[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

CIS AND *TRANS* β-AROYLACRYLIC ACIDS AND SOME DERIVATIVES[1]

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The study with respect to ring-chain tautomerism, of various α- and β-substituted β-aroylacrylic acids and their derivatives (1), and especially of the amides of *cis* and *trans* β-(4-bromobenzoyl)-α-methylacrylic acids (1g), has led to the present investigation, for comparative purposes, of the β-(4-bromobenzoyl)acrylic series (I–II). In this series, which carries no substituent on the ethylene linkage, the unsaturated system was expected to be sterically very labile and chemically reactive, and to show little if any tendency to exist or to function in cyclic forms such as XII or XX. This expectation is supported in part by the early studies on *trans* β-benzoylacrylic acid and nuclear-substituted analogs where the *cis* forms have been so far obtained only in the esters and not in the free acids themselves (2).

trans β-(4-Bromobenzoyl)acrylic acid (I) has been made from maleic anhydride by the Friedel-Crafts reaction (3), and it has the normal properties expected of the type. It forms an acid chloride, dissolves in sodium bicarbonate, reacts with strong alkali to undergo self-condensation, is reduced readily to the saturated ketonic acid (4), and can be converted into the methyl ester by diazomethylation, by acid catalyzed methylation, by methanolysis of the acid chloride, and by the action of methyl iodide on the silver salt. The reaction with an excess of diazomethane proceeds beyond the ester formation, to produce the pyrazoline, which presumably has the structure VIII. Incidentally, it is noteworthy that this same pyrazoline was obtained also from the *cis* acid (II) and from both the *cis* and *trans* esters (III and IV), and that no stereo or structural isomer was detected, a result which is comparable with the similar pyrazoline formation from *cis* and *trans* dibenzoylethylenes (5).

Although the α-methyl derivative of the *trans* acid, I, readily undergoes rearrangement under the influence of sunlight to the *cis* isomer (1c), early attempts similarly to isomerize the *trans* β-aroylacrylic acids which are *without* ethylenic substituents have consistently failed (2a). This resistance to isomerization is in contrast to the susceptibility of the *trans* esters to this reaction. Conditions have now been found, however, under which the *trans* to *cis* inversion of the acids can be effected, and it involves simply the choice of a favorable solvent. In the case of I the favorable solvents are benzene and acetone, and in the case of β-benzoylacrylic acid itself, acetone. No inversion (of I) occurred in the solvents chloroform, ether, or ethanol, and exposure of the solid material to light, either as a dry powder or as a suspension in benzene, gave a polymer, pre-

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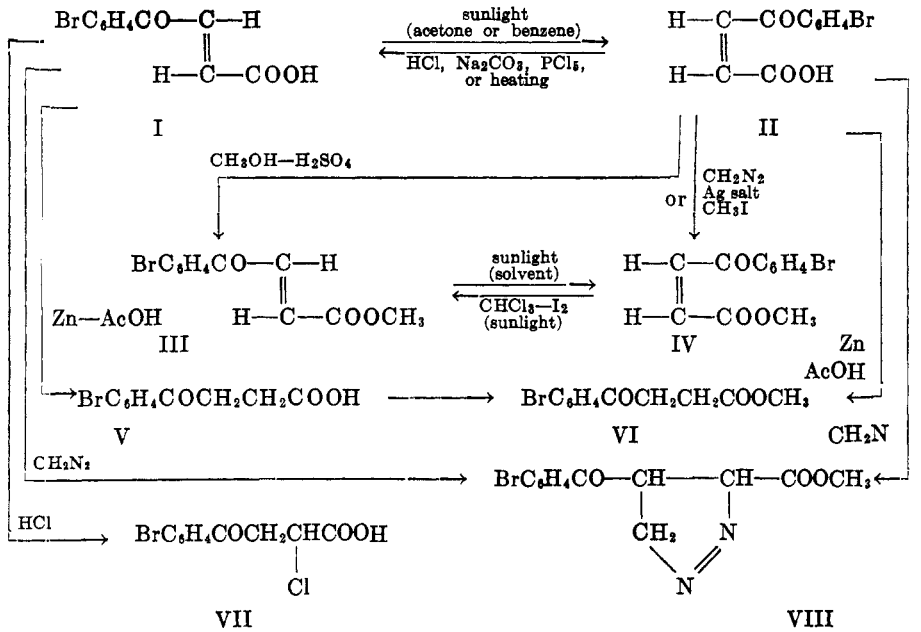


sumably analogous to truxillic acid and to the polymer of β-(4-methoxybenzoyl)-acrylic acid (2c).

Ready solubilities of *cis* β-benzoylacrylic acid and the 4-bromo derivative (II) in sodium bicarbonate indicate these compounds to be actually, or to function, in the open-chain form and not in the cyclic or γ-hydroxylactone form. As was to be expected, the free *cis* acids are very labile and undergo rearrangement back to the *trans* forms readily. This transformation was effected by the action of dilute hydrochloric acid, sodium carbonate, sunlight on a chloroform solution containing a trace of iodine, or heating above the melting points.

A further test of the stability of the *cis* acid (II) under exposure to sunlight in chloroform, ether, or ethanol, was made to see if the failure to achieve *trans* to *cis* inversion in these solvents was due to instability or to side reactions. In ether and ethanol only part of the *cis* acid was recovered after 24 hours exposure, but no *trans* acid could be isolated, whereas in chloroform the product was mainly the *trans* isomer.

The *cis* acids are converted by diazomethane, and through the silver salts by methyl iodide, into the *cis* esters, which are readily obtainable also by the sunlight inversion of the *trans* esters. Methanol-sulfuric acid esterification, however, of the *cis* acid (II) produces the *trans* ester (III).

