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Factor group, Spectroscopic and Thermal studies on Creatininium hydrogen oxalate monohydrate

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ABSTRACT

Creatinine: A chemical waste molecule that is generated from muscle metabolism. Creatinine is produced from creatine, a molecule of major importance for energy production in muscles. Approximately 2% of the body's creatine is converted to creatinine every day. Creatinine is transported through the bloodstream to the kidneys. The kidneys filter out most of the creatinine and dispose of it in the urine. Although it is a waste, creatinine serves a vital diagnostic function. Creatinine has been found to be a fairly reliable indicator of kidney function. As the kidneys become impaired the creatinine will rise. Abnormally high levels of creatinine thus warn of possible malfunction or failure of the kidneys. Because of this biological importance creatinine treated with oxalic acid and the crystals were grown by slow evaporation technique at ambient temperature. The FT-IR and FT-Raman spectra of this crystal have been recorded and analyzed at room temperature. Further, these molecular vibrations are correlated with the different functional groups by factor group analyses, theoretically. A pronounced change is observed in the N–H stretching frequency of the NH_2 group. It is proposed that the amide NH_2 group is influence by the intermolecular hydrogen bond in this complex. . Thermogravimetric analysis and differential thermal analysis have also been carried out to study the thermal behavior of Creatininium hydrogen oxalate monohydrate crystals.

Keywords: Creatininium hydrogen oxalate monohydrate, FT-IR and FT-Raman spectra, TGA/DTA studies, Factor group analysis

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INTRODUCTION

Creatinine anhydride [$C_4H_7N_3O$] is found in muscle tissue and blood, also it is excreted in the urine as a metabolic waste. Urinary excretion of creatinine is relatively constant from day to day, and reflects mainly the amount of muscle tissue in the body. Therefore the amounts of various components of urine are often expressed relative to creatinine. It is mainly filtered by the kidney, though a small amount is actively secreted. There is little-to-no tubular reabsorption of creatinine. If the filtering of the kidney is deficient, blood levels rise. As a result, creatinine blood levels may be used to calculate creatinine clearance (ClCr), which reflects the Glomerular Filtration Rate (GFR). The GFR is clinically important because it is a measurement of renal function. However, in cases of severe renal dysfunction, the creatinine clearance rate will be overestimated because the active secretion of creatinine will account for a larger fraction of the total creatinine cleared. Measurement of creatinine levels in serum and determination of renal clearance of creatinine are widely used for laboratory diagnosis of renal and muscular function [1].

In the gas phase, the imino tautomer is probably more stable [2], while in a sufficiently acidic medium, creatinine is protonated apparently at N3, forming the creatininium cation with strongly delocalized charge [3, 4]. Creatinine, being a natural metabolite of creatine, is an important bioligand. The presence of several donor groups in its main tautomeric forms determines its strong coordination capacity. The complexation ability towards a number of metal ions: Ag(I), Hg(II), Cd(II), Zn(II), Co(II), Ni(II), Cu(II), Pt(II), Pd(II) was studied [5]. Similarly studies of organic – inorganic hybrid materials, including aminoacids and various inorganic acids [6] have received a great deal of attention in recent years because of their electrical, magnetic and optical properties.

Hydrogen bonds in hybrid compounds are of interest because of their widespread biological occurrence. In particular, N-H…O hydrogen bonds are predominant in determining the formation of secondary structure elements in proteins and base- pairing in nucleic acid and their biomolecular interactions. The crystal structure of creatinine with organic/ inorganic acid complexes reported are creatininium nitrate [7], creatininium oxalate monohydrate [8], Creatinium dipicolinate monohydrate [9] etc. The complexes were studied to understand the hydrogen bonding of creatinine with other acids, hence the stability and reactivity of the complexes. Based on the above specifics, in the present investigation, creatinine was treated with the oxalic acid and the title compound was crystallized.

