A Molecular Orbital Study of Diastereofacial Selectivity in the Diels-Alder Reaction

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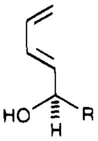
The AM1 molecular orbital method is used to predict the face selectivity for six different Diels-Alder reactions. The predictions are based upon fully optimized and fully characterized transition states for each possible conformation of the 12 different transition states. Agreement with the available experimental literature is quite satisfactory. The contributions to the various transition-state energies are discussed. A combination of steric and electronic effects appears to control the selectivities.

Introduction

The recent interest in the face selectivity of the Diels-Alder reaction has focused on three sets of experimental results for acyclic **1**,[1] semicyclic **2**,[2] and cyclopentadienes **3**.[3] In addition, the extensive studies in the isodicyclopentadiene series **4**[4] raise interpretative questions that need to be addressed by modern theoretical methods. The variation in face selectivity with the allylic substituent on diene[2,3] and the nature of the dienophilic partner[1,4] require elucidation.



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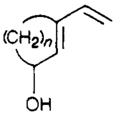

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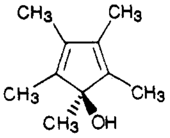

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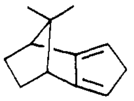

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Three distinct methods have been used to interpret the observed face selectivities. Hehre has computed the favored electrostatic interactions of the reactants, assuming these to be indicative of the relative energetics of the transition states.[5] A second way to rationalize selectivity uses FMO arguments. An empirical rule suggested that relative face selectivities for the Diels-Alder reactions of chirally functionalized dienes and dienophiles should be of opposite sign. This rule was based on the idea that the stereogenic center had different conformations best suited to interact with the HOMO or the LUMO of the substituted reactant.[6,7] In the isodicyclopentadiene series, the idea of orbital tilting or pyramidalization of the diene in the ground state led naturally into stabilizing one of two possible transition states because of better HOMO-LUMO overlap.[4] There have been no reports of applications of the orbital tilting approach to noncyclic systems.[8] A third approach is to directly calculate the transition states (TS) for the cycloaddition to both possible faces of the π system perturbed by the adjacent stereogenic center.

There have been many calculations of the Diels-Alder transition state (discussed in more detail below); however, the results described in this paper are the first to evaluate the effect of a noncyclic stereogenic center on face selectivity in the Diels-Alder reaction. The most closely related calculations are those of Houk and Liotta. Houk studied the transition states for the 1,3 dipolar cycloaddition of fulminic acid to an acyclic ethylene with an adjacent chiral center using a blend of ab initio and MM2 calculations. He noted that the preferred conformation of the stereogenic center in the transition state had the oxygen function "inside", i.e., directed toward the group attached to the distal sp^2 carbon, or syncoplanar (see Figure 1B). Face selectivity was controlled by minimization of steric hindrance to approach of fulminic acid by the remaining groups of the chiral carbon.[9] Houk has also applied this approach to the isodicyclopentadiene problem.[10] Liotta applied MINDO/3 calculations of transition states to Diels-Alder reactions involving dienophiles with stereogenic centers within cyclic systems. The energies of single TS's of two diastereomeric dienophiles were compared to predict their relative reactivities.[11]

Modelling of the transition state for the Diels-Alder reaction has been one of the more controversial subjects in the field of theoretical organic chemistry. There have been many reported calculations on the archetypical reaction between ethylene and butadiene.[12] Several have predicted a symmetrical, while others an unsymmetrical, TS. The method that we have used for this study, AM1, has been reported to predict a symmetrical TS when RHF calculations are performed, but an extremely unsymmetrical TS (and even a possible biradical intermediate) when the same methodology is used in a specific 3 × 3 configuration interaction (CI) procedure. In this procedure, the SCF calculation is done on the open-shell biradical state. the two other states are constructed by either demoting an electron from the higher singly occupied orbital or

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[1] (a) Tripathy, R.; Franck, R. W.; Onan, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 3257 and references therein. (b) An additional example that appeared too late to be referenced in (a); Fleming, I. *Pure Appl. Chem.* **1988**, *60*, 71.

[2] (a) Fisher, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4625. (b) Tripathy, R.; Franck, R. W.; Onan, K. D., submitted for publication.

[3] Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1988**, *110*, 4074.

[4] Paquette, L. A.; Gugelchuk, M. *J. Org. Chem.* **1988**, *53*, 1835 and references therein, the most recent paper in an extensive series.

[5] Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 663.

[6] Franck, R. W.; Argade, S.; Subramaniam, C. S.; Frechet, D. M.; *Tetrahedron Lett.* **1985**, *26*, 3187-3190.

[7] (a) Kozikowski, A. P.; Jung, S. H.; Springer, J. P. *Chem. Commun.* **1988**, 167. (b) It is noteworthy that Fleming in ref 1b also interprets his result using argumentation implicit in ref 6 and 7a.

[8] N. Kaila, unpublished AM1 calculations, Hunter College 1988.

[9] Houk, K. N.; Duh, H.-y.; Wu, Y.-D.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754 and references therein.

[10] (a) Brown, F. K.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 1971. (b) Brown, F. K.; Houk, K. N.; Burnell, D. J.; Valenta, Z. *J. Org. Chem.* **1987**, *52*, 3050.

[11] Fraser-Reid, B.; Underwood, R.; Osterhout, M.; Grossman, J. A.; Liotta, D. *J. Org. Chem.* **1986**, *51*, 2152.

