Synthesis and Absorption Spectra of Some 6-Hydroxythiazolo[3,2-*a*]-benzimidazoles and Their Quaternary Derivatives

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A series of substituted 6-Hydroxythiazolo[3,2-*a*]benzimidazoles has been synthesized. Their quaternary derivatives showed characteristic absorption maxima at longer wavelengths in visible region. The spectral study of parent compounds in the visible region shows a red shift at higher pH which is attributed to the dipolar nature of these compounds.

The chemotherapeutic importance of imidazole derivatives is well recognized.[1-3] The effectiveness of condensed heterocycles containing thiazole and imidazole rings as antiprotozoal agents,[4] anticonvulsants,[5] antidepressants,[6] antihelminthic agents,[7-10] antidiabetic,[11] and as inhibitors of dihydrofolate[12] led us to synthesize a new series of thiazolobenzimidazoles in a manner analogous to Schmid and Czerney's[13] synthesis of 8-hydroxypyrido[1,2-*a*]benzimidazole. Rudner[14] synthesized some of the 6-hydroxy-substituted thiazolo[3,2-*a*]benzimidazoles by the condensation of substituted 2-aminothiazoles with *p*-benzoquinone in acetic acid. We followed the same procedure and obtained more new compounds of the above series. A study of their finer structure through spectral analysis was made. The thiazolobenzimidazoles so obtained were quaternized with ethyl bromide giving the corresponding 9-ethyl-6-hydroxythiazolo[3,2-*a*]benzimidazolium bromides. These quaternary compounds gave intense yellow color with dilute aqueous alkali due to the formation of phenol betaines.[15-16] The colored betaines could be extracted in the chloroform layer giving a deep violet color. The color was discharged on acidification which is the reversal of the mode of formation of these betaines.

Experimental

All the reagents were thoroughly dried and purified before use. All melting points were determined on Kofler instrument and were uncorrected. IR spectra were recorded on a Perkin-Elmer 577 spectrophotometer in KBr. UV absorption spectra were scanned in Beckman spectrophotometer, Model DU-2.

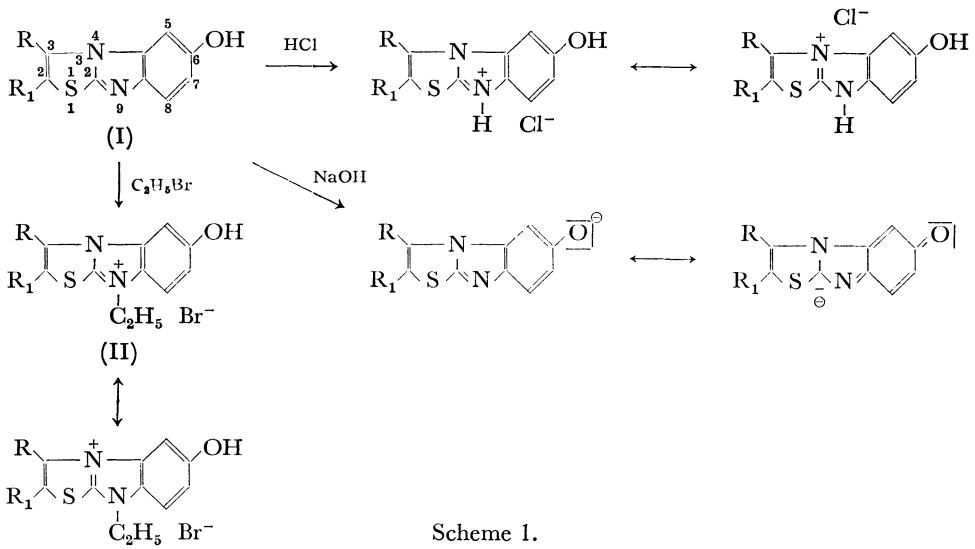
2-Aminothiazoles: These compounds were prepared by known method.[17]

*6-Hydroxythiazolo[3,2-*a*]benzimidazoles (I).* A solution of *p*-benzoquinone (0.01 mol) in glacial acetic acid (10 ml) was added in small portions to the substituted 2-aminothiazole (0.01 mol) in acetic acid (10 ml) with shaking. The mixture was left aside for 30 min. After addition of 20 ml of 50% aq HCl, the solution was diluted with water, and extracted with ether to remove any unreacted quinone and hydroquinone. The resulting solution was made alkaline with aq sodium carbonate when the desired compound precipitated. After treatment with charcoal in ethanol, the compound was recrystallized from ethanol. The yields, mp; *etc.* are given in Table 1.

