as a dynamic method for determining, with fair precision, the concentration of the H^+ ion.
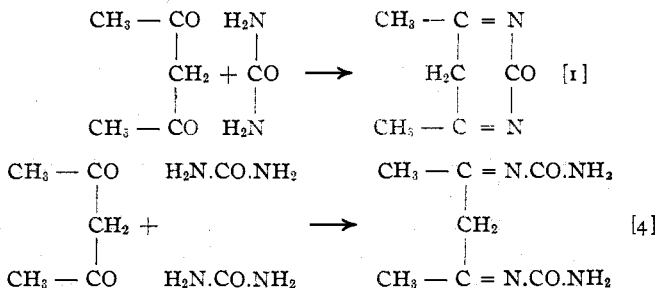
BERKELEY, CALIF.

THE CONSTITUTION OF ACETYLACETONE-UREA.
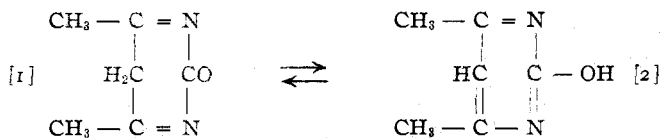
BY WILLIAM J. HALE.

As first reported by Evans[1] and shortly afterwards by A. and C. Combes,[2] the condensation of acetylacetone and urea may proceed in either of two ways. The more stable product, called by Evans, acetylacetone-urea and the second, called diurimidoacetylacetone, were described at length in a second contribution.[3] The condensations were looked upon as proceeding in the following manner:

$$CH_3 — CO \quad H_2N \qquad\qquad CH_3 — C = N$$
$$\quad | \qquad\qquad | \qquad\qquad\qquad | \qquad\qquad |$$
$$\qquad CH_2 + CO \longrightarrow \qquad H_2C \quad CO \quad [1]$$
$$\quad | \qquad\qquad | \qquad\qquad\qquad | \qquad\qquad |$$
$$CH_3 — CO \quad H_2N \qquad\qquad CH_3 — C = N$$

$$CH_3 — CO \quad H_2N.CO.NH_2 \qquad CH_3 — C = N.CO.NH_2$$
$$\quad | \qquad\qquad\qquad\qquad\qquad\qquad\qquad |$$
$$\quad CH_2 + \qquad\qquad \longrightarrow \qquad\qquad CH_2 \qquad [4]$$
$$\quad | \qquad\qquad\qquad\qquad\qquad\qquad\qquad |$$
$$CH_3 — CO \quad H_2N.CO.NH_2 \qquad CH_3 — C = N.CO.NH_2$$

The ease with which this acetylacetone-urea gave salts with heavy metals was thought to be due to its ready transformation into an enolic form [2]:

$$CH_3 — C = N \qquad\qquad\qquad CH_3 — C = N$$
$$\quad | \qquad\qquad | \qquad\qquad\qquad\qquad | \qquad\qquad |$$
$$[1] \quad H_2C \quad CO \rightleftarrows \qquad HC \quad C — OH \quad [2]$$
$$\quad | \qquad\qquad | \qquad\qquad\qquad\qquad || \qquad\qquad ||$$
$$CH_3 — C = N \qquad\qquad\qquad CH_3 — C — N$$

If this assumption were correct we should have, for consideration, a 2-hydroxypyrimidine; a compound of the type described by Hale and Brill[4] in work upon urea and a β-dialdehyde. With the exception of certain uracil derivatives,[5] which may exist in such tautomeric form, we note a marked absence of description of 2-hydroxypyrimidines in the literature. It seemed well, therefore, to undertake further investigation upon this product of Evans' in order to study the distinctive properties of 2-hydroxypyrimidines as a class.

According to Evans, the usual reactions characteristic of an hydroxyl

[1] J. prakt. Chem., [2] 46, 352 (1892).
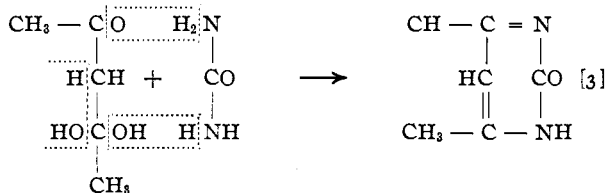[2] Bull. soc. chim., [3] 7, 791 (1892).
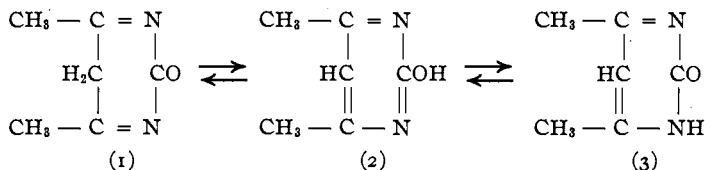[3] J. prakt. Chem., [2] 48, 489 (1893).
[4] THIS JOURNAL, 34, 82 (1912).
[5] J. prakt. Chem., [2] 47, 201 (1893).