EXPERIMENTAL

Preparation

Crystals of creatininium oxalate monohydrate were crystallized from an aqueous solution of creatinine and oxalic acid with a stoichiometric ratio of 1:1 at low temperature by slow evaporation. After 6 days, needle-shaped, transparent and colorless crystals of creatininium oxalate monohydrate were obtained.

Single crystal XRD studies

Unit cell parameters and structure of creatininium oxalate monohydrate crystal were determined from single-crystal X-ray diffraction data obtained with a Bruker SMART APEX CCD area detector diffractometer (graphite-monochromated, MoK$_\alpha$ = 0.71073 Å).

Unit cell dimensions	a = 9.1728 (7)Å α = 90°
	b = 6.3520 (5) Å β = 90°
	c = 16.6567 (12) Å γ = 90°
Volume	V = 970.51 (13) Å^3

Hence, the crystalline phase is confirmed and the CIF of the creatinine oxalate monohydrate is used for further calculations.

Vibrational spectroscopic measurements

Infrared spectral measurements were made with a Nexus 670 FTIR spectrometer with a resolution of ~1–2 cm^{-1} over the range 4000–400 cm^{-1}, the samples being mixed with KBr powder and pressed into discs under high pressure. The disc was used to obtain good spectra. Radiation of 1064 nm from the same Nexus 670 FT Raman spectrometer of Nd:YAG laser was used as the source of excitation. The laser power was maintained at 1.5 watts. The spectral range is in the range of the 3600 – 100 cm^{-1} for stokes lines and 2000 – 200 cm^{-1} in anti-stokes lines. The measured spectral lines had a resolution of 2–3 cm^{-1} in the same range of the wavenumber. Indium-Gallium Arsenide detector is used as a detector.

Thermal Analysis

Thermo gravimetric analysis (TGA) and Differential Thermal Analysis (DTA) were carried out for the crystals using a SDT Q600 thermal analyzer. A powder sample was used for the analysis in the temperature range of 28 ºC to 600ºC with a heating rate of 25°C/min in the air atmosphere.

RESULTS AND DISCUSSION

Crystal structure and factor group analysis

The unit cell of the crystal is determined using Bruker SMART APEX CCD area-detector diffractometer. The unit cell has four formula units (Z = 4). The crystal structure and information about the hydrogen bonds were determined in x-ray diffraction study [8]. The asymmetric unit contains one creatininium cation, one oxalate anion and one water molecule (Figure 1). The H atom of the oxalic acid is migrated to the N site of the creatinine leading to the expected creatininium cation and oxalate anion. This is reflected in the spectrum from the wave numbers of the functional groups N-H and COO^-.

