[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

1,2-Dihydroquinoline

BY WILLIAM S. JOHNSON AND BENNETT G. BUELL

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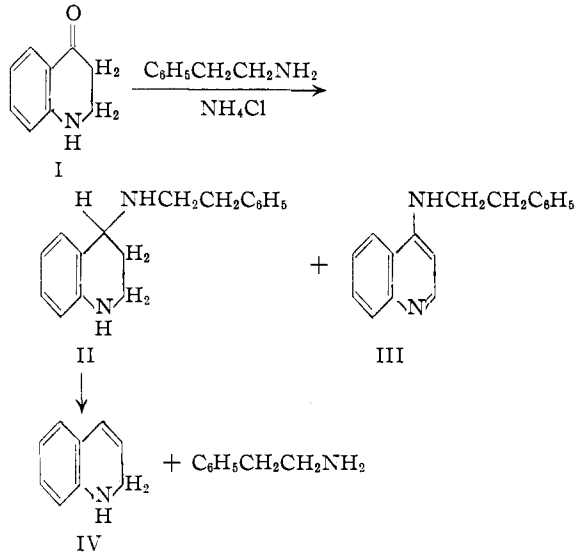
Authentic 1,2-dihydroquinoline, the presumed intermediate in the Skraup quinoline synthesis, has been prepared by pyrolysis of 4-(β-phenylethylamino)-1,2,3,4-tetrahydroquinoline (II) which was obtained with III as a disproportionation product in the condensation of 4-keto-1,2,3,4-tetrahydroquinoline (I) with β-phenylethylamine. The structure of the new dihydroquinoline was proved by compositional analysis, molecular weight determination, dehydrogenation to quinoline, hydrogenation to tetrahydroquinoline and ultraviolet spectrographic analysis. In the course of this study some interesting observations were made on the structures of Schiff bases and eneamines derived from aromatic amines.

1,2-Dihydroquinoline (IV) has interested chemists for many years, particularly since it has been the generally accepted intermediate in the Skraup quinoline synthesis. In 1881 Koenigs[1] described the reduction of quinoline with zinc and ammonia to give a substance, m.p. 161–162°, having the empirical formula of a dihydroquinoline. This material, however, proved to be dimeric,[2] and appeared to consist of a mixture of isomers.[3] In 1924 Räth[4] reported the preparation of "1,2-dihydroquinoline," b.p. 226°, in 90% yield from *o*-toluidine and chloroacetal. This product, however, was clearly shown to have none of the expected properties of dihydroquinoline,[5] and proved to be a mixture consisting in large part of 2-methyl-4-ethylaniline.[6]

Reduction of quinoline with sodium in liquid ammonia,[7] or by electrolysis[8] evidently gives 1,4-dihydroquinoline (or di- or polymers); hence the 1,2-isomer has not to our knowledge yet been described. The elusive nature of this simple compound as compared with the homologs having an N-alkyl substituent[9] is not surprising in view of the tendency of compounds probably containing the 1,2-dihydroquinoline system to undergo facile dehydrogenation.[10,11]

In the present communication the preparation and structure proof of 1,2-dihydroquinoline is described.

In the course of a study of the reaction of 4-keto-1,2,3,4-tetrahydroquinolines with primary amines,[12] the parent substance (I) was condensed with β-phenylethylamine by heating in benzene solution with ammonium chloride. Under these conditions the Schiff base, presumably formed as the primary product, underwent disproportionation to 4-(β-phenylethylamino)-quinoline (III) and the tetrahydro compound (II). The former was crystallized from the concentrated reaction mixture in 97% yield (based on the equation I → II + III), and the latter was left as an oily product which gave an oily acetyl derivative having the expected composition. When the residual oil (after removal of III) was heated at reduced pressure the tetrahydro



