π-Facial selectivity in Diels–Alder reactions of cyclopentadienes having π-systems at 5-positions and the solvent effect †

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The orbital mixing rule is successfully applied to the prediction of the π-facial selectivity in the Diels–Alder reactions of cyclopentadienes having π-systems at 5-positions, by taking into consideration the relative energies of the π-HOMO of the diene and the π and π* orbitals on the substituent. When the π orbital lies high enough to interact with the π-HOMO, the participation of the π* orbital in the mixing is negligible. The rule gives a prediction of *syn* π-facial selectivity. The FMO extends and distorts inwardly to favor the reaction at the *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 π* orbital plays a predominant role. The rule gives a prediction of *anti* π-facial selectivity (Case B: Ψ(FMO) = π-HOMO + π* − σ). The prediction was examined by theoretical calculation of the FMO's of the model dienes **1d**, **e**, and **f** (Cp–X: X = CHO, CH=NOH, and CH=CH_2), and substantiated by the reactions of the corresponding pentamethylcyclopentadienes **2d**, **e**, and **f** (Cp*–X: X = CHO, CH=NOH, and CH=CH_2) with *N*-phenylmaleimide at 25 °C in CCl_4 to give products with *syn*:*anti* ratios of 0:100, 50:50 and 34:66, respectively. The new modeling of the solvent effects on the π-facial selectivity in the reactions of the amphoteric diene **2e** was proposed as an application of the orbital mixing rule. Enhancement of *syn* π-facial selectivity is expected in a solvent which is a Lewis base. Under the conditions, the orbital mixing of Case A would be enhanced, since the hydrogen-bond formation between the solvent and the hydroxy hydrogen of **2e** should raise the π and π* orbitals. The prediction was substantiated by the observation of considerable enhancement of *syn* π-facial selectivity in solvents such as CF_3CH_2OH, pyridine, THF, MeOH, EtOH, Et_3N, TMEDA and HMPA relative to CCl_4, toluene and AcOH.

Introduction

5-Substituted cyclopentadiene C–X is the simplest diene having an unsymmetrical π-plane.[1] In principle, the diene can react with dienophiles at either face. However the dienes having 5-acetoxy,[2] 5-hydroxy,[3] 5-methoxy,[3b,4] 5-fluoro,[5] 5-chloro,[3b,6] and 5-amino[3b] substituents were reported to react with highly *syn* π-facial preference. It becomes intriguing to inquire what leads to the observed contrasteric reactivity.

Some hypotheses to explain the π-facial selectivity have been reported.[7] Anh reported that the selectivity in the reactions of 5-acetoxycyclopentadiene, Cp–OAc, was ascribed to the stabilization by the interaction between the LUMO of a dienophile and the n-orbital of the alkoxy oxygen of the acetoxy moiety.[8] Ohwada and we recently pointed out that the theory is mistaken.[7a,b] The interaction destabilizes the system since the LUMO and the n-orbital should be out of phase. Kahn and Hehre reported that the selectivity was dependent on the electrostatic interaction.[9] They suggested that the approach of a dienophile to a diene would occur *syn* to the directing allylic functionality for groups having lone pairs, although Fallis[10] and Koizumi[11] argued against the theory. Macaulay and Fallis[3b] claimed that the selectivity could be explained in terms of "Cieplak effects".[7d,12] Coxon[13] and McEvoy[14] agreed with this proposal, although semiempirical calculations reported by Werstiuk and Ma[15] and us[16] provided no concrete support for the proposal. Recently, Poirier and Burnell reported a theoretical study to show that the selectivity was primarily due to steric hindrance between a dienophile and the 5-positioned substituent.[17]

We had proposed that the nonequivalent extension of the frontier molecular orbital (FMO) of the diene Cp–X (X = heteroatom substituent) is the major contributor to the selectivity.[16,18–20] The orbital mixing rule[18] is the most convenient way to evaluate the nonequivalency. This rule predicts the phases of the FMO formed by the interaction of two orbitals as perturbed by a third. The original description of this rule[18] included an application to the π-facial selectivity of 5-chlorocyclopentadiene. More recently, it has been successfully applied to the first prediction of *syn* π-facial preference in the reactions of the cyclopentadienes **1a**–**c** having substituents of π-systems at 5-positions.[21] The FMO's were expected to distort to favor the *syn*-attack due to π-HOMO–σ mixing through the overlap interaction with π orbital on the substituents. The prediction was substantiated by observation in the reactions of the corresponding pentamethylcyclopentadienes **2a**–**c** (Cp*–X: X = CN, CO_2H, CO_2R).

5-Formylcyclopentadiene **1d** (or **2d**: Cp*–CHO), a typical candidate for this class of dienes, was also straightforwardly predicted to react with *syn* π-facial preference. However, quite contrarily, Adam *et al.* reported that the diene **2d** reacted with exclusive *anti* π-facial selectivity.[22] They simply described the selectivity as being due to the steric repulsion between the formyl moiety and dienophiles at the *syn* attack transition state.

