8. Glycoside formation decreases to a great extent the number of organisms that will attack a sugar.

9. Substitution of an amino group on the second carbon atom of glucose does not appreciably affect the fermentability of the sugar.

10. Gulonic acid, erythritol, and 1,2-isopropylideneglucose were not fermented by most of the organisms.

11. Glucose ethyl mercaptal, 1,2-5,6-diisopropylideneglucose, 1,2-isopropylidene-3,5-benzylideneglucose, and glucuronic acid were not fermented by any organism.

12. In general, any departure from the original structure of a naturally-occurring sugar renders the sugar less likely to be fermented by microorganisms.

CHICAGO, ILLINOIS RECEIVED AUGUST 27, 1937

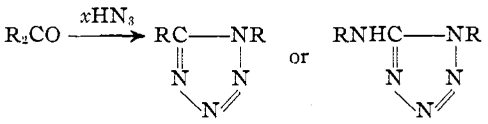
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reaction of Hydrazoic Acid with Benzil[1]

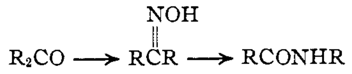
BY M. A. SPIELMAN AND F. L. AUSTIN

K. F. Schmidt[2,3,4] has published several papers on the reaction between hydrazoic acid and ketones in the presence of sulfuric acid or similar reagents. With one equivalent of hydrazoic acid the product is an amide. Two or more equivalents of hydrazoic acid lead to tetrazoles, alkylaminotetrazoles, or both.

$$R_2CO + HN_3 \longrightarrow RCONHR + N_2$$

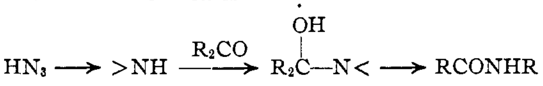


In his first paper Schmidt formulates the reaction as first yielding an oxime which then undergoes the Beckmann rearrangement.



$$R_2CO \longrightarrow R\overset{\overset{\text{NOH}}{\|}}{C}R \longrightarrow RCONHR$$

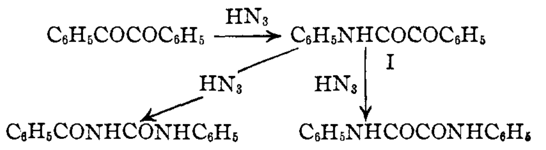
Later papers make no mention of the hypothesis but give the impression that the essential factor is the imino diradical >NH which adds to the carbonyl group to form a univalent nitrogen derivative of a type once in favor as an intermediate in several molecular rearrangements. In a footnote[3] the idea is attributed to Stollé.



$$HN_3 \longrightarrow {>}NH \xrightarrow{R_2CO} R_2\overset{\overset{\text{OH}}{|}}{C}\text{—}N{<} \longrightarrow RCONHR$$

Although the Schmidt reaction has been used in a few instances[5] it has never been extensively studied, and the experiments here described were undertaken with the idea of expanding our knowledge of the field. No α-diketone has been investigated, and benzil was selected as an example of this type of compound. The present paper reports its reaction with hydrazoic acid.

Benzil and hydrazoic acid, in the presence of sulfuric acid at 0–10°, give as the principal product 30–60% of the theoretical yield of benzoylphenylurea, II. The first fission undoubtedly takes place unsymmetrically, as phenylglyoxanilide, I, is the only ketonic intermediate possible.



II III

A second Schmidt reaction, resulting in bond rupture between the two carbonyl groups, would then lead to the main product, II. There is some evidence for this view in the fact that oxanilide, III, which would be formed by insertion of an imino group between the carbonyl and phenyl group, is also found in small amounts. The relative yield of products indicates that in the second step division between the two carbonyls is the more rapid reaction.

The oxime which by means of the Beckmann rearrangement produces benzoylphenyl urea is benzil γ-dioxime,[6] but this compound is stable to hydrazoic–sulfuric acid, and the Beckmann rearrangement as a factor is thus clearly eliminated. The preformation of imino radicals is also improbable because of the fact that hydrazoic

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[1] This work was supported in part by the Wisconsin Alumni Research Foundation.

[2] Schmidt, *Acta Acad. Aboenisis Mata. et Phys.*, 2 (1924); *C. A.* **19**, 3248 (1925).

[3] Schmidt, *Ber.*, **57**, 704 (1924).

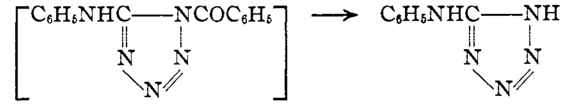
[4] Schmidt, *Friedl.*, **15**, 221, 333 (1926); **16**, 2862 (1928); German Patents 427,858, 439,041, 479,016.

[5] Ruzicka Goldberg, Hürbin and Boeckenoogen, *Helv. Chim. Acta*, **16**, 1323 (1933); v. Braun and Heymons, *Ber.*, **63**, 502 (1930).