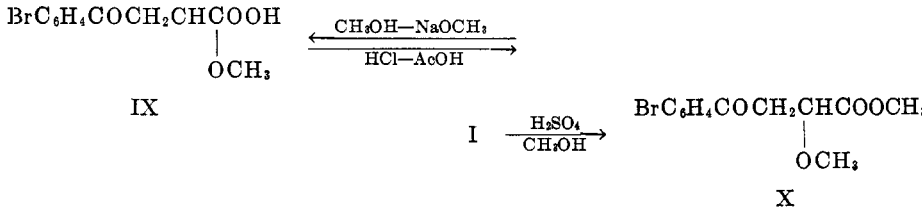
The hypothetical and as yet unknown *cis* acid chlorides are of particular interest in connection with ring-chain tautomerism. However, attempts to make the acid chloride of II failed. The reaction between the acid and phosphorus pentachloride at −35° evidently caused rearrangement before the acid chloride had formed completely, as shown by the production of a mixture of the *trans* acid chloride and the *trans* acid. The *trans* acid chloride on exposure to

sunlight in sodium-dried benzene gave only resinous products. From these results it appears unlikely that the *cis* acid chlorides can be made by the usual procedures.

The *trans* ester (III) seems to be definitely more easily isomerized to the *cis* isomer in the sunlight than is the *trans* acid (I), as shown by the fact that the transformation occurred in all of those solvents tried in which the *trans* acid was not affected, namely, chloroform, ether and ethanol.

Hydrogen chloride adds readily to *trans* β-bromobenzoylacrylic acid to give the expected addition compound, VII. This addition compound was converted back to the *trans* acid by treatment with sodium acetate in conc'd acetic acid.

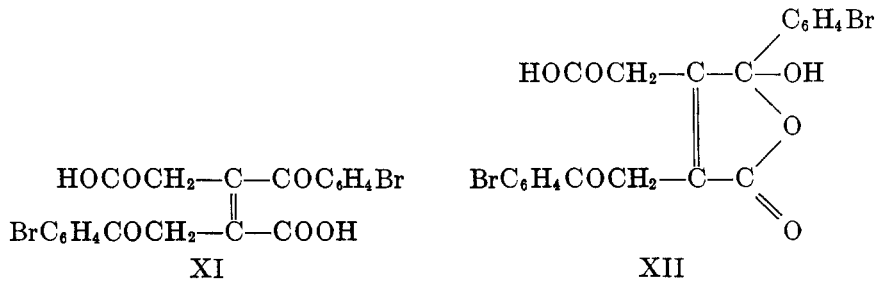
Sodium methoxide in methanol causes addition of methanol to the *trans* acid to give presumably the α-methoxy compound (IX), and this product is easily converted back to the *trans* acid by the action of a hydrochloric-acetic acid mixture. Methanol and sulfuric acid, by the method of Newman (6), converted the *trans* acid into the ester of a methanol addition product, presumably X.



The assumption that these addition reactions have placed the methoxyl in the α-position is suggested by analogy to *trans* β-(4-methoxybenzoyl)acrylic acid (2e), where the structure of such an addition compound has been demonstrated independently. These reactions are of interest in connection with the addition of alcohols to dibenzoylethylene, where the alkoxyfuran is the result (7).

The Structure of the Dimolecular Condensation Product

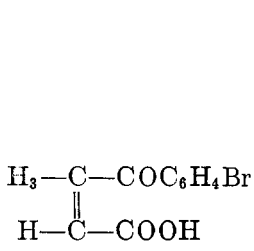
The attempt to hydrolyze both the *cis* and *trans* β-(4-bromobenzoyl)acrylic esters with alcoholic sodium hydroxide produced, instead of the expected *trans* acid, a dimolecular compound which can be obtained also from the *trans* acid under the same conditions. The compound was expected to be a self-condensation product of the type XI, possibly analogous to the cyclic compound obtained from dibenzoylethylene under similar conditions (8). Investigation of this compound leads us to believe that it has a quite different type of cyclic structure, however, namely, XII.



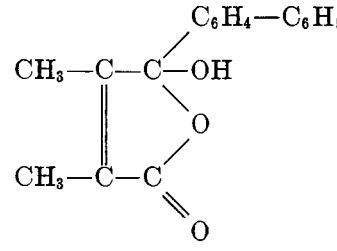
The evidence for a dibasic acid structure such as XI is the ready formation of a dimethyl ester; the evidence more specifically for the cyclic structure, XII, is the very weakly acidic character of one of these ester-forming groups. The neutral equivalent as determined by titration with standard alkali and phenolphthalein or thymolphthalein was 445 and 461, as compared with the theoretical of 510 for a monobasic acid and 225 for a dibasic acid. Obviously the second acidic group is very weakly acidic, although it responds to diazomethylation to give the dimethyl ester.

In a further investigation of the nature of the acidic groups, a potentiometric titration was carried out and the *p*H was plotted against standard alkali; this gave a first inflection point at about *p*H 6.9 and a second at about *p*H 9–10, and a neutral equivalent of 448 (as compared with the 510 calculated for the monobasic acid). The resulting solution, after this titration, was then treated with a small excess of standard alkali under refluxing to complete the conversion of the hydroxyfuranone carboxylic acid to the disodium salt; it was then cooled (to $-5°$ to slow down cyclization of the dibasic acid when it was liberated), and was back-titrated with standard acid just beyond the first inflection point (at about *p*H 10) to determine the excess of alkali used. The solution was allowed to come to room temperature and the back-titration was continued beyond the end-point, which was assumed to cover the conversion of the disodium salt to the free dimolecular compound (XII); this gave a neutral equivalent of 285 as compared with the value of 255 for a dibasic acid. These results demonstrate the existence of the second and weakly acidic group, and support the hydroxyfuranone carboxylic acid structure XII.

