

# Ab Initio Study of Diels–Alder Reactions of Cyclopentadiene with Ethylene, Isoprene, Cyclopentadiene, Acrylonitrile, and Methyl Vinyl Ketone

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**Abstract:** Ab initio molecular orbital calculations have been used to investigate the structures and energetics for the reactants and transition states of Diels–Alder reactions between cyclopentadiene and ethylene, isoprene, cyclopentadiene, acrylonitrile, and methyl vinyl ketone (MVK). Geometry optimizations were performed with both RHF/3-21G and RHF/6-31G\* calculations, and the energies were computed to the MP3/6-31G\*//6-31G\* level in each case. Calculations of the vibrational frequencies permitted computation of the enthalpies and entropies of activation. Though the structural results are very similar for the two basis sets, the computed activation enthalpies are sensitive to the treatment of the correlation energy. The reactivity order and the enthalpies of activation reach good accord with experimental results at the MP3 level. The stereochemical preferences of the reactions were investigated; for both isoprene and MVK, the *endo-cis* transition states are favored. The observed strong *endo* preference for cyclopentadiene dimerization is also reproduced as well as the lack of stereoselectivity for the addition of acrylonitrile.

In view of its synthetic value and status as a prototypical pericyclic reaction, the Diels–Alder reaction continues to be an important subject for computational studies. Significant progress has been made in understanding the nature of transition states and the levels of ab initio theory that are required to reproduce experimental kinetic data. Bernardi and co-workers through MCSCF calculations have supported a concerted, synchronous pathway for the parent reaction of ethylene plus 1,3-butadiene.<sup>1</sup> A nagging issue was then resolved by Bach et al., who demonstrated that convergence to the experimental activation energy for the parent reaction could be achieved by use of a basis set with polarization functions and extensive treatment of the correlation energy (MP4SDTQ/6-31G\*<sup>2</sup>). In addition, Houk and co-workers have established the ability of ab initio calculations to reproduce observed reactivity orders and stereoselectivities, provided insights into the origins of the variations in reactivity, and illuminated other important issues such as the effects of Lewis acids on transition-state structure and energetics and the preference for *s-cis* forms of conjugated dienophiles in transition states.<sup>3–6</sup> Overall, most ab initio studies have focused on relatively simple reactions of 1,3-butadiene with geometry optimizations using basis sets without polarization functions and with little, if any, treatment of the correlation energy. In this setting, results of ab initio calculations are reported here for the reactions of cyclopentadiene with five dienophiles: ethylene, isoprene, cyclopentadiene, acrylonitrile, and methyl vinyl ketone. Geometry optimizations have been carried out with the 6-31G\* basis set, and the correlation energy has been computed to the MP3 level in each case. Computation of the vibrational frequencies has also permitted calculation of the enthalpies and entropies of activation. The level of ab initio theory that is required for

reproducing experimental data over a wide reactivity range is established, and key points concerning stereoselectivity and dienophile conformation are addressed.

## Computational Methods

The ab initio molecular orbital calculations were executed with the GAUSSIAN 90 program on Silicon Graphics 4D/35 and Cray Y-MP2E computers.<sup>7</sup> Geometries for all structures were fully optimized by means of analytical energy gradients in restricted Hartree–Fock calculations with the split-valence 3-21G and 6-31G\* basis sets; the latter includes a set of d-type polarization functions on all nonhydrogen atoms.<sup>8</sup> Electron correlation energies were computed via second- and third-order Møller–Plesset perturbation theory with the 6-31G\* basis set and frozen core orbitals (MP3/6-31G\*//6-31G\*). This level of theory is comparable to configuration interaction with full double excitations for the noncore MO's.<sup>8</sup> The possible intermediacy of diradicals has not been considered through MCSCF or UHF calculations; the earlier ab initio studies support concerted mechanisms for Diels–Alder reactions, and the accord is good between the present results and experiment on reactivity and stereoselectivity.

Vibrational frequencies were calculated at the 6-31G\* level for all reactants and transition states, which were confirmed to have zero and one imaginary frequency, respectively. The frequencies were scaled by a factor of 0.91<sup>9</sup> and used to compute the zero-point vibrational energies, their thermal corrections, and the vibrational entropies. This enabled calculation of the enthalpies and entropies of activation at 298 K.<sup>8</sup> Scaled vibrational frequencies below 500 cm<sup>-1</sup> were treated as classical rotations in computing the vibrational energy, i.e.,  $E_{\text{vib}} = RT/2$ . The imaginary frequency for transition states was ignored in all calculations.

## Results and Discussion

For organizational purposes, the transition-state structures and stereoselectivity for each reaction will be discussed first one at a time. The relative reactivities of the dienophiles are then addressed in comparison with experimental data.<sup>10–17</sup> The

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Table I. Electronic Energies (hartrees) and Relative Energies (kcal/mol) of Reactants in Diels–Alder Reactions

reactant	3-21G//3-21G		6-31G*//3-21G		6-31G*//6-31G*		MP2/6-31G*//6-31G*		MP3/6-31G*//6-31G*		MP2/6-31G*//6-31G*	
	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$	$E_{\text{rel}}$
ethylene	-77.600 988 2		-78.031 694 2		-78.031 718 1		-78.284 342 0		-78.305 357 5			
<i>s-cis</i> -isoprene	-192.875 715 0	3.12	-193.951 370 3	3.61	-193.951 485 0	3.60	-194.586 255 9	3.57	-194.628 342 5	3.47		
<i>gauche</i> -isoprene	-192.877 561 9	1.96	-193.953 325 6	2.38	-193.953 446 0	2.37	-194.588 349 7	2.26	-194.630 263 1	2.26		
<i>s-trans</i> -isoprene	-192.880 687 4	0.0	-193.957 123 4	0.0	-193.957 228 3	0.0	-194.591 946 2	0.0	-194.633 864 4	0.0		
cyclopentadiene	-191.717 079 7		-192.791 379 8		-192.791 720 9		-193.423 514 3		-193.456 553 4			
acrylonitrile	-168.820 400 4		-169.767 766 6		-169.768 015 0		-170.292 716 1		-170.307 433 3			
<i>s-cis</i> -MVK	-228.522 040 1	0.0	-229.805 429 4	0.0	-229.806 306 2	0.0	-230.483 801 0	0.0	-230.511 740 5	0.0	-230.508 595 0	0.0
<i>s-trans</i> -MVK	-228.518 929 4	1.95	-229.805 005 5	0.27	-229.805 907 0	0.25	-230.483 238 1	0.35	-230.511 702 5	0.02	-230.508 263 7	0.21

