4,5-Dicyanopyridazine: a 1,2-Diazine Superheterodiene for [4 + 2] Cycloaddition Reactions

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Unlike other electron-deficient pyridazines, the title compound **1** is found to represent a valuable synthon for hetero Diels–Alder reactions with different unactivated dienophiles.

1,2,4-Triazines and 1,2,4,5-tetrazines have been extensively employed over the past decades as excellent azadienes in cycloaddition processes with a variety of dienophiles, and the value of these reactions as synthetic tools is generally recognized.[1] However, only minor attention has been devoted to the pyridazine system, probably due to some discouraging conclusions on its reactivity, well documented by the following statement: 'Although 1,2-diazines substituted with electron-withdrawing substituents have been shown to participate in inverse electron demand Diels–Alder reactions with the more reactive electron-rich dienophiles, they fail to react with unactivated alkynes and alkenes.'[2] With this in mind, and after we discovered that compound **1**, easily available from the corresponding diester,[3] can perform under relatively mild conditions a [4 + 2] cycloaddition with a double bond of 2,3-dimethylbuta-1,3-diene,[4] we undertook a systematic study of its behaviour towards different 2π electron counterparts.

When the dicyano derivative **1** was allowed to react with an excess of phenyl- and trimethylsilyl-acetylene (molar ratio 1 : 5) in chloroform at 110 °C in a sealed tube, the biphenyl **2a** and phthalonitrile **2b** were obtained in 68 and 71% yields, respectively (Scheme 1).†

On the other hand, treatment of **1** with cyclohexene under the same conditions afforded the diene **3** as the predominant product (50%) together with a minor amount (20%) of the tetrahydronaphthalene **4**.

Similarly, compound **1** was found to react even with an electron-poor alkene such as methyl acrylate, and the polyfunctionalized aromatic derivative **5** was isolated in 58% yield.

Although attempts to carry out a direct benzoannelation reaction on 1-methylpyrrole under different conditions gave the dicyanoindole **6** only in modest yields (15–17%), more satisfactory results were achieved with indole (1 equiv., xylene, 150 °C) and 1-methylindole (1 equiv., chloroform, 110 °C), which were easily converted into the difunctionalized carbazoles **7a** and **7b** in 59 and 53% yields, respectively.

These preliminary findings clearly challenge the previous claim, showing that 4,5-dicyanopyridazine **1** exhibits an exceptional reactivity in cycloaddition reactions, due to favourable electronic effects matched with a lack of any steric hindrance. It therefore represents a much more attractive heterodiene for such reactions than the other derivatives of the same system previously tested,[1,5] including the corresponding tetraester regarded so far as the most efficient for some troublesome experiments.[6]

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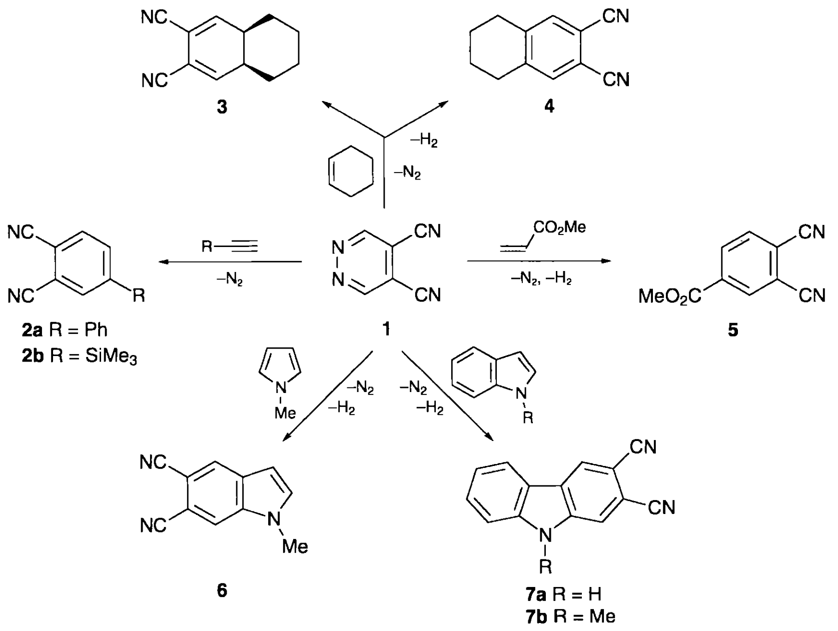

Scheme 1

Footnote

† Whereas the previously known compounds **2b** and **6** were identified on the basis of the literature data,[7,8] the structures of the new products **2a**, **3**, **4**, **5**, **7a** and **7b** followed from analytical and spectral evidence.

References

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