

tetrazole is unknown⁴ may be explained by these effects of electron withdrawal. From the present work it appears that the nitro group in the 6-position of pyridotetrazole and the thiazole group in tetrazolobenzthiazole-1,3 have comparable effect in destabilizing the tetrazole ring, whereas the thiazole dioxide group, e.g., VIb, is demonstrably more effective. These conclusions allow the prediction that electron donating substituents will stabilize the pyridotetrazole ring system relative to an isomeric azide. Investigations are now being carried out to test this hypothesis.

Experimental¹⁶

Trimethylenetetrazole.—A solution of 4.15 g. (0.04 mole) of thiopyrrolidone,¹⁷ 11.36 g. (0.08 mole) of methyl iodide and 40 ml. of benzene was stored at room temperature for 4 hours. A pale yellow solid reprecipitated from an ethanol and ether mixture as a colorless solid, 9.79 g., which was dissolved in 20 ml. of water and neutralized with 15 ml. of 5 *N* sodium hydroxide. The aqueous solution was saturated with salt and extracted with ether. From the dried ether extracts, 1.39 g. of crude 2-methylmercaptopyrrolone was obtained as residue after evaporation. To this residue was added 14 ml. of a chloroform solution of hydrogen azide (from 0.02 mole of sodium azide¹⁸). The solution, after standing for 44 hours, was refluxed 2.5 hours. Trimethylenetetrazole, a solid residue after removal of solvent by distillation, recrystallized from xylene as small colorless needles, m.p. 109–110° (lit.⁶ m.p. 110°), 0.89 g. (20%).

Literature methods were followed for the preparation of compounds II,⁹ IV,¹² V¹⁴ and VI.¹⁵

(16) We are indebted to Mr. R. T. O'Connor, Southern Regional Research Laboratory, for infrared and ultraviolet absorption data.

(17) J. Tafel and P. Lawaczek, *Ber.*, **40**, 2842 (1907).

(18) H. Wolff, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 327.

Infrared absorption data for compounds I, II, IV, V and VI are found in Table I.

Chromatography.¹⁹—Ascending chromatograms of analytically pure samples of IV and V were developed on strips of Whatman No. 2 filter paper using benzene or chloroform as eluents in the presence of ultraviolet light. Chromatograms near 0° were obtained by immersing the entire chamber in ice-water and those above room temperature were obtained by heating a paper containing an initial spot for 5 to 10 minutes at the desired temperature and then developing at room temperature. In all cases the solvent front was allowed to ascend 3 to 4 inches from the origin. Concentration of material at a spot was judged by intensity of fluorescence in ultraviolet light. It was assumed that the moving spot corresponds to a less polar species (presumably tetrazole) whereas the stationary spot corresponds to a polar species¹⁹ (presumably azide).

An ethanolic solution of 6-nitropyridotetrazole (V) was chromatographed at 0°, 25° and near 25° immediately after heating at 70°. Eluent was benzene except at 0° where chloroform was used. At each temperature two spots were obtained, one at the origin and one just behind the solvent front. At 0° the residual spot at the origin was weak and the spot which traveled with the solvent was very strong. Both spots were of nearly equal intensity at 25°, and at higher temperatures the residual spot at the origin became very strong as the traveling spot nearly disappeared.

Similar results were obtained with an ethanolic solution of 1,5-tetrazolobenzthiazole-1,3 (IV). The intensity of the traveling spot varied from very strong at 0°, to strong at 25°, to disappearance at 100° while the intensity of the residual spot at the origin varied from very weak at 0°, to medium at 25°, to very strong at 100°.

Satisfactory eluents have not been found for similar chromatographic study of pyridotetrazole and trimethylenetetrazole (I).

(19) E. Lederer and M. Lederer, "Chromatography," Elsevier Publishing Co., New York, N. Y., 1953, p. 75.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

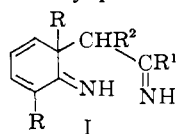
The Fischer Indole Synthesis. VI. A Non-aromatic Intermediate and a New Class of Hydroindoles¹

BY ROBERT B. CARLIN AND D. PETER CARLSON²

RECEIVED FEBRUARY 24, 1959

2,6-Dimethylphenylhydrazine has been prepared from 2,6-xylydine by a much improved procedure and converted to acetophenone 2,6-dimethylphenylhydrazone (II). Treatment of the latter with zinc chloride in nitrobenzene at 120° led to a mixture from which five products were isolated: a crystalline solid C₂₄H₂₅NO₂ of unknown structure (trace); 2,6-xylydine (8%); acetophenone (trace); 2-phenyl-4,7-dimethylindole (III, 4%); and the chief product, 2-phenyl-3a,5-dimethyl-3a,4,7,7a-tetrahydro[3H]pseudoindolone-4 (IV, 33%). The structure of III was established by independent synthesis and that of IV substantially by degradation to 2,6-dimethyl-2-(β-phenylethyl)-cyclohexanone, which was also synthesized independently. In the course of the degradation of IV, evidence was obtained suggesting that IV has a *cis* ring junction. A mechanism previously proposed to account for the formation of 2-carbethoxy-4,7-dimethylindole from ethyl pyruvate 2,6-dimethylphenylhydrazone readily accounts also for the formation of IV, a new kind of indole derivative; in fact, a single non-aromatic intermediate of type I would be expected to give rise to both III and IV.

The behavior of 2,6-disubstituted arylhydrazones thus far investigated in the Fischer indole synthesis has been rationalized by postulating non-aromatic



(1) Submitted by D. Peter Carlson in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Carnegie Institute of Technology. The work reported here has been the subject of a Communication to the Editor (*THIS JOURNAL*, **79**, 3605 (1957)).

(2) Allied Chemical and Dye Co. Fellow, 1956–1957.

intermediates of structure I. When R is halogen, it may undergo allylic rearrangement with or without exchange of halogen with the promoting agent (a zinc or a stannous halide), and the product is then a 5,7-dihalogenoindole.³ Also when R is halogen, it may be substituted by hydrogen, particularly when a stannous halide is the promoter; a 7-monohalogenoindole is the product of this reaction.⁴ In one case in which R was methyl, a small amount of

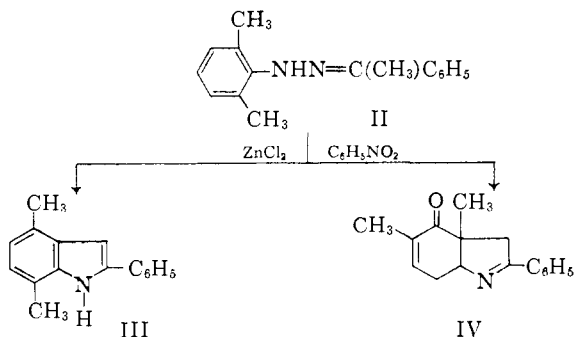
(3) (a) R. B. Carlin and E. E. Fisher, *THIS JOURNAL*, **70**, 3421 (1948); (b) R. B. Carlin and G. W. Larson, *ibid.*, **79**, 934 (1957).

(4) R. B. Carlin, J. G. Wallace and E. E. Fisher, *ibid.*, **74**, 990 (1952); R. B. Carlin and L. M. Amoros-Marin, *ibid.*, **80**, 730 (1958).

a 4,7-dimethylindole, resulting from a 1,2-migration of methyl, was isolated.⁵ In this paper an account is given of an investigation of the behavior of acetophenone 2,6-dimethylphenylhydrazone (II) in the Fischer reaction. The observations reported here may again be rationalized in terms of an intermediate of structure I; indeed, the chief product from II has the carbon skeleton of I ($R = \text{CH}_3$, $R^1 = \text{C}_6\text{H}_5$, $R^2 = \text{H}$).

Owing to the fact that 2,6-dimethylphenylhydrazine could be obtained from the rather dear 2,6-xylylidine in only 18-25% yields⁶ by the usual procedure, the 2,6-dimethylphenylhydrazone whose behavior in the Fischer reaction was the subject of a previous investigation⁵ was prepared by the Japp-Klingemann reaction. This preparative method does not lead to arylhydrazones of simple ketones, however, and since most of our earlier studies on the Fischer reaction had involved 2,6-disubstituted phenylhydrazones of simple ketones, especially acetophenone, it was desirable to continue using simple ketone derivatives in order to minimize the number of variables. These considerations made it essential to discover a useful synthesis of 2,6-dimethylphenylhydrazine. An investigation of the standard preparative method, which involves the reduction of cold diazotized 2,6-xylylidine with stannous chloride and hydrochloric acid for about an hour, disclosed that when the reduction step was allowed to proceed for 24 hours while the cold solution gradually warmed to room temperature, 2,6-dimethylphenylhydrazine was formed in 70-95% yields. This observation substantiated those of Hunsberger, *et al.*,⁷ whose work on the preparation of a number of arylhydrazines had not yet been published.