The successful application of the potentiometric titration method above led us to undertake a similar study of two simpler compounds, in one of which this type of ring-chain tautomerism is involved. *cis* β-(4-Bromobenzoyl)-α-methylacrylic acid, which is believed to be open-chain (XIII), was titrated against standard alkali and back-titrated with standard acid. Both of these titrations gave normal curves in the plots against *p*H; the midway inflection points fell at about *p*H 7 and the values of the neutral equivalents in two runs were 259 and 272 as compared with the calculated value of 269. This demonstrated a normal carboxyl group as formulated in XIII.



XIII



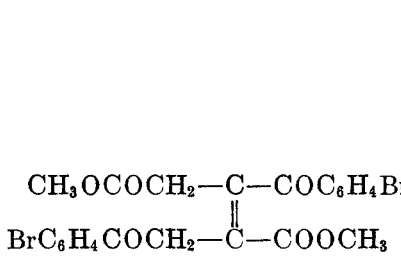
XIV

On the other hand, α,β-dimethyl-β-(*p*-xenoyl)acrylic acid (XIV) gave such a flat curve on direct and back-titrations, with the inflection points at *p*H 9 to

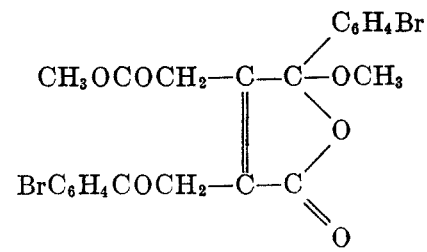
10, that an accurate determination of the neutral equivalent was not obtained; however, in the two titrations, values of 242 and 275 were obtained as compared with a theoretical of 247. This clearly indicates a very weakly acidic compound, and supports the cyclic structure which has been proposed on the basis of insolubility in sodium bicarbonate (1a).

Limited attempts to obtain further evidence for the cyclic structure of the dimolecular condensation product (XII) through characteristic reactions such as acylation and reduction, were not successful.

The compound (XII) reacts, as mentioned above, with diazomethane, with methanol-sulfuric acid, and through the silver salt with methyl iodide, to give the dimethyl ester apparently of a dibasic acid; and the diester is readily hydrolyzed back to the original dimolecular compound by hydrochloric and acetic acids. The open-chain formulation of the diester (XV) is preferred over the cyclic structure (XVI) in view of the mode of formation by diazomethane and through the silver salt by methyl iodide; however, it should be stressed that the cyclic structure, which might have been expected from a methanol-sulfuric acid esterification (1c), is not necessarily excluded on the basis of this evidence [*cf.* the diazomethylation of 4-benzoyl-2,5-diphenyl-2-hydroxyfuranone-3 (9)].



XV



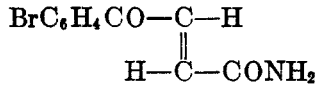
XVI

The structure of the dimolecular product is still, perhaps, open to some questions. It would appear from the fact of ring-chain tautomerism demonstrated above, that the condensation has gone unsymmetrically as formulated, because otherwise in neither of the two possible symmetrical modes of condensation would one have expected the product to have been capable of this type of ring-chain tautomerism. In the open-chain form there are two possible locations for the double bond, one of which would probably be the more stable because of the conjugation between carboxyl and 4-bromobenzoyl groups. The location indicated in the hydroxyfuranone structure XII, however, might well involve an equal or even stronger stabilizing influence; in any case it best accounts for the observed properties of the compound, especially the difficulty of reduction which is incompatible with an unsaturated 1,4-keto acid formulation.

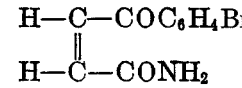
As to the mechanism of the condensation reaction which leads to this product, two possibilities may be suggested: one, the enolization of the system to an allene enolate, followed by a Michael-type condensation with a second molecule; and the other, 1,4- addition of the elements of water or alkali to give an enolate, followed by a Michael-type condensation of this enolate with an unchanged molecule, and subsequent loss of a molecule of water or alkali (*cf.* 8b).

The Amides of the β-(4-Bromobenzoyl)acrylic Acids

The primary amide of the *trans* acid (XVII) was made by the action of dry ammonia on a chloroform solution of the acid chloride. It had been determined previously that ammonia does not add to the conjugated system under these conditions as it had been found to do under other conditions (10).



XVII



XVIII

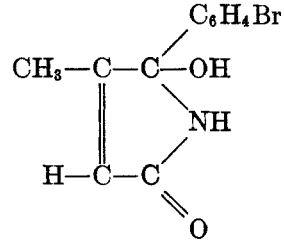
The *cis* amide (XVIII) could not be made as had been hoped through a *cis* acid chloride, but it is easily obtained by the sunlight inversion of the *trans* compound. It is in turn easily rearranged back to the *trans* isomer. The chloroform-iodine-sunlight combination which is usually used for this inversion gave amorphous products and a blue coloration; however, the inversion was readily accomplished by the action of dilute ethanol solution containing disodium phosphate.

Both the *cis* and *trans* amides were converted by methanol and hydrochloric acid into the *trans* ester (III). Hydrolysis by hydrochloric and acetic acids or by sodium acetate and acetic acid gave only intractable products; but the use of sulfuric and nitrous acids led to the formation of moderate yields of the *trans* acid.

Reduction of the *cis* and *trans* amides gave the expected saturated keto amide (XIX).

