Thermal Racemisation of N-Unsubstituted and Various N-Substituted S-o-Methoxyphenyl S-Phenyl Sulphimides by Pyramidal Inversion [1]
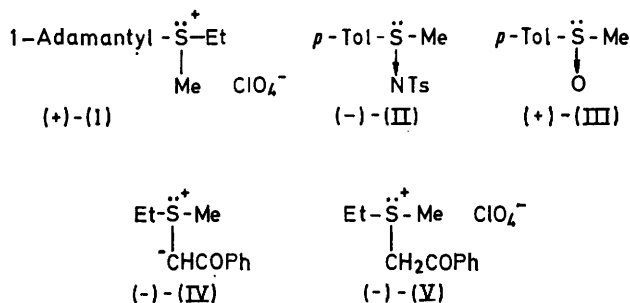
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The rates of the thermal racemisation by pyramidal inversion of optically active N-unsubstituted and N-substituted S-o-methoxyphenyl S-phenyl sulphimides have been measured. In the case of N-arylsulphonylsulphimides [Ar^{1}S($\stackrel{..}{\cdot}$NSO$_2$Ar^2)Ar^3] and N-acylsulphimides [Ar^{1}S($\stackrel{..}{\cdot}$NCOR)Ar^2], the electron-withdrawing group (Ar^2 or R) retarded the rate of pyramidal inversion. In keeping with the observed trend, the enormous rate differences among the sulphoxide, the sulphimide, and the sulphonium ylide, each having a semi-polar bond, are considered to be predominantly due to the differences of electronegativities of the atoms bonded to sulphur (O 3.5, N 3.0, C 2.5). Intramolecular hydrogen bonding between the oxygen atom of the o-methoxy-group and the hydrogen atom of the imino-group plays an important role in the pyramidal inversion of S-o-methoxyphenyl S-phenyl sulphimide. A correlation has been found between the pyramidal inversion and the i.r. stretching frequency (ν_{S-N}) of the S^{IV}–N bond of sulphimides.

IT was recently shown that optically active S-alkyl S-p-tolyl N-tosylsulphimides are thermally racemised at 80—100 °C through pyramidal inversion.[2] In comparing the rate of racemisation with those of the analogous sulphoxide and sulphonium salt, the rates fall in the following sequence, sulphonium salt $\gg$ sulphimide $\gg$ sulphoxide, approximately in the relative order 10^{12}, 10^7, and 1, respectively, based on the rates for (+)-1-adamantylethylmethylsulphonium perchlorate (I),[3] (−)-S-methyl S-p-tolyl N-tosylsulphimide (II),[2] and (+)-S-methyl S-p-tolyl sulphoxide (III).[4] Darwish and Tomilson reported that (−)-ethylmethylsulphonium phenacylide (IV) is racemised ca. 200 times faster than the corresponding (−)-sulphonium perchlorate (V).[5]

These enormous rate differences among typical trivalent sulphur compounds each with a semi-polar linkage have been interpreted on the basis of the following three factors, (a) $2p$–$3d$ π bond formation, (b) electronic repulsion between lone pairs of two adjacent

(+)-(I)   1-Adamantyl-$\stackrel{\stackrel{..}{+}}{\underset{\underset{Me\quad ClO_4^-}{|}}{S}}$-Et   (−)-(II)   p-Tol-$\stackrel{..}{\underset{\underset{NTs}{|}}{S}}$-Me   (+)-(III)   p-Tol-$\stackrel{..}{\underset{\underset{O}{|}}{S}}$-Me