Acetophenone 2,6-dimethylphenylhydrazone (II), prepared from the now available 2,6-dimethylphenylhydrazine, proved to be unstable in air. Although it could be stored under a nitrogen atmosphere in a refrigerator for perhaps a few weeks, it was ordinarily used immediately following its preparation. When II in nitrobenzene was heated with zinc chloride to about 120°, a spontaneous temperature rise indicated the onset of reaction. The mixture was maintained at about 120° for an hour before separation into its components. Five products were isolated, and four of these were completely characterized. The latter proved to be 2,6-xylylidine



(5) R. B. Carlin, W. O. Henley, Jr., and D. P. Carlson, *THIS JOURNAL*, **79**, 5712 (1957).

(6) Our figure. H. Frantzen, A. Onsager and G. Faerden, *J. prakt. Chem.*, [2] **97**, 336 (1918), reported "less than 30% yields."

(7) I. M. Hunsberger, E. R. Shaw, J. Fugger, R. Ketcham and D. Lednicer, *J. Org. Chem.*, **21**, 394 (1956).

(8%) acetophenone (trace), 2-phenyl-4,7-dimethylindole (III, 4%) and the main product, 2-phenyl-3a,5-dimethyl-3a,4,7,7a-tetrahydro[3H]pseudoindolone-4 (IV, 33%). The fifth product, a crystalline solid isolated in less than 1% yield whose composition corresponded to the formula $\text{C}_{24}\text{H}_{26}\text{NO}_2$, cannot yet be assigned a proven structure.

2,6-Xylylidine was characterized as its phenylthiourea derivative and acetophenone as its 2,4-dinitrophenylhydrazone. The structure of III was established by an independent synthesis from acetophenone 2,5-dimethylphenylhydrazone. Samples from the two sources had identical melting and mixed melting points, as did their maroon picrates, and the infrared spectra were also essentially identical.

Proof of Structure of Compound IV.—Unlike the indole III, which was effectively neutral, IV was basic in nature. It crystallized from ether as its hemihydrate, $\text{C}_{18}\text{H}_{17}\text{NO} \cdot \frac{1}{2}\text{H}_2\text{O}$, m.p. 92-101°. Fractional crystallization, chromatography and liquid-liquid extraction failed to narrow the melting range or to disclose the presence of impurities. The hydrochloride, the picrate and a crystalline molecular compound of IV with III all formed without water of crystallization, but regeneration of IV from any of these derivatives led again to a hemihydrate with the original melting range. This evidence suggested that the broad melting range was a true property of the hemihydrate and not an indication that the compound IV was impure.

The infrared spectra (Fig. 1) of IV and of its hydrochloride, measured in chloroform solution, strongly indicated the presence in the molecule of an α,β -unsaturated ketone function (6.01μ both in IV and in its hydrochloride).⁸ An intense band at 6.22μ in the spectrum of the base IV corresponded to a band of similar intensity at 6.24μ in the spectrum of the hydrochloride, but the latter also had in it an intense band at 6.12μ that was not present in the spectrum of the base. Witkop has observed that the imine double bond ($\text{C}=\text{N}$) usually gives rise to an infrared band just beyond 6μ ; in the corresponding hydrochloride this band is shifted about 0.13μ toward shorter wave lengths, and new bands typical of ammonium and immonium salts appear in the 4.0-4.3 and 5.80-5.12 μ regions.⁹ Inasmuch as the spectrum of the hydrochloride of IV included a broad band at 4.10μ and sharper but weaker bands at 5.08 and 5.24 μ , none of which appeared in the spectrum of IV itself, these, together with the 6.12μ band were attributed to $\text{C}=\text{NH}^+$ and the 6.24μ band was associated with conjugated phenyl, as were the bands at about 6.32 and 6.68 μ .⁸ The intense 6.22μ band in the spectrum of the base IV then was presumably the sum of two unresolved bands, one assigned to $\text{C}=\text{N}$ and one to conjugated phenyl.

The ultraviolet absorption spectra of IV in ethanol and in 0.1 N ethanolic hydrochloric acid (Fig. 2) supported the structural assignments derived from the infrared spectra. In neutral ethanol, the spectrum showed a single intense band at 242 m μ

(8) Cf. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London, 1954.

(9) B. Witkop, *Experientia*, **10**, 420 (1954); *THIS JOURNAL*, **78**, 2873 (1956).

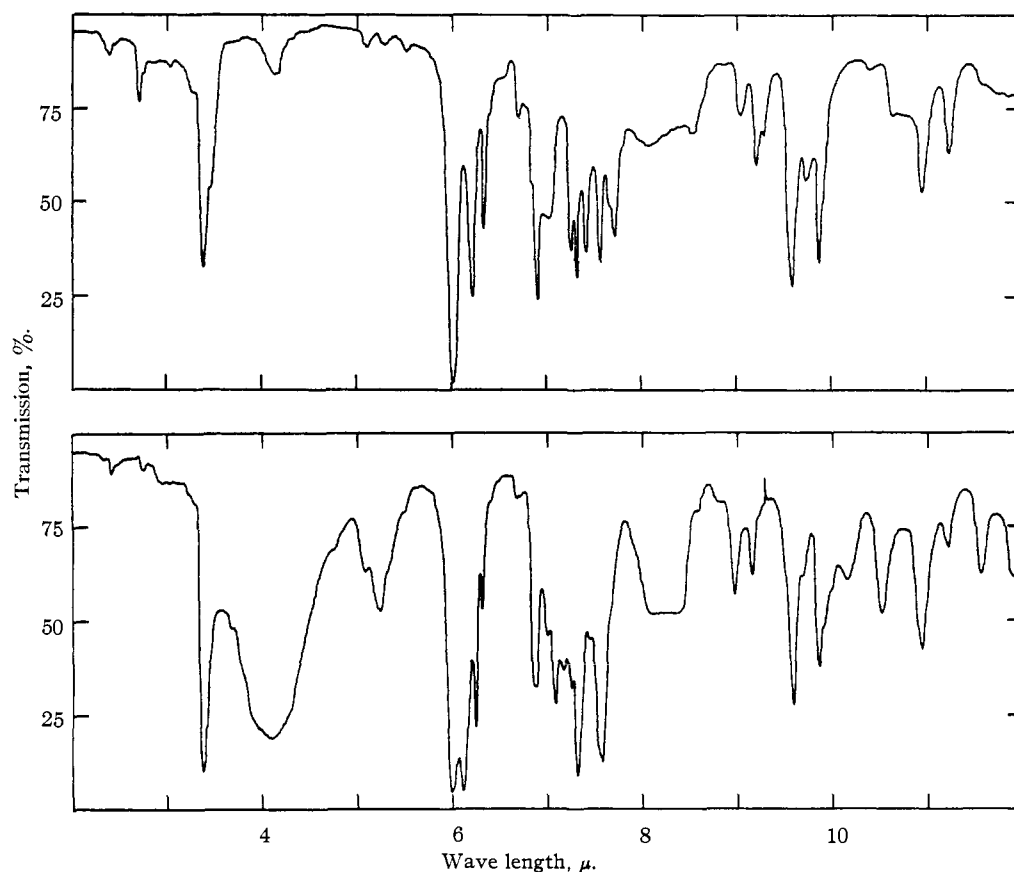


Fig. 1.—The infrared absorption spectra of IV (top) and of IV hydrochloride (bottom); *ca.* 25 mg./ml. in chloroform.

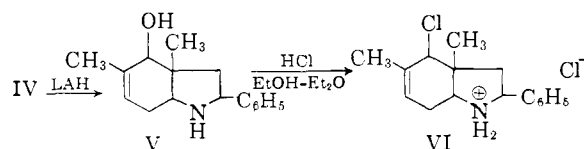
(ϵ 21,500); the spectrum of the acid solution showed a weaker band at the same wave length (ϵ 10,500) and a new band at $273\text{ m}\mu$ (ϵ 16,500). The ultraviolet absorption bands of α,β -disubstituted α,β -unsaturated ketones are known to occur in the range $245 \pm 5\text{ m}\mu$,¹⁰ and Witkop⁹ has observed that imines (C=N) absorb in the same region in neutral solution but that the absorption maxima may be displaced as much as $50\text{ m}\mu$ toward longer wave lengths in acid solutions. The $232\text{ m}\mu$ band from the neutral solution is therefore considered to be the sum of both the imine and the unsaturated carbonyl bands; in acid solution the carbonyl band remains, but the absorption caused by the imine chromophore has shifted to $273\text{ m}\mu$.

