Thermal and Photochemical Cycloaddition Reactions of Thiocarbonyls: a Qualitative Molecular Orbital Analysis

Varanasi Pushkara Rao, Jayaraman Chandrasekhar,* and Vaidhyanathan Ramamurthy*
Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

A comprehensive analysis of thermal and photochemical reactions of thiocarbonyls has been undertaken within the PMO framework employing MINDO/3 orbital energies and wavefunctions. The model is generally successful in rationalizing the observed regiochemistry of such reactions. In particular, the indicated regiochemistry for [4 + 2] thermal cycloadditions of saturated thiones to 2-substituted dienes, for the dimerization of α,β-unsaturated thiones, and for the photochemical cycloadditions of thioketones and thioenones are all in agreement with experimental observations. Interesting predictions are also made concerning cycloadditions of saturated, conjugated, and arylalkyl thiones which have not yet been studied experimentally. The analysis reveals the decisive role played by secondary orbital interactions in determining the observed product selectivity in the photochemical reactions between thioenone and olefins.

Cycloaddition reactions of thiocarbonyls, both thermal and photochemical, have attracted considerable attention over the last decade.[1] It has become evident that the reactivity in these systems cannot be understood on the basis of a simple extrapolation of the well known behaviour of carbonyl compounds. In order to unravel the origins of the distinctive chemical behaviour of thiocarbonyl compounds, especially in cycloaddition reactions, we have undertaken a comprehensive molecular orbital investigation. Our goal is to obtain a qualitative understanding of the frontier orbital control of the reactivity patterns in photo and thermal cycloaddition reaction of thioketones and thioenones using MINDO/3 orbital energies and wavefunctions.

A few PMO analyses on some isolated thiocarbonyl systems have been attempted before, with varying degrees of success.[2–4] A systematic study of thermal [4 + 2] cycloaddition reactions of thiones to olefins using *ab initio* wavefunctions has also been reported.[5] The latter calculations provide a convenient calibration to the present investigation. Our study is more extensive as it examines photochemical reactivity as well as a number of additional types of thermal cycloaddition reactions. The use of the MINDO/3 method has enabled us to examine a large variety of systems without making serious geometric assumptions. Earlier calculations generally employed assumed or partially optimized geometries. This is a potential source of error, especially for several unsaturated thiones considered in this work.

We now demonstrate that the PMO model[6] in conjunction with the MINDO/3 formalism adequately accounts for the observed products both in thermal and photochemical cycloaddition reactions. In addition, several interesting predictions are made for systems that have not yet been studied experimentally.

Computationals

MINDO/3 calculations[7] were carried out on a number of saturated and conjugated thiones with alkyl and/or aryl substitutents **(1)**—**(13)**. A few related carbonyl compounds **(14)**—**(18)** were also examined for comparison. Orbital energies and eigenvectors were computed for a variety of representative electron-rich and -poor olefins and dienes **(19)**—**(33)** which are the reaction partners in the cycloadditions considered in this study. Both 1- and 2-substituted dienes were examined. Full geometry optimization was performed in each case with the single assumption that non-hydrogen atoms lie in a plane.

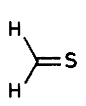
Table 1. MO coefficients of π and π* orbital of thiones

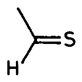
	π(HOMO)				π*(LUMO)			
Thione	$-C_\beta$	$-C_\alpha$	C	S	$-C_\beta$	$-C_\alpha$	–C	S
(1)			0.53	0.85			0.85	0.53
(2)			0.45	0.83			0.80	0.52
(3)			0.41	0.83			0.77	0.51
(4)	0.48	0.40	0.28	0.73	0.52	0.24	0.67	0.48
(5)	0.52	0.43	0.24	0.68	0.53	0.25	0.66	0.47
(6)	0.48	0.38	0.26	0.72	0.47	0.21	0.67	0.48
(7)	0.46	0.47	0.20	0.66	0.55	0.20	0.59	0.44
(8)	0.41	0.47	0.16	0.60	0.51	0.30	0.56	0.43
(9)	0.43	0.48	0.12	0.55	0.52	0.31	0.55	0.42
(10)	0.26	0.47	0.16	0.61	0.33	0.28	0.59	0.43
(11)	0.33	0.45	0.10	0.50	0.49	0.30	0.52	0.40
(12)	0.28	0.44	0.18	0.64	0.30	0.25	0.61	0.44
(13)	0.39	0.25	0.26	0.76	0.41	0.16	0.63	0.48

Results and Discussion

The general trends in orbital polarization (Table 1) and orbital energies (Figure 1) of the various thiocarbonyl compounds considered in this study are discussed first. The calculated data are then used to predict the regiochemistry of several types of thermal cycloaddition reactions involving thiones and thioenones. Finally the photobehaviour of these systems is examined. In these two sections, the principal frontier orbital interactions are first identified using symmetry and orbital energy-gap criteria. Preferred reactive sites are then determined by matching the atoms with the largest coefficients in the appropriate frontier orbitals. The qualitative analysis is deliberately kept simple. Potential complications due to electrostatic effects, dependence of the interaction integrals on the specific atom pair involved,[8] and variation in the transition-state geometry with substituents are all ignored, since even an approximate attempt to include these factors would necessitate the introduction of several empirical parameters.

Trends in the Orbital Coefficients and Energies of Thiocarbonyls.—Orbital energies. The energies of orbitals of principal interest for the thiocarbonyl fragment, namely the π_{CS} level, the sulphur *p*-type lone pair (HOMO), and the π^*_{CS} orbital (LUMO) are shown schematically in Figure 1. In the parent thioformaldehyde the π^*_{CS} orbital energy is 1.50 eV lower than that calculated for the π^*_{CS} orbital of formaldehyde. On the other hand, both the HOMO and the π_{CS} orbitals are calculated to be higher in energy than the corresponding orbitals in


(1)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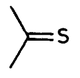
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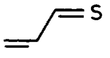
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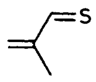
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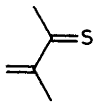
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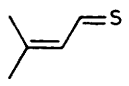
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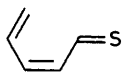
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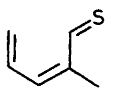
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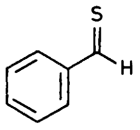
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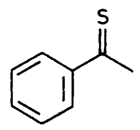
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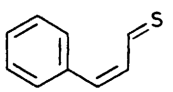
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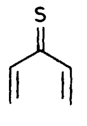
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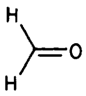
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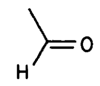
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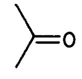
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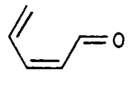
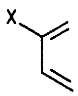
(17)


(18)

(19) X = CN
(20) X = $\mathrm{COOCH_3}$
(21) X = $\mathrm{COCH_3}$
(22) X = $\mathrm{CH{=}CH_2}$
(23) X = $\mathrm{OCOCH_3}$
(24) X = $\mathrm{OCH_3}$

(25) X = $\mathrm{NH_2}$
(26) X = OH
(27) X = $\mathrm{CH_3}$
(28) X = CN
(29) X = CHS



