Elucidation of Selectivity Difference in the Diels-Alder Reactions of 6,6-Disubstituted Cyclohexa-2,4-dienone

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Recently it was reported that cycloaddition of 6,6-disubstituted cyclohexa-2,4-dienone, **1** with cyclopentadiene gave solely the adduct of type I, while its reaction with 1,3-cyclohexadiene gave both II and III. Semiempirical MO calculations were done to elucidate the origin of the selectivity difference between the two dienes. Cycloaddition of **1** with cyclopentadiene is controlled thermodynamically to give only **1**-diene adduct by ΔG values of 10.6-20.3 kcal/mol, while its reaction with 1,3-cyclohexadiene does not show **1**-diene/**1**-dienophile selectivity due to similar stabilities of the two adducts. Thermodynamic parameters also show that *endo* adducts are more favourably formed in the cycloadditions of **1** with both cyclopentadiene and 1,3-cyclohexadiene, which coincides with experimental observations. Cope rearrangements of *endo* adducts are another avenue to convert between **1**-diene and **1**-dienophile.

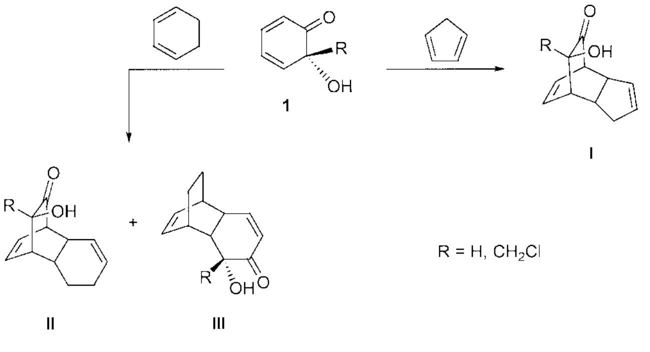
Keywords : Cycloaddition, Diels-Alder reaction, Cyclohexa-2,4-dienone, Semiempirical MO.

Introduction

Much interest has been focused on the pericyclic reactions of conjugated polyenes due to their potential for easy creation of complex carbocyclic systems.[1,2] 2,4-Cyclohexadienones are emerging as valuable intermediates in organic synthesis,[3-6] because of their various chemical behavior. However, multiple modes of addition could be occurred during their cycloaddition with conjugated polyenes.[7]

In the syntheses of variously annulated bicyclo[2.2.2]-octenones, cycloadditions of 6,6-disubstituted cyclohexa-2,4-dienone **1** with cyclopentadiene gave only adduct of type I, while its reaction with 1,3-cyclohexadiene gave both II and III[8] (Scheme 1). Considering the structural similarity in cyclopentadiene and 1,3-cyclohexadiene, and that Diels-Alder reaction is carried out more easily when dienophile has electron-withdrawing group,[9] this observations are quite interesting.

It has been reported that the reactions of variously substituted cyclohexa-2,4-dienones with cyclopentadiene involve the intermediate formation of norbornene system, where cyclopentadiene behaves as diene, which then rearranges to give a less strained product, adduct of type I.[5a] However, it cannot be excluded that some of the adduct might have been formed directly by addition of the cyclohexadienone to a double bond of the cyclopentadiene.



Scheme 1

On the other hand, Singh and coworkers have shown that cyclohexa-2,4-dienones behave as diene in the reaction with 1,3-cyclohexadiene, and that while the type III adducts failed to undergo the Cope rearrangement to type II adducts, the type II adducts smoothly rearranged to type III adducts.[8b] But they did not ruled out the possibility of a competitive reaction in which 1,3-cyclohexadiene behaves as diene.

In order to obtain a deeper insight into the origin of different behaviour of **1** in these reactions, we have performed semiempirical PM3[10] computations for these reactions and discussed the experimental results with thermodynamic parameters obtained.

Computations

All calculations were performed with PM3 method by using MOPAC93,[11] and convergence criteria were increased by 100 times using keyword PRECISE. Transition states were located by using the eigenvector following procedure (EF)[12] and characterized by confirming the presence of only one negative eigenvalue in the Hessian matrix. In addition, intrinsic reaction coordinate (IRC) method[13] was used to confirm both minima.

Results and Discussion

Frontier molecular orbitals were examined in the first place, in order to see if there is any aspect to make cyclopentadiene react only in one mode. PM3-optimized energy diagram of frontier molecular orbitals of **1**(R=CH$_3$), cyclopentadiene, and 1,3-cyclohexadiene is shown in Figure 1.