Spectroscopic evidence therefore pointed to the presence of an α,β -disubstituted α,β -unsaturated carbonyl function, an imine function that was probably conjugated, and a conjugated phenyl. Incidentally, a weak band at $2.72\text{ }\mu$ in the infrared spectrum of IV but not in that of its hydrochloride was assigned to water (of crystallization). The presence of a ketone carbonyl group was confirmed by the preparation of a crystalline oxime. The spectroscopic evidence, together with the molecular formula and the structure II of the starting material, suggested what proved to be the correct structural representation for IV, and the transformations to be described are formulated from this expression.

Support for the incorporation of an α,β -unsaturated carbonyl system into the structure of IV was

(10) R. B. Woodward, *THIS JOURNAL*, **64**, 76 (1942).

derived from its behavior when treated with lithium aluminum hydride in ether. The product of this reaction was a colorless, viscous oil that failed to crystallize. The composition of this oil and that of its crystalline picrate were consistent with the empirical formula $\text{C}_{18}\text{H}_{21}\text{NO}$, a tetrahydro derivative of IV. The infrared spectrum included bands at 2.76 (OH), 3.0 (NH), 6.16 (C=C) and at 6.24 and $6.75\text{ }\mu$ (non-conjugated phenyl).⁸ When an ether solution of this oil was treated with ethanolic hydrochloric acid, and when the resulting mixture was permitted to evaporate to dryness on the steam-bath, the crystalline product proved to be a chloride hydrochloride, $\text{C}_{18}\text{H}_{20}\text{NCl}\cdot\text{HCl}$. The ease with which the reduction product of IV underwent replacement of its hydroxyl group by chlorine was consistent with the assignment to these groups of allylic positions and with the formulations of the products as V and VI.



Evidence bearing on the nature of the skeletal structure of IV came from a series of reactions beginning with the hydrogenation of IV in acetic acid over Adams catalyst. This reaction led to oil from which two crystalline tetrahydro derivatives of IV could be separated. Although the infrared spectra of the two substances showed significant differences,

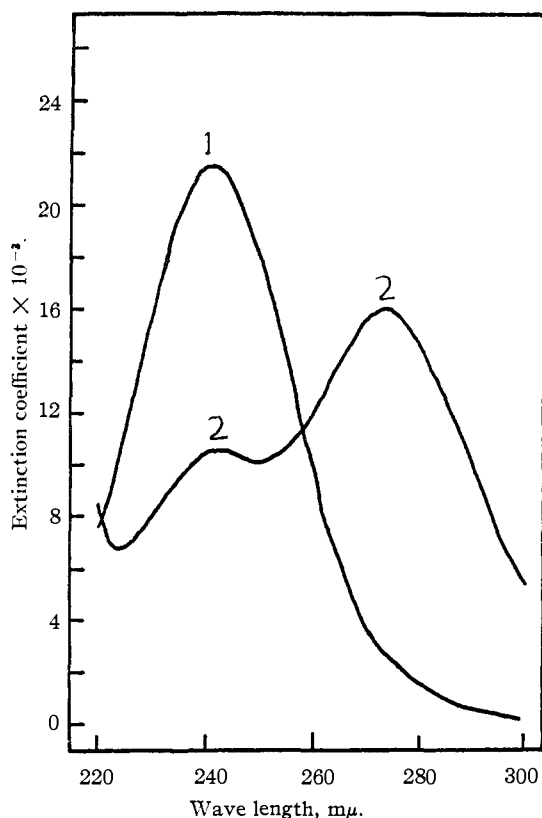
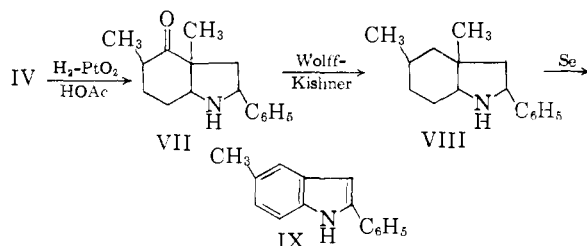


Fig. 2.—The ultraviolet absorption spectra of IV in (1) ethanol and in (2) ethanolic 0.1 *N* hydrochloric acid.

both included bands at 2.98 (NH), 5.90 (unconjugated C=O) and at 6.24 and 6.70 μ (unconjugated phenyl). These compounds apparently were stereoisomeric modifications of VII. Wolff-Kishner

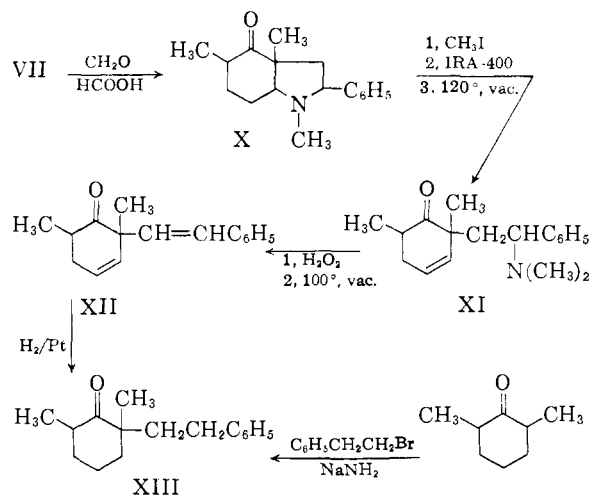


reduction of VII led to an oil characterized as its crystalline hydrobromide and assigned the structure VIII. When a mixture of VIII and selenium was heated to 290°, the mixture yielded a very small amount of a crystalline solid, m.p. 205–208°, which gave a positive Ehrlich test (for indoles) and whose composition accorded with the formula $C_{14}H_{13}N$. Although the sample was evidently not thoroughly purified, insufficient amounts were obtained to permit both further purification and comparisons with specimens of known structures. Of the five known monomethyl-2-phenylindoles, only 2-phenyl-5-methylindole (IX), m.p. 214–216°, melted as high as the selenium degradation product of VIII. Therefore, an authentic specimen of IX was prepared from phenacylaniline and excess *p*-toluidine by the Bischler method.¹¹ A mixture of this com-

(11) P. E. Verkade and E. F. J. Janetzky, *Rec. trav. chim.*, **62**, 763 (1943).

pound with a sample of the dehydrogenation product melted at 208–212°, and the ultraviolet absorption spectra were identical. Although the presence of impurities in the dehydrogenation product apparently were responsible for two bands in the infrared spectrum that were not present in the spectrum of authentic IX, the former spectrum contained all the bands present in the latter. The assignment of structure IX to the dehydrogenation product therefore appeared justified. That this product was obtained in very small yield from VIII was not surprising in view of previous reports that even octahydroindole derivatives with no angular substituents are dehydrogenated by selenium to indoles in poor yield.¹²

Conclusive proof of the structure of the carbon skeleton of IV was obtained by converting IV to 2,6-dimethyl-2-(β -phenylethyl)-cyclohexanone (XIII) through a series of steps formulated in the following expressions. This series of steps also provided evidence suggesting that IV has a *cis* ring junction.



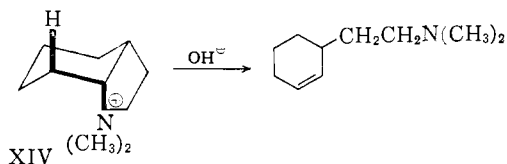
The tetrahydro derivative VII in either of its crystalline isomeric modifications afforded the same viscous, oily N-methyl derivative X when treated with formaldehyde and formic acid. Samples of X derived from the isomeric forms of VII were identified by means of their boiling points, refractive indices and infrared spectra. Only one crystalline product (X), m.p. 42–44°, could be separated from the oily product, but the infrared spectra of the crystalline compound and of the oil that remained after the crystals had been separated indicated that stereoisomers of X had been formed. The partial epimerization that occurs during methylation of VII almost certainly must involve ring position number 5, for none of the other three asymmetric centers (ring positions 2, 3a and 7a) is in a position to undergo facile equilibration of configurations. It is therefore reasonable to conclude that the stereoisomeric forms of VII also can be considered epimers about ring position 5.

The methiodide of X was formed in 57% yield when a solution of X and methyl iodide in dioxane was boiled for 22 hours. An aqueous solution of

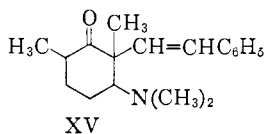
(12) Shin-itero Fujisie and Kozo Tiba, *Bull. Chem. Soc. Japan*, **14**, 478 (1939).

the methiodide was allowed to trickle through a column of Amberlite IRA-400 (hydroxide form), and the methohydroxide thereby formed was decomposed by heating it to 120° under reduced pressure. The product was a basic oil that was characterized as its crystalline methiodide, m.p. 158–213°, which, unlike the methiodide of X, formed immediately when the oil was mixed with methyl iodide. The composition of the new methiodide agreed satisfactorily with the formula $C_{19}H_{28}NOI$, and its wide melting range was ascribed, at least in part, to stereoisomerism centered at the same carbon atom responsible for the stereoisomeric modifications of VII and X.

