ABSTRACT

Rotational barriers in heterocyclic sulphenamides; trapping of sulphenylnitrenes

by Brian David Judkins B.Sc.

The first part of this work is an investigation of the reason for the abnormally high barrier to rotation around the N-N bond in certain N-quinolone substituted sulphenamides. Some mechanisms by which diastereoisomers of the above compounds could interconvert are also examined. Extension of this work lead to resolution of N-benzyl-N-(1,2-dihydro-2-oxoquinolin-1-yl) glycine as a result of the N-N chiral axis. The thermal stability of some heterocyclic sulphenamides is also investigated.

A study of the reaction of some alkylhydrazines with arylsulphenyl chlorides is described and some mechanisms proposed for the fragmentation of the intermediate sulphenylhydrazides.

The trapping of dinitrobenzenesulphenylnitrene with alkenes and other reagents is described as well as a study of the stereospecificity of its addition to cis-1-phenylpropene. The generation and attempted trapping of other sulphenylnitrenes is also investigated.

ROTATIONAL BARRIERS IN HETEROCYCLIC SULPHENAMIDES; INTERMOLECULAR TRAPPING OF SULPHENYLNITRENES

by

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A thesis presented for the degree of
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To my Parents

STATEMENT

The accompanying thesis submitted for the degree of Doctor of Philosophy entitled 'Rotational barriers in heterocyclic sulphenamides; intermolecular trapping of sulphenylnitrenes' is based on work conducted by the author in the Department of Chemistry of the University of Leicester between the period October 1976 and October 1979.

All the work recorded in this thesis is original unless acknowledged in the text or by references. None of the work has been submitted for another degree in this or any other university.

Signed B.D. Tudkin.....

1981

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Fellow research workers who made my three years so enjoyable.
Finally, I am indebted to the S.R.C. for my grant.

CONTENTS

ABBREVIATIONS

Me - methyl	Ac - acetyl
Et - ethyl	Ph - phenyl
Pr^i - isopropyl	Ar - aryl
Bu^n - $CH_3(CH_2)_3$-	Ar^1 - 2,4-dinitrophenyl
Bu^t - Me_3C-	Tos - 4-methylphenylsulphonyl
DMSO - dimethylsulphoxide	THF - tetrahydrofuran
DMF - dimethylformamide	

$\Delta G^{\ddagger}$ values are measured in kcal mol^{-1} throughout.

e.u. (entropy units) have units cal K^{-1} mol^{-1}.

All temperatures are measured in °C except where indicated.

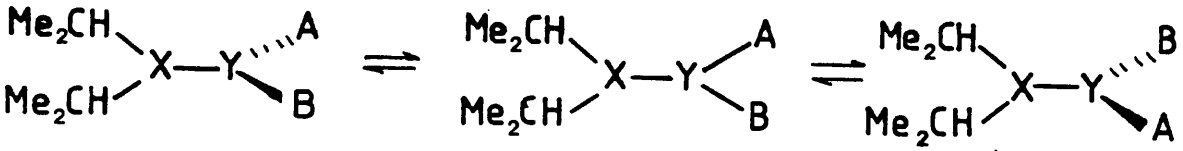
CHAPTER 1

Rotational isomerism around some single bonds: Inversion at nitrogen

Restricted rotation around a single bond can be caused by (a) steric effects or (b) electronic effects. In the latter case, steric effects usually contribute to the overall barrier as well. In this review chapter, restricted rotation around S-N and N-N bonds and the use of n.m.r. spectroscopy in investigating these phenomena will be examined.

1.1 The use of dynamic n.m.r. spectroscopy in determining the energy barrier of conformational processes

In the hypothetical molecule [1], rotation around the X-Y bond is assumed to occur at a rate measurable by n.m.r. (all other rotation and inversion processes are assumed fast). Although the X-Y bond is



[1]

not a chiral axis (i.e. the molecule is not resolvable) because of the identical substituents on X, the prochiral isopropyl substituents enable the slow rotation to be followed by n.m.r.. When rotation around X-Y is fast on the n.m.r. time-scale (i.e. $>10^2$ rotations per second), the isopropyl methyl groups appear as one doublet. However, when rotation is slow, the methyl groups within each isopropyl become magnetically non-equivalent, and appear as two doublets of equal intensity. On increasing the temperature of the system, the rate of rotation around X-Y will increase, and the two doublets coalesce into one doublet. $\Delta G^{\ddagger}$ for the X-Y rotation can then be calculated at the

coalescence temperature by using the expressions:[1]

$$k_c = \frac{\pi \Delta\nu}{\sqrt{2}} \quad \ldots\ldots \quad (a)$$

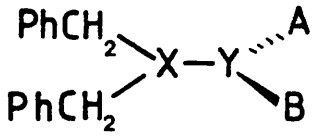
and $$k_c = \frac{k_B T_c}{h} \exp\left[-\frac{\Delta G^{\ddagger}}{RT_c}\right] \quad \ldots\ldots \quad (b)$$

where T_c = coalescence temperature (in kelvin), k_c = rate of rotation around X-Y at T_c, $\Delta\nu$ = frequency separation of coalescing signals (in Hz, measured at temperatures lower than T_c), k_B = Boltzmann's constant, h = Planck's constant and R = the gas constant. When (a) and (b) are combined, and the constant terms inserted, the following expression results:

$$\Delta G^{\ddagger} = \frac{4.574\ T_c}{1000}\left[9.9722 + \log_{10}\frac{T_c}{\Delta\nu}\right] \quad \ldots\ldots \quad (c)$$

with $\Delta G^{\ddagger}$ in kcal mol^{-1}.

The above equation is valid for uncoupled signals (the methyl doublets above are uncoupled to <u>each other</u>). It must be modified, however, in the case where the signals are coupled to each other, as in the case of molecule [2]. When rotation around X-Y is slow on the



[2]

n.m.r. time scale here, the benzyl groups remain equivalent, but the protons within each benzyl group become magnetically non-equivalent. Since they will then couple each other, an AB system will result, which

will coalesce into a singlet as the temperature is raised. At T_c, equation (d) is valid:[2]

$$k_c = \pi \sqrt{\frac{\Delta\nu^2 + 6J_{AB}^2}{2}} \qquad \ldots\ (d)$$

where J_{AB} = coupling constant between the signals. This means equation (c) must be modified to:

$$\Delta G^{\ddagger} = \frac{4.574\ T_c}{1000}\left[9.9722 + \log_{10} T_c - \log_{10}\sqrt{\Delta\nu^2 + 6J_{AB}^2}\right] \qquad \ldots\ (e)$$

Validity of expressions (c) and (e)

Kost and Raban[3] have investigated the accuracy of the above expressions, and they find equation (c) is valid for equally intense coalescing singlets and doublets as long as $\Delta\nu$ is greater than 3Hz. For unequally intense coalescing singlets or doublets, $\Delta\nu$ must be greater than 4Hz for acceptable results. Equation (e) gives acceptable results when $\Delta\nu$ is greater than J_{AB}.

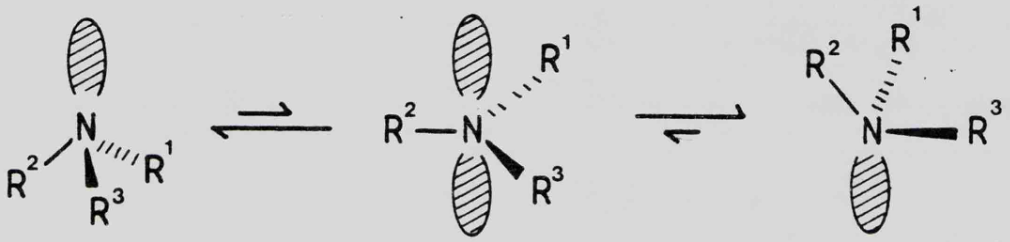
Another inaccuracy results from having to measure $\Delta\nu$ at below the coalescence temperature as $\Delta\nu$ may be temperature dependent. Its value at T_c sometimes has to be extrapolated from lower temperature measurements. However, Kost and Zeichner[4] showed that for the uncoupled case [equation (c)], $\Delta\nu = W_{\frac{1}{2}}$ at T_c, where $W_{\frac{1}{2}}$ = width at half height of the coalescing signal, and this can be substituted directly into (c). For AB systems, k_c can be evaluated graphically from the width at half height at T_c and the coupling constant at lower temperature, J_{AB} (which is not temperature dependent[5]).

As a result of the above work, coalescence temperatures give accept-

able accuracy (believed to be ±0.3 kcal mol^{-1}) in the calculation of free energies of activation.

1.2 Inversion at pyramidal nitrogen

Inversion at the nitrogen pyramid takes place via re-hybridisation of the nitrogen atom from sp^3 to sp^2. As a result, the hybridisation of the nitrogen lone pair orbital changes from sp^3 to p in the planar transition state [3].



[3]

Inversion at nitrogen and other atoms has been well reviewed,[6,7,8] and a summary of the main factors affecting inversion will be given here.

(a) Effect of ring strain

In simple alkylamines, the inversion barrier is low, being less than 6 kcal mol^{-1}. However, incorporation of the nitrogen atom into a small ring system increases the inversion barrier as the ring size becomes smaller. Thus a comparison of the cyclic amines [4], [6], [8] and [10] in table 1 reveals the inversion barrier to be highest for the three membered ring (aziridine) species [10].

These results can be explained by the increased ring strain in the transition state relative to the ground state. During inversion it is

necessary for the bond angles to increase ideally to 120°, and this process is more inhibited in aziridines in which the bond angles of the ring are formally close to 60°.

(b) Effect of heteroatoms bonded to nitrogen

When a heteroatom is bonded directly to nitrogen the inversion barrier can be noticeably changed. With strongly inductively electron withdrawing substituents the inversion barrier is increased, and two effects seem to operate; firstly, the -I effect of the heteroatom demands increased p character in the N-X bond (X = N, O, Cl), and so reduces the availability of a p orbital for the nitrogen lone pair, thus making the necessary re-hybridisation in the transition state more difficult. Secondly, heteroatoms usually possess lone pairs of electrons themselves, and unfavourable lone pair - lone pair interactions are increased in the transition state. E.g. [4]-[9] in table 1, in which the N-chloramines have higher inversion barriers than the corresponding alkylamines.

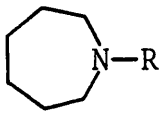
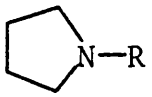
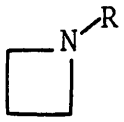
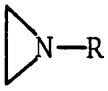
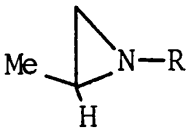
When the two effects of ring strain and heteroatom substitution are combined, it is possible to isolate the two invertomers at room temperature, e.g. [22] was separated into two diastereoisomeric forms by Brois[16] in 1968 using preparative g.l.c. This was the first example of diastereoisomerism caused by slow nitrogen inversion.

(c) Steric effects

As the size of the substituents on nitrogen is increased, the greater becomes the steric strain in the ground state relative to the less hindered transition state. Hence the more bulky substituents lower the inversion barrier as seen in aziridines [10]-[12] in table 1.

TABLE 1

Inversion at nitrogen in some cyclic amines

			$\Delta G^{\neq}$	ref.
	[4]	R = Me	6.8	9
	[5]	R = Cl	9.2	9
	[6]	R = Me	8.3	9
	[7]	R = Cl	10.3	9
	[8]	R = Me	10.0	9
	[9]	R = Cl	13.4	9
	[10]	R = Me	~22	10
	[11]	R = Et	19.4	11
	[12]	R = Bu^t	17.0	12
	[13]	R = SO_2Ph	12.4	13
	[14]	R = COMe	<6	14
	[15]	R = 4-$MeOC_6H_4$	12.5	15
	[16]	R = Ph	11.2	15
	[17]	R = 4-ClC_6H_4	11.0	15
	[18]	R = 3-$CF_3C_6H_4$	10.7	15
	[19]	R = 4-$CF_3C_6H_4$	10.0	15
	[20]	R = 4-$NO_2C_6H_4$	8.2	15
	[21]	R = SPh	13.1	13
	[22]	R = Cl	>24	16

(d) Electronic effects

Conjugation reduces the inversion barrier since delocalisation of the nitrogen lone pair occurs better in the planar transition state. This significantly reduces the inversion barrier as is seen in [13] and [14] in table 1.

Lehn and Mislow[15] evaluated inversion barriers for substituted aryl aziridines [15]-[20] in table 1 and subjected the results to a Hammett analysis.[17] A good correlation with σ^- was found, with a ρ value of 2.8. This indicates the nitrogen lone pair conjugates better with the more electron deficient aryl ring in the transition state for inversion.

Divalent sulphur also lowers the inversion barrier when compared to an alkyl substituent, despite the possibility of lone pair - lone pair repulsion in the transition state (aziridine [21] in table 1). This result is discussed in section 1.4(c).

1.3 Rotational barriers in hydrazines

This subject has been reviewed recently.[18] The magnitude of the barrier to rotation depends greatly on the hybridisation of the nitrogen atoms involved, as well as the nature of the substituents. A few typical cases are examined below.

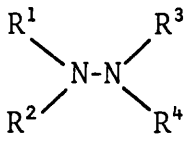
(a) Bipyramidal hydrazines

The barrier to rotation around the N-N bond is low in these cases and complicated by the associate process of N inversion. Table 2 illustrates some free energies of activation for bipyramidal hydrazines.

In [23] and [24], slow rotation around the N-N bond (with fast N inversion) will not be visible by n.m.r. because of the symmetry of the molecules. Hence the measured barriers must be due to N inversion (although N-N rotation is probably also slow in these cases[19]). Fletcher and Sutherland[20] assigned the barriers in [25]-[27] to N-N rotation with fast N inversion. Indeed, in [25] and [26] each nitrogen has identical substitution, and will have the same inversion barrier. When N inversion is slow, two AB systems should be visible for the

TABLE 2

Bipyramidal hydrazines - activation data



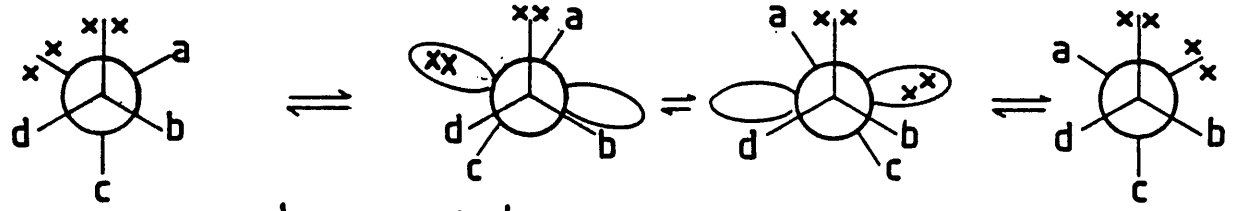
		T_c	$\Delta G^{\ddagger}$	ref.
[23]	$R^1=R^2=CH_2Ph$, $R^3=R^4=H$	-106	8.0	19
[24]	$R^1=R^2=R^3=R^4=CH_2Ph$	-105	8.2	19
[25]	$R^1=R^3=CH_2Ph$, $R^2=R^4=Et$	- 51	10.7	20
[26]	$R^1=R^3=CH_2Ph$, $R^2=R^4=CHMe_2$	- 46	11.2	20
[27]	$R^1=R^2=R^3=CH_2Ph$, $R^4=Et$	- 53	10.8	20

benzyl protons. However, only one is seen below the coalescence temperature, with no further changes down to -100°. Also, [26] with the more bulky substituents than [25] has a higher barrier than [25]; the reverse would be expected for a rate determining N inversion [see section 1.2(c)]. Similarly in [27] only two benzyl groups, presumably those at R^1 and R^2 produce an AB system below T_c; the third remains a singlet. Fletcher and Sutherland[20] again explain this in terms of rapid N inversion and slow N-N rotation, but this appears to be an over-simplification. Katritzky[21] and Shvo[22] discuss these results in more detail and show a combination of rotation and inversion is the rate-determining process for racemisation (and thus coalescence of n.m.r. signals).

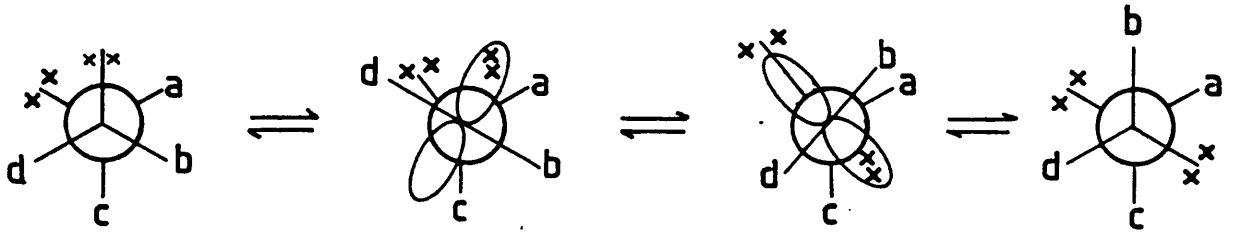
Katritzky[21] specifies two types of inversion process which occur in bipyramidal hydrazines: one in which eclipsing interactions of substituents occur, and a second in which they are avoided. The concept of two inversion barriers arose from the behaviour of certain cyclic bipyramidal hydrazines in which both types of barrier could be

measured. Katritzky's proposal was later modified by Nelsen[23] who suggested that it was eclipsing of the two lone pairs which was responsible for the higher energy inversion process (see scheme 1).

Scheme 1



'non-passing' (low energy) inversion

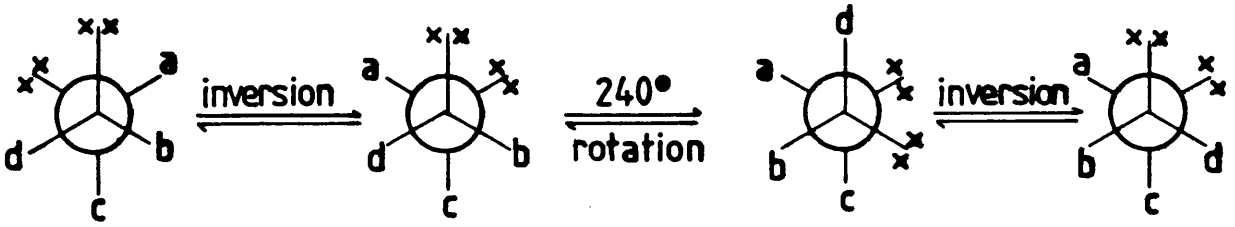


passing (high energy) inversion

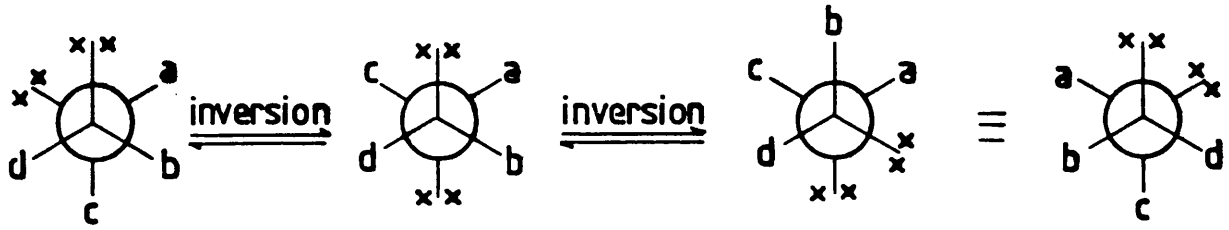
Both these processes enable racemisation to occur (and hence bring about coalescence of prochiral groups in the n.m.r. - see scheme 2). The 'passing inversion' is of higher energy; in addition to the eclipsing interaction between the lone pairs during the inversion, the trans conformation [28] is of higher energy than the gauche [29]. Present evidence[24] indicates the preferred conformation is one in which there is a 90° angle between the lone pairs (for simplicity in the diagrams above this has been taken as 60°).

The behaviour of hydrazines [23]-[27] has been discussed by Shvo[18] in the light of these ideas; the barriers in [23] and [24] were assigned to 'non-passing' inversion (in these cases rotation is not

Scheme 2



Racemisation via 'non-passing' inversions



[29] [28]

Racemisation via 'passing' inversions

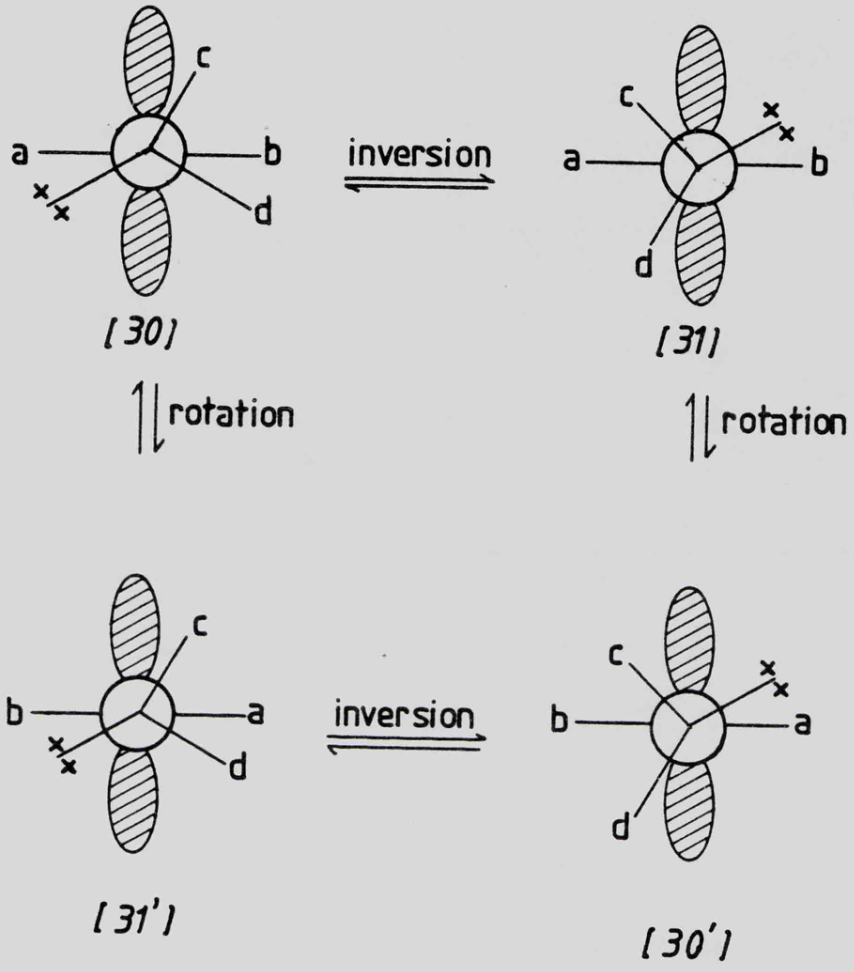
required to cause racemisation because of the symmetry of the molecules), whereas a careful analysis of the symmetry properties of [25]-[27] reveal that either the 240° rotational step in the 'non-passing' inversion scheme for racemisation or the 'passing' inversion mechanism could be responsible for their observed n.m.r. behaviour.

(b) Pyramidal-planar hydrazines

The conformational processes in this system are shown in scheme 3.

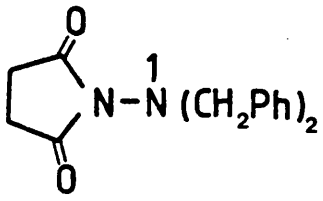
The enantiomers [30] and [30′], [31] and [31′] are interconverted by rotation then inversion (or vice versa). The inversion process can occur without eclipsing of lone pairs and substituents, with the lone pairs retaining a 90° angle to each other. Rotation must involve eclipsing interactions, however, and this is found to be the rate determining stereochemical process for racemisation. In fact, in [32]

Scheme 3



pyramidal-planar hydrazines

slow N-N rotation is not seen by n.m.r. because of the symmetry of the molecule, but slow inversion at N-1 ought to render the protons within each benzyl group diastereotopic. However, no change is seen in the n.m.r. of [32] even at -130° (except for loss of resolution).[19] This strongly implies the barriers in [33]-[37] in table 3 are due to slow N-N rotation.



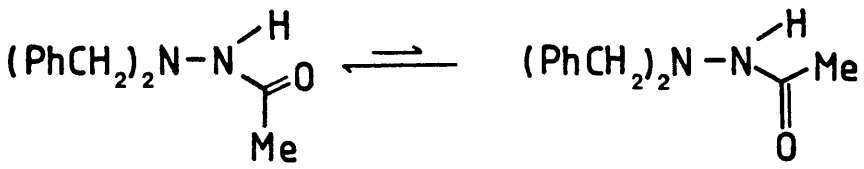
[32]

TABLE 3

Pyramidal-planar hydrazines - activation data

		T_c	$\Delta G^{\neq}$	
	[33] R = 2,4-dinitrophenyl	59	16.6	
	[34] R = 2,4,6-trinitrophenyl	50	16.4	
$(PhCH_2)_2N$-NHR	[35] R = 2-pyrimidyl	- 34	11.7	ref. 19
	[36] R = E-CH_3CO	39	15.5	
	[37] R = Z-CH_3CO	<-100°	<9.3	

There is a wide difference in behaviour between the E and Z-acetyl derivatives [36] and [37] ([36] and [37] are interconverted by rotation around the C-N bond; this occurs with an activation energy of 18.2



E

[36]

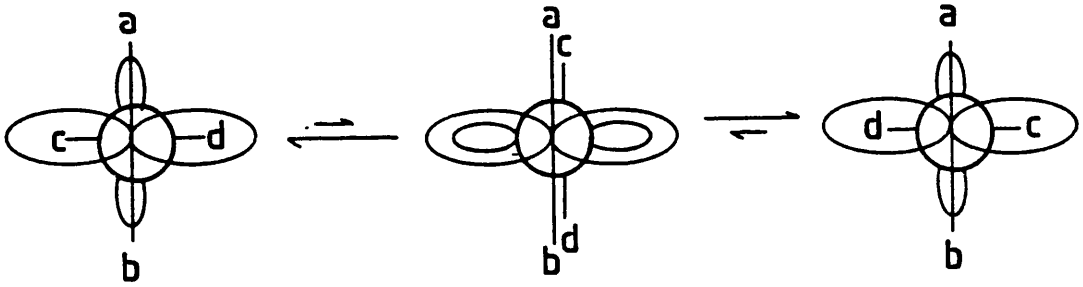
Z

[37]

kcal mol^{-1}[19]). Apparently, there is greater steric hindrance in the transition state for rotation in the E isomer than the Z isomer. It appears, therefore, that the magnitude of the N-N barrier is very sensitive to the size of the substituents on nitrogen.

(c) Biplanar hydrazines

In these systems, rotation is the only process available for degenerate racemisation. The transition state for rotation [38]



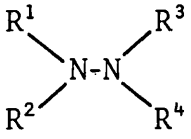
[38]

involves simultaneous eclipsing of lone pairs and substituents. This fact, coupled with the closer proximity of the lone pairs results in larger rotational barriers than in cases (a) or (b) above. Sutherland et al.[20,25,26] have studied barriers in these types of hydrazines in table 4.

In [39] and [40], the effect of bulkier substitution in increasing the barrier is clearly demonstrated. In [41] rotation around both N-C$^{=O}$ bonds also occurs slowly on the n.m.r. time scale. At -40°, four methoxy methyl signals and four benzyl AB systems are visible, owing to restricted rotation around the N-N and two N-C amide bonds, giving rise to four diastereoisomers. On increasing the temperature, the methoxy signals coalesce into one, and the AB systems coalesce into one AB system. It appears at this point that the rotation around the

TABLE 4

Biplanar hydrazines - activation data

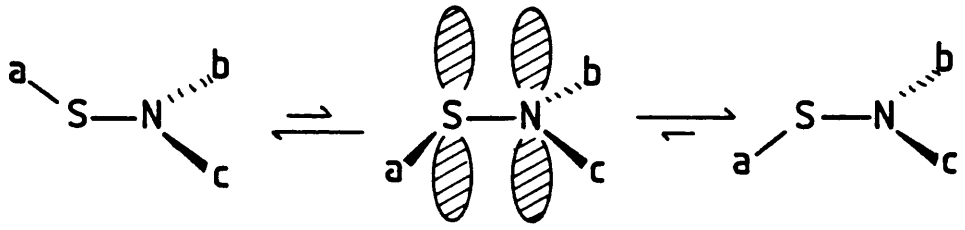


		T_c	$\Delta G^{\ddagger}$	ref.
[39]	$R^1=R^3=CH_2Ph$, $R^2=R^4=COPh$	117	19.6	20
[40]	$R^1=R^3=CHMe_2$, $R^2=R^4=COPh$	147	23.5	20
[41]	$R^1=R^3=CH_2Ph$, $R^2=R^4=CO_2Me$	192	23.5	25
[42]	$R^1=R^3=CH_2Ph$, $R^2=R^4=COMe$	188	23.4	25
[43]	$R^1=R^3=CH_2Ph$, $R^2=R^4=COCH_2Ph$	190	23.3	25
[44]	$R^1=CH_2Ph$, $R^3=H$, $R^2=R^4=COCH_2Ph$	4	13.2	25
[45]	$R^1=R^3=Ph$, $R^2=R^4=CH_2Ph$	13	14.2	26

two amide bonds is now fast on the n.m.r. time scale, with slow N-N rotation. Coalescence of the AB system occurs at 192° to one singlet, indicating an associated barrier of 23.5 kcal mol^{-1}, much higher than the hydrazines examined in (a) or (b). The lower barrier in the N-H compound [44] is probably a result of less steric hindrance in the transition state for rotation, while in [45], the hybridisation of the nitrogen atoms is probably between sp^2 and sp^3 and so there would be less hindrance in the rotational transition state.

1.4 Restricted rotation around the S-N bond in sulphenamides

In a sulphenamide [46] there can exist a barrier to rotation (torsion) around the S-N bond.[27] If the rate of nitrogen inversion is assumed fast (and so is effectively planar when time averaged), then the planar conformation [47] may be represented as the transition

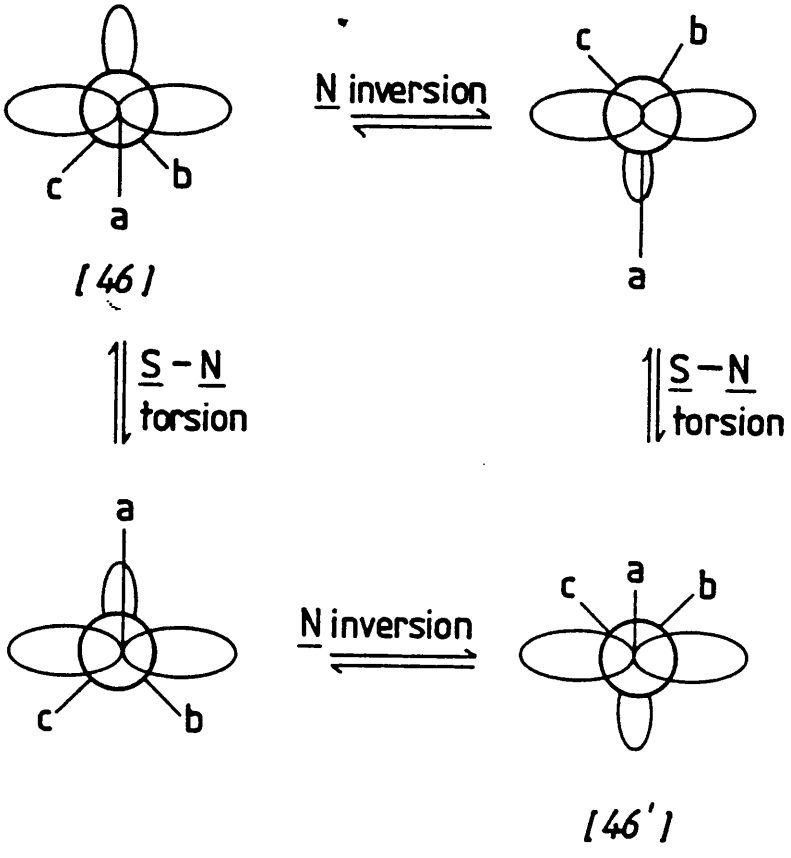


[46] [47] [46']

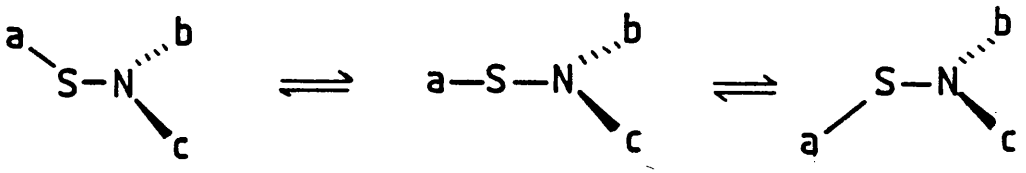
state in which eclipsing between lone pairs and substituents occurs. The S-N bond is a chiral axis; [46] and [46'] are enantiomers and their interconversion may be referred to as degenerate racemisation. When the sulphenamide nitrogen is pyramidal, a combination of rotation and inversion is necessary to bring about racemisation.

SCHEME 4

Conformational processes in sulphenamides



Degenerate racemisation could also occur by inversion at sulphur:



[46] [46']

By employing prochiral substituents on nitrogen, it is possible to follow the degenerate racemisation of [46] by variable temperature n.m.r.. Raban et al.[27] found that these barriers were highest in sulphenamides containing electron withdrawing groups attached to sulphur (table 5).

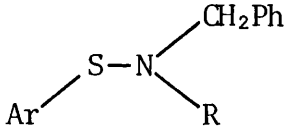
Energy barriers were much higher in the dinitrophenyl derivatives [50] and [51] than in the phenyl and tolyl derivatives [48] and [49]. Similarly, the bulky, electron withdrawing trichloromethyl group allowed barriers to be measured for a series of sulphenamides [52]-[56]. The results indicate a rate determining S-N rotation for racemisation.

The rate of inversion at divalent sulphur is not known with much certainty, but inversion barriers in sulphoxides (range 35-42 kcal mol^{-1})[28] and sulphonium salts (~25 kcal mol^{-1})[29] are substantially higher than the energy barriers in table 5. Unfortunately to date there have been no theoretical calculations on the inversion barrier at divalent sulphur.

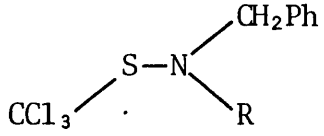
The barriers in [52]-[56] are increased with increased size of R; the reverse would be expected for a rate determining inversional process [section 1.2(c)]. For the S-N rotation process, a bulkier R

TABLE 5

Sulphenamides - activation data

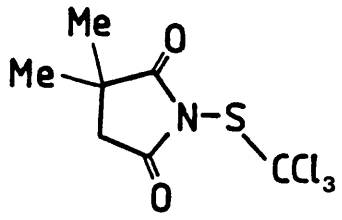


		T_c	$\Delta G^{\ddagger}$	ref.
[48]	Ar = Ph, R = $CHMe_2$	<-70°	<10.5	27
[49]	Ar = $pMeC_6H_4$, R = $CHMe_2$	<-70°	<10.5	27
[50]	Ar = 2,4-dinitrophenyl, R = $CHMe_2$	66	16.9	this work
[51]	Ar = 2,4-dinitrophenyl, R = Ph	78	17.8	27



[52]	R = Me	17	14.4	27
[53]	R = CH_2Ph	27	14.9	
[54]	R = Et	40	15.6	
[55]	R = $CHMe_2$	48	16.0	
[56]	R = 1-adamantyl	68	16.9	

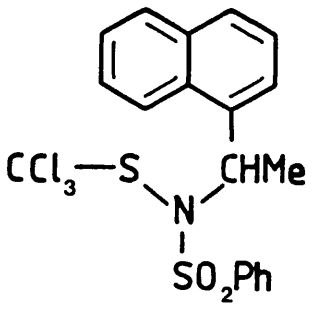
group increases the unfavourable eclipsing interactions in the transition state, thus raising the barrier. A convincing proof that S-N rotation is rate determining was found in [57]; the barrier found,



[57]

11.8 kcal mol^{-1}[27] is much higher than one would expect for N inversion - the nitrogen is certainly almost planar here, with a very low energy to inversion (an X-ray crystal structure of the related N N′-bis-succinimidyl showed the nitrogen atoms to be planar[30]) so the barrier in [57] must be due to slow rotation around the S-N bond.

Resolution of [58] as a result of the S-N chiral axis has been achieved.[31] The barrier in [58] was found to be 18.3 kcal mol^{-1} ($T_c = 78°$).



[58]

This barrier is somewhat higher than in the sulphenamides [52]-[56], and is probably caused by the bulkier substituents. As a result of the extra chirality in the 1-(1-naphthyl)ethyl substituent, [58] exists as

two diastereoisomers at room temperature (ratio 2:1 from n.m.r. integration of the methyl doublets) on the n.m.r. time scale, although interconversion is rapid on the isolation time scale.

By starting with optically pure R-(+)-1-(1-naphthyl)ethylamine, the sulphenamide [58] was prepared with the two diastereoisomers having RR and RS configuration. Crystallisation of [58] proceeds with 'second order asymmetric induction',[32] and the major diastereoisomer in the equilibrium mixture can be isolated pure, $[\alpha]_D^{28°} = -62°$ (c = 0.02, MeCN). The diastereoisomer is conformationally stable in the solid state at room temperature, but racemises rapidly in solution above -50°. An X-ray crystal structure[33] on the pure diastereoisomer showed it to have the RR configuration. The sulphenamide nitrogen was found to be virtually planar, probably because of resonance delocalisation into the neighbouring sulphonyl group (rather than the presence of the sulphenyl sulphur) which stabilises the planar nitrogen (see X-ray structure of [118] in Chapter 2). The CSN bond angle of 104° suggests the sulphur is sp^3 hybridised, and the conformation adopted was one in which repulsion between the lone pairs was minimised.

(a) Possible causes of the rotational barrier

In order to explain the increase of the rotational barrier with increasingly electronegative substituents, two hypotheses were initially proposed. These were (p-d) π bonding and negative hyperconjugation.

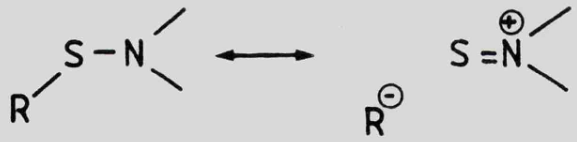
(i) (p-d) π bonding

In this hypothesis, the lone pair on nitrogen may be donated into an empty sulphur 3d orbital, thus giving rise to a partial double bond. This resonance is destroyed in the transition state for rotation,

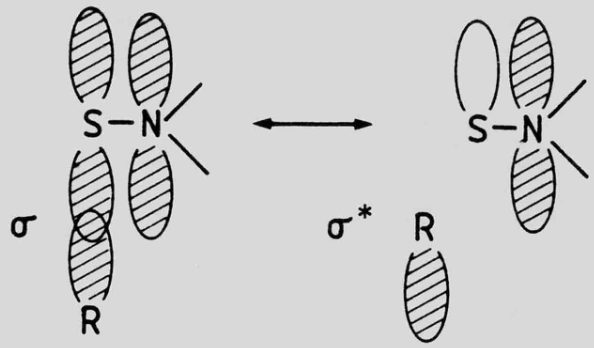
thus giving rise to the rotational barrier. An objection to this hypothesis is the large difference in energy between the orbitals involved, which would result in poor overlap. However, with electronegative substituents on sulphur, the 3d orbitals contract with concomitant lowering of their energy. It is then possible in theory therefore for such overlap to occur, assuming the aryl ring also conjugates with the 3d orbitals. Indeed, the possibility of (p-d) π bonding did offer a good rationale for the effect of polar substituents in sulphenamides (vide infra).

(ii) Negative hyperconjugation

Negative hyperconjugation involves the donation of the nitrogen lone pair into the antibonding orbital of the neighbouring R-S bond, i.e. in valence bond terms:



In molecular orbital terms, one can draw the above two possibilities as in [59] and [60] below.



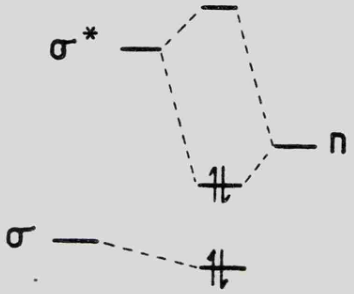
[59] *[60]*

In effect, the n and σ^* orbitals can form two molecular orbitals in

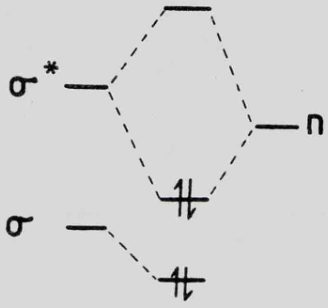
which the resulting bonding orbital represents a net stabilisation. This stabilisation is bigger for a more electronegative substituent as the σ* and n orbitals are then closer in energy, thus increasing the interaction between them (Scheme 5).

Scheme 5

M.O. diagram illustrating negative hyperconjugation



For R not electronegative in [59] and [60] (i.e. $\Delta G^{\neq}$ small)



For R electronegative in [59] and [60] (i.e. $\Delta G^{\neq}$ large)

This results in a stabilisation of the conformation in which the R-S bond bisects the R^1-N-R^2 plane. No such stabilisation is possible for other conformations, thus giving rise to the rotational barrier.

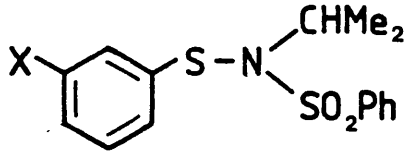
In this hypothesis, resonance effects through the R-S bond are not possible, so only the inductive influence of R should be important. -

(iii) Lone pair - lone pair repulsion

Another possibility is increased lone pair - lone pair repulsion in the transition state for rotation. See the introduction to this section on this point.

(b) The effect of polar substituents on the S-N rotational barrier in acyclic sulphenamides

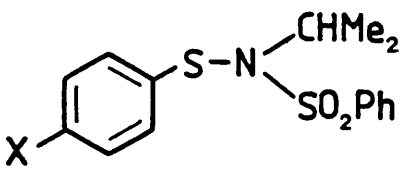
In order to investigate the above hypotheses, Raban and Jones synthesised a variety of N-sulphonylsulphenamides [61]-[64] (X = MeO, Me, H, Cl, NO_2) in which the rotational barriers are all between 13-20 kcal mol^{-1}.[34] The results were subjected to a Hammett analysis,[17] and the ρ values (corrected to 300 K as ρ is temperature dependent) evaluated.



[61]

$\Delta G^{\ddagger}$ v σ_m

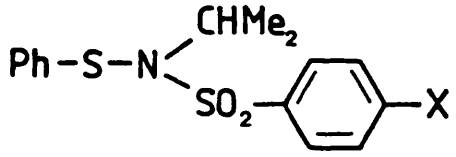
$\rho_{300} = -0.9 \pm 0.1$



[62]

$\Delta G^{\ddagger}$ v σ_p

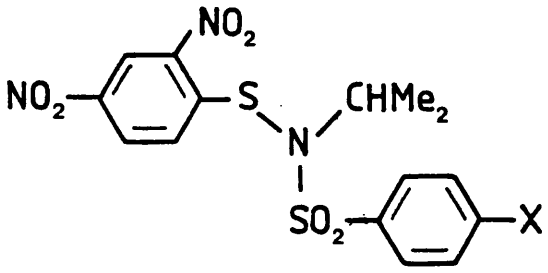
$\rho_{300} = -1.9 \pm 0.2$



[63]

$\Delta G^{\ddagger}$ v σ_p

$\rho_{300} = 0$



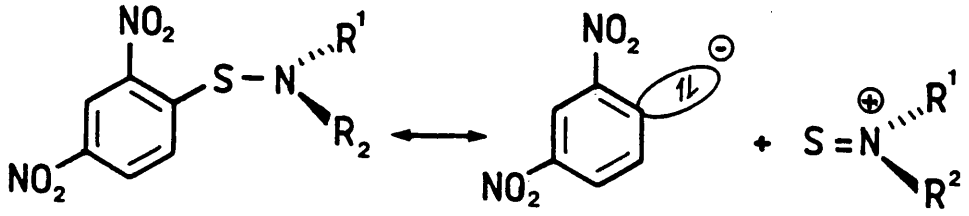
[64]

$\Delta G^{\ddagger}$ v σ_p

$\rho_{300} = 0.9 \pm 0.1$

It is clear that increasing electron withdrawal from the divalent sulphur increases the rotational barrier, and the greater effect in the para substituted series [62] over [61] indicates that resonance effects are important. Thus an Exner plot[35] ($\Delta G^{\ddagger}$ for [62] v $\Delta G^{\ddagger}$ for corresponding [61]) had a slope of 4.5 against 1.14 expected if only inductive effects were important (the substituted benzoic acids gave a slope of 1.14). This appears to rule out the negative hyperconjugation hypothesis

in which only inductive effects can operate; in this system the aryl anion [65] has the negative charge located in a σ orbital orthogonal to



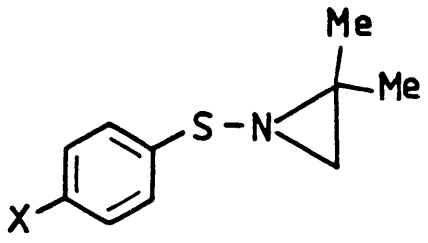
[65]

the π system, and so cannot gain extra stabilisation by resonance. However with (p-d) π bonding resonance effects would be expected to be important, and the increasing electron withdrawal from the divalent sulphur atom would in theory lower the energy of the 3d orbitals, enabling such bonding to occur. Raban and Jones[34] assign the torsional barriers in [63] ($\Delta G^{\ddagger}$ = 13.5 kcal mol^{-1}) to steric effects alone (i.e. eclipsing of substituents in the transition state). However, (p-d) π bonding becomes appreciable with more electronegative substituents in the divalent sulphur aryl ring, giving rise to partial double bond character in the ground state. The effect of substitution in the series [64] is the reverse of [61] and [62]; this may be accounted for by assuming the sulphonyl sulphur atom is able to compete for the nitrogen lone pair when electronegative substituents are placed in the sulphonyl aryl ring, thus reducing the bond order of the sulphenyl S-N bond.

It appears that (p-d) π bonding can add up to 7 kcal mol^{-1} to the rotational barrier in addition to the steric contribution of ~13 kcal mol^{-1} in these systems.

(c) Substituent effects in arylsulphenylaziridines

A series of p-substituted arylsulphenylaziridines have been prepared and the $\Delta G^{\ddagger}$ values evaluated were all between 12-13 kcal mol^{-1}.[36†] In N-arylaziridines, p-substituents have a direct effect on the magnitude of the inversion barrier, as a result of (p-p) π conjugation in the transition state for inversion (a ρ value of 2.8 was obtained).[15] However in the sulphenylaziridines [66], very little dependence on



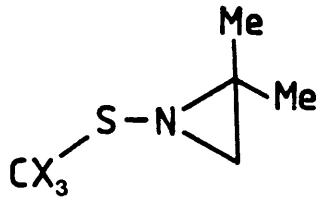
[66]

$\rho_{300} = -0.2 \pm 0.1$

substituents was found, with electron withdrawing substituents having slightly higher inversion barriers than for other members of the series. If (p-d) π bonding were occurring here, a result similar to the N-arylaziridines [15]-[20] should obtain. It is possible that there is an equal degree of (p-d) π bonding in the ground state and transition state, but this seems unlikely.

Abnormally low inversion barriers were obtained for the N-trihalomethylsulphenylaziridines [67] and [68].[36] They were much lower than could be accounted for by steric effects alone (when $\Delta G^{\ddagger}$ for inversion

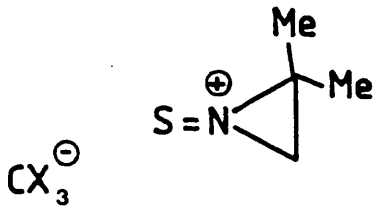
† That the rate determining step for racemisation in sulphenylaziridines is N inversion and not S-N rotation has been demonstrated by Lehn and Wagner (ref. 37).



[67] X=F, ΔG^{+} = 10·4 kcal mol^{-1}

[68] X=Cl, ΔG^{+} = 9·2 kcal mol^{-1}

was plotted against Taft's steric parameter[38] for a series of sulphenylaziridines, a good correlation was obtained, but the inversion barriers in [67] and [68] were 2-2.5 kcal mol^{-1} lower than expected). It is possible that negative hyperconjugation is the cause in these two cases; the resonance form [69] for n-σ* bonding is stabilised by the



[69]

electronegative trihalomethyl carbanion. This leads to increased stabilisation of the planar transition state to inversion.

(d) Objections to the negative hyperconjugation and (p-d) π bonding hypotheses

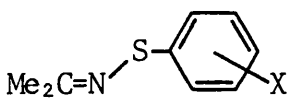
Although negative hyperconjugation is a possible explanation for the inversion barriers in sulphenylaziridines, the results from the sulphonylsulphenamide series indicate that resonance effects are important (vide supra) whereas only the inductive effect is important for negative hyperconjugation.

