# Mechanistic Studies in the Chemistry of Urea. Part 8.[1] Reactions of Urea, 1-Methylurea, and 1,3-Dimethylurea with Some Acyloins and Butane-2,3-dione (Diacetyl) in Acid Solution

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Urea and 1-methylurea react with both aromatic and aliphatic acyloins to form 4-imidazolin-2-ones but, under the same reaction conditions, 1,3-dimethylurea does not react. However, 1,3-dimethylurea does react with diacetyl to form 4,4'-methylenebis-(1,3,5-trimethyl-4-imidazolin-2-one) (4a). The carbon atom lost in the formation of (4a) is eliminated as formaldehyde. We propose a reaction mechanism which involves formation of an oxetan ring. With 1-methylurea and urea the main products of reaction with diacetyl are the bicyclic compounds (6a—c). However, it is possible that reactions analogous to that leading to the formation of (4a) also occur and that the carbonium ion (5c) is the coloured species formed in the well known colorimetric procedure for the determination of urea concentrations in biological liquids.

In this series of reports on the reactions of urea and *N*-alkylureas with dicarbonyl compounds we come now to consider reactions with butane-2,3-dione (diacetyl). The unexpected products obtained posed a number of mechanistic problems and occasioned a study of the acid-catalysed reactions of urea and *N*-methylureas with a number of acyloins. These simpler reactions will be reported first.

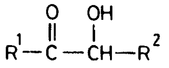
## RESULTS AND DISCUSSION

Acyloins are known [2,3] to react with ureas in the presence of an acid to give 4-imidazolin-2-ones but the success of this reaction appears to depend upon both *N*-methylation of the urea and substitution of the acyloin. We therefore investigated the reactions of urea, 1-methylurea, and 1,3-dimethylurea with various acyloins under standard conditions, *i.e.* in refluxing benzene with added trifluoroacetic acid (TFA). Detailed spectral data of the products are given in the Experimental section.

(a) *Acetoin* (1a).—Reaction with urea proceeds readily to give the expected product 4,5-dimethyl-4-imidazolin-2-one (2a).[2] With 1-methylurea we obtained 1,4,5-trimethyl-4-imidazolin-2-one (2b), which was identified mainly from the $^{13}$C n.m.r. spectrum which showed the present of two nearly identical methyl groups, one *N*-methyl group, two olefinic carbons with slightly different shifts, and one carbonyl carbon. The formation of (2b) does not agree with the statement [4] ' the acyloins of the aliphatic series (which) fail to react with substituted ureas '. However, there was no reaction between acetoin and 1,3-dimethylurea.

(b) *Propionoin* (1b).—Reaction with urea gave the expected product, *viz.* (2c), which was identified by spectral data. With 1-methyl- and 1,3-dimethyl-urea unreacted starting material was recovered. Lack of reaction with the former, when compared to reaction with acetoin, must be due to increased steric factors.

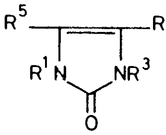
(c) *α-Hydroxybenzyl Methyl Ketone* (1c).—Reaction with urea gave the expected product (2d). All the spectral data are consistent with this structure. There was also reaction with 1-methylurea but, as the acyloin is unsymmetrical, there is the problem of the position of the *N*-methyl group. In the $^{1}$H n.m.r. spectrum of (2b) the protons of the *N*-methyl group have a chemical shift of δ 3.12, while those of the present compound are at δ 2.48. This upfield shift suggests that the methyl group is adjacent to the phenyl group with consequent magnetic shielding. The product is, therefore, (2e).



$$R^1-\overset{\overset{O}{\|}}{C}-\overset{\overset{OH}{|}}{CH}-R^2$$

(1)

a; $R^1 = R^2 = Me$
b; $R^1 = R^2 = Et$
c; $R^1 = Me, R^2 = Ph$
d; $R^1 = R^2 = Ph$



(2)

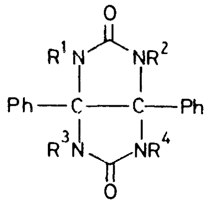
a; $R^1 = R^3 = H, R^4 = R^5 = Me$
b; $R^1 = R^4 = R^5 = Me, R^3 = H$
c; $R^1 = R^3 = H, R^4 = R^5 = Et$
d; $R^1 = R^3 = H, R^4 = Me, R^5 = Ph$
e; $R^1 = Me, R^3 = H, R^4 = Me, R^5 = Ph$
f; $R^1 = Me, R^3 = H, R^4 = R^5 = Ph$

All the other spectral data are in agreement with this assignment.

