A Study of the Chlorination of Crotonic Acid and Related Compounds

being a Thesis submitted for the Degree of Master of Science in the University of London

by

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ABSTRACT: "A Study of the Chlorination of Crotonic Acid and Related Compounds"

The chlorination of crotonic acid and of crotonaldehyde was studied under various conditions with particular reference to the products of the reactions.

The reaction of crotonic acid with chlorine was carried out in water saturated with sodium chloride, in nitromethane, and in chloroform. In the first of these three solvents the products appeared to be entirely those which would be expected if the reaction proceeded through a two-stage mechanism in which the first stage involved electrophilic attack by a chlorine molecule on the α-carbon atom, followed by reaction of the carbonium ion so formed with any nucleophile present in the solution. In nitromethane the products were more unexpected, and appeared to consist largely of α-chloro-β-hydroxybutyric acid, even when the reaction was carried out in dry solvent. A mechanism involving the intermediate formation of a lactone ring is suggested for this reaction. The chlorination which was carried out in chloroform produced, apart from αβ-dichlorobutyric acid, a product which has not yet been identified conclusively, but which, at the moment, appears to be α-chlorovinylacetic acid. A mechanism by which this could have been formed is suggested.

One quantitative determination of the amounts of the two isomers of αβ-dichlorobutyric acid produced by the chlorination in chloroform of crotonic acid was made, using the method of isotopic dilution. It was shown that not more than 2% of the isomer formed by cis addition of the halogen was produced under these conditions.

The chlorination of crotonaldehyde was also carried out in chloroform. The reaction was faster than the corresponding reaction of the acid, and the products, after oxidation, consisted entirely of the two isomers of αβ-dichlorobutyric acid, the one formed by cis addition to the aldehyde being present to an extent of about 20%. A nucleophilic mechanism is suggested for this reaction.

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The work presented in this Thesis was carried out in the laboratories of the Chemistry Department of Bedford College, University of London, during the period September 1961 to September 1962.

The author wishes to thank Prof. P.B.D. de la Mare for his help and guidance during this work. She also wishes to thank Mr. R. Mitchell for technical assistance, and Dr. R. Bolton for assistance with this thesis.

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I. INTRODUCTION

INTRODUCTION

Ia. The mechanisms of the additions of halogens to olefinic substances.

Under most conditions, the addition of halogens to unsaturated systems involves an initial electrophilic attack by the halogen molecule. The halogen molecule is at least partially polarised in the sense $X^{\delta+} -- X^{\delta-}$, and it is the positive end of the dipole which attacks the olefin first. The experimental evidence for this has been summarised by Williams[1], and includes the facts that electron-releasing substituents in the molecule accelerate the addition rate, while electron-withdrawing substituents retard it[2,3], and that the actual charge on the molecule is important, undissociated acids reacting much more slowly than their anions[4].

While electrophilic attack by the halogen molecule is most common for additions to olefins, it is possible under certain conditions for nucleophilic attack to initiate reaction. This can occur if there is a sufficiently powerful electron-withdrawing substituent in the molecule. The possibility of the nucleophilic addition of halogens was first envisaged by Ingold[2] and this mechanism has been shown to be operative in the

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(1) Williams, Trans. Faraday Soc., 1941, 37, 749.
(2) Ingold and Ingold, J., 1931, 2354.
(3) Anatakrishnan and Ingold, J., 1935, 984, 1396.
(4) Robertson, Clare, McNaught, and Paul, J., 1937, 335.

case of the acid-catalysed addition of halogens to αβ-unsaturated aldehydes, ketones, nitro-compounds, and nitriles[1]. These reactions are catalysed by strong acids, and the effect of structure on the rate of the reaction is quite different from that observed in electrophilic additions. It is generally considered that in these reactions the rate-determining step involves a nucleophilic attack by the halogen on the positively-charged carbon atom produced by the addition of a proton to, for example, the aldehyde:

$$R.CH{=}CH.CHO + H^{+} \rightleftharpoons R.\overset{+}{C}H.CH{=}CH(OH)$$

Nucleophilic addition is, however, an exception to the general rule, and most of the work which has been carried out on the addition of halogens to olefinic compounds has been on the far more usual electrophilic reactions.

The reaction of halogens with olefins, at least in polar solvents, is a two-stage process. This has been shown by the fact that the second stage can be brought about either by the second half of the halogen molecule or by any other nucleophilic reagents, such as solvent molecules or added anions, which may be present in the reaction mixture. (see p. 3)

Another characteristic of the reaction is that it is stereochemically 'trans'. This has been shown, for example,

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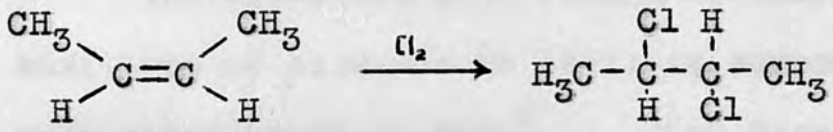
(1) de la Mare, Ann. Repts. on Progress Chem., 1950, 47, 126.

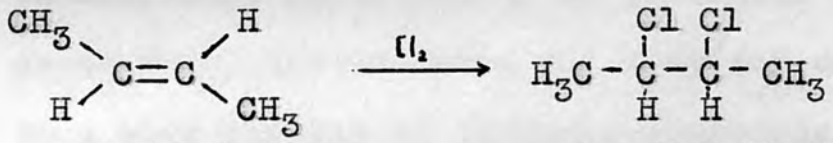
$$R.CH{=}CHR' + Br_2 \rightarrow R.\overset{+}{C}H.CHR'Br + Br^-$$

$$R.\overset{+}{C}H.CHR'Br \begin{cases} \xrightarrow{Br^-} R.CHBr.CHBr.R' \\ \xrightarrow{Cl^-} R.CHCl.CHBr.R' \\ \xrightarrow{H_2O} R.CHOH.CHBr.R' + H^+ \end{cases}$$

by Lucas and Gould[1] for the addition of chlorine to but-2-ene. They found that the addition of chlorine to cis-but-2-ene gave dl-threo-2,3-dichlorobutane, while addition to trans-but-2-ene produced the erythro-compound.



cis-but-2-ene dl-2,3-dichlorobutane



trans-but-2-ene meso-2,3-dichlorobutane

The product in each case is that formed by the 'trans' addition of chlorine to the respective but-2-ene. In neither case was any sign of the other diastereoisomer found.

This 'trans' addition is explained by the formation, or partial formation, of a bridge between the two olefinic carbon atoms by the electrophilic halogen. This would necessitate the subsequent attack by the nucleophile taking place from the side of the molecule opposite to that from which the first group entered it.

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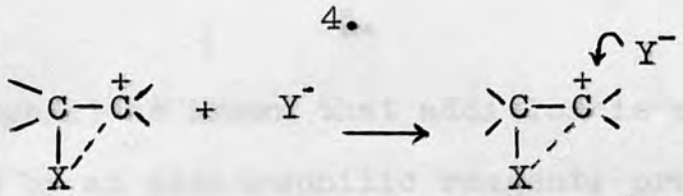
(1) Lucas and Gould, J. Amer. Chem. Soc., 1941, 63, 2541.



The exact nature of the intermediates involved, however, is not known. In particular, it is not known whether the halogen-halogen bond in the molecule which initiates the reaction is broken in the first, rate - determining stage of the process or whether the whole of the halogen molecule is involved in the intermediates[1,2].

The situation with regard to the kinetics of the additions of halogens to olefinic compounds has been summarised by de la Mare[3]. They have been studied extensively, particularly by Robertson who, with various co-workers, investigated the kinetics of halogen addition to a wide variety of olefinic compounds using, mainly, acetic acid as solvent. Chlorine additions are usually second order reactions with the rate proportional to $[A][X_2]$ where A is the unsaturated compound and X_2 is the halogen. Bromine addition can show second, third, or even higher, order kinetics depending on the conditions under which it takes place.

In general, far less is known about the reaction paths, intermediates, and products of the addition of halogens to olefins than is known about the kinetics of the reactions.

(1) Roberts and Kimball, J. Amer. Chem. Soc., 1937, 59, 947.
(2) Waters, Caverhill, and Robertson, J., 1947, 1168.
(3) de la Mare, Quart. Revs., 1949, III, 126.

Although it is known that addition is usually initiated by attack by an electrophilic reagent, probably the halogen molecule, details of the subsequent stages are by no means fully understood. The exact nature of the intermediates which are involved in the reactions is not known, for example; nor is it known how, and at what stage, the ratio of products is determined under various conditions. Also, although the stereochemistry of these halogen addition reactions is known to be 'trans' in the systems studied, it is not known whether this is the case under other conditions such as, for example, the acid-catalysed nucleophilic addition of halogens to aldehydes. In the case of aprotic solvents the situation is even more obscure than that for hydroxylic solvents, to which most of the above information, and most of what is known at present concerning the mechanisms of halogen addition reactions in solution, applies. In non-hydroxylic solvents, although the products are frequently simpler than in hydroxylic media, the kinetics are much more complicated and very little is understood about them. The situation is complicated by the fact that, in non-dissociating solvents, halogen additions tend to have less reproducible rates than in dissociating solvents, and induction periods are frequently observed[1]. The rate of addition is very

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(1) Williams, Trans. Faraday Soc., 1941, 37, 749.

sensitive to small amounts of polar catalysts such as hydrogen bromide, iodine, and water, and is also accelerated by packing the reaction vessel with glass beads[1]. This indicates that a heterolytic mechanism is operating, but details of it are unknown.

(1) Robertson, Clare, McNaught, and Paul, J., 1937, 335.

Ib. Side reactions which accompany the addition of halogens to olefins.

The attack of an electrophilic reagent upon an olefinic compound is generally considered to lead to the formation of a carbonium ion as an intermediate of the reaction. There are then several ways in which the carbonium ion can react. The first of these is by the attack of a nucleophile from the side of the molecule opposite to that at which the first group entered. This leads to the 'trans' addition which has been described above. The carbonium ion can also react with the elimination of a proton either from the carbon atom to which the entering group is attached or from a neighbouring carbon atom.

These three possibilities are very well illustrated in the case of iso-butylene[1], which reacts with hypochlorous acid in water with the formation of the following three compounds:

$$(CH_3)_2C{=}CH_2 + H_2\overset{+}{O}Cl \longrightarrow \begin{cases} (CH_3)_2C(OH).CH_2Cl & (87.6\%) \\ CH_2{=}C(CH_3).CH_2Cl & (12.0\%) \\ (CH_3)_2C{=}CHCl & (0.4\%) \end{cases}$$

The reaction is considered to go through a carbonium ion which then either reacts with a nucleophile to give an

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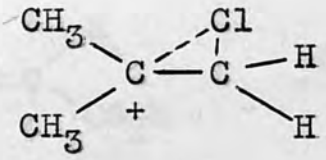
(1) de la Mare and Salama, J., 1956, 3337.

addition product or loses a proton to give an olefinic compound. The direction of elimination of the proton depends on inductive, electromeric, and steric factors within the molecule. In the case of carbonium ions containing only alkyl substituents, the systems upon which most of the work on elimination reactions has been carried out, the direction of elimination is largely controlled by the electromeric effects of the substituents[1]. In the case of iso-butylene, however, if this were the only factor operating it would lead to elimination from the chloromethyl group and the formation of 1-chloro-2-methylpropene as the main olefinic product. The fact that this does not occur has been attributed by de la Mare and Salama to the interaction between the carbonium ion and the chlorine atom.



This is considered to hold the ion in a configuration which is unfavourable for elimination from the chloromethyl group, and this leads to elimination from one of the methyl groups. The same applies for the chlorination of iso-butylene under aprotic conditions, where 3-chloro-2-methylpropene is again the main product.

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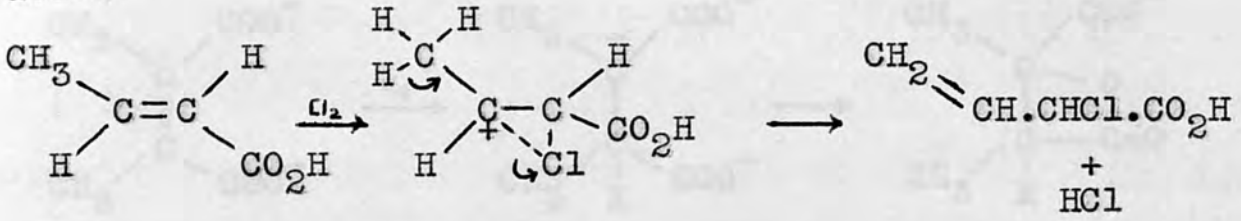
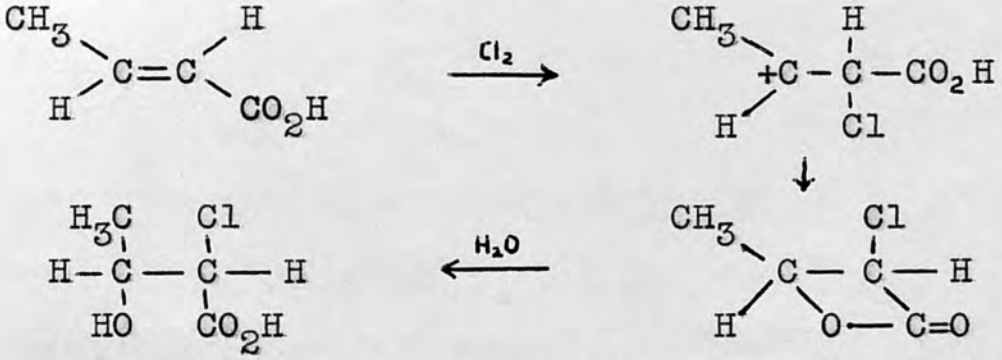
(1) Dhar, Hughes, Ingold, Mandour, Maw, and Woolf, J., 1948, 2093.

If this chlorine-carbonium ion interaction determines the position of proton loss for iso-butylene, it might also be expected to do so in the case of crotonic acid. In this case it would lead to the production of α-chlorovinylacetic acid.



No account of such a reaction being described for an unsaturated acid has been found in the literature.

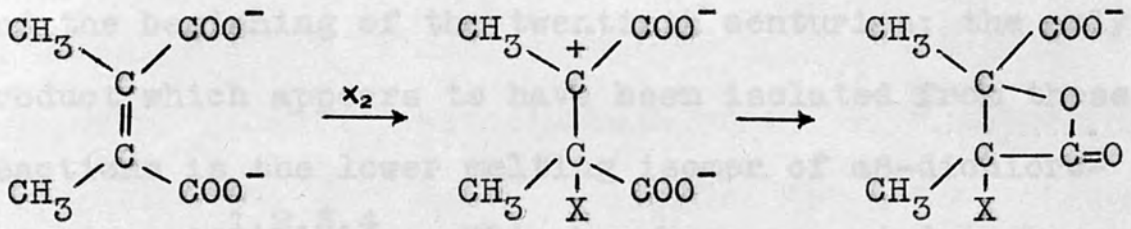
For an unsaturated acid such as crotonic acid, there is another possible form of interaction within the molecule which must be considered. This is interaction between the carboxyl group of the acid and the carbonium ionic centre.



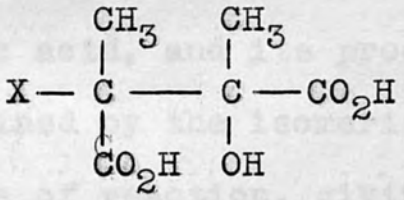
The formation of a lactone ring, which could probably be opened by reaction with water as shown, would lead to the production of hydrogen chloride, as the elimination reactions do. This type of interaction has been demonstrated by Bartlett and Tarbell[1] in dimethylmaleic and

(1) Bartlett and Tarbell, J. Amer. Chem. Soc., 1937, 59, 407.

dimethylfumaric acids. They found that when the sodium salt of either of these two acids was treated with chlorine water or with bromine water a β-lactone could be isolated from the reaction mixture.



On standing for several hours in 5% sulphuric acid at room temperature, the lactone ring was opened irreversibly to form the halohydrin acid,



Ic. Previous work on the crotonic acid system itself.

(1) Products:

Most of the previous work on the chlorination of crotonic acid was carried out at the end of the nineteenth and the beginning of the twentieth centuries; the only product which appears to have been isolated from these reactions is the lower melting isomer of αβ-dichlorobutyric acid[1,2,3,4]. This has been reported to be produced by the action of chlorine on either the 'cis' or the 'trans' isomer of crotonic acid. It is the compound which is formed by the 'trans' addition of chlorine to trans-crotonic acid, and its production from cis-crotonic acid is explained by the isomerisation of the latter under the conditions of reaction, giving the trans isomer which could then add chlorine in the normal way. The preparation of the lower melting isomer of αβ-dichlorobutyric acid has been carried out in chloroform, carbon tetrachloride, or carbon disulphide solutions, both with and without illumination by sunlight. The higher melting isomer of αβ-dichlorobutyric acid has only been prepared by the addition of hydrogen chloride to either α-chlorocrotonic acid[3,4], or α-chloroeβ-hydroxybutyric acid[5]. A pure sample

(1) Wislicenus, Ann., 1888, 248, 283.
(2) Michael and Browne, Am. Chem. J., 1887, 9, 281.
(3) Michael and Schulthess, J. prakt. Chem., 1892, 46(2), 238, 258.
(4) Michael and Bunge, Ber., 1908, 41, 2907.
(5) Melikoff and Petrenko-Kriskchenko, Ann., 1891, 266, 371.

of melting point 78° has not been isolated from the latter reaction. Both these reactions take place only slowly and under vigorous conditions.

The reactions of both isomers of αβ-dichlorobutyric acid with alkali have been studied by several workers. When the reaction is carried out without cooling using either aqueous or alcoholic alkali, both of the αβ-dichlorobutyric acids appear to give a mixture of the two geometric isomers α-chlorocrotonic acid (I) and α-chloro-*iso*crotonic acid (II). The higher melting isomer gives largely α-chlorocrotonic acid of m.p. 99°, and the lower melting isomer largely the α-chloro-*iso*crotonic acid of m.p. 66°.[1,2,3,4,5] When, on the other hand, the reaction mixture is kept cold, treatment of the lower-melting isomer of αβ-dichlorobutyric acid with aqueous alkali has been reported to yield entirely α-chloro-*iso*crotonic acid[4,5].