Similarly, the sulphenylsulphonamides can accommodate a (p-d) π bonding hypothesis, but the sulphenylaziridines cannot, in view of

their lack of substituent effects. Davis et al.[39] examined the barrier to inversion in a series of N-sulphenylimines [70]-[74]; the barriers were considerably lower than the corresponding oximes.[40] Calculations

TABLE 6

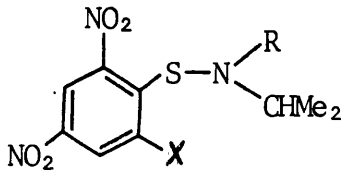
Inversion barriers in some N-sulphenylimines



		T_c	$\Delta G^{\ddagger}$	
[70]	X = H	104	20.3	ref. 39
[71]	X = pCl	110	20.6	
[72]	X = pBr	111	20.7	
[73]	X = mNO_2	108	20.5	
[74]	X = pNO_2	116	20.8	

had suggested[41] that (p-d) π bonding would be maximised if the adjacent N lone pair to the S 3d orbitals were in a p orbital (viz. the linear transition state for inversion in N-sulphenylimines), and this could account for the lower barriers in N-sulphenylimines than oximes. However, it is clear from Table 6 that the magnitude of the inversion barrier is unaffected by the nature of X (as in the sulphenylaziridines), and this casts doubt on the importance of (p-d) π bonding in these systems.

Raban and Yamamoto[42] found that trinitrobenzenesulphenamides had lower rotational barriers than dinitrobenzenesulphenamides. In view of the importance of electron withdrawing substituents in augmenting the rotational barrier in sulphenamides, the introduction of a third nitro group appears to cause steric inhibition of resonance; for [75] and



		T_c	$\Delta G^{\ddagger}$	ref.
[75]	X = H, R = $CHMe_2$	105	20.6	42
[76]	X = NO_2, R = $CHMe_2$	62	17.6	42
[77]	X = H, R = Tos	115	20.1	34
[78]	X = NO_2, R = Tos	-11	14.2	42

[77] the aryl ring is likely to be in the CSN plane, so that conjugation of the sulphur $3p_z$ orbital occurs with the aryl ring.† However, the third nitro group could render this conformationally unfavourable because of steric hindrance. Loss of resonance of the sulphur atom with the aromatic ring results in less lowering of the sulphur 3p orbital energy therefore less efficient 3p-2p interaction; i.e. a lower barrier to rotation using Kost's M.O. description (vide infra). An analogy here is the increased basicity of NN-dimethyl-2,4,6-trinitroaniline[44] ($pK_{BH^+} = -6.55$) in which steric inhibition of resonance prevents the nitrogen lone pair from interacting with the aryl ring, so the basicity is increased 3500 times over that of 2,4,6-trinitroaniline[45] ($pK_{BH^+} = -10.1$).

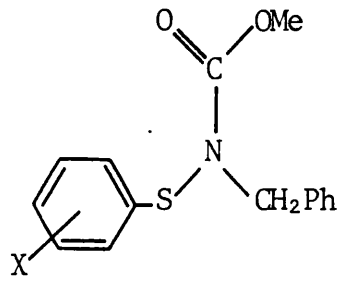
A convincing demonstration of the unimportance of (p-d) π bonding in acyclic sulphenamides was demonstrated by Kost and Zeichner[46] who measured rotational barriers around both the amide C-N and S-N bonds in the series of sulphenylbenzylurethanes [79]-[85] in table 7 by using the benzyl CH_2 in the n.m.r. If (p-d) π bonding is augmenting the rotational barrier in the nitro substituted compounds, it follows that

---

† In the X-ray crystal structure of 2-(2,4-dinitrobenzenesulphenylamino)-2,3,4,5-tetraphenyl-(2H)pyrrole [269] (see 7.3), the plane of the dinitrophenyl ring was found to be within 5° of the CSN plane.[43]

TABLE 7

Rotational barriers in sulphenylbenzylurethanes



		$\Delta G^{\ddagger}$	
		S-N	C-N (amide)
[79]	X = p-OMe	8.7	12.1
[80]	X = p-Me	9.1	12.1
[81]	X = H	9.4	12.1
[82]	X = p-Cl	9.5	12.0
[83]	X = m-NO_2	9.9	12.0
[84]	X = p-NO_2	10.9	12.0
[85]	X = 2,4-$(NO_2)_2$	16.2	12.3

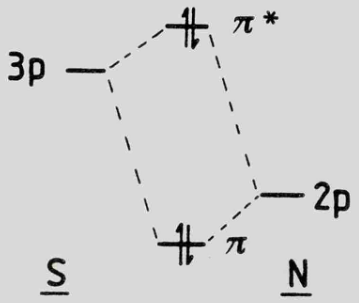
the amide rotational barrier be reduced, as the same lone pair is involved in both rotational barriers. In the event, the amide barrier was found to be independent of X, unlike the behaviour of the S-N bond. One cannot assume that (p-d) π bonding stabilises both ground state and transition state for amide rotation equally, as conjugation between the nitrogen and carbonyl group is non-existent at the transition state for amide rotation.

(e) A molecular orbital model to account for sulphenamide rotation barriers

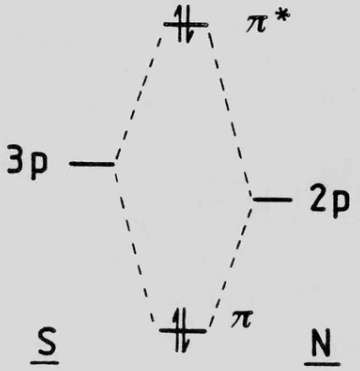
Kost and Sprecher[47] have proposed a model for sulphenamide rotational barriers based on a lone pair - lone pair repulsions. In this model, a non-bonding π interaction between the two lone pairs occurs; this interaction has a net destabilising effect and is the transition state for rotation. The interaction can be illustrated in M.O. terms as in Scheme 6.

Scheme 6

M.O. model for sulphenamides



(a) for non-electronegative substituent at sulphur



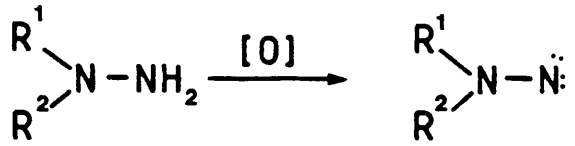
(b) for electronegative substituent at sulphur

In (a) the sulphur 3p orbital is higher in energy than the nitrogen 2p orbital (or the nitrogen sp^3 hybrid for a pyramidal nitrogen). However with an electronegative substituent on sulphur, the energy of the 3p orbital is reduced, with concomitant increase in the destabilising interaction; as a result, the rotational barrier increases, in agreement with experimental results. Similarly, electron withdrawal from nitrogen has the reverse effect, as expected (as in the series [64]). This model also rationalises the results in the sulphenylbenzylurethanes [79]-[85]. For amide rotation, the S-N bond remains in the ground state (as the two rotations required for racemisation occur sequentially) and as a result substituent effects will not affect the barrier as through resonance is absent. Similarly, the low rotational barriers in sulphenylaziridines are accounted for; the nitrogen lone pair has increased s character, and so a lower energy. This increases the energy difference between the lone pairs, thus reducing the repulsive interaction, and so the rotational barrier.

CHAPTER 2

2.1 N-nitrenes

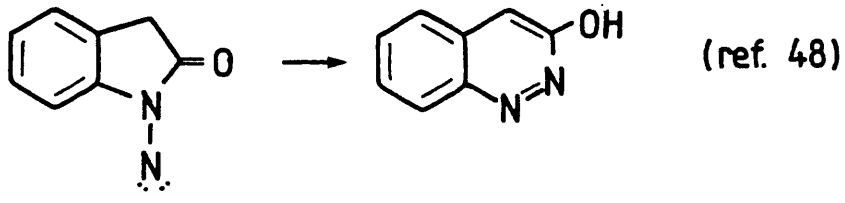
The research described in this thesis stems from the reaction of N-nitrenes [86] with allyl aryl sulphides to give sulphenamides. The N-nitrenes employed, prepared by oxidation of the parent N-amino compound, invariably have the second nitrogen as part of a heterocyclic ring system. They can be divided into two categories:- (a) those which have low energy intramolecular reactions available, and thus



[86]

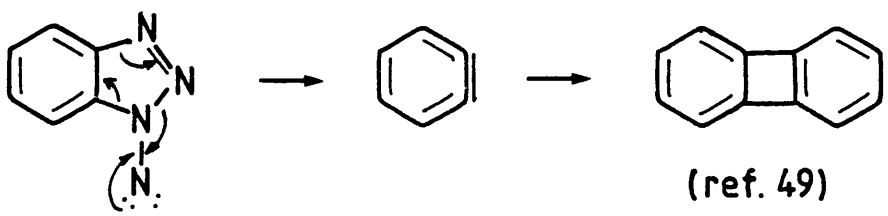
cannot be trapped intermolecularly, and (b) those which undergo intermolecular reactions including deamination and tetrazene formation; these can be trapped with a variety of reagents.

In the first category are the nitrenes derived from N-amino-oxindole [87],[48] N-aminobenzotriazole [88],[49] and N-aminobenzotriazinone [89],[50] which give products derived from intramolecular rearrangement (for [87]), and fragmentation:



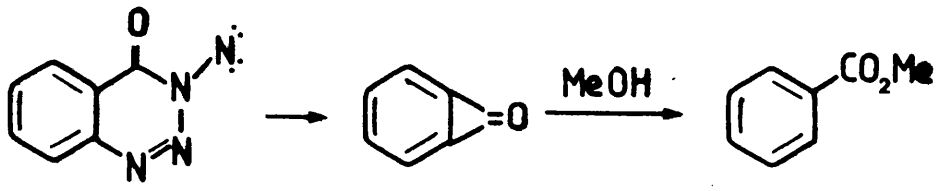
(ref. 48)

[87]



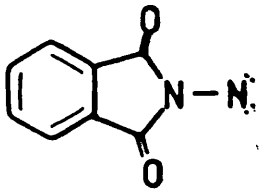
(ref. 49)

[88]



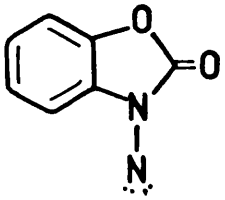
[89] (ref. 50)

Representatives of the second category are the nitrenes [90]-[93]:



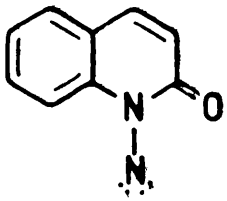
'phthalimidonitrene'

[90]



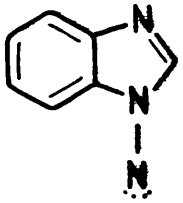
'benzoxazolinonenitrene'

[91]



'quinolonenitrene'

[92]



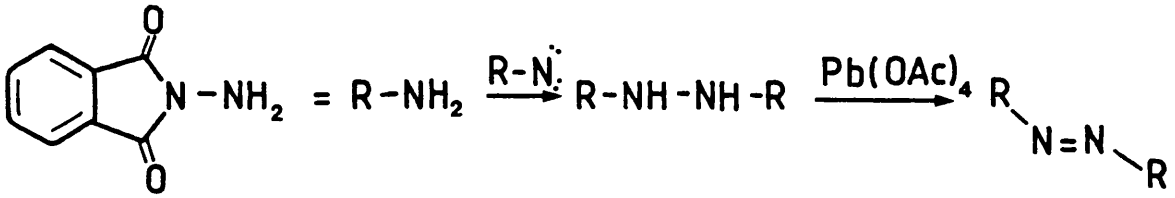
'benzimidazolenitrene'

[93]

Such nitrenes can be trapped by a variety of reagents including alkenes,[51] alkynes,[52] allenes,[53] sulphoxides,[54] and aromatic compounds.[55,56]

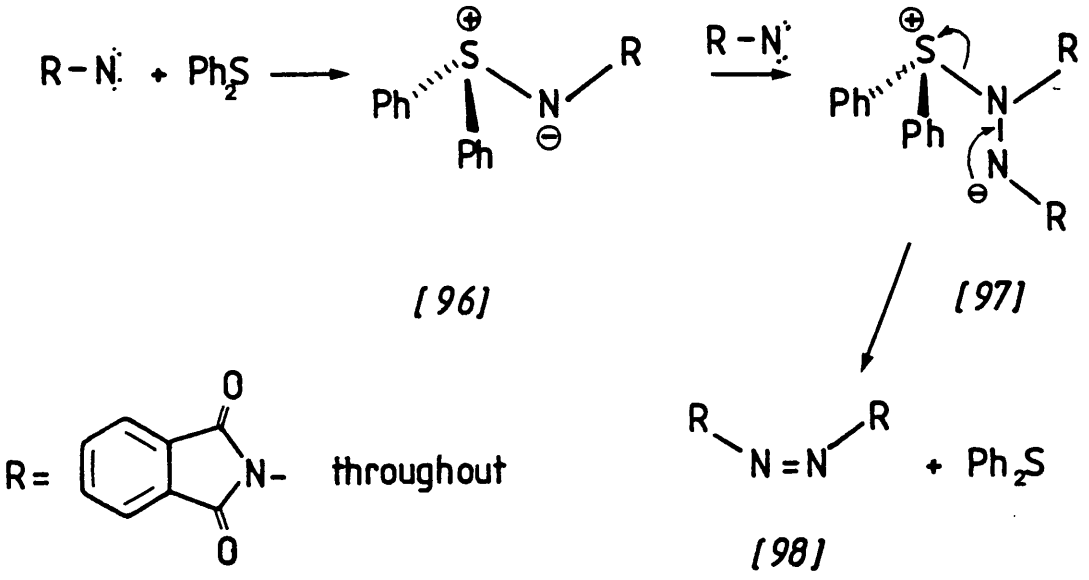
2.2 The behaviour of phthalimidonitrene in the presence of diphenyl sulphide

When N-aminophthalimide [94] is oxidised by lead tetra-acetate in the absence of a trap, a variety of products are obtained.[57] One of these is trans-diphthaloyl tetrazene [95] whose formation may be rationalised by attack of phthalimidonitrene [90] on an unchanged N-aminophthalimide molecule:



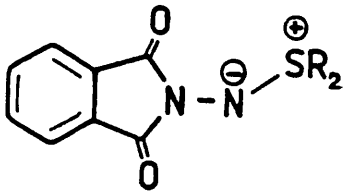
[94] [95]

However, in 1970, Jones[58] observed that the stereochemistry of the product [95] was changed from trans to cis in the presence of diphenyl sulphide. He rationalised this result by proposing a sulphilimine intermediate [96] which was attacked by another phthalimidonitrene molecule to give [97]. Breakdown of [97] gave cis-diphthaloyltetrazene [98] in 70% yield.



[96] [97] [98]

More recently, Rees et al.[59] have isolated stable sulphilimines from phthalimidonitrene and dialkyl sulphides, e.g. [99] and [100] which are stable at 0°, but revert back to phthalimidonitrene and

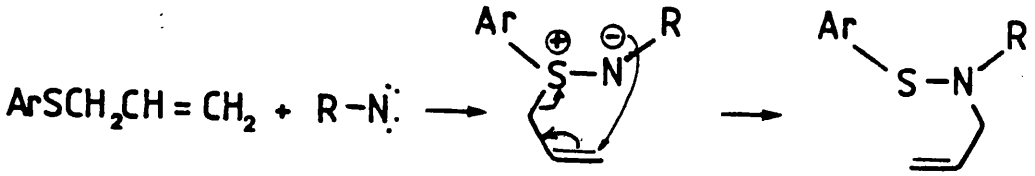


[99] R = Me
[100] R = Et

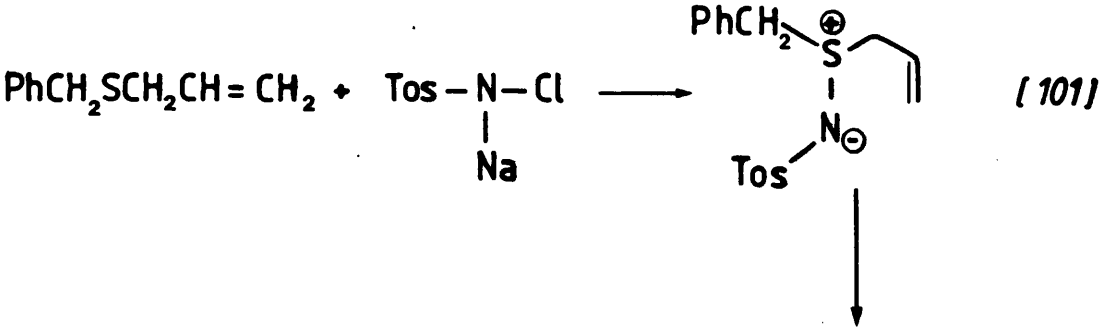
dialkyl sulphide in boiling benzene, and thus are a useful alternative way to generate the nitrene [90].

2.3 The reaction of N-nitrenes with allyl aryl sulphides

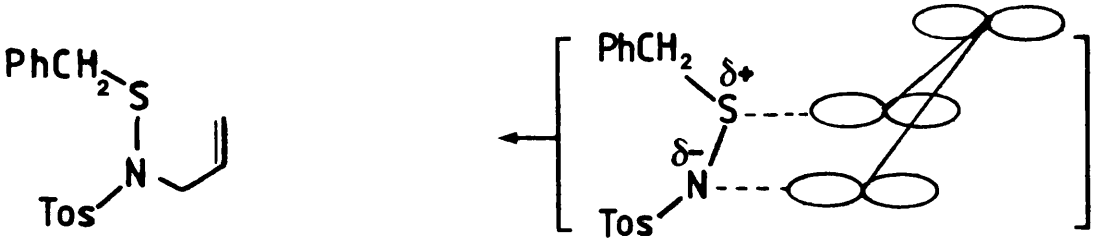
The sulphilimine intermediate [96] can be diverted from reaction with a further nitrene molecule by incorporating an allyl substituent into the sulphide and encouraging a [2,3]-sigmatropic rearrangement to



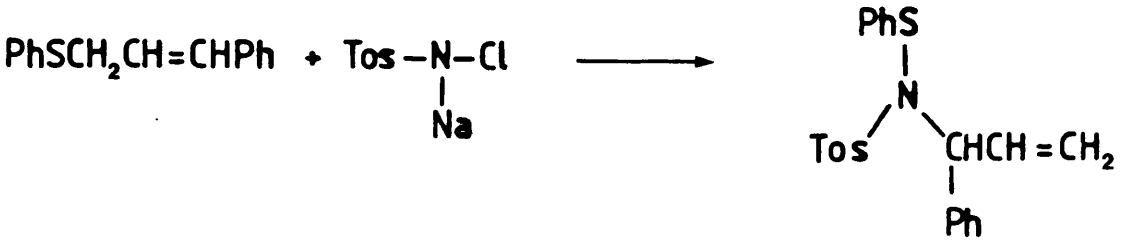
occur. The occurrence of such a rearrangement in sulphilimines was first demonstrated by Challenger et al.,[60,61,62] who reacted allyl sulphides with chloramine-T. Some of the sulphilimines so formed could be isolated at room temperature and rearranged on warming, e.g. allyl benzyl sulphide and chloramine-T[61] gave a stable sulphilimine [101] which rearranged at its melting point into the sulphenylsulphonamide [102]. However with cinnamyl phenyl sulphide, rearrangement occurred spontaneously to give [103].[62]



[101]

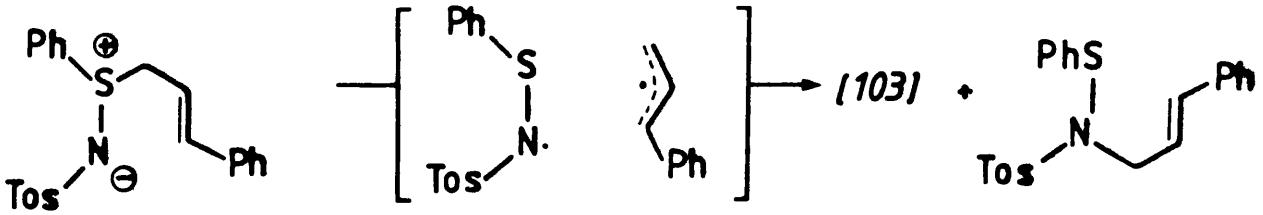


[102]



[103]

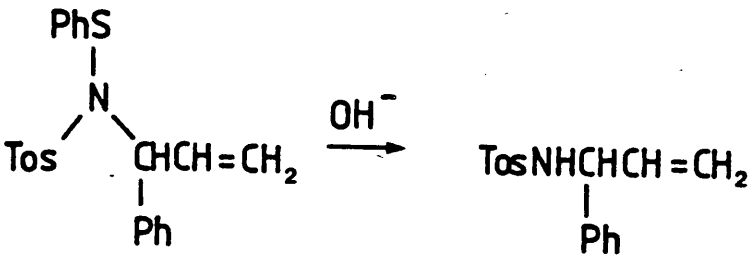
There is an alternative radical process possible for this type of reaction:[63]



[104]

However, if this pathway was significant, substantial amounts of [104] should be formed as well as [103], whereas in the event only [103] was isolated in 71% yield. Its structure was proved by alkaline hydrolysis to [105]; [106] was synthesised for comparison and shown

to be a different compound.[62]



[105]

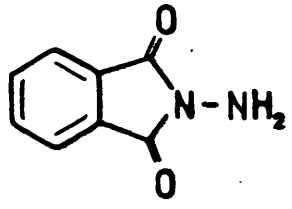
$TosNHCH_2CH=CHPh$

[106]

When N-aminophthalimide was oxidised with lead tetra-acetate in the presence of allyl 4-chlorophenyl sulphide [107], a 61% yield of the sulphenamide [108] was isolated.[64] Similarly [109] was obtained in 60% yield using trans-but-2-enyl 4-chlorophenyl sulphide [110].

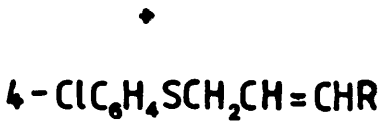
These products are presumably formed by [2,3]-sigmatropic rearrangement of the sulphilimine [111]. 9% of cis-diphthaloyltetrazene [98] was isolated in each case. Analogous sulphenamides [112] and [113] were obtained using N-aminobenzoxazolinone [114] in place of N-aminophthalimide, in similar yields.[64] When the preparation of [113] was carried out at -10°, no evidence was obtained for the intermediate sulphilimine [115] by n.m.r. examination of the reaction mixture at this temperature. Also absent from the n.m.r. spectrum were signals due to [116] which could be formed via the radical mechanism for the rearrangement. The major pathway for the rearrangement thus appears to be the concerted sigmatropic rearrangement.

Evidently, the rearrangement occurs more easily here than in the cases examined by Challenger et al. whose sulphilimines all bear a sulphonyl group on the nitrogen atom. This stabilises the ground state



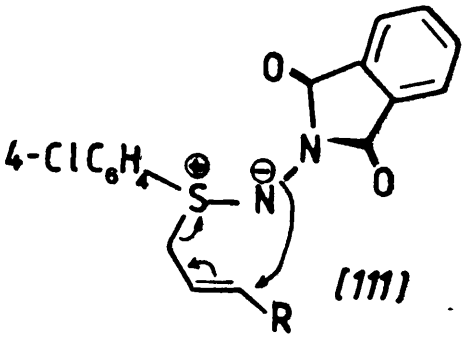
[94]

+

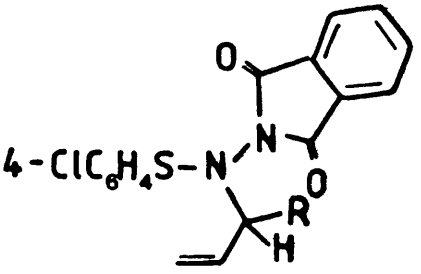


[107] R = H
[110] R = Me

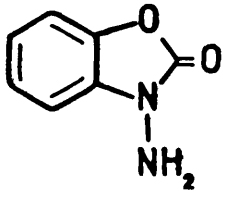
$Pb(OAc)_4$ / CH_2Cl_2



[111]

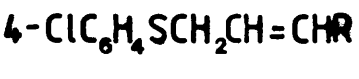


[108] R = H
[109] R = Me



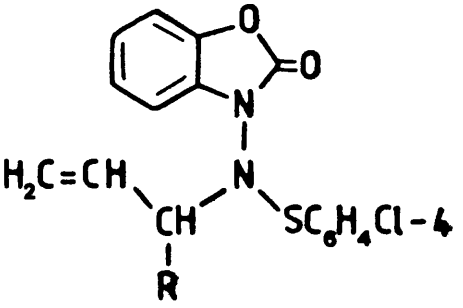
[114]

+

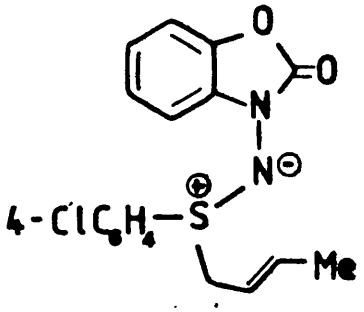


[107]
[110]

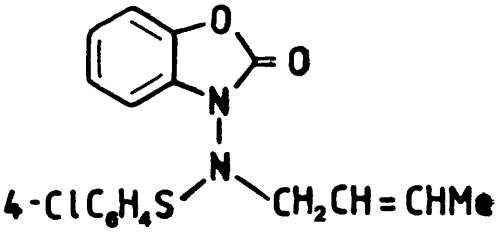
$Pb(OAc)_4$ / CH_2Cl_2



[112] R = H
[113] R = Me

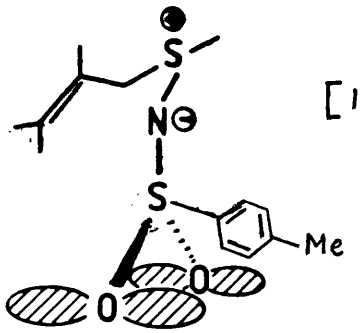


[115]



[116]

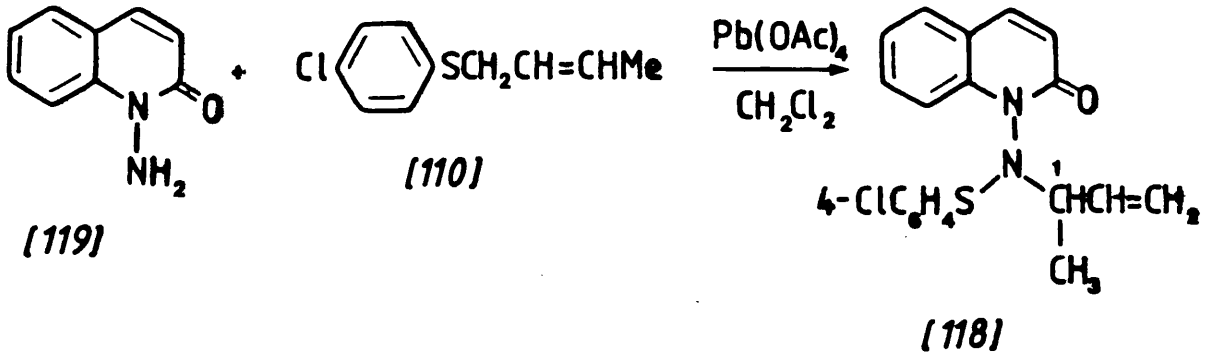
relative to the transition state - this delocalisation is destroyed in the transition state for rearrangement [117].[63] No such resonance delocalisation is possible in the sulphilimines [111] and [115] so rearrangement occurs spontaneously.



[117]

2.4 N.m.r. spectra of N-(heteroaryl) arylsulphenamides

The n.m.r. behaviour of the sulphenamides [108], [109], [112], [113], and the sulphenamide [118] prepared from N-aminoquinolone [119], trans-but-2-enyl 4-chlorophenyl sulphide [110], and lead tetra-acetate were found to be significantly different.[64]



[119] [110] [118]

Whereas the phthalimido compounds [108] and [109] showed no unusual n.m.r. features, the benzoxazolinone compound [113] showed a broad signal for the C-1 methyl doublet at 27°. At higher temperatures than this only one methyl doublet was seen (δ1.42 in $CDCl_3$ at 59°), but at lower temperatures, two doublets were visible (δ1.36 and 1.42, ratio

2:3 in $CDCl_3$ at -54°). Evidently, at lower temperatures additional chirality is established in the molecule which, in addition to that at C-1 gives rise to diastereoisomers whose presence is revealed by n.m.r..

The corresponding quinolone derivative [118] also shows two doublets for the C-1 methyl group, but in contrast to [118] no coalescence is seen up to 100°, above which temperature thermal decomposition occurs. The ratio of the two doublets (δ_{Me}0.93 and 1.48 in $CFCl_3$) initially present was 2:1 respectively, but changed on heating to reach an equilibrium value of 4:5 after 1h at 80°. Repeated recrystallisation from 60°-80° petrol of the crude reaction mixture removed the lower field doublet (present initially in the lesser amount), and gave a pure sample showing the δ0.93 methyl doublet. The other diastereoisomer having the δ1.48 methyl doublet could be obtained pure by careful chromatography over Kieselgel.

The extra chirality in [118] which enables separation of these diastereoisomers could be accounted for by any of the following three processes:

(a) slow rotation around the N-N bond

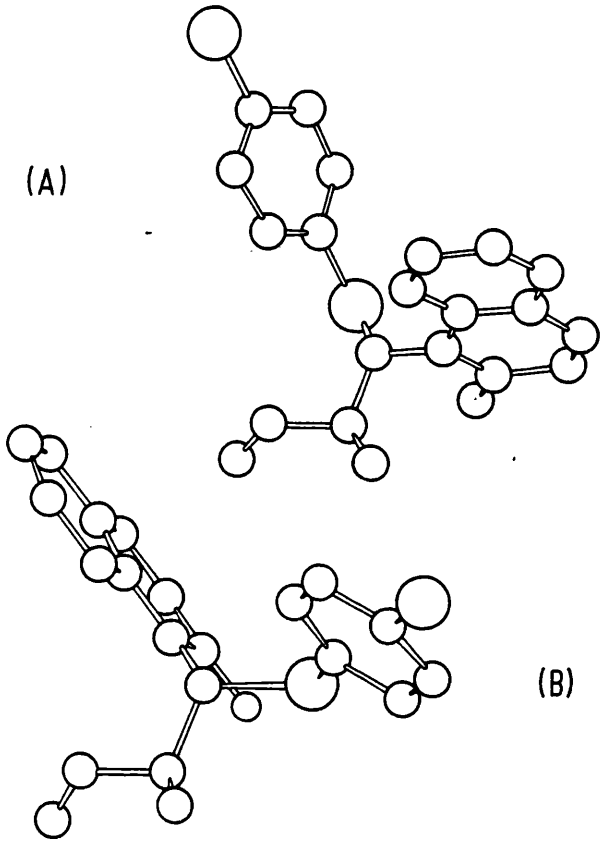
(b) slow rotation around the S-N bond

(c) slow inversion at the sulphenamide nitrogen.

Other possibilities which in principle could account for diastereoisomerism in [118] are considered to be of too low energy, e.g. restricted rotation around the C-N bond[65] (the rotational barrier around the C-N bond in trimethylamine is only 4.4 kcal mol^{-1} [66]).

Of the three possibilities above, support for (a) comes from the fact that the symmetrical phthalimido group in [109] cannot sustain a chiral axis, and this would account for the lack of diastereoisomers in [109]. However, it seems curious that there should be such a large

difference in the energy barriers to N-N bond rotation between the benzoxazolinone substituted sulphenamide [113] and the quinolone analogue [118]. An attempt to resolve the problem was made by determining the X-ray crystal structures of the diastereoisomers of [118][67] (fig. 1).



Crystal structures of *N*-(1,2-dihydro-2-oxoquinolin-1-yl)-*N*-(1-methylallyl)-*p*-chlorobenzenesulphenamide: top (A) (methyl doublet δ 1.48); bottom (B) (methyl doublet δ 0.93)

Figure 1

Inspection of the two structures, however, reveals that whereas

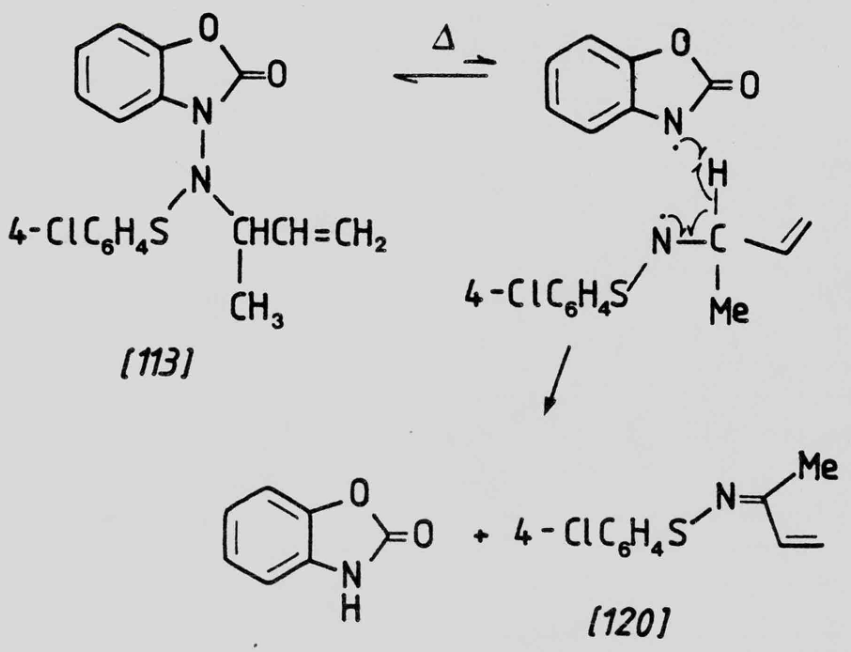
the chirality of the 1-methylallyl group is the same, the pyramidal sulphenamide nitrogen and the N-N and S-N bonds all have opposite chirality, so the factor responsible for the diastereoisomerism of [118] cannot be deduced directly from these structures.

Chapter three of this work is concerned with the synthesis of derivatives of [118] in order to ascertain which of the processes (a), (b) or (c) allows isolation of its diastereoisomers.

2.5 Thermal stability of the sulphenamides

Thermal decomposition of the above sulphenamides takes place at significantly different temperatures. The phthalimido derivatives [108] and [109] were the most stable, with substantial amounts of starting material being recovered even after refluxing in bromobenzene (156°). However, the benzoxazolinone derivatives are completely decomposed in boiling benzene within one hour. Atkinson and Symons[68] have shown this decomposition to take place at least in part *via* homolysis of the N-N bond, followed by proton abstraction by the benzoxazolinone radical to give benzoxazolinone and the sulphenylimine [120]. The two intermediate radicals were identified by e.s.r. spectroscopy, and the same e.s.r. signals could be observed at as low a temperature as 48°. If the barrier which separates the two diastereoisomers of [113] and [118] is restricted rotation around the N-N bond, then these e.s.r. results suggest that N-N homolysis-recombination may be an alternative route to rotation for interconversion of the diastereoisomers.

The corresponding quinolone derivative [118] was found to be intermediate in stability between [109] and [113]; it decomposed in boiling toluene over 5h to give 2-hydroxyquinoline and the sulphenylimine [120].

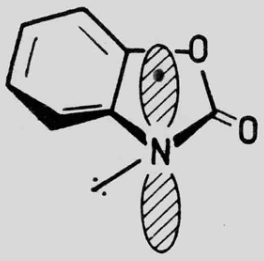


[113]

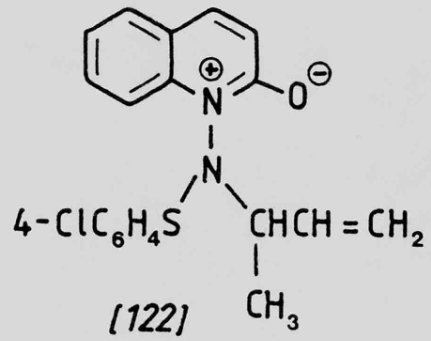
[120]

It is possible to rationalise the thermal stability of [109], [113] and [118] by consideration of the intermediate heterocyclic radicals. The benzoxazolinone radical [121] would be more extensively delocalised than the corresponding phthalimido radical. Also, the loss of amide resonance caused by N-N σ bond bending in the transition state for N-N homolysis of [113] is offset by compensation from the ring oxygen.

The greater thermal stability of [118] relative to [113] may be a result of the resonance contributor [122] to the quinolone ring system;



[121]



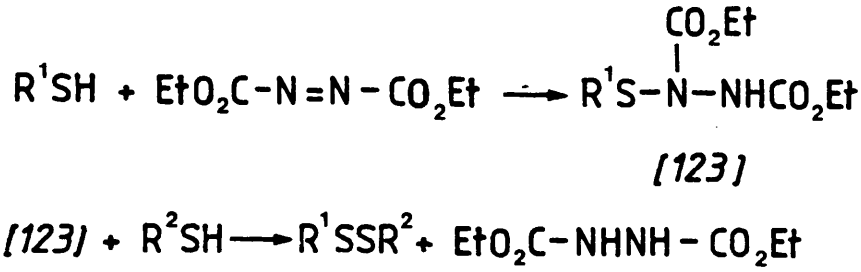
[122]

this aromatic resonance energy must be lost during formation of an analogous radical to [121] on homolysis.

2.6 Other examples of compounds containing the N-N-S^{II} unit

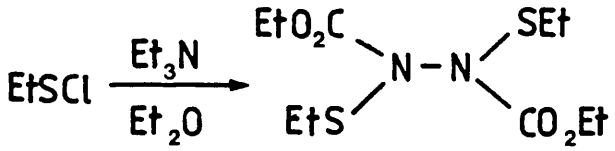
Very few examples of N-N-S^{II} species are known in the literature, and all the examples prepared to date contain one or more electron withdrawing substituents (e.g. $>C=O$) on the nitrogen atoms.

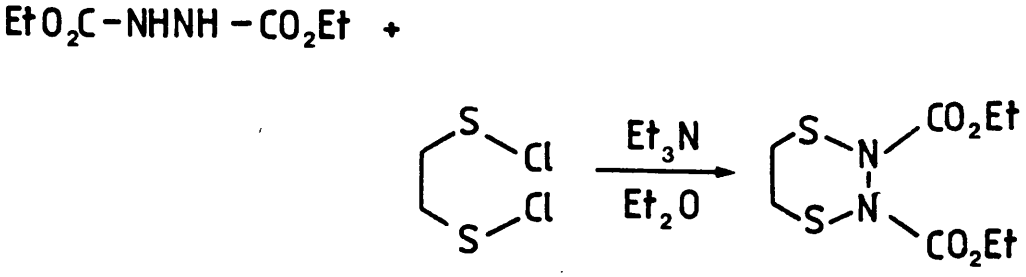
Mukaiyama and Takahashi[69] were able to add aliphatic thiols to the azo function of diethyl azodicarboxylate. The adduct formed, [123], could then be treated with a second thiol to give unsymmetrical disulphides:



[123]

Similar compounds were obtained by Linke et al. who sulphenylated diethyl hydrazodicarboxylate:[70]

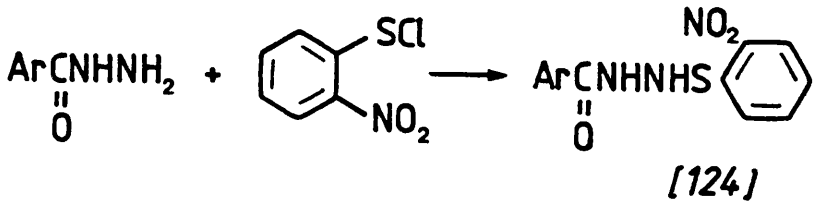




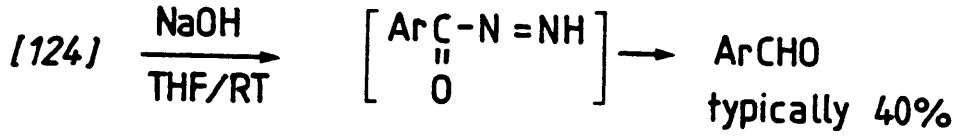
[67%]

Cacchi and Paolucci[71] were able to sulphenylate hydrazides with o-nitrophenylsulphenyl chloride and the resulting sulphenylhydrazides

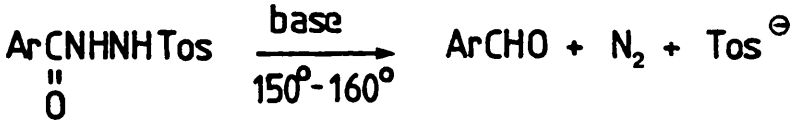
[124] were degraded by base at room temperature to give aldehydes in moderate yields.



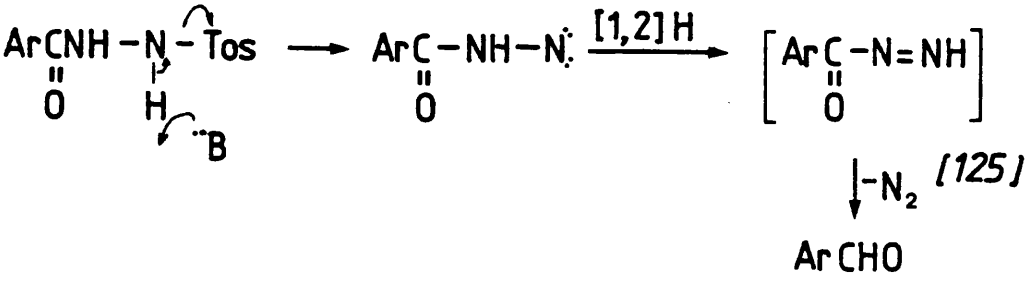
[124]



The reaction of [124] with base resembles the McFadyen-Stevens reaction,[72,73] in which a tosyl group is the leaving group instead of an o-nitrophenylthio group:



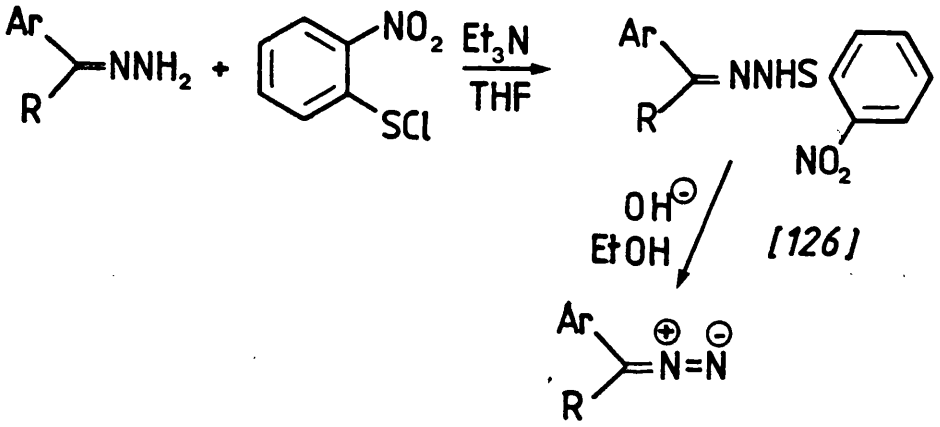
This reaction is believed[73] to proceed <u>via</u> an α-elimination to a nitrene which rapidly tautomerises <u>via</u> an α-insertion to the azo species [125]:



However, much more vigorous conditions are required here than in Cacchi and Paolucci's reaction and this implies the phenylthio group is a better leaving group than the tosyl group in this case.

Anselme and Dana[74] were able to prepare sulphenylated hydrazones

[126] which on treatment with base gave diazo compounds by a similar mechanism involving α-elimination of the arylthio group.



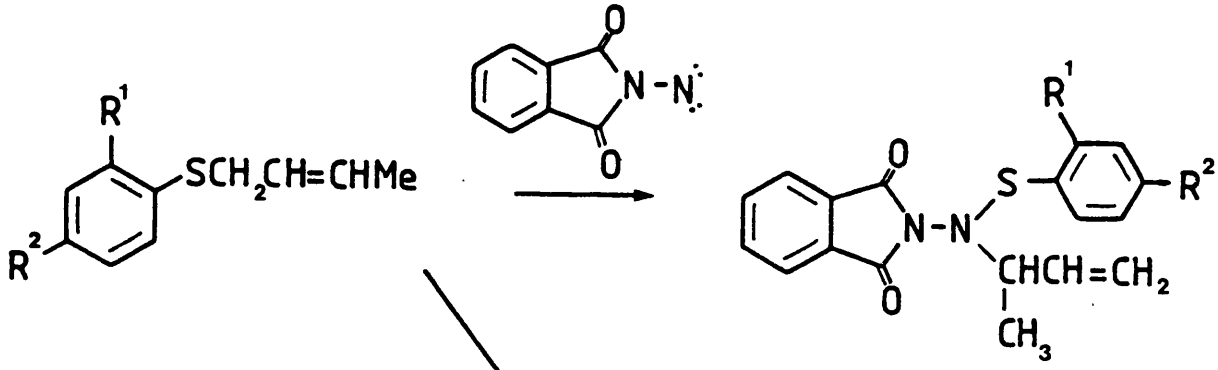
As mentioned earlier, the interesting feature of these isolable N-N-S^{II} species is the presence of electron withdrawing substituents on the nitrogen atoms, as in [123] and [124], or delocalisation of the terminal nitrogen lone pair into a π framework as in [126], which it seems are required if the resulting compound is to be stable. No simple sulphenylated hydrazines containing only alkyl or aryl groups were found in the literature, and chapter five of this work describes some attempts to prepare such species.

CHAPTER 3

Investigation of rotational barriers in N-(N-heteroaryl) aryl-sulphenamides

3.1 S-(nitroaryl) sulphenamides

In order to obtain more information on the conformational processes in the N-(N-heteroaryl) arylsulphenamides, the derivatives [129]-[133] were synthesised using the appropriate nitrene precursor, and allyl aryl sulphide.



[127] $R^1 = NO_2, R^2 = H$
[128] $R^1 = R^2 = NO_2$

[129] $R^1 = NO_2, R^2 = H$
[130] $R^1 = R^2 = NO_2$
[131] $R^1 = H, R^2 = NO_2$

[134] R = H
[50] $R = NO_2$

[132] R = H
[133] $R = NO_2$

The sulphenamides [129] and [130] were found to exhibit variable temperature n.m.r. behaviour; in both cases coalescence of the methyl

doublets at C-1 and the S-aryl H-6 proton were observed; two doublets for each were seen at temperatures lower than T_c, and one at higher temperatures. As the N-N bond is not a chiral axis in [129]-[131] because of the symmetry of the phthalimido group, the coalescence observed indicates rotation around the S-N bond is becoming faster on the n.m.r. time scale as the temperature is raised. The fact that [130] has a higher barrier than [129], and the similarity of the magnitude of the energy barriers with the alkyl analogues [134] and [50] also bears this out. The 4-nitro compound [131] did not show any splitting of the methyl doublet down to -88°;[75] this appears to be due to accidental chemical shift equivalence of the methyl groups rather than a low rotational barrier. The rotational barrier in [50] had already been determined by Raban et al.[27] in d^8-toluene as solvent; however, in $CDCl_3$ a larger chemical shift difference of the benzyl CH_2 protons was obtained, enabling a more accurate determination of $\Delta G^{\ddagger}$ and a comparison of the barriers of [129], [130], [132], [133], [134] and [50] in the same solvent. The results are shown in table 8.

The similarity of the barriers in [129] and [130] with [134] and [50] indicate the S-N rotational barrier is not noticeably affected by substitution of the phthalimido group for an alkyl group. The n.m.r. behaviour of the N-quinolone S-2,4-dinitrophenylsulphenamide [133] shows interesting features; at room temperature two diastereoisomers are indicated as for [118] from the methyl doublets at δ1.27 and 1.50. However, at -40° and 220 MHz, four methyl doublets are clearly visible at δ1.18, 1.32, 1.50 and 1.60 (ratio 7.3:1:2:4.3 respectively). Also four types of S-aryl H-6 proton and four types of quinoline H-3 are visible in the same ratio as above (see fig. 2). Presumably the four diastereoisomers result from slow rotation around the N-N and S-N bonds

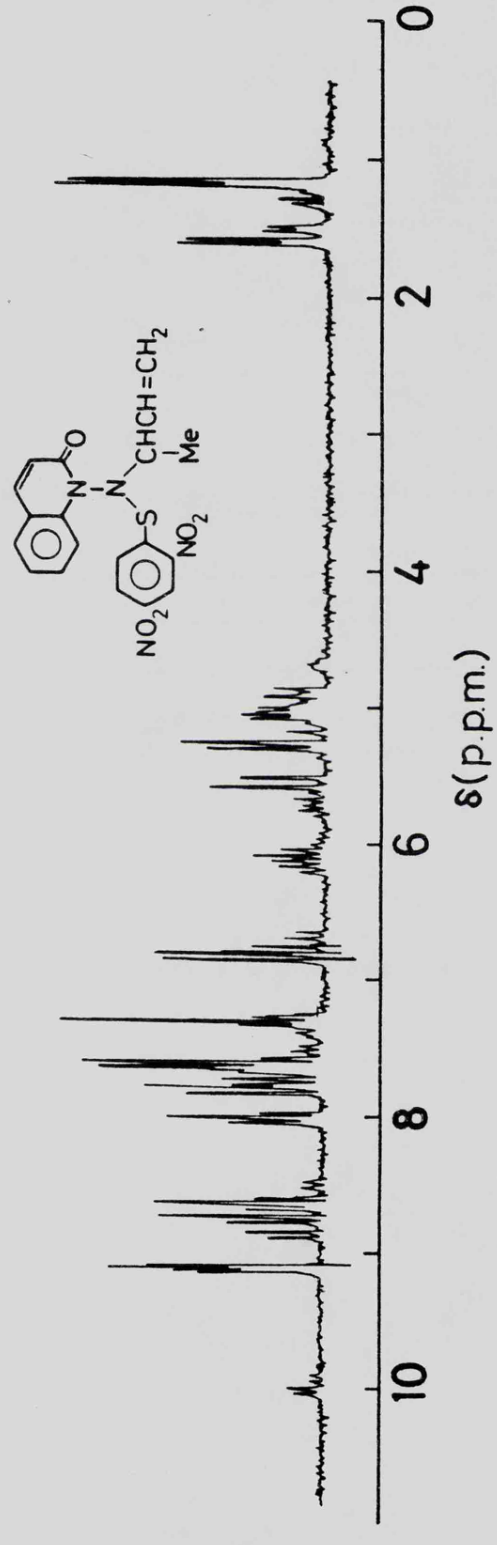


Figure 2

N.m.r. spectrum of (133) at -40° ($CDCl_3$).

