Ab initio study of the Diels–Alder reactions of prop-2-enethial

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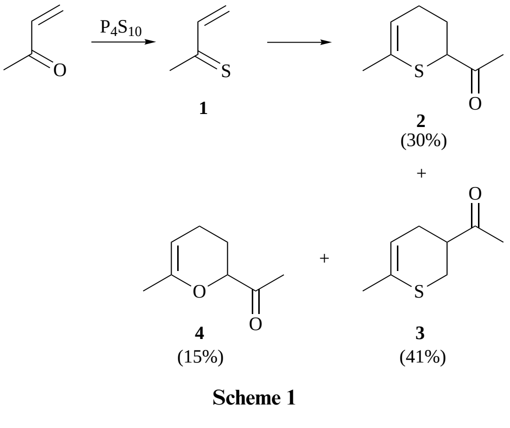
The Diels–Alder reactions of prop-2-enethial with ethene, propene, methoxyethene, ethenenitrile and prop-2-enal have been examined at the MP4SDTQ/6-31G*//MP2/6-31G* level. The activation energy for the reaction with ethene is 54.48 kJ mol^{-1}, which is much lower than the barrier for the reactions of ethene with butadiene or prop-2-enal. The lowest barrier (32.01 kJ mol^{-1}) occurs in the reaction with prop-2-enal. The transition states for all of the reactions are quite similar and are synchronous, as evaluated using bond orders derived from the topological method. Application of FMO theory does predict the effect of substituent on activation barriers. There is little regioselectivity and significant *endo* selectivity only in the case where the dienophile is prop-2-enal.

The preparation of heterocycles is an intensely studied area of synthetic organic chemistry. Perhaps the most useful preparative method is the Diels–Alder cyclization, which can readily assemble the ring, incorporate a heteroatom, and set up to four stereocenters in a single synthetic step. A recent monograph contains hundreds of citations of examples of the hetero-Diels–Alder reaction.[1]

The orbital symmetry rules and frontier molecular orbital (FMO) theory form a powerful predictive tool, allowing for effective design of synthetic strategies. One of our research themes has been to explore the utility and validity of these simple theories towards understanding reactions where a heteroatom is embedded in the π-backbone. Specifically, the Diels–Alder reactions of phosphaalkenes and phosphaalkynes obey these rules.[2] In this paper, we report *ab initio* calculations on the Diels–Alder reaction of prop-2-enethial with a number of dienophiles in order to determine activation energies, regio- and stereo-selectivity, and compare them with the predictions from FMO theory.

Background

The earliest clear example of a Diels–Alder reaction involving an α,β-unsaturated thiocarbonyl as the diene component appears in the work of Lipkowitz and Mundy.[3] Thioketone **1** is formed *in situ* and reacts to give **2** and (preferentially) **3**, in contrast to the dimerization of methyl vinyl ketone which gives only **4** (see Scheme 1). These results are completely consistent with FMO theory, with the regioselectivity dominated by the large coefficient on S in the LUMO of **1**.



1

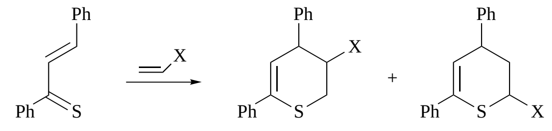
2 (30%)

4 (15%)

3 (41%)

Scheme 1

In a series of papers, Motoki and co-workers have examined the regiochemistry of the Diels–Alder cycloaddition involving unsaturated thioketones.[4–8] For example (see Scheme 2), while the reaction of thioketone **5** with acrylonitrile or acrylamide is in agreement with FMO predictions,[4] the reaction with butyl vinyl ether gives the regioisomer opposite to that predicted by FMO.[5] Their arguments rested on the dominant interaction being between the LUMO of the thioketone and the HOMO of the dienophile.



