π-Facial Selectivity in the Diels–Alder Reaction of 5-Substituted 1,3-Cyclopentadienes#

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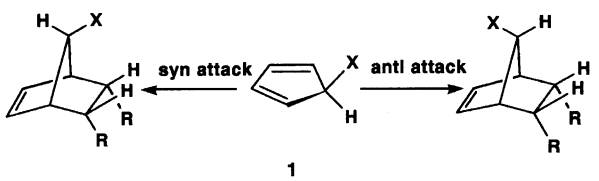
Theoretical and experimental studies are presented about π-facial selectivities in Diels–Alder reactions of 5-substituted cyclopentadienes (**1**). The HOMO and the NHOMO of **1** were readily predicted from the orbital mixing rule to be distorted to favor the *syn*- and *anti*-attack, respectively. The frontier orbital is dependent on the *n*-orbital energy (ε_n) of the substituent relative to the π-HOMO energy (ε_π) of the diene. For $\varepsilon_\pi > \varepsilon_n$, the *syn* π-facial selectivity is predicted since the HOMO contains the diene π-HOMO as the main component. For $\varepsilon_\pi < \varepsilon_n$, the anti π-facial selectivity is predicted since the π-HOMO most contributes to the NHOMO. For $\varepsilon_\pi \simeq \varepsilon_n$, the loss of π-facial selectivity is predicted since the HOMO and the NHOMO both contribute to the reaction. The qualitative theory was examined by *ab initio* molecular orbital calculation on **1** (X=NH_2, PH_2, AsH_2, OH, SH, SeH, F, Cl, and Br) and PM3 calculation of the activation energies on Diels-Alder reactions of **1** (X=NH_2, PH_2, AsH_2, SbH_2, OH, SH, SeH, TeH, F, Cl, Br, and I) with maleic anhydride. The observed selectivities of chalcogen-substituted cyclopentadienes (X=SPh and SePh) were in agreement with the theoretical prediction.

The π-facial selectivity has been one of the most fundamental and attractive subjects of theoretical and experimental studies. Increasing attention has been focused on that of the Diels–Alder reaction of 5-substituted cyclopentadienes (**1**) (Scheme 1).[1—10] For instance, the following π-facial stereoselectivities were reported: 1) 5-hydroxy-,[10g] 5-acetoxy-,[10f] 5-fluoro-,[10h] and 1,2,3,4,5-pentachlorocyclopentadiene[10i,10j] reacted with dienophiles with *syn*-π-facial selectivity; 2) 5-alkyl or 5-trimethylsilyl group lead to the opposite stereochemical results (Scheme 1).[10a,10c,10d,10e] The selectivity of the latter examples is simply attributable to the steric repulsion between the substituents and dienophiles.

The origin of the *syn* selectivity has been the subject of intensive studies. Some theories have been developed for the selectivities.[1—5] The orbital mixing rule[1] was presented to predict the direction of the nonequivalent orbital extension (orbital distortion) caused by the asymmetric perturbation of substituents. Its application to the 5-chlorocyclopentadiene (**1**: X=Cl) was successful in explaining the *syn*-facial selectivities. Anh[2] proposed the nonbonded attraction between the heteroatom and dienophiles. Kahn, Hehre et al.[3] proposed that the electrostatic potentials should control the selectivities. The predictions and interpretations based on the theories have been in agreement with the observed selectivities.[10] Recently, π-facial stereoselectivities in the Diels–Alder reactions of 5-heteroatom-substituted cyclopentadienes were observed to depend on the heteroatom (O, S, and Se) substituents.[11,12] Fallis explained the dependence on the basis of Cieplak concept.[12b]



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Scheme 1.

In this paper, we apply the orbital mixing rule[1] to the heteroatom dependent π-facial selectivities. The selectivities are proposed to be controlled by nonequivalent extension of the frontier orbitals, which is determined by the energy of the *n*-orbital on heteroatom relative to the π-HOMO energy of the diene moiety. The qualitative theory was examined by *ab initio* molecular orbital calculation on the cyclopentadienes (X=NH_2, PH_2, AsH_2, OH, SH, SeH, F, Cl, and Br) and PM3 calculation of the activation energies on Diels–Alder reactions of **1** (X=NH_2, PH_2, AsH_2, SbH_2, OH, SH, SeH, TeH, F, Cl, Br, and I) with maleic anhydride. The experimental study of the Diels–Alder reaction of chalcogen-substituted cyclopentadienes (X=SPh and SePh) was fully described.

Results and Discussion

Theoretical Prediction. The Diels–Alder reaction is one of the text book examples used in the illustration of the frontier orbital theory. In order to distinguish the Diels–Alder reaction from the 2+2 cycloaddition reaction, we need only know the phase property (symmetry) of the frontier orbitals. The amplitude (the coefficient of the p_π atomic orbital) of the frontier orbitals at the reaction centers are additionally required to predict the regioselectivities of the Diels–Alder reactions. However, neither orbital symmetry nor amplitude has anything to do with the π-facial selectivities. The nonequivalent orbital extension caused by σ, π mixing makes difference between the *syn*- and *anti*-faces of

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plane-unsymmetrical conjugated molecules.

The frontier orbital distortion favorable for the Diels–Alder reaction is shown in Fig. 1. The mixing of s-orbital results in the orbital extension on a π-face and the contraction on the other (Fig. 1a). The relation with the π-facial selectivity is straightforward. The distance between the reaction centers (C(1) and C(4)) in the diene is longer than that between C(5) and C(6) in the dienophile. The geometrical feature suggests that the dienophiles prefer the π-face where the p-orbital lobes at the reaction centers of the dienes are close to each other (Fig. 1b). The p-orbital axis rotation is caused by the mixing of the $p_{\sigma(x)}$ components.

The nonequivalent extension of the π-orbitals of the plane-unsymmetrical dienes (**1**) is caused by mixing of the low-lying σ-orbitals of the carbon framework through the interaction with the high-lying orbitals (n) on the 5-substituents.[1)] The frontier orbital is the π-HOMO of the diene part. The orbital is antisymmetric with respect to reflection in the plane containing the saturated carbon and its substituents. The same symmetry is required for the perturbing orbital on X. The symmetric σ-orbitals for the bonds between the saturated carbon and the heteroatom is forbidden to interact with the π-HOMO. Antisymmetric orbitals on X are here represented by the nonbonding (n)-orbital. The orbital mixing rule shows that the direction of the frontier orbital extension is controlled by the relative energies of the π-HOMO (ε_π) and the n-orbital (ε_n). The π-HOMO of the diene moiety can be the HOMO or the NHOMO of the whole molecule after the perturbation. So, we classify the dienes into the three classes:

(**A**) $\varepsilon_\pi > \varepsilon_n$; (**B**) $\varepsilon_\pi \simeq \varepsilon_n$; (**C**) $\varepsilon_\pi < \varepsilon_n$.