Table II. Electronic Energies (hartrees) of Transition Structures in Diels–Alder Reactions with Cyclopentadiene as Diene

dienophile	TS stereochem	3-21G//3-21G		6-31G*//3-21G		6-31G*//6-31G*		MP2/6-31G*//6-31G*		MP3/6-31G*//6-31G*	
		$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$
ethylene		-269.270 158 5		-270.759 745 4		-270.760 230 9		-271.691 019 8		-271.726 315 7	
isoprene	<i>endo-cis</i>	-384.545 661 0		-386.679 234 9		-386.680 167 1		-388.001 134 2		-388.053 742 7	
	<i>exo-cis</i>	-384.544 358 6		-386.677 059 3		-386.677 922 7		-387.998 811 5		-388.051 552 8	
	<i>endo-trans</i>	-384.545 171 5		-386.678 644 9		-386.679 451 0		-388.000 140 6		-388.052 902 8	
	<i>exo-trans</i>	-384.543 054 9		-386.675 970 2		-386.676 774 0		-387.997 535 9		-388.050 289 1	
cyclopentadiene	<i>endo</i>	-383.386 000 2		-385.516 988 5		-385.518 435 2		-386.838 420 9		-386.880 104 6	
	<i>exo</i>	-383.383 544 8		-385.513 128 4		-385.514 362 5		-386.833 252 4		-386.875 785 0	
acrylonitrile	<i>endo</i>	-360.496 106 3		-362.501 622 7		-362.502 558 2		-363.707 611 5		-363.734 464 8	
	<i>exo</i>	-360.496 539 4		-362.501 731 6		-362.502 612 5		-363.707 714 0		-363.734 516 1	
methyl vinyl ketone	<i>endo-cis</i>	-420.199 530 1		-422.540 254 7		-422.542 194 3		-423.903 887 9		-423.942 928 6	
	<i>exo-cis</i>	-420.201 186 1		-422.539 683 4		-422.541 677 4		-423.903 426 4		-423.942 536 7	
	<i>endo-trans</i>	-420.193 376 2		-422.536 287 7		-422.538 047 4		-423.899 440 9		-423.938 998 0	
	<i>exo-trans</i>	-420.189 814 2		-422.532 108 5		-422.534 157 7		-423.895 612 5		-423.935 243 2	

Table III. Electronic Activation Energies (kcal/mol) of Diels–Alder Reactions with Cyclopentadiene as Diene

dienophile	TS stereochem	3-21G//3-21G		6-31G*//3-21G		6-31G*//6-31G*		MP2/6-31G*//6-31G*		MP3/6-31G*//6-31G*	
		$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$	$E_{\text{a}}$	$E_{\text{a}}(\text{rel})$
ethylene		30.06		39.74		39.66		10.57		22.34	
isoprene	<i>endo-cis</i>	32.70	0.0	43.47	0.0	43.16	0.0	8.99	0.0	23.01	0.0
	<i>exo-cis</i>	33.51	0.81	44.83	1.36	44.57	1.41	10.45	1.46	24.39	1.38
	<i>endo-trans</i>	33.00	0.30	43.84	0.37	43.61	0.45	9.61	0.62	23.54	0.53
	<i>exo-trans</i>	34.33	1.63	45.52	2.05	45.29	2.13	11.25	2.26	25.18	2.17
cyclopentadiene	<i>endo</i>	30.22	0.0	41.27	0.0	40.79	0.0	5.40	0.0	20.71	0.0
	<i>exo</i>	31.76	1.54	43.69	2.42	43.35	2.56	8.64	3.24	23.42	2.71
acrylonitrile	<i>endo</i>	25.96	0.27	36.10	0.07	35.88	0.03	5.41	0.07	18.53	0.04
	<i>exo</i>	25.69	0.0	36.03	0.0	35.85	0.0	5.34	0.0	18.49	0.0
methyl vinyl ketone	<i>endo-cis</i>	24.84	1.04	35.49	0.0	35.04	0.0	2.15	0.0	15.92	0.0
	<i>exo-cis</i>	23.80	0.0	35.85	0.36	35.36	0.32	2.44	0.29	16.16	0.24
	<i>endo-trans</i>	28.71	4.91	37.98	2.49	37.64	2.60	4.94	2.79	18.38	2.46
	<i>exo-trans</i>	30.94	7.14	40.60	5.11	40.08	5.04	7.34	5.19	20.74	4.82

computed electronic energies for the reactants and transition states are recorded in Tables I and II. The resultant electronic activation energies are in Table III, Table IV contains the zero-point vibrational energies and other properties computed from the vibrational frequencies, and Table V lists the computed thermodynamic activation parameters.

**Cyclopentadiene + Ethylene.** The computed structures for the reactants and transition state are illustrated in Figures 1 and 2. Molecular structures for ground states are known to be well represented at the 6-31G\* level with average errors in bond lengths of 0.02 Å and in bond angles of ca. 1°. As in previous studies of the reactions of ethylene with 1,3-butadiene and 2-azabuta-diene,<sup>2,6</sup> little difference is found between the transition-state

structures computed at the 3-21G and 6-31G\* levels (Figure 2). For the reaction of ethylene and cyclopentadiene, a synchronous transition-state structure is obtained with forming bond lengths of 2.205 (3-21G) and 2.193 Å (6-31G\*). This pattern is maintained for all the transition states considered here; the largest difference between forming bond lengths from the two basis sets is 0.07 Å. Only the 6-31G\* results are described from here on. Going around the six-membered ring in the transition state (Figure 2), the 6-31G\* bond lengths are 2.193, 1.389, 1.392, 1.389, 2.193, and 1.382 Å, which are strikingly similar to the 6-31G\* bond lengths for the ethylene plus 1,3-butadiene transition state: 2.201, 1.377, 1.393, 1.377, 2.201, and 1.383 Å.<sup>2</sup>

**Cyclopentadiene + Isoprene.** The reaction with isoprene is more complicated in view of the eight possible transition states corresponding to *endo* and *exo* stereochemistry, the dienophile conformation being *s-cis* or *s-trans*, and reaction of either double bond in the dienophile. For isoprene itself, *gauche* and *s-trans* minima were located, and the structure of an *s-cis* transition state with  $C_s$  symmetry was also obtained (Figure 3). The relative energies show little sensitivity to the computational level with the *s-cis* and *gauche* forms 3.47 and 2.26 kcal/mol above the *s-trans* conformer from the MP3 calculations (Table I). The CCCC dihedral angle for the *gauche* structure is computed to be 43.2°.