Fig 1: Scheme diagram of creatininium oxalate monohydrate

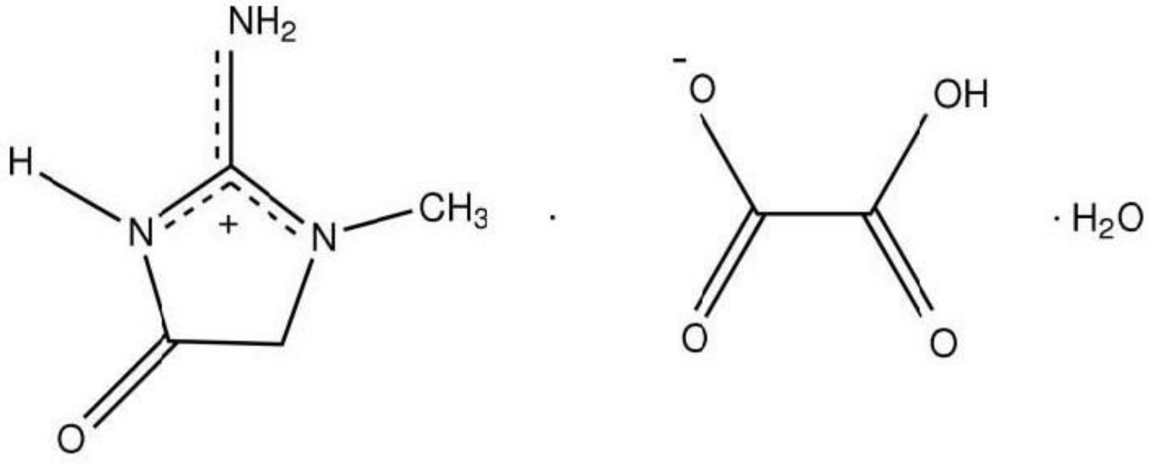


Table 1. Crystallographic Data

Particulars	Creatininium oxalate monohydrate
Molecular Formula	$C_4H_8N_3O^+.C_2HO_4^-.H_2O$
Molecular weight	221.18
Unit cell dimensions	a = 9.1728(7) Å
	b = 6.3520(5) Å
	c = 16.6567(12) Å
Volume	970.51(13) Å^3
Crystal system	Orthorhombic
Space group	P_{nma}

Factor Group Analysis

Factor group analysis is a method used for determining symmetry of vibrations. The numbers of normal modes of the crystals creatininium oxalate monohydrate were determined by group theory analysis using the correlation method based upon the symmetry of the molecules, 618 normal modes are predicted. These genuine modes can be decomposed into the irreducible representations of the factor group as

$\Gamma_{crystal} = 78A_g + 77B_{1g} + 77B_{2g} + 77B_{3g} + 78A_u + 77B_{1u} + 77B_{2u} + 77B_{3u}$. Factor group analysis using the standard correlation method was carried out (10,11)

Table 2 :Factor group analysis of creatininium oxalate monohydrate $C_4H_8N_3O^+.C_2HO_4^-.H_2O$; space group: *Pnma* = D_{2h}; z = 4

	Modes and degrees of freedom for each species		Site symmetry C_1	Factor group analysis C_{2h}
Creatininium $C_4H_8N_3O^+$	Vibrational	192	A	$48A_g+48B_{1g}+48B_{2g}+48B_{3g}$ $+48A_u+48B_{1u}+48B_{2u}+48B_{3u}$
Oxalate $C_2HO_4^-$	Vibrational	48	A	$21A_g+21B_{1g}+21B_{2g}+21B_{3g}$ $+21A_u+21B_{1u}+21B_{2u}+21B_{3u}$
Water H_2O	Vibrational	12	A	$3A_g+3B_{1g}+3B_{2g}+3B_{3g}$ $+3A_u+3B_{1u}+3B_{2u}+3B_{3u}$
	Translational	12	A	$3A_g+3B_{1g}+3B_{2g}+3B_{3g}$ $+3A_u+3B_{1u}+3B_{2u}+3B_{3u}$
	Libration	12	A	$3A_g+3B_{1g}+3B_{2g}+3B_{3g}$ $+3A_u+3B_{1u}+3B_{2u}+3B_{3u}$

$$\Gamma_{\mathrm{vibrational}} = 72\mathrm{A_g} + 72\mathrm{B_{1g}} + 72\mathrm{B_{2g}} + 72\mathrm{B_{3g}} + 72\mathrm{A_u} + 72\mathrm{B_{1u}} + 72\mathrm{B_{2u}} + 72\mathrm{B_{3u}};$$

$$\Gamma_{\mathrm{translational}} = 3\mathrm{A_g} + 3\mathrm{B_{1g}} + 3\mathrm{B_{2g}} + 3\mathrm{B_{3g}} + 3\mathrm{A_u} + 3\mathrm{B_{1u}} + 3\mathrm{B_{2u}} + 3\mathrm{B_{3u}};$$

