Synthesis, crystal structure and solubility of C₆H₁₄N₄O₂ C₄H₄O₄·2H₂O

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Abstract

Synthesis, crystal structure and solubility of a new non-linear optical material L-arginine maleate dihydrate have been reported here. From the solubility studies with different solvents, water was found to be the most suitable one. Title compound crystallized in the triclinic space group P1 with Z=1 and unit cell dimensions a=5.264(3) Å, b=8.039(3) Å, c=9.784(3) Å, α=106.19(3)°, β=97.24(3)°, γ=101.66(2)°. The present complex of L-arginine contains a positively charged zwitterionic arginine molecule and a negatively charged semi-maleate ion. The molecules are held together by a three-dimensional network of hydrogen bonds.

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1. Introduction

L-Arginine is one of the essential amino acids widely distributed in biological substances. The functions and role of L-arginine molecules in living matter are characterized by strong basicity of the guanidyl group. As a result L-arginine forms a number of salts with organic and inorganic acids showing non-linear optical properties [1,2]. L-Arginine maleate dihydrate (C₆H₁₄N₄O₂ C₄H₄O₄·2H₂O) is one of these L-arginine salts which is a complex of strongly basic amino acid, carboxylic acid and provides useful information in relation to molecular interaction in present day biological systems and to prebiotic self-organism [3]. It is also a non-linear optical material with second harmonic generation efficiency 1.68 times that of KDP [4]. A long range program being pursued in our laboratory for the synthesis, crystal growth and characterization of crystalline complexes of amino acid and carboxylic acid. One such complex involving acetic acid has already been studied by us and reported elsewhere [5]. In continuation of these studies we have synthesized L-arginine maleate dihydrate (abbreviated as LAMD). Detailed studies on the synthesis, single crystal growth of large sized LAMD and characterization of LAMD have already been communicated [4]. In this present communication we have reported the results of crystal and molecular structure determination of LAMD by using X-ray diffraction data along with solubility studies.

2. Experimental section

2.1. Synthesis of LAMD

L-Arginine maleate dihydrate LAMD (C₆H₁₄N₄O₂, C₄H₄O₄·2H₂O) was synthesized by the reaction between a weak organic acid, maleic acid (C₄H₄O₄) and the strongly basic amino acid, L-arginine (Lobachemie) taken in equimolar proportions. Purification of the synthesized salt was done by repeated crystallization from aqueous solution.

2.2. Solubility and single crystal growth

For growth of single crystals of LAMD of optical quality suitable solvent was selected. For this selection the solubility of LAMD was determined in different mixed solvents like water, ethanol and water (1:1), acetone and water (1:1) as a function of temperature in the temperature range 30–50 °C. Thermostatically controlled vessels (100 ml) were filled with different solutions of LAMD with some undissolved LAMD and stirred for 24 h. On the next day, a small amount
of solution from each vessel was pipetted out and its composition was determined gravimetrically. This experiment was repeated for different temperatures. Single crystals of LAMD were then grown by solvent evaporation of the saturated aqueous solution of LAMD at constant temperature (35 °C). A constant temperature bath with ± 0.03 °C error in temperature had been used for this purpose.

2.3. Crystal structure determination

Single crystal X-ray diffraction data were collected with a specimen of dimensions 0.17 × 0.21 × 0.33 mm³ cut out from the as grown crystals. A Bruker AXS diffractometer was used to collect the intensity data using Mo Kα radiation. Least square refinement of 25 reflections in the range 20–30° revealed the lattice parameters as

\[
a = 5.264(3) \text{ Å}, \quad b = 8.039(3) \text{ Å}, \quad c = 9.784(3) \text{ Å}, \quad \alpha = 106.19(3)^\circ, \quad \beta = 97.24(3)^\circ, \quad \gamma = 101.66(2)^\circ.
\]

LAMD crystallizes in the triclinic system with non-centric space group \( P1 \). The crystal data, parameters used for data collection and reliability factor are summarized in Table 1.

