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REACTION OF DIMETHYLFORMAMIDE DIETHYLACETAL WITH 2,2-DIMETHYL-4,6-DIOXO-1,3-DIOXANE (MELDRUM'S ACID)

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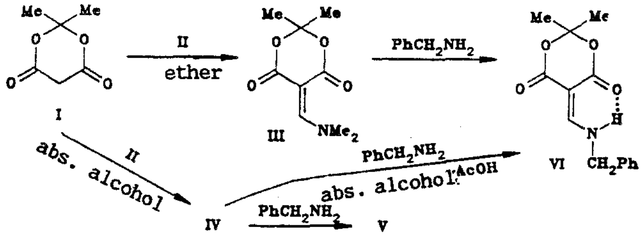
Depending on the conditions of carrying out the reaction of dimethylformamide diethylacetal with the Meldrum's acid, either 2,2-dimethyl-4,6-dioxo-5-(N,N-dimethylaminomethylene)-1,3-dioxane or N,N,N^1N^1-tetramethylformamidinium salt of 2,2-dimethyl-4,6-dioxo-5-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)methylene-1,3-dioxane are formed. The two compounds can react with primary amines to form N-substituted 2,2-dimethyl-4,6-dioxo-5-aminomethylene-1,3-dioxanes.

It is known [2, 3] that 2,2-dimethyl-4,6-dioxo-1,3-dioxane (Meldrum's acid) (I) reacts with dimethylformamide diethylacetal II to form 2,2-dimethyl-4,6-dioxo-5-(N,N-dimethylaminomethylene)-1,3-dioxane (III). In the course of our investigations on the synthesis and properties of different enaminocarbonyl compounds, we studied this reaction in a greater detail.



Under usual conditions, i.e., when acetal II was added to the solution of Meldrum's acid in alcohol, a compound was obtained, which gave the same data of elementary analysis as enamine III, but its melting point was 30°C higher than that described in [2, 3]. In analogy with the products of the reaction of amide acetals with malonitrile [4], we assumed that in this case an ionic compound is obtained, i.e., an N,N,N^1,N^1-tetramethylformamidinium salt of 2,2-dimethyl-4,6-dioxo-5-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)methylene-1,3-dioxane (IV). In the mass spectrum of this compound a peak of ion (A) 296† is observed, which has a molecular weight one unit lower than that of the anionic part of the molecule. On further decomposition, peaks 238 $[A-Me_2CO]^{+\cdot}$, 194 $[A-Me_2CO-CO_2]^{+\cdot}$, 166 $[A-Me_2COCO_2-CO]^{+\cdot}$, 150 $[A-Me_2CO-2CO_2]^{+\cdot}$ are formed, which confirms the suggested structure of the anion of IV. When the sample is heated in an ionic source above 200°C, a peak 101 appears in the spectrum, which probably belongs to the tetramethylformamidinium cation. In the PMR spectrum of compound IV in CD_3OD, proton signals are observed of the 2,2-dimethyl groups at 1.70 ppm, dimethylamino groups at 3.29 and 3.35, a narrow singlet of the CH-anionic part of the molecule at 8.34, and a broadened singlet of the CH proton of the formamidinium cation at 7.80 ppm. It is important that in the solution of salt IV in CD_3OD, there is a slow exchange of the CH proton in the anion for deuterium, and after a week, the intensity of this signal decreases to 30% of the initial one.

It is known [5] that amidines, and especially amidinium salts, readily undergo transmination reactions. This serves as a basis for the preparation of salts of the type of IV, containing different amidinium components as cation. We took the reaction of salt IV with benzylamine as an example, and showed that under mild conditions, a transamination reaction takes place of the cationic part of the molecule with the formation of N-benzyl-N^1,N^1-dimethylformamidinium salt (V). In the PMR spectrum of this salt in CD_3OD, the following

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*For Communication 51, see [1].
†Here and below, the m/z values are given for ion peaks.

