[CONTRIBUTION FROM THE LABORATORY FOR ORGANIC CHEMISTRY OF THE TECHNICAL HIGH SCHOOL, DELFT, HOLLAND]

The Diazotization of Very Weakly Basic Amines

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Measurements in relation to the velocity of the diazotization reaction with different quantities of hydrochloric acid[1] have led to the conclusion that this reaction proceeds between the *ammonium* salt and nitrous acid. Now the concentration of the amino salt in the solution is directly proportional to the degree of the basicity of the amine. In consequence of the researches published in a previous communication[2] it follows that the substituents in the benzene nucleus exert a twofold *opposing* influence on the velocity of the diazotization reaction: (1) *a diminution of the velocity* with the negativeness of the substituent in consequence of the reduced basicity of the amine, the basicity *decreasing* in the order: *meta, para, ortho;* (2) *an increase of velocity* as the substituent is more negative, in consequence of the influence of the group on the velocity of transposition of the ammonium group, the velocity *increasing* in the order: *meta, para, ortho.* If in consequence of the reduced basicity hydrolysis is so much advanced that no ammonium salt is present in the usual concentrations of mineral acid, no diazotization is to be expected. Theoretically this can be anticipated with very highly negative substituted amines. Instances of this kind are known in chemical literature. Trichloro-, tribromo- and 2,4-dinitroaniline, *e. g.*, are only diazotizable under conditions of highly increased concentrations of mineral acid. Also many cases are known in which even under these conditions diazotization is not successful.

An example of such an amine is picramide.

The advantage owing to sulfuric acid being a strong acid which can be employed in high concentrations is nullified by the fact that it combines with all the nitrous acid, as is proved by following experiments.

A solution of aniline in sulfuric acid (1.84) has been mixed during an hour with the theoretical quantity of nitrosylsulfuric acid; temp. 0°. Concentrated nitric acid (d. 1.51) is added in excess, temp. 0°. After two hours the reaction mixture is poured into a solution of potash and coupled with β-naphthol. The product of coupling existed in the main as *m*-nitrobenzene-azo-β-naphthol, m. p. 193°, and contained only a very small quantity of benzene-azo-β-naphthol, m. p. 133°. We may conclude therefore that the diazotization with nitrosylsulfuric acid does *not* take place or proceeds very slowly, *as otherwise the primarily formed diazonium compound will resist nitration.*[3]

Still more convincing evidence may be obtained in the following way.

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(1) Schoutissen, These Delft, Editors Nygh and v. Ditmar, Rotterdam.

(2) Böeseken, Brandsma and Schoutissen, *Proc. Royal Society, Amsterdam,* Feb. 28, 1920.

(3) Schoutissen, *Rec. trav. chim.,* **40**, 763 (1921).

p-Aminobenzaldehyde (2.5 g.) is dissolved in 30 cc. of concentrated sulfuric acid and mixed with 1.45 g. of sodium nitrite in 15 cc. of sulfuric acid (1.84) temp. 0°. After two hours nitrobenzene is added, *p*-aminobenzaldehyde precipitating. No diazotization has taken place.

Therefore the writer has tried to release the nitrous acid from nitrosylsulfuric acid with the aid of a compound that does not neutralize the advantages of the strong acid medium. This is possible by *weak* acids. Among these phosphoric acid offers the most advantages as it does not congeal even at temperatures of −20°, so that the decomposition of the diazonium compounds can be avoided; moreover it does not give rise to the formation of troublesome by-products in the reaction of coupling as *e. g.* indophenols, as is the case if glacial acetic acid is used.[4]

Experimental

2,4-Dinitraniline (3 g.) is dissolved in 15 cc. of sulfuric acid (1.84). To this solution cooled to 0° is added nitrosylsulfuric acid prepared from a little more than the theoretical quantity of sodium nitrite and 15 cc. of sulfuric acid (1.84). While stirring vigorously 60 cc. of phosphoric acid (1.7) is added, temp. 0°. After one-half hour 2 g. of urea is added and finally the reaction mixture is poured onto ice. The very weak yellow-colored diazonium solution was totally clear; no unchanged amine could be seen.

