should be taken into account in future consideration of the problem of specificity of enzyme action.

We are greatly indebted to the Carnegie Institution of Washington for grants in aid of this investigation.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA.]

THE ACTION OF BASIC REAGENTS ON SCHIFF'S BASES. I. THE CHLORALNITRANILINE GROUP.

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Received August 23, 1919.

Theoretically a great many compounds are included under the designation of Schiff's Bases, since it comprehends all condensation products of primary aromatic amines with aldehydes and ketones of every description. Actually a considerable number of Schiff's Bases have been described, beginning with the first mention of such products by Laurent and Gerhardt,[1] who condensed aniline with benzaldehyde. But H. Schiff[2] made the first real study of the reaction, condensing a humber of amines and aldehydes. The reaction is indicated by the equation:

$$R.CHO + 2R.NH_2 = R.CH(NHR)_2 + H_2O.$$

These bases are stable, as a rule though a small number are sensitive to light and may be decomposed readily by hot water. Among these are compounds of the *meta* series and certain naphthylamine derivatives. The investigations of Schiff's Bases in the organic laboratory of the University of North Carolina have dealt only with three aldehydes, chloral, vanillin and piperonal, but with a wide variety of amines.

It has been noted generally by observers that Schiff's Bases are sensitive to acids, being resolved into their constituents by strong hydrochloric acid. Their behavior toward basic reagents however has been quite generally overlooked. Wallach[3] noted that the condensation product of aniline and chloral was slowly decomposed by aqueous potash but rapidly by alcoholic potash, giving aniline, chloroform and phenylisocyanide. The presence of the two latter substances indicate that the decomposition takes place in 3 stages. This uninteresting behavior with alcoholic potash undoubtedly caused later investigators of Schiff's Bases to pass by this reaction. One of us[4] observed that the condensation product of chloral and *p*-nitraniline was changed immediately by alcoholic potash from a yellow substance to a brilliant red one. Upon puri-

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[1] *Compt. rend.*, **30**, 404 (1850).

[2] *Ann. Chem. Pharm.*, **131**, 118 (1864).

[3] *Ann.*, **173**, 278 (1874).

[4] Wheeler and Glenn, *J. Elisha Mitchell Sci. Soc.*, **19**, 63 (1903).

fying the product, however, a yellow compound was obtained in which one chlorine atom was replaced by the hydroxyl group

$CCl_3CH(NHNO_2C_6H_4)_2 + KOH = CCl_2OH.CH(NHNO_2C_6H_4)_2 + KCl.$

The red compound appeared to be an intermediate product for it disappeared when the reaction mixture was poured into water. It was then found that sodium methylate reacted similarly, replacing one chlorine atom by the methoxy group. In all of the reactions with the *o*- and *p*-nitraniline condensation products a brilliant red substance appeared only to disappear in the presence of water. All of the products are of a rich yellow color. We now find that sodium ethylate has a similar action and also that the *o*-nitraniline condensation product acts analogously to the *para* compound. The method of preparation of Wheeler and Glenn has been decidedly improved by dissolving or suspending the amines in acetone instead of alcohol. The reaction is almost immediate, the quality of the product is much better and the yield is much increased.

Although the *o*- and *p*-nitraniline condensation products of chloral readily yield these stable derivatives, the *m*-nitraniline product was found to be very sensitive to basic reagents. It is resolved at once in the cold into its constituents. The behavior then of Schiff's Bases toward basic reagents depends upon the nature of the substituents in the benzene ring of the amine and also upon whether it is a *meta* compound or not.

Experimental Part.

I. Behavior of *N,N'*-β,β,β-trichloroethylidene-bis-*o*-nitraniline.

***N,N'*-β,β,β-Dichlorohydroxyethylidene-bis-*o*-nitraniline,** $CCl_2OHCH(NHNO_2C_6H_4)_2$.—The trichloro compound was prepared according to the directions of Wheeler and Weller.[1] Its reaction with alcoholic potash was tested by allowing a mixture to stand 36 hours. A brown flocculent precipitate of indefinite melting point settled out. Another mixture was warmed a few moments and poured into 4 volumes of water. A yellow substance which melted at 142° after several recrystallizations was obtained but the yield was only 40%. The following plan was finally adopted: Five g. of the trichloro compound was suspended in 25 cc. of acetone and 15 cc. of a 10% alcoholic potash solution was added. The mixture became dark red immediately. It was warmed until it began to boil and was at once poured into 5 volumes of ice-water. After standing a few hours to insure full crystallization the precipitate was filtered off. The yield was 4.4 g. or about 91% of the theoretical amount. The crude product melted at 139–140° but upon recrystallization from alcohol the melting point was raised to 143°.

Subs., 0.1582; AgCl, 0.1186.

Calc. for $C_{14}H_{12}O_5N_4Cl_2$: Cl, 18.37. Found: 18.52.

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[1] THIS JOURNAL, 24, 1063 (1902).

