

CCCXCI.—*The Addition of Halogens to Unsaturated Acids and Esters. Part II. The Addition of "Bromine Chloride" to Phenylpropionic Acid.*

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It has been shown in Part I (this vol., p. 1955) that an equimolecular mixture of bromine and chlorine, dissolved in carbon tetrachloride ("bromine chloride" solution), reacts additively with cinnamic acid to form the two externally compensated stereoisomerides corresponding to the formula $C_6H_5 \cdot CHCl \cdot CHBr \cdot CO_2H$.

Similar experiments with phenylpropionic acid in the place of cinnamic acid have now given a mixture from which, by fractional crystallisation from light petroleum, two, and only two *acids* have been isolated. These are the geometrical isomerides which theory demands from the structural formula $C_6H_5 \cdot CCl : CBr \cdot CO_2H$.

By exposure of a chloroform solution of the higher-melting acid (129°), mixed with a little bromine, to direct sunlight, this acid was almost entirely converted into its lower-melting isomeride (112°). The latter acid was unaffected by such treatment.

This transformation is parallel to that of the other $\alpha\beta$ -dihalogeno-

cinnamic acids, since, under similar conditions, the higher-melting (m. p. 139°) $\alpha\beta$ -dibromocinnamic acid is partly transformed into its lower-melting (m. p. 100°) isomeride (Roser and Haselhoff, *Annalen*, 1888, **247**, 140), and the lower-melting (m. p. 101°) $\alpha\beta$ -dichlorocinnamic acid undergoes isomerisation into the higher-melting (m. p. 121°) acid (Stoermer and Heymann, *Ber.*, 1913, **46**, 1349). The stable transformation products in both of these cases possessed the *cis*-configuration, as will be shown.

The interconvertibility of the β -chloro- α -bromocinnamic acids is indicative of their geometrically, and not structurally isomeric relationship; thus the addition of "bromine chloride" corresponds to that of bromine to phenylpropionic acid in non-hydroxylic solvents, since in this case also a mixture of the two geometrically isomeric $\alpha\beta$ -dibromocinnamic acids is formed (Roser and Haselhoff, *loc. cit.*).

The corresponding addition of chlorine, however, gives rise to only one product, namely, *cis*- $\alpha\beta$ -dichlorocinnamic acid (m. p. 121°) (Nissen, *Ber.*, 1892, **25**, 2665), but this apparent anomaly can probably be explained by the extremely labile nature of the lower-melting (100°) *trans*-isomeride (Stoermer and Heymann, *loc. cit.*).

The positions occupied by the respective halogen atoms in the chlorobromocinnamic acids have been determined by a study of the chlorobromoindone which is produced when the lower-melting (112°) isomeride is treated with cold concentrated sulphuric acid; this reaction, moreover, establishes the *cis*-configuration of this acid. The higher-melting acid is therefore the *trans*-isomeride, and this conclusion is borne out by the fact that it is not affected by treatment with sulphuric acid.

Indeed, it has been found most convenient to prepare the chlorobromoindone directly from the product of the interaction of phenylpropionic acid and "bromine chloride," since the indone was readily separable from the residual *trans*-acid by solution in hot light petroleum.

Although this indone has the same melting point (105°) as that of the compound shown by Roser and Haselhoff (*Annalen*, 1888, **247**, 148) to be 2-chloro-3-bromo-1-ketoindene, yet an examination of its reactions has led to the conclusion that it is isomeric with the latter, and possesses the structure designated by 3-chloro-2-bromo-1-ketoindene. The evidence adduced for such a structure is based on the fact, definitely established by Schlossberg (*Ber.*, 1900, **33**, 2425), that the halogen atom which occupies the α -position to the phenylene group (*i.e.*, the 3-position) is the more readily replaceable by univalent atoms or radicals.

The chlorobromoindone obtained from *cis*-chlorobromocinnamic

acid condensed readily with aniline, to form an anilido-derivative identical with that obtained by Roser and Haselhoff (*loc. cit.*) from 2 : 3-dibromoindone, which was therefore 2-bromo-3-anilidoindone.

The fact that as a result of this condensation hydrogen chloride is eliminated (as a quantitative experiment proved) establishes the structure of the substance as 3-chloro-2-bromoindone. Additional evidence favouring such a structure is afforded by the fact that the analogous piperidyl derivative was identical with that prepared by Roser and Haselhoff from 2 : 3-dibromoindone and piperidine.

Furthermore, an authentic specimen of 2-chloro-3-bromoindone, prepared by boiling 2 : 3-dichloroindone with alcoholic potassium bromide (Roser and Haselhoff) proved to be non-identical with the new chlorobromoindone, as was evinced by a mixed melting point, and by the non-identity of their *oximes*.

