Effects of pressure on organic reactions III: the base-catalyzed reduction of diisobutylketone

Author(s)
Moriyoshi, Takashi; Hirata, Masahiro

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EFFECTS OF PRESSURE ON ORGANIC REACTIONS III

The Base-Catalyzed Reduction of Diisobutylketone

BY TAKASHI MORIVOSHI AND MASAHIRO HIRATA

The rate of the base-catalyzed reduction of diisobutylketone to carbinol in n-butanol solution has been measured in the range 96~112°C at pressures up to 1.450 bar. The reaction is kinetically of second order in both ketone and base, and is accelerated by pressure. The energies of activation at 1 bar and 964 bar are 26.4 kcal/mole and 26.6 kcal/mole, respectively, and the volume of activation is about -13 cm³/mole at 99.00~100.2°C. These results show favorably that the slow step is a bimolecular reaction, probably the hydrogen abstraction between two ketone-alkoxide adducts formed in rapidly established initial equilibrium. In addition, it may be deduced that the acceleration of the reaction under pressure arises predominantly from the enhanced addition of alkoxide anion to ketone.

Introduction

The reduction of ketones by primary alcohols in the presence of alkaline has been well-known1). Although it may appear that the reaction is of Meerwein-Ponndorf-Verley type2), represented as R'COR'' + RCH₂OH → R'CH(OH)R'' + RCHO, the mechanism has not been established.

In the course of the investigation related with the self-condensation of ketone3), we attempted to subject diisobutylketone to the action of sodium butoxide in n-butanol under pressure. The main product was the corresponding carbinol, and the other condensation products from ketone were not isolated.

Then, in order to make some mechanistic explanations about the reaction, a kinetic study has been made of the reduction of diisobutylketone under such conditions as in this paper.

Experimental

Materials

Diisobutylketone was first distilled under reduced pressure. The middle fraction was dried over

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3) T. Moriyoshi and K. Mikami, This Journal, 38, 50 (1968)
night by standing over anhydrous potassium carbonate and then fractionally distilled twice, bp. 70.0~
70.4°C/20 mm. n-Butanol was refluxed over freshly burned lime for 3 hours and distilled. The alcohol
obtained was subsequently dried with anhydrous potassium carbonate and finally fractionally distilled,
bp. 116.5~116.8°C. The sodium butoxide solution used as catalyst was prepared by dissolving metal-
lic sodium in pure n-butanol under reflux in the stream of dry nitrogen to avoid moisture. The other
chemicals used were of reagent grade and were purified by conventional means when necessary.

**Analytical method**

The rate of reaction was followed by determining the concentration of unchanged diisobutylketone
by the gas chromatographic technique. The estimation of its amount from chromatogram was made by
application of the internal standardization method with iso-amyl alcohol as a standard substance.
The analysis was performed with a Shimazu gas chromatograph model GC-1C, fitted with 7.5m of
Ucone 500 column, at 150°C with 16.5 ml/sec, the flow rate of helium carrier gas. Since a linear
relationship was satisfactorily found between the weight ratio of diisobutylketone to iso-amyl alcohol
and the ratio of their peak heights rather than the peak areas, the calibration factor obtained from this
relation was used to determine the amount of reactant from the chromatogram of the reaction mixture.
Analytical error in this method was within ±1 per cent.

**Kinetic measurements**

The reaction mixtures were prepared by the weight method using diisobutylketone, sodium
butoxide solution and n-butanol as solvent, and the concentrations were expressed in terms of their
molalities. The initial concentration of diisobutylketone was about 4.6 mole/kg-solvent in all runs.
The concentration of butoxide in the mixture was determined by titration with the standard 0.18
n-hydrochloric acid in 50 per cent aqueous methanol solution.

The rates at ordinary pressure and high pressures were measured by using the apparatus and
the technique similar to that described in the previous paper[5]. The reaction vessel was placed in an
oil-bath controlled within ±0.05°C. Pressure was measured with a calibrated Bourdon gauge.

