pale yellow blade-like prisms separated which melted at 151–152° to a transparent yellow oil. These were dried in a current of air until free from the odor of acetic anhydride. They could then be heated to 110° without any loss of weight but meanwhile assumed a bright lemon yellow color. Nitrogen determination:

Calc. for $C_5H_8O_2N_2S$: N, 17.5. Found: 17.4. The analysis of a later preparation gave 17.6% and 17.5%.

If diacetyl thiourea is crystallized from a concentrated solution in acetic anhydride it separates in the form of a bright lemon-yellow product. If allowed to crystallize slowly from a dilute solution larger crystals are obtained which are pale yellow and transparent. On heating to 100° they assume a bright lemon-yellow color, losing nothing in weight and retaining their original form.

Monoacetyl Urea.—One gram of urea was dissolved in 10 cc. of acetic anhydride by boiling and the heating continued for one hour at 100°. On cooling, clusters of colorless prisms separated, melting at 212°. These were dried at 110° with no loss in weight.

Calc. for $C_3H_6O_2N_2$: N, 27.4. Found: 27.3.

URBANA, ILL.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON HYDANTOINS. XXXIII. THE CONDENSATION OF CINNAMIC ALDEHYDE WITH HYDANTOINS.[1]

BY TREAT B. JOHNSON AND RICHARD WRENSHALL.

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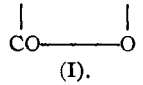
Erlenmeyer's method of synthesizing α-amino acids, the first step of which involves the condensation of hippuric acid with an aldehyde giving an azlactone (I), has found a wide application for the preparation of amino



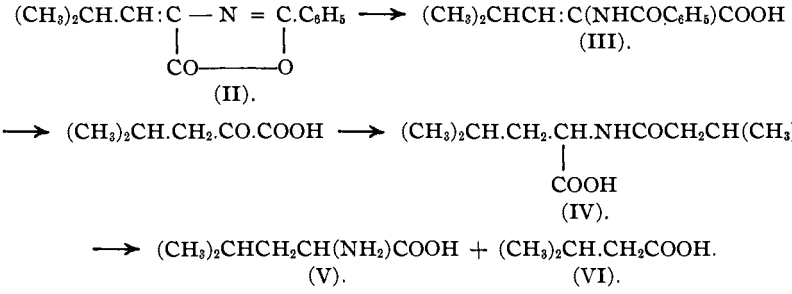
(I).

acids containing aromatic groups. The majority of the aromatic aldehydes which have been studied, have been shown to condense smoothly with hippuric acid giving good yields of the corresponding azlactones. Attempts to synthesize aliphatic α-amino acids by application of Erlenmeyer's method with aliphatic aldehydes have been attended with very little success. Erlenmeyer and Kunlin[2] were the first to apply the method with an aliphatic aldehyde with the object of developing a new synthesis of leucine (V). They condensed isobutylaldehyde with hippuric acid

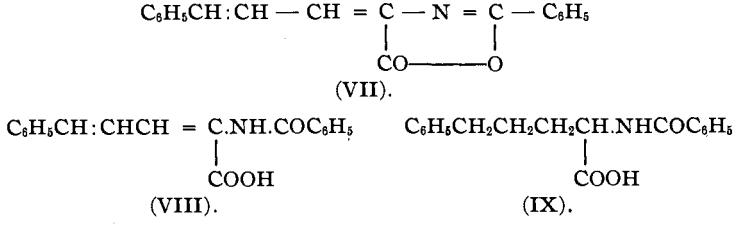
[1] Part of a dissertation presented by Mr. Richard Wrenshall to the Faculty of the Graduate School of Yale University, 1915, in candidacy for the Degree of Doctor of Philosophy.

