.61.

Elution with chloroform-ether mixtures removed a light tan amorphous solid, probably containing some of the preceding ketone which, upon reprecipitation from methanol-water, yielded a light tan sample (0.085 g.), m.p. ~ 98–101°; ν_{NH} 3410s, $\nu_{C=O}$ 1698mw, $\nu_{C=C}$ 1625m cm.$^{-1}$ in Nujol. Further elution with ether and with methanol removed only brown amorphous material.

4-Methyl-4-(1-methyl-3-indolyl)-2-pentanone (VIb) (C.G.R.). Concentrated hydrochloric acid (4.00 g.) was added to a solution of 1-methylindole (5.24 g., 0.0398 mole) and mesityl oxide (4.00 g., 0.0408 mole) in 95% ethanol (30 cc.), causing almost immediate separation of an oil. More ethanol (20 cc.) was added, but the mixture did not become homogeneous for about 10 min. The solution was kept at room temperature for 7.5 hr. and then poured into water and extracted with ether. The ether extract was washed with aqueous sodium bicarbonate solution and the ether evaporated. The residual pale yellow oil (9.0 g.) was distilled in a bulb tube, giving a pale yellow oil (2.60 g., 0.0113 mole, 28%), b.p. 170–190° (0.35 mm.); ν_{NH} 3380, $\nu_{C=O}$ 1700 cm.$^{-1}$ on the oil. Three more vacuum distillations yielded a colorless oil, highly fluorescent to ultraviolet light, b.p. 152–154° (bath temperature; 0.15 mm.); λ_{max} in 95% ethanol: 225 mμ (log ϵ 4.54), 290 (3.75).

Anal. Calcd. for $C_{15}H_{19}NO$ (229.31): C, 78.56; H, 8.35; N, 6.11. Found: C, 78.57; H, 8.34; N, 6.46.

The oily nonvolatile residue (4.3 g.) was assumed to consist largely of 1,1′-dimethyl-3,3′-isopropylidenebisindole, and possibly 1-methylindole trimer.

The oxime was obtained in 98% yield from reaction of the ketone with hydroxylamine hydrochloride and sodium acetate; white crystals from ethanol-water, m.p. 118–118.5°; λ_{max} in 95% ethanol: 226 mμ (log ϵ 4.56), 291 (3.75); ν_{OH} 3240, $\nu_{C=N}$ 1669 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, 74.02; H, 8.21; N, 11.52.

2,4-Bis(1-methyl-3-indolyl)-4-methyl-2-pentene (IX) *or 4,4-bis(1-methyl-3-indolyl)-2-methyl-2-pentene* (Vb) (C.G.R.). In the unsuccessful hope of introducing a methyl group into the 3-position and inducing cyclization to VIII, 4-methyl-4-(1-methyl-3-indolyl)-2-pentanone (2.29 g., 0.0100 mole) and methyl iodide (8.52 g., 0.060 mole) were heated at 140–150° in an autoclave for 1 hr. and allowed to cool overnight. The products were poured into water, extracted with ether, the ether extract washed with aqueous sodium bicarbonate solution, and the ether and methyl iodide evaporated. The dark residual oil was dissolved in 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°) and chromatographed on alumina (60 g.). Elution with the same solvent gave an oil (1.53 g., 67%). Distillation in a bulb tube gave an oil (1.06 g., 46%), b.p. 135–145° (0.06 mm.), and two more distillations gave an analytical sample of starting material, b.p. 140–142° (bath temperature; 0.10 mm.).

Anal. Calcd. for $C_{15}H_{19}NO$ (229.31): C, 78.56; H, 8.35; N, 6.11. Found: C, 78.27; H, 8.39; N, 6.23.

The ultraviolet spectrum was the same as that of the starting material and the oxime was identical by mixed melting point (118–118.5°) comparison with the oxime of the starting material.

The dark distillation residue gave tan crystals, m.p. 145–150°, upon treatment with ethanol. Crystallization from ethanol gave light tan crystals (0.190 g., 0.000555 mole, 11%), m.p. 176–178°, and two more recrystallizations from ethanol gave light tan needles, m.p. 177.5–178°; λ_{max} in 95% ethanol: 227 mμ (log ϵ 4.79), 287 inflection (4.12), 293 (4.13). The infrared spectrum in Nujol shows no olefinic band at higher frequency than the conjugated double bond band at 1612 cm.$^{-1}$

Anal. Calcd. for $C_{24}H_{26}N_2$ (342.46): C, 84.17; H, 7.65; N, 8.18. Found: C, 83.89; H, 7.62; N, 8.24.