compound II did not distil; instead a mixture of two relatively volatile components was obtained. The lower boiling fraction was β-phenylethylamine, and the higher boiling portion (86–91.5° (0.2 mm.)) obtained in 76% yield, appeared to consist mainly of what proved to be 1,2-dihydroquinoline (see below) contaminated with some β-phenylethylamine. The dihydroquinoline fraction solidified on cooling, and could be recrystallized, although in poor recovery, from dilute methanol saturated with carbon dioxide (to retain the β-phenylethylamine as the soluble carbonate or carbamate[13]). The pure specimen was obtained as colorless hexagonal plates, m.p. 72–74.5°, which sublime nicely at reduced pressure. It has the molecular formula C_9H_9N as shown by carbon–hydrogen analysis and molecular weight determination by the Raoult cryoscopic method. The new substance has a naphthalene-like odor and on exposure to air it gradually turns to an oil with the odor of quinoline. This oily product was indeed identified as quinoline through the picrate and by ultraviolet spectroscopy (see below). Attempts to prepare the picrate gave an unstable mixture from which only the picrate of quinoline could be isolated.[14]

The ultraviolet spectrum of our dihydroquinoline is shown in Fig. 1. As the alcoholic solution stood in air, the λ_{max} at 343 mμ gradually dropped and the sharp band at 312 mμ characteristic of quinoline

(1) W. Koenigs, *Ber.*, **14**, 98 (1881).
(2) E. Lellmann, *ibid.*, **22**, 1337 (1889).
(3) V. Vincenzi, *Gazz. chim. ital.*, [2] **24**, 97 (1894).
(4) C. Räth, *Ber.*, **57B**, 550 (1924).
(5) J. Meisenheimer and E. Stotz, *ibid.*, **58B**, 2330 (1925).
(6) W. König and R. Buchheim, *ibid.*, **58B**, 2868 (1925).
(7) C. M. Knowles and G. W. Watt, THIS JOURNAL, **65**, 410 (1943).
(8) V. V. Levchenko, *Zhur. Obschei Khim* (*J. Gen. Chem.*), **18**, 1237 (1948) [*C. A.*, **43**, 955 (1949)].
(9) M. Freund, *Ber.*, **37**, 4666 (1904).
(10) G. R. Clemo and W. H. Perkin, *J. Chem. Soc.*, 1608 (1924).
(11) H. Gilman and D. A. Shirley, THIS JOURNAL, **72**, 2181 (1950).
(12) W. S. Johnson and B. G. Buell, *ibid.*, **74**, 4513 (1952).
(13) E. Katchalski, C. Berliner-Klibanski and A. Berger, *ibid.*, **73**, 1829 (1951).
(14) *Cf.* the behavior of the picrates of the N-alkyldihydroquinolines (ref. 9).

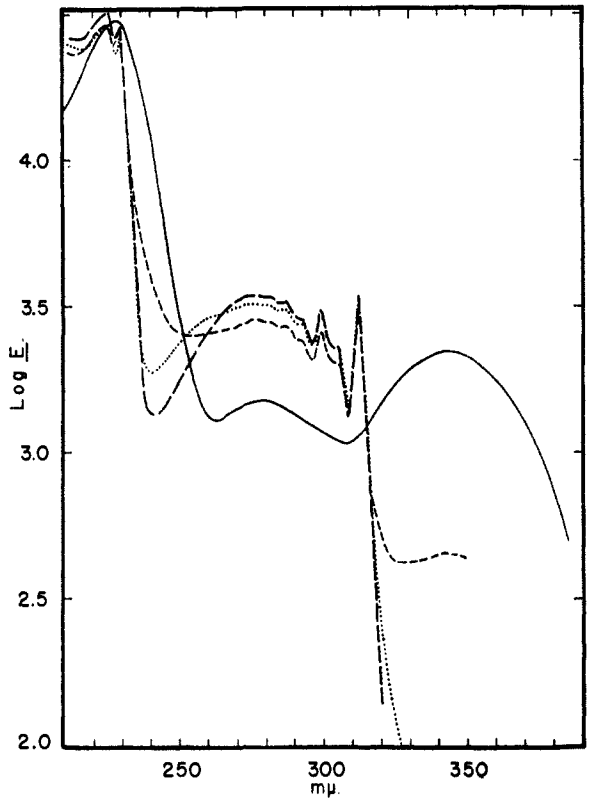


Fig. 1.——, 1,2-Dihydroquinoline; - - - -, after 2 days (in alcohol); . . . . . , after 16 days (in alcohol); — — —, quinoline.