[2] *Ann.*, **316**, 145 (1901).

in the usual manner but obtained a very poor yield of the corresponding azlactone represented by Formula II. Like the azlactones derived from aromatic aldehydes, this was converted into the corresponding acrylic acid (III) by hydrolysis with aqueous sodium hydroxide. This transformation was nearly quantitative. In order to convert the acrylic acid (III) into leucine these investigators apparently made no attempts to reduce it to the corresponding saturated acid and then remove the benzoyl group by hydrolysis according to the general practice. On the other hand, they heated the unsaturated acid under pressure with aqueous ammonia when it was transformed into the peptide combination represented by Formula IV. The latter then underwent hydrolysis, giving a mixture of leucine (V) and isovalerianic acid (VI). No statement is made in their paper regarding the yield of leucine. The important steps of this synthesis may be represented as follows:



The only other aliphatic aldehyde to be investigated, so far as the writers are aware, is cinnamic aldehyde which, as Erlenmeyer and Matter[1] have shown, condenses normally with hippuric acid forming the corresponding unsaturated azlactone represented by Formula VII. The latter on careful hydrolysis with dilute alkali was transformed into the unsaturated acid (VIII). In this case also, no attempt was made to reduce this unsaturated compound to the saturated acylamino acid (IX). In other words, the synthesis of the higher homolog of phenylalanine, *viz.: α-amino-d-phenylvalerianic acid* has been accomplished by the malonic ester method only.[2]



[1] *Ann.*, **337**, 270 (1904).

[2] Braun and Kruber, *Ber.*, **45**, 389 (1912).

Wheeler and Brautlecht[1] were the first to show that cinnamic aldehyde will condense with hydantoins by preparing 1-phenyl-2-thio-4-cinnamalhydantoin from 1-phenyl-2-thiohydantoin by interaction with cinnamic aldehyde. The yield of their condensation product was recorded as being equivalent to 93.6% of the theoretical. We now find that plain hydantoin and also 2-thiohydantoin condense with this aldehyde forming the corresponding 4-cinnamalhydantoin (XIII), and 4-cinnamalthiohydantoin (XXI), respectively. The yields in both cases were good. Theoretically, these two unsaturated hydantoins as well as Erlenmeyer's and Matter's[2] azlactone (VII), should be capable of existing in more than one modification. In fact, in the case of the azlactone (VII), Erlenmeyer and Matter state that they encountered difficulties in its purification and actually assumed that they were probably dealing with stereoisomeric forms which were inseparable. We examined very carefully both of our condensation products, in hopes of detecting here stereisomers,[3] but no evidence was found that would point to the conclusion that either substance existed in more than one form.

2-Thio-4-cinnamalhydantoin (XXI), was desulfurized smoothly by vigorous treatment with chloroacetic acid, giving the hydantoin (XIII). Therefore, for the synthesis of the amino acid (XV) one can start either with hydantoin or 2-thiohydantoin. It was our experience, however, that it is more practical to start with hydantoin and prepare the cinnamalhydantoin by direct condensation. Both the cinnamalhydantoin (XIII) and the thiohydantoin (XXI) behave in an analogous manner when reduced in alkaline solution with sodium analgam. The corresponding hydantoic acids, which are represented by Formulas XIV and XXII, respectively, were formed. The corresponding hydantoins (XVIII) and (XXIII) were easily obtained by digesting their respective hydantoic acids with hydrochloric acid. The unsaturated thiohydantoin (XXIII) was easily desulfurized by digestion with chloroacetic acid and transformed into the hydantoin (XVIII).

The hydantoic acid (XIV) is very stable in the presence of alkalis. However, it slowly underwent decomposition when digested for a long time with strong, aqueous, barium hydroxide solution and was transformed into *the α-amino acid* (XV). This new amino acid dissolves in about 100 parts of boiling water and separates, on cooling, in beautiful, colorless, distorted needles which are tasteless. It is very soluble in alcohol and melts at 247–248° with decomposition. The yield of pure amino acid formed by hydrolysis was 82% of the theoretical,

[1] *Ann. Chem. J.*, **45**, 446 (1911).

[2] *Loc. cit.*

[3] Johnson and Hadley, THIS JOURNAL, **37**, 171 (1915); Johnson and Bates, *Ibid.*, **37**, 383 (1915).

while the yield of the acid, if based on the quantity of hydantoin originally used in its synthesis, was only about 25% of theory.

The α-amino acid (XV) reacts normally with ammonium thiocyanate, in the presence of acetic anhydride,[1] forming nearly quantitatively the acylthiohydantoin (XIX). The latter was converted, by hydrolysis with hydrochloric acid, into the same 2-thiohydantoin (XXIII) as was formed by digesting the thiohydantoic acid (XXII) with hydrochloric acid.