(30) X = OH
(31) X = $\mathrm{CH_3}$
(32) X = CN
(33) X = Cl

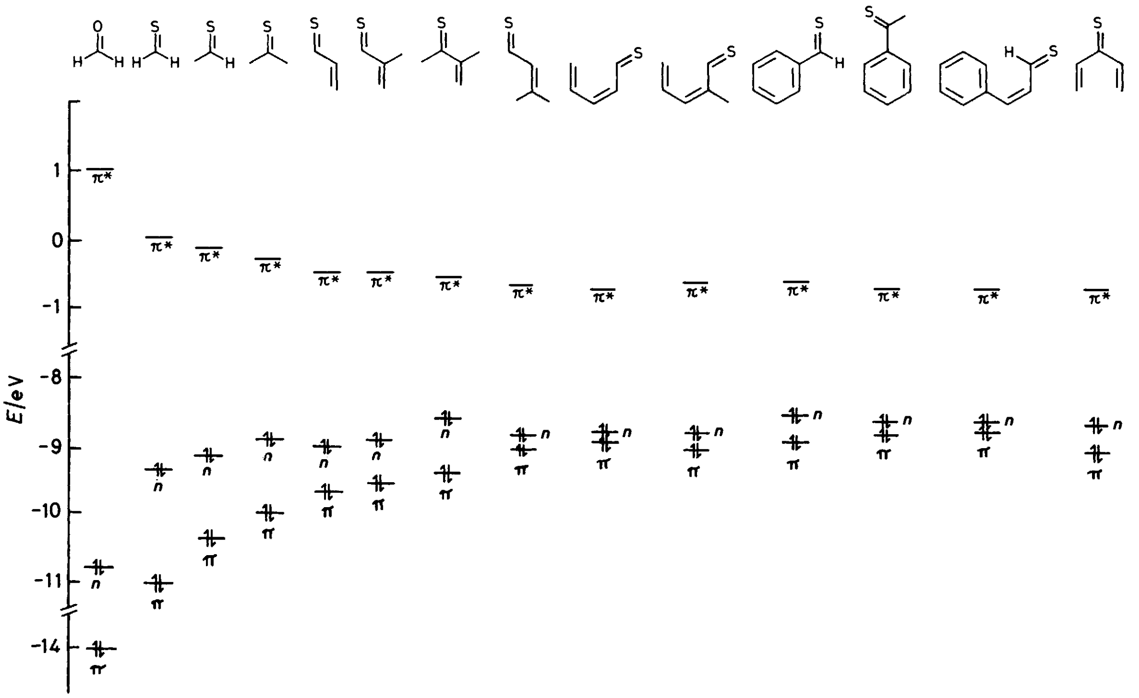
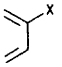
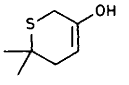
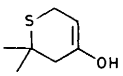
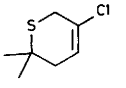
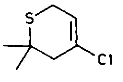
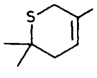
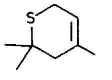
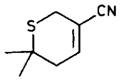
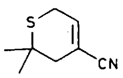


Figure 1. Schematic representation of the energy levels (eV) of key MOs of thiones. The occupancy indicated corresponds to the ground state in each case

Table 2. Energy gaps of the frontier orbital interactions (eV), the preferred interaction, and the possible and predicted regioisomers for the thermal cycloaddition of thioacetone and 2-substituted butadienes

Diene  X =	ΔE_1 [T(H)-D(L)]/ eV	ΔE_2 [T(L)-D(H)]/ eV	Perferred interaction	Possible regioisomers		Preference in regioisomers
OH	11.05	8.43	T(L)-D(H)	 (39a)	 (39b)	(39b) ≫ (39a)
Cl	10.69	9.05	T(L)-D(H)	 (40a)	 (40b)	(40b) ≫ (40a)
CH_3	11.01	8.76	T(L)-D(H)	 (41a)	 (41b)	(41a) > (41a)
CN	10.68	8.89	T(L)-D(H)	 (42a)	 (42b)	(42b) > (42a)

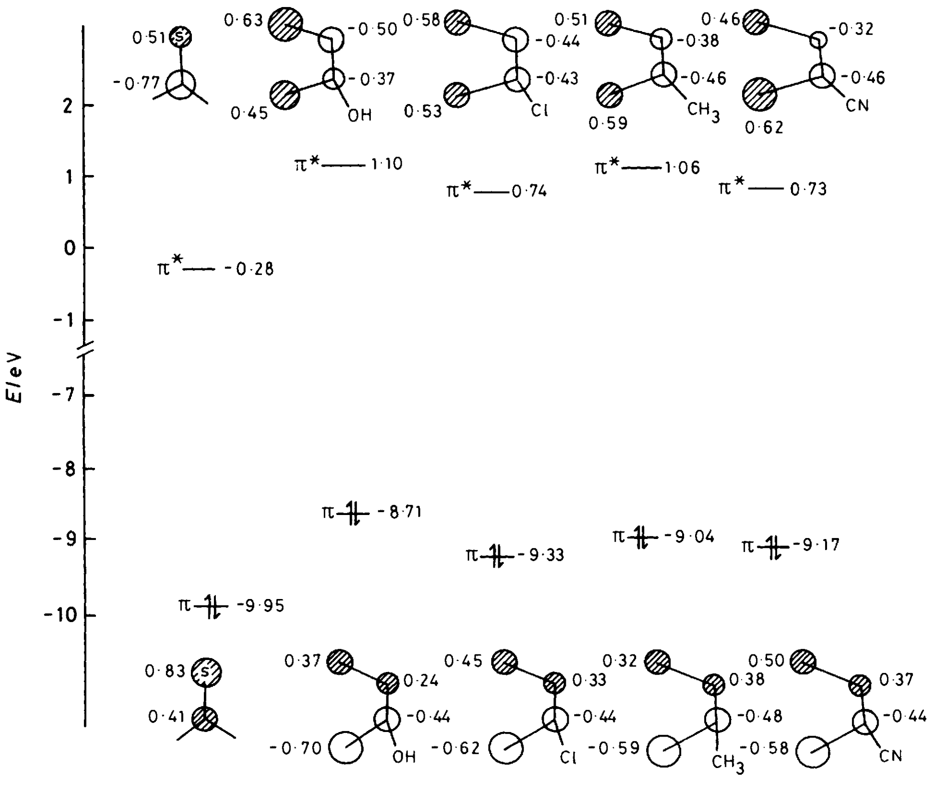


Figure 2. The energies (eV) and coefficients of the frontier orbitals involved in the [4 + 2] cycloaddition between thioacetone and 2-substituted dienes

formaldehyde by 1.44 and 3.35 eV, respectively. These trends are in qualitative accord with experimental observations.[9] Thiocarbonyl compounds are both more electrophilic (lower LUMO) and more nucleophilic (high HOMO) than carbonyl compounds.

The substituent effects on these orbital energies are in general accord with substituent effects on alkenes and carbonyl compounds.[10] Electron-donating groups raise the π_{CS} orbital the most and lower the π^*_{CS} orbital to a lesser extent (Figure 1). Conjugating substituents, such as the vinyl group, produce similar shifts, although the effect is more dramatic on the π^*_{CS} level. Extending the conjugation does not alter the π^*_{CS} energy appreciably although the π_{CS} level is raised. Electron-donating groups on conjugated thiones raise the π_{CS} energy even further.

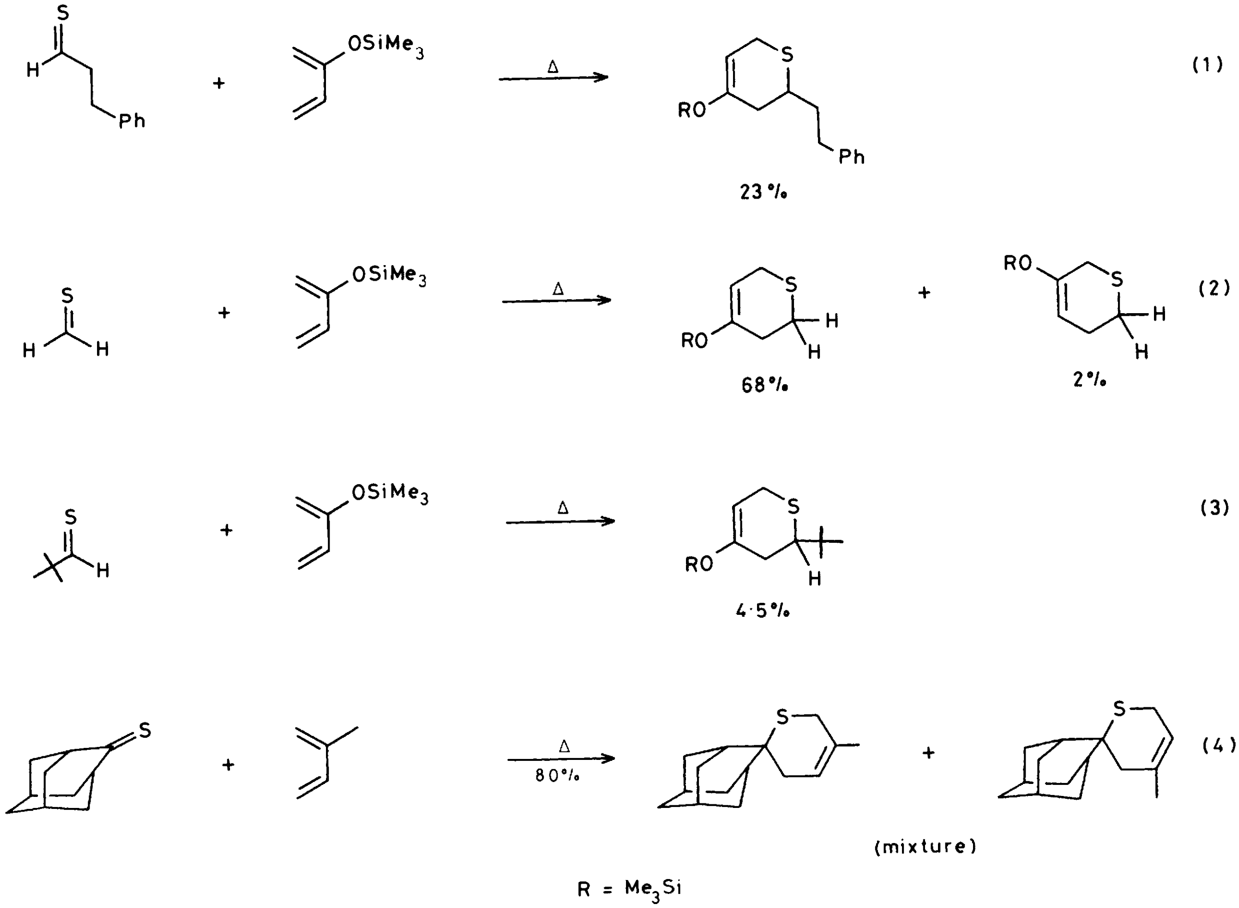
Orbital Coefficients.—The atomic orbital coefficients of the π_{CS} and π^*_{CS} orbitals of thioformaldehyde are highly unsymmetrical (Table 1). The coefficient on sulphur is large in the π orbital, while the π^* orbital exhibits an opposite polarization. While this trend is similar to that in formaldehyde, substituents affect these polarizations in substantially different ways. Electron-donating substituents such as the methyl group do not alter the coefficients on the S atom in either the π or the π^* orbital. On the other hand, conjugating substituents reduce the LUMO polarization by decreasing the coefficient on the thiocarbonyl carbon to an appreciable extent. In addition, conjugating substituents increase the π_{CS} polarization by decreasing the coefficient of the thiocarbonyl carbon. The effect of additional alkyl groups on conjugating thione π coefficients is negligible.

