Ab Initio Molecular Orbital Study of Reactivity of Active Alkyl Groups. II. Deprotonation of Some Acyclic Carbonyl Compounds with Methoxide Anion

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The present report describes studies on the reaction mechanisms of an α -proton abstraction from acetone (MMK), methyl ethyl ketone (MEK), methyl isopropyl ketone (MIPK) and methyl *tert*-butyl ketone (MTBK) using CH_3ONa in CH_3OD solution. The activation energies for the deuterium exchange reaction of active methyl group of the ketones MMK, MEK, MIPK and MTBK were 11.87, 12.14, 12.29 and 13.14 kcal·mol⁻¹, respectively. The deprotonation reaction mechanisms of the methyl alkyl ketones with methoxide anion were studied by *ab initio* molecular orbital method. Optimized geometries and energies of all complexes consisting of two molecules were calculated by 6-31+G basis set. The correlation between the activation energies and the differences in calculated energies of the transition state (E_{TS}) and the H-bonded encounter complex I (E_I) was fairly good. It is shown that the mechanisms of the deprotonation reactions can be explained with a simple model consisting of a methyl alkyl ketone and a methoxide anion.

Keywords acyclic carbonyl compound; methyl alkyl ketone; active alkyl group; deuterium exchange; deprotonation; methoxide anion; rate constant; activation energy; *ab initio* MO method

The electrophilic displacement reactions of active alkyl compounds (AH) with electrophilic reagents (E) using base catalysts (B^-) are shown by Eqs. 1 and 2. There are several types of base catalysts, almost all of which involve a proton transfer in at least one step. A prior ionization of the starting material is followed by a reaction with reagents to give the products:

There are a number of reports on these reactions,¹⁾ which fall into two groups depending on whether the rate determining step is Eq. 1 or 2. Examples of the former include the deuterium exchange and the halogenation reactions for many organic compounds containing an acidic hydrogen atom. Examples of the latter reactions include the condensation of acetone to diacetone alcohol and many similar condensations in organic chemistry, such as the Claisen and Michael reactions. Recently the detailed mechanisms of the electrophilic reactions have been studied and have been noteworthy in the synthesis of acyclic ketone derivatives, especially in regioselective and stereospecific synthesis.²⁾

The first deprotonation step shown in Eq. 1 consists of the following three items, *i.e.*, (i) formation of an H-bonded encounter complex I (C-I), $\text{A} \cdots \text{H} \cdots \text{B}^-$, (ii) proton transfer *via* a complex TS (TS), $[\text{A} \cdots \text{H} \cdots \text{B}]^-$ to form a new complex II (C-II), $\text{A}^- \cdots \text{H} - \text{B}$, and (iii) separation into an anion molecule A^- and a neutral HB, as shown in Chart 1.

In general, it depends on the bulkiness of the substituents in the ketones or in the bases, whether the configurations of the enolates produced in the deprotonation step of the ketones with the bases become (*Z*)- or (*E*)-form (Fig. 1). Models of a six or five-membered ring in the transition state have been proposed by Ireland and Moreland to

predict and explain the compositions of (*Z*)- or (*E*)-form of the enolates.³⁾

We reported previously a study on the mechanisms of deprotonation reactions of acetaldehyde and methane with three bases (NH_2^- , OH^- , F^-) by *ab initio* molecular orbital (MO) method using the 6-31+G basis set. The order of the deprotonation ability of these bases, *i.e.*, $\text{NH}_2^- > \text{OH}^- > \text{F}^-$ could be reasonably explained when the deformation energy was taken into account in calculating the energies of the complexes in each reaction pathway.⁴⁾

In the present study, to further investigate the mechanism of the first step shown in Chart 1, five acyclic carbonyl compounds, CH_3COR (MHK: $\text{R} = \text{H}$, MMK: $\text{R} = \text{CH}_3$, MEK: $\text{R} = \text{C}_2\text{H}_5$, MIPK: $\text{R} = \text{CH}(\text{CH}_3)_2$, and MTBK: $\text{R} = \text{C}(\text{CH}_3)_3$) were used, and the rate constants of the deuterium exchange reactions of CH_3COR with CH_3OD were measured in the presence of CH_3ONa using gas chromatography/mass spectrometry (GC/MS). The activation energies for the reactions of four methyl alkyl ketones were determined from the Arrhenius plots. Furthermore, an *ab initio* MO calculation on the deprotonation step was carried out using a simple model consisting of two molecules in which the oxygen atom of CH_3O^- approached the hydrogen atom of the active alkyl group of CH_3COR along the axis of the C—H bond. Optimized geometries and energies of complexes in each case were calculated using the 6-31+G basis set. In this paper we studied the reactivities of a proton of the methyl and alkyl group in

Fig. 1

Chart 1

CH_3COR by means of the chemical kinetics and the MO calculations of the chemical reaction energies.

