Synthesis of 1,4,2,5-Dithiadiazines, a New Heterocyclic System, from Aminosulphines (Thioamide *S*-Oxides)

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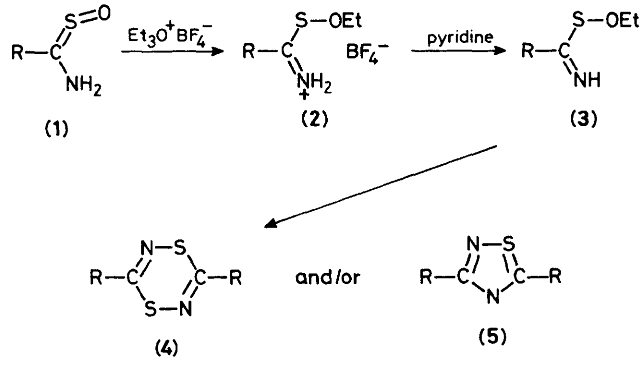
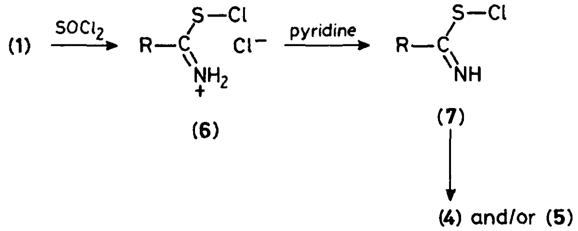
Treatment of aryl aminosulphines (thiobenzamide *S*-oxides) with either $Et_3O^+BF_4^-$ or $SOCl_2$, followed by base, leads to 1,4,2,5-dithiadiazines.

We report here a synthesis of 1,4,2,5-dithiadiazines, a new heterocyclic system, from aminosulphines (thioamide *S*-oxides). While exploring the chemistry of sulphines[1] we have investigated the reaction of thioamide *S*-oxides with electrophilic reagents with the aim of establishing which nucleophilic site in these molecules, N, S, or O, reacts preferentially. Reactions of sulphines with electrophilic reagents have received little attention.[1] The reaction of $Ph_2C{=}S{=}O$ with $Et_3O^+BF_4^-$ was reported to give *O*-alkylation to unstable, hygroscopic salts which on hydrolysis form benzophenone.[2] Simple aliphatic sulphines react with alkanesulphinyl chloride to give an initial reaction at the sulphine oxygen atom.[3] The reaction of thiobenzamide *S*-oxide, the same type of aminosulphines as investigated here, with electrophiles such as $(CF_3CO)_2O$, BF_3–diethyl ether, or anhydrous $CaCl_2$, gives 2,5-diphenyl-1,2,4-thiadiazole.[4]

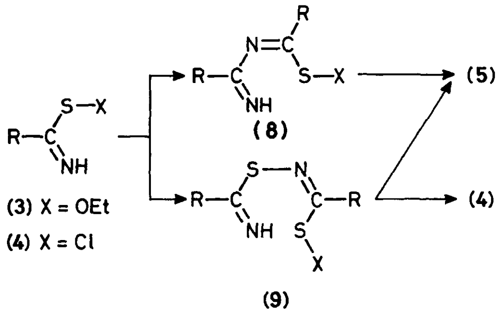
Treatment of thiobenzamide *S*-oxide (**1a**) with $Et_3O^+BF_4^-$ (CH_2Cl_2, 25 °C, 10 min) gave the stable salt (**2a**) [yield 75%; m.p. 104—105 °C (from CH_2Cl_2–diethyl ether); $\nu_{max.}$ ($CHCl_3$) 3280, 3140, 1615, and 1065 cm^{-1}; ^1H-n.m.r. ($CDCl_3$) δ 1.50 (t, 3H, *J* 6.0 Hz, Me), 4.37 (q, 2H, *J* 6.0 Hz, CH_2), 7.5—7.9 (m, 5H, Ar), 8.23 and 8.87 (2 × br.s, 2H, NH_2)]. Subsequently, iminium salt (**2a**) was deprotonated with an excess of pyridine (CH_2Cl_2, 25 °C, 1 h) with the aim of preparing the corresponding α-imino sulphenate (**3a**).† Instead heterocycle (**4a**) was isolated by flash column chromatography on silica gel (light petroleum–ethyl acetate 20 : 1) [yield 30%; m.p. 102—104 °C (from light petroleum)]. No characteristic i.r. absorption was observed for the imine bond. Similarly substituted thiobenzamide *S*-oxides (**1c**—**e**) were converted into the corresponding salts (**2c**—**e**). Treatment with base led to the respective heterocycles (**4c**—**e**). Isolation of the salts (**2**) was not necessary; a one-pot procedure can also be followed. In the case of the 4-chloro compound (**2f**) no (**4f**) was formed, but instead the 1,2,4-thiadiazole (**5f**) was obtained. This type of



Scheme 1



Scheme 2



Scheme 3

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† Treatment of the iminium salts derived from secondary thioamide *S*-oxides with base leads to isolable α-imino sulphenates: B. G. Lenz and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, in the press (*cf.* ref. 5).

