

SYNTHESIS OF 7-BROMO/8,9-DIMETHYLPHENOTIAZINE SULFONES

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ABSTRACT

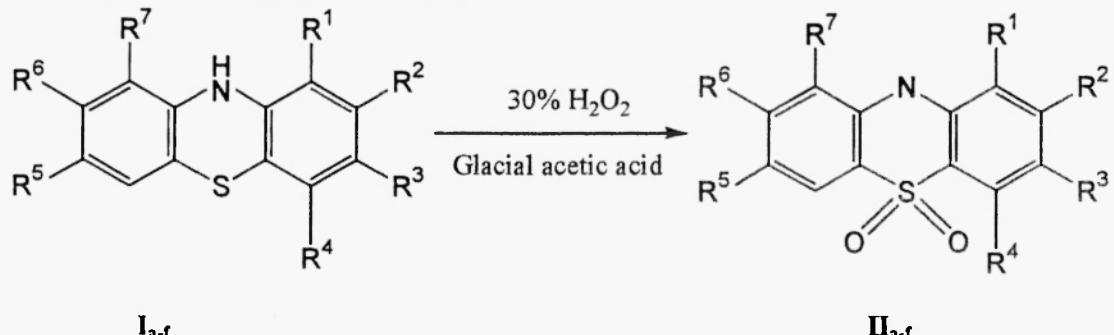
The synthesis of 7-bromo/8,9-dimethylphenothiazine sulfones is reported. 7-Bromo/8,9-dimethylphenothiazine sulfones were prepared by the oxidation of their corresponding phenothiazines by 30% hydrogen peroxide in glacial acetic acid. The structure of newly synthesized compounds has been confirmed by the elemental analysis, IR and ¹H NMR spectral studies.

INTRODUCTION

Phenothiazine sulfones constitute an important class of heterocycles posses a wide spectrum of pharmacological / biological activities.¹⁻¹¹ The oxidation of sulfide linkage in phenothiazines to dioxide leads to an interesting class of heterocyclic sulfones not only the medicinal and industrial point of view, but also from structural aspects. It has stimulated our interest to understand oxidation behaviour of phenothiazines and to investigate changes in infrared and nuclear magnetic spectra caused by the conversion of sulfide linkage to sulfones¹²⁻¹⁶.

RESULTS AND DISCUSSION

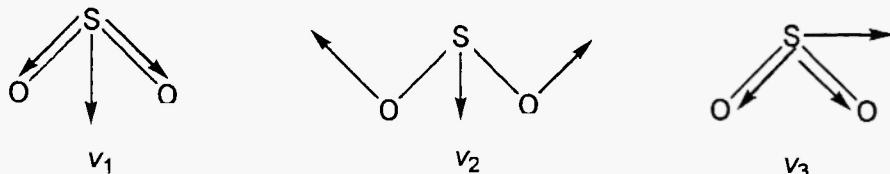
The title compounds have been synthesized by corresponding phenothiazines. Phenothiazines were prepared by the Smiles rearrangement of 2-amino-5-bromo/3,4-dimethylbenzenethiols with a halonitrobenzenes. 7-Bromo/8,9-dimethyl-10H-phenothiazines-5,5-dioxides (**II_{a-f}**) have been prepared by treating phenothiazine with 30% hydrogen peroxide in glacial acetic acid (Scheme I).



Compound	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷
II _a	Cl	H	H	H	Br	H	H
II _b	H	H	Cl	H	Br	H	H
II _c	NO ₂	H	Cl	Cl	Br	H	H
II _d	NO ₂	H	CF ₃	H	Br	H	H
II _e	H	H	Cl	H	H	CH ₃	CH ₃
II _f	H	Cl	Cl	H	H	CH ₃	CH ₃

