The method described also practically eliminates the error due to solvent action of the solutions on the beakers, etc., used in the determination. A common practice in cement analysis is to catch the filtrate and washings from the calcium oxalate precipitate in a No. 6 beaker and boil or evaporate down to 100 to 150 cc. before precipitation of the magnesia. Whether this solution is kept ammoniacal during the evaporation, or, as more commonly practiced, rendered acid as soon as it is placed over the source of heat, a considerable solvent action takes place on the beaker during the operation. In numerous experiments made in actual determinations and also on blanks on reagents, water, etc., absolutely free from lime and silica, this contamination was found at times to run as high as 0.0030 gram silica, equivalent on a 0.5 gram sample, to 0.60 per cent. silica, and 0.0024 gram, equivalent to 0.48 per cent. lime. While this silica possibly might not come down in the subsequent magnesia precipitate, the lime, if not previously removed, undoubtedly would, and would not be removed by a double precipitation of the ammonium magnesium phosphate. The resulting magnesia would consequently be high, contaminated with lime, obtained, not from cement itself, but from the glassware. If this lime were removed and added to that originally obtained in the regular course of analysis, a high lime determination would result. In the regular methods of analysis used a greater or less solvent action also occurs in the operations preceding the actual precipitation of calcium oxalate. In the rapid method described the solution is in contact with glass only a very short time before the precipitation of the lime, the solvent action is reduced to a minimum, and the possible error from this source is entirely obliterated by the fact that the potassium permanganate used in titration is standardized by a cement run under exactly the same conditions as the regular determinations.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF TEXAS.]

ACTION OF MUSTARD OILS AND ISOCYANATES ON HYDRAZO ACIDS.

BY J. R. BAILEY.

Received June 11, 1904.

INTRODUCTION.

HYDRAZO compounds, as a rule, do not react readily with mustard oils,[1] although they react more readily with isocyanates.[2] In

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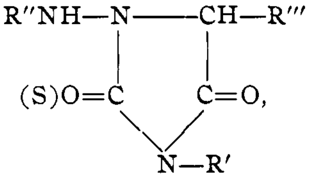
[1] *Ber. d. chem. Ges.*, **25**, 3115.
[2] *Ibid.*, **23**, 490.

an investigation of semicarbazinopropionic acid ethyl ester,[1] the author, in conjunction with S. F. Acree, observed that this substance reacts with mustard oils, and further experiments have shown that α-hydrazo acids, in general, easily form compounds with both mustard oils and isocyanates; in fact, these reactions might well serve to characterize hydrazo acids. From the study of semicarbazinopropionic acid.[2] semicarbazinoisobutyric acid,[3] hydrazoisobutyric acid,[4] and phenylhydrazoisobutyric acid,[5] it appears probable that all α-hyrazo acids will show a similar behavior toward mustard oils and isocyanates.

The reaction product of a mustard oil on a hydrazo acid is not a simple addition product of one molecule on the other, but is this product minus one molecule of water. Although in the case of the isocyanates on hydrazo acids it is possible, sometimes, to isolate the primary reaction products, the latter also readily undergo ring condensation with the loss of water. The substances obtained are thiohydantoins and hydantoins, respectively, of the general formula



where R′, R″, R‴ represent, as usual, aliphatic or aromatic radicals. These formulas are proved conclusively by the chemical behavior of the substances in question.

Hydrazoisobutyric acid, $COOH(CH_3)_2CNHNHC(CH_3)_2COOH$, gives with phenyl mustard oil a body which the analysis shows to be a condensation product of these two molecules minus a molecule of water. The substance so obtained is a monobasic acid, as is indicated by the titration with alkalies and the formation of esters. The possibility of the substance being a thiazole is excluded by the fact that it is readily desulphurized with mer-

[1] *Ann. Chem.* (Liebig). **303**, 83.

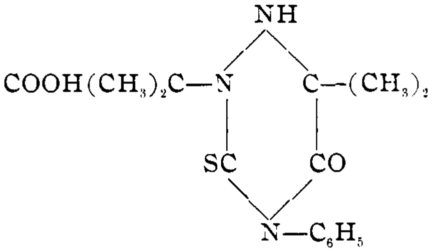
[2] *Loc. cit.*

[3] *Ann. Chem.* (Liebig), **283**, 33: *Am. Chem. J.*. **28**, 401.

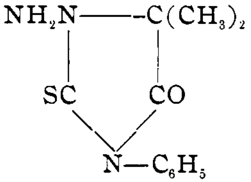
[4] *Ann. Chem.* (Liebig). **290**, 25.

[5] *Ber. d. chem. Ges.*, **25**, 3323.

curic oxide, yielding a substance identical with the reaction produc of phenylisocyanate on hydrazoisobutyric acid. The possibilit of a triazine, constituted as follows,

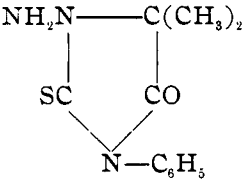


is excluded by the behavior of the substance toward aqueous hydrochloric acid. Hydrochloric acid yields as a reaction product substance that is undoubtedly 1-amino-5-dimethyl-3-phenyl-2 thiohydantoin,



In the formation of this substance an isobutyric acid radical i eliminated from the molecule, giving, as primary reaction products

$(CH_3)_2C(OH)COOH$[1] and



Such a reaction is analogous to the formation of hydrazine from hydrazinoisobutyric acid[2] and of hydrazine from 6-hydrazinopyridinecarboxylic acid-(3)[3] under the influence of aqueous hydrochloric acid. The formation of an aminothiohydantoin by the action of hydrochloric acid on the aminoisobutyric acid thiohydantoin, as described above, is further in accordance with the fol-

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[1] No attempt was made to isolate this substance.

[2] *Ann. Chem.* (Liebig), **290**, 18.

