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The Chemistry of Nitrile Sulphides

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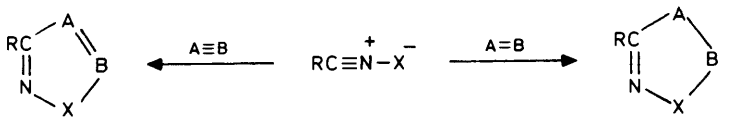
1 Introduction

1,3-Dipolar cycloaddition reactions are one of the most widely used and versatile preparative methods in heterocyclic chemistry.[1] With more than a dozen classes of 1,3-dipoles and numerous types of unsaturation able to fill the role of dipolarophile the scope for synthesis is immense.

Particular attention has been paid to the nitrilium betaines (Scheme 1). Nitrile



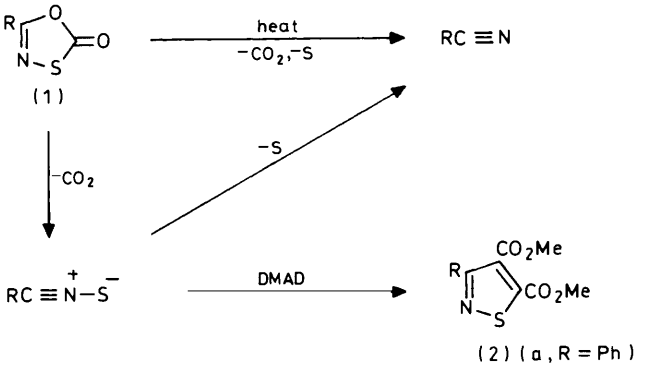
Scheme 1

oxides ($RC{\equiv}N^{+}{-}O^{-}$) have a long and varied history with the parent fulminic acid[2] and benzonitrile oxide[3] being first reported in 1800 and 1886 respectively. Their chemistry has been explored[4] in great depth: they are formed with ease from readily accessible precursors, they have been identified as transient intermediates in a variety of reactions, and cycloadditions involving numerous dipolarophiles have been accomplished. Moreover, utilizing their facile stereospecific cycloaddition to alkenes and manipulation of the resulting 2-isoxazolines (4,5-dihydroisoxazoles) they are a key component of a novel and versatile approach[5] to natural product synthesis which is attracting widespread current interest.

Nitrile imines ($RC{\equiv}N^{+}{-}N^{-}R$)[4b] and ylides ($RC{\equiv}N^{+}{-}C^{-}R_2$),[6] although possessing a less extensive literature, are nevertheless readily generated, have a wide range of cycloaddition reactions, and are often the intermediate of choice for the construction of five-membered heterocycles incorporating C=N–N and C=N–C.

Nitrile ylides, imines, and oxides all feature prominently in the recent two-volume monograph[1] (edited by Padwa) entitled '1,3-Dipolar Cycloaddition

[1] '1,3-Dipolar Cycloaddition Chemistry', ed. A. Padwa, Wiley, 1984.
[2] E. Howard, *Phil. Trans. R. Soc. London*, 1800, 204.
[3] S. Gabriel and M. Koppe, *Ber.*, 1886, **19**, 1145.
[4] (*a*) C. Grundmann and P. Grünanger, 'The Nitrile Oxides', Springer-Verlag, 1971; (*b*) P. Caramella and P. Grünanger, Ref. 1, ch. 3.
[5] (*a*) A. P. Kozikowski, *Acc. Chem. Res.*, 1984, **17**, 410; (*b*) V. Jäger, I. Müller, R. Schohe, M. Frey, R. Ehrler, B. Hafelle, and D. Schroter, *Lect. Heterocycl. Chem.*, 1985, **9**, 79.
[6] H.-J. Hansen and H. Heimgartner, Ref. 1, ch. 2.



Scheme 2

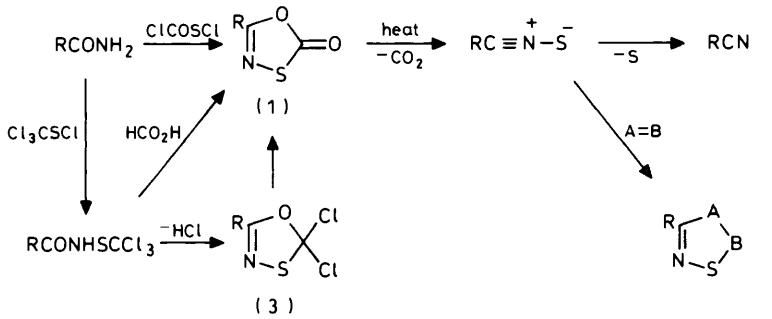
Chemistry', which has deservedly become the definitive work on the subject. In contrast nitrile sulphides ($RC{\equiv}N^{+}{-}S^{-}$), the only other nitrilium betaine for which cycloaddition reactions are known, have received much less attention and their chemistry has not previously been reviewed. By analogy, they should be uniquely well suited for the synthesis of five-membered heterocycles incorporating C=N–S. Various of these (*e.g.* 1,2,4-thiadiazoles,[7] isothiazoles[8]) show useful biological activity, and generally applicable synthetic methods are therefore in demand. The nitrile sulphides have the potential to satisfy this need. Nitrile sulphides are also of interest from a theoretical point of view as they represent a rare case of an *N*-sulphide. Whereas *N*-oxides are commonplace the only comparable *N*-sulphide is the recently detected dinitrogen sulphide (N_2S).[9,10]

Since they were first reported[11] in 1970 there has been a steady, though not heavy, flow of papers devoted to their chemistry. It is the purpose of this review to gather together this literature, to assess what has been achieved, and to identify future applications. Also included is a brief discussion of the closely related but largely unexplored nitrile selenides ($RC{\equiv}N^{+}{-}Se^{-}$).

2 Discovery

The first clear evidence for the existence of nitrile sulphides was provided in 1970 by Franz and Black.[11] Stimulated by a report[12] that oxathiazolone (1a) decomposes on heating to benzonitrile, sulphur, and carbon dioxide they surmised that this process might involve initial decarboxylation to benzonitrile sulphide followed by loss of sulphur (Scheme 2). To test this hypothesis they repeated the thermolysis in the presence of dimethyl acetylenedicarboxylate

[7] (*a*) F. Kurzer, *Adv. Heterocycl. Chem.*, 1982, **32**, 285; (*b*) J. E. Franz and O. P. Dhingra, in 'Comprehensive Heterocyclic Chemistry', ed. A. R. Katritzky and C. W. Rees, Pergamon, 1984, Ch. 4.25.
[8] D. L. Pain, B. J. Peart, and K. R. H. Wooldridge, Ref. 7*b*, 4.17.
[9] C. Wentrup, S. Fischer, A. Maquestiau, and R. Flammang, *J. Org. Chem.*, 1986, **51**, 1908.
[10] H. Bender, F. Carnovale, J. B. Peel, and C. Wentrup, *J. Am. Chem. Soc.*, 1988, **110**, 3458.
[11] J. E. Franz and L. L. Black, *Tetrahedron Lett.*, 1970, 1381.
[12] A. Senning and P. Kelly, *Acta Chem. Scand.*, 1967, **21**, 1871.



Scheme 3

(DMAD), a well-established dipolarophile. From the reaction mixture they isolated isothiazoledicarboxylate (2a), the anticipated [3 + 2]-cycloadduct.

Since this initial report, nitrile sulphides have been generated from several sources and other cycloaddition reactions have been identified. Although all have so far proved to be too unstable to isolate at ambient temperature, they have been detected spectroscopically using matrix isolation techniques (*vide infra*).

3 Methods of Generation

As nitrile sulphides are transient intermediates prone to decomposition it is necessary for synthetic applications for them to be generated *in situ* in the presence of the dipolarophile. In this section the various sources will be described and the most efficient identified.

There are two general approaches involving either thermal or photolytic reactions. Of these the former group are more useful synthetically, while the latter are suitable for matrix isolation and spectroscopic investigations.