The basic oil formed by heating the methohydroxide from X was assigned the structure XI on the basis of its composition, its behavior on exhaustive methylation, and on the basis of the observations reported by King and Booth¹³ on the products of the Hofmann decompositions of *cis*- and *trans*-N-methyloctahydroindole methohydroxides. The *cis* isomer, which can assume a conformation in which a *trans*, coplanar arrangement of the H-C-C-N⁺ system obtains (XIV), undergoes smooth decomposition to 3- β -dimethylaminoethylcyclohexene; the *trans* isomer, which cannot assume a similar alignment of the four essential atoms, decomposes to a mixture of dimethyl-(2-vinylcyclohexyl)-



amine and a dimeric ether. Even though the presence of the 2-phenyl group in the methohydroxide of X might be expected to lend increased importance to the Hofmann reaction leading to the isomer XV of XI from either *cis*- or *trans*-X metho-

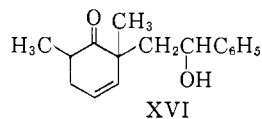


hydroxide, we are inclined to interpret the smooth conversion of X methohydroxide to olefin at relatively low temperatures as an indication that X has the *cis* configuration required to produce the most favorable conformation for olefin formation. If this interpretation is correct, then XI should be the chief product, but it is important to emphasize that no direct experimental evidence now at hand eliminates the possibility that XV may also be present.

The methohydroxide from XI, prepared from the methiodide by the procedure used to form X methohydroxide, underwent decomposition to a clear oil while the water was being distilled under reduced pressure from its solution. The decomposition product, however, was not the expected bis-olefin XII but was instead a substance containing the elements of XII plus the elements of water.

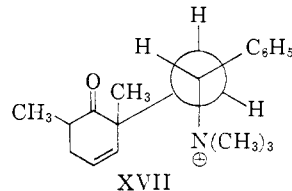
(13) F. E. King and H. Booth, *J. Chem. Soc.*, 3798 (1954); H. Booth and F. E. King, *ibid.*, 2688 (1958).

The oil was characterized as a crystalline oxime, $C_{16}H_{21}NO_2$, m.p. 185–187°, and it also formed a derivative, m.p. 94–97°, when treated with phenyl isocyanate. Hydrogenation over Adams catalyst in ethanol solution afforded a dihydro derivative, also an oil characterized as its crystalline oxime, m.p. 126–127°. The decomposition product dissolved in concentrated hydrochloric acid, but the solution soon deposited a gummy solid. These observations were in accord with the assignment of the benzylic alcohol structure XVI to the decompo-



sition product, which would be the result of a substitution rather than of an elimination reaction from XI methohydroxide. Substitution reactions of this nature appear to be characteristic of quaternary ammonium salts containing groups of the benzyl type,¹⁴ so that the formation of XVI and trimethylamine rather than of XI and methanol would be expected from the thermal decomposition of XI methohydroxide. However, nothing further is to be gained by speculating on the reason for the formation of the compound tentatively formulated as XVI until a rigorous demonstration of its structure is carried out.

The failure of XI methohydroxide to undergo an elimination reaction to form XII may be explained not only by referring to the expected ease with which it should form XVI but also by considering the stereochemistry of the quaternary cation derived from XI. A Newman formulation for one of the two conformations required for Hofmann elimination is given by expression XVII. In both this and the other possible conformation



the space-consuming ring and the trimethylammonio group (isosteric with *t*-butyl) are required to occupy positions that models indicate to be in forbiddingly close juxtaposition. Certainly both of the conformations required for Hofmann elimination are substantially less stable than the third staggered conformation, from which Hofmann elimination is difficult or impossible.

The Cope amine oxide elimination reaction¹⁵ has been shown to proceed by a predominantly *cis* steric course.¹⁶ It follows that the same stereochemical features that tend to inhibit Hofmann elimination from XI methohydroxide

(14) von Braun, *Ann.*, **362**, 1 (1911); see also H. R. Snyder and J. H. Brewster, *This Journal*, **71**, 291 (1949).

(15) A. C. Cope, T. T. Foster and P. H. Towle, *This Journal*, **71**, 3929 (1949).

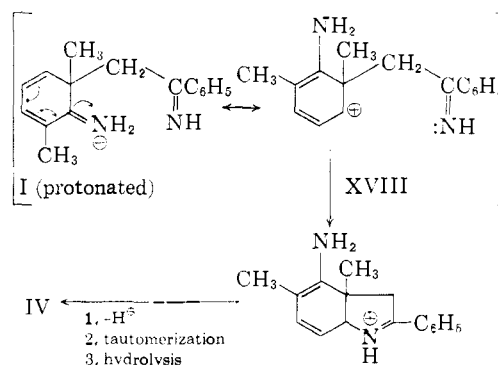
(16) D. J. Cram and J. E. McCarthy, *ibid.*, **76**, 5740 (1954); A. C. Cope and C. L. Baumgardner, *ibid.*, **79**, 960 (1957); A. C. Cope and E. M. Acton, *ibid.*, **80**, 355 (1958).

should tend to promote the Cope elimination from XI oxide. In a test of this hypothesis XI was converted by hydrogen peroxide to its oxide, which was characterized as the picrate, and the oxide was decomposed at 100° (15–20 mm.) to a neutral oil that was not purified sufficiently to yield completely satisfactory analytical results. However, hydrogenation in methanol over Adams catalyst converted this oil to another oil which was characterized as its oxime. That the hydrogenation product was 2,6-dimethyl-2-(β -phenylethyl)-cyclohexanone (XIII) was demonstrated by synthesizing XIII from 2,6-dimethylcyclohexanone and β -phenylethyl bromide in the presence of sodamide and showing that the infrared spectra of the two oils were essentially identical, as were the infrared spectra of the two crystalline oximes, which also had identical melting points, alone or mixed. Inasmuch as hydrogenation of the Cope elimination product from XI oxide had been shown to produce XIII, the Cope elimination product itself must have had the structure XII. It is worthy of note here that had the product of Hofmann elimination from X methoxide been partly or entirely XV, rather than XI, the structure of the Cope elimination product would still have been XII; therefore the proof of structure of IV by its degradation ultimately to XIII is not affected by the question whether XI or XV or both properly represent the Hofmann product.

The structure XIII has in it the entire carbon skeleton of IV; only the nitrogen atom of IV has been removed in the course of the degradation scheme. Therefore, the proof of structure of XIII (by synthesis) also proves the carbon skeleton of IV, including the angular methyl group at position 3a; for the reactions employed in the degradation of IV to XIII include none that are associated with carbon skeleton rearrangements. The proof of structure of XIII also fixes the position of the carbonyl group in IV. The demonstration of the carbon system of IV and the location of the ketone function leaves as the only remaining problems in the complete structure of IV the positions of the nitrogen atom and of the double bonds (other than the carbonyl). The nitrogen is shown to be cyclic by the fact that two degradative steps were required to separate it from the organic molecule. The assigned position is certainly the most probable one for a cyclic nitrogen in IV, and that this assignment is correct is attested by the isolation of 2-phenyl-5-methylindole (IX) in three steps from IV. The carbon-carbon double bond of IV is fixed in the 5-position by the evidence cited above that shows the presence of an α,β -unsaturated carbonyl function. Likewise, the spectroscopic evidence attesting the presence of conjugated imine and of conjugated phenyl fixes the remaining unsaturation between the 1- and 2-positions. Thus the proof of structure of IV is complete.

Discussion.—The conversion of ethyl pyruvate 2,6-dimethylphenylhydrazone to 2-carbethoxy-4,7-dimethylindole was rationalized by means of a mechanism that combined the essential features of certain current views on the mechanism of the Fischer reaction with portions of presently ac-

cepted mechanisms of the *para* Claisen rearrangement and of the dienone-phenol rearrangement.⁵ The principal feature of this mechanism is a postulated non-aromatic intermediate I. Exactly the same mechanism now may be used to explain the formation of 2-phenyl-4,7-dimethylindole (III) from acetophenone 2,6-dimethylphenylhydrazone (II). However, in this instance the same non-aromatic intermediate (I, R = CH₃, R¹ = C₆H₅, R² = H) can account not only for the formation of III but for that of IV as well. If the conjugate acid of I, written in structure and conformation XVIII, undergoes not only the methyl migration that leads eventually to III but also formation of a new C-N bond, the product should readily lose a proton, tautomerize and hydrolyze to afford IV.



Thus, the formation of III and IV from II may be interpreted as evidence supporting the postulate that a non-aromatic intermediate of type I is common to the formation of both III and IV.

The proposed mechanisms for the formation of III and IV require that the 1-nitrogen of the arylhydrazone (that attached to the aromatic ring) be retained in III and lost from IV. Experiments now in progress are designed to discover whether this predicted behavior is in fact observed.

