469. *Substitution at an Olefinic Carbon. The Reactions of the Ethyl β-Chlorocrotonates with Nucleophiles.*

By D. Emyr Jones, R. O. Morris, C. A. Vernon, and R. F. M. White.

Ethyl β-chloro-*cis*- and -*trans*-crotonate * have been found to undergo relatively rapid nucleophilic displacement of halogen with a number of nucleophiles in ethanol solution. The reactions are of the second order and, with sulphur-containing nucleophiles such as the ethylthio ion, $^-$SEt, give, in the main, products with unchanged geometric configuration. The configurations of the products have been established by the use of nuclear magnetic resonance spectroscopy. Experiments with deuterated ethanol as solvent showed that the reactions are not of the " elimination-addition " type. The mechanisms of these reactions, and of nucleophilic displacements at an olefinic carbon atom generally, are discussed.

Nucleophilic replacement of halogen in simple vinyl halides is known to be difficult. The reasons for this and for the obviously analogous case of simple aryl halides have been discussed by various authors.[1,2,3] Nevertheless, there are numerous reports of apparent nucleophilic replacement of a vinylic halogen atom, and a summary of these has been given by Miller and Yonan.[4]

A priori, it is reasonable to suppose that nucleophilic replacement of an atom attached to an ethylenic carbon atom will be favoured by the structural factors which favour nucleophilic aromatic substitution, *i.e.*, the process $\mathrm{XHC{=}CHCl} + \mathrm{Y}^- \longrightarrow \mathrm{XHC{=}CHY} + \mathrm{Cl}^-$, will be assisted if X is strongly electron-withdrawing. However, several other reaction paths, the most important of which involves elimination followed by addition, can lead to the same products, *i.e.*:

The best conditions for observing the substitution are, therefore, those in which (*a*) X is strongly electron-withdrawing and (*b*) Y^- is weakly nucleophilic towards hydrogen.

In seeking a system we noted that Autenreith,[5] between 1887 and 1890, showed that the halogen atom of the isomeric β-chlorocrotonic acids is easily displaced by a variety of nucleophiles. With reagents of the type RO^- the same product was obtained from both chloro-acids. With reagents of the type RS^-, on the other hand, the two chloro-acids gave different products. The properties of each pair of products, however, showed them to be geometric isomers. Autenreith concluded, largely from consideration of melting points and other simple physical properties, that these reactions proceed with retention of geometric configuration. Scheibler and Voss,[6] working with the ethyl esters rather than the free acids, later arrived at essentially similar conclusions.

The systems investigated by these early workers obviously provide favourable conditions for observing nucleophilic substitution at an ethylenic carbon atom (*i.e.*, X = $\mathrm{CO_2H}$, $\mathrm{CO_2Et}$, strongly electron-withdrawing; Y = EtS^-, weakly nucleophilic towards hydrogen), and their results constitute a strong *a priori* case for supposing that the reactions studied were actually of this type. We decided, therefore, to investigate these and other

---

* Throughout this paper the terms *cis* and *trans* refer to the crotonic acid structure. For example, ethyl *β*-ethylthio-*cis*-crotonate denotes a compound with the methyl and ethoxycarbonyl groups in the *cis*-relation, as in ethyl crotonate.

[1] Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185.
[2] Gold, *J.*, 1951, 1430.
[3] Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273.
[4] Miller and Yonan, *J. Amer. Chem. Soc.*, 1957, **79**, 5931.
[5] Autenreith, *Ber.*, 1887, **20**, 1531; 1896, **29**, 1639. *Annalen*, 1889, **254**, 222; 1890, **259**, 332.
[6] Scheibler and Voss, *Ber.*, 1920, **53**, 382.

similar reactions, by modern methods. The ethyl esters presenting fewer complications than the free acids, we studied the ester reactions, especially those with the sulphur-containing nucleophiles, in some detail by kinetic, isotopic, and stereochemical techniques. The results leave no doubt that the early workers were substantially correct: nucleophilic substitution occurs easily in these systems and, under certain conditions, proceeds largely with retention of geometric configuration. Preliminary accounts of our work have already been published.[7,8]

Recently, two other groups of workers have investigated reactions involving nucleophilic substitution at an ethylenic carbon. Miller and Yonan [4] studied the reactions between iodide ions and *cis*- and *trans*-ω-bromo-4-nitrostyrene and gave an important theoretical discussion of the reactions. Montanari [9] and Modena [10-13] and their colleagues have studied the reactions of 1-chloro-2-phenylsulphonylethylene and similar compounds with a variety of nucleophiles. The results of these workers and of the present investigation appear to be entirely consistent and are summarised below.

EXPERIMENTAL

(A) *Materials*.—β-*Chlorocrotonic acids*. These acids were made by a modification of Geuther's method.[14] A suspension of phosphorus pentachloride (1 kg.) in benzene (350 g.) was kept at 0° with stirring. Ethyl acetoacetate (330 g.) was added in small portions during 3 hr. The mixture was set aside at 0° for 24 hr. Ice-cold water was added slowly (6 hr.), with efficient stirring and at a low temperature. The mixture was then left overnight. The aqueous layer was repeatedly extracted with ether. The benzene layer was extracted with sodium hydrogen carbonate solution and these extracts, after acidification, were extracted with ether. Ether was removed from the combined ether extracts, leaving a mixture of crude β-chlorocrotonic acids (30%).

To obtain the pure acids, the crude mixture was steam-distilled. The *cis*-acid was obtained from the distillate and, after sublimation, had m. p. 60·3—60·6°. The *trans*-acid, which is not steam-volatile, was recrystallised from light petroleum (b. p. 60—80°) and had m. p. 93·8—94·0°.

Ethyl β-*chlorocrotonates*. The crude mixture of acids was esterified as described by Scheibler and Voss.[6] The mixed esters (90%) were fractionated under reduced pressure through a long, helix-packed column. Ethyl β-chloro-*cis*-crotonate had b. p. 48·4—48·5°/10 mm., n_D^{25} 1·4512 (Found: C, 48·6; H, 6·1; Cl, 24·2. Calc. for $C_6H_9O_2Cl$: C, 48·5; H, 6·1; Cl, 23·9%). Ethyl β-chloro-*trans*-crotonate had b. p. 69·5—69·7°/10 mm., n_D^{25} 1·4562 (Found: C, 48·5; H, 6·1; Cl, 24·5%).

Ethyl β-*chloro*-α-*methylcrotonate*. β-Chloro-α-methylcrotonic acid was made from ethyl methylacetoacetate and phosphorus pentachloride as described above. The crude acid (52%) appeared to consist of only one isomer. Esterification with ethanol gave the ethyl ether, b. p. 61·1°/10 mm., n_D^{25} 1·4551 (Found: C, 50·95; H, 6·7; Cl, 23·1. Calc. for $C_7H_{11}O_2Cl$: C, 51·85 H, 6·8; Cl, 21·9%). The acid and the ester are of unknown geometric configuration. Attempts to prepare the other isomer (cf. Otto and Berkurts [15]) failed.

1-*Bromo*-2-p-*chlorophenyl*-1,2-*diphenylethylene*. The *cis*- and the *trans*-form of this compound were prepared by Koelsch's method.[16] The lower-melting compound had m. p. 104° (Found: C, 65·4; H, 4·05. Calc. for $C_{20}H_{16}ClBr$: C, 64·9; H, 3·8%). The higher-melting form had m. p. 158° (Found: C, 64·7; H, 4·2%).

1-*Chloropropene*. The two isomers of this were prepared by treating 1,1-dichloropropane (112 g.) with sodium ethoxide (from 23 g. of sodium) in absolute ethanol (500 c.c.). The

---

[7] Jones and Vernon, *Nature*, 1955, **176**, 791.
[8] Morris, Vernon, and White, *Proc. Chem. Soc.*, 1958, 303.
[9] Montanari, *Bull. Sci. Fac. Chim. ind.* (*Bologna*), 1958, **31**, 16 and references given there.
[10] Modena, *Ricerca sci.*, 1958, **28**, 341.
[11] Maioli and Modena, *Gazzetta*, 1959, **89**, 854.
[12] Modena and Todesco, *Gazzetta*, 1959, **89**, 856.
[13] Modena, Todesco, and Tanti, *Gazzetta*, 1959, **89**, 878.
[14] Geuther, *Z. Chem.*, 1871, **14**, 237.
[15] Otto and Berkurts, *Ber.*, 1885, **18**, 847.
[16] Koelsch, *J. Amer. Chem. Soc.*, 1932, **54**, 2045, 2487.

solution was refluxed for 2 hr. and then distilled. The distillate boiling up to 78° was collected and washed several times with distilled water. After drying, the product was fractionated. *cis*-1-Chloropropene had b. p. 32·1—32·8°/760 mm., n_D^{25} 1·4028; *trans*-1-chloropropene had b. p. 37·2—38·0°/760 mm., n_D^{25} 1·4022. These constants are in agreement with those of Hatch and Perry [17] who determined the configuration of these compounds.

Ethanethiol and thiophenol. These were commercial samples, dried and fractionated; they had b. p. 35° and 168·5—169·0° respectively. Both were stored under nitrogen.