group failed entirely in this compound; neither benzoyl nor acetyl esters could be prepared; no definite compound could be obtained by the action of methyl iodide upon the dry silver salt; and the alkali salts were obtainable only with difficulty by reason of marked hydrolysis. From such evidence we are led at once to the conclusion that a true imino base is most likely present.

A very careful study of the condensation products of acetylacetone and urea has been conducted by de Haan.[1] His work indicated the imino formula [3] as a possible structure for acetylacetone-urea, and a mode of condensation represented as follows:

$$
\begin{array}{ccc}
CH_3 - C\,O \quad H_2N & & CH - C = N \\
| \qquad | & & | \quad | \\
H\,CH \; + \; CO & \longrightarrow & HC \quad CO \;\;[3] \\
| \qquad | & & \| \quad | \\
HO\,C\,OH \; H\,NH & & CH_3 - C - NH \\
| & & \\
CH_3 & &
\end{array}
$$

Tautomeric, with this product, de Haan assumed that a quinoid form [1] must be considered in order to account for certain color changes in the compound itself and in its derivatives. He does not, however, argue to the exclusion of the enolic form proposed by Evans, hence we have, for our consideration, the following possible tautomeric formulas:

$$
\begin{array}{ccc}
CH_3 - C = N & CH_3 - C = N & CH_3 - C = N \\
| \quad | & | \quad | & | \quad | \\
H_2C \quad CO \;\rightleftharpoons & HC \quad COH \;\rightleftharpoons & HC \quad CO \\
| \quad | & \| \quad \| & \| \quad | \\
CH_3 - C = N & CH_3 - C - N & CH_3 - C - NH \\
(1) & (2) & (3)
\end{array}
$$

As first prepared, acetylacetone-urea crystallizes from water with 2 molecules of water of hydration. These crystals, prepared with care and without access of light, are perfectly colorless. When, however, this aqueous solution falls under the influence of heat, or light, lemon-yellow crystals are obtained; the same product as that which results upon exposing the colorless crystals to direct sunlight. Both forms of crystals lose their two molecules of water by long standing in the air but better over calcium chloride. de Haan has shown conclusively that a colorless nitrate can be prepared from the colorless form of crystals, and likewise a red-colored nitrate from the colored form. From a series of optical measurements upon the colorless and colored forms of acetylacetone-urea scarcely no difference could be detected between the two. The relation between the colorless and colored forms may well be represented as in [3] and [1], respectively. Though de Haan gives preference to the imino form, he maintains that the second possible structure for the colorless

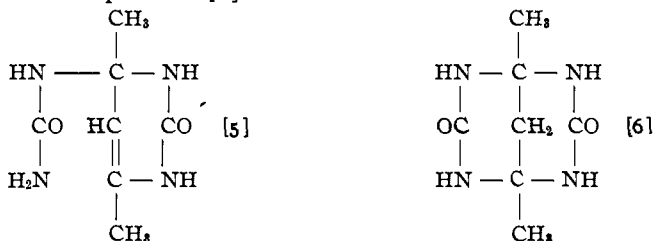[1] Rec. trav. chim., 27, 162 (1908).

compound, namely an enolic form of dimethylketopyrimidine [2], must be considered. This latter is, of course, the structure already proposed by Evans to explain the tendency toward salt formation in the compound. Without doubt, we may conclude that the original formula assigned by Evans to acetylacetone-urea, the quinoid form [1], may be taken to represent the colored product. For the colorless substance there remain therefore the two possibilities [2] or [3], for which we shall select that one best substantiated by the facts at hand.