[12] (a) Dewar, M. J. S.; Olivella, S.; Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 5650. (b) Ortega, M.; Oliva, A.; Lluch, J. M.; Bertran, J. *Chem. Phys Lett.* **1983**, *102*, 317. (c) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1985**, *25*, 4609. (d) Houk, K. N.; Lin, Y.-T.; Brown, F. K. *J. Am. Chem. Soc.* **1986**, *108*, 554. (e) Bernardi, F.; Bottoni, A.; Robb, M. A.; Field, M. J.; Hillier, I. H.; Guest, M. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1051.

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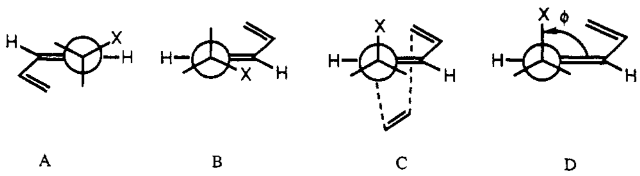

Figure 1. Conformations of transition states. In A, B, and C, X is in the *anticoplanar*, *syncoplanar*, and *away* positions respectively. The dihedral angle, ϕ, is defined as in D, where the positive direction is indicated by the arrowhead. ϕ is positive on the *si* face and negative on the *re* face regardless of the direction of the approaching dienophile.

promoting one from the lower singly occupied orbital. In our hands, we have found that 3×3 CI of this type works well for bond dissociation reactions[13] since the TS's for such reactions are usually fairly similar to the radical pairs. This procedure converges to the sum of the energies of the two independent radicals (as calculated using the half electron method[14]) at large separation of the radicals. On the other hand, we have found that 2×2 CI (using the RHF, doubly occupied ground state to perform the SCF calculation) is a better procedure for molecular rearrangements (such as the Cope rearrangement[15]) where there is considerable bond formation at both the bond-making and bond-breaking positions. In the report[16] of the 3×3 CI AM1 calculation of the Diels–Alder TS (the higher or first TS in this report), one can see that the biradical state has the least weight of the three states considered in the CI, yet it is the state for which the SCF calculation was performed. The other two states, the completely paired ground state and the paired doubly excited state, which have weighting coefficients of −0.933 and 0.356, respectively, after CI, are likely to be inadequately described by simply demoting or promoting an electron using imperfect SCF orbitals (for comparison, the weighting coefficients for the biradical state is 0.055). We therefore believe that this calculation could lead to a misleading model of the TS.

Bernardi has recently reported that a fully optimized MCSCF ab initio treatment of the reaction between butadiene and ethylene has two competing reaction channels: one synchronous and another asynchronous.[17] This is in accord with a suggestion by Dewar that both reaction paths might (in general) exist.

We are currently repeating the optimization of the transition state for butadiene and ethylene using 2×2 CI as described above. The preliminary results indicate that the TS will be much closer to the symmetric structure than that predicted by the earlier report. We, therefore, consider the RHF TS to be a reasonable model for the calculation of the TS's for the reactions of the chiral molecules that we have considered.

In this paper, we report calculations for the Diels–Alder cycloadditions of ethylene, acrolein, and methyl propiolate with pentadienes substituted so that C-5 is stereogenic, $CH(OR_1)(R_2)$ (reactions I–IV, VIII, and IX, Table I).

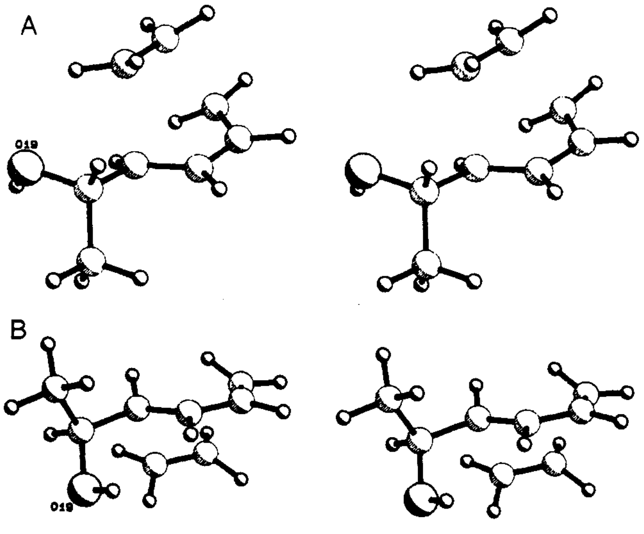

Figure 2. Transition states for reaction I (A *like*, B *unlike*).

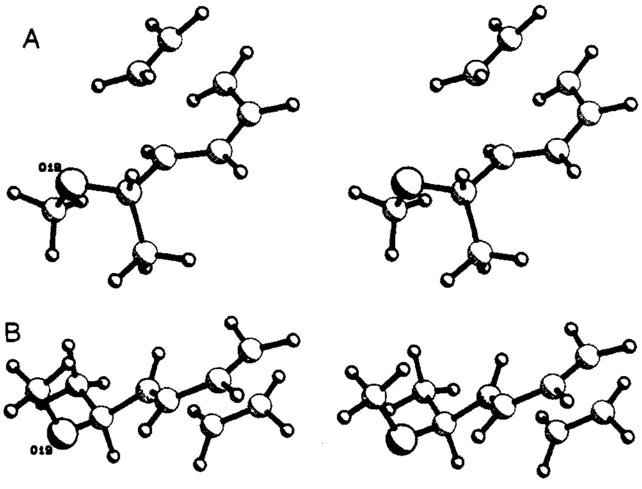

Figure 3. Transition states for reaction II (A *like*, B *unlike*).