TABLE 8

Rotational barriers in S-(nitroaryl)sulphenamides

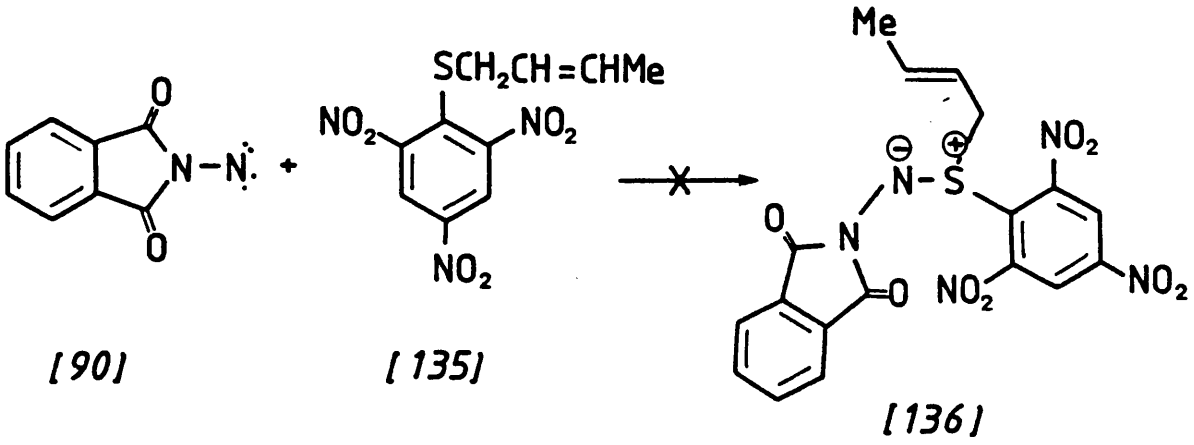
	T_c	$\Delta\nu$(Hz)	$W_{\frac{1}{2}}$(Hz)	$\Delta G^{\ddagger}$
[129]	-2[a]	4.5		14.6
[130]	39[a]	5.0		16.8
[132]	-24 ± 5[b]	≈40		12.3 ± 0.7
[133]	0 ± 5[b]	115 ± 10		12.9 ± 0.3
[134]	26[c]		8.0	14.9
[50]	66[c]		9.0	16.9

[a] coalescence temperature of the C-1 methyl doublets
[b] coalescence temperature of the S-aryl H-6 proton
[c] coalescence temperature of the benzyl CH_2 protons

plus the chiral centre at C-1. On raising the temperature, the four methyl doublets coalesce into two doublets between -18° and +9°; as in [130], this appears to be due to rotation around the S-N bond becoming fast on the n.m.r. time scale. The S-aryl H-6 proton coalesces at 0 ± 5° enabling an approximate free energy of activation of 12.9 ± 0.3 kcal mol^{-1} to be calculated. The 2-nitrophenyl analogue of [133], [132] shows two methyl doublets at room temperature (δ_{Me} 1.17 and 1.55 ppm, $CDCl_3$), as in [118] and [133], but no separation in these is seen on lowering the temperature; however, a coalescence of the S-aryl H-6 proton is seen around -24°, so presumably the methyl doublets are accidentally equivalent as in [131]. The coalescence temperature of the S-aryl H-6 proton in [132] is ~25° lower than in [133] giving an associated barrier of 12.3 ± 0.7 kcal mol^{-1}. The lower barrier in this case is expected for rotation around the S-N bond. Hence it is clear

that restricted rotation around the S-N bond is not responsible for the diastereoisomerism in [118].

It was of interest to attempt the preparation of analogous trinitrobenzenesulphenamides and investigate their rotational barriers but, unfortunately, the N-nitrenes employed did not react with trans-but-2-



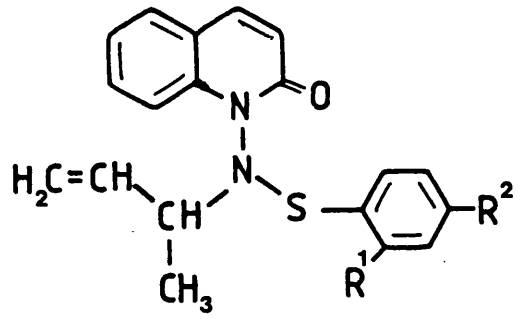
[90] [135] [136]

enyl trinitrophenyl sulphide [135]. Failure to form the desired sulphenamide may be due to the necessity of forming a positive charge on the sulphur atom of the intermediate sulphilimine [136], adjacent to the strongly electron withdrawing trinitrophenyl group.

3.2 Magnitude of the energy barrier separating the diastereoisomers of [118] and [132]

As stated earlier (2.4), the diastereoisomers of [118] equilibrate on heating. Those of [132] do likewise at slightly lower temperatures. The kinetics of equilibration were investigated by n.m.r. - a solution of a pure (or nearly pure) diastereoisomer (obtained by recrystallisation) was dissolved in chlorobenzene and the equilibration followed by integration of the methyl doublets over a period of time. By obtaining rate constants at different temperatures it was possible to evaluate

the activation parameters for this interconversion (see appendix 1):



[118] $R^1=H$, $R^2=Cl$

[132] $R^1=NO_2$, $R^2=H$

	E_A	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$ (e.u.)	$\Delta G^{\ddagger}$
[118][a]	27.1 ± 0.8	26.4 ± 0.8	0.9,[b] 0.4[c] ± 2.2	26.1,[b] 26.3[c]
[132][d]	23.8 ± 0.5	23.1 ± 0.5	-6.5,[b] -7.3[c] ± 1.4	25.3,[b] 25.6[c]

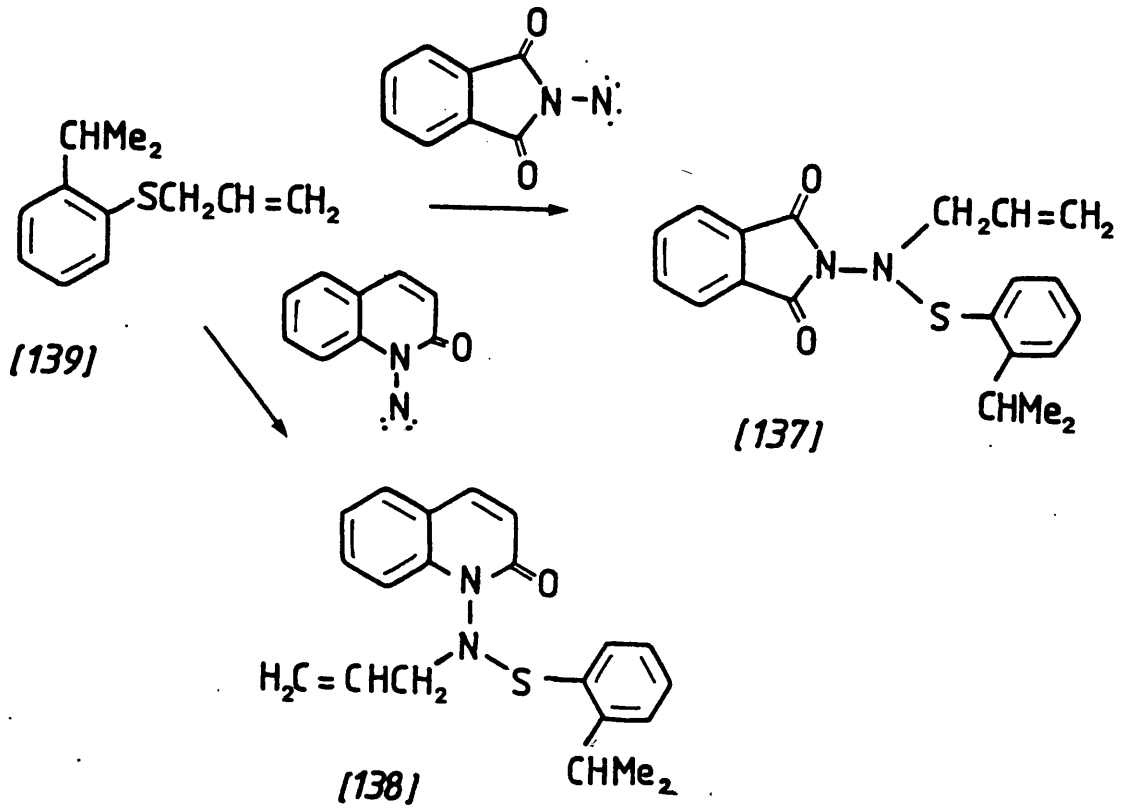
[a] from four different temperatures
[b] minor diastereoisomer
[c] major diastereoisomer
[d] from three different temperatures

The $\Delta G^{\ddagger}$ values for [118] and [132] are similar, implying that the same process interconverts the diastereoisomers; the differences in the entropies of activation may be due to differences in solvation between the ground state and transition state. The results must be interpreted with caution, however; the results for [132] were measured at three different temperatures only, so the error margins may be larger than given above.

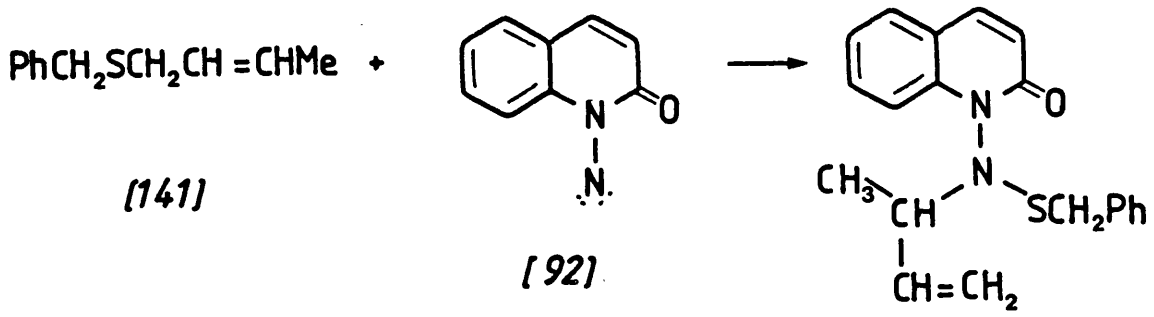
3.3 The cause of the high barrier to interconversion of the diastereoisomers in [118] and [132]

The sulphenamides [137] and [138] were synthesised from the approp-

riate nitrene and allyl 2-isopropyl phenyl sulphide [139]. A clear difference in behaviour of their diastereotopic isopropyl methyl n.m.r.



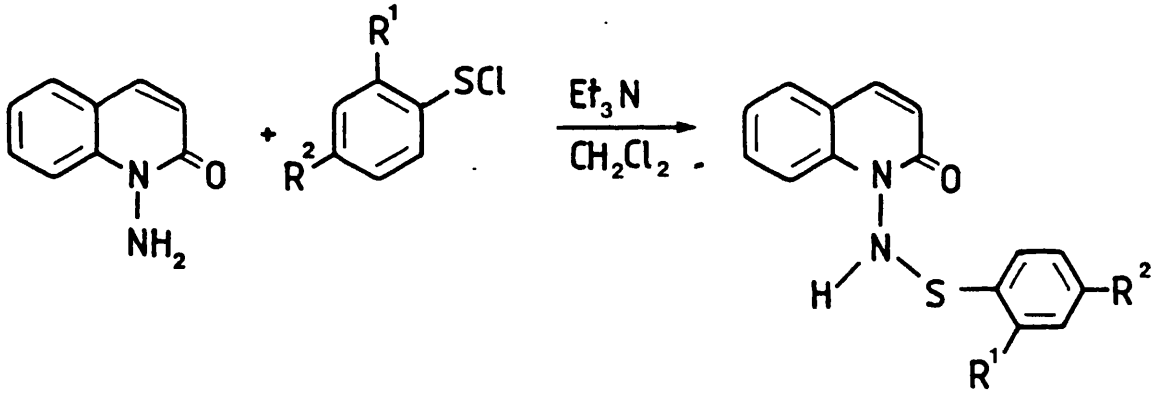
signals was seen. [137] showed only one doublet (δ_{Me} 1.18, $CDCl_3$), but [138] showed two doublets (δ_{Me} 0.82 and 1.02, d^8-toluene), which were unchanged at 100° in the n.m.r., above which temperature thermal decomposition occurs. Evidently, replacement of the 1-methylallyl substituent by allyl does not drastically affect the size of the energy barrier. Similarly, the sulphenamide [140] prepared from quinolone-nitrene [92] and benzyl trans-but-2-enyl sulphide [141] existed as two diastereoisomers at room temperature (δ_{Me} 0.95 and 1.45, $CDCl_3$). The ratio initially obtained in the crude reaction product was 4:1 (δ_{Me} 0.95 : 1.45 respectively) which changed to 1.2:1 after 2h in boiling ethanol. The rate of interconversion is slightly slower than [118], but again the barrier to interconversion is high; it appears that the



[141] [92] [140]

S-aryl ring in [118] does not play a significant role in causing its diastereoisomerism, as the barrier remains high when it is substituted by a smaller CH_2Aryl unit as in [140].

However, removal of the N-allyl substituent did have a profound effect on the rotational barrier. Compounds [142] and [143] were

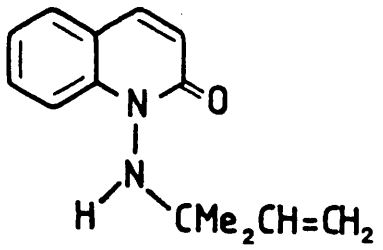


[142] $R^1 = R^2 = NO_2$

[143] $R^1 = CHMe_2$, $R^2 = H$

synthesised from N-aminoquinolone and the appropriate sulphenyl chloride in dichloromethane in the presence of triethylamine as proton scavenger. Examination of the S-aryl signals of [142] in the n.m.r. spectrum indicated only one compound to be present in the temperature range examined (-11° to +50°), unlike [133], which exists as two diastereoisomers at room temperature. The isopropyl derivative [143] only shows one methyl doublet at room temperature unlike the N-allyl

analogue [138]; at -50° and 220 MHz, two methyl doublets are just visible, the coalescence temperature being somewhat higher than this (probably in the range -35 ± 10°). Evidently removal of the N-allyl group reduces the energy barrier considerably. Removal of the arylthio



[144]

group as in [144] also reduces the barrier; a coalescence of the diastereotopic methyl singlets was noted at around room temperature.[76] The magnitude of the associated barrier, 16.2 ± 0.8 kcal mol^{-1} is in the range typical for an sp^2/sp^3 hybridised hydrazine; it seems certain the barriers observed in [143] and [144] are due to restricted rotation around the N-N bond. A most significant result came from the n.m.r.

TABLE 9

Rotational barriers around the N-N bond in N-(N-heteroaryl) arylsulphenamides

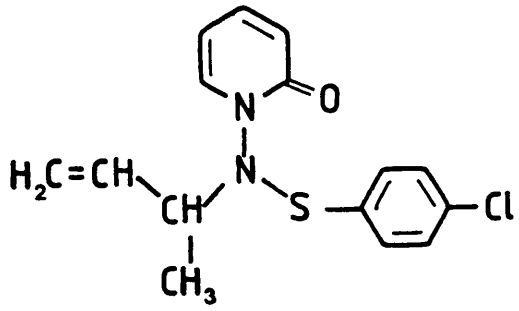
	T_c	$\Delta\nu$(Hz)	$W_{\frac{1}{2}}$(Hz)	J_{AB}	k_c[a](Hz)	$\Delta G^{\ddagger}$
[143]	-35 ± 10[b]	2.0				13.1 ± 0.6
[144]	25 ± 10[b]	2.0-5.0[c]				16.2 ± 0.8
[145]	32	36				15.2
[147]	28		12.0	12.5	76	15.0

[a] rate of exchange at T_c

[b] rough estimate

[c] $\Delta\nu$ was strongly temperature dependent

spectrum of the pyridone derivative [145]. Here, two methyl doublets



[145]

were observed at -40°, but they coalesced on warming ($T_c = 32°$) and only one doublet was seen in chlorobenzene at 101°. The energy barrier in this case, 15.2 kcal mol^{-1}, is 11 kcal mol^{-1} lower than [118]; removal of the benzene ring therefore, as in [145] reduces the barrier considerably. This result rules out (c) in chapter 2 (slow N inversion) as the cause of the diastereoisomerism in [118]; the pyridone ring in [145] is smaller than the quinolone ring in [118] and this should lead to an increase in the inversion barrier [see 1.2(c)]. The fact that a much lower barrier is observed in [145] indicates that a high rotational barrier around the N-N bond is present in [118]. This is probably caused by the steric interaction of substituents on the sulphenamide nitrogen (sulphur, allyl or 1-methylallyl) with the peri H-8 of the quinolone ring. It appears that both the sulphur and allyl substituents are unable to pass the H-8 proton since if either is removed, the high rotational barrier disappears. Further support of this explanation comes from the quinazolone substituted sulphenamides [146] and [147].†

In [146] two diastereoisomers exist at room temperature as indicated from the C-1 methyl doublets (δ 1.10 and 1.65, $CDCl_3$). In this case

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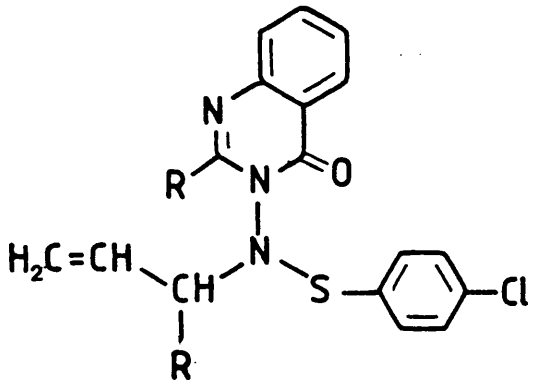
† Restricted rotation around the C-N(3) bond in 2-benzyl 3-aryl-quinazol-4-ones has been studied by Colebrooke et al. (Ref. 77).



[146] R = Me

[147] R = H

the initial ratio was 3.3:1 respectively and changed to 1:1.8 after 1h in boiling benzene (80°). This rate of interconversion of the diastereoisomers is very similar to [118]. Indeed, the quinazolone 2-methyl substituent has a similar steric bulk to the quinolone benzene ring in [118] in terms of inhibiting rotation around the N-N bond. The quinazolone [147] is sterically similar to the pyridone [145] and the rotational barrier obtained from coalescence of the N-allyl CH_2 protons from an ABX system to an A_2X system is very similar to that of [145] (see table 9).

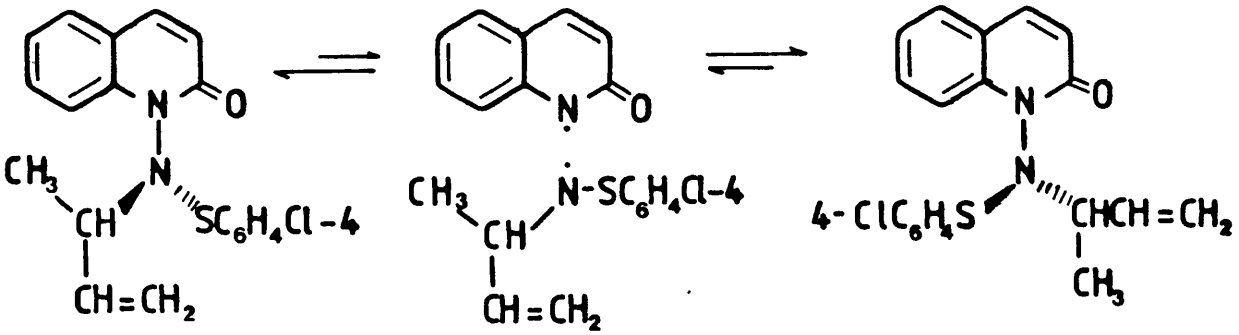
3.4 Mechanism of interconversion of the diastereoisomers of [118] and derivatives

Although the rotational barrier around the N-N bond is high in [118], [132], [133], [138], [140] and [146] there are two other plausible mechanisms by which the diastereoisomers may interconvert besides simple rotation around the N-N bond. These are (a) by homolysis-radical recombination of the N-N bond and (b) via a reverse [2,3]-sigmatropic rearrangement back to the sulphilimine. In both cases, the actual rotational barrier is assumed to be higher than the barrier to interconversion of the diastereoisomers. Another possible mode of interconversion, bimolecular exchange of the N-N bonds does not occur here as the rate of interconversion is independent of concentration, i.e.

first order.

(a) N-N homolysis-recombination

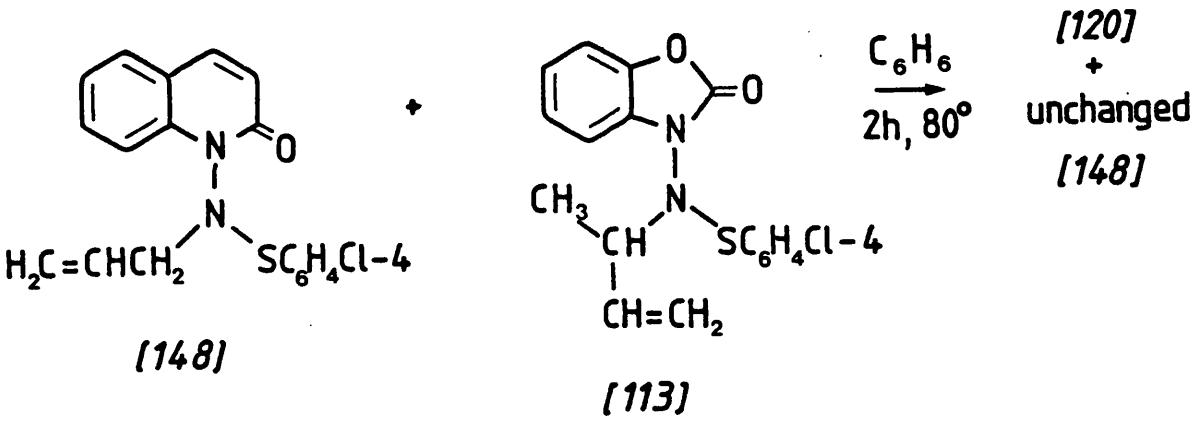
This pathway is illustrated below. It derives some support from the fact that the benzoxazolinone analogue [113] (chapter 2.3) is known to decompose via N-N bond homolysis with the intermediate radicals



[118]

being identifiable by e.s.r. spectroscopy even at 48°, at which point little decomposition occurs.[68] However, although diastereoisomer interconversion of [118] proceeds rapidly at 80°, it did not show any e.s.r. signals at this temperature; nor was the n.m.r. spectrum affected by CIDNP effects. Also, interconversion via a pair of radicals should have an appreciably positive entropy of activation (e.g. racemisation of benzyl aryl sulphoxides[28] proceeds via a radical pair, with entropies of activation of ca. +25 e.u.) - formation of a pair of radicals would increase the 'freedom' of the system. The entropy of activation for equilibration of the diastereoisomers of [118], however, is virtually zero. As a check, the cross-over experiment below was tried.

On refluxing a mixture of [113] and [148] in benzene, [113] decomposes into benzoxazolinone and the sulphenylimine [120] as described

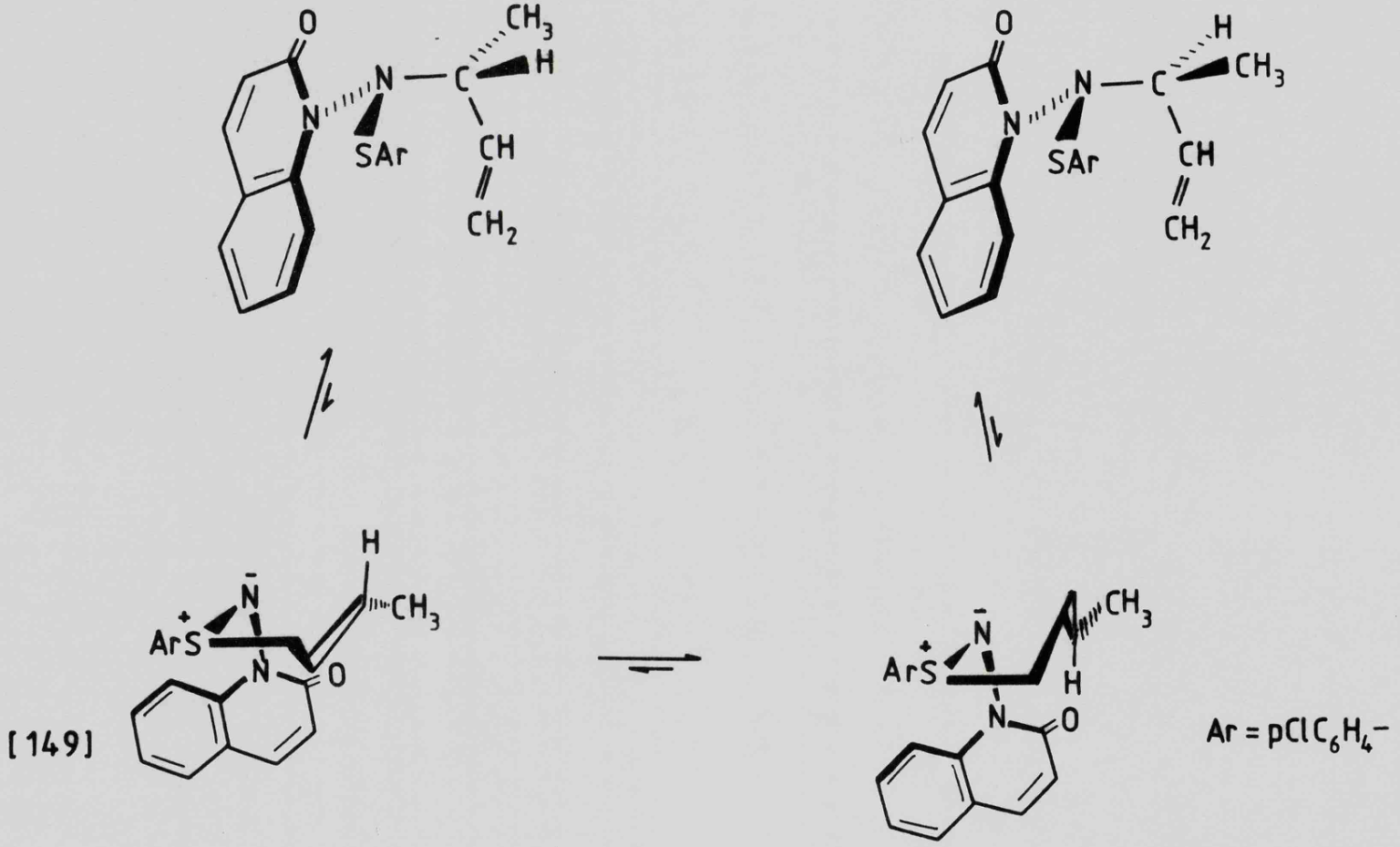


in 2.5. At this temperature, the rate of interconversion of the diastereoisomers of [118] proceeds at a measurable rate (equilibration is practically complete in ca. 40 mins. at this temperature), and hence the homolysis of the N-N bond should be proceeding at the same rate if this is the mechanism. Provided that [148] is behaving the same as [118], then on heating [113] and [148] in boiling benzene, some [118] may be formed from cross-over of the four radicals formed. In the event, no [118] was detected and [148] was recovered unchanged at the end of the experiment. This, in conjunction with the evidence above appears to rule out this hypothesis as the mechanism for interconversion (see also appendix II).

(b) Reverse [2,3]-sigmatropic rearrangement

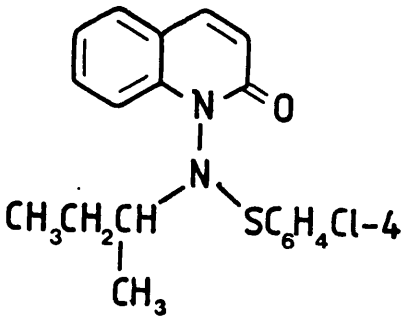
This pathway involves a reverse [2,3]-sigmatropic shift to the sulphilimine [149]. Allyl sulphoxides racemise in an analogous pathway via the sulphenate ester.[28] The sulphilimine [149] may adopt two conformations for the rearrangement, as illustrated overleaf in Scheme 7. Interconversion of diastereoisomers can occur by two paths here: firstly, by rotation of the quinolone N-N bond in [149] or, secondly, if the N-N bond remains fixed, then equilibration may occur by interconversion of the sulphilimine conformers before the second sigmatropic rearrangement occurs (i.e. interconversion of the two 'envelope'

Scheme 7



Possible route for interconversion of diastereoisomers of (118)

forms). The net result is no change in the chirality of the N-N bond but a change of the chirality in the asymmetric C-1 carbon atom in [118] (as illustrated above). Synthesis of the saturated derivative [150] should determine the importance of this route, as a reverse



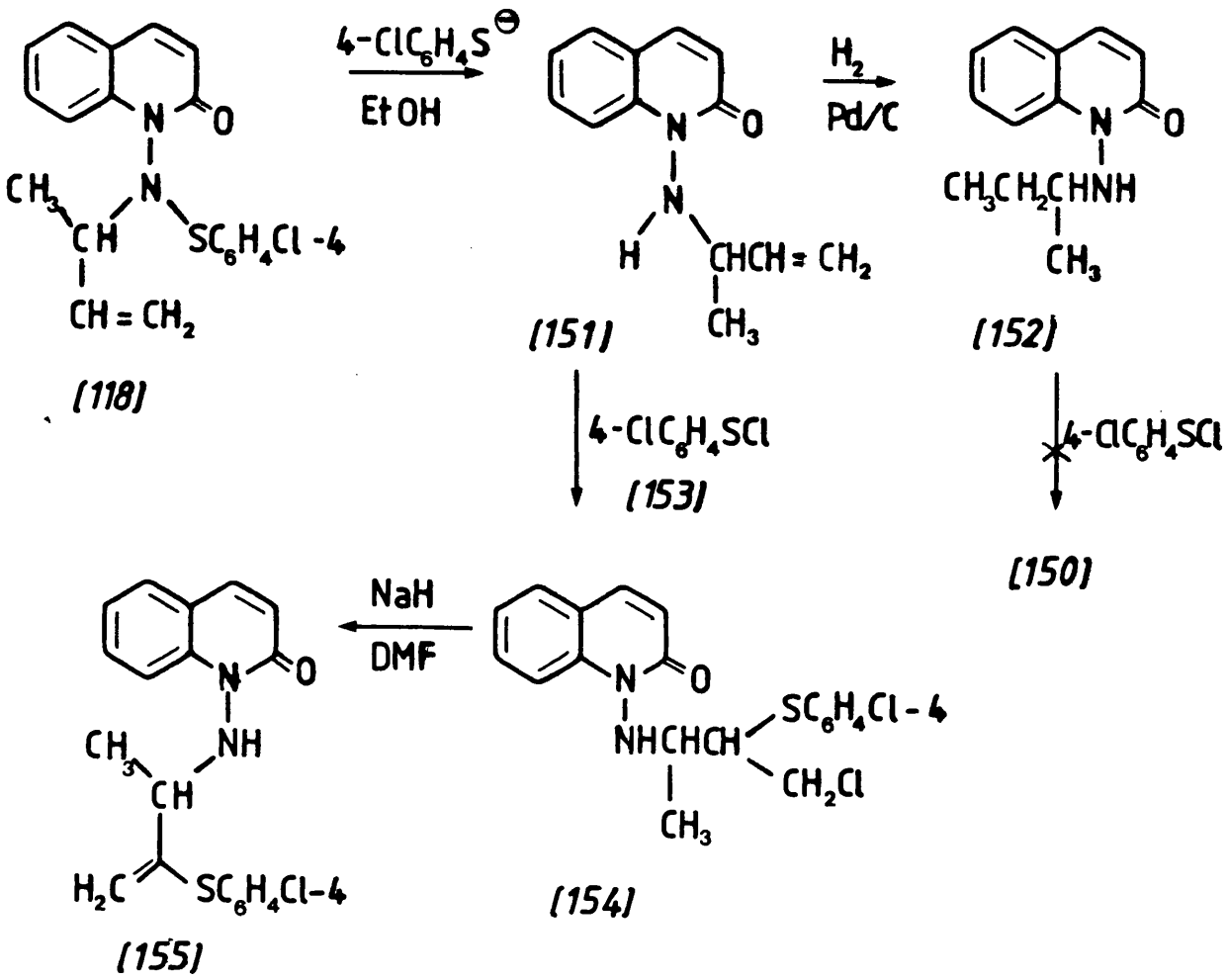
(150)

[2,3]-sigmatropic shift is not possible here; if this is the rate determining step in [118] then the barrier should increase in [150].

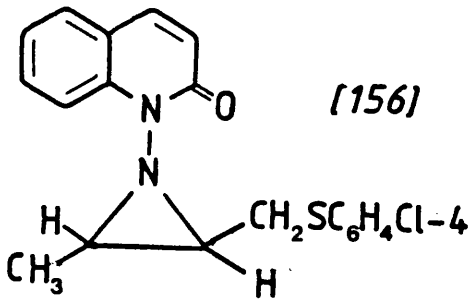
Synthesis of [150]

As direct catalytic hydrogenation of [118] is not feasible because of the lability of the S-N bond and the presence of sulphur which would poison the catalyst, the scheme below was devised for its synthesis.

Reaction of [118] with 4-chlorophenylthiolate in ethanol gave [151] in 71% yield and a virtually quantitative yield of bis(4-chlorophenyl) disulphide. Hydrogenation of [151] gave [152] in 74% yield. Unfortunately, [152] would not react with 4-chlorophenylsulphenyl chloride [153] even in the presence of sodium hydride; it appears that the N-H of [152] is very weakly basic and the anion is not generated by sodium hydride. The N-H is also sterically inhibited from attacking the electron deficient sulphur atom of the sulphenyl chloride. The unsaturated material [151] does react with the sulphenyl chloride, by addition over the double bond, the N-H function being unaffected.



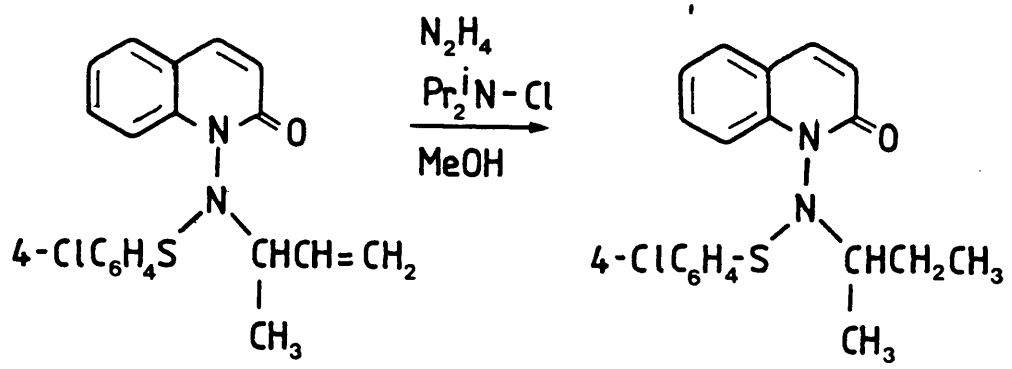
Addition of sulphenyl halides to alkenes occurs via an episulphonium salt[78] and is mainly anti-Markovnikov in this case, with apparently only one diastereoisomer being formed predominantly. Dehydrohalogenation of the adduct [154] with sodium hydride in DMF gave the vinyl sulphide [155]; the presence of two broad singlets at δ4.7 and 5.3 in the n.m.r. spectrum indicates two geminal olefinic C-H protons; a multiplet at δ4.0 sharpened to a quartet after exchange with D_2O; this must be the proton adjacent to the N-H. The N-H at δ5.75 appeared as a doublet and was removed by D_2O. Only the anti-Markovnikov adduct could give [155] on dehydrohalogenation; the Markovnikov must give a product containing two vicinal olefinic protons, which would couple with each other in the n.m.r. spectrum. Some of the aziridine [156] might also



[156]

be expected from the Markovnikov adduct if the nitrogen anion was generated by sodium hydride. However, only [155] was isolated.

Direct reduction of [118] to [150] was eventually found to occur using di-imide (generated from hydrazine and N-chlorodi-isopropyl-amine[79]). Reduction of a mixture of the diastereoisomers of [118]



[118] [150]

(ratio δ_{Me} 0.93 : 1.48 = 63 : 37) gave [150] containing doublets at δ_{Me} 1.30 and 1.90 (in chlorobenzene); the remaining aliphatic signals were second order. When the reduction was performed on a pure diastereoisomer of [118] (δ_{Me} 0.93), [150] was obtained in 43% yield after chromatography over Kieselgel. Some reduction of the S-N bond also occurred, and 34% of [152] was also isolated from the chromatography. The n.m.r. spectrum of [150] obtained this way did not show the methyl doublet at δ1.90, but the signal at δ1.30 was clearly visible, just clear of the other aliphatic signals. On heating to 82°

in chlorobenzene, the signal at δ1.30 diminished in intensity to become partly obscured by the other aliphatic signals and the other doublet at δ1.90 increased in intensity. After 40 mins., the n.m.r. resembled that obtained initially from the reduction of the mixture of diastereoisomers of [118]. This rate of equilibration appears to be very similar to the unsaturated compound [118]. Thus it appears that the double bond in the alkyl side chain does not affect the rate of interconversion of the diastereoisomers.

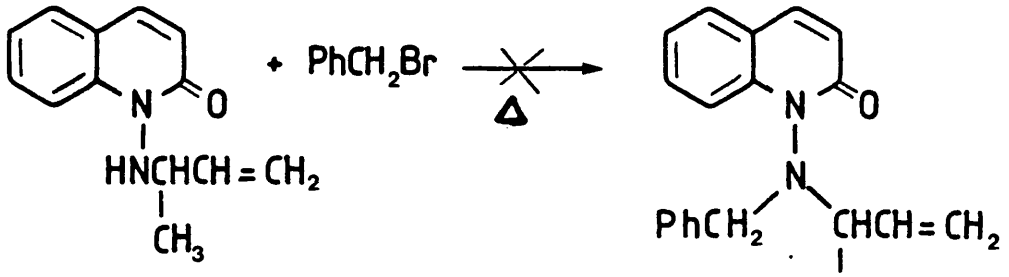
The only reasonable mechanism that remains for interconversion of the diastereoisomers, therefore, is simple rotation around the N-N bond. A further indication that this is the case is given in chapter 4.

CHAPTER 4

Resolution of N-benzyl N-(1,2-dihydro-2-oxoquinolin-1-yl) glycine

4.1 Rotational barriers in N-dibenzylaminobenzoxazolinone and N-dibenzylaminoquinol-2-one

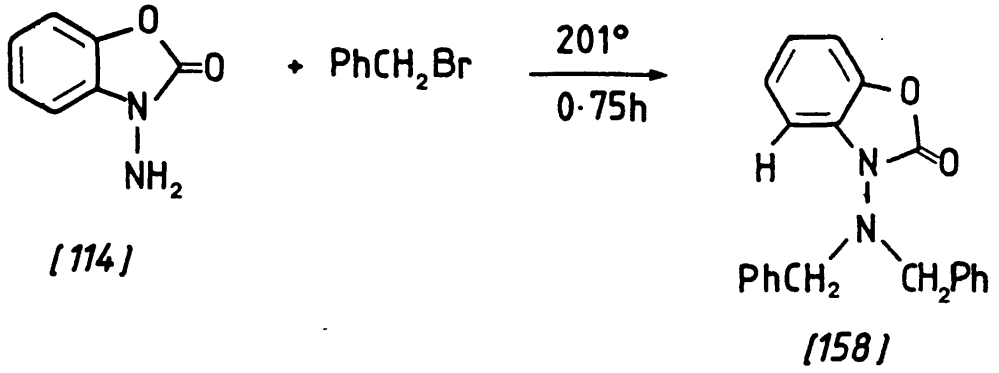
It was of interest to synthesise some dialkylaminoquinol-2-one derivatives to see whether they also showed high barriers to rotation around the N-N bond. Initial experiments were centred on the preparation of [157].



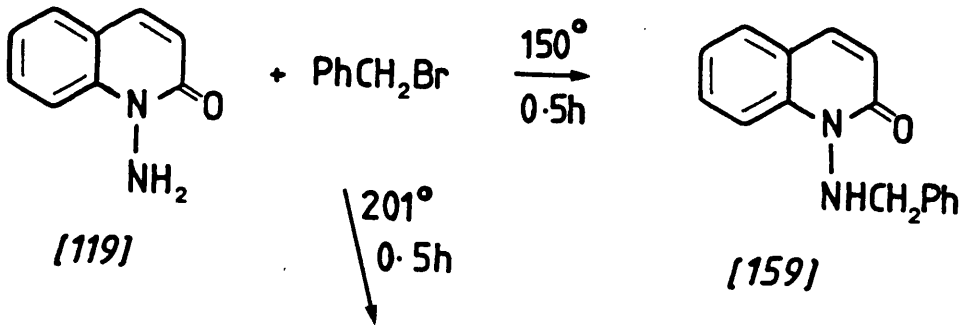
[151] *[157]*

Unfortunately, the forcing conditions required to alkylate the unreactive N-H of [151] caused its decomposition in the presence of benzyl bromide or benzyl chloride, and no [157] was obtained.

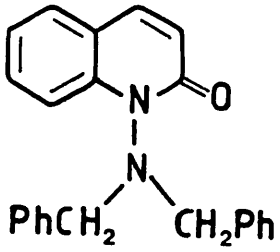
However, more success was achieved in the alkylation of N-aminoquinolone [119] and N-aminobenzoxazolinone [114] by benzyl bromide.



[114] *[158]*



[119] [159]

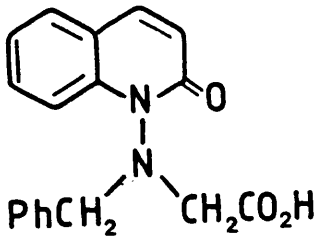


[160]

On refluxing N-aminobenzoxazolinone with benzyl bromide for 45 min., the major product isolated was the dibenzyl derivative [158] in 19% yield after Kieselgel chromatography. In [158] the benzyl protons are diastereotopic, and appear as an AB system at room temperature (δ4.4 ppm, J_{AB} 12.6 Hz, $CDCl_3$). On raising the temperature, the AB system reversibly collapses to a singlet. The coalescence temperature T_c of 95° corresponds to an energy barrier of 18.4 kcal mol^{-1}, for rotation around the N-N bond.

N-aminoquinolone gave either the mono or dibenzyl derivatives depending on the reaction conditions. At 150° for 30 min., the major product was the mono-benzylated material [159] in 23% yield. Refluxing benzyl bromide (201°) gave the dibenzyl compound [160] as the major product in 12% yield after purification by Kieselgel chromatography. The n.m.r. behaviour of [160] is different to [158]. Here an AB system (δ4.6, J_{AB} = 12.5 Hz, $CDCl_3$) is visible, but no coalescence or line broadening of these signals occurs even at 179° in nitrobenzene. For a coalescence temperature >190°C in [160], then $\Delta G^{\ddagger}$ must be >23.5 kcal mol^{-1} which is above the isolation time scale for resolution of

enantiomers at room temperature. Therefore, in theory, it is possible to resolve the N-N bond in such compounds, and the acid [161] was

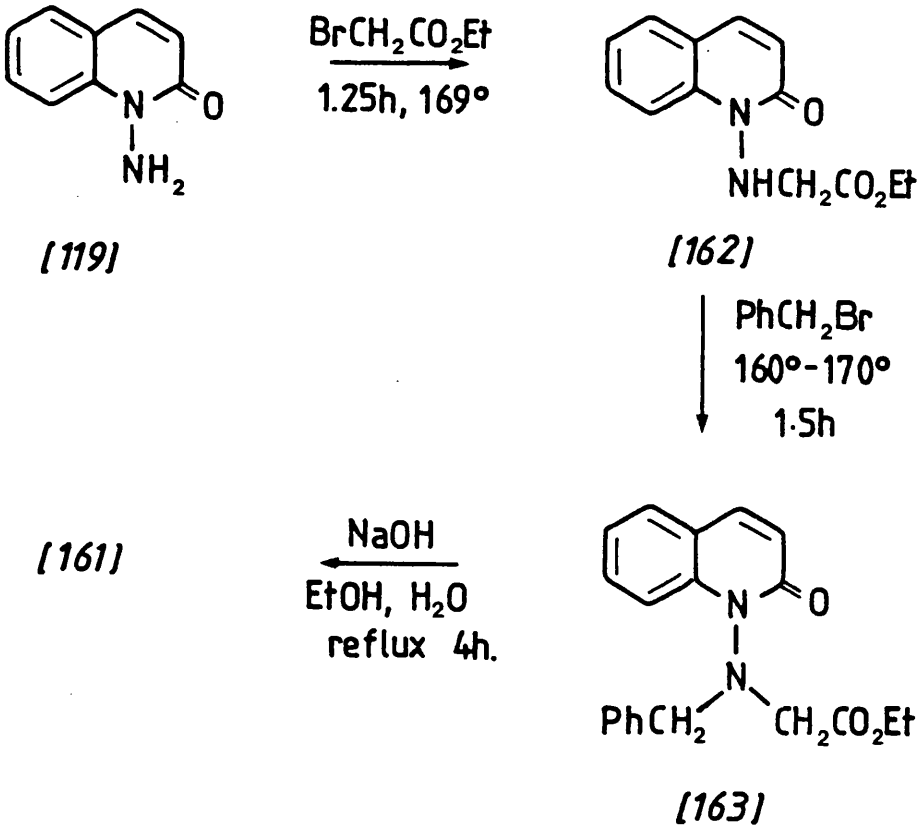


[161]

selected as the target molecule to attempt this.

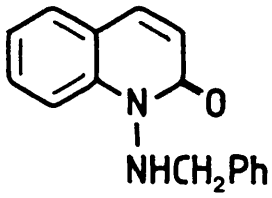
4.2 Synthesis of [161]

The successful route to [161] is shown below.



[119] *[162]* *[161]* *[163]*

An alternative way of making the ethyl ester [163] is to prepare the monobenzyl derivative [159], and react this with ethyl bromoacetate,



[159]

$BrCH_2CO_2Et$ → 169°, 1·5h → [163] + unreacted [159]

but this route was found to give lower yields, and involved more difficult chromatographic separations. The successful route involved alkylation of N-aminoquinolone by refluxing ethyl bromoacetate (b.p. 169°) for 1.25h to give a 33% yield of the mono-alkylated material [162]; no disubstitution occurred. [162] was then alkylated by benzyl bromide at 160°-170° for 1.5h to give the ethyl ester [163] in 41% yield. The n.m.r. spectrum of this compound in $CDCl_3$ showed an AB system for the benzyl CH_2 protons, but not the glycine CH_2 protons, which were accidentally equivalent. Hydrolysis of the ethyl ester gave the acid [161] in 10% overall yield from N-aminoquinolone. The n.m.r. spectrum of the acid [158] in chlorobenzene showed AB systems at δ4.25 (J_{AB} 12.6 Hz, $-CH_2Ph$) and 3.97 (J_{AB} 17.4 Hz, $-CH_2CO_2H$) indicating slow rotation around the N-N bond in this material.

4.3 Resolution of [161]

The ℓ-(-)-phenylethylamine salt of [161], [164] was not crystalline, but its n.m.r. spectrum (fig. 3) was very informative. Both the benzyl and glycine CH_2 signals are duplicated, indicating the presence of diastereoisomeric salts. The benzyl protons showed up as two AB systems in benzene, δ_{CH_2} 4.60 and 4.65 (J_{AB} 12.4 and 12.6 Hz respectively), and the glycine CH_2 protons likewise, δ_{CH_2} 4.02 and 4.06 (J_{AB} 16.4 and 16.6 Hz respectively). The C-1 methyl doublets of the amine remained a single doublet, however.

