New syntheses of aryl isothiocyanates from *N*-arylimino-1,2,3-dithiazoles

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Treatment of *N*-arylimino-1,2,3-dithiazoles 2 with ethylmagnesium bromide (2 equiv.) gives the corresponding aryl isothiocyanates 13, providing a very mild two-step conversion of $ArNH_2$ into ArNCS avoiding hazardous reagents; alternatively the iminodithiazoles 2 can be converted into cyanothioformanilides 11 which rapidly give the same isothiocyanates with 1 equiv. of the Grignard reagent.

4,5-Dichloro-1,2,3-dithiazolium choride **1**, which is readily prepared from chloroacetonitrile and disulfur dichloride, reacts rapidly with anilines in dichloromethane at room temperature to give the stable 5-(*N*-arylimino)-4-chloro-5*H*-1,2,3-dithiazoles **2** usually in very high yield.[1–3] These iminodithiazoles are susceptible to intramolecular (*e.g.* **3**) and intermolecular (*e.g.* **4**) nucleophilic substitution at both sulfur and both carbon atoms of the dithiazole ring and, in consequence, have proved to be very versatile synthetic intermediates. They can be converted in one step into the 2-cyano derivatives of benzoxazoles **5**,[2] benzothiazoles **6**,[2] benzimidazoles **7**,[4] benzoxazin-4-ones **8**,[3] benzothiazin-4-ones **9**[3] and 4-alkoxyquinazolines **10**,[5] and into the acyclic *N*-arylcyanothioformamides **11**.[3] Opening of the dithiazole ring by aliphatic amines (*e.g.* **4**) has also been shown by Kim and co-workers to be synthetically useful.[6] In all of these reactions the latent cyano group in the reagent **1** has been generated and retained in the products. We now find that with the more powerfully nucleophilic Grignard reagents, opening of the dithiazole ring is accompanied by elimination of the cyano group. A commercial solution of ethylmagnesium bromide (2 equiv.) in THF was added dropwise to a heated solution of the iminodithiazole **2** in THF under argon, and heated at reflux for 1 h. Hydrolysis followed by extraction of the product with dichloromethane and purification by column chromatography afforded the isothiocyanates **13** (45–60%) (Method A, Table 1). Similar yields were obtained from reactions run at room temperature overnight. Transposing this procedure to a open microwave oven specially designed for organic synthesis gave very similar results (reaction times, yields). An excess of ethylmagnesium bromide (5–6 equiv.) gave more complex reactions with lower yields of isothiocyanates.

The ready conversion of iminodithiazoles **2** into aryl isothiocyanates **13** is a new reaction of the heterocyclic ring, which provides a novel route to isothiocyanates. This mild two-step conversion of primary aromatic amines into isothiocyanates avoids the use of carbon disulfide and thiophosgene, and high temperature reactions.[7]

Opening of the dithiazole ring by the Grignard reagent is probably initiated by attack at S-2 and generation of the cyano group (Scheme 1), as with other nucleophiles.[6] Attack by a second molecule of the Grignard reagent on the same sulfur could result in formation of the isothiocyanate, dialkyl sulfide

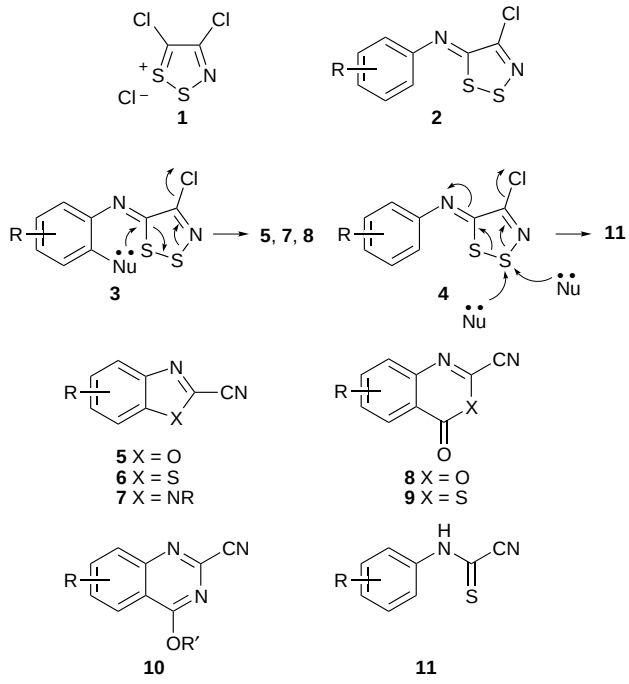
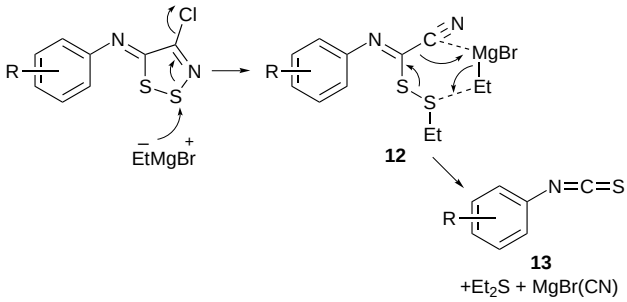