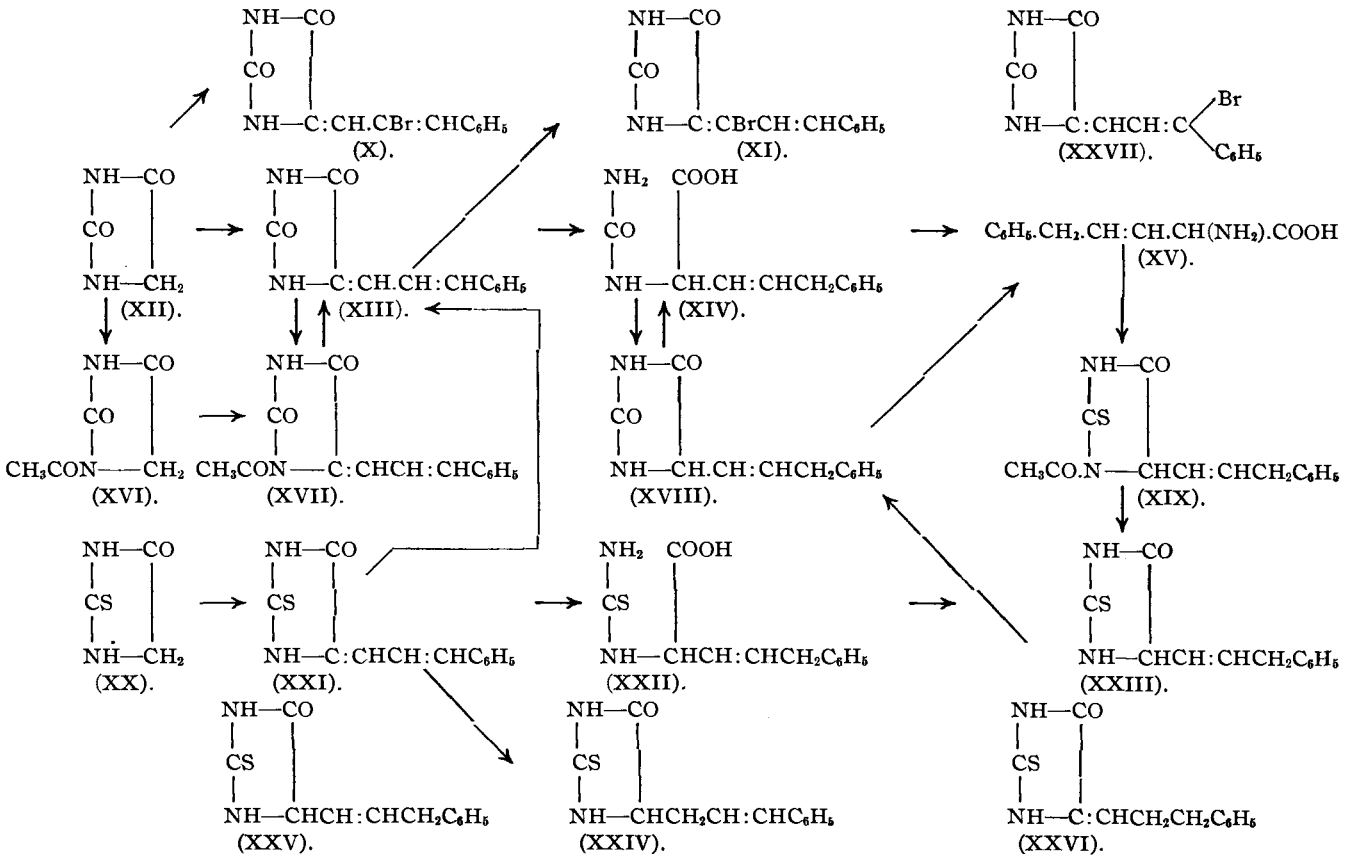
We also investigated the behavior of 2-thio-4-cinnamalhydantoin (XXI) when digested in acetic acid with zinc dust. Under these conditions the hydantoin (XXIII) was not produced, but another product was formed whose constitution has not yet been established. The loss of yellow color on reduction indicates a destruction of the double bond in position 4 of the hydantoin. Whether this double bond is reduced independently, as in the case of other aldehyde-condensation products, forming the hydantoin (XXIV), or whether the change actually involves an addition of hydrogen at the Thiele 1,4-union in the hydantoin (XXI), giving a stereoisomer (XXV), remains to be decided. The third possible isomer represented by Formula XXVI should be formed by condensation of 2-thiohydantoin with phenylpropylaldehyde. A complete investigation of these interesting changes will be carried out at a future date.

