EFFECT OF PRESSURE ON THE ACID-CATALYZED ENOLIZATION OF ACETONE AND ACETOPHENONE IN VARIOUS ETHANOL–WATER SOLVENTS. ORIGIN OF THE ENTHALPY–ENTROPY COMPENSATION EFFECT[1]

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Received March 17, 1964

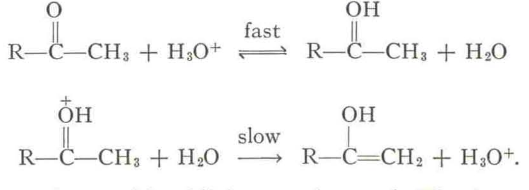
ABSTRACT

The effect of pressure, temperature, and solvent composition on the rate of the acid-catalyzed enolization of acetone and acetophenone, and the solvent deuterium isotope effect for the enolization of acetophenone, have been measured by following the iodination. The solvent deuterium isotope effect ($k^{\mathrm{D_2O}}/k^{\mathrm{H_2O}}$) for the enolization of acetophenone in 16.2% w/w ethanol–water is $2.50 \pm \sim 0.05$, which undoubtedly proves that there is a pre-equilibrium proton transfer. The effect of solvent in the range water to 33.4% w/w ethanol in water on the rate of enolization of both acetone and acetophenone is small at atmospheric pressure, but is about four times larger at 3 kbar. This cannot be explained on simple electrostatic grounds, and indicates that any simple electrostatic explanation of the solvent effect at atmospheric pressure is invalid. The volumes of activation for the enolizations are strongly dependent on the solvent, that for acetone varying from $-2.1 \pm \sim 0.5$ to $-6.9 \pm \sim 0.7$ cm^3 mole^{-1} between solvents water and 33.4% w/w ethanol in water.

An examination has been made of the enthalpy–entropy compensation effect. It is shown that in general if the rate or equilibrium constant of a reaction does not change with changing conditions (such as solvent, substituents, etc.) then either the quantities of activation at constant pressure, $\Delta H_p^{\ddagger}$ and $\Delta S_p^{\ddagger}$, or the corresponding quantities at constant volume, $\Delta U_v^{\ddagger}$ and $\Delta S_v^{\ddagger}$, must vary in a compensating manner, and the existence of an energy–entropy compensation effect is inevitable. For the enolization of acetone and acetophenone in ethanol–water mixtures, $\Delta U_v^{\ddagger}$ and $\Delta S_v^{\ddagger}$ vary only slightly with solvent, whereas $\Delta H_p^{\ddagger}$ and $\Delta S_p^{\ddagger}$ vary in a compensating manner. The main causes of the compensation effect in the constant-pressure parameters are, in a sense, the change with changing solvent of the thermal expansion of the solvent and of the volume of activation of the reaction. On the other hand, both the constant-pressure and the constant-volume parameters vary with substituent from acetone to acetophenone, and the constant-volume parameters vary the more.

1. INTRODUCTION

The acid-catalyzed enolization of ketones is a well-studied reaction (1). It can be conveniently followed by the halogenation (2–5) and the deuterium exchange (6) of the ketones, and by their racemization (7) if they have an asymmetric α-carbon atom. The rates of all these processes are usually identical, and when followed by halogenation they are of zero order in halogen, the zero-order rate constant being itself of first order in both ketone and catalyst. The mechanism of enolization when catalyzed by strong acids is accepted on good grounds to be (see ref. 1 for discussions)



$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}CH_3 + H_3O^+ \xrightleftharpoons{\text{fast}} R{-}\overset{\overset{\overset{+}{O}H}{\|}}{C}{-}CH_3 + H_2O}$$

$$\mathrm{R{-}\overset{\overset{\overset{+}{O}H}{\|}}{C}{-}CH_3 + H_2O \xrightarrow{\text{slow}} R{-}\overset{\overset{OH}{|}}{C}{=}CH_2 + H_3O^+.}$$

Halogenation then occurs by rapid addition to the enol. The incorporation of a molecule of water in the transition state is not kinetically proved. There is, however, little doubt

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Canadian Journal of Chemistry. Volume 42 (1964)

that it occurs, on the grounds that analogy with the observed base catalysis (1) suggests that water is itself acting as a base. In addition, the entropy of activation, which is usually about -15 cal deg^{-1} mole^{-1} (8), strongly suggests (9–11) that a water molecule is incorporated into the transition state.

Few measurements have been made of the volumes of activation of proton abstraction reactions, and for purposes of comparison with other reactions the volume of activation of the acid-catalyzed enolization of acetone and acetophenone would be interesting. In addition, there are several other points of interest. In the first place, few systematic measurements have been made of the effect of solvent on volumes of activation, and the iodination of ketones is a suitable example of a particular class of reaction that would be worth studying. In the second place, the rate of the reaction is little affected by solvent. It is shown in Section 2 of this paper that for such a reaction, the enthalpy and entropy of activation at constant pressure, or the energy and entropy of activation at constant volume, or both, must vary with solvent so as to compensate one another in the free-energy (energy–enthalpy compensation effect). It is of interest to determine whether only one set of parameters has an appreciable compensation effect or whether both have.

We have therefore measured the effect of temperature and pressure on the rates of the acid-catalyzed iodination of acetone and acetophenone in several ethanol–water mixtures. There was no firm evidence that the iodination of acetophenone goes by a pre-equilibrium proton transfer. The solvent deuterium isotope effect on the rate has therefore been measured to verify it.

2. THE ENTHALPY–ENTROPY COMPENSATION EFFECT

It is frequently found that the enthalpy and entropy changes, ΔH and ΔS, of a reaction, either of its rate or its equilibrium, change with changing conditions in the same direction, so that the changes can be said to compensate one another partially in the free energy ΔG $(= \Delta H - T\Delta S)$. The changing conditions can be a change of solvent for a given reaction, a change of substituents in a series of compounds undergoing a similar reaction, and so on. This compensation has frequently been called the enthalpy–entropy compensation effect. The existence of this effect is frequently considered surprising. The purpose of the following discussion is to show that it is in fact inevitable for many reactions and other processes except in special circumstances.

We first emphasize that processes can be considered to occur at constant pressure or at constant volume (or of course with neither pressure nor volume constant, but these conditions are less interesting). The most useful free energy for constant-pressure processes is the Gibbs free energy, and we have, using the subscript p to indicate the constant-pressure condition

$$\Delta G_p = \Delta H_p - T\Delta S_p. \tag{1}$$

The most useful free energy for constant-volume processes is the Helmholtz free energy A, and we have

$$\Delta A_v = \Delta U_v - T\Delta S_v \tag{2}$$

where U is the intrinsic energy, and the subscript v indicates constant-volume conditions. If the rate or equilibrium constant of a reaction is a function of temperature and pressure and not of the extent of reaction then

$$\Delta G_p = \Delta A_v. \tag{3}$$