sym-TRIAZINES. HYDROLYSIS AND CYCLIZATION OF 1,3,5-TRIAZINE SERIES MONONITRILES

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The routes of base and acid hydrolysis of sym-triazine mononitriles has been studied for aqueous or aqueous-alcohol media. Depending on the pH of the medium, the concentration of reagents, and the temperature it was found that the hydrolysis led to the formation of amides, oxo or alkoxy 1,3,5-triazines, or to an unstable sym-triazine carboxylic acid, the latter leading to formation of substituted sym-triazines. A novel series of tetrazolotriazines has been prepared by the reaction of the mononitriles with sodium azide and their alkylation has been studied.

Keywords: 2-carbamoyl-sym-triazines, 2-[tetrazol-5-yl]-sym-triazines, 6H-sym-triazines, 2-cyano-sym-triazines.

The high biological activity and broad spectrum of possible areas of use of sym-triazine derivatives are responsible for the increase in their interest. We have previously obtained a series of novel 2-cyano-4,6-disubstituted 1,3,5-sym-triazines and investigated some of their reactions. Bearing in mind the availability of the starting compounds and simplicity of the synthesis of such mononitriles it was of interest to study routes of hydrolytic conversion of the cyano group in acid and base media and also to use these mononitriles as intermediate products in the preparation of related tetrazolotriazines via cyclization reactions with sodium azide.

With this in view we have investigated the base and acid hydrolysis of the mononitriles according to Scheme 1.

It was found that refluxing the starting nitrile 1a with a solution of a two-fold excess of NaOH or KOH in 50% aqueous alcohols CnH2n+1OH (n = 1-4) solutions gave the 4-alkoxy derivatives 2a-d in about 85% yield in place of the expected sym-triazine-4-carboxylic acid salt. All of the constants and spectra were identical to the compounds prepared by alkylation of 2-oxo[1,2-dihydro]-4,6-disubstituted 1,3,5-triazines as reported by us previously [6].

Evidently, in base hydrolysis conditions using an aqueous alcohol medium the C–C≡N bond in position 2 of the sym-triazine ring becomes so labile that the cyano group of such a mononitrile behaves as a pseudohalogen and can be eliminated by the action of such active nucleophiles as alcohols.

* For Communication 6 see [1].
It was found that the nature of the hydrochloric acid hydrolysis of the nitriles 1 depends both on the concentration of acid and on the reaction temperature. Hence even simple solution of these nitriles in 15% hydrochloric acid at room temperature leads to formation of the 2-oxo derivatives 3a-j, identical in properties to those reported before [6]. At the same time, the use of conc. HCl also at room temperature leads to formation of the 2-carbamoyl-substituted 4a-j in 63-75% yield (Table 1) with the spectroscopic parameters given in Table 2. Finally, heating a solution of the nitrile 1a in conc. HCl for 1-2 h at 80-95°C gave the 2,4-bis(1-morpholyl)sym-triazine 5, probably as a result of decarboxylation of the unstable intermediate acid. Acid hydrolysis of the starting nitrile 1d containing a methoxy group in the triazine ring under analogous conditions gave the sym-triazinone 6.

The amides 4a-j and compounds 5, 6 obtained are white, finely crystalline powders which are higher melting and with lower solubility in organic solvents than the starting nitriles 1a-j.

The composition and structure of the hydrolysis products were confirmed by a combination of their elemental analysis, IR, 1H NMR, and mass spectroscopic data.

The IR spectra of compounds 4 show the presence of strong, narrow absorption bands at 1660-1695 cm⁻¹ which are characteristic of νC=O and broad absorptions at 3240-3430 cm⁻¹ for νNH. The IR spectra of compounds 5a,b do not show the absorption bands characteristic of the amide or carboxyl groups while the spectrum of compound 6a contains absorption bands for carbonyl and NH group stretching vibrations (Table 2). The 1H NMR spectra show signals for the protons of all the substituents surrounding the sym-triazine ring, the number of which correspond to those expected from the integrated curve data. A common feature of the