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The Fischer Reaction of Cyclohexanone Mesitylhydrazone. Evidence of a 1,4-Methyl Migration[1]

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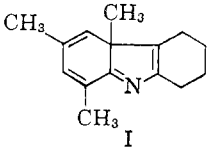
RECEIVED MAY 31, 1962

Cyclohexanone mesitylhydrazone (IV) was transformed in boiling acetic acid into 6,7,8-trimethyl-1,2,3,4-tetrahydrocarbazole (Vb), which was synthesized independently from cyclohexanone 2,3,4-trimethylphenylhydrazone. 5,6,8-Trimethyl-1,2,3,4-tetrahydrocarbazole (Va) was synthesized from cyclohexanone 2,4,5-trimethylphenylhydrazone and shown to be different from Vb. The tetrahydrocarbazoles, though quickly destroyed by air oxidation, could be dehydrogenated by chloranil in xylene under nitrogen to stable, crystalline carbazoles. The tetrahydrocarbazoles underwent air oxidation in ether solution, in the absence of added catalyst, to form crystalline 11-hydroperoxytetrahydrocarbazolenines (VII) which rearranged characteristically in chloroform or ethanol solution to stable ketolactams (VIII). The structures of VIII were demonstrated by their hydrolysis to ketoaminoacids (IX) and by their cyclization to 2,3-cyclopenteno-4-quinolones (X). The conversion of IV to Vb is believed to proceed through a pathway analogous to those proposed for previously investigated 2,6-dimethylphenylhydrazones, except that a 1,4-migration of a methyl group is postulated to have occurred.

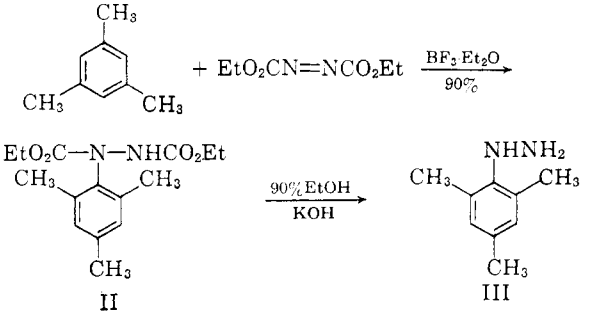
The conversion of cyclohexanone mesitylhydrazone in acetic acid to a substance $C_{15}H_{19}N$, which was isolated and characterized only as its black picrate, m.p. 171°, was reported some time ago.[3]



I

Structure I was tentatively proposed for the product. The later observation[4] that acetophenone 2,6-xylylhydrazone is transformed by zinc chloride in nitrobenzene to 2-phenyl-4,7-dimethylindole and a hydroindolone derivative prompted a more detailed examination of the product derived from cyclohexanone mesitylhydrazone, some of the results of which were briefly described in a Communication.[5] The present article is intended to comprise a complete account of the investigation.

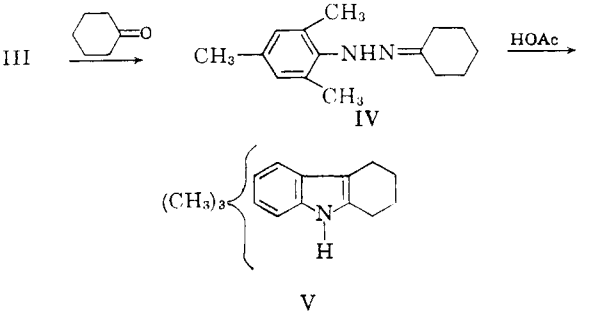
The preparation of cyclohexanone mesitylhydrazone, which was not reported by the former investigators,[3] required a satisfactory synthetic route to mesitylhydrazine. At the time when this work was undertaken, the only recorded preparation of mesitylhydrazine was that by Franzen, *et al.*,[6] who reported its synthesis from mesidine, through diazotization and reduction, in 7.5% yield. Later, Hunsberger and his associates[7] reported an improvement on Franzen's synthesis that afforded mesitylhydrazine in about 30% yield. An extension and adaptation of Huisgen's synthesis of 1,2-dicarbalkoxy-1-arylhydrazines from alkylbenzenes and azodicarboxylic esters,[8] however, led to a much more satisfactory preparative method, both from the point of view of yields obtained and of time expended. A separate communication will describe this method and its application to the preparation of a number of arylhydrazines; for the present, it should be sufficient to indicate that mesitylhydrazine is available in 80% over-all yield from mesitylene in two steps. Mesitylhydrazine (III), though a crystalline solid



II III

was too sensitive to air to be characterized by analysis; however, its crystalline dicarbethoxy derivative II was characterized, and the structure of III was further demonstrated by its hydrogenation to mesidine, identified as its N-acetyl derivative. Cyclohexanone mesitylhydrazone (IV), prepared from III and cyclohexanone, likewise was too air-sensitive to permit preparation for analysis.

When IV was boiled in acetic acid for thirty minutes under nitrogen, ammonium acetate separated, and treatment of the solution with picric acid afforded a black picrate whose analysis and m.p. 171° coincided with those formerly reported.[3] Although the picrate was itself stable, the crystalline base V, obtained from the picrate by the action of 5% sodium hydroxide, was extremely sensitive to air. A freshly prepared sample of V, treated im-



IV V

(1) Support of this investigation by Grant NSF-G4377 from the National Science Foundation is gratefully acknowledged.

