inch Vigreux column. Since distillation at normal pressure gave decomposition in some cases, reduced pressure was used. Results are summarized in Table I.

Summary

1. Silicon tetraacetate and substituted acetoxysilanes have been prepared from the corresponding chlorides and anhydrous sodium acetate in an anhydrous solvent.

2. The physical properties of some substituted acetoxysilanes are recorded.

3. Seven of the compounds reported are new.

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[CONTRIBUTION FROM THE CENTRAL RESEARCH DEPARTMENT, MONSANTO CHEMICAL COMPANY]

The Synthesis of Amino-substituted Phosphonic Acids. I

BY GENNADY M. KOSOLAPOFF

The purpose of this paper is to present the general synthetic schemes which have been used in this Laboratory over the course of several years for the syntheses of typical representatives of amino-substituted phosphonic acids.

The amino-aromatic phosphonic acids have been prepared either by reduction of the corresponding nitro derivatives by means of tin and hydrochloric acid[1] in poor yields or by the ammonolysis of the corresponding chloro derivatives in satisfactory yields.[2] Since the nitro derivatives are more readily available in some cases than are the chloro derivatives, we investigated the former reaction scheme and found that good yields of the amino-acids can be obtained when the reduction is effected by sodium sulfide solutions.

In the case of aliphatic or aralkyl acids having the amino-group on the aliphatic portion of the molecule, there are several general synthetic methods which have to be selected according to the type of amino-phosphonic acid desired. In the case of an ω-amino derivative there is the choice between the ammonolysis of the ω-halo derivative or the coupling of the ω-halo derivative with potassium phthalimide, following by the removal of the phthalic acid portion by hydrolysis. The latter reaction is the more desirable one because of the lack of side-reactions. Furthermore, in a number of instances, the reaction may be advantageously inverted, *i. e.*, N-ω-haloalkylphthalimides may be reacted with trialkyl phosphites and the products hydrolyzed to the desired ω-aminoalkanephosphonic acids.

If the amino group is desired on the same carbon atom as the phosphono group, the choice lies between: (a) the ammonolysis of an α-halophosphonic acid, obtainable either by the addition of phosphorus trichloride to the appropriate aldehyde or ketone or by reduction of an appropriate α-keto derivative to the hydroxy derivative, followed by conversion of the hydroxy group to a halo-substituent, and (b) the reduction of a variety of nitrogen derivatives of α-keto-phosphonic acids. The choice between the various possibilities is conditioned primarily by the availability of the necessary intermediates.

(1) Michaelis and Benzinger, *Ann.*, **188**, 275 (1877).

(2) Bauer, THIS JOURNAL, **63**, 2137 (1941).

There are two additional preparatory methods for amino-phosphonic acids which, however, appear to be rather limited in scope. The conversion of dichlorosphosphites of methylolamides into the corresponding dichlorides of acylated aminomethanephosphonic acid[3] is limited to the aminomethane acid. The other is the Hofmann degradation of the C-amide of the appropriate phosphonocarboxylic acid, which method was used by Finkelstein[4] to prepare β-aminoethanephosphonic acid. This procedure gives satisfactory results with the simpler members of the class but may be limited in the application to derivatives sensitive under the conditions of the Hofmann reaction.

The typical procedures are presented in the experimental part.

Experimental

I. Amino-aromatic Phosphonic Acids

A. Phosphanilic Acid.—The method used by Bauer[2] needs only the comment that for the preparation of larger amounts of the product, the use of a hydrogenation apparatus of 2–3 liter capacity is to be preferred over the use of sealed tubes.