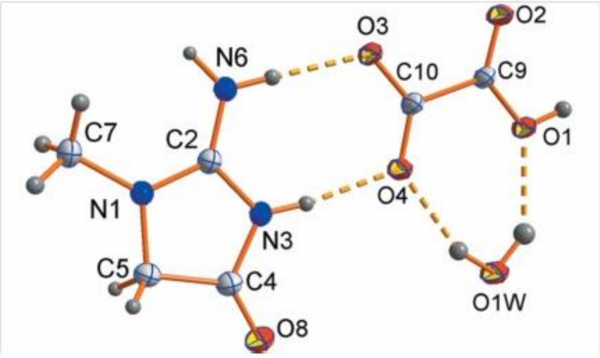
$$\Gamma_{\mathrm{rotational}} = 3\mathrm{A_g} + 3\mathrm{B_{1g}} + 3\mathrm{B_{2g}} + 3\mathrm{B_{3g}} + 3\mathrm{A_u} + 3\mathrm{B_{1u}} + 3\mathrm{B_{2u}} + 3\mathrm{B_{3u}};$$

$$\Gamma_{crystal}^{total} = 78\mathrm{A_g} + 78\mathrm{B_{1g}} + 78\mathrm{B_{2g}} + 78\mathrm{B_{3g}} + 78\mathrm{A_u} + 78\mathrm{B_{1u}} + 78\mathrm{B_{2u}} + 78\mathrm{B_{3u}};$$

$$\Gamma_{\mathrm{acoustic}} = \mathrm{B_{1g}} + \mathrm{B_{2g}} + \mathrm{B_{3g}} + \mathrm{B_{1u}} + \mathrm{B_{2u}} + \mathrm{B_{3u}};$$

$$\Gamma_{crystal} = \Gamma_{crystal}^{total} - \Gamma_{acoustic} = 78\mathrm{A_g} + 77\mathrm{B_{1g}} + 77\mathrm{B_{2g}} + 77\mathrm{B_{3g}} + 78\mathrm{A_u} + 77\mathrm{B_{1u}} + 77\mathrm{B_{2u}} + 77\mathrm{B_{3u}}$$

Fig 2: Structural view of creatininium oxalate monohydrate which shows R_2^2(7) and R_2^2(8) ring motif



Vibrational Analysis

The normal modes of vibrations are classified into skeletal or fingerprint vibrations that involve many of the atoms to move the same extent and characteristic group vibrations, which involve only a small portion of the molecule. The crystal creatininium oxalate monohydrate is identified with many functional groups like, NH_2, NH, CH_3, CH_2, C=O, C-N, COO^-, C-O(H) and C-C-O. In addition skeletal vibrations like C-C, C-C-C, C-C-N, C-N-C and N-C-N also exist in this compound. The characteristic wavenumbers of these groups are expected to change in their intensity and position according to their environment and the hydrogen bonding association in the crystal packing. The crystal packing is stabilized through the classical N-H…O and O-H…O interactions and non-classical C-H…O interactions (8). The asymmetric unit itself contains ring R_2^2(8) motif (12). These enriched hydrogen bonds are expected to change the position and intensity of the wavenumbers considerably. The observed infrared and Raman spectra are presented in Figures 3 and 4 respectively. The observed wavenumbers together with the proposed assignments are given in Table 3.

