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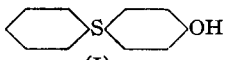
THE PREPARATION AND BACTERIOLOGICAL STUDY OF CERTAIN THIAZOLE AZO DYES.*

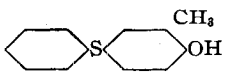
BY W. A. LOTT AND W. G. CHRISTIANSEN.

In view of the recent demonstrations of the germicidal activity of divalent sulphur compounds such as *p*-hydroxy diphenyl sulphide, I,



(I)

prepared by Hilbert and Johnson (1), and 3-methyl 4-hydroxy diphenyl sulphide, II, and 3-ethyl 4-hydroxy diphenyl sulphide, III,



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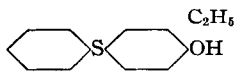
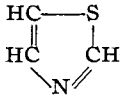


(III)

prepared by E. Moness, W. Braker and W. G. Christiansen (2), it seemed possible that divalent ring sulphur, as it appears in, for example, the thiazole heterocyclic ring  might also carry bactericidal activity. The most readily available

starting material of this type was the easily synthesized amino thiazole, IV,

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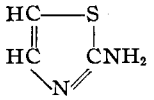
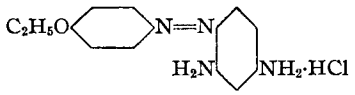
* Scientific Section, A. PH. A., Madison meeting, 1933.



(IV)

Inasmuch as some azo dyes such as 4-ethoxy 2′,4′-diamino azobenzene monohydrochloride, V (Serenium), are bactericidal, it was thought that



(V)

compounds containing both the ring divalent sulphur and the azo groupings might be useful bactericides. Some compounds of this type have been prepared by diazotizing amino thiazole and coupling with phenolic substances.

PREPARATION OF AMINO THIAZOLE.

The amino thiazole was prepared by the method of V. Trauman (3) in which 53 Gm. of thiourea in 250 cc. water was condensed with 100 Gm. α,β-dichlorethyl ether. After the two liquid layers merged, refluxing was continued 10 minutes, after which the reaction mixture was evaporated until the characteristic odor of the α,β-dichlorethyl ether had disappeared. After making the solution strongly alkaline it was extracted repeatedly with ether.

The combined residue from these ether extracts was recrystallized out of alcohol, and a yield of 30 Gm. of red crystalline amino thiazole of melting point 88.5° to 90.5° C. was obtained.

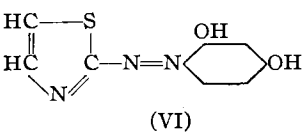
Analysis: Found—S, 31.94%. Calculated for $C_3H_4N_2S$: S, 32.00%.

PREPARATION OF THIAZOLE AZO RESORCINOL.

The diazotization of amino thiazole was very slow and incomplete by the usual method, but when all of the sodium nitrite is added at one time to the acidified solution of the amino thiazole, thereby obtaining a high concentration of nitrous acid, an acceptable yield of the diazonium salt is obtained.

5 Gm. of amino thiazole (0.5 mol.) was dissolved in 13 cc. of hydrochloric acid (1.5 mol.) and 125 cc. water. This was diazotized at 0–5° C. by adding 3.5 Gm. of $NaNO_2$ as fast as possible without allowing the temperature to rise above 5° C., using efficient agitation and an external cooling bath of ice and salt. Thereupon, 5.5 Gm. resorcinol in 10 cc. of cold water was added. The precipitated azo dye was agitated without cooling for an hour in order to induce its change from a gelatinous material to a granular one.

4.5 Gm. of crude material having a low sulphur content was obtained. Repeated reprecipitation out of alkaline solution by dilute HCl gave about 1.5 Gm. of material which was shown by analysis to be thiazole azo resorcinol, VI,



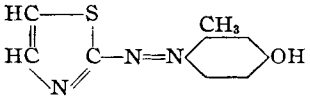
(VI)

Analysis: Found—S, 14.99%. Calculated for $C_9H_7O_2N_3S$: S, 14.47%.

Bacteriological test showed that although this substance (when dissolved in aqueous alkali) had no germicidal activity, it inhibited growth of both Typhoid and Staphylococcus at a dilution of 1 to 8000.

PREPARATION OF THIAZOLE AZO-*m*-CRESOL.

5 Gm. of amino thiazole was dissolved in 100 cc. 20% H_2SO_4 and diazotized at 0–5° C. with 3.5 Gm. $NaNO_2$, the latter being added as in the above preparation. When the excess of HNO_2 was very low, as indicated by starch iodide papers, 5.4 Gm. meta-cresol in 10 cc. water at 0° C. and enough 10% NaOH to keep it in solution were added. After agitating two hours at room temperature, the precipitated dye became granular. This was filtered and reprecipitated several times out of alkaline solution by dilute HCl. A yield of 5.8 Gm. of thiazole azo *m*-cresol, VII, was obtained.

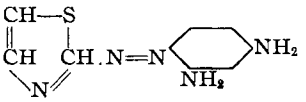


(VII)

Analysis: Found—S, 13.33%. Calculated for $C_{10}H_7ON_3S$: S, 14.60%.

Although this material showed no germicidal action it inhibited the growth of Typhoid and Staphylococcus at dilutions up to 1 to 16,000. The dye was dissolved in water with a minimum quantity of sodium hydroxide for germicidal test.

By coupling diazotized amino thiazole with metaphenylene diamine a dye was obtained which probably had the following structure:



This product was not obtained in a sufficiently pure form to warrant biological tests.

The biological tests on compounds reported herein were made in the Biological Research Laboratories of E. R. Squibb & Sons and we gratefully acknowledge their assistance.

SUMMARY.

Thiazole azo resorcinol and thiazole azo *m*-cresol were prepared by the diazotization of amino thiazole with subsequent coupling of the diazonium salt with the respective phenols. Although solutions of these two azo dyes failed to kill, they restrained the growth of Typhoid and Staphylococcus in dilutions of 1 to 8000 and 1 to 16,000, respectively.

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