Ab Initio Molecular Orbital Study of the Reactivity of Active Alkyl Groups. V. Nitrosation Mechanism of Acetone with syn-Form of Methyl Nitrite

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The mechanisms of nitrosation of acetone through sodium enolate [CH₃COCH₂CH(CH₃)₂]⁺ (1) or naked enolate [CH₃COCH₂CH(CH₃)₂]⁻ (2) with methyl nitrite CH₃OONO (3), and the reactivity of the syn-form of 3 (syn-3) during the C–N bond formation process were investigated using ab initio molecular orbital (MO) methods. Our results have demonstrated the predominant formation of 4E when the complex [CH₃COCH₂NO(OCH₃)]⁻ Na⁺ was produced kinetically via a metal-chelated pericyclic transition state (TSCHELA TED), in which the O³ atom of syn-3 was coordinated to the Na⁺ atom of 1. Thus the reaction of RCOCH₂ (1) with tert-butyl nitrite in THF.4) Thus the nitrosation of active alkyl compounds, such as acetone and 2-butanone, the rate-determining step of the nitrosation is

RCOCHR’+R’ONO → [RCOCR’]=NOH (1)

In the case of the nitrosation of the methyl or ethyl group of carbonyl compounds, such as acetone and 2-butaneone, the E-form of the hydroxyimino compound was predominantly obtained.1–5 On the other hand, a E/form (E/Z) ratio of 2.3 was observed for the nitrosation of 3-methyl-1-phenylbutan-1-one (PhCOCH₂CH(CH₃)₂) (5) with tert-butyl nitrite in THF.5) Thus the E/Z ratio decreased with increasing bulkiness of the R and R’ groups of RCOCH₂R’.
As shown in Eq. 1, alkyl nitrite R’ONO exists as either the syn- or anti-conformer. The proportion of the anti-form of R’ONO was found to increase in the order R’=CH₃<primary<secondary<tertiary.5) The E/Z ratio of the hydroxyimino compound increased when methyl nitrite (3) was used in place of tert-butyl nitrite in the nitrosation of 5,6) which indicated that the E/Z ratio is affected by the conformation of R’ONO. Our experimental and theoretical investigations on the mechanisms of nitrosation have shown that the E/Z ratio varied significantly with the participation of the counter cation M⁺ of the base catalyst.4,7,9) Consequently, two types of transition state models (TS) during the C–N bond formation process were proposed to elucidate the variation of the E/Z ratio in various solvents; specifically, the TS models were 1) metal-chelated pericyclic transition state (TSCHELA TED) and 2) open-chain transition state without metal (TSOPEN).4,7) Previous calculations of the nitrosation of sodium enolate [CH₃COCH₂CH(CH₃)₂]⁻ Na⁺ (1) with the anti-form of 3 (anti-3) have shown that Z-1-hydroxyimino-2-oxo-propane (4Z) was obtained predominantly, with the nitrosation proceeding via TSCHELA TED.4) In the case of naked enolate [CH₃COCH₂CH(CH₃)₂]⁻ (2), the reaction with anti-3 afforded not only 4Z but also 4E via TSOPEN.7)

In the present study, the mechanisms of the stereochemical nitrosation of 1 or 2 with syn-form of 3 (syn-3), as opposed to anti-3, were investigated by ab initio MO methods using the same two transition state models as described above.3,5) Our studies have shown the predominant formation of 4E when the complex [CH₃COCH₂NO(OCH₃)]⁻ Na⁺ was produced via TSCHELA TED, with the O³ atom of syn-3 coordinated to the Na⁺ atom of 1. On the other hand, similar coordination between the O³ atom of anti-3 to the Na⁺ atom of 1 was not observed in TS, as described in the previous paper.4)

Experimental

Computational Procedures
MO calculations were carried out using the Gaussian 98 program. The optimized geometries in the TS were initially determined using HF/6-31G, followed by intrinsic reaction coordinate (IRC) calculations. For the energies of the complexes, calculations were performed using similar methods, MP3/6-31+G(HF/6-31G), as previously described.4) The structure of syn-3 was used to provide the initial geometries for the C–N bond formation process.

Results and Discussion

For the studies on the nitrosation mechanisms between 3 and 1 or 2, TSCHELA TED or TSOPEN models, respectively, were adopted for the C–N bond formation process. In this report, the influence of the conformation of alkyl nitrite on the nitrosation mechanism was investigated using syn-3, as opposed to anti-3, which was described in previous papers.4) As shown in Chart 1, MO calculations for the formation of 4 were carried out stepwise as follow: The nitrosation of 1 or 2 with syn-3 (Eq. 2) to yield 4 was divided into two processes, the C–N bond forming process via TSCHELA TED (Eq. 3-1) or via TSOPEN (Eq. 3-2), the final elimination process shown as Eq. 4. MO calculations were carried out for Eq. 3-1 and 3-2, followed by the elimination processes (Eq. 4). Two pathways (paths A, B) were considered with TS₁ and -B in Fig. 2 arising from the difference of the geometrical orientation of 3 toward 1.4) Initially, the geometries of the transition states (TS₁ and TS₁) were determined, and subsequently those of

Fig. 1. Conformers of Alkyl Nitrite, R’ONO

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C-I\textsubscript{Na} and C-II\textsubscript{Na} (or C-I and C-II) were obtained from TS\textsubscript{1Na} (or TS\textsubscript{I}) using the IRC method, respectively. The active hydrogen atom in the H–C\textsubscript{2} bond of C-II\textsubscript{Na} was attacked by the base CH\textsubscript{3}O\textsuperscript{−}, followed by demethoxylation occurred, and lastly by deprotonation to give C-IV\textsubscript{Na}. The details of the complexes (C-I\textsubscript{Na}—C-IV\textsubscript{Na}) in Chart 1 were described below.