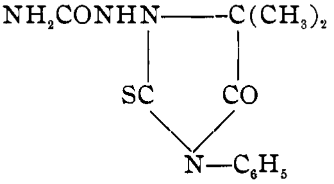
[3] *Ber. d. chem. Ges.*, **36**, 1114.

lowing facts: The same substance is formed from hydrazinoisobutyric acid and phenyl mustard oil. The substance yields, with benzaldehyde, a yellow reaction product that is identical with a substance obtained from benzalhydrazinoisobutyric acid,

$$C_6H_5CH{=}NNHC(CH_3)_2COOH,$$[1]

and phenyl mustard oil. It might seem anomalous that a substance, constituted like the aminothiohydantoin in question, does not possess basic properties, but Traube and Hoffa,[2] and later Busch and Holzmann[3] observed that aminothiohydantoins do not form salts with acids.

The substance obtained by the action of phenyl mustard oil on semicarbazinoisobutyric acid must also contain the thiohydantoin ring and be constituted as follows:



The above constitution is deduced from the fact that this compound wih hydrochloric acid yields 1-amino-5-dimethyl-3-phenyl-2-thiohydantoin, the constitution of which was established above. In this reacion the carbonamido radical of the ureidothiohydantoin is eliminated by interaction with a molecule of water. From the foregoing it appears probable that all α-hydrazo acids will react with mustard oils in a way similar to α-amino acids.[4]

5-Methyl-1-ureido-3-phenyl-2-thiohydantoin shows a peculiar behavior toward barium hydroxide in that it passes into 1,5-dihydro-3-oxy-5-phenylimido-4,1,2-thiodiazol-1-propionic acid, a reaction which may be interpreted by supposing the thiohydantoin ring hydrolyzed and the thiodiazole formed from this intermediary product by the elimination of a molecule of ammonia:

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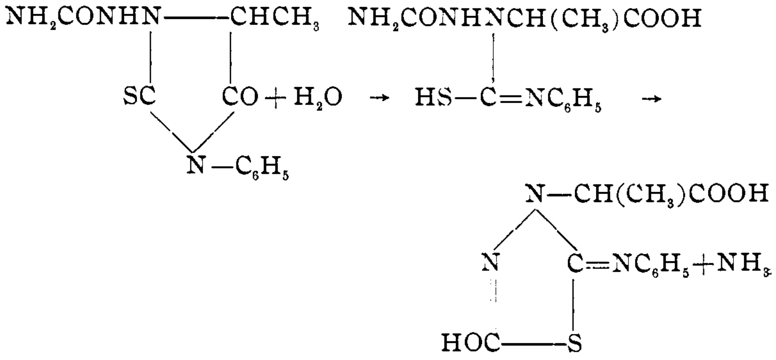
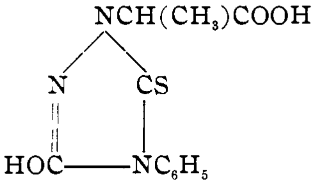
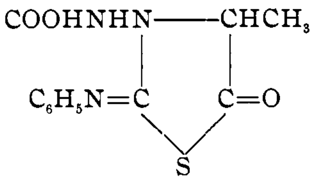
[1] *Ann. Chem.* (Liebig). **290**, 16.
[2] *Ber. d. chem. Ges.*. **31**, 322.
[3] *Ibid.*, **34**, 322.
[4] *Ibid.*, **17**, 420; **24**, 3278.



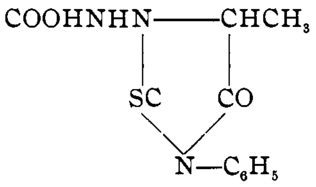
Another structural formula that would conform to the analytical data is a triazole,



Such a substance is a cyclic amide and its formation in the presence of an alkali would not be expected, whereas thiazoles can be formed in alkaline solution.[1] Furthermore, the stability of the molecule toward mercuric oxide indicates that the sulphur is in a ring nucleus.



or



also represents a structural formula, in harmony with the analytical data, but improbable, in view of the instability of carbamic acids. This thiodiazole titrates as a dibasic acid and forms an amide, esters and a benzoyl derivative, properties which accord with the behavior of the somewhat similarly constituted triazoles of the general formula,

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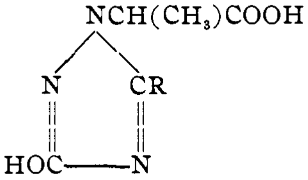
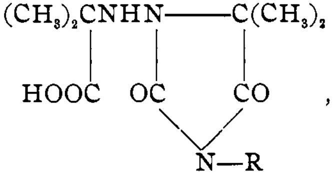
[1] *Ann. Chem.* (Liebig), 189, 382.

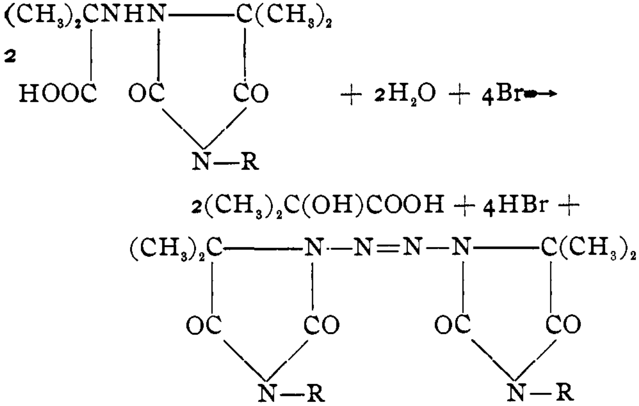


described by Bailey and Acree.[1]

The thiohydantoins of the general formula,



show an interesting behavior toward bromine water. Thiele and Hauser[2] studied the action of bromine water on hydrazoisobutyric acid derivatives and found that azo compounds are formed. As one of the imide hydrogens of the hydrazo groups is substituted in the substances under discussion, the formation of azo compounds is excluded here. It was found that the reaction products are tetrazones, a class of substances, the first representatives of which were prepared by E. Fischer.[3] The formation of these substances can be represented as follows:



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[1] *Ber. d. chem. Ges.*, **33**, 1520.

