Since fluidities (reciprocal viscosities) are more convenient to use in certain cases than viscosities, they are included in the tables and are plotted in Fig. 2. The resulting curves deviate somewhat from straight lines, a slight sag being noted in each case.

Plotting log viscosities against temperatures resulted in curves which deviated from straight lines to about the same extent as did the fluidity curves.

The fluidity curves, however, approach straight lines nearly enough so that they may be easily extended to temperatures beyond those actually determined, at least to those temperatures of importance in the commercial application of the esters.

Acknowledgment.—The author wishes to express his appreciation of the assistance of W. deC. Crater, who kindly prepared the samples used in this investigation.

Summary

The viscosities of highly purified samples of propylene glycol dinitrate, ethylene glycol dinitrate, trimethylene glycol dinitrate, diethylene glycol dinitrate and glycerol trinitrate were measured in c. g. s. units (poises) at five-degree intervals over the temperature range 10 to 60°, inclusive, and the results compared with previously reported values. The corresponding fluidities were calculated and reported.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

RESEARCHES ON HYDANTOINS. XLIX. A NEW REARRANGEMENT LEADING TO THE FORMATION OF 4-AMINOHYDANTOIN DERIVATIVES

BY R. M. HERBST[1] AND T. B. JOHNSON

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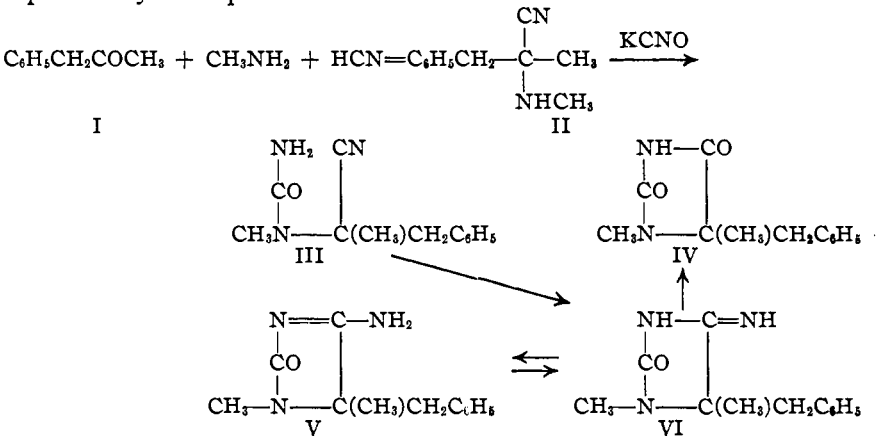
In the course of an investigation dealing with the synthesis of 5,5-dialkylated hydantoins from ketones, the authors had occasion to study the applicability of a series of reactions suggested for the preparation of 1,5,5-trialkyl-hydantoins. Tiemann and Piest[2] first showed that the Strecker synthesis of α-amino acids could be modified to include N-alkylamino acids if an amine is used in place of ammonia in the reaction with aldehyde or ketone cyanhydrins. Biltz and Slotta[3] applied this phase of the Strecker–Tiemann reaction to the synthesis of 1-alkyl-hydantoins. We have now employed the same series of reactions described by Biltz and Slotta under modified experimental conditions for the preparation of 1,5,5-trialkyl-

[1] Eli Lilly Company Graduate Scholar, 1928–1929.

[2] Tiemann and Piest, *Ber.*, **14**, 1982 (1881); **15**, 2028 (1882).

[3] Biltz and Slotta, *J. prakt. Chem.*, **113**, 233 (1926).

hydantoins. The method of operating is illustrated by the synthesis of 1,5-dimethyl-5-benzylhydantoin from methyl benzyl ketone which is expressed by the equations



A careful study of these reaction changes has now revealed a mechanism of ring formation which has not been observed, hitherto, in the hydantoin series. The α-methylureido-α-methyl-β-phenylpropionitrile (III), prepared as an intermediate in this synthesis, undergoes a molecular rearrangement on boiling in water solution to form 1,5-dimethyl-5-benzyl-4-aminohydantoin (V or VI). The transformation is perfectly analogous to that which was observed by Pschorr,[4] who encountered a similar reaction in the synthesis of α-aminoquinolines from *o*-aminocinnamylcyanides. Traube[5] and Conrad[6] have described analogous rearrangements leading to the formation of ring compounds in the synthesis of barbituric acid and derivatives.

Jongkees[7] has prepared 4-iminohydantoin-1-acetamide, in which the imino group is easily replaced by oxygen by warming with dilute hydrochloric acid. His technique involved cyclization in ammoniacal solution. Our compound shows a much greater stability than Jongkees' hydantoin, and is not affected by boiling even with fairly strong hydrochloric acid. The amino group can be replaced with oxygen, however, by treatment with nitrous acid, analogous to the conversion of cytosine into uracil studied by Kossel and Steudel[8] and later by Wheeler and Johnson.[9] These facts favor the amino V, in preference to the imino structure VI, for the cyclic compound.