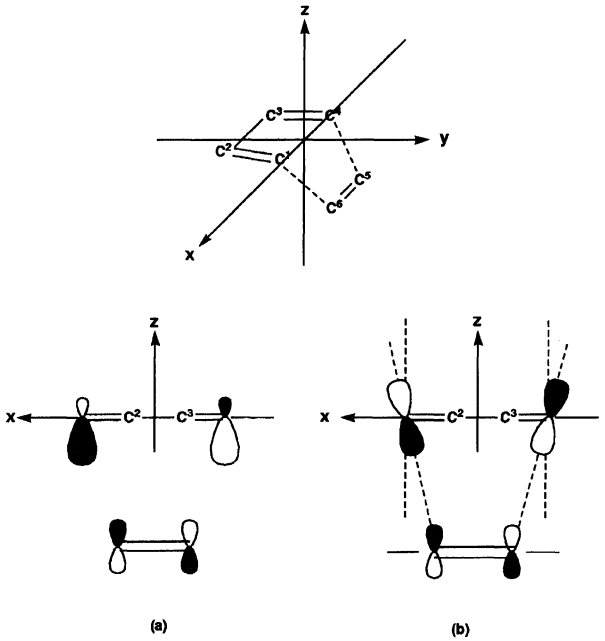


Fig. 1. Favorable orbital distortion for the Diels–Alder reactions.

In case **A**, the π-HOMO of the diene part is modified by an out-of-phase combination with the low-lying n-orbital to be the HOMO of the whole molecule. The π-HOMO further mixes the σ-orbitals in such a way that σ and n are out of phase (Fig. 2a) since $\varepsilon_\pi > \varepsilon_\sigma$. Both s-component in the σ-orbital and p_σ-orbital are out of phase with the n-orbital. The HOMO at the reaction centers, C(1) and C(4), extends more in the *syn*-face due to the s-orbital mixing. The $p_{\sigma(x)}$ orbital interact with the n-orbital more strongly at the lobe extending within the five-membered ring. The inner lobe is out of phase with the n-orbital. The phase relation implies that the mixing of the $p_{\sigma(x)}$ orbital rotates the *syn*-lobe of the $p_{\pi(z)}$ orbital axis inwardly. As a result, the distortion of the frontier orbital or the HOMO in this case is suitable for the reaction on the *syn*-face of the diene.

In case **C**, the predominant component of the HOMO of the 5-substituted cyclopentadienes is the n-orbital ($C_n > C_\pi$) since $\varepsilon_\pi < \varepsilon_n$. The HOMO is not the frontier

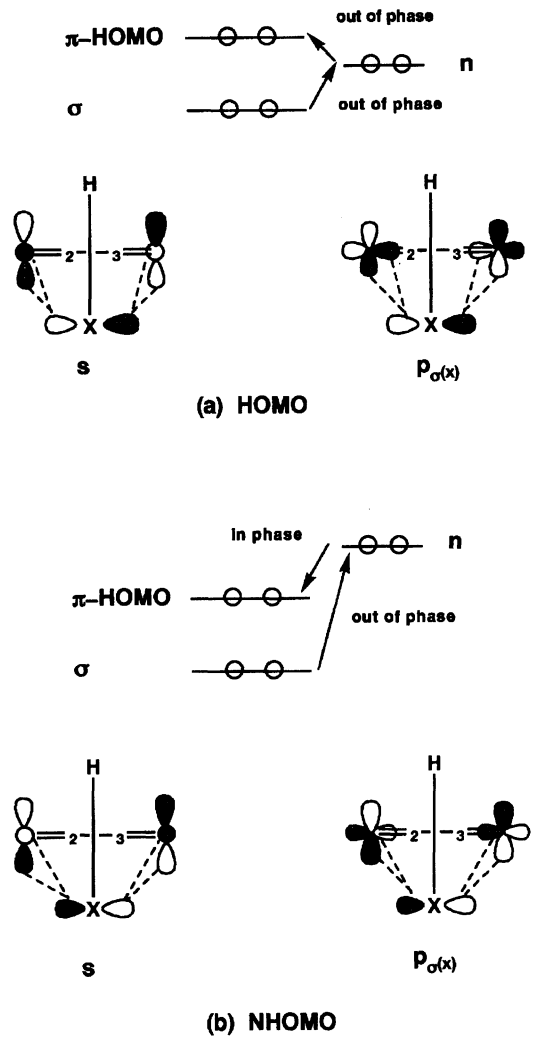


Fig. 2. Orbital mixing rule applied to the nonequivalent extension of the HOMO and NHOMO of 5-X-cyclopentadienes.

orbital for the Diels–Alder reactions. The π-HOMO of the diene part interacts with the high-lying n-orbital to be transformed into an orbital of the 5-substituted cyclopentadienes lower in energy than the HOMO. This orbital is denoted by the NHOMO. The NHOMO should be the frontier orbital. The π-HOMO is in phase with n, σ and n being out of phase (Fig. 2b). The NHOMO extends in a way opposite to the HOMO. The anti π-facial stereoselectivity is expected.

In case **B**, the π-HOMO appreciably contributes to HOMO and NHOMO. Both orbitals can play significant roles in the Diels–Alder reactions. The loss of π-facial stereoselectivity is expected.

The frontier orbital distortion of 5-substituted cyclopentadienes has been predicted to be controlled by the relative energies of the n-orbital. For low-lying n-orbitals the frontier orbital of the cyclopentadienes is the HOMO which is distorted to favor the *syn*-attack. For high-lying n-orbitals the frontier orbital is the NHOMO which is distorted to favor the *anti*-attack.

Molecular Orbital Calculation. The molecular geometries of the cyclopentadienes (X=NH_2, PH_2, AsH_2, OH, SH, SeH, F, Cl, and Br) were optimized by *ab initio* molecular orbital calculations with the STO-3G basis set.[14] The orbital energies and the AO coefficients of the HOMO and NHOMO are summarized in Table 1. The calculations confirmed the prediction by the orbital mixing rule that the HOMO and NHOMO are distorted to favor the *syn*- and *anti*-attack of dienophiles, respectively.