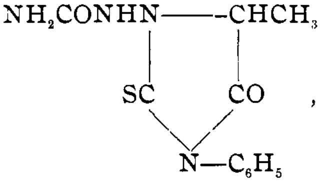
[2] *Ann. Chem.* (Liebig), **290**, 5.

[3] *Ibid.*, **190**, 166.

The amount of bromine used in this reaction was far in excess of that indicated by the equation, doubtless due to the bromination of the hydroxyisobutyric acid formed. Only one of these tetrazones, the one where R represents C_2H_5, was obtained in a condition pure enough for a satisfactory analysis. An attempt to determine the molecular weight, with chloroform as a solvent, of the tetrazone where R represents CH_3 gave results which indicate that a reaction of some kind is produced when these tetrazones are dissolved in chloroform. This fact offers a possible explanation of the slight discrepancies, in the case of two of the three tetrazones investigated, between the analytical data and the structural formulas ascribed to them. The study of these substances, as well as the study of the oxidation products of the corresponding thiohydantoins, will be continued.

Experimental Part.

PART I.—ACTION OF MUSTARD OILS ON HYDRAZO ACIDS.



5-Methyl-1-ureido-3-phenyl-2-thiohydantoin,[1] was first prepared as follows: Six grams of semicarbazinopropionic acid ethyl ester and 5 grams of phenyl mustard oil in alcoholic solution were heated to boiling one-half hour. At the end of this time 7.5 grams of the reaction product had crystallized out. The filtered solution, on evaporation to a small bulk and precipitation with ether, yielded a further small amount of the thiohydantoin. As the ester of the semicarbazino acid is somewhat difficult to obtain, the following method of preparing the hydantoin is to be preferred: One mole of freshly prepared semicarbazinopropionitrile[2] is allowed to stand two weeks with an aqueous solution of 0.5 mole of barium hydroxide in order to form the amide, and the barium is then removed as sulphate. The solution is now evaporated to

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[1] The phenyl and allyl compounds were first prepared and analyzed conjointly with S. F. Acree.

[2] *Ann. Chem.* (Liebig), **303**, 79; *Am. Chem. J.*, **28**, 596.

a pasty mass and to this is added 1 mole of phenyl mustard oil, together with 10 cc. of 95 per cent. alcohol for each gram of nitrile employed. The alcoholic solution, after being boiled one hour, is evaporated to a small bulk and precipitated with ether. About 1 gram of the thiohydantoin is obtained for each gram of the nitrile employed. The thiohydantoin can be crystallized from water, alcohol or acetic ether. It crystallizes from methyl alcohol in aggregates of short, colorless prisms, as seen under the microscope, which decompose to a yellow liquid at 206°. An alcoholic solution of this substance does not produce a coloration with ferric chloride. On heating the thiohydantoin with hydrochloric acid the carbonamide radical is eliminated and an aminothiohydantoin formed. Treated with 0.5 mole of barium hydroxide at a temperature of 60°, the thiohydantoin ring is hydrolyzed and, by the elimination of ammonia, a thiodiazole formed. These reaction products are described further on.

Calculated for $C_{11}H_{12}O_2N_4S$: C, 50.00; H, 4.54; N, 21.21; S, 12.12. Found: C, 49.71; H, 4.72; N, 21.37; S, 12.04.

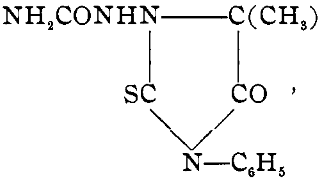
5-Methyl-1-ureido-3-allyl-2-thiohydantoin, prepared similarly to the corresponding phenyl compound by the action of allyl mustard oil on the ethyl ester of semicarbazinopropionic acid in alcoholic solution, melts at 167° to a clear liquid.

Calculated for $C_8H_{12}O_2N_4S$: C, 42.10; H, 5.26; N, 24.56; S, 14.03. Found: C, 41.87; H, 5.53; N, 24.65; S, 13.92.

5-Methyl-1-ureido-3-ethyl-2-thiohydantoin was prepared, similarly to the foregoing allyl compound, by the action of ethyl mustard oil on the semicarbazino ester. It crystallizes from alcohol in radiating bunches of short, microscopic prisms, which melt at 153°, apparently undecomposed, to a clear liquid.

Calculated for $C_7H_{12}O_2N_4S$: C, 38.89; H, 5.56; N, 25.93. Found: C, 38.86; H, 5.58; N, 26.21.

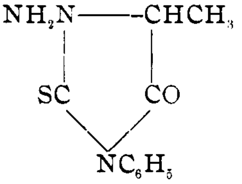
5-Dimethyl-1-ureido-3-phenyl-2-thiohydantoin,



was prepared in acetic ether solution from semicarbazinoisobutyric acid ethyl ester[1] and phenyl mustard oil by boiling the mixture one-half hour. Attempts to prepare the substance from other derivatives of this semicarbazino acid were without success. This thiohydantoin is readily soluble in alcohol, chloroform, acetic ether and benzene, difficultly soluble in water and as good as insoluble in ether and petroleum ether. It is best purified by precipitation from an alcoholic solution with ether. It decomposes at 191°, with gas evolution, to a clear liquid. Heated one hour with concentrated hydrochloric acid in a sealed tube at 140°, the substance passes into aminodimethylphenylthiohydantoin.

