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Enhanced *Endo* Selectivity in 1,3-Dipolar Cycloaddition of Pyrazolone *N,N*-Dioxides with Dipolarophiles Having Ether and Carbonyl Groups. Role of the Remarkably Long N-N Bond

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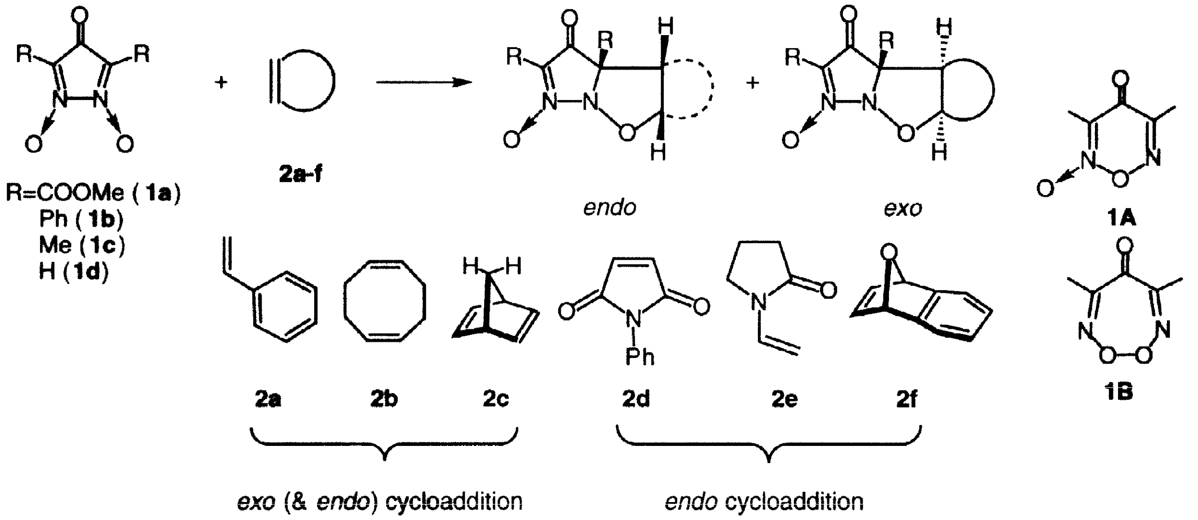
Abstract: The X-ray analysis of 2,5-dimethylpyrazolone *N,N*-dioxides (**1c**) revealed that the N-N bond is remarkably long [1.650(4) Å]. Inspection of the crystal packing diagram suggested that the interaction between the nitrogen atoms of the dioxides and the carbonyl oxygen is operative, indicating the presence of a molecular complex before the formation of the TS in the 1,3-dipolar cycloaddition.

In the previous papers,[1] we reported the 1,3-dipolar cycloaddition behavior of 3,5-disubstituted pyrazolone *N,N*-dioxides (**1a-c**)[2] toward various unsaturated compounds. It was noted that the *exo* 1:1 cycloadducts were predominantly formed in styrene (**2a**), 1,5-cyclooctadiene (**2b**) and norbornadiene (**2c**), whereas the ***endo*** cycloadducts were obtained in dipolarophiles bearing carbonyl or ether oxygen [*N*-phenylmaleimide (**2d**), *N*-vinylpyrrolidinone (**2e**) and epoxynaphthalene (**2f**)]. The PM3 calculation[3] predicted that the parent pyrazolone dioxide would have a very low LUMO energy level and a remarkably long N-N bond length exceeding 1.7 Å.



In this paper, we discussed the observed *endo/exo* selectivity based on the X-ray analysis and MO calculation data.

First of all, we clarified the structure of 2,5-dimethylpyrazolone *N,N*-dioxide (**1c**).[4a] The computer-generated drawing of the crystal structure is depicted in Fig. 1. The result gave a definitive evidence for the *N,N*-dioxide structure, ruling out the alternative structure[2b] (**1A** or **1B**). However, the N-N bond length was found to be remarkably elongated [1.650(4) Å], suggesting that the dioxide has a different electronic character from that of the nonelongated structure. Inspection of the X-ray structure of **1c** indicates that the structure of the nitrone moiety closely resembles the remaining nitrone moiety of the cycloadduct of epoxynaphthalene and **1a**.[1b, 5]