The tetrahydroindolone derivative IV apparently represents a new class of hydroindoles. Efforts will be made to expand the study of its chemistry and to investigate the preparation and properties of other members of the series.

Experimental¹⁷

2,6-Dimethylphenylhydrazone.—With vigorous stirring 215 g. of 2,6-xylydine (Eastman Kodak Co.) was added to a solution of 445 ml. of concentrated hydrochloric acid and 200 ml. of water. The mixture was chilled to -5°, stirring was maintained, and a solution of 131 g. of sodium nitrite in 200 ml. of water was added dropwise. The clear orange diazonium solution was maintained at about 0° and stirred while a solution of 900 g. of stannous chloride dihydrate in 1200 ml. of 1:1 hydrochloric acid was added over a 4-hour period. The yellowish slurry was stirred as it was permitted to warm to room temperature and stirring was continued for another 24 hours. The pale yellow tin complex salt was collected by filtration, dried on the funnel and washed with ether. The 600 g. of dry complex salt was stirred into 1300 ml. of water, and the slurry was stirred vigorously while it was treated with a solution of 450 g. of sodium hydroxide in 600 ml. of water; the temperature of the mixture was maintained at or below 15°. The crude hydrazine was extracted from the mixture with two 700-ml. portions of ether, and the ether solutions were washed with water and dried over magnesium sulfate. The dried ether solution was diluted with ether to 3 l., the diluted solution

(17) Melting points are corrected.

was divided into two equal parts, and each was treated with dry hydrogen chloride until precipitation of the hydrazine hydrochloride was complete. The filtered hydrochloride was washed with ether and dried: yield 220 g. (72%), m.p. 204° dec. (sealed tube). A sample recrystallized from ethanol formed satiny, flat needles, m.p. 211° dec. (sealed tube).

Anal. Calcd. for $C_8H_{13}N_2Cl$: C, 55.64; H, 7.59; N, 16.23. Found: C, 55.63; H, 7.51; N, 16.22.

In one run 2,6-dimethylphenylhydrazine itself was isolated. It formed long, white needles, m.p. 36–40°, from petroleum ether (b.p. 30–60°). The compound decomposed rapidly in air.

Acetophenone 2,6-Dimethylphenylhydrazone (II).—A solution prepared by warming a mixture of 172 g. of 2,6-dimethylphenylhydrazine hydrochloride with a solution of 80 g. of sodium acetate in 500 ml. of water and 1500 ml. of methanol was heated to the boiling point and treated with 135 g. of acetophenone. Heating was maintained for a few minutes as a yellow oil began to separate from solution. The mixture was swirled as it was allowed to cool, and the yellow oil crystallized into large clumps of yellow needles. The mixture was chilled for a few hours in a refrigerator, filtered and the lumps crushed. The crude hydrazone weighed 210 g. (88%) after 4 hours drying in a vacuum desiccator. Three recrystallizations from methanol afforded bright yellow, flat needles, m.p. 55.5–58°. This material could be stored only for a few hours in a vacuum desiccator before marked decomposition became apparent. It proved impossible to dry a sample for analysis without decomposing it.

Action of Zinc Chloride in Nitrobenzene on Acetophenone 2,6-Dimethylphenylhydrazone (II).—A solution of 232 g. of freshly prepared II in 750 ml. of nitrobenzene was stirred with a Hershberg stirrer as it was treated with 375 g. of zinc chloride and then heated to 120°. At this temperature the color of the mixture quickly changed from orange to dark brown, and the temperature of the mixture rose rapidly. The mixture was cooled intermittently in order to maintain its temperature in the range 120–130°. After 15 minutes the temperature fell below 120°, and thereafter it was heated for 45 minutes to sustain the temperature in the 120–130° range. The mixture was steam distilled to remove the nitrobenzene.

The nitrobenzene layer of the steam distillate was extracted with 200 ml. of 10% hydrochloric acid, and a red oil separated when the acid extract was made basic with sodium hydroxide. The red oil was extracted into ether, and the ether solution was washed with water and dried over magnesium sulfate. A sample of the 10 g. of red oil that remained after removal of the ether was treated with phenyl isothiocyanate. The crystalline phenylthiourea derivative formed colorless prisms, m.p. 179–179.5°, from acetone-acetic acid. A sample prepared from authentic 2,6-xylylidine melted at 177–179°, and there was no mixed m.p. depression. The m.p. 186–187° has been reported.¹⁸

Anal. Calcd. for $C_{16}H_{16}N_2S$: C, 70.29; H, 6.29; N, 10.93; S, 12.49. Found: C, 70.22; H, 6.38; N, 11.18; S, 12.68.

The non-volatile residue from the steam distillation was extracted into 2 l. of ether. After the aqueous layer was removed, the ether layer was washed with 20% sodium hydroxide to dissolve suspended inorganic material, then washed with water and dried over magnesium sulfate. Concentration of the ether solution to a volume of 1 l. and cooling the concentrate overnight in the refrigerator caused the separation of 50.5 g. of a brown crystalline solid. Further concentration of the mother liquor afforded an additional 19.0 g. of similar crystals. Complete removal of the ether from the filtrate left 84.0 g. of a black tar. In some runs no crystalline material separated from the cooled, concentrated ether solution. In these cases all of the ether was removed, and the entire product was subjected to the treatment normally accorded the black tar fraction.

The 69.5 g. of crystalline solid was distilled at 15 μ through a short Vigreux column and thereby separated into two fractions: (1) 51.5 g., b.p. 137.5–142°; (2) 7.5 g., b.p. 146–149°. Both fractions were yellow oils that crystallized when scratched. The 84 g. of black tar was also separated into two fractions by distillation at 50 μ : (a)

22 g., b.p. 60–130°; (b) 34.4 g., b.p. 130–155°. The non-volatile residue from this distillation weighed 24 g.

Distillation fraction a was dissolved in ether, and the solution was extracted with 10% aqueous hydrochloric acid. When the acid extract was made basic with aqueous sodium hydroxide, only a black tar was obtained from which no crystalline substance could be isolated. The ether solution was washed with water and dried over magnesium sulfate. Removal of the ether left an orange oil that had the odor of nitrobenzene. A small sample of this oil was dissolved in ethanol, and the solution was added to a solution of 2,4-dinitrophenylhydrazine in ethanol containing a little sulfuric acid. An orange crystalline solid separated immediately; after crystallization from ethanol-ethyl acetate, this solid formed short, orange needles, m.p. 247–249°, which, when mixed with authentic acetophenone 2,4-dinitrophenylhydrazone, m.p. 250°, caused no m.p. depression.

Distillation fractions 2 and b, 41.9 g., were dissolved in about 250 ml. of ether, and the solution was extracted with 150 ml. of 10% aqueous hydrochloric acid. The washed ether solution was dried over anhydrous magnesium sulfate. Removal of the ether left 8.8 g. of a viscous, orange oil, whose solution in acetone gave an intense greenish-red color when treated with Ehrlich reagent. When 10 g. of neutral oil obtained in this manner was distilled at 1–2 mm., 7.5 g. of orange, oily distillate was collected which crystallized when scratched. Two recrystallizations from petroleum ether (b.p. 65–110°) afforded 3 g. of nearly white needles, m.p. 64–66°, undepressed by admixture with authentic 2-phenyl-4,7-dimethylindole (III), m.p. 65.5–66.5° (see below). A sample of the solidified distillate when treated with ethanolic picric acid formed a picrate, dark maroon needles from ethanol, m.p. 169–171°.¹⁹

The acid extract of distillation fractions 2 and b, when made basic with aqueous sodium hydroxide, precipitated 33.3 g. of a light yellow solid. This material, together with distillation fraction 1, was dissolved in 500 ml. of boiling ether. Cooling this solution in the refrigerator caused the separation of 20.7 g. of large, colorless crystals. The filtrate was extracted with 200 ml. of 10% aqueous hydrochloric acid, and the yellow solid that precipitated when the acid extract was made basic with 10% aqueous sodium hydroxide was dried and dissolved in 1.2 l. of boiling ether. The cooled solution deposited 49 g. of colorless crystals. Concentration of the mother liquors and subsequent cooling produced an additional 10.1 g. of the same material. In all, three fractions of these crystals totaling 79.8 g. of 2-phenyl-3a,5-dimethyl-3a,4,7,7a-tetrahydro[3H]pseudoindolone-4 (IV), m.p. 88–101°, was collected.

The non-volatile residue from the second distillation (24 g.) was dissolved in 100 ml. of acetone. After several days storage in the refrigerator, this solution had deposited 0.85 g. of a crystalline white solid which formed fluffy, white needles, m.p. 176–178°, from acetone.

