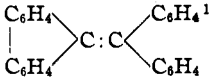
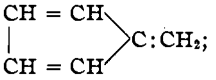
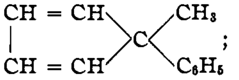
It appears established that azulene is closely related to the sesquiterpenes. From no other class of compounds have hydrocarbons been obtained which show such intense color. Colored hydrocarbons which have so far been prepared, are characterized by complex structure or a dense arrangement of the atoms, the intensity of the color increasing with the size of the molecule; for example:

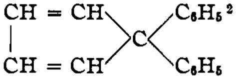




1. Yellow.



2. Red liquid.



3. Deep red solid.

Rubicen, a red hydrocarbon, $C_{26}H_{14}$, m. p. 306°.[3]

It is obvious that in azulene we have an entirely different and unique chemical compound. We hope, in a subsequent communication, to collect further data on this interesting substance.

The writer wishes here to acknowledge his indebtedness to Dr. Francis D. Dodge for helpful suggestions as well as for aid in obtaining material used in connection with the above work.

LABORATORY OF THE DODGE AND OLCOTT CO.,
BAYONNE, N. J.

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

RESEARCHES ON HYDANTOINS. XXIX. GEOMETRICAL ISOMERISM IN THE HYDANTOIN SERIES.

BY TREAT B. JOHNSON AND SIDNEY E. HADLEY.

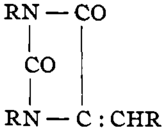
Received November 19, 1914.

In order that geometrical isomerism may be shown in an unsaturated carbon compound, two fundamental conditions must be fulfilled: first, that the molecule contains a double bond between two of its carbon atoms, and second, that the two radicals linked to each of these two carbon atoms must be different. Theoretically, the accepted structural formula of an *aldehyde-hydantoin* condensation product (I) fulfills both these conditions and consequently a hydantoin of this type might be expected to occur in *cis*- and *trans*-modifications. The constitutions of such isomeric forms might be expressed by the two graphic Formulas II and III, respectively. Several unsaturated compounds of this type (I) have been prepared in this laboratory, but hitherto we have not detected the occurrence of more than one modification. In this paper we will now discuss the first case of this type of isomerism so far observed in the hydantoin series.

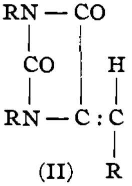
[1] Graebe, *Ber.*, 26, 2334 (1892); 25, 3146 (1891).

[2] Thiele, *Ber.*, 33, 668, 851, 3395 (1900); *Ibid.*, 36, 842 (1903); *Ann.*, 319, 226 (1901).

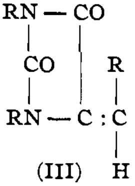
[3] Pummerer, *Ber.*, 45, 294 (1912).



(I)

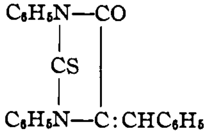


(II)

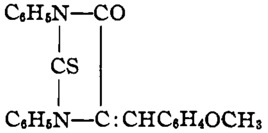


(III)

1,3-Diphenyl-2-thiohydantoin (VI), which was first synthesized in this laboratory by Wheeler and Brautlecht,[1] condenses with benzaldehyde and anisic aldehyde forming the corresponding condensation products represented by Formulas IV and V, respectively. The benzal compound (IV), which is the only one of the two hydantoins of any interest in this investigation, was found by Wheeler and Brautlecht to melt at 194°. Having occasion to prepare this hydantoin we found, to our surprise, on repeating this experiment, that the hydantoin (m. p. 194°) described by Wheeler and Brautlecht[2] is not the only product of this reaction. In fact we were able to isolate an isomeric product which melted several degrees lower than Wheeler and Brautlecht's hydantoin. This modification, however, was formed in such small quantities and possessed such unfavorable properties that we were unable to establish conclusively its constitution by chemical means. The structure of the modification melting at 197° was proved by the fact that it underwent reduction with hydriodic acid giving the hydantoin (IX) previously described by Johnson and Shepard.[3]



(IV)



(V)

Notwithstanding the fact that the hydantoin (IV), melting at 197°, is a stable and definite compound, it undergoes a remarkable change when it is desulfurized by digestion with chloroacetic acid. It combines with this halogen acid, giving apparently an addition product, which can easily be broken down by acid hydrolysis forming smoothly two well defined isomeric hydantoins. We have now concluded that these are geometrical isomers of *1,3-diphenyl-4-benzalhydantoin* whose structures may be represented by Formulas VII and VIII. They melt at 192° and 152°, respectively. The higher melting modification, which we have represented as the *trans*-form, is the chief product of the reaction. The lower melting form, or *cis*-modification, is not formed in large amount

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[1] *Am. Chem. Jour.*, 45, 446 (1911).