(2) Submitted by Mead S. Moores in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Carnegie Institute of Technology.

(3) C. S. Barnes, K. H. Pausacker and W. E. Badcock, *J. Chem. Soc.*, 730 (1951).

(4) R. B. Carlin and D. P. Carlson, *J. Am. Chem. Soc.*, **79**, 3605 (1957); **81**, 4673 (1959).

(5) R. B. Carlin and M. S. Moores, *ibid.*, **81**, 1259 (1959).

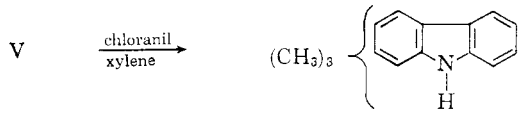
(6) H. Franzen, A. Onsager and G. Faerden, *J. prakt. Chem.*, [2] **97**, 350 (1918).

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

(8) R. Huisgen, F. Jakolo, W. Siegel and A. Cadus, *ibid.*, **590**, 1 1954).

mediately with picric acid, gave the black picrate again; however, after standing in air for an hour, another sample yielded very little picrate. One sample of V, after having been subjected for two weeks to efforts to recrystallize it in air, had turned to a mucilaginous mass, from which a new crystalline compound, $C_{15}H_{19}NO_2$, could be isolated in approximately 20% yield. When V was boiled in xylene solution with chloranil under normal conditions, it was converted into refractory blue and green powders. Thus it became clear that V could be manipulated successfully only in an inert atmosphere, and accordingly all of the succeeding operations upon it were carried out in a glove-box provided with an atmosphere of dry, oxygen-free nitrogen.

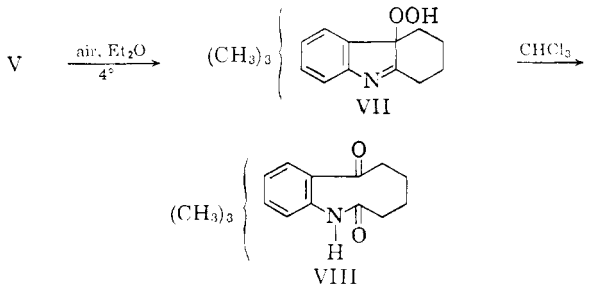
The infrared spectrum of the base V showed an N–H stretching band at 2.87μ. This, together with other features of the ultraviolet and infrared spectra, rendered extremely unlikely the structure I previously proposed[3] and suggested instead a tetrahydrocarbazole structure. That V actually possessed this skeletal structure was demonstrated by two observations: (a) the conversion of V by chloranil in xylene solution under nitrogen to a stable, crystalline substance exhibiting all of the properties to be expected of a carbazole (VI); and



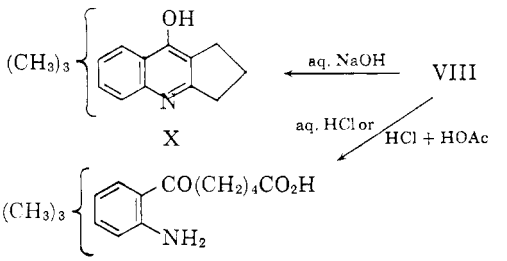
VI

(b) its transformation to a crystalline hydroperoxide when its ether solution was exposed to the action of air at 4°.

Witkop and his collaborators,[9] among others who had studied the air oxidation of tetrahydrocarbazole, had demonstrated that tetrahydrocarbazole is converted by air to 11-hydroperoxytetrahydrocarbazolenine which is transformed by acids or in polar solvents to a ketolactam, which in turn is characterized by its acid hydrolysis to a keto amino acid and its cyclization in base to a cyclopenteno-4-quinolone derivative. Analogously, V was converted to the moderately stable, crystalline hydroperoxide VII when its ether solution was exposed to air. This structural assignment was supported by the spectral properties of VII and by its rearrangement in ethanol solution to a stable, crystalline substance having the properties of the ketolactam VIII. Incidentally, this crystalline

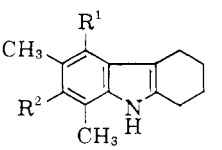


solid, m.p. 172°, was identical with the crystalline material isolated from the product of an effort to crystallize a sample of V in air for two weeks. Acid hydrolysis of VIII afforded a stable ketoamino acid IX, plus a substance having the properties to be expected of the quinolone derivative X, which could also be obtained from VIII by the action of sodium hydroxide.[10]



IX(major) + X(minor)

The behavior of the base V and its transformation products therefore left no reasonable doubt of its tetrahydrocarbazole skeletal structure. Only the positions occupied by the three methyl groups, shown by analytical data to be present in the base and in the derivatives (XI–X) obtained from it, remained to be established. Analogy with the reactions of the 2,6-xylylhydrazones of acetophenone[4] and of ethyl pyruvate[11] suggested that the hydrazone IV might well have undergone an *ortho* migration of one methyl group during its conversion to V, in which case the three methyl groups in V would occupy the 5-, 6- and 8- positions (Va).



