1,3-Dipolar Cycloaddition Reactions of Nitrilium Betaines with Aryl Thiocyanates[1] and Selenocyanates

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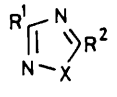
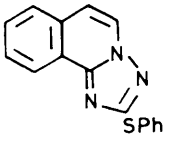
The carbon–nitrogen triple bond of aryl thiocyanates acts as a dipolarophile in 1,3-dipolar cycloadditions. Reaction with nitrile oxides, nitrile sulphides, and benzonitrile *N*-phenylimide yields, respectively, 5-arylthio-1,2,4-oxadiazoles, -thiadiazoles and -triazoles. Aryl selenocyanates behave similarly forming 5-arylseleno-1,2,4-oxadiazoles and -thiadiazoles from nitrile oxides and sulphides. Divergent pathways are followed by the reactions of secondary amines such as piperidine with 5-arylthio-1,2,4-oxadiazoles and -thiadiazoles, the former yielding 5-piperidyl-1,2,4-oxadiazoles and the latter dihydro-1,2,4-thiadiazole-5-thiones.

The 1,3-dipolar cycloaddition reactions of nitrilium betaines ($RC{\equiv}N^{+}{-}X^{-}$ where X = CR_2, NR, O, S) are widely used for the synthesis of 5-membered heterocycles incorporating the C=N–X unit.[2] Particular effort has been devoted to their reactions with nitriles which provide access to 4*H*-imidazoles (**1**), 1,2,4-triazoles (**2**), 1,2,4-oxadiazoles (**3**), and 1,2,4-thiadiazoles (**4**). The variety of biological activity shown by such heterocycles[3] has given added impetus to these studies. The dipolarophilicity of aliphatic nitriles is generally low, that of their aromatic analogues somewhat higher, while the presence of electron-withdrawing substituents results in much greater reactivity. Trichloroacetonitrile[4,5] and ethyl cyanoformate,[6,7] for example, give high yields of oxadiazoles and thiadiazoles with, respectively, nitrile oxides and nitrile sulphides.

We have explored the reactions of aryl thiocyanates and selenocyanates with some nitrile oxides, nitrile sulphides, and benzonitrile *N*-phenylimide as a possible route to 5-arylthio- and 5-arylseleno-oxadiazoles, -thiadiazoles and -triazoles. Cycloadditions to the carbon–nitrogen triple bond of cyanates have been described previously and afford, for example, 5-aryloxy-1,2,4-oxadiazoles (**3**; R^2 = OAr) with nitrile oxides.[8] In contrast, thiocyanates have received such less attention, the formation of the triazoloisoquinoline (**5**) from isoquinoline *N*-imide being a rare example.[9] 1,3-Dipolar cycloadditions to selenocyanates appear to be unknown.



(**1**) X = CR_2
(**2**) X = NR
(**3**) X = O
(**4**) X = S



(**5**)

Results and Discussion

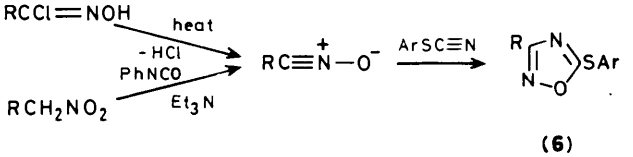
1,3-Dipolar Cycloadditions to Aryl Thiocyanates.—We first examined the reactions of thiocyanates with nitrile oxides generated either by thermal dehydrochlorination of the corresponding hydroximoyl chloride[10] or, in the case of acetonitrile oxide, by dehydration of nitroethane[11] using phenyl isocyanate and triethylamine.

A solution of benzohydroximoyl chloride and 1-naphthyl thiocyanate (1:1) in xylene was heated under reflux until evolution of hydrogen chloride had ceased. Removal of the solvent and chromatography of the residue afforded 5-(1-naphthylthio)-3-phenyl-1,2,4-oxadiazole (**6**; R = Ph, Ar = 1-naphthyl) (79%). Although the possibility of direct interaction between the hydroximoyl chloride and the thiocyanate cannot be ruled out, the most likely reaction pathway involves initial loss of HCl followed by 1,3-dipolar cycloaddition of the resulting benzonitrile oxide to the carbon–nitrogen triple bond of the thiocyanate (Scheme 1). The effect of substituents in the

Table. Cycloaddition of nitrilium betaines to aryl thiocyanates and selenocyanates

1,3-Dipole $RC{\equiv}\overset{+}{N}{-}X^{-}$			Dipolarophile N≡C–Y–Ar	Cycloadduct (%)[a]
R	X	Y	Ar	
Ph	O	S	1-Naphthyl	(**6a**) (79)
$4\text{-}O_2NC_6H_4$	O	S	1-Naphthyl	(**6b**) (75)
$4\text{-}O_2NC_6H_4$	O	S	$4\text{-}O_2NC_6H_4$	(**6c**) (52)
$4\text{-}O_2NC_6H_4$	O	S	$2,4\text{-}(O_2N)_2C_6H_3$	(**6d**) (51)
$4\text{-}O_2NC_6H_4$	O	S	$2\text{-Cl-}4,6\text{-}(O_2N)_2C_6H_2$	(**6e**) (66)
Me	O	S	1-Naphthyl	(**6f**) (39)
Me	O	S	$4\text{-}O_2NC_6H_4$	(**6g**) (48)
$4\text{-}MeC_6H_4$	S	S	$2\text{-Cl-}4,6\text{-}(O_2N)_2C_6H_2$	(**9a**) (37)
Ph	S	S	$2\text{-Cl-}4,6\text{-}(O_2N)_2C_6H_2$	(**9b**) (43)
$4\text{-}MeOC_6H_4$	S	S	$2\text{-Cl-}4,6\text{-}(O_2N)_2C_6H_2$	(**9c**) (20)
$4\text{-}MeC_6H_4$	S	S	$2,4\text{-}(O_2N)_2C_6H_3$	(**9d**) (17)
$4\text{-}MeOC_6H_4$	S	S	$2,4\text{-}(O_2N)_2C_6H_3$	(**9e**) (26)
$4\text{-}MeC_6H_4$	S	S	$4\text{-}O_2NC_6H_4$	(**9f**) (17)
$4\text{-}MeOC_6H_4$	S	S	$4\text{-}O_2NC_6H_4$	(**9g**) (10)
$4\text{-}MeOC_6H_4$	S	S	1-Naphthyl	(**9h**) (2)
Ph	NPh	S	1-Naphthyl	(**12**) (59)
Ph	O	Se	$2,4\text{-}(O_2N)_2C_6H_3$	(**13a**) (72)
Ph	O	Se	1-Naphthyl	(**13b**) (77)
Ph	O	Se	$4\text{-}O_2NC_6H_4$	(**13c**) (58)
$4\text{-}O_2NC_6H_4$	O	Se	$2,4\text{-}(O_2N)_2C_6H_3$	(**13d**) (55)
Ph	S	Se	$2,4\text{-}(O_2N)_2C_6H_3$	(**14a**) (15)
$4\text{-}MeC_6H_4$	S	Se	$2,4\text{-}(O_2N)_2C_6H_3$	(**14b**) (18)