The above trends in the orbital polarization and energies of thiocarbonyl compounds obtained in our study are in fair agreement with *ab initio* results of Houk *et al.*[5] wherever a comparison is possible.

Thermal [4 + 2] *Cycloaddition Reactions of Thiocarbonyls.—Case* 1: *reaction between thiones and* 2-*substituted dienes.* Several cycloadditions which fall under this category have been studied experimentally.[5,11] Of these, reactions involving 2-trimethylsiloxybuta-1,3-diene (the Danishefsky diene) have received special attention. In order to predict the regiochemistry for this set of reactions, we utilised eigenvalues and orbital coefficients of thioacetone (**3**), 2-methylbutadiene (**31**), 2-hydroxybutadiene (**30**), 2-chlorobutadiene (**33**), and 2-cyanobutadiene (**32**) (Figure 2).

Of the two possible stabilizing two-electron interactions, that involving the thione (T)LUMO and the diene (D)HOMO is predicted to be more dominant on the basis of the small orbital energy gap (Table 2) for all the systems considered. Furthermore, the D(HOMO) polarisation is also qualitatively similar in all cases. As is well known, 2-donor substituents in a diene affect the π bond to which they are directly attached more than the remote double bond.[10] The coefficient at C-1 is therefore considerably greater than at C-4. The differential polarization at these two centres is a direct function of the π donor ability of the substituent. As a result, the regioisomer **b** is preferred over **a** (Table 2), the preference being the greatest for OR substituents. Weakly π donating halide and alkyl groups as well as the π acceptor cyano groups (which influence the LUMO more than the HOMO) are indicated to give a mixture of regioisomers **a** and **b** with a slight excess of **b**.

Related cycloaddition reactions which have been well studied experimentally[5,11] are shown in Scheme 1. These results are uniformally compatible with the above predictions. Thus the preferred regioisomer in the reaction with Danishefsky diene [equations (1)—(3), Scheme 1] is similar to the one predicted for 2-hydroxybutadiene. In the case of the reaction between adamantanethione and isoprene [equation (4)],[11] the lack of



R = Me$_3$Si

Scheme 1.

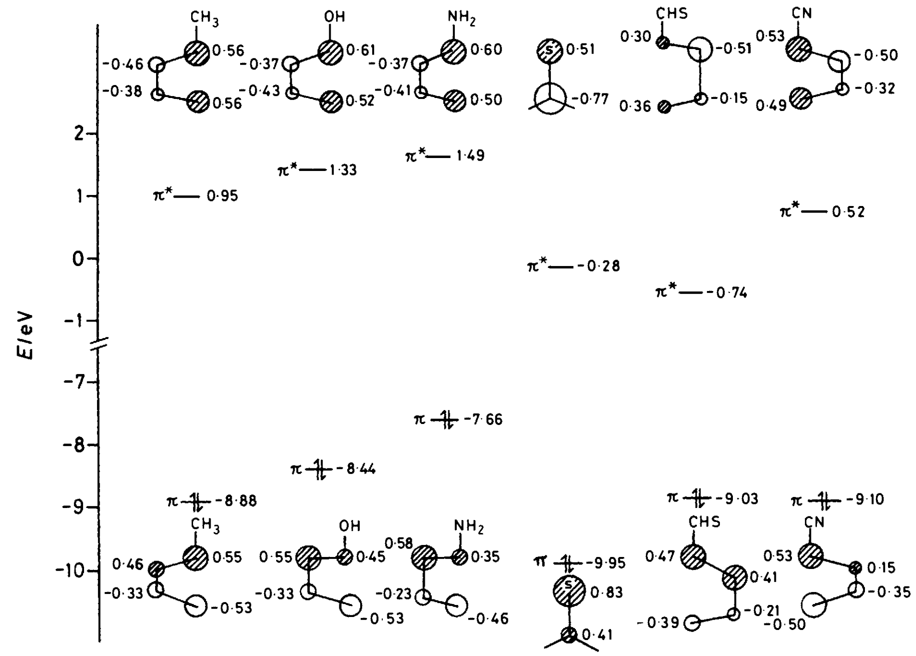
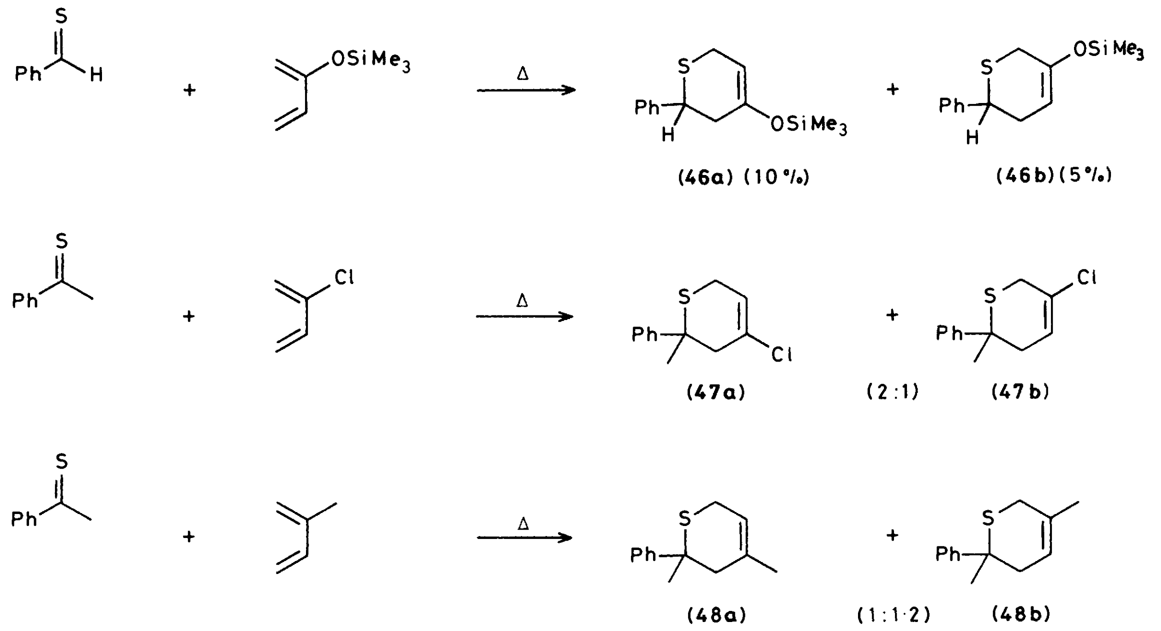


Figure 3. The energies (eV) and coefficients of the frontier orbitals involved in the [4 + 2] cycloaddition between thioacetone and 1-substituted dienes

much regioselectivity is in accord with the reduced orbital polarization calculated for the 2-methyl substituent (Figure 2).