Crystal structure was solved by direct method using the program SIR97 [6] and refined by full matrix least squares with program SHELXL97 [7] to an R value of 0.030. All the non-hydrogen atoms were refined anisotropically while the hydrogen atoms, all found in ΔF map were refined with isotropic thermal parameters. The ORTEP drawing was performed with ORTEP3 program [8] and that of molecular packing with CAMERON [9].

### Table 1

| Chemical formula          | \((C_6H_{15}N_4O_2)^{+} + (C_4H_7O_4)^{-} \cdot 2H_2O\) |
|---------------------------|----------------------------------------------------------|
| Molecular weight          | 326.32                                                   |
| System                    | Triclinic                                                |
| Space group               | \( P1 \)                                                  |
| \( a \) (Å)               | 5.624(3)                                                 |
| \( b \) (Å)               | 8.039(3)                                                 |
| \( c \) (Å)               | 9.784(3)                                                 |
| \( \alpha \) (°)          | 106.19(3)                                                |
| \( \beta \) (°)           | 97.24(3)                                                 |
| \( \gamma \) (°)          | 101.66(2)                                                |
| Cell volume               | 382.02                                                   |
| Formula units/unit cell   | 1                                                        |
| \( D_{calc} \) (Mg/m³)    | 1.4184                                                   |
| \( \mu \) (cm⁻¹)          | 1.223                                                    |
| Diffrauctose              | Bruker AXS                                               |
| Radiation                 | Mo Kα (\( \lambda = 0.7126 \) Å)                        |
| \( \Theta \) range (degree)| 2.21–27.69                                              |
| Range of \( h, k, l \)    | \(-6 < h < 6, \quad -10 < k < 10, \quad -12 < l < 12\) |
| Reflections measured      | 4010                                                     |
| Independent reflections   | 3045                                                     |
| Observed reflections \([F_o > 4\sigma(F_o)]\) | 2988                                                   |
| Structure solution        | Direct methods                                           |
| Refinement method         | Full-matrix least squares on \( F^2 \)                  |
| No. of parameters         | 288                                                      |
| Final \( R \) and \( R_w \)| 0.0300 and 0.0824 for all 3045 rf                      |
| Weighting expression      | \( \frac{1}{\sigma^2(F_o^2) + (0.0608P)^2 + (0.001P)} \) |

3. Results and discussion

3.1. Selection of solvent

Fig. 1 shows the solubility graph of LAMD in three different solvents. From this curve we find that solubility of LAMD in mixed solvents (ethanol and acetone in water) is almost constant with temperature and hence are unsuitable for crystal growth. In pure water, the solubility of LAMD increases with the increase of temperature up to 45 °C. After that solubility curve becomes parallel to the temperature axis. So water was selected as a potentially suitable solvent for the growth of LAMD in the temperature region 30–45 °C. Now from the nature of solubility curve and values of solubility coefficient \((dS/dT)/S_0\) at different temperatures (where \( S \) is the solubility and \( T \) is the temperature, \( S_0 \) is the solubility at \( T_0 \)) we found that there exists two temperature zones for crystal growth. Temperature zone 30–38 °C where the solubility coefficients vary from 0.003 to 0.012 °C⁻¹ is suitable for crystal growth by solvent evaporation method at constant temperature whereas the temperature zone 38–45 °C where the solubility coefficients range between 0.012 and 0.046 °C⁻¹ is ideal for growth of crystal by slow cooling method. Crystals of LAMD grown by solvent evaporation method at 35 °C are shown in Fig. 2.

3.2. Description of crystal structure

The final atomic coordinates and \( U_{equ} \) are given in Table 2. Interatomic distances, bond angles and details of the hydrogen bonding scheme are given in Tables 3 and 4, respectively. The projection of the atomic arrangement viewed down the \( a \) axis is shown in Fig. 3. The molecular geometry shows that arginine molecule consists of two terminal groups, one is the carboxyl group C5, C6, O1, O2 and the other is a guanidyl group N1, C1, N2, N3.