(−)-(IV)   Et-$\stackrel{\stackrel{..}{+}}{\underset{\underset{^-CHCOPh}{|}}{S}}$-Me   (−)-(V)   Et-$\stackrel{\stackrel{..}{+}}{\underset{\underset{CH_2COPh}{|}}{S}}$-Me ClO$_4^-$

atoms, and (c) electronegativity.[1,5-10] A variety of N-substituted sulphimides [R^{1}S($\stackrel{..}{\cdot}$NZ)R^2] can now be readily prepared and are good models for understanding the nature of the factors which affect pyramidal in-

version of trivalent sulphur compounds by making use of the polar effect of the substituent Z. In this paper the results obtained for the thermal racemisation by pyramidal inversion of the (−)-S-o-methoxyphenyl S-phenyl sulphimides (VI)—(IX) are described.
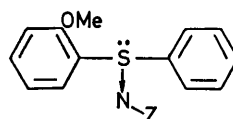
(VI)   Z = SO$_2$Ar
(VII) Z = COR
(VIII) Z = CH$_2$CH$_2$CN
(IX)   Z = H

a; Ar = p-MeOC$_6$H$_4$, R = Pr^i
b; Ar = p-MeC$_6$H$_4$, R = Me
c; Ar = R = Ph
d; Ar = p-ClC$_6$H$_4$, R = CF$_3$

RESULTS AND DISCUSSION

The rates of thermal racemisation of sulphimides were measured over the temperature range 65—85 °C by a semi-automatic polarimeter. The cell containing a 0.06—0.18M solution was sealed after replacing air with dry nitrogen. All the polarimetric rate constants were cleanly of first order over 1—3 half-lives. Except for the specific rotation, the product was completely identical with the starting sulphimide (t.l.c., i.r., and n.m.r.).

Thermal racemisation of optically active sulphimides may proceed by one of the three routes, (a) pyramidal inversion, (b) dissociation by an S_N1 mechanism, or (c) bimolecular exchange (Scheme 1).[9] Among these, pathway (c) is eliminated, since the rate of racemisation is of the first order with respect to the sulphimide. Moreover, the fact that the only product is the original

[1] Preliminary communication, M. Moriyama, N. Furukawa, T. Numata, and S. Oae, Chem. Letters, 1976, 275.

[2] N. Furukawa, K. Harada, and S. Oae, Tetrahedron Letters, 1972, 1377.

[3] R. Scartazzini and K. Mislow, Tetrahedron Letters, 1967, 2719.

[4] D. R. Rayner, A. J. Gordon, and K. Mislow, J. Amer. Chem. Soc., 1968, **90**, 4854.

[5] D. Darwish and R. L. Tomilson, J. Amer. Chem. Soc., 1968, **90**, 5938.

[6] B. C. Menon and D. Darwish, Tetrahedron Letters, 1973, 4119.

[7] D. Darwish and S. K. Datta, Tetrahedron, 1974, **30**, 1155.

[8] S. J. Campbell and D. Darwish, Canad. J. Chem., 1974, **52**, 2953.

[9] J. B. Lambert, ' Topics in Stereochemistry,' Wiley, New York, 1971, vol. 6, p. 19.

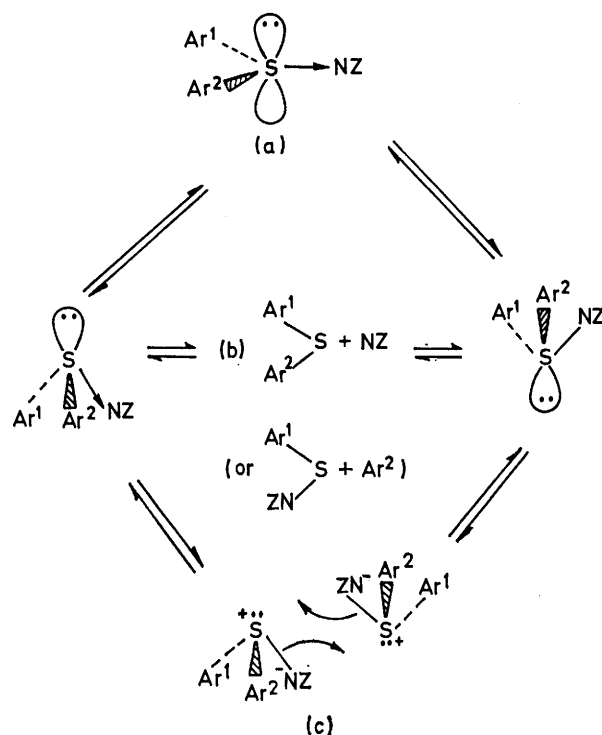[10] A. Rauk, L. C. Allen, and K. Mislow, Angew. Chem. Internat. Edn., 1970, **9**, 400.

sulphimide also eliminates a mechanism involving C–S and S–N bond fission [pathway (b)]. Thus, thermal racemisation of the sulphimides is considered to proceed *via* the pyramidal inversion process (a).