1,3-Dimethylurea did not react with α-hydroxybenzyl methyl ketone.

(d) *Benzoin* (1d).—Reaction with urea gave a product which was identical with that (3a) obtained by reaction of urea and benzil. This had been prepared and characterised previously.[5] Benzoin is known to be oxidised readily to benzil and this is the simplest explanation of the above observation. With 1-methylurea the situation is more complicated. The product, which is insoluble in every solvent suitable for recrystallisation, did not melt sharply. This suggested that it was a mixture. Benzil is known to react with 1-methylurea to give (3b) [5] but the $^1$H n.m.r. spectrum of the product had chemical shifts of $\delta$ 2.96 and 3.14, corresponding to two different *N*-methyl groups, only one of which is right for (3b). We assume that this is due to concomitant formation of (2f) and (3b). The mass spectrum of the product had peaks at *m/e* 250 and 322, which are molecular ion peaks for the two products. Other spectral data were not diagnostic. It appears that reaction of benzoin with 1-methylurea occurs at a rate similar to that of oxidation to benzil.

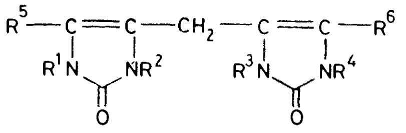
Under the experimental conditions there was no reaction between benzoin and 1,3-dimethylurea, although it is claimed [4] that reaction can occur to give 1,3-dimethyl-4,5-diphenyl-4-imidazolin-2-one. Our results do not support the view that, in reaction with *N*-substituted ureas, acyloins of the aliphatic series react differently from those of the aromatic. The simplest explanation for the lack of reactivity of 1,3-dimethylurea is a steric one.



(3)

a; $R^1 = R^2 = R^3 = R^4 = H$

b; $R^1 = R^3 = H$, $R^2 = R^4 = Me$



(4)

a; $R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = Me$

b; $R^1 = R^4 = Me$, $R^2 = R^3 = H$, $R^5 = R^6 = Ph$

c; $R^1 = R^4 = H$, $R^2 = R^3 = Me$, $R^5 = R^6 = Ph$

d; $R^1 = R^3 = Me$, $R^2 = R^4 = H$, $R^5 = R^6 = Ph$

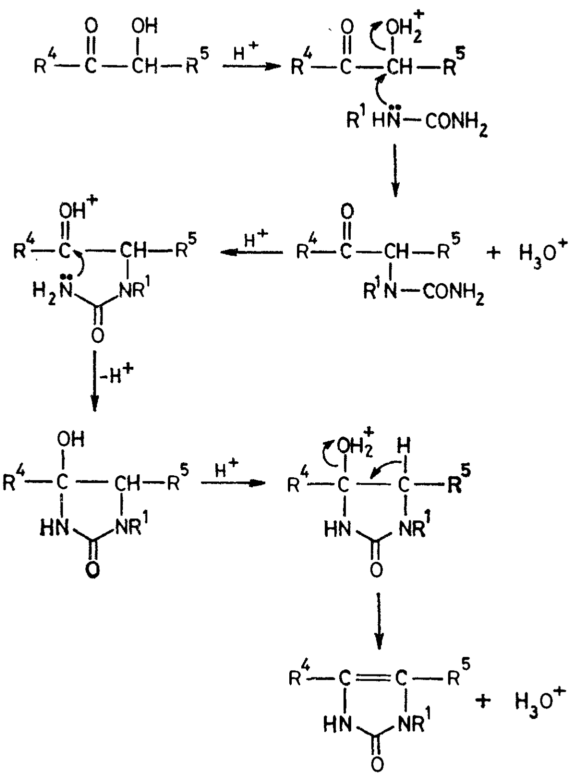
e; $R^1 = R^3 = Me$, $R^2 = R^4 = H$, $R^5 = R^6 = Me$

f; $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6 = Me$

We propose a general mechanism, shown in Scheme 1, for the reaction of urea with acyloins in the presence of an acid. As with other reactions in this series, the driving force is the elimination of the elements of water whenever this is possible. In Scheme 1 we have shown attack of the hydroxy-bearing carbon atoms preceding attack at the other carbon. The reverse may occur, but the last step in both cases is loss of the elements of water to form a double bond. As formation of (2e) occurs, rather than the other isomer, it appears that the greater basicity of the methylated nitrogen is more significant than any steric hindrance.

All the imidazolin-2-ones prepared, apart from (2f), gave intense colours in acid solution. We are not, at present, able to explain this effect.

