Effect of pyridine on the regio- and stereo-chemistry in the addition of bromine chloride to α,β-unsaturated aldehydes and ketones†

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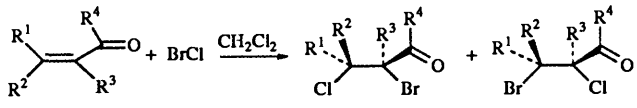
The addition of bromine chloride (BrCl) in methylene dichloride (CH_2Cl_2) in the presence and absence of acid scavengers such as pyridine to the following α,β-unsaturated aldehydes, ketones and esters is described: acrylaldehyde 1, methyl vinyl ketone 2, phenyl vinyl ketone 3, (*E*)-crotonaldehyde 4, (*E*)-pent-3-en-2-one 5, (*E*)-4-phenylbut-3-en-2-one 6, 4-methylpent-3-en-2-one 7, methyl isopropenyl ketone 8, 3-phenylbut-3-en-2-one 9, cyclohex-2-enone 10, methyl acrylate 11, (*E*)-methyl crotonate 12 and methyl methacrylate 13. The majority of the aldehydes and ketones gave primarily anti-Markovnikov (AM) bromo chloride regioisomer in the absence of pyridine. In most cases the Markovnikov (M) regioisomer increased significantly in the presence of pyridine. Addition of BrCl to 4, 5, 6 and 10 became stereospecific (*erythro*) in the presence of pyridine. The stereospecificity of addition to ester 12 was high with or without pyridine. These data were interpreted as follows: in the absence of an acid scavenger, an acid-catalysed reaction is involved, initiated by attack of proton on the carbonyl oxygen. When traces of acid are removed by an acid scavenger, the reactions proceed through a bromonium ion–chloride ion intermediate. The esters reacted only *via* a bromonium ion giving essentially the same mixture of regioisomers with and without acid scavenger.

In recent papers, we described the bromination[1] and chlorination[2] of α,β-unsaturated ketones and esters in methanol to give methoxy halides and dihalides. In the presence of acid scavengers such as pyridine and *N*-bromosuccinimide (NBS), a significant increase in the Markovnikov (M)‡ methoxy halide regioisomer occurred with the ketones but not the esters. The effect of acid scavengers was ascribed to the inhibition of an acid-catalysed reaction§ and the emergence of a halonium ion pathway. The esters apparently followed the halonium mechanism under all conditions.

In the study reported here, we proposed to determine whether the acid-catalysed reaction was operative in the reaction of BrCl with α,β-unsaturated aldehydes and ketones in an inert solvent such as methylene dichloride (CH_2Cl_2). An acid-catalysed reaction would be indicated by the formation of a high percentage of AM bromo chloride regioisomer which becomes substantially lower in the presence of acid scavengers. We suspected that an acid-catalysed reaction might be involved in the reaction of BrCl with α,β-unsaturated aldehydes and ketones since an earlier preliminary investigation[3] showed an unexpectedly high percentage of AM regioisomer when BrCl was added to a few α,β-unsaturated ketones and an aldehyde.

Results and discussion

BrCl was added to the α,β-unsaturated aldehydes and ketones listed in Table 1 and the esters in Table 2. In most cases, mixtures of Markovnikov (M) and anti-Markovnikov (AM) bromo chlorides were formed as outlined in the following reaction:



1 Acrylaldehyde $R^1 = R^2 = R^3 = R^4 = H$
2 Methyl vinyl ketone $R^1 = R^2 = R^3 = H$; $R^4 = Me$
3 Phenyl vinyl ketone $R^1 = R^2 = R^3 = H$; $R^4 = Ph$
4 (*E*)-Crotonaldehyde $R^1 = R^3 = R^4 = H$; $R^2 = Me$
5 (*E*)-Pent-3-en-2-one $R^1 = R^3 = H$; $R^2 = R^4 = Me$
6 (*E*)-4-Phenylbut-3-en-2-one $R^1 = R^3 = H$; $R^2 = Ph$; $R^4 = Me$
7 4-Methylpent-3-en-2-one $R^1 = R^2 = R^4 = Me$; $R^3 = H$
8 Methyl isopropenyl ketone $R^1 = R^2 = H$; $R^3 = R^4 = Me$
9 3-Phenylbut-3-en-2-one $R^1 = R^2 = H$; $R^3 = Ph$; $R^4 = Me$
10 Cyclohex-2-enone R^1 and $R^4 = -(CH_2)_3-$; $R^2 = R^3 = H$
11 Methyl acrylate $R^1 = R^2 = R^3 = H$; $R^4 = OCH_3$
12 (*E*)-Methyl crotonate $R^1 = R^3 = H$; $R^2 = Me$; $R^4 = OCH_3$
13 Methyl methacrylate $R^1 = R^2 = H$; $R^3 = Me$; $R^4 = OCH_3$

