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THE EFFECT OF PRESSURE AND TEMPERATURE ON THE BASE-CATALYZED CONDENSATION OF CYCLOHEXANONE

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The base-catalyzed condensation of cyclohexanone to ketol in ethanol solution has been kinetically investigated in the range 0.68～9.75°C and 1～2,000 kg/cm^2. The activation energy and entropy at 1 atm are 12.7 kcal/mole and −33.1 cal/deg·mole, which are both quite close to the results in the absence of the solvent. The activation volume is −7.4 cm^3/mole at 0.68°C and −7.8 cm^3/mole at 9.75°C. From these results, it may be reasonably concluded that the transition state is not so much polar and the acceleration of a reaction can be mainly attributed to the structural effect.

Introduction

Hitherto, a few attempts have been made to study the self-condensation of cyclohexanone under pressures. It was found by Newitt *et al.*[1] that 2-cyclohexenyl-cyclohexanone was obtained in poor yield at 60°C and 4,500 atm. In 1938, Sapiro and Shu-Lin P'eng[2] measured the effect of pressure on the equilibrium in a mixture involving aniline at temperatures up to 130°C and at pressures up to 5,000 atm. Furthermore, recently Bengelsdorf[3] has observed that the condensation of cyclohexanone to dodecahydrotriphenylene easily occurred even in the absence of a catalyst at 300°C and 35,000 atm.

In contrast to these observations, it has been found in the previous studies[4][5] that the condensation in the presence of sodium methoxide at relatively lower temperatures leads chiefly to the formation of 1-cyclohexanol-2-cyclohexanone, that is, ketol. Though the rate of this reaction was measured dilatometrically in the absence of the solvent at 1 atm, the effect of pressure on the rate has been examined only in part. Then, in order to take more precise information about the effects of pressure and temperature, we have kinetically investigated the ketol condensation of cyclohexanone in an ethanol solution involving sodium ethoxide.

Experimentals

Materials

Cyclohexanone was purified by means of the bisulfite addition compound[6]. The precipitate was

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1) D. M. Newitt, R. P. Linstead, R. H. Sapiro and E. J. Boorman, *J. Chem. Soc.*, **1937**, 876
2) R. H. Sapiro and Shu-Lin P'eng, *ibid.*, **1938**, 1171
3) see S. D. Hamann, "Physico-Chemical Effects of Pressure", p. 189, Butterworths, London, (1957)
4) T. Kume, T. Moriyoshi and T. Hamamoto, *Preprint of the 6th Symposium on High Pressure*, p. 4, (1964)
5) T. Moriyoshi, T. Hamamoto and K. Mikami, *Preprint of the 9th Symposium on High Pressure*, p. 125, (1967)
6) C. E. Garland and E. E. Reid, *J. Am. Chem. Soc.*, **47**, 2333 (1925)

decomposed with concentrated sodium carbonate solution, and then the ketone layer separated was distilled two times (bp. 52.5°C/20 mmHg). Ethanol was purified by the Lund-Bjerrum magnesium method[7]. Alcoholic sodium ethoxide solution used as the catalyst was prepared by dissolving metallic sodium in pure ethanol. The other chemicals were of reagent grade and were used without further purification.

Apparatus

The high pressure apparatus used is shown in Fig. 1, which is a piston-cylinder pressure vessel with jacket and is combined with a hydraulic press.

In operation, a glass syringe with a teflon cup containing the reaction mixture was placed in the pressure vessel, which was filled with ethanol as pressure-transmitting fluid and kept at constant temperature by circulating water from the thermostat to the jacket. The pressure was produced by forcing the piston into the cylinder by the action of the press and measured indirectly from the reading of the gauge at the press side.

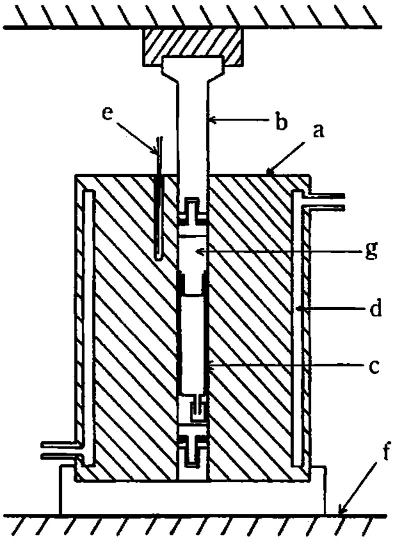

Fig. 1 High pressure apparatus
a pressure vessel
b piston
c glass syringe
d jacket
e thermocouple
f press rum
g ethanol