Fig 3: Infrared spectrum of creatininium oxalate monohydrate

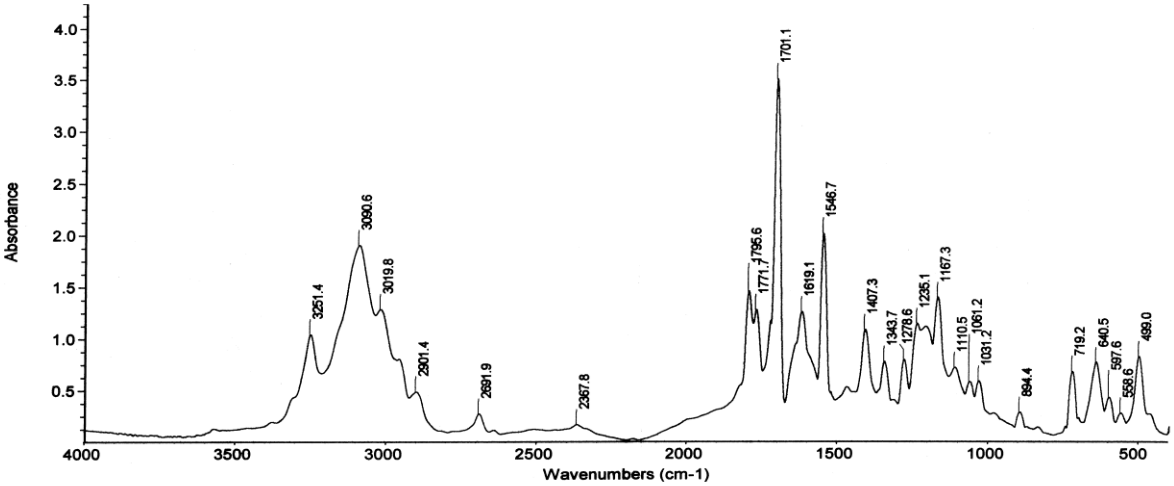


Fig 4: Raman spectrum of creatininium oxalate monohydrate

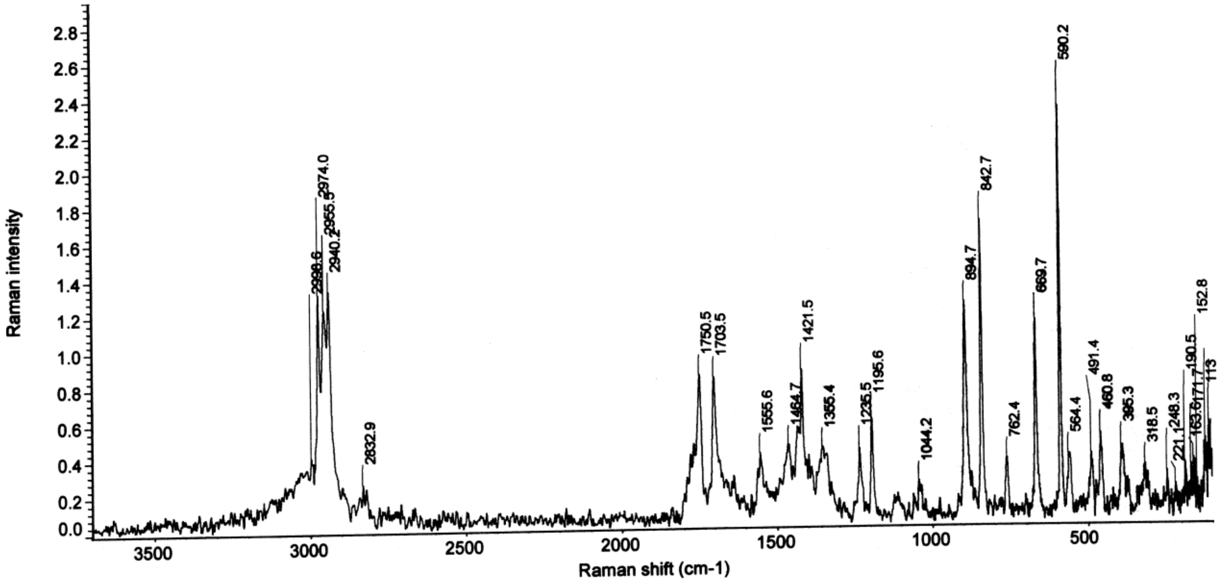


Table 3. Observed vibrational ($\bar{\nu}$) bands for creatininium oxalate monohydrate

Infrared $\bar{\nu}$ / cm^{-1}	Raman $\bar{\nu}$ / cm^{-1}	Assignment
3251.4		O-H & C-O(H) str.; N-H...O str.
3090.6		NH_2 asym. str.
3019.8	2998.6	NH_2 sym. str. ; Aromatic C-H str.
	2974.0	CH_3 asym str.; (C)O-H str.
	2955.5	CH_3 sym str.
	2940.2	CH_2 asym str.
2901.4		CH_2 sym str.
	2832.9	Overtone and combination
2691.9		
2367.8		
1795.6		
1771.7	1750.5	
1701.1	1703.5	

