Non-isothermal decomposition of 4-(5-(4-fluoro-3-phenoxyphenyl)-4,5-dihydro-3-(3,4-dimethoxyphenyl) pyrazol-1-yl)benzonitrile under Nitrogen atmosphere

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ABSTRACT

pyrazoline namely 4-(5-(4-fluoro-3-phenoxyphenyl)-4,5-dihydro-3-(3,4-dimethoxyphenyl)pyrazol-1-yl)benzonitrile (DMPCN) was synthesized by the cyclization of (E)-3-(3-fluoro-4-phenoxyphenyl)-1-(3,4-dimethoxyphenyl)prop-2-en-1-one and 4-cyano phenyl hydrazine in the presence of sodium hydroxide. The yield of pyrazoline is more than 85%. The synthesized compound was purified by crystallization using ethanol. The structure of the synthesized compound was assigned on the basis of the spectral data. IR, ^{1}H NMR, ^{13}C NMR and Mass spectra showed that expected absorption frequencies and signals of DMPCN. The thermal decomposition of synthesized compound was studied by Thermogravimetry / Derivative thermogravimetry analysis (TG-DTG) under dynamic Nitrogen atmosphere at different heating rates of 10, 15 and 20 K min^{-1}. The kinetic parameters were estimated using model-free (Friedman, Kissinger-Akahira-Sunose (KAS) and Flynn-Wall-Ozawa (FWO)) and model-fitting method (Coats-Redfern (CR)). The most probable fitting kinetic model was also determined.

Keywords: TG-DTG, model free methods, model fitting method, kinetic models, thermodynamic parameters, Invariance.

1. Introduction

Heterocyclic compounds are a group of organic compounds containing rings in which one or more of the carbon atom is replaced by an atom other than carbon, usually nitrogen, oxygen, sulphur or other hetero atoms. Heterocyclic compounds containing nitrogen are most abundant with great biological applicability than those containing oxygen or sulphur. Pyrazolines as a class of nitrogen containing heterocyclic compounds have many medicinal applications. The pharmacological and antitumor activities of many compounds containing

pyrazoline rings have been reviewed[1].They are reported to be potential extractants and powerful drugs[2]. It is also reported that many pyrazoline derivatives have found applications in both pharmaceutical and agrochemical fields[3-5]. Pyrazolines used as pesticide coating material agents[6]. pyrazoline derivatives have been found to possess considerable biological activities, which stimulated the research activity in this field. They have several prominent effects, such as antibacterial[7], antifungal[8], antihistaminic[9], antimycobacterial[10], anticancer[11], antitumor[12], analgesic[13], anticonvulsant[14], antiproliferative activity[15], antitubercular[16], cardiovascular activity[17], antioxidant[18], antidepressant[19], antidiabetic[20], anti-inflammatory[21], herbicidal[22]. Recently these classes of compounds are reported to possess potential antiviral activity against flavivirus[23] and HIV[24]. Literature survey reveals that no work has been reported on thermal decomposition of Pyrazoline under non-isothermal decomposition in the presence of dynamic nitrogen atmosphere. This prompted us to carry out the synthesis, spectral characterization and thermal studies of 4-(5-(4-fluoro-3-phenoxyphenyl)-4,5-dihydro-3-(3,4-dimethoxyphenyl)pyrazol-1-yl)benzonitrile (DMPCN)

2. Procedure

2.1. Materials

Starting materials obtained from commercially sources Sigma alrich chemicals of AnalaR grade 3,4-dimethoxy acetophenone, 4-cyanophenylhydrazine, Sd fine chemicals of AnalaR grade 4-fluoro-3-phenoxy benzaldehyde were used without purification. Analytical grade solvents like ethanol, ethyl acetate, hexane and dimethyl sulfoxide (DMSO) were used as such without further purification.