Calculated for $C_{12}H_{14}O_2N_4S$: C. 51.80; H, 5.04; N, 20.14; S, 11.51. Found: C, 51.67; H, 4.96; N, 20.19; S, 11.97.

1-Amino-5-methyl-3-phenyl-2-thiohydantoin,



—Seven grams of the corresponding ureidomethylphenylthiohydantoin, suspended in 100 cc. of concentrated hydrochloric acid were heated one hour in a sealed tube at 120°. Upon cooling the solution nothing immediately separated out, but, after letting off a slight pressure that was present and shaking the tube, the entire solution became filled with crystals. A little more than 2 grams of this new substance were thus obtained. On evaporating the filtrate to a small bulk and adding water a considerable amount of the original substance was recovered, unchanged. The compound crystallizes from water, or better, from alcohol, in long, slender, colorless, bayonet-shaped prisms, which melt at 150°, undecomposed. The substance is very soluble in chloroform, even in the cold, and difficultly soluble in alcohol and ether.

Calculated for $C_{10}H_{11}ON_3S$: C, 54.30; H, 4.98; N, 19.00. Found: C, 54.18; H, 5.20; N, 18.98.

Treated with phenyl mustard oil in boiling alcoholic solution, aminomethylphenylthiohydantoin reacts to form a substituted sul-

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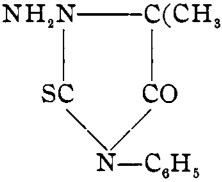
[1] *Am. Chem. J.*, **28**, 402.

phourea, which separates from very dilute alcoholic solution in short, slender, microscopic prisms. This substance decomposes at 223° to a red liquid.

The analysis gave 15.48 per cent. N. Calculated for $C_{17}H_{16}ON_4S_2$, 15.73 per cent.

1-Amino-5-dimethyl-3-phenyl-2-thiohydantoin,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was obtained in several ways. It is formed similarly to the preceding compound, when dimethylureidophenylthiohydantoin is heated in concentrated hydrochloric acid under pressure at 140°. The compound crystallizes beautifully from alcohol in long needles, which melt undecomposed at 173°. It is readily soluble in cold chloroform, in benzene and in glacial acetic acid, more difficultly soluble in carbon disulphide and very difficultly soluble in water. The substance does not possess basic properties, but otherwise shows the characteristic reactions of a hydrazine. Two other methods of preparing this substance are described further on.

The analysis gave 17.75 per cent. N. Calculated for $C_{11}H_{13}ON_3S$, 17.87 per cent.

Reaction Product of Phenyl Mustard Oil on Aminodimethylphenylthiohydantoin.—The aminothiohydantoin was boiled with a slight excess of phenyl mustard oil in glacial acetic acid for one hour and the reaction product then precipitated by the addition of water. The same substance can be obtained by boiling hydrazinoisobutyric acid in acetic acid solution with an excess of mustard oil, when the acid reacts with 2 molecules of mustard oil. The behavior of hydrazino acids toward mustard oils can well serve to characterize the former substances.[1] For analysis the substance is best crystallized from glacial acetic acid, in which it is difficultly soluble. It is only slightly soluble in alcohol. It decomposes at about 233°.

The analysis gave 15.09 per cent. N. Calculated for $C_{18}H_{13}ON_4S_2$, 15.14 per cent.

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[1] Compare *Ann. Chem.* (Liebig), 290, 16.

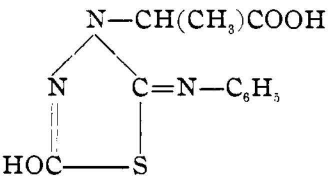
Reaction Product of Benzaldehyde on Aminodimethylphenylthiohydantoin.—The aminodimethylphenylthiohydantoin was heated in a test-tube with an excess of benzaldehyde until drops of water were formed on the side of the tube. The excess of aldehyde was then allowed to oxidize in the air and the benzoic acid thus formed was removed with ammonium hydroxide and the remaining trace of aldehyde with petroleum ether. The residue crystallized from alcohol as a light yellow substance, melting undecomposed at 135°. The hydrazone is more readily soluble in water than the corresponding aminothiohydantoin.

The analysis gave 12.93 per cent. N. Calculated for $C_{18}H_{17}O$ N_3S, 13.00 per cent.

The foregoing substance was also prepared from benzalhydrazinoisobutyric acid, $C_6H_5CH=N.NHC(CH_3)_2COOH$. The hydrazone in alcoholic solution was neutralized with potassium hydroxide and to this was added a little over one molecule of phenyl mustard oil. After boiling one-half hour, the solution, on cooling, solidified. The alcohol was next distilled off and the excess of mustard oil washed out with petroleum ether. The residue was then taken up with water and from the aqueous solution a substance was precipitated by the addition of hydrochloric acid. This proved identical with the reaction product of benzaldehyde on dimethylaminophenylthiohydantoin.

Calculated for $C_{18}H_{17}ON_3S$: C, 66.87; H, 5.26; N, 13.00. Found: C, 66.72; H, 5.22; N, 12.91.

1,5-Dihydro-3-oxy-5-phenylimido-4,1,2-thiodiazole-1-propionic acid.



—Ten grams of methylureidophenylthiohydantoin and 7 grams of barium hydroxide in 100 cc. of water were heated at 65° for four hours. The solution was then filtered and the thiodiazole precipitated by acidifying with hydrochloric acid. The yield of thiodiazole was 7.5 grams. The substance, after two crystallizations from water, melted at 220° with gas evolution to a brownish yellow liquid. From water it crystallizes in radiating bunches of very fine needles. It is readily soluble in alcohol and chloroform, more difficultly soluble in ether and benzene. With ferric chloride the thiodiazole gives characteristic color reactions; in absolute alcohol it gives, with an alcoholic solution of ferric chloride, a greenish blue color, which, on the addition of a few drops of water, becomes an intense blue. This blue color in less than a minute's time passes into an amethyst color and, on further dilution, the solution, after standing some time, assumes a faint green color. The thiodiazole titrates as a dibasic acid, requiring only a little less than the calculated two molecules of sodium hydroxide for neutralization. With mercuric chloride in alcoholic solution it gives a very difficultly soluble double salt, which was not further investigated. An attempt to split off aniline, by heating the thiodiazole with concentrated hydrochloric acid, was not successful. In contrast to the thiohydantoins, discussed in this paper, an ammoniacal solution of the thiodiazole can be boiled with mercuric oxide without forming mercuric sulphide.

