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# REACTION OF HALOGENS WITH SOME α,β-UNSATURATED ALDEHYDES AND KETONES

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Abstract: Mechanisms are proposed to account for evidence indicating that some simple α,β-unsaturated aldehydes and ketones do not react with halogens by the expected attack on the C=C bond.

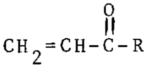
We would like to report several unusual aspects of the reactions of some α,β-unsaturated aldehydes and ketones with halogens ($Br_2$,$Cl_2$,BrCl). For example, when we added $Br_2$ in $CH_2Cl_2$ to phenyl vinyl ketone (1) we were surprised to observe that the reaction occurred extremely rapidly - almost violently. Furthermore, we established that the regiochemistry of the product (2) from addition of BrCl was exclusively α-bromo-β-chloro:

$$CH_2{=}CH{-}\overset{\overset{O}{\|}}{C}{-}\phi + BrCl \qquad \underset{Cl}{\underset{|}{CH_2}}{-}\underset{Br}{\underset{|}{CH}}{-}\overset{\overset{O}{\|}}{C}{-}\phi$$

1 2

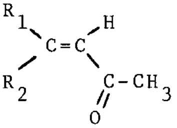
Based on our previous studies on the additions of the halogens to methyl acrylate,[1] methyl crotonate,[1] methyl isocrotonate,[1] and ethyl sorbate,[2] we assumed that the halogenation of 1 would be very slow[3] and give both regioisomers.[4]

The reactions of the halogens with 1 and the following α,β-unsaturated carbonyl compounds were instantaneous and gave exclusively α-bromo-β-chloro products with BrCl: acrolein (3), methyl vinyl ketone (4), cis-(5) and trans-3-penten-2-one (6). Competitive rate studies (bromination) of 3 and 4 with 1-hepten



$$CH_2{=}CH{-}\overset{\overset{O}{\|}}{C}{-}R$$

3: R=H
4: R=$CH_3$



5: $R_1$=H, $R_2$=$CH_3$
6: $R_1$=$CH_3$,$R_2$=H

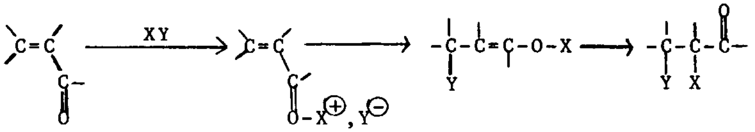
provide a quantitative insight into the great reactivity of the carbonyl compounds: 3/1-heptene = 2.71; 4/1-heptene = 4.04.

The literature contains essentially no mention of this unexpected reactivity Years ago, Ingold and Anatakrishnan[5] observed that 3 reacted rapidly with bromine in the presence of hydrogen bromide, but there was no mention of bromination without acid catalyst. At about the same time, White and Robertson[6] reported that crotonaldehyde reacted rapidly with $Cl_2$ compared to crotonic acid.

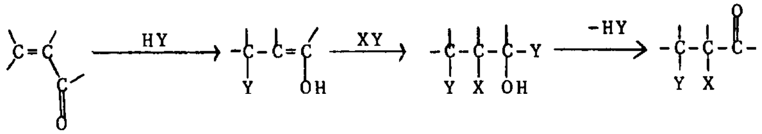
We assume that the mechanism of reaction cannot involve electrophilic attack of halogen on the C=C bond since the rate and regiochemistry data do not support this mechanism.[3,4] Further evidence against electrophilic attack on the C=C bond was provided by analysis of the stereochemistry of the dichlorides from chlorination [7] of 5 and 6. Chlorination of 5 was non-stereospecific, with both 5 and 6 giving identical ratios of dichloride diastereomers (ratio= 93:7).[8] Based on our previous studies, [1,2] we would have predicted that the additions would be stereospecific if electrophilic attack on the C=C bond occurred.[9]

Two other mechanisms are possible. One (Mechanism A) involves initial attack of halogen on the oxygen, and the other (Mechanism B) involves initial addition of a trace of HY to give a highly reactive enol. These two mechanisms are outlined below, where X and Y equal halogen:

