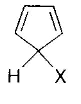
Effects of the π and π* Orbitals of the 5-Unsaturated Substituents on the π-Facial Selectivities in the Diels-Alder Reactions of Cyclopentadienes

Masaru Ishida,* Hiroki Kobayashi, Shingo Tomohiro, Hiroaki Wasada,† and Satoshi Inagaki*
Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-11
†*Faculty of Regional Studies, Gifu University, Yanagido, Gifu 501-11*

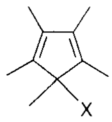
(Received September 8, 1997; CL-970691)

The exclusive anti-π-facial selectivity in the Diels-Alder reaction of 5-formylpentamethylcyclopentadiene, Cp*-CHO, was proposed to come from the π-HOMO distortion of the diene due to the perturbation by low-lying π* orbital on the substituent. The role of the π* orbital was experimentally substantiated by a considerable amount of syn-attack products in the reactions of Cp*-CH=NOH and Cp*-CH=CH_2 having high-lying substituent π* orbitals.

Recently, the orbital mixing rule[1,2] was applied to the prediction of the selectivity[3] in the Diels-Alder reactions of cyclopentadienes having substituents of π-systems at 5-positions, such as 5-cyano-, 5-carboxy-, and 5-(ethoxycarbonyl)cyclopentadienes, **1a**, **1b**, and **1c**.[4] Syn-π-facial preference observed in the reactions of the corresponding pentamethylcyclopentadienes **2a,b,c** was in good agreement with the predicted nonequivalency of π-HOMO due to σ mixing through the interaction with the π-orbital on the substituents.[5] These results allowed us to deduce that 5-formylcyclopentadiene **1d** (or **2d**), a typical candidate of this class of dienes, should react with syn π-facial preference. However, Adam et al. reported that the diene **2d** (X= CHO) reacts with exclusive anti π-facial selectivity.[6]



1a-f



2a-f

a: X= C≡N,
b: X= CO_2H,
c: X= CO_2Et,
d: X= CHO,
e: X= CH=NOH,
f: X= CH=CH_2

In this paper, we will disclose the origin of the selectivity in the reaction of 5-formyl diene **2d** and demonstrate that the orbital mixing rule is generally applicable to the reactions of cyclopentadienes having 5-substituents of π-systems, when the relative energies of the π-HOMO of the diene and the π and π* orbitals on the substituent, $\varepsilon_{\pi\text{-HOMO}}$, ε_{π}, and ε_{π^*}, are considered.

Application of the orbital mixing rule to such a system was classified into two categories, depending on the relationship of the orbital energies, $\varepsilon_{\pi\text{-HOMO}}$, ε_{π}, and ε_{π^*} (Figure 1). When the π* orbital lies much higher than the π-HOMO, the participation of the π* orbital in the orbital mixing is negligible. The π-HOMO of the diene combines with the low-lying π orbital out of phase and mixes the σ orbital of carbon framework out of phase with respect to the π orbital. The resulting FMO distorts to favor the reaction at syn side of the substituent (Case A: Ψ(FMO)= π-HOMO - π + σ).

On the other hand, when the π* orbital lies low enough to interact with the π-HOMO, the participation of the π* orbital needs to be taken into account. This is the case with **1d** (or **2d**). Combination of the π-HOMO with the high-lying π* orbital in phase, followed by mixing of the σ orbital out of phase with the π* orbital gives the FMO, which distorts to favor the reaction at anti side of the substituent (Case B: Ψ(FMO)= π-HOMO + π* - σ).

