

found to kill 1 cc. of a 24-hour culture of *B. Typhosus* and also of *staphylococcus aureus* within two minutes. Five cc. of a 1:10 dilution killed 0.1 cc. of a 24-hour culture of *B. Typhosus* within two minutes.

This solution was found to possess solvent properties similar to Dakin's solution.

This solution has also been found to be excellent for sterilizing maggot eggs used for the production of larvæ for cleaning wounds.

It is superior to the bichloride of mercury solution hitherto employed for this purpose in that, when the iodine solution is used, fewer eggs are killed and complete sterility is obtained.

In presenting the formulas for those two new non-proprietary solutions of iodine to the medical and pharmaceutical professions, it is believed that a contribution has been made which will be appreciated from the combined standpoint of economy and efficiency.

CONTRIBUTED BY THE IODINE SCHOLARSHIP OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE UNDER THE DIRECTION OF THE IODINE FELLOWSHIP OF THE MELLON INSTITUTE.

NITROSYL CHLORIDE WITH ALCOHOLS AND ALDEHYDES.

BY FRANK A. LEE AND E. V. LYNN.

As has been demonstrated (1, 2, 3), aliphatic hydrocarbons react with nitrosyl chloride to form isonitroso compounds. It has also been shown (4) that alkyl ketones undergo similar change and, at the same time, some of them (5) are chlorinated. Similarly, it has been found that certain alcohols (6) are readily converted to the corresponding nitrites. In view of the generic relationship, it seemed of interest to determine the effect upon aldehydes.

In 1903, Bouveault and Wahl (6) showed that nitrosyl chloride will react with certain alcohols in the presence of pyridine to form nitrites. All these alcohols were of fairly high molecular weight, the simplest one being isoamyl alcohol. We have now applied this reaction to other compounds with similar results and find that pyridine is not necessary with those of low molecular weight. It is notable also that this reaction apparently does not take place with glycerin, menthol and benzyl alcohol.

The aldehydes evidently react in a manner analogous to that of isonitroso-ketones (5), giving rise to chlorides of the corresponding acids. Benzaldehyde gave benzoyl chloride and benzoic acid; acetaldehyde probably behaves in a similar way to a smaller extent. This ability of nitrosyl chloride to chlorinate is in conformity with previous experiments on ketones (5).

EXPERIMENTAL.

The nitrosyl chloride which was employed was made according to the method as previously described (4).

Ethyl Nitrite.—Absolute ethyl alcohol was placed in a vessel surrounded by a freezing mixture of ice and salt and the gas was run in to the point of saturation, as judged by the appearance of a deep reddish brown color. The product was poured into ice water, and a considerable effervescence and separation of yellow liquid followed. This yellow liquid was removed, washed with a cold solution of sodium

carbonate, and dried over anhydrous potassium carbonate. Distillation of this product gave an amount boiling below 18° C. equivalent to 70 per cent of the theoretical. Analysis by the gasometric method of the United States Pharmacopœia showed a purity of 97 per cent.

0.179 Gm. gave 56 cc. NO at 22° C. and 760 mm.

0.130 Gm. gave 41 cc. NO at 21° C. and 760 mm.

Percentage of NO found: 38.8 and 39.2; calculated: 40.0.

Because of the rapidity of the formation of the ethyl nitrite, the possibility of the production of sweet spirit of nitre by this method was considered. Should nitrosyl chloride be passed into an excess of ethyl alcohol, the ethyl nitrite formed would be in solution in alcohol. Hydrochloric acid is a by-product of the reaction. Subsequent neutralization of the acid, followed by an assay to determine the nitrite content of the product, and dilution to the required strength with alcohol is the procedure that should be carried out.

The work described under the preparation of ethyl nitrite was repeated, using isopropyl, normal butyl and tertiary butyl alcohols. The corresponding nitrites were obtained in each case. It should be made clear, however, that pyridine, equal in quantity to the alcohol used, should be present when nitrites are made from tertiary alcohols. It appears that unless this is done, satisfactory products cannot be obtained. As the molecular weight of the alkyl group increases, it was found that more satisfactory yields are obtained when pyridine is used.

Nitrite of Methyl Diethyl Carbinol.—The alcohol, which was made by means of the Grignard reaction, was saturated with nitrosyl chloride in the presence of an equal quantity of pyridine, the whole being kept at about -10° C. by means of a freezing mixture. The product was added to cold water and the yellow oil which separated was dried, treated with more pyridine, and then resaturated with the gas. After repeating the process once more, the oil was submitted to distillation under reduced pressure. The product is a pale yellow liquid with very little odor. It decomposes if boiled under atmospheric pressure but distills unchanged at 24° C. under 10 mm. From 40 Gm. of the alcohol there were obtained 32 Gm. of nitrite, a yield of 62 per cent.

0.191 Gm. gave 35.0 cc. NO at 20° C. and 740 mm.

0.180 Gm. gave 33.0 cc. NO at 18° C. and 736 mm.

Percentage of NO found: 22.2 and 22.3; calculated: 22.9.

Nitrite of Triethyl Carbinol.—The alcohol was made by the Grignard method and saturated with nitrosyl chloride in the presence of pyridine as before. The product was a yellowish liquid with slight nitrite-like odor, boiling at 36° C. under 10-mm. pressure. Like the previous compound, it decomposes when boiled under atmospheric pressure. The yield was 55 per cent of theoretical.

