[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

β-Propiolactone. IX. The Kinetics of Attack by Nucleophilic Reagents upon the Alcoholic Carbon of β-Propiolactone

BY PAUL D. BARTLETT AND GILBERT SMALL, JR.

Previous papers have described the polymerization of β-propiolactone,[1] and its reaction with salts,[2,3] with alcohols,[4] with phenols,[5] with Grignard reagents,[6] with acids, acid chlorides and anhydrides.[7] The present paper reports the beginning of a program directed toward the study of the mechanisms of these reactions. It is evident from the nature of the products that both strong and weak nucleophilic reagents are able to perform displacement reactions of the S_N2 type[8] upon the saturated alcoholic carbon atom of β-propiolactone. In the present work the rates of these reactions have been measured for a series of such reagents, covering a range of more than four powers of ten in reactivity.

Experimental

β-Propiolactone provided by the B. F. Goodrich Company was redistilled. The material used boiled at 45.8° under 8 mm. pressure. The experiments here reported were all carried out in a thermostat at 25.00 ± 0.01°. The reactions were carried out in glass-stoppered flasks from which 5-ml. aliquots were withdrawn by pipets at suitable intervals and analyzed either for lactone or for the reagent.

Reaction with Sodium Thiosulfate.—The reaction of β-propiolactone with sodium thiosulfate is so rapid as to require solutions of 0.01 *M* or lower concentration for convenient study. The concentration of thiosulfate was followed in the solution by iodimetric titration. Figure 1 shows a typical kinetic run between β-propiolactone and sodium thiosulfate at initial concentrations of 0.00670 and 0.01059 *M*, respectively. The reaction was followed to more than 90% completion. The initial concentration of the lactone was determined as the difference between initial and final concentrations of thiosulfate ion. The validity of this procedure is supported by the consistent linearity of the plots.

Reaction with Other Reagents.—The rate of reaction between β-propiolactone and thiosulfate ion (k_2 = 0.186 liter/mole sec.) is sufficiently great to offer a convenient method for the determination of β-propiolactone in aqueous solution. In the reaction of this lactone with other reagents its concentration was determined by pipetting 5 cc. of the reacting solution into 50 cc. of water containing a suitable known excess of standard sodium thiosulfate. From the known rate constant, the concentration of thiosulfate and the minimal excess in which it is present, one can calculate the proper period of standing to accomplish 99.8% consumption of the lactone. This was a satisfactory method of analysis in all cases except that of the reaction with hydroxyl ion which was rapid enough to compete with thiosulfate during the analysis. In the determination of the rate of reaction with hydroxyl ion, therefore, the reagent was titrated with standard acid.

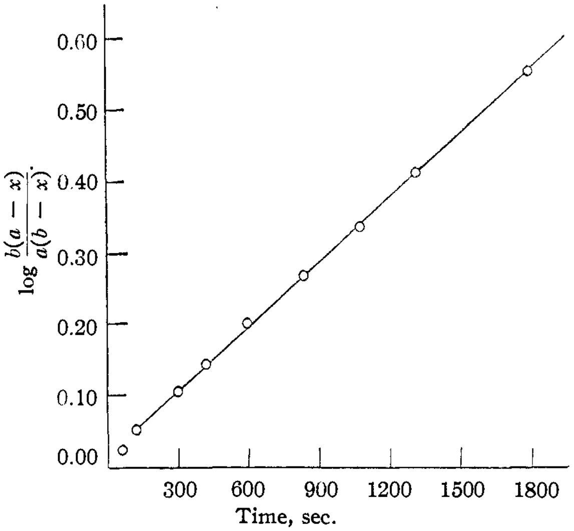

Fig. 1.—Reaction of 0.00670 *M* β-propiolactone with 0.01059 *M* sodium thiosulfate at 25°.

The initial concentrations of chloride, bromide, iodide and thiocyanate were determined by titration of the reacting solution with silver nitrate immediately after its preparation. In the comparatively slow reactions with chloride and bromide ions, concentrations of the reactants of the order of 1-2 *M* were used in order to make the reaction occur at a convenient rate and to render reaction of the lactone with water negligible. It has been previously observed[9] that β-propiolactone is not affected by strong aqueous acid in moderate concentrations; therefore, hydrochloric, hydrobromic and hydriodic acids were used in these kinetic experiments rather than their salts in order to ensure against slight alkalinity which would seriously disturb the kinetics.

