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

Ring-Chain Tautomerism of the *cis*-β-Aroyl-β-bromoacrylic Acids[1,2]

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The Friedel-Crafts reaction with bromomaleic anhydride gave largely *cis*-β- and some *trans*-α-bromo-β-aroylacrylic acids, and involved halogen displacement by aluminum chloride in one case. *trans*-Dehydrobrominations of the *erythro* and *threo* dibromides of the β-aroylacrylic acids and esters gave respectively the *cis*- and *trans*-β-bromo derivatives, presumably by a concerted mechanism. Absorption spectra show the *cis*-β-bromo acid to be acyclic in the solid state and partly cyclic in solution. Acid and irradiation-catalyzed inversions indicate that the *trans* acids and esters are the labile higher-energy stereoisomers. Effects of solvent, acid, and base on the ring-chain equilibrium were studied spectroscopically. The following cyclic derivatives were made: ester, acid chloride, acetate, and amide (γ-hydroxylactam). The acyclic *cis*-ester relative to the cyclic *cis* ester is the stable form, and is obtainable from the labile-cyclic ester under acid catalysis and from the cyclic acid chloride by 1,4-methanolysis. The labile-cyclic *cis* ester was made by 1,2-methanolysis of the cyclic acid chloride in the presence of silver ion, presumably through an ionization mechanism. Differences in the effect of the β-bromine and of a β-methyl on the ring-chain tautomerism are explained in electronic terms. *para*-Halogens increase and *para*-methoxyl decreases the degree of cyclization at eq uilibrium in solution.

In continuation of studies on ring-chain tautomerism of *cis*-β-aroylacrylic acids it was of interest to determine the effects of one or two halogen atoms substituted on the ethylene linkage for comparison with the previously investigated effects of one or two methyl groups,[4-11] because the bromine atom is close to the methyl group in size but is electronically quite different. This paper deals mainly with the more accessable β-bromo derivatives[12-14] and their higher-melting *p*-bromo analogs II–VII.

The β-benzoyl-α- and β-bromoacrylic acids and their esters. The *first bromo acid* (*cis*-β-bromo, IIIa, m.p. 108°) was made by Bogert and Ritter[12] by dehydrohalogenation of the dibromides of β-benzoylacrylic acid (Va, VIa), and later by Rice[13] *via* the Friedel-Crafts reaction on bromomaleic anhydride (I). The *cis* configuration was assigned[13] correctly but on the inconclusive basis of diazomethylation to the IIIa-ester obtainable also from the ester dibromides by dehydrobromination and sunlight stereoinversion of the resulting IVa-ester.[13] That this was the β-bromo acid, contrary to earlier formulation,[12] was proved by the isolation from the Friedel-Crafts reaction mixture of a small amount of a *second bromo acid* (*α-bromo*, probably *trans*, IIa, m.p. 125°) the structure of which was proved by ozonolysis.[13] A *third bromo acid* (*trans*, β-bromo, IVa, m.p. 105°) corresponding to the IVa-ester,[13] was later isolated[14] in small amounts. The assigned configurations of IIIa and IVa are confirmed by the relationships described below.

The Friedel-Crafts condensation of bromomaleic anhydride (I) with bromobenzene using aluminum chloride gave two compounds,[5] as it did with benzene. One was the expected *cis*-β-bromo acid III (55%). The other (yellow, 20%) was the presumably-*trans*-α-chloro analog of II resulting from displacement of the ethylenic bromine atom, which was subsequently made directly from chloromaleic anhydride. The use of aluminum bromide in the reaction with bromomaleic anhydride to preclude halogen exchange, gave a 46% yield of the *cis*-β-bromo acid III and 23% of the presumably-*trans*-α-bromo acid II.

(1)(a) This work was supported in small part by a contract with the Office of Ordnance Research, U. S. Army and a research grant from the National Science Foundation. (b) Presented in a paper at the 136th Meeting of the American Chemical Society, Atlantic City, September 1959, Abstracts p. 19p.

(2)(a) H. Moncure, Jr., Ph.D. Dissertation, University of Virginia, July 1958. (b) A few of the experiments here reported were carried out by Joseph P. Feifer, and some aspects of the problems and data involved will be presented in a later paper (c).

(3) Du Pont Teaching Fellow, 1957–58. (b) Use of staff laboratory of the Chemistry Committee, Department of Electrical Engineering, U. S. Naval Academy, during 1955, is gratefully acknowledged. (c) Present location, Polychemicals Department, E. I. du Pont de Nemours & Co., Wilmington, Del.

(4) R. E. Lutz, P. S. Bailey, C.-K. Dien, and J. W. Rinker, *J. Am. Chem. Soc.*, **75**, 5039 (1953).

(5) J. W. Rinker, Ph.D. Dissertation, University of Virginia, 1954.

(6) R. E. Lutz, D. T. Merritt, and M. Couper, *J. Org. Chem.*, **4**, 95 (1939).

(7) R. E. Lutz and A. W. Winne, *J. Am. Chem. Soc.*, **56**, 445 (1934).

(8) R. E. Lutz and R. J. Taylor, *J. Am. Chem. Soc.*, **55**, (a) 1168, (b) 1585 (1933).

(9)(a) C. T. Clark, Dissertation, University of Virginia, 1958. (b) R. E. Lutz and C. T. Clark, *J. Org. Chem.*, **25**, 346 (1960); [(c) Correction: on page 248 in the paragraph following formula X the solid α-methyl acid Xb was by mistake included with the β-methyl acid Xa as cyclic in the solid state; the data in the Table 1[9b] show it to be acyclic.]

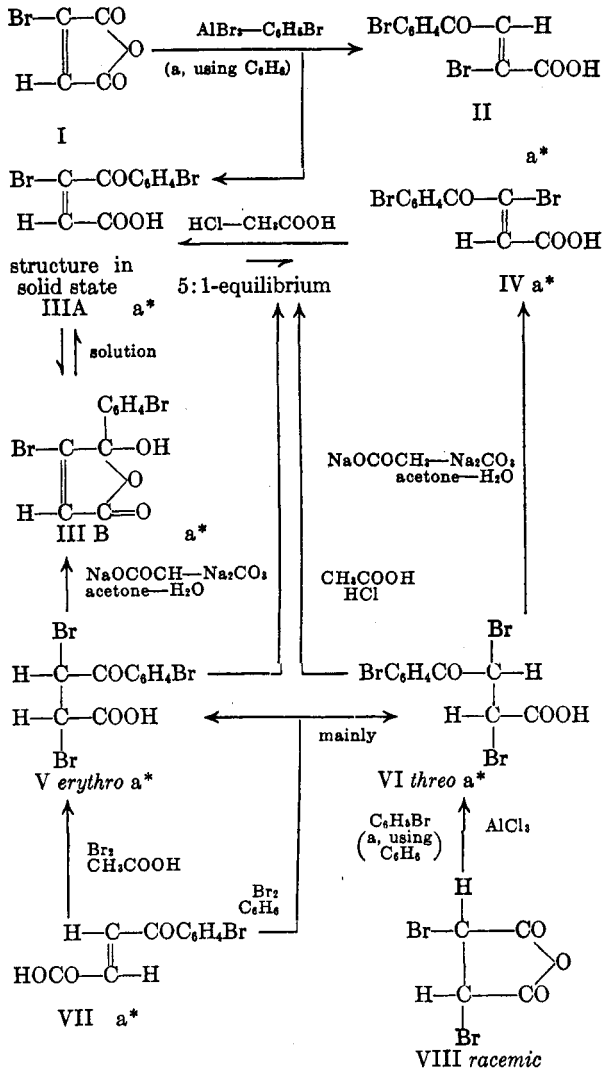
(10) R. E. Lutz and M. Couper, *J. Org. Chem.*, **6**, 77 (1941).

(11) R. E. Lutz and F. H. Hill, *J. Org. Chem.*, **6**, 175 (1941).

(12) M. Bogert and J. Ritter, *J. Am. Chem. Soc.*, **47**, 526 (1925).

(13) G. P. Rice, *J. Am. Chem. Soc.*, **52**, 2094 (1930) and references cited therein.