The puzzling selectivity prompted us to develop a general theory to predict the selectivity in the reactions of the dienes **1** (and **2**) having substituents of π-systems at 5-positions.[23] We will demonstrate herein that the orbital mixing rule is generally applicable to the prediction, when the relative energies of the

† Calculated Z-matrices and heats of formation of the stationary structures of compounds **1d**–**f** as global minima and other local minima of the cyclopentadienes **1d**–**f** and their relative total energies (Fig. 6) are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/a9/a910191h/

π-HOMO of the diene **1** (and **2**) and the π and the π* orbitals of the substituent (hereinafter referred to as $\varepsilon_{\pi\text{-HOMO}}$, ε_{π}, and ε_{π^*}, respectively) are considered. The qualitative theory was examined by theoretical calculation of FMO's at the RHF/6-31G* level. The experimental studies of the Diels–Alder reactions of the corresponding pentamethylcyclopentadienes **2** were fully described in detail. A new modeling of the solvent effects on the π-facial selectivity in the reactions of the amphoteric diene **2e** (Cp*–CH=NOH) was proposed based on the orbital mixing rule and examined experimentally.

1a	X= CN	**2a**	X= CN
1b	X= CO_2H	**2b**	X= CO_2H
1c	X= CO_2R	**2c**	X= CO_2Et
1d	X= CHO	**2d**	X= CHO
1e	X= CH=NOH	**2e**	X= CH=NOH
1f	X= $CH=CH_2$	**2f**	X= $CH=CH_2$

Results and discussion

Theoretical prediction

The orbital mixing rule on the basis of perturbation theory gave a prediction of the interaction among more than two molecular orbitals. An orbital (Ψ_{Ai}) of a system, say A, mixes into itself the other orbital (Ψ_{Aj}) of A, which is originally orthogonal to Ψ_{Ai} through the interaction with Ψ_{Bk} of the other system. The sign relation of Ψ_{Ai}, Ψ_{Aj}, and Ψ_{Bk} in the perturbed orbital $\Psi_{Ai'}$ is definitely given by the rule and dependent on the relative orbital energies.[18]

Application of the rule to the prediction of non-equivalent extension of the FMO's of the cyclopentadienes **1** was classified into two categories, depending on the relationship of the orbital energies, $\varepsilon_{\pi\text{-HOMO}}$, ε_{π}, and ε_{π^*} (Fig. 1).

When the π lies high enough to interact with the π-HOMO, the participation of the π* in the orbital mixing is negligible. According to the orbital mixing rule, the π-HOMO of the diene combines with the low-lying π out of phase and mixes the low-lying σ-orbital of the carbon framework out of phase with the π. Consequently, the mixing of the π-HOMO and the σ-system of the diene is perturbed by the low-lying π of the substituent in such a way that both diene orbitals contribute to the FMO in an out of phase manner relative to the π of the substituent. The FMO extends and distorts inwardly to favor the reaction at the *syn* side of the substituent (Case A: Ψ(FMO) = π-HOMO − π + σ).

On the other hand, when the π* lies low enough to interact with the π-HOMO, the participation of the π* needs to be taken into account. This is the case with **1d**. Again, according to the orbital mixing rule, combination of the π-HOMO with the high-lying π* in phase is followed by mixing of the low-lying σ out of phase with the π*. Consequently, the FMO contains an in phase contribution of the π-HOMO and an out of phase contribution of the σ relative to the π* of the substituent. The resulting FMO extends and distorts inwardly at the *anti* side of the substituent (Case B: Ψ(FMO) = π-HOMO + π* − σ). In this case, observation of *anti* π-facial selectivity is expected.

MO Calculation and discussion

The theory was examined by theoretical calculation. The molecular geometry of 5-formylcyclopentadiene **1d** was fully optimized by *ab initio* molecular orbital calculation[24] at the

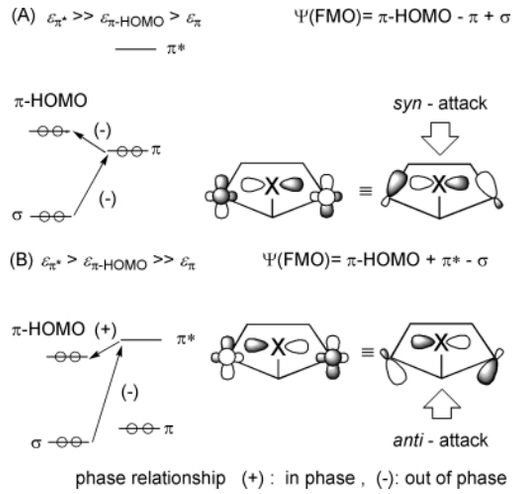


Fig. 1 Direction of nonequivalent extension of the FMO of 5-substituted cyclopentadiene **1** (Cp–X) on the basis of the orbital mixing rule, where X is a carbon substituent of a π-system.