Of the two α-chlorocrotonic acids the *cis* isomer, of m.p. 66°, is the thermodynamically less stable isomer and can be converted into the 'trans' form by treatment with pyridine hydrochloride in pyridine[6], by heating in a sealed tube at 150-60° for twelve hours[7], or even slowly on steam

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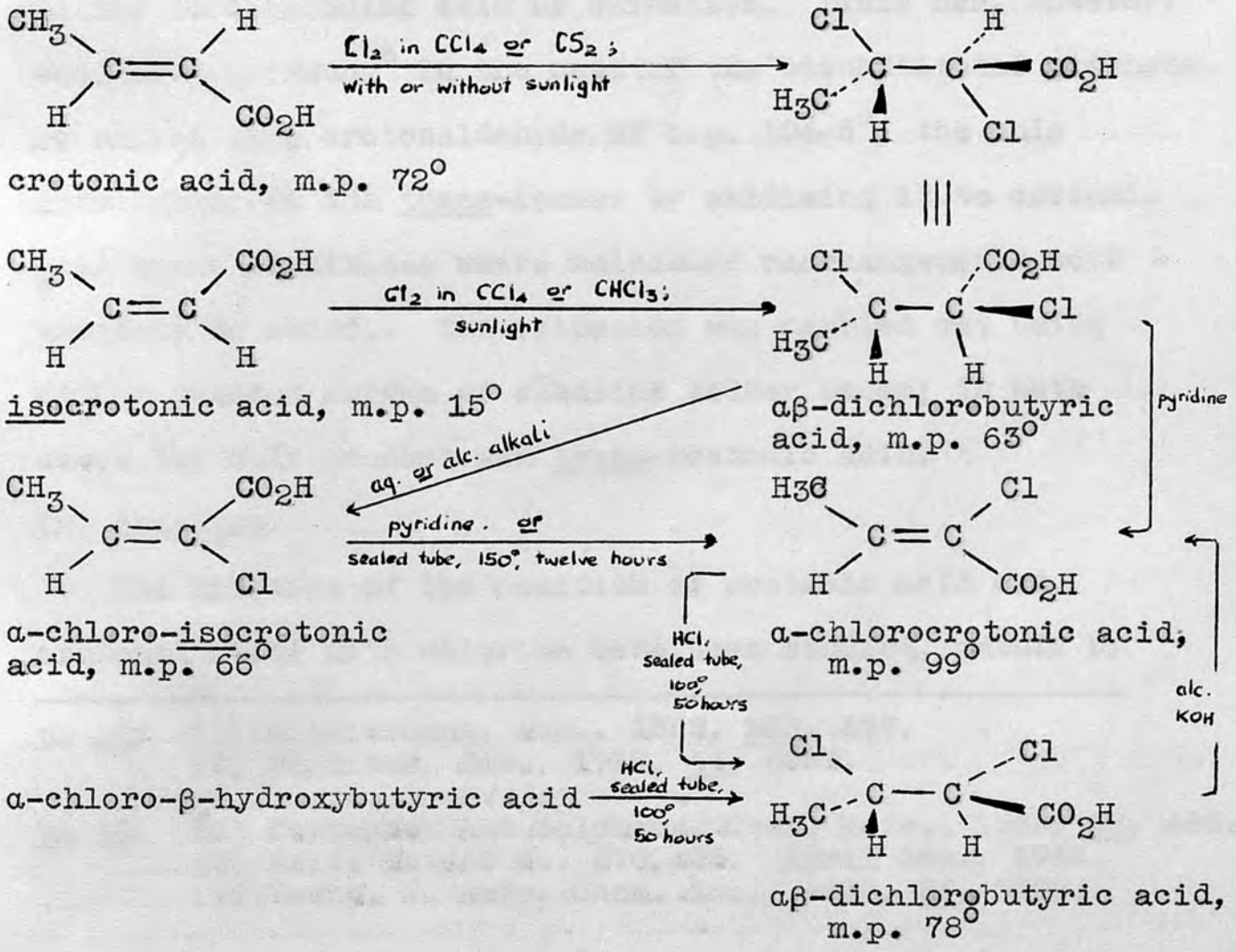
(1) Michael and Browne, Am. Chem. J., 1887, 9, 284.
(2) Michael and Schulthess, J. prakt. Chem. 1892, 46 (2), 255.
(3) Melikoff, Ann., 1886, 234, 203.
(4) Wislicenus, Ann., 1888, 248, 288.
(5) Wislicenus, Ber., 1887, 20, 1008.
(6) Pfeiffer, Ber., 1910, 43, 3045.
(7) Michael and Pendleton, J. prakt. Chem., 1888, 38 (2), 4.

distillation[1].

The trans-isomer of α-chlorocrotonic acid has been prepared by heating the lower melting isomer of αβ-dichlorobutyric acid with pyridine, a reaction which is thought to involve the intermediate formation of α-chloro-isocrotonic acid which is then converted by the action of pyridine hydrochloride into the trans-isomer[2].

The complete scheme for the formation of the chlorination products of crotonic acid, giving the conditions under which the reactions have been carried out is as follows:



The situation with regard to the halogenation of croton-aldehyde has been summarised by Fernandez and Solomons in a recent review[1]. Direct chlorination at room temperature has been reported to give αβ-dichlorobutyraldehyde. On warming this to 50° in the presence of chlorine and water a third chlorine atom is added to give the trichloro-derivative of the saturated aldehyde, 2,2,3-trichlorobutanal monohydrate[2]. The stereochemistry of the αβ-dichlorobutyraldehyde prepared by this chlorination does not appear to be known, and there seems to have been no attempt to relate its structure to that of the corresponding acid by oxidation. This has, however, been done by Young[3] in the case of the unsubstituted aldehyde. He showed that crotonaldehyde of b.p. 104-5°, the only form known, is the trans-isomer by oxidising it to crotonic acid under conditions where molecular rearrangements were unlikely to occur. The oxidation was carried out using either gaseous oxygen or alkaline silver oxide; in both cases the only product was trans-crotonic acid.

(2) Kinetics:

The kinetics of the reaction of crotonic acid and crotonaldehyde with chlorine have been studied, mainly by

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p. 13: (1) Wislicenus, Ann., 1888, 248, 337.
(2) Pfeiffer, Ber., 1910, 43, 3039.

p. 14: (1) Fernandez and Solomons, Chem. Revs., 1962, 62, 485.
(2) Brit. Patent No. 576,435. April 3rd., 1946.
(3) Young, J. Amer. Chem. Soc., 1932, 54, 2498.

Robertson and co-workers, who only appear to have used acetic acid as solvent[1,2,3]. In this solvent the rate of addition of chlorine to crotonic acid is unaltered by the presence of hydrogen chloride, and the reaction appears to involve electrophilic attack by the halogen molecule and to take place with second order kinetics. The rate of addition of bromine, on the other hand, shows marked catalysis by hydrogen bromide and also by acids such as sulphuric acid. It is thought to involve a nucleophilic mechanism, and this is born out by the fact that the relative rates of bromine addition to various unsaturated acids in the presence of hydrogen bromide in acetic acid are in the reverse order to the electrophilic rate of chlorine addition in the same solvent, i.e.

$$CH_2{=}CH.CO_2H > CH(CH_3){=}CH.CO_2H > C(CH_3)_2{=}CH.CO_2H$$

for nucleophilic bromine additions.

The kinetic order of these nucleophilic halogen additions is largely of the kinetic form

$$-d[X_2]/dt = k.[A][H^+][X_2].$$

In acetic acid, crotonic acid adds bromine at concentrations of about 0.1M showing third order kinetics, but at lower concentrations the reaction tends to show autocatalysis,

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(1) White and Robertson, J., 1939, 1509.
(2) de la Mare and Robertson, J., 1945, 888.
(3) Morton and Robertson, J., 1945, 129.

and follows no clear kinetic order.

The addition of both chlorine and bromine to crotonaldehyde in acetic acid takes place by a nucleophilic mechanism. The reaction rate is strongly increased by the presence of acids, and the rate of addition is very much faster than that of the corresponding acid. If an electrophilic mechanism had been involved, the aldehyde would have been less reactive than the acid, and also chlorine would be expected to react more rapidly than bromine, the reverse of what actually happens. The following results have been found for the addition of chlorine and bromine to crotonic acid and crotonaldehyde in acetic acid and support the above mechanisms.

Addition in acetic acid at 24°

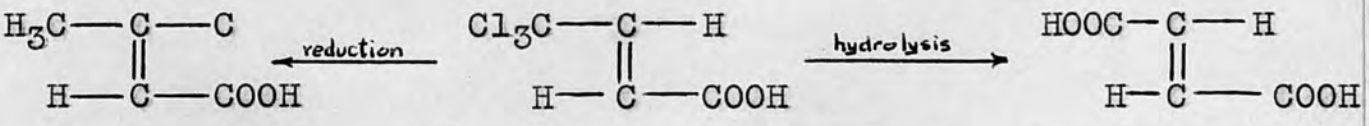
	$CH(CH_3)=CH.CO_2H$	$CH(CH_3)=CH.CHO$
Bromine addn. k_2 (+0.25 mol. sulphuric acid)	ca. 0.01	ca. 1000
Chlorine addn. k_2 (+0.25 mol. sulphuric acid)	0.62	43

There does not appear to have been any attempt to isolate the products of these reactions.

Id. The stereochemistry of crotonic acid and its chlorination products.

A knowledge of the stereochemistry of the compounds with which this work is concerned -- namely, the two isomers of crotonic acid, α-chlorocrotonic acid, αβ-dichlorobutyric acid, crotonaldehyde, and αβ-dichlorobutyraldehyde -- was of primary importance.

A determination of the stereochemistry of the two crotonic acids and the two α-chlorocrotonic acids has been reported by Auwers and Wesseback[1]. They related the configurations of the two isomers of crotonic acid, m.p. 72° and 15°, to the known configurations of fumaric and maleic acids. This was done through γ-trichlorocrotonic acid, which can be smoothly hydrolysed at 0° to give fumaric acid, and can also be reduced to give the isomer of crotonic acid of m.p. 72°. The configuration of fumaric acid is known to be <u>trans</u> and therefore, since neither the hydrolysis nor the reduction affects the double bond, the higher melting form of crotonic acid is shown to have the <u>trans</u> configuration.

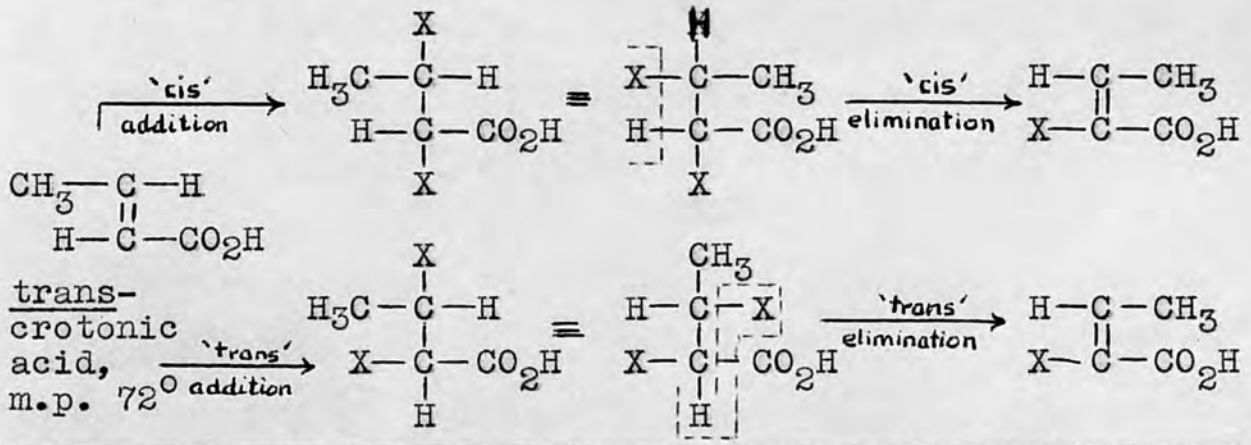


crotonic acid, m.p. 72°. γ-trichlorocrotonic acid. fumaric acid.

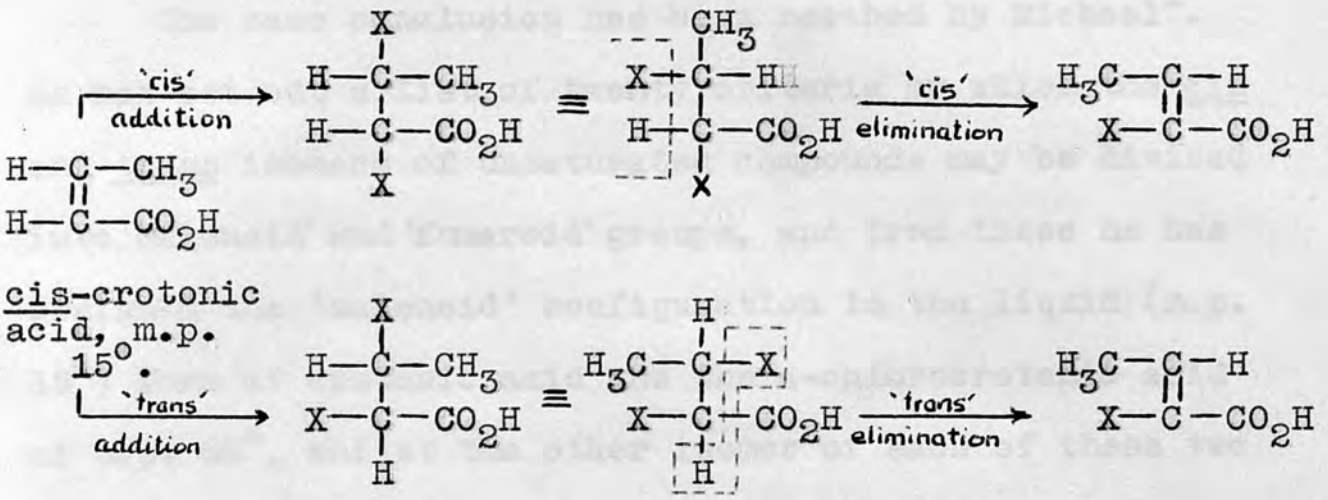
(1) Auwers and Wisseback, Ber., 1923, <u>56</u>, 721.

The lower melting form of crotonic acid must, therefore, have the cis configuration.

The stereochemistry of the halogenated crotonic acids has been deduced from this merely by a consideration of the reactions of the two isomers of crotonic acid with chlorine, working on the assumption that "additions and eliminations concerning halogens and hydrogen halides in ethylenic and acetylenic derivatives take place 'normally' with the same orientation. Whether this is cis or trans orientation is immaterial for the following discussion; it is only essential that if cis addition is accepted, the elimination of hydrogen halide also takes place in the cis sense, and correspondingly for the alternate proposition"[1]. Working on this basis the following schemes are possible for the addition of halogens to the two isomers of crotonic acid and the elimination of hydrogen halide from the products:



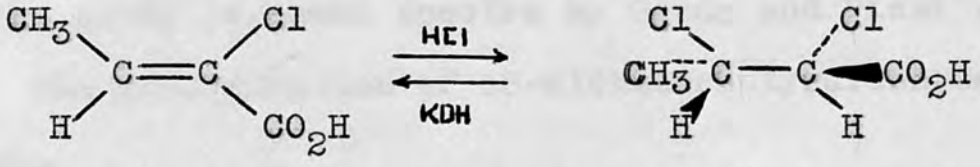
(1) "..dass Anlagerung und Abspaltung bei Äthylen- und Acetylen-Derivaten, solange es sich um Halogen und Halogenwasserstoff handelt, 'normalerweise' in gleicher Stellung erfolgen. Ob dies die cis- oder die trans-Stellung ist.... ist für die folgenden Betrachtungen gleichgültig; wesentlich ist nur, dass bei Annahme von cis-Addition auch der Austritt von Halogenwasserstoff in cis-Lage vor sich geht, und entsprechend" Auwers and Wisseback, Ber., 1923, 56, 722



From this it can be seen that whichever way the reaction takes place, the α-halogen derivative produced has the opposite configuration from which it is formed. Unfortunately, as is shown in the scheme on p. 13, both isomers of crotonic acid have given the same isomer of αβ-dichlorobutyric acid, that with m.p. 63°. The trans-isomer of crotonic acid is, however, the thermodynamically more stable one and the additions to cis-crotonic acid have all been carried out in the presence of sunlight, under which conditions it can be converted into the trans isomer before reaction with chlorine. From this it is assumed that it is trans-crotonic acid which adds on chlorine in the normal manner, known now to be trans, to give the lower melting isomer of αβ-dichlorobutyric acid. The α-chlorocrotonic acid of m.p. 66° which is formed by the elimination of hydrogen chloride from this must, therefore, have the cis configuration, and the isomer of m.p. 99°, the trans configuration.

The same conclusion has been reached by Michael[1]. He has set out a list of twenty criteria by which the cis and trans isomers of unsaturated compounds may be divided into 'malenoid' and 'fumaroid' groups, and from these he has assigned the 'malenoid' configuration to the liquid (m.p. 15°) form of crotonic acid and the α-chlorocrotonic acid of m.p. 66°, whilst the other isomer of each of these two compounds is given the 'fumaroid' configuration.

Once the configurations have been assigned to the crotonic acids and α-chlorocrotonic acids, those of the two forms of αβ-dichlorobutyric acid follow. The isomer of m.p. 78° is produced by the 'trans' addition of hydrogen chloride to trans-α-chlorocrotonic acid, and can be converted back into the latter compound by alkali. The configuration of this compound must therefore be as shown below:



α-chlorocrotonic acid, m.p. 99°.

αβ-dichlorobutyric acid, m.p. 78°.