Scheme I : Synthesis of 7-bromo/8,9-dimethylphenothiazine sulfones

The IR spectra of phenothiazines sulfones have been recorded both in potassium bromide pellets and in chloroform solution. All the synthesized phenothiazine sulfones exhibit a sharp intense peak in the region 1390-1300 cm⁻¹ which can be ascribed to the asymmetric stretching (ν_3) mode of sulfonyl group which in the solid state splits into three bands in the region 1420-1330 cm⁻¹, 1355-1250 cm⁻¹ and 1270-1200 cm⁻¹. The asymmetric stretching vibrations in sulfones is strongly affected on passing from solution to the crystalline state. The symmetric stretching vibrations (ν_1) of phenothiazines sulfones give rise to a doublet in potassium bromide pellets in the region 1180-1100 cm⁻¹ whereas in solution it appears in the region 1180-1080 cm⁻¹. These frequencies are slightly affected by the state of aggregation. The bond appearing in the region 600-500 in phenothiazine sulfones can be attributed to bending vibrations (ν_2) on passing from solution to the crystalline state.



In all the phenothiazines sharp peaks in KBr discs are observed in region (3380-3215 cm⁻¹) due to N-H stretching vibrations and shifted to slightly higher frequency (3420-3370 cm⁻¹) in corresponding sulfones.

NMR spectra of each synthesized phenothiazine sulfones (II_{a-f}) exhibit a singlet in the region δ 8.91-9.98 ppm due the N-H proton. All compound (II_{a-f}) exhibit a multiplet in the region δ 5.78-8.62 ppm due to aromatic protons. In compound (II_{e,f}) two singlets are observed in the region δ 3.16-3.24 ppm and δ 1.16-1.27 ppm assigned to CH₃ protons at C₈ and C₉, respectively.

EXPERIMENTAL

All the melting points are uncorrected. The purity was checked by thin layer chromatography using various non-aqueous solvents and characterized by their spectral studies. The infrared spectra have been recorded on FTIR spectrometer MAGNA IR 550

NICOLET using both of KBr discs as well as chloroform. The NMR spectra were recorded on 90MHz on Jeol FX 90 Q FT NMR spectrometer in CDCl_3 using TMS as an internal standard. Physical and analytical data of synthesized compounds are summarized in **Table 1**.

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

Compound	R¹	R²	R³	R⁴	R⁵	R⁶	R⁷	M.P. °C	% yield	Molecular Formula	Found (Calculated)		
	C	H	N	XII	XIII	XIV					C	H	N
II_a	Cl	H	H	H	Br	H	H	178	46	$\text{C}_{12}\text{H}_7\text{O}_2\text{NSBrCl}$	(41.81) 41.77	(2.03) 2.00	(4.07) 4.05
II_b	H	H	Cl	H	H	Br	H	198	39	$\text{C}_{12}\text{H}_7\text{O}_2\text{BrNSCl}$	(41.81) 41.80	(2.03) 2.01	(4.07) 4.05
II_c	NO_2	H	Cl	Cl	H	Br	H	199	64	$\text{C}_{12}\text{H}_7\text{O}_4\text{N}_2\text{SBrCl}_2$	(41.81) 41.81	(1.18) 1.15	(6.60) 6.61
II_d	NO_2	H	CF_3	H	H	Br	H	219	78	$\text{C}_{12}\text{H}_6\text{O}_4\text{N}_2\text{SF}_3\text{Br}$	(41.81) 41.45	(1.48) 1.51	(6.91) 6.66
II_e	H	H	Cl	H	H	CH_3	CH_3	120	42	$\text{C}_{14}\text{H}_{12}\text{SO}_2\text{NCl}$	(57.24) 57.20	(4.09) 4.05	(4.77) 4.77
II_f	H	Cl	Cl	H	H	CH_3	CH_3	164	50	$\text{C}_{14}\text{H}_{11}\text{SO}_2\text{NCl}_2$	(51.22) 51.20	(3.35) 3.35	(4.26) 4.25

Preparation of 7-bromo-8/9-dimethylphenothiazine sulfones(II_{a-f})

30% Hydrogen peroxide (5ml) was added to the solution of phenothiazine (**I**, 0.01 mole) in glacial acetic acid (20 ml) and refluxed for fifteen minutes. Heating was stopped and another lot of hydrogen peroxide (5 ml) was added. The reaction mixture was 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 from ethanol.

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