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HALOGENATION OF UNSATURATED ESTERS—II

ADDITION OF Cl_2, BrCl AND Br_2 TO METHYL ESTERS OF MONOCHLOROPROPENOIC ACIDS

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Abstract—The addition of chlorine, bromine chloride and bromine to methyl 2-chloropropenoate 1, methyl *cis* - 3 - chloropropenoate 2 and methyl *trans* - 3 - chloropropenoate 3 under ionic and radical conditions gave regioisomer mixtures. Both *trans*- and *cis*-addition of halogen species was observed, bromine preferentially adding to the non-halogenated carbon atom.

INTRODUCTION

In a recent paper[1] we reported a study dealing with halogen (Cl_2, Br_2 and BrCl) additions to methyl *trans* - 2-butenoate, methyl *trans* - 2 - methyl - 2 - butenoate and methyl 3 - methyl - 2 - butenoate. Bromine chloride addition was found to produce 2 - bromo - 3 - chloro regioisomer as the main product. Bromine chloride additions to unsaturated compounds have received some attention in the literature.[2–7] Studies on the addition of bromine chloride to methyl acrylate, methyl isocrotonate and methyl crotonate under ionic and radical conditions have been reported by Heasley *et al.*[3] The main product under ionic conditions was in every case 2 - bromo - 3 - chloro regioisomer. Radical addition of BrCl (under UV-radiation) to methyl acrylate was reported to produce exclusively methyl 3 - bromo - 2 - chloropropanoate, while additions to 2-butenoates gave regioisomer ratios similar to those from ionic additions.

To investigate the effect that a chlorine substituent (bound to the double bond) might have on the regiochemistry of bromine chloride addition to α,β-unsaturated ester double bond, we chose methyl 2-chloropropenoate and *cis*- and *trans*-3-chloropropenoates as substrates. The mutual relative proportions of addition products are compared to those received from methyl substituted butenoates.[1] Studies dealing with additions of unsymmetric halogens to halogen substituted double or triple bonds are few in literature.[2]

EXPERIMENTAL

Materials. Methyl 2-chloropropenoate **1** was prepared from methyl 2,3-dichloropropanoate[8] by heating with sulphuric acid and distillating the elimination product from the reaction mixture.[9] Methyl *cis*- **2** and *trans* - 3 - chloropropenoates **3** were prepared as described earlier.[10]

Halogenations of **1–3** were performed as described earlier.[1] To a sample of 1 mmol of each gas chromatographically pure substrate an equivalent amount of halogen in CCl_4 solution was added. The reactions were carried out in dark and light at $-5 \ldots +5°$. The reactions were followed by GC and found to proceed slowly in dark but much faster in light. The reactivity order of halogens towards the substrates was found to be $Br_2 > BrCl > Cl_2$.

HX eliminations with triethylamine (Fluka) were carried out as described earlier.[1] The elimination products were identified by gas chromatography-mass spectrometry (GC–MS) by comparing with authentic samples prepared by halogenating (Cl_2, Br_2, BrCl) methyl propynoate.[2]

Instruments used for experimental measurements. The gas chromatographic analyses were performed with a Perkin–Elmer Sigma 3 gas chromatograph equipped with a flame-ionization detector and connected to a Hewlett–Packard Model 3390A Reporting Integrator. A vitreous silica (WCOT) OV-101 quartz capillary column (25 m × 0.30 mm i.d.) was used with N_2-carrier gas flow-rate of 1 ml/min. The mass spectra were run with a Varian MAT-212 mass spectrometer with a Varian Model 3700 gas chromatograph (SE-30 quartz capillary column) and a Spectro System MAT-188 data processor. The NMR spectra were obtained by a 60 MHz Perkin–Elmer R 12 B and a JEOL FX-60 NMR spectrometers.

RESULTS AND DISCUSSION

The following compounds were formed in the reactions of **1–3**: methyl 2,2,3 - trichloro - **4**, 2,3,3 - trichloro - **5**, 2 - bromo - 2,3 - dichloro - **6**, 3 - bromo - 2,2 - dichloro - **7**, 2-bromo - 3,3 - dichloro - **8**, erythro 3 - bromo - 2,3-dichloro - **9a**, threo 3 - bromo - 2,3 - dichloro - **9b**, 2-chloro - 2,3 - dibromo - **10**, erythro 3 - chloro - 2,3 - dibromo - **11a** and threo 3 - chloro - 2,3 - dibromopropanoate **11b**.