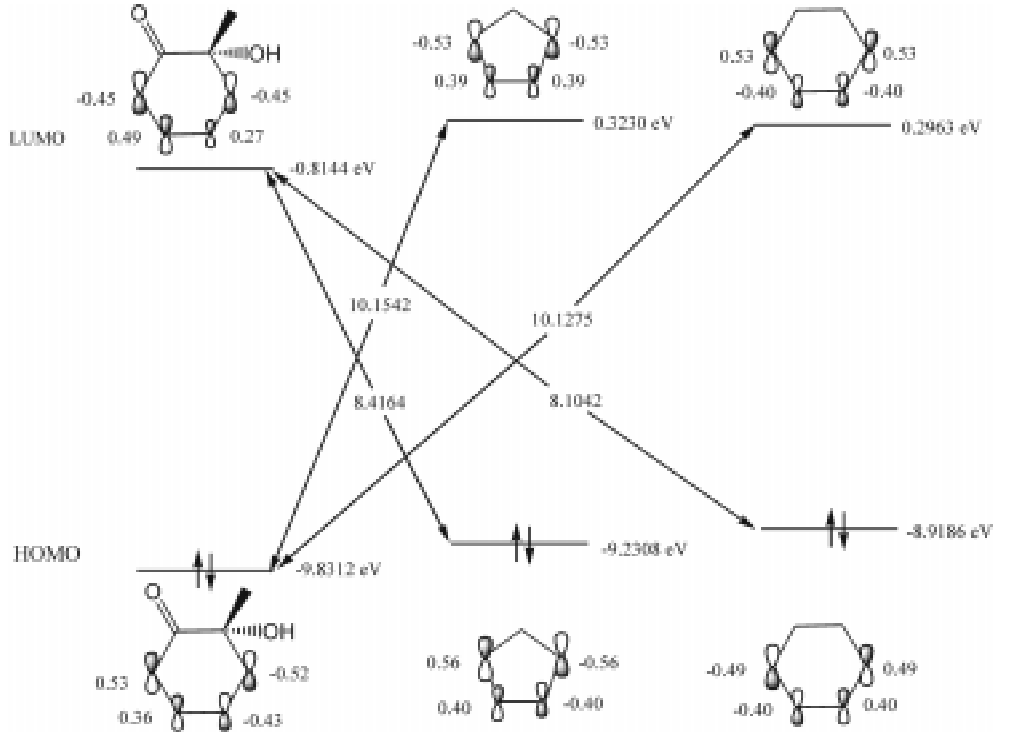


Figure 1. PM3-optimized energy diagram of frontier molecular orbitals of **1** ($R=CH_3$), cyclopentadiene, and cyclohexadiene. Part of coefficients of the FMOs are depicted.

The interaction between LUMO of **1**($R=CH_3$) and HOMO of cyclopentadiene is more favourable than the inteaction between HOMO of **1**($R=CH_3$) and LUMO of cyclopentadiene in terms of energy by 1.74 eV, although both interactions are symmetry-allowed. Frontier molecular orbital interaction energy, ΔE_{FMO}, for the cycloaddition between two molecules can be estimated by[14]

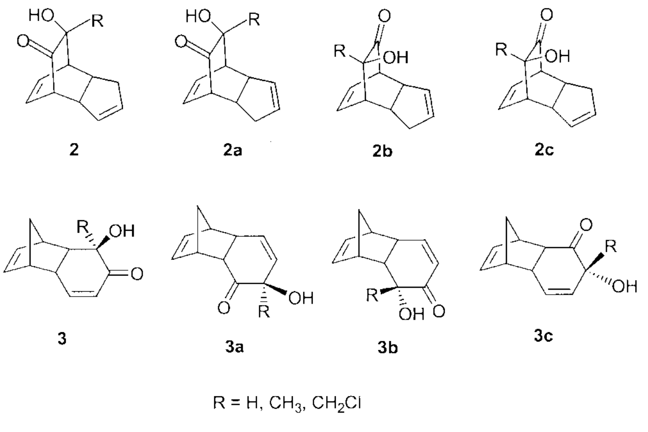
$$\Delta E_{FMO} = 2\gamma^2\left[\frac{(C_{A1H}C_{B1L}+C_{A2H}C_{B2L})^2}{E_{AH}-E_{BL}}+\frac{(C_{A1L}C_{B1H}+C_{A2L}C_{B2H})^2}{E_{BH}-E_{AL}}\right]$$

where γ is the resonance integral of the two interacting lobes at each of the reaction sites, C and E refer to particular eigenvector coefficient and eigenvalue, respectively. Subscripts A and B refer to the two reacting molecules, 1 and 2 refer to the two reaction sites, and H and L refer to HOMO and LUMO. ΔE_{FMO} values were compared for the two reaction modes in the interaction between **1**($R=CH_3$) and cyclopentadiene. The reaction of **1**($R=CH_3$) as dienophile ($-0.11\gamma^2$ eV) is slightly more favourable than that as diene ($-0.092\gamma^2$ eV), although both reactions are symmetry-allowed. Energy is more favourable for the interaction between LUMO of **1**($R=CH_3$) and HOMO of 1,3-cyclohexadiene, as is the same aspect in the reaction of **1**($R=CH_3$) with cyclopentadiene, by 2.02 eV. Again, the reaction of **1**($R=CH_3$) as dienophile ($-0.10\gamma^2$ eV) is slightly more favourable than that as diene ($-0.094\gamma^2$ eV) as regards to frontier molecular orbital interaction energy. Analysis of FMO did not give the grounds for the selectivity of the reaction of **1** with cyclopentadiene.

We have sought all the stationary points for possible reaction paths in the cycloadditions of **1** with cyclopentadiene and 1,3-cyclohexadiene.

Cycloadditions with cyclopentadiene. Scheme 2 shows all feasible structures resulted from cycloadditions of **1** with cyclopentadiene. While **2**, **2a**, **2b**, and **2c** could be expected when cyclopentadiene reacts as dienophile, **3**, **3a**, **3b**, and **3c** could be obtained when it reacts as diene. All structures could have a pair of cis junctions, *i.e.*, *endo* and *exo* additions.