Evans prepared acetylacetone-urea by allowing urea and acetylacetone to react in alcoholic solution in the presence of a large quantity of either concentrated sulfuric or hydrochloric acid. From the corresponding salts, which crystallize out, the free substance was easily obtained in aqueous solution by the action of barium carbonate or silver oxide, respectively. In place of this acetylacetone-urea Evans found that, by use of a much smaller quantity of acid and a relatively large portion of urea (2 molecules), an entirely different product resulted, a so-called diurimido-acetylacetone in the form of the corresponding acid salt. To this product Evans assigned the structure [4]. In solubilities and melting point ($197°$) it was found not much unlike those of acetylacetone-urea. When the hydrochloride in aqueous solution was warmed with silver oxide, acetylacetone-urea and free urea were obtained. Though the presence of one free ureide group may thus be confirmed, the presence of only one is not established. There remained, therefore, the supposition that we had here two free ureide groups until the work of de Haan gave us the correct interpretation of the structure of this compound, namely, that of a monoureide of a ring substance, this same acetylacetone-urea ring.

de Haan best prepared this product by allowing an absolute alcoholic solution of urea (2 molecules) and acetyl acetone (1 mol) to stand for several days. The colorless crystals separating out are practically insoluble in alcohol, but fairly soluble in water. This substance is the principal product obtained when acetylacetone and urea are allowed to react without any large quantity of acid condensing agent. The constitution [5] assigned by de Haan makes it a 6-ureido-4,6-dimethyl-2-keto-2,3,6,1-tetrahydropyrimidine, or as de Haan reported, a 4,6-dimethyl-2-ketopyrimidine-urea.
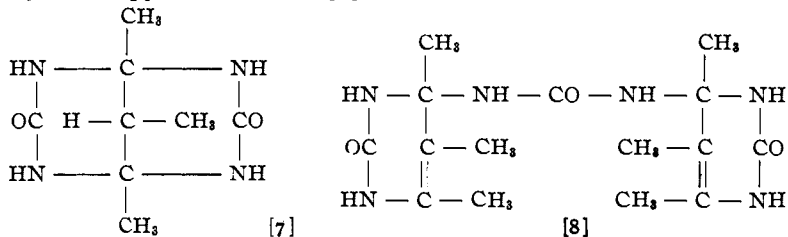
Readily acted upon by nitric acid with evolution of gas, the presence of only one free urea group is indicated; the residue is the nitrate of dimethylketopyrimidine. Again, by the action of strong alkali, the liberation of ammonia corresponded with the decomposition of one free urea group, and gave a residue of dimethylketopyrimidine alkali salt. As might be expected, a small quantity of crystals of this dimethylketopyrimidine-urea were obtained when unimolecular quantities of dimethyl-ketopyrimidine and urea reacted together.

According to the method of M. Combes, complete solution between acetylacetone and urea is effected when they are warmed together for several hours upon a water bath. Upon cooling and digestion of the crystalline mass with alcohol, a small quantity of an insoluble product, melting at 290°, is left undissolved. From the alcoholic solution, however, a considerable amount of the dimethylketopyrimidine-urea is obtained by crystallization. The insoluble substance is obtained in somewhat better yield when acetylacetone and an excess of two molecules of urea are allowed to stand in aqueous solution at room temperature. The yellow tinged crystals separating out were investigated by de Haan and called 2,4-diureinopentane [6].

$$
\begin{array}{ccc}
& CH_3 & \\
& | & \\
HN \!\!-\!\!\!-\!\!\!- C \!\!-\!\! NH & \\
| & | & | \\
CO & HC & CO \quad [5] \\
| & \| & | \\
H_2N & C \!\!-\!\! NH \\
& | \\
& CH_3
\end{array}
\qquad
\begin{array}{ccc}
& CH_3 & \\
& | & \\
HN \!\!-\!\! C \!\!-\!\! NH & \\
| & | & | \\
OC & CH_2 & CO \quad [6] \\
| & | & | \\
HN \!\!-\!\! C \!\!-\!\! NH \\
& | \\
& CH_3
\end{array}
$$

After somewhat longer standing of this aqueous reaction-mixture, a small quantity of crystals of dimethylketopyrimidine-urea make their appearance. This diureinopentane is produced in small quantities only. It is not acted upon by cold nitric acid, and thus the absence of a ureide chain is confirmed. By prolonged action of nitric acid or boiling with dilute acid, decomposition of the molecule ensues and dimethylketopyrimidine nitrate results. This production of diureinopentane from aqueous reaction-mixtures recalls somewhat the condensation between urea and diacetyl leading to the production of dimethylglycoluril,[1] the properties of which differ in no marked extent from this substance.