1619.1		NH_2 asym def.
1546.7	1555.6	COO^- asym str; NH_2 sym def.
	1464.7	C-N asym str.; CH_2 rock
1407.3	1421.5	CH_3 asym def.
1343.3	1365.4	CH_3 sym def.; CH_2 wag; O-H i.p. def.
1278.6		C – OH i.p.def.
1235.1	1235.5	CH_2 twist
	1195.6	CH i.p.def.
1167.3		NH_2 rock
1110.5		Phenol O-H & C-O Stretch
1061.2		C-C-N asym str.; CH_2 wag.
1031.2	1044.2	C-N sym Str. ; CH_3 rock.
894.4	894.7	C – C – N sym str.
	842.7	C – C str; H_2O rocking
	762.4	Aromatic C-H Bending
719.2		CH_2 rock
	669.7	COO^- sciss.
640.5		O-C=O def.
597.6	590.2	C-C=O def.
558.6	564.4	COO^- wag
499.0	491.4	H_2O wag
	460.8	COO^- rocking
	395.3	C – N def.
	318.5	C – C tor
	248.3	Lattice vibration
	221.1	
	190.5	

	171.7	
	163.6	
	152.8	
	113	

Spectra of aromatic compounds in the infrared region, from 4000 to 800 cm^{-1} contain bands that are characteristic of the aromatic group. These bands are primarily associated with the motion of the benzene ring at the aromatic C-H bonds (13). The high wave number region around 3500-1500 cm^{-1} consist the bands due to NH_2, CH_3, CH_2, C=O, COO^-, C-N, N-H and C-H stretching vibrations. The low wave number region around 1500-450 cm^{-1} contains bands due to deformation, twisting and rocking vibrations of the various groups. The skeletal vibrations are all coupled together and they occur in the region around 1150-500 cm^{-1}. The lattice vibrations occur below 400 cm^{-1}.

Vibration of Creatininium Cation

The structural investigation of the tile compound reveals the protonation on the N site of the creatinine molecule and its cationic nature. The asymmetric unit of the tile compound contains one creatininium cation and one oxalate anion and one water molecule. The expected proton transfer from oxalic acid to creatinine occurs at N3 of the imidazolyl ring. This result in an increase in the C2—N3 bond distance and a decrease of C2-N6 compared with the corresponding values found in the neutral creatinine molecule [14].

The creatininium cation is linked to anion through three two centered N-H…O and one two centered O-H…O hydrogen bonds. This strong and moderate hydrogen bonds lead to downshifting of the stretching mode of vibrations in high wave number region. The NH_2 asymmetric stretching frequency is observed in the 3090.6 cm^{-1} in the Raman spectrum which is superimpose of the bands due to the $-CH_3$, $-CH_2-$ and –OH stretching frequencies. The same is observed at 3123 cm^{-1} in the infrared spectrum as a broad medium band. As well, the amine group, NH_2, shows the bending vibrational wavenumbers in the regions of 1660-1610 cm^{-1}. The band at 1619.1 cm^{-1} in infrared is assigned for NH_2 asymmetric deformation mode and NH_2 symmetric deformation mode assigned at 1546.7 cm^{-1} in infrared spectrum & 1555.6 cm^{-1} in Raman spectrum.

The C-N asymmetric stretching modes of vibrations lie in the expected region. It is observed as a band in the in Raman spectrum at 1464.7 cm^{-1}. Normally, this band is observed along with the $-CH_2$ rocking frequency, the fundamental of which is observed near 700 cm^{-1}. The same case is repeated here with the fundamental of rocking frequency is observed at 719.2 cm^{-1} as a band. The band at 1464.7 cm^{-1} is observed for C-N asymmetric stretching in Raman spectrum.