(14) R. E. Lutz, *J. Am. Chem. Soc.*, **52**, 3423 (1930). The formation reported here of the *trans* β-bromo acid has not been repeated in numerous attempts.[2,5]



In C_6H_4Br, Br is *para*. * The "a" compounds IIa–VIIa constitute the parent phenyl series, where phenyl replaces *p*-bromophenyl.

show the acyclic character of the acid and the lack

The α-bromo structure of the acid II is certain by difference from the *cis-trans* β-bromo pair (established below). It did not undergo irradiation-inversion into the stereoisomer which remains unknown. It was converted into an acyclic ester by diazomethane, by methanolic hydrogen chloride or hydrogen bromide, and by phosphorus pentachloride followed by methanolysis. No displacement of the α-bromine atom by chlorine occurred as happened in hydrogen chloride-catalyzed esterification of the parent acid IIa.[13] The ester was hydrolyzed by acetic-hydrobromic acid mixture. The acid both in the solid state and in chloroform solution showed two strong infrared absorption bands at *ca.* 5.85 and 6.00 μ and no lactone carbonyl absorption at *ca.* 5.7 μ; and it showed strong ultraviolet absorption maxima at 275 and 270 mμ in chloroform and in ethanol solutions, respectively, values which correspond to the maximum of 282 mμ for the ester in ethanol. These absorptivities of detectable equilibration with a cyclic or γ-hydroxylactone form, which would very probably have been involved to some small extent at least were the compound of *cis* configuration. These facts support but do not prove the *trans* configuration.

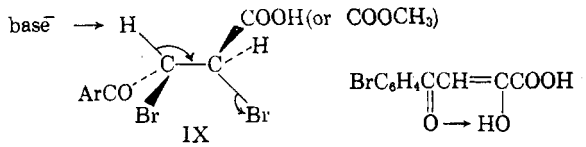
The *trans*-α-chloro acid was oxidized by potassium permanganate to *p*-bromobenzoic acid and was reduced to β-(*p*-bromobenzoyl)propionic acid. The location of the α-chlorine atom was presumed on the assumption that this product resulted from aluminum chloride-induced 1,4-addition-enolization of the reactive α,β-unsaturated ketone system of the α-bromo acid by hydrogen chloride, and subsequent elimination of hydrogen bromide, an exchange which is like that presumed to occur during the hydrogen chloride-catalyzed esterification of IIa.[13] The occurrence of the halogen exchange in the Friedel-Crafts reaction with bromobenzene but not with benzene, may be attributed to a significant activation of the conjugated system by the *p*-bromine atom.

Bromomaleic anhydride has reacted in two ways with bromobenzene and with benzene, corresponding to the similar reactions of citraconic anhydride with bromobenzene.[4] The citraconic anhydride reaction with benzene, however, differed in that both the α and β-methyl products had the *cis* configuration of the starting material. A hydrogen *alpha* to the β-aroyl group seems to be necessary for *cis*- to-*trans* inversion during this type of reaction, but even then inversion does not always occur.

Stereochemistry and mechanism of the dehydrohalogenation reactions. The *erythro*-dibromide V needed for these studies was made by addition of bromine in acetic acid to *trans*-β-(*p*-bromobenzoyl)-acrylic acid(VII). When the bromination was carried out in benzene, however, a mixture of dibromides was produced from which the predominant *threo*-dibromide VI could readily be isolated. In the formation of the corresponding dibromides of the parent benzoylacrylic acid Va and VIa, there was a similar solvent effect, the polar acetic acid favoring formation of the *erythro*-dibromide Va, and the less polar benzene leading to a separable mixture of the diastereoisomers in which the *threo* isomer VIa predominated.*cf.* [14] Actually the *threo* isomers of both series (VI and VIa) were better obtained by the stereochemically unequivocal Friedel-Crafts synthesis from *racemic*-dibromosuccinic anhydride (VIII).*cf.* [12–14]

It has been reported that sodium acetate in acetic acid converts both dibromides Va and VIa into the same *cis* unsaturated β-bromo acid,[12] presumably *via* the enolization mechanism (XIA), whereas methanolic potassium acetate dehydrobromination of the noncrystalline ester dibromide consisting largely of the *threo* isomer (VIa-ester) gives mainly the *trans*-β-bromo ester (of IVa),[13] presumably by concerted *trans*-elimination (IX).

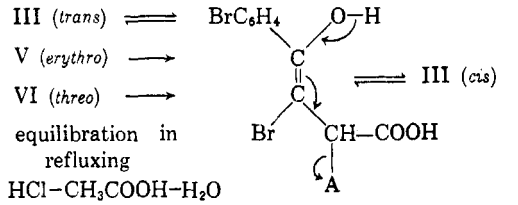
The *cis*-β-bromo unsaturated acid III, first obtained[5] from I by the Friedel-Crafts reaction described above, may be prepared in better yield (78%) by *trans*-dehydrobromination of the *erythro*-dibromide V[15] using the heterogeneous combination, sodium acetate, sodium carbonate, and acetone containing 2–4% of water.[14] The *trans* acid IV was obtained by similar *trans*-dehydrobromination of the *threo*-dibromide VI. The esters of the *erythro* and *threo* dibromides prepared by diazomethylation of the acids V and VI, also underwent *trans*-dehydrobrominations under these conditions to the esters of IIIA and IV, respectively. And comparable *trans*-dehydrobrominations of the parent benzoylacrylic acid dibromides Va and VIa gave the unsaturated acids IIIa and IVa, respectively. It may be concluded from the consistently *trans* character of these reactions that under these particular conditions they all proceed by a concerted mechanism and through the conformation formulated in IX.



IX

X

In acid-catalyzed dehydrobrominations,[2b] brought about by refluxing concentrated acetic–hydrochloric acid mixture, the *threo*-dibromide VI reacted readily, albeit with considerable loss of material and partly to give the enol X. The main product was impure *cis* unsaturated acid III from which were isolated a pure sample of III and a trace of the *trans* acid IV. The *erythro*-dibromide V under the same conditions reacted only partly but also gave a mixture of the β-bromo acids consisting largely of the *cis* isomer III. Both the *cis*- and the *trans*-β-bromo acids III and IV in separate experiments under these same conditions were converted into similar equilibrium mixtures in which the *cis* acid was shown by infrared analysis to predominate in a ratio of 5–1 over the *trans* acid, and from which also pure samples of the *cis* acid were isolated. It was thus shown under these conditions that *cis-trans* equilibration is induced under these strongly acidic conditions, and that the ratio of stereoisomers formed in the dehydrobrominations is essentially and necessarily independent of the mechanism of dehydrobromination. It may reasonably be presumed that the acid-catalyzed dehydrohalogenations proceed through enolization to XIa and that the *cis-trans* interconversions go by 1,4-addition-enolization through XIb.



XI

A = a, Br; b, Cl, OH, or OCOCH₃

These reactions may be compared with the dehydrohalogenations of the dibromosuccinic acids where concerted *trans* reactions occur,[16] the chalcone dibromides where concerted and enolization mechanisms evidently compete,[17] and the 1,2-dibenzoylethylene dihalides where the enolization mechanism seems important.[18]

cis-trans and Ring-chain relationships in the β-(p-bromobenzoyl)-β-bromoacrylic series. The interconversions of the *cis*- and *trans*-β-bromo acids, and of the acyclic-*cis*, the cyclic-*cis* and the *trans* methyl esters, are shown in XII–XIV. The configuration of the *cis* acid III, and by difference the configuration of the *trans* isomer IV, were established by ring-chain relationships.

The *cis* acid *in the solid state* was shown to be acyclic (IIIA) by its infrared absorption bands at 5.85 and 5.95 μ representing carboxyl and bromobenzoyl groups respectively, by the absence of γ-lactone carbonyl absorptivity at *ca.* 5.7 μ, and by the close correspondence of these absorptivities with those of the *trans* acid whose bands fall at 5.84 and 6.00 μ. It is unlike the β-methyl analog which is cyclic in the solid state,[9] and it is like the α-methyl analog which is acyclic in this state.[9c]

In *solution* the *cis*-β-bromo acid is in mobile ring-chain equilibrium (IIIA⇌IIIB). At 10% concentrations in chloroform and in ethanol it showed three strong infrared absorption bands at 5.7, 5.9, and 6.0 μ; and it was roughly estimated from relative absorption intensities that the acyclic-to-cyclic ratios were on the order of 7 to 3 and 6 to 4, respectively. At extremely high dilution, $5 \times 10^{-5}M$, in chloroform and in ethanol, the ultraviolet absorptivities at 273 and 268 mμ were ε 12,800 and 12,100, respectively, showing a marked equilibrium shift toward predominence of the acyclic form; this effect is explainable in terms of increased ionization to the highly absorbing acyclic anion and concomitant decrease in the concentra-

(15) It should be noted that in the preliminary experiments in this field the preparations of the β-bromo acids by dehydrohalogenation of the dibromides were confused by mistaken identities and similar melting points of the dibromides and by the variant effect of conditions on the stereochemistry of the dehydrobrominations. When the identity and correct structures of materials were finally established it became apparent that the special conditions described produced consistent *trans*-dehydrobromination as now formulated (*cf.* refs. 2a, 5).