The contribution of the π-HOMO of the diene part or the n-orbital to the HOMO and the NHOMO were shown to be highly dependent on X (OH, SH and SeH). For X=OH, the π-HOMO is the main component of the HOMO. The contribution of the π-HOMO was estimated from the coefficient C_n of the n-orbital (p_x-AO) for the lone pair on X. The coefficient (0.137) is small. The contribution of the n-orbital to the HOMO is 2%. The HOMO is localized on the diene parts (98%). The *syn*-selectivity was predicted. For X=SH, the coefficients of p-atomic orbital at C(1) are very similar in the HOMO (0.368) and the NHOMO (0.384). The π-HOMO is equally contained in both of the HOMO (47%) and the NHOMO (52%). Furthermore, the energy gap between the HOMO and the NHOMO is rather small relative to that of **1** (X=OH), both orbitals can be expected to participate in the Diels–Alder reactions (*syn*/*anti* selectivity). For X=SeH, the coefficient of p-atomic orbital at C(1) is larger in the NHOMO. The π-HOMO contributes two times more to the NHOMO (63%) than to the HOMO (36%). The anti selectivity is predicted. The prediction is confirmed by the experimental observation[11a] (see the next section). The dienes having oxygen, sulfur, and selenium substituents are classified into the case **A** (*syn*), **B** (*syn*/*anti*), and **C** (*anti*), respectively.[15a] This is in complete agreement with the preceding results.

Irrespective of X=NH_2, PH_2, and AsH_2, the HOMO localizes on the diene part. The *syn* selectivity is predicted (Case **A**). No remarkable signs of the heteroatom dependence of the selectivity were found in the results of the MO calculations.[15b] The *syn* selectivity of 5-amino-1,2,3,4,5-pentamethylcyclopentadiene reported by Fallis[12] is in agreement with the prediction.

For 5-halogen-substituted cyclopentadienes, the HOMO contains the π-HOMO of the diene part as the predominant component. The dienes are expected to react with *syn* selectivity (Case **A**).[15c] In fact, *syn* π-facial selectivity has been observed in the reactions of 5-fluoro-[10h] and 1,2,3,4,5-pentachlorocyclopentadiene.[10i,10j] However, 5-chloro-, 5-bromo-, and 5-iodocyclopentadienes were reported to give *syn*/*anti*, *anti*-, and *anti*-attack, respectively.[10k,10l] Steric hindrance may dominate over the π-facial selectivity for X=Br.

The prediction by the orbital mixing rule was examined by the activation energies of Diels–Alder reactions of the dienes **1** (X=NH_2, PH_2, AsH_2, SbH_2, OH, SH, SeH, TeH, F, Cl, Br, and I) with maleic anhydride calculated by PM3 method (MOPAC ver 6.0).[16] The results are summarized in Table 2.

The activation energies for the dienes **1** (X=OH, SH, and SeH) confirmed the prediction in good agreement with the observed selectivities.[10f,10g,11a] The calculations showed slight preference of the *syn*-attack on **1** (X=OH). The *anti* selectivity was shown to increase in the order of X=SH<SeH<TeH. The *anti* selectivity for (X=TeH) remains to be examined in an experimental manner.

The calculated activation energies for X=F showed the *syn* selectivity in agreement with the prediction and the observation. The preference of the *anti*-attack increases in the order of Cl<Br<I, while the *syn* selectivity is predicted by the orbital distortion. In fact, the *anti* selectivity was observed for the dienes (X=Br and I).[10k,10l] Steric hindrance may dominate over the selectivity for X=Br and I.

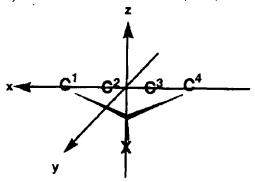
For X=NH_2, PH_2, and AsH_2, the calculated activation energies showed the *anti* selectivity in contradiction with the prediction. However, *syn* selectivity was observed in the reaction of 5-amino-1,2,3,4,5-pentamethylcyclopentadiene.[12] The agreement with the prediction suggests that the orbital distortion should play a predominant role, and that the PM3 calculations should overestimate the preference of the *anti*- to the *syn*-attack. More reliable calculations or experiments are required for the definite conclusion about the selectivities for X=NH_2, PH_2, AsH_2, and SbH_2.

The bond lengths of C(5)–X and C(5)–H of the cyclopentadienes at the transition states were summarized in Table 3. The σ-bond (C(5)–X or C(5)–H) on the side opposite to dienophile is longer than that of the starting diene. These results can be attributable to the σ–π^* interaction (Fig. 3). Since the σ orbital on the opposite

Table 1. Frontier Orbitals (HOMO, NHOMO) of 5-Substituted Cyclopentadienes

Diene	Orbital	Energies	Coefficients at C(1)[a,b] and X					Selectivity
1: X=		eV		C_{pz}^{π}	C_{px}^{σ}	C_{s}^{σ}	C_{p}^{n}	(Observed)
NH_2	HOMO	−7.206	C(1)	0.522	0.014	−0.028	0.151[c,d]	*syn*
			[C(4)	−0.519	0.039	0.015]		(*syn*[e])
	NHOMO	−8.919	C(1)	0.052	−0.185	0.133	−0.795[c,f]	
			[C(4)	−0.134	−0.076	−0.045]		
PH_2	HOMO	−6.941	C(1)	0.514	0.008	−0.026	0.243[c,d]	*syn*
			[C(4)	−0.498	0.008	0.002]		
	NHOMO	−7.829	C(1)	0.110	−0.102	0.091	−0.687[c,f]	
			[C(4)	−0.223	−0.004	−0.007]		
AsH_2	HOMO	−5.632	C(1)	0.503	0.013	−0.029	0.296[c,d]	*syn*
			[C(4)	−0.485	0.001	0.002]		
	NHOMO	−7.838	C(1)	0.152	−0.009	0.081	−0.688[c,f]	
			[C(4)	−0.252	0.001	−0.004]		
OH	HOMO	−7.374		0.523	0.028	−0.022	0.137	*syn*
	NHOMO	−9.578		0.081	−0.202	0.114	−0.829	(*syn*[g,h])
SH	HOMO	−6.857		0.368	0.063	−0.061	0.730	*syn/anti*
	NHOMO	−7.619		0.384	−0.073	0.061	−0.693	(*syn/anti*[i]), *anti*[h])
SeH	HOMO	−6.857		0.319	0.057	−0.059	0.804	*anti*
	NHOMO	−7.700		0.426	−0.055	0.047	−0.606	(*anti*[i])
F	HOMO	−7.448		0.526	0.026	−0.019	0.084	*syn*
	NHOMO	−10.72		0.055	−0.250	0.104	−0.689	(*syn*[j])
Cl	HOMO	−7.789		0.525	0.020	−0.016	0.176	*syn*
	NHOMO	−10.20		0.092	−0.121	0.070	−0.950	(*syn*[k]), *syn/anti*[l])
Br	HOMO	−7.453		0.495	0.028	−0.027	0.364	*syn*
	NHOMO	−8.663		0.197	−0.085	0.066	−0.931	(*anti*[l])

a) Definition of X, Y, and Z axes.