*9-Ethyl-6-hydroxythiazolo[3,2-*a*]benzimidazolium Bromides (II).* A mixture of I (0.01 mol) and ethyl bromide (0.01 mol) in a minimum quantity of acetone was boiled under reflux for 1 h. The solvent was evaporated to dryness under reduced pressure and the residue was crystallized from ethanol–ether. The yields, mp *etc.* are given in Table 2.

Discussion

All these compounds are deep colored powdery substances, insoluble in water but are readily soluble in ethanol. They do not melt upto 330 °C. The structure of these compounds has been determined on the basis of IR spectra and elemental analysis. The IR spectra of these compounds showed bands at 3210, 1200 (phenolic OH), 1610(C=N), 1310(C–N), and 1440 cm^{-1} (aromatic



Scheme 1.

Table 1. 6-Hydroxythiazolo[3,2-*a*]benzimidazoles (I)

Compd No.	R	R_1	Molecular formula	Analysis (%)		Yield %	UV spectra					
				Calcd	Found		Ethanol		0.1 M HCl		0.1 M NaOH	
							λ_{max} nm	log ε	λ_{max} nm	log ε	λ_{max} nm	log ε
1	C_6H_5	H	$C_{15}H_{10}N_2OS$	C, 67.6	67.4	55	230	4.13				
				H, 3.7	3.6		258	3.93	315	3.40	312	3.53
				N, 10.5	10.4		350	3.39	375	3.47	450	3.55
2	CH_3	H	$C_{10}H_8N_2OS$	C, 58.8	58.6	40	236	4.01				
				H, 3.9	3.7		253	3.95	310	3.43	305	3.54
				N, 13.7	13.5		357	3.56	366	3.71	435	3.43
3	CH_3	$COOC_2H_5$	$C_{13}H_{12}N_2O_3S$	C, 56.5	56.4	57	240	3.98				
				H, 4.3	4.1		255	3.90	313	3.41	308	3.51
				N, 10.1	9.9		361	3.78	372	3.35	415	3.29
4	H	CH_3	$C_{10}H_8N_2OS$	C, 58.8	58.5	36	244	3.80				
				H, 3.9	3.8		272	3.74	321	3.37	310	3.48
				N, 13.7	13.5		355	3.40	370	3.5	427	3.35
5	CH_3	C_6H_5	$C_{16}H_{12}N_2OS$	C, 68.5	68.1	25	245	3.60				
				H, 4.28	4.1		278	3.57	329	3.8	324	3.2
				N, 10.0	9.8		364	3.60	385	3.3	450	3.7
6	*p*-$CH_3C_6H_4$	H	$C_{16}H_{12}N_2OS$	C, 68.5	68.3	40	238	3.76				
				H, 4.28	4.20		275	3.54	325	3.6	318	3.3
				N, 10.0	9.7		362	3.65	380	3.5	445	3.46
7	*p*-BrC_6H_4	H	$C_{15}H_9N_2OSBr$	C, 52.1	52.0	39	245	3.69				
				H, 2.5	2.3		267	4.35	319	3.38	312	3.43
				N, 8.1	8.1		357	3.81	384	3.40	449	3.61
8	*p*-HOC_6H_4	H	$C_{15}H_{10}N_2O_2S$	C, 63.8	63.5	48	248	4.01				
				H, 3.54	3.32		272	4.41	315	3.46	308	3.28
				N, 9.95	9.67		352	3.87	377	3.38	438	3.72
9	2-Thienyl	H	$C_{13}H_8N_2OS_2$	C, 57.3	57.1	53	251	4.31				
				H, 2.94	2.78		277	4.13	334	3.84	325	3.63
				N, 10.2	10.1		368	3.61	387	3.61	453	3.57
10	2-Naphthyl	H	$C_{19}H_{12}N_2OS$	C, 72.1	71.8	35	254	3.84				
				H, 3.78	3.52		279	4.12	339	3.51	322	3.31
				N, 8.86	8.75		372	3.71	383	3.47	451	3.57

