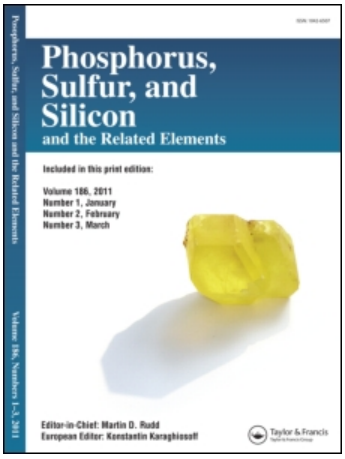

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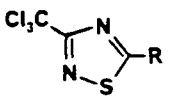
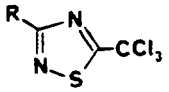
Nitrile sulphides, generated by thermal decarboxylation of 1,3,4-oxathiazol-2-ones, undergo 1,3-dipolar cycloaddition to trichloroacetonitrile yielding 5-trichloromethyl-1,2,4-thiadiazoles (45–66%). The reaction of the cycloadducts with secondary amines has also been examined.

The widespread use of Terrazole (**1**, R=OEt) as a pesticide has led to extensive investigation of the chemistry of 3-trichloromethyl-1,2,4-thiadiazoles.[1] In contrast, the 5-trichloromethyl analogues (**2**) appear to be unknown. We now report that a straightforward synthetic route to (**2**) is provided by the 1,3-dipolar cycloaddition of nitrile sulphides ($RC{\equiv}N^{+}{-}S^{-}$) to trichloroacetonitrile.



(1)



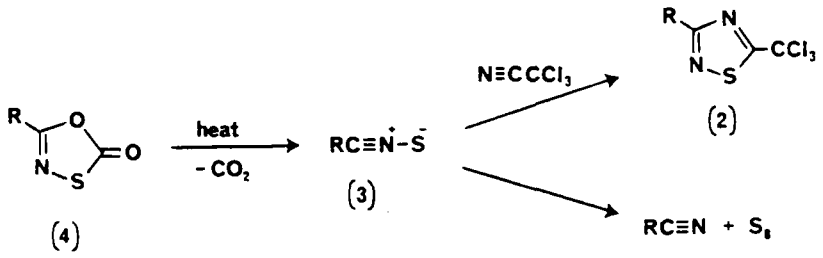
(2)

RESULTS AND DISCUSSION

The nitrile sulphides (**3**) were generated by thermal decarboxylation[2] of 1,3,4-oxathiazol-2-ones (**4**), which are readily available from the corresponding carboxamide by treatment with chlorocarbonylsulphenyl chloride.

A solution of the oxathiazolone and trichloroacetonitrile (1 : 10 molar ratio) in dry toluene or xylene was heated under reflux for 3–4 days. Removal of the solvent and excess dipolarophile afforded a mixture of the 5-trichloromethyl-1,2,4-thiadiazole (**2**)

*Author to whom all correspondence should be addressed.



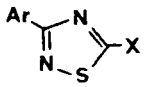
(2-4) a ; R = p-ClC_6H_4
b ; R = C_6H_5
c ; R = p-$MeOC_6H_4$
d ; R = p-MeC_6H_4

SCHEME 1

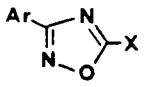
(45–66%), sulphur, the corresponding nitrile, and traces of unreacted oxathiazolone, which were separated by chromatography. The formation of sulphur and nitriles as by-products is a common feature of reactions involving nitrile sulphides and has been attributed[3] to fragmentation of (**3**) competing with the cycloaddition process (Scheme 1).

The identity of the products follows from their analytical and spectroscopic data. Their ^{13}C n.m.r. spectra show characteristic peaks at 172–174 (C-3) and 190–191 ppm (C-5) for the heterocyclic carbons, and at 88–89 ppm for CCl_3. The corresponding values[4] for the ring carbons of the structurally similar 3-aryl-5-ethoxycarbonyl-1,2,4-thiadiazoles (**5**) are 173–175 (C-3) and 178–179 ppm (C-5). (**2**) also shows an absorption at 1600 cm^{-1} (C=N) in the infrared.

The activating influence of electron-withdrawing substituents attached to the nitrile has been established previously.[3] The yields of cycloadduct in the present case suggest that trichloroacetonitrile is a stronger dipolarophile than aromatic nitriles but is weaker than ethyl cyanoformate. A similar trend is evident for the analogous reactions with nitrile oxides,[5] 5-trichloromethyl-1,2,4-oxadiazoles (**6**) being formed in good yield from trichloroacetonitrile.