de Haan further studied the condensation of urea with the two methyl derivatives of acetylacetone. Monomethylacetylacetone condensed very slowly with urea in the presence of sulfuric acid, but better by simple fusion of the two substances alone. In aqueous solution they also condensed and yielded both 2,4-diureino-3-methylpentane [7] and 4,5,6-trimethyl-2-ketopyrimidine-urea [8], the latter the more soluble in alcohol:

$$
\begin{array}{ccc}
& CH_3 & \\
& | & \\
HN \!\!-\!\!\!-\!\!\!- C \!\!-\!\!\!-\!\!\!- NH & \\
| & | & | \\
OC & H\!\!-\!\!C\!\!-\!\!CH_3 & CO \\
| & | & | \\
HN \!\!-\!\!\!-\!\!\!- C \!\!-\!\!\!-\!\!\!- NH \\
& | \\
& CH_3 \quad [7]
\end{array}
\qquad
\begin{array}{c}
\begin{array}{ccccc}
CH_3 & & & & CH_3 \\
| & & & & | \\
HN\!\!-\!\!C\!\!-\!\!NH\!\!-\!\!CO\!\!-\!\!NH\!\!-\!\!C\!\!-\!\!NH \\
| & | & & & | \\
OC & C\!\!-\!\!CH_3 & & CH_3\!\!-\!\!C & CO \\
| & | & & \| & | \\
HN\!\!-\!\!C\!\!-\!\!CH_3 & & CH_3\!\!-\!\!C\!\!-\!\!NH
\end{array} \\
[8]
\end{array}
$$

[1] Franchimont and Klobbie, *Rec. trav. chim.*, 7, 251 (1888). See also Widman, *Ber.*, 19, 2477 (1886).

Either of these products, practically colorless, when carefully treated with nitric acid, gives the yellow crystals of 4,5,6-trimethyl-2-ketopyrimidine [9] as nitrate.

$$
\begin{array}{cc}
CH_3 - C & = N \\
| & | \\
CH_3 - C & CO \quad [9] \\
| & | \\
CH_3 - C & - NH
\end{array}
$$
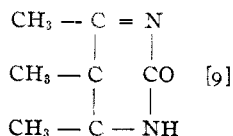
The free product (melting point 209–10°) is colorless and resembles the dimethyl derivative previously described. The tendency here to develop color is only slight; neither by heat upon its aqueous solution nor by action of methyl iodide upon its alkali salt is any color change observed. Nitric acid alone seems able to bring about this change to a yellow salt.

In the study of dimethylacetylacetone and urea, colorless crystals of 2,4-diureino-3,3-dimethylpentane were obtained in small quantity. By the action of nitric acid the methyl groups are lost and possibly a 4,6-dimethyl-5,5-dihydroxy-2-ketopyrimidine produced.

Extensive work upon the condensation of aldehyde with this acetylacetone-urea was carried out by Stark.[1] It was thought that the methylene group of the quinoid form [1] would readily lend itself to condensation with aldehydes. Stark, however, found that the methyl groups, since they were attached to carbon atoms possible of double ties with another atom, entered more readily into this condensation; a tendency, according to the structure, that may be compared with α-quinaldine reactions. With piperidine as condensing agent, one which favors strongly the keto-pyrimidine formula, the monobenzal, obtained from benzaldehyde and the pyrimidine, appears in colorless form, showing therefore that the condensation must have proceeded from formula [3] to the structures shown in [10]. It is readily soluble in alcohol, and, under the influence of light, heat and possibly benzaldehyde itself, it goes over into the quinoid form, whereupon a second methyl group becomes possible of reaction, giving thus a golden yellow dibenzal of formula [11]:
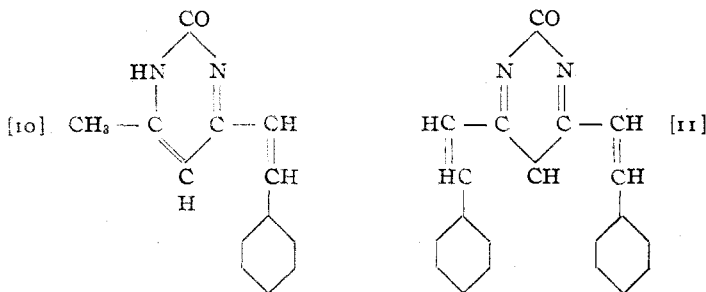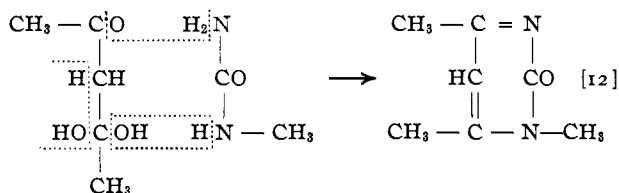

With p-oxybenzaldehyde and vanillin, the first condensation products

[1] Ber., 42, 699 (1909).

are only difficultly soluble and hence do not readily tautomerize. Consequently the monobenzal derivatives only are formed. These mono derivatives, however, develop color with acids, and thus enter into quinoid form.