2.2. Methods

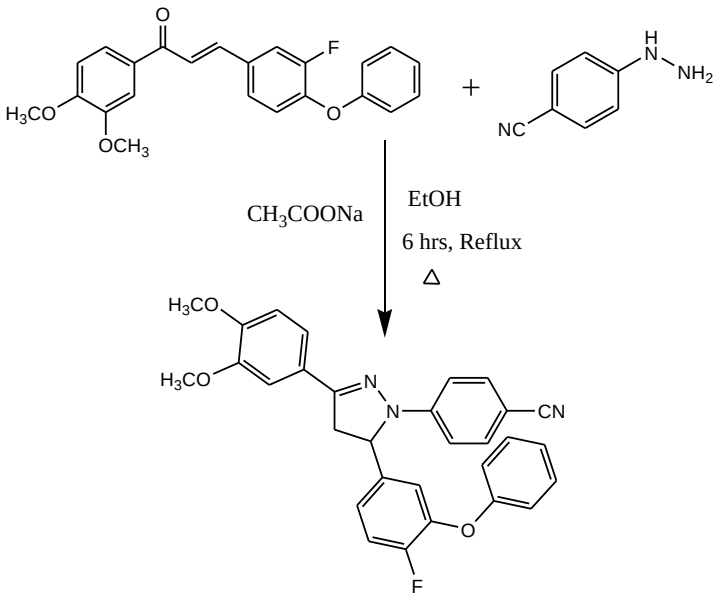
Analytical Thin Layer Chromatography (TLC) was performed on pre-coated plastic sheets of silica gel G/UV-254 of 0.2 mm thickness. Melting points of the synthesized compound was determined in open-glass capillaries on a Mettler FP51apparatus and recorded in ^{0}C without correction. FT-IR measurement was done as KBr pellets for solids using SHIMADZU-2010 Fourier transform Infra-Red (FT-IR) spectrophotometer (4000- 400 cm^{-1}). The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d6 using TMS as internal standard with Bruker 400 MHz and 100 MHz high resolution NMR spectrometer.

2.3. Thermal analysis

The simultaneous TGA/DTG curves were obtained with the thermal analysis system model Perkin Elmer TGA 4000 V1.04 at IIT-Madras, India. The TG analysis of DMPCN was carried out under dynamic nitrogen atmosphere using Perkin Elmer Pyris TGA 4000 (0-200 ml min^{-1}) in an 180 µl ceramic pan with a sample at the heating rates of 10,15 and 20 K min-1 from 35 to 900 °C. In order to ensure the uniformity of temperature of the sample and good reproducibility, small amounts (5 mg) were taken. The sample temperature controlled by thermocouple, did not exhibit any systematic deviation from the present linear temperature programme. The kinetic parameters *E*a and A were calculated using Microsoft Excel Software®.

3. Synthesis of 4-(5-(4-fluoro-3-phenoxyphenyl)-4,5-dihydro-3-(3,4-dimethoxyphenyl) pyrazol-1-yl) benzonitrile (DMPCN)

An appropriate equi-molar quantities of (*E*)-3-(3-fluoro-4-phenoxyphenyl)-1-(3,4-dimethoxyphenyl)prop-2-en-1-one (Chalcone) (0.20 mmol), 4-cyanophenylhydrazine (0.20 mmol) and anhydrous sodium acetate (0.5 g) was refluxed[25] in (15 mL) ethanol for 6hrs (Scheme-1). The completion of the reaction was monitored by TLC. The reaction mixture was cooled, and poured into ice cold water. The precipitate was filtered, dried and subjected to column chromatography using hexane and ethyl acetate (3:1) as eluent.



Scheme -1 Reaction pathway for the synthesis of 4-(5-(4-fluoro-3-phenoxyphenyl)-4,5-dihydro-3-(3,4-dimethoxyphenyl)pyrazol-1-yl)benzonitrile (DMPCN)

Physical and Spectral data

IR νcm^{-1}: 1595.49; ^{1}H NMRδ(ppm): 3.351(H_a, 1H-*dd*)ppm, 3.692(H_b, 1H-*dd*)ppm, 5.087ppm(H_c, 1H-*d*), 6.694 -7.088(*m*, Aromatic protons)ppm, 3.239 ppm (-CH_3, 6H-*s*) ; ^{13}C NMRδ(ppm): 157.243(C=N)ppm, 40.779(C_α)ppm, 65.332(C_β)ppm, 55.971, 55.936 (C-OCH_3)ppm; Mass m/z; 493[M+], 474, 467, 432, 391, 356, 306, 188, 137, 102; m.p. 87°C; Yield : 89% ; Molecular Formula: $C_{30}H_{24}FN_3O_3$.

3.1 Thermal analysis of DMPCN

The thermograms of pure DMPCN recorded in a dynamic nitrogen atmosphere at different heating rates of 10, 15 and 20 K min^{-1} are presented in Fig-1. The thermal decompositions process of DMPCN stars at 483K and ends at 823 K with endothermic nature.