Stereoisomers of each adduct of **1** in Scheme 2 were not considered, because they did not show stability difference. Computations were performed for R=H, CH_3, and CH_2Cl of



Scheme 2

Table 1. PM3-calculated thermodynamic parameters[a] for the Diels-Alder reactions of **1** with cyclopentadiene in kcal/mol at 298 K

Compounds		ΔH_f	S[b]	ΔH	ΔS[b]	ΔG	$\Delta H^{\neq}$	$\Delta S^{\neq}$[b]	$\Delta G^{\neq}$
1	R = H	-47.2	78.1						
	CH_3	-53.0	84.3						
	CH_2Cl	-54.0	86.4						
cyclopentadiene		31.7	65.3						
2-*endo*	R = H	-45.2	92.9	-29.7	-50.5	-14.6	36.7	-49.6	51.5
	CH_3	-50.8	97.9	-29.5	-51.7	-14.1	37.2	-51.5	52.6
	CH_2Cl	-52.2	100.3	-29.9	-51.4	-14.6	36.6	-47.9	50.9
2-*exo*	R = H	-45.3	91.8	-29.8	-51.6	-14.4	37.7	-47.5	51.9
	CH_3	-47.4	96.5	-26.1	-53.1	-10.3	42.4	-48.6	56.9
	CH_2Cl	-49.2	99.1	-26.9	-52.6	-11.2	41.5	-48.5	56.0
2a-*endo*	R = H	-45.2	92.9	-29.7	-50.5	-14.6	36.9	-49.4	51.6
	CH_3	-50.9	97.9	-29.6	-51.7	-14.2	37.3	-47.9	51.6
	CH_2Cl	-51.8	100.4	-29.5	-51.3	-14.2	37.5	-47.9	51.8
2a-*exo*	R = H	-45.2	92.4	-29.7	-51.0	-14.5	37.9	-47.0	51.9
	CH_3	-47.8	98.1	-26.5	-51.5	-11.1	42.1	-47.7	56.3
	CH_2Cl	-49.4	99.8	-27.1	-51.9	-11.6	41.5	-48.0	55.8
2b-*endo*	R = H	-45.2	92.7	-29.7	-50.7	-14.6	35.4	-46.8	49.4
	CH_3	-50.7	98.7	-29.4	-50.9	-14.2	36.0	-47.0	50.0
	CH_2Cl	-52.1	100.6	-29.8	-51.1	-14.6	35.8	-47.3	49.9
2b-*exo*	R = H	-43.0	92.5	-27.5	-50.9	-12.3	37.8	-48.7	52.3
	CH_3	-47.6	98.0	-26.3	-51.6	-10.9	39.9	-48.9	54.5
	CH_2Cl	-49.0	100.0	-26.7	-51.7	-11.3	39.6	-48.8	54.1
2c-*endo*	R = H	-45.3	92.7	-29.8	-50.7	-14.7	35.7	-46.9	49.7
	CH_3	-50.7	98.7	-29.4	-50.9	-14.2	36.2	-47.0	50.2
	CH_2Cl	-52.1	100.6	-29.8	-51.1	-14.6	36.0	-47.3	50.1
2c-*exo*	R = H	-43.2	92.6	-27.7	-50.8	-12.6	36.9	-48.5	51.4
	CH_3	-48.0	98.2	-26.7	-51.4	-11.4	40.1	-47.3	54.2
	CH_2Cl	-49.6	100.3	-27.3	-51.4	-12.0	39.9	-51.1	55.1
3-*endo*	R = H	-30.4	87.6	-14.9	-55.8	1.7	37.7	-50.6	52.8
	CH_3	-31.7	93.8	-10.4	-55.8	6.2	41.1	-51.7	56.5
	CH_2Cl	-33.4	100.2	-11.1	-51.5	4.3	40.6	-51.3	55.9
3-*exo*	R = H	-30.7	89.2	-15.2	-54.2	1.0	38.0	-52.1	53.5
	CH_3	-34.4	95.3	-13.1	-54.3	3.1	38.6	-50.9	53.8
	CH_2Cl	-35.9	97.1	-13.6	-54.6	2.7	38.1	-51.1	53.3
3a-*endo*	R = H	-29.8	89.9	-14.3	-53.5	1.7	36.0	-50.3	51.0
	CH_3	-35.1	95.3	-13.8	-54.3	2.4	36.2	-48.6	50.7
	CH_2Cl	-37.6	97.4	-15.3	-54.3	0.9	36.3	-50.9	51.5
3a-*exo*	R = H	-32.9	89.1	-17.4	-54.3	-1.2	36.6	-50.4	51.6
	CH_3	-37.2	95.5	-15.9	-54.1	0.2	36.2	-50.9	51.4
	CH_2Cl	-38.9	96.9	-16.6	-54.8	-0.3	36.0	-51.4	51.3
3b-*endo*	R = H	-29.4	88.5	-13.9	-54.9	2.5	37.1	-51.4	52.4
	CH_3	-33.0	95.1	-11.7	-54.5	4.5	39.0	-50.9	54.2
	CH_2Cl	-34.4	97.0	-12.1	-54.7	4.2	38.6	-51.0	53.8
3b-*exo*	R = H	-32.5	87.9	-17.0	-55.5	-0.5	37.0	-47.5	51.2
	CH_3	-34.9	97.3	-13.6	-52.3	2.0	40.5	-50.5	55.6
	CH_2Cl	-36.3	99.7	-14.0	-52.0	1.5	40.3	-45.8	54.0
3c-*endo*	R = H	-31.6	89.0	-16.1	-54.4	0.1	36.4	-51.8	51.8
	CH_3	-35.9	95.5	-14.6	-54.1	1.5	37.2	-50.7	52.3
	CH_2Cl	-37.6	96.8	-15.3	-54.9	1.1	36.9	-51.3	52.2
3c-*exo*	R = H	-32.9	91.6	-17.4	-51.8	-2.0	34.6	-47.4	48.7
	CH_3	-37.6	95.4	-16.3	-54.2	-0.1	34.9	-48.4	49.3
	CH_2Cl	-38.8	97.5	-16.5	-54.2	-0.3	34.9	-48.5	49.4

