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KINETICS OF THE ACID-CATALYZED INTERCONVERSION OF 3-HYDROXYCYCLOHEXANONE AND 2-CYCLOHEXENONE: REINTERPRETATION OF THE DECOMPOSITION OF 3-ALKOXYALLYLIC ALCOHOLS

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A VERY useful synthesis of α,β-unsaturated aldehydes and ketones involves reduction of the enol ether of a β-dicarbonyl compound and treatment of the resulting hydroxy enol ether with aqueous acid (equation 1).[1-11] In the course of studying the mechanisms of several reactions which center about

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[1] R.L. Frank and H.K. Hall, Jr., J.Amer.Chem.Soc. **72**, 1645 (1950).

[2] P. Siefert and H. Schinz, Helv.Chim.Acta **34**, 728 (1951).

[3] J.P. Blanchard and H.L. Goering, J.Amer.Chem.Soc. **73**, 5863 (1951).

[4] R.B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W.M. McLamore, J.Amer.Chem.Soc. **74**, 4225 (1952).

[5] H. Conroy, J.Amer.Chem.Soc. **74**, 3046 (1952).

[6] E.A. Braude and O.H. Wheeler, J.Chem.Soc. 320 (1955).

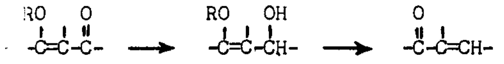
[7] O.P. Vig, T.P. Sharma and S.M. Mukherji, Chem. & Ind. 381 (1956).

[8] R.D. Campbell and H.M. Gilow, J.Amer.Chem.Soc. **82**, 2389 (1960).

[9] R.F. Church, R.E. Ireland and J.A. Marshall, Tetrahedron Letters No. 1, 34 (1961); the authors are grateful to Professor Ireland for communicating his results to us prior to publication and for many stimulating discussions of this problem.

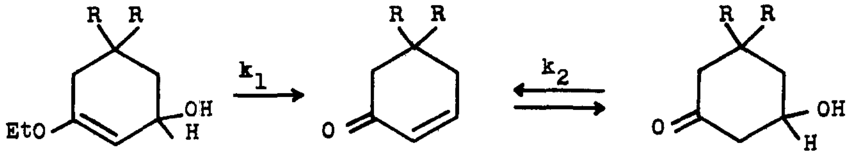
[10] G.F. Woods, P.H. Griswold, Jr., B.H. Armbrecht, D.I. Blumenthal and R. Plapinger, J.Amer.Chem.Soc. **71**, 2028 (1949), employing Grignard reagents in the first step, used the scheme to prepare unsaturated ketones with another substituent at C_β.

[11] J.F. Arens and D.A. Van Dorp, Rec.Trav.Chim. **67**, 973 (1948) prepared the intermediates by a different method.



$$\overset{RO}{\overset{|}{-C}}=\overset{|}{C}-\overset{O}{\overset{\|}{C}}- \longrightarrow \overset{RO}{\overset{|}{-C}}=\overset{|}{C}-\overset{OH}{\overset{|}{C}}H- \longrightarrow \overset{O}{\overset{\|}{-C}}-\overset{|}{C}=CH- \qquad (1)$$

β-hydroxy ketones, we have obtained kinetic information which clarifies the mechanism of reaction (1) and contradicts most previous interpretations.[2-5,8,10]



I II III

Treatment of 3-ethoxy-2-cyclohexenone[12] with lithium aluminum hydride furnished the alcohol (I, R=H), b.p. 69°/0.7 mm, n_D^{25} 1.4843 (Found: C, 67.33; H, 9.84) which was stable toward alkali and in the absence of moisture. The compound was converted quantitatively to cyclohexenone (II, R=H) by 10^{-3} M hydrochloric acid at 0° or by solution in water at room temperature; in neither case could any hydroxy ketone (III) be found. The alcohol (I, R=CH_3) b.p. 99.0-100.5°/5 mm (Found: C, 70.68; H, 10.60) prepared by reduction of 5,5-dimethyl-3-ethoxy-2-cyclohexenone[1] was equally sensitive to "hydrolysis". The rate of formation of cyclohexenone from I (R=H) was followed spectrometrically at 25.2° C in both phosphate and ammonia buffers between pH 7 and 9. The reaction is clearly acid-catalyzed, with first-order rate constants k_1 (min^{-1}) described by the equation: $\log k_1 = -0.945\ pH + 5.52$.

