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RESEARCH IN THE FIELD OF FUNCTIONALLY SUBSTITUTED AZINES. SYNTHESES OF IMIDAZOLIDINYL-sym-TRIAZINES

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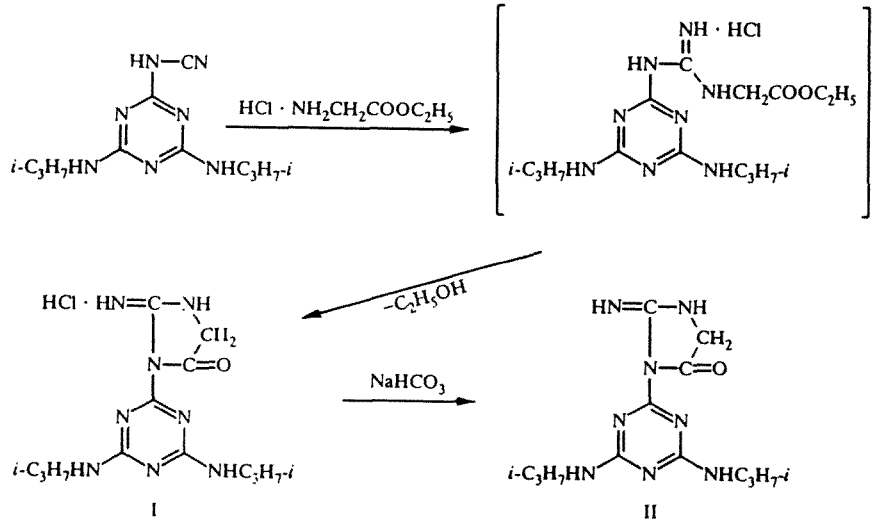
New approaches have been developed for the application of cyanamino-sym-triazines in the synthesis of imidazolidinyl-sym-triazines.

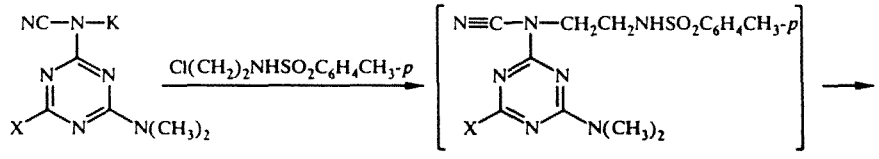
It had been shown previously that iminoimidazolidinyl-sym-triazines are formed in the ammonolysis, aminolysis, or hydrazinolysis of triazinylmalonic esters [1, 2, 3]. Also, a number of analogous compounds had been synthesized by the action of N-chloroacetylglycine esters or chloroacetylanilides on the potassium salts of cyanamino-sym-triazines [4, 5].

Here we are presenting results obtained in the development of new approaches in the use of cyanamino-sym-triazines in synthesis of the compounds indicated above, as these compounds may be of definite interest as potential physiologically active substances.

We have shown that the hydrochloride of the ethyl ester of glycine, upon interaction with 2-cyanamino-4,6-bisisopropylamino-sym-triazine, probably through the intermediate formation of a guanidino-sym-triazine hydrochloride with an open chain, is capable of forming the iminoimidazolidinyl-sym-triazine hydrochloride I, which is converted by the action of aqueous sodium bicarbonate to the free base II.



Intramolecular imination also takes place in the interaction of potassium salts of cyanamino-sym-triazines with N-(2-chloroethyl)sulfonamides, which also results in the formation of the cyclic guanidines III.



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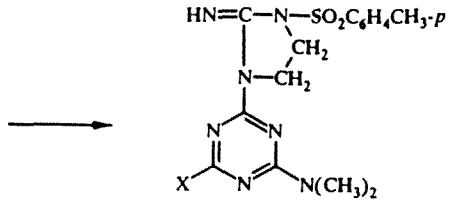
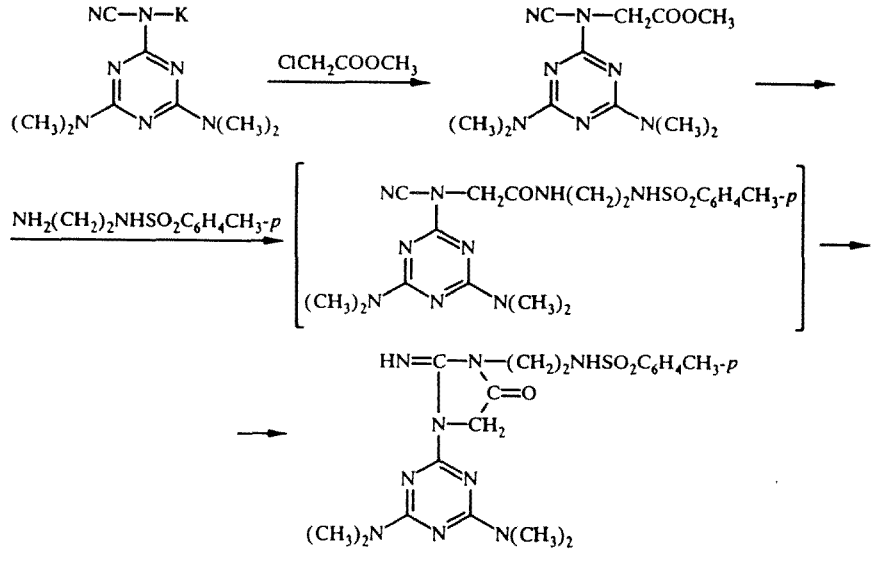


IIIa,b

IIIa) X = $N(CH_3)_2$, b) X = SCH_3

Compounds of the type of III have also been synthesized by a different path based on conversion of cyanamino-sym-triazines to the previously described N-cyano-N-carbonylmethoxymethylamino-sym-triazines [6], with their subsequent aminolysis by an N-(2-aminoethyl)sulfonamide.



EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer in white mineral oil, PMR spectra on a Varian T-60 instrument. TLC was performed on Silufol-254 plates, eluent acetone–hexane 1:1 or 1:2, development with 2% $AgNO_3$ + 0.4% BPB [bromphenol blue] + 0.4% citric acid.

Elemental analyses of the synthesized compounds for C, H, and N matched the calculated values.

2-(2-Imino-5-oxoimidazolidinyl-1)-4,6-bisisopropylamino-sym-triazine (II, $C_{12}H_{20}H_8O$) and Its Hydrochloride (I, $C_{12}H_{20}N_8O \cdot HCl$). To a suspension of 2.35 g (10 mmoles) of 2-N-cyanamino-4,6-bisisopropylamino-sym-triazine in 10-12 ml of butanol, 1.4 g (10 mmoles) of the hydrochloride of the ethyl ester of glycine was added, along with several crystals of hydroquinone. The mixture was heated for 10-12 h at 120°C; after cooling, 20-25 ml of absolute ether was added, and the precipitated crystals of compound I were filtered off. Yield 2.25 g (65%), mp > 350°C.

A 2.14-g quantity (6.5 mmoles) of compound I was dissolved in 10 ml of water, the solution was neutralized with 0.55 g (6.5 mmoles) of sodium bicarbonate, and the resulting crystals of compound II were filtered off. Yield 1.9 g (95%), mp 337-339°C (acetone–water, 1:4), R_f 0.48 (acetone–heptane, 7:3). IR spectrum, cm^{-1}: 1570, 1600 (C=N), 1660 (C=O), 3110, 3250 (NH), M^+ 292.

2-(2-Imino-3-p-toluenesulfaimidazolidinyl-1)-4,6-bisdimethylamino-sym-triazine (IIIa, $C_{17}H_{24}N_8O_2S$). To a suspension of 1.23 g (5 mmoles) of the potassium salt of 2-cyanamino-4,6-bisdimethylamino-sym-triazine in 6 ml of DMF, 1.18 g (5 mmoles) of β-chloroethyl-p-toluenesulfamide was added. The mixture was heated for 12-14 h at 70°C. The resulting

precipitate of compound IIIa was filtered off and air-dried. Yield 1.45 g (71%), mp 228-230°C (DMSO), R_f 0.34 (acetone–hexane, 1:1). IR spectrum, cm^{-1}: 1580, 1600 (C=N, C=O), 3270 (NH). PMR spectrum (DMSO-d_6), ppm: 2.3 (3H, s, CH_3), 2.92 [12H, s, $N(CH_3)_2$], 3.75 (4H, s, CH_2-CH_2), 7.2-7.8 (4H, m, Ph), 8.6 (1H, br.s, NH).

2-(2-Imino-3-p-toluenesulfaimidazolidinyl-1)-4-methylthio-6-dimethylamino-sym-triazine (IIIb, $C_{16}H_{21}N_7O_2S_2$). From 1.23 g (5 mmoles) of the potassium salt of 2-cyanamino-4-methylthio-6-dimethylamino-sym-triazine in 6 ml of DMF and 1.18 g (5 mmoles) of β-chloroethyl-p-toluenesulfamide, obtained 1.4 g (70%) of compound IIIb by a procedure similar to that described above, mp 206-208°C, R_f 0.66 (acetone–hexane, 1:1). IR spectrum, cm^{-1}: 1560, 1600 (C=N, C=O), 3270 (NH). PMR spectrum (DMSO-d_6), ppm: 2.63 (3H, s, CH_3), 2.54 (3H, s, SCH_3), 2.90 [6H, s, $N(CH_3)_2$], 3.75 (4H, s, CH_2-CH_2), 7.2-7.8 (4H, m, Ph), 8.6 (1H, m, NH).

2-(2-Imino-3-p-toluenesulfaminoethyl-4-oxoimidazolidinyl-1)-4,6-bisdimethylamino-sym-triazine (IV, $C_{19}H_{27}N_9O_3S$). A mixture of 1.4 g (5 mmoles) of 2-N-methoxycarbonylmethyl-4,6-bisdimethylamino-sym-triazine and 1.07 g (5 mmoles) of β-aminoethyl-p-toluenesulfamide in 6 ml of methanol was heated for 30 h in a sealed ampul in a boiling water bath. After cooling the mixture, the crystalline precipitate was filtered off, washed with water, and air-dried. Yield 1.8 g (71%), mp 228-230°C (DMSO). R_f 0.45 (acetone–hexane–NH_4OH, 10:10:1). IR spectrum, cm^{-1}: 1520, 1600, 1620 (C=N, C=C), 1710 (C=O), 3280 (NH).

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