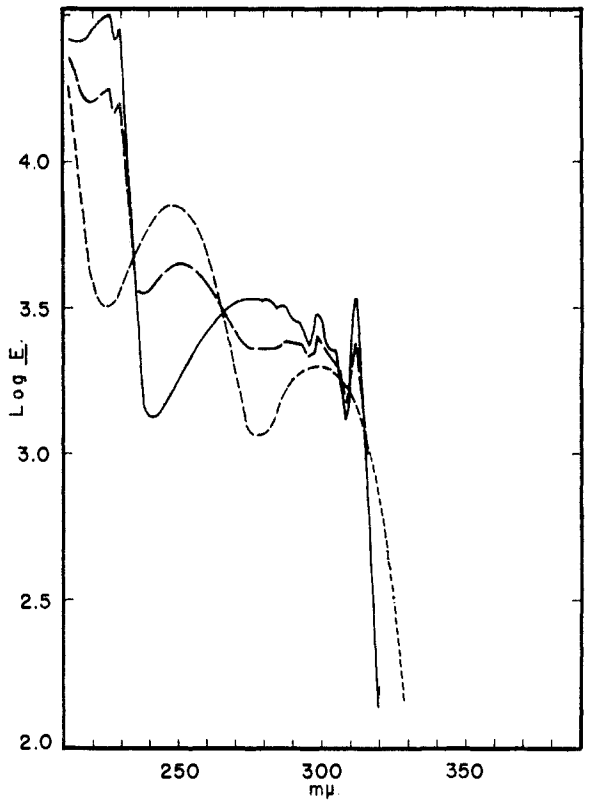
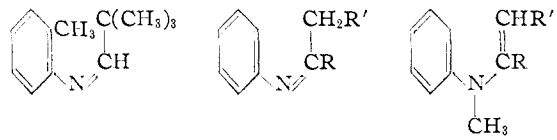


Fig. 2.——, Quinoline; - - - -, 1,2,3,4-tetrahydroquinoline; — — —, 50% quinoline–50% tetrahydroquinoline.

appeared. After two days the spectrum was practically identical with that of quinoline (see Fig. 1). That this change is a true dehydrogenation, and not a disproportionation into quinoline and tetrahydroquinoline, may be seen by a comparison with the spectrum of a 1:1 mixture of these two substances (Fig. 2).

The dihydroquinoline gave oily products on acetylation, benzoylation and nitrosation. On catalytic hydrogenation, the amount of hydrogen calculated to saturate one double bond was absorbed, and 1,2,3,4-tetrahydroquinoline was isolated and identified by mixture melting points of the benzoyl derivative.

The foregoing results conclusively established that the 74° compound is a dihydroquinoline, with the heterocyclic ring undoubtedly carrying the two extra hydrogen atoms. The only remaining question is the decision as to whether these hydrogens are located at the 1,2-, 1,4- or 3,4-position. The λ_{max} at 343 (log ϵ 3.35) shows that the double bond in the heterocyclic ring is conjugated with the benzene nucleus. If the bond were not conjugated, as in 1,4-dihydroquinoline, the spectrum would be expected to resemble that of 1,2,3,4-tetrahydroquinoline (Fig. 2) which absorbs at considerably shorter wave lengths. Eneamines of the general formula VII (*e.g.*, R = C_2H_5, R′ = C_3H_7)[15] may be considered open models of 1,4-dihydroquinoline and these compounds, which lack both the alkyl substituent in the benzene nucleus as well as the additional ring absorb as expected (see below) at even shorter wave lengths than tetrahydroquinoline. The 1,4-dihydroquinoline structure may therefore be reasonably excluded for our compound.



