

SHORT
COMMUNICATIONS

New Synthesis of 5,6-Dihydrothiazolo[3,2-*b*][1,2,4]triazoles

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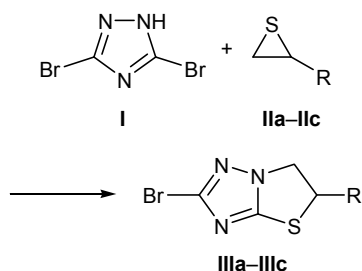
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Fused 5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole system may be constructed in several ways: (1) by reaction of 1,2,4-triazole-3(5)-thiols with 1,2-dibromoethane [1, 2], (2) by cyclization of 3-allylsulfanyl-1,2,4-triazoles by the action of iodine [3], and (3) by reaction of 3,5-dibromo-1-(thiiran-2-ylmethyl)-1,2,4-triazole with nucleophiles [4]. In the first two methods, isomeric 5,6-dihydrothiazolo[2,3-*c*][1,2,4]triazoles are formed as by-products [1–3].

We now propose a new one-step procedure for the synthesis of 5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole derivatives by reaction of 3,5-dibromo-1,2,4-triazole with thiiranes. 5,6-Dihydrothiazolo[3,2-*b*][1,2,4]triazoles **IIIa–IIIc** were synthesized in 44–67% yield by heating triazole **I** with an equimolar amount of thiirane **IIa–IIc** in dimethylformamide in the presence of potassium hydroxide. The structure of compounds **IIIa–IIIc** was confirmed by elemental analysis and IR and ¹H and ¹³C NMR spectroscopy.



R = H (**a**), morpholinomethyl (**b**), MeOCH₂ (**c**).

Unsymmetrical thiiranes **IIb** and **IIc** gave rise to 5-substituted dihydrothiazolo[3,2-*b*][1,2,4]triazoles **IIIb** and **IIIc**. Their structure was proved by independent synthesis of 2-bromo-5-morpholinomethyl-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (**IIIb**) from 3,5-dibromo-1-(thiiran-2-ylmethyl)-1,2,4-triazole and morpholine [4]. Samples of **IIIb** prepared by different

methods showed no depression of the melting point on mixing, and their IR spectra completely coincided. These data indicated that the thiirane ring is opened according to the Krasuskii rule [5].

2-Bromo-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (IIIa). A solution of 2.26 g (10 mmol) of triazole **I**, 0.56 g (10 mmol) of KOH, and 0.60 g (10 mmol) of thiirane (**IIa**) in 20 ml of DMF was heated for 5 h at 45–50°C. The mixture was diluted with water to a ratio of 1:10 and extracted with ethyl acetate (2×50 ml), and the extract was evaporated. Yield 0.98 g (48%), mp 115–117°C (from *i*-PrOH). ¹H NMR spectrum, δ, ppm: 3.87–4.01 m (2H, SCH₂), 4.31–4.46 m (2H, NCH₂). ¹³C NMR spectrum, δ_C, ppm: 33.21 (C⁵), 47.19 (C⁶), 142.89 (C²), 159.67 (C^{3a}). Found, %: C 23.42; H 2.04; N 20.31. C₄H₄BrN₃S. Calculated, %: C 23.31; H 1.96; N 20.39.

2-Bromo-5-morpholinomethyl-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (IIIb). A solution of 1.59 g (7 mmol) of triazole **I**, 0.39 g (7 mmol) of KOH, and 1.10 g (7 mmol) of thiirane **IIb** in 15 ml of DMF was heated for 2 h under reflux. The mixture was cooled and diluted with water until a solid separated, and the precipitate was filtered off. Yield 1.43 g (67%), mp 163.5–165°C (from *i*-PrOH). IR spectrum, ν, cm⁻¹: 2968, 2932, 2863, 2812, 1479, 1428, 1299, 1223, 1115. Found, %: C 35.34; H 4.35; N 18.24. C₉H₁₃BrN₄OS. Calculated, %: C 35.42; H 4.29; N 18.36.

2-Bromo-5-methoxymethyl-5,6-dihydrothiazolo[3,2-*b*][1,2,4]triazole (IIIc) was synthesized as described above for compound **IIIb** from 2.26 g (10 mmol) of triazole **I** and 1.04 g (10 mmol) of thiirane **IIc** in the presence of 0.56 g (10 mmol) of KOH. The mixture was diluted with water to a ratio of 1:10 and extracted with diethyl ether (3×40 ml), and the extract was evaporated. Yield 1.09 g (44%), mp 69–70°C

(from *i*-PrOH–hexane). ^1H NMR spectrum, δ , ppm: 3.42 s (3H, OCH₃), 3.65 d (2H, 5-H, $^3J = 7.0$ Hz), 4.26–4.42 m (2H, NCH₂), 4.46–4.58 m (1H, SCH). Found, %: C 29.01; H 3.14; N 16.68. C₆H₈BrN₃OS. Calculated, %: C 28.81; H 3.22; N 16.80.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer at 300 and 75 MHz, respectively, using CDCl₃ as solvent and reference. The IR spectra were measured in KBr on an Infracum FT-02 spectrometer. Thiirane (**IIa**) was commercial product (from Aldrich). Thiirane **IIb** was synthesized according to the procedure reported in [5], and thiirane **IIc** was prepared as described in [6].

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