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From tetrazoles via hydrazonoyl chlorides to 1,3,4-thiadiazole oligomers†

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Abstract

5-Substituted tetrazoles react rapidly with Appel salt **1** at room temperature to give hydrazonoyl chlorides (**14**) in high yield. 5-Aminotetrazole reacts further to give an extended bis-imine (**6**) which, with triphenylphosphine at room temperature, rapidly gives 1,3,4-thiadiazoles **15** and **17**. The mono-imines **14** react similarly to give simpler thiadiazoles **18** in high yield. By repetition of the tetrazole formation and Appel salt–triphenylphosphine sequence, these 2-cyanothiadiazoles **18** are converted in high yield into thiadiazole dimers and trimers **21**, $n=1$ and 2. These reactions are explained mechanistically.

Keywords: tetrazoles; nitriles; 1,3,4-thiadiazoles; oligomers.

5-Arylimino-4-chloro-1,2,3-dithiazoles **2** are stable yellow crystalline solids readily prepared in high yield from anilines and 4,5-dichloro-1,2,3-dithiazolium chloride **1** ('Appel salt') itself readily available from chloroacetonitrile and disulphur dichloride.[1] Formation of the iminodithiazoles **2** is a general reaction which we have extended to a wide range of aromatic and heteroaromatic amines because of the synthetic versatility of **2**.[2] This derives from their reactivity towards inter- and intra-molecular nucleophilic attack at S-1, S-2 and C-5 of the dithiazole ring driven by regeneration of the latent cyano group.[3] Some of these reactions transform the dithiazole ring only, such as treatment with triphenylphosphine in CH_2Cl_2 at room temperature to give the cyanothioformanilides **3** in high yield,[4] whilst others involve cyclisation onto the adjacent aromatic ring.[2] However treatment of 5-aminotetrazole monohydrate **4** with Appel salt (1.1 equiv.) under standard conditions (with pyridine in CH_2Cl_2 at room temperature) took a very different course, giving none of the corresponding imine **5**. Nitrogen was evolved from the unusually complex reaction mixture from which a very low yield of the unexpected product **6**

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† Dedicated with admiration and affection to Harry H. Wasserman on the occasion of his 80th birthday.

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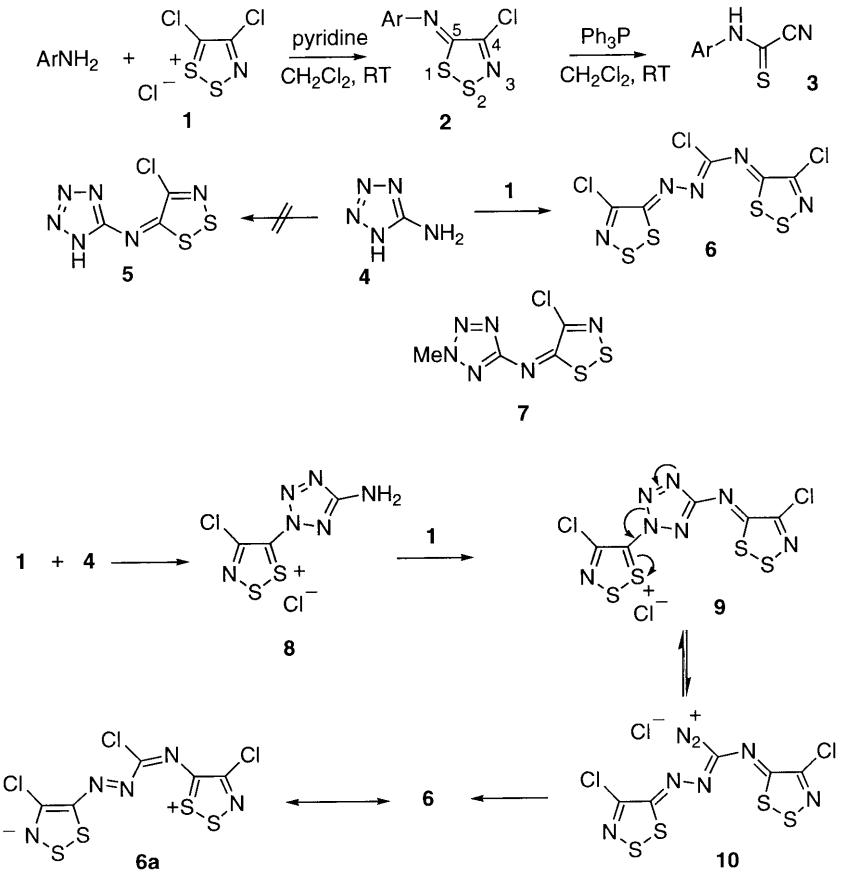
(8%) was isolated as long red needles. Its structure was deduced from analysis, spectroscopy and mechanistic considerations (Scheme 1) and was confirmed by X-ray crystallography.[5] This product is derived from 1 mol of tetrazole **4** and 2 mol of Appel salt **1** with loss of N_2 and 3 HCl; with 2 equiv. of **1**, its yield rose to 20% but was not increased further with more Appel salt.



