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In fact, *L*-threonine

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Abstract

It is shown that three papers published recently by Allen Moses *et al*. on "*L*-threoninium phosphate", "*L*-threoninium sodium fluoride" and "*L*-threoninium tartrate" are completely erroneous. In fact, only crystals of *L*-threonine were obtained in all cases.

Keywords: *L-threoninium phosphate; L-threoninium sodium fluoride; L-threoninium tartrate; L-threonine; improper characterization; misinterpretation*

Graphical abstract:

L-threonine + Sodium fluoride → L-threonine
and NOT
L-threoninium sodium fluoride

Highlights

- *L*-threoninium phosphate (**I**) is in fact *L*-threonine
- *L*-threoninium sodium fluoride (**II**) is in fact *L*-threonine
- *L*-threoninium tartrate (**III**) is in fact *L*-threonine
- **I** to **III** were improperly characterized due to misinterpretation of experimental data

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Introduction

In contrast to other amino acids, only very few salts are known for *L*-threonine (*L*-Thr) which include the isostructural (*L*-ThrH)Cl and (*L*-ThrH)Br, $(L\text{-ThrH})_2SO_4.H_2O$ and (*L*-ThrH) picrate [1]. Although some reports on "*L*-threonine acetate", "*L*-threonine formate", "*L*-threonine diformate", "*L*-threonine zinc acetate", "*L*-threonine phthalate", "Urea *L*-threonine" and "*L*-threonine phosphate" have appeared in the literature, all these were proved to be *L*-threonine crystals and not any "new salts" as had been claimed [2-9]. *A priori*, the phosphate salt of *L*-threonine viz. $(L\text{-ThrH})H_2PO_4$ can exist, since such a salt $(DL\text{-ThrH})H_2PO_4$ has been reported for *DL*-threonine [10]. In a very early case study of salts of amino acids Fleck and Petrosyan had demonstrated that many amino acid salts reported in the literature are improperly characterized and identified typical errors in compound characterization for example characterizing a new crystal based on unit cell data and incorrect interpretation of spectral data [2]. The use of incorrect nomenclature for chemical name of crystals is another common error in many of these papers [2,7]. Despite the case study and several critical comments [2-9] erroneous papers continue to be published in the scientific literature especially in the area of nonlinear optical crystals. It has also been shown that an erroneous publication can serve as the basis for subsequent erroneous papers [3,9]. In this context we are disappointed to mention that a claim of Chinnappan et al of having grown crystals of *L*-threoninium phosphate [11] which has already been proved to be erroneous [7] happens to be the basis for a paper by Allen Moses *et al* on "*L*-threoninium phosphate" (**I**) [12] and two more papers by the same group on "*L*-threoninium sodium fluoride" (**II**) [13] and "*L*-threoninium tartrate" (**III**) [14]. We have titled our present manuscript as "In fact, *L*-threonine" because all three compounds (**I**), (**II**) and (**III**) are *L*-threonine as shown below.

Comments

"*L*-threoninium phosphate" (**I**) [12]

The report on (**I**) is based on the erroneous paper [11]. Although Allen Moses *et al* [12] write that the structure of the "*L*-threoninium phosphate" crystal was reported in [11] this is incorrect. Interestingly the authors of [11] were reporting on the phosphate ester *viz*. *O*- Phospho-*L*-threonine ($H_2O_3POCH(CH_3)CH(NH_2)COOH$) under the name "*L*-threonine phosphate" which actually is a salt of formula (*L*-ThrH)H_2PO_4. The incorrect name is not surprising because the authors considered possible the formation of a phosphate ester in an aqueous medium, as a result of the coupling reaction of the –OH group of L-Thr with H_3PO_4 resulting in release of a water molecule. However, the authors of [11] did not compare their unit cell parameters and space group with those of *O*- Phospho-*L*-threonine [15] considering their crystal as new. The *O*- Phospho-*L*-threonine is commercially available as a reagent. The space group *P*na2_1 indicated in the abstract of [11] cannot be correct because it is not compatible with the presence of optically active *L*-threonine in the structure of assumed crystal. In fact, the coincidence of the cell parameters, infrared spectrum and thermal curves indicates that the obtained crystal is *L*-threonine with space group *P*$2_12_12_1$ [7]. The authors of [11] tried to substantiate the presence of the phosphate group in the molecule by assigning several peaks in the spectrum of *L*-threonine to vibrations of the phosphate group, but it would be easier to compare the obtained spectrum with the spectrum of *L*-threonine. The report on (**I**) [12] is a typical occurrence of an erroneous paper based on another one and an example for incorrect nomenclature. However, the authors of [12] confuse phosphoric acid (H_3PO_4) with phosphorous acid (H_3PO_3). Moreover, they believe that the structure of phosphorous acid is $P(OH)_3$ instead of $(HO)_2PH(O)$. In result of this they believe that the obtained "*L*-threoninium phosphate" crystal is $(HO)_2POCH(CH_3)CH(NH_2)COOH$. The coincidence of the cell parameters, powder XRD pattern, infrared spectrum and thermal curves of "*L*-threoninium phosphate" crystal confirms beyond doubt that the obtained crystal is *L*-threonine.

"*L*-threoninium sodium fluoride" (**II**) [13]

The report on (**II**) is yet another example for both improper compound characterization and incorrect nomenclature. In this paper [13] the confusion begins in the title as the name for (**II**) is incorrect, the

correct / acceptable names being "*L*-threonine sodium fluoride" or "*L*-threoninium sodium difluoride". Although in the section on Materials synthesis and growth the authors write that *L*-threonine ($C_4H_9NO_3$) and sodium fluoride (NaF) were taken in 2:1 molar ratio, the reaction scheme $C_4H_9NO_3 + NaF \rightarrow [C_4H_9NO_3Na^+]F^-$ indicates otherwise suggesting the composition to be 1:1 *L*-Thr.NaF.