Anal. Calcd. for $C_{24}H_{28}NO_2$: C, 80.19; H, 7.01; N, 3.90. Found: C, 80.34; H, 7.04; N, 3.79.

A bis-oxime was formed by the pyridine method,²⁰ colorless prisms from ethanol, m.p. 239–240°.

Anal. Calcd. for $C_{24}H_{27}N_3O_2 \cdot C_2H_5OH$: C, 71.69; H, 7.64; N, 9.65. Found: C, 71.16; H, 7.54; N, 9.72.

The major infrared absorption bands of the product $C_{24}H_{28}NO_2$ included two in the carbonyl region at 5.86 and 5.92 μ . The former is assigned to unconjugated carbonyl and the latter to aryl ketone carbonyl. (Acetophenone shows its carbonyl band at 5.93 μ .) In addition, three bands at 6.22, 6.32 and 6.68 μ were assigned to conjugated phenyl. No bands appeared in the O–H or N–H stretching regions. The ultraviolet spectrum measured in ethanol solution showed a single maximum at 246 m μ (ϵ 25,700); in ethanolic 0.1 N hydrochloric acid two bands appeared at 250 and 273 m μ (ϵ 17,700 and 20,000, respectively). This behavior is quite similar to that manifested by IV under similar conditions. The two bands observed in the acid solution are assigned to the C_6H_5CO and to $C=NH^+$, respectively, while the single band in neutral ethanol is considered to be

(19) C. F. H. Allen, D. M. Young and M. R. Gilbert, *J. Org. Chem.*, **2**, 235 (1937), reported the m.p. 171–172°.

(20) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," fourth ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 254.

(18) H. Busch and W. Schmidt, *Ber.*, **62**, 1455 (1929).

TABLE I
 SOME DERIVATIVES OF TETRAHYDROINDOLONE (IV)

Derivative	M.p., °C.	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
Mol. compd. (III-IV)	114.5-115 ^a	C ₂₂ H ₃₂ N ₂ O	83.44	83.49	7.00	7.22	6.08	6.15
Picrate	224 dec. ^b	C ₂₂ H ₂₀ N ₄ O ₈	56.41	56.19	4.30	4.02	11.96	12.20
Hydrochloride	214 dec. ^c	C ₁₆ H ₁₇ NO·HCl	69.68	69.74	6.58	6.49	5.08	5.16
Oxime	230 dec. ^d	C ₁₆ H ₁₈ N ₂ O	75.56	75.56	7.13	7.25	11.02	11.20

^a White cubes from ethanol. ^b Bright yellow cubes from acetone. ^c Small white crystals from ethanol-ether. ^d Prepared by pyridine method²⁰; fluffy white threads from ethyl acetate.

the sum of those owing to C₆H₅CO and C=N. The spectroscopic and chemical behavior of C₂₄H₂₈NO₂ therefore suggests a structure formed by the conjugate addition of acetophenone to IV.

Characterization of 2-Phenyl-3a,5-dimethyl-3a,4,7,7a-tetrahydro[3H]pseudindolone-4 (IV).—A sample of IV, m.p. 88-101°, gave large, colorless, prismatic needles, m.p. 92-101°, from ether.

Anal. Calcd. for C₁₆H₁₇NO·½H₂O: C, 77.39; H, 7.31; N, 5.64; mol. wt., 249. Found: C, 77.46; H, 7.31; N, 5.68; mol. wt. (Menzies-Wright, 4 detns.), 241-264.

In the course of one of the early preparations of IV from II, the residue from the steam distillation was subjected to high vacuum sublimation. The sticky yellow solid was crystallized from *n*-heptane and recrystallized from ethanol. Its composition (Table I) suggested that it was a molecular compound formed from equimolar amounts of III and IV. This supposition was confirmed by isolating both III and IV from this substance, as follows. Treatment of a solution of 2.5 g. of a solution of this compound in 25 ml. of ethanol with a solution of 3.0 g. of picric acid in 25 ml. of ethanol at the boiling point caused the immediate separation of the picrate of IV (Table I), from which IV could be regenerated by treatment with lithium hydroxide.²¹ The ethanolic filtrate from IV picrate was made basic with excess aqueous sodium hydroxide, and the mixture was extracted with benzene. Removal of the benzene and recrystallization of the residue from *n*-hexane gave white needles, m.p. 65.5-66.5°, alone or when mixed with the indole III.

In addition to the molecular compound and a picrate, IV was also converted to a crystalline hydrochloride and a crystalline oxime (Table I). None of the derivatives contained water of crystallization.

The broad melting range of IV cast some doubt on its purity and homogeneity, despite the fact that pure, sharp-melting derivatives were formed from it. Therefore, samples of IV were subjected to fractional crystallization from ether, to chromatography on alumina from petroleum ether solution and to counter-current distribution in a 54-plate Craig machine. In the latter procedure the sample was distributed between cyclohexane and a hydrochloric acid-potassium chloride buffer of pH 1.6. The ultraviolet absorption spectrum of a sample from each plate that contained detectable amounts of organic solute was measured. In every case the curve was of the same shape as that of IV in cyclohexane, and each curve had its maximum at 237 mμ. The concentration of IV in each plate was computed from the intensity of absorption at 237 mμ, and the distribution curve was plotted from the data thus gathered. The curve showed no indication of heterogeneity of the original sample. Since the other separation procedures also disclosed no heterogeneity, the broad melting range of IV was attributed to the nature of the hemihydrate.

2,5-Dimethylphenylhydrazine.—A procedure identical with that employed to prepare 2,6-dimethylphenylhydrazine, except that the solution was stirred for only 0.5 hour at 0° after the stannous chloride-hydrochloric acid solution had been added, gave an ether solution from which 2,5-dimethylphenylhydrazine was isolated as long, white crystals when the ether was removed. Slurrying with petroleum ether (b.p. 30-60°) and subsequent filtration gave a 46% yield of a product of m.p. 73-75°.²²

Acetophenone 2,5-dimethylphenylhydrazone.—When a solution of 26 g. of 2,5-dimethylphenylhydrazine, 26 g. of acetophenone and 2 ml. of glacial acetic acid in 250 ml. of ethanol was boiled for 10 minutes and then cooled, a thick

slurry of the hydrazone was formed. The white solid weighed 43 g. (95%), m.p. 107-108.5°. Owing to its instability, a satisfactory analytical sample could not be prepared; however, it could be stored for a short time under nitrogen in a refrigerator.

2-Phenyl-4,7-dimethylindole (III) from Acetophenone 2,5-Dimethylphenylhydrazine.—A mixture of 33 g. of acetophenone 2,5-dimethylphenylhydrazone, 54 g. of zinc chloride and 400 ml. of nitrobenzene was stirred vigorously and heated to 130-140° for 25 minutes. The residue that remained after the nitrobenzene had been removed by steam distillation was dissolved in benzene, and the benzene solution was extracted with 10% aqueous hydrochloric acid and then with water before it was dried over Drierite. Removal of the benzene left a tarry residue which was subjected for 8 hours to sublimation at 120° (1 μ). The sublimate, 8.0 g. (26%) of an orange solid, after three recrystallizations from *n*-heptane and a vacuum sublimation at 90° (1 μ), gave colorless needles, m.p. 65.5-66.5°.

Anal. Calcd. for C₁₆H₁₈N: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.60; H, 7.17; N, 6.24.

The picrate, prepared as described above, formed dark maroon needles, m.p. 170.5-171.5°, undepressed in the mixture of samples from the two sources.

The synthesis of III by two independent routes has been reported previously, but it was isolated only as an oil that formed a picrate, reddish-brown needles, m.p. 171-172°.¹⁹

Reduction of IV with Lithium Aluminum Hydride.—A solution of 8.2 g. of IV in 100 ml. of anhydrous ether was added to a stirred mixture of 6.5 g. of powdered lithium aluminum hydride in 100 ml. of anhydrous ether at such a rate that smooth boiling was maintained. After an additional half-hour boiling, excess reagent was destroyed by addition of water; then the mixture was treated with 160 ml. of 20% aqueous sodium potassium tartrate, and the ether layer was washed with water and dried over Drierite. Removal of the ether left a viscous, nearly colorless oil from which no crystalline solid could be obtained. Distillation of the oil gave a colorless, viscous distillate (V), b.p. 171-178° (1-2 mm.). A center cut, b.p. 173° (1-2 mm.), was selected for analysis.

Anal. Calcd. for C₁₆H₂₁NO: C, 78.97; H, 8.70; N, 5.76. Found: C, 79.17; H, 8.44; N, 5.80.

The picrate of V crystallized from an ethanol solution of the oil and picric acid. Recrystallization from aqueous ethanol gave yellow needles, m.p. 186-187°.

