other proteins. The greatest change in isoelectric point (from 4.6 to 3.2) was found in the azocasein, the product containing the most arsenic. This is to be expected since the isoelectric point of a protein is at least partially determined by the numbers of free acidic and basic groups.

Our results on the coupling of casein seem to agree with those of Kapeller-Adler and Boxer[3] who found an arsenic content of 8.20% (8.10, 8.19, 8.33), when an excess of diazotized *p*-arsanilic acid was used. Our product contained an average of 8.32% arsenic (8.10, 8.55).

Experimental

4-Arsonophenylazoproteins.—Casein, ovalbumin, pumpkin seed globulin and beef serum protein were coupled with *excess* diazotized *p*-arsanilic acid following the method of Landsteiner and van der Scheer.[4]

Anal.[5] Azocasein, Found: As, 8.10, 8.55. Azovalbumin, Found: As, 3.62, 3.43. Azopumpkin seed globulin, Found: As, 6.22. Azobeef serum protein, Found: As, 3.56.

Isoelectric point determinations on both the original proteins and the azoproteins were carried out using the method of Hawk, Oser and Summerson.[6]

ISOELECTRIC POINTS

	Original protein	Azoprotein
Casein	4.6	3.2
Ovalbumin	5.2	4.3
Pumpkin seed globulin	5.3	4.6
Beef serum protein	>6.2	<6.2

---

(3) R. Kapeller-Adler and G. Boxer, *Biochem. Z.*, **285**, 55 (1936).

(4) K. Landsteiner and J. van der Scheer, *J. Exp. Med.*, **45**, 1045 (1927).

(5) A modification of the method of F. E. Cislak and C. S. Hamilton, THIS JOURNAL, **52**, 638 (1930), was used in the arsenic analyses.

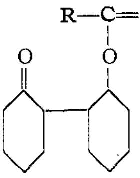
(6) P. B. Hawk, B. L. Oser and W. H. Summerson, "Practical Physiological Chemistry," Twelfth Edition, The Blakiston Company, Philadelphia, Pa., 1947, p. 160.

DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF LOUISVILLE SCHOOL OF MEDICINE
LOUISVILLE, KY.
RECEIVED SEPTEMBER 18, 1950

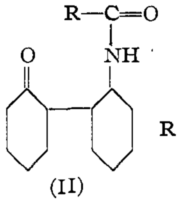
Acid-catalyzed Reactions of Nitriles. IV. Condensation of Cyclohexanone with Nitriles

BY EUGENE E. MAGAT

In a recent communication, Bruson, Riener and Riener[1a] have shown that cyclohexanone condenses with nitriles, in the presence of aluminum chloride, to yield compounds whose properties have suggested that they are imino-ethers of the aldol of cyclohexanone having the general formula (I). It is the purpose of this paper to report evidence which indicates that the products are in reality the isomeric amides of 1-(2-oxocyclohexyl)-cyclohexylamine (II).[1b]



(I)



(II)

R = CH_3

The following properties of the reaction product contradict the assignment of structure (I).

(1) Tertiary alcohols do not form imino-ethers as do primary and secondary alcohols; the tertiary alcohols rather lose water to form unsaturated compounds.[2] (2) Imino-ethers are usually unstable at high temperatures and gradually decompose to the original nitrile and alcohol,[3] whereas the condensation product can be distilled at 175–225° at 0.5–1 mm. without decomposition. (3) Imino-ethers are basic compounds which form stable salts with acids. If the condensation product were an imino-ether it should be necessary to neutralize the hydrochloric acid salt, which would form in the presence of aluminum chloride, before isolating the free imino-ether. However, no neutralization step is necessary in the isolation of (I). (4) The infrared absorption spectrum of the condensation product shows bands at 3.03, 3.25, 6.00 and 6.45 microns characteristic of the peptide linkage –CO–NH–.[4] These bands are sufficiently intense to show a high concentration of –CO–NH– groups. The infrared spectrum is shown in Fig. 1.

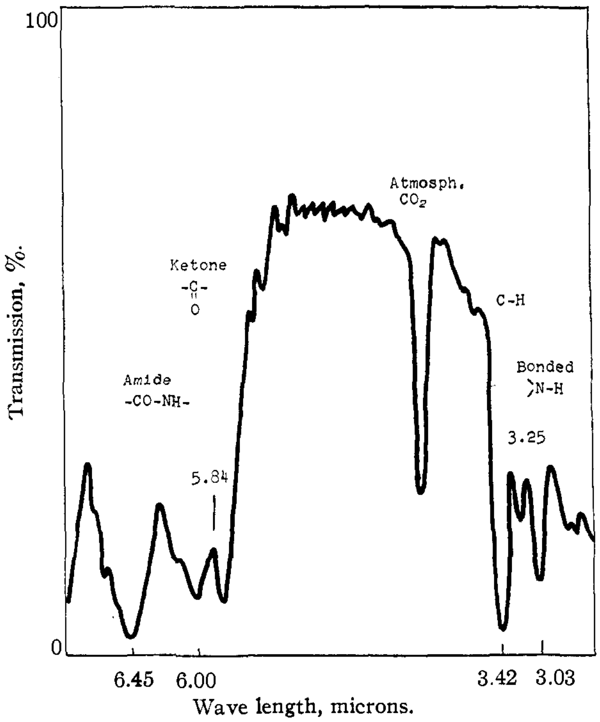


Fig. 1.—Infrared spectrum of reaction product of acetonitrile and cyclohexanone, 0.001 inch thick. Tracings of spectra recorded on Perkin-Elmer Infrared Spectrometer Model 12C with rock-salt prism in accordance with instruction manual.

