

SYNTHESIS AND CHARACTERIZATION OF TRISODIUM PHOSPHONETRIACETATE*

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A new carboxyphosphine ligand, which is the phosphorus analogue of nitrilotriacetic acid, was synthesized from phosphorus trichloride and the Reformatsky reagent followed by hydrolysis of the ester formed. It was isolated as the trisodium salt, $\text{P}(\text{CH}_2\text{COONa})_3 \cdot 2 \text{H}_2\text{O}$, which is stable in the air and soluble in water. The free acid was obtained only in solution. The ligand was characterized by a number of methods and its properties necessary for study of the coordination behaviour were established.

Phosphinetriacetic acid, $\text{P}(\text{CH}_2\text{COOH})_3 = \text{H}_3\text{X}$, represents the last member of the series of carboxyphosphines with the general formula $(\text{C}_6\text{H}_5)_{3-n}\text{P}(\text{CH}_2\text{COOH})_n$. The first two members of the series ($n = 1, 2$) were described in previous papers¹⁻³. According to the literature, attempts to synthesize the last member have so far been unsuccessful⁴⁻⁹. Its trimethyl ester was obtained from phosphorus trihalides and organometallics bearing carboxymethyl groups⁴⁻⁶; the hydrolysis of the ester, however, is not complete⁶. Another precursor of phosphinetriacetic acid is formed in the reaction of phosphorus tribromide with some enamines⁷. Attempted hydrolysis of the carbenium salts formed was accompanied by extensive P—C bond cleavage and characterizable products could be obtained only after oxidation to phosphine oxide⁸. The phosphine halide — bromozincethyl acetate reaction (which is obviously general and was used successfully in the synthesis of phenylphosphine-diacetic acid²) seemed to proceed in a complicated manner with phosphorus trichloride⁹ and the triethyl ester of phosphinetriacetic acid which was believed to be formed was seriously contaminated and could not be purified. The only product obtained using this method was the crystalline phosphine oxide triester after oxidation of the crude reaction mixture with gaseous oxygen⁹. Other possible methods for the synthesis of phosphinetriacetic acid include alkylation of alkaline phosphide¹⁰ and reduction of phosphine oxide with silanes leaving the carbonyl unchanged^{11,12}.

This work was carried out to test various methods for the synthesis of the desired ligand. After some modifications, the method of Kirtz⁹ was found to be the most

* Part XI in the series Compounds Structurally Related to Complexones; Part X.: This Journal 43, 2853 (1978).

advantageous. The structure of the product obtained and its potential complexing ability were investigated.

EXPERIMENTAL

Phosphorus trichloride and ethyl bromoacetate were fractionated before use. Solvents were purified and deaerated by standard methods. Deuterium oxide with isotopic purity of 99.5% and a 20% solution of DCl in D₂O were the products of Alfa Inorganics. Other chemicals were C.P. products from Merck and Lachema.

The apparatus and methods used were described in previous papers^{1,2}. NMR spectra were taken on Varian HA-100 (¹H, 100.1 MHz) and Varian XL-100 (³¹P, 40.5 MHz) instruments. Thermal decomposition in the air was followed on a Derivatograph instrument.

The microdetermination of C, H and P was supplemented by the iodometric titration of P(III) with starch indicator. The equivalent weight of the acid was found by titration with sodium hydroxide either visually with phenolphthalein indicator or using Gran's method¹³. Sodium was determined argentometrically as sodium chloride after exchange on a Dowex-2 column (Cl-form). The purity of the samples was checked by TLC (silica gel, solvent systems: CHCl₃-MeOH 10:1 for esters and CHCl₃:i-PrOH:NH₃:H₂O 10:10:1:1 for acids).

Ligand Synthesis

In pure dry nitrogen, 750 ml of absolute ether was refluxed under stirring with 200 g of zinc chips (3.06 mole) and 0.3 g of iodine was added. After decoloration, the addition of 3 ml of ethyl bromoacetate resulted in slight opalescence of the ether indicating the start of the reaction. Without external heating, the total amount of 330 ml of ethyl bromoacetate (3.02 mole) was added at a rate necessary to keep the ether boiling vigorously. The reaction mixture was then stirred for one hour under reflux and a further 450 ml of ether was added. At -25°C to -30°C, the solution of 79 ml of phosphorus trichloride (0.90 mole) in 100 ml of ether was added dropwise. After warming to room temperature with stirring, the excess organometallic was destroyed by adding 100 ml of water with cooling. The ether layer was washed under nitrogen successively with 500, 300, 200 and 100 ml of water and dried over sodium sulphate. The ether was removed under reduced pressure to leave 130 g of the crude triethyl ester of phosphinetricetic acid. The product was vacuum distilled in amounts of 10–15 g* to yield 61.3 g of the light yellow liquid (yield 23.3%) which is oxidized rapidly in the air to give the corresponding phosphine oxide⁹.