XIX

The *cis* amide (XVIII) is insoluble in sodium hydroxide in contrast to the α-methyl derivative which is soluble under these conditions (1g). This fact, coupled with the others outlined above, especially reduction and the facile interchange between the *cis* and *trans* forms, indicates that the *cis* compound is of the open-chain type, and not cyclic as the α-methyl derivative (XX) seems clearly to be.



XX

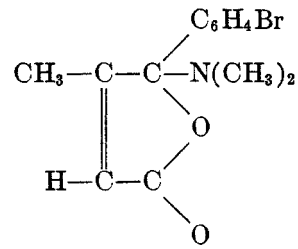
The reaction between aqueous methylamine and the *trans* acid chloride gave an alkali-soluble non-basic product of melting point 204° and empirical formula $C_{11}H_{12}BrNO_3$, which is to be investigated later.

Dimethylamine in benzene solution converts the *trans* acid chloride into the *trans* amide, which is hydrolyzed to the *trans* acid by hydrochloric and acetic acids. This amide is reduced easily to the saturated keto amide. It is rearranged to the *cis* isomer by the action of sunlight on a solution in acetone, but not in the other solvents which were effective in the isomerization of the *trans* esters.

The *cis* dimethylamide was hydrolyzed by hydrochloric and acetic acids but gave the *trans* acid together with some *trans* amide; the latter product indicated that the configurational inversion preceded hydrolysis. The *cis* dimethylamide is quickly converted back into the *trans* isomer by the chloroform-iodine-sunlight combination.

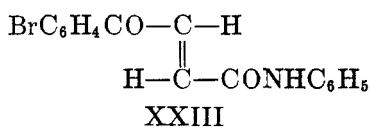
From the foregoing facts it is clear that the *cis* dimethylamide is open-chain (XXI), and unlike the α-methyl analog which appears to be cyclic (XXII) (1g).

XXI

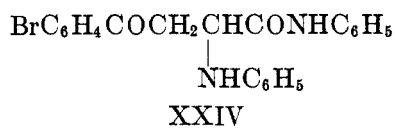


XXII

The *trans* acid chloride reacted in benzene with aniline to give two products, the anilide (XXIII), and the anilide addition product which is presumed to be XXIV.



XXIII



XXIV

The anilide (XXIII) was easily reduced to the saturated compound. Hydrolysis led to intractable products, but methanolysis led to a new and unknown compound (see experimental part). Repeated attempts to isomerize it by the action of sunlight failed.

The *trans* acid chloride reacted with N-methylaniline to give exclusively the N-methylanilide without further addition such as occurred with aniline. It was reduced to the saturated amide, which was made also from the saturated ester by the action of N-methylanilinomagnesium bromide. Like the anilide, the N-methyl derivative could not be isomerized to the *cis* form, and resisted hydrolysis and methanolysis. The action of hydrochloric and acetic acids, however, produced a new compound, the analysis of which indicated the empirical formula $C_{17}H_{14}BrNO_2$; this and the possibly analogous compounds obtained from the anilide (above) and from the N-methylanilide in the α-methyl series,[3] are still to be investigated.

[3] See Ref. 1g, page 195–196.

The foregoing studies obviously have been limited because of the non-availability of the *cis* acid chloride, and it is hoped that a way may yet be found to make this interesting compound.

EXPERIMENTAL PART[4]

trans β-(4-Bromobenzoyl)acrylic acid (*I*) was prepared by a modification of the procedure of Kohler and Woodward (3), by adding maleic anhydride to a mixture of bromobenzene, aluminum chloride, and tetrachloroethane (35°) and heating for two hours on a water-bath at 45–52°; yield 74%; recrystallized from benzene.

The *acid chloride* (3) was made by the action of phosphorus pentachloride on a carbon disulfide solution; crystallized from isooctane; melting point 104–104.5°.

trans Methyl β-(4-bromobenzoyl)acrylate (*III*) was made in the following ways: (*a*) The *trans* acid chloride was reacted with methanol (20 hours at room temperature). (*b*) An ether solution of less than the calculated amount of diazomethane was added slowly to a sample of the acid; the unchanged acid was recovered by extraction with sodium bicarbonate [the production of the pyrazoline (VIII) was minimized by this procedure]. (*c*) A solution of the acid in sodium bicarbonate was treated with silver nitrate and the precipitated silver salt was filtered, suspended in methanol and methyl iodide, and the mixture refluxed for ten minutes. The silver iodide was filtered and the solution diluted with water to precipitate the ester. (*d*) A solution of the *trans* acid in saturated methanolic hydrogen chloride was allowed to stand for 12 hours. Neutralization with 5% sodium carbonate gave an oil which was purified by evaporation at 131° under 8 mm. onto a cold-finger condenser (the yield was poor). (*e*) A solution of the acid in methanol containing a small amount of conc'd sulfuric acid was refluxed for 2.5 hours.

The ester was crystallized from dilute methanol; melting point 77°.

Anal. Calc'd for $C_{11}H_9BrO_3$: C, 49.10; H, 3.37. Found: C, 48.72; H, 3.37.

Hydrolysis of the ester was effected in a 4:10 by volume mixture of conc'd hydrochloric and acetic acids upon refluxing for one hour.

cis β-(4-Bromobenzoyl)acrylic acid (*II*). A solution of 21 g. of the *trans* acid (I) in 700 ml. of acetone was exposed to sunlight for 60 hours. Approximately 100 ml. of this solution was evaporated in a current of air and the white residue was recrystallized from benzene; yield 2.2 g.; melting point, 129°, solidifying at 133° and melting again at 162°.

