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Thermal study of synthesized 1,2,4-triazole compounds and their kinetic parameter evaluation

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ABSTRACT

A series of 1,2,4-Triazole derivatives were synthesized by condensation reaction. These synthesized compounds ($MM4_{c\text{-}e}$) were characterized by FT-IR, NMR, mass spectral and elemental analysis. The thermal stabilities of these compounds ($MM4_{c\text{-}e}$) were investigated by simultaneous TGA and DSC methods. The decomposition steps and thermal behaviour of ($MM4_{c\text{-}e}$) were investigated. The kinetic parameters such as order of reaction (n), energy of activation (E_a), pre-exponential factor (A), entropy of activation ($\Delta S^{\#}$), enthalpy of activation ($\Delta H^{\#}$) and Gibbs free energy of activation ($\Delta G^{\#}$) were evaluated using by Freeman-Carroll method.

Keywords*:* Freeman–Carroll method, TGA-DTA and DSC analysis, kinetics data

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INTRODUCTION

1,2,4-Triazole and its derivatives represent one of the most biologically active class of heterocyclic compounds. 1,2,4-triazole derivatives are known to exhibit antimicrobial agent. In recent years, a literature review revealed that 1,2,4-triazole derivatives belong to an significant moiety of heterocyclic compounds. 1,2,4-Triazole represent a group of heterocyclic compounds with a diverse of biological and pharmaceutical important are also being persued. 1,2,4-Triazole derivatives are known to exhibit antimicrobial [1-5], antitubercular [6-8], anticancer [9], anti-inflammatory [10], anticonvulsant [11], analgesic [12], antiviral [13], cytotoxic agent [14] antioxidant activity [15], aromatase inhibitor [16] and antimalerial agents [17]**.**

Thermal analysis is used for the investigation of the thermal behaviour of newly synthesized compounds such as presence of intermediates, degradation process, melting and final known composition. All thermal techniques simply measure the change of a specific property of a material as a function of temperature. The thermal techniques in the pharmaceutical sciences have great importance because of collective information obtained about the behavioural changes in the synthesized compounds when undergo to thermal changes at elevated temperature. Looking the importance of the subject and in continuation to our work in the field of thermal analysis of newly synthesized heterocyclic compounds, the present study focused on synthesis of 1,2,4-triazole derivatives and their thermal behaviour at elevated temperature.

EXPERIMENTAL SECTION

Melting points are determined on a Gallenkamp melting point apparatus and are uncorrected. Completion of reaction and purity of synthesized compounds were checked on thin layer chromatography (TLC), TLC was performed throughout the reaction on Merck silica gel GF_{254} aluminium sheets using mixture of benzene: ethyl acetate (8:2 V/V) as mobile phase and visualized under ultraviolet (UV) light or iodine vapour. Both compounds were purified by combi flash chromatography using ethyl acetate: hexane as eluent. Elemental analysis (% C, H, N) is carried out by a Perkin-Elmer 2400 CHN analyzer. IR spectra of compounds have been recorded on Thermo-Nicolet FT-IR-200 spectrophotometer in KBr disc (cm^{-1}). ^1H NMR and ^{13}C NMR spectra are recorded on Bruker DRX (200 MHz) spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard. Chemical shifts are reported in parts per million (δ_{ppm}). Mass spectra of synthesized compounds ($MM4_{a-b}$**)** were carried out by using the shimadzu GC-MS (Shimadzu 2010 plus) direct probe method. TGA and DSC of compounds ($MM4_{c-e}$) were scanned on a Perkin Elmer TGA and DSC (model No. Pyris-1) instrument under N_2 atmosphere at heating rate of 10 °C min^{-1}. Compounds ($MM4_{c-e}$**)** were synthesized by using Random synthesizer Syrris IKA-RCA with safety control.

1,2,4 triazole derivatives were synthesized according to method reported elsewhere [18-19].

