OXIDATION OF 1-AMINOALKYLIDENE-1,1-DIPHOSPHONIC ACIDS BY BROMINE IN BICARBONATE

I. S. Alfer'ev, I. L. Kotlyarevskii,
and N. V. Mikhalin

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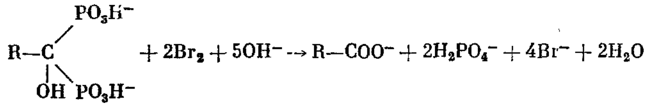
It is known [1] that 1-hydroxyalkylidene-1,1-diphosphonic acids are oxidized quantitatively by bromine in bicarbonate solutions to carboxylic acids and phosphate:

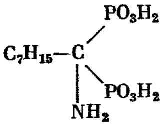


$$R-C(PO_3H^-)(OH)(PO_3H^-) + 2Br_2 + 5OH^- \rightarrow R-COO^- + 2H_2PO_4^- + 4Br^- + 2H_2O$$

Information on the mechanism of the reaction is not given in [1]; however, it is noted that some condensation products of 1-hydroxyalkylidenediphosphonic acids which do not contain a free OH group in the α position with respect to the P atom are stable toward the action of bromine. This fact points to an important role of the OH group in this reaction.

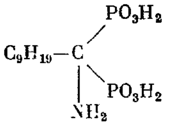
For clarification of the role of the α substituent in such reactions, the study of oxidation of 1-aminoalkylidene diphosphonic acids, which are similar in structure, under these same condition, seems to be useful. Literature data dealing with this problem are absent.

With this aim, we have studied the oxidation of 1-aminooctylidene-1,1-diphosphonic (I) and 1-aminodecylindene-1,1-diphosphonic (II) acids by bromine in $KHCO_3$ solution at room temperature:



$C_7H_{15}-C(PO_3H_2)_2(NH_2)$

(I)



$C_9H_{19}-C(PO_3H_2)_2(NH_2)$

(II)

Under the conditions mentioned, the acids (I) and (II) are oxidized by bromine with great speed, ~2 moles of bromine are consumed per 1 mole of acid. However, the end products of oxidative dephosphorylation, instead of the carboxylic acids expected in analogy with the reaction of amides given above, proved to be nitriles. The formation of nitriles in aqueous medium is at least unusual, since, as a rule, dehydrating agents are used for their preparation. During the oxidation of (I), caprylonitrile is obtained with 57% yield, and during the oxidation of (II), caprinitrile with 39% yield. The identical nature of the nitriles obtained with known specimens we demonstrated by the methods of GLC and IR spectroscopy, and in the case of caprylonitrile, in addition, by comparison of physical constants of the specimen. Yields of the nitriles proved to be far from stoichiometric, although the starting aminodiphosphonic acids entered into the reaction completely and were not found in the reaction mixtures after oxidation. Neither were the expected secondary products, carboxylic acids and their amides, found. Phosphate and surface-active substances, the structures of which we did not establish, were contained in the aqueous layers after extraction of the nitriles. This substance was not successfully isolated from the acidified oxidate of acid (I) in a form suitable for analysis. Caprylic acid was found among the products of acid hydrolysis of this substance. It is important to note that the reaction of oxidation of (I) and (II) with bromine does not proceed in acid medium and stops even upon reduction of the pH to 4-5.

For explanation of the formation of nitriles during the oxidative dephosphorylation of 1-aminoalkylidenediphosphonic acids, one of the possible schemes of reaction can be suggested:

