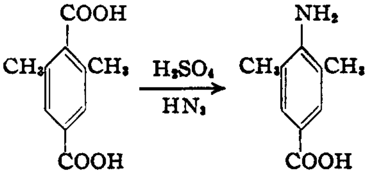
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY]

The Mechanism of the Schmidt Reactions and Observations on the Curtius Rearrangement[1]

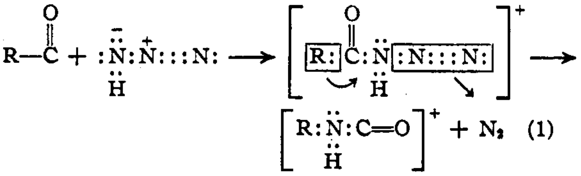
BY MELVIN S. NEWMAN AND HYMAN L. GILDENHORN[2]

During studies on the synthesis of 4-amino-2,6-dimethylbenzoic acid we made an observation which gave us a clue as to the mechanism of the Schmidt reactions[3] and led us to predict that the Curtius rearrangement should be acid catalyzed. In this paper we present mechanisms for the reactions of hydrazoic acid with acids and other compounds and also demonstrate that the Curtius rearrangement is catalyzed by protonic and non-protonic acids.

The original observation which gave the impetus to this work was the fact that 2,6-dimethylterephthalic acid, I, yielded 4-amino-3,5-dimethylbenzoic acid, II, in the Schmidt reaction. Since the hindered carboxyl group reacted exclusively we were struck by the similarity between this Schmidt reaction and the sulfuric acid esterification of 2,4,6-trimethylbenzoic acid.[4] Since the mechanism for this esterification involves an oxocarbonium ion,[4,5] it seemed logical to propose a similar intermediate for the Schmidt reaction. Accordingly we submit that the Schmidt reaction with acids may proceed by an electrophilic attack of an oxocarbonium ion on nitrogen accompanied by a rearrangement.[6] The function of the sulfuric acid is to convert the acid, RCOOH, into an oxocarbonium ion, R—C^{+}=O, or a dihydroxycarbonium ion, R—C^{+}(OH)$_2$.[7] The carbonium ion then attacks the nitrogen atom in hydrazoic acid which is attached to hydrogen. The unstable initial adduct loses nitrogen as a molecule of N_2 leaving the remaining nitrogen electronically deficient. This in turn sets up forces which cause the R group originally attached to the carbonium-carbon to rearrange to the nitrogen. In this migration the R group carries with it the pair of electrons which originally bound it to the carbonium-carbon. The final resulting electron-deficient complex may either remain as such in the reaction medium or, on dilution with water, react with water to yield the final products.

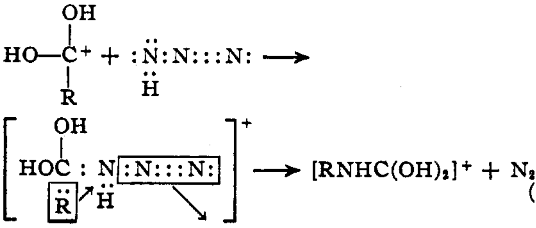


I II



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C} + :\underset{\ddot{H}}{\overset{-}{\ddot{N}}}:\overset{+}{N}:::N: \longrightarrow \left[\boxed{R:}\overset{\overset{\displaystyle O}{\|}}{C}:\underset{\ddot{H}}{\ddot{N}}\boxed{:N:::N:}\right]^{+} \longrightarrow \left[R:\underset{\ddot{H}}{\ddot{N}}:C{=}O\right]^{+} + N_2 \quad (1)$$

$$[RNHCO]^{+} + H_2O \longrightarrow RNH_3^{+} + CO_2 \quad (1a)$$



$$HO{-}\underset{R}{\overset{OH}{C^{+}}} + :\underset{\ddot{H}}{\ddot{N}}:N:::N: \longrightarrow \left[HO\underset{\boxed{\ddot{R}}}{\overset{OH}{C}} : \underset{\ddot{H}}{N}\boxed{:N:::N:}\right]^{+} \longrightarrow [RNHC(OH)_2]^{+} + N_2 \quad (2)$$

