SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF THIAZOLO [5,4-b] PYRIDINE ANALOGS OF PIPEMIDIC ACID.

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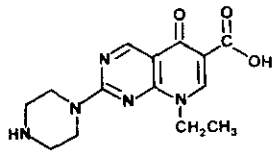
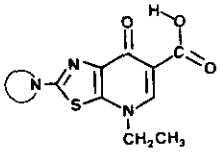
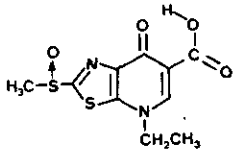
As we were interested in sulfur analogs of the quinolone chemotherapeutics, we synthesized a series of thiazolo [5,4-b] pyridine compounds. The 2-methylthiazolo [5,4-b] pyridine structure was already described by Masui and Tamura (1). Our aim was to prepare analogs of the pipemidic acid (I) type : 2-substituted-7-ethyl-4,7-dihydro-4-oxothiazolo [5,4-b] pyridine-5-carboxylic acids (II).



I



II



III

According to the method of Cook (2) 5-amino-2-mercaptothiazol was prepared. After S-alkylation, the 5-amino-2-methylthiothiazol was condensed with diethyl ethoxymethylenemalonate. Thermal cyclisation, N-alkylation, alkaline hydrolysis of the ester group and oxydation with m-chloroperoxybenzoic acid afforded III. Nucleofilic displacement of the methylsulfoxyde group with various cyclic amines yielded the desired compounds (II). None of the new compounds prepared showed any antibacterial activity in vitro.

(1) Masui T., Tamura T., Jap. Patent 71 43. 792 ; 71, 43. 793 ; 71 43. 794 (25.12.1971).

(2) A.H.Cook, I.Heilbron and A.L.Levy, J. Chem. Soc., 201 (1948).