Dry $Li^{36}Cl$. An aqueous 6N-solution containing $H^{36}Cl$ was neutralised with lithium hydroxide and washed with acetone into a solution of inactive lithium chloride (2·7 g.) in acetone. The solvent was removed *in vacuo* and the solid was extracted with dry acetone (Soxhlet). The solvent was again removed and the solid was then heated without fusion in a Rowe crucible in a stream of dry hydrogen chloride.

Solvents. Acetone was dried over anhydrous potassium carbonate and distilled. Ethanol was dried by refluxing with sodium ethoxide and ethyl phthalate and then distilled.[18]

Sodium (30 g.) was dissolved in dry ethanol (300 ml.). Deuterium oxide (25 g.; 97·7% D_2O) and ethyl phthalate (277 g.) were added and the mixture was refluxed. The ethanol was distilled off and then refractionated from more sodium and ethyl phthalate. The deutero-ethanol (600 c.c.) had b. p. 78·3—78·4°/769 mm. and contained *ca.* 30% of $C_2H_5{\cdot}OD$.

(B) *Kinetic Measurements.*—The reactions of the ethyl β-chlorocrotonates and of β-chloro-α-methylcrotonate with ethoxide ions (sodium ethoxide) in ethanol were followed by titration of the residual base at appropriate time intervals. Good second-order rate coefficients were obtained in each run. The values of k_2 (l. mole^{-1} sec.$^{-1}$) are summarised in Table 1.

TABLE 1.

Temp.	[RCl]	[EtO⁻]	10^3k_2	Temp.	[RCl]	[EtO⁻]	10^3K_2
	Et β-chloro-*cis*-crotonate				Et β-chloro-*trans*-crotonate		
−11·5°	0·05	0·086	1·04	0°	0·04	0·0816	0·915
0	0·05	0·0716	4·28	20	0·04	0·0800	10·2
0	0·05	0·0872	4·11 *	30·9	0·04	0·0764	34·8
0	0·05	0·2565	3·33				
20·0	0·05	0·0783	35·2		Et β-chloro-α-methylcrotonate		
				34·9	0·1307	0·1942	0·71
				44·6	0·0983	0·1857	1·90
				63·4	0·1008	0·1782	12·0

* The reactions are not, in the mathematical sense, strictly of second order since k_2 decreases slightly as [EtO⁻] increases. This effect, which may be partly due to incomplete dissociation of sodium ethoxide and partly to a salt effect, is common in reactions involving a neutral and a negatively charged species. It does not imply, however, that a concomitant first-order process is present. In all cases no reaction was observed in the absence of sodium ethoxide, even at elevated temperatures.

In a few runs both the rate of disappearance of base and the rate of appearance of chloride ions were determined. The rate coefficients, calculated from the two sets of data were the same within experimental error. The following is typical: for ethyl β-chloro-*cis*-crotonate, [LiOEt] = 0·10, temp. = 20·0°, k_2 (disappearance of EtO⁻) = $2{\cdot}60 \times 10^{-2}$, k_2 (appearance of Cl⁻) = $2{\cdot}65 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$.

For the reactions with thioethoxide and thiophenoxide ions, the procedure was as follows. A weighed amount of the pure thiol was added to ethanol containing an equivalent amount of sodium ethoxide, and the reacting solution was allowed to come to thermostat-temperature. Organic chloride was added and aliquot parts were withdrawn at appropriate times in the usual way. Titration was carried out either in ethanol to lacmoid, or in aqueous solution with Methyl Red–Bromocresol Green, as indicator. Good second-order rate coefficients were obtained in each run. The following result with ethyl β-chloro-α-methylcrotonate (0·100M) and sodium thioethoxide (0·1647M) in ethanol at 60·0° is typical:

Time (sec.)	0	180	360	540	720	1020	1320	1620
x (mole/l.)	0·00	0·0102	0·0188	0·0251	0·0312	0·0402	0·0475	0·0537
10^3k_2 (l. mole^{-1} sec.$^{-1}$)	—	3·58	3·63	3·47	3·47	3·53	3·53	3·55
Time (sec.)	1920	2220	2820	3420	4020	4620	∞	
x (mole/l.)	0·0586	0·0626	0·0698	0·0749	0·0792	0·0822	0·1000	
10^3k_2 (l. mole^{-1} sec.$^{-1}$)	3·53	3·50	3·52	3·49	3·50	3·45	—	

---

[17] Hatch and Perry, *J. Amer. Chem. Soc.*, 1949, **71**, 3262.

[18] Manske, *J. Amer. Chem. Soc.*, 1931, **53**, 1106.

It was found that the presence of excess of thiol had no appreciable effect on the rates, *i.e.*, the rates are insensitive to changes in the ratio RS^- : EtO^-. The results are summarised in Table 2 where k_2 is in l. mole^{-1} sec.$^{-1}$.

Some kinetic runs on the *cis-* and *trans*-1-chloropropenes were also carried out. The procedures were as before except that, because of the high reaction temperatures, the sealed-tube technique was necessary. The results (k_2 in l. mole^{-1} sec.$^{-1}$; temp. 129°) are given in Table 3. 1-Bromo-2-*p*-chlorophenyl-1,2-diphenylethylenes were found to be unreactive both towards ethoxide and thioethoxide ions in ethanol at 160°. It was estimated that the rate coefficients did not exceed 10^{-7} l. mole^{-1} sec.$^{-1}$ in any of the four reactions tried.

Reaction between the ethyl β-chlorocrotonate and dry $Li^{36}Cl$ was studied with ethanol as solvent. With both isomers the rates of exchange were immeasurably small at 100°. At higher temperatures slow exchange was, however, observed. For the *cis*-compound the rate coefficient was found to be *ca.* 6 × 10^{-5} l. mole^{-1} sec.$^{-1}$ at 150°. This value must, however, be regarded as an upper limit to the value of the true exchange rate, since, at 150°, ethyl β-chlorocrotonates undergo slow solvolysis in ethanol.

TABLE 2.

Compound	Temp.	Thiol	[RCl]	$[RS^-]$	10^3k_2
Et β-chloro-*cis*-crotonate	−11·5°	EtSH	0·05	0·0760	0·797
	−9·5	,,	,,	0·0805	0·994
	0	,,	,,	0·0830	2·43
	20·0	,,	,,	0·0785	15·1
	0	PhSH	0·055	0·0960	0·055
	20·0	,,	,,	0·0988	0·385
	25·1	,,	,,	0·0955	0·600
Et β-chloro-*trans*-crotonate	−11·5	EtSH	0·05	0·0757	1·71
	0	,,	,,	0·0809	5·60
	20·0	,,	,,	0·0768	32·4
	0	PhSH	0·055	0·0975	0·223
	20·0	,,	,,	0·0957	1·78
	25·1	,,	,,	0·0956	2·75
Et β-chloro-α-methylcrotonate ...	34·9	EtSH	0·1051	0·1776	0·447
	49·9	,,	0·0959	0·1684	1·66
	60·0	,,	0·100	0·1647	3·45

TABLE 3.

Compound	Nucleophile (N)	[RCl]	[N]	10^6k_2
cis-1-Chloropropene	EtO^-	0·2830	0·0796	335
	EtS^-	0·2870	0·0873	46
trans-1-Chloropropene	EtO^-	0·2920	0·0946	2·6
	EtS^-	0·2890	0·0758	1·92

(C) *Products.*—The following procedure, with appropriate minor modifications for particular materials, was used in all cases. Solutions of the organic chloride and of the nucleophile were allowed to reach thermal equilibrium in a thermostat-bath at the desired temperature. The solutions were mixed and reaction was allowed to continue for a predetermined time. In the experiments at elevated temperatures the reaction flask was sealed. The concentrations of the reactants were usually *ca.* 0·5M, *i.e.*, not far removed from those used in the kinetic experiments. The volume of solution and the reaction time were so chosen that at least 25 g. of product were formed. At the end of the reaction time, the mixture was poured into a large volume (*e.g.*, 5 l. for 350 c.c. of solution) of ice-cold water which was then repeatedly extracted with ether. The combined ether extracts were reduced in volume and dried ($MgSO_4$). Ether was then removed by distillation. The resulting product, if solid, was recrystallised. Liquid products were distilled, under reduced pressure, through an efficient fractionating column with small hold-up.

(a) *Ethyl β-chloro-*cis*-crotonate and ethoxide ions.* From a reaction in ethanol (150 c.c.) with [RCl] = 0·71M, and [NaOEt] = 0·85M, at 0° for 24 hr., there was obtained as sole product ethyl β-ethoxycrotonate (88%), m. p. 30·2°, b. p. 81°/13 mm (Found: C, 60·44; H, 8·8. Calc. for $C_8H_{14}O_3$: C, 60·75; H, 8·9%). With 2,4-dinitrophenylhydrazine in warm aqueous hydrochloric acid this gave ethyl acetoacetate 2,4-dinitrophenylhydrazone, m. p. 90°, whilst alkaline hydrolysis gave β-ethoxycrotonic acid, m. p. 135°.