We now turn to a consideration of the reaction of 1,3-dimethylurea with butane-2,3-dione. Refluxing the reactants in benzene and TFA resulted in formation of water and a purple solution. Removal of solvent left a viscous mass, which was purified by column chromatography to yield crystals. This material has a molecular formula of $C_{13}H_{20}N_4O_2$ and must be formed from the condensation of two molecules of 1,3-dimethylurea and two molecules of butane-2,3-dione with elimination of four molecules of water and *one carbon atom.* In Part 5 we reported [6] that a similar reaction occurred between 1-phenylpropane-1,2-dione and 1-methylurea, and Kuono and Ueda [7] reported a similar reaction with t-butylurea.



SCHEME 1

The i.r. spectrum of the product suggested the presence of carbonyl groups and carbon–carbon double bonds. The 360 MHz $^1$H n.m.r. spectrum was unexpectedly simple: two pairs of *N*-methyl groups ($\delta$ 2.89 and 2.81), two identical methyl groups ($\delta$ 1.68), and a methylene group at low field ($\delta$ 3.25). This gives the correct total of 20 protons. The $^{13}$C n.m.r. spectrum was equally simple, with only six resonances; this suggested a symmetrical molecule. Apart from the peaks assigned to the methyl groups, the *N*-methyl groups, and the carbonyl groups, there are two others at $\delta$ 112.60 and

115.03 p.p.m. These are correct for carbons of an unsymmetrical double bond. The remaining resonance was at δ 19.00 p.p.m., and in the off-resonance spectrum became a triplet and was identified as that due to the methylene group. As the peak in the $^1$H n.m.r. spectrum is not split by geminal coupling, the methylene group appears not to be part of a ring.

There are several structures of different degrees of credibility, analogous to those shown in Part 5,[6] which are consistent with the spectral data. Fortunately discussion of their relative merits can be avoided as we have an *X*-ray crystal structure of the product.[8] It is 4,4′-methylenebis-(1,3,5-trimethyl-4-imidazolin-2-one) (4a). This molecule has all the features deduced from the spectral data; it is also symmetrical.

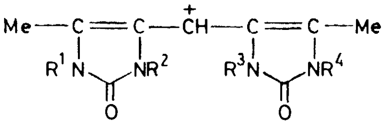
We can now propose a definite structure for the product of reaction of 1-methylurea and 1-phenylpropane-1,2-dione, which we were not able to do when Part 5 [6] was written. The proposed structure is (4) with $R^5 = R^6 =$ Ph, but it is difficult to be certain about the relative positions of the two *N*-methyl groups. There are three possibilities, (4b—d). In the 360 MHz $^1$H n.m.r. spectrum two different *N*-methyl groups are indicated with δ 1.19 and 1.50. This could mean (4d) or a mixture of (4b and c). As the integrals for the two peaks are different, (4d) is not possible and we must have a mixture containing unequal amounts of (4b and c). This is confirmed by two unequal peaks at δ 3.01 and 3.13, corresponding to two different methylene groups. The discussion (see later) concerning the mechanism of formation of (4a) applies to that of (4b and c).

The reaction mixture from which (4a) was obtained was deep purple and we found we could generate this coloured material from (4a). Acidification of an aqueous solution gave a purple solution, the intensity of which increased with time. The rate of colour intensification was increased by blowing oxygen through the solution and by addition of an oxidising agent. Compound (4a) is a ‘ skipped ’ diene and therefore readily susceptible to radical oxidation at the methylene group to give a hydroperoxide.[9] Protonation of this and elimination of hydrogen peroxide would give the carbonium ion (5a), which is related to the cyanine dyes. The positive charge can be delocalised on one of the two outer nitrogens with formation of a conjugated, chromophoric system. This, we suggest, is the origin of the colour. The reaction is analogous to the generation of the tropylium ion from cycloheptatriene by autoxidation in strong acid.[10]

A solution of (4a) in chloroform is initially colourless but turns purple on standing. Chloroform normally contains some acid due to oxidation. Formation of colour is diminished if light and oxygen are excluded. However, addition of phosphorus pentachloride (a Lewis acid) resulted in immediate production of the colour. Lewis acids generate carbonium ions and are known to convert cycloheptatriene into the tropylium cation.[11]

Formally (5a) is generated from (4a) by removal of a hydride ion and further proof of the identity of the coloured species came from the reaction of (4a) with triphenylmethyl perchlorate.[12] The colour appeared immediately. Thus, formation of (5a) is proved beyond doubt and we now know what highly coloured species may be formed by reaction of ureas with α-diketones.

Urea and 1-methylurea do not react with butane-2,3-dione in the same manner as 1,3-dimethylurea. With 1-methylurea a crystalline product was obtained, of formula $C_8H_{14}N_4O_2$. The same product was obtained by reaction in ethanol saturated with HCl. This compound results from the reaction of two molecules of 1-methylurea with one molecule of the dione and elimination of two molecules of water.