The data in Table 1 show that the percentages of AM and M regioisomers for the majority of the aldehydes and ketones were significantly influenced by the presence of the acid scavenger pyridine, leading to an increase in M regioisomer. Pyridine was required only in a small amount. Introduction of acid led to an increase in the AM regioisomer with acrylaldehyde (gaseous HCl and HBr) and methyl isopropenyl ketone (gaseous HCl). These alkenes were chosen because they gave a large amount of M bromo chloride without pyridine. The ratio of regioisomers from esters **11** and **12** was unaffected by pyridine. *N*-Bromosuccinimide (NBS) showed the same effect as pyridine, except with **1**, but was more difficult to use than pyridine and was examined in only selected cases.

The results in Tables 1 and 2 parallel our earlier studies with

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‡ We have used the terms Markovnikov (M) and anti-Markovnikov (AM) as follows: the M regioisomer refers to compounds where the electrophile (Br with Br_2; Cl with Cl_2; Br with BrCl) is on the carbon which is β to the carbonyl group; the AM regioisomer has the electrophile on the α carbon.

§ Formation of trace acid (probably HCl from BrCl) may result from oxidation of impurities in the solvents, substitution of a proton in the methyl ketones and slow free radical halogenation of CH_2Cl_2.

Table 1 Reaction of bromine chloride (BrCl) with aldehydes and ketones in methylene dichloride (CH_2Cl_2)

Compound	Halogen system	Bromo chlorides (%)[a] AM	M	M:AM ratio	*erythro* and *trans* for **10** (%)[b]
1	BrCl	85	15	0.18	
	BrCl/Pyr[c]	58	42	0.72	
	BrCl/NBS	85	15	0.18	
	BrCl/HCl	94	6	0.06	
	BrCl/HBr	94	6	0.06	
2	BrCl	91	9	0.10	
	BrCl/Pyr	52	48	0.92	
3	BrCl	90	10	0.11	
	BrCl/Pyr	70	30	0.43	
4	BrCl	100	0	0.00	66
	BrCl/Pyr	75	25	0.33	97
5	BrCl	93	7	0.07	48
	BrCl/Pyr	70	30	0.43	94
	BrCl/NBS	67	33	0.49	
6	BrCl	100	0	0.00	88
	BrCl/Pyr	100	0	0.00	100
7	BrCl	100	0	0.00	
	BrCl/Pyr	100	0	0.00	
8	BrCl	76	24	0.32	
	BrCl/Pyr	57	43	0.75	
	BrCl/NBS	62	38	0.61	
	BrCl/HCl	95	5	0.05	
9	BrCl	90	10	0.11	
	BrCl/Pyr	72	28	0.39	
10	BrCl	100	0	0.00	68
	BrCl/Pyr	79	21	0.27	100

[a] The reproducibility of these data is ± 5%. [b] The percentages of *erythro* and *trans* involve both M and AM isomers. [c] Pyr = pyridine, in a 1:10 molar ratio with alkene.

Table 2 Reaction of bromine chloride (BrCl) with selected esters

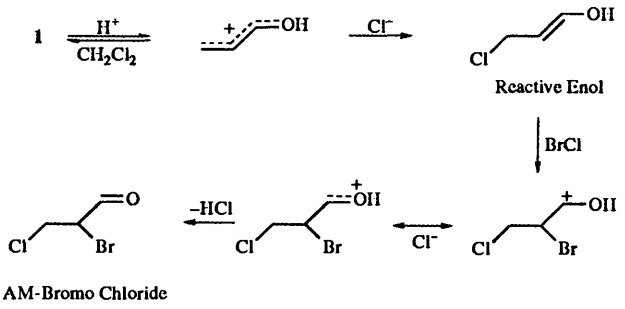
Ester	Halogen system	Bromo chlorides (%)[a] AM	M	M:AM ratio	*erythro* and *trans* for **10** (%)[b]
11[b]	BrCl	83	17	0.20	
12[b]	BrCl	75	25	0.33	98
	BrCl/Pyr	79	21	0.27	98
13	BrCl	75	25	0.33	
	BrCl/Pyr	71	29	0.41	

[a] The reproducibility of these data is ± 5%. [b] See ref. 4.