Mechanism A - Carbonyl Attack

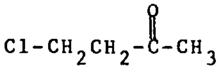


Mechanism B - Enol Formation

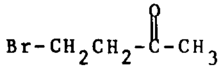


Preliminary data suggest that $Cl_2$ and BrCl are adding by Mechanism B.[10,11] Here is the evidence: The rates of addition of $Cl_2$ and BrCl to 4 in a stirred slurry of $NaHCO_3/CH_2Cl_2$ are slowed significantly ($Cl_2$, ca. 0.5 hr; BrCl, ca. 2 hrs).[12] Moreover, the effect of $NaHCO_3$ appears to be related to the removal of catalytic amounts of HCl since we have established that HCl adds instantly to 4 in $CH_2Cl_2$ to give 4-chlorobutan-2-one (7), but, in the $NaHCO_3/CH_2Cl_2$ slurry, the acid is completely neutralized before addition to give 7 can occur.

Sodium bicarbonate, $NaHCO_3$, does not affect the rate of addition of $Br_2$ to 4, suggesting that Mechanism A may be involved in this case.[13] Again, we have established that the addition of HBr to give 4-bromobutan-2-one (8) can be prevented with the $NaHCO_3/CH_2Cl_2$ slurry.[14]

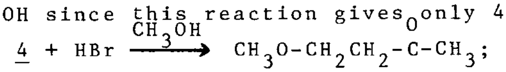

$Cl-CH_2CH_2-\overset{O}{\overset{\|}{C}}-CH_3$

7


$Br-CH_2CH_2-\overset{O}{\overset{\|}{C}}-CH_3$

8

Further support for Mechanism A in the addition of $Br_2$ to 4 comes from preliminary studies on the bromination of 4 in methanol ($CH_3OH$). We have established that 8 is a major product in this reaction, along with dibromide, 4-methoxybutan-2-one (9), and the β-methoxy, α-bromo addition product (10). 8 Does not result from addition of HBr to 4 in $CH_3OH$ since this reaction gives only 4-methoxybutan-2-one (9):

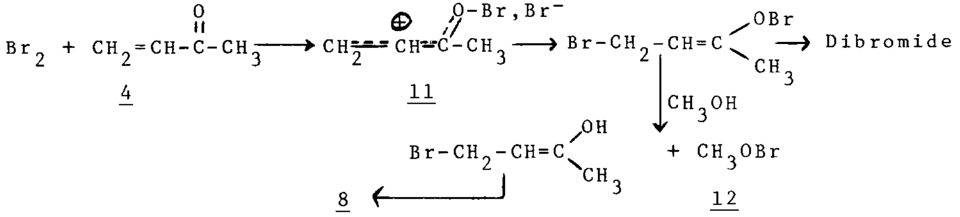


$$4 + HBr \xrightarrow{CH_3OH} CH_3O\text{-}CH_2CH_2\text{-}\overset{O}{C}\text{-}CH_3$$

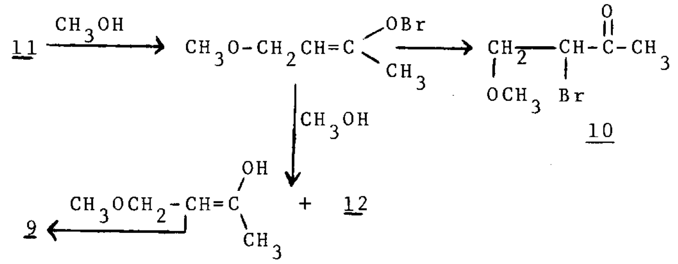
; No 8 is formed.

9

We suggest that 8 is formed by a series of reactions involving initial attack of $Br_2$ on the carbonyl group of 4 (Mechanism A), conceivably as shown below:



9 and 10 Are formed by attack of methanol on intermediate 11:



Methyl hypobromite (12) can add to 4 to give the β-methoxy, α-bromo addition product.[15,16] 4-Chlorobutan-2-one (11) is not formed when $Cl_2$ or BrCl react with 4 in $CH_3OH$. At this time, we do not have an explanation for the apparent differences in mechanisms in the reactions of $Br_2$ and the other halogens with 4.

