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β-Propiolactone. XII. Mechanisms Involved in the Reaction of β-Propiolactone with Acids and Bases

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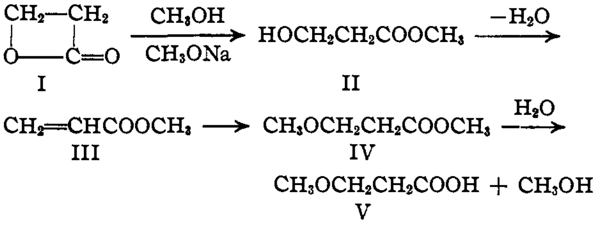
β-Propiolactone reacts with absolute methanol containing a small amount of sodium methoxide to yield methyl hydracrylate but in the presence of larger amounts of sodium methoxide the product is β-methoxypropionic acid. The series of reactions summarized in the equations are shown to account for these facts. An explanation is offered for the apparently opposite effects of acid and basic media upon the methanolysis and phenolysis of β-propiolactone.

The reaction of β-propiolactone with alcohols and with phenols has been described in two previous papers of this series.[1,2] In both cases products were obtained according to the conditions of reaction in which the alkoxy or aryloxy group was attached at either the carbonyl carbon or the β-carbon of the reacting lactone. The present experiments concern the mechanism of the alkaline methanolysis of β-propiolactone (I). From these results and a few supplementary experiments conclusions are drawn concerning the mechanism of reaction involved with phenol under basic and acidic conditions as well.

The Alkaline Methanolysis of β-Propiolactone

It was mentioned in Part V of this series[1] that methyl hydracrylate (II) is produced in an exothermic reaction as β-propiolactone is added to well cooled alcohol containing a small amount of sodium alkoxide as alkaline catalyst. It was observed in the course of the same work[3] that in the presence of a molal equivalent of sodium methoxide the product, instead of being methyl hydracrylate, was β-methoxypropionic acid formed in good yield. Superficially one might conclude from such an observation that the attack of methoxide ion upon the β-carbon atom of the lactone was of higher order in methoxide ion than attack at the carbonyl group. Actually investigation shows that β-methoxypropionic acid is the end-product of a chain of reactions involving (1) normal methanolysis of the lactone, (2) base-catalyzed dehydration of methyl hydracrylate to yield methyl acrylate (III), (3) addition of alcohol to methyl acrylate[4,5,6]



to yield methyl β-methoxypropionate (IV), and finally hydrolysis of this ester by the water produced in the second step. The occurrence of this series of reactions has been verified first by showing that if the products are isolated in a total of eight minutes time methyl hydracrylate can be found in 17% yield even under conditions which a little later yield only the β-methoxy acid. Secondly, we have shown that the same final product results whether β-propiolactone or methyl hydracrylate be added to a mole of sodium methoxide in methanol. Methyl acrylate under these conditions is converted to methyl β-methoxypropionate but acrylic acid is precipitated as its sodium salt. A small amount of solid precipitated during the alkaline methanolysis of the lactone was identified as a mixture of sodium acrylate with a smaller amount of sodium β-methoxypropionate.

Methanolysis in Neutral and Acid Solutions

Methanolysis in neutral solution was shown[1] to yield β-methoxypropionic acid. This is what one would expect if the behavior of methanol is analogous to that of water which attacks a β-lactone directly with Walden inversion in the absence of base or of very strong acid.[7] As previously shown,[8,9] the concentration of strong acid must exceed 0.01 molar in water before its effect is felt in the appearance of acid-catalyzed attack at the carbonyl group of β-propiolactone. If, as is reasonable to suppose, methanol is a somewhat stronger base than water, still higher concentrations of acid might be necessary in order to bring out a mechanism of methanolysis differing from that in neutral absolute methanol. The results reported in Part V are consistent with these expectations and support a rather close analogy between water and methanol in their behavior toward the β-lactone. If high enough acidities were studied in methanol we should expect the point of attack to shift again to the carbonyl group, leading to methyl hydracrylate, methyl polyhydracrylate formed by the attack of the primary product as an alcohol upon lactone, and probably some dehydration products as well.

Reaction of β-Propiolactone with Phenol

An oversimplified comparison between the behavior of propiolactone toward methanol and toward phenol has the appearance of a paradox. In contrast to the methanol system, the most acidic conditions of attack by phenol lead to phenyl hydracrylate while the most alkaline lead to β-phenoxypropionic acid. The behavior in acid is undoubtedly due to the conditions under which

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[1] T. L. Gresham, J. E. Jansen, F. W. Shaver, J. T. Gregory and W. L. Beears, THIS JOURNAL, 70, 1004 (1948).

[2] T. L. Gresham, J. E. Jansen, F. W. Shaver, R. A. Bankert, W. L. Beears and M. G. Prendergast, *ibid.*, 71, 661 (1949).

[3] T. L. Gresham and co-workers, private communication.

[4] T. Purdie and W. Marshall, *J. Chem. Soc.*, 59, 468 (1891).

[5] C. F. Koelsch, THIS JOURNAL, 65, 437 (1943).

[6] C. E. Rehberg, M. B. Dixon and C. H. Fisher, *ibid.*, 68, 544 (1946).

[7] A. R. Olson and R. J. Miller, *ibid.*, 60, 2687 (1938).

[8] H. Johansson, Lund Univ. Annual, New Series, Division 2, Volume 12, No. 8, 1915.

