CYCLIZATION REACTIONS OF NITRILES.

26.* SYNTHESIS, STRUCTURE, AND PROPERTIES OF 2-AMINO-4-METHYLTHIO-5-CYANO-6(IH)-PYRIMIDINETHIONE


2-Amino-4-methylthio-5-cyano-6(1H)-pyrimidinethione has been prepared via treatment of N-cyanodimethyldithioimidate or 1,1-di(methylthio)-2-thiocarbamoyl-2-cyanoethylene with cyanothioacetamide or cyanamide. The structure of the complex formed between 2-amino-4-methylthio-5-cyano-6(1H)-pyrimidinethione and urea has been studied by x-ray structural analysis. Thiieno[2,3-d]pyrimidines and thiazolo[3,2-c]pyrimidinium salts have been synthesized based on the 6(1H)-pyrimidinethione.

The preparation of 5-cyano-6(1H)-pyrimidinethiones based on active methylene nitriles has been described in the literature. Thus, for instance, 2-amino-1-acetylthiocarbamoyl-1-cyanoethylene cyclizes to give 2,4-dimethyl-5-cyano-6(1H)-pyrimidinethione [2]. Related thiones have been synthesized by treatment of ethoxymethylenemalonitriles with thioamides [3]. It was therefore of interest to examine the reactions of alkoxymethylene cyanamides [4] and alkoxymethylene carbamic acid esters [5] with cyanothioacetamide. The structures and chemical properties of 5-cyano-6(1H)-pyrimidinethiones have received practically no attention until recently.

We have studied the reaction of N-cyanodimethyldithioimidate (I), which is easily accessible, with cyanothioacetamide (II). In ethanol solution in the presence of sodium ethoxide at 45-50°C the reaction proceeds regioselectively to give sodium 2-amino-4-methyl-5-cyano-6-pyrimidinethiolate (III) (method A). The 6-pyrimidinethiolate (III) could also be obtained from cyanamide V and 1,1-di(methylthio)-2-thiocarbamoyl-2-cyanoethylene (IV) in the presence of sodium ethoxide (method B). The formation of salt III in these reactions is accompanied by elimination of methyl mercaptan, which prevents oxidation of the pyrimidinethione to disulfide. 2-Amino-4-methylthio-5-cyano-6(1H)-pyrimidinethione (VI) was isolated after acidification of salt III in ethanol solution with hydrochloric acid.

*For Communication 25, see [1].

The IR spectrum of salt III differs from the spectrum of the pyrimidinethione in that the CN absorption band has been shifted 18 cm\(^{-1}\) to lower frequency and its intensity has been simultaneously increased. This is a consequence of the increased degree of conjugation in the \(\text{N}=\text{C}=\text{S}^-\) chain III. Comparison of these results with the data obtained in a structural study of 3-cyano-2-pyridinethiolates [6-8] reveals that in compounds III the sulfur atom possesses a formal negative charge. Based on IR and PMR spectroscopic analysis, compound VI exists in the thione form. The PMR spectrum of pyrimidinethione VI contains a broad singlet for the NH group proton signal. The IR spectrum of VI further contains a C=S absorption band in the 1200 cm\(^{-1}\) region, which is not present in the IR spectrum of salt III.

Treatment of pyrimidinethione VI with urea gave a complex VII, whose structure was studied by x-ray structural analysis. The atomic coordinates are given in Table 1. In Fig. 1 the bond lengths and bond angles in complex VII are shown. The six-membered ring heterocycle is approximately planar; the atomic deviations from the average plane do not