Experimental

Instruments GC/MS of reaction products was obtained by the electron impact (EI) on a Shimadzu GC-MS 6020 instrument. A glass column (50 cm $\times$ 2.5 mm i.d.) packed with Porapak P was used. The temperature of the column oven was maintained at 120 °C. The carrier gas was helium with a linear velocity of 20 ml $\cdot$ min⁻¹. The temperature of the injection port and the transfer line was kept at 140 °C and that of the ion source at 250 °C. Ionization energy and trap current were 20 eV and 70 μA , respectively. The accelerating voltage was 3.5 kV. A thermo-regulator used for the reactions was a Model K4R (Lauda, West Germany).

Materials CH_3OD and methyl alkyl ketones of guaranteed reagent grade were purchased from Merck and Tokyo Kasei Kogyo Co., Ltd., respectively. Carbonyl compounds were purified by distillation before use. Concentrations of CH_3COR in CH_3OD were as follows: acetone (MMK); 0.0379 M, methyl ethyl ketone (MEK); 0.0337 M, methyl isopropyl ketone (MIPK); 0.0326 M, methyl *tert*-butyl ketone (MTBK); 0.0225 M. The CH_3OD solutions of CH_3ONa (0.025%, 0.05%) were prepared from 0.1% solution (0.0437 M).

Kinetic Measurement A reaction solution was prepared by adding a CH_3OD solution of CH_3ONa (0.1 ml) to a CH_3OD solution of CH_3COR (0.5 ml). The deuterium exchange reactions of the alkyl groups were carried out at desired temperature for the determination of rate constants and activation energies of the deprotonation reactions (MMK: 0.025%; 33–15 °C, 0.05%; 18–6 °C, 0.1%; 6––6 °C, MEK: 0.025%; 39–21 °C, 0.05%; 24–15 °C, 0.1%; 12–0 °C, MIPK: 0.025%; 39–21 °C, 0.05%; 27–15 °C, 0.1%; 18–3 °C, MTBK: 0.025%; 42–24 °C, 0.05%; 30–18 °C, 0.1%; 24–6 °C). The residual amounts of active alkyl protons were measured at regular time and temperature intervals (3 min, 3 °C, respectively) by molecular and fragment ions in the mass spectra. The mass spectra were measured 3 times under the same reaction conditions as described above and the rate of the reaction was determined by the decrease in intensity of the ions. It was assumed that the bond cleavage of deuterated alkyl ketones was the same pattern as that of a starting material in mass spectra.

Computational Procedure The molecular orbital calculations were carried out with the GAUSSIAN80^{5a)} and GAUSSIAN82^{5b)} programs using the SCF method with 6-31+G^{5c)} basis set, which incorporates diffuse functions not only on the oxygen atoms of CH_3O^- and the conjugate acid CH_3OH , but also on the carbon atom in the enolates participating in the reaction. No diffuse function was contained in the basis set for the other first row atoms in the starting material. Geometry optimization was performed by the energy gradient method.⁶⁾ As a model of the deprotonation process, the oxygen atom of CH_3O^- approached the active hydrogen atom of methyl or alkyl groups along the axis of the

C–H bond.

Results and Discussion

Deuterium Exchange Reaction of Active Alkyl Groups Using Methoxide Anion in Methanol- d_1 The rate determining step in the reaction shown in Eqs. 1 and 2 depends strongly on the species of electrophilic reagents. In this study, deuterium exchange reactions were carried out to determine the rate constants and the activation energies of the first step, *i.e.*, the deprotonation step for acyclic ketones. The rate constants of the reaction of active alkyl groups with CH_3O^- were determined by measuring the time-course of the decrease in intensity of the fragment ion peaks, *e.g.* $[\text{CH}_3\text{CO}]^+$, or the molecular ion peak M^+ in the mass spectra as shown in Fig. 2.

In this reaction, deuterium atoms were consecutively substituted for hydrogen atoms in active alkyl groups. The mass number of the fragment ion $[\text{CH}_3\text{CO}]^+$ increased in single increments from m/z 43 to m/z 46 with the lapse of reaction time. The relative intensity (RI) of the fragment ion peak *e.g.*, of m/z 43 was determined by the ratio of the intensity of ion peak m/z 43 to the sum of the intensities of four peaks, m/z 43, 44, 45, and 46. According to Beutelman, the isotope effect (k_H/k_D) for the enolate formation of 2-methyl-3-pentanone with lithium diisopropylamine in tetrahydrofuran is about 3.⁷⁾ Strictly speaking, correction of the isotope effect has to be made by analysis of the data, but in the present study this was precluded. To minimize the consequences of errors inherent in the method of analysis, the rates were evaluated from the variation of the relative intensities of the ion in the first half-life.