Va, $R^1 = CH_3$, $R^2 = H$
Vb, $R^1 = H$, $R^2 = CH_3$

A synthesis of Va was therefore undertaken. The starting material, 2,4,5-trimethylphenylhydrazine, was prepared from pseudocumene by the azo ester synthesis used to convert mesitylene to its hydrazine. The structure of this new hydrazine was also established by reduction to the corresponding aromatic amine and characterization of the latter through its crystalline acetyl derivative. The corresponding cyclohexanone trimethylphenylhydrazone (IVa), like its isomer IV, an easily oxidized crystalline solid, was converted in boiling acetic acid to a substance that formed a black picrate, m.p. 171°. Although a mixture of this picrate and that obtained from cyclohexanone mesitylhydrazone (IV) exhibited a melting point depression of a few degrees, the significance of this observation was obscured by the fact that both picrates melted with decomposition. The facile oxidation in air of the base derived from the picrate made doubtful the validity of comparing the properties of this material

(9) B. Witkop, *J. Am. Chem. Soc.*, **72**, 1428 (1950); B. Witkop and J. B. Patrick, *ibid.*, **73**, 2188, 2196 (1951).

(10) Assignment of structures to the compounds VIII-X, and isomers to be referred to presently, was substantially aided by comparisons of their spectra with those of authentic samples of the parent substances (without methyl groups). Dr. Hans Dressler, Koppers Research Laboratories, generously supplied us with the parent ketolactam, and the quinolone and ketoamino acid derivatives were prepared from it by published procedures.[9]

(11) R. B. Carlin, W. O. Henley, Jr., and D. P. Carlson, *J. Am. Chem. Soc.*, **79**, 5712 (1957).

with those of the specimen obtained from IV. However, dehydrogenation of the new base in xylene solution by chloranil under nitrogen afforded a crystalline trimethylcarbazole (VIa), m.p. 143°, some 15° higher than the melting point of the trimethylcarbazole (VI) obtained from V. Furthermore, the ketolactam VIIIa obtained from the new base by air oxidation and rearrangement could not be obtained crystalline, and the melting point of the keto amino acid IXa, derived from VIIIa by acid hydrolysis, differed by more than 20° from that of the keto amino acid IX obtained from VIII. It was thus clear that the structure Va was not the correct one for the product derived from cyclohexanone mesitylhydrazone IV.

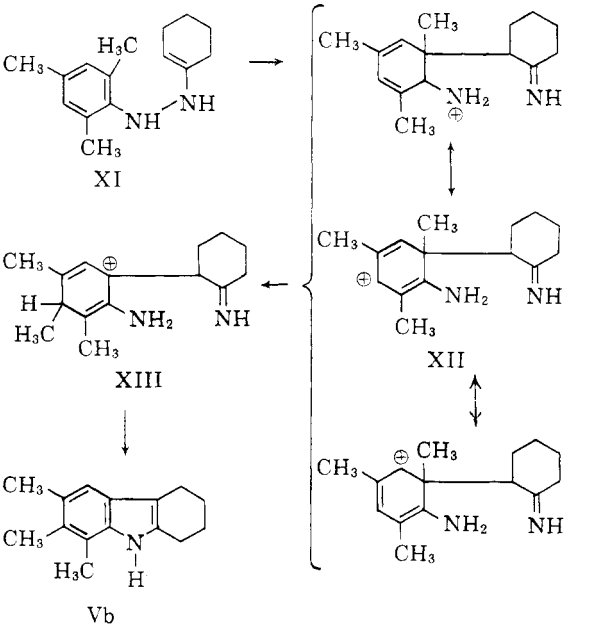
Barring a wholesale rearrangement of methyl groups from their original positions in IV, an unlikely development under the conditions imposed in the conversion of IV to V, then only one remaining feasible structure, Vb, may be written for the product derived from IV. Therefore, a synthesis of Vb was undertaken from hemimellitene, using a series of steps precisely analogous to those employed in converting mesitylene and pseudocumene to the tetrahydrocarbazoles derived from them. The structure of 2,3,4-trimethylphenylhydrazine (IIIb) was also established by reduction to the corresponding aromatic amine and characterization of the latter through its known crystalline acetyl derivative.

As was the case with Va, the product Vb of the transformation of cyclohexanone 2,3,4-trimethylphenylhydrazone (IVb) in boiling acetic acid was isolated as a black picrate, m.p. 171°. This time, however, no melting point depression was observed when a sample of this compound was mixed with the picrate derived from V. In addition, the trimethylcarbazole VIb and the several oxidation products (VIIb–Xb) derived from the new base, were identical in every detectable respect with the corresponding compounds (VI–X) obtained from cyclohexanone mesitylhydrazone (IV). Thus, the base derived from the latter has the structure Vb.

This conclusion, to be sure, rests on the assumption that widespread methyl migrations have not occurred during the conversions of the corresponding hydrazones to the tetrahydrocarbazoles. That this assumption is valid is indicated by the observation that the cyclohexanone arylhydrazones derived from pseudocumene and hemimellitene give different tetrahydrocarbazoles. In the unlikely event that the conditions that bring about the formation of the tetrahydrocarbazoles induced generalized methyl group rearrangements, then all three of the cyclohexanone arylhydrazones would have been expected to afford the same trimethyltetrahydrocarbazole.

