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Spectroscopic and Physical Studies on the Oxidation of Some 4H-1,4-Benzothiazines with Hydrogen Peroxide in Acetic Acid

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A suitable route for the preparation of 4H-1,4-benzothiazine sulphones with hydrogen peroxide and acetic acid has been reported. The synthesis of 4H–1,4-benzothiazines, consisting of 2-aminothiophenol with β-diketone/β-ketoester in dimethyl sulphoxide, is described. The infrared spectral investigation on the pure samples of 4H-1,4-benzothazines and its sulphones showed the remarkable shifting of characteristic vibrational bands towards higher frequencies in sulphones.

INTRODUCTION

4H-1,4-benzothiazine sulphones constitute an interesting class of heterocyclic sulphones which find a number of applications in medicine[1–4] and in industry[5]. It is considered worthwhile to convert benzothiazines to sulphones to investigate their oxidation behaviour.

Different oxidising agents have been used for the oxidation of benzothiazines to their sulphones. The oxidation of benzothiazines has been accomplished with potassium permanganate[6] and potassium permanganate in 50% acetic acid[7]. The literature survey reveals that some substituted 4H-1,4-benzothiazin-1,1-dioxides have been prepared by the oxidation of 2-(hydroxyethylthio)-cyclohexanol in hydrogen peroxide[8] followed by cyclisation with sodium hydroxide, by thermal cyclisation of N-(benzylsulphonylphenyl)-glycine[9] and by the ozonolysis of *o*-nitrophenylsulphone followed by catalytic hydrogenation[10] in 20% yield. Maschmeier[11] have synthesised sulphones by electrosynthesis.

In the present communication 4H-1,4-benzothiazine sulphones in almost quantitative yield have been prepared by carrying out oxidation of 4H-1,4-benzothiazines by 30% hydrogen peroxide in glacial acetic acid (Scheme 1).

EXPERIMENTAL

The melting points of all the synthesised 4H-1,4-benzothiazine sulphones are uncorrected. The purity of all the compounds was checked by thin layer chromatography. The IR spectra were recorded on Perkin-Elmer spectrophotometer model 577 in both potassium bromide discs and in chloroform solution. The ^{1}H NMR spectra were recorded at 90 MHz using TMS as an internal standard in $CDCl_3$ solution.

Preparation of 4H-1,4-benzothiazines (I)

Synthesis of 4H-1,4-benzothiazines[12, 13] required for the preparation of sulphones has already been published.

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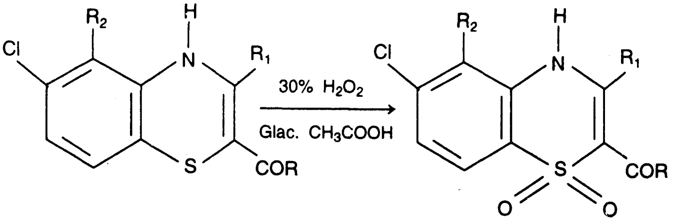

(I) (II)

IIa. $R = OCH_3$; $R_1 = R_2 = CH_3$
b. $R = OC_2H_5$; $R_1 = R_2 = CH_3$
c. $R = C_6H_5$; $R_1 = R_2 = CH_3$
d. $R = C_6H_4—Cl(p)$; $R_1 = R_2 = CH_3$
e. $R = C_6H_4—CH_3(p)$; $R_1 = R_2 = CH_3$
f. $R = CH_3$; $R_1 = R_2 = CH_3$
g. $R = C_6H_4—Br(p)$; $R_1 = R_2 = CH_3$
h. $R = C_6H_5$; $R_1 = C_6H_5$; $R_2 = CH_3$
i. $R = OCH_3$; $R_1 = CH_3$; $R_2 = H$
j. $R = C_6H_3—(OCH_3)_2(m, p)$; $R_1 = CH_3$; $R_2 = H$
k. $R = C_6H_4—OCH_3(m)$; $R_1 = CH_3$ $R_2 = H$

Scheme 1

Preparation of 4H-1,4-benzothiazine sulphones (II)

Respective 4H-1,4-benzothiazine (I; 0.01 mol) in glacial acetic acid (20 mL) and 30% hydrogen peroxide (3 mL) was refluxed for 15 minutes at 50–60°C.

TABLE-1
PHYSICAL CHARACTERISATION DATA OF II

Comp. No.	Molecular formula	m.p.* [°C]	Yield [%]	% Calcd./(found)	
				N	S
IIa	$C_{12}H_{12}ClNO_4S$	252	65	4.64 (4.62)	10.61 (10.59)
IIb	$C_{13}H_{14}ClNO_4S$	293	68	4.44 (4.41)	10.14 (10.11)
IIc	$C_{17}H_{14}ClNO_3S$	278	55	4.03 (4.01)	9.20 (9.15)
IId	$C_{17}H_{13}Cl_2NO_3S$	312	60	3.66 (3.65)	8.37 (8.32)
IIe	$C_{18}H_{16}ClNO_3S$	282	57	3.87 (3.85)	8.85 (8.84)
IIf	$C_{12}H_{12}ClNO_3S$	286	72	4.90 (4.87)	11.20 (11.17)
IIg	$C_{17}H_{13}BrClNO_3S$	305	64	3.28 (3.25)	7.50 (7.46)
IIh	$C_{12}H_{16}ClNO_3S$	245	48	3.42 (3.36)	7.81 (7.75)
IIi	$C_{11}H_{10}ClNO_4S$	375	75	4.87 (4.83)	11.13 (11.09)
IIj	$C_{18}H_{16}ClNO_5S$	285	70	3.56 (3.51)	8.13 (8.05)
IIk	$C_{17}H_{14}ClNO_4S$	318	65	3.85 (3.81)	8.80 (8.76)

*All compounds were crystallised from ethanol and give C, H analysis satisfactorily.