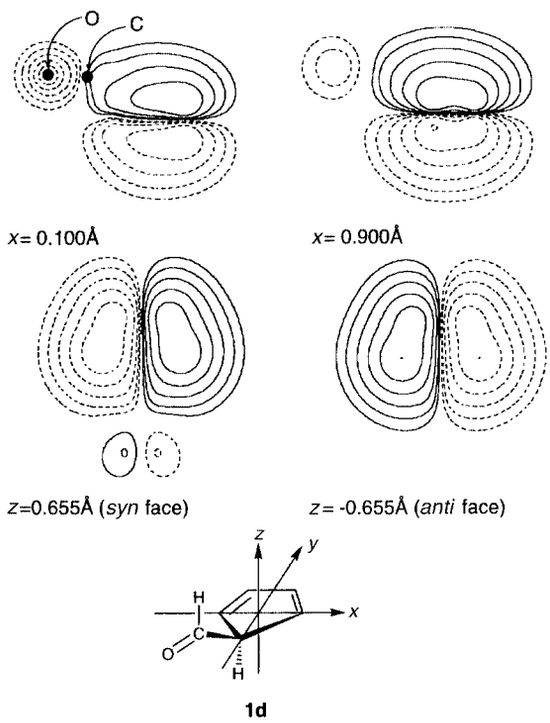
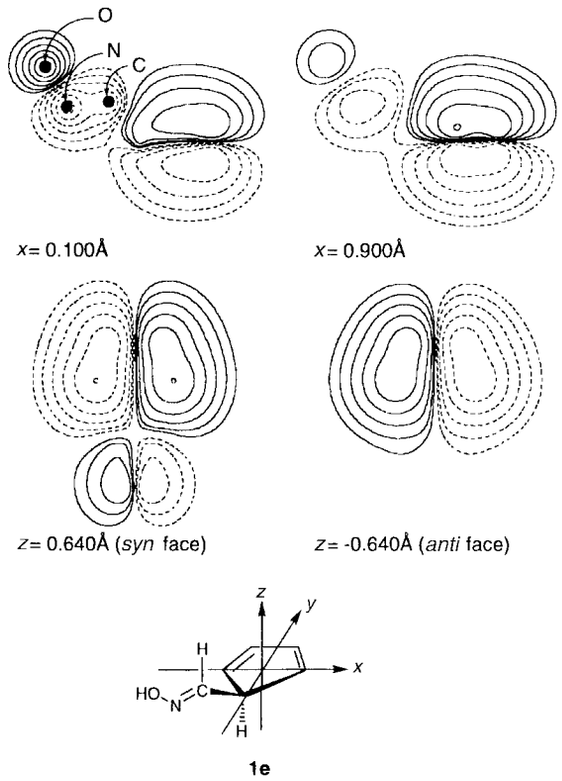


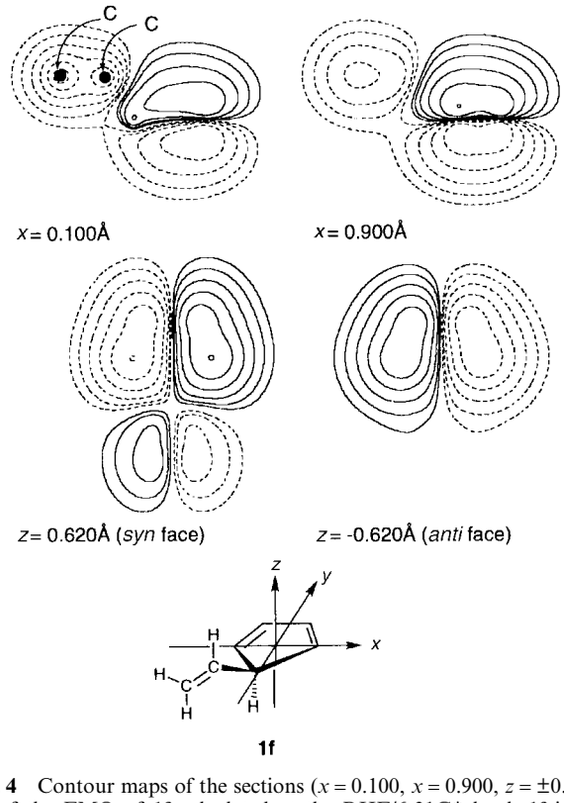
Fig. 2 Contour maps of the sections ($x = 0.100$, $x = 0.900$, $z = \pm 0.655$ Å) of the FMO of **1d** calculated at the RHF/6-31G* level. **1d** is C_s symmetric with respect to the *yz* plane. The Cp ring is in the *xy* plane and C-1 and C-4 carbons are on the *x* axis at the space coordinates of (1.175. 0. 0) and (−1.175. 0. 0), respectively. The absolute value of the largest contour line is 5.0×10^{-3} AU (exception: 1.25×10^{-3} AU for the plot of the $x = 0.100$ Å section). The heights of adjacent contours differ by a factor of 2.