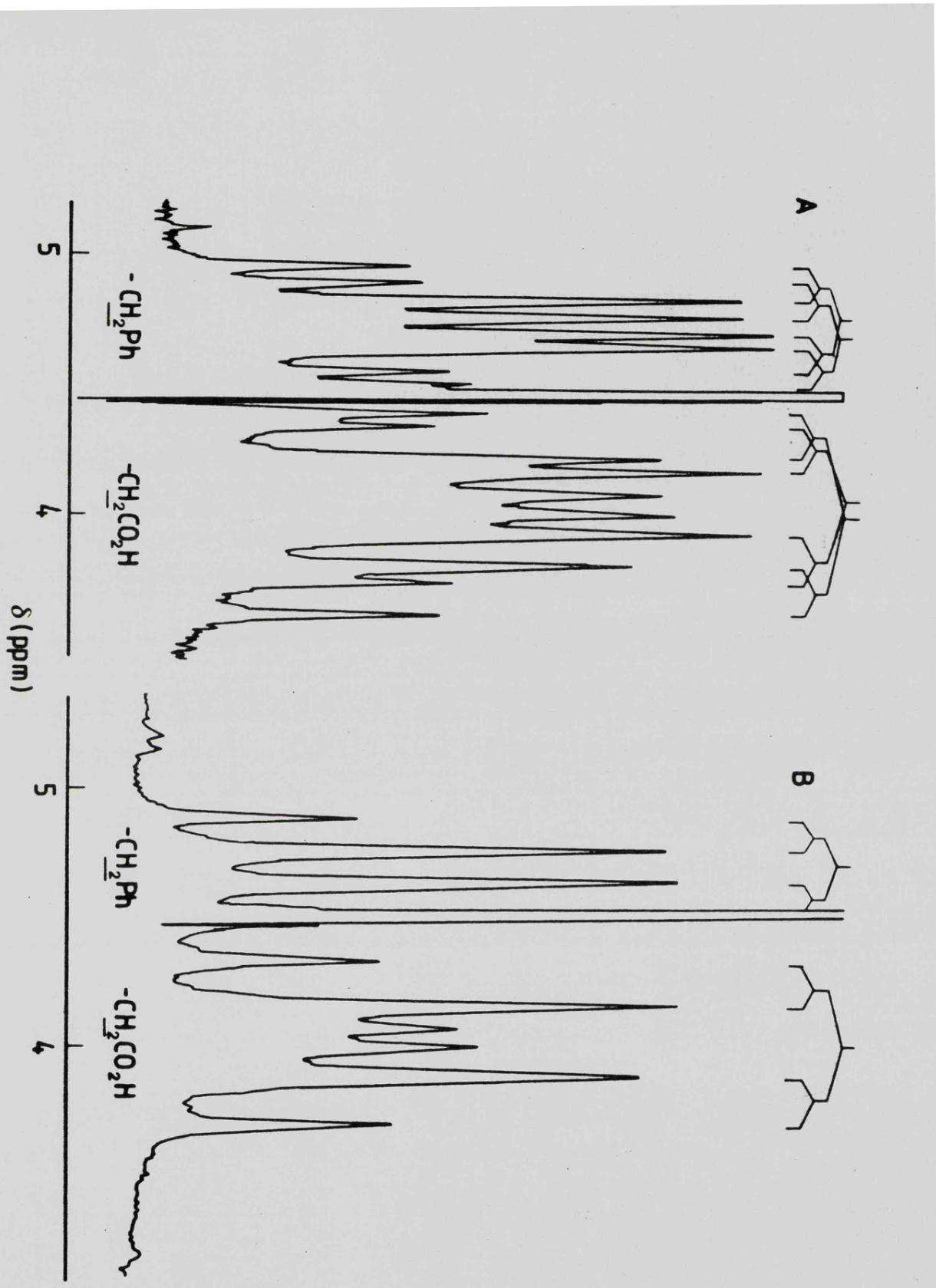
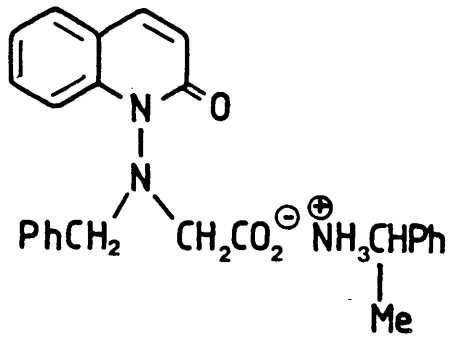


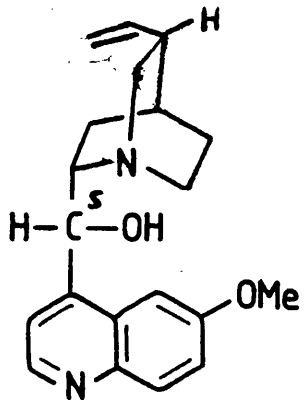
Figure 3

A. NMR spectrum of racemic [164]

B. NMR spectrum of resolved [164]



[164]



l-(-)-quinine

[165]

A crystalline salt of the acid [161] and ℓ-(-)-quinine [165] was obtained; the mixture of salts derived from the racemic acid had $[\alpha]_D^{28} = -75.6°$ (c = 1.37, EtOH). On recrystallisation from ethanol-ether (1:12), crystalline material of $[\alpha]_D^{27} = -99°$ (c = 0.3, EtOH) was obtained. A second recrystallisation from the same mixture changed the rotation to -101.3° (c = 0.3, EtOH), and this was unchanged after a third recrystallisation. Decomposition of the salt with mineral acid, followed by addition of an equimolecular amount of ℓ-(-)-phenylethylamine to the liberated [161] gave the salt [164] whose n.m.r. spectrum showed removal of the AB systems at δ4.02 and 4.65 (fig. 3) indicating this material to be n.m.r. optically pure (>95%). When [164] was treated with mineral acid, the acid [161] obtained was then carefully recrystallised from light petroleum - ethyl acetate; after removal of a small amount of racemic acid, the ℓ-(-)-acid crystallised out, m.p. 88-90°, $[\alpha]_D^{25} = -64.8°$ (c = 1.175, EtOH). After a few minutes above its melting point, the melt solidified and re-melted at 147-148°, the melting point of the racemic acid. This indicates that the acid racemises on heating.

4.4 Investigation of the racemisation of [161]

The rate of racemisation k_r of [161] was calculated at two different temperatures, boiling ethanol (78°) and boiling methanol (65°) on partly resolved samples of the acid. This enabled an approximate value for the activation energy to be calculated. The results are given in table 10.

TABLE 10

Racemisation of N-benzyl-N-(1,2-dihydro-2-oxoquinolin-1-yl) glycine [161]

T = 65°

Time/s	$-[\alpha] \times 10^3$	$\text{Log}_{10}\left(\frac{\alpha}{\alpha_o}\right)$
0	58	0
4200	44	0.120
9600	30	0.286
13200	22	0.421

T = 78°

Time/s	$[\alpha] \times 10^3$	$\text{Log}_{10}\left(\frac{\alpha}{\alpha_o}\right)$
0	190	0
3200	61	0.493
4200	42	0.656
7200	14	1.136

On plotting the log terms against time, a straight line results of slope equal to $k_r/2.303$ (fig. 4). Rate constants were obtained using a least squares line-fitting computer program:

T	k_r/s^{-1}	Half-life (τ) (mins.)	Correlation coefficient (r)
65	$7.30 \pm 0.09 \times 10^{-5}$	158.3	0.9985
78	$3.62 \pm 0.05 \times 10^{-4}$	31.9	0.9997

From this, approximate activation parameters can be calculated:

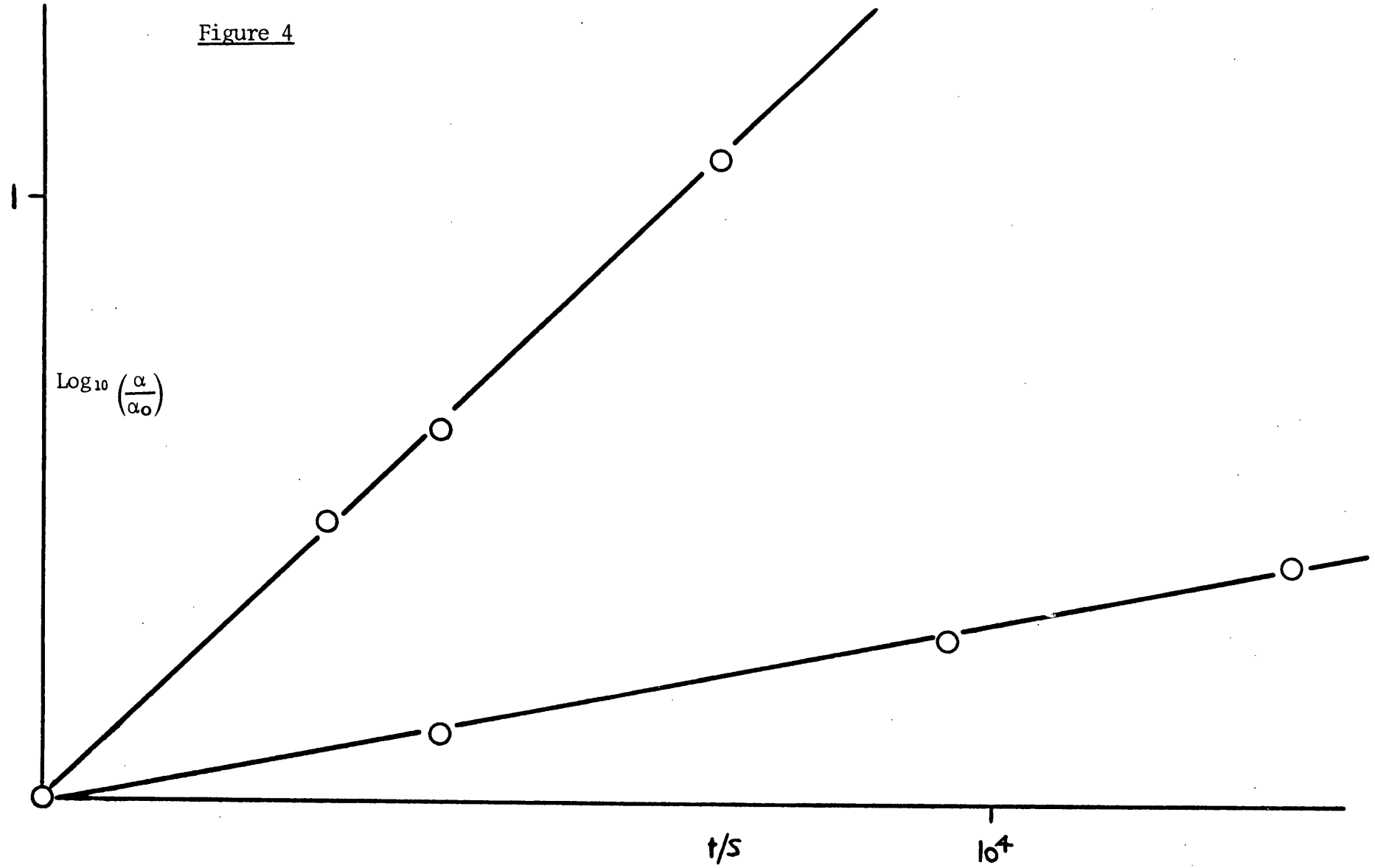
E_A (kcal mol^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (e.u.)	$\Delta G^{\ddagger}$
26.9 ± 0.4	26.3 ± 0.4	0.1 ± 1.2	26.2 ± 0.4

The margin of error for $\Delta G^{\ddagger}$ is probably greater than indicated above, as different solvents were used to evaluate the rate constants, and also any inaccuracies owing to temperature variation are not included above. However, a small $\Delta S^{\ddagger}$ is expected for a rotational process, and the $\Delta G^{\ddagger}$ obtained is very similar to the sulphenamides [118] and [132] (see 3.2); this implies that the same factors are involved in augmenting the rotational barrier around the N-N bond in each case.

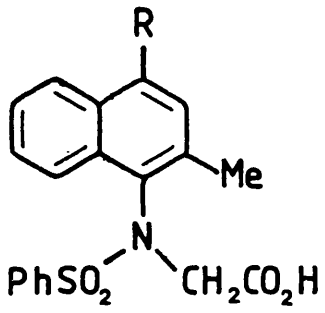
The lower barrier in [158] is presumably a result of the skewed H-8 hydrogen (itself a consequence of the five membered oxazolinone geometry) which enables the benzyl CH_2 groups to pass the plane of the heterocycle more easily. The same explanation seems likely to hold for the sulphenamide [113] (2.4) ($T_c = 27°$, $\Delta G^{\ddagger}$ = 15.5 kcal mol^{-1}), although the alternative possibility of N-N homolysis-recombination to interconvert the diastereoisomers in this case has not yet been disproven.

The closest analogues to [161] are the N-benzenesulphonyl N-naphthyl-glycine derivatives [166] which are resolvable owing to slow rotation around the aryl (C)-N bond.[80] The rate of racemisation at 118° was found to be dependent on the nature of R - the half-lives of the

Figure 4

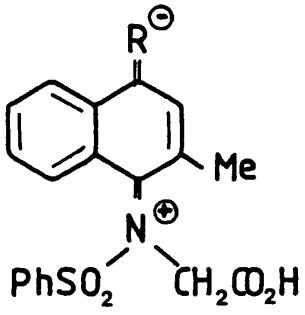


optically-active acids were found to vary between 40 mins. for R = CN and NO_2 to 8h for R = MeO ($\Delta G^{\ddagger} \approx$ 29-31 kcal mol^{-1} for $\Delta S^{\ddagger} = 0$). This result indicates a stronger resonance interaction between the nitrogen lone pair and naphthalene ring when an electron withdrawing group is present on the ring, stabilising the planar transition state for C-N rotation, [167], and lowering the rotational barrier.



[166]

R=CN, NO_2, H, Me, MeO



[167]

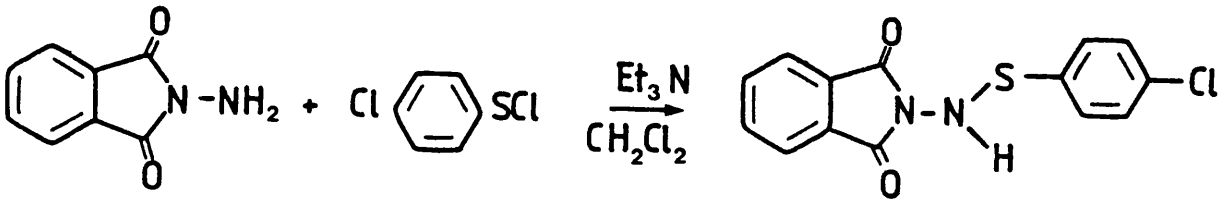
Unlike in [161], the barriers in [166] are wholly steric in nature, being caused by the bulky benzenesulphonyl group being unable to pass the peri H-8 and 2-methyl substituents of the naphthalene ring. This system has some resemblance to atropisomerism in biphenyl derivatives, whereas the barriers in the quinolone systems discussed have substantial electronic contributions to their overall barriers.

CHAPTER 5

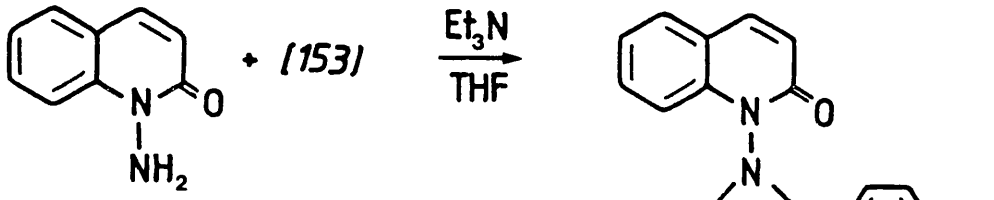
Thermal stability of heterocyclic sulphenamides: attempted preparation of some sulphenylhydrazides

5.1 Stability of some heterocyclic sulphenamides

In 2.5, the thermal stability of some sulphenamides was discussed. In order to extend this work, the sulphenamides [168] and [169] were synthesised to test their stability. It was found that they effervesced



[94] *[153]* *[168]*

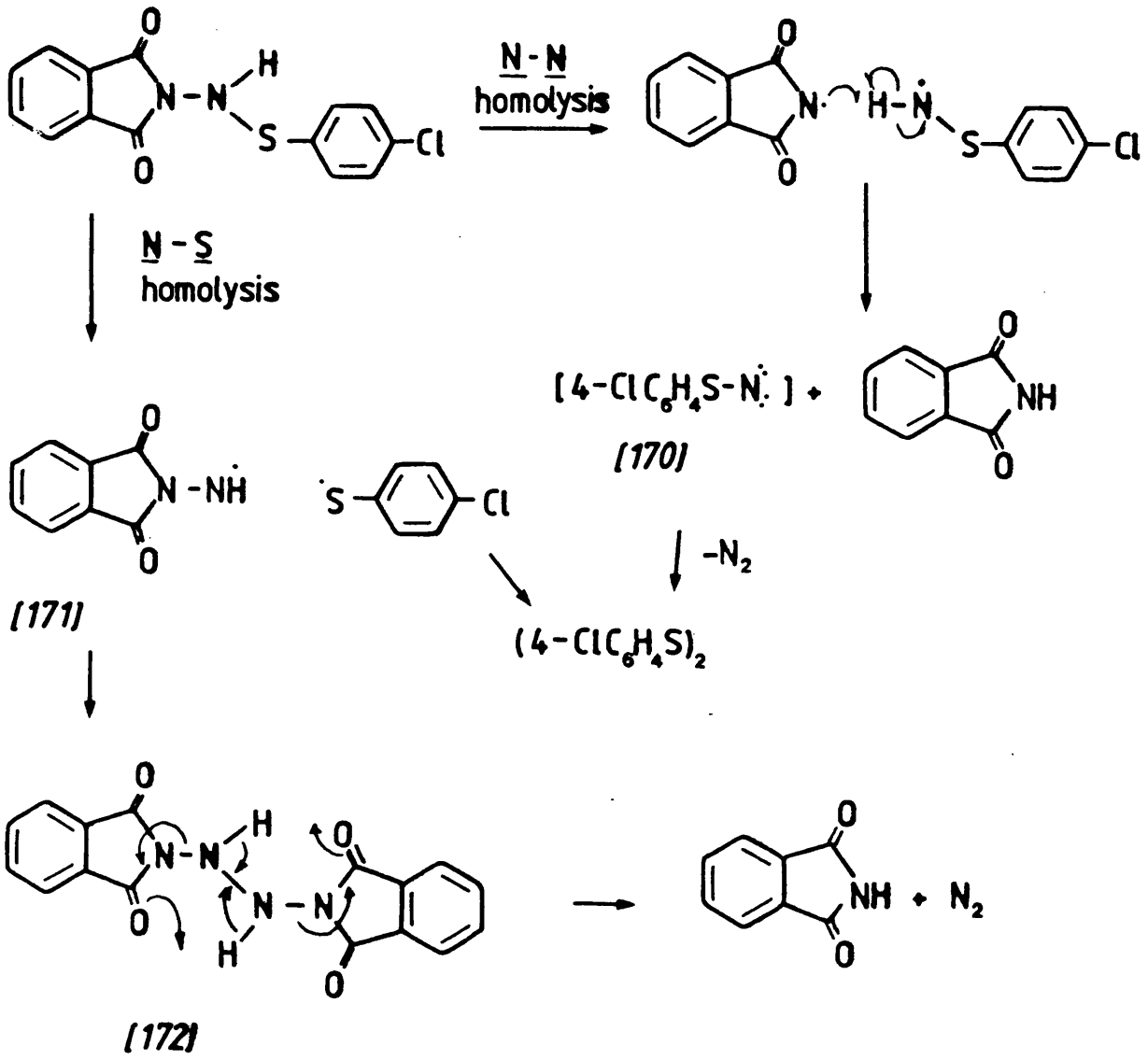


[119] *[169]*

vigorously at their melting points (the related derivatives [142] and [143] did likewise). On isolation of the products of pyrolysis of [168] and [169], the corresponding heterocycles, phthalimide or quinolin-2(1H)-one were obtained together with bis(4-chlorophenyl) disulphide. Two mechanisms may be proposed to account for the products, involving initial homolysis of the N-N or S-N bonds. In the N-N homolysis mechanism, the heterocyclic radical may abstract a proton from the thio-imino radical to give the parent heterocycle (phthalimide or quinolin-2(1H)-one), and the sulphenylnitrene intermediate [170]

which subsequently dimerises and then fragments to bis(4-chlorophenyl) disulphide and nitrogen (scheme 8). The trapping of such a nitrene

SCHEME 8

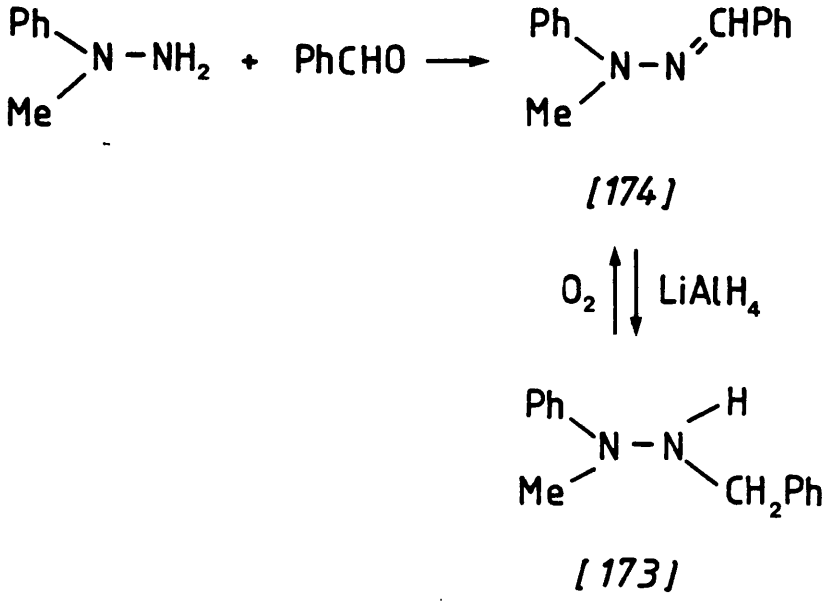


forms the second part of this work. An alternative mechanism involves homolysis of the N-S bond to give the hydrazyl radical [171], and a thiolate radical. These may dimerise to the disulphide and tetrazane [172]; the latter is known[57,81] to fragment in the manner shown to give the heterocycle and nitrogen. It may be possible to distinguish

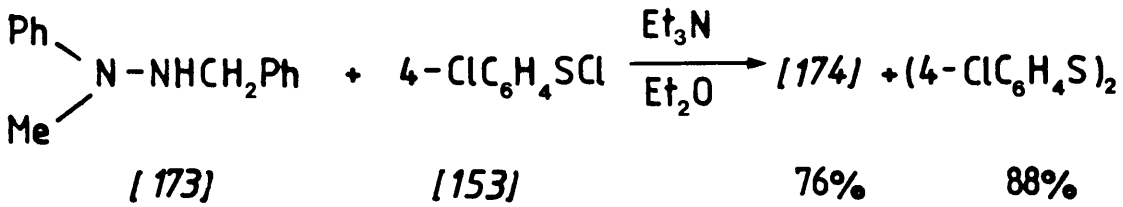
between these pathways by e.s.r. spectroscopy or spin trapping experiments, but this was not attempted. It was found that [169] decomposes at lower temperatures than [168] in solution, e.g. in boiling xylene for 15 min., [169] is completely decomposed, whereas [168] is only slightly affected. This implies that the N-N homolysis mechanism occurs as previous work[64] had shown that the stability of the heterocyclic radicals would indicate the phthalimide radical to be less easily formed (see 2.5). Hydrogen abstraction by the heterocyclic radical also has some precedent since the phthalimido radical is known to be a good hydrogen abstracter.[82]

5.2 Reaction of 2-benzyl-1-methyl-1-phenylhydrazine with 4-chlorophenylsulphenyl chloride

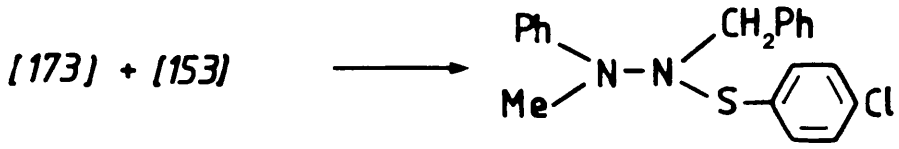
2-Benzyl-1-methyl-1-phenylhydrazine [173] was synthesised from 1-methyl-1-phenylhydrazine by condensation with benzaldehyde followed by reduction with lithium aluminium hydride under forcing conditions. Compound [173] is readily oxidised by air back to the starting hydrazone



Scheme 9

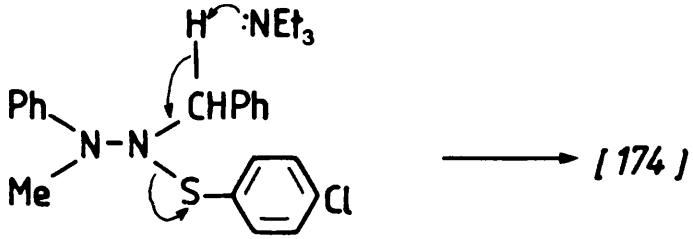


[173] [153] 76% 88%

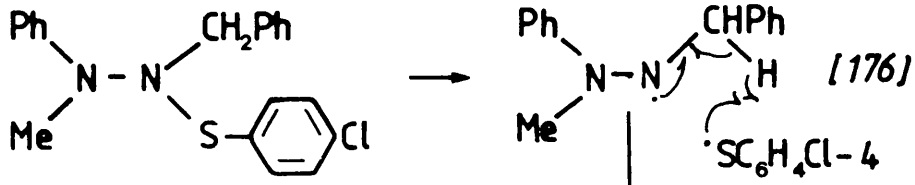


[175]

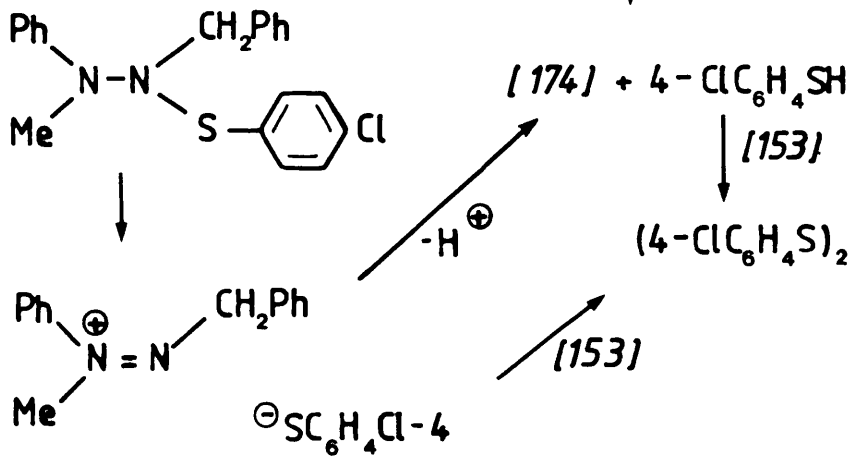
(a)

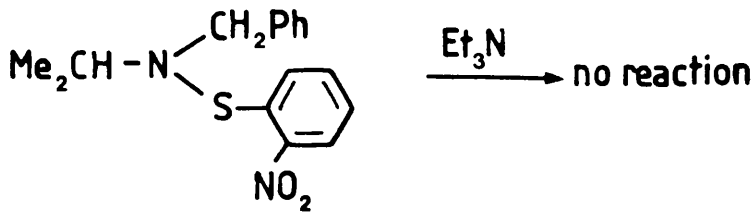


(b)



(c)





[134]

[174]. The hydrochloride of [173] is stable, however, and was used to characterise the hydrazine.

When [173] was treated with 4-chlorophenylsulphenyl chloride [153] in ether at 0° in the presence of triethylamine, it was found that two moles of [153] were required to consume all of [173], and the only two products isolated were the hydrazone [174] and bis(4-chlorophenyl) disulphide. No evidence for the sulphenylhydrazide [175] was obtained at all, even at -40° (by n.m.r.). Three mechanisms could account for these products (scheme 9).

As a control experiment for the E2 elimination [mechanism (a)], the sulphenamide [134] was stirred in triethylamine at room temperature for 1h and no change occurred; this suggests mechanism (a) is unlikely. When the reaction was done in an e.s.r. tube and quenched at -196° a few seconds after adding the sulphenyl chloride, a weak radical signal was seen ($g = 2.006$), but no splitting was seen as the sample was in the solid state. This signal could be the hydrazyl radical [176], and indicates that some of the breakdown of [175] goes <u>via</u> a radical pathway [mechanism (b)]. The major pathway to the products is probably the anchimerically assisted SN1 mechanism (c). This would fit in with the stability of the sulphenylhydrazides discussed in 2.6 in which the terminal nitrogen lone pair is not available for anchimeric assistance owing to amide or π delocalisation. The availability of this lone pair is evidently of fundamental importance in determining the stability of the sulphenylhydrazide.

5.3 <u>Reaction of 1,1-dibenzylhydrazine with 4-chlorophenylsulphenyl chloride</u>

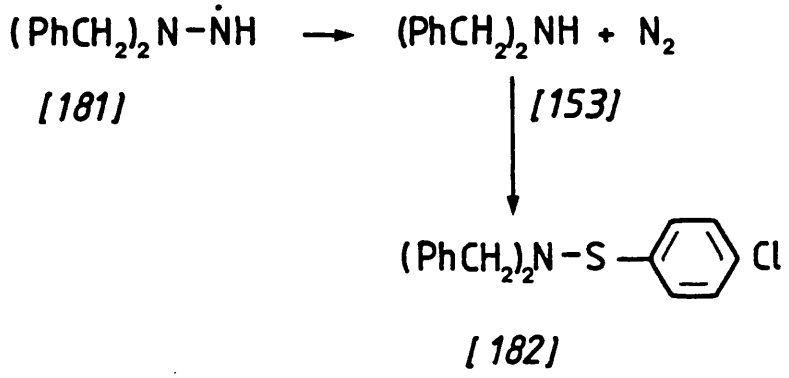
When 1,1-dibenzylhydrazine was treated with 1 mole of 4-chloro-

phenylsulphenyl chloride in ether at 0° in the presence of triethylamine, the isolated products were bis(4-chlorophenyl) disulphide, 93% bibenzyl [177], 43% and benzaldehyde dibenzylhydrazone [178], 45%. The latter two compounds are classic decay products of dibenzylaminonitrene [179],[83] and the likely mechanism is given in scheme 10.

The N-nitrene may fragment to bibenzyl[84] or be captured by another mole of 1,1-dibenzylhydrazine to give the hydrazone [178]. Another known decay product of the nitrene [179] is tetrabenzyltetrazene [180],[85] but no trace of this compound was detected in the crude reaction mixture by t.l.c. or n.m.r. comparison with an authentic sample; the benzyl CH_2 protons of [180] resonate at δ4.3, and no such signal was seen in the n.m.r. of the crude reaction product.

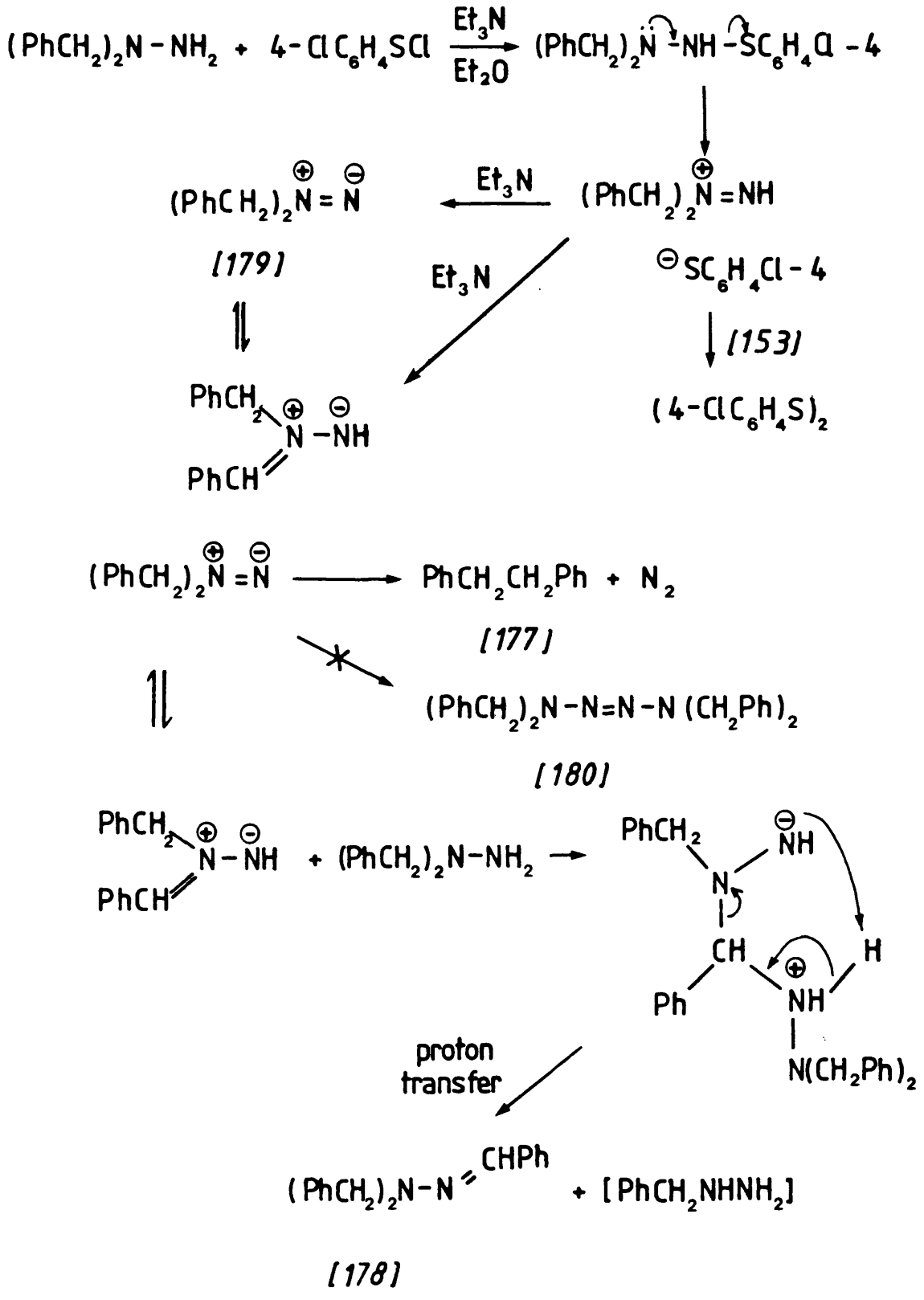
The mechanism of formation of [178] (proposed by Koga and Anselme[83]) is far from proven, but this hydrazone has also been isolated in several other oxidations of 1,1-dibenzylhydrazine.[86]

A free radical mechanism is unlikely as the resulting hydrazyl radical [181] is known to decay at the diffusion controlled limit to dibenzylamine and nitrogen:[87]



If this process occurred in the above reaction then substantial quantities of dibenzylamine or [182] ought to be isolated; the benzyl protons of [182] appear at δ4.0, but no signals were seen at this

Scheme 10


(PhCH2)2N-NH2 + 4-ClC6H4SCl
Et3N
Et2O
(PhCH2)2N-NH-SC6H4Cl-4
(PhCH2)2N=N
Et3N
(PhCH2)2N=NH
[179]
Et3N
SC6H4Cl-4
[153]
(4-ClC6H4S)2
PhCH2
N-NH
PhCH
(PhCH2)2N=N
PhCH2CH2Ph + N2
[177]
(PhCH2)2N-N=N-N(CH2Ph)2
[180]
PhCH2
N-NH
PhCH
+ (PhCH2)2N-NH2
PhCH2
NH
N
CH
H
Ph
NH
N(CH2Ph)2
proton
transfer
(PhCH2)2N-N=CHPh
+ [PhCH2NHNH2]
[178]

position in the n.m.r. spectrum of the crude reaction product, and neither was any dibenzylamine detected.

It is interesting to note that the sulphonylhydrazide [183] is stable at room temperature.[88] The results obtained in 5.2 and 5.3

$$(PhCH_2)_2N-NHSO_2Ph$$

[183]

verify the statement in 2.6 that the thiolate anion is a better leaving group than the sulphinate anion in these systems, and that the terminal nitrogen lone pair must be inhibited from anchimerically assisting cleavage of the S-N bond by resonance delocalisation, if the resulting N-N-S^{II} compounds are to be stable at room temperature. The possibility of anchimeric assistance in the cleavage of the S-N bond is known to reduce the stability of other sulphenamides,[89] and is borne out by the results above.

CHAPTER 6

PART 2

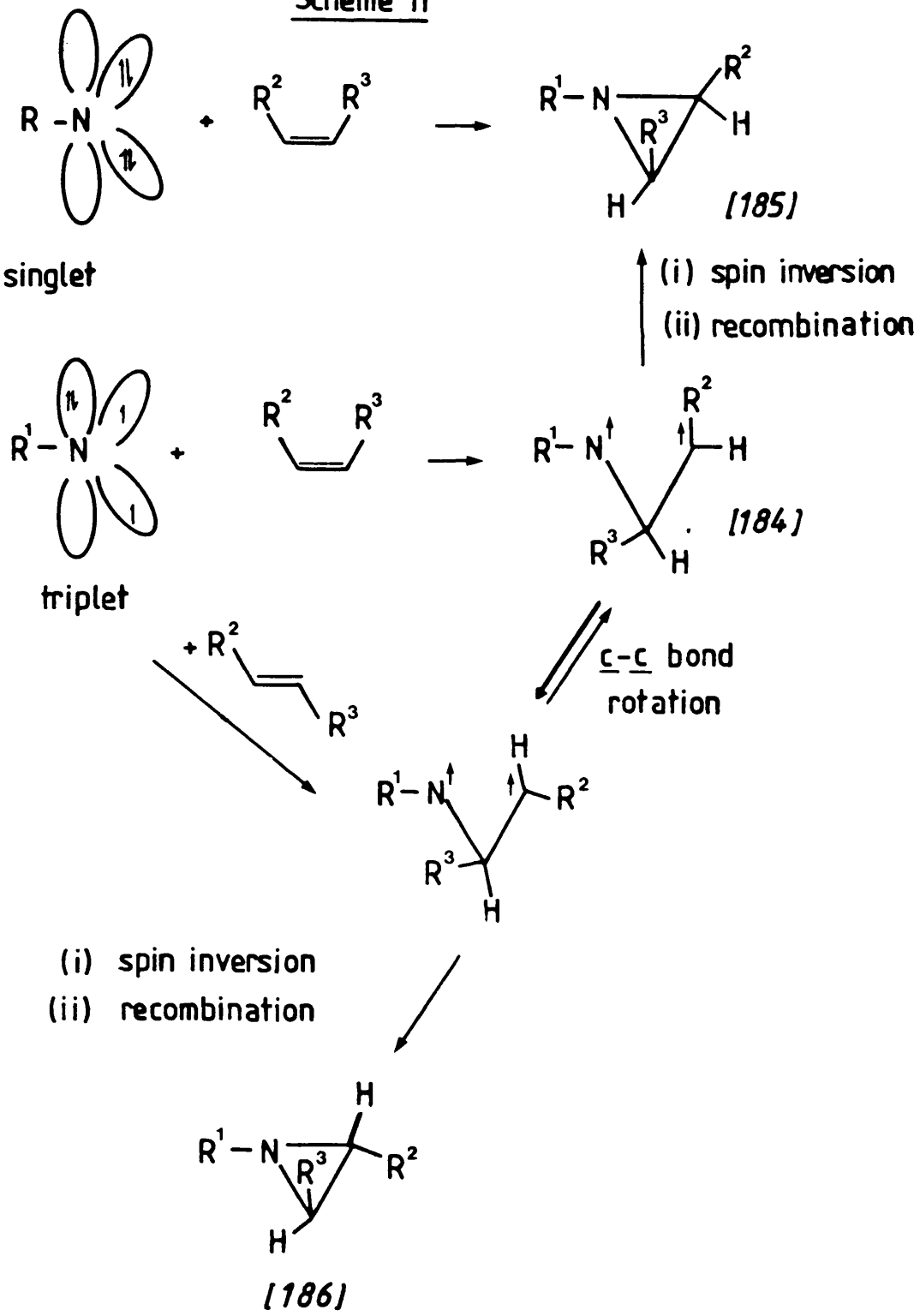
Introduction

In this chapter, the behaviour of various nitrenes which can be trapped intermolecularly will first be briefly examined.

6.1 Skell's hypothesis[90,91]

Nitrenes may undergo cycloaddition to alkenes to give aziridines. With cis substituted alkenes, some nitrenes give aziridines in which the substituents are orientated trans; indeed, occasionally the same mixture of aziridines may be formed from both cis and trans alkenes. An adaptation of Skell's hypothesis (originally conceived for the case of carbenes) explains these results in terms of the spin state of the reacting nitrene. Whereas addition of the singlet nitrene to the alkene is concerted so that the alkene configuration is retained, addition of the triplet state goes via a biradical intermediate [184] (scheme 11) in which the spins of the unpaired electrons are the same (parallel). Before bond formation to give the aziridine can occur, these spins must be paired. Since the time required for a spin inversion is greater than the time required for rotation around a C-C bond, stereospecificity is lost and both aziridines [185] and [186] are formed. Exceptionally, in some systems spin inversion may be faster than bond rotations, where the latter is abnormally slow, e.g. this is one of the explanations which has been proposed to account for the reaction products of dibromocarbene with dihaloalkenes.[92] Although originally empirically derived, the Skell hypothesis has been elaborated by Hoffmann with theoretical calculations,[93] and appears to hold for

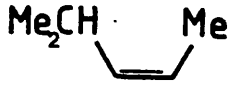
Scheme 11


singlet
triplet
(i) spin inversion
(ii) recombination
[185]
[184]
c-c bond rotation
(i) spin inversion
(ii) recombination
[186]

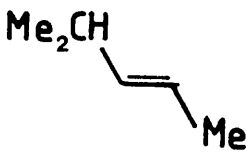
many triplet nitrenes and carbenes.

6.2 Ethoxycarbonylnitrene

Lwowski and McConaghy[94,95] have examined the behaviour of ethoxycarbonylnitrene [187] with cis and trans-4-methyl-pent-2-ene [188] and [189]. The nitrene was generated either thermolytically or photo-



[188]



[189]

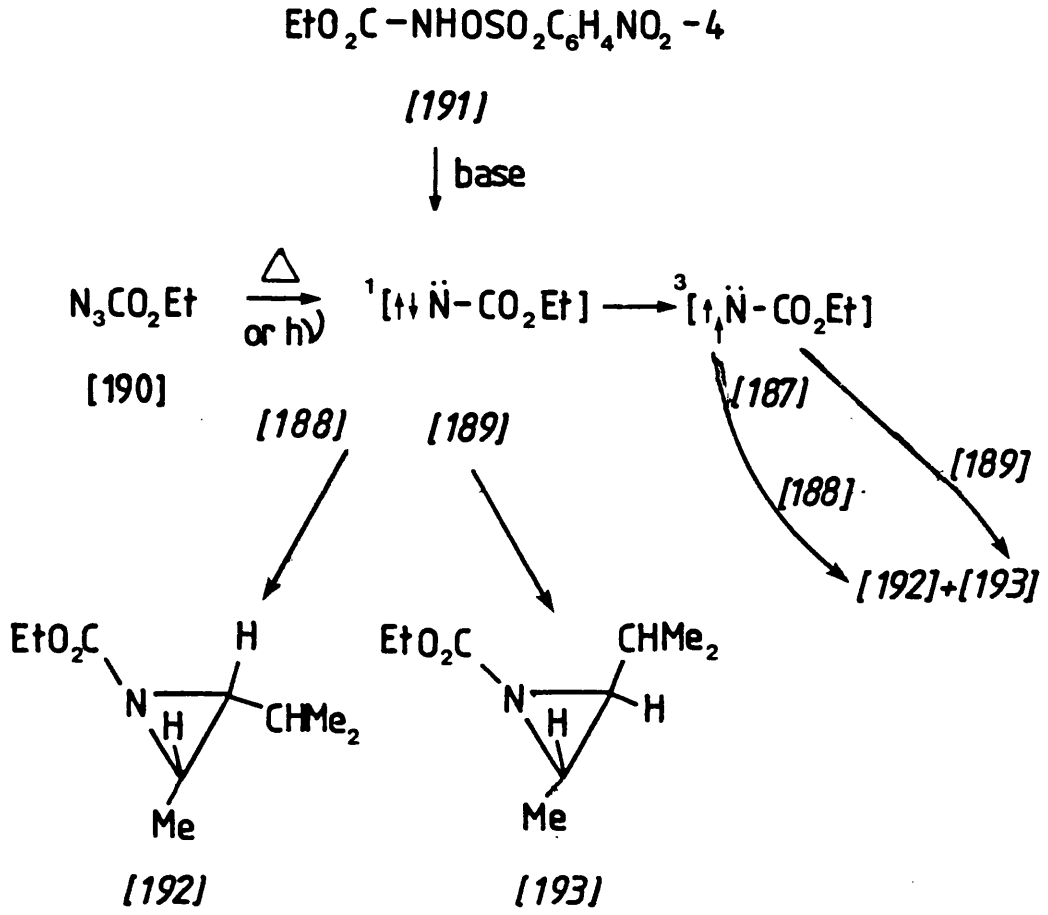
lytically from ethyl azidoformate [190], or by base catalysed α-elimination from the N-(4-nitrobenzenesulphonyloxy)urethane [191] (scheme 12). Like all heterolytic methods, the singlet state of the nitrene is generated by this reaction. However, decay to the triplet state may occur if this is the ground state (which it is in the case of [187]). On electronic grounds alone the triplet state is expected to be the ground state (by Hund's rules), but the nature of the substituents may alter this. Lwowski found that in the reaction of [187] with [188] or [189], the addition was highly stereoselective at high concentration of alkene, e.g. at 33 mole % of [188] in dichloromethane, 92% of the cis aziridine [192] was isolated, and 8% of the trans aziridine [193], when the nitrene was generated by the α-elimination route. When generated in the presence of an alkene, the singlet nitrene may add to the alkene or decay to the triplet state. The former process predominates at high concentration but with increasing dilution more of the singlet state decays to the triplet by collisions with the inert solvent molecules. As a result, the reaction becomes

TABLE 11

Addition of $\dot{N}$-CO_2Et to [188] and [189]

alkene conc. mole %	% [193] from [188] using thermolysis route	nitrene generated by α-elimination % [193] from [188]	% [192] from [189]
100	14		
33	18	7.8	2.6
10	33	17.5	
5	41	26	8.0
3.3		34	
2.5		37.5	
1.5		43	12.3
1.0	54		

Scheme 12

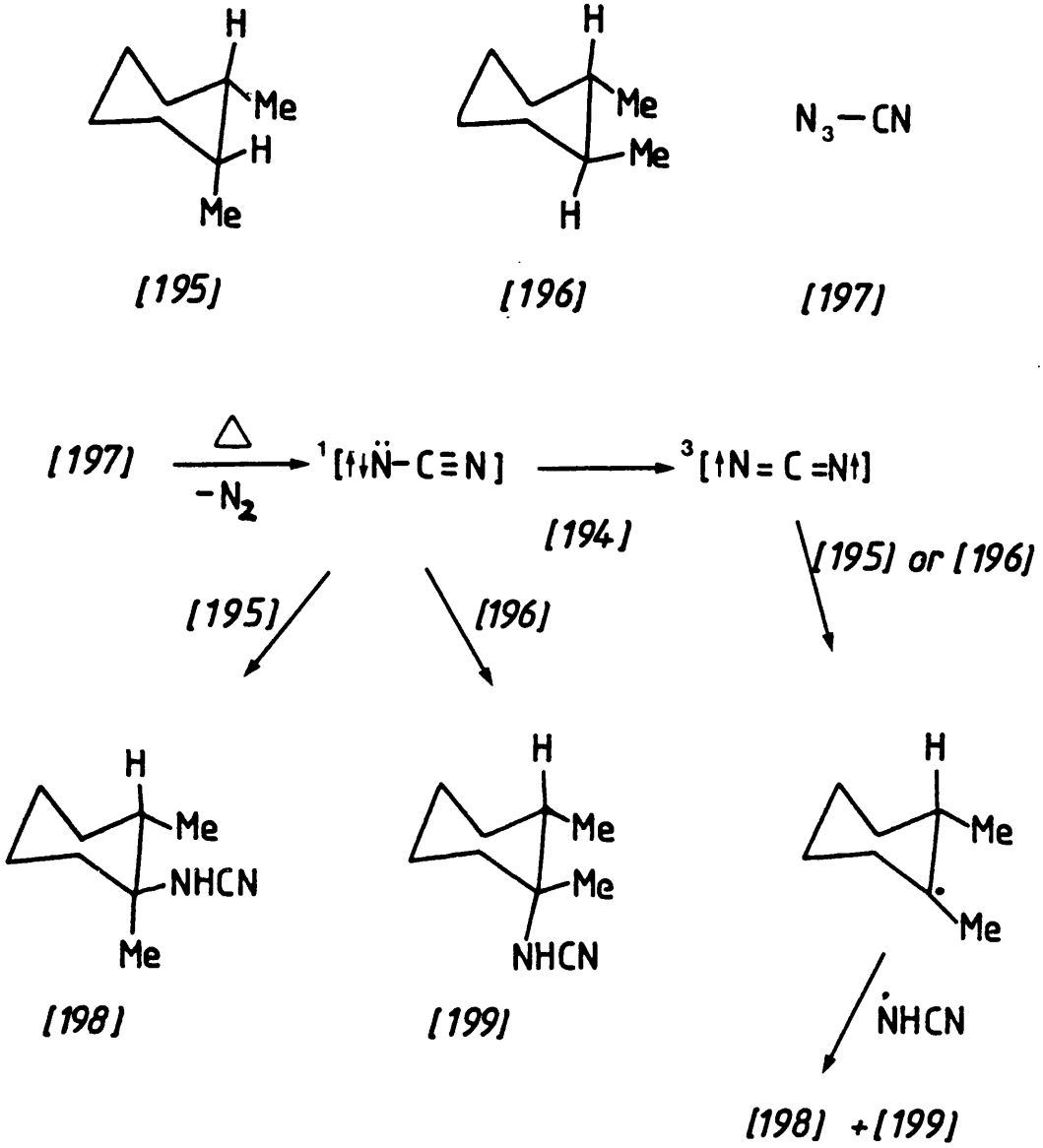


less stereoselective, with a greater amount of the 'wrong' aziridine formed. Both cis and trans 4-methylpent-2-ene give this result. With the ratios of aziridines being different even at high dilution (and still apparently changing even at this high dilution) it appears that a proportion of the aziridines produced are still being derived from the singlet state at this dilution.

