[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE STATE UNIVERSITY OF IOWA]

NITROGEN TRICHLORIDE AND UNSATURATED KETONES

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Unsaturated aliphatic hydrocarbons react with nitrogen trichloride to form N-dichloro-C-chloro amines. Thus with 2-butene, 2-chloro-3-dichloro-aminobutane is obtained.[1] Reaction will also take place with benzene and toluene but mixtures are obtained which are difficult to separate.[2]

The present work was carried out in order to study the effect of the presence of the carbonyl group on the addition reactions of nitrogen trichloride and to compare the reaction of nitrogen trichloride on benzalacetophenone with the reaction of phosphorus trichloride on this compound as studied by Conant.[3]

The reaction of this unsaturated ketone with nitrogen trichloride takes place in carbon tetrachloride solution with the evolution of a large amount of nitrogen, the formation of ammonium chloride, the dichloride of benzalacetophenone and an N-dichloro-C-chloro-amino ketone (I). This compound was first converted into a C-chloro-amino ketone (II) by treatment with concentrated hydrochloric acid. The reducing action of hydrochloric acid on the chloro-amino group was first reported by Berg.[4]

The C-chloro-amino ketone formed by this reaction was isolated as the hydrochloride and on further reduction with sodium amalgam yielded the corresponding amino alcohol (III). The molecular weight of this amino alcohol and that of the corresponding amino ketone, which would have been formed had the ketone group not been reduced, are so nearly the same that a nitrogen analysis does not suitably differentiate between them. Since several acyl derivatives of this compound were found to be oils, the acetylation value was determined with acetic anhydride.[5]

This showed the presence of an hydroxyl group. Since there was the possibility of the formation of a pinacol in the reduction of the ketone,[6] a molecular-weight determination was made. This indicated that the product was not a pinacol. In order to prove the position of the amino group this amino alcohol was also prepared from the monoxime of dibenzoylmethane by the action of sodium amalgam. This shows Compound III to be a β-amino alcohol, indicating that the chloro-amino

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[1] Coleman and Howells, THIS JOURNAL, **45**, 3084 (1923).

[2] Coleman and Noyes, *ibid.*, **43**, 2211 (1921).

[3] Conant, *ibid.*, **42**, 830 (1920).

[4] Berg, *Bull. soc. chim.*, [3] **7**, 542 (1892).

[5] Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, **1904**, Vol. I, p. 152.

[6] Buchka, *Ber.*, **10**, 1714 (1877).

group, in the primary addition, added to the carbon atom farthest from the ketone group. The reactions for the addition and for the proof of the structure of the product are as follows:

$C_6H_5CH{=}CHCOC_6H_5 + NCl_3 = C_6H_5CH(NCl_2)CH(Cl)COC_6H_5$ (I)

$C_6H_5CH(NCl_2)CH(Cl)COC_6H_5 + 2HCl = 2Cl_2 + C_6H_5CH(NH_2)CH(Cl)COC_6H_5$ (II)

$C_6H_5CH(NH_2)CH(Cl)COC_6H_5 + 4H = C_6H_5CH(NH_2)CH_2CH(OH)C_6H_5$ (III)

$C_6H_5C(:NOH)CH_2COC_6H_5 + 6H = C_6H_5CH(NH_2)CH_2CH(OH)C_6H_5$ (III)

No attempt was made to separate racemic mixtures. The preparation of derivatives and the determination of physical properties did not indicate the presence of more than one racemic mixture.

In other addition reactions of benzalacetophenone, where the ketone group is not involved, the negative part of the adding molecule attaches itself to the carbon atom farthest from the carbonyl group. Thus with hydrogen chloride[7] the chlorine atom goes to the β-position, as does also the cyanide group when hydrogen cyanide[8] is used. With ammonia and amines[9] the part containing the nitrogen atom goes to the β-position. This is true of other unsaturated ketones, having been investigated with ammonia and mesityl oxide[10] and particularly well investigated with amines[11] and various unsaturated ketones.

While it might be possible to explain the formation of product (I) by a series of reactions following a 1,4 addition to the conjugated system, similar to that which occurs with phosphorous trichloride, it seems more probable that the addition involves only the —C=C— linkage, as in the typical addition to unsaturated hydrocarbons.

Experimental Part

The Preparation of the Hydrochloride of 1-Amino-2-chloro-1,3-diphenylpropanone-3.—One hundred and twenty g. of benzalacetophenone was dissolved in 800 cc. of dry carbon tetrachloride in a flask fitted with a mercury-sealed stirrer and connected to a gasometer. The solution was cooled to 0° and 350 cc. of a carbon tetrachloride solution containing 220 mg. moles of nitrogen trichloride was added slowly through a separatory funnel. The nitrogen trichloride was prepared and analyzed by the method described by Coleman and Noyes[2] with the modifications as described by Coleman and Howells.[1]

The time required for the addition was about three hours. The evolution of nitrogen began in a few minutes and continued for some time after all of the solution had been run in. The reaction mixture was allowed to stand overnight, during which time it came to room temperature. A small amount of ammonium chloride was filtered off and analyzed. The filtrate contained the dichloride of benzalacetophenone and an N-dichloro-C-chloro-amino ketone and was shaken with 50 cc. of concentrated hydrochloric acid. After 30 minutes, 50 cc. of water was added and the hydrochloride of 1-amino-2-chloro-1,3-diphenylpropanone-3 filtered off. The average yield of the crude

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[7] Rupe and Schneider, *Ber.*, **28**, 957 (1895).

[8] Hann and Lapworth, *J. Chem. Soc.*, **85**, 1358 (1904).

[9] Tambor and Wildi, *Ber.*, **31**, 349 (1898).

[10] Sokoloff and Latschinoff, *Ber.*, **7**, 1777 (1874).