(b) *Ethyl β-chloro-*trans*-crotonate and ethoxide ions.* From a reaction in ethanol (150 c.c.), with [RCl] = 0·75M, and [NaOEt] = 0·85M, at 0° for 24 hr., there was obtained ethyl β-ethoxycrotonate (87%), m. p. and mixed m. p. 30·2° (Found: C, 60·5; H, 8·9. Calc. for $C_8H_{14}O_3$: C, 60·75; H, 8·9%). Experiments with different times and concentrations gave no other products.

(c) *Ethyl* β-*chlorocrotonates and phenoxide and* p-*nitrophenoxide ions.* Both isomers, on reacting with sodium phenoxide in ethanol (78°; 7 hr.) gave the same liquid product, b. p. 144°/14 mm., n_D^{25} 1·5159. Mild hydrolysis of the compound with acid gave ethyl acetoacetate, identified as 2,4-dinitrophenylhydrazone. Similar reactions with sodium *p*-nitrophenoxide gave a solid product, m. p. 86°. The two products are presumed to be ethyl β-phenoxycrotonate and ethyl β-*p*-nitrophenoxycrotonate respectively.

(d) *Ethyl* β-*chloro*-α-*methylcrotonate and ethoxide ion.* The sole product isolated from a mixture (250 ml.), containing RCl (0·49M), NaOEt (0·50M) after 2 hr. at 78°, was a liquid (82%), b. p. 82°/10 mm., m. p. −5°, n_D^{25} 1·4161, whose infrared spectrum was consistent with its formulation as ethyl β-ethoxy-α-methylcrotonate.

(e) *Ethyl* β-*chloro*-cis-*crotonate and thioethoxide ions.* (i) A reaction in ethanol (350 c.c.) with [RCl] = 0·77M, [NaSEt] = 0·58M, at 0° for 24 hr., gave 41 g. of liquid product. On distillation at 6 mm., six fractions were obtained. Fraction 3 (2·8 g.), from its physical properties, b. p. 36—95°, n_D^{25} 1·5030, was identified as unchanged ethyl β-chloro-*cis*-crotonate. Fractions 4 (24·0 g.; b. p. 94—96°, n_D^{25} 1·5078) and 6 (4·8 g., b. p. 117°, n_D^{25} 1·5185) were the isomeric ethyl β-ethylthiocrotonates which for convenience will be referred to as (L) and (H), *i.e.*, lower- and higher-boiling respectively.

A number of experiments gave similar results. By assuming that each intermediate fraction contains only two components, its composition can be calculated from its refractive index. The total yield of (L) and (H) and the proportion in which they are formed can then be obtained. Table 4 presents the results of separate experiments expressed in this way. The average yield of these esters in these experiments was *ca.* 90%. Considering the procedure involved, this is an acceptable figure: less than a 10% loss in handling could not have been expected. It was indeed shown that, recovery, by the method described, from an ethanol solution containing known amounts of sulphides, was about 90%.

TABLE 4. *Products of the reaction between ethyl* β-*chloro*-cis-*crotonate and sodium ethyl sulphide in ethanol.*

[RCl] (M)	[NaSEt] (M)	Temp.	Reaction time (hr.)	Yield (%)	(L) (%)	(H) (%)
0·76	0·60	0	24	83	88	12
0·202	0·174	0	0·7	94	87	13 *
0·77	0·58	0	24	91	82	18
0·77	0·60	0	24	88	82	18
0·77	0·59	78	0·75	90	88	12

* 52% reaction.

It may be concluded, therefore, that the reaction between ethyl β-chloro-*cis*-crotonate and thioethoxide ions in ethanol gives the two isomers (L) and (H) in the ratio 85 : 15 (±3). This ratio is, as can be seen from the results in Table 4, not sensitive to considerable changes in temperature, reagent concentration, and reaction time.

(ii) Properties of esters (L) and (H). The esters were pure [Found for (L): C, 55·3; H, 7·7; S, 18·3; for (H): C, 55·5; H, 7·9; S, 18·4. Calc. for $C_8H_{14}O_2S$: C, 55·1; H, 8·1; S, 18·4%).

Physical data, after several distillations of large quantities, were: Ester (L), b. p. 108—109°/10 mm., 113°/17 mm., n_D^{25} 1·5079, $\lambda_{max.}$ 2800 Å (ε 18,000). Ester (H), b. p. 131—132°/10 mm., 136°/17 mm., n_D^{25} 1·5190, $\lambda_{max.}$ 2900 Å (ε 12,000).

Treatment of esters (L) and (H) with hydrochloric acid gave free thiol. Addition of 2,4-dinitrophenylhydrazine to the resulting solution gave the ethyl acetoacetate hydrazone (m. p. 90°).

Boiling ester (L) with alcoholic potassium hydroxide for 5 hr. gave an acid, m. p. 90·5° (Found: C, 49·7; H, 6·9. Calc. for $C_6H_{10}O_2S$: C, 49·3; H, 6·85%). Similar treatment of ester (H) gave an acid, m. p. 114·0—114·3° (Found: C, 49·5; H, 6·2; S, 21·7. Calc. for $C_6H_{10}O_2S$: C, 49·3; H, 6·85; S, 21·9%). These two acids, the isomeric β-ethylthiocrotonic acids, were prepared by Autenreith [5] who recorded m. p. 92° and 112° respectively.

These properties are consistent with the view that esters (L) and (H) are the geometric isomers of ethyl β-ethylthiocrotonate. The infrared and nuclear magnetic resonance spectra are described below. At room temperatures (L) is the stable form. A sample of ester (H), kept for 7 months, was found to have completely isomerised into form (L). However, ester (H) can be distilled without isomerisation at <20 mm. In some of the early experiments an "air-bleed" was used as a device to prevent bumping during distillation but this caused extensive isomerisation of form (H); the use of glass wool overcomes this difficulty.

(f) *Ethyl* β-*chloro*-trans-*crotonate and thioethoxide ions.* This reaction gave, as with the *cis*-compound, a product containing unchanged starting material and esters (L) and (H) (see Table 5).

TABLE 5. *Reaction at* 0°.

[RCl] (M)	[NaSEt] (M)	Reaction time (hr.)	Yield (%)	(L) (%)	(H) (%)
0·34	0·29	24	93	8	92
0·77	0·67	24	86	9	91

(g) *Ethyl* β-*chlorocrotonate and thioethoxide ions in the presence of excess of ethanethiol.* Experiments in which either chloro-compound was left for prolonged periods with sodium ethyl sulphide and excess of ethanethiol gave, as products, ester (L) and ethyl ββ-diethylthiobutyrate. The following is typical: the reaction in ethanol (350 c.c.) of ethyl β-chloro-*trans*-crotonate (0·73M) and sodium ethyl sulphide (0·83M) in the presence of ethanethiol (0·83M) gave, after 5 days at 0°, a product, which on distillation yielded, besides small intermediate fractions, ester (L) (17 g.), b. p. 80°/3 mm., n_D^{25} 1·5001, and the diethylthio-ester (5 g.), b. p. 104—105°/3 mm., n_D^{25} 1·4930 (Found: C, 51·1; H, 8·4; S, 27·1. Calc. for $C_{10}H_{20}O_2S_2$: C, 50·9; H, 8·5; S, 27·1%).

An authentic sample of the dithiobutyrate was prepared as follows: ethyl acetoacetate (40 g.) was condensed with ethanethiol (43 g.) by dry hydrogen chloride. The mixture rapidly separated (30 min.) into two layers. The upper oily layer was washed, dried, and distilled, giving a slightly yellow liquid, b. p. 127°/8 mm., n_D^{25} 1·4922, apparently identical with the above. Both substances on treatment with base in ethanol gave ester (L).

(h) *Ethyl* β-*chlorocrotonates and thioethoxide ions in deuteroethanol.* The products were isolated as described above. Samples of solvent (*ca.* 2 g.) and of the β-ethylthio-esters were placed in a platinum boat contained in a silica tube (60 × 1 cm.). Air, dried by sulphuric acid and by passage through a trap cooled by liquid oxygen, was slowly passed over the sample and thence through a catalyst consisting of a mixture of copper oxide and dry lead chromate. The catalyst was heated to 700—800° and the sample slowly vaporised by heat. The products of combustion were condensed in a trap cooled by alcohol–carbon dioxide. Small samples (*ca.* 4 mg.) of the water obtained were heated with purified zinc dust at 400° for 4 hr. The hydrogen produced was analysed mass-spectrometrically. The results are tabulated.

Compound	[NaSEt] (M)	Reaction time * (min.)	Yield (%)	(L) (%)	(D) (%)
Ethanol	—	—	—	—	0·88
Et β-chloro-*cis*-crotonate	0·90	10	85	82	<0·1
Et β-chloro-*trans*-crotonate †	0·90	20	90	11	<0·1

* At 0°. † Concn. 1·195M.

If one hydrogen atom in the esters had been isotopically equilibrated with the solvent, the percentage of deuterium in the hydrogen samples would have been 0·88 × 6/14 = 0·37. Some difficulty was experienced in the conversion of the water into hydrogen and rather small amounts of hydrogen were obtained. Under these circumstances the limit of detection of deuterium was considered to be *ca.* 0·1%; no more than this was found from the ester.

