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# An MO Study of the Reaction Mechanism of Photoisomerization from Isoxazole *via* Azirine Intermediate to Oxazole

Hidetsugu TANAKA, Yoshihiro OSAMURA, Toshio MATSUSHITA,
and Kichisuke NISHIMOTO*

*Department of Chemistry, Faculty of Science, Osaka City University, Sumiyoshi-ku, Osaka 558*

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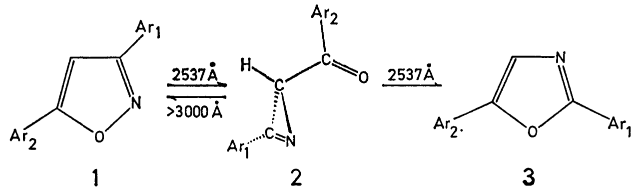
The reaction mechanism of photoisomerization of isoxazoles and the wavelength dependent photochemistry of azirine intermediates which are the photoisomerization reaction intermediates are investigated theoretically by means of *ab initio* MO-CI calculation. The present calculation shows that the lowest excited singlet state, $S_1$, of azirine intermediate is an $(n\rightarrow\pi^*)$ state localized at the carbonyl chromophore, while the $S_2$ state is assigned to be an $(n\rightarrow\pi^*)$ state localized at the ketimine chromophore. Intersystem crossing from $S_1$ to $T_1$ states of azirine intermediate causes the N–C bond rupture of azirine ring and leads to isoxazole. On the other hand, azirine intermediate in the $S_2$ state proceeds to the C–C bond break of azirine ring and converts to oxazole *via* intersystem crossing to the $T_1$ state.

Some of five-membered heterocycles undergo the isomerization reactions in which two of ring atoms interchange their positions under the influence of UV-visible light. For instance, 2-substituted thiophenes were found to rearrange into 3-substituted thiophenes,1) and 1,4-dimethylimidazoles into 1,2-dimethylimidazoles.2) These reactions have been supposed to proceed *via* bridged-valence intermediates similar to those in the photochemical rearrangements of benzene derivatives.3) Singh and his co-workers have studied the photochemical isomerization of diarylisoxazoles (**1**) to diaryloxazoles (**3**) and proposed an alternative mechanism which proceeds *via* the three-membered intermediates.4) This reaction is of compelling interest both experimentally and theoretically, since 2-aroyl-3-aryl-2*H*-azirines(**2**) have the reactivity strongly depending upon the wavelength of irradiation light.4c)



In the present study, *ab initio* MO-CI calculations have been carried out for isoxazole (**1a**) (a: $Ar_1=Ar_2=H$, see Fig. 1), 2*H*-azirine-2-carbaldehyde (**2a**), and oxazole (**3a**) which are the parent molecules of **1**, **2**, and **3**, respectively.5) On the basis of the calculated results, the reaction scheme and the wavelength dependency of the reactivity of **2** are discussed.

## Calculations

*Ab initio* MO calculations of **1a**, **2a**, and **3a** are carried out with the STO-3G minimal basis set using the GAUSSIAN 70 program package.6) The excited states of these species are calculated within the singly excited configuration interaction (SECI) procedure. In the SECI calculations, all the singly excited configurations are included except the inner-shell excitations.

The ground-state geometries of **1a**, **2a**, and **3a** are optimized using the STO-3G minimal basis set. Figure 2 shows the optimized geometries and those determined by means of double resonance modulated microwave spectroscopy7) in parentheses. The agreement between the calculated and the observed geometry is satisfactory.