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**Table IV.** Computed Thermodynamic Properties of Reactants and Transition Structures in Diels–Alder Reactions<sup>a</sup>

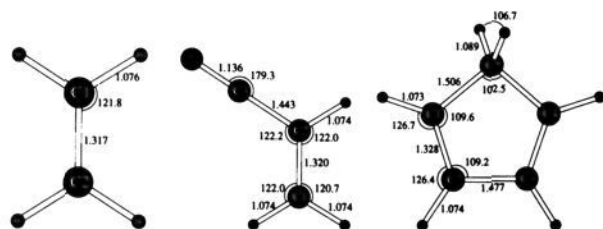
structure	stereochem	$E_{\text{vib}}$ (0)	$\Delta E_{\text{vib}}$ (298)	$S_{\text{vib}}$ (298)	$S_{\text{trans}}$ (298)	$S_{\text{rot}}$ (298)
ethylene		31.28	0.13	0.54	35.93	15.80
ethylene–cyclopentadiene		88.22	2.26	10.15	39.54	26.82
<i>s-trans</i> -isoprene		67.60	2.00	10.57	38.57	25.55
isoprene–cyclopentadiene	<i>endo-cis</i>	124.56	4.14	25.69	40.59	29.29
	<i>exo-cis</i>	124.61	4.14	25.25	40.59	29.39
	<i>endo-trans</i>	124.61	4.14	24.51	40.59	29.31
	<i>exo-trans</i>	124.68	4.14	25.17	40.59	29.39
cyclopentadiene		56.46	0.91	3.80	38.48	24.47
cyclopentadiene–cyclopentadiene	<i>endo</i>	113.09	3.18	17.45	40.55	28.77
	<i>exo</i>	113.09	3.19	17.16	40.55	28.89
acrylonitrile		30.53	0.88	4.19	37.83	23.14
acrylonitrile–cyclopentadiene	<i>endo</i>	87.60	3.02	17.23	40.24	28.51
	<i>exo</i>	87.64	3.02	17.11	40.24	28.54
<i>s-cis</i> -MVK		53.09	1.85	11.50	38.66	25.36
MVK–cyclopentadiene	<i>endo-cis</i>	110.35	3.96	25.89	40.64	29.20
	<i>exo-cis</i>	110.40	3.95	25.26	40.64	29.31
	<i>endo-trans</i>	110.29	3.99	24.25	40.64	29.26
	<i>exo-trans</i>	110.32	3.99	25.36	40.64	29.35

<sup>a</sup> Vibrational frequencies from 6-31G\*/6-31G\* calculations scaled by 0.91. Energies in kcal/mol, entropies in cal/mol·K.

**Table V.** Computed Thermodynamic Quantities for Diels–Alder Reactions with Cyclopentadiene as Diene<sup>a</sup>

dienophile	TS stereochem	$\Delta E_{\text{elec}}^b$ (0)	$\Delta E_{\text{vib}}$ (0)	$\Delta \Delta E_{\text{vib}}$ (298)	$\Delta E_{\text{trans}}$ (298)	$\Delta E_{\text{rot}}$ (298)	$\Delta S_{\text{vib}}$ (298)	$\Delta S_{\text{trans}}$ (298)	$\Delta S_{\text{rot}}$ (298)	$\Delta H^\ddagger$ (298)	$\Delta S^\ddagger$ (298)	$\Delta G^\ddagger$ (298)
ethylene		22.34	0.48	1.22	−0.89	−0.89	5.81	−34.87	−13.45	21.66	−42.51	34.34
isoprene	<i>endo-cis</i>	23.01	0.50	1.23	−0.89	−0.89	11.32	−36.46	−20.73	22.37	−45.87	36.05
	<i>exo-cis</i>	24.39	0.55	1.23	−0.89	−0.89	10.88	−36.46	−20.63	23.80	−46.21	37.57
	<i>endo-trans</i>	23.54	0.55	1.23	−0.89	−0.89	10.14	−36.46	−20.71	22.95	−47.03	36.97
	<i>exo-trans</i>	25.18	0.62	1.23	−0.89	−0.89	10.80	−36.46	−20.63	24.66	−46.29	38.46
cyclopentadiene	<i>endo</i>	20.71	0.17	1.36	−0.89	−0.89	9.85	−36.41	−20.17	19.87	−46.73	33.80
	<i>exo</i>	23.42	0.17	1.37	−0.89	−0.89	9.56	−36.41	−20.05	22.59	−46.90	36.57
acrylonitrile	<i>endo</i>	18.53	0.61	1.23	−0.89	−0.89	9.24	−36.07	−19.10	17.99	−45.93	31.69
	<i>exo</i>	18.49	0.65	1.23	−0.89	−0.89	9.12	−36.07	−19.07	18.00	−46.02	31.72
methyl vinyl ketone	<i>endo-cis</i>	15.92	0.80	1.20	−0.89	−0.89	10.59	−36.50	−20.63	15.54	−46.54	29.42
	<i>exo-cis</i>	16.16	0.85	1.19	−0.89	−0.89	9.96	−36.50	−20.52	15.83	−47.06	29.86
	<i>endo-trans</i>	18.38	0.74	1.23	−0.89	−0.89	8.95	−36.50	−20.57	17.98	−48.12	32.33
	<i>exo-trans</i>	20.74	0.77	1.23	−0.89	−0.89	10.06	−36.50	−20.48	20.37	−46.92	34.36

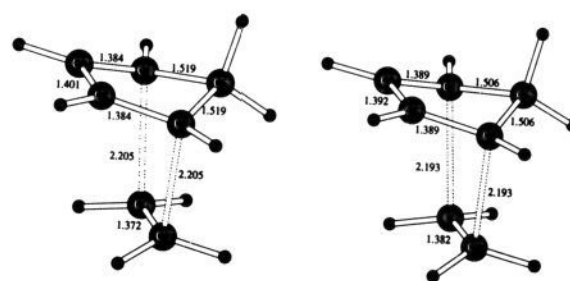
<sup>a</sup> Energies in kcal/mol and entropies in eu (cal/mol·K). Vibrational frequencies from 6-31G\*/6-31G\* optimizations. <sup>b</sup> MP3/6-31G\*\*//6-31G\*.