Analysis

The rate of reaction was followed by a small modification of Bryant and Smith's method[8], in which the carbonyl content was determined by the oximation with hydroxylamine hydrochloride; 2 m*l* of the reaction mixture, initially 0.80 mole in ketone, was added to 16 m*l* of an ethanolic solution, containing 0.2 mole of hydroxylamine hydrochloride, 0.15 mole of pyridine and bromphenol blue as the indicator. After the completion of oximation (2 hours at room temperature was sufficient for the reactant and product), the solution was titrated with 0.4 N standard methanolic solution of sodium hydroxide, and

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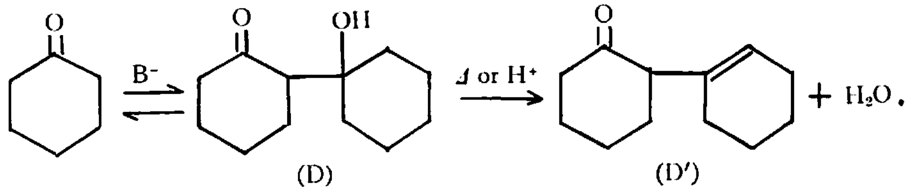
[7] H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931)
[8] W. M. D. Bryant and D. M. Smith, *J. Am. Chem. Soc.*, **57**, 57 (1935)

then was compared with that resulted from the initial reaction mixture without any catalyst to ensure the end point of titration. Analytical error in this procedure was within ±0.3 per cent. Small corrections for the alkaline used as catalyst and for the adjustment of the end point were made to calculate the conversion of ketone.

Rate calculation

In previous studies[4)5)], it had been proved that cyclohexanone in basic medium condensed to 1-cyclohexanol-2-cyclohexanone (D), *i.e.*, ketol, which was easily dehydrated to 2-cyclohexenyl-cyclohexanone (D′) by the heating or the action of acidic reagents as follows:



(1)

Since the ketol seems to be unlikely dehydrated under the present conditions, the concerned reaction may be regarded as a reversible process between dimeric ketol and ketone. Hence, the rate constant k of condensation was calculated according to the rate equation

$$kt = \frac{X_e}{C_{KO}(1-X_e^2)} \ln\left\{\frac{(1-X\cdot X_e)}{X_e-X}\cdot X_e\right\}, \tag{2}$$

where C_{KO} is the initial concentration of ketone, X and X_e are the conversions of that at any time t and equilibrium, respectively.

Results

The results of kinetic measurements are shown in Figs. 2 and 3, and the apparent second order rate constants obtained from the slopes are listed in Table 1. These values were corrected for compression and thermal expansion of the solvent, which are taken by extrapolating Bridgman's data[9)].

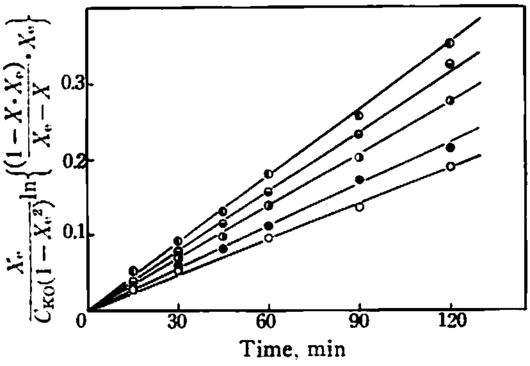


Fig. 2 Plots of $\frac{X_e}{C_{KO}(1-X_e^2)}\ln\left\{\frac{(1-X\cdot X_e)}{X_e-X}\cdot X_e\right\}$ *vs.* time at 0.68°C
○: 1 kg/cm², ●: 500 kg/cm²,
◑: 1,000 kg/cm², ◒: 1,500 kg/cm²,
◐: 2,000 kg/cm²

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9) P. W. Bridgman, *Proc. Am. Acad. Arts Sci.*, **49**, 3 (1913)

The equilibrium constants were determined by allowing the reaction mixtures to remain for over 24 hours at given conditions, and are also listed in Table 1.

