SINGLE CRYSTAL X-RAY STUDY AND THERMAL ANALYSIS OF 5, 5-DIMETHYLCYCLOHEXANE 1, 3-DIONE AND ITS DERIVATIVES

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ABSTRACT

X- ray crystallography is an important modern technique for determination of structure of a molecule. 5, 5- dimethylcyclohexane 1, 3-dione and its derivatives are synthesized. Single crystal of synthesized compound has been studied by X-ray crystallography. Oak Ridge Thermal Elipsoid Plot (ORTEP), Crystal data and structure refinement for compound shows that molecules are inter molecularly hydrogen bonded with hydrogen atom of NH group. A linear chain of molecules is formed via N-H…O hydrogen bonding with x y z…x 1+y z and N…O while the distance noticed is 2.865 Å. Thermogravimetric analysis (TGA) of synthesized compounds has been performed to obtain order of reaction and energy of activation which will be helpful in determining the biological potentials. Thermo gravimetric analysis of almost all synthesized compounds indicates that all molecules decompose in two steps. The first step starts around 95^0c to $350~^0$c and the second step extends from $267~^0$C to $657~^0$C. Compound 5 decomposes in three stages which correspond to 71^0C to 106^0C, $106~^0$C to 218^0C and 218^0C to 506^0C. It is very clear from the results that all molecules have order of reaction (η) of 0.8.The calculated energy of activation indicates an increase in Ea from first stage to second stage for all compounds except compound 5. The energy of activation (Ea) is very high (13.85 kJ) during first stage. It decreases to 6.59 KJ for second stage; while a significant increase (9.87 KJ) is noticed during third stage of compound 5.

KEYWORDS: X- Ray crystallography, Thermal Ananlysis, 5, 5-dimethylcyclohexane 1, 3-dione.

INTRODUCTION

X-ray crystallography is a powerful tool for obtaining the structure of different molecules. The distance between two bonded atoms is the measure of the bond strength and its bond order. The initial X-ray crystallographic studies showed the various types of bonding in compounds. In the field of organometallic chemistry, the X-ray structure of ferrocene initiated scientific studies of sandwich compounds while that of Zeise's salt encouraged research into "back bonding" and metal-pi complexes. X-ray crystallography had a pioneering role in the development of supramolecular chemistry in elucidating the structures of the crown ethers. The imidazole molecules were characterized. [1] and the reports revealed that X-ray structure of dimedone complexed with human cyclophilin A was studied.[2] Single crystal X-ray diffraction is a powerful method which gives the 3D conformation of the molecules and its stereochemistry. As one can get the precise bond distances and angular relations among the atoms in molecules from X-ray studies, this has helped to design required molecular structure.[3] Some of the physical properties as well as activities can be correlated to the structure of compounds. Numerous molecular structures of organic, biologically important molecules, natural products, synthetic drugs, inorganic, organometallic, metal clusters, high-energy materials, catalytically active coordination compounds are determined with this technology. X-ray crystallography is now used routinely by scientists to determine how a pharmaceutical drug interacts with its protein target and what changes might improve in it.[4] Single-crystal X-ray analysis has three basic steps -to obtain an adequate crystal, the proper placement of a crystal and the data processing. The first and often most difficult step is to obtain an adequate crystal of the material under study. The crystal should be sufficiently large, pure in composition and regular in structure, with no significant internal imperfections such as cracks or twinning. In the second step, the crystal is placed in an intense beam of X-rays, usually of a single wavelength (monochromatic X-rays), producing the regular pattern of reflections. The diffracted intensity from a crystal is recorded at every orientation of the crystal. Multiple data sets have to be collected, to have complete set of diffracted intensities. In the third step, data is processed and combined computationally with complementary chemical information to produce and

refine a model of the arrangement of atoms within the crystal. The final, refined model of the atomic arrangement gives definite crystal structure. The geometrical parameters and H-Bonding are calculated and all the data are stored in a public database library. The major factor affecting the quality of single-crystal structure is the size of crystal and regularity. Recrystallization is a commonly used technique to improve these factors. Single crystal mounted on a goniometer head is placed in the X-ray beam. The diffracted intensities are recorded on film/detector/CCD camera. The Unit cell parameters can be determined using few reflections. Depending on cell parameters – cell length and cell angle they are classified as Triclinic, Monoclinic, Orthorhombic, Tetragonal, Cubic, Hexagonal or Trigonal.

