

Does an '*L*-arginine doped orthophosphoric acid' crystal exist?

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Abstract

The reactive nature of aqueous orthophosphoric acid (H_3PO_4) towards *L*-arginine (*L*-Arg), to form a phosphate salt namely *L*-arginine phosphate monohydrate (LAP), rules out the doping of any *L*-arginine into H_3PO_4 . Hence, the reported claim of growth of '*L*-arginine doped orthophosphoric acid' crystals by Saradha et al (K. Saradha, S. Bangaru, G. Muralidharan, Thermoluminescence, optical absorption, photoluminescence, FT-IR and XRD studies on *L*-arginine doped orthophosphoric acid, J. Lumin. 142 (2013) 184-188)) is untenable.

Keywords: *L*-arginine; orthophosphoric acid; *L*-arginine phosphate monohydrate; *L*-arginine doped orthophosphoric acid.

1. Introduction

The study of non-centrosymmetric crystals is a frontier area of research and hence many groups are working on the crystal growth and characterization of new compounds, which can find applications in non-linear optics (NLO). The naturally occurring α -amino acids are known to form several compounds with many inorganic and organic reagents for example mineral and organic acids due to the reactivity characteristics of the amino ($-NH_2$) or the carboxylic acid ($-COOH$) functional groups of the amino acids. The compounds thus obtained crystallize in non-centrosymmetric space groups in view of the chiral nature of the starting α -amino acids (excepting glycine) and thus possess non-linear properties. This has prompted several new research groups to venture into the above type of work by employing amino acids as reagents for new product syntheses. However, some researchers claiming growth of a new NLO material do not take into consideration some simple facts for example

i) the quantity as well as the reactivity characteristics of the reagents used for new compound formation ii) reported literature on the crystals under study and related compounds iii) proper interpretation of spectroscopic (IR, UV-Vis) and structural (X-ray) data and report incorrect data. Several such erroneous reports were brought to the attention of the scientific community by Fleck and Petrosyan in a case study of salts of amino acids [1]. In spite of publication of this case study describing in detail the several difficulties in the crystal growth and characterization of NLO materials, more cases of incorrect claims continue to appear in the literature in the area of crystal growth of NLO materials [2-14]. The recent report by Saradha *et al* [15] titled '*Thermoluminescence, optical absorption, photoluminescence, FT-IR and XRD studies on L-arginine doped orthophosphoric acid*' is one such erroneous paper. While the terminology '*L-arginine doped orthophosphoric acid*' gives an impression that the authors of [15] have doped (incorporated) small amounts of *L-arginine* into the crystal structure of orthophosphoric acid, the work described does not concern with growth of any doped crystals as will be shown below.

2. What can be incorporated into the crystal structure of orthophosphoric acid?

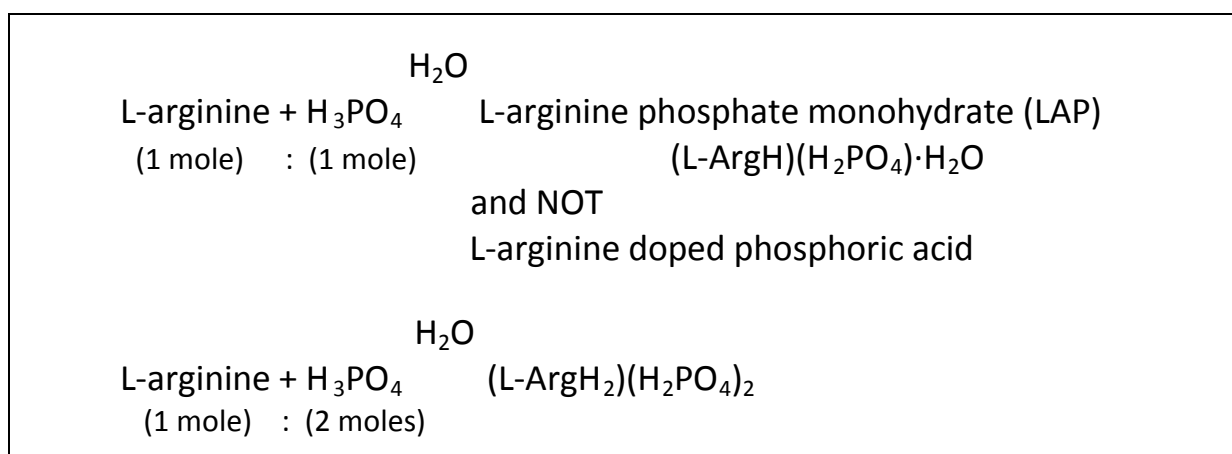
In a recent paper I have shown the usefulness of structural chemistry principles to determine beforehand, which atom or ion or molecule can be incorporated into the known crystal structure of a compound [14]. Using this approach, the structure of orthophosphoric acid (H_3PO_4) is first analyzed to predict which ion or molecule can be incorporated into the crystal structure of H_3PO_4 . Orthophosphoric acid represented by the formula H_3PO_4 is a low melting solid (m.p. 42.35°) and is a tetrahedral molecule with the P atom at the centre of the tetrahedron. If some H atoms in the crystal structure are substituted by D, a partially deuterated phosphoric acid viz. $\text{H}_{3-x}\text{D}_x\text{PO}_4$ can be obtained which is an example of incorporation (doping) of D atoms for the H atoms. A similar case can be made out for the substitution of P by As. The incorporation of any neutral molecule in orthophosphoric acid