Reaction of dihydroresorcinol with β-mercaptoethanol and p-toluenesulfonic acid in benzene furnished both the mono-hemithioketal, b.p. 90°/0.05 mm (Found: C, 55.61; H, 7.0), and the bis-hemithioketal, m.p. 61°

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[12] E.G. Meek, J.H. Turnbull and W. Wilson, J.Chem.Soc. 811 (1953).

(Found: C, 51.72; H, 7.09). Reduction of the former with lithium aluminum hydride yielded the corresponding alcohol, b.p. 110-111°/0.5 mm (Found: C, 54.96; H, 8.11; S, 18.36) which was converted by refluxing in acetone with Raney nickel to 3-hydroxycyclohexanone (III, R=H) b.p. 75.0-75.5°/0.25 mm, n_D^{25} 1.4831 (Found: C, 63.17; H, 8.89). The hydroxy ketone was not measurably affected by 10^{-3} M hydrochloric acid. In 0.10-5.0 M hydrochloric acid, either the hydroxy ketone (III) or cyclohexenone (II) is converted to an equilibrium mixture in which (II)/(III) = 2.36 ± 0.09 (average of 10 experiments).

Measurement of the rate of dehydration of III in 0.10-5.0 M hydrochloric acid gave values for the first-order rate constant k_2 which were accurately proportional to neither acid concentration nor the Hammett acidity

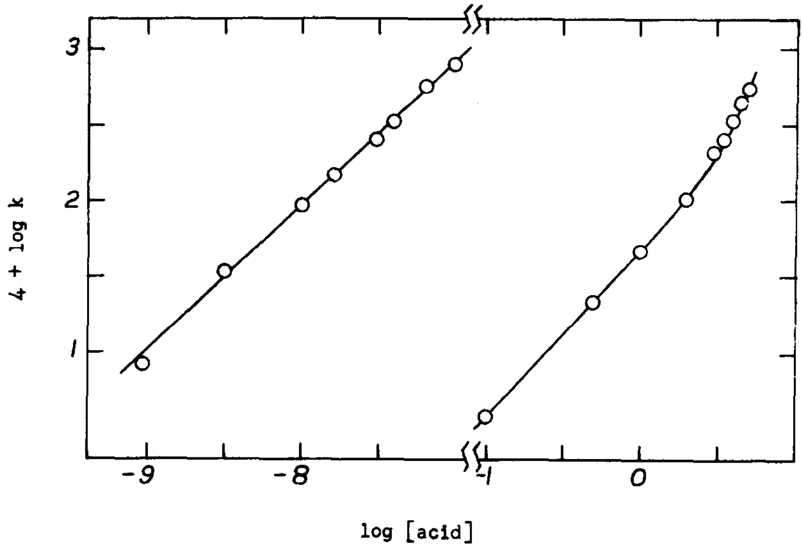
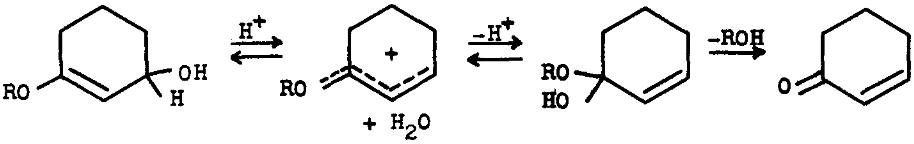


FIG. 1.

First-order rate constants (min^{-1}) for the formation of cyclohexenone from 3-ethoxy-2-cyclohexen-1-ol (left) and from 3-hydroxycyclohexanone (right) at 25.2°.

function h_o, although both conditions were approximated at the lower acidities.[13] Comparison of the rates of formation of cyclohexenone from I and from III (Fig. 1) shows that the hydroxy ketone dehydrates too slowly by a factor of ca. 10^8 to be an intermediate, as has been assumed,[2-5,8,10] in the "hydrolysis" of the hydroxy enol ethers. Thus some especially favored path from I to II takes precedence over the normal hydrolysis of the enol ether function. Consideration of the kinetic information and the well-known rearrangement of allylic alcohols[14] leads us to suggest the mechanism of equation (2). A more detailed discussion will follow.



(2)

We are indebted to Gwyn V. Hudson for some exploratory experiments, and to the National Institutes of Health for partial support (RG 5780).

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[13] Similar kinetic behavior in the acid-catalyzed dehydration of certain acyclic β-hydroxy ketones has been reported: D.S. Noyce and W.L. Reed, J.Amer.Chem.Soc. **80**, 5539 (1958).

[14] E.A. Braude, Quart.Rev. **4**, 407 (1950) clearly anticipated this mechanism for the reaction under discussion.