

Ring-opening desulfurization of 1,2,3-thiadiazolium salts with *N*-nucleophiles

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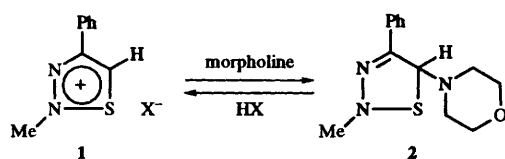
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The 1,2,3-thiadiazolium chlorides **4a, b** react with benzylamine, aniline, phenylhydrazine, hydroxylamine and *N*-methylhydroxylamine at low temperature to yield the 1-arylamino-1,4-diazadienes **5–9** which have been fully characterized by NMR spectroscopy.

1,2,3-Thiadiazoles are well known heterocycles which exhibit three important types of reactions. Firstly, they decompose thermally or photochemically with extrusion of nitrogen, yielding thiirenes and thioketenes as primary products.¹ Secondly, thiadiazoles unsubstituted at the 5-position lose nitrogen under the influence of strong bases to give alkynethiolates,² which have found some interesting applications.³ Thirdly, thiadiazoles can undergo rearrangement reactions when appropriate substituents are placed at the 4- or 5-position.⁴

1,2,3-Thiadiazolium salts have also been studied to some extent, particularly in connection with the synthesis of mesoionic compounds and azathiapentalenes.⁵ Three methods are available for preparing the salts; these are (i) methylation of the thiadiazole ring at the N-2 and/or N-3 position,⁵ (ii) bromine oxidation of arylhydrazones derived from active methylene thioamides,⁶ and (iii) treatment of α -methylene-ketone arylhydrazones with thionyl chloride.⁷

In the present work the third method was used to obtain a series of 2-aryl-1,2,3-thiadiazolium salts having a hydrogen atom at the 5-position, and the reactivity of these salts towards *N*-nucleophiles was investigated. Only one such reaction has been reported briefly in the literature; namely the addition of morpholine onto the salt **1** to give the nonaromatic product **2**, as well as the reverse reaction with mineral acids.⁸ We have now found a new reactivity pattern which is described below.



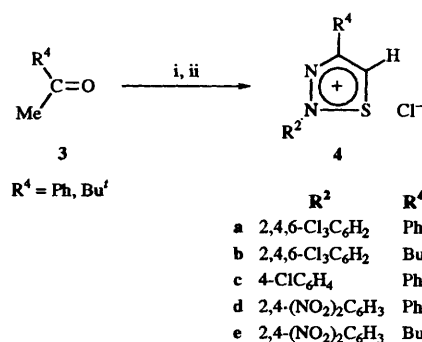
The thiadiazolium salts **4a–e** were synthesized in two steps from acetophenone and pinacolone as shown in Scheme 1. Their ¹³C NMR spectra are informative for the electron distribution in the ring. In Table 1 we compare the chemical shifts of the ring carbon atoms with published data for other salts and neutral heterocycles.^{5a,9} It is apparent that the introduction of an N-2 substituent has a small upfield effect on the resonance position of C-4 ($\Delta\delta < 7$ ppm) and a strong downfield effect on C-5 ($\Delta\delta = 13–31$ ppm) where the deshielding parallels the electron-withdrawing capacity of R². Thus, the ¹³C NMR spectra reflect the electron-deficiency at C-5, which is the centre of attack for nucleophiles.

Two thiadiazolium salts, **4a** and **4b**, were selected to react with benzylamine, aniline, phenylhydrazine, hydroxylamine and *N*-methylhydroxylamine. The reactions occurred readily below 0 °C in acetonitrile, and the results are shown in Scheme

Table 1 ¹³C NMR data for ring carbons of 1,2,3-thiadiazoles and their salts (R⁵ = H)^a

R ²	R ⁴	Solvent	C-4	C-5	Ref.
—	H	CDCl ₃	147.3	135.8	9
Me	H	(CD ₃) ₂ SO	147.1	149.9	5a
—	Ph	CDCl ₃	163.9	130.9	9
Me	Ph	(CD ₃) ₂ SO	158.1	143.7	5a
4-ClC ₆ H ₄	Ph	CDCl ₃	157.0	153.2	This work
2,4,6-Cl ₃ C ₆ H ₂	Ph	CDCl ₃	157.8	157.9	This work
2,4-(NO ₂) ₂ C ₆ H ₃ ^b	Ph	CD ₂ Cl ₂	<i>c</i>	160.3	This work
—	Bu ^t	CDCl ₃	173.5	129.0	9
Me	Bu ^t	(CD ₃) ₂ SO	169.4	143.7	5a
2,4,6-Cl ₃ C ₆ H ₂	Bu ^t	CDCl ₃	168.8	158.5	This work
2,4-(NO ₂) ₂ C ₆ H ₃ ^d	Bu ^t	CD ₂ Cl ₂	169.1	160.1	This work