Characterization data for both derivatives are summarized here in
Procedure for synthesis with elemental and characterization data of 3-methoxy benzoyl chloride; compound (1)
Synthesis of intermediate step was carried out using standard methods available in the literature. A brief notation is given here. A mixture of 5.0 gm 3-methoxy benzoic acid and 7.5 mL thionyl chloride in 250 mL RBF was refluxed about 8 hrs, after completion of reaction; excess thionyl chloride was distilled and allowed the solution at room temperature to get a solid product of 3-methoxy benzoyl chloride (**1**). The characterization data are summarized here.

IR (KBr) ν max, cm^{-1}: IR (KBr) $_{\nu max}$, cm^{-1}: 3059 (Ar–C–H stretching), 1038 (Ar–O–C stretching), 1466 (Ar–CH_3 bending), 758 (C–Cl stretching). 1H NMR ($CDCl_3$, 200 MHz) δ: 7.204-7.940 (m, 4H, Ar–H), 3.706 (s, 3H, methoxy, Ar–OCH_3) ppm. 13C NMR ($CDCl_3$, 100 MHz) 115.3-160.4 (benzene ring, C–H, 6C), 167 (benzene ring, $^-$C=O 1C), 55.6 (Ar–OCH_3, 1C) ppm. MS: *m/*z (relative abundance; %), $M^{+\bullet}$ 171 a. m. u. anal Calcd (%) for $C_8H_7ClO_2$: C, 56.32; H, 4.14; N, 0.00%; Found: C, 56.32; H, 4.13; N, 0.00%.

Procedure for synthesis with elemental and characterization data of 3-methoxybenzoyl isothiocyanate; compound (**2**)
A solution of 3-methoxy benzoyl chloride (**1**) (0.01mole) in dry acetone (50mL), ammonium thiocyanate (0.01mole) was added with constant stirring at room temperature. Reaction mixture was stirred for an hour, and after the completion of reaction, the formed precipitate of ammonium chloride was filtered, while the filtrate containing 3-methoxy benzoyl isothiocyanate (2).

IR (KBr) ν_{max}, cm^{-1}: 3058 (Ar–C–H stretching), 1037 (Ar–O–C stretching), 1465 (Ar–CH_3 bending), 757 (C–Cl stretching), 2116 (–N=C stretching of isothiocynate), 1119 (–C=S stretching). ^1H NMR ($CDCl_3$, 200 MHz) δ: 7.206-7.945 (m, 4H, Ar–H), 3.708 (s, 3H, methoxy, Ar–OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 115.6-160.3 (benzene ring, C–H and C-O, 7C), 166.8 (attached to benzene ring, C-C 1C), 55.7 (Ar–OCH_3, 1C) ppm. MS: *m/*z (relative abundance; %), $M^{+\bullet}$ 194 a. m. u. anal Calcd (%) for $C_9H_7NO_2S$: C, 55.94; H, 4.65; N, 7.25%; Found: C, 55.93; H, 4.64; N, 7.23%.

Procedure for synthesis with elemental and characterization data of 5-(3-methoxyphenyl)-1-phenyl-1*H*-1,2,4-triazole-3(2*H*)-thione; compound (**3**)

The phenyl hydrazine (0.01mole) was added in the filtrate, then the reaction mixture was refluxed for 5 hr, solid product was filtered, washed with water and cold acetone to get compound (3).

IR (KBr) ν_{max}, cm^{-1}: 3056 (Ar–C–H stretching), 1041 (Ar–O–C stretching), 1468 (Ar–CH_3 bending), 1665 (–C=N stretching), 1117 (–C=S stretching).^1H NMR ($CDCl_3$, 200 MHz) δ: 7.208-7.940 (m, 9H, Ar–H), 3.705 (s, 3H, methoxy, Ar–OCH_3), 4.105 (s, 1H, Ar–NH, secondary amine) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 111.61-129.26 (C–H and C–C, triazole and benzene ring, 11C), 163.07 (–C=S, triazole ring, 1C), 161.68 (–C–OCH_3, attached to

methoxy, 1C), 139.55 (–C=N, triazole ring, 1C), 58.13 (Ar–OCH_3, 1C) ppm. MS: *m/*z (relative abundance; %), $M^{+\bullet}$ 282 a. m. u. anal Calcd (%) for $C_{15}H_{13}N_3OS$: C, 66.58; H, 4.62; N, 14.83%; Found: C, 66.55; H, 4.60; N, 14.81%.
Procedure for synthesis with elemental and characterization data of 2-(((4-fluorophenyl)amino)methyl)-5-(3-methoxyphenyl)-1-phenyl-1*H*-1,2,4-triazole-3(2*H*)-thione ($MM4_c$)