Further confirmation of the quinoid structure for acetylacetone-urea, in colored form, has been clearly presented by Stark in his later contributions.[1] The work of Majima[2] upon alkylguanidines and acetoacetic ester would indicate also this quinoid structure for the colored product. So also this structure has been indicated by St. Angerstein[3] and again by Wheeler and Jamieson[4] from entirely different sources.

Throughout the work of Evans, de Haan, Stark, and others no mention is made of investigating an alkyl derivative of urea in connection with the ketone. It seemed advisable, therefore, to bring into this study the possible reactions between acetylacetone and monomethylurea. If Evans' theory of a diurimido product were correct then we might hope to obtain the corresponding symmetrical dimethyl-diurimido-acetylacetone (cf. 4). Again, by condensation in alcoholic solution with great concentration of acid, we should obtain an acetylacetone-methylurea [12] in the following manner:

$$
\begin{array}{ccc}
CH_3 - CO \quad H_2N & & CH_3 - C = N \\
\qquad | \qquad | & & \qquad | \quad | \\
H \cdot CH \qquad CO & \longrightarrow & HC \quad CO \quad [12] \\
\qquad | \qquad | & & \qquad \| \quad | \\
HO \cdot C \cdot OH \quad H \cdot N - CH_3 & & CH_3 - C - N - CH_3 \\
\qquad | & & \\
CH_3 & &
\end{array}
$$

Though the greatest care was exercised in order that the condensation between these substances might proceed in the presence of only the smallest amount of acid (method of Evans' above), scarcely enough to form the corresponding salt, there separated from the alcoholic solutions in each and every case the same colorless crystalline mass as was obtained when greater concentrations of acid were employed. Analyses and properties indicated that the product was not a simple ureide but one of ring structure, and this again not of the possible quinoid form of acetylacetone-urea, but a methyl derivative of the imino form [3]. If we retain the name acetylacetone-urea for the colored or quinoid structure we may logically call the imino form a dimethyl-2-ketopyrimidine and consequently this new product will be a 3,4,6-trimethyl-2-keto-2,3-dihydropyrimidine [12].

In fact the ease, with which this pyrimidine derivative is formed, would suggest that even with urea a similar condensation to ring structure should

[1] Ber., **42**, 708 (1909); Ibid., **42**, 1126 (1909); Ann., **381**, 143 (1911).
[2] Ber., **41**, 176 (1908).
[3] Ibid., **34**, 3756 (1901).
[4] Am. Chem. J., **32**, 356 (1904).

not be unexpected in the presence of mild condensing agents; a result exactly in keeping with de Haan's conclusions that Evans' diurimido-acetylacetone is merely a derivative of acetylacetone-urea, which latter is really the first product of the reaction.

When methylurea and acetylacetone are warmed together on the water bath or allowed to stand either in alcoholic or aqueous solutions, no marked reaction takes place, though from alcoholic solutions a small quantity of the methylpyrimidine could be removed. With this condensation proceeding so well in the presence of acid, it appears most difficult to accomplish without the acid condensing agent, a result not unlikely with alkyl ureas. In similar manner many efforts were made to condense unsymmetrical dimethylurea with acetylacetone by means of acid, and thus possibly obtain a simple ureide of chain structure, but in each case no positive results were obtained. Though such condensation may possibly be effected by other means, the failure in presence of acid is the point of comparison here made. If a mono-ureide of the ketone is produced, its stability seemingly is not assured till further condensation into ring form is effected.

The product of the condensation between methylurea and acetyl-acetone is much more soluble in the ordinary solvents than the corresponding ketopyrimidine of Evans. Reactions indicate the absence of any free ureide group. The position of the methyl group upon the 3-N atom was confirmed by the Herzig-Meyer reaction by which methyl iodide was given off only at very high temperatures. This trimethyl-ketopyrimidine, unlike the dimethyl derivative, refuses altogether to give metallic salts; there can be then no ionizable hydrogen. With the N-alkyl firmly fixed the reactions for a tertiary nitrogen atom always persisted under many possible reactions.

The ease of formation of this trimethylketopyrimidine, without the production of an intermediate diurimido product, argued strongly for a similar procedure when urea and acetylacetone entered into condensation, though here with less speed than in the former case where an imino hydrogen is well situated to effect the ring closing. There is also no tendency for the methylurea condensation product to combine with another molecule of the alkyl urea to produce a possible pyrimidine-methylurea in analogy with the urea condensation [cf. 5]. The loss of acid characteristics in the trimethylketopyrimidine possibly explains this further inactivity toward a second molecule of the base, urea, in effecting this result.

