1,2-Thiazines and Related Heterocycles. Part 3.[1] The Mechanism and Regioselectivity of the Cycloadditions of N-Sulphinylamino Compounds with Dienes

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A kinetic investigation indicates the mechanism of reaction of ethyl N-sulphinylcarbamate with 1,1'-bicyclohexenyl to be pericyclic. It is argued that N-sulphinylamino compounds, in general, cycloadd to dienes by a similar mechanism. Contradictions in the literature concerning the regioselectivity shown in the reactions of N-sulphinylamino compounds with unsymmetrical dienes are resolved. The suitability of Hückel frontier orbitals in accounting for observed regioselectivities is investigated. For the systems studied it is possible to define regioselectivity ratios for the reactions which are independent of the nature of the transition state. A consideration of the regioselectivity ratios given by various parameterisations of the NSO group, together with the probable nature of the transition state, shows that the regioselective behaviour of sulphinylamino compounds is comprehensible in the frontier orbital approximation.

The cycloadditions of N-sulphinylamino compounds such as PhN=S=O to dienes yielding 1,2-thiazine S-oxides were discovered more than 30 years ago by Wichterle and Roček.[2,3] The chemistry of these and related heterocumulenes have been reviewed by various authors.[4-9] In most of the literature it is implicit in the terminology, e.g. the use of dienophile and Diels–Alder,[4,9-11] that a pericyclic mechanism of cycloaddition is understood and some authors[10,11] are explicit in their assumption. There appears, however, to be a dearth of quantitative evidence and, moreover, contradictions among those authors who have specifically considered mechanism. Macaluso and Hamer[12] investigated the reversible cycloaddition of N-sulphinylbenzenesulphonamide, PhSO₂N=S=O, with cyclopentadiene and determined the equilibrium constant at various temperatures. The derived thermodynamic parameters fell 'within the general pattern' of Diels–Alder reactions. Mock and Nugent[13,14] investigated the cycloaddition of N-sulphinyltoluenesulphonamide with the isomeric hexa-2,4-dienes: although the E,E- and E,Z-diastereoisomers gave cycloadducts which were stereochemically consistent with a pericyclic mechanism, since the highly sterically overcrowded Z,Z-diastereoisomer did not, these authors opted for an economy of mechanism and inferred a dipolar two-step path for all the cycloadditions.

A two-step mechanism of cycloaddition involving electrophilic attack by sulphinyl sulphur on the most nucleophilic double bond of the diene could, for example, account for the regioselectivity reported[15] for reaction (i) of Scheme 1 but not so that in reaction (ii).[16] It has also been shown[17] that the kinetic product of a cycloaddition is not necessarily the thermodynamically (sterically) preferred product [Scheme 1, reaction (iii)] which implies an electronic control of the regioselectivity.

The opposite regioselectivities reported for reactions (i) and (ii) of Scheme 1 were inferred by Soviet workers[15,16] from the structure of the but-3-enylamines obtained on hydrolysis of the cycloadducts [reaction (iv)]. In general, the butenylamines were isolated and characterised and the distinction between possible isomers made on the basis of the i.r. absorptions of their different vinyl groups. Interestingly, Sasaki et al.[18] found PhN=S=O to add to myrcene with the opposite orientation to that found for isoprene by Kataev and Plemenkov;[16] it is surprising that variation of the structure of the diene C(2) alkyl group should apparently change the orientation of addition. Also, the isolation of principal adducts for characterisation,
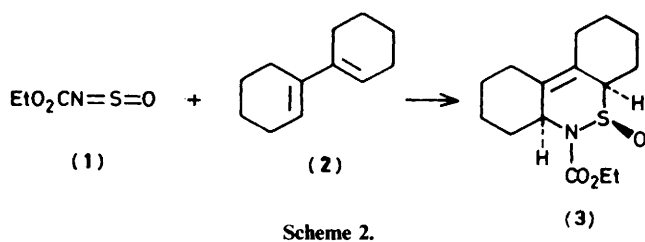
Scheme 1.

Scheme 2.

(4)   (5)
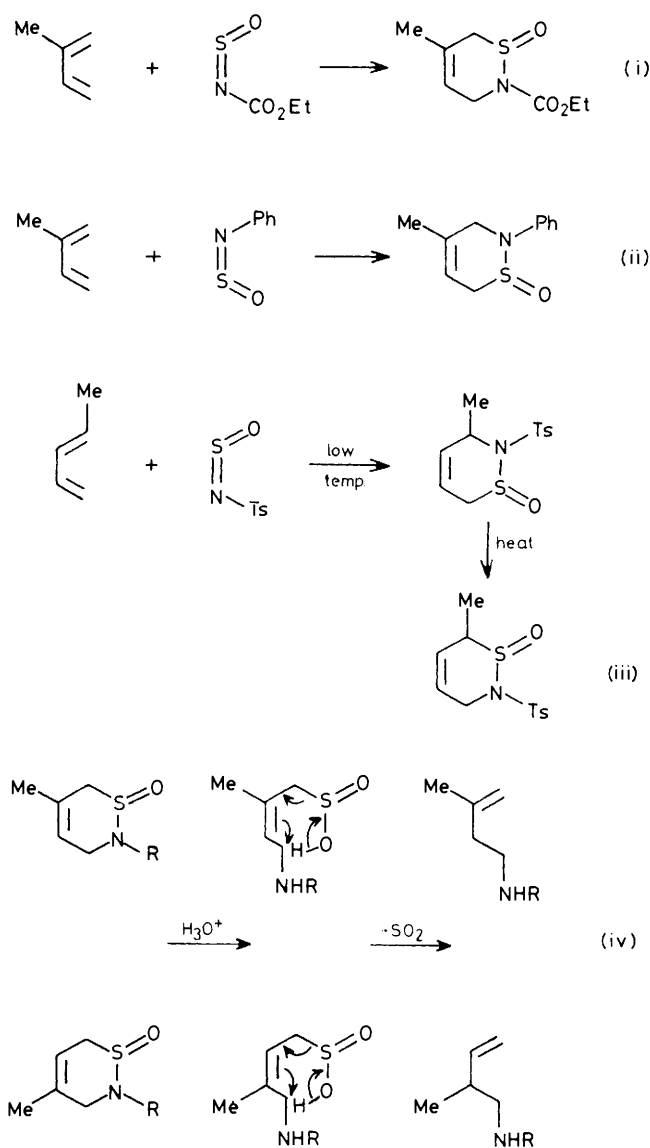
Table 1. Kinetic results for the cycloaddition of ethyl N-sulphinyl-carbamate to 1,1'-bicyclohexenyl