[a] Based on 1,3-dipole



(**6**)

Scheme 1.

dipolarophile was examined for the reaction of 4-nitrobenzonitrile oxide with 1-naphthyl, 4-nitrophenyl, 2,4-dinitrophenyl and 2-chloro-4,6-dinitrophenyl thiocyanates. The results (see the Table) showed little variation in yield.

3-Methyl-5-arylthio-1,2,4-oxadiazoles, (**6f**) and (**6g**), were prepared from the appropriate thiocyanate and acetonitrile oxide formed by treatment of nitroethane with phenyl isocyanate and a catalytic amount of triethylamine. The diphenylurea formed as a by-product was removed by filtration and the adducts separated from unchanged thiocyanate by chromatography.

The identity of the products follows from their analytical and spectroscopic properties. In the ^{13}C n.m.r. spectra there are distinctive peaks for the carbons of the heterocycle at 167—169 (C-3) and at 173—179 p.p.m. (C-5). These values are comparable with those of other 3-aryl-1,2,4-oxadiazoles,[12] such as (**3**; $R^1 = R^2 = Ph$) [169.0 (C-3), 175.1 (C-5)] and (**3**; $R^1 = 4\text{-}O_2NC_6H_4$, $R^2 = Pr^i$) [166.5 (C-3), 187.4 (C-5)]. The chemical shift for C-5 is substituent-dependent, ranging from 178.1 for (**6b**) to 173.1 p.p.m. for (**6e**) but, as expected, the values for C-3 show little variation. In the mass spectra the main fragmentation (Figure 1, path *a*) involves cleavage between the heterocycle and the arylthio group yielding (**7**); when R = 4-$O_2NC_6H_4$ this is invariably followed by loss of NO_2. Such behaviour is unusual for 1,2,4-oxadiazoles which normally[13] fragment at according to paths *b* and *c*. Fragments attributable to paths *b* and *d* are also observed.

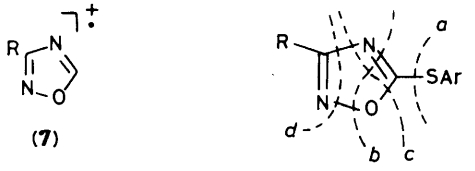
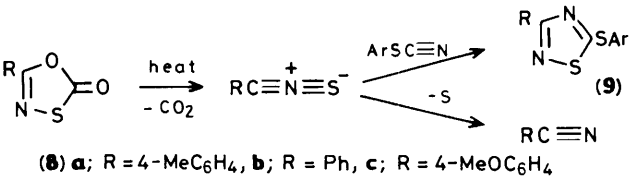


Figure 1.

Having established that typical nitrile oxides would cycloadd to thiocyanates the corresponding reaction with nitrile sulphides was examined. These are short-lived species[7] which usually give much lower yields of cycloadducts than the other nitrilium betaines. They are therefore necessarily generated *in situ* in the presence of the dipolarophile. The method chosen was thermal decarboxylation of oxathiazolones (**8**),[14] which are readily accessible by treatment of the corresponding carboxamide with chlorocarbonylsulphenyl chloride. Heating



(**8**) **a**; R = 4-MeC_6H_4, **b**; R = Ph, **c**; R = 4-$MeOC_6H_4$

Scheme 2.

under reflux of a xylene solution of 2-chloro-4,6-dinitrophenyl thiocyanate with oxathiazolone (**8a**), the precursor of 4-toluonitrile sulphide, yielded a mixture of sulphur, 4-toluonitrile (46%), and the 5-arylthio-1,2,4-thiadiazole (**9a**) (37%), which were separated by chromatography. The formation of sulphur and nitriles as by-products is a common feature of nitrile sulphide chemistry and is attributed[7] to fragmentation competing with cycloaddition (Scheme 2); the other thiocyanates reacted similarly. The yields of adducts (Table) proved to be more substituent dependent than was the case for the nitrile oxides, ranging from 43% for (**9b**) to as little as 2% (**9h**). Electron withdrawing groups in the thiocyanate increase its dipolarophilicity.

The spectroscopic properties of the cycloadducts are broadly similar to those of known 1,2,4-thiadiazoles. Their ^{13}C n.m.r. spectra are characterised by peaks at 172—175 (C-3) and 178—185 p.p.m. (C-5), compared with 173.4 and 187.6 p.p.m. for compound (**4**; $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = Ph$),[15] 173—175 and 178—179 p.p.m. for (**4**; $R^1 = Ar$, $R^2 = CO_2Et$),[15] and 172—174 and 190—191 p.p.m. for (**4**; $R^1 = Ar$, $R^2 = CCl_3$).[5] In the mass spectra all the fragments can be attributed to cleavage at C(3)–N(4) and C(5)–S(1) (Figure 2, path *a*) or at S(1)–N(2) and C(3)–N(4) (path *b*), similar to those reported for simple 3,5-diaryl-1,2,4-thiadiazoles.[16] There is no evidence for cleavage between the heterocycle and the arylthio group, the predominant fragmentation for the corresponding 1,2,4-oxidiazoles.

