phenate, ethyl phenyl sulfide and diphenyl disulfide.

2. An attempt has been made to formulate a mechanism through which the ethyl phenyl sulfide and diphenyl disulfide could be formed.

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

# The Reactions of Certain Gamma Ketonic Acids. I. Ketonic Beta Lactones

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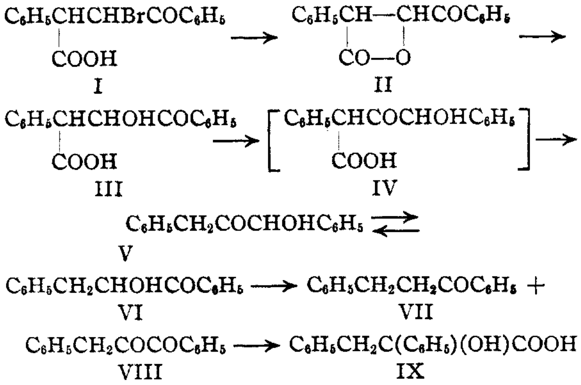
By brominating phenyl benzoyl propionic acid it is possible to obtain two stereoisomeric monobromo derivatives which have bromine as well as benzoyl in the beta position. These derivatives are excellent material for investigating the extent to which the properties of beta bromo acids are affected by their configuration. We are employing them for a study of beta lactones because, despite many excellent investigations, there still is much that is mysterious with respect to the mechanism by which these 4-ring compounds are formed and the manner in which they behave.

In this paper we deal only with the higher melting of the two beta bromo acids, and with the reactions which it was necessary to study before undertaking to determine the relative rates at which the two stereoisomers form lactones and the speed with which the lactone rings are opened. When this bromo acid is dissolved in dilute aqueous solutions of weak bases it is rapidly converted into a beta lactone which is precipitated almost as fast as it is formed, and a hydroxy acid which remains in solution. Of the three types of products that are commonly formed when beta bromo acids react with bases—beta lactone, hydroxy acid and ethylenic compound—this acid yields but two, no ethylenic compound—in this case benzalacetophenone—being formed under any conditions.

Only one of the two possible stereoisomeric beta lactones is formed from the higher melting bromo acid and this lactone constitutes more than 90% of the product, the remainder being a mixture of the two possible beta hydroxy acids. Since a similar mixture of hydroxy acids is formed very slowly by the action of weak bases on the lactone, rate measurements will be necessary to determine whether the acids are secondary products or whether the lactone and the hydroxy acids are formed concurrently from some common intermediate.

The action of strong bases is much more complicated; even in dilute solutions strong bases induce a series of reactions which end in secondary products that are only remotely related to the substances from which they arise



$$\underset{\text{I}}{\underset{\text{COOH}}{C_6H_5\overset{|}{C}HCHBrCOC_6H_5}} \longrightarrow \underset{\text{II}}{\underset{\text{CO—O}}{C_6H_5CH—CHCOC_6H_5}} \longrightarrow$$

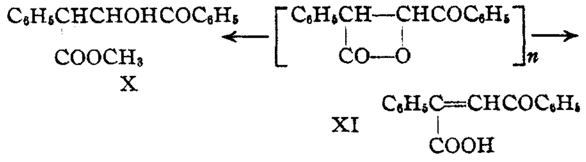
$$\underset{\text{III}}{\underset{\text{COOH}}{C_6H_5\overset{|}{C}HCHOHCOC_6H_5}} \longrightarrow \underset{\text{IV}}{\left[\underset{\text{COOH}}{C_6H_5CHCOCHOHC_6H_5}\right]} \longrightarrow$$

$$\underset{\text{V}}{C_6H_5CH_2COCHOHC_6H_5} \rightleftarrows$$

$$\underset{\text{VI}}{C_6H_5CH_2CHOHCOC_6H_5} \longrightarrow \underset{\text{VII}}{C_6H_5CH_2CH_2COC_6H_5} +$$

