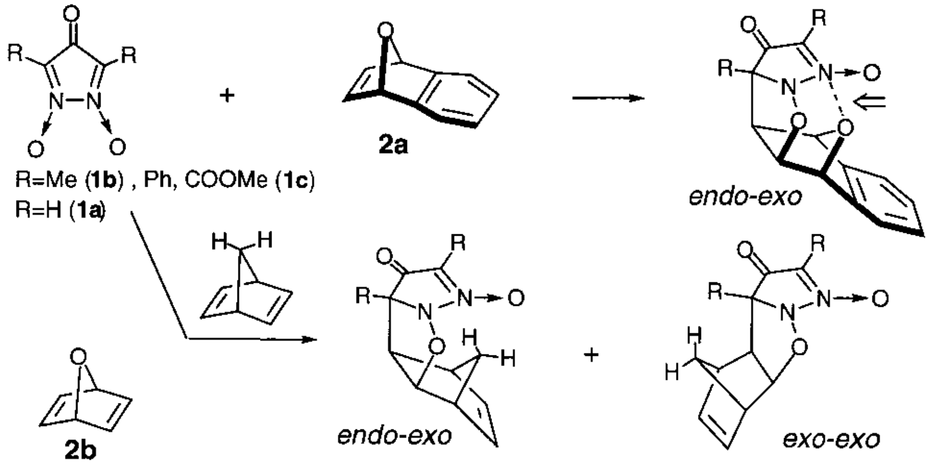
1,3-DIPOLAR CYCLOADDITION BEHAVIOR OF PYRAZOLONE *N,N*-DIOXIDES TOWARD EPOXYNAPHTHALENE. EFFECTIVE SECONDARY N···O INTERACTION BETWEEN ADDENDS

Yasuyuki Yoshitake, Masashi Eto, and Kazunobu Harano*[†]

Faculty of Pharmaceutical Sciences, Kumamoto University, 5-1 Oe-hon-machi,
Kumamoto 862, Japan

Abstract- Cycloaddition of pyrazolone *N,N*-dioxides (**1**) with epoxynaphthalene (**2a**) gave *endo* 1,3-dipolar cycloadduct. The origin of the high *endo* selectivity was explored by MO analysis of the transition structure. *Ab initio* calculation at several levels indicates that the orientation complex (OC) forms prior to the formation of the transition state (TS). The interaction between the oxygen of **2a** and the nitrogen of the >N→O group of **1** binds two addends together in both OC and TS.

In the previous papers,[1] we reported the cycloaddition behavior of 3,5-disubstituted pyrazolone *N,N*-dioxides (**1**) toward various unsaturated compounds. In the 1,3-dipolar reaction of **1** with epoxynaphthalene (**2a**), the *endo-exo* cycloadduct was produced stereoselectively, whereas the reaction of **1** with norbornadiene gave a mixture of *endo-exo* and *exo-exo* isomers.



Scheme 1

In the X-Ray structure of the cycloadduct (**3ca**) of 3,5-dimethoxycarbonylpyrazolone *N,N*-dioxide (**1c**) with **2a**, we found the presence of very close contact between the epoxy oxygen and the nitrogen atom of the remaining >N→O group, which is reproduced by MP2/3-21G calculation (Figure 1).