A. Thermal Methods.—The most widely used routes are based on cycloreversion of five-membered heterocycles which already contain the C=N–S unit, particularly 1,3,4-oxathiazol-2-ones. However, acyclic precursors such as thioacyl diphenylsulphimides and alkyliminosulphur difluorides have also been employed.

(i) *From* 1,3,4-*Oxathiazol-2-ones.* Decarboxylation of oxathiazolones (1), the reaction in which benzonitrile sulphide was originally identified, remains the method of choice and has been used for the generation of numerous substituted analogues. The precursors usually have a good shelf-life and are readily prepared from the corresponding carboxamide, either in two stages using perchloromethyl mercaptan followed by formic acid [12] or triethylamine,[13] or directly by treatment with chlorocarbonylsulphenyl chloride[14] (Scheme 3). The former route is

[13] E. Müllbauer and W. Weiss, Belgian patent, 680644 (1966), British patent 1079348 (1967); *Chem. Abstr.*, 1968, **68**, 69000.

[14] M. M. Kremlev, A. I. Tarsenko, and I. V. Koval, *Vop. Khim., Khim. Tekhnol.*, 1973, **30**, 40; *Chem. Abstr.*, 1974, **81**, 3837.

assumed to involve hydrolysis of an intermediate dichlorooxathiazole (3).

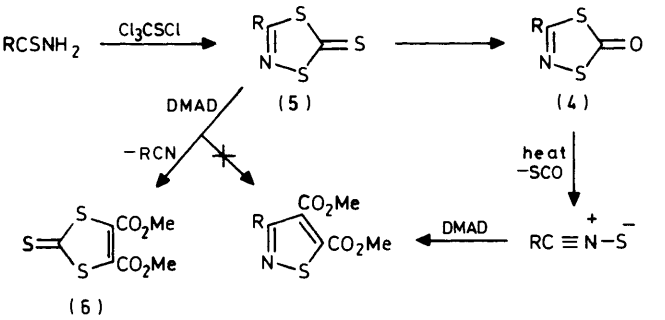
Various substituents can be accommodated including phenols,[15–17] esters,[16–19] nitriles,[20,21] and alkenes [18,22,23] in addition to simple alkyl and aryl groups. Nucleophiles, *e.g.* primary and secondary amines, which react with oxathiazolones[24–26] must be excluded. Thermolysis of the parent oxathiazolone (1; R = H)[27] affords hydrogen cyanide and isothiocyanic acid rather than formonitrile sulphide.

Nitrile sulphides are generated conveniently for cycloaddition reactions by heating the oxathiazolone with an excess of the dipolarophile at 110—160 °C in an inert solvent (*e.g.* xylene, chlorobenzene). Nitriles and sulphur as by-products are commonly observed even with reactive dipolarophiles; in the absence of dipolarophile the nitrile is formed quantitatively. The decarboxylation involves a thermally allowed $_{\sigma}2_s + _{\sigma}2_s + _{\pi}2_s$ process. The reaction is accelerated by electron-donating substituents indicative of development of partial positive charge in the transition state at the 5-position of the heterocyclic ring.[20] Lewis acids such as BF_3 also accelerate decomposition but result in lower adduct yields.[28]

(ii) *From* 1,4,2-*Dithiazol*-5-*ones*. Closely related to oxathiazolones (1) are dithiazolones (4) and thiones (5) in which the ring oxygen is replaced by sulphur. By analogy, these are potential sources of nitrile sulphides by extrusion of SCO and CS_2 respectively. Thiones (5) have been prepared from thioamides with thiophosgene–carbon disulphide[29] or better using perchloromethyl mercaptan[30,31] (Scheme 4). Thione to ketone conversion is achieved by treatment with mercury(II) acetate,[30] $KMnO_4$,[32] or benzonitrile oxide.[30]

Dithiazolones (4) are more stable than the corresponding oxathiazolones fragmenting only slowly (75—200 h) to nitrile, sulphur, and CO_2 in refluxing mesitylene. In the presence of DMAD isothiazoles are formed in good yield, implicating nitrile sulphides as intermediates.[33] The more forcing conditions

[15] A. Senning and J. S. Rasmussen, *Acta Chem. Scand.*, 1973, **21**, 2161.
[16] P. A. Brownsort and R. M. Paton, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1339.
[17] P. A. Brownsort, PhD Thesis, University of Edinburgh, 1987.
[18] P. A. Brownsort, R. M. Paton, and A. G. Sutherland, *Tetrahedron Lett.*, 1985, **26**, 3727.
[19] R. K. Howe, T. A. Gruner, and J. E. Franz, *J. Org. Chem.*, 1977, **42**, 183.
[20] R. K. Howe, T. A. Gruner, L. G. Carter, L. L. Black, and J. E. Franz, *J. Org. Chem.*, 1978, **43**, 3736.
[21] R. K. Howe and B. R. Shelton, *J. Org. Chem.*, 1981, **46**, 771.
[22] W. Beck, E. Leidl, M. Keubler, and U. Nagel, *Chem. Ber.*, 1980, **113**, 1790.
[23] R. M. Paton, I. Stobie, and R. M. Mortier, *Phosphorus Sulfur*, 1983, **15**, 137.
[24] G. Westphal, A. Weise, and A. Otto, *Z. Chem.*, 1977, **17**, 295.
[25] A. Rajca, D. Grobelny, S. Witek, and M. Zbirovsky, *Synthesis*, 1983, 1032.
[26] M. C. McKie, PhD Thesis, University of Edinburgh, 1988.
[27] (*a*) B. Bak, O. J. Nielsen, and H. Svanholt, *J. Mol. Spectroscop.*, 1977, **68** 169; (*b*) B. Bak, J. J. Christiansen, O. J. Nielsen, and H. Svanholt, *Acta Chem. Scand.*, 1977, **31A**, 666.
[28] R. K. Howe and J. E. Franz, *J. Org. Chem.*, 1974, **39**, 962.
[29] H. Behringer and D. Deichmann, *Tetrahedron Lett.*, 1967, 1013.
[30] D. Noel and J. Vialle, *Bull. Soc. Chim. Fr.*, 1967, 2239.
[31] D. J. Greig, M. McPherson, R. M. Paton, and J. Crosby, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1205.
[32] M. S. Chauhan and D. M. KcKinnon, *Can. J. Chem.*, 1976, **54**, 3879.
[33] D. J. Greig, R. M. Paton, J. G. Rankin, J. F. Ross, and J. Crosby, *Tetrahedron Lett.*, 1982, 5453.



Scheme 4

required and less straightforward access to the dithiazolones makes them a less attractive source.

The reaction between dithiazolethione (5) and DMAD takes a different course[31] yielding dithiolethione (6) rather than nitrile sulphide-derived products. Direct interaction between thione (5) and the dipolarophile in a cyclo-substitution reaction is the most likely mechanism.

(iii) *From* 1,3,4-*Oxathiazoles and* 4,5-*Dihydro*-1,2,4-*thiadiazoles.* 1,3,4-Oxathiazoles (7),[34] prepared at 135 °C from nitrile sulphides and activated carbonyl compounds (*e.g.* $Cl_3CCOCCl_3$, CF_3COPh), decompose slowly at higher temperatures (*ca.* 160 °C) regenerating the original carbonyl compound and nitrile sulphide, which can be trapped with alkynes and nitriles.[35] The rate of this retro-1,3-dipolar cycloaddition is critically substituent-dependent, being rapid for R′ = R″ = CCl_3 and slow for R′ = H, R″ = CCl_3. Benzonitrile sulphide is also a likely intermediate in the reported[36] thermal decomposition of the fluorene-8-spiro derivative (7; R = Ph, R′R″ = $C_{13}H_{10}$), which was prepared by cyclization of fluorenethione *S*-benzoylimide.

Similar behaviour is observed[37] for 4,5-dihydro-1,2,4-thiadiazoles (8), the cycloadducts of nitrile sulphides with imines (Scheme 5). Prolonged heating at 160 °C results in cycloreversion to the nitrile sulphide which can be trapped with DMAD and ethyl cyanoformate (ECF).