5

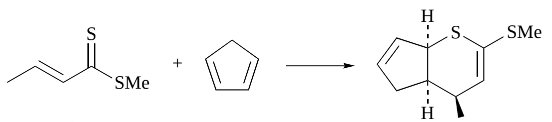
X = CN, CONH$_2$

X = OBu

Scheme 2

Further, Motoki reported complete *endo* selectivity in the reaction of **5** with dimethyl or dimenthyl fumarate.[8] *Endo* selectivity has also been reported in the dimerization of thioamides[9] and dithioesters.[10]

A number of other reports of the Diels–Alder reactions of α,β-unsaturated thioketones indicate again generally consistent agreement with FMO predictions.[11–13] We note that attempts to get the dithioester **6** to react as a dienophile proved fruitless; it did not react with furan[14] and reacts as the diene fragment in the [4 + 2]cycloaddition with cyclopentadiene[15] in an *endo* fashion only (Scheme 3). It should also be noted that the thio-Diels–Alder reaction generally occurs at lower temperatures than typically needed for these types of cycloadditions, often occurring at or below room temperature.[4,7,9,11]



6

Scheme 3

While there has been no theoretical study of the Diels–Alder reaction of α,β-unsaturated thiocarbonyl compounds, a detailed examination of the Diels–Alder reaction between butadiene and thioformaldehyde[16] does bear upon our examinations. In particular, the activation energy for the reaction of thioformaldehyde was found to be much lower than for the reaction with formaldehyde. The low barrier is consistent with

Table 1 Activation (E_a) and reaction (E_{rxn}) energies (kJ mol^{-1}) for reactions (1)–(9)[a]

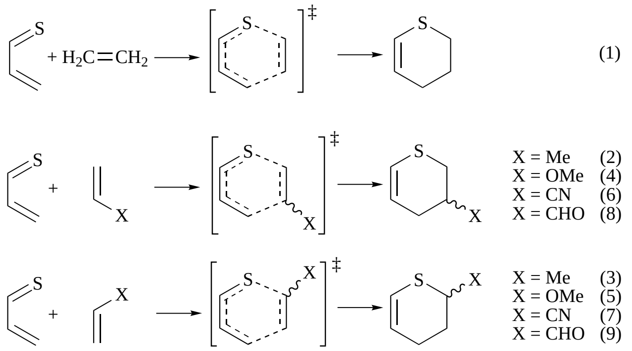
Reaction	E_a	E_{rxn}
(1)	54.48	−163.59
(2) *endo*	53.81	−159.95
(2) *exo*	56.99	−159.95
(3) *endo*	55.73	−161.75
(3) *exo*	52.47	−164.18
(4) *endo*	65.14	−142.72
(4) *exo*	64.10	−150.79
(5) *endo*	66.40	−148.32
(5) *exo*	60.08	−144.93
(6) *endo*	47.53	−158.74
(6) *exo*	51.17	−153.93
(7) *endo*	50.25	−152.71
(7) *exo*	48.58	−147.95
(8) *endo-cis*	37.28 (31.59)[b]	−154.05
(8) *exo-cis*	46.53 (40.84)[b]	−153.84
(8) *endo-trans*	43.26	−154.05
(8) *exo-trans*	45.19	−153.84
(9) *endo-cis*	32.01 (26.32)[b]	−155.77
(9) *exo-cis*	39.16 (33.47)[b]	−149.16
(9) *endo-trans*	47.07	−155.77
(9) *exo-trans*	47.00	−149.16

[a] Evaluated at MP4SDTQ/6-31G*//MP2/6-31G*. [b] Number without parentheses is the activation energy relative to the most stable conformer of acrolein (*s-trans*) and the number within parentheses is that relative to *s-cis*-acrolein.

experimental observation, similar to that of the unsaturated species noted above, that thioaldehydes undergo Diels–Alder reaction at or below room temperature. The extreme reactivity of the thiocarbonyl was attributed to the weak C=S π-bond, its low LUMO energy,[17] reduced repulsive lone pair–butadiene interactions due to the long C–S distance, and reduced strain in the butadiene to interact with the ends of the dienophile. Many of these features should also play a role in the chemistry of the unsaturated thiocarbonyl compounds.

Computational method

We report here on the Diels–Alder reactions between prop-2-enethial and a variety of dienophiles: ethene, propene, methoxyethene, ethenenitrile and prop-2-enal. Reactions (1)–(9) are shown in Scheme 4. For the substituted ethenes, for each regioisomer, there are two orientations of attack, *exo* and *endo*, leading to products having pseudoaxial or pseudoequatorial substitution. We will label the transition structures (TS) as **TS*No***, where ***N*** will indicate the reaction number and ***o*** will be ***x*** for *exo* attack or ***n*** for *endo* attack, and the products will be similarly labeled as **P*No***. For the TSs of reactions (8) and (9), the acrolein fragment can be in the *s-cis* or *s-trans* arrangement, labeled by a trailing ***c*** or ***t***, respectively.