will have to occur in the interstitial space of the crystalline H_3PO_4 , which exhibits a H-bonded layer structure in which each $\text{PO}(\text{OH})_3$ tetrahedron is linked to six others by weak (O-H \cdots O) H-bonds [16]. The well-known crystalline compound $\text{H}_3\text{PO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$ which contains half mole of the neutral molecule namely H_2O per mole of H_3PO_4 , is not called as a water doped phosphoric acid crystal but is referred to as phosphoric acid hemihydrate. The crystal structure of the hemihydrate consists of two unique tetrahedral H_3PO_4 molecules and a H_2O molecule which are linked into a three-dimensional H-bonded network [17]. To the best of my knowledge no neutral molecule has been incorporated in the crystal structure of orthophosphoric acid so far, resulting in a doped crystal of formula $(\text{H}_3\text{PO}_4) \cdot \text{X}_n$ (X = neutral molecule; $n < 1$) excepting the recent claim of doping of *L*-arginine [15], which can be ruled out based on the chemistry of H_3PO_4 and *L*-Arg.

3. Reactivity characteristics of orthophosphoric acid towards *L*-arginine

Aqueous solutions of phosphoric acid are always used in the laboratory, the commonly used reagent being 85% H_3PO_4 , which is a commercially available form of phosphoric acid. In aqueous solution, H_3PO_4 behaves as a medium-strong acid. The property of *L*-Arg to function as a base is well documented by its reaction with different acids forming salts [18-20]. The acid-base reactions of aqueous H_3PO_4 with the amino acid *L*-arginine which has two available sites for protonation namely guanidyl and α -amino group, has been well studied. In these reactions small amounts of H_2O_2 are added to prevent microbe formation for isolation of crystals and the product depends on the mole ratio of *L*-Arg: H_3PO_4 (Scheme 1). Use of equimolar quantities results in the formation of the salt *L*-arginine phosphate monohydrate (LAP) of composition $(\text{L-ArgH})(\text{H}_2\text{PO}_4) \cdot \text{H}_2\text{O}$ crystallizing in the monoclinic space group $P2_1$ [18, 19]. In contrast, use of two or more moles of H_3PO_4 results in the formation of an anhydrous solid of composition $(\text{L-ArgH}_2)(\text{H}_2\text{PO}_4)_2$ crystallizing in the orthorhombic space group $P2_12_12_1$ [20]. Thus it can be seen that the reactive nature of H_3PO_4 towards *L*-Arg in

aqueous medium to form a mono or bis dihydrogenphosphate salt rules out formation of any doped crystalline product of formula $(\text{H}_3\text{PO}_4) \cdot (\text{L-arginine})_n$ ($n \leq 1$) containing free phosphoric acid. In view of the above mentioned chemistry, the so called '*L*-arginine doped phosphoric acid' cannot actually exist and hence such a crystal can never be grown from an aqueous solution. Therefore, the synthetic protocol (reaction scheme) reported in [15] showing a free phosphoric acid for the product crystal is conceptually wrong.



Scheme 1

4. On the non-existent '*L*-arginine doped orthophosphoric acid' crystal

The authors of [15] who claim to have doped *L*-arginine into orthophosphoric acid have unfortunately not taken into consideration the well-known acid-base chemistry of these reagents used for the crystal growth. It is not clear if the use of the term '*L*-arginine doped orthophosphoric acid' is an unintentional error or a statement of the authors to claim that a novel doped crystal different from the known LAP crystal has been grown. It is noted that these authors have cited the work in this area by Monaco *et al* [18] which describes the synthesis of LAP and the paper by Petrosyan *et al* [20] reporting on the anhydrous 1:2 compound $(\text{L-ArgH}_2)(\text{H}_2\text{PO}_4)_2$. In addition, the work of Premkumar *et al* [21] reporting growth of pure and urea or thiourea doped LAP crystal without any substantiation for the so called doping was also cited. However, the doping of urea or thiourea in LAP also appears to

be incorrect based on a structural analysis of LAP which does not have any interstitial space to accommodate urea or thiourea. Saradha et al [15] have described in detail how their crystal growth method is different from that of the authors of [21]. The above facts clearly show that the authors of [15] were very well aware of the formation of LAP from aqueous solutions of H_3PO_4 and *L*-Arg. Hence it is not clear as to why these authors claim to have grown a doped crystal employing a synthetic method known to give crystals of a phosphate salt. The authors compare the IR spectrum of their so called doped crystal with that of LAP which is incorrectly referred to as *L*-arginine phosphate indicating that this crystal is anhydrous thus causing more confusion. Several inconsistencies are noted in the work of Saradha et al, some of which are discussed below.

