COMPLEX KINETICS OF ACID-CATALYSED HALOGENATION OF ALIPHATIC KETONES:

α-METHYL SUBSTITUENTS EFFECTS ON ENOLISATION AND ENOL KETONISATION RATES.

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Our knowledge of the slow ketone-enol interconversion for saturated aliphatic ketones is practically limited (1) to the enolisation rate constants which are easily accessible but whose interpretation in terms of structural effects is generally unsatisfactory. The kinetic study of the bromination and iodination, at very low halogen concentration, in a strongly acidic medium, makes it possible to examine the reverse reaction, the ketonisation affecting prototropy.

Under our experimental conditions, two rate constants are determined (2), the catalytic enolisation constant ($k_1 = K_{X_2C} \cdot k_1'$ [1]), and the apparent enol halogenation constant (bromination and iodination) ($k_{II}^2 = k_1 \cdot k_{X_2}/k_{-1} = K_E \cdot k_{X_2}$ [2]), corresponding to the mechanism:
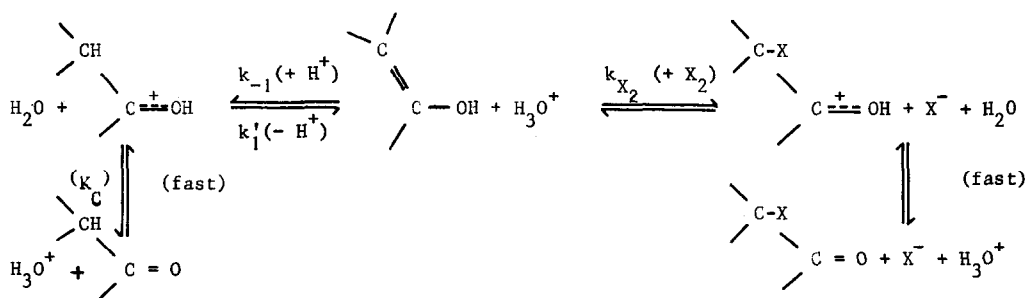
The ratio of these two experimental constants corresponds in fact, to that of the rate constants for ketonisation and halogenation of the enol or, in other terms, competitive electrophilic additions of proton and halogen:

$$k_1/k_{II}^{X_2} \;=\; k_{-1}/k_{X_2} \qquad\qquad [3]$$

These constants have been measured for three ketones: acetone, diethylketone and di-iso-propylketone.

TABLE I

Absolute and relative (*) enolisation rate constants (k_1) (3)
and ketonisation-halogenation rate ratios (k_{-1}/k_{X_2})

Enol	k_1 (**) ($M^{-1} sec.^{-1}$)		k_{-1}/k_{Br_2}		k_{-1}/k_{I_2}	
	abs.	rel.	abs.	rel.	abs.	rel.
$CH_3 - C(OH) = CH_2$ (a)	$2.5.10^{-5}$	1	$1.4.10^{-6}$	1	$1.5.10^{-6}$	1
$CH_3-CH_2-C(OH)=CH-CH_3$ (b)	$2.4.10^{-5}$	0.96	$0.24.10^{-6}$	0.17	$0.23.10^{-6}$	0.16
$(CH_3)_2CH - C(OH) = C(CH_3)_2$ (b)	$0.16.10^{-5}$	0.064	$0.036.10^{-6}$	0.026	$0.033.10^{-6}$	0.022

(a) $\left[H_2SO_4 \right] = 0.1$ M;   (b) : $\left[H_2SO_4 \right] = 0.5$ M
ketone concentration ca. 10^{-2} M
Initial analytical bromine or iodine concentrations : $10^{-5} - 5.10^{-7}$ M
(*) relative to acetone
(**) Determined from both bromination and iodination measurements.

The variations of k_{-1}/k_{X_2} must be considered in the light of information obtained on the reactivity of enols, or of their ethers, with halogens or the proton. We have shown (preceding communication) that, for the three enols studied here, iodine and bromine react with a given enol at very similar rates. This result may be attributed either to diffusion limited kinetics or to a low degree of transition state polarity. In either cases, the elementary constants (k_{X_2}) should depend little on enol structure. This we have confirmed by an investigation of the bromination of enol ethers (4) which serve as a good model for enols. Rate constants for ethyl vinyl ethers are only very slightly modified by α- or β-methyl substituents.

