sulfuric acid in 30 cc. of water. The solution was then made alkaline and extracted with ether. The ether was extracted with aqueous hydrochloric acid. This solution was then evaporated to dryness. The yield of di-*n*-butylamine hydrochloride was 7.8 g.

Separation of Amine Mixtures.—A mixture of 10 g. of aniline, 10 g. of methylaniline, and 10 g. of dimethylaniline was suspended in a 10% excess of cold 10% aqueous sodium hydroxide. To the cold suspension 27 g. (about 20% excess) of methanesulfonyl chloride was added during about ten minutes. The temperature was never above 25° and was usually about 10–15°. When the methanesulfonyl chloride had reacted, the solution was extracted with ether. The ether was evaporated and this residue was again treated with methanesulfonyl chloride and aqueous alkali as before.

After the second treatment the derivative of the primary amine was obtained by acidifying the combined alkaline solutions. The yield was 10.2 g. (55% of the theoretical amount). The unchanged tertiary amine was extracted from the ether solution with hydrochloric acid and the ether was then evaporated. The residue weighed 10.5 g. (60% of the theoretical amount) and was the pure secondary amine derivative. The tertiary amine was recovered to the extent of about 95% from the acid solution.

When the composition of the amine mixture was not known the results were never as satisfactory as those described above. Prolonged action of the sulfonyl chloride converted the primary amines to alkali-insoluble derivatives. These are undoubtedly the disulfonyl derivatives although they were not isolated and characterized.

Summary

Several methanesulfonamides have been prepared and characterized. They make suitable derivatives for many amines and they are more readily hydrolyzed than most sulfonamides. Some difficulties are encountered when methanesulfonyl chloride is used as a reagent for the separation of unknown amine mixtures.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

RESEARCHES ON PYRIMIDINES. CVI. LEUCO BASES OF A NEW CLASS OF DYESTUFFS CONTAINING PYRIMIDINE RINGS

BY TREAT B. JOHNSON

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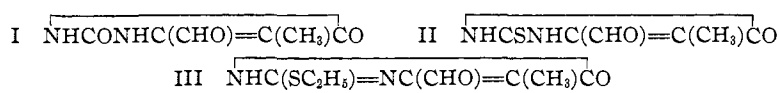
Certain representatives of the aniline dyes hold a place of great importance in the chemotherapy of bacterial diseases, and their practical use for the disinfection of tissues has received increased attention during recent years.[1] Some of these combinations, especially members of the triphenylmethane series, are highly bactericidal. Gentian violet and magenta, for example, have been shown to be able to inhibit growth of staphylococci and streptococci in culture media in dilutions as high as 1:100,000 to 1:1,000,000. It is important also to note that several of these dyestuffs

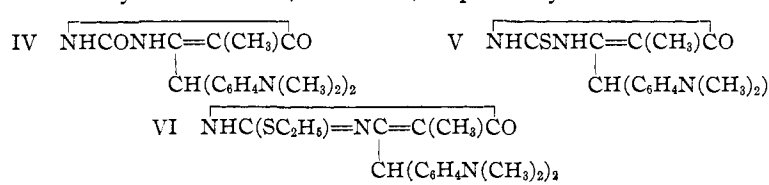
[1] J. W. Churchman, *J. Am. Med. Assocn.*, **79**, 1657 (1922); *Chim. industrie*, **10**, 212 (1923); *Stain Tech.*, **1**, 27, 103 (1926); *Ind. Eng. Chem.*, **18**, 1322 (1926).

exhibit a remarkable variation in activity toward different bacterial organisms, a property which bears a close relationship to chemotherapy.

Notwithstanding the scientific interest that has been created in these compounds[2] and the increased attention that they have received by clinicians and bacteriologists, we have at present very little information regarding the relation of chemical constitution to their bactericidal and bacteriostatic properties, and also regarding the mechanism of their bactericidal activities. As a preliminary undertaking in the development of a new program of research on germicides the writer investigated, (with his co-workers) some new condensation reactions of certain pyrimidine aldehydes. The reactions reported at this time serve to illustrate the condensation possibilities of three typical pyrimidine aldehydes with aromatic bases under experimental conditions favoring the formation of leuco bases in the triphenylmethane series. The aldehydes thus far studied are derivatives of thymine as represented by Formulas I, II and III, respectively.