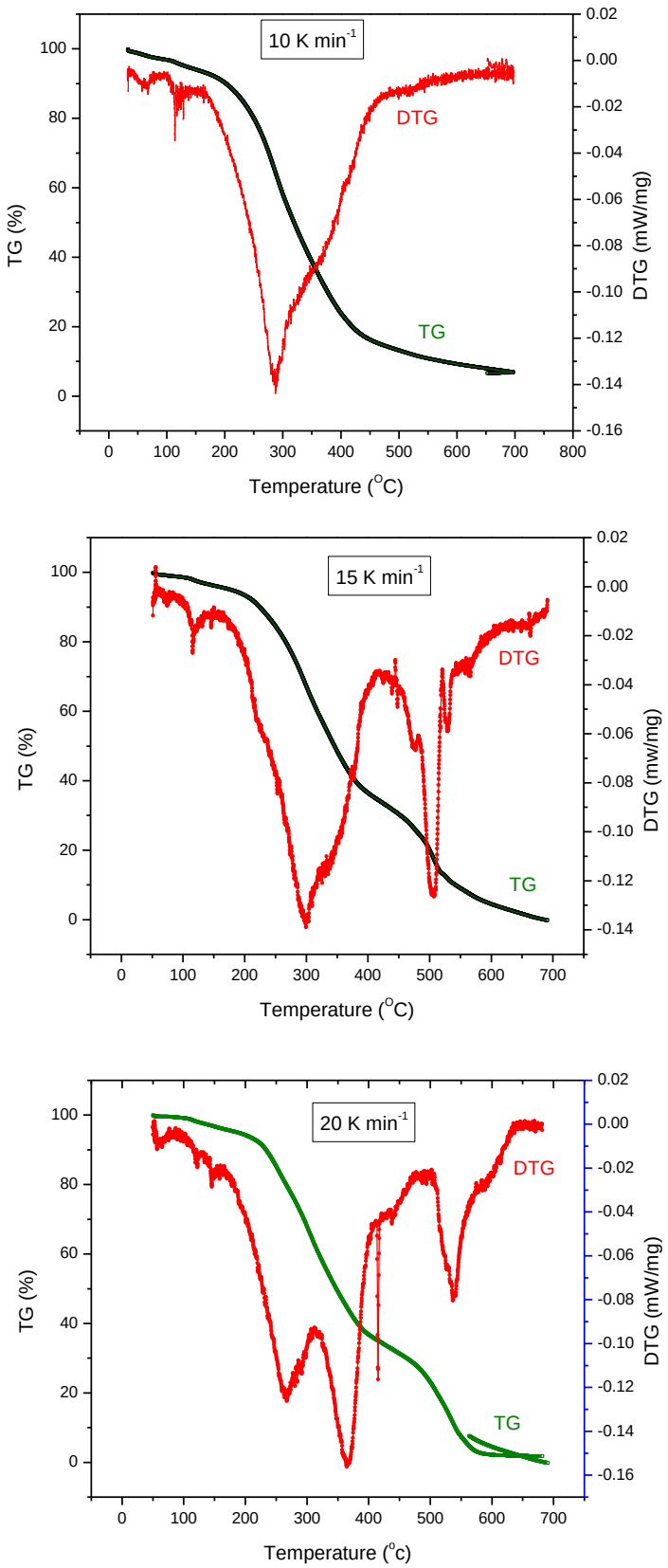


Fig -1 TG – DTG curves of DMPCN at 10, 15 and 20 K min^{-1} heating rates in nitrogen atmosphere

3.2 Model-free analysis

All results of non-isothermal TG analyses under dynamic nitrogen atmosphere and typical results are shown in Fig-2. The obtained TG analysis data for the described stages of the compound DMPCN was analyzed to determine the activation energy for a different level of conversion using eqn. (1).

$$\ln\left(\beta / T^{2}\right) = \ln\left[\frac{AE_{a}}{g(\alpha)\,R}\right] - \frac{E_{a}}{RT} \qquad \text{---------- (1)}$$

The non-isothermal decomposition kinetics of DMPCN is first analyzed by model-free methods *viz.*, Friedman,[26] Flynn-Wall-Ozawa,[27] and Kissinger-Akahira-Sunose[28,] (Table - 1) show that the variation of apparent activation energy E_a, as a function of extent of conversion α, for decomposition of DMPCN. E_a values slightly variation in the conversion range of $0.1 \leq \alpha \leq 0.95$. It was pointed out[29] that when E_a changes with α, the Friedman, KAS and FWO isoconversional methods lead to different values of E_a. The applied isoconversional methods do not suggest a direct way for evaluating either the pre-exponential factor (A) or the analytical form of the reaction model f(α), for the investigated decomposition process of DMPCN.