[a] ΔH_f = Heat of formation. ΔH, ΔS, and ΔG refer to reaction enthalpy, reaction entropy, and Gibbs free energy of reaction, respectively. $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta G^{\neq}$ refer to activation enthalpy, activation entropy, and Gibbs free energy of activation, respectively. [b] cal/(K·mol).

Table 2. Comparison of thermodynamic parameters between **1**-diene and **1**-dienophile for the Diels-Alder reaction of **1** with cyclopentadiene in kcal/mol

	$\Delta\Delta G^{\neq}$	$\Delta\Delta G$		$\Delta\Delta G^{\neq}$	$\Delta\Delta G$
(**2**-*endo*)-(**3**-*endo*)			(**2**-*endo*)-(**3**-*endo*)		
R = H	-1.3	-16.3	R = H	-1.6	-15.4
CH_3	-3.9	-20.3	CH_3	3.1	-13.4
CH_2Cl	-5.0	-18.9	CH_2Cl	2.7	-13.9
(**2a**-*endo*)-(**3a**-*endo*)			(**2a**-*exo*)-(**3a**-*exo*)		
R = H	0.6	-16.3	R = H	0.3	-13.3
CH_3	0.9	-16.6	CH_3	4.9	-11.3
CH_2Cl	0.3	-15.1	CH_2Cl	4.5	-11.3
(**2b**-*endo*)-(**3b**-*endo*)			(**2b**-*exo*)-(**3b**-*exo*)		
R = H	-3.0	-17.1	R = H	1.1	-11.8
CH_3	-4.2	-18.7	CH_3	-1.1	-12.9
CH_2Cl	-3.9	-18.8	CH_2Cl	0.1	-12.8
(**2c**-*endo*)-(**3c**-*endo*)			(**2c**-*exo*)-(**3c**-*exo*)		
R = H	-2.1	-14.8	R = H	2.7	-10.6
CH_3	-2.1	-15.7	CH_3	4.9	-11.3
CH_2Cl	-2.1	-15.7	CH_2Cl	5.7	-11.7

1 to see if substituent effect exist.

Table 1 shows thermodynamic parameters for the cycloaddition reaction of **1** with cyclopentadiene at 298 K.

Themodynamic parameters of *endo* and *exo* adduct were compared to see if there are stability differences that could result in *endo*/*exo* selectivity; the difference of Gibbs free energy of reaction, ΔΔG (*endo*-*exo*) and the difference of Gibbs free energy of activation, $\Delta\Delta G^{\neq}$ (*endo*-*exo*) reveal that adducts which arise from the reaction of **1** as diene (**1**-diene) are all favourable for *endo* addition by 0.1-3.8 kcal/mol and 0.3-5.1 kcal/mol, respectively. Adducts which arise from the reaction of **1** as dienophile (**1**-dienophile) are all favourable for *exo* addition by Gibbs free energies of reaction of 0.7-3.1 kcal/mol, while Gibbs free energy of activation do not show consistency.

Both **1** and cyclopentadiene could function as diene in Diels-Alder cycloaddition, hence it is necessary to find **1**-diene/**1**-dienophile selectivity. Themodynamic parameters of **1**-diene and **1**-dienophile were compared to see if there are stability differences that could result in **1**-diene/**1**-dienophile selectivity (Table 2).

The differences of Gibbs free energy of reaction for all *endo* adducts and *exo* adducts are favourable for **1**-diene cycloaddition by 10.6-20.3 kcal/mol, while the differences of Gibbs free energy of activation, which range from 0.1 kcal/mol to 5.7 kcal/mol, do not show consistency. This reveals that **1**-diene/**1**-dienophile selectivity for the cycloaddition of **1** with cyclopentadiene was thermodynamically controlled. Potential energy diagrams for the cycloadditions of **1** with cyclopentadiene are shown in Figure 2.

It is interesting that **1**-diene *endo* adducts can be formed through Cope rearrangement of 1-dienophile *endo* adducts and *vice versa*. Table 3 shows thermodynamic parameters for the Cope rearrangement of *endo* adducts of **1** with cyclopentadiene.