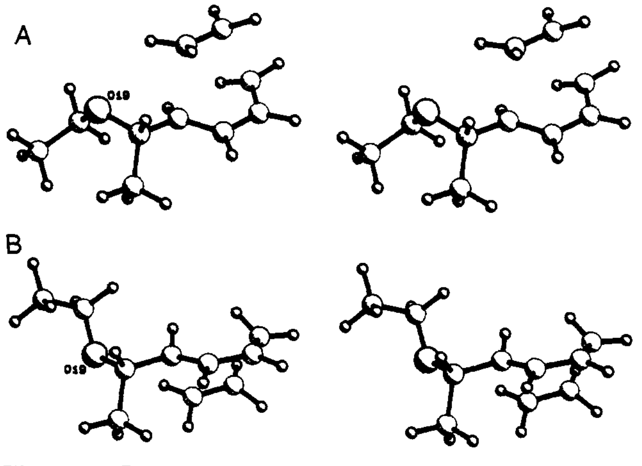

Figure 4. Transition states for reaction III (A *like*, B *unlike*).

Methods

The RHF, AM1 method was used throughout. In each of the cases considered, all six possible transition states[18] (3 rotamers, each, for both the like, attack from *si* face for

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[13] (a) Dannenberg, J. J.; Rayez, J. C.; Rayez-Meaume, M. T.; Halvick, P. *THEOCHEM* **1985**, *128*, 342. (b) Dannenberg, J. J.; Tanaka, K *J. Am. Chem. Soc.* **1985**, *107*, 671. (c) Huang, X. L.; Dannenberg, J. J., unpublished results.

[14] Dewar, M. J. S.; Hashwall, J. A.; Vernier, C. G. *J. Am. Chem. Soc.* **1968**, *90*, 1953.

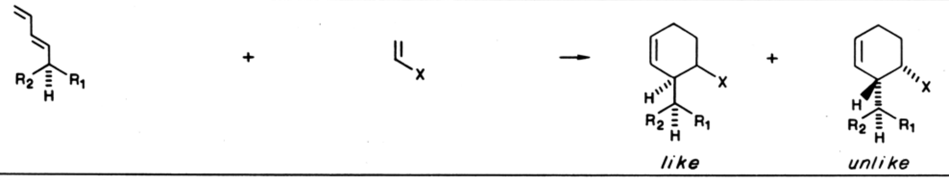
[15] Miller, L. S.; Grohmann, K.; Dannenberg, J. J. *J. Am. Chem. Soc.* **1983**, *105*, 6862.

[16] Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1986**, *108*, 5771.

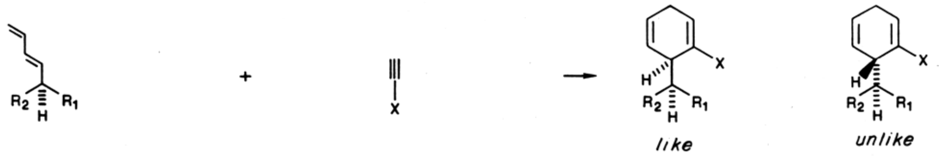
[17] Bernardi, F.; Bottoni, A.; Field, M. J.; Guest, M. F.; Hillier, I. H.; Robb, M. A.; Venturini, A. *J. Am. Chem. Soc.* **1988**, *110*, 3050.

[18] In this paper, we use the term "transition state" to correspond to any saddle point connecting the reactants and products. Strictly speaking, "transition state" should only apply to the lowest possible saddle point.

Table I



				like		unlike	reaction
5 ($R_1 = CH_3$; $R_2 = OH$)	+	12 (X = H)	→	15	+	16	reaction I
6 ($R_1 = CH_3$; $R_2 = OCH_3$)	+	12	→	17	+	18	reaction II
7 ($R_1 = CH_3$; $R_2 = OC_2H_5$)	+	12	→	19	+	20	reaction III
8 ($R_1 = C_2H_5$; $R_2 = OCH_3$)	+	12	→	21	+	22	reaction IV
9 ($R_1 = CH_3$; $R_2 = H$)	+	12	→	23			reaction V
10 ($R_1 = H$; $R_2 = OH$)	+	12	→	24			reaction VI
11 ($R_1 = H$; $R_2 = OCH_3$)	+	12	→	25			reaction VII
6	+	13 (X = CHO)	→	26	+	27	reaction VIII



				like		unlike	reaction
6	+	14 ($X = CO_2CH_3$)	→	28	+	29	reaction IX

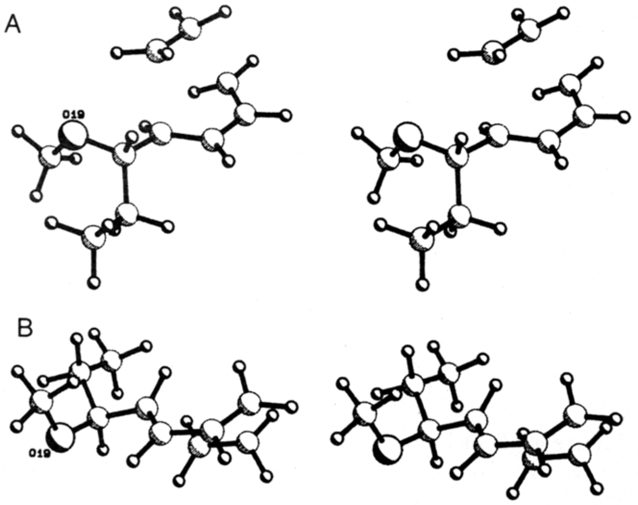


Figure 5. Transition states for reaction IV (A *like*, B *unlike*).