Table 1. Synthesis of iminium salts (**2**) and 1,4,2,5-dithiadiazines (**4**).[a]

	R	Yield of (**2**)/%	M.p./°C	Procedure[b]	Yield[c] of (**4**)/%	M.p./°C	Yield[c] of (**5**)/%
a	Ph	75	104—105	A	30	102—104	
				B	48		
b	4-Me-C_6H_4	93[d]	110—112	B	39[d]	153—154	
c	3-Me-C_6H_4	[e]		A	27[d]	81—82	21[d,f]
d	2-Me-C_6H_4	[e]		A	4[d]	135—137	
				B	50		
e	4-MeO-C_6H_4	[e]		B	46[d]	155—157.5	
f	4-Cl-C_6H_4	[e]		A			49[g]
				B			9

[a] All compounds gave correct elemental analyses. [b] Procedure A: $Et_3O^+BF_4^-$ followed by pyridine. Procedure B: $SOCl_2$ followed by pyridine. [c] All compounds isolated by flash column chromatography on silica gel [light petroleum–ethyl acetate, except (**4c**) (CCl_4) and (**4d**) (CCl_4–1% MeCN). [d] See footnote ‡. [e] Not isolated. [f] M.p. 55—57 °C (ref. 7 m.p. 49.5 °C). [g] M.p. 151—153 °C (ref. 8 m.p. 161—162 °C).

heterocycle was also obtained from (**2c**) as the second product (Scheme 1). Yields of this reaction (procedure A) are listed in Table 1.

An alternative method of preparing (**4**) from (**1**) is initial treatment with thionyl chloride (1 equiv.) (CH_2Cl_2, −78 °C, 5 min) and subsequent treatment with excess of pyridine (−78 °C, 10 min; 25 °C, 1 h) (Scheme 2). The initially formed iminium salts (**6**) are too unstable to allow isolation. The results of this procedure B are compiled in Table 1. Note that using this method (**4f**) was still not formed from (**1f**).

The structure of the new heterocyclic system was determined by an *X*-ray diffraction analysis of (**4e**).[6]

It seems reasonable to propose the sulphenates (**3**)† and (**7**), respectively, as primary intermediates. The formation of the heterocycles (**4**) and (**5**) can be rationalized as follows (Scheme 3). Nucleophilic attack of the imine nitrogen on the imine carbon atom leads to intermediate (**8**) which then expels the X-group to give (**5**). Alternatively, the S–X bond can be attacked by the imine nitrogen atom yielding intermediate (**9**). Reaction of the NH group with the S–X function leads to the six-membered heterocycle (**4**), whereas displacement of the S–X group by the imine nitrogen gives (**5**). It is probable that for an electron-withdrawing R substituent, such as 4-chlorophenyl, the electrophilicity of the imine carbon atom is enhanced to such an extent that either intermediate (**8**) is formed preferentially, or intermediate (**9**) produces the 5-membered ring exclusively.

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References

1 B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, 1982, **101**, 1.
2 L. Carlsen and A. Holm, *Acta Chem. Scand., Ser. B*, 1976, **30**, 277.
3 E. Block and A. A. Bazzi, *Tetrahedron Lett.*, 1982, **23**, 4569.
4 J. R. Cashman and R. P. Hanzlik, *J. Org. Chem.*, 1982, **47**, 4645.
5 J. M. M. Smits, J. H. Noordik, B. G. Lenz, and B. Zwanenburg, *Cryst. Struct. Commun.*, 1982, **11**, 1625.
6 J. M. M. Smits, J. H. Noordik, B. G. Lenz, and B. Zwanenburg, *Acta Crystallogr., Sect. C*, submitted for publication. This analysis shows that the molecule is not planar, but has a puckered twisted structure.
7 S. Ishikawa, *Sci. Pap. Inst. Phys. Chem. Res. Jpn.*, 1927, **7**, 237; *Chem. Zentralbl.*, 1928, **1**, 1764; *Chem. Abstr.*, 1928, **22**, 1581.
8 G. Kresze, A. Horn, R. Philippson, and A. Trade, *Chem. Ber.*, 1965, **98**, 3401.

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‡ Selected spectroscopic data: (**2b**) ν_{max} ($CHCl_3$) 1620 and 1060 cm^{-1}, ^1H n.m.r. δ 1.45 (t, 3H, *J* 6.9 Hz, CH_2Me), 2.37 (s, 3H, Me), 4.30 (q, 2H, *J* 6.9 Hz, CH_2), 7.23 and 7.64 (ABq, 4H, *J* 6.3 Hz, Ar). (**4b**) ^1H ($CDCl_3$) δ 2.37 (s, 6H, Me), 7.20 and 8.84 (ABq, 8H, *J* 7.8 Hz, Ar). (**4c**) ^1H ($CDCl_3$) δ 2.38 (s, 6H, Me), 7.25—8.10 (m, 8H, Ar). (**5c**) ^1H ($CDCl_3$) δ 2.35 (s, 6H, Me), 7.25—7.8 (m, 8H, Ar). (**4d**) ($CDCl_3$) ^1H δ 2.43 (s, 6H, Me), 7.15—7.5 (m, 8H, Ar). (**4e**) ^1H δ 3.80 (s, 6H, Me), 6.87 and 7.87 (ABq, 8H, *J* 8.2 Hz, Ar).