# Heterocylic Studies. Synthesis of 9-Hydroxybenzimidazo[2,1-*b*]-benzothiazoles and Their Quaternary Derivatives

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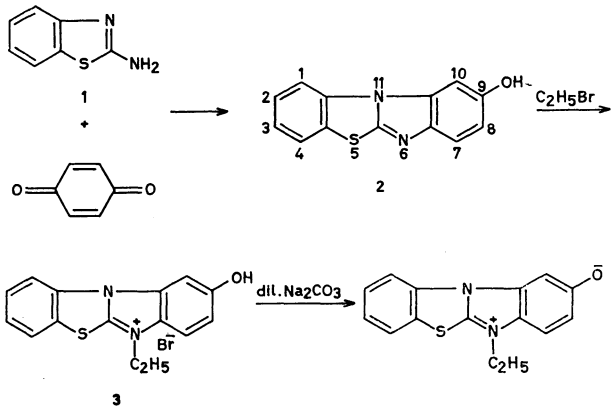
**Synopsis.** A series of substituted 9-hydroxybenzimidazo[2,1-*b*]benzothiazoles has been synthesized. The position of phenolic hydroxyl group in these compounds has been ascertained on the basis of spectral data.

Benzimidazole derivatives exhibit pronounced antiviral activity.[1] Thiabendazole[2-(4-thiazolyl)benzimidazole] is well known for its use as the leading anthelmintic for the control of most gastrointestinal nematodes of man, with exception of Trichuris species.[2-4] It was therefore worthwhile to synthesize some new compounds containing benzimidazole moiety and study their mode of formation through spectral data.

Recently we have reported the synthesis of 6-hydroxy [1,3,4]thiadiazolo[2,3-*b*]benzimidazoles.[5] In this paper we report the synthesis of some new 9-hydroxybenzimidazo[2,1-*b*]benzothiazoles (**2**), obtained by the reaction of 2-aminobenzothiazoles (**1**) with *p*-benzoquinone.




Quaternization of **2** with ethyl bromide yields 6-ethyl-9-hydroxybenzimidazo[2,1-*b*]benzothiazolium bromide (**3**), as evidenced by the work of Paudler and Blewitt for the site of protonation and *N*-methylation of imidazo-[1,2-*a*]pyridines.[6] Compound **3** gave intense yellow color with dil alkali due to the formation of the phenol betaines.[7,8]

## 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 on a Beckman spectrophotometer, Model DU-2.

*6-Hydroxybenzimidazo[2,1-*b*]benzothiazoles (2).* A solution of *p*-benzoquinone (0.01 mol) in glacial acetic acid (10 ml) was added in small portions to the substituted 2-aminobenzothiazoles (0.01 mol) in glacial acetic acid (10 ml) with constant shaking. The mixture was refluxed for 2 h and left aside for 5—7 d. To the reaction mixture 20 ml of 50% HCl was added and the solution was diluted with water, and then extracted with ether to remove any unreacted quinone and hydroquinone. The resulting solution was just neutralized with aq sodium carbonate. A crude solid product was obtained. It was filtered, washed well with water, and then recrystallized from an appropriate solvent after decolorizing with charcoal in ethanol till it gave a single spot on TLC with aq ethanol.

*6-Ethyl-9-hydroxybenzimidazo[2,1-b]benzothiazolium Bromides (3).* A mixture of **2** (0.01 mol) and ethyl bromide (0.01 mol) was taken in minimum quantity of acetone. The reaction mixture was boiled under reflux on a water bath for 1 to 2.5 h. The solvent was evaporated to dryness under reduced pressure. The residue was recrystallized from ethanol–ether mixture.

Table 1. 9-Hydroxybenzimidazo[2,1-*b*]benzothiazoles (**2**)

| Starting thiazole | Molecular formula | Mp $\theta_m$/°C | Yield % | Calcd (%) | Found (%) | UV Spectra: Ethanol $\lambda_{max}$/nm | log ε | 0.1 M HCl $\lambda_{max}$/nm | log ε | 0.1 M NaOH $\lambda_{max}$/nm | log ε |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2-Amino-benzothiazole[9] | $C_{13}H_8N_2OS$ | 321—322 | 53 | C, 65.0 | 64.7 | 245 | 3.60 | | | | |
| | | | | H, 3.3 | 3.1 | 271 | 3.97 | 326 | 3.71 | 315 | 3.51 |
| | | | | N, 11.6 | 11.5 | 341 | 3.86 | 374 | 3.81 | 442 | 3.43 |
| 2-Amino-6-methoxy benzothiazole[10] | $C_{14}H_{10}N_2O_2S$ | 307 | 45 | C, 66.1 | 65.9 | 248 | 3.61 | | | | |
| | | | | H, 3.9 | 3.6 | 279 | 4.00 | 330 | 3.67 | 322 | 3.59 |
| | | | | N, 11.0 | 10.8 | 348 | 3.82 | 273 | 3.91 | 451 | 3.47 |
| 2-Amino-5,5-dimethyl-4,5,6,7-tetrahydro-benzothiazol-7-one[11] | $C_{15}H_{14}N_2O_2S$ | 345 (decomp) | 35 | C, 62.8 | 62.6 | 250 | 3.86 | | | | |
| | | | | H, 4.9 | 4.7 | 292 | 4.05 | 335 | 3.57 | 325 | 3.47 |
| | | | | N, 9.7 | 9.6 | 364 | 3.74 | 391 | 3.81 | 483 | 3.34 |
| 2-Amino-4,5,6,7-tetra-hydrobenzothiazole[12] | $C_{13}H_{12}N_2OS$ | 297 | 33 | C, 63.1 | 62.9 | 257 | 3.51 | | | | |
| | | | | H, 4.9 | 4.6 | 305 | 4.15 | 321 | 3.41 | 315 | 3.61 |
| | | | | N, 11.0 | 10.7 | 357 | 4.07 | 401 | 3.76 | 476 | 3.54 |
| 2-Amino-6-methyl-4,5,6,7-tetrahydro-benzothiazole | $C_{14}H_{14}N_2OS$ | 314 | 38 | C, 65.1 | 64.8 | 254 | 3.67 | | | | |
| | | | | H, 5.4 | 5.3 | 301 | 4.09 | 318 | 3.56 | 310 | 3.57 |
| | | | | N, 10.8 | 10.5 | 352 | 4.10 | 397 | 3.82 | 471 | 3.42 |