A mixture of compound (3) (0.01mole), formaldehyde (0.01mole) and 4-fluoro aniline (0.01mole) in 1,4-dioxan (50mL) was stirred for 22 hrs. After a completion of the reaction, neutralize it with liquor, ammonia solution then poured in water, and in this mixture, ethyl acetate was added for the extraction of the final compound ($MM4_c$). Distilled the solvent, get a compound ($MM4_a$), and recrystalized with methanol. The structure of compound $MM4_c$ is shown in figure 1.

Other series of compounds ($MM4_{c-e}$) were prepared by using a similar method and their physico-chemical data are summerized in Table-1.

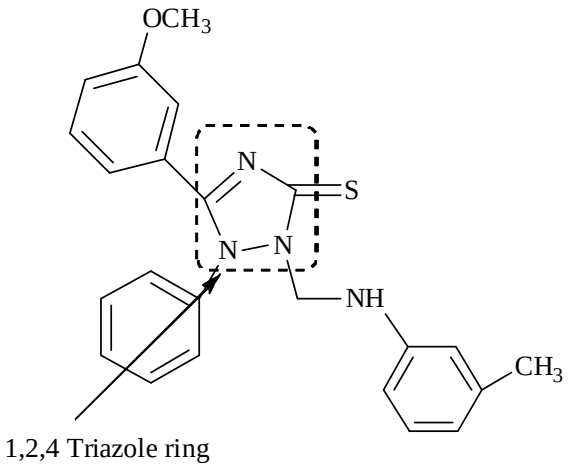

Figure 1 Structure of compound MM4c

Table 1 Physico chemical data of compounds ($MM4_{c-e}$) obtained from DSC technique

Compound' Code	Peak Temp /ºC (Endo)	On set Temp/ºC	End set Temp/ºC
$MM4_c$	207.83	186.11	218.59
$MM4_d$	226.14	213.46	230.34
$MM4_e$	215.45	203.24	222.39

IR (KBr) ν_{max}, cm^{-1}: 2985 & 3058 (Ar–C–H stretching), 1039 (Ar–O–C stretching), 1398 (Ar–CH_3 bending), 755 and 789 (C–H out of plane), 1598 (–C=N stretching), 1120 (–C=S stretching), 1398 (C–F stretching). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.224-8.449 (m, 13H, Ar–H), 3.567 (s, 3H, methoxy, Ar–OCH_3), 3.428 (s, 1H, Ar–NH, secondary amine), 3.785 (d, 2H, –CH_2) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 111.23-141.64 (C–H, C–N and –C–C triazole and benzene ring, 15C), 187.23(–C=S, 1C), 160.13 (–C–OCH_3, attached to methoxy, 1C), 161.87 (–C=N, triazole ring, 1C), 55.78 (Ar–OCH_3, 1C), 75.35 (N–CH_2, attached to triazole ring, 1C), 143.47 (–C–NH, 1C), 148.65 (C–F benzene ring, 1C) ppm. MS: *m/*z (relative abundance; %), $M^{+\bullet}$ 407 a. m. u. anal Calcd (%) for $C_{22}H_{19}FN_4OS$: C, 65.01; H, 4.71; N, 13.78%; Found: C, 65.01; H, 4.70; N, 13.76%.

