SYNTHESIS AND SPECTRAL STUDIES OF 4H-1,4-BENZOTHIAZINE S,S-DIOXIDES (SULFONES)

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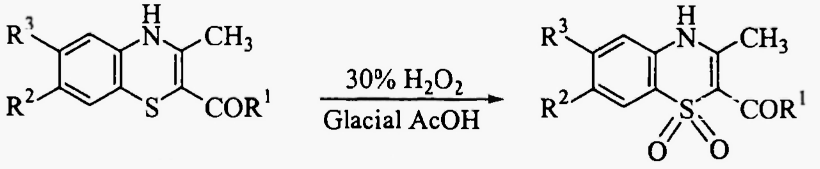
Abstract : The oxidation of 4H-1,4-benzothiazines by 30% hydrogen peroxide in glacial acetic acid leads to the formation of 4H-1,4-benzothiazine S,S-dioxides. The IR and ^1H NMR spectral studies are also included.

Introduction

4*H*–1,4–Benzothiazine–S,S–dioxides form an interesting class of heterocyclic compounds[1,2] of therapeutic[3-5] and industrial[6] importance. These applications have stimulated our interest to understand the oxidation behaviour of 4*H*–1,4–benzothiazines S,S-dixoides in order to correlate the structural changes caused by the conversion of sulfide linkage into S,S–dioxide in IR and NMR spectra.

Result and Discussion

In the present work, 4*H*–1,4–benzothiazine S,S-dioxides (Scheme 1, IIa-h) have been prepared by the oxidation of 4*H*–1,4–benzothiazines (I) by 30% hydrogen peroxide in glacial acetic acid. 4H,1,4-Benzothiazines[7,8] were prepared by the condensation and oxidative cyclization of 2–amino–5–methoxy/4-sulfonylbenzenethiol with β-diketones in dimethylsulfoxide.



I

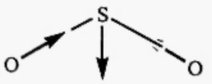
IIa-h

$R^1 = C_6H_4\text{–}Br(m), C_6H_4\text{–}CH_3(m), C_6H_4\text{–}OC_2H_5(p), C_6H_4\text{–}C_2H_5(p)$

$R^2 = OCH_3, H; R^3 = SO_3H, H$

Scheme 1

Infrared spectra of all the newly synthesized 4H-1,4-benzothiazine-S,S-dioxides have been recorded both in potassium bromide pellets and chloroform solution. All the 4*H*–1,4–benzothiazine S,S-dioxides exhibit three characteristic absorption bands due to sulfonyl group corresponding to three normal modes of vibrations[9,10] in the molecule of sulfurdioxide as shown :

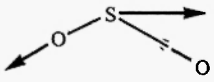


$\nu_1 = 1151\ cm^{-1}$

symmetric

$\nu_2 = 519\ cm^{-1}$

bending



$\nu_3 = 1361\ cm^{-1}$

asymmetric

All the benzothiazine S,S-dixoides exhibit a single sharp band in the region 1384–1300 cm^{-1} in chloroform solution corresponding to the asymmetric stretching mode of vibrations of sulfonyl group. While in solid state, this absorption band (ν_3), splits into three bands in the region 1395–1305 cm^{-1}, 1365–1285 cm^{-1} and 1265–1255 cm^{-1}. The symmetric stretching vibrations (ν_1) give rise to a doublet in the region 1205–1150 cm^{-1} and 1150–1105 cm^{-1} in KBr pellets and chloroform respectively. The bending vibrations (ν_2) in sulfur dioxide exhibit a medium absorption band in the low frequency region at 570–520 cm^{-1}.By comparing the vibrational frequencies of 4H-1,4-benzothiazine S,S-dioxides and their parent 4H,1,4-benzothiazines, it is found that vibrational frequency corresponding to each substituent is shifted to higher frequency in the corresponding benzothiazine S,S-dioxide.A sharp band appearing in the region 1665–1605 cm^{-1} due to >C=O stretching vibrations in 4*H*–1,4–benzothaizmes is shifted to higher frequency region 1685–1630 cm^{-1} in the corresponding S,S-dioxides. The shifting of absorption band to higher frequency region is attributed to –I effect of the SO_2 group combined with the mesomeric effect operating in the same direction which hinder the conjugation of lone pair of electrons at nitrogen with carbonyl group. A band observed in the region 3385–3270 cm^{-1} in 4*H*–1,4–benzothaizines due to free N–H vibrations is shifted to higher frequency region 3410–3335 cm^{-1} in the corresponding S,S-dioxides. And a medium intensity band appearing at 1060–1000 cm^{-1} in 4H-1,4–benzothaizines due to C–S stretching vibrations is shifted to higher frequency 1070–1025 cm^{-1} in the corresponding S,S-dioxides.