SCHEME 1

The first-order polarimetric rate constants of the thermal racemisations of compounds (VI) and (VII) are given in Tables 1 and 2, respectively.

TABLE 1

Rate constants of thermal racemisation for sulphimides (VI) [a]

Sulphimide	$T/°C$	$10^5 k/s^{-1}$	k/k_{Ph} [b]
(VIa)	75	4.38 ± 0.10	1.21
(VIb)	65	1.10 ± 0.01	
	75	3.72 ± 0.05	1.03
(VIc)	65	0.97 ± 0.01	
	75	3.61 ± 0.04	1.00
	85	10.2 ± 0.2	
(VId)	75	3.06 ± 0.05	0.85

[a] Rates were measured in 0.06M chloroform solution. [b] Relative rate constants at 75 °C with sulphimide (VIc) as standard.

The electronic effects of the substituents on the rate of thermal racemisation are in the following order, *p*-MeO > *p*-Me > H > *p*-Cl for N-sulphonylsulphimides (VI), and Pr^i > Me > Ph > CF_3 for N-acylsulphimides

(VII). However, the range of relative rate constants of these compounds are rather small as indicated in Tables 1 and 2. Values of log $k_{racemisation}$ of these N-sulphonyl- and N-acyl-sulphimides can be correlated with σ and σ* values giving small negative ρ and ρ* (−0.31 and −0.22) values, respectively. Thus, a strong electron-withdrawing group attached to nitrogen retards the rate of pyramidal inversion.

An electron-withdrawing substituent on the nitrogen atom should reduce both $2p$–$3d$ formation of π S^{IV}–N bond, and lone pair–lone pair electron repulsion, because

TABLE 2

Rate constants of thermal racemisation for sulphimides (VII) [a]

Sulphimide	$T/°C$	$10^5 k/s^{-1}$	k/k_{Me} [b]
(VIIa)	75	1.21 ± 0.05	1.12
(VIIb)	75	1.08 ± 0.01	1.00
(VIIc)	65	0.150 ± 0.005	
	75	0.545 ± 0.008	0.50
	85	1.92 ± 0.05	
(VIId)	75	0.246 ± 0.004	0.23

[a] Rates were measured in 0.06M chloroform solution. [b] Relative rate constants at 75 °C with sulphimide (VIIb) as standard.

it substantially reduces the electron density on nitrogen. Since both factors should diminish the energy barrier for pyramidal inversion, they cannot account for all the observed substituent effects.

Thus, the effect of the electronegativity (inductive effect) of the substituent needs to be invoked to explain the inversion barrier of the sulphimides. The pyramidal structure of a sulphimide with a strong electron-withdrawing (electronegative) substituent, such as the trifluoroacetyl group, would be substantially stabilised in the ground state.[11,12] This conclusion is supported by X-ray analyses for N-sulphonyl- and N-acyl-sulphimides.[13-16] The pyramidal structure of a sulphimide with a weakly electron-withdrawing substituent on nitrogen approaches a planar structure with a somewhat shorter S–N bond.* This is in accord with the fact that the N-tosylsulphimide (VIb) was racemised 15 times faster than the N-trifluoroacetyl derivative (VIId) (see Tables 1 and 2 and Figure).