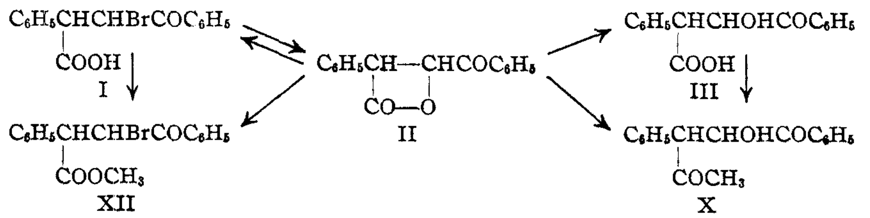
$$\underset{\text{VIII}}{C_6H_5CH_2COCOC_6H_5} \longrightarrow \underset{\text{IX}}{C_6H_5CH_2C(C_6H_5)(OH)COOH}$$

Another fertile cause of secondary products is polymerization. When the bromo acid is dissolved in concentrated aqueous solutions of bases, the solutions soon precipitate sparingly soluble, oily salts or insoluble and infusible solids which have the same composition as the readily soluble lactone. Similar polymers are formed with great rapidity when the lactone is dissolved in a polar solvent containing a trace of a weak base. These products are mixtures representing various degrees of polymerization. Some of them can be crystallized from acetone, many can be converted into the methyl ester of a monomeric hydroxy acid, and pyridine transforms all of them as well as the monomeric lactone into *cis* phenyl benzoyl acrylic acid



$$\underset{\text{X}}{\underset{\text{COOCH}_3}{C_6H_5CHCHOHCOC_6H_5}} \longleftarrow \left[\underset{\text{CO—O}}{C_6H_5CH—CHCOC_6H_5}\right]_n \longrightarrow \text{XI}\ \underset{\text{COOH}}{C_6H_5C{=}CHCOC_6H_5}$$

In marked contrast to these involved effects of bases, the reactions between the lactone and acidic reagents are simple and explicit. Aqueous solutions of sulfuric acid convert the lactone quantitatively into a single hydroxy acid and methyl alcoholic solutions convert it into the corresponding methyl ester. Similarly, concentrated aqueous hydrobromic acid, acting on the lactone, quantitatively regenerates the bromo acid from which it arose and methyl alcoholic hydrobromic acid forms the methyl ester of this acid. All these reactions in acid solutions are entirely free from racemization and therefore quite probably also from inversion.



## Experimental

Although the reaction between the bromo acid and bases may give rise to a variety of secondary products it can be controlled without great difficulty. The formation of hydroxy acids can be reduced to a minimum by employing a sufficiently weak base, and polymerization can be obviated completely by operating in sufficiently dilute solutions. For the purpose of preparation both these conditions are met adequately when the bromo acid is dissolved in a cold dilute solution of sodium bicarbonate.

Substitution of the carbonate for the bicarbonate leads to an increase in the amount of hydroxy acids and to contamination of the lactone with hydroxy ketone, and concentrated carbonate adds a considerable quantity of polymers to the impurities. Dilute caustic alkalies also produce mainly lactone but unless this is extracted as fast as it is formed[1] it disappears rapidly and gives rise to the entire list of secondary products.

These methods in which the lactone is precipitated or extracted are ill adapted for rate measurements. For this purpose it is better to resort to alcoholic solutions. With alcoholic solutions of alkaline hydroxides by-products are inevitable but methyl alcoholic sodium methylate serves admirably; in sufficiently dilute solutions the lactone is the only product.

**Preparation of the Lactone.**—Ten grams of the pure bromo acid[2] is dissolved as rapidly as possible with vigorous shaking in a liter of 1% aqueous sodium bicarbonate. Perfectly pure acid forms a clear colorless solution which becomes cloudy within a minute and soon begins to deposit crystalline lactone. At the ordinary temperature the reaction is complete in less than three hours. The lactone is then collected on a filter, thoroughly washed with water and recrystallized from methyl alcohol. The yield is about 90%.

Much more concentrated solutions of bicarbonate may be used and larger quantities of the bromo acid may be dissolved in the same volume of solution but under these conditions the lactone frequently is contaminated with the sparingly soluble sodium salt of the bromo acid and polymerizes completely during recrystallization.

**α-Phenyl-β-benzoyl Propiolactone, II.**—The lactone is readily soluble in all common organic solvents except petroleum ether. It usually separates in thin plates from the aqueous solutions in which it is formed but crystallizes from organic solvents in needles melting at 95°.