Discussion

The formation of the tetrahydrocarbazole Vb from cyclohexanone mesitylhydrazone (IV) may be rationalized by means of a mechanism analogous in most respects to those proposed previously[4,11] to account for products derived from 2,6-disubstituted phenylhydrazones. If the ene-amine tautomer XI, or one of its conjugate acids, is first converted to the intermediate XII, three of whose contributing structures are formulated, the latter may be transformed by three successive more or less conventional 1,2-migrations or by a single (unconventional) 1,4-migration to the intermediate XIII, from which the aromatic ring may be restored by loss of a proton, and the heterocyclic ring closed in the normal way to provide Vb. Of course, the question of the sequence of these events may not yet be answered with certainty. For example, the closure of the heterocyclic ring could precede, accompany or succeed the methyl group migrations; arguments can be advanced to support any of these hypotheses, but no definitive evidence known to us permits of a sure distinction.



The question of the nature of the methyl group migration that accompanies this reaction is substantially more significant. Although work now in progress in this Laboratory is designed to provide evidence leading to a settlement of this question, no decisive argument is now known to us. Nevertheless, at the present time we are inclined to favor the hypothesis of a single 1,4-migration on the following grounds.

First, a series of 1,2-migrations must almost certainly pass through an intermediate such as XIV. Intermediates altogether analogous to XIV have been postulated[4,11] to precede the formation of 1,2-methyl migration products derived from the 2,6-xylylhydrazones of acetophenone and ethyl pyruvate; therefore, if XIV is indeed formed from XII, there is no obvious reason why it should not be converted to the tetrahydrocarbazole Va, through loss of a proton and subsequent ring closure, rather than continue through two more 1,2-methyl migrations to reach the intermediate XIII.

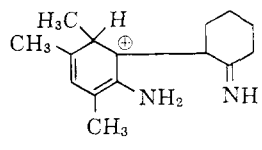
Second, the direct 1,4-methyl migration appears simple and uncomplicated by comparison with the sequence of 1,2-migrations. A single transition state, XV, bridges the conversion from XII to XIII, and this transition state seems altogether reasonable to us, both on the basis of structure and geometry and on the grounds of precedent. Al-

TABLE I

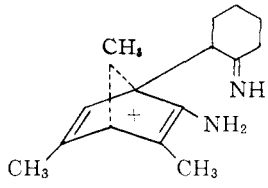
THE FISCHER REACTIONS OF CYCLOHEXANONE 2,4,5-TRIMETHYLPHENYLHYDRAZONE AND CYCLOHEXANONE 2,3,4-TRIMETHYLPHENYLHYDRAZONE AND THE CHARACTERIZATION OF THE PRODUCTS

Compound	Yield, %	M.p., °C.	Anal. calcd., % C	H	N	Anal. found, % C	H	N
Cyclohexanone 2,4,5-trimethylphenylhydrazone (IVa)	95	*Ca.* 100					[a]	
5,6,8-Trimethyltetrahydrocarbazole picrate	77	171 d.[b]	57.01	5.01	12.66	56.90	5.00	12.18
5,6,8-Trimethyltetrahydrocarbazole (Va)	83	115–125					[a]	
1,3,4-Trimethylcarbazole (VIa)	34[c]	143–143.5	86.08	7.22	6.69	85.39	7.03	6.82
5,6,8-Trimethyl-11-hydroperoxytetrahydrocarbazolenine (VIIa)[d]	92	145 d.	73.44	7.81	5.71	73.08	7.80	5.71
8,9,11-Trimethyl-1-benzazonidine-2,7-dione (VIIIa)	100	Glass					[e]	
ω-(2-Amino-3,5,6-trimethylbenzoyl)-valeric acid (IXa)	5[f]	150–150.5	68.41	8.04	5.32	68.99	7.84	5.40
5,6,8-Trimethyl-2,3-cyclopenteno-4-quinolone (Xa)	74[f]	Black at 300	79.26	7.54	6.16	77.59[g]	7.57	6.15
Cyclohexanone 2,3,4-trimethylphenylhydrazone (IVb)	100	.....					[a]	
6,7,8-Trimethyltetrahydrocarbazole picrate	57	171–172 d.						
6,7,8-Trimethyltetrahydrocarbazole (Vb)	88	81–86					[a]	
1,2,3-Trimethylcarbazole (VIb)	20[c]	127.5–128.5	86.08	7.22	6.69	85.57	7.03	6.65
6,7,8-Trimethyl-11-hydroxyperoxytetrahydrocarbazolenine (VIIb)[d]	85	134 d.	73.44	7.81	5.71	72.46	7.81	5.77
9,10,11-Trimethyl-1-benzazonidine-2,7-dione (VIIIb)	73	171–172						
ω-(2-Amino-3,4,5-trimethylbenzoyl)-valeric acid (IXb)	39[f]	146–149	68.41	8.04	5.32	68.56	7.84	5.50
6,7,8-Trimethyl-2,3-cyclopenteno-4-quinolone (Xb)	30[f]	Black at 300	79.26	7.54	6.16	78.00[g]	7.56	6.49

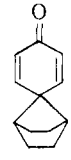
[a] The compound was too easily air oxidized to permit preparation for analysis. [b] Mixture m.p. with IV picrate was 163° dec. [c] Despite precautions to protect the tetrahydrocarbazoles from air during dehydrogenation, partial oxidation occurred. Highly colored reaction mixtures were common. In one dehydrogenation of Va only 2% of VIIa was isolated. [d] These hydroperoxides were formed by occasional aeration of ether solutions of the tetrahydrocarbazoles during storage at 4° (tetrahydrocarbazole itself remained unchanged under these conditions). The hydroperoxides were analyzed without further purification. Peroxide assay of VIIa was 90% after one day of storage at room temperature, 84% after 74 days; peroxide assay of VIIb was 93% after 20 days. [e] Compound VIIIa could not be purified for analysis. [f] Treatment of 1-benzazonidine-2,7-dione with 2 *N* hydrochloric acid gave an 86% yield of ω-(2-aminobenzoyl)-valeric acid as the only isolable product, but VIIIa and VIIIb (identical with VIII) when treated with 2 *N* hydrochloric acid gave mixtures of the products of hydrolysis and cyclization. In fact, VIIa gave a 33% yield of Xa on attempted rearrangement to VIIIa in methanol, so easily is the cyclization effected. [g] The quinolones gave consistently low carbon values on repeated analyses.