Elemental and characterization data of 2-(((3-chlorophenyl)amino)methyl)-5-(3-methoxyphenyl)-1-phenyl-1*H*-1,2,4-triazole-3(2*H*)-thione ($MM4_d$).
IR (KBr) ν_{max}, cm^{-1}: 2923 (Ar–C–H stretching), 3318 (Ar–O–H stretching), 1040 (Ar–O–C stretching), 1463 (Ar–CH_3 bending), 756 and 856 (C–H out of plane), 1659 (–C=N stretching), 1118 (–C=S stretching). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.878-8.751 (m, 13H, Ar–H), 3.724 (s, 3H, methoxy, Ar–OCH_3), 3.733 (s, 1H, Ar–NH, secondary amine), 3.887 (d, 2H, –CH_2) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 110.86-140.43 (C–H, C–N and –C–C triazole and benzene ring, 15C), 187.27 (–C=S, 1C), 160.54 (–C–OCH_3, attached to methoxy, 1C), 162.62 (–C=N, triazole ring,

1C), 55.72 (Ar–OCH_3, 1C), 75.39 (N–CH_2, attached to triazole ring, 1C), 148.83 (C–NH, 1C), 135.16 (C–Cl, benzene ring, 1C) ppm. MS: *m/*z (relative abundance; %), $M^{+\bullet}$ 423 a. m. u. anal Calcd (%) for $C_{22}H_{19}ClN_4OS$: C, 62.48; H, 4.53; N, 13.25%; Found: C, 62.47; H, 4.52; N, 13.23%.

Elemental and characterization data of 2-(((2,5-dimethylphenyl)amino)methyl)-5-(3-methoxyphenyl)-1-phenyl-1*H*-1,2,4-triazole-3(2*H*)-thione ($MM4_e$).
IR (KBr) ν_{max}, cm^{-1}: 2985 & 3060 (Ar–C–H stretching), 3378 (Ar–O–H stretching), 1035 (Ar–O–C stretching), 1472 (Ar–CH_3 bending), 755 and 856 (C–H out of plane), 1698 (–C=N stretching), 1117 (–C=S stretching). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 6.945-8.738 (m, 12H, Ar–H), 3.749 (s, 3H, methoxy, Ar–OCH_3), 3.765 (s, 1H, Ar–NH, secondary amine), 3.432 (d, 2H, –CH_2), 3.587 (s, 6H, Ar–CH_3, benzene ring) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) 110.62-139.31 (C–H, –C–N and –C–C triazole and benzene ring, 16C), 162.13 (C–H, 1C), 187.51 (–C=S, 1C), 55.87 (Ar–OCH_3, methoxy, 1C), 161.28 (–C=N, triazole ring, 1C), 74.86 (N–CH_2, attached to triazole ring, 1C), 161.67 (C–NH, 1C), 18.43 and 25.72 (Ar–CH_3, 2C) ppm. MS: *m/*z (relative abundance; %), $M^{+\bullet}$ 417 a. m. u. anal Calcd (%) for $C_{24}H_{24}N_4OS$: C, 69.20; H, 5.81; N, 13.45%; Found: C, 69.19; H, 5.79; N, 13.43%.

RESULTS AND DISCUSSION

Thermal behaviour of compound $MM4_c$
TGA thermogram of compound $MM4_c$ is depicted in figure-2 and it is evident from the figure-2 that $MM4_c$ is thermally stable up to about 200°C and followed single step degradation. The mass loss involved over the decomposition temperature range from 200 to 400 ℃.

The final residue was obtained at 400 with 21.17%. Freeman-Carroll plot is depicted in figure-3 and the DSC curve of compound $MM4_c$ is depicted in figure-4.