For the calculation of the geometry of TS\textsubscript{CHELATED}, two types of the TS\textsubscript{1Na} complex (TS\textsubscript{1Na}−O\textsubscript{2} and TS\textsubscript{1Na}−O\textsubscript{3}) were obtained. The terms TS\textsubscript{1Na}−O\textsubscript{2} and TS\textsubscript{1Na}−O\textsubscript{3} refer to the complexes in which the O\textsubscript{2} atom and O\textsubscript{3} atom of syn-3, respectively, are coordinated to the Na\textsuperscript{+} atom of I. In the case of the nitrosation of I with anti-3, the O\textsubscript{3} atom in anti-3 did not coordinate to the Na\textsuperscript{+} atom in the TS, as described previously.

The differences of the behavior between syn-3 and anti-3 in the TS can be explained as steric influence of the methyl group of 3. In the case of nitrosation of I using anti-3, the negative charge of the O\textsuperscript{3} atom in anti-3 increased with the decreasing distance of C–N bond between 1 and 3, and hence the binding site of Na\textsuperscript{+} migrated more easily from O\textsubscript{3} atom to the O\textsuperscript{2} atom as the reaction proceeded.

C–N Bond Formation of the Sodium Enolate of Acetone with syn-Form of Methyl Nitrite via TS\textsubscript{CHELATED}

The geometries, bond parameters (Å), and calculated energies of the optimized complexes, C-I\textsubscript{Na}, TS\textsubscript{1Na}, and C-II\textsubscript{Na}, are shown in Figs. 2 and 3. The complexes C-II\textsubscript{Na}−O\textsubscript{2}−A and -B were derived from C-I\textsubscript{Na}−O\textsubscript{2}−A and -B were derived from C-I\textsubscript{Na}−O\textsubscript{3}−A via TS\textsubscript{1Na}−O\textsubscript{2}−A (path A) and -B (path B), respectively, as shown in Fig. 2. The complexes C-II\textsubscript{Na}−O\textsubscript{3}−A and -B were derived from C-I\textsubscript{Na}−O\textsubscript{3}−A via TS\textsubscript{1Na}−O\textsubscript{2}−A (path A) and -B (path B), respectively, as shown in Fig. 3. (Eq. 3-1). The designations, C-I\textsubscript{Na}−O\textsubscript{2}−C and C-I\textsubscript{Na}−O\textsubscript{3}−C, refer to complex C-I\textsubscript{Na} with coordination between the Na\textsuperscript{+} atom of I to the O\textsubscript{2} or O\textsubscript{3} atoms, respectively, of syn-3. The energies (kcal), which are shown in parenthesis, are the differences between the energies of TS\textsubscript{1Na} and C-I\textsubscript{Na}, specifically, the activation energies during the C–N bond formation process. Among the available paths, path A in Fig. 3 (4.74 kcal) was kinetically the most favorable path in the formation of C-II\textsubscript{Na}. The final geometries of CH\textsubscript{3}COCH\textsubscript{2}NO moieties for each C-II\textsubscript{Na} structures (Figs. 2, 3) show completion of the C–N bond formation. The transformation from TS\textsubscript{1Na} to C-II\textsubscript{Na} also involved structural changes in the [CH\textsubscript{3}COCH\textsubscript{2}]\textsuperscript{−}Na\textsuperscript{+} moiety, from the enol- to the keto-form. In the structures of C-II\textsubscript{Na}−O\textsubscript{2}−A and C-II\textsubscript{Na}−O\textsubscript{2}−A, two leaving groups, CH\textsubscript{3}O\textsuperscript{−} and H\textsuperscript{2}, were arranged nearly antiperiplanar to one another (∠H\textsubscript{2}C\textsubscript{2}NO\textsubscript{3}=174.8°, 137.9°), respectively. This conformation indicated that the elimination reaction of these groups was facile with non-energy barrier. The structure of C-II\textsubscript{Na}−O\textsubscript{2}−A was similar to that of the complex produced in the nitrosation of I with anti-3.\textsuperscript{4) The eliminations of CH\textsubscript{3}O\textsuperscript{−} group and H\textsuperscript{2} atom in C-II\textsubscript{Na}−O\textsubscript{2}−A with a base afforded 4Z, as described in the previous paper.\textsuperscript{5) The N−O− bond length in both C-II\textsubscript{Na}−O\textsubscript{2}−A and C-II\textsubscript{Na}−O\textsubscript{2}−B was shown to be considerably exceeded during the C–N bond formation process.