The thermal and kinetic parameters for various synthesized molecules along with mass spectra correlations had been evaluated.[5] Thermal analysis of organic compounds illustrates the properties such as energy of activation and order of reaction.[6] Organic moieties, when used as a medicament, its stability and energy of activation become essential, fundamental added properties. These properties give an account of precise action on the specific pathogens. To achieve such properties these remarks become very essential. Thermal analysis sounds out with mass spectrum analysis. This investigation has very high value in medical field.

MATERIALS AND METHOD
Preparation of 5, 5-dimethylcyclohexane 1, 3-dione and its derivatives –
The compounds were synthesized under anhydrous conditions by utilizing equimolar reactants (Dimedone **1** with aniline & substituted anilines **2, 4, 6, 8, 10 & 12**) using anhydrous $MgSO_4$ as dehydrating agent. The reaction mixture was refluxed for two hours in methanol. The progress of the reaction was monitored by TLC. The reaction mixture was separated from $MgSO_4$. The solvent was removed under vacuum to get crude solid. Repeated crystallization from ethanol gives crystalline product. Purity of the molecule was confirmed by TLC [7,8,9]. The melting points of all synthesized compounds were matched with the standard. Various compounds were synthesized as reported in Scheme 1.

Single crystal X-ray Crystallographic study.
The single crystal for **Compound 5** was developed by crystallization using ethanol. Slow evaporation of the solvent furnished a single crystal, which was examined by X-ray crystallographic method and collected required information for the crystal. The compound **5** was collected at $T = 296$ K, on SMART APEX CCD. Single Crystal X-ray diffractometer using Mo-Kα radiation (λ = 0.7103 Å) to a maximum θ range of 25.00°was used. Crystal to detector distance was 6.05 cm, 512 x 512 pixels / frame. Oscillation / frame -0.3°, maximum detector swing angle = −30.0°, beam center = (260.2, 252.5), in plane spot width = 1.24, SAINT integration

was employed. SADABS correction was utilized. Structures were solved by direct methods using SHELXTL.[10] The facts were corrected for Lorentzian, polarization and absorption effects. SHELX-97 was used for structure solution when full matrix least squares refinement on F^2 was maintained. Hydrogen atoms were included in the refinement as per the riding model. The refinements were carried out using SHELXL-97.[11]

Thermal analysis
Thermal analysis is performed in air- atmosphere. The powdered sample (0.040 to 0.060 g.) in weighing tube was charged. It was made compact by tapping. The weight was recorded. The experiment was started from room temperature to 700 ^{0}C with a heating rate of 3 ^{0}C /min. The thermo gram followed the decrease in sample weight with the linear increase in temperature. Thermal and kinetic parameters like order of reaction (η) and energy of activation (Ea) were determined from computer programmed of rising temperature expression given by Coats and Red Fern. Order of reaction was changed until a straight line with maximum correlation coefficient value was obtained from the plot using the expression.

$$\ln [1-(1-x)^{1-n}] / [(1-n)T^2] \text{ vs. } 1/T \text{ ------ } 1$$

Energy of activation was obtained from slope of the plot as, Ea = slope x R, where R is gas constant (8.314 k J/mol). Analytical data obtained from TGA for all compounds were given (Table 1). The decomposition of the compounds in various stages temperatures has been accomplished. The energy of activation and order of reaction have been commuted from the plots reported (fig. 9 to11).

Scheme 1

5,5-dimethylcyclohexane-1,3-dione   Aniline   3,3-dimethyl-5-(phenylamino)cyclohexanone
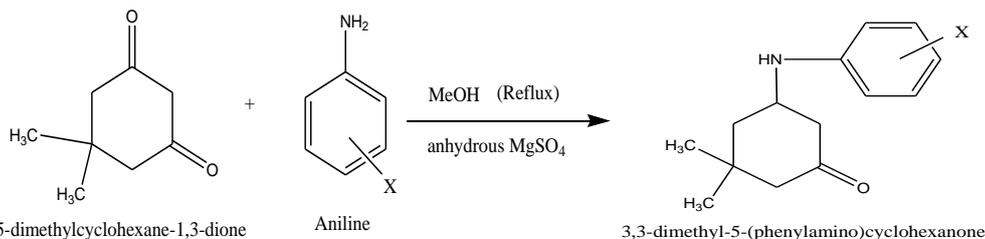
Here,   X = H   (Substituent 2)   X = H   (Compound 3 / L_1)
= o-CH$_3$ (Substituent 4)   = o-CH$_3$ (Compound 5 / L_2)
= m-CH$_3$ (Substituent 6)   = m-CH$_3$ (Compound 7 / L_3)
= p-CH$_3$ (Substituent 8)   = p-CH$_3$ (Compound 9 / L_4)
= m-Cl   (Substituent 10)   = m-Cl   (Compound 11 / L_5)
= *p*-Cl   (Substituent 12)   = *p*-Cl   (Compound 13 / L_6)