0.138 Gm. gave 22.2 cc. NO at 18° C. and 746 mm.

0.190 Gm. gave 30.6 cc. NO at 19° C. and 746 mm.

Percentage of NO found: 19.8 and 19.7; calculated: 20.7.

Nitrite of Diethyl Propyl Carbinol.—The alcohol was prepared as were the foregoing ones. The reaction with nitrosyl chloride and pyridine gave 61 per cent of a yellowish liquid with slight odor of nitrites, boiling at 48° C. under 10-mm. pressure, and decomposing when boiled under atmospheric pressure.

0.168 Gm. gave 24.5 cc. NO at 17° C. and 744 mm.

0.151 Gm. gave 22.3 cc. NO at 15° C. and 732 mm.

Percentage of NO found: 18.0 and 18.1; calculated: 18.8.

Thymol.—A solution of thymol in carbon tetrachloride was saturated with nitrosyl chloride at room temperature. The red solution gradually turned green and deposited a greenish brown precipitate of nitrosothymol. The yield amounted almost to theoretical. The melting point was found to be 163° C.

Antipyrine.—In view of the easy transformation of thymol, antipyrine was treated in a similar manner, using chloroform as the solvent. There was an immediate green color and a rapid formation of a brown precipitate of nitrosoantipyrine. The yield obtained was 80 per cent.

Other Alcohols.—Although several of them seemed to react readily with nitrosyl chloride, the nitrites of glycerin, benzyl alcohol, ethylene glycol, menthol, trimethylene chlorhydrin and chloretone were not obtained under the experimental conditions used. Glycerin reacted to a limited extent, but the chief product appeared to be acrolein by dehydration.

Benzaldehyde.—Benzaldehyde was treated with a solution of sodium carbonate and occasionally shaken, for several days, to remove free acid. It was then separated, dried, and distilled in an atmosphere of nitrogen. The distillate, which was found to be free from benzoic acid, was treated repeatedly with nitrosyl chloride until saturated, keeping the mixture at all times in an atmosphere of nitrogen or carbon dioxide. Without allowing the air to enter the container, it was exposed to direct sunlight. The red color was changed to yellow. More nitrosyl chloride was run in under the same conditions and the mixture was exposed to the sunlight, as before. After several such treatments, the product was fractionated under ordinary pressure. From 46 Gm. of the original aldehyde, 14 Gm. of unchanged material and 7 Gm. of benzoyl chloride were obtained. This latter fraction, of course, had an odor of benzoyl chloride and was readily convertible to benzamide and benzoic acid in the usual way. The residue from distillation was solid and proved to be almost entirely benzoic acid. The recrystallized material had a melting point of 120–121° C.

There is a possibility that the benzoyl chloride might be formed from benzoic acid previously produced by an oxidizing action of nitrosyl chloride. In order to determine whether this is the case, a sample of pure benzoic acid was dissolved in benzene, saturated with the gas, and exposed to the sunlight for several days. The product, however, gave no evidence of containing any benzoyl chloride.

Acetaldehyde.—Purified acetaldehyde was dissolved in three times its volume of benzene, treated with nitrosyl chloride, and exposed to the sunlight. In a very short time the reddish brown color had disappeared, and, at the same time, a straw-colored, heavy, viscous oil separated. The benzene mixture was treated several times in the same way. Finally, it was removed and distilled. The part boiling below 55° C. was warmed with water to decompose any acetyl chloride and the water solution was analyzed. Evidences of the presence of acetic acid were obtained. Another part of the distillate was heated with aniline and the resulting mixture was extracted with hot water. Crystals, which responded to tests for acetanilid, separated on cooling. While the results do not prove that acetyl chloride was produced, it would seem reasonable to conclude that such was the

case. However, the amount of conversion was too small to permit any closer identification.

The oily precipitate was found to be non-volatile in a vacuum, even at high temperatures. It reacted readily with water or alcohol to produce a white, amorphous solid, which possessed no characteristic melting point and contained no nitrogen or chlorine. It was probably a polymerized aldehyde, but it was not examined further.

SUMMARY.

1. All aliphatic alcohols tried give nitrites by treatment with nitrosyl chloride. With increase in molecular weight, pyridine as a condensation agent is necessary. When nitrites of tertiary alcohols are being prepared, pyridine should be used. The nitrites of diethyl propyl carbinol, triethyl carbinol and methyl diethyl carbinol were also made. The nitrite of diethyl propyl carbinol was made by others, as noted, but the product was not vacuum distilled and physical data were not determined.

2. Benzyl alcohol, glycerin, ethylene glycol, trimethylene chlorhydrin, menthol and chloretone gave no nitrites under the experimental conditions used.

3. Thymol and antipyrine are converted to the corresponding nitroso compounds.

4. Benzaldehyde is converted to benzoyl chloride and benzoic acid. Acetaldehyde apparently behaves in a somewhat similar manner.

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SUGGESTED ASSAYS FOR SOME N. F. PREPARATIONS.*

1. ANTISEPTIC SOLUTION.

BY S. W. GOLDSTEIN.

The most important ingredient of Antiseptic Solution, N. F. V, from the standpoint of therapeutic value, is probably boric acid. A method for the determination of the latter, therefore, appears to be desirable. The procedure suggested on page 129 is one for the direct titration of boric acid and has been found to give concordant results.

- Reagents.*—1. Glycerin
2. 0.1 N Sodium hydroxide solution
3. Phenolphthalein test solution.

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