

Synthesis And Characterization Of Novel 3-Substituted-1,2,4-Triazolo-[3,4-B]Benzothiazole Derivatives

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Abstract

2-nitro-4-chloro aniline **1** on treatment with sodium thiocyanate in acetic acid afforded 2-amino-4--nitro-6-chloro benzothiazole **2**. Compound **2** in ethylene glycol was heated at 150 °C with 80% hydrazine hydrate to get 2-hydrazino 4-nitro-6-chloro- benzothiazole **3**. This hydrazino compound **3** on heating with benzaldehyde / 4-hydroxy benzaldehyde / 2-nitro benzaldehyde to obtain corresponding hydrazones (**4a-4c**). These hydrazones (**4a- 4c**) in benzene independently were refluxed on water bath for three hours with Attenburrow's MnO₂ to obtain 3- phenyl (**5a**)/4'-hydroxy phenyl (**5b**) / 2'-nitro phenyl(**5c**) -5-nitro-7-chloro-1,2,4-triazolo-[3,4-b]-benzothiazoles respectively.

Keywords : triazole benzothiazole, hydrazone, oxidative cyclization;

1. Introduction

Five-membered aromatic heterocyclic systems containing three heteroatoms at symmetrical positions have attracted considerable interest because of their diverse physiological properties. Derivatives of 1,2,4-triazole have been reported to exhibit a broad range of pharmacological activities, including antibacterial and antifungal properties. 1,2,4-Triazolo[3,4-b]-benzothiazole chemistry has been investigated by several researchers. Brooker and Vanlare reported an early preparation of this fused heterocyclic system. Subsequent studies described 3-substituted derivatives, including 3-methyl and 3-phenyl analogues, by cyclization or oxidation of suitable benzothiazole.

Several synthetic approaches to the triazolo-[3,4-b]-benzothiazole nucleus have subsequently been reported, including routes involving 2-hydrazinobenzothiazole, thiosemicarbazide derivatives, hydrazones, lead tetraacetate, nitrobenzene, ferric chloride, bromine/acetic acid and photochemical methods. The literature also contains reports describing biological evaluation of substituted benzothiazole and triazole derivatives.

The present work was undertaken to prepare substituted 1,2,4-triazolo-[3,4-b]-benzothiazole derivatives bearing nitro and chloro substituents on the benzothiazole ring and different aromatic substituents at the triazole ring. The synthetic approach consists of preparation of a substituted aminobenzothiazole, conversion to its hydrazino derivative, condensation with aromatic aldehydes, and oxidative cyclization with activated manganese dioxide.

Experimental

Melting points were determined in open capillaries and are uncorrected. Infrared spectra were recorded in Nujol / potassium bromide pellets on Bomem MB 104FT infrared spectrophotometer. ¹HNMR spectra were obtained on a Gemini 200 Mz spectrometer with TMS as an internal standard and mass spectra on FT VG-7070H mass spectrometer using the GI technique at 70 eV. Elemental analysis was carried out on a Heraeus CHN-O Rapid analyser. Purity of the compound was checked by TLC and elemental analysis.

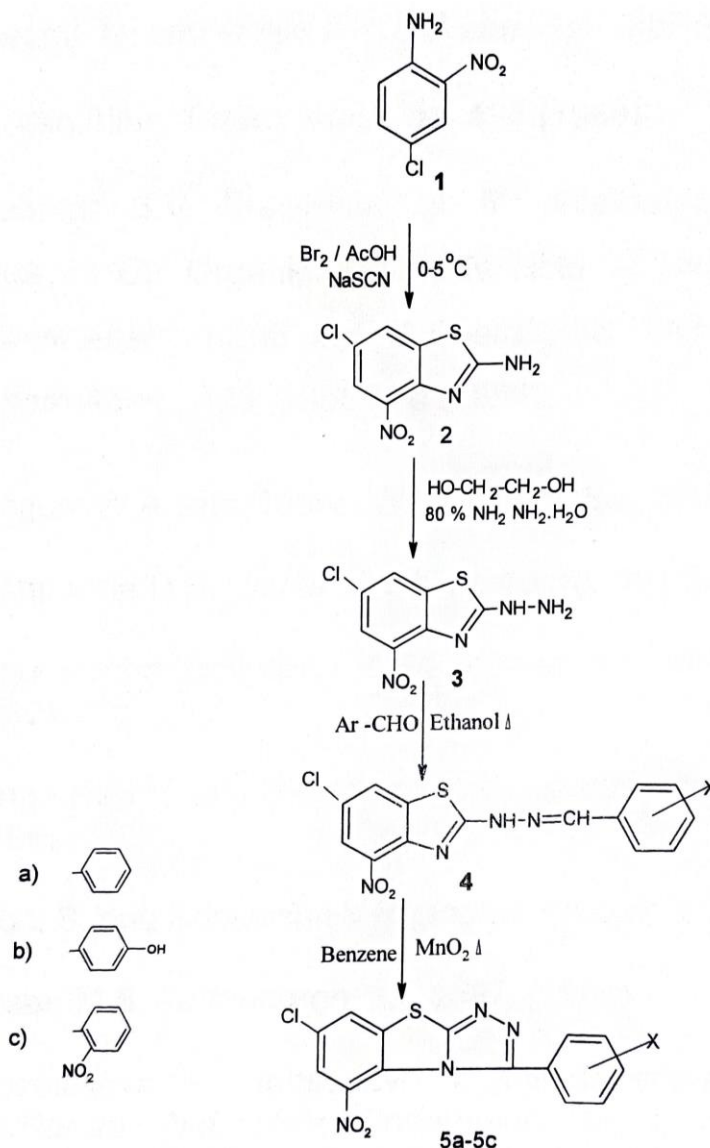
Synthesis of 2-Amino-4-nitro-6-chlorobenzothiazole