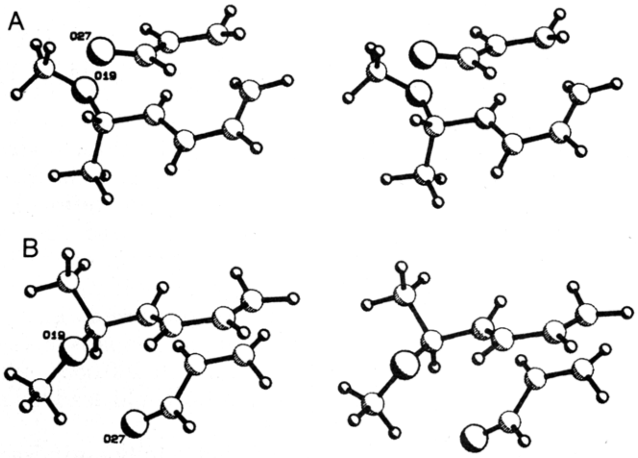


Figure 6. Transition states for reaction VIII (A *like*, B *unlike*).

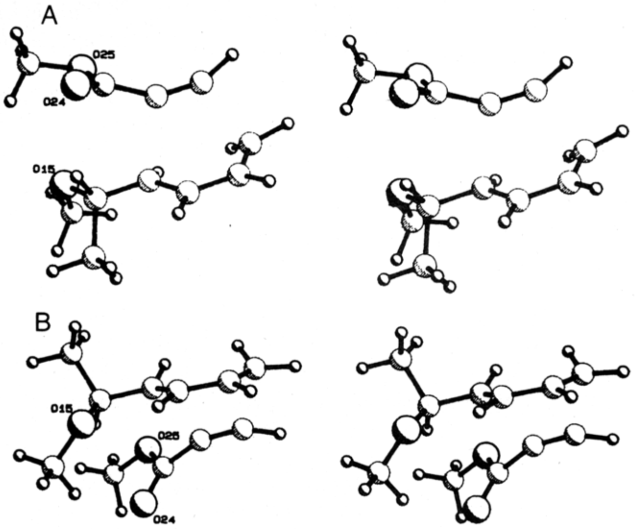


Figure 7. Transition states for reaction IX (A *like*, B *unlike*).

S chiral group, and unlike, attack from *re* face for *S* chiral group)[19] were individually optimized with respect to all internal degrees of freedom. All possible rotamers about the relevant bonds in the substituent groups on the chiral center were also considered. The transition states were fully characterized by calculating the force constants, only one of which was negative in each case studied. This required a significant number of calculations as convergence to points with more than one negative force constant was quite common. In general the second negative force constant would be for a torsional mode about a bond either to or within one of the substituents on the chiral center. Calculations were also performed for the reactants and products. A total of 47 individual transition states were characterized, each involving up to 84 independent internal degrees of freedom.

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[19] We use the Seebach–Prelog convention (Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654–660) describing the relative topicities of the approach or addition to the face of an enantiomer, e.g., addition to the *si* face of the double bond with an adjacent *R* allylic center is *unlike*.

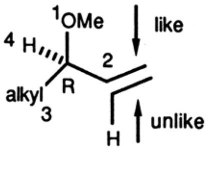

Table II. Geometric and Energetic Parameters for the Best (*like* and *unlike*) Transition States for Reactions I-IX[a]

reaction	product	ϕ	$\Delta H_{act.}$	ΔH_f	bond length long	bond length short
I	**15**	167.4	25.50	-14.11	2.166	2.072
I	**16**	-38.1	25.91	-14.11	2.161	2.078
II	**17**	168.1	25.69	-7.69	2.154	2.071
II	**18**	28.0	26.30	-7.69	2.174	2.067
III	**19**	170.7	26.02	-13.23	2.163	2.072
III	**20**	175.7	26.22	-13.23	2.169	2.061
IV	**21**	168.7	25.66	-13.62	2.166	2.067
IV	**22**	22.4	26.15	-13.62	2.184	2.042
VIII	**26**	177.5	25.57	-40.69	2.287	1.995
VIII	**27**	0.8	25.98	-40.69	2.326	1.975
IX	**28**	182.6	33.44	-50.70	2.174	2.056
IX	**29**	-9.5	32.30	-50.70	2.295	1.992

[a] Long bond is always the bond to the substituted carbon of the diene. $\Delta H_{act.}$ and ΔH_f in kcal/mol, distances in Å, angles in deg. See Figure 1D for the definition of dihedral angle ϕ.