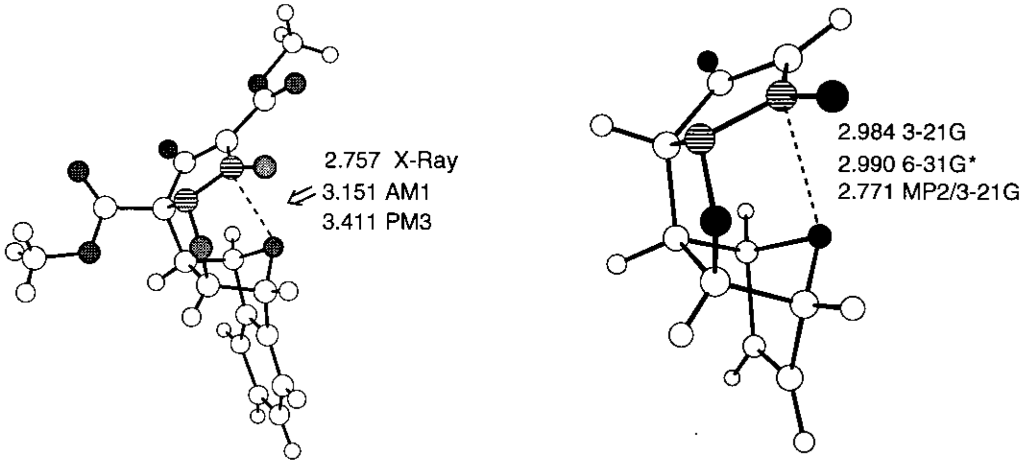


Figure 1. X-Ray and Semiempirical MO Structures of the *endo* cycloadduct (**3ca**) of **1c** and **2a** and the *ab initio* structures of model cycloadduct (*endo* **3ab**) of **1a** and epoxybenzene (**2b**).

These facts prompted us to consider that similar interaction must be operative in the transition state playing a leading role in determination of the stereoselectivity. This paper deals with the theoretical confirmation of the secondary interaction between the addends using the *ab initio* MO calculation.

RESULTS AND DISCUSSION

The model reaction selected for the present study is that of unsubstituted pyrazole *N,N*-dioxide (**1a**) with epoxybenzene (**2b**) which is a simplified form of epoxynaphthalene (**2a**). The energies of the *endo*/*exo* transition states for 1,3-dipolar cycloaddition reactions of **1a** with epoxybenzene are listed in Table 1. In PM3,[2] 3-21G and 6-31G* calculations,[3] the *exo* TS is slightly more stable than the *endo* TS, whereas the STO-3G and MP2/3-21G calculations predicted that the *endo* adduct is predominant.

Table 1. Energies of the Transition States for Cycloaddition of **1a** with Epoxybenzene (**2b**)[a)]

Method	E_{endo}	E_{exo}	ΔE (E_{endo} - E_{exo})
PM3	101.531[b)]	101.211[b)]	0.320[c)]
STO-3G	-743.7612	-743.7608	-0.251
3-21G	-753.4320	-753.4332	0.753
6-31G*	-753.4466	-753.4479	0.816
MP2/3-21G	-750.7976	-750.7958	-1.130

a) *Exo* attack with respect to epoxybenzene. b) Heat of formation (ΔHf) c) ΔHf_{endo} - ΔHf_{exo}

The exclusive *endo* cycloadduct formation is considered to be destined to occur by an additional factor before formation of the TS. As described above, the X-Ray structure of the *endo* adduct (**3ca**) and the *ab initio* TS structures gave us a clue to solve the problem.

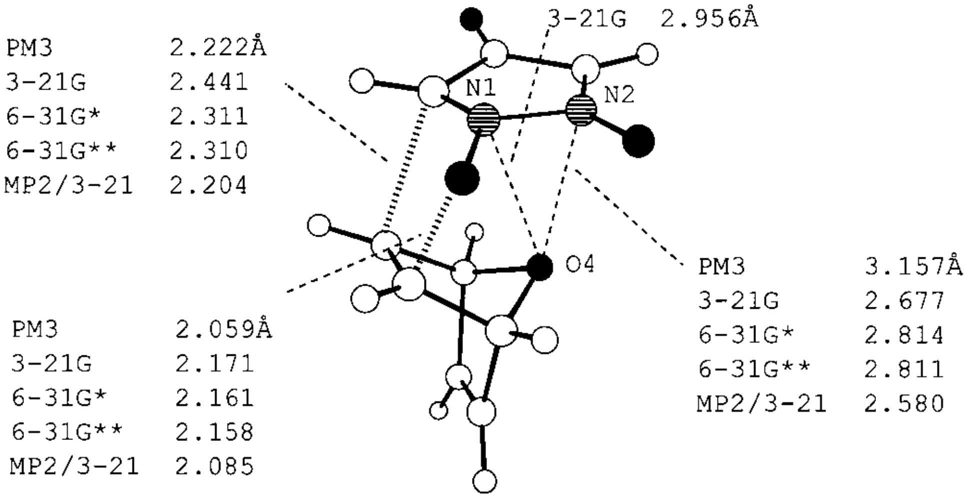


Figure 2. Partially formed C--C and C--O Bond Lengths and N--O Short Contacts in the *endo* Transition State (**TSab**)