Condensation of 1-Methylindole and methyl isobutyl ketone in ethanolic hydrochloric acid (C.G.R.). (*A*) *At lower concentration.* A solution of 1-methylindole (1.50 g., 0.0114 mole), methyl isobutyl ketone ($n_D^{25.5}$ 1.3935, 5.19 g., 0.0517 mole), and concentrated hydrochloric acid (1.5 g.) in 95% ethanol (15 cc.) was kept at room temperature for 14 days. The solution was then poured into water, extracted with ether, the ether extract washed with aqueous sodium bicarbonate solution, and the ether evaporated. The residual oil partially

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(19) By William C. Kuryla, 1960.

(20) Section added to manuscript, May 1, 1961.

crystallized on standing. It was extracted with methanol, leaving a white solid (0.61 g., 0.00286 mole, 25%) m.p. 147–149°. Two crystallizations from methanol yielded *6,12-diisobutyl-5,6,11,12-tetrahydro-5,6,11,12-tetramethylindolo[3,2-b]carbazole* (XII) *or 4,6-bis(1-methyl-3-indolyl)-2,6,8-trimethyl-4-nonene* (XIII) as white crystals, m.p. 148–150°; λ_{max} in 95% ethanol: 230 mμ (log ε 4.51), 287 (3.83), 293 (3.84). The infrared spectrum in Nujol shows no olefinic band at higher frequency than the conjugated double bond band at 1611 cm.$^{-1}$

Anal. Calcd. for $C_{15}H_{19}N$ (213.31): C, 84.45; H, 8.98; N, 6.57. Found: C, 84.75; H, 9.11; N, 6.96.

The residual oil from evaporation of the methanol extract was distilled in a bulb tube, giving a yellow-orange oil (0.72 g., 0.00244 mole, 21%), b. p. 145–155° (bath temperature; 0.002 mm.), n_D^{26} 1.5758. Three further distillations yielded *4-(1-methyl-3-indolyl)-2,6,8-trimethyl-3,5-nonadiene* (XV), b.p. 138° (0.002 mm), $n_D^{25.5}$ 1.5775.

Anal. Calcd. for $C_{21}H_{29}N$ (295.45): C, 85.36; H, 9.89; N, 4.74. Found: C, 85.06; H, 9.66; N, 5.15.

The 1,3,5-trinitrobenzene derivative prepared in methanol had a m.p. of 106–107° and was identical with the sample described in part B, as shown by mixed melting point (105.5–106.5°) comparison.

(*B*) *At higher concentration.* A solution of 1-methylindole (2.50 g., 0.0190 mole), methyl isobutyl ketone (n_D^{25} 1.3936, 8.65 g., 0.0863 mole), and concentrated hydrochloric acid (2.5 g.) in 95% ethanol (20 cc.) was kept at room temperature for 14 days. The solution was poured into water, extracted with ether, and the ether evaporated. The residual oil (4.30 g.) was chromatographed on alumina (200 g.) using 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°), giving a pale yellow oil (4.21 g., 0.0143 mole, 75%). Distillation in a bulb tube at 210–230° (0.45 mm.) resulted in extensive pyrolysis, because of the relatively poor vacuum employed. Two redistillations yielded *4-(1-methyl-3-indolyl)-2,6,8-trimethyl-3,5-nonadiene* (XV) in a slightly impure state, b.p. 116° (0.002 mm.), $n_D^{25.5}$ 1.5695; λ_{max} in 95% ethanol:225 mμ (log ε 4.28), 244 inflection (4.08), 250 (4.12), 258 inflection (4.04), 305 (4.05), 316 (4.09), 329 (3.89); $\nu_{C=C}$ 1649, 1610 cm.$^{-1}$ on the liquid.

Anal. Found: C, 84.78; H, 9.68; N, 5.29.

The 1,3,5-trinitrobenzene derivative was prepared in methanol; after two crystallizations from methanol, it formed dark violet crystals, m.p. 103–104°.