**Figure 1.** 6-31G\* optimized geometries for ethylene, acrylonitrile, and cyclopentadiene (bond lengths in Å and angles in deg throughout). Atom numbering in the figures reflects computational convenience rather than conventional rules.

These results are consistent with earlier experimental and ab initio studies of isoprene, which indicate the *gauche* form with a dihedral near 40° is less stable than the *s-trans* rotamer by 2–3 kcal/mol.<sup>18</sup> For 1,3-butadiene itself, MP3/6-311++G\*\* calculations give corresponding values of 38° and 2.40 kcal/mol for the *gauche* form and 3.59 kcal/mol for the *s-cis* structure.<sup>19</sup> The similarity of the energetic results for 1,3-butadiene and isoprene is curious since one might expect introduction of the 2-methyl group to destabilize the *s-trans* conformer preferentially on steric grounds, as in the case of acrolein versus methyl vinyl ketone (vide infra).

The four transition states for the reaction of the less substituted double bond in isoprene were located, as illustrated in Figure 4. Experimentally, this is known to be the more reactive double bond.<sup>20</sup> The computed energetic order of the transition states is



**Figure 2.** 3-21G (left) and 6-31G\* (right) optimized geometries for the transition state of the ethylene + cyclopentadiene reaction.

the same at all computational levels, and the relative energies are very similar at all levels above 3-21G//3-21G (Table III). The *endo-cis* transition state is the lowest in energy, as for the reaction of acrolein and 1,3-butadiene.<sup>3</sup> The preference for the *endo-cis* form over the *endo-trans* alternative is 0.5 kcal/mol at the MP3 level for the isoprene reaction, and 0.6 kcal/mol for the acrolein example at the 6-31G\*\*//3-21G level.<sup>3</sup> In both cases, attainment of the *cis*-like structure in the transition state is accompanied by an energetic penalty of ca. 2 kcal/mol owing to the preferences for the *s-trans* forms of the dienophiles. Loncharich et al. have identified the lower LUMO energy for the *s-cis* rotamer of the dienophile as a key component in its greater electrophilicity.<sup>3</sup> It is well known that ease in achieving the *s-cis* form enhances the reactivity of dienes in Diels–Alder reactions.<sup>21</sup> The present results

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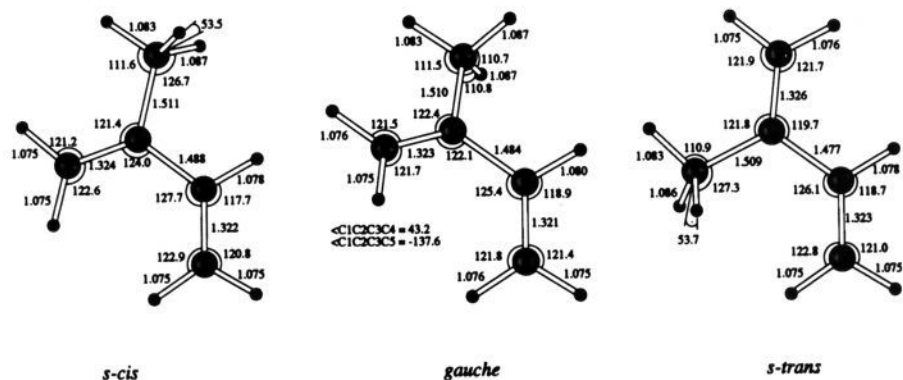


Figure 3. 6-31G\* optimized geometries for the *s-cis*, *gauche*, and *s-trans* conformers of isoprene. The *s-cis* form is a transition state.

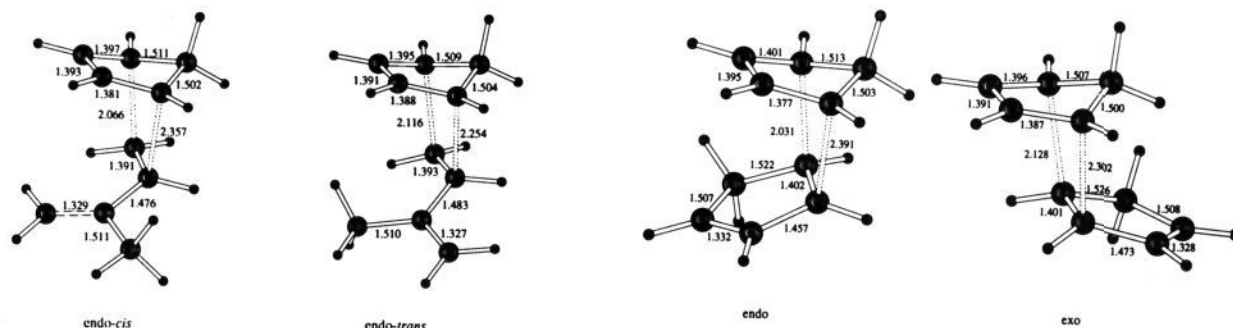


Figure 5. 6-31G\* optimized geometries of the *endo* and *exo* transition states for the Diels–Alder dimerization of cyclopentadiene.

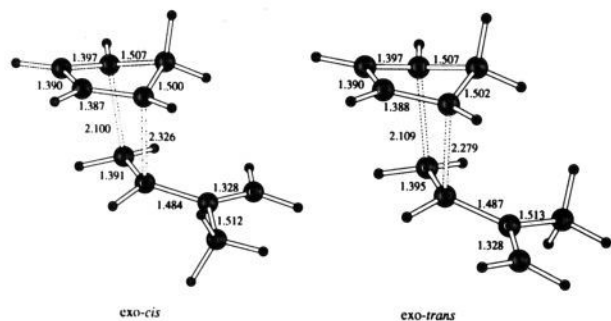


Figure 4. 6-31G\* optimized geometries of the four transition states for the isoprene + cyclopentadiene reaction.

for isoprene and methyl vinyl ketone (vide infra) and those for acrolein<sup>3</sup> establish that ease in achieving the *s-cis* conformation also promotes the reactivity of dienophiles.

