

## New Syntheses of 1 $\lambda^4$ ,2,4-Benzothiadiazines

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**Summary** *N*-Arylbenzamidines react with *N*-chlorosuccinimide and either sulphenyl chlorides or sulphenamides to give 1 $\lambda^4$ ,2,4-benzothiadiazines (**1**).

Few examples of sulphur(IV)-nitrogen ylides have been reported in which the sulphur-nitrogen bond forms part of a ring system, although such ylides should have a varied and interesting chemistry on the basis of that known for the open-chain analogues.<sup>1</sup> We now describe new routes to one group of such ylides: the 1 $\lambda^4$ ,2,4-benzothiadiazines (**1**).

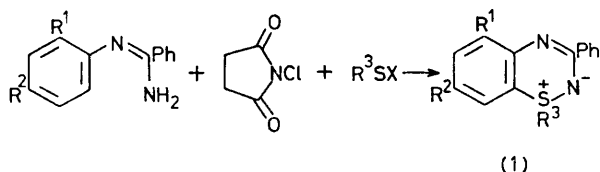
*N*-Arylbenzamidines react with *N*-chlorosuccinimide and 4,4'-thiobismorpholine at  $-20^\circ\text{C}$  in dichloromethane to give, after a basic workup, 1-(4-morpholino)-1,2,4-benzothiadiazines. If sulphenyl chlorides are used in place of 4,4'-thiobismorpholine, the products are 1-alkyl- or 1-aryl-1,2,4-benzothiadiazines (Scheme 1). These latter reactions can also be carried out at room temperature or

4-(phenylthio)morpholine can be used in place of the corresponding sulphenyl chlorides. Representative examples of the ylides prepared by these methods, and typical reaction conditions, are given in the Table.

TABLE. 1 $\lambda^4$ ,2,4-Benzothiadiazines (**1**)

Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Method <sup>a</sup>	Yield /% <sup>b</sup>	M.p. / $^\circ\text{C}$
(1a)	H	Cl	Morpholino	A	49	147—149 <sup>c</sup>
(1b)	Cl	H	"	A	43	129—130
(1c)	H	Me	"	A	60	156—157
(1d)	H	H	Ph	A	56	173—175 <sup>d</sup>
(1e)	H	Me	Ph	A	82	137—138
				B	86	
				C	30	
				D	34	
(1f)	Cl	H	C <sub>6</sub> H <sub>4</sub> Me-4	A	70	119—120
(1g)	H	Me	Me	B	20 <sup>e</sup>	171—172 <sup>d</sup>
(1h)	H	Me	Et	B	20 <sup>e</sup>	179—180 <sup>d</sup>

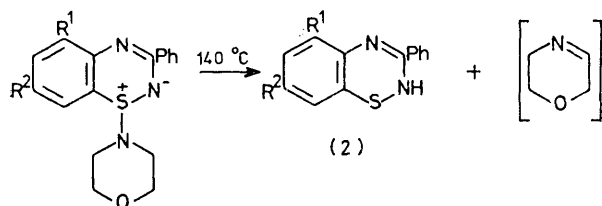
<sup>a</sup> Method A: equimolar amounts of the amidine, *N*-chlorosuccinimide, and 4,4'-thiobismorpholine or the sulphenyl chloride in dichloromethane are stirred at  $-20^\circ\text{C}$  for 1 h then at  $20^\circ\text{C}$  for 2 h. The solution is then washed with aqueous sodium hydroxide and the product obtained from the organic solution by layer chromatography. Method B: the procedure is identical to that of method A except that the reagents are mixed and stirred at  $20^\circ\text{C}$  for 2 h, followed by brief heating under reflux. Method C: the *N*-chloroamidine and the sulphenyl chloride are mixed and stirred in dichloromethane for 0.5 h, followed by heating for 0.5 h. Method D: the amidine, *N*-chlorosuccinimide, and 4-(phenylthio)morpholine are mixed in equimolar amounts and are stirred in dichloromethane at  $20^\circ\text{C}$  for 2 h, followed by brief heating. <sup>b</sup> Yields are for isolated products, which have been characterised by analytical and spectroscopic methods. <sup>c</sup> Lit.,<sup>5</sup> m.p. 167—168 $^\circ\text{C}$ . <sup>d</sup> Picrate. <sup>e</sup> Yields are for recrystallised picrates; n.m.r. spectroscopy of the crude benzothiadiazines (oils) indicated much higher yields.