After the desired time, the sample removed from the vessel was cooled and pipetted into the
weighed amount of iso-amyl alcohol, whose peak gave approximately the same height as that of the
reactant in the chromatogram, and then the total mixture was finally weighed. Subsequently, the
solution was neutralized with ethanolic hydrochloric acid solution and the supernatant solution was
chromatographed.

**Analysis of products**

A large amount (ca. 200 ml) of the reaction mixture, containing nearly the same contents as in
kinetic runs, was heated for 41 hours at 105°C for the seperation of products. After the neutralization
with hydrochloric acid, the unchanged reactant and the products were extracted with ether from the
resulting solution. The extract was dried with anhydrous potassium carbonate, filtered and ether was
removed by evaporation. The residue was distilled under reduced pressure in the stream of dry nitro-
gen, and two fractions were isolated. The first fraction as the main product was colorless oil, bp.

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62.4~63.4°C/5.5 mm, d²⁰ 0.8092, nD° 1.4209, and gave an infra-red spectrum containing a strong absorption band of OH stretching near 3,470 cm⁻¹, as shown in Fig. 1.

![Infra-red spectra](image)

Fig. 1 Infra-red spectra
a: diisobutylketone
b: main product
c: by-product

From these evidences, this product was identified as diisobutylcarbinol.

The second fraction obtained in poor yield, no more than about 3 per cent to carbinol, was lightly yellowish oil, bp. 92.8~94.0°C/0.36 mm. nD²⁰ 1.4677, and exhibited a strong band due to C=O stretching at 1690 cm⁻¹ in the spectrum.


These results suggest that the by-product will be dehydrated trimer made from the aldol condensation of n-butylaldehyde formed by oxidation of solvent, but it is doubtful because the characteristic band of C=C stretching cannot be found in the spectrum.

**Results**

First, in order to determine an appropriate rate equation applicable to the present results, various equations were examined. Consequently, it was confirmed that the second order rate equation,

\[
\frac{1}{C} - \frac{1}{C₀} = kₙt
\]
where \( C_0 \) is the initial concentration of ketone and \( C \) the concentration of that at any time \( t \), was obeyed preferably at constant base concentrations over the range of measured conversion, usually up to about 30 per cent of complete reaction.

Some kinetic plots are illustrated in Figs. 2 and 3, and the apparent second order rate constants

![Figure 2](image1.png)

![Figure 3](image2.png)

**Table 1** Rate constants for the base-catalyzed reduction of diisobutylketone

<table>
<thead>
<tr>
<th>( T, \degree C )</th>
<th>( P, \text{bar} )</th>
<th>( [C_0] \text{ mole•kg}^{-1} )</th>
<th>( 10^7 k_m \text{ kg•mole}^{-1}•\text{sec}^{-1} )</th>
</tr>
</thead>
<tbody>
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<td>95.95</td>
<td>1</td>
<td>2.05</td>
<td>4.67</td>
</tr>
<tr>
<td>95.95</td>
<td>964</td>
<td>2.05</td>
<td>6.58</td>
</tr>
<tr>
<td>98.85</td>
<td>964</td>
<td>2.05</td>
<td>8.60</td>
</tr>
<tr>
<td>99.00</td>
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<td>5.19</td>
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<tr>
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<td>1.81</td>
<td>6.42</td>
</tr>
<tr>
<td>99.00</td>
<td>964</td>
<td>1.81</td>
<td>7.75</td>
</tr>
<tr>
<td>99.00</td>
<td>1,160</td>
<td>1.82</td>
<td>8.39</td>
</tr>
<tr>
<td>99.45</td>
<td>1</td>
<td>0.785</td>
<td>0.467</td>
</tr>
<tr>
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<td>1</td>
<td>1.22</td>
<td>2.50</td>
</tr>
<tr>
<td>99.45</td>
<td>1</td>
<td>1.64</td>
<td>4.43</td>
</tr>
<tr>
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<td>2.03</td>
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</tr>
<tr>
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<td>479</td>
<td>2.03</td>
<td>8.61</td>
</tr>
<tr>
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<td>964</td>
<td>2.02</td>
<td>10.2</td>
</tr>
<tr>
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<td>1,450</td>
<td>2.01</td>
<td>12.1</td>
</tr>
<tr>
<td>105.42</td>
<td>1</td>
<td>2.06</td>
<td>12.0</td>
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<td>16.3</td>
</tr>
<tr>
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<td>1</td>
<td>2.06</td>
<td>19.0</td>
</tr>
<tr>
<td>111.55</td>
<td>1</td>
<td>2.06</td>
<td>19.0</td>
</tr>
</tbody>
</table>
$k_a$ were obtained from their slopes. All the results are summarized in Table 1. The mean error in $k_a$ was about within ± 2 per cent.

