[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND BIOLOGY OF THE STATE UNIVERSITY OF MONTANA]

THE ANTISEPTIC ACTION OF THE ZINC CHLORIDE SALT OF ANILINE[1]

BY J. W. HOWARD AND F. D. STIMPERT

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Introduction

In connection with the investigation of the use of zinc chloride as a condensing agent in the preparation of anilides our attention was called to the fact that the chemical and physical data in the literature[2] concerning a possible side product of the reaction, namely the double salt of aniline with zinc chloride [$(C_6H_5NH_2)_2\ ZnCl_2$], were very meager.

This salt further interested us in that it offered an opportunity to compare the bactericidal action of a compound with its constituent compounds.

The medicinal use of zinc chloride is generally that of an antiseptic or disinfectant, being applied either as a solid or in solution.

While aniline has not been used for these purposes, the fact that it is a compound of known toxicity suggested that a study of its bactericidal action might be of value as well as a comparison of this action with that of zinc chloride and with its double salt with zinc chloride.

In order to make the data concerning the salt of aniline with zinc chloride more complete as well as to make the bactericidal comparisons mentioned the following study has been carried out.

Experimental Part

Zinc Chloride.—Fused, U. S. P. sticks of commercial quality were used in making the solution.

Aniline.—The usual constant-boiling fraction of freshly distilled aniline was used.

Zinc Chloride Salt of Aniline.—Ten g. of aniline was thoroughly mixed with 7.5 g. of finely ground, fused zinc chloride. This mixture was allowed to stand for one hour after the heat of the reaction had subsided. The reaction product was extracted with boiling 95% alcohol, from which the salt readily crystallized on cooling; yield, 11 g.

The needles soften slightly at 230° and melt at 255°. The salt is soluble to the extent of 0.64 g. in 100 cc. of water at 20°; 0.87 g. in 100 cc. of 0.4% hydrochloric acid at 20°; 0.066 g. in 100 cc. of 95% alcohol at 20°. It is also only very slightly soluble in carbon disulfide, chloroform, benzene or ethyl ether. It is somewhat more soluble in methyl alcohol or acetone. It is slowly decomposed by 3 *N* sodium carbonate solution, readily by 1 *N*

[1] Presented before the Division of Chemistry of Medicinal Products at the 66th meeting of the American Chemical Society, Milwaukee, Sept. 10–14, 1923.

[2] Schiff, *Jahresber.*, **1863**, 413. Lachowicz and Bandrowski, *Monatsh.*, **9**, 512 (1888). Tombeck, *Compt. rend.*, **124**, 961–3 (1897). Base, *Am. Chem. J.*, **20**, 646 (1898). Hodges, *Chem. News*, **103**, 52 (1911). Reddelien, *Ann.*, **388**, 165 (1912).

sodium hydroxide or boiling water. The water solution becomes slightly cloudy on standing for several days at room temperature.

Calc. for $C_{12}H_{14}N_2ZnCl_2$: N, 8.71. Found: 8.72, 8.75.

Bactericidal Studies.—For this purpose a 6% solution of zinc chloride, a 3% solution of aniline and a 0.6% solution of the zinc chloride salt of aniline were used. The latter two solutions were made in these concentrations because of their limited solubilities in water. The zinc chloride solution was made stronger than the others, as preliminary experiments indicated that this was necessary for comparative purposes.

These solutions were so diluted as to make a total of 5 cc. in each case. To each of these portions of 5 cc. was added 0.1 cc. of a 24-hour broth culture of *staphylococcus aureus* that had been transplanted on 2 successive days. At 5-minute intervals a 5mm. loop was transplanted from these solutions in 10 cc. of broth and incubated for 48 hours. An examination was made of the broth for positive and negative cultures by cloudiness. These results were then checked by plating 1 cc. of the 48-hour broth culture and incubating for 48 hours. These results were further checked by direct plating from the bacteria suspensions in the original solutions and incubating.

TABLE I

RESULTS

Dilutions Cc. soln.	Cc. water	Time in minutes 5	10	15	20	
6% Zinc chloride solution						
5	...	−	−	−	−	
4	+1	+	+	+	−	
2.5	+2.5	+	+	+	+	(few)
2	+3	+	+	+	+	(few)
0.5	+4.5	+	+	+	+	
3% Aniline solution						
5	...	−	−	−	−	
4	+1	+	−	−	−	
3	+2	+	+	−	−	
2	+3	+	+	+	−	
1	+4	+	+	+	+	

This would indicate that aniline has about four times the disinfectant power of zinc chloride in solution.

TABLE II

0.6% Solution of zinc chloride salt of aniline
5 cc. of solution

Time in minutes	5	10	15	20	25	30	35
Results.....	+ (strong)	+ (strong)	+ (mod.)	+ (few)	+ (few)	−	−

As this table indicates, there would be no object in diluting this solution further. The colony counts here indicated a gradual but marked decrease

with increase in time. The 15- and 20-minute plates on comparison with the aniline and zinc chloride plates of the same times and dilution show clearly a stronger antiseptic action. Predicting from the curve obtained from the aniline solution, in order to compare on a time basis with the salt solution, the results would seem to indicate that the salt has about 1.3 times the disinfecting power of aniline and about 5 times that of zinc chloride.

When the salt solution was allowed to stand for a week at room temperature, it became somewhat cloudy and lost the power to kill the bacteria in even the 30- or 35-minute periods.

Summary

1. The double salt of aniline with zinc chloride has been prepared and physical and chemical data have been added to those already existing.

2. Its bactericidal action has been found to be greater than that of either aniline or zinc chloride.

MISSOULA, MONTANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

STUDIES ON REACTIONS RELATING TO CARBOHYDRATES AND POLYSACCHARIDES.[1] V. THE USE OF ACETYLENE FOR THE SYNTHESIS OF CYCLIC ACETALS

BY HAROLD S. HILL[2] AND HAROLD HIBBERT

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In a previous communication[3] the authors have pointed out the structural relationship existing between cyclic acetals and polysaccharides, that is, that the carbonyl-hydroxyl condensation reaction involved in cyclic acetal formation is without doubt duplicated, either inter- or intramolecularly, or both, when simple sugars condense to form di-, tri-, or polysaccharides. In view of this relationship the belief was expressed that a thorough investigation of the simpler cyclic derivatives would afford a promising means of attack for the problem of the nature of the complex molecules of starch, inulin, cellulose, etc. It is in the course of this work that a new and improved method for the synthesis of cyclic acetals has been developed.

Earlier investigators have prepared cyclic acetals from acetaldehyde and ethylene glycol,[4] trimethylene glycol,[4b] 1,2-propylene glycol,[5] glycerol,[6]

[1] The title has been altered so as to be more in accord with present, and proposed future investigations (Hibbert).

[2] Antoine Chiris Co. Research Fellow.

[3] Hibbert and Hill, THIS JOURNAL, **45**, 734 (1923).

[4] (a) Würtz, *Compt. rend.*, **53**, 378 (1861); *Ann.*, **120**, 328 (1861); (b) Lochert, *Ann. chim. phys.*, [6] **16**, 26 (1889). (c) Clark, *J. Chem. Soc.*, **101**, 1803 (1912).

[5] Gramont, *Compt. rend.*, **97**, 173 (1883); *Bull. soc. chim.*, **41**, 361 (1884).

[6] Harnitzky and Menschutkin, *Ann.*, **136**, 126 (1865).