Solvent	T/K	$10^2 k/$ $dm^3 mol^{-1} s^{-1}$	Activation parameters
C_6H_6	281.2	0.79 ⎤	$\Delta S^{\ddagger}$ −176.9 J K^{-1} mol^{-1}
(2.28)[a]	288.2	1.06 ⎪	
	298.2	1.80 ⎬	$\Delta H^{\ddagger}$ 30.3 kJ mol^{-1}
	308.2	2.60 ⎪	
	318.2	3.99 ⎦	$\Delta G^{\ddagger}$ 83.0 kJ mol^{-1} at 298 K
$C_2H_4Cl_2$ (10.65)[a]	281.2	2.99	

[a] Dielectric constant at 20 °C; source: 'American Institute of Physics Handbook,' McGraw-Hill, New York, 1957, 2nd. edn., table 5d—7.

together with the instrumental limitations 20—30 years ago, leads to the impression that the cycloadditions of interest are regiospecific. This is unlikely, whatever their mechanism, since 2-methylation of buta-1,3-diene is only a minor perturbation. The investigation described below is intended to clarify these various observations.

Results and Discussion

(a) *The Cycloaddition of Ethyl* N-*Sulphinylcarbamate to* 1,1'-*Bicyclohexenyl.*—(i) *Choice of reactants.* Although N-sulphinylsulphonamides are readily prepared by reaction of a sulphonamide with $SOCl_2$, their distillation to purity requires inconveniently high vacua.[4] We therefore chose to use ethyl N-sulphinylcarbamate (1); this material is equally readily prepared, from urethane, and is easily fractionated.[19,20] The substituent, CO_2Et, on the sulphinylamino group is of an electronic character comparable with $ArSO_2$ and should confer a similar electrophilicity; the regioselectivity in cycloaddition of N-sulphinylcarbamates to unsymmetrical dienes parallels that of N-sulphinylsulphonamides.[4,15]

For the diene component of the reaction we took 1,1'-bicyclohexenyl (2).[21] This was chosen for its symmetry, which circumvents problems of regioselectivity, and for its convenient gas-chromatographic retention time, g.l.c. being the method of analysis selected for monitoring the progress of reaction. Each of the carbons of the diene in (2) is 'alkylated' and thus (2) should be rather more reactive towards electrophiles than the hexa-2,4-dienes. We expect, therefore, that our reactants should have a propensity for two-step mechanism at least as great as those of Mock and Nugent.[13]

(ii) *Nature of the product.* Although, in principle, the cycloaddition of (1) and (2) could lead to diastereoisomeric products differing in relative configurations at S and the ring-junction carbon atoms, the reaction in fact occurs cleanly to give a single adduct (3) whose structure has been determined.[22] The S–O bond is *trans* to both of the ring junction C–H bonds.

(iii) *Kinetics.* The reaction of (1) and (2) in benzene was found to be of first order in each reactant. For rate measurements they were allowed to react in equimolar concentrations, the course of reaction being followed by observing the decrease in
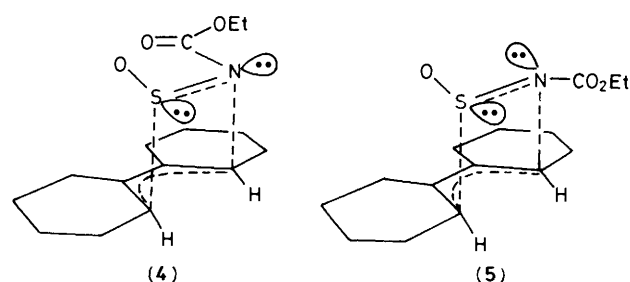
concentration of (2) with time relative to an internal standard. The rates obtained for reaction in different solvents and at different temperatures are presented in Table 1 together with derived activation parameters.

The results are characteristic of a pericyclic reaction: the entropy of activation is typically of large negative magnitude and the enthalpy of activation, amounting to 36% of the free energy of activation, is small. These imply a highly ordered, early transition state in which occurs a concerted making and breaking of bonds. The solvent effect, shown for a moderate increase in solvent polarity, is small, indicating little separation of charge in the transition state, again consistent with pericyclic character. (We attempted to obtain rate measurements in both acetonitrile and nitromethane without success. Despite careful drying, the dienophile was destroyed in these solvents which may indicate a reaction with solvent.)