For both the *cis* and *trans* transition states, the preference for *endo* approach of isoprene is about 1.5 kcal/mol at the MP3 level (Table III). The qualitative prediction is undoubtedly correct based on numerous precedents,<sup>21</sup> though experimental data for this specific Diels–Alder reaction do not appear to be available. The lower symmetry and conjugation in the dienophile now cause the lengths of the two forming bonds to differ by 0.14–0.29 Å with the largest difference for the preferred *endo-cis* transition state. Though the asynchronism is not large, it is in the direction expected from resonance models that favor retention of allylic character in the dienophile component of the transition state. This pattern is found in all cases for unsymmetrical, conjugated dienophiles here and elsewhere.<sup>3–6</sup>

**Cyclopentadiene Dimerization.** The 6-31G\* transition states for the two possible Diels–Alder dimerizations of cyclopentadiene are illustrated in Figure 5. Experimentally, the thermal reaction is observed to yield only the *endo* product.<sup>17</sup> The present results are consistent with this; the computed difference in electronic energies for the transition states is 2.7 kcal/mol from the MP3 calculations (Table III). The asynchronism is greater for the

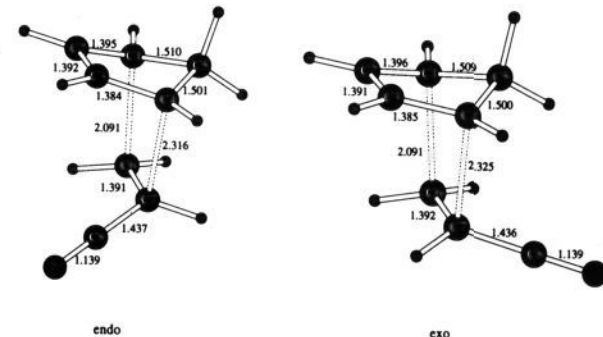


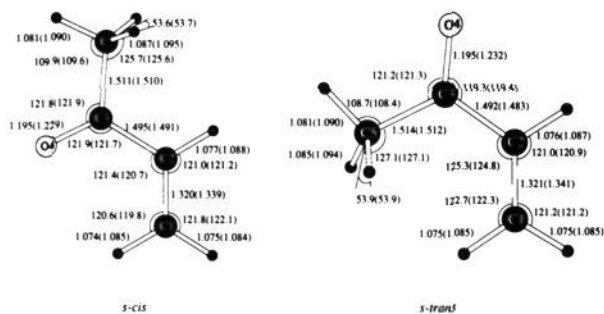
Figure 6. 6-31G\* optimized geometries of the *endo* and *exo* transition states for the acrylonitrile + cyclopentadiene reaction.

lower-energy transition state with a difference of 0.36 Å in the two forming C–C bond lengths. In every case examined here, the forming bond lengths at the transition state are between 2.0 and 2.4 Å in length from both the 3-21G and 6-31G\* optimizations. There is also balance about 2.2 Å; the two bond lengths always total about 4.4 Å; e.g., if one bond length is near 2.1 Å, the other is near 2.3 Å.

**Acrylonitrile + Cyclopentadiene.** The 6-31G\* transition states for the *exo* and *endo* approaches of acrylonitrile are shown in Figure 6. The asynchronism is a little less than with isoprene or cyclopentadiene as dienophiles. The two transition states are essentially isoenergetic at all levels above 3-21G//3-21G (Table III). This is consistent with experimental observations,<sup>12</sup> as discussed further below. The corresponding bond lengths in the two transition states are also the same to within 0.01 Å. Moreover, it is notable that in every case the changes in bond lengths between the reactants and transition states are small. The four preexisting bonds in the forming six-membered ring, naturally, undergo the largest variations; however, these are notably constant at about +0.07 Å and –0.07 Å for the bonds with increasing and decreasing bond order. The other bond lengths are essentially unchanged.

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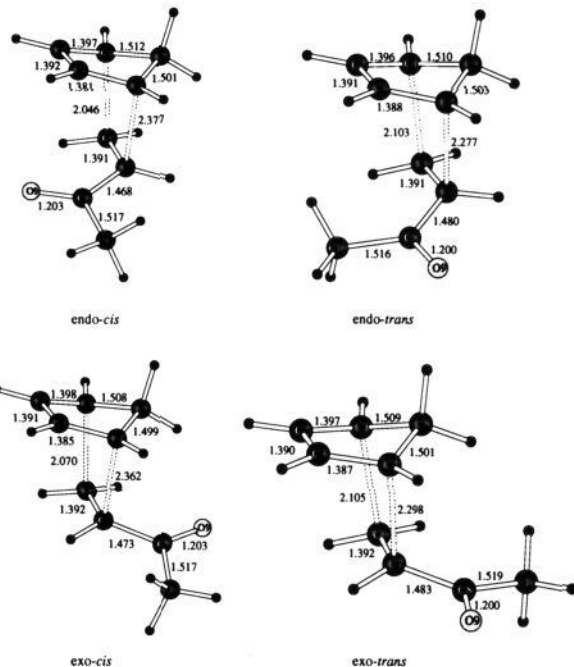


**Figure 7.** 6-31G\* and MP2/6-31G\* (in parentheses) optimized geometries for the *s-cis* and *s-trans* conformers of methyl vinyl ketone.

For example, in the acrylonitrile case, the C–CN, C≡N, and diene C1–C5 and C4–C5 bond lengths change by less than 0.01 Å between reactants (Figure 1) and transition states (Figure 6). Thus, in searching for Diels–Alder transition states, good starting geometries are obtained by adopting standard bond lengths and bond angles for the reactants, making the four changes of  $\pm 0.07$  Å, and setting the two forming bonds at 2.2 Å.