The dependence of the base concentration on the rate at 1 bar is shown graphically in Fig. 4, and a straight line with slope 2.0 is drawn through the points, except at the lowest concentration of base, to show the validity of the relation:

$$k_a = 1.65 \times 10^{-7} [C_n]^{1.0},$$

where $[C_n]$ denotes the concentration of base. The fourth order kinetics in the same manner, that is, second order in both aldehyde and alkaline, had been observed in some cases of Cannizzaro reaction.

The Arrhenius plots of the second order constants $k_a$ at 1 bar and 964 bar are given in Fig. 5, in which from the slopes of the straight lines the energies of activation are calculated to be 26.4 kcal/mole and 26.6 kcal/mole, respectively.

The rate constants as a function of pressure at two temperatures are shown in Fig. 6. The volume of activation $\Delta V^*$ estimated graphically using the equation,

$$\left( \frac{\partial \ln k_a}{\partial P} \right)_T = - \frac{\Delta V^*}{RT},$$

is $-12.9$ cm$^3$/mole at 99.00°C and $-12.6$ cm$^3$/mole at 100.27°C.

Discussion

The base-catalyzed reduction of diisobutylketone to corresponding carbinol is found to be kinetically of second order in ketone and also of second order in base from the observed results, and then the reaction sequence may be given as follows:

\[
\begin{align*}
\text{iso-C}_4\text{H}_9\text{C}=\text{O} + \text{iso-C}_4\text{H}_9\text{O}^- & \xrightleftharpoons{k_1 \quad k_{-1}} \text{iso-C}_4\text{H}_9\text{O}^- \text{iso-C}_4\text{H}_9\text{C}=\text{O} \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \Quad
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\[ \text{rate} = k_2 \left( \frac{k_1 [K] [B^-]}{k_{-1} + 2k_2[A^-]} \right)^{1/2}, \]  

where \( k \)'s are the rate constants and the brackets denote the concentration terms.

In the limiting case where \( k_{-1} \gg 2k_2[A^-] \), the equation reduces to

\[ \text{rate} = k_2K_1^{1/2}[B^-]^{3/2}, \]  

where \( K_1 \) is the equilibrium constant for the first step (i), which is consistent with the present kinetic results, that is, the reduction is of second order in both ketone and base as shown in Fig. 4. Thus, the apparent second order rate constant \( k_a \) observed experimentally is given by

\[ k_a = k_2K_1[B^-]^{3/2}. \]  

Since the pressure dependence on the concentration term, which is given in the molality scale, could be eliminated, the effect of pressure on the rate constant may be expressed by

\[ \left( \frac{\partial \ln k_a}{\partial P} \right)_T = \frac{(2dV_1 + dV_2^*)}{RT}, \]  

where \( dV_1 \) represents the volume change of the first step (i) and \( dV_2^* \) the volume of activation for the second step (ii). Hence, the actually observed value of \( dV^* \) may be given as a composite quantity from the following terms

\[ dV^* = 2dV_1 + dV_2^* \]  

The first equilibrium step involves no change in ionic charge and consequently no large change in the electrostriction of solvent, but a new covalent bond between ketone and butoxide anion is formed so that obviously the over-all change in volume \( dV_1 \) should be slightly negative. The second step may be assumed to be the bimolecular abstraction of hydrogen between two ketone-alkoxide adducts. The volume of activation in this step reflects the contraction due to the formation of a partial valence bond \((O\cdots H)\) outweighing the stretching of \( C-H \) bond and further the expansion caused by the dispersal of ionic charge.

