[Contribution from the Cobb Chemical Laboratory, University of Virginia]

CIS-β-(*p*-BROMOBENZOYL)-α-METHYLACRYLIC ACID AND ITS ESTERS

ROBERT E. LUTZ, DANIEL T. MERRITT, Jr.,* and MONROE COUPER

Received February 2, 1939

Cis- and *trans*-β-(*p*-bromobenzoyl)-β-methylacrylic acids,† BrC_6H_4-$COC(CH_3) = CHCOOH$, and their esters, have been investigated in some detail.[1] Of the two possible stereoisomeric α-methyl acids, $BrC_6H_4COCH = C(CH_3)COOH$, only the *trans* form has previously been prepared; it was made from mesaconyl chloride by the Friedel-Crafts reaction on bromobenzene, the reaction stopping at this stage in contrast with the analogous reaction on benzene which goes further to give the expected unsaturated 1,4-diketone. The Friedel-Crafts reaction between citraconic anhydride and bromobenzene gave largely the *cis* β-methyl derivative and only a small amount of α-methyl acid which, however, proved to be the *trans* compound, stereochemical inversion having occurred.

In continuation of investigations on unsaturated 1,4-ketonic acid systems and on the ring-chain tautomerism involved,[1] it seemed worthwhile to prepare and study the hitherto unknown *cis* α-methyl acid, II. The synthesis, which is being reported at this time, was accomplished in a simple way through rearrangement of the *trans* acid, I, by exposure in a suitable solvent to the action of sunlight. The various intertransformations of the *cis* and *trans* acids and the methyl esters are summarized in the accompanying diagram (1).

Reduction of the new *cis* acid gives β-bromobenzoyl-α-methylpropionic acid, V, which has already been made by a similar reduction of the *trans* acid, I. The position of the methyl group, previously established by hydrolysis of the *trans* acid to *p*-bromoacetophenone,[1] has been confirmed by synthesis of this acid from methylacetoacetic ester, VII, through the monoethyl ester of mesaconic acid, VIII, followed by a Friedel-Crafts reaction on the acid chloride, IX, and hydrolysis of the resulting *trans* ethyl ester, X, as outlined in diagram (2).

---

* The larger part of the work described in this paper was presented by the second author in a thesis for the M.A. degree (1936).

† These acids have previously been called the β-bromobenzoylcrotonic acids.

[1] (*a*) Lutz and Taylor, *J. Am. Chem. Soc.*, **55**, 1168 (1933); (*b*) Lutz and Winne, *ibid.*, **56**, 445 (1934); (*c*) Lutz, *ibid.*, **56**, 1378 (1934).

The *cis* α-methyl acid undergoes rearrangement to the more stable *trans* isomer when exposed to the action of sunlight in a chloroform solution with iodine as catalyst or through contact with alcoholic alkali, conditions under which the *cis* β-methyl acid is stable. It dissolves readily without significant lag in sodium bicarbonate solution in contrast with the *cis* β-methyl acid which dissolves slowly.

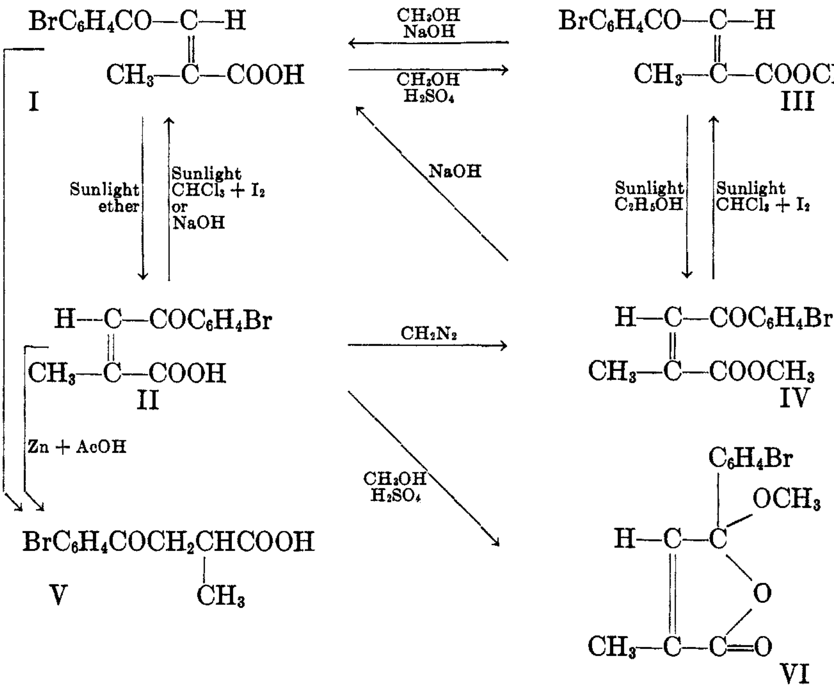


Diagram (1)