C–N Bond Formation of the Naked Enolate of Acetone with syn-Form of Methyl Nitrite via TS\textsubscript{CHELATED} The geometries, bond parameters (Å), and calculated energies of the optimized complexes (C-I, TS1, C-II, and C-II\textsubscript{Na}) derived via TS\textsubscript{CHELATED} and both paths (A and B; Eq. 3-2) are shown in Fig. 4. The geometry of C-II\textsubscript{Na}−B is the mirror image of that of C-II\textsubscript{Na}−O\textsubscript{2}−A, and therefore the complex C-II\textsubscript{Na}−B, as well as C-II\textsubscript{Na}−O\textsubscript{2}−B, afforded 4Z via the subsequent elimination reaction, as described previously.\textsuperscript{6) The two leaving groups, CH\textsubscript{3}O\textsuperscript{−} and H\textsuperscript{2}, in C-II\textsubscript{Na}−B were nearly antiperiplanar to one another. The conformation of C-II\textsubscript{Na}−B indicated that the subsequent elimination reaction can easily occur with non-energy barrier to afford 4E.

Elimination of Methoxide and Proton from C-II\textsubscript{Na} with a Base Figure 5 shows the geometries and calculated energies of C-IV\textsubscript{Na} complexes, which were derived from the corresponding C-II\textsubscript{Na} with non-energy barrier in the elimination processes. Initially, the CH\textsubscript{3}O\textsuperscript{−} group of C-II\textsubscript{Na}−O\textsubscript{2}−A, as well as that in C-II\textsubscript{Na}−B, was eliminated using base CH\textsubscript{3}O\textsuperscript{−}, followed by deprotonation of the active hydrogen atom of the H–C\textsubscript{2} bond to yield 4Z as shown in C-IV\textsubscript{Na}−O\textsubscript{2}−A. Similarly,
Fig. 2. C–N Bond Formation Process of Nitrosation of Sodium Enolate of Acetone with $\text{syn-3}$ via $\text{TS}_{1_{\text{Na-O}}}$

Imaginary frequency modes are shown with bold arrows in the structures of the transition states.

Fig. 3. C–N Bond Formation Process of Nitrosation of Sodium Enolate of Acetone with $\text{syn-3}$ via $\text{TS}_{1_{\text{Na-O}}}$

Imaginary frequency modes are shown with bold arrows in the structures of the transition states.
C-IVNa–O3-B was obtained as 4Z from C-IINa–O3-B. In contrast, although the elimination reaction proceeded through mechanisms similar to that for C-IINa–O2-A, C-IV Na–O3-A was obtained as 4E from C-II Na–O3-A. C-IV Na-A was obtained as 4E from C-IIINa-A. As a note, hydroxyimino compound was not formed in the elimination process of C-IINa–O2-B with a base.

Concluding Remarks

Our studies have shown that the complex C-IINa–O3-A was

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Fig. 4. C–N Bond Formation Process of Nitrosation of Naked Enolate of Acetone with syn-3 via TS\_OPEN

Imaginary frequency modes are shown with bold arrows in the structures of the transition states.

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Fig. 5. Elimination Process of Nitrosation
formed kinetically most readily as the intermediate of the reaction between \(1\) and \(\text{syn-3}\) via \(\text{TS}_{\text{CHELATED}}\) with the \(\text{O}^3\) atom coordinated to the \(\text{Na}^+\) atom. The active hydrogen atom of the \(\text{H}–\text{C}_2\) bond in \(\text{C-II}_{\text{Na}}–\text{O}^3\)-\(\text{A}\) reacted with base \(\text{CH}_3\text{O}^-/\text{H}_2\text{O}\), and the reaction induced the demethoxylation of \(\text{3 moiety in C-II}_{\text{Na}}–\text{O}^3\)-\(\text{A}\) with non-energy barrier, followed by deprotonation to give \(\text{4E}.\) \(\text{4E}\) was obtained from the other complex, \(\text{C-II}_{\text{Na}}–\text{A}\), which consisted of the naked enolate \(\text{2}\) and \(\text{syn-3}\). For the formation of \(\text{4E}\) in the nitrosation of \(\text{CH}_3\text{COCH}_3\) with \(\text{3}\), the geometry of \(\text{3}\) in the complex must be in the \(\text{syn}\)-form during the process of the formation of \(\text{C-II}_{\text{Na}}\). Furthermore, it is required that the \(\text{O}^3\) atom of \(\text{syn-3}\) moiety is coordinated to the \(\text{Na}^+\) atom in these complexes.

The \(E/Z\) ratio of the hydroxyimino compound decreases when \(\text{tert-butyl nitrite having a predominant anti-form is used in place of \(\text{syn-3}\) in the nitrosation, since the \(\text{O}^3\) atom in \(\text{tert-butyl nitrite does not coordinate to the \(\text{Na}^+\) atom in the TS unless the conformation is transformed by the steric hindrance.}

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\textbf{References and Notes}