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SYNTHESIS OF 2-(*o*-HYDROXYPHENYL)BENZOTHIAZOLE AND OF 2-(*o*-HYDROXYPHENYL)BENZOTHIAZOLINE[1]

ROBERT G. CHARLES and HENRY FREISER

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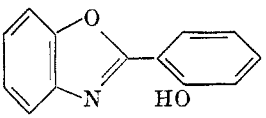
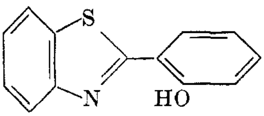
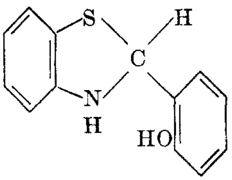
In the course of an investigation of the structure and behavior of organic chelating agents analogous to 8-hydroxyquinoline, it was decided to study the behavior of 2-(*o*-hydroxyphenyl)benzoxazole (I) and its sulfur analog, 2-(*o*-hydroxyphenyl)benzothiazole (II) (1). This latter compound is described several places in the literature (2, 3) as being the product of the condensation of salicylaldehyde and *o*-aminobenzenethiol. Our attempts to prepare II in this manner resulted in a product which was found to react with metals in a strikingly different manner than did the benzoxazole, I. This suggested to us the possibility that we had prepared 2-(*o*-hydroxyphenyl)benzothiazoline (III).



I. 2-(*o*-Hydroxyphenyl) benzoxazole



II. 2-(*o*-Hydroxyphenyl) benzothiazole



III. 2-(*o*-Hydroxyphenyl) benzothiazoline

The formation of the benzothiazoline was suggested by Claaz (4) but was disputed by later workers (3). The fact that III is actually formed in the condensation of *o*-aminobenzenethiol and salicylaldehyde receives support from the work of Lankelma (5) who prepared a number of thiazolines and showed that they could be oxidized to the corresponding thiazoles. While the compounds of interest in the present study were not included in Lankelma's work, they are quite similar to those he prepared [2-phenyl-5-chlorobenzothiazoline, 2 (*o*-chlorophenyl)benzothiazoline, and their corresponding thiazoles].

In view of these facts, it is apparent that it was necessary to establish whether the compound obtained from *o*-aminobenzenethiol and salicylaldehyde was II or III. To accomplish this, the synthesis of II was attempted by an independent method; that is, by the condensation of *o*-aminobenzenethiol and salicylamide in a manner analogous to the method used to synthesize I. The compound obtained by this reaction had nearly the same appearance and melting point as the reaction product when salicylaldehyde was used, but which was shown to be different from the following considerations: (a) a mixture melting point of the two compounds exhibited a depression, (b) the reactions of the two compounds with metal ions were entirely different, the supposed

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benzothiazoline reacting with many more metals than the benzothiazole whose reactions with metals greatly resembled those of the analogous benzoxazole (I), (c) the ultraviolet absorption spectra of the two substances were entirely different (see Figure 1), (d) the analytical results for C, H, and N were in accord with their supposed structures.

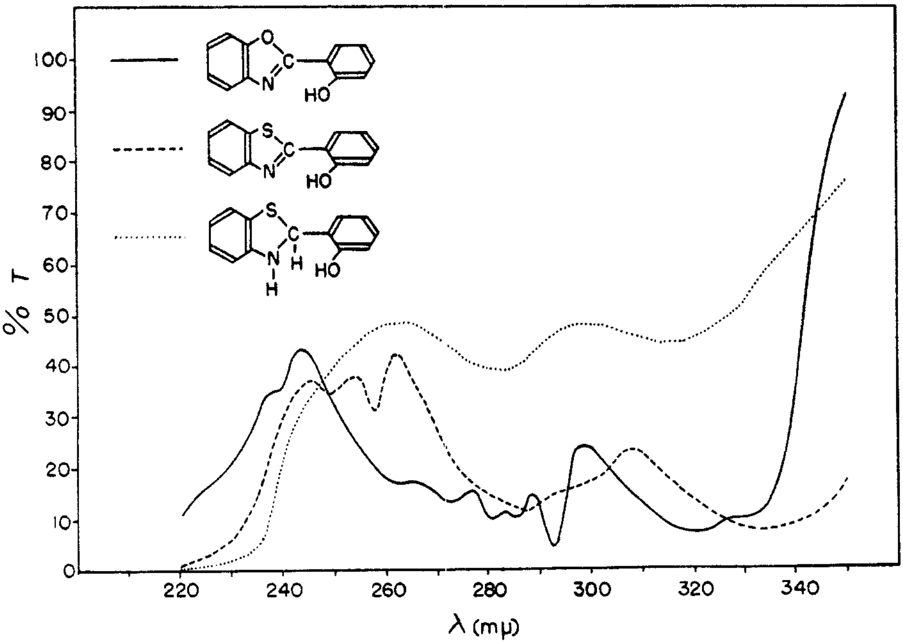
By analogy with the synthesis of the benzoxazole (I), there can be little doubt that the condensation product of *o*-aminobenzenethiol and salicylamide is the benzothiazole (II). This is strengthened by the fact that water and ammonia were given off during the reaction as would be expected from the equation,

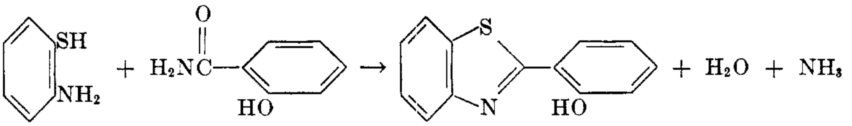
FIGURE 1

ULTRAVIOLET ABSORPTION SPECTRA IN 95% ALCOHOL.