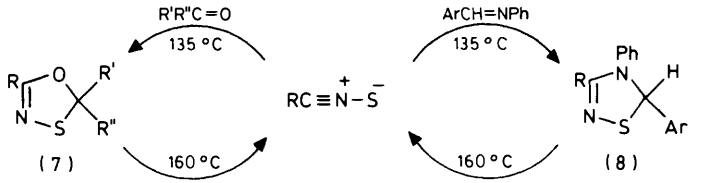
With few alternative routes available to such oxathiazoles and dihydrothiadiazoles they offer little advantage synthetically.

[34] (*a*) R. M. Paton, J. F. Ross, and J. Crosby, *J. Chem. Soc., Chem. Commun.*, 1979, 1146; (*b*) A. M. Damas, R. O. Gould, M. M. Harding, R. M. Paton, J. F. Ross, and J. Crosby, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2991.

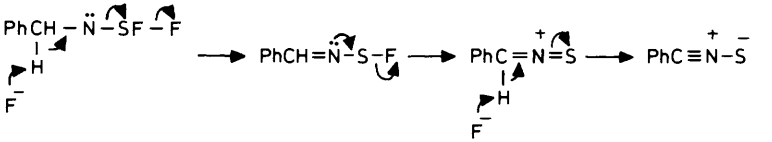
[35] (*a*) R. M. Paton, F. M. Roberton, J. F. Ross, and J. Crosby, *J. Chem. Soc., Chem. Commun.*, 1980, 714; (*b*) R. M. Paton, F. M. Robertson, J. F. Ross, and J. Crosby, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1517.

[36] (*a*) E. M. Burgess and H. R. Penton, *J. Am. Chem. Soc.*, 1973, **95**, 279; (*b*) *J. Org. Chem.*, 1974, **39**, 2884.

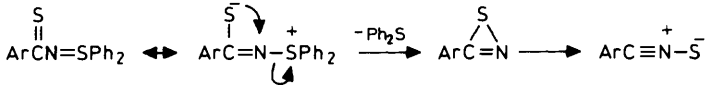
[37] R. O. Gould, R. M. Paton, J. F. Ross, M. D. Walkinshaw, and J. Crosby, *J. Chem. Res.*, 1986, (*S*) 156, (*M*) 1372.



Scheme 5



Scheme 6



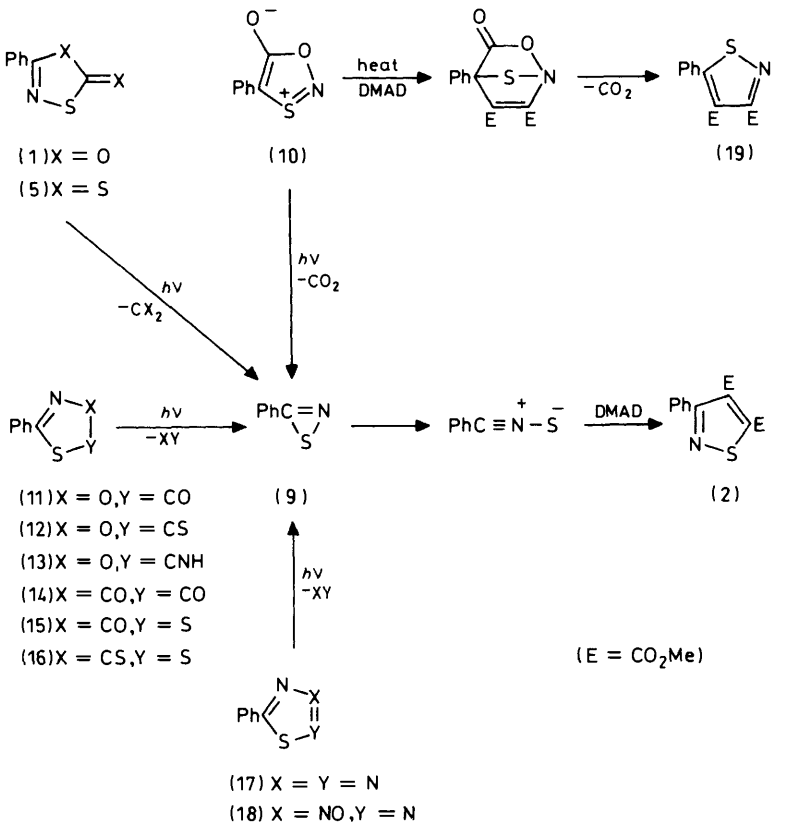
Scheme 7

(iv) *From (Alkylimino)sulphur Difluorides.* (Benzylimino)sulphur difluoride, prepared from benzylamine and SF_4, on heating with NaF and 18-crown-6-polyether at 130 °C in the presence of DMAD yields isothiazole (2a).[38–40] The reaction is believed to involve 1,3-elimination of two moles of HF to form benzonitrile sulphide as illustrated in Scheme 6. Acetonitrile sulphide and trifluoroacetonitrile sulphide have also been generated by this approach.[41]

(v) *From* N-*Thioacyl Diphenylsulphinimides.* Thermolysis at 50—70 °C of *N*-thioaroyl diphenylsulphimides, prepared by treatment of diphenylsulphimide with methyl dithiobenzoates, affords the corresponding nitriles together with diphenyl sulphide and sulphur. In the presence of electron-poor alkynes, isothiazoles are formed[42]—presumably *via* thiazirine and nitrile sulphide intermediates (Scheme 7).

B. Photochemical Methods.—Benzonitrile sulphide has been invoked[43–53] as a transient intermediate in photofragmentation reactions of various five-membered heterocycles incorporating C, N, and S (Scheme 8). In each case the process is believed to involve extrusion of a small inorganic fragment (CO_2, COS, CS_2, N_2, N_2O, HNCO) forming the unstable 4π-antiaromatic thiazirine (9), followed by rearrangement to the corresponding nitrile sulphide. Spectroscopic evidence for these intermediates is presented in Section 5.

[38] J. R. Grunwell and S. L. Dye, *Tetrahedron Lett.*, 1975, 1739.
[39] M. J. Sanders, S. L. Dye, A. G. Miller, and J. R. Grunwell, *J. Org. Chem.*, 1979, **44**, 510.
[40] M. J. Sanders, *Diss. Abstr.*, 1979, **40B**, 1181; *Chem. Abstr.*, 1980, **92**, 5782.
[41] M. J. Sanders, and J. R. Grunwell, *J. Org. Chem.*, 1980, **45**, 3753.
[42] H. Yoshida, H. Taketani, T. Ogata, and S. Inokawa, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 3124.



Scheme 8

In the presence of DMAD the expected isothiazoles (2) are formed; yields are generally poor, ranging from 5% for dithiazolethione (16)[50] to 29% for mesoionic oxathiazolone (10),[52] and are invariably lower than those for the thermal methods described above. Nitrile sulphide-derived products are also formed on

[43] H. Gotthardt, *Tetrahedron Lett.*, 1971, 1277.
[44] A. Holm, N. Harrit, K. Bechgaard, O. Buchardt, and S. E. Harnung, *J. Chem. Soc., Chem. Commun.*, 1972, 1125.
[45] H. Gotthardt, *Chem. Ber.*, 1972, **105**, 188.
[46] A. Holm, N. Harrit, and N. H. Toubro, *J. Am. Chem. Soc.*, 1975, **97**, 6197.
[47] I. R. Dunkin, M. Poliakoff, J. J. Turner, N. Harrit, and A. Holm, *Tetrahedron Lett.*, 1976, 873.
[48] A. Holm, N. Harrit, and N. H. Toubro, *Tetrahedron*, 1976, **32**, 2559.
[49] A. Holm, N. Harrit, and I. Trabjerg, *J. Chem. Soc., Perkin Trans. 1*, 1978, 746.
[50] A. Holm and N. H. Toubro, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1445.
[51] A. Holm, J. J. Christiansen, and C. Lohse, *J. Chem. Soc., Perkin Trans. 1*, 1979, 960.
[52] H. Gotthardt, F. Reiter, and K. Kromer, *Liebigs Ann. Chem.*, 1981, 1025.
[53] N. Harrit, A. Holm, I. R. Dunkin, M. Poliakoff, and J. J. Turner, *J. Chem. Soc., Perkin Trans. 2*, 1987, 1227.

photolysis of 3-ethyl-5-phenyl-1,2,3,4-thiatriazolium tetrafluoroborate.[50] By-products are commonplace: *e.g.* isothiocyanates from thiatriazoles (17) and ethyl benzoylformate from mesoionic compound (10). These are formed in addition to benzonitrile, the expected photodecomposition product of benzonitrile sulphide. Thermolysis, rather than photolysis, of compound (10) with DMAD yields the isomeric isothiazole-3,4-dicarboxylate (19) resulting from cycloaddition to the thiocarbonyl imine moiety.[52,54] Photofragmentation of 3,4-disubstituted 1,2,5-thiadiazoles affords nitriles and sulphur consistent with nitrile sulphide formation;[55] however, attempts to trap the 1,3-dipole proved unsuccessful.

