Chlorination of α,β-Unsaturated Ketones and Esters in the Presence of Acid Scavengers

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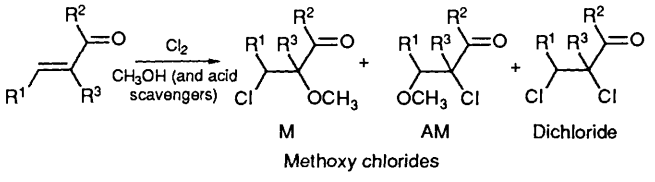
The chlorination of a series of α,β-unsaturated ketones and esters by Cl_2 in CH_3OH, with and without acid scavengers such as *N*-chlorosuccinimide (NCS), pyridine and 2,6-lutidine, is described. Methyl vinyl ketone and cyclohex-2-enone have also been chlorinated in ethanol. Mixtures of Markovnikov(M) and anti-Markovnikov(AM) methoxy chlorides and dichlorides are formed in most cases; phenyl vinyl ketone gives no M products in the absence of pyridine, M methoxy chloride is not formed with (*E*)-4-chlorobut-3-en-2-one under any conditions, pyridine has no effect on the product ratios and methyl 3-chlorobut-2-enoate forms only dichloride. Chlorination of the ketones in the presence of the pyridines results in a significant increase in the M regioisomer (except for methyl isopropenyl ketone and the ketones mentioned), giving M:AM ratios which are similar to the corresponding esters. Ratios for the esters are not affected significantly by pyridine. We ascribe the effect of the pyridine bases to the elimination of acid and the acid-catalysed mechanism, permitting the chlorination to occur *via* a carbon–carbon π-bond (chloronium ion) mechanism. The rate of chlorination of methyl vinyl ketone is retarded by pyridine but is still considerably faster than methyl acrylate. NCS, in contrast to *N*-bromosuccinimide (NBS) reported previously, has no effect on the M:AM ratio. The chlorination of methyl vinyl ketone with NCS and HCl gives markedly different results from Cl_2.

Recently we reported on the bromination by Br_2 of α,β-unsaturated ketones and esters in methanol, in the presence of acid scavengers such as *N*-bromosuccinimide (NBS) and other bromoamides.[1] This study showed that bromination of the ketones in the presence of an acid scavenger led to a significant increase in the Markovnikov to anti-Markovnikov (M:AM) ratio, probably by eliminating a rapid acid-catalysed addition, and by delivering bromine to the carbon–carbon π-bond as a bromine–bromoamide complex for both ketones and esters. In the present paper, we have extended the investigation to the chlorination of α,β-unsaturated ketones and esters by Cl_2 in methanol (and, in certain cases, ethanol), in the presence of potential acid scavengers such as *N*-chlorosuccinimide (NCS), pyridine and 2,6-lutidine.

Results

Chlorination of the Ketones and Esters.—Several α,β-unsaturated esters and ketones were chlorinated by Cl_2 in methanol in the presence of potential acid scavengers, NCS, pyridine (Pyr), and 2,6-lutidine (Lut). The reactions are shown in Scheme 1, and the results are summarized in Tables 1 and 3.



Scheme 1

In most cases, mixtures of anti-Markovnikov (AM) and Markovnikov methoxy chlorides (M, methoxy adjacent to the carbonyl group) and dichlorides (DiCl) were formed.

Methyl vinyl ketone (**1**) and cyclohex-2-enone (**7**) were chlorinated in ethanol and the data are shown in Table 2. Cyclohex-2-enone **7** was chlorinated in ethanol because of difficulty in separating the methoxy chlorides and dichlorides. Considerable substitution product, 2-chlorocyclohex-2-enone, was formed in the chlorination of **7** in ethanol: with pyridine, 53% and without, 10%. The products were stable to the reaction conditions, so the substitution product must arise from attack of base (Cl^-, solvent or pyridine) on the intermediate chloronium ion. Data from the chlorination of **1** in ethanol are included for comparison purposes.

Effect of NCS and the Pyridines.—The data in Tables 1 and 3 for selected ketones and esters show that chlorination in the presence of NCS has no significant effect on the M:AM ratio, which is in contrast to our previous study[1] on the bromination of α,β-unsaturated ketones and esters, in which the M:AM ratio was shown to increase markedly in the presence of NBS. Apparently, NCS does not form a complex with Cl_2, as NBS does with Br_2. On the other hand, chlorination of the ketones in the presence of pyridine and 2,6-lutidine (see Tables 1 and 2) shows a significant increase in the amount of Markovnikov regioisomer in all cases except for **6**. In the presence of pyridine, M:AM ratios for ketones **1**, **4** and **5** compare favourably with esters **8**, **9** and **10**, respectively. The M:AM ratios for the esters (Table 3) were not affected significantly by the presence of pyridine.

Effects of Added Acid and Lithium Chloride on the Product Ratios.—Chlorination of ketones **1** and **5** in the presence of gaseous HCl, in an amount equivalent to Cl_2, resulted in a decrease in the M:AM ratio. The ratio became 0.00 with **1** and 1.79 with **5**. The original ratio was restored when pyridine was present. Chlorination of **1** with lithium chloride had no effect on

Table 1 Chlorination of α,β-unsaturated ketones in methanol

Ketone	Halogen system	Products (%)			
		Methoxy chlorides			
		AM	M	Dichloride	M:AM ratio
Methyl vinyl ketone **1**	Cl_2	21	2	77	0.10
	Cl_2/NCS	30	2	68	0.07
	Cl_2/Pyr[a]	52	28	20	0.54
	Cl_2/Pyr(1:2)	56	28	16	0.50
	Cl_2/Pyr(2:1)	42	16	42	0.38
	Cl_2/Lut(1:1)	50	29	21	0.58
Phenyl vinyl ketone **2**	Cl_2	18	0	82	0.00
	Cl_2/NCS	10	0	90	0.00
	Cl_2/Pyr	42	32	26	0.76
tert-Butyl vinyl ketone **3**[b]	Cl_2	27	9	64	0.33
	Cl_2/Pyr	53	22	25	0.42
(*E*)-Pent-3-en-2-one **4**	Cl_2[c]	35	2	63	0.06
	Cl_2/Pyr[d]	54	14	32	0.26
Methyl isopropenyl ketone **5**	Cl_2	16	38	46	2.38
	Cl_2/Pyr	33	53	14	1.61
(*E*)-4-Chlorobut-3-en-2-one **6**[e]	Cl_2 and Cl_2/Pyr	26	0	74	0.00

[a] Cl_2: Pyr ratios are 1:1 unless indicated otherwise. [b] Bromination (%, with and without NBS): 70(17); 14(2); 16(81); M:AM, 0.2(0.14). [c] Ratio of diastereoisomers (AM and DiCl), *erythro*:*threo* = 93:7. [d] Ratio of diastereoisomers (AM and DiCl), *erythro*:*threo* = 98:2. [e] Bromination (%), same with and without NBS: AM, 10; DiBr, 90.