B. *p*-Aminobenzylphosphonic Acid.—*p*-Nitrobenzylphosphonic acid[5] (20 g.) was suspended in 75 cc. of water and was brought into solution by the addition of dilute sodium hydroxide solution to *p*H 9. This solution was treated with 42 g. of sodium sulfide nonahydrate ($Na_2S\cdot 9H_2O$) in 100 cc. of water and was heated for one hour to 90–95°. The cooled solution was carefully acidified by hydrochloric acid, evaporated to dryness and the precipitate extracted with 50 cc. of concentrated hydrochloric acid. The acid filtrate was diluted to 80 cc. and treated with 25% sodium hydroxide until just acid to congo red. The *p*-aminobenzylphosphonic acid was filtered off upon cooling; yield was 65%. The acid is a pale yellow powder, which melts with decomposition at 323–325°, and is amphoterically soluble.

Anal. Calcd.: N, 7.4. Found: N, 7.29, 7.56.

II. Aminoaliphatic Phosphonic Acids

A. 2-Aminoethane Phosphonic Acid.—β-Bromoethylphthalimide (39 g.) and triethyl phosphite (26 g.) were heated to 160° for four and one-half hours in an apparatus described earlier[6]; approximately 80% of the theoretical amount of ethyl bromide was collected in the receiver. The residual oil was shaken out with 25 cc. of hexane and was treated with 150 cc. of 48% hydrobromic acid. The mixture was refluxed for five hours and cooled. The

(3) J. Pikl, U. S. Patents 2,304,156 and 2,328,358.

(4) Finkelstein, THIS JOURNAL, **68**, 2397 (1946).

(5) Litthauer, *Ber.*, **22**, 2144 (1889).

(6) Kosolapoff, THIS JOURNAL, **66**, 109 (1944).

phthalic acid precipitate was filtered off and the filtrate was evaporated to constant weight by an infrared lamp. The viscous brown residue was taken up in 100 cc. of ethyl alcohol and was treated slowly with a slight excess of aniline to precipitate 2-aminoethanephosphonic acid, which after recrystallization from 50% alcohol, was obtained in 50% over-all yield in the form of tiny plates which resinify at 265° and melt at 285°. Finkelstein's product[4] is reported to melt at 281–282°.

B. α-Amino-α-phenylethanephosphonic Acid.—α-Chloro-α-phenylethanephosphonic acid[7] (89.5 g.) was added, with stirring and cooling, to 500 cc. of concentrated ammonium hydroxide contained in a one-liter round bottomed flask. The stoppered flask was allowed to stand for two weeks at room temperature. The suspension was filtered by suction to yield 63 g. of crude ammonium salts of the corresponding hydroxy derivative, which were not investigated further. The mother liquor from the above was evaporated to dryness. The residue was treated with 25 cc. of water and was carefully acidified by hydrochloric acid to yield 10 g. of α-amino-α-phenylethanephosphonic acid, as tiny colorless flakes. This was dissolved in 1:1 hydrochloric acid and precipitated by 20% sodium hydroxide at congo red end-point. Yield was 10 g. (12%); m. p. 214–215° (with some decomposition).

Anal. Calcd.: N, 6.96. Found: N, 6.75, 6.92.

C. α-Aminobenzylphosphonic acid ("Phenylphosphonoglycine").—Diethyl benzoylphosphonate[8] readily yields the *p*-nitrophenylhydrazone, m. p. 126°, and the 2,4-dinitrophenylhydrazone, m. p. 171–172°, on heating with the corresponding hydrazines in alcohol.

