

SYNTHESIS OF 3-BROMO-1-METHYL PHENOTHIAZINE SULFONES

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ABSTRACT

The synthesis of 3-bromo-1-methyl phenothiazine sulfones has been reported. The phenothiazines have been synthesized via Smiles rearrangement by the reaction of 2-amino-5-bromo-3-methyl benzenethiol with halonitrobenzene. 3-Bromo-1-methyl phenothiazine sulfones were synthesized by the oxidation of their corresponding phenothiazines by 30% hydrogen peroxide in glacial acetic acid. The structure of newly synthesized compounds have been confirmed by the elemental analysis, IR and ¹H NMR spectral data.

Key word : Sulfones, Phenothiazine

INTRODUCTION

Phenothiazine sulfones constitute an important class of heterocyclic sulfones, which possess a wide spectrum of biological and pharmacological activities¹⁻¹⁰. The oxidation of sulfide linkage in phenothiazine to dioxide leads to an interesting class of heterocyclic compounds not only from medicinal and industrial point of view, but for structural investigations also. It has stimulated our interest to understand oxidation behaviour of phenothiazine and to investigate the changes in infra red and nuclear magnetic spectra caused by the conversion of sulfide linkage to sulfones¹¹⁻¹⁴

EXPERIMENTAL

All the melting points are uncorrected. The purity of all the synthesized compounds have been checked by thin layer chromatography using various non-aqueous solvent systems and characterized by their spectral studies. The infra red spectra were recorded with FT – IR spectrometer MAGNA IR 550 NICOLET using both KBr discs as well as chloroform. The ¹H NMR spectra have been scanned at 90 MHz on Jeol FX 90 FT NMR spectrometer in CDCl₃ using TMS as an internal standard. Physical and analytical data of the synthesized compounds are summarized in Table – I.

Table 1: Physical and analytical data of phenothiazine sulfones (II_{a-f})

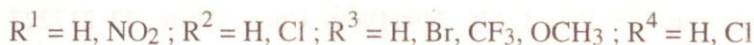
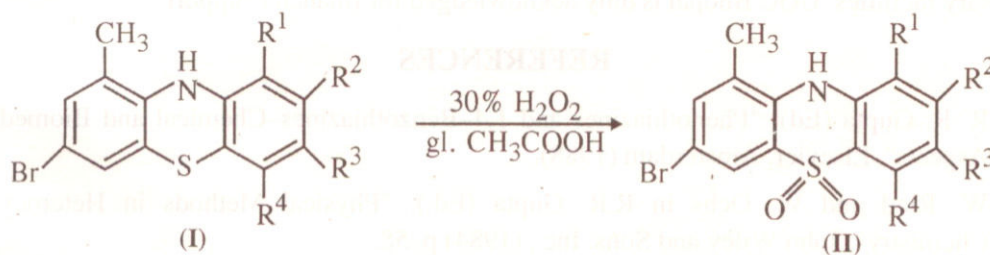
Comp.	R ¹	R ²	R ³	R ⁴	M.P. °C	% Yield	Molecular Formula	% Found (Calcd.)		
								C	H	N
II _a	H	H	Cl	H	198	25	C ₁₃ H ₉ BrClNO ₂ S	43.73 (43.51)	2.50 (2.51)	3.91 (3.90)
II _b	H	H	Br	H	232	30	C ₁₃ H ₉ Br ₂ NO ₂ S	38.93 (38.70)	2.24 (2.23)	3.46 (3.47)
II _c	N	N	CF ₃	N	158	43	C ₁₄ H ₉ BrF ₃ NO ₂ S	43.05 (42.85)	2.31 (2.29)	3.56 (3.57)
II _d	N	N	OCH ₃	N	198	52	C ₁₄ H ₁₂ BrNO ₃ S	47.67 (47.45)	3.39 (3.38)	3.96 (3.95)
II _e	NO ₂	H	CF ₃	H	270	60	C ₁₄ H ₈ BrF ₃ N ₂ O ₄ S	38.68 (38.44)	1.85 (1.83)	6.42 (6.40)
II _f	NO ₂	Cl	H	Cl	186	58	C ₁₃ H ₇ BrCl ₂ N ₂ O ₄ S	35.50 (35.61)	1.60 (1.59)	6.38 (6.39)