RHF/6-31G* level to be a C_s symmetric structure as the global minimum.[25] The nonequivalency of the FMO of **1d** was confirmed based on contour maps (Fig. 2). The map at the section of $x = 0.100$ Å clearly indicated the in phase relationship between the π-HOMO and the π*. The contour of the highest absolute value of the maps of the section of $x = 0.900$ Å (inside of C-1) appeared at the *anti* side of the formyl moiety. The difference between the maps ($z = \pm 0.655$Å) is very subtle. Very small contours of the highest value appeared in the map of the section of $z = -0.655$ Å (*anti* face), but not in the map of the section of $z = 0.655$ Å (*syn* face). The FMO does distort inwardly and extend at the *anti* side of the substituent. These results showed complete agreement with not only the prediction



1e

Fig. 3 Contour maps of the sections ($x = 0.100$, $x = 0.900$, $z = \pm 0.640$ Å) of the FMO of **1e** calculated at the RHF/6-31G* level. **1e** is C_s symmetric with respect to the *yz* plane. The Cp ring is in the *xy* plane. The C-1 and C-4 carbons are at the space coordinates of (1.75. 0. 0) and (−1.75. 0. 0), respectively. The absolute values of the contour lines are the same as in Fig. 2.



1f

Fig. 4 Contour maps of the sections ($x = 0.100$, $x = 0.900$, $z = \pm 0.620$ Å) of the FMO of **1f** calculated at the RHF/6-31G* level. **1f** is C_s symmetric with respect to the *yz* plane. The Cp ring is in the *xy* plane. The C-1 and C-4 carbons are at the space coordinates of (1.74. 0. 0) and (−1.174. 0. 0), respectively. The absolute values of the contour lines are the same as in Fig. 2.

from the orbital mixing rule of Case B, but also the observed *anti* π-facial selectivity in the reaction of **2d**.

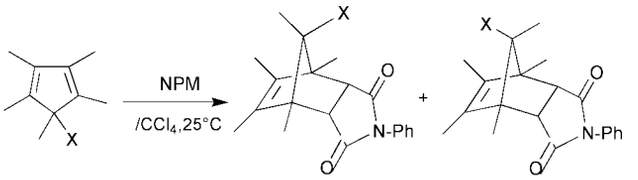
The nonequivalency of the FMO of **1d** is attributable to the low-lying π* and π orbitals of the formyl moiety. This led to the consequence that the orbital mixing of Case B is able to be turned into Case A by the replacement of the oxygen atom by less electronegative atoms such as nitrogen and carbon. In this context, 5-[(hydroxyimino)methyl]- and 5-vinylcyclopentadienes, **1e** and **1f**, were considered. The π and π* orbitals of the hydroxyimino and the vinyl moieties should be more high-lying than those of the formyl moiety of **1d**.[26] This simple prediction was examined by theoretical calculation of the FMO's at the RHF/6-31G* level. The molecular geometries of the dienes **1e** and **1f** were fully optimized to be C_s symmetric structures as global minima.[24,25] The FMO's were examined based on contour maps (Figs. 3 and 4). In Fig. 3, the map at the section of $x = 0.100$ Å showed the out of phase relationship between the π-HOMO and the π of the substituents as in the prediction of Case A. The highest contour at the section of $x = 0.900$ Å (inside of C-1) appeared at the *syn* side of the substituent. The highest contours at the sections of $z = \pm 0.640$ Å appeared at the section of $z = 0.640$ Å (*syn* face) but not at the section of $z = -0.640$ Å (*anti* face). Similarly, in Fig. 4, the map at the section of $x = 0.100$ Å showed the out of phase relationship between the π-HOMO and the π. The highest contour at the section of $x = 0.900$ Å (inside of C-1) appeared at the *syn* side of the substituent. The highest contours at the sections of $z = \pm 0.620$ Å appeared at $z = 0.620$ Å (*syn* face) not at $z = -0.620$ Å (*anti* face). The *z* slices were taken at these values to show the differences most distinctly. These results showed that the FMO's of **1e** and **f** distort inwardly and are large at the *syn* faces to favor the reactions at the *syn* side of the substituents.