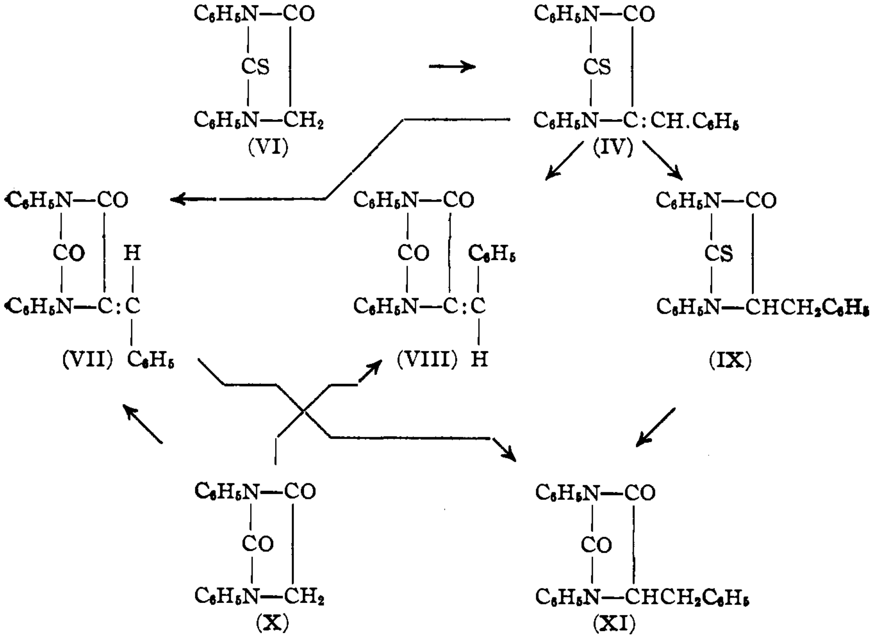
[2] The true melting point of this hydantoin is 197°.

[3] THIS JOURNAL, 36, 1735 (1914).

and is characterized by its greater solubility. That this interesting case of hydantoin isomerism is to be explained by the presence of the double bond in the unsaturated molecule is established by the fact that both modifications (VII and VIII) undergo reduction smoothly with hydriodic acid, giving the same saturated compound—*1,3-diphenyl-4-benzylhydantoin* represented by Formula XI. This hydantoin has previously been described by Johnson and Shepard.[1]

We have now made the interesting observation that these same two isomeric modifications of 1,3-diphenyl-4-benzalhydantoin are also formed by condensation of 1,3-diphenylhydantoin[2] (X) with benzaldehyde. Wheeler and Hoffmann[3] state that this hydantoin does not condense with anisic aldehyde when heated with it in the presence of sodium acetate, acetic acid and acetic anhydride. With benzaldehyde the condensation can easily be brought about with smooth formation of hydantoins. The *trans*-modification, however, is the chief product of the reaction. Both forms were isolated and their identity with the two hydantoins obtained by desulfurization of 1,3-diphenyl-4-benzalthiohydantoin completely established.

These various transformations are expressed by the following formulas:



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[1] *Loc. cit.*

[2] Bischoff and Häusdörfer, *Ber.*, 25, 2274 (1892).

[3] *Am. Chem. J.*, 45, 368 (1911).

Experimental Part.

1,3-Diphenylthiohydantoin (VI).—This hydantoin, which served as the starting point in our investigation, was prepared according to the directions of Wheeler and Brautlecht[1] by heating ethyl anilinoacetate with phenylisothiocyanate. While this compound is easily obtained in quantity by this method, we have observed, however, that it is not the only product of the reaction. In several cases we have obtained a secondary product which melts several degrees higher than the diphenylthiohydantoin (212°). Whether we are dealing here with an unique case of isomerism or polymerization will be decided by a further investigation.

1,3-Diphenylhydantoin (X).—This hydantoin[2] is easily obtained by desulfurization of 1,3-diphenylthiohydantoin. This was accomplished by digestion of the thiohydantoin with chloroacetic acid. Fifteen grams of the thiohydantoin and 150 g. of chloroacetic acid were digested with 50 cc. of water, on a sand bath, for 9 hrs. The mixture was then diluted with water, when a gummy product was obtained. This was separated from the water solution and finally heated with boiling hydrochloric acid when thioglycollic acid and diphenylhydantoin were formed. The latter was purified by recrystallization from alcohol and melted at 139°. The yield of purified material was 10.5 g.

