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Reaction of azahetarylguanidines with trichloroacetonitrile

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Abstract

Separate reaction of benzimidazolyl-2-guanidine and benzothiazolyl-2-guanidines with trichloroacetonitrile was investigated. 2,4-Diamino[1,3,5]triazino[1,2-*a*]benzimidazole and 2,4-diimino[1,3,5]triazino[2,1-*a*][1,3]benzothiazoles were found to be products of the reaction. The structures of the compounds obtained were established using ¹H NMR spectroscopy.

Key words: triazines, benzimidazoles, benzothiazoles, guanidines, cyclization.

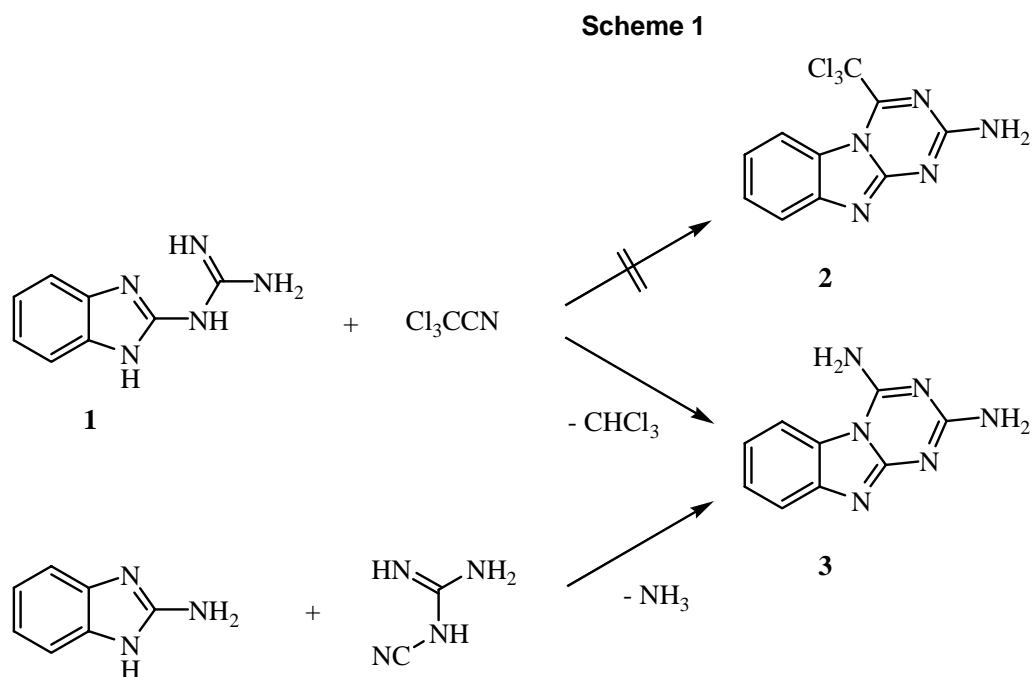
Introduction

The heterylguanidines (e.g. benzimidazolyl-2-guanidines and benzothiazolyl-2-guanidines) represent valuable synthons in heterocyclic syntheses. Particularly, a number of one-carbon cyclizing reagents was reported [1] to react with heterylguanidines to afford fused 1,3,5-triazines. It was also reported [2] that heterocyclization of structurally related heterylamidines using trichloroacetonitrile proceeded with the elimination of ammonia and subsequent formation of trichloromethyl substituted 1,3,5-triazine ring. The current study was carried out to investigate the possibility of similar reaction using azahetarylguanidines.

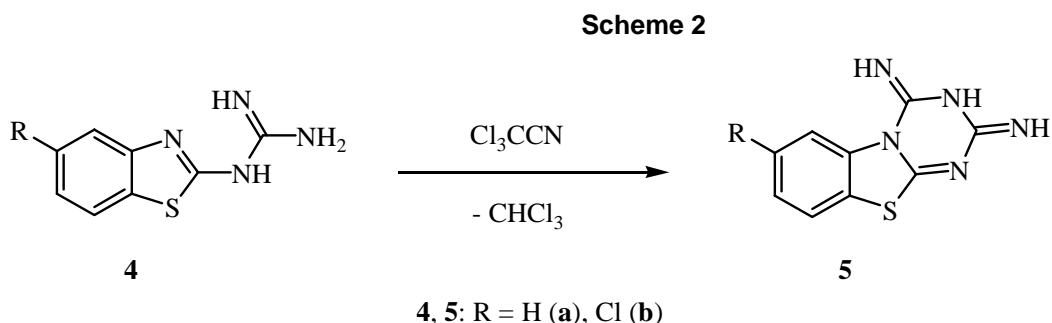
Results and Discussion

Benzimidazolyl-2-guanidine (**1**) and benzothiazolyl-2-guanidines (**4**) were obtained as described previously [1].