^a The salts refer to tetrafluoroborates when R² = Me and to chlorides when R² = aryl. ^b This salt is very sensitive to moisture and decomposes in wet dimethyl sulfoxide to give α -formylbenzaldehyde 2,4-dinitrophenylhydrazone. ^c Not observed. ^d In wet dimethyl sulfoxide this salt decomposes to give α -formylpivaldehyde 2,4-dinitrophenylhydrazone.

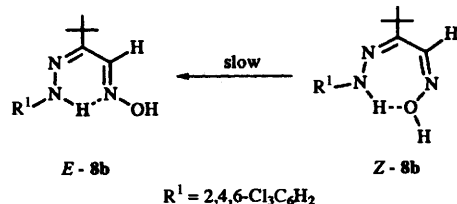


Scheme 1 Reagents: i, R²NHNH₂; ii, SOCl₂

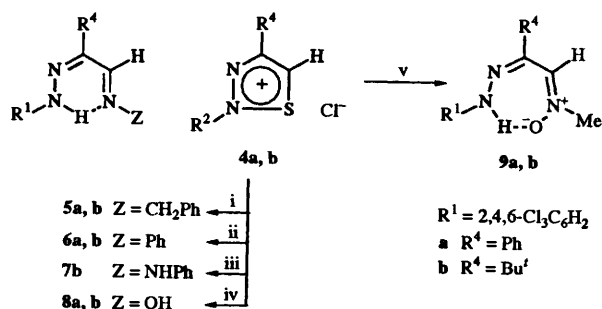
2. In all cases sulfur was eliminated as evidenced by microanalyses and mass spectral analyses. The structures were further established on the basis of the ¹H and ¹³C NMR spectra.† The lowfield NH resonances in the ¹H NMR spectra point to intramolecular hydrogen bonding and an *s-cis* configuration of the 1,4-diazadiene moiety. Furthermore, the CH=N structural unit of the imines **5a, b** and **6a, b**, and the hydrazone **7b** have the *E*-configuration since their ¹J_{CH} coupling constants lie between 156 and 160 Hz.¹⁰ The product **8a** isolated from salt

† Spectral results have been treated as a Supplementary publication [Sup. No. 57102 (3 pp.)]. For details of the scheme see 'Instructions for Authors' (1995), *J. Chem. Soc., Perkin Trans. 1*, 1995, Issue 1.

4a and hydroxylamine also has the *E*-configuration ($^1J_{\text{CH}}$ 165 Hz), whereas the two geometrical oximes were formed from salt **4b**. They were separated by chromatography and exhibit $^1J_{\text{CH}}$ coupling constants of 163 Hz for *E*-**8b** and 178 Hz for *Z*-**8b**. The latter is not planar and shows a homo-allyl coupling between CH=N and NH of 1 Hz. In chloroform solution at room temperature *Z*-**8b** isomerizes slowly into *E*-**8b** within 5 days.



The seven-membered hydrogen-bonded structure found in *Z*-**8b** is also present in the reaction products **9a, b** ($\delta_{\text{NH}} \approx 10$). Here, the *Z* configuration of the nitron function was determined by a homonuclear NOE experiment, carried out on compound **9b**. Thus, selective irradiation of the *tert*-butyl hydrogens at δ 1.22, or the *N*-methyl hydrogens at δ 3.91, causes a 13–15% increase of the CH=N singlet at δ 7.43, indicating a *cis*-relationship of these atoms.