*Anal.* Calcd. for $C_{16}H_{12}O_3$: C, 76.2; H, 4.8; mol. wt., 252. Found: C, 76.2; H, 4.9; mol. wt., 250.

**Action of Sodium Bicarbonate. α-Phenyl-β-hydroxy-β-benzoyl Propionic Acid, III.**—The filtrate from the lactone when acidified and thoroughly extracted with ether, yielded a small quantity of a mixture of two acids which were separated by systematic fractional recrystallization from ether and petroleum ether. One of these acids was identified as the beta hydroxy acid which had been obtained in earlier work[3] but the principal component of the mixture proved to be a second hydroxy acid which is more soluble in water and organic solvents, crystallizes in fine needles and melts at 132°.

*Anal.* Calcd. for $C_{16}H_{14}O_4$: C, 71.1; H, 5.2. Found: C, 71.0; H, 5.2.

In proof of the structure of this acid it was established that when its solution in methyl alcohol is saturated with hydrogen bromide it is converted into the methyl ester of the bromo acid which had been used in preparing the lactone.

A similar mixture of beta hydroxy acids was obtained by shaking the lactone with aqueous bicarbonate. The reaction was exceedingly slow. Thus after shaking 10 g. of very finely ground lactone continuously for fifteen days with a nearly saturated solution of the bicarbonate, slightly more than 2.0 g. was recovered by filtration and extraction with ether. The aqueous solution yielded 8.5 g. of a mixture containing the two hydroxy acids in approximately equal quantities. No other products were formed.

**Action of Strong Bases: Hydroxy Dibenzyl Ketone (V) and α-Hydroxy-β-phenyl Propiophenone VI.**—An ethereal solution containing 10 g. of the lactone was shaken for an hour with 100 cc. of 5% aqueous sodium hydroxide. The aqueous layer first turned yellow and then became almost colorless again. The ethereal layer became yellow more slowly but retained its color. The aqueous layer by the usual manipulations yielded 0.3 g. of an acid which melted

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[1] Johanson, *Ber.*, **55**, 649 (1922).

[2] Kohler and Goodwin, THIS JOURNAL, **49**, 224 (1927).

[3] Ref. 2, p. 223.

at 165° and which was identified as phenyl benzyl hydroxy acetic acid (IX) by analysis and by comparison with a sample prepared as directed by Widman.[4]

The yellow ethereal layer, on concentration, deposited a colorless solid which crystallized from ether and petroleum ether in fine white needles and melted at 115°.

*Anal.* Calcd. for $C_{15}H_{14}O_2$: C, 79.6; H, 6.2. Found: C, 79.4; H, 6.4.

This same product was also formed when either of the two hydroxy acids was dissolved in cold sodium hydroxide or in warm sodium carbonate. Its structure was established by an independent preparation from dibenzyl ketone

$$C_6H_5CH_2COCH_2C_6H_5 \longrightarrow C_6H_5CH_2COCHBrC_6H_5 \longrightarrow C_6H_5CH_2COCHOHC_6H_5$$

The requisite bromo dibenzyl ketone has heretofore been prepared with bromine vapor but we found that it can be obtained equally well by brominating the ketone in carbon tetrachloride in the usual manner. Thus 15 g. of the ketone brominated in 50 cc. of carbon tetrachloride with 11.4 g. of bromine gave 13.8 g. of recrystallized bromo ketone melting at 48–50°—a yield of 66%.

In order to replace the bromine with hydroxyl, 0.7 g. of the bromo ketone was boiled with 400 cc. of water for two hours during which time nearly all of it dissolved. The filtered solution on cooling deposited the hydroxy ketone in fine white crystals which melted at 113–114° and were found to be identical with the product obtained from the lactone.

