Use of Piperidine-1-sulphenyl Chloride as a Sulphur-transfer Reagent in Reactions with Diamines: The Preparation of Sulphur–Nitrogen Heterocycles

Martin R. Bryce
Department of Chemistry, University of Durham, South Road, Durham DH1 3LE

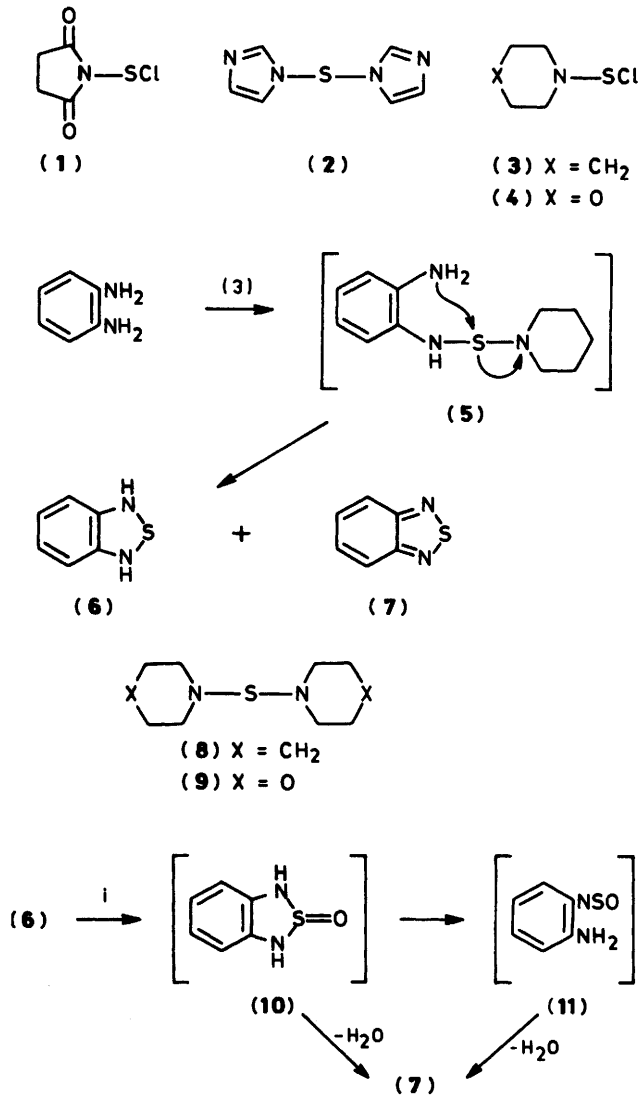
The use of piperidine-1-sulphenyl chloride (**3**) as a sulphur-transfer reagent in reactions with diamines is described. The reaction of (**3**) with *o*-phenylenediamine yielded the dihydro-2,1,3-benzothiadiazole (**6**) and benzothiadiazole (**7**). Oxidation of (**6**) with *m*-chloroperoxybenzoic acid yielded (**7**). The reactions of (**3**) with 1,8-diaminonaphthalene and 1,4,5,8-tetra-aminonaphthalene yielded the 1,2,6-thiadiazine derivatives (**14**) and (**16**); possible mechanisms are discussed. 1,2-Diamino-*N,N'*-dimethylethane and (**3**) yielded the tetrahydrothiadiazole (**17**), whereas 1,3-diaminopropane and (**3**) afforded the novel N–S–N chain compound (**19**). The reactions of morpholine-1-sulphenyl chloride (**4**) with aromatic diamines gave the same products in low yields.

The importance of sulphur-transfer reagents in the synthesis of sulphur-containing heterocyclic compounds is well known and has been emphasized in a recent review.[1] New reagents of general formulae RNSCl or RNSNR, *e.g.* (**1**) and (**2**), with a nitrogen heterocycle as a leaving group, have been developed as alternatives to sulphur dichloride for introducing a sulphur atom between nitrogen, oxygen, or sulphur.[2] These reagents are more convenient to use than SCl_2 as they are easy to purify, do not disproportionate, and do not bring about unwanted chlorination reactions. The related reagents piperidine-1-sulphenyl chloride (**3**) and morpholine-1-sulphenyl chloride (**4**), although known for over twenty years,[3] have received scant attention[4–7] and their potential as sulphur-transfer reagents remains largely unexplored. We were attracted by an early communication which reported the reaction of aniline and some derivatives with compound (**3**) to yield products of general formula ArNH–S–NHAr.[4] We have extended this work and now describe reactions of both compounds (**3**) and (**4**) with selected aromatic and aliphatic diamines to yield new heterocyclic products.