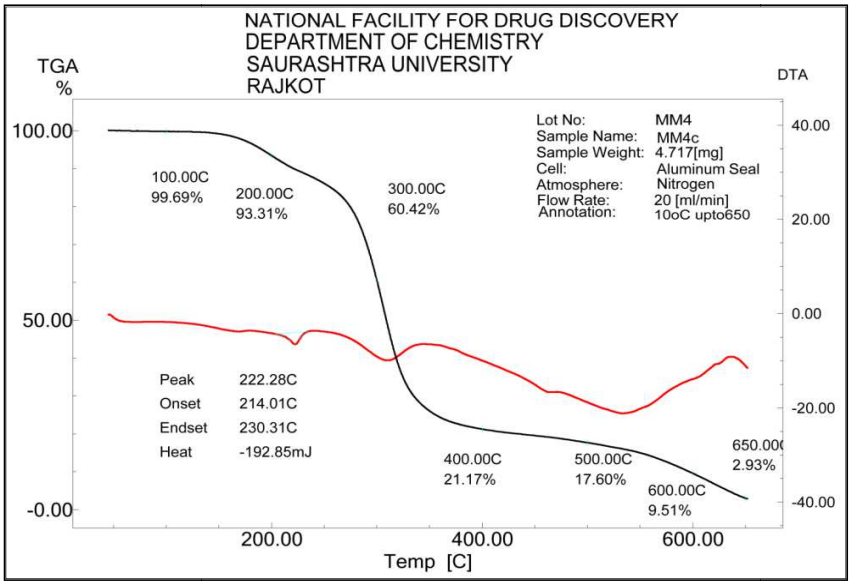

Figure-2 Simultaneous TGA thermogram of compound ($MM4_c$) at the heating rate of 10 °C/min in an N_2 atmosphere

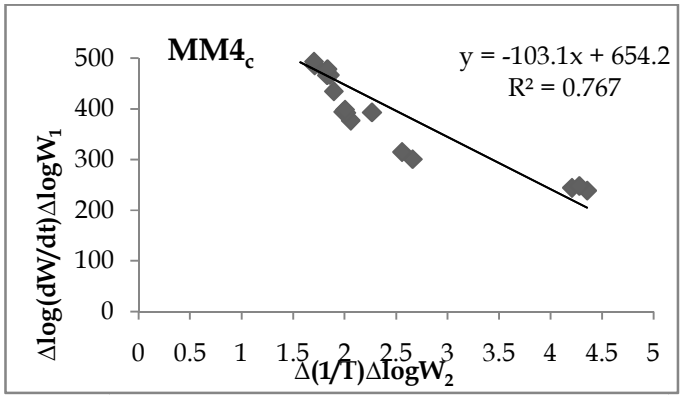

Figure-3 Freeman-Carroll plot for compound $MM4_c$

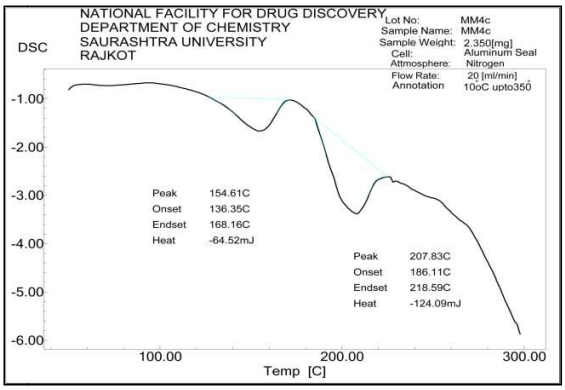

Figure-4 DSC thermogram of compound $MM4_c$ at the heating rate of 10 °C/min in an N_2 atmosphere

Endothermic transition was found at 200 °C and corresponding $\Delta H^{\#}$ was -124.09 $Jmol^{-1}deg^{-1}$, which was due to melting of $MM4_c$. The least square values (R^2= 0. 767) of E_a, A, $\Delta S^{\#}$, $\Delta H^{\#}$ and $\Delta G^{\#}$ were determined as 8.0818 *k*J mol^{-1}, 0.1534 s^{-1} -101.22 *k*J mol^{-1}, 3.251 *k*J mol^{-1} and 62.063 *k*J mol^{-1} respectively.