C. Miscellaneous Methods.—Nitrile sulphides have been proposed as intermediates in the oxidative dimerization of thioamides to 3,5-disubstituted-1,2,4-thiazdiazoles.[56–59] Although nitriles are often formed as by-products and such thiadiazoles are formally 1,3-dipolar cycloadducts of nitrile sulphides and nitriles, in most cases there is scant evidence for the reaction proceeding in this way. Indeed, the low dipolarophilicity of unactivated aromatic nitriles suggests that nitrile sulphides are not involved and that alternative oxidative pathways are more likely.

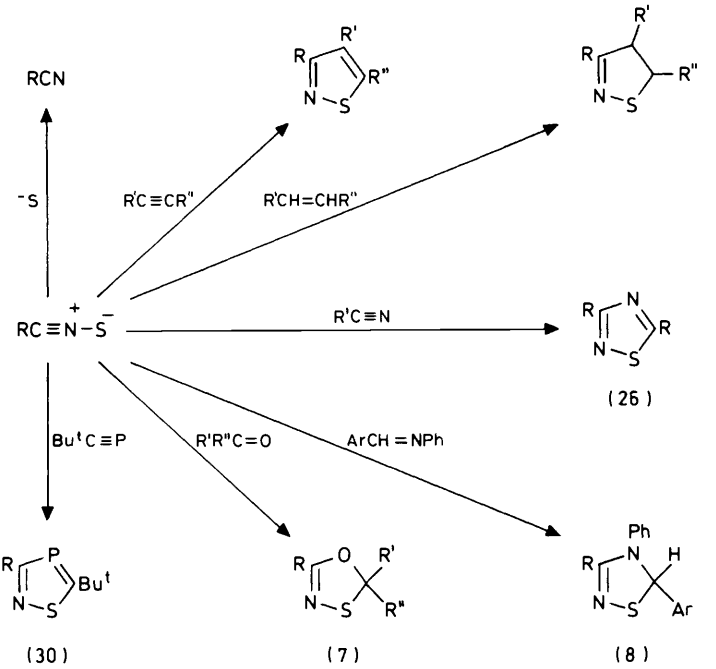
4 Reactions

Whereas some nitrile oxides can be isolated and characterized at room temperature all nitrile sulphides reported so far are thermally unstable and can only be detected using low-temperature matrix isolation techniques. Rapid desulphuration to the corresponding nitrile occurs in solution. However, generation *in situ* in the presence of suitably activated dipolarophiles allows 1,3-dipolar cycloaddition reactions to be accomplished. Optimum yields are obtained by using an excess of dipolarophile and maintaining a low concentration of the nitrile sulphide thus minimizing decomposition, a process for which the mechanism has not been firmly established but which is known to be higher than first order.

The range of established cycloaddition reactions is limited compared with the other nitrilium betaines. Dipolarophiles examined to date and described below comprise alkynes, alkenes, nitriles, imines, carbonyl compounds, and phosphaalkynes (Scheme 9). The mechanisms of desulphuration and cycloaddition are discussed in Section 6.

A. Cycloaddition to Alkynes.—Historically the first dipolarophile to be examined, DMAD remains the most widely used for trapping nitrile sulphides.[11,16,18,20,23,33,35,37–46,50,52,60–62] Isothiazole-4,5-dicarboxylates are

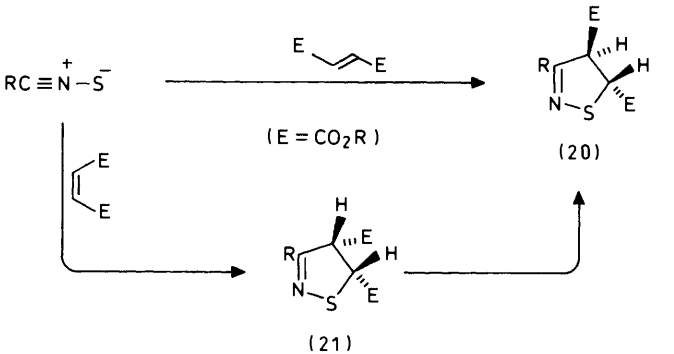
[54] H. Gotthardt, *Tetrahedron Lett.*, 1971, 1281; *Chem. Ber.*, 1972, 196.
[55] T. S. Cantrell and W. S. Haller, *J. Chem. Soc., Chem. Commun.*, 1968, 977.
[56] M. Bahadir, S. Nitz, H. Parlar, and F. Korte, *J. Agric. Food Chem.*, 1979, **27**, 815.
[57] M. T. M. El-Wassimy, K. A. Jorgensen, and S.-O. Lawesson, *Tetrahedron*, 1983, **39**, 1729.
[58] M. Machida, K. Oda, and Y. Kanaoka, *Tetrahedron Lett.*, 1984, **25**, 409.
[59] Y. Takikawa, K. Shimada, K. Sato, S. Sato, and S. Takizawa, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 995.



Scheme 9

formed in yields as high as 96%,[20] and other electron-poor alkynes (*e.g.* dibenzoylacetylene[42]) react similarly. Alkyl propiolates give a mixture of 4- and 5-carboxylates, the isomer ratio depending on both the nitrile sulphide and its source. For benzonitrile sulphide generation from oxathiazolone (1a) affords nearly equal amounts of the two regioisomers, whereas there is a slight preference for the 4-substituted product using benzyliminosulphur difluoride as precursor,[39] possibly due to protonation of the dipolarophile by hydrogen fluoride, the co-product. Of examples examined so far only trifluoroacetonitrile sulphide shows pronounced regioselectivity, the 5-carboxylate predominating (5:1). This general lack of regioselectivity contrasts with the behaviour of nitrile oxides for which 5-carboxylates are often the major products.[4] Isothiazole-4-carboxylates can also be prepared by thermal decarboxylation of isothiazole-4,5-dicarboxylates.[20,62] The yields of cycloadducts decrease as the alkyne becomes less electron poor: *e.g. ca.* 50% for ethyl phenylpropiolate,[20] traces for ethyl butynoate,[20] and only nitrile and sulphur are formed with diphenylacetylene.[42]

[60] R. K. Howe and J. E. Franz, *J. Chem. Soc., Chem. Commun.*, 1973, 524.
[61] (*a*) R. M. Mortier, R. M. Paton, and I. Stobie, *J. Chem. Soc., Chem. Commun.*, 1983, 901; (*b*) R. M. Mortier, R. M. Paton, G. Scott, and I. Stobie, *Br. Polymer J.*, 1987, **19**, 303.
[62] M. C. McKie and R. M. Paton, *J. Chem. Res.*, 1987, (*S*) 245, (*M*), 2051.