![Fig. 1. Solubility curve of LAMD as a function of temperature in different solvents.](image-url)
connected through an aliphatic chain. Crystal structure analysis of LAMD reveals that the arginine molecule exists as a positively charged zwitterion in which the guanidyl and amino groups are protonated and the carboxyl group is deprotonated as evident from C–O distances [1.229–1.265 Å]. Thus, π–π* transition occurs in the carboxylate and guanidyl groups, which give rise to the NLO properties in LAMD. The anion is the singly negatively charged maleic acid in which one of the two carboxyl functional groups of maleic acid has been deprotonated. The bond lengths and angles of L-arginine molecule as listed in Table 3 are compared with those of other salts of L-arginine [10–12] and found to be in well agreement with each other. The C–N bond length which connects the guanidyl group with carbon chain is as usual shorter (1.452 Å) than the normal C–N single bond length and also observed in other salts of l-arginine [10–12]. The three C–N bonds in guanidyl group are nearly equal in length with a variation from 1.319 to 1.334 Å. All the angles N–C–N in guanidyl group are almost equal to 120°. The fact that one of the carboxyl group of maleic acid is deprotonated by giving the hydrogen atom attached to oxygen (O4M) is evident from the values of C–O bond distances in maleic acid group. The maleic acid is interconnected with the arginine molecule through three N–H···O hydrogen bonds formed between N2 with O3M, O4M and N3 with O3M. Different molecules in the crystal lattice are interconnected through several

Table 3

| Principal intramolecular distances (Å), and bond angles (°) in LAMD |
|---------------------------------------------------------------|
| **Atoms** | **Bond distances (esd)** | **Bond angles (°)** |
|-----------|--------------------------|---------------------|
| N1–C1     | 1.3189(12)               | N1–C1–N2            | 119.41(10) |
| N2–C1     | 1.3213(14)               | N2–C1–N3            | 120.13(3)  |
| C1–N3     | 1.3338(6)                | N1–C1–N3            | 120.45(4)  |
| N3–C2     | 1.4523(14)               | N3–C2–C1            | 122.12(3)  |
| C2–C3     | 1.5187(6)                | N3–C2–C3            | 112.03(3)  |
| C3–C4     | 1.5175(13)               | C2–C3–C4            | 109.06(3)  |
| C4–C5     | 1.5293(6)                | C3–C4–C5            | 116.46(3)  |
| C5–N4     | 1.4914(15)               | C4–C5–C6            | 111.61(4)  |
| C5–C6     | 1.5332(13)               | C5–C6–O1            | 109.03(8)  |
| C6–O1     | 1.2651(14)               | O1–C6–O2            | 118.67(7)  |
| C6–O2     | 1.2288(13)               | C5–C6–O1            | 115.15(10) |
| O1M–C1M   | 1.2835(12)               | O1–C6–O2            | 126.17(10) |
| O2M–C1M   | 1.2166(16)               | O1M–C1M–O2M         | 120.45(9)  |
| C1M–C2M   | 1.4985(10)               | O2M–C1M–C2M         | 119.49(4)  |
| C2M–C3M   | 1.3310(15)               | O1M–C1M–C2M         | 120.05(3)  |
| C3M–C4M   | 1.4925(16)               | C1M–C2M–C3M         | 131.00(4)  |
| C4M–O3M   | 1.2343(14)               | C2M–C3M–C4M         | 129.86(13) |
| C4M–O4M   | 1.2712(8)                | C3M–C4M–O4M         | 119.61(4)  |

Table 4

Possible hydrogen bonds

| D–H···O | H–O | D–O | D–H···O |
|---------|-----|-----|---------|
| N2–H2N2–O4M | 2.016(14) | 2.836(2) | 177.44(9) |
| N3–H1N3–O3M | 2.065(13) | 2.946(2) | 178.37(10) |
| O2W–H1W2–O1W | 2.663(25) | 3.186(2) | 176.25(25) |
| N1–H2N1–O1i | 2.167(9) | 2.946(1) | 170.86(4) |
| O1W–H2W1–O1i | 1.982(34) | 2.765(2) | 155.74(8) |
| N2–H2N1–O2i | 2.208(16) | 2.934(2) | 166.22(5) |
| O2W–H1W2–O2i | 2.597(32) | 3.076(2) | 135.69(20) |
| N4–H1N4–O4ii | 1.922(15) | 2.838(2) | 174.46(16) |
| O2W–H2W2–O1Wiii | 1.820(36) | 2.784(2) | 162.81(12) |
| N4–H3N4–O2Wiii | 1.867(20) | 2.800(2) | 176.01(11) |
| O1W–H1W1–O3Miv | 2.117(18) | 2.873(1) | 167.39(4) |