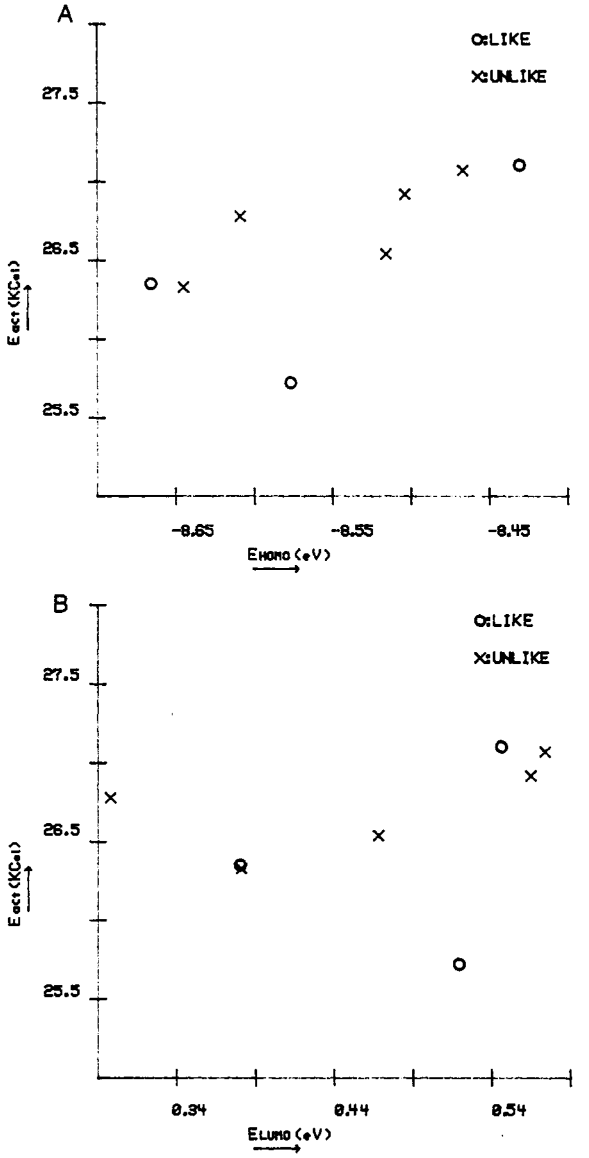

Figure 8. Variation of calculated activation energies (kcal/mol) with HOMO (A) and LUMO (B) energies eV).

Results and Discussion

The results of the calculations are presented in Table II-VI, and Figures 2-11. The activation energies are close to what is expected for Diels-Alder reactions of this class. The activation enthalpy of the reaction of ethylene with butadiene has been estimated to be 27-34 kcal/mol at 298 °C in the gas phase.[20] Activation enthalpies for the reactions of our model dienes with ethylene (see Table II) range between 25.5 and 26.3 kcal/mol. The higher activation enthalpy for reaction with acrolein parallels the observation of Dewar that RHF calculations do not properly account for the effect of substituting CN groups for H on the dienophile.[21] The gas-phase Diels-Alder

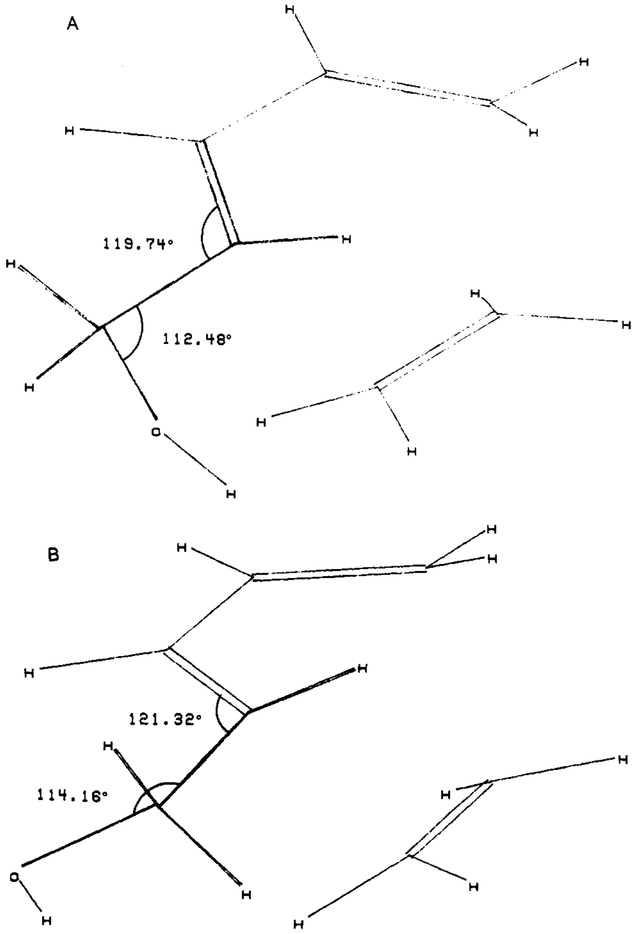

Figure 9. Transition states for reaction VI (A *anticoplanar*, B *syncoplanar*).

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(20) Dewar, M. J. S.; Olivella, S.; Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 5650. The analysis (in footnote 38) is based upon reports of Rowley, D.; Steiner, H. *Discuss. Faraday Soc.* **1951**, *10*, 198. Barnard, J. A.; Parrott, J. K. *J. Chem. Soc. Faraday Trans. 1*, **1976**, 2404. Uchiyama, M.; Tomioka, T.; Amano, A. *J. Phys. Chem.* **1964**, *68*, 1878. Townshend, R. E.; Ramunni, G.; Segal, G. Hehre, W. J.; Salem, L. *J. Am. Chem. Soc.* **1976**, *98*, 2190.

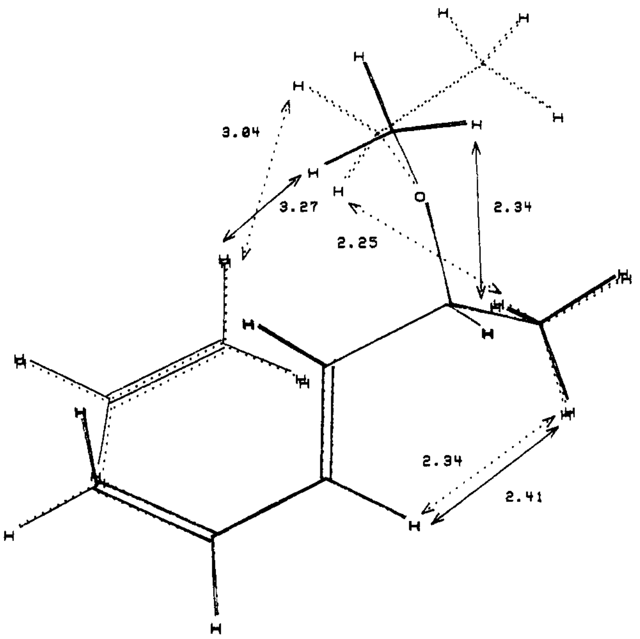

Figure 10. Superposition of the transition states for reactions II (solid line) and III (broken line). Distances are in Å.