$$RNH\overset{+}{C}(OH)_2 \longrightarrow RNH_3^{+} + CO_2 \quad (2a)$$

Evidence supporting the first alternative was obtained by showing that with sulfuric and hydrazoic acids: (A) methyl 2,4,6-trimethylbenzoate, which has been shown to yield $(CH_3)_3C_6H_2C^{+}{=}O$ ions in the cold in sulfuric acid solution,[8] is converted into mesidine (2,4,6-trimethylaniline) at 0°; (B) 2,4,6-trimethylbenzoic acid which likewise yields $(CH_3)_3C_6H_2C^{+}{=}O$ ions in the cold in sulfuric acid solution[8] is converted into mesidine, even at 0°; (C) benzoic acid, which yields mainly $C_6H_5C^{+}(OH)_2$ ions in the cold in sulfuric acid, does not yield aniline in the cold. This evidence indicates that oxocarbonium ions[5] react readily with hydrazoic acid but does not exclude the pos-

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[1] Part of the material herein presented is contained in the M.S. thesis presented by H. L. G. to the Ohio State University in June, 1947. This also formed the basis for part of the address given by M. S. N. to the Organic Symposium in Boston, Massachusetts, June 12, 1947. Additional work on the Schmidt reaction carried out in the Department of Chemistry of the Massachusetts Institute of Technology by Dr. Conrad Schuerch with Professor E. H. Huntress, executed independently of but concurrently with the present paper, will shortly be presented to THIS JOURNAL.

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[3] Wolff in Adams "Organic Reactions," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 309–310. Under the heading of Schmidt reactions are included the reactions of organic compounds with sulfuric and hydrazoic acids.

[4] Newman, THIS JOURNAL, 63, 2431 (1941).

[5] As a suitable system for the nomenclature of simple carbonium ions we propose that the central electron deficient carbon atom be used as a root and that the attached groups be named as usual. Thus $(CH_3)_3C^{\bullet}$ would be called trimethylcarbonium ion, $CH_3C^{+}(OH)_2$ would be called methyl dihydroxy carbonium ion, and CH_3—C^{+}=O, methyl oxo carbonium ion. For more complicated carbonium ions a more systematic nomenclature would be necessary.

[6] It is to be understood throughout our discussion that the intermediate stages pictured in formulas have no significance other than to indicate formation and loosening of the bonds involved and to indicate driving forces for the reactions.

[7] The activated form for hydrazoic acid proposed by Hurd in Gilman's "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1938, p. 699, is merely one of the contributing resonance structures and does not require sulfuric acid for its existence. See Hendricks and Pauling, THIS JOURNAL, 47, 2904 (1925); Langseth and Nielsen, *Phys. Rev.*, 44, 326 (1933); and Brockway and Pauling, *Proc. Natl. Acad. Sci.*, 19, 860 (1933).

[8] Newman, Kuivila and Garrett, THIS JOURNAL, 67, 704 (1945).

sibility that dihydroxycarbonium ions[5] may also react as shown in equation 2. However, the reaction with dihydroxycarbonium ions is undoubtedly much slower. This difference in reactivity of these two types of carbonium ions is strikingly illustrated by the course of the reaction in the case of I. Findings B and C (above) are also to be noted.

The fragments, $(RNHCO)^+$ and $[RNHC(OH)_2]^+$, react with water to yield the amine and carbon dioxide. In some cases, at least, carbon dioxide is evolved directly from the sulfuric acid solution. We noticed that the fragment $(RNHCO)^+$ should also be the species first formed when an isocyanate is dissolved in sulfuric acid. When we added phenyl isocyanate to sulfuric acid there was an immediate evolution of carbon dioxide and aniline was isolated from the reaction mixture.