The other isomer of αβ-dichlorobutyric acid on reaction with alkali gives cis-α-chlorocrotonic acid, and thus, together with the fact that it is formed by the 'trans' addition of chlorine to trans-crotonic acid, its configuration is undetermined.

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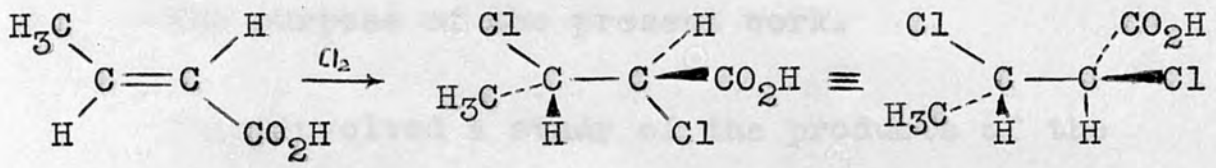
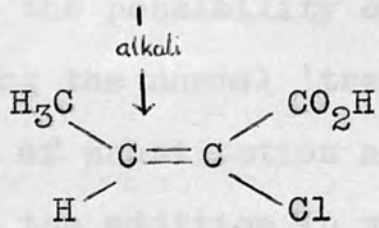
(1) Michael, J. prakt. Chem., 1895, 52 [2], 344.



crotonic acid,
m.p. 72°

αβ-dichlorobutyric acid,
m.p. 63°



α-chloroisocrotonic acid,
m.p. 66°

These configurations for crotonic acid and its halogenated products have also been described in several other papers by Michael[1,2,3].

The configuration of the only known form of crotonaldehyde has been shown to be 'trans' by oxidation to the corresponding acid (see p. 14). Confirmatory evidence has been obtained by the study of Raman spectra by Gredy and Piaux[4].

The configuration of αβ-dichlorobutyraldehyde is not known.

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(1) Michael, J. prakt. Chem., 1889, 40[2], 29.
(2) Michael, J. prakt. Chem., 1895, 52[2], 359.
(3) Michael, J. prakt. Chem., 1907, 75[2], 112.
(4) Gredy and Piaux, Compt. rend., 1934, 198, 1235.

Ie. The purpose of the present work.

This involved a study of the products of the chlorination of crotonic acid under various conditions with special reference to the possibility of observing any 'cis' addition accompanying the normal 'trans' addition to the acid. The amount of substitution and other side reactions which accompany the addition in various solvents was of interest. It was also hoped to compare the products of chlorination of crotonic acid and crotonaldehyde, and to attempt to correlate them with the different mechanisms by which each reacts.

Most of the aspects which have been studied have been examined only in an incomplete way, but it is felt that a number of significant and novel points have been established.

II. EXPERIMENTAL

EXPERIMENTAL

IIa. Preparation and characterisation of reference materials

The first stage in the experimental work involved the preparation and characterisation of the four materials required for reference purposes:

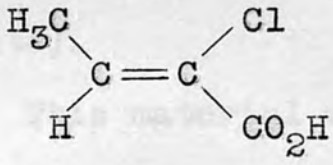
(i) α-chlorocrotonic acid;

(ii) lower melting isomer of αβ-dichlorobutyric acid;

(iii) α-chloro*iso*-crotonic acid;

(iv) higher melting isomer of αβ-dichlorobutyric acid.

(1) α-Chlorocrotonic acid



This was prepared by Roberts' method[1].

$$CH_3.CHCl.CCl_2.CH(OH)_2 \xrightarrow{HNO_3} CH_3.CHCl.CCl_2.CO_2H$$

$$CH_3.CHCl.CCl_2.CO_2H \xrightarrow[H_2O]{Zn} CH_3.CH{:}CCl.CO_2H$$

Butyl chloral hydrate (50 g.) was added to concentrated nitric acid (100 ml.) and kept at 30-35° for one-and-a-half hours, being shaken occasionally. The mixture was left to stand at room temperature for about twenty-four hours and was then distilled, everything boiling below 135° being collected. The residue, on cooling, gave colourless

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(1) Roberts, J., 1938, 779.

crystals to which water (250 ml.) was added, followed by zinc dust (30 g.) in small portions. The mixture was then heated on the steam-bath for about three hours, cooled, and was acidified with concentrated hydrochloric acid (30 ml.). Some of the acid precipitated as a white solid. The whole was extracted with ether, and the combined ethereal extracts were washed with water and dried over sodium sulphate. On removal of the ether, the residue solidified as colourless crystals of α-chlorocrotonic acid, which were recrystallised from water.

Three preparations were carried out, giving yields of 30%, 75%, and 74% respectively (calculated on butyl chloral hydrate).

This material was characterised by means of

(a) melting point: 98.5-99° (lit,[1] 99-100°)

(b) infra red spectrum: see Section IV;

(c) S-benzyl thiuronium derivative: m.p. 189°,

(d) methyl ester: b.p. 160° (lit[2], 161°),

(e) neutralisation equivalent: 120 (calc., 120.5)

(2) Lower melting isomer of αβ-dichlorobutyric acid, m.p. 63°

Several attempts were made to prepare this material, firstly by the method of Michael and Bunge[3]. They cooled a solution of crotonic acid in carbon tetrachloride in ice,

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(1) Roberts, J., 1938, 779.
(2) Auwers, Ber., 1912, 45, 2806.
(3) Michael and Bunge, Ber., 1908, 41, 2910.

and added an equimolar quantity of chlorine in carbon tetrachloride. According to the reference, the addition proceeded rapidly in bright sunlight, and the pale yellow colour of the solution showed the reaction to be complete within a short time. Little bright sunlight was available to us, however, and for most of the attempts, ultra violet lamps had to be used.

(a) Crotonic acid and a slight excess of chlorine were dissolved in carbon tetrachloride, and the solution was cooled in ice and irradiated with ultra violet light and as much sunlight as was available for varying lengths of time. In most cases, only very small yields of the required dichlorobutyric acid were obtained. The reaction appeared to proceed much faster in sunlight than with the ultra violet lamp, being very slow in the latter case. The best result was a 33% yield (calculated on crotonic acid) obtained by standing a cold carbon tetrachloride solution of crotonic acid and a slight excess of chlorine in bright sunlight for six-and-a-half hours.

(b) An attempt to catalyse the reaction by using a trace of benzoyl peroxide resulted in an oily product from which no solid could be obtained.

(c) The best, and most consistent, results were obtained by using a trace of iodine as a catalyst.

Crotonic acid, a slight excess of chlorine, and a

trace of iodine were dissolved in carbon tetrachloride and the solution allowed to stand at room temperature for twenty-four hours. At the end of this time the mixture was only pale yellow in colour. The solvent was removed under reduced pressure, and the resulting oil was chromatographed on a silica-gel column. Two main fractions were obtained:

(i) the required low melting isomer of αβ-dichlorobutyric acid (65% by weight of the total product),

(ii) an oil (21% by weight of the total product) with an infra red spectrum very similar to that of a product obtained by chlorinations in water and in nitromethane and shown to be α-chloro-β-hydroxybutyric acid.

The low melting isomer of αβ-dichlorobutyric acid was recrystallised from light petroleum (b.p. 60-80°).

It was characterised as follows:

(a) melting point: 62.5-62.8° (lit[1], 63°);

(b) infra red spectrum: see Section IV;

(c) S-benzylthiuronium derivative: m.p. 141°;

(d) neutralisation equivalent: 155 (calc., 157);

(e) conversion to α-chloro<u>iso</u>-crotonic acid on treatment with sodium hydroxide in the cold.

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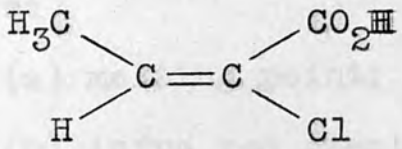
(1) Michael and Bunge, Ber., 1908, <u>41</u>, 2910.

(3) α-Chloroiso-crotonic acid:



This was prepared by the carefully controlled dehydrochlorination of the lower melting isomer of αβ-dichlorobutyric acid[1].

The αβ-dichlorobutyric acid was covered with water and cooled in ice. Sodium hydroxide solution (10%; approximately 2.5 molar excess) was then slowly added so that the temperature of the mixture did not rise above 5°. The reaction mixture was left in the refrigerator overnight, and was then acidified with concentrated hydrochloric acid and again left in the refrigerator. After about three hours, a solid began to separate and was shown to be α-chloroiso-crotonic acid. It was recrystallised from light petroleum (b.p. 60-80°).

The aqueous mother liquors were extracted with ether and the extracts were dried over sodium sulphate. The ether was removed, leaving aslightly oily solid, the infra red spectrum of which showed it to be very largely α-chloro-iso-crotonic acid.

The yield, including the slightly oily product, was 84%.

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(1) Wislicenus, Ann., 1888, 248, 288.

The α-chloro*iso*-crotonic acid was characterised as follows:

(a) melting point: 66.5-67° (lit[1], 66.2-66.5°);

(b) infra red spectrum: see Section IV;

(c) S-benzyl thiuronium derivative: m.p. 120-1°;

(d) neutralisation equivalent: 117 (calc., 120.5).

(4) *Higher melting isomer of αβ-dichlorobutyric acid, m.p. 78°.*

This was prepared by the addition of hydrogen chloride to α-chlorocrotonic acid[2,3].

Three preparations were carried out. In the first, dry hydrogen chloride was passed into cold, concentrated hydrochloric acid (50 ml.) until the solution was saturated at 0°. The solution was then added to α-chlorocrotonic acid (2 g.) in a thick-walled glass tube, which was subsequently sealed and heated at 100° for fifty hours. The tube was then opened, and the liquid was almost neutralised with powdered sodium carbonate before extraction with ether. The ethereal extracts were dried over sodium sulphate, the solvent was removed, and the resulting oil was purified by chromatography on a silica-gel column. Two main fractions were obtained. The larger amount consisted of unchanged α-chlorocrotonic acid; the other smaller fraction was impure higher melting isomer of αβ-dichlorobutyric acid.

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(1) Wislicenus, Ann., 1888, 248, 288.
(2) Michael and Schulthess, J. prakt. Chem., 1892, 46[2], 259.
(3) Michael and Bunge, Ber., 1908, 41, 2911.

For the next two preparations, the concentrated hydrochloric acid was added to the α-chlorocrotonic acid and the solution in the tube was then saturated with dry hydrogen chloride so that the minimum of hydrogen chloride was lost. The procedure was then as before. In these cases, however, chromatography of the total product on a silica-gel column gave three compounds. These were the isomeric αβ-dichlorobutyric acids and unchanged α-chlorocrotonic acid. In the first of these two preparations they were in the approximate ratios by weight of one part of α-chlorocrotonic acid to two parts each of the two dichlorobutyric acids. In the second case, very little α-chlorocrotonic acid was left, and the two αβ-dichlorobutyric acids were again present in approximately equal amounts.

The higher melting isomer of αβ-dichlorobutyric acid was recrystallised from light petroleum (b.p. 60-80°).

It was characterised as follows:

(a) melting point: 77.5-78° (lit[1], 78°);

(b) infra red spectrum: see Section IV;

(c) conversion to α-chlorocrotonic acid on treatment with sodium hydroxide in the cold.

(d) S-benzyl thiuronium derivative: m.p. 124°

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(1) Michael and Bunge, Ber., 1908, 41, 2911.

Separation of products using silica-gel columns

The reaction products from most of the experiments carried out were separated using silica-gel columns.

The columns were made up by using petroleum (b.p. 40-60°); about 150 ml. of silica-gel slurry was used per gram of material. The material to be separated was dissolved in light petroleum (b.p. 40-60°) together with a little ether, and was eluted from the column using light petroleum containing increasing proportions of ether. Fractions (50 ml.) were taken, and the solvent was blown off using the draught from a fume cupboard.

For most separations, it was found to be sufficient to elute with a solution of ether in light petroleum (b.p. 40-60°; 1:4), and to change to pure ether only for the last fractions. Most products were removed from the column using the former eluent. For example, in the separation of a mixture of crotonic acid, α-chlorocrotonic acid, and the lower melting isomer of αβ-dichlorobutyric acid, the compounds (ca. 0.3 g., each) were dissolved in a mixture of ether and light petroleum (b.p. 40-60°) and were eluted with a solution of ether in light petroleum (b.p. 40-60°; 1:4). The solids emerged from the column in the following order:

(1) low melting αβ-dichlorobutyric acid,

(2) α-chlorocrotonic acid,

(3) crotonic acid.

Quite a good separation was obtained, and although there was some overlap between the fractions, this was not very great.

α-Chloro<u>iso</u>-crotonic acid is removed at about the same time as α-chlorocrotonic acid, and the other isomer of αβ-dichlorobutyric acid appears between these two and crotonic acid itself.

IIb. Chlorination of crotonic acid in water saturated with sodium chloride.

Crotonic acid (1 g.) was dissolved in water completely saturated with sodium chloride (60 ml.). A slow stream of chlorine was passed through the solution for one-and-a-half hours. The organic matter was extracted with ether, the solvent was removed, and the remaining oily product was purified on silica-gel (p. 30). Two fractions were obtained, the first being removed by ether - light petroleum (1:4), and the second by pure ether.

(i) The first fraction comprised about 48% by weight of the total product and consisted of the lower melting isomer of αβ-dichlorobutyric acid.

(ii) The second fraction, 52% by weight of the total product, eluted as an oil but, on standing, the later fractions of this slowly solidified to give a slightly oily material, m.p. 58-59°. The infra red spectrum of both the oil and the solid were measured (see Section IV). On standing for several days, both the infra red spectrum and the melting point of the solid changed. The melting point had increased considerably, and on recrystallisation from a mixture of ether and light petroleum (b.p. 60-80°) a value of 85-86.5° was found.

The same compound was obtained as the total product by the chlorination of crotonic acid in water without added sodium chloride. It was shown to be α-chloro-β-hydroxybutyric acid by the following means:

(a) found (BC 276*): C, 35.45; H, 5.02; Cl, 25.77; O, 33,0
Calculated for $C_4H_7ClO_3$:
C, 34.65; H, 5.10; Cl, 25.58; O, 34.62%.

(b) neutralisation equivalent: 140.
Calculated for $C_3H_6ClO.COOH$: 138.5.

(c) exists in two forms,
(i) unstable, m.p. 58-9°; (ii) stable, m.p. 85-86.5°;
α-Chloro-β-hydroxybutyric acid exists in two forms, m.p. 60-1° and m.p. 86°. [1]

(d) with aqueous sodium hydroxide in the cold it gave an oil which, on long standing, partially solidified to give a solid, m.p. 75-84°; α-chloro-β-hydroxybutyric acid reacts with potassium hydroxide to give $CH_3.\underset{\backslash O /}{CH.CH}.CO_2H$ of m.p. 84°. [2]

(e) reaction with sodium hydroxide gave exactly one equivalent of hydrogen chloride liberated per mole of compound;

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(1) Smith, Z. phys. Chem., 1936, 177[A], 139.
(2) Melikoff, Ann., 1891, 266, 358.

(*) Analyses normally by A. Bernhardt; departmental reference numbers are given here.

(f) heating with concentrated sulphuric acid gave α-chlorocrotonic acid; so does α-chloro-β-hydroxy-butyric acid[1];

(g) the infra red spectra of both forms indicate the presence of an -OH group (Section IV).

Attempts to prepare an S-benzyl thiuronium derivative of this compound were unsuccessful.

Chlorination in water saturated with sodium chloride, at pH 7.6-8.0

pH 76.-

One attempt was made to chlorinate crotonic acid in a solution of water completely saturated with sodium chloride and keeping the acid as the anion throughout. This was done using an autotitrator. It was set to maintain the pH of the solution at between 7.6 and 8.0 throughout the chlorination, which was carried out as before. Unfortunately, the autotitrator could only cope with very dilute solutions of crotonic acid, and the total weight of product isolated at the end of the chlorination was only 0.06 g.. This was purified by chromatography (p. 30) and two fractions were obtained, the first being very much smaller than the second.

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(1) Melikoff, Ann., 1891, 266, 358, 361

The larger fraction was α-chloro-β-hydroxybutyric acid; the smaller fraction was eluted at the same time as the lower melting isomer of αβ-dichlorobutyric acid, but there was insufficient of it for its infra red spectrum to be studied.

IIc. Chlorinations in nitromethane.

Several chlorinations of crotonic acid were carried out using nitromethane as solvent. The earlier experiments showed that considerably more than one gram molecule of chlorine was being consumed per gram molecule of acid which reacted, and also that large amounts of hydrogen chloride were being produced. The reactions in nitromethane were thus carried out under two sets of conditions. In the first of these, an excess of chlorine was used, and both the amounts of this consumed and the products of the reaction were determined. In the second, the acid was in excess, and the amount of hydrogen chloride produced was estimated.

The nitromethane which was used in the later experiments was carefully dried by fractional distillation, and the chlorine was dried by passing it through concentrated sulphuric acid.

The following is a typical example of a reaction in which an excess of chlorine was used.

Crotonic acid (0.42 g., 4.9×10^{-3} mole) was dissolved in nitromethane (25 ml.) in a dark, long-necked, 250-ml. flask. An approximately 0.5$\underline{\underline{M}}$ solution of chlorine in nitromethane was made up, the concentration being determined by the need for 25 ml. of the solution to give about a three-fold molar excess of chlorine. Two portions of this (2 ml. each) were

run into an excess of potassium iodide solution, a quantity (25 ml.) was added to the crotonic acid solution, and finally another two portions (2 ml. each) were run into potassium iodide solution. The four solutions of iodine in potassium iodide were titrated against sodium thiosulphate solution, and the following values were found for the volume of 0.1$\underline{\underline{N}}$-sodium thiosulphate solution which was equivalent to 2 ml. of chlorine solution: (1) 19.92 ml., (2) 19.75 ml., (3) 18.95 ml., (4) 18.84 ml..

It was assumed that a fairly accurate estimate of the chlorine concentration could be obtained by averaging the above values. This gave a value of 12.1×10^{-3} moles of chlorine in the 25 ml. of solution which was added to the crotonic acid.

