CATALYTIC ACTIVITY OF MERCURY SALTS IN CERTAIN ELECTROPHILIC REACTIONS OF DIKETENE

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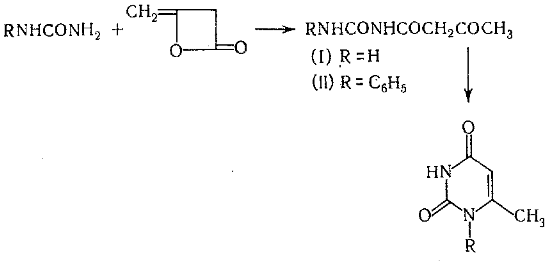
It is known that diketene reacts with weakly basic nitrogen compounds, as a rule, at increased temperature and in the presence of pyridine as a catalyst [1-3]. We have established that under the influence of mercury salts, diketene is also capable of reacting at an appreciable rate at room temperature with such weakly nucleophilic reagents as urea, phenylurea, urethane, and dimedon methylenamine.

In the interaction of diketene with urea and phenylurea in acetic acid solution with an addition of catalytic amounts of $Hg(OOCCH_3)_2$, the ureide (I) and 1-phenylureide (II) of acetoacetic acid are formed in yields of 79 and 55%, respectively. Analogous results are given by the use of HgO and $(CH_3CONH)_2Hg$ as catalysts. In the presence of $HgCl_2$, Hg_2SO_4, $HgSO_4$, and $Hg(NO_3)_2$, on the other hand, acetoacetylation is accompanied by a substantial thermal effect, inducing cyclization of the ureides (I) and (II) to the corresponding uracils (III) and (IV). In addition, BF_3 etherate, H_2SO_4, $ZnCl_2$, $CaCl_2$, $MgSO_4$, $AlCl_3$, $AgNO_3$, $Pb(OOCCH_3)_2$, $Cu(OOCCH_3)_2$, $FeCl_3$, H_2PtCl_6, and $(CH_3)_2Hg$ in acetic acid medium have no appreciable catalytic effect upon the condensation of urea with diketene (3 h, 20°). In the absence of mercury salts, acetoacetylation of urea and phenylurea proceed, as is well known [1, 4], only at increased temperatures and lead to the formation of the uracils (III) and (IV)

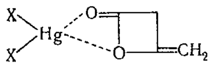


(III) R=H; (IV) R=C_6H_5

The catalytic action of mercury salts can be explained by the formation of a reactive metallic derivative of the type of (V) or by activation of the carbonyl group of diketene in the intermediate complex (VI)

$$O{=}C(NHHgOOCCH_3)_2$$

(V)



(VI)

Some of the experimental data that we obtained are rather convincing evidence in support of the second hypothesis. $Hg(OOCCH_3)_2$ and $HgSO_4$ do not react with urea in acetic acid solution at room temperature during a 24-h contact of the reagents, while under the action of diketene upon a known mercury derivative (V) [5] under normal conditions, the reaction product (III) can be isolated in a yield of only 16% of the theoretical. In addition, mercury salts proved capable of catalyzing the decomposition of diketene in acetic acid medium, forming acetone, acetic anhydride, 2,6-dimethylpyrone, 2,6-dimethylpyronecarboxylic acid, and 2,2,4-trimethyl-6-keto-1,3-dioxene (VIII). These multistep conversions probably proceed with the participation of the mixed anhydride (VII) and acetoacetic acid according to the following scheme

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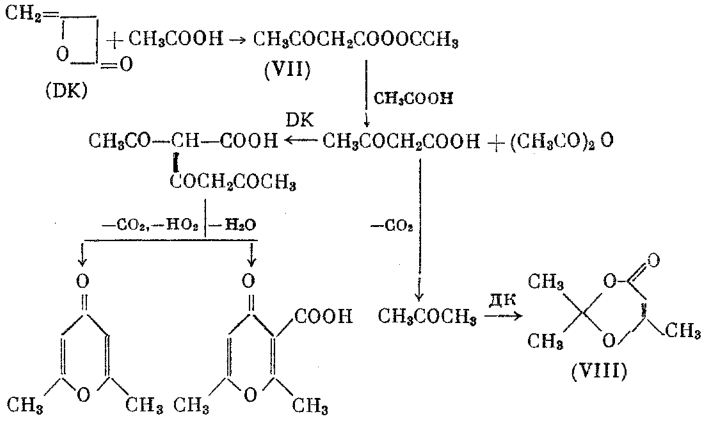
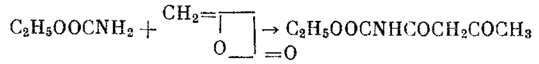
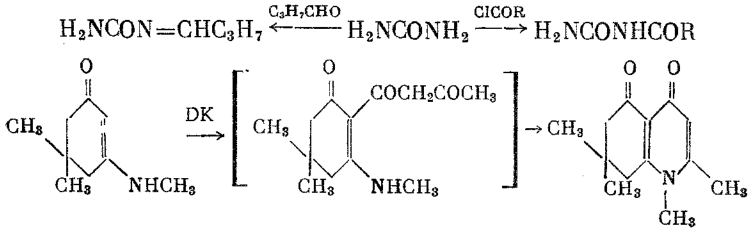