Consequently, the new indone must be formed by the elimination of water from *cis*- β -chloro- α -bromo- β -phenylacrylic acid, m. p. 112°, and since this is directly obtainable from its isomeride, m. p. 129°, the latter must possess the *trans*-configuration. The following table summarises the physical properties of these new chlorobromocinnamic acids and the already known $\alpha\beta$ -dihalogenocinnamic acids :

Cinnamic acid.	M. p.	Crystalline form.	Solubility.	Stability.
β -Chloro- α -bromo-	<i>cis</i> 112°	Needles	More sol.	Stable
	<i>trans</i> 129	Plates	Less „	Labile
$\alpha\beta$ -Dibromo-	<i>cis</i> 100	Needles	More „	Stable
	<i>trans</i> 139	Plates	Less „	Labile
$\alpha\beta$ -Dichloro-	<i>cis</i> 121	Plates	Less „	Stable
	<i>trans</i> 100	Rhombic tablets	More „	Labile

The new chlorobromocinnamic acids are seen to possess physical properties analogous in every respect with those of their dibromocongeners.

The positions taken up by the constituent atoms of the “ bromine chloride ” molecule when this unites with phenylpropionic acid—the more negative atom uniting with the β -carbon atom—are the same as in the case where cinnamic is substituted for phenylpropionic acid.

By a series of experiments conducted as described in Part I, “ bromine chloride ” has been found to react with phenylpropionic acid at a much more rapid rate than either bromine or chlorine alone, the reaction being of the bimolecular type, without an inhibition period. Thus in yet another way is the reaction parallel to that for cinnamic acid and “ bromine chloride.”

The action of bromine and chlorine dissolved in carbon tetrachloride on the *cis*-isomerides of the three pairs of $\alpha\beta$ -dihalogeno-

cinnamic acids above described (the *trans*-isomerides were not employed owing to their ready transformation into the *cis*-acids) is interesting.

The nature and extent of these reactions were determined by a series of experiments conducted as already described by Williams and James (this vol., p. 344). The mixed solutions of acid and halogen were sealed up in colourless glass bulbs and exposed to dull light, the residual halogen after definite time-intervals being determined by breaking the bulbs under potassium iodide and titrating the liberated iodine with standard thiosulphate.

The results obtained with bromine showed that in all three cases the amount of this halogen which disappeared was extremely small even after several weeks, and may even then have been due to substitution in the phenyl radical, so that no bromine addition products could be prepared.

$\alpha\beta$ -Dichlorocinnamic acid formed an addition product with chlorine, *viz.*, $\alpha\alpha\beta\beta$ -tetrachloro- β -phenylpropionic acid, m. p. 130°. This is the one product expected on theoretical grounds; it contains *no* asymmetric carbon atoms and is therefore not potentially optically active.

The results for $\alpha\beta$ -dibromocinnamic acid and chlorine indicated that some replacement of the bromine in the acid by chlorine occurred, but no recognisable product could be isolated and there was no further reaction when the concentration of the total halogen was approximately half its initial value. This attainment of an approximate "equilibrium" may be ascribed either to the formation of an actual equilibrium between original acid, replaced acid, chlorine and bromine, or to the total disappearance of the chlorine by its substitutive and additive reactions, in which case the residual halogen would be the bromine liberated by replacement, which would be practically inert towards these acids.

A similar partial replacement of bromine by chlorine, and attainment of an approximate "equilibrium," occurred in the reaction between β -chloro- α -bromocinnamic acid and chlorine, but in this case about five-sixths of the halogen had disappeared at that stage. The main product of this reaction was the dichloride of the chloro-bromo-acid, *viz.*, $\alpha\beta\beta$ -trichloro- α -bromo- β -phenylpropionic acid, m. p. 127°, but a small quantity of $\alpha\alpha\beta\beta$ -tetrachloro- β -phenylpropionic acid was also formed.

The former of these products is the only addition compound expected on theoretical grounds: it contains only one asymmetric carbon atom, and may therefore be resolvable.

Corresponding experiments with "bromine chloride" in place of the pure halogens indicated that it did not react as a molecule of

such in these cases, the chlorine portion only appearing to be reactive.

The properties of the dichloro- and chlorobromo-cinnamic acids of forming addition products with chlorine but not with bromine, and of the replacement of part of the bromine by chlorine in the case of the latter acid, are not unique. For instance, tetraphenylethylene forms no addition product with bromine (Behr, *Ber.*, 1870, **3**, 753) but yields with chlorine a dichloride (Norris, Thomas, and Brown, *Ber.*, 1910, **43**, 2940). Further it has recently been shown by Meisenheimer (*Annalen*, 1927, **456**, 142) that triphenylbromoethylene, although it does not unite with bromine, reacts with excess of chlorine with replacement of the bromine atom and formation of a dichloride of the resulting product, triphenyltrichloroethane.

EXPERIMENTAL.

When a suspension of phenylpropionic acid in carbon tetrachloride was treated at 0° and in the dark with "bromine chloride" (1 mol.) dissolved in the same solvent, the acid gradually went into solution. After a few hours the solvent was removed by evaporation in a vacuum, and the resulting crystalline mass dissolved in hot chloroform. On adding light petroleum to this solution until cloudy and allowing it to cool, colourless crystalline plates and clusters of straw-coloured needles were deposited. The mother-liquid was decanted, and the mixture of crystals warmed with light petroleum; the needles alone went into solution. The plates, after being washed with more hot light petroleum, melted at 129° (Found: Br, 30.0; Cl, 13.8. $C_9H_6O_2ClBr$ requires Br, 30.6; Cl, 13.6%). The hot petroleum from the first extraction deposited, on cooling, clusters of long, straw-coloured needles, m. p. 112° (Found: Br, 30.0; Cl, 13.7%). The proportion of the higher- to the lower-melting *chlorobromocinnamic acid* was approximately 1:4. A successful separation of the two acids could not be accomplished by any of the other methods commonly employed in similar cases.