The amount of chlorine used up, and a rough estimate of the rate at which it reacted, were determined by withdrawing samples from the reaction vessel at various time intervals and titrating them. The values found showed that after three minutes, the first time taken, only $\underline{ca}. 2.4 \times 10^{-3}$ moles of chlorine remained. This decreased further to a value of 1.8×10^{-3} moles by the end of ten minutes and appeared to remain constant at this point.

The results of this (i) and the other two experiments in which the amount of chlorine consumed was determined may be summarised:

(i) Initially: 4.9×10^{-3} moles crotonic acid,
12.1×10^{-3} moles chlorine.
Finally (10 mins.): 1.8×10^{-3} moles chlorine: i.e.
10.3×10^{-3} moles chlorine consumed.

(ii) Initially: 17.4×10^{-3} moles crotonic acid,
57.8×10^{-3} moles chlorine.
Finally: 20.6×10^{-3} moles chlorine, i.e.
37.2×10^{-3} moles chlorine consumed.

(iii) Initially: 17.4×10^{-3} moles crotonic acid,
55.9×10^{-3} moles chlorine.
Finally: 19.9×10^{-3} moles chlorine, i.e.
36.0×10^{-3} moles chlorine consumed.

The reaction of crotonic acid with an excess of chlorine in nitromethane is thus a rapid one, going to completion within about ten minutes, and about two moles of chlorine appear to be consumed for every mole of crotonic acid which reacts.

The products of the reaction were next determined. This was done about ninety minutes after mixing the reactants. The solvent was removed from the solution by distillation under reduced pressure, and the remaining oily material was purified by chromatography on silica-gel. Two fractions were obtained. The first was eluted by ether - light petroleum (1:4) mixture, and its infra red spectrum showed it to be the

lower melting isomer of αβ-dichlorobutyric acid contaminated with another material (A) whose spectrum was unlike that of any of the other compounds which had been obtained in this work (see Section IV). The second fraction emerged from the column as an oil by using pure ether as eluent. Its infra red spectrum was identical with that of the oily form of α-chloro-β-hydroxybutyric acid, which was obtained by the chlorination of crotonic acid in water (p. 32). In this case also, on leaving the oil to stand and scratching the surface of it, it slowly solidified to give the higher melting isomer of α-chloro-β-hydroxybutyric acid. The identity of these two solids was shown as follows:

(a) identical infra red spectrum;

(b) identical analyses (BC 275 and BC 276);

(c) similar behaviour with sodium hydroxide and with concentrated sulphuric acid;

(d) identical melting points, and an undepressed mixed melting point.

None of the lower melting isomer of α-chloro-β-hydroxybutyric acid was isolated from the chlorinations which were carried out in nitromethane.

So far as the quantities of each product of this reaction were concerned, some overlapping always occurred between the fractions which emerged from the column, and

also a certain amount of material appeared either to remain behind on the column or to be volatilised during the process of solvent removal. This made an accurate estimation of the amount of each product very difficult. The following values are rough estimates for the three experiments in which the yields of the isolated products were investigated. The amounts given as percentages are by weight of the total material which was eluted from the column.

α-chloro-β-hydroxybutyric acid: (i) 75%, (ii) 77%, (iii) 76%.

In each case, the remaining material was the lower melting isomer of αβ-dichlorobutyric acid mixed with the unknown material 'A'. Thus about 76% by weight of the total product isolated from the chlorination of crotonic acid in dry nitromethane was α-chloro-β-hydroxybutyric acid.

The next step involved the determination of the amount of hydrogen chloride which was produced during these reactions. The following is typical of the experiments in which this was done.

The reaction was carried out in a dark, 250-ml., iodine flask, the stopper of which was coated with silicone grease to minimise the loss of hydrogen chloride. It was also found helpful to stand the reaction vessel in a bath of cold water, because the heat of reaction, together with the large amount of hydrogen chloride evolved, tended to blow the stopper out of the flask.

Crotonic acid (0.7 g., 8.1×10^{-3} mole) was dissolved in nitromethane (25 ml.) in the iodine flask. A solution of chlorine in nitromethane was then made up, and the concentration was adjusted so that 25 ml. of the solution would give slightly less than a two-fold molar excess of chlorine (ca. 0.6$\underline{\underline{M}}$). Two portions (2 ml.) of the chlorine solution were added to excess of potassium iodide solution, a quantity (25 ml.) was added to the crotonic acid solution and the flask was immediately stoppered, and finally two more portions (2 ml.) were run into potassium iodide solution. The solutions of iodine in potassium iodide were once again titrated against sodium thiosulphate, and the following values were found for the volume of 0.1$\underline{\underline{N}}$-sodium thiosulphate which was equivalent to 2 ml. of the chlorine solution:
(1) 20.85 ml., (2) 20.80 ml., (3) 16.82 ml., (4) 16.40 ml..

The average of these gave the initial amount of chlorine as 11.7×10^{-3} moles.

On adding the chlorine to the crotonic acid solution, the colour immediately changed to dark-green, and then rapidly became pale blue; the solution became hot. The colour did not change further over a period of about two hours. At the end of this time, water was added around the rim of the iodine flask, and the stopper was slowly removed so that all the hydrogen chloride which was expelled from the flask was trapped in the water. The nitromethane layer was extracted

with water several times, and the aqueous extracts were washed with ether. The hydrogen chloride content of the aqueous solution was then estimated by Volhard's method, giving a value of 10.5×10^{-3} moles of hydrogen chloride. Titration of the pale blue nitromethane solution showed that it contained no chlorine.

The following values were found for the relative amounts of chlorine consumed and hydrogen chloride produced in the various experiments in which this was determined:

Crotonic acid	Chlorine	Hydrogen chloride
(i) 41×10^{-3}	36×10^{-3}	32×10^{-3} moles.
(ii) 13×10^{-3}	25×10^{-3}	23×10^{-3} moles.
(iii) 29×10^{-3}	46×10^{-3}	42×10^{-3} moles.
(iv) 81×10^{-4}	117×10^{-4}	105×10^{-4} moles.

Chlorination in nitromethane saturated with hydrogen chloride.

One chlorination of crotonic acid was carried out in dry nitromethane saturated with dry hydrogen chloride. This was done using an approximately three-fold molar excess of chlorine; the procedure was exactly the same as before excepting that all the nitromethane used was first saturated with dry hydrogen chloride.

The reaction appeared to be slightly faster than the corresponding one which was carried out in the absence of added hydrogen chloride, and had gone to completion within

five minutes. The results obtained were the following:

Initially:	5.9×10^{-3}	moles crotonic acid,
	13.7×10^{-3}	moles chlorine;
Finally (4 mins.):	0.8×10^{-3}	moles chlorine, i.e.
	12.9×10^{-3}	moles chlorine consumed.

Once again, the solvent was removed from the reaction mixture under reduced pressure, and the total oily product was purified by chromatography (p. 30). In this case, three fractions appeared. The first two emerged from the column after elution with ether - light petroleum (1:4), but the separation between them was poor. The infra red spectrum showed that the first fraction was the lower melting isomer of αβ-dichlorobutyric acid, again contaminated with the same unknown compound 'A' as before; from the second fraction, a small amount of a solid of m.p. 105-6° was isolated (see Section IV for infra red spectrum). The third fraction was eluted from the column by pure ether and was once again shown to be α-chloro-β-hydroxybutyric acid. The relative amounts of each fraction, given as percentages by weight of the total product obtained from the column, were:

(i) lower melting isomer of αβ-dichlorobutyric acid together with unknown compound 'A': 14%,

(ii) unknown compound of m.p. 105-6° ('B'): 9%,

(iii) α-chloro-β-hydroxybutyric acid: 74%.

Thus if the chlorination is carried out in nitromethane

saturated with hydrogen chloride, the ratio of chlorine consumed to crotonic acid which reacts is the same as for the reaction with pure nitromethane as solvent; the amount of α-chloro-β-hydroxybutyric acid which is produced is unchanged; and the same isomer of αβ-dichlorobutyric acid is produced. The only apparent differences are that the reaction is probably slightly faster than in pure nitromethane, and that the compound 'B' of m.p. 105-6° was not isolated from the previous reaction.

Chlorination of methyl crotonate in nitromethane.

Two chlorinations of methyl crotonate were carried out in nitromethane. The first was studied to estimate the amount of chlorine which was consumed during the reaction; the other was to determined the amount of hydrogen chloride which was produced.

In the first experiment, an approximately three-fold molar excess of chlorine was used. It was found that the chlorine was consumed very much more slowly than in the corresponding reaction with crotonic acid; in the case of methyl crotonate, the reaction required approximately three-and-a-half hours to reach completion, while for crotonic acid no more chlorine was consumed after ten minutes. Once again, however, about two moles of chlorine were used up per mole of methyl crotonate which was present in the

reaction mixture, as is shown in the following results:

Initially: 20.0×10^{-3} moles methyl crotonate,
58.8×10^{-3} moles chlorine;
Finally ($3\frac{1}{2}$ hrs.): 18.9×10^{-3} moles chlorine, i.e.
39.9×10^{-3} moles chlorine used up.

(See p. 38 for crotonic acid values)

In the next experiment, a slightly less than two-fold molar excess of chlorine was used, and the hydrogen chloride which was produced in the reaction was determined. The reaction mixture was allowed to stand for four-and-a-half hours before the flask was opened, but apart from this the procedure was the same was that described for the similar analysis in the chlorination of crotonic acid. The following results were obtained:

Methyl crotonate: 20.0×10^{-3} moles;
Chlorine consumed: 39×10^{-3} moles;
Hydrogen chloride liberated: 32×10^{-3} moles.

(See p. 42 for crotonic acid values)

Thus in the chlorination of methyl crotonate in nitromethane, as in the case of crotonic acid itself, two moles of chlorine are consumed per mole of methyl crotonate, and almost one mole of hydrogen chloride is produced per mole of chlorine which reacts. The difference between the two reactions is that methyl crotonate reacts much more

slowly than crotonic acid.

Because of the unexpectedly large amount of chlorine which was consumed, and hydrogen chloride which was liberated, during these reactions, several checks were carried out in an attempt to discovered any discrepancies or sources of error.

A blank run was carried out using chlorine and nitromethane alone, but it was found that there was little loss of chlorine during one-and-a-half hours. In other words, in this space of time there was no perceptible reaction between chlorine and either nitromethane or any impurities it might have contained.

The method used to estimate the amount of hydrogen chloride produced during these reactions was also checked by studying the chlorination of anisole in nitromethane. It was found that 1.00 moles of chlorine reacted to give 1.03 $\pm$ 0.01 moles of hydrogen chloride, and hence no great errors could have arisen from the method used for the estimation of hydrogen chloride.

The reaction of α-chlorocrotonic acid with chlorine in nitromethane was also checked. Little loss of chlorine occurred over one-and-a-half hours, and only unchanged α-chlorocrotonic acid was obtained at the end of the reaction upon removal of the solvent.

IId. Chlorination of crotonic acid in chloroform.

In all these experiments, the chloroform was freed from traces of ethanol by passing a continuous stream of water through it for about three or four hours. It was dried over sodium sulphate and redistilled immediately before use. The chlorine was dried, using concentrated sulphuric acid.

The methods used for the determination of the amount of chlorine and hydrogen chloride involved in the reaction were the same as those already described (p. 36ff.). The concentrations of crotonic acid were also similar; i.e. of the order of 1 g. in 100 ml. of solution.

Two experiments were carried out with an approximately three-fold molar excess of chlorine, the rate at which the chlorine was consumed being determined. In the first, the reaction mixture was allowed to stand at room temperature for about twenty-four hours. The reaction appeared to take place in two stages. A plot of concentration of chlorine against time showed that for the first thirty minutes there was a fairly rapid decrease in the chlorine concentration. After this, the graph levelled out considerably and showed a continuous, slow, linear decrease in the amount of chlorine present. A control run, carried out under identical conditions but without the crotonic acid, showed that although

some of the linear decrease in the chlorine concentration could be attributed to loss of chlorine to the atmosphere, this did not account for all of it by any means. The amount of chlorine which was present at the various stages of the reaction was as follows:

Initially: 8.3×10^{-3} moles crotonic acid,
26.1×10^{-3} moles chlorine.

At the end of the 'fast' reaction (ca. 30 minutes):
20.2×10^{-3} moles chlorine; i.e.
5.9×10^{-3} moles chlorine consumed;

After 100 minutes, 19.5×10^{-3} moles chlorine, i.e.
6.6×10^{-3} moles chlorine consumed;

After 24 hours (final value):
12.5×10^{-3} moles chlorine, i.e.
13.6×10^{-3} moles chlorine consumed.

The control run indicated that at least 2.5×10^{-3} moles of chlorine, and possibly more, were lost to the atmosphere under these conditions.

At the end of twenty-four hours, the solvent was removed under reduced pressure and the remaining material was purified by chromatography on silica-gel. Three fractions were obtained, which emerged from the column in the following order:

(i) the lower melting isomer of αβ-dichlorobutyric acid, which was eluted with ether - light petroleum (1:4);

(ii) an oil, 'X', the infra red spectrum of which was different

from that of any other compound which had been obtained in this work (see Section IV), also eluted with ether - light petroleum (1:4);

(iii) unchanged crotonic acid, removed by elution with pure ether.

The αβ-dichlorobutyric acid and 'X' were present in the approximate ratios by weight of 1,2 : 1 respectively.

From the amount of crotonic acid recovered from the column it was estimated that no more than 65% of the original crotonic acid was consumed. There is probably a little loss of crotonic acid during the removal of the solvent from the column fractions.

A second experiment was carried out under the same conditions as the previous one, but in this case the reaction was stopped after 100 minutes by removing both the excess of chlorine and the solvent under reduced pressure. Once again, there was an initial fairly fast reaction and the rate of chlorine consumption slowed down considerably after about thirty minutes. The following values were found:

Initially: 8.4×10^{-3} moles crotonic acid,
20.7×10^{-3} moles chlorine;

After 30 minutes: 14.0×10^{-3} moles chlorine, i.e.
6.7×10^{-3} moles chlorine consumed;

After 100 minutes (final value):
13.6×10^{-3} moles chlorine, i.e.

7.1×10^{-3} moles chlorine consumed.
A control run again indicated that about 2×10^{-3} moles of chlorine were probably lost to the atmosphere under these conditions. The loss largely occurred when the solution was disturbed by withdrawing samples for titration.

The total oily product of this reaction was purified by chromatography on silica-gel. Three fractions were obtained, emerging from the column in the following order:

(i) lower melting isomer of αβ-dichlorobutyric acid, which was eluted with ether - light petroleum (1:4);

(ii) crotonic acid, which was eluted mainly with pure ether;

(iii) an oily material, 'Y', the infra red spectrum of which seemed to be different from that of any of the other compounds which had been obtained in this work, was eluted with pure ether. There was considerable overlapping with the last crotonic acid fractions.

The amount of crotonic acid obtained from the column again indicated that about 65% of the crotonic acid had reacted under these conditions. The third fraction, 'Y', emerged from the column at the same time as the last half of the crotonic acid fraction, and was therefore heavily contaminated with crotonic acid. This made it very difficult either to form an estimate of the amount of 'Y' or to identify it. The position at which it was eluted from the column, however, showed it to be different from the other

unidentified compound 'X', which had been obtained in the previous experiment.

The amount of hydrogen chloride produced during the chlorination of crotonic acid in chloroform was also determined. An excess of crotonic acid was used, and the procedure was the same as that already described. (p. 41). In chloroform, however, it was found necessary to leave the reaction mixture to stand for about two days before the disappearance of the yellow colour from the solution showed that all the chlorine had reacted.

The following results were obtained:

Crotonic acid (initially): 12.2×10^{-3} moles;

Chlorine consumed: 3.9×10^{-3} moles;

Hydrogen chloride produced: 1.5×10^{-3} moles;

The products of this reaction were separated on a silica-gel column, and the following fractions were obtained:

(i) lower melting isomer of αβ-dichlorobutyric acid;

(ii) crotonic acid;

(iii) the same unidentified compound, 'Y', which was obtained by using an excess of chlorine and stopping the reaction after one hundred minutes.

The large excess of crotonic acid in the total product made it very difficult to determined the relative amounts of either of the other two fractions. Therefore, a further experiment was carried out, on a larger scale and using

only a slight excess of crotonic acid. The reaction mixture was allowed to stand for two days at room temperature before it became colourless. The solvent was then removed under reduced pressure, and the product was purified by chromatography on silica-gel. Three fractions resulted:

(i) lower melting isomer of αβ-dichlorobutyric acid;

(ii) crotonic acid;

(iii) unidentified compound, 'Y'.

In this case, the fraction containing crotonic acid was much smaller than in the previous experiments, and the latter portion of the 'Y' fraction was almost free from it. There was, however, too much overlap for the relative amounts of the fractions to be accurately weighed, and determined. The ratio by weight of αβ-dichlorobutyric acid and 'Y' was very approximately, 2:1. The amount of crotonic acid which was present at the end of the reaction indicated that about one mole of the acid had reacted with each mole of chlorine.

Chlorination of crotonic acid in chloroform in the presence of traces of iodine.

One experiment only was carried out. The chloroform contained just sufficient iodine to colour it. An approximately three-fold molar excess of chlorine was used, and the rate at which it reacted was determined as before. The shape of the plot of chlorine concentration against time was much the same as that of the corresponding reaction in the

absence of iodine. For about the first thirty minutes a fairly rapid decrease in chlorine concentration occurred, after which the graph levelled out slightly, but the rate of loss of chlorine continued to be faster than in the absence of iodine. The following values were found:

Initially: 9.0×10^{-3} moles crotonic acid,
23.7×10^{-3} moles chlorine;

After 30 minutes: 14.8×10^{-3} moles chlorine, i.e.,
8.9×10^{-3} moles chlorine consumed;

After 100 minutes: 13.0×10^{-3} moles chlorine; i.e.,
10.7×10^{-3} moles chlorine consumed;

After three days: 2.9×10^{-3} moles chlorine, i.e.
20.8×10^{-3} moles chlorine consumed.