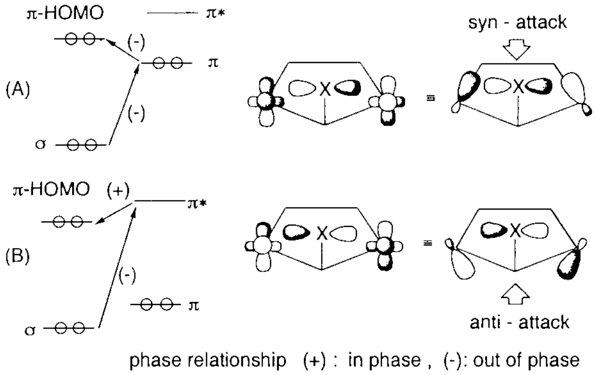


Figure 1. Direction of nonequivalent extension of the FMO of 5-substituted cyclopentadiene **1** Cp-X on the basis of the orbital mixing rule, where X is a carbon substituent of a π-system.

The predictions were examined by theoretical calculations. The molecular geometry of **1d** was optimized by ab initio calculation (RHF 6-31G*)[7] to be a Cs symmetric structure. The contour map of the section of x= 0.100Å of the FMO clearly indicated the in phase relationship between the π-HOMO and the π*. The FMO does distort to favor the reaction at the anti side of the formyl moiety in agreement not only with the prediction from the orbital mixing rule of case B, but also with the observed selectivity in the reaction of **2d** (**1d**: Figure 2).

The theoretical prediction was substantiated by the selectivities in the reactions of the modified dienes, 5-[(hydroxyimino)methyl]- and 5-vinylpentamethylcyclopentadienes, **2e** and **2f**. Since the orbital mixing of case A should be more significant in those dienes,[8] it is expected that the reactions of the dienes give syn-attack products at least to some extent, although it had been implied that anti addition was the exclusive mode of cycloaddition with the reaction between **2f** and maleic anhydride.[9] On the other hand, if the reason of the anti selectivity in the reaction of **2d** was largely steric repulsion as reported by Adam et. al,[6] the dienes should react with exclusive anti π-facial selectivity.

At first, ab initio molecular orbital calculation of the model dienes **1e** and **1f** was performed (RHF 6-31G*). In consonance with the prediction from the mixing rule of case A, the contour map of the FMO of **1f** at the section of x= 0.100 Å showed the out of phase relationship between the π-HOMO of the diene and the π on the vinyl moiety (**1f**: Figure 2).[10] The FMO distorts inwardly on the syn sides of the vinyl moiety.

The dienes **2e**[11] and **2f**[9] were prepared and subjected to the reactions with N-phenylmaleimide (NPM) in carbon tetrachloride

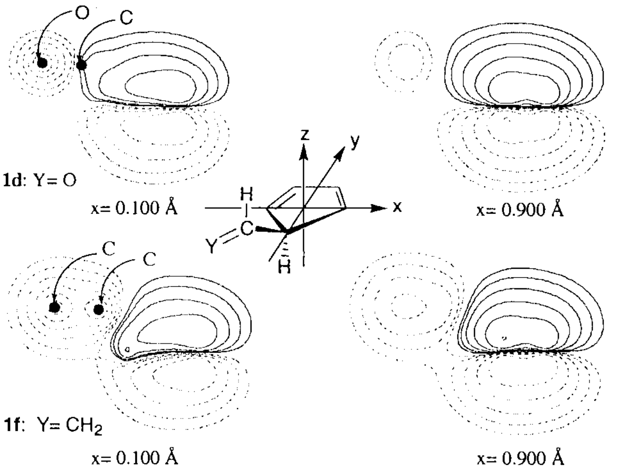
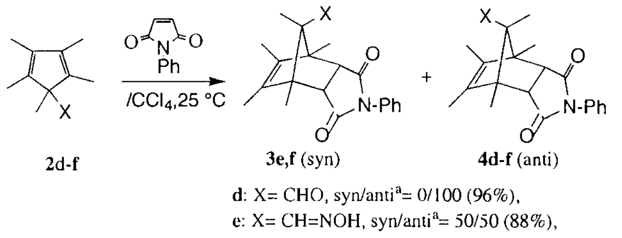


