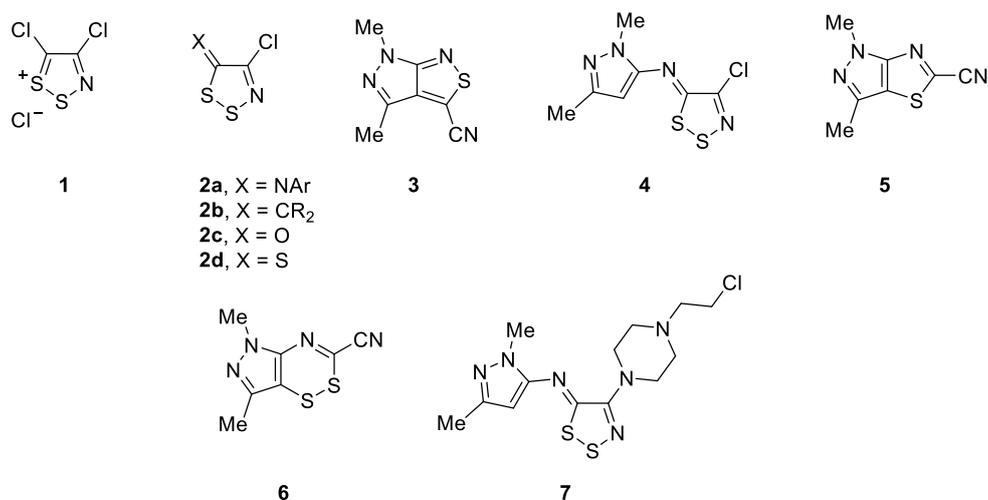


Adventures with S,N-Heterocycles

Maria Koyioni, Panayiotis A. Koutentis

*Department of Chemistry, University of Cyprus, 1 University Avenue, 2109, Nicosia, Cyprus
maria.g.koyioni@gmail.com*

4,5-Dichloro-1,2,3-dithiazolium chloride (Appel salt) **1**, which is readily prepared from chloroacetonitrile and disulfur dichloride, is a useful reagent for the preparation of various 4-chloro-5*H*-1,2,3-dithiazoles **2**. Appropriately substituted 5*H*-dithiazoles **2** are useful precursors to an increasing variety of cyano-substituted heteroarenes. During our investigations on the chemistry of 1,2,3-dithiazoles, we investigated the reaction of Appel salt **1** with 5-aminopyrazoles. 1,3-Dimethyl-5-aminopyrazole gives as main products 6*H*-pyrazolo[3,4-*c*]isothiazole-3-carbonitrile **3** and 4-chloro-*N*-(pyrazol-5-yl)-5*H*-1,2,3-dithiazol-5-imine **4** the ratio of which can be modified by adjusting the pH of the reaction medium. Single crystal X-ray crystallography supports the structure of 4,6-dimethyl-6*H*-pyrazolo[3,4-*c*]isothiazole-3-carbonitrile **3** which was previously misassigned, in the literature, as the 4,6-dimethyl-1*H*-pyrazolo[3,4-*d*]thiazole-5-carbonitrile **5**. Furthermore, thermolysis of 4-chloro-*N*-(pyrazol-5-yl)-5*H*-1,2,3-dithiazol-5-imine **4** gives the correct 1*H*-pyrazolo[3,4-*d*]thiazole-5-carbonitrile **5**.¹ During our investigation on the thermolysis of pyrazolimine **4** we also observed the formation of 1,2,4-dithiazine **6**. The rarity of this ring system prompted us to investigate its formation further and we developed a two-step one-pot procedure for accessing these systems in good yield. The 1,2,4-dithiazine **6** thermolysed to give the pyrazolo[3,4-*d*]thiazole **5** in quantitative yield.² During our investigations for the formation of the 1,2,4-dithiazine **5** we encounter another interesting ring transformation on reaction of dithiazolimine **4** with 1,4-diazabicyclo[2.2.2]octane (DABCO). The reaction gives 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **7**. Optimized reaction conditions are developed and applied to a variety of 4-chloro-5*H*-1,2,3-dithiazoles **2**. The products are obtained in very good yields and can be further manipulated on the 2-chloroethyl moiety by reaction with various nucleophiles leaving intact the dithiazole ring.³



1. Koyioni, M.; Manoli, M.; Manolis, J. M.; Koutentis, P. A. *J. Org. Chem.* **2014**, *79*, 4025-4037.
2. Koyioni, M.; Manoli, M.; Koutentis, P. A. *J. Org. Chem.* **2014**, *79*, 9717-9727.
3. Koyioni, M.; Manoli, M.; Koutentis, P. A. *J. Org. Chem.* **2016**, *81*, 615-631.