Symmetry codes: (i) x+1, y, z+1; (ii) x+1, y, z; (iii) x−1, y−1, z−1; (iv) x, y, z+1.

U_{eqq} = 1/3 \sum_{i<j} u_{ij} a_i a_j a_i a_j.
intermolecular hydrogen bonds that exist mainly in between guanidyl nitrogen (N1,N2), carboxyl oxygen (O1,O2), amino nitrogen (N4) and water molecules. A list of hydrogen bonds is given in Table 4. The least square plane calculation (Table 5) also shows that both the guanidyl and carboxyl groups are truly planar compared to carbon chain which is nearly planar. But as a whole l-arginine molecule is not strictly planar as evident from the dihedral angles formed between carbon chain, carboxyl and guanidyl groups. The atoms belong to maleic acid are also planar with one of the oxygen (O3M) atom slightly displaced from the mean plane. Projection of crystal structure (molecular packing) of l-arginine maleate dihydrate viewed along b axis is shown in Fig. 4. In this figure, hydrogen bonds are indicated by broken lines. As shown in Fig. 4, the crystal structure consists of alternate layers of arginine molecules and maleic acid group stacked along the b axis and held together by hydrogen bonds.

### 4. Conclusions

A new complex (LAMD) of l-arginine and carboxylic acid was synthesized and optical quality crystal was grown from its aqueous solution. From solubility study water was found to be potentially suitable solvent for growth of LAMD. From crystal structure analysis, the π–π\* transition in the carboxylate and guanidyl group is established which accounts for the non-linearity of LAMD. The complex is made up of positively charged zwitterionic arginine molecule and negatively charged semi-maleate ions. The arginine molecules aggregate into layers with the maleate

| Atom                | Distance from mean plane (Å) |
|---------------------|------------------------------|
| C5                  | 0.0011(4)                    |
| C6                  | 0.0042(4)                    |
| O1                  | 0.0014(4)                    |
| O2                  | 0.0016(4)                    |
| N4\*                | 0.5292(4)                    |
| C4\*                | 1.3942(4)                    |
| C1                  | 0.0023(10)                   |
| N2                  | 0.0043(14)                   |
| C1                  | 0.0068(10)                   |
| N3                  | 0.0023(10)                   |
| C2\*                | 0.0162(10)                   |
| C2                  | 0.0300(11)                   |
| C3                  | 0.0257(11)                   |
| C4                  | 0.0359(11)                   |
| C5                  | 0.0315(11)                   |
| N3\*                | 0.2172(11)                   |
| N4\*                | 1.0816(11)                   |
| C4M                 | 0.0041(10)                   |
| C4M                 | 0.0088(14)                   |
| C3M                 | 0.0013(14)                   |
| C2M                 | 0.0040(14)                   |
| C1M                 | 0.0016(14)                   |
| O1M                 | 0.0015(10)                   |
| O3M\*               | 0.0141(10)                   |
| O2M\*               | 0.0098(14)                   |

### Table 5

| Plane–plane Angles (esd) | Dihedral angle (°) between the least square planes |
|--------------------------|-----------------------------------------------|
| 1–2                      | 66.02(4)                                      |
| 2–3                      | 11.96(5)                                      |
| 3–1                      | 77.98(4)                                      |

\* Atoms not included in LSQ plane calculation.
ions in between the layers. The molecules are held together by three-dimensional network of hydrogen bonds.

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Fig. 4. Crystal structure of LAMD viewed down the b axis, with hydrogen bonds indicated by dashed lines.