Enol Formation by Elimination of Alkyl Groups: Structural Effects on the Fragmentation of Ketones in Acidic Media

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THE fragmentation of ketones, in which the α- and β-carbons in one alkyl chain are both tertiary, in acidic media, has not previously been reported.[1] This reaction has, in fact, been studied only as a secondary reaction[2,3] following upon the metathetical transpositions of di-t-alkyl ketones.[4] The fragmentation of 3,3,4,4-tetramethylpentan-2-one, for example, in concentrated sulphuric acid gives methyl isopropyl ketone and isobutene.[3]

Preliminary experiments showed that 3,3,4,4-tetramethylpentan-2-one was much more stable than 4,4-diethyl-5,5-dimethylhexan-3-one in 95% w/w sulphuric acid; the relative reactivity[5] was of the order of 2 times 10^3. This difference seemed remarkably large for a reaction whose rate-determining step, according to Zook *et al.*,[2] appears to be the irreversible formation of an enol by the elimination of a tertiary alkyl group (R^1) α to the functional group: (I) → (II) (Scheme).

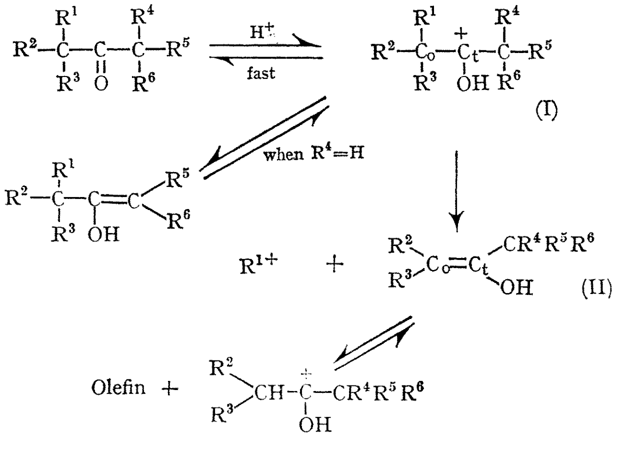
We have, therefore, studied the reaction in detail, and kinetic data for the first-order fragmentation are presented in the Table.[6]

The influence of three structural parameters on the fragmentation rate has been analysed: the nature of the group eliminated R^1, the environment of the origin carbon $E(C_o)$, and the environment of the carbon terminal $E(C_t)$.[7]

An increase in the number of carbon atoms in R^1, $E(C_o)$ or $E(C_t)$ leads, in all but one case, to an increase in the fragmentation rate by a factor on average; 20 for R^1; 6·5 for $E(C_o)$; and 2 for (EC_t), per carbon atom (Table). The three effects are largely independent of each other.

Release of steric strain at the origin carbon, as well as the stability of the cation $(R^1)^+$, are instrumental in determining the reactivity.

The consequences of modification of the other alkyl chain appear more complex. The variation in reactivity observed in the series of ketones (1)—(5) cannot be readily explained in terms of the predominant effects of steric or polar factors.



SCHEME

The reactivity sequence $R^6 = H < Me < Et > Pr^n$ [ketones (1)—(4)] is the inverse of that observed for the enolisation rate of the same ketones [formation (III)] in acidic media.[8] Furthermore, the replacement of the α'-hydrogens of $CR^4R^5R^6$ by methyl groups leads to an increase in the fragmentation rate [ketones (1) and (5)] despite the unfavourable interactions, which must arise

Rate constants for elimination of R^1 *in fragmentation of αβ-ditertiary ketones in* 95% *w/w* H_2SO_4 *at* 25°*

Ketone	R^1	R^2	R^3	R^4	R^5	R^6	$10^6 k$ (sec.$^{-1}$)
1	Bu^t	Me	Me	H	H	H	4
2	,,	,,	,,	,,	,,	Me	10
3	,,	,,	,,	,,	,,	Et	17
4	,,	,,	,,	,,	,,	Pr^n	13
5	,,	,,	,,	Me	Me	Me	55
6	,,	Et	,,	H	H	H	30
7	,,	,,	,,	,,	,,	Me	56
8	,,	,,	,,	,,	,,	Et	109
9	t-C_5H_{11}	Me	,,	,,	,,	H	89
10	,,	,,	,,	,,	,,	Me	193
11	,,	Et	,,	,,	,,	H	560

* Products were separated and estimated by g.l.c. They were identified by their i.r. and n.m.r. spectra.

in the formation of enol (II), between the C_t-t-butyl and the C_0 methyl groups [ketone (5)]. This suggests that charge delocalization by hyperconjugation with the α′-hydrogens in (I) tends to hinder breaking of the R^1–C_0 bond.

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[1] C. A. Grob, *Angew. Chem. Internat. Edn.*, 1967, **6**, 1.

[2] H. D. Zook, W. E. Smith, and J. L. Greene, *J. Amer. Chem. Soc.*, 1957, **79**, 4436.

[3] M. Stiles and R. P. Mayer, *Chem. and Ind.*, 1957, 1357.

[4] J. E. Dubois and P. Bauer, *J. Amer. Chem. Soc.*, 1968, **90**, 4510 and 4511.

[5] P. Bauer, Doctoral Thesis, University of Paris, 1968, N° CNRS AO 2508.

[6] The ketones were prepared by metathetical transpositions of di-t-alkyl ketones (ref. 4), or by the reaction of an acid chloride with the Grignard of 1,1,2,2-tetramethylpropyl chloride (J. E. Dubois, M. Chastrette, and C. Létoquart, *Compt. rend.*, 1967, **264**, *C*, 1124).

[7] In order to express the results and discussion concisely, we have adopted a notation for the analysis of structural effects which has already been used for alkyl group migrations (ref. 4). Fragmentation involves the migration of the C_0–R^1 bond pair. The origin and terminal carbon atoms are C_0 and C_t in the ion (I). The environments of the origin carbon $E(C_0)$ and the terminal carbon $E(C_t)$ consist of the groups R^2 and R^3, and $-CR^4R^5R^6$ and OH respectively.

[8] J. E. Dubois and J. Toullec, *Chem. Comm.*, in the press.