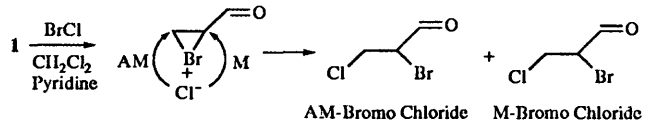
Br_2[1] and Cl_2[2] in CH_3OH where acid scavengers lead to an increase in M regioisomers. Our explanation for the data in Table 1 is that, in the absence of pyridine, BrCl addition occurs predominantly by an acid-catalysed reaction for all aldehydes and ketones except **8** and **9**, and that in the presence of pyridine a bromonium ion pathway is followed, leading to more M regioisomer. The esters react by the bromonium ion pathway under all conditions.

The two mechanisms are outlined in Scheme 1 using acrylaldehyde **1** for the purposes of illustration. The acid-catalysed reaction should lead to the AM regioisomer because attack of the electrophile (Br) on the enol π-bond will generate a carbocation which is stabilized by resonance with the neighbouring oxygen. Because of strong bridging in the bromonium ion in Scheme 1, the ring should be opened to give both M and AM regioisomers. The strong bridging results from the destabilization of charge on the α and β carbons by the carbonyl group. This argument does not apply to ketones **6** and **7** where the bridging in the intermediate ions is unsymmetrical due to stabilization by the phenyl ring in **6** and alkyl groups in **7**, resulting in charge development on the β carbon.

Mechanism involving acid catalysis



Mechanism involving a bromonium ion



Scheme 1

Perhaps a few comments on the variations in certain M/AM ratios are in order. The increase in M regioisomers for **1** and **2** in the presence of pyridine compared to the corresponding ester **11** suggests that the carbonyl groups of the aldehyde and ketone may accelerate the ring-opening of the intermediate bromonium ion to a greater extent than the carbonyl of the ester.¶ This points to S_N2 character in the ring-opening step. On the other hand, an increase in AM for **4** and **5** compared to their unsubstituted analogues **1** and **2**, where the methyl groups in the former pair can stabilize the charge on the β-carbon, seems to correlate with S_N1 character in the ring-opening step of **4** and **5**. This increase is in contrast with our earlier study where (*E*)-methyl crotonate **12** gave less AM than methyl acrylate **11**.[4] Apparently subtle changes in the effect of substituents can alter the mechanism. This sensitivity may explain why Korhonen *et al.*[5] in a study of the addition of BrCl to α,β-unsaturated esters proposed an S_N1 mechanism for the ring-opening step and we suggested an S_N2 mechanism for **11** and **12** and an S_N1 mechanism for (*Z*)-methyl crotonate.

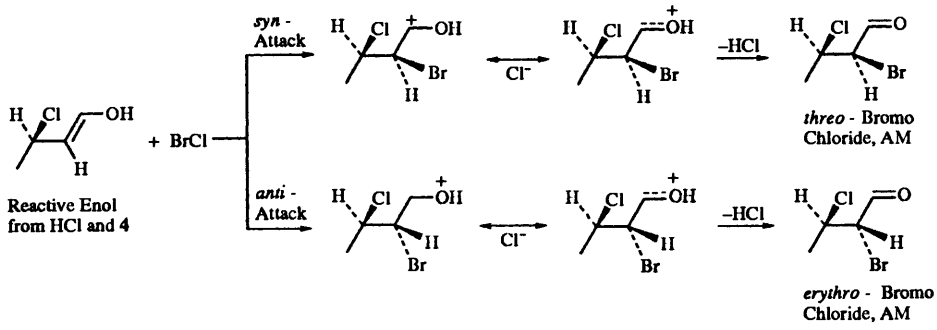
Apparently **8** undergoes significant attack at the C–C π-bond (bromonium ion mechanism) even in the absence of pyridine since the amount of M regioisomer is high. The data show that the acid-catalysed mechanism becomes significant if excess acid is added. Assuming that the increase in π-bond attack for **8** was due to stabilization of positive charge on the α-carbon by the α-methyl group, we anticipated greater M regioisomer with **9** where the phenyl ring should stabilize the charge more than the methyl group. Surprisingly, the M regioisomer was lower with the phenyl derivative **9**.