Chlorination and bromination

The reactivity order of the substrates towards chlorine was found to be 2-chloro > *trans* - 3 - chloro > *cis* - 3 - chloro. Formation of methyl 3,3-dichloropropanoate as a side product from 3-chloropropenoates was confirmed by comparing with an authentic sample[8] by GC–MS.

In the brominations (in dark) the reactivity order was *trans* - 3 - chloro > *cis* - 3 - chloro > 2 - chloro. Bromine added to the double bond evidently by both *cis*- and *trans*-addition, the *trans*-addition product, however, dominating, as expected. The erythro/threo ratios obtained in the brominations both in dark and light are given in Table 1. Isomerization of substrates prior to addition may have occurred to some extent in the brominations, since unknown halogenated compounds with lower GC retention times were detected to have been formed.[7]

Bromine chloride addition

The reactivity order with bromine chloride is 2 - chloro ≧ *trans* - 3 - chloro > *cis* - 3 - chloro. Also sub-

Table 1. Relative product proportions from Br_2 and BrCl additions to compounds (1–3)

Methyl ester of	Br_2 addition		BrCl addition			
	Diastereomer ratio[a]		Regioisomer ratio 2-Br-3-Cl:3-Br-2-Cl		Diastereomer ratio[a] of 3-Br-2-Cl regioisomer	
	In light	In dark	In light	In dark	In light	In dark
2-Chloropropenoic acid **1**	One product	One product	45 : 55	40-47:53-60	One product	One product
cis-3-Chloropropenoic acid **2**	92 : 8	32 : 68	47 : 53	98 : 2	83 : 17	45 : 55
trans-3-Chloropropenoic acid **3**	96 : 4	62 : 38	31 : 69	88 : 12	82 : 18	94 : 6

[a]Erythro: threo.

stantial amounts of bromine addition products were detected in BrCl addition mixture to **1** and **3**, but only trace amount (~ 1%) in the addition to **2** in dark.

The relative product proportions from BrCl additions to **1–3** are included in Table 1. As shown by the diastereomeric ratios, the additions of bromine chloride to **2** and **3** were non-stereospecific. Erythro 3 - bromo - 2,3 - dichloropropanoate **9a** would have been the expected product from a stereospecific *trans*-addition of unsymmetrical BrCl molecule to **2** and the threo form **9b** from the corresponding addition to **3**. *Cis* - 3 - chloro isomer showed, however, appreciable amount (45%) of *trans*-addition. At least one stereospecific *trans*-addition of bromine chloride from mixtures of bromine and chlorine has been reported.[6]

In CCl_4 a glass-surface catalyzed reaction may occur and give *cis*-addition product.[7,11] Isomerization of the starting compounds prior to addition reactions was noticed to occur in the presence of bromine, but surely not to the extent to explain the product distributions.

The electrophilic addition of BrCl to a double bond is believed to pass through a cyclic bromonium ion intermediate. The regiochemistry of products depends on the direction of substitution (S_N) by chloride ion in the bromonium ion. The adjacency of the electron withdrawing carbonyl group would suggest chloride ion attack to carbon atom 2. S_N2 type reactions are known[12] to be accelerated by a neighbouring carbonyl group. Only in the case of 2-chloropropenoate substantial amount of the expected 3-bromo-2-chloro regioisomer (Markownikov product) is produced. In the cyclic intermediate from **1** a competitive chloride ion attack to carbon atom 3 (non-halogenated carbon) could be favoured by the small steric size of hydrogen atoms.

The almost quantitative β attack (attack to the carbon atom 3) by chloride ion within *cis* - 3 - chloropropenoate **2** is possible to explain by an unsymmetrically bridged bromonium ion suggested by Heasley *et al.*[3] for methyl *cis* - 2 - butenoate (isocrotonate).

The formation of 3 - bromo - 2,3 - dichloro regioisomer **9a**, **9b** from **2** seems to occur by both *cis*- and *trans*-addition of the halogen species. The almost quantitative predominance of erythro 3 - bromo - 2,3 - dichloropropanoate **9a** over the threo form refers to the *cis*-addition of the electrophilic (Br^+) and nucleophilic (Cl^-) species to **3**.