Beckman Spectrophotometer; 1 cm. quartz cells; 1 mμ band width.

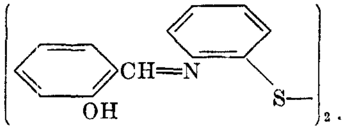
Concentration in all cases—6.67 x 10⁻⁵ M.



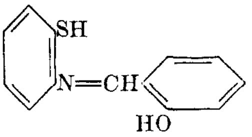


and also by the fact that there is considerable similarity between the ultraviolet spectra of I and that of the supposed benzothiazole.

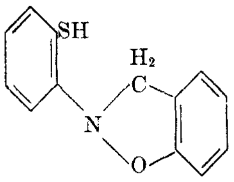
That the compounds III and II are the only two likely possibilities for the reaction products is indicated by the fact that the molecular weights for the products were found to be within experimental error of those calculated for II and III, thus eliminating such possibilities as the disulfide



A further indication that II and III are the only possibilities is given by the fact that only one acid dissociation constant was found for each in the pH region characteristic of phenols rather than of thiophenols. This eliminates such possibilities as:



or



Also, it should be mentioned that no infrared absorption band which could be assigned to an —SH group could be found in the spectrum of the product of either the salicylaldehyde or the salicylamide condensations.

The infrared absorption spectra of the assumed benzothiazoline further substantiated proof of structure by the occurrence of a sharp absorption band at 3.12 μ which was completely absent in the spectrum of the compound prepared from salicylamide. This absorption band falls in the range assigned to N—H vibrations (6).

EXPERIMENTAL

2-(o-Hydroxyphenyl)benzothiazoline. A somewhat simpler method than that described in the literature (4) was used. *o*-Aminobenzenethiol (12.5 g., 0.1 mole) was mixed in an Erlenmeyer flask with 12.2 g. (0.1 mole) of salicylaldehyde. After a few minutes at room temperature the mixture evolved heat, became cloudy, and slowly solidified. After the reaction was complete, the mixture was recrystallized several times from alcohol-water mixtures and dried *in vacuo*. The purified substance consisted of yellowish needles with a faint characteristic odor. The yield of the unpurified compound was nearly quantitative. However, there were considerable losses on recrystallization. The melting point depended somewhat on the rate of heating, since melting was accompanied by some decomposition. M.p. (with preheating to 130°), 136–137° (corr.). The compound was analyzed for C, H, and N by the Microorganic Analytical Laboratory at the University of Pittsburgh.

Anal. Calc'd for $C_{13}H_{11}NOS$: N, 6.11; C, 68.09; H, 4.84.
Found: N, 6.50; C, 68.15; H, 4.72.

The Rast method for determining molecular weights (7) was found unsatisfactory for this compound, due to decomposition. The molecular weight was determined cryoscopically by determining the freezing point of dilute solutions in 1,4-dioxane, using the cryoscopic constant of 4.9, listed by Reilly and Rae (8). Data: 0.2554 g. substance; 25.72 g. solvent; $\Delta t = 0.22°$; M. W.: calc'd 229, found 221. Acid dissociation constant determined potentiometrically in 50 v/v% dioxane-water at 25° = 6.0×10^{-11}.

2-(o-Hydroxyphenyl)benzothiazole. *o*-Aminobenzenethiol (25 g., 0.2 mole) was mixed with 27.4 g. (0.2 mole) of salicylamide in a round-bottom flask and heated on an oil-bath.

At about 220°, evolution of ammonia and water began. The bath temperature was maintained at 240–250° for five hours. The reaction product was vacuum-distilled. The fraction boiling below 175° at 3 mm. was discarded. The product distilled in the range 175–193° (mainly at 190–193°) at 3 mm. and solidified in the receiving flask as a light yellow solid. The yield of distilled solid was 32.5 g. (72%). The product was further purified by recrystallizing several times from alcohol-water mixtures and was dried *in vacuo.* M.p. 132–133° (corr.). Mixture melting point with 2-(*o*-hydroxyphenyl)benzothiazoline 120–130° (corr.).

Anal. Calc'd for $C_{13}H_9NOS$: C, 68.70; H, 3.99.

Found: C, 69.06; H, 3.90.

Molecular weight (cryoscopically in dioxane): wt. of substance 0.5005 g.; wt. of solvent 25.61 g.; $\Delta t = 0.43°$; M. W. calc'd 227; M. W. found 223. The recrystallized substance consists of slightly yellowish, nearly colorless, needles which are nearly odorless. Acid dissociation constant determined potentiometrically in 50 v/v% dioxane-water at 25° = 4.3×10^{-11}.

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PITTSBURGH 13, PENNA.

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