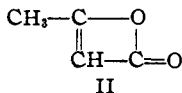
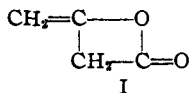


[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

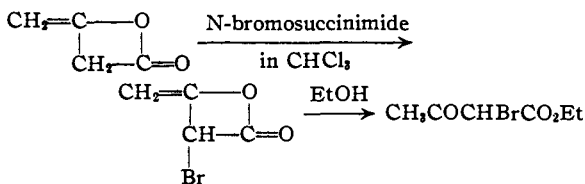
Studies Relating to the Structure of Ketene Dimer¹

BY A. T. BLOMQUIST AND FRANKLIN H. BALDWIN

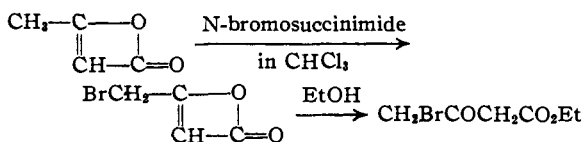
Ziegler's² development of specific reagents for halogenation of the allyl position suggested a useful application in securing additional chemical evidence for the structure of ketene dimer. Consideration of the most reliable evidence to date indicates structures I and II as being the most likely ones for ketene dimer.³



If structure I is the correct representation of ketene dimer, halogenation with Ziegler's reagents should afford halogen derivatives directly convertible to α -haloacetoacetic esters



However, should structure II be the true one for ketene dimer, a similar series of reactions would lead to γ -haloacetoacetic esters

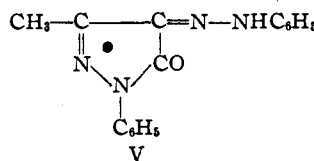
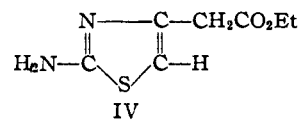
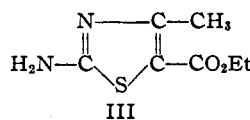


These formulations are, of course, also based on the assumption that Ziegler's reagents halogenate the allyl position in oxygenated unsaturated compounds as in unsaturated hydrocarbons.

Treatment of ketene dimer in chloroform solution with N-bromosuccinimide gave a highly unstable bromo derivative which reacted smoothly with ethyl alcohol to yield exclusively α -bromoacetoacetic ester. Similarly, chlorination with N,2,4-trichloroacetanilide followed by reaction with ethyl alcohol gave only α -chloroacetoacetic ester.

The two α -haloacetoacetic esters were characterized by conversion to two known solid derivatives. Reaction with thiourea gave, in each case, ethyl 2-amino-4-methylthiazole-5-carboxylate (III)⁴ and none of the ethyl-2-aminothiazolyl-4-acetate (IV) derivable from γ -haloacetoacetic

esters.⁵ Phenylhydrazine converted both α -halogen esters into 3-methyl-1-phenyl-4-phenylhydrazono-5-pyrazolone (V).⁶



It is significant that there was no evidence for the presence of γ -haloacetoacetic esters in the reaction products. Although it has been demonstrated that there is no tendency for α -chloroacetoacetic ester to rearrange to its γ -isomer, α -bromoacetoacetic ester may rearrange to γ -bromoacetoacetic ester under certain conditions. The rearrangement of γ -haloacetoacetic esters to the α -isomers has not been observed.⁷

The isolation of the direct products of halogenation of ketene dimer in pure form has not been realized as yet but work along this line is being continued.

Experimental⁸

Materials.—Ketene dimer was prepared as described in "Organic Syntheses."⁹ N-Bromosuccinimide, m. p. 160–161°; was prepared by the method of Lengfeld and Stieglitz.¹⁰ N,2,4-Trichloroacetanilide was prepared as described by Orton and Reed.¹¹

Bromination of Ketene Dimer.—To a solution of 8.4 g. (0.1 mole) of freshly distilled ketene dimer in 200 cc. of chloroform there was added, at room temperature with vigorous stirring, a solution of 17.8 g. (0.1 mole) of N-bromosuccinimide in 700 cc. of chloroform. The volume of the mixture was reduced to 400 cc. by distillation at atmospheric pressure from a steam-bath. The succinimide which precipitated was removed by filtration and to the filtrate there was added 10 cc. of absolute alcohol and 2 drops of triethylamine. After refluxing for one hour the reaction mixture was fractionated under reduced pressure. α -Bromoacetoacetic ester (9 g., 43% based on ketene dimer) was obtained as a fraction boiling at 125–127° at 25 mm. It was characterized by the following two derivatives:

Ethyl 2-Amino-4-methylthiazole-5-carboxylate.—Using the method of Epprecht⁴ 0.5 g. of α -bromoacetoacetic ester gave 0.5 g. (80%) of the thiazole derivative: m. p. 171–172° (Epprecht⁴ gave the m. p. as 175–176°).

(5) Steude, *Ann.*, **261**, 30 (1891); Conrad and Schmidt, *Ber.*, **29**, 1043 (1896).

(6) Schönbrodt, *Ann.*, **263**, 193 (1889); Buchka and Sprague, *Ber.*, **22**, 2548 (1899).

(7) Hantzsch, *Ber.*, **27**, 356, 3168 (1894).

(8) All boiling points and melting points reported are uncorrected.

(9) "Organic Syntheses," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 127–128.

(10) Lengfeld and Stieglitz, *Am. Chem. J.*, **16**, 215 (1893).

(11) Orton and Reed, *J. Chem. Soc.*, **91**, 1554 (1909).

(1) This paper is an abstract of a portion of the thesis submitted by Franklin H. Baldwin to the Graduate Faculty of Cornell University for the M.S. degree in June, 1947.

