is undoubtedly the same acid, but containing a trace of some impurity which persistently clings to it.

The ether extract, obtained by extraction of the barium salts, yielded on spontaneous evaporation of the ether a straw-colored residue having the consistency of vaseline. This was decomposed by warming in a water bath with dilute hydrochloric acid, and the clear oil which separated, extracted with ether. By spontaneous evaporation of the ether, there was obtained a clear, yellow oil. This oil readily decolorizes bromine water, and is soluble in dilute alkalies, from which it is regenerated when acidified. It showed no tendency to crystallize until after standing for about three months, when a crystalline substance separated. The crystals were spread on a porous plate to remove the adhering oil, and then washed with a little cold alcohol, whereby the substance was obtained nearly white. After two recrystallizations from acetic acid, and another from ether in a freezing mixture, it melted at 86–90° to a slightly turbid oil which became perfectly clear at 100° and decomposed with bubbling at about 150°. It dissolves easily in warm dilute ammonium hydroxide, and is reprecipitated in a flocculent form when acidified with hydrochloric acid. This substance shows all of the properties of the ditetradecylsuccinic acid which melts at 95°.

The oil from which the above acid was obtained showed strong properties of unsaturation. Unfortunately, the amount available was so small that further investigation of it was impossible.

MADISON, WIS.

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

THE CONSTITUTION OF ACETYLACETONE-THIOUREA.

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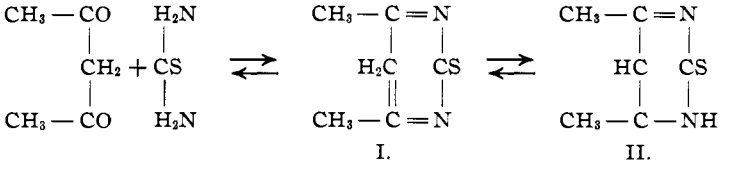
The constitution of acetylacetone-urea has been shown by de Haan,[1] and again by one of us,[2] to accord primarily with the formula advanced by Evans[3] and at the same time to exist in a tautomeric imino, or colorless form. The ordinary product was considered quinoid in structure and possessed a decided yellow color. The condensation of thiourea with acetylacetone is described by Evans[4] as proceeding in exactly analogous manner to the condensation of urea with this diketone and yielding two distinct condensation products. From the properties of these two products it seemed that their exact structures might be open to question. de Haan has shown conclusively that the so-called diurimido-acetylacetone

[1] *Rec. trav. chim.*, **27**, 162 (1908).
[2] THIS JOURNAL, **36**, 104 (1914).
[3] *J. prakt. Chem.*, [2] **48**, 489 (1893).
[4] *Ibid.*, **48**, 503 (1893).

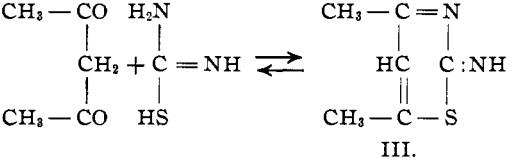
is a pyrimidine at base and not a chain product; in similar manner in a subsequent paper we shall attempt to account for the structure of the so-called dithiourimido-acetylacetone—one of these two condensation products just mentioned. The other product, called by Evans acetylacetone-thiourea, accords with this exact constitution and proceeds from a direct ring condensation between the ketone and thiourea:



I. Acetylacetone-thiourea or 4,6-dimethyl-2-thio-2,5-dihydropyrimidine.

II. 4,6-Dimethyl-2-thio-2,3-dihydropyrimidine.

The possibility of thiourea condensing in its pseudo form must also be considered. The product would accord with the metathiazine formula (III)



III.

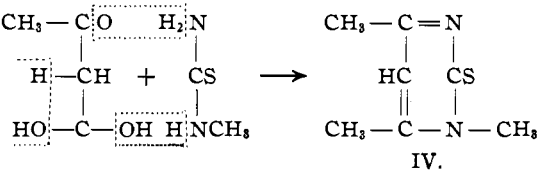
In the former case we might expect a third tautomer bearing a mercaptan group, and in the latter case this identical mercapto compound may easily be derived by the second possible manner of condensation. The possibility of such a result, however, is at once dismissed when it is recalled that acetylacetone-thiourea scarcely blackens moist mercuric oxide or basic lead acetate solution, even by prolonged boiling—a property not in keeping with the presence of a free mercaptan group. This distinct characteristic is almost indicative of Formula III where sulfur is held in the ring. The inference of, however, and the entire basis for such metathiazine structure, is overthrown by the ease with which the *n*-methyl ether of acetylacetone-thiourea gives up its sulfur to these mild desulfurizing agents. We are, therefore, brought to the conclusion that only Formulas I and II can be presented for consideration—structures similar in every respect to the two possible tautomeric formulas for acetylacetone-urea.