1,3-Diphenyl-4-benzal-2-thiohydantoin (IV).—Wheeler and Brautlecht[1] first prepared this compound by condensing benzaldehyde with 1,3-diphenylthiohydantoin and found it to melt at 194°. We now find on repeating this experiment that this hydantoin is not the only product of this reaction. While this hydantoin, which we found to melt at 197°, is the chief product formed we have observed that it is accompanied by two other substances of characteristic properties. One of these is apparently a stereoisomeric modification of the hydantoin (melting at 197°) and the other is apparently identical with the substance of unknown constitution, which is formed by heating phenylisothiocyanate with ethylanilinoacetate.

The condensations were generally carried out in the following manner: Forty-seven grams of the diphenylthiohydantoin, 40 g. of benzaldehyde and 76 g. of anhydrous sodium acetate are dissolved in 245 cc. of hot glacial acetic acid and the solution heated in an oil bath at 150° for 12–14 hrs. The acid solution is then diluted copiously with cold water and cooled, when the crude hydantoin separates in a granular condition. The yield of crude material varies somewhat but generally is between 90–98% of the theoretical. On digesting this crude product with glacial acetic acid, all dissolves with the exception of a small amount of yellow material which generally melts above 280°. On cooling the acetic acid solution

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[1] *Loc. cit.*

[2] Bischoff and Häusdörfer, *Loc. cit.*

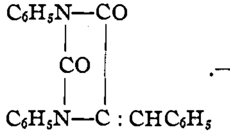
the diphenylbenzalhydantoin separates at once and is easily obtained in a pure condition (m. p. 197°) by recrystallization from acetic acid. After separation of the diphenylbenzalhydantoin a dark red acetic acid filtrate is always obtained, which contains apparently a small amount of a substance isomeric with the hydantoin melting at 197°. This can be isolated in an impure condition by evaporating the acetic acid filtrate at 100° to remove acetic acid and then triturating the gummy residue with hot alcohol. The coloring material and isomer are removed by this treatment, leaving behind the 1,3-diphenyl-4-benzalthiohydantoin. On cooling the alcoholic solution the isomer separates as a red powder having no definite melting or decomposition point. It was not present in large amount. A nitrogen determination gave (Kjeldahl):

Calc. for $C_{22}H_{16}ON_2S$: N = 7.8; found: N = 7.36.

In another experiment when we used 10 g. of the thiohydantoin, 15 g. of sodium acetate, 11 g. of benzaldehyde and 50 cc. of glacial acetic acid, we obtained 13 g. of the hydantoin melting at 196–197°. This yield was nearly the theoretical amount.

1,3-Diphenyl-4-benzyl-2-thiohydantoin (IX).—This hydantoin has been described in a previous paper by Johnson and Shepard.[1] We now find that the same compound is also formed by reduction of the above benzalthiohydantoin with hydriodic acid in the presence of phosphorus. This was accomplished by digesting the hydantoin with the halogen acid and phosphorus in acetic acid solution. The hydantoin was purified by crystallization from alcohol. It separated in rosets of needles which melted at 130°. Analysis (Kjeldahl):

Calc. for $C_{22}H_{18}ON_2S$: N = 7.8; found: N = 7.53.



$$\begin{array}{l} C_6H_5N\text{—}CO \\ \quad\ \ | \qquad | \\ \quad\ CO \quad\ | \\ \quad\ \ | \qquad | \\ C_6H_5N\text{—}C : CHC_6H_5 \end{array}$$

(*trans*)-1,3-Diphenylbenzalhydantoin, .—This new hydantoin is easily obtained by desulfurization of the corresponding 2-thiohydantoin. Three grams of the thiohydantoin (melting at 197°) and 30 g. of chloroacetic acid were digested for 2 hrs. A clear solution was obtained. This was then diluted with water when a light yellow, gummy product separated. After separation from the water this substance was then boiled with strong hydrochloric acid when it was completely changed into the above hydantoin. The yield of crude material was 2.7 g. The hydantoin was purified by crystallization from glacial acetic acid. It separated from this solvent, on cooling, in light yellow prisms with tetrahedral form and melted at 192°. They did not respond to a test for sulfur. Nitrogen determination (Kjeldahl):

Calc. for $C_{22}H_{16}O_2N_2$: N = 8.22; found: N = 8.39, 8.11.

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[1] *Loc. cit.*

(*cis*)-1,3-Diphenylbenzalhydantoin.—In another experiment we used the following proportions: 14 g. of diphenylbenzalthiohydantoin, 140 g. of chloroacetic acid and 47 cc. of water. These were heated for 5 hrs. when a similar result was obtained as in the previous experiment. The gummy product was decomposed in the usual manner by digesting with hydrochloric acid and the resulting crude hydantoin then purified by crystallization from acetic acid. The hydantoin melting at 192° was obtained as before. After separation of this substance the acetic acid filtrate was then concentrated and cooled, when we obtained a crystalline substance which melted at 145–152°. This was identified as an *isomer* of 1,3-diphenyl-4-benzalhydantoin. It was purified by crystallization from glacial acetic acid and separated in rosets of prisms which melted sharply at 150–152°. It did not rearrange into the *trans*-modification when heated at 192°. The yield of purified material was 1 g. Analysis (Kjeldahl):

Calc. for $C_{22}H_{16}O_2N_2$: N = 8.22; found: N = 8.03.