[11] Kohn, *Monatsh.*, **28**, 423 (1907); *ibid.*, **28**, 461 (1907).

hydrochloride from a large number of runs was about 10%, calculated from the nitrogen trichloride used. This was dissolved in the least possible amount of hot methyl alcohol and precipitated by the addition of a large amount of dry ether. The compound melted with decomposition at 206–208° (uncorr.).

Anal. Subs., 0.1009, 0.1016: 19.96, 19.67 cc. of 0.01634 *N* HCl. Calcd. for $C_{15}H_{14}ClON.HCl$: N, 4.73. Found: 4.53, 4.43.

Subs., 0.1096, 0.1048: 7.45, 7.02 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{15}H_{14}ClON.HCl$: Cl, 23.96. Found: 24.10, 23.76.

Benzoyl-1-amino-2-chloro-1,3-diphenylpropanone-3.—This compound was obtained from the amine hydrochloride by acylation with benzoyl chloride according to the usual Schotten-Baumann procedure. The product after recrystallizing several times from benzene melted at 186–187° (uncorr.).

Anal. Subs., 0.2605: 7.14 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{22}H_{18}ClO_2N$: Cl, 9.76. Found: 9.72.

1-Amino-1,3-diphenylpropanol-3.—Five g. of the hydrochloride was dissolved in 80 cc. of methyl alcohol and 20 cc. of water; 290 g. of 2.5% sodium amalgam was added slowly, with stirring, and with the addition of 6 *N* hydrochloric acid rapidly enough to keep the solution just acid to litmus. The alcohol was boiled off and the free amine extracted from an alkaline solution with ether. The amine was extracted from the ether by 6 *N* hydrochloric acid, the layers were separated and the ether was boiled out of the aqueous layer. The free amine was obtained as a flocculent precipitate by making the solution alkaline. On recrystallizing the product seven times from benzene, the melting point was 122–124° (uncorr.). The product did not contain chlorine, as was shown by the Beilstein test.

Anal. Subs., 0.1254: 5.30 cc. of 0.1038 *N* HCl. Calcd. for $C_{15}H_{17}NO$: N, 6.17. Found: 6.14.

Acetylation Value.—Subs., 0.2422: 2.26 mg. equiv. of acetic anhydride. Calcd. for one OH and one NH_2, 2.00. Found: 2.12.

Since this value and others similarly obtained were slightly higher than the theoretical, a similar test was made with benzylamine. This gave an acetylation value of 1.10 instead of 1.00. Possibly in both cases a small amount of the diacetylamino compound is formed.

Molecular Weight Determination.—The boiling-point method was used. Subs., 0.3973: 94.0 g. of benzene: boiling-point elevation, 0.053°. Calcd. for $C_{15}H_{17}NO$: 227. Found: 214.

Preparation of the Amino Alcohol from the Monoxime of Dibenzoylmethane.—The monoxime of dibenzoylmethane was prepared according to the method of Wislicenus.[12] It was reduced with sodium amalgam by the same method used in the reduction of the hydrochloride of the aminochloro ketone and yielded the same product; m. p. 122–124° (uncorr.). Mixed melting points showed no depression. Compound (III) is therefore a β-amino alcohol.

Anal. Subs., 0.1229: 5.18 cc. of 0.1038 *N* HCl. Calcd. for $C_{15}H_{17}NO$: 6.17. Found: 6.10.

Summary

1. The reaction of nitrogen trichloride with benzalacetophenone in carbon tetrachloride solution has been shown to form among other products 1-dichloro-amino-2-chloro-1,3-diphenylpropanone-3. The addi-

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[12] Wislicenus, *Ann.*, **308**, 250 (1899).

tion is probably a simple addition to the —C═C— bond and does not involve the ketone group.

2. This compound was reduced to 1-amino-2-chloro-1,3-diphenylpropanone-3 by concentrated hydrochloric acid and on further reduction with sodium amalgam 1-amino-1,3-diphenylpropanol-3 was obtained.

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A QUANTITATIVE STUDY OF THE INFLUENCE OF SODIUM ACETATE, SODIUM BORATE, SODIUM CITRATE AND SODIUM PHOSPHATE UPON THE ACTIVITY OF PANCREATIC AMYLASE

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In continuation of our study of the nature and properties of pancreatic amylase it became important to obtain further quantitative information on the influence of electrolytes upon its action. The first series of experiments described briefly here deal with the sodium salts of acetic, boric, citric and phosphoric acids.

Data dealing with the influence of these salts upon enzymic activity have been reported from time to time by various investigators but unfortunately they are conflicting and hard to interpret because of failure to recognize the simultaneous importance of other factors such as the hydrogen-ion activities of the solutions, the concentrations of substrates and electrolytes and the value of strictly comparable data obtained under parallel conditions.

Experiments were, therefore, planned in which each of these factors was carefully considered.

Experimental

The general plan was to study the influence upon the amylase activity, of each salt alone in solutions in which the hydrogen-ion activities differed at close intervals (by about 0.1 *P*H) and then to make a quantitative parallel comparison of the influence of the different salts, the solutions being adjusted in each case to the hydrogen-ion activity which had been found to favor the optimal activity of the enzyme in the presence of that salt.

The same preparation of pancreatin was used throughout and its activity measured under constant conditions, half-hour hydrolyses of 2% starch at 40°. The hydrogen-ion activity of each starch solution used was measured electrometrically at room temperature.

As has been shown in earlier papers from this Laboratory,[1] amylase

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[1] Sherman and co-workers, This Journal, **32**, 1073, 1087 (1910); **33**, 1195 (1911); **34**, 1104 (1912); **35**, 1617, 1784 (1913); **37**, 623 (1915); **41**, 231 (1919); **43**, 2461 (1921).