V VI VII

The spectrum of our dihydroquinoline is similar to that of *o*-aminostyrene (Fig. 3), which has the double bond conjugated with the aromatic nucleus and thus serves as the open model for the 1,2-dihydro structure. The bathochromic shift of about 29 mμ in the maxima of the bicyclic compound is expected (*cf.* the spectrum of 1,2-dihydronaphthalene, which is 23 mμ toward the longer wave length than that of the open chain analog, *o*-methylstyrene).[16] The spectrum of the dihydroquinoline was also compared with that of 2,2,4-trimethyl-1,2-dihydroquinoline and found to be strikingly similar (Fig. 3). On the basis of the spectrum of the latter the possibility that this substance, originally called "acetone anil," is the 1,4-dihydroquinoline derivative[17] is eliminated.

The spectrum of the Schiff base V, which represents the open chain model of a 3,4-dihydroquinoline, bears very little resemblance to that of our dihydroquinoline (Fig. 3). The compound V,

(15) P. R. Lucas and M. J. Hoch, *Bull. soc. chim.*, [5] **3**, 918 (1936).

(16) (a) C. S. Marvel and W. J. Peppel, THIS JOURNAL, **61**, 895 (1939); (b) P. Ramart and M. J. Hoch, *Bull. soc. chim.*, [5] **5**, 848 (1938).

(17) D. Craig, THIS JOURNAL, **60**, 1458 (1938).

which was prepared by the condensation of *o*-toluidine with pivalic aldehyde, was chosen for this study, because the position of the double bond is unambiguous. The Schiff bases of Lucas and Hoch[15] of the general structure VI could exist in the tautomeric eneamine form VII (H in place of CH_3). The spectrum of the authentic Schiff base V, however, proved to resemble closely those reported for the presumed Schiff bases,[15] which accordingly are best represented by the originally proposed formula V.

Experimental[18,19]

1,2-Dihydroquinoline.—A mixture of 10.00 g. of 4-keto-1,2,3,4-tetrahydroquinoline, m.p. 42–44.5°, 9.30 g. of β-phenylethylamine, $n^{28}D$ 1.5282, 60 mg. of ammonium chloride and 50 ml. of dry benzene was heated under reflux for 17 hours. The solution was concentrated and cooled, and 2.92 g. of 4-(β-phenylethylamino)-quinoline,[12] m.p. 155.5–159.5°, crystallized. The filtrate was diluted to about 40 ml. with benzene, and refluxed for an additional 12 hours with a water separator attached as in the preparation of III.[12] After concentration and cooling, the solution yielded an additional 5.30 g. of III, m.p. 146.2–156°. The residual oil remaining upon evaporation of the solvent from the filtrate was distilled from a Claisen flask at reduced pressure. With the bath temperature at 195–230° the following fractions were taken: (1) 1.44 g., b.p. 90–95° (22 mm.), $n^{29}D$ 1.5264; (2) 0.82 g., b.p. 52–78° (0.2 mm.); (3) 1.33 g., b.p. 78–86° (0.2 mm.), $n^{30}D$ 1.565; (4) 1.21 g., b.p. 86–91.5° (0.2 mm.), $n^{30}D$ 1.587; (5) 2.19 g., b.p. 91.5 (0.2 mm.), $n^{30}D$ 1.598. Fraction (1) consisted of fairly pure β-phenylethylamine, and fractions (2) and (3) appeared to consist largely of this material. Fractions (4) and (5) apparently consisted mainly of 1,2-dihydroquinoline contaminated with some β-phenylethylamine which was detected as the benzoyl derivative, m.p. 114–116°, in very small yield from the benzoylation of fraction (5).

Fraction (4) was dissolved in about 10 ml. of methanol, and the solution was saturated with carbon dioxide at a temperature slightly below that of the room. Water was then added drop by drop until crystallization occurred. Since 1,2-dihydroquinoline is rather unstable in this medium, the colorless plates were separated by filtration after about 10 minutes. The yield after drying *in vacuo* over potassium hydroxide was 0.447 g., m.p. 65–71°. A single recrystallization of material of this quality from dilute methanol, followed by sublimation at 65–70° (0.1 mm.) gave hard colorless hexagonal plates, m.p. 72–74.5°.