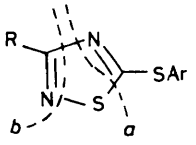
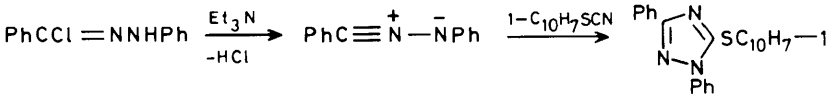


Figure 2.

Benzonitrile *N*-phenylimide (**10**) was chosen as a representative nitrilimine for reaction with thiocyanates. It was generated by dehydrochlorination[11] of the hydrazonoyl chloride (**11**) (Scheme 3). Heating of a solution of compound (**11**) and 1-naphthyl thiocyanate in toluene in the presence of triethylamine yielded, after removal of triethylamine hydrochloride and chromatography, the 5-arylthiotriazole (**12**) (59%). Similar reactivity has been reported[8] for phenyl cyanate with the same nitrile imine. The ease of the process suggests that a variety of 5-arylthio-1,2,4-triazoles should be readily accessible by this approach.



Scheme 3.

1,3-*Dipolar Cycloadditions to Aryl Selenocyanates.*—The reactions of aryl selenocyanates with nitrile oxides and nitrile sulphides closely parallel those of the corresponding thiocyanates. Treatment of 2,4-dinitrophenyl selenocyanates with benzonitrile oxide, generated as described earlier by thermal dehydrochlorination of benzohydroximoyl chloride, yielded the 5-arylseleno-1,2,4-oxidiazole (**13a**) (72%) (Table). 1-Naphthyl and 4-nitrophenyl selenocyanates reacted similarly forming compounds (**13b**) (77%) and (**13c**) (58%). Likewise 4-nitrobenzonitrile oxide reacted with 2,4-dinitrophenyl selenocyanate to

give (**13d**) (55%). The spectroscopic properties of the adducts are generally similar to those derived from the thiocyanates. Typical δ_C values for both heterocyclic ring carbons lie in the range 167—171 p.p.m., representing little change at C-3 but a shift to lower frequency for C-5 of *ca.* 5 p.p.m. compared with the corresponding 5-arylthio derivatives. In the mass spectra the main fragmentation pathway involves cleavage between the heterocycle and the arylseleno group-forming ion (**7**).

Thermolysis of oxathiazolones (**8**; R = Ph, 4-MeC_6H_4) in the presence of 2,4-dinitrophenyl selenocyanate yielded the 5-arylseleno-1,2,4-thiadiazoles (**14a** and **b**) indicative of 1,3-dipolar cycloaddition of benzonitrile sulphide (or 4-toluonitrile sulphide) to the carbon–nitrogen triple bond. In the ^{13}C n.m.r. spectra of the adducts the absorptions for C-3 lie in the range 173—174 p.p.m. (very similar to those of the 5-arylthio analogues), while the C-5 peaks appear at 174—176 p.p.m., corresponding to a shift to lower frequency of 4—5 p.p.m. Electron impact-induced [3 + 2]-cycloreversion is the principal fragmentation pathway in the mass spectrum.

Reactions of 5-*Arylthio*-1,2,4-*oxadiazoles* (**6**) *and Thiadiazoles* (**9**) *with Amines.*—We have previously reported[5] divergent pathways for the reaction of piperidine with the 5-trichloromethyl oxadiazoles (**3**; $R^2 = CCl_3$) and thiadiazoles (**4**; $R^2 = CCl_3$). The former undergo nucleophilic substitution[17] yielding 5-amino derivatives (**3**; $R^2 = NR_2$), while the latter afford[5] the amides (**4**; $R^2 = CONR_2$), presumably by nucleophilic attack at the carbon of the CCl_3 group. A similar trend is evident in the present work. Treatment of the oxadiazole (**6e**) with piperidine yielded the 5-piperidyl compound (**15**), presumably *via* nucleophilic displacement of 2-chloro-4,6-dinitrobenzenethiol. On the other hand, the thiadiazole (**9a**) with the same amine gave a mixture of the piperidylarene (**16**) and 3-(4-tolyl)-1,2,4-thiadiazole-5(4*H*)-thione (**17**). The assignment of structure to the latter compound is supported by a distinctive ^{13}C n.m.r. peak at 201 p.p.m. (C=S), an i.r. absorption at 3 370 cm^{-1} (NH), and a fragment peak in the mass spectrum at *m/z* 149 attributable to 4-$MeC_6H_4CNS^+$. Formula (**18**) is also possible. The corresponding reaction of (**9a**) with morpholine also yielded compound (**17**) together with the substituted arenes (**19**) and (**20**). Likewise compounds (**21**) and (**22**) were formed on treatment of (**9b**) with butylamine. These products are consistent with nucleophilic attack by the amine at C-1 of the 5-arylthio group and displacement of 3-aryl-1,2,4-thiadiazole-5-thiol which is isolated as its thione tautomer.

sulphur. While some 5-arylthio derivatives have been prepared[18] by other methods, the seleno analogues have not been reported previously. The dipolarophilicity of the thiocyanates and selenocyanates appear to be very similar.