In a second experiment, in which the diazotization took place under the same circumstances, after coupling with β-naphthol in the mixture of the acids during one hour, the azo compound was isolated by pouring into water. The precipitate was boiled with ethyl alcohol. It was formed in the calculated quantity.

It appears from both experiments that the diazotization of 2,4-dinitraniline according to this new method proceeds *quantitatively.*

2,6-Dibromo-*p*-nitraniline is diazotized in the same way. The diazonium solution is poured with vigorous stirring into a concentrated solution of potassium iodide, to which some pieces of ice are added. After some hours the iodine compound is washed with water, sodium thiosulfate and finally with water again. The crude product melted at 149–150°; yield 98–99%. After some recrystallizations from alcohol, the 2,6-dibromo-4-nitroiodobenzene is separated in colorless prisms, m. p. 153.5°.

Anal. Calcd. for $C_6H_2O_2NBr_2I$: Br, 39.3; I, 31.2. Found: Br, 39.5; I, 30.9.

2,6-Dibromo-*p*-nitraniline (5.92 g.) is diazotized and coupled with 3 g. of β-naphthol in 15 cc. of glacial acetic acid. At once a rapid coupling takes place. After about one and one-half hours the mixture is poured into water. The crude product is boiled with alcohol; yield 99%, m. p. 218°; after three crystallizations from toluene, m. p. 221–222°; reddish-brown needles or prisms with a pronounced green metallic surface reflex. In sulfuric acid (1.84) the substance dissolves with red color. The alcoholic solution gives with a drop of sodium hydroxide a reddish-violet coloration.

Anal. Calcd. for $C_{16}H_9O_3N_3Br_2$: Br, 35.5. Found: Br, 35.3.

2,6-Dichloro-*p*-nitraniline (4.14 g.) is diazotized in the same way and poured into an ice-cold solution of potassium iodide; yield 6.09 g. The product was of a pale yellow

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(4) Schoutissen, *Rec. trav. chim.*, **40**, 753 (1921). After a part of the experiments based upon the above-mentioned considerations had been carried out the communication of Misslin, *Helv. Chim. Acta*, **3**, 626 (1920), appeared. His method bears much resemblance to our procedure as he releases the nitrous acid by means of glacial acetic acid.

color, m. p. 153°. The product is readily soluble in benzene and toluene, moderately in alcohol and ether. After steam distillation and crystallization from alcohol the compound was obtained as colorless needles, m. p. 153°.

Anal. Calcd. for $C_6H_2NO_2Cl_2I$: C, 22.6; H, 0.63; Cl, 22.2; I, 39.94. Found: C, 22.6; H, 0.66; Cl, 22.2; I, 39.7.

The diazo compound of this amine is coupled with β-naphthol, operating in the same way as indicated for the dibromo compound; yield 97%. The product crystallizes from boiling toluene in long, red, flattened prisms with a marked surface reflex, m. p. above 270°.

Anal. Calcd. for $C_{16}H_9O_3N_3Cl_2$: Cl, 19.5. Found: Cl, 19.4.

Picramide (3.3 g.) is dissolved in 15 cc. of nitrobenzene. To this solution is added 1 g. of sodium nitrite in 10 cc. of concentrated sulfuric acid. The mixture is cooled with salt and ice to about −10°. Now under vigorous stirring 20 cc. of phosphoric acid (1.7) is dropped into this solution, the temperature not being allowed to exceed 0°. After one-half hour 2 g. of powdered urea is added, afterward a little more than the theoretical quantity of β-naphthol. The pale yellow colored diazonium solution turns to reddish-brown. After about one-half hour the reaction mixture is poured onto water: the azo compound remains dissolved in the nitrobenzene layer. By the addition of alcohol to the nitrobenzene solution the product is isolated; yield 80–90%. The compound is crystallized from much glacial acetic acid or from boiling nitrobenzene: red needles with metallic reflex, m. p. above 260° with decomposition. The solution in sulfuric acid (1.84) is indigo blue. In alcohol, benzene and ligroin the substance is insoluble. The alcoholic suspension gives on addition of a trace of caustic potash an intense red color; in thin layers this color appears as blue however.