If the regiochemistry of the products from BrCl additions to **1–3** are compared to those from the parent esters, methyl acrylate[3] and methyl *trans* - 2 - butenoate,[1,3] the chlorine substituent seems to force the cyclic intermediate to open so that the bromine atom remains attached to the previously non-halogenated double bond carbon.

The reaction of **1** with BrCl differed from those of **2** and **3** in that it gave the regioisomers almost in the same ratio in dark and in light (Table 1), while **2** and **3** gave the 3 - bromo - 2 - chloro regioisomer as the main product in light. Dibromo addition products were formed also from *cis* - 3 - chloropropenoate **2** with BrCl in light. The ratio of BrCl/Br_2 addition products from both 3-chloropropenoates was 42 : 30 in light.

Are the reactions of **1–3** with BrCl occurring by an ionic reaction in dark? To avoid halogen radicals formation, the reactions have been done in dark and in dilute CCl_4 solutions. No concomitant radical reaction with *cis* - 3 - chloro isomer **2** could have occurred as shown by the clear difference in the regiochemistry of products formed in dark and in light. The formation of a greater extent of 3 - bromo - 2,3 - dichloro regioisomers **9a**, **9b** from **3** might be attributed to a concomitant radical reaction. If this was the case and some **9a**, **9b** was formed by a radical reaction, then the difference in the product distributions from *cis*- and *trans* - 3 - chloro isomers would be still less. Further, the reactivity order observed with BrCl was 2 - chloro ≧ *trans* - 3 - chloro > *cis* - 3 - chloro. Though the reaction of 2-chloro substrate was fastest, the similar regioisomer ratios (in dark and light) might refer to a concomitant radical reaction. "The radical conditions" in this study mean only that the reactions were allowed to proceed in normal light without UV-irradiation (or direct sun light). Hence, it is also possible that the light reaction was in fact ionic of nature.

Identification

The substrates were eluted on the OV-101 non-polar column used in the order **1** ≲ **3** < **2** and their halogenation products in the order dichloro < bromochloro < dibromo as previously reported also for the halogenated methyl butanoates.[1]

Methyl 2,2,3- **4** and 2,3,3,-trichloropropanoates **5** are known compounds.[13,14] Both BrCl and Br_2 addition products, **6–11** show scarcely detectable molecular ion peaks in their mass spectra. The α-cleavage, $(M\text{-}COOCH_3)^+$, gives rise peaks of which isotopic dis-

tributions differ between ions containing two bromine and one chlorine atoms and on the other hand two chlorine and one bromine atoms. The regioisomers from BrCl addition to **1** gave clearly different mass spectra. Erythro and threo forms **9a**, **9b** and **11a**, **11b** gave nearly identical mass spectral fragmentation. The mass spectra of the addition compounds will be published later in detail.

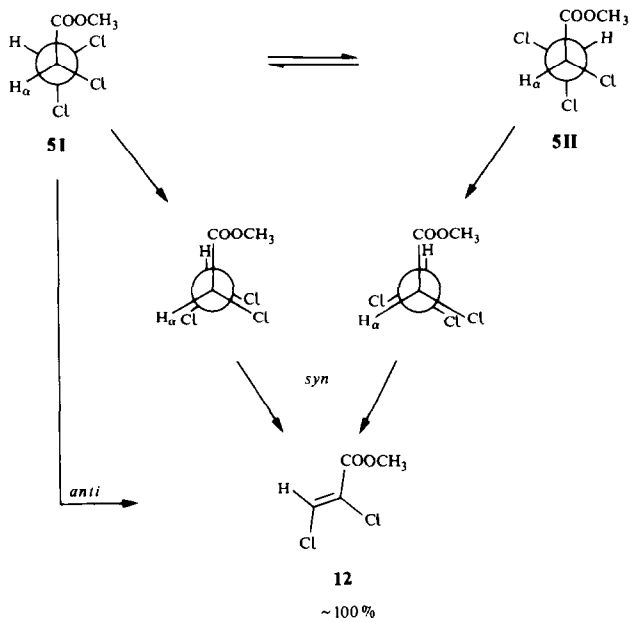
Dehydrohalogenation

Dehydrohalogenation with triethylamine from the halogenation products of *cis*- and *trans* - 3 - chloropropenoates gave 2,3-dihalopropenoates.