Experimental

The analytical methods for monitoring the reactions and the instruments used for recording i.r., ^1H and ^{13}C n.m.r., and mass spectra were as previously described.[19] The oxathiazolones (**8a**—**c**) were prepared by established literature methods.[15,20]

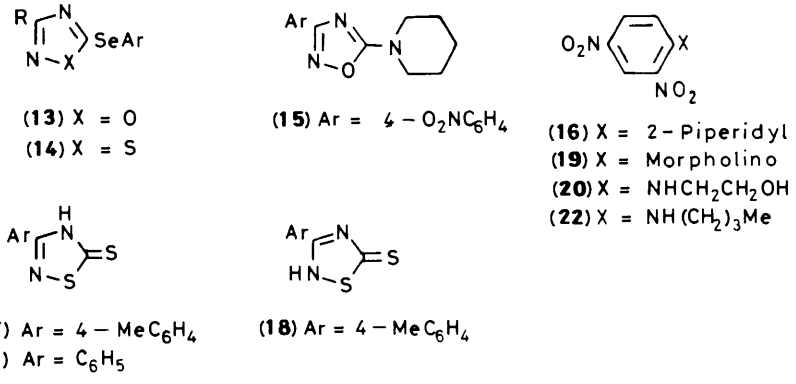
Reactions of Nitrile Oxides with Aryl Thiocyanates and Selenocyanates.—The aryl nitrile oxides were generated *in situ* by thermal dehydrochlorination of the corresponding hydroximoyl chloride. The general method was to heat under reflux a solution of the thiocyanate or selenocyanate and hydroximoyl chloride (1:1) in dry xylene until evolution of HCl had ceased (14—18 h). After removal of the solvent the 3-aryl-5-arylthio- or arylseleno-1,2,4-oxadiazole cycloadduct was separated from unchanged thiocyanate or selenocyanate by chromatography (silica; hexane–dichloro-methane). By this method the following were prepared:

5-(1-*Naphthylthio*)-3-*phenyl*-1,2,4-*oxadiazole* (**6a**): 79%, m.p. 85 °C (from hexane) (Found: C, 70.8; H, 4.1; N, 9.2. $C_{18}H_{12}N_2OS$ requires C, 71.0; H, 4.0; N, 9.2%); δ_C ($CDCl_3$; 20 MHz) 176.2 (C-5), 168.8 (C-3), 135.7, 134.2, 131.9, 131.0, 127.7, 127.2, 126.6, 125.5, 125.0 (12 × ArCH), 134.1, 128.5, 126.2, and 122.3 (ArC); *m/z* 304 (M^+) 201 ($C_{11}H_7NOS^+$), 185 ($C_{11}H_7NS^+$), 145 ($C_8H_5N_2O^+$), 127 ($C_{10}H_7^+$), 119 ($C_7H_5NO^+$), and 77 ($C_6H_5^+$).

5-(1-*Naphthylthio*)-3-(4-*nitrophenyl*)-1,2,4-*oxadizole* (**6b**); 75%, m.p. 168.5 °C (from hexane–dichloromethane) (Found: C, 61.8; H, 3.3; N, 12.3. $C_{18}H_{11}N_3O_3S$ requires C, 61.9; H, 3.2; N, 12.0%); δ_C (CD_2Cl_2; 50 MHz) 178.1 (C-5), 167.6 (C-3), 149.9, 134.8, 134.5, 132.7, 122.5 (ArC), 136.4, 132.7, 129.2, 128.6, 128.3, 127.3, 126.1, 125.3, and 124.2 (11 × ArCH); *m/z* 349 (M^+), 201 ($C_{11}H_7NOS^+$), 190 ($C_8H_4N_3O_3^+$), 185 ($C_{11}H_7NS^+$), 159 ($C_{10}H_7S^+$), 144 ($C_8H_4N_2O^+$), and 127 ($C_{10}H_7^+$).

3-(4-*Nitrophenyl*)-5-(4-*nitrophenylthio*)-1,2,4-*oxadiazole* (**6c**); 52%, 145 °C (from methanol) (Found: C, 56.7; H, 5.0; N, 20.3. $C_{14}H_8N_4O_5S$ requires C, 56.9; H, 5.1; N, 20.4%); δ_C ($CDCl_3$; 20 MHz) 175.7 (C-5), 167.3 (C-3), 149.5, 148.8, 133.4, 131.6 (ArC), 134.5, 128.3, 124.5, and 124.0 (8 × ArCH); *m/z* 344 (M^+), 190 ($C_8H_4N_3O_3^+$), 180 ($C_7H_4N_2O_2S^+$), 164 ($C_7H_4N_2O_3^+$), 144 ($C_8H_4N_2O^+$), and 134 ($C_7H_4NS^+$).

5-(2,4-*Dinitrophenylthio*)-3-(4-*nitrophenyl*)-1,2,4-*oxadiazole* (**6d**); 66%, 150.5 °C (from dichloromethane) (Found: C, 43.2; H, 1.8; N, 18.0. $C_{14}H_7N_5O_7S$ requires C, 43.2; H, 1.8; N, 17.9%); δ_C [$(CD_3)_2SO$; 20 MHz] 172.8 (C-5), 167.6 (C-3), 149.6, 147.1,



In conclusion, the results described herein illustrate a general synthetic route to 5-arylthio- and 5-arylseleno-1,2,4-oxadiazoles and -thiadiazoles. The cycloadditions involving nitrile oxides occur readily and provide easy access to the oxadiazoles. The nitrile sulphides react similarly forming 1,2,4-thiadiazoles, but in lower yield due to competing fragmentation to nitrile and

147.0, 133.5, 131.1 (ArC), 133.9, 128.7, 128.5, 124.6, and 121.3 (7 × ArCH); *m/z* 389 (M^+), 190 ($C_8H_4N_3O_3^+$), 179 ($C_7H_3N_2O_2S^+$), 164 ($C_7H_4N_2O_3^+$), and 144 ($C_8H_4N_2O^+$).

5-(2-*Chloro*-4,6-*dinitrophenylthio*)-3-(4-*nitrophenyl*)-1,2,4-*oxadiazole* (**6e**); 51%, m.p. 132 °C (from ethanol) (Found: C, 39.5; H, 1.5; N, 16.6. $C_{14}H_6ClN_5O_7S$ requires C, 39.7; H, 1.4; N, 16.5%); δ_C (CD_3COCD_3; 50 MHz) 173.1 (C-5), 167.0 (C-3), 153.5, 149.2, 148.9, 141.9, 130.7, 125.7 (ArC), 127.8, 123.4, and 118.3 (6 × ArCH); *m/z* 425, 423 (M^+), 388 [$(M - Cl)^+$], 263, 261 ($C_7H_2ClN_2O_5S^+$), 190 ($C_8H_4N_3O_3^+$), 164 ($C_7H_4N_2O_3^+$), and 144 ($C_8H_4N_2O^+$).