The diazonium solution of 5 g. of picramide is coupled with phenol. The azo compound can be isolated from the nitrobenzene layer by the addition of ligroin and carbon tetrachloride; yield nearly the theoretical. The compound dissolves in nitrobenzene, benzene, glacial acetic acid and alcohol; it is less soluble in carbon disulfide and carbon tetrachloride, very little in ligroin. The solution in sulfuric acid (1.84) is orange-yellow. The alcoholic solution gives with a drop of caustic potash a red color; in thin layers the color is blue. The azo compound dissolves in 2 *N* potassium hydroxide with a red color; this disappears however very quickly, especially when the solution is warmed.[5] The compound is crystallized from benzene and separated in short, thick needles, which show a metallic reflex, m. p. 194°.

Anal. Calcd. for $C_{12}H_7O_7N_5$: N, 21.03. Found: N, 20.74.

In the same way the product of coupling with anisole was obtained, yield about 80%. The compound was crystallized by dissolving the impure product in benzene and adding ligroin gradually as pointed, orange needles, m. p. 148°. The compound dissolves in nitrobenzene, benzene, alcohol, ether, glacial acetic acid, chloroform and acetone and is insoluble in ligroin. With sulfuric acid (1.84) an orange-yellow color appears. The color turns from yellow to red by the addition of a drop of potassium hydroxide to the alcoholic solution; this solution is also *red* in thin layers.

Anal. Calcd. for $C_{13}H_9O_7N_5$: N, 20.18. Found: N, 19.94.

The diazo solution of 5 g. of picramide was coupled with 3 g. of phenetole, yield 6.5 g. After dissolving the crude product in benzene and cautiously adding ligroin the product separated in red leaflets with metallic surface luster, m. p. 171–172°. With concentrated sulfuric acid an orange-red color appears. The alcoholic solution turns to red on the addition of alkali; in thin layers the color is red as well. It seems, there-

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(5) According to Borsche, *Ber.*, **54**, 1287 (1921), decomposition takes place, evolving nitrogen, picric acid and phenol.

fore, that for the change in color to blue of these azo compounds, which possess several nitro groups, a free hydroxyl group is required.

Anal. Calcd. for $C_{14}H_{11}O_7N_5$: N, 19.38. Found: N, 19.11.

In the same way the product of the coupling of **2,4,6-trinitro-5-aminoanisole** with **phenol** has been isolated. After recrystallization from benzene orange needles are obtained, m. p. 165°. The yellow-orange alcoholic solution turns to red upon the addition of a drop of 2 *N* potassium hydroxide; in thin layers the color is *indigo blue.*

Anal. Calcd. for $C_{13}H_9O_8N_5$: N, 19.29. Found: N, 19.04.

The azo compound of **trinitroaminoanisole** with **anisole** crystallizes in the same way in thick, red needles; yield 82%, m. p. 118°. In concentrated sulfuric acid the substance dissolves with a yellow color. The alcoholic solution turns to red on the addition of a drop of potassium hydroxide. In thin layers the color is red as well.

Anal. Calcd. for $C_{14}H_{11}O_8N_5$: N, 18.56. Found: N, 18.34, 18.42.

2,4,6-Trinitro-5-aminophenetole can also be diazotized in exactly the same way. After coupling with *phenol* the azo compound is obtained in a yield of 82%. This substance possesses the same properties as the coupling product of trinitroaminoanisole with phenol. It crystallizes from the benzene solution upon the gradual addition of light petroleum in long orange-red needles, m. p. 149°.

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Summary

A new procedure of diazotization has been worked out, which, as is illustrated with several instances, creates the possibility of diazotizing very weakly basic amines.

The principle of this method is based on the one hand upon the use of concentrated sulfuric acid in order to obtain a formation of amine salt, as far as possible; on the other hand, upon the release of nitrous acid from nitrosylsulfuric acid by adding phosphoric acid.

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