by crystallization, first from methyl alcohol and finally from ligroin. It proved to be identical with the original benzoate prepared by the action of the unsymmetrical benzoylphenylhydrazine on β-orthotoluquinone.

The Action of Unsymmetrical:—Benzoyltolylhydrazine on β-Orthotoluquinone:—Tolylazometacresol Benzoate, $C_6H_3(CH_3)(OC_7H_5O)(N_2C_6H_4CH_3)$ (1 : 3 : 4).—This reaction with the tolylhydrazine was carried out under the same condition as with the phenylhydrazine described above. There was thus obtained an orange colored solid melting at 93°.

Analysis: Calculated for $C_{21}H_{18}N_2O_2$: C, 76.36; H, 5.45.
Found: C, 75.71; H, 5.64.

Tolylazometacresol benzoate is slightly soluble in cold methyl and ethyl alcohol and readily so in hot benzene and ligroin. It is deposited from ligroin in the form of light orange colored needles. When dissolved in sulfuric acid and the resulting solution poured into water tolylazometacresol, $C_6H_3(CH_3)(OH)(N_2C_6H_4CH_3)$(1 : 3 : 4), was deposited as an orange-red solid which on crystallization from ligroin melted at 148°.

Analysis: Calculated for $C_{14}H_{14}N_2O$: C, 74.33; H, 6.19.
Found: C, 74.24; H, 6.13.

Tolylazometacresol readily dissolves in hot ligroin, crystallizing out in the form of thin lath-shaped crystals, orange-red in color. Like the other orthohydroxyazo compounds it is very slightly soluble in alkalies. It is isomeric with the paratolylazoparacresol, $C_6H_3(CH_3)(N_2C_6H_4CH_3)$ (OH)(1 : 3 : 4), described by Nölting and Kohn.[1] When benzoylated by dissolving in alcohol containing sodium ethylate and adding benzoyl chloride, tolylazometacresol benzoate is formed, identical with the compound formed by the action of the unsymmetrical benzoyltolylhydrazine on β-orthotoluquinone.

COLUMBUS, OHIO.

[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

HYDANTOINS: THE REDUCTION OF ALDEHYDE CONDENSATION-PRODUCTS OF 1-PHENYL-2-THIOHYDANTOIN.

[FOURTH PAPER.]

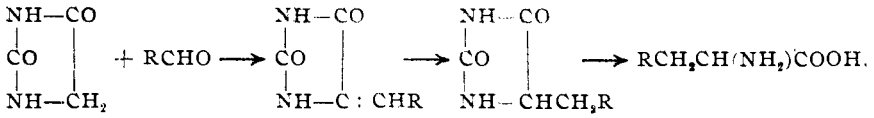
BY TREAT B. JOHNSON AND CHARLES A. BRAUTLECHT.

Received July 20, 1911.

In a previous paper from this laboratory, Wheeler and Hoffman[2] have described a new and practical method of synthesizing phenylalanine and tyrosine. They condense hydantoin with benzaldehyde and anisaldehyde, forming 4-benzal- and 4-anisalhydantoins respectively. When these unsaturated compounds are warmed with hydriodic acid they are reduced at the double bond and transformed quantitatively into the

[1] *Ber.*, **17**, 354.
[2] *Am. Chem. J.*, **45**, 368.

corresponding alkyl hydantoins, which are then hydrolyzed with acids or alkalies giving the α-amino-acids. This method of synthesizing an α-amino-acid is represented by the following formulas:



I. II. III. IV.

(R = C_6H_5 —, $CH_3OC_6H_4$ —, etc.)

Not only hydantoin I condenses smoothly with aldehydes, but it has also been observed that the methylene hydrogens of the phenylthiohydantoins V are likewise reactive towards aldehydes and these also condense with aromatic aldehydes giving the corresponding benzal-derivatives VI.[1] It was therefore of interest to determin the behavior of these aldehyde condensation products of thiohydantoins towards reducing agents. In this paper, we shall discuss only derivatives of 1-phenyl-2-thiohydantoin V.