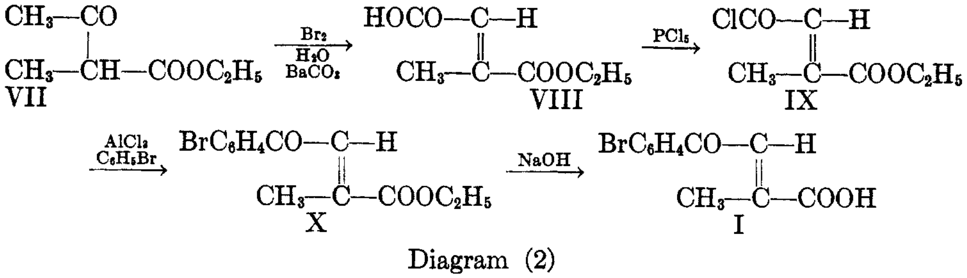


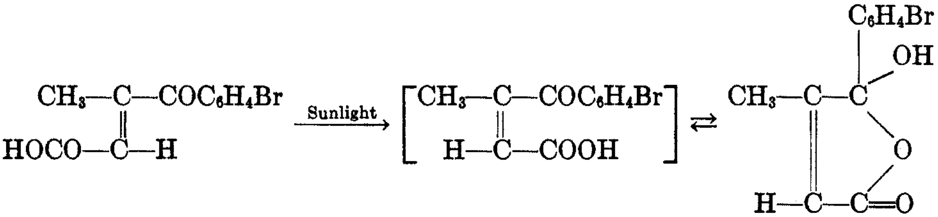
Diagram (2)

The open-chain *cis* ester, IV, was prepared in the customary way by the action of diazomethane on the *cis* acid, and also by the action of sunlight on a solution of the *trans* ester III. It undergoes inversion to the *trans* ester when exposed to sunlight in chloroform solution with iodine as catalyst. Hydrolysis by means of alcoholic alkali usually gives the *trans* acid exclusively, although in one isolated experiment hydrolysis was accomplished without stereochemical inversion.

The isomeric cyclic ester, VI, is obtained by esterification of the *cis* acid by Fischer's method. The cyclic structure is shown by the refractive index which differs from that of the open-chain ester in the expected degree and direction,[2] and by the fact that, unlike the open-chain ester, this isomer is not rearranged to the *trans* ester by the action of sunlight on a chloroform-iodine solution. Hydrolysis under alkaline conditions gives the *trans* acid.

It is evident from the various reactions cited above, that the *cis* configuration is inherently less stable in the α- than in the β-methyl series. This point is best illustrated by the relative stabilities of the sodium salts of the acids in alkaline solution where presumably only the open-chain structures are involved.

The *cis* β-methyl acid, XII, as already pointed out,[1b] probably exists chiefly or exclusively in the cyclic lactonol form, XII*b*, since it dissolves slowly in sodium bicarbonate solution in contrast with the *trans* acid, XI, which dissolves rapidly.



XI XII*a* XII*b*

Pertinent to this is the fact that the *cis* acid is not rearranged into the *trans* isomer by the action of sunlight on a chloroform-iodine solution in contrast with the rapid inversion of the open-chain *cis* ester under these conditions (and also the ready inversions in the reverse direction from *trans* to *cis* by the action of sunlight alone). The unique stability of the *cis* β-methyl acid toward stereochemical inversion might conceivably be accounted for if this acid were assumed to exist exclusively in the lactonol form, XII*b*; however, this explanation is questionable since the more acidic open-chain form must be present in equilibrium in solution as shown by methylation with diazomethane to the open-chain ester.

In this connection, we have made ultraviolet absorption measurements

---

[2] *Cf.* Auwers and Heinze, *Ber.*, **52**, 584 (1919); Meerwein, *J. prakt. Chem.*, **116**, 253 (1927).

on the *cis* β-methyl acid, XII, and on its open-chain and cyclic methyl esters and have observed a definite absorption band for the open-chain ester at about 2550–2700 Å, but no marked absorption in this region for the cyclic ester or for the free acid. A more careful investigation with better equipment is needed before these results can be regarded as conclusive. Nevertheless, there appears to be little doubt from these results that the *cis* acid is structurally like the cyclic ester and unlike the open-chain ester and that it exists chiefly in the cyclic form, XII*b*.