(See p. 48 ff. for the values of the reaction rate in the absence of iodine).

At the end of three days the solvent was removed under reduced pressure, together with the excess of chlorine, and the oily product was separated by chromatography on silica-gel. Two fractions were obtained:

(i) lower melting isomer of αβ-dichlorobutyric acid;

(ii) unidentified product 'X' which had previously been obtained from the chlorination of crotonic acid in chloroform using an excess of chlorine and allowing the reaction to proceed for about twenty-four hours.

The relative weights of the two fractions were about

1.5 parts of αβ-dichlorobutyric acid to 1 part of 'X'; no crotonic acid was found at the end of the reaction.

Chlorination of crotonic acid in chloroform containing dry hydrogen chloride.

All chloroform used in this experiment was about 0.15N in hydrogen chloride. An approximately three-fold molar excess of chlorine was used, and the rate at which it disappeared from the solution was estimated. The following values were found:

Initially: 8.0×10^{-3} moles crotonic acid,
23.2×10^{-3} moles chlorine;

After 30 minutes: 14.6×10^{-3} moles chlorine, i.e.;
8.6×10^{-3} moles chlorine consumed;

After 100 minutes: 13.4×10^{-3} moles chlorine, i.e.,
9.8×10^{-3} moles chlorine consumed;

After three days: 5.0×10^{-3} moles chlorine, i.e.,
18.2×10^{-3} moles chlorine consumed.

These values are very similar to those obtained for the chlorination of crotonic acid in chloroform containing a trace of iodine (see p. 53).

The products of this reaction were determined as before. Four fractions were eluted from the silica-gel column, emerging in the following order:

(i) lower melting isomer of αβ-dichlorobutyric acid,

(ii) unidentified product 'X';

(iii) unchanged crotonic acid;

(iv) a very small amount of an oily material whose infra red spectrum was very similar to that of the oily form of α-chloro-β-hydroxybutyric acid. The position at which this compound emerged from the column was also the same as that of α-chloro-β-hydroxybutyric acid.

The relative weights of the other two fractions were approximately 1.3 parts of αβ-dichlorobutyric acid to 1 part of 'X'. From the amount of unchanged crotonic acid recovered no more than about 76% of the original charge had reacted.

These results indicated that the unidentified compound 'Y' was an unsaturated substitution product formed with the liberation of hydrogen chloride, and that it could be further chlorinated to give 'X'. Both the position at which it was eluted from the column and its infra red spectrum showed that 'Y' was neither α-chlorocrotonic acid, nor α-chloro<u>iso</u>-crotonic acid, nor a mixture of the two. The most likely answer seemed to be that it was α-chlorovinylacetic acid.

This compound would be expected to isomerise on treatment with sodium hydroxide to give α-chlorocrotonic acid; 'Y' (0.2 g.) was therefore treated with sodium hydroxide solution (5 ml., 2.5$\underline{\underline{N}}$) and allowed to stand at room temperature

for thirty minutes. The product was separated by chromatography on silica-gel, giving two fractions. The first consisted of a little impure α-chlorocrotonic acid (5-10 mg.); the remainder of the material was an unidentifiable oil.

Another attempt was made to isomerise 'Y', this time after esterification, by Rambaud's method[1]. The material was esterified by boiling it with acidic methanol, and the alcoholic solution was rendered just neutral to phenolphthalein using N-sodium hydroxide. A further equivalent (based on the initial weight of 'Y') of N-sodium hydroxide was added, and the solution was allowed to stand at room temperature for thirty minutes before being acidified. Chromatography of the product upon silica-gel gave two fractions. The first, about 50% by weight of the total, consisted of α-chlorocrotonic acid which was identified by its melting point and by its infra red spectrum. The second fraction had the same infra red spectrum as the main product obtained by treating the free acid with sodium hydroxide.

This isomerisation seemed to indicate that 'Y' was, in fact, α-chlorovinylacetic acid.

The other unidentified compound from the chlorination of crotonic acid in chloroform, 'X', was formed by the further chlorination of 'Y'. The infra red spectrum of 'X' was unchanged by further chromatography on silica-gel. The analysis of the oil, however, indicated that it was not a

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(1) Rambaud, Bull., 1934, 1352.

pure compound. If the analysis figures are calculated on the basis of four carbon atoms present in the molecule, the results are:

C, 4.00; H, 6.2; O, 2.2; Cl, 1.5. (BC 301)

IIe. Isotopic dilution experiments for the quantitative determination of the products from the chlorination of crotonic acid in chloroform.

These experiments were carried out in order (a) to obtain an accurate quantitative measure of the amount of the lower melting isomer of αβ-dichlorobutyric acid produced under these conditions, (b) to estimate the maximum possible amount of the other isomer of αβ-dichlorobutyric acid which was formed.

The method adopted for the quantitative determination of a particular product (P) by isotopic dilution was as follows. The reaction was carried out using radioactive chlorine ($^{36}Cl_2$, of known radioactivity, S_{Cl}) and then to a solution in which a known weight of this had undergone reaction a known weight (y) of the pure, inactive product P was added. The component P was separated from the rest of the products, purified, and its radioactivity (S_p) was determined. The weight (x) of P produced in the original reaction may be calculated from the equation

$$S_p = \frac{x}{x + y} \cdot S_{Cl} \; ; \quad \underline{i}.\underline{e}. \quad x = \frac{y}{[(S_{Cl}/S_p) - 1]} \; ;$$

where S_p and S_{Cl}, the radioactivities of the pure, diluted sample of P and of the original chlorine respectively were in each case calculated per unit concentration of chlorine.

The counter used in these experiments was of the type conventionally used for liquids. It had previously been calibrated by using material of known specific activity and was known to count approximately one disintegration in fifty for ^{36}Cl dissolved in acetone. Whenever possible, the concentration of the solution to be counted was arranged so that 10 ml. gave 500-600 counts per minute, and a total count of about 10,000 was made. From this a value for the background radioactivity was subtracted, found by carrying out a count, lasting for approximately the same length of time, with pure solvent (acetone) in the tube.

The chlorine used was obtained as the gas, sealed under atmospheric pressure. Its specific activity was 41.4 μC/mM., and its total activity was 21.6 μC.

An approximately 0.1$\underline{M}$ solution of inactive chlorine in chloroform (55 ml.) was made up. To this, the active chlorine was added as follows. The ampoule containing the active chlorine was such that about 10 ml. of solvent could be added to it above the seal, which could be broken simply by hitting it gently with a glass rod. The ampoule was cooled to about -40° in drikold-methanol, and chloroform (10 ml.) was added to the top. The ampoule was opened by making a small hole in it, when the chloroform was drawn slowly into it, dissolving the chlorine. The ampoule was then inverted into the solution of inactive chlorine and, as it slowly

warmed to room temperature, the active solution was driven out into the inactive one.

Meanwhile, crotonic acid (1.0590 g., 12.31×10^{-3} mole) was dissolved in chloroform (10 ml.) in a dark, 250-ml. iodine flask. Two portions (2 ml.) of the active, diluted chlorine solution were run into excess of potassium iodide, a quantity (50 ml.) was added to the crotonic acid solution, and the flask was immediately stoppered, and finally one portion (2 ml.) was run into potassium iodide solution. The three solutions of iodine in potassium iodide were titrated with sodium thiosulphate solution in order to find the initial chlorine concentration. The following values were found for the volume of 0.1$\underline{\underline{N}}$-sodium thiosulphate which was equivalent to 2 ml. of the chlorine solution:

(1) 2.46 ml.; (2) 2.38 ml.; (3) 2.10 ml..

It was very difficult to decided which value of the chlorine concentration was the correct one to take as a measure of the strength of the chlorine solution added to the crotonic acid. It seemed reasonable to assume that the same loss of chlorine occurred between taking sample (2) and the addition of the chlorine to the crotonic acid solution as that which occurred between taking samples (1) and (2). If this were so, 2.30 ml. of 0.1$\underline{\underline{N}}$-sodium thiosulphate were equivalent to 2 ml. of the chlorine solution; hence 50 ml. of solution contained 2.88×10^{-3} moles of chlorine.

This gave the initial chlorine concentration. The specific activity of the chlorine (S_{Cl}) initially was found by converting the remaining active chlorine to chloride by extracting the solution in chloroform (5 ml.) several times with aqueous sulphur dioxide. The combined aqueous extract was made up to 50 ml. with water, and the amount of chloride in two 20-ml. samples was determined by Volhard's technique. This gave an average value of 0.513×10^{-3} mole of chloride ion in the 50 ml. of aqueous solution. The activity of the remaining solution was next determined. Two dilutions were made using acetone:

(i) 2 ml. diluted to 50 ml.;

(ii) 5 ml. diluted to 100 ml..

Samples (10 ml.) were counted. After subtraction of the background count for pure acetone, this gave

(i) 578 counts per minute;

(ii) 717 counts per minute.

These values were converted to specific activities by making use of the known chloride concentration of the aqueous solution:

(i) 1.408×10^{8} counts/minute/mole of chloride;

(ii) 1.398×10^{8} counts/minute/mole of chloride.

Thus, the specific activity of the initial chlorine was $1.40_3 \times 10^{8}$ counts/minute/gram atom of chlorine, or $2.80_6 \times 10^{8}$ counts/minute/mole.

The chloroform solution which remained after extraction with aqueous sulphur dioxide was also counted. This gave a count which corresponded to a total activity of about 0.006 μC in the 5 ml. of chloroform, compared with about 1.6 μC in the aqueous solution obtained by extraction with aqueous sulphur dioxide.

The amount of hydrogen chloride which was produced during the reaction was determined. The reaction mixture was allowed to stand at room temperature for about three days, by the end of which the yellow colour had disappeared from the solution, showing that all the chlorine had reacted. The chloride ion was determined in exactly the same way as for the inactive cases. The following results were obtained:

Crotonic acid initially: 12.31×10^{-3} mole;

Chlorine consumed: 2.88×10^{-3} mole;

Hydrogen chloride liberated: 1.32×10^{-3} mole.

Total volume of reaction solution after extraction of the hydrogen chloride: 61 ml..

The total activity of the reaction product was then determined.

(1) Two counts were made using different dilutions of the total reaction solution. These gave average values of 12.48 μC for the 61 ml. of solution. Adding the activity of the hydrogen chloride (4.17 μC) gave the total activity accounted for as 12.48 + 4.17 = 16.65 μC.

(2) The total activity of the product without the solvent was also found.

The solvent was removed from a sample (2 ml.) of the reaction mixture by use of an air-blast. The residue was diluted with acetone suitably, and counted. This gave the value of 12.67 μC for the activity of the 61 ml. of solution.

If the average of the two values found in (1) and (2) above are taken, 12.58 μC is the activity of the product which remained in the chloroform. On adding 4.17 μC to this, to allow for the hydrogen chloride, the total activity which can be accounted for by this means is 16.75 μC. There were, however, 2.88×10^{-3} moles of chlorine of specific activity 2.806×10^{8} counts/minute/mole put into the reaction mixture; this amounts to 18.20 μC. In an attempt to account for the residual radioactivity, the aqueous solution into which the hydrogen chloride had been extracted was checked. It was found to contain a total activity of 5.20 μC of which only 4.17 μC were due to the hydrogen chloride.

This, therefore, gave the total activity of the reaction mixture's products to be 12.58 μC in the chloroform solution, and 5.20 μC in the aqueous solution; that is, 17.78 μC compared with the 18.20 μC which were put into the solution.

(a) The amount of the lower melting isomer of αβ-dichlorobutyric acid produced in the above reaction was determined. Pure, inactive, lower melting isomer of αβ-dichlorobutyric

acid (1.0009 g.) was added to 25 ml. of the reaction solution (total volume, 61 ml.). The solvent was removed under reduced pressure, and the residue was separated by chromatography on silica-gel. About 0.8 g. of a slightly impure lower melting isomer of αβ-dichlorobutyric acid was obtained. This was recrystallised twice from light petroleum (b.p. 60-80°) and its specific activity was determined at each stage.

(i) 1.097×10^7 counts/minute/g. atom of chlorine;

(ii) 1.117×10^7 counts/minute/g. atom of chlorine;

(iii) 1.177×10^7 counts/minute/g. atom of chlorine; m.p., 62.5-62.8°.

The solvent was evaporated off from all the solutions containing the lower melting isomer of αβ-dichlorobutyric acid, and the total material was used to make the elimination product, α-chloro<u>iso</u>-crotonic acid. The specific activity of the α-chloro<u>iso</u>-crotonic acid was measured:
1.157×10^7 counts/minute/g. atom of chlorine; m.p. 64-66°.

The S-benzylthiuronium derivative of this compound was then made and its specific activity was measured before and after crystallisation from water:

(i) 1.097×10^7 counts/minute/g. atom of chlorine; m.p. 118-20°.

(ii) 1.155×10^7 counts/minute/g. atom of chlorine; m.p. 120-21°.

The average of the values for the three pure compounds gave the specific activity of the chlorine in the lower melting αβ-dichlorobutyric acid isomer as 1.162×10^{7} counts per minute per g. atom . The amount of this compound which was produced in the reaction was then calculated. The results were 0.095 g. in 25 ml., or 0.2209 g. in the total 61 ml.. On the basis of the 2.88×10^{-3} moles of chlorine which were put into the reaction mixture, this amounted to a 48.9%yield of lower melting αβ-dichlorobutyric acid isomer.

(b) An attempt was also made to estimate the maximum possible amount of the higher melting isomer of αβ-dichlorobutyric acid which was produced during the chlorination of crotonic acid in chloroform.

Unfortunately, none of the higher melting αβ-dichlorobutyric acid isomer was available for this experiment, and so the dilution technique had to be carried out using the elimination product, α-chlorocrotonic acid. The method could, however, only give a maximum possible yield for the amount of the higher melting isomer formed, since it had been shown (p. 56) that α-chlorovinylacetic acid on treatment with sodium hydroxide under similar conditions produced a little α-chlorocrotonic acid (2-5% yield).

The solvent was removed from a sample (25 ml.) of the reaction solution (total volume, 61 ml.) under reduced pressure, and sodium hydroxide was added to the total

remaining material in the cold. After standing at 0° for twenty-four hours, inactive α-chlorocrotonic acid (0.5000 g.) was added to the solution. The product was purified by chromatography on silica-gel after acidification and extraction with ether. About 0.23 g. of moderately pure α-chlorocrotonic acid was obtained. The specific activity of this material was determined both before and after recrystallisation from water:

(i) 0.346×10^7 counts/minute/g. atom of chlorine, m.p. 95-8°;
(ii) 0.044×10^7 counts/minute/g. atom; m.p. 98-9°.

The whole of the α-chlorocrotonic acid was then used in the preparation of its S-benzylthiuronium derivative. This was recrystallised several times from water, and its specific activity was measured at each stage:

(i) 0.249×10^7 counts/minute/g. atom of chlorine;
(ii) 0.115×10^7 counts/minute/g. atom.; m.p. 188.5-189°;
(iii) 0.102×10^7 counts/minute/g. atom;
(iv) 0.089×10^7 counts/minute/g. atom.;
(v) 0.084×10^7 counts/minute/g. atom.: m.p. 189°.

It was evident that this was not going to decrease the specific activity to the value of 0.044×10^7 counts/minute/g. atom of chlorine which had been found for the α-chlorocrotonic acid itself. The S-benzylthiuronium derivative of α-chlorocrotonic acid was analysed to ensure that the material of m.p. 189° was indeed this:

Found (BC 352); C, 50.67; H, 5.05; Cl, 12.24; N, 9.63; O, 11.41; S, 11.07%. $C_{12}H_{13}ClN_2O_2S$ requires C, 50.24; H, 5.28; Cl, 12.36; N, 9.77; O, 11.15; S, 11.18%.

It was assumed that the value of 0.084×10^7 counts/minute/g. atom was the correct value for the specific activity as it was a consistent member of a series of values. If this was due entirely to the original presence of the higher melting isomer of αβ-dichlorobutyric acid, it would correspond to a 2% yield calculated on the amount of chlorine which reacted. It could, however, equally as well be due to a conversion of α-chlorovinylacetic acid to α-chlorocrotonic acid. These results only show, therefore, that not more than 2% of the higher melting isomer of αβ-dichlorobutyric acid can have been formed.

Summarising the results obtained from the isotopic dilution experiment:

Crotonic acid initially: 12.31×10^{-3} moles;

Chlorine: 2.88×10^{-3} moles;

Hydrogen chloride: 1.32×10^{-3} moles (45.8%)

Lower melting αβ-dichlorobutyric acid: 48.9%

Higher melting αβ-dichlorobutyric acid: 2% maximum.

All percentages of the products formed were calculated on the basis of the chlorine consumed. They account for a total of 96.7% of the chlorine used.

IIf. Chlorination of crotonaldehyde in chloroform.

The identification of the products of the chlorination of crotonaldehyde in chloroform involved the oxidation of the aldehydes to their corresponding acids. The procedure adopted was that of oxidation using an acid solution of potassium permanganate.

Three experiments were carried out, the first two using an approximately two-fold molar excess of chlorine, and the third using a two-fold excess of aldehyde in order to determine the amount of hydrogen chloride which was produced. The first two chlorinations were carried out at 0^{o}, and the third at room temperature. The crotonaldehyde was redistilled immediately before use, and the experimental procedure was then the same as that used with crotonic acid. The chlorination of crotonaldehyde in chloroform seemed to be much more rapid than the corresponding reaction with crotonic acid, however, and in the chlorination which was carried out using an excess of crotonaldehyde the chlorine was completely consumed after about fifteen minutes.

At the end of the reaction, the solvent was removed under reduced pressure, and the product (ca. 1 g.) was treated with acid permanganate solution (5 g. potassium permanganate in 40 ml. 2N-sulphuric acid). The solution was heated under reflux on a water-bath for about two

hours. It was then extracted with ether and the product was purified by chromatography on silica-gel. In the case of the two experiments which were carried out using an excess of chlorine, two fractions only were obtained. They both were eluted from the column using ether - light petroleum (1:4) and consisted of the two isomers of αβ-dichlorobutyric acid. From the chlorination which was carried out using an excess of aldehyde there was, in addition to these two products, a third, oily fraction which was eluted with pure ether and which was presumably the product of the reaction of crotonaldehyde with acid potassium permanganate.