The pure compound is brilliant yellow, crystallizing from alcohol in prisms, m. p. 143°. It is soluble in about 30 parts of hot alcohol and 120 parts of cold alcohol. It is very soluble in acetone and in chloroform, slightly soluble in ligroin and insoluble in water. It turns red with alcoholic potash. Strong acids decompose it. If heated with conc. hydrochloric acid, it dissolves, and a precipitate then forms which again dissolves. On pouring this solution into water, *o*-nitraniline crystallizes out.

***N,N'*-β,β,β-Dichloromethoxyethylidene-bis-*o*-nitraniline,** $CCl_2OCH_3CH(NHNO_2C_6H_4)_2$.—Two g. of the trichloro compound was suspended in 20 cc. of acetone and to this was added 10 cc. of a sodium methylate solution containing 5 g. of sodium per 60 cc. of methyl alcohol. The mixture became dark at once. It was heated to boiling and at once poured into 4 volumes of ice water. The yellow precipitate weighed 1.75 g. or 89% of the theoretical amount. The crude substance melted at 140° but after several recrystallizations from alcohol the melting point was raised to 147°.

Subs., 0.2874; AgCl, 0.2049.
Calc. for $C_{15}H_{14}O_5N_4Cl_2$: Cl, 17.69. Found: 17.60.

The pure substance is bright yellow, crystallizing from alcohol in rectangular plates, m. p. 147°. It is soluble in about 25 parts of boiling alcohol and 100 parts of cold alcohol. It turns dark red with alcoholic potash. With hot aqueous potash the red color finally becomes purple.

***N,N'*-β,β,β-Dichloroethoxyethylidene-bis-*o*-nitraniline,** $CCl_2OC_2H_5CH(NHNO_2C_6H_4)_2$.—The reaction of sodium ethylate upon the trichloro compound was carried out as with sodium methylate. The crude precipitate weighed 1.8 g. or 88% of the theoretical amount. It melted at 132° but on recrystallizing from alcohol the melting point was raised to 135°.

Subs., 0.2846; AgCl, 0.2000.
Calc. for $C_{16}H_{16}O_5N_4Cl_2$: Cl, 17.13. Found: 17.38.

The pure substance is a very brilliant, yellow compound, crystallizing from alcohol in rectangular plates, m. p. 135°. It is soluble in about 50 parts of boiling alcohol and 100 parts of cold alcohol. Its behavior is analogous to that of the methoxy compound.

II. Behavior of *N,N'*-β,β,β-Trichloroethylidene-bis-*m*-nitraniline.

No derivatives of the *meta* compound could be obtained with alcoholic potash, sodium methylate or sodium ethylate. In no case was a red coloration produced. The precipitate obtained on pouring the reaction mixture into water consisted of *m*-nitraniline. The decomposition was immediate and took place in the cold.

III. Behavior of *N,N'*-β,β,β-Trichloroethylidene-bis-*p*-nitraniline.

The derivatives of this compound with alcoholic potash and sodium methylate were described by Wheeler and Glenn. Their method was improved by suspending the trichloro compound in acetone, but a little longer heating was required than with the *ortho* compound. The yield was increased to 78% of the theoretical amount for the hydroxy derivative and to 87% for the methoxy compound. These compounds are described in the *Review of American Chemical Research*, **9**, 559 (1903) as "Derivatives of Trichloroethylidenedi-*p*-nitrophenamine." But the nomenclature is changed in this paper to conform to the plan adopted in the Decennial Index of *Chemical Abstracts*. The ethoxy compound described below is new.

N, *N'*-β,β,β - **Dichloroethoxyethylidene-bis-*p*-nitraniline,** $CCl_2OC_2H_5$-$CH(NHNO_2C_6H_4)_2$.—Five g. of the trichloro compound was suspended in 75 cc. of acetone and 25 cc. of sodium ethylate solution (5 g. of sodium per 60 cc. of ethyl alcohol) was added. The deep red mixture was heated on the steam bath for 10 minutes and then poured into 5 volumes of ice-water. The precipitate weighed 4.5 g. or 88% of the theoretical amount. It melted at 140° but after purifying by alcohol at 147°.

Subs., 0.2149; AgCl, 0.1491.

Calc. for $C_{16}H_{16}O_5N_2Cl_2$: Cl, 17.13. Found: 17.12.

The pure substance is bright yellow, crystallizing from alcohol in fan-shaped crystals, m. p. 147°. It gives a deep red color with alcoholic potash and the alcoholates. Heated with aqueous potash a green color is obtained instead of a purple. Heated with conc. hydrochloric acid it yields *p*-nitraniline hydrochloride.

Summary.

1. Schiff's Bases obtained by condensing *o*- and *p*-nitraniline with chloral yield hydroxy, methoxy and ethoxy derivatives with alcoholic potash, sodium methylate and sodium ethylate. In each case one chlorine atom is replaced.
2. The *m*-nitraniline-chloral product is so sensitive to these basic reagents that each of them in the cold breaks it up into its constituents.
3. The nitro group in the benzene ring of the amine stabilizes the Schiff's base to such an extent that basic reagents yield derivatives, though this is not true when it is in the *meta* position.

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