Anal. Calcd. for C_9H_9N: C, 82.40; H, 6.92; mol. wt., 131. Found: C, 82.40; H, 7.03; av. mol. wt., 126.5.[20]

The ultraviolet absorption spectrum was determined immediately on the pure material after dissolution in alcohol: λ_{max} 228 mμ (log ε 4.48), 278 (3.18), 343 (3.35). The solution was then saturated with oxygen, and the spectrum redetermined after 2 days, then again after 16 days. The results of these determinations are shown in Fig. 1.

Reaction of 1,2-dihydroquinoline with benzoyl chloride and aqueous potassium hydroxide gave a gummy product which was not obtained crystalline. Similar results were obtained on treatment of the base with acetic anhydride. Reaction with nitrous acid at 5° gave an orange oil. Treatment of a sample of the base, m.p. 66–72° with picric acid in alcohol, gave what appeared to be a mixture from which an apparently homogeneous fraction was isolated as red rods, m.p. 202–203.5°. The m.p. was not depressed on admixture with authentic (yellow) quinoline picrate, m.p. 202.5–203.5°.

Anal. Calcd. for $C_{15}H_{10}O_7N_4$: C, 50.28; H, 2.81. Found: C, 50.80; H, 3.03.

Some *yellow* needles, m.p. 199.5–203°, undepressed on admixture with quinoline picrate, were also isolated from the mixture.

(18) All melting points are corrected.

(19) The ultraviolet spectra were determined in 95% alcohol solution on a Beckman quartz spectrophotometer.

(20) Average of two semi-micro determinations (0.06- and 0.14-g. scale) by the Raoult cryoscopic method in a Beckmann freezing point apparatus.

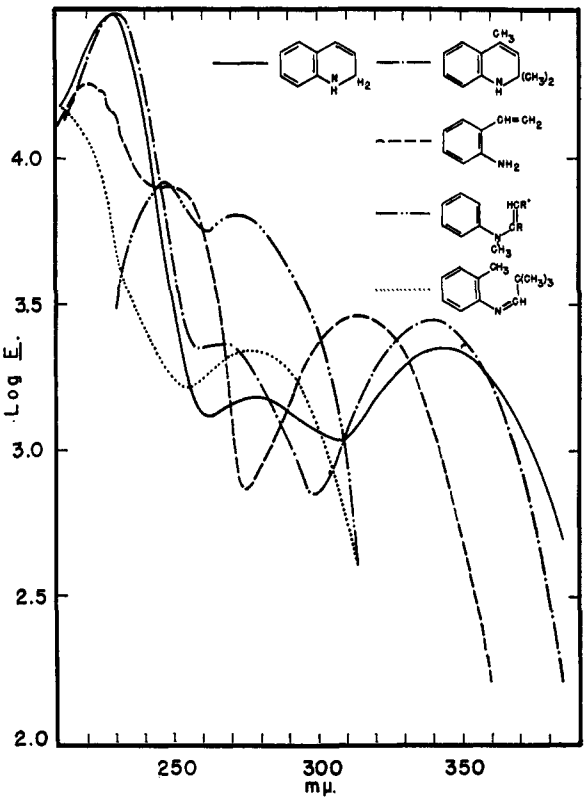


Fig. 3.

Conversion of 1,2-Dihydroquinoline to Quinoline.—In addition to the spectrographic demonstration of this reaction in air (see above), the following experiments were performed. A sample of 1,2-dihydroquinoline was allowed to stand in dilute methanol solution for several days. The brown oily product which then had a quinoline-like odor was converted to the picrate in the usual manner. It crystallized from alcohol in the form of yellow needles, m.p. 201–203.5°, undepressed on admixture with authentic quinoline picrate.

Anal. Calcd. for $C_{15}H_{10}O_7N_4$: C, 50.28; H, 2.81. Found: C, 50.13; H, 2.82.

The sulfate, prepared from material treated in dilute methanol as above, crystallized from alcohol as tan prisms, m.p. 162–164°, undepressed on admixture with authentic quinoline sulfate, m.p. 162.5–164.5°.

1,2-Dihydroquinoline in acetone solution was found to decolorize almost instantaneously 2% aqueous potassium permanganate solution in the cold. The product obtained after the reagent was added until the color persisted was shown to be quinoline by conversion to the yellow picrate, m.p. 202.5–204.3°, as described above.