The results of the three chlorinations may be summarised:

(i) Reactants: crotonaldehyde: 17.1×10^{-3} moles;
chlorine: 40.0×10^{-3} moles;

Products: (a) lower melting isomer of αβ-dichlorobutyric acid,
(b) higher melting isomer of αβ-dichloro-butyric acid.

Ratio: (a) to (b):: 4.2:1

(ii) Reactants: crotonaldehyde: 51.4×10^{-3} moles;
chlorine: 121×10^{-3} moles;

Products: (a) lower melting isomer of αβ-dichlorobutyric acid,
(b) higher melting isomer of αβ-dichloro-

butyric acid

Ratio: (a) to (b) :: 4.2:1

(iii) Reactants: crotonaldehyde: 16.9×10^{-3} mole;

chlorine: 8.6×10^{-3} mole;

Products: (a) hydrogen chloride: 0.15×10^{-3} mole;

(b) lower melting isomer of αβ-dichloro-butyric acid;

(c) higher melting isomer of αβ-dichloro-butyric acid;

(d) unidentified product, possibly from the reaction of crotonaldehyde with acid potassium permanganate.

Ratio: (b) to (c) :: 3.7 : 1 by weight.

The lower melting isomer of αβ-dichlorobutyric acid was treated with acid permanganate under the conditions used for the above oxidations, in order to ensure that the conditions were not such as to convert the lower melting form into its higher melting isomer. However, the lower melting isomer of αβ-dichlorobutyric acid was not changed by this treatment.

Thus, the reaction of crotonaldehyde with chlorine in chloroform differs markedly from the corresponding reaction of crotonic acid (a) in that much less substitution accompanies the addition, and (b) in the formation of the

higher melting isomer of αβ-dichlorobutyric acid, presumably arising from the oxidation of the corresponding isomer of αβ-dichlorobutyraldehyde. There was no sign of this compound in the products of chlorination of crotonic acid under any of the conditions studied in the present work.

III. DISCUSSION

DISCUSSION

The products of the reaction of crotonic acid with chlorine under a variety of conditions have been studied; they depend critically upon these reaction conditions. Straightforward addition is not the only reaction which takes place under any of the conditions which have been studied here. It has also been shown that for crotonic acid very little, if any, 'cis' addition accompanies the normal 'trans' addition of chlorine. This applies both for uncatalysed and catalysed reactions.

In the case of crotonaldehyde, on the other hand, both 'cis' and 'trans' addition appear to take place under the conditions of study. The only products which have been isolated after the oxidation of the chlorination products are the two isomeric αβ-dichlorobutyric acids.

The individual reactions are discussed below.

IIIa. Reactions of α-chlorocrotonic acid with hydrogen chloride.

The reaction was carried out in an attempt to prepare the higher melting isomer of αβ-dichlorobutyric acid. This compound would have been the only product if the reaction had taken place simply by the 'trans' addition of hydrogen chloride to α-chlorocrotonic acid.

In fact, it was the only product which was

mentioned by Michael and Schulthess or by Michael and Bunge[1,2]. In the present work, however, the two αβ-dichlorobutyric acids were obtained in approximately equal yields, and the question arises as to how the lower melting isomer came to be produced. There are two possible explanations of the experimental fact. Either 'cis' addition accompanies the normal 'trans' addition, or the α-chlorocrotonic acid isomerises under the conditions of the experiment to give α-chloro*iso*-crotonic acid which then reacts with hydrogen chloride by 'trans' addition. It has already been suggested that this might happen 'in reverse' by Michael and Bunge[2]. They explained the partial isomerisation of the lower melting isomer of αβ-dichlorobutyric acid, when it was treated with hydrogen chloride under the same conditions as this experiment, by suggesting that it decomposed to give α-chloro*iso*-crotonic acid which isomerised to give α-chlorocrotonic acid which then added hydrogen chloride by 'trans' addition. Further work is needed to establish the course of the reaction under the conditions of the present experiments.

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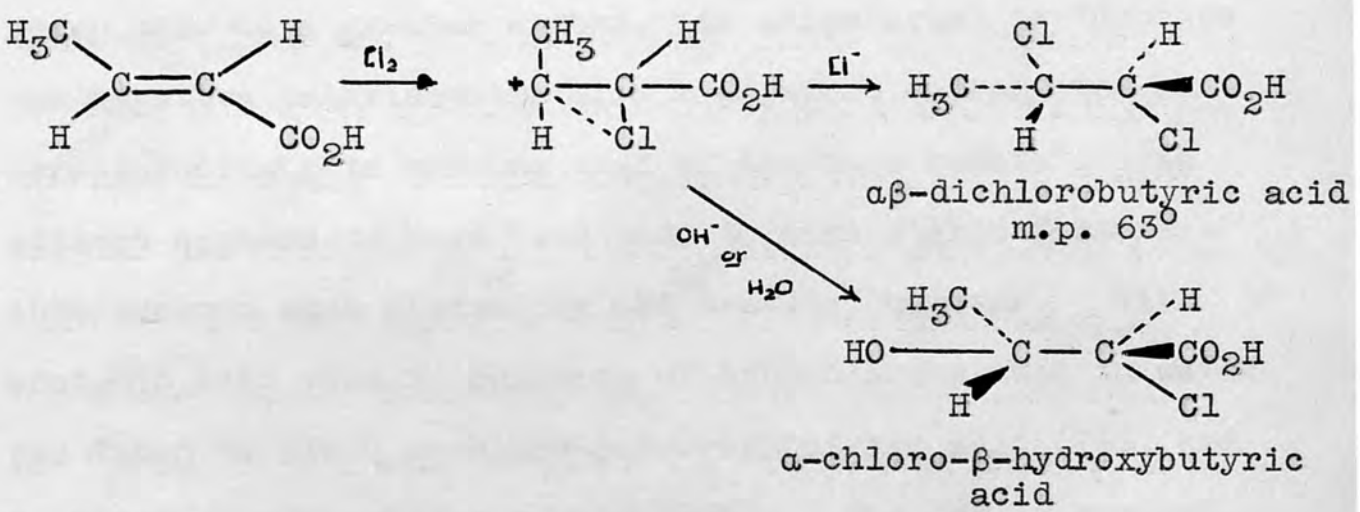
(1) Michael and Schulthess, J. prakt. Chem., 1892, *46*[2], 259.
(2) Michael and Bunge, Ber., 1908, *41*, 2911.

IIIb. Chlorination of crotonic acid in water saturated with sodium chloride.

The products which were isolated from this reaction were those expected if the addition took place by a two-stage mechanism in which the first step involved electrophilic attack by the halogen. This would produce a carbonium ion which could then react with any nucleophiles present in the reaction mixture, in this case chloride ions, hydroxyl ions, and water molecules, with the production of a mixture of αβ-dichlorobutyric acid and α-chloro-β-hydroxybutyric acid (p. 32) -- in this case, in approximately equal amounts.



The isomer of αβ-dichlorobutyric acid which has been isolated from these reactions is that which is formed by 'trans' addition of chlorine to <u>trans</u>-crotonic acid. In the case of α-chloro-β-hydroxybutyric acid, both isomers have been obtained. However, this would be expected, since

the compound with the lower melting point (60-1°) has been reported by Smith[1] to be converted into the other isomer (m.p. 86°) simply by recrystallisation. The lower melting compound is the one which has been obtained by the addition of hypochlorous acid to trans-crotonic acid,[2] while the higher melting isomer has been obtained by the corresponding reaction of cis-crotonic acid.[3]

The reaction of crotonic acid with hypochlorous acid has been studied by Farmer and his co-workers.[4] They carried out this addition with a number of unsaturated acids in an attempt to determine the orientating influence of the carboxyl group. The results indicated that the carboxyl group and, to a greater extent, its anion acted to "depress the negative polarisations of the adjacent carbon atom and correspondingly to enhance that of the more remote". No attempt appears to have been made to take steric factors into account when discussing the results, however. With crotonic acid itself, addition of hypochlorous acid in water was found to yield α-chloro-β-hydroxybutyric acid (74%) and β-chloro-α-hydroxybutyric acid (26%). The latter was not isolated by Melikoff[2,3] nor has it been found in the present work, although the methods used to isolate the products do not exclude the possibility that it was present to some extent.

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(1) Smith, Z. physik. Chem., 1936, 177[A], 139.
(2) Melikoff, Ann., 1886, 234, 197.
(3) Melikoff, Ann., 1891, 266, 358.
(4) Bloomfield, Farmer, and Hase, J., 1933, 800.

IIIc. Chlorination of crotonic acid and of methyl crotonate in nitromethane.

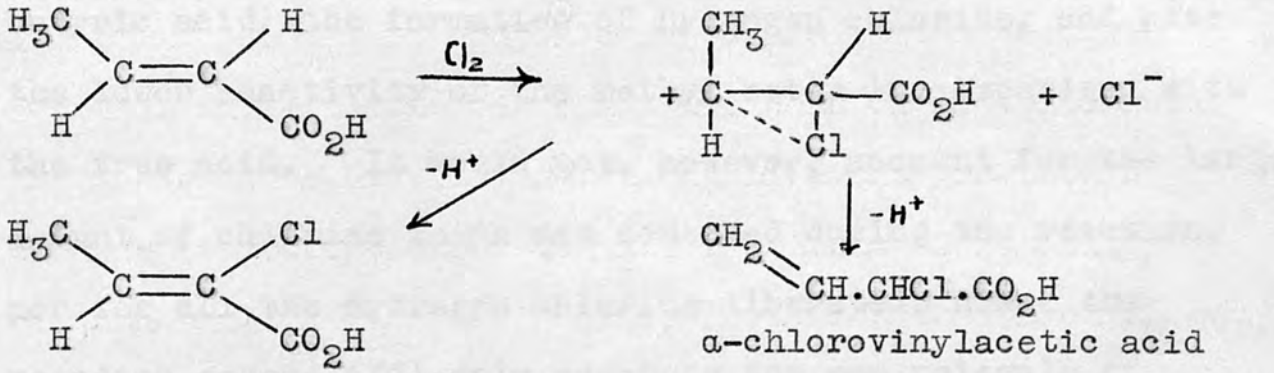
The products of the chlorination of crotonic acid in nitromethane were totally unexpected. Nitromethane is an aprotic solvent which has the fairly high dielectric constant of 37, and which possesses little nucleophilic activity. It was expected, therefore, that addition of the halogen would be the predominant reaction of chlorine with crotonic acid in this solvent. It was found, however, that only about 24% by weight of the total product which was isolated from the reaction was the lower melting isomer of αβ-dichlorobutyric acid, the compound formed by the trans addition of chlorine to crotonic acid. This was contaminated by a very small amount of material of unknown composition, but the remaining 76% of the isolated product was α-chloro-β-hydroxybutyric acid, and this compound was obtained even when the nitromethane was carefully dried by fractional distillation and the other starting materials were kept dry also. The α-chloro-β-hydroxybutyric acid was obtained as the same proportion of the total product when the chlorination was carried out in nitromethane saturated with hydrogen chloride. The reaction appeared to be slightly faster under these conditions, but was always complete within ten minutes even in the absence of hydrogen chloride. The results for the chlorination in pure nitromethane also

indicated that about two molecules of chlorine were consumed for each molecule of crotonic acid, and that when the reaction was carried out using an excess of crotonic acid about one molecule of hydrogen chloride was produced by each molecule of chlorine. The reactions of methyl crotonate with chlorine in nitromethane were very much slower than the corresponding reactions of the acid, but once again about two molecules of chlorine were consumed for each molecule of methyl crotonate, and one molecule of hydrogen chloride was produced per molecule of chlorine consumed. The products of the reaction were not examined further.

None of these results is easy to explain. The production of hydrogen chloride and the formation of α-chloro-β-hydroxybutyric acid in a supposedly dry system can first be considered.

The hydrogen chloride could be produced by an substitution reaction in which a carbonium ion was formed as the first stage of the reaction, and which subsequently lost a proton from either of two possible carbon atoms (see p. 79). The unsaturated product of the reaction would thus have to react with water, possibly at a later stage such as during the working up of the reaction mixture, to give α-chloro-β-hydroxybutyric acid. This explanation appears to be very unlikely, since α-chlorocrotonic acid has been shown to be unaffected by the conditions of the

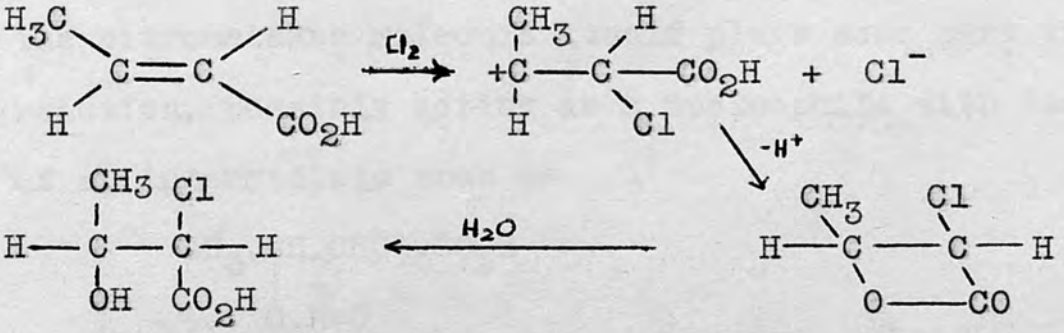
Reaction Scheme I.



experiment, and under normal conditions α-chlorovinylacetic acid does not react with water.

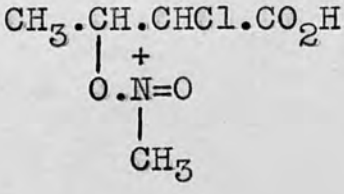
The other way in which hydrogen chloride could be produced in this system is through a reaction path involving the interaction of the carboxyl group of the acid with the carbonium ion centre, forming a lactone ring (see p. 9). This would probably not be very stable and it is reasonable to suppose that it could be opened by reaction with water possibly during the working up process when the nitromethane solution was saturated with water.

Reaction Scheme II.



This would explain the production of α-chloro-β-hydroxy-butyric acid, the formation of hydrogen chloride, and also the lower reactivity of the methyl ester in comparison with the free acid. It would not, however, account for the large amount of chlorine which was consumed during the reaction, nor for all the hydrogen chloride liberated, since the reaction scheme (II) only accounts for one molecule of chlorine per molecule of crotonic acid. It is possible, however, that the extra chlorine and hydrogen chloride could partly be accounted for by the small amount of product of unknown composition which was isolated with the αβ-dichloro-butyric acid fraction. Another point which must be taken into consideration is the fact that the total yields from these experiments were only about 50%, or less, calculated on the amount of crotonic acid initially. This makes it possible that some of the products were never isolated, and that it was these which were using up more than one molecule of chlorine for each molecule of crotonic acid.

Another possibility which must be considered is that the nitromethane molecule itself plays some part in the reaction, possibly acting as a nucleophile with the formation of an intermediate such as



which could later decompose. This, however, appears unlikely and still would not account for the large amount of chlorine consumed, and hydrogen chloride liberated.

Much further work is needed, but at the moment the formation of the lactone ring appears to be the most likely explanation for the production of α-chloro-β-hydroxy-butyric acid in this reaction.

IIId. Chlorination of crotonic acid in chloroform.

Chloroform is an aprotic solvent with a dielectric constant of about six. The addition of halogens to olefins has not been studied extensively in such media, and little appears to be known either about the mechanisms of the reactions or about their products. The addition of bromine to ethylcinnamate is one reaction which has been studied in chloroform solution, however[1]. The reaction followed third order kinetics as shown by the rate equation

$$-d[Br_2]/dt = k[A][Br_2]^2.$$

The reaction is catalysed by iodine, but the extent of the catalysis is less than for the corresponding reaction in the less polar solvent, carbon tetrachloride. The corresponding reaction with chlorine has not been investigated, nor has much attention been paid to the products of the reaction.

In the present work, the chlorination of crotonic acid in chloroform was carried out under four different conditions:

(i) using a deficiency of chlorine in pure chloroform;
(ii) using an excess of chlorine in pure chloroform;
(iii) using chloroform containing dry hydrogen chloride (0.15N);
(iv) using chloroform containing a trace of iodine.

The products which were obtained either by using excess or a deficiency of chlorine and stopping the reaction after about one molecule of chlorine had been consumed per molecule of crotonic acid were the lower melting isomer of αβ-dichloro-

(1) Waters, Caverhill, and Robertson, J., 1944, 1168.

butyric acid, hydrogen chloride, and a compound which, at the moment, appears to be α-chlorovinylacetic acid (p. 55). These three compounds were obtained in approximately the same molar quantities, and an isotopic dilution experiment showed that the αβ-dichlorobutyric acid accounted for 49% of the reacting chlorine. If the chlorination was allowed to proceed beyond this point, both for the catalysed and for the uncatalysed reactions, a slow reaction of α-chlorovinylacetic acid with chlorine took place and the final product consisted of the lower melting isomer of αβ-dichlorobutyric acid and an impure product or mixture of products which has not yet been identified. Rambaud[1] has reported that α-chlorovinylacetic acid absorbs bromine in chloroform to give a mixture of several dibromides, but he has not succeeded in purifying them.