Calculated for $C_{11}H_{11}O_3N_3S$: C, 49.81; H, 4.15; N, 15.85; S, 12.08. Found: C, 49.61; H, 3.90; N, 15.89; S, 12.20.

Titration of the thiodiazole with N/10 NaOH:

0.2156 gram substance required 15.75 cc. N/10 NaOH; calculated, if dibasic, 16.26 cc.

0.2180 gram substance required 16.05 cc. N/10 NaOH; calculated, if dibasic, 16.44 cc.

For the titration the acid was dissolved in alcohol and phenolphthaleïn used as an indicator.

1,5-Dihydro-3-oxy-5-phenylimido-4,1,2-thiodiazole-1-propionic Acid Ethyl Ester.—The ester was prepared by boiling 3 grams of the acid with 50 cc. of 4 per cent. alcoholic hydrochloric acid one hour. The solution was then evaporated to dryness and taken up with water. The ester is a monobasic acid, readily soluble in alkalies and ammonia, and difficultly soluble in water. It is more soluble in benzene, and more difficultly soluble in ether and alcohol, than the acid. For the analysis the substance was purified by crystallization from benzene and finally from dilute alcohol. It melts undecomposed at 171°. The color reactions produced in an alcoholic solution of the ester with ferric chlorides are very similar to those observed in the case of the corresponding acid.

Calculated for $C_{13}H_{15}O_3N_3S$: C, 53.24; H, 5.12. Found: C, 53.48; H, 5.24.

In the titration of the ester in alcoholic solution with N/10 NaOH with phenolphthaleïn as indicator, 0.5920 gram substance required 20.3 cc.; calculated, 20.2 cc.

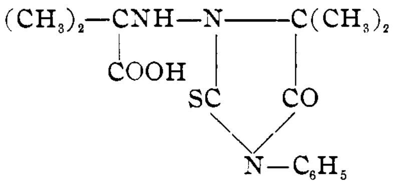
Benzoyl Derivative of the Ester.—This substance may be prepared from the sodium salt of the ester by boiling this with 1 molecule of benzoyl chloride in benzene solution. It is readily soluble in alcohol and benzene and best purified by crystallization from the latter. It crystallizes in broad, thin plates, which melt undecomposed at 110°. Unlike the ester and acid, the benzoyl derivative of the ester gives no color reaction with ferric chloride.

The analysis gave 10.63 per cent. N. Calculated for $C_{20}H_{19}O_4N_3S$, 10.58 per cent.

1,5-Dihydro-3-oxy-5-phenylimido-4,1,2-thiodiazole-1-propionic Acid Amide.—Three grams of the ethyl ester were dissolved in 50 cc. of alcoholic ammonia and the solution allowed to stand one month. On evaporation of the alcohol the amide remained as an ammonium salt. This was dissolved in water and the amide precipitated with hydrochloric acid. For purification the substance was twice crystallized from alcohol. It melts at 228° with gas evolution to a brownish yellow liquid.

The analysis gave 21.46 per cent. N. Calculated for $C_{11}H_{12}O_2N_4S$, 21.21 per cent.

5-Dimethyl-3-phenyl-1-isobutyric-acid-amino-2-thiohydantoin,[1]



—After numerous experiments the following method was found to give the best results in the preparation of the above thiohydantoin: Twenty-five grams of hydrazoisobutyric acid and 20 grams of phenyl mustard oil in 100 cc. of glacial acetic acid as solvent are heated one hour to boiling. The acetic acid is now removed for the greater part by distillation *in vacuo* and the hydantoin precip-

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[1] The preparation of the phenyl and allyl derivatives, as well as the esters described under the phenyl compound, was carried out conjointly with P. T. Miller.

itated by the addition of water. This method gave a yield of about 92 per cent. of the theoretical, although the hydrazo acid was not quite pure. The thiohydantoin thus obtained is readily soluble in ether, alcohol, chloroform and benzene, less readily soluble in carbon disulphide and rather difficultly soluble in water. The thiohydantoin differs from hydrazoisobutyric acid in that it does not possess basic properties and is, therefore, not readily soluble in acids. For analysis the substance was crystallized from benzene and ether. It melts at 153°. The presence of a carboxyl group is shown by the formation of esters and the presence of an imide group by the formation of a nitroso compound. The thiohydantoins, obtained by the action of mustard oils on hydrazoisobutyric acid, are readily desulphurized with mercuric oxide. The products thus obtained are described further on. Hydrochloric acid eliminates the isobutyric acid radical, yielding aminodimethylphenylthiohydantoin, the reaction product of hydrochloric acid on ureidodimethylphenylthiohydantoin and of phenyl mustard oil on hydrazinoisobutyric acid.

Calculated for $C_{15}H_{19}O_3N_3S$: C, 56.07; H, 5.92; N, 13.09; S, 9.97. Found: C, 56.46; H, 6.13; N, 13.09; S, 9.97.

Titration of the Dimethylphenylisobutyric-acid-aminothiohydantoin with N/10 NaOH:

0.1829 gram substance required 5.7 cc. N/10 NaOH; calculated, if monobasic, 5.7 cc. N/10 NaOH.