[9] P. D. Bartlett and G. Small, Jr., THIS JOURNAL, 72, 4867 (1950).

the experiment is carried out. Phenol is the solvent and the acidity is produced by the addition of a small amount of concentrated sulfuric acid. The basicity of phenol is enormously lower than that of methanol (if we were to estimate this difference by analogy to the corresponding amines, aniline and methylamine, we should set the factor at about 10^5). The acidity required to promote rapid attack at the carbonyl group by the acid mechanism is therefore reached in phenol at much lower stoichiometric acid concentrations than in methanol or water. An acid concentration which in methanol still permits the examination of the uncatalyzed attack of solvent will in phenol reveal the limiting acid-catalyzed mechanism as it is observed in very strongly acidic aqueous or methanolic solutions. This mechanism is in all cases attack at the carbonyl group.

The fact that sodium phenoxide attacks β-propiolactone by a displacement reaction at the β-position instead of behaving like methoxide ion and attacking at the carbonyl group requires consideration of still another mechanistic factor. Attention has often been called[9] to the fact in displacement reactions of this type that the nucleophilic reactivity of a reagent is not strictly proportional to its basicity. The phenoxides well illustrate this in that they are relatively vigorous reagents in displacement reactions with ethylene oxides toward which the more strongly basic hydroxyl ion is relatively inert. Although the reason for this is not understood it is a recognized fact that sodium phenoxide occupies an intermediate position between the strongly basic hydroxyl ion which will always attack the carbonyl group by preference and the weakly basic but strongly nucleophilic iodide ion which will always attack the β-carbon by preference. In summarizing the comparison of methanol and phenol with water we may then say that of the three mechanisms of lactone hydrolysis which may be observed in water as we pass from the most strongly basic to moderately acidic solutions, only the neutral and basic mechanisms are clearly observed in methanol over a range of acidity where only the neutral and acidic mechanisms are observed in phenol.

In comparing the yields of β-aryloxypropionic acids obtained from various substituted sodium phenoxides the Goodrich workers[2] found that the most basic phenoxides in general gave the poorest yields. This is contrary to what would be expected if the yield were a measure of the rate of nucleophilic attack of the phenoxide ion upon the lactone. It will be noted, however, that the conditions under which this reaction was carried out were conditions of competition between the phenoxide ion and the hydroxyl ion produced by acid–base interchange with the water which was used as solvent. Since hydroxyl ion strongly promotes normal ester hydrolysis of the lactone, this appears as an important competing reaction with attack by the phenoxide. Such competition is reduced to a minimum in the solutions of those phenoxides whose reaction is most nearly neutral in aqueous solution. Since any one of the phenoxides would be capable of giving 100% yield of β-aryloxypropionic acid in the absence of competition, the table of yields by the various phenoxides actually measures the effectiveness of the competition by hydroxyl ion diverting lactone away from reaction with the phenoxide.

Experimental

Reaction of β-Propiolactone with Methoxide at Low Concentration.—β-Propiolactone (72 g., 1 mole) was added dropwise with stirring to a solution of 2 g. (0.04 mole) of sodium methoxide in 192 g. (6 moles) of absolute methanol. During the addition the reaction was cooled in an acetone–Dry Ice mixture. The base was neutralized with an equivalent quantity of concentrated hydrochloric acid. The solution was filtered and the filtrate distilled at reduced pressure. There was obtained 89 g. (85%) of methyl hydracrylate boiling from 78–81°. Calcd. for $C_4H_8O_3$: sapn. equiv., 104.1. Found: sapn. equiv., 105.5.

Reaction of β-Propiolactone with Methoxide at High Concentration.—A solution of sodium methoxide was prepared by dissolving 15 g. (0.27 mole) of sodium methoxide in 192 g. (6 moles) of methanol. β-Propiolactone (72 g., 1 mole) was added and the solution worked up as above. The products included 7 g. (6%) of methyl β-methoxypropionate (b.p. 60°, 40 mm.) and 54 g. (52%) of β-methoxypropionic acid (b.p. 115–120°, 20 mm.).

In a similar experiment an acid titration on the resulting solution showed that 58% of the lactone had undergone a reaction consuming base.

The reactions starting with methyl acrylate, methyl hydracrylate and acrylic acid were performed in similar fashion.

Identification of Material Precipitated in Reaction with Strong Base.—The precipitate was collected on a filter, washed with methanol and with ether. It was then dissolved in water, in which it was very soluble, and extracted with three portions of ether of 100 cc. each. The water solution was acidified with concentrated hydrochloric acid and extracted with six 100-cc. portions of ether. The 18-cc. liquid residue left upon evaporation of the ether was distilled under diminished pressure. Most of the material was in a fraction which was distilled first at 200 mm., then redistilled under atmospheric pressure. It boiled at 140°, was acidic, gave an unsaturation test with permanganate and partially polymerized in the distilling column. It was therefore acrylic acid. The remaining material was distilled at 115° under 18 mm. pressure and was identified as β-methoxypropionic acid.

Isolation of Methyl Hydracrylate from Methanolysis of β-Propiolactone in Concentrated Alkali.—Sodium (23 g., 1 mole) was dissolved in 300 cc. of absolute methanol. This solution was strongly cooled by an acetone–Dry Ice mixture and vigorously stirred while 72 g. (1 mole) of β-propiolactone was added drop by drop. As soon as the addition was complete 1 mole of concentrated hydrochloric acid was added. The total time of reaction to this point was eight minutes. The mixture was filtered and the filtrate was fractionated under diminished pressure. The product included 18 g. (17%) of methyl hydracrylate boiling at 78–81° under 18 mm. pressure.

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