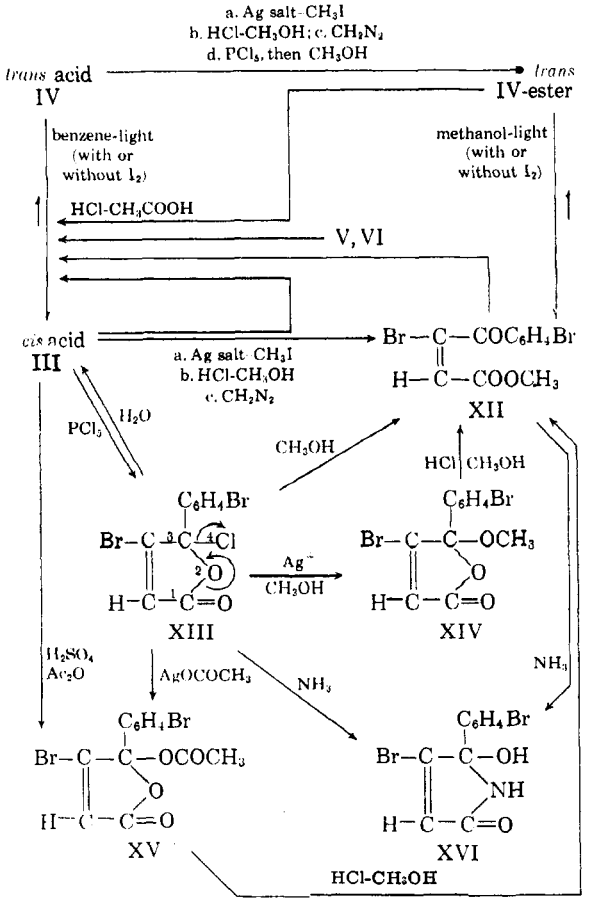
(16) W. G. Young, D. Pressman, and C. Coryell, *J. Am. Chem. Soc.*, 61, 1640 (1939).

(17) R. E. Lutz, D. F. Hinkley, and R. H. Jordan, *J. Am. Chem. Soc.*, 73, 4647 (1951).

(18)(a) R. E. Lutz and M. G. Reese, *J. Am. Chem. Soc.*, 81, 127 (1959); *cf.* also (b) J. B. Conant and R. E. Lutz, *J. Am. Chem. Soc.*, 47, 886 (1925); (c) R. E. Lutz and W. R. Smithey, Jr., *J. Org. Chem.*, 16, 51 (1951).

tion of the cyclic form. Addition of a small amount of hydrochloric acid to the $5 \times 10^{-5}M$ ethanol solution diminished the ultraviolet absorptivity at the maximum only slightly; but at this same concentration in glacial acetic acid to which was then added 10% by volume of concentrated hydrochloric acid, the drop in absorptivity was greater, indicating 10–20% decrease in concentration of the still-predominent acyclic form. These equilibrium shifts were in the direction and magnitude predicted of repression of ionization of the more acidic acyclic form and increased protonation of the probably more basic cyclic form. Addition of an excess of sodium hydroxide to the $5 \times 10^{-5}M$ ethanol solution on the other hand, increased ϵ to 14,500,[5] showing approach to complete conversion to the acyclic anion.

The structure of the acyclic *cis* methyl ester XII obtained by esterifications of III, and that of the cyclic ester XIV obtained under speical conditions of methanolysis of the acid chloride XIII, were proved by the relation of their absorption spectra to that of the *trans* ester, a necessarily acyclic reference compound. The acyclic-*cis* ester and the *trans* ester had similar ultraviolet and infrared absorptions which were characteristic of the unsaturated 1,4-keto-ester system, namely: maxima of 270 and 275 mμ, ϵ 12,000 and 13,000 (in ethanol); prominent pairs of bands at 5.84, 6.00 μ and 5.85, 6.00 μ respectively, corresponding in each pair to carbomethoxy and bromobenzoyl groups respectively; and absence of γ-lactone type carbonyl absorptivity at *ca.* 5.7 μ. The cyclic-*cis* ester XIV showed sharply decreasing absorptivity over the range 225 to 285 mμ, lack of absorption maximum or shoulder at *ca.* 270 mμ, γ-lactone-type carbonyl absorption at 5.65 μ, and the absence of acyclic-type carbonyl absorption at *ca.* 5.85 and 6.0 μ.



Acid catalysts as used in the methanolic hydrogen chloride esterifications of the *cis* and *trans* acids III and IV, did not cause configurational inversion, but did bring about cyclic-acyclic *cis*-ester equilibration (XII⇌XIV) favoring the acyclic form which thereby was shown to be the more stable of these two forms. This ring-chain relationship is in some degree of correspondence with that between the cyclic and acyclic *cis* acids where the acyclic is the dominant form and the cyclic the minor form; but it is contrary to the relationships in the analogous β-methyl series where both cyclic acid and cyclic ester are the more stable forms.[4,5]

The refluxing acetic-hydrochloric acid combination hydrolyzed both the *trans* and the acyclic-*cis* esters to *cis-trans* equilibrium mixtures consisting chiefly of the *cis* acid.

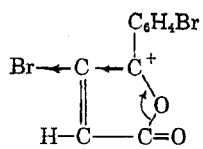
Both the *cis* and the *trans* acids in benzene, chloroform, or methanol solution were converted by sunlight irradiation into *cis-trans* photoequilibrium mixtures in which the *cis* isomer predominated. The ratios of *cis* to *trans*, approached from either direction, were approximately 9 to 1 and 2.5 to 1, respectively, in benzene and in chloroform. The *trans* ester in methanol was converted by sunlight irradiation into a similar mixture consisting largely of the acyclic *cis* isomer. The presence of iodine during irradiations did not appear significantly to alter the course of these isomerizations or the photoequilibrium positions, either for the acids or for the esters. These relationships are in contrast to those in the β-methyl series where interconversions of stable-*trans* and labile-*cis* esters were brought about, *trans*-to-*cis* by sunlight irradiation in the absence of iodine, and *cis*-to-*trans* by irradiation with iodine present.

Acid catalysis in refluxing concentrated acetic-hydrochloric acid mixture converted both *cis*- and *trans*-β-bromo acids to the same thermodynamic equilibrium mixture of the stereoisomers of approximately 5 to 1 *cis-trans* ratio. Although the strong acid present had been shown to shift the acyclic-cyclic-*cis* equilibrium (IIIA⇌IIIB) appreciably toward the cyclic form, the acyclic form IIIA was still predominent and the effect was clearly insufficient to account for predominance of the *cis* form in the *cis-trans* equilibrium. It is therefore concluded that the acyclic-*cis* configuration is the lower in energy and the *trans* higher, and that the photoequilibria are not far from true thermody-

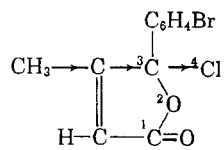
namic equilibria. These relationships are in contrast to those of the β-methyl analogs where the labile *cis* isomer is also produced from the *trans* isomer under the above equilibrating conditions,[2b] but where it is chiefly in the cyclic form under the strongly acid conditions and where the energy of cyclization must be decisive.[19,20]

The cyclic acid chloride XIII was obtained from the acid by the action of phosphorus pentachloride, and it was slowly hydrolyzed by water back to the acid. Its cyclic character was shown both in the solid state and in solution by ultraviolet and infrared absorptions. In iso-octane it showed no aroyl ultraviolet absorption maximum; rather, the absorptivity diminished continuously over the range 230–290 mμ. In the solid state its one infrared carbonyl absorption band was in the γ-lactone carbonyl range at 5.70 μ, whereas the acyclic form would have shown two distinctly different bands, at 6.0 μ for the aroyl group and 5.6 μ for the chlorocarbonyl.

This cyclic acid chloride reacted relatively slowly with methanol to give *directly* the stable-acyclic ester XII under build-up of a small hydrogen chloride concentration which in separate experiment was shown to be insufficient to cause cyclic-to-acyclic ester rearrangement. The labile-cyclic *cis* ester XIV was obtained only by the action of methanolic silver nitrate on the cyclic acid chloride. Two methanolysis mechanisms therefore must be involved,[cf. 21] solvent attack at the lactone carbonyl in a concerted 1,4-reaction with the conjugated system numbered in XIII, and 3,4-reaction by initial silver ion attack at the γ-chloride and through the resonance-stabilized cation XVII.