Scheme 10

B. Cycloaddition to Alkenes.—Whereas the cycloaddition of nitrile sulphides to acetylenes described above is one of several synthetic approaches to isothiazoles[8] the corresponding reaction with olefins is the only method developed so far for 2-isothiazolines (4,5-dihydroisothiazoles). The process is most efficient for electron-poor alkenes, although norbornene-type unsaturation also shows adequate reactivity.[62,63]

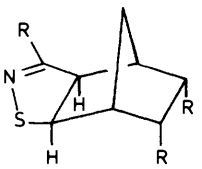
With dialkyl fumarates 2-isothiazoline-*trans*-4,5-dicarboxylates (20) are formed in 50—80% yield.[63,64] The stereochemistry of the products is evident from their ^{1}H n.m.r. spectra which show couplings for H(4)–H(5) of *ca.* 4 Hz, comparable with those observed for analogous 2-isoxazoline-*trans*-4,5-dicarboxylates. For diethyl 3-phenyl-2-isothiazoline-*trans*-4,5-dicarboxylate the structure has been confirmed by *X*-ray crystallography.[64]

N-Phenylmaleimide[41,63] and maleic anhydride[38] afford the expected *cis*-adducts with $J_{H(4)H(5)}$ 11 Hz. In contrast dialkyl maleates yield *trans*-isothiazolines (20), identical to those formed from fumarate esters.[26,64] The isomerization may occur in an initially-formed *cis*-adduct (21) (Scheme 10) or in the dipolarophile prior to cycloaddition. The corresponding reaction of nitrile oxides with maleate esters also give *trans*-products at elevated temperatures; the *cis*-adduct, which can be isolated at room temperature, isomerizes on heating.[65]

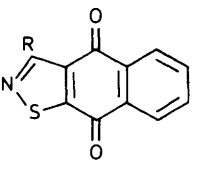
The yield of cycloadduct, as with acetylenes, is dependent on the nature of the dipolarophile. Acrylate esters afford a mixture of 2-isothiazoline-4- and 5-carboxylates with little regioselectivity.[63,64] No reaction is observed with tetraethyl ethenetetracarboxylate,[63] presumably because of steric effects, or with the double bond of tetracyanoethene; instead 1,2,4-thiadiazoles are formed by cycloaddition to one or more of the nitrile groups.[63] β-Nitrostyrene and 3-nitrostyrene are similarly unreactive.

Norbornene-type double bonds, which are strong dipolarophiles towards nitrile

[63] R. K. Howe and J. E. Franz, *J. Org. Chem.*, 1978, **43**, 3742.
[64] J. F. Ross, PhD Thesis, University of Edinburgh, 1981.
[65] A. Rahman and L. Clapp, *J. Org. Chem.*, 1976, **41**, 122.



(22)



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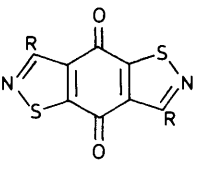

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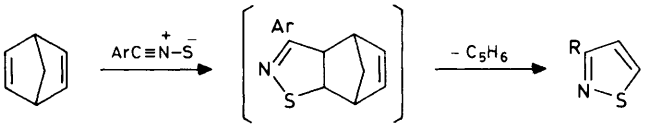


(25)

Scheme 11

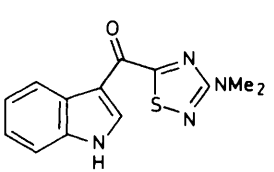
oxides,[4] also react with nitrile sulphides. *exo*-Adducts (22) have been isolated from norbornene itself[62] and from dimethyl 5-norbornene-*cis,endo*-2,3-dicarboxylate.[63]

The reaction of nitrile sulphides with alkenes can be used as a route to isothiazoles. 2-Isothiazolines are readily dehydrogenated (DDQ[63] or NaOCl[64]) and, in some cases, isothiazoles are the isolated products from alkene–nitrile sulphide reactions. For example, isothiazoloquinones, (23) and (24), are formed from *p*-naphthoquinone and *p*-benzoquinone respectively, presumably by *in situ* oxidation by excess quinone of an intermediate isothiazoline.[66] Ethyl α-chloro- and β-pyrrolidinyl-acrylates both afford isothiazoles *via* cycloaddition followed by elimination of HCl and pyrrolidine respectively.[63]

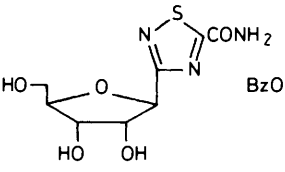
3-Arylisothiazoles (25) unsubstituted at both 4- and 5-positions, formally adducts between nitrile sulphides and acetylene, are produced using norbornadiene which acts as an acetylene equivalent. By analogy with nitrile oxides and imines the process is presumed[62] to involve the cycloaddition–cycloreversion pathway illustrated in Scheme 11. Isothiazoles (25) can also be prepared by thermal extrusion of C_2H_4 and CO_2 from 3-arylisothiazole 3- and 4-carboxylates and 4,5-dicarboxylates under flash vacuum pyrolysis conditions.[62]

C. Cycloaddition to Nitriles.—Reaction of nitrile sulphides with nitriles provides a versatile preparative route to 1,2,4-thiadiazoles [(26), Scheme 9], an important class of heterocycles showing a range of biological activity.[7] Whereas traditional methods such as oxidation of thioamides are well suited for symmetrically substituted derivatives,[7] *e.g.* 3,5-diphenyl-1,2,4-thiadiazole is readily prepared from thiobenzamide, the nitrile sulphide cycloaddition approach allows controlled introduction of different substituents at the 3- and 5-positions.[16,19,21,23,28,61,67,68]

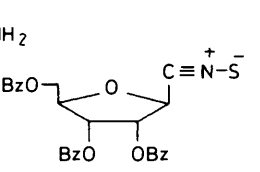
[66] R. M. Paton, J. F. Ross, and J. Crosby, *J. Chem. Soc., Chem. Commun.*, 1980, 1194.



(27)



(28)



(29)

Nitriles are surprisingly reactive towards nitrile sulphides. For most dipolarophiles the yields of cycloadduct obtained from nitrile sulphides are much less than those from nitrile oxides. Indeed, cycloadditions involving nitrile sulphides generally require strongly activated dipolarophiles. Towards nitriles, however, the reactivities of these two nitrilium betaines are more comparable although still favouring nitrile oxides. As with other dipolarophiles the yield of cycloadducts is strongly substituent-dependent and is greatly increased by electron-withdrawing groups. Ethyl cyanoformate (ECF),[16,23,28,61] α-ketonitriles,[26,69] and trichloroacetonitrile[67] are the most reactive, readily affording 50—95% of 5-substituted 1,2,4-thiadiazoles. ECF is a particularly useful trap for nitrile sulphides; not only is it highly reactive but it also often affords crystalline adducts and its moderate boiling point (*ca.* 115 °C) facilitates its removal from the reaction mixture. Simple arenenitriles,[19,21,28,35] dichloroacetonitrile,[26] aryl thio- and seleno-cyanates,[68] and ethyl cyanoacetate[28] give substantially smaller amounts. 1,2,4-Thiadiazoles unsubstituted at the 5-position (26; R′ = H), formally the cycloadduct of HCN, are accessible by decarboxylation of their 5-carboxylate derivatives.[28]

Symmetrically substituted thiadiazoles are sometimes observed[28,64] as by-products. For example 4-chlorobenzonitrile sulphide and benzonitrile yield 3,5-diphenyl-1,2,4-thiadiazole (26, R = R′ = Ph) (7%) in addition to the expected 3-(4-chlorophenyl)-5-phenyl compound (26; R = 4-ClC_6H_4, R′ = Ph). Its formation is attributed[28] to the presence of benzonitrile sulphide arising either by sulphuration of benzonitrile by S_n (n = 1—8) or by sulphur atom transfer between 4-chlorobenzonitrile sulphide and benzonitrile.

Recent applications include the synthesis of the cytotoxic marine natural product dendrodoine (27) from dimethylaminoformonitrile sulphide and indole-3-carbonitrile,[69] and the ribovasin analogue (28)[70] *via* the protected β-D-ribofuranosylcarbonitrile sulphide (29) and ECF.