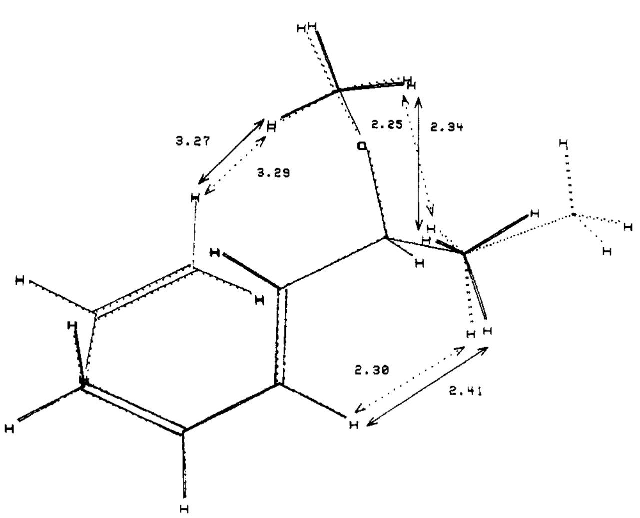

Figure 11. Superposition of the transition states for reactions II (solid line) and IV (broken line). Distances are in Å.

reaction of butadiene and acrolein is reported to have an activation energy of 19.7 kcal/mol ($A = 1.46 \times 10^9$) in the temperature range of 155–332 °C.[22] We have not found appropriate quantitative gas-phase activation energy data for reactions similar to reaction IX with an acetylenic dienophile. However, qualitative reports suggest that acetylenic dienophiles react more slowly than their ethylenic counterparts in solution.[1a,23]

Table III. Comparison of Calculated and Experimental Selectivities for Diels–Alder Reactions[a]

reactn	$\Delta\Delta H_{\mathrm{act.}}$(calcd), kcal/mol	$\Delta\Delta H_{\mathrm{act.}}$(expt), kcal/mol
I	0.4	
II	0.6	
III	0.2	
IV	0.5	
VIII	0.4	0.9[1a,entry 8]
IX	-1.1	-0.6[1a,entry 18]

[a] $\Delta\Delta H_{\mathrm{act.}}$ is defined as *unlike* – *like*.

It is immediately apparent that AM1 successfully predicts the face selectivities for the cases studied (Table III, assuming that the minor structural differences between the theoretical and experimental examples are insignificant). One should note that the selectivity is inverted upon changing from ethylenic to an acetylenic dienophile in both the theoretical and experimental determinations. The calculations correctly predict the predominance of endo product for the reactions with acrolein. One should note that the structure of the favored endo transition state has the carbonyl group anti to the double bond.[24] The syn arrangement would allow for greater secondary overlap.[25]

In the cases for reaction with ethylene and acrolein the like transition state is favored for each reaction studied. Furthermore, the best *like* transition state always has the OR group in the plane of the diene and extended away from the diene (we shall refer to this conformation as *anticoplanar*, see Figure 1A for definitions). In this conformation, the alkyl group can point away from the dienophile, leaving the sterically less demanding hydrogen directed toward the incoming dienophile (see Figures 2A, 3A, 4A, 5A, and 6A). If the dienophile were to approach from the other face (*unlike*), the alkyl group would hinder its approach (for example, see Figure 4B) unless the chiral group changes its conformational position. In fact, the preferred transition state for most of the *unlike* reactions has the alkoxyl group rotated by close to 180° into the *syncoplanar* position. This moves the alkyl group to the opposite face of the diene, thereby allowing the dienophile to approach from the less hindered side (see Figures 2B, 3B, 5B, and 6B). Reaction III is an exception because the ethoxy is larger than the methyl group. It, therefore, prefers the less hindered, anticoplanar position while the alkyl group becomes positioned toward the approaching dienophile (see Figure 4B). The energy differences between the syncoplanar and anticoplanar conformations is less for unlike than like transition states since both conformations are sterically demanding only in the unlike (see discussion below). Significantly, the alkoxyl group prefers to be (approximately) in the plane of the diene in the favored transition states for both *like* and *unlike* reactions of all the dienes. The dienophile approaches from what is the less hindered side after this first criterion is met. Thus, the face selectivity appears to be due to a combination of steric and electronic effects.

We sought, in several different ways, to determine the nature of whatever electronic effects might be important. Most of the detailed analysis described below will refer to

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(21) A referee has suggested that Dewar's observations about the RHF calculations taken together with two other recent reports[26] imply that AM1 may be deficient for transition states involving nitrogens. We have results that imply the reverse. In particular, AM1/CI[18c] better describes bond cleavage than does MNDO/CI.[13a,b] One should note that the calculations in ref 26 were also at the RHF level. It is likely that open-shell calculations and/or CI are necessary to correctly describe the energetics of reactions involving bond formation or bond breaking.

(22) Kistiakowsky, G. B.; Lacher, J. R. *J. Am. Chem. Soc.* **1936**, *38*, 123.

(23) Activation energies for comparable reactions of cyclopentadiene with maleic anhydride and dimethyl acetylenedicarboxylate are 8.5 kcal/mol (at -60 to -40 °C) and 14.1 kcal/mol (at 10 °C) Craig, D.; Shipman, J. J.; Fowler, R. B. *J. Am. Chem. Soc.* **1961**, *83*, 2885. Greiger, R. A.; Eckert, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 7149.