Anal. Calcd. for C₂₂H₂₄N₄O₈: C, 55.93; H, 5.12; N, 11.86. Found: C, 55.66; H, 5.28; N, 11.80.

A chloride hydrochloride was formed when an ether solution of V was treated with ethanolic hydrogen chloride and the resulting solution evaporated to dryness. The residual white solid formed fine, white needles, m.p. 199-201° dec., from absolute ethanol ether.

Anal. Calcd. for C₁₆H₂₁NCl₂: C, 64.44; H, 7.10; N, 4.69. Found: C, 64.24; H, 7.46; N, 4.31.

2-Phenyl-3a,5-dimethyloctahydroindolone-4 (VII).—A solution of 29.6 g. of the tetrahydroindolone derivative IV in 75 ml. of glacial acetic acid was shaken for 2 hours with hydrogen at 55 p.s.i. in the presence of 0.1 g. of Adams catalyst. The solution was filtered free of catalyst, poured into excess cooled 20% aqueous sodium hydroxide, and the insoluble oil was extracted into 100 ml. of ether. The ether solution was washed with water and dried over magnesium sulfate. Removal of the ether left a yellow oil, which was dissolved in 100 ml. of petroleum ether (b.p. 65-110°). When the vessel containing the refrigerated solution was scratched, 13.0 g. (45%) of fluffy, white needles separated,

(21) A. Burger, *THIS JOURNAL*, **67**, 1615 (1945).

(22) C. Willgeroat and W. Lindenberg, *J. prakt. Chem.*, [2] **71**, 398 (1905), reported the m.p. 78°.

m.p. 91–93°. Recrystallization from the same solvent gave a sample of m.p. 92.5–93.5°.

Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.94; H, 8.86; N, 5.60.

The oxime, prepared by the pyridine method,²⁰ formed white needles, m.p. 177–179°, from cyclohexane–ethyl acetate.

Anal. Calcd. for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.32; H, 8.39; N, 10.83.

The mother liquors from the crystals of m.p. 92.5–93.5° were concentrated to dryness under reduced pressure, and the residue was dissolved in petroleum ether (b.p. 30–60°). The refrigerated solution deposited 13.25 g. (46%) of a tan solid, m.p. 39–48°. This material was purified by distillation, b.p. 164–166° (1–2 mm.). A sample of the distillate, after five recrystallizations from petroleum ether (b.p. 30–60°), yielded clusters of white needles, m.p. 56.5–58°, from petroleum ether. This substance is an epimer of the higher-melting modification.

Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 79.01; H, 8.80; N, 5.67.

The oxime, also prepared by the pyridine method,²⁰ formed clumps of white needles, m.p. 162–164°, from cyclohexane.

Anal. Calcd. for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.44; H, 8.40; N, 10.74.

Wolff–Kishner Reduction of the Octahydroindolone VII.—A mixture of 3.5 g. of VII, m.p. 91–93°, 40 ml. of ethylene glycol, 3.75 ml. of 85% hydrazine hydrate and 5.0 g. of potassium hydroxide was heated at the boiling point (137°) for 1.5 hours. Water was distilled from the mixture until the temperature of the latter rose to 195°, and then boiling was continued at this temperature for 4.5 hours. The cooled mixture was poured into 200 ml. of water, and the water-insoluble oil was extracted into ether. The ether solution was washed with water, dried over magnesium sulfate, and the ether was removed. The residual 3.0 g. of straw-colored oil, the crude reduction product VIII, was converted to a solid hydrobromide derivative when a solution of 3.0 g. of crude VIII in 5 ml. of ethanol was treated with 3 ml. of 48% aqueous hydrobromic acid. The solution was diluted with 25 ml. of water, the dilute solution was filtered and the filtrate was evaporated to dryness. The pasty residue was washed with a little ether, and the remaining 3.9 g. of sticky yellow solid was recrystallized from ether–absolute ethanol to afford 1.64 g. of a yellow solid, m.p. 202–210°. Two additional recrystallizations from the same solvent gave fine, bright yellow needles, m.p. 206–218°. The broad m.p. range probably indicates the presence of stereoisomers.

Anal. Calcd. for $C_{16}H_{21}NBr$: C, 61.93; H, 7.80; N, 4.51. Found: C, 61.64; H, 7.86; N, 4.49.

2-Phenyl-5-methylindole (IX) by Dehydrogenation of VIII.—A mixture of 2.0 g. of VIII and 4.0 g. of powdered selenium was heated at 290° for 6 hours, cooled and extracted with ether. The filtered ether solution was extracted with 10% hydrochloric acid and with water, then the ether was removed. The residual black tar, heated at 80–110° (1 μ), evolved 0.5 g. of a mobile yellow oil and also a small quantity of a yellow solid. This solid, recrystallized from petroleum ether (b.p. 65–110°), gave 10 mg. of a fluffy white solid, m.p. 198–202°, whose acetone solution gave an intense, cherry-red color when treated with Ehrlich reagent. Another recrystallization from petroleum ether gave a sample melting at 205–208°, but attempts to effect further purification were abandoned because of scarcity of the material. A mixture of this substance with authentic 2-phenyl-5-methylindole (IX), m.p. 214–216°, melted at 208–212°. The ultraviolet absorption spectra of the two samples were identical, and the infrared spectra differed only in the presence of a weak band at 7.25 μ and a medium band at 12.37 μ in the spectrum of the selenium dehydrogenation product that did not appear in that of authentic IX.

Anal. Calcd. for $C_{15}H_{13}N$: C, 86.92; H, 6.32. Found: C, 86.71; H, 6.55.

2-Phenyl-5-methylindole (IX) by the Bischler Method.¹¹—When phenacylaniline and *p*-toluidine in 1:9 molar ratio were subjected to the Bischler procedure,¹¹ IX was obtained as fluffy, buff-colored fine needles, m.p. 214–216°.²³

(23) A. Bischler, *Ber.*, **25**, 2870 (1892), reported the m.p. 213°.

2-Phenyl-1,3a,5-trimethyloctahydroindolone-4 (X).—A mixture of 12.35 g. of the octahydroindolone VII, m.p. 47–53°, and 6.65 g. of 88% formic acid was treated with 4.56 g. of 36% formaldehyde in accordance with a published procedure.²⁴ The cooled reaction mixture was poured into 20 ml. of 25% aqueous sodium hydroxide, and the oily product was extracted with ether. The ether solution was washed with water, dried over magnesium sulfate, and the ether was removed. Distillation of the oily residue gave 9.35 g. of a colorless oil, b.p. 145–147° (1–2 mm.), n_D^{20} 1.5338. Refrigeration of a solution of 6 g. of this oil in 25 ml. of petroleum ether (b.p. 65–110°) caused the separation of 3.75 g. of a white crystalline solid. The mother liquor was distilled at 100–125° (0.01 mm.), and 1.97 g. of a colorless distillate, n_D^{20} 1.5338, was collected. A solution of this oil in 3 ml. of petroleum ether (b.p. 30–60°) deposited another 0.34 g. of white crystalline solid after 2 weeks refrigeration. Three recrystallizations of the combined crystalline solids from the same solvent afforded colorless cubes, m.p. 42–44°.

Anal. Calcd. for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.12; H, 9.16; N, 5.48.

The oxime, prepared by the pyridine method,²⁰ formed short, white needles, m.p. 138–140°, from petroleum ether.

Anal. Calcd. for $C_{17}H_{24}N_2O$: C, 74.96; H, 8.88; N, 10.29. Found: C, 75.26; H, 8.89; N, 10.18.

When the stereoisomer of VII, m.p. 91–93°, was subjected to the same methylation procedure, the product was a colorless oil, b.p. 149–150° (1–2 mm.), n_D^{20} 1.5332. The infrared spectrum of this oil was identical with that prepared from the VII stereoisomer of m.p. 47–53°. Although only one crystalline form of the methylation product X could be isolated, the infrared spectra of the oil, of the solid and of the oily residue left after removal of the solid suggested that another stereoisomeric form of X was present.

The methiodide of X was prepared by boiling a solution of 9.35 g. of X and 10 ml. of colorless methyl iodide in 15 ml. of dioxane for 22 hours. The mixture was diluted with 25 ml. of ether, and 8.25 g. (57%) of dark yellow solid, m.p. 222–224° dec., was collected by filtration, washed with ether and recrystallized from water. Repeated recrystallizations from absolute ethanol gave short, nearly colorless needles, m.p. 228° dec.

Anal. Calcd. for $C_{18}H_{23}NOI$: C, 54.14; H, 6.56; N, 3.51. Found: C, 54.27; H, 6.65; N, 3.61.