The data in Table 1 indicate that the prochiral aldehyde and ketones show a significant increase in *erythro* (**4**, **5**, **6**) and *trans* (**10**) stereoisomers in the presence of pyridine‖ In the case of ester **13**, the percentage of *erythro* was unaffected by pyridine. The effect of pyridine on the stereochemistry of BrCl addition to aldehyde **4** and ketones **5**, **6**, **10** can be explained on the basis of a change from an acid-catalysed reaction to one involving a bromonium ion in the presence of pyridine. As described in Scheme 2, using **4** as an example, both *erythro* and *threo* products would be anticipated from the non-stereospecific acid-catalysed reaction with *E*-aldehydes and *E*-ketones. With respect to the chlorine atom in Scheme 2, *threo*-products should result from *syn* attack and *erythro*- from *anti*. However, the

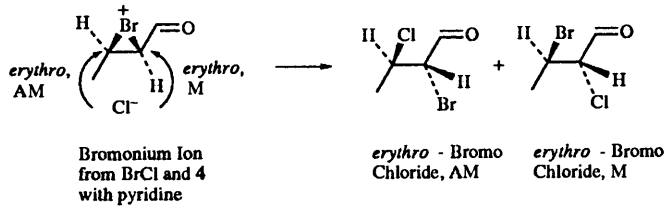
¶ See ref. 6 for a discussion of the acceleration of S_N2 reactions by various carbonyl groups.

‖ A preliminary investigation showed that the addition of Cl_2 and Br_2 to these aldehydes and ketones also became nearly stereospecific (*erythro*) in the presence of pyridine.

Stereochemistry in a Reaction Involving Acid Catalysis



Stereochemistry in a Reaction Involving a Bromonium Ion



Scheme 2

bromonium ion pathway should give only M and AM *erythro* stereoisomers with *E*-starting compounds. It should be noted that all of the M regioisomers for the *E*-aldehydes and *E*-ketones with BrCl were found to have *erythro* stereochemistry even without pyridines. This is as expected since the M regioisomers must arise exclusively from attack of Cl^- on a bromonium ion. A small amount of acid-catalysed attack apparently accompanies the bromonium ion mechanism since some *threo* stereoisomer is formed.

With cyclohex-2-enone **10**, the enol intermediate (acid-catalysed reaction) can be attacked *syn* and *anti* to the chlorine on the β-carbon, analogous to **4** in Scheme 2, leading to both *cis* and *trans* bromo chlorides, respectively. In the presence of pyridine, a bromonium ion must be involved since only *trans* products are observed.

The relative rates of reaction of BrCl with **5** and **12** were determined in the presence and absence of pyridine. In the absence of pyridine, reaction occurred entirely with **5**. In the presence of pyridine, **5** reacted approximately four times faster than **12**. These results parallel our earlier studies[2,3] where the reactions in the absence of acid scavengers were observed to be faster and suggest that the acid-catalysed reaction is faster than the reaction involving a bromonium ion. It is not clear why the reaction of the ketone with BrCl, in the presence of pyridine, is faster than the ester.

Experimental

Materials and instrumentation

The starting aldehydes, ketones and esters were obtained commercially in high purity except for **3**[1] and **9**[6] which were synthesized as reported previously. All other reagents and solvents, except bromine chloride (BrCl), were obtained in high purity and used without further purification. BrCl was prepared in CCl_4 as reported previously.[4] BrCl in CH_2Cl_2 is less stable than in CCl_4 but, if it is stored in foil at refrigerator temperature, the molarity drops only 10% over several days.

Mass spectra were obtained at 70 eV on a Hewlett-Packard (HP) 5890 GLC interfaced with an HP 5970B mass selective detector. Results are expressed as *m/z* and as relative intensity (%). Products were analysed on an HP 5890II GLC with a 25 m, methyl silicone capillary column. NMR spectra were obtained on a Hitachi 1500 spectrometer with Me_4Si as the reference standard. IR spectra were obtained on a Nicolet 610 FT-IR interfaced with an HP 5890II GLC.

Reaction conditions

Sufficient bromine chloride (*ca.* 1.5 mol dm^{-3} in CCl_4 or CH_2Cl_2) was added to react with *ca.* 50% of the alkene. Products were analysed directly by GLC. In some cases the products were dehydrohalogenated by adding triethylamine (10 mol excess) directly to the reaction mixture. The product solution was extracted three times with 40 cm^3 of 1 mol dm^{-3} HCl and, after drying over $MgSO_4$, was analysed by GLC.