From the literature it is known that when diketene is heated in benzene in the presence of sodium phenolate, a mixture of dihydracetic acid and 2,6-dimethylpyrone is formed [6], while in acetic acid medium in the absence of any catalyst, a mixture of acetone and acetic anhydride is formed [7].

The appreciable catalytic effect of mercury salts can also be noted in the condensation of butyraldehyde and carboxylic acid chlorides with urea, as well as in the reaction of diketene with urethane and dimedon methylenamine





(IX)

From the data of elementary analysis, it follows that acetoacetylation of a dimedon enamine is accompanied by cyclization, and the substance thereby formed evidently possesses the structure (IX).

EXPERIMENTAL

Interaction of Diketene with Urea. To a suspension of 1.5 g urea and 0.2 g $Hg(OOCCH_3)_2$ in 5 ml of acetic acid at ~20° we added 3 ml of diketene. The reaction was accompanied by a slight thermal effect, and the temperature rose by 10°. After 3-h mixing at room temperature, the solution was diluted with ether, and the precipitate was filtered off. We obtained 2.8 g (79%) of the ureide of acetoacetic acid (I) with m.p. 142-144° (in a block preliminarily heated to 120°), which gave no depression of the melting point in a mixed sample with a known specimen (m.p. 146-147°) [1]. In the absence of mercury acetate, diketene does not react with urea under analogous conditions.

To a suspension of 1.5 g urea and 0.19 g $HgSO_4$ in 5 ml acetic acid we added 3 ml of diketene. The reaction proceeded with a substantial evolution of heat, and the mixture began to boil after 10 min. After 3-h standing at room temperature and the treatment described above, we obtained 2.2 g (61%) of 6-methyluracil (III) with m.p. 308-310°, giving no depression of the melting point when mixed with a known sample (m.p. 310-312°) [1].

Interaction of Diketene with Phenylurea. Analogously, from 1.7 g of phenylurea and 1.5 ml diketene in the presence of $Hg(OOCCH_3)_2$ we obtained 1.5 g (55%) of the 1-phenylureide of acetoacetic acid (II) with m.p. 144-145°, giving no depression of the melting point when mixed with a known sample (m.p. 143-144°) [4].

Interaction of Diketene with Urethane. A mixture of 1.8 g of urethane, 1.8 ml of diketene, and 0.42 g of $Hg(OOCCH_3)_2$ was exposed at room temperature for 36 h. After evaporation, the residue was dissolved in 15 ml of ether, and upon cooling to −70°, 0.82 g (24%) of the acetoacetyl derivative of urethane with m.p. 65-71° was isolated. After recrystallization from a mixture of heptane and benzene (3 : 1), the substance melted at 70-73° and gave no depression of the melting point when mixed with a known sample (m.p. 77-78°) [3].

Acylation of Urea. To 3.1 g of acetyl chloride, 0.6 g $Hg(OOCCH_3)_2$, and 1.2 g urea were added with mixing; the temperature of the reaction mixture thereupon rose to 38°; the mixture was left for 12 h at ~20°, then treated with water. A total of 0.7 g (34%) acetylurea with m.p. 208-209° was filtered off; it gave no depression of the melting point when mixed with a known sample (m.p. 210-212°) [2].

From 7.4 g of propionyl chloride, 1.2 g urea, and 0.6 g $Hg(OOCCH_3)_2$, we obtained 0.6 g (25%) propionylurea with m.p. 206-207° under the conditions of the preceding experiment. In the literature, a melting point of 210-211° is cited for propionylurea [2].

Under analogous conditions, but without $Hg(OOCCH_3)_2$ or in the presence of $HgSO_4$, urea does not react with carboxylic acid chlorides.