b) The coefficients at C(4) of the unsymmetrical cyclopentadienes **1** (X=NH_2, PH_2, and AsH_2) are in parentheses. c) $C_p^n=(C_{px}^{n\,2}+C_{py}^{n\,2}+C_{pz}^{n\,2})^{1/2}$ d) The coefficients C_s^n of HOMO's for X=NH_2, PH_2, and AsH_2 are 0.079, 0.193, and 0.222, respectively; See Ref. 15b. e) See Ref. 12b. f) The coefficients C_s^n of NHOMO's for X=NH_2, PH_2, and AsH_2 are 0.387, −0.512, and −0.478, respectively; See Ref. 15b. g) See Refs. 10f and 10g. h) See Ref. 12. i) See Ref. 10a. j) See Ref. 10h. k) See Refs. 10i and 10j. l) See Ref. 10k.

side is parallel with the π* orbital, σ-bond electrons on the opposite side are able to delocalize much more effectively than that on the same side. The electron-donating σ-bond on the opposite side stabilizes the transition state. The σ–π* delocalization may contribute to π-facial selectivity. Coxon and McDonald reported similar bond lengthenings to argue for the Cieplak effect, which emphasized the electron delocalization from the antiperiplanar σ-bond at the 5-position to the incipient σ-bonds at the transition states.[13b] However, the bond lengthenings cannot be necessarily convincing evidence for the Cieplak effect, but can be explained in terms of the σ–π* interaction without assuming the incipient σ bonds at the transition state.

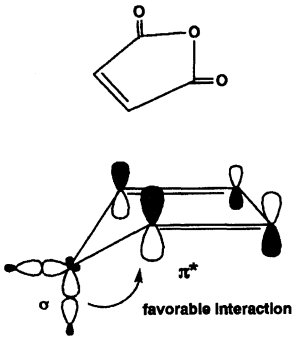


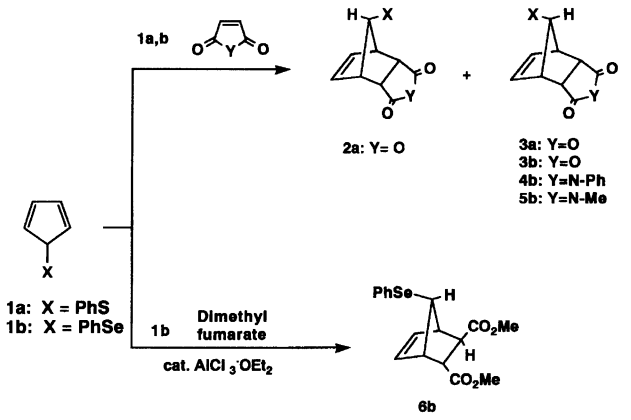
Fig. 3. σ–π* Interaction at the transition state of Diels–Alder reaction.

Experimental Confirmation. Diels–Alder reactions of substituted cyclopentadienes (**1a,b**: X=PhS

and PhSe) were investigated.[11a] The cyclopentadienes were generated in situ and immediately reacted with dienophiles (Scheme 2). The results are summarized in Table 4.

5-Phenylthio-1,3-cyclopentadiene (**1a**) was prepared from the reaction of cyclopentadienylthallium with benzenesulfenyl chloride in carbon tetrachloride.[17] After removal of precipitated thallium chloride, maleic anhydride was immediately added since the diene **1a** readily undergoes [1,5] proton shift.[10a,17,18] The reaction mixture was allowed to stand at −20 °C for 12 h to give a 4:6 mixture of *syn*- and *anti*-attack products, *endo*-8- and *exo*-8-phenylthio-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione, (**2a** and **3a**) [isolated yields: **2a** (as the corresponding diacid **2a'**); 21%, **3a**; 28%].[19,20] The low π-facial selectivity of the reaction of **1a** substantiated the prediction and forms a contrast to the high *syn* selectivities observed for X=OR.[10f,10g,12]

5-Phenylseleno-1,3-cyclopentadiene (**1b**) reacted with *anti* selectivity. The seleno diene **1b** was prepared from benzeneselenenyl bromide and cyclopentadienylthallium in carbon tetrachloride.[10a] The diene **1b** was rather stable than **1a**. The diene **1b** reacted with maleic anhydride at 10 °C to give *anti*-attack product, *exo*-8-phenylseleno-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione (**3b**) exclusively in 69% yield. Reaciton of **1b** with *N*-phenyl- and *N*-methylmaleimide gave the corresponding *anti*-attack products, 2-phenyl and 2-methyl-*exo*-8-phenylseleno-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (**4b** and **5b**) in 32 and 34% yields, respectively. ^{1}H NMR monitoring of the reaction mixture showed no sign of the other stereoisomer. In the presence of aluminum chloride etherate, the diene **1b** reacted with dimethyl fumarate to give the *anti*-attack product, *exo*-7-phenylseleno-*endo*-5,*exo*-6-bis(methoxycarbonyl)bicyclo[2.2.1]hept-2-ene (**6b**) in 34% yield. The selectivity of the diene **1b** was also exactly in agreement with the prediction by the orbital mixing rule.



Scheme 2.

Table 2. PM3 Calculation of Activation Energy of Diels–Alder Reaction of the Diene **1** with Maleic Anhydride

Diene **1** X=	Activation energy (kcal mol^{-1}) *syn*-Attack		*anti*-Attack	$\Delta E_{syn-anti}$
NH_2	32.508	>	31.601	0.91
PH_2	39.622	>	32.499	7.12
AsH_2	41.411	>	33.611	7.79
SbH_2	36.730	>	32.019	4.71
OH	31.127	<	31.449	−0.32
SH	36.200	>	32.973	3.23
SeH	35.601	>	32.145	3.46
Teh	35.996	>	31.253	4.74
F	29.643	<	32.478	−2.84
Cl	32.162	>	32.100	0.06
Br	34.163	>	32.382	1.78
I	39.225	>	34.294	4.93

Conclusion

The π-facial selectivities in Diels–Alder reactions of the 1,3-cyclopentadienes having 5-heteroatom substituents was predicted in terms of the direction of the nonequivalent orbital extension. *Ab initio* molecular orbital calculation on the cyclopentadiene **1** confirmed the frontier orbital distortion. PM3 calculation of the activation energies on Diels–Alder reactions of **1** (X=NH_2, PH_2, AsH_2, SbH_2, OH, SH, SeH, TeH, F, Cl, Br, and I) with maleic anhydride and experimental examination of chalcogen-substituted cyclopentadienes **1a,b** (X=PhS and PhSe) substantiated a part of the theoretical prediction.