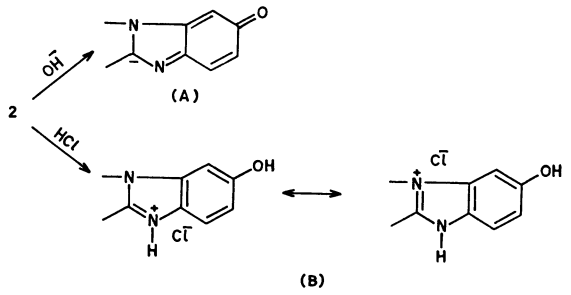
TABLE 2. 6-ETHYL-9-HYDROXYBENZIMIDAZO[2,1-*b*]-BENZOTHIAZOLIUM BROMIDE (**3**)

| Molecular formula | Mp $\theta_m$/°C | Yield % | Calcd (%) | Found (%) | UV Spectra Ethanol $\lambda_{max}$/nm | log ε |
|---|---|---|---|---|---|---|
| $C_{15}H_{13}N_2OSBr$ | 274 | 41 | N, 8.0<br>Br, 22.9 | 7.9<br>22.6 | 260<br>507 | 3.41<br>3.66 |
| $C_{16}H_{15}N_2O_2SBr$ | 287 | 37 | N, 7.7<br>Br, 22.0 | 7.4<br>21.7 | 263<br>512 | 3.81<br>3.75 |
| $C_{17}H_{19}N_2O_2SBr$ | 337 | 25 | N, 7.2<br>Br, 21.4 | 6.9<br>21.2 | 268<br>517 | 3.34<br>3.75 |
| $C_{15}H_{17}N_2OSBr$ | 256 | 38 | N, 7.9<br>Br, 22.6 | 7.7<br>22.5 | 275<br>542 | 3.64<br>3.51 |
| $C_{16}H_{19}N_2OSBr$ | 304 | 42 | N, 7.6<br>Br, 21.7 | 7.3<br>21.4 | 272<br>548 | 3.91<br>3.72 |

## Discussion

The structure of compounds **2** has been determined on the basis of IR, UV spectra, and elemental analysis. The IR spectra of these compounds showed bands at 3340, 1210 (phenolic OH), 1625 (C=N), 1315 (C–N), and 1450 $cm^{-1}$ (aromatic ring). Electronic absorption spectra of **2** have been studied which have a bearing on their finer structure, particularly with regards to the position of phenolic hydroxyl group which could be either on 9th or 8th carbon atom.

Compounds **2** show the characteristic bathochromic shifting of the absorption maximum in the longer wavelengths in both acid and alkaline medium.

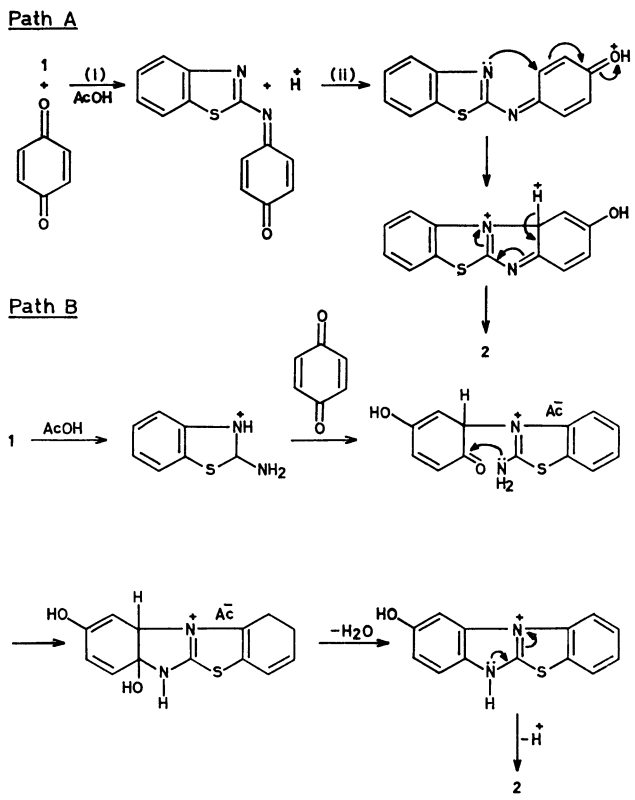



In alkaline medium this red shift of about 100 nm is more pronounced and is ascribed to the quinonoid structure (A) as one of the contributing form to the total structure. In acid medium (about 40 nm) it should be due to the salt formation (B).

The quaternary compounds **3** show a further red shifting of absorption maxima in the visible region ($\lambda_{max}$>500 nm) (Table 2). This may be attributed to salt formation and contribution of the dipolar betaine structure in ethanol.

The formation of **2** can be explained by the following mechanisms.

Whichever of the two mechanisms cited here may be taking place, the position of phenolic hydroxyl group remains ascertained as meta to the bridgehead nitrogen atom and para to second imidazole nitrogen, through either of these routes.

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