In a third experiment we obtained, after desulfurization of 15 g. of 1,3-diphenyl-4-benzal-2-thiohydantoin, 10.5 g. of the *trans*-hydantoin melting at 192° and 1.5 g. of the *cis*-modification melting at 152°.

The Condensation of Benzaldehyde with 1,3-Diphenylhydantoin.—1,3-Diphenylhydantoin undergoes condensation with benzaldehyde giving *cis*- and *trans*-1,3-diphenyl-4-benzalhydantoins. The yield, however, of the *cis*-modification is very small. In our first experiment the condensation was effected by digesting 5 g. of the diphenylhydantoin and 3 g. of benzaldehyde with 15 g. of sodium acetate, 10 cc. of acetic anhydride and 20 cc. of glacial acetic acid for 4 hrs. at 150°. On cooling the resulting solution and then diluting with water the hydantoin separated. This was purified by recrystallization from acetic acid and melted at 192°. This same result was also obtained when the condensation was effected in the presence of potassium acetate. In neither of these experiments did we detect the presence of any *cis*-diphenyl-4-benzalhydantoin melting at 152°. It was only by working with larger quantities of material that we were finally able to isolate the *cis*-modification. In a third experiment 47 g. of the diphenylhydantoin were condensed with benzaldehyde according to the described conditions. After pouring the reaction mixture into water, to separate the crude hydantoin, and then crystallizing from acetic acid, we obtained 28 g. of the *trans*-hydantoin, melting at 192°. The acetic acid filtrates were then combined and evaporated at 100° to remove the excess of acetic acid when we obtained a dark red, gummy residue. This product was triturated with warm 95% alcohol and the mixture allowed to stand for several hours, when we finally obtained about 5–6 g. of a semisolid substance insoluble in the alcohol. This was separated from adhering oil by filtering and purified by recrystallization from acetic acid. After the first crystallization this melted at 130–150°, indicating a mixture of the two isomeric hydantoins. Separation was finally effected by fractional crystallization from acetic acid. The *cis*-modification is more soluble in this solvent than the *trans*-form and in this case sufficient material was available to enable us to isolate the *cis*-modification. It crystallized from acetic acid in needles which melted at the same temperature as the hydantoin obtained by desulfurization of the corresponding 2-thiohydantoin. A mixture of the two substances melted at 150–2°.

Reduction of *cis*- and *trans*-1,3-Diphenyl-4-benzalhydantoin.

1,3-Diphenyl-4-benzylhydantoin (XI).—This hydantoin, which has been described in a previous paper by Johnson and Shepard,[1] is formed when the *cis*- and *trans*-modifications of 1,3-diphenyl-4-benzalhydantoin are reduced with hydriodic acid. This was accomplished by digesting the unsaturated hydantoins in glacial acetic acid with hydriodic acid and in presence of a little red phosphorus. After the reduction was complete the solution was then diluted with water when the hydantoin separated as a gum. In some experiments the excess of acetic acid was first removed by evaporation at 100°, but under both conditions the same gum was obtained. This was purified by dissolving in ether, washing with a little bisulfite solution to remove a trace of iodine and then drying the ether solution over anhydrous calcium chloride. On allowing the ether to evaporate the hydantoin was finally obtained in a crystalline condition melting at 58–62°. The compound is very hygroscopic. It is extremely soluble in cold alcohol, ether, benzene acetic acid, acetone, chloroform, ethylacetate and ligroin but practically insoluble in water. It does not dissolve in cold sodium hydroxide solution. The compound agreed in all its properties with Johnson and Shepard's *1,3-diphenyl-4-benzylhydantoin.*

NEW HAVEN, CONN.

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

RESEARCHES ON PYRIMIDINES. LXXIII. ALKYLATION OF 2-MERCAPTOPYRIMIDINES.

BY TREAT B. JOHNSON AND HOWARD W. HAGGARD.

Received November 23, 1914.

The papers so far published from this laboratory on the alkylation of *2-mercapto-6-oxypyrimidines* have been confined to a description of results obtained from the study of mercapto compounds in which the mercapto grouping contained a saturated alkyl radical, *viz.*, CH_3-, C_2H_5-, $C_6H_5CH_2$-, etc. In all of the cases examined, with one exception, mercapto groups of this type have favored substitution in the 1- and 3-positions of the pyrimidine ring. With these results at hand it then became

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[1] *Loc. cit.*