Time-Course of Decrease in Intensity of Fragment Ion Peaks in Mass Spectra of Methyl Alkyl Ketones The mass spectrum of MMK showed the molecular ion M^+ at m/z 58 together with the fragment ion $[\text{CH}_3\text{CO}]^+$ at m/z 43 as the base peak (Fig. 2a). The intensities of M^+ and the ion at m/z 43 decreased, the mass number of each ion increased one at a time with the progress of the deuterium exchange reactions, and the intensities of the ions having larger mass numbers increased successively. The rate of the decrease in

Fig. 2. Mass Spectra of Methyl Alkyl Ketones CH_3COR
(a), MMK; (b), MEK; (c), MIPK; (d), MTBK.

intensity of M^+ was twice that of the ion at m/z 43.

The mass spectrum of MEK gave the molecular ion M^+ at m/z 72 together with the fragment ions $[CH_3CH_2]^+$ at m/z 29 and $[CH_3CO]^+$ at m/z 43 as the base peak, respectively (Fig. 2b). With the progress of the deuterium exchange reactions, the intensities of M^+ and of the ions at m/z 43 and 29 decreased, the mass number of each ion increased one by one, and the intensities of the ions having larger mass numbers increased successively. The rate of the reduction in intensity of the ion at m/z 43 was about 3 times faster than that of the ion at m/z 29. The rate of the decrease in intensity of M^+ coincided with the sum of those of the individual ions at m/z 43 and 29. This indicates that a $CH_3CO-CH_2CH_3$ bond cleaves exclusively.

The mass spectrum of MIPK showed the molecular ion M^+ at m/z 86, accompanied by the duplicate ions $[CH(CH_3)_2]^+$ and $[CH_3CO]^+$ at m/z 43 as the base peak (Fig. 2c). In addition, cleavage of the $CH_3-COCH(CH_3)_2$ bond in the molecule resulted in the formation of a characteristic ion $[COCH(CH_3)_2]^+$ at m/z 71. The intensities of M^+ and the fragment ions at m/z 43 and 71 decreased and the mass number of each ion increased one by one with the progress of the deuterium exchange reactions, and the intensities of the ions having larger mass numbers increased successively. The rate of the decrease in intensity of the ion at m/z 71 was very slow compared with that of the ion at m/z 43.

The mass spectrum of MTBK gave the molecular ion M^+ at m/z 100 together with the ions $[CH_3CO]^+$ at m/z 43 and $[C(CH_3)_3]^+$ at m/z 57 as the base peak, respectively (Fig. 2d). As the deuterium exchange reactions proceeded, the intensities of M^+ and the fragment ion at m/z 43 decreased, the mass number of each ion increased one by one, respectively, and the ions having larger mass numbers increased successively. On the other hand, no change in time. The rate of intensity decrease of M^+ was in fair agreement with that of the ion at m/z 43. The above results in the mass spectrum indicate that only the $CH_3CO-C(CH_3)_3$ bond is cleaved.

The rate of the deuterium exchange reaction of active

TABLE I. Rate Constants (k) of Deuterium Exchange Reaction of CH_3COR with CH_3O^- at 25 °C ($M^{-1} \cdot s^{-1}$)

CH_3COR	R	k_{Me}	k_R	k_M	$k_{Me}/k_{Me(MMK)}$	
					This work	Warkentin ^{a)}
MMK	CH_3	0.549	—	1.116	1.0	1.0
MEK	CH_2CH_3	0.295	0.082	0.381	0.54	0.5
MIPK	$CH(CH_3)_2$	0.222	0.042	0.302	0.40	0.34
MTBK	$C(CH_3)_3$	0.117	—	0.116	0.21	0.16

a) Ref. 8e.

TABLE II. Calculated Energies for Reactants, Products and Complexes of Methyl Groups of CH_3COR with CH_3O^- in Deprotonation Reaction of CH_3COR with CH_3O^- (a.u.)

CH_3COR	R	E_R	E_I	E_{TS}	E_{II}	E_P
MHK	H	-267.20278	-267.23094	-267.22489	-267.24717	-267.22669
MMK	CH_3	-306.23487	-306.26353	-306.25366	-306.27374	-306.24960
MEK	CH_2CH_3	-345.25439	-345.28295	-345.27304	-345.29351	-345.26957
MIPK	$CH(CH_3)_2$	-384.27143	-384.30276	-384.29216	-384.31360	-384.29431
MTBK	$C(CH_3)_3$	-423.28712	-423.32100	-432.30771	-423.32896	-423.31015

alkyl hydrogen atom using a base catalyst CH_3O^- can be represented by Eq. 3, where k is the rate constant and $[CH_3COR]$ stands for the concentration of CH_3COR in CH_3OD solution. This reaction is pseudo-first-order, since CH_3O^- is a catalyst and its concentration remains constant during a run (Eq. 4).