XIV



XV



XVI

though no precedent for a 1,4-methyl migration across a six-membered carbocyclic ring is known to us, the 1,4-migration of a methoxyl group in a similar system evidently has been observed, and apparent intermediates containing 1,4-bridged cyclohexanes have been isolated from 1,4-disubstituted cyclohexanes undergoing nucleophilic substitution and/or elimination. For example, Noyce and Bastian[12] have shown that acetolysis of *trans*-4-methoxycyclohexyl-1-*t*-tosylate gives, among other products, *trans*-4-methoxycyclohexyl-1-*t* and 4-*t* acetates, the latter of which must have arisen by a 1,4-methoxy migration, presumably through an intermediate bridged oxonium ion. Barner, Dreiding and Schmid[13] isolated the bridged spirodienone XVI from the products of the action of potassium *t*-butoxide on *trans*-4-(4-hydroxyphenyl)-cyclohexyl tosylate in *t*-butyl alcohol; and Heine[14] isolated 1,4-epoxycyclohexane from the alkaline and neutral hydrolysis products of *trans*-4-chlorocyclohexanol. In all of these instances, 1,4-bridged cyclohexane intermediates evidently were involved. Examples of anchimeric assistance rendered by groups in the 4-position to nucleophilic substitution at the 1-cyclohexyl system are perhaps less rigorously established,[15] but the weight of these examples suggests the generality of the phenomenon. When viewed against this background, the proposal of a 1,4-methyl migration through a transition state such as XV does not seem to constitute a radical departure.

Even if the correct pathway for the transformation of cyclohexanone mesitylhydrazone (IV) to Vb is a 1,4-methyl migration, the difference between the behavior of IV and that of the 2,6-xylylhydrazones of acetophenone and ethyl pyruvate,[4,11] which undergo 1,2-methyl migrations, requires explanation. Do the 2,6-xylylhydrazones generally show 1,2-methyl migrations, while mesitylhydrazones yield 1,4-rearrangements? Or are the 1,4-rearrangements typical of cyclohexanone arylhydrazones? Or is the nature of the rearrangement dependent chiefly on the medium? Experiments

(12) D. S. Noyce and B. N. Bastian, *J. Am. Chem. Soc.*, **82**, 1246 (1960).

(13) R. Barner, A. S. Dreiding and H. Schmid, *Chemistry & Industry*, **36**, 1437 (1958).

(14) H. W. Heine, *J. Am. Chem. Soc.*, **79**, 6268 (1957).

(15) *Cf.* H. L. Goering and L. Sims, *ibid.*, **79**, 6270 (1957); C. D. Nenitzescu and C. Curcaneanu, *Ber.*, **70**, 346 (1937); L. N. Owen and P. A. Roberts, *J. Chem. Soc.*, 320 (1949).

now in progress are intended to provide some answers to these questions.

Experimental[16]

N,N'-Dicarbethoxy-2,4,6-trimethylphenylhydrazine (II).—The method reported by Huisgen[8] was modified as follows. A solution of 300 g. of mesitylene (Matheson, Coleman and Bell) in 400 ml. of boron trifluoride etherate was treated with 314 ml. of ethyl azodicarboxylate in one portion. The mixture was shaken and cooled so that the temperature was maintained between 25 and 30°. A thick slurry formed within 30 minutes. When the temperature of the mixture no longer tended to rise spontaneously, the mixture was set aside overnight. The slurry was diluted with 200 ml. of ether, the mixture was chilled to 0° and then filtered. The solid was washed on the filter with 100 ml. of ether, then slurried in 2 l. of water with a high speed stirrer, again collected by filtration and dried at 100°. The white-to-cream crystals (530 g., 90%, m.p. 155–158°) were sufficiently pure for use in the preparation of mesitylhydrazine (III). A sample recrystallized from ethanol had m.p. 159–160°.

Anal. Calcd. for $C_{15}H_{22}N_2O_4$: C, 61.20; H, 7.53; N, 9.52. Found: C, 61.67; H, 7.61; N, 9.57.[17]

Mesitylhydrazine (III).—A solution of 45 g. of potassium hydroxide in 100 ml. of ethanol was added to 50 g. of the dicarbethoxymesitylhydrazine (II) in an alkali-resistant flask. The mixture was boiled under nitrogen for 24 hours, cooled to 25° and filtered. Part of the solvent was removed under water-pump pressure, and the mixture was diluted with ether, refiltered and then extracted with a little water. The ether solution was dried over magnesium sulfate and the ether removed. The residue comprised 13 g. of III, m.p. 59–61° (under nitrogen).

