A New Ring Interconversion: 3-Azido-1,2,4-thiadiazoles from the Reaction of Thionyl Chloride with 1-Alkyl-5-aminotetrazoles

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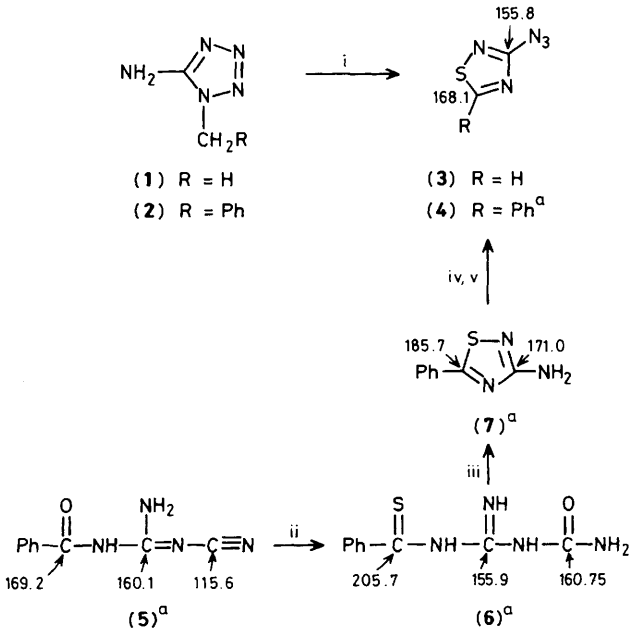
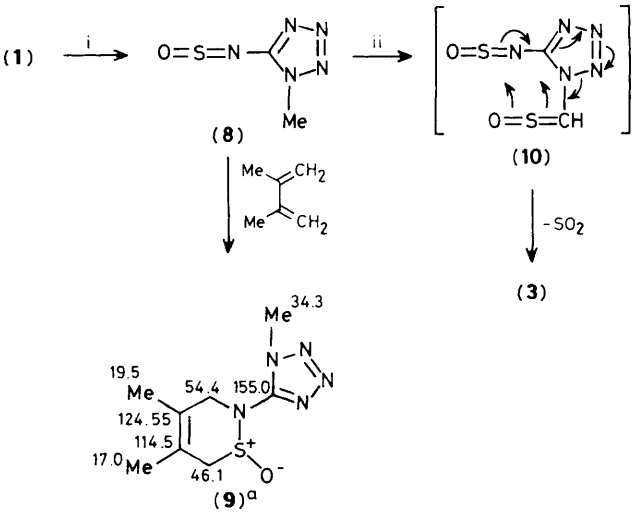
Heating of some 1-alkyl-5-aminotetrazoles with thionyl chloride gave 3-azido-1,2,4-thiadiazoles in a reaction involving 5-*N*-sulphinylaminotetrazoles as intermediates.

Our studies[1,2] of the reaction of thionyl chloride with acyclic heteroallylic systems, –C(Me)=N–XH–, led us to investigate cyclic systems with alkyl and amino groups in 1,2-positions. We now report an interesting new reaction observed on prolonged heating† of the 1-alkyl-5-aminotetrazoles (**1**) and (**2**) with an excess of thionyl chloride in dry *p*-xylene when the new 3-azido-1,2,4-thiadiazoles (**3**) and (**4**) were obtained in 20% and 30% yields, respectively. These compounds were accompanied by decomposition resins and extensive separation procedures requiring column chromatography combined with solvent extractions were necessary to isolate them. Their structures were established by ^1H and ^{13}C n.m.r. spectra (Scheme 1) and from the strong azide stretching band at 2140 (±2) cm^{-1} in the i.r. spectra. These assignments were further confirmed by an unequivocal synthesis of compound (**4**) *via* diazotisation‡ of the amine (**7**) (Scheme 1). 3-Amino-5-phenyl-1,2,4-thiadiazole (**7**) was synthesised from (**5**) by the Kurzer route originally reported[3] thirty years ago (Scheme 1). The intermediate (**6**) was first reported[3] with a structure containing benzoyl and thiourea moieties, *i.e.* with the oxygen and sulphur atoms interchanged, but the ^{13}C n.m.r. spectrum (Scheme 1) showed it to have the Ph–C(=S)– moiety and the structure (**6**). The structure of this compound was recently pointed out by Ollis and coworkers from u.v. and mass spectral data.[4] The compounds (**3**) and (**4**) appear to be the first reported 3-azido-1,2,4-thiadiazole derivatives despite the many other derivatives of this ring system.[5] This new ring interconversion may be viewed as a heterocyclic analogue of the reaction of thionyl chloride with *ortho*-toluidines which gives benzisothiazoles.[6,7] It requires two moles of the reagent and probably proceeds *via* the intermediates (**8**) and (**10**)