XVII



XVIII

A striking phenomenom is revealed in the contrast between the above-described 1,4-methanolysis of the cyclic acid chloride XIII and the 3,4-methanolysis under comparable conditions (in the absence of silver nitrate) of the analogous β-methyl cyclic acid chloride XVIII directly to the cyclic ester (which in that series is thermodynamically the more stable of the acyclic-cyclic pair). These different reactions of the two cyclic acid chlorides XIII and XVIII, involving different effects of the β-bromine atom and the β-methyl group which must operate in the initial reaction step, may be explained in terms of the strong electron-attracting *vs.* electron-repelling effects (XVII and XVIII) which would respectively increase and lessen the activity of the lactone carbonyl groups, and respectively lessen and increase the ionizability of the γ-chloride. While kinetics control the courses of these two types of reactions of the acid chlorides, the results fortuitously are the same as they are under acid-catalyzed equilibration of the acyclic and cyclic *cis* ester.

It would seem that the electronic differences between the β-bromine atom and the β-methyl group are of primary importance in affecting the ring-chain equilibrium position in the two series, but it should be noted that nevertheless the steric effects probably are more important in an over-all sense in permitting the necessary ring-chain equilibria in which the electronic effects can operate effectively and distinctively. This steric situation does not exist in the parent β-aroylacrylic series without ethylenic substituents where no cyclization whatever has been observed, and where the β-hydrogen atom in its electronic behavior lies between the bromine atom and the methyl group of the two β-derivatives.

The cyclic acetate XV was made not only by the action of silver acetate on the cyclic acid chloride XIII but also by acid catalyzed acylation of the acid. The latter reaction showed the product to be more stable than the unknown acyclic acetate which would have the high activity of a mixed anhydride. Acid-catalyzed alcoholysis through equilibrium control converts the cyclic acetate XV into the acyclic ester, XII, which is the more stable of the two ester forms.

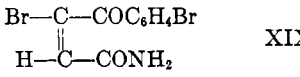
The action of concentrated ammonium hydroxide in dioxane on the *cis*-cyclic acid chloride XIII caused slow ammonolysis to the γ-hydroxylactam XVI the nature of which was shown by the absence of an ultraviolet absorptivity maximum or shoulder at *ca.* 270 mμ. The single infrared absorption peak at 5.95 μ distinguishes it from the alternative cyclization product, the γ-aminolactone, which would have its carbonyl band at a much shorter wave length.[cf. 9] Ammonolysis of the cyclic-*cis* ester took place slowly and gave the same γ-hydroxylactam XVI. Mechanistically it seems likely that concerted (1,4-) reaction has occurred by attack of ammonia at the lactone carbonylcarbon of XIII, and that the acyclic-*cis* ester has undergone primary attack

(19) The complicated stereochemical stability relationships which hold in the β-bromo- and β-methylaroylacrylic acid series seem to be transposed in the 1,2-dibenzoylmethyl and bromoethylenes where the *trans* methyl and the *cis* bromo derivatives appear to be the labile higher-energy forms. In the aroylacrylic series the effective steric bulk of the β-bromine atom is not much less than that of a β-methyl group. Plane scalar models based on Pauling bond lengths[cf. 20] show similar total group overlaps in both *cis* and *trans* forms but show in the *cis* form a significantly greater localization of overlaps of the important aroyl group in its sandwiched position between the β-bromine (or methyl) and the carboxyl or carbomethoxyl group.

(20)(a) L. Kuhn, R. E. Lutz, and C. R. Bauer, *J. Am. Chem. Soc.*, **72**, 5058 (1950). (b) R. E. Lutz and C.-K. Dien, *J. Org. Chem.*, **23**, 1861 (1958).

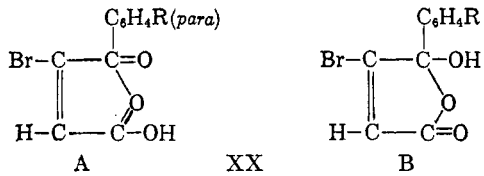
(21)(a) N. O. V. Sonntag, *Chem. Revs.*, **52**, 237 (1953); (b) G. E. K. Branch and A. C. Nixon, *J. Am. Chem. Soc.*, **70**, 3135 (1948).

by ammonia at the carbonyl of the carbomethoxyl group; in both cases these attacks would lead first to the hypothetical acyclic-*cis* amide XIX which would promptly cyclize.



XIX

Effects of p-substitutions on the ring-chain equilibrium position of cis-β-benzoyl-β-bromoacrylic acid were studied in extension of earlier work on the *cis*-α-methyl[5] and α-phenyl[22]-β-benzoylacrylic acids and on the α-hydroxyethylaminodesoxybenzoins[23] where *para* substitutions of chlorine and methoxyl in the benzoyl group markedly affect the equilibrium position, seemingly under the over-all requirement of existence of ring-chain equilibrium. Two additional *cis*-β-aroyl-β-bromoacrylic acids were therefore made, the *p*-chloro and *p*-methoxy derivatives XXa and XXd, where the two substituents relative to hydrogen of the unsubstituted molecule XXc involve opposite electronic effects, attractive and donative respectively.



A XX B

a. R = Cl; b. R = Br; c. R = H; d. R = OCH_3. Approximate relative % of cyclic form in 10% chloroform solution: a. 50; b. 30–40; c. 30; d. zero.

The *p*-methoxy-β-bromo *cis* acid XXd was made from the known *trans-p*-methoxybenzoylacrylic acid by bromination in acetic acid to the presumably-*erythro* dibromide, followed by *trans*-dehydrobromination which required significantly more drastic conditions than used for Va and V (doubtless because of lessening of the activity of the α-hydrogen by the *p*-methoxyl group). The β-location of the bromine atom is certain from the mode of reaction. The *cis* configuration was proved by the formation of two esters, the acyclic by diazomethylation and the cyclic by methanolysis of the cyclic acid chloride in the presence of silver nitrate, which were characterized by ultraviolet and infrared absorptions.

The *p*-chloro *cis* acid XXa was similarly made, and its configuration was proved by characterizing ultraviolet and infrared absorptions which showed a well balanced ring-chain equilibrium in solution.

All four of the acids XXa-d are acyclic in the solid state as shown by their pairs of infrared absorption bands at the wave lengths corresponding to aroyl carbonyl and carboxyl groups and by their lack of γ-lactone absorption. It is interesting to note that the sizable wave length difference between the ketone-carbonyl infrared absorptions of the *p*-chloro and *p*-methoxy compounds, the former at 5.95 μ and the latter at 6.02 μ, reflects the opposite electronic effects of these two substituents.

In solution in chloroform or in ethanol the *p*-methoxy acid XXd is largely acyclic as shown by the infrared absorption spectra which contain no 5.7 γ-lactone bands. The other three acids, XXa–c, all show well balanced ring-chain equilibria.

Although it is not possible in the absence of pure acyclic form precisely to measure the ring-chain ratios, we have made estimates from the per cent transmittancies of the compounds at the three bands characteristic of the γ-lactone, carboxyl, and keto groups at *ca.* 5.70, 5.85, and 6.00 μ respectively, on the assumption that the *relative* absorbancies of these groups are similar and not seriously affected by the *para* substituent, an assumption which seems reasonable from the several measurements of absorptivities made on the acyclic and cyclic derivatives under these conditions. The estimates given under XX show that electronically-opposite *para* substituents actually have a significant effect on the degree of cyclization in 10% solution in chloroform. The strongly electron-attracting *p*-chlorine atom which must activate the ketone carbonyl group, significantly increases cyclization, whereas *p*-methoxyl as a powerful electron-donating group which must deactivate the keto carbonyl, practically eliminates cyclization. These effects are comparable with those obtained in the α-methyl-β-aroylacrylic acid[5] and the α-hydroxyethylaminodesoxybenzoin series,[23a] where *p*-chlorine in the benzoyl group increases cyclization somewhat and *p*-methoxyl suppresses it.

EXPERIMENTAL[24]

erythro("normal")-β-Benzoylacrylic acid dibromide (Va)[14] was best prepared by slow addition of 0.4 mole of bromine to 0.4 mole of VIIa in 200 ml. of concd. acetic acid at room temperature with stirring and gentle warming at the end. Pouring into water and crystallization of the resulting precipitate from benzene (or toluene) gave 122.5 g. of a mixture of isomers, m.p. 120–128°. Two further crystallizations gave 55 g. (40%) of pure *erythro* Va of melting point 147–148°. A mixture of Va and VIa melted at 101–130°.

threo("iso")-β-Benzoylacrylic acid dibromide VIa[14] was made in one operation from 49 g. (0.5 mole) of molten

(22)(a) C. L. Browne, Ph.D. Dissertation, University of Virginia, 1953. *cf.*[23] (b) C. L. Browne and R. E. Lutz, *J. Org. Chem.*, **18**, 1638 (1953).