The production of α-chlorovinylacetic acid by the chlorination of crotonic acid in chloroform is of interest because it appears to be the first time that such a substitution reaction has been reported for an unsaturated acid. The path taken which leads to the production of α-chlorovinylacetic acid rather than α-chlorocrotonic acid as a result of proton loss from the reaction intermediate is presumably the same as that which has been described for iso-butylene[2] (p. 7). That is, after the initial attack

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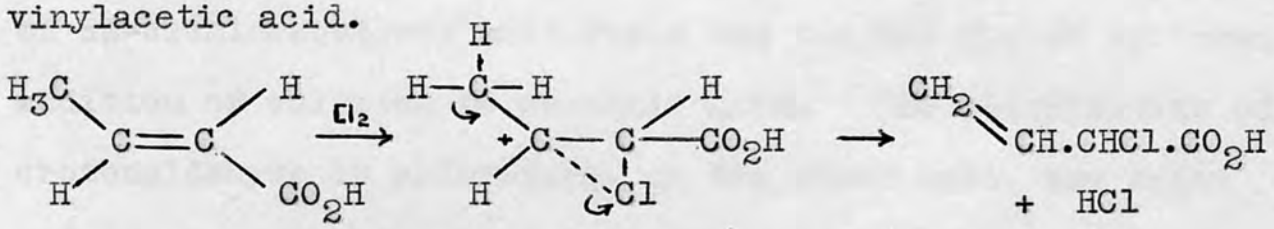
(1) Rambaud, Bull., 1934, 1317.
(2) de la Mare, and Salama, J., 1956, 3337.

by the chlorine molecule, the interaction of the entering chlorine atom with the carbonium ion which is formed is considered to hold the ion in a configuration which is unfavourable for the elimination of a proton from the α-carbon atom, and thus leads to significant elimination from the methyl group (C_γ) and the production of α-chloro-vinylacetic acid.



Chloroform is the only solvent in which the exact yield of the two isomers of αβ-dichlorobutyric acid was determined by an isotopic dilution experiment. This was carried out partly to obtain an accurate value for the extent of formation of the lower melting isomer, but mainly to discover the maximum possible amount of the higher melting isomer which was produced. This is the compound which would result from the cis addition of chlorine to crotonic acid, but it was found that for the reactions in chloroform that a maximum (and perhaps spurious) value of less than 2% of this isomer was formed. This result shows that in this solvent little, if any, cis addition accompanies the 'normal' trans addition of chlorine to crotonic acid.

IIIe. Chlorination of crotonaldehyde in chloroform.

The chlorination of crotonaldehyde in chloroform was completely different from the corresponding reaction of crotonic acid. In the latter case a continuous, slow reaction of chlorine took place over a period of several days, hydrogen chloride was one of the products, and the only isomer of αβ-dichlorobutyric acid found was the one formed by 'trans' addition of chlorine to crotonic acid. The chlorination of crotonaldehyde in chloroform, on the other hand, was rapid and complete within about fifteen minutes. Very little hydrogen chloride was produced and the products, after oxidation under conditions which were unlikely to cause rearrangement, consisted of the two isomers of αβ-dichlorobutyric acid containing 20% of the higher melting isomer.

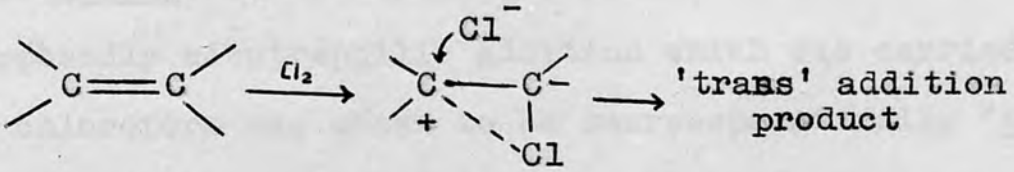
If the reaction which was taking place in chloroform was the 'normal' electrophilic addition of chlorine to the aldehyde or the acid, the former would be expected to react more slowly, and the reversal of this order of reactivity indicates that, at least for the aldehyde, a nucleophilic attack by the chlorine molecule initiates reaction. The stereochemistry of such reactions does not appear to be known, as there is no report of the products having been studied. In the present case, the production of both isomers of αβ-dichlorobutyric acid (after oxidation) shows that the mechanism of this reaction must be different from that of the

electrophilic addition reaction, and seems to take place in such a way that both *cis* and *trans* additions of the halogen can occur.

IIIf. Relationships between the reactions which have been discovered for the crotonic acid systems and those which are known to take place with other olefinic compounds.

This work, although very incomplete, has served to demonstrate the different types of reaction which can take place when chlorine is added to an olefin. Most of these types of reaction have been shown to occur in the crotonic acid system and, in a few cases, the results obtained have helped to throw some light upon the mechanism of the reactions involved.

The stereospecificity of the electrophilic addition of chlorine to an olefin has, for example, been demonstrated. The generally accepted mechanism for the electrophilic addition of chlorine to olefins is thought to lead to 'trans' addition because of the interaction of the entering halogen atom with the carbonium ionic centre. This would necessitate the subsequent attack of the nucleophile taking place from the opposite side of the molecule to that from which the first group entered it.



There are numerous examples of this, but the actual degree of stereospecificity involved is only

known in a few specific cases. In the work of Lucas and Gould on the addition of chlorine to cis- and trans-but-2-ene,[1] for example, the only addition product which was isolated in each case was that formed by the trans addition of the halogen to the olefin. The methods used however did not eliminate the possibility of a small amount of the product of cis addition being present, although there was no evidence that it was there to any appreciable extent.

The addition of bromine to maleic and fumaric acids has also been shown to be largely 'trans' in character[2]. Here the addition to maleic acid has been shown to give not less than 80% of d,l-dibromosuccinic acid, whilst the corresponding addition to fumaric acid gives largely meso-dibromosuccinic acid. In both cases, however, the presence of a small proportion of the other isomer was not eliminated.

In the present investigations there was no sign of the product from the cis addition of chlorine to crotonic acid (trans) under any of the conditions studied, and the supposedly electrophilic addition which was carried out in chloroform was shown to be stereospecifically 'trans' to the extent of at least 96%. This was demonstrated

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1. Lucas and Gould, J. Amer. Chem. Soc., 1941, 63, 2541.
2. McKenzie, J., 1912, 101, 1196.

by an isotopic dilution experiment in which it was found that no more than 4%, and probably less, of the total addition product (2% of the total chlorine consumed) could have been the compound formed by the cis addition of chlorine to crotonic acid. Thus, for crotonic acid at least, the electrophilic addition of chlorine to the olefin has been shown to be very nearly stereospecifically 'trans'. The supposedly nucleophilic addition to crotonaldehyde, on the other hand, was found to be much less stereospecific, cis addition accompanying the trans to an extent of about 20%. This points towards a definitely mechanistic difference between the two reactions.

The various reactions which can accompany the electrophilic addition of halogens to olefins have also been demonstrated in the crotonic acid system. There can be three general divisions made: those which involve a competition between the second half of the halogen molecule and one or more external nucleophiles in the second stage of the reaction; those which involve internal competition with a group which is already present in the molecule; and those which involve proton-loss.

There are numerous examples in the literature of the first of these three groups, reactions which have been used to demonstrate the two-stage mechanism of the electro-

philic addition mechanism. The external nucleophile may take the form of an added salt as, for example, in the addition of bromine to ethylene in an aqueous solution of sodium chloride or sodium nitrate.[1] Alternatively, the reaction may be completed by a nucleophilic solvent molecule such as that of water, when the same reaction is carried out in the absence of added ions.[2]

$$CH_2{=}CH_2 + Br_2 \longrightarrow {}^{+}CH_2.CH_2Br + Br^-$$

$${}^{+}CH_2.CH_2Br \xrightarrow{Br^-} BrCH_2.CH_2Br$$

$$\xrightarrow[Cl^-]{aq.\ NaCl} ClCH_2.CH_2Br$$

$$\xrightarrow[NO_3^-]{aq.\ NaNO_3} (NO_3)CH_2.CH_2Br$$

$$\xrightarrow{H_2O} (OH)CH_2.CH_2Br + H^+$$

The extent to which the reaction is diverted depends upon the nucleophilic power of the competing anion and on the concentration in which it is present in the solution.

This type of competition with an external species has been identified in the crotonic acid system. The reaction which was carried out in the presence of water saturated with sodium chloride is the obvious example. Here the first stage of the reaction involved attack by an electrophilic halogen molecule with the formation of a positively charged carbonium ion. This could then react either with the added chloride ions or with the other half

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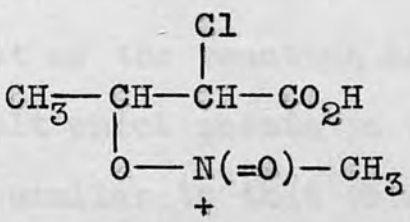
1. Francis, J. Amer. Chem. Soc., 1925, 47, 2340.
2. Read and Williams, J., 1917, 240.

of the halogen molecule, or with the solvent. When the reaction was carried out in the absence of added chloride ions, the total product appeared to be α-chloro-β-hydroxybutyric acid; in other words, the nucleophilic water molecules succeeded in eliminating completely the chlorine from the second stage of the reaction. In the presence of added chloride ions, however, competition between the water molecules and the chloride ions in the second stage of the reaction resulted in approximately equal yields of αβ-dichlorobutyric acid and α-chloro-β-hydroxybutyric acid. Here the water was present in about a ten-fold molar excess over the chloride ions, but this was balanced by the greater nucleophilic character of the halide ions.

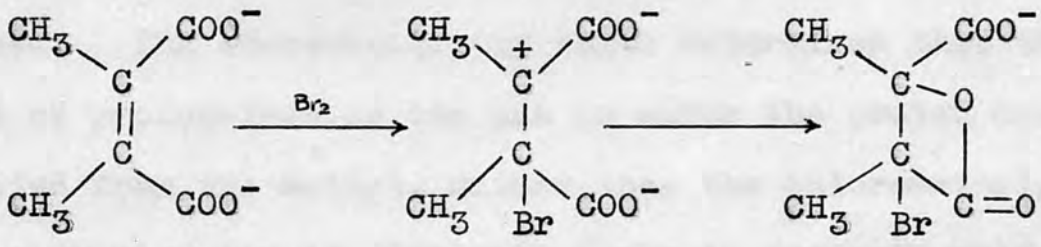
The possibility of a solvent molecule intervening in the reaction also exists in the case of the chlorination which was carried out in nitromethane. Here the interpretation of the results must take into account the possibility of some sort of interaction of a nitromethane molecule with the carbonium ion to produce an unstable intermediate of the type:



This does not seem to be the most probable explanation of the results obtained, since nitromethane has very

little nucleophilic character, but it may be a contributing factor to some extent.

The second group of side reactions which may have been identified in the crotonic acid system consists of those in which the halogen molecule has to compete with a group which is already present in the olefin in the second stage of the reaction. The best example of this is the one involving dimethylmaleic acid and dimethylfumaric acid[1] which has already been mentioned (see Introduction).



Dimethylmaleic acid dianion

Here the carboxyl group successfully competes with the bromide ions for the positively charged carbon atom, with the formation of a lactone ring.

In the crotonic acid system it seems probable that a similar type of interaction occurs during the reaction of chlorine with crotonic acid in nitromethane. Here the main product of the reaction is α-chloro-β-hydroxybutyric acid, a result which points to the possible formation of a lactone ring, similar to that obtained with dimethylmaleic acid, as an intermediate of the reaction.

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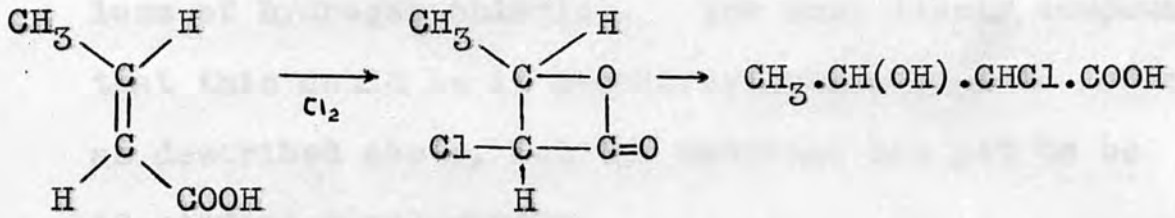
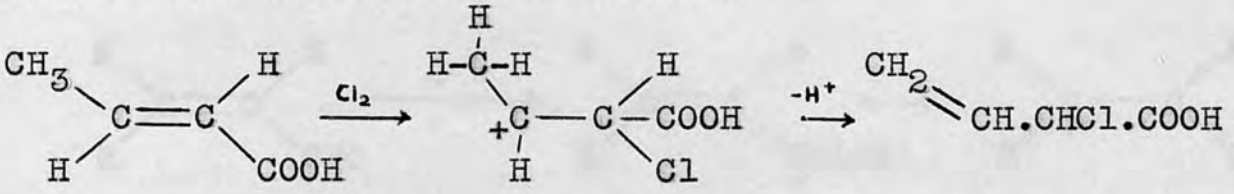
1. Bartlett and Tarbell, J. Amer. Chem. Soc., 1937, 59, 407.



The third group of reactions which are known to accompany the electrophilic addition of halogens to olefins under certain conditions, those which involve the loss of a proton from the carbonium ion intermediate, are also believed to take place in the crotonic acid system. The example of the reactions of iso-butylene with hypochlorous acid[1] has already been mentioned. The stereochemistry which determines that the main product of proton-loss is the one in which the proton has been eliminated from the methyl, rather than the chloromethyl, group of the carbonium ion is likely to apply to crotonic acid as much as to iso-butylene. This would lead to the production of α-chlorovinylacetic acid from crotonic acid, and in fact appears to be one of the processes occurring when crotonic acid reacts with chlorine in chloroform.



The isolated product consisted of the lower melting isomer of αβ-dichlorobutyric acid accompanied by an approximately equal amount of a material which was formed by the

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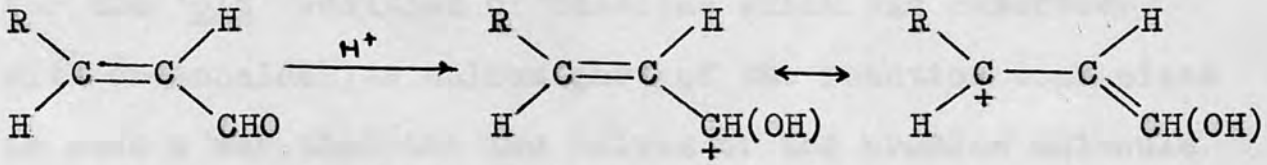
1. de la Mare and Salama, J., 1956, 3337.

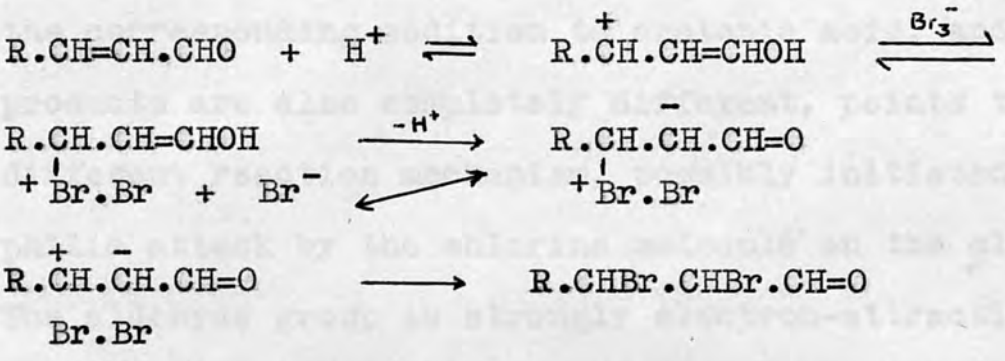
loss of hydrogen chloride. The most likely compound that this could be is α-chlorovinylacetic acid formed as described above, but the material has yet to be identified conclusively.

All the above remarks apply to the 'normal' type of addition reaction, that in which the reaction is initiated by electrophilic attack upon an olefin with the formation of a positively charged carbonium ion. This ion can then react in a number of ways depending upon the conditions of the experiment. The situation with regard to the nucleophilic addition of halogens to olefins is much less clearly understood and very little is in fact known about either the reaction paths involved or the products of these reactions. For the acid-catalysed nucleophilic addition of a halogen to an αβ-unsaturated acid or aldehyde the first step is thought to involve the addition of a proton, forming a positive charge centre which could then resonate over the molecule



Apart from the fact that the next step presumably involves attack by the nucleophilic end of a polarised halogen molecule upon one of the positively charged carbon atoms, little is known about the subsequent stages of the

reactions, which are thought to be complex. A suggested reaction path for the nucleophilic addition of bromine, catalysed by hydrogen bromide, to an aldehyde is as follows:[1]



In other words, what is thought to happen here is that the nucleophilic mechanism serves solely to bring the bromine molecule into a position which is sterically favourable for the final electrophilic attack. This would be expected to leads to '<u>trans</u>' addition of the halogen to the aldehyde as the subsequent reaction would be the same as for the electrophilic mechanism described above. This reaction path would not, therefore, account for the '<u>cis</u>' addition of chlorine which was observed with crotonaldehyde unless part of the reaction took place in such a way that the two halves of the bromine molecule attacked the olefin more or less simultaneously from the same side.