Experimental

Melting points were determined using a Yanagimoto melting point apparatus and are uncorrected. IR spectra were measured on a JASCO grating IR spectrometer IR-G. ^{1}H NMR spectra were recorded on Hitachi R-22 (90 MHz) and JEOL-JNM-GX 270 (270 MHz) with tetramethylsilane as an internal standard. EIMS were recorded on Hitachi RMU-6M, Shimadzu QP-1000, or Shimadzu 9020-DF spectrometer at an ionizing voltage of 20 eV. Elemental analyses were performed by Elemental Analyses Center of Osaka University or Elemental Analysis Center, Department of Pharmacy, Kyoto University.

Preparation of the Cyclopentadienes 1a,b. 5-Phenylthio-1,3-cyclopentadiene (1a). To a suspension of cyclopentadienylthallium (3.234 g, 10.0 mmol) in carbon tetrachloride (30 mL), a solution of benzenesulfenyl chloride (1.446 g, 10.0 mmol) in carbon tetrachloride (10 mL) was added dropwise for 30 min at −20 °C under vigorous stirring. After stirring for additional 30 min, thallium chloride was removed by filtration to give a solution of 5-phenylthio-1,3-cyclopentadiene (**1a**, 10 mmol) in carbon tetrachloride. The solution was kept at −20 °C to avoid self polymerization and isomerization of the diene and was used for the following reactions without further purification.

Table 3. PM3 Optimized Bond Lengths of C(5)–X and C(5)–H of the Cyclopentadienes Having 5-Heteroatom Substituents at the Transition States of Diels–Alder Reactions with Maleic Anhydride

1		Substrate	Transition states/Å		
X		Diene	$syn(\Delta_{syn-Diene})$		$anti(\Delta_{anti-Diene})$
NH_2	C(5)–X	1.477	1.470 (−0.007)	<	1.479 (0.002)
	C(5)–H	1.117	1.121 (0.004)	>	1.114 (−0.003)
PH_2	C(5)–X	1.908	1.921 (0.013)	<	1.927 (0.019)
	C(5)–H	1.107	1.116 (0.009)	>	1.108 (0.001)
AsH_2	C(5)–X	2.002	2.016 (0.014)	<	2.021 (0.019)
	C(5)–H	1.107	1.116 (0.009)	>	1.108 (0.001)
SbH_2	C(5)–X	2.174	2.165 (−0.009)	<	2.178 (0.004)
	C(5)–H	1.101	1.111 (0.010)	>	1.103 (0.002)
OH	C(5)–X	1.400	1.391 (−0.009)	<	1.400 (0.000)
	C(5)–H	1.112	1.118 (0.006)	>	1.110 (−0.002)
SH	C(5)–X	1.819	1.807 (−0.012)	<	1.823 (0.004)
	C(5)–H	1.115	1.124 (0.009)	>	1.114 (−0.001)
SeH	C(5)–X	1.948	1.933 (−0.015)	<	1.948 (0.000)
	C(5)–H	1.106	1.118 (0.012)	>	1.107 (0.001)
TeH	C(5)–X	2.214	2.190 (−0.024)	<	2.207 (−0.007)
	C(5)–H	1.101	1.113 (0.012)	>	1.103 (0.002)
F	C(5)–X	1.360	1.357 (−0.003)	<	1.368 (0.008)
	C(5)–H	1.112	1.114 (0.002)	>	1.109 (−0.003)
Cl	C(5)–X	1.770	1.756 (−0.014)	<	1.778 (0.008)
	C(5)–H	1.112	1.117 (0.005)	>	1.110 (−0.002)
Br	C(5)–X	1.944	1.922 (−0.022)	<	1.945 (0.001)
	C(5)–H	1.106	1.113 (0.007)	>	1.106 (0.000)
I	C(5)–X	2.024	2.004 (−0.020)	<	2.026 (0.002)
	C(5)–H	1.111	1.117 (0.006)	>	1.111 (0.000)

5-Phenylseleno-1,3-cyclopentadiene (1b). Similarly to the synthesis of the diene **1a**, the solution of 5-phenylseleno-1,3-cyclopentadiene (2.0 mmol) in carbon tetrachloride was prepared from cyclopentadienylthallium (647 mg, 2.4 mmol) and benzeneselenenyl bromide (472 mg, 2.0 mmol) at 20 °C. The solution was used for the following reactions without further purification. ^{1}H NMR ($CDCl_3$) δ=4.72 (brs, 1H, CH–SePh), 6.47 (m, 4H, HC=CH), 7.1—7.6 (m, 5H, Ar).

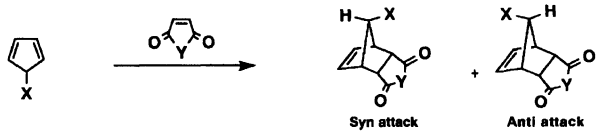
Diels–Alder Reaction of the Diene 1a,b with Dienophiles. *endo*-8-Phenylthio-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione (2a) and *exo*-8-Phenylthio-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione (3a). Maleic anhydride (980 mg, 10.0 mmol) was added to a solution of 5-phenylthio-1,3-cyclopentadiene (**1a**, 10.0 mmol) in carbon tetrachloride (55 mL) and allowed to stand at −20 °C for 12 h. After removal of the solvent, an aliquot of the residue was dissolved in C_6D_6 and subjected to ^{1}H NMR spectroscopy which showed a triplet peak at δ=5.70 due to the olefinic protons of the *syn*-attack product **2a** and a triplet-doublet at δ=5.76 due to the olefinic protons of the *anti*-attack **3a** in the integration ratio of 40:60.[21] The residue was treated with carbon tetrachloride (20 mL) to give a mixture of the *anti*-attack product **3a** and maleic anhydride (950 mg, ca. 1:1) as yellow powder. Removal of maleic anhydride in vacuo (80 °C/4 Torr, 1 Torr=133.322 Pa) gave 758 mg (28%) of pure **3a** (Fig. 4) The mother liquid was concentrated and dissolved in tetrahydrofuran (45 mL). To the solution, potassium hydroxide (579 mg, 10.2 mmol) in water (2 mL) was added followed by acidification to give 580 mg of the *syn*-attack product as the diacid, *endo*-7-(phenylthio)bicyclo[2.2.1]hept-5-ene-*endo*-2,*endo*-3-dicarboxylic acid (**2a′**) in the yield of 21%. Treatment of **2a′** with acetic anhydride gave **2a**.

