Dihydrogen Tetrametaphosphate, \([\text{P}_{4}\text{O}_{12}\text{H}_{2}]^{2–}\):

Synthesis, Solubilization in Organic Media, Preparation of

The MIT Faculty has made this article openly available. **Please share**
how this access benefits you. Your story matters.

| Citation | Jiang, Yanfeng, et al. “Dihydrogen Tetrametaphosphate, \([\text{P}_{4}\text{O}_{12}\text{H}_{2}]^{2–}\):
| As Published | http://dx.doi.org/10.1021/JA5058339 |
| Publisher | American Chemical Society (ACS) |
| Version | Final published version |
| Accessed | Fri Apr 05 00:29:44 EDT 2019 |
| Citable Link | http://hdl.handle.net/1721.1/113228 |
| Terms of Use | Article is made available in accordance with the publisher’s policy and may be subject to US copyright law. Please refer to the publisher’s site for terms of use. |
| Detailed Terms | |
Dihydrogen Tetrametaphosphate, $[P_4O_{12}H_2]^{2-}$: Synthesis, Solubilization in Organic Media, Preparation of its Anhydride $[P_4O_{11}]^{2-}$ and Acidic Methyl Ester, and Conversion to Tetrametaphosphate Metal Complexes via Protonolysis

Yanfeng Jiang,‡ Khetpakorn Chakarawet,† Andrea Laura Kohout,‡ Matthew Nava,‡ Nadia Marino,§,¶ and Christopher C. Cummins*†

†Department of Chemistry, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, United States
‡Dipartimento di Chimica e Tecnologie Chimiche, Università della Calabria, via P. Bucci 14/c, 87036 Rende, (CS), Italy
§Department of Chemistry, Syracuse University, Syracuse, New York 13244-4100, United States

Supporting Information

ABSTRACT: Dihydrogen tetrametaphosphate $[P_4O_{12}H_2]^{2-}$ (1) can now be synthesized and isolated as its PPN salt ([PPN]$^+ = [N(PPh_3)_2]^+$) via treatment of $[PPN]_4[P_4O_{12}]$ with trifluoroacetic anhydride in wet acetone; this simple procedure affords the oxoacid salt in 94% yield. A $pK_a$ of 15.83 ± 0.11 in acetonitrile was determined. $[P_4O_{11}H_2]^{3-}$ reacts with the dehydrating agent $N,N'$-dicyclohexylcarbodiimide to afford tetrametaphosphate anhydride $[P_4O_{11}]^{2-}$ (2) in 82% yield, also as the PPN salt. From 2 a monohydrogen tetrametaphosphate ester $[P_4O_{10}(OH)(OMe)]^{2-}$ (3, 96%) was derived by addition of methanol, illustrating that 2 can function as a reagent for chemical phosphorylation. Addition of water to 2 regenerates 1 quantitatively. Deprotonation of 1 by metal amides in the +2 oxidation state led to the unconventional monomeric tin(II) $\kappa^6$ tetrametaphosphate $[Sn(P_4O_{12})]^2-$ (4, 78%, a molecular analog of SnO) and binary dimeric chromium(II) bis($\mu_2$-$\kappa^2$) derivative $[Cr_2(P_4O_{14})]^4-$ (5, 82%). Structural data stemming from single-crystal X-ray diffraction studies for the PPN salts of anions 1–5 are also reported.

The study of cyclic phosphates was initially undertaken almost two centuries ago coinciding with the advent of modern chemistry. The early interest in this fundamentally important research area has not yet translated into a modern field of vigorous activity, although applications in materials science and conventional coordination chemistry have been reported sporadically. This class of molecules, the cyclic phosphates, is also strongly implicated in prebiotic chemistry. Recognizing that a significant opportunity for the expansion of cyclic phosphate chemistry could be realized by synthesizing an organic-media soluble acid form of tetrametaphosphate, we set out to investigate if a convenient entry point into this domain could be identified. Herein, we report a simple and high-yielding procedure for the preparation of a previously unknown organosoluble form of dihydrogen tetrametaphosphate, which is demonstrated to be a potent precursor not only to its corresponding anhydride and methyl ester but also to metal tetrametaphosphates. This is a powerful new strategy in cyclic phosphate chemistry: the synthesis of tetrametaphosphate metal complexes via protonolysis.