5-(2,4-*Dinitrophenylseleno*)-3-*phenyl*-1,2,4-*oxadiazole* (**13a**): 72%, m.p. 176 °C (from ethanol–dichloromethane) (Found: C, 42.7; H, 2.0; N, 14.1. $C_{12}H_8N_4O_5Se$ requires C, 43.0; H, 2.1; N, 14.3%); δ_C [$(CD_3)_2SO$; 20 MHz] 168.9, 168.8 (C-3 and C-5), 146.6, 145.4, 136.8, 125.4 (ArC), 132.6, 131.9, 129.3, 128.7, 127.2, and 121.2 (8 × ArCH); *m/z* 392 (M^+) 289 ($C_7H_3O_5Se^+$), 247 ($C_6H_3N_2O_4Se^+$), 145 ($C_8H_5N_2O^+$), 119 ($C_7H_5NO^+$), 103 ($C_7H_5N^+$), and 77 ($C_6H_5^+$).

5-(1-*Naphthylseleno*)-3-*phenyl*-1,2,4-*oxadiazole* (**13b**): 77%, m.p. 86—87 °C (from ethanol) (Found: C, 61.6; H, 3.3; N, 7.9. $C_{18}H_{12}N_2OSe$ requires C, 61.4; H, 3.4; N, 8.0%); δ_C ($CDCl_3$; 20 MHz) 170.9, 168.7 (C-3 and C-5), 136.9, 131.7, 131.1, 128.6, 127.6, 127.5, 127.3, 126.6, 125.8 (12 × ArCH), 134.5, 134.3, 126.3, and 122.2 (ArC); *m/z* 352 (M^+), 249 ($C_{11}H_7NOSe^+$), 233 ($C_{11}H_7NSe^+$), 207 ($C_{10}H_7Se^+$), 145 ($C_8H_5N_2O^+$), 127 ($C_{10}H_7^+$), 115 ($C_8H_5N^+$), 103 ($C_7H_5N^+$), and 77 ($C_6H_5^+$).

5-(4-*Nitrophenylseleno*)-3-*phenyl*-1,2,4-*oxadiazole* (**13c**): 58%, m.p. 109—111 °C (from ethanol) (Found: C, 48.5; H, 2.8; N, 12.0. $C_{14}H_9N_3O_3Se$ requires C, 48.6; H, 2.6; N, 12.1%); δ_C ($CDCl_3$; 20 MHz) 169.2, 168.7 (C-3 and C-5), 148.4, 131.7, 125.8 (ArC), 135.3, 131.4, 128.7, 127.3, and 124.3 (9 × ArCH); *m/z* 347 (M^+), 202 ($C_6H_4NO_2Se^+$), 145 ($C_8H_5N_2O^+$), 119 ($C_7H_5NO^+$), 103 ($C_7H_5N^+$), and 77 ($C_6H_5^+$).

5-(2,4-*Dinitrophenylseleno*)-3-(4-*nitrophenyl*)-1,2,4-*oxadiazole* (**13d**); 55%, m.p. 144—146 °C (from ethanol–dichloromethane) (Found: C, 38.7; H, 1.6; N, 16.2. $C_{14}H_7N_5O_7Se$ requires C, 38.6; H, 1.6; N, 16.1%); δ_C [$(CD_3)_2SO$; 20 MHz) 170.0, 167.6 (C-3 and C-5), 149.5, 146.7, 145.4, 132.8, 128.8 (ArC), 137.1, 131.3, 128.8, 124.6, and 121.4 (6 ArCH); *m/z* 437 (M^+), 289 ($C_7H_3N_3O_5Se^+$), 247 ($C_6H_3N_2O_4Se^+$), 190 ($C_8H_4N_3O_3^+$), 164 ($C_7H_4N_2O_3^+$), 148 ($C_7H_4N_2O_2^+$), 144 ($C_8H_4N_2O^+$), and 102 ($C_7H_4N^+$).

Acetonitrile oxide was prepared *in situ* by dehydration of nitroethane. The general method was to add dropwise a solution of the thiocyanate (10 mmol) and phenyl isocyanate (30 mmol) in toluene (20 ml) to a solution of nitroethane (15 mmol) and triethylamine (0.5 ml) in toluene (20 ml). The mixture was stirred for 16 h when the precipitate of diphenylurea was removed by filtration and the filtrate concentrated and chromatographed on silica. Elution with hexane–ethyl acetate yielded unchanged thiocyanate followed by cycloadduct. By this method the following were prepared:

3-*Methyl*-5-(1-*naphthylthio*)-1,2,4-*oxadiazole* (**6f**); 39%, m.p. 93—94 °C (from ethanol) (Found: C, 64.3; H, 4.3; N, 11.8. $C_{13}H_{10}N_2OS$ requires C, 64.4; H, 4.2; N, 11.6%); δ_C $CDCl_3$; 20 MHz) 176.1 (C-5), 167.7 (C-3), 135.6, 131.9, 128.6, 127.6, 126.6, 125.5, 124.9 (ArCH), 134.2, 134.0, 122.3 (ArC), and 11.3 (Me); *m/z* 242 (M^+), 201 ($C_{11}H_7NOS^+$), 185 ($C_{11}H_7NS^+$), 159 ($C_{10}H_7S^+$), 127 ($C_{10}H_7^+$), and 83 ($C_3H_3N_2O^+$).

3-*Methyl*-5-(4-*nitrophenylthio*)-1,2,4-*oxadiazole* (**6g**): 48%, m.p. 143—145 °C (from ethanol) (Found: C, 45.4; H, 3.2; N, 17.9. $C_9H_7N_3O_3S$ requires C, 45.6; H, 3.0; N, 17.7%); *m/z* 237 (M^+), 196 ($C_7H_4N_2O_3S^+$), 180 ($C_7H_4N_2O_2S^+$), 134 ($C_7H_4NS^+$), and 83 ($C_3H_3N_2O^+$).