Thermal of compound $MM4_d$ is depicted in figure 5 and it is evident from the figure that $MM4_d$ is thermally behaviour of compound $MM4_d$

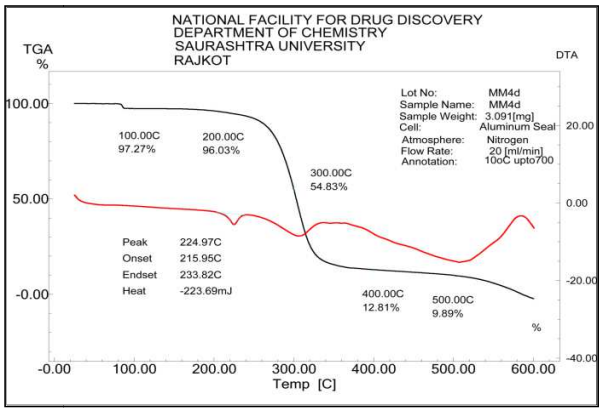

Figure 5 Simultaneous TGA thermogram of compound $MM4_d$ at the heating rate of 10 °C/min in an N_2 atmosphere

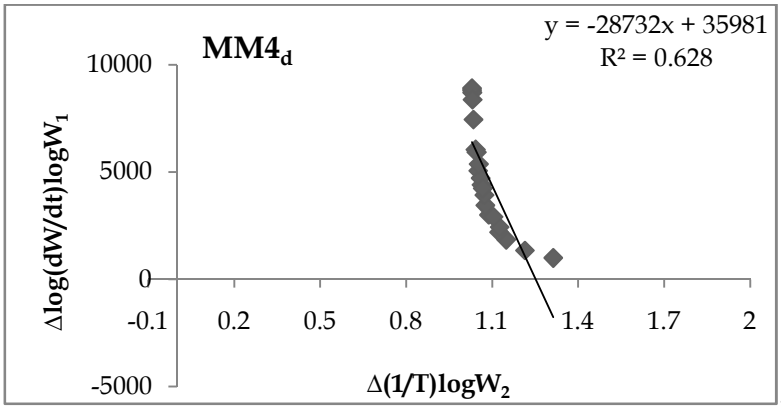

Figure-6 Freeman-Carroll plot for compound $MM4_d$

TGA thermogram stable up to about 200 ℃ and followed single step degradation. The mass loss involved over the decomposition temperature range from 400 to 400 ℃. The final residue was obtained at 400°C with 12.81%. Freeman-Carroll plot is depicted in figure-6. Endothermic transition was found at 226.14 ℃ and corresponding $\Delta H^{\#}$ was -53.10 $Jmol^{-1}deg^{-1}$, which was due to melting of $MM4_d$. The least square values (R^2= 0.628) of E_a, A, $\Delta S^{\#}$, $\Delta H^{\#}$ and $\Delta G^{\#}$ were determined as 7.2301 kJ mol^{-1}, 0.1179 s^{-1} -101.60 kJ mol^{-1}, 2.432 kJ mol^{-1} and 61.573 kJ mol^{-1}respectively. Negative magnitude of $\Delta S^{\#}$ established that transition state was much in orderly state for compound $MM4_d$.

Thermal behaviour of compound $MM4_e$

TGA thermogram of compound $MM4_e$ is depicted in figure-7 and it is evident from the figure that $MM4_e$ is thermally stable up to about 200℃ and followed single step degradation. The weight loss involved over the decomposition temperature range from 200 to 400 ℃. The final residue was obtained at 400°C with 16.72%. Freeman-Carroll plot is depicted in figure-8.

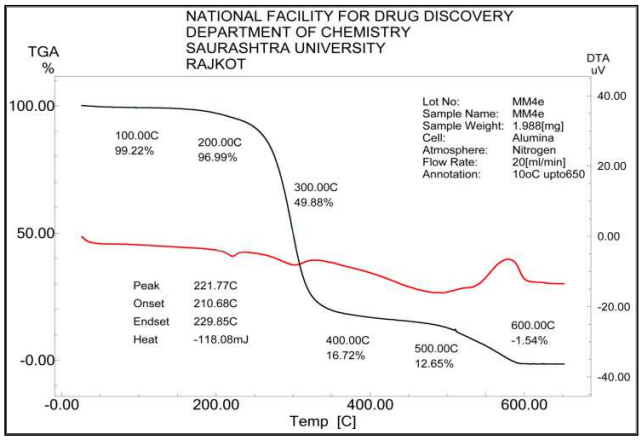

Figure 7 Simultaneous TGA thermogram of compound $MM4_e$ at the heating rate of 10 °C/min in an N_2 atmosphere

