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INTERACTION OF α,β-UNSATURATED KETONES WITH HYDROGEN HALIDES. ADDITION VS. SALT FORMATION

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The protonation of α,β-unsaturated ketones in strong non-nucleophilic acids, such as sulfuric and perchloric acids, has recently been studied in detail.[1] However, the interaction of these compounds with nucleophilic acids, such as the hydrogen halides, has not been investigated in a systematic manner. We wish to report that while many unsaturated carbonyl compounds add the hydrogen halides across the double bond readily,[2] others are only protonated on the carbonyl oxygen to give relatively stable salts, which show no tendency toward addition.

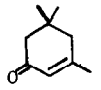
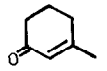
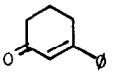
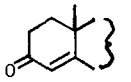
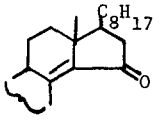
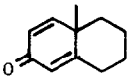
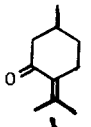
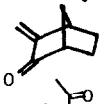
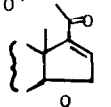
We have recently reported[3] the first example of isolation of a crystalline salt from HBr and an aliphatic enone, isophorone (1). We have now investigated a number of other enones and related compounds. Their behavior with the hydrogen halides and with sulfuric acid is summarized in the table. The reactions were readily followed by the changes in the NMR spectra when excess HX gas was bubbled into a solution of the enone in $CDCl_3$ at room temperature.

In the cases where salt formation was observed, a deshielding of all the peaks of the starting enone occurred, the amount of deshielding approximately reflecting the expected charge density at each carbon atom. For example, vinyl protons α to the carbonyl group were deshielded by ca. 1 ppm. The spectra were essentially identical to the spectra in H_2SO_4, thus verifying that protonation was complete.[1] That protonation occurred only on oxygen was shown by the lack of exchange of the vinyl protons of the enones in D_2SO_4 solution.[4]

In all cases where addition of HX occurred, the NMR spectra observed immediately after mixing of the reagents were those expected for the β-halo ketones, which could be isolated essentially pure by removal of the solvent. Thus, the common methods of addition, such as

TABLE

INTERACTION OF ENONES WITH HX

No.	Compound: Name	Compound: Formula	Reaction with: HCl	HBr	HI	H_2SO_4
1	isophorone		none	salt	salt	salt
2	3-methylcyclohexenone		none	salt	salt	salt
3	3-phenylcyclohexenone		none	salt	salt	salt
4	16-dehydroprogesterone		none	salt	salt	salt
5	3 β-acetoxy-5 α-cholest-8(14)-en-15-one		none	salt	salt	salt
6	10-methyldecalin-1,4-dien-3-one		salt	salt	salt	salt
7	cyclohexenone		none	none	adds	polymerizes
8	cyclopentenone		none	none	adds slowly	polymerizes
9	pulegone		adds	adds	adds	salt
10	3-methylenenorbornan-2-one		adds	adds	adds	polymerizes
11	16-dehydroprogesterone		adds	adds	adds	salt
12	dibenzalacetone	$\phi CH{=}CHC(=O)CH{=}CH\phi$	salt or adds	salt or adds	salt or adds	salt
13	chalcone	$\phi CH{=}CHC(=O)\phi$	salt or adds	salt or adds	salt or adds	salt
14	methyl vinyl ketone	$CH_2{=}CHC(=O)CH_3$	adds	adds	adds	polymerizes
15	ethyl acrylate	$CH_2{=}CHC(=O)OEt$	none	adds	adds	polymerizes
16	methyl ethynyl ketone	$HC{\equiv}CC(=O)CH_3$	adds	adds	adds	polymerizes

allowing the enones to stand for prolonged periods in HOAc-HX solution[2] would seem to be unnecessary, as would indirect synthetic methods.[5]

As is the case with isophorone,[3] the enones which formed salts with HBr or HI absorbed a maximum of two moles of the hydrogen halide. The $HX_2^{\ominus}$ salts are believed to be the major species in solution under these conditions. A number of attempts to obtain crystalline HBr salts from these compounds gave only colored oils.

The cyclohexadienone 6 is worthy of comment. With HBr in $CDCl_3$ at 25°, protonated 6 undergoes the dienone-phenol rearrangement with a half-life of ca. three days. This is consistent with Vitullo's recent findings[6] that protonation of cyclohexadienones occurs prior to rearrangement in sulfuric acid. The weaker acid HCl protonates 6 to the extend of ca. 10% under our conditions, whereas the enones are not protonated at all. Saturated ketones are not even protonated to an extent detectable by NMR by the stronger acid HBr. The findings are consistent with the relative basicities of the compounds.[7]

Although many examples of addition reactions of this type are known,[2] reports of salt formation are very rare. Examples are known in which an enone grouping is inert to addition during addition of HX to an isolated double bond in the same molecule.[8,9] In one such case, Wolinsky[9] has shown that carvone hydrobromide is completely protonated in HBr-HOAc solution and does not add HBr, though no characterization of the salt was attempted. β-phenyl substituted enones, such as dibenzalacetone (12) and chalcone (13) have long been known[10] to form highly colored salts with the hydrogen halides. However, these are unstable and rearrange to the addition products readily. Isolation of the salts seems to be an artefact of their insolubility in non-polar media, since addition occurs readily if the salts are dissolved in a more polar solvent, such as nitromethane.

The fundamental difference between the enones which form salts and those which form addition compounds is seen to involve the thermodynamic stability of the addition products which would be formed. Doubtedlessly, protonation preceeds the attack of $X^{\ominus}$ to give the addition product. In the cases in which the addition product would be sterically crowded, by forcing a group into an axial position or other similar reason, the addition step is blocked and the salt is observed. Just such cases are represented by compounds 1-6. An earlier hypothesis,[11] that cisoid enones undergo addition and transoid ones form salts with hydrogen halides is shown to be untenable from the results with compounds 5, 7, and 8.

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10. Cf. D. Vorlander and C. Tubandt, Ber., 37, 1644 (1904).

11. J. N. Marx, 161st. National ACS Meeting, Los Angeles, Abstr. ORGN. No. 105.