(23)(a) C. E. Griffin and R. E. Lutz, *J. Org. Chem.*, **21**, 1131 (1956); (b) R. E. Lutz and C. E. Griffin, *J. Org. Chem.*, **25**, 928 (1960).

(24) Melting points are "corrected." Ultraviolet absorption spectra were determined using (a) a Beckman DU Quartz spectrophotometer, or (b) a Perkin-Elmer Spectrocord 4000A. Infrared absorptions were determined using Perkin-Elmer (c) model 21 or (d) an "Infracord," and those by J. W. Rinker (ref. 5) were on a Baird double beam instrument. (e) The % refers to transmittancies when solvent transmittancies for both chloroform and ethanol were 90%. (f) The infrared absorptions in ethanol were made using a silver chloride cell. (g) The infrared determinations were by J. P. Feifer. (h) Microanalyses were by Mrs. Thomas Jensen and Mrs. James Logan.

maleic anhydride by slow addition of 80 g. (0.5 mole) of bromine, gentle heating for 1.5 hr., cooling to room temperature, dissolving in 200 ml. of pure benzene, adding 134 g. (1 mole) of anhydrous aluminum chloride portionwise under stirring, and allowing the mixture to stand overnight. Hydrolysis in dilute hydrochloric acid (ice) and recrystallization of the dried product from benzene gave 128 g. (76%) of VIa, m.p. 147–149°.

While bromination of VIIa in chloroform gave a mixture of isomeric dibromides,[14] bromination in carbon tetrachloride (Rice[13]) gave predominently the *threo* isomer VIa. In a typical experiment 0.04 mole of VIIa in 35 ml. of hot carbon tetrachloride was treated with 0.04 mole of bromine. Cooling gave 55% of nearly pure *threo* dibromide VIa, m.p. 141–145°.

trans-β-Benzoyl-β-bromoacrylic acid (IVa)[13,14] *by trans dehydrohalogenation.* After many unsuccessful attempts[5,14] the following directions were developed.

A mixture of 31 g. (0.09 mole) of *threo*-dibromide VIa, 15 g. (0.18 mol.) of sodium acetate, 6 g. of sodium carbonate, 200 ml. of pure acetone and 4 ml. of water, was shaken for 2 hr., dissolved in 1 l. of water, and acidified with 50 ml. of 50% hydrochloric acid. The precipitated oil crystallized on standing. Three crystallizations from 1:1 benzene–petroleum ether (b.p. 30–60°) gave 7 g. (36%) of pure *trans* acid IVa, m.p. 105°; identified by mixture melting point and infrared absorption.[14] This acid like the *trans* *p*-bromo analog IV formed a cottoney mass of needle-like crystals in contrast to the *cis* analogs III and IIIa which gave granular crystals under these conditions (and formed large octahedra on slow crystallizations[cf. 13]).

Absorption maxima: in chloroform, 263 mμ, ε 12,400; μ, 5.88s, 6.00s; in potassium bromide pellet, μ 5.82s, 6.00s.

cis-β-Benzoyl-β-bromoacrylic acid (IIIa)[12] *by trans dehydrohalogenation.* In repeating the earlier preparation[14] results depended on composition of the dibromide mixture. Pure *threo* dibromide Va gave only non-crystalline product and in no case was the "third isomer"[14] (IVa) obtained. The following procedure was successful.

A mixture of 11 g. of *erythro*-dibromide Va, 15 g. of sodium acetate, 3.5 g. of sodium carbonate, 75 ml. of acetone, and 5 ml. of methanol was refluxed for 4 hr. After filtering, the solid was suspended in water; acidification gave an oil which slowly crystallized upon standing in a vacuum dessicator; yield 5.1 g. (61%) m.p. 100–107°; recrystallized, it melted at 109°.

In another experiment under shaking at room temperature (24 g. of Va, 11 g. of sodium acetate, 4 g. of sodium carbonate, 150 ml. of acetone, and 3 ml. of water) the yield was 60%.

Absorption maxima: mμ, in chloroform, 257, ε 9,000; in 95% ethanol, 255, ε 10,600; in basic ethanol, 244, ε 12,200; in acidified ethanol; 255, ε 10,400; μ in chloroform 5.70 (60%),[24a] 5.90 (25%), 6.00 (27%); in 95% ethanol, 5.70 (38%), 5.90 (28%), 5.98 (22%); in potassium bromide pellet, 5.95s, 6.00s.

trans-to-cis Rearrangements (IVa to IIIa) were effected by 5-day sunlight irradiation of a benzene solution of 1 g. of IVa, and of a similar solution of 0.15 g. containing enough iodine to impart persistent color throughout the experiment. The product in each case was crystallized from benzene–petroleum ether (b.p. 30–60°) mixture (m.p. 106–108°) and identified by mixture melting point. The yield of pure IIIa in the first case was 50%, but it was small in the second where however no IVa was actually recovered.

Cyclic-cis-β-benzoyl-β-bromoacrylic acid chloride (β-bromo-γ-chloro-γ-phenylcrotolactone). A mixture of 21 g. of IIIa and 21 g. of phosphorus pentachloride was stirred until reaction was complete and then filtered from excess reagent. The phosphorus oxychloride was evaporated *in vacuo*. Recrystallization from iso-octane gave 13.5 g. (69%), m.p. 68°.

Anal. Calcd. for $C_{10}H_6BrClO_2$: C, 43.91; H, 2.21. Found: C, 43.75; H, 2.58. Absorption maxima: none in chloroform, ε decreasing through 7,000 at 250 mμ and 800 at 285 mμ to zero at 305 mμ. In potassium bromide pellet, 5.68s μ.

Acyclic-cis-β-benzoyl-β-bromoacrylic methyl ester (IIIAa-ester)[13] was obtained by methanolysis of the crude cyclic acid chloride under warming, then chilling to crystallize. After recrystallizations from methanol it melted at 85–86°.[cf. 13]

Absorption maxima: in absolute ethanol, 255 mμ, ε 11,800; in potassium bromide pellet, μ, 5.85s, 6.00s.

Cyclic-cis-β-benzoyl-β-bromoacrylic methyl ester (β-bromo-γ-methoxy-γ-phenylcrotolactone) (IIIBa-methyl ether). A solution of 2 g. of the cyclic acid chloride and 1.3 g. of silver nitrate in 200 ml. of methanol gave an immediate precipitate of silver chloride. After warming, filtering, concentrating, and adding water, 1.8 g. was obtained. Vacuum sublimation gave 1.5 g. (50%), m.p. 63–64°.

Anal. Calcd. for $C_{11}H_9BrO_3$: C, 49.09; H, 3.37. Found: C, 48.87; H, 3.32. Absorption maxima: mμ, none in 95% ethanol, ε decreasing through 10,800 at 225 mμ and 2,200 at 255 mμ to zero at 305 mμ; μ, KBr pellet, 5.70s.

Poorer yields were obtained using freshly precipitated silver oxide in methanol.

Conversion of cyclic to acyclic methyl ester (IIIBa-ether to IIIAa-ester) occurred in 70% yield in saturated methanolic hydrogen chloride (refluxing 4 hr.).

trans(?)-β-Benzoyl-α-bromoacrylic acid (IIa).[14] Absorption maxima: mμ, in 95% ethanol, 255, ε 10,400; in basic ethanol 255, ε 10,400; in acidified ethanol, 260, ε 11,400; μ, in chloroform, 5.88s, 6.00s; μ in 95% ethanol, 5.90s; 6.00s; μ in potassium bromide pellet, 5.88s, 6.00s.

erythro-β-(p-Bromobenzoyl)acrylic acid dibromide (V). A 300-ml. concd. acetic acid solution of 52 g. of VII[25] was treated under stirring with 11 g. of bromine (0.5 hr.). Pouring into ice gave a yellow oil which slowly solidified; 64 g. (m.p. 140–155°). Repeated recrystallizations from benzene and from 1:1 benzene–petroleum ether (b.p. 30–60°) mixture gave 19 g. (23%), m.p. 170–171° (25°-mixture melting point depression with *threo* isomer VI).

Anal. Calcd. for $C_{10}H_7Br_3O_3$: C, 28.94; H, 1.71. Found: C, 28.82; H, 1.67.

threo-β-(p-Bromobenzoyl)acrylic acid dibromide (VI)[5,15] was prepared like V but using benzene as reaction solvent. Concentrating and cooling gave 76% melting at 165–168°; recrystallized from benzene, it melted at 171°.

Anal.[5] Calcd. for $C_{10}H_7Br_3O_3$: C, 28.94; H, 1.71. Found: C, 28.99; H, 1.79.