Scheme 4

Previous studies of Diels–Alder reactions, including hetero-Diels–Alder reactions, have reached a common conclusion concerning the effect of computational level.[18–25] Activation energies are too large at the HF level, are too small at MP2, and are in reasonable agreement with experiment when evaluated at the MP4 level. The same trend has been found with the reactions examined here. Therefore, while we have first optimized the structures at HF/6-31G*, we report here only the MP2/6-31G* optimized geometries and single point energies at MP4SDTQ(fc). Zero-point energies were obtained at HF/6-31G* and have been scaled by 0.89. We have shown that this level is adequate for obtaining geometries of organosulfur compounds.[26] The activation and reaction energies for reactions (1)–(9) are listed in Table 1. All calculations were performed using GAUSSIAN94.[27]

Topological electron density analysis[28] was used to determine bond orders (BO), using the empirical relation given in eqn. (10).

$$\mathrm{BO(X{-}Y)} = \exp[A(\rho(\boldsymbol{r}_c) - B)] \tag{10}$$

X–Y	A	B	
C–C	6.458	0.252	ref. 30
C–S	13.43	0.187	ref. 26

The values of the electron density at the bond critical points $\rho(\boldsymbol{r}_c)$ were determined using a locally modified version of EXTREME.[29]

Results

Geometries

Products. The MP2/6-31G* optimized geometries of the Diels–Alder products for reactions (1)–(9) are sketched in Fig. 1 (see Supplementary Materials). The calculated 3,4-dihydro-2*H*-thiopyrans display common features, with the ring geometry relatively unaffected by substitution. The exception is the S–C2 distance. When C2 is unsubstituted, the S–C2 distance is 1.811 to 1.815 Å. When C2 carries a methyl or cyano substituent (**P3** and **P7**) the bond lengthens to 1.824 Å, presumably due to a steric interaction with sulfur. When C2 carries the formyl group the S–C2 is longer than when the group is on C3, but the effect is not as strong as with the other substituents.

Methoxy substitution on C2 leads to an extreme geometric change; the S–C2 distance is very long (1.845 Å) in **P5*x*** while it is short (1.810 Å) in **P5*n***. Concomitant changes in the C2–O distance also occur with these, 1.411 in **P5*x*** and 1.423 Å in **P5*n***. These structural differences reflect the anomeric effect. In the simple MO model of the anomeric effect (whereby a lone pair donates into an adjacent antibonding orbital) one can easily understand the geometric distortions observed in **P5**. In **P5*n***, the sulfur lone pair is parallel to the σ_{CO}* and donation into this orbital lengthens the C–O bond and shortens the C–S, though the magnitude of this change is small. In **P5*x***, the sulfur lone pairs are gauche to the σ_{CO}* and no donation occurs. Instead, the lone pair on oxygen donates into the σ_{CS}* giving rise to a short C–O bond and a long C–S bond. The magnitude of this change is much larger than in **P5*n***.

Transition states. The MP2/6-31G* optimized geometries of the TSs are presented in Fig. 2 (see Supplementary Materials). The bond distances within the forming ring for all TSs are listed in Table 2. What is most striking about these distances is how little variation there is due to regiochemistry or substitution. This is particularly apparent in the bonds that have orders between 1 and 2; the S–C6 distance ranges from 1.653 to 1.671 Å, the others have smaller ranges: 1.411 to 1.424 Å for C5–C6, 1.369 to 1.386 Å for C4–C5, and 1.374 to 1.388 Å for C2–C3.

The average C3 · · · C4 forming distance in these TSs is 2.323 Å. This is slightly longer than the typical value found in TSs for pericyclic reactions of hydrocarbons[31] but is understandable. In the TSs examined here, the second forming bond is between C