Heating was stopped and another lot of hydrogen peroxide (5 mL) was added. The reaction mixture was again refluxed for 4 h. The excess of solvent was removed by distillation under reduced pressure and the solution was poured in to a beaker containing crushed ice. The yellow residue obtained was filtered off, dried, and crystallised from ethanol. The physical data of 4H-1,4-benzothiazine sulphones are summarised in Table-1.

RESULTS AND DISCUSSION

All the 4H-1,4-benzothiazine sulphones exhibit three characteristic intense absorption bands in the region 1395–1240 cm^{-1}, 565–515 cm^{-1} and 1165–1130 cm^{-1} in the solid state as well as in chloroform solution. These bands are analogous to the three fundamental absorption bands *viz.*, 1151, 519 and 1361 cm^{1} in the sulphur dioxide molecule and can be assigned to three normal modes of vibration[15, 16] (Fig. 1).

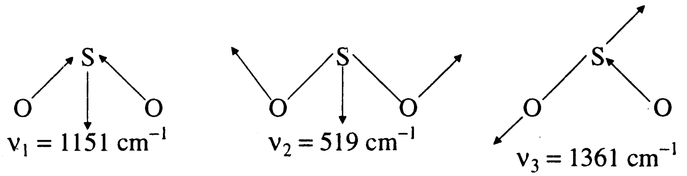

Fig. 1

All the 4H-1,4- benzothiazine sulphones exhibit an intense peak in the region 1395–1378 cm^{-1} in chloroform solution due to the asymmetric stretching mode of the sulphonyl group, but in solid state this absorption band splits into three and appears in the regions 1395–1375 cm^{-1}, 1350–1310 cm^{-1} and 1285–1240 cm^{-1}. The asymmetric vibration in the sulphones is strongly affected on passing from solution to the crystalline state. The symmetric stretching vibrations ν_1 give rise to a high intensity doublet and in some cases a broad signal in the region 1165–1115 cm^{-1}, whereas in chloroform solution it appears at 1160–1130 cm^{-1}. Hence, these frequencies are affected only to a very small extent by the state aggregation. The banding vibrations ν_2 in sulphur dioxide exhibit medium absorption bands in the low frequency region 560–512 cm^{-1} and appear as a doublet or sometimes as a singlet band with an inflection. In the IR spectra of sulphuryl halides, this absorption is reported below 600 cm^{-1} and assigned to fundamental vibrations[17, 18]. Analogously the bands in 4H-1,4-benzothiazine sulphones in the region 570–525 cm^{-1} can be ascribed to sulphur dioxide scissoring and rocking vibrations (Table-2).

The present work deals with the substituent vibrations, both in sulphones and in their parent benzothiazines and have been summarised in Table-3. The vibrational frequency corresponding to each substituent is shifted to higher frequency in benzothiazine sulphones. 4H-1,4-Benzothiazines exhibit a band at 1640–1550 cm^{-1} due to ν(C=O) stretching vibrations, but it is shifted to higher frequencies 1700–1665 cm^{-1} in the corresponding sulphones. This is in agreement with increased electron acceptor ability of the hetero-aromatic nucleus in the sulphones as compared to the parent nucleus. The lone pair of electrons at nitrogen is withdrawn more effectively towards the ring and it conjugates less effectively with carbonyl group, and results in higher carbonyl group frequencies. The –I effect of the sulphur dioxide group combines with mesomeric effect operating in the same direction and also hinders the conjugation of lone pair of electrons at nitrogen with the carbonyl group. A sharp intense peak observed in the region 3360–3220 cm^{-1} in 4H-1,4-benzothiazines due to free N—H stretching vibrations is shifted to higher frequency region 3420–3315 cm^{-1} in the corresponding

TABLE-2

CHARACTERISTIC IR VIBRATION OF SULPHONYL GROUP IN KBr AND $CHCl_3$ (cm^{-1})