Figure 2. Contour maps of the FMO of **1d** and **1f** (at the sections of x= 0.100 and 0.900 Å) calculated with 6-31G* basis set. The dienes are Cs symmetric with respect to yz plane. The Cp rings are in xy plane and C-1 and C-4 carbons of **1d** and **1f** are at (±1.175. 0. 0) and (±1.180. 0. 0), respectively. The absolute value of the largest contour line is 1.25×10^{-3}AU for the plot of the x= 0.100 Å section and 5.0×10^{-3}AU for the plot of the x= 0.900 Å section. The heights of adjacent contours differ by a factor 2. The contours of the highest absolute value in the plots of **1d** and **1f** (x= 0.900 Å section) are observed at the anti and syn sides of the substituents, respectively.

at 25 °C. In both cases, formation of considerable amount of syn attack products **3e** and **3f** was observed.[11,12] In contrast, the reaction of **2d** with NPM gave exclusive formation of the anti attack product **4d** (Scheme 1). These results very clearly attest to the correctness of the prediction based on the orbital mixing rule.



2d-f **3e,f** (syn) **4d-f** (anti)

d: X= CHO, syn/anti[a]= 0/100 (96%),
e: X= CH=NOH, syn/anti[a]= 50/50 (88%),
f: X= $CH=CH_2$, syn/anti[a]= 33/67 (66%).

Scheme 1. [a]Products ratios and yields were determined on the basis of ^{1}H-NMR.

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture of Japan (**1996**, C2: No.08640680 and **1997**, A1: No.08305034).

References and Notes

1 a) S. Inagaki and K. Fukui, *Chem. Lett.*, **1974**, 509. b) S. Inagaki, H. Fujimoto, and K. Fukui, *J. Am. Chem. Soc.*, **98**, 4054 (1976).

2 a) M. Ishida, T. Aoyama, and S. Kato, *Chem. Lett.*, **1989**, 663. b) M. Ishida, Y. Beniya, S. Inagaki, and S. Kato, *J. Am. Chem. Soc.*, **112**, 8980 (1990). c) M. Ishida, T. Aoyama, Y. Beniya, S. Yamabe, S. Kato, and S. Inagaki, *Bull. Chem. Soc. Jpn.*, **66**, 3430 (1993). d) M. Ishida, S. Kakita, and S. Inagaki, *Chem. Lett.*, **1995**, 469.

3 Recent reports on π-facial selectivity in Diels-Alder reactions of 5-substituted cyclopentadienes: a) J. M. Coxon and D. Q. McDonald, *Tetrahedron Lett.*, **33**, 651 (1992). b) R. A. Poirier, C. C. Pye, J. D. Xidos, and D. J. Burnell, *J. Org. Chem.*, **60**, 2328 (1995). c) L. C. Burry, J. N. Bridson, and D. J. Burnell, *J. Org. Chem.*, **60**, 5931 (1995) and references cited therein. d) M. A. Wellman, L. C. Burry, J. E. Letourneau, J. N. Bridson, D. O. Miller, and D. J. Burnell, *J. Org. Chem.*, **62**, 939 (1997) and references cited therein. e) Review: A. G. Fallis and Y.-F. Lu, in "Advances in Cycloaddition" ed by D. P. Curran, JAI Press, Inc., Greenwich, CT(**1993**), Vol. *3*, pp 1 and references cited therein. f) Review: M. Ishida and S. Inagaki, *J. Synth. Org. Chem. Jpn.*, **52**, 649 (1994) and references cited therein.

4 M. Ishida, S. Tomohiro, M. Shimizu, and S. Inagaki, *Chem. Lett.*, **1995**, 739.

5 5-Ethynylcyclopentadiene CpC≡CH is also expected to react at syn-face. Computation of the selectivity in the reactions of CpC≡N and CpC≡CH with ethylene was reported: See Ref. 3b.

6 W. Adam, U. Jacob, and M. Prein, *J. Chem. Soc., Chem. Commun.*, **1995**, 839.

7 Gaussian 94, Revision C.3, M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA (1995).

8 The π* and π orbitals on the substituents of **1e** and **1f** lie much higher than those of **1d**. The orbital energies, ε_π and ε_π* of the mother compound H-X (RHF 6-31G*): H-X: (ε_π[AU], ε_π*[AU]), X= CHO (-0.5270, 0.1475), X= CH=NOH (-0.3982, 0.1785), X= $CH=CH_2$ (-0.3794, 0.1861).