In their work identifying the key intermediate in ATP synthetic routes developed by Todd and Khorana, Glonek, Kleps, and Myers (GKM) definitively characterized cyclic adenosine triphosphate which rapidly decomposed to ATP upon contact with water. GKM concluded that “it is likely that trimetaphosphate esters including that of adenosine will be found only in a nonaqueous milieu, such as the lipid portions of cell organelles.” The requirement of anhydrous media for the preparation of cyclic phosphate esters is universal not only in the synthesis of phosphate nucleosides but also in previous attempts to access the acid forms of cyclic phosphates. In 1956, Griffith reported that under furnace conditions the reaction of phosphoric acid with sodium dihydrogen phosphate afforded cyclic phosphate acids. However, an unrefined structure was reported, and there was an ensuing debate on the composition of the obtained polycrystalline form. Structurally well-characterized cyclic phosphate acids are a tetraakis(3,5-xylidinium) dihydrogen cyclohexaphosphate dihydrate and a sodium monohydrogen trimetaphosphate.

Why are the acid forms of metaphosphate rings so rare? One reason could be associated with their essentially strong acidity, as implicated by the titration of sodium tri- and tetrametaphosphate with nitric acid. Following the “anhydrous principle,” we investigated whether a lipophilic organic cation, such as $[PPN]^+$ ([PPN]$^+ =$ bis(triphenylphosphine)iminium), could facilitate access to dihydrogen tetrametaphosphate in nonaqueous media by protonation of its tetrametaphosphate salt with a strong acid. Treatment of $[PPN]_4[P_4O_{12}]$·5H$_2$O$^{3f}$ with 1 equiv of trifluoroacetic anhydride in acetone at £23 °C resulted in the formation of a single new cyclic phosphate species 1, which exhibits a singlet resonance at $-25.6$ ppm in its $^{31}$P$^1$ H NMR spectrum. Upon addition of a dehydrating agent such as DCC (DCC = $N,N'$-dicyclohexylcarbodiimide) to the reaction mixture, the $^{31}$P$^1$ H NMR
NMR spectrum displayed two triplet signals at −24.4 and −32.5 ppm in an A2B2 spin system, characteristic for the small ultraphosphate [P4O12H2]2− (2, Scheme 1).15 These results suggest that 1 is the oxoacid dianion dihydrogen tetrametaphosphate [P2O12H2]3−. Indeed, we were able to isolate the PPN salt of 1 as an analytically pure solid in 94% yield. The presence in 1 of acidic P−OH groups is evidenced by a broad singlet at 14.03 ppm in the 1H NMR spectrum recorded in CD3CN at 23 °C. However, in solution these terminal acidic hydrogens are mobile; this being a general property of hydrogen-bonded oxoacids.16 The behavior of 1 is reflected in its 31P{1H} NMR spectrum which displays a single singlet resonance.

It should be emphasized that the synthesis of 1 is so facile that the reaction can be carried out on gram scales under open air conditions using commercial solvents and reagents as received. Trifluoroacetic acid reacts with H2O from either the solvent or [PPN]2[P4O12]-·5H2O to in situ generate trifluoroacetic acid (TFA), which can then protonate [P4O12]4−. Acetone was identified as the most convenient solvent as it delivers a simple purification process. The simplicity of the purification procedure in acetone is primarily attributed to the lower solubility of [PPN]2[1] (this precipitates out of or crystallizes from the reaction mixture) relative to the byproduct [PPN]-·[CF3COO]. It should be noted that strong Bronsted acids such as TFA, trichloric acid, and triflic anhydride also react with [P4O12]4− to afford 1 in good isolated yields. In comparison, no formation of 1 was observed when [P4O12]4− was treated with a weaker Bronsted acid such as acetic acid.

The solid-state structure of [PPN]2[1] was established using single-crystal X-ray diffraction, and the resulting model of the dianion in C2 symmetry is depicted in Figure 1. The hydrogen atoms (placed at calculated positions and refined using a riding model) are arranged in a mutual 1,5 disposition. The most prominent feature is the presence of intramolecular hydrogen bonds between the protons and neighboring P−O−hydrogen-bond acceptors showing a short O21⋯O12A distance of 2.731(5) Å.17 Such hydrogen-bonding interactions may contribute to the stability of 1 in both the solid state and in organic solvents. The P−OH bond length of 1.5096(19) Å is intermediate between the long bridging P−O distances and the short external P−O distances.