Diels–Alder reactions of 1,2,3,4,5-pentamethylcyclopentadienes having 5-substituents of π-systems. The FMO's of the dienes **1e** and **1f** distort to favor the reactions at the *syn* side of substituents due to the orbital mixing of Case A. The prediction was examined experimentally. To avoid complication due to [1,5]-hydrogen rearrangement, the reactions of the corresponding pentamethylcyclopentadienes **2e** and **2f** were investigated.[27] If the reason for the *anti* π-facial selectivity of **2d** was largely steric repulsion as reported by Adam *et al.*,[22] the dienes should react with exclusive *anti* π-facial selectivity, since the (hydroxyimino)methyl and vinyl moieties are rather bulky compared with the formyl moiety. On the other hand, from the orbital mixing rule, the reactions of the dienes **2e** and **2f** should give the *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.[28]

The dienes **2e** and **2f** were prepared from the treatment of **2d** with hydroxylamine and from the treatment of hexamethyl Dewer benzene with hydrogen chloride by the procedures of Hellmann *et al.*,[28] respectively. The dienes were subjected to reactions with *N*-phenylmaleimide (NPM) in carbon tetrachloride at 25 °C (Table 1). In both cases, formation of a considerable amount of *syn* attack products **3e** and **3f** was observed. In order to compare these results fairly with those of Adam and co-workers, the control experiment of **2d** with NPM was performed under similar conditions. The reaction indicated exclusive formation of the *anti* attack product **4d**. These results very clearly attest to the correctness of the prediction based on the orbital mixing rule.

Application of the orbital mixing rule to the prediction of solvent effects. The next step in our study was the application of the orbital mixing rule to the prediction of solvent effects on the π-facial selectivity in the Diels–Alder reactions of the amphoteric dienes **2e**. There have been many reports of solvent effects in the reactions, however most of them focused on the kinetics,[29] especially on the rate enhancement of the reaction in

Table 1 π-Facial selectivities in the Diels–Alder reactions of **2d**, **2e** and **2f** with *N*-phenylmaleimide (NPM)



2 **3** **4**

Diene	X	Products	Selectivity[a] *syn*:*anti*
2d	CHO	**4d**	0:100
2e	CH=NOH	**3e**, **4e**	50:50
2f	$CH=CH_2$	**3f**, **4f**	34:66

[a] π-Facial selectivity was determined on the basis of ^{1}H NMR of the crude mixture.

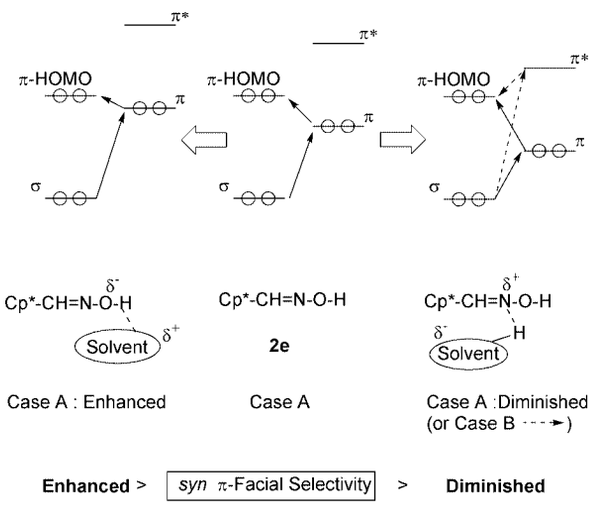


Fig. 5 Prediction of solvent effects on the π-facial selectivity in the Diels–Alder reactions of **2e**.

water.[30] The concepts of the modeling systems were based on hydrophobic or solvophobic packing of a diene and dienophile, entropy-driven aggregation, and high internal pressure of water. The FMO concept gave another approach, which included interaction between solvent and dienophile.[29e,f]

Our modeling is very simple (Fig. 5). Enhancement of *syn* π-facial selectivity is expected in a solvent which is a Lewis base. Under the conditions, the orbital mixing of Case A would be enhanced, since the hydrogen-bond formation between the solvent and the hydroxy hydrogen of **2e** should raise the π and π* orbitals. On the other hand, the reverse is expected when the solvent is acidic. Protonation at the nitrogen atom of **2e** should lower the π and the π* orbitals, where the mixing of Case A would be diminished or, in the extreme case, switched into Case B.

The prediction was examined experimentally. Reactions of the diene **2e** with NPM were performed under nitrogen atmosphere in various solvents at 25 °C for 12 h. After removal of the solvent, the residue was subjected to ^{1}H NMR, from which the *syn*:*anti* ratio of the products was established.

The results are summarized in Table 2.