(iv) *Mechanism.* The weight of evidence is that sulphinylamino compounds exist in their ground states in the *Z*-configuration about the N–S bond.[23–28] If ethyl N-sulphinylcarbamate enters a pericyclic transition state in this configuration the stereospecific product (3) requires an orientation of reactants as in (4); subsequent retention of configuration at S but ready inversion at N in the product is expected. If, however, the dienophile enters the transition state in the *E*-configuration, the stereospecific product requires there to be a strong preference for overlap of the sulphinyl group rather than of the ester group with the diene as in (5).

Since we have shown that an electrophilic sulphinylamino compound most probably cycloadds to an electron-rich diene by a pericyclic mechanism, we suggest that dienophiles of comparable electrophilicity, such as N-sulphinylsulphonamides, also cycloadd by the same mechanism. Mock and Nugent's[13] observations would then be explained by pericyclic reaction for the *E,E*- and *E,Z*-diastereoisomers of hexa-2,4-diene with a change of mechanism for the highly hindered *Z,Z*-diastereoisomer. Furthermore, less electrophilic compounds such as N-sulphinylanilines, which cycloadd, would also be expected to do so by the concerted route.

(b) *Regioselectivity of Addition of* $EtO_2CN=S=O$ *and* $PhN=S=O$ *to Isoprene.*—(i) $EtO_2CN=S=O$. The N-sulphinylurethane and isoprene were stirred in dry benzene at ambient temperature for 72 h. After removal of the solvent the residue, an oil which corresponded to a quantitative yield of adduct, was examined by ^{13}C n.m.r. spectrometry; it clearly comprised two isomers in proportions of *ca.* 13 : 1 as estimated from the relative intensities of the resonances of the heterocyclic methylene carbons which showed significantly different chemical shifts between the two isomers (see Experimental section). The major isomer was isolated by vacuum distillation and hydrolysed in aqueous acid to give an N-(but-3-enyl)urethane which manifested the expected pair of alkenic carbon resonances. In an off-resonance experiment one of these showed a triplet splitting and the other a singlet. This clearly indicates the hydrolysate to be N-(3-methylbut-3-enyl)urethane confirming that the major adduct of $EtO_2CN=S=O$ and isoprene is 2-

ethoxycarbonyl-5-methyl-3,6-dihydro-1,2-thiazine 1-oxide as indicated in Scheme 1, reaction (i).

(ii) PhN=S=O. N-Sulphinylaniline and an excess of isoprene were mixed and stored, at ambient temperature but protected from moisture, for 3 weeks. On chilling, a solid adduct separated which was isolated and washed with cyclohexane. The product, on examination by ^{13}C n.m.r. spectrometry, clearly showed the presence of two isomers in proportions of 2:1. Comparison of the ^{13}C n.m.r. spectra of these adducts with those from $EtO_2CN=S=O$ and isoprene also clearly indicated the major isomers obtained from the two dienophiles to be similar as were the two minor isomers. It was shown in an additional experiment where PhN=S=O was treated with isoprene at 70 °C that the proportion of minor adduct increased, so confirming the mixture obtained at ambient temperature to be the kinetic product. It was also shown, by comparing the single adducts obtained from the two dienophiles with 2,3-dimethylbuta-1,3-diene, that the carbon resonances of the 3,6-dihydro-1,2-thiazine 1-oxide heterocycle are insensitive to the nature of the N-substituent. It follows, therefore, from the similarity of the major adducts from the two dienophiles that both cycloadditions have the same regioselectivity and that that hitherto accepted for the reaction of PhN=S=O with isoprene [Scheme 1, reaction (ii)] is erroneous.

(c) *Prediction of Regioselectivity of Cycloaddition.*—(i) *The regioselectivity ratio.* Second-order perturbation theory gives equation (1) for the stabilisation ΔE which accompanies the interaction of the occupied orbitals of a molecule with the unoccupied orbitals of a co-reactant, and *vice versa*. In equation

$$\Delta E = \left(\sum_r^{occ} \sum_s^{unocc} - \sum_s^{occ} \sum_r^{unocc} \right) 2(\Sigma c_{ra}c_{sb}\beta_{ab})^2/(E_r - E_s) \quad (1)$$

(1) c_{ra} is the coefficient at atom a in molecular orbital r of the one reactant, c_{sb} is the coefficient at atom b in the molecular orbital s of the other reactant, β_{ab} is the resonance integral for the interaction in the transition state of the atoms a and b, and E_r and E_s are the energies of the molecular orbitals r and s.[29] The principal contributions to ΔE come from the interactions of those molecular orbitals which are close in energy, *i.e.* the frontier orbitals, as the denominators in equation (1) are then small. In the frontier orbital approximation, equation (1) is thus simplified to a two-term expression, the one corresponding to interaction of the HOMO of the diene with the LUMO of the dienophile and the other to the interaction of the LUMO of the diene with the HOMO of the dienophile. Thus, for example, ΔE for the addition of isoprene to a sulphinylamino compound RN=S=O according to Scheme 3, path (i), is given by equation

$$0.5\Delta E = (ap\beta_{CN} + bq\beta_{CS})^2/E_1 + (cr\beta_{CN} + ds\beta_{CS})^2/E_2 \quad (2)$$

(2) where a—d and p—s are coefficients of the frontier orbitals and E_1 and E_2 are their separations in energy as indicated in Figure 1; the β terms are resonance integrals for the forming σ-bonds. In Figure 1, cycloaddition is depicted as being of 'normal electron demand' *i.e.* the major interaction involves the HOMO of the diene and the LUMO of the dienophile.[30,31] Isoprene, with an inductively donating substituent, is electron rich and hence has relatively high energy frontier orbitals; sulphinyl-amino compounds, on account of their content of electro-negative heteroatoms, are expected to possess frontier orbitals of relatively low energy.