$$v = k[CH_3O^-][CH_3COR] \quad (3)$$

$$v = k'[CH_3COR] \quad (4)$$

$$k' = k[CH_3O^-]$$

The deuterium exchange reaction was treated as effectively irreversible during the first half-life. The values k were estimated by the rate of decrease in intensities of the molecular ion M^+ and the fragment ions. Logarithms of the relative intensities of the ions were plotted against time and a linear relationship between them was obtained with a good correlation coefficient ($r=0.99$) in all cases except in MIPK ($r=0.95$). The rate constants k of the reaction of CH_3COR with CH_3O^- at 25 °C are summarized in Table I.

The rate constants k_{Me} , k_R , and k_M shown in the table were obtained by calculation based on the decrease in intensities of the ions $[CH_3CO]^+$, $[R]^+$, and M^+ in the mass spectra, respectively. The sum of k_{Me} and k_R for both alkyl groups across carbonyl group is expected to be equal to k_M . Actually, it was confirmed that both $2 \times k_{Me}$ and k_M for MMK have the same values within experimental errors. In the case of MEK, the sum of k_{Me} and k_R was in good agreement with k_M , and for MTBK, k_{Me} was in accord with k_M . The value of the rate constant k_{Me} for acetyl group in MIPK could not be determined directly from the intensity

Fig. 3. Arrhenius Plots for Deuterium Exchange Reaction of Active Methyl Group of CH_3COR

○, MMK (correlation coefficient $r=0.997$); △, MEK ($r=0.998$); □, MIPK ($r=0.981$); □, MTBK ($r=0.999$). Open symbols: 0.025% CH_3ONa , half-closed symbols: 0.05% CH_3ONa , closed symbols: 0.1% CH_3ONa .

of the ion at m/z 43, because this ion was comprised of two components $[\text{CH}_3\text{CO}]^+$ and $[\text{CH}(\text{CH}_3)_2]^+$ as described above. The rate constant k_{Me} , therefore, was calculated from the difference between k_{M} and k_{R} for the fragment ion at m/z 71. The value of the rate constant k_{R} obtained from the peak at m/z 71 involved some experimental errors, because of the weak intensity of the peak and a slight decrease in intensity of the peak with the lapse of time. The ratio $k_{\text{Me}}/k_{\text{Me(MMK)}}$ decreases in proportion with bulk of the alkyl groups, and these values are similar to those ascertained by Warkentin *et al.* using nuclear magnetic resonance (NMR) spectrometry.⁸⁾ The value of the rate constant per hydrogen atom $k_{\text{Me}}/3$ for methyl group is about twice that for methylene group $k_{\text{R}}/2$ in the case of MEK. Such comparison of the rate constants per hydrogen atom must be considered when the reactivities of the reaction sites of ketones are investigated. The reaction of a hydrogen atom of MMK proceeds about 4 times as fast as that of a methylene hydrogen atom of MEK.

The activation energies of the deuterium exchange reactions of four ketones, MMK, MEK, MIPK and MTBK were evaluated from the slopes of Arrhenius plots as shown in Fig. 3. The activation energies of each active methyl group in MMK, MEK, MIPK and MTBK were 11.87, 12.14, 12.29 and 13.14 $\text{kcal}\cdot\text{mol}^{-1}$, respectively. In addition, the activation energies for a methylene proton in MEK and a methine proton in MIPK were 13.87 and 14.83 $\text{kcal}\cdot\text{mol}^{-1}$, respectively.

Optimized Geometries and Energies of Complexes for Deprotonation Reaction of Active Alkyl Groups with Methoxide Anion The mechanisms for the deprotonation reactions of MHK, MMK, MEK, MIPK, and MTBK with CH_3O^- were studied by the *ab initio* MO method with 6-31+G basis set. First, the stable geometries of reactants in a ground state were calculated, and then a model consisting of two molecules, *i.e.*, a ketone CH_3COR and a

base CH_3O^- , was used to calculate the geometries and the energies of complexes in the deprotonation process. In the simple model, the oxygen atom of CH_3O^- approached the hydrogen atom of CH_3COR along the axis of the alpha C-H bond in the ketones having the most stable conformation. The calculated energies of reactants (E_{R}), products (E_{P}), and complexes (E_{I} , E_{TS} , E_{II}) in the reaction of CH_3COR with CH_3O^- are presented in Table II.

The reaction of MHK with NH_2^- or OH^- showed single-well potential-energy curves as reported previously.⁴⁾ On the other hand, the reaction profiles for the deprotonation of CH_3COR with CH_3O^- differed from that of MHK with OH^- and indicated double-well potential-energy curves in all reaction systems as shown in Fig. 4.