Anal. Calcd. for $C_{27}H_{32}N_4O_6$ (508.56): C, 63.76; H, 6.34; N, 11.02. Found: C, 64.04; H, 6.45; N, 11.18.

Diacid from maleic anhydride adduct of XV: *3-isobutyl-6-isopropyl-3-methyl-5-(1-methyl-3-indolyl)-4-cyclohexene-1,2-dicarboxylic acid* (H.S.D.). Solutions of the 1:2-condensation product of 1-methylindole and methyl isobutyl ketone (0.65 g., 0.0022 mole) in benzene (5 cc.) and technical grade maleic anhydride (0.216 g., 0.0022 mole) in benzene (15 cc.) were combined, and the resulting solution was refluxed for 45 min. Evaporation of the red solution left a dark red oil, which was dissolved in benzene. Addition of petroleum ether (b.p. 60–68°) caused separation of a brown crystalline solid (0.30 g.). Recrystallization from benzene–petroleum ether (b.p. 60–68°), with charcoal, gave whitish crystals (0.22 g., 0.00053 mole, 24%), m.p. 118–136.5°. Three more recrystallizations from benzene–petroleum ether (b.p. 60–68°) yielded fluffy colorless needles (0.073 g., 8%), m.p. 131–134°; λ_{max} in 95% ethanol:247 mμ (log ε 3.93), 298 (3.44); ν_{OH} 3600–2300 (broad), $\nu_{C=O}$ 1759s, $\nu_{C=C}$ 1609m cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{25}H_{33}NO_4$ (411.52): C, 72.96; H, 8.08; N, 3.40. Found: C, 72.50; H, 8.39; N, 3.52.

Self-condensation of 4-(3-indolyl)-2-butanone (XVI) *in ethanolic hydrochloric acid* (C.G.R). A solution of 4-(3-indolyl)-2-butanone[14,15] (1.0 g., 0.0053 mole) and water (2.0 cc.) in ethanol (20 cc.) was cooled in an ice bath and saturated with hydrogen chloride. The solution was kept in the ice bath for 0.5 hr. and at room temperature for 1.25 hr. The red-brown solution was diluted with water, extracted with ether, and the ether evaporated. The residual light brown semisolid (0.210 g.), m.p. 114–118°, was dissolved in 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°) and chromatographed on alumina (10 g.). Elution with the same solvent gave a partially crystalline oil. Crystallization from methanol gave a white solid (0.070 g., 0.000196 mole, 7%), m.p. 240–245°. Four recrystallizations from methanol-water yielded *6-(3-indolyl)-4-methyl-3-skatyl-3-hexene-2-one* (XVIII) as white crystals, m.p. 241.5–242.5°; λ_{max} in 95% ethanol: 226 mμ (log ε 4.63), 250 (4.11), 275 inflection (3.95), 283 (3.98), 291 (3.95), 309 inflection (3.60); ν_{NH} 3400, $\nu_{C=O}$ 1698, $\nu_{C=C}$ 1607 (strong, conjugated) cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{24}H_{24}N_2O$ (356.45): C, 80.86; H, 6.79; N, 7.86. Found: C, 80.71; H, 7.13; N, 7.95.

The acidic aqueous layer was made alkaline, extracted with ether, and the ether evaporated. The residual reddish oil was dissolved in 1:1 (by volume) benzene–petroleum ether (b.p. 60–68°) and chromatographed on alumina (15 g.). Elution with the same solvent gave an oil, which crystallized. Washing with methanol gave white needles (0.030 g., 0.000084 mole, 3%), m.p. 245–250°. Two recrystallizations from benzene-methanol yielded *3-(3,4,4a,9a-tetrahydro-2-carbazolyl)-2-oxo-1,2,3,4,4a,9a-hexahydrocarbazole* (XX?) as white needles, m.p. 246–249°; λ_{max} in 95% ethanol: 238 mμ (log ε 4.12), 283 (3.82); ν_{NH} 3320, $\nu_{C=O}$ 1694, $\nu_{C=C}$ 1650, 1607 cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{24}H_{24}N_2O$ (356.45): C, 80.86; H, 6.79; N, 7.86. Found: C, 81.50; H, 6.85; N, 7.87.

The mixed melting point with the compound extracted from acidic solution was depressed.

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