Table 2 Chlorination of α,β-unsaturated ketones in ethanol

Ketone	Halogen system	Products (%)			
		Ethoxy chlorides			
		AM	M	Dichloride	M:AM ratio
Methyl vinyl ketone **1**	Cl_2	8	1	91	0.12
	Cl_2/Pyr	22	14	64	0.64
Cyclohex-2-enone **7**	Cl_2	8	0	92	0.00
	Cl_2/Pyr	17	5	78	0.29

Table 3 Chlorination of α,β-unsaturated esters in methanol

Esters	Halogen system	Products (%)			
		Methoxy chlorides			
		AM	M	Dichloride	M:AM ratio
Methyl acrylate **8**	Cl_2	53	27	20	0.51
	Cl_2/NCS	46	27	27	0.59
	Cl_2/Pyr	55	29	16	0.53
(*E*)-Methyl crotonate **9**[a]	Cl_2	70	13	17	0.19
	Cl_2/NCS	67	8	25	0.12
	Cl_2/Pyr	67	8	25	0.12
Methyl methacrylate **10**	Cl_2	36	52	12	1.44
	Cl_2/Pyr	32	55	13	1.72
Methyl 3-chloroprop-2-enoate **11**[b]	Cl_2	—	—	100[c]	—

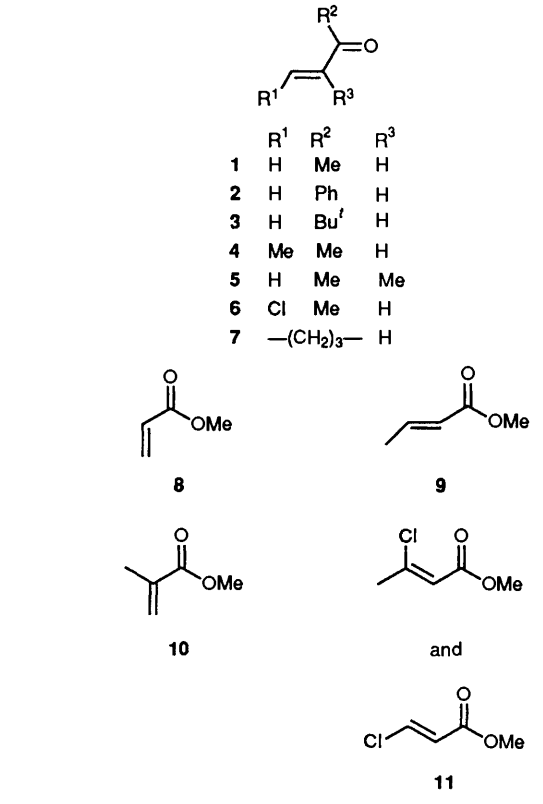
[a] The *threo* diastereoisomers (M + AM + DiCl) were <1%. [b] A mixture of *E*- and *Z*-isomers was used. Pyridine had no effect on the products. [c] Isomeric methyl 2,3-dichlorobut-2-enoates were also formed.

the M:AM ratio but led to an increase in the dichloride. The dichloride formed was proportional to the amount of LiCl added, both with and without pyridine.

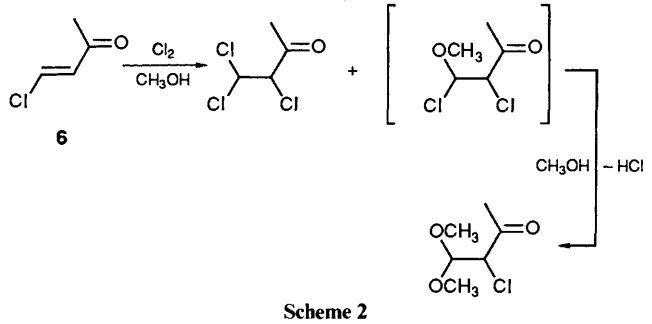
Reaction of Chlorine with Pyridine in Methanol.—UV spectroscopic studies established that Cl_2 and pyridine (also 2,6-lutidine) reacted to form a chlorine–pyridine complex, which existed in equilibrium with non-complexed chlorine; non-complexed chlorine was present even with a pyridine:chlorine ratio of 2:1. We assume that the chlorinating agent in these reactions is the non-complexed chlorine.*

Considerations on the Chlorination of (E)-4-*Chlorobut*-3-*en*-2-*one* **6**.—We established that 1,2-dichloro-1-methoxybutan-3-one solvolysed immediately in CH_3OH to 2-chloro-1,1-dimethoxybutan-3-one. Therefore, we assume that 1,2-dichloro-1-

* Bellucci[2] has shown that bromination occurs more rapidly with Br_2 than with Br_2-pyridine complex. By analogy, Cl_2 should be more reactive in chlorination reactions than its corresponding complex.



methoxybutan-3-one is the kinetic product in the chlorination of (*E*)-4-chlorobut-3-en-2-one (**6**), and that it is converted to 2-chloro-1,1-dimethoxybutan-3-one. Hence, the latter compound represents the anti-Markovnikov (AM) product (Scheme 2). No Markovnikov product was detected.