First, as CH_3O^- approaches a hydrogen atom of the active alkyl group in CH_3COR , a stable C-I is formed. Further approach of CH_3O^- to the hydrogen atom lengthens the C-H bond and leads to the formation of a stable C-II *via* the transition state TS. Finally, enolate and methanol are produced. The differences in energies between each of the complexes are all shown in Table III. The difference between the reactivity of MHK with OH^- and with CH_3O^- may be attributable to the steric effects and the proton affinity of the bases (OH^- : 390.7, CH_3O^- : 379.2 $\text{kcal}\cdot\text{mol}^{-1}$).⁹⁾ The interaction energies for the complex C-I consisting of MHK with OH^- and with CH_3O^- were -17.8 and -16.7 $\text{kcal}\cdot\text{mol}^{-1}$, respectively,⁴⁾ whereas

TABLE III. Differences between Calculated Energies of Complexes of Methyl Groups of CH_3COR with CH_3O^- ($\text{kcal}\cdot\text{mol}^{-1}$)

CH_3COR	R	$E_{\text{P}} - E_{\text{R}}$	$E_{\text{I}} - E_{\text{R}}$	$E_{\text{TS}} - E_{\text{I}}$	$E_{\text{II}} - E_{\text{TS}}$	$E_{\text{P}} - E_{\text{II}}$
MHK	H	-15.00	-17.67	3.79	-13.98	12.85
MMK	CH_3	-9.24	-17.98	6.20	-12.60	15.14
MEK	CH_2CH_3	-9.52	-17.92	6.22	-12.84	15.02
MIPK	$\text{CH}(\text{CH}_3)_2$	-14.36	-19.66	6.65	-13.45	12.10
MTBK	$\text{C}(\text{CH}_3)_3$	-14.45	-21.26	8.34	-13.34	11.80

Fig. 4. Comparison of Reaction Profiles for the Deprotonation of Methyl Group of CH_3COR with CH_3O^- Using 6-31+G Basis Set
MHK,; MMK, —; MEK, ---; MIPK, — · —; MTBK, — — —.

Fig. 5. Potential Energy for $\text{C}_2\text{-C}_3$ Bond Rotation from 0° (a) to 180° (c) of a Dihedral Angle

TABLE IV. Calculated Energies for Reactants, Products and Complexes of MEK or MIPK with CH_3O^- in Deprotonation Reaction of MEK or MIPK with CH_3O^- (a.u.)

Compound	Reaction site	E_R	E_I	E_{TS}	E_{II}	E_P
MEK	CH_3	-345.25439	-345.28295	-345.27304	-345.29351	-345.26957
	$\text{CH}_2\text{CH}_3(\text{Z})^a$	-345.25439	-345.28306	-345.26970	-345.29022	-345.26472
	$\text{CH}_2\text{CH}_3(\text{E})^b$	-345.25439	-345.28093	-345.26744	-345.28368	-345.26217
MIPK	CH_3	-384.27143	-384.30276	-384.29216	-384.31360	-384.29431
	$\text{CH}(\text{CH}_3)_2$	-384.27143	-384.30091	-384.28596	-384.30312	-384.28313

a) Product has a Z-form. b) Product has an E-form.

TABLE V. Differences between Calculated Energies of Complexes of MEK or MIPK with CH_3O^- ($\text{kcal}\cdot\text{mol}^{-1}$)

Compound	Reaction site	$E_P - E_R$	$E_I - E_R$	$E_{TS} - E_I$	$E_{II} - E_{TS}$	$E_P - E_{II}$
MEK	CH_3	-9.52	-17.92	6.22	-12.84	15.02
	$\text{CH}_2\text{CH}_3(\text{Z})^a$	-6.48	-17.99	8.39	-12.88	16.00
	$\text{CH}_2\text{CH}_3(\text{E})^b$	-4.88	-16.65	8.47	-10.19	13.50
MIPK	CH_3	-14.36	-19.66	6.65	-13.46	12.10
	$\text{CH}(\text{CH}_3)_2$	-7.34	-18.49	9.38	-10.77	12.54

a) Product has a Z-form. b) Product has an E-form.

there was a distinct difference between the reaction profile for the deprotonation of MHK with OH^- and with CH_3O^- . In the reaction of MHK with OH^- , no transition state was obtained,⁴⁾ while the reaction profile for the deprotonation of MHK with CH_3O^- had a double-well potential-energy surface ($E_{TS} - E_I = 3.79 \text{ kcal}\cdot\text{mol}^{-1}$). From the above results, it may be assumed that the difference of reactivity between OH^- and CH_3O^- with MHK is mainly due to the steric effect in TS.