The CH_3 asymmetric and symmetric stretching modes are expected to occur nearly at 2980 - 2900 cm^{-1}, respectively. In this compound, the presence of Raman line at 2974 cm^{-1}

correspond to asymmetric stretching vibration and 2955 cm^{-1} correspond to the CH_3 symmetric mode. Generally, the wavenumbers of the CH_2 vibrational modes depend on its immediate environment. The stretching modes of the CH_2 group usually occur in the region 3100-2800 cm^{-1}. A Raman line at 2940.2 cm^{-1} is assigned to CH_2 asymmetric stretching mode of vibration and 2901.4 cm^{-1} is assigned to CH_2 symmetric stretching mode in infrared spectrum. A Raman line at 1421.5 cm^{-1} is due to CH_3 asymmetric deformation and 1407.3 cm^{-1} is due to CH_3 symmetric deformation in Infrared spectra [15,16]. The spectral lines in the region of 1000-1100 cm^{-1} are due to C-N symmetric stretching vibrations. A Raman band at 1044.2 cm^{-1} is due to the rocking mode of the CH_3 group vibration coupled with the C-N symmetric stretching frequency. The same is observed at 1031.2 cm^{-1} in the IR spectrum as a weak band.

There is one CH_3 group in the creatininium cation which is performing the deformation vibration. This deformation mode is observed at 1422 cm^{-1} in Raman spectrum as a medium intensity band. The bending frequencies like wagging, twisting and rocking modes of CH_2 vibrations have been greatly influenced in the spectra. Generally, the wagging modes of CH_2 groups are expected to spread out over a wide frequency region, viz., 1357-1170 cm^{-1}. Here, the CH_2 wagging mode is observed as at 1061.2 cm^{-1} in infrared spectrum. The rocking frequencies of the CH_2 group are observed at 719.2 cm^{-1} in IR spectrum.

Vibration of Oxalate anion

The observed assignments of the oxalate anion are coinciding well [17]. The ionized carboxylic group gives rise to antisymmetric COO^- stretch at 1600-1570 cm^{-1} and symmetric COO^- stretch around 1400 cm^{-1}. In the present compound lines at 1546.7 cm^{-1} in the IR spectrum and 1555.6 cm^{-1} in Raman spectrum has been assigned to asymmetric stretching mode vibrations of ionized carboxylic group (COO^-). A peak at 1343.3 cm^{-1} in IR spectrum and in Raman spectrum the peak at 1365.4 cm^{-1} are corresponds to COO^- symmetric stretching mode of vibration. These bands are lower than the expected range owing to strong hydrogen bonding interactions which was revealed in the X-ray crystallographic data.

The rocking, wagging, scissoring in-plane and out-of-plane deformation modes of COO^- ionized carboxylic group are expected at 502, 577 and 665 cm^{-1}, respectively. For the title compound, the rocking mode at 460.8 cm^{-1} in Raman spectrum and the wagging mode appears at 558.6 cm^{-1} in IR spectrum and 564.4 cm^{-1} in Raman spectrum. The scissoring deformation mode is identified at 669.7 cm^{-1} in Raman spectrum.

