

to have been previously recorded. 5.15 g. substance made up to 50 cc. with chloroform, in a 2 dcm. tube at 20°, rotated 96.5° V. to the right, therefore, $[\alpha]_D^{20} = +162.3^\circ$. When this octacetate was dissolved in acetic anhydride with a small amount of zinc chloride, no change in its specific rotation of +147.4° could be detected after heating the solution to 100° repeatedly. Evidently there is only one trehalose octacetate.

Observations on Sucrose Octacetate.—Sucrose octacetate was prepared by the acetylation of sugar with acetic anhydride and pyridine bases, and also with acetic anhydride and sodium acetate. After recrystallization, it melted at 69° (uncorr.) and in chloroform $[\alpha]_D^{20} = +59.6^\circ$. Herzfeld¹ has found the m. p. 67°. In this case again it was not possible to obtain any evidence of the existence of an isomeric sucrose octacetate, since the specific rotation of its solution in acetic anhydride containing a trace of ZnCl₂ did not change on heating. These results with the octacetates of trehalose and sucrose are not unexpected since the parent disaccharides are not reducing sugars, do not combine with phenylhydrazine, do not exhibit mutarotation, nor occur in alpha and beta forms, and consequently do not have the type of structure which accounts for the existence of alpha and beta modifications of the aldoses and ketoses and their derivatives.

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THE CONDENSATION OF ALDEHYDE DIACETATES AND OF PHENYLHYDRAZONES WITH 2-THIOHYDANTOIN.

By BEN H. NICOLET.

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Five years ago, Wheeler and Hoffman² made the discovery that aromatic aldehydes can be condensed with hydantoin by boiling with glacial acetic acid and fused sodium acetate, giving compounds of Type I. Wheeler and Brautlecht³ applied the reaction to substituted 2-thiohydantoins, and Wheeler, Nicolet and Johnson⁴ showed that it worked equally well with 2-thiohydantoin itself.

These condensation products are readily reduced to benzyl (II), or substituted benzyl hydantoins,⁵ and these in turn are readily hydrolyzed to phenylalanine (III), or substituted phenylalanines. In most cases this method for preparing substituted phenylalanines compares favora-

¹ *Ber.*, 13, 267 (1880); *Z. Ver. D. Zuckerind.*, 1887, 422.

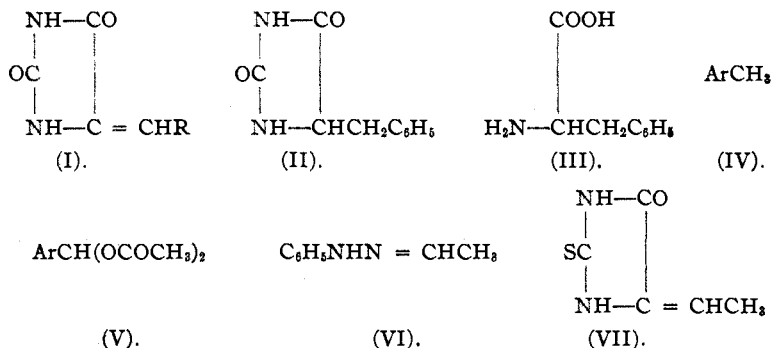
² H. L. Wheeler and C. Hoffman, *Am. Chem. J.*, 45, 368.

³ H. L. Wheeler and C. A. Brautlecht, *Loc. cit.*, 446.

⁴ H. L. Wheeler, B. H. Nicolet and T. B. Johnson, *Loc. cit.*, 46, 456.

⁵ Wheeler and Hoffman, *Loc. cit.*; T. B. Johnson and C. A. Brautlecht, *This Journal*, 33, 1531 (1911).

bly with that of the younger Erlenmeyer.¹ Johnson and his various co-workers have made use of it for the preparation of a number of phenylalanine and tyrosine derivatives.



During the last few years, considerable interest has been shown in the preparation of nucleus-substituted phenylalanines not hitherto found to occur as protein constituents, for use in the study of the chemistry of metabolism. As some of the acids desired are bound to require for their preparation aldehydes which cannot readily be bought, nor easily prepared in the pure state, a method was desirable which would obviate the necessity of isolating the aldehydes before condensation with hydantoins. This seems now to have been found in the use of either the α -diacetates or the phenylhydrazones, instead of the free aldehydes.

One of the simplest methods for the laboratory preparation of many aromatic aldehydes, is the oxidation of the corresponding methyl derivatives (IV) with chromic anhydride in acetic acid and acetic anhydride solution. This reaction yields the aldehyde diacetates (V). Ordinarily these are readily hydrolyzed to the aldehydes, but occasionally they are so difficultly soluble in water that the hydrolysis is unsatisfactory. In any case, the subsequent distillation with steam, and purification by means of the bisulfite, are operations that would willingly be avoided. Benzal diacetate reacts normally with 2-thiohydantoin, and there is no apparent reason why this reaction should not be a general one.

Where the regeneration of the aldehyde is not required, the phenylhydrazone is one of the favorite derivatives for its isolation and purification. It may often be found preferable to substitute phenylhydrazones for the free aldehydes when the latter are not themselves readily isolated. Benzal phenylhydrazone condenses normally with 2-thiohydantoin, and the reaction is evidently a very general one, since even phenyl glucosazone can be so condensed.