Although for an acid-catalysed reaction it is presumably the carbonium ion formed by the addition of a

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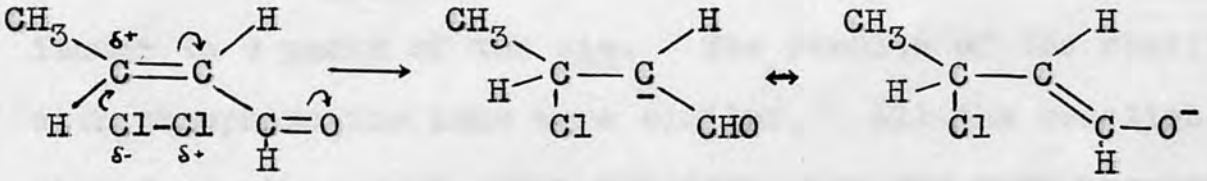
1. de la Mare and Robertson, J., <u>1950</u>, 2838.

proton and not the olefin itself which is attacked, in a reaction such as the addition of chlorine to crotonaldehyde in the absence of added acid this may not be so. The fact that this reaction is considerably faster than the corresponding addition to crotonic acid, and that the products are also completely different, points to a different reaction mechanism, possibly initiated by nucleophilic attack by the chlorine molecule on the olefin itself. The aldehyde group is strongly electron-attracting, and may polarise the molecule sufficiently to allow nucleophilic attack to occur on the β-carbon atom, with the formation of a carbon anion:



The results obtained with crotonaldehyde have served to show that this reaction is not stereospecific, as 'cis' addition accompanies 'trans' to an extent of about 20% in chloroform. In considering the possible ways in which this could occur, the known reactions of carbon anions are of interest. Some such reactions are known in which inversions of configuration have been shown to occur, an example being the reaction of ethyl β-chlorocrotonate with nucleophiles.[1] Both cis and trans ethyl β-chlorocrotonates

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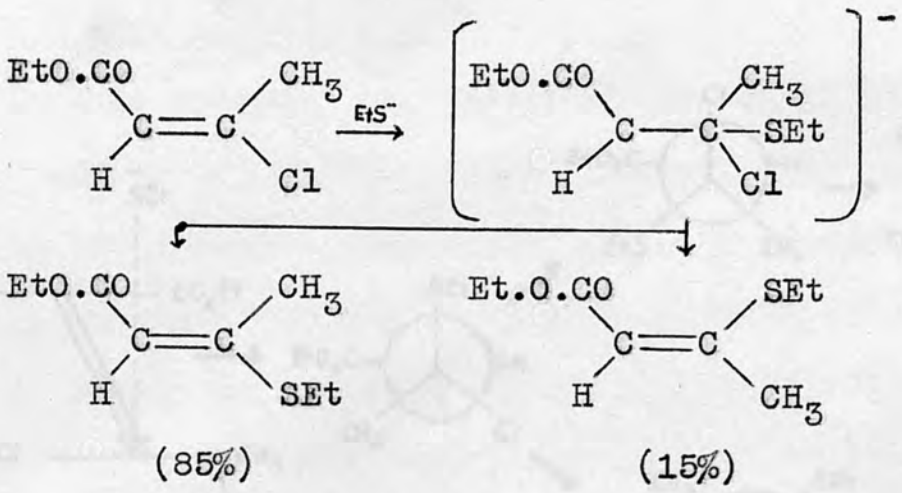
1. Jones, Morris, Vernon, and White. J., 1960, 2349.

were allowed to react with thioethoxide and thiophenoxide ions in ethanol, and the products of the reactions were studied. Fairly rapid nucleophilic displacement of chlorine took place, and it was found that although in each case the reaction proceeded largely with retention of geometric configuration, in no case was it completely stereospecific, some proportion of the other isomer always being found. For example, the reaction between ethyl β-chloroiso-crotonate and thioethoxide ions in ethanol was found to give the two isomers of ethyl β-thioethoxy-crotonate in the ratio of 85 parts of the cis isomer to 15 parts of the trans. The corresponding reactions of ethyl α-chlorotrans-crotonate gave 91 parts of the trans isomer to 9 parts of the cis. The results of the reactions with thiophenoxide ions were similar. All the reactions showed simple second order kinetics with the rate proportional to $[RCl][X^-]$. These results were explained by a mechanism involving an initial attack by the nucleophile with the formation of a carbanion intermediate, the negative charge being distributed over the molecule by resonance. This carbanion could then react with the loss of chloride ion as shown. (next page)

The exact geometry of the intermediate formed in this reaction is not known, but the various ways in which the observed products might have been obtained are discussed



in the paper. These explanations had to take into account the fact that reactions of the type

$$Ph.SO_2.CH{:}CHCl + X^- = Ph.SO_2.CH{:}CHX + Cl^-$$

had been shown to take place with retention of the configuration with the nucleophiles MeO^-, EtO^-, PhO^-, and N_3^-. [1,2]

In the explanation which was adopted, it was assumed that the approach of the nucleophile was at right angles to the plane of the olefin; the departing ion left along the same or a reciprocal path; and the groups attached to the distal carbon atom remained in the original plane of the molecule in the intermediate. The steric course of the reaction of the chloro-esters with thioethoxide ions would then be as follows, the negative charge on the intermediates resonating between the oxygen and the α-carbon atoms.

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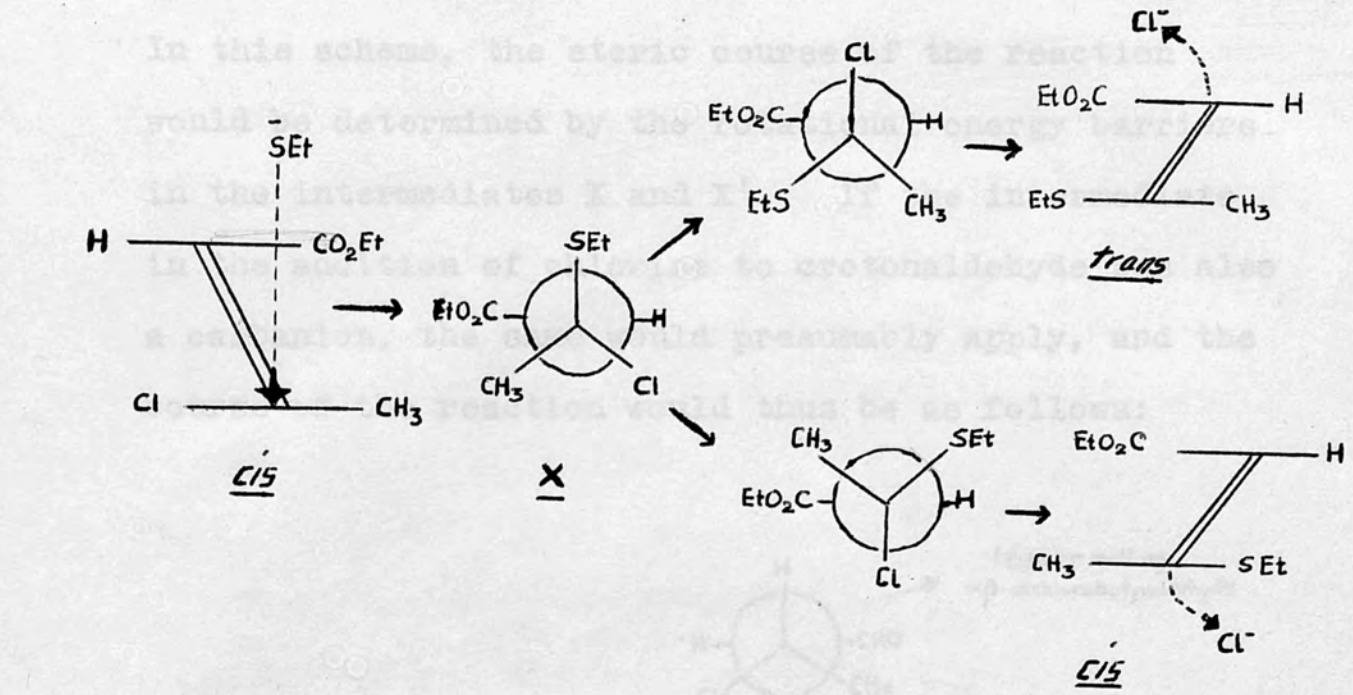
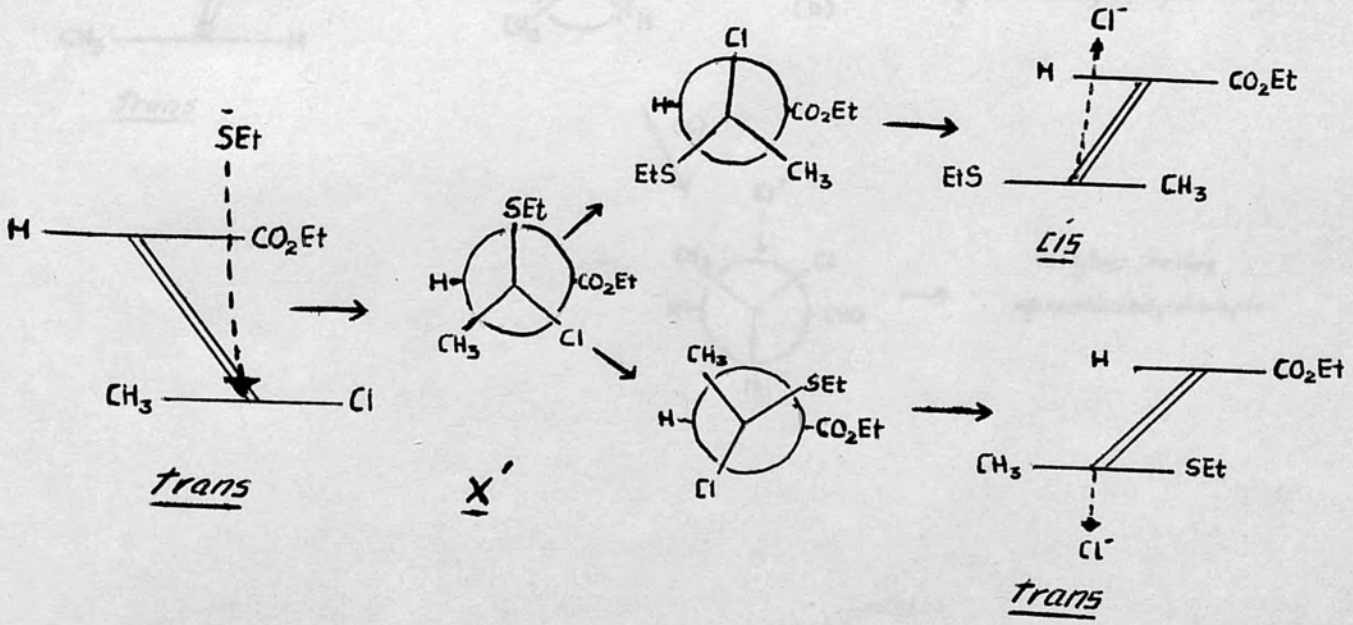
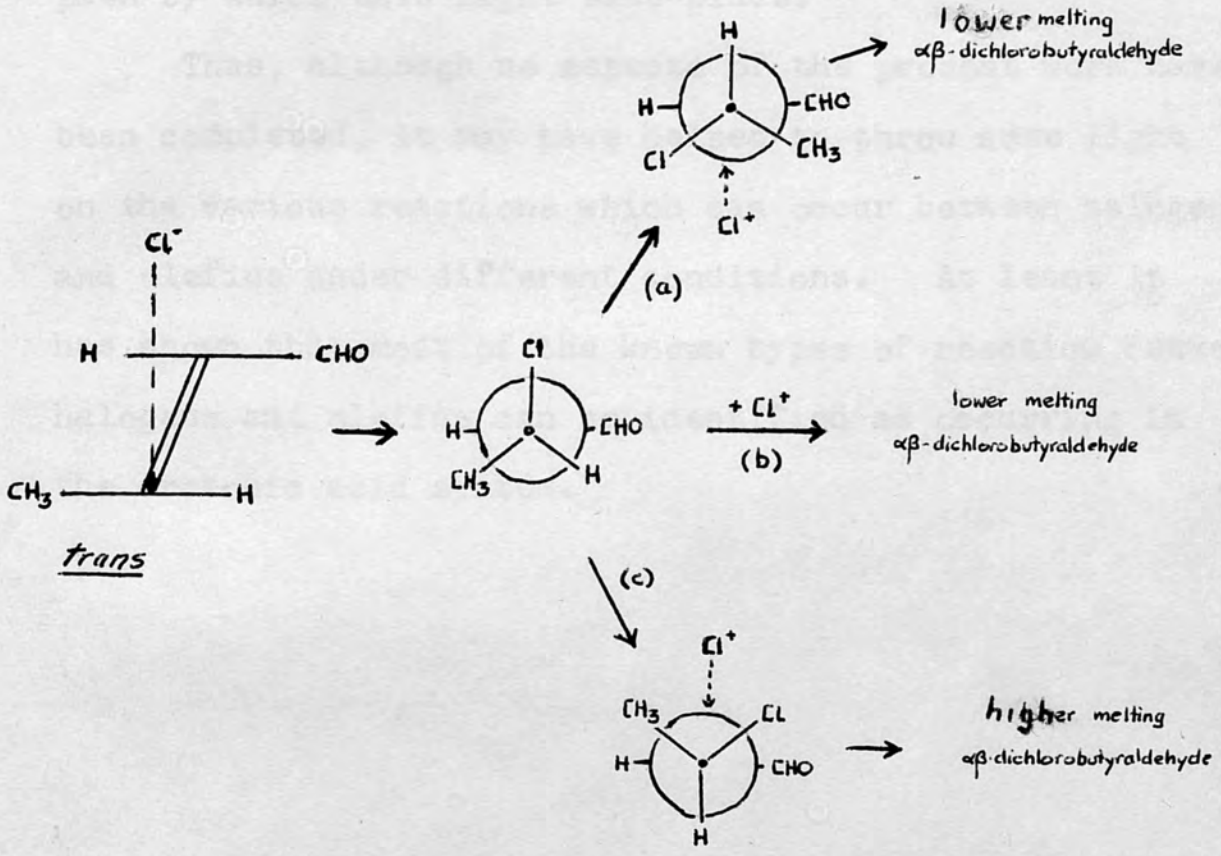
1. Modena, Ricerca sci., 1958, 28, 341.
2. Modena et al., Gazzetta, 1959, 89, 854, 856, 878.


SEt
H
CO2Et
Cl
CH3
cis
X
EtO2C
H
EtS
CH3
Cl
trans
Cl⁻
CH3
SEt
cis


SEt
H
CO2Et
CH3
Cl
trans
X'
Cl
CO2Et
EtS
CH3
cis
Cl⁻
trans

In this scheme, the steric course of the reaction would be determined by the rotational energy barriers in the intermediates X and X'. If the intermediate in the addition of chlorine to crotonaldehyde was also a carbanion, the same would presumably apply, and the course of the reaction would thus be as follows:



This would explain the production of both isomers of α/β-dichlorobutyraldehyde, the relative amounts depending on the rotational energy barriers of the intermediate.

Although much work is still needed in order to establish the mechanism for the nucleophilic addition of halogens to olefins, the above suggests a possible path by which this might take place.

Thus, although no aspects of the present work have been completed, it may have helped to throw some light on the various reactions which can occur between halogens and olefins under different conditions. At least it has shown that most of the known types of reaction between halogens and olefins can be identified as occurring in the crotonic acid system.

IV. TABLE OF INFRA-RED SPECTRA

Wavelengths given in μ.

[facing p. 103]

IV. TABLE OF INFRA-RED SPECTRA

Wavelengths given in μ.

Crotonic acid	3.25m	5.90s	6.05m	7.65s	8.20m
				7.80m	8.60w
α-Chlorocrotonic acid	3.20m	5.98s	6.15m	7.60w	8.60w
				7.75s	8.95w
α-Chloroiso-crotonic acid	3.15m	5.90s	6.15m	7.50w	8.60w
				7.95s	8.95w
Lower melting αβ-dichlorobutyric acid	3.25m	5.80s		7.10m	8.05w
				7.72s	8.35s
				7.95w	8.85w
Higher melting αβ-dichlorobutyric acid	3.25m	5.80s		7.10m	8.20w
				7.85s	8.35s
				7.95w	
α-Chloro-β-hydroxy-butyric acid [oily form]	2.95s	5.80s		7.10m	8.15w
	3.15m			7.25m	8.40s
	3.35s			7.80s	8.95s
α-Chloro-β-hydroxy-butyric acid [m.p. 58-9°]	2.95s	5.85s		7.10m	8.10m
				7.80s	8.40s
α-Chloro-β-hydroxy-butyric acid [m.p. 85-86.5°]	2.97s	5.92s		7.10m	8.25w
				7.80s	8.85m
				7.90m	
Materials obtained from the chlorination of crotonic acid					
Oil 'A'		5.80s	6.90w	7.00w	8.40m
				7.25m	8.60w
				7.80m	
Solid 'B', m.p. 105-6°	3.20m	5.98s		7.92s	8.60w

The bands at the 3.3-3.6 μ and 6.7-7.4 μ regions were

9.10w	10.35s	11.20w		13.90m	14.50m
	10.75m	11.90w			
9.75w	10.50s	11.10s		13.45s	16.40m
		11.85m			
9.70w	10.10m	11.80m		13.00s	
	10.35s			13.90m	
	10.90s				
9.20w	10.60m	11.15m	12.38s	13.25w	14.50s
9.45w	10.90s				
9.80m					
9.02w	10.10m	11.20m	12.35s	13.95s	15.60m
9.20m	10.60m	11.70w	13.00w		16.70m
9.85w	10.93s				
9.20s	10.50s	11.40s	12.20m	13.35w	14.30m
9.55w		11.60m	12.60m		15.10w
9.00s	10.60s	11.65s	12.55s		14.15s
9.20s					15.50m
9.55w					
9.15m	10.40s	11.10w	12.18s	13.90m	14.30m
9.35s	10.60m	11.43s			14.85m

in nitromethane solution [see Experimental Section]

9.25m	10.30s	11.00w	12.40w		15.20m
9.45w		11.55w			
9.90s					
9.15w	10.70m		12.25m	13.80w	15.00w
9.65m					16.65m
9.85s					

obscured by Nujol in the case of all solid compounds.

[facing p. 105]

IV. TABLE OF INFRA-RED SPECTRA (contd.)

Wavelengths are given in μ.

Materials obtained from the chlorination of crotonic acid

Oil 'X', obtained in using an excess of chlorine.		5.85s	6.15w	7.05m 7.25m 7.95s	8.55s
Oil 'Y', obtained in using a deficiency of chlorine [α-chlorovinyl-acetic acid?]	3.15m 3.35s	5.80s	6.05m 6.95m	7.25m 7.75s	8.50s 8.75w

The bands at the 3.3-3.6 μ and 6.7-7.4 μ regions were

in chloroform (see Experimental Section)

9.22w	10.30m	11.20m	12.50m	13.80w	15.40s
9.47m		11.60w			
9.82m					
9.05m	10.35m	11.15w	12.55w	13.40w	14.50s
9.40m	10.90w	11.58w			
9.95m		11.95m			

obscured by Nujol in the case of all solid compounds