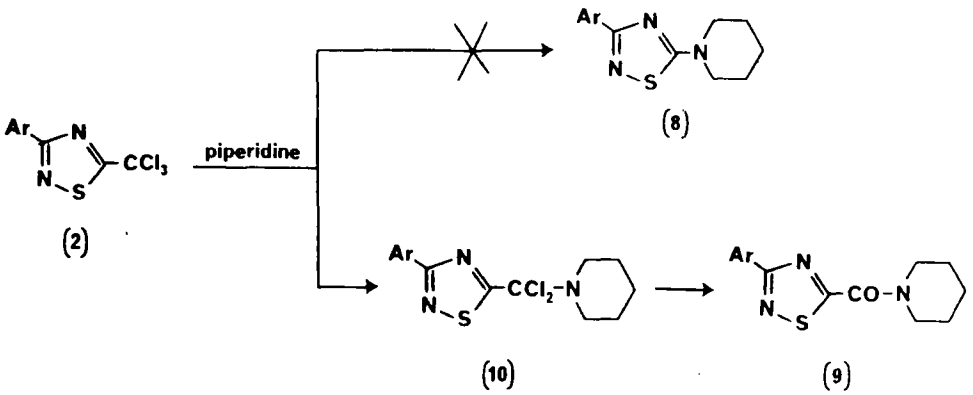


(5) X = CO_2Et
(8) X = NR_2



(6) X = CCl_3
(7) X = NR_2

The trichloromethyl group in (**6**) can be displaced by nucleophiles; e.g. secondary amines yield the dialkylamino derivatives (**7**).[6] Similar behaviour for the thiadiazole series would give (**8**). We therefore examined the reaction of the 5-trichloromethyl-



SCHEME 2

1,2,4-thiadiazoles with piperidine as a representative secondary amine. Treatment of (**2d**) with excess piperidine in chloroform under reflux followed by chromatography on silica yielded a white solid. Its spectroscopic properties, however, were not those anticipated for the dialkylamino compound (**8**). The mass spectrum showed a parent ion peak at m/z 287, 28 greater than that required for (**8**, Ar = p-ClC_6H_4). Furthermore, there were extra peaks in the infrared at 1625 cm^{-1} and in the ^{13}C n.m.r. spectrum at 157.7 ppm. This data indicated the presence of a carbonyl group in addition to the expected aryl, thiadiazole, and piperidine components. The identity of the product was confirmed as the amide (**9d**), in which the piperidine and thiadiazole are separated by a carbonyl group, by preparation of an authentic sample from piperidine and the ethoxycarbonylthiadiazole (**5**, Ar = p-ClC_6H_4). (**2a**) reacted similarly with piperidine forming (**9a**), and with morpholine to give the corresponding morpholinocarbonylthiadiazole.

The formation of (**9**) is consistent with nucleophilic displacement of chloride ion from the trichloromethyl group, followed by hydrolysis during work up of the resulting dichloro compound (**10**) (Scheme 2).

EXPERIMENTAL

The analytical methods for monitoring the reactions and the instrumentation used for recording i.r., ^1H and ^{13}C n.m.r., and mass spectra were as previously described.[7] The 5-aryl-1,3,4-oxathiazol-2-ones (**4a–d**) and 5-ethoxycarbonyl-3-(p-tolyl)-1,2,4-thiadiazole were prepared by established literature routes.[2,8]

Synthesis of 3-Aryl-5-trichloromethyl-1,2,4-thiadiazoles (**2**). These were prepared by heating under reflux a solution of the appropriate oxathiazolone and excess trichloroacetonitrile (1 : 10) in toluene (*ca* 100°C) or xylene (110–115°C), as described below for 3-*p*-chlorophenyl-5-trichloromethyl-1,2,4-thiadiazole. After removal of the solvent and excess trichloroacetonitrile by evaporation under reduced pressure, the products were separated from sulphur and nitrile by-products and traces of unreacted oxathiazolone by chromatography on silica.

3-(p-Chlorophenyl)-5-trichloromethyl-1,2,4-thiadiazole (**2a**). A solution of 5-(p-chlorophenyl)-1,3,4-oxathiazol-2-one (5.0 g, 23.4 mmol) and trichloroacetonitrile (34 g, 235 mmol) in toluene (50 ml) was heated under reflux for 186 h. Removal of the solvent and excess nitrile left a brown solid which was chromatographed on silica (Merck silica gel, 5% deactivated) to yield 3-(*p*-chlorophenyl)-5-trichloromethyl-1,2,4-thiadiazole (**2a**) (4.33 g, 59%) as a white crystalline solid (from ethanol), m.p. 86–87°C. (Found: C, 34.3; H, 1.3; N, 8.8. $C_9H_4Cl_4N_2S$ requires C, 34.4; H, 1.3; N, 8.9%); ν_{max} (Nujol) 1600 cm^{-1} C=N); δ_C ($CDCl_3$, 20 MHz) 190.8 (C-5), 172.8 (C-3), 137.1 and 130.2 (4ArC), 129.5 and 128.9 (ArCH), and 88.0 (CCl_3).