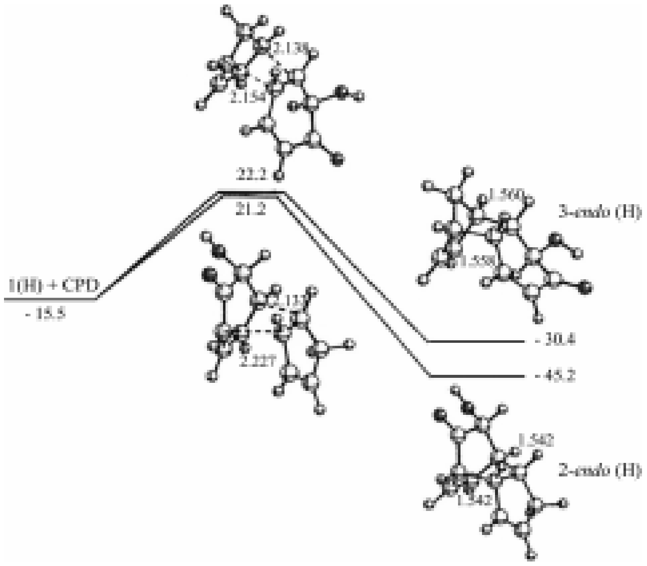
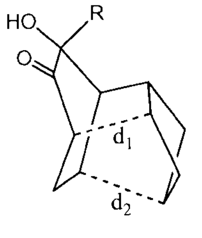


Figure 2. Potential energy (ΔH_f) diagram for the cycloadditions in compound **1** (R=H) with cyclopentadiene (CPD) calculated by the PM3 Hamiltonian. Energies and interatomic distances are given in kcal/mol and angstrom, respectively.

Table 3. PM3-calculated thermodynamic parameters for the Cope rearrangement of the adducts of **1** with cyclopentadiene in kcal/mol at 298 K

Reactions	ΔH	ΔS^a	ΔG	$\Delta H^{\neq}$	$\Delta S^{\neq a}$	$\Delta G^{\neq}$
3-*endo* to **2**-*endo*						
R = H	-14.8	5.3	-16.4	51.9	4.3	50.6
CH_3	-19.1	4.1	-20.3	48.0	2.8	47.2
CH_2Cl	-18.8	0.1	-18.8	48.9	-0.5	49.0
3a-*endo* to **2a**-*endo*						
R = H	-15.4	3.0	-16.3	52.6	1.5	52.2
CH_3	-15.8	2.6	-16.6	53.4	1.0	53.1
CH_2Cl	-14.2	3.0	-15.1	54.8	1.1	54.5
3b-*endo* to **2b**-*endo*						
R = H	-15.8	4.2	-17.1	49.6	3.6	48.5
CH_3	-17.7	3.6	-18.8	47.8	2.5	47.1
CH_2Cl	-17.7	3.6	-18.8	47.7	2.6	46.9
3c-*endo* to **2c**-*endo*						
R = H	-13.7	3.7	-14.8	56.0	2.3	55.3
CH_3	-14.8	3.2	-15.8	54.6	1.9	54.0
CH_2Cl	-14.5	3.8	-15.6	54.9	2.5	54.2

[a] cal/(K·mol)

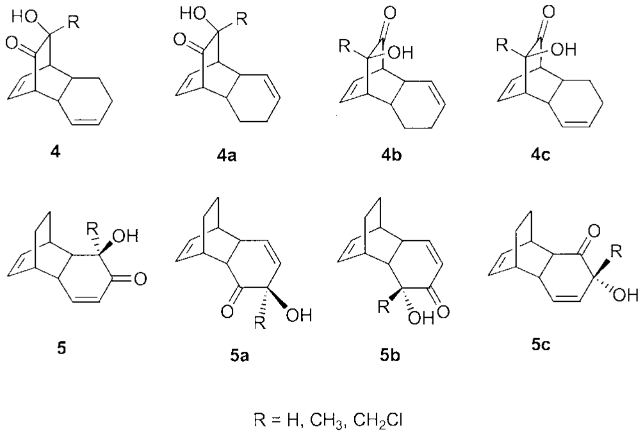


TS_{2-3}

Gibbs free energies of activation and Gibbs free energies of reaction for the Cope rearrangement of **1**-dienophile *endo* adducts are in the range of 46.9 to 55.3 kcal/mol and -14.8 to

-20.3 kcal/mol, respectively. The values of Gibbs free energy of activation could be compared with those for the retro Diels-Alder reaction, which are in the range of 63.9 to 67.5 kcal/mol for **1**-diene adducts and 48.3 to 53.6 kcal/mol for **1**-dienophile adducts. d_1 and d_2 values at ground state vary from *ca.* 1.55 Å of normal C-C single bond distance to the range of 3.62 Å-4.09 Å, and those values at transition state are in the range of 2.24 Å-2.29 Å.

The experimental results for cycloadditions of **1** with cyclopentadiene, which gave only **1**-diene adduct without giving **1**-dienophile, might be explained with more favourable Gibbs free energies of reaction by 10.6-20.3 kcal/mol, that is, **1**-diene/**1**-dienophile selectivity for the cycloaddition of **1** with cyclopentadiene was thermodynamically controlled at reversible reaction conditions. Considering the values of Gibbs free energy of activation for the Cope rearrangement of **1**-dienophile *endo* adducts and those for the retro Diels-Alder reaction of **1**-dienophile adducts, Cope rearrangement of **1**-dienophile *endo* adducts is another way of converting of **1**-dienophile *endo* adduct to **1**-diene *endo* adduct. Besides, *endo*/*exo* selectivities of **1**-diene adducts are all favourable for *endo* adducts in terms of both Gibbs free energy of activation and Gibbs free energy of reaction. These results reveal that **1**-diene *endo* adducts are most favourably formed in the cycloadditions of **1** with cyclopentadiene, which coincide with experimental observations.[5a,8a]



Scheme 3

Cycloadditions with 1,3-cyclohexadiene. Scheme 3 shows all feasible structures resulted from cycloadditions of **1** with 1,3-cyclohexadiene. While **4**, **4a**, **4b**, and **4c** could be expected when 1,3-cyclohexadiene reacts as dienophile, **5**, **5a**, **5b**, and **5c** could be obtained when it reacts as diene. All structures could have a pair of *cis* junctions, *i.e.*, *endo* and exo additions.