9 W. Schäfer and H. Hellmann, *Angew. Chem.*, **79**, 566 (1967).

10 The calculation of **1e** gave similar results.

11 All new compounds gave ^{1}H-, ^{13}C-, mass spectroscopic (EI, CI) and analytical data consistent with the assigned structures. **2e:** mp 129-130°C; ^{1}H-NMR($CDCl_3$, 400MHz) δ 1.11 (s, 3H, CH_3), 1.73 (s, 6H, $2CH_3$), 1.80 (s, 6H, $2CH_3$), 6.60 (s, 1H, CH=N), 8.25 (s, 1H, OH); **4d:** mp 133-135°C; ^{1}H-NMR($CDCl_3$, 270MHz) δ 0.95 (s, 3H, CH_3), 1.47 (s, 6H, $2CH_3$), 1.70 (s, 6H, $2CH_3$), 3.12 (s, 2H, 2CH), 7.05-7.44 (m, 5H, Ph), 9.60 (s, 1H, CHO); **4d** displayed an NOE between the methyl protons at δ 0.95 and the methyne protons at δ 3.12. **3e**: mp 197-198°C; ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.87 (s, 3H, CH_3), 1.43 (s, 6H, $2CH_3$), 1.63 (s, 6H, $2CH_3$), 3.27 (s, 2H, 2CH), 7.04-7.45 (m, 5H, Ph),7.38 (s, 1H, C$\underline{H}$=N) 7.59 (s, 1H, OH); **3e** displayed an NOE between the imino proton at δ 7.38 and the methyne protons at δ 3.27. **4e:** mp 227-228°C; ^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.03 (s, 3H, CH_3), 1.35 (s, 6H, $2CH_3$), 1.65 (s, 6H, $2CH_3$), 3.16 (s, 2H, 2CH), 7.05-7.49 (m, 5H, Ph), 7.35 (s, 1H, C$\underline{H}$=N), 7.94 (s, 1H, OH); **4e** displayed an NOE between the methyl protons at δ 1.03 and the methyne protons at δ 3.16. **3f**: mp 115-116°C; ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.83 (s, 3H, CH_3), 1.29 (s, 6H, $2CH_3$), 1.62 (s, 6H, $2CH_3$), 3.12 (s, 2H, CH), 5.21 (dd, 1H, CH=C$\underline{H}$H, J=17.5 and 1.0 Hz) 5.30 (dd, 1H, CH=CH$\underline{H}$, J=11.5, and 1.0 Hz), 5.80 (dd, 1H, C$\underline{H}$=CH_2, J=17.5Hz, 11.5Hz), 7.05-7.60 (m, 5H, Ph); **3f** displayed an NOE between the olefinic proton at δ 5.80 and the methyne protons at δ 3.12. **4f:** mp 121-123°C; ^{1}H-NMR($CDCl_3$, 400MHz) δ 0.94 (s, 3H, CH_3), 1.26 (s, 6H, $2CH_3$), 1.62 (s, 6H, $2CH_3$), 3.12 (s, 2H, 2CH), 5.01 (dd, 1H, CH=CH$\underline{H}$, J=17.5 and 1.0Hz), 5.14 (dd, 1H, CH=C$\underline{H}$H, J= 11.5 and 1.0 Hz), 5.78 (dd, 1H, C$\underline{H}$=CH_2, J=17.5 and 11.5 Hz), 7.05-7.43 (m, 5H, Ph); **4f** displayed an NOE between the methyl protons at δ 0.94 and the methyne protons at δ 3.12.

12 The importance of π-orbital participation is further supported by exclusive anti π-facial selectivity in the reaction of 5-ethyl-1,2,3,4,5-pentamethylcyclopentadiene: See Ref. 6.