SCHEME 1

above, and in these conditions various alternative procedures can be used. For example, *N*-chloroamidines can be used in place of the amidines and *N*-chlorosuccinimide, which suggests that the reactions involve chlorination of the amidine at an early stage. Sulphenamides such as

The structures proposed for these products are supported by the following observations. (a) The ylides (**1a**)—(**1c**) were converted into 2*H*-1,2,4-benzothiadiazines (**2**), presumably by way of a cycloelimination reaction (Scheme 2),

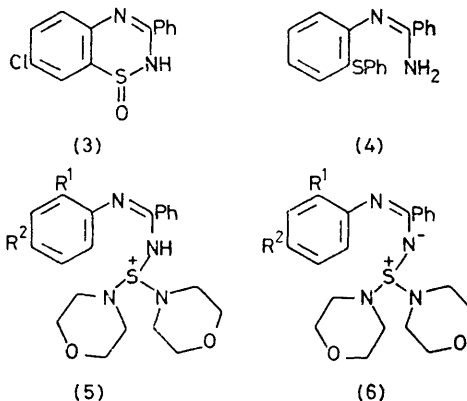


SCHEME 2

when they were heated in chlorobenzene. Compound (**2a**) has been reported previously;<sup>2</sup> a specimen was prepared by the literature route and was shown to be identical to the product of pyrolysis of the ylide (**1a**). (b) Acid hydrolysis of the ylide (**1a**) gave the known<sup>2</sup> thiadiazine 1-oxide (**3**), a specimen of which was prepared independently. (c) Oxidation of the amidine (**4**) with *N*-chlorosuccinimide gave the ylide (**1d**) in high yield, this reaction being a recognised method of preparing the analogous open-chain sulphimides.<sup>3</sup>

The mechanism by which these ylides are formed has not been established. The *N*-chlorosuccinimide probably acts as a chlorinating agent towards the amidines, but it can also complex with the sulphur(II) components under these conditions.<sup>4</sup> It might be expected that azasulphonium salts [*e.g.*, (**5**)] would be formed and that the benzothiadiazines would then be produced by cyclisation of these salts. Their role is uncertain, however. The reaction of *N*-arylamidines, *N*-chlorosuccinimide, and 4-(phenylthio)morpholine, when carried out at  $-20^{\circ}\text{C}$ , gave as major

products the open-chain sulphimides (**6**). These ylides could be induced to cyclise only under fairly vigorous conditions; for example, the benzothiadiazines (**1**) were slowly formed when the sulphimides (**6**) were heated under reflux in toluene for several hours in the presence of an acid. It may be that the nature of the substituents in salts such as (**5**), or in sulphurane precursors to these salts, plays a crucial role in determining their rate of cyclisation.



A limited number of  $\text{S}^{\text{IV}}$  benzothiadiazines has hitherto been available from the reaction of amidines with bis-(*N*-tosyl)sulphur di-imide<sup>2</sup> or with sulphur dichloride.<sup>5</sup> The present work extends the range of available ylides greatly, and thereby, provides a means of specific *ortho* substitution, by electrophilic sulphur, of *N*-arylamidines.

We thank Esso Chemical Limited for generous support, and Dr. T. Colclough for valuable discussions.

(Received, 17th August 1978; Com. 904.)

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<sup>3</sup> T. L. Gilchrist, C. J. Moody, and C. W. Rees, *J.C.S. Perkin I*, 1975, 1964.

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<sup>5</sup> L. N. Markovskii, E. A. Darmokhval, and E. S. Levchenko, *Zhur. Org. Khim.*, 1973, **9**, 2039.