Action of Hydrochloric Acid on Dimethylphenylisobutyric-acid-aminothiohydantoin.—Five grams of the thiohydantoin were heated at 140°-160° with 60 cc. concentrated hydrochloric acid in a sealed tube for one hour. On cooling the tube it was found that complete solution had been effected. However, after letting off the pressure in the tube 2.4 grams of a new substance quickly separated out. The substance was prepared for analysis by crystallization from methyl alcohol and benzene.

Calculated for $C_{11}H_{13}ON_3S$: C, 56.17; H, 5.53; N, 17.87; S, 13.62. Found: C, 56.17; H, 5.77; N, 17.86; S, 13.75.

This substance has the same melting-point, 173°, as the reaction product already described of hydrochloric acid on 5-dimethyl-1-ureido-3-phenyl-2-thiohydantoin, and the two preparations, when mixed in equal amounts and crystallized from alcohol, form crystals, which possess a constant melting-point of 173°. The two preparations are, therefore, undoubtedly identical. The same substance may also be prepared from hydrazinoisobutyric acid, $NH_2NHC(CH_3)_2COOH$, and phenyl mustard oil, when they are allowed to react in molecular proportion. The hydrazine is dissolved in a little water and to this is added the mustard oil in alcohol and the mixture is then heated about twenty minutes to boiling. The aminothiohydantoin can be separated from a little of the reaction product of 2 molecules of mustard oil on the hydrazinoisobutyric acid by dissolving out the former with chloroform. A third body, readily soluble in alcohol, is formed in small amount in this reaction, but this was not investigated.

Nitroso Derivative of 5-Dimethyl-3-phenyl-1-isobutyric-acid-amino-2-thiohydantoin.—When double the calculated amount of sodium nitrite in concentrated aqueous solution is slowly added to a cold glacial acetic acid solution of the thiohydantoin a nitroso body is formed and may be precipitated by pouring the acetic acid solution into a large excess of water. The substance, purified by crystallization from a benzene-ligroin mixture, melted with gas evolution to a brown liquid at 166°. It shows the Liebermann reaction.

The analysis gave 16.06 per cent. N. Calculated for $C_{15}H_{18}O_4N_4S$, 16 per cent.

Ethyl Ester of 5-Dimethyl-3-phenyl-1-isobutyric-acid-amino-2-thiohydantoin.—To effect esterification, 3 grams of the acid were put into 110 cc. of 4 per cent. alcoholic hydrochloric acid and the solution boiled one hour. The alcohol was then distilled off, the residue taken up with water, and the ester precipitated with sodium bicarbonate. Purified by crystallization from dilute methyl alcohol, it melted at 84°. By evaporation of the benzene solution of the ester, it can be obtained in large four-sided prisms.

The analysis gave 12.11 per cent. N. Calculated for $C_{17}H_{23}O_3N_3S$, 12.04 per cent.

Methyl Ester.—This ester, prepared similarly to the ethyl ester, is much more difficultly soluble in alcohol. It melts undecomposed at 142°.

Calculated for $C_{16}H_{21}O_3N_3S$: C, 57.31; H, 6.27; N, 12.54; S, 9.55. Found: C, 57.47; H, 6.37; N, 12.66; S, 9.75.

5-Dimethyl-3-allyl-1-isobutyric-acid-amino-2-thiohydantoin can be obtained in almost theoretical yield by the method employed in the preparation of the corresponding phenyl compound. The substance, purified by recrystallization from benzene, melts undecomposed at 121°. It can be crystallized from water in very pointed diamond-shaped plates.

Calculated for $C_{12}H_{19}O_3N_3S$: C, 50.53; H, 6.67; N, 14.74. Found: C, 50.62; H, 6.82; N, 14.92.

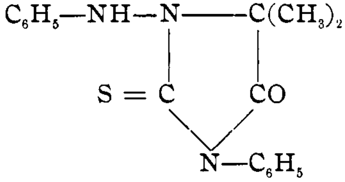
5-Dimethyl-3-ethyl-1-isobutyric-acid-amino-2-thiohydantoin, purified by crystallization from dilute alcohol and then from benzene, melted undecomposed at 110°.

Calculated for $C_{11}H_{19}O_3N_3S$: C, 48.35; H, 6.96; N, 15.38; S, 11.72. Found: C, 48.41; H, 6.64; N, 15.47; S, 11.63.

5-Dimethyl-3-methyl-1-isobutyric-acid-amino-2-thiohydantoin, purified similarly to the corresponding ethyl compound, melts apparently undecomposed to a clear liquid at 129°.

The analysis gave 16.20 per cent. N. Calculated for $C_{10}H_{17}O_3N_3S$, 16.22 per cent.

5-Dimethyl-3-phenyl-1-phenylamino-2-thiohydantoin,[1]



—This substance, prepared in glacial acetic acid solution by allowing phenyl mustard oil and phenylhydrazoisobutyric acid to react in molecular proportion, was purified by crystallization from alcohol, acetic ether and finally benzene. It melts, apparently undecomposed, at 206°. This thiohydantoin is readily soluble in common organic solvents, petroleum ether excepted, and almost insoluble in water.

Calculated for $C_{17}H_{17}ON_3S$: C, 65.59; H, 5.47; N, 13.50; S, 10.29. Found: C, 65.64; H, 5.73; N, 13.53; S, 10.18.

5-Dimethyl-3-ethyl-1-phenylamino-2-thiohydantoin, prepared similarly to the foregoing compound from ethyl mustard oil and phenylhydrazoisobutyric acid, and purified by crystallization from dilute alcohol and petroleum ether, melts at 85°.

The analysis gave 15.94 per cent. N. Calculated for $C_{13}H_{17}ON_3S$, 15.97 per cent.

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[1] The investigation of the behavior of mustard oils toward phenylhydrazoisobutyric acid was carried out conjointly with Ernest Anderson.

