Regio- and Stereo-specificity of Cycloaddition Reactions of Sulphines with Diphenylnitriliminet

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Sulphines (thione *S*-oxides) undergo cycloaddition reactions with diphenylnitrilimine to yield in a regiospecific manner 1,3,4-thiadiazoline 1-oxides, with the exception of thiofluorene *S*-oxide, which gave the other regioisomer (a 1,2,3-thiadiazoline 1-oxide) as a by-product. The products obtained from cyclisation with geometrically isomeric sulphines indicate that steric integrity is lost during the reaction. This stereomutation does not come about by sulphine isomerization prior to reaction but is caused by product equilibration afterwards. It is shown that the steric integrity is lost by ring opening–ring closure of the cycloaddition product. A ring expansion of the addition product similar to the penam–cepham conversion is described.

CYCLOADDITION reactions of cumulenes with 1,3-dipoles serve as an important source of a great variety of heterocyclic compounds.[1] In this respect cycloadditions with sulphines (thione *S*-oxides) are of special interest, since these heterocumulenes have a bent structure allowing the existence of geometrical isomerism.[2] This structural property of sulphines enables us to investigate the stereochemistry of the cyclization as well as the regiochemistry. From the synthetic point of view these cycloadditions are of interest since they lead directly to heterocyclic compounds containing the sulphoxide function.

Previously we reported on the cycloaddition reactions of sulphines with diazoalkanes,[3] nitrile oxides,[4] nitrile ylides,[5] and nitrones.[6] This paper gives a full account [7] of the cycloaddition reactions of sulphines with diphenylnitrilimine $PhC^{+}=N-\bar{N}Ph$ (DPNI).

Diphenyl sulphine (1a) gave with DPNI, generated [8] *in situ* from *N*-(α-chlorobenzylidene)-*N'*-phenylhydrazine and triethylamine, the cycloadduct (2a) in 68% yield. The structure of this adduct was assigned on the basis of spectral data, $\nu_{max.}$ 1 070 (SO) and 1 535 (C=N) cm^{-1}, combustion analysis, and independent synthesis. Oxidation of 2,4,5,5-tetraphenyl-Δ^2-1,3,4-thiadiazoline (3a) (see Scheme 1), obtained [9] from the cycloaddition of thiobenzophenone and DPNI, gave the corresponding *S*-oxide which was identical with adduct (2a). The structure of adduct (3a) was firmly established by Huisgen *et al.*[9] Sulphines (1b and c) similarly gave the adducts (2b) (62%) and (2c) (85%). The reaction of thiofluorenone *S*-oxide with DPNI was reported [7] to yield solely adduct (2d). However, in view of the deviant results obtained with this sulphine and benzonitrile oxide,[4] the reaction of (1d) and DPNI was carefully re-examined. Indeed, a second product (4) was isolated in low yield (15%) in addition to the predominant adduct (2d) (54%). The structure of the minor product (4) was apparent from the correct elemental analysis and particularly the i.r. band at 1 125 cm^{-1} (sulphinamide [10]). Chemical proof for structure (2d) was provided by the thermolytic behaviour of the corresponding sulphone (5d). Heating in benzene (80 °C) gave quantitative liberation of sulphur dioxide while benzonitrile as well as the anil (6d) were isolated in high yields. This two-fold extrusion process

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[1] H. Ulrich, 'Cycloaddition Reactions of Heterocumulenes', Academic Press, New York, 1967.

[2] J. F. King and T. Durst, *J. Amer. Chem. Soc.*, 1963, **85**, 2676; *Canad. J. Chem.*, 1966, **44**, 819; B. Zwanenburg, L. Thijs, and J. Strating, *Tetrahedron Letters*, 1967, 3453; B. Zwanenburg and J. Strating, *Quart. Reports Sulfur Chem.*, 1970, **5**, 79; B. F. Bonini, L. Lunazzi, G. Maccagnani, and G. Mazzanti, *J.C.S. Perkin I*, 1973, 2314; A. Tangerman and B. Zwanenburg, *Tetrahedron Letters*, 1973, 79; Th. W. Hummelink, *J. Cryst. Mol. Struct.*, 1974, **4**, 87, 373.

[3] B. F. Bonini, G. Maccagnani, A. Wagenaar, L. Thijs, and B. Zwanenburg, *J.C.S. Perkin I*, 1972, 2490; B. Zwanenburg, A. Wagenaar, L. Thijs, and J. Strating, *ibid.*, 1973, 73; L. Thijs, A. Wagenaar, E. M. M. van Rens, and B. Zwanenburg, *Tetrahedron Letters*, 1973, 3589.

[4] B. F. Bonini, G. Maccagnani, G. Mazzanti, L. Thijs, H. P. M. M. Ambrosius, and B. Zwanenburg, *J.C.S. Perkin I*, 1977, 1468.

[5] B. F. Bonini, G. Maccagnani, G. Mazzanti, and B. Zwanenburg, *Gazzetta*, 1977, **107**, 289.

[6] B. F. Bonini, G. Maccagnani, G. Mazzanti, P. Pedrini, and B. Zwanenburg, *Gazzetta*, 1977, **107**, 283.

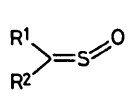
[7] B. F. Bonini, G. Maccagnani, L. Thijs, and B. Zwanenburg, *Tetrahedron Letters*, 1973, 3569.

[8] R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, 1962, **17**, 3.

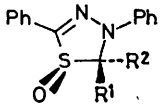
[9] R. Huisgen and W. Mack, *Chem. Ber.*, 1972, **105**, 2815.

[10] L. J. Bellamy, 'Advances in Infrared Group Frequencies', Methuen, London, 1968.

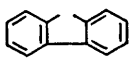
is only feasible for adduct (2d), not for (4). Similarly, the sulphone derived from (2a) gave upon heating SO_2, benzonitrile, and anil (6a) (see Scheme 1).