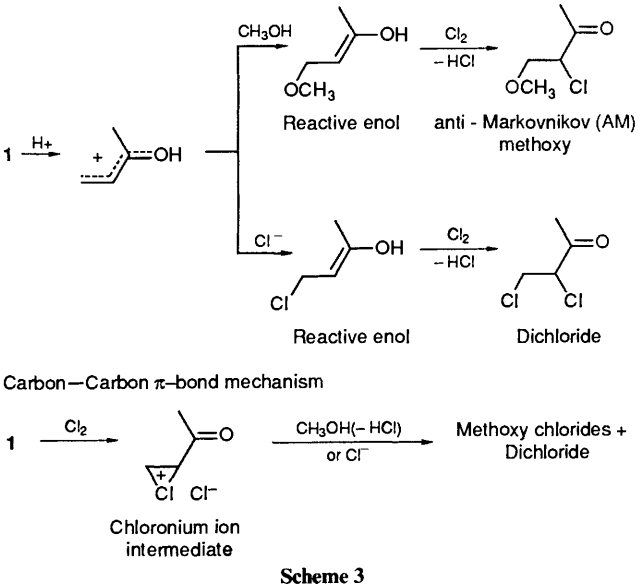
Scheme 2

Comparisons of the Reactivities of **1** *and* **8** *with* Cl_2 *in Methanol, with and without Pyridine.*—The reaction of **1** with Cl_2 was complete before an aliquot could be removed for titration. With pyridine, the reaction half-time was 20 s. For **8**, the reaction half-times, with and without pyridine, are 10 and 8 min, respectively.

Reactions of **1** *in Methanol with NBS and NCS and their Respective Acids, HBr and HCl.*—NBS, **1** and HBr in CH_3OH gave the same products as Br_2 and **1** in CH_3OH. In contrast, NCS, **1** and HCl in CH_3OH gave very different products from Cl_2. With NCS, anti-Markovnikov methoxy chloride was the main product (90%), with some dichloride (10%). Dichloride was formed in largest amounts with Cl_2 (see Table 1).

Discussion

We propose that the rapid chlorination reactions of the α,β-unsaturated ketones, in the absence of pyridine, occur by an acid-catalysed mechanism, involving a reactive enol, as shown in Scheme 3. Support for this mechanism is based on the



Scheme 3

following: (*a*) a preponderance of anti-Markovnikov (AM) product in all cases except ketone **5**; (*b*) an increase in AM product when acid (HCl) is added to the reaction of **1**; and (*c*) a non-stereospecific addition to **4**.

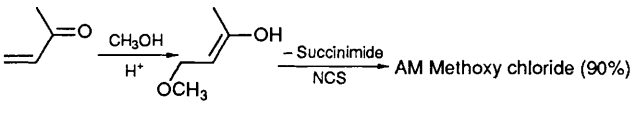
In the presence of pyridine the M:AM ratios for the ketones increased significantly (except for ketones **5** and **6**) and, in the case of ketones **1**, **4** and **5**, compared favourably to those of the corresponding esters **8**–**10**. For the esters, and the ketones in the presence of pyridine, we suggest that chlorination occurs *via* a carbon–carbon π-bond mechanism (Scheme 3). The slower rate of reaction for the ketones, the similarities of the M:AM ratios for the analogous ketones and esters, and the high stereospecificity of addition to ketone **4** support this mechanism. It seems reasonable to assume that the esters are reacting *via* the chloronium ion since the reactions are slow, and the addition to ester **9** is highly stereospecific.

The increase in dichloride formation when the chlorination is conducted in the presence of LiCl, both with and without pyridine, supports mechanisms with nucleophilic steps such as those described in Scheme 3. The involvement of a pyridine–chlorine complex to account for increases in the M:AM ratios in the presence of pyridine seems unlikely, since such a complex would also be involved in the chlorination of the esters, and significant changes in the M:AM ratio are not observed in this case. Furthermore, as has already been mentioned, free chlorine is present in the pyridine solutions, and molecular chlorine should chlorinate faster than the complex.

We assume that the decrease in the rate of chlorination of ketone **1** in the presence of pyridine is due primarily to the removal of acid catalyst. Reduction in the concentration of molecular chlorine may also be involved to some extent, and must be a major factor in the decrease with ester **8**. We have no explanation for the fact that ketone **1** in the presence of pyridine is still considerably more reactive than ester **8**.

The data with ketone **1** show that NBS and NCS react very differently with their respective acids. Apparently NBS and HBr react rapidly to give Br_2, thus removing acid from solution. NCS, on the other hand, does not react with HCl to generate Cl_2, but probably directly chlorinates the reactive methoxy enol intermediate to give AM product as shown in Scheme 4.

The percentages of dichlorides in the presence of pyridine was significantly lower for all of the ketones except **6**. Perhaps the chloride ion is more effective as a nucleophile with the conjugate acid of the ketone than with the chloronium ion (Scheme 3).



1 Reactive enol

Scheme 4

The M:AM ratios for **3** and **5** in the absence of pyridine are higher than would have been anticipated from the other ketones. This is particularly true in the case of **5**, where the value is comparable to that of the corresponding ester **10**. Examination of models show that the carbon–oxygen π-bonds (carbonyl groups) and the carbon–carbon π-bonds in **3** and **5** may not be coplanar, due to steric interaction between the methyl or *tert*-butyl group and the group (proton or methyl) on the carbon adjacent to the carbonyl group. Non-planarity would mean that the rate of acid-catalysed addition to **3** and **5** would be retarded, producing less AM product, and attack at the carbon–carbon π-bond would predominate, resulting in an elevated M:AM ratio. We have no explanation for the decrease in the M:AM ratio for **5** in the presence of pyridine.

Data from the chloroketone **6** and chloroester **11** are anomalous. Apparently **6** does not react by an acid-catalysed mechanism since the data is the same with and without pyridine. It is not clear why only dichloride is formed with ester **11**.

Experimental

Materials and Instrumentation.—The starting ketones and esters have been reported previously,[1] except for **3**, **6**, **11** and 4-methoxybut-3-en-2-one. Ketone **3** was synthesised by the Mannich reaction using pinacolone, paraformaldehyde and dimethylamine hydrochloride, and was identified by its NMR spectrum and boiling point: b.p. (obs.) 43–45 °C/40 mmHg (lit.,[3] b.p. 48–50 °C/50 mmHg). Ketone **6** was prepared as described in the literature.[4] 4-Methoxybut-3-en-2-one and NCS were obtained from the Aldrich Chemical Company. Chlorine, high purity grade, was purchased from the Matheson Company. HPLC grade methanol was used. Ester **11** was synthesised by treating methyl propiolate with HCl gas in CH_3OH.