These substituent effects are probably the first example to reveal the small but pronounced effect of electronegativity on the pyramidal stability of a trivalent sulphur compound. Analogously, in phosphines and arsines, the predominant influence upon pyramidal stability is considered to be the electronegativity of the ligand rather than *p*–*d* π bond formation.[17,18]

On the basis of these results for N-substituted sulphimides, it seems reasonable to assume that the

* The sum of the bond angles around the sulphur atom and the S–N bond distance of sulphimides $R^1S(:NZ)R^2$ are as follows: R^1, R^2, Z, sum of bond angles (°), bond distance (Å) Me, Me, $MeSO_2$, 307.0, 1.633;[13] Ph, Ph, *p*-TolSO₂, 308.5, 1.628;[14] Me, Me, CCl_3CO, 302.7, 1.667;[15] Et, Et, $CHCl_2CO$, 302.3, 1.673.[16]

[11] J. F. Kincaid and F. C. Henriques, jun., *J. Amer. Chem. Soc.*, 1940, **62**, 1474.

[12] C. C. Levin, *J. Amer. Chem. Soc.*, 1975, **97**, 5649.

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[14] A. Kalman, B. Duffin, and A. Kucsman, *Acta Cryst.*, 1971, **B27**, 586.

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[17] R. D. Baechler and K. Mislow, *J. Amer. Chem. Soc.*, 1971, **93**, 774.

[18] R. D. Baechler, J. P. Casey, R. J. Cook, G. H. Senkler, jun., and K. Mislow, *J. Amer. Chem. Soc.*, 1972, **94**, 2859.

enormous rate differences among sulphoxides, the sulphimide, and sulphonium ylides, each with a semi-polar bond, may be attributable mainly to the electro-negativity of the atom adjacent to sulphur (O 3.5, N 3.0,
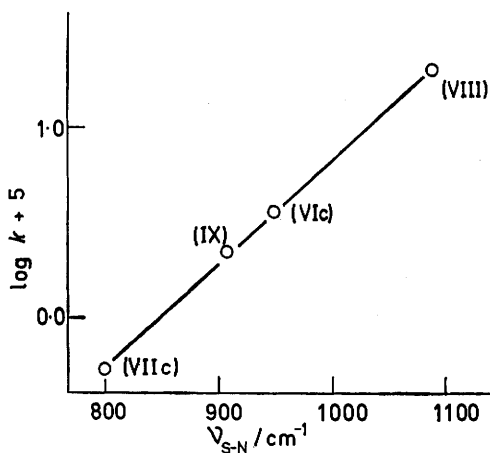
Correlation of log $k_{\text{racemisation}}$ at 75 °C with i.r. stretching frequency for sulphimides (VI)—(IX)

C 2.5). Since the difference in electronegativity due to the inductive effect of the substituent on the nitrogen atom of the sulphimides is small by comparison with

sulphonium ylide. Furthermore, the S–O double bond character of the sulphoxide is larger than that of the S–N bond of the sulphimide or the S–C bond of the sulphonium ylide,[19] and hence the ground state of the sulphoxide is more stabilised than those of the latter two.

The detailed features of pyramidal inversion were investigated for S-o-methoxyphenyl S-phenyl sulph-imide (IX) which is the simplest sulphimide and the one most structurally analogous to sulphoxide. In-spection of the activation parameters in Table 3 reveals that normal activation entropy values for pyramidal inversion were obtained for the racemisation of the sulphimides (VIc) and (VIIc) but not for sulphimide (IX); it was well known that the activation entropies observed for pyramidal inversion of the analogous sulphoxide, N-tosylsulphimide, and sulphonium ylide are close to zero.[2,4,8] However, in the case of sulph-imide (IX), $\Delta S^{\ddagger}$ in a nonpolar solvent ($\Delta S^{\ddagger}$ −12.3 cal mol^{-1} K^{-1}) is more negative by ca. 10 cal mol^{-1} K^{-1} than for N-substituted sulphimides.