(1)



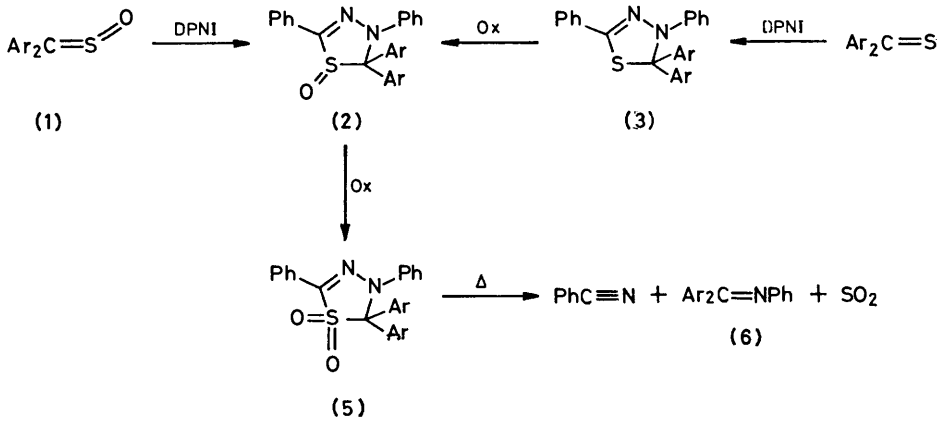
(2)

a; $R^1 = R^2 =$ Ph
b; $R^1 = R^2 = 4\text{-MeOC}_6H_4$
c; $R^1 = R^2 = 4\text{-MeC}_6H_4$
d; R^1, R^2 = 
e; R^1 = Ph, $R^2 = 2\text{-MeC}_6H_4$
f; $R^1 = 2\text{-MeC}_6H_4$, R^2 = Ph
g; R^1 = Ph, R^2 = 1-naphthyl
h; R^1 = 1-naphthyl, R^2 = Ph
i; $R^1 = 4\text{-MeC}_6H_4$, $R^2 = 4\text{-ClC}_6H_4$
j; $R^1 = 4\text{-ClC}_6H_4$, $R^2 = 4\text{-MeC}_6H_4$
k; R^1 = Ph, R^2 = PhS
l; R^1 = PhS, R^2 = Ph
m; R^1 = Ph, R^2 = Me
n; R^1 = Me, R^2 = Ph

The results with the sulphines (1a—d) show a high degree of regiospecificity for the cycloaddition with DNPI. The regiochemistry is the same as that observed for the cycloaddition reactions of DNPI and the corresponding diaryl thioketones,[9] this in spite of the fact that the distribution [11,12] and other molecular parameters [13] differ considerably. This observation, that the orientation of thioketones and its *S*-oxides in cycloaddition reactions with DNPI is the same, is consistent with the results obtained previously with other 1,3-dipoles, *viz.* diazoalkanes [3] and benzonitrile oxide.[4] The orientation in cycloadditions with heterodipolarophiles usually obeys the principle of maximum gain in σ-bond energy,[12] meaning that the reactants join in such a manner that the best compensation for the π-bond energy lost is achieved in the combined energy of the two newly formed σ-bonds. Apparently, attachment of an oxygen atom to the C=S function does not affect the outcome of this energy balance.

Having established the regiochemistry of the cycloaddition, the stereochemistry was investigated by treating geometrically isomeric sulphines with the 1,3-dipole. From the reaction of the isomers of phenyl *o*-tolyl sulphine (1e and f) with DPNI the same predominant adduct was isolated to which tentatively the *anti*-structure (2e) was assigned (see Experimental section). In both cases the n.m.r. spectrum of the crude product mixture showed in addition to the methyl signal of (2e) at δ 2.38 an absorption at δ 2.07 attributable to the methyl group of the *syn*-adduct (2f). On the basis of integration the *anti* : *syn* ratio was 9 : 1. However, the *syn*-adduct (2f) could not be isolated probably because of isomerization to the *anti*-isomer during chromatography. Attempts to prepare both adducts (2d and f) by oxidation of the parent thiadiazoline also resulted in the formation of one strongly dominating isomer which turned out to be identical with the *anti*-adduct (2e) obtained during the cycloadditions of (1e and f). Similarly, cycloaddition of the isomers (1g and h) with DPNI gave only one adduct (2g). The sterically hindered isomers of mesityl phenyl sulphine failed to react, demonstrating that the cycloaddition with DNPI is sensitive to steric hindrance as observed [4] for other 1,3-dipoles with sulphines. In order to minimize the influence of steric factors the *E*- and *Z*-isomers of *p*-chlorophenyl *p*-tolyl sulphine (1i and j) were subjected to cycloaddition with DPNI. With (1i) a mixture of the diastereoisomeric adducts (2i and j) was obtained in the ratio 1 : 1 whereas (1j) gave the product ratio of 2 : 3. Oxidation of the parent thiadiazoline gave a ratio of (2i and j) of 1 : 2. The *E*- and *Z*-isomers of phenyl phenylthio sulphine (1k and l) both yielded the same adduct (2k).

All the experiments conducted with the geometrically isomeric sulphines indicate that the steric integrity is lost during the cycloaddition. This result is surprising since



(1) (2) (3) (5) (6)

SCHEME 1

[11] J. P. Snyder and D. N. Harpp, *J.C.S. Chem. Comm.*, 1972, 1305; F. Bernardi, G. Maccagnani, and A. Mangini, *Anales de Quim.*, 1974, **70**, 1199; J. van Lierop, A. van der Avoird, and B. Zwanenburg, *Tetrahedron*, 1977, **33**, 359.