As can be seen from Table –1 the variation of apparent activation energy E_a, as a function of extent of conversion α, for decomposition of DMPCN. The average value of E_a is 62.50 ± 2.66 kJ mol^{-1} for FWO methods coincide with Friedman and KAS methods (56.71 ± 1.39 kJ mol^{-1}, Friedman; 55.84 ± 1.99 kJ mol^{-1}, KAS).

Table-1 Temperatures corresponding to the same degree of conversion at different heating rates for DMPCN

α	Heating Rates			FWO method			KAS method			Friedman method	
	10 (K min^{-1})	15 (K min^{-1})	20 (K min^{-1})	*E*a (kj mol^{-1})	ln*A* (A min^{-1})	r	*E*a (kj mol^{-1})	ln*A* (A min^{-1})	r	*E*a (kj mol^{-1})	r
0.10	481.65	494.84	504.75	57.68	4.05	-1.000	52.47	3.96	-1.000	56.57	-1.000
0.15	491.18	507.14	514.16	58.36	4.07	-0.990	53.04	3.97	-0.990	57.21	-0.990
0.20	511.10	525.11	536.05	60.23	4.10	-1.000	54.66	4.00	-1.000	57.86	-1.000
0.25	526.69	546.61	550.31	60.13	4.10	-0.960	54.30	3.99	-0.950	57.72	-0.900
0.30	539.69	559.11	565.08	61.71	4.12	-0.980	55.74	4.02	-0.970	58.04	-0.880
0.35	547.49	570.92	570.61	58.00	4.06	-0.910	51.71	3.95	-0.880	53.46	-0.760
0.40	556.15	577.97	581.79	61.51	4.12	-0.960	55.24	4.01	-0.940	57.85	-0.870
0.45	563.94	586.88	589.81	61.10	4.11	-0.950	54.69	4.00	-0.930	55.52	-1.000
0.50	573.47	591.51	602.41	64.83	4.17	-1.000	58.43	4.07	-1.000	57.10	-0.850
0.55	582.14	600.79	612.15	64.52	4.17	-1.000	57.94	4.06	-1.000	54.45	-0.800
0.60	592.53	613.51	623.36	63.94	4.16	-0.990	57.16	4.05	-0.990	55.94	-0.960
0.65	603.79	620.24	636.24	64.98	4.17	-1.000	58.04	4.06	-1.000	58.26	-0.930
0.70	615.92	634.01	649.90	64.70	4.17	-1.000	57.53	4.05	-1.000	56.87	-0.910
0.75	628.05	649.28	663.22	64.58	4.17	-1.000	57.20	4.05	-1.000	55.74	-0.960
0.80	640.18	658.96	676.95	64.70	4.17	-1.000	57.11	4.05	-1.000	57.48	-0.990
0.85	654.04	681.59	689.70	64.68	4.17	-0.980	56.88	4.04	-0.970	58.80	-0.840
0.90	668.76	697.33	706.32	64.71	4.17	-0.980	56.65	4.04	-0.970	55.81	-0.780
0.95	680.56	710.05	719.63	64.69	4.17	-0.980	56.42	4.03	-0.970	56.17	-0.980
				62.50	**±2.66**		**55.84**	**±1.99**		**56.71**	**±1.39**