6.3 Cyanonitrene

The reaction of cyanonitrene [194] with cis and trans-1,2-dimethyl-cyclohexane [195] and [196] is similar in principle to that described above.[96] Thermolysis of cyanogen azide [197] (scheme 13) gives singlet cyanonitrene which then decays to the highly resonance stabilised

Scheme 13



triplet state. In the reaction with [195] and [196], the nitrene inserts into the tertiary C-H bonds. The singlet state may do this in a concerted fashion, but the triplet state first abstracts a hydrogen atom to give a pair of radicals with spins parallel; only after spin inversion is the product formed. As the tertiary radical formed is planar, both stereoisomeric products [198] and [199] are obtained. Thus the system resembles the addition of singlet and triplet nitrenes to alkenes. In neat [195] or [196], the reaction is stereospecific

(table 12) but on dilution with dichloromethane, decay from singlet to triplet may occur *via* collisions with solvent molecules, and as a result both stereoisomers [198] and [199] are formed. 'Heavy atom' solvents, e.g. dibromomethane are known to increase the rate of

TABLE 12

Reaction of :N-CN with [195] and [196]

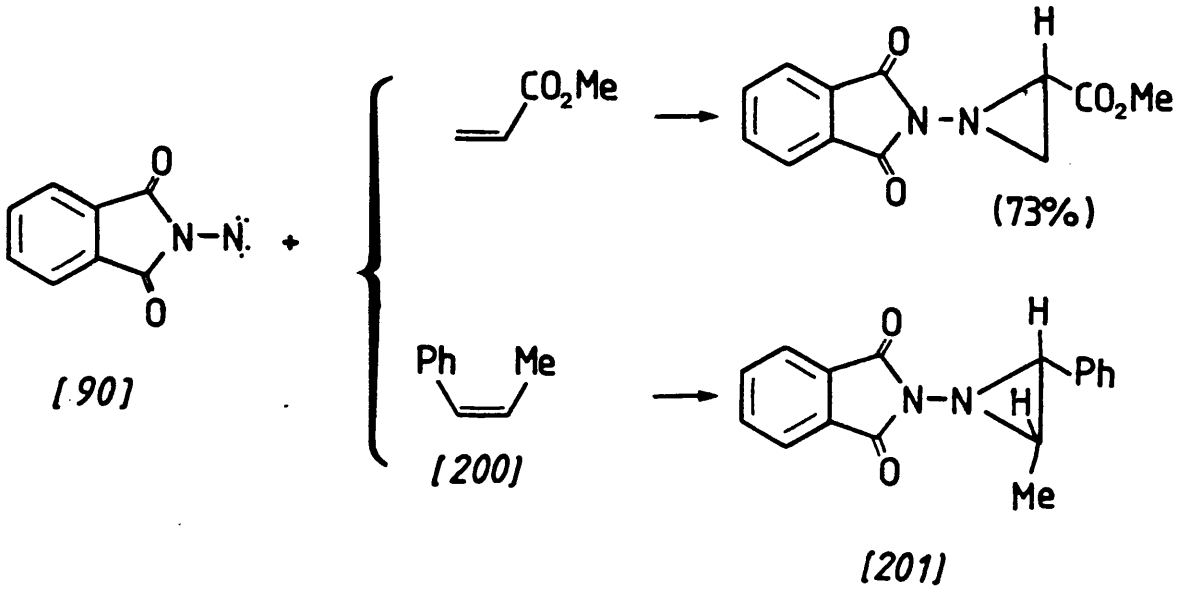
solvent	conc. of hydrocarbon (volume %)	hydrocarbon used	% [198]	% [199]
neat	100	[195]	>98	< 2
	100	[196]	< 2	>98
CH_2Cl_2	10	[195]	75	25
	2	[195]	62	38
	10	[196]	36	64
	2	[196]	39	61
CH_2Br_2	10	[195]	52	48
	10	[196]	52	48

singlet-triplet transitions by a spin-orbit coupling mechanism.[97] Indeed, in dibromomethane as solvent, containing 10% [195] or [196], the same ratio of [198] or [199] was obtained in each case, thus indicating reaction only of the triplet state.

Cyanonitrene also adds to alkenes, but the reaction is complicated by the fact the nitrene precursor, the azide [198], also readily adds to alkenes *via* a 1,3-dipolar mechanism.

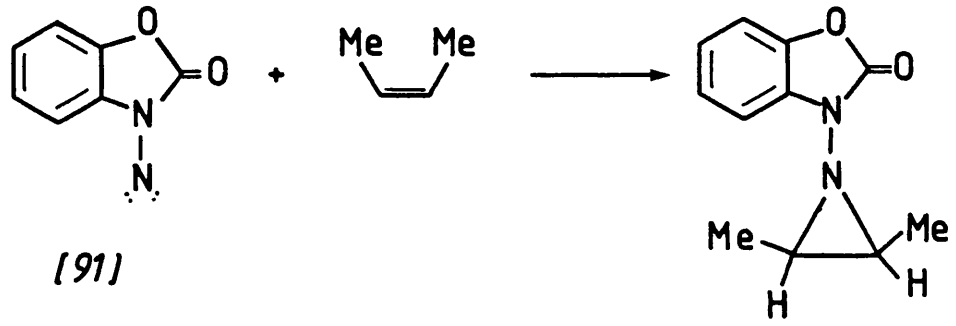
6.4 N-nitrenes (see also 2.1 and 2.2)

At present, the only N-nitrenes which are known to be trapped intermolecularly by alkenes are those in which the second nitrogen is part of a heterocyclic ring (see 2.1). Such nitrenes react with a variety of alkenes including electron deficient ones such as the acrylates:[51]

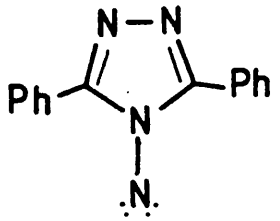


Such behaviour is unusual for a nitrene which, normally being electrophilic, reacts only with electron-rich alkenes.

Addition of benzoxazolinonenitrene [91] to cis and trans but-2-ene was found to be stereospecific even at high dilution.[48] Phthalimidonitrene [90] also adds stereospecifically to the butenes, and, as has

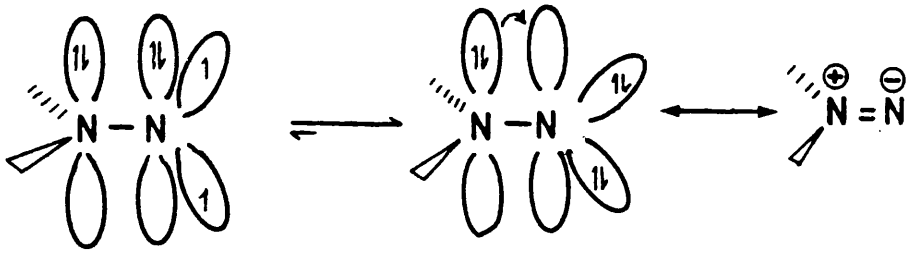


been found in this work, to cis-1-phenylpropene [200], at low concentration of [200] in dichloromethane. In the latter case, the driving force for rotation within the derived triplet biradical would be strong. The s-triazolo-N-nitrene [202] also adds stereospecifically

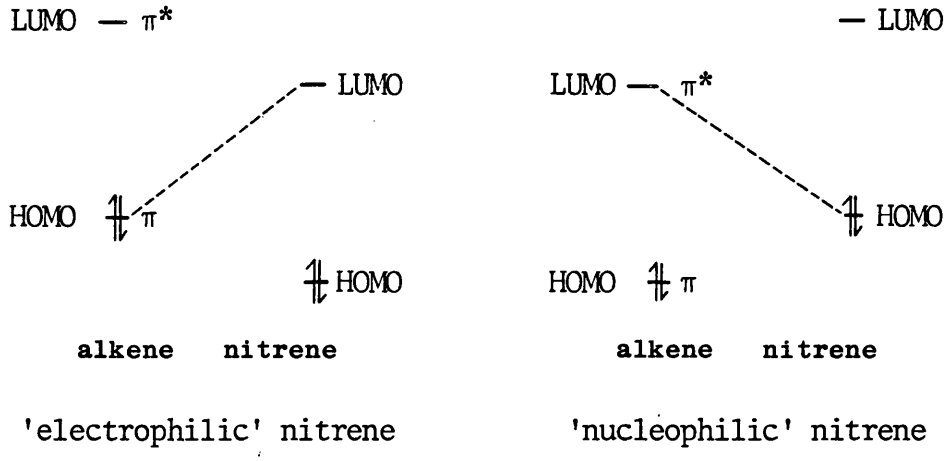


[202]

to [200].[98] The behaviour of the above nitrenes indicates that reaction occurs only via the singlet state. In these N-nitrenes, the singlet state appears to be resonance stabilised by the adjacent nitrogen whereas the triplet state is not, and as a result the singlet state is the ground state.

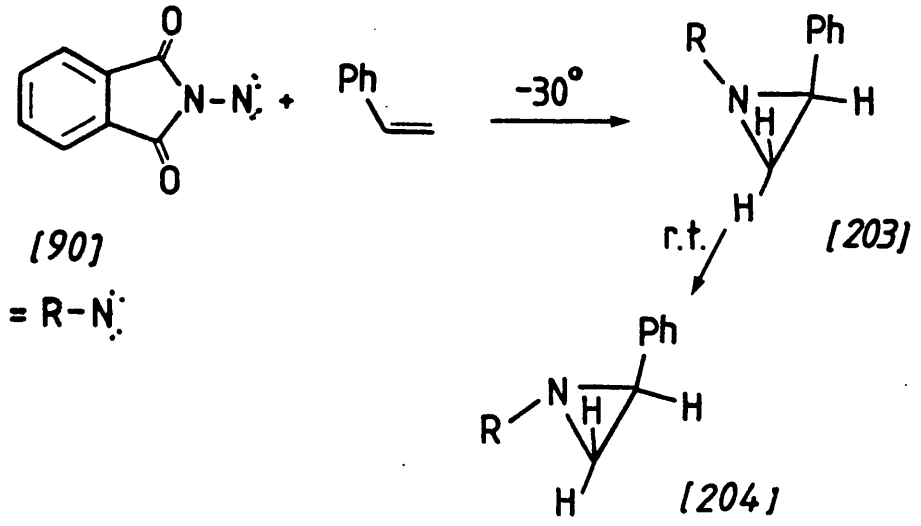


The reaction with both electron-rich and electron-deficient alkenes may be accounted for by an extension of an explanation devised by Jones et al.[99] for some aromatic carbenes. It is assumed that the HOMO-LUMO orbitals of the nitrene and alkene are of similar energy; in the case of the electrophilic nitrene the $HOMO_{alkene}$-$LUMO_{nitrene}$ interaction is stronger, owing to these orbitals being closer in energy than the other pair. The net effect is donation of electrons from alkene to nitrene, with the reverse applying for the nucleophilic



nitrene, the $HOMO_{nitrene}$-$LUMO_{alkene}$ interaction being dominant. With an ambiphilic nitrene, either interaction may predominate, depending on the nature of the alkene.

A further peculiarity of these N-nitrenes is that they show syn selectivity in reaction with alkenes, the more hindered aziridine invertomer often being the first formed. For example, addition of phthalimidonitrene to styrene at -30° gives the syn invertomer [203];[100] at this temperature nitrogen inversion is retarded. On warming to over

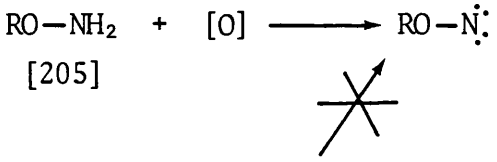


0°, the thermodynamically more stable [204] is formed. The kinetically formed invertomer [203] is initially formed as a result, it is proposed,

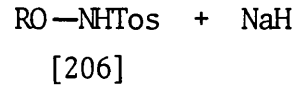
of favourable secondary orbital interactions between the phenyl group of the styrene and a carbonyl group in the phthalimido ring. A similar selectivity is observed using dienes as traps, and this requires that the dienes adopt the s-cis conformation to enable secondary orbital interactions to occur. A similar syn selectivity is also shown by many carbenes[101] although the selectivity with free carbenes (as opposed to carbenoids) is not large.

6.5 O-nitrenes

Little work has been done on these species; at present, the only successful way of generating them is by oxidation of the corresponding hydroxylamine [205]:

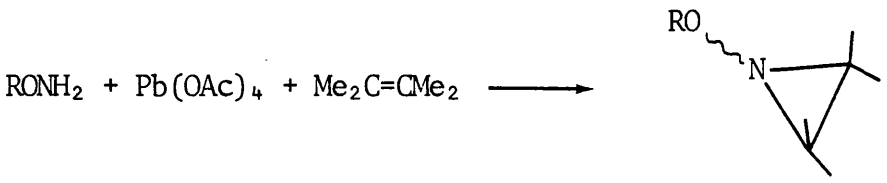


[205]



[206]

α-elimination of a tosyl group from an N-sulphonyl-O-aryl(alkyl)-hydroxylamine [206] failed to give nitrene derived products.[102] Brois[103] obtained a 30% yield of the alkoxyaziridine [207] on oxidation of O-methylhydroxylamine with lead tetra-acetate in the presence of 2,3-dimethylbut-2-ene:



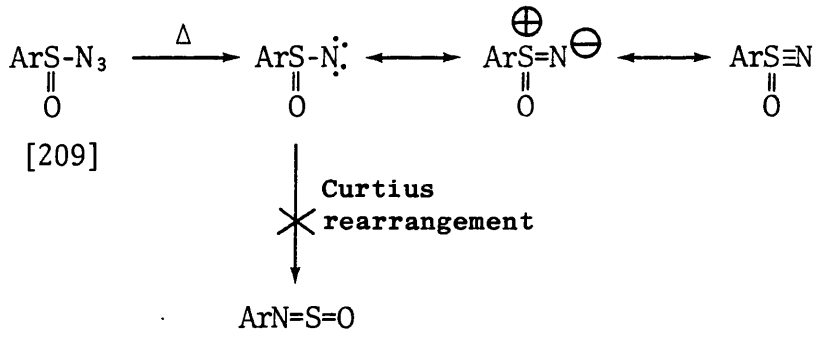
[207] R = Me

[208] R = $Me(CH_2)_3$

N-n-butoxynitrene gave an analogous aziridine [208] in 40% yield.[102] The reaction of this nitrene with cis and trans but-2-ene was found to be stereospecific by gas chromatographic mass spectrometry.[104] Some theoretical calculations[105] had predicted a singlet ground state for N-nitrenes and O-nitrenes, and these are verified by the above results.

6.6 Sulphinylnitrenes

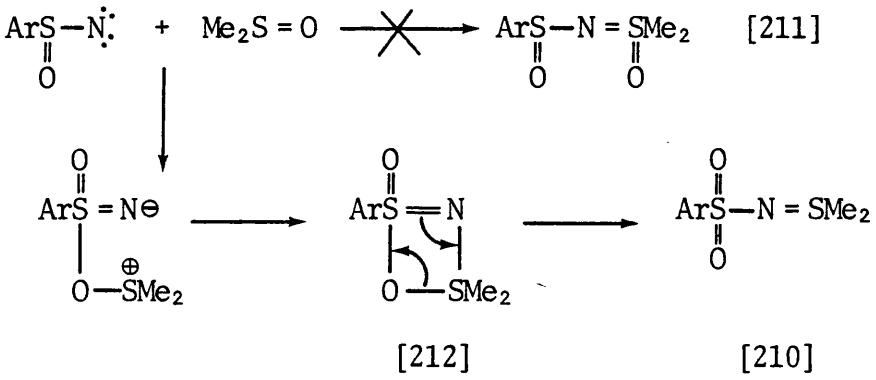
There is one report of a sulphinylnitrene intermediate.[106] Sulphinyl azides can be prepared by careful reaction of sulphinyl chlorides with sodium azide at low temperatures (<-20°) in an inert solvent. These azides [209] readily evolve nitrogen on warming, and give a variety of products. A sulphinylnitrene intermediate is postulated. Its failure to undergo the Curtius rearrangement[107] is accounted for by its



stabilisation by resonance, which reduces its ground state energy. The nitrene was trapped by DMSO, but the product isolated was the sulphilimine [210], and not the expected sulphoximine [211]. [210] is thought to arise by oxygen transfer via the sulphurane [212].

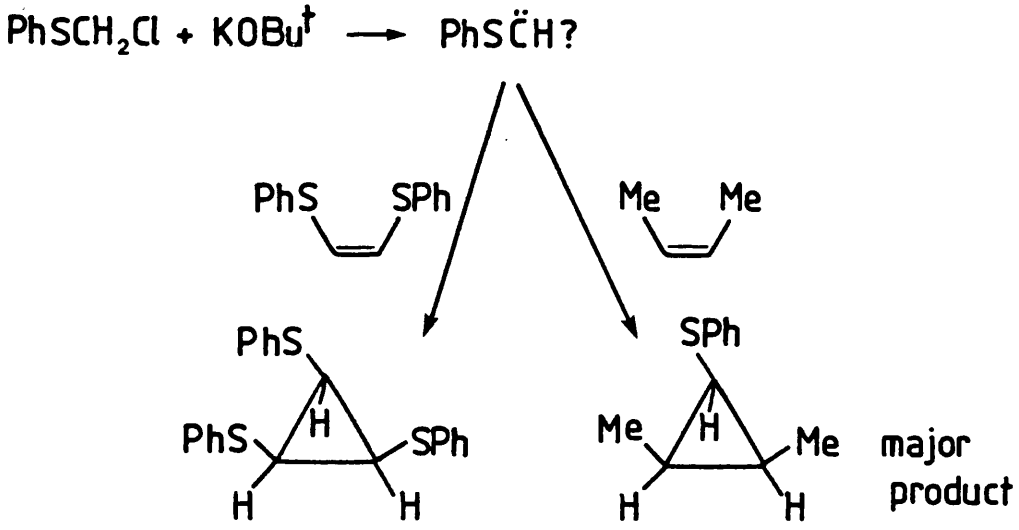
6.7 Sulphenylcarbenes

To date sulphenylcarbenes have only been generated by α-elimination



[212] [210]

of 1-chloroalkyl sulphides. However, this method of formation may also give a carbenoid type intermediate. The reaction of phenylthiocarbene generated this way with cis and trans but-2-ene was found to be stereospecific,[108] and in the case of cis-but-2-ene a syn selectivity of 7:1 was observed. Similarly, reaction with cis-1,2-bis(phenylthio) ethene only gave the all cis adduct [213]. Such behaviour indicates a



[213]

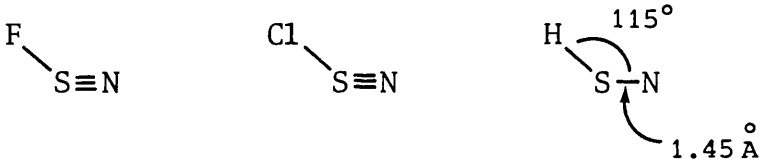
carbenoid rather than a free carbene.

Addition of a crown ether (e.g. 18-crown-6) is thought to result in a carbene rather than a carbenoid, probably by complexation of the metal. Using this reagent, the addition of methylthio-chlorocarbene

to the but-2-enes was found to be stereospecific,[109] indicating a singlet ground state for this carbene. There is no report to date of phenylthiocarbene being similarly generated in the presence of a crown ether.

6.8 Sulphenylnitrenes

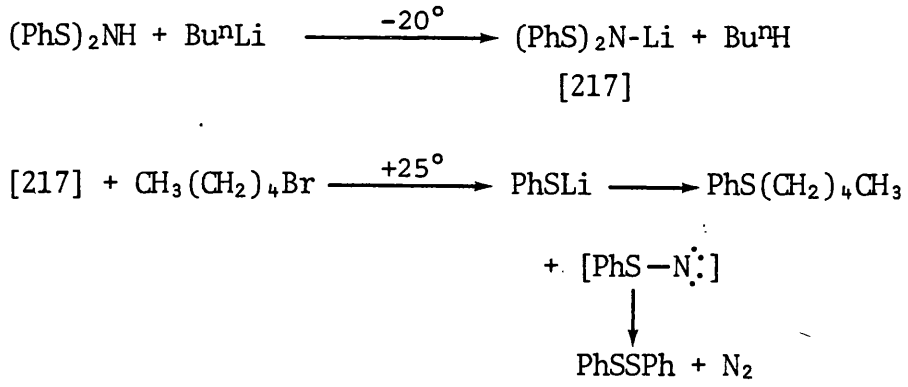
Very little is known about these species. Fluoro[110] and chlorothiazyne[111] [214] and [215] are known compounds which trimerise readily. Spectroscopic studies[112,113] indicate they have a bent structure with short S-N bonds (1.45 Å as compared to 1.7 Å in a sulphenamide S-N bond[67]), i.e. formally the structures may be written as:



[214] [215] [216]

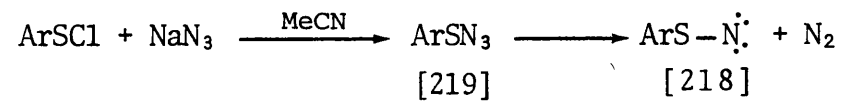
A theoretical study[105] on [216] indicated an S-N bond order of 2.54 with the nitrogen having approximately one unit of negative charge for the singlet state of [216]; whether this is also the ground state was not determined.

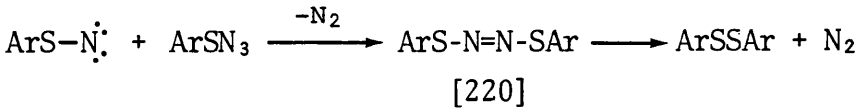
A sulphenylnitrene intermediate was proposed in the decomposition of the sulphenimide anion [217]:[114]



The anion is stable at -20° but at room temperature fragments as shown. The authors did not attempt to trap the nitrene which they suggested subsequently decayed to diphenyl disulphide.

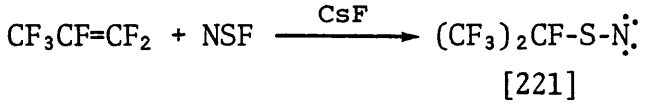
An attempt to prepare sulphenyl azides failed.[115] Even at -40° the reaction of an arylsulphenyl chloride with sodium azide spontaneously evolved nitrogen, and disulphides were the eventual products. It seems possible that the sulphenylnitrene [218] formed attacks a molecule of sulphenyl azide [219], and the collapse of the bis(arylthio)di-imide [220] gives diaryl disulphide:





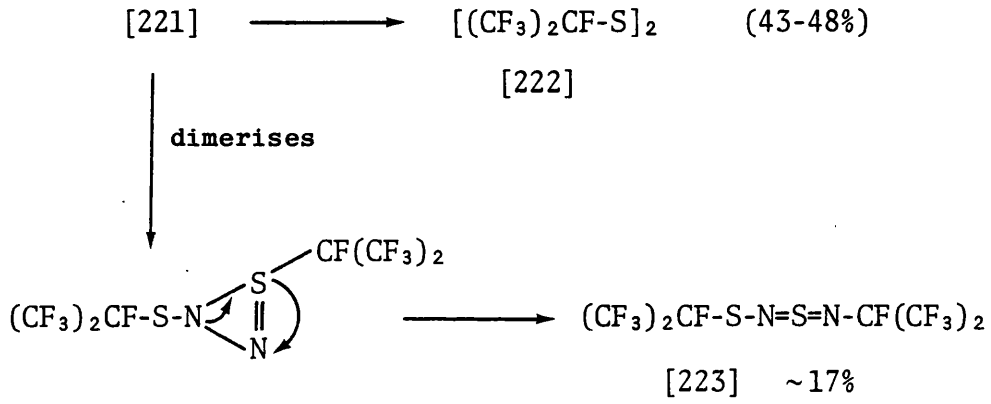
Ar = phenyl, 4-tolyl, 4-nitrophenyl, 2,4-dinitrophenyl

An intermediate sulphenylnitrene has been proposed from reaction of perfluoropropene and thiazyl fluoride in the presence of caesium fluoride:[116]

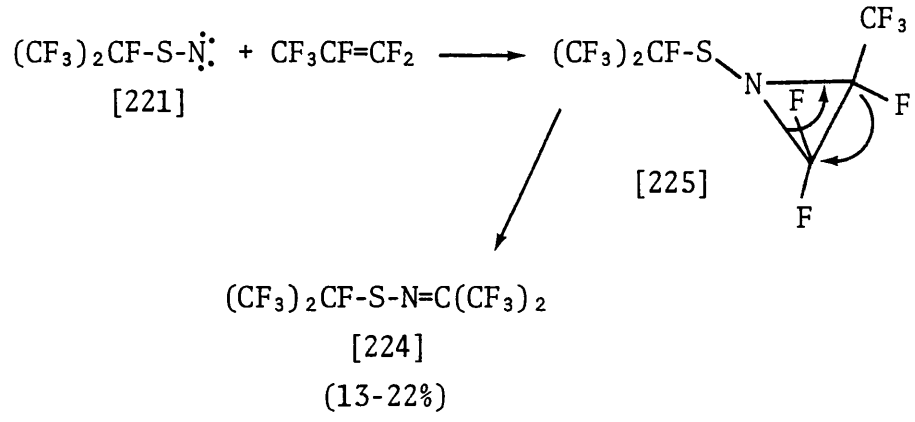


[221]

The nitrene [221] dimerises and fragments to the corresponding disulphide [222] which is the major product (43-48%) although another decay product [223] is formed:



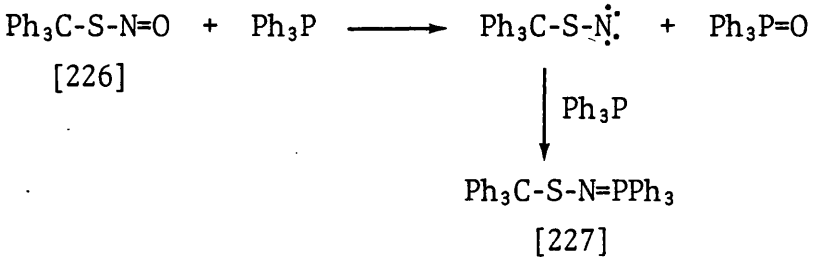
A product derived from nitrene addition to excess perfluoropropene is obtained, i.e. the sulphenylimine [224].



This is probably formed from thermal decomposition of the initially formed aziridine [225] under the reaction conditions (130°, 16-24h). Other haloaziridines are known to decompose in a manner similar to

that shown.[51]

One postulated sulphenylnitrene intermediate has been intermolecularly trapped:[117] deoxygenation of tritylthionitrite [226] with triphenylphosphine gave the sulphenylphosphin-imide [227]:



$Ph_3C\text{-}S\text{-}N{=}O + Ph_3P \longrightarrow Ph_3C\text{-}S\text{-}\ddot{N}: + Ph_3P{=}O$

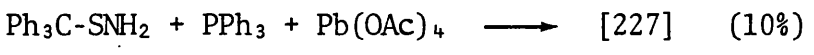
[226]

Ph_3P

$Ph_3C\text{-}S\text{-}N{=}PPh_3$

[227]

The same adduct was isolated by oxidation of the sulphenamide [228] by lead tetra-acetate in the presence of triphenylphosphine in low yield.



$Ph_3C\text{-}SNH_2 + PPh_3 + Pb(OAc)_4 \longrightarrow$ [227] (10%)

[228]

Deoxygenation of [226] by triphenylphosphine in DMSO gave [227] but also the sulphoximine [229] in 11% yield.

$Ph_3C\text{-}S\text{-}N{=}O + Ph_3P + DMSO \longrightarrow$ [227] + $Ph_3C\text{-}S\text{-}N(=O)(=SMe_2)$

[229]

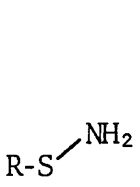
CHAPTER 7

The trapping and spin state of 2,4-Dinitrobenzenesulphenylnitrene

In chapter five reference was made to a sulphenylnitrene intermediate in the decomposition of [168] and [169]. In this chapter, the trapping of such an intermediate is described.

7.1 Synthesis of nitrene precursors

The primary sulphenamides [230]-[234] were used as nitrene precursors, being relatively easy to synthesise, and oxidation by lead tetra-acetate was expected to generate the nitrene intermediates [235]. The sulphenamides [231] and [234] were conveniently prepared by treatment of the corresponding sulphenyl chloride with excess ammonia in aqueous acetonitrile. This reaction fails with 4-chlorobenzenesulphenyl chloride [153], the product being the disulphenamide (sulphenimide) [236].



[230] R = PhC(=O)-
[231] R = 2-nitrophenyl
[232] R = 4-nitrophenyl
[233] R = 4-chlorophenyl
[234] R = 2,4-dinitrophenyl = Ar^1

$$RSNH_2 + Pb(OAc)_4 \longrightarrow \underset{[235]}{R\text{-}S\text{-}N\cdot} + Pb(OAc)_2 + 2AcOH$$

$$(4\text{-}ClC_6H_4S)_2NH$$

[236]

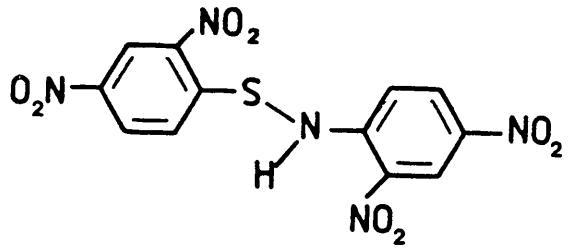
Instead [233] was synthesised by amination of 4-chlorobenzenethiol by hydroxylamine-O-sulphonic acid in aqueous base. [233] is an unstable oil which disproportionates to [236] and ammonia on standing at room

temperature. It is stable at -20°, however.

The amination method was used to prepare the known sulphenamides [230] and [232], and gave good yields.

7.2 Oxidation of [230]-[234] by lead tetra-acetate

When [230]-[234] were oxidised by lead tetra-acetate in dichloromethane, gas evolution was noted in all cases. However, on work up, [230] only gave elemental sulphur and an intractable polymer. In the cases of [231]-[233] the corresponding disulphides were obtained; however from [234] an insoluble yellow material was isolated in 41% yield. It had two types of dinitrophenyl ring protons in its n.m.r. spectrum, and a mass peak at 381 in its mass spectrum. The structure [237] fits this data, and an alternative synthesis of this compound

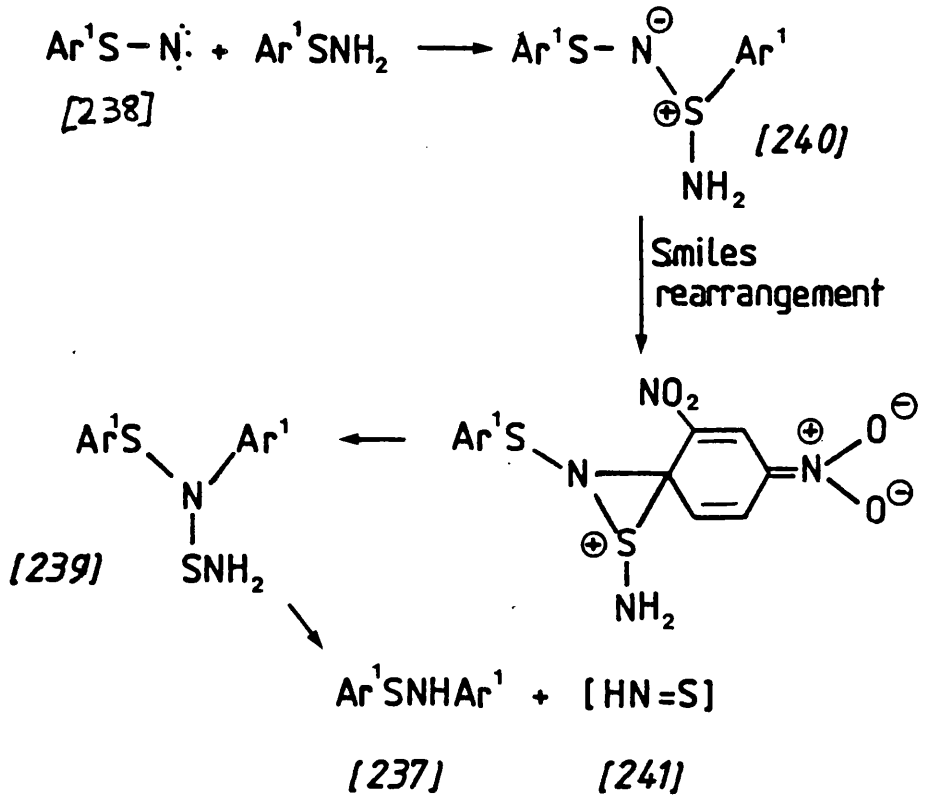


(237)

from 2,4-dinitroaniline and 2,4-dinitrobenzenesulphenyl chloride (in the presence of sodium hydride) supported the assigned structure. The N-H of [237] is acidic and a blue anion is readily generated in dilute base, or on column chromatography over basic alumina. The anion of [237] is stabilised by the electron withdrawing dinitrophenyl ring, and adjacent sulphur atom.

There are two possible mechanisms for the formation of [237] from [234], both involving the Smiles rearrangement.[118] If attack of 2,4-

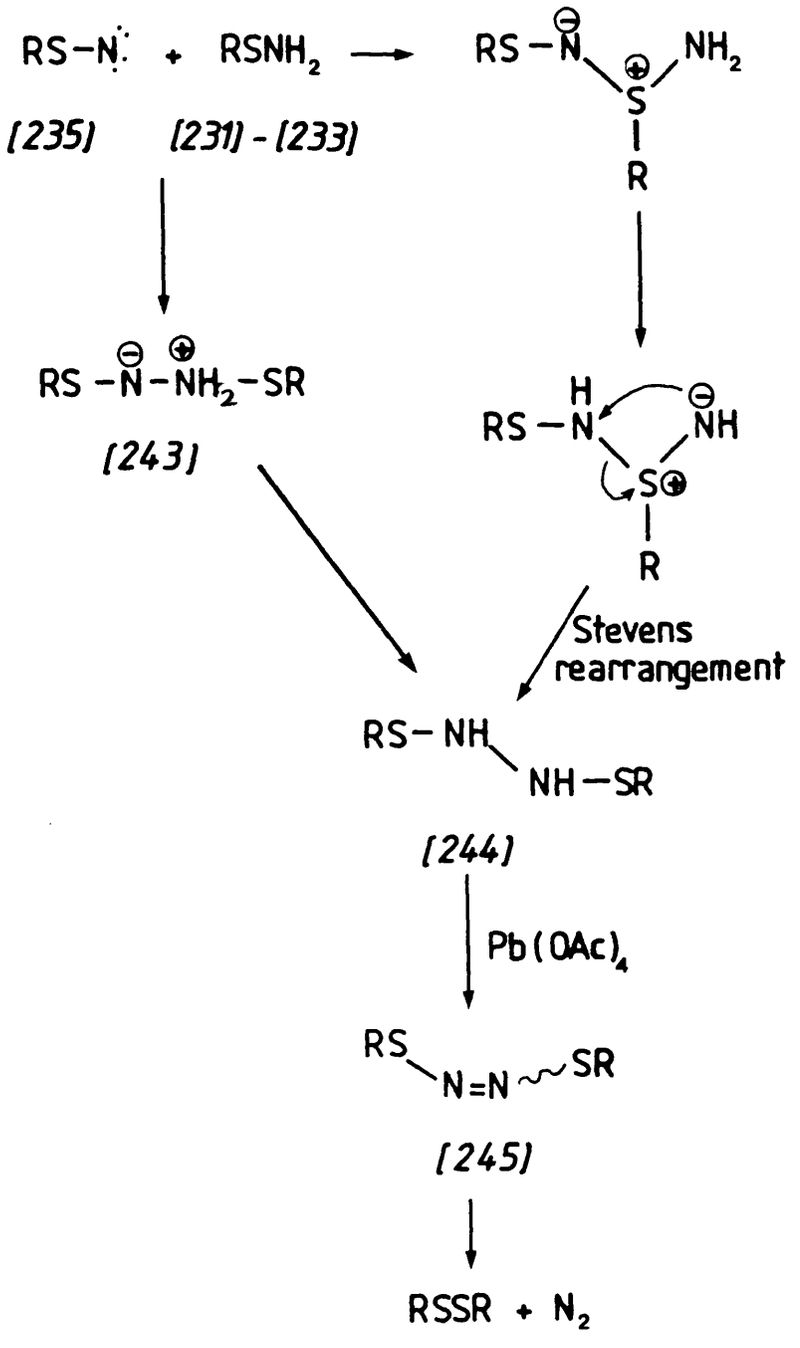
dinitrobenzenesulphenylnitrene [238] occurs on the sulphur atom of the starting sulphenamide, a Smiles rearrangement to give [239] could occur via the key intermediate [240] which fragments to [237] and thionitroxyl [241]. It is possible that the thionitroxyl is further oxidised under the reaction conditions, possibly leading to evolution

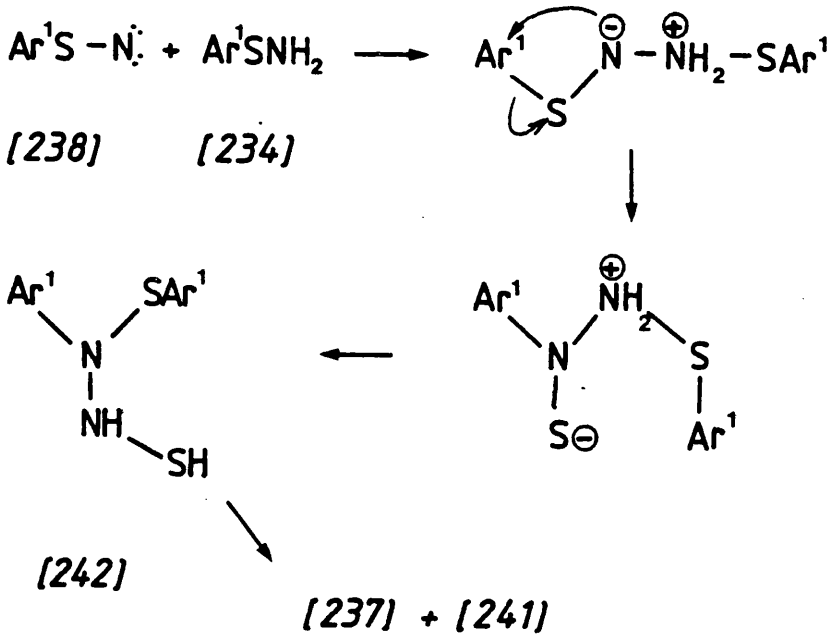


of nitrogen. An alternative mechanism for formation of [237] involves attack by the nitrene [238] on the nitrogen atom of [234] followed by consecutive Smiles/Stevens rearrangements to give the intermediate [242].

For the sulphenamides [231]-[233], attack of the nitrenes may occur initially on nitrogen or sulphur, as above, but in these cases, the aryl rings cannot act as electron sinks for the Smiles rearrangement, and so disulphide formation occurs.

[244] may be formed by attack on nitrogen followed by proton


RS–N: + RSNH2
[235]
[231] - [233]
RS–N–S(R)–NH2
RS–N–NH2–SR
[243]
Stevens rearrangement
RS–NH
NH–SR
[244]
Pb(OAc)4
RS
N=N
SR
[245]
RSSR + N2



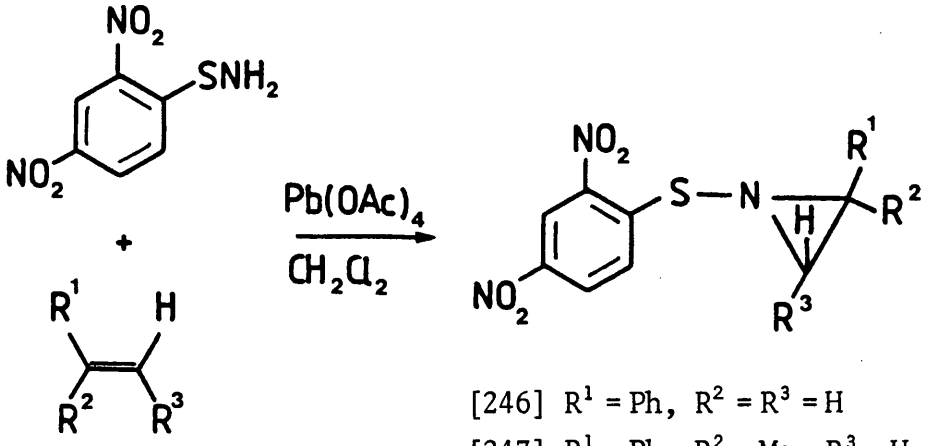
transfer, or alternatively by initial attack on sulphur followed by a Stevens rearrangement. Further oxidation by lead tetra-acetate gives the disulphides and nitrogen via the (unknown) bis(arylsulphenyl)diimide [245].

7.3 The trapping of 2,4-dinitrobenzenesulphenylnitrene [238]

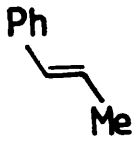
(a) Trapping with alkenes

When 2,4-dinitrobenzenesulphenamide [234] was oxidised in the presence of methyl acrylate, ethyl cinnamate, 3,3-dimethylbut-1-ene or 2-acetylbenzofuran, no trapping occurred, and only the sulphenamide [237] was isolated. However, oxidation of [234] in the presence of more electron-rich alkenes gave aziridines (scheme 14). With a five molar excess of styrene, the resulting aziridine [246] exhibited characteristic aziridine ring signals in its n.m.r. spectrum; δ3.15 (dxd, J 4 × 7Hz, aziridine H-2), 2.65 (d, J 4Hz, aziridine H-3 cis to phenyl), and 2.60 (d, J 7Hz, aziridine H-3 trans to phenyl). An aziridine ring structure is assigned to [246] as it could be readily

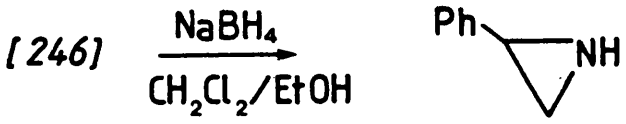
Scheme 14

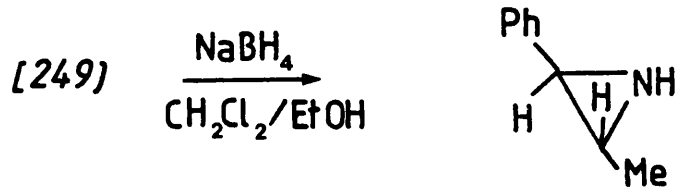


[246] $R^1 = Ph$, $R^2 = R^3 = H$
[247] $R^1 = Ph$, $R^2 = Me$, $R^3 = H$
[249] $R^1 = Ph$, $R^2 = H$, $R^3 = Me$
[250] $R^1 = R^3 = Me$, $R^2 = H$
[251] $R^1 = CH=CH_2$, $R^2 = R^3 = H$
[255] $R^1 = H$, $R^2 = Ph$, $R^3 = Me$



[248]

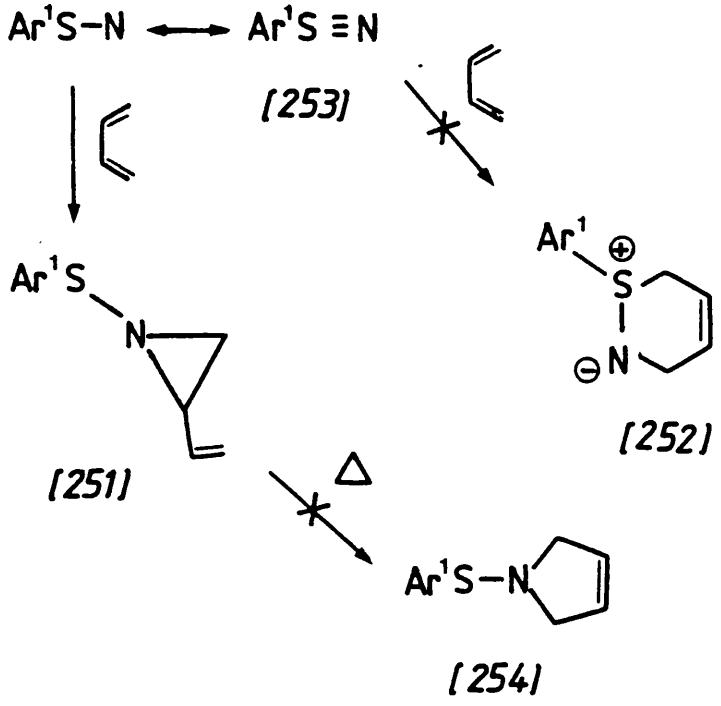




reduced by sodium borohydride in ethanol/dichloromethane to the known[119] 2-phenylaziridine in 44% yield.

Although the yield of [246] from [234] was moderate (38%), the

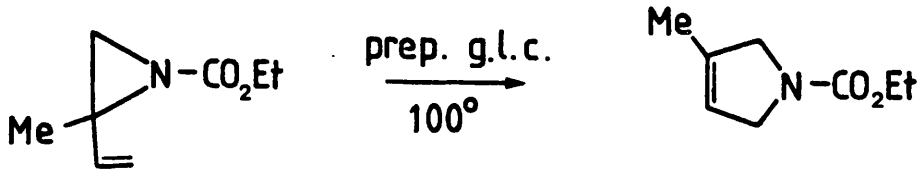
methylstyrenes gave much better yields of aziridines. 2-phenylpropene gave a 61% yield of the aziridine [247], and trans-1-phenylpropene [248] gave a 64% yield of the aziridine [249]. Compound [249] could be reduced by sodium borohydride to the known[119,120] trans-2-methyl-3-phenylaziridine in 56% yield. Trans-but-2-ene gave a 38% yield of the aziridine [250], and addition to buta-1,3-diene occurred to give the aziridine [251] in 58% yield. In this latter reaction [251] was the only nitrene-alkene adduct isolated; another possible product [252], resulting from Diels-Alder addition, could arise if the resonance structure [253] was contributing strongly to the nature of the reactive intermediate, but no evidence for the presence of [252] was obtained.



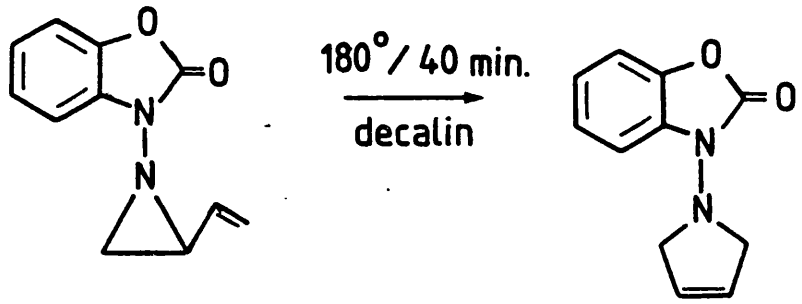
The thermal stability of [251] was of interest; other vinyl aziridines are known to ring expand to pyrrolines on heating.

However, [251] was unchanged at its melting-point (113°) and stronger heating resulted in charring and decomposition; the pyrroline [254] (and its thermal stability), however, is unknown.

Ref.



121



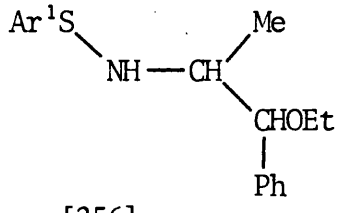
122

(85%)

With cis-1-phenylpropene [200], examination of the n.m.r. spectrum of the crude reaction product revealed the presence of signals due to the trans substituted aziridine [249] as well as signals due to another aziridine which was subsequently shown to be the cis isomer [255] (this reaction is examined in detail in 7.5).

(b) Chromatographic behaviour of [249] and [255]

When the crude reaction product from the reaction of [234], [248] and lead tetra-acetate was chromatographed over basic alumina with light petroleum-ethyl acetate, the aziridine [249] was not obtained but instead a 20% yield of the ethanolysis product [256]. This material



[256]

possibly results from a small concentration of ethoxide ion being

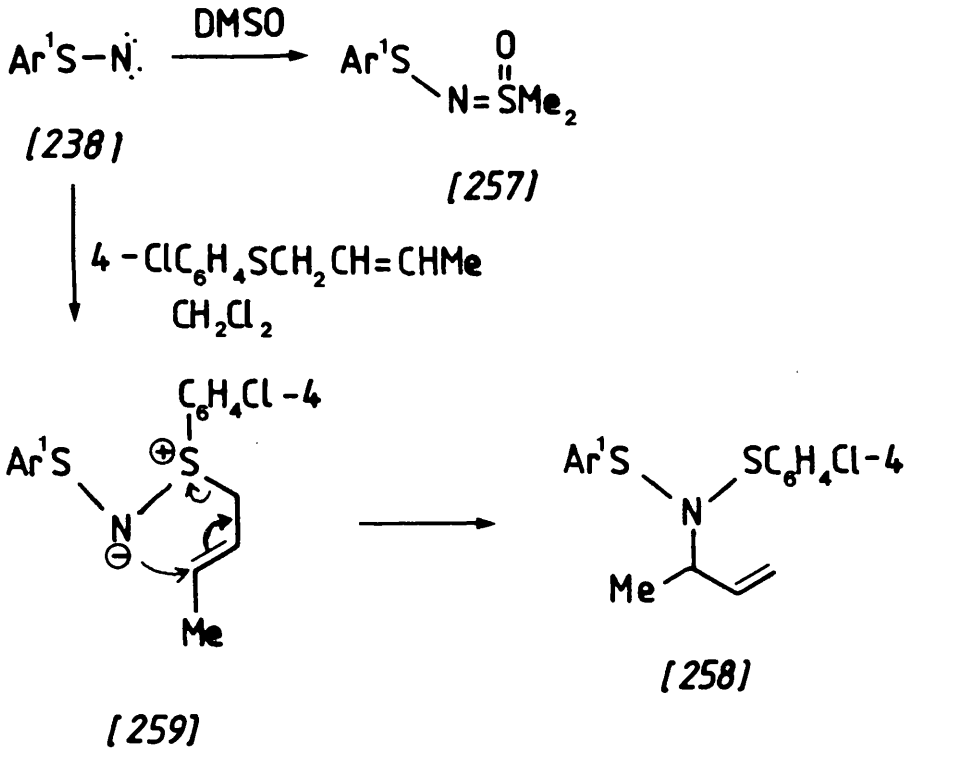
present under the conditions of the chromatography resulting from hydrolysis of ethyl acetate by the basic alumina. Indeed, on treatment of [249] with sodium ethoxide in ethanol a low yield of [256] was obtained.