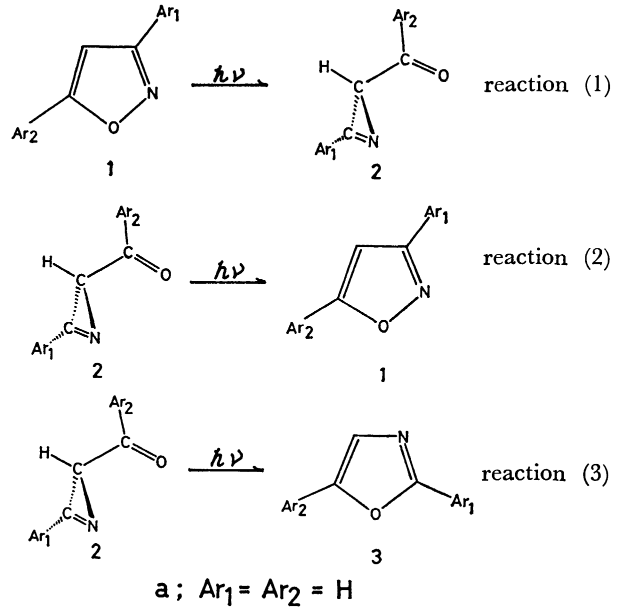
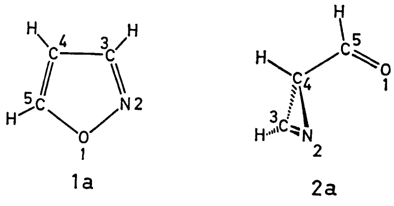


Fig. 1. Steps in the photoisomerization of isoxazole to oxazole.

The numbering of atoms of **1a** and **2a** is as follows.



## Results and Discussion

*Excited States of **1a**.* The energy levels and their assignments of the ground ($S_0$) and some low-lying excited states of **1a**, **2a**, and **3a** at the optimized ground-state geometries are shown in Fig. 3.

Before discussing the mechanism of the reactions

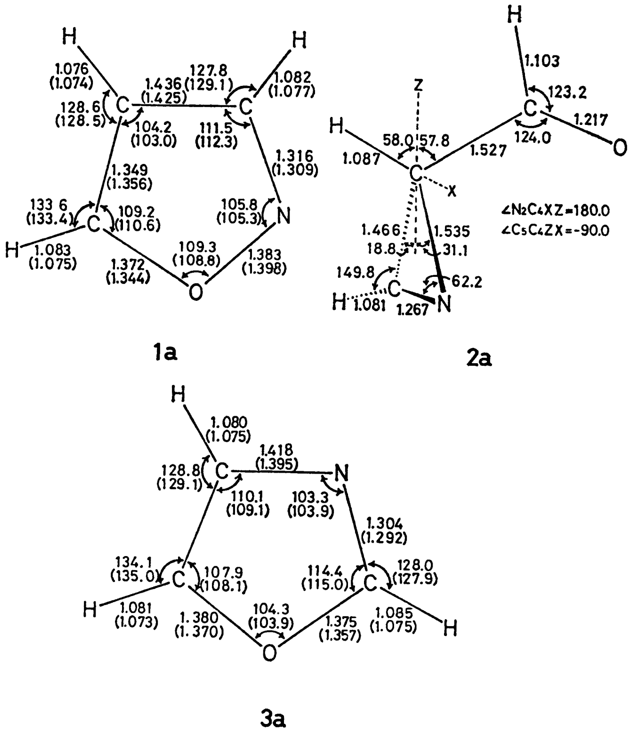


Fig. 2. Optimized ground-state geometries of **1a**, **2a**, and **3a**. **1a** and **3a** have a $C_s$ symmetry. Values in parentheses are those determined by the experiments, see Ref. 7. Units are shown in Å and degree.

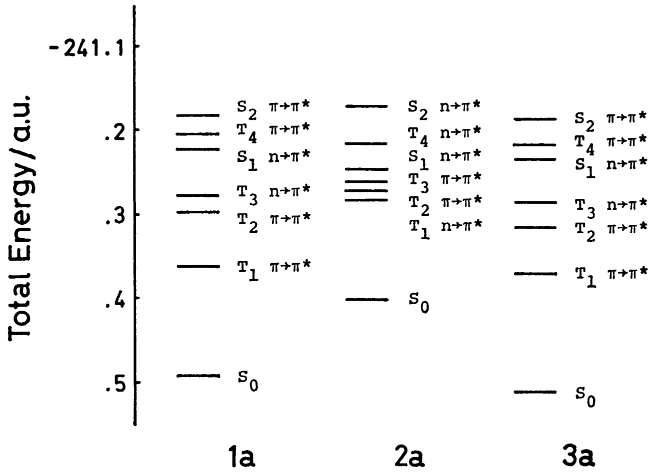


Fig. 3. State energies of the ground($S_0$) and some low-lying excited states calculated by vertical excitation approximation.