Preparation of 3-bromo-1-methyl phenothiazine sulfones (II_{a-f})

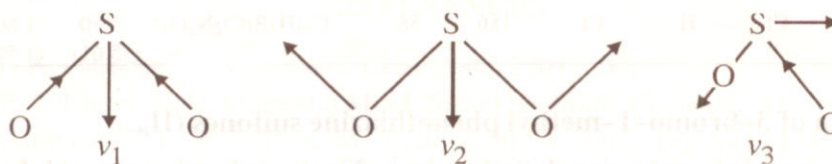
To a solution of phenothiazine (I; 0.01 mole) in 20 mL of glacial acetic acid, 5 mL of 30% hydrogen peroxide was added and refluxed for fifteen minutes. Heating was stopped and another lot of hydrogen peroxide (5 mL) was added. The reaction mixture was again refluxed for 3–4 hrs. The contents were poured in a beaker containing crushed ice. The yellow residue obtained was filtered off, washed with water and crystallized with ethanol.

RESULTS AND DISCUSSION

The title compounds have been synthesized by corresponding phenothiazines. Phenothiazines were prepared by the Smiles rearrangement of 2-amino-5-bromo-3-methyl benzenethiol with halonitrobenzenes. 3-Bromo-1-methyl phenothiazine sulfones have been prepared by treating phenothiazine with 30% hydrogen peroxide in glacial acetic acid (Scheme-1).

**Scheme-1**

The IR spectra of phenothiazine sulfones have been scanned in potassium bromide pellets as well as chloroform. All the synthesized phenothiazine sulfones exhibit a sharp intense peak in the region $1370\text{--}1345\text{ cm}^{-1}$ which can be assigned to the asymmetric stretching (ν_3) mode of sulfonyl group while in the solid state, this absorption band splits into three bands in the region $1375\text{--}1350\text{ cm}^{-1}$, $1320\text{--}1280\text{ cm}^{-1}$ and $1290\text{--}1265\text{ cm}^{-1}$. The asymmetric stretching vibrations in sulfones are strongly affected on passing from solution to the crystalline state. The symmetric stretching vibrations (ν_1) of phenothiazine sulfones give rise to a doublet in potassium bromide pellets in the region $1180\text{--}1140\text{ cm}^{-1}$ whereas in solution, it appears in the region $1178\text{--}1140\text{ cm}^{-1}$. These frequencies are slightly affected due to the state of aggregation. The bands appeared in the region $582\text{--}545\text{ cm}^{-1}$ and $550\text{--}580\text{ cm}^{-1}$ in phenothiazine sulfones can be attributed to bending vibrations (ν_2) on passing from solution to the crystalline state.



In all the synthesized phenothiazine sulfones, peaks in potassium bromide discs are observed in the region $3450\text{--}3370\text{ cm}^{-1}$ due to N-H stretching vibrations and a medium intensity band appeared at $1090\text{--}1060\text{ cm}^{-1}$ due to C-S stretching vibration.

^1H NMR spectra of each synthesized phenothiazine sulfones (**II_{a-f}**) exhibit a singlet in the region δ 9.80–8.50 ppm due to N-H proton. All compounds (**II_{a-f}**) exhibit a multiplet in the region δ 8.98–6.70 ppm due to aromatic protons. Compound **II_d** exhibit a singlet in the region δ 5.37 ppm due to OCH_3 protons at C_7 . All compounds (**II_{a-f}**) exhibit a singlet in the region δ 2.14–2.02 ppm due to CH_3 protons at C_1 .

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