The lactone yielded about 4 g. of this hydroxy ketone. The yellow residue left after the hydroxy ketone had been removed as completely as possible was a mixture of low melting substances that was extremely difficult to separate. A portion of it, when tested with *o*-phenylenediamine, gave a colorless solid which melted at 97° and which was identified as the quinoxaline from phenyl benzyl diketone. The remainder by cautious fractionation with low boiling petroleum ether finally yielded another colorless solid which crystallized in prisms and melted at 66°. This substance proved to be the isomeric hydroxy ketone VI. Its structure was established by an independent preparation from benzylacetophenone

$$C_6H_5CH_2CH_2COC_6H_5 \longrightarrow C_6H_5CH_2CHBrCOC_6H_5 \longrightarrow C_6H_5CH_2CHOHCOC_6H_5$$

The saturated ketone was brominated in ether at the ordinary temperature, and the resulting $\alpha$-bromo compound was purified by recrystallization from methyl alcohol. It separated in needles and melted at 56–57°.

*Anal.* Calcd. for $C_{15}H_{13}OBr$: Br, 27.7. Found: Br, 27.6.

The bromo compound was converted into the hydroxyl compound by prolonged boiling with a dilute solution of sodium bicarbonate. The resulting hydroxy ketone was identical with the product from the lactone.

**Action of Pyridine.**—When the bromo acid is dissolved in pyridine it is very rapidly converted into the pyridine salt of *cis* phenyl benzoyl acrylic acid XI, but when it is extracted from an ethereal solution with a dilute aqueous solution of the base it forms a pyridine salt which crystallizes in colorless needles, melts and dissociates with brisk effervescence at about 135°.

*Anal.* Calcd. for $C_{21}H_{18}O_3NBr$: C, 61.1; H, 4.4. Found: C, 60.9; H, 4.6.

The salt is not affected by prolonged shaking with water and it can be recrystallized from boiling methyl alcohol.

Traces of pyridine, like traces of potassium acetate, generally induce polymerization in methyl alcoholic or acetone solutions of the lactone, but when excess of pyridine is added the polymer redissolves and both the lactone and the polymer are converted quantitatively into the same unsaturated acid that is formed from the bromo acid.

**Action of Acids, $\alpha$-Phenyl-$\beta$-hydroxy-$\beta$-benzoyl Propionic Acid.**—A mixture of 5.0 g. of the lactone and 250 cc. of 10% sulfuric acid was boiled for 20 hours, then cooled and extracted with ether. The dried ethereal solution, concentrated and diluted with petroleum ether, deposited 5.0 g. of the hydroxy acid melting at 132°. No isomeric hydroxy acid and no other product could be detected.

**Action of Acid and Methyl Alcohol, Methyl $\alpha$-Phenyl-$\beta$-hydroxy-$\beta$-benzoyl Propionate X.**—A solution containing 2.0 g. of the lactone and 2 drops of sulfuric acid in 10 cc. of methyl alcohol was set aside for twenty-four hours, then poured into bicarbonate and cracked ice, and extracted with ether. The ether solution yielded 2 g. of a hydroxy ester isomeric with the one previously described.[2] The same ester was obtained by esterifying the hydroxy acid melting at 132° with diazomethane. It crystallizes in small prisms and melts at 89°.

*Anal.* Calcd. for $C_{17}H_{16}O_4$: C, 71.8; H, 5.6. Found: C, 71.7; H, 5.6.

**Action of Hydrobromic Acid.**—A suspension of 2.0 g. of the finely ground lactone in 10 cc. of 40% hydrobromic acid was shaken mechanically and tested at intervals for unchanged lactone. After ten hours the melting point indicated about 50% conversion, and after twenty-four hours the lactone had been completely converted into the same bromo acid from which it had been formed. Neither the isomeric bromo acid nor the hydroxy acid could be detected.

**Action of Hydrobromic Acid and Methyl Alcohol.**—A solution of 2 g. of the lactone in a mixture of 20 cc. of methyl alcohol and 10 cc. of 40% hydrobromic acid was left to itself for twenty-four hours then treated in the usual manner. It yielded 2.4 g. of the methyl ester of the higher melting bromo acid and a small quantity of the ester of the hydroxy acid, but none of the isomeric esters could be detected.

## Summary

This paper contains a description of $\alpha$-phenyl-$\beta$-benzoyl propiolactone, including the conditions in which it is formed, its polymerization and its reactions with basic and acidic reagents.

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(4) Widman, *Ber.*, **49**, 484 (1916).