(1), (2), and (3) (see Fig. 1), it is of interest to examine the relation between the geometrical deformations and the state energy variation in the low-lying states of **1a** and **2a**. Several geometrical parameters are varied independently from the ground-state geometry. In **1a**, it is found that all of three geometrical variations, the $C_5$–$C_4$–$C_3$–$N_2$ torsional angle $\theta$ (by which the $N_2$ atom rises from the molecular plane and the $O_1$–$N_2$ bond is weakened), the $C_3$–$C_4$–$C_5$–$O_1$ torsional angle $\eta$ (by which the $O_1$ atom stands up from the molecular plane and the $O_1$–$N_2$ bond is weakened), and the rotational angle with respect to the perpendicular bisector of the $C_3$–$N_2$ bond $\gamma$ (by which the $O_1$–$N_2$ and the $C_3$–$C_4$ bonds are weakened simultaneously), give the rather flat potential curves in every excited states (see Figs. 4(a)—4(c)). The results of the independent geometrical variations show that the minima in the potential curves of the $S_1$ state appear at $\theta=12.3°$ (depth is *ca.* 1.0 kcal mol$^{-1}$), $\eta=17.2°$ (*ca.* 2.3 kcal mol$^{-1}$), and $\gamma=9.9°$ (*ca.* 0.7 kcal mol$^{-1}$).

*Excited States of* ***2a***. $T_1$ and $S_1$ states of this intermediate are (n→π*) states of the carbonyl chromophore and the $T_4$ and $S_2$ states are (n→π*) states of the ketimine chromophore. Since the $C_5$=$O_1$ and the $C_3$=$N_2$ parts are perpendicular to each other, the excited states related these parts do not mix.

There are two ways of the reaction in the excited azirine intermediate. One is the $N_2$–$C_4$ bond break and the $O_1$–$N_2$ bond formation (reaction (2)), and the other is the $C_3$–$C_4$ bond break and the $O_1$–$C_3$ bond formation (reaction (3)). The former is described by the change of the $N_2$–$C_3$–$C_4$ bond angle $\delta$ (which causes the $N_2$–$C_4$ bond scission) and the out-of-plane torsional angle of the azirine ring (the $C_4$–