While the aldehyde condensation products of plain hydantoin are reduced at the double bond when digested with hydriodic acid, we now find that the corresponding derivatives of 1-phenyl-2-thiohydantoin are not reduced by this reagent. Benzalphenylthiohydantoin VI, for example, was recovered unaltered after 2 hours' digestion in glacial acetic acid with an excess of iodine and red phosphorus. Also no reduction to the corresponding benzylhydantoin VII took place by the action of ferrous sulfate in an ammoniacal solution or with zinc dust and acetic acid. Aluminium amalgam effected only a partial reduction of the hydantoin. A practically quantitative transformation into the alkyl hydantoin, however, took place by reduction of the benzal hydantoins with sodium amalgam. 1-Phenyl-2-thio-4-benzal-, 1-phenyl-2-thio-4-piperonal- and 1-phenyl-2-thio-4-anisalhydantoins were converted in this manner into 1-phenyl-2-thio-4-benzyl-, 1-phenyl-2-thio-4-piperonyl- and 1-phenyl-2-thio-4-anisylhydantoins respectively.

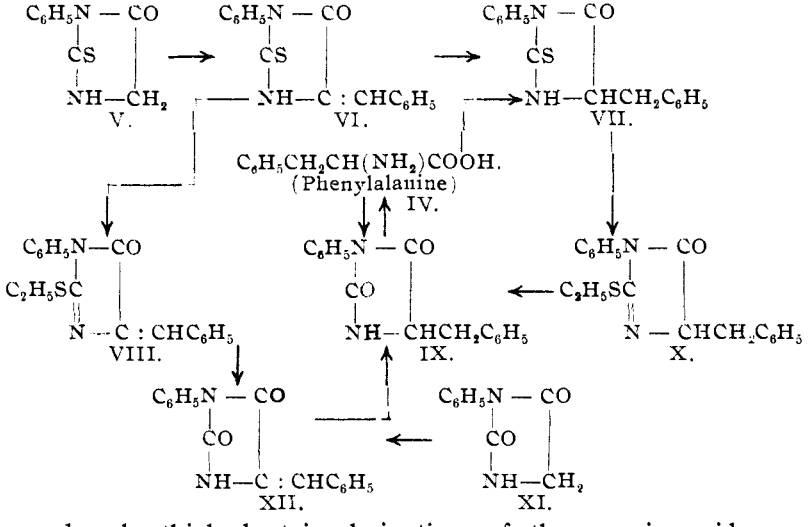
The thiohydantoin VII, formed by reduction of 1-phenyl-2-thio-4-benzalhydantoin, VI, was identical with that obtained by the action of phenylisothiocyanate on phenylalanine,[2] IV. When this hydantoin was warmed with ethylbromide, in the presence of alkali, the corresponding 2-ethylmercapto-derivative X was formed. On hydrolysis with acids, ethylmercaptan was evolved and this compound was converted into the same substance—1-phenyl-4-benzylhydantoin, IX—as was obtained by the action of phenylisocyanate on phenylalanine.[3]

[1] Wheeler and Brautlecht, *Am. Chem. J.*, **45**, 446.

[2] Brautlecht, *J. Biol. Chem.*, **10**, No. 2 (1911).

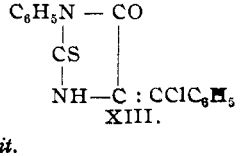
[3] Mouneyrat, *Ber.*, **33**, 2393.

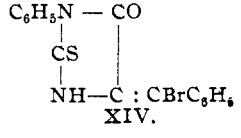
Wheeler and Brautlecht[1] have previously shown that 1-phenyl-2-thio-4-benzalhydantoin, VI, can easily be desulfurized in a similar manner, giving 1-phenyl-4-benzalhydantoin, XII. We now find that this benzal derivative, XII, is reduced smoothly by the action of sodium amalgam, giving the hydantoic acid $C_6H_5NHCONHCH(C_7H_7)COOH$.[2] This was then converted into 1-phenyl-4-benzylhydantoin, IX, by the action of hydrochloric acid. These various transformations are represented by the following structural formulas:



The 1-phenyl-2-thiohydantoin derivatives of the α-amino-acids are far more stable than the corresponding unsubstituted hydantoins studied by Wheeler and Hoffman.[2] The latter compounds underwent hydrolysis smoothly by the action of acids and alkalies, giving amino-acids. All attempts to hydrolyze, on the other hand, 1-phenyl-2-thio-4-benzylhydantoin, VII, to phenylalanine by digestion with sodium or barium hydroxide were unsuccessful. Because of this pronounced stability, the aldehyde condensation products of 1-phenylthiohydantoin are, therefore, of no value for the synthesis of amino-acids.