Scheme 1.

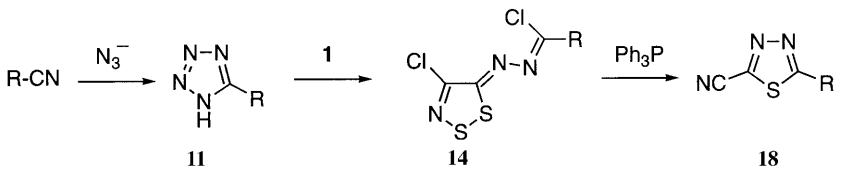
It is possible that **6** is formed from **1** and **4** via the normal iminodithiazole **5**, but this appears unlikely since several other 5-substituted tetrazoles **11** (see below) react entirely analogously with Appel salt at N-2. 5-Amino-2-methyltetrazole, with its N-2 position blocked, reacts normally at the exocyclic amino group to give a high yield (89%) of the stable iminodithiazole **7**.

We therefore propose that **1** and **4** give the 2,5-disubstituted tetrazole **8**, which then reacts with more Appel salt to give **9**. With the strongly electron-withdrawing dithiazolium group on N-2, **9** could equilibrate with the stabilised diazonium tautomer **10** which with chloride would give the trichloro compound **6** isolated. X-Ray crystallography[5] shows **6** to be planar with the configuration shown and extensively delocalised (**6**↔**6a**). This accounts for its deep red colour and the observed inertness of the central 'imidoyl' chloride towards hydrolysis.

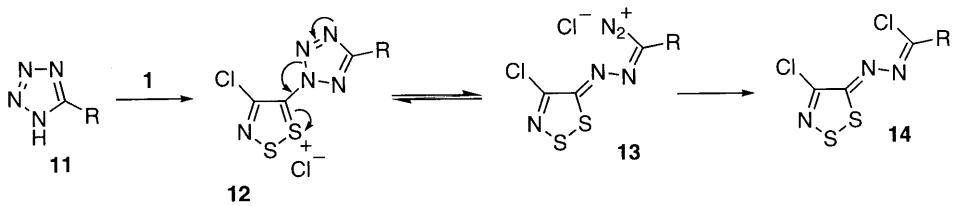
To seek support for the mechanism of Scheme 1 we investigated the reaction of a series of tetrazoles **11**, where the amino group is replaced by substituents inert towards Appel salt. The 5-substituted tetrazoles **11a**–**h** (Table 1) were prepared in high yields by the addition of azide ions to R–CN.[6] If these tetrazoles react with **1** in the same way as the 5-amino compound **4**, the

dithiazolium salts **12** (Scheme 2) would be formed; since **12** cannot react further with Appel salt it could equilibrate directly with the stabilised diazonium chloride **13** and hence give the hydrazonoyl chlorides **14** analogous to **6**. This is exactly what was observed with all the tetrazoles **11a**–**h** upon treatment with **1** (1.1 equiv.) in CH_2Cl_2 at room temperature; the products **14** were isolated in high yield as yellow to red solids (Table 1). These were stable except for the 5-phenoxy compound **14f**, which decomposed rapidly in the solid state, and the 5-chloroethyl compound **14h**, which decomposed slowly. Structures **14** were based on analytical and spectroscopic data and on their conversion into 1,3,4-thiadiazoles **18** (below).

Table 1
Synthesis of hydrazonoyl chlorides **14** and 5-substituted 2-cyano-1,3,4-thiadiazoles **18**



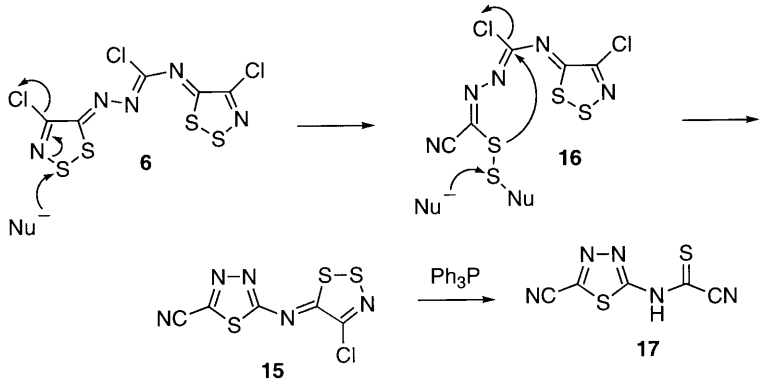
R	**11**	**14** yields (%)	**18** yields (%)
Ph	**11a**	**14a** (87)	**18a** (80)
4-$MeOC_6H_4$	**11b**	**14b** (94)	**18b** (99)
4-NCC_6H_4	**11c**	**14c** (76)	**18c** (72)
4-$O_2NC_6H_4$	**11d**	**14d** (95)	**18d** (92)
2-Thienyl	**11e**	**14e** (86)	**18e** (76)
PhO	**11f**	**14f** (56)	**18f** (75)
MeS	**11g**	**14g** (78)	**18g** (73)
$ClCH_2CH_2$	**11h**	**14h** (75)	**18h** (90)



Scheme 2.