In general, the reactivities of the reactants increase with the gap between the energies of the reactants and those of the products under the dominance of the thermodynamic control. The differences $E_P - E_R$ of calculated energies were in conflict with the experimental data for the deuterium exchange reactions shown in Table I. On the other hand, the differences $E_{TS} - E_I$ enlarged with the bulk of substituents "R" in CH_3COR and reasonably explained the reactivities of the methyl groups in CH_3COR . The values of $E_{TS} - E_I$ for the reactions of the ketones, MHK, MMK, MEK, MIPK and MTBK with CH_3O^- were 3.79, 6.20, 6.22, 6.65 and 8.34 $\text{kcal}\cdot\text{mol}^{-1}$ respectively, as shown in Table III. The differences $E_{TS} - E_I$ for the reactions of MMK or MTBK with CH_3O^- increased by a factor of about 1.6 or 2.2 compared with that for MHK, respectively.

Both MEK and MIPK have two different α -protons, that is, methyl and methylene protons in MEK, methyl and methine protons in MIPK. All of the carbon and oxygen atoms of the enolate produced by the deprotonation of methine proton in MIPK lie on the same plane; therefore, no regioisomers exist in the optimized geometries. On the other hand, in MEK, (Z)- and (E)-isomers shown in Fig. 1 are produced by the deprotonation of methylene proton. It is well known that the favored structure of MEK has the conformation shown in Fig. 5a.¹⁰⁾ A stable conformation of MEK (a) leads to an unstable conformation (c) with additional energy of about $2.8 \text{ kcal}\cdot\text{mol}^{-1}$ through a relatively unstable conformation (b) by the rotation of ethyl group as shown.

Fig. 6. Relation between Observed Activation Energies and Differences of Calculated Energies of Complexes ($E_{TS} - E_I$)

1, MMK; 2, MEK-methyl group; 3, MIPK-methyl group; 4, MTBK-methyl group; 5, MEK-ethyl group; 6, MIPK-isopropyl group.

A (Z)-enolate is produced by a deprotonation of methylene proton in the stable conformation. To obtain an (E)-enolate, it is necessary to rotate an ethyl group at least 90 degrees from stable conformation and then to deprotonate an appropriate proton on methylene carbon atom with CH_3O^- . The arrows in Fig. 5 indicate the deprotonated proton leading to the (E)-enolate. The calculated energies of complexes for two reaction sites in the unsymmetrical ketones and for the formation of (Z)- and (E)-isomer from MEK are shown in Table IV. The difference in energies between each of the complexes is summarized in Table V.

The differences $E_P - E_R$ indicate that methyl group reacts thermodynamically more easily than ethyl or isopropyl group with CH_3O^- . The differences $E_{TS} - E_I$ for the deprotonation reaction of methyl group are smaller than those of another alkyl group, i.e., a proton in methyl group reacts more easily than that in ethyl or isopropyl group with CH_3O^- , and this is consistent with the experimental data shown in Table I. In the present study the reaction of CH_3COR with CH_3O^- was carried out at ca. 0–30 °C in a protic solvent. Under these reaction conditions it is generally said that a thermodynamic enolate is formed.¹¹⁾ Consequently, it can be considered that the (Z)-enolate is generated from the ketone in stable form shown in Fig. 5a in the deuterium exchange reaction. Therefore, circle number 5 in Fig. 6 is designated using the values of $E_{TS} - E_I$ calculated from the stable structure in the process of the formation of the (Z)-enolate. Figure 6 shows the plots of the observed activation energies of the deuterium exchange reactions of methyl alkyl ketones versus the $E_{TS} - E_I$ shown in Tables III and V. A linear relationship between the

TABLE VI. Optimized Geometries of Reactants, Products and Complexes between $\text{CH}_3\text{COCH}_2\text{CH}_3$ with CH_3O^-