These properties are in accord with structure (II). In addition, the following properties of the reaction product are also in accord with structure (II): (a) Ketone derivatives are formed. (b) Amides are, in general, soluble in concentrated hydrochloric acid and are reprecipitated unchanged

---

(1) (a) Bruson, Riener and Riener, THIS JOURNAL, **70**, 483 (1948); (b) A similar formulation has been suggested by Mowry and Ringwald, *ibid.*, **72**, 4439 (1950).

(2) Migrdichian, "The Chemistry of Organic Cyanogen Compounds," Reinhold Publishing Corp., New York, N. Y., 1947, p. 86.

(3) *Ibid.*, p. 84.

(4) Richards and Thompson, *J. Chem. Soc.*, 1248 (1947).

upon dilution with water. (c) Amides of primary amines where the amino group is attached to a tertiary carbon atom yield an olefin, an acid and ammonia upon steam distillation with 10% sulfuric acid.[5]

Cyclohexanone probably goes to cyclohexenylcyclohexanone in the presence of aluminum chloride and the condensation of cyclohexenylcyclohexanone and a nitrile is similar to the reaction of cyclohexene with hydrogen cyanide in the presence of aluminum chloride to give a 30% yield of N-formylcyclohexylamine[6] and to the reaction of nitriles and tertiary olefins to give N-tertiary alkyl amides.[5]

Acknowledgment.—The assistance of Dr. J. R. Downing of the Chemical Department, E. I. du Pont de Nemours and Company, Inc., is gratefully acknowledged for the interpretation of the infrared data.

---

(5) Ritter and Minieri, THIS JOURNAL, **70**, 4045 (1948).

(6) Wieland and Dorrer, *Ber.*, **63**, 404 (1930).

CAROTHERS RESEARCH LABORATORY
RAYON TECHNICAL DIVISION
E. I. DU PONT DE NEMOURS AND CO., INC.
WILMINGTON, DELAWARE RECEIVED OCTOBER 11, 1950

Methyl *n*-Propyl Ketone and its Conversion to *n*-Propylpyridine

BY RAYMOND P. MARIELLA AND ROGER STANSFIELD

In agreement with earlier workers,[1-4] ethyl formate was found to condense with the methyl group of methyl *n*-propyl ketone in the presence of sodium. This was established by converting the product (I) into the pyridone (II) and subsequent degradation to *n*-propylpyridine.

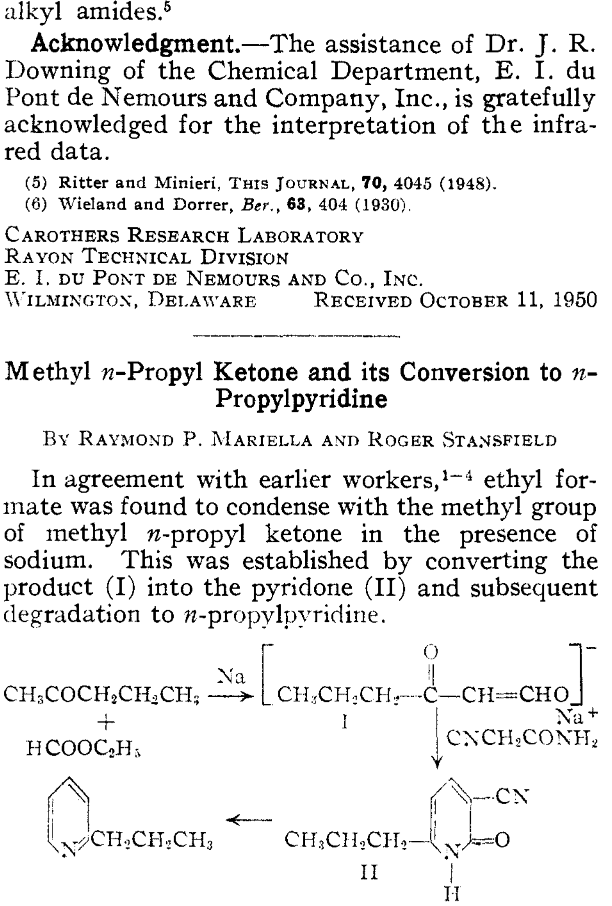


Fig. 1.

However, the condensation might have occurred partly at the methylene group, since the pyridone (II) could not be isolated in better than a 37% yield. The condensation product (I) was obtained in a 74% yield. These results are interesting because the previous workers had indicated that the methyl group was the only site of condensation. It was possible to isolate the free hydroxymethylene ketone as a colorless liquid, but in a poor yield (13%), as it decomposed rapidly.