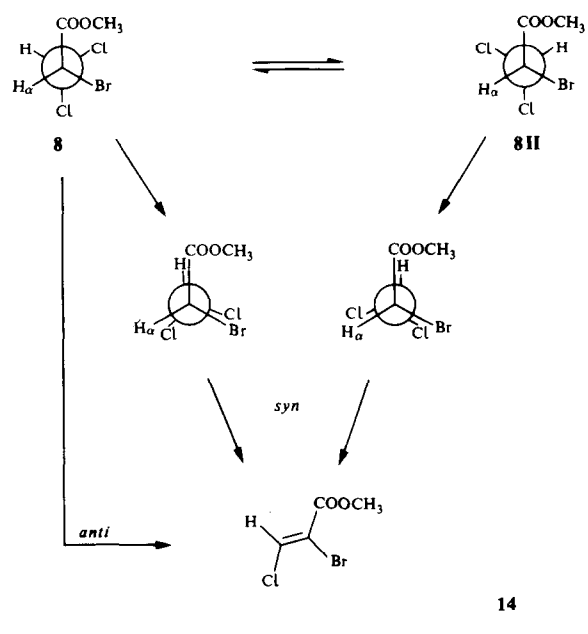
HX elimination with triethylamine from halogenated esters is known to be initiated by attack of the base exclusively on the acidic α-hydrogen.[3] Two halogen substituents on the β-carbon seem to accelerate HX elimination, which was in some cases almost instantaneous. It would seem, at least in the case of 3 - chloro - 2,3 - dibromopropanoates **11a**, **11b**, that HX elimination is faster (easier) from the erythro form.

In the absence of α-hydrogen no HX elimination was observed within the halogenated derivatives of 2-chloropropenoate **1**. The identification of these compounds **4**, **6**, **7** and **10** was based on their mass and ^{1}H NMR spectra.

The triethylamine treatment of **5** gives methyl *cis* - 2,3 -



Scheme 1. HCl elimination from methyl 2,3,3-trichloropropanoate **5**.



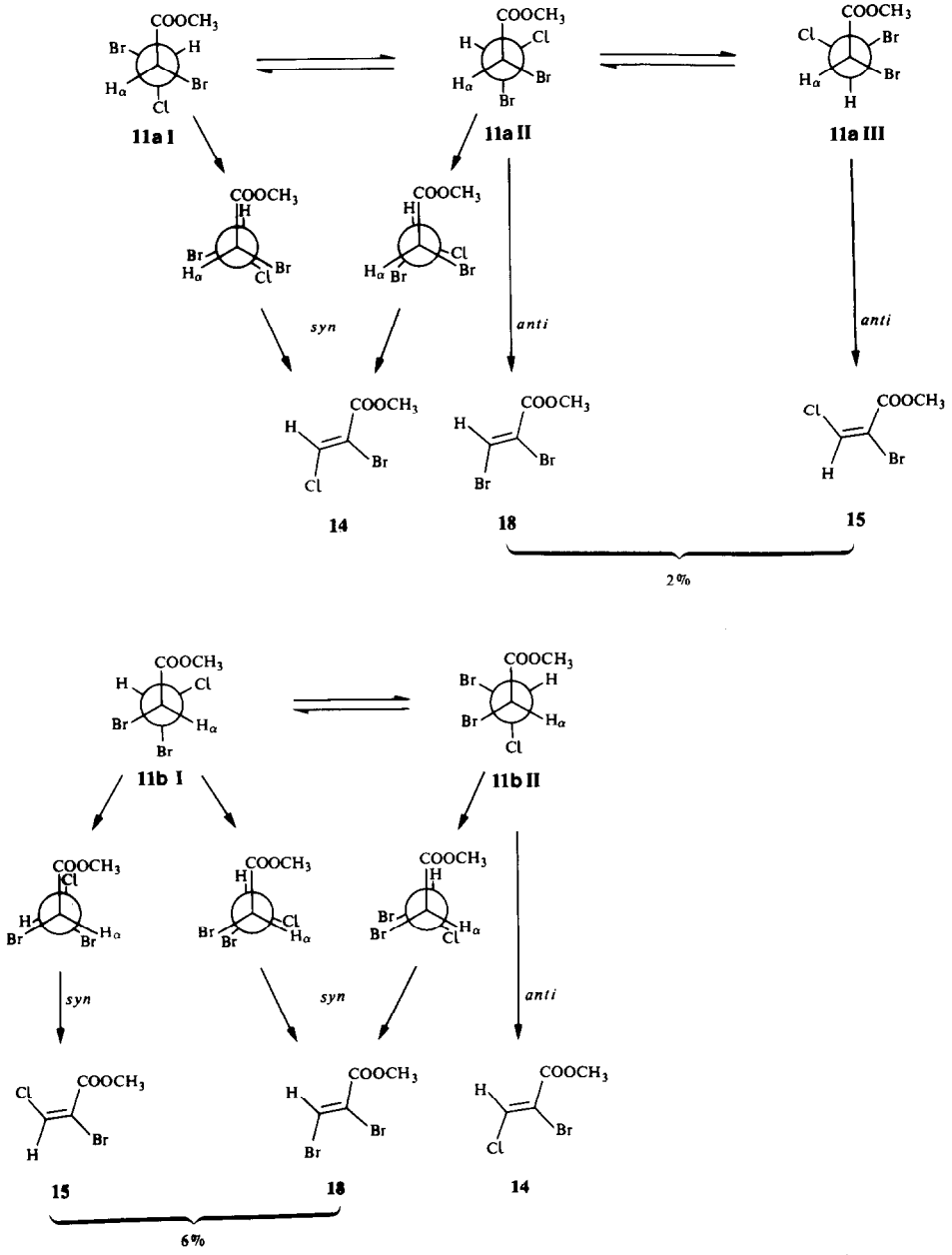
Scheme 2. HCl elimination from methyl 2 - bromo - 3,3 - dichloropropanoate **8**.