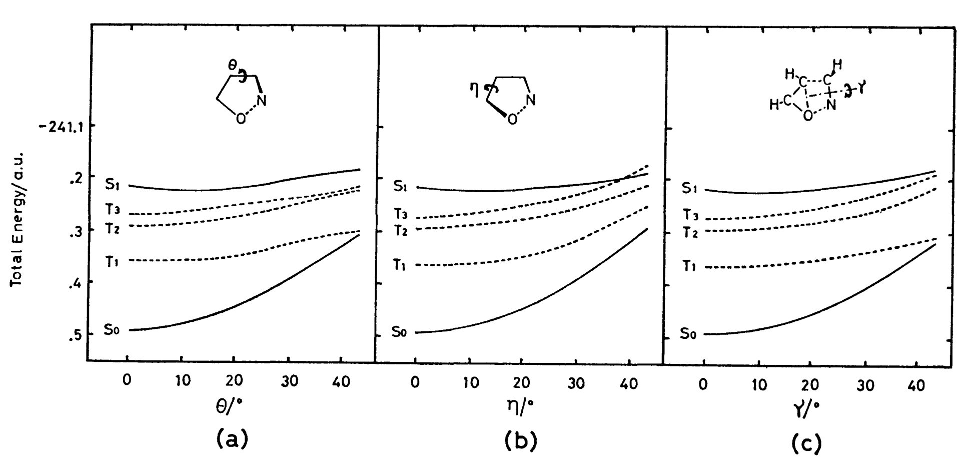
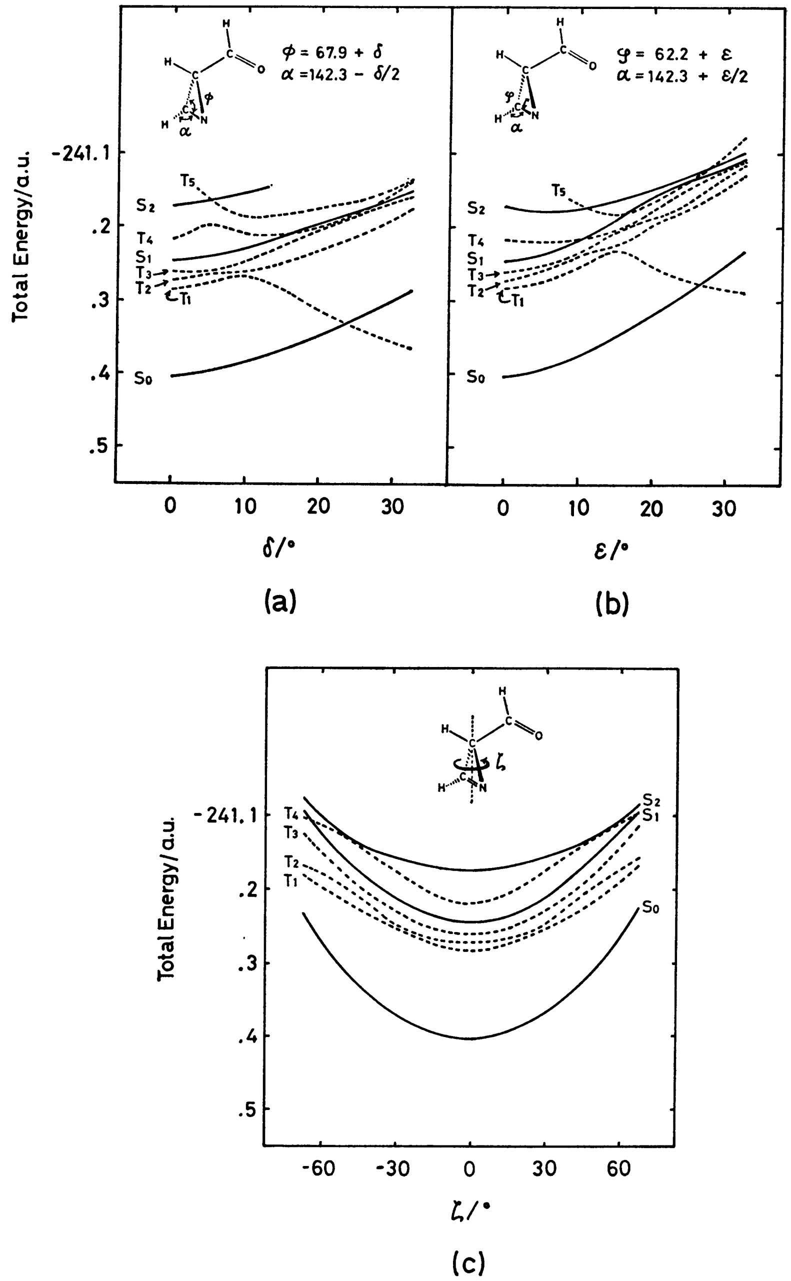


Fig. 4. State energy variations of **1a** by the deformations of (a) the $C_5$–$C_4$–$C_3$–$N_2$ torsional angle $\theta$, (b) the $C_3$–$C_4$–$C_5$–$O_1$ torsional angle $\eta$, and (c) the rotational angle with respect to the perpendicular bisector of the $N_2$–$C_3$ bond $\gamma$ relative to the ground-state geometry.



(a) (b)

(c)

Fig. 5. State energy variations of **2a** by the deformations of (a) the $N_2$–$C_3$–$C_4$ bond angle δ, (b) the $C_3$–$N_2$–$C_4$ bond angle ε, and (c) the out-of-plane torsional angle of azirine ring (the $C_4$–$N_2$–$C_3$ plane) ζ relative to the ground-state geometry.

