



## Direct Synthesis of 2-Cyanobenzimidazoles and the Generation of S<sub>2</sub>

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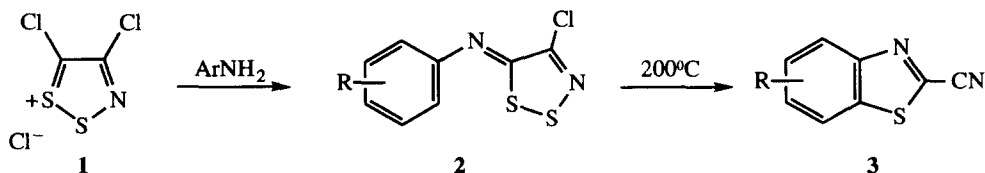
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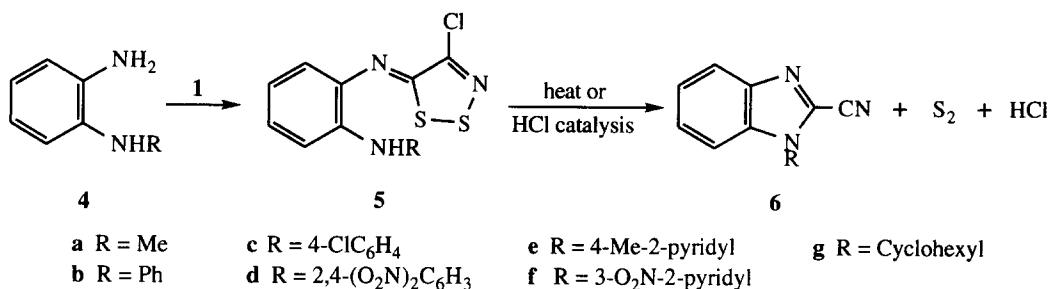
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**Abstract:** 2-Cyanobenzimidazoles **6** are readily prepared from 1,2-diaminobenzenes **4** and 4,5-dichloro-1,2,3-dithiazolium chloride **1**, either directly or through thermal or acid-catalysed rearrangement of the isolated imine intermediates **5**; thermolysis of the imine **5b** at 140-150°C simultaneously generates diatomic sulfur, S<sub>2</sub>, as shown by its interception.

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*N*-Arylimino-4-chloro-5H-1,2,3-dithiazoles **2** are readily prepared by the reaction of 4,5-dichloro-1,2,3-dithiazolium chloride **1** with primary aromatic amines in dichloromethane (DCM) at room temperature.<sup>1,2</sup> They show interesting biological activity<sup>3</sup> and have considerable synthetic utility.<sup>2,4</sup> For example, pyrolysis of the imines **2** gave 2-cyanobenzothiazoles **3** by cyclization of the *ortho*-carbon onto sulfur with liberation of the other sulfur atom and hydrogen chloride.<sup>2</sup> It occurred to us that if the aryl ring had a nucleophilic *ortho*-substituent, cyclization could involve attack of this nucleophile at the imino-carbon to form a new heterocyclic ring with loss of both sulfur atoms from the dithiazole ring. Thus with an *o*-amino group present, as in **5**, a 2-cyanobenzimidazole **6** could be formed, and this proved to be so.





Our standard method for preparing the *N*-arylimines **2** involves stirring the amine with the salt **1** in DCM at room temperature, followed by the addition of pyridine (2 equiv.) after 30min.<sup>2</sup> This proved to be unsuitable for the preparation of the *o*-aminophenylamines **5** since these started to cyclize to the benzimidazoles **6** under the developing acidic conditions. However, if pyridine (2 equiv.) was added at the beginning of the reaction, preferably with tetrahydrofuran (THF) as solvent, the intermediate imines **5**<sup>5</sup> could be isolated, mostly in very good yield, after from 1 to 5 hours at room temperature. The yields of **5a-g** were 36,<sup>6</sup> 79, 79, 68, 62, 80 and 70% respectively.

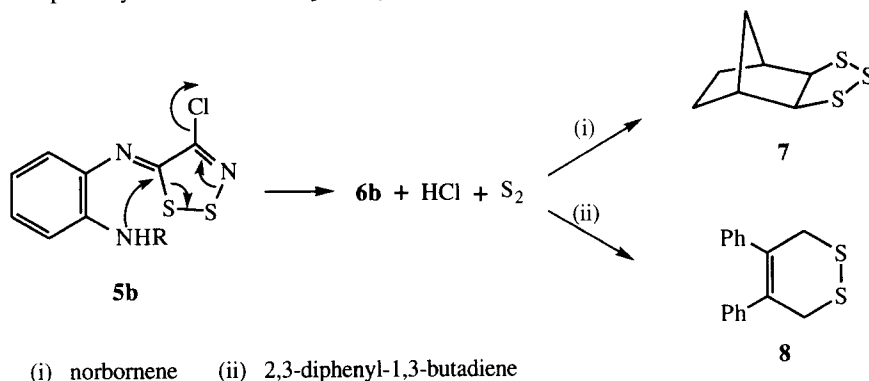
Upon thermolysis most of the imines **5** gave the corresponding 1-substituted-2-cyanobenzimidazoles **6**<sup>5</sup> in fair to good yields. Reaction conditions ranged from boiling in benzene for 10 min (**5a**) to heating neat at 160°C for 2h (**5g**). As expected, the more nucleophilic amines rearranged at lower temperatures, and the very poorly nucleophilic dinitroanilino compound **5d** and nitropyridylamino compound **5f** failed to undergo rearrangement at temperatures up to 180°C.