In inert solvents such as CCl_4 and toluene, the diene reacted with the ratio of *syn*:*anti* = 50:50 (Entries 1 and 2). In relatively basic solvents such as CF_3CH_2OH, pyridine, THF, MeOH, EtOH, Et_3N, TMEDA and HMPA, considerable enhancement of *syn* π-facial selectivity was observed (Entries 3–10). The *syn* selectivity in the reactions of **2e** showed a tendency to be enhanced with increasing order of base strength of

Table 2 Solvent effects on the π-facial selectivity in Diels–Alder reactions of **2e** (and **2f**) with *N*-phenylmaleimide (NPM)

Entry	Solvent	*syn*:*anti*[a]
1	CCl_4	50:50 (34:66)[b]
2	Toluene	50:50
3	CF_3CH_2OH	56:44
4	Pyridine	58:42
5	THF	60:40 (36:64)[b]
6	MeOH	61:39
7	EtOH	65:35
8	Et_3N	67:33
9	TMEDA	67:33
10	HMPA	74:26 (38:62)[b]
11	AcOH	44:56 (36:64)[b]

[a] The ratios were determined on the basis of ^{1}H NMR. [b] The ratios in parentheses are those of the reactions of the vinyl diene **2f** (Cp*–$CH=CH_2$).

solvents, although the enhancement was qualitative and did not follow the basicity of the solvent in a systematic way. The following are typical examples. The reactions in alcohols such as CF_3CH_2OH, MeOH, and EtOH gave products with the ratio of *syn*:*anti* = 56:44, 61:39, and 65:35, respectively. The reactions in amines such as pyridine, Et_3N and TMEDA gave products with the ratio of *syn*:*anti* = 58:42, 67:33 and 67:33, respectively. The highest ratio of 74:26 was observed in the reaction in HMPA, which was reported to be an "extraordinarily strong donor" solvent by Mayer *et al.*[31] In contrast to these results, in inert solvents such as CCl_4 and toluene, the diene reacted with the ratio of *syn*:*anti* = 50:50. The reaction in AcOH gave products with the ratio of *syn*:*anti* = 44:56 (Entry 11). Decreasing *syn* π-facial selectivity was observed, however it was not very marked. The situation could be ascribed to the equilibrium between the diene **2e** and the diene **2e** protonated at the nitrogen atom. Under equilibrium conditions, only the diene **2e** would act as an active species, since the protonated diene is less reactive due to the low-lying HOMO. In order to avoid the equilibrium, use of more acidic solvents such as HCOOH and CF_3COOH was attempted. However, in both cases, significant decomposition of the diene **2e** was observed.

The possibility of solvent effects owing to the interaction between the dienophile and the solvent was completely ruled out by the reactions of the diene **2f**, which contains the inert vinyl moiety at the 5-position. The results were in sharp contrast to those for the diene **2e**. The *syn*:*anti* ratios were almost constant without dependence on the solvents (Table 2: Entries 1, 5, 10 and 11). The reason for the *anti* selectivity (*syn*:*anti* = 34:66) in the reactions of **2f** is not clear at the present time. We tentatively attribute this to the repulsive interaction between the vinyl moiety and NPM in the *syn*-attack transition state. Thermodynamic control was completely ruled out, since neither isomerization nor decomposition of the products **3e**, **3f**, **4e**, and **4f** was found to occur under the reaction conditions.

These results clearly demonstrated the correctness of our modeling of the solvent effects.

Conclusion

We have demonstrated a successful application of the orbital mixing rule to the prediction of the π-facial selectivity in the Diels–Alder reactions of cyclopentadienes having a substituent of π-systems. The rule is also found to be applicable for the prediction of solvent effects on the selectivity in the reactions of the amphoteric diene **2e**.

It is noteworthy that, among the qualitative theories, only the orbital mixing rule gave clear predictions.

Experimental

Melting points were determined using a Yanagimoto melting point apparatus and are uncorrected. NMR spectra were recorded on JEOL-JNM-GX 270 (270 MHz) or α-400 (400 MHz) instruments with tetramethylsilane as an internal standard. Mass spectra were recorded on a Shimadzu QP-1000 or a Shimadzu 9020-DF spectrometer. Elemental analyses were performed by the Elemental Analyses Center of the Department of Pharmacy of Kyoto University.

5-[(Hydroxyimino)methyl]-1,2,3,4,5-pentamethylcyclopentadiene (2e)

To an aqueous solution of hydroxylamine prepared from hydroxylamine hydrochloride (3.5 g, 50.4 mmol) and sodium hydroxide (5.8 g, 145 mmol) in water (10 cm^3) at 0 °C was added a solution of 5-formylpentamethylcyclopentadiene (**2d**, 615 mg, 3.75 mmol) in ethanol (10 cm^3). After refluxing for 1 h, the reaction mixture was extracted with dichloromethane (20 $cm^3 \times 3$). The combined extracts were dried over anhydrous sodium sulfate. Removal of the solvent quantitatively gave **2e** as a white solid. **2e**: mp 129–130 °C (from hexane); (Found: C, 73.4; H, 9.55; N, 7.8. $C_{11}H_{17}NO$ requires C, 73.7; H, 9.55; N, 7.8%); δ_H(400 MHz; $CDCl_3$) 1.11 (3H, s, Me), 1.73 (6H, s, Me), 1.80 (6H, s, Me), 6.60 (1H, s, C*H*=NOH), 8.25 (1H, s, CH=NO*H*); δ_C(100 MHz; $CDCl_3$) 10.1, 11.3, 14.8, 58.6, 136.9, 137.7, 154.1; *m*/*z* (EI, 20 eV) 179 (M^+, 69%); 135 ($M^+ - CH$=NOH, 100%); *m*/*z* (CI) 180 ($M^+ + 1$, 100%).