Table 4 shows thermodynamic parameters for the cyclo-

Table 4. PM3-calculated thermodynamic parameters[a] for the Diels-Alder reactions of **1** with 1,3-cyclohexadiene in kcal/mol at 298 K

Compounds		ΔH_f	S^b	ΔH	ΔS^b	ΔG	$\Delta H^{\neq}$	$\Delta S^{\neq b}$	$\Delta G^{\neq}$
1	R = H	-47.2	78.1						
	CH_3	-53.0	84.3						
	CH_2Cl	-54.0	86.4						
cyclohexadiene		20.3	72.0						
4-*endo*	R = H	-51.0	97.7	-24.1	-52.4	-8.5	39.0	-54.6	55.3
	CH_3	-56.8	102.6	-24.1	-53.7	-8.1	39.3	-56.5	56.1
	CH_2Cl	-57.7	105.2	-24.0	-53.2	-8.1	39.5	-53.0	55.3
4-*exo*	R = H	-51.4	96.9	-24.5	-53.2	-8.6	39.7	-52.4	55.3
	CH_3	-53.2	98.0	-20.5	-58.3	-3.1	44.8	-53.9	60.9
	CH_2Cl	-54.4	103.8	-20.7	-54.6	-4.4	44.8	-50.4	59.8
4a-*endo*	R = H	-50.8	97.8	-23.9	-52.3	-8.3	38.5	-57.7	55.7
	CH_3	-56.7	102.7	-24.0	-53.6	-8.0	39.4	-53.0	55.2
	CH_2Cl	-57.7	105.1	-24.0	-53.3	-8.1	39.5	-53.0	55.3
4a-*exo*	R = H	-51.2	97.5	-24.3	-52.6	-8.6	40.3	-52.0	55.8
	CH_3	-54.9	102.7	-22.2	-53.6	-6.2	43.8	-49.4	58.5
	CH_2Cl	-57.1	103.3	-23.4	-55.1	-7.0	43.4	-50.9	58.6
4b-*endo*	R = H	-50.9	97.5	-24.0	-52.6	-8.3	37.9	-51.9	53.4
	CH_3	-56.5	103.4	-23.8	-52.9	-8.0	38.5	-55.5	55.0
	CH_2Cl	-57.8	105.4	-24.1	-53.0	-8.3	38.3	-52.5	54.0
4b-*exo*	R = H	-48.8	95.8	-21.9	-54.3	-5.7	41.1	-54.0	57.2
	CH_3	-54.1	101.8	-21.4	-54.5	-5.2	41.9	-53.9	58.0
	CH_2Cl	-55.4	103.9	-21.7	-54.5	-5.5	41.7	-54.2	57.9
4c-*endo*	R = H	-51.0	97.4	-24.1	-52.7	-8.4	37.8	-51.9	53.3
	CH_3	-56.4	103.5	-23.7	-52.8	-8.0	38.4	-55.5	54.9
	CH_2Cl	-57.8	105.4	-24.1	-53.0	-8.3	38.2	-52.6	53.9
4c-*exo*	R = H	-49.8	97.4	-22.9	-52.7	-7.2	39.6	-53.2	55.5
	CH_3	-54.3	103.1	-21.6	-53.2	-5.7	42.7	-52.4	58.3
	CH_2Cl	-55.6	101.6	-21.9	-56.8	-5.0	42.5	-52.8	58.2

Table 4. Continued

Compounds		ΔH_f	S^b	ΔH	ΔS^b	ΔG	$\Delta H^{\neq}$	$\Delta S^{\neq b}$	$\Delta G^{\neq}$
5-*endo*	R = H	-51.2	93.1	-24.3	-57.0	-7.3	38.6	-54.4	54.8
	CH_3	-52.2	98.5	-19.5	-57.8	-2.3	42.7	-54.4	58.9
	CH_2Cl	-54.1	100.2	-20.4	-58.2	-3.0	40.6	-52.7	56.3
5-*exo*	R = H	-48.6	92.7	-21.7	-57.4	-4.6	40.1	-53.6	56.1
	CH_3	-51.9	98.5	-19.2	-57.8	-2.0	42.1	-53.5	58.1
	CH_2Cl	-53.5	101.1	-19.8	-57.3	-2.7	41.7	-53.7	57.7
5a-*endo*	R = H	-51.3	93.2	-24.4	-56.9	-7.4	36.3	-50.9	51.5
	CH_3	-55.1	99.5	-22.4	-56.8	-5.5	36.8	-49.5	51.6
	CH_2Cl	-57.2	101.5	-23.5	-56.9	-6.5	36.8	-49.4	51.5
5a-*exo*	R = H	-50.9	94.0	-24.0	-56.1	-7.3	38.2	-54.3	54.4
	CH_3	-55.3	99.6	-22.6	-56.7	-5.7	39.2	-53.4	55.1
	CH_2Cl	-56.9	100.9	-23.2	-57.5	-6.1	39.1	-53.9	55.2
5b-*endo*	R = H	-49.1	94.0	-22.2	-56.1	-5.5	38.5	-54.9	54.9
	CH_3	-52.3	99.6	-19.6	-56.7	-2.7	40.6	-54.7	56.9
	CH_2Cl	-53.8	101.3	-20.1	-57.1	-3.1	40.1	-51.7	55.5
5b-*exo*	R = H	-51.4	92.5	-24.5	-57.6	-7.3	38.9	-53.6	54.9
	CH_3	-51.0	97.2	-18.3	-59.1	-0.7	43.6	-56.0	60.3
	CH_2Cl	-53.6	100.0	-19.9	-58.4	-2.5	42.3	-55.0	58.7
5c-*endo*	R = H	-51.3	93.1	-24.4	-57.0	-7.4	37.0	-52.8	52.7
	CH_3	-55.4	99.6	-22.7	-56.7	-5.8	38.2	-51.7	53.6
	CH_2Cl	-57.1	100.9	-23.4	-57.5	-6.3	40.0	-52.5	55.7
5c-*exo*	R = H	-51.6	92.3	-24.7	-57.8	-7.5	36.5	-53.6	52.5
	CH_3	-55.8	99.6	-23.1	-56.7	-6.2	39.4	-54.0	55.5
	CH_2Cl	-57.1	101.5	-23.4	-56.9	-6.4	37.5	-50.6	52.6