[4] Pschorr, *Ber.*, **31**, 1289 (1898).
[5] Traube, *ibid.*, **33**, 1371 (1900); *Ann.*, **331**, 64 (1904).
[6] Conrad, *ibid.*, **340**, 310 (1905).
[7] Jongkees, *Rec. trav. chim.*, **27**, 287–326 (1908).
[8] Kossel and Steudel, *Z. physiol. Chem.*, **38**, 49 (1903),
[9] Wheeler and Johnson, *Am. Chem. J.*, **29**, 492 (1903).

This rearrangement suggests a possible reaction mechanism for the conversion of ureido-nitriles into hydantoins by means of aqueous hydrochloric acid. Generally this transformation is expressed as one involving, first, hydrolysis of the nitrile to the corresponding hydantoic acid, and then a molecular condensation to form the hydantoin. According to the new conception the change to ring structure first involves a formation of the intermediate imino compound VI, which is unstable in the presence of strong hydrochloric acid and is decomposed immediately, giving the normal hydantoin. On the other hand, in the absence of hydrochloric acid, or under conditions where we have a low hydrogen-ion concentration, the imino compound may undergo tautomerization to form the isomeric and more stable aminohydantoin V, which is not attacked by acids. In the above rearrangement we have an excellent example apparently of this tautomeric change, and it is a molecular transformation which possesses considerable biochemical interest. This tautomerization is undoubtedly influenced by the character of the groups substituted in the hydantoin ring on nitrogen and carbon.

The rapidity with which hydantoins are formed from ureido-nitriles, the reaction being almost instantaneous, lends support to the belief that something other than the hydrolysis of a cyanide group to carboxyl is involved in this reaction. The unique behavior of the ureido-nitrile suggests a mechanism of reaction which is far more general than we have hitherto realized.

Experimental

α-Methylamino-α-methyl-β-phenylpropionitrile, II.—Seven and nine-tenths cc. (0.2 mole) of anhydrous hydrocyanic acid and 6.2 g. (0.2 mole) of dry methylamine are dissolved in a thoroughly cooled solution of 26.8 g. (0.2 mole) of methyl benzyl ketone in 25 cc. of absolute ethyl alcohol. After the solution has stood at room temperature in a well-stoppered bottle for twenty-four hours, it is taken up in 200 cc. of ether, washed with cold water and dried over sodium sulfate. The hydrochloride of α-methylamino-α-methyl-β-phenylpropionitrile is then precipitated by passing dry hydrogen chloride into the ethereal solution. It separates first as an oil, which on continued treatment with hydrogen chloride changes to a colorless, crystalline solid, melting at 106–108°[10] with decomposition, after sintering at 102°. The yield of hydrochloride is 35 g. (85%). The hydrochloride decomposes slowly on standing, and cannot be kept over long periods. Heating in non-anhydrous solvents causes methylamine hydrochloride and hydrocyanic acid to split off with regeneration of the ketone.

Anal. Calcd. for $C_{11}H_{15}N_2Cl$: N, 13.30. Found: N, 13.14, 13.09.

The free methylamino-nitrile, obtained by evaporating the solvent from an ethereal solution at room temperature under reduced pressure, decomposes easily on heating, and cannot be distilled even in vacuo without serious decomposition.

α-Methylureido-α-methyl-β-phenylpropionitrile, III.—During the course of an hour 25 g. of finely ground potassium cyanate is added to a cold suspension of 35 g. of α-methylamino-α-methyl-β-phenylpropionitrile hydrochloride in 100 cc. of glacial acetic acid. After standing in a cool place for fifteen hours, the reaction mixture is poured into

[10] All melting points are corrected.

500 cc. of ice water. On standing in the refrigerator, α-methyl-ureido-α-methyl-β-phenylpropionitrile separates as a flocculent white solid, which is filtered off through a Büchner funnel, washed with water and air-dried. The yield of crude material is 28 g. (77.5%). It crystallizes from 50% alcohol in colorless needles, melting at 130–131°.

Anal. Calcd. for $C_{12}H_{15}ON_3$: N, 19.35. Found: N, 18.91, 18.93.

1,5-Dimethyl-5-benzylhydantoin, IV.—Twenty-eight grams of crude α-methyl-ureido-α-methyl-β-phenylpropionitrile is suspended in 100 cc. of 20% hydrochloric acid. On warming the methylureido-nitrile dissolves and the hydantoin begins to precipitate almost immediately. After heating for one hour on the steam-bath, the suspension is cooled, filtered through a Büchner funnel and the residue washed with cold water. The yield of crude hydantoin is 23 g. (82%). Recrystallization from 50% alcohol, decolorizing with norite if necessary, yields a product melting at 134–135°.

Anal. Calcd. for $C_{12}H_{14}O_2N_2$: N, 12.84. Found: N, 12.92, 12.81.

An attempt to decompose the hydantoin to the corresponding methylamino acid was unsuccessful. After refluxing 5 g. of the hydantoin for one hundred hours with saturated barium hydroxide solution, 4.5 g. of the unchanged hydantoin was recovered.