The observed volume of activation for the reduction is \(-13 \text{ cm}^3/\text{mole}\) as a whole, and there is no way of measuring \( dV_1 \) and \( dV_2^* \) directly. However, one can approach to the estimation of these values by considering other analogous reactions. If the change of volume accompanying a reaction of the same type, \( A + B^- \rightarrow AB^- \), as the first step would be roughly taken as being comparable to \(-5 \text{ cm}^3/\text{mole}\) for the reaction, \( I_e + I^- \rightarrow I_3^- \) \(6\), then it follows from the equation (5) that \( dV_2^* \approx -3 \text{ cm}^3/\text{mole} \).

A possible transition state from the proposed mechanism may be presumably represented as follows:

In view of the reaction type, the hydrogen abstraction by adduct anion is rather similar to exchange reactions, in which a new bond is formed and another is broken simultaneously as in the ionic displacement reactions. \( \Delta V^\ast \) for the process of this kind has been observed to range from -5 to -10 cm\(^3\)/mole\(^\circ\) on the average. Also, the chain transfer reaction for the analogous reactions, involving only the structural contribution except for that of steric hindrance, has about -11 cm\(^3\)/mole\(^\circ\) for \( \Delta V^\ast \). In comparison with these results, the value of \( \Delta V^\ast \) estimated above is apparently large enough.

As shown above, the transition state formed from two bulky anions appears to make a ring structure linked loosely, and there is some dispersal of ionic charge in the reaction sites, which should lead to solvent relaxation and result in the increase in volume, possibly accompanied by some steric exhaustion of solvent from the partly formed ring structure. Consequently, it follows from these considerations that the volume lost in this activation process should be less than expected by analogy with the exchange and the chain transfer reactions, and that the observed acceleration of the reaction at high pressures is probably caused by a shift of the preliminary equilibrium in favor of the adduct form.

The energies of activation evaluated at two pressures are larger than that for the self-condensation of ketone\(^\circ\) by a factor of about 2, and this suggests the reaction will be energetically hard to occur. In addition, the entropies of activation at 1 bar and 964 bar, which are calculated from the rate constant divided by the second power of the concentration of base, are \(-21.2 \) cal/deg·mole and \(-20.0 \) cal/deg·mole, respectively. There is no appreciable change with pressure in these activation parameters.

The volume of activation can also be divided thermodynamically into two terms,

\[
\Delta V^\ast = \left( \frac{\partial A^\ast}{\partial P} \right)_T
\]

\[
= \left( \frac{\partial A^\ast}{\partial P} \right)_T - T \left( \frac{\partial A^\ast}{\partial T} \right)_P
\]

Calculating from the differences of two activation parameters between 1 bar and 964 bar according to the above equation, the value of \( \Delta V^\ast \) is \(-10.7 \) cm\(^3\)/mole at 99.00\(^\circ\)C and \(-10.8 \) cm\(^3\)/mole at 100.27\(^\circ\)C, in fairly good agreement with that from the pressure dependence of the reaction rate.


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The present argument for the mechanism of the studied reduction seems to be still unsound and may involve somewhat illogical reasoning, because there is no doubt that in such a non-aqueous concentrated solution of base various species will exist and their functions as catalyst are complex. Therefore, more exact description about this will be possible from further experimental results.

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Department of Chemical Engineering
Faculty of Engineering
Tokushima University
Tokushima, Japan