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TABLE 1. Characteristics of Compounds Synthesized

Compound	mp, °C*	Found, %			Empirical formula	Calc., %			Yield, % (method)
		C	H	N		C	H	N	
III	125—126	54,3	6,6	7,3	$C_9H_{13}NO_4$	54,3	6,6	7,0	84
IV	158—159	54,5	6,6	7,3	$C_{18}H_{26}N_2O_8$	54,3	6,6	7,0	43
V	144—144,5	59,8	6,2	6,1	$C_{23}H_{28}N_2O_8$	60,0	6,1	6,1	71
VI	167—168	64,5	5,8	5,4	$C_{14}H_{15}NO_4$	64,4	5.8	5,4	82 (A) 90 (B)

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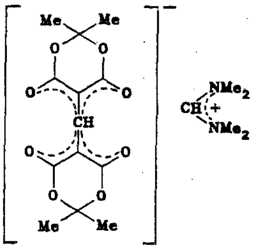
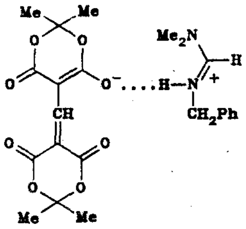
*The solvent for compounds III, V, VI was isopropanol, and for IV a 1:2 mixture of isopropanol and ethyl acetate.

signals are observed: 1.68 (2,2-Me_2); 3.08 and 3.32 (NMe_2); 4.58 (CH_2); 7.37 (Ph), 8.18 (CH-anion) and 8.55 ppm (CH-cation). It is interesting that in this case, when the solution of salt V is held in deuteromethanol, there is no decrease in the signal of the CH-anionic part of the molecule, i.e., no deuterio-exchange is observed. This is probably due to the possible existence in salt V (in contrast to the case with salt IV) of a strong intermolecular hydrogen bond between the cation and anion. The presence of this bond decreases the partial negative charge on the CH-anionic carbon atom, and thus appreciably retards the deutero-exchange. To a certain extent, this supposition is confirmed by the very weak field position of the $\overset{+}{N}H$ group signals in the PMR spectrum (9.46 ppm in DMSO-D_6, 9.67 ppm in $CDCl_3$).



IV



V

In other words, the delocalization of the negative charge in the anionic part of the molecule of IV is much greater than it is in the anion of salt V.

It was interesting to examine the problem of the stability of type IV salts in an acid medium. In this case a reaction with nucleophilic reagents with a cleavage of the C—C bond is possible. In fact, when the reaction of salt IV with benzylamine was carried out under acid catalysis conditions, such a splitting of the C—C bond was observed with the formation of 2,2-dimethyl-4,6-dioxo-5-(N-benzylaminomethylene)-1,3-dioxane (VI).

In compound VI there is an intramolecular hydrogen bond, as indicated by the value of $^3J_{CH,NH}$ = 14.7 Hz, showing a transoid disposition of C—H and N—H protons. The presence of this H-bond is also confirmed by the fairly weak field position of the proton signal of the NH group (δ 9.83 ppm in $CDCl_3$).

And, lastly, in conclusion we found the conditions for carrying out the reaction of the Meldrum's acid I with acetal II, in which enamine III is formed. To obtain compound III, the process should be carried out in a nonpolar solvent, in the absence of excess of acid I. In this case, the reaction proceeds mainly selectively, and compound III is formed in a high yield, although according to the PMR spectroscopy data, under these conditions a small admixture of salt IV is present in the technical grade material.

The enamine III obtained is readily transaminated with benzylamine to form the above described N-benzylenamine VI.

EXPERIMENTAL

The IR spectra were run on a Perkin-Elmer 457 spectrophotometer in mineral oil, and the PMR spectra on a Varian XL-200 spectrometer, using TMS as internal standard. The mass spectra were obtained on a Varian MAT-112 spectrometer with direct introduction of the sample into the ionic source. The temperature of the ionization chamber was 180°C and the energy of the ionizing electrons 70 eV. The melting points were determined on a type Boetius heating stage.

The physical constants, yields, and analytical characteristics of the compounds synthesized are listed in Table 1.