Reactions employing pyridine as the acid scavenger were conducted by adding 0.1 mol of pyridine per mol of alkene to the reaction mixture prior to adding BrCl. NBS as the acid scavenger was added to the reaction solution until a slight excess was obtained. It was established that pyridine did not react with any of the bromo chlorides.

Reactions involving the addition of acid were conducted as follows: HCl or HBr/CH_2Cl_2 solutions were prepared by bubbling HCl or HBr gas into CH_2Cl_2 at 0 °C until a saturated solution of *ca.* 1 mol dm^{-3} was obtained as determined by titration. Just prior to addition of BrCl, the appropriate amount of HCl/CH_2Cl_2 or HBr/CH_2Cl_2 reagent was added to the alkene solution to give a solution of *ca.* 0.1 mol dm^{-3}.

Yields for all reactions were determined by GLC using internal standards and exceeded 75% in all cases.

The relative rates of reaction of BrCl with **5** and **12** were conducted as follows: equimolar amounts of **5** and **12** were dissolved in CH_2Cl_2 with and without pyridine. Sufficient BrCl was added to react with *ca.* 10% of one of the alkenes. The reactions were followed by GLC.

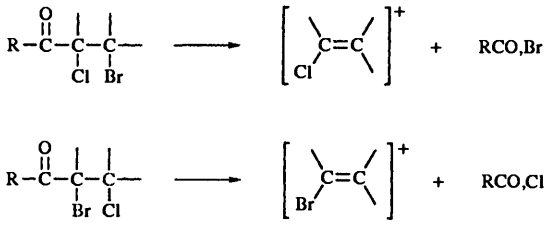
Identification of the products

Many of the products have been previously reported. Products which are new to this study were identified from the ^1H NMR, mass and IR spectra of crude samples and elimination to haloalkenes in several cases. No attempt was made to isolate pure bromo chlorides because of the difficulties involved: several of the products were unstable and decomposed rapidly;

all of the bromo chlorides were contaminated with trace amounts of dichlorides and dibromides (from the small amounts of Cl_2 and Br_2 in equilibrium with BrCl) and were impossible to remove.

Ratios of bromo chloride regioisomers were determined by one or more of the following procedures: (*a*) direct GLC analysis; (*b*) GLC analysis of elimination products (haloalkenes); (*c*) NMR analysis. The procedure used for each starting compound is listed: **1**: *a,b*; **2**: *b*; **3**: *b*; **4**: *a*; **5**: *a*; **6**: *a,b*; **7**: *a*; **8**: *a,c*; **9**: *a*; **10**: *a*; **11**: *b*; **12**: *a*; **13**: *c*.

The structures of the regioisomers were established in certain cases by comparing the mass spectra of the elimination products (haloalkene) with those of the authentic haloalkenes, prepared by dehalohalogenation of the known dichloride or dibromide. Starting compounds in this category are **1**, **2**, **3**, **6** and **11**. Many of the regioisomers (**1**, **4**, **5**, **6**, **8**, **9** and **12**) were established by recognizing the following fragmentations (possibly concerted) in the mass spectrometer:



R = H, CH_3 or CH_3O

With M regioisomers, chloroalkene ions were major; bromoalkene ions were minor. The opposite was true with AM regioisomers. For **6**, formation of only the AM regioisomer was confirmed by the presence of the C_6H_5CHCl fragment in the mass spectrum and the absence of the C_6H_5CHBr fragment, as well as by the other mass spectrum and elimination proofs. For **7**, structural proof for exclusive formation of the AM regioisomer depended on unambiguous synthesis of the M regioisomer and correlation of the methyl protons on C-4 in the AM bromine chloride regioisomer with the corresponding methyl protons in the dichloride but not the dibromide. For **13**, structures of the regioisomers were established by comparing the chemical shifts of the methyl protons on C-2 in the regioisomers with the chemical shifts of the methyl protons on the C-2 in the authentic dichloride and dibromide of methyl methacrylate.

The assignment of *erythro*, *threo* was based on the assumption that the sole isomer produced on the addition of BrCl to *E*-isomers in the presence of pyridine has the *erythro* configuration because of *anti* attack of chloride ion on the bromonium ion.

It was established that all bromo chloride regioisomers reported in this study were stable to reaction and analysis conditions.