With the structure of the trimethylketopyrimidine so well in hand, it appeared all the more possible to establish the structure of the dimethyl-ketopyrimidine of Evans by a simple methylation. If the methyl group entered upon an hydroxyl, as shown in the constitution [2] supported both by Evans and de Haan, we should have a trimethyl derivative

entirely different from the one just described. If, on the other hand, the methylation took place on the imino group, as shown in [3], we should have accordingly a 3,4,6-trimethylketopyrimidine of the identical structure as that product obtained from methylurea and acetylacetone, constituting a clear and direct proof of the structure of the colorless dimethylketopyrimidine.

Attempts to carry out this methylation of Evans' product were at first unsuccessful. Both Evans and de Haan describe the failure attending the reaction of alkyl iodides upon the silver or alkali salts of the ketopyrimidine. In such cases, however, a deep red colored product could be separated from the reaction-mixture. Attempts were then made to methylate, by means of dimethylsulfate, but the product here, as in the previous method, turned quickly to a deep red color. The residue from the action of methyl iodide upon the silver salt was indeed beautifully crystalline but gave, in aqueous solution, a copious yellow precipitate of silver iodide when treated with a soluble silver salt. This presence of iodide-ion indicated an ammonium salt and possibly here an alkyl iodide addition product to one of the nitrogen atoms. Further work showed the correctness of this view. In order to test further this possibility, a methyl alcoholic solution of the free dimethylketopyrimidine was warmed over a water bath with methyl iodide. After a short time the solution, upon spontaneous evaporation, gave colorless needle-like clusters of crystals. These, when removed and analyzed, confirmed our supposition and established the substance as a simple addition product of the free dimethylpyrimidine and methyl iodide. In the action of this halide upon the silver salt of the pyrimidine, there is no doubt a first formation of trimethylketopyrimidine and then, later, an alkyl iodide addition product of the latter.
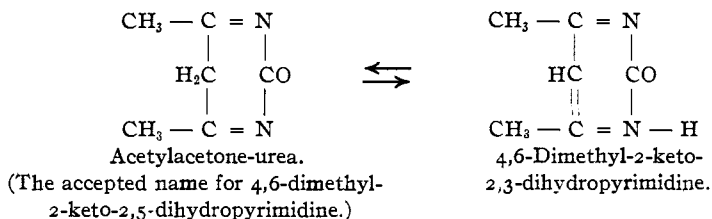
By reason of this great tendency to form addition products with alkyl halides and acid salts, an entirely different method for methylation was undertaken. This method consisted in the use of diazomethane of v. Pechmann. The anhydrous dimethylketopyrimidine was dissolved in chloroform (or methyl alcohol) and the vapors of diazomethane led into the solution, after which the vessel was closed and set aside for an hour or more. Upon spontaneous evaporation of this solution, there appeared colorless crystals of trimethylketopyrimidine melting at 63°. identical in all respects with that trimethyl derivative obtained by condensation of methyl urea and acetylacetone. It is thus seen that the alkylation by diazomethane takes place upon the imino hydrogen atom. It matters not if the starting point be the dried yellow quinoid form, the acetylacetone-urea according to Evans' formula, as the tautomeric imino form is readily produced and methylation proceeds in the manner outlined. If the supposition of Evans and de Haan were correct and a

possible hydroxyl group here present, then this action of diazomethane would lead at once to a methoxyl derivative. The product, however, does not contain a methoxyl group and, hence, we conclude that the colorless form of the dimethylketopyrimidine exists alone in the imino type.

The trimethylketopyrimidine obtained by alkylation showed a somewhat greater tendency to take on a red color than that product from the condensation of methyl urea and acetylacetone. Though the cause of the red color is unknown it has been thought due to a possible tautomerization, or shifting, of the methyl group to the 5-carbon atom. The product thus formed would coincide exactly in constitution with the trimethyl derivative [9] of de Haan, but as this latter has been shown to be even less colored than the free dimethylketopyrimidine, the hypothesis lacks substantiation. The trimethylketopyrimidine remains much longer colorless when confined *in vacuo.*

In order, now, to prove the constitution of the addition product resulting from the action of methyl iodide upon dimethylketopyrimidine there remained only to treat this addition product with alkali and liberate, if possible, a trimethyl derivative. The chloroform extract of this methyl iodide addition product, when treated in aqueous solution with potassium hydroxide, gave upon spontaneous evaporation, the reddish tinged crystals of the 3,4,6-trimethyl-2-ketopyrimidine, thus proving that the addition product can readily be converted into the trimethyl derivative, and further indicating the possible addition of methyl iodide to that nitrogen in the imino group.