The reaction pictured in equation (1) takes place at a temperature determined by the ease with which the acid in question yields appreciable quantities of oxocarbonium ion, $R{-}C^+{=}O$. In the case of 2,6-dimethylterephthalic acid, I, and 2,4,6-trimethylbenzoic acid, a temperature of 10° or lower is sufficient because of the tendency of these acids to undergo complex ionization[8,9] in sulfuric acid according to equation (3).[10]

$$RCOOH + 2H_2SO_4 \rightleftarrows R{-}C^+{=}O + H_3O^+ + 2HSO_4^- \quad (3)$$

But in the case of benzoic acid and many other acids, a temperature of 35 to 50° is required for the Schmidt reaction (equation 2). Acids of this type ionize according to equation 4 in sulfuric acid.[10]

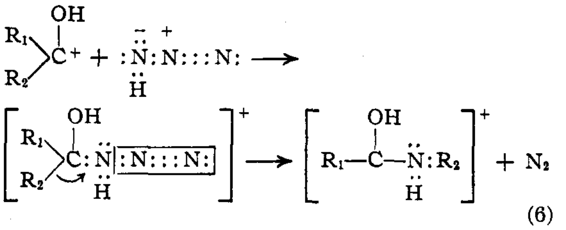
$$RCOOH + H_2SO_4 \rightleftarrows RC^+(OH_2) + HSO_4^- \quad (4)$$

The dihydroxycarbonium ions,[5] $RC^+(OH_2)$, thus formed evidently do not react with hydrazoic acid as easily as do the oxocarbonium ions,[5] $R{-}C^+{=}O$. The higher reaction temperature required for many Schmidt reactions may be needed to shift the equilibrium shown in equation 5 to the right or to provide a higher temperature for the reaction of the less reactive dihydroxycarbonium ions as shown in equation (2).

$$RC^+(OH)_2 \rightleftarrows R{-}C^+{=}O + H_2O \quad (5)$$

Should it prove possible to produce appreciable concentrations of oxocarbonium ions from acids of the benzoic type at lower temperatures by altering the reaction medium, we would expect reaction with hydrazoic acid. Thus it may be that reaction at low temperatures of a system with hydrazoic acid to yield nitrogen will prove to be a means of determining the presence of oxocarbonium ions, barring complications involving hydrazoic acid.

In the case of Schmidt reactions with aldehydes and ketones a similar mechanism has been used to account for the products formed.[11] The reaction of the hydroxycarbonium ion[5] formed from aldehydes and ketones in sulfuric acid[10] with hydrazoic acid is shown in equation 6.

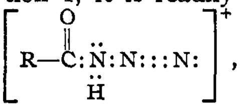


(6)

It should be pointed out that many of these reactions proceed at low temperatures. The complex ion formed loses a proton to yield an amide. In this connection it should prove interesting to compare the migration aptitudes of various groups in the Schmidt reaction with those obtained by Bachmann in the case of the rearrangement of symmetrical pinacols.[12] The qualitative results reported for a few ketones show that the migration aptitudes are roughly what one would expect using data from pinacol rearrangements.[11,12]

Further application of the principles outlined above allow reasonable mechanisms to be postulated for the reaction of a variety of other compounds with hydrazoic acid under acid conditions.[13]

If we return to the first reaction stage of equation 1, it is readily seen that this intermediate,



$$\left[\mathrm{R{-}\overset{\overset{\displaystyle O}{\|}}{C}{:}\underset{H}{\overset{..}{N}}{:}N{:}{:}{:}N{:}}\right]^+$$

, could likewise be obtained by the addition of a proton to an acid azide. Therefore, since the Schmidt reaction takes place readily at 35 to 50° and most azides decompose in solvents only at higher temperatures, we were led to predict that the Curtius reaction should be acid catalyzed.[14] This prediction was verified by showing that the rate of decomposition of benza-

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[9] Raymond A. Craig has shown in unpublished work that acid I has an i factor of 2.4. Although the exact i factor for this acid could not be predicted its magnitude is in the region expected if one considers that the i factor of 2,4,6-trimethylbenzoic acid is 4 and that for 2,6-dimethylbenzoic acid is about 3.5. Thus substitution of the 4-methyl group by hydrogen causes a decrease in i factor (see Treffers and Hammett, THIS JOURNAL, **59**, 1708 (1937)). Further substitution of a carboxyl group in the 4-position, as in I, would be expected to produce a further decrease in the i factor.

[10] See Hammett "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 45–56.

[11] See Sanford, Blair, Arroya and Sherk, THIS JOURNAL, **67**, 1941 (1945), for a comparison of mechanisms involving hydrazoic acid and hydroxylamine-O-sulfuric acid.