2a: Mp 91—93 °C (AcOEt/hexane=1:5); IR (KBr) 1860, 1780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.40 (m, 2H, H-4,7), 3.58 (t, J=1.4 Hz, 1H, CH–SPh), 3.94 (dd-like m, 2H, H-3a,7a), 6.40 (t-like m, 2H, CH=CH), 7.3—7.4 (m, 5H, Ph); ^{1}H NMR (C_6D_6) δ=2.73 (m, 2H, H-4,7), 2.90 (t, J=1.4 Hz, 1H, CH–SPh), 3.07 (dd-like m, 2H, H-3a,7a), 5.67 (t-like m, 2H, CH=CH), 6.9—7.1 (m, 5H, Ph); ^{13}C NMR (Acetone-d_6) δ=46.7, 50.1, 69.1, 128.4, 130.2, 132.2, 134.5, 137.3, 172.5 (*C=O); EIMS (20 eV), m/z (rel intensity) 272 (M^+, 27), 244 (18), 199 (100), 174 (45), 135 (11), 110 (13), 91 (49), 85 (61). Found: C, 65.92; H, 4.55%. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44%.

2a′: Mp 144 °C (decomp); IR (KBr) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$+d_6-DMSO) δ=3.0 (m, 2H, CH), 3.12 (brs, 1H, CH–SPh), 3.50 (m, 2H, CH), 5.5 (br, H_2O + COOH), 6.25 (t-like m, 2H, CH=CH), 7.0—7.3 (m 5H, Ph); EIMS (20 eV), m/z (rel intensity), 290 (M^+, 4), 272 (22), 244 (15), 198 (97), 174 (85), 141 (14), 135 (15), 110 (26), 99 (24), 98 (24), 91 (43), 72 (100). Found: C, 61.97; H, 4.89%. Calcd for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86%.

3a: Mp 165—168 °C (AcOEt/hexane=1:1); IR (KBr) 1860, 1785 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.40 (brs, 1H, CH–SPh), 3.65 (brs, 4H, CH), 6.37 (brs, 2H, CH=CH), 7.2—7.4 (m, 5H, Ph); ^{1}H NMR (C_6D_6) δ=2.37 (dd-like m, 2H, H-3a, 7a), 2.57 (brs, 1H, CH–SPh), 2.95 (m, 2H, H-4, 7), 5.74 (td-like m, 2H, CH=CH), 6.9—7.2 (m, 5H, Ph); ^{13}C NMR (Acetone-d_6) δ=46.9, 51.5, 70.3, 127.3, 129.9, 130.7, 134.8,

Table 4. Diels–Alder Reaction of Cyclopentadienes Having Chalcogen-Substituents at 5-Positions



Run	Diene X=	Dienophile Y=	Product (%)[a]	addition ratio *syn* : *anti*[b]
1	**1a** SPh	O	**2a** (21)[c] **3a** (28)	40 : 60
2	**1b** SePh	O	**3b** (69)	0 : 100
3		NPh	**4b** (32)	0 : 100
4		NMe	**5b** (34)	0 : 100
5		Dimethyl fumarate	**6b** (34)[d]	0 : 100
	OAc	Ethylene		100 : 0[e]
	OH	Dimethyl fumarate	R= COOMe	100 : 0[f]

a) Isolated yields based on PhSCl or PhSeBr. b) The ratios were determined on the basis of ^{1}H NMR. c) Yield of the diacid **2a**′. d) In the presence of an equimolar amount of $AlCl_3$·OEt_2. e) See Ref. 10f. f) See Ref. 10g.

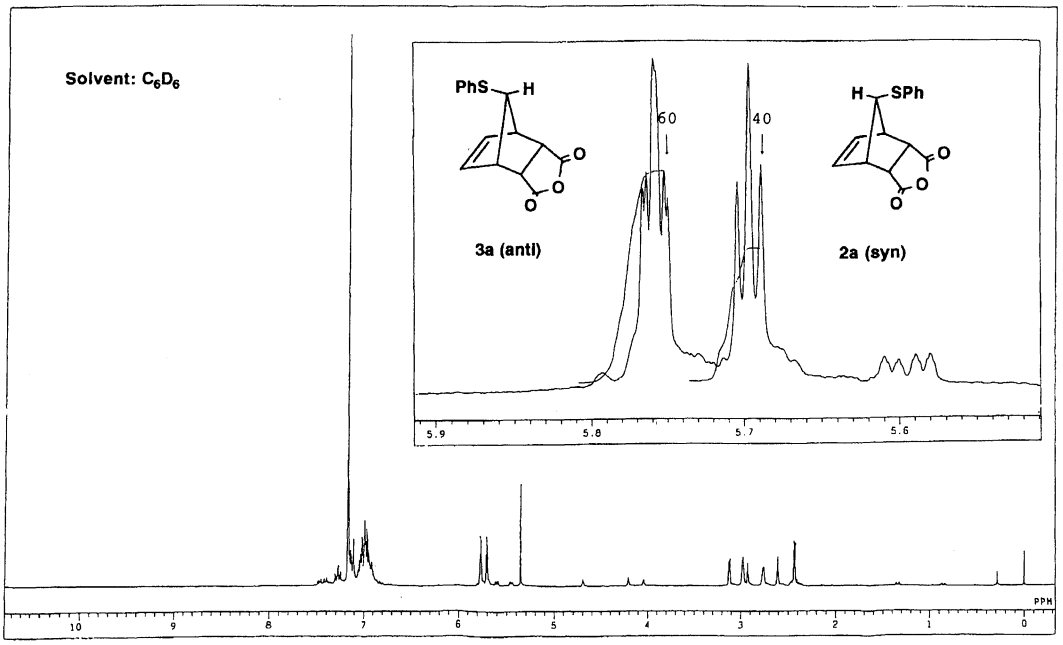


Fig. 4. 270 MHz ^{1}H NMR spectrum of the reaction mixture of the diene **1a** with maleic anhydride.

136.7, 171.8 (*C=O); EIMS (20 eV), *m/z* (rel intensity) 272 (M^+, 33), 244 (10), 199 (100), 174 (12), 135 (19), 110 (12), 91 (51). Found: C, 66.23; H, 4.53%. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44%.