The free acetylacetone-thiourea is almost colorless when pure—a point in favor of the tautomeric imino form (II). However, when a thio group is present the absence of marked color cannot be taken as argument against the quinoid structure. In the application of Hinsberg's test for the presence of a secondary amine (or imino) group, only negative results could

be obtained; a result identical with that[1] obtained with acetylacetone-urea, which is known to exist in both keto and imino forms, and consequently due no doubt to the strongly negative thio group. The action of diazomethane upon this acetylacetone-thiourea, both in methyl alcohol and in chloroform solutions, failed to give any appreciable quantity of a methyl ether corresponding to that which was readily and quantitatively prepared when diazomethane acted upon acetylacetone-urea. This result was unexpected and can only be used as an argument against the imino form (II) for the free substance. The compound, therefore, may be regarded as existing primarily in its quinoid structure, namely, that of the 2,5-dihydro derivative (I): a 4,6-dimethyl-2-thio-2,5-dihydropyrimidine. The tendency toward formation of salts is to be looked upon, however, as proceeding from the imino form. The process was found slow and in nowise complete.

The preparation, not only of this *n*-methyl ether but also of the thio ether, was accomplished by condensation of acetylacetone with methyl thiourea, $NH_2.CS.NHCH_3$, and on the other hand with methyl iminothiocarbamate, $NH_2.C(SCH_3):NH$, respectively.

The condensation with methyl thiourea proceeded readily in acid solution:



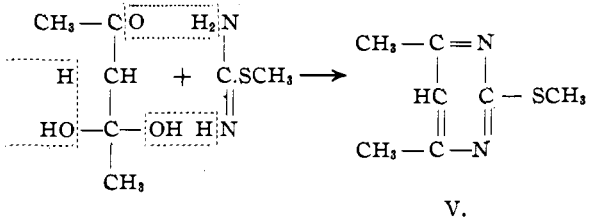
IV.

The free substance, melting at 156.5°, is colorless and is easily blackened by warming with mild desulfurizing agents. The resistance of the sulfur in acetylacetone-thiourea to these same agents is therefore no longer apparent when one of the nitrogen atoms carries a substituent. The complete desulfurization of the ether, and replacement of sulfur by oxygen, was accomplished by several hours' boiling with an aqueous solution of chloroacetic acid. The product hereby obtained is naturally identical with that product prepared by the condensation of acetylacetone and methylurea.[2] The structure (IV) therefore of the ether of acetylacetone-thiourea is established. The desulfurization of acetylacetone-thiourea itself by means of chloroacetic acid was found to give acetylacetone-urea as expected.

Condensation of acetylacetone with methyl iminothiocarbamate, *i. e.*, pseudomethyl-thiourea, proceeded well in alkaline solution:

[1] THIS JOURNAL, 36, 113 (1914).

[2] *Ibid.*, 36, 114 (1914).



V.

The oil separating out is somewhat difficult to purify, but the free product obtained by distillation *in vacuo* agreed in all respects with the thio ether (m. p. 24°) prepared by Wheeler and Jamieson.[1] We started with the product which Dixon[2] made by the action of thiourea upon methyl chlorocarbonate. Upon melting this methyl pseudo-thioallophanate, we secured the pseudomethyl-thiourea in the form of its hydrochloride. Wheeler and Jamieson condensed the methyl iodide addition product of thiourea with acetylacetone in the presence of alkali. The structure of their addition product, as investigated by Bernthsen and Klinger[3] and by Werner[4] and others, corresponds with that of a methyl ether of iminothiocarbamic acid in the form of its hydrogen iodide salt and consequently should enter into the condensation in the same manner as the hydrochloride salt employed by us. Furthermore, this thioether or 2-methylmercapto-4,6-dimethylpyrimidine, may best be prepared directly from free acetylacetone-thiourea by methylation with methyl iodide and sodium methylate. No matter by which of these three possible methods the methyl mercapto derivative is prepared, it is slowly transformed into the corresponding keto derivative, with consequent loss of mercaptan, when boiled for several hours with concentrated hydrobromic acid. This keto derivative is again the free acetylacetone-urea melting at 210°. Its production from acetylacetone-thiourea directly or through the intermediate step of a methylmercapto derivative, taken together with its corresponding production in the form of a methyl ether of acetylacetone-urea by the action of chloroacetic acid upon the methyl ether of acetylacetone-thiourea leave no room for doubt upon the constitution of the thiourea condensation product. The free acetylacetone-thiourea therefore may be looked upon as of the quinoid type (I) in equilibrium with a small proportion of the rather inactive imino type (II).