The solid material collected by the first filtration was acidified with hydrochloric acid, and the acid layer was extracted with ether. The aqueous phase was then made basic with sodium hydroxide and the basic solution extracted with ether. The combined ether extracts were dried over magnesium sulfate, and evaporation of the ether left as a residue an additional 10 g. of III. The total yield of III was 90%.

The facile air oxidation of III precluded the preparation of a satisfactory sample for analysis.

Hydrogenolysis of Mesitylhydrazine (III) to Mesidine.—A solution of 7.6 g. of III in 50 ml. of glacial acetic acid was treated with approximately 1 ml. of Raney nickel slurry, and the mixture was subjected to the action of hydrogen at 900 p.s.i. at 50° for 2 hours. The filtered solution was concentrated to about 15 ml. under water-pump pressure, diluted with water, cooled to 0°, and made basic by the addition of sodium hydroxide pellets. Ammonia was evolved from the basic mixture, which was extracted with ether. The ether extract was dried over magnesium sulfate and the ether removed. Treatment of the residual oil with 1:1 acetic anhydride–glacial acetic acid afforded 6.7 g. (75%) of N-acetylmesidine, m.p. 216–217°, alone or when mixed with an authentic specimen.

Cyclohexanone Mesitylhydrazone (IV).—A mixture of 17.6 g. of mesitylhydrazine (III) and 12 g. of cyclohexanone was warmed in a nitrogen atmosphere on a steam-cone. Water and excess cyclohexanone were removed under water-pump pressure, and the residual clear, pale yellow oil solidified on cooling. The crystalline hydrazone (24.8 g., 92%, m.p. 45–47°) was not sufficiently stable in air to permit the preparation of a satisfactory analytical sample.

Action of Glacial Acetic Acid on Cyclohexanone Mesitylhydrazone (IV).—The initially pale yellow solution of 24.8 g. of IV in 50 ml. of glacial acetic acid under nitrogen became deep orange-red as the temperature rose spontaneously from 25° to 70° in 10 minutes. The color turned to dark green as the solution was heated to the boiling point. After boiling for 30 min., the solution was treated with 58 g. of 85% picric acid in 100 ml. of hot glacial acetic acid. Cooling the mixture to room temperature effected the separation of 38 g. of solid material, which was collected by filtration. The filtrate yielded nothing that could be characterized.

The solid was digested in hot water and filtered. The residual black picrate (15.3 g., 32%, m.p. 156–163° dec.) was purified by recrystallization from benzene. The analytical sample had the m.p. 171–172° dec.

Anal. Calcd. for $C_{15}H_{19}N \cdot C_6H_3N_3O_7$: C, 57.01; H, 5.01; N, 12.66. Found: C, 57.61; H, 5.00; N, 12.87.

The hot aqueous solution from the filtration of the black picrate afforded 21.7 g. (82%) of ammonium picrate.

The isolation of cyclohexanone mesitylhydrazone (IV) was not necessary to the success of the preparation of the black picrate. In fact, the yield of black picrate from cyclohexanone and mesitylhydrazine (III) could be raised to 55% if the latter in equal molar amounts were subjected to the action of glacial acetic acid under the same conditions used to convert IV to the black picrate.

6,7,8-Trimethyl-1,2,3,4-tetrahydrocarbazole (V) from the Black Picrate Derived from IV.—A slurry of 10 g. of the black picrate in ether was treated with 5% aqueous sodium hydroxide under nitrogen. The clear, deep red ether solution was dried over magnesium sulfate, which also absorbed the red color. The ether was removed from the now light tan solution by evaporation under reduced pressure at room temperature. The residue formed a mass of crystals (4 g., 83%, m.p. 92–98° (under nitrogen)).

A portion of freshly prepared V, treated with picric acid in ethanol, afforded the black picrate, m.p. 171° dec.; samples after exposure to air gave little or no black picrate under the same conditions. All manipulations of V to be described subsequently were carried out in a nitrogen atmosphere, usually in a glove-box.

Satisfactory analytical specimens of V could not be prepared; the spectra were measured on solutions of freshly prepared V. The ultraviolet spectrum (cyclohexane) showed values of λ_{max} (mμ), $\epsilon \times 10^{-4}$: 226, 3.44; 277, 0.92. The infrared spectrum (chloroform) was: 2.87m, 3.43i, 3.48i, 6.27w, 6.84i, 6.93i, 7.35m, 7.65m, and 11.66 m μ.

1,2,3-Trimethylcarbazole (VI) from V.—Treatment of 2.14 g. of V in xylene solution with 4.90 g. of chloranil[18] afforded the theoretical amount of tetrachlorylhydroquinone and 1.5 g. (70%) of brown crystals of crude trimethylcarbazole VI. The crude material was purified first by decolorizing its benzene solution with alumina, and then by sublimation of the solid in a high vacuum and finally by recrystallization from benzene. The analytical specimen comprised colorless platelets, m.p. 127.5–128.5°. Analyses of this and other carbazoles obtained not only in the work described here but in other work to be reported later yielded good values for hydrogen and nitrogen, but consistently low carbon values. The ultraviolet absorption spectrum (cyclohexane) was characteristic of simple carbazoles: λ_{max} (mμ), $\epsilon \times 10^{-4}$: 218, 2.92; 238, 4.4; 259, 1.12; 286, 1.21; 292, 1.50; 297, 2.08; 322, 0.41; 337, 0.35; infrared spectrum (chloroform): 2.85m, 2.95w, 3.45m, 6.17m, 6.30w, 6.69m, 6.83i, 7.25w, 7.46w, 7.64i, and 7.86 mμ.

