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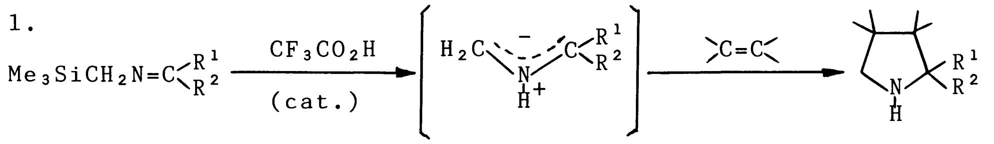
The Origin of Regio- and Stereoselectivities in 1,3-Cycloadditions of Azomethine Ylides Generated from N-(Benzylidene)trimethylsilylmethylamine and the Related Compounds[1)]

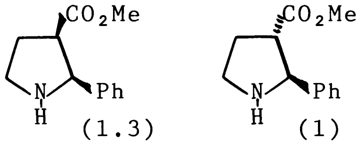
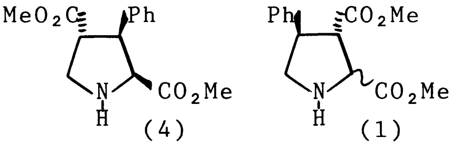
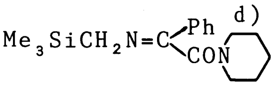
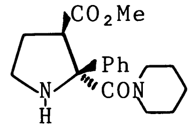
Nobuyuki IMAI, Hiroaki TOKIWA, Yukio AKAHORI, and Kazuo ACHIWA*
Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka 422

The frontier molecular orbital theory (*ab initio* procedures) was found to clearly explain the regio- and stereoselectivities in 1,3-dipolar cycloadditions of the azomethine ylides to conjugated olefins yielding the pyrrolidines.

Recently accumulated results[2)] on 1,3-dipolar cycloadditions of the azomethine ylides generated from N-(benzylidene)trimethylsilylmethylamine and the related compounds to conjugated olefins indicated that most of these reactions proceeded regio- and stereospecifically to give the corresponding pyrrolidines as illustrated in Table 1. On the other hand, the frontier molecular orbital theory[3)] has much successfully contributed to the theoretical development of cycloadditions.[4)] Houk et al. explained the regioselectivities in 1,3-dipolar cycloadditions of several types of ylides including simple azomethine ylides, based on this theory.[5)]

Table 1.



Substrate	Dipolarophile	Product[a)]	Regioselectivity / % Stereoselectivity / %
$Me_3SiCH_2N=CHPh$[b)]	$H_2C=CHCO_2Me$	 (1.3) (1)	≈100 57
$Me_3SiCH_2N=CHCO_2Me$[c)]	$PhCH=CHCO_2Me$	 (4) (1)	80 ≈100
 d)	$H_2C=CHCO_2Me$		≈100 ≈100

a) Ratio of the isomers is described in parentheses.
b) Unpublished data.
c) N. Imai, Y. Terao, and K. Achiwa, Heterocycles, 23, 1107(1985).
d) K. Achiwa, N. Imai, T. Motoyama, and M. Sekiya, Chem. Lett., 1984, 2041.

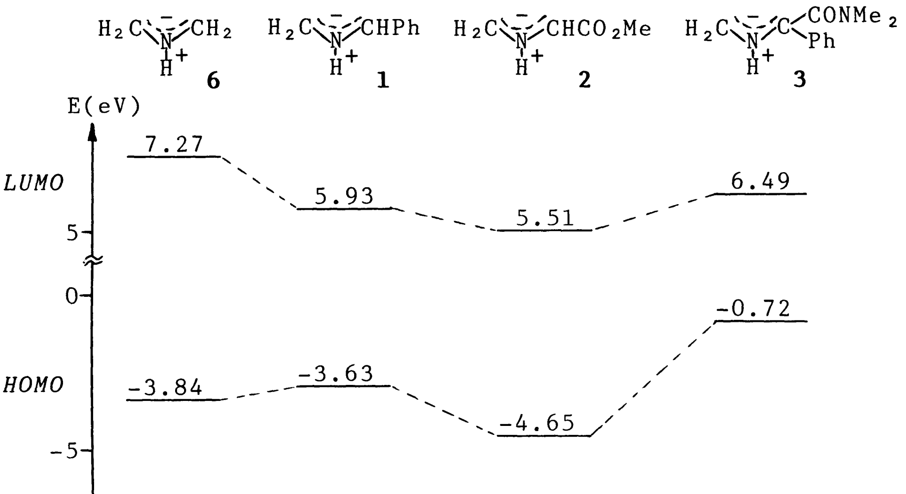


Fig. 1. The frontier orbital energies for azomethine ylides.