PART II. ACTION OF PHENYLISOCYANATE ON HYDRAZO ACIDS. DESULPHURIZATION OF THIOHYDANTOINS.

α-Ureido-α,β-diphenylurea,

$$C_6H_5NHCON(C_6H_5)NHCONH_2.$$[1]

—To prepare this substance phenylsemicarbazide,

$$NH_2CONHNHC_6H_5,$$

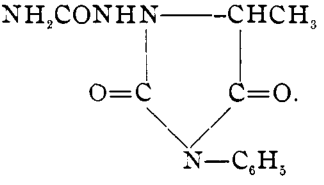
and an excess of phenylisocyanate are allowed to react for several hours in boiling benzene. The insoluble reaction product is then filtered off and purified by crystallization from alcohol, in which it is difficultly soluble. It melts with gas evolution to a clear liquid at 210°. Unlike phenylisocyanate, phenyl mustard oil does not react with phenylsemicarbazide at the boiling temperature of benzene.

Calculated for $C_{14}H_{14}O_2N_4$: C, 62.22; H, 5.19; N. 20.74. Found: C, 62.24; H, 5.29; N, 21.00.

Action of Phenylisocyanate on Semicarbazinopropionic Acid Ethyl Ester.—Two grams of $NH_2CONHNHCH(CH_3)COOC_2H_5$ were suspended in 50 cc. of benzene and then 1.5 grams of phenylisocyanate added. Reaction took place immediately with considerable elevation of temperature and the ester quickly dissolved. To complete the reaction the solution was boiled one hour. The benzene was next distilled off and the residue crystallized from alcohol and acetic ether. The new substance melts at 163°. The analysis shows this substance to be a simple addition product of the isocyanate on the semicarbazino ester, *i. e.*, α-phenylcarbonamidesemicarbazinopropionic acid ethyl ester, $NH_2CONHN(CONHC_6H_5)CH(CH_3)COOC_2H_5$.

Calculated for $C_{13}H_{18}O_4N_4$: C, 53.06; H, 6.12; N, 19.05. Found: C, 53.00; H, 6.24; N, 19.29.

The above substance, when boiled in water solution, readily splits off alcohol, giving 5-methyl-1-ureido-3-phenylhydantoin,



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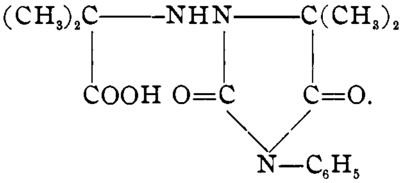
[1] The investigation of the reaction products of phenylisocyanate on phenylsemicarbazide and on semicarbazinopropionic acid ethyl ester was carried out conjointly with P. T. Miller.

This latter substance crystallizes from acetic ether in long, very slender needles, which decompose at about 219°.

Calculated for $C_{11}H_{12}O_3N_4$: C, 53.23; H, 4.84. Found: C, 53.24; H, 4.97.

5-Dimethyl-3-phenyl-1-isobutyric-acid-aminohydantoin,



—This substance was obtained by desulphurizing the corresponding 2-thiohydantoin, already described, and also by allowing phenylisocyanate to react on hydrazoisobutyric acid in glacial acetic acid solution. One hundred cc. of glacial acetic acid, in which were dissolved 10 grams of phenylisocyanate and 16 grams of hydrazoisobutyric acid, were boiled one hour, the acetic acid was then boiled off *in vacuo,* and the residue crystallized from alcohol. In this way 12.5 grams of the hydantoin were obtained. The alcohol, on evaporation, yielded a large amount of s-diphenylurea and 2 grams of the hydantoin. The latter was dissolved with sodium bicarbonate and then regained by precipitation with hydrochloric acid. The substance is difficultly soluble in benzene, almost insoluble in ether and water, and readily soluble in hot alcohol. From the latter it crystallizes in characteristic prisms with wedge-shaped end faces. It melts at 205° to a light brown liquid. Like the corresponding 2-thiohydantoin, it titrates as a monobasic acid.

Calculated for $C_{15}H_{10}O_4N_3$: C, 59.02; H, 6.23; N, 13.77. Found: C, 58.93; H, 6.24; N, 13.83.

0.4128 gram substance required 13.48 cc. N/10 NaOH; calculated, if monobasic, 13.53 cc. N/10 NaOH.

Ethyl Ester of 5-Dimethyl-3-phenyl-1-isobutyric-acid-aminohydantoin.—This ester was prepared similarly to the ethyl ester of the corresponding 2-thiohydantoin. It is readily soluble in alcohol, benzene and ether, and difficultly soluble in petroleum ether and water. For the analysis it was twice crystallized from ether, from which it separates in large hexagonal prisms. The substance melts undecomposed at 98°.

Calculated for $C_{17}H_{23}O_4N_3$: C, 61.26; H, 6.91; N, 12.61. Found: C, 61.14; H, 6.89; N, 12.66.

Action of Mercuric Oxide on 5-Dimethyl-3-phenyl-1-isobutyric-acid-amino-2-thiohydantoin.—Three grams of the above thiohydantoin were converted into the sodium salt by dissolving it in the calculated amount of N/10 NaOH, and this solution, diluted to 150 cc., was heated for one hour in a boiling water-bath with a large excess of mercuric oxide. The solution was then filtered and a substance precipitated by acidifying with hydrochloric acid that proved identical in every respect with the reaction product, already described, of phenyl isocyanate on hydrazoisobutyric acid.

Calculate for $C_{15}H_{19}O_4N_3$: C, 59.02; H, 6.23; N, 13.77. Found: C, 58.88; H, 6.25; N, 13.81.