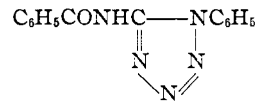
[6] Beckmann and Köster, *Ann.*, **274**, 19 (1893).

acid is unchanged by sulfuric acid in the cold, and the presence of the ketone is necessary for its decomposition. In other words, if hydrazoic acid does not break down unless a ketone is present, it is difficult to see how it can first decompose to the imino diradical which then reacts by addition.

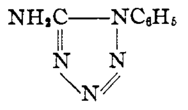
With benzil the Schmidt reaction is more than usually complicated by the large number of by-products. Benzoic acid and aniline which are formed in small amounts need no particular hypothesis to account for their presence. More interesting are two acids and a feeble base which were identified, respectively, as 5-anilinotetrazole, V,[7] 1-phenyl-5-benzamidotetrazole, VI,[7] and 1-phenyl-5-aminotetrazole, VII.[8] The presence of these compounds would be predicted on the basis of the aminotetrazole reaction which generally concurs with the Schmidt reaction, even when amides or tetrazoles are desired. Compound IV which should also be expected is too easily hydrolyzed for isolation.[7] An obvious theory for the origin of the aminotetrazole by-products is that they result from the reaction of hydrazoic acid with benzoylphenylurea, II, analogous to the manner in which they are formed from benzoylphenylthiourea and hydrazoic acid (in the presence of lead oxide).[7] This is not the case, however, as benzoylphenylurea is unaffected by the reagents used. Aminotetrazoles, therefore, are the product of side reactions, and consecutive reactions are not involved. Further evidence was brought out in experiments in which a large excess of hydrazoic acid was used. Amounts of by-products were essentially the same.



IV V



VI



VII

Experimental Part

The method of preparing hydrazoic acid was substantially that of v. Braun.[9] Molar quantities of sulfuric acid were added dropwise to wet sodium azide under chloroform at 0–5°. After two hours of stirring the sodium sulfate was washed several times by decantation. The combined chloroform washings were dried over sodium sulfate and assayed by titrating an aliquot portion with aqueous sodium hydroxide using phenolphthalein as indicator. The yield was 85–90% of the theoretical.

In carrying out the Schmidt reaction several methods were tried, and best results were obtained by adding the sulfuric acid to a chloroform solution of hydrazoic acid and the ketone, rather than the reverse order of addition used by Schmidt and others. Many runs were made with minor modifications of isolation procedure; of these, one is given in detail.

In a 3-necked flask fitted with stirrer, dropping funnel and thermometer, and surrounded by an ice–salt bath, was placed 10.2 g. of benzil and 120 cc. of chloroform containing two molar equivalents of hydrazoic acid. Twenty cc. of concd. sulfuric acid was added during an hour while the temperature was not allowed to rise above 5°. After five hours of stirring the layers were separated.

The chloroform layer, on evaporation, yielded only 0.5 g. of solids from which washing with ether extracted 0.2 g. of benzoic acid, m. p. 122°. From the insoluble residue was obtained after crystallization from dioxane an equal amount of oxanilide; m. p. and mixed m. p. 248–249°.

The sulfuric acid layer from the reaction mixture was diluted with ice water and filtered from the bulky mass designated as the *main precipitate*. The filtrate was made alkaline and extracted with ether in a continuous extractor. The ether was concentrated to 5 cc. and filtered from 0.5 g. of pale yellow scales, m. p. 159–160°, which were identified as 1-phenyl-5-aminotetrazole, VII, by comparison with a synthetic specimen. Evaporation of the ether left a few drops of brown oil characterized as aniline by conversion to benzanilide; m. p. 160–161°.

The main precipitate was washed twice with dilute sodium hydroxide and, after drying, with several portions of ether. This left a residue of 5.4 g. of fairly pure benzoylphenylurea, m. p. 202°. One crystallization from benzene or dioxane raised the melting point and mixed melting point to 206°.

The sodium hydroxide extract was acidified, filtered and exhaustively extracted with ether. The ether extract was concentrated to 5 cc. and the crystals which separated were combined with the precipitate obtained before extraction and recrystallized. There was isolated 0.8 g. of the characteristically feathery needles of 5-anilinotetrazole, V, m. p. 209–210°. The 5-cc. ether filtrate yielded 0.5 g. of difficultly purified benzoic acid.

The ether washings from the main precipitate gave, after evaporation, about 0.25 g. of a weakly acidic substance which melted at 158° after crystallization from dilute methanol. It was characterized as 1-phenyl-5-benzamidotetrazole, VI, by acid hydrolysis to the free amine, VII. A better procedure for collecting a maximum yield of this particular by-product is to omit the alkali wash, crystallize the crude benzoylphenylurea from benzene, evaporate the mother liquor and crystallize the residue several times from methanol. The yield is then 1.3 g.

Stability of Benzil γ-Dioxime and Benzoylphenylurea.—Each was treated exactly as in the Schmidt reaction and was recovered unchanged.

Summary

Benzil reacts with hydrazoic acid in the presence of sulfuric acid to form principally N-phenyl-N′-

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[7] Stollé and Henke-Stark, *J. prakt. Chem.*, **124**, 261 (1930).