Scheme 1. i, $SOCl_2$ (excess), *p*-xylene, heat; ii, H_2S, EtOH (aq); iii, H_2O_2; iv, $NaNO_2$ (aq), HCl; v, NaN_3 (aq).
[a] ^{13}C N.m.r. shifts are shown.



Scheme 2. i, $SOCl_2$, benzene; ii, $SOCl_2$, *p*-xylene, heat.
[a] ^{13}C N.m.r. shifts ($CDCl_3$) are shown.

(Scheme 2). The formation of the latter intermediate (**10**) is the difficult step requiring prolonged careful heating which must be sufficiently high to give carbon sulphinylation but not so high as to cause extensive decomposition. The *N*-sulphinyl intermediate (**8**) was isolated under milder conditions and also using dry benzene as solvent. It was characterised as an

† Typically, a mixture of 1-benzyl-5-aminotetrazole (500 mg) in purified dry *p*-xylene (20 ml) was treated with purified thionyl chloride (0.3 ml) at ambient temperatures and heated at 120 °C for 24 h. The solution was cooled at ambient temperatures, treated with further thionyl chloride (0.3 ml), heated at 120 °C for a further 24 h, and evaporated. The residue (which showed an i.r. band 2142 cm^{-1}) was dissolved in chloroform (30 ml) and the solution was washed with (a) 10% sodium carbonate solution (b) water, and evaporated. The residue was separated on an alumina column using an eluant gradient range of light petroleum (b.p. 60—80 °C)–diethyl ether (20 : 1 v/v) to pure diethyl ether which eluted some sulphur and a number of gums. The azide (**4**) which still remained on the column was then eluted with chloroform and isolated as a brown gum which was further purified by extraction into boiling n-pentane to give an off-white waxy oil (**4**) (30%) on evaporation of the pentane.

‡ A solution of the amine (**7**) (500 mg) (m.p. 139 °C from light petroleum, b.p. 40—60 °C, lit.,[3] m.p. 132—134 °C) in a mixture of water (10 ml), ethanol (5 ml), and conc. hydrochloric acid (5 ml) at −5—0 °C was treated dropwise with aqueous $NaNO_2$ (1.5 g, 8 ml) over 50 min followed by aqueous NaN_3 (1.6 g, 8 ml) over 30 min and stirred for 1 h. Insoluble intractable material was extracted into chloroform. The chloroform extract was washed with water, evaporated, and the residue extracted into boiling n-pentane to give the azide (**4**) (20%) as a waxy oil (i.r. spectrum identical with the sample from the thionyl chloride reaction).

interesting Diels–Alder adduct with 2,3-dimethylbutadiene, (**9**) [m.p. 103—104 °C, from chloroform–pentane (b.p. 40—60 °C)]. Heating of compound (**8**) in *p*-xylene only led to decomposition but when it was heated in *p*-xylene containing 1 mole of thionyl chloride the azide (**3**) was readily formed in the same yield as from the direct reaction of compound (**1**) with thionyl chloride. These results suggest the possibility that α,β-amino and alkyl substituents in other appropriate heterocycles might also be linked with a sulphur atom if treated with thionyl chloride under correct conditions. The reactions of other *N*-sulphinylamines such as (**8**) are being examined.

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