2-Phenyl-*exo*-8-formyl-4,5,6,7,8-pentamethyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (4d)

To a solution of the diene **2d** (234 mg, 1.40 mmol) in carbon tetrachloride (20 cm^3) was added 346 mg (2.00 mmol) of *N*-phenylmaleimide (NPM). The mixture was stirred at 25 °C for 12 h. After removal of the solvent, the residue was subjected to ^{1}H NMR to show exclusive formation of the product **4d** (96% yield). Pure sample was obtained by flash chromatography (eluent: hexane–ethyl acetate = 3 : 1, R_f = 0.20) followed by recrystallization from ethyl acetate.

4d: mp 133–135 °C; (Found: C, 74.55; H, 6.9; N, 4.3. $C_{21}H_{23}NO_3$ requires C, 74.75; H, 6.9; N, 4.15%); δ_H(270 MHz; $CDCl_3$) 0.95 (3H, s, Me), 1.47 (6H, s, Me), 1.70 (6H, s, Me), 3.12 (2H, s, CH), 7.05–7.44 (5H, m, Ph), 9.60 (1H, s, CHO); **4d** displayed an NOE between the methyl protons at δ 0.95 and the methyne protons at δ 3.12. δ_C(67.5 MHz; $CDCl_3$) 10.9, 11.6, 12.4, 51.6, 59.6, 77.2, 126.6, 128.7, 129.3, 131.5, 137.0, 175.7, 205.7; *m*/*z* (EI, 20 eV) 337 (M^+, 28%), 164 (54%), 136 (100%); *m*/*z* (CI, isobutane) 338 ($M^+ + 1$, 100%).

2-Phenyl-*endo*-8-[(hydroxyimino)methyl]-4,5,6,7,8-pentamethyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (3e) and 2-phenyl-*exo*-8-[(hydroxyimino)methyl]-4,5,6,7,8-pentamethyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (4e)

To a solution of the diene **2e** (179 mg, 1.00 mmol) in carbon tetrachloride (20 cm^3) was added 173 mg (1.00 mmol) of NPM. The mixture was stirred at 25 °C for 12 h. After removal of the solvent, the residue was subjected to ^{1}H NMR to show formation of a mixture of **3e** and **4e** with the ratio of 50 : 50. Pure samples were obtained by flash chromatography (isolated yield 88%; eluent: hexane–ethyl acetate = 3 : 1, R_f = 0.38 for **3e** and 0.26 for **4e**) followed by recrystallization from hexane–ethyl acetate = 1 : 1. **3e**: mp 197–198 °C; (Found: C, 71.3; H, 6.80; N, 7.75. $C_{21}H_{24}N_2O_3$ requires C, 71.6; H, 6.80; N, 7.95%); δ_H(400 MHz; $CDCl_3$) 0.87 (3H, s, Me), 1.43 (6H, s, Me), 1.63 (6H, s, Me), 3.27 (2H, s, CH), 7.04–7.45 (5H, m, Ph), 7.38 (1H, s, C*H*=NOH), 7.59 (1H, br s, CH=NO*H*); **3e** displayed an NOE between the imino proton at δ 7.38 and the methyne protons at δ 3.27. δ_C(100 MHz; $CDCl_3$) 11.4, 12.1, 13.3, 51.2, 60.0, 67.8, 126.6, 128.4, 129.1, 131.9, 135.0, 152.9, 176.4; *m*/*z* (EI, 20 eV) 352 (M^+, 100%), 335 ($M^+ - OH$, 46%); *m*/*z* (CI, isobutane) 353 ($M^+ + 1$, 46), 337 ($M^+ - Me$, 71%), 335 ($M^+ - OH$, 100%).