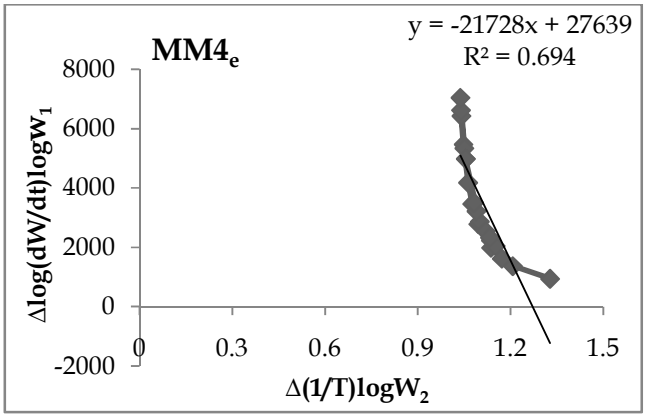

Figure-8 Freeman-Carroll plot for compound $MM4_e$

Endothermic transition was found at 215.45 ℃ and corresponding $\Delta H^{\#}$ was -43.58 $Jmol^{-1}deg^{-1}$, which was due to melting of MM4e. The least square values (R^2= 0.694) of E_a, A, $\Delta S^{\#}$, $\Delta H^{\#}$ and $\Delta G^{\#}$ were determined as 69.2428 kJ mol^{-1}, 456390.4 s^{-1} -93.447 kJ mol^{-1}, 64.487 kJ mol^{-1}, 118.50 kJ mol^{-1}respectively. Negative magnitude of $\Delta S^{\#}$ established that transition state was much in orderly state for compound $MM4_e$. Thermal data and kinetic parameters of the synthesized molecule are presented in tables 2 and 3 respectively. The degradation of the compound is involved a variety of reactions namely rearrangement, bond cleavage, branching, etc. Methoxy, dimethyl, and chloro

substitute groups are electro-negative in nature and therefore, selective cleavage took place as of this structure of the thiazolidine ring, which further underwent a series of reactions and ultimately degraded into low molecular mass substance.

Table 2 TGA results of 1,2,4-triazole compounds ($MM4_{c-e}$)

Compound Code	Temp. range /°C	% Weight loss (Total)	Assignment
$MM4_c$	100-600	90.49	Single step decomposition
$MM4_d$	100-500	90.11	Single step decomposition
$MM4_e$	100-500	87.35	Single step decomposition

Table 3 Thermodynamic data of the thermal decomposition of 1,2,4-triazole compounds ($MM4_{c-e}$)

Compound Code	TGA range/°C	E_a/ kJmol^{-1}	A/S^{-1}	$\Delta S^{\#}$ /Jdeg^{-1}	$\Delta H^{\#}$/ kJ mol^{-1}	$\Delta G^{\#}$/ kJ mol^{-1}
$MM4_c$	100-650	8.8081	0.1534	-101.22	3.251	62.063
$MM4_d$	100-500	7.2301	0.1179	-101.60	2.432	61.057
$MM4_e$	100-500	69.2928	0.4564	-93.447	64.487	118.50

Table 4 Decomposition temperature, final temperature, percentage weight loss of 1,2,4-triazole compounds obtained from TGA ($MM4_{c-e}$)

Compound Code	T_0,	T_{10}, /°C	T_f/ °C	T_{max}/ °C	Decomposition Range °C	% Wt. loss	% Residue
$MM4_c$	100	217	600	500	100-500	82.40	17.60
$MM4_d$	100	259	600	500	100-500	90.11	9.89
$MM4_e$	100	253	600	500	100-500	87.35	12.65

CONCLUSION

1,2,4-triazole derivatives ($MM4_{c-e}$) were prepared successfully using standard protocols with some modifications to yield title compounds. Three targeted titled compounds were further characterized by various spectral techniques.