Mass spectral analyses were obtained at 70 eV on a Hewlett-Packard 5890 GC interfaced with an HP5970B mass selective detector. Results are expressed as *m/z* and as relative intensity (%). Products were analysed on a Hewlett-Packard 5890 GC with a 25 m, methyl silicone capillary column. NMR spectra were obtained on a Varian T60A spectrometer with Me_4Si as the reference standard. Coupling constants are given in Hz. IR spectra were obtained on a Hewlett-Packard 5890II gas chromatograph (GLC) interfaced with a Nicolet 710 FT-IR spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, USA.

Reaction Conditions.—Chlorination reactions were conducted as follows: to a stirred solution of the alkene (0.04 mole fraction) in methanol or ethanol (overall volume, *ca.* 15 cm^3) at room temperature was added sufficient Cl_2 (1–2 mol dm^{-3} in CCl_4 or CH_2Cl_2) to consume *ca.* 50% of the alkene. Reaction mixtures were analysed directly by GLC. The reaction solution was saturated with NCS as was done previously with NBS.[1] The pyridines were introduced prior to chlorination.

The dichlorides did not react with methanol to give the methoxy chlorides. The ratios of M:AM regioisomers were not affected by the presence of Cl_2, NCS or the pyridines, and they did not change on standing.

Yields (%) were determined for selected reactions by either NMR or GLC: **1**: 88, 51(Pyr): **2**: 97; **3**: 88 with and without pyridine; **4**: 90, 93(Pyr); **5**: 88, 94(Pyr); **6**: 71 without pyridine; **8**: 91, 85(Pyr); **9**: 90, 89(Pyr): **10**: 70.

Unless indicated, products were isolated by preparative GLC. The methoxy chlorides were synthesised for preparative GLC from the appropriate alkene and CH_3OCl in methanol, using the procedure reported previously.[5]

Identification of the Products.—Evidence for the structures of the products reported in Tables 1–3 was obtained as follows: all structures were established by their mass spectra, most by their NMR spectra, and some by elemental analyses. In certain cases the products were too unstable to be isolated in pure form for elemental analysis, or even NMR spectra. Certain methoxy chlorides and dichlorides could not be separated sufficiently for adequate elemental analyses.

Bromination products, for comparison with those from chlorination, are described for the ketones not reported previously.[1] GLC analysis conditions and retention times are reported for each compound.

Chlorination of Methyl Vinyl Ketone **1**.—*3-Chloro-4-methoxybutan-2-one.* δ_H 2.37 (s, 3 H), 3.45 (s, 3 H), 3.83 (d, 3 H, *J* 6.0) and 4.33 (q, 1 H, *J* 6.0). The NMR spectrum was recorded on a product synthesised from **1** and NCS in CH_3OH, with one drop of H_2SO_4. The mass spectrum was identical to that of the product from **1** and Cl_2 in CH_3OH; *m/z* 101 (M − Cl, 19%), 75 (11), 95 and 93 (M − 43, 0.21 and 0.59), 64 and 62 (C_2H_3Cl, 6.3 and 18), 45 (CH_2OCH_3, 31) and 43 (CH_3CO, 100).

4-Chloro-3-methoxybutan-2-one. This compound was not isolated in pure form although its methoxy protons were observed at 3.71 ppm in the NMR spectrum of the mixture of the two regioisomers, which were isolated by preparative GLC. *m/z* 95 and 93 (M − 43, 0.21 and 0.59), 58 (73), 45 (1.6) and 43 (C_2H_3O, 100).

Elemental analysis was performed on a mixture of the two regioisomers (Found: C, 43.2; H, 6.65; Cl, 27.2. Calc. for $C_5H_9ClO_2$: C, 43.97; H, 6.6; Cl, 25.96%).

3,4-Dichlorobutan-2-one. δ_H 2.30 (3 H), 3.80 (d, 1 H, *J* 6.0), 3.90 (d, 1 H, *J* 6.0) and 4.39 (t, 1 H, *J* 6.0); *m/z* 144, 142 and 140 (M^+, 0.10, 0.54 and 0.73), 101.99 and 97 (M − 43, 0.12, 0.66 and 1.0) and 43 (C_2H_3O, 100). B.p. (obs.) 38–50 °C/5 mmHg (lit.,[6] 65–70 °C/16 mmHg).

The anti-Markovnikov and Markovnikov regioisomers and the dichloride were separated on the capillary column with the following retention times/min, respectively, by programming from 35–60 °C at 1.5 °C min^{-1}: 16.6, 18.5 and 15.8.

3-Chloro-4-ethoxybutan-2-one. δ_H 1.20 (t, 3 H, *J* 7.0), 2.31 (s, 3 H), 3.37–3.84 (m, 7 H) and 4.22 (t, 1 H, *J* 6.0); *m/z* 115 (M − Cl, 17), 59 (C_3H_7O, 12) and 43 (C_2H_3O, 100).

4-Chloro-3-ethoxybutan-2-one. δ_H 1.29 (t, 3 H, *J* 7.0), 2.19 (s, 3 H) and 3.34–3.95 (m, 8 H); *m/z* 109 and 107 (M − 43, 6 and 19), 81 and 79 (C_2H_4ClO, 21 and 69), 44 (36) and 43 (C_2H_3O, 100). The retention times/min for the anti-Markovnikov and Markovnikov regioisomers, under the same conditions used for the methoxy chlorides were 20.6 and 22.4, respectively. The compounds were too unstable for elemental analysis.

Chlorination of Phenyl Vinyl Ketone **2**.—*2-Chloro-3-methoxy-1-phenylpropan-1-one.* δ_H 3.40 (s, 2 H), 3.60–4.96 (m, 2 H), 5.10 (t, 1 H, *J* 7.0), 7.21–7.77 (m, 3 H) and 7.81–8.30 (m, 2 H); *m/z* 163 (M − Cl, 7), 136 (M − C_2H_3Cl, 14), 105 (C_7H_5O, 100), 77 (C_6H_5, 54), 51 (20) and 45 (11). (Found: C, 60.6; H, 5.2; Cl, 18.1. Calc. for $C_{10}H_{11}ClO_2$: C, 60.45; H, 5.54; Cl, 17.8%).