RESULTS AND DISCUSSION

Single crystals of the compound are grown by slow evaporation of ethanol during crystallization. Pale yellow coloured crystals have an approximate size (0.18 x 0.12 x 0.06 mm^3) and one of them was employed for data collection. Hemisphere data acquisition is used. The instrument is run for following factors such as: total scans = 3, total frames = 1271, exposure / frame = 10.0 sec / frame. The   θ range (2.18 to 25.0 °) is used. Completeness of the scans observed at θ of 25.0 ° which is 99.9 % for C$_{15}$ H$_{19}$ N O.H$_2$O having molecular weight, M = 247.32. Crystals belong to orthorhombic, space group P2$_1$2$_1$2$_1$, a = 7.6469 (8), b = 11.3899 (12), c = 16.3274 (18) Å, V = 1422.1(3) Å^3, Z = 4, D$_c$ = 1.160 g /cc, μ (Mo–K$_\square$) = 0.076 mm^{-1}, 7246, reflections measured, 2503 unique [I>2σ(I)], R value is 0.0603 and wR2 is = 0.1360. Largest difference peak and hole is observed at 0.239 and -0.295 e. Å $^{-3}$. The compound crystallizes along with a solvent water molecule which is hydrogen bonded to carbonyl oxygen atom.

Oak Ridge Thermal Ellipsoid Plot (ORTEP) for compound **5** is presented (Fig.1). Crystal data and structure refinement for Compound 5 are given (Table 1). It is seen (Fig. 2) when viewed down C axis. Molecules are inter molecularly hydrogen bonded with hydrogen atom of NH group. A linear chain of molecules is formed via N-H…O hydrogen bonding with x y z…x 1+y z and N…O while the distance noticed is 2.865 Å. (Fig.3).

Thermo gravimetric analysis of all synthesized compounds except compound **5** indicates that all molecules decompose in two steps. Thermal analysis describes the loss of each fragment. For all compounds the first step starts around 95^{0}c to 350 ^{0}c and the decomposition in second step extends from 267 ^{0}C to 657 ^{0}C. Compound **5** decomposes in three stages which correspond to 71^{0}C to 106^{0}C, 106 ^{0}C to 218^{0}C and 218^{0}C to 506^{0}C.

 In compound **3**, decomposition starts very slowly from 99 ^{0}c. The loss is seen from o.3 to 18 % up to 312^{0}C. The weight loss of 34.66 % & 49.50 % (cal.35.81& 42.79%)

is seen for C$_6$H$_5$ and C$_6$H$_5$ NH fragments between temperatures 328 to 338 ^{0}C. The loss of 64.83 % (cal.64.19 %) is examined at 363^{0}C for a loss of C$_8$H$_{12}$NO. At 346°C loss of 58.83% (cal.57.23%) corresponds to C$_8$H$_{12}$O molecule. The loss in weight is significant up to 371 ^{0}C and remains constant up to 480 ^{0}C where 72 % loss is detected. A sharp decrease is watched   up to 490 ^{0}C .Continuous loss in weights viewed up to 560 ^{0}C for 97.66 % weight loss. The details are in (Table 2, Fig.4).

In compound **5,** loss of water of crystallization at 97 ^{0}C corresponding to 7.28 % (cal.7.86%) is observed. The loss of toluene, C$_7$H$_7$, in the range 299^{0}C to 308 ^{0}C 36.40 % to 44.17 % (cal.38.74%) is noted. It is the loss of C$_7$H$_8$N which corresponds to loss of 44.17% (cal 46.29%) at 308 ^{0}C.The removal of dimedone moiety, C$_8$H$_{11}$O correlates to 52.42 % loss (cal 53.71%).The irradiated molecule of C$_8$H$_{12}$0N corresponds to 62.04% (cal 60.26%) at 320 ^{0} (Table 2, Fig 5).