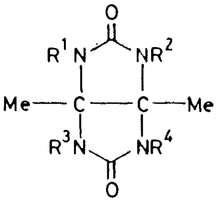


(5)

a; $R^1 = R^2 = R^3 = R^4 = Me$

b; $R^1 = R^3 = Me,\ R^2 = R^4 = H$

c; $R^1 = R^2 = R^3 = R^4 = H$



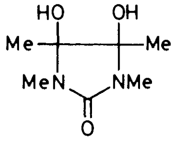
(6)

a; $R^1 = R^4 = Me,\ R^2 = R^3 = H$

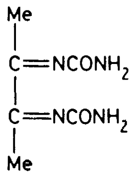
b; $R^1 = R^3 = Me,\ R^2 = R^4 = H$

c; $R^1 = R^2 = R^3 = R^4 = H$

The i.r. spectrum indicated the presence of NH and carbonyl groups. The $^1$H n.m.r. spectrum was rather complex with seven singlets. These we ascribe to three methyl groups, two *N*-methyl groups, and two NH groups. The spectrum could indicate an unsymmetrical molecule or a mixture of isomers. We propose the latter, (6a and b). In (6a) the two methyl groups are identical but in (6b) they differ. Each contains only one type of *N*-methyl and NH group. These structures were confirmed by the $^{13}$C n.m.r. spectrum of the product. There is evidence for two different carbonyls (one in each isomer) and five peaks in the range δ 16.23—28.00 p.p.m. corresponding to the five different methyl groups. There were three different tertiary carbons (the peaks



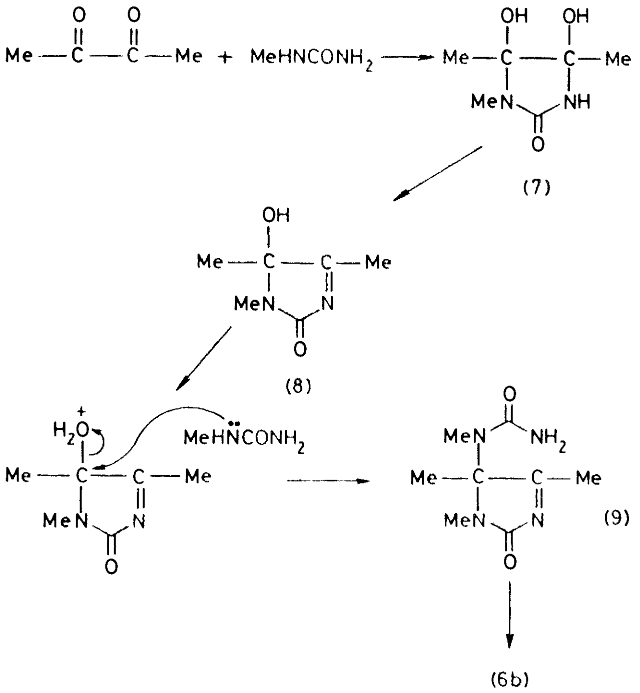
(10)



(11)

remained as singlets in the off-resonance spectrum) at δ 78.56, 82.34, and 86.62 p.p.m., one in (6a) and two in (6b).

We propose a mechanism for the formation of (6b) (Scheme 2) which is similar to that suggested previously[5] for the reaction of 1-methylurea with benzil. The crucial intermediate is (8), formed by elimination of water in acid conditions from the diol (7). If (8) is protonated on the hydroxy-group a good leaving group (water) is formed and displacement by a second 1-methylurea molecule forms (9). Ring closure occurs by addition across the carbon–nitrogen double bond, probably by *N*-protonation and generation of a carbonium ion which reacts with the nucleophilic $NH_2$ group. Attack of protonated (8) by the other end of the 1-methylurea molecule gives (6a), rather than (6b), and so the mixture of isomers is explained.



Scheme 2

The intermediacy of (8) explains why 1,3-dimethylurea does not form a product analogous to (6). The diol (10) cannot eliminate water to give a double bond in the ring. Thus, this reaction pathway is blocked and an entirely different one gives (4a) as the main product. A similar effect was noted in the reaction of 1,3-dimethylurea with benzil[5] and with 1-phenylpropane-1,2-dione.[6] With the former a hydantoin formed, while the latter gave a spiro-compound. With urea products analogous to (6) were obtained.