The experiment, therefore, excludes mechanisms requiring isotopic equilibrium of one hydrogen atom in the ester molecules with solvent: it does not, as it stands, exclude the possibility that some exchange may have occurred.

(j) *Ethyl* β-*chlorocrotonates and thiophenoxide ions.* The pattern of the results was similar to that obtained with thioethoxide ions. Reaction mixtures obtained from either chloro-ester gave (*a*) unchanged chloro-ester (in cases where [RCl] > [NaSPh]) and (*b*) the isomeric ethyl β-phenylthiocrotonates (L′) and (H′). A typical experiment was as follows: on reaction in ethanol (350 c.c.) of ethyl β-chloro-*trans*-crotonate (0·774M) and sodium phenyl sulphide (0·65M), at 0° for 60 hr., there were obtained 47·5 g. of product. Fractionation gave the

Fraction	B. p./mm.	n_D^{25}	Wt. (g.)	Ester	Fraction	B. p./mm.	n_D^{25}	Wt. (g.)	Ester
1	71°/13	1·4568	4·9	Unchanged	4	133—139°/3	1·5725	12·5	
2	up to 133°/3	1·5128	1·0		5	139—142°/3	1·5750	5·3	
3	133°/3	1·5676	8·0	L′	6	142—143°/3	1·5760	15·0	H′

tabulated fractions. It will be observed that the fractionation is not as sharp as with the ethylthio-compounds, owing, no doubt, to the lower pressures required. The estimates of the proportions of esters L′ and H′ are correspondingly less precise (Table 6).

TABLE 6. *Products of reactions of ethyl β-chlorocrotonates with thiophenoxide ions at* 0°.

Compound	[RCl] (M)	[NaSPh] (M)	Reaction time (min.)	Yield (%)	(L′) (%)	(H′) (%)
Et β-chloro-*cis*-crotonate ...	0·81	0·61	46	89	93	7
,, ,, ...	0·77	0·63	60	81	83	17
Et β-chloro-*trans*-crotonate	0·77	0·65	60	89	36	64

The ester L′ (Found: C, 64·7; H, 6·5; S, 14·1. Calc. for $C_{12}H_{10}O_2S$: C, 94·6; H, 6·3; S, 14·4%) had b. p. 127—129°/1·5 mm., 133°/3 mm., n_D^{25} 1·5670; ester H′ (Found: C, 64·6; H, 6·4%) had b. p. 134—136°/1·5 mm., 143°/3 mm., n_D^{25} 1·5760.

Both esters gave thiophenol on mild acidic hydrolysis. The resulting solution gave the same 2,4-dinitrophenylhydrazone (m. p. 90°) as ethyl acetoacetate under the same conditions.

Hydrolysis of ester L′ with alcoholic potassium hydroxide gave an acid, m. p. 172—174° (cf. Autenreith's value [5] of 176°) (Found: C, 61·5; H, 5·2; S, 16·5. Calc. for $C_{10}H_{10}O_2S$: C, 61·8; H, 5·2; S, 16·5%). Ester H′ similarly gave an acid, m. p. 135—136° (cf. Autenreith's value,[5] 155°) (Found: C, 61·7; H, 5·1; S, 16·3%).

Reaction mixtures containing excess of thiophenol gave, on prolonged standing, ester L′ and a fraction, b. p. 142°/3 mm., n_D^{25} 1·6000. This fraction was, by analogy, considered to be ethyl ββ-diphenylthiobutyrate; it was not further characterised, partly because, owing to some decomposition on distillation, it was difficult to obtain pure.

(k) *Ethyl β-chloro-α-methylcrotonate and thioethoxide ions.* Reaction in ethanol (300 c.c.), with [RCl] = 1·03M, [NaSEt] = 0·83M, at 60° for 20 min., gave only one product, a colourless liquid, b. p. 112—113°/9 mm., n_D^{25} 1·5088, presumably ethyl β-ethylthio-α-methylcrotonate. On this basis the yield was 73% (Found: S, 17·9. Calc. for $C_9H_{10}O_2S$: S, 17·0%. C and H analyses gave erratic results, possibly because the compound readily polymerises).

(l) cis-1-*Chloropropene with ethoxide and thioethoxide ions.* The reaction of *cis*-1-chloropropene with ethoxide ions in ethanol at 129° gave, apparently as sole product, methylacetylene. With thioethoxide ions under the same conditions a liquid (73%), b. p. 113—114°/760 mm., n_D^{25} 1·4723, was obtained, which decolorised bromine in carbon tetrachloride, formed an addition complex with mercuric chloride and was presumably 1-ethylthiopropene.

(C) *Configurations of Esters* (L), (H), (L′), *and* (H′).—A variety of methods were used in an attempt to determine the geometric configurations of these compounds, namely (*a*) conversion into compounds of known configuration, (*b*) dipole-moment measurements, (*c*) infrared spectroscopy, and (*d*) nuclear magnetic resonance spectroscopy. Only the last two gave useful information: the first two will, therefore be described only in outline.

(a) *Reaction of esters* (L) *and* (H) *with Raney nickel.* The object was to carry out the reaction, $EtS{\cdot}CMe{:}CH_2{\cdot}CO_2Et \longrightarrow Me{\cdot}CH{:}CH{\cdot}CO_2Et$. Since the configurations of the ethyl crotonates are known, the configurations of the sulphides would follow, granted the assumption that no change in geometry occurs during the reaction. This might not be a bad assumption: Zederic *et al.*,[19] for example, showed that desulphurisation of certain optically active sulphones and sulphoxides proceeded without loss of optical activity although the corresponding sulphide racemised under the conditions used.

Raney nickel was prepared from Raney alloy by the method of Mozingo *et al.*[20] This preparation was too active: treatment of ester (L) or (H) gave only ethyl butyrate. The nickel was, therefore, deactivated by treatment with ammonia and acetone. Ester (L) then gave unchanged starting material, ethyl butyrate, and ethyl *trans*- and *cis*-crotonate, identified by vapour-phase chromatography. It was found, however, that the Raney nickel caused

---

[19] Zederic, Bonner, and Greenlee, *J. Amer. Chem. Soc.*, 1957, **79**, 1696.
[20] Mozingo, Wolf, Stanton, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013.

ready isomerisation of ethyl *cis*-crotonate into the *trans*-isomer. Many attempts to prepare a nickel which did not produce this isomerisation were unsuccessful.

(b) *Dipole-moment measurements.* Dipole moments were determined in conventional manner by measuring the polarisation in a non-polar solvent (benzene) at a number of different concentrations. The resonance technique was employed with a concentric dielectric cell and a standard condenser. The difference between the values for esters L and H is too small for diagnostic purposes (see Table 7), especially since the group moments for CO_2Et and SEt do not lie along the directions of the bonds linking these groups to the molecule.[21]

TABLE 7.

Compound	Dipole moment (D)	Compound	Dipole moment (D)
Et β-chloro-*cis*-crotonate	1·43	Ester L	2·22
Et β-chloro-*trans*-crotonate ...	2·45	Ester H	2·56

(c) *Infrared spectra.* The spectra of the chloro-esters and -acids, of esters L, H, L′, and H′, and the acids derived from them (L_A, H_A, L'_A, H'_A respectively) were examined in the region 2—16 μ with Grubb–Parsons grating spectrometer (G.S. 2A) fitted with a double-beam attachment. The liquids were examined as such, the solids as mulls in Nujol. Table 8 gives the main frequencies found. The assignments to specific modes of vibration are based on tables given by Bellamy.[22] The relevance of these spectra to the determination of the configurations of esters L and H, etc., is examined in the Discussion section.

TABLE 8. *Infrared maxima (cm.*$^{-1}$*) for* (1) *ethyl* β-*chlorocrotonate,* (2) β-*chlorocrotonic acid,* (3) *ethyl* β-*ethylthiocrotonate,* (4) β-*ethylthiocrotonic acid,* (5) *ethyl* β-*phenylthiocrotonate,* (6) β-*phenylthiocrotonic acid; column* (7) *is the probable assignment.*

(1)		(2)		(3)		(4)		(5)		(6)		(7)
cis	*trans*	*cis*	*trans*	L	H	L_A	H_A	L′	H′	L'_A	H'_A	
1712	1721	1692	1698	1701	1689	1678	1672	1698	1695	1667	1667	C=O str
1631	1637	1634	1634	1592	1577	1597	1570	1595	1587	1590	1587	C=C str
								1580	1580	1577	1572	C=C ar str
								1473	1473			
1437	1420			1439	1477			1437	1437			CH_2 deform
1374	1372			1372	1372							
1361	1359			1361	1362			1362	1364			
1326	1300			1332	1325			1330	1323			
				1299w	1297w							
1266				1264	1264			1264	1267w			
		1236	1229			1233	1227			1238	1230	
1189	1183			1183	1183			1185	1185			C–O ester str
			1112w		1117	1110			1115			
	1101							1101	1101			
1086		1092		1094	1092			1089	1091			
					1054			1066w	1066w			
1037	1046			1043	1044			1042	1044			
1000w	1000w			1000w	1000w			1022w	1022w			
								1000w	1000w			
	952w				965w				965w			
917	944w	916	912	*922*	955w	917	916	*919*	*950*w	915	916	
860	*843*	*858*	*856*	*834*	*818*	*840*	*819*	*849*	*823*	*845*	*825*	=C–H out-of-plane deform
				793w	792w	787						
				747w	763w			751	751	750	754	
			715				718			713	713	
				701	696w			706	706	706		
			680		684w	689	690	690	691			
685	656	668		659w	649		662		644			C–Cl and C–S str
					628w							

---

[21] Le Fèvre, " Dipole Moments," Methuen, London, 1938.

