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On the existence of "L-arginine acetamide"

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Abstract We argue that the "L-arginine acetamide" crystal reported by Anitha et al. (J Therm Anal Calorim 119:785–789, 2015) is actually the well-known monoclinic form of anhydrous L-arginine hydrochloride crystal.

Keywords L-Arginine acetamide · L-Arginine hydrochloride · Improper characterization

Comment

The authors of a recent paper [1] claim to have grown a so-called L-arginine acetamide crystal by the slow evaporation of an aqueous solution containing L-arginine (L-Arg) and acetamide in equimolar ratio. The name "L-arginine acetamide" means that the obtained crystal is a 1:1 adduct viz. L-Arg·CH_3CONH_2. However, the authors consider that they obtained a compound of formula $H_2NC(NH)NH(CH_2)_3CH(NH_2)CONH(CO)CH_3$ (Fig. 1), whose actual systematic name is *N*-acetyl-2-amino-5-guanidinopentanamide.

According to the authors of [1], the "L-arginine acetamide" crystal is monoclinic (space group $P2_1$) with $a = 20.29$ Å; $b = 5.18$ Å; $c = 9.54$ Å; $\beta = 91.68°$. These cell parameters differ from the reported data for L-arginine dihydrate and anhydrous L-arginine [2] as well as trigonal [3] and orthorhombic [4] forms of acetamide, indicating that the title crystal is different from either of the starting materials. The authors write: "*The crystal structure is elucidated using standard crystallographic procedure*." The determination of unit cell parameters can be considered as standard crystallographic procedure for identification of previously known crystals, but not for new crystals. For formulating new crystals, unit cell data are not enough and can lead to erroneous conclusions [5]. The authors provided also the infrared spectrum and thermogravimetric curves, which according to them confirm the composition and structure of the obtained crystal. We cannot agree with the authors in this point. Then, the authors added an erratum [6], where an alternate reaction scheme and a different formula ($H_2NC(CH_3)NC(NH)NH(CH_2)_3CH(NH_2)COOH$) were proposed for the title crystal (Fig. 2). The authors retained the earlier name "L-arginine acetamide" even though the systematic name for the proposed formula is (*E*)-2-amino-5-(3-(1-aminoethylidene)guanidino)pentanoic acid. The reaction scheme explaining the formation of the title crystal due to the coupling of the carbonyl group (>C=O) of acetamide with the $-NH_2$ group of the guanidine moiety of L-arginine forming an imine (Schiff base) is incorrect because Schiff base formation is a characteristic reaction of aldehydes or ketones and not that of an amide [7].

However, this reaction scheme contains the essential information, that is, the presence of HCl, which helped us to clear up what actually was obtained by the authors. The use of HCl can lead to formation of L-arginine hydrochlorides: L-Arg·HCl·H_2O (monoclinic), L-Arg·HCl (monoclinic) [8, 9], L-Arg·HCl (triclinic) [10], L-Arg·2HCl·H_2O (orthorhombic) [11, 12]. Triclinic L-Arg·HCl and orthorhombic L-Arg·2HCl·H_2O can be excluded, because obtained crystal is monoclinic. The crystal L-Arg·HCl·H_2O also can be excluded because obtained crystal decomposes above 200 °C. Comparison of unit cell

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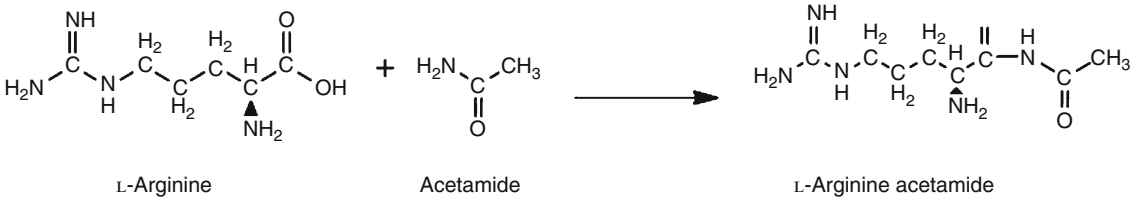

Fig. 1 Reported reaction scheme for "L-arginine acetamide" in [1] (reproduced with permission)

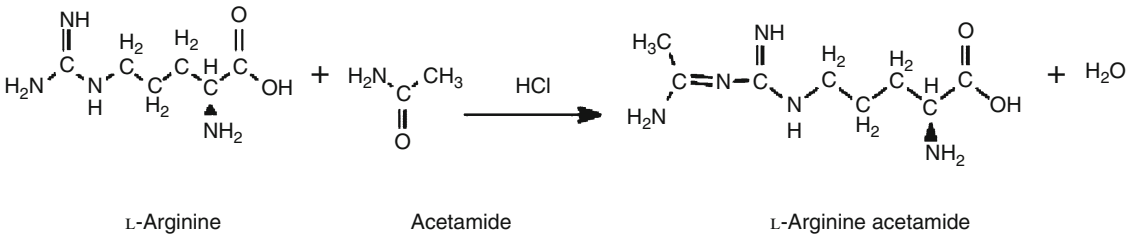

Fig. 2 Alternate reaction scheme for "L-arginine acetamide" given in [6] (reproduced with permission)

parameters of monoclinic L-Arg.HCl ($a = 5.33$ Å, $b = 9.46$ Å, $c = 20.07$ Å, $\beta = 90.5°$, space group $P2_1$) [9] with that of "L-arginine acetamide" shows that they are close to that of [1], but differ by other designation of the axes. It is worth mentioning that the authors of [1] reported the calculated density as 1.271 g cm^{-3} for $Z = 2$. It is not clear how they calculated this value. For assumed composition, relative molecular mass is 215.25 and actual calculated density for $Z = 2$ is 0.713 g cm^{-3} and 1.426 g cm^{-3} for $Z = 4$.

In summary, we have shown that a so-called L-arginine acetamide crystal reported by Anitha et al. [1] is actually the well-known monoclinic form of L-arginine hydrochloride crystal.

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