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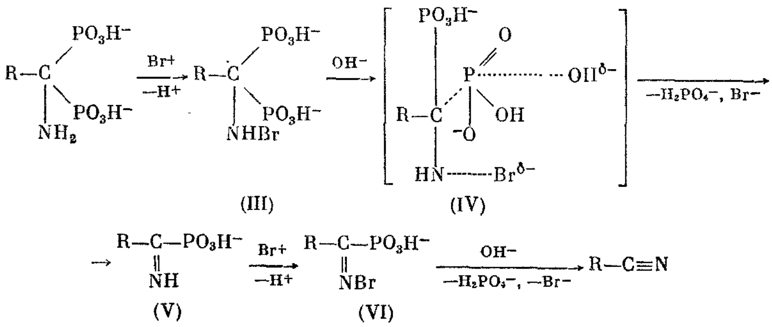
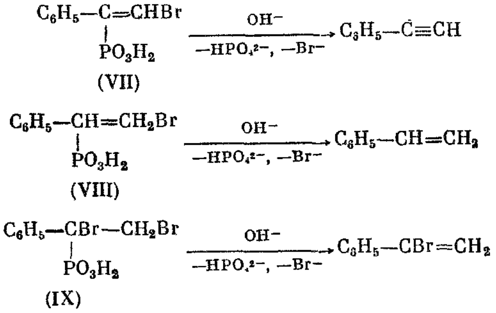


According to the scheme, the first stage of the reaction is electrophilic bromination of the amino group of the original acid, the possibility of which under the conditions of the reaction is confirmed by the results of [2], where different N-halogen amines were obtained under similar conditions. The N-bromoamine (III) which forms is later subjected to bimolecular 1,2-elimination under the action of the base (most probably OH^- ion) and, splitting off $H_2PO_4^-$ and Br^- ions, gives the imine (V), which again is subjected to electrophilic bromination, forming the N-bromoimine (VI). The last, eliminating $H_2PO_4^-$ and Br^- ions, in the end forms the nitrile.

The structure of the transitional complex (IV) of the elimination reaction which we have proposed is analogous to the structure of the transitional complex in normal bimolecular 1,2-elimination reactions, for example, dehydrohalogenation and dehydration. Although in the literature we have not found a demonstration of the existence of elimination in which the phosphonate group plays the role of the electrophilic leaving particle, results exist [3] which to a significant degree confirm the possibility of such a reaction. In [3] it was observed that, in alkaline medium, 2-bromo-1-phenylethenylphosphonic acid (VII) forms phenylacetylene, 2-bromo-1-phenylethenylphosphonic acid (VIII) forms styrene, and 1,2-dibromo-1-phenylethylphosphonic acid (IX) forms α-bromostyrene, splitting off phosphate and bromide ions:



(VII)

$$C_6H_5\underset{PO_3H_2}{\underset{|}{C}}{=}CHBr \xrightarrow[-HPO_4^{2-},\ -Br^-]{OH^-} C_6H_5{-}C{\equiv}CH$$

(VIII)

$$C_6H_5\underset{PO_3H_2}{\underset{|}{CH}}{=}CH_2Br \xrightarrow[-HPO_4^{2-},\ -Br^-]{OH^-} C_6H_5{-}CH{=}CH_2$$

(IX)

$$C_6H_5\underset{PO_3H_2}{\underset{|}{CBr}}{-}CH_2Br \xrightarrow[-HPO_4^{2-},\ -Br^-]{OH^-} C_6H_5{-}CBr{=}CH_2$$

The absence of information about the structure of the secondary products of the reaction does not allow us to make any suggestions in regard to the path of its formation.

For confirmation or disproof of the proposed scheme, further studies are necessary. If the proposed scheme is successfully confirmed, then by analogy, with a high degree of probability, an analogous scheme will be suggested (with the initial formation of hypobromite) for the oxidation of 1-hydroxyalkylidene-1,1-diphosphonic acids.

EXPERIMENTAL

Gas–liquid chromatographic analysis was carried out on Chrom-3 apparatus, column 1 m × 6 mm, with 0.5% Apiezon on glass, nitrogen gas carrier, flame-ionization detector. Thin-layer chromatography was carried out on plates of Siluful. For the phosphorus-containing products, the system enanthic acid–25% aqueous NH_3–water–methanol (7 : 7 : 16 : 4 by volume) was used, with development by spraying with a mixture of 0.04 ml saturated aqueous $FeCl_3$, 2 g of salicyclic acid, 50 ml of water, and 3 ml of pyridine. For products not containing phosphorus, the system $CHCl_3$–CH_3OH (3 : 1 by volume) was used, with development in an iodine chamber.