In the discussion of single crystal X-ray diffraction analysis, the authors provide lattice parameters and state that "*The unit cell parameters are in good agreement with the reported values [10]*". It could be assumed that the crystal was previously obtained in Ref. "[10]" quoted in [13]. Actually, the Ref. "[10]" quoted in [13] is the well-known paper [16] on *L*-threonine. Does this not mean that authors confirm the obtaining of "*L*-threoninium sodium fluoride" by agreement of cell parameters with those of *L*-threonine!? Hence, we do not find it surprising that the powder patterns of the two crystals (**I**) [12] and (**II**) [13] are the same; it is surprising that the authors of [12] and [13] did not notice this. Comparison of the IR spectra of (**I**) and (**II**) [12, 13] shows that in the spectrum of (**II**) a new peak appeared at 1703 cm^{-1}; all other peaks in both spectra are the same. We do not undertake to explain how this peak could appear. However, it will be interesting to know the explanations of the authors: "*A new peak at 1703 cm^{-1} due to the influence of sodium fluoride atoms present in LTSF crystal* [15]". Interestingly, in the table where peaks were assigned this band is missing. The Ref. "[15]" in [13] is quoted incorrectly, should be Optik 127 (2016) 1922-1925. Additionally, they write: "*The peak at 3168 cm^{-1} is due to NH_3^+ asymmetric stretching confirms bonding between Na-S atoms*…" and also "*The C-N double bond on the formation of LTSF is observed from N-C-N stretching band at 1480 cm^{-1}*". It is hard to imagine what kind of crystal structure the authors had in mind when they mentioned Na-S and N-C-N bonds. Moreover, a peak at 933 cm^{-1} is assigned to C-F stretching vibration. So, the authors assume that fluorine is not an anion but is covalently bonded to carbon atom.

In their discussion of Elemental analysis [13] the authors write: "*Energy dispersive X-ray (EDX) analysis is a most reliable method to identify the elements presence in the grown crystal*". About inappropriate use of EDX data for compound characterization see the Ref. [17]. According to [13] atomic percentage of C, O, F and Na are 40.9, 31.5, 10.4 and 9.7 respectively. Meanwhile calculated

atomic percentage of (**II**) are H(47.37), C(21.05), O(15.79), N(5.26), F(5.26), Na(5.26). Thus, the EDX data analysis does not confirm the composition of the crystal.

"*L*-threoninium tartrate" (**III**) [14]

The authors of [14] claim to have obtained their crystal from an aqueous solution containing equimolar quantities of *L*-threonine ($C_4H_9NO_3$) and *L*-tartaric acid ($C_4H_6O_6$) by slow evaporation. One might expect the formation of a salt *viz*. *L*-threoninium hydrogen *L*-tartrate $(C_4H_{10}NO_3)^+(C_4H_5O_6)^-$ or an adduct *L*-threonine.*L*-tartaric acid, if they interact with each other or a mixture of crystals of *L*-threonine and *L*-tartaric acid, if they do not interact. As described earlier for (**I**) the authors of [14] reporting on "*L*-threoninium tartrate" (**III**) had in mind not any crystals of the salt *L*-threoninium hydrogen *L*-tartrate $(C_4H_{10}NO_3)^+(C_4H_5O_6)^-$, but a neutral molecule $C_9H_{15}NO_7$ (HO-CH_2-CH(OH)-CH(NH_2)-C(O)-C(O)-CH(OH)-CH(OH)-C(O)-CH_3). It is not clear how an extra carbon can occur in the product when the reactants had a total of 8 carbons. As in the case of (**I**) the authors of [14] consider possible the formation of a neutral molecule in an aqueous medium as a result of a dehydration reaction. In this case one might expect a molecule having composition $C_8H_{13}NO_8$ and not $C_9H_{15}NO_7$. As discussed earlier for (**I**) and (**II**) the authors of [14] did not determine the structure of **III**. Instead, they limited themselves to determining the parameters of orthorhombic unit cell: a=5.157 Å, b=7.757 Å, c=13.636 Å. However, for new crystals, the determination of the unit cell parameters cannot substitute the determination of the crystal structure [18]. These unit cell parameters are in good agreement with those of (**I**) and (**II**) and *L*-threonine [16]. Thermal curves of (**III**) also in good agreement with those of (**I**) and (**II**). As in the case of the spectrum of (**II**) a new peak appeared at 1736 cm^{-1} in the spectrum of (**III**). All other peaks in the IR spectra of (**I**, **II**, **III**) are the same. Again, we do not undertake to explain how this peak could appear.

So, in this case also the obtained crystal (**III**) in fact is *L*-threonine. The authors of [12-14] can confirm this by determining the structures of the crystals of **I**, **II**, **III**.

Conclusions

In summary, the names given for (**I**), (**II**) and (**III**) are inconsistent with the proposed chemical formula. Crystals of "*L*-threoninium phosphate" (**I**), "*L*-threoninium sodium fluoride" (**II**) and "*L*-threoninium tartrate" (**III**) reported by Allen Moses et al. [12-14] are in fact crystals of *L*-threonine. Erroneous conclusions about their existence arose because of improper characterization and misinterpretation of experimental data.

Declaration of conflict of interest: None

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