In some cases the *N*-arylimines **5** rearranged to the benzimidazoles **6** in solution (DCM) at room temperature; thus **6a**, **6b**, and **6c** were isolated in 31,<sup>6</sup> 93 and 80% yield respectively. This was traced to the pronounced catalytic effect of hydrogen chloride upon this rearrangement. Addition of pyridine (2 equiv.) to the reaction mixture suppressed the spontaneous rearrangement, and if a little hydrogen chloride was bubbled into the reaction solution, benzimidazole formation was very rapid.

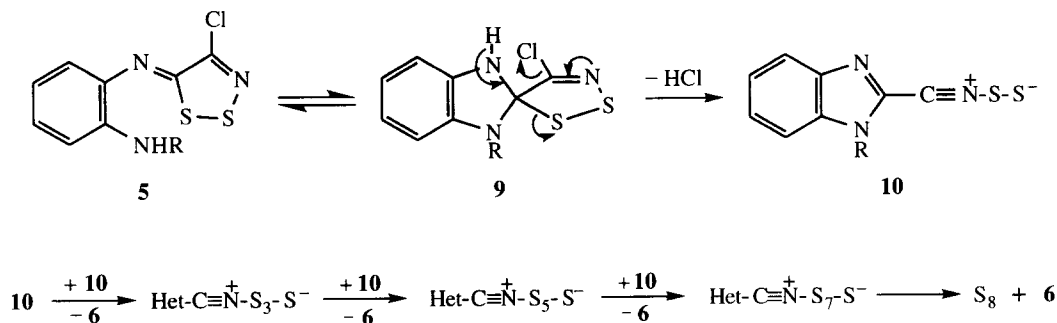
By omission of pyridine it was possible to convert the amines **4** into the benzimidazoles **6** in one step, without isolation of the imines **5**. This worked for amines without electron withdrawing groups, at room temperature in DCM over 24-48h; thus **4** (R = Me, Ph, PhCH<sub>2</sub> and 3,4-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>) gave the corresponding benzimidazoles **6** in yields of 30-70%.

The mechanism suggested above for the transformation of **5** into **6** requires the formal loss of S<sub>2</sub> and HCl and it is possible that the sulfur atoms are actually extruded as singlet diatomic sulfur, S<sub>2</sub>.<sup>7</sup> Whenever 2-cyanobenzimidazoles were formed S<sub>8</sub> was also formed and could be isolated in high yield, up to 95% from **5a**, **b**, and **c**. In an attempt to intercept S<sub>2</sub> the imine **5b** was heated in norbornene at 140-150°C for 4h in a sealed tube; benzimidazole **6b** was isolated (72%) together with the trisulfide **7** (78%) which is known to be characteristic of the reaction of S<sub>2</sub> with norbornene.<sup>8</sup> Decomposition of imine **5b** at a lower temperature, in boiling toluene, did not give the trisulfide **7** although benzimidazole **6b** was formed (69%). Similarly, in the

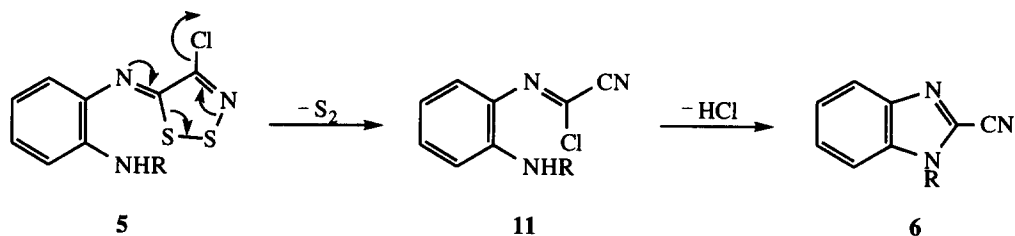
presence of 2,3-diphenylbutadiene the S<sub>2</sub> Diels-Alder adduct **8**<sup>7</sup> (25%) was obtained after reaction at 140-150°C for 3h in a sealed tube; at lower temperatures **8** was not produced although the benzimidazole **6b** was again formed. Very similar results were obtained with the (less stable) methylamino imine **5a**. In the presence of 2,3-diphenylbutadiene the Diels-Alder adduct **8** was not obtained when imine **5a** was heated in boiling toluene (2.5h), in boiling xylene (4h), or in a sealed tube at 110°C for 2h, although in all cases S<sub>8</sub> was isolated (60-75%). Thus it seems that S<sub>2</sub> is generated only at the higher, and S<sub>8</sub> at the lower temperatures, suggesting two decomposition pathways for the imines **5**, possibly as shown in Schemes 1 and 2.



At the lower temperature (Scheme 1) the reaction may involve reversible attack of the *o*-amino group on the dithiazole ring, as proposed above, to give the spiro compound **9** which aromatises with loss of HCl to give the nitrile disulfide **10** which could undergo extension of the sulfur chain with final formation of S<sub>8</sub>. At the higher temperature the spiro compound **9** could fragment completely to the 2-cyanobenzimidazole, HCl and S<sub>2</sub> or alternatively (Scheme 2) S<sub>2</sub> could be extruded directly, with formation of the cyanoimidoyl chloride **11** which then cyclises to the benzimidazole **6**. We have previously isolated such cyanoimidoyl chlorides, in the absence of a neighbouring nucleophile, from high temperature decomposition of *N*-arylimino-1,2,3-dithiazoles.<sup>2</sup>



Scheme 1



Scheme 2

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