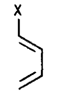
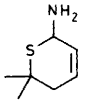
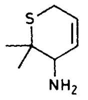
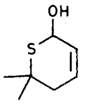
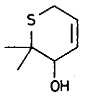
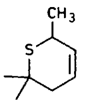
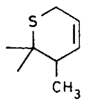
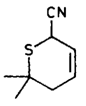
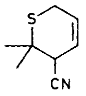
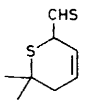
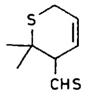
It is interesting to compare the present results with earlier theoretical examination of these systems. The regioselectivity for the reaction involving the Danishefsky diene was correctly predicted by the *ab initio* calculation of Houk *et al.*[5] However, CNDO/2 calculations for equation (4) (Scheme 1) predicted only one isomer, in disagreement with experiment.[11] It was found necessary to invoke additional geometric factors to account for the formation of both isomers. These comparisons suggest that the use of MINDO/3 orbital energies and coefficients with fully optimized geometries represent a reliable and adequate model to predict the regioselectivity of thione cycloaddition reactions.

Interestingly, the frontier orbitals of arylalkyl thione and saturated thiones are polarized in the same direction, although the degree of polarization is less for the former (Table 1). Therefore, the trends in the product distribution for the reactions of arylalkyl thiones with dienes should parallel those predicted for saturated thiones, but with reduced selectivity. Comparison of the observed regioselectivity in the cycloaddtion reactions of arylalkyl thiones with 2-substituted dienes (Scheme 2)[12] with the corresponding data for saturated thiones (Scheme 1) confirms the above prediction.



Scheme 2.

Table 3. Energy gaps of the frontier orbital interactions (eV), the preferred interaction, and the possible and predicted regioisomers for the thermal cycloaddition of thioacetone and 1-substituted butadiene

Diene  X =	ΔE_1 [T(H)–D(L)]/ eV	ΔE_2 [T(L)–D(H)]/ eV	Preferred interaction	Possible regioisomers		Preference in regioisomers
NH_2	11.44	7.38	T(L)–D(H)	 (34a)	 (34b)	**(34a)** ≫ **(34b)**
OH	11.28	8.16	T(L)–D(H)	 (35a)	 (35b)	**(35a)** ≫ **(35b)**
CH_3	10.90	8.60	T(L)–D(H)	 (36a)	 (36b)	**(36a)** ~ **(36b)**
CN	10.47	8.82	T(L)–D(H)	 (37a)	 (37b)	**(37b)** ≳ **(37a)**
CHS	9.21	8.75	T(L)–D(H) T(H)–D(L)	 (38a)	 (38b)	**(38b)** ≫ **(38a)**

Case 2: reactions between thiones and 1-substituted dienes. Prompted by the success of the PMO analysis in predicting the regioselectivity of cycloaddition reactions between thiones and 2-substituted dienes, we have extended our investigation to the reactions involving 1-substituted dienes although they have not so far been studied experimentally. The present analysis leads to unequivocal predictions of regiochemistry in these additions and should therefore be of considerable interest for future experimental work.

Three kinds of 1-substituted diene have been considered: butadiene with a donor (NH_2, OH, CH_3), acceptor (CN), and conjugating substituent (CHS). The calculated eigenvalues and eigenvectors of the π(HOMO) and π*(LUMO) in these molecules are provided in Figure 3. The data for the reactant partner, thioacetone, are shown in the middle.

1-Donor substituents destabilize both the HOMO and LUMO of a diene, especially the former. Therefore, the interaction between D(HOMO) and T(LUMO) is clearly favoured in such systems (Table 3). The LUMO of thioacetone is strongly polarized towards the thiocarbonyl carbon. In the π(HOMO) of the diene, the donor group tends to increase the coefficient at C-4 relative to C-1. Therefore, a single regioisomer with the donor group close to sulphur is predicted (Table 3). Since the increase in the π-orbital energy as well as the difference between C-4 and C-1 coefficients follow the order $CH_3 < OH < NH_2$, the regioselectivity of cycloaddition of the corresponding 1-substituted diene should follow a similar trend. Interestingly, the other possible stabilizing frontier orbital interaction, D(LUMO)–T(HOMO), also leads to the same regioselectivity. We can therefore safely conclude that thermal cycloaddition reactions between 1-donor substituted dienes and thioacetone are highly regioselective, particularly if the substituents are strong π-donor groups.

The effect of an acceptor group at the 1-position of the diene is to decrease the energy of both the π-HOMO and π-LUMO. Therefore, cycloaddition of dienes such as 1-cyanobutadiene to olefins has generally been considered as an example of Diels–Alder reactions with inverse electron demand.[13] However, in the present case of reaction with thioacetone, the major interaction still remains D(HOMO)–T(LUMO), with the alternative frontier orbital interaction characterized by a much larger energy gap (Table 3). Since the HOMO of 1-cyanobutadiene shows only a small difference in the coefficients at C-1 and -4, both regioisomers (**37a** and **b**) are expected, with a slight preference for the latter.

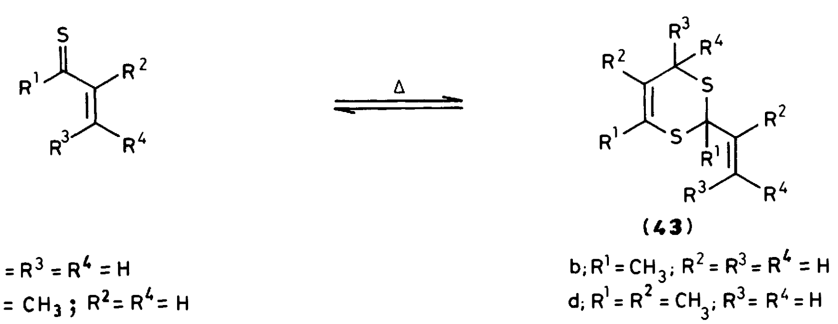
We have also considered the reaction between thioacetone and 1-thioformylbutadiene. There are several reactive sites in the latter molecule. If the diene unit is part of a cisoid ring system, it may prefer to function as the 4π-fragment of a cycloaddition with thioacetone. We analyse the regioselectivity of such a reaction in this case. Alternative modes of cycloaddition involving thioenone groups are considered later.

The thioformyl group reduces the energy of both π(HOMO) and π*(LUMO) of butadiene substantially. Both frontier orbital interactions, D(HOMO)–T(LUMO) and D(LUMO)–T(HOMO), are favourable to equal extents (Δ*E* 8.75 and 9.21 eV, respectively). In both the D(HOMO) and D(LUMO), the coefficients at C-1 and -4 differ by only a modest amount. However, the two favourable orbital interactions reinforce each other to lead to the product (**38b**) preferentially (Table 3).

As noted earlier, the frontier orbital polarizations for arylalkyl thiones parallel those of saturated thiones. Therefore, the conclusions drawn in this section are generally applicable for the reactions between arylalkyl thiones and 1-substituted dienes as well.

Case 3: *dimerization of* α,β-*unsaturated thiones.* One of the most interesting reactions among thermal cycloadditions of thiocarbonyls is the dimerization of α,β-unsaturated thiones. The characteristic feature of this cycloaddition is that the same species acts as both diene and dienophile. Potentially both the C=C and C=S units can act as the dienophilic partner. In each case two regioisomers are possible. Thus one would expect four possible dimers resulting from the dimerization of an α,β-unsaturated thione. For predicting the preferred product(s) both D(HOMO)–T(LUMO) and T(HOMO)–D(LUMO) interactions have to be considered, because these two energy separations are identical. Among the four possible orientations (Figure 4) the one which has a 1,3 S–S linkage would be the most preferred as a result of optimum matching of MO coefficients for both stabilizing interactions (Figure 5). Thus PMO theory predicts the exclusive formation of regioisomer (**44b**) for this reaction. This reaction was studied experimentally and the observed product orientation is the same as that predicted here (Scheme 3).[8] MO coefficients from an earlier *ab initio* study (STO-3G) failed to predict the observed regioselectivity of this reaction. It was found necessary to invoke a strong dependence of the relative magnitudes of C–C, C–S, and S–S interaction integrals on the geometry of the transition state.[8] It is gratifying that MINDO/3 formalism predicts the observed regioisomer (**43**) without such an involved argument.

It is to be noted that the analogous carbonyl compound, *i.e.* acrolein, undergoes dimerization to give an entirely different kind of product (Scheme 3). The present MINDO/3 study as also a few earlier PMO approaches[14] rationalize the observed orientation in this case. As seen from Figure 6, the C=C unit in acrolein prefers to be the dienophilic component leading to (**45a**) as the exclusive product (Scheme 4).



Scheme 3.