When the mixed chlorobromocinnamic acids obtained by addition of "bromine chloride" to phenylpropionic acid were rubbed with excess of cold concentrated sulphuric acid, a dark brown solution was formed, which, when poured into a large volume of cold water, yielded a quantity of golden-yellow flocks. Hot light petroleum dissolved the coloured constituent of the dried product, leaving undissolved a small proportion (about one-fifth of the original mixture) of small colourless plates of the higher-melting chlorobromocinnamic acid (m. p. 129°). The petroleum extract deposited *3-chloro-2-bromo-1-ketoindene* in clusters of golden-yellow needles,

m. p. 105° (Found : Br, 32·7; Cl, 10·9. C_9H_4OClBr requires Br, 32·9; Cl, 10·8%).

The indone, when warmed with excess of aniline in alcoholic solution, yielded bright scarlet needles of 2-bromo-3-anilidoindone, m. p. 170°, as described by Roser and Haselhoff (*loc. cit.*). That hydrogen chloride was eliminated by this condensation is proved by the following results :

0·204 G. of the indone was treated with alcoholic aniline, and the anilido-compound removed. The filtrate gave 0·1220 g. of silver halide, which was not reduced in weight when warmed in a stream of chlorine, and was hence silver chloride (Calc. for 100% evolution of hydrogen chloride : AgCl, 0·1200 g.).

The chlorobromoindone, when treated with piperidine as for aniline, gave bright red tables of 3-piperidyl-2-bromo-1-ketoindene, m. p. 117° (decomp.) (Roser and Haselhoff, *loc. cit.*).

By boiling the indone in alcoholic solution with hydroxylamine hydrochloride, pouring the mixture into water, and crystallising the precipitated yellow powder from alcohol, 3-chloro-2-bromo-1-ketoindene oxime was obtained as silky yellow needles, m. p. 194° (decomp.) (Found : Br, 30·1; Cl, 14·1. $C_9H_5ONClBr$ requires Br, 30·9; Cl, 13·7%).

2-Chloro-3-bromo-1-ketoindene, prepared as described by Roser and Haselhoff, melted at 105°; a mixture of this and the above-described 3-chloro-2-bromo-1-ketoindene melted indefinitely at 65—100°. The oxime of the former compound, prepared as described for the latter, melted at 184° (decomp.) (Found : Br, 30·3; Cl, 13·6%).

The results of kinetic experiments with phenylpropionic acid and "bromine chloride," bromine, and chlorine, respectively, are summarised in the table. The corresponding figures for cinnamic acid and these reagents are given for comparison purposes. Experiments were conducted at 0°, in the dark, and in carbon tetrachloride solution. The bimolecular velocity coefficient $k = 1/t \cdot x/a(a - x)$, is calculated on the basis of t in hours and concentrations (a and x) in g.-mols. per litre.

Acid.	Reagent.	Limits of k .	Mean k .
Phenylpropionic	{ Bromine chloride	4·43—3·76	4·11
	{ Bromine	0·0733—0·0680	0·0700
	{ Chlorine	0·0540—0·0344	0·0420
Cinnamic	{ Bromine chloride	133—96·3	104
	{ Bromine	0·173—0·041	0·146
	{ Chlorine	0·265—0·153	0·209

Although phenylpropionic acid is more unsaturated than cinnamic acid, the halogens react with the former at a slower rate than with the latter. The hydrogen atoms in the cinnamic acid side chain probably play an important part in this connexion.

cis- $\alpha\beta$ -Dichlorocinnamic acid, treated with chlorine (1 mol.) in carbon tetrachloride solution, and exposed to diffused light for 5 weeks, yielded a product which crystallised from carbon tetrachloride in colourless prisms, m. p. 130° (Found: Cl, 48.8. $C_9H_6O_2Cl_4$ requires Cl, 49.2%). The product is therefore $\alpha\alpha\beta\beta$ -tetrachloro- β -phenylpropionic acid.

cis- β -Chloro- α -bromocinnamic acid reacted with chlorine, with partial replacement of bromine by chlorine, and formation of the corresponding addition product, $\alpha\alpha\beta\beta$ -tetrachloro- β -phenylpropionic acid in small amount, the main product being the dichloride of the original chlorobromo-acid, viz., $\alpha\beta\beta$ -trichloro- α -bromo- β -phenylpropionic acid, m. p. 127° (Found: Br, 24.0; Cl, 31.7. $C_9H_6O_2Cl_3Br$ requires Br, 24.0; Cl, 32.0%). The products were separated by fractional crystallisation from carbon tetrachloride.

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