Geometrical parameter	Optimized geometries $r(\text{\AA})$, $\angle(^{\circ})$								
	Reactants	$-\text{CH}_3^a)$				$-\text{CH}_2\text{CH}_3^a)$			
		C-I	TS	C-II	Products	C-I	TS	C-II	Products
Bond length									
$r(\text{C}^1-\text{O}^2)$	1.219	1.229	1.243	1.282	1.281	1.229	1.245	1.290	1.289
$r(\text{C}^1-\text{C}^3)$	1.506	1.496	1.448	1.381	1.379	1.507	1.520	1.525	1.539
$r(\text{C}^3-\text{H}^4)$	1.080	1.082	1.083	1.077	1.076	1.082	1.082	1.086	1.083
$r(\text{C}^3-\text{H}^5)$	1.085	1.089	1.087	1.076	1.078	1.086	1.088	1.087	1.087
$r(\text{C}^3-\text{H}^6)$	1.085	1.096	1.350	2.198	—	1.084	1.082	1.085	1.087
$r(\text{C}^1-\text{C}^7)$	1.511	1.512	1.527	1.534	1.550	1.500	1.443	1.375	1.369
$r(\text{C}^7-\text{C}^8)$	1.526	1.525	1.526	1.531	1.528	1.523	1.522	1.508	1.509
$r(\text{C}^7-\text{H}^9)$	1.088	1.086	1.085	1.086	1.088	1.097	1.382	2.162	—
$r(\text{C}^7-\text{H}^{10})$	1.088	1.088	1.089	1.089	1.088	1.092	1.090	1.079	1.079
$r(\text{C}^8-\text{H}^{11})$	1.084	1.086	1.087	1.089	1.090	1.085	1.088	1.084	1.091
$r(\text{C}^8-\text{H}^{12})$	1.082	1.083	1.083	1.086	1.082	1.084	1.084	1.095	1.091
$r(\text{C}^8-\text{H}^{13})$	1.082	1.084	1.082	1.081	1.082	1.086	1.093	1.092	1.091
$r(\text{H}^{6(9)}-\text{O}^{14})$	—	1.858	1.277	0.968	0.950	1.855	1.244	0.968	0.950
$r(\text{O}^{14}-\text{C}^{15})$	1.399	1.398	1.408	1.430	1.436	1.399	1.407	1.432	1.436
$r(\text{C}^{15}-\text{H}^{16})$	1.107	1.103	1.096	1.082	1.076	1.103	1.097	1.085	1.076
$r(\text{C}^{15}-\text{H}^{17})$	1.107	1.103	1.093	1.085	1.082	1.103	1.092	1.081	1.082
$r(\text{C}^{15}-\text{H}^{18})$	1.107	1.104	1.093	1.081	1.082	1.103	1.093	1.082	1.082
Bond angle									
$\angle \text{O}^2\text{C}^1\text{C}^3$	121.1	123.4	125.1	126.7	127.3	120.8	118.0	115.4	115.8
$\angle \text{C}^1\text{C}^3\text{H}^4$	109.8	110.4	112.8	120.1	120.4	110.4	109.7	109.5	108.4
$\angle \text{C}^1\text{C}^3\text{H}^5$	110.6	109.2	113.3	121.5	121.6	110.0	109.4	108.9	111.7
$\angle \text{C}^1\text{C}^3\text{H}^6$	110.6	109.4	109.3	90.0	—	109.0	111.2	113.2	111.7
$\angle \text{O}^2\text{C}^1\text{C}^7$	121.8	121.2	118.7	115.5	116.0	123.9	125.3	126.5	126.3
$\angle \text{C}^1\text{C}^7\text{H}^8$	113.9	114.3	114.1	112.3	113.3	114.5	116.2	122.1	121.7
$\angle \text{C}^1\text{C}^7\text{H}^9$	107.9	106.8	107.9	110.7	108.9	106.6	106.1	90.0	—
$\angle \text{C}^1\text{C}^7\text{H}^{10}$	107.9	107.5	107.4	107.0	108.9	107.1	111.2	119.3	120.1
$\angle \text{C}^7\text{C}^8\text{H}^{11}$	110.4	110.5	110.8	111.6	111.1	109.7	110.5	109.3	110.9
$\angle \text{C}^7\text{C}^8\text{H}^{12}$	111.1	110.9	110.7	110.7	110.6	110.6	110.3	113.0	112.7
$\angle \text{C}^7\text{C}^8\text{H}^{13}$	111.1	111.4	110.9	109.3	110.6	112.2	113.5	112.8	112.7
$\angle \text{C}^1\text{C}^{3(7)}\text{O}^{14}$	—	109.4	109.3	90.0	—	106.6	106.1	90.0	—
$\angle \text{H}^{6(9)}\text{O}^{14}\text{C}^{15}$	—	169.2	114.6	111.0	114.4	177.6	116.0	110.9	114.4
$\angle \text{O}^{14}\text{C}^{15}\text{H}^{16}$	114.0	113.5	112.3	111.2	105.9	113.4	112.3	111.0	105.9
$\angle \text{O}^{14}\text{C}^{15}\text{H}^{17}$	114.0	113.4	112.0	111.1	111.4	113.6	111.5	107.8	111.4
$\angle \text{O}^{14}\text{C}^{15}\text{H}^{18}$	114.0	113.6	111.9	107.3	111.4	113.5	112.5	110.0	111.4
Dihedral angle									
$\angle \text{O}^2\text{C}^1\text{C}^3\text{H}^4$	0.0	−15.4	18.6	6.4	0.0	−3.9	−24.3	−54.1	0.0
$\angle \text{O}^2\text{C}^1\text{C}^3\text{H}^5$	120.6	104.2	146.8	176.6	180.0	116.8	94.3	62.7	119.8
$\angle \text{O}^2\text{C}^1\text{C}^3\text{H}^6$	−120.6	−138.4	−101.4	−90.0	—	−126.2	−146.0	−176.0	−119.8
$\angle \text{C}^3\text{C}^1\text{O}^2\text{C}^7$	180.0	180.0	180.0	180.0	180.0	180.0	180.0	180.0	180.0
$\angle \text{O}^2\text{C}^1\text{C}^7\text{C}^8$	0.0	1.2	10.3	48.3	0.0	9.8	−14.8	−6.8	0.0
$\angle \text{O}^2\text{C}^1\text{C}^7\text{H}^9$	123.2	125.6	133.8	172.3	122.3	134.6	105.8	90.0	—
$\angle \text{O}^2\text{C}^1\text{C}^7\text{H}^{10}$	−123.2	−122.2	−112.1	−71.0	−122.3	−112.9	−146.0	−176.0	180.0
$\angle \text{C}^1\text{C}^7\text{C}^8\text{H}^{11}$	180.0	179.6	181.0	186.5	180.0	178.8	175.5	15.6	180.0
$\angle \text{C}^1\text{C}^7\text{C}^8\text{H}^{12}$	59.7	59.6	60.7	66.3	59.0	60.1	56.6	−103.5	59.8
$\angle \text{C}^1\text{C}^7\text{C}^8\text{H}^{13}$	−59.7	−59.8	−58.2	−52.7	−59.0	−60.2	−63.4	135.7	−59.8
$\angle \text{O}^2\text{C}^1\text{C}^{3(7)}\text{O}^{14}$	—	−138.4	−101.4	−90.0	—	134.6	105.8	90.0	—
$\angle \text{C}^1\text{C}^{3(7)}\text{O}^{14}\text{C}^{15}$	—	100.4	83.6	52.5	—	−177.8	−191.7	−46.7	—
$\angle \text{H}^{6(9)}\text{O}^{14}\text{C}^{15}\text{H}^{16}$	—	0.1	−2.3	−42.6	180.0	−2.1	−15.6	−91.2	180.0
$\angle \text{H}^{6(9)}\text{O}^{14}\text{C}^{15}\text{H}^{17}$	60.0	120.1	117.7	78.3	61.3	−122.1	−135.1	149.8	61.3
$\angle \text{H}^{6(9)}\text{O}^{14}\text{C}^{15}\text{H}^{18}$	−60.0	−119.9	−122.0	−162.7	−61.3	117.9	104.6	29.6	−61.3