Anal. Calc'd for $C_{10}H_7BrO_3$; C, 47.08; H, 2.77. Found: C, 47.00; H, 3.02.

The remainder of the original solution after similar treatment and recrystallization from benzene gave largely the *trans* acid.

To avoid this extensive reversion to the *trans* acid during purification, the crude *cis* acid was dissolved quickly in already-boiling benzene, and the solution was immediately and rapidly filtered and cooled.

The sunlight inversion worked equally well in benzene as solvent.

The *cis* acid is soluble in sodium bicarbonate or carbonate and is recovered without isomerization upon acidification with 6 *N* hydrochloric acid.

Rearrangement to the *trans* acid was effected as follows: (*a*) heating in benzene solution (*b*) suspending in benzene containing a trace of hydrochloric acid, for ten minutes; and (*c*) exposure of a solution in chloroform to sunlight for 24 hours. Attempts to make a *cis* acid chloride with phosphorus pentachloride in carbon disulfide at −35° gave only *trans* products. Exposure of samples of the *cis* acid in ether and in 95% ethanol to sunlight for 24 hours gave considerable non-crystalline material and some unchanged *cis* acid, but none of the *trans* compound.

cis Methyl β-(4-bromobenzoyl)acrylate (*IV*) was prepared as follows: (*a*) A solution of the *trans* ester in benzene was exposed to sunlight for 15 hours. (*b*) An ethereal solution of diazomethane was added to a slight excess of the acid (II), and the unchanged acid was

[4] All melting points are "corrected".

removed by sodium bicarbonate. (*c*) A solution of the *cis* acid in 5% sodium carbonate was neutralized with acetic acid, and treated with silver nitrate to precipitate the silver salt which was filtered and treated with methanol and methyl iodide for 3 hours.

The ester was crystallized repeatedly from dilute ethanol. It melted at 56.5°.

Anal. Calc'd for $C_{11}H_9BrO_3$: C, 49.10; H, 3.37. Found: C, 49.19; H, 3.65.

Rearrangement to the trans ester was effected by exposure of a chloroform solution containing a trace of iodine to sunlight for 15 hours.

Attempted hydrolysis by solution at room temperature in 100% sulfuric acid (several minutes) and pouring into crushed ice, gave unchanged *cis* ester.

β-(4-Bromobenzoyl)propionic acid (*V*) was obtained by zinc dust-conc'd acetic acid reduction (2 minutes at boiling temperature) of samples of both the *cis* and *trans* acids, and the product (m.p. 149°) was identified by mixture melting point with an authentic sample (4).

β-(4-Bromobenzoyl)propionic acid methyl ester (*VI*) was made by the following procedures: (*a*) An excess of ethereal diazomethane was added to a sample of the acid (V). (*b*) A mixture of the *cis* or *trans* esters with 70% ethanol was treated with an excess of sodium hydrosulfite with refluxing for one hour and dilution with water.

It was recrystallized repeatedly from dilute ethanol and melted at 51.5°.

Anal. Calc'd for $C_{11}H_{11}BrO_3$: C, 48.73; H, 4.09. Found: C, 48.62; H, 4.17.

β-(4-Bromobenzoyl)-α-chloropropionic acid (*VII*). A suspension of the *trans* acid (I) in conc'd hydrochloric acid, after standing for 36 hours, gave a flocculent mass at the top of the solution, which was decanted from unchanged material at the bottom. It was recrystallized from benzene, and melted at 129.5°.

Anal. Calc'd for $C_{10}H_8BrClO_3$: C, 41.23; H, 2.76. Found: C, 41.07; H, 3.00.

Elimination of hydrogen chloride was effected by the action of a refluxing 5% solution of sodium acetate in conc'd acetic acid for 15 minutes; the *trans* acid (I) was recovered and identified.

β-(4-Bromobenzoyl)-α(?)-methoxypropionic acid (*IX*). One gram of the *trans* acid (I) was added to a solution of 0.16 g. of sodium in 25 ml. of methanol; after standing 16 hours the mixture was diluted with water and neutralized with 6 *N* hydrochloric acid. The product was crystallized from benzene; yield 0.63 g. (63%); melting point 115.6°.

Anal. Calc'd for $C_{11}H_{11}BrO_4$: C, 46.01; H, 3.86. Found: C, 46.25; H, 4.02.

Elimination of methanol was effected by the action of a 4:10 by volume mixture of conc'd hydrochloric and acetic acids (refluxing for 30 minutes). The *trans* acid (I) was recovered and identified by mixture melting point.

β-(4-Bromobenzoyl)-α(?)-methoxypropionic methyl ester (*X*). A solution of 1.29 g. of the *trans* acid in 16 ml. of 100% sulfuric acid, after standing for seven minutes, was poured into ice-cold methanol [*cf.* method of Newman (6)]. Dilution with water, extraction with ether, washing with sodium carbonate, evaporation of the solvent and evaporation of the residue at 120–130° and 2–3 mm. pressure onto a cold-finger condenser, gave 1.27 g. of product. Repeated crystallization from petroleum ether gave long needles of melting point 44–45°.

Anal. Calc'd for $C_{12}H_{13}BrO_4$: C, 47.85; H, 4.35; OCH_3, 20.60. Found: C, 47.79; H, 4.55; OCH_3, 19.69.

4-(4-Bromobenzoyl)-3-carbomethoxypyrazoline (*VIII*). Samples of the *cis* and *trans* acid and esters were added in each case to solutions of an excess of diazomethane in ether and allowed to stand until the reactions appeared to be complete. The products were the same; the compound was crystallized from dilute methanol or ethanol; melting point 120–121°.