3-Chloro-2-methoxy-1-phenylpropan-1-one. This compound was isolated, together with its regioisomer, by preparative GLC from the reaction of **2** with CH_3OCl in methanol. It was not obtained in pure form. The following peaks in the NMR spectrum could be assigned to the regioisomer: δ_H 3.44 (s, 3 H) and 4.58 (t, 3 H). The chemical shifts of the other protons were identical with those of the AM regioisomer. The percentage

of M and AM regioisomers, as calculated from the NMR spectrum, agreed with the percentage from GLC analysis. *m/z* 105 (C_7H_5O, 97), 95 and 93 (C_3H_6ClO, 3 and 10), 77 (C_6H_5, 100), 51 (44) and 45 (0.4) (Found: C, 59.5; H, 5.4; Cl, 18.9. Calc. for $C_{10}H_{11}ClO_2$ (mixture of regioisomers): C, 60.45; H, 5.54; Cl, 17.88%). The sample used for elemental analysis was contaminated with some dichloride.

2,3-*Dichloro*-1-*phenylpropan*-1-*one*. δ_H 3.68–4.40 (m, 2 H), 5.20 (dd, 1 H, *J* 6.0, *J* 8.0), 7.34–7.78 (m, 3 H) and 7.83–8.27 (m, 2 H); *m/z* 204 and 202 (M^+, 0.09 and 0.12), 105 (C_7H_5O, 100), 77 (49) and 51 (20) (Found: C, 53.6; H, 4.4; Cl, 35.3. Calc. for $C_9H_8Cl_2O$: C, 53.20; H, 3.94; Cl, 34.98%).

The anti-Markovnikov and Markovnikov regioisomers and the dichloride were separated on the capillary column with the following retention times/min, respectively, by programming from 125–190 °C at 5 °C min^{-1}: 8.8, 9.0 and 8.4.

Chlorination and Bromination of tert-*Butyl Vinyl Ketone* **3**.—2-*Chloro*-1-*methoxy*-4,4-*dimethylpentan*-3-*one*. δ_H 1.18 (s, 9 H), 3.30 (s, 3 H), 3.64 (m, 2 H) and 4.55 (dd, 1 H, *J* 5.5, 8.5); *m/z* 143 (M − Cl, 2.4), 85 (C_5H_9O, 16), 58 (C_3H_6O, 7), 57 (C_4H_9, 100), 45 (C_2H_5O, 17) and 41 (40).

1-*Chloro*-2-*methoxy*-4,4-*dimethylpentan*-3-*one*. δ_H 1.18 (s, 9 H), 3.41 (s, 3 H), 3.74 (m, 2 H) and 4.20 (t, 1 H, *J* 6); *m/z* 93 and 95 (M − C_5H_9O, 17 and 6), 58 (C_3H_6O, 100), 57 (C_4H_9, 44), 43 (C_3H_7, 23) and 41 (C_3H_5, 29).

Elemental analysis for a mixture of the regioisomers (Found: C, 53.8; H, 8.5; Cl, 20,4. Calc. for $C_8H_{15}ClO_2$: C, 53.78; H, 8.40; Cl, 19.89%).

1,2-*Dichloro*-4,4-*dimethylpentan*-3-*one*. δ_H 1.25 (s, 9 H), 4.04 (m, 2 H) and 4.90 (dd, 1 H, *J* 4.8, 10); *m/z* 125 (M − C_4H_9, 0.3), 101, 99 and 97 ($C_2H_3Cl_2$, 0.3, 1.8 and 2.8), 85 (C_5H_9O, 16), 57 (C_4H_9, 100), 41 (C_3H_5, 47) and 39 (C_3H_3, 14). This compound was too unstable for elemental analysis.

2-*Bromo*-1-*methoxy*-4,4-*dimethylpentan*-3-*one*. δ_H 1.20 (s, 9 H), 3.29 (s, 3 H), 3.70 (m, 2 H) and 4.55 (dd, 1 H, *J* 5.5, 9); *m/z* 143 (M − Br, 12), 85 (17), 58 (8), 57 (100), 55 (14), 45 (15), 41 (36) and 39 (11).

1-*Bromo*-2-*methoxy*-4,4-*dimethylpentan*-3-*one*. δ_H 1.22 (s, 9 H), 3.45 (s, 3 H) and 4.21 (m, 3 H); *m/z* 139 and 137 (M − $C_5H_{10}O$, 16 and 16), 58 (C_3H_6O, 69), 57 (100), 43 (21), 41 (38) and 39 (11).

1,2-*Dibromo*-4,4-*dimethylpentan*-3-*one*. δ_H 1.28 (s, 9 H), 3.80 (m, 2 H) and 4.81 (dd, 1 H, *J* 3.7, 10.9); *m/z* 189, 187 and 185 (M^+, 0.9, 2.0 and 1.0), 108 and 106 (C_2H_3Br, 2.6 and 2.6), 85 (23), 57 (100), 55 (C_4H_7, 11), 41 (40) and 39 (13) (Found: C, 31.25; H, 4.5; Br, 58.9. Calc. for $C_7H_{12}Br_2O$: C, 30.91; H, 4.45; Br, 58.76%).

The anti-Markovnikov and Markovnikov regioisomers and dihalides were separated on the capillary column with the following retention times/min, respectively, by programming from 80–160 °C at 5 °C min^{-1}. Chlorination: 7.7, 8.7 and 7.9; bromination: 9.3, 10, 4 and 11.9.

Chlorination of (E)-*Pent*-3-*en*-2-*one* **4**.—3-*Chloro*-4-*methoxypentan*-2-*one* (erythro). δ_H 1.26 (d, 3 H, *J* 6.0), 2.27 (s, 3 H), 3.32 (s, 3 H) and 3.57–4.34 (m, 2 H); *m/z* 115 (M − Cl, 0.04), 78 and 76 (C_2HClO, 8 and 26), 75 (21), 59 (C_3H_7O, 74) and 43 (C_2H_3O, 100).

(threo) *m/z* 115 (M − Cl, 0.04), 78 and 76 (C_2HClO, 8 and 20), 75 (18), 59 (C_3H_7O, 85) and 43 (C_2H_3O, 100).

4-*Chloro*-3-*methoxypentan*-2-*one*. Only one stereoisomer, *erythro*, was observed. δ_H 1.50 (d, 3 H, *J* 5.0), 2.16 (s, 3 H), 3.53 (s, 3 H) and 3.57–4.34 (m, 2 H); *m/z* 109 and 107 (M − 43, 22 and 67), 72 (C_4H_8O, 93).