[22] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1954.

(d) *Nuclear magnetic resonance spectra.* Proton resonance spectra were obtained with a Varian (V4300B) high-resolution spectrometer operating at 40 Mc. Samples were contained in tubes of 5 mm. outside diameter. Where necessary a capillary of water was used as an external reference. The effects of field inhomogeneities were reduced by spinning the sample. Spectra were referenced by the side-band technique.[23] Measurements were made directly on the liquid esters. The chloro-acids were dissolved in carbon tetrachloride: the other acids were examined as their sodium salts in solution in deuterium oxide. Chemical shifts were calculated, in parts per million, from the function $f_r = 10^6(H_s - H_r)/H_r$, where H_s and H_r are the resonance fields for the sample and the reference sample respectively. Susceptibility corrections have not been made. The differences in susceptibility for a *cis–trans*-pair would, in any case, be expected to be small.[23] However, in all cases except for the chloro-acids, spectra were obtained for approximately 2 : 1 mixtures of each pair of isomers. These spectra confirmed that the shifts of certain peaks were real and were not due to susceptibility differences.

FIG. 1. *Proton magnetic resonance spectrum of ethyl β-chloro-*cis*-crotonate.*

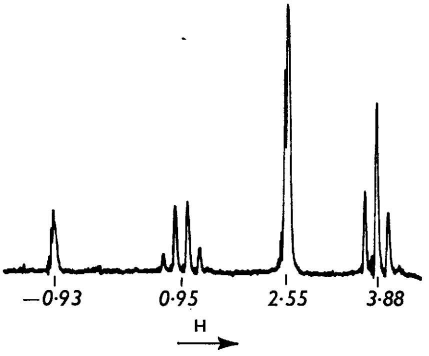


FIG. 2. *Proton magnetic resonance spectrum of a 1 : 2 mixture of ethyl β-chloro-*cis*-crotonate and its *trans*-isomer.*

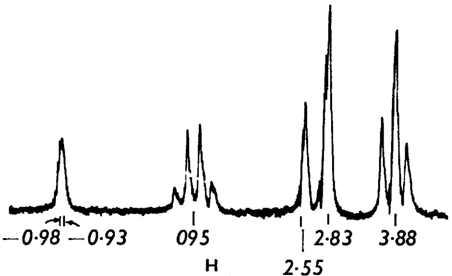


Fig. 1 shows the spectrum of ethyl β-chloro-*cis*-crotonate. The triplet and quartet at 3·88 and 0·95 p.p.m. are characteristic of the ethyl group. From its position [24] and relative area the peak at 2·55 p.p.m. is assigned to the *C*-methyl protons. Similarly the peak at −0·93 p.p.m. arises from the olefin-proton. Weak coupling between these two types of protons splits the *C*-methyl proton peak into a doublet and the olefinic-proton peak into a quartet (incompletely resolved in the spectrum illustrated). The separation between components of these multiplets is *ca.* 1·5 c./sec. The spectra of the other compounds were assigned by similar arguments.

TABLE 9. *Chemical shifts* (δ) (p.p.m.).

Compound	*C*-Me protons		Olefinic protons	
Et β-chloro-*cis*-crotonate	2·55	0·27	−0·93	−0·05
Et β-chloro-*trans*-crotonate	2·83		−0·98	
β-Chloro-*cis*-crotonic acid	2·25	0·25	−1·25	0·00
β-Chloro-*trans*-crotonic acid	2·50		−1·25	
Ester L	2·70	0·10	−0·40	−0·30
,, H	2·80		−0·70	
Acid L_A	2·63	0·07	−0·73	−0·25
,, H_A	2·70		−0·98	
Ester L′	2·70	0·68	−0·18	−0·57
,, H′	3·38		−0·75	
Acid L'_A	2·75	0·55	−0·80	−0·25
,, H'_A	3·30		−1·05	
Maleic acid	—		−2·05	−0·53
Fumaric acid	—		−2·53	

Fig. 2 shows the spectrum of a mixture of ethyl β-chloro-*trans*- and -*cis*-crotonate in the approximate ratio 2 : 1. The shift in the *C*-methyl proton signal, obtained by external reference, is real, and, from the relative areas, in the correct direction. Other spectra of

---

[23] Selwood, " Magnetochemistry," Interscience Publ. Inc., New York, 1943.

[24] Gutowsky, *Ann. New York Acad. Sci.*, 1958, **70**, 786.

mixtures were similar. Table 9 summarises the chemical shifts observed. The significance of the observed shifts and their use in assigning configurations are discussed in the next section.

DISCUSSION

Configuration of the Products.—The results show that the isomeric ethyl β-chlorocrotonates react readily, in ethanol solution, with a variety of nucleophiles. Chloride ion is released and the products are of the general formula $X\cdot CMe=CH\cdot CO_2Et$, where X^- is the nucleophile. For example, with ethoxide ions both chloro-esters give a substance which from its analysis, reactions, and infrared spectrum is shown to be the substitution product, ethyl β-ethoxycrotonate. With thioethoxide or thiophenoxide ions two compounds are formed from each chloro-ester. From their analyses, chemical reactions, ultraviolet, infrared, and nuclear magnetic resonance spectra, these have, in each case, been shown to be the two geometric forms of the substitution product.

It is clearly of importance to determine the configurations of the ethyl β-ethylthiocrotonates (L and H) and of the corresponding phenylthio-compounds (L′ and H′). As described in the Experimental section, experiments with Raney nickel and dipole moment measurements gave little useful information. However, the infrared spectrum (Table 8) of ethyl β-chloro-*cis*-crotonate has a strong band at *ca.* 920 cm.$^{-1}$, which for the *trans*-isomer is replaced by two weak absorptions near 950 cm.$^{-1}$. Strong absorptions near 920 cm.$^{-1}$ also occur for esters (L) and (L′); for the isomers (H) and (H′) these, again, are replaced by two weak absorptions near 950 cm.$^{-1}$. This indicates that esters L and L′ are related to *cis*-crotonic acid and esters H and H′ to *trans*-crotonic acid. The other diagnostically useful feature of the spectra supports this. All six esters and their corresponding acids show a strong band in the region 810—860 cm.$^{-1}$, presumably due to out-of-plane deformation of the system =C–H. For the chloro-ester and the acid with the *trans*-configuration this band occurs at lower frequency. This pattern is repeated with the other compounds. Taken together, therefore, the information indicates that the L series has the *cis*- and the H series the *trans*-configuration.

However, the infrared spectra of these compounds are complicated. In designating the geometric configurations we have used only a small number of the observed frequencies. We did not consider, therefore, that the configurations could be regarded as firmly established solely in this way. The proton nuclear resonance spectra, however, gave much less ambiguous information. Table 9 shows that, for the compounds of known configuration, the chemical shifts for the *C*-methyl protons are smaller in the *cis*- than in the *trans*-configurations. For the other substances studied the shift for each of the compounds designated L was consistently smaller than that for its H isomer. The spectra of mixtures of isomers (cf. Fig. 2) showed that these differences did not arise from differences in bulk susceptibility. Consequently, irrespective of the origin of these effects, we may assign all the L compounds to the *cis*- and all the H compounds to the *trans*-series.

The configurations of the β-methylglutaconic acids have recently been determined by Jackman and Wiley [25] in a similar way. The method is probably widely applicable and the origin of the observed separation in the *C*-methyl proton resonances for each pair of isomeric compounds is of interest. Models show that weak hydrogen-bonding between the hydrogen of the methyl group and the carbonyl-oxygen is possible in the *cis*-compounds. It is known [26] that hydrogen bonding usually shifts proton resonance to lower field strengths and it is, therefore, reasonable to suppose that it accounts for the effects in the present case.

The chemical shifts for the olefinic protons are also of interest. Except for the chloro-compounds, the olefinic proton resonance occurs at lower field strengths in the *trans*-compounds (*i.e.*, those with the olefinic hydrogen and the substituent, X, in *cis*-relation:

---

[25] Jackman and Wiley, *Proc. Chem. Soc.*, 1958, 196.

[26] Korinek and Schneider, *Canad. J. Chem.*, 1957, **35**, 1157.

X = Cl, SEt, SPh). Owing to the diverse nature of the β-substituent X, it is probable that more than one effect is being observed. In the compounds which contain the phenyl group, for example, ring currents from the aromatic nucleus [27] may contribute to the shift. In the chloro-compounds the distance between the interacting groups is larger and the effect is correspondingly smaller. The results for maleic and fumaric acid presumably reflect weak hydrogen-bonding between the olefinic proton and the carboxyl group when these have the *cis*-relation and are to be compared with the effects described above for the *C*-methyl protons in the crotonic acid series.