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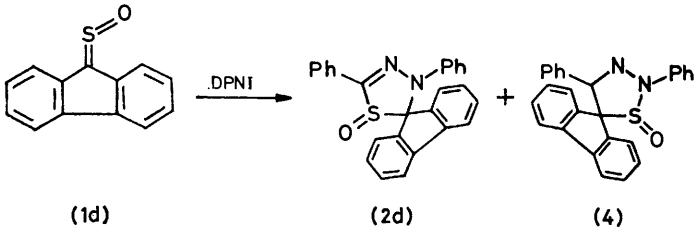
[13] J. P. Snyder, *J. Org. Chem.*, 1973, **38**, 3965.

other 1,3-dipoles such as diazoalkanes [14] and benzonitrile oxide [4] showed a stereospecific cyclization. In view of this an explanation invoking a non-concerted cycloaddition process seems rather unlikely. On the other hand,



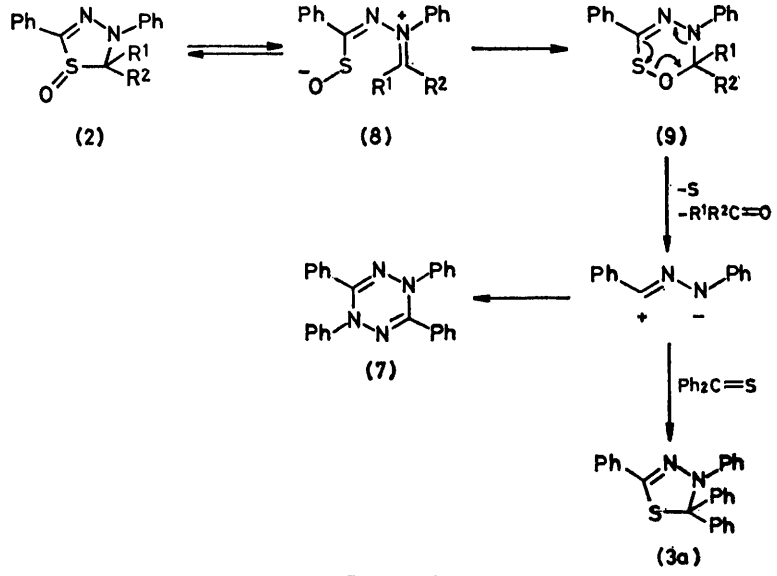
SCHEME 2

both isomerization of the sulphines prior to cycloaddition and product equilibration afterwards would account for the loss of steric integrity.

Pyramidal inversion of the sulphoxide function [15,16] in the adducts (2) seems unlikely, since the configurational stability of sulphoxides is usually rather high. In this case interaction of the imine bond and/or the lone pair at N-4 with the sulphoxide function may lower the inversion barrier.[15]

The arrangement of atoms –N(4)–C(5)–S(=O) present in the adducts is also encountered in the five-membered ring of the penicillin skeleton. It is therefore suggested that the stereomutation of (2) bears some resemblance to the conversion of (*R*)-penicillin sulphoxide into the (*S*)-sulphoxide,[17] which is believed to proceed *via* the intermediacy of a ring-opened product,[18] *viz.* a sulphenic acid. In the present case the ring opening–ring closure (2) ⇄ (8) is thought to be responsible for the loss of stereospecificity in the cycloaddition.

In order to provide evidence for this mechanism the



SCHEME 3

Isomerization of sulphines in the presence of triethylamine was observed [equilibrium ratio 88 : 12 for (1e) : (1f) and 69 : 31 for (1k) : (1l)]. Reliable information on isomerization during cyclization can be provided by recovering sulphines from incomplete reactions. Such experiments were conducted with (1e, f, k, and l); in all cases the recovered sulphine had the original configuration. Therefore, isomerization prior to cycloaddition is not a likely explanation for the non-stereospecificity.

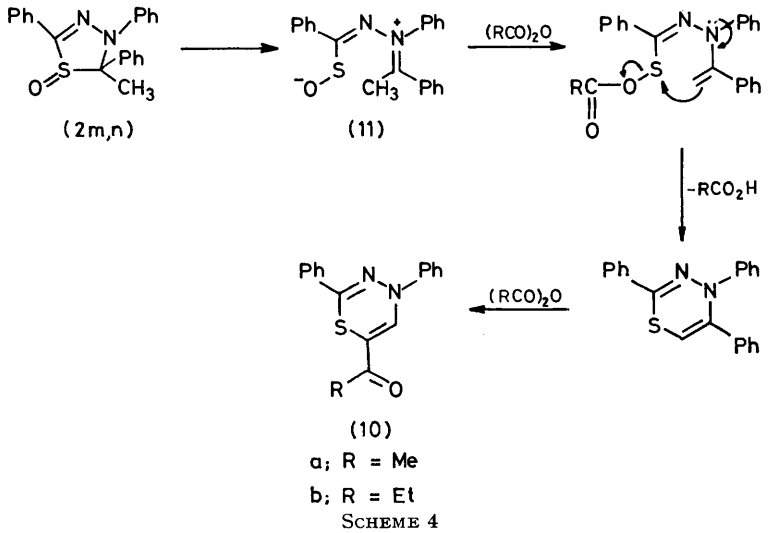
Support for product equilibration was provided by the equilibration of mixtures of (2i and j) in the ratios 1 : 1 and 1 : 2, on standing or heating, to give the ratio 3 : 2. Similar behaviour was found for the isomeric adducts (2k and l).

mixture of adducts of (2m and n), obtained from the cycloaddition of *E*- + *Z*-methyl phenyl sulphine (1m and n), was treated with trimethylsilyl chloride and hexamethyldisilazane. Similar conditions were used to trap [19] the intermediate sulphenic acid during the equilibration of penicillin sulphoxides. However, no silylated sulphenate was isolated but the dimer of the 1,3-dipole, *viz.* (7), instead. The formation of (7) is rationalized as outlined in Scheme 3. The ring-opened sulphenate (8) can close in two fashions. Reaction of the ambident sulphenate at the sulphur atom leads to the five-membered ring (2), whereas closure *via* the oxygen atom produces the six-membered ring (9), which upon fragmentation gives DPNI, the ketone $R^1R^2C{=}O$, and sulphur. Dimerization of DPNI leads to (7). Heating the adduct (2a)