These aldehydes all condense smoothly with dimethylaniline in the presence of zinc chloride, giving the corresponding leuco compounds represented by Formulas IV, V and VI, respectively. These combinations



are leuco pyrimidine-malachite greens in which one benzene cycle of leuco malachite green has been replaced by a pyrimidine ring. All three of these leuco compounds are colorless substances and undergo oxidation in acid solution, giving soluble dyestuffs which dye silk fiber with beautiful effects. It is our belief that a program of research involving the study of these combinations can be organized which will aid in advancing our present knowledge of the chemotherapy of dyestuffs. Structural changes can be incorporated easily in the pyrimidine cycle, which will enable us to synthesize new dyestuffs in an orderly manner.

Experimental Part

p-**2-Tetramethyldiaminodiphenyl-2-thiothyminylmethane, V.**—In order to prepare this leuco compound we used the following reagents: 1 gram of 2-thiothymine aldehyde[3]

[2] J. H. Kolmer, "Chemotherapy of Bacterial Diseases, The Newer Knowledge of Bacteriology and Immunology," University of Chicago Press, Chicago, Illinois, **1928**.

[3] Johnson and Cretcher, *J. Biol. Chem.*, **26**, 99 (1916).

(II), 3 cc. of dimethylaniline and 2 g. of fused zinc chloride. These reagents were mixed and heated in a flask at 100° for four hours. The mixture was stirred intermittently during the heating period. The excess of dimethylaniline was then removed by distillation with steam and the waxy residue left behind washed several times with water and finally dissolved in hot alcohol. On cooling, the leuco compound separated in the form of large, colorless blocks which melted at 212–214° to an oil. The leuco compound is practically insoluble in water. The yield was 1.6 g.

Anal. Calcd. for $C_{22}H_{26}ON_4S$: N, 14.2; S, 8.1. Found: N, 14.1, 14.2; S, 7.94.

***p*-2-Tetramethyldiaminodiphenyl-2-ethylmercaptothyminylmethane, VI.**—The procedure followed in preparing this new leuco compound corresponded exactly to that described in the previous experiment for the synthesis of the thio analog. The compound was insoluble in water but very soluble in warm alcohol. It crystallized from the latter solvent in long, colorless needles which melted at 218–219°. The yield was 1.8 g. from one gram of the aldehyde (III).

Anal. Calcd. for $C_{24}H_{30}ON_4S$: N, 13.2. Found: N, 13.0, 13.1.

The aldehyde used in this synthesis (III) has already been described in an earlier paper.[3]

***p*-2-Tetramethyldiaminodiphenylthyminylmethane, IV.**—The aldehyde (I) used in the preparation of this compound has likewise been described in our earlier work.[3] The leuco compound was found to be insoluble in water but very soluble in boiling alcohol. It crystallized from the latter solvent in the form of flat prisms or plates and melted at 197–198°. The yield was 1.8 g. from one gram of the pyrimidine aldehyde.

Anal. Calcd. for $C_{22}H_{26}O_2N_4$: N, 14.8. Found: N, 14.9, 14.8.

Summary

1. Aldehyde derivatives of thymine condense smoothly with dimethylaniline in the presence of zinc chloride to give stable leuco pyrimidine bases corresponding to the leuco base of malachite green.

2. Their oxidation products will be investigated in this Laboratory.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE MASSACHUSETTS AGRICULTURAL EXPERIMENT STATION]

EFFECT OF HEAT ON MALIC ACID[1]

BY FRED W. MORSE

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During a study of the cranberry, samples of the fruit were dried before making the subsequent analysis. The berries were cut in halves, spread in thin layers on trays and placed in a large, steam-heated drying-oven, where the temperature ranged around 85°. They remained in the oven for about three days; then they were cooled in the air, weighed, ground in an iron mortar and preserved in bottles.

When total acids were determined in these samples, the results appeared to be low when compared with data obtained from fresh cranberries.

[1] Published with the approval of the Director of the Massachusetts Agricultural Experiment Station.