Table 2 Bond distances (Å) in **TS1**–**TS9**

	Forming bonds		Diene			Dienophile
Compound	C···C	C···S	C6–S	C5–C6	C4–C5	C2–C3
TS1	2.320	2.566	1.658	1.417	1.374	1.374
TS2*n*	2.356	2.551	1.660	1.418	1.374	1.377
TS2*x*	2.361	2.553	1.660	1.417	1.374	1.378
TS3*n*	2.302	2.621	1.658	1.419	1.375	1.376
TS3*x*	2.323	2.595	1.656	1.419	1.374	1.375
TS4*n*	2.315	2.430	1.671	1.410	1.379	1.387
TS4*x*	2.336	2.418	1.670	1.412	1.378	1.388
TS5*n*	2.143	2.694	1.662	1.411	1.386	1.382
TS5*x*	2.226	2.644	1.660	1.414	1.380	1.381
TS6*n*	2.366	2.459	1.658	1.418	1.374	1.382
TS6*x*	2.381	2.447	1.658	1.418	1.373	1.383
TS7*n*	2.250	2.652	1.659	1.418	1.379	1.382
TS7*x*	2.258	2.656	1.657	1.419	1.377	1.381
TS8*nc*	2.493	2.432	1.658	1.421	1.369	1.378
TS8*nt*	2.374	2.487	1.658	1.419	1.373	1.379
TS8*xc*	2.439	2.474	1.656	1.421	1.370	1.377
TS8*xt*	2.383	2.486	1.658	1.419	1.372	1.380
TS9*nc*	2.304	2.777	1.653	1.424	1.374	1.374
TS9*nt*	2.302	2.634	1.656	1.421	1.374	1.378
TS9*xc*	2.274	2.703	1.655	1.420	1.375	1.375
TS9*xt*	2.279	2.625	1.657	1.420	1.375	1.380

and S, which must be longer than a forming C–C bond, thereby stretching the forming C–C bond from the normal distance. The shortest C3···C4 distances occur in the two TSs for reaction (5), with a particularly short distance in **TS5*n***. The longest C3···C4 distances appear in **TS8*nc*** and **TS8*xc***, where we also note that their *trans* isomers have C3···C4 distances that are much shorter.

There is little variation of the C2···S distance in these TSs, with an average value of 2.56 Å. The shortest C2···S distances are in the TSs for reaction (4) while the longest distances are found in **TS9*nc*** and **TS9*xc***. We note that these extrema come in pairs corresponding to the different regioisomers: shortest C···C in reaction (5), shortest C···S in reaction (4); longest C···C in reaction (8), longest C···S in reaction (9).

Lastly, a trend in the distances of the forming C···C and C···S bonds relative to the parent [reaction (1)] is observed. For the reactions where the substituent is attached to C3 [reactions (2), (4), (6) and (8)], the C···C bond is longer and the C···S bond is shorter than in the parent. On the other hand, for the reactions where the substituent is placed on C2 [reactions (3), (5), (7) and (9)], the C···C bond is shorter and the C···S bond is longer than in the parent. Since this effect is independent of the type of substituent, we can dismiss an electronic cause and consider that the larger steric interaction (relative to H) caused by the substituent approaching the diene leads to the longer distance.

Energies

Activation and reaction energies evaluated at MP4SDTQ(fc)/6-31G*//MP2/6-31G* are listed in Table 1. While no experimental data exists to which we can compare our results, previous theoretical studies of other Diels–Alder reactions at this computational level provide activation and reaction energies in good agreement with experiments.[17–24]

The activation energy for reaction (1) is 54.48 kJ mol^{-1}. This is substantially smaller than for the parent Diels–Alder reaction butadiene + ethylene [E_a(MP4SDQ/6-31G*) = 132.88 kJ mol^{-1}][21] and for the reaction of acrolein with ethylene[32] [E_a(MP4/6-31G* = 101.21 kJ mol^{-1}]. In addition, the activation energy for the reaction of 1-phosphabuta-1,3-diene with ethylene is 76.57 kJ mol^{-1}.[21]

The reaction of propene with prop-2-enethial shows little kinetic selectivity. The transition states **TS2*n*** and **TS3*x*** differ in energy by only 1.34 kJ mol^{-1}. **P3*x*** is the thermodynamic product. The reaction with ethenenitrile also shows little kinetic preference, with **TS6*n*** favored by only 1.05 kJ mol^{-1}. In this case, the thermodynamic and kinetic products are the same, **P6*n***. For these systems, there is little *endo*/*exo* selectivity; the difference between these two pathways is no greater than 3.8 kJ mol^{-1}.

The reaction with methoxyethene proceeds most easily through **TS5*x***, which lies 4.35 kJ mol^{-1} below **TS4*x***, while **P4*x*** is the most stable product. While reaction (4) shows little *endo*/*exo* selectivity, the *exo* pathway is favored by 6.32 kJ mol^{-1} for reaction (5).