One of the possible reasons for the more negative value of $\Delta S^{\ddagger}$ for sulphimide (IX) is an ability to engage in either intramolecular or inter-molecular association in the transition state which is larger than that in the ground state. Intermolecular associ-ation can be ruled out in view of the fact

TABLE 3

Rate constants and activation parameters for thermal racemisation of sulphimides (VI)—(IX) [a]

Sulphimide	Solvent	T/°C	10^5k/s^{-1}	$\Delta H^{\ddagger}$ [d]/ kcal mol^{-1}	$\Delta S^{\ddagger}$ [d]/ cal mol^{-1} K^{-1}
(IX)	CHCl$_3$	65	0.807 ± 0.04	23.6	−12.3
		75	2.22 ± 0.03		
		75	2.23 ± 0.03 [b]		
		85	6.08 ± 0.10		
	C$_6$H$_6$	75	1.46 ± 0.04		
		85	4.03 ± 0.06		
		85	4.18 ± 0.07 [c]		
	EtOH	75	1.70 ± 0.03		
		85	5.50 ± 0.08		
	Pyridine	75	1.68 ± 0.06		
		85	5.62 ± 0.04		
(VIII)	CHCl$_3$	65	6.42 ± 0.02		
		75	19.8 ± 0.5		
(VIc)	CHCl$_3$	75	3.61 ± 0.04	27.6	0.0 [e]
(VIIc)	CHCl$_3$	75	0.545 ± 0.008	30.0	3.3 [f]

[a] Rates were measured in 0.06M solution except where noted. [b] In 0.102M solution. [c] In 0.182M solution. [d] Activation para-meters were calculated from rate constants obtained at three different temperatures. [e] Calculated from data in Table 1. [f] Calcul-ated from data in Table 2.

that of the different atoms attached directly to sulphur, this explanation of the small difference of rates due to the substituent on nitrogen is quite rational.

As for the large stabilisation of the sulphoxide, two factors could contribute in addition to the electro-negativity effect. Greater electron repulsion may result between the unshared electron pairs on the sulphur and oxygen (three lone pairs) atoms of the sulphoxide in going from the pyramidal ground state to the planar transition state than for the nitrogen (two lone pairs) of the sulphimide or carbon (one lone pair) of the

that the rate of racemisation does not vary when the concentration of sulphimide (IX) is increased about three-fold in benzene solution (see Table 3), since if intermolecular interaction exists, the rate of racemis-ation should be changed by changing the concentration. Furthermore, sulphimide (IX) was confirmed to exist as a monomer by the freezing point depression method.[20]

On the other hand, an intramolecular hydrogen bond would be formed between the oxygen atom of the o-methoxy-group and the hydrogen atom of the imino-group. As illustrated in Scheme 2, the dihedral angle

[19] C. E. Mixan and J. B. Lambert, J. Org. Chem., 1973, 38, 1350.

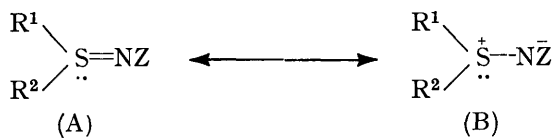[20] M. Moriyama, K. Kuriyama, T. Iwata, N. Furukawa, T. Numata, and S. Oae, Chemistry Letters, 1976, 363.

between the sp^3 lone pair electrons of the sulphur atom and the sp^2 lone pair electrons of nitrogen is known to be ca. 180° by X-ray analysis;[14,16] this conformation

ground state   transition state

SCHEME 2
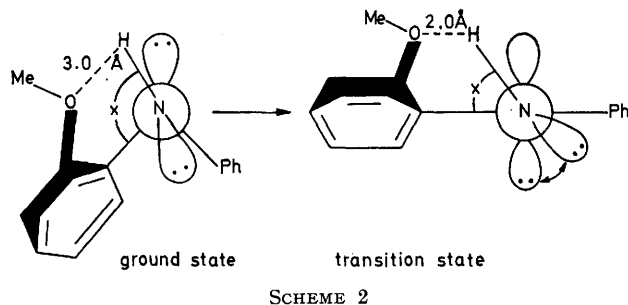
would minimise both lone pair–lone pair electron repulsion and steric hindrance of the substituents. In a planar transition state, the dihedral angle would be diminished by lone pair electron repulsion between the p lone pair electrons of the sulphur atom and the sp^2 lone pair electrons of nitrogen. Thus, the distance (ca. 3.0 Å) between the o-methoxy-oxygen atom and the imino-hydrogen atom in the pyramidal ground state may be reduced (ca. 2.0 Å) in the transition state, and hence intramolecular hydrogen bonding between these groups would become effective in the transition state.[21] Consequently, intramolecular association seems more realistic in accounting for the unusual thermal racemisation of sulphimide (IX).

