Some Nucleophilic Addition Reactions of Halogenated 2-Oxetanones (1)

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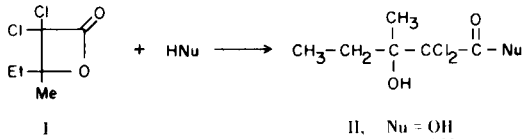
The cycloaddition of halogenated ketenes and carbonyl compounds produces halogenated 2-oxetanones (2). We have recently reported on the decarboxylation of such compounds and the effect the halogen substituents have on decarboxylation (3). The purpose of this report is to describe some nucleophilic addition reactions of some halogenated 2-oxetanones and the effect the halogens have on this reaction.

Many nonhalogenated 2-oxetanones are so susceptible to decarboxylation and/or polymerization when heated or in the presence of certain nucleophiles that nucleophilic addition reactions cannot be studied (4). However, it has been well established that halogenated 2-oxetanones are much less susceptible to decarboxylation and thus are well suited for nucleophilic addition studies (3). 2-Oxetanones can react with a nucleophile to undergo acyl-oxygen cleavage or alkyl-oxygen cleavage. The type of cleavage is usually dependent upon the medium in which the reaction is conducted. Ohse, Palm, and Cherdron have recently reported that 3,3-dimethyl-4-trichloromethyl and 3,3-dimethyl-4-bis-(trichloromethyl)-2-oxetanones react with several different types of nucleophiles and undergo only acyl-oxygen cleavage (5). This cleavage was independent of the nature of the medium of the reaction. The electronegative trichloromethyl substituent in the 4-position is apparently responsible for the exclusive acyl-oxygen cleavage.

We have examined the reaction of 3,3-dichloro-4-ethyl-4-methyl-2-oxetanone with water, methanol and dimethylamine and the reactions occurred as illustrated.

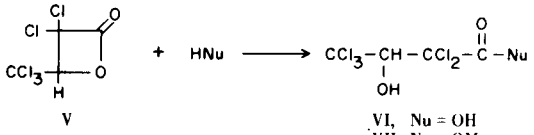


I

II, Nu = OH
III, Nu = OMe
IV, Nu = NMe_2

The reactions paralleled the nucleophilicity of the nucleophiles; *e.g.*, dimethylamine gave a quantitative yield at 0-5°, methanol a 50% yield after 48 hours at 50° and water a 15% yield after 4 days at 60-65°. Some decarboxylation accompanied the hydrolysis reaction.

The reaction of 3,3-dichloro-4-trichloromethyl-2-oxetanone with the same three nucleophiles also occurred to yield only the acyl-oxygen cleavage products as illustrated.



V

VI, Nu = OH
VII, Nu = OMe
VIII, Nu = NMe_2

This 2-oxetanone is considerably more reactive than I. Compound V reacts with dimethylamine at -78° and upon warming to room temperature a quantitative amount of amide is produced. There is some indication of a nucleophilic displacement of a halogen as evidenced by some dimethylamine hydrochloride. Compound V reacts with methanol at room temperature to immediately produce a quantitative yield of ester and with water at 70° in two hours to produce an 80% yield of hydroxy acid.

The exclusive acyl-oxygen cleavage with the two halogenated 2-oxetanones investigated is probably the result of the electronegative substituents increasing the electrophilicity of the carbonyl carbon atom. The increased reactivity of V and the exclusive acyl-oxygen cleavage of the trichloromethyl-2-oxetanones studied by Ohse and coworkers is probably due to the trichloromethyl substituent stabilizing the negative charge on oxygen in the transition state.

The results of this investigation are summarized in the following conclusions:

1. Halogenated 2-oxetanones undergo only acyl-oxygen cleavage.

2. The trichloromethyl substituent in the 4-position of the 2-oxetanone ring exerts a strong influence on the reactivity.

3. The nature of the nucleophile does not influence the type of cleavage but does influence the rate of the reaction.

4. Halogenated 2-oxetanones are more reactive to nucleophilic addition than nonhalogenated 2-oxetanones.

EXPERIMENTAL

3,3-Dichloro-4-ethyl-4-methyl- and 3,3-dichloro-4-trichloromethyl-2-oxetanones were prepared by *in situ* cycloadditions of dichloroketene with methyl ethyl ketone and chloral, respectively as previously described (2,6).

2,2-Dichloro-3-hydroxy-3-methylpentanoic Acid (II).