5. Inconsistencies in the paper by Sarada et al [15]

The authors state under the heading experimental techniques, '*L-Arginine doped orthophosphoric acid single crystals were grown using slow evaporation techniques at room temperature. L-Arginine and orthophosphoric acid were taken in the equimolar ratio and dissolved in excess water ...*' However, the authors actually employed 40 g each of *L*-Arg and H_3PO_4 which amounts to 1:1.78 mole ratio if solid H_3PO_4 was used and not equimolar ratio of H_3PO_4 :*L*-Arg. If instead the commercial 85% H_3PO_4 had been used then the ratio will be 1:1.5 mole. From such a reaction stoichiometry, a mixture of 1:1 (LAP) and the 1:2 product reported by Petrosyan *et al* [20] can be expected. The reported infrared spectrum indicates that the sample used for this study is LAP and not $(L\text{-ArgH}_2)(\text{H}_2\text{PO}_4)_2$. However most of the assignments of the bands for example 409 and 1406 cm^{-1} for N-H stretching, 1598 cm^{-1} for C-H stretching, bands below 1000 cm^{-1} for carboxylate vibrations and band at 1129 cm^{-1} for carbonyl stretching are incorrect.

The compound discussed under the heading X-ray diffraction analysis is LAP (but not the doped crystal), where the authors claimed that they determined the structure and stated, '*The*

structure of LAP was solved by the direct method and refined by the full matrix least squares fit technique employing the SHELXL program. The X-ray data of LAP single crystal is presented in Fig. 4. It is observed that LAP is orthorhombic in structure with space group of $P2_12_12_1$. The lattice parameter values $a = 10.89 \text{ \AA}$, $b = 7.91 \text{ \AA}$, $c = 7.34 \text{ \AA}$ are in good agreement with the reported values'. By the phrase 'full matrix' the authors probably meant full matrix. However the structure determination is not supported by any other refinement results (for example CIF file) and hence this result is unacceptable. It is not clear why an X-ray powder pattern is referred to as X-ray data of LAP single crystal. For the Sohncke space group $P2_12_12_1$ the value of Flack parameter [22] is not listed, and one wonders how the space group can be reported without solving the structure. The claim of the authors that the lattice parameter values are in agreement with reported values (namely Ref. 20 in their paper which is also [20] here) is not only inappropriate but quite misleading because the values (only a , b , and c and not space group) actually agree with those for LAP (Table 1) reported in [19] but the space group for LAP is $P2_1$. The values in [20] are the cell data for the anhydrous 1:2 compound $L\text{-Arg}\cdot 2\text{H}_3\text{PO}_4$ reported by Petrosyan *et al* which crystallizes in $P2_12_12_1$. The claim of the authors 'Intense green light has been observed in Orthophosphoric acid sample was used as the reference material' appears to be incorrect because H_3PO_4 crystallizes in the centrosymmetric space group $P2_1/c$ and hence not expected to exhibit SHG [2-4].

Table 1. Unit cell data of LAP, *L*-arginine doped orthophosphoric acid and $L\text{-Arg}\cdot 2\text{H}_3\text{PO}_4$

| Compound | a (Å) | b (Å) | c (Å) | β (°) | Space Group | Ref |
|--|----------|----------|-----------|-------------|-------------------|------|
| <i>L</i> -arginine phosphate monohydrate (LAP) | 10.85(2) | 7.91(1) | 7.32(2) | 98.0(1) | $P2_1^{\#}$ | [19] |
| <i>L</i> -arginine doped orthophosphoric acid | 10.89* | 7.91* | 7.34* | -- | $P2_12_12_1^{\$}$ | [15] |
| $L\text{-Arg}\cdot 2\text{H}_3\text{PO}_4$ | 7.000(1) | 9.681(2) | 21.756(4) | 90 | $P2_12_12_1^{\#}$ | [20] |

*No esd's given; [#]Space group from structure determination; ^{\\$}No CIF file reported

4. Conclusions

In summary, it is shown that a so called ‘*L*-arginine doped phosphoric acid’ crystal cannot exist in view of the reactive nature of aqueous orthophosphoric acid (H_3PO_4) towards *L*-arginine (*L*-Arg).

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