$N_2$–$C_3$ plane) ζ. The latter is described by the change of the $C_3$–$N_2$–$C_4$ bond angle ε (which causes the $C_3$–$C_4$ bond scission) and the geometrical parameter ζ. These three geometrical parameters are varied independently from the ground-state geometry. The results for some low-lying states are given in Fig. 5. Other geometrical parameters are also varied, but such geometrical deformations destabilize considerably any state. Therefore, only the geometrical parameters δ and ε can contribute to the initial stage in the reactions (2) and (3). In other words, the character of the reaction coordinate is varied from δ or ε to ζ gradually as the reaction proceeds.

While the $S_1$ state does not mix with the $S_2$ state at $\delta=\varepsilon=0$, the geometrical deformations cause the mixing of excited states each other. Let us consider the mechanism of the $N_2$–$C_4$ bond scission due to the geometrical deformation δ. As Fig. 5(a) shows, the $T_1$ state becomes more stable at large δ. Therefore, this state promotes the $N_2$–$C_4$ bond scission. Since both the $S_1$ and $T_1$ states are $(n\rightarrow\pi^*)$ states of the carbonyl chromophore, and their energy separation is rather small, the intersystem crossing (ISC) between these states may rapidly occur. Thus, the excitation to the $S_1$ state leads to the $N_2$–$C_4$ bond scission *via* ISC to the $T_1$ state.

On the other hand, the geometrical deformation ε makes both the $T_1$ and $S_1$ states unstable, while it makes the $S_2$ state stable (see Fig. 5(b)). But the $T_1$ state becomes much stable at large ε. Therefore,

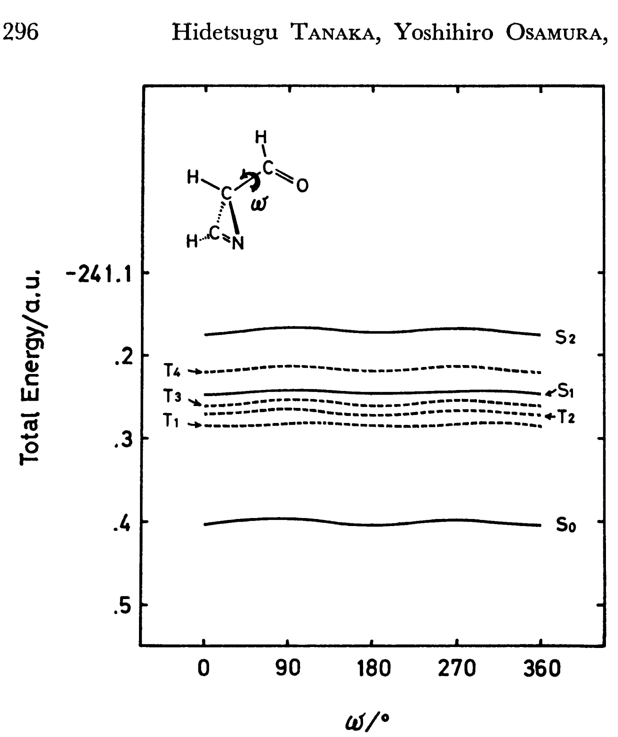


Fig. 6. State energy variation of **2a** by the rotation of CHO group ω. When ω=0° or 360°, **2a** is *s-trans* form. When ω=180°, it is *s-cis* form.

the $C_3$–$C_4$ bond scission occurs *via* ISC from the $S_2$ to $T_1$ states.

In the ground state, the *s-trans* form of **2a** is slightly stable than the *s-cis* form (*ca.* 0.5 kcal $mol^{-1}$). However, the *s-cis* form is of advantage to initiate the reactions. Energy variation with the rotation of the CHO group in the low-lying states is given in Fig. 6. The rotational barriers are calculated to be *ca.* 5.2 kcal $mol^{-1}$, *ca.* 2.6 kcal $mol^{-1}$, and *ca.* 5.1 kcal $mol^{-1}$ for the $S_0$, $S_1$, and $S_2$ states of **2a**, respectively. These energy barriers are rather small and, therefore, might obstruct the initiation of reaction.