3-Phenyl-5-trichloromethyl-1,2,4-thiadiazole (**2b**). (48%) m.p. 74–75°C (from ethanol). (Found: C, 38.6; H, 1.8; N, 9.8. $C_9H_5Cl_3N_2S$ requires C, 38.7; H, 1.8; N, 10.0%); δ_C ($CDCl_3$, 20 MHz) 190.5 (C-5), 173.9 (C-3), 131.7 (PhC), 130.8, 128.6, 128.2 (5PhCH), 88.1 (CCl_3).

3-(p-Methoxyphenyl)-5-trichloromethyl-1,2,4-thiadiazole (**2c**). (45%) m.p. 90–91°C. (Found: C, 38.7; H, 2.3; N, 8.8. $C_{10}H_7Cl_3N_2OS$ requires C, 38.8; H, 2.3; N, 9.0%); δ_C ($CDCl_3$, 50 MHz) 190.2 (C-5), 173.7 (C-3), 161.7 and 124.8 (ArC), 129.9 and 114.0 (4ArCH), 88.5 (CCl_3) and 55.1 (OMe).

3-(p-Tolyl)-5-trichloromethyl-1,2,4-thiadiazole (**2d**). (66%) m.p. 70–71°C (from ethanol). (Found: C, 46.6; H, 2.4; N, 9.4. $C_{10}H_7Cl_3N_2S$ requires C, 46.9; H, 2.4; N, 9.5%); δ_C ($CDCl_3$, 20 MHz) 190.3 (C-5), 174.0 (C-3), 141.1 and 129.2 (ArC), 129.3 and 128.2 (4ArCH), 88.2 (CCl_3), and 21.3 (Me).

Preparation of 5-(piperidinocarbonyl)-3-(p-tolyl)-1,2,4-thiadiazole (**9d**). A solution of 5-ethoxycarbonyl-3-*p*-tolyl-1,2,4-thiadiazole (2.0 g, 8.1 mmol) and piperidine (10 ml) in chloroform (30 ml) was heated under reflux for 4.5 h. After removal of the solvent and excess amine by evaporation under reduced pressure the residue was recrystallised from ethanol to yield 5-piperidinocarbonyl-3-(*p*-tolyl)-1,2,4-thiadiazole (**9d**) (2.1 g, 90%) as a white crystalline solid, m.p. 86°C. (Found: C, 62.5; H, 5.9; N, 4.8. $C_{15}H_{17}N_3OS$ requires C, 62.7; H, 6.0; N, 4.6%); ν_{max} (Nujol) 1625 cm^{-1} (C=O); δ_C ($CDCl_3$, 20 MHz) 185.2 (C-5), 173.0 (C-3), 157.7 (C=O), 140.5 and 129.7 (ArC), 129.2 and 127.9 (4 ArCH), 47.3, 44.2, 26.4, 25.5 and 24.2 (CH_2) and 21.2 (Me); *m/z* 287 ($\underline{M}^+$), 203 [($\underline{M}$—$C_5H_{10}N$)$^+$], 149 ($ArCNS^+$), 117 ($ArCN^+$).

Reaction of 3-Aryl-5-trichloromethyl-1,2,4-thiadiazoles with secondary amines. A mixture of 3-(*p*-tolyl)-5-trichloromethyl-1,2,4-thiadiazole (**2d**) (0.52 g, 1.8 mmol) and piperidine (10 ml) in chloroform (30 ml) was heated under reflux for 5 h. Removal of the solvent and excess amine, followed by chromatogrphay (silica/petrol-EtOAc, 6 : 1) yielded 5-piperidinocarbonyl-3-(*p*-tolyl)-1,2,4-thiadiazole (0.33 g, 65%), m.p. and mixed m.p. 85–86°C. The spectroscopic data for the product were identical to those of the authentic sample.

Similar treatment of (**2a**) with piperidine afforded *3-(p-chlorophenyl)-5-piperidinocarbonyl-1,2,4-thiadiazole* (**9a**) (72%), m.p. 103°C (Found: C, 54.4; H, 4.5; N, 13.5. $C_{14}H_{14}ClN_3OS$ requires C, 54.6; H, 4.6; N, 13.6%). The corresponding reaction of (**2a**) with morpholine yielded 3-(*p*-chlorophenyl)-5-morpholinocarbonyl-1,2,4-thiadiazole (27%), m.p. 174–175°C (Found: $\underline{M}^+$, 309.03330. $C_{13}H_{12}ClN_3O_2S$ requires $\underline{M}$, 309.03385).

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