Reaction of urea with butane-2,3-dione under the same reaction conditions gave a white crystalline material of molecular formula $C_6H_{10}N_4O_2$. Lugosi *et al.*[13] suggested structure (11) for this material but there is evidence against this. It was difficult to obtain spectral data for the product as it is insoluble in the usual organic solvents. However, it does dissolve in TFA and the material may be recovered unchanged from this solvent. In the $^{13}C$ n.m.r. spectrum there is only one resonance at low field (the carbonyl group) but (11) requires a second due to the C=N group. There is, however, a tertiary carbon at δ 80.6 p.p.m.. These data are consistent with (6c) which is the analogue of the product obtained from 1-methylurea. Other spectral data are consistent with this structure. A mechanism analogous to that of Scheme 2 explains the formation of (6c).

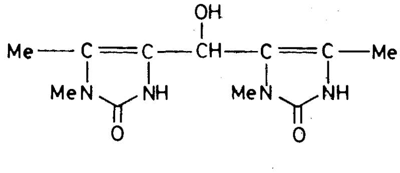
The filtrate obtained after the removal of the mixture of (6a and b) and of (6c) from the reaction mixture was highly coloured and suggested formation of another reaction product. In view of our identification of the coloured material obtained by reaction of 1,3-dimethylurea as the carbonium ion (5a), it seems probable that the above colours are due to (5b and c). As will be seen later in the discussion of the mechanism of formation of (4a), there is nothing to stop urea and 1-methylurea reacting in the same way. However, we were unsuccessful in isolating and characterising (4e or f) from the coloured filtrates. It is possible that carbonium ion formation is complete and neither (4e or f) is present. With the reaction of 1,3-dimethylurea some (4a) must remain unchanged, although the colour of the solution does indicate that (5a) forms spontaneously. With 1-methylurea and urea the main products of reaction are, of course (6a—c); these are highly insoluble and immediately removed from the reaction mixture, leaving little material to form (4e and f).

Some evidence was obtained for formation of (5b). Removal of solvent from the filtrate left a yellow gum which did not crystallise, but a cream solid was obtained on neutralisation of a methanolic solution by aqueous ammonia and addition of acetone. As this material was filtered off it became dark brown on contact with air. However, this was avoided when filtration was carried out under dry nitrogen. Once the material was obtained dry it was stable in a tightly sealed container. Addition of a little of this material to water produced a deep golden solution. It was found to be insoluble in all the regular organic solvents and, therefore, we were unable to purify it by recrystallisation.

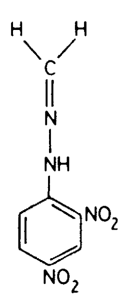
The material was hygroscopic, as well as impure, and no meaningful elemental analysis could be obtained. The $^1H$ n.m.r. spectrum (in $D_2O$) had only peaks corresponding to methyl groups and *N*-methyl groups and there was a very large $H_2O$ peak. The i.r. spectrum (KBr disc) had a broad peak in the NH–OH region and another in the C=C–C=O region. Alkaline potassium permanganate was decolorised by a solution of the material, suggesting the presence of carbon–carbon double bonds. We suggest that the material isolated is the methanol (12), probably as a hydrate, which, in solution, forms the coloured carbonium ion (5b).

There is support for this from the $^{13}C$ n.m.r. spectrum in aqueous solution. There are peaks centred at δ 26.07, 55.26, 60.41, and 161.51 p.p.m. corresponding to methyl, two *N*-methyl groups, and the carbons of the double bond which, because of the positive charge, have all moved down field from the equivalent values in (4a). The carbonium ion centre and the carbonyl group did not appear in the spectrum.

We were equally unsuccessful in obtaining positive direct identification of the coloured product obtained by reaction of urea and butane-2,3-dione. Repetition of the isolation procedure described above yielded a cream solid which was hygroscopic, air-sensitive, and soluble only in water. However, we are sure that the colour is due to (5c), partly because of the evidence adduced for the formation of (5a), and partly because we have found it impossible to find any other suitable chromophoric system which can form from urea and an α-diketone. This identification is important as reaction between urea and diacetyl mono-oxime in acid is used as a colorimetric procedure for the measurement of urea concentrations in biological liquids during medical diagnosis.[14] The method is widely used and appears to be highly specific for urea. Until now the chemistry has been unknown. In acid solution the mono-oxime is hydrolysed to the diketone which then, we suggest, reacts with urea to form (4f). Radical oxidation of (4f) in acid solution generates the coloured species (5c). In the very dilute solutions used in biological assays (6c) is not precipitated. When (6c) is dissolved in concentrated acid it is converted into (5c).