Anal. Calcd. for $C_{15}H_{15}N$: C, 86.08; H, 7.22; N, 6.69. Found: C, 85.32; H, 7.37; N, 6.85.

11-Hydroperoxy-6,7,8-trimethyl-1,2,3,4-tetrahydrocarbazolenine (VII).—An ether solution of 6,7,8-trimethyl-1,2,3,4-tetrahydrocarbazole (V) was stored in a stoppered flask at 4°. The stopper was removed periodically and the contents of the flask swirled to replenish the air supply. Within 12 hours a mass of crystals had formed which were collected by filtration and the mother liquor concentrated and returned to storage at 4°. This procedure was repeated until crystalline product no longer formed from the mother liquors. Roughly 80% of the product was collected during the first 12 hours. The yield was about 85% of colorless needles, m.p. 134° dec.; infrared spectrum (Nujol mull): 3.24m, 6.20i, 7.49m, 7.72w, 7.85w, 8.46w, 8.78w, 9.14m, 10.14m, and 11.50 mμ.

9,10,11-Trimethyl-1-benzazonidine-2,7-dione (VIII) was obtained by repeated crystallizations of VII from hot ethanol in air. The analytical specimen had the m.p. 171.5–172.5°; infrared spectrum (chloroform): 2.97w, 3.42m, 6.01i, 6.27w, 6.91m, 7.27m, 7.66m, and 8.86mμ. This spectrum was markedly similar to that of 1-benzazonidine-2,7-dione, the parent substance.[10]

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.08; H, 7.90; N, 5.55.

One specimen of VIII was also prepared directly from V in the course of an effort to purify V by recrystallization from cyclohexane in air. Repeated efforts lasting over a period of 2 weeks led only to a pasty white mass from which VIII was finally isolated in about 20% yield by crystallization

(16) Melting points are corrected.

(17) Sample first prepared by Dr. Robert J. Laufer.

(18) B. M. Barclay and N. Campbell, *J. Chem. Soc.*, 530 (1945).

from ethanol. The product was identified with a sample of VIII prepared from VII by m.p., mixed m.p., and the identity of the infrared spectra.

Transformations of Ketolactam VIII in Acid and Base. A. In Sodium Hydroxide.—A 100-mg. sample of 9,10,11-trimethyl-1-benzazonidine-2,7-dione (VIII) was stirred with 10 ml. of 2 *N* aqueous sodium hydroxide at room temperature for an hour. The resulting slurry was made acidic with 2 *N* aqueous hydrochloric acid. A white, flocculent precipitate soon separated from the clear, water-white solution initially formed after addition of the acid. The solid, separated by filtration, comprised 86 mg. of 6,7,8-trimethyl-2,3-cyclopenteno-4-quinolone hydrochloride, which darkened without melting above 300°. When the acidic filtrate was made basic with 2 *N* aqueous sodium hydroxide and the solution cooled, 3 mg. of the quinolone X, which darkened without melting above 200°, separated and was isolated by filtration. Purification was effected by recrystallization from methanol.

Although good analytical values for hydrogen and nitrogen could be obtained by combustion of X, repeated purifications failed to yield samples from which satisfactory values for carbon could be obtained. Infrared spectra (Nujol mulls) were taken: quinolone base: 3.1w, 3.28w, 6.16m, 6.22m, 6.40i, 6.47m, 6.64i, 7.00m, 7.40m, 7.64w, 7.97w, 8.97w μ; hydrochloride: 3.10w, 6.12m, 6.40i, 6.46m, 6.62m, 6.73m, 7.60w, 8.04i, 8.95mμ. The infrared spectrum of the quinolone base is markedly similar to that of 2,3-cyclopenteno-4-quinolone, the parent substance without methyl groups.[10]

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 80.09; H, 7.64; N, 5.86.

B. By Hydrochloric Acid.—A 200-mg. sample of the ketolactam VIII was stirred in 8 ml. of hot 2 *N* aqueous hydrochloric acid for 30 minutes. Filtration of the hot slurry afforded 56 mg. (30%) of the solid quinolone X hydrochloride, identified by its infrared spectrum. The yellow filtrate was neutralized with sodium bicarbonate and then acidified with acetic acid, which brought about the separation of 84 mg. (39%) of 2-amino-3,4,5-trimethylbenzoylvaleric acid (IX). The analytical sample, m.p. 146–149°, was recrystallized from benzene; infrared spectrum (chloroform): 2.86w, 3.02w, 3.44m, 5.87i, 6.12i, 6.19i, 6.31i, 6.52m, 6.62w, 6.90mμ. This spectrum is nearly identical with that obtained from a sample of δ-(*o*-aminobenzoyl)-valeric acid, the parent compound obtained by acid hydrolysis of the parent ketolactam.[10]

Anal. Calcd. for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.56; H, 7.84; N, 5.50.

N,N'-Dicarbethoxy-2,4,5-trimethylphenylhydrazine (IIa) was prepared from pseudocumene (Aldrich Chemical Co., Inc.) by the same method used to synthesize II. The crude product, m.p. 110–115°, was obtained in 86% yield. The analytical specimen, obtained by recrystallization from ethanol, had m.p. 114–115°.

