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SYNTHESIS OF PYRIMIDINES AND THIAZOLO[5,4-d]PYRIMIDINES
III. THE N.M.R. SPECTRUM OF THIAZOLO[5,4-d]PYRIMIDINE*.

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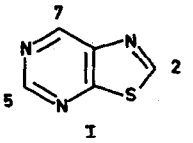
Numerous thiazolo[5,4-d]pyrimidines have been synthesized as potential purine antagonists. In a recent paper[1], Suzuki, Sugiura, Naito and Inoue discuss the N.M.R. spectrum of the parent compound (I). The three peaks at

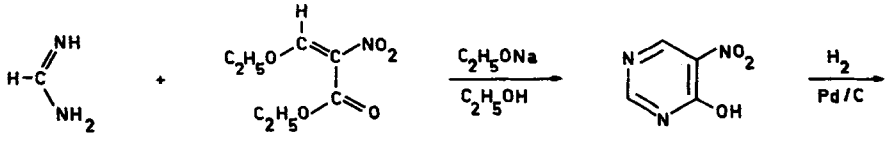


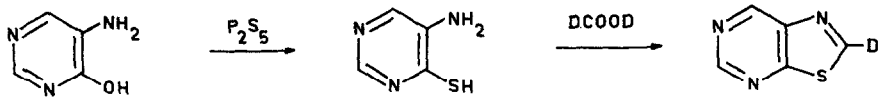
I

551.5, 553 and 569 ± 0.5 c/s (from TMS at 60 Mc/s in deuterochloroform) are assigned respectively to the protons attached at the 7-, 5- and 2- position. Although quite reasonable, the evidence provided by the authors, based on the signal shapes, seemed to us not convincing. Accordingly, we have prepared two deutero derivatives of the ring system and compared their N.M.R. spectra with that of the parent compound (I).

2-Deuterothiazolo[5,4-d]pyrimidine (II).

This compound has been obtained by the following scheme :



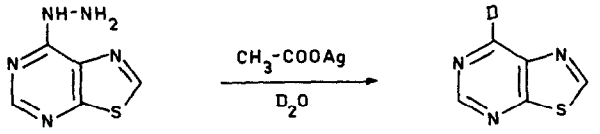


II

Condensation of formamidine and ethyl β-ethoxy-α-nitroacrylate affords 4-hydroxy-5-nitropyrimidine (m.p. 190-192°; m.p.[2] 192°)(several amidines have been condensed in the same way[3]). Catalytic reduction of this product yields 5-amino-4-hydroxypyrimidine (m.p. 206-208°; m.p.[4] 211-212°, [5] 206-208°). Subsequent treatment with phosphorus pentasulfide in boiling pyridine gives 5-amino-4-mercaptopyrimidine (m.p. 207° (decomp.); m.p.[6] 207° (decomp.) in high yield. Cyclization is carried out by refluxing 5-amino-4-mercapto-pyrimidine in dideuteroformic acid (E. Merck) for a short period (35 min.; Yield 33 %).

7-Deuterothiazolo[5,4-d]pyrimidine (III).

The introduction of a deuterium label in position 7 was conveniently achieved by a method recently developed by several workers[7-9]. 7-Hydrazinothiazolo [5,4-d]pyrimidine[5] is converted to the deuterated derivative III by oxidation with silver acetate in heavy water (yield 21 %).



III

N.M.R. spectra.

Chemical shifts and recording conditions are given in the table.

Table

compounds	chemical shifts (c/s) H_2	H_5	H_7
thiazolo[5,4-d]pyrimidine (I)	551.4	552.4	568.4
2-deutero " " " (II)		552.6	568.3
7-deutero " " " (III)	551.1	552.4	

The spectra were recorded on a Varian A-60 spectrometer operating at 60 Mc/s with TMS as internal standard. The compounds were examined in deuterochloroform at a concentration of 5.9 %. Chemical shifts were measured with an accuracy of $\pm$0.2 c/s.

The spectrum of thiazolo[5,4-d]pyrimidine (I) shows two peaks whose intensities are in the ratio 1:2 : a low field singlet and two almost superimposed signals[1]. In the spectrum of the 2-deuterated derivative (II), the low field singlet is still present while the second peak is a broadened singlet at 552.6 c/s. The spectrum of the 7-deuterated compound (III) shows only one peak which is split into two lines on an expanded scale.

The results obtained are not consistent with the conclusion of Inoue and co-workers[1]. The proton in the 2-position is the most shielded rather than the most deshielded while the low field singlet arises from the proton in the 7-position. Going downfield, the correct order of chemical shifts is H_2, H_5, H_7.

A detailed account of our work, including measurements in other solvents, will be published at a later date.

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