

Short Note

Synthesis of 4-[10*H*-Phenothiazin-10-yl(1*H*-tetrazol-5-yl)-methyl]phenol

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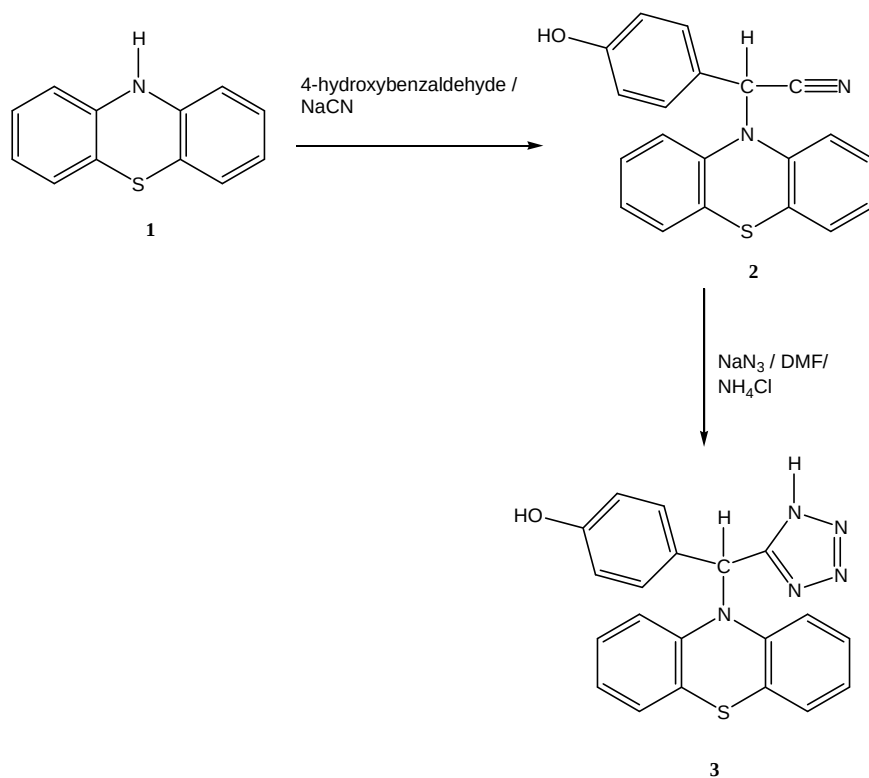
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Abstract: This present work aims at synthesizing a novel tetrazole from phenothiazine. Phenothiazine is converted into a nitrile by reacting it with 4-hydroxybenzaldehyde, sodium metabisulphite and sodium cyanide. The nitrile on treatment with NaN₃/DMF yielded the corresponding tetrazole. The tetrazole obtained was characterized by IR, ¹H NMR, EI-MS and elemental analysis.

Keywords: 4-[10*H*-phenothiazin-10-yl(1*H*-tetrazol-5-yl)methyl]phenol; (4-hydroxy-phenyl)(10*H*-phenothiazin-10-yl)acetonitrile

Introduction

Tetrazole and its derivatives gained scientific interest ever since its discovery. Tetrazoles are reported to possess a wide spectrum of biological activities including antifungal [1], antiinflammatory [2], central nervous system stimulant activity [3], antiallergic activity [4], etc. Phenothiazine compounds also possess potential biological activities [5,6]. In this paper, we would like to report the synthesis of a novel tetrazole from phenothazine.



Synthesis

Preparation of (4-hydroxyphenyl)(10H-phenothiazin-10-yl)acetonitrile (2)

To a stirred solution of sodium metabisulphite (5.2 g, 0.05 mol) in 20 mL of water was added 4-hydroxybenzaldehyde (6.1 g, 0.05 mol). Phenothiazine **1** (9.9 g, 0.05 mol) was added after 15 min. The reaction mixture was cooled in an ice bath and then it was stirred for 30 min. A solution of sodium cyanide (2.45 g, 0.05 mol) in 20 mL of water was added dropwise and stirring was continued for 6 h. It was kept over night. The product **2** was filtered, washed with excess of water and dried. The crude product was recrystallised from aqueous acetic acid. The yield of the product is 60%.

Melting Point: 175-177 °C.

IR (KBr pellet, cm^{-1}): 2235 (Nitrile).

^1H NMR (90 MHz, CDCl_3): 7.2-7.4 (m, 8H, ArH), 7.9 (d, $J = 7.2$ Hz, 2H, *o*-protons), 7.0 (d, $J = 3.4$ Hz 2H, *m*-protons), 7.5 (s, 1H, OH-phenolic), 3.95 (s, 1H, C-H).

MS (m/z): 331 ($M + 1$)⁺ (20%), 199 (100%).

Elemental Analysis: Calculated: C, 72.70; H, 4.27; N, 8.48. Found: C, 72.82; H, 4.34; N, 8.39.

Preparation of 4-[10H-phenothiazin-10-yl(1H-tetrazol-5-yl)methyl]phenol (3)

A mixture of (4-hydroxyphenyl)(10H-phenothiazin-10-yl)acetonitrile **2** (3.3 g, 0.01 mol), sodium azide (1.0 g, 0.01 mol), dimethylformamide (10 mL) and ammonium chloride (5.3 g, 0.1 mol) was heated in an oil bath for 7 h at 125 °C. The solvent was removed at reduced pressure. The reaction mixture was dissolved in 100 mL of distilled water and acidified with concentrated hydrochloric acid to pH 2. The solution was cooled to 5 °C in an ice bath. The tetrazole **3** obtained was filtered, washed with water and recrystallised from aqueous methanol. The yield of the product is 60%.

Melting Point: 189-191 °C.

IR (KBr pellet, cm^{-1}): 3610 (s), 3341 (s), 3184 (w), 3099 (w), 2918 (w), 1596 (s), 1571 (m), 1282 (w), 1263 (w), 1035 (m), 751 (s), 737 (m), 717 (w).

^1H NMR (90 MHz, CDCl_3): 7.25 (s, 8H, ArH), 7.5 (d, $J = 6.4$ Hz, 2H, *o*-protons), 7.1 (d, $J = 3.0$ Hz, 2H, *m*-proton), 3.9 (s, 1H, C-H), 7.8 (s, 1H, -OH phenolic).

MS (m/z): 373 (M^+) (20%), 199 (100%).

Elemental Analysis: Calculated: C, 64.33; H, 4.05; N, 18.75. Found: C, 64.47; H, 4.12; N, 18.63.

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