(24) Optimized molecular orbital calculations tend to favor the exo rather than endo transition state, although only studies using cyclic dienophiles have been carried out (Sodupe, M.; Oliva, A.; Bertran, J.; Dannenberg, J. J. *J. Org. Chem.* **1989**, *54*, 2488). A report to the contrary is in error (Fox, M. A.; Cardona, R.; Kiwiet, N. J. *J. Org. Chem.* **1987**, *52*, 1469). A subsequent paper will deal with this problem in detail.

(25) For a discussion of secondary orbital effects, see: Gleiter, R.; Bohm, M. C. *Pure Appl. Chem.* **1983**, *55*, 237 and references cited therein.

(26) (a) Grierson, L.; Perkins, M. J.; Rzepa, H. S. *J. Chem. Soc., Chem. Commun.* **1987**, 1779. (b) Rzepa, H. S. *J. Chem. Res.* **1988**, 224.

Table IV. Comparison of the Different Transition-State Structures Characterized for Reaction II[a]

			bond length				charge	π density
product	ϕ	$\Delta H_{act.}$	long	short	HOMO	LUMO	(on oxygen)	
17	168.1	25.7	2.154	2.071	−8.574	0.516	−0.278	0.166
17	227.0	26.3	2.169	2.066	−8.669	0.377	−0.280	0.163
17	56.4	27.1	2.180	2.058	−8.434	0.543	−0.276	0.160
18	28.0	26.3	2.174	2.067	−8.648	0.378	−0.275	0.168
18	174.6	26.5	2.175	2.058	−8.519	0.465	−0.279	0.156
18	76.8	26.8	2.198	2.037	−8.612	0.295	−0.275	0.167
18	−33.4	26.9	2.165	2.071	−8.507	0.562	−0.276	0.155
18	199.0	27.0	2.166	2.069	−8.467	0.571	−0.281	0.154

[a] Long bond is always the bond to the substituted carbon of the diene. $\Delta H_{act.}$ in kcal/mol; HOMO and LUMO in eV; bond lengths in Å; charges and densities in atomic units. See Figure 1D for the definition of dihedral angle ϕ.

the reaction of diene **6** with ethylene, which is typical of all the reactions with ethylene. The corresponding data for the other reactions are not presented for brevity.

First, we examined the HOMO's and LUMO's in the transition states. There is no apparent correlation of either MO with that of the best conformation of the transition state for each reaction (see Table IV and Figure 8). Both the HOMO and LUMO of the best transition state are more average than extreme.

Second, we examined the charge densities at the oxygen and at the π positions in the diene and dienophile. Again, no correlation is evident. In fact neither the charge nor the π density on oxygen changes by any significant amount (see Table IV).

We examined the selectivities for dienes **5**–**8**, which have alkyl and alkoxyl groups of varying bulk attached to the chiral center, in the hope of distinguishing the electronic effects (which should remain constant) from the steric effects. The selectivities of these reactions, as well as, their transition-state structures, are quite similar (Figures 2–5). One should note that II shows slightly more selectivity than III or IV (see below for discussion).

In order to investigate whether the methyl, hydroxy, or methoxy group has a natural preference for one conformational position on the chiral center, we next studied the TS's involving achiral dienes that contained only one of these groups and H's on the saturated carbon. Thus, we calculated the transition-state energies for the reactions of 1,3-hexadiene (**9**), 5-hydroxy-1,3-pentadiene (**10**), and 5-methoxy-1,3-pentadiene (**11**). For 1,3-hexadiene, the methyl group showed little preference between the *anticoplanar* or *away* (away from the incoming dienophile) positions, but the conformation with the methyl oriented toward the dienophile was disfavored by 0.78 kcal/mol. On the other hand, for both the hydroxy and methoxy dienes, **10** and **11**, the OR group exhibited a clear preference for the *anticoplanar* position. The *syncoplanar* position is next best (0.34 and 1.04 kcal/mol higher with OH and OCH_3, respectively) followed by the *away* position (see Table V).

In order to minimize steric interference to the incoming alkene dienophile, the transition state should have the allylic hydrogen as the group closest to the trajectory of bond formation. Thus, the alkoxyl and alkyl groups should be in either the *coplanar* or *away* positions, leaving the hydrogen oriented toward the dienophile. The calculations on the reaction of 1,3-hexadiene with ethylene have indicated that the alkyl group has no preference for either of the two acceptable positions. The determinations of the TS's for the reactions of **10** and **11** with ethylene show that the OR group favors the *anticoplanar* position and strongly disfavors the *away* position, preferring the *syncoplanar* position to the latter. Only the *like* transition state can accommodate the preferences of both the alkyl and alkoxyl groups. In the *unlike* transition state, the alkoxyl group is forced to take the less favored *syncoplanar* position to avoid forcing the methyl group toward the dienophile.

Table V. Activation Energies for Reactions V, VI, and VII as a Function of the Dihedral Angle (ϕ) in Degrees (See Figure 1D for Definition)

reactn	product	ϕ	$\Delta H_{act.}$, kcal/mol
V	**23**	−97.6	25.9
V	**23**	−171.4	25.9
V	**23**	28.0	26.7
VI	**24**	179.4	25.1
VI	**24**	25.6	25.4
VI	**24**	−110.1	26.1
VI	**24**	−53.5	26.5
VII	**25**	180.5	26.1
VII	**25**	37.5	27.2
VII	**25**	−43.2	27.9

The preference of the OR group to be (nearly) coplanar with the diene seems to clearly be of electronic origin. Nevertheless, we are unable to find a simple correlation with orbital energy or electronic density that is symptomatic of the effect. The interaction is likely of too complex a nature to be effectively simplified. The preference for *anti* rather than *syn* coplanar seems to be, at least partially, of steric origin. This can be seen from the bond angles in the optimized *anticoplanar* and *syncoplanar* transition states for 5-hydroxy-1,3-pentadiene (**10**). The OCC and adjacent CCC angles increase by about 2° upon going from the *anticoplanar* to the *syncoplanar* transition state (see Figure 9). The OR groups tend to be twisted slightly more out of the plane for the *unlike* than the *like* transition states, presumably to reduce the steric interaction within the reactants.