In case of compounds **7** and **9** loss of C$_7$H$_7$ molecule match to 39.00 %and 37.58% (cal 39.74%) at 310 ^{0}C and 323 ^{0}C respectively. The loss of 46.00. % and 45.55 % (cal 46.29%) at 357 ^{0}C and 335 ^{0}C respectively ,are comparable to the species C$_8$H$_7$N .The results show consistency for the loss of C$_8$H$_{11}$O , which match with 53.8% and 53.00% (cal. 53.71%) at 429 ^{0}C and 340 ^{0}C.The removal of C$_8$H$_{12}$ON at 465 ^{0}C and 359 ^{0}C are consistent with 60.40 % (cal.60.26%) for both compounds **7** and **9**. (Table 2 Fig. 6&7).

The observed results for compounds **11** and **13** exhibit characteristic removal of halogen, chlorine atom at 312 ^{0}C and 323 ^{0}C with the loss of 13.21 % and 15.00% (cal 14.25%) respectively. The removal of aromatic chloro moiety, C$_6$H$_4$Cl, tally with 42.95 % and 44.00 % (cal 44.69%) at 348 ^{0}C and 400 ^{0}C respectively. The expulsion of C$_6$H$_5$NCl with 47.90% and 50.00 % (cal 50.80%) at 357 ^{0}C and 413 ^{0}C respectively match well with the calculated value The results are found to match well to the removal of C$_8$H$_{12}$ON with 55.28% and 55.00 % (cal.55.42%)   loss at 366 ^{0}C and 420 ^{0}C for the compounds**11** and **13** respectively. (Table 2 Fig. 8 &9).