Although iminodithiazoles like **2** are thermally very stable, the red solution of bis-iminodithiazole **6** in warm DMSO slowly faded to yellow; the change was complete in 4 h at 50°C and a yellow crystalline product **15** (Scheme 3) was isolated (25%). The presence of a conjugated cyano group and the loss of the elements of SCl_2 suggested that one of the dithiazole rings had been opened, probably by nucleophilic attack by DMSO, especially since **6** was stable in CH_2Cl_2, acetone, ethanol and chloroform at temperatures above 50°C. Attack on sulphur in the appropriate dithiazole ring (Scheme 3) will generate a cyano group and nucleophilic sulphur suitably placed (**16**) to cyclise to a cyano-1,3,4-thiadiazole; this suggested structure **15** for the yellow product, and X-ray crystallography confirmed the configuration shown.[5] A thiophile stronger than DMSO should be more effective in this reaction; as mentioned above Ph_3P rapidly converts iminodithiazole **2** into cyanothioformamides **3** under very mild conditions. Bis-

iminodithiazole **6** was therefore treated similarly; after 30 min it gave the same yellow product **15** (25%) plus the analogous orange cyanothioformamide **17** (20%). The latter presumably arose from opening of the second dithiazole ring in **6** by PPh_3, and indeed reaction of **6** with excess of PPh_3 (5 equiv.) gave **17** (85%) exclusively (Scheme 3). Triphenylphosphine oxide and sulphide were also isolated in almost quantitative yield in accord with a previously proposed mechanism.[4]



Scheme 3.

The hydrazonoyl chlorides **14**, from 2-substituted tetrazoles and Appel salt **1**, responded in exactly the same way to attack by PPh_3. With 2 equiv. of PPh_3 in CH_2Cl_2 at room temperature for 15 min, compounds **14a**–**h** all gave the corresponding 5-substituted-2-cyano-1,3,4-thiadiazoles **18**, together with $Ph_3P{=}O$ and $Ph_3P{=}S$, in high yields (Table 1), presumably by the same mechanism as before (Scheme 3). This transformation provides good support for the structures assigned to **14**. The sequence of reactions, shown in Table 1, provides a very mild, high-yielding synthesis of 1,3,4-thiadiazoles **18** from nitriles via the tetrazoles **11** and dithiazoles **14**. This new route has the useful feature of directly giving the reactive 2-cyano derivatives, which are rare 1,3,4-thiadiazole derivatives only made before by multi-step processes.[7] Furthermore, the starting cyanide, RCN, is converted into a new cyanide **18** and so the sequence of Table 1 can be repeated to give a series of unsymmetrical thiadiazole oligomers of precisely known structure, with a cyano group at one end and various groups, including strong electron donors, at the other. So far we have shown (Table 2) that this route gives high yields of the highly fluorescent dimers **21**, $n=1$, and trimers **21**, $n=2$ (Table 2). A few such trimers have been made before by classical 1,3,4-thiadiazole ring forming sequences.[8]

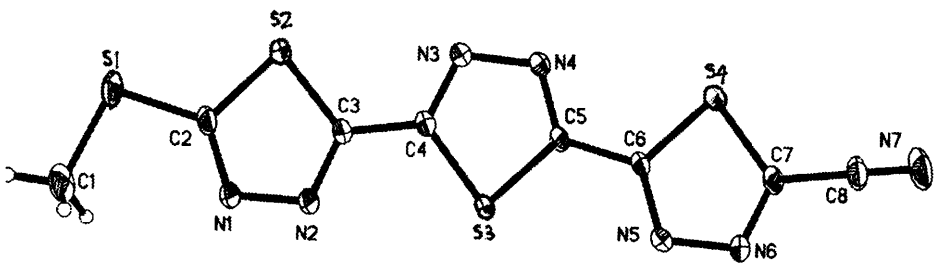


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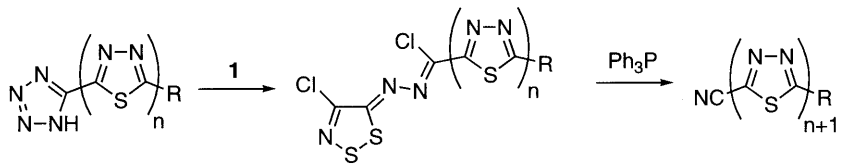
Table 2
Synthesis of dimers and trimers of 1,3,4-thiadiazoles



	19 yields (%)		**20** yields (%)		**21** yields (%)	
	R = Ph	R = SMe	R = Ph	R = SMe	R = Ph	R = SMe
$n=1$	94	97	88	84	80	85
$n=2$	92	89	90	87	64	79

The structure of trimer **21** (R = SMe, $n=2$) was confirmed by X-ray diffraction; in the crystal the heterocyclic rings are nearly coplanar, with the all-*anti* orientation shown. Well-defined conjugated oligomers, related to polythiophenes, are important as active compounds in field effect transistors and light-modulating and light-emitting devices with properties that can surpass those of the corresponding polymers.[9]

Acknowledgements

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