When benzimidazolyl-2-guanidine (**1**) was heated in ethanol, 2,4-diamino substituted compound **3** was formed instead of the expected trichloromethyl substituted **2** (Scheme 1). The presence of two amino groups in the structure was supported by two D₂O exchangeable signals at 6.84 and 7.83 ppm in the ¹H NMR spectrum. The 2,4-diamino[1,3,5]triazino[1,2-*a*]benzimidazole (**3**) was identical to the one obtained from the reaction of 2-aminobenzimidazole with cyanoguanidine according to [3].



The reaction of benzothiazolyl-2-guanidines (**4**) with trichloroacetonitrile was found to give 2,4-diimino[1,3,5]triazino[2,1-*a*][1,3]benzothiazoles (**5**) (Scheme 2). The signal of the exocyclic NH at C-4 atom of the heterocyclic nucleus exhibited a downfield shift in ^1H NMR spectra (9.79-9.83 ppm) due to anisotropic effect of the phenylene part of the molecule.



In conclusion, trichloroacetonitrile was found to serve as one-carbon cyclizing reagent in the reactions with azaheterylguanidines. The ring closure proceeded with the introduction of an amino (imino) group during the formation of the 1,3,5-triazine ring and was accompanied by elimination of chloroform.

Experimental procedures

Melting points (uncorrected) were determined on a Gallenkamp melting point apparatus. ^1H NMR spectra were recorded on a Bruker DPX-300 spectrometer, using $\text{DMSO-}d_6$ as a solvent and TMS as an internal reference.

Reaction of heterylguanidines with trichloroacetonitrile.

A solution of appropriate heterylguanidine **1** or **4** (5.0 mmol) and 0.55 ml (5.5 mmol) trichloroacetonitrile in ethanol (10 ml) was heated under reflux for 3-8 h. After cooling, the product was filtered. 2,4-Diamino[1,3,5]triazino[1,2-*a*]benzimidazole (**3**) was washed with ethanol and dried. 2,4-Diimino[1,3,5]triazino[2,1-*a*][1,3]benzothiazoles (**5**) were recrystallized from ethanol.

*2,4-Diamino[1,3,5]triazino[1,2-*a*]benzimidazole (3).*

Yield 90%, mp > 360°C (lit. [4]: > 360°C).

¹H NMR (300 MHz, DMSO-*d*₆): δ 6.84 (2H, br.s, C(2)NH₂), 7.10 (1H, t, *J* = 7.5 Hz, H-8), 7.28 (1H, t, *J* = 7.5 Hz, H-7), 7.44 (1H, d, *J* = 7.5 Hz, H-9), 7.83 (2H, br.s, C(4)NH₂), 8.08 (1H, d, *J* = 7.5 Hz, H-6).

*2,4-Diimino[1,3,5]triazino[2,1-*a*][1,3]benzothiazole (5a).*

Yield 64%, mp 232-234°C.

¹H NMR (300 MHz, DMSO-*d*₆): δ 7.19-7.37 (3H, m, H-7, H-8 and H-9), 7.59 (1H, dd, *J* = 7.3, 1.7 Hz, H-9), 7.60 (1H, s, NH), 7.65 (1H, s, NH), 9.79 (1H, s, NH).

*7-Chloro-2,4-diimino[1,3,5]triazino[2,1-*a*][1,3]benzothiazole (5b).*

Yield 57%, mp 214-216°C.

¹H NMR (300 MHz, DMSO-*d*₆): δ 7.30 (1H, dd, *J* = 8.7, 1.9 Hz, H-8), 7.50 (1H, d, *J* = 1.9 Hz, H-6), 7.57 (1H, d, *J* = 8.7 Hz, H-9), 7.67 (1H, s, NH), 7.75 (1H, s, NH), 9.83 (1H, s, NH).

References

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