The reaction between prop-2-enal and prop-2-enethial is complicated by the number of isomeric pathways. The reactions involving the *cis* isomer of acrolein are favored by 5.98 kJ mol^{-1} in reaction (8) and 15.06 kJ mol^{-1} in reaction (9). In the *cis* cases, the *endo* TSs are preferred by 9.25 kJ mol^{-1} for reaction (8) and 7.15 kJ mol^{-1} in reaction (9). The *endo*/*exo* selectivity for the *trans* cases is small. Overall, the lowest TS is **TS9*nc***, which is 5.27 kJ mol^{-1} below the next lowest barrier, **TS8*nc***.

Relative to the parent, reaction (1), the methyl substituent barely lowers the activation energy, while the stronger donor methoxy group raises the activation energy. On the other hand, the withdrawing groups cyano and formyl both lower the barrier. The effect of the formyl group is quite dramatic: the barrier is reduced by 23.0 kJ mol^{-1} to only 32.01 kJ mol^{-1}.

For all cases where the substituent is on C3 [reactions (2), (4), (6) and (8)] the *endo* TS is favored. On the other hand, the *exo* TS is favored for all cases where the substituent is on C2 except for reaction (9) with acrolein in the *s-cis* conformation. In this case, the *endo* TS lies 7.15 kJ mol^{-1} below the *exo* TS.

Topological electron density analysis

We have employed the topological electron density method to evaluate the bond order in the transition states using the empirical expression given in eqn. (10). These results are listed in Table 3. There are two striking patterns in this table [neglecting reaction (5) for a moment]. First, the bond orders of the butadiene and ethylene fragment are nearly identical for each bond in each reaction. Secondly, the sum of the bond orders of the 'active' bonds in the transition state is seven for each reaction. The bond order of the 'active' bonds in the reactant and product is also seven. These trends suggest a synchronous reaction. The two new σ-bonds are not formed to the same extent in the TS, with the C–S bond trailing the C–C bond.

Table 3 Bond orders in **TS1**–**TS9**

	Forming bonds		Diene			Dienophile	
Compound	C···C	C···S	C6–S	C5–C6	C4–C5	C2–C3	Sum[a]
TS1	0.30	0.14	1.66	1.63	1.61	1.66	7.00
TS2*n*	0.30	0.14	1.67	1.63	1.61	1.66	7.01
TS2*x*	0.30	0.14	1.67	1.64	1.61	1.65	7.01
TS3*n*	0.31	0.12	1.59	1.65	1.57	1.67	6.91
TS3*x*	0.31	0.13	1.62	1.65	1.58	1.66	6.94
TS4*n*	0.31	0.15	1.68	1.65	1.59	1.68	7.06
TS4*x*	0.30	0.16	1.68	1.65	1.60	1.67	7.06
TS5*n*	0.35	0.10	1.41	1.68	1.43	1.62	6.58
TS5*x*	0.33	0.10	1.47	1.67	1.49	1.62	6.68
TS6*n*	0.28	0.16	1.68	1.64	1.64	1.59	7.00
TS6*x*	0.28	0.16	1.67	1.64	1.64	1.59	6.98
TS7*n*	0.30	0.14	1.73	1.63	1.62	1.61	7.04
TS7*x*	0.31	0.14	1.73	1.62	1.61	1.61	7.02
TS8*nc*	0.28	0.16	1.68	1.63	1.65	1.59	7.04
TS8*nt*	0.28	0.16	1.66	1.64	1.62	1.60	6.96
TS8*xc*	0.28	0.16	1.67	1.63	1.64	1.60	6.97
TS8*xt*	0.28	0.16	1.66	1.64	1.63	1.60	6.97
TS9*nc*	0.31	0.14	1.70	1.64	1.61	1.65	7.04
TS9*nt*	0.28	0.14	1.70	1.62	1.62	1.64	7.01
TS9*xc*	0.31	0.14	1.70	1.64	1.60	1.65	7.04
TS9*xt*	0.30	0.14	1.71	1.63	1.62	1.63	7.03

[a] Sum of the bond orders of the active bonds.