Acrylaldehyde 1. The regioisomers of bromochloropropanal have been reported previously.[3] Conditions used for GLC analysis involved programming from 45–180 °C at 5 °C min^{-1}. Retention times/min were: 3-bromo-2-chloropropanal, 7.90; 2-bromo-3-chloropropanal, 8.00.

Methyl vinyl ketone 2. The regioisomers of bromochlorobutan-2-one, 3-bromobut-3-en-2-one and 3-chlorobut-3-en-2-one have been reported previously.[3] Retention times/min, under the conditions reported for **1**, are, respectively: 10.4, 5.82 and 4.04.

Phenyl vinyl ketone 3. The regioisomers of bromochloro-1-phenylpropan-1-one, 2-bromo-1-phenylprop-2-en-1-one and 2-chloro-1-phenylprop-2-en-1-one have been reported previously.[3] Conditions used for GLC analysis involved programming from 110–195 °C at 10 °C min^{-1}. Retention times/min were, respectively: 11.0, 8.25 and 7.09.

(*E*)-Crotonaldehyde 4. The regioisomers and stereoisomers of bromochlorobutanal were identified by the NMR spectrum of the mixture and IR and mass spectra of the individual isomers: δ_H 1.40–2.09 (m, 3 H), 4.10–4.76 (m, 2 H), 9.20–9.71 (m, 1 H), *erythro* and *threo* (AM)-2-bromo-3-chlorobutanal; *m/z* 188, 186, 184 (M, 0.16, 0.75, 0.54), 157, 155 (M − HCO, 0.33, 0.25), 150, 148 (M − HCl, 0.55, 0.53), 143, 141 (M − CHO, 0.27, 0.31), 122, 120 (M − HOCl, 0.42, 0.40), 65, 63 (CH_3CHCl, 1.7, 6.2), 41 (C_2HO, 100). Confirming peaks in the IR spectra (ν/cm^{-1}) for the previous pair of isomers: CH_3, 2997; CHO, 2834, 2724; C=O, 1744. There were differences between the isomers in the fingerprint region.

erythro-(M)-3-bromo-2-chlorobutanal, *m/z* 186 (M, 0.46), 159, 157, 155 (M − HCO, 0.76, 2.8, 2.4), 109, 107 (CH_3CHBr, 1.5, 3.1), 78, 76 (M − CHOBr, 0.31, 0.88), 0.41 (C_2HO, 100). Confirming peaks in the IR spectrum (ν/cm^{-1}): CH_3, 2996; CHO, 2832, 2723; C=O, 1749. Conditions used for GLC, GLC-FTIR and GLC-MS analyses involved programming from 45–120 °C at 10 °C min^{-1}. Retention times/min were: AM 7.28; AM 7.56; M, 7.14.

(*E*)-Pent-3-en-2-one 5. The regioisomers of bromochloropentan-2-one[5] have been reported previously. Conditions used for GLC analysis involved programming from 45–180 °C at 5 °C min^{-1}. Retention times/min were, respectively: *erythro* (AM), 12.3; *threo* (AM), 12.8 and *erythro* (M), 12.2.

(*E*)-4-Phenylbut-3-en-2-one 6. *erythro* and *threo* 3-bromo-4-chloro-4-phenylbutan-2-one (AM). These stereoisomers were identified by the NMR spectrum of the mixture and the IR and mass spectra of the individual isomers: δ_H 2.41 (s, 3 H), 4.58–5.39 (m, 2 H), 7.40 (s, 5 H); *m/z* (same for both isomers) 226, 224 (M − HCl, 0.21, 0.24), 184, 182 (M − CH_3COCl, 0.21, 0.21), 183, 181 (M − Br, 13, 33), 127, 125 (C_6H_5CHCl, 4.1, 11.5), 43 (CH_3CO, 100); IR spectrum (ν/cm^{-1}): C=O, 1738. Specific proofs for the exclusive presence of the AM regioisomer: C_6H_5CHCl was present, C_6H_5CHBr was absent in the mass spectrum; elimination of the bromo chloride product with triethyl amine gave exclusively the vinyl bromide, 3-bromo-4-phenylbut-3-en-2-one, which was confirmed by comparison with the authentic vinyl bromide prepared by elimination of 3,4-dibromo-4-phenylbutan-2-one with triethylamine. Mass and IR spectra of the vinyl bromide are: *m/z* 226, 224 (M, 18, 19), 211, 209 (M − CH_3, 4.6, 4.8), 183, 181 (M − CH_3CO, 5.2, 5.8), 43 (CH_3CO, 100); IR spectrum (ν/cm^{-1}): C=O, 1708; C=C, 1599. Conditions used for GLC, GLC-FTIR and GLC-MS analyses were the same as with the dichlorides. Retention times/min were: vinyl bromide, 10.3; *erythro*, 11.4; *threo*, 11.5.