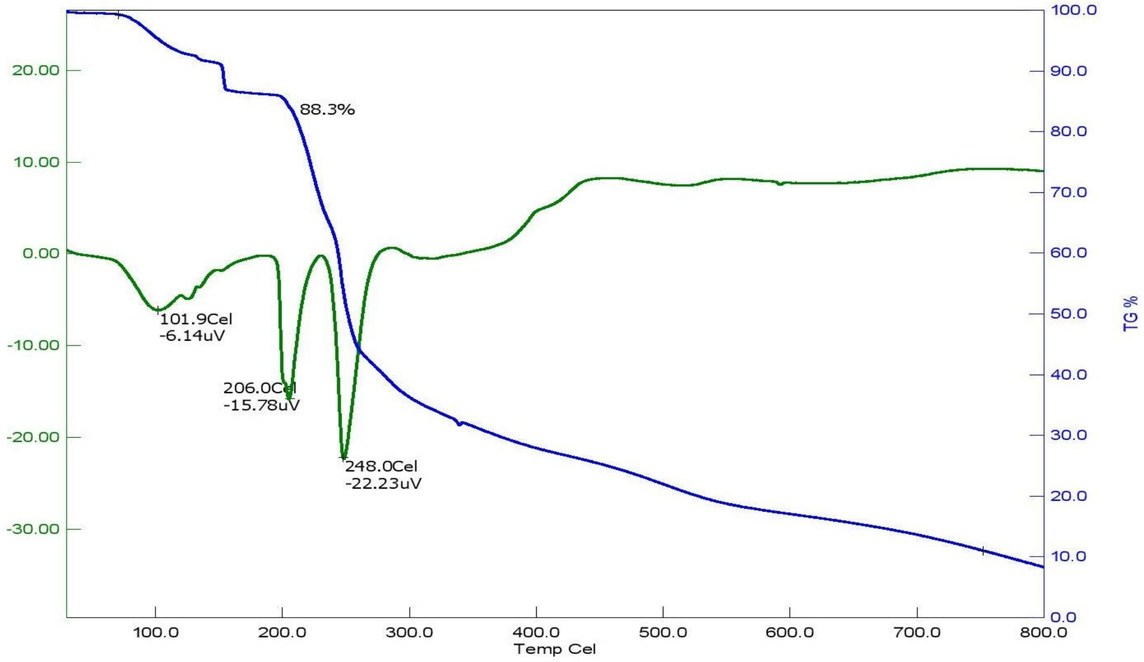
The O-C=O deformation mode is observed as a line at 640.5 cm^{-1} in IR spectrum. Normally, the absorption bands in the region 3600 - 3200 and 3100 - 2800 cm^{-1} are due to O-H and C-H stretching vibrational modes of phenol. The presence of O-H group and the O…H bond involved in the hydrogen bonding interactions give rise to a moderate intensity line at 3228 cm^{-1} in Raman in overtone with the water in the KBr pellet. The O-H in-plane deformation mode is observed at 1343.3 cm^{-1} in IR spectrum and 1365.4 cm^{-1} in Raman spectrum.

Thermal Analysis

From TGA, it is observed that creatininium oxalate monohydrate has very good thermal stability upto 206 ºC. There is no phase transition or decomposition in the material. The endothermic peak at 206 ºC is due to melting of the crystal and immediately afterwards it starts to decompose. The decomposition occurs in two steps. The first weight loss occurring between 101.9ºC and 206ºC. The second weight loss occurring between 206ºC and 248ºC. The final residue (above 500ºC) has the combination of the carbon, hydrogen and nitrogen atoms. The above decomposition points are confirmed in the TGA curve.

The DTA is shown in Figure 5. The two weak endothermic peaks observed in the temperature 206ºC and 248ºC. Also, the first endothermic peak may be the melting point of the compound. This is accompanied by mild exothermic peak at 440ºC is due to the decomposition of the organic compound.

Fig 5: TGA/DTA Thermogram of creatininium oxalate monohydrate



CONCLUSION

The infrared and Raman vibrational modes of creatininium oxalate monohydrate have been assigned. The title compound is confirmed from the x-ray unit cell determination. The migration of hydrogen from oxalic acid to the N site of the creatinine and the formation of the creatininium cation and oxalate anion is confirmed in x-ray structural preliminary investigation. The same is reiterated in the spectral investigations with the carboxylate and -NH fundamental frequencies. Further the skeletal vibrations are assigned to the corresponding group. The downshifting of several stretching wavenumbers together with increases in many of the deformation wavenumbers confirms the existence of extensive intermolecular hydrogen bonds.

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