**Methyl Vinyl Ketone + Cyclopentadiene.** As in the case of acrolein and 1,3-butadiene,<sup>3</sup> there are four possible transition states for the reaction of methyl vinyl ketone (MVK) and cyclopentadiene corresponding to MVK being *s-cis* or *s-trans* and the approach being *endo* or *exo*. The structures of the two conformers of MVK were optimized and found to have CCCO dihedral angles of 0° and 180° (Figure 7), which is consistent with previous ab initio and spectroscopic investigations.<sup>22</sup> The energy difference between the conformers is sensitive to the computational level; the *s-trans* conformer is actually higher in energy by a declining amount from 1.95 kcal/mol at the 3-21G/3-21G level to 0.02 kcal/mol from the MP3 calculations (Table I). Surprisingly, this is qualitatively incorrect; an infrared and Raman investigation found the *s-trans* form to have the lower enthalpy by 0.80 kcal/mol in the gas phase, and solution-phase values have been reported in the range 0.34–0.49 kcal/mol.<sup>23</sup> MP2/6-31G\*//MP2/6-31G\* calculations were also performed for the two conformers and still favor the *s-cis* isomer by 0.21 kcal/mol. Based on the difference between the MP2 and MP3 results in Table I, it is likely that the *s-trans* form would have the lower energy by about 0.1 kcal/mol at the MP3/6-31G\*/MP2/6-31G\* level. However, Wiberg and co-workers in a broader study of carbonyl compounds used the MP2/6-31G\* geometries in MP3/6311+G\*\* single point calculations and obtained an energy difference of 0.60 kcal/mol correctly favoring the *s-trans* conformer.<sup>24</sup> Aside from the computational saga, it is important to note that the *cis/trans* energy difference is much smaller for MVK than for acrolein (2.0 kcal/mol)<sup>3</sup> or 1,3-butadiene and isoprene (ca. 3 kcal/mol). This should contribute to enhanced reactivity for MVK as a dienophile, since the penalty is lower for achieving the more electrophilic *s-cis* geometry, and provide a greater *cis* over *trans* preference for the transition states. It also suggests that replacement of the methyl group in MVK by bulkier substituents might further enhance the reactivity by increasing the *s-cis* population.

The structures of the four transition states, optimized at the 6-31G\* level, are illustrated in Figure 8. Although MVK is the strongest electron acceptor among the dienophiles considered here, the asynchronism for the transition states, as reflected in the difference between the lengths of the two forming bonds, is only marginally greater than for isoprene and acrylonitrile and slightly less than for cyclopentadiene as dienophiles (Figures 4–6). The



**Figure 8.** 6-31G\* optimized geometries of the four transition states for the methyl vinyl ketone + cyclopentadiene reaction.

*endo-cis* transition state is again found to be the lowest in energy; however, the ordering of the other transition states is not the same as for isoprene (Table III). As expected, the *trans* transition states are less competitive owing to the smaller *cis/trans* energy difference. The *endo-trans* transition state is now 2.46 kcal/mol higher in energy than the *endo-cis* from the MP3 calculations, which can be compared to the 0.53-kcal/mol difference for the isoprene reaction. Even if one corrects for the ca. 0.6-kcal/mol underestimate of the *s-cis/s-trans* energy difference for MVK, it appears that the intrinsic energetic benefit for reaction of the *cis* forms of the dienophiles is 2–3 kcal/mol over the *trans*. This is also consistent with the earlier results for the reaction of acrolein and 1,3-butadiene; the *endo-cis* over *endo-trans* preference is 0.6 kcal/mol, which overcomes an *s-trans* over *s-cis* preference for acrolein of 1.8 kcal/mol at the 6-31G\*/3-21G level.<sup>3</sup> Furthermore, in that study, it was demonstrated that the *s-trans/s-cis* energy difference was the same for acrolein in the transition-state geometries as in the ground states.<sup>3</sup> For MVK, the *exo-cis* transition state is the next lowest in energy, only 0.24 kcal/mol above the *endo-cis* alternative. The *endo* stereoselectivity is qualitatively correct, as discussed more below.

Some computational effort has also been directed at the products of the reactions, and, in the cases of the reaction of cyclopentadiene with MVK and cyclopentadiene dimerization, complete minimum energy reaction paths have been traced at the 3-21G level.<sup>25,26</sup> As illustrated in Figure 9, 3-21G//3-21G structures have been obtained for the *endo* and *exo* products of the reaction between MVK and cyclopentadiene. Two different rotamers were optimized for both possibilities by starting from the four transition-state structures. The C=O bond eclipses one of the adjacent C–C bonds of the norbornene in each case. The computed energies from 6-31G\*/3-21G calculations are much closer than for the transition states; the relative energies in kcal/mol are 0.0 for *exo-cis*, 0.09 for *exo-trans*, 0.68 for *endo-cis*, and 0.75 for *endo-trans*. There should be an additional rotational isomer in both cases with the C=O bond eclipsing the adjacent C–H bond. Experimentally, data are available for equilibration of the corresponding carbomethoxy derivatives; the *exo* to *endo* free-energy difference is 0.0 kcal/mol for methyl bicyclo[2.2.1]-

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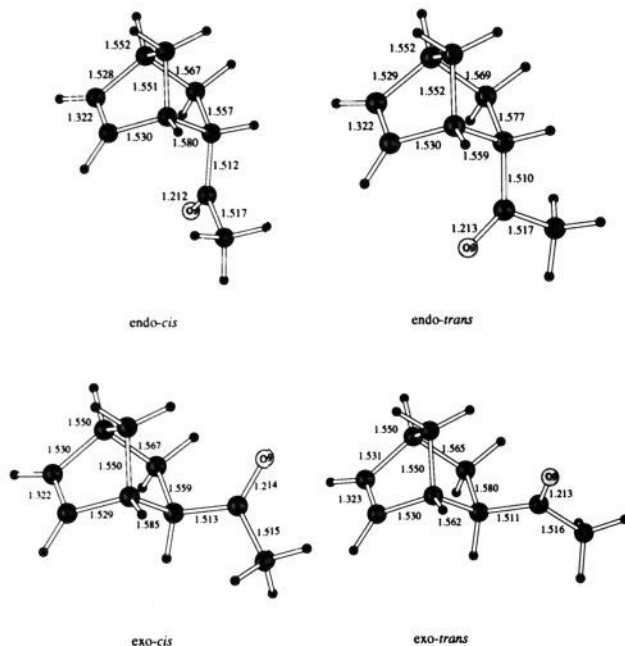


Figure 9. 3-21G optimized geometries of *endo* (top) and *exo* (bottom) products from the methyl vinyl ketone + cyclopentadiene reaction.

hept-5-ene-2-carboxylate and rises to 0.5 kcal/mol for the norbornane analogues.<sup>27</sup>