2-Nitro-6-chloroaniline (17.24 g) and sodium thiocyanate (12 g) were dissolved in glacial acetic acid (50 ml). The solution was cooled in a freezing mixture. Bromine (4 ml) in glacial acetic acid (26 mL) was added with stirring while maintaining the temperature below 25 °C. The mixture was allowed to stand for 1 h at room temperature. The resulting hydrobromide was dissolved in hot water and neutralized with 10% NaOH to obtain the free base. The amine was filtered, washed with water and recrystallized from aqueous alcohol to give 13 g of product. The reported melting point was 97–98 °C. IR (KBr): 3435 cm⁻¹ (Asymmetric stretching of -NH₂), 3345 cm⁻¹ (N-H Symmetrical stretching of -NH₂), 3054 cm⁻¹ (Ar-H stretching), 1635 cm⁻¹ (-C=N stretching), 1320 cm⁻¹ (Ar-C-O stretching), ¹HNMR (CDCl₃) : δ 6.5 (broad, 2H, NH₂), δ 7.0-7.5 (two singlet, 2H, Ar-H),

Synthesis of 2-Hydrazino-4-nitro-6-chlorobenzothiazole

Hydrazine hydrate (80%) was taken in a flask and cooled to 5 °C. Concentrated HCl (6 mL) was added with stirring. The flask was kept at room temperature for a few minutes, after which the benzothiazole starting material (6 g) was added portion wise. Ethylene glycol (24 mL) was then added. The reaction mixture was heated at 140–160 °C on an oil bath for 3 h and then cooled. The separated 2-hydrazino-4-nitro-6-chlorobenzothiazole was filtered, washed with cold water and crystallized from ethyl alcohol. The reported melting point was 90 °C. IR (KBr) : 3330 cm⁻¹ (asymmetric N-H stretching of –NH₂), 3210 cm⁻¹ (symmetric N-H stretching of –NH₂)

Scheme



Condensation with aldehyde to form hydrazone

2-Hydrazino-4-nitro-6-chlorobenzothiazole (2.30 g) was dissolved in ethanol (20 ml). Aldehyde / 4-hydroxy benzaldehyde / 2-nitro benzaldehyde in ethanol (20 ml) was added and the reaction mixture was refluxed on a water bath for 1.5 h. After cooling, the solid product was collected and recrystallised in aq. alcohol..

Oxidative Cyclization of hydrazone

The hydrazone (0.5 g) was taken in dry benzene (25 ml). Attenbarrow's activated manganese dioxide (1 g) was added and the mixture was refluxed on a water bath for 3 h. The hot mixture

was filtered, the benzene was removed by evaporation, and the solid product was recrystallized from hot ethanol. IR (KBr): Band due to N-H stretching absent. compound 5b shows 3275 cm⁻¹ (O-H stretching),

Results and Discussion

The structures of these tricyclic triazolo benzothiazoles (5a- 5cf) were assigned on the basis of their spectral data The I. R. spectra of these triazolo benzothiazoles, observed the absence of strong bands in the region 3450cm⁻¹ - 3100 cm⁻¹ due to -NH stretching , however the absence of broad singlet in PMR spectra of these triazolo benzothiazole in the region δ 2.5 - δ 4.5 confirms the formation of cyclised products.

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