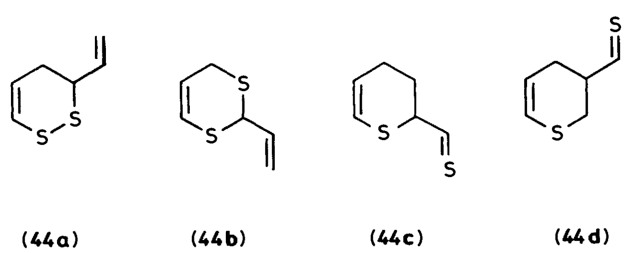


Figure 4. Possible orientations of addends in the dimerization of thioacrolein

Case 4: *cycloaddition between* α,β-*unsaturated thiones and dienes.* Although cycloadditions of this type have not received much attention experimentally, we have attempted to predict the course of these cycloadditions using frontier orbital interactions. The important stabilizing interactions, possible product orientations, and the preference in regioisomers are summarized in Table 4.

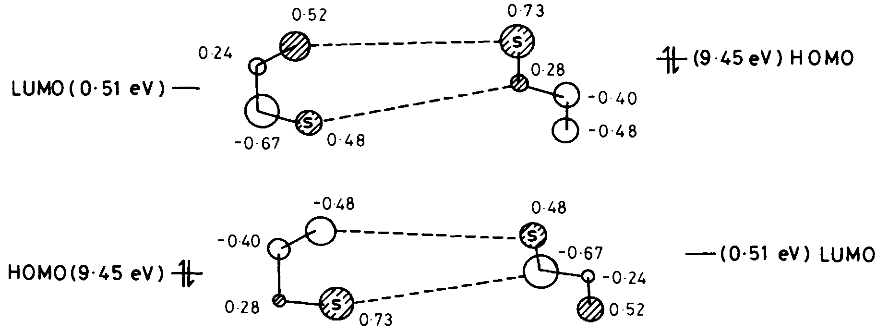
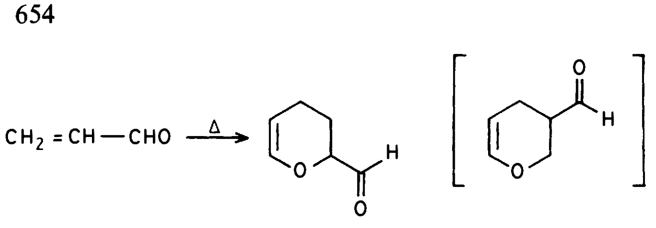


Figure 5. Frontier orbital interactions in the preferred orientation of the addends showing optimum coefficient matching



(45a) **(45b)**

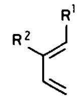
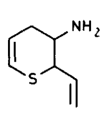
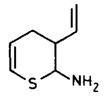
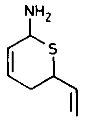
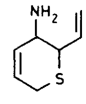
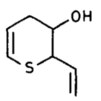
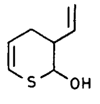
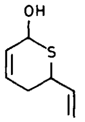
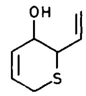
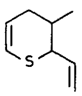
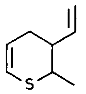
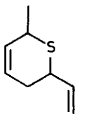
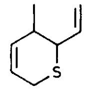
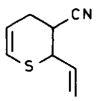
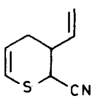
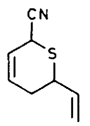
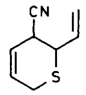
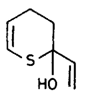
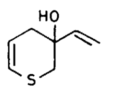
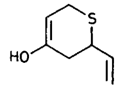
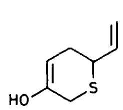
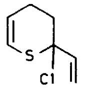
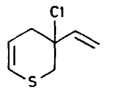
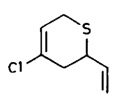
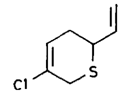
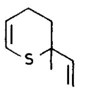
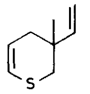
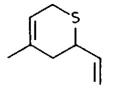
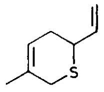
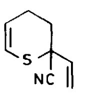
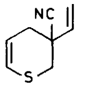
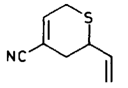
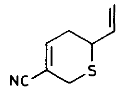
Not observed experimentaly

Scheme 4.

Since both reactions partners are 4π systems, different modes of [4 + 2] cycloadditions are possible. The reaction pattern would be influenced by the conformational restrictions placed on the thioenone and diene. Thus a thioenone locked in a transoid ring can function only as a dienophile. Orbital coefficients of the π and π* frontier MO clearly show that the C=S rather than the C=C fragment will act as the dienophile. In fact, the additional conjugation produces only a minor perturbation on the thione unit. Therefore, the preferred products in the reaction with 2- and 1-substituted dienes exactly parallel those derived in Cases 1 and 2 respectively. The predictions are summarized in the last column of Table 4.

If the conjugated thione is present in the cisoid form two types

Table 4. Energy gaps of the frontier orbital interactions (eV), the preferred interaction, and the possible and predicted regioisomers for the thermal cycloaddition of conjugated thione and dienes (both 1- and 2-substituted dienes)

 R^1(R^2 = H)/ R^2(R^1 = H)	ΔE_1 [CT(H)-D(L)]/ eV	ΔE_2 [CT(L)-D(H)]/ eV	Preferred interaction	Preferred regioisomers in the cycloaddition between thioenone and diene: 1 Conjugated thione as a diene partner	2 Conjugated thione as a dienophilic partner
R^1 = NH$_2$	11.14	7.15	CT(L)-D(H)	 ~ 	 > 
OH	10.98	7.93	CT(L)-D(H)	 ~ 	 > 
CH$_3$	10.60	8.37	CT(L)-D(H)	 ~ 	 ~ 
CN	10.17	8.59	CT(L)-D(H)	 ~ 	 ~ 
R^2 = H	10.75	8.20	CT(L)-D(H)	 ~ 	 > 
Cl	10.39	8.82	CT(L)-D(H)	 ~ 	 > 
CH$_3$	10.71	8.53	CT(L)-D(H)	 ~ 	 > 
CN	10.38	8.66	CT(L)-D(H)	 ~ 	 > 

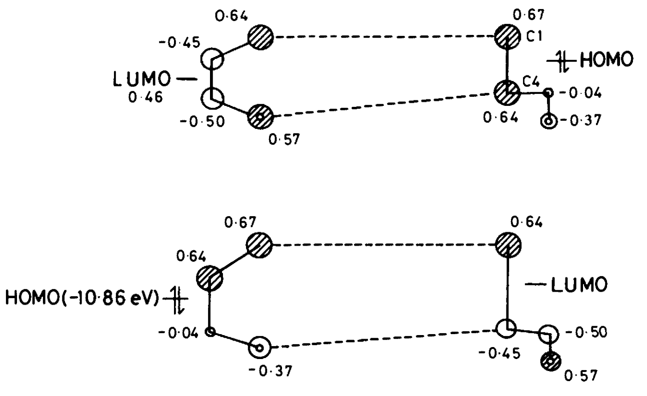


Figure 6. Frontier orbital interactions in the preferred orientation of addends showing optimum coefficient matching

of addition products can be expected. (1) The products resulting from the addition of conjugated thione to the substituted double bond of the diene and (2) the products resulting from the addition of conjugated thione to the unsubstituted double bond of the diene system. The frontier orbital interaction between the conjugated thione LUMO and the diene HOMO is clearly the dominant one, irrespective of the nature of substitution on the diene (Table 4). Based on the coefficients of relevant MOs, the addition is predicted to occur preferentially to the substituted double bond of the diene. Further, since the LUMO coefficients on the terminal atoms of the conjugated thione are nearly the same, the two possible regioisomers resulting from this addition should be formed to the same extent.

Photochemical [2 + 2] *Cycloaddition Reactions of Thioketones.*—Extensive studies by us[15] and others[16] have shown that the excited-state behaviour of thiocarbonyl compounds towards olefins is quite different from that of carbonyl analogues. We now attempt to rationalize the experimental observations concerning excited thioketones using PMO theory. The utility of PMO theory for explaining several features of Paterno–Buchi reactions has already been demonstrated.[17] The present study further establishes the usefulness of PMO theory in providing a unified description of photoreactivity preferences for another series of related molecules.

Cycloaddition reactions of excited alkyl, aryl, and α,β-unsaturated thiones with ground-state olefins are considered here. Both $n\pi^*$ and $\pi\pi^*$ reactivity have been examined. In each case, regioselectivity and, when different reaction centres are present, site selectivity are derived. The basis for the theoretical predictions is the general orbital interaction diagram involving an excited thione (T) and an olefin (Figure 7).