(12)



(13)

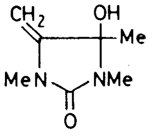
We now come to propose a reaction mechanism for the formation of (4a) from butane-2,3-dione and 1,3-dimethylurea. Anything said in this section applies equally to the formation of (4b—f) from the appropriate diketone and urea. The first problem is the fate of the missing carbon atom. Evolution of carbon dioxide was detected during the course of the azeotropic distillation but this could have resulted from elimination of formaldehyde, oxidation to formic acid, and decomposition at the temperature of refluxing benzene.

Reaction between butane-2,3-dione and 1,3-dimethylurea does proceed in aqueous sulphuric acid at room temperature and $^{13}$C n.m.r. evidence shows that the product is again (4a). We attempted to demonstrate formation of formaldehyde in this reaction mixture by blowing through nitrogen and passing this gas into a solution of dimedone, but the result was negative. However, it is known [15] that, in acid solution, formaldehyde forms a stable trimer and this may not be removed from the reaction mixture by the passage of nitrogen.

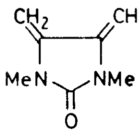
However, we were successful in isolating the 2,4-dinitrophenylhydrazone (DNP) of formaldehyde (13) from the reaction mixture. An excess of 1,3-dimethylurea was used so that no unchanged butane-2,3-dione, which could itself form a DNP, remained. Addition of 2,4-dinitrophenylhydrazine to the reaction mixture after 1 h yielded a yellow solid which was identified as the DNP of formaldehyde by a comparison of its $^{1}$H n.m.r. spectrum whth that of an authentic sample. There is a characteristic double doublet centred at δ 6.95 p.p.m. due to geminal coupling of the methylene group of (13). We think, therefore, that the reaction mechanism involves elimination of formaldehyde. There are precedents for this in related reactions. The Friedel–Crafts reaction of anisole with 2-t-butyloxiran to give 2-(4-methoxyphenyl)-2-methylbutane involves loss of a methylene group as formaldehyde.[16]

Obviously formation of (4a) involves a number of intermediates. We attempted to detect some of these by examination of the $^{13}$C n.m.r. spectra of the reaction mixture taken at intervals during 5 h. However, it transpired that reaction is complete after 0.5 h, the time taken to collect the first spectrum. This spectrum did contain a few peaks in the range δ 84—103 p.p.m., in addition to those expected for (4a), and these can be assigned to polymers of formaldehyde. The same peaks were noticed in the spectrum of acidified formalin.

In considering other reactions of urea with diketones we have suggested [5,6] that the first product of reaction is a diol, (10) in this reaction, and that further reaction is governed by the tendency of such compounds to eliminate the elements of water in the presence of acid. The intermediate (10) cannot form a double bond in the ring but can form one, or two, exocyclic double bonds, to give (14) or (15). The second of these cannot be the key intermediate as such a compound could not occur in the routes to (4b—d). On the other hand, compounds of type (4) form only if at least one substituent on the diketone is a methyl group and so (14) is a possible intermediate.



(14)

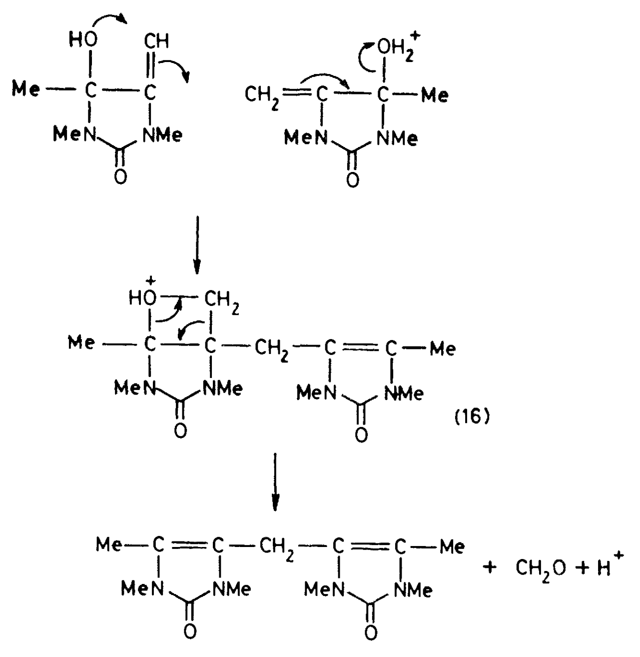


(15)

Compounds of type (4) are 4-imidazolin-2-ones which, as we have shown, form readily under our experimental conditions, from acyloins and urea. However, there are two reasons why we reject the intermediacy of acyloins in a mechanism for the formation of (4) from a diketone. First, conversion of a diketone to an acyloin requires reduction and our conditions are, if anything, oxidising. This is evidenced by the reaction of urea with benzoin, where products from reaction with benzil were obtained. Second, we were unsuccessful in effecting reaction between any acyloin and 1,3-dimethylurea. Compound (4a) forms readily from 1,3-dimethylurea.