Anal. Calcd. for $C_{15}H_{22}N_2O_4$: C, 61.20; H, 7.53; N, 9.52. Found: C, 61.02; H, 7.67; N, 9.53.

That the derivative had the assigned structure, rather than that of one of the isomers, was established by reductive cleavage of IIa with hydriodic acid and red phosphorus in acetic acid.[8] The aromatic amine isolated from the reaction mixture was converted by acetic anhydride to its N-acetyl derivative, m.p. 164° alone or when mixed with an authentic specimen[19] of 2,4,5-trimethylacetanilide.

Efforts to separate and identify isomers of IIa in the reaction mixture that produced it proved unsuccessful.

(19) Prepared by the method of B. Schultz, *Ber.*, **42**, 3605 (1909), who reported the m.p. 164°.

2,4,5-Trimethylphenylhydrazine (IIIa) was prepared in nearly quantitative yield from IIa by the method described for the conversion of II to III. The trimethylphenylhydrazine, m.p. 121–122°, was too susceptible to air oxidation to permit the preparation of a satisfactory analytical specimen.

N,N'-Dicarbethoxy-2,3,4-trimethylphenylhydrazine (IIb) was prepared in 60% yield from hemimellitene[20] by the method described for the preparation of II. The white crystalline material obtained from the reaction mixture had m.p. 148–149°; the analytical specimen, obtained by recrystallization of the crude material from ethanol, had m.p. 151–152°.

Anal. Calcd. for $C_{15}H_{22}N_2O_4$: C, 61.20; H, 7.53; N, 9.52. Found: C, 60.70; H, 7.62; N, 9.60.

Reductive cleavage of a sample of IIb by hydriodic acid and red phosphorus in acetic acid[8] afforded 2,3,4-trimethylaniline, isolated and identified as its N-acetyl derivative, m.p. 139–140°.[21]

Again, a search of the reaction mixture from which IIb was isolated for its isomer proved fruitless.[22]

2,3,4-Trimethylphenylhydrazine (IIIb) was prepared in 80% yield from IIb by the procedure used to convert II to III. The crystalline product IIIb, m.p. 105–106°, was too readily attacked by air to permit preparation of a satisfactory analytical specimen.

A solution of 4.2 g. of IIIb in 25 ml. of glacial acetic acid to which about 1 ml. of Raney nickel slurry had been added was shaken with hydrogen at 900 p.s.i. at 50° for 2 hours. The mixture was filtered free of catalyst, concentrated, and the concentrate was treated with acetic anhydride. The white, crystalline product (2.8 g., m.p. 139–140°) had the same infrared spectrum as the product derived directly from IIb by the action of hydrogen iodide and red phosphorus; a mixture of the two specimens showed no m.p. depression.

The conversion of the trimethylphenylhydrazine IIIa through the series IVa–Xa and that of IIIb through the series IVb–Xb were carried out by employing the same procedures used to convert III through IV–X. Infrared spectra of all products were measured, and in every case those of the "b" series were identical with their analogs derived from mesitylhydrazine. The infrared spectra of the "a" series, on the other hand, were in every case sensibly different, though similar in their general characteristics. Mixed m.p. determinations, carried out whenever analogous products were crystalline and possessed definitive melting points, led to the same conclusions. Yields, melting points and analytical data for the compounds of the "a" and "b" series are listed in Table I.

Infrared Spectra in the "a" Series.—5,6,8-Trimethyl-1,2,3,4-tetrahydrocarbazole (Va) (chloroform): 2.88m, 3.44i, 3.50i, 6.24w, 6.86m, 6.93m, 6.28w, 7.58m, 11.70wμ; 1,3,4-trimethylcarbazole (VIa) (chloroform): 2.85m, 3.00w, 3.42m, 6.20m, 6.64m, 6.87i, 7.18m, 7.49m, 7.57m, 7.70iμ; 5,6,8-trimethyl-11-hydroperoxytetrahydrocarbazolenine (VIIa) (Nujol mull): 3.28m, 6.18m, 7.88w, 8.22w, 8.77w, 9.15m, 10.14m, 11.50mμ; 8,9,11-trimethyl-1-benzazonidine-2,7-dione (VIIIa) (chloroform): 2.97w, 3.43m, 6.03i, 6.80m, 6.92m, 7.27m, 7.78m, 9.06wμ; δ-(*o*-aminobenzoyl)-valeric acid (IX) (chloroform): 2.86w, 3.01w, 3.44m, 5.83i, 6.08m, 6.19w, 6.30m, 6.51w, 6.82w, 7.02m, 7.11wμ; 5,6,8-trimethyl-2,3-cyclopenteno-4-quinolone (Xa) (Nujol mull): 2.94m, 3.40w, 6.18m, 6.26w, 6.44m, 6.61i, 6.84m, 7.01m, 7.15wμ.

(20) J. E. Nickels and W. J. Heintzelman, *J. Org. Chem.*, **15**, 1142 (1950).

(21) M. G. Barclay, A. Burawoy and G. H. Thomson, *J. Chem. Soc.*, 109 (1944), reported the m.p. 140°.

(22) 3,4,5-Trimethylacetanilide is reported by E. Nölting and S. Forel, *Ber.*, **18**, 2681 (1885), to have m.p. 164°.