4-Methylpent-3-en-2-one 7. 3-Bromo-4-chloro-4-methylpentan-2-one (AM), the sole regioisomer in the addition of BrCl to **7**, was identified by its NMR, IR and mass spectra. Dehydrochlorination with triethylamine occurred too slowly to be used in identification since decomposition of the vinyl bromide product became a complicating factor. 4-Bromo-3-chloro-4-methylpentan-2-one (M) was synthesized unambiguously by the addition of HBr to the vinyl chloride, 3-chloro-4-methylpent-3-en-2-one, and was shown to be absent in the reaction mixture. 3-Bromo-4-chloro-4-methylpentan-2-one (AM), δ_H 1.79 (s, 3 H), 1.83 (s, 3 H), 2.41 (s, 3 H), 4.57 (s, 1 H) (the methyl singlet—conformer—is closer to the dichloride than the M regioisomer); *m/z* 178, 176 (M − HCl, 0.07, 0.09), 173, 171, 169 (M − CH_3CO, 0.06, 0.22, 0.17), 136, 134 (M − CH_3OCl, 52, 50), 43 (CH_3CO, 100); confirming peaks in the IR spectrum (ν/cm^{-1}): C=O, 1740. 4-Bromo-3-chloro-4-methylpentan-2-one (M), δ_H 1.91 (s, 3 H), 1.93 (s, 3 H), 2.42 (s, 3 H), 4.50 (s, 1 H) (the methyl singlet—conformer—is closer to the dibromide than the AM regioisomer); *m/z* 171, 169 (M − CH_3CO, 0.10, 0.08), 135, 133 (M − Br, 0.31, 0.69), 92, 90 (M − CH_3OBr, 12, 38), 43 (CH_3CO, 100); confirming peaks in the IR spectrum (ν/cm^{-1}): C=O, 1743.

Conditions used for GLC, GLC-FTIR and GLC-MS analyses involved programming from 70–150 °C at 2.5 °C

min $^{-1}$. Retention time/min for 3-bromo-4-chloro-4-methylpentan-2-one was 11.

Methyl isopropenyl ketone 8. The regioisomers of bromochloro-3-methylpropan-2-one were identified by the NMR spectrum of the mixture and IR and mass spectra of the individual isomers: M, δ_H 1.80 (s, 3 H), AM, 1.95 (s, 3 H), M, 2.40 (s, 3 H), AM, 2.43 (s, 3 H), M and AM, 3.77–4.31 (m, 2 H); 3-bromo-4-chloro-3-methylbutan-2-one (AM), *m/z* 200, 198 (M, 0.37, 0.31), 122, 120 (M − CH_3COCl, 24, 25), 43 (CH_3CO, 100). IR spectrum (ν/cm^{-1}): C=O, 1734. 4-Bromo-3-chloro-3-methylbutan-2-one (M), *m/z* 200, 198 (M, 0.17, 0.14), 121, 119 (M − Br, 1.1, 3.2), 78, 76 (M − HCOBr, 0.94, 2.8), 43 (CH_3CO, 100). IR spectrum (ν/cm^{-1}): C=O, 1736. Conditions used for GLC, GLC-FTIR and GLC-MS analyses were the same as for **1**. Retention times/min were: M, 11.8; AM, 12.0

3-Phenylbut-3-en-2-one 9. The regioisomers of bromochloro-3-phenylbutan-2-one were identified by the NMR spectrum of the mixture, the IR spectrum of the AM regioisomer and the mass spectra of the individual isomers: δ_H 2.31 (s, 3 H), 2.65–2.86 (m, 2 H), 7.43 (s, 5 H); 2-bromo-3-chloro-3-phenylbutan-2-one (AM), *m/z* 221, 219, 217 (M − CH_3CO, 0.19, 0.73, 0.54), 184, 182 (M − CH_3COCl, 26, 26), 103 ($C_6H_5C_2H_2$, 100), 43 (CH_3CO, 51); IR spectrum (ν/cm^{-1}): C=O, 1725; 3-bromo-2-chloro-3-phenylbutan-2-one (M), *m/z* 219, 217 (M − CH_3CO, 1.3, 0.82), 140, 138 (M − CH_3COBr, 26, 83), 103 ($C_6H_5C_2H_2$, 63), 43 (CH_3CO, 100). Conditions used for GLC, GLC-FTIR and GLC-MS analyses involved programming from 100–180 °C at 10 °C min^{-1}. Retention times/min were: M, 10.9; AM, 11.2.