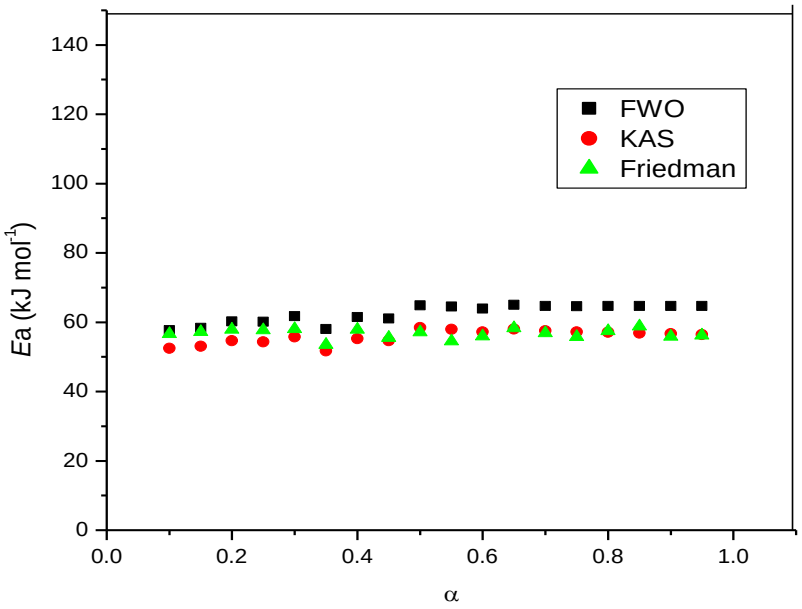


Fig – 2 Plot of *E*a verses α for DMPCN

3.3 Model-fitting analysis

After model-free analysis is performed, model-fitting can be done in the conversion region where apparent activation energy is approximately constant where a single model may fit. The non-isothermal kinetic data of DMPCN at $0.1 \leq \alpha \leq 0.95$ where model-free analyses indicate that activation energy approximately constant, were then fitted into each of the 15 models are listed in Table – 2. As shown in Table - 2 for the applied method,[30] Arrhenius parameters (E_a , ln A) exhibit strong dependence on the reaction model chosen.

Table 2 Arrhenius parameters for non-isothermal decomposition of DMPCN

Kinetic model	β=10 Kmin^{-1}			β=15 Kmin^{-1}			β=20 Kmin^{-1}		
	***E*a (kJ mol^{-1})**	**ln*A* (A min^{-1})**	**r**	***E*a (kJ mol^{-1})**	**ln*A* (A min^{-1})**	**r**	***E*a (kJ mol^{-1})**	**ln*A* (A min^{-1})**	**r**
P2	5.26	-3.27	-0.846	5.11	-3.03	-0.828	4.95	-2.85	-0.813
P3	0.33	-6.94	-0.138	0.13	-7.61	-0.051	-0.04	-3.40	0.015
P4	-2.12	-5.39	0.747	-2.35	-5.27	0.764	-2.52	-3.99	0.780
F1	33.53	4.51	-0.997	33.76	4.67	-0.995	33.67	4.80	-0.995
F2	53.54	9.71	-0.981	54.10	9.80	-0.981	54.04	9.88	-0.981
F3	78.70	16.01	-0.954	79.68	16.01	-0.955	79.66	16.02	-0.955
D1	59.05	16.77	-0.981	59.76	16.91	-0.980	59.75	17.01	-0.978
D2	56.65	8.19	-0.985	57.15	8.24	-0.983	57.05	8.30	-0.982
D3	66.14	9.12	-0.994	66.78	9.12	-0.993	66.71	9.17	-0.993
D4	59.76	7.49	-0.989	60.30	7.52	-0.987	60.21	7.58	-0.986
A2	12.02	-0.82	-0.992	11.97	-0.58	-0.990	11.84	-0.40	-0.989
A3	4.83	-3.17	-0.976	4.69	-2.92	-0.967	4.55	-2.74	-0.963
A4	1.26	-5.23	-0.818	1.07	-5.10	-0.731	0.93	-5.02	-0.662
R2	25.99	1.76	-0.986	26.11	1.94	-0.983	25.98	2.09	-0.982
R3	23.91	1.45	-0.978	24.01	1.64	-0.976	23.87	1.80	-0.974

3.4 Invariant kinetic parameter (IKP) analysis

The apparent kinetic parameters for the thermal decomposition in dynamic nitrogen atmosphere for DMPCN are represented in ln *A versus* E_a (Fig - 3). The evaluation of the invariant kinetic parameters is performed using the super correlation eqn(2). The plot of a_β *versus* b_β, E_{inv} and ln A_{inv} values were obtained from the slope and intercept of the straight line.