For P(CH₂COOC₂H₅)₃ (C₁₂H₂₁O₆P, m.w. 292.3) calculated: 49.31% C, 7.24% H, 10.60% P; found: 49.11% C, 7.32% H, 10.83% P.

56.4 g of the ester (0.193 mole) was dissolved under nitrogen in 450 ml of ethanol and a solution of 27 g NaOH (0.675 mole) in 300 ml of water was added. After standing at 0°C overnight, two layers separated. The lower layer was treated with 1500 ml of absolute ethanol, the crystalline precipitate was collected, washed with absolute ethanol and ether and dried at 25°C/130 Pa. A white crystalline powder (39.2 g, total yield 15.3%) with m.p. 304–306°C (dec.) was obtained.

For P(CH₂COONa)₃ · 2 H₂O (C₆H₁₀O₈Na₃P, m.w. 310.1) calculated: 23.24% C, 3.25% H, 9.99% P, 22.24% Na; found: 22.94% C, 3.42% H, 10.25% P, 9.81% P(III), 22.50% Na.

* The heating is connected with partial decomposition; when larger amounts were used, the initial loss of vacuum completely stopped the distillation. Using 10–15 g, the main part of the sample distilled at 171–173°C (260 Pa, bath temperature 200–210°C) after an initial temporary pressure increase to 1 kPa.

RESULTS AND DISCUSSION

After testing a number of other possible methods, the described procedure was chosen as giving the best results. Comparable yields of the trisodium salt were also obtained from the ester⁹ $\text{O}=\text{P}(\text{CH}_2\text{COOC}_2\text{H}_5)_3$ after reduction with trichlorosilane¹¹, but the purity of the product was less satisfactory.

Other solvent systems were also tried for the hydrolysis of $\text{P}(\text{CH}_2\text{COOC}_2\text{H}_5)_3$. Hydrolysis in 96% ethanol is incomplete as an insoluble intermediate separates out. The precipitate is $\text{P}(\text{CH}_2\text{COONa})_2\text{COOC}_2\text{H}_5$ as was confirmed by the IR spectrum⁶. In aqueous ethanol, no solubility complications occur and the hydrolysis is fast and complete.

All attempts to obtain crystalline free acid led to uncharacterizable products. The main methods tried included acidification with a strong mineral acid followed by extraction with various solvents, precipitation of the slightly soluble barium salt and its metathesis with the calculated amount of sulphuric acid, ion exchange, *etc.* All these methods yield solutions of H_3X in water or polar organic solvents.

The trisodium phosphinetriacetate dihydrate is stable in the air and fairly soluble in water. On heating, it is first dehydrated between 60 and 110°C to give the stable anhydrous salt. A complicated decomposition begins to take place around 300°C in accordance with the observed m.p.

The IR and NMR spectra of the triethyl ester and trisodium salt display characteristic bands of carboxyphosphines⁶.

$\text{P}(\text{CH}_2\text{COOC}_2\text{H}_5)_3$: 442 w $\nu(\text{PC})$, 595 m, 738 w, 891 w, 943 w, 1033 m, 1119 s $\nu_s(\text{COC})$, 1270 vs $\nu_{\text{as}}(\text{COC})$, 1380 w, 1410 w $\delta(\text{CH}_2)$, 1472 w $\delta(\text{CH}_3)$, 1732 vs $\nu(\text{C}=\text{O})$, 2885 vw $\nu_s(\text{CH}_3)$, 2915 vw vs $\nu(\text{CH}_2)$, 2950 w $\nu_{\text{as}}(\text{CH}_2)$, 2992 m $\nu_{\text{as}}(\text{CH}_3)$.

$\text{P}(\text{CH}_2\text{COONa})_3 \cdot 2 \text{H}_2\text{O}$: 445 m $\nu(\text{PC})$, 504 w, 568 mb, 725 w, 781 w, 832 w, 868 w, 928 m, 1060 m, 1138 s, 1204 m, 1375 vs $\nu_s(\text{COO})$, 1428 w $\delta(\text{CH}_2)$, 1595 vs $\nu_{\text{as}}(\text{COO})$, 1620 sh $\delta(\text{H}_2\text{O})$, 2920 sh $\nu_s(\text{CH}_2)$, 2950 m $\nu_{\text{as}}(\text{CH}_2)$, 3300 s, vb $\nu(\text{H}_2\text{O})$; (w = weak, m = medium, s = strong, v = very, sh = shoulder, b = broad).

Similarly, the NMR spectra correspond to the proposed structure: $\text{P}(\text{CH}_2\text{COOC}_2\text{H}_5)_3$: ^1H (CDCl_3 , against tetramethylsilane): CH_3 1.26 ppm triplet ($J = 7$ Hz, 9.3 H), OCH_2 4.16 ppm multiplet ($J = 7$, 5.9 H), PCH_2 2.69 ppm doublet ($J = 3.5$, 3.8 H). ^{31}P (acetone- d_6 , against 85% H_3PO_4): +34.7 ppm multiplet ($J_{\text{PH}} = 4$).