The thermal behaviour of compounds ($MM4_{c-e}$) was carried out using TGA-DTA and DSC techniques. In all the three cases, endothermic reaction, and one-step degradation was observed. Thermodynamic and kinetic parameters were calculated using Freeman-Carroll method; this suggests that degradation process was dominated by first order reaction. The assessment of thermal stability to understand structural relationship of three synthesized derivatives of 1,2,4-triazole is of great importance looking to the importance of 1,2,4-oxo-thiazolidine in pharmaceutical chemistry. Significant variation of thermal stabilities is expected in three derivatives of 1,2,4-triazole due to their structural modification. It has been found that small structural changes of hydrazide moiety can modify substantially the thermal behavior. Approach of this work is to study the thermal behavior of two compounds in non-isothermal system.

Overall, the aim of our present study is achieved successfully and three compounds of 1,2,4-triazole were prepared. The findings suggest that the compounds possess good thermal stability and hence, can be used further for medicinal use after successful completion of all necessary protocols.

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REFERENCES

[1] H Bayrak; A Demirbas; N Demirbas; KA Sengu. *Eur. J. Med. Chem.*, **2009**, 44, 4362–4366.
[2] K Sztanke; T Tuzimski; J Rzymowska; K Pasternak; M Kandefer-Szerszen. *Eur. J. Med. Chem.*, **2009**, 43, 404-419.

[3] BS Holla; B Kallurya; KR Sridhar; E Drake; LM Thomas; KK Bhandary; MJ Levine. *Eur. J. Med. Chem*., **1994**, 29, 301–308.
[4] ZA Kaplancikli; G Turan-Zitouni; A Ozdemir; G Revail. *Eur. J. Med. Chem*., **2008**, 43(1), 155–159.
[5] R Mishra; R Kumar; S. Kumar; J Majeed; M Rashid; S. Sharma. *J. Chil. Chem. Soc*; **2010**, 55 (3), 359–362.
[6] I Kucukguzel; SG Kucukguzel; S Rollas; M Kiraz. *Bioorg. Med. Chem. Lett*; **2001**, 11, 1703-1707.
[7] L Zahajska; V Klimesova; J Koci; K Waisser; J Kaustova. *Arch. Pharm. Med. Chem*; **2004**, 337, 549-555.
[8] A Foroumadi; Z Kiani; F Soltani; *IL Farmaco*; **2003**, 58, 1073-1076.
[9] MS Karthikeyan; DJ Prasad; B Poojary; K Subrahmanya Bhat; BS Holla; NS Kumari. Bioorg. *Med. Chem;* 14 (2006) 7482-7489.
[10] MF El-Shehry; AA Abu-Hashem; EM El-Telbani. *Eur. J. Med. Chem*; **2010**, 45, 1906-1911.
[11] J Chen; XY Sun; KY Chai; JS Lee; MS Song; ZS Quan. *Bioorg. Med. Chem*., **2007**, 15, 6775-6781.
[12] AA El-Emam, TM Ibrahim. *Arzn-Fors/Drug Res*., **1991**, 41 (12), 1260–1264.
[13] M Kritsanida; A Mouroutsou; P Marakos; N Pouli; S Papakonstantinou-Garoufalias; C Pannecouque; M Witvrouw; E De Clercq. *Farmaco*., **2002**, 57, 253–257.
[14] T. Mosmann; *J. Immu. Meth;* **1983**, 65, 55–63.
[15] PB Bandgar; SS Gawande; RG Bodade; JV Totre; CN Khobragade. *Bioorg. Med. Chem*., **2010**, 18(3), 1364–1370.
[16] RW Brueggemeier; CH John; SD Edgar. *Endocrine. Rev*; **2004**, 26, 331–345.
[17] V Patil; W Guerran; C Po; DB Benicewicz; SI Khan; BL Tekwani; AK Oyelere. *Bio-org. Med. Chem*; **2010**, 18 (1), 415-425.
[18] DR Godhani; DB Sanja; AM Sanghani; PB Dobariya. *Ind. J. Het. Chem*., **2011**, 20, 411-412.
[19] DR Godhani; AM Sanghani; DB Sanja; PB Dobariya. *J. Ind. Chem. Soc*., **2012**, 89, 971-974.