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# DEUTERIUM ISOTOPE EFFECTS IN THE THERMAL DECOMPOSITION OF β-HYDROXY KETONES AND β-HYDROXY ESTERS

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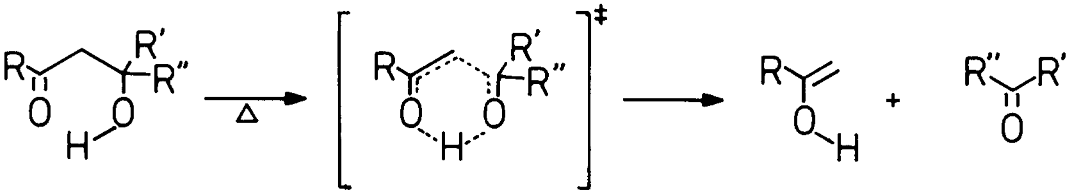
**Summary:** Small primary and cumulative secondary isotope effects are determined experimentally by thermolysis of various β-hydroxy ketones and β-hydroxy esters.

It has been previously shown[1,2,3], that β-hydroxy-ketones may be pyrolyzed to mixtures of aldehydes and ketones, and β-hydroxy-esters decompose thermally to a mixture of the corresponding ester and aldehyde or ketone. A cyclic six-membered transition state was proposed based on the products, kinetics, and activation parameters of the reaction.



R = $CH_3$, $C_2H_5O$ ;R',R" = H, $CH_3$

The proposed mechanism was further supported by the observation[4] that the bicyclic compound, 3,3-dimethyl-1-(1-hydroxy-1-methyl ethyl) bicyclo [2.2.1] hepta-2-one, which is essentially stable to heat, cannot form a cyclic transition state without forming a double bond at the bridgehead (Bredt's rule)[5].

As a complement to the above study we now present kinetic measurements of the thermal decomposition of the compounds listed in Table I and Table II with the purpose of studying both the possible primary kinetic deuterium effect and the cumulative β-deuterium effect.

Diluted xylene solution of β-hydroxy ketones and diluted toluene solution of β-hydroxy esters were pyrolyzed in sealed tubes at 178.1°C and 206.0°C respectively.

TABLE I

Rate Constants and Kinetic Isotope Effect of Pyrolysis of β-Hydroxy Ketone (178.1°C)

| β-Hydroxyketone | $10^4k$ sec$^{-1}$ | $k_H/k_D$ |
|---|---|---|
| 4-Hydroxy-4-methyl-2-pentanone | 1.13 | - |
| 4-Deuteroxy-4-methyl-2-pentanone | 0.567 | 1.99 |
| 4-Hydroxy-4-methyl-2-pentanone d-11 | 0.601 | 1.88 |

Quantitative analysis, using gas-liquid chromatography of the products of the thermal decomposition of β-hydroxy ketones, showed that acetone is by far the principal product of the reaction, with a yield of 95%. This product was identified by glc retention time and and by a 2,4-dinitrophenylhydrazone derivative.

TABLE II

Rate Constants and Kinetic Isotope Effect of Pyrolysis of β-Hydroxy Esters (206°C)

| β-Hydroxy Esters | $10^6k$ sec$^{-1}$ | $k_H/k_D$ |
|---|---|---|
| Ethyl-3-hydroxy-3-methylbutanoate | 2.76 | - |
| Ethyl-3-deuteroxy-3-methylbutanoate | 1.40 | 1.97 |
| Ethyl-3-hydroxy-3-methyl-$d_3$-4,4,4-$d_3$ butanoate | 1.82 | 1.52 |

The same analysis was applied to the thermal decomposition of β-hydroxy esters, where the ketone and ethyl acetate are the principal products of the reaction. Each reaction was followed to at least four half-lives. Good first-order kinetics were observed, the first-order plots being linear for all the periods during which the reaction was followed.

The results for the primary isotope effect suggest that the previously proposed six-membered cyclic transition-state characterized by partial bonds between H (or D) and the two oxygens of the carbonyl and the hydroxyl is correct. It is known that the magnitude of the primary isotope effect in a hydrogen-transfer reaction varies with the symmetry of the transition state and is at a maximum when the hydrogen is symmetrically bonded to the atoms between which it is being transferred.

Some doubts have been expressed about this hypothesis[6], but in the previous cases it was considered that hydrogen transfer is linear. In our case, the hydrogen transfer is not linear. The O-H bond is not stretched to its breaking point, but it does bend, so that the hydrogen atom may become attached to another part of the molecule. It is the bending rather than the stretching which is converted into translation motion.[7,8] Since vibration frequencies for bending are much lower than those for stretching, the zero-point energy lost in the transition state will be small, and therefore the primary kinetic deuterium effect should be small.

By observing the value of the kinetic β-deuterium effect, it is most probable that these data represent small β-secondary isotope effects, so no H(or D) attached to the carbons would be lost in the rate-controlling step of the reaction, but it is conceivable that these effects could represent primary effects for only one of the C-H(C-D) bonds.

β-Hydroxy ketones were obtained by the aldol condensation synthesis[9] β-hydroxy esters by the Reformatsky reaction[10] and deuteroxy compounds were obtained by stirring the corresponding β-hydroxy compound with 99.5% $D_2O$.

The kinetic method used was that described previously[1]. A 2700 Varian Aerograph with thermal conductivity detector was used. Thermolysis was carried out in carefully washed glass tubes, 2 mm i.d. and 50 mm length. The sealed ampules containing the β-hydroxy ester (4% V/V) and benzene (4% V/V) as an internal standard in xylene solution (92% V/V) were placed in a boiling solvent thermostatic bath whose temperature was checked by using a standardized thermometer. At regular intervals, the ampules were removed and the amount of acetone and ethyl acetate produced was determined by glc.

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