Interaction of Urea with Butyraldehyde. A mixture of 1 g urea, 5 ml butyraldehyde, and 0.2 g $Hg(OOCCH_3)_2$ was mixed for 30 min at ~20°. The solid reaction product was washed with ether, water, and methanol, yielding 1.8 g (100%) of a polymer substance with m.p. 153-156°, corresponding in composition to monobutyrylideneurea. Found %: C 51.32, 51.41; H 8.71, 8.86; N 24.02, 23.92. $C_5H_{10}ON_2$. Calculated %: C 52.40; H 8.76; N 24.60. Under analogous conditions, but without $Hg(OOCCH_3)_2$, the reaction proceeds in 11% yield.

Production of Dimedon Methylenamine. A mixture of 2.8 g dimedon and 4 ml of 30% aqueous methylamine was exposed for 12 h at ~20°, then evaporated under vacuum, and the residue heated for 30 min at 100°. Yield 2.1 g (70%) of dimedon methylenamine, m.p. 150-151° (ethyl acetate–methanol mixture). Found %: N 9.38, 9.12. $C_9H_{15}ON$. Calculated %: N 9.14.

Interaction of Dimedon Methylenamine with Diketene. A solution of 1.5 g dimedon methylenamine and 1.5 ml diketene in 25 ml of acetic acid was boiled for 3 h. After removal of the solvent, the residue was treated with a mixture of acetone and ether, and the precipitate filtered off. Yield 1.8 g (80%) of a substance with the presumed structure (IX) with m.p. 224-225°. After recrystallization from dioxane, m.p. 227-229°. Found %: C 71.08, 71.11; H 7.88, 7.91; N 6.53, 6.56. $C_{13}H_{17}O_2N$. Calculated %: C 71.20; H 7.80; N 6.39.

To a mixture of 1.2 g dimedon methylenamine and 0.3 g $Hg(OOCCH_3)_2$ in 3 ml acetic acid we added 1.2 ml of diketene, after 3-h standing at 20° and the treatment described above, we obtained 0.9 g (53%) of substance (IX) with m.p. 224-225°. Under the same conditions, but without $Hg(OOCCH_3)_2$, we isolated 0.7 g of contaminated (IX) with m.p. 210-215°.

Decomposition of Diketene in Acetic Acid under the Influence of Mercury Salts. A mixture of 15 ml diketene, 15 ml acetic acid, and 0.2 g $Hg(OOCCH_3)_2$ was kept for 3 days at ~20°, then 16 g of the fraction with b.p. up to 145°, containing acetone, acetic acid, and acetic anhydride, was distilled off. The residue was treated with ether, and the undissolved crystals (3.4 g, m.p. 105-110°) were filtered off and chromatographed on Al_2O_3, activity II. Elution with chloroform yielded 1.7 g of 2,6-dimethylpyrone with m.p. 130-132°, giving no depression of the melting point in a mixture with a known sample (m.p. 130-132°). The mother liquor remaining after removal of the crystalline mixture was evaporated and redistilled under vacuum, yielding 2.4 g of a fraction with b.p. 60-120° (7 mm). When it was chromatographed on Al_2O_3, activity II, we isolated 0.4 g 2,2,4-trimethyl-6-keto-1,3-dioxine (VIII) with b.p. 82-83° (7 mm); n_D^{20} 1.4630; λ_{max} (in alcohol) 248 mμ (ε 5530) (elution with ether) and 1.4 g 2,6-dimethylpyrone with m.p. 130-131° (elution with chloroform). For (VIII) obtained by the reaction of diketene with acetone [8], the following data are cited: b.p. 65-67° (2 mm); n_D^{20} 1.4636; λ_{max} (in alcohol) 247.5 mμ (log ε 3.92). The presence of 2,4-dimethylpyronecarboxylic acid [9] (methyl ether R_f 0.38, Al_2O_3, activity II, system acetone–heptane, 1 : 1) was detected by thin-layer chromatography in the crystalline mixture with m.p. 105-110°. The same compounds are formed in the decomposition of diketene in acetic acid in the presence of $HgSO_4$; however, in this case the reaction is accompanied by a substantial thermal effect.

CONCLUSIONS

Mercury salts exert a catalytic effect upon the acetoacetylation of urea, urethane, and dimedon methylenamine, as well as on the reaction of urea with butyraldehyde and carboxylic acid chloride.

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