It will be observed that the configurational assignments based on the proton resonance spectra agree with those based, although more tentatively, on the infrared spectra. Table 10, summarising the relevant physical data, shows that the *cis*-isomer is the more volatile and the lower-melting, except for the β-phenylthiocrotonic acid.

TABLE 10. *Properties of substituted ethyl crotonates.*

Compound	B. p./mm.	n_D^{25}	M. p. of derived acid
Et β-ethylthio-*cis*-crotonate (L)	108—109°/10	1·5079	90·5°
Et β-ethylthio-*trans*-crotonate (H)	131—132°/10	1·5190	114—114·2°
Et β-phenylthio-*cis*-crotonate (L′)	133°/3	1·5670	172—174°
Et β-phenylthio-*trans*-crotonate (H′)	143°/3	1·5760	135—136°

The methods used above are successful provided both isomers of a pair are available. Ethyl β-ethoxycrotonate has, however, been obtained only in one form. Its configuration and that of the corresponding phenoxy-derivative, which is also known only in one form, cannot, therefore, be determined by the methods described. However, they are probably both in the *cis*-form. Compounds X·CMe⁚CH·CO$_2$Et of known configurations (X = Cl, SEt, Ph) are stable in the *cis*-configuration. It is reasonable to suppose that where X = OEt or OPh the isomer isolated is the stable one. Chemical evidence obtained by Arndt [28] for the ethoxy-compound and by Ruhemann and Wragg [29] for the phenoxy-compound also suggests that both have the *cis*-configuration.

Ethyl β-chloro-α-methylcrotonate and its ethoxy- and ethylthio-derivative are also known only in one isomeric form. For these there is no evidence justifying assignment of configuration.

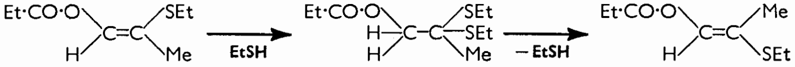
Kinetic and Stereochemical Course of the Reaction.—Each of the isomeric ethyl β-chlorocrotonates with either thioethoxide or thiophenoxide ions gave products which were isolated in both geometric forms. It was necessary, for two reasons, to establish that the amounts isolated reflected the isomeric composition of the reaction mixtures. First, in fractional distillation losses of the highest-boiling fraction (here the *trans*-esters) are usually the greatest, because of residual liquid in the column and pot. In our experiments this source of error was minimised by working with relatively large amounts of products (more than 25 g.) and by using an efficient fractionating column with a small hold-up. Secondly, recovery of the *trans*-esters can also be reduced by thermal isomerisation during distillation. In some of our early experiments this undoubtedly occurred but it was found that by careful drying of the products and by working at sufficiently low pressures the effect could be eliminated. In the experiments quoted in the Experimental section it is considered that no isomerisation occurred during distillation with the ethylthio-compounds. The isolated *trans*-ester could be redistilled without change. With the phenylthio-compounds, however, a little isomerisation may have occurred.

Next we had to show that none of the product arises from a secondary process. Obvious possibilities are isomerisation, during the reactions, of either the substrate or the products. The first of these was easily eliminated. In all the product runs quoted the chloro-ester was in excess, and in each case starting material was recovered in approximately the

[27] Pople, *J. Chem. Phys.*, 1956, **24**, 1111.
[28] Arndt, *Ber.*, 1940, **73**, 779.
[29] Ruhemann and Wragg, *J.*, 1901, 1185.

expected amount; no fractions corresponded to isomerised chloro-ester. Further, isomerisation of either chloro-ester would have produced deviations of a characteristic kind in the kinetics, and none such was observed.

Isomerisation in the products can, however, occur under certain conditions. For, example, it was found that ethyl β-ethylthio-*trans*-crotonate on treatment, in ethanol, with thioethoxide ions and excess of ethanethiol isomerised by the annexed route.



These reactions, and similar reactions with the phenylthio-compounds, would reduce the amounts of the *trans*-product in the reaction mixtures. It was found, however, that prolonged reaction times and a large excess of thiol were necessary before isomerisation produced in this way became important. The reaction of the *cis*-chloro-ester and thioethoxide ions was investigated, with this point in mind, in some detail. The results (Table 4) show that variations in reagent concentration, reaction time, and temperature produced no large change in the relative amount of *trans*-product isolated. Only after allowing the product to stand for prolonged periods with excess of ethanethiol was a significant change observed. It was concluded, therefore, that, with thioethoxide ions as nucleophiles, providing the reactions were carried out with an excess of chloro-ester, no significant isomerisation of the product occurred.

Table 11 gives the mean values obtained in the product experiments (generally at 0°; at 78° results did not differ significantly). It shows that the reactions of the two ethyl β-chlorocrotonates with thioethoxide or thiophenoxide ions proceed largely with retention of geometric configuration, but are not completely stereospecific. Since ethyl β-ethylthio- and β-phenylthio-*trans*-crotonate are thermodynamically unstable they cannot be artefacts: formation of products with inverted configuration from the *cis*-chloro-ester is, therefore, unequivocal. The origin of products with *cis*-configuration in the reactions of the *trans*-chloro-ester is less firmly established. With thioethoxide ion *ca.* 9% of ethyl β-ethylthio-*cis*-crotonate is, apparently, formed; and in our opinion this amount could not have been formed, under the conditions of the reaction, from the main product. This reaction also, therefore, is not entirely stereospecific. With thiophenoxide ion, however, it seems likely that some of the *cis*-product isolated may have been formed by secondary processes, for reasons given above.

TABLE 11. *Results of product experiments.*

[RCl] = 0·2—0·8M, *ca.* 20% excess. Usually *ca.* 40 g. of chloro-ester used. Yields *ca.* 90%.

Chloro-ester	Nucleophile	Product (%) * *cis*	Product (%) * *trans*	No. of runs
cis	EtS^-	85	15	6
trans	,,	9	91	3
cis	PhS^-	88	12	2
trans	,,	36	64	2
cis	EtO^-	(100)	(0)	2
trans	,,	(100)	(0)	2
cis	PhO^-	(100)	(0)	2
trans	,,	(100)	(0)	1

* Parentheses denote cases where only one isomer is known.

The steric course of the reactions with ethoxide and phenoxide ions remains unknown; and, since only one of the isomers can be prepared in each case, it is impossible to decide if any of the products isolated have been formed by secondary isomerisation. This also applies to the reaction of ethyl β-chloro-α-methylcrotonate.

All the reactions showed simple second-order kinetics, *i.e.*, the rate law was uniformly $v = k_2[RCl][X^-]$. In the absence of the nucleophile X^-, no detectable solvolysis occurred unless the temperature exceeded 100°. No disturbance indicating isomerisation of substrate or build-up of intermediates was found. Within the limits of our analytical methods the expected stoicheiometry was obtained with respect both to the appearance of chloride ion and to the disappearance of nucleophile.

Table 12 summarises the kinetic parameters obtained. The rate coefficient for the reaction between ethyl β-chloro-*trans*-crotonate and ethoxide ions in ethanol at 0° (k_2 = 0·000915 l. mole^{-1} sec.$^{-1}$) has been taken at unity. The relative rates refer to 0° and to concentrations [RCl] *ca.* 0·05 and [X^-] *ca.* 0·10M. The results show that the reactions of ethyl β-chloro-α-methylcrotonate with ethoxide or thioethoxide ions are slower than the corresponding reactions with either of the β-chlorocrotonates. The precise rate factors depend on which configuration is chosen for comparison, but, irrespective of this, it is clear that the methyl group slows the reaction by factors which, at 0°, are around 10^2—10^3.

TABLE 12.

Compound	Nucleophile	Relative k_2	E (kcal./mole)	$\log_{10} B$
Et β-chloro-*trans*-crotonate	EtO^-	[1]	19·2	12·4
,, ,, ,, ...	EtS^-	6·12	14·5	9·39
,, ,, ,, ...	PhS	0·24	16·0	9·19
Et β-chloro-*cis*-crotonate	EtO^-	4·49	17·6	11·8
,, ,, ,, ...	EtS^-	2·66	14·1	8·71
,, ,, ,, ...	PhS^-	0·060	15·3	8·13
Et β-chloro-α-methylcrotonate	EtO^-	0·011	20·5	11·4
,, ,, ,, ...	EtS^-	0·013	16·7	8·49

Other comparisons are harder to make. The simplest statement might be that the reactions of both isomeric ethyl β-chlorocrotonates with ethoxide and thioethoxide ions are of approximately the same rate at any temperature over the range studied, while the reactions with thiophenoxide ions are significantly slower. More precise comparisons are of little value. For example, for the *trans*-chloro-ester at 0° the relative rates are EtO^- 1, EtS^- 6·12, and PhS^- 0·24, and at 100° 12·0, 1·0, and 0·12 respectively. The activation energies, however, show a clear trend. The order is $EtO^- > PhS^- > EtS^-$ for both isomers. The differences between the reactions with ethoxide and thioethoxide ions are particularly large; 4·7 and 3·5 kcal./mole for the *trans*- and the *cis*-isomer respectively.

