Pyridazine Derivatives and Related Compounds, Part 3 [1]

Some Reactions with 4-Cyano-3(2H)-pyridazinethione

Ali Deeb*, Abdel Naby Essawy, Fathy Yasmine, and Rida Fikry

Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Egypt

Z. Naturforsch. **46b**, 835–837 (1991); received May 7/October 19, 1990

4-Cyano-5,6-diphenyl-3(2H)-pyridazinethione, 3-Amino-5,6-diphenylpyridazine-4-carbonitrile

The reaction of 5-amino-3,4-diphenylthieno[2,3-c]pyridazine-6-carboxamide **2** with formamide, acetic anhydride and carbon disulphide yielded pyrimido[4',5':4,5]thieno[2,3-c]pyridazin-4-one derivatives. Pyrimido[4,5-c]pyridazinethione and dithione derivatives were obtained by cyclocondensation of 3-amino-5,6-diphenylpyridazine-4-carbonitrile (**8**) with phenyl isothiocyanate and carbon disulphide, respectively. Tetrahydropyridazino[3,4-b]-quinoline (**11**) was prepared by reaction of **8** with cyclohexanone in presence of zinc chloride.

In the course of a program directed to the synthesis of pyridazines annelated with various five and six membered heterocycles, we undertook the synthesis of thieno[2,3-c]pyridazine and its pyrimidine condensed system, which the pyrimidine ring is a frequent partner in polycyclic heterocyclic system of biological significance [2].

The direct route into this ring system proved to be the reaction of 5-amino-3,4-diphenyl[2,3-c]pyridazine-6-carboxamide (**2**) with formamide to yield 8,9-diphenylpyrimido[4',5':4,5]thieno[2,3-c]pyridazin-4(3H)-one (**3**). The preparation of the required 5-amino-3,4-diphenylthieno[2,3-c]pyridazine-6-carboxamide (**2**) was accomplished using the procedure in the following equations (Scheme 1) and employed nucleophilic substitution by chloroacetamide at the 2-position of 4-cyano-5,6-diphenyl-3(2H)-pyridazinethione (**1**) [3], with subsequent base promoted intermolecular ring formation [4].

Treatment of **2** with acetic anhydride under mild conditions afforded the 5-acetamido derivative (**4**), which underwent smooth cyclization to 2-methyl-8,9-diphenylpyrimido[4',5':4,5]thieno[2,3-c]pyridazin-4(3H)-one (**5**).

Condensation of **5** with 4-nitrobenzaldehyde furnished the corresponding 6-(4-nitro)styryl derivative (**6**).

Compound **2** was also reacted with carbon disulphide in the presence of potassium hydroxide to

give 2-mercapto-8,9-diphenylpyrimido[5',4':2,3]-thieno[5,4-c]pyridazin-4(3H)-one (**7**).

In a previous work [3], compound **1** was readily methylated with dimethyl sulphate; the resulting 3-methylthio derivative, readily reacted with ammonium acetate in acetic acid to give the 3-amino derivative (**8**), which represents a versatile building block for the synthesis of various fused pyridazines.

It was reported that the reaction of *o*-aminonitriles with carbon disulphide [5], aryl isothiocyanate [6] and cyclohexanone [7] yielded condensed pyrimidinethione and aminoquinoline derivatives.

Based on these results, it was found that compound **8** reacted with carbon disulphide to give 3,4-diphenylpyrimido[4,5-c]pyridazine-5,7(6H,8H)-dithione (**9**), and reacts with phenyl isothiocyanate to give 3,4-diphenyl-7-phenylaminopyrimido[4,5-c]pyridazine-5(6H)-thione (**10**). The reaction of **8** with cyclohexanone in presence of one molar equivalent of ZnCl₂ leads to a 1:1 complex of the expected amino derivative **11** and zinc chloride. 5-Amino-3,4-diphenyl-6,7,8,9-tetrahydropyridazino[3,4-b]quinoline (**11**) was liberated by treatment of this complex with alkali (Scheme 2).

The structures of compounds **1–11** were established on the bases of their analytical and spectral data (see Table I).

Experimental

Melting points are uncorrected. ¹H NMR spectra were recorded on a Hitachi Perkin-Elmer Va 60 spectrometer with TMS as an internal stan-

* Reprint requests to Dr. A. Deeb.