Hydrolysis of enol ethers, the slow step of which is the addition of a proton to the double bond (5), is formally analogous to enol ketonisation (see ref 2 c) as far as the rate determining step is concerned, therefore, it is a good model for an analogy of structural effects. α- and β-methyl substituents alter (6,7) the hydrolysis rate constants of ethyl vinyl ethers much more markedly than the rate constants of bromination.

These properties of enols and their ethers lead us to propose the

hypothesis that the variations in k_{-1}/k_{X_2} are caused predominantly by variations in the keto-
nisation constants.

Following the enol-enol ether analogy, the structural effects on this
ratio could be compared with the hydrolysis constants of the corresponding ethers of the enols
of acetone, diethylketone and di-iso-propylketone. Although the hydrolysis constants of these
ethers are not known (except $CH_3 - C(OEt) = CH_2$ (7))we can anticipate important or predominant
β(relative to OH-group)-methyl substituents effects, analogous to those which arise for
β-methyl substituted ethyl vinyl ether:

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TABLE II

Relative hydrolysis rate constants for β-methyl vinyl ethers

(water-dioxan). (6)

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EtO - CH = CH$_2$			1
	cis		0.29
EtO - CH = CH - CH$_3$	{		
	trans		0.12
EtO - CH = C(CH$_3$)$_2$			0.03

Each β-methyl substituent causes a decrease in the hydrolysis rate cons-
tant. This result has been interpreted (6) in terms of hyperconjugation. Here, the same effects
on k_{-1}/k_{X_2} are observed, both in direction and in magnitude. That is, the effects of methyl
substituents on the β-carbon relative to the OH group lead to a decrease in the ketonisation
rate constant (8), if we suppose that these are the most important effects. Analogously, we
attribute the bulk of these variations to hyperconjugative effects; methyl substituents sta-
bilize the enol and destabilize the intermediate hydroxy-oxocarbonium ion.

These conclusions lead us to reexamine the variations in the rate cons-
tant of the reverse reaction, enolisation. If it is accepted that there is some sort of re-
lationship (rate constant vs. equilibrium constant) between the rate constant k_1' of the rate
determining step of the enolisation and the equilibrium constant k_1'/k_{-1} (as is generally ob-
served in the proton transfer reactions), the hyperconjugative effects observed for ketoni-
sation, i.e. on k_{-1}, must operate in the opposite sense on k_1' and thus modify the overall e-
nolisation constant k_1. These effects are compatible with the apparent identity between the
enolisation constants of acetone and diethylketone if one takes into account a statistical
factor for the labile hydrogen atoms; they do not, however, provide an explanation of the
low value of the enolisation constant of di-iso-propylketone (see tableI). To explain this
behaviour one should think of a supplementary factor which opposes the hyperconjugative effects
which favor the most substituted enol formation. For such a ketone, the interaction between
cis iso-propyl and methyl groups, which would hinder the enol formation, should in all

likelyhood be considered. Consequently for this ketone, the stability constant of the enol (K_E) should be small in spite of its stabilisation by hyperconjugation. In agreement with this, studies of the variations of $k_{II}^{X_2}$, assuming k_{X_2} to be constant, yield a relatively small value for this ketone. We find the value of $k_{II}^{X_2}$ for acetone to be 17, for diethylketone 105, and would expect a value much greater than 44 for di-iso-propylketone, if hyperconjugative effects alone were operative. This cis steric effect is probably responsible, in whole or in part, for the low value of the enolisation rate constant, although we are not presently able to determine its influence on each one of the rate and equilibrium constants for this reaction.

REFERENCES

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8) We have observed an analogous effect on the ratio of ketonisation and bromination rate constants, in aqueous acetic acid, for $tBuCOCH_3$ and $tBuCOCH_2CH_3$ (see ref. 2b).