Especially interesting was the behavior of cinnamalhydantoin (XIII) towards aceticanhydride. It has been our previous experience that aldehyde condensation products of this type have not shown a tendency to interact with aceticanhydride. We now find that this compound (XIII), is transformed by the action of this reagent into the corresponding acetylhydantoin represented by Formula XVII. The yield was excellent. The structure of this compound was established by the fact that the same hydantoin was formed by condensation of Siemonsen's[2] 3-acetylhydantoin with cinnamicaldehyde. 4-Cinnamalhydantoin (XIII), does not add bromine in acetic acid solution to form a saturated compound or a dibromoderivative. On the other hand, it interacts with the halogen in a similar manner as does benzalhydantoin,[3] and forms a monobrom substitution product with evolution of hydrobromic acid. We have represented this hydantoin by Formula XI. The same hydantoin is also formed by treatment of the hydantoin (XIII) with an excess of bromine. That the bromine does not substitute in the β-position was established by the fact that a different bromohydantoin (X) was formed

[1] Johnson and Nicolet, THIS JOURNAL, **33**, 1973 (1911); Johnson, *Am. Chem. J.*, **49**, 68 (1913).

[2] *Ann.*, **333**, 111 (1904).

[3] Wheeler, Hoffmann and Johnson, *J. Biol. Chem.*, **10**, 147 (1911).


NH—CO
CO
NH—C:CH.CBr:CHC6H5
(X).
NH—C:CBrCH:CHC6H5
(XI).
NH—C:CHCH:C
Br
C6H5
(XXVII).
NH—CH2
(XII).
NH—C:CH.CH:CHC6H5
(XIII).
NH2 COOH
NH—CH.CH:CHCH2C6H5
(XIV).
C6H5.CH2.CH:CH.CH(NH2).COOH
(XV).
CH3CON—CH2
(XVI).
CH3CON—C:CHCH:CHC6H5
(XVII).
NH—CH.CH:CHCH2C6H5
(XVIII).
CH3CO.N—CHCH:CHCH2C6H5
(XIX).
CS
NH—CH2
(XX).
NH—C:CHCH:CHC6H5
(XXI).
NH—CHCH:CHCH2C6H5
(XXII).
(XXIII).
NH—CHCH:CHCH2C6H5
(XXV).
NH—CHCH2CH:CHC6H5
(XXIV).
NH—C:CHCH2CH2C6H5
(XXVI).

by condensation of bromocinnamic aldehyde[1] $C_6H_5CH : CBrCHO$ with hydantoin. The only other monobromo derivative theoretically possible, if we disregard those where the halogen is substituted in the benzene ring, would be the bromohydantoin represented by Formula XXVII. This we have temporarily eliminated because it seems very improbable that bromine would substitute in a propenyl grouping on the carbon joined to phenyl. In other words, the interesting results which we have obtained is not what would be expected if the 1,4-union in the hydantoin (XIII), interacted with bromine in accordance with Thiele's law. The study of these compounds will be continued.

The various transformations discussed above are represented by the preceding structural formulas.

Experimental Part.

4-Cinnamal Hydantoin (XIII).—This hydantoin is easily obtained according to the following procedure: A mixture of 10 g. of hydantoin, 14 g. of cinnamic aldehyde, 50 g. of fused sodium acetate and 50 cc. of glacial acetic acid are heated for 6 hours in an oil bath at 130–140°. The resulting product is then cooled and finally warmed with 500 cc. of water until thoroughly disintegrated, in order to dissolve all the sodium acetate. The hydantoin is insoluble in the water and separates as a brown crystalline powder. The yield of crude material is generally about 15.5 g. or 72% of the theoretical. The hydantoin is easily purified by crystallization from hot, glacial acetic acid and separates, on cooling, as clusters of canary yellow prisms which melt at 272–273° to a red oil with decomposition. The hydantoin crystallizes from 95% alcohol in stout prisms or long, slender prisms, depending on the strength of the solution and the temperature of crystallization. The compound is insoluble in water and very difficultly soluble in ether. Analysis:

Calc. for $C_{12}H_{10}O_2N_2$: N, 13.08. Found: N, 12.95, 13.12.