a) Underlines indicate the deprotonated protons.

differences $E_{\text{TS}} - E_1$ and the activation energies with the good correlation coefficient ($r=0.966$) is obtained. The good correlation indicates that the environment of each complex, *e.g.*, solvation, *etc.*, resembles closely the others in the deprotonation process of the reaction of acyclic carbonyl compounds with CH_3O^- and that the simple model consisting of ketone and CH_3O^- , can explain quite reasonably the reactivities of the deprotonation reactions dealt with in this paper.

The optimized geometries of reactants, products and

complexes between MEK with CH_3O^- are presented in Table VI, and in Fig. 7 each of the complexes is represented by an ORTEP drawing.

The geometries of C-I and C-II are similar to those of reactants and products, respectively. A proton which migrates from MEK to CH_3O^- is situated in the neighborhood of the middle position between the oxygen atom of CH_3O^- and the carbon atom of alkyl group in TS. The distances between hydrogen and carbon or oxygen atom are 1.382 and 1.244 Å, respectively. A dihedral angle

Fig. 7. ORTEP Drawing of Complexes of $\text{CH}_3\text{COCH}_2\text{CH}_3$ with CH_3O^-

(a), complex of methyl group of MEK with CH_3O^- ; (b), complex of ethyl group of MEK with CH_3O^- ; which gives (Z)-enolate.

between the carbonyl $\text{C}=\text{O}$ bond and the alpha $\text{C}-\text{H}$ bond is 105.8 degrees in TS. The calculated geometries in TS are similar to those described in previous papers.¹²⁾ Methyl group of CH_3O^- moves from a sterically stable position (Fig. 7, C-I) toward the oxygen atom of carbonyl group by rotating around the axis of $\text{C}-\text{H}$ bond, and at the same time, CH_3O^- abstracts the proton of the active alkyl group as shown in Fig. 7, C-II. It can be said that the mechanism of the deprotonation reaction of CH_3COR with CH_3O^- in CH_3OH is illustrated reasonably by the simple model shown in Chart 1 and Fig. 7.

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