Note: Compounds No. **1**, **2**, **4**, **5** are reported.[14]

Table 2. 9-Ethyl-6-hydroxythiazolo[3,2-*a*]benzimidazolium bromides (II)

Compd No.	R	R_1	Molecular formula	Mp °C	Yield %	Analysis (%)		UV, Ethanol	
						Calcd	Found	λ_{max} nm	log ε
1	C_6H_5	H	$C_{17}H_{15}N_2OSBr$	310	40	N, 7.43	7.41	260	3.84
						Br, 21.3	21.2	510	4.00
2	CH_3	H	$C_{12}H_{13}N_2OSBr$	299	35	N, 8.94	8.89	265	3.65
						Br, 25.5	25.4	525	3.90
3	CH_3	$COOC_2H_5$	$C_{15}H_{17}N_2O_3SBr$	317	25	N, 7.27	7.16	257	3.45
						Br, 20.7	20.5	515	3.85
4	H	CH_3	$C_{12}H_{13}N_2OSBr$	285	25	N, 8.94	8.92	253	3.50
						Br, 25.5	25.3	530	3.64
5	CH_3	C_6H_5	$C_{18}H_{17}N_2OSBr$	360	30	N, 6.88	6.86	250	3.50
						Br, 19.5	19.3	512	3.81
6	*p*-$CH_3C_6H_4$	H	$C_{18}H_{17}N_2OSBr$	293	40	N, 6.88	6.85	264	3.72
						Br, 19.5	19.4	526	3.94
7	*p*-BrC_6H_4	H	$C_{17}H_{14}N_2OSBr_2$	288	37	N, 7.48	7.37	260	3.40
						Br, 21.3	21.0	512	3.81
8	*p*-HOC_6H_4	H	$C_{17}H_{15}N_2O_2SBr$	280	41	N, 7.17	7.09	255	3.38
						Br, 20.5	20.1	508	3.63
9	2-Thienyl	H	$C_{15}H_{13}N_2OS_2Br$	326	51	N, 7.34	7.31	271	3.71
						Br, 20.9	20.6	535	3.56
10	2-Naphthyl	H	$C_{21}H_{17}N_2OSBr$	304	45	N, 6.58	6.37	276	3.51
						Br, 18.5	18.3	519	3.87

ring breathing).

A study of the absorption spectra of various substituted 6-hydroxythiazolo[3,2-*a*]benzimidazoles in ethanol at different pH shows a bathochromic shifting of the absorption maxima in both acidic and alkaline media. The observed bathochromic shift might be explained by the canonical quinonoid structure shown in Scheme 1. Same phenomenon is observed when these compounds are quaternized with ethyl bromide which results into further red shifting of absorption maxima in visible region.

For the sake of comparison of the absorption spectra of these title compounds (I), 8-hydroxypyrido[1,2-*a*]-benzimidazole was synthesized by the method described by Schmid and Czerney.[13] A study of its absorption spectra in ethanol under various conditions (Table 3) also shows a red shifting of absorption band in the longer wavelengths in alkaline medium whereas in acid medium the spectra remain practically unaltered.

Table 3. Absorption spectra of 8-hydroxypyrido[1,2-*a*]benzimidazole

S. No.	Compound	λ_{max}/nm (log ε)			
1	Parent base in ethanol	—	360 (3.78)	300 (3.76)	248 (4.5)
2	Parent base in alkaline ethanol	405 (3.87)	—	268—270 (4.49)	242 (4.36)
3	Parent base in acidic ethanol	—	358 (3.94)	292 (3.71)	238 (4.17)

It has been observed by Edger *et al.*[18] that the 5- or 6-chlorobenzimidazoles do not show any shifting of absorption maxima in ethanolic solution of different pH. It indicates that the presence of 6-hydroxyl group in these title compounds which being more acidic causes the molecule to attain greater dipolar character at different pH thereby facilitating absorption in the longer wavelengths.

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