γ-Phenylpropenylhydantoic Acid (XIV).—This acid is formed by reduction of the above hydantoin with sodium amalgam. Eight and two-tenths grams of the preceding hydantoin were dissolved in a solution containing 2.5 g. of potassium hydroxide in 100 cc. of water. After diluting further with 260 cc. of water and warming to 60–65°, 110 g. of 3% sodium amalgam were added slowly, keeping the temperature of the solution between 50–65°. After heating for 1.5 hours the reduction was complete, and no cinnamalhydantoin separated on acidifying the solution with hydrochloric acid. During the reduction, the color of the solution changed from yellow to pale green. The fluid was decanted from mercury, cooled and finally acidified with hydrochloric acid, when the hydantoic acid separated. The yield was 7.0 g. This acid is very soluble in hot water and alcohol. It was purified for analysis by recrystalliza-

[1] Zincke and Hagen, *Ber.*, **17**, 1814 (1884).

tion from hot water and separated in the form of colorless, diamond-shaped plates which melted from 142–161° with decomposition. The melting point is very indefinite and varies according to the rate of heating. An attempt to reduce cinnamalhydantoin with stannous chloride and hydrochloric acid was unsuccessful.

Calc. for $C_{12}H_{16}O_3N_2$: N, 11.86. Found: N, 11.80, 11.94.

α-Amino-δ-phenylpentenic Acid, $C_6H_5CH_2.CH:CH.CH(NH_2)COOH$. —This new α-amino acid was obtained by digesting the 7.0 g. of the hydantoic acid, described above, with 50 g. of barium hydroxide in 200 cc. of water for 50 hours. After this treatment the hydrolysis was complete and no ammonia was evolved. Then 150 cc. of water were added and the solution boiled to dissolve all the amino acid. After filtering from barium carbonate the excess of barium was precipitated as barium sulfate by adding the required amount of sulfuric acid. The solution, freed from sulfate and barium, was then concentrated to a volume of about 150 cc. and cooled, whereupon practically all of the amino acid present separated in a crystalline condition. It was purified by crystallization from boiling water, a little bone-coal being added to remove all color. It crystallized in long, colorless needles which melted at 247–248° to a yellow oil with some decomposition. The acid is very soluble in alcohol and dissolves in about 100 parts of boiling water.

Calc. for $C_{11}H_{15}O_2N$: N, 7.25. Found: N, 7.17, 7.26.

4-(γ-Phenylpropenylhydantoin) (XVIII).—This hydantoin is formed smoothly by digesting the above hydantoic acid with hydrochloric acid. One hour's boiling with 25% hydrochloric acid is sufficient to close the ring. The hydantoin crystallizes from 95% alcohol in long needles which melt at 160–161° to a clear oil without effervescence.

Calc. for $C_{12}H_{14}O_2N_2$: N, 12.84. Found: N, 12.67, 12.79.

2-Thio-3-acetyl-4-(γ-phenylpropenyl)-hydantoin (XIX.)—Two grams of α-amino-δ-phenylpentenic acid were warmed on the steam bath with 2 g. of dry ammonium thiocyanate and 10 cc. of acetic anhydride for one hour at 100°. The orange-colored solution which was obtained, was then allowed to stand over night when this acetylhydantoin separated in the form of yellow prisms. The yield was 2.5 g., being equivalent to 90.5% of theory. It was purified by recrystallization from 80% alcohol, using enough of the solvent so that crystallization did not commence above the room temperature. The compound always separated as an oil if the solution was too concentrated. The hydantoin crystallized in orange-colored plates which melted at 97–98° to an oil without effervescence. It was difficultly soluble in water and quite soluble in alcohol and ether.

Calc. for $C_{14}H_{16}O_2N_2S$: N, 10.14. Found: N, 10.03, 9.95.