Dihydrogen tetrametaphosphate 1 is not stable in aqueous solution in that it generates an acidic medium in which the formation of linear phosphates and phosphoric acid can be detected by 31P{1H} and 1H NMR spectroscopy. However, 1 shows significant stability toward H2O in organic solvents such as acetonitrile and acetone, as no decomposition was detected after 48 h at 23 °C for an acetonitrile solution of 1 containing 50 equiv of H2O. The dianionic character of 1 serves to inhibit nucleophilic attack at the phosphorus atoms. Such an anion stabilization effect is commonly observed in the chemistry of general anionic phosphate diesters.18

The instability of 1 in aqueous solution hampers measurement of its acidity in water. Nevertheless, the pK1a of 1 in acetonitrile was determined by UV−vis spectrophotometric titration of [PPN]2[P4O12H2] coupled with 2,4-dinitrophenol (pK1a = 16.66 in MeCN) as a chromophore.19 A pK1a value of 15.83 ± 0.11 was thereby obtained for 1 in acetonitrile, corresponding to an intermediate acidity between that of TFA (pK1a = 12.65 in MeCN) and acetic acid (pK1a = 3.51 in MeCN),20 this being in agreement with the experimental observation that 1 can be prepared by protonation of tetrametaphosphate with TFA but not with acetic acid.

We further pursued the isolation of the observed small ultraphosphate 2.15 It was reported to be an important intermediate in the hydrolysis of P4O1021 and a key phosphorylating precursor to esters of orthophosphate and linear polyphosphate.22 However, neither an isolation procedure nor structural characterization was available until now.23 The reaction of 1 with a stoichiometric amount of DCC in acetonitrile led to the quantitative formation of 2 (as its PPN salt), which was isolated as an analytically pure solid in 82% yield after removing the byproduct dicyclohexylurea (DCU) that precipitated from the reaction mixture. Since ultraphosphate was originally defined as an infinite cross-linked polymer of high viscosity,15,24 2 would be more aptly described as the anhydride of dihydrogen tetrametaphosphate.

The solid-state structure of 2 was established via an X-ray diffraction study and is shown in Figure 1. The two negatively charged terminal phosphates are bent away from each other probably due to electrostatic repulsion making the two six-membered rings of the bicyclic structure that share a P1−O3−P3 bridge adopt boat and chair conformations.

Treatment of 2 with acetonitrile (H2O content ≤0.5 w/w%) at 23 °C regenerates 1 in quantitative in situ yield and in a 68% isolated yield. The reaction likely occurs via nucleophilic attack of H2O with concomitant rupture of the phosphoanhydridic P1−O3−P3 bridge. In a similar manner, the P1−O3−P3 bridge of 2 can also be cleaved by other hydroxy nucleophiles such as methanol, in that case yielding an acidic tetrametaphosphate methyl ester (Scheme 2). The reaction of 2 with 50 equiv of methanol at 23 °C afforded within 30 min the quantitative formation of methanolysis product [P4O10(OH)(OMe)]2− (3). The 31P{1H} NMR spectrum of 3 revealed a triplet at −24.6 ppm.

Figure 1. Solid-state molecular structures of [P4O12H2]3− (1) and [P4O12]4− (2) with ellipsoids at the 50% probability level.
(Scheme 3). 119Sn NMR spectroscopy revealed a singlet at 800.57 ppm, consistent with the coordination of the cyclic phosphate to the tin center. As the reaction generates only the volatile HN(SiMe3)2 as byproduct, the PPN salt of [PPN]2[Sn(P4O12)] could still be achieved at room temperature within 24 h. Although the existence of the so-called "ethyl metaphosphate" (Langheld ester) has been reported,25 compound 3 now represents the first example of a structurally characterized metaphosphate ester (Figure 2).

Figure 2. Solid-state molecular structure of [P4O10(OH)(OMe)]2− (3) with ellipsoids at the 30% probability level.

In the structure of 3 (Figure 2), the hydroxyl and methyl residues are located on opposing phosphoryl residues and intramolecular O−H···O hydrogen bonding17 between the hydroxyl and neighboring P−O− bond is indicated, with a O32···O21 distance of 2.617(9) Å.