Reaction of β-Propiolactone with Water.—In conformity with the report of Johansson[9] we have observed that the hydrolysis of β-propiolactone in solutions of perchloric acid from 0.01 to 0.05 *M* is independent of the concentration of the acid. The unimolecular rate constant in five determinations averaged 5.59×10^{-5} sec.$^{-1}$.

Reaction with Acetate Ion.—In contrast to the other reagents studied in this work, acetate ion yields a reaction with β-propiolactone which appears to be of first order during any particular run. This is due to the fact that the β-acetoxypropionate ion, which is the direct product of attack of the acetate ion on β-propiolactone, is a reagent of nucleophilic activity very similar to that of acetate ion itself. The product of the reaction is a mixture of sodium salts of acids with neutral equivalent greater than that (132.1) calculated for β-acetoxypropionic acid. For example, the measured neutral equivalent of the product from 0.45 *M* acetate ion and 0.47 *M* lactone was 161.2 while the

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(1) T. L. Gresham, J. E. Jansen and F. W. Shaver, THIS JOURNAL, **70**, 998 (1948).

(2) T. L. Gresham, J. E. Jansen, F. W. Shaver and J. T. Gregory, *ibid.*, **70**, 999, 4277 (1948).

(3) T. L. Gresham, J. E. Jansen and F. W. Shaver, *ibid.*, **70**, 1001, 1003 (1948).

(4) T. L. Gresham, J. E. Jansen, F. W. Shaver, J. T. Gregory and W. L. Beears, *ibid.*, **70**, 1004 (1948).

(5) T. L. Gresham, J. E. Jansen, F. W. Shaver, R. A. Bankert and Marie G. Prendergast, *ibid.*, **71**, 661 (1949).

(6) T. L. Gresham, J. E. Jansen, F. W. Shaver and R. A. Bankert, *ibid.*, **71**, 2807 (1949).

(7) T. L. Gresham, J. E. Jansen and F. W. Shaver, *ibid.*, **72**, 72 (1950).

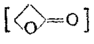
(8) See E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941), for definitions of terms.

(9) H. Johansson, Lund Univ. Annual, New Series, Division 2 Volume 12, No. 8, 1915.

average neutral equivalent from 2.78 M acetate and 0.056 M lactone was 134.2. Thus by using acetate ion in great excess it was possible to make the acetate ion compete successfully with the acetoxypropionate ion in reaction with the lactone. Although the kinetics in any one run was of the first order the value of the rate constant was proportional to the acetate ion concentration. The bimolecular rate constant for the reaction of acetate ion with β-propiolactone is taken to be 3.1×10^{-4} which is the mean of two determinations made at the largest acetate:lactone ratio. Table I records the results of this series of determinations of rate constants.

TABLE I

PSEUDO-UNIMOLECULAR RATE CONSTANTS FOR REACTION OF PROPIOLACTONE WITH ACETATE ION IN WATER AT 25°

$[AcO^-]_0$	[]	$k_{obsd.} \times 10^4$ sec.$^{-1}$	$\frac{k_{obsd.}}{[AcO^-]_0} \times 10^4$
2.733	0.220	8.81	3.23
2.782	.0558	8.46	3.04
0.4534	.472	1.56	3.44
3.462	.222	12.8	3.68
3.487	.223	12.8	3.67
2.755	.0556	8.72	3.16