Experimental Part.

Acetylacetone-thiourea (I).—The method employed by Evans was found satisfactory in every respect. Two grams of thiourea were dissolved in 40 cc. of alcohol, 2 g. of acetylacetone then added and during cooling 50

[1] *Am. Chem. J.*, **32**, 356 (1904).
[2] *J. Chem. Soc.*, **83**, 566 (1903).
[3] *Ber.*, **11**, 492 (1878).
[4] *J. Chem. Soc.*, **57**, 283 (1890).

drops of concentrated sulfuric acid admitted to flask. After a day or two the yellow crystalline mass was filtered off and taken up in water. To this solution freshly precipitated barium carbonate was added to neutral reaction. The clear filtrate from the barium salts was then evaporated to dryness upon steam bath and this mass extracted with absolute alcohol. Upon further evaporation of the clear alcoholic solution to small volume the light yellow colored prisms of acetylacetone-thiourea make their appearance. The pure substance melts at 210° (uncor.). This compound is readily soluble in water or chloroform, from which latter it may be precipitated by ligroin in small colorless crystals; it is fairly soluble in alcohol, crystallizing best from this solvent; it is slightly soluble in benzene, ethylacetate, acetone or ether and insoluble in ligroin. It forms insoluble salts with metal ions of barium, silver and mercury as has been noted by Evans. The preparation of this acetylacetone-thiourea as a hydrochloride, using concentrated hydrochloric acid as a condensing agent, is also described by Evans, but the method was not found as practical as that where sulfuric acid is used.

Complete desulfurization of acetylacetone-thiourea was accomplished by the method of Wheeler and Liddle.[1] Two grams of the substance in solution with 15 cc. of water containing 2 g. of chloroacetic acid were boiled under a reflux condenser for a period of 4 or 5 hours. The mixture was then evaporated upon a steam bath and the residue treated with 90% alcohol. The part remaining undissolved was colorless. This colorless hydrochloride was next dissolved in a little water and the solution almost neutralized with alkali, when it was again evaporated to dryness upon the steam bath. The solid mass was now extracted with benzene to remove the free base. This latter came out of the concentrated benzene solution in colorless prisms melting at 198° and proved to be identical in all respects with the acetylacetone-urea of Evans. The two melted separately, and also when mixed, at this constant point.

Condensation of Acetylacetone with Methyl Thiourea.—One gram methyl thiourea and 1 g. acetylacetone in 10 cc. of alcohol are treated with 20 drops of conc. hydrochloric acid, and the yellow solution allowed to stand. The beautiful yellow prisms of the hydrochloride separate out over night. The hydrochloride was crystallized from alcohol for analysis.

0.2038 g. air-dried salt gave 0.1525 g. AgCl. Calc. for $C_7H_{10}N_2S.HCl$: HCl, 19.13%. Found: HCl, 19.04%.

The free substance—the 3,4,6-trimethyl-2-thio-2,3-dihydro pyrimidine, (IV), may be obtained directly from the hydrochloride by adding alkali to its aqueous solution and extracting this neutral mixture with chloroform. If the original reaction-mixture, before removing the hydrochloride, is allowed to evaporate spontaneously to dryness, and then its aqueous

[1] *Am. Chem. J.*, 40, 549 (1908).

solution neutralized with alkali and extracted with chloroform, practically a quantitative yield of the methyl ether is obtained; any methyl thiourea unacted upon will remain undissolved by the chloroform. This colorless methyl ether is insoluble in ligroin or ether; readily soluble in water, chloroform, acetone or alcohol, crystallizing from concentrated solutions in either; and fairly soluble in ethyl acetate or benzene. It is best purified by crystallization from the latter, giving small needles melting at 156.5°. Prolonged boiling with concentrated hydrochloric is without action upon this product. This therefore verifies its structure as a *n*-methyl ether. By gentle warming with basic lead acetate solution, moist mercuric oxide or ammoniacal silver nitrate, a blackening or sulfide formation is observed.