[14] L. Thijs, A. Wagenaar, E. M. M. van Rens, and B. Zwanenburg, *Tetrahedron Letters*, 1973, 3589.
[15] A. Rauk, L. C. Allen, and K. Mislow, *Angew. Chem.*, 1970, **82**, 453; A. Rauk, J. D. Andose, W. G. Frick, R. Tang, and K. Mislow, *J. Amer. Chem. Soc.*, 1971, **93**, 6507.
[16] P. H. Lauer, ' Steric Aspects of Sulfur Chemistry,' ed. A. Senning, Marcel Dekker, New York, 1972, vol. 3.
[17] D. H. R. Barton, F. Comer, and P. G. Sammes, *J. Amer. Chem. Soc.*, 1969, **91**, 1529; R. A. Archer and P. V. De Marco, *ibid.*, p. 1530.
[18] T. S. Chou, J. R. Burgtorf, A. L. Ellis, S. R. Lammert, and S. P. Kukolja, *J. Amer. Chem. Soc.*, 1974, **96**, 1609.
[19] T. S. Chou, *Tetrahedron Letters*, 1974, 725.

in the presence of thiobenzophenone provided a means to trap DPNI to yield the product (3a) in addition to benzophenone and sulphur.*

Confirmatory evidence for the suggested equilibration *via* (2) ⇌ (8) was obtained by treating the adduct mixture (2m and n) with acetic anhydride in benzene for 6 h at 80 °C. Thiadiazine (10a) was isolated in 70% yield. The structure of this product was established on the basis of a correct elemental analysis and spectral data (i.r., n.m.r., and mass). The formation of (10a) is readily explained as outlined in Scheme 4. The primary



SCHEME 4

ring-opened product (11) [*cf.* (8)] is trapped by acetic anhydride as a mixed anhydride. The enamine function reacts in a nucleophilic fashion with the sulphur atom now bearing a good leaving group. The thiadiazine thus formed is acylated by acetic anhydride as expected for the enamine part of this molecule.[20] Propionic anhydride similarly gave product (10b) in 60% yield.

The formation of the six-membered ring (10) bears analogy with the conversion of penicillin sulphoxide to cephalosporin (penam–cepham conversion).[21]

In conclusion, sulphines react with DPNI to give thiadiazoline *S*-oxides with a high degree of regiospecificity. The cycloaddition is non-stereospecific due to equilibration of the adducts *via* a ring opening–ring closure mechanism.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 257 grating spectrometer. N.m.r. spectra were obtained with JEOL C-60HL or Varian HA 100 and T-60 spectrometers (Me_4Si as internal standard). Mass spectra were recorded with a JEOL JMS D100 spectrometer.

All experiments were carried out under nitrogen and with dry solvents. *N*-(α-Chlorobenzylidene)-*N'*-phenylhydrazine was prepared as described in ref. 8. Sulphines were prepared as reported previously [22] by oxidation of the corresponding thiocarbonyl compounds with *m*-chloroperbenzoic acid.

2,4,5,5-*Tetraphenyl*-Δ²-1,3,4-*thiadiazoline* 1-*Oxide* (2a).—A solution of triethylamine (1.00 g, 10.0 mmol) in benzene (5 ml) was added slowly to a stirred solution of diphenyl sulphine (1a) (1.07 g, 5.0 mmol) and DPNI precursor (1.15 g, 5.0 mmol) in benzene (25 ml). After heating at reflux for 0.5 h, the mixture was allowed to react at 20 °C for 20 h. The precipitated Et_3NHCl (0.55 g) was filtered off and the filtrate concentrated *in vacuo*. The residue was chromatographed on a silica gel column. Elution with benzene gave unchanged precursor (0.20 g); elution with benzene–ether (1 : 1) gave the *adduct* (2a) (1.40 g, 68%), m.p. 167—168 °C (from methanol) (Found: C, 76.8; H, 4.75; N, 6.8; S, 7.85. $C_{26}H_{20}N_2OS$ requires C, 76.45; H, 4.9; N, 6.85; S, 7.85%), $\nu_{max.}$ (CCl_4) 1 070 cm^{-1} (SO), δ ($CDCl_3$) 6.8—8.1 (m, ArH). The adduct (2a) was identical in all respects with that prepared by cycloaddition of diphenylnitrilimine and thiobenzophenone [23] and subsequent oxidation as follows. A solution of monoperphthalic acid (mPPA) (0.45 mmol) was added at 0 °C to the adduct (3a) (0.18 g, 0.46 mmol) in ether (10 ml). After 24 h the phthalic acid was filtered off, the filtrate was concentrated and the residue was chromatographed on silica. Elution with benzene afforded adduct (2a) (0.17 g, 91%).

2,4,5,5-*Tetraphenyl*-Δ²-1,3,4-*thiadiazoline* 1,1-*Dioxide* (5a).—Adduct (2a) (0.7 g, 1.69 mmol) in ether (30 ml) was treated with mPPA (8.9 mmol) for 60 h at 5 °C. Removal of the phthalic acid, concentration of the filtrated *in vacuo*, and chromatography on silica gel gave the *sulphone* (5a) (0.44 g, 61%), m.p. 118—119 °C [from CH_2Cl_2–hexane (1 : 1)] (Found: C, 72.8; H, 4.9; N, 6.45; S, 7.35. $C_{26}H_{20}N_2SO_2$

* An alternative explanation for the formation of (3a) from (2a) and thiobenzophenone could be a retro-1,3-dipolar cycloaddition reaction giving DPNI and (1a). Preferential cyclization with thiobenzophenone would then give (2a). However, the sulphine (1a) which is stable under these conditions, was not detected. Therefore, this rationale is rejected.