D. Cycloaddition to Carbonyl Compounds.—1,3,4-Oxathiazoles [(7), Scheme 9], the adducts of nitrile sulphides and carbonyl compounds,[34] are a rare class of heterocycles accessible only with difficulty by other means.[36,71] The cycloaddition occurs only when the carbonyl group is activated by electron-withdrawing

[67] D. J. Greig, M. McPherson, R. M. Paton, and J. Crosby, *Phosphorus Sulfur*, 1986, **26**, 151.
[68] D. J. Greig, D. G. Hamilton, M. McPherson, R. M. Paton, and J. Crosby, *J. Chem. Soc., Perkin Trans. 1*, 1987, 607.
[69] I. T. Hogan and M. Sainsbury, *Tetrahedron*, 1984, **40**, 681.
[70] D. K. Buffel, B. P. Simons, J. A. Deceuninck, and G. J. Hoornaert, *J. Org. Chem.*, 1984, **49**, 2165.

groups, *e.g.* hexachloroacetone, chloral, α,α,α-trifluoroacetophenone[34] and methyl benzoylformate.[72] The oxathiazoles, like the oxathiazolones from which they are formed, have a planar heterocyclic ring with a localized C=N double bond. Dehydrochlorination of chloral-derived compound (7; R′ = H, R″ = CCl_3) affords dichloromethylene derivative (7; R′R″ = CCl_2), which is formally the adduct between a nitrile sulphide and C=O of dichloroketene.

All the oxathiazoles are themselves thermally labile and cyclorevert[35] on heating to nitrile sulphide and carbonyl fragments (Scheme 5). Subsequent decomposition of the nitrile sulphide gives the corresponding nitrile quantitatively.

E. Cycloaddition to Imines.—Schiff bases formed from aniline and *para*-substituted benzaldehydes cycloadd to nitrile sulphides affording 3,4,5-trisubstituted-4,5-dihydro-1,2,4-thiadiazoles [(8), Scheme 9]. Yields for the few reported examples[37] are very low ($\leqslant 13\%$) even when the *para*-group is electron withdrawing.

Although various 4,5-dihydro-1,2,4-thiadiazoles have been known for many years, *e.g.* Hector's base and Dost's keto compound,[73] previous examples have sp^2-hybridization at C(5) and a near planar heterocyclic ring. In contrast, for the nitrile sulphide-derived analogues (8) both C(5) and N(4) are sp^3-hybridized resulting in a fold in the ring about the S(1)–N(4) vector.

Their thermolytic behaviour closely parallels that of the 1,3,4-oxathiazoles described above. On heating they undergo retro-1,3-dipolar cycloaddition to nitrile sulphides and imines (Scheme 5).

This system has not been studied in depth and the imines used so far have been of low reactivity. By inclusion of electron-attracting groups in the dipolarophile component greater yields may be expected.

F. Cycloaddition to Phosphaalkynes.—t-Butylphosphaacetylene ($Bu^tC{\equiv}P$) is a sufficiently strong dipolarophile to cycloadd to several nitrilium betaines including benzonitrile sulphide.[74,75] Thermal decarboxylation of phenyloxathiazolone (1a) in the presence of $Bu^tC{\equiv}P$ affords 5-t-butyl-3-phenyl-1,2,4-thiazaphasphole [(30), Scheme 9] (82%), the first example of this class of heterocycle. Traces of compound (30) are also formed from mesoionic precursor (10), accompanying the 3-t-butyl-5-phenyl isomer, which is the expected mesoionic cycloaddition product.[75]

G. Intramolecular Cycloaddition Reactions.—Intramolecular 1,3-dipolar cycloaddi-

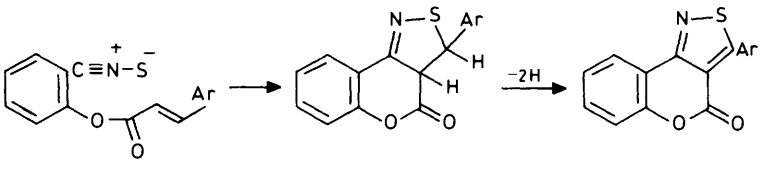
[71] (*a*) N. Haake, B. Eichenauer, and K. H. Ahrens, *Z. Naturforsch.*, 1974, **29B**, 284; (*b*) W. S. Levchenko, L. V. Budnik, V. N. Kalinin, and A. A. Kisilenko, *Zh. Org. Khim.*, 1982, **18**, 2549; *Chem. Abstr.*, 1983, **98**, 125987.

[72] H. C. Gibbard and R. M. Paton, unpublished observations.

[73] (*a*) A. R. Butler, C. Glidewell, and D. C. Liles, *Acta Crystallogr.*, 1978, **34B**, 3241; (*b*) A. F. Cuthbertson, C. Glidewell, H. D. Holden, and D. C. Liles, *J. Chem. Res.*, 1979, (*S*) 316, (*M*) 3714 and references therein.

[74] W. Rösch and M. Regitz, *Synthesis*, 1987, 689.

[75] W. Rösch, H. Richter, and M. Regitz, *Chem. Ber.*, 1987, **120**, 1809.



(31) (32)

Scheme 12

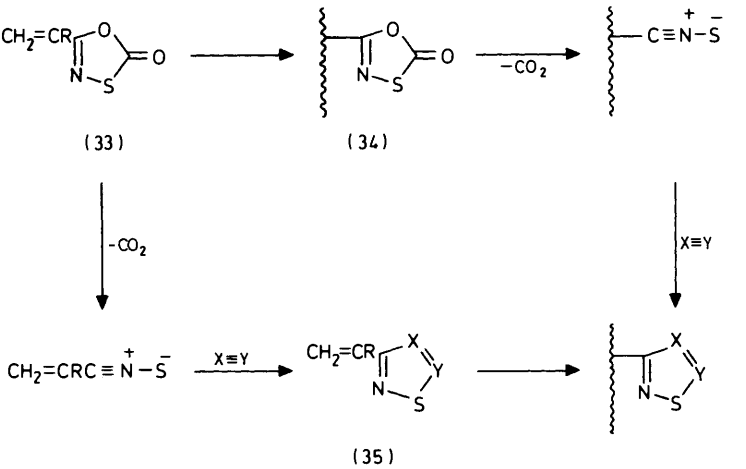
tion reactions find widespread application for the construction of fused heterocyclic systems and examples have been reported[76] for most 1,3-dipoles including the nitrilium betaines. Whereas nitrile oxides have been examined in great detail, particularly for natural product synthesis,[5a] it is only recently that the first cases involving nitrile sulphides have been described.[18]

o-Cinnamoyloxybenzonitrile sulphides (31), which incorporate an adjacent 1,3-dipole and activated dipolarophile, were generated by thermal decarboxylation of the corresponding oxathiazolones. They yield isothiazolocoumarins (32), presumably *via* the intramolecular cycloaddition–dehydrogenation pathway illustrated in Scheme 12. The same fused isothiazoles (32) are also formed directly from benzonitrile sulphides bearing *o*-arylpropiolyloxy substituents. A similar approach has been used[17] to form 3-phenylisothiazolo[4,3-*c*]quinoline-4-(5*H*)-ones from phenylpropiolamidobenzonitrile sulphide.

H. Polymeric Nitrile Sulphides.—The cycloaddition reactions of polymeric 1,3-dipoles are an ideal means of preparing polymers bearing pendant heterocycles. Examples include nitrile imines,[77] azides,[78] and nitrile sulphides.[61] Free radical-initiated polymerization of α-alkenyloxathiazolones (33) with styrene or methyl methacrylate (MMA) affords[61,79] oxathiazolone-containing polymers (34). Thermal decarboxylation generates polymer-bound nitrile sulphides which are efficiently trapped[61] in the presence of reactive dipolarophiles such as DMAD, ECF, and chloral (Scheme 13). An alternative route to such polymer-linked heterocycles involves initial cycloaddition of α-alkenylnitrile sulphides[23] to form adducts (35) with polymerizable substituents, and subsequent co-polymerization with styrene or MMA. The latter method has the advantage of yielding products free from contamination by nitriles which, unlike the corresponding monomer reactions, are necessarily retained in the polymer when the former approach is used.