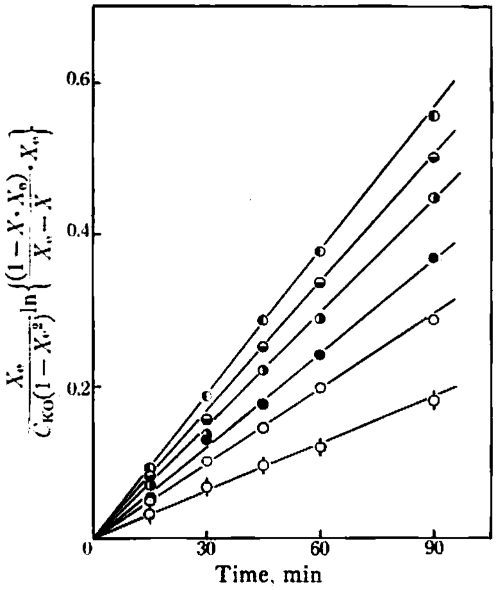


Fig. 3 Plots of $\frac{X_e}{C_{KO}(1-X_e^2)}\ln\left\{\frac{(1-X\cdot X_e)}{X_e-X}\cdot X_e\right\}$ *vs.* time at 9.75°C

○: 1 kg/cm², ●: 500 kg/cm²,
◑: 1,000 kg/cm², ⊖: 1,500 kg/cm²,
◖: 2,000 kg/cm² ⦶: 1 kg/cm² and 4.25°C

Table 1 Rate and equilibrium constants for the condensation of cyclohexanone ([cyclo-C_6H_5O]=0.80 mole, [C_2H_5ONa]=0.040 mole)

Temp., °C	P, kg cm^{-2}	10^5k, l mole^{-1} sec^{-1}	10^2K, l mole^{-1}
0.68±0.03	1	2.61	7.27
	500	3.06	10.1
	1,000	3.53	13.7
	1,500	3.99	18.2
	2,000	4.40	23.4
4.25±0.04	1	3.56	5.74
9.75±0.09	1	5.51	4.57
	500	6.46	6.09
	1,000	7.50	7.94
	1,500	8.47	10.1
	2,000	9.35	12.5

Table 2 Activation and thermodynamic parameters for the condensation of cyclohexanone

P, kg cm^{-2}	Activation parameters		Thermodynamic parameters	
	E, kcal mole^{-1}	$\Delta S^{\neq}$, cal deg^{-1} mole^{-1}	ΔH, kcal mole^{-1}	ΔS, cal deg^{-1} mole^{-1}
1	12.7	−33.1	−8.41	−48.4
500	12.7	−32.6	−9.13	−50.4
1,000	12.8	−32.1	−9.86	−52.5
1,500	12.8	−31.8	−10.6	−54.6
2,000	12.8	−31.5	−11.2	−56.4

Fig. 4 shows the Arrhenius plots of the rate constants at each pressure, from which the activation energies and entropies are obtained and are shown in Table 2.

The effect of temperature on the equilibrium is shown by the van't Hoff plots (*i.e.*, $\log(K/T)$ *vs.* $1/T$) in Fig. 5. The thermodynamic parameters obtained from these plots are also shown in Table 2.

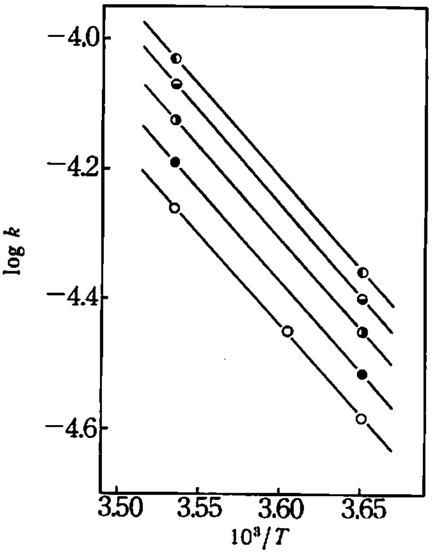


Fig. 4 Arrhenius plots at various pressures
○: 1 kg/cm^2, ●: 500 kg/cm^2,
◑: 1,000 kg/cm^2, ◒: 1,500 kg/cm^2,
◐: 2,000 kg/cm^2