The reaction of *o*-phenylenediamine with compound (**3**) in anhydrous ether at −20 °C yielded a mixture of dihydro-2,1,3-benzothiadiazole (**6**) (45%) and 2,1,3-benzothiadiazole (**7**) (15%) along with dipiperidino sulphide (**8**) (10%). The formation of the 2,1,3-benzothiadiazole system (**7**) from *o*-phenylenediamine and a variety of sulphur-transfer reagents [*e.g.* $SOCl_2$,[8] PhNSO,[9] and $(PhSO_2N)_2S$[9]] is well known, and although compound (**6**) has been postulated as an intermediate on at least one occasion,[10] it has never been isolated before. The reaction with piperidinesulphenyl chloride can be considered to proceed *via* intermediate (**5**) and displacement of the anion of piperidine, which will react further to form piperidinium hydrochloride. The dihydrothiadiazole (**6**) is a pale yellow solid that is stable at room temperature, but solutions of (**6**) in methanol, chloroform, or acetonitrile rapidly darken and on evaporation yield tars. An attempt to isolate the sulphoxide (**10**) from peracid oxidation of the dihydrothiadiazole (**6**) was unsuccessful; the only isolated product was the thiadiazole (**7**). This can be readily explained by dehydration of the sulphoxide (**10**), or by ring opening of (**10**) to the *N*-sulphinylamine (**11**) which could then dehydrate to give (**7**) (Scheme 1).

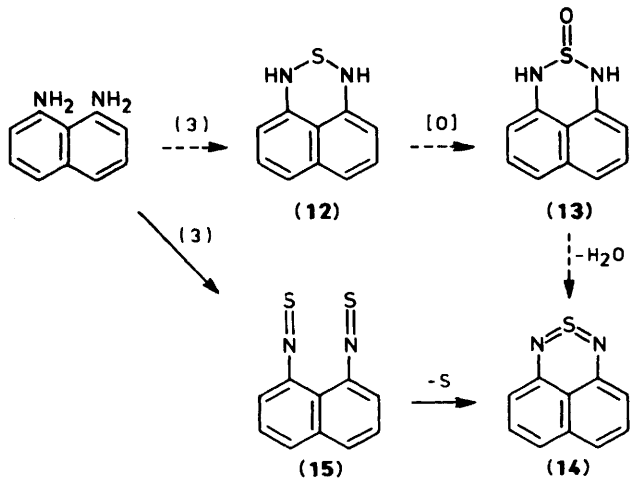
The reaction of *o*-phenylenediamine with morpholine-1-sulphenyl chloride (**4**) also gave products (**6**) and (**7**), but in low yields; the major product was the sulphide (**9**).

The reaction of 1,8-diaminonaphthalene with piperidine-1-sulphenyl chloride yielded the known[11] thiadiazine (**14**) (62%) as the only identifiable product. No evidence for a compound containing the expected NH–S–NH grouping could be obtained. The mechanism of formation of product (**14**) is unclear