Bis-oxathiazolones [*e.g.* 1,2-bis(2-oxo-1,3,4-oxathiazol-5-yl)-ethane, a potential precursor of succinonitrile sulphide] have also been utilized[80] to vulcanize styrene–butadiene rubbers. It is doubtful that the process involves cycloaddition between nitrile sulphides to the alkene units. Whereas the latter are known to

[76] A. Padwa, Ref. 1, Ch. 12.
[77] J. K. Stille, *Makromol. Chem.*, 1972, **154**, 49.
[78] H. L. Cohen, *J. Polym. Sci., Polym. Chem. Ed.*, 1981, **19**, 1337.
[79] R. M. Paton, I. Stobie, and R. M. Mortier, *J. Polym. Sci., Polym. Lett. Ed.*, 1983, **21**, 145.
[80] J. Crosby, British patent 1509406 (1975); *Chem. Abstr.*, 1977, **86**, 156824.



Scheme 13

form[81] bis-isoxazoline crosslinks with dinitrile oxides, it is unlikely that they would be sufficiently good dipolarophiles to react with nitrile sulphides. A mechanism involving vulcanization by a reactive form of sulphur resulting from decomposition of nitrile sulphides is more probable, a hypothesis supported by the observation that *mono*functional analogues such as compound (1a) also effect crosslinking.

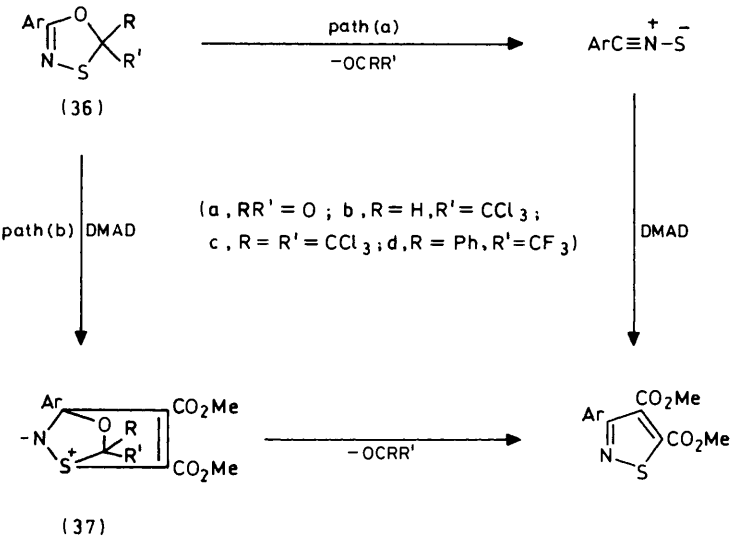
5 Matrix Isolation and Spectroscopic Detection

The thermal instability of nitrile sulphides prevents spectroscopic investigation at room temperature. They have however been detected when generated photolytically at cryogenic temperatures using matrix isolation techniques.

Irradiation (400—470 nm) of 4-phenyl-1,2,3-oxathiazolylium-5-olate (10) at 85 K in diethyl ether–isopentane–ethanol (EPA) and isopentane–methylcyclohexane (MPH) glasses or a PVC film results in formation of benzonitrile sulphide as one of the primary photoproducts.[44,46,49,53] Its u.v. spectrum shows characteristic $\lambda_{max.}$ values at 335 ($\varepsilon = 6.7 \times 10^3$ l.mol^{-1} cm^{-1}), 324, 313, 295, and 240 nm. In EPA the spectrum remains unchanged on warming to 140 K at which point the glass melts and the nitrile sulphide decomposes to benzonitrile (70%). In PVC traces of benzonitrile sulphide are still detectable at room temperature. Fragmentation to nitrile and sulphur is also accomplished by irradiation at 335 nm, one of the absorption maxima. The same u.v. spectrum is obtained on photolysis of 5-phenyl-1,2,3,4-thiatriazole (17),[46,49] its 3-oxide (18),[49] and oxathiazolone (1a).[49]

Benzonitrile sulphide has also been detected by i.r. spectroscopy.[53] After irradiation of mesoionic compound (10) in PVC a peak is observed at 2 185

[81] J. Crosby, R. M. Paton, R. A. C. Rennie, and J. Tanner, British patent, 147691 (1973); *Chem. Abstr.*, 1975, **82**, 141047.



Scheme 14

cm^{-1}. It is assigned to benzonitrile sulphide as it appears before benzonitrile, it is efficiently photolysed at 335 nm, and it behaves during warm-up in PVC as benzonitrile sulphide does when monitored by u.v. spectroscopy. The value of 2 185 cm^{-1} compares with 2 288 cm^{-1} for benzonitrile oxide,[82] 2 228 cm^{-1} for benzonitrile *N*-phenylimide,[83] and 1 926 cm^{-1} for benzonitrile methylide,[84] suggesting a nitrilium betaine-like structure ($RC{\equiv}N^{+}{-}X^{-}$) comparable to those assigned to nitrile oxides and imines, rather than the allene-like skeleton of nitrile ylides ($RC^{-}{=}N^{+}{=}CH_2$).

Formation of benzonitrile sulphide from compounds (1a), (10), (17), and (18) is believed[45–53] to proceed *via* thiazirene (9) (Scheme 8), and evidence for the existence of this unstable species in PVC at 10—15 K has been presented.[49] Although it has not been detected directly its presence is implied by the formation of benzonitrile sulphide on heating (20 → 140 K) a sample of thiatriazole (17) which had previously been photolysed at 10 K.

6 Mechanistic Aspects

A. Evidence for Nitrile Sulphides.—Evidence for the existence of nitrile sulphides is based on spectroscopic measurements of matrix-isolated samples at cryogenic temperatures (Section 5) and trapping reactions in solution.

Formation of isothiazoles and 1,2,4-thiadiazoles respectively from reactions of oxathiazolones (36a) with DMAD and ECF, both well-established dipolarophiles,

[82] R. H. Wiley and B. J. Wakefield, *J. Org. Chem.*, 1960, **25**, 546.
[83] N. H. Toubro and A. Holm, *J. Am. Chem. Soc.*, 1980, **102**, 2093.
[84] (*a*) O. L. Chapman and J.-P. Le Roux, *J. Am. Chem. Soc.*, 1978, **100**, 282; (*b*) E. Orton, S. T. Collins, and G. C. Pimentel, *J. Phys. Chem.*, 1986, **90**, 6139.

strongly indicates nitrile sulphides as intermediates. It does not however, prove that they are involved and alternative pathways to the observed products must be considered. Mechanisms involving zwitterions can be discounted in view of the isolation of both regioisomers from reactions with propiolate esters.[20] However, cycloadduct formation is consistent not only with intermediate formation of nitrile sulphides (Scheme 14, path a), but also with a mechanism (path b) involving direct interaction between the dipolarophile and precursor (36) to form adduct (37), followed by elimination of CO_2.

That path (a) involving a discrete nitrile sulphide intermediate is operative rather than path (b) is demonstrated both by kinetic measurements and by competition experiments. Howe *et al.*[20] established that the rate constant for the consumption of oxathiazolone (36a, Ar = Ph) is first order and independent of concentration of DMAD. Furthermore, the rate constants for the formation of isothiazole and benzonitrile, the by-product of the reaction, are also first-order and equal to the rate constant for the disappearance of the oxathiazolone. Complementary evidence is provided by competition experiments performed by Ross *et al.*[35] Thermolysis of four sources, oxathiazolone (36a, Ar = 4-$MeOC_6H_4$) and three oxathiazoles (36b—d, Ar = 4-$MeOC_6H_4$), in the presence of ethyl propiolate as trapping agent afforded the same regioisomeric ratio (1.33 ± 0.02) of isothiazole-4- and 5-carboxylates. These results imply generation of a common intermediate (4-$MeOC_6H_4C{\equiv}N^+{-}S^-$) from each source. The involvement of nitrile sulphides as discrete intermediates in these reactions is thus firmly established.

B. Theoretical Treatment.—Frontier molecular orbital (FMO) theory has frequently been used to rationalize the reactivity of nitrilium betaines and the regioselectivity of their cycloaddition reactions.[1] For nitrile ylides the process is regarded as dipole-HOMO–dipolarophile-LUMO controlled, *i.e.* type I in the Sustmann classification.[85] Nitrile imines and oxides are categorized type II where both sets of frontier orbitals (dipole-HOMO–dipolarophile-LUMO and dipole-LUMO–dipolarophile-HOMO) must be considered.