For the reactions involving the acetylenic dienophile, IX, *unlike* selectivity is observed. The *like* transition state, with the alkoxy anticoplanar, is less favored than the *unlike* due to the unfavorable steric interaction between the methoxy groups on both the diene and the dienophile. This interaction does not occur in the *unlike* transition state as the methoxy on the diene is *syncoplanar* and out of the way of the dienophile methoxy (see Figure 7). Kozikowski in ref 7 predicted a similar transition state. Clearly, subtle interactions in the transition states can play an important role.

Of particular interest is the prediction that reaction II be considerably more selective than III and slightly more selective than IV. This appears to be due to the interactions between the hydrogens on the alkyl and alkoxyl groups with those on both the diene and dienophile. In reaction II, there is one fewer carbon in the chain from the end of the alkyl to the end of the alkoxyl groups than in III and IV. In the transition states for reactions III and IV, the repulsive interactions between the hydrogens on the ends of these chains forces the transition state to assume a less favorable conformation than for II. The dif-

Table VI. Minimum Energy Rotational Conformations for Starting Dienes (in Their Respective s-Trans Conformations)[a]

diene	ϕ	H_f
5	-14.6	-30.6
6	151.3	-24.2
7	151.4	-29.7
8	178.9	-30.1

[a] The dihedral angle (ϕ) is defined analogously to the corresponding angle in the transition states (see Figure 1D). H_f in kcal/mol; angles in deg.

ferences between the rotational conformation of the alkyl group attached to the oxygen are particularly evident (See Figures 10 and 11). The added repulsion between the H's on the terminal carbons of the ethyl and methyl groups (on III) vs the two methyl groups (on II) causes the alkoxyl alkyl group to rotate by about 60°. This causes one of the H's on this group to more closely approach the incoming dienophile, leading to greater repulsions between the diene and the dienophile in reaction III (3.07 Å vs 3.27 Å for reaction II, see Figure 10). Because of this, the bond lengths are longer in the transition states for III than for II. In addition, the H's on the alkyl and alkoxyl groups, as well as the H's on the alkyl group and the diene, are closer in the transition state for reaction III than for II. Comparison of the transition states for reactions IV and II leads to similar observations, except that the differences are much less (see Figure 11).

The need to completely optimize the transition states can be seen from the ranges of energies and bond lengths for the bonds being formed in the various rotamers about the C–C bond linking the chiral center to the diene (shown in Tables II and IV) for all of the individual transition states that have been studied. The longer bond is always that to the substituted end of the diene, as would be expected to stabilize the small amount of biradical character of the transition state. It is seen that the energy differences between rotamers of the same TS are of the same order of magnitude as the differences between the like and unlike TS's. Furthermore, the variation in the optimized bond lengths (2.326–2.154 Å and 1.975–2.078 Å for the long and short bonds, respectively) for *all* of the *different* TS's and rotamers confirms the need for complete optimization of the TS's.

AM1 calculations on the reagent dienes (see Table VI) indicate that the OR group prefers to be nearly in the anticoplanar position with the exception of **5** for which the OR group is syncoplanar. This observation suggests that the conformation of the reagents does not always provide good indications of the eventual transition-state geometries. Calculations on the preferred products of the specific reactions studied here suggest that four of the six cases have conformations that correlate with the reagents. In reactions I and IX, the conformation of the allylic groups in the starting reagents and the products do not correlate. These observations might be due to one or more of several possibilities. First, if the transition state were early along the reaction path, it would be expected to resemble the reagents. In this case the conformation of the reagent diene would be expected to be the same as in the transition state. Second, the product might have a conformation that is related to that of the starting material in that the rotational isomer of the product can be achieved from the reagent without traversing a rotational barrier. We shall define such a situation as a conformational correlation between reagent and product. In such a case, it is likely that the transition state have a similar conformation to that of the reagent. If the preceding were untrue, the conformation would have to change along with the reaction path from reagent to transition state, and again from transition state to product. While this is not impossible, it is unlikely. Third, there may be an energetic preference for a specific conformation in the transition state that is qualitatively different from those in the reagents and, perhaps, the products.

Therefore, in those cases where a conformational correlation between reagents and products exists, it is reasonable to suppose that the transition state has a conformation corresponding to the reagent and the product. In such cases, it may be reasonable to predict face selectivity on the basis of the conformation of the reagent dienes. The four such cases (II, III, IV, and VIII) studied here are in accord with this suggestion.

Conclusion

To the extent that is verifiable by current experiments, the AM1 RHF method, with complete geometrical optimization, is adequate for predicting the face selectivities for the reactions studied. This is true despite the inability of RHF calculations to correctly predict substituent effects of the dienophile upon the activation energies. No single effect seems to dominate the predicted selectivities. Rather, they appear to result from a combination of electronic and steric interactions. The electronic effects are not clearly manifest in any simple parameter, such as HOMO/LUMO properties, charges, or π densities. They seem to involve more subtle interactions that require specific calculations on each transition state. Our data show that predictions made by assuming that the conformations of the ground states of the reactants are reflected in the transition states are not uniformly correct. The sensitivity of the calculated activation energies to relatively small changes in molecular structure underscores the importance of complete geometrical optimization when performing calculations such as those reported here.

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