Strictly aliphatic aldehydes have not hitherto been condensed with

¹ E. Erlenmeyer, Jr., *Ber.*, **30**, 2981 (1897); *Ann.*, **307**, 146 (1899).

hydantoin derivatives. The higher aldehydes would be expected to react normally, but the lower members of the series are too volatile to stand heating to the required temperatures, except in a sealed tube. Here the phenylhydrazone seems to solve the difficulty, for ethylidene-phenylhydrazine (VI) condenses with 2-thiohydantoin to give 2-thio-4-ethylidenehydantoin (VII), the first compound¹ of Type I, in which R is an alkyl group.

Experimental Part.

Condensation of Benzal Diacetate with 2-Thiohydantoin.—The condensation was made in the usual manner. One and seven-tenths grams of 2-thiohydantoin,² 3.5 g. (calc. 3.05 g.) benzal diacetate, and 5 g. fused sodium acetate, were added to 20 g. glacial acetic acid, and the mixture boiled for two hours under a reflux condenser in a metal bath. On diluting with water, 2-thio-4-benzal hydantoin separated, and was freed from any diacetate that might possibly be present by dissolving in dilute alkali and reprecipitating. It melted at 258°, and was identical with the product obtained by Wheeler, Nicolet, and Johnson.³ The yield was 1.9 g. of the pure product, or 61.3%.

Condensation of Benzal Phenylhydrazone with 2-Thiohydantoin.—One and two-tenths grams of 2-thiohydantoin was condensed as described above with 2.5 g. (calc. 2.0 g.) benzal phenylhydrazone. Addition of water precipitated a mixture of 2-thio-4-benzal hydantoin and unaltered phenylhydrazone, from which dilute alkali dissolved only the former. On acidifying, 1.13 g. benzal thiohydantoin was obtained, corresponding to a yield of 54%.

Both of these yields will undoubtedly be somewhat improved by working with larger quantities.

2-Thio-4-ethylidenehydantoin, VII.—Three grams of 2-thiohydantoin were condensed with a slight excess of acetaldehyde phenylhydrazone by boiling for two hours with sodium acetate in acetic acid. Addition of water precipitated the crude compound, which was purified by solution in alkali and crystallization from alcohol, in which it is readily soluble hot, and moderately soluble cold. It forms a yellow-brown crystalline powder which melts rather indefinitely at 253°, and is only very slightly

¹ Since this paper was written, Dr. Treat B. Johnson has called the writer's attention to a paper by Pinner and Lifschutz (*Ber.*, 20, 2350 (1887)), in which a compound said to be 4-ethylidenehydantoin was described. It was prepared by the fusion of α -chlorocrotonylurea, and named "ethylidene metapyrazolone." The few properties of this substance there described have caused both Dr. Johnson and myself to question whether the substance in question might not have been 4-methyluracil. This point, and also some anomalies that have been noted in the condensation of ethylidene-phenylhydrazine with 3-benzoyl-2-thiohydantoin, will be further investigated.

² THIS JOURNAL, 33, 1978 (1911).

³ *Am. Chem. J.*, 46, 470 (1911).

soluble in water. The analysis shows it to be 2-thio-4-ethylidene hydantoin. Nitrogen (Kjeldahl).

Calc. for $C_6H_8ON_2S$: N = 19.72%. Found: N = 19.57%.

PITTSBURGH, PA.

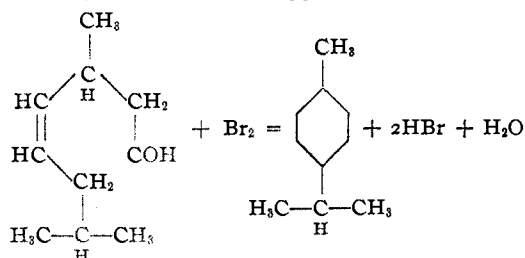
[CONTRIBUTION FROM THE LABORATORY OF THE DODGE & OLCOTT Co.]

ISOPULEGOL PHOSPHONIC ACID.

By FRANCIS D. DODGE.

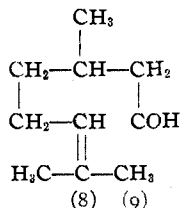
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The characteristic constituent of the essential oil of citronella is an aldehyde, having the composition $C_{10}H_{18}O$, and known as citronellal aldehyde, or citronellal. In an investigation of this oil, in 1889,¹ the writer found that this aldehyde was an aliphatic or open-chain compound, singly unsaturated, and hence homologous with acrolein. This was one of the first examples of open-chain compounds closely related to the terpene series, and the first clue to its structure was afforded by the conversion into *p*-cymene, an aromatic hydrocarbon frequently found as the final transformation product of many terpene derivatives. To explain this reaction, the following formula was suggested:



which would appear to locate the relative positions of the methyl and isopropyl groups, but leaves the position of the unsaturation undetermined. The location of the double bond was deduced from the apparent formation of iso-valerianic acid on oxidation. Semmler² also reported this acid as an oxidation product of the aldehyde, but this was found later to be erroneous.

In 1896, citronellal was made the subject of an investigation by Tiemann



¹ *Am. Chem. J.*, **11**, 456 (1889).

² *Ber.*, **24**, 201 (1891).