The stabilisation associated with the alternative cycloaddition of isoprene and RN=S=O to give the regioisomeric adduct [Scheme 3, path (ii)] is given by equation (3). If equations (2) and

$$0.5\Delta E' = (aq\beta_{CS} + bp\beta_{CN})^2/E_1 + (cs\beta_{CS} + dr\beta_{CN})^2/E_2 \quad (3)$$
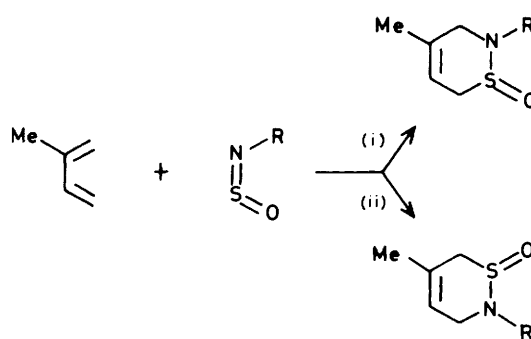
Scheme 3.
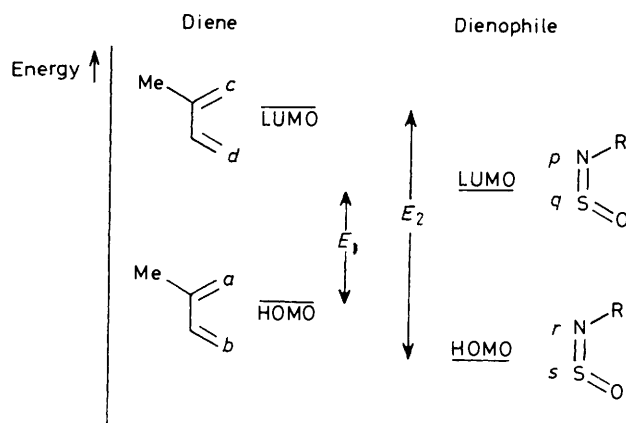

Figure 1. Labelling of frontier orbitals for the cycloaddition of isoprene to a sulphinylamino compound RN=S=O

(3) are expanded and subtracted, it is readily shown that the difference in stabilisations, $\Delta\Delta E = \Delta E - \Delta E'$, for the two modes of addition is given by equation (4).

$$0.5\Delta\Delta E = [p^2(a^2 - b^2)/E_1 + r^2(c^2 - d^2)/E_2]\beta_{CN}^2 - [q^2(a^2 - b^2)/E_1 + s^2(c^2 - d^2)/E_2]\beta_{CS}^2 \quad (4)$$

For cycloaddition to be regioselective, $\Delta\Delta E \neq 0$; regio-selectivity in favour of path (i) requires $\Delta\Delta E > 0$, whence we have equation (5).

$$[p^2(a^2 - b^2)/E_1 + r^2(c^2 - d^2)/E_2]\beta_{CN}^2 > [q^2(a^2 - b^2)/E_1 + s^2(c^2 - d^2)/E_2]\beta_{CS}^2$$

i.e. $$R_r = \frac{[E_2 p^2(a^2 - b^2) + E_1 r^2(c^2 - d^2)]}{[E_2 q^2(a^2 - b^2) + E_1 s^2(c^2 - d)^2]}$$

$$> (\beta_{CS}/\beta_{CN})^2 \quad (5)$$

We term R_r a *regioselectivity ratio* for its value determines which path is calculated to predominate in the frontier orbital approach. It is useful to define R_r for thereby the results of MO calculations on the individual reactants are combined into a term which is independent of the resonance integrals, appropriate to bonds forming in the transition state, whose values depend on assumptions about the mathematical form of the orbitals, the transition state geometry, the synchronism of bond formation, *etc.* [Unfortunately, in the general case where more than two different kinds of bond may form in the alternative regioisomers, it is not possible to separate the β values in this way since cross-terms which arise in the expansions of expressions corresponding to equations (2) and (3) do not then cancel.]

Table 2. Overlap integrals S_{AB},[b] and critical regioselectivity ratios R_c,[a] for various interplanar separations z

$z/\text{Å}$	S_{CS}	S_{CN}	R_c
1.75	0.336	0.256	0.70
2.00	0.294	0.188	1.00
2.25	0.228	0.128	1.28
2.50	0.168	0.086	1.63
2.75	0.117	0.051	2.15
3.00	0.079	0.032	2.49

[a] Interpolated from the tables given in ref. 32. [b] $R_c = (14.7S_{CS}/23.0S_{CN})^2$.

The critical value of R_r, R_c, is given by $R_c = (\beta_{CS}/\beta_{CN})^2$ and, obviously, can be estimated from a consideration of the resonance integrals of the σ-bonds formed during the cycloaddition, on the assumption that these are essentially constant for both orientations. In approximate MO methods it is assumed that the resonance integrals are proportional to overlap integrals S_{AB}, which are available from various compilations, e.g. $\beta_{AB} = 0.5(\beta_A{}^0 + \beta_B{}^0)S_{AB} = \beta_{AB}{}^0 S_{AB}$.