2-Thio-4-(γ-phenylpropenyl)-hydantoin (XXIII).—In order to obtain this hydantoin the above acetyl derivative was suspended in strong hydrochloric acid and the mixture heated on a steam bath until the acid was expelled by evaporation. This operation was repeated four times, in order to insure complete hydrolysis, when the thiohydantoin was obtained as a brittle, orange-colored product melting at 124–125° to a turbid oil. This material was insoluble in water, but very soluble in alcohol. It could not be crystallized from 95% alcohol, for even on spontaneous evaporation of the solvent at room temperature it deposited in the form of a gum. From 60% alcohol it separated on slow cooling, in the form of cream-colored plates. More of this same material was obtained by mixing the alcohol filtrate with hydrochloric acid and evaporating to dryness. When perfectly pure the thiohydantoin crystallizes from dilute alcohol as needles or distorted prisms which melt at 126–127° to an oil. A mixture of this hydantoin and the corresponding acetyl compound melted at 85°.

Calc. for $C_{12}H_{14}ON_2S$: N, 11.96. Found: N, 11.78, 11.76.

Desulfurization of 2-Thio-4-(γ-phenylpropenyl)-hydantoin (XXIII) with Formation of 4-(γ-phenylpropenyl)-hydantoin (XVIII).—This change can be accomplished easily by heating the thiohydantoin with a 10% aqueous solution of chloroacetic acid at 140° for 4 hours. Under these conditions the sulfur is completely removed and, on cooling, the acid solution, the hydantoin is obtained in the form of needles which melt at 160°. The operation of boiling the thiohydantoin with chloroacetic acid was not effective in removing the sulfur.

2-Thio-4-cinnamalhydantoin (XXI).—Eight grams of 2-thiohydantoin, which were prepared according to the method of Johnson and Nicolet,[1] were heated with 8.5 g. of cinnamic aldehyde, 40 g. of fused sodium acetate and 60 cc. of glacial acetic acid for 2 hours at 130°. The resulting mixture was then cooled and the solid mixture warmed with 400 cc. of water until completely disintegrated. The hydantoin was obtained as a brownish yellow product insoluble in water. The yield of crude material was 13 g. or 85% of the theoretical. It was purified for analysis by crystallization from glacial acetic acid and melted at 262–263°.

It was noticed that this material, on crystallization from the acetic acid, separated, while the solution was very hot, in the form of red, prismatic columns but after the temperature of the solution had fallen below 70° it then deposited in long, slender, yellow needles. By proper regulation of the temperature and application of fractional crystallization it was possible to separate the two forms.

The red product melted at 262–263° to an oil without apparent decomposition and was identified as *2-thio-4-cinnamalhydantoin* (XXI).

[1] *Loc. cit.*

On drying for 2 hours at 125° it lost only 0.1% of its weight. It was insoluble in water and soluble in alcohol. It was less soluble in alcohol and glacial acetic acid than the cinnamalhydantoin.

Calc. for $C_{12}H_{10}ON_2S$: N, 12,17. Found: N, 11.98.

On taking the melting point of the yellow modification it was noticed that it turned red at about 140 to 160° and then melted at the same temperature as the red compound, namely, 262–263°. In fact, the yellow form was identified as the red hydantoin containing acetic acid of crystallization. A sample of the yellow modification, which was washed with ether and then dried at ordinary temperature, gave the following results on analysis:

Calc. for $C_{12}H_{10}ON_2S.CH_3COOH$: N, 9.65. Found: N, 9.59, 9.68.

After drying at 125° for 3 hours and finally for 4 hours at 145° the hydantoin was then analyzed for nitrogen when the following results were obtained:

Calc. for $C_{12}H_{10}ON_2S$: N, 12.17. Found: N, 11.93, 12.03.

From these results it is evident that the yellow modification of the thiohydantoin contains one molecule of acetic acid of crystallization.

Reduction of 2-Thio-4-cinnamalhydantoin with Sodium Amalgam. γ-Phenylpropenylthiohydantoic Acid (XXII).—Two grams of the thiocinnamalhydantoin were dissolved in the least possible amount of 10% sodium hydroxide solution and enough water was added to bring the volume up to 150 cc. The temperature of this solution was then kept between 65–75° and the hydantoin reduced by adding 100 g. of 3% sodium amalgam in small portions at a time. The color of the solution changed from orange to an apple green during this operation. After the reaction was complete the solution was then acidified with hydrochloric acid, when this hydantoic acid separated as an oil. Hydrogen sulfide was also evolved indicating partial decomposition. The hydantoic acid showed no tendency to crystallize on long standing. It was dissolved in ether, dried and the solvent allowed to evaporate spontaneously, but even after such treatment only a gum was obtained, which refused to crystallize after standing for 2 weeks. Its constitution was established by the fact that it was converted into the corresponding hydantoin by digestion with hydrochloric acid. This was accomplished by suspending the hydantoic acid in strong hydrochloric acid and heating on the steam bath to remove the hydrochloric acid. After repeating this treatment 3 times we finally obtained the thiohydantoin, which deposited as a brittle, resinous product melting at 120–130°. It was purified by crystallization from 50% alcohol and separated in cream-colored crystals which melted at 127° without effervescence. A mixture of this substance with some 2-thio-4-(γ-phenylpropenyl)-hydantoin, described above, melted at the same temperature.