4e: mp 227–228 °C; (Found: C, 71.45; H, 6.85; N, 7.8. $C_{21}H_{24}N_2O_3$ requires C, 71.6; H, 6.8; N, 7.95%); δ_H(400 MHz; $CDCl_3$) 1.03 (3H, s, Me), 1.35 (6H, s, Me), 1.65 (6H, s, Me), 3.16 (2H, s, CH), 7.05–7.49 (5H, m, Ph), 7.35 (1H, s, C*H*=NOH), 7.94 (1H, br s, CH=NO*H*); **4e** displayed an NOE between the methyl protons at δ 1.03 and the methyne protons at δ 3.16. δ_C(100 MHz; $CDCl_3$) 11.5, 12.1, 12.8, 51.5, 60.3, 69.7, 126.5, 128.5, 129.1, 131.9, 136.0, 154.3, 176.1; *m*/*z* (EI, 20 eV) 352 (M^+, 100%), 335 ($M^+ - OH$, 51%); *m*/*z* (CI) 353 ($M^+ + 1$, 100%), 337 ($M^+ - Me$, 80%), 335 ($M^+ - OH$, 53%).

2-Phenyl-*endo*-8-vinyl-4,5,6,7,8-pentamethyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (3f) and 2-phenyl-*exo*-8-vinyl-4,5,6,7,8-pentamethyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (4f)

To a solution of the diene **2f** (324 mg, 2.00 mmol) in carbon tetrachloride (30 cm^3) was added 350 mg (2.02 mmol) of NPM. The mixture was stirred at 25 °C for 12 h. After removal of the solvent, the residue was subjected to ^{1}H NMR to show formation of a mixture of the products **3f** and **4f** in the ratio of 34 : 66. Pure samples were obtained by flash chromatography (isolated yield 66%; eluent: hexane–ethyl acetate = 1 : 20, R_f = 0.17 for **3f** and 0.13 for **4f**) followed by recrystallization from hexane.

3f: mp 115–116 °C; (Found: C, 78.65; H, 7.55; N, 4.25. $C_{22}H_{25}NO_2$ requires C, 78.8; H, 7.45; N, 4.3%); δ_H(400 MHz; $CDCl_3$) 0.83 (3H, s, Me), 1.29 (6H, s, Me), 1.62 (6H, s, Me), 3.12 (2H, s, CH), 5.21(1H, dd, *J* = 17.5 and 1.0, CH=C*H*H), 5.30 (1H, dd, *J* = 11.5 and 1.0, CH=CH*H*), 5.80 (1H, dd, *J* = 17.5 and 11.5, C*H*=CHH), 7.05–7.60 (5H, m, Ph); **3f** displayed an NOE between the olefinic proton at δ 5.80 and the methyne protons at δ 3.12; δ_C(100 MHz; $CDCl_3$) 11.6, 11.9, 13.2, 51.5, 60.6, 69.5, 118.9, 126.6, 128.3, 129.1, 132.1, 135.4, 138.6, 176.8; *m*/*z* (EI, 20 eV) 335 (M^+, 32%), 162 (100%); *m*/*z* (CI, isobutane) 336 ($M^+ + 1$, 100).

4f: mp 121–123 °C; (Found: C, 78.75; H, 7.65; N, 4.1. $C_{22}H_{25}NO_2$ requires C, 78.8; H, 7.45; N, 4.3%); δ_H(400 MHz; $CDCl_3$) 0.94 (3H, s, Me), 1.26 (6H, s, Me), 1.62 (6H, s, Me), 3.12 (2H, s, Me), 5.01 (1H, dd, *J* = 17.5 and 1.0, CH=C*H*H), 5.14 (1H, dd, *J* = 11.5 and 1.0, CH=CH*H*), 5.78 (1H, dd, *J* = 17.5 and 11.5, C*H*=CHH), 7.05–7.43 (5H, m, Ph); **4f** displayed an NOE between the methyl protons at δ 0.94 and the methyne protons at δ 3.12; δ_C(100 MHz; $CDCl_3$) 11.5, 11.8, 13.3, 51.9, 60.5, 70.3, 117.3, 126.6, 128.3, 129.1, 132.1, 135.4, 139.7, 176.6; *m*/*z* (EI, 20 eV) 335 (M^+, 74%), 162 (100%); *m*/*z* (CI, isobutane) 336 ($M^+ + 1$, 100%).

Solvent effects in the reactions of the dienes 2e and 2f with NPM

Typical procedures: a solution of the diene **2e** (0.2 mmol) and NPM (0.2 mmol) in a solvent (2.0 cm^3) was stirred at 25 °C under nitrogen atmosphere. After 12 h, disappearance of **2e** was detected by TLC. The solvent was removed *in vacuo* (or the mixture was poured into water then extracted with pentane (20 $cm^3 \times 3$) followed by concentration). Without further purification, the residue was subjected to ^{1}H NMR, from which the *syn* : *anti* ratio of the products was established. The yields were also estimated from ^{1}H NMR to be almost quantitative.

As control experiments, the isolated adducts **3e**, **3f**, **4e**, and **4f** were treated with the solvents under the reaction conditions. After removal of the solvents, the residues were subjected to ^{1}H NMR to show recovery of the adducts. Neither isomerization nor decomposition was observed.

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