3-Methyl-5-dimethyl-1-isobutyric-acid-aminohydantoin.—After several experiments, the following method of preparing this hydantoin was adopted as giving the best yield: The corresponding 2-thiohydantoin is dissolved in a slight excess of ammonium hydroxide and then an excess of mercuric oxide added. Reaction takes place in the cold, with an elevation of temperature in the solution, and the mercuric oxide is quickly blackened. The solution is allowed to stand fifteen hours with occasional shaking. At the end of this time the hydantoin is isolated in the manner described under the 3-phenyl compound. This method gave a yield of 7.7 grams of hydantoin from 12 grams of the thiohydantoin. It is not at all necessary to purify the thiohydantoin, as even a very impure substance yields an almost pure product. This hydantoin is readily soluble in alcohol, ether and benzene, and crystallizes beautifully from water in slender prisms, melting at 169°.

Calculated for $C_{10}H_{17}O_4N_3$: C, 49.38; H, 7.00; N, 17.28. Found: C, 49.26; H, 7.11; N, 17.24.

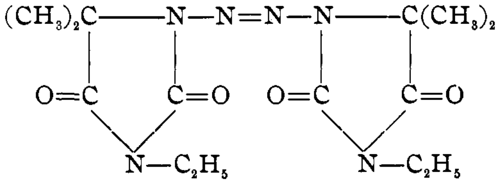
3-Ethyl-5-dimethyl-1-isobutyric-acid-aminohydantoin was prepared similarly to the foregoing substance by desulphurizing the corresponding 2-thiohydantoin. It has about the same solubility as the 3-methyl compound and crystallizes from water in long, slender needles, which melt at 140°.

Calculated for $C_{11}H_{19}O_4N_3$: C, 51.36; H, 7.39. Found: C, 51.29; H, 7.43.

5-Dimethyl-3-allyl-1-isobutyric-acid-aminohydantoin, obtained by desulphurizing the corresponding 2-thiohydantoin, was purified by crystallization from water and ether. It crystallizes in thin, prismatic plates, which melt at 114°.

Calculated for $C_{12}H_{19}O_4N_3$: C, 53.53; H, 7.06; N, 15.61. Found: C, 53.23; H, 7.09; N, 15.77.

1-Azo-5-dimethyl-3 ethylhydantoin,[1]



—The aminoisobutyric-acid-hydantoins, as well as the corresponding thiohydantoins, behave as reducing agents toward bromine water or potassium permanganate. Although these oxidation products have not been thoroughly investigated, the analyses thus far made indicate that they are tetrazones. The method of preparing these substances is to suspend the hydantoin in water, or better, to dissolve it in alcohol, and then add bromine water until the bromine produces a faint, permanent yellow color. A large amount of the bromine is probably used in brominating the oxyisobutyric acid split off in this reaction. Three grams of dimethylethylisobutyric-acid-aminohydantoin required 510 cc. $^9/_{100}$ N bromine water. In this experiment 1.9 grams of the tetrazone were obtained. The tetrazones here described are very difficultly soluble in almost all solvents thus far tried, except chloroform and glacial acetic acid. They can be obtained snow-white by precipitation with petroleum ether from a chloroform solution, but this method of crystallization does not seem to effect complete purification. For analysis the azodimethylethylhydantoin was twice crystallized from alcohol and thus obtained as a crystalline white substance, which melts with gas evolution at 234°.

Calculated for $C_{14}H_{22}O_4N_6$: C, 49.70; H, 6.51; N, 24.85. Found: C, 49.64; H, 6.59; N, 24.88.

1-Azo-3-methyl-5-dimethylhydantoin was prepared similarly to the preceding 3-ethyl compound. It was purified by precipitation

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[1] This nomenclature is not strictly in accordance with the recognized use of the term "azo," which is employed to designate the group N=N doubly joined to carbon, but this extended application of the term here removes the difficulty that would arise were it attempted to embody the term "tetrazone" in the name of these substances.

from a chloroform solution with petroleum ether. The product thus obtained decomposed at about 278°. The nitrogen determinations, which were made on different preparations, were between 0.5 per cent. and 1 per cent. below the theoretical in each case.

Calculated for $C_{12}H_{18}O_4N_6$: C, 46.45; H, 5.85; N, 27.10. Found: C, 46.22; H, 5.90; N, 26.36, 26.16, 26.60.

1-Azo-5-dimethyl-3-phenylhydantoin was prepared and purified similarly to the foregoing tetrazone. It decomposes to a brown liquid at 270° with gas evolution. The product analyzed had the external appearance of purity, but the analytical data do not conform closely to the formula given this substance.

Calculated for $C_{22}H_{22}O_4N_6$: C, 60.83; H, 5.07; N, 19.35. Found: C. 61.85; H, 5.26; N, 18.71, 18.90.

NOTES.

Stationary Hempel Apparatus.—The apparatus shown in the accompanying sketch was devised by Mr. W. J. Knox, of Pittsburg, and has been in constant use for a number of years with no radical modifications.

To a horizontal frame, near to and parallel to the edge of the working-bench, is attached a horizontal rod, D, about ⅝ inch in diameter, on which the pipettes may be suspended from appropriate hooks attached to the frame of the pipette, while to a vertical rod, secured to frame and bench, are fastened the burette and leveling tube in such a manner as to permit free lateral motion. The prolong of the burette is bent at right angles to the burette and parallel to the graduations. The capillary tubes of the pipettes are also bent to 90°, so that only a single rubber connection is necessary to attach the pipette to the burette. At the top of the burette is a 3-way cock, A, the second outlet, E, being the stem of the cock. At the bottom of the leveling tube is a cock, C. Burette and leveling tube are connected by a Y-tube to one branch of a 3-way cock, B, the other branches of which are connected, respectively, to an overhead reservoir and drain.

The *modus operandi* is as follows: With C closed, open A to burette and fill burette with water by opening B to supply. Close A and attach sample bottle to prolong of burette. Pass enough