Reactions of Nitrile Sulphides with Aryl Thiocyanates and Selenocyanates.—The aryl nitrile sulphides were generated by thermal decarboxylation of the corresponding 5-substituted-1,3,4-oxathiazole-2-one.[14] The general method was to heat under reflux a solution of the thiocyanate or selenocyanate and oxathiazolone (1:1) in dry xylene until h.p.l.c. or t.l.c. analysis indicated complete consumption of the oxathiazolone (12—18 h). Removal of the solvent and chromatography of the residue (silica; hexane–dichloromethane or ethyl acetate) yielded sulphur, followed by nitrile, thiadiazole cycloadduct, and unchanged thiocyanate. Traces of thiocyanate were removed by Kugelrohr distillation. By this technique the following were prepared:

5-(2-*Chloro*-4,6-*dinitrophenylthio*)-3-(4-*tolyl*)-1,2,4-*thiadiazole* (**9a**): 37%, m.p. 100—101 °C (from hexane–chloroform) (Found: C, 43.8; H, 2.2; N, 13.5. $C_{15}H_9ClN_4O_4S_2$ requires C, 44.1; H, 2.2; N, 13.7%); δ_C ($CDCl_3$; 20 MHz) 180.0 (C-5), 172.6 (C-3), 153.6, 148.0, 142.5, 130.3, 128.8, 128.0 (ArC), 141.0, 129.2, 127.9, 118.1 (6 × ArCH), and 21.2 (Me); *m/z* 410, 408 (M^+), 373 (M^+ – Cl), 364, 362 ($M^+ - NO_2$), 247, 245 ($C_7H_2ClN_2O_4S_2^+$), 149 ($C_8H_7NS^+$), 117 ($C_8H_7N^+$), and 91 ($C_8H_7^+$). 4-Toluonitrile (46%) was formed as a by-product.

5-(2-*Chloro*-4,6-*dinitrophenylthio*)-3-*phenyl*-1,2,4-*thiadiazole* (**9b**): 43%, m.p. 112—113 °C (from ethanol–chloroform) (Found: C, 42.4; H, 1.8; N, 14.0. $C_{12}H_7ClN_4O_4S_2$ requires C, 42.5; H, 1.8; N, 14.2%); δ_C ($CDCl_3$; 20 MHz), 180.2 (C-5), 172.5 (C-3), 153.7, 148.1, 142.6, 131.5, 130.3 (ArC), 130.7, 128.5, 128.1, 128.0, and 118.1 (7 × ArCH); *m/z* 396, 394 (M^+), 359 (M^+ – Cl), 350, 348 ($M^+ - NO_2$), 247, 245 ($C_7H_2ClN_2O_2S_2^+$), 135 ($C_7H_5NS^+$), 103 ($C_7H_5N^+$), and 77 ($C_6H_5^+$).

5-(2-*Chloro*-4,6-*dinitrophenylthio*)-3-(4-*methoxyphenyl*)-1,2,4-*thiadiazole* (**9c**): 20%, m.p. 156 °C (from ethanol–chloroform) (Found: C, 42.2; H, 2.2; N, 13.0. $C_{15}H_9ClN_4O_5S_2$ requires C, 42.4; H, 2.1; N, 13.2%); δ_H ($CDCl_3$; 80 MHz), 8.68 (1 H, d, *J* 3 Hz, ArH), 8.60 (1 H, d, *J* 3 Hz, ArH), 8.01 (d, *J* 9 Hz, 1 H, ArH), 6.92 (1 H, d, *J* 9 Hz, ArH), and 3.84 (3 H, s, Me); *m/z* 426.424 (M^+), 389 (M^+ – Cl), 165 ($C_8H_7NOS^+$), 133 ($C_8H_7NO^+$). 4-Methoxybenzo-nitrile (42%) was formed as a by-product.

5-(2,4-*Dinitrophenylthio*)-3-(4-*tolyl*)-1,2,4-*thiadiazole* (**9d**): 17%, m.p. 159—161 °C (from hexane–dichloromethane) (Found: C, 47.8; H, 2.7; N, 14.8. $C_{15}H_{10}N_4O_4S_2$ requires C, 48.1; H, 2.7; N, 15.0%); δ_C ($CDCl_3$; 50 MHz), 179.0 (C-5), 175.0 (C-3), 146.3, 146.0, 141.7, 139.7, 129.2 (ArC), 131.1, 129.6, 128.4, 127.5, 121.2 (7 ArCH), and 21.5 (CH_3); *m/z* 374 (M^+), 328 ($M^+ - NO_2$), 257 ($C_7H_3N_3O_4S_2^+$), 211 ($C_7H_3N_2O_2O_2S_2^+$), 149 ($C_8H_7NS^+$), 117 ($C_8H_7N^+$), and 91 ($C_8H_{17}^+$).

5-(2,4-*Dinitrophenylthio*)-3-(4-*methoxyphenyl*)-1,2,4-*thiadiazole* (**9e**): 26%, m.p. 138—139 °C (from ethanol–toluene) (Found: C, 46.4; H, 2.4; N, 14.1. $C_{15}H_{10}N_4O_5S_2$ requires C, 46.1; H, 2.6; N, 14.4%); δ_C ($CDCl_3$; 50 MHz), 178.5 (C-5), 174.5 (C-3), 161.9, 145.9, 145.5, 139.8, 125.1 (ArC), 130.9, 129.9, 127.4, 121.1, and 114.1 (7 × ArCH); *m/z* 390 (M^+), 344 ($M^+ - NO_2$), 298 ($M^+ - 2NO_2$), 165 ($C_8H_7NOS^+$), and 133 ($C_8H_7NO^+$).