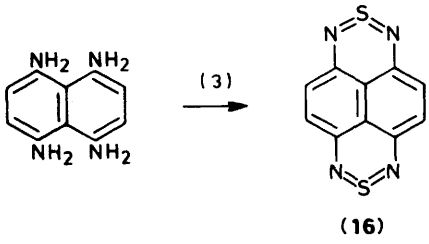


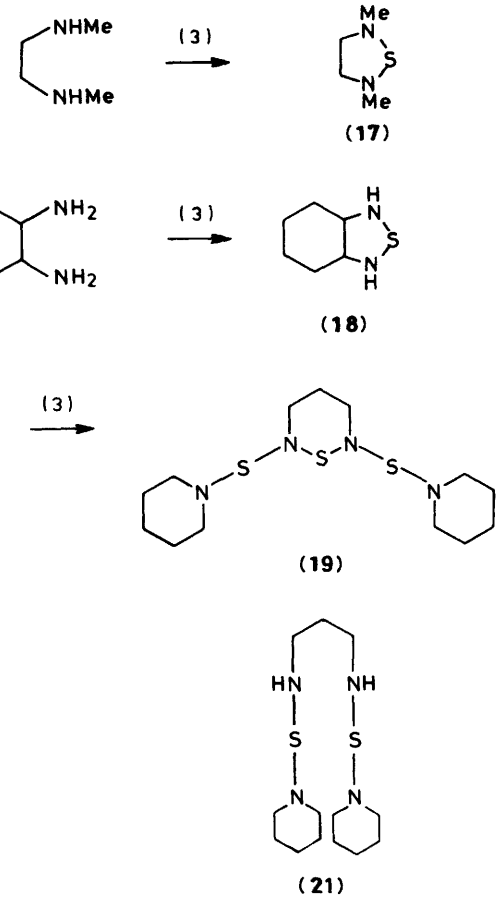
Scheme 1. *Reagents:* i, *m*-$ClC_6H_4CO_3H$ (1 equiv.)

(Scheme 2). A route *via* the intermediate (**12**) followed by oxidation to give (**13**) and subsequent dehydration to yield product (**14**) seems most unlikely, as the reaction was performed in the absence of air or moisture. Moreover, authentic



Scheme 2.





sulphoxide (**13**) (from 1,8-diaminonaphthalene and *N*-sulphinylaniline)[11] did not yield the thiadiazine (**14**) when treated with the reagent (**3**) under these conditions. An alternative route for the formation of compound (**14**) could involve the loss of sulphur from the bis(thionitroso) compound (**15**) which would be expected to be very unstable. Sulphur eliminations of this type leading to acyclic sulphur di-imides have been reported very recently.[12] However, our attempts to trap a transient thionitroso group with 2,3-dimethylbutadiene or cyclopentadiene, for which there are precedents,[4,5,12] were unsuccessful.

The reaction of 1,4,5,8-tetra-aminonaphthalene with piperidinesulphenyl chloride yielded the analogous bis(1,2,6-thiadiazine) derivative (**16**) (25%), previously prepared from a salt of the tetra-amine and sulphur dioxide.[13] Again, no product containing an NH group was identified. The molecular and electronic structure of (**16**) have recently been studied in some detail to probe the ambiguous aromatic properties of the molecule.[14] A lower yield of the product (**14**) from 1,8-diaminonaphthalene was obtained when the morpholine derivative (**4**) was used instead of the piperidine derivative (**3**), and again the major product was dimorpholino sulphide (**9**). These low yields for the reactions of compound (**4**) led us to concentrate on the piperidine derivative (**3**) for reactions with aliphatic diamines.

Three aliphatic 1,2-diamines were tried. Addition of compound (**3**) to 1,2-diaminoethane lead to an intractable tar, but 1,2-diamino-*N*,*N*'-dimethylethane gave the known tetrahydrodimethylthiadiazole (**17**) (30%), previously prepared using *N*,*N*'-thiobisphthalimide as the sulphur-transfer reagent.[15] 1,2-Diaminocyclohexane and compound (**3**) gave a very low yield of a product that could not be obtained analytically pure, but for which the mass spectrum (*m*/*z* 144) and n.m.r. and i.r. spectroscopic data (in particular the presence of a secondary NH) suggested structure (**18**), analogous to product (**6**) from *o*-phenylenediamine.