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Table 1. X-Ray and Calculated Bond Lengths (Å) of **1c**

Method	N→O	N=C	N-N	C=O	C-C
X-ray	1.226(4)	1.295(4)	1.650(4)	1.209(4)	1.467(4)
AM1	1.185	1.346	1.623	1.223	1.496
PM3	1.209	1.328	1.730	1.205	1.496
3-21G	1.283	1.275	1.546	1.204	1.484
6-31G*	1.208	1.277	1.518	1.186	1.482
MP2/6-31G*	1.213	1.317	1.806	1.238	1.470
B3LYP/6-31G*	1.214	1.300	1.723	1.220	1.482

In order to know an origin of the bond elongation, we performed the MO calculation. The structural data calculated by semiempirical[3] and *ab initio* methods with several basis sets[6] are listed in Table 1. The N-N bond length is significantly affected by the computational level, ranging from 1.518 to 1.806 Å. The RHF/3-21G and 6-31G* values are remarkably shorter than the X-ray value. The MP2/6-31G* and B3LYP/6-31G* calculated bond lengths are much longer than the others. The AM1 calculated bond length (bond order 0.553) is near the experimental value.

The AM1 calculations of some model compounds (**1d**, **3** and **4**) indicate that the substitution of the carbonyl moiety with ethylene or aminoethylene significantly shortens the N-N bond length [1.662 Å (>C=O) → 1.600 Å ($>C=CH_2$) → 1.551 Å ($>C=CHNH_2$)]. The *ab initio* calculations show a similar trend (Fig. 2). These results suggest that the bond elongation is derived from its antiaromatic character which can be rationalized in terms of the cyclic conjugation theory (see Figure in ref. 7). The compound **1d** is considered to be antiaromatic whereas the compound **4** has an aromatic character.

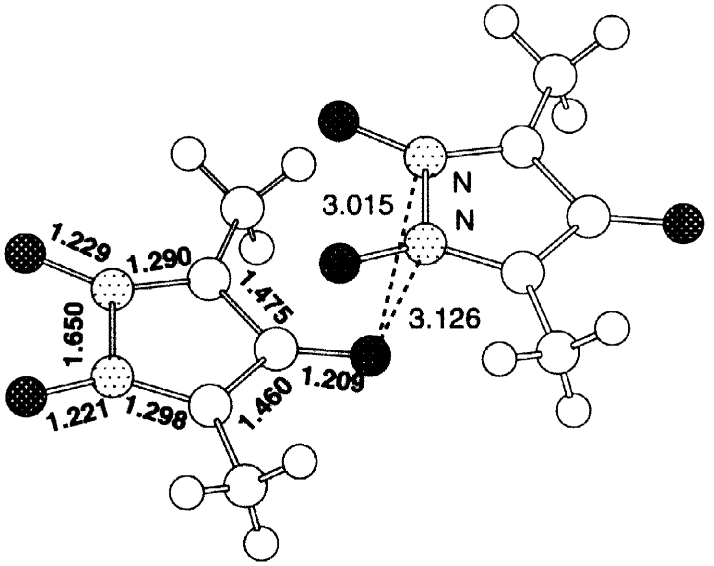
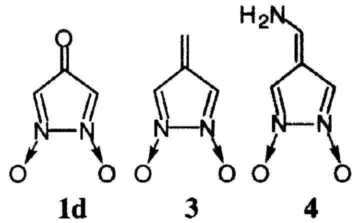


Fig. 1. Intermolecular Contacts (Å) in the Crystal of **1c**.