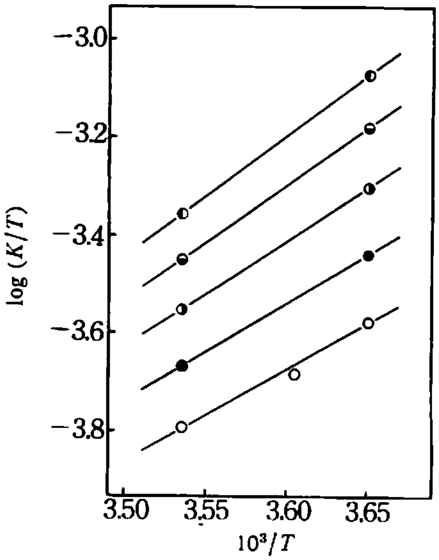


Fig. 5 van't Hoff plots at various pressures
○: 1 kg/cm^2, ●: 500 kg/cm^2,
◑: 1,000 kg/cm^2, ◒: 1,500 kg/cm^2,
◐: 2,000 kg/cm^2

The values of $\log k$ and $\log K$ as a function of pressure at two temperatures are shown together in Fig. 6. From the slope of each curve estimated graphically, the activation volume and the volume change of complete reaction at 1 atm were obtained and the values are given in Table 3.

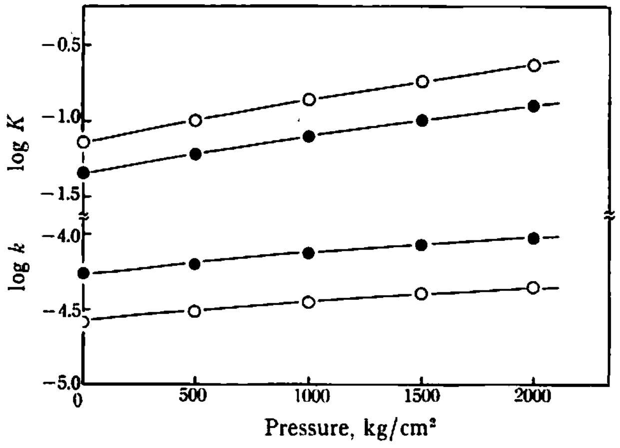


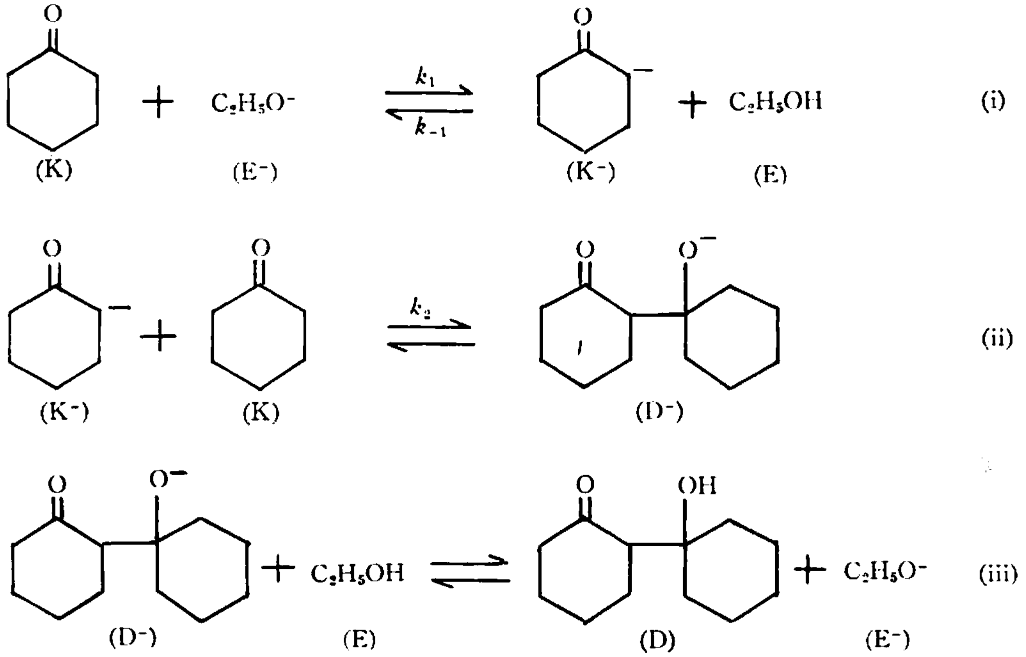
Fig. 6 Plots of $\log k$ *vs.* P and $\log K$ *vs.* P at two temperatures
○: 0.68°C, ●: 9.75°C