The interactions favouring the reaction between the $\pi\pi^*$ excited thione and the olefin are (i) a three-electron interaction between π(T) and π(O) and (ii) one-electron interaction between π*(T) and π*(O) (Figure 7). Both interactions have the correct orbital phase relationship for a concerted reaction. The reactivity would depend on the magnitude of the orbital energy gaps for these two pairs of MOs. The preferred regiochemistry can be predicted from the MO coefficients of these interacting orbitals.

For the reaction involving $n\pi^*$ excited thione and an olefin only one stabilizing interaction is possible; either (i) a three-electron interaction between *n*(T) and π(O) or (ii) a one-electron interaction between π*(T) and π*(O) (Figure 7). Simultaneous operation of the two interactions is precluded by the different orientations of the two sets of orbitals. Generally the former interaction dominates leading to diradical intermediates. The regiochemical outcome of the reaction is then determined simply by the relative stabilities of the diradicals.

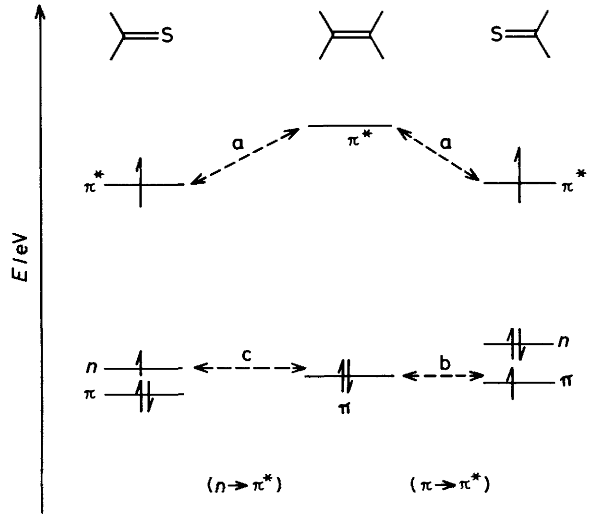


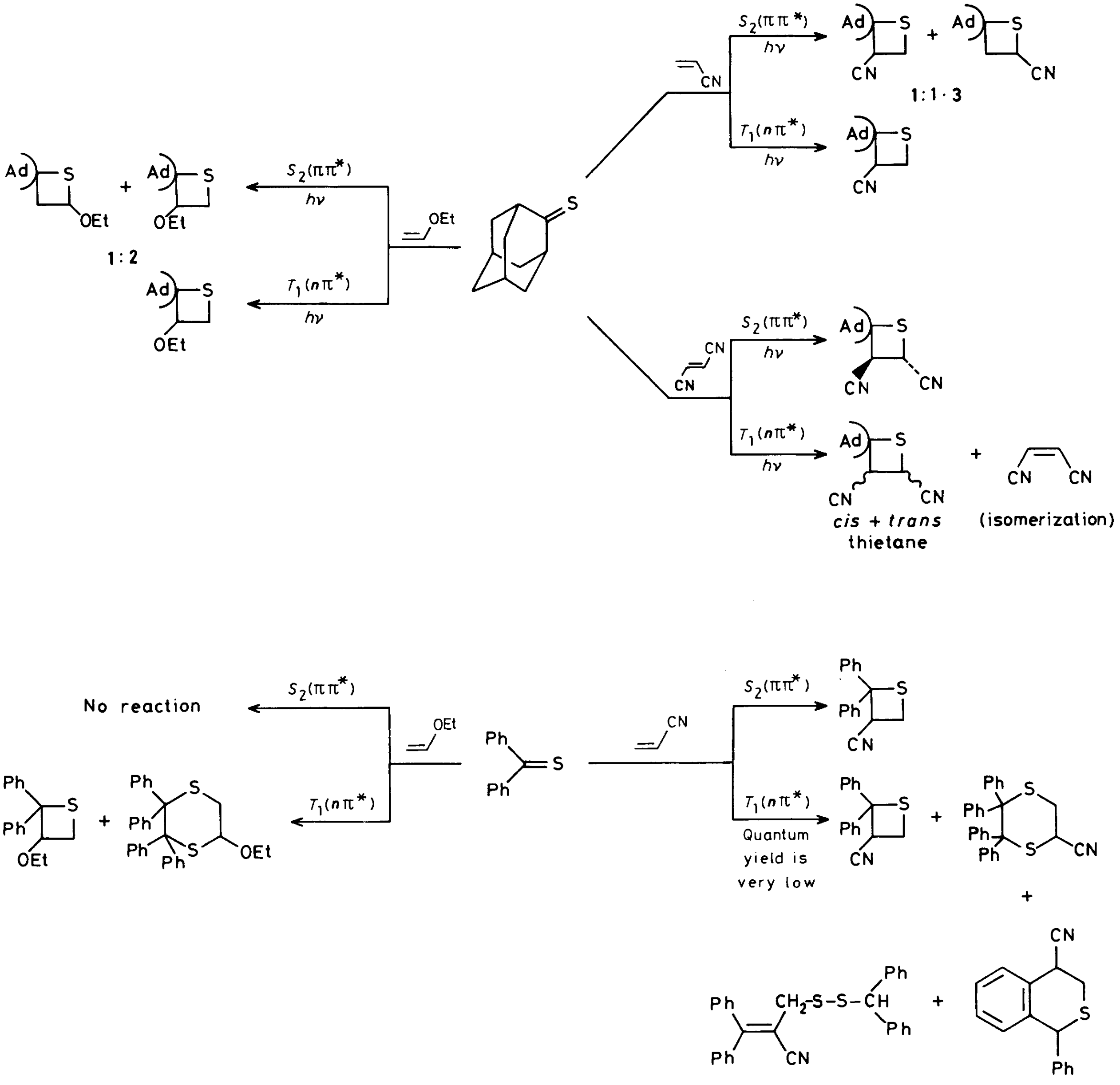
Figure 7. General interaction diagram showing possible stabilizing interactions in a photocycloaddition reaction between an olefin and a thione in its $n\pi^*$ and $\pi\pi^*$ excited states

A couple of serious assumptions in the present analysis should be made clear. The first of these is the utilization of ground-state eigenvalues and functions for predicting excited state reactivity. However, no simple alternative is evident. Use of eigenvalues and functions of singly occupied molecular orbitals of the excited state is one possibility. But even this choice may prove counterproductive since the approximations inherent in the semiempirical MINDO/3 procedures introduce a greater measure of unrealiability in the excited state eigenfunctions and -values.

The second serious assumption pertains to the multiplicity of the excited state involved. It is very difficult to differentiate between singlet- and triplet-state reactivities in a simple PMO analysis. However, all the reactions considered here involving the $\pi\pi^*$ excited state proceed *via* the singlet state, while those involving the $n\pi^*$ excited state correspond to the triplet state. It is therefore possible that a comparison between the reactivity of $n\pi^*$ and $\pi\pi^*$ states involves some error. However, the PMO model should prove reliable within a series of reactions involving exclusively $\pi\pi^*$ or $n\pi^*$ excited states. In particular, the regiochemical preferences (rather than relative rates) predicted for these photoreactions should be nearly as accurate as those obtained for the corresponding thermal reactions.

Dialkyl Thiones.—Saturated thiones such as adamantanethione and di-t-butyl thioketone have been reported to undergo cycloaddition reactions with both electron-rich and -deficient olefins to yield thietanes.[18] These reactions have been suggested to originate from both the second excited singlet state (S_2,$\pi\pi^*$) and the lowest triplet state (T_1,$n\pi^*$) (Scheme 5). The orbital interaction diagram for the photocycloaddition between a model saturated thione, thioacetone (T), and an electron-poor and -rich olefin (O) (acrylonitrile, AN; methyl vinyl ether, MVE) is shown in Figure 8. The regioselectivity preferences based on Figure 8 are discussed below.

Regioselectivity in $n\pi^*(T_1)$ *reaction.* From Figure 8 it is clear that among the two possible stabilizing interactions between the $n\pi^*$ excited thione and olefin, the major interaction is the one between the *n*-orbital of thione and the π-orbital of olefin. The result of such an interaction is to facilitate the formation of a diradical intermediate. The preferred product orientations are

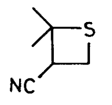


Scheme 5.

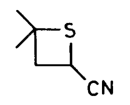
likely to be controlled by the relative stability of the diradicals. On this basis, products (**49a**) (in the reaction with AN) and (**50a**) (in the reaction with MVE) are expected to be formed preferentially. Experimental results (Scheme 5) are compatible with these predictions.