However, a cleaner reaction occurred between 1,3-diaminopropane and the sulphur reagent (**3**) to afford a colourless crystalline solid. Microanalytical and mass spectroscopic data implied a molecular formula $C_{13}H_{26}N_4S_3$ and ^1H n.m.r. data suggested a highly symmetrical structure without an NH group. I.r. spectra confirmed the absence of NH and the presence of one or more N–S groups ($\nu_{max.}$ 758 cm^{-1}). Taken together this evidence identifies the product as the 1,2,6-thiadiazine derivative (**19**) (30%). The formation of compound (**19**) requires three equivalents of sulphenyl chloride (**3**) and could proceed *via* intermediate (**20**) or (**21**); however, attempts to isolate an intermediate by using a decreasing molar proportion of (**3**) led only to progressively lower yields of the product (**19**). The failure to isolate the intermediate (**20**) could be due to the high acidity of the NH proton resulting from lone pair donation from nitrogen to sulphur. This high acidity would favour the reaction of the sulphenyl chloride with compound (**20**) rather than with diaminopropane. Also, it is known that the presence of three contiguous sp^3 hybridised heteroatoms can be a cause of instability in heterocyclic systems.[16] Compound (**19**) provides the first example of a derivative of the fully saturated 1,2,6-thiadiazine ring system, and its formation represents a novel route to an N–S–N chain compound.

Attempts to obtain the 1,2,7-thiadiazepine ring system by reaction of 1,4-diaminobutane with piperidinesulphenyl chloride (**3**) gave only intractable tars.

Experimental

N.m.r. spectra were recorded on a Brüker HX90E spectrometer or a JEOL PFT 100 spectrometer (at Bristol University) with tetramethylsilane as internal standard. Mass spectra were

recorded on an A.E.I. MS9 spectrometer. I.r. spectra were recorded as Nujol mulls, unless otherwise stated, using a Perkin-Elmer 577 instrument. Microanalyses were obtained on a Perkin-Elmer CHN240 elemental analyser. M.p.s were recorded on a Kofler micro-heating stage and are uncorrected. Column chromatography was performed on alumina Brockman activity II. Ether refers to diethyl ether.

Reactions of Piperidine-1-sulphenyl Chloride (**3**) *with Diamines: General Procedure.*[4]—A solution of sulphenyl chloride (**3**)[3] (3.0 g, 20 mmol) in dry ether (20 ml) was added dropwise with stirring to a solution of diamine (20 mmol) in dry ether (50 ml) at −20 °C. The solution was stirred at −20 °C overnight. Piperidinium hydrochloride was removed by filtration and the ether evaporated under reduced pressure at room temperature to yield the crude product.

Reaction with o-phenylenediamine. Addition of ice-cold methanol to the crude product precipitated an orange solid. Recrystallisation from methanol afforded 1,3-*dihydro*-2,1,3-*benzothiadiazole* (**6**) (1.13 g, 45%), m.p. 130—132 °C (Found: C, 52.0; H, 4.1; N, 20.4. $C_6H_6N_2S$ requires C, 52.5; H, 4.4; N, 20.3%); *m/z* 138 (M^+); δ_H ($CDCl_3$) 7.72 (2 H, br s, NH) and 6.9—7.3 (4 H, m, ArH); $\nu_{max.}$ 3 340 cm^{-1} (NH). Column chromatography of the residue, with hexane–ether (4:1 v/v) as eluant, gave impure compound (**6**) (0.2 g, 10%), 2,1,3-benzothiadiazole (**7**) (0.34 g, 15%) (identical by mixed m.p. with an authentic sample[9]), and dipiperidino sulphide (**8**) (0.20 g, 10%), m.p. 73—76 °C (lit.,[17] 75—76 °C).

Reaction with 1,8-diaminonaphthalene. Recrystallisation of the crude product from acetone yielded naphtho[1,8-*cd*][1,2,6]-thia(S^{IV})diazine (**14**) (2.3 g, 62%), identical by i.r. and mixed m.p. with an authentic sample.[11] When the reaction was carried out in the presence of 2,3-dimethylbutadiene (20 mmol) or cyclopentadiene (20 mmol) the only isolated product was the thiadiazine (**14**) (50—60%).

Reaction with 1,4,5,8-tetra-aminonaphthalene. Recrystallisation of the crude product from 1,2-dichloroethane yielded naphtho[1,8-*cd*:4,5-*c'd'*]bis[1,2,6]thia(S^{IV})diazine (**16**) (1.2 g, 25%), m.p. 287—288 °C (lit.,[13] 288—290 °C) (i.r. spectrum identical with the literature data).[13]

Reaction with 1,2-diaminoethane. Evaporation of the solvent gave a red tar from which nothing could be obtained pure.