Preparation and Hofmann Decomposition of the Methohydroxide of X.—A slurry formed by treating 30 g. of Amberlite IR-400 resin (chloride form) with 100 ml. of 20% aqueous sodium hydroxide was poured into a 25-mm. diameter glass tube, the alkaline solution was permitted to drain from the resin, and the latter was washed with distilled water until the washings were neutral to litmus. A solution of 6.75 g. of X methiodide in 300 ml. of warm water was allowed to trickle through the column, then the resin was washed with water until the washings were neutral to litmus (ca. 250 ml.). The water was removed from the eluate and washings at 15–20 mm. on the steam-bath; the 5.0 g. of yellow glassy residue gave only a faint positive test with silver nitrate. The glass was ground to a hygroscopic yellow powder which decomposed at 120° (1 μ) to a dark liquid. An ether extract of this liquid, after removal of the ether, afforded 2.7 g. (59%) of a pale yellow oily distillate, b.p. 115° (1 μ), n_D^{20} 1.5305. This oil comprised compound XI, or XV, or a mixture of the two. Its methiodide formed immediately when 1.4 g. of the oil was treated with 1.6 g. of colorless methyl iodide. After brief heating on the steam-bath, the mixture was diluted with a little ether, and 2.2 g. (ca. 100%) of a white solid was collected which formed a cloudy melt at 152° and then decomposed at about 200°. Recrystallization from ether–absolute ethanol afforded small white crystals, m.p. 158–213° dec. The melting range, together with the analytical data, suggest that the salt is a mixture of isomers, possibly diastereomers.

Anal. Calcd. for $C_{19}H_{23}NOI$: C, 55.21; H, 6.83; N, 3.39. Found: C, 55.33; H, 7.18; N, 3.26.

Preparation and Decomposition of the Methohydroxide of XI (and/or XV).—A solution of 2.9 g. of the methiodide described in the preceding paragraph in 70 ml. of warm

(24) H. T. Clark, H. B. Gillespie and S. W. Weisshaus, *THIS JOURNAL*, **55**, 4571 (1933).

water was allowed to trickle through a 2.5×10 cm. column of Amberlite IR-400 resin (hydroxide form, prepared as described), and the resin was washed with 100 ml. of water. The water was removed from the eluate and washings on the steam-bath at 15–20 mm., and the residual base underwent decomposition to a clear oil as soon as the water was gone. The product was extracted with ether, the ether was removed and the residue distilled (10 μ , bath temperature 95–105°) to yield 0.71 g. of a colorless oil, n_D^{20} 1.5512.

An oxime, prepared by the pyridine method,²⁰ was a white solid, m.p. 185–187°, from ethanol.

Anal. Calcd. for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.23; H, 8.07; N, 5.28.

Hydrogenation of a sample of the oil, n_D^{20} 1.5512, in ethanol solution over Adams catalyst at 60 p.s.i. for 1 hour produced another oil, from which an oxime was also prepared by the pyridine method.²⁰ It was a fluffy white solid, m.p. 129–130° from cyclohexane.

Anal. Calcd. for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.59; H, 8.72; N, 5.80.

Preparation and Decomposition of the Oxide of XI (and/or XV).—A solution of the amine oxide in 20 ml. of water was prepared from 1.6 g. of XI (and/or XV) in accordance with the procedure of Cope, Foster and Towle.¹⁵ Addition of a 3-ml. aliquot from this solution to a solution of 0.2 g. of picric acid in 15 ml. of water effected the precipitation of about 0.4 g. of a yellow solid which formed fine, light yellow needles, m.p. 133–134.5°, after three recrystallizations from aqueous ethanol.

Anal. Calcd. for $C_{24}H_{28}N_4O_9$: C, 55.81; H, 5.46; N, 10.85. Found: C, 56.13; H, 5.56; N, 10.95.

The remaining 17 ml. of amine oxide solution was concentrated at 40–50° (15–20 mm.); removal of all the water left a viscous sirup that crystallized to a waxy solid. This material was heated at 100° (15–20 mm.) for 1.5 hours, and an ether solution of the residual oil was extracted with 20 ml. of 10% hydrochloric acid, washed with water and dried over magnesium sulfate. Distillation of this oil at 10 μ (bath temperature 130°) gave about 0.5 g. (43%) of a colorless oil, n_D^{20} 1.5625. While its analysis did not accord satisfactorily with the formulation XII, it indicated that XII could indeed be the chief component.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 83.60; H, 7.71.

Hydrogenation of the amine oxide elimination product (0.8 g.) in 25 ml. of absolute methanol over 0.1 g. of Adams catalyst at 50 p.s.i. for 1.5 hours gave a solution from which a light yellow oil remained after removal of the catalyst and

methanol. Distillation of this oil at 10 μ (bath temperature 90–100°) produced 0.7 g. of a mobile, faintly yellow oil, n_D^{20} 1.5182; infrared spectrum (pure liquid, 0.025-mm. cell): 3.32sh, 3.44i, 3.50i, 5.87i, 6.23w, 6.68m, 6.89i, 7.28m, 7.36sh, 7.62w, 8.08w, 8.52w, 8.90m, 9.10w, 9.32w, 9.50w, 9.72w, 9.96m, 10.16m, 10.48m, 11.62m, 11.88w, 13.32m, 13.66m, 14.34i.

The oxime, prepared by the pyridine method,²⁰ gave white needles, m.p. 114–115.5°, from ethanol.

2,6-Dimethyl-2-(β -phenylethyl)-cyclohexanone (XIII).—A warm, stirred suspension of 9.0 g. of powdered sodium amide in 150 ml. of dry benzene was treated with 23 g. of 2,6-dimethylcyclohexanone.²⁶ After ammonia evolution had ceased, 37 g. of β -phenylethyl bromide (Eastman Kodak Co.) was added, and the mixture was stirred at the boiling point for 18 hours. After addition of 100 ml. of water, the benzene solution was separated, dried over magnesium sulfate, and the benzene was removed. Distillation of the oily residue afforded three fractions: (1) b.p. 52–70° (12–13 mm.), 11.8 g. (52%) of unchanged 2,6-dimethylcyclohexanone; (2) b.p. 85–95° (12–13 mm.), 8.5 g. of an unidentified oil; (3) b.p. 145–155° (1–2 mm.), 17 g. (40%) of XIII. Redistillation of fraction 3 yielded a water-clear liquid, b.p. 143° (1–2 mm.), n_D^{20} 1.5205. Its infrared spectrum, determined on the pure liquid, was identical in every respect with that of the liquid derived by hydrogenation of the amine oxide elimination product.

Anal. Calcd. for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.20; H, 9.66.

The oxime, prepared by the pyridine method²⁰ and recrystallized from petroleum ether (b.p. 65–110°) and then twice from ethanol, formed white needles, m.p. 115–116°. A mixture with the oxime formed from the liquid derived by hydrogenation of the amine oxide elimination product showed no m.p. depression.

Anal. Calcd. for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.51; H, 9.28; N, 5.64.

Absorption Spectra.—Ultraviolet absorption spectra were determined by means of a Cary automatic recording spectrophotometer equipped with 1-cm. quartz cells. Infrared spectra were measured by a Perkin-Elmer model 21 infrared spectrophotometer equipped with sodium chloride optics.

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(25) R. B. Carlin, *THIS JOURNAL*, **67**, 928 (1945).

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Chelates of β -Diketones. I. Enolization, Ionization and Spectra

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Observations have been made concerning the properties of two series of β -diketones, one in which electronic factors are varied by the introduction of substituents in the *m*- and *p*-positions of dibenzoylmethane, and a second in which the steric requirements of the R-groups in $RCOCH_2COR$ are varied by progressive branching. Increasing the steric requirements of the R-groups in the aliphatic series increases the degree of enolization to such an extent that dipivaloylmethane has no detectable diketo form in the pure liquid. As the degree of enolization increases, the acidity of the enol decreases. Two series of β -diketones have been prepared and studied in order to observe the effects of electronic and steric effects upon properties such as acidity, enolization and spectra. In one series electronic effects were varied by introduction of *m*- and *p*-substituents in the dibenzoylmethane structure. The second series consisted of symmetrical aliphatic diketones in which the bulk of the terminal alkyl groups was varied.

Experimental

Diaroylmethanes.—All of the diaroylmethanes (1,3-diaroyl-1,3-propanediones), except 3,3'-dinitrodibenzoylmeth-

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ane, were prepared by Claisen condensations of ethyl benzoates with acetophenones using the procedure described by Adams and Hauser⁴ with minor modifications. The physical constants and yield data are reported in Table I.

3,3'-Dinitrodibenzoylmethane.—1,3-Di-(3-nitrophenyl)-propenone (3,3'-dinitrochalcone) was prepared in 89% yield by the condensation of *m*-nitroacetophenone with *m*-nitrobenzaldehyde, m.p. 211–214°. The chalcone was converted to the dibromide in 44% yield by reaction with

(4) J. T. Adams and C. R. Hauser, *THIS JOURNAL*, **66**, 1220 (1944).