[20] P. W. Hickmott and H. Suschitzky, *Chem. and Ind.*, 1970, 1188.

[21] P. G. Sammes, *Chem. Rev.*, 1976, **76**, 113.

[22] B. Zwanenburg, L. Thijs, and J. Strating, *Rec. Trav. chim.*, 1967, **86**, 577; B. F. Bonini, S. Ghersetti, G. Maccagnani, and G. Mazzanti, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 419; B. Zwanenburg, L. Thijs, and J. Strating, *Rec. Trav. chim.*, 1971, **90**, 614; B. Zwanenburg, L. Thijs, and A. Tangerman, *Tetrahedron*, 1971, **27**, 1731; A. Tangerman and B. Zwanenburg, *J.C.S. Perkin II*, 1974, 1413.

[23] R. Huisgen, R. Grashey, M. Seidel, H. Knupfer, and R. Schmidt, *Annalen*, 1962, **658**, 169.

requires C, 73.55; H, 4.75; N, 6.6; S, 7.55%), $\nu_{max.}$ (CCl_4) 1 125 and 1 330 cm^{-1} (SO_2), δ ($CDCl_3$) 6.8—8.1 (m, ArH). Heating of (5a) (43.11 mg, 0.1015 mmol) for 15 min in benzene (5 ml) at 80 °C gave benzonitrile and *N*-diphenylmethyleneaniline (6a) in quantitative yield. The yields were determined by g.l.c. analysis (column 20% SE 30; 250°). The SO_2 liberated during the thermolysis was trapped in 0.1N-NaOH (50 ml). Titration of the absorbed SO_2 with I_2 indicated a 100% yield.

2,4-Diphenyl-5,5-bis-(p-*methoxyphenyl*)-Δ²-1,3,4-*thiadiazoline* 1-*Oxide* (2b).—As described for (2a), bis-(*p*-methoxyphenyl) sulphine (1b) (0.67 g, 2.46 mmol) gave the *adduct* (2b) (0.71 g, 62%), m.p. 137—138 °C (from methanol) (Found: C, 71.4; H, 4.9; N, 5.7; S, 6.9. $C_{28}H_{24}N_2O_3S$ requires C, 71.75; H, 5.15; N, 5.95; S, 6.85%), $\nu_{max.}$ (CCl_4) 1 070 cm^{-1} (SO), δ ($CDCl_3$) 3.81 (3 H, s, OMe), 3.86 (3 H, s, OMe), and 6.5—8.1 (18 H, m, ArH).

*2,4-Diphenyl-5,5-di-*p-*tolyl-*Δ²-1,3,4-*thiadiazoline* 1-*Oxide* (2c).—As decribed for (2a), di-*p*-tolyl sulphine (1c) (1.50 g, 6.20 mmol) gave the *adduct* (2c) (2.30 g, 85%), m.p. 152—153 °C (from methanol) (Found: C, 77.6; H, 5.5; N, 6.5; S, 7.2. $C_{28}H_{24}N_2OS$ requires C, 77.0; H, 5.55; N, 6.4; S, 7.35%), $\nu_{max.}$ (CCl_4) 1 070 cm^{-1} (SO), δ ($CDCl_3$) 2.30 (3 H, s, Me), 2.36 (3 H, s, Me), and 6.9—8.2 (18 H, m, ArH). As described for (2a), adduct (2c) (0.20 g, 0.46 mmol) gave upon oxidation with mPPa (1.5 mmol) *2,4-diphenyl-5,5-di-*(p-*tolyl-*Δ²-1,3,4-*thiadiazoline* 1,1-*dioxide* (5c) (0.03 g, 14%), m.p. 107—108 °C (Found: C, 73.2; H, 5.4; N, 6.05. $C_{28}H_{24}N_2O_2S$ requires C, 74.3; H, 5.35; N, 6.2%), $\nu_{max.}$ (CCl_4) 1 125 and 1 330 cm^{-1} (SO_2), δ ($CDCl_3$) 2.37 (6 H, s, Me) and 6.8—8.3 (18 H, m, ArH). During the isolation and purification spontaneous fragmentation of (5c) was observed. Thermolysis of (5c) gave SO_2, benzonitrile, and anil (6c).

Cycloaddition with Thiofluorenone S-*Oxide* (1d).—As described for (2a), sulphine (1d) (1.06 g, 5.0 mmol), triethylamine (1.0 g, 10.0 mmol), and DPNI precursor (1.15 g, 10.0 mmol) gave after elution with benzene fluorenone (0.2 g, 22%) and *2′,4′-diphenylfluorene-9-spiro-5′-*Δ³′-*1′,2′,3′-thiadiazoline* 1′-*oxide* (4) (0.3 g, 15%), m.p. 154—155 °C (from methanol) (Found: C, 76.0; H, 4.35; N, 6.95%; *M*, 406.2061. $C_{26}H_{18}N_2OS$ requires C, 76.8; H, 4.45; N, 6.9%; *M*, 406.2045), $\nu_{max.}$ (CCl_4) 1 125 cm^{-1} (SO), δ (CS_2) 6.6—8.2 (*m*, ArH), *m/e* 406 (M^+, 87%), 358 (M^+ − SO, 100), and 253 (M^+ − [PhNNSO], 79%). Elution with benzene–ether (10 : 1) afforded *2′,4′-diphenylfluorene-9-spiro-5′-*Δ²′-*1′,3′,4′-thiadiazoline* 1′-*oxide* (2d) (1.1 g, 54%), m.p. 173—174 °C (from ethanol) (Found: C, 76.65; H, 4.5; N, 6.9; S, 7.9. $C_{26}H_{18}N_2OS$ requires C, 76.8; H, 4.45; N. 6.9; S, 7.9%), $\nu_{max.}$ (CCl_4) 1 070 cm^{-1} (SO), δ (CS_2) 6.6—8.2 (m, ArH). As described for (2a), oxidation of (2d) 0.25 g, 1.36 mmol) with mPPA (3.6 mmol) for 6 days at 5 °C gave the *sulphone* (5d) (0.17 g, 30%), m.p. 146—147 °C [from CH_2Cl_2–hexane (1 : 1)] (Found: C, 73.3; H, 4.35; N, 6.6; S, 7.6. $C_{26}H_{18}N_2O_2S$ requires C, 73.9; H, 4.3; N, 6.65; S, 7.6%), $\nu_{max.}$ (CCl_4) 1 335 and 1 135 cm^{-1} (SO_2) and unchanged sulphoxide (2d). Thermolysis of (5d) afforded SO_2, benzonitrile, and fluorenone anil [24] (6d).