The absence of an hydroxyl group in Evans' product is no longer in question. The complete failure of acetylacetone-urea to react with acetyl chloride or benzoyl chloride led to this early assumption. The presence, however, of an imino group in our accepted formula, naturally leads to the supposition that benzene sulfochloride (Hinsberg's test) should react with this substance. Practically the only exceptions to Hinsberg's reaction are just those of this type of compounds where a secondary nitrogen atom is situated adjacent to a carbonyl group and functions thus both as acid and base. Repeated and persistent efforts in carrying out this test, both for the colored and colorless forms of the dimethylketopyrimidine, failed to give any appreciable quantity of product insoluble in the alkali. This failure of reaction, however, can not be construed, as just pointed out, to negative other results. The tautomerism between the colored acetylacetone-urea and its colorless form, 4,6-dimethyl-2-ketopyrimidine, must lie between the formulas here shown:

$$CH_3 - C = N$$
$$H_2C \quad CO \quad \rightleftarrows \quad$$
$$CH_3 - C = N$$

Acetylacetone-urea.
(The accepted name for 4,6-dimethyl-
2-keto-2,5-dihydropyrimidine.)

$$CH_3 - C = N$$
$$HC \quad CO$$
$$CH_3 - C = N - H$$

4,6-Dimethyl-2-keto-
2,3-dihydropyrimidine.

Experimental Part.

Acetylacetone-urea (1).—The method of preparation was, in general, that described by Stark.[1] Ten grams of urea were dissolved in 160 grams of alcohol and to the cooled solution 10 grams of acetylacetone and 30 grams of concentrated sulfuric acid added as quickly as possible. The well-mixed solution (set aside in ice-box) deposited crystals within a few hours; all told, about 12 grams of the sulfate salt were obtained. When a solution of this sulfate is boiled for a few minutes with barium carbonate and the clear filtrate evaporated nearly to dryness over a water bath, there separate, upon standing, large yellow prisms of the acetyl-acetone-urea [1], containing two molecules of water of crystallization.

4,6-Dimethyl-2-keto-2,3-dihydropyrimidine (3).—When the reaction-mixture just described for the preparation of acetylacetone-urea is set aside in the dark and the salt separating out dissolved in a small quantity of water and digested with an emulsion of freshly precipitated barium carbonate, a clear filtrate, free from sulfate-ion, is easily obtained. This solution, by spontaneous evaporation in the absence of light, gives beautiful colorless crystals of the dimethylketopyrimidine.

0.4782 gram air-dried salt lost over $CaCl_2$ 0.1082 gram H_2O.

Calculated for $C_6H_8ON_2.2H_2O$: H_2O, 22.50%. Found: H_2O, 22.62%.

The colorless product, just as the colored product, contains exactly two molecules of water of crystallization. The two products, as already stated, differ scarcely at all in crystalline form. de Haan describes them as monoclinic, but in the case of the colorless, there is a slightly greater difference in the angles between the faces in the zone of the ortho-diagonal than in the other. They each melt at 197°.

A potassium salt can be prepared from an aqueous solution of these products. It is, however, completely decomposed by the action of carbon dioxide in the air. The application of Hinsberg's test by warming a small quantity of these products with benzene sulfochloride and sufficient alkali, gave no appreciable quantity of oily or insoluble matter. The white insoluble silver salt is readily prepared by adding silver nitrate to an aqueous solution of either the yellow or colorless products. The red crystalline substance, obtained by action of methyl iodide upon the silver salt, suspended in methyl alcohol, is very soluble in water. It showed

[1] *Ber.*, **42**, 699 (1909).

reactions for an iodide and is undoubtedly a methyl addition product of the trimethylketopyrimidine first formed. Mercuric chloride also gives an insoluble salt with the pyrimidine. Platinic chloride does not give an addition product.

Acetylacetone-urea Methyl Iodide Addition Product.—$C_6H_8ON_2.CH_3I$.—One gram of the well dried yellow acetylacetone-urea was dissolved in 10 to 25 cc. of methyl alcohol and a few grams of methyl iodide added. The contents of the flask were heated to boiling for an hour or two under a reflux condenser, and afterwards allowed to evaporate in vacuum desiccator. The colorless crystals of the addition product slowly separate, but upon standing in the air, readily develop a red color. The yield was 1.9 grams, or 88% of the theoretical value.