Anal. Calc'd for $C_{12}H_{11}BrN_2O_3$: C, 46.32; H, 3.56; N, 9.01. Found: C, 46.58; H, 2.88; N, 8.76.

Di-(4-bromobenzoyl)-dicarboxycyclobutane [*dimer of β-(4-bromobenzoyl)acrylic acid*]. A suspension of 2 g. of the *trans* acid (I) in 150 ml. of benzene was exposed for eight hours to sunlight. Upon heating to boiling, solution occurred and on cooling 0.57 g. (28%) of the dimer crystallized as colorless plates. Recrystallization from ethanol brought the melting

point to 249°. Exposure to sunlight for 36 hours, of the powdered solid, held between two plates of glass, gave the same compound.

Anal. Calc'd for $C_{20}H_{14}Br_2O_6$: C, 47.08; H, 2.76; mol. wt. 510. Found: C, 46.84; H, 2.91; mol. wt. 456.

Sublimation at 150° at 7 mm. pressure gave the *trans* acid (I) in small yield.

The dimolecular condensation product, 3-(4-bromophenacyl)-4-carboxymethyl-5-hydroxy-5-(4-bromophenyl)furanone-2 (XII). A suspension of 15 g. of the *trans* acid (I) in 528 ml. of 4% sodium hydroxide was stirred for 1.5 hours. Acidification gave 10.4 g. (67%) of XII. Hydrolysis of samples of both the *cis* and *trans* esters (IV and III) by sodium hydroxide in 40% ethanol (20 hours at room temperature) gave this same product. It crystallized as elongated rectangular plates from dilute ethanol and melted at 177.5°. It could also be crystallized from 95% ethanol or ethyl acetate.

Anal. Calc'd for $C_{20}H_{14}Br_2O_6$: C, 47.08; H, 2.76; Neut. eq. 510. Found: C, 46.95; H, 2.82. Neut. eq. 460.

This compound was not changed upon treatment with (*a*) phosphorus pentachloride at room temperature followed by hydrolysis; (*b*) conc'd sulfuric acid, dissolving at room temperature; (*c*) conc'd acetic and hydrochloric acids (at 150–160° for 4 hours); (*d*) conc'd acetic acid, red phosphorus, and iodine [according to Fuson and Grey (11)]; (*e*) stannous chloride in conc'd acetic and hydrochloric acids (refluxing for 30 minutes); (*f*) sunlight on an acetone solution, for 4 days; and (*g*) acetic anhydride or acetyl chloride plus a small amount of conc'd sulfuric acid (one hour at room temperature).

Only intractable products were obtained upon vacuum distillation, heating with phosphorus pentachloride at 100°, heating with phosphorus pentoxide at 100°, and treatment with sodium hydrosulfite in solution in 5% sodium carbonate (refluxing for one hour). Some of these experiments were tried because at first the compound was thought to be the α-hydroxy acid resulting from water addition.

Potentiometric titrations with standard sodium hydroxide and back-titrations with standard hydrochloric acid were carried out, using a Beckman *p*H meter.

The dimethyl ester (XV or XVI) of the condensation product (XII), was prepared (*a*) by the action of an excess of ethereal diazomethane; (*b*) by the action of 25 ml. of methanol and 2.5 ml. of conc'd sulfuric acid (refluxing for one hour) on 1.5 g. of XII; yield 1.34 g.; (*c*) as follows: a suspension of 1 g. of the acid (XII) in 1 ml. of 10% sodium hydroxide was diluted with 25 ml. of methanol; 5 ml. of 1 *N* silver nitrate was added; the precipitate was filtered, suspended in a mixture of 40 ml. of methanol and 4 ml. of methyl iodide, and the mixture was refluxed for 20 minutes and filtered; evaporation of the filtrate in a current of air gave a solid which was crystallized from methanol; yield 0.3 g.; and (*d*) by a procedure similar to (*c*) but using the *cis* acid (II) which is evidently condensed to XII under the influence of the strong alkali.

The three samples prepared above were shown to be identical by mixture melting point. The compound was purified by repeated crystallizations from dilute ethanol and melted at 121°.

Anal. Calc'd for $C_{22}H_{18}Br_2O_6$: C, 49.10; H, 3.37; mol. wt. 538. Found: C, 49.10; H, 3.78; mol. wt. 506.

Hydrolysis by a 4:10 by volume mixture of conc'd hydrochloric and acetic acids (refluxing for one hour) regenerated XII which was identified by mixture melting point.

The compound (XV) was recovered unchanged (*a*) after treatment with sodium hydrosulfite in 70% ethanol (refluxing for one hour), and (*b*) upon exposure in acetone solution for 4 days to the action of sunlight.

trans β-(4-Bromobenzoyl)acrylic amide (XVII). Dry ammonia was bubbled through a 100-ml. chloroform solution of 14.5 g. of *trans* β-(4-bromobenzoyl)acrylyl chloride for one hour. The resulting yellow crystalline precipitate was recrystallized from ethanol; yield 8 g.; the melting point after repeated crystallizations was 185° decomp.

Anal. Calc'd for $C_{10}H_8BrNO_2$: N, 5.51. Found: N, 5.50.

This amide was insoluble in 10% sodium hydroxide. It gave a purple coloration and

intractable product upon attempted hydrolysis by conc'd acetic and hydrochloric acid mixture, and by sodium acetate in conc'd acetic acid (heating). *Hydrolysis* was effected as follows: one gram of the amide in 10 ml. of cold conc'd sulfuric acid was treated with 1 g. of sodium nitrite in 5 ml. of water, and the mixture was warmed on the water-bath till the evolution of gas ceased. The resulting precipitate was crystallized from benzene (0.6 g.) and identified upon repeated crystallization as largely the *trans* acid. (This procedure with an excess of the reagent applied directly to the *trans* acid gave chiefly 4-bromobenzoic acid).