In an alternative synthesis 98 g. (1 mole) of stirred molten maleic anhydride was treated with 160 g. (1 mole) of bromine, added slowly, with heating at 80–90° until disappearance of bromine color. Ethylene dichloride (250 ml.) and 330 g. (2.5 moles) of anhydrous aluminum chloride were added, and after standing overnight the solution was decanted from excess aluminum chloride and treated dropwise under stirring with 157 g. of bromobenzene. After evolution of hydrogen chloride ceased, hydrolysis, evaporation of solvent, and recrystallization from benzene gave 303 g. of crude VI, m.p. 155–160° (71%), identified by recrystallization and mixture melting point with the sample made from VII (above).

Using carbon disulfide as the reaction solvent (above) gave poorer yields.

cis-β-(p-Bromobenzoyl)-β-bromoacrylic acid (III). A mixture of 10 g. of *erythro*-dibromide V, 5 g. of sodium acetate, 2 g. of sodium carbonate, 50 ml. of pure acetone, and 2 ml. of water was shaken for 1 hr.; the sodium salt of III separated. Solution in water and acidification gave an oil from which a solid slowly crystallized. Recrystallization from 1:1 benzene–petroleum ether (b.p. 30–60°) mixture gave 6 g. (78%), m.p. 144–145°.

Anal.[5] Calcd. for $C_{10}H_6Br_2O_3$: C, 35.95; H, 1.81. Found: C, 35.98; H, 1.88. Absorption maxima: mμ in chloroform,[24b]

(25) D. Papa, E. Schwenk, F. Vellani, and E. Klingsberg, *J. Am. Chem. Soc.*, **70**, 3356 (1948).

272 ϵ 12,340; in 95% ethanol,[24a] 267[5], ϵ 14,500; in concd. acetic acid,[24b] 269–270, ϵ 10,970; in 4:10 by volume concd. hydrochloric–acetic acid mixture,[24b] 273, ϵ 8,670; μ[24a] in chloroform, 5.70 (33%), 5.90 (12%), 6.00 (11%); in 95% ethanol, 5.70 (48%), 5.88 (45%) (shoulder), 5.97 (36%); in potassium bromide pellet, 5.85s, 5.95s.

trans-β-(p-Bromobenzoyl)-β-bromoacrylic acid (IV).*cf.*[5] A mixture of 19.1 g. of VI, 10 g. of sodium acetate, 4 g. of sodium carbonate, 100 ml. of pure acetone, and 2 ml. of water, after shaking for 1 hr., deposited sodium salt of IV which upon filtering and acidifying gave 14 g. (92%) of IV, melting at 143–148°. Upon recrystallizations from 2:1 benzene–petroleum ether (b.p. 30–60°) mixture it melted at 153–154°.

Anal.[5] Calcd. for $C_{10}H_6Br_2O_3$: C, 39.95; H, 1.81. Found: C, 35.98; H, 1.86. Absorption maxima: mμ, in chloroform, 275, ϵ 16,000; in 95% ethanol[5], 270, ϵ 15,050; in basic ethanol[5] 269, ϵ 17,800. μ, in potassium bromide pellet, 5.84s, 6.00s.

Ozonolysis attempts on both III and IV under different conditions including those used on maleic acid[26] gave only *p*-bromobenzoic acid and none of the expected glyoxylic acid.

trans-β-(p-Bromobenzoyl)-β-bromoacrylic acid methyl ester (IV-ester) (five preparations). (a) *trans*-Acid IV, treated in the usual way with ethereal diazomethane, gave a 96% yield. (b) The silver salt of IV was precipitated from a solution of 4.5 g. of IV in 100 ml. of water and 1.5 g. of sodium hydroxide by addition of a solution of 25 g. of silver nitrate in 50 ml. of water; it was filtered and suspended in methanol–methyl iodide mixture with shaking for 20 hr.; yield 67%. (c) IV was treated for 5 hr. with refluxing saturated methanolic hydrogen chloride; yield 58%. (d) The acid chloride XIII was freshly prepared by the action of phosphorus pentachloride on IV, transferred to iso-octane, treated with Darco and cooled to −20° (light yellow platelets); it was then treated at room temperature with methanol from which the IV-ester crystallized on cooling. Recrystallization gave 43%. (e) VI-ester was dehydrohalogenated as described below.

The IV-ester, purified by recrystallizations from methanol, melted at 83–84°.

Anal. Calcd. for $C_{11}H_8Br_2O_3$: C, 37.96; H, 2.32. Found: C, 37.80; H, 2.38. Absorption maxima: mμ in 95% ethanol, 275, ϵ 15,400; μ, 5.78s, 6.02s.

Hydrolysis (of IV ester) by alkali gave intractable products.

trans-β-(p-Bromobenzoyl)acrylic acid (VII) *methyl ester.*[27,28] A mixture of 7 g. of the *trans* acid, 3.5 ml. of methanol, 8 ml. of ethylene dichloride, and 1 ml. of concd. sulfuric acid, was refluxed for 3 hr., and was then washed with dilute sodium carbonate and with water.[28] Evaporation and two crystallizations from methanol gave 3.5 g. (47%), m.p. 77–78°.

The threo-dibromide of VIII *ester* (used in non-crystalline form), was obtained (a) by addition of bromine to VII-ester in carbon tetrachloride and evaporation, and (b) by the action of ethereal diazomethane on the *threo*-dibromide VI and evaporation of the solvent.

*Dehydrobrominations of threo-*VI*-ester.* (a) A solution of 2.5 g. of VII-ester [(a) above] in methanol containing 2 g. of potassium acetate, was refluxed for 5 min. Work-up and crystallization from methanol gave 2 g. (62%) of pure IV-ester. (b) A mixture of 10 g. of VI [(b) above], 5 g. of sodium acetate, 2 g. of sodium carbonate, 50 ml. of acetone, and 1 ml. of water, after shaking for 1 hr. and standing overnight, was filtered from 2.6 g. of product; an additional 3.7 g. was obtained upon diluting the filtrate with water and chilling; the combined and nearly pure IV-ester (78%) was identified by mixture melting point.

Acyclic-cis-β-(p-bromobenzoyl)-β-bromoacrylic acid methyl ester (XII) was prepared in five ways: (a) By acid-catalyzed methanolysis of the acid III (as for IV-ester above); yield 90%. (b) By the action of methyl iodide on the silver salt of the *cis* acid III (as with the *trans* acid IV above); yield 35%. (c) By the action of ethereal diazomethane on the acid III (as with IV); yield 92%. (d) By dehydrobromination of 5 g. of *erythro*-V-ester (described below) by a mixture of 5 g. of sodium acetate, 1 g. of sodium carbonate, 25 ml. of acetone, and 1 ml. of methanol (refluxing for 0.5 hr.), diluting with water, and inducing crystallization; yield 50%. (e) By methanolysis of the cyclic *cis* acid chloride XIII, described below. The various samples were shown to be identical by mixture melting points.

The ester was recrystallized from methanol, m.p. 119–120°.

Anal. Calcd. for $C_{11}H_8Br_2O_3$: C, 37.96; H, 2.32. Found: C, 37.90; H, 2.38. Absorption maxima: mμ in 95% ethanol, 270, ϵ 13,000. μ in potassium bromide pellet, 5.85s, 6.00s.

erythro-β-(p-Bromobenzoyl)acrylic acid methyl ester dibromide (V-ester) was obtained in near-quantitative yield by ethereal-diazomethylation of the acid, V; it was recrystallized from methanol, m.p. 90–90.5°.

Anal. Calcd. for $C_{11}H_9Br_3O_3$: C, 30.79; H, 2.11. Found: C, 30.91; H, 2.26.

Hydrolysis of XII by refluxing a 4:10 (by volume) concd. hydrochloric–acetic acid mixture gave a mixture consisting predominently of the *cis* acid and some *trans* acid, from which 28% of purified *cis* acid III was isolated and identified.

Acid-catalyzed dehydrobrominations of threo and erythro dibromides VI and V were accomplished by refluxing for 1 hr. solutions of 1-g. samples in mixtures of 4 ml. of concd. hydrochloric and 10 ml. of concd. acetic acids, followed by pouring into ice water and allowing the resulting emulsions to stand overnight. In each of two *experiments on the threo acid VI* the total of products was extracted by ether. In one case the partially crystalline material was fractionally crystallized from dilute ethanol and gave as the first crop 7% of an enol which gave a positive ferric chloride color test, m.p. 158–163°; this was identified as X by ultraviolet absorption spectrum and mixture melting point with an authentic sample; the next crop (29%) was a *cis-trans* acid mixture (largely III), m.p. 130–142°, which on crystallization from benzene melted at 142–146° and was identified by mixture melting point as nearly pure III. The other run, from which no enol X was isolated, gave a mixture of III and IV (56%) from which 17% of pure III and a trace of pure IV were obtained upon fractional crystallization from benzene–petroleum ether (b.p. 30–60°) mixture; these were identified by mixture melting points.