Experimental[5]

Since the experimental details parallel those published before,[6] only the essential features will be mentioned.

3-Cyano-6-*n*-propyl-2(1)-pyridone (II).—From 46 g. of sodium metal ribbon in 1.5 l. of dry ether, by the addition of 172 g. of methyl *n*-propyl ketone (b.p. 101.3° at 752 mm.) and 148 g. of ethyl formate, there was obtained 200 g. (74% yield) of crude sodium salts as a yellow powder.

A solution of 136 g. of the above sodium salt and 90 g. of cyanoacetamide in 500 ml. of water, containing piperidine acetate catalyst, after refluxing for 3 hours, gave 100 g. of crude brown product.

A sample was recrystallized several times from absolute alcohol and resulted in white needles, m.p. 153°.

Anal. Calcd. for $C_9H_{10}N_2O$: C, 66.24; H, 6.18; N, 17.2. Found: C, 66.23; H, 6.41; N, 16.9.

The 100 g. obtained above represented very crude material since the m.p. was over a wide range, 120–145°. One recrystallization and treatment with Norit gave 60 g. (37% yield) of yellow prisms, m.p. 142–148°. An investigation of the mother liquor showed the presence of a dark-brown solid, softening in the range 50–110°, which appeared to be a complex mixture. Many attempts at purification using alcohol, acetone or glacial acetic acid as crystallizing solvents did not improve the melting point.

The Free Hydroxymethylene Ketone.—Fifteen grams of sodium salt was treated with excess sulfuric acid and shaken with ether. The ether was dried and removed *in vacuo*, leaving a dark-red liquid. Distillation gave 1.7 g. (13% yield) of colorless liquid, b.p. 51° at 16 mm., $n^{24}D$ 1.4190 and d^{24}_4 1.009. This liquid rapidly darkened.

6-*n*-Propyl-2(1)-pyridone-3-carboxylic Acid.—A solution of 50 g. of recrystallized cyanopyridone (II) in 500 ml. of concentrated hydrochloric acid was refluxed for 6 hours and gave 49 g. (88%) of the acid. A sample was recrystallized several times from water, colorless powder, m.p. 160°.

Anal. Calcd. for $C_9H_{11}NO_3$: N, 7.7. Found: N, 7.8.

6-*n*-Propyl-2-pyridol.—From 31 g. of pyridone acid, by heating at 335° for 15 minutes, there was obtained 21.5 g. (92%) of colorless long needles. Sublimation produced short needles, m.p. 88–89°.

Anal. Calcd. for $C_8H_{11}NO$: N, 10.2. Found: N, 10.4.

6-Chloro-2-*n*-propylpyridine.—From a solution of 20 g. of pyridol and 33 g. of phosphorus pentachloride in 25 ml. of phosphorus oxychloride, there was obtained 7 g. (33%) of a colorless liquid, b.p. 81.0–81.2° at 6 mm., $n^{20}D$ 1.5164, $n^{25}D$ 1.5135 and d^{25}_{25} 1.073.

Anal. Calcd. for $C_8H_{10}ClN$: N, 9.0. Found: N, 8.6.

2-*n*-Propylpyridine.—From 6.5 g. of the chloropyridine, using palladium-on-charcoal in acid solution, there was obtained 6.0 g. (92%) of colorless needles of 2-*n*-propylpyridine hydrochloride. The free base had the following physical constants: b.p. 166–167° at 750 mm., d^{25}_{25} 0.912, and $n^{20}D$ 1.4925. The derivatives had the following melting points: picrate 74°, chloroplatinate 161–162° and chloroaurate, 77–80°, and did not depress the m.p. of authentic samples.[7]

---

(1) L. Claisen and N. Stylos, *Ber.*, **21**, 1148 (1888).

(2) E. Benary, H. Meyer and K. Charisius, *ibid.*, **59**, 110 (1926).

(3) E. Benary, *ibid.*, **59**, 600 (1926).

(4) W. Gruber and H. Schlogl, *Monatsh.*, **81**, 83 (1950).

(5) Analyses by Misses Virginia Hobbs and Margaret Hines.

(6) R. P. Mariella, THIS JOURNAL, **69**, 2670 (1947).

(7) R. P. Mariella, L. Peterson and R. Ferris, *ibid.*, **70**, 1494 (1948).

CHEMICAL LABORATORY
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS RECEIVED OCTOBER 26, 1950

Quinoxaline Studies. II. The Preparation of 2-Hydroxy-3,6-dimethylquinoxaline and 2-Hydroxy-3,7-dimethylquinoxaline

BY BURTON MARKS[1] AND HARRY P. SCHULTZ

The condensation of 3,4-diaminotoluene with pyruvic acid was reported by Hinsberg[2] to produce a quinoxaline of undetermined structure melting at 220°. A low yield of another quinoxaline, m.p. 238°, presumably 2-hydroxy-3,7-dimethylquinoxa-

---

(1) Abstracted in part from a thesis by Burton Marks, presented to the Graduate Faculty of the University of Miami, in partial fulfillment of the requirements for the degree of Master of Science in chemistry, August, 1950.

(2) O. Hinsberg, *Ann.*, **237**, 351 (1887).