Values of S_{CS} and S_{CN}, calculated from Mulliken's[32] tables for Slater orbitals, for $C(2p)$–$S(3p)$ and $C(2p)$–$N(2p)$ σ-overlap at various separations of the interacting atoms, are given in Table 2. Appropriate $\beta_A{}^0$ and $\beta_B{}^0$ and hence $\beta_{AB}{}^0$ are available for different MO methods; e.g. in CNDO/2 $\beta_{CN}{}^0$ is 23 and $\beta_{CS}{}^0$ is 14.7 eV.[33] It is clear from Table 2 that for separations likely to encompass those in transition states for cycloaddition, $S_{CS}/S_{CN} > 1$; the more so the greater the separation. The disparity is not entirely compensated by the fact that $\beta_{CS}{}^0/\beta_{CN}{}^0 < 1$, thus R_c increases approximately linearly with the separation of the presumed parallel planes of the diene and dienophile.

Houk and his co-workers[34] assumed an interplanar separation of 1.75 Å in the cycloadditions of 1,3-dipoles formed from first-period elements. Since we find that the full C–S bond ultimately formed in adduct (3) is 1.79 Å in length,[22] it is improbable that in the cycloadditions of sulphinylamino compounds the interplanar separation in the transition state will be so small. We note, however, in Table 2 that an interplanar separation of 2 Å corresponds conveniently to an R_c value of 1 and so we adopt this.

(d) *Calculations.*—There is ample evidence that Hückel frontier orbitals are often satisfactory for predicting the regioselectivity of cycloadditions;[35–38] indeed they can be more reliable than more sophisticated molecular orbitals. It has been suggested[38] that the exaggeration in the description of the electron distribution which characterises Hückel MO in fact models in some degree the perturbation which occurs as the reactants begin to combine. We therefore investigated the Hückel frontier orbitals of sulphinylamino compounds in order to account for their regioselectivity of cycloaddition.

(i) *Previous calculations.* Although Hückel orbitals for many dienes are available from the literature,[37] there have been far fewer calculations for sulphinylamino compounds. Plemenkov and Kataev[39] reported Hückel calculations for PhN=S=O modelled in three ways: in the first, the $(p–d)\pi$ bond of the O–S link was orthogonal to the $(p–p)\pi$ system of the rest of the molecule; in the second, the authors followed Longuet–Higgins[40] and assumed pd^2 hybridisation at S which allowed π overlap throughout the molecule; in the third model a polar S–O bond was assumed, conferring 'allylic' character on the N=S⁺–O⁻ moiety. The properties of *N*-sulphinylaniline were interpreted with varying degrees of success in terms of these models.

Oskam and his co-workers[41] have reported CNDO/S calculations for various *N*-sulphinylanilines and a modified

CNDO/S calculation, designed to improve the description of bonding at S, for PhN=S=O itself. The calculated orbital energies were used in the interpretation of photoelectron spectra. The modified procedure gave the better account but both types of calculation, and experiment, indicated the S–O bond to be strongly polarised. There appear to be few reports of relevant calculations on other types of sulphinylamino compound.[25]

(ii) *Selection of Hückel parameters.* In parameterising the sulphinylamino group we follow literature precedents in the selection of Coulomb integrals:[42] h_N 0.5 is the value usually taken for pyridine-like nitrogen; h_S 1.0 was the value used by Kataev and Plemenkov[39] in their 'allylic' model of N=S⁺–O⁻, and the high value seems consistent with the positively polarised sulphur that this structure suggests. We have taken h_O as 1.0 for sulphinyl oxygen; this value, normally used for carbonyl oxygen, seems more appropriate than the value (2.0) used by Kataev and Plemenkov in that it reflects better the negative polarisation of O. The selection of resonance integrals is less straightforward. The polarised allylic structure N=S⁺–O⁻ suggests different bond orders for the N–S and S–O links; both bonds involve a first- and a second-period element and there is less agreement in the literature as to how these should be parameterised than for bonds restricted to first-period elements only. Accordingly, we elected to vary $k_{N=S}$ and $k_{S=O}$ and to judge the results using the derived regioselectivity ratios.

For the remaining atoms in the dienophiles investigated we have used literature precedent for both h and k values. In modelling the ester function of ethyl *N*-sulphinylcarbamate, the ester oxygen was accounted for by adopting an auxiliary inductive parameter[42] of 0.1 for the carbonyl carbon atom rather than by specific parameterisation of the heteroatom.

(iii) *Evaluation and use of regioselectivity ratios.* In Table 3 are presented the regioselectivity ratios for $EtO_2CN=S=O$ and PhN=S=O reacting with isoprene. The ratios were evaluated using equation (5) and the frontier orbital coefficients and energies for isoprene quoted by Anh and his co-workers.[37] Recalling the critical value, $R_c = 1$, which was adopted earlier, we note that for all values of $k_{N=S}$ examined R_r for PhN=S=O exceeds R_c when $k_{S=O}$ is 0.5 and 0.6. We therefore discard calculations using these parameters as they predict the wrong regioselectivity for this dienophile. The remaining calculations, however, all predict the correct regioselectivity for both dienophiles.