Catalytic Hydrogenation of 1,2-Dihydroquinoline.—A solution of 0.132 g. of 1,2-dihydroquinoline, m.p. 63–72°, in 10 ml. of alcohol was hydrogenated over 0.08 g. of 30% palladium-on-carbon[21] at room temperature and atmospheric pressure. After 17.5 hours the uptake of gas ceased and 99% of the calculated volume of hydrogen for saturation of one double bond was absorbed. The residual oil obtained upon filtration and evaporation of solvent was benzoylated by the Schotten–Baumann procedure, and thus 0.189 g. (79% yield) of crude benzoyl derivative, m.p. 70–74°, was obtained. Recrystallization from dilute alcohol gave 0.111 g. of colorless rods, m.p. 74–75.2°, undepressed on admixture with authentic N-benzoyl-1,2,3,4-tetrahydroquinoline, m.p. 74–75.5°.

Isolation of 4-(β-Phenylethylamino)-1,2,3,4-tetrahydroquinoline.—The condensation of 7.10 g. of 4-keto-1,2,3,4-tetrahydroquinoline with 6.60 g. of β-phenylethylamine was carried out, as described above, in 60 ml. of benzene with 10

(21) R. P. Linstead and S. L. S. Thomas, *J. Chem. Soc.*, 1127 (1940).

mg. of zinc chloride as the catalyst. After 26 hours, 4.54 g. of 4-(β-phenylethylamino)-quinoline was isolated, and upon evaporation of the filtrate 8.85 g. of oil remained. A 1.00-g. sample of this oil was treated with excess picric acid in ethanol, and 0.439 g. of an orange picrate, m.p. 182.5–187° (soft at 180°) separated. Repeated recrystallization from alcohol gave yellow needles, m.p. 182–196°, undepressed on admixture with 4-(β-phenylethylamino)-quinoline picrate, m.p. 198–199° (soft at 184–186°).[12] Decomposition of the picrate with potassium hydroxide solution gave the free base, m.p. 156–158.5°, undepressed on admixture with authentic material.[12]

The deep red filtrate from the isolation of the crude picrate above yielded no further crystalline material, so was decomposed with an excess of 6 *N* potassium hydroxide solution, and extracted with benzene. The benzene solution was washed repeatedly with dilute potassium hydroxide to complete the decomposition of picrate, followed by 5% hydrochloric acid to remove the amine. The acid solutions were made alkaline, and the amine taken up in ether, washed with water, then with saturated sodium chloride solution and dried over anhydrous potassium carbonate. On evaporation of the ether, 0.57 g. (42% yield considered as 4-(β-phenylethylamino)-1,2,3,4-tetrahydroquinoline) of pale yellow oil remained. Attempts to effect crystallization failed, nor could a crystalline phosphate be obtained. The oil was acetylated by refluxing with an excess of acetic anhydride, and the product evaporatively distilled. The main fraction which came over at 175–188° (0.01 mm.) was about 1% high in the analysis for carbon indicating the presence of some monoacetyl derivative. This product was, therefore, taken up in ether, washed with 5% hydrochloric acid, recovered from the ether as above, and again evaporatively distilled. The product coming over at 150–165° (0.05–0.08 mm.) was obtained as an almost colorless glass, which proved to be the **diacetyl derivative of** II.

Anal. Calcd. for $C_{21}H_{24}O_2N_2$: C, 74.97; H, 7.19. Found: C, 75.05; H, 7.14.

o-Aminostyrene was prepared by reduction of *o*-nitrophenylethyl alcohol followed by base-catalyzed dehydration of the amino alcohol according to the procedures of Sabetay, Bleger and de Lestrange.[22] Our specimen of the amino alcohol had the following properties: b.p. 135–136° (0.6 mm.), $n^{19}D$ 1.5882 (reported[22] b.p. 147–148° (3.5 mm.), $n^{19}D$ 1.5849). Our sample of *o*-aminostyrene was obtained as a colorless oil, b.p. 111.7–111.9° (20 mm.), $n^{21}D$ 1.6100 (reported[22] b.p. 104–105° (15 mm.), $n^{20}D$ 1.6101). The acetate m.p. 94–95.6° (reported[22] 94.5°) was crystallized from benzene–petroleum ether (60–65°). The ultraviolet spectrum (Fig. 3) was determined on the freshly distilled material. λ_{max} 221 mμ (log ε 4.25), 250 (3.90), 314 (3.46).