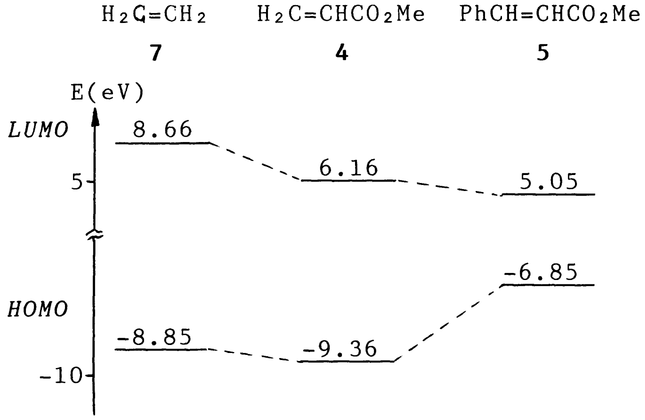


Fig. 2. The frontier orbital energies for dipolarophiles.

We carried out the *ab initio* molecular orbital calculation at the STO-3G level$^{6,7)}$ on the fully optimized geometry$^{8)}$ of azomethine ylides (**1**, **2**, **3**$^{9)}$) and dipolarophiles (**4**, **5**) for explaining the regio- and stereoselectivities in the 1,3-dipolar cycloadditions (Table 1) from the same viewpoint. As the frontier molecular orbital (HOMO, LUMO) energies of non-substituted azomethine ylide (**6**), **1**, **2**, and **3** are illustrated in Fig. 1 and those of ethylene (**7**), **4**, and **5** are illustrated in Fig. 2, the influence of substituted groups of azomethine ylides and dipolarophiles on their HOMO and LUMO energies is the same as that of dienes and dienophiles in general Diels-Alder reactions.$^{10)}$ Therefore, as shown in Fig. 3, all these reactions are controlled by the ylides' HOMO according to the Sustmann's classification.$^{11)}$ The frontier molecular orbital interactions between the dipoles (**1**, **2**, **3**) and the dipolarophiles (**4**, **5**) are indicated in Fig. 4 from the viewpoint of the frontier molecular orbital theory, in which the most developed lobe in HOMO of electron donors (dipoles) interacts the most developed lobe in LUMO of electron accepters (dipolarophiles). These calculated results agree with the experimental regioselectivities. And the stereoselectivities are explained by the secondary molecular orbital interaction$^{12)}$ between the ester orbitals and the phenyl ones of dipoles or dipolarophiles as indicated in Fig. 4.

It should be noted that the low stereoselectivity in the reaction of **1** with **4** was caused from the weakened secondary orbital interaction due to the less coplanarity between the azomethine group and the phenyl nuclei,$^{13)}$ that the low regioselectivity of **2** with **5** resulted from the similar LCAO coefficient values of the olefinic part in **5**, and that the stereospecificity in the reaction of **3** with **4** was enhanced by the steric hindrance between the rotated amide group of **3** and the ester of **4** in the stereoisomer-forming transition state.$^{14)}$

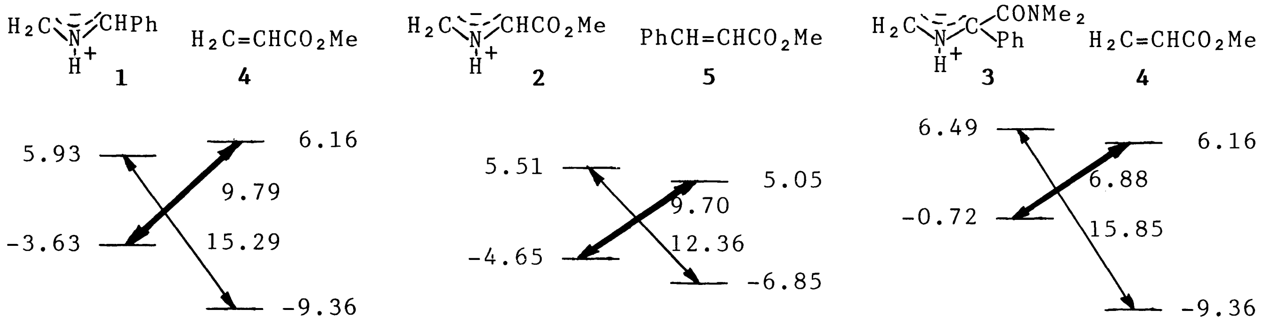


Fig. 3. HOMO-LUMO correlation diagram in 1,3-dipolar cycloaddition.