*Reaction (1)*: ***1a→2a.*** In order to estimate the reaction path and the height of the barrier roughly, the geometies in the excited states are partly optimized (only several geometrical parameters are chosen) along the reaction paths which are infered from the results of independent variations of geometrical parameters given in Figs. 4 and 5.

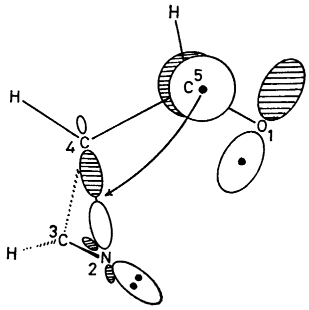
It is well known that the bond break and creation cannot be described correctly in terms of singly excited configurations only. Thus, all valence singly excited configurations and the doubly and triply excited configurations from three highest occupied (HO) MO's to three lowest unoccupied (LU) MO's ((S+D+T)-ECI) are included in the present optimization procedure. As a result of partial optimization, the energy in $S_1$ state of **1a** descents along the reaction path. On the other hand, the $T_1$ state has an energy hill (the roughly estimated height is about 40 kcal $mol^{-1}$, see Fig. 8), so that this reaction would proceed hardly in the triplet state. These results are in good agreement with the experimental results that the reaction (1) could not be sensitized with benzophenone, acetophenone, or acetone.[4]

As Fig. 4 shows, the $O_1$–$N_2$ bond of **1a** becomes loose in the excited states. This is in accordance with the experiments that the compounds containing the O and N atoms adjacently such as isoxazoline derivatives are easily cleft at the O–N bond under the influence of UV-visible light.[8]

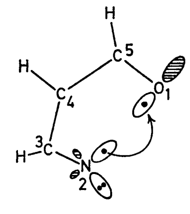
Let us consider this reaction in terms of the concept of orbital interaction.[9] The $\sigma$-type LUMO in **1a** is the *anti*-bonding orbital located at the $O_1$–$N_2$ bond. When a planar molecule such as isoxazole distorts with the out-of-plane motion, the $\sigma$-type LUMO becomes to mix with the occupied $\pi$ MO's. In addition, since both O and N atoms have negative net charges and lone pair electrons, they repel each other by the electrostatic force. Thus, this force may be helpful for the twisting out-of-plane motion at the $O_1$–$N_2$ bond. This is the same as in the case of peroxides and hydrazines in which O–O and N–N bonds are broken very easily. In the excited states, the orbital mixing easily occurs because the $\sigma$-type LUMO is close energetically to $\pi^*$ orbital and the out-of-plane distortion easily occurs, so that the $O_1$–$N_2$ bond break is promoted.

At the $S_1$ state of **1a**, the $O_1$–$N_2$ bond is cleft and a biradical might be formed at the $N_2$–$C_3$–$C_4$ part. Subsequently, the internal conversion (IC) into the ground state leads to the ring closure at the $N_2$ and $C_4$ atoms. Consequently, one can expect that the $O_1$–$N_2$ bond scission and the $N_2$–$C_4$ bond formation occur with nearly concerted manner.

*Reaction(2)*: ***2a→1a.*** As Fig. 5(a) shows, this reaction is favor to start from the $S_1$ or $T_1$ states which are (n→$\pi^*$) states localized at the $C_5$=$O_1$ chromophore. Therefore, in these excited states, electron charge density accumulates on the $C_5$ atom. The negative charge populated on the $C_5$ atom might delocalize into the $\sigma$-type LUMO of the three-membered ring which is the *anti*-bonding orbital ($\sigma^*_{C-N}$) of the $N_2$–$C_4$ bond.