It is very clear from the results obtained by applying Coats and Redfern equation that all molecules have order of reaction (η) of 0.8. The calculated energy of activation from the same formula indicates an increase in Ea from first stage to second stage for all compounds except compound **5.** The results are reported (Table 2). The energy of activation (Ea) is very high (13.85 kJ) during first stage. It decreases to 6.59 KJ for second stage, while a significant increase (9.87 KJ) is noticed during third stage of compound **5.**
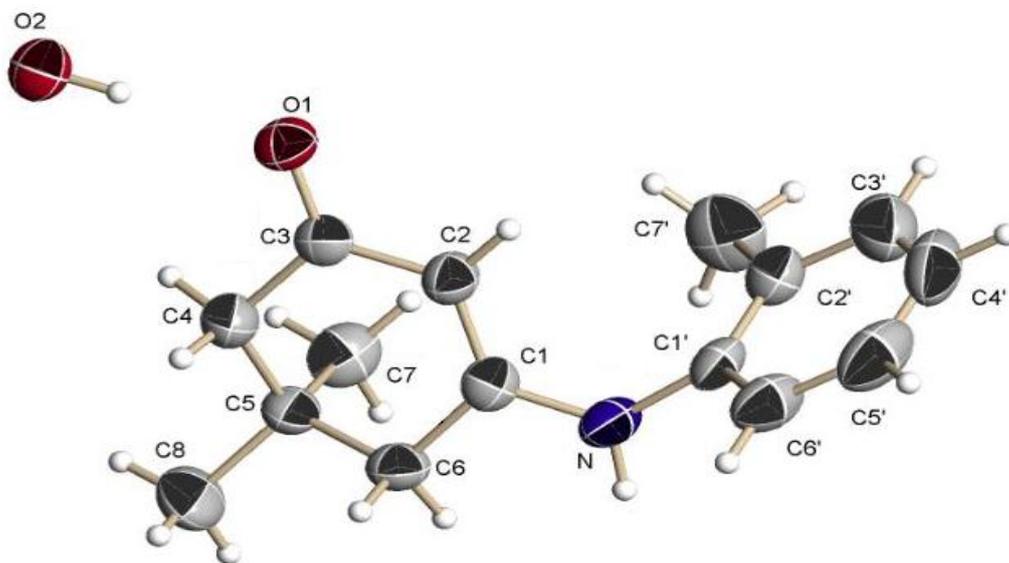
Fig. 1: ORTEP diagram of the Compound 5.
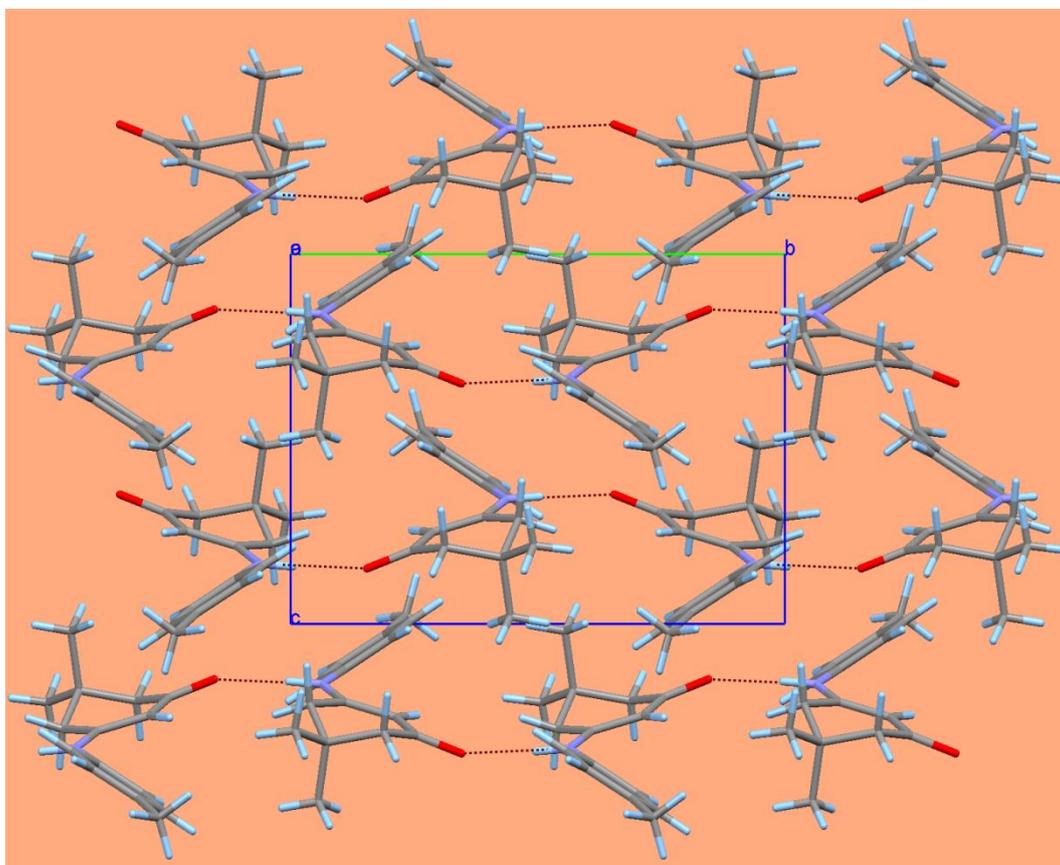
Fig. 2: Molecule Packing – viewed down A axis.
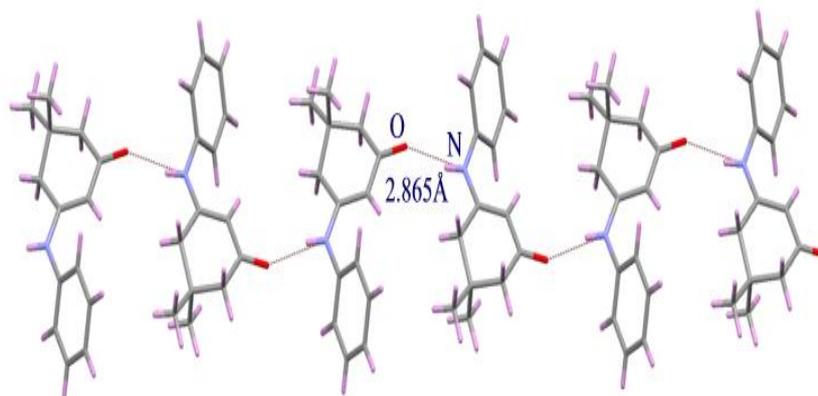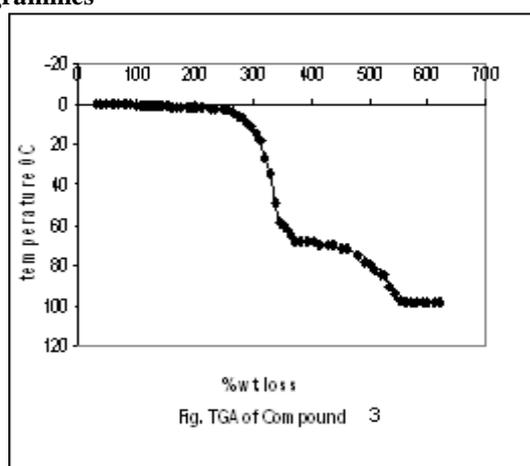
Fig. 3: ORTEP representation showing hydrogen bonding.