**Relative Reactivity and Kinetic Parameters.** In order to facilitate comparisons with experimental kinetic data, the enthalpies and entropies of activation were computed for the reactions. The enthalpy change at 298 K is given by eq 1 where

$$\Delta H^{298} = \Delta E_{\text{elec}}^0 + \Delta E_{\text{vib}}^0 + \Delta(\Delta E_{\text{vib}})^{298} + \Delta E_{\text{trans}}^{298} + \Delta E_{\text{rot}}^{298} + P\Delta V \quad (1)$$

the six terms on the right are the changes in electronic energy, the zero-point vibrational energy, the thermal correction to the vibrational energy, the classical translational energy, the classical rotational energy, and the work term which equals  $-RT$  for the present reactions.<sup>8</sup> The entropy change consists of vibrational, translational, and rotational components that are computed from standard statistical thermodynamic formulas.<sup>8</sup> The key results are summarized in Tables IV and V. Table IV contains the zero-point vibrational energies, their thermal corrections, and the entropy terms for the reactants and transition states from the 6-31G\*\*/6-31G\* calculations. These are combined with the electronic energy changes from the MP3 calculations to yield the computed enthalpies, entropies, and free energies of activation in Table V. Corresponding experimental results could be found or derived from rate data and the Eyring equation except for the isoprene reaction (Table VI). The listed experimental activation parameters correspond to a 1 atm standard state for appropriate comparison with the computed results. For conversion to concentration units with a 1 mol/L standard state,  $RT$  needs to be added to  $\Delta H^\ddagger$  and  $R \ln RT/P$  to  $\Delta S^\ddagger$ , i.e., 0.6 kcal/mol and 6.3 cal/mol K at 293 K and 1 atm.

As shown in Table III, the computed electronic activation energies are very sensitive to the computational level. This has been well documented for the parent Diels–Alder reaction<sup>2</sup> and is reasonable in view of the importance of correlation energy changes for bond-making and/or bond-breaking processes. The activation energies are too high by 10–20 kcal/mol from the 3-21G and 6-31G\* calculations. Inclusion of only the MP2 contributions overestimates the correlation energy changes,<sup>2,6</sup>

Table VI. Experimental Rates and Activation Parameters for Diels–Alder Reactions with Cyclopentadiene as Diene<sup>a</sup>

dienophile	medium	$k^{293} \times 10^6$	$\Delta H^\ddagger$	$\Delta S^\ddagger$	ref	
ethylene	gas	0.000083	22.5	–32.1	10	
	cyclopentadiene	gas	0.45	15.5	–38.9	11
		CCl <sub>4</sub>	0.89	15.9	–36.1	11
acrylonitrile	dioxane	0.36	16.7	–35.3	12	
	dioxane	0.94	16.1	–35.3	13	
	isooctane	8.1	14.0	(–38.3) <sup>b</sup>	14	
	benzene	7.1	12.0	–45.3	15	
MVK	dioxane	10.4	13.9	(–38.3) <sup>b</sup>	13	
	isooctane	59.4	12.8	(–38.3) <sup>b</sup>	14	
	methanol	755.0	11.4	(–38.3) <sup>b</sup>	14	
acrolein	gas	7.1	14.0	–38.5	16	
	benzene	126.0	10.9	–43.4	15	

<sup>a</sup> Rate constants  $k$  in L/mol-sec.  $\Delta H^\ddagger$  in kcal/mol,  $\Delta S^\ddagger$  in cal/mol-K; 1 atm standard state used for  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ . <sup>b</sup> Assumed.

while proceeding to the MP3 level brings the activation energies within a few kilocalories/mole of experimental values.<sup>2</sup> For the reactions of cyclopentadiene with ethylene, cyclopentadiene, acrylonitrile, and MVK, the computed activation enthalpies from the MP3 calculations are 21.7, 19.9, 18.0, and 15.5 kcal/mol (Table V), which compare well with the experimental values of 22.5, 15.5, 14.0, and 12.8 for the gas phase or isooctane solution (Table VI). Importantly, the order of reactivity of the dienophiles is correct, while it is less well represented at the lower computational levels. For example, at the MP2 level including the zero-point corrections, the computed activation energy for acrylonitrile is 0.4 kcal/mol greater than for cyclopentadiene as dienophile, and the significantly lower activation energy for cyclopentadiene than ethylene as dienophile is not obtained from the 6-31G\* and 3-21G calculations.

In the calculations on the reaction of ethylene and 1,3-butadiene,<sup>2</sup> the computed electronic activation energy was lowered from 26.86 kcal/mol at the MP3/6-31G\*\*//6-31G\* level to 21.86 kcal/mol at the MP4SDTQ/6-31G\*\*//6-31G\* level. Thus, some lowering of the present MP3 values for the activation enthalpies is anticipated by extending the correlation treatment. This would likely further enhance the accord with the experimental values for the present cases except for the ethylene plus cyclopentadiene reaction. It should be realized that there is some uncertainty in the experimental activation parameters, as indicated in Table VI. Some of the discrepancies, e.g., for acrylonitrile and acrolein, are beyond the range that can reasonably be attributed to solvent effects.<sup>14,21</sup>

Another point from Table V that should be noted is the lower reactivity predicted for isoprene than ethylene. This seems surprising since conjugation should narrow the HOMO/LUMO gap and make frontier orbital interactions more favorable. The predicted activation enthalpy for cyclopentadiene dimerization is lower than for the reaction with ethylene. As discussed above, cyclopentadiene as dienophile undoubtedly benefits from the enforced *s-cis* geometry. For isoprene, the benefit of attaining the *s-cis* form for the transition-state stabilization is largely cancelled by the intrinsic *s-cis/s-trans* energy difference. Thus, the lower reactivity of isoprene than cyclopentadiene is reasonable, though an experimental test for ethylene versus isoprene is desirable. Factors favoring ethylene would be less delocalization for its  $\pi$ -orbitals and minimal steric demands.