Mechanism.—There are several formally possible mechanisms consistent with the observation that the ethyl β-chlorocrotonates react with a variety of nucleophiles by second-order processes giving substitution products. These are:

(*a*) A mechanism in which addition of the nucleophile is followed by loss of chloride ion. If, for the moment, geometry is neglected, this can be formulated as:

$$\mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH{=}CMeCl} \longrightarrow \mathrm{Et{\cdot}CO{\cdot}O{\cdot}\bar{C}H{\cdot}CMeClX} \longrightarrow \mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH{=}CMeX}$$

If addition of X^- and loss of Cl^- occur together the mechanism becomes a synchronous substitution process.

(*b*) A mechanism in which base-catalysed elimination of hydrogen chloride is followed by addition to the triple bond thus formed:

$$\mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH{=}CMeCl} \xrightarrow[X^-]{} \mathrm{EtCO{\cdot}O{\cdot}C{\equiv}C{\cdot}Me} \xrightarrow[HX]{} \mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH{=}CMeX}$$

(*c*) A mechanism involving prototropic rearrangement as the first step. The sequence might be:

$$\mathrm{Et{\cdot}CO{\cdot}CH{=}CMeCl} \rightleftharpoons \mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CCl{=}CH_2}\ (\mathrm{I}) \longrightarrow \begin{array}{c}\mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}C{\equiv}CH} \\ \mathrm{or\ Et{\cdot}CO{\cdot}O{\cdot}CH{=}C{=}CH_2}\end{array} \longrightarrow \mathrm{Et{\cdot}CO{\cdot}O{\cdot}CH{=}CMeX}$$

Mechanism (*c*) is unlikely for several reasons. First, the equilibrium between ethyl β-chlorocrotonate and the intermediate (I) will be very unfavourable for the formation of the latter; for example, in an analogous system,[30] ethyl 1-chlorovinylacetate is readily

[30] Morris, Ph.D. Thesis, London, 1959.

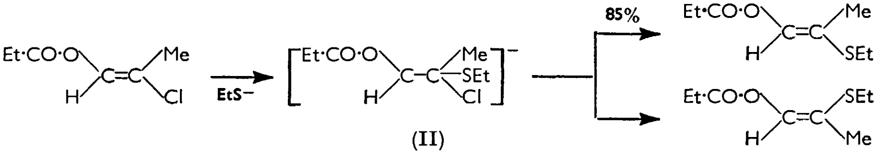
converted into ethyl α-chlorocrotonate by both ethoxide and thioethoxide ions. Secondly, elimination of hydrogen chloride from the intermediate (I) is unlikely to be rapid, particularly with the sulphur-containing nucleophiles. Mechanism (*c*) would not account, therefore, for the ease of the overall reactions or for the relatively small differences between the rates for the reactions with different nucleophiles, although it remains a formal possibility for the reactions involving ethoxide ions.

Mechanism (*b*) can also be rejected, at least for the reactions with thioethoxide and thiophenoxide ions. The arguments are: First, this mechanism requires that the same isomeric product, or, at least, the same mixture of isomers, shall be produced from both chloro-esters. Since this is not the case, the reactions can involve mechanism (*b*) either only for one of the isomeric chloro-esters or only as a minor concomitant to some other mechanism for one or both of the chloro-esters. Neither of these possibilities is attractive. The similarity in the kinetic parameters for the reactions with any particular nucleophile argues against a different reaction path for each isomer. Further, since the isomer ratios in which the products are formed do not appear to change significantly with temperature it seems likely that only one reaction path is important. Secondly, the relative reactivities of the chloro-esters towards ethoxide and thioethoxide ions are inconsistent with mechanism (*b*). If either isomer reacted with thioethoxide ions by this mechanism the more strongly basic ethoxide ion would be expected to produce a large increase in rate. Thirdly, the studies on ethyl β-chloro-α-methylcrotonate show that reactions similar to those of the isomeric ethyl β-chlorocrotonates occur, even when, for structural reasons, mechanism (*b*) is precluded.

In order to confirm the conclusions from these arguments the reaction of both of the ethyl β-chlorocrotonates with thioethoxide ion were carried out in deuteroethanol. Mechanisms (*b*) and (*c*) require that, under these conditions, isotopic exchange would be complete for one of the hydrogen atoms in the product. This was found not to be the case. Consequently mechanisms (*b*) and (*c*) can be excluded for the reactions with thioethoxide ions and, by analogy, for the similar case of thiophenoxide ions. These reactions are, therefore, firmly established as substitution processes [mechanism (*a*)].

It is not possible, at the moment, to be equally certain about the reactions with ethoxide ion. Since only one substitution product can be obtained and since the deuterium test has not yet been applied, it remains possible that one of the isomers, presumably the *trans*-isomer, reacts by mechanism (*b*). It is, of course, true that the results with ethyl β-chloro-α-methylcrotonate show that a reaction path other than (*b*) is available with ethoxide ions. Nevertheless, the mechanism of these reactions cannot yet be regarded as established.

Mechanism (*a*) can proceed either as a synchronous process or with the formation of an intermediate adduct. This distinction recalls the previous controversy over the similar case of nucleophilic aromatic substitution.[3] The view now prevailing, largely due to Bunnett's work, is that, at least in sufficiently activated systems, reaction occurs through an intermediate adduct of some stability.[31] In the reactions of the ethyl β-chlorocrotonates with thioethoxide and thiophenoxide ions there seems no doubt that a similar intermediate adduct is formed. No other formulation of the mechanism can accommodate easily the fact that *both* isomeric forms of the product are produced in each of the reactions. The reaction of the *cis*-chloro-ester with thioethoxide ions, for example, must be represented



---

[31] Bunnett, *Quart. Rev.*, 1958, **12**, 1.

as occurring through the intermediate (II). Irrespective of the precise geometry of the intermediate, it is clearly similar to that formed in the aromatic system, since (*a*) the carbon atom undergoing substitution has become tetrahedral and (*b*) the negative charge can be distributed by resonance.

Although the data obtained in this investigation are rather limited a number of kinetic similarities between the two kinds of substitution emerge. First, replacement at an olefinic carbon requires an activating group. For example, the reaction between ethyl β-chloro-*cis*-crotonate and thioethoxide ions is, at 129°, *ca.* 10^6 times faster than the corresponding reaction (which also gives a replacement product) with *cis*-1-chloropropene. However, from the work of Truce and his colleagues,[32] it seems likely that the latter compound reacts by the elimination-addition mechanism [*i.e.*, (*b*)]. The activating effect of the ethoxycarbonyl group is, therefore, greater than this comparison would indicate. It is significant in this respect that neither isomer of 1-bromo-2-*p*-chlorophenyl-1,2-diphenylethylene reacts appreciably with thioethoxide ions at 160°. These reactions are, therefore at least 10^9 times slower than that of the *cis*-chloro-ester. Thus the ethoxycarbonyl group is powerfully activating in vinyl substitution: its effect is much greater than in aromatic systems.[3] Comparison of ethyl β-chloro-α-methylcrotonates with the ethyl β-chlorocrotonates shows that a methyl group attached to the olefinic carbon one atom removed from the centre of substitution reduces the rate 100—1000-fold. Again there is a qualitative similarity to nucleophilic aromatic substitution, but, as with the ethoxycarbonyl group, the effect is much greater in the vinylic system. For example, a *para*-methyl group in 1-chloro-2,4-dinitrobenzene reduces the rate of substitution by ethoxide ions [33] only by a factor of *ca.* 6. The behaviour of chloride ion as a nucleophile provides another similarity between the vinyl and aromatic systems. The rate coefficient for the reaction of the *cis*-chloro-ester with chloride ion is at least 10^6 times slower than with the thioethoxide ion. Bevan and Hirst,[34] working with *p*-fluoronitrobenzene, found similar large differences.

Other recent investigations of nucleophilic vinyl substitution appear to be consistent with our results. Miller and Yonan [4] studied the reactions of the isomeric ω-bromo-*p*-nitrostyrenes with iodide ion in diethylene glycol monobutyl ether at ~200°. The reactions, compared with ours, are very slow and have high activation energies (23·9 and 27·9 kcal./mole for the *cis*- and the *trans*-isomer respectively). Although the primary products of substitution could not be isolated, it was shown by a method based on selective dehydrohalogenation of *cis*-isomers, that the reaction proceeded largely with retention of configuration. These authors state that "the experimental data almost exclude mechanisms which invert the carbon at the reactive site."

Modena and his co-workers [10-13] following the earlier work of Montanari,[9] studied reactions of the type:

$$\mathrm{Ph{\cdot}SO_2{\cdot}CH{=}CHCl} + \mathrm{X^-} \longrightarrow \mathrm{Ph{\cdot}SO_2{\cdot}CH{=}CHX} + \mathrm{Cl^-}$$

They found retention of configuration with both isomers with the nucleophiles $\mathrm{MeO^-}$, $\mathrm{EtO^-}$, $\mathrm{PhO^-}$, and $\mathrm{N_3^-}$. Electron-releasing groups in the *para*-position of the benzene ring reduced the rate: electron-withdrawing substituents had the opposite effect. The reactions of the corresponding sulphoxide, $\mathrm{Ph{\cdot}SO{\cdot}CH{=}CHCl}$ with $\mathrm{MeO^-}$ and $\mathrm{PhS^-}$ also preceeded with retention of configuration. The rates of all these reactions are of the same order of magnitude as those in the present study: clearly the groups $\mathrm{Ph{\cdot}SO_2}$ and $\mathrm{Ph{\cdot}SO}$, like $\mathrm{Et{\cdot}CO_2}$ are good activating groups.