<p style="text-align:center">Calculated for $C_7H_{11}ON_2I$: I, 47.71; found: 47.83.</p>

Methylation of Acetylacetone-urea.—As previously stated, the action of methyl iodide upon the silver salt of the dimethylketopyrimidine, as well as the action of dimethyl sulfate upon this substance, gave no satisfactory results, owing to the formation of addition products and deep coloration which these underwent. The use of diazomethane, however, proved most satisfactory. In accordance with the method of v. Pechmann[1] the yellow vapors of diazomethane were led into a cooled chloroform solution of the dried acetylacetone-urea and the vessel stoppered and allowed to stand for an hour or two. Upon spontaneous evaporation of the solution in a vacuum desiccator, colorless crystals of the free trimethylketopyrimidine were obtained. Recrystallized from benzene, the product melted at 63° and proved identical in all other respects with the trimethylketopyrimidine prepared from methylurea and acetylacetone as described below. When the two were mixed the melting point of the mixture remained constant at 63°.

Condensation of Methylurea with Acetylacetone.—Six grams of methyl urea and 9 grams of acetylacetone were dissolved in 30 cc. of alcohol and cooled. To this mixture, 30 grams of concentrated sulfuric acid were added and the flask with its contents set aside in a cool place. The further addition of a little alcohol, in the course of a day or two, increases somewhat the total precipitation of crystals. At the end of three days 16.6 grams of crystalline product had separated. This product, a sulfate, was dissolved in a small quantity of water and the solution neutralized with sodium hydroxide, and then extracted with chloroform. From the chloroform extract 9.4 grams of the colorless base were obtained, *i. e.*, practically 84% of the theoretical amount of trimethylketopyrimidine possible from the weight of methylurea taken. In the form of sulfate, this product crystallizes well from alcohol.

<p style="text-align:center">H_2SO_4 calculated for $C_7H_{10}ON_2.H_2SO_4$: 41.53; found: 41.89.</p>

[1] *Ber.*, **28**, 851 (1895).

The condensation of methylurea and acetylacetone was also conducted in the presence of only sufficient sulfuric acid to form the calculated amount of sulfate, and at the same time an excess of the urea (2 mol) used. It was hoped that, by this means, a compound of the type described by Evans as a diurimido derivative might be prepared. In all cases the crystalline product obtained was no greater in weight than that where molecule to molecule was used. By analysis, the salt, crystallized from alcohol, accorded with the previous results:

H_2SO_4 calculated for $C_7H_{10}ON_2.H_2SO_4$: 41.53; found: 41.98.

We may conclude, therefore, that the pyrimidine ring is formed at once in this acid reaction-mixture. The free substances obtained by neutralizing the sulfate salt, obtained either by the use of concentrated acid or by this latter method, melted at the same point, 63°, and proved identical. 3,4,6-Trimethyl-2-keto-2,3-dihydropyrimidine is readily soluble in water, alcohol, chloroform, acetone or acetic ester; fairly soluble in ether, benzene, carbon disulfide; and insoluble in ligroin. It crystallizes well from benzene and melts at 63°.

0.2055 gram substance gave 0.4593 gram CO_2 and 0.1387 gram H_2O.
0.1634 gram substance gave 30.9 cc. N_2 (25°, 739.3 mm. over H_2O).

Calculated for $C_7H_{10}ON_2$: C, 60.82; H, 7.30; N, 20.31.
Found: C, 60.95; H, 7.55; N, 20.53.

This product of condensation, as before stated, is identical with the trimethylketopyrimidine obtained by methylation of acetylacetone-urea. It is, however, in a much purer form, requiring but one or two crystallizations for final purification.

The preparation of this trimethylketopyrimidine, by condensation in the presence of hydrochloric acid, was found equally as practical as with sulfuric acid, but with a somewhat longer period of time necessary. The hydrochloride salt crystallizes well from alcohol in colorless prisms.

Calculated for $C_7H_{10}ON_2.HCl$: HCl, 20.88; found: 20.78.

Zeisel's method, for the determination of methoxyl groups, gave negative results with this trimethylketopyrimidine, but at high temperatures, 200–300°, Herzig and Meyer's method succeeded in driving off methyl iodide sufficient to indicate that, at least, one methyl group attached to a nitrogen atom was present in the molecule.

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THE RELATION BETWEEN THE BOILING POINT AND COMPOSITION OF A MIXTURE OF ETHYLIODIDE AND ETHYL ALCOHOL.

By SARAT CHANDRA JANA AND JITENDRA NATH SEN GUPTA.

The boiling points, or the vapor pressures, of mixtures of liquids have been determined by many investigators. For non-miscible liquids, such