EXPERIMENTAL

The problem of preparation of the *cis* β-bromobenzoyl-α-methylacrylic acid (II) became one of getting the *trans* acid (I) consistently in good yield. The *trans* acid is formed in small amounts in the Friedel-Crafts reaction on citraconic anhydride and it is separated with difficulty from the major product, *cis* β-bromobenzoyl-β-methylacrylic acid (II). This separation was facilitated by taking advantage of the slow rate of solution of the latter in aqueous sodium carbonate solution. If the mixture of solids is extracted by digesting with successive portions of sodium carbonate solution and filtered, the *trans* acid (I) together with some *cis* acid (XII) is leached out, leaving nearly pure *cis* β-bromobenzoyl-β-methylacrylic acid as the residue. This source of the *trans* α-methyl acid is inadequate, of course, as a means of preparation of large quantities.

The best yields of the *trans* acid were obtained in the Friedel-Crafts reaction on mesaconyl chloride, but we have been unable to find conditions which would give consistently the favorable yields obtained in several individual experiments, such as that reported previously.[1a] A great variety of conditions, using mesaconyl chloride, carbon disulfide, and bromobenzene, with varying amounts of aluminum chloride, time of heating, temperature, and order of adding reagents, gave yields varying from 19–25%, although in two instances (not duplicable) the yields reached 50%. When nitrobenzene was used as the solvent, the mixture being allowed to stand for five to seven days at room temperature, consistent yields of 40% were obtained. While these yields have been bettered and do not represent the maximum, this method seems the best so far worked out since it gives the most consistent results. Under these conditions standing for a still longer time gave poorer yields and a product of poorer quality.

In a typical experiment a mixture of 25 g. of mesaconyl chloride, 75 g. of bromobenzene, 70 g. of anhydrous aluminum chloride, and 100 cc. of nitrobenzene was allowed to stand for one week at room temperature, and was then decomposed in ice and hydrochloric acid, the nitrobenzene solution then being washed with water. The product was isolated either by steam distillation and extraction of the residue with ether, or by diluting the nitrobenzene solution with benzene, cooling and allowing the mixture to stand, the *trans* acid (I) crystallizing slowly. The yield was 40%.

The *methyl ester (III)* was prepared by refluxing a solution of 20 g. of the acid and 20 cc. of concd. sulfuric acid in 200 cc. of methanol for one hour. On diluting with a little water, 20 g. of nearly pure methyl ester separated.

Cis-*β-bromobenzoyl-α-methylacrylic acid (II)*.—One gram of the *trans* acid (I) in 40 cc. of ether was exposed to direct sunlight for twelve hours. The ether was partly evaporated, benzene was added, and the rest of the ether was boiled off. The colorless *cis* acid then separated and was recrystallized from benzene; m.p. 97°; yield 0.8 g.

Anal. Calc'd for $C_{11}H_9BrO_3$: C, 49.1; H, 3.4.
Found: C, 49.5; H, 4.0.

When ethanol was used in the above experiment no inversion took place.

Reduction of a sample of the *cis* acid (II) with zinc and concentrated acetic acid, in the usual way, gave β-bromobenzoyl-α-methyl propionic acid (V), which was identified by mixture melting point with a sample prepared by the similar reduction of the *trans* acid (I).

Isomerization back to the *trans* acid (I) was effected by exposing a solution of the *cis* acid in chloroform solution containing iodine to the action of sunlight for twelve hours. A sample of 0.5 g. of the *cis* acid was converted quantitatively into the *trans* isomer upon standing overnight in dilute ethanol containing 0.01 g. of sodium hydroxide.

The synthesis of the trans *acid (I). Mesaconyl-α-ethyl acid ester (VIII)*, prepared according to the method of Anschütz[3] from methyl acetoacetic ester (VII), was converted into the acid chloride (IX) by means of phosphorus pentachloride. Without removing the phosphorus oxychloride, the acid chloride was treated with carbon disulfide, bromobenzene, and aluminum chloride, and the reaction mixture was decomposed in ice and acid. The oily ester which was produced (X) was hydrolyzed with dilute alcohol and sodium hydroxide, and a good yield of the *trans* acid (I) was isolated and identified.

Cis-*β-bromobenzoyl-α-methylacrylic methyl ester (IV)* was obtained as an oil by exposure of one gram of the *trans* ester (III) in alcohol solution to direct sunlight for ten hours. This oil was hydrolyzed with 0.15 g. of sodium hydroxide in 70 cc. of 40% ethanol (the mixture being allowed to stand overnight). The mixture was diluted with water, extracted with ether, and acidified, and the *cis* acid was extracted with ether, 0.7 g. of nearly pure material being obtained on evaporation of the solvent.

Several other attempts to hydrolyze the ester (III), using alcohol, water, and sodium hydroxide, gave only *trans*-β-bromobenzoyl-α-methylacrylic acid (I). We did not, however, make an exhaustive study to determine the necessary conditions for effecting hydrolysis without inversion of the configuration.