Cycloaddition with Sulphines (1e *and* f).—The reaction with the *E*-sulphine (1e) (0.82 g, 3.6 mmol) was carried out as described for (1a). After heating for 0.5 h, the mixture was stirred for 48 h at 20 °C. After filtration, evaporation of the solvent, and chromatography on silica [benzene–ether (1 : 1)] a 9 : 1 mixture of the adducts (2e and f) (1.10 g, 72%) was obtained. Upon crystallization from methanol only *adduct* (2e) was obtained, m.p. 132—133 °C (Found: C, 75.85; H, 5.3; N, 6.6; S, 7.6. $C_{27}H_{22}N_2OS$ requires C, 76.75; H, 5.25; N, 6.65; S, 7.6%), $\nu_{max.}$ (CCl_4) 1 070 cm^{-1} (SO), δ (CS_2) 2.38 (3 H, s, Me) and 6.7—8.0 (19 H, m, ArH). The minor component having a methyl signal at δ 2.07 (CS_2) could not be isolated. The tentative assignment of the *anti*-structure to the more stable isomer (2e) and the *syn*-structure (2f) was based on the position of the methyl signals in comparison with that of the parent compound (3e), δ 2.27.

The reaction with the *Z*-isomer (1f) was performed in the same manner. After chromatography and crystallization from methanol adduct (2e) was isolated (54%). As described for (3a), 2-methylthiobenzophenone (3.0 g, 14.2 mmol) gave *2,4,5-triphenyl-5-tolyl-*Δ²-*1,3,4-thiadiazoline* (3e) (3.25 g, 57%), m.p. 173—174 °C (from methanol) (Found: C, 80.1; H, 5.6; N, 7.8. $C_{27}H_{22}N_2S$ requires C, 79.8; H, 5.45; N, 6.9%), δ(CS_2) 2.27 (3 H, s, Me) and 6.5—8.0 (19 H, m, ArH). Adduct (3e) (2.5 g, 6.1 mmol) was oxidized with mPPA (6.1 mmol) in ether (50 ml) for 3 days at 5 °C. After removal of the phthalic acid and evaporation of the solvent, the product was chromatographed on alumina. Elution with benzene gave starting material (0.55 g), elution with benzene–ether (10 : 1) gave a 10 : 1 mixture of (2e and f). The ratio of the products was determined by the integration of the 2-Me signals at δ (CS_2) 2.07 and 2.38 and is essentially the same as in the cycloaddition of sulphines (1e and f).

Oxidation of adduct (2e) (0.22 g, 0.48 mmol) with *m*-chloroperbenzoic acid (0.200 g, 1.00 mmol) in ether–$CHCl_3$ (3 : 1; 20 ml) for 16 h at 20 °C gave, after removal of *m*-chlorobenzoic acid with aqueous $NaHCO_3$ and chromatography, benzonitrile (0.35 g, 71%) and *anil* (6e) (0.105 g, 80%), m.p. 100—103 °C (from methanol) (Found: C, 88.5; H, 6.3; N, 5.0. $C_{20}H_{17}N$ requires C, 88.55; H, 6.25; N, 5.15%), $\nu_{max.}$ (KBr) 1 620 cm^{-1} (C=N), δ ($CDCl_3$) 2.01 (3 H, s, Me) and 6.65—7.80 (14 H, m, ArH). The intermediate sulphone (5e) fragmented spontaneously during the oxidation.

Isomerization of Sulphines (1e *and* f).—*E*-Sulphine (1e) (0.40 g, 1.75 mmol), triethylamine (0.5 ml), and Et_3N,HCl (0.30 g, 2.20 mmol) in benzene (15 ml) were heated at reflux for 0.5 h. After standing for 24 h at 20 °C, the mixture was filtered and concentrated *in vacuo*. The relative amounts of *E*- and *Z*-sulphine were determined by the integration of the methyl signals at δ 2.14 and 2.24. The *E* : *Z* ratio was 88 : 12 after 24 h. When *Z*-sulphine (1f) was used instead the *E* : *Z* ratio was 84 : 16 after 24 h.

Cycloaddition with Sulphines (1g *and* h).—As described for (2a), sulphine (1g) (0.080 g, 0.30 mmol), DPNI precursor (0.100 g, 0.43 mmol), and triethylamine (0.10 g, 1.00 mmol) in benzene (15 ml) gave after chromatography *adduct* (2g) (0.117 g, 85%), m.p. 154—155 °C (from dioxan) (Found: C, 77.7; H, 4.7; N, 6.0. $C_{30}H_{22}N_2OS$ requires C, 78.6; H, 4.85; N, 6.1%), $\nu_{max.}$ (KBr) 1 060 cm^{-1} (SO), δ ($CDCl_3$) 6.66—8.01 (18 H, m, ArH) and 8.01—8.44 (4 H, m, ArH). Similarly sulphine (1h) (0.180 g, 0.68 mmol) gave adduct (2g) (0.200 g, 64%), which appeared to be identical in all respects with the product obtained from the cyclization of sulphine (1g).