$\text{P}(\text{CH}_2\text{COONa})_3 \cdot 2 \text{H}_2\text{O}$: ^1H (D_2O against tert-BuOH): CH_2 1.25 ppm singlet, HDO 3.46 ppm singlet. ^{31}P (D_2O , against 85% H_3PO_4): +30.7 ppm singlet ($J_{\text{PH}} < 2$).

In solution the X^{3-} anion successively binds three protons to give the free acid. The corresponding equilibria were studied in water and 50% v/v dioxane by the pH-titration method at $25 \pm 0.1^\circ\text{C}$ and $I = 0.1$ (NaClO_4). The titration curves were treated by the MINQUAD program¹⁴ which minimizes the sum of the squared

residual concentrations $U = \sum(\Delta c_i)^2$. The final values of the logarithms of the stability constants (three times their standard deviations) of the complexes HX^{2-} , H_2X^- and H_3X are 5.43 (0.02), 9.20 (0.02), 11.93 (0.03) for aqueous solutions and 7.16 (0.02), 12.26 (0.04), 16.37 (0.04) for 50% dioxane. The reliability of these constants is illustrated by the value of the R -factor, $R = \sum \Delta c_i / \sum c_i$, which is equal to 0.016 (water, 211 data points) and 0.019 (50% dioxane, 132 data points).

The mechanism of the successive proton bonding was elucidated from the IR spectra of Na_3X in deuterium oxide at various acidity values¹⁵. The regions corresponding to the antisymmetrical stretching of dissociated carboxyl (around 1580 cm^{-1}) and of undissociated carboxyl (around 1720 cm^{-1}) were studied. From the spectra it follows that the protons are bound to carboxyls whereas the phosphorus atom is not protonized. Hence, phosphinetriacetic acid differs from its higher homologue – phosphinetripropionic acid^{16,17}, the first proton of which is bound to the lone electron pair of phosphorus to form a betain structure. The evident reason for this difference is the inductive effect of the carboxyls¹⁸ which lowers the basicity of phosphorus in phosphinetriacetate more effectively because of the separation of the carboxyl and phosphorus by only one methylene group.

The low basicity of phosphorus in H_3X is also reflected in a low affinity for further protons. Protonization occurs only in strong acid where changes in the far UV

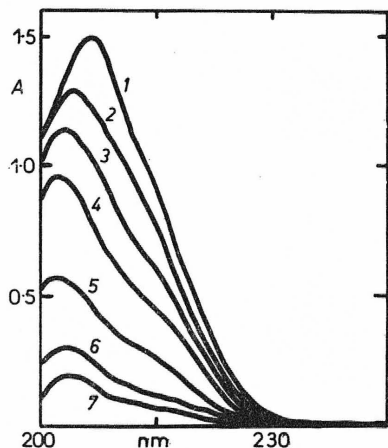


FIG. 1

The UV Spectrum of $5 \cdot 10^{-4}\text{M-Na}_3\text{X}$ in 1 cm cells

1 pH 9.5 to 0.48M-HClO₄; 2 1.014M;
3 1.555M; 4 2.00M; 5 2.92M; 6 3.54M; 7 4.84 to
8.0M-HClO₄.

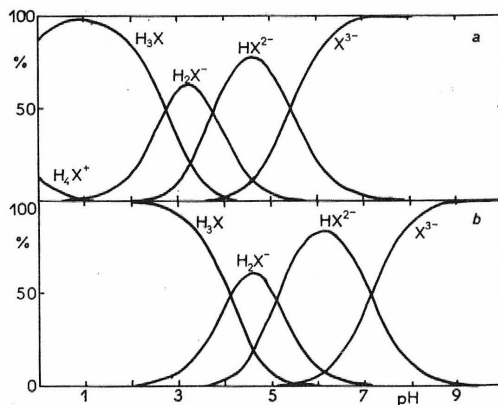


FIG. 2

Distribution Diagrams of the Acidobasic Forms of the Ligand

a water, b 50% dioxane.

spectra typical for the protonization of phosphorus^{1,2} occur. The spectra depicted in Fig. 1 can be interpreted in terms of equilibrium $H_3X + H^+ \rightleftharpoons H_4X^+$. The constant $K_0 = [H_4X^+]/[H_3X][H^+]$ is a linear function of the ionic strength (*i.e.* strong acid concentration) according to the relationship $K_0 = -0.36 + 0.50 I$. Analogous measurements in 50% dioxane could not be carried out because of the proximity of the absorption edge of the solvent.

Hence, phosphinetriacetic acid in solution displays pronounced amphoteric behaviour; the distribution of the acidobasic forms is depicted in Fig. 2. The ligand is potentially multidentate and capable of bonding through phosphorus and carboxyls. Work on its coordinating behaviour is in progress.

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