Methanolysis of the amide was effected by a 3:50 by volume mixture of conc'd hydrochloric acid and methanol under refluxing for 1.9 hours. The main product was a tar from which the *trans* acid was isolated in small amounts by vacuum evaporation at 157°.

trans β-(4-Bromobenzoyl)acrylic dimethylamide, $BrC_6H_4COCH{=}CHCON(CH_3)_2$. Dry dimethylamine was absorbed in a benzene solution of the *trans* acid chloride. The product crystallized as yellow rectangular plates from 33% ethanol; melting point 118–119.5°.

Anal. Calc'd for $C_{12}H_{12}BrNO_2$: N, 4.96. Found: N, 4.90.

It was insoluble in sodium hydroxide and hydrochloric acid. *Hydrolysis* by 1:10 by volume conc'd hydrochloric and acetic acids (refluxing for 20 hours) gave the *trans* acid (I). Hydrolysis with 10% sodium hydroxide (15 days at room temperature) gave a compound of melting point 183–196° which was not investigated.

trans β-4-(Bromobenzoyl)acrylic anilide (XXIII) was prepared from 40 g. of the *trans* acid chloride and 32.8 g. of aniline in 250 ml. of benzene (34 hours at room temperature). The crude solid precipitate was crystallized from benzene (9.5 g.); pale yellow needles; melting point 196–197°.

Anal. Calc'd for $C_{16}H_{12}BrNO_2$: N, 4.67. Found: N, 4.59.

The benzene filtrates gave the anilide addition compound, *β-(4-bromobenzoyl)-α(?)-(N-phenylamino)propionic anilide (XXIV)*, as a solid, which was purified by leaching with ethanol; 10.8 g. of melting point 146–147.5°. Further leaching with boiling ethanol left colorless needles of melting point 163–164°.

Anal. Calc'd for $C_{22}H_{19}BrN_2O_2$: N, 6.62. Found: N, 6.93.

The *trans* anilide (XXIII) was insoluble in sodium hydroxide. Hydrolysis under a variety of conditions gave intractable products. Attempts at sunlight inversion in acetone, methanol, and ethanol failed.

The action of saturated methanolic hydrogen chloride under an atmosphere of nitrogen, refluxing for 6 hours, gave a small yield of a *new compound*; it crystallized as fine yellow platelets from methanol; melting point 178.5–179°.

Anal. Calc'd for $C_{17}H_{14}BrNO_2$: C, 59.32; H, 4.10. Found: C, 58.75; 59.15; H, 4.17; 4.18.

trans β-(4-Bromobenzoyl)acrylic N-methylanilide, $BrC_6H_4COCH{=}CHCON(CH_3)C_6H_5$, was prepared from 12 g. of the *trans* acid chloride by interaction with 10 ml. of methylaniline in 100 ml. of acetone (12 hours at room temperature). Dilution with ice-water gave a product which was crystallized from ethanol; 12.9 g.; yellow trapezoidal prisms; melting point 138–140°.

Anal. Calc'd for $C_{17}H_{14}BrNO_2$: N, 4.07. Found: N, 4.06.

Attempts at hydrolysis with acids and inversion by the action of sunlight failed.

The action of conc'd hydrochloric and acetic acids (a 1:8 mixture by volume) under reflux for 15 hours gave a yield of about 50% of a *new compound* which was purified by repeated crystallizations from 70% ethanol; colorless needles of melting point 158°.

Anal. Calc'd for $C_{17}H_{14}BrNO_2$: C, 59.32; H, 4.10; N, 4.07. Found: C, 59.04; H, 4.50; N, 4.12; 4.02.

This compound was insoluble in 10% sodium hydroxide; it was not changed upon treatment with (*a*) sodium acetate in conc'd acetic acid (refluxing for 4 hours), (*b*) stannous chloride in conc'd hydrochloric and acetic acids, and (*c*) ethereal diazomethane. Oxidation by potassium permanganate of a suspension of 0.15 g. of the compound in 10% sodium hydroxide gave a 46% yield of 4-bromobenzoic acid.

cis β-(4-Bromobenzoyl)acrylic amide (XVIII). A solution of 3.69 g. of the *trans* amide (XVII) in 225 ml. of ethanol, exposed to sunlight for 7 hours, and evaporated in a current

of air, gave a colorless residue which was crystallized from benzene; yield, 3.45 g.; the melting point after further crystallizations from chloroform was 130–135° decomp.

Anal. Calc'd $C_{10}H_8BrNO_2$: C, 47.27; H, 3.17; N, 5.51. Found: C, 47.12; H, 3.49; N, 5.27.

The compound was insoluble in 10% sodium hydroxide. It was resinified by the action of sunlight in a chloroform solution containing iodine. *Inversion* to the *trans* amide was accomplished by the action of a 10% solution of disodium phosphate in 70% ethanol (refluxing for 50 minutes). *Hydrolysis* by sulfuric acid and sodium nitrite (as with the *trans* amide) gave a low yield of the *trans* acid and a considerable amount of 4-bromobenzoic acid. *Methanolysis* by saturated methanolic hydrogen chloride (12 hours at room temperature) gave a small yield of the *trans* ester.

cis β-(Bromobenzoyl)acrylic N-dimethylamide, (XXI), was prepared by the action of sunlight for 20 days on an acetone solution of the *trans* compound. The reaction was not successful in methanol or ethanol. The compound was crystallized from a benzene-ligroin mixture; melting point 77.5–78.5°.