Nitrile sulphides have not been examined rigorously from a theoretical point of view. However, some rationalizations and predictions have been made on simple electronegativity grounds and on the basis of CNDO/2 SCFMO calculations. Since sulphur is little more electronegative than carbon, nitrile sulphides should have LUMO and HOMO energy levels only slightly lower than those of nitrile ylides. By analogy they are expected to react readily with electron-poor acetylenic esters with predominantly dipole HOMO control. The observed[20] order of reactivity for such esters (DMAD > ethyl propiolate > ethyl phenylpropiolate > ethyl but-2-ynoate) is consistent with this hypothesis. CNDO/2 SCFMO calculations[39] performed on benzonitrile sulphide, with geometry optimization of the N–S bond and standard geometry for the rest of the molecule, lead to broadly similar conclusions. The energy difference between the

[85] R. Sustmann, *Pure Appl. Chem.*, 1974, **40**, 569.

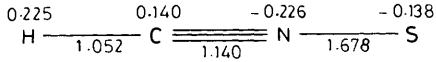


Figure 1

HOMO of benzonitrile sulphide and the LUMO of electron-deficient acetylenes is calculated to be *ca.* 1eV less than the alternative dipole-LUMO–dipolarophile-HOMO interaction. Nitrile sulphides are therefore expected to show more dipole-HOMO control than the corresponding nitrile oxides.

Explanation and prediction of regioselectivity are necessarily less precise. The CNDO/2 calculations[39] indicate that the largest orbital coefficient is associated with sulphur in the HOMO but with carbon in the LUMO. Cycloaddition to propiolate esters is thus expected to afford predominantly isothiazole-4-carboxylates under dipole-HOMO control and 5-carboxylates under dipole-LUMO control. Whereas benzonitrile oxide reacts with methyl propiolate to give mainly isoxazole-5-carboxylate (*ca.* 4:1),[4] the same alkyne with benzonitrile sulphide affords a 50/50 mixture of regioisomers. Although some lack of selectivity can be attributed to the higher temperatures used for nitrile sulphide reactions, these results are also consistent with the CNDO/2 prediction of increased dipole-HOMO–dipolarophile-LUMO interaction for nitrile sulphides compared with nitrile oxides.

Ab initio calculations have been performed[27b,51] on the parent, but as yet unidentified, formonitrile sulphide (HCNS). Geometry optimization indicates a linear structure with the bond lengths and atomic charges shown in Figure 1. The estimated N–S bond order is 1.0. It is predicted to be less stable than the known isomeric isothiocyanic acid (HNCS) (−490.153 44 *vs.* −490.212 38 hartrees). The calculations also suggest a value of *ca.* 5.4 D for the dipole moment.

C. Desulphuration.—The thermal and photochemical behaviour of nitrile sulphides is very different from that of nitrile oxides. The latter rearrange to the isomeric isocyanates,[4] with oxazirenes and acyl nitrenes as likely intermediates. In contrast photolysis of nitrile sulphides at cryogenic temperatures or allowing the sample to warm above 100 K results in desulphuration.

The mechanism of this process has been the subject of some debate. *Ab initio* MO calculations[27b,51] suggest that extrusion of a singlet sulphur atom, S(^{1}D), is endothermic (*ca.* 100 kJ), but formation of atomic sulphur in the ground state, S(^{3}P), is exothermic (*ca.* 40 kJ) although spin-forbidden.

The rate of decay is strongly concentration-dependent. The process appears to be unimolecular in dilute ethanol,[51] but substantial deviations from first-order kinetics occur in non-polar solvents and at higher concentration. Flash photolysis studies in ethanol at 10—30 °C enabled decomposition rates and relative stabilities of several arenenitrile sulphides (4-XC_6H_4CNS) to be examined. Half-life times varied from 0.21 ms for X = Br to 0.87 ms for X = MeO. A Hammett ρ-value of 2.2 was obtained for a limited range of substituents (X = H, Me, MeO) indicating stabilization of the nitrile sulphides by electron-donating groups.

The following observations provide evidence for higher order reactions. Firstly, isolated samples are stable only in an inert matrix.[53] In EPA glass the compound is consumed as soon as the glass melts (140 K); in PVC it is still detectable at room temperature. Secondly, the yields of 1,3-dipolar cycloadducts are remarkably dilution-dependent; for example, the yield of 3,5-diphenyl-1,2,4-thiadiazole from benzonitrile sulphide in neat benzonitrile increases from 14% at reactant ratio 1:10 to 74% at 1:100. Moreover, portionwise addition of the precursor[21] or slow delivery by means of a syringe pump[62] also raises the yield substantially. These results are not consistent with a unimolecular process as the sole mechanism for the decomposition of nitrile sulphides. Reactions that may account for the deviations from first-order kinetics include bimolecular collisions of nitrile sulphides and scavenging by sulphur atoms or short sulphur chains (Scheme 15).

$$2\ RCNS \longrightarrow RCN + RCNS_2 \longrightarrow RCN + S_2 \longrightarrow S_8$$

$$RCNS + S_x\ (x=1\text{-}7) \longrightarrow RCN + S_{x+1} \longrightarrow S_8$$

Scheme 15

These observations are of considerable significance for synthetic applications. By maintaining a low concentration of nitrile sulphide, respectable yields of cycloadducts can be achieved for less reactive dipolarophiles.

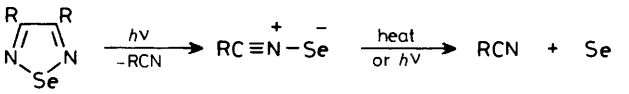
7 Nitrile Selenides

Much less is known about nitrile selenides ($RC{\equiv}N^{+}{-}Se^{-}$) than their sulphur analogues. There is good evidence[86,87] for their existence at low temperatures (< 100 K), but so far attempts to trap them as 1,3-dipolar cycloadducts, *e.g.* with DMAD, have failed.

The approach used to detect these short-lived species was very similar to that successfully employed for isolating and studying nitrile sulphides. On photolysis of 3,4-diphenyl-1,2,5-selenadiazole (38a) at 85 K in PVC film or EPA glass, or at 20 K in a nitrogen matrix, a transient was observed with $\lambda_{max.}$ at *ca.* 255, 325, 360, and 390 nm. An i.r. peak at 2 200 cm^{-1} in N_2 (2 190 cm^{-1} in PVC) was also detected and similar spectra were obtained from the isomeric 3,5-diphenyl-1,2,4-selenadiazole. The thermal and photochemical behaviour of the transient is consistent with benzonitrile selenide. On heating above 100 K or irradiation (300 or 360 nm) selenium was deposited and the signals attributed to benzonitrile selenide replaced by those of benzonitrile (Scheme 16).

Under similar conditions 1,2,5-selenadiazole (38b) and its dimethyl derivative (38c) also afforded short-lived species. These were tentatively assigned to the parent formonitrile selenide ($HC{\equiv}N^{+}{-}Se^{-}$) and acetonitrile selenide. The failure of

[86] C. L. Pedersen and N. Hacker, *Tetrahedron Lett.*, 1977, 3981.
[87] C. L. Pedersen, N. Harrit, M. Poliakoff, and I. Dunkin, *Acta Chem. Scand.*, 1977, **31B**, 848.



(38) (a, R = Ph; b, R = H; c, R = Me)

Scheme 16

trapping reactions, even with a reactive dipolarophile, can be attributed to nitrile selenides being less stable and more prone to fragmentation than the sulphides.

8 Conclusion

The cycloaddition reactions of nitrile sulphides described in this review provide a route to several classes of heterocycles which are accessible only with difficulty by other means. Although additions to most of the common dipolarophiles have been reported, some simple systems have yet to be examined. These include thiones and azo compounds, both of which are reactive towards other nitrilium betaines. There is thus scope for the synthesis of further unusual sulphur–nitrogen heterocycles.

The limited reactivity of nitrile sulphides, the high temperatures usually required, together with their tendency to desulphurate are restrictions on their more widespread use. There is therefore a need for alternative sources which retain the easy access and good shelf-life of current precursors, particularly oxathiazolones, but can be used under less forcing conditions.

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