[8] Stollé, *Ber.*, **55**, 1289 (1922).

[9] Von Braun, *Ann.*, **490**, 125 (1931).

benzoylurea. Side reactions yield benzoic acid, aniline, and aminotetrazoles. The latter are not the product of consecutive reactions. The Schmidt reaction does not involve the Beckmann rearrangement or imino diradicals.

MADISON, WISCONSIN RECEIVED OCTOBER 30, 1937

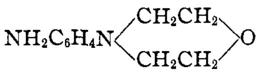
[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, COLLEGE OF CITY OF NEW YORK]

Alkanolamines. III. Reactions of Chloronitrobenzenes with Ethanolamines

BY M. MELTSNER, L. GREENSTEIN, G. GROSS AND M. COHEN

In a previous communication from this Laboratory, Kremer[1] confirmed the reduction action of monoethanolamine as first reported by Meltsner,[2] *et al.* In addition to reduction products of nitrochlorobenzenes, Kremer also obtained condensation products, *e. g.*, 2-(*o*-nitroanilino)-ethanol from *o*-nitrochlorobenzene and monoethanolamine in the presence of sodium carbonate.

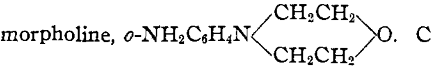
The present paper reports the results of additional experiments on the nitrohalides with mono-, di- and triethanolamines. The ethanolamines may bring about reduction to the azoxy, azo or amino compound, condensation, hydrolysis or combinations of these reactions. Condensations do not require the use of sodium carbonate as previously reported, although the yield may be greater in presence of the alkali carbonate. The addition of sodium hydroxide increases the yield of azo compounds.

Diethanolamine leads to the formation of a compound which is believed to be 2-aminophenylmorpholine,  $NH_2C_6H_4N\left<\begin{matrix}CH_2CH_2\\CH_2CH_2\end{matrix}\right>O$ by condensation with *o*-nitrochlorobenzene and the reduction of the condensation product. Further identification of this compound is being undertaken. The presence of water and excess ethanolamine favor condensation. Triethanolamine produces no condensation product.

Experimental

Reaction of *o*-Nitrochlorobenzene with Diethanolamine.—Thirty grams of *o*-nitrochlorobenzene was placed in a 3-necked flask fitted with a reflux condenser and a dropping funnel. The temperature was raised to 175–180° in an oil-bath and then 126 g. of diethanolamine was added dropwise. The heating was continued for a total of three hours. The reaction mixture was treated with ice to complete precipitation and filtered. The insoluble residue, after further washing with cold water, was recrystallized from alcohol and yielded orange crystals, m. p. 134°, which proved to be 2,2′-dichloroazobenzene.

The filtrate was steam distilled. The distillate after extraction with ether and acidification of the extract yielded *o*-chloroaniline hydrochloride. The residue from the steam distillation was acidified and steam distilled. The ether extract of the distillate yielded yellow crystals, m. p. 44° and identified as *o*-nitrophenol.

The residue was made alkaline, evaporated as much as possible on a water-bath and then distilled under vacuum. The fraction collected at 155–175° (20 mm.), which contained some diethanolamine, on standing deposited white crystals. These crystals were recrystallized several times from benzene and then gave a melting point of 133–134°. They were soluble in water, almost insoluble in ether. A fusion test for elements showed the presence of nitrogen but no chlorine. It reduces ammoniacal silver nitrate at 100°. Evaporation of the crystals with hydrochloric acid leaves a white solid which contains chlorine and melts at 200°. The compound is probably *o*-aminophenylmorpholine,  $o\text{-}NH_2C_6H_4N\left<\begin{matrix}CH_2CH_2\\CH_2CH_2\end{matrix}\right>O$. Calcd. N, 15.73. Found, N, 15.51.

Reaction with Diethanolamine and Water.—Sixty-three grams of water was added to the diethanolamine and the solution added as in the previous experiment. After heating for three hours at 175–180° the mixture was treated with ice water and filtered. The filtrate was steam distilled and further treated as in the previous experiment.

The residue, insoluble in the ice water, was steam distilled to separate any unreduced nitrochlorobenzene.

Reaction with Monoethanolamine and Water.—Twenty-four grams of water was added to 48 g. of monoethanolamine and the solution added dropwise to 30 g. of *o*-nitrochlorobenzene. The temperature was kept at 175° for three hours. Ice water was added and the mixture filtered. The filtrate was steam distilled and yielded *o*-chloroaniline. The residue insoluble in ice water was dissolved in boiling benzene, cooled, and petroleum ether added. On standing crystals separated out. The crystals were identified as 2-(*o*-nitroanilino)-ethanol.

Summary

Mononitrohalides of benzene yield reduction, hydrolytic and condensation products when treated with ethanolamines, except that *m*-nitro-

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[1] C. B. Kremer, THIS JOURNAL, **59**, 1681 (1937).

[2] M. Meltsner, C. Wohlberg and M. J. Kleiner, *ibid.*, **57**, 2554 (1935).