A crystalline sodium salt is formed when a mixture of a small amount of the hydantoin with an equivalent amount of a 5% solution of sodium hydroxide in 95% alcohol is evaporated in a vacuum desiccator. Solutions of mercuric chloride, calcium chloride and magnesium sulfate precipitate the corresponding salts when added to aqueous solutions of the sodium salt of the hydantoin. The mercury salt precipitates as a flocculent white solid, whereas the calcium and magnesium salts separate as colorless needles.

1,5-Dimethyl-5-benzyl-4-aminohydantoin.—When a solution of α-methylamino-α-methyl-β-phenylpropionitrile in hot water is boiled momentarily, 1,5-dimethyl-5-benzyl-4-aminohydantoin crystallizes out on cooling in a practically quantitative yield, in the form of small, colorless needles, melting at 267–268° with charring.

Anal. Calcd. for $C_{12}H_{15}ON_3$: N, 19.35. Found: N, 19.32, 19.27.

The aminohydantoin is readily soluble in dilute mineral acids, but insoluble in alkalies, which precipitate it unaltered from its solutions in acids. Boiling with acids or alkalies does not affect the aminohydantoin. It forms a characteristic mono-hydrochloride and picrate.

On treating with nitrous acid, as described by Kossel and Steudel[8] for the conversion of cytosine to uracil, an acidic compound is obtained, crystallizing from 50% alcohol in plates and melting at 134–135°. Mixed with 1,5-dimethyl-5-benzyl-hydantoin the melting point is unchanged.

The hydrochloride of **1,5-dimethyl-5-benzyl-4-aminohydantoin** is prepared by pouring a solution of the aminohydantoin in 95% alcohol saturated with hydrogen chloride into dry ether. On standing the hydrochloride precipitates as a colorless crystalline solid, melting at 218–223° with decomposition.

Anal. Calcd. for $C_{12}H_{16}ON_3Cl$: N, 16.57; Cl, 14.00. Found: N, 16.65; Cl, 13.93.

The picrate of **1,5-dimethyl-5-benzyl-4-aminohydantoin** crystallizes as yellow needles when a solution of equal amounts of the aminohydantoin and picric acid in a slight excess of boiling water is cooled. After recrystallization from 50% alcohol it melts at 226–227° with decomposition.

Anal. (Kjeldahl–Gunning). Calcd. for $C_{18}H_{18}O_8N_6$: N, 18.83. Found: N, 18.97.

Summary

1. 1,5-Dimethyl-5-benzylhydantoin and its 4-amino derivative have been prepared.

2. A new rearrangement leading to hydantoin derivatives substituted in the 4-position with an amino group has been described.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

THE MECHANISM OF CARBOHYDRATE OXIDATION. XII. THE ACTION OF POTASSIUM HYDROXIDE ON *l*-ARABINOSE AND *d*-XYLOSE

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When the hexose sugars, glucose, mannose, fructose and galactose are treated with aqueous solutions of potassium hydroxide, it is found that the amounts of certain reaction products are definitely dependent upon the normality of the solutions used and also upon the temperature employed. In a recent report, Shaffer and Friedman[1] have shown that the concentration of the sugar is also an important factor in the reaction of the hexose sugar under these conditions.

Since it is conceivable that pentose sugars may be formed as intermediate compounds in reactions involving the decomposition of hexose sugars in alkaline solutions, it becomes of much interest to know whether the products formed in a similar decomposition of the pentoses will show the same general relationship to the experimental conditions used as the hexose sugars do under similar circumstances. To obtain data with reference to this point was the principal objective in these experiments. For our experimental purposes we used the two easily accessible five-carbon atom sugars, *l*-arabinose and *d*-xylose. A similar study concerning the theoretically possible intermediate trioses has been made in this Laboratory previously.[2]

Experimental

(a) **Materials.**—All materials used in these experiments were examined for their purity by well-known laboratory methods.

(b) **Manipulation. Lactic, Acetic and Formic Acids.**—A 100-cc. round-bottomed pyrex flask containing 25 cc. of potassium hydroxide of the desired normality was attached to a mechanical agitator placed in a thermostat. After sufficient time had elapsed for the flask and its contents to come to the desired temperature (25, 50 or 75°), 1.875 g. (0.5*M*) of the crystalline *l*-arabinose or *d*-xylose was added through a large funnel whose stem had been shortened. Usually ten samples, including different normalities and duplicates, were started within the period of an hour. As in all the previous studies in this series, the agitation of these solutions was continued for forty-eight hours. Owing to the difficulties arising from the deposition of moisture during the preparation of the reacting systems at 75°, it was found more convenient to place the sugar in the flask first and then add the standard alkali solution. The general procedure from this

[1] Shaffer and Friedman, *J. Biol. Chem.*, **86**, 345 (1930).

[2] (a) Evans and Hass, THIS JOURNAL, **48**, 2703 (1926); (b) Evans and Cornthwaite, *ibid.*, **50**, 486 (1928).