0.1296 g. subs. gave 22.5 cc. N_2 (26°, 729.1 mm. over H_2O). Calc. for $C_7H_{10}N_2S$: N, 18.19%. Found: 18.36%.

One gram of this ether was dissolved in 15 cc. water containing 1 g. of chloroacetic acid and the mixture boiled in flask under reflux condenser for 3 hours. The contents of the flask were then neutralized with NaOH and extracted with chloroform. The chloroform extract, upon evaporation gave a low melting product which, when recrystallized from benzene, melted at 63° and corresponded in all other characteristics with the methyl ether of acetylacetone-urea (m. p. 63°) described by one of us in a previous paper.

Condensation of Acetylacetone with Pseudomethyl-thiourea.—The preparation of pseudomethyl-thiourea was in exact accord with the method described by Dixon.[1] Methyl chlorocarbonate was allowed to condense with thiourea and the crystalline product heated upon a water bath till the evolution of carbon dioxide had ceased and the hydrochloride of pseudomethyl-thiourea remained as residue. Attempts to condense this pseudomethyl-thiourea with acetylacetone in the presence of acids as condensing agents did not give good results. The tendency for desulfurization is apparent when free acids are present. In the presence of alkali, however, the condensation runs smoothly though here also decomposition into cyanamide has been noted. Five grams acetylacetone were added to a cold aqueous solution of 5 g. pseudomethyl-thiourea hydrochloride in 25 cc. of water containing also 2.5 g. of potassium hydroxide. The clear solution was allowed to stand one day, when an oil was found to have separated. This oil, shaken out with ether, dried over solid potassium hydroxide, and distilled *in vacuo*, gave a small quantity of distillate solidifying when cold to a colorless crystalline substance melting at 24°. This was found identical with the 2-methylmercapto-4,6-dimethylpyrimidine (V) (m. p. 24°) obtained by Wheeler and Jamieson[1] when acetylacetone was condensed in alkaline solution with the methyl iodide addition product by thiourea. Just as the product prepared according to the method of

[1] *Loc. cit.*

Wheeler, so also this product from our preparation was submitted to the action of concentrated hydrobromic acid for 3 to 4 hours under a reflux condenser. Mercaptan was copiously liberated and the contents of flask finally evaporated to dryness upon a steam bath. The residue taken up in water was just neutralized with alkali and again reduced to dryness upon steam bath. From this final residue, by extraction with benzene, a product is obtained which upon crystallization from alcohol melts at 198° and is identical with Evans acetylacetone-urea. The methylmercaptan therefore had been transformed into the corresponding keto derivative.

Methylation of Acetylacetone-Thiourea.—The addition of alkyl haloids to the free sulfur atom of acetylacetone-thiourea, just as with thiourea itself, is naturally to be expected. By the action of sodium methylate upon this addition product, which was made but not analyzed, we should expect to obtain the methyl thio ether or methylmercapto derivative of our pyrimidine. 0.6 g. of sodium was dissolved in 10 cc. methyl alcohol and 3.5 g. of acetylacetone-thiourea added. Into this solution 3.5 g. of methyl iodide (which must not be in excess of calculated quantity) in a few cc. of methyl alcohol were then admitted to the flask and the mixture warmed gently under a reflux condenser (over water bath) till neutral reaction appeared. The methyl alcohol was now removed by evaporation and the residue extracted with ether. The ether removed an excellent yield of the almost pure crystalline 2-methylmercapto-4,6-dimethylpyrimidine melting at 24°. When this latter was treated with concentrated hydrobromic acid, as before described, a quantitative yield of the acetylacetone-urea (198°) was obtained. The methylation, therefore, of acetylacetone-thiourea in its methylmercapto form is readily accomplished through the intermediate step of its alkyl halide addition product.

In attempting to methylate acetylacetone-thiourea by means of diazomethane, as was readily accomplished with acetylacetone-urea,[1] no positive results could be obtained. Methyl alcohol and chloroform also were used as solvents. From both solutions the greater part of acetylacetone-thiourea was recovered. In one or two instances it seemed that traces of both the thio ether and the imino ether were present but confirmatory tests were lacking. We are led therefore to the conclusion that acetylacetone-thiourea functions primarily as a quinoid base. The formation of thio ethers is only possible through the preliminary addition of an alkyl salt and consequently all tests to show the possible tautomerization for existence of mercapto group in this free base must have failed. The imino form then must be considered the normal tautomer and in reactivity placed far below the corresponding imino form of acetylacetone-urea.

ANN ARBOR, MICH.

[1] *Loc. cit.*