In an *experiment on the erythro-dibromide* V, upon cooling the solution, pouring into ice water and allowing to stand overnight, filtration gave 35% of unchanged V which was identified. Ether extraction of the filtrate, evaporation, and one crystallization from benzene–petroleum ether (b.p. 30–60°) mixture, gave 0.26 g. of colorless solid mixture of III and IV, m.p. 125–128°, (34%) which infrared spectroanalysis showed to consist of approximately 5:1 amounts of the *cis* and *trans* acids III and IV.

Sunlight irradiation-equilibrations of the cis and trans β-bromo acids (III *and* IV) *and their methyl esters.* (a) *trans*-to-*cis* Inversions (IV to III) were accomplished by 5-day sunlight irradiations of solutions of 1 g. of IV in benzene with and without iodine present. The yields of pure III (isolated) were 70 and 50% respectively with no actual recovery of IV in either case (though IV evidently was present in the residues). (b) Another 5-day sunlight irradition of a 35-ml. purified benzene solution of 1.22 g. of pure *cis* acid III, and evaporation of the solvent, gave 1.19 g. (98%) of colorless solid residue of melting point 135–141°. The infrared absorption spectrum of pure *cis* acid in po-

(26) R. M. Dorland and H. Hibbert, *Can. J. Research*, 18B, 30 (1940).

(27) R. E. Lutz and G. W. Scott, *J. Org. Chem.*, 13, 284 (1948).

(28) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, 70, 3135 (1948).

tassium bromide pellets shows peaks at 9.7 and 10.5 μ which are not present in the spectrum of the *trans* isomer, and the spectrum of the pure *trans* isomer has a band at 11.8 μ which is not present in the spectrum of the *cis* isomer. From the infrared absorption spectrum of the mixture obtained by irradiation it was shown by quantitative comparison of absorptivities at these distinctive wave lengths that the ratio of *cis* form to the *trans* was approximately 8–10 to 1. (c) Attempts at *cis*-to-*trans* inversion (III to IV) by 5-day sunlight irradiations of benzene-iodine solutions of III led to recovery only of III; IV, although not actually isolated, was evidently present in equilibrium amount. (d) In two experiments $5 \times 10^{-5}M$ chloroform solutions of the *cis* and *trans* acids III and IV, which showed absorption maxima of ϵ 12,290 and 15,160, respectively, at 273 mμ, gave practically identical absorption spectra after 4 hr. of sunlight irradiation, with ϵ 13,110 at 273 mμ. By proportions the equilibrium was shown to involve 71.5% *cis* and 28.5% *trans* isomers. (e) After sunlight irradiation for 3 days of a methanol solution of *cis* acid III, only III was recovered. (f) Isomerization of *trans* IV-ester by 5-day irradiation of a methanol solution gave II as the only pure product isolated. (g) After similar 3-day irradiation of the *cis* ester XII, with iodine present throughout the reaction, cooling gave 50% of pure unchanged XII and a second crop of crystals which was shown by infrared spectroanalysis to be a mixture of XII and the *trans* IV-ester.

Acid-catalyzed cis-trans equilibrations of the β-bromo acids III and IV were carried out on 1-g. samples by the 1-hr. action of refluxing 4:10 (by volume) concd. hydrochloric-acetic acid mixture. The resulting solutions were poured into ice water and allowed to crystallize overnight. Usually first crops of pure *cis* acid III were obtainable. The total of products in each case (isolation often completed by ether extraction of the aqueous mixture) was intimately mixed and showed a melting range in the region 130–145°, 85–88%. Infrared spectroanalysis in potassium bromide pellet of products from either *cis* or *trans* acids III or IV gave the same equilibrium ratios of 5-*cis* to 1-*trans*.

Cyclic-cis-β-(p-bromobenzoyl)-β-bromoacrylic acid chloride [β-bromo-γ-chloro-γ-(*p*-bromophenyl)crotolactone] (XIII). A mixture of 5 g. of phosphorus pentachloride and 5 g. of *cis* acid III was stirred until completion of reaction, filtered from excess reagent, and evaporated under reduced pressure. The residue was recrystallized from isooctane; 4 g. (76%) m.p. 91–92°. The use of thionyl chloride, with one Darco treatment, gave 50%.

Anal. Calcd. for $C_{10}H_5Br_2ClO_2$: C, 34.07; H, 1.43. Found: C, 34.23; H, 1.58. Absorption maxima: in isooctane, ϵ decreasing from 12,200 at 235 mμ through 6,400 at 255 mμ, 5,600 at 260 mμ, to 500 at 280 mμ.

Hydrolysis of XIII with water, under shaking for 2 days, was incomplete. In fractional crystallization of the products from isooctane half of the starting material was recovered; the next fractions on recrystallization from benzene gave 2.5 g. of pure *cis* acid III which was identified by mixture melting point. *Methanolysis* required prolonged refluxing of a methanol solution (3 hr.), whereupon cooling gave 70% of pure acyclic *cis* ester XII (identified by mixture melting point.)

Cyclic acetate of cis-β-(p-bromobenzoyl)-β-bromoacrylic acid [γ-acetoxy-β-bromo-γ-(*p*-bromophenyl)crotolactone] (XV).[5] (a) A solution of 5 g. of III in 150 ml. of concd. acetic acid and 1 ml. of concd. sulfuric acid was maintained at 10° for 0.5 hr. and hydrolyzed in ice water. Recrystallizations of the precipitate from ethanol gave 1.45 g. (26%), melting at 121°.

Anal. Calcd. for $C_{12}H_8Br_2O_4$: C, 38.33; H, 2.14. Found: C, 38.39; H, 2.08. Absorption[5]: in 95% ethanol[24a] ϵ decreasing from 230 mμ to close to zero at 280 mμ. In chloroform, μ, 5.58–5.67s (bifurcation). (b) A suspension of freshly precipitated silver acetate from 1 g. of silver nitrate in concd. acetic acid, was treated with an acetic acid solution of 1 g. of the cyclic acid chloride XIII (shaking for 18 hr.). After filtering and adding water, crystallization of the resulting precipitate from methanol gave 1 g. (91%) of XV melting at 118°.

Methanolysis catalyzed by hydrogen chloride (refluxing for 5 hr.) gave acyclic-*cis* ester XIV in 69% yield (identified by mixture melting point).

Cyclic-cis-β-(p-bromobenzoyl)-β-bromoacrylic methyl ester [β-bromo-γ-(*p*-bromophenyl)-γ-methoxycrotolactone] (XIV). Warming a methanol solution of 2 g. of the *cis* (cyclic) acid chloride XIII and 1 g. of silver nitrate, filtering, and concentrating the solution, gave 1.5 g. (75%) of pure cyclic-*cis* ester XIV, m.p. 87–88°.

Anal. Calcd. for $C_{11}H_8Br_2O_3$: C, 37.96; H, 2.32. Found: C, 37.68; H, 2.62. Absorption maxima: in 95% ethanol, decreasing ϵ from 15,300 at 225 mμ through 900 at 275 mμ to zero at 285 mμ. μ, in potassium bromide pellet, 5.65s.

The metastability (persistence) of the labile cyclic-*cis* ester XIV in the presence of the small amount of acid generated during methanolysis of the cyclic acid chloride XIII is evident from the very fact that this ester was isolated in the above experiment. It was demonstrated in a separate experiment. After 10 min., refluxing of a methanol solution of XIV containing an added equivalent amount of nitric acid, XIV was recovered unchanged.

Intramolecular transmethylation of 0.5 g. of cyclic-*cis* ester XIV by methanolic hydrogen chloride under refluxing for 3 hr., and cooling the solution, gave 0.3 g. (60%) of nearly pure acyclic-*cis* ester XII.

Cyclic-amide of β-(p-bromobenzoyl)-β-bromoacrylic acid [β-bromo-γ-(*p*-bromophenyl)-γ-hydroxycrotolactam] (XVI), (a) *from the cyclic-cis acid chloride* XIII. A solution of 3 g. of XIII in 25 ml. of purified dioxane was treated with 10 ml. of 16*N* ammonium hydroxide (3 hr. at room temperature and refluxing for 1 hr.) and was evaporated. Crystallization of the residue gave 3 g. (94%) of XVI. (b) *From the cyclic-cis ester* XIV, suspended in 16*N* ammonium hydroxide (2 days), the yield was 21%. It was recrystallized from benzene or chloroform, m.p. 165° dec.