N-(*o*-Methylphenyl)-2,2-dimethylpropylimine (V).—To 7.76 g. of freshly distilled *o*-toluidine was added gradually with cooling (ice-bath) 6.4 g. of pivalic aldehyde, b.p. 72–73°,[23] according to the general procedure of Campbell, Sommers and Campbell[24] for the preparation of aldimines. After the addition was complete the solution became cloudy, and solid potassium hydroxide was added to absorb the droplets of water. After standing overnight, the oil was decanted and distilled through a 6-in. Vigreux column. The main fraction boiling at 51–51.2° (0.1 mm.) amounted to 4.18 g. A center cut was employed for determination of the ultraviolet spectrum, $n^{26}D$ 1.5030, λ_{max} 279 mμ (log ε 3.34).

Anal. Calcd. for $C_{12}H_{17}N$: C, 82.23; H, 9.78. Found: C, 81.99; H, 10.01.

When mixed with dilute hydrochloric acid this substance hydrolyzed readily as the odor of pivalic aldehyde was evident immediately, although the Schiff base appeared to dissolve only gradually. The 2,4-dinitrophenylhydrazone prepared directly from the Schiff base was obtained as yellow rods, m.p. 209.6–210.8°, undepressed on admixture with the 2,4-dinitrophenylhydrazone of pivalic aldehyde, m.p. 209.6–210.8°.

Preparation of Other Materials for Spectroscopy.—The quinoline was prepared by converting Skraup quinoline (Eastman Kodak Co., synthetic) to the sulfate by addition of a slight excess of sulfuric acid to an ethanol solution of the base. The salt was recrystallized several times from alcohol, and finally from glacial acetic acid until it melted constantly at 162–164°. The quinoline regenerated from this salt was distilled through a 6-in. Vigreux column, giving material b.p. 119.5° (22 mm.), $n^{25}D$ 1.6218, λ_{max} 226 mμ (log ε 4.51), 230 (4.46), 277 (3.54), 299.5 (3.48), 312.5 (3.53).

1,2,3,4-Tetrahydroquinoline was obtained as a by-product in the reduction of 4-keto-1,2,3,4-tetrahydroquinoline with lithium aluminum hydride. The base was identified by preparation of the benzoyl derivative, m.p. 74–75.5 (reported[25] 76°) and the hydrochloride, m.p. 182–183.5° (reported[26] 180–181°). The fractionated material boiled at 140° (30 mm), $n^{26}D$ 1.5922, λ_{max} 248 mμ (log ε 3.86), 299 (3.30). **2,2,4-Trimethyl-1,2-dihydroquinoline** was prepared by the reaction between acetone and aniline according to the procedure of Craig.[17] It was purified *via* the hydrochloride which was obtained as colorless rods, m.p. 207–210° (dec.). The free base, regenerated in the usual manner, was evaporatively distilled at 90–95° (0.02 mm.) giving a colorless solid with a violet fluorescence, m.p. 26–28° (reported[17] 26–27°), λ_{max} 230 mμ (log ε 4.49), 267 (3.36), 341 (3.44).

The spectrum for compound VII reproduced in Fig. 3 was taken from Lucas and Hoch.[15]

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(22) S. Sabetay, J. Bleger and Y. de Lestrange, *Bull. soc. chim.*, [4] **49**, 3 (1931).

(23) This material was prepared by an unpublished procedure of Drs. B. F. Aycock and R. Johnson, involving the reaction of *t*-butylmagnesium chloride with N-methylformanilide.

(24) K. N. Campbell, A. H. Sommers and B. K. Campbell, THIS JOURNAL, **66**, 82 (1944).

(25) J. v. Braun and A. Steindorff, *Ber.*, **37**, 4723 (1904).

(26) L. Hoffmann and W. Königs, *ibid.*, **16**, 727 (1883).