Results and Discussion

Previous work has demonstrated that β-lactones are capable of yielding bimolecular displacement reactions with cleavage of the bond between the alcoholic carbon and oxygen,[10-13] and that when the alcoholic carbon is a center of asymmetry such reactions occur with Walden inversion. Since open-chained esters and γ- and δ-lactones show a strong preference for normal ester hydrolysis with cleavage adjacent to the carboxyl carbon, the direct displacement reaction of a β-lactone must be associated with activation of the CO-bond through ring strain. This suggests a resemblance between the attack of reagents upon β-propiolactone, on the one hand, and upon ethylene oxides and ethylenesulfonium ions, on the other hand. In Table II are assembled the bimolecular rate constants measured in this work for reaction of the several nucleophilic reagents with β-propiolactone and the unimolecular rate constant measured in acid solution and assumed to correspond to direct attack of water upon the lactone. We assume this mechanism for the water reaction rather than a unimolecular self-ionization for two reasons. First, racemization is not observed in the neutral water reaction of β-butyrolactone[12] which, reacting at a secondary carbon atom, would be more likely to display the S_N1 mechanism than would β-propiolactone. Second, the observed reaction in dilute acid solution is much more rapid than the best estimate which has been given[14] of the rate of an ionization process in a primary halide ($k_1 = 1.5 \times 10^{-7}$ for neopentyl bromide at 95° in 70% aqueous ethanol). These constants are expressed as relative rate constants compared to the constant for chloride ion taken as unity and these are compared with similar reactivity series toward β-chloroethylethylenesulfonium ion by Ogston and Holiday and toward epichlorohydrin by Brønsted, Kilpatrick and Kilpatrick. The relative reactivities of chloride, iodide, thiocyanate and thiosulfate ions are all the same within a factor of less than 2 toward β-propiolactone as toward β-chloroethylethylenesulfonium ion, the difference between the fastest and slowest reagent being slightly over a thousand-fold. Three reagents are considerably more reactive toward the lactone than toward the sulfonium ion: water by a factor of 6, acetate ion by a factor of a little over 3 and hydroxyl ion by a factor of 17.6. The large difference in the case of hydroxyl ion is a strong indication that this reagent attacks β-propiolactone primarily by a mechanism of normal ester hydrolysis at the carbonyl group, a mechanism not available in the case of the ethylenesulfonium ion. Since the solutions of sodium acetate were slightly alkaline, it is possible that a certain amount of hydroxyl ion reaction is included in the measured rate of reaction with acetate ion. Unless the situation with β-propiolactone is very different from what it is with β-butyrolactone,[12,13] the high relative reactivity of water cannot be explained as due to a mechanism of normal ester hydrolysis.

TABLE II

RATE CONSTANTS IN AQUEOUS SOLUTION AT 25° FOR ATTACK OF NUCLEOPHILIC REAGENTS UPON β-PROPIOLACTONE AND OTHER SUBSTANCES

	β-Propiolactone		Relative k toward		
Reagent	k_2, l./mole sec.	Relative k	β-Chloroethylethylenesulfonium ion[b]	Epichlorohydrin[c]	Trimethylcarbonium ion[b]
H_2O	5.6×10^{-5a}	0.31	0.05	0.04	0.28
CH_3COO^-	3.0×10^{-4}	1.7	0.48	0.54	
Cl^-	1.8×10^{-4}	(1.0)	(1.0)	(1.0)	(1.0)
Br^-	6.0×10^{-4}	3.3	.....	5.2	
I^-	3.0×10^{-3}	17.0	31.0	85.0	
SCN^-	3.8×10^{-3}	21.0	32.0	57.0	
$S_2O_3^=$	1.9×10^{-1}	1050	1286	....	1.9
OH^-	1.2	6700	381	Very small	

[a] Unimolecular rate constant, sec.$^{-1}$. [b] A. G. Ogston and E. R. Holiday, *Trans. Faraday Soc.*, **44**, 49 (1948). [c] J. N. Brønsted, M. Kilpatrick and M. Kilpatrick, THIS JOURNAL, **51**, 428 (1929).

The relative reactivities toward epichlorohydrin are strikingly similar to those toward the ethylenesulfonium ion except for a factor of 3 in the case of the iodide ion in favor of attack upon epichlorohydrin and except for the well-known puzzle of the behavior of hydroxyl ion whose reactivity toward epichlorohydrin is so small as to be negligible in comparison to its reactivity toward either the ethylenesulfonium ion or the β-lactone. As a matter of interest the relative reactivities reported by Ogston for water, chloride ion and thiosulfate ion toward the trimethylcarbonium ion are included in Table II. As pointed out by the British

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(10) B. Holmberg, *Svensk. Kem. Tid.*, **30**, 190, 215 (1918).

(11) F. A. Long and A. R. Olson, *J. Phys. Chem.*, **41**, 267 (1937).

(12) A. R. Olson and R. J. Miller, THIS JOURNAL, **60**, 2687 (1938).

(13) A. R. Olson and J. L. Hyde, *ibid.*, **63**, 2459 (1941).

(14) I. Dostrovsky and E. D. Hughes, *J. Chem. Soc.*, 166 (1946).

authors the trimethylcarbonium ion appears as a highly undiscriminating reactant, doubtless in consequence of its very great instability.

Further work is in progress on the mechanisms of reaction of β-propiolactone with these and other types of reagents.

Acknowledgment.—The authors are grateful to the B. F. Goodrich Company for a grant in support of this work and for the supply of β-propiolactone, and to Drs. T. L. Gresham and J. E. Jansen for interesting discussions.