2,2-Dimethyl-4,6-dioxo-5-(N,N-dimethylaminomethylene)-1,3-dioxane (III). A solution of 7.5 g (52 mmoles) of acid I in 22 ml of acetone was added dropwise at 22-25°C to a solution of 19.8 ml of N,N-dimethylformamide diethylacetal (II) in 135 ml of dry ether. The mixture was stirred for 1 h at room temperature, and cooled, and 8.7 g of compound III were filtered. IR spectrum: 1725, 1675 cm^{-1} (C=O). PMR spectrum: ($CDCl_3$): 1.72 (2,2-Me_2); 3.32 and 3.42 (NMe_2); 8.14 ppm (=CH). Mass spectrum: 199 $[M]^{+\cdot}$, 142 $[M-Ch_3COCH_2]^+$, 141 $[M-(CH_3)_2CO]^+$, 98 $[M-(CH_3)_2COCO_2]^{+\cdot}$, 58 $[(CH_3)_2CO]^{+\cdot}$.

N,N,N^1,N^1-Tetramethylformamidinium Salt of 2,2-Dimethyl-4,6-dioxo-5-(2,2-dimethyl-4,6-dioxi-1,3-dioxan-5-yl)methylene-1,3-dioxane (IV). A 12.2 ml portion of acetal II was added dropwise at 20-25°C to a suspension of 8.5 g (59 mmoles) of compound I in 95 ml of absolute alcohol. The mixture was stirred at room temperature for 2 h, 0.6 ml of acetal was added, and stirring was continued for another 1 h 30 min. The mixture was evaporated, the residue was ground with petroleum ether, and then with ethyl acetate, and 10.2 g of compound IV were filtered.

N-Benzyl-N^1,N^1-dimethyl Formamidinium Salt of 2,2-Dimethyl-4,6-dioxo-5-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)methylene-1,3-dioxane (V). A mixture of 3.98 g (10 mmoles) of salt IV, 1.1 ml (10 mmoles) of benzylamine and 25 ml of absolute alcohol was stirred at room temperature for 1 h 30 min, then evaporated, and the residue was ground with petroleum ether, and then with water to yield 2.7 g of salt V.

Evaporation of the aqueous mother liquor and recrystallization of the residue from ethyl acetate gave an additional 0.55 g of compound V.

2,2-Dimethyl-4,6-dioxo-5-(N,benzylaminomethylene)-1,3-dioxane (VI). A. A mixture of 1.99 g (5 mmoles) of salt IV, 1.64 ml (15 mmoles) of benzylamine, catalytic amounts (3 drops) of acetic acid and 20 ml of absolute alcohol was stirred for 3 h at room temperature. The mixture was cooled and 0.2 g of compound VI was filtered. The mother liquor was evaporated, the residue was ground with isopropanol, and an additional 0.88 g of compound VI was obtained.

B. A 1.1 ml portion (10 mmoles) of benzylamine was added dropwise at 25°C to a solution of 1.99 g (10 mmoles) of compound III in 25 ml of absolute alcohol. The mixture was stirred at room temperature for 1 h and 30 min, and cooled, and 2.35 g of compound VI were filtered. IR spectrum: 3260 (NH), 1720, 1665 cm^{-1} (C=O) PMR spectrum ($CDCl_3$): 1.70 (2,2-Me_2); 4.62 (CH_2); 8.23 (=CH); 7.25-7.45 (C_6H_5); 9.83 ppm (NH); $^3J_{NH,CH_2}$ = 6 Hz, $^3J_{NH,CH}$ = 14.7 Hz. Mass spectrum: 261 $[M]^{+\cdot}$, 246 $[M-CH_3]^+$, 203 $[M-(CH_3)_2CO]^{+\cdot}$, 204 $[M-CH_3COCH_2]^+$, 174 $[M^{+\cdot}-(CH_3)_2CO-CHO]^+$, 159 $[M-(CH_3)_2CO-CO_2]^{+\cdot}$, 130 $[M-(CH_3)_2CO-CO_2-CHO]^+$, 91 $[PhCH_2]^+$, 58 $[(CH_3)_2CO]^{+\cdot}$.

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