$$a_\beta = \ln A_{inv} - b_\beta E_{inv} \quad \text{--------} \quad (2)$$

For DMPCN, for AKM - {D1; D2; D3 ;} the plots of ln *A versus* E_a have highest correlation coefficient gave a_β and b_β from the slope and intercept, respectively. From the plot of a_β *versus* b_β, we determined (Table-3) invariant kinetic parameters E_{inv}=55.61 ± 0.37 kJ mol^{-1} and ln A_{inv}=9.62 ± 1.17 *A* min^{-1} (Table - 4) with good linear plot *r*=0.998. For these groups, the invariant activation energy is almost equal to 55.61 ± 0.37 kJ mol^{-1} in comparison with FWO, Friedman and KAS methods (56.71 ± 1.39 kJ mol^{-1}, Friedman; 55.84 ± 1.99 kJ mol^{-1}, KAS)

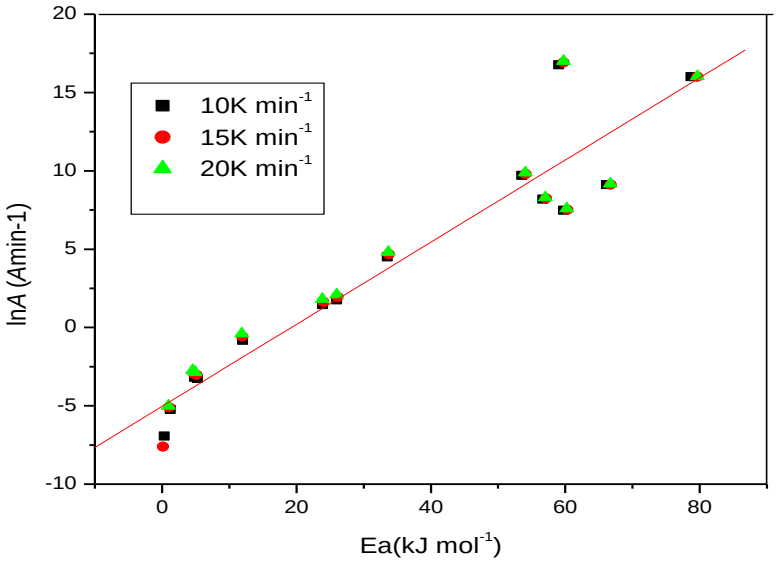


Fig – 3 Dependency of frequency factor on extent of conversion using the Coats – Redfern method for DMPCN

3.5 Kinetic model determination

The most suitable kinetic model for decomposition process of DMPCN is D3 (Diffusion - Jander). By introducing the derived reaction model $g(\alpha) = [1-(1-\alpha)^{1/3}]^2$, the following eqn(3)[31] is obtained.

$$[1-(1-\alpha)^{1/3}]^2 = \frac{AE_a}{R\beta} p(x) \quad \text{---------- (3)}$$

The plot of $[1-(1-\alpha)^{1/3}]^2$ against E_a p(x)/Rβ at the different heating rates is shown in Fig-4, the most suitable model for the decomposition process is second order model D3. The activation energy E_a and the frequency factor A were found to be $E_a = 62.50 \pm 2.66$ kJ mol^{-1} and $A = 6.91\times 10^{10}$ min^{-1} (ln A = 24.96). The obtained value of ln A coincide with the average value of Friedman isoconversional intercept ln [A f(α)] = 24.93.

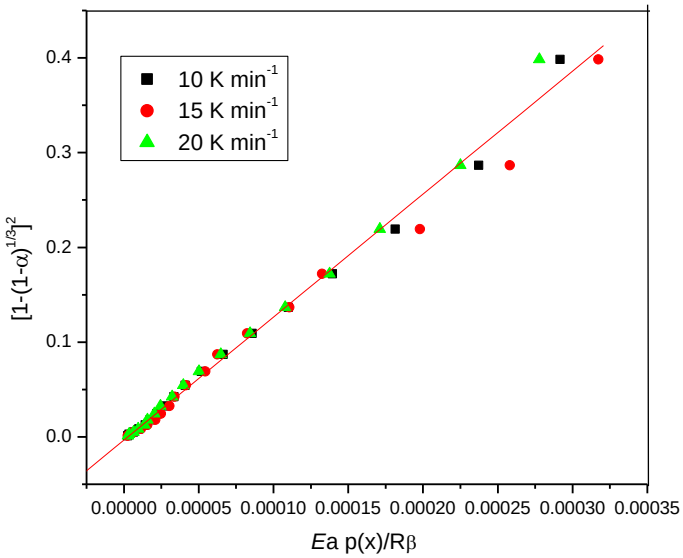


Fig – 4 Determination of A value by plotting $[1-(1-\alpha)^{1/3}]^2$ against E_a p(x)/Rβ for the decomposition process of DMPCN at different heating rates (β)