Anal. Calcd. for $C_{10}H_7Br_2NO_2$: C, 36.06; H, 2.12; N, 4.20. Found: C 36.30; H, 2.21; N, 4.21. Absorption: in 95% ethanol, no maximum, ϵ dropping through 7,800 at 225 mμ and 2,400 at 240 mμ to zero at 300 mμ.

Attempts to prepare β-(p-bromobenzoyl)propiolic acid by dehydrohalogenations of the *cis* and *trans* acids III and IV using triethylamine, quinoline, or sodium acetate were unsuccessful.

Bromomaleic anhydride (I)[28] was prepared from *meso*-dibromosuccinic acid; b.p. 117°/25 mm.; 95°/8.5 mm.; 71°/1 mm. Purity was shown by *Anal.* (calcd. for C_4HBrO_3: C, 27.15; H, 0.57. Found: C, 26.92; H, 0.52). The Friedel-Crafts reaction with bromobenzene and aluminum chloride in carbon disulfide (3 hr.), hydrolysis, evaporation of the solvent, and filtering, gave crystals and a yellow oil. Recrystallization of the former from benzene gave 55% of III, m.p. 145–148°, (identified by mixture melting point with sample above). From the yellow oil, bright yellow crystals formed on standing. Repeated crystallizations from benzene and from 95% acetic acid gave 24% of the α-chloro analog of II (see below), m.p. 165–166° (analysis was 1.2 to 2.5% low in carbon) and showed no mixture melting point depression with *trans*-α-chloro compound (see below).

trans(?)-β-(p-Bromobenzoyl)-α-bromoacrylic acid (II). In a second experiment on 41 g. of I, using 130 g. of aluminum bromide and 200 ml. of carbon disulfide (5 hr.), after hydrolysis and evaporation of the solvent, 36 g. (47%) of crystals was obtained which after purification melted at 142–145° and was identified by mixture melting point as III. The residual oil crystallized (18 g., 23%) and upon recrystallizations from 2:1 by volume water–acetic acid mixture melted at 154.5–155°.

Anal. Calcd. for $C_{10}H_6BrO_3$: C, 35.95; H, 1.81. Found: C, 35.58; H, 1.68. Absorption: maximum, in chloroform, 275 mμ, ϵ 16,600; in 98% ethanol, 270 mμ, ϵ 17,000.

Reduction of II by zinc and acetic acid (below 40°) gave β-(*p*-bromobenzoyl)propionic acid[cf. 27] (identified by mixture melting point). *Attempts to isomerize* II by 5-day sunlight irradiation of a benzene solution, and by a refluxing 4:10 (by volume) concd. hydrochloric-acetic acid mixture (1 hr.), gave unchanged material as the only crystalline product.

trans(?)-β-(p-Bromobenzoyl)-α-bromoacrylic acid methyl ester (II-ester) was made from 1-g. samples of the acid II by: (a) ethereal diazomethane (58% yield); (b) treatment with phosphorus pentachloride, filtering, take-up in isooctane, addition of methanol, and warming (yield 49%); (c) passing hydrogen bromide through a refluxing methanol solution of II (yield 38%, and 13% of unchanged II); and (d) similarly using hydrogen chloride (yield 29%). Recrystallizations were from methanol, melting point 81–82°.

Anal. Calcd. for $C_{11}H_8Br_2O_3$: C, 37.96; H, 2.32. Found: C, 37.84; H, 2.70. Absorption maxima: in 95% ethanol, 282 mμ, ε 16,000; in potassium bromide pellet, μ, 5.78s, 6.04s.

Hydrolysis of II-ester by 4:10 (by vol.) concd. hydrobromic-acetic acid mixture (refluxing for 1 hr.) gave 35% of II; it was recrystallized from benzene–petroleum ether (b.p. 30–60°) mixture and identified by melting point 155° and mixture melting point. After *irradiation* of a methanol solution for 5 days, 66% of II-ester was recovered and identified, and no other crystalline producted was isolated.

trans(?)-β-(p-Bromobenzoyl)-α-chloroacrylic acid (analog of II). The sample closest to analytical purity was obtained in 15% yield from chloromaleic anhydride by the Friedel-Crafts reaction as described above but using ethylene dichloride as the solvent.

After repeated crystallizations from benzene, acetic acid, and petroleum ether (b.p. 30–60°) it melted at 164–165° and gave no mixture melting point depression with the sample isolated above. Analyses for carbon were consistently high by 0.86–0.97%. It showed strong absorptivity at 275 mμ.

Oxidation by aqueous alkaline permanganate gave *p*-bromobenzoic acid (identified). *Reduction* by zinc and acetic acid (below 40°) gave β-(*p*-bromobenzoyl)propionic acid 68% (identified by mixture melting point[27]).

trans(?)-β-(p-Bromobenzoyl)-α-chloroacrylic acid methyl ester. Both of the above samples of the acid, esterified by ethereal diazomethane, gave this same ester; it was recrystallized from methanol and vacuum-sublimed, m.p. 91–92° (no mixture melting point depression).

Anal. Calcd. for $C_{11}H_8BrClO_3$: C, 43.52; H, 2.66. Found: C, 43.55; H, 2.67.

cis-β-(p-Chlorobenzoyl)-β-bromoacrylic acid,[cf. 25] XXa. *erythro-β-*(*p*-Chlorobenzoyl)acrylic acid dibromide[25] was obtained in 26% yield, m.p. 148–150°, from the first crystalline fraction obtained after bromination of the *trans-β-*(*p*-chlorobenzoyl)acrylic acid in acetic acid (for analogies see V and VII). Conversion by sodium acetate in 2% (by volume) acetone-water mixture in the usual way gave the *cis-β-*bromo acid in 56% yield (pure); it was crystallized from benzene–petroleum ether (b.p. 30–60°), m.p. 147–148°.

Anal. Calcd. for $C_{10}H_6BrClO_3$: C, 41.48; H, 2.08. Found: C, 41.40; H, 2.41. Absorption maxima: μ, in chloroform, 5.65s, 5.90s; 5.95s; in potassium bromide pellet, 5.84s, 5.95s.

erythro-β-(p-Methoxybenzoyl)acrylic acid dibromide, made like V by bromination of *trans-β-*(*p*-methoxybenzoyl)acrylic acid[25] in concd. acetic acid, was crystallized from 1:1 (by volume) benzene–petroleum ether (b.p. 30–60°) mixture; m.p. 147.5–148°.

Anal. Calcd. for $C_{11}H_{10}Br_2O_4$: C, 36.09; H, 2.75. Found: C, 36.31; H, 2.89.

cis-β-(p-Methoxybenzoyl)-β-bromobenzoylacrylic acid (XXd). Dehydrobromination of 3.95 g. of the *erythro* dibromide (above) by 2.5 g. of sodium acetate, 0.8 g. of sodium carbonate, 25 ml. of acetone, and 0.5 ml. of water, was achieved by warming the mixture on a water bath for 3 hr., dilution with water, and acidification. The ether extract of the resulting oil upon drying over calcium chloride and evaporating gave 1.5 g. (77%) melting at 139–141°. After recrystallizations from 1:1 benzene–petroleum ether (b.p. 30–60°) mixture it melted at 144–145°.

Anal. Calcd. for $C_{11}H_9BrO_4$: C, 46.34; H, 3.18. Found: C, 46.28; H, 3.21. Absorption maxima: in 95% ethanol, 295 mμ, ε 13,800; in basic ethanol, 290 mμ, ε 13,800; in acidified ethanol, 295 mμ, ε 13,800. μ, in chloroform, 5.90s, 6.00s; in potassium bromide pellet, 5.82s, 6.02s.

Acyclic-cis-β-(p-methoxybenzoyl)-β-bromoacrylic methyl ester was obtained in 40% yield by the action of ethereal diazomethane on the *cis* acid XXd. It was purified by vacuum sublimation, m.p. 85–86°.

Anal. Calcd. for $C_{12}H_{11}BrO_4$: C, 48.18; H, 3.70. Found: C, 48.18; H, 3.41.

Cyclic-cis-β-(p-methoxybenzoyl)-β-bromoacrylic methyl ester [β-bromo-γ-methoxy-γ-(*p*-methoxyphenyl)crotolactone] was obtained in 10% yield by the action of phosphorus pentachloride on the acid XXd followed by treatment with a suspension of silver oxide in methanol. After vacuum sublimation it melted at 116–117°.

Anal. Calcd. for $C_{12}H_{11}BrO_4$: C, 48.19; H, 3.68. Found: C, 48.07; H, 3.93. Absorption maximum: in potassium bromide pellet, 5.70s μ.

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