Thermogrammes

Figure 4
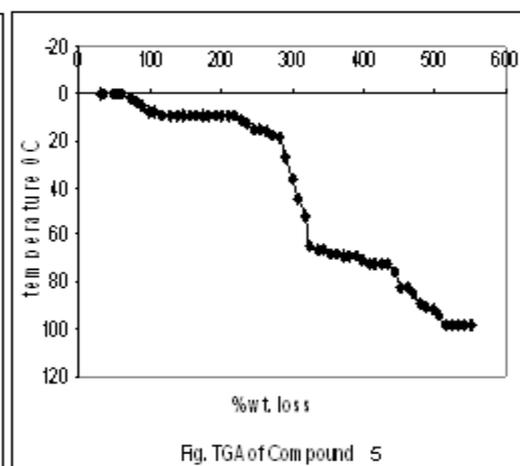

Figure 5

Figure 6

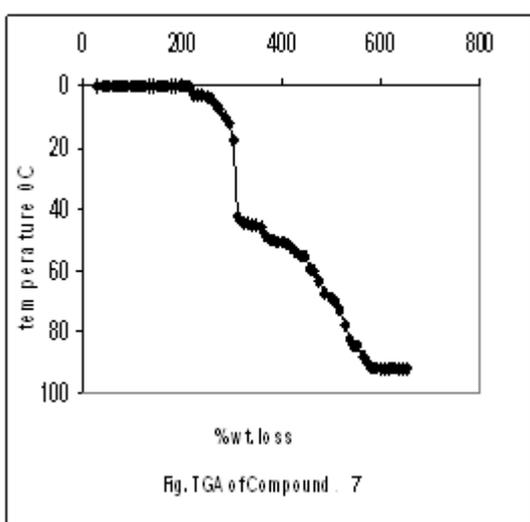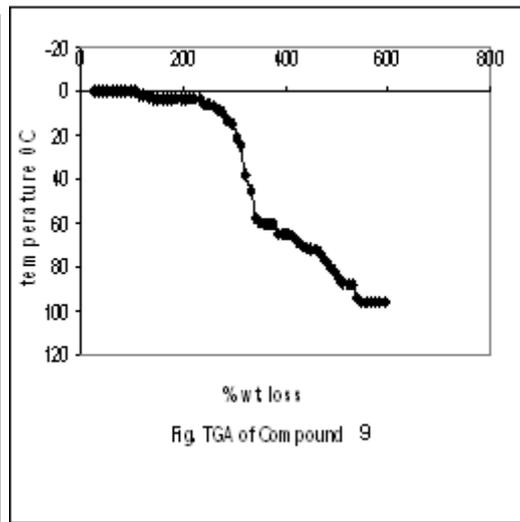**Figure 7**
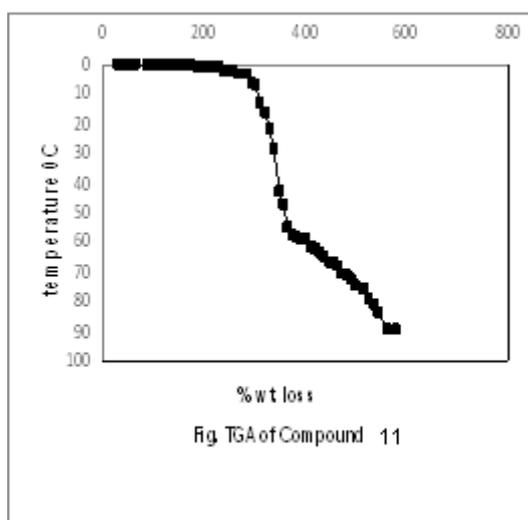
Figure 8
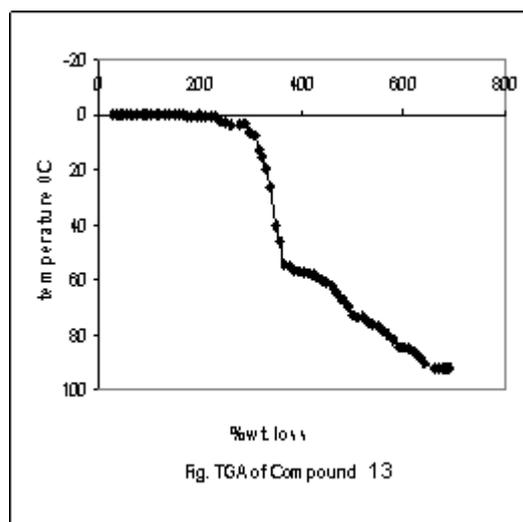
Figure 9