Anal. Calc'd for $C_{12}H_{12}BrNO_2$: C, 51.08; H, 4.29. Found: C, 51.29; H, 4.53.

The compound is insoluble in 10% sodium hydroxide, is converted back to the *trans* isomer by the action of sunlight on a chloroform-iodine solution, and is converted to a mixture of the *trans* acid and *trans* amide by the action of conc'd hydrochloric and acetic acids (1:10 by volume, refluxing for 5 hours).

β-(4-Bromobenzoyl)propionic amide (XIX). (*a*) Raney nickel hydrogenation at atmospheric pressure and room temperature, of samples of the *trans* amide, in ethanol, gave XIX in 70% yield. (*b*) Reduction of the *cis* amide under the same conditions, and also by sodium hydrosulfite in 70% ethanol (refluxing for 45 minutes), gave 10% yields only of XIX. It crystallized as rectangular plates melting at 174–175°.

Anal. Calc'd for $C_{10}H_{10}BrNO_2$: N, 5.47. Found, N, 5.62.

Hydrolysis with 1:10 by volume conc'd hydrochloric and acetic acids (refluxing for 2 hours) gave the acid V.

β-(4-Bromobenzoyl)propionic N-dimethylamide, $BrC_6H_4COCH_2CH_2CON(CH_3)_2$. (*a*) Reduction of either the *cis* or *trans* N-dimethylamides by adding a solution of the amide in a small amount of ethyl acetate to a mixture of an excess of stannous chloride in a 1:2 conc'd hydrochloric-acetic acid mixture (room temperature for one hour) gave the saturated amide in 92 and 90% yields respectively. (*b*) Reduction of the *trans* amide by sodium hydrosulfite in 70% ethanol (refluxing) gave a small yield of the saturated amide and a large amount of a sulfur-containing water-soluble compound of melting point above 237°; the latter compound evidently is a bisulfite addition compound, and was not investigated.

Repeated crystallizations of the saturated amide from benzene-ligroin mixtures gave colorless rectangular plates of melting point 106–107°.

Anal. Calc'd for $C_{12}H_{14}BrNO_2$: C, 50.72; H, 4.97. Found: C, 50.95; H, 5.44.

Hydrolysis as above gave the saturated acid.

β-(4-Bromobenzoyl)propionic anilide, $BrC_6H_4COCH_2CH_2CONHC_6H_5$, was made in nearly quantitative yield by the stannous chloride reduction method described above; it crystallized as needles from ethanol; melting point 145–146°.

Anal. Calc'd for $C_{16}H_{14}BrNO_2$: N, 4.22. Found: N, 3.93.

Hydrolysis by a 1:10 conc'd hydrochloric-acetic acid mixture (refluxing for 16 hours) gave the acid (V).

β-(4-Bromobenzoyl)propionic N-methylanilide, $BrC_6H_4COCH_2CH_2CON(CH_3)C_6H_5$, was obtained in 90% yield by the action of sodium hydrosulfite in 70% ethanol under refluxing for one hour, and in 85% yield upon stannous chloride reduction by the method described above. It was made also in small yield by a modification of the method of Kuhn (12, 1g) by the action of N-methylanilinomagnesium bromide in ether and benzene. It crystallized from 60% ethanol as rectangular needles melting at 101.5–103°.

Anal. Calc'd for $C_{17}H_{16}BrNO_2$: N, 4.05. Found: N, 4.03.

Hydrolysis by 1:10 by volume conc'd hydrochloric-acetic acids (refluxing for 5 hours) gave incomplete hydrolysis to the acid (V).

cis β-Benzoylacrylic acid. A solution of 1 g. of *trans* β-benzoylacrylic acid in 30 ml. of

acetone was exposed to sunlight for 15 hours and evaporated under a current of air. The white residue crystallized as fine needles from benzene and melted at 84.5°.

Anal. Calc'd for $C_{10}H_8O_3$: C, 68.18; H, 4.50. Found: C, 67.98; H, 4.38.

Inversion back to the *trans* isomer was effected by (*a*) exposure of a chloroform solution, containing a trace of iodine, to sunlight; (*b*) heating a sample to 100°; (*c*) solution in 5% sodium carbonate and liberation by 6 *N* hydrochloric acid and extraction with ether; and (*d*) suspension in benzene containing a trace of conc'd hydrochloric acid.

Esterification to the *cis* ester was effected by the action of the calculated amount of standardized ethereal diazomethane, extraction of unreacted acid by 5% sodium carbonate, and evaporation of the solvent. Acidification of the carbonate solution gave a small amount of *trans* acid which must have been the result of isomerization of that part of the *cis* acid which had escaped methylation.

SUMMARY

β-Benzoyl and β-(4-bromobenzoyl)acrylic acids have been obtained in the very labile *cis* forms. These are methylated by diazomethane to the esters.

β-(4-Bromobenzoyl)acrylic acid reacts with an excess of diazomethane to give the pyrazoline. Hydrogen chloride and methanol addition products have been obtained.

The action of alkali produced a dimolecular condensation product which appears to be a hydroxyfuranone carboxylic acid. Potentiometric titrations demonstrated the ring-chain tautomerism of this product. It gave a dimethyl ester.

The β-(4-bromobenzoyl)acrylic amide and N,N-dimethylamide were made and converted by the action of sunlight into *cis* isomers. The anilide and N-methylanilide were also prepared but these could not be obtained in *cis* forms.

The evidence accumulated leads to the conclusion that the *cis* β-aroylacrylic acids and amides, without substituents on the ethylene linkage, are open-chain and will not easily, if at all, react in the sense of the cyclic forms.

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