Table 3 Activation volumes and volume changes of complete reaction for the condensation of cyclohexanone at 1 atm

Temp., °C	$\Delta V^{\ddagger}$, cm^3 mole^{-1}	ΔV, cm^3 mole^{-1}
0.68	−7.4	−15.2
9.75	−7.8	−13.7

Discussion

The condensation of base-catalyzed cyclohexanone to ketol is essentially similar to aldol condensation and related reactions, and the reaction sequence can be given as follows:



In these steps, if the initial carbanion formation (i) is rapid and reversible, and if its subsequent attack (ii) of the carbanion on carbonyl group is the rate determining step, then the rate is given by

$$\text{rate}=\frac{k_1 k_2[E^-]}{k_{-1}[E]}[K]^2 \tag{3}$$

or

$$\text{rate}=K_1\cdot k_2\frac{[E^-]}{[E]}[K]^2, \tag{4}$$

where k's are the rate constants, K_1 is the equilibrium constant for the first step (i) and brackets denote the concentration terms. The reaction is thus second order in ketone and first order in base. This is in agreement with the present kinetic results. The apparent second order rate constant, k, experimentally observed is given as follows:

$$k=K_1\cdot k_2\frac{[\mathrm{E}^-]}{[\mathrm{E}]}. \qquad (5)$$

Assuming the pressure dependences on the concentration terms to be identical, the effect of pressure on the rate constant is

$$\left(\frac{\partial \ln k}{\partial P}\right)_T=-\frac{(\Delta_1 V+\Delta_2 V^{\neq})}{RT}, \qquad (6)$$

where $\Delta_1 V$ is the partial molal volume change in the equilibrium step (i) and $\Delta_2 V^{\neq}$ the activation volume in the step (ii).

In the equilibrium step, neither the number of molecules nor the number of ionic charges changes, so that $\Delta_1 V$ may be assumed probably to be small. Hence, the observed values of $\Delta V^{\neq}$ could be presumed to be roughly close to that of the rate determining step.

Since the transition state for the present reaction is not thought to be so much polar from the structure and properties of the concerned molecule, the solvation effect is presumably small and not significant. In agreement with this, it has been found that the values of activation energy and entropy at 1 atm, shown in Table 2, are quite close to their values ($E=13.2$ kcal/mole, $\Delta S^{\neq}=-35.1$ cal/deg·mole) from the dilatometric measurement[5] for the base-catalyzed condensation in the absence of the solvent. Consequently, the acceleration of the reaction can be reasonably ascribed to the decrease in volume caused in the transition state by the partial formation of C–C bond between the concerned molecules. The relatively large negative activation entropies also seem to result from substantial losses in translational and rotational freedom in the activation process.

From the values in Tables 2 and 3, $(\Delta\Delta V^{\neq}/\Delta T)_P$ and $(\Delta\Delta S^{\neq}/\Delta P)_T$ is $-0.044\,\mathrm{cm^3/deg\cdot mole}$ and $-0.043\,\mathrm{cm^3/deg\cdot mole}$, respectively, and it was shown that the following thermodynamic relation in the activation process holds approximately,

$$\left(\frac{\partial \Delta V^{\neq}}{\partial T}\right)_P=-\left(\frac{\partial \Delta S^{\neq}}{\partial P}\right)_T. \qquad (7)$$

As shown in Table 3, the effect of temperature on the activation volume and the volume change of complete reaction are as follows:

$$\left(\frac{\partial \Delta V^{\neq}}{\partial T}\right)_P<0 \quad \text{and} \quad \left(\frac{\partial \Delta V}{\partial T}\right)_P>0,$$

from which the thermal expansion, β, for respective species may be suggested to be in the order:

$$\beta_{\mathrm{ketol}}>\beta_{\mathrm{ketone}}>\beta_{\neq},$$

where the subscript, $\neq$, denotes the activation complex in the reaction.

The over-all enthalpy and entropy changes at 1 atm are a little more negative, compared with the values $\Delta H=-7.8$ kcal/mole and $\Delta S=-32$ cal/deg·mole for acetone, which were found by Koelichen[10] in the solution containining 60 per cent water, and this is probably due to the structural difference in

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10) K. Koelichen, *Z. Physik. Chem.*, 33, 129 (1900); A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", p. 339, John Wiley and Sons, Inc., New York (1961)

ketones.

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