The pyramidal inversion of the sulphimides was investigated in terms of the $S^{IV}-N$ bond character. Interestingly, the rate of pyramidal inversion decreases as the frequency of the i.r. band characteristic of the $S^{IV}-N$ bond decreases (Figure).

The electronic nature of the $S^{IV}-N$ bond of sulphimides is an interesting problem. At present, a resonance hybrid of forms (A) and (B) is considered reasonable based on the data obtained from i.r., u.v., and X-ray

(A)   (B)

analyses,[14,22-25] though the semi-polar form is predominant, e.g. 55% for N-sulphonyl derivatives (VI).[19]

The importance of structure (B) may be enhanced by electron-withdrawing substituents Z, and this may decrease the $S^{IV}-N$ stretching frequency. Indeed, the order of the stretching frequencies for N-alkyl- (1 091 cm^{-1}), N-carbamoyl- (960—1 039 cm^{-1}),[26] N-sulphonyl- (950 cm^{-1}), and N-acyl-sulphimides (794—815 cm^{-1})[27,28] are qualitatively in accord with the values expected on the basis of the above considerations, though sulphimide (IX) exhibits a lower frequency (907 cm^{-1})[29,30] than the N-sulphonylsulphimides (VI) contrary to expectation. This decrease in frequency [a higher contribution from structure (B)] corresponds to the increase of the pyramidal inversion barrier by electron-withdrawing substituents.

The equation derived from the straight line in the Figure, log $k = 0.005\ 47\nu_{S-N} - 9.63$, can be used to predict the $S^{IV}-N$ stretching frequency from the rate constant for racemisation of other N-substituted sulphimides, and vice versa.

EXPERIMENTAL

Preparation of Optically Active S-o-Methoxyphenyl S-Phenyl Sulphimides.—The title compounds were prepared by the method described in the literature.[31,32] Specific rotations in chloroform (c ca. 1) at 22—27 °C are as follows: (VIa) -32; (VIb) -94.8; (VIc) -77.2; (VId) -73.8; (VIIa) -145; (VIIb) -74; (VIIc) -76; (VIId) -61.3; (VIII) -135; and (IX) $-64.1°$.

Kinetic Procedure.—A solution (2 ml) containing an optically active sulphimide was sealed in a 1.0 cm cell after substitution of air by dry nitrogen. The sealed cell was placed in a bath maintained to within ±0.2 °C. After the cell was returned rapidly to room temperature, the rate was measured directly by checking the rotation (α) using a Yanagimoto OR-10 polarimeter. The rotation was measured 4—5 times and the average value of α was used in the calculation (average deviation $\pm0.002°$). At the completion of runs, the solutions were checked for decomposition by t.l.c., n.m.r., and i.r. The pseudo-first-order rate constants were evaluated by the equation, log $\alpha_0/\alpha_t = kt/2.303$, where α_0 and α_t are the rotation at times 0 and t, respectively. The rate constants were determined from 2—4 independent runs and the average value was used.

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[29] N. Furukawa, T. Omata, T. Yoshimura, T. Aida, and S. Oae, Tetrahedron Letters, 1972, 1619.
[30] The same tendency has been observed for SS-diphenyl N-(p-substituted phenyl)sulphimides, T. Yamamoto, M. Yamauchi, and M. Ookawara, Abstracts (Part II), 34th Annual Meeting of Chemical Society of Japan, Kanagawa, 1976, p. 795.
[31] M. Moriyama, S. Oae, T. Numata, and N. Furukawa, Chem. and Ind., 1976, 163.
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