1-Aminoalkylidene-1,1-diphosphonic Acids (I) and (II). The acids were obtained by the modified method of [4], mixing 0.1 mole of the appropriate nitrile, 0.3 mole of PBr_3, 0.12 mole of H_3PO_3, and 40 ml of dioxane during cooling by ice. The mixture was stirred 3 h at ~20° to homogenization, left 5 days, dissolved in AcOH, left 1 day more, poured into water, and for hydrolysis of the condensed products was held 7 h on a steam bath in an open cup. Then the mixture was diluted with isopropanol, and the 1-aminoalkylidene-1,1-diphosphonic acids were filtered off and carefully washed with boiling isopropanol. Yield of (I) was 65%; results of pH-metric titration: found: eq_2 145.0; calculated: eq_2 144.6. Yield of (II) 63%; found: eq_2 163.4; calculated: eq_2 158.6. Found: C 37.83; H 8.25%. Calculated for $C_{10}H_{25}NO_6P_2$: C 37.86; H 7.94%. Acids (I) and (II) were chromatographically pure. The application of the method of [5] for synthesis of (I) and (II) gives significantly poorer results.

Oxidation of Acids (I) and (II). To a mixture of 1.45 g (5 mmoles) of (I), 7.0 g of $KHCO_3$, and 6 ml of water during intense stirring at ~20°, 0.5 M solution of Br_2 in 10% aqueous KBr was added dropwise. Decolorization of the Br_2 occurred immediately, and in this case CO_2 was evolved and drops of an organic phase were formed. After the addition of 20 ml (10 mmoles) of the Br_2 solution, the decolorization stopped. To the mixture was added another 5 ml of the Br_2 solution, held 15 min, and extracted with hexane. The hexane extract was dried over K_2CO_3, filtered, and the solvent distilled off in vacuum. The amount of 0.36 g (57%) of caprylonitrile was obtained. The product (GLC, 60°) did not contain volatile impurities. The IR spectrum of this product did not show noticeable absorption in the regions 1650-1690 and 3200-3600 cm^{-1}, which are characteristic for amides. After sublimation in vacuum, 0.31 g of a product was obtained which was identical with a known specimen of caprylonitrile, bp 70-72° (10 torr), compare [6, 7]. IR spectrum (CCl_4): 2260 cm^{-1} (CN).

The aqueous phase was acidified with HCl to pH of 0 and extracted with hexane in order to find caprylic acid. Extracted substances were not found in the hexane layer. Then the aqueous phase was extracted with ether, the ether was distilled off, and an uncrystallized syrupy product was obtained which was easily soluble in water. This was hydrolyzed with 5% HCl for 5 h at boiling point. Among the hydrolysis products, caprylic acid was found by the TLC method but noticeable amounts of caprylamide were not found.

A mixture of 0.32 g (1 mmole) of (II), 1 g of $KHCO_3$, 1.5 ml of water, and 6 ml of 0.5 M Br_2 solution being introduced into the reaction mixture, after extraction with hexane, drying, and distilling off of the hexane, 0.06 g of caprylonitrile was obtained which did not contain volatile impurities (GLC, 80°), yield 39%. The IR spectrum ($-C\equiv N$ 2255 cm^{-1}) was identical with the spectrum of a known specimen. Carrying out the reaction in this case was complicated by frothing of the solution, and extraction of the nitrile by strong emulsification. In order to stratify the emulsion, the mass was held 40 min at 40°.

CONCLUSIONS

The unusual reaction of dephosphorylation of 1-aminoalkylidene-1,1-diphosphonic acids by bromine in bicarbonate solutions, leading to the formation of nitriles, has been observed.

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