Cycloaddition with Sulphines (1i *and* j).—Sulphine (1i) (0.200 g, 0.76 mmol) was treated with DPNI precursor (1.00 mmol) in the presence of triethylamine (0.20 g, 2.00 mmol) in benzene (20 ml) as described for (2a). After standing for 3 days at 20 °C the mixture was worked up in the usual way to give a 1 : 1 mixture of adducts (2i and j) (0.312 g, 90%)

[24] G. Reddelieu, *Ber.*, 1910, **42**, 4760.

as an oil, $\nu_{max.}$ (neat) 1 065 cm^{-1} (SO), δ ($CDCl_3$) 2.58 and 2.65 (3 H, s, ratio 1 : 1, Me), 7.0—7.7 (16 H, m, ArH), and 7.0—8.2 (2 H, m, ArH). A solution of (2i and j), ratio 1 : 1, in chloroform changed upon standing or heating at reflux to a ratio of 2 : 3. Sulphine (1j) (0.24 g, 0.91 mmol) in benzene (20 ml) gave, as for (1i), a 2 : 3 ratio of adducts (2i and j). Efforts to separate (2i and j) were unsuccessful. The adducts (2i and j) were prepared independently by oxidation of (3i). The latter was obtained by cyclization of 4-chloro-4′-methylthiobenzophenone (0.54 g, 2.20 mmol) with DPNI precursor (0.507 g, 2.20 mmol) and triethylamine (0.30 g, 3.00 mmol) in benzene (40 ml). After standing for 24 h at 20 °C the mixture was filtered, the filtrate was concentrated *in vacuo* and the residue was crystallized from ethyl acetate–MeOH (10 : 1) to give thiadiazoline (3i) (0.69 g, 91%), m.p. 141—144 °C, δ ($CDCl_3$) 2.70 (3 H, s, Me) and 7.0—8.1 (18 H, m, ArH). Oxidation of (3i) (0.30 g, 0.68 mmol) was performed by treatment for 2 h at 0 °C with *m*-chloroperbenzoic acid (0.13 g, 0.68 mmol) in $CHCl_3$–ether (1 : 1; 30 ml). After standing for 12 h at 20 °C *m*-chlorobenzoic acid was removed with aqueous $NaHCO_3$ and the mixture was chromatographed (preparative t.l.c., development with benzene, elution with ether) to afford adducts (2i and j) (0.30 g, 97%) in the ratio of 1 : 2. On standing the ratio changed to 2 : 3, as determined by integration of the methyl signals at δ 2.58 and 2.65. The assignment of these signals to (2i and j) is arbitrary.

Cycloaddition with Sulphines (1k *and* l).—As described for (2a), a 3 : 1 mixture of sulphines (1k and l) (0.35 g, 2.13 mmol) gave one adduct (2k) (0.87 g, 93%). It is assumed that the *anti*-isomer (2k) is thermodynamically more stable because of less steric hindrance. An analytical *sample* of (2k) was obtained by recrystallization from methanol, m.p 163—166 °C (decomp.) (Found: C, 70.7; H, 4.5; N, 6.4; S, 14.5. $C_{25}H_{20}N_2OS_2$ requires C, 70.9; H, 4.6; N, 6.35; S, 14.55%), $\nu_{max.}$ (KBr) 1 060 cm^{-1} (SO), δ ($CDCl_3$) 7.1—8.3 (m, ArH). When the cycloaddition was carried out with either the pure *E*- or *Z*-isomer one adduct was isolated. When the reaction of the *E*-isomer (1k) with DPNI was worked up after an incomplete reaction, the adduct (2k) (35%) as well as the starting sulphine (59%) were isolated. The geometry of the recovered sulphine was completely (>98%) retained, as determined by n.m.r. and t.l.c. Similarly, in case of the *Z*-isomer (1l), the adduct (2k) (33%) and sulphine (1l) (57%) were obtained. The n.m.r. spectrum as well as t.l.c. showed that the geometry of the recovered sulphine was completely (>98%) unchanged.

Isomerization of Sulphines (1k *and* l).—A solution of sulphine (1k) (0.10 g, 0.44 mmol) and triethylamine (0.10 g, 1.0 mmol) in benzene (5 ml) was allowed to stand at 20 °C. After removal of the volatiles the ratio of sulphines (1k and l) was determined by n.m.r. After standing for 12 h no isomerization was detected, but after 4 days the ratio of (1k and l) was 69 : 31. Similarly, the *Z*-isomer (1l) equilibrated to the same ratio (69 : 31) of the *E*- and *Z*-isomers.

Methyl Phenyl Sulphine (1m *and* n).—A solution of mPPA (22.0 mmol) in ether was added slowly at 0 °C to a stirred solution of thioacetophenone [25] (6.0 g, 44.1 mmol) in ether (60 ml). The precipitated phthalic acid was removed by filtration, the filtrate was concentrated, and the residue was chromatographed on a silica gel column. Elution with benzene gave the excess of thione and acetophenone; further elution with benzene–ethyl acetate (10 : 1) afforded *methyl phenyl sulphine* (1.6 g, 48%) as a 5 : 1 mixture of the *Z*- and *E*-isomers (Found: C, 63.4; H, 5.2; S, 21.3. C_8H_8OS requires C, 63.1; H, 5.3; S, 21.05%), $\nu_{max.}$ (CS_2) 1 070 and 1 090 cm^{-1} (CSO), δ (CS_2) 2.16 and 2.47 (3 H, s, ratio 1 : 5, Me) and 7.1—7.2 (5 H, m, ArH). The geometry of these sulphines was determined by the chemical shifts in C_6D_6 (ASIS),[26]