3,4-*Dichloropentan*-2-*one* (*erythro*) δ_H 1.68 (d, 3 H, *J* 6.0), 2.34 (s, 3 H) and 4.08–4.80 (m, 2 H); *m/z* 156 and 154 (M^+, 0.15 and 0.24), 78 and 70 (C_2HClO, 17 and 54) and 43 (C_2H_3O, 100).

(*threo*) *m/z* C_2HClO, 78 (17) and 76 (49); CH_3CO, 43 (100).

Because of the closeness in retention times, the methoxy chlorides and dichloride products from the various reactions were isolated by preparative GLC and analysed by NMR spectroscopy, using the differences in the chemical shifts of the 5-methyl protons. Retention times of the products, programmed from 70–120 °C at 10 °C min^{-1} were: *erythro*: anti-Markovnikov and dichloride, 4.9; Markovnikov, 5.03. *threo*: anti-Markovnikov and dichloride, 5.2. At lower temperatures, the anti-Markovnikov regioisomer and dichloride, for both *erythro* and *threo* forms, separated slightly, with the dichloride having the shorter retention time. The dichloride was synthesised by chlorination in CH_2Cl_2, and the methoxy chlorides were prepared using CH_3OCl.

The neat compounds, both dichloride and methoxy chloride, decomposed on standing, even in the cold, and therefore gave elemental analyses with considerable error.

Chlorination of Methyl Isopropenyl Ketone **5**.—3-*Chloro*-4-*methoxy*-3-*methylbutan*-2-*one*. δ_H 1.68 (s, 3 H), 2.37 (s, 3 H), 3.45 (s, 3 H) and 3.71 (d, 2 H, *J* 2.0); *m/z* 109 and 107 (M − C_2H_3O, 0.1 and 0.5), 78 and 76 (M − $C_3H_6O_2$, 10 and 74), 75 (38), 45 (C_2H_5O, 46) and 43 (C_2H_3O, 100).

4-*Chloro*-3-*methoxy*-3-*methylbutan*-2-*one*. δ_H 1.35 (s, 3 H), 2.22 (s, 3 H), 3.31 (s, 3 H) and 3.72 (s, 2 H); *m/z* 152 and 150 (M^+, 0.05 and 0.09), 109 and 107 (M − C_2H_3O, 29 and 93) and 43 (C_2H_3O, 89). A satisfactory elemental analysis of a mixture of the regioisomers could not be obtained because of contamination by dichloride.

3,4-*Dichloro*-3-*methylbutan*-2-*one*. δ_H 1.81 (s, 3 H), 2.45 (s, 3 H) and 4.01 (d, 2 H, *J* 2.8); *m/z* 158, 156 and 154 (M^+, 0.09, 0.5 and 0.8), 78 and 76 (C_2H_5Cl, 17 and 55) and 43 (C_2H_3O, 100) (Found: C, 39.0; H, 5.3; Cl, 45.45. Calc. for $C_5H_8Cl_2O$: C, 38.71; H, 5.2; Cl, 45.80%).

The anti-Markovnikov and Markovnikov regioisomers, and the dichloride were separated on the capillary column with the following retention times/min, by programming from 35–120 °C at 25 °C min^{-1}: 5.4, 5.9 and 5.5, respectively.

Chlorination and Bromination of 4-*Chlorobut*-3-*en*-2-*one* (**6**) *and* 4-*Methoxybut*-3-*en*-2-*one*.—Chlorination of **6** in CH_3OH gave 1,1,2-trichlorobutan-3-one and 2-chloro-1,1-dimethoxybutan-3-one in 71% yield. We assume that the 2-chloro-1,1-dimethoxybutane was derived from solvolysis of the authentic anti-Markovnikov (AM) product, 1,2-dichloro-1-methoxybutan-3-one, since we established in a separate experiment that 1,2-dichloro-1-methoxybutan-3-one, prepared from the chlorination of 4-methoxybut-3-en-2-one in CH_2Cl_2 reacts immediately with CH_3OH to give 2-chloro-1,1-dimethoxybutan-3-one. All efforts to detect the Markovnikov (M) product, 1,1-dichloro-2-methoxybutan-3-one failed. Only the peak for trichloride disappeared during elimination with triethylamine. If the M regioisomer were present, we would expect it to eliminate. No new peaks appeared. Chlorination in ethanol did not produce the M regioisomer. Also, methyl hypochlorite, CH_3OCl, which was used with other alkenes to make the regioisomers, failed to react with **6** to give either M or AM regioisomers. 1,1,2-Trichlorobutan-3-one is stable in CH_3OH and eliminates only slowly when pyridine is present. Upon standing in CH_3OH, **6** was slowly converted to 4-methoxybut-3-en-2-one, and then to 1,1-dimethoxybutan-3-one.

The products from the chlorination of the above compounds were unstable and could not be isolated by preparative GLC. Their structures were established from their mass and NMR spectra. NMR spectra were made on a crude reaction mixture where GLC analysis had confirmed that the compound under consideration was the major component.

1,1,2-*Trichlorobutan*-3-*one*. This compound was prepared by chlorination of **6** in CH_2Cl_2. GLC analysis indicated a high

yield. δ_H 2.40 (s, 3 H), 4.52 (d, 1 H, *J* 6.0) and 6.08 (d, 1 H, *J* 6.0); *m/z* 159 (M − CH_3, 0.002), 137, 135, 133 and 131 (M − C_2H_3O, 0.04, 0.22, 0.70 and 0.73), 100, 48 and 96 ($C_2H_2Cl_2$, 1.7, 11.1 and 16.9), 63 and 61 (C_2H_2Cl, 2.6 and 6.3) and 43 (C_2H_3O, 100).

1,2-*Dichloro*-1-*methoxybutan*-3-*one*. This compound was prepared by chlorination of 4-methoxybut-3-en-2-one in CH_2Cl_2. GLC analysis indicated a high yield. δ_H 2.35 (s, 3 H), 3.60 (s, 3 H), 4.28–4.29 (m, 1 H) and 5.57–5.78 (m, 1 H); *m/z* 137 and 135 (M − Cl, 0.87 and 3.10), 94 and 92 (C_3H_5ClO, 14 and 41), 85 ($C_4H_5O_2$, 6.5), 81 and 79 (C_2H_4ClO, 2.0 and 7.0) and 43 (C_2H_3O, 10.0).