Summary

The rates of reaction of β-propiolactone with chloride, bromide, iodide, acetate, thiocyanate, thiosulfate and hydroxyl ions have been measured and found to be of the second order. The lactone reacts with first order kinetics at 25° in aqueous solutions of perchloric acid from 0.01 to 0.05 M. The reaction with thiosulfate is rapid enough to be adapted to the quantitative determination of β-propiolactone in solution. Acetate ion is the only reagent of this group whose reaction with β-propiolactone in dilute solution always is attended by substantial polymerization. Except for water and hydroxyl ion, the latter of which is believed to attack the lactone by a mechanism of normal ester hydrolysis, the relative reactivities of the reagents are quite parallel to the reported reactivities of the same reagents toward the β-chloroethylethylenesulfonium ion and toward epichlorohydrin.

CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 2, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE LABORATORY FOR NUCLEAR SCIENCE AND ENGINEERING OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Kinetics and Mechanism of the Acid-Catalyzed Reaction of Diphenyldiazomethane with Ethyl Alcohol[1,2]

BY JOHN D. ROBERTS AND WARREN WATANABE

Although the acid-catalyzed solvolysis reactions of diazoacetic ester have been thoroughly studied, both from the standpoint of kinetics and of mechanism,[3] comparatively little attention has been paid to the possible analogous reactions of other substituted diazomethanes. While it was early reported that in the acid-induced decomposition of several aliphatic and aryl diazomethanes in inert solvents the rate of evolution of nitrogen gas increases with increasing acid strength,[4] no parallel measurements appear to have been carried out in polar solvents.

We have found that diphenyldiazomethane reacts smoothly and in high yield with ethyl alcohol, in the presence of a strong acid, p-toluenesulfonic acid, to give ethyl benzhydryl ether. Minor by-products, comprising less than

$$(C_6H_5)_2CN_2 + C_2H_5OH \xrightarrow{H^{\oplus}} C_2H_5OCH(C_6H_5)_2 + N_2$$

5% of the total yield, are diphenylketazine, $(C_6H_5)_2C{=}N{-}N{=}C(C_6H_5)_2$, and tetraphenylethylene. In the absence of acid, diphenylketazine is obtained as the major product, together with some of the ether, through a thermal and a photochemical decomposition.[5] The presence of tetraphenylethylene appears to be due to a simultaneous acid-catalyzed reaction which proceeds in ethyl alcohol solution only to a negligible extent.

With several classes of acids the acid-catalyzed reaction with solvent is accompanied or superseded by a reaction in which the acid anion appears in the product. Thus hydrochloric acid both catalyzes the reaction with solvent and reacts directly with diphenyldiazomethane to form benzhydryl chloride. In ethyl alcohol solution (as well as in inert solvents)[5,6] carboxylic acids yield mostly the benzhydryl esters of the acids, while with strongly acidic phenols, phenol ethers are the major product.

In the present investigation the kinetics of the simple acid-catalyzed reaction as well as the more complex case of the hydrochloric acid reaction have been studied and certain aspects of the mechanisms of these reactions have been considered.

Experimental

Technique of Rate Measurements.—The rates of all reactions were followed by measuring the rate of decrease in concentration of diphenyldiazomethane by the spectrophotometric method described earlier.[7] The solvent was absolute ethyl alcohol. All measurements were made at constant ionic strength, with anhydrous lithium perchlorate as the inert salt. As a rule stock solutions of all reactants were made up and thermostated at least an hour before the start of the reaction. The reaction mixtures were prepared at zero time and rapidly transferred to a Corex cell already in place in the thermostated cell compartment of the Beckman spectrophotometer. The rate of the reaction was followed by measuring the decrease in optical density at 525 mμ with time. By this method

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[1] Supported in part by the joint program of the Office of Naval Research and the Atomic Energy Commission.

[2] Presented at the Atlantic City Meeting of the American Chemical Society, September, 1949.

[3] (a) Bredig and Ripley, *Ber.*, **40**, 4015 (1907); (b) Fraenkel, *Z. physik. Chem.*, **60**, 202 (1907); (c) Snethlage, *Z. Elektrochem.*, **18**, 539 (1912); (d) Brønsted and Duus, *Z. physik. Chem.*, **117**, 299 (1925).

[4] Staudinger and Gaule, *Ber.*, **49**, 1897 (1916).

[5] Staudinger, Anthes and Pfenninger, *ibid.*, **49**, 1928 (1916).

[6] Hardegger, El Heweihi and Robinet, *Helv. Chim. Acta*, **31**, 439 (1948).

[7] Roberts, McElhill and Armstrong, THIS JOURNAL, **71**, 2923 (1949).