In order to narrow down further the range of acceptable parameters we proceed as follows. For each dienophile, the observed ratio of regioisomers ρ is equal to the ratio of the rates at which they are formed, provided one observes a kinetic product, *i.e.*

$$\rho = k_{(i)}[\text{diene}][\text{dienophile}]/k_{(ii)}[\text{diene}][\text{dienophile}]$$
$$= k_{(i)}/k_{(ii)}, \text{ for homocompetitive reactions.}$$

Applying the Arrhenius equation and taking logarithms gives $\ln\rho = \Delta E_{(ii)}{}^{\ddagger}/RT - \Delta E_{(i)}{}^{\ddagger}/RT$ after cancellation of pre-exponential factors on the ground that, for homocompetitive reactions, these will be very similar, *i.e.* we have equation (6).

$$\Delta\Delta E^{\ddagger} = RT \ln\rho \qquad (6)$$

Recalling that for addition of PhN=S=O to isoprene the ratio of regioisomers is 2:1 and for $EtO_2CN=S=O$ it is 13:1 we have equation (7), for ambient temperature.
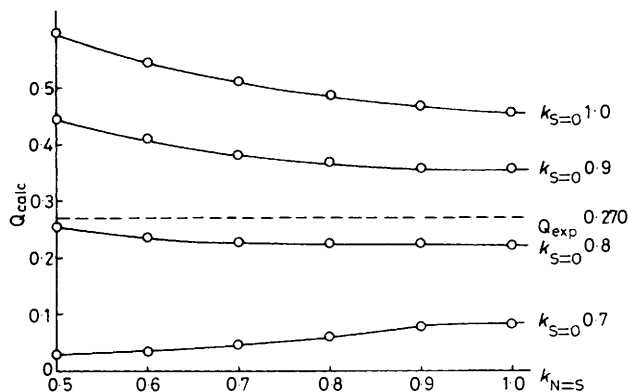
$$\Delta\Delta E^{\ddagger}{}_{(\text{PhNSO})}/\Delta\Delta E^{\ddagger}{}_{(\text{EtO}_2\text{CNSO})} = \ln2/\ln13$$
$$\text{i.e. } Q_{\text{exp.}} = 0.270 \qquad (7)$$

For each dienophile, equation (4) can be expressed as equation (8), using definitions of R_r and R_c given earlier where t

Table 3. Regioselectivity ratios for the cycloaddition of EtO_2CNSO and PhNSO to isoprene[a]

$k_{S=O}$	0.5		0.6		0.7		0.8		0.9		1.0	
$k_{N=S}$	EtO_2CNSO	PhNSO	EtO_2CNSO	PhNSO	EtO_2CNSO	PhNSO	EtO_2CNSO	PhNSO	EtO_2CNSO	PhNSO	EtO_2CNSO	PhNSO
0.5	0.544	1.917	0.320	1.406	0.154	0.952	0.019	0.595	−0.096	0.314	−0.196	0.093
0.6	0.542	1.671	0.361	1.294	0.201	0.949	0.061	0.649	−0.061	0.391	−0.170	0.179
0.7	0.549	1.509	0.385	1.217	0.233	0.940	0.093	0.683	−0.034	0.449	−0.148	0.246
0.8	0.545	1.383	0.396	1.157	0.252	0.927	0.115	0.703	−0.013	0.496	−0.135	0.297
0.9	0.534	1.296	0.400	1.107	0.262	0.909	0.127	0.712	−0.004	0.520	−0.130	0.338
1.0	0.521	1.213	0.392	1.057	0.262	0.889	0.129	0.734	−0.001	0.535	−0.131	0.363

[a] The Hückel frontier orbitals of isoprene used were: HOMO $E_H = 0.570\beta$, terminal coefficients C(1) $a = 0.653$, C(4) $b = -0.551$; LUMO $E_L = -0.643\beta$, terminal coefficients C(1) $c = 0.564$, C(4) $d = 0.619$, from ref. 37.

**Figure 2.** Variation of $Q_{calc.}$ with $k_{N=S}$ for $k_{S=O}$ 0.7—1.0

$$0.5\Delta\Delta E = (R_r/R_c - 1)[q^2(a^2 - b^2)/E_1 +$$
$$s^2(c^2 - d^2)/E_2]\beta_{CS}{}^2$$
$$= (R_r/R_c - 1)t\beta_{CS}{}^2 \qquad (8)$$

replaces the term in square brackets. Whence, on setting R_c to unity and cancelling $\beta_{CS}{}^2$, we have equation (9).

$$\Delta\Delta E_{(PhNSO)}/\Delta\Delta E_{(EtO_2CNSO)} =$$
$$[(R_r - 1)t]_{PhNSO}/[(R_r - 1)t]_{EtO_2CNSO} = Q_{calc.} \qquad (9)$$

If it is assumed that the difference in perturbational stabilisations $\Delta\Delta E$ is proportional to the difference in regioisomeric activation energies $\Delta\Delta E^{\ddagger}$ for each dienophile, the computed values $Q_{calc.}$ may be compared with the experimental Q_{exp}. By working in ratio the need is avoided to specify β_{CS}, the proportionality constant relating $\Delta\Delta E$ and $\Delta\Delta E^{\ddagger}$, and the β unit of energy in which the Hückel orbital energies are found.

