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BASE-INDUCED REARRANGEMENT AND ELIMINATION OF 2-HALO-SUBSTITUTED 1-AMINOETHANE-1,1-DIPHOSPHONIC ACIDS

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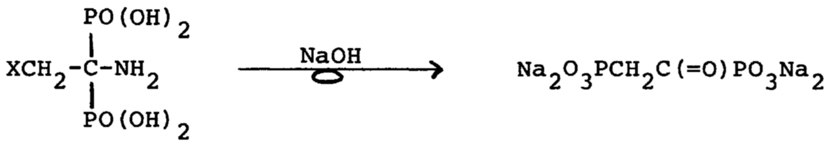
A base-induced rearrangement involving a 1,2-shift of a phosphono group from carbon to carbon was found in 2-halo-substituted 1-aminoethane-1,1-diphosphonic acids. In 2,2-dichloro-substituted 1-aminoethane-1,1-diphosphonic acid, each of the geminal phosphono groups underwent a 1,2-shift and an elimination, respectively, to give phosphonoacetic acid.

Rearrangement of organophosphorus compounds involving a 1,2-shift of a phosphono[$-PO(OH)_2$] group from carbon to carbon has recently attracted considerable interests.$^{1)}$ We now report a new base-induced rearrangement of 2-halo-substituted 1-aminoethane-1,1-diphosphonic acids($\underline{\underline{1}}$) and the same rearrangement accompanied by a fragmentation of 2,2-dichloro-substituted 1-aminoethane-1,1-diphosphonic acid.$^{2)}$

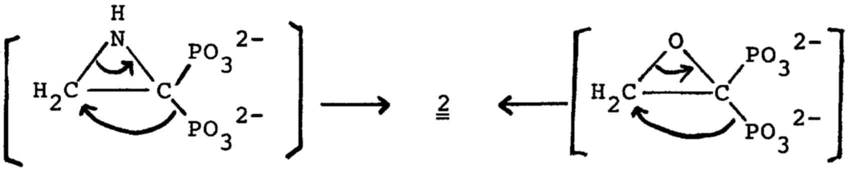
Three grams of 1-amino-2-chloroethane-1,1-diphosphonic acid was treated with 100 ml of 1M aqueous solution of NaOH with stirring at room temperature. Ammonia gas was evolved. The solution was evaporated under reduced pressure. The oily residue crystallized on cooling. Recrystallization from 1:1 water-acetone mixture gave 3.3 g (85%) of hydrated tetrasodium 1-oxoethane-1,2-diphosphonate($\underline{\underline{2}}$). Found: C, 7.35; H, 1.29; P, 20.79%. Calcd for $C_2H_4O_8P_2Na_4$: C, 7.55; H, 1.30; P, 19.98%. ^1H and ^{31}P NMR and IR spectral data were identical with those reported in the literature.$^{1a)}$ Analogous rearrangements were observed for the fluoro- and bromo-substituted derivatives.



$$XCH_2C(NH_2)(PO(OH)_2)_2 \xrightarrow{NaOH} Na_2O_3PCH_2C(=O)PO_3Na_2 \quad (1)$$

1(X= F, Cl, Br) 2

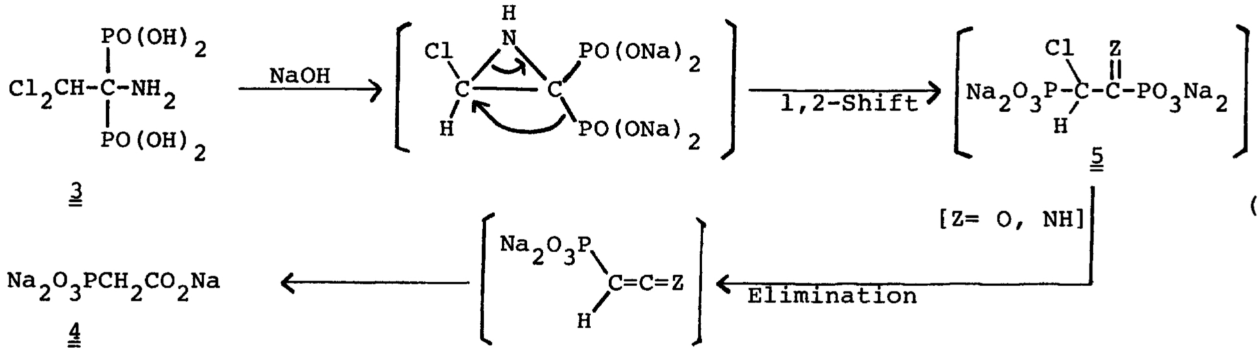
It is well known that the fragmentation of 2-haloalkane-1-phosphonic acid in aqueous solution of NaOH yields the corresponding alkene, phosphoric acid, and halide.[3] But under the same conditions, 1 was readily dehydrohalogenated to give 2, wherein one of the geminal phosphono groups had undergone a 1,2-shift. This $PO(OH)_2$ group migration to the neighbouring carbon seems to be assisted by an amino group in a similar manner as a hydroxy group in the base-induced rearrangement of 2-chloro-1-hydroxyethane-1,1-diphosphonic acid.[1a]