The experimental entropies of activation range from –32 to –45 cal/mol-K (Table VI), while the computed results are all near –46 cal/mol-K except for the value of –42.5 in the case of ethylene with cyclopentadiene. Computations at this level reproduce experimental entropies for ground-state molecules very well.<sup>8</sup> For example, the computed entropies at 298 K for ethylene and isoprene are 52.25 and 74.68 cal/mol-K (Table IV), and the

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experimental values are 52.54 and 75.44 cal/mol·K.<sup>28</sup> It may also be noted that the experimental entropy change for the overall reaction of ethylene + 1,3-butadiene → cyclohexene is -44.9 cal/mol·K, which is similar to the present computed activation entropies. Conversion of the experimental rate data to obtain the activation parameters in Table VI for the reactions of ethylene and cyclopentadiene as dienophiles did require extrapolation from higher temperatures to 293 K. However, this does not appear to be a major source of error. For example, when the 6-31G\* results are used to compute the entropy of activation at 400 K for the cyclopentadiene dimerization, which is in the temperature range of the rate measurements, -46.6 cal/mol·K is obtained. Thus, there is essentially no change from the computed value in Table V (-46.7 cal/mol·K), and the experimental value changes only from -38.9 at 293 K to -40.1 cal/mol·K at 400 K. For the reaction of ethylene and cyclopentadiene, the computed and experimental entropies of activation at 550 K are -42.3 and -34.6 cal/mol·K, again similar to the room temperature values in Tables V and VI.

The discrepancy between the experimental and computed activation entropies might suggest that the computed transition-state structures are too tight or product-like. This may result from a need to progress to larger basis sets with incorporation of the correlation energy in the geometry optimizations or from the single-configuration wave functions that have been used here, and will be an interesting point to pursue in future studies. However, there is fundamental uncertainty in comparing activation entropies for bimolecular reactions in the gas phase and solution.<sup>29-31</sup> For a 1 M solution, there is restricted translational motion owing to the presence of the solvent molecules compared to the 1 M gas. One way of estimating the effect is to consider that the "free volume" in a liquid is about 1% of the molar volume.<sup>29</sup> This leads to a roughly  $R \ln 100 = 9$  cal/mol·K more negative activation entropy for a bimolecular reaction in the gas phase than in solution owing to the -1 change in the number of molecules between the reactants and transition state. Another approach is to consider a cycle involving Trouton's rule ( $\Delta S_{\text{vap}} \approx 21$  cal/mol·K) and dilution of a pure liquid to a 1 M solution; this yields corrections of 10-15 cal/mol·deg for the entropy change.<sup>31</sup> Such corrections could easily account for the discrepancy between the present computed, gas-phase activation entropies, and the mostly solution-phase experimental data. However, this difference is not clearly apparent in comparing the limited experimental data for reactions that have been studied both in the gas phase and in solution (Table VI). A definite decision on the magnitude of the corrections cannot be made in the absence of uniformly high-accuracy determinations of activation entropies for several Diels-Alder reactions in the gas phase and different solvents.

Finally, the stereoselectivities can be considered more appropriately than before by comparing the differences in free energies of activation in Tables V and VII. For cyclopentadiene dimerization, the computed favoring of *endo* addition by 2.8 kcal/mol is consistent with the essentially exclusive observation of *endo* dimer. For acrylonitrile with cyclopentadiene, both theory (0.03 kcal/mol) and experiment in hexane (0.06 kcal/mol) find a slight preference for *endo* addition. For MVK with cyclopentadiene, the *endo-cis* transition state is computed to be 0.44 kcal/mol lower in free energy than the *exo-cis* one; the experimental *endo* preference appears to be somewhat greater, though it is medium dependent and is probably less in the gas phase than the 0.80 kcal/mol in excess cyclopentadiene. As a reviewer noted, the

Table VII. Experimental Endo/Exo Product Ratios for Diels-Alder Reactions with Cyclopentadiene as Diene

dienophile	medium	T, K	endo/ exo	$\Delta\Delta G^\ddagger$ , kcal/mol	ref
cyclopentadiene	cyclopentene	427	>49	>3.30	17
acrylonitrile	hexane	313	1.11	0.06	12
	dioxane	313	1.49	0.25	12
	ethanol	313	1.87	0.39	12
MVK	cyclopentadiene	298	3.85	0.80	14
	ethanol	298	8.5	1.27	14
	water	298	25.0	1.91	14

*endo/exo* selectivity for MVK is computed to be greater for the *trans* transition states than the *cis* ones in Table V. It is then tempting to consider that the enhanced *endo* selectivity in the hydrogen-bonding solvents might arise from a switch to the more polar *trans* forms, which are also less shielded for hydrogen bonding at the carbonyl oxygen.<sup>32</sup> However, this scenario would require that both *trans* transition states become lower in free energy than the *endo-cis* form. It is unlikely that differential solvation could fully overcome the gas-phase preferences of 3-5 kcal/mol for the *endo-cis* transition state (Table V). Reaction field calculations have been performed on the four analogous transition states for the reaction of cyclopentadiene and methyl acrylate.<sup>32</sup> The computed differences in free energies of solvation are 0.4-1.2 kcal/mol in a medium with a dielectric constant of 78.<sup>32</sup>

The present gas-phase results for acrylonitrile and MVK indicate that the intrinsic electronic driving force for *endo* selectivity is not strong, irrespective of its origin from secondary-orbital interactions or favorable van der Waals' interactions. The much greater preference for *endo* addition in cyclopentadiene dimerization can be attributed to a steric clash between the methylene group hydrogens in the *exo* transition state (Figure 5). This is reflected in the lengthening of the adjacent forming CC bond from 2.031 Å for the *endo* transition state to 2.128 Å in the *exo* one.

## Conclusion

The present results demonstrate the ability of ab initio calculations at the MP3/6-31G\*//6-31G\* level to accurately predict relative reactivities and stereoselectivities for typical Diels-Alder reactions over a wide reactivity range, and to provide quantitatively reasonable estimates of the enthalpies and entropies of activation. This appears to be the minimal computational level for generally satisfactory quantitative results. However, the constant discrepancy of ca. 8 cal/mol·K between the computed and observed entropies of activation raises the possibility that the transition-state structures at this level are too product-like, though new experimental measurements for gas-phase versus solution entropies of activation are desirable to confirm an expected translational entropy correction. The results for isoprene and methyl vinyl ketone as dienophiles in conjunction with earlier results for acrolein establish the greater intrinsic reactivity of the *s-cis* form of conjugated dienophiles, which may provide synthetic opportunities.

**Acknowledgment.** Gratitude is expressed to the National Science Foundation for support of the work at Yale and to Professors K. N. Houk, K. B. Wiberg, and C. F. Wilcox for helpful discussions.

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