When the mixture of aziridines obtained from the reaction of sulphenamide [234], cis-1-phenylpropene [200] and lead tetra-acetate were chromatographed over basic alumina with light petroleum-ether, it was found that the trans aziridine [249] was selectively destroyed, enabling convenient isolation of pure cis aziridine [255] in 18% yield.

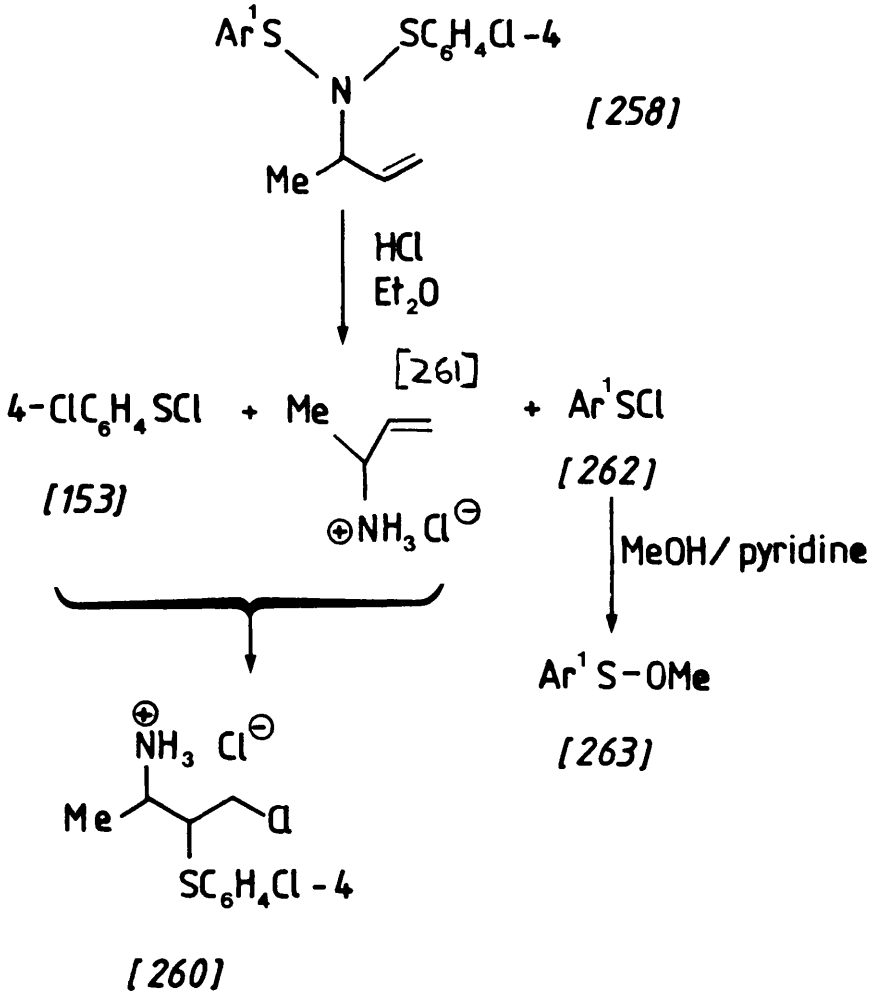
(c) Trapping of [238] with other reagents

Nitrene [238] was trapped by DMSO if the latter was used as solvent for the reaction. Sulphoximine [257] was isolated in 28% yield. This reaction contrasts with that of the sulphinylnitrene[106] discussed in 6.6 where oxygen transfer occurs to give a sulphonylsulphilimine. In the case above the methyl singlets of [257] resonate at δ3.4 indicating a sulphoximine structure, and this was the only adduct obtained. (A sulphinylsulphilimine structure would be expected to give methyl singlets between δ2.5-3 p.p.m.).

Allyl aryl sulphides are excellent traps for [238] as they are for N-nitrenes; e.g. trans-but-2-enyl 4-chlorophenyl sulphide gave a 74% yield of an orange oil identified as the mixed sulphenimide [258] presumably formed via a [2,3]-sigmatropic rearrangement of the intermediate sulphilimine [259]. To date, no mixed sulphenimides have been reported, and the above reaction is an easy method of generating them. Assignment of structure of [258] was supported by spectral data and also isolation of [260] from treatment of the material with dry hydrogen chloride in ether. Initially the two S-N bonds are cleaved to give the amine salt [261] and the two sulphenyl chlorides [153] and [262]. 4-

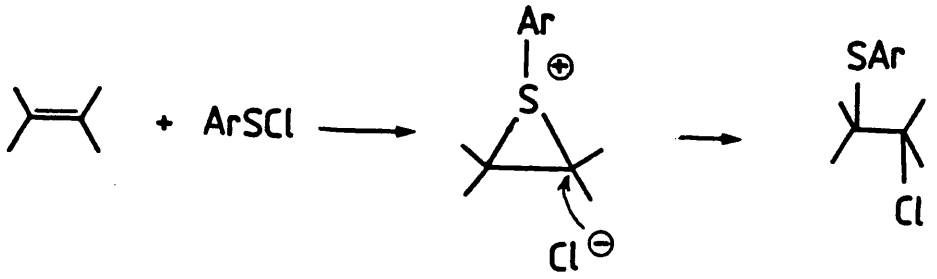


[238] [257] [259] [258]



[258] [153] [262] [263] [260]

Chlorobenzenesulphenyl chloride [153] is more reactive in electrophilic addition to alkenes than the 2,4-dinitrophenyl analogue as the more stable episulphonium salt [264] is formed;[78] a dinitrophenyl ring



[264]

discourages formation of a positive charge on the adjacent sulphur atom. Hence [261] reacts with [153] to give the isolated salt [260] in 46% yield. Although the regiospecificity of addition has not been proved, it is probably anti-Markovnikov by analogy with [154] (see 3.4). The dinitrobenzenesulphenyl chloride formed in the above reaction was trapped by methanol to give the known crystalline sulphenate ester in 82% yield.

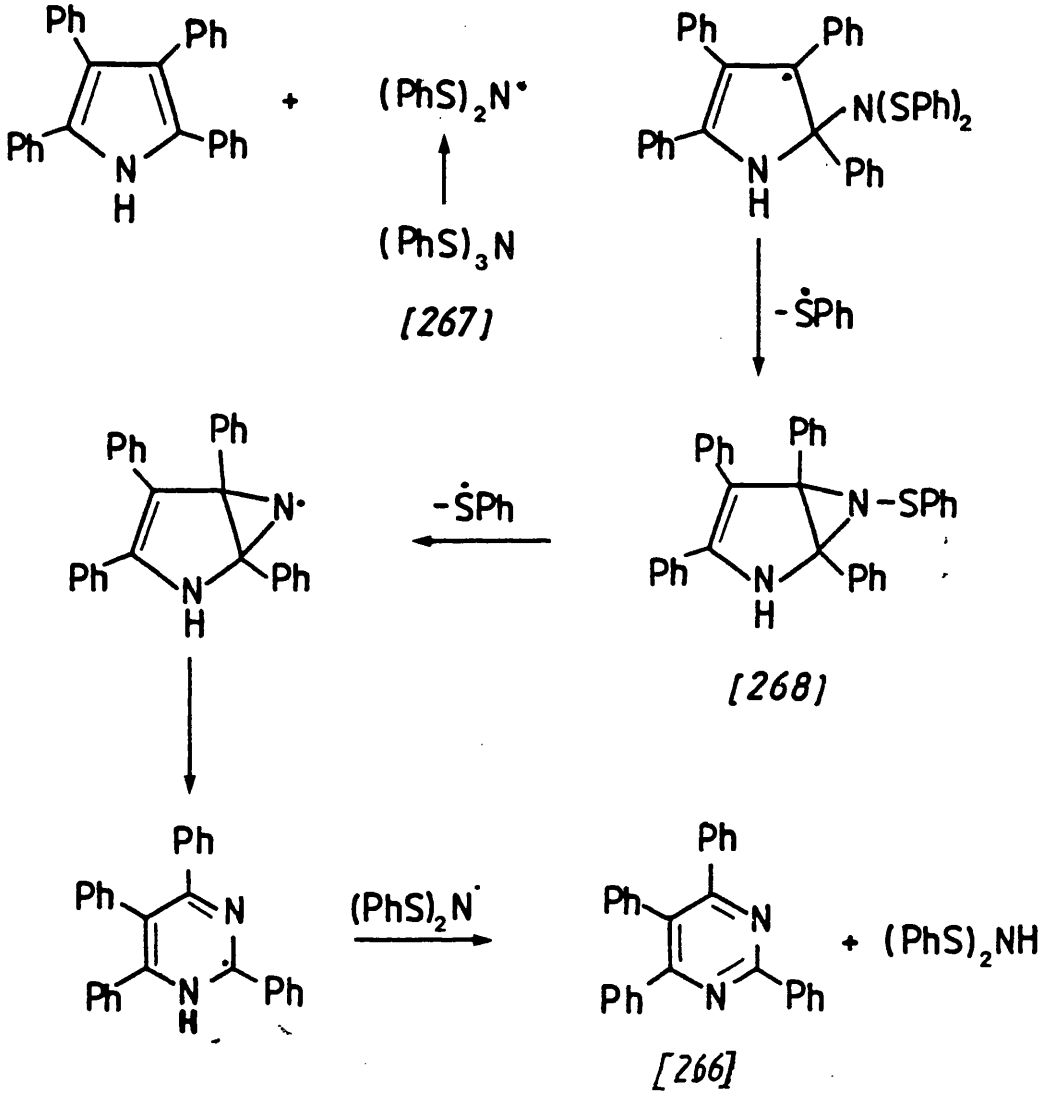
(d) Reaction of [238] with tetraphenylpyrrole [265]

When the sulphenamide [234] was oxidised in the presence of tetraphenylpyrrole [265] in dichloromethane, three products other than unreacted [265] and a small amount of [237] were obtained. A colourless crystalline material identified as 2,4,5,6-tetraphenylpyrimidine [266] was obtained in 47% yield. This material was originally obtained by Barton *et al.*[123] by heating tris(benzenesulphenyl)nitride [267] with [265].

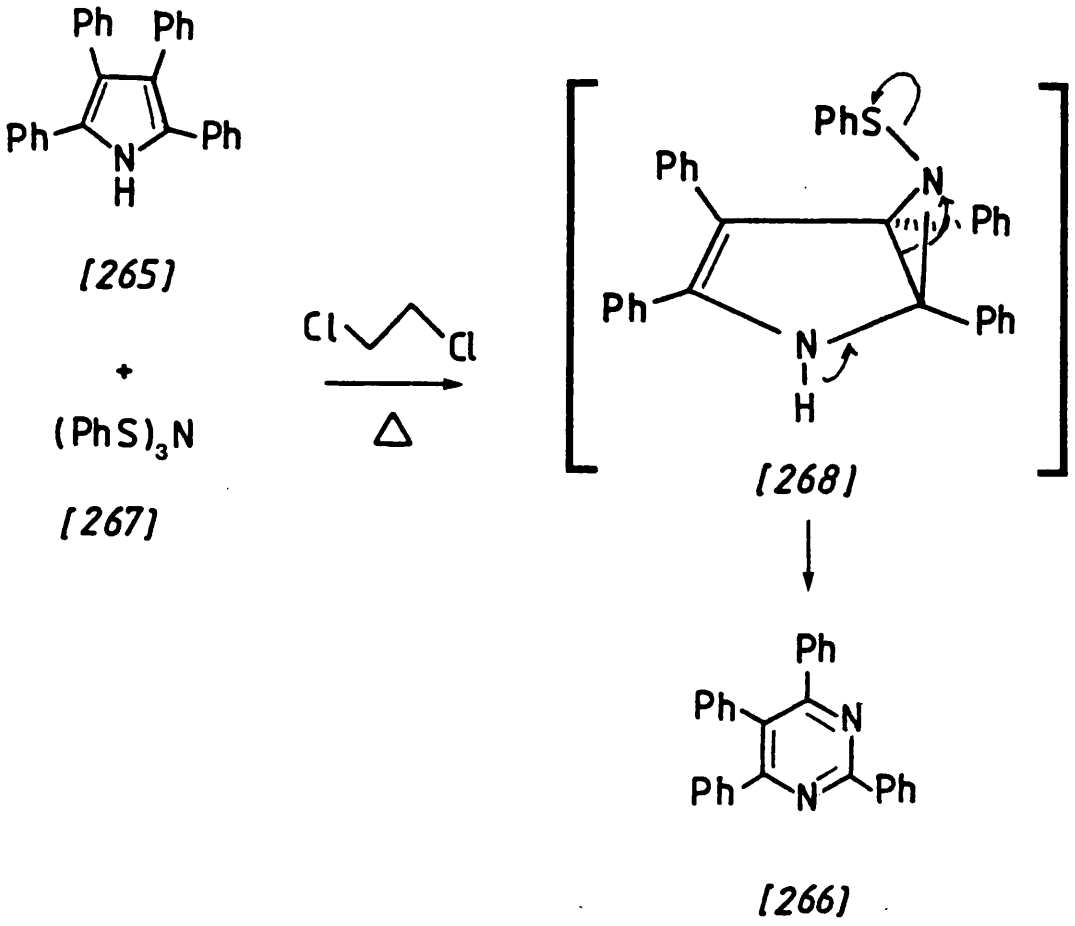
The authors[123] proposed a sulphenylaziridine intermediate [268] which may undergo heterolytic ring expansion to [266], although the authors proposed a free radical mechanism for this transformation under

SCHEME 15

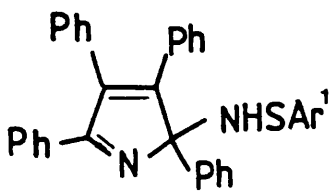
Reaction of tris(benzenesulphenyl)nitride with tetraphenylpyrrole



their conditions (see scheme 15). However, the heterolytic mode of decomposition of [268] seems more likely, since concerted loss of the mercaptide anion with disrotatory[124] aziridine ring opening generates an aromatic ring system directly. It seems likely that the 2,4-dinitrophenyl analogue of [268] is the first formed product in the reaction of the nitrene [238] with tetraphenylpyrrole [265]; some of this then gives

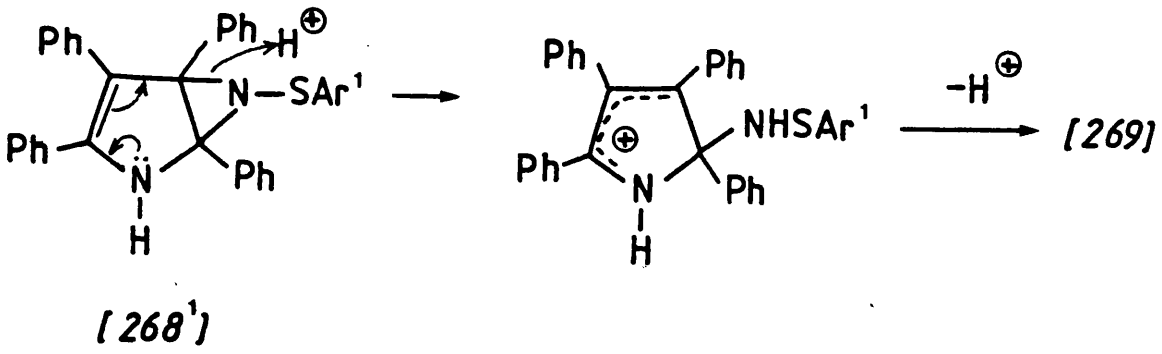


the pyrimidine [266]. In addition to [266], two coloured materials were identified by chromatography. One, obtained in low yield was not identified, but the second more polar compound was identified as a 1:1 nitrene-tetraphenylpyrrole adduct by n.m.r. and elemental analysis. The structure of this compound was subsequently determined by X-ray diffraction[43] as the (2H) pyrrole derivative [269]. [269] is unstable



[269]

in ethanol solution, reverting to the pyrimidine [266]. A probable mechanism for the formation of [269] from [268] is shown below.

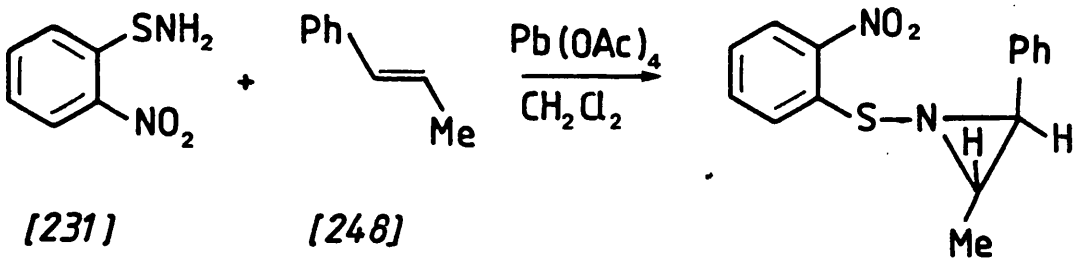


[268']

Acid catalyzed ring opening of [268] by acetic acid (formed from the lead tetra-acetate oxidation) leads to [269]. The pyrimidine [266] is also formed on heating the (2H) pyrrole to its melting point (172°). When the nitrene reaction was carried out in acetic acid as solvent,[125] virtually no pyrimidine was formed and the yield of [269] increases, thus supporting the idea that [269] is formed by an acid catalyzed process.

7.4 Trapping of the nitrenes derived from [230]-[233]

The attempted trapping of the nitrenes derived from [230], [232] and [233] with a variety of reagents all failed. The benzoyl derivative [230] gave no trapping with methyl acrylate, styrene or 4-chlorophenyl crotyl sulphide [110], the 4-nitro derivative [232] gave no trapping with [110], styrene or DMSO, although with trans-1-phenylpropene [248] a very low yield of an aziridine was detectable by n.m.r. - the characteristic aziridine pattern signals being visible between δ2 and 3. The 4-chloro derivative [233] gave no products with [110], methyl acrylate, trans-1-phenylpropene or buta-1,3-diene, and in each case the products obtained were identical with those obtained in the absence of any trapping reagents (7.2). However, [231] did give a 58% yield of the aziridine [270] with trans-1-phenylpropene. The n.m.r. spectrum of [270] is very similar to the dinitrophenyl analogue [249].

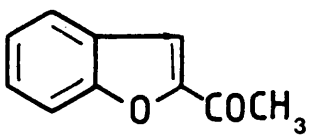


[231] [248] [270]

It is not clear why the 2-nitro substituted sulphenylnitrene is trappable whereas the 4-nitro substituted compound is not; nor is it clear why the electron withdrawing (di)nitrophenyl ring is necessary for trapping. One possibility is that the sulphenamide precursor [234] is less reactive towards the derived nitrene [238]. Thus in the cases of the 4-chloro and 4-nitrophenylsulphenyl nitrenes, the greater affinities of these nitrenes for their precursors, the sulphenamides [232] and [233] explains the absence of trapping and subsequent disulphide formation, whereas the presence of a nitro group in the ortho position of [231] and [234] may deactivate them sterically as well as electronically to attack from their derived nitrenes. The steric effect may be the factor which allows the trapping of Haake's tritylsulphenylnitrene[117] by triphenylphosphine and DMSO.

Some clarification of the behaviour of these nitrenes could be obtained by finding alternative methods of generating them which could minimise attack on the precursor, and which could eliminate the possibility of the lead complex [271] (lead nitrenoid) as the true reactive intermediate and not the free nitrene. Such a possibility has been

[271]

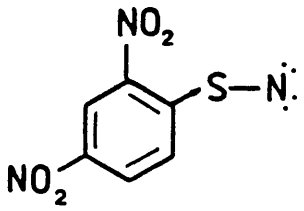


[272]

eliminated for phthalimidonitrene [90] by use of its 2-acetylbenzofuran adduct which, when heated, is a source of the nitrene.[126] 2-Acetylbenzofuran [272] was tried as a trap for [238] but, unfortunately, no adduct was isolated.

7.5 The spin state of dinitrobenzenesulphenylnitrene [238]

Good evidence for the free nitrene [238] as the reactive intermediate



[238]

in the oxidation of sulphenamide [238] results from the study of its reaction with cis and trans-1-phenylpropene [200] and [248] in detail.

Discussion

A number of points may be raised from the results shown in table 13. Firstly, reaction of the nitrene [238] with the trans alkene [248] is stereospecific giving [249] in all solvents examined (runs 2, 3, 11 and 13). The cis alkene [200], however, gives a mixture of the aziridines [249] and [255]. In benzene as solvent (runs 7-9), the ratio of [249]:[255] obtained was 50:50 as it was also in neat cis alkene (run 1), but in dichloromethane as solvent, the ratio of [249]:[255] obtained was approximately 3:1 with five molar equivalents of alkene and 5:1 in a more dilute solution of alkene, with one molar equivalent of alkene. An unusual feature is the lack of a dilution effect - in runs 1, 7, 8 and 9 the same ratios of [249]:[255] were obtained despite changes in

TABLE 13

Reaction of 1-phenylpropenes with [238]

Run no.	solvent	Alkene conc. (moles %)	1-phenylpropene	Alkene mole equivs.	% aziridines trans/cis	aziridines % yield
1	neat	100	cis	18.2	50 50	
2		19.3	trans	5.3	>98 <2	64
3		2.9	"	0.87	>98 <2	51
4	CH_2Cl_2	23.1	cis	5.0	77 23	65
5		15.8	"	5.0	79 21	69
6		3.7	"	1.0	83 17	42
7		29.8	"	5.1	52 48	
8	C_6H_6	20.7	"	5.0	50 50	55
9		5.0	"	5.1	50 50	
10		5.0	"	1.0	73 27	31
11	CH_2Br_2	20.8	trans	6.4	>98 <2	
12		17.3	cis	5.1	79 21	55
13	CH_3CN	9.6	trans	3.5	>98 <2	
14		13.2	cis	5.0	71 29	26

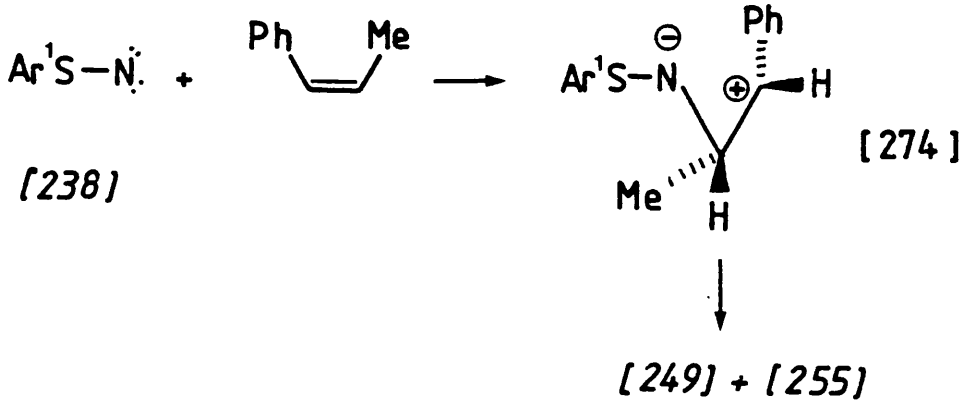
Competition experiment with allyl 4-chlorophenyl sulphide [107] in benzene

Run no.	Alkene conc. (moles %)	Sulphide conc. (moles %)	Alkene mole equivs.	Sulphide mole equivs.	% aziridines trans/cis	product ratio sulphenimide [275]/aziridines
8	20.7	-	5.0	-	50 50	0 100
15	20.5	2.1	5.1	0.51	72 28	77 23

concentration from 100 to 5 moles %.

These results contrast with the classical increased non-stereospecific addition or insertion obtained with ethoxycarbonylnitrene or cyanonitrene; they could be accounted for by proposing the generation of sulphenylnitrene [238] in its singlet state (by heterolytic fragmentation of the intermediate lead complex [271]) which then rapidly decays to the triplet state before reacting with the alkene. The fact that the same ratio of aziridines are not formed from both cis and trans alkenes, even in dibromomethane, contrasts with the behaviour of cyanonitrene and could be accounted for by proposing a slow rate of C-C bond rotation in the intermediate triplet biradical [273] relative to spin inversion; leading to some retention of stereospecificity (scheme 16). Such an explanation is eliminated by the result of run 15, a competition experiment with allyl 4-chlorophenyl sulphide [107] in which the change in the ratio of aziridines produced is impossible to rationalise with a wholly triplet state reaction (vide supra).

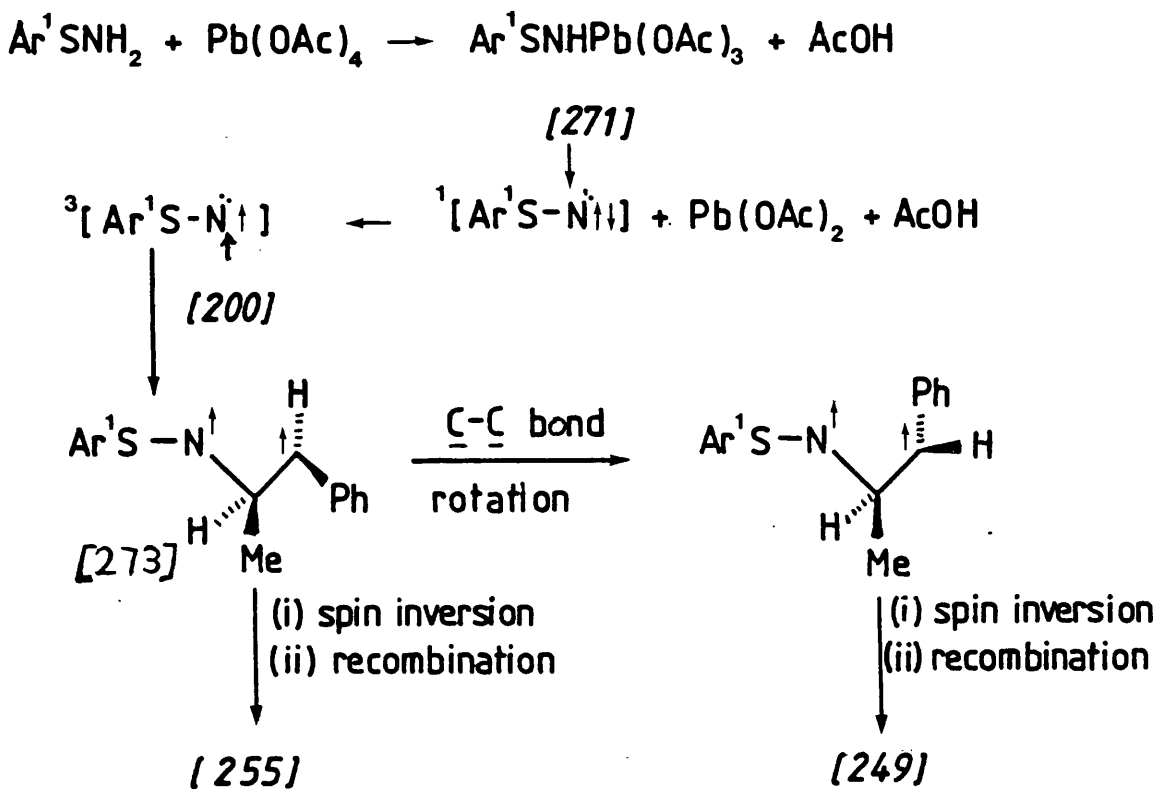
An alternative explanation involves dipolar addition of the nitrene to the alkene:



[238] [274] [249] + [255]

Dipolar intermediates are very sensitive to the nature of the solvent employed, and the dipolar intermediate [274] ought to be stabilised intermolecularly by a polar solvent enabling more C-C bond rotations to

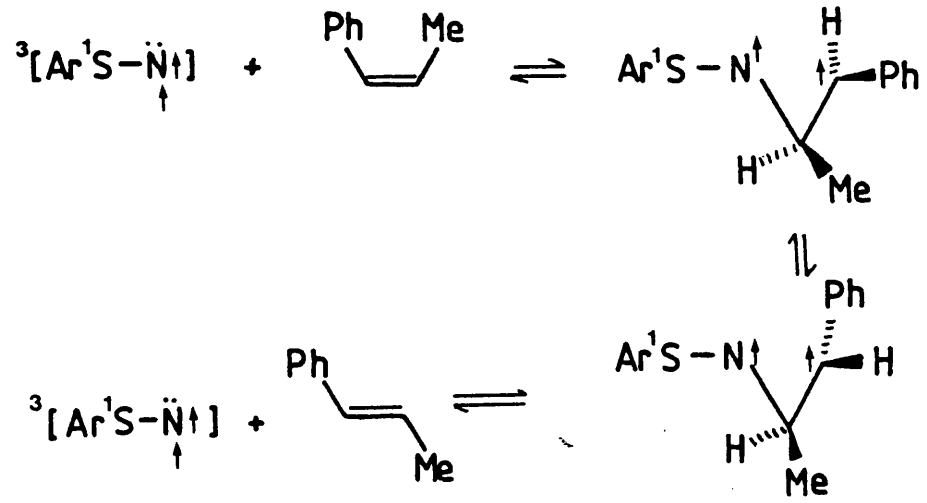
Scheme 16



occur before ring closure, leading to greater loss of stereospecificity. Hence the reaction of [238] with [200] in acetonitrile should give increased amounts of the trans aziridine [249] if this mechanism were operative but, in fact, the same ratios of [249]:[255] were obtained in acetonitrile (runs 13, 14) as in dichloromethane, which appears to rule out the dipolar mechanism of addition.

A most unusual feature was the change in the ratio of [249]:[255] on

lowering the number of equivalents of alkene present, keeping all other variables constant. In run 6, a slight change was noticeable, but the effect was more marked in benzene solution (cf. runs 9 and 10). This was accounted for by the observation that partial isomerisation of the cis alkene occurred during the reaction. The cis alkene [200], initially >98% pure by g.l.c., was found to consist of 25% cis and 75% trans alkene when recovered after the reaction under conditions of run 6. Control experiments show this to be a genuine reaction effect. Thus, with one molar equivalent of cis alkene present, the trans alkene formed during the reaction can compete more effectively with the cis alkene for the nitrene if the concentration of the latter present initially is lower. A possible mechanism for the isomerisation is reversible addition of the triplet state of [238] to the alkene:

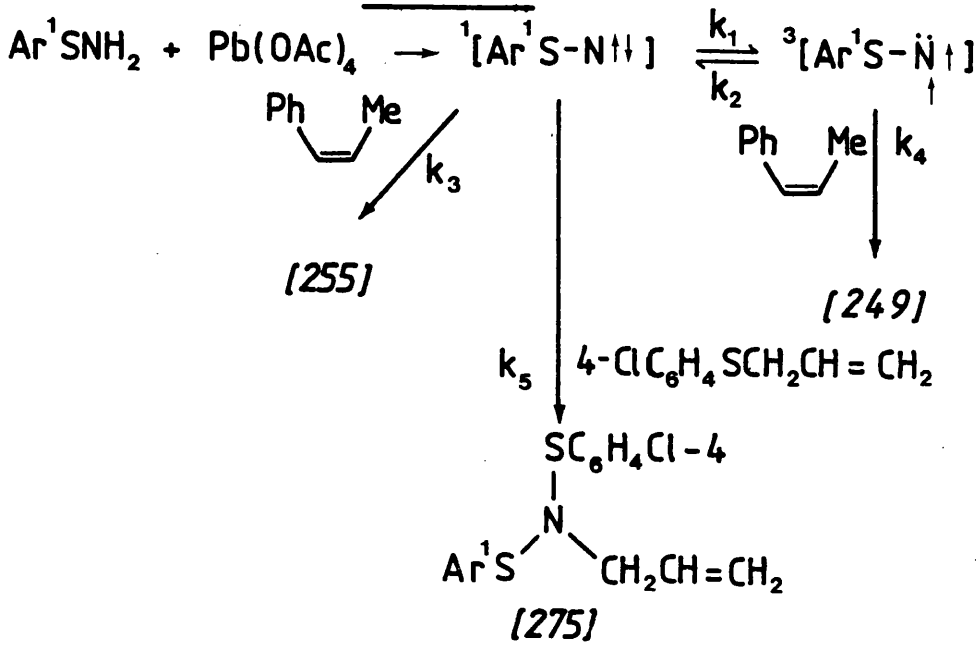


In principle, any free radical present in the reaction may induce isomerisation of the alkene and may also induce polymerisation; however, no evidence for polymerisation of the alkene was observed in the above reactions.

A most significant result was a competition experiment involving the cis alkene [200] and allyl 4-chlorophenyl sulphide [107] (run 15). The

ratio of aziridines produced was changed from 1:1 to 5:2 trans:cis with the allyl sulphide present and the major part of the reaction product was derived from the allyl sulphide despite its ten-fold lesser concentration. Reaction of the nitrene [238] with the sulphide must be a singlet state reaction involving donation of a lone pair of electrons on sulphur to a vacant p orbital on the nitrene (cf. the reaction of bis(ethoxycarbonyl)carbene with allyl sulphides[127]); the triplet state has no suitable vacant low-lying orbitals for such a reaction. As a result, it is difficult to rationalise the change in the ratio of the aziridines [249] and [255] if the reaction of the nitrene [238] with alkenes is purely that of the triplet state. It seems likely that the nitrene is generated in its singlet state and some of this is being syphoned off by the allyl sulphide leading to a greater proportion of triplet derived products from the alkene. To resolve the conflicting evidence it may be proposed that the singlet and triplet states of [238] are close in energy and in rapid thermal equilibrium, i.e. k_1 and k_2 (scheme 17) are faster than k_3 and k_4, and, as a result, no dilution effect would be observed. The rate of equilibration, however, may be close to the rate of reaction with the allyl sulphide (k_5) giving rise to the observed effect. Unfortunately, experimental difficulties in measuring the ratio of aziridines [249] and [255] at low concentration, prohibit increase in the allyl sulphide concentration any further. However, it seems likely that the reaction of the triplet state of [238] with [200] gives only the trans aziridine [249], i.e. the rate of bond rotation is fast relative to spin inversion. Considerable steric hindrance must be present in the initially formed biradical from the cis alkene as isomerisation to the trans alkene attests, and also reaction of the nitrene [238] with the trans alkene [248] is stereo-

Scheme 17

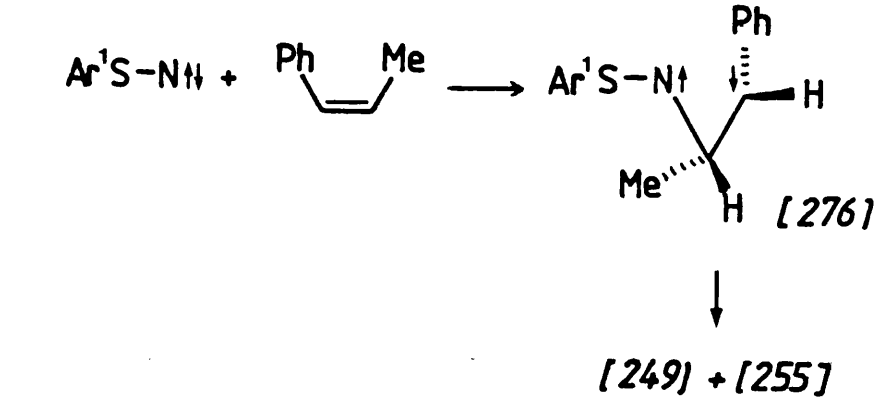


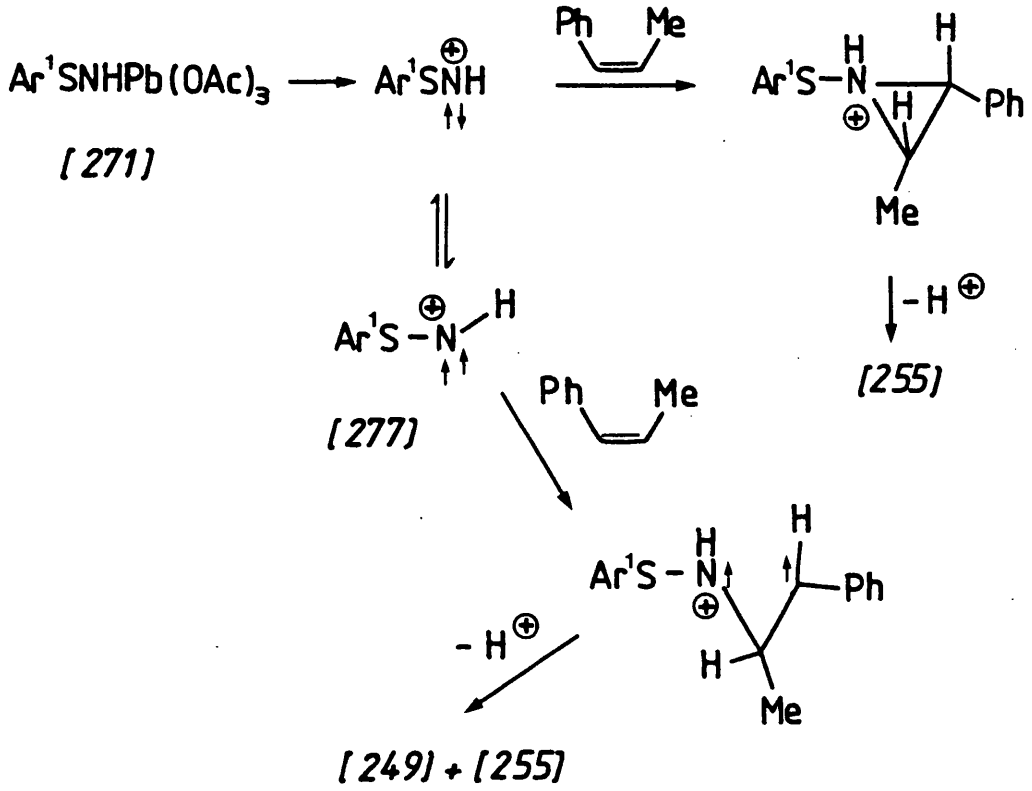
specific. It may be proposed that the delicate balance between the energies of the singlet and triplet states is displaced in benzene relative to the other solvents used.

This competition experiment with allyl sulphide also eliminates a singlet biradical intermediate [276] which could, in principle, give rise to both aziridine products. In this case, introduction of allyl sulphide into the reaction ought not to affect the ratio of aziridines produced.

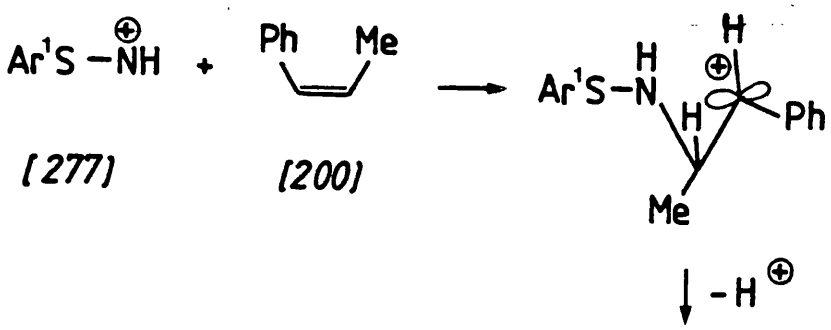
However, the above results do not preclude the nitrenium ion [277] as being the true reactive intermediate in the reactions discussed.

It seems unlikely that this species is the true reactive intermediate as the strongly electron withdrawing 2,4-dinitrophenylthio group would be expected to destabilise an adjacent positive charge. It also seems





more likely that the singlet nitrenium ion would add to the alkene [200] in the manner shown below rather than in a concerted fashion.[128] This would lead to both aziridines being formed from the singlet state, and one would expect a predominance of the trans-aziridine [249] to be formed instead of the 50:50 mixture of the two formed in benzene.



[277] [200] [249]+[255]

A similar rapid equilibration of singlet and triplet states has been proposed for some arylcarbenes, e.g. diphenylcarbene[129] and 9-xanthylcarbene,[130] as well as dihalocarbenes.[92] Here the situation is complicated by formation of C-H insertion products as well as cyclopropanes in reactions with alkenes. As the cyclopropanes are generated almost stereospecifically it is believed that these are singlet derived, whereas the triplet state gives insertion products. In the presence of oxygen (a triplet scavenger) the amount of insertion products are reduced. In the case of the nitrene [238], very little change is noted when oxygen is excluded under the conditions of run 8 when the ratio of [249]:[255] changed from 50:50 to 54:46, implying that some triplet state is being diverted by oxygen under the normal reaction conditions. Such a change with oxygen must be faster than the rate of equilibration (k_1 and k_2), i.e. the triplet state is being reacted too fast for equilibrium to be re-established.

EXPERIMENTAL

Instrumentation

Melting points (m.p.'s) were determined with a Kofler hot stage and are uncorrected.

I.r. spectra of crystalline compounds were determined using Nujol mulls, and liquid compounds as thin films using a Perkin Elmer 237 spectrometer.

N.m.r. spectra were measured using Varian T-60, EM 390 and JEOL PS-100 spectrometers, and ^{13}C spectra using a JEOL FX-60 Fourier-transform spectrometer. 220 MHz spectra were obtained by courtesy of PCMU Harwell.

Temperatures were measured with a calibrated Comark copper-constantan thermocouple, and are believed to be accurate to ±2°.

Mass spectra were obtained with a V.G. Micromass 16B instrument, and accurate mass spectra were obtained by courtesy of PCMU Harwell.

U.v. spectra were determined on a Unicam SP-800 spectrophotometer.

Gas-Liquid chromatography (g.l.c.) was performed on a Pye series 104 gas chromatogram.

Optical rotations were measured on a Perkin-Elmer 141 polarimeter.

Physical data

I.r. spectra are measured in units of cm^{-1}. The following abbreviations are used in determining i.r. data:

br - broad	m - medium
s - strong	w - weak

N.m.r. spectra chemical shifts are expressed in p.p.m. on the δ scale relative to internal tetramethylsilane. The following abbreviations are used in recording n.m.r. data:

J - coupling constant (in Hz)

s - singlet; d - doublet; t - triplet; q - quartet

m - multiplet; dxd - double doublet

Ar - aromatic signals

AB - AB system

Mass spectra were determined in units of mass relative to charge (m/e).

Basic experimental

THF and 1,4-dioxan were obtained pure and dry by refluxing and distillation from lithium aluminium hydride and used immediately.

Diethyl ether was dried over sodium wire.

DMF, acetonitrile and dichloromethane were dried by distillation from calcium hydride.

Triethylamine was dried by refluxing and distillation from potassium hydroxide pellets and stored over potassium hydroxide pellets.

Light petroleum refers to the fraction b.p. 60-80° unless otherwise stated.

Wet solvents from aqueous extractions were dried with anhydrous sodium sulphate.

Basic alumina for column chromatography is UG1 (S. Lancaster & Co.) and neutral alumina is Woelm (BDH) deactivated with 5% water (to Brockmann Grade III). Kieselgel is PF_{254} (Merck).

All small scale distillations (<2g) were carried out in a Kugelröhr oven and bulb tube, and the b.p. quoted as the oven temperature.

PART I

EXPERIMENTAL

CHAPTER 3

N-Aminophthalimide [94]

- was prepared by the method of Drew and Hatt[131] in 52% yield from phthalimide and hydrazine hydrate. The crude material was recrystallised from acetonitrile, m.p. 196-200° (decomp.) (lit.[131] 200-205°);
i.r. 3370w, 3290w, 1790m, 1730s, 1620m, and 720s.

1-Aminoquinolin-2(1H)-one [119]

- was prepared by the method of Rees et al.[51] in 77% yield from quinolin-2(1H)-one[132] and hydroxylamine-O-sulphonic acid.[133] The product was recrystallised from ethyl acetate-light petroleum, m.p. 128-129° (lit.[134] 130°);
i.r. 3300w, 3200w, 1660s, 1175m, 900w, 830s, and 700s.

3-Amino-2-methylquinazolin-4(3H)-one

- was prepared by the method of Rees et al.[51] from methyl 2-acetamidobenzoate and hydrazine hydrate in 73% yield. The product was recrystallised from light petroleum-benzene, m.p. 144-146° (lit.[135] 152°);
n.m.r. ($CDCl_3$) 8.2 (dxd, J 2×7Hz, quinaz. H-5), 7.8-7.3 (m, 3×ArH), 5.0 (br s, $-NH_2$), and 2.7 (s, $-CH_3$).

1-Aminopyridin-2(1H)-one

Pyridin-2(1H)-one (6.6g, 69.5 mmol) was dissolved in 2M potassium hydroxide solution (250 ml) and hydroxylamine-O-sulphonic acid (23.4g, 207 mmol) added portionwise over a period of 20 min. to the stirring mixture at 70°. The solution was cooled, the precipitated potassium sulphate separated, and the filtrate extracted with dichloromethane (5×50 ml). The combined organic extracts were dried and evaporated, and the residue recrystallised from ethyl acetate-light petroleum to give the title compound (0.6g, 8%) m.p. 63-65° (lit.[136] 64-66°).

2-Nitrobenzenethiol

- was prepared by the method of Claasz[137] by reduction of bis(2-nitrophenyl) disulphide with D(+) Glucose in alkaline solution. The crude material was recrystallised from carbon tetrachloride (yield 54%) m.p. 47° (lit.[138] 61°).

trans-But-2-enyl 2-nitrophenyl sulphide [127]

A solution of sodium (1.05g, 45.65 mmol) in ethanol (40 ml) was prepared, and 2-nitrobenzenethiol (7g, 45.16 mmol) added. The mixture was stirred at 0° and trans-1-bromo-but-2-ene (7g, 51.86 mmol) added dropwise. After stirring overnight at room temperature, ethanol was evaporated in vacuo, the mixture poured into water and ether extracted (×2). The ether extracts were dried and evaporated and the residue distilled giving the title compound as a yellow oil (b.p. 145-160°/ 1 mmHg), pure enough to be used directly in the preparation of the sulphenamides below (yield 5.9g, 63%). An analytical sample was obtained by low temperature recrystallisation from ethanol, m.p. 25-26° (Found: C, 57.4; H, 5.35; N, 6.6. $C_{10}H_{11}NO_2S$ requires C, 57.4; H, 5.3; N, 6.7%);

n.m.r. ($CDCl_3$) 8.15 (d, J 8Hz, Ar H-3), 7.6-7.1 (m, 3×ArH), 6.0-5.4 (m, 2×alkene H), 3.6 (d, J 6Hz, further split, CH_2), and 1.7 (d, J 6Hz, $-CH_3$);

i.r. 3040w, 1595s, 1565s, 1510s, 1340s, 960s, and 740s;

m.s. 209 (M^+), 179, 155, 139, 138, 125, 124, 91 and 55 (base).

2,4-Dinitrobenzenethiol

- was prepared by the method of Willgerodt[139] in 67% yield from sodium sulphide and 1-chloro-2,4-dinitrobenzene; m.p. 126-128° (lit.[139] 131°).

trans-But-2-enyl 2,4-dinitrophenyl sulphide [128]

- was prepared by the method of Bost et al.[140] in 40% yield from 2,4-dinitrobenzenethiol and trans-1-bromobut-2-ene using 2-methoxyethanol as solvent. The crude product was recrystallised from methanol m.p. 89-94° (lit.[141] 98.5-99°);

n.m.r. ($CDCl_3$) 9.0 (d, J 2.5Hz, Ar H-3), 8.4 (dxd, J 2.5 × 9Hz, Ar H-5), 7.6 (d, J 9Hz, Ar H-6), 6.0-5.3 (m, 2 × alkene H), 3.7 (br d, J 6Hz, $-CH_2$), and 1.7 (br d, J 7Hz, $-CH_3$).

Potassium 2,4,6-trinitrobenzenethiolate[142] and trans-but-2-enyl 2,4,6-trinitrophenyl sulphide [135]

A solution of potassium hydroxide (4.56g, 80 mmol) in methanol (20 ml) was prepared and divided into two portions. To the first, water (2.16g, 120 mmol) was added, and the mixture saturated with gaseous hydrogen sulphide. The second portion of potassium hydroxide solution was then added, giving a methanolic solution of $K_2S.5H_2O$. This solution was added dropwise to a stirring mixture of 1-chloro-2,4,6-trinitrobenzene (4.95g, 20 mmol) in methanol (40 ml) cooled to 10° under nitrogen. After addition the mixture was stirred at 10° for 0.5h, the precipitated solids were separated and suspended in ethanol (50 ml), and trans-1-bromobut-2-ene (3.2g, 23.7 mmol) added at ambient temperature with stirring. Stirring was continued for 4h at room temperature, then the mixture was heated under reflux for 0.5h. The solution was then evaporated in vacuo, and partitioned between dichloromethane (30 ml) and water (30 ml). The dichloromethane layer was separated, washed with water (30 ml), dried, evaporated, and the residue chromatographed over basic alumina (50g) with light petroleum - chloroform (1:1) as eluant, which gave the sulphide [135] as a yellow oil (4.0g, 67%);

n.m.r. ($CDCl_3$) 8.7 (s, 2 × ArH), 5.9-5.1 (m, 2 × alkene H), 3.5 (br d, J 6.5Hz, CH_2), and 1.5 (br d, J 6Hz, $-CH_3$);
i.r. 3080w, 1595s, 1540s, 1345s, 1055m, 965m, 910m, and 730s.