1-Phenyl-2-thio-4-benzalhydantoin, VI, is attacked by chlorine and bromine in glacial acetic acid solution giving 4-(α-chlorobenzal)-1-phenyl-2-thiohydantoin, XIII, and 4-(α-bromobenzal)-1-phenyl-2-thiohydantoin, XIV, respectively.



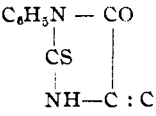


[1] *Loc. cit.*

[2] Fischer and Mouneyrat, *Ber.*, 33, 2383.

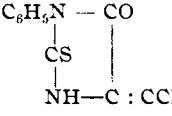
Experimental Part.

1-Phenyl-2-thio-4-benzalhydantoin,



—The method for preparing this compound has been described in a previous paper.[1] The sulfur in this hydantoin is very firmly bound. The compound is not changed by digestion with concentrated hydrochloric acid while the corresponding 2-ethylmercapto-derivative[1] is transformed, under similar conditions, into the oxygen hydantoin. The hydantoin dissolves in barium hydroxide solution, giving, apparently, a salt of the corresponding benzalthiohydantoic acid. This acid, however, was not isolated. After digestion of the hydantoin with an excess of the alkali for 10 hours and then acidifying the solution with hydrochloric acid the unaltered benzalthiohydantoin was obtained. The hydantoin was not changed by digestion with sodium ethylate in alcohol solution. Two grams of the finely pulverized hydantoin were suspended in a mixture of 400 cc. of water and 100 cc. of a 1 per cent. solution of hydrogen dioxide and the mixture boiled for 2 hours. There was apparently no oxidation under these conditions. We recovered 1.9 grams of the original thiohydantoin and the aqueous filtrate gave no test for sulfuric acid.

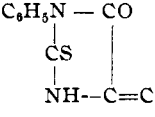
4-(α-Chlorobenzal)-1-phenyl-2-thiohydantoin,



—This compound was prepared by passing chlorine gas into cold, glacial acetic acid in which was suspended 1-phenyl-2-thio-4-benzalhydantoin. The same compound was formed whether one molecular proportion or a large excess of chlorine was used. It was purified for analysis by crystallization from acetic acid or alcohol and separated from hot solutions, on cooling, in colorless prisms, which melted at 236–237° to a clear oil. The hydantoin is very difficultly soluble in alcohol. Analysis (Kjeldahl):

Calculated for $C_{16}H_{11}ON_2SCl$: N, 8.90; found, 8.72.

4-(α-Bromobenzal)-1-phenyl-2-thiohydantoin,



—From 1-phenyl-2-thio-4-benzalhydantoin and one molecular proportion

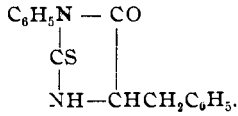
[1] Wheeler and Brautlecht, *Loc. cit.*

of bromine as in the preparation of the preceding chloro compound. It is soluble in boiling acetic acid, alcohol and acetone and crystallizes from alcohol in yellow plates, which melt at 211° with decomposition. The yield was about 60 per cent. of the calculated. It was dried for analysis at 100°. Analysis (Kjeldahl):

Calculated for $C_{18}H_{11}ON_2SBr$: N, 7.80; found, 7.86.

The Reduction of 1-Phenyl-2-thio-4-benzalhydantoin:

1-Phenyl-2-thio-4-benzylhydantoin,



—Forty grams of the benzalhydantoin were dissolved in dilute sodium hydroxide solution and an excess of sodium amalgam suspended in the solution. There was an immediate reaction with reduction at the double bond and the solution gradually lost its yellow color. After allowing to stand for about 19 hours, at ordinary temperature, in order to obtain a complete reduction, the solution was warmed to dissolve a crystalline sodium salt, which had separated, and the solution decanted from the mercury. An excess of hydrochloric acid was then added and the solution evaporated to dryness when the hydantoin was obtained, contaminated with sodium chloride. The salt was dissolved by trituration with water and the benzyl-hydantoin then crystallized from boiling alcohol. It separated in colorless prisms which melted at 187° to a clear oil. The yield was nearly quantitative. The hydantoin was identical with that obtained by the action of phenylmustard oil on phenylalanine.[1] A mixture of the two melted at exactly the same temperature. Analysis (Kjeldahl):

Calculated for $C_{16}H_{14}ON_2S$: N, 9.93; found, 9.89.

