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LETTERS TO THE EDITOR

New Method For Synthesis of 4-Tosyl-5-chlorothiazole-2-thiol Derivatives

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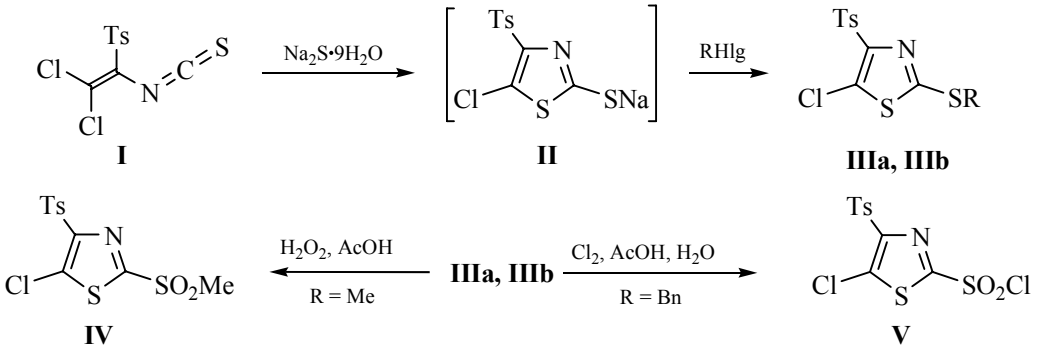
Thiazole derivatives containing sulfonyl groups in positions 2 and 4 are interesting objects to study nucleophilic substitution in the thiazole ring [1–3].

A method for synthesis of 2,4-disulfo-5-chlorothiazol via cyclocondensation of 1-tosyl-2,2-dichloroethenylisothiocyanate **I** with thiols in the presence of pyridine hydrochloride is known [1]. A disadvantage of this method is handling with volatile thiols, when alkylsulfonyl group has to be introduced at position 2 of the thiazole ring.

We have found that isothiocyanate **I** undergos cyclocondensation with sodium sulfide to form sodium 4-tosyl-5-chlorothiazole-2-thiolate **II**. The latter was methylated or benzylated to give the corresponding derivatives **IIIa** and **IIIb** with quantitative yields. Oxidation of compounds **IIIa** and **IIIb** was further carried out by hydrogen peroxide or chlorine in acetic acid to obtain new thiazole derivatives, 2-(methylsulfonyl)-4-tosyl-5-chlorothiazole **IV** and 4-tosyl-5-chlorothiazole-2-sulfonyl chloride **V**. Composition and structure of the compounds **IV** and **V** were confirmed by elemental analysis, IR and NMR spectroscopy. In particular, IR spectra of compounds **IV** and **V** contained strong absorption bands at 1155–1180 and 1325–1385 cm^{-1} assigned to the two SO_2 groups (Scheme 1).

2-(Methylsulfanyl)-4-tosyl-5-chlorothiazole (IIIa). 1-Tosyl-2,2-dichloroethenylisothiocyanate **I** [4], 56.74 g (184 mmol), was added portionwise to a suspension of 47.32 g (197 mmol) of sodium sulfide nonahydrate in 200 mL of ethanol upon cooling to 5–10°C within 1 h. After stirring during 2 h, a solution of 12.58 mL (202 mmol) of methyl iodide in 20 mL of ethanol was added dropwise to the mixture at 10–15°C within

Scheme 1.



R = Me (**a**), Bn (**b**).

2.5 h. Then the reaction mixture was diluted with 300 mL of water, and the precipitated compound **IIIa** was filtered off. Yield 99% (58.06 g), colorless crystals, mp 98°C (MeOH) (mp 94–95°C [1]). IR spectrum (KBr), ν, cm^{-1}: 1149 w, 1326 w (SO_2). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.41 s (3H, CH_3C), 2.65 s (3H, CH_3S), 7.49 d (2H, C_6H_2, $^3J_{HH}$ 8.2 Hz), 7.87 d (2H, C_6H_2, $^3J_{HH}$ 8.2 Hz).

2-(Benzylsulfanyl)-4-tosyl-5-chlorothiazole (IIIb) was prepared similarly from 18.49 g (60 mmol) of 1-tosyl-2,2-dichloroethenylisothiocyanate **I**, 15.13g (63 mmol) sodium sulfide nonahydrate, and 7.49 mL (63 mmol) of benzyl bromide. Yield 91% (21.72 g), colorless crystals, mp 86°C (MeOH) (mp 69–70°C [1]). IR spectrum (KBr), ν, cm^{-1}: 1150 w, 1332 w (SO_2). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.42 s (3H, CH_3), 4.43 s (2H, CH_2), 7.19–7.35 m (5H, C_6H_5), 7.51 d (2H, C_6H_2, $^3J_{HH}$ 7.6 Hz), 7.88 d (2H, C_6H_2, $^3J_{HH}$ 7.6 Hz).

2-(Methylsulfonyl)-4-tosyl-5-chlorothiazole (IV). 12 mL of 35% aqueous hydrogen peroxide solution was added to a suspension of 13.97 g (43.7 mmol) of **IIIa** in 45 mL of acetic acid. After refluxing the mixture during 1 h, 6 mL of 35% aqueous hydrogen peroxide solution was added to it, and the mixture was further refluxed during 0.5 h. After cooling, compound **IV** was filtered off. Yield 89% (13.70 g), colorless crystals, mp 179°C (EtOAc). IR spectrum (KBr), ν, cm^{-1}: 1155 w, 1326 w, 1339 w (SO_2). ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 2.44 s (3H, CH_3C), 3.31 s (3H, CH_3S), 7.37 d (2H, C_6H_2, $^3J_{HH}$ 8.0 Hz), 7.95 d (2H, C_6H_2, J_{HH} 8.0 Hz). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ_C, ppm: 21.8, 42.1, 128.6, 130.2, 136.0, 138.0, 146.1, 150.6, 163.3. Found, %: C 37.73; H 3.08; Cl 10.19; S 27.29. $C_{11}H_{10}ClNO_4S_3$. Calculated, %: C 37.55; H 2.86; Cl 10.08; S 27.34.

4-Tosyl-5-chlorothiazole-2-sulfonyl chloride (V). Chlorine was bubbled through a suspension of 6.60 g (16.7 mmol) of compound **IIIb** in 120 mL of acetic acid and 12 mL of water upon cooling to 5–10°C and stirring, during 1 h. The reaction mixture was incubated at the same temperature during 12 h, and the precipitate was filtered off. Yield 76% (4.71 g), colorless crystals, mp 145°C (CCl_4). IR spectrum (KBr), ν, cm^{-1}: 1157 w, 1182 w, 1340 w, 1386 w (SO_2). ^1H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm: 2.47 s (3H, CH_3), 7.40 d (2H, C_6H_2, $^3J_{HH}$ 8.5 Hz), 7.99 d (2H, C_6H_2, $^3J_{HH}$ 8.5 Hz). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ_C, ppm: 21.4, 128.4, 129.9, 135.2, 139.3, 146.1, 150.5, 160.2. Found, %: C 32.31; H 1.92; Cl 18.72; N.57. $C_{10}H_7Cl_2NO_4S_3$. Calculated, %: C 32.26; H 1.90; Cl 19.05; N 3.76.

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