2-Thio-4-(γ-phenylallyl)-hydantoin? (XXIV).—This was obtained by partial reduction of 2-thio-4-cinnamalhydantoin. Two and one-half grams of the cinnamalhydantoin were dissolved in sufficient glacial acetic acid to form a clear solution at 65°; 20 g. of zinc dust were added and the solution then warmed for 1.5 hours at 65–75°. It was found that boiling the solution caused an evolution of hydrogen sulfide. During the first half hour the color of the solution changed from chrome yellow to pale apple green, but after this no further color change was noticed. After the reduction was complete the acid solution was cooled and filtered into an excess of cold dilute hydrochloric acid, whereupon this unsaturated hydantoin separated at once as a salmon-colored, curdy precipitate. This substance was dissolved again in pure acetic acid and the precipitation with hydrochloric acid repeated in order to remove all traces of zinc. The hydantoin was extremely soluble in all the common organic solvents. It was finally dried at 40° and then heated for an hour at 100° when it was obtained as a powder having no definite melting point. The substance began to contract at 175°, when heated in a capillary tube, giving a red gum at 185° which became partially fluid at 190°. The yield was quantitative. The compound immediately decolorized a dilute acetone solution of potassium permanganate showing the presence of an unsaturated grouping.

Calc. for $C_{12}H_{12}ON_2S$: N, 12.07. Found: N, 11.87, 11.76.

Desulfurization of 2-Thio-4-cinnamalhydantoin with Formation of 4-Cinnamalhydantoin.—An attempt was made to desulfurize this 2-thiohydantoin by boiling 2.5 g. of the compound for 6 hours with 5 g. of chloroacetic acid in 50 cc. of water. The hydantoin did not dissolve and as there was no change in its appearance by this treatment 5 g. more of chloroacetic acid were added and the digestion continued for 14 hours. Even after this prolonged treatment the hydantoin had undergone no change and melted at 253°. The hydantoin was then heated in a bomb tube for 6 hours with 7 g. of chloroacetic acid (4 molecular proportions) and 15 cc. of water. On opening the tube there was no pressure and the cinnamalhydantoin was suspended in the acid solution. This was separated by filtration, dissolved in dilute sodium hydroxide solution and finally precipitated by addition of hydrochloric acid. The hydantoin was then purified by crystallization from glacial acetic acid. It melted at 272–273° to a red oil with effervescence. It gave no test for sulfur.

The Action of Bromine on 4-Cinnamalhydantoin, 4-(α-Bromocinnamal)-hydantion (XI).—One and five-tenths grams of the cinnamalhydantoin were dissolved in 200 cc. of glacial acetic acid and the temperature of the mixture kept at 50–60° while the calculated amount of bromine vapor (1.12 g.) was aspirated through the solution. After the bromine had been completely absorbed, the excess of acetic acid was removed by evapora-

ting under diminished pressure and the solution cooled, when the bromohydantoin separated in the form of yellow needles which were purified by recrystallization from acetic acid. The substance melted at 290–295° with decomposition. This melting point is not definite and varies according to the rate of heating. The hydantoin is insoluble in water and moderately soluble in alcohol.

Calc. for $C_{12}H_9O_2N_2Br$: N, 9.55. Found: N, 9.20, 9.26.