Benzylisopropylamine

Isopropylamine (11.0g, 186.4 mmol) and benzyl chloride (10.0g, 79 mmol) were stirred at room temperature for 36h. The reaction product was poured into dilute hydrochloric acid (1M, 200 ml) and extracted with ether (3 × 30 ml). The aqueous layer was basified with sodium hydroxide solution (2M, 200 ml) and extracted with ether (2 × 50 ml). The combined ether extracts were washed with water (30 ml), dried, evaporated and the residue distilled *in vacuo* to give benzylisopropylamine (5.2g, 44%) b.p. 75-80°/6 mmHg (lit.[143] 64-66°/4 mmHg);
n.m.r. (CCl_4) 7.2 (m, 5 × ArH), 3.7 (s, $-C\underline{H}_2Ph$), 2.8 (m, J 6.5Hz, $-C\underline{H}Me_2$), 1.05 (d, J 6.5Hz, 2 × CH_3), and 0.8 (br s, exch. D_2O, -NH).

N-Benzyl-N-isopropyl-2-nitrobenzenesulphenamide [134]

This was prepared using Raban's procedure[27] from benzylisopropylamine (4.0g, 26.85 mmol) and 2-nitrobenzenesulphenyl chloride (2.7g, 14.25 mmol). The crude product (4.0g, 93%) was recrystallised from methanol, m.p. 58-60° (Found: C, 63.6; H, 6.0; N, 9.3. $C_{16}H_{18}N_2O_2S$ requires C, 63.55; H, 6.0; N, 9.3%);
n.m.r. ($CDCl_3$) 8.2-7.95 (m, 2 × ArH), 7.6-7.0 (m, 7 × ArH), 4.16 (br s, $-C\underline{H}_2Ph$), 3.36 (m, J 6.5Hz, $-C\underline{H}Me_2$), and 1.15 (d, J 6.5Hz, 2 × CH_3). At -4°, the δ4.16 becomes an AB system, J_{AB} 13.7Hz (T_c 26°), and δ1.15 becomes two doublets, δ1.10 and 1.20 (J 6.5Hz);
i.r. 1600m, 1580m, 1510s, 1350m, 1310s, 770s, 750s, and 720s.

Allyl 4-chlorophenyl sulphide [107]

- was prepared by the literature method[144] from ethanolic sodium 4-

chlorobenzenethiolate and allyl chloride in 87% yield. The crude product was distilled, b.p. 74-82°/0.3 mmHg.

trans-But-2-enyl 4-chlorophenyl sulphide [110]

- was prepared using the same procedure as for allyl 4-chlorophenyl sulphide in 87% yield. It was purified by recrystallisation from light petroleum at low temperature as previously described.[64]

2-Isopropylbenzenethiol[145]

- Benzenethiol (27.5g, 0.25 mol) and anhydrous aluminium trichloride (5g, 37.45 mmol) were stirred under nitrogen in a three necked flask (100 ml) fitted with two dry ice condensers. Propene (5.25g, 0.125 mol) was added slowly *via* one dry ice condenser over 25 min., the mixture being cooled in an ice salt bath. After stirring a further 20 min., benzene (40 ml) was added, then water (40 ml) cautiously. The organic layer was separated, washed with water (20 ml), and then extracted with sodium hydroxide solution (2 × 70 ml, 2M). The combined alkaline extracts were acidified with concentrated hydrochloric acid, and re-extracted with ether (2 × 50 ml). The ether extracts were dried and evaporated and the residual oil distilled *in vacuo* with a Vigreux column. After removal of unchanged benzenethiol (11g) b.p. 45-55°/ 7 mmHg, 2-isopropylbenzenethiol was obtained (4.95g, 26%) b.p. 80-100°/ 7 mmHg.

Allyl 2-isopropylphenyl sulphide [139]

- was prepared from 2-isopropylbenzenethiol (5g, 32.9 mmol) and allyl chloride (3g, 39.2 mmol) using the literature method[144] for the preparation of allyl 4-chlorophenyl sulphide. The crude product (5.4g, 85%) was distilled, b.p. 90-100°/2 mmHg;

n.m.r. ($CDCl_3$) 7.5-7.0 (m, 4 × ArH), 6.2-5.6 (m, :CH), 5.4-4.9 (m, :CH_2),

3.5 (d, further split, J 7Hz, $C\underline{H}_2S$ superimposed on 3.5 [m, J 6.5Hz, $-C\underline{H}Me_2$]), and 1.2 (d, J 6.5Hz, $2 \times CH_3$);

i.r. 3070w, 3050w, 1635m, 1580m, 1470s, 1050s, 980s, 910s, and 750s.

Benzyl trans-but-2-enyl sulphide [141]

- was prepared using the procedure[144] for allyl 4-chlorophenyl sulphide in 85% yield from benzyl mercaptan and trans-1-bromobut-2-ene. The product was distilled, b.p. 115-120°/3 mmHg (lit.[146] 137-139°/18 mmHg);

n.m.r. ($CDCl_3$) 7.2 (br s, $5 \times$ArH), 5.5 (m, $2 \times$alkene H), 3.6 (s, $-C\underline{H}_2Ph$), 3.0 (m, $-SC\underline{H}_2$), and 1.7 (d, J 6Hz, $-C\underline{H}_3$).

Reaction of Nitrenes with Allyl Aryl Sulphides; General Procedure

The N-amino compound (1 mol. equiv.) and the allyl aryl sulphide (1.2-1.5 mol. equiv.) were stirred in dichloromethane (10 ml per g amino compound) and powdered lead tetra-acetate (1 mol. equiv.) was added portionwise over 15 min. to the magnetically stirred solution. After a further 20 min. the mixture was filtered and the separated solids washed with dichloromethane. The filtrate was evaporated, and the residue chromatographed over basic alumina using light petroleum - ethyl acetate (9:1) which eluted unchanged allyl aryl sulphide. Further elution with light petroleum - ethyl acetate (1:1) yielded the sulphenamides. The following sulphenamides were prepared in this way:

N-(1,2-dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-2-nitrobenzene-sulphenamide [132] - from 1-aminoquinolin-2(1H)-one and trans-but-2-enyl 2-nitrophenyl sulphide [127] as lemon coloured crystals (59%) (from ethanol) m.p. 143-143.5° (Found: C, 62.1; H, 4.7; N, 11.4. $C_{19}H_{17}N_3O_3S$ requires C, 62.1; H, 4.7; N, 11.4%);

n.m.r. ($CDCl_3$) 8.72 and 8.20 (2xd, J 8Hz, Ar H-3 and H-6), 8.05-7.05

(m, 6× ArH + quinoline H-4), 6.70 (d, J 9.5Hz, quinoline H-3), 6.4-6.0 (m, :CH), 5.5-5.1 (m, :CH_2), 5.1-4.8 (m, NC<u>H</u>), and 1.55 and 1.17 (2xd, J 7Hz, 2× CH_3); two diastereoisomers are indicated by the duplicated methyl signals at δ1.55 and 1.17 whose ratio in the crude mixture was 1:3. Repeated recrystallisation from acetonitrile gave the predominant diastereoisomer (δ_{Me} 1.17), m.p. 141-142°;

<u>i.r.</u> 1650s, 1592s, 1560s, 1505s, 1335s, 825s, and 725s.

<u>N-(1,2-Dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-2,4-dinitrobenzenesulphenamide [133]</u> - from 1-aminoquinolin-2(1H)-one and <u>trans</u>-but-2-enyl 2,4-dinitrophenyl sulphide [128] as yellow crystals (18%) (from ethanol - acetonitrile) m.p. 162-163° (Found: C, 55.2; H, 4.2; N, 13.5. $C_{19}H_{16}N_4O_5S$ requires C, 55.3; H, 3.9; N, 13.6%);

<u>n.m.r.</u> ($CDCl_3$, 51°) 9.20 (d, J 9Hz, Ar H-6), 9.00 (d, J 2Hz, Ar H-3), 8.50 (dxd, J 2× 9Hz, Ar H-5), 8.0-7.2 (m, 4× ArH + quinoline H-4), 6.70 and 6.68 (2xd, J 9.5Hz, quinoline H-3), 6.4-5.7 (m, :CH), 5.5-4.8 (structured m, NC<u>H</u> and :CH_2) and 1.50 and 1.27 (2xd, J 7Hz, 2× CH_3); two diastereoisomers evident as in [132] above. At -40° and 220MHz, four methyl doublets were observed at δ1.60, 1.50, 1.32 and 1.18 (ratio 4.3:2:1:7.3) as a result of slow <u>N</u>-<u>N</u> and <u>S</u>-<u>N</u> bond rotation on the n.m.r. time scale;

<u>i.r.</u> 1660s, 1590s, 1560m, 1510s, 1340s, 830m, 750s, and 730s.

<u>N-Allyl-N-phthalimido-2-isopropylbenzenesulphenamide [137]</u> - from <u>N</u>-aminophthalimide and allyl 2-isopropylphenyl sulphide [139], as crystals (30%) (from light petroleum) m.p. 93.5-95° (Found: C, 67.9; H, 5.8; N, 8.0. $C_{20}H_{20}N_2O_2S$ requires C, 68.2; H, 5.7; N, 7.95%);

<u>n.m.r.</u> ($CDCl_3$), 8.26 (dxd, J 2× 7Hz, Ar H-6), 7.85-7.55 (m, 4× phthalimido H), 7.4-7.1 (m, 3× ArH), 6.2-5.8 (m, :CH), 5.3-5.0 (m, :CH_2), 4.20 (d, J 7Hz, NC<u>H</u>$_2$), 2.98 (m, J 6.5Hz, -C<u>H</u>Me_2) and 1.18 (d, J 6.5Hz,

2 × CH_3);

i.r. 3070w, 1790w, 1730s, 885s, 795s, 760s, and 720s.

N-Allyl-N-(1,2-dihydro-2-oxoquinolin-1-yl)-2-isopropylbenzene-sulphenamide [138] - from 1-aminoquinolin-2(1H)-one and allyl 2-isopropylphenyl sulphide [139] as crystals (36%) (from light petroleum [b.p. 40-60°]) m.p. 60-61.5° (Found: C, 71.9; H, 6.3; N, 8.0. $C_{21}H_{21}N_2OS$ requires C, 72.0; H, 6.3; N, 8.0%);

n.m.r. ($C_6D_5CD_3$) 8.0-7.65 and 7.30-6.75 (m, 8 × ArH + quinoline H-4), 6.55 (d, J 9.5Hz, quinoline H-3), 6.1-5.6 (m, :CH), 5.20-4.25 (structured m, CH_2N and $:CH_2$), 3.40 (m, J 7Hz, $-CHMe_2$), and 1.02 and 0.82 (d, J 7Hz, 2 × CH_3);

i.r. 3075w, 1670s, 1600s, 820s, 755s, and 740s.

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-benzylsulphenamide [140] - from 1-aminoquinolin-2(1H)-one and benzyl trans-but-2-enyl sulphide [141] as crystals (31%) (from light petroleum) m.p. 84-88° (Found: C, 71.3; H, 6.0; N, 8.35. $C_{20}H_{20}N_2OS$ requires C, 71.4; H, 6.0; N, 8.3%);

n.m.r. ($CDCl_3$) 7.8-7.0 (m, 9 × ArH + quinoline H-4), 6.63 and 6.58 (2xd, J 9.5Hz, quinoline H-3), 6.2-5.8 (structured m, :CH), 5.4-5.0 (structured m, $:CH_2$), 4.9-4.5 (m, NCH), 4.25 (AB, J_{AB} 12.5Hz, $-CH_2Ph$), and 1.45 and 0.90 (2xd, J 7Hz, 2 × CH_3);

i.r. 1650s, 1595s, 1240m, 1010w, and 830s.

N-(1,2-Dihydro-2-oxopyridin-1-yl)-N-(1-methylallyl)-4-chlorobenzene-sulphenamide [145] - from 1-aminopyridin-2(1H)-one and trans-but-2-enyl 4-chlorophenyl sulphide [110] as crystals (47%) (from light petroleum) m.p. 84-86° (Found: C, 58.9; H, 5.0; N, 9.1. $C_{15}H_{15}ClN_2OS$ requires C, 58.7; H, 4.9; N, 9.1%);

n.m.r. ($CDCl_3$, -40°) 7.35 (br s, 7 × ArH), 6.64 and 6.58 (2xd, J 9.5Hz,

pyridine H-3), 6.05-4.4 (structured m, NCH̲CH̲=CH̲$_2$) and 1.41 and 1.05 (2xd, J 6.5Hz, 2 × CH$_3$). Coalescence of the doublets at δ1.41 and 1.05 (ratio 2:1) occurs at 30-35°, and at 101° a single doublet is present, δ(PhCl) 1.29;

i.r. 3070w, 1660s, 1590s, 1535m, 930w, and 765w.

N-(3,4-Dihydro-2-methyl-4-oxoquinazolin-3-yl)-N-(1-methylallyl)-4-chlorobenzenesulphenamide [146] - from 3-amino-2-methylquinazol-4(3H)-one and trans-but-2-enyl 4-chlorophenyl sulphide [110] as crystals (60%) (from light petroleum [b.p. 80-100°]) m.p. 127-129° (Found: C, 61.2; H, 4.9; N, 11.4. $C_{19}H_{18}ClN_3OS$ requires C, 61.4; H, 4.9; N, 11.3%);

n.m.r. ($CDCl_3$) 8.20 (d, J 8Hz, quinazolone H-5), 7.8-7.2 (m, 7 × ArH), 6.2-4.6 (m, NCH̲CH̲=CH̲$_2$), 2.40 (s, quinazolone CH$_3$) and 1.65 and 1.10 (d, J 6.5Hz, 2 × CH$_3$). No coalescence of signals at δ1.65 and 1.10 occurs up to 100° but the initial ratio of 1:3.3 changes to 1.84:1 after 1h at 80°;

i.r. 1680s, 1590s, 1000s, 920s, 810s, 760s, and 690s.

N-Allyl-N-(3,4-dihydro-4-oxoquinazolin-3-yl)-4-chlorobenzenesulphenamide [147] - from 3-aminoquinazolin-4(3H)-one[147] and allyl 4-chlorophenyl sulphide [107] as crystals (29%) (from ethanol) m.p. 85-86° (Found: C, 59.3; H, 4.1; N, 12.3. $C_{17}H_{14}ClN_3OS$ requires C, 59.4; H, 4.1; N, 12.2%);

n.m.r. ($C_6D_5CD_3$) 8.25 (d, J 7Hz, quinazolone H-5), 7.85 (s, quinazolone H-2), 7.55 (d, J 8Hz, quinazolone H-8), 7.36-6.8 (m, 6 × ArH), 5.8-5.4 (m, :CH), 5.0-4.75 (m, :CH$_2$) and 4.15 (br s, NCH̲$_2$). The signal at δ4.15 sharpens to a doublet at +50° (J 7Hz) but at -42° becomes an ABX system (J 7 × 12.5Hz);

i.r. 3060w, 1680s, 1600s, 875s, 805s, 770s, and 690s.

N-Allyl-N-(1,2-dihydro-2-oxoquinolin-1-yl)-4-chlorobenzenesulphenamide [148] - from 1-aminoquinolin-2(1H)-one and allyl 4-chlorophenyl sulphide [107] as crystals (49%) (from light petroleum) m.p. 83.5-85° (Found: C, 63.1; H, 4.5; N, 8.2. $C_{18}H_{15}ClN_2OS$ requires C, 63.1; H, 4.4; N, 8.2%);

n.m.r. ($CDCl_3$) 7.9-7.2 (m, 8 × ArH + quinoline H-4), 6.7 (d, J 9.5Hz, quinoline H-3), 6.4-5.0 (structured m, 3 × alkene H), 4.5 (br d, J 6.5Hz, NCH_2);

i.r. 1650s, 1595s, 1240m, 1010w, and 830s.

N-(1-Methylallyl)-N-phthalimido-2-nitrobenzenesulphenamide [129]

This was formed from N-aminophthalimide and trans-but-2-enyl 2-nitrophenyl sulphide [127]. The crude reaction mixture was chromatographed over basic alumina; elution with light petroleum - ether (4:1) gave unchanged [127]. Further elution with ether gave the title compound (32%) as pale yellow crystals (from ethanol) m.p. 125-127° (Found: C, 58.5; H, 4.2; N, 11.3. $C_{18}H_{15}N_3O_4S$ requires C, 58.5; H, 4.1; N, 11.4%);

n.m.r. (CD_2Cl_2) 9.06 (d, J 9Hz, Ar H-6), 8.26 (d, J 2× 7Hz, Ar H-3), 7.96-7.70 and 7.35 (m and dxd, J 8× 8Hz, 6× ArH), 6.16-5.76 (m, :CH), 5.30 (br d, J 5Hz, H-3 cis), 5.05 (d, J 10Hz, H-3 trans), 4.6-4.3 (m, NCH) and 1.34 (d, J 6.5Hz, CH_3). At -24°, two methyl doublets, δ1.36 and 1.31, and two aryl H-6 signals, δ9.08 and 9.01 are visible, with coalescence at 0°;

i.r. 1780m, 1730s, 1565s, 1500s, 1305m, 945m, 730s, and 705s;

m.s. 396 (M^+), 314, 251, 250, 223, 215, 154, 138, 104 (base), 77, and 55.

N-(1-Methylallyl)-N-phthalimido-2,4-dinitrobenzenesulphenamide [130]

This was formed from N-aminophthalimide and trans-but-2-enyl 2,4-dinitrophenyl sulphide [128]. The crude reaction mixture was purified by chromatography over Kieselgel; elution with light petroleum - ethyl acetate (5:1) gave unchanged [128] followed by the title compound (39%) as yellow crystals (from methanol - chloroform) m.p. 146-147° (Found: C, 51.7; H, 3.4; N, 13.4. $C_{18}H_{14}N_4O_6S$ requires C, 51.2; H, 3.4; N, 13.5%);

n.m.r. ($CDCl_3$) 9.35, 9.28 (2xd, J 9.5Hz, Ar H-6), 9.05 (d, J 2.5Hz, Ar H-3), 8.60 (dxd, J 2.5 × 9Hz, Ar H-5), 7.84 (br s, 4 × phthalimido H), 6.16-5.68 (m, :CH), 5.45-5.00 (m, :CH_2), 4.7-4.3 (m, C<u>H</u>CH_3), and 1.42 and 1.36 (2xd, J 6.5Hz, 2 × CH_3). On warming, these last two signals coalesce at 39°; those of the Ar H-6 do likewise at 43°. At 48°, one methyl doublet is seen at δ1.40;

i.r. 3100w, 1790w, 1730s, 1590s, 1510s, 940s, 880s, 830s, and 720s.

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-4-chlorobenzenesulphenamide [118]

- was prepared by the method of Atkinson and Awad[64] from 1-aminoquinolin-2(1H)-one and trans-but-2-enyl 4-chlorophenyl sulphide [110] in 54% yield. The predominant diastereoisomer (δ_{Me} 0.93) was obtained by repeated recrystallisation from light petroleum (three times); m.p. 74-75° (lit.[64] 76.5-78°).

N-(2,3-Dihydro-2-oxobenzoxazol-3-yl)-N-(1-methylallyl)-4-chlorobenzenesulphenamide [113]

- was prepared by the method of Atkinson and Awad[64] from 3-aminobenzoxazol-2(3H)-one[48] and trans-but-2-enyl 4-chlorophenyl sulphide [110] in 46% yield. The crude material was recrystallised from light petroleum, m.p. 72-73° (lit.[64] 74°).

Attempted reaction of phthalimidonitrene with trans-but-2-enyl 2,4,6-trinitrophenyl sulphide [135]

- using the above procedure, N-aminophthalimide and trans-but-2-enyl 2,4,6-trinitrophenyl sulphide [135] gave a crude product, which on chromatography over basic alumina or Kieselgel with light petroleum - chloroform (1:1) as eluant gave first unreacted allyl sulphide [135]; further elution with chloroform - ethyl acetate (1:1) then ethyl acetate alone gave trans-diphthaloyltetrazene [95] (24%) m.p. 260° (decomp.) (lit.[57] 265-271°). No other homogeneous product was isolated from the reaction.

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-2,4-dinitrobenzenesulphenamide [142]

1-Aminoquinolin-2(1H)-one (1.42g, 8.88 mmol) and triethylamine (0.92g, 9.11 mmol) were dissolved in dichloromethane (70 ml) and a solution of 2,4-dinitrobenzenesulphenyl chloride (2.13g, 9.08 mmol) in dichloromethane (70 ml) was added dropwise at room temperature to the stirred mixture over a period of 0.5h. The mixture was heated under reflux for 1h then stirred overnight at room temperature. The precipitated bis(2,4-dinitrophenyl) disulphide was separated, and the filtrate washed with water, dried, and evaporated. Chromatography of the residue over basic alumina using dichloromethane gave more bis(2,4-dinitrophenyl) disulphide (total 0.5g, 28%). Further elution with ethyl acetate and ethyl acetate - ethanol (3:1) gave the title compound (0.89g, 28%) as yellow crystals (from acetonitrile) m.p. 197° (decomp.) (Found: C, 50.4; H, 2.9; N, 15.9. $C_{15}H_{14}N_4O_5S$ requires C, 50.3; H, 2.8; N, 15.6%);

n.m.r. ($[CD_3]_2SO$) 9.3 (s, exch. D_2O -NH), 9.0-8.7 (m, Ar H-3, -5, -6), 8.0 (d, J 9.5Hz, quinoline H-4), 7.9-7.2 (m, 4 × quinoline ArH), and 6.8 (d, J 9.5Hz, quinoline H-3);

i.r. 3200w, 1650s, 1590s, 1510s, 1340s, 840w, and 830w;
m.s. 358 (M^+), 200, 199, 183, 159, 145 (base), 122, 117, and 89.

Bis(2-isopropylphenyl) disulphide

2-Isopropylbenzenethiol (4.95g, 32.57 mmol) and iodine (7.0g, 55.12 mmol) were shaken in chloroform (20 ml) and water (20 ml) for 1.5h. The mixture was rendered basic with sodium carbonate solution (2M), and sodium thiosulphate solution added until the excess of iodine was removed. The organic layer was separated and the aqueous layer extracted with a further portion of chloroform (20 ml). The chloroform extracts were dried and evaporated and the residue purified by chromatography over basic alumina with light petroleum eluant. The product recrystallised from light petroleum (b.p. <40°) m.p. 46-52° (lit.[148] 58.5-60°) (4.0g, 81%). The material was pure as judged by n.m.r.; n.m.r. ($CDCl_3$) 7.7-6.8 (m, 8 × ArH), 3.5 (m, J 7Hz, 2 × CH), and 1.2 (d, J 7Hz, 4 × CH_3).

2-Isopropylbenzenesulphenyl chloride

To a saturated solution of chlorine in carbon tetrachloride (80 ml) at -5° was added a solution of bis(2-isopropylphenyl) disulphide (4.0g, 13.24 mmol) in carbon tetrachloride (20 ml) over a period of 0.25h. The mixture was evaporated in vacuo and the residue distilled to give the title compound (4.7g, 95%) as a red liquid, b.p. 110-120°/0.7 mmHg; n.m.r. ($CDCl_3$) 7.9-7.1 (m, 4 × ArH), 3.7 (m, J 7Hz, CH), and 1.3 (d, J 7Hz, 2 × CH_3).

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-2-isopropylbenzenesulphenamide [143]

1-Aminoquinolin-2(1H)-one (0.8g, 5.0 mmol) and triethylamine (0.53g, 5.25 mmol) were dissolved in dichloromethane (20 ml) and a solution of 2-isopropylbenzenesulphenyl chloride (0.95g, 5.09 mmol) in dichloro-

methane (20 ml) was added over a period of 0.5h with stirring at room temperature. The mixture was stirred for 0.5h then heated under reflux for 0.5h. The cooled mixture was washed with hydrochloric acid (1%, 20 ml), water (20 ml), dried and evaporated. The residue was chromatographed over basic alumina with light petroleum - ethyl acetate (5:1) as eluant which gave bis(2-isopropylphenyl) disulphide (30%). Elution with ethyl acetate gave the title compound (0.42g, 27%) as crystals (from light petroleum - ethyl acetate) m.p. 117-119° (decomp.) (Found: C, 69.5; H, 5.7; N, 9.1. $C_{18}H_{18}N_2OS$ requires C, 69.65; H, 5.85; N, 9.0%);

n.m.r. ($CDCl_3$) 7.92 (s, exch. D_2O, -NH), 7.66-7.04 (m, 8 × ArH + quinoline H-4), 6.60 (d, J 9.5Hz, quinoline H-3), 3.38 (m, J 6.5Hz, CH), and 1.05 (d, J 6.5Hz, 2 × CH_3); at -50° and 220MHz the doublet (δ1.05) separated into two doublets δ1.09 and 1.10 (J 6.5Hz);

^{13}C n.m.r. ($CDCl_3$) 160.6 (>C=O), 150.4-115.7 (14 × ArC + C-4, C-3), 30.65 (CH), and 23.8 (2 × CH_3);

i.r. 3200m, 1650s, 1595s, 825m, and 755m.

Cross-over experiment between [113] and [148]

N-(2,3-Dihydro-2-oxabenzoxazol-3-yl)-N-(1-methylallyl)-4-chlorobenzenesulphenamide [113] (293mg, 0.846 mmol) and N-allyl-N-(1,2-dihydro-2-oxoquinolin-1-yl)-4-chlorobenzenesulphenamide [148] (116mg, 0.339 mmol) were dissolved in benzene (3 ml) and heated under reflux for 2h. Benzene was evaporated and the residue chromatographed over basic alumina (15g). Elution with light petroleum gave 1-methyl-1-vinyl-N-(4-chlorophenyl)sulphenylimine [120] (120mg, 67%) as a yellow oil. Elution with light petroleum - ethyl acetate (1:1) gave unchanged [148] (101mg) in which no [118] was visible by n.m.r.

1-(1-Methylallylamino)quinolin-2(1H)-one [151]

An ethanolic solution of sodium 4-chlorobenzenethiolate was prepared by dissolving sodium (0.3g, 13.04 mmol) in ethanol (50 ml) and adding 4-chlorobenzenethiol (1.4g, 9.69 mmol). To this solution was added N-(1,2-dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-4-chlorobenzenesulphenamide [118] (2.2g, 6.17 mmol), and the mixture heated under reflux for 1.5h. The ethanol was evaporated under reduced pressure and the residue partitioned between chloroform (50 ml) and sodium hydroxide solution (1M, 30 ml). The chloroform layer was washed with water, dried and evaporated and the oily residue purified by chromatography over basic alumina (90g). Elution with light petroleum - ethyl acetate (9:1) gave bis(4-chlorophenyl) disulphide (1.24g, 70%) identical with authentic material. Further elution with ethyl acetate gave the title compound (1.0g, 76%) as crystals (from light petroleum) m.p. 80.5-81° (Found: C, 73.0; H, 6.6; N, 13.0. $C_{13}H_{14}N_2O$ requires C, 72.9; H, 6.6; N, 13.1%);

n.m.r. ($CDCl_3$) 7.61 (d, J 9.5Hz, quinoline H-4), 7.96-6.98 (m, 4 × ArH), 6.67 (d, J 9.5Hz, quinoline H-3), 6.51 (br s, exch. D_2O, -NH), 6.0-5.6 (structured m, :CH), 5.0-4.7 (m, $:CH_2$), 4.08-3.64 (m, NCH), and 1.23 (d, J 7Hz, $-CH_3$);

i.r. 3240m, 1650s, 1590s, 1005w, 930s, 830s, and 760s;

m.s. 214 (M^+), 199, 160, 159, 146, 145 (base), 131, 117, 103, 89, and 55.

4-Chlorobenzenesulphenyl chloride [153]

- was prepared by the method of Kharasch et al.[149] in 90% yield by chlorinolysis of 4-chlorobenzenethiol. The product was distilled in vacuo, b.p. 85-90°/5 mmHg (lit.[149] 86-90°/5 mmHg);

n.m.r. (CCl_4) 7.5 (AA'BB', 4 × ArH).

Reaction of 1-(1-methylallylamino)quinolin-2(1H)-one [151] with 4-chlorobenzenesulphenyl chloride

1-(1-Methylallylamino)quinolin-2(1H)-one (0.45g, 2.10 mmol) and 4-chlorobenzenesulphenyl chloride (0.5g, 2.79 mmol) were dissolved in chloroform (10 ml) and heated under reflux for 20 min. The chloroform was evaporated and the residue chromatographed over basic alumina (40g) eluting with light petroleum - ethyl acetate (9:1) which gave bis(4-chlorophenyl) disulphide (120mg). Elution with ethyl acetate gave 1-(3-chloro-2-[4-chlorophenylthio]-1-methylpropylamino)quinolin-2(1H)-one [154] (380mg, 46%) as crystals (from ethanol) m.p. 139-139.5° (Found: C, 58.1; H, 4.5; N, 7.2. $C_{19}H_{18}Cl_2N_2OS$ requires C, 58.0; H, 4.6; N, 7.1%);

n.m.r. ($CDCl_3$) 8.2-7.2 (m, 8 × ArH + quinoline H-4), 6.92 (d, J 9.5Hz, quinoline H-3), 6.45 (br s, exch. D_2O, -NH), 4.2-3.6 (m, 4 × aliphatic H) and 1.32 (d, J 7Hz, $-CH_3$);

i.r. 3265w, 1645s, 1585s, 1090m, 1005m, 815s, and 750s;

m.s. 396/394/392 (M^+), 358/356, 233/231, 213, 187, 149, and 145.

Reaction of [154] with sodium hydride

1-(3-Chloro-2-[4-chlorophenylthio]-1-methylpropylamino)quinolin-2(1H)-one [154] (123mg, 0.313 mmol) was stirred in freshly distilled DMF (1.5 ml) and sodium hydride dispersion (50%, 20mg, 0.42 mmol) added. After 1h at room temperature, the mixture was poured into water (5 ml) and triturated, giving a white solid which was recrystallised from ethanol and identified as 1-(2-[4-chlorophenylthio]-1-methylallylamino)-quinolin-2(1H)-one [155] (70mg, 63%) m.p. 119.5-121° (Found: C, 63.9; H, 4.8; N, 7.8. $C_{19}H_{17}ClN_2OS$ requires C, 63.95; H, 4.8; N, 7.85%);

n.m.r. ($CDCl_3$) 8.0 (d, J 8Hz, quinoline H-8), 7.7-7.0 (m, 7 × ArH + quinoline H-4), 6.60 (d, J 9.5Hz, quinoline H-3), 5.75 (br d, J 4Hz,

exch. D_2O, -NH), 5.3 (br s, :CH cis to sulphur), 4.7 (br s, :CH trans to sulphur), 4.0 (m, NCHMe; becomes q, J 6.5Hz after D_2O exchange), and 1.28 (d, J 6.5Hz, $-CH_3$);

i.r. 3230w, 1660s, 1590s, 1090m, 1010m, 860m, 830s, and 760s.

1-(1-Methylpropylamino)quinolin-2(1H)-one [152]

1-(1-Methylallylamino)quinolin-2(1H)-one [151] (1.0g, 4.67 mmol) and 10% palladium on charcoal (0.4g) were stirred in ethanol (25 ml) and hydrogenated at atmospheric pressure until uptake of hydrogen ceased (2h). The reaction product was filtered and evaporated and passed down a short column of basic alumina (10g) with ethyl acetate eluant which gave the title compound as crystals (from light petroleum) m.p. 63-65° (0.74g, 73%) (Found: C, 72.05; H, 7.4; N, 12.75. $C_{13}H_{16}N_2O$ requires C, 72.2; H, 7.5; N, 12.95%);

n.m.r. ($CDCl_3$) 8.00 (d, J 9Hz, quinoline H-8), 7.75 (d, J 9.5Hz, quinoline H-4), 7.7-7.1 (m, 3 ×ArH), 6.75 (d, J 9.5Hz, quinoline H-3), 5.7 (br s, exch. D_2O, -NH), 3.35 (m, NCHMe), and 1.8-0.8 (m, 8 ×aliphatic H);

i.r. 3280s, 1655s, 1595s, 1410m, 1230m, 1145m, 830s, 750s, and 740m.

Attempted reaction of [152] with 4-chlorobenzenesulphenyl chloride

1-(1-Methylpropylamino)quinolin-2(1H)-one [152] (300mg, 1.39 mmol) and triethylamine (220mg, 2.18 mmol) were dissolved in dry ether (2 ml) and a solution of 4-chlorobenzenesulphenyl chloride (390mg, 2.18 mmol) in ether (3 ml) added and the mixture stirred at room temperature for 3 days. The reaction product was filtered and evaporated, and the residue chromatographed over basic alumina (10g) with light petroleum - ethyl acetate (9:1) eluant which gave bis(4-chlorophenyl) disulphide (144mg). Further elution with ethyl acetate gave back [152] (255mg, 85% recovery).

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-N-(1-methylpropyl)-4-chloro-benzenesulphenamide [150]

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-4-chloro-benzenesulphenamide [118] (0.120g, 0.337 mmol, δ_{Me} 0.93 diastereoisomer) and hydrazine hydrate (0.9g, 18.0 mmol) were dissolved in methanol (7 ml) at 0°, and a solution of N-chlorodi-isopropylamine[150] (2.44g, 18.0 mmol) in methanol (4 ml) added very slowly with stirring. After 1.5h at 0°, the methanol was removed and dichloromethane (10 ml) and water (10 ml) added. The dichloromethane layer was washed with water, dried and evaporated. N.m.r. revealed partial conversion to [150]. The above material was re-dissolved in methanol (8 ml) and hydrazine hydrate (1.0g, 20 mmol) added and the mixture cooled to 0°. N-chlorodi-isopropylamine (2.70g, 20 mmol) in methanol (5 ml) was added slowly as above. The above work up procedure gave an oil whose n.m.r. spectrum showed the absence of olefinic protons. The residue was purified by chromatography over Kieselgel (5g) with dichloromethane eluant which gave bis(4-chlorophenyl) disulphide (15mg, 31%). Further elution gave the title compound [150] (52mg, 43%) as a glass. Further elution with dichloromethane gave 1-(1-methylpropylamino)quinolin-2(1H)-one [152] (25mg, 34%) identical with authentic material.

Spectral data for [150]:

n.m.r. ($CDCl_3$) 8.0-7.0 (m, 8 × ArH + quinoline H-4), 6.70 (d, J 9.5Hz, quinoline H-3), 4.10 (m, NCHMe), and 2.2-0.8 (m, 5 × aliphatic H including d, J 7Hz at δ1.00, $-CH_3$);

m.s. 360/358 (M^+), 303/301, 215/213, 188/186, 145 (base), 117, and 108;

accurate mass - m/e 301.0205. Calc. for $C_{15}H_{10}ClN_2OS$ 301.0202, and m/e 213.0375. Calc. for $C_{10}H_{12}ClNS$ 213.0377.

EXPERIMENTAL

CHAPTER 4

Reaction of 1-(1-methylallylamino)quinolin-2(1H)-one [151] with benzyl bromide

1-(1-Methylallylamino)quinolin-2(1H)-one [151] (117mg, 0.547 mmol) was heated at reflux under nitrogen with benzyl bromide (2 ml) for 1h. Benzyl bromide was removed in vacuo, and t.l.c. of the residue (neutral alumina, light petroleum - ethyl acetate 3:1) showed five components to be present, one of which had the same R_f as quinolin-2-(1H)-one. Examination of the 60MHz n.m.r. spectrum of the crude reaction product showed the absence of olefinic protons and methyl doublets which would have been found in the expected product [157]. Shortening the reaction time lead to substantial recovery of the starting material [151].

3-(Dibenzylamino)benzoxazolin-2(3H)-one [158]

3-Aminobenzoxazolin-2(3H)-one (400mg, 2.67 mmol) and benzyl bromide (2 ml) were heated under reflux (201°) for 0.75h under nitrogen. Excess benzyl bromide was distilled off in vacuo and the residue poured into 50% concentrated ammonia solution (20 ml), and extracted with dichloromethane (2 × 15 ml). The organic extracts were dried and evaporated, and the residue purified by chromatography over Kieselgel (25g) with light petroleum - ethyl acetate (2:1) as eluant, which gave, after elution of residual benzyl bromide, the title compound as crystals (from ethanol), m.p. 112-114° (167mg, 19%) (Found: C, 76.3; H, 5.55; N, 8.4. $C_{21}H_{18}N_2O_2$ requires C, 76.3; H, 5.5; N, 8.5%);
n.m.r. ($CDCl_3$) 7.5-7.0, 6.8 (m, 14 × ArH), and 4.40 (AB, J_{AB} 12.5Hz, 2 × $C\underline{H}_2Ph$);
i.r. 1750s, 1250m, 1120m, 1010m, 990m, 750s, 700s, and 670s.

1-(Benzylamino)quinolin-2(1H)-one [159]

1-Aminoquinolin-2(1H)-one (0.6g, 3.75 mmol) was heated with benzyl

bromide (4 ml) under nitrogen at 150° for 0.5h. Excess of benzyl bromide was removed by distillation in vacuo, and the residue partitioned between dichloromethane (20 ml) and sodium hydroxide solution (1M, 20 ml). The dichloromethane layer was washed with water, dried, evaporated, and the residue chromatographed over Kieselgel (20g). Excess of benzyl bromide was eluted with light petroleum, then further elution with light petroleum - ethyl acetate (2:1) gave initially the dibenzylamino compound [160] in low yield, then the title compound (216mg, 23%) as crystals (from light petroleum), m.p. 64-65°;
n.m.r. ($CDCl_3$) 8.2-7.1 (m, 9 × ArH + quinoline H-4), 6.70 (d, J 9.5Hz, quinoline H-3), 6.2 (br t, J 7.5Hz, exch. D_2O, -NH), 4.2 (br d, J 7.5Hz, becomes singlet after D_2O shake, -CH_2Ph).

1-(Dibenzylamino)quinolin-2(1H)-one [160]

1-Aminoquinolin-2(1H)-one (0.6g, 3.75 mmol) was heated under reflux with benzyl bromide (6 ml) under nitrogen for 0.5h. Excess of benzyl bromide was removed by distillation in vacuo and the residue worked up as for [159] above. Chromatography over Kieselgel (20g) with light petroleum - ethyl acetate (2:1) eluant, gave, after elution of residual benzyl bromide, the title compound (160mg, 12%) as crystals (from light petroleum - chloroform) m.p. 81-82° (Found: C, 81.0; H, 6.0; N, 8.2. $C_{23}H_{20}N_2O$ requires C, 81.15; H, 5.9; N, 8.2%);
n.m.r. ($CDCl_3$) 8.0 (d, J 9Hz, quinoline H-8), 7.54 (d, J 9.5Hz, quinoline H-4), 7.4-6.9 (m, 13 × ArH), 6.64 (d, J 9.5Hz, quinoline H-3), and 4.58 (AB, J_{AB} 12.5Hz, 2 × -CH_2Ph);
i.r. 1655s, 1600s, 990m, 830s, 750s, and 700s.

N-(1,2-Dihydro-2-oxoquinolin-1-yl)glycine ethyl ester [162]

1-Aminoquinolin-2(1H)-one (5.0g, 31.25 mmol) and ethyl bromoacetate (25 ml) were heated under reflux for 1.25h under nitrogen. Ethyl

bromo-acetate was removed by distillation in vacuo and dichloromethane (20 ml) added. The organic layer was washed with 50% concentrated ammonia solution (2 × 20 ml), water (10 ml), dried, evaporated and the residue purified by chromatography over basic alumina (230g) with light petroleum - ethyl acetate (4:1) eluant which gave impurities. Further elution with ethyl acetate and ethyl acetate - ethanol (19:1) gave the title compound (2.5g, 33%) crystals (from light petroleum - chloroform) m.p. 74-75° (Found: C, 63.2; H, 5.8; N, 11.2. $C_{13}H_{14}N_2O_3$ requires C, 63.4; H, 5.7; N, 11.4%);

n.m.r. ($CDCl_3$) 8.1-7.1 (m, 4 × ArH + quinoline H-4), 6.7 (d, J 9.5Hz, quinoline H-3), 6.1 (t, J 6Hz, exch. D_2O, -NH), 4.2 (q, J 7Hz, $-C\underline{H}_2CH_3$), 3.8 (d, J 6Hz, $-NHC\underline{H}_2CO$), and 1.2 (t, J 7Hz, $-CH_3$);

i.r. 3280m, 1735s, 1650s, 1590s, 1220s, 1200s, 1010m, 830s, and 730s;

u.v. λ_{max} 270, 278 and 332 nm.

N-Benzyl-N-(1,2-dihydro-2-oxoquinolin-1-yl)glycine ethyl ester [163]

The above ester [162] (1.82g, 7.40 mmol) was heated with benzyl bromide (10 ml) at 160-170° (oil bath) for 1.5h with stirring under nitrogen. The benzyl bromide was removed in vacuo and dichloromethane (15 ml) added. The organic layer was washed successively with sodium hydroxide solution (1M, 2 × 10 ml), water, and dried. Evaporation gave an oil which was purified by chromatography over basic alumina (60g) with light petroleum - ethyl acetate (4:1) as eluant which gave residual benzyl bromide. Further elution with light petroleum - ethyl acetate (1:1) gave the title ester as an oil which was distilled in vacuo, b.p. (Kugelröhr) 195-200°/0.15 mmHg. Yield 1.03g (41%);

n.m.r. ($CDCl_3$) 8.40 (d, J 9Hz, quinoline H-8), 7.65 (d, J 9.5Hz, quinoline H-4), 7.65-7.10 (m, 8 × ArH), 6.68 (d, J 9.5Hz, quinoline H-3), 4.57 (AB, J_{AB} 12.5Hz, $-C\underline{H}_2Ph$), 4.25 (s, $COC\underline{H}_2N$), 4.05 (q, J 7Hz, $-C\underline{H}_2CH_3$),

and 1.15 (t, J 7Hz, -CH_3).

Reaction of 1-(benzylamino)quinolin-2(1H)-one [159] with ethyl bromo-acetate

1-(Benzylamino)quinolin-2(1H)-one (200mg, 0.8 mmol) and ethyl bromo-acetate (2 ml) were heated at reflux under nitrogen for 1.5h. Excess of ethyl bromo-acetate was removed in vacuo and the residue partitioned between dichloromethane (10 ml) and 50% concentrated ammonia solution (10 ml). The dichloromethane layer was washed with water (10 ml), dried and evaporated. Examination of the n.m.r. spectrum of the crude reaction product showed it consisted mainly of starting material with a small amount (~10%) of the desired product [163]. Examination of t.l.c. plates of the mixture in a variety of solvent systems failed to separate the two components widely enough to enable viable chromatographic separation in comparison to the alternative synthesis of [163].

N-Benzyl-N-(1,2-dihydro-2-oxoquinolin-1-yl)glycine [161]

The ethyl ester [163] (1.50g, 4.46 mmol) and sodium hydroxide solution (2M, 11 ml) were heated under reflux for 4h with sufficient ethanol to ensure homogeneous solution (30 ml). The ethanol was removed in vacuo and the solution extracted with dichloromethane (2 × 10 ml); the aqueous layer was then acidified with concentrated hydrochloric acid (3 ml) and extracted with dichloromethane (3 × 15 ml). The dichloromethane extracts were dried and evaporated, and the residue (foam) recrystallised from light petroleum - ethyl acetate to give white crystals of the title acid, m.p. 147-148° (980mg, 71%) (Found: C, 69.9; H, 5.3; N, 8.9. $C_{18}H_{16}N_2O_3$ requires C, 70.1; H, 5.2; N, 9.1%); n.m.r. ($CDCl_3$) 8.9 (br s, -CO_2H), 8.2 (d, J 8Hz, quinoline H-8), 7.8 -7.0 (m, 8 × ArH + quinoline H-4), 6.75 (d, J 9.5Hz, quinoline H-3), 4.5 (s, -CH_2Ph), and 4.25 (s, -CH_2CO_2H). In PhCl as solvent, the δ4.5

signal appears as an AB system at δ4.25 (J_{AB} = 12.6Hz) and the δ4.25 signal likewise, at δ3.97 (J_{AB} = 17.4Hz);

i.r. 2600br m, 1720s, 1650s, 1580s, 1280s, 1260s, 765s, 750s, 740s, and 700s.

L-(-)-1-phenylethylamine salt of the acid [161], [164]

The acid [161] (400mg, 1.30 mmol) and L-(-)-1-phenylethylamine (158mg, 1.305 mmol) were dissolved in dichloromethane (5 ml). The solution was filtered and evaporated and examined by n.m.r. spectroscopy. The material could not be induced to crystallise;

n.m.r. (C_6D_6) 4.60 and 4.65 (2 × AB, J_{AB} 12.5 and 12Hz respectively, -CH_2Ph) and 4.06 and 4.02 (2 × AB, J_{AB} 16.4 and 16.6Hz respectively, -$CH_2CO_2^{\ominus}$). After resolution of the acid [161] (below) and re-formation of [164], n.m.r. revealed the AB systems at δ4.02 and 4.65 had been removed.

Resolution of the acid [161] with L-(-)-quinine

The acid [161] (460mg, 1.494 mmol) and dried L-(-)-quinine (483.5mg, 1.494 mmol) were dissolved in chloroform (5 ml) and heated under reflux for 5 min. On cooling, the solution was filtered and evaporated, and the resulting foam had $[\alpha]_D^{28}$ = -75.6° (c = 1.37, EtOH). It was dissolved in ethanol (2 ml) and ether (15 ml) added. The mixture was cooled in ice and scratched to initiate crystallisation. After some crystallisation had occurred, more ether (5 ml) was added and the solution stood overnight at -5°. The resulting solid (400.6mg) was separated and had $[\alpha]_D^{27}$ = -99.0° (c = 0.3, EtOH). After two more crystallisations from ethanol - ether (1:12), the resulting quinine salt (233.7mg, 25%) had m.p. 128-132° and $[\alpha]_D^{24}$ = -101.3° (c = 0.3, EtOH). It was dissolved in dichloromethane (5 ml), washed with dilute sulphuric acid (2M, 3 × 5 ml),

water (5 ml), dried and evaporated to give the acid [161] (117.7mg) which was carefully recrystallised from ethyl acetate - light petroleum. After removal of some racemic [161] (4.4mg, m.p. 141-142°) the optically pure (n.m.r.) laevoratory acid crystallised, m.p. 88-90° (100.0mg, 22%), $[\alpha]_D^{25} = -64.8°$ (c = 1.175, EtOH).

The mother liquors of the recrystallisation of the quinine salt were converted to the acid [161] as described above, and contained (approximately) a 30% enantiomeric excess of the (+) acid (from n.m.r. examination of the L-(-)-1-phenylethylamine salt).

Rate of racemisation of the acid [161]

A sample of optically active (+) acid (400mg) was dissolved in ethanol and heated under reflux. At measured intervals, the mixture was evaporated in vacuo at room temperature and made up to 10 ml with ethanol in a volumetric flask, and the optical rotation measured. The above procedure was repeated until four readings of rotation at known times were obtained. The above process was repeated (on a fresh sample of acid) in boiling methanol.

EXPERIMENTAL

CHAPTER 5

N-Phthalimido-4-chlorobenzenesulphenamide [168]

N-Aminophthalimide (5.0g, 30.87 mmol) was suspended in dichloromethane (150 ml) containing triethylamine (3.5g, 34.65 mmol) with stirring at 0°. 4-Chlorobenzenesulphenyl chloride (5.5g, 30.73 mmol) in dichloromethane (80 ml) was added over a 40 min. period. After a further 2h, the mixture was filtered to remove unchanged N-aminophthalimide (0.28g), washed with water (2 × 20 ml), dried and then evaporated, and the residue purified by chromatography over basic alumina. Elution with light petroleum - ethyl acetate (4:1) gave bis(4-chlorophenyl) disulphide (1.32g, 30%) m.p. 69-70° (from light petroleum) identified by i.r. and mixed m.p. comparison with authentic material. Elution with ethyl acetate gave the title compound (3.45g, 37%) as crystals (from ethanol) m.p. 156° (decomp.) (Found: C, 55.2; H, 3.0; N, 9.2. $C_{14}H_9ClN_2O_2S$ requires C, 55.2; H, 3.0; N, 9.2%);
n.m.r. ($CDCl_3$) 7.87 (s, 4 × phthalimido H), 7.68-7.24 (AA'BB', 4-Cl $C_6\underline{H}_4S$), and 6.30 (s, exch. D_2O, -NH);
i.r. 3260s, 1795w, 1725m, 885s, 840s, 800s, and 705s;
m.s. 306/304 (M^+), 162, 161, 158, 147, 144, 143, 104 (base), and 77.

N-(1,2-Dihydro-2-oxoquinolin-1-yl)-4-chlorobenzenesulphenamide [169]

1-Aminoquinolin-2(1H)-one (1.5g, 9.38 mmol) was dissolved in dry THF containing triethylamine (1.0g, 9.90 mmol) and a solution of 4-chlorobenzenesulphenyl chloride (1.7g, 9.49 mmol) in dry THF (30 ml) added dropwise with stirring over a 20 min. period. After a further 1h, the mixture was filtered and evaporated and the residue recrystallised from light petroleum - ethyl acetate to give the title compound (1.25g, 44%) m.p. 143-145° (decomp.) (Found: C, 59.6; H, 3.7; N, 9.3. $C_{15}H_{11}ClN_2OS$ requires C, 59.5; H, 3.7; N, 9.25%);
n.m.r. ($CDCl_3$) 8.0 (br s, exch. D_2O, -NH), 7.66 (d, J 9.5Hz, quinoline

H-4), 7.6-7.1 (m, 8 × ArH), and 6.64 (d, J 9.5Hz, quinoline H-3);

i.r. 3220m, 1650s, 1595s, 850s, 820s, 760s, and 750s;

u.v. λ_{max} (CH_3CN) 272 ($\varepsilon = 8465$) and 334 ($\varepsilon = 3950$) nm.;

m.s. 304/302 (M^+), 288/286, 160, 159, 158, 145 (base), 144, 143, 117, 108, 90, 89, and 62.