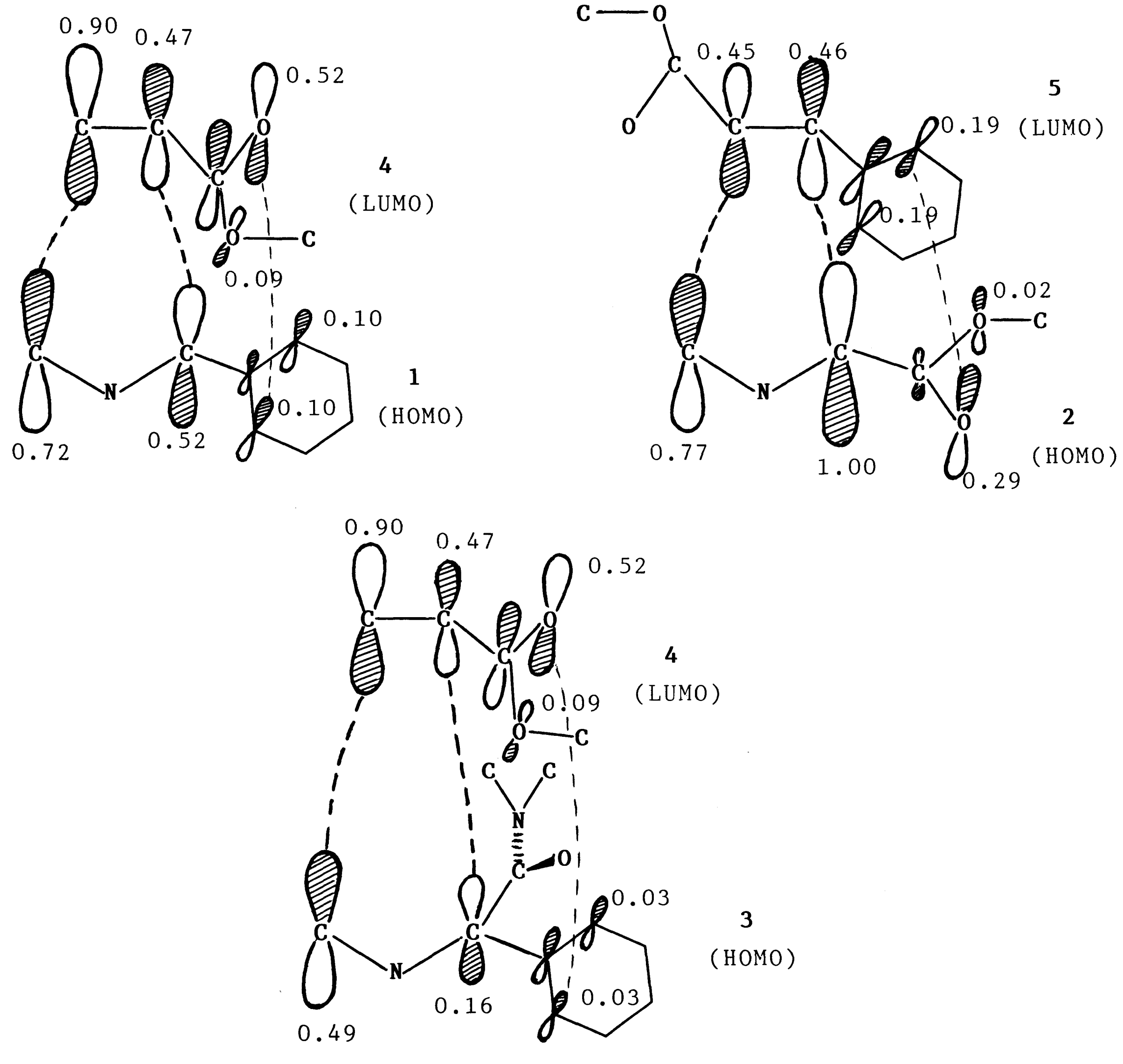


Fig. 4. The frontier molecular orbital interaction between dipoles and dipolarophiles in 1,3-dipolar cycloaddition. The numerals beside the lobes indicate the frontier electron densities.

The successful explanation on the regio- and stereoselectivities in the reaction of the complex azomethine ylides may emphasize the importance of the molecular orbital consideration on this type of cycloadditions.

References

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14) In the fully optimized geometry of **3**, the amide group rotated at a twisted angle of 69.0° with the plane of azomethine and phenyl groups. The stabilization by the amide group rotation is 9.2 kcal/mol.

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