dichloropropenoate **12** as the only elimination product (Scheme 1). Compound **12** is most probably formed from the rotamer **5I** by HCl *anti*-elimination. Rotamers **5I** and **5II** are evidently the dominating ones. The third rotamer with two chlorine atoms around $COOCH_3$ group could only give *trans* - 2,3 - dichloropropenoate **13** by *anti*-elimination. Since the elimination process was followed by gas chromatograph and only trace amount of *trans*-form was observed, the *cis*-form is not believed to be formed by isomerization from the *trans*-isomer. Besides, the *cis–trans* mixtures of 2,3-dichloropropenoates were found to keep unchanged by storing at room temperature.

Trans - 2,3 - dibromopropenoic acid has been reported to isomerize easily to the *cis*- form in dilute CCl_4 solution, especially, in the presence of bromine.[7] The same phenomenon was observed in this study within 2,3-dichloropropenoates **12** and **13** when bromine was added to the mixture of *cis*- and *trans*-forms.

2 - Bromo - 3,3 - dichloropropanoate **8** shows the analogous elimination with **5** as illustrated in Scheme 2. The only elimination product observed was at all stages *cis* - 2 - bromo - 3 - chloropropenoate **14**.

Scheme 3 illustrates the possible HX elimination routes from 3 - chloro - 2,3 - dibromopropanoate diastereomers **11a**, **11b**. Erythro form **11a** gave almost quantitatively (98%) of *cis* - 2 - bromo - 3 - chloropropenoate **14** by *syn*-elimination. The triethylamine elimination was made to a 96 : 4 mixture of **11a/11b**. In general HX elimination is believed to occur by *anti*-elimination as in Schemes 1 and 2 and in Scheme 3 for the threo form, but **14** cannot be formed from any of the rotamers **I–III** of **11a** by *anti*-elimination. The slight amounts of *trans* - 2 - bromo - 3 - chloro - **15** and *cis* -



Scheme 3. HX elimination from methyl erythro and threo 3 - chloro - 2,3 - dibromopropanoates **11a**, **11b**.

2,3 - dibromo isomers **18** observed could come from either diastereomer **11a** or **11b** by routes shown in Scheme 3. Pure **11b** would have offered the access to the accurate ratio of elimination products from the threo form but the elimination was made to a mixture containing 68% of **11b** and 32% of **11a**.

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