[12] See Wallis in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, p. 969–970. Dr. P. A. S. Smith, University of Michigan, has informed us that he is studying this problem now.

[13] See the entire chapter of ref. 3 above.

[14] No mention of acid catalysis in the Curtius reaction is made either in the chapter on this reaction by Smith in "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 337, *et seq.*, or in the chapter by Wallis and Lane, *ibid.*, p. 267, *et seq.* Since this article was written, Dr. Smith (see ref. 12) pointed out that Th. Curtius, *J. prakt. Chem.*, [2] **50**, 291 (1894), mentions briefly the decomposition of azides in ether containing hydrogen chloride.

zide in acetic acid was increased progressively by separate additions of chloroacetic, dichloroacetic, trichloroacetic and sulfuric acids. The rate of decomposition of benzazide in dioxane was also markedly increased by hydrogen chloride and by boron trifluoride.[15] We are now studying some quantitative aspects of this catalytic reaction.

Experimental[16]

3,5-Dimethyl-4-aminobenzoic Acid, II.—To a stirred mixture of 4.7 g. of pure 2,6-dimethylterephthalic acid[17] in 20 cc. of 100% sulfuric acid and 15 cc. of chloroform at 25° was added 1.05 g. of sodium azide over a period of two and one-half hours. After stirring for another fifteen minutes, the mixture was poured on ice and neutralized with sodium hydroxide. The chloroform layer was separated and the aqueous layer acidified with dilute hydrochloric acid. The white solid which separated was collected and dried. It weighed 2.3 g. (87% based on azide used) and melted with darkening and decomposition from 240 to 250°. After two recrystallizations from alcohol white crystals of pure II were obtained. The melting point of 251 to 252° with decomposition[18] was determined in a copper block by heating from 30 to 200° in ten minutes and then heating at a rate of 4° per minute.

Anal. Calcd. for $C_9H_{11}O_2N$: C, 65.4; H, 6.7; N, 8.5. Found: C, 64.9, 65.0; H, 6.6, 6.8; N, 8.5, 8.7.

This amino acid was diazotized and coupled with β-naphthol to yield a brilliant orange-red product, m. p. 285.5 to 288° with decomposition, when recrystallized from absolute alcohol (m. p. procedure same as for II).

Anal. Calcd. for $C_{19}H_{16}O_3N_2$: C, 71.2; H, 5.0; N, 8.8. Found: C, 71.0, 71.0; H, 5.2, 5.4; N, 8.8, 8.9.

In another experiment, the diazonium solution was heated with added copper sulfate[19] to yield a small amount of colorless crystals, m. p. 222–224°, of 3,5-dimethyl-4-hydroxybenzoic acid[20] on crystallization from benzene.

Further evidence for the structure of II was obtained in decarboxylation experiments. Our amino acid decarboxylated with difficulty whereas Noyes[17] reported that the isomeric 2,6-dimethyl-4-aminobenzoic acid decarboxylates readily. On heating our acid with a little copper carbonate[21] a small amount of an amine was obtained which formed an acetate, m. p. 170–174° after crystallization from alcohol and from benzene. The melting point of the acetate of *sym-m*-xylidine is 140.5°[22] whereas that of *vic-m*-xylidine melts at 177°.[23]

Schmidt Reactions at Low Temperature.—In two parallel experiments 5 g. of benzoic and 2,4,6-trimethylbenzoic acids were dissolved in 100% sulfuric acid and the solutions were cooled at 0°. Equivalent amounts of sodium azide were added to each solution during one hour. From the former no gas was evolved but from the latter a brisk evolution of nitrogen took place. Carbon dioxide was also formed but no carbon monoxide. After stirring an additional half hour the solutions were poured on ice. From the former a negligible amount of aniline was isolated but from the latter 51% of mesidine was obtained. The mesidine was identified as its formyl derivative, m. p. 175.5–176.5°.[24] We also prepared the 1,3,5-trinitrobenzene addition product of mesidine and found it to form deep reddish-brown needles, m. p. 133.5–134.0°.[25]

Anal. Calcd. for $C_{15}H_{16}O_6N_4$: C, 51.7; H, 4.6; N, 16.1. Found: C, 51.7, 51.9; H, 4.8, 5.0; N, 16.1, 16.2.