As seen in the *endo* **TSab**, the forming N--O and C--C bond distances calculated at RHF levels are longer than those obtained by MP2/3-21G calculation, which are comparable to the PM3 distances. The interatomic distance between N1 (and N2) and O4 is interesting. The 3-21G calculation indicates that the N2----O4 (2.677Å) is shorter than the N1----O4 (2.956Å). The 6-31G* and 6-31G** N2----O4 distances is 2.814 and 2.811 Å, respectively, slightly longer than the X-Ray distance (2.757Å) of the *endo* adduct (**3ca**).

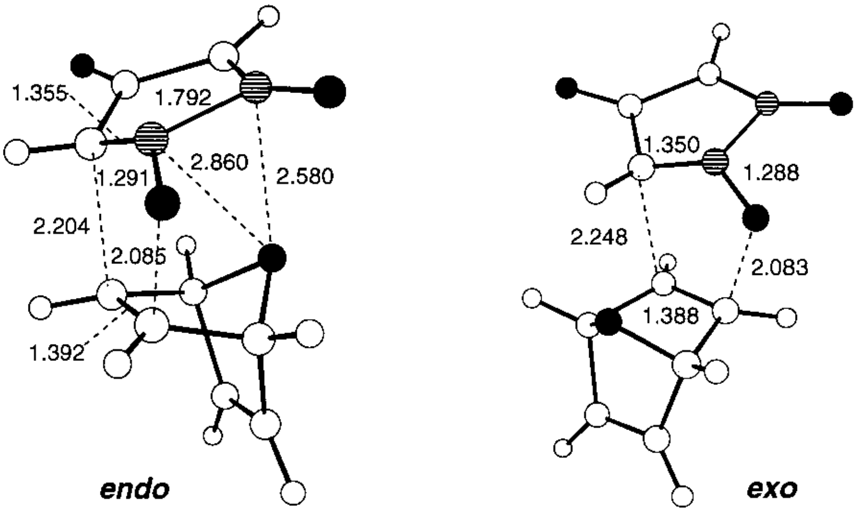


Figure 3. Geometries of MP2/3-21G **TSab**

The PM3 distance is 3.157Å, which may be overestimated than the actual value.[4]

The MP2/3-21G TS geometries leading to the *endo* and *exo* adducts are depicted in Figure 3, wherein the N----O close contact of the *endo* TS is 2.580 Å, considerably shorter than the sum of the VDW distance of N and O atoms.

Based on these consideration and observation of a charge-transfer (CT) complexation[5] between **1c** and electron-rich dipolarophiles such as *N*-vinylcarbazole,[1b] we arrived at the conclusion that the initial interaction leading to *endo* cycloaddition involves orientation complexes of CT type.

In order to obtain information about the formation of orientation complex between **1a** and **2b**, we calculated various geometries of the molecular complexes, in which two addends were placed 3.0Å apart and fully optimized. The most stable structure of complex calculated at the 6-31G* level is depicted in Figure 4. The stabilization energy due to complexation is 5.8 kcal mol^{-1}, in which the two N----O distances are 3.020 and 3.062Å, respectively.[6]