$^a\Delta H_f$ = Heat of formation. ΔH, ΔS, and ΔG refer to reaction enthalpy, reaction entropy, and Gibbs free energy of reaction, respectively.$\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta G^{\neq}$ refer to activation enthalpy, activation entropy, and Gibbs free energy of activation, respectively.^{b}cal/(K·mol).

addition reaction of **1** with 1,3-cyclohexadiene at 298 K.

Themodynamic parameters of *endo* and *exo* adduct were compared to see if there are stability differences that could result in *endo*/*exo* selectivity; The difference of Gibbs free energy of reaction, $\Delta\Delta G$ (*endo*-*exo*) and the difference of Gibbs free energy of activation, $\Delta\Delta G^{\neq}$ (*endo*-*exo*) reveal that **3**-diene adducts are favourable for *endo* addition by 1.1-5.0 kcal/mol and 0.0-4.8 kcal/mol, respectively. **1**-Dienophile adducts are favourable for e*ndo* addition by Gibbs free energies of activation of 1.3-3.7 kcal/mol, while Gibbs free energies of reaction do not show notable difference.

Table 5. Comparison of thermodynamic parameters between **1**-diene and **1**-dienophile for the Diels-Alder reaction of **1** with 1,3-cyclohexadiene in kcal/mol

	$\Delta\Delta G^{\neq}$	$\Delta\Delta G$		$\Delta\Delta G^{\neq}$	$\Delta\Delta G$
(**4**-*endo*)-(**5**-*endo*)			(**4**-*exo*)-(**5**-*exo*)		
R = H	0.5	-1.2	R = H	-0.8	-4.0
CH_3	-2.8	-5.8	CH_3	2.8	-1.1
CH_2Cl	-1.0	-5.1	CH_2Cl	2.1	-1.7
(**4a**-*endo*)-(**5a**-*endo*)			(**4a**-*exo*)-(**5a**-*exo*)		
R = H	4.2	-0.9	R = H	1.4	-1.3
CH_3	3.6	-2.5	CH_3	3.4	-0.5
CH_2Cl	3.8	-1.6	CH_2Cl	3.4	-0.9
(**4b**-*endo*)-(**5b**-*endo*)			(**4b**-*exo*)-(**5b**-*exo*)		
R = H	-1.5	-2.8	R = H	2.3	1.6
CH_3	-1.9	-5.3	CH_3	-2.3	-4.5
CH_2Cl	-1.5	-5.2	CH_2Cl	-0.8	-3.0
(**4c**-*endo*)-(**5c**-*endo*)			(**4c**-*exo*)-(**5c**-*exo*)		
R = H	0.6	-1.0	R = H	3.0	0.3
CH_3	1.3	-2.2	CH_3	2.8	0.5
CH_2Cl	-1.8	-2.0	CH_2Cl	5.6	1.4

Themodynamic parameters of **1**-diene and **1**-dienophile were compared to see if there are stability differences that could result in **1**-diene/**1**-dienophile selectivity (Table 5).

The differences of Gibbs free energy of reaction between **1**-diene and **1**-dienophile are favourable for **1**-diene cycloaddition by 0.9-5.8 kcal/mol for *endo* adducts, but do not show consistancy for exo adducts within 0.5-4.5 kcal/mol. And the differences of Gibbs free energy of activation, which range from 0.5 kcal/mol to 5.6 kcal/mol, do not show consistency for both *endo* and *exo* adducts. These results are quite different from the results of the cycloaddition of **1** with cyclopentadiene which show reactions are thermodynamically controlled; the differences of Gibbs free energy of reaction are insignificant compared to those of 10.6-20.3 kcal/mol for cycloaddition with cyclopentadiene. Potential energy diagrams for the cycloadditions of **1** with 1,3-cyclohexadiene are shown in Figure 3.

Table 6 shows thermodynamic parameters for the Cope rearrangement of *endo* adducts of **1** with 1,3-cyclohexadiene.