Table 1: Crystal data and structure refinement for Compound 5.

Empirical formula	$C_{15}H_{19}NO.H_2O$
Crystal size	$0.18 \times 0.12 \times 0.06 \ mm^3$
Formula weight	248.34
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a:6469 (8) A^o, b:390 (1) A^o c: 16.327(2) A^o, α: 90 ^{o} β:90 ^{o} γ:90 ^{o}
Volume and Z	1422.1 (3) and 4
Calculated density	1.160 g/cc
Absorption coefficient , F(000)	0.076 mm A^{-1} , 540
Theta range for data collection	2.18 to 25.00 ^{o}
Index ranges 14 ‹ =k ‹ =10.	-9‹ =h‹ =6, -13‹ =k‹ =13,-18‹ =l‹ =19
Reflections collected	7246
Independent refle.	2503 [R(int) = 0.0483]
Completeness to theta	99.9 %
Data/restraints/parameters	2503 /0/174
Goodness-of-fit on F^2	1.059
Final R indices [I › 2 sigma (I)] 0.1867	Rl = 0.0603, wR2 = 0.1360
R indices (all data) 0.2007	Rl = 0.0907, wR2 = 0.1485
Largest diff. peak and hole	0.239 and – 0.295 e. A A $^{-3}$

Table 2: Thermogravimetric parameters for all compounds ($RT = 29 \ ^0C$).

Comp	Stage No.	Temp. Range ^0C	% weight loss (Cal.)	% weight loss (Obs.)	Loss of Probable molecule	Order of Reaction (η)	Ea (KJ)
	I	RT to 360	64.18	64.09	$C_8H_{12}NO$	0.8	3.4
3	II	360 to 560	35.81	36	C_6H_5	0.8	10.93
	I	RT to 100	7.28	7.28	H_2O	0.8	13.85
5	II	100 to 320	55.80	54.97	$C_8H_{12}NO$	0.8	6.59
	III	320 to 500	36.89	35.56	C_6H_5	0.8	9.87
	I	RT to 460	60.17	60.4	$C_8H_{12}NO$	0.8	4.13
7	II	460 to 750	39.68	39.60	C_7H_7	0.8	11.93
	I	RT to 360	60.17	60.40	$C_{18}H_{12}NO$	0.8	6.46
9	II	360 to 700	39.68	39.05	C_7H_7	0.8	10.90
	I	RT to 365	55.31	55.28	$C_8H_{12}NO$	0.8	4.0
11	II	365 to 600	44.49	43.92	C_6H_4Cl	0.8	10.07
	I	RT to 380	55.31	55.45	$C_8H_{12}NO$	0.8	4.70
13	II	380 to 750	44.49	44.00	C_6H_4Cl	0.8	10.95

CONCLUSIONS

X-ray crystallographic study depicts that compound **5** is orthorhombic and intermolecular hydrogen bonding is observed as N - H----O. Thermal and kinetic parameters of all compounds exhibit decomposition in various stages at diverse temperatures. The invstigated order of reaction and activation energy   may be helpful in metabolic path ways, chemical reactions, catalysts etc.

ACKNOWLEDGEMENT

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