The stereochemistry of the products **2a** and **3a** was assigned on the basis of NOE difference studies (solvent: C_6D_6, Fig. 5). In the case of the product **2a**, irradiation of the CH–SPh proton at $\delta = 2.90$ produced positive en-

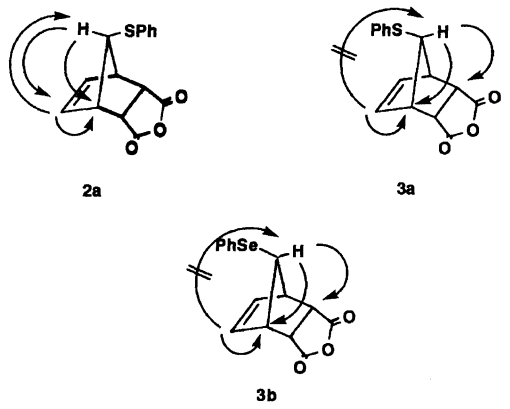


Fig. 5. NOE study of the products **2a**, **3a**, and **3b**.

hancement of the 4,7 and the olefinic protons at $\delta=2.73$ and 5.67, respectively. Upon irradiation of the olefinic proton at $\delta=5.67$, positive NOE's were observed for CH–SPh and H-4,7 protons at $\delta=2.90$ and 2.95. On the other hand, in the case of the product **3a**, irradiation of the CH–SPh proton at $\delta=2.57$ produced strong enhancement of the H-3a, 7a and the H-4,7 protons at $\delta=2.37$ and 2.95, respectively. Upon irradiation of the olefinic proton at $\delta=5.74$, a strong NOE was observed only for H-4,7 protons at $\delta=2.95$.

***exo*- 8- Phenylseleno- 3a, 4, 7, 7a- tetrahydro- 4, 7-methanoisobenzofuran-1,3-dione (3b).** A solution of maleic anhydride (196 mg, 2.0 mmol) in carbon tetrachloride (20 mL) was added at 10 °C to a solution of 5-phenylseleno-1,3-cyclopentadiene (**1b**, 2.0 mmol) in carbon tetrachloride (30 mL). The mixture was kept at 10 °C for 84 h to give 440 mg (69%) of the *anti*-attack product **3b** as colorless solid: Mp 121—124 °C (CH_2Cl_2/hexane); IR (KBr) 1860, 1790 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=3.30$ (brs, 1H, CH–SePh), 3.62 (dd-like m, 2H, CH), 3.70 (m, 2H, CH), 6.37 (td-like m, 2H, HC=CH), 7.1—7.5 (m, 5H, Ar); ^1H NMR (C_6D_6) $\delta=2.35$ (dd-like m, 2H, CH), 2.53 (brs, 1H, CH–SePh), 3.03 (brs, 2H, CH), 5.74 (brs, 2H, CH=CH), 6.9—7.3 (m, 5H, Ph); ^{13}C NMR (Acetone-d_6) $\delta=47.1$, 52.4, 66.0, 127.9, 129.9, 130.7, 133.7, 135.8, 171.5 (*C=O); EIMS (20 eV) *m/z* (rel intensity) 320 (M^+, 43), 222 (27), 142 (28), 141 (100), 135 (28), 91 (41). Found: C, 56.16; H, 3.83%. Calcd for $C_{15}H_{12}O_3Se$: C, 56.44, H, 3.79%.

The *exo* stereochemistry of the product **3b** was similarly confirmed on the basis of NOE difference studies (solvent: C_6D_6).

2-Phenyl-*exo*-8-phenylseleno-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)dione (4b). *N*-Phenylmaleimide (346 mg, 2.0 mmol) was added to a solution of the diene **1b** (2.0 mmol) in carbon tetrachloride (23 mL) and was kept at 12 °C for 40 h to give 251 mg (32%) of the *anti*-attack product **4b**: Mp 210—214 °C (CCl_4); IR (KBr) 1770, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=3.39$ (brs, 1H, CH–SePh), 3.48 (dd-like m, 2H, H-3a, 7a), 3.73 (m, 2H, H-4, 7), 6.32 (td-like m, 2H, HC=CH), 7.1—7.6 (m, 10H, Ph); EIMS *m/z* (rel intensity), 395 (M^+, 50), 238 (59), 222 (37), 210 (13), 173 (31), 141 (100), 119 (21), 91 (79). Found: C, 63.68; H, 4.39; N, 3.29%. Calcd for $C_{21}H_{17}O_2NSe$: C, 63.96; H, 4.35; N, 3.55%.

Preparation of 4b from 3b. To a solution of **3b** (160 mg, 0.5 mmol) in ether (20 mL), aniline (47 mg, 0.5 mmol) was added and the solution was refluxed for 30 min. After removal of the solvent, the residue was dissolved in toluene (30 mL) and refluxed for 3 h in the presence of molecular sieves (4A) to give, after workup, 58 mg (30%) of **4b** whose spectra were identical with those of **4b** obtained from the reaction of **1b** and *N*-phenylmaleimide.

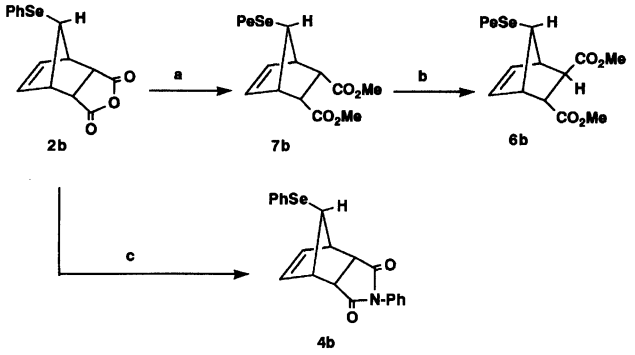
2-Methyl-*exo*-8-phenylseleno-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione (5b). *N*-Methylmaleimide (222 mg, 2.0 mmol) was added to a solution of 2.0 mmol of the diene (**1b**) in carbon tetrachloride (23 mL) and was kept at 10 °C for 40 h to give, after workup, 242 mg (37%) of the *anti*-attack product **5b**: Mp 144—147 °C (CCl_4); IR (KBr) 1762, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=2.83$ (s, 3H, N–CH_3), 3.32 (m, 3H, CH), 3.62 (m, 2H, CH), 6.15 (td-like m, 2H, HC=CH), 7.2—7.6 (m, 5H, Ph); EIMS (20 eV) *m/z* (rel intensity) 333 (M^+, 24), 222 (12), 176 (81), 141 (42), 119 (8), 91 (100). Found: C, 57.74; H, 4.63; N, 3.96%. Calcd for $C_{16}H_{15}O_2NSe$: C, 57.84; H, 4.55; N, 4.21%.