3,3-Dichloro-4-ethyl-4-methyl-2-oxetanone (0.05 mole) was stirred with 100 ml. of water at 60-65°. After 4 days, the organic layer was separated from the aqueous layer. Vpc analysis of the organic layer revealed some decarboxylation product along with the starting 2-oxetanone. The aqueous layer was slowly evaporated and the hydroxy acid crystallized in a 15% overall yield, m.p. 82°; ir, 1722 cm^{-1}; nmr (deuterioacetone): δ 1.0 (t, 3H), 1.5 (s, 3H), 1.80 (m, 2H), 2.2 (m, 1H).

This acid was converted to the corresponding methyl ester (III).

Methyl 2,2-Dichloro-3-hydroxy-3-methylpentanoate (III).

Compound I (0.05 mole) was added to a stirred 50 ml. portion of methanol at 50°. The progress of the reaction was followed by vpc. After 48 hours, only 50% of the starting 2-oxetanone had disappeared and the corresponding ester formed. Fractional distillation afforded the ester at 53° at 0.25 mm; ir, 1720 cm^{-1}; nmr (deuterioacetone): δ 1.0 (t, 3H), 1.45 (s, 3H), 1.85 (q, 2H), 3.8 (s, 4H).

Anal. Calcd. for $C_7H_{12}Cl_2O_3$: C, 39.90; H, 5.59. Found: C, 39.71; H, 5.62.

N,N-Dimethyl-2,2-dichloro-3-hydroxy-3-methylpentanamide (IV).

Compound I (0.05 mole) was added to a stirred solution of dimethylamine (0.06 mole) in 100 ml. of ether at 0-5°. Upon warming to room temperature, the ether was evaporated and the amide distilled in quantitative yield at 70-75° at 0.5 mm; ir, 1640 and 1670 cm^{-1}; nmr (deuterioacetone): δ 1.0 (t, 3H), 1.45 (s, 3H), 2.0 (q, 2H), 3.25 (m, 6H), 4.65 (s, 1H).

Anal. Calcd. for $C_8H_{15}Cl_2NO_2$: C, 42.11; H, 6.58. Found: C, 42.61; H, 6.62.

2,2,4,4,4-Pentachloro-3-hydroxybutanoic Acid (VI).

3,3-Dichloro-4-trichloromethyl-2-oxetanone (0.05 mole) was stirred with 100 ml. of water at 70°. After 2 hours, the organic layer had gone into solution. The water was slowly evaporated and the acid crystallized from solution in 80% yield, m.p. 180°, ir, 1725 cm^{-1}; nmr (deuterioacetone): δ 2.2 (s, 1H), 5.2 (s, 1H).

Anal. Calcd. for $C_4H_3Cl_5O_3$: C, 17.36; H, 1.08. Found: C, 17.31; H, 0.98.

Methyl 2,2,4,4,4-Pentachloro-3-hydroxybutanoate (VII).

Compound V (0.05 mole) was slowly added to a stirred 50 ml. portion of dry methanol at room temperature. The reaction was exothermic and upon evaporation of the solvent and distillation of the residue, there was obtained a quantitative yield of the ester, b.p. 100° at 0.05 mm; m.p. 72°; ir, 1740 cm^{-1}; nmr (deuterioacetone): δ 3.92 (s, 3H), 5.2 (m, 1H), 7.1 (m, 1H).

Anal. Calcd. for $C_5H_5Cl_5O_3$: C, 20.65; H, 1.72. Found: C, 20.23; H, 1.65.

N,N-Dimethyl-2,2,4,4,4-pentachloro-3-hydroxybutanamide (VIII).

Compound V (0.05 mole) was added to a stirred solution of dimethylamine in 100 ml. of ether at -78°. Upon warming to room temperature, a small amount of amine hydrochloride precipitated from solution. The reaction mixture was filtered and the ether evaporated to yield the crystalline amide, m.p. 123°; ir, 1635 and 1670 cm^{-1}; nmr (deuterioacetone): δ 2.0 (s, 1H), 3.1 (s, 6H), 5.4 (s, 1H).

Anal. Calcd. for $C_6H_8Cl_5NO_2$: C, 23.72; H, 2.63. Found: C, 23.53; H, 2.71.

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(1) Support of this study by the Robert A. Welch Foundation and a North Texas State University Faculty Research Grant is gratefully acknowledged.

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