BRIEF COMMUNICATIONS

ALKYLATION OF AMINOTHIAZOLES

V. Alkylation of 2-Ethylamino-4-Methyl-Thiazole*

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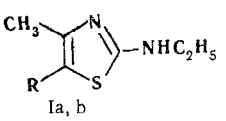
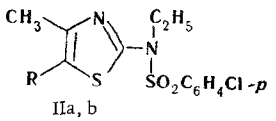
Alkylation of 2-ethylamino-4-methylthiazole with isopropanol and tert-butanol in 85% H_2SO_4 gave 2-ethylamino-4-methyl-5-alkylthiazoles. The structure of the resultant compounds is shown by lack of diazo coupling and formation of p-chlorobenzenesulfonyl derivatives.

It was previously shown [1] that 2-methylamino-4-methylthiazoles readily undergo alkylation by secondary and tertiary alcohols to give 2-methylamino-4-methyl-5-alkylthiazoles. To ascertain to what extent alkylation of 2-alkylaminothiazoles at position 5 in the thiazole ring is general, we carried out alkylation of 2-ethylamino-4-methylthiazole with isopropanol and tert-butanol. It was found also in this case that one alkyl group was introduced to form type I compounds. The alkylation products did not undergo diazo coupling with p-nitrophenyldiazonium compound (see [2]), while treatment with p-chlorobenzenesulfonyl chloride gave acyl derivatives. Hence it can be assumed that here too the alkyl group enters at position 5 in the thiazole ring, giving 2-ethylamino-4-methyl-5-alkylthiazole (I). Obviously the acyl derivatives are 2-(N–p-chlorobenzenesulfonyl)ethylamino-4-methyl-5-alkylthiazoles (II). Formation of the isomeric 2-ethylimino-3-p-chlorobenzenesulfonyl-4-methyl-5-alkylthiazolines (III) is less probable, but we intend to make a special study of the problem.

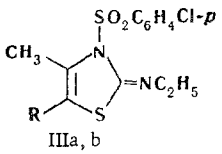


Ia, b



IIa, b

a R = *i*-C_3H_7
b R = *t*-C_4H_9



IIIa, b

EXPERIMENTAL

2-Ethylamino-4-methylthiazole. This was prepared from 1-ethylthiourea and bromoacetone similar to the synthesis of 2-amino-4-methylthiazole [3]. After vacuum-distillation, bp 107–110° (3–4 mm), it was obtained as an oil which crystallized on standing; colorless prisms mp 52–53° (ex n-octane). It couples with a p-nitrophenyldiazonium salt to give a brick-red color (in pyridine vapor), on moistening with a 1 M solution of alkali, the color changed to blue. Found: N 19.69%. Calculated for $C_6H_{10}N_2S$. N 19.69%. The picrate was prepared by precipitating the base with ethanol with picric acid. Minute yellow needles, mp 178° (ex AcOH). Found: N 18.74%. Calculated for $C_6H_{10}N_2S \cdot C_6H_3N_3O_7$ N 18.85%.

2-(N-p-chlorobenzenesulfonyl)ethylamino-4-methylthiazole. A mixture of 1.4 g (0.01 mole) 2-ethylamino-4-methylthiazole, 2.2 g (0.01 mole) p-chlorobenzene sulfonyl chloride, 1 g Na_2CO_3, and 15 ml acetone was refluxed for 1 hr, poured into water, the solid precipitate filtered off, and recrystallized from EtOH, mp 79–80°. Found: N 8.78%. Calculated for $C_{12}H_{13}ClN_2O_2S_2$:

Standard method of alkylation. 5.68 g (0.04 mole) 2-ethylamino-4-methylthiazole was dissolved in 70 ml 85% H_2SO_4, and at 20° for tert-butanol and 80° for isopropanol, the anhydrous alcohol (0.08 mole) added dropwise. The reaction mixture was held at the stated temperature for 10 hr (4 hr for isopropanol), cooled, poured onto ice and neutralized with conc. NH_4OH, using ice cooling. The solid alkylation product was filtered off and dried.

2-Ethylamino-4-methyl-5-tert-butylthiazole (Ib). Yield 8 g (94%). After vacuum-distillation it had bp 125–127° (3–4 mm), yield 6.4 g (80%). Coarse colorless transparent plates, mp N 14.13% (ex n-octane). Found: N 14.53%. Calculated for $C_{10}H_{18}N_2S$. N 14.13%. Picrate, yellow leaflets mp 181–182° (ex AcOH). Found: N 16.41%. Calculated for $C_{10}H_{18}N_2S \cdot C_6H_3N_3O_7$. N 16.39%.

2-(N-p-chlorobenzenesulfonyl)ethylamino-4-methyl-5-tert-butylthiazole (IIb). Prepared similarly to the unsubstituted analog. Colorless crystals, of irregular shape, mp 82.5°. Found: N 7.81%. Calculated for $C_{16}H_{21}ClN_2O_2S_2$. N 7.52%.

2-Ethylamino-4-methyl-5-isopropylthiazole (Ia). Yield 7 g (95%). Bp 113–115° (3–4 mm). After vacuum-distilling yield 84%. Colorless crystals of irregular shape, mp 83–84° (ex n-heptane). Found: N 15.60%. Calculated for $C_9H_{16}N_2S$. N 15.20%. Picrate, yellow leaflets mp 171–172° (ex AcOH). Found: N 16.71%. Calculated for $C_9H_{16}N_2S \cdot C_6H_3N_3O_7$. N 16.94%.

2-(N-p-chlorobenzenesulfonyl)ethylamino-4-methyl-5-isopropylthiazole (IIa). Pale-brown needles mp 94–95° (ex EtOH). Found: N 7.98%. Calculated for $C_{15}H_{19}ClN_2O_2S_2$. N 7.81%.

REFERENCES

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*For Part IV see [1].