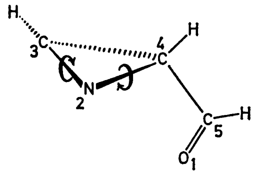


Thus, this type of orbital interaction and also the strain of the three-membered ring promote the $N_2$–$C_4$ bond scission. Since $\sigma^*_{C-C}$ orbital of the azirine ring lies much higher than $\sigma^*_{C-N}$ orbital, it does not mix with $\pi^*_{C-O}$ orbital so efficiently as $\sigma^*_{C-N}$ orbital. The reaction does not experience nitrene be-



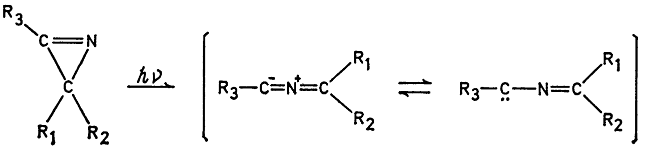
cause one of unpaired electrons is on the $O_1$ atom. That is, this reaction proceeds by above mentioned manner.

*Reaction (3)*: ***2a→3a***. As Fig. 5(b) shows, (n→π*) states of the $C_3$=$N_2$ chromophore, $S_2$ and $T_4$ states, become stable with the increase in the $C_3$–$N_2$–$C_4$ bond angle, because the hybridization on the N atom is varied from $sp^2$ to sp due to the removal of an electron from the lone-pair orbital of N atom (Walsh's rule).10) Bigot *et al.* have shown that the ring opening of 2*H*-azirine occurs *via* ISC from $^1$(n→π*) to $^3$(n→π*) states.11) The present results accord with theirs. But this ring opening would not occur with retaining the plane of azirine ring. The following motion would be also helpful for the ring opening.



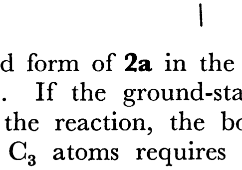
In fact, the present calculation shows that this conrotatory motion gives the descending potential curve in the $T_1$ state and leads to the $O_1$–$C_3$ bond formation.

Padwa *et al.*12) and Schmid *et al.*13) have reported that 2*H*-azirines undergo the irreversible ring opening at the C–C bond to give nitrile ylides as the reactive intermediates. These intermediates can be intercepted



with dipolarophiles to form five-membered heterocyclic rings or other type of isomers.14) With this analogy, Ullman and Singh have proposed nitrile ylide intermediates as the precursor of oxazole in the reaction (3).4b,15) In order to examine whether the reaction (3) proceeds *via* this intermediate or not, the state energy variation due to the deformation of the $C_3$–$N_2$–$C_4$ bond angle of the nitrile ylide intermediate $\chi$ is calculated. The result is shown in Fig. 7. The decrease of $\chi$ in the ground state indicates the slow energy ascent. One can expect that the nitrile ylide intermediate in the ground state transforms to an oxazole with relative low activation energy.

However, the ground-state nitrile ylide has a linear structure at the $C_3$–$N_2$–$C_4$ part, while the lowest excited state nitrile ylide is carbenic and has a bent structure such as



The ring opened form of **2a** in the triplet state seems to be biradical. If the ground-state nitrile ylide is formed during the reaction, the bond formation between $O_1$ and $C_3$ atoms requires too much motion of nuclei, which contravenes the principle of least motion.16) Therefore, it might be concluded that **3a** is formed without any intermediacy, that is, with almost one-step reaction.

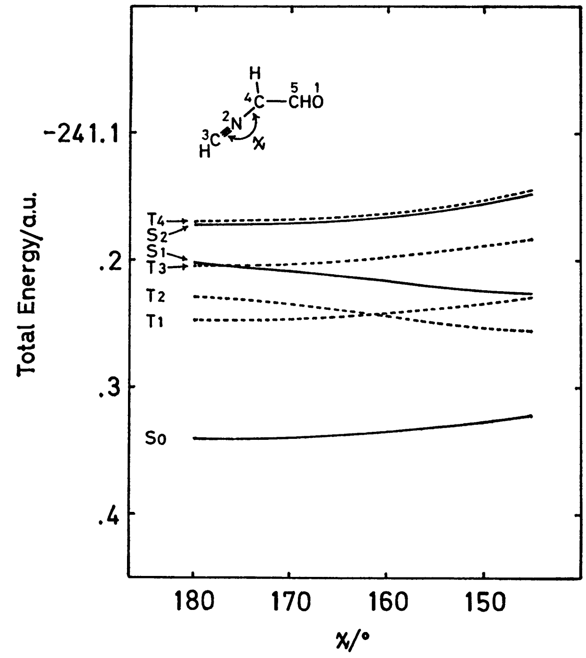
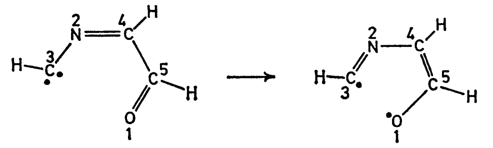