Regioselectivity in $\pi\pi^*(S_2)$ reactions. In the reaction between $\pi\pi^*$ excited thioacetone and acrylonitrile the matching of MO coefficients for the $\pi(T)$–$\pi(O)$ interaction predicts the regioisomer (**49a**) whereas that for the $\pi^*(T)$–$\pi^*(O)$ interaction favours the opposite regioisomer (**49b**). Since both the interactions are believed to be responsible in bringing about the cycloaddition, both the regioisomers are expected to be formed. The corresponding reaction has been studied experimentally using adamantanethione as the excited reactant and the observed regiochemistry is the same as that predicted here (Scheme 5).

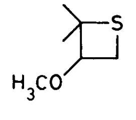
In the reaction between $\pi\pi^*$ excited thioacetone and methyl vinyl ether, both $\pi(T)$–$\pi(O)$ and $\pi^*(T)$–$\pi^*(O)$ interactions predict the regioisomer (**50a**). The corresponding regioisomer is indeed the major product in the experimentally studied cycloaddition between adamantanethione and ethyl vinyl ether (Scheme 5) although the sterically less hindered regioisomeric thietane is also observed in smaller amounts.



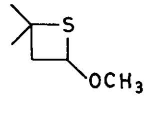
(**49a**)



(**49b**)



(**50a**)



(**50b**)

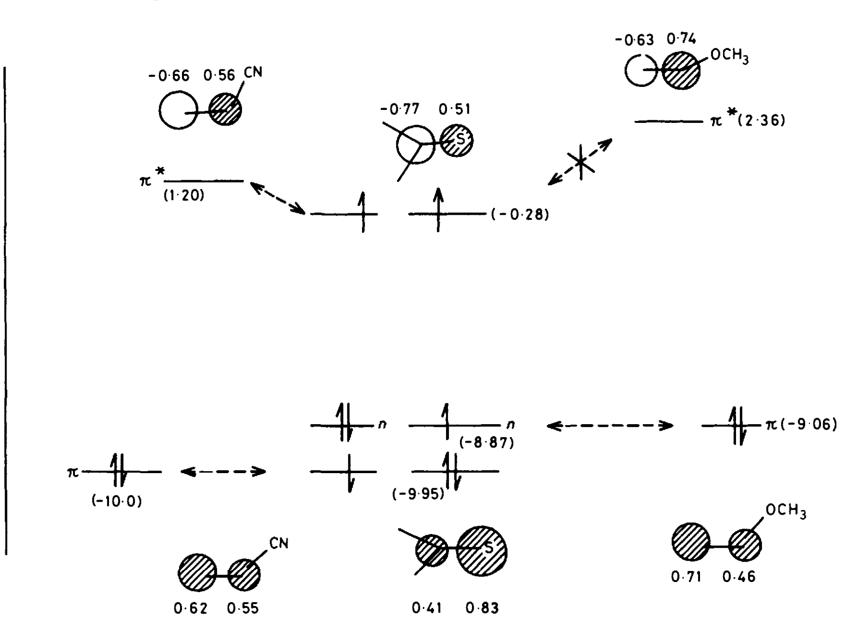
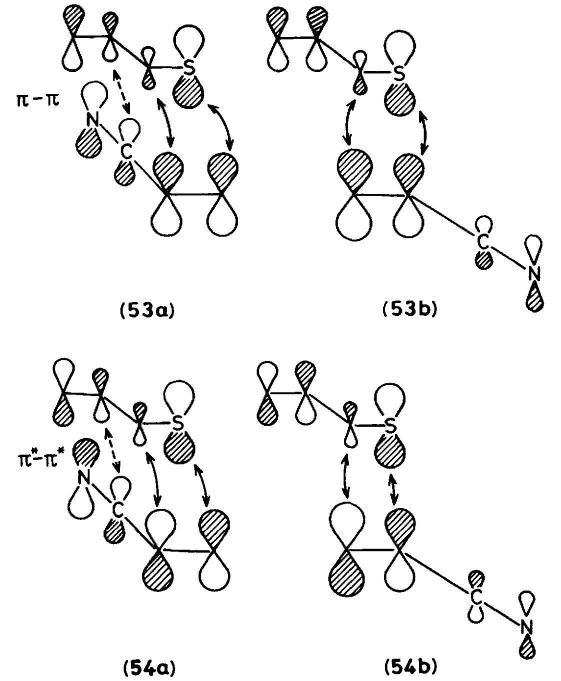


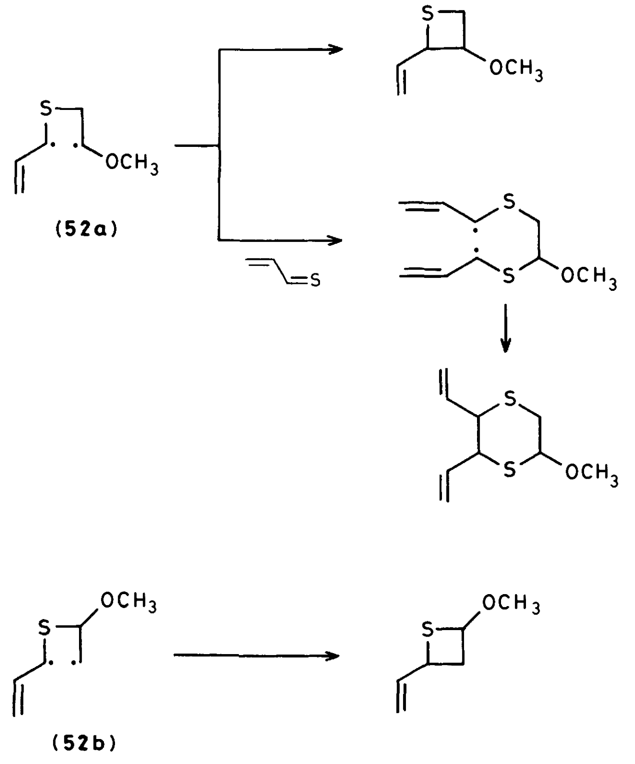
Figure 8. Interaction diagram for the photocycloaddition between thioacetone and acrylonitrile and methyl vinyl ether



(53a) **(53b)**

(54a) **(54b)**

Figure 9. Frontier orbital interaction in two orientations for the photocycloaddition between ππ* excited thioacrolein and acrylonitrile. Secondary orbital interactions are shown as dotted lines



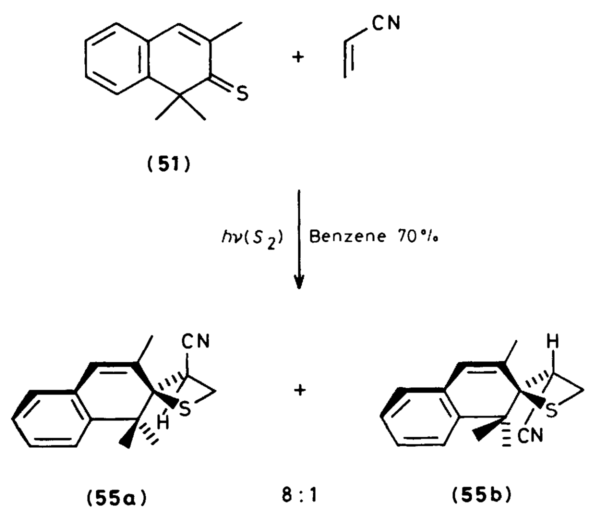
(52a)

(52b)

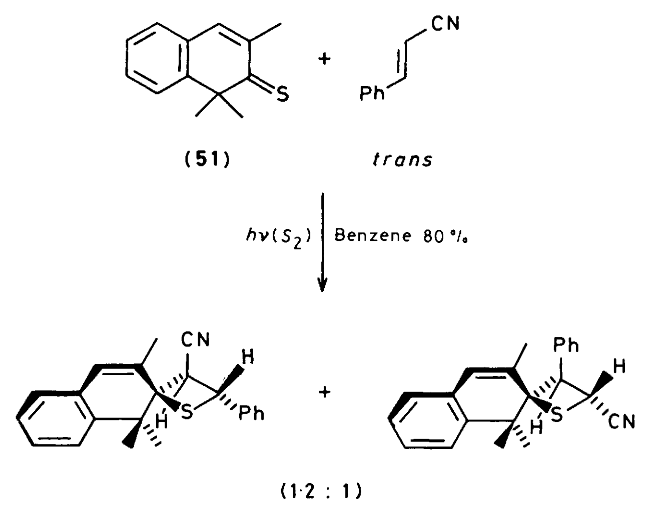
α,β-*Unsaturated Thiones.*—The orbital interaction diagram for the cycloaddition between a model thioenone, *viz.* thioacrolein, and an olefin (acrylonitrile, methyl vinyl ether) is shown in Figure 9. Clearly, the reactivity of the *n*π* state of the thione is dominated by the *n*(T)–π(O) interaction on the basis of the energy gap. Therefore, the stability order of the resulting diradicals determines the product distribution. For the reaction between thioacrolein and methyl vinyl ether, diradical (**52a**) is expected to be more stable than (**52b**). Experimentally,[19] the products observed in the reaction between *n*π* excited 1,1,3-trimethyl-2-thioxo-1,2-dihydronaphthalene (**51**) and ethyl vinyl ether are derived from a diradical smilar to (**52a**).