Attempts to reduce 1-phenyl-2-thio-4-benzalhydantoin with ferrous sulfate in ammoniacal solution, with zinc dust and acetic acid and with hydriodic acid were unsuccessful. In one experiment four grams of the benzalhydantoin were digested on the steam bath with 200 cc. of water, 300 cc. of concentrated ammonia and 2 molecular proportions of ferrous sulfate for 17 hours. We recovered, after this treatment, about 2.5 grams of pure unaltered hydantoin. Again, 4 grams of the benzalhydantoin were dissolved in 60 cc. of boiling glacial acetic acid, 2 grams of zinc dust added, and the mixture boiled for 3.5 hours. Over two grams of unaltered benzalhydantoin were recovered. In another experiment, 1.6 grams of the benzalhydantoin and 1.5 grams of iodine were dissolved in glacial acetic acid, 0.4 gram of red phosphorus suspended

[1] Brautlecht, *Loc. cit.*

in the solution and the liquid then boiled for 2 hours. There was no evidence of a reduction and the benzalhydantoin was recovered unaltered.

Reduction with Aluminium Amalgam.—Three grams of the benzalhydantoin were dissolved in 300 cc. of dilute sodium hydroxide solution and four grams of amalgamated aluminium filings suspended in the solution. After allowing the reaction to proceed for about 18 hours and then acidifying with hydrochloric acid we obtained the benzylhydantoin mixed with unaltered material. The yield was small. The experiment was repeated and the hydantoin reduced for 60 hours with an excess of aluminium amalgam. Under these conditions, we still recovered the greater proportion of the benzalhydantoin unaltered.

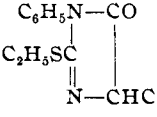
Reduction of 1-Phenyl-4-benzalhydantoin.[1]—Four grams of this hydantoin, which was prepared by the desulfurization of 1-phenyl-2-thio-4-benzalhydantoin as described in a previous paper, were dissolved in 50 cc. of dilute sodium hydroxide solution and reduced with 68 grams of 2.5 per cent. sodium amalgam. A crystalline sodium salt separated from the aqueous solution, which was first dissolved by warming, and the solution then acidified with hydrochloric acid. The corresponding hydantoic acid, $C_6H_5NH.CONHCH(CH_2C_6H_5)COOH$,[2] separated and melted at about 180°–1° with effervescence. Analysis (Kjeldahl):

Calculated for $C_{16}H_{16}O_3N_2$: N, 9.86; found, 9.88.

When this hydantoic acid was digested with hydrochloric acid it was converted into the hydantoin described by Mouneyrat,[3] melting at 173° to an oil. Analysis (Kjeldahl):

Calculated for $C_{16}H_{14}O_2N_2$: N, 10.45; found, 10.49.

1-Phenyl-2-ethylmercapto-4-benzylhydantoin,



—This hydantoin was obtained as a viscous oil by alkylation of 1-phenyl-2-thio-4-benzylhydantoin with ethylbromide in presence of sodium ethylate. It showed no signs of crystallizing after standing two days. When this mercaptohydantoin was digested with hydrochloric acid mercaptan was evolved immediately and a quantitative yield of 1-phenyl-4-benzylhydantoin[4] obtained. It melted at 180°–181° and was identical with the hydantoin obtained by reduction of 1-phenyl-4-benzalhydantoin. A mixture of the two products melted at exactly the same temperature. When 1-phenyl-4-benzylhydantoin was digested for a long time with barium hydroxide it underwent hydrolysis, giving phenyl-

[1] Wheeler and Brautlecht, *Loc. cit.*

[2] Fischer and Mouneyrat, *Loc. cit.*

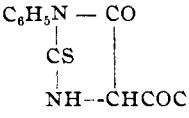
[3] *Loc. cit.*

[4] Mouneyrat, *Loc. cit.*

alanine, melting at 263° (N = 8.31 per cent.), carbon dioxide, aniline and, apparently, other decomposition products.

Action of Alkali on 1-Phenyl-2-thio-4-benzylhydantoin.—Attempts to hydrolyze this hydantoin to phenylalanine by digestion with sodium or barium hydroxide were unsuccessful. This stability in the presence of alkali was remarkable. Three and one-half grams of the hydantoin were suspended in a strong barium hydroxide solution and the mixture boiled on a sand-bath for 8 to 9 hours. The greater proportion of the hydantoin was recovered unaltered, while the rest had undergone decomposition giving tarry products. No phenylalanine was identified. In a second experiment, the benzylhydantoin was recovered unaltered after long digestion (8–10 hours) in strong sodium hydroxide solution.