Formation of (4a) does not appear to proceed by condensation of two molecules of butane-2,3-dione before reaction with 1,3-dimethyurea. The diketone was refluxed with benzene and TFA for 5 h, much longer than required for formation of (4a), but no water was formed. Apart from some tar, most of the diketone was recovered unchanged. Also, self-condensation is not catalysed by urea as no reaction occurred when 1,3-dimethylurea was replaced by 1,1,3,3-tetramethylurea.

These considerations lead us to suggest that (14) is the crucial intermediate in the formation (4a) and that the departing carbon leaves as formaldehyde. We propose the mechanism shown in Scheme 3. The condensation step is reaction of a molecule of (14) with another molecule which has been protonated to provide water as a leaving group. The driving force is the leaving of water and movement of the double bond, which generates an incipient carbonium ion on the exocyclic methylene group. Reaction of this with the electron-rich double bond of the other molecule of (14) and cyclisation to give an oxetan ring, although not readily predicted, is not unreasonable. The process envisaged is not unlike the acid-catalysed aldol condensation where one molecule of the enol form of acetone reacts with a molecule of the protonated keto-form. Oxetans are known to decompose readily to give a double bond and a keto-compound. In a recent paper [17] intermediate formation of an oxetan ring and decomposition to give a double bond in a steroid system has been proposed. Therefore, loss of formaldehyde from (16) to give (4a) is an expected process. Thus, we can rationalise the formation of (4a) with only the rather unexpected step involving formation of the oxetan ring. We have been unable to find any other reaction mechanism which accounts for the facts in as acceptable a manner.



SCHEME 3

## EXPERIMENTAL

The method of azeotropic removal of water has been described previously. Parentheses in the $^{13}C$ n.m.r. spectra indicate the form in the off-resonance spectrum.

Acetoin (5 ml), urea (3 g), and TFA (3 ml) were refluxed in benzene for 4 h. On cooling a solid separated and the crystals of 4,5-dimethyl-4-imidazolin-2-one (2a) were washed with acetone (yield 80%), m.p. 290° (decomp.) [lit.,[2] 290° (decomp.)], *m/e* 112 ($M^+$), $\nu_{\text{max.}}$ (mull) 3 130 (NH), 1 685 (C=O), and 1 665 $cm^{-1}$ (C=C), $\delta_H$ (TFA) 2.14 (6 H, s) and 9.96 (1 H, s), $\delta_C$ (TFA) 8.7 (q), 119.5 (s), and 151.2 (s) p.p.m.

A similar reaction with 1-methylurea gave 1,4,5-*trimethyl-4-imidazolin-2-one* (2b) (yield 70%), m.p. 185°, *m/e* 126 ($M^+$), $\nu_{\text{max.}}$ (mull) 3 150 (NH), 1 685 (C=O), and 1 650 $cm^{-1}$ (C=C), $\delta_H$ ($CDCl_3$) 1.94, 1.98 (6 H, s), 3.12 (3 H, s), and 11.49 (1 H, s), $\delta_C$ ($CDCl_3$) 8.3, 9.20, 26.9 (q), 112.2 (s), 113.8 (s), and 154.6 (s) p.p.m. (Found: C, 56.4; H, 7.85; N, 22.3. $C_6H_{10}N_2O$ requires C, 57.1; H, 8.0; N, 22.2%).

Reaction of urea with propionion gave 4,5-*diethyl-4-imidazolin-2-one* (2c) (yield 75%), m.p. 284°, *m/e* 140 ($M^+$), $\nu_{\text{max.}}$ 3 140 (NH), 1 690 (C=O), and 1 670 $cm^{-1}$ (C=C), $\delta_H$ ([$^2H_6$]DMSO) 1.02 (6 H, t, *J* 8 Hz), 2.22 (4 H, q, *J* 8 Hz), 8.52 (1 H, s), and 9.50 (1 H, s), $\delta_C$ (TFA) 13.9 (q), 18.3 (t), 125.3 (s), and 151.2 (s) p.p.m. (Found: C, 59.7; H, 8.65; N, 19.55. $C_7H_{12}N_2O$ requires C, 59.95; H, 8.6; N, 20.0%).