In the [2 + 2] photocycloaddition involving ππ* excited thioenone two reactive sites, C=C and C=S, are possible. Since both the π(HOMO) and π*(LUMO) have large coefficients on the C=S fragment the site selectivity is unequivocal in this case. Experimentally, photocycloaddition of (**51**) to acrylonitrile shows the same site selectivity exclusively.[20]

For the preferred cycloaddition reaction, two regioisomers are possible. Each of these in turn can have the vinyl and cyano substituents *cis* or *trans* to each other. The primary frontier



Scheme 6.



Scheme 7.

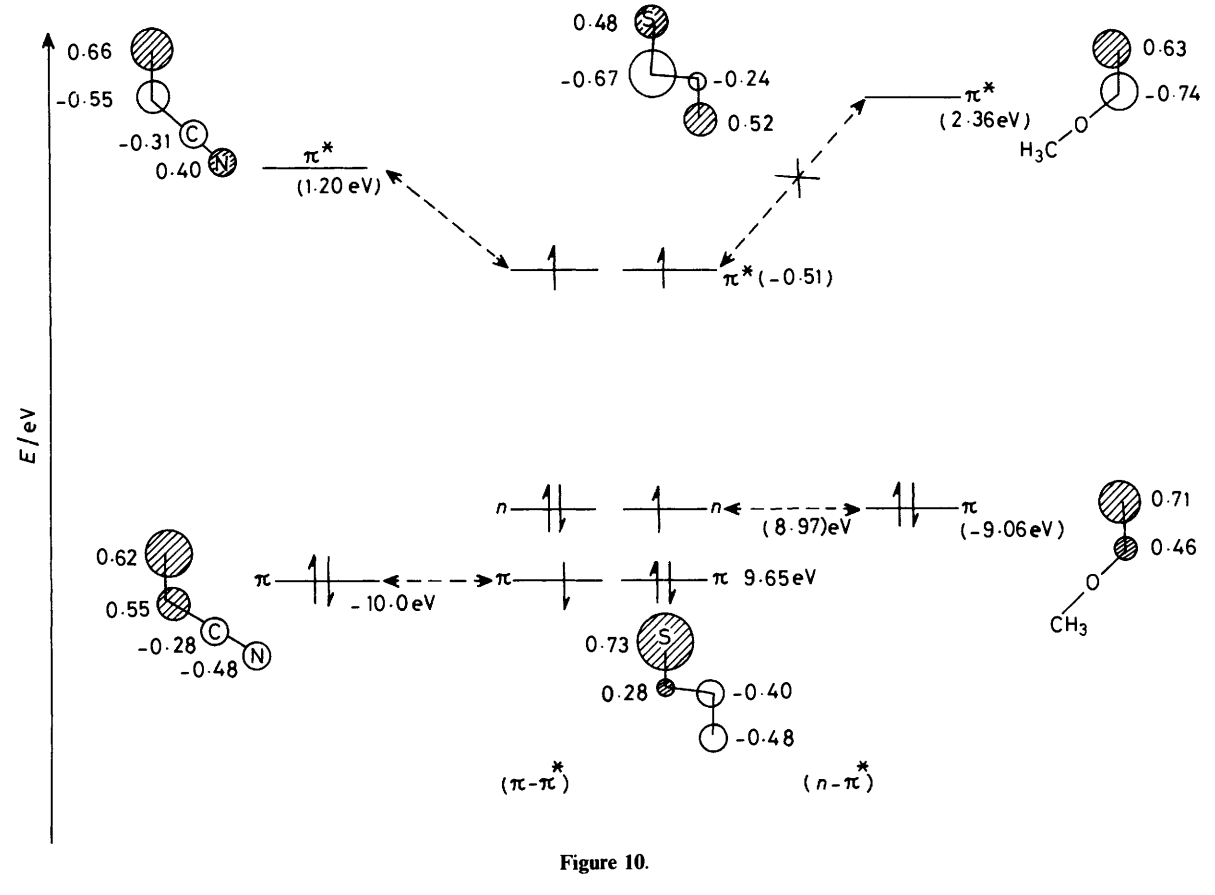


Figure 10.

orbital interactions at the four centres are not affected by the relative orientation of the substituents. The interaction of the π(T)–π(O) orbital pair is stabilizing to a larger extent in orientation (**53a**) compared with that of (**53b**). Therefore, the preferred thietane regioisomer should have the vinyl and cyano groups on adjacent carbon atoms (2,3-disubstituted thietane). On the other hand, the second frontier orbital interaction, π*(T)–π*(O), which is somewhat less effective due to a larger energy separation, favours the opposite regioisomer in which the cyano group is closer to sulphur (2,4′-disubstituted thietane). Experimentally, the photochemical cycloaddition between thione (**51**) and acrylonitrile leads to the exclusive formation of products corresponding to the former regioisomer. While this can be attributed to the dominance of π(T)–π(O) interaction over that of π*(T)–π*(O), another factor may also be responsible. A secondary interaction between the cyano and vinyl substituents is likely for both the π(T)–π(O) and π*(T)–π*(O) orbital pairs [see (**53a**) and (**54b**)]. The orbital phases are seen to be perfectly matched in these systems to produce an additional stabilization (Figure 10). Of course, such secondary orbital stabilization is possible only if the two 4π-addends are placed one above the other leading to the regioisomer with the substituents *cis* to each other. Interestingly, of the two products obtained in the experimental study [(**55a** and **b**), Scheme 6], the major isomer has the nitrile group oriented towards the olefinic bond (**55a**). This additional selectivity clearly supports the importance of secondary orbital interactions in these systems. Similar interactions are also expected in the reactions of an α,β-unsaturated thione with olefins having electron-withdrawing groups such as $COOCH_3$ and $COCH_3$. The MO coefficients at the carbonyl group in these substituents have a sizeable magnitude and the correct phase to lead to additional stabilization as in (**53a**) and (**54a**). The observed products are entirely consistent with this analysis. Furthermore, the observed regiochemistry in the cycloaddition of (**51**) with cinnamonitrile (Scheme 7) further provides evidence for the role of secondary orbital interactions in these systems.

The PMO analysis presented for thioenones are also applicable to diaryl thiones, since the frontier orbital energies and polarizations are similar in the two systems (Figure 1 and Table 1). This accounts for the parallel photochemical behaviour of diarylthiones (lower section of Scheme 5)[21] and thioenones.

Conclusions.—The PMO method in conjunction with MINDO/3 molecular orbital energies and coefficients is generally successful in rationalizing the regiochemistry of thermal and photochemical cycloaddition reactions involving thiocarbonyls. In particular, the indicated regiochemistry for (1) [4 + 2] cycloaddition reactions of saturated thiones and 2-substituted dienes, (2) the dimerization of α,β-unsaturated thiones, and (3) the photochemical cycloaddition reactions of saturated and unsaturated thiones are all in agreement with experimental observations. The present analysis also leads to unequivocal predictions of regiochemistry for the cycloadditions involving saturated, conjugated, and aryl thiones which have not yet been experimentally examined. Some of these results should therefore be of considerable interest for future experimental work. Special attention is drawn to the following predictions.

(1) Thermal cycloaddition reactions of saturated thiones and 1-donor substituted dienes should be highly regioselective.

(2) The dienophilic nature of transoid α,β-unsaturated thiones and aryl thiones should be similar to that of saturated thiones. Therefore, thermal cycloaddition reactions involving those thiones with 2-substituted dienes should exhibit parallel regioselectivities.

(3) Thermal cycloaddition of cisoid α,β-unsaturated thione to 1- or 2-substituted dienes should preferentially occur at the more substituted double bond of the diene, although regioselectivity is predicted to be low.

One of the most interesting cases examined in this study is the photocycloaddition of α,β-unsaturated thiones to olefins with electron-withdrawing substituents. The PMO model convincingly rationalizes the three levels of selectivity observed in such systems; the preferred reaction site (C=S *versus* C=C), regiochemistry of the products (2,3-disubstituted thietane *versus* 2,4′-disubstituted thietane), and the preferred orientation of the substituents (*cis versus trans*). The secondary orbital interactions invoked for these systems deserve to be tested and exploited by additional experimental and theoretical work.

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