***exo*-8-Phenylseleno-*endo*-5,*exo*-6-bis (methoxycarbonyl)bicyclo[2.2.1]hept-2-ene (6b).** To a mixture of dimethyl fumarate (144 mg, 1.0 mmol) and aluminum chloride etherate (208 mg, 1.0 mmol) in carbon tetrachloride (25 mL), a solution of the diene **1b** (1.0 mmol) in carbon tetrachloride was added and the mixture was allowed to stand at 10 °C for 12 h to give, after usual workup, 125 mg (34%) of the *anti*-attack adduct, (**6b**): Colorless needles; mp 79 °C (ether/hexane=1 : 75); IR (KBr) 1722 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=2.81$ (d, $J=4.58$ Hz, 1H, CH), 3.40 (m, 1H, CH), 3.41 (m, 1H, CH), 3.52 (m, 1H, CH), 3.57 (m, 1H, CH), 3.66 (s, 3H, CH_3), 3.73 (s, 3H, CH_3O), 6.13 (dd, $J=5.7$, 2.1 Hz, **H**C=CH), 6.34 (dd, $J=5.7$, 2.7 Hz, HC=C**H**), 7.2—7.5 (m, 5H, Ph); EIMS (20 eV) *m/z* (rel intensity) 366 (M^+, 47), 222 (61), 209 (39), 177 (22), 165 (34), 149 (26), 142 (26), 141 (100), 113 (45). Found: C, 55.89; H, 4.98%. Calcd for $C_{17}H_{18}O_4Se$: C, 55.90; H, 4.97%.

Structural Elucidation of 6b. The *anti*-attack product **3b** (319 mg, 1.0 mmol) was treated with *t*-BuOK (112 mg, 1.0 mmol) in methanol (10 mL) at 25 °C for 30 min to give the corresponding half ester in 98% yield. A solution of the half ester (344 mg, 0.98 mmol) in methanol/benzene (1 : 1, 50 mL) was refluxed for 12 h in the presence of *p*-toluenesulfonic acid (10 mg) to give 251 mg (69%) of the dimethyl ester, *exo*-7-phenylseleno-*endo*-5,*endo*-6-bis-(methoxycarbonyl)bicyclo[2.2.1]hept-2-ene (**7b**). The ester **7b** (742 mg, 2.0 mmol) was treated with *t*-BuOK (45 mg, 0.4 mmol) in refluxing methanol (40 mL) for 3 h to give, after workup, 584 mg (79%) of the ester **6b** whose spectra was in agreement with those of **6b** obtained from the reaction of the diene **1b** and dimethyl fumarate (Scheme 3).

7b: Mp 64—65 °C (ether/hexane=5 : 3); IR (KBr) 1725 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=3.17$ (brs, 1H, CH–SePh), 3.37 (brs, 2H, CH), 3.42 (brs, 2H, CH), 3.61 (s, 6H, CH_3O), 6.33 (brs, 2H, HC=CH), 7.2—7.5 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) $\delta=47.7$, 51.7, 52.5, 63.2, 127.4, 129.1, 130.2, 133.8, 134.5, 171.6 (*C=O); EIMS (20 eV) *m/z* (rel intensity) 366 (M^+, 26), 222 (61), 209 (62), 177 (22), 149 (45), 145 (31), 142 (26), 141 (100), 113 (51). Found: C, 55.75; H, 4.92%. Calcd for $C_{17}H_{18}O_4Se$: C, 55.90; H, 4.97%.

The *ab initio* molecular orbital calculations with



Scheme 3. **a**. *t*-BuOK/MeOH, 25 °C, 30 min, then TsOH/(MeOH+benzene 1:1), reflux, 12 h: yield 69%; **b**. *t*-BuOK/MeOH, reflux, 3 h: yield 79%; **c**. Ph–NH_2/ether, reflux 30 min then toluene reflux 3 h: yield 30%.

GAUSSIAN 80 and 82 programs which were carried out on FACOM M-782 computer at Nagoya University computer center and HITAC M-680H computer at the Institute for Molecular Science, respectively. The PM3 molecular orbital calculations with MOPAC Ver 6.0 program were carried out on Convex computer at Nara University of Education. This work was supported in part by Grant-in Aid for Scientific Research on Priority Area "Theory of Chemical Reactions" from the Ministry of Education, Science and Culture. We also gratefully acknowledge support of this work by Nippon Polyurethane Industry Co., Ltd. and Asahi Yukizai Kogyo Co., Ltd.

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15) a) The heteroatom dependence of the π-facial selectivities is consistent with the observed ionization potentials of $(CH_3)_2Y$ (Y=O, S, Se, Te) relative to cyclopentadiene. The ionization potentials indicate that the orbital energy increases in the order of $\varepsilon_{n(O)}$ (−10.04 eV)<$\varepsilon_{n(S)}$ (−8.71 eV)≃$\varepsilon_{\pi(\text{cyclopentadiene})}$ (−8.566 eV)<$\varepsilon_{n(Se)}$ (−8.40 eV)<$\varepsilon_{n(Te)}$ (−7.89 eV): S. Cradock and R. A. Whiteford, *J. Chem. Soc., Farady Trans. 2*, **68**, 281 (1972); b) The ionization potentials of $(CH_3)_3Y$ (Y=N: −8.54 eV, P: −8.60 eV, As: −8.65 eV, Sb: −8.48 eV) are almost unchanged from nitrogen to antimony. The similar n-orbital energy levels have been proposed to be due to the increase of the s-character in the order of N<P<As<Sb: S. Elbel, H. Bergmann, and W. Ensslin, *J. Chem. Soc., Farady Trans. 2*, **70**, 555 (1974); c) This is consistent with the observed ionization potentials of CH_3X [F: −13.05 eV, Cl: −11.03 eV, Br: −10.54 eV, I: −9.54 eV] much lower than that of cyclopentadiene (−8.566 eV): J. W. Robinson, "Handbook of Spectroscopy," CRC Press, Boca Raton, FL (1974), Vol. 1.

16) The *syn*/*anti* transition-state energy differences calculated at the HF/3-21G level by Hehre et al. supported our simple rationale, while they interpreted the results in terms of steric and electrostatic arguments (T. -M. Chao, J. Baker, and W. J. Hehre, private communication of August 28 (1990) prior to publication of the preliminary report,[11b] for which we thank Prof. Hehre)

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19) The ratio was determined on ^{1}HNMR. The adduct **2a** was isolated as the diacid **2a′**, since fractional recrystallization gave **2a** in low yields.

20) To avoid confusion, the prefix *exo* was employed to

show the relative stereochemistry at the methano bridge when the substituent at the position is on the same side of the olefinic bridge (**3a**,**b**, **4b**, **5b**, and **6b**). When the substituent at the methano bridge is on the side remote from the olefinic bridge, the prefix *endo* is used (**2a**, **a**′).

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