Table 4 HOMO and LUMO energies (au)

Compound	HOMO	LUMO
prop-2-ene-1-thial	−0.3384	0.0376
ethene	−0.3744	0.1839
propene	−0.3570	0.1929
methoxyethene	−0.3400	0.2114
ethenylnitrile	−0.3977	0.1030
prop-2-enal	−0.3975	0.0994

The exception to the above statement are the results for reaction (5). The bond order sum is 6.58 and 6.68 in the two isomeric TSs, due to a smaller bond order for the diene fragment C6–S and C4–C5 bonds. This is not reflected in the bond distances; these bond distances are quite comparable to the analogous bonds in the other TS.

Discussion

The main focus of this study is two-fold: to judge the nature of the reaction mechanism and the applicability of FMO to this heteroatomic system. Before addressing these issues, we first compare the effect of the sulfur substitution. The activation energy for reaction (1) is 54.48 kJ mol^{-1}. This barrier is much smaller (75.31 kJ mol^{-1}) than for the all-carbon case and 46.02 kJ mol^{-1} lower than when the heteroatom is oxygen. It is somewhat lower even than the case where the heteroatom is phosphorus. This low barrier is completely consistent with experiments which find that thiocarbonyls undergo Diels–Alder reactions at low temperature. The weak π-bond of the C–S double bond and its low LUMO, high HOMO (discussed below) account for this low barrier.

We next discuss the reaction mechanism. While we did not explicitly look for a non-concerted TS, the geometry optimizations were permitted the freedom to reorient if desired. Other studies of Diels–Alder reactions have suggested that the concerted pathway is favored over the stepwise reaction.[23,32,33] In all of the cases examined here there is a single TS connecting reactant to product, supporting a concerted reaction.

The geometries of the TSs for all nine reactions are remarkably similar. The diene and dienophile fragments are virtually unchanged in all of the TSs. The only variation, and it is fairly small, is in the forming C···C and C···S bonds. The TS with the longest C···S distance (**TS9*nc***) has the lowest activation barrier, while the TS with the longest C···C distance (**TS8*nc***) has the next lowest barrier. The TS with the shortest C···C distance (**TS5*n***) has the highest activation barrier, while the TS with the shortest C···S distance (**TS4*x***) has the third highest barrier. However, there is no correlation between either C···C or C···S distances with the activation energy.

The relative lengths of the forming C···C and C···S bonds in the TSs do fall within two distinct categories. The TSs for reactions (2), (4), (6) and (8) have longer C···C distances and shorter C···S distances than in **TS1**. On the other hand, the TSs for reactions (3), (5), (7) and (9) have shorter C···C distances and longer C···S distances than **TS1**. Since within each group, the effect is the same regardless of whether the substituent is an electron donor or acceptor, a steric interaction is the likely cause of this trend. In the first group, the substituent is attached to the carbon involved in the forming C···C bond, resulting in a lengthening of this forming bond. The substituent is attached to the carbon forming the C···S bond in the second group, resulting in a lengthened C···S distance in the TSs.

There is very little variation in bond orders when the substituents are changed, excluding reaction (5). The very consistent values of the bond orders in the diene and dienophile fragments of around 1.7, including the C6–S bond, suggests that the TSs are synchronous. This is difficult to assess simply on the basis of geometries alone, since the distances to S are so different to C–C distances. Further bond order is conserved in these TSs, which by itself does not confirm synchronicity, it does certainly support the claim. We have noted bond conservation in other Diels–Alder reactions.[21,22,25]

A concerted Diels–Alder reaction involving a thioaldehyde is probably to be expected. A synchronous TS is another matter. The symmetry of the system is entirely broken, not just by a substituent, but within the π-backbone as well. Nevertheless, based on empirical bond orders (a better basis for judgment than simply examining distances since it directly reflects the electronic distribution and is not complicated by inherent differences in distances involving different atom pairs) these TSs are synchronous—bonds are broken and made to quite similar extents.

The traditional thinking has been that in terms of FMO arguments, prop-2-enethial participates in the Diels–Alder reaction principally through the interaction of its LUMO with the HOMO of the dienophile.[3–5] As seen in Table 4, the LUMO of prop-2-enethial is quite low in energy, and this approach at first seems reasonable. If this is the dominant interaction, then the activation energies should decrease in going from ethene to propene to methoxyethene, since the HOMO energy rises in this series. In fact, the opposite trend in activation energy is found. Furthermore, with the electron withdrawing substituents on the dienophile, [reactions (6)–(9)] the activation energy is reduced, relative to the reaction with ethene [reaction (1)].