2-*Chloro*-1,1-*dimethoxybutan*-3-*one*. This compound was synthesised either by chlorination of 4-methoxy-3-but-2-enone in CH_3OH or by solvolysis of 1,2-dichloro-1-methoxybutan-3-one in CH_3OH. GLC analyses indicated that the yields of both reactions were high. The NMR and mass spectra were made on the crude product from the chlorination of 4-methoxybut-3-en-2-one. δ_H 2.31 (s, 3 H), 3.36 (s, 3 H), 3.40 (s, 3 H), 4.02–4.20 (m, 1 H) and 4.47–4.82 (m, 1 H); *m/z* 165 (M − H, 0.10), 137 and 135 (M − CH_3O, 0.92 and 2.9), 131 (M − Cl, 1.6), 94 and 92 (C_3H_5ClO, 5.0 and 16), 75 ($C_3H_7O_2$, 78), 43 (C_2H_3O, 100).

The compounds, in the order listed above, were analysed on the capillary column with the following retention times/min, by programming from 45–90 °C at 5 °C min^{-1}: 11.5, 11.5 and 13.0, respectively.

All of the products encountered in the bromination of **6** and 4-methoxybut-3-en-2-one were unstable, and decomposed rapidly when the solvent was removed. Therefore, NMR spectra were performed directly on reaction mixtures. 1,2-Dibromo-1-methoxybutan-3-one solvolysed rapidly in CH_3OH to give 3-bromo-1,1-dimethoxybutan-3-one. No Markovnikov regioisomer was detected. The product ratio from the bromination of **6** in CH_3OH was the same with and without NBS: 1,2-dibromo-1-chlorobutan-3-one (90%) and 2-bromo-1,1-dimethoxybutan-3-one (AM, from solvolysis of 1,2-dibromo-1-methoxybutan-3-one, 10%).

1,2-*Dibromo*-1-*chlorobutan*-3-*one*. This compound was prepared by the bromination of **6** in CH_2Cl_2. GLC analysis on the capillary column, programmed from 75–130 °C at 5 °C min^{-1}, showed two peaks with retention times/min 11.5 (82%) and 11.6 (18%), respectively. The two compounds were assumed to be diastereoisomers, since their mass spectra were identical. δ_H 2.44 (s, 3 H), 4.60–4.93 (m, 1 H) and 5.90–6.18 (m, 1 H); *m/z* 225, 223, 221 and 219 (M − C_2H_3O, 0.55, 0.23, 0.36 and 0.17), 144, 142 and 140 (C_2H_2Cl, 0.5, 2.2 and 1.8), 143, 141 and 139 (C_2HBrCl, 0.14, 0.39 and 0.25), 91 and 89 (C_3HClO, 0.6 and 4.7) and 43 (C_2H_3O, 100).

1,2-*Dibromo*-1-*methoxybutan*-3-*one*. This compound was synthesised by the bromination of 4-methoxybut-3-en-2-one in CH_2Cl_2. Its retention time was 9.4 min under the analysis of conditions mentioned above. δ_H 2.09 (s, 3 H), 3.29 (s, 3 H). 4.24–4.88 (m, 1 H) and 5.87–6.18 (m, 1 H); *m/z* 181 and 179 (M − Br, 7.7 and 8.2), 138 and 130 (M − Br–C_2H_3O, 4.7 and 5.0), 85 ($C_4H_5O_2$, 14) and 43 (C_2H_3O, 100).

2-*Bromo*-1,1-*dimethoxybutan*-3-*one*. This compound was synthesised by bromination of 4-methoxybut-3-en-2-one in CH_3OH. Its retention time was 9.4 min under the conditions listed above. δ_H 2.27 (s, 3 H), 3.38 (s, 3 H), 3.40 (s, 3 H), 4.00–4.29 (m, 1 H) and 4.56–4.83 (m, 1 H); *m/z* 138 and 136 (C_3H_4BrO, 7.4 and 7.3), 85 ($C_4H_5O_2$, 11) 75 (C_3H_7O, 100) and 43 (C_2H_3O, 94).

Chlorination of Cyclohex-2-enone **7**.—2-*Chloro*-3-*ethoxycyclohexanone*. δ_H 1.20 (t, 3 H, *J* 7.0), 1.54–2.27 (m, 4 H), 3.58 (q, 2 H, *J* 7.0) and 3.71–4.36 (m, 6 H). The above compound was isolated from a chlorination mixture using column chromatography. Its NMR spectrum was similar to the spectrum from the analogous methoxy bromide,[1] except for the ethyl group in the present case. *m/z* 178 and 176 (M^+, 0.21 and 0.59), 141 (M − Cl, 8.5), 133 and 131 (M − C_2H_5O, 0.66 and 2.1), 83 (C_5H_7O, 100), 85 (C_5H_9O, 65) and 57 (C_7H_5O, 99). The above compound was too unstable for elemental analysis.

3-*Chloro*-2-*ethoxycyclohexanone*. The evidence for the structure of this compound is based entirely on its mass spectrum. It is a significant product (22%) in the reaction of cyclohex-2-enone with C_2H_5OCl. *m/z* 176 (M^+, 0.59), 141 (M − Cl, 6.2), 98 ($C_5H_6O_2$, 36), 97 ($C_5H_5O_2$, 40), 85 (C_5H_9O, 88) and 57 (C_7H_5O, 100).

2,3-*Dichlorocyclohexanone*. The structure of the dichloride was confirmed by elimination with diethylamine to give the monochloride, whose m.p. compared favourably to that reported in the literature.[7] The dichloride decomposed during attempted distillation. The NMR spectrum of the crude material supported the structure, as did the mass spectrum. δ_H 1.10–3.15 (m, 6 H) and 3.82–4.86 (m, 2 H); *m/z* 168 and 166 (M^+, 4.8 and 7.7), 133 and 131 (M − Cl, 51 and 16), 104 and 102 (C_5H_7Cl, 11 and 36), 90 and 88 (C_4H_5Cl, 31 and 100) and 77 and 75 (C_3H_4Cl, 16 and 47).

2-*Chlorocyclohex*-2-*enone*. The structure of this compound was confirmed, as described above, by comparing its m.p. with that reported in the literature, and from its NMR and mass spectra. δ_H 1.80–2.32 (quintet, 2 H), 2.32–2.84 (m, 4 H) and 6.89–7.30 (t, 1 H); *m/z* 132 and 130 (M^+, 29 and 92), 104 and 102 (C_5H_7Cl, 28 and 100), 91 and 89 (C_4H_6Cl, 15 and 49) and 76 and 74 (C_3H_3Cl, 20 and 67).