In a second experiment 2 g. of 4-cinnamalhydantoin were dissolved in 200 cc. of glacial acetic acid and 4 molecular proportions of bromine (3 g.) aspirated through the solution. The same temperature conditions were maintained as in the first experiment. There was a large excess of bromine which did not react with the hydantoin. This was expelled with the excess of acetic acid by heating under diminished pressure. On cooling we obtained the same compound as was formed in our first experiment, namely, *bromocinnamalhydantoin*. In other words, there was no tendency for the bromine to add at the double bond of the allyl group. After crystallization from glacial acetic acid the compound melted at 290–295° with decomposition.

Calc. for $C_{12}H_9O_2N_2Br$: N, 9.55. Found: N, 9.34, 9.36.

4-(β-Bromocinnamal)-hydantoin (X).—This hydantoin was prepared by condensing bromocinnamic aldehyde[1] with hydantoin. The following proportions were used: 10 g. of the aldehyde, 5 g. of hydantoin, 25 g. of anhydrous sodium acetate, 20 cc. of glacial acetic acid and 20 cc. of acetic anhydride. After heating for 1.5 hours at 130° the mixture was then cooled and triturated with cold water when we obtained 6.0 g. of the crude hydantoin. This compound was unstable and a certain amount of decomposition always took place when attempts were made to purify it by crystallization. A product was finally isolated by crystallization from glacial acetic acid which crystallized in clusters of yellow prisms and melted at 226–227° with decomposition. Work had to be abandoned on this compound because it or the monobromocinnamic aldehyde caused acute and very painful dermititis on the hands of the experimenter.

Calc. for $C_{12}H_9O_2N_2Br$: N, 9.55. Found: N, 9.7.

3-Acetyl-4-cinnamalhydantoin (XVII.)—It was observed during the condensation of hydantoin with cinnamic aldehyde, when some acetic anhydride was incorporated with the acetic acid, that the condensation product always contained two products, one of which was cinnamalhydantoin melting at 273° and the other a substance, which melted much lower, was more insoluble in glacial acetic acid and contained less nitrogen. It was impossible to isolate it in a pure condition. In order to determine whether this secondary product might be an acetyl derivative, 1.5 g. of the

[1] Zincke and Hagen *Loc. cit.*

cinnamalhydantoin were heated with 30 cc. of acetic anhydride for 4 hours at 140–150°. There was no apparent reaction at first but after heating for about an hour most of the hydantoin had disappeared and a new product began to deposit in the form of needles. On continued heating all the cinnamalhydantoin changed to this modification. This was identified as the acetyl derivative of cinnamalhydantoin and crystallized from glacial acetic acid as yellow prisms, which melted at 241–242° without any apparent decomposition. This hydantoin was less soluble in glacial acetic acid than cinnamalhydantoin.

Calc. for $C_{14}H_{12}O_3N_2$: N, 10.94. Found: N, 10.96, 10.94.

This hydantoin easily underwent hydrolysis when warmed with hydrochloric acid was changed into cinnamalhydantoin. This was crystallized from glacial acetic acid and melted at 272–273° with decomposition.

In order to determine whether the acetyl group in this new hydantoin was linked to the 1- or 3-position of the ring 3-acetylhydantoin[1] (XVI) was condensed with cinnamic aldehyde by heating in the presence of sodium acetate, acetic acid and acetic anhydride. After heating for 3.5 hours at 130–135° the fused mass was cooled and then triturated with 500 cc. of cold water when the above acetylhydantoin separated in a crystalline condition. The yield was excellent. It was purified by crystallization from acetic acid and melted at 241–242°. A mixture of this substance with some of the acetyl compound described above melted at the same temperature.

Calc. for $C_{14}H_{12}O_3N_2$: N, 10.94. Found: N, 10.9.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON PYRIMIDINES. LXXV. PYRIMIDINE ALDEHYDES AND THEIR BIOCHEMICAL INTEREST (THIOURACILALDEHYDE).

BY TREAT B. JOHNSON AND LEONARD H. CRETCHER, JR.

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So far as the writers are aware, no cyclic aldehydes of the pyrimidine series have been described in the literature. Such unsaturated combinations should manifest great reactivity and consequently a knowledge of their chemistry is especially desirable, because of the probability that they will prove of value for the future synthesis of new pyrimidine combinations of great biochemical interest. A description of three aldehydes of this series of cyclic compounds will be given in this paper. One of these, *2-thiouracil-4-aldehyde* (I), can be obtained easily in quantity for synthetical work.

[1] Siemonsen, *Loc. cit.*