Comp. No.	ν_1 ($\nu_{sym}(SO_2)$)		$\nu_2((\nu(SO_2))$		$\nu_3((\nu_{asym}(SO_2))$	
	KBr	$CHCl_3$	KBr	$CHCl_3$	KBr	$CHCl_3$
IIa	1150	1142	540	536	1390	1395
	1140	1135	520	518	1320	
					1250	
IIb	1160	1155	550	543	1375	1378
	1145	1142	535	529	1340	
					1260	
IIc	1152	1145	548	538	1385	1387
	1148	1143	535	526	1335	
					1250	
IId	1160	1155	540	545	1380	1385
	1145	1142	525	520	1310	
					1260	
IIe	1162	1160	540	534	1390	1390
	1155	1148	520	515	1315	
					1280	
IIf	1140	1135	535	530	1395	1390
	1135	1132	515	512	1320	
					1240	
IIg	1155	1147	565	560	1390	1385
	1140	1130	530	527	1345	
					1250	
IIh	1150	1144	542	540	1375	1380
	1140	1136	550	522	1335	
					1270	
IIi	1165	1160	545	540	1395	1395
	1140	1135	530	525	1330	
					1240	
IIj	1150	1142	535	531	1385	1392
	1145	1137	520	515	1310	
					1250	
IIk	1145	1147	555	548	1385	1395
	1135	1130	530	523	1350	
					1265	

sulphones. A band of medium intensity in the region 1080–1045 cm^{-1} appears due to ν(C—S) stretching vibrations and is shifted to higher frequency region 1110–1085 cm^{-1} in corresponding sulphones. The oxidation of sulphide linkage in 4H-1,4-benzothiazines results in the change of vibrational modes due to the strong electron withdrawing nature of sulphur dioxide group.

TABLE-3
IR SPECTRAL DATA OF 4H-1,4-BENZOTHIAZINES AND THEIR SULPHONES IN KBr (cm^{-1})

Compund	ν(N—H)	ν(C=O)	ν_{asym}(C—S)
Ia/IIa	3370	1620	1085
	3415	1690	1105
Ib/IIb	3400	1630	1090
	3410	1670	1105
Ic/IIc	3410	1600	1170
	3430	1650	1110
Id/IId	3390	1680	1075
	3400	1700	1095
Ie/IIe	3320	1590	1085
	3440	1660	1105
If/IIf	3360	1590	1070
	3385	1670	1095
Ig/IIg	3340	1620	1090
	3345	1650	1110
Ih/IIh	3320	1595	1095
	3335	1645	1110
Ii/IIi	3300	1600	1080
	3330	1660	1105
Ij/IIj	3310	1570	1065
	3315	1655	1095
Ik/IIk	3280	1580	1085
	3295	1645	1110

^{1}H NMR spectra (Table-4) of each synthesised 4H-1,4-benzothiazine sulphones exhibits a singlet in the region δ(10.05–8.96) due to N—H proton. All compounds exhibit a multiplet in the region δ(8.14–6.12) due to aromatic ring protons. In compounds IIa–h a singlet is observed in the region δ(2.30–1.73) assigned to CH_3 protons at C_5. A singlet is observed in all the compounds except IIh in the region δ(2.35–1.89) due to CH_3 protons at C_3. In compounds IIa and IIi a singlet appears at δ3.75 and δ3.79 respectively due to OCH_3 protons as $COOCH_3$ at C_2. In compound IIf a singlet is observed at δ2.18 due to CH_3 protons as $COCH_3$ at C_2. In compound IIe a singlet is observed at δ2.21 due to CH_3 protons at *para* position in benzoyl side chain at C_2. Compound IIb exhibits quartet and a triplet in the regions δ(4.65–3.75) and δ(1.20–0.82) respectively due to CH_2 and CH_3 protons of C_2H_5 as $COOC_2H_5$ at C_2. In compound IIk a singlet appears at δ4.65 due to OCH_3 protons at *para* position in benzoyl side chain at

C_2. In compound IIj two singlets are observed at δ4.03 and δ3.89 due to OCH_3 protons at *meta* and *para* positions in benzoyl side chain at C_2.

TABLE-4

^1H NMR SPECTRAL DATA (δ, ppm) OF 4H-1,4-BENZOTHIAZINE SULPHONES

Comp	NH^s	arom.^{m}	$3\text{-}CH_3{}^s$	$5\text{-}CH_3{}^s$	Other protons
IIa	9.32	8.14–7.40	2.26	2.18	3.75 (OCH_3 at 2–C)^s
IIb	10.05	7.13–6.10	2.30	2.03	4.65–3.75 (CH_2 at 2–C)^t, 1.20–0.82 (CH_3 at 2–C)^q
IIc	8.96	7.60–6.12	2.35	2.30	—
IId	9.53	7.65–6.15	1.89	1.73	—
IIe	9.83	8.09–6.35	2.25	1.83	2.21 (CH_3) at benzoyl side chain at 2–C^s
IIf	9.07	8.03–6.94	2.04	1.63	2.18 (CH_3 at 2–C)^s
IIg	9.35	7.53–6.11	2.18	1.90	—
IIh	9.82	8.10–6.25	—	2.06	—
IIi	9.67	8.53–7.49	2.13	—	8.79 (OCH_3 at 2–C)^s
IIj	9.58	7.83–6.19	2.24	—	4.03 and 3.89 (OCH_3 at *m*- and *p*-position of benzoyl side chain at 2–C)^s
IIk	9.34	7.76–6.15	1.93	—	4.65 (OCH_3 at *m*- position of benzoyl side chain at 2–C)^s

^{s}Singlet, ^{t}triplet, ^{q}quartet, ^{m}multiplet

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