(2)

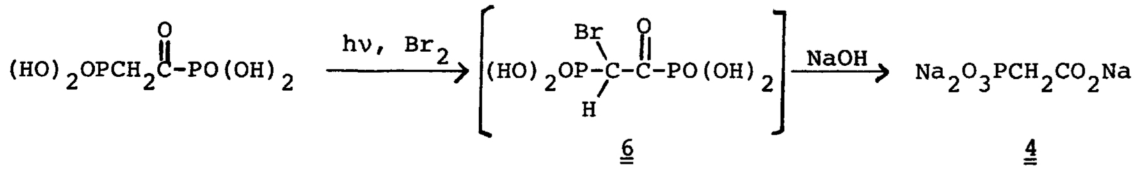
Moreover, we found a novel fact that 1-amino-2,2-dichloroethane-1,1-diphosphonic acid(3, 3.0 g) was transformed to trisodium phosphonoacetate(4) on treatment with 100 ml of 1M aqueous solution of NaOH in a similar manner as above. The aqueous solution of 4 was acidified with conc. HCl and evaporated under reduced pressure. Ethanol was added to the residue, and the precipitated NaCl was filtered. The filtrate was evaporated. The residue was recrystallized from acetic acid to give 1.5 g of the free acid of 4, which was identified by comparing its melting point[142-143°C] and ^1H NMR spectrum[$\delta(D_2O)$: 2.52 (d, J_{PCH} 8.2 Hz)] with an authentic sample prepared by other method.[4]

It may be reasonable to consider that this reaction proceeds in two stages. The first stage involving a 1,2-shift of one of the geminal $PO(OH)_2$ groups, which will take a path similar to that of the base-induced rearrangement of 1 to 2, gives an intermediate(5). The second stage may consist of a fragmentation of 5, which is similar to a fragmentation of 2-haloalkane-1-phosphonic acid to an unsaturated compound. The resulting ketene and/or ketenimine derivatives, being very sensitive to water, would instantly be converted to 4.



(3)

An evidence favoring this scheme was provided by our observation. Namely, 1-bromo-2-oxoethane-1,2-diphosphonic acid(6),[5] derived from a free acid of 2(1.0 g) by photobromination, was successfully decomposed *in situ* by treatment with 30 ml of 1M aqueous solution of NaOH to give 0.9 g of 4 (89%).



(4)

It is most of interest that one of the geminal $PO(OH)_2$ groups in 1-aminoethane-1,1-diphosphonic acids with a halogen atom at 2-position underwent a 1,2-migration, and each of the geminal $PO(OH)_2$ groups in the acid with two chlorine atoms at 2-position underwent a 1,2-migration and an elimination respectively.

A full account of this work will be published elsewhere.

References and Footnotes

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2) These aminodiphosphonic acids were prepared in the following manner. A mixture of phosphorus trichloride(27.4 g, 0.2 mol) and phosphonic acid(16.4 g, 0.2 mol) was stirred at 60°C until the viscous and homogeneous solution was formed. Then, the mixture was cooled to room temperature, and the corresponding nitrile (0.1 mol) was added dropwise with stirring. The reaction mixture was allowed to stand for an additional hour and poured into cold water(150 ml). The solution was evaporated to dryness under reduced pressure. After the addition of water(300 ml) to the residue, the solution was re-evaporated to dryness to expel the residual hydrochloric acid. When the solution was concentrated to one-fourth of its original volume, the product precipitated as a white crystalline precipitate. This was filtered and recrystallized from water.

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5) Although 1-bromo-2-oxoethane-1,2-diphosphonic acid(6) could be isolated, it did not precipitate as crystals. Beilstein's Test strongly indicated the presence of halogen atoms.

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