An interesting study of non-activated vinyl substitution has been made by Carra and Beltrame.[35] They found the second-order rate coefficients for the reaction of $\mathrm{Ph_2C{=}CHCl}$

---

[32] Truce, Boudakian, McManimie, and Heine, *J. Amer. Chem. Soc.*, 1956, **78**, 2743.

[33] Bevan, Hughes, and Ingold, quoted by Bunnett and Zahler, ref. 3.

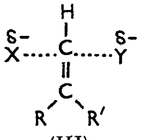
[34] Bevan and Hirst, *J.*, 1956, 254.

[35] Carra and Beltrame, *Gazzetta*, 1959, **89**, 2027.

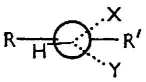
with ethoxide ion in ethanol to be $2{\cdot}44 \times 10^{-6}$ l. mole^{-1} sec.$^{-1}$ at 130°. The corresponding bromide reacted about four times more readily. Replacement of the two phenyl groups by two methyl groups increased the rate. The activation energies of all the reactions were high, greater than 30 kcal./mole. It seems possible that, although substitution occurs with the diphenyl compound, the dimethyl analogue reacts by a mechanism similar to our (*c*).

Several theoretical discussions [2,3,4] have been given of a one-stage displacement on an olefinic carbon which would be the analogue of the S_N2 mechanism for a saturated carbon. In the transition state (III) the carbon atom undergoing substitution has linear *sp*-hybridisation. Of the remaining two *p*-orbitals, one forms the π-bond and the other binds X and Y. As Gold [2] pointed out, such a reaction path would give inversion of geometric configuration. However, we agree with the view expressed by Miller and Yonan [4] that in such a reaction path the reaction centre is highly shielded and for most cases (and certainly in the ethyl β-chlorocrotonates) at least one of the pairs, R,X and R′,Y, would be within bonding distance.

The alternative one-stage displacement mechanism involves a tetrahedral arrangement at the reactive centre (IV), and leads to retention of configuration. Neither of these processes adequately explain our results, although there is a formal possibility that the products of retained configuration arise *via* (IV) and those of inverted configuration arise from a different reaction *via* (III). However, we have already given reasons for supposing that the isomeric products are found, in any given reaction, from a common intermediate.



(III)



(IV)

The observed facts can be accounted for by assuming (*a*) that the approach of the nucleophile is at right angles to the plane of the olefin, (*b*) that the chloride ion, by the principle of microscopic reversibility, departs along the same or a reciprocal path, and (*c*) that in the intermediate the groups attached to the distal olefinic carbon remain in the original plane of the molecule. For the reactions between the chloro-esters and thioethoxide ion, the sequence of events is shown in Fig. 3. The intermediate (X) (and similarly for X′) is presumably a hybrid of (X_1) and (X_2). Since the ethoxycarbonyl group produces so large an effect on the rate, (X_2) must be the important structure, and, on a time average, the group Et•CO_2 and the atom H remain in their original plane. In order for the reactions to proceed, the intermediates X and X′ must, by rotation, pass into the rotamers Y_1 or or Y_2 and Y_1' or Y_2'. In each case, the intermediates pass through conformations in which certain groups are eclipsed. Table 13 gives a list of these.

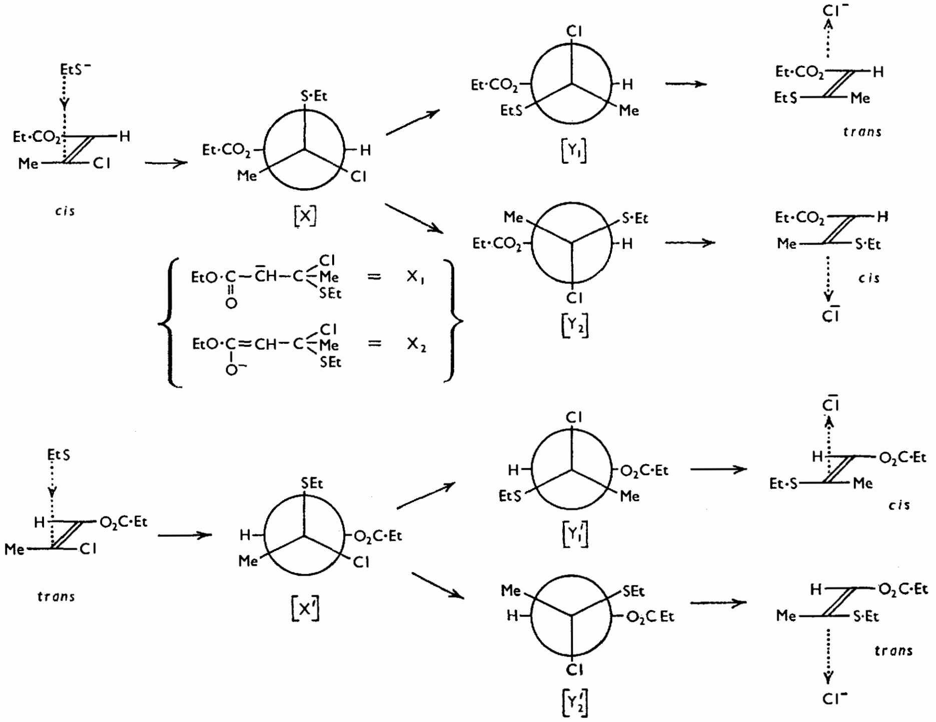
TABLE 13.

Transformation	Steric course	Eclipsed pairs
$X \longrightarrow Y_1$	Inversion	EtS, Et·CO_2; Cl, H
$X \longrightarrow Y_2$	Retention	Me, Et·CO_2–
$X' \longrightarrow Y_1'$	Inversion	EtS, H; Et·CO_2, Cl
$X' \longrightarrow Y_2'$	Retention	Me, H

Models show that some steric compression is to be expected for the pairs EtS, Et•CO_2, and EtCO_2, Cl, and possibly for Et•CO_2, Me. Hence X and X′ will pass more easily into Y_2 and Y_2' than into Y_1 and Y_1'. The differences in the energy barriers must, in fact, be slight. For the *cis*-chloro-ester, which gives 85% of the product with retained configuration, the energy difference must be *ca.* 1 kcal./mole.

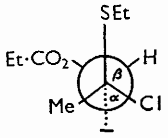
In the above scheme the steric course of the reactions is determined by the rotational

FIG. 3.



energy barriers in the intermediates X and X′. On this basis substitution at an olefinic centre could, by suitable choice of groups, be made to follow any steric course. For example, compounds of type X·CH=CHCl should show a more pronounced tendency to give products with retained configurations than those of type X·CH=CRCl (X is a strongly activating group and R is any group other than H). It is, perhaps, noteworthy in this respect that, whereas ethyl β-chlorocrotonates (R = Me) gives some inverted products, the reactions studied by Miller and Yonan [4] and by Modena and his colleagues,[10–13] in both cases with compounds of type X·CH=CHCl, gave only products retaining their configuration. A compound with a relatively bulky group R would also be of interest. On the theory given above, whereas the isomer with *trans*-relation between R and X should behave normally, *i.e.*, react largely with retention of configuration, *cis*-relation between R and X should favour inversion.

Our analysis is based on the assumption that the groups attached to the distal olefinic carbon atom remain in the plane of the molecule. If this is not the case, then as Miller and Yonan [4] have pointed out, the situation is more complicated. Consider the intermediate Z, formed from the *cis*-chloro-ester and thioethoxide ion. If elimination of chloride occurs *trans* to the electron pair, then retention results from inversion at the distal carbon atom and rotation through the angle α, at the reaction centre. Inverted products result from rotation at the reaction centre through the angle (β). However, there seems no particular reason for assuming *trans*-elimination. It is at least conceivable that, for reasons of overlap loss of chloride ion occurs when the electron pair and the chlorine atom are in *cis*-relation. It seems that in either event the steric course of the reaction will be governed by the factors discussed above.



(Z)

It must be stressed that out detailed analysis applies only to the reactions of the ethyl β-chlorocrotonates with thioethoxide and thiophenoxide ions. The reactions with ethoxide ion and the reactions of ethyl β-chloro-α-methylcrotonate, although probably of the same form, are not yet sufficiently understood for detailed analysis.

One of us (C. A. V.) thanks Professor S. I. Miller (Illinois Institute of Technology) and Dr. G. Modena (University of Bologna) for very helpful and stimulating discussions. The encouragement and advice of Professor Hughes and Sir Christopher Ingold are also acknowledged. We thank the Department of Scientific and Industrial Research for a maintenance grant (to R. O. M.).

William Ramsay and Ralph Forster Laboratories,
Gower St., London, W.C.1.

[*Received, January* 11*th*, 1960.]