The lowest activation energy occurs in reaction (9), and examination of the HOMO–LUMO gaps suggests that in this case, each HOMO–LUMO interaction participates nearly equally. This is also likely in the reaction with ethenenitrile. The trend in activation energies thus is best accounted for not by a simple $\mathrm{HOMO_{dienophile}}$–$\mathrm{LUMO_{diene}}$ interaction, but a combination of this one and the $\mathrm{HOMO_{diene}}$–$\mathrm{LUMO_{dienophile}}$ interaction, with the latter becoming more important as the substituent becomes more electron withdrawing. In fact, the $\mathrm{HOMO_{diene}}$–$\mathrm{LUMO_{dienophile}}$ gap alone accounts for the entire trend in barrier heights, if one neglects that this energy gap is larger than the $\mathrm{HOMO_{dienophile}}$–$\mathrm{LUMO_{diene}}$ gap.

With the non-conjugating substituents the *endo*/*exo* selectivity is small. The largest is in reaction (5) where the *exo* methoxy group is favored by 6.32 kJ mol^{-1}. On the other hand, there is substantial preference for the *endo* position in both reaction (8) and (9) when acrolein is in the *s-cis* conformation and little preference when in the s-*trans* conformation. The *s-cis* conformation allows for maximum secondary orbital interactions in the *endo* orientation.

In fact, secondary orbital interactions account for the observation that the reactions with the substituent on C3 favor the *endo* TS while the *exo* TS is favored when the substituent is on C2. Secondary orbital interactions require the substituent orbitals to interact with either the 2 or 3 position of the diene. In the cases where the substituent is on the carbon making the new bond to sulfur [reactions (3), (5), (7) and (9)], the substituent is directed away from the interior of the diene component, unlike the other cases where the substituent lies above one of the interior carbon atoms. Furthermore, the distance between the substituent and the nearest interior carbon of the diene is longer in the *endo* TSs of reactions (3), (5), (7) and (9) than in the *endo* TSs of reactions (2), (4), (6) or (8). Therefore, in the reactions where the substituent is on C2, secondary interactions are poor and steric interactions dominate, thereby favoring the *exo* pathway. These high-level calculations continue to support the notion of secondary orbital interactions in Diels–Alder TSs and are in agreement with experiments.[8–10]

Lastly, there is little regioselectivity in these reactions. In the reaction with propene or methoxyethene, the substituent in the 2 position is favored by 1.34 and 4.27 kJ mol^{-1}, respectively. Ethenenitrile reacts preferentially to give the product with the nitrile in the 3 position, but the difference in TS energies is only 1.05 kJ mol^{-1}. These selectivities are in agreement with the work of Motoki.[4–7] The largest selectivity is in the reaction with acrolein, where the 2 position is favored by 5.27 kJ mol^{-1}, however, this is not the major product observed by Lipkowitz and Mundy.[3] One note of caution is that the small energy differences predicted between the different regioisomers implies that solvent effects or the effect of the other substituents present on the thioaldehydes used in the experiments may be determining the regio-outcome.

Conclusions

High level *ab initio* calculations on the Diels–Alder reaction of prop-2-enethial lead to a number of observations. The conjugated thial is much more reactive towards a dienophile than a diene, conjugated aldehyde or conjugated phosphaalkene. The transition state of this Diels–Alder reaction is concerted and remarkably synchronous, even though symmetry is broken within the π-backbone in addition to the substituent upon the dienophile. The reaction is not dictated by just the $\mathrm{LUMO_{diene}}$–$\mathrm{HOMO_{dienophile}}$ interaction, but rather the $\mathrm{LUMO_{dienophile}}$–$\mathrm{HOMO_{diene}}$ interaction, which is smaller than the other frontier interaction, and correlates with the activation energies. There is a definite *endo* preference in the reaction with a conjugated dienophile. The regioselectivity is small for all cases examined, though in general in agreement with experiment.

Supplementary materials

Figs. 1 and 2, which contain drawings of the products and transition states including pertinent distances and angles are available (SUPP. PUB. NO. 57318, 8 pp.).†

Acknowledgements

We are grateful to the National Science Foundation for support of this research.

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† For details of the Supplementary Publications Scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 2*, available *via* the RSC Web pages (http://www.rsc.org/authors).

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Paper 7/05343F
Received 23*rd July* 1997
Accepted 8*th October* 1997