In Figure 2 are plotted values of $Q_{calc.}$ versus $k_{N=S}$ for $k_{S=O}$ 0.7 to 1.0. It is evident that $Q_{calc.} = Q_{exp.}$ for $0.8 < k_{S=O} < 0.9$ and all values of $k_{N=S}$. Of the calculations performed, that which gives the closest correspondence of $Q_{calc.}$ with $Q_{exp.}$ has $k_{N=S}$ 0.5, $k_{S=O}$ 0.8. This would imply a lesser bond order for N–S than for S–O in the dienophiles studied, which does not accord well with the allylic structure, $N=S^+-O^-$. However, $Q_{calc.}$ is essentially independent of $k_{N=S}$ for higher values of the latter so $k_{N=S}$ can always be chosen to exceed the optimal $k_{S=O}$ which occurs at ca. 0.83. Thus a choice of, for example, $k_{N=S}$ 0.9, $k_{S=O}$ 0.83 reflects a reduced overlap in bonds to sulphur by comparison with those between first-period elements, and of the S–O bond vis à vis the N–S bond. (Frontier orbitals for both dienophiles, obtained using these resonance integrals and other parameters as indicated earlier, are depicted in Figure 3.) The aim is not, however, to find the best ad hoc parameterisation but
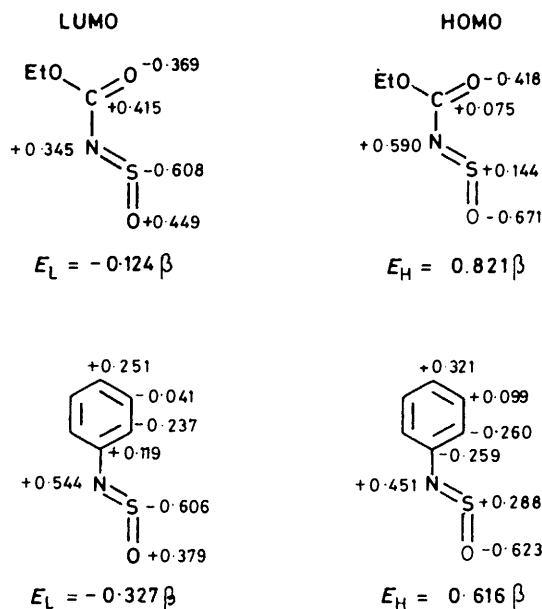
Figure 3. Optimised Hückel frontier orbitals for $EtO_2CN=S=O$ and $PhN=S=O$

rather to show that Hückel frontier orbitals, sensibly found, may be used to comprehend the pericyclic reactivity of sulphinylamino compounds and this, we suggest, has been done.

(e) *Conclusions.*—Experimental evidence has been provided that the addition of $EtO_2CN=S=O$ to 1,1'-bicyclohexenyl is pericyclic rather than electrophilic. It seems probable, therefore, that potentially less electrophilic sulphinylamino compounds, such as PhN=S=O, which also cycloadd to dienes, will react in a similar way.

The preferred orientation of cycloaddition of $EtO_2CN=S=O$ to isoprene has been confirmed and the proportions of the regioisomers found; the preferred orientation of addition of PhN=S=O to the same diene has been corrected and the proportions of the regioisomers found for this case also. The fact that the less electrophilic sulphinylamino compound is the least regioselective implies that the mechanism underlying the selectivity is not electrophilic in character. The regioisomeric preferences for both dienophiles can be consistently accounted for in the frontier orbital approach using Hückel orbitals. The treatment necessarily involves arbitrary choice of parameters and assumptions of transition state geometry, but these, when taken together, have some coherence.

A shortcoming of our approach is that it offers no direct explanation of the stereospecificity of addition of $EtO_2CN=S=O$

Table 4. [13]C Chemical shifts of the regioisomers from the cycloaddition of sulphinylamino dienophiles RN=S=O to isoprene

R	Isomer	C(3)	C(4)	C(5)	C(6)	Me	R			
CO₂Et	Major	39.0	118.6	122.0	52.5	24.2	14.1	63.2	153.9	
	Minor	42.0	108.2	132.7	49.0	21.2	14.1	60.2	153.9	
Ph	Major	42.1	119.1	122.4	53.3	24.2	121.6	124.8	129.2	145.9
	Minor	45.6	109.2	132.5	49.9	21.4	121.4	124.9	129.2	146.0

to 1,1'-bicyclohexenyl to give (3), the Hückel method taking no account of the possibility of geometrical isomerism about the N–S bond in sulphinylamino compounds. We note, however, that the Hückel calculations do show the phase of the LUMO of the dienophile at the carbonyl carbon to be appropriate for a secondary bonding overlap with the HOMO of the diene at the adjacent interior sp^2 carbon. See Figure 3. (This is analogous to the secondary overlap which has been invoked to explain the *endo* addition of maleic anhydride to cyclopentadiene.[42]) The same is not true, however, at the sulphinyl oxygen. The stereochemistry of the S–O bond is thus not explicable in terms of direct secondary interaction, but may be explained by a combination of secondary interaction involving carbonyl carbon with a residuum, in the transition state, of those forces which constrain sulphinylamino compounds to the Z-configuration in their ground states.[25] This would require the transition state to have a geometry as in (4) and to occur early on the reaction co-ordinate, which accords with the activation parameters measured.

Experimental

(a) *Materials.*—(i) *Ethyl* N-*sulphinylcarbamate.* Thionyl chloride (31 g) in benzene (31.5 cm³) and pyridine (39.5 cm³) in benzene (10.5 cm³) were added in parallel streams with efficient stirring to ethyl carbamate (22.2 g) in benzene (12.5 cm³). After the initial exotherm, the mixture was stirred for 1 h, then filtered to remove pyridine hydrochloride; benzene and other volatiles were removed on the rotary evaporator and the residue was distilled to give *ethyl* N-*sulphinylcarbamate* (25.2 g, 94%) as a light yellow oil, b.p. 23 °C at 0.5 mmHg (lit.,[20] 48 °C at 12 mmHg).

(ii) N-*Sulphinylaniline.* N-Sulphinylaniline was prepared by the method of Kresze et al.,[4] b.p. 70 °C at 6 mmHg (lit.,[4] 80 °C at 12 mmHg).

(iii) 1,1'-*Bicyclohexenyl.* The pinacol obtained from cyclohexanone using the method of Corey et al.[43] was dehydrated by the procedure described by Isabelle et al.[21] to give 1,1'-bicyclohexenyl, b.p. 68 °C at 0.5 mmHg (lit.,[21] 68 °C at 0.4 mmHg).