GLC analyses were performed by programming from 90–130 °C at 5 °C min^{-1}. Retention times/min were: anti-Markovnikov, 10.2; Markovnikov, 10.4; dichloride, 8.8; monochloride, 8.0.

Chlorination of Methyl Acrylate **8**.—*Methyl* 2-*chloro*-3-*methoxypropanoate*. δ_H 3.37 (s, 3 H), 3.78 (s, 3 H) and 4.20 (t, 1 H, *J* 7.0). The methylene protons were partially obscured by the singlet at 3.78 ppm. *m/z* 123 and 121 (M − CH_3O, 0.69 and 2.0), 117 (M − Cl, 6.2), 95 and 93 (M − $C_2H_3O_2$, 1.24 and 3.8), 59 ($C_2H_3O_2$, 5.9) and 45 (C_2H_5O, 100).

Methyl 3-*chloro*-2-*methoxypropanoate*. δ_H 3.45 (s, 3 H), 3.76 (s, 3 H) and 3.53–4.10 (m, 3 H); *m/z* 124 and 122 (M − CH_2O, 2.2 and 7.2), 95 and 93 (M − $C_2H_3O_2$, 32 and 100), 59 ($C_2H_3O_2$, 7.0) and 43 (C_2H_3O, 100) [Found: C, 39.1; H, 5.85; Cl, 23.1. Calc. for $C_5H_9O_3Cl$ (mixture of regioisomers): C, 39.36; H, 5.95; Cl, 23.24%].

Methyl 2,3-*dichloropropanoate*. This compound has been described previously.[8]

The anti-Markovnikov regioisomers and the dichloride were separated on the capillary column with the following retention times/min, respectively, by programming from 45–100 °C at 3 °C min^{-1}): 11.7, 12.7 and 10.9, respectively.

Chlorination of Methyl (E)-*Crotonate* (**9**).—*Methyl* 2-*chloro*-3-*methoxybutanoate*. The structure of this compound was established by elemental analysis (mixture of regioisomers), and by comparison of its NMR spectrum with that reported previously.[9]

Methyl 3-*chloro*-2-*methoxybutanoate*. The structure of this compound was confirmed by elemental analysis and its mass spectrum. *m/z* 109 and 107 (M − $C_2H_3O_2$, 32 and 100), 65 and 63 (CH_3CHCl, 0.015 and 0.042), 59 ($C_2H_3O_2$, 11) and 57 (C_3H_5O, 78) [Found: C, 43.1; H, 6.4; Cl, 21.3. Calc. for $C_6H_{11}O_3Cl$ (mixture of regioisomers): C, 43.3; H, 6.65; Cl, 21.28%].

Methyl 2,3-*dichlorobutanoate*. This compound has been described previously.[8]

The anti-Markovnikov and Markovnikov regioisomers and the dichloride were separated on the capillary column with the

following retention times/min, by programming from 40–100 °C at 3 °C min^{-1}: 15.2, 15.6 and 14.7, respectively.

Chlorination of Methyl Methacrylate (**10**).—*Methyl 2-chloro-3-methoxy-2-methylpropanoate.* δ_H 1.70 (s, 3 H), 3.36 (s, 3 H), 3.76 (3 H) and 3.57–3.90 (m, 2 H); *m/z* 109 and 107 (M − $C_2H_3O_2$, 1.4 and 4.6) and 43 (C_2H_3O, 100).

Methyl 3-chloro-2-methoxy-2-methylpropanoate. δ_H 1.45 (s, 3 H), 3.25 (s, 3 H), 3.61 (s, 2 H) and 3.76 (s, 3 H); *m/z* 117 (M − CH_2Cl, 18), 109 and 107 (M − $C_2H_3O_2$, 31 and 100), 57 ($C_2H_3O_2$, 88) and 45 (4). Elemental analysis of a mixture of the regioisomers (Found: C, 43.0; H, 6.6; Cl, 23.0. Calc. for $C_6H_{11}ClO_3$: C, 43.24; H, 6.61; Cl, 21.32%). The regioisomers were contaminated with a trace of dichloride.

Methyl 2,3-dichloro-2-methylpropanoate. δ_H 1.95 (s, 3 H), 4.00 (s, 3 H) and 3.76–4.35 (m, 2 H); *m/z* 113 and 111 (M − $C_2H_3O_2$, 9 and 15), 78 and 76 (C_2HClO, 32 and 100) (Found: C, 35.5; H, 4.8; Cl, 41.6. Calc. for $C_5H_8Cl_2O_2$: C, 35.09; H, 4.68; Cl, 41.15%).

The anti-Markovnikov and Markovnikov regioisomers and the dichloride were separated on the capillary column, with the following retention times/min by programming from 50–120 °C at 3 °C min^{-1}: 12.61, 14.71 and 12.37, respectively.

Synthesis and Chlorination of Methyl (E)- *and* (Z)-3-*Chloroprop-2-enoate* (**11**).—A mixture of isomers (*ca.* 50:50) of **11** was obtained by adding gaseous HCl to methyl propiolate in CH_3OH. (The reaction did not occur in CH_2Cl_2.) The mass spectra of the *E*- and *Z*-isomers were identical. *m/z* 122 and 120 (M^+, 9 and 2.9), 91 and 89 (M − CH_3O, 100 and 31), 63 and 61 (C_2H_2Cl, 33 and 11) and 59 ($C_2H_3O_2$, 8). Confirming peaks in the IR spectra (ν/cm^{-1}) for *E*- and *Z*-isomers, respectively: 2853 and 2860 (CH_3O), 1749 and 1750 (CO) and 1613 and 1620 (C=C). Exclusive for *E*, 939 (CH=CH, *trans*); for *Z*, 806 (CH=CH).

Methyl 2,3,3-trichloropropanoate. m/z 163, 161 and 159 (M − CH_3O, 4 and interference with next peak), 159, 157 and 155 (M − Cl, interference, 6 and 9), 135, 133 and 131 ($C_2H_2Cl_3$, 5, 16 and 16), 100, 98 and 96 ($C_2H_2Cl_2$, 9, 62 and 100) and 59 ($C_2H_3O_2$, 100). Confirming peaks in the IR spectrum (ν/cm^{-1}).

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