Thermal decomposition of [168]

The sulphenamide [168] (130mg, 0.427 mmol) was heated in a sublimation tube at 190° and 15 mmHg for 5 min. Effervescence was observed and a white solid (26.5mg) sublimed over, subsequently identified as phthalimide by comparison with an authentic sample. The residue was chromatographed over basic alumina with light petroleum - ethyl acetate (9:1) as eluant which eluted bis(4-chlorophenyl) disulphide, identical with an authentic sample (45mg, 73%). Further elution with ethyl acetate gave more phthalimide (total 35mg, 56%).

Pyrolysis of [168] (50mg) in refluxing xylene (1 ml) for 0.25h gave only a small amount of the above decomposition products, with much [168] remaining (by t.l.c.).

Thermal decomposition of [169]

The sulphenamide [169] (106mg, 0.35 mmol) was heated in a sublimation tube at 150° and 15 mmHg for 10 mins. Effervescence occurred, but no sublimation was observed. The residue was chromatographed over basic alumina (4g). Elution with light petroleum - ethyl acetate (9:1) gave bis(4-chlorophenyl) disulphide (16mg, 32%) identical with authentic material. Elution with ethyl acetate - ethanol (1:1) gave quinolin-2-(1H)-one (20.7mg, 41%) as a crystalline solid (from water) m.p. 196-198° (lit.[132] 199-200°);

i.r. 3400br m, 1670s, 1560m, 830s, and 770s.

On conducting the pyrolysis of [169] (40mg) in boiling xylene (1 ml) for 0.25h, t.l.c. examination revealed complete decomposition to the above products.

Benzaldehyde methylphenylhydrazone [174]

1-Methyl-1-phenylhydrazine[151] (9.8g, 80.33 mmol) was dissolved in a mixture of glacial acetic acid (15 ml) and water (10 ml) and freshly distilled benzaldehyde (9.8g, 92.45 mmol) in glacial acetic acid (50 ml) added. The mixture was heated on a steam bath for 2h. The mixture was cooled in ice and the precipitated hydrazone (13.7g, 81%) separated, washed with water, and dried, m.p. 103-104.5° (lit.[152] 104-104.5°);

n.m.r. ($CDCl_3$) 7.8 (m, PhC<u>H</u>:), 7.4-6.8 (m, 10 × ArH), and 3.25 (s, $-CH_3$);

i.r. 1590s, 1110m, 930s, and 760s.

2-Benzyl-1-methyl-1-phenylhydrazine [173]

Benzaldehyde methylphenylhydrazone (2.2g, 10.48 mmol) in 1,4-dioxan (40 ml) was added to a stirred suspension of lithium aluminium hydride (950mg, 25 mmol) in 1,4-dioxan (40 ml) under nitrogen and the mixture heated under reflux for 17h. Addition of ethyl acetate and water destroyed excess lithium aluminium hydride, then the mixture evaporated in vacuo. Ether (50 ml) was added and the inorganic solids separated. The solution was dried, evaporated and the resulting oil distilled, b.p. 175-195°/3 mmHg (Kugelröhr) giving the title compound as an oil (2.16g, 97%). The hydrazine was fairly rapidly oxidised in air back to the hydrazone [174];

n.m.r. (CCl_4) 7.5-6.5 (m, 10 × ArH), 3.8 (s, $-C\underline{H}_2Ph$), 3.2 (br s, exch. D_2O, -NH), and 2.8 (s, $-CH_3$);

i.r. 3300w, 1600s, 1500s, 1030m, 760s, and 700s.

2-Benzyl-1-methyl-1-phenylhydrazine hydrochloride

The above hydrazine (600mg, 2.83 mmol) was dissolved in dry light petroleum (b.p. 40-60°, 20 ml) and dry hydrogen chloride was passed into the mixture for 2 mins. The solution was evaporated under reduced pressure and the residue recrystallised from ethyl acetate, m.p. 117-122° (330mg, 46%) (Found: C, 67.4; H, 6.8; N, 11.4. $C_{14}H_{17}ClN_2$ requires C, 67.6; H, 6.9; N, 11.3%).

Reaction of hydrazine [173] with 4-chlorobenzenesulphenyl chloride [153]

The hydrazine [173] (420mg, 1.98 mmol) and pyridine (313mg, 3.96 mmol) were dissolved in dry ether (30 ml), and a solution of 4-chlorobenzenesulphenyl chloride (709mg, 3.96 mmol) in dry ether (30 ml) added slowly to the stirring mixture over a period of 0.5h at 0° under nitrogen. After a further 0.5h, the precipitated pyridine hydrochloride was separated, and the filtrate evaporated. The residue was chromatographed over basic alumina (40g). Elution with light petroleum - ethyl acetate (9:1) gave bis(4-chlorophenyl) disulphide (500mg, 88%). Further elution afforded benzaldehyde methylphenylhydrazone [174] (316mg, 76%) identical with authentic material.

The same products were identifiable by n.m.r. when the reaction was conducted at -40° without allowing the solution temperature to rise over -35°.

Control experiment: treatment of sulphenamide [134] with triethylamine

N-Benzyl-N-isopropyl-2-nitrobenzenesulphenamide [134] (100mg) was stirred in triethylamine (2 ml) for 1h at ambient temperature. Examination by t.l.c. after this period (Al_2O_3; light petroleum - ethyl acetate 5:1) showed only the presence of starting sulphenamide [134]

at R_f 0.8. On evaporation of the triethylamine under reduced pressure, [134] was recovered in quantitative yield.

1,1-Dibenzylhydrazine

- was prepared by the method of Dewar and Jennings[23] in 24% yield from benzyl chloride and hydrazine hydrate. The product after recrystallisation from light petroleum (b.p. 40-60°) melted at 52-54° (lit.[153] 55°);

i.r. 3400w, 3330w, 1610s, 1500s, 760s, and 700s.

Reaction of 1,1-dibenzylhydrazine with 4-chlorobenzenesulphenyl chloride

1,1-Dibenzylhydrazine (1.9g, 8.96 mmol) and triethylamine (1.0g, 9.90 mmol) were dissolved in dry ether (20 ml) with stirring at 0° under nitrogen. 4-Chlorobenzenesulphenyl chloride (1.6g, 8.94 mmol) in dry ether (30 ml) was added over a period of 0.5h, then stirring continued for a further 3h. The mixture was filtered and evaporated, and the residue chromatographed over Kieselgel (100g) with light petroleum eluant, which gave initially bis(4-chlorophenyl) disulphide (1.19g, 93%) identical with authentic material. Further elution gave colourless crystals of 1,2-diphenylethane [177] (385mg, 43% corrected for unreacted 1,1-dibenzylhydrazine) m.p. 47-49° (from ethanol) (lit.[154] 53°) with n.m.r. and i.r. identical to authentic material;

n.m.r. ($CDCl_3$) 7.20 (br s, 10 × ArH), and 2.90 (s, 2 × -CH_2Ph);

i.r. 3080w, 3040w, 3010w, 1600m, 1060w, 1020w, 740s, and 690s.

Further elution with light petroleum - ether (9:1) gave a second crystalline solid subsequently identified as benzaldehyde dibenzylhydrazone [178] (672mg, 45% corrected for unreacted 1,1-dibenzylhydrazine) m.p. 79.5-81° (from ethanol) (lit.[155] 85°), identical in all respects with the material synthesised below. Further elution with

ether gave unreacted 1,1-dibenzylhydrazine (855mg).

Benzaldehyde dibenzylhydrazone [178]

1,1-Dibenzylhydrazine (300mg, 1.415 mmol) was dissolved in a warm mixture (~50°) of glacial acetic acid (6 ml) and water (4 ml), and freshly distilled benzaldehyde (150mg, 1.415 mmol) in glacial acetic acid (7 ml) added. The mixture was heated at 70° for 10 min., then cooled, and the precipitated product separated and recrystallised from ethanol to give benzaldehyde dibenzylhydrazone (306mg, 72%) m.p. 81-83° (lit.[155] 85°);

n.m.r. ($CDCl_3$) 7.8 (m, PhC<u>H</u>:), 7.4-6.8 (m, 15 × ArH), and 3.25 (s, 2 × -C<u>H</u>$_2$Ph);

^{13}C n.m.r. ($CDCl_3$) 137.5, 131.7, 128.4-125.4 (15 × ArC + PhC<u>C</u>=N) and 57.8 (2 × PhC<u>H</u>$_2$);

i.r. 1600m, 1570m, 1500s, 1130m, 880m, 760s, and 695s;

m.s. 300 (base, M^+), 209, 181, 166, and 91.

Tetrabenzyl-2-tetrazene [180]

1,1-Dibenzylhydrazine (210mg, 0.991 mmol) was dissolved in dichloromethane (2 ml) and cooled to 5°. A solution of lead tetra-acetate (500mg, 1.128 mmol) in dichloromethane (10 ml) was added slowly over a period of 0.25h with stirring. After a further 0.5h the precipitated lead salts were separated, the filtrate evaporated and the residue recrystallised from light petroleum to give the title compound (85mg, 41%) m.p. 94-98° (lit.[155] 98-99°);

n.m.r. ($CDCl_3$) 7.1 (br s, 20 × ArH) and 4.3 (s, 4 × -C<u>H</u>$_2$Ph).

NN-Dibenzyl-4-chlorobenzenesulphenamide [182]

Dibenzylamine (500mg, 2.525 mmol) was dissolved in dry ether (10 ml) containing triethylamine (250mg, 2.475 mmol) with stirring at room

temperature. A solution of 4-chlorobenzenesulphenyl chloride (450mg, 2.514 mmol) in dry ether (10 ml) was added over a 10 min. period. After a further 1h, the precipitate was separated and the ether removed to give the crude product (606mg, 71%) as a colourless oil; n.m.r. ($CDCl_3$) 7.15 (AA'BB', 4 × p$ClC_6\underline{H}_4$ - superimposed on m, 10 × ArH) and 4.00 (s, 2 × -$C\underline{H}_2Ph$).

PART II

EXPERIMENTAL

CHAPTER 7

2-Nitrobenzenesulphenamide [231] and 2,4-dinitrobenzenesulphenamide [234]

A solution of the appropriate sulphenyl chloride (20 mmol) in acetonitrile (50 ml) was added at ambient temperature over a period of 0.5h to a stirred mixture of ammonia solution (d, 0.88, 40 ml) and acetonitrile (30 ml). After a further 0.5h, saturated sodium chloride solution (100 ml) was added, and the organic layer separated, washed with saturated sodium chloride solution, dried and evaporated and the residue recrystallised from ethanol to give:

2-Nitrobenzenesulphenamide [231] (80%) m.p. 122-125° (lit.[155] 128°);

n.m.r. ($CDCl_3$) 8.2-7.2 (m, 4 × ArH) and 2.75 (br s, exch. D_2O, $-NH_2$);

i.r. 3380w, 3300w, 3100w, 1590m, 1560m, 1340s, 1310s, and 730s.

2,4-Dinitrobenzenesulphenamide [234] (85%) m.p. 119-120° (lit.[157] 119-120°);

n.m.r. ($CDCl_3$) 9.15 (br d, J 2Hz, Ar H-3), 8.5 (br d, J 2Hz, Ar H-5 and H-6), and 2.85 (br s, exch. D_2O, $-NH_2$);

i.r. 3410w, 3320w, 3100w, 1590s, 1500s, 1340s, 1300m, and 730s.

Benzoylsulphenamide [230]

- was prepared by the method of Raasch[158] from thiobenzoic acid and hydroxylamine-O-sulphonic acid. The crude material (65%) was recrystallised from ethanol m.p. 81-84° (lit.[158] 88.5-90°).

4-Nitrobenzenesulphenamide [232]

4-Nitrobenzenethiol (1.55g, 10 mmol) was dissolved in water (100 ml) containing potassium hydroxide (700mg, 12.28 mmol) and to the filtered solution was added a solution of hydroxylamine-O-sulphonic acid (2.5g, 22.12 mmol) and potassium hydroxide (1.5g, 26.32 mmol) in water (20 ml) (cooled to 10°) with stirring. The resulting precipitate (the title compound) was separated,

washed with water and dried (1.44g, 85%) m.p. 105-106° (lit.[159] 101-103°).

4-Chlorobenzenesulphenamide [233]

To a solution of potassium hydroxide (1.85g, 32.46 mmol) and 4-chlorobenzenethiol (3.3g, 22.84 mmol) in water (50 ml) was added with stirring at ambient temperature a cooled (10°) solution of hydroxylamine-O-sulphonic acid (3.1g, 27.43 mmol) and potassium hydroxide (1.55g, 27.19 mmol) in water (10 ml). The resulting mixture was extracted with dichloromethane (2 × 20 ml), and the combined extracts were washed with water, dried and evaporated to give the title compound as a highly unstable colourless oil (1.67g, 46%).

This material decomposes to the bis(sulphenimide) [236] m.p. 137-138° over a period of a few hours at room temperature, but is stable for several weeks at -40°;

n.m.r. ($CDCl_3$) 7.2 (m, 4 × ArH) and 2.65 (br s, exch. D_2O, $-NH_2$);

i.r. 3380s, 3300s, 1470s, 1390s, 1090s, 1010s, 810s, and 785m.

Derivitisation of [233] with acetone

The sulphenamide [233] (1.0g, 6.27 mmol), ammonium chloride (catalyst, 200mg) and acetone (2.5 ml) were stirred in ethanol (10 ml) for 18h at ambient temperature. The mixture was filtered and evaporated and the residue chromatographed over basic alumina (35g) with light petroleum - ethyl acetate (9:1) as eluant, which gave the acetone derivative of [233], 1,1-dimethyl-N-(4-chlorophenyl)sulphenylimine (220mg, 18%) m.p. 51-53° (from light petroleum, b.p. <40°) (lit.[160] 40-41°);

n.m.r. ($CDCl_3$) 7.4 (AA'BB', 4 × ArH), and 2.10 and 2.05 (2 × s, 2 × CH_3).

Further elution with light petroleum - ethyl acetate (3:1) gave bis-

(4-chlorophenyl)sulphenimide [236] (390mg, 41%) resulting from thermal decomposition of [233];

n.m.r. ($CDCl_3$) 7.2 (br s, 8 × ArH), and 4.7 (br s, -NH).

Oxidation of [230]-[234] by lead tetra-acetate in the absence of trapping reagents

The sulphenamide (1 mol. equiv.) was stirred in dichloromethane (10 ml per gm) and powdered lead tetra-acetate (1 mol. equiv.) added portionwise over a period of 15 mins. Gas evolution was noted in all cases. Stirring was continued a further 15 mins., then dichloromethane was added. The mixture was filtered and evaporated and the residue chromatographed over basic alumina with conditions shown for each sulphenamide.

Benzoylsulphenamide [230] - elution with light petroleum gave a pale yellow solid identified as elemental sulphur (35%) m.p. 116-119°. The remainder of the product was intractable.

4-Chlorobenzenesulphenamide [233] - elution with light petroleum - ethyl acetate (9:1) gave bis(4-chlorophenyl) disulphide (75%) m.p. 68-70° (from light petroleum) (lit.[161] 71.5°);

i.r. 1900w, 1100s, 1010s, and 820s.

No other product was obtained.

4-Nitrobenzenesulphenamide [232] - elution with light petroleum - ethyl acetate (1:1) gave bis(4-nitrophenyl) disulphide (33%) m.p. 191° (from acetic acid) (lit.[162] 181°).

No other product was isolated.

n.m.r. ($CDCl_3$) 8.20 and 7.55 (J 9Hz, AA'BB');

i.r. 1590m, 1560m, 1500s, 1330s, 1090m, 840s, 830s, and 725s.

2-Nitrobenzenesulphenamide [231] - elution with ether gave bis(2-nitrophenyl) disulphide (49%) m.p. 191-196° (from acetic acid) (lit.[163] 192-

195°). The remainder of the material was polymeric.

i.r. 1590m, 1560m, 1510s, 1335s, 1310s, 1250m, 1100m, 1035m, 850m, and 730s.

2,4-Dinitrobenzenesulphenamide [234] - elution with ethyl acetate - methanol (99:1) gave a yellow solid identified as N-2,4-dinitrobenzene-S-2,4-dinitrobenzenesulphenamide [237], (41%) m.p. 231° (decomp.) (from nitrobenzene) (Found: C, 38.5; H, 2.0; N, 17.9. $C_{12}H_7N_5O_8S$ requires C, 37.8; H, 1.85; N, 18.4%; figures are correct for 6% occluded nitrobenzene);

n.m.r. (DMSO) 9.80 (s, -NH), 8.98 and 8.90 (2xd, J 3Hz, Ar H-3 and H-3'), 8.40 and 8.20 (2xdd, J 3 × 9Hz, Ar H-5 and H-5'), and 7.80 and 7.65 (2xd, J 9Hz, Ar H-6 and H-6');

i.r. 3330w, 3320w, 3100w, 1620s, 1600s, 1520s, 1350s, 1320s, 860m, 830s, 740s, and 730s;

m.s. 381 (M^+), 199 (base), 183, 153, 150, and 123.

Alternative synthesis of [237]

2,4-Dinitroaniline (500mg, 2.732 mmol) was added to a stirring suspension of sodium hydride (150mg, 50% dispersion, 3.125 mmol) in acetonitrile (80 ml). A solution of 2,4-dinitrobenzenesulphenyl chloride (650mg, 2.772 mmol) in acetonitrile (30 ml) was added dropwise over a period of 0.5h. After a further 0.5h, dilute hydrochloric acid (2M, 5 ml) was cautiously added, then water (30 ml). The precipitate was separated, and the filtrate concentrated giving more solid. The combined solids were chromatographed over basic alumina (60g). Elution with ethyl acetate - methanol (4:1) gave the title compound (200mg, 19%) as crystals (from nitrobenzene), identical in all respects with the material obtained above.

Cis-1-phenylpropene [200]

- was prepared by the method of Coussement et al.[164] in 67% yield from decarboxylation of Z-methylcinnamic acid with copper and quinoline. The crude product was distilled, b.p. (Kugelröhr) 120-125° /80 mmHg;

g.l.c. (3% OV 225, 75°, N_2 flow rate 48 ml min^{-1}).

Rt 5.2 (cis) and 7.2 (trans) min. Ratio 98:2.

n.m.r. ($CDCl_3$) 7.20 (br s, 5×ArH), 6.40 (dxd, J 1.6×11.5Hz, H-1), 5.70 (dxq, J 7×11.5Hz, H-2), and 1.78 (dxd, J 1.6×7Hz, $-CH_3$).

Tetraphenylpyrrole [265]

- was prepared by the method of Davidson[165] in 58% yield from benzoin, ammonium acetate, acetic acid and zinc dust. The product was recrystallised from acetonitrile, m.p. 217-217.5° (lit.[165] 214°).

Trapping of nitrenes derived from [230]-[234] by alkenes. General procedure.

The sulphenamide (1 mol. equiv.) and the alkene (5 mol. equiv.) (gaseous alkenes were condensed and measured directly into the reaction flask at 0°) were dissolved in dichloromethane (7 ml per gm. sulphenamide) and powdered lead tetra-acetate (1 mol. equiv.) added portionwise over 15 mins., with stirring at room temperature (0° for gaseous alkenes). After a further 15 mins., the mixture was diluted with dichloromethane, filtered and evaporated, and the residue chromatographed over neutral alumina (Brockmann Grade 3). Elution with light petroleum gave unreacted alkene. Further elution with ether gave the aziridines. The following aziridines were obtained in this way:

1-(2,4-dinitrobenzenesulphenyl)-2-phenylaziridine [246] from 2,4-dinitrobenzenesulphenamide and styrene (38%) as yellow crystals (from light petroleum - chloroform), m.p. 110-112° (Found: C, 52.8; H, 3.5;

N, 13.1. $C_{14}H_{11}N_3O_4S$ requires C, 53.0; H, 3.5; N, 13.2%);

n.m.r. ($CDCl_3$) 9.10 (br s, Ar H-3), 8.35 (br s, Ar H-5 and H-6), 7.35 (m, 5 × phenyl H), 3.15 (dxd, J 4 × 7Hz, aziridine H-2), 2.65 (d, J 4Hz, aziridine H-3 cis to phenyl), and 2.60 (d, J 7Hz, aziridine H-3 trans to phenyl);

i.r. 3100w, 1590s, 1510s, 1330s, 1300s, 1050m, 740s, 730s, and 695s;

m.s. 317 (M^+), 188, 180, and 119.

trans-1-(2,4-Dinitrobenzenesulphenyl)-2-methyl-3-phenylaziridine [249] from 2,4-dinitrobenzenesulphenamide and trans-1-phenylpropene (64%) as orange crystals (from ethanol) m.p. 115-117° (Found: C, 54.4; H, 4.0; N, 12.7. $C_{15}H_{13}N_3O_4S$ requires C, 54.4; H, 3.95; N, 12.7%);

n.m.r. ($CDCl_3$) 8.95 (d, J 2.5Hz, Ar H-3), 8.45 (d, J 8.5Hz, Ar H-6), 8.25 (dxd, J 2.5 × 8.5Hz, Ar H-5), 7.25 (br s, 5 × phenyl H), 3.00 (d, J 3.5Hz, aziridine H-3), 2.85 (dxq, J 3.5 × 5.5Hz, aziridine H-2), and 1.60 (d, J 5.5Hz, $-CH_3$);

i.r. 3100w, 1595s, 1520s, 1330s, 1300s, and 730s.

When the crude reaction mixture in the preparation of [249] was chromatographed over basic alumina instead of neutral alumina, with light petroleum - ethyl acetate (4:1) as eluant, N-(2-ethoxy-1-methyl-2-phenylethyl)-2,4-dinitrobenzenesulphenamide [256] was obtained (20%) as yellow crystals (from light petroleum - ethyl acetate) m.p. 88-89° (Found: C, 53.9; H, 5.0; N, 11.2. $C_{17}H_{19}N_3O_5S$ requires C, 54.1; H, 5.1; N, 11.1%);

n.m.r. ($CDCl_3$) 9.0 (s, Ar H-3), 8.2 (structured m, Ar H-5 and H-6), 7.25 (m, 5 × phenyl H), 4.40 (d, J 5Hz, -CHOEt), 3.75-2.85 (m, CHMe + N-H + OCH_2), and 1.35 and 1.10 (structured m, 2 × CH_3);

i.r. 3340w, 3080w, 1580s, 1520s, 1500m, 1340s, 1300s, 1070s, 910s, 755s, and 700s.

1-(2,4-dinitrobenzenesulphenyl)-2-methyl-2-phenylaziridine [247] from 2,4-dinitrobenzenesulphenamide and 2-phenylpropene as an orange glass (61%);

n.m.r. ($CDCl_3$) 9.0 (d, J 1.5Hz, Ar H-3), 8.30 (m, Ar H-5 and H-6), 7.35 (m, 5 × phenyl H), 2.75 (br s, aziridine H-3 cis to phenyl), 2.40 (br s, aziridine H-3 trans to phenyl), and 1.80 (s, $-CH_3$);

i.r. 3100w, 1585s, 1515s, 1335s, 1300s, and 740s.

trans-1-(2,4-dinitrobenzenesulphenyl)-2,3-dimethylaziridine [250] from 2,4-dinitrobenzenesulphenamide and trans but-2-ene (38%) as orange crystals (from ethanol) m.p. 137-138.5° (Found: C, 44.7; H, 4.2; N, 15.65. $C_{10}H_{11}N_3O_4S$ requires C, 44.6; H, 4.1; N, 15.6%);

n.m.r. ($CDCl_3$) 9.10 (d, J 2.5Hz, Ar H-3), 8.50 (d, J 8Hz, Ar H-6), 8.30 (dxd, J 2.5 × 8Hz, Ar H-5), 2.40-2.10 (m, 2 × aziridine H), and 1.40 (d, J 5.5Hz, 2 × CH_3);

i.r. 3110w, 1590s, 1510s, 1340s, 1300s, 1080m, 1050m, 1030m, 910s, 820s, and 730s.

1-(2,4-dinitrobenzenesulphenyl)-2-vinylaziridine [251] from 2,4-dinitrobenzenesulphenamide and buta-1,3-diene (58%) as orange crystals (from ethanol) m.p. 113-115° (Found: C, 45.1; H, 3.45; N, 15.8. $C_{10}H_9N_3O_4S$ requires C, 44.9; H, 3.4; N, 15.7%);

n.m.r. ($CDCl_3$) 9.10 (d, J 1.5Hz, Ar H-3), 8.40 (d, J 1.5Hz, Ar H-5 + H-6), 5.9-5.2 (structured m, 3 × alkene H), 2.70 (dxdxd, J 3.7 × 6.8 × 6.8 Hz, aziridine H-2), 2.40 (d, J 3.7Hz, aziridine H-3 cis to vinyl), and 2.38 (d, J 6.8Hz, aziridine H-3 trans to vinyl);

i.r. 3100w, 1590s, 1515s, 1380s, 1300s, 1050s, 920m, 740s, and 730s.

trans-1-(2-nitrobenzenesulphenyl)-2-methyl-3-phenylaziridine [270] from 2-nitrobenzenesulphenamide and trans-1-phenylpropene as a yellow oil (58%);

n.m.r. ($CDCl_3$) 8.30 (dxd, J 2.5 × 8Hz, Ar H-3), 7.65-7.10 (m, 8 × ArH), 2.90 (d, J 4Hz, aziridine H-3), 2.75 (dxq, J 4 × 6Hz, aziridine H-2), and 1.55 (d, J 6Hz, -Me).

With the sulphenamides [230], [232] and [233] no trappable products were obtained using the above procedure and the same products were isolated as in the absence of trapping reagents.

Reaction of trans-1-(2,4-dinitrobenzenesulphenyl)-2-methyl-3-phenyl-aziridine [249] with sodium ethoxide/ethanol

Sodium (50mg, 2.174 mmol) was dissolved in ethanol (10 ml) and the aziridine [249] added (200mg, 0.604 mmol), and the mixture stirred at ambient temperature for 0.5h. Dilute hydrochloric acid (2M, 3 ml) was then added and the mixture extracted with dichloromethane (2 × 5 ml). The organic extracts were dried and evaporated, and examination of the n.m.r. spectrum of the residue showed the presence of the sulphenamide [256], (ca. 10%) with the rest of the material being unchanged [249].

Reaction of 2,4-dinitrobenzenesulphenamide [234], lead tetra-acetate and cis-1-phenylpropene [200]

Using the general procedure given above, a mixture of two aziridines was revealed by n.m.r. of the crude reaction mixture. On chromatography over neutral alumina, the mixture of aziridines could be obtained pure. One component could be identified as the trans isomer [249]. The other isomer could be obtained by chromatography over basic alumina with ether as eluant (after removal of excess alkene with light petroleum) and was identified as cis-1-(2,4-dinitrobenzenesulphenyl)-2-methyl-3-phenylaziridine [255] (18%) as yellow crystals (from ethanol) m.p. 109-110° (Found: C, 54.3; H, 3.9; N, 12.7. $C_{15}H_{13}N_3O_4S$ requires C, 54.4; H, 3.95; N, 12.7%);

n.m.r. ($CDCl_3$) 9.05 (d, J 2.5Hz, Ar H-3), 8.50 (d, J 9Hz, Ar H-6), 8.35 (dxd, J 2.5 × 9Hz, Ar H-5), 7.35 (br s, 5 × phenyl H), 3.40 (d, J 7.3Hz, aziridine H-3), 2.65 (dxq, J 5.5 × 7.3Hz, aziridine H-2), and 1.20 (d, J 5.5Hz, $-CH_3$);

i.r. 3120w, 3090w, 1595s, 1515s, 1330s, 1300s, 1050m, 910s, 830m, 740m, and 730s.

Reaction of sulphenylaziridines with sodium borohydride

The sulphenylaziridine (0.3 mmol) was stirred in ethanol (1.5 ml) and dichloromethane (2 ml) at room temperature, and powdered sodium borohydride (1.2 mmol) added portionwise over a 2 min. period. After stirring a further 10 min. the mixture was poured into water (10 ml) and rapidly extracted with dichloromethane (2 × 5 ml). The organic extracts were dried, evaporated and distilled to give the aziridines:-

2-phenylaziridine - from 1-(2,4-dinitrobenzenesulphenyl)-2-phenyl-aziridine [246] as a colourless oil (45%) b.p. (Kugelröhr) 95-100°/2 mmHg (lit.[119] 94-95°/10 mmHg);

n.m.r. ($CDCl_3$) 7.25 (s, 5 × ArH), 3.00 (dxd, J 3.3 × 6Hz, aziridine H-2), 2.15 (d, J 6Hz, aziridine H-3 trans to phenyl), 1.75 (d, J 3.3Hz, aziridine H-3 cis to phenyl), and 1.10 (s, -NH);

i.r. 3300w, 1580s, 1495s, 750s, and 700s.

trans-2-methyl-3-phenylaziridine - from trans-1-(2,4-dinitrobenzene-sulphenyl)-2-methyl-3-phenylaziridine [249] as a colourless oil (56%) b.p. (Kugelröhr) 110-115°/2 mmHg (lit.[119] 96-97°/10 mmHg);

n.m.r. ($CDCl_3$) 7.20 (m, 5 × phenyl H), 2.65 (d, J 2.8Hz, aziridine H-3), 2.10 (dxq, J 2.8 × 5.5Hz, aziridine H-2), 1.35 (d, J 5.5Hz, -Me), and 1.20 (br s, -NH);

i.r. 3300w, 1600m, 1490s, 1450s, 840m, and 740s.

Reaction of 2,4-dinitrobenzenesulphenamide [234], lead tetra-acetate and DMSO

The sulphenamide [234] (0.5g, 2.326 mmol) was dissolved in DMSO (3 ml) with stirring at ambient temperature, and lead tetra-acetate (1.04g, 2.346 mmol) added portionwise over a period of 10 mins. After a further 10 min. the mixture was poured into water (20 ml) and extracted with dichloromethane (2 × 30 ml). The combined dichloromethane extracts were washed with water (20 ml), dried and evaporated, and the residue purified by chromatography over neutral alumina (40g). Elution with ether - ethyl acetate (9:1) gave N-(2,4-dinitrobenzene)-2,4-dinitrobenzenesulphenamide [237] (111mg, 25%). Further elution with ethyl acetate and ethyl acetate - methanol (4:1) afforded N-(2,4-dinitrobenzenesulphenyl)-SS-dimethylsulphoximine [257] (190mg, 28%) as chocolate-brown crystals (from ethanol) m.p. 212-215° (decomp.) (Found: C, 33.2; H, 3.1; N, 14.4. $C_8H_9N_3O_5S_2$ requires C, 33.0; H, 3.1; N, 14.4%);

n.m.r. ($[CD_3]_2SO$) 8.85 (d, J 2.5Hz, Ar H-3), 8.37 (dxd, J 2.5 × 9Hz, Ar H-5), 8.20 (d, J 9Hz, Ar H-6), and 3.30 (s, 2 × CH_3);

i.r. 3120w, 1600s, 1590s, 1510s, 1345s, 1220m, 1030s, 830m, 745m, and 740s;

m.s. 291 (M^+), 197, 181, 147, 119, and 76 (base).

Reaction of 2,4-dinitrobenzenesulphenamide [234], trans-but-2-enyl 4-chlorophenyl sulphide [110] and lead tetra-acetate

2,4-Dinitrobenzenesulphenamide (450mg, 2.093 mmol) and trans-but-2-enyl 4-chlorophenyl sulphide (600mg, 3.031 mmol) were stirred in dichloromethane (3.5 ml) at room temperature and lead tetra-acetate (1.09g, 2.46 mmol) was added portionwise over a period of 10 mins. After a further 30 mins., the mixture was filtered and evaporated and

chromatographed over basic alumina (50g) with light petroleum - ether (9:1) as eluant which gave back unchanged allyl sulphide (250mg). Further elution with ether gave N-(1-methylallyl)-S-(4-chlorobenzene)-S-(2,4-dinitrobenzene)sulphenimide [258] (640mg, 74%) as an orange oil;

n.m.r. ($CDCl_3$) 9.0 (d, J 2Hz, Ar H-3), 8.35 (dxd, J 2 × 9Hz, Ar H-5), 7.80 (d, J 9Hz, Ar H-6), 7.30 (AA'BB', 4 × ArH), 6.10-5.70 (structured m, $C\underline{H}=CH_2$), 5.30-5.0 (structured m, $CH=C\underline{H}_2$), 4.05 (m, $NC\underline{H}$), and 1.35 (d, J 7Hz, $-CH_3$);

i.r. 3100w, 2850w, 1590s, 1510s, 1470m, 1340s, 1300s, 1080m, 1040m, 910m, 825s, 735s, and 725s.

Reaction of [258] with hydrogen chloride

The sulphenimide [258] (680mg, 1.653 mmol) was dissolved in dry ether (25 ml) and dry hydrogen chloride passed into the ice-cooled mixture for 0.5h. After a further 1h at 0°, the precipitated white solid which had formed was separated, and the filtrate evaporated and re-dissolved in dry ether (10 ml). This solution was added slowly to a stirring mixture of methanol (1 ml), pyridine (0.5 ml) and dry ether (10 ml) at ambient temperature, over a 10 min. period. After a further 10 min., the mixture was filtered and evaporated, and the residue recrystallised from methanol to give yellow crystals of O-methyl-S-2,4-dinitrobenzenesulphenate [262] (310mg, 81%) m.p. 120-122° (lit.[166] 125°);

n.m.r. ($CDCl_3$) 9.05 (d, J 2Hz, Ar H-3), 8.50 (dxd, J 2 × 9Hz, Ar H-5), 7.90 (d, J 9Hz, Ar H-6), and 4.0 (s, $-CH_3$).

The initially precipitated white solid was identified as 1-chloro-2-(4-chlorophenylthio)-3-butylamine hydrochloride [260] (215mg, 45%) m.p. 131-134° (from light petroleum - acetone) (Found: C, 41.9; H, 4.9; N, 4.9. $C_{10}H_{14}Cl_3NS$ requires C, 41.9; H, 4.9; N, 4.9%);

n.m.r. ($CDCl_3$) 8.80 (br s, $-NH_3^{\oplus}$), 7.40 (AA'BB', 4 × ArH), 4.10-3.40 (m, 4 × aliphatic H), and 1.57 (d, J 6Hz, $-CH_3$);

i.r. 3200-2800br, 1600m, 1520s, 1100s, 1020s, 970m, and 830s.

Reaction of 2,4-dinitrobenzenesulphenamide [234] with tetraphenylpyrrole [265] and lead tetra-acetate

2,4-Dinitrobenzenesulphenamide (1.2g, 5.582 mmol) and tetraphenylpyrrole (2.1g, 5.792 mmol) were stirred in dichloromethane (24 ml) at ambient temperature and powdered lead tetra-acetate (2.5g, 5.64 mmol) added over a 10 min. period. After a further 30 min., dichloromethane (50 ml) was added, and the mixture filtered and evaporated. The residue was purified by chromatography over Kieselgel (110g) with light petroleum - dichloromethane (2:1) as eluant which eluted a mixture of two colourless compounds (1.8g). On fractional recrystallisation from dichloromethane - ethanol, 2,4,5,6-tetraphenylpyrimidine [266] was obtained (1.08g, 48%) m.p. 195-196° (lit.[123] 195-196°) with spectral data identical to that reported by Barton[123] et al. The mother liquors gave unreacted tetraphenylpyrrole (588mg, 28%). Further elution with light petroleum - ether (1:1) gave an orange solid (100mg), which was not identified, followed by a yellow crystalline solid (from dichloromethane - ethanol) m.p. 172-174°, identified by X-ray crystallographic studies as 2-(2,4-dinitrobenzenesulphenylamino)-2,3,4,5-tetraphenyl-(2H)-pyrrole [269] (600mg, 18%) (Found: C, 70.3; H, 4.3; N, 9.1. $C_{34}H_{24}N_4O_4S$ requires C, 69.85; H, 4.1; N, 9.6%);

n.m.r. ($CDCl_3$) 8.85 (d, J 2.5Hz, Ar H-3), 8.15 (d, J 8Hz, Ar H-6), 7.85 (dxd, J 2.5 × 8.5Hz, Ar H-5), 7.7-6.4 (m, 20 × phenyl H), and 4.8 (s, -NH);

i.r. 3300w, 3100m, 1600s, 1520s, 1340s, 1300s, 1045s, 910m, 740m, 730m, and 695s;

m.s. 385, 384 (base), 371, 304, 279, 187, and 177;

u.v. λ_{max} (CH_2Cl_2) 271 and 332 nm.

Control experiments on cis-1-phenylpropene [200]

(i) Cis-1-phenylpropene (100mg, 97:3 cis:trans by g.l.c.) and acetic acid (two drops) were stirred at room temperature for 0.5h. Diethyl ether (10 ml) was added, and the mixture extracted with 8% sodium bicarbonate solution (5 ml), washed with water (5 ml) and dried. G.l.c. of the solution (3% OV 225, 75°, N_2 flow rate 48 ml min^{-1}) revealed no change in the proportion of trans alkene present (3%).

(ii) Cis-1-phenylpropene (100mg, 97:3 cis:trans by g.l.c.) and lead tetra-acetate (100mg) were dissolved in dichloromethane (1 ml) and stirred at room temperature for 0.5h. Ether (3 ml) was added, and the solution allowed to percolate through a small column of alumina (5g). G.l.c. of the resulting solution revealed no change in the proportion of the trans alkene present (3%).

Control experiment on aziridines [249] and [255]

A mixture of aziridines [249] and [255] (250mg, ratio 1:1), allyl 4-chlorophenyl sulphide [107] (220mg) and lead tetra-acetate (310mg) were stirred in dichloromethane (2 ml) at room temperature for 2h. The solution was percolated through a small column (5g) of neutral alumina and evaporated. N.m.r. of the residue revealed no change in the proportion of [249]:[255].

Addition of phthalimidonitrene [90] to cis-1-phenylpropene [200]

N-aminophthalimide (0.81g, 5.0 mmol) and cis-1-phenylpropene [200] (0.6g, 5.085 mmol) were dissolved in dichloromethane (4 ml) and powdered lead tetra-acetate (2.2g, 4.966 mmol) added over a period of 0.25h, at room temperature. After a further 1h, the precipitated lead

salts were separated and the residue chromatographed over neutral alumina (25g). Elution with light petroleum yielded unchanged alkene. Further elution with light petroleum - ethyl acetate (1:1) afforded cis-2-methyl-3-phenyl-1-phthalimidoaziridine [201] (270mg, 20%) as pale yellow crystals (from ethanol) m.p. 81-82° (Found: C, 73.4; H, 5.05; N, 10.1. $C_{17}H_{14}N_2O_2$ requires C, 73.4; H, 5.1; N, 10.1%); n.m.r. ($CDCl_3$) 7.8-7.2 (m, 9 × ArH), 3.70 (d, J 8.0Hz, aziridine H-3), 2.95 (dxq, J 6 × 8Hz, aziridine H-2), and 1.25 (d, J 6Hz, $-CH_3$); i.r. 1765w, 1730s, 1700s, 1610w, 1160m, 1030m, 1020m, 895s, and 710s.

APPENDICES

APPENDIX I

Raw kinetic data for determination of energy barrier separating the diastereoisomers of [118] and [132]

In order to evaluate the energy barriers for the sulphenamides [118] and [132], the following equations, valid for first order reversible reactions were applied:

$$\text{Isomer A} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{Isomer B} \qquad K = \frac{k_1}{k_{-1}} \qquad \ldots\ldots \text{(a)}$$

$$(k_1 + k_{-1})t = 2.303 \log_{10} \left[\frac{\%\text{ B in equilibrium mixture} - \%\text{ B in starting mixture}}{\%\text{ B in equilibrium mixture} - \%\text{ B at time t}} \right]$$

$\ldots\ldots$ (b)

when the log term is plotted against time, a straight line with slope $\frac{k_1 + k_{-1}}{2.303}$ results.

The results from the graph in conjunction with relationship (a) enable the forward and reverse rate constants to be calculated at the temperature in question. A least squares line-fitting computer program was used to evaluate the rate constants.

The Arrhenius equation (c) was then employed to evaluate the activation energies:

$$2.303 \log_{10} k = -\frac{E_A}{RT} \qquad \ldots\ldots \text{(c)}$$

On plotting $\log_{10} k$ against $1/T$, the slope of the resulting straight line = $-E_A/2.303\,R$ where R = the gas constant.

From the activation energy, E_A, the activation enthalpy, $\Delta H^{\ddagger}$ may be directly evaluated:

$$E_A = \Delta H^{\ddagger} + RT \qquad \ldots\ (d)$$

(for first order reactions in solution)

The activation entropy, $\Delta S^{\ddagger}$, can be evaluated using relationship (e):

$$\log_{10} k = \log_{10} \left[\frac{e\, k_B\, T}{h}\right] + \frac{\Delta S^{\ddagger}}{2.303R} - \frac{E_A}{2.303RT} \qquad \ldots\ (e)$$

where k_B = Boltzmann's constant and h = Planck's constant.

Having obtained the enthalpy and entropy, the free energy of activation may be evaluated using:

$$\Delta G^{\ddagger} = \Delta H^{\ddagger} - T.\Delta S^{\ddagger} \qquad \ldots\ (f)$$

Experimental

The sulphenamide (15mg) was dissolved in chlorobenzene (0.6 ml) in an n.m.r. tube and placed inside the n.m.r. probe. After a period of 5 min. to allow temperature equilibration, the diastereoisomeric methyl doublets of the sample were repeatedly integrated until equilibrium was achieved.

Results

N-(1,2-dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-2-nitrobenzene-sulphenamide [132]

Isomer A	δ_{Me}	1.17 p.p.m.	$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B$
Isomer B	δ_{Me}	1.55 p.p.m.	

In this case K = 1.5 (i.e. 40% A, 60% B at equilibrium).

(i) T = 52°

Time t/s	N.m.r. integration A : B		% A : B		$\left[\frac{54.9}{(60-x)}\right]$	$\log_{10}\left[\frac{54.9}{(60-x)}\right]$
0	157	8.5	94.9	5.1	1	0
1260	108	14	88.5	11.5	1.1320	0.0539
2160	101	21	82.8	17.2	1.2827	0.1081
3060	97	27	78.2	21.8	1.4371	0.1575
3720	92	32	74.8	25.2	1.5776	0.1980
8580	75	51	59.5	40.5	2.8154	0.4495
9660	67	51	56.8	43.2	3.2679	0.5143
10800	60	51	54.0	46.0	3.9214	0.5934
12000	64	57	52.9	47.1	4.2558	0.6290
13020	59	55	51.8	48.2	4.6525	0.6677
14130	58	59	49.6	50.4	5.7188	0.7573

(ii) T = 60°

Time t/s	N.m.r. integration A : B		% A : B		$\left[\frac{54.9}{(60-x)}\right]$	$\log_{10}\left[\frac{54.9}{(60-x)}\right]$
0	157	8.5	94.9	5.1	1	0
1100	102	29	77.9	22.1	1.4485	0.1610
1560	99	36	73.3	26.7	1.6486	0.2171
2460	86	45	65.6	34.4	2.1445	0.3313
3325	75	52	59.0	41.0	2.8895	0.4608
4290	68	58	54.0	46.0	3.9214	0.5934
5190	64	63	50.4	49.6	5.2788	0.7225
6360	67	72	48.2	51.8	6.6951	0.8257

(iii) T = 67°

Time t/s	N.m.r. integration A : B		% A : B		$\left[\frac{54.9}{(60-x)}\right]$	$\log_{10}\left[\frac{54.9}{(60-x)}\right]$
0			94.9	5.1	1	0
870	71	25	74.0	26.0	1.6147	0.2081
1560	61	39	61.0	39.0	2.6143	0.4173
2160	54	45	54.5	45.5	3.7862	0.5782

Evaluation

T	no. of points	r	$k_1/10^{-4}\ s^{-1}$	$k_{-1}/10^{-4}\ s^{-1}$
52	11	0.999	0.7371	0.4914
60	8	0.998	1.834	1.223
67	4	0.999	3.735	2.490

r = correlation coefficient

For activation parameters, see 3.2.

N-(1,2-dihydro-2-oxoquinolin-1-yl)-N-(1-methylallyl)-4-chlorobenzene-sulphenamide

Isomer A δ_{Me} 0.93
Isomer B δ_{Me} 1.48

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B$$

In this case K = 1.25.

(i) T = 63.5°

Time t/s	N.m.r. integration A : B	% A : B	$\left[\frac{39.8}{(55.7-x)}\right]$	$\log_{10}\left[\frac{39.8}{(55.7-x)}\right]$
0	74 14	84.1 15.9	1	0
2220	65 21	75.6 24.4	1.272	0.0976
3780	55 22	71.4 28.6	1.469	0.1670
5580	46 23	66.7 33.3	1.777	0.2497
7620	44 31	58.7 41.3	2.764	0.4415
12300	40 36	52.6 47.4	4.795	0.6808
13980	36 35	50.7 49.3	6.219	0.7937

(ii) T = 70°

Time t/s	N.m.r. integration A : B	% A : B	$\left[\frac{43.3}{(55.7-x)}\right]$	$\log_{10}\left[\frac{43.3}{(55.7-x)}\right]$
0	106 15	87.6 12.4	1	0
540	124 26	82.7 17.3	1.128	0.0522
2100	102 46	68.9 31.1	1.760	0.2455
2880	95 52	64.1 35.9	2.187	0.3399
3780	87 57	60.4 39.6	2.689	0.4296
4860	89 71	55.6 44.4	3.832	0.5834
5880	77 70	52.4 47.6	5.346	0.7280
6600	65 61	51.6 49.4	5.932	0.7732
7380	60 61	49.6 50.4	8.170	0.9912

(iii) T = 76°

Time t/s	N.m.r. integration A : B	% A : B	$\left[\frac{39.7}{(55.7-x)}\right]$	$\log_{10}\left[\frac{39.7}{(55.7-x)}\right]$
0	63 12	84.0 16.0	1	0
780	54 20	73.0 27.0	1.383	0.1409
1320	50 26	65.8 34.2	1.847	0.2665
1980	46 33	58.2 41.8	2.856	0.4557
2580	45 36	55.6 44.4	3.513	0.5457
3060	40 37	51.9 48.1	5.224	0.7180

(iv) T = 82°

Time t/s	N.m.r. integration A : B	% A : B	$\left[\frac{31.8}{(55.7-x)}\right]$	$\log_{10}\left[\frac{31.8}{(55.7-x)}\right]$
0	153 : 48	76.1 : 23.9	1	0
600	117 : 62	67.2 : 32.8	1.389	0.1428
1080	104 : 78	57.2 : 42.8	2.465	0.3918
1620	94 : 90	52.1 : 48.9	4.676	0.6699
2040	86 : 95	47.5 : 52.5	9.937	0.9972

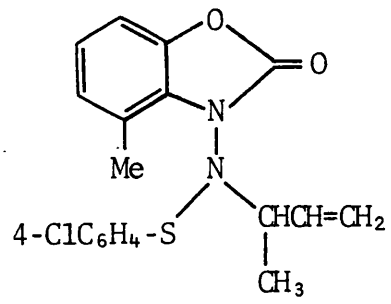
Evaluation

T	no. of points	r	$k_1/10^{-4}$ s^{-1}	$k_{-1}/10^{-4}$ s^{-1}
63.5	7	0.996	0.7441	0.5993
70	9	0.999	1.570	1.256
76	6	0.995	2.978	2.383
82	5	0.982	6.261	5.009

For activation parameters, see 3.2.

APPENDIX 2

The sulphenamide [278] has been synthesised[125] and its n.m.r. behaviour investigated:



[278]

It was found that this compound exhibited two distinct C-1 methyl doublets (δ1.18 and 1.50, $CDCl_3$) at room temperature, which were initially in the ratio 3:1 but over a period of eleven hours at room temperature this changed to 1:1. This indicates an approximate $\Delta G^{\ddagger}$ value of $\approx$23 kcal mol^{-1}, which is appreciably higher than the analogue [113] lacking the 4-methyl substituent (see 2.4, 2.5 and 3.4), for which coalescence of the C-1 methyl doublets occurs at 27° ($\Delta G^{\ddagger}$ ~15.5 kcal mol^{-1}). This evidence shows the process which interconverts the diastereoisomers of [113] and [278] is rotation around the N-N bond, and not the N-N homolysis - recombination mechanism. This higher barrier results owing to greater steric hindrance in the transition state for rotation caused by interaction of the sulphur or methylallyl substituents on nitrogen with the 4-methyl substituent of the benzoxazolinone ring.

For the N-N homolysis - recombination mechanism, a lower energy barrier would be predicted as the 4-methylbenzoxazolinone radical would be more thermodynamically stable than the analogous benzoxazolinone radical. Also, it is believed that the initial step in the

homolysis mechanism is the deformation of the N-N bond out of the plane of the heterocycle, relieving the peri interaction with the 4-methyl substituent. In fact, the sulphenamide [278] decomposes readily; standing in solution at room temperature for 5 days is sufficient for complete decomposition, to 4-methylbenzoxazolinone and the thio-oxime [120].

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