Mesidine from Methyl 2,4,6-Trimethylbenzoate.—To a solution of 5.2 g. of methyl 2,4,6-trimethylbenzoate in 40 cc. of concentrated sulfuric acid at 40° was added slowly 1.56 g. of sodium azide. The gases evolved amounted to 1020 cc., almost twice the theory for nitrogen. No tests on this gas were made other than to show it contained carbon dioxide and did not contain carbon monoxide. The reaction mixture was poured on ice and the mesidine formed was extracted from the alkaline solution and distilled. It boiled at 80° at 2 mm. and was isolated in 79% yield (based on azide). From the acid portion of the reaction mixture was recovered 13% of 2,4,6-trimethylbenzoic acid.

Acid Catalyzed Curtius Rearrangements.[26]—Qualitative experiments on the effect of acids on the decomposition of benzazide at 75° were carried out in a 500-cc., three-necked flask fitted with a sealed stirrer and dropping funnel and connected to an azotometer. Various acids were added to the acetic acid to make 50 mole per cent. solutions. The apparatus was equilibrated at 75° and was then pinched off and the flask cooled. A solution of benzazide in 10 cc. of acetic acid was then sucked in through the separatory funnel, followed by a rinse with 5 cc. of acetic acid. The pinchcock was then removed and the flask heated to 75°. The times required for collection of one-half of the total volume of gas evolved were as follows: acetic acid, 20 minutes; chloroacetic acid, 13 minutes; dichloroacetic acid, 10 minutes; trichloroacetic acid, 7 minutes; 2.5 cc. of 100% sulfuric acid in 50 cc. of acetic acid, 10 minutes; 50 mole per cent. sulfuric in acetic, 6 minutes. When benzazide was added to 100% sulfuric acid, an explosion occurred.[15] In three experiments in dioxane, the time for dioxane was 60 minutes, for a solution of 9 g. of boron trifluoride in 50 cc. of dioxane, 7 minutes, and for 2.3 g. of hydrogen chloride in 65 cc. of dioxane, 6 minutes.

Summary

A mechanism for the Schmidt reactions of acids and certain esters with hydrazoic acid in sulfuric acid solution is proposed.

Catalysis of the Curtius rearrangement of benzazide by protonic and non-protonic acids has been demonstrated.

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[15] The following references mention explosions or catalysis of decomposition of azides by acids: *Ber.*, **58**, 1221 (1925); *Ann.*, **469**, 44 (1929); *Helv. Chim. Acta.*, **15**, 935 (1932), **16**, 349 (1933); *Rec. trav. chim.*, **53**, 988 (1934).

[16] All melting points corrected. Microanalyses by W. J. Polglase, O. S. U.

[17] Noyes, *Am. Chem. J.*, **20**, 789 (1898).

[18] Fittig and Brueckner, *Ann.*, **147**, 40 (1868), give a m. p. of 235° and Wheeler and Hoffman, THIS JOURNAL, **44**, 120 (1922), 242° for this compound.

[19] Lassar-Cohn "Arbeitsmethoden," Leipzig, 1923, p. 136.

[20] Thiele and Eichwede, *Ann.*, **311**, 372 (1900). The isomeric 2,6-dimethyl-4-hydroxybenzoic acid melts at 185°, Rabe and Spence, *Ann.*, **342**, 351 (1905).

[21] Fieser "Experiments in Organic Chemistry," D. C. Heath Co., New York, N. Y., 1941, p. 201.

[22] Wroblewski, *Ann.*, **207**, 96 (1881).

[23] Hodgkinson and Limpach, *J. Chem. Soc.*, **77**, 67 (1900).

[24] Hantzsch and Lucas, *Ber.*, **28**, 751 (1895).

[25] Noelthing and Sommerhof, *ibid.*, **39**, 77 (1906), give 120–122° as the melting point of this derivative.

[26] For a study of solvent effect on the rate of Curtius rearrangement of benzazide, see Newman, Lee and Garrett, THIS JOURNAL, **69**, 113 (1947).