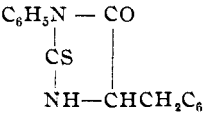
1-Phenyl-2-thiohydantoin-4-glyoxylic Acid,



—1-Phenyl-2-thiohydantoin and a molecular proportion of diethyl oxalate were dissolved in absolute alcohol containing the required amount of sodium ethylate (1 mol.). There was no apparent evidence of any reaction. After standing at ordinary temperature for 3 days the excess of alcohol was then expelled, the residue dissolved in dilute sodium hydroxide solution and the glyoxylic acid precipitated by addition of hydrochloric acid. It crystallizes from 95 per cent. alcohol as pale yellow needles, which melt at 240° with effervescence. A mixture of the acid and the original 1-phenyl-2-thiohydantoin melted at about 210°. The yield was 82 per cent. of the theoretical. Analysis (Kjeldahl):

Calculated for $C_{11}H_8O_4N_2S$: N, 10.67; found, 10.48.

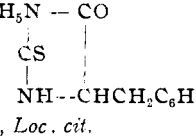
1-Phenyl-2-thio-4-(p-methoxybenzyl)-hydantoin,



—A quantitative yield of this hydantoin was obtained by dissolving 1-phenyl-2-thio-4-anisalhydantoin[1] in dilute alkali and then reducing with sodium amalgam. It crystallizes from alcohol in slender, colorless prisms, which melt at 171° to a clear oil. Analysis (Kjeldahl):

Calculated for $C_{17}H_{16}O_2N_2S$: N, 8.97; found, 8.70, 8.81.

1-Phenyl-2-thio-4-piperonyl hydantoin,



[1] Wheeler and Brautlecht, *Loc. cit.*

—From 1-phenyl-2-thio-4-piperonalhydantoin[1] by reduction with sodium amalgam. The yield was about 70 per cent. of the calculated. It is difficultly soluble in alcohol and separates from hot solutions in straw-colored needles, which melt at 172–173° to a clear oil. It was dried for analysis at 100°. Analysis (Kjeldahl):

Calculated for $C_{17}H_{14}O_3N_2S$: N, 8.59; found, 8.57.

NEW HAVEN, CONN.

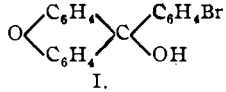
[CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN.]

THE CONDENSATION OF *p*-DIBROMOBENZENE WITH XANTHONE; A CONTRIBUTION TO THE KNOWLEDGE OF QUINOCARBONIUM SALTS.

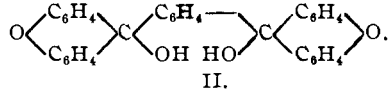
L. H. CONE AND C. J. WEST.

Received July 20, 1911.

Gomberg and Cone[2] found that by the action of xanthone upon the products resulting from dibromobenzene and magnesium two xanthenols resulted. One (I) is *p*-bromophenylxanthenol; the second (II), which they did not investigate, is *p*-phenylenedixanthenol.



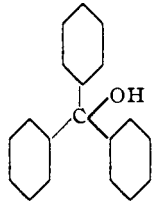
I.



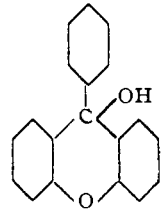
II.

This observation confirms that made by Houben,[3] who first showed that in the Barbier-Grignard reaction either one or both of the bromine atoms of *p*-dibromobenzene may react with magnesium. We have found that the reaction may be thrown largely in favor of the mono- or di-xanthenol compound, depending upon the amount of magnesium (and correspondingly of xanthone) used.

It has been shown[4] that there is a close analogy between triphenylcarbinol (III) on the one hand and phenylxanthenol (IV) on the other,



III.



IV.

[1] Wheeler and Brautlecht, *Loc. cit.*

[2] *Ann.*, **370**, 178 (1909).

[3] *Ber.*, **33**, 3796 (1905).

[4] Gomberg and Cone, *Ann.*, **370**, 142 (1909); *Ibid.*, **376**, 183 (1910); see also Gomberg and West, THIS JOURNAL, **33**, 1211 (1911).