Table -3 The compensation effect parameters for several combinations of kinetics models for DMPCN

β (K min $^{-1}$)	AKM			AKM -{ D1}		
	aβ (Amin^{-1})	bβ (mol J^{-1})	r	aβ (Amin^{-1})	bβ (mol J^{-1})	r
10	-5.0374	0.2622	0.952	-4.9235	0.2437	0.979
15	-4.9203	0.2589	0.948	-4.8071	0.2405	0.975
20	-4.0688	0.2453	0.942	-3.9295	0.2262	0.978

β (K min -1)	AKM { D1; D3}			AKM - {D1 ;D3 ;D4}		
	aβ (Amin^{-1})	bβ (mol J^{-1})	r	aβ (Amin^{-1})	bβ (mol J^{-1})	r
10	-5.0364	0.2534	0.982	-5.1351	0.2659	0.990
15	-4.9200	0.2502	0.978	-5.0162	0.2627	0.986
20	-4.0584	0.2357	0.983	-4.1709	0.2482	0.993

β (K min -1)	AKM - {D1 ;D3; D4; P3}			AKM - {D1 ;D3; D4; P3 ; D2}		
	aβ (Amin^{-1})	bβ (mol J^{-1})	r	aβ (Amin^{-1})	bβ (mol J^{-1})	r
10	-4.6778	0.2568	0.993	-4.7455	0.2664	0.998
15	-4.3832	0.2503	0.993	-4.4478	0.2597	0.997
20	-4.1709	0.2482	0.993	-4.2337	0.2575	0.997

β (K min -1)	AKM - {D1 ;D3; D4; P3 ; D2 ; A2}		
	aβ (Amin^{-1})	bβ (mol J^{-1})	r
10	-4.9027	0.2687	0.999
15	-4.6117	0.2621	0.998
20	-4.4035	0.2601	0.998

Table – 4 IKP for several combinations of kinetics model for DMPCN

Kinetic model	***E*inv (kJmol^{-1})**	**ln*A* inv (A min^{-1})**	**r**
AKM	58.79	10.34	0.997
AKM - {D1}	58.14	9.21	0.998
AKM { D1; D3}	56.71	9.3	0.998
AKM - {D1 ;D3 ;D4}	55.61	9.62	0.998
AKM - {D1 ;D3; D4; P3}	55.49	9.56	0.981
AKM - {D1 ;D3; D4; P3 ; D2}	54.74	9.82	0.981
AKM - {D1 ;D3; D4; P3 ; D2 ; A2}	54.23	9.66	0.980

3.6 Thermodynamic parameters

From the DTG curves, the peak temperature for DMPCN is 561, 572 and 579 K at different heating rates at 10, 15 and 20 K min^{-1}. These peak temperatures were used to determine single point kinetic parameters.[28] The obtained E_a values were 9.16 kJ mol^{-1}.

Table - 5 Values of kinetic and thermodynamic parameters for thermal decomposition of DMPCN in dynamic nitrogen atmosphere

Parameter	**Value**
E_a (kJ mol^{-1})	9.16
ln A (A min^{-1})	18.56
$\Delta G^{\neq}$ (kJ mol^{-1})	146.59
$\Delta H^{\neq}$ (kJ mol^{-1})	86.89
$\Delta S^{\neq}$ (JK^{-1} mol^{-1})	-104.29
r	-0.999

The thermodynamic parameters, $\Delta S^{\#}$, $\Delta H^{\#}$ and $\Delta G^{\#}$ were determined at the peak temperature T_P in the DTG curves for the corresponding stage.[32] Since the temperature characterizes the higher rate of decomposition and therefore, it is an important parameter. As can be seen from Table-5, the value of $\Delta S^{\#}$ for the compound is negative. It means that the corresponding activated complex were with higher degree of arrangement than the initial state.[33] The positive values of $\Delta H^{\#}$ and $\Delta G^{\#}$ show that they are connected with absorption of heat and are attributed to non-spontaneous process.[32,34]

4. Conclusion

The compound chosen for this study decomposed into a single stage with the absorption of heat. The kinetic model for the decomposition mechanism is D3. The thermal