We are currently examining the products of the reactions of 4, 5, and 6 with the halogens in $NaHCO_3/CH_2Cl_2$. Preliminary results indicate that: the yields for $Br_2$ and BrCl are similar with or without base, but are significantly lower for $Cl_2$ in base; the regiochemistry for 4 and BrCl is unchanged in base; base has no major effect on the stereochemistry in the addition of the halogens to 5 and 6. These preliminary results may suggest that in the presence of base either $Cl_2$ and BrCl are reacting slowly by Mechanism B, or that base has caused a switch to Mechanism A.

All reactions were done at 0.02 - 0.04 mol fraction in olefin, at room temperature, and at low completion (ca. 20%). Yields were high (ca. 85%), except as indicated with chlorine and base. The structures of all products were established by nmr and ir. Whenever possible physical properties were compared to reported values. All dihalides were converted, using the elimination procedure reported previously,[1] to α-halo, α,β-unsaturated carbonyl compounds whose structures were confirmed by nmr and ir. This elimination procedure was also used to establish the regiochemistry of the BrCl adducts.

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1. V.L. Heasley, D. Spaite, D.F. Shellhamer, and G.E. Heasley, *J. Org. Chem.*, **44**, 2608 (1979).
2. D.F. Shellhamer, V.L. Heasley, J.E. Foster, J.K. Luttrull, and G.E. Heasley, *J. Org. Chem.*, **42**, 2141 (1977).
3. The reaction of methyl acrylate with comparable amounts of bromine is very slow (19 hrs).[1]
4. BrCl addition to methyl acrylate and the methyl crotonates gave both the α-bromo-β-chloro and α-chloro-β-bromo regioisomers, with the latter being the minor product.[1] We anticipated that the carbonyl group in the ketones and aldehydes might accelerate α-attack by chloride in the intermediate halonium ions giving a greater amount of the α-chloro-β-bromo regioisomer. (See reference 1 for a discussion of the effect of carbonyl groups on $S_N^2$ reactions.
5. S.V. Anatakrishnan and C.K. Ingold, *J. Chem. Soc*., 1935, 1396.
6. E.P. White and P.W. Robertson, *J. Chem. Soc.*, 1939, 1509.
7. Ratios of diastereomers from addition of $Br_2$ and BrCl to **5** and **6** were identical for each halogen, but these data may not be valid since **5** is converted to **6** during the course of the reaction.
8. The principal diastereomer is probably *erythro* (the most stable from model studies) since oxidation of the dichloride from *trans*-3-penten-2-ol (an *erythro* isomer--assuming anti addition of $Cl_2$) gave only the major diastereomer. Oxidation of the dichloride from the *cis*-alcohol gave the minor diastereomer.
9. We have observed that the chlorination and bromination[1] of methyl isocrotonate are highly stereospecific.
10. The regiochemistry of BrCl addition cannot be used to distinguish between Mechanisms A or B because either mechanism should give the α-bromo-β-chloro regioisomer. In Mechanism A, the carbonyl will attack the bromine atom, and in Mechanism B, the enol addition product will release HCl.
11. The enol mechanism has been postulated in the chlorination of cinnamaldehyde in acetic acid. However, no rate enhancement was reported. (M.C. Cabaleiro, C.J. Cooksey, M.D. Johnson, B.E. Swedland, and J.G. Williams, *J. Chem. Soc*., *Perkin II*, 1968, 1026).
12. The decrease in rate is not due to the formation of an unreactive electrophile since the color disappeared instantly when 1-heptene was added.
13. The relative rate (**4**/1)-heptene) was unaffected by $NaHCO_3$.
14. Less HBr than HCl can be removed by base, but 1% HBr (compared to the bromine) in the presence of $NaHCO_3$ produced no **8**.
15. $CH_3OBr$ (**12**) readily adds to alkenes: V.L. Heasley, C.L. Frye, G.E. Heasley, K.A. Martin, D.A. Redfield, and P.S. Wilday, *Tetrahedron Lett*. **18**, 1573 (1970).
16. We have observed that alkyl hypochlorites exchange chlorine rapidly with alcohols, supporting the suggestion that the intermediate hypobromite will react with $CH_3OH$ to give **12**.

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