	1d	3	4
AM1	1.662Å	1.600Å	1.551Å
B3LYP/6-31G*	1.739Å	1.673Å	1.607Å
MP2/6-31G*	1.815Å	1.733Å	1.659Å

Fig. 2. Effect of Aromaticity on the N-N Bond Length of Some Model Compounds

The LUMO of the parent dioxide localizes in the vicinity of the elongated N-N bond (Fig. 4).[8] This suggests that the ON-NO moiety behaves as a strong acceptor toward electron-rich functional groups. In fact, the crystal packing diagram supported this assumption. As can be seen in Fig. 1, the molecules are arranged in a nearly parallel disposition (interplanar distance: *ca.* 3 Å) with a head to tail relationship, in which the two nitrogen atoms of **1c** link with the carbonyl oxygen of an adjacent molecule and the linkage is reinforced by the hydrogen bondings between the methyl groups and the oxygen atoms of the N-O groups. The N--O interactions observed in the crystal packing indicate that the 1,3-dipolar cycloadditions with dipolarophiles bearing carbonyl or ether oxygen might meet a similar interaction before the formation of transition states. Figures 3 and 5 show the molecular complex (**MC**) geometries optimized by AM1 and 6-31G* calculations.[9a] The calculated complexes take conformations in which the dipolarophile moiety is close to the reaction site of the 1,3-dipole, very favorable for the transformation to the corresponding transition states leading to the *endo* cycloadducts.

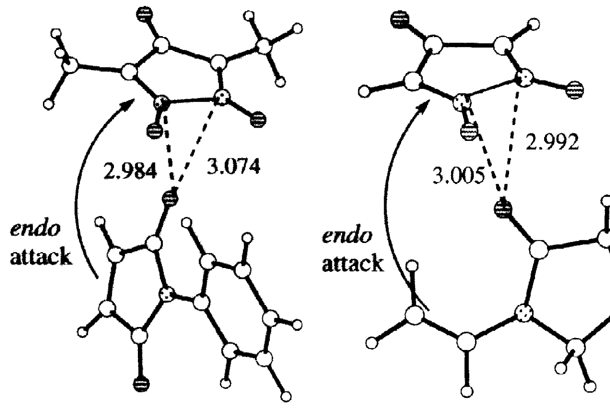


Fig. 3. Molecular Complexes (**MC**) leading to the *endo* TS's Calculated by AM1 for Cycloaddition of **1c** with **2d,e**

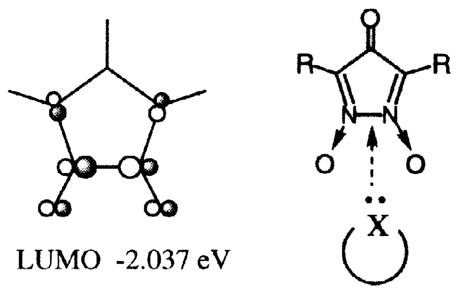


Fig. 4. LUMO of **1d** and Donor-Acceptor Interaction of **1** with Electron-rich Compounds

The AM1 intrinsic reaction coordinate (IRC) calculation supports this assumption. Fig. 5 shows the geometrical change along the reaction pathway for the model reaction of parent dioxide and epoxynaphthalene (**2f**). During the progress of the reverse reaction, the intermolecular N--O distance was kept within 3.2Å. The complex (**MC**) is stabilized by -2.5 kcal/mol.[9b]

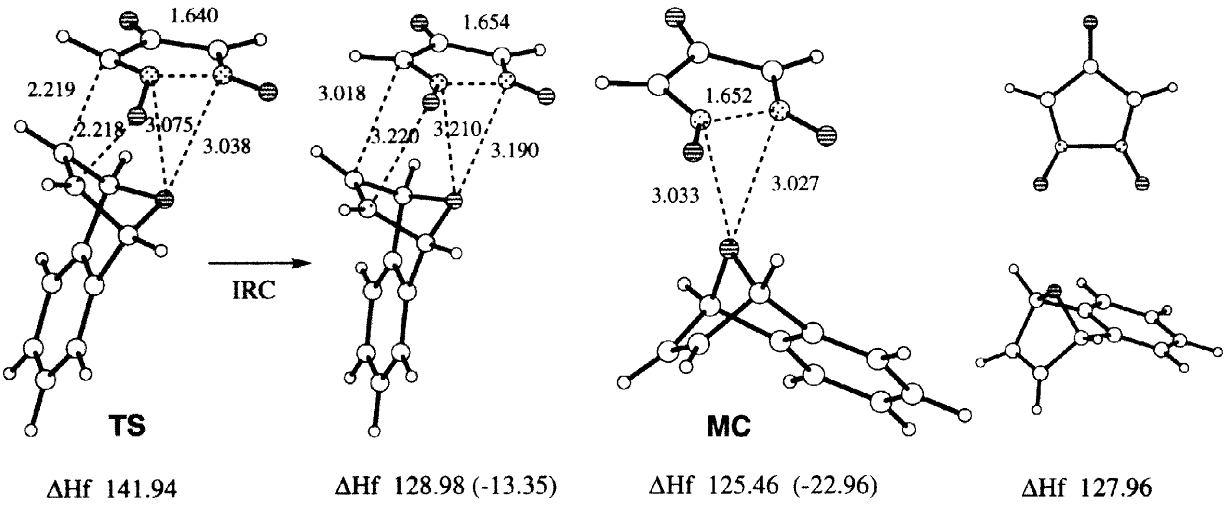


Fig. 5 AM1 Geometries and Heats of formation (kcal/mol) derived from the TS and IRC Calculations for the Cycloaddition of **1d** with **2f**.