(2) Ziegler, *et al.*, *Ann.*, **581**, 80 (1942).

(3) "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 127–128.

(4) Epprecht, *Ann.*, **276**, 79 (1894); Conrad, *Ber.*, **29**, 1044 (1896).

3-Methyl-1-phenyl-4-phenylhydrazono-5-pyrazolone. Following the procedure of Buchka and Sprague,⁶ 1.3 g. of α -bromoacetoacetic ester gave 1.5 g. (50%) of the pyrazolone derivative: m. p. 154° (Buchka and Sprague⁶ reported the m. p. at 157°).

Chlorination of Ketene Dimer.—In a flask protected against atmospheric moisture there was placed a solution of 8.4 g. (0.1 mole) of ketene dimer in 100 cc. of chloroform, a solution of 23.8 g. (0.1 mole) of N,2,4-trichloroacetanilide in 200 cc. of chloroform was added, and the mixture refluxed for twenty hours. The reaction mixture was then reduced to a volume of 150 cc., cooled in an ice-salt-bath, the precipitated 2,4-dichloroacetanilide filtered, and 4.6 cc. of absolute alcohol added to the chloroform solution. This mixture was then refluxed for six hours, concentrated to 50 cc., and again cooled to precipitate additional dichloroacetanilide. The liquid residue was then fraction-

ated under reduced pressure giving 6.0 g. (35% based on ketene dimer) of α -chloroacetoacetic ester: b. p. 100–110° (25 mm.).

This chloroester was characterized in the same manner as described for α -bromoacetoacetic ester: ethyl 2-amino-4-methylthiazole-5-carboxylate, m. p. 172–173°; 3-methyl-1-phenyl-4-phenylhydrazono-5-pyrazolone, m. p. 155–157°.

Summary

Chemical evidence, based on halogenation of the allyl position, is presented in support of that lactone structure for ketene dimer which has the exocyclic carbon-carbon double bond.

ITHACA, N. Y.

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

Many-membered Carbon Rings. I. Cyclization of Some Bifunctional Ketenes¹

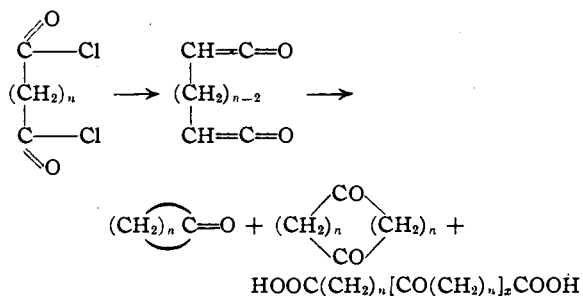
BY A. T. BLOMQUIST AND R. D. SPENCER²

In the course of investigations in this Laboratory with respect to certain derivatives of many-membered carbon rings it was decided to investigate the possibilities of a new method of cyclization involving bifunctional ketenes. Sauer³ in his investigation of ketene dimers from acid halides observed that the bifunctional ketene derived from adipyl chloride gave a 40% yield of α -carbethoxycyclopentanone when treated with ethyl alcohol while sebacyl chloride yielded only a polymeric ketene derivative with no evidence of the formation of cyclic compounds. In these experiments no attempt was made to achieve significantly greater dilution than that employed in the preparation of monofunctional ketene dimers. Ziegler⁴ and subsequently Hunsdiecker⁵ have shown that high dilution is essential for the formation of many-membered rings in satisfactory yields by their methods. Ruzicka's method⁶ was not adaptable to the application of the dilution principle and, consequently, the yields of the larger rings formed by his method were quite low.

We reported in a recent communication⁷ the results obtained when the dilution principle was applied to the formation of the bifunctional ketene prepared from sebacyl chloride by dehydrohalogenation with triethylamine. There was some evidence for the formation of traces of cyclononane as a product of the reaction, but none was isolated. A 16% yield of crude 1,10-cyclooctadecanedione was obtained. We have now pre-

pared cycloheptanone and 1,8-cyclotetradecanedione from suberic acid as well as cyclopentadecanone and 1,16-cyclotriacontanedione from thapsic acid.

The following general equation indicates the products obtained upon hydrolysis and decarboxylation of the ketene derivatives without making any attempt to show the structure of these intermediates themselves. The structure of ketene dimer and the aldoketene dimers is still a controversial issue.^{8,9}



In the course of the cyclization reaction much ketene polymer is formed. Part of this is ether insoluble and remains with the triethylamine hydrochloride. The ether soluble polymeric material is easily separable from the desired cyclic products after the mixture has been hydrated and decarboxylated with alcoholic potassium hydroxide. Presumably the polymers afford polyketodibasic acids which are soluble in aqueous alkali.

The original experimental procedure has been

(8) Hanford and Sauer, "Organic Reactions," John Wiley and Sons, New York, Vol. III, 1946, pp. 127–128.

(9) Recent work in this Laboratory, cf. Blomquist and Baldwin, THIS JOURNAL, 69, 29 (1947), supports the following structure for ketene dimer $\text{CH}_2 = \text{C} - \text{CH}_2$.



(1) Abstracted from a dissertation submitted by R. D. Spencer in June, 1947, to the Graduate Faculty of Cornell University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) du Pont Postgraduate Fellow in Chemistry, 1946–1947.

(3) Sauer, THIS JOURNAL, 69, 2444 (1947).

(4) Ziegler, Eberle and Ohlinger, Ann., 504, 94–130 (1933), and succeeding papers by Ziegler and his co-workers.

(5) Hunsdiecker, Ber., 75B, 1190–1197 (1942), and succeeding papers.

(6) Stoll and Rouve, Helv. Chim. Acta, 27, 1570–1583 (1944).

(7) Blomquist and Spencer, THIS JOURNAL, 69, 472 (1947).