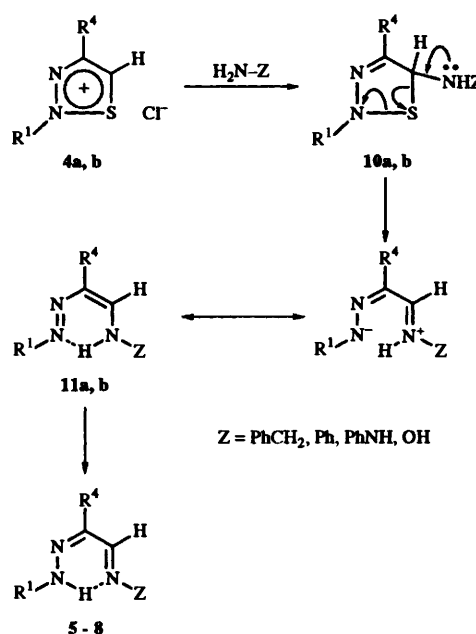
Scheme 2 Reagents: i, PhCH₂NH₂; ii, PhNH₂; iii, PhNHNH₂; iv, NH₂OH; v, MeNH₂

A rationalization of the mechanism of formation of the products is outlined in Scheme 3. After nucleophilic attack at C-5 of the salts **4a, b**, the resulting adducts **10a, b** eliminate sulfur and yield the 1,2-diazadienes **11a, b**. These compounds then tautomerize into the thermodynamically more stable 1,4-diazadienes **5a, b**–**8a, b**. A similar mechanism accounts for the formation of the nitrones **9a, b**. Differentiation between the tautomers **11a, b** and **5–9** was essentially based on the ¹³C NMR spectra, where the ipso carbon of the trichlorophenyl R¹ substituent resonates as a double triplet, thus coupled both with NH and the *meta* hydrogens. This coupling is also observed for the *ortho* trichlorophenyl carbons. In the cases of **6a, b** and **7b**, the ipso, *ortho* and *para* *N*-phenyl resonances were compared with those of appropriate model compounds¹¹ and confirmed the structure assignment.

Experimental

Typical procedure for the salts

4-Phenyl-2-(2,4,6-trichlorophenyl)-1,2,3-thiadiazolium chloride 4a. Acetophenone *N*-(2,4,6-trichlorophenyl)hydrazone (3 g, 9.6 mmol) was added in portions over a period of 30 min to thionyl chloride (25 cm³) at –30 °C, and the reaction mixture



Scheme 3

was stirred for 3 h at room temperature. The excess of thionyl chloride was removed under reduced pressure, and the residue washed with diethyl ether and dried to give the salt **4a** (3.3 g, 91%), mp 161–167 °C.

Note: The following salts were similarly obtained: **4b** (72%), mp 158–161 °C; **4c** (79%), mp 186–196 °C; **4d** (85%), mp 132–135 °C and **4e** (95%), mp 137–138 °C.

Typical procedure for the 1,4-diazadienes

4-Benzyl-2-phenyl-1-(2,4,6-trichloroanilino)-1,4-diazabutadiene 5a. To a solution of the salt **4a** (1 g, 2.6 mmol) in acetonitrile (10 cm³), cooled in a solid CO₂–acetone bath, was added dropwise benzylamine (0.8 g, 3 equiv.). After being stirred for 2 h, the reaction mixture was brought to room temperature and the precipitated benzylamine hydrochloride was filtered off. The filtrate was chromatographed on silica gel with dichloromethane–light petroleum (1:2) as the eluent to give compound **5a** (0.57 g, 53%), mp 122–123 °C (red needles from chloroform) (Found: C, 60.5; H, 3.9. C₂₁H₁₆Cl₃N₃ requires C, 60.53; H, 3.87%); *m/z* 415/417/419 (*M*⁺, 1.5/1.4/0.5%), 221 (*M*⁺ – C₆H₂Cl₃NH, 19), 118 (PhCH₂N≡CH, 12), 107 (21), 106 (PhCH₂NH⁺, 36), 91 (C₇H₇⁺, 100), 79 (22) and 77 (Ph⁺, 24).

Note: The following compounds were similarly obtained: **5b** (77%), mp 68–70 °C (yellow crystals from light petroleum), **6a** (14%), mp 142–145 °C (red needles from diethyl ether), **6b** (30%), mp 104–108 °C (yellow crystals from light petroleum), **7b** (63%), mp 122–125 °C (yellow crystals from dichloromethane–hexane), **8a** (38%), mp 116–119 °C (yellow crystals from light petroleum), **8b** (31% *E* isomer and 38% *Z* isomer), mp 100–102 °C for the *E* isomer and 91–95 °C for the *Z* isomer (both beige crystals from dichloromethane–light petroleum, 1:1), **9a** (32%), mp 126–129 °C (yellow crystals) and **9b** (85%), mp 181–184 °C (yellow crystals).

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