Table 1 Synthesis of aryl isothiocyanates **13** from 5-(*N*-arylimino)-1,2,3-dithiazoles **2** and cyanothioformanilides **11**[a,b]

Starting material	R	Product **13**	Yield (%)	Mp/°C
2a	H	**a**	54	oil[c]
2b	2-F	**b**	50	oil[c]
2c	2-CN	**c**	55 (A); 76 (B)[d]	64
2d	4-MeO	**d**	44 (A); 75 (B)	oil[c]
2e	4-CN	**e**	60	123[c]
2f	3,4-$(MeO)_2$	**f**	50	oil
2g	2-CN, 4,5-$(MeO)_2$[e]	**g**	46 (A); 54 (B)	134
2h	3,4-(OCH_2CH_2O)	**h**	47 (A); 73 (B)	74
11d	4-MeO	**d**	93[f]	oil
11g	2-CN, 4,5-$(MeO)_2$	**g**	70[f]	134
11h	3,4-(OCH_2CH_2O)	**h**	92[f]	74

[a] All compounds were characterised by IR, NMR and HRMS. [b] Aryl isothiocyanates **13**: typical procedures from 5-(*N*-arylimino)-4-chloro-5*H*-1,2,3-dithiazoles **2**. *Method A*: Under an argon atmosphere, a solution of ethylmagnesium bromide (2 mmol, 1 m in THF) was added dropwise to a solution of the 5-imino-1,2,3-dithiazole **2** (1 mmol) in boiling THF (5 ml). The brown mixture obtained was heated for about 1 h, the reaction being followed by TLC. After addition of CH_2Cl_2 (20 ml) the solution was washed with water, the organic layer dried over sodium sulfate and the solvent evaporated. The crude product was then purified by column chromatography with light petroleum–CH_2Cl_2. The same procedure was transposed to a open microwave oven in a quartz reactor (Synthewave S402 Prolabo® microwave reactor monomode system which has variable speed rotation, visual control, irradiation monitor, infrared measurement and continuous feedback temperature controlled by PC computer). The products were purified as above. [c] Compound commercially available. [d] (A): method A; (B): method B (see above). [e] Treatment of the iminodithiazole **2g** with benzylmagnesium bromide gave the same yield of isothiocyanate **13g** as EtMgBr. [f] EtMgBr (1 equiv.), THF 50 °C, 30 min.



Scheme 1

and cyanide anion, possibly assisted by electrophilic catalysis in a cyclic transition state as shown in **12** (Scheme 1). It has been shown that treatment of some *N*-arylcyanothioformamides **11** with pyrrolidine gave minor amounts of thioureas, where the cyano group had been replaced by the amine, and the corresponding aryl isothiocyanate was proposed as a possible intermediate.[6a]

N-Aryliminodithiazoles **2** can be easily converted into cyanothioformanilides **11** in high yield by treatment with triphenylphosphine (2 equiv.) in undried CH_2Cl_2 at room temperature for 1–3 h.[3] We now find that HCN is also eliminated from these formanilides **11** by ethylmagnesium bromide (1 equiv.) in THF to give the isothiocyanates **13** in high yield. The two steps, **2** → **11** → **13**, can be readily combined (Method B, Table 1).

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