Reaction with N,N'-dimethyl-1,2-diaminoethane. Evaporation of the solvent gave a tarry residue. Column chromatography [eluant, hexane–ether (4:1 v/v)] separated 2,5-dimethyltetrahydro-1,2,5-thiadiazole (**17**) (0.71 g, 30%), *m/z* 118 (M^+); m.p. 125—127 °C (lit.,[15] 125—127 °C).

Reaction with 1,2-diaminocyclohexane. Evaporation of solvent gave an oil which was a mixture of at least three components by t.l.c. Column chromatography [eluant, hexane–ether (3:1 v/v)] separated a viscous yellow oil identified as hexahydro-2,1,3-benzothiadiazole (**18**) (0.27 g, 10%) (Found: C, 49.2; H, 8.6; N, 20.5. Calc. for $C_6H_{12}N_2S$: C, 50.0; H, 8.3; N, 19.4%); *m/z* 144 (M^+); δ_H ($CDCl_3$) 7.5 (2 H, br s, NH), 2.9 (2 H, m, C*H*NH), and 1.8—1.4 (8 H, m, CH_2); $\nu_{max.}$ 3 335 cm^{-1} (NH). Further purification of compound (**18**) by preparative scale t.l.c. or vacuum distillation was unsuccessful. No other products could be separated.

Reaction with 1,3-diaminopropane. Diamine (1.8 g, 25 mmol) and piperidine-1-sulphenyl chloride (**3**) (30 g, 0.2 mmol) yielded an oil which was dissolved in methanol (12 ml) and left at −20 °C for a week. Colourless crystals were filtered off and recrystallised from methanol to afford 2,6-*bis(piperidinosulphenyl)*-3,4,5,6-*tetrahydro*-1H-1,2,6-*thiadiazine* (**19**) (2.5 g, 30%), m.p. 108—109 °C (Found: C, 47.0; H, 7.8; N, 16.6; S, 29.1. $C_{13}H_{26}N_4S_3$ requires C, 46.7; H, 7.8; N, 16.7; S, 28.7%); *m/z* 116 $(C_5H_{10}NS)^+$, and 102 $(C_3H_6N_2S)^+$ (M^+ absent); δ_H ($CDCl_3$) 3.8 (4 H, m), 3.0 (8 H, m), and 1.5 (14 H, br s); $\nu_{max.}$ 1 210 (C–N), 758 cm^{-1} (N–S), (NH absent). Chromatography of the residue gave oils which could not be purified.

Reactions of Morpholine-1-sulphenyl Chloride (**4**) *with Diamines.*—Reactions were carried out on the same scale and under the same conditions as those detailed above for piperidinesulphenyl chloride.

Reaction with o-phenylenediamine. Isolated products were the dihydrothiadiazole (**6**) (10%), the thiadiazole (**7**) (10%), and dimorpholino sulphide (**9**)[17] (20%).

Reaction with 1,8-diaminonaphthalene. Isolated products were the thiadiazine (**14**) (8%) and the sulphide (**9**) (15%).

Reaction of Dihydrobenzothiadiazole (**6**) *with m-Chloroperoxybenzoic Acid.*—To a stirred solution of the dihydrothiadiazole (**6**) (0.42 g, 3 mmol) in dry chloroform (50 ml) under nitrogen was added *m*-chloroperoxybenzoic acid (0.50 g, 3 mmol) in portions during 15 min. The mixture was stirred at room temperature for 1 h and then washed with aqueous Na_2CO_3. The organic layer was dried ($MgSO_4$) and evaporated to leave a red oil. Vacuum sublimation (80 °C, 10 mmHg) separated the 2,1,3-benzothiadiazole (**7**) (0.20 g, 48%), identical with material described above.

Reaction of the Sulphoxide (**13**) *with Piperidine-1-sulphenyl Chloride* (**3**).—A mixture of sulphenyl chloride (**3**) (1.5 g, 10 mmol), piperidinium hydrochloride (0.6 g, 5 mmol), and the sulphoxide (**13**)[18] were stirred overnight at −20 °C in dry ether (20 ml). The mixture remained colourless with no appearance of the intense blue colour characteristic of the thiadiazine (**14**).

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