^{1}H NMR spectra of 4*H*–1,4–benzothiazine S,S-dioxides exhibit a singlet in the region δ 8.42–9.51 ppm due to N–H proton. The multiplet observed in the region δ 6.34–8.46 ppm is due to aromatic protons. Compounds (IIe–h) exhibits a singlet in the region δ 3.68–3.84 ppm due to OCH_3 protons. The compounds (IIb) and (IIf) exhibit a singlet at δ 1.82–1.85 ppm due to CH_3 protons at benzoyl side chain at C_2. All the compounds show a singlet in the region δ 1.99–2.50 ppm which can be assigned to CH_3 protons at C_3. The compounds (IIc) and (Ilg) exhibits a triplet and quartet in the region δ 1.35–1.37 ppm and δ 3.76–4.12 ppm due to CH_3 and CH_2 protons of OC_2H_5 group at *p*–position in benzoyl side chain at C_2. A quartet at δ 2.55–2.66 ppm and triplet at δ 1.20 ppm are observed in the compounds (IId) and (IIh) due to CH_2 and CH_3 protons of C_2H_5 group at *p*–position in benzoyl side chain at C_2.

Table 1 : Physical data of substituted 4H–1,4–benzothiazine S,S-dioxides (IIa–h)

	Compound			M.P.	Yield	Molecular	% Found (Calcd.)			
	R^1	R^2	R^3	°C	%	formula	C	H	N	S
I	II	III	IV	V	VI	VII	VIII	IX	X	XI
a.	C_6H_4–Br(*m*)	H	SO_3H	220	25	$C_{16}H_{12}NO_6S_2Br$	41.26 (41.92)	2.62 (2.64)	3.01 (3.05)	13.95 (13.99)
b.	C_6H_4–CH_3(*m*)	H	SO_3H	179	33	$C_{17}H_{15}NO_6S_2$	52.18 (51.89)	3.87 (3.84)	3.60 (3.56)	16.33 (16.29)
c.	C_6H_4–OC_2H_5(*p*)	H	SO_3H	170	16	$C_{18}H_{17}NO_7S_2$	51.64 (51.05)	4.06 (4.04)	3.36 (3.30)	15.18 (15.14)
d.	C_6H_4–C_2H_5(*p*)	H	SO_3H	106	21	$C_{18}H_{17}NO_6S_2$	52.75 (53.05)	4.18 (4.20)	3.38 (3.43)	15.68 (15.73)
e.	C_6H_4–Br(*m*)	OCH_3	H	152	32	$C_{17}H_{14}NO_4SBr$	50.32 (50.00)	3.48 (3.45)	3.46 (3.43)	7.91 (7.85)
f.	C_6H_4–CH_3(*m*)	OCH_3	H	109	21	$C_{18}H_{17}NO_4S$	62.73 (62.95)	4.97 (4.99)	4.06 (4.08)	9.28 (9.33)
g.	C_6H_4–OC_2H_5(*p*)	OCH_3	H	98	29	$C_{19}H_{19}NO_5S$	61.45 (61.11)	5.15 (5.12)	3.79 (3.75)	8.61 (8.58)
h.	C_6H_4–C_2H_5(*p*)	OCH_3	H	122	40	$C_{19}H_{19}NO_4S$	64.09 (63.84)	5.38 (5.35)	3.95 (3.91)	9.01 (8.97)

Experimental

The melting points of all the synthesized 4*H*–1,4–benzothiazine S,S-dioxides are uncorrected. The purity of all the compounds was checked by thin layer chromatography using various non-aqueous solvent systems. The infrared spectra were recorded on a NICOLET MAGNA FT IR spectrophotometer model 550 in KBr discs. NMR spectra were recorded at 90 MHz on Jeol FX 90Q FT NMR spectrometer using TMS as internal standard. The physical data of newly synthesized compounds are tabulated in Table-1.

Preparation of substituted 4*H*–1,4–benzothiazine S,S-dioxides (IIa–h)

30% Hydrogen peroxide (5 ml) was added to the solution of 4*H*–1,4–benzothiazine (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 hours. The excess of solvent was removed by distillation under reduced pressure and the concentrated solution was poured into a beaker containing crushed ice. The yellow residue obtained was filtered off, washed with water and crystallized from ethanol.

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