Gibbs free energies of activation for the Cope rearrange-

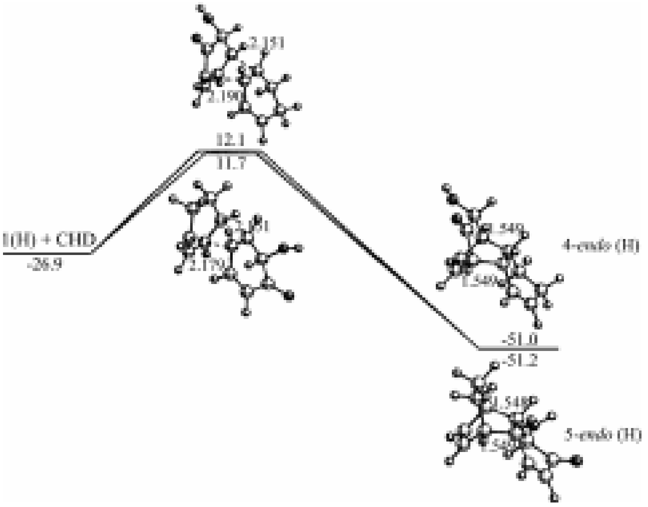


Figure 3. Potential energy (ΔH_f) diagrams for the cycloaddition in compound **1** (R=H) with 1,3-cyclohexadiene (CHD) calculated by the PM3 Hamiltonian. Energies and interatomic distances are given in kcal/mol and angstrom, respectively.

ment of **1**-dienophile *endo* adducts and **1**-diene *endo* adducts are in the range of 55.7 to 63.3 kcal/mol and 60.2 to 64.3, respectively. The values of Gibbs free energy of activation could be compared with those for the retro Diels-Alder reaction, which are in the range of 57.0 to 62.2 kcal/mol for **1**-dienophile adducts and 61.7 to 65.5 kcal/mol for **1**-diene adducts. And Gibbs free energies of reaction for the Cope rearrangement of **1**-dienophile *endo* adducts are small in the range of -0.9 to -5.8 kcal/mol. d_1 and d_2 values at ground state vary from *ca*. 1.55 Å of normal C-C single bond distance to the range of 3.62 Å-4.23 Å, and those values at transition state are in the range of 2.12 Å-2.17 Å.

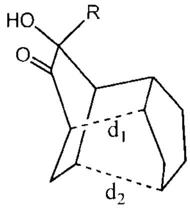
The observations in the cycloadditions of **1** with 1,3-cyclohexadiene, which gave both **1**-diene adduct and **1**-dienophile adduct, might be explained by small differences of Gibbs free energy of reaction of 0.5-5.8 kcal/mol. These insignificant differences of Gibbs free energy of reaction could be compared with those of 10.6-20.3 kcal/mol for cycloaddition of **1** with cyclopentadiene which gave solely **1**-diene adduct.

Endo/*exo* selectivities of **1**-diene adducts are favourable for *endo* adducts in terms of both Gibbs free energy of activation and Gibbs free energy of reaction, while the selectivity of **1**-dienophile adducts are favourable for *endo* adducts in terms of Gibbs free energy of activation. This result coincides with experimental observation that *endo* adducts are formed in the cycloadditions of **1** with 1,3-cyclohexadiene.[8b] Nonetheless, Cope rearrangements of **1**-dienophile *endo* adduct to **1**-diene *endo* adduct do not accord with the experimental observation; Although Cope rearrangements of **1**-dienophile *endo* adduct to **1**-diene *endo* adduct are slightly more favourable than those of **1**-diene *endo* adduct to **1**-dienophile *endo* adduct in terms of Gibbs free energies of reaction, they observed only Cope rearrangement of **1**-diene *endo* adduct to **1**-dienophile *endo* adduct.

Table 6. PM3-calculated thermodynamic parameters for the Cope rearrangement of the adducts of **1** with 1,3-cyclohexadiene in kcal/mol at 298 K

Reactions	ΔH	ΔS^a	ΔG	$\Delta H^{\neq}$	$\Delta S^{\neq a}$	$\Delta G^{\neq}$
5-*endo* to **4**-*endo*						
R = H	0.2	4.6	-1.2	61.6	2.4	60.9
CH_3	-4.6	4.1	-5.8	57.0	1.8	56.5
CH_2Cl	-3.6	5.0	-5.1	57.7	2.4	57.0
5a-*endo* to **4a**-*endo*						
R = H	0.5	4.6	-0.9	61.7	1.8	61.2
CH_3	-1.6	3.2	-2.6	61.7	3.3	60.7
CH_2Cl	-0.5	3.6	-1.6	62.3	0.2	62.2
5b-*endo* to **4b**-*endo*						
R = H	-1.8	3.5	-2.8	58.0	1.9	57.4
CH_3	-4.2	3.8	-5.3	56.3	1.5	55.9
CH_2Cl	-4.0	4.1	-5.2	56.2	1.8	55.7
5c-*endo* to **4c**-*endo*						
R = H	0.3	4.3	-1.0	63.9	2.1	63.3
CH_3	-1.0	3.9	-2.2	62.3	1.5	61.9
CH_2Cl	-0.7	4.5	-2.0	62.5	1.9	61.9

[a]cal/(K·mol)



$TS_{4\text{-}5}$

All above results imply that cycloadditions of **1** with cyclopentadiene are controlled thermodynamically to give only **1**-diene adducts, while its reactions with 1,3-cyclohexadiene do not show **1**-diene/**1**-dienophile selectivity due to similar stabilities of the two adducts. Thermodynamic parameters show that *endo* adducts are more favourably formed in the cycloadditions of **1** with both cyclopentadiene and 1,3-cyclohexadiene, which coincides with experimental observations. Cope rearrangements of *endo* adducts are another avenue to convert between **1**-diene and **1**-dienophile.

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