5-(4-*Nitrophenylthio*)-3-(4-*tolyl*)-1,2,4-*thiadiazole* (**9f**): 17%, m.p. 144—144.5 °C (Found: C, 54.9; H, 3.2; N, 12.7. $C_{15}H_{11}N_3O_2S_2$ requires C, 54.7; H, 3.4; N, 12.7%); δ_C ($CDCl_3$; 20 MHz), 185.0 (C-5), 173.3 (C-3), 148.5, 140.9, 137.3, 129.3 (ArC), 134.0, 129.3, 128.1, 124.6 (ArCH), and 21.3 (Me); *m/z* 329 (M^+), 212 ($C_7H_4N_2O_2S_2^+$), 149 ($C_8H_7NS^+$), 117 ($C_8H_7N^+$), and 91 ($C_8H_7^+$). 4-Toluonitrile (70%) was formed as a by-product.

3-(4-*Methoxyphenyl*)-5-(4-*nitrophenylthio*)-1,2,4-*thiadiazole* (**9g**): 10%, m.p. 152 °C (from hexane–dichloromethane) (Found: C, 52.2; H, 3.2; N, 12.0. $C_{15}H_{11}N_3O_3S_2$ requires C, 52.2; H, 3.2; N, 12.2%); δ_C ($CDCl_3$; 20 MHz), 184.8 (C-5), 173.1 (C-3), 161.5, 148.6, 137.5, 124.9 (ArC), 134.1, 129.8, 124.7, and 114.0 (8 × ArCH), and 55.2 (Me); *m/z* 345 (M^+), 212 ($C_7H_4N_2O_2S_2^+$), 165 ($C_8H_7NOS^+$), and 133 ($C_8H_7NO^+$).

3-(4-*Methoxyphenyl*)-5-(1-*naphthylthio*)-1,2,4-*thiadiazole* (**9h**): 2%, m.p. 108—110 °C (Found: C, 65.4; H, 3.9; N, 7.8. $C_{19}H_{14}N_2OS_2$ requires C, 65.1; H, 4.0; N, 8.0%); *m/z* 350 (M^+),

217 ($C_{11}H_7NS_2^+$), 185 ($C_{11}H_7NS^+$), 165 ($C_8H_7NOS^+$), 159 ($C_{10}H_7NS^+$), 133 ($C_8H_7NO^+$), and 127 ($C_{10}H_7^+$). 4-Methoxybenzonitrile (85%) was formed as a by-product.

5-(2,4-*Dinitrophenylseleno*)-3-*phenyl*-1,2,4-*thiadiazole* (**14a**): 15%. m.p. 137—139 °C (from ethanol–chloroform) (Found: C, 41.1; H, 2.0; N, 13.6. $C_{14}H_8N_4O_4SSe$ requires C, 41.3; H, 2.0; N, 13.8%); δ_C (CD_3COCD_3; 50 MHz), 174.3, 173.9 (C-3 and C-5), 146.3, 145.4, 138.1, 131.5 (ArC), 131.9, 130.2, 128.2, 127.5, 127.4, and 120.4 (8 × ArCH); *m/z* 408 (M^+), 362 ($M^+ - NO_2$), 305 ($C_7H_3N_3O_4SSe^+$), 259 ($C_7H_3N_2O_2SSe^+$), 135 ($C_7H_5NS^+$), and 77 ($C_6H_5^+$).

5-(2,4-*Dinitrophenylseleno*)-3-(4-*tolyl*)-1,2,4-*thiadiazole* (**14b**): 18%, m.p. 174—175 °C (from ethanol–chloroform) (Found: C, 42.6; H, 2.4; N, 13.2. $C_{15}H_{10}N_4O_4SSe$ requires C, 42.8; H, 2.4; N, 13.3%); δ_C ($CDCl_3$; 50 MHz), 175.8, 173.3 (C-3 and C-5), 146.6, 145.5, 141.5, 139.7, 129.2 (ArC), 131.8, 129.6, 128.4, 127.7, 121.3 (7 × ArCH), and 21.4 (Me); *m/z* 422 (M^+), 376 ($M^+ - NO_2^+$), 305 ($C_7H_3N_3O_4SSe^+$), 259 ($C_7H_3N_2O_2SSe^+$), 149 ($C_7H_7NS^+$), 117 ($C_7H_7N^+$), and 91 ($C_7H_7^+$). 4-Toluonitrile (70%) was formed as a by-product.

Reaction of Benzonitrile N-*Phenylimide with* 1-*Naphthyl Thiocyanate*.—A solution of *N*-phenylbenzohydrazonoyl chloride (0.50 g, 2.2 mmol), 1-naphthyl thiocyanate (400 mg, 1.9 mmol), and triethylamine (0.25 ml) in dry toluene (15 ml) was heated under reflux for 16 h. Removal of triethylamine hydrochloride and chromatography (silica; hexane–ethyl acetate) yielded 5-(1-*naphthylthio*)-1,3-*diphenyl*-1,2,4-*triazole* (**12**) (490 mg, 59%) as a yellow oil (Found: M^+, 379.113371. $C_{24}H_{17}N_3S$ requires *M*, 379.1143 13); δ_C ($CDCl_3$; 50 MHz) 161.9 (C-3), 150.3 (C-5), 136.8, 133.6, 132.8, 130.0, 126.6 (ArC), 132.4, 129.4, 128.9, 128.5, 128.2, 127.9, 126.5, 126.0, 125.9, 125.0, 124.6, and 124.3 (17 × ArCH); *m/z* 379 (M^+), 194 ($C_{13}H_{10}N_2^+$), 185 ($C_{11}H_7NS^+$), 159 ($C_{10}H_7S^+$), 127 ($C_{10}H_7^+$), 103 ($C_7H_5N^+$), 91 ($C_6H_5N^+$), and 77 ($C_6H_5^+$).