Reaction of urea with α-hydroxybenzyl methyl ketone gave 4-*methyl-5-phenyl-4-imidazolin-2-one* (2d) (yield 45%), m.p. 290° (decomp.) (lit.,[18] 285°), *m/e* 174 ($M^+$), $\nu_{\text{max.}}$ 3 180 (NH), 1 690 (C=O), and 1 650 $cm^{-1}$ (C=C), $\delta_H$ (TFA) 2.36 (3 H, s) and 7.42 (5 H), $\delta_C$ (TFA) 10.2, 82.6, 85.3, 127.9—132.6, 137.2, and 161.6 p.p.m.

With 1-methylurea the product is 3,4-*dimethyl-5-phenyl-4-imidazolin-2-one* (2e) (yield 55%), m.p. 170°, *m/e* 188 ($M^+$), $\nu_{\text{max.}}$ 3 460 (NH), 1 690 (C=O), and 1 675 $cm^{-1}$ (C=C), $\delta_H$ ([$^2H_6$]DMSO) 0.78 (3 H, s), 2.48 (3 H, s), 7.18—7.32 (5 H, m), and 5.90 (1 H, s), $\delta_C$ ([$^2H_6$]DMSO) 24.4, 24.8, 85.6, 91.9, 126.7, 127.95, 128.1, 139.0, and 158.7 p.p.m. (Found: C, 69.95; H, 6.35; N, 14.7. $C_{11}H_{12}N_2O$ requires C, 70.2; H, 6.4; N, 14.9%).

α-Hydroxybenzyl methyl ketone (1c) was prepared from mandelamide by the method of Hey.[19]

Butane-2,3-dione and 1,3-dimethylurea were allowed to react under reflux for 40 min, benzene and TFA removed by evaporation, and the residue purified by elution from an alumina column (type H) with chloroform. Removal of chloroform left a gum which crystallised on standing and the product was recrystallised from methanol to give 4,4′-*methylenebis-*(1,3,5-*trimethyl-4-imidazolin-2-one*) (4a) (yield 54%), m.p. 218°, *m/e* 264 ($M^+$) $\nu_{\text{max.}}$ (mull) 1 690 (C=O) and 1 660 $cm^{-1}$ (C=C), $\delta_H$ ($CDCl_3$) 1.99 (6 H, s), 3.09 (6 H, s), 3.17 (6 H, s), and 3.58 (2 H, s), $\delta_C$ ($CDCl_3$) 8.41 (q), 19.00 (t), 27.35 (q), 112.60 (s), 115.03 (s), and 153.53 (s) p.p.m. (Found: C, 59.05; H, 7.95; N, 21.3. $C_{13}H_{20}N_4O_2$ requires C, 59.05; H, 7.6; N, 21.2%).

The reaction time for 1-methylurea was 2 h. After removal of benzene and TFA methanol was added to the residue and the solid filtered off. The filtrate was deep orange. The solid was recrystallised from DMSO and washed with acetone to give a mixture of 1,3a,4,7a-*tetramethyl-*(6a) and

1,3a,6,7a-*tetramethyl-tetrahydroimidazo*[4,5-d]*imidazole*-2,5-*dione* (6b) (yield 62%), m.p. 305°, *m/e* 198 ($M^+$), $\nu_{max.}$ 3 290 (NH) and 1 730 cm$^{-1}$ (C=O), $\delta_H$ ([$^2H_6$]DMSO; 100°) 1.39—1.49 (12 H, 3s), 2.61 (3 H, s), 2.78 (9 H, s), 7.33 (3 H, s), and 7.55 (1 H, s), $\delta_C$ (TFA) 16.23, 19.09, 22.25, 26.25, 28.00, 78.56 (s), 82.34 (s), 86.62 (s), 162.78 (s), and 163.25 (s) p.p.m. (Found: C, 48.5; H, 7.3; N, 28.2. $C_8H_{14}N_4O_2$ requires C, 48.45; H, 7.1; N, 28.25%).

The above procedure was repeated for the reaction of urea with butane-2,3-dione to give 3a,7a-*dimethyltetrahydroimidazo*[4,5-d]*imidazole*-2,5-*dione* (6c) (yield 70%), m.p. 348°, *m/e* 170 ($M^+$), $\nu_{max.}$ 3 240 (NH), 1 720, and 1 670 cm$^{-1}$ (C=O), $\delta_H$ (TFA) 1.80 (6 H, s) and 7.30br (2 H, s), $\delta_C$ (TFA) 21.86 (q), 80.64 (s), and 164.10 (s) p.p.m. (Found: C, 42.35; H, 5.95; N, 32.95. $C_6H_{10}N_4O_2$ requires C, 42.4; H, 6.0; N, 32.75%).

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