Since 1 can be delivered in anhydrous form and is soluble in organic solvents, it is uniquely suitable for synthesizing metal tetrametaphosphate complexes by protonolysis leading to replacement of simple basic ligands. Moreover, due to its diacidic nature 1 is commensurate for reaction with metals in the +2 oxidation state. Herein we tested the reactivity of 1 with a pair of metal(II) bis(hexamethyldisilazide) complexes leading to exemplary binary metal(II) tetrametaphosphate systems.

The reaction of [PPN]2[1] with 1 equiv of Sn(HMDS)2 (selected as a representative p-block metal amide, HMDS = hexamethyldisilazide) in acetonitrile at 23 ℃ afforded within 15 min a new species 4 showing a singlet in its 31P{1H} NMR spectrum at −23.54 ppm, which is slightly downfield from that of 1 (Scheme 3). 119Sn NMR spectroscopy revealed a singlet at 800.57 ppm, consistent with the coordination of the cyclic phosphate to the tin center. As the reaction generates only the volatile HN(SiMe3)2 as byproduct, the PPN salt of 4 was easily isolated as analytically pure solid with the formula [PPN]2[Sn(P4O12)] in 78% yield. The structure of anion 4 was established by an X-ray diffraction study to be the C4v symmetric tin(II) κ4 tetrametaphosphate (Figure 3). The tin vertex is centered above the four-membered face consisting of four oxygen atoms, resulting in a tetragonal pyramidal geometry. The Sn−O distances were found to be in the range of 2.187(6) to 2.2240(16) Å. The O−Sn−O angles between neighboring phosphates are quite similar to each other varying from 78.6(2) to 75.90(4)°.

Previous reports of tin(II) in a similar C4v all-oxygen binding site were focused upon tungstostannate(II) heteropolyanions26 and tridentate alkoxyl tin(II) clusters.27 In fact, the solid-state tin(II) oxide SnO has tin(II) in nearly an identical C4v environment consisting of four oxide ions as reported by Moore and Pauling,28 making 4 an excellent molecular mimic of a known solid oxide material. To the best of our knowledge, 4 also represents the first example of κ4 tetrametaphosphate coordination to a metal. The lone pair electrons at the tin(II) center are expected to be localized in an orbital very rich in s character in view of Bent’s rule considerations.29

We further examined the reactivity of 1 toward the d-block metal(II) amide Cr(HMDS)2(THF)2.30 Addition of 1 equiv of [PPN]2[1] to a purple-brown solution of Cr(HMDS)2(THF)2 at 23 ℃ rapidly afforded a pale-green solution. The 31P{1H} NMR spectrum of this new species is silent in the phosphate region, suggesting that the tetrametaphosphate is coordinated to a paramagnetic chromium(II) center. After workup, a pale-gray solid was isolated in 82% yield. The solid-state structure of 5 was identified as a binary chromium(II) tetrametaphosphate dimer [Cr2(P4O12)2]+ (5, Scheme 3, Figure 3) by X-ray diffraction. Each chromium adopts a square planar configuration. The Cr···Cr distance of 2.9020(13) Å suggests a very weak Cr···Cr interaction.
interaction. Compound 5 represents the first example of a binary metal(II) tetrametaphosphate dimer. In the case of most other $\kappa^2$ tetrametaphosphate complexes, such as those bearing $d^0$ Rh and Ir centers, typically only one tetrametaphosphate ligand is involved with two metal moieties bonded on either side of the $P_2O_4$ mean plane. However, an example of the $M_2(P_4O_{12})_2$ configuration observed here for anion $S$ with approximate $D_{2d}$ symmetry has been reported previously for titanium. We have described a simple preparative procedure for an organic-media soluble salt of the strong Brønsted acid $[P_4O_{12}]^{2−}$. The development of the chemistry of cyclophosphates was very significant in the 1930s, but their full potential was not realized until the 1970s, and it has been shown that they can be used as precursors to numerous derivatives. The use of available free of charge via the Internet at http://pubs.acs.org.

The authors declare the following competing interest(s): A provisional patent containing the material in this paper has been filed by MIT.

**REFERENCES**

(1) “The development of the chemistry of cyclophosphates was very slow, spreading along almost two centuries”. Quote from André Durif, ref 32; see also references therein.