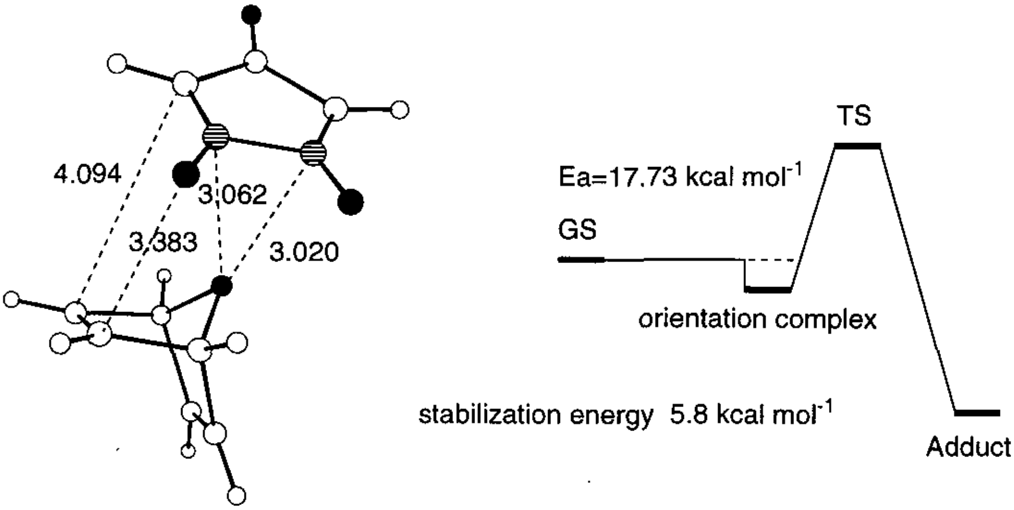
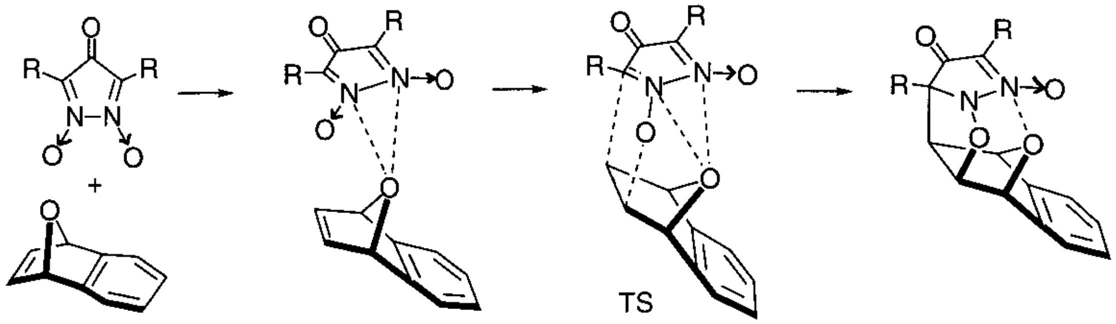


Figure 4. 6-31G* Geometry of Orientation Complex and Stabilization Energy

Along the progress of the cycloaddition (addends → orientation complex → TS → cycloadduct), the two addend are loosely united by the N2----O< interaction with the distance being kept among 2.8-3.0Å (Scheme 2).

The highly negative entropies of activation ($\Delta S^{\ddagger}$)[7] which were observed in the reactions of 3,5-disubstituted pyrazolone *N,N*-dioxides (**1b,c**) with **2a** reflect crowded transition states in which freedom of motion is unduly hindered. The 1,3-dipolar reactions exhibit entropies of activation ranging from -29 to -33 e.u. For example, the $\Delta S^{\ddagger}$ for the reaction of **1b** with **2a** is about 12 e.u. lower than that reported for the reaction of phenyl-*N*-methylnitrone with methyl methacrylate (Table 2). The extra N2--O< interaction besides the N1--O< attraction in pyrazolone *N,N*-dioxides obviously adds to the crowding in the transition state.



Scheme 2

Table 2. Activation Parameters for the 1,3-Dipolar Reactions of Phenyl-*N*-methylnitrone and Pyrazolone *N,N*-Dioxides with Some Dipolarophiles.

1,3-Dipole/Dipolarophile[a]	$\Delta H^{\ddagger}$(kcal mol^{-1})	$\Delta S^{\ddagger}$(e.u.)
phenyl-*N*-methylnitrone/methyl methacrylate[b]	15.7	-32
phenyl-*N*-methylnitrone/2-vinylpyridine[b]	10.7	-29
1b/2a	12.7	-46
1c/2a	9.4	-43

a) in toluene. b) ref. 8.

As shown in Figure 4, the 6-31G* geometry of the orientation complex is very similar to the TS structure, which is favorable for the movement to the *endo* TS. On the other hand, the transformation from the orientation complex to the *exo* TS is considered to require a large structural change which is energetically unfavorable.

At present, the ^{1}H-NMR spectral evidence for the presence of the orientation complex among **1b,c** and **2a** in solution could not be obtained.

The study of weak interactions to control the stereo, peri and regioselectivities is in progress.

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† E-mail: harano@gpo.kumamoto-u.ac.jp

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