Cyclohex-2-enone 10. The regioisomers of bromochlorocyclohexanone were identified by NMR spectra of reaction products with and without pyridine, mass spectra of the individual isomers and IR spectra of the AM stereoisomers: NMR spectrum of product without pyridine, δ_H 1.77–3.40 (m, 6 H), 4.12–4.84 (m, 2 H) and NMR spectrum of product with pyridine, δ_H 1.79–3.43 (m, 6 H), 4.24–5.02 (m, 2 H); *cis*- and *trans*-2-bromo-3-chlorocyclohexanone (AM, stereoisomers gave the same MS): *m/z* 214, 212, 210 (M, 2.8, 11.7, 8.9), 177, 175 (M − Cl, 4.0, 4.3), 176, 174 (M − HCl, 6.8, 6.9), 133, 131 (M − Br, 18, 44), 67 (C_4H_3O, 100); confirming peaks in the IR spectra (ν/cm^{-1}) of the *cis* and *trans* AM isomers for C=O are, respectively: 1741 and 1741; *trans*-3-bromo-2-chlorocyclohexanone (M), *m/z* 214, 212, 210 (M, 0.73, 2.8, 2.3), 176, 174 (M − HCl, 0.32, 0.32), 133, 131 (M − Br, 28, 84), 105, 103 (C_6H_8Cl, 8.1, 24), 77, 75 (17, 53), 67 (C_4H_3O, 100).

Our conclusion that only the AM stereoisomers are formed in the absence of pyridine is based on the fact that both isomers gave the same mass spectra, suggesting *cis*, *trans* stereoisomers. In the presence of pyridine, the third bromo chloride isomer must be a regioisomer since another stereoisomer is not expected. Without an acid scavenger (pyridine), AM regioisomers would be anticipated, since chlorination and bromination of **10** in CH_3OH led exclusively to AM orientation. With pyridine, the assignment of *trans* stereochemistry is based on the assumption that involvement of a bromonium ion would be anticipated, leading to the *trans* isomer. Conditions used for GLC, GLC-FTIR and GLC-MS analyses involved programming from 70–150 °C at 10 °C min^{-1}. Retention times/min were: *trans* AM, 9.46; *cis* AM, 10.3; *trans* M, 9.52.

Methyl acrylate 11. The regioisomers of methyl bromochloropropanoate have been reported previously.[4]

(*E*)-Methyl crotonate 12. The regioisomers of the methyl 3,4-bromochlorobutanoates have been reported previously.[4] Under the conditions reported for **1**, their retention times/min were: AM, 13.7; M, 14.5.

Methyl methacrylate 13. The regioisomers of methyl bromochloro-2-methylpropanoate were identified by the NMR, IR and mass spectra of the mixture of regioisomers: methyl 3-bromo-2-chloro-2-methylpropanoate (M), δ_H 1.90 (s, 3 H); methyl 2-bromo-3-chloro-2-methylpropanoate (AM), δ_H 2.01 (s, 3 H); two regioisomers together, δ_H 3.89 (s, 3 H), 3.71–4.39 (m, 2 H) (it was discussed earlier how the chemical shifts of the methyl protons in the bromine chloride, dichloride and dibromide were used to distinguish between the M and AM regioisomers). *m/z* 216 (M + 2, 0.28), 187, 185, 183 (M − OCH_3, 0.56, 1.9, 1.5), 183, 181, 179 (M − Cl, 1.5, 3.5, 3.6), 159, 157, 155 (5.1, 20, 15), 122, 120 (M − CH_3OCOCl, 53, 57), 78, 76 (M − CH_3OCOBr, 10, 31), 59 (CH_3CO_2, 100); IR spectrum (ν/cm^{-1}): C=O, 1764. Conditions used for GLC, GLC-FTIR and GLC-MS analyses involved programming from 50–120 °C at 5 °C min^{-1}. Retention time/min for the peak of a mixture of the two regioisomers was 11.2.

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