[CONTRIBUTION FROM THE THOMPSON LABORATORY OF THE PHILLIPS EXETER ACADEMY]

The Mutarotation of a Beta Lactone

BY E. P. KOHLER AND C. L. BICKEL[1]

Earlier papers by Kohler and co-workers[2,3] describe the two stereoisomeric beta bromo acids obtained by brominating α-phenyl-β-benzoylpropionic acid and also the relative rates at which the bromo acids form beta lactones.

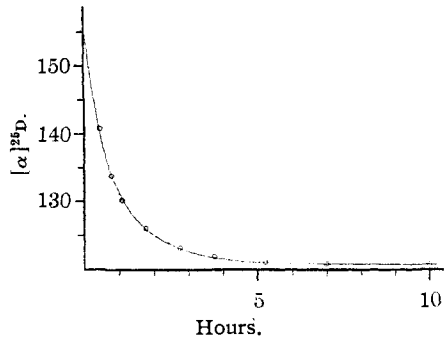
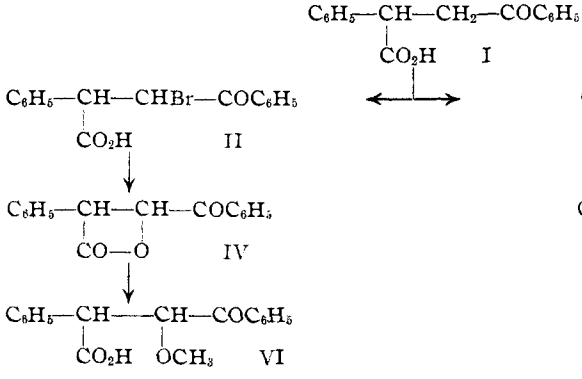


Fig. 1.

These two beta lactones behave differently in methanol solution, a difference which was not suspected until the optically active substances were investigated. The dextro modification of α-phenyl-β-benzoylpropionic acid I gives two optically active stereoisomeric bromo acids II and III. One of the bromo acids II readily forms an optically active beta lactone IV; optically active beta lactone V is formed much more slowly from the stereoisomeric bromo acid III.



A methanol solution of beta lactone IV shows a rapid loss in optical activity for some hours, followed by a much slower gain in activity which at room temperature is not complete for several weeks. Figure 1 shows the mutarotation stage while Fig. 2 includes the second stage as well.

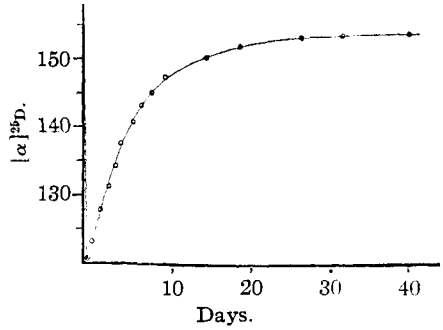
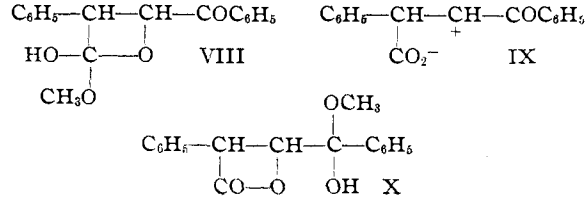


Fig. 2.

If the methanol solution is worked up before the minimum point of the curve is passed, the lactone is recovered unchanged. Beyond this point, however, two substances can be isolated from the solution, the lactone and the methyl ether VI of the β-hydroxy acid. A solution which exhibits no further change in activity yields nothing but the methyl ether.

Since the rotations of the beta lactone IV and the methyl ether VI are about the same, the pronounced mutarotation of the solution must involve an intermediate substance which gives rise to the methyl ether. Three possible intermediates VIII, IX, and X are suggested but there is as yet no evidence to support or discount any of them. Each offers the possibility of mutarotation by a change in the nature of the groups attached to an asymmetric center.



(1) The junior author was private assistant to the late Professor E. P. Kohler when the mutarotation of certain beta lactones was first observed. While the bulk of the experimental work was completed prior to Professor Kohler's death, the junior author is solely responsible for the preparation of the manuscript.

(2) Kohlerand Kimball, THIS JOURNAL, **56**, 729 (1934).

(3) Kohler, Peterson and Bickel, *ibid.*, **56**, 2000 (1934).

The racemic beta lactone, which is an equimolecular mixture of the optically active beta lactone IV and its optical opposite, also reacts slowly at room temperature with methanol to give a racemic methyl ether VII, identical in structure with VI. Either of these methyl ethers can be obtained more readily by boiling the methanol solution of the beta lactone for twenty-four hours. No other products were found.