In summary, the dioxides recognizes the carbonyl and ether oxygens to form molecular complexes to give the *endo* adducts. The charge transfer complex formation between **1a** and electron-rich species supports this assumption.[10]

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References and Notes

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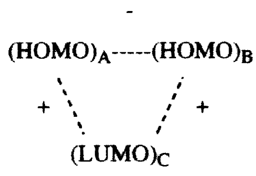
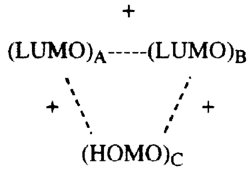
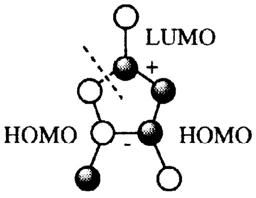
4. a) Crystal Data; $C_5H_6N_2O_3$ (**1b**), M=142.1. Orthorhombic, Space group $P2_12_12_1$, a=9.695(3), b=14.986(2), c=4.668(3) Å, V=678.1(4) Å^3, Dc=1.392 gcm^{-3}, Z=4. The reflection data were measured on RIGAKU AFC7R four-circle autodiffractometer with a graphite monochromated Mo-Kα radiation (50 kV-150 mA) and a rotating anode generator. A total og 951 reflections were collected. The structure was solved by the direct method.[4b] The block-diagonal least-square refinements based on 718 observed reflections (Fo >3.0σF) converged with weighted agreement factors (Rw) of 0.050. All calculations were performed on a Sun 4/2 work station with the Universal Crystallographic Computation Program (UNICS III).[4c] b) Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. "MULTAN78, a System of Computer Programs for Automatic Solution of Crystal structures from X-ray Diffraction Data", University of York, York, England, 1978. c) Sakurai, T.; Kobayashi, K. *Rikagaku Kenkyusho Hookoku*, **1979**, 55, 69.; Kawano, S. *Koho, Comput. Center Kyushu Univ.*, **1983**, 16, 113.
5. The N-N distance of the adduct is 1.493(3) Å.
6. Gaussian 94, Revision D.4, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian, Inc., Pittsburgh PA*, 1995.
7. a) There are two ways of dividing three systems according to their roles. They are two donors and one acceptor (case 1) and two acceptors and one donor (case 2). In case 1, the orbital phase relation for stabilization has been found to be in phase (+) between the HOMO of the donor A and the LUMO of the acceptor C, in phase between the HOMO of the donor B and the LUMO of the acceptor C, and out of phase (-) between (HOMO)$_A$ and (HOMO)$_B$. In case 2, each relation should be in phase between (LUMO)$_A$ and (HOMO)$_C$, between (LUMO)$_B$ and (HOMO)$_C$, and between (LUMO)$_A$ and (LUMO)$_B$.[7b] b) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.*, **1976**, 98, 4693-4701; Inagaki, S.; Hirabayashi, Y. *J. Am. Chem. Soc.*, **1977**, 99, 7418-7423.

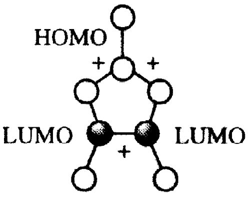


case 1



case 2





8. The NLUMO consists of π-orbitals.
9. a) The 6-31G* calculation gave a similar molecular complex for the reaction of **1d** and epoxybenzene. b) The AM1 heats of formation in **1d** and **1f** were 74.3 and 53.6 kacl/mol, respectively.
10. A preliminary study indicates that the second-order rate-constants decreased with the increase of the concentration of dipolarophiles.[11]
11. Andrews, L. J.; Keefer, R. M. *J. Am. Chem. Soc.*, **1955**, 77, 6284-6289.