METHOD FOR THE SYNTHESIS OF 2-AMINO-5-[(5-METHYLFUR-2-YL)-METHYL]THIAZOLE

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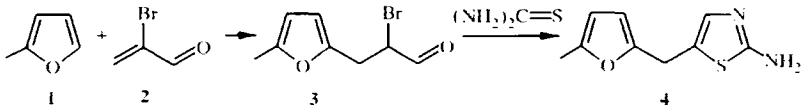
Derivatives of 2-aminothiazole containing substituents at position 5 are less readily available than the 4-substituted analogs, and this is due to the comparatively limited range of α-halogen-substituted aldehydes used in the synthesis of thiazole derivatives by the Hantsch method [1, 2]. Earlier we proposed a method for the production of 2-amino-5-R-benzylthiazoles by the reaction of the products from the chloroarylation of acrolein $ArCH_2CH(Cl)CHO$ with thiourea [3]. In the present work we demonstrated the possibility of realizing a scheme without the participation of diazo compounds for the synthesis of 2-aminothiazoles containing a 5-R-2-furylmethyl group at position 5. The reaction of sylvane (**1**) with α-bromoacrolein (**2**) gave aldehyde **3**, which readily underwent cyclization in reaction with thiourea and formed compound **4**.



1 2 3 4

2-Bromo-3-(5-methylfur-2-yl)propanal (3). To a mixture of sylvane **1** (18 ml) and acetic acid (5 ml) at 35°C we added dropwise α-bromoacrolein (27 g). After 3 h the reaction mixture was distilled under vacuum. Yield of aldehyde **3** 23.9 g (55%); bp 114-115°C (10 mm Hg), n_D^{20} 1.5234. Found, %: C 44.10; H 4.02; Br 36.65. $C_8H_9BrO_2$. Calculated, %: C 44.26; H 4.18; Br 36.81.

2-Amino-5-[(5-methylfur-2-yl)methyl]thiazole (4). A solution of thiourea (0.8 g) and aldehyde **3** (2.2 g) in ethanol (15 ml) was boiled for 2 h. The reaction mixture was dissolved in water and made alkaline. The precipitate was recrystallized from ethanol. Yield 1.4 g (72%); mp 85-86°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.20 (3H, s, CH_3); 3.88 (2H, s, CH_2); 5.95 (1H, d, CH_{furan}); 5.98 (1H, d, CH_{furan}); 6.71 (1H, s, $CH_{thiazole}$); 6.73 (2H, br. s, NH_2). Found, %: C 55.42; H 5.08; N 14.35. $C_9H_{10}N_2OS$. Calculated, %: C 55.64; H 5.19; N 14.42.

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