The isomeric optically active beta lactone V does not exhibit mutarotation in methanol and does not react with methanol under the conditions which produce the methyl ether VI.

Experimental Part

The resolution of α-phenyl-β-benzoylpropionic acid I has been adequately described in a previous paper.[4]

The methods employed in obtaining the bromo acids II and III as well as the beta lactones IV and V were identical with those used for the racemic substances.[2,3]

The polarimetric studies were carried out in methanol, using Pyrex polarimeter tubes described previously.[4] The methanol was distilled from oxalic acid through an all Pyrex system, using a good column.

The Methyl Ether VI.—The methyl ether was prepared either by allowing a methanol solution of beta lactone IV to stand until no further change in rotation of the solution was observed, or by boiling the solution for twenty-four hours. The methyl ether was then isolated in the usual way.

The analyses and physical properties of these new substances are given in the following tables:

Substance	Theory, % C	Theory, % H	Found, % C	Found, % H	$[\alpha]^{25}D$
II	57.7	3.9	57.8	4.1	+157°
III	57.7	3.9	57.3	4.0	+ 90°
IV	76.1	4.8	76.0	5.0	+155°[a]
V	76.1	4.8	76.0	5.0	+ 92°
VI	71.8	5.7	71.8	5.7	+153°
VII	71.8	5.7	71.7	5.9	

Substance[b]	Crystal form	Solubility	M. p., °C.	Mixed m. p., °C.[c]
III	Needles	v. s. ether; s. methanol	148	180
IV	Needles	s. ether, methanol; i. pet. ether	75	96
V	Needles	s. ether, sl. s. methanol	130	148
VI	Plates	v. s. ether; s. methanol; sl. s. pet. ether	132	117
VII	Plates	Same as VI	117	

[a] From Fig. 1 by extrapolation to zero time. [b] Bromo acid II has so far failed to give a crystalline solid. The rotation and analysis were run on the oil obtained by treating the lactone IV with 2% HBr in acetic acid. The identity of the oil is certain, however, since it regenerated lactone IV by the action of 1% aqueous sodium bicarbonate solution. [c] The optical opposite of each active compound derived from the dextro acid was prepared from the levo acid by identical methods. The mixed melting point in each case was the same as the melting point of the corresponding racemic compound. Moreover, the identity of each "synthetic" racemate was proved by a mixed melting point with the known racemic compound.

Summary

The two beta lactones formed from the beta bromo acids of dextro α-phenyl-β-benzoylpropionic acid behave quite differently in methanol. The one lactone exhibits mutarotation and also gives the methyl ether of α-phenyl-β-benzoyl-β-hydroxypropionic acid; the other lactone does not.

EXETER, NEW HAMPSHIRE RECEIVED FEBRUARY 8, 1941

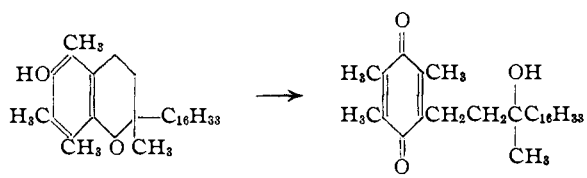
(4) Bickel, THIS JOURNAL, **60**, 928 (1938).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, MERCK & CO., INC.]

Interrelation of α-Tocopherol and α-Tocopherylquinone

BY M. TISHLER AND N. L. WENDLER

The oxidation of α-tocopherol has been the subject of much discussion ever since the sensitivity of this vitamin factor to oxidants was first demonstrated.[1] Under mild conditions ferric chloride or silver nitrate converts natural α-tocopherol into a yellow liquid which was designated by John and his collaborators as α-tocopherylquinone, II.[2]



α-Tocopherol, I II

The stability of the quinone to chromic oxide indicated that the hydroxyl group in the side chain is tertiary, confirming[2] the chroman structure, I, for α-tocopherol as proposed by Fernholz.[3] Kar-

(1) Olcott, *J. Biol. Chem.*, **107**, 471 (1934); Evans, Emerson and Emerson, *ibid.*, **113**, 319 (1936).

(2) (a) John, *Z. physiol. Chem.*, **252**, 222 (1938); (b) John, Dietzel and Emte, *ibid.*, **257**, 173 (1939); (c) John and Emte, *ibid.*, **261**, 24 (1939).

(3) Fernholz, THIS JOURNAL, **60**, 700 (1938).