(iv) *Solvents.* AnalaR benzene was dried by standing over sodium wire before use. 1,2-Dichloroethane was distilled first from P₄O₁₀, then redistilled under nitrogen from CaH₂ and used immediately. Unless the solvent was freshly prepared, 1,2-dichloroethane solutions developed colouration under the conditions of kinetic measurements and inconsistent results were obtained.

(b) *Kinetics.*—Standard solutions in the appropriate solvent were prepared of ethyl N-sulphinylcarbamate (25 cm³; 1.0 × 10⁻³ mol dm⁻³) and 1,1'-bicyclohexenyl (25 cm³; 1.0 × 10⁻³ mol dm⁻³), the latter also containing 1-chloro-2-nitrobenzene (1.0 × 10⁻³ mol dm⁻³) to serve as internal standard. These were equilibrated thermally at the chosen temperature then, in triplicate, 5 cm³ aliquot portions were mixed and the progress of reaction followed by monitoring the disappearance of the diene,

relative to the internal standard, by g.l.c.: column, 1.5 m, OV 225, 3% on Chromasorb W; oven temperature 108 °C; nitrogen carrier gas, flow ca. 50 cm³ min⁻¹. The quantity of residual diene at any time was determined by triangulation and comparison of peak areas for diene and standard, response factors for the conditions having been previously determined. The rate constants were obtained graphically by plotting $x/a(a - x)$ versus time where a is the initial concentration of diene and $(a - x)$ its measured remaining quantity; slopes of the graphs, equal to the second-order rate constants, were obtained by a least mean squares treatment of the plots. The rate constants presented in Table 1 are averages of the replicate analyses for each conditon and have estimated errors of ca. 6%.

(c) *Cycloadditions to Isoprene.*—(i) EtO₂CN=S=O. The N-sulphinylurethane (13.5 g) and an excess of isoprene were stirred in dry benzene, in a stoppered flask, at room temperature for 72 h. After removal of solvent and excess of isoprene the residual oil (20.1 g, 99%) was divided into two parts. The major part was distilled to give 2-ethoxycarbonyl-5-methyl-3,6-dihydro-1,2-thiazine 1-oxide as an oil, b.p. 128—129 °C at 0.5 mmHg (lit.,[15] 130—131 °C at 0.6 mmHg). [13]C N.m.r. spectrometry on the distillate in CDCl₃ showed the presence of eight resonances. See Table 4.

The identification of the material as the 5-methyl and not the 4-methyl derivative was confirmed in the following experiment. The purified adduct (7.0 g) was refluxed for 0.5 h in hydrochloric acid (16 cm³, 10%) and the resultant N-(methylbut-3-enyl)urethane was extracted into ether, isolated, and distilled, b.p. 42—44 °C at 0.5 mmHg (lit.,[15] 67—68 °C at 1.0 mmHg), to give an oil showing carbon resonances as follows: δ 14.9, 22.4, 38.8, 40.0, 61.5, 112.2, 144.0, and 158.9 p.p.m. In an off-resonance experiment the alkenic resonances at δ 112.2 and 144.0 p.p.m. showed triplet and singlet multiplicities, respectively, and there was no alkanic doublet. This confirms the product to be N-(3-methylbut-3-enyl)urethane, consistent only with a 5-methyl substituent in the heterocycle; a 4-methyl substituent would require doublet resonances for one alkenic and one alkanic carbon of the hydrolysate. See Scheme 1, reaction (iv).

The minor part of the original adduct was examined, unpurified, by [13]C n.m.r. spectrometry: major resonances were observed at chemical shifts identical with those of the thiazine described above and, in addition, minor resonances were observed corresponding to the resonances of the ring carbons of its regioisomer; the resonances of the ester groups of the two isomers were similar (Table 4). The relative proportions of the two isomers (13:1) were determined from the relative mean intensities of the resonances of the heterocyclic methylene carbons, which are expected to be similarly relaxed.

(ii) PhN=S=O. N-Sulphinylaniline (1.4 g) and an excess of isoprene reacted at ambient temperature on storing, in a stoppered flask, for three weeks. On chilling, a solid adduct (1.0 g) separated which was isolated by filtration, and washed with a small amount of cyclohexane. The [13]C n.m.r. spectrum of the

product obtained, for solution in $CDCl_3$, without further refinement showed the presence of two isomers; see Table 4. Their relative proportions (2 : 1) were found as described above for the isomers from $EtO_2CN=S=O$.

For the high-temperature reaction, $PhN=S=O$ (1.4 g), dissolved in an excess of isoprene, was sealed in a Carius tube and heated 24 h at 70 °C. On chilling, the adduct (1.6 g) crystallised; on isolation, it was shown by ^{13}C n.m.r. spectrometry to comprise the same two isomers as the ambient temperature product but now in proportions of ca. 3:2. Since the relative proportion of minor isomer has increased on increasing the temperature, we infer the mixed isomers to constitute the kinetic product of cycloaddition at each temperature.

It is evident from Table 4 that for each dienophile the chemical shifts of the ring carbons of the respective major isomers correspond as do those of the minor isomers and that, consequently, both cycloadditions have the same regioselectivity, though to different degree as shown by the different proportions of the regioisomers.

(c) *Hückel Calculations.*—Calculations were performed on the University of York's DEC System 10 computer using a program originally written by Dr. D. R. Burnham.

Acknowledgements

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