Fig. 7. State energy variation of nitrile ylide intermediate by the decrease of the $C_3$–$N_2$–$C_4$ bond angle $\chi$.



## Concluding Remarks

As Figs. 4 and 5 show, any geometrical deformation greatly destabilizes the ground states of both **1a** and **2a**, which suggests that these reactions hardly occur thermally.

As mentioned above, the azirine intermediate has different two reactive states, $S_1$ and $S_2$ states. These states are almost localized at the C=O and C=N chromophores, respectively, and lead to different reaction products each other *via* different reaction paths. This is the reason why the azirine intermediate has the wavelength dependent photochemistry.

From the calculated results, the mechanism of the photoisomerization of isoxazole can be summarized as follows;

Reaction (1): Isoxazole in the lowest $^1$(n→π*) state interconverts to azirine intermediate in the ground state through the $N_2$–$C_3$–$C_4$–$C_5$ torsional deformation which leads to the $O_1$–$N_2$ bond scission and the $N_2$–$C_4$ bond formation simultaneously.

Reaction (2): The $S_1$ state of azirine intermediate is an (n→π*) state of the carbonyl chromophore. The deformation of the $N_2$–$C_3$–$C_4$ bond angle in the $T_1$ state produced through the ISC from the $S_1$ state causes the $N_2$–$C_4$ bond rupture. Subsequently, odd electrons on the $O_1$ and $N_2$ atoms combine to form the $O_1$–$N_2$ bond, leading to the formation of isoxazole.

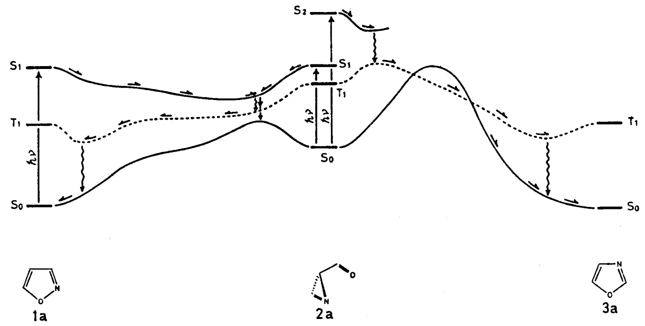


Fig. 8. The possible mechanism of the photoisomerization of isoxazole to oxazole infered from the present (S+D+T)ECI calculation.

This reaction does not experience nitrene.

Reaction (3): Azirine intermediate in $S_2$ state which is an (n→π*) state of the ketimine chromophore causes the $C_3$–$C_4$ bond rupture by the deformation of the $C_3$–$N_2$–$C_4$ bond angle. It is possible to follow the conrotatory motion in such a ring opening process. The transformation to oxazole proceeds *via* ISC from the $S_2$ to $T_1$ states. The doubly and triply excited configurations have an effect of small modification in this reaction.5) This reaction does not experience any intermediacy.

The possible reaction path of photoisomerization reaction of isoxazoles to oxazoles through azirine intermediates can be shown pictorially in Fig. 8.

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5) In order to compare the electronic structure of **1a** and **2a** with those of **1** and **2**, CNDO/S-CI calculations are carried out for 3,5-diphenylisoxazole and 2-benzoyl-3-phenyl-2*H*-azirine($Ar_1=Ar_2=C_6H_5$ in Fig. 1). See, H. Tanaka, T. Matsushita, Y. Osamura, and K. Nishimoto, *Int. J. Quantum Chem.*, **18**, 463 (1980).

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