Yoshihisa Mizuno and Kikuo Adachi: Benzothiazoles. IV. Some Interesting Exchange Reaction between 2-Alcoxy-6-nitrobenzothiazoles and Alcohols **

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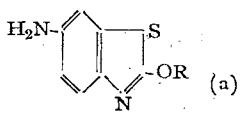
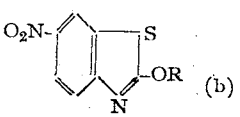
During a recent study of derivatives of 2-alcoxy-6-amino-benzothiazole (a), strong bacteriostatic agent against virulent human tubercle bacilli [1], a quantity of 2-alcoxy-6-nitrobenzothiazole (b) was required. Some of these substances (2-ethoxy and 2-butoxy-6-nitrobenzothiazoles) have been synthesized by Takahashi and Taniyama[2], and others[3] from *p*-nitroaniline by a four-stage process developed from the earlier work by Kaufman and co-workers[4].



(a)



(b)

For the preparation of 2-alcoxy-6-nitrobenzothiazole in quantity a simpler synthesis seemed desirable, and accordingly, possible alternative routes were examined, one of which proved to be satisfactory. Phenylmethylthiocarbamate was subjected to ring closure by a modification of Jacobson's method[5] and the 2-methoxybenzothiazole thus obtained was transformed into 6-nitroderivative and it was converted in an almost quantitative yields to 6-nitro-2-alcoxybenzothiaiazoles ($R=C_2H_5$, C_3H_7, C_4H_9) by 15 minutes' boiling with corresponding alcohols in the presence of a small amount of sodium hydroxide. Further investigation of this exchange reaction with higher alcohols and mercaptans will be continued.

Experimental

(1) Methoxybenzothiazole—30 g. of phenylmethylthiocarbamate ($C_6H_5NHCSOCH_3$), dissolved in 300 cc. of 10% sodium hydroxide solution was added under stirring in portions into a mixture of 150 g. of potassium ferricyanide and 300 cc. of water at 90~95° during 40 minutes. After the addition, the reaction mixtrue was stirred for another 30 minutes at the same temperatue. 2-Methoxybenzothiazole thus produced was extracted with ether. The residue obtained by removing the ether was subjected to steam distillation. 13.5 g. of the oily base which boiled at 115~120/11 mm. was obtained. The yield was 45%. Its picrate melted at 102~103 (uncorr.).

(2) To the solution of 13.5 g. of the base prepared by dissoliving in 55 cc. of conc. sulfuric acid (98%) was added a mixture of 11 cc. of nitric acid (d=1.54) and 8 cc. of conc. sulfuric acid (98%) at 2~3°. After standing at room temperature for an hour, the reaction mixture was poured onto ice. The amorphous substances were collected and washed with cold water. 18.5 g. of air-dried material was obtained. After one recry-

stallization from methanol 11.2 g. of 2-methoxy-6-nitorobenzothiazole, m. p. 165～166° was obtained in an yield of 72%.

(3) 2-Alcoxy-6-nitrobenzothiazoles—To a mixture of 1 g. of powdered sodium hydroxide, 3 cc. of water and 30 cc. of ethanol, was added 0.5 g. of 6-nitro-2-methoxybenzothiazole and the mixture was boiled on a steam bath for 15 minutes. During the boiling crystals separated. After 15 minutes' boiling, the yellow (sometimes red) mixture was poured into 300 cc. of water, acidified by 20 cc. of conc. hydrochloric acid. 0.55 g. of 2-ethoxy-6-benzothiazole, m. p. 146～147°, was obtained. The yield was quantitative. Recrystallization from 100 cc. of ethanol gave 0.48 g. of pure 2-ethoxy-6-nitrobenzothiazole in 90% yield The mixed melting point was not depressed with authentic sample obtained from 2-chloro-6-nitrobenzothiazole and sodium ethoxide according to the usual procedure.

2-Propoxy-6-nitrobenzothiazole, m. p. 84～85, and 2-butoxy-6-nitrobenzothiazole were obtained by almost the same procedure in satisfactory yields, (73 and 72%). Anal. calcd. for $C_{10}H_{10}N_2O_3S$: C, 50. 42; H, 4.20; N, 11. 77. Found: C, 49. 8; N, 11.75.

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