Cycloaddition with the Sulphines (1m *and* n).—A mixture of sulphines (1m and n) (*E* : *Z* ratio 1 : 5) (1.5 g, 10.0 mmol) was treated with DPNI as described for (1a). After standing for 35 h the reaction mixture was filtered, the solvent was removed, and the residue was chromatographed on a silica gel column. Elution with benzene gave DNPI precursor (0.9 g). Elution with benzene–ether (10 : 1) gave acetophenone and *adducts* (2m and n) (0.92 g, 44%), *Z* : *E* ratio 2 : 5, m.p. 160—169 °C (Found: C, 72.5; H, 5.2; N, 7.9; S, 9.2. $C_{21}H_{18}N_2OS$ requires C, 72.8; H, 5.25; N, 8.05; S, 9.25%), $\nu_{max.}$ (KBr) 1 055 cm^{-1} (SO), δ ($CDCl_3$) 1.80 and 2.01 (3 H, s, ratio 2 : 5) and 6.7—8.0 (15 H, m, ArH), *m/e* 346 (M^+), 330 ($M^+ - O$) and 315 ($M^+ - OMe$). The major isomer with the methyl signal absorbing at the lowest field (δ 2.01) has the *anti*-structure (2n) (deshielding of methyl by the adjacent sulphoxide function). The adducts (2m and n) were also obtained as follows. Thioacetophenone (3.40 g, 25.0 mmol) was treated with DPNI precursor (5.76 g, 25.0 mmol) and triethylamine (5.05 g, 50.0 mmol) in benzene (150 ml). After stirring for 24 h at 20 °C the mixture was worked up in the usual way. Elution with light petroleum (b.p. 60—80 °C) gave unchanged precursor (1.2 g) and with benzene gave *5-methyl-3,4,5-triphenyl-Δ²-1,3,4-thiadiazoline* (3m) (2.8 g, 43%), m.p. 84 °C (from ethanol) (Found: C, 75.95; H, 5.55; N, 8.35. $C_{21}H_{18}N_2S$ requires C, 76.3; H, 5.5; N, 8.5%), δ (CS_2) 2.13 (3 H, s, Me) and 6.8—8.0 (15 H, m, ArH). Oxidation of adduct (3m) (0.9 g, 2.73 mmol) with *m*-chloroperbenzoic acid (0.55 g, 2.73 mmol) at −30 °C for 2 h in ether (30 ml) gave after filtration the adducts (2m and n) (0.62 g), in the ratio of 3.7 : 1. The mother liquor afforded, after removal of the acid and solvents, a second crop of adducts (2m and n) (0.1 g, total yield 76%).

Silylation of Adducts (2m *and* n).—Adducts (2m and n) (ratio 1 : 5; 0.20 g, 0.59 mmol) in benzene (20 ml) were treated with Me_3SiCl (1.0 ml). After stirring for 3 h at 20 °C the mixture was filtered and the filtrate was concentrated and chromatographed (preparative t.l.c., development with benzene, elution with ether), affording acetophenone (0.030 g, 40%) and 1,3,4,5-tetraphenyl-1,2,4,5-tetrazine (7) (0.040 g, 36%). The product obtained in this reaction was identical in all respects with the dimer [8] of DPNI.

Trapping of the Intermediate Sulphenic Acid.—A mixture of adducts (2m and n) (0.40 g, 1.16 mmol) and acetic anhydride (12 ml) in benzene (40 ml) was heated at reflux. After 6 h the solvent was removed and the residue was chromatographed (preparative t.l.c., development with benzene, elution with ether) to give *6-acetyl-2,4,5-triphenyl-1,3,4-thiadiazine* (10a) (0.30 g, 70%), m.p. 129—132 °C (from methanol) (Found: C, 74.4; H, 4.8; N, 7.6. $C_{23}H_{18}N_2OS$ requires C, 74.55; H, 4.9; N, 7.55%), $\nu_{max.}$ (KBr) 1 700 (CO) and 1 590 cm^{-1} (C=N), δ ($CDCl_3$) 2.04 (3 H, s, Me) and 6.4—7.4 (15 H, m, ArH), *m/e* 370 (M^+), 327 (M^+ — MeCO), 295 [M^+ — (MeCO + S)], 194 (PhC=N–NPh), and 180 (PhN=CPh).

Similarly *2,4,5-triphenyl-6-propionyl-1,3,4-thiadiazine* (10b) (0.23 g, 60%) was obtained from the adducts (2m and

[25] J. W. Scheeren, P. H. J. Ooms, and R. J. F. Nivard, *Synthesis*, 1973, 149.

[26] A. Tangerman and B. Zwanenburg, *Tetrahedron Letters*, 1973, 79.

n) (0.34 g, 1.0 mmol) and propionic anhydride (7.5 ml), m.p. 104—106 °C (from methanol) (Found: C, 74.3; H, 5.2; N, 7.3. $C_{24}H_{20}N_2OS$ requires C, 75.0; H, 5.25; N, 7.3%), $\nu_{max.}$ ($CHCl_3$) 1 700 (CO) and 1 590 cm^{-1} (C=N), δ ($CDCl_3$) 0.94 (3 H, t, J 7 Hz, Me), 2.23 (2 H, q, CH_2), and 7.0—7.7 (15 H, m, ArH), *m/e* 384 (M^+).

Reaction of Adduct (2a) *with Thiobenzophenone*.—Adduct (2a) (0.20 g, 0.48 mmol) and thiobenzophenone (0.097 g, 0.48 mmol) dissolved in benzene (15 ml) were heated at reflux for 10 h. After filtration, the filtrate was concentrated *in vacuo* and the residue was chromatographed (preparative t.l.c., development with benzene, elution with ether) to give benzophenone (0.08 g, 92%) and thiadiazoline (3a) (0.174 g, 92%), m.p. 163—164 °C (from ethanol).

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