The distillation of the ester is attended by decomposition at the end of the distillation, when appreciable amounts remain in the still; this was felt to be the reason for the rather low yield of the phosphonate. Accordingly, the crude reaction mixture, after removal of traces of residual triethylphosphite and benzoyl chloride under reduced pressure, was taken up in 300 cc. of ethanol containing an equimolar amount of *p*-nitrophenylhydrazine. The solution was refluxed for one hour and cooled, to yield 55% of the *p*-nitrophenylhydrazone in the first crop. Evaporation of the mother liquor gave 34% additional product. Recrystallization from alcohol gave 85% pure hydrazone, m. p. 126°. Ten grams of the hydrazone in 250 cc. of ethanol was treated with hydrogen, which was slowly bubbled through the solution in the presence of 2% palladium–charcoal catalyst, for two hours. The pale yellow solution was filtered, and the filtrate concentrated to 25 cc. This residue was treated with a solution of 21.4 g. of $Na_2S \cdot 9H_2O$ in 100 cc. of water and heated to 90–95° for two hours. On cooling, 150 cc. of concentrated hydrochloric acid was added to the dark solution, the precipitated sulfur was filtered off and the mixture was refluxed for four hours, with gradual concentration to about 100 cc. Fifty cubic centimeters of concentrated hydrochloric acid was then added and the solution was evaporated to dryness by an infrared lamp. The residue was extracted with 150 cc. of warm ethanol and the extract was neutralized with aniline to yield 4 g. of α-aminobenzylphosphonic acid, which after recrystallization from 90% ethanol, formed almost colorless fine flaky crystals, which decomposed at 165°. The product was however contaminated with traces of the aniline salt, no means having been found for a satisfactory purification.

Anal. Calcd.: N, 7.5. Found: N, 7.9, 8.0.

D. ω-Aminopropanephosphonic Acid.—Forty grams of 3-bromopropanephosphonic acid was dissolved in the smallest amount of water and added slowly to ice-cold, stirred, concentrated ammonium hydroxide (1 liter). The mixture was allowed to stand for two weeks, after which it was filtered and the filtrate was evaporated to dryness. After acidification with concentrated hydrochloric acid, evaporation to dryness and extraction of the solid residue with ethanol, the extract was neutralized with aniline to yield 10 g. (36.5%) ω-aminopropanephosphonic acid, which after recrystallization from dilute ethanol, formed colorless needles, which resinified and melted at 274°.

Anal. Calcd.: N, 10.05. Found: N, 9.72, 9.65.

Summary

The available methods of synthesis of aminophosphonic acids are discussed and the examples of their applications are given.

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(7) Conant and Coyne, THIS JOURNAL, **44**, 2530 (1922).

(8) Kabachnik and Rossiiskaya, *Bull. Acad. Aci. U. S. S. R., cl. sci. chim.*, 364–374 (1945); *C. A.*, **40**, 4688[5] (1946).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Reaction of the Dioxane–Sulfotrioxide Reagent with Aniline. Classification of the Sulfamic Acids

BY CHARLES D. HURD AND NORMAN KHARASCH[1]

Reaction of the dioxane–sulfotrioxide reagent with aniline has been mentioned[2] as resulting in the formation of phenylsulfamic acid ($C_6H_5NHSO_3H$). Our interest in the possible existence of this acid in the free state led us to study this reaction in some detail.

The sulfonation of aniline with one molar proportion of dioxane–sulfotrioxide was carried out in carbon tetrachloride solution at ice-bath temperatures. The product proved to be a mixture of phenylammonium phenylsulfamate with a smaller proportion of sulfanilic acid.

In accord with the work of Suter and co-workers,[2] we believe that the first product of the reaction is phenylsulfamic acid; but that this does not exist as such, and stabilizes itself by forming the phenylammonium salt. The formation of phenylammonium phenylsulfamate, under these conditions, agrees with the work of Wagner,[3] who obtained it by sulfonation of aniline with pyridine–sulfotrioxide. Willcox,[4] using dimethylaniline–sulfotrioxide, obtained analogous results. The simultaneous formation of sulfanilic acid was not reported, however, by these earlier workers. The product of reaction of aniline with dioxane–sulfo-

(1) Present address: University of Southern California, Los Angeles, Calif.

(2) Suter, Evans and Kiefer, THIS JOURNAL, **60**, 538 (1938).

(3) Wagner, *Ber.*, **19**, 1157 (1886).

(4) Willcox, *Ann. Chem. J.*, **32**, 459 (1904).