Esterification of the *cis* acid with diazomethane in ether solution took place rapidly with the evolution of nitrogen. The ester was obtained as an oil, and again attempts to induce it to crystallize failed. It was converted back to the *trans* ester by exposing it to sunlight in chloroform solution containing iodine. It distilled at 146° under 2 mm. pressure, but at higher pressures or under prolonged heating it was partly rearranged into the *trans* ester. To minimize this inversion during distillation a sample was evaporated in the high-vacuum oven at 85–90° and collected dropwise on a cold finger condenser, the refractive index being followed on the consecutive drops. The first few drops showed a slightly low index of refraction, and the bulk of the material showed a practically constant value of n_D^{25} 1.5763 to 1.5765 and a dispersion of (n_F-n_C) 0.0237.

Anal. Calc'd for $C_{12}H_{11}BrO_3$: C, 50.9; H, 3.9; Br, 28.2.
Found: C, 50.8; H, 3.7; Br, 28.0.

4-Bromophenyl-4-methoxy-2-methylcrotolactone (the cyclic methyl ester of *cis* β-bromobenzoyl-α-methylacrylic acid) (VI) was prepared by refluxing a solution of 10 g. of the *cis* acid (II) and 10 cc. of concentrated sulfuric acid in 100 cc. of methanol for half an hour, and diluting with water. The product was an oil boiling at 162° at 2 mm. pressure. It did not crystallize. It contained a small amount of the *trans*

---

[3] ANSCHÜTZ, *Ann.*, **353**, 149 (1907).

ester, formed undoubtedly through rearrangement by the acid catalyst used in the esterification, even when the amount of acid and time of heating were minimized.

In a typical experiment a solution of 2 g. of *cis* acid and 1 cc. of concentrated sulfuric acid in 20 cc. of methanol was refluxed for 30 minutes, cooled, diluted with water, and made slightly alkaline. The oily ester was extracted with ether, and distilled dropwise in the vacuum oven onto a cold finger condenser, the refractive index becoming quickly constant on successive drops at n_D^{25} 1.5675; dispersion (n_F-n_C) 0.0202. Even this product, however, contained traces of the *trans* ester and could not be regarded as really pure in spite of the constant refractive index.

Anal. Calc'd for $C_{12}H_{11}BrO_3$: C, 50.9; H, 3.9; Br, 28.2.
Found: C, 51.0; H, 3.9; Br, 28.0.

The cyclic ester was slowly hydrolyzed by dilute alcohol and sodium hydroxide, and gave the *trans* acid (I) in good yield. Exposure to sunlight in chloroform containing iodine was without effect.

Preliminary experiments show that it is not as easily reduced as the analogous cyclic ester of β-bromobenzoyl-β-methylacrylic acid.

*β-(*p*-Bromobenzoyl)-α-methylpropionic methyl ester,* $BrC_6H_4COCH_2CH(CH_3)COOCH_3$.—A sample of the acid (V) was treated with an ether solution of an excess of diazomethane, reaction taking place immediately. After standing, the solution was shaken, first with 10% hydrochloric acid, then with 10% sodium hydroxide, and finally with water. From the ether solution the oily ester was obtained. It could not be induced to crystallize. Distillation dropwise onto a cold finger condenser or ordinary distillation under 2 mm. pressure gave a colorless oil boiling at 147–148° of n_D^{25} 1.5460 and dispersion (n_F-n_C) 0.0312.

Anal. Calc'd for $C_{12}H_{13}BrO_3$: C, 50.5; H, 4.6.
Found: C, 50.6; H, 4.7.

Hydrolysis was easily accomplished by refluxing for one minute a solution of the ester in dilute methanol containing an excess of sodium hydroxide, the corresponding acid (V) being produced in good yield.

Inversion of trans-*β-(*p*-bromobenzoyl)-β-methylacrylic acid*‡ was brought about by exposure of its solution in methanol for 4 hours to the direct action of sunlight. The *cis* acid was isolated by concentration of the solution to the point of crystallization and identified by mixture melting point.

Cis-*β-(*p*-bromobenzoyl)-β-methylacrylic acid*‡ was recovered unchanged when subjected to the action of sunlight for 6 hours in chloroform solution containing enough iodine to maintain a definite iodine coloration throughout the experiment.

Cis-*β-(*p*-bromobenzoyl)-β-methylacrylic methyl ester* was prepared in nearly quantitative yield by the action of an excess of diazomethane in ether solution on the *cis* acid; this product was identical with a sample prepared by the silver salt method.[1b]

SUMMARY

The preparation of *cis*-β-bromobenzoyl-α-methylacrylic acid and its open-chain and cyclic methyl esters is reported. Inversions to and from the *trans* isomers are described.

The difference in properties of the α- and β-methyl types and the greater stability of the *cis* configuration in the β-methyl series, are considered.

Evidence is presented indicating that the β-methyl acid has the lactonol structure.

---

‡ These two experiments were carried out by Mr. F. B. Hill, Jr.