Reaction of Compound (**6e**) *with Piperidine*.—A solution of the oxadiazole (**6e**) (600 mg, 1.4 mmol) and piperidine (10 ml) in chloroform (30 ml) was heated under reflux for 2 days. Removal of the solvent and excess piperidine followed by chromatography of the residue on silica yielded 3-(4-*nitrophenyl*)-5-*piperidyl*-1,2,4-*oxadiazole* (**15**) (260 mg, 67%); m.p. 144 °C (from ethanol) (Found: C, 56.7; H, 5.0; N, 20.3. $C_{13}H_{14}N_4O_3$ requires C, 56.9; H, 5.1; N, 20.4%); δ_C ($CDCl_3$; 20 MHz), 171.2 (C-5), 166.8 (C-3), 149.0, 133.9 (ArC), 127.9, 123.6 (4 × ArCH), 46.9, 25.0, and 23.5 (5 CH_2); *m/z* 274 (M^+), 190 ($C_8H_4N_3O_3^+$), 164 ($C_7H_4N_2O_3^+$), 144 ($C_8H_4N_2O^+$), and 112 ($C_6H_{10}NO^+$).

Reaction of Compound (**9a**) *with Amines*.—A solution of the thiadiazole (**9a**) (406 mg, 1.0 mmol) and piperidine (10 ml) in chloroform (40 ml) was heated under reflux for 1 h. Removal of the solvent and excess piperidine followed by chromatography of the residue on silica yielded 1-*chloro*-3,5-*dinitro*-2-*piperidylbenzene* (**16**) (210 mg, 74%), m.p. 125—126 °C (Found: C, 46.1; H, 4.2; N, 14.7. $C_{11}H_{12}ClN_3O_4$ requires C, 46.2, H, 4.2; N, 14.7%); δ_H ($CDCl_3$; 200 MHz), 8.40 (1 H, d, *J* 3 Hz, ArH), 8.33 (1 H, d, *J*3 Hz, ArH), 3.1 (4 H, m, 2 × CH_2), and 1.7 (6 H, m, 3 CH_2); δ_C ($CDCl_3$; 50 MHz), 148.1, 144.1, 139.6, 132.8 (ArC), 128.8, 120.4 (ArCH), 51.6, 15.8, and 23.5 (5 × CH_2); *m/z* 287, 285 (M^+); and 3-(4-*tolyl*)-1,2,4-*thiadiazole*-5-(2H)- or 4(*H*)-*thione* (**17**) or (**18**) (120 mg, 56%), m.p. 176—178 °C (Found: C, 51.8; H, 4.1; N, 13.2. $C_9H_8N_2S_2$ requires C, 51.9; H, 3.9; N, 13.4%); $\nu_{max.}$(Nujol) 3 370 (NH), 1 430, 1 250 cm^{-1} ($CSNR_2$); δ_H [$(CD_3)_2SO$; 80 MHz] 8.1—7.3 (4 H, m, ArH), and 2.5 (3 H, s, Me); δ_C [$(CD_3)_2SO$; 50 MHz], 201.2 (C=S), 160.3 (C=N), 141.7, 124.8 (ArC), 129.4, 127.2 (4 ArCH), and 20.9 (Me); *m/z* 208 (M^+), 149 ($C_8H_7NS^+$), 117 ($C_8H_7N^+$), and 91 ($C_7H_7^+$).

The corresponding reaction with morpholine yielded compound (**17**) (63%), 1-*chloro*-3,5-*dinitro*-2-*morpholinobenzene* (**19**) (82%) [m.p. 157—160 °C (Found: C, 41.6; H, 3.4; N, 14.9. $C_{10}H_{10}ClN_3O_5$ requires C, 41.7; H, 3.5; N, 14.6%); δ_H ($CDCl_3$; 80 MHz), 8.43 (1 H, d, *J*, 3 Hz, ArH), 8.39 (1 H, d, *J* 3 Hz, ArH), 3.84 (4 H, m, 2 CH_2), and 3.28 (4 H, m, 2 CH_2); δ_C ($CDCl_3$; 20 MHz), 146.6, 145.1, 140.9, 133.4 (ArC), 128.8, 120.1 (ArCH), 66.7, and 50.2 (4 CH_2); *m/z* 289, 287 (M^+)], and 1-*chloro*-3,5-*dinitro*-2-(2-*hydroxyethylamino*)*benzene* (**20**) (16%) [(Found: C, 36.6; H, 3.1; N, 16.3. $C_8H_8ClN_3O_5$ requires C, 36.7; H, 3.1; N, 16.1%); δ_H ($CDCl_3$; 80 MHz), 8.79 (1 H, d, *J* 3 Hz, ArH), 8.29 (1 H, d, *J* 3 Hz, ArH), 7.9 (1 H, s, NH), 3.8 (4 H, m, 2 × CH_2), and 2.2 (1 H, s, OH); *m/z* 263, 261 (M^+), and 232, 230 ($M^+ - CH_2OH$)].

Treatment of compound (**9b**) with butylamine yielded 3-*phenyl*-1,2,4-*thiadiazole*-5-(2H)- or (3H)-*thione* (**21**), (58%), m.p. 156.5—158 °C (Found: C, 49.5; H, 2.9; N, 14.5. $C_8H_6N_2S_2$ requires C, 49.5; H, 3.1; N, 14.4%); *m/z* 194 (M^+), 135 ($C_7H_5ND^+$), 103 ($C_7H_5N^+$), and 77 ($C_8H_5^+$); and 2-*butylamino*-1-*chloro*-3,5-*dinitrobenzene* (**22**), (92%) (Found: C, 43.7; H, 4.4; N, 15.5. $C_{10}H_{12}ClN_3O_4$ requires C, 43.9; H, 4.4; N, 15.4%); $\nu_{max.}$(Nujol) 3 360 (NH), 1 515, and 1 325 cm^{-1} (NO_2); δ_C ($CDCl_3$; 20 MHz), 145.6, 135.2, 133.8, 121.8 (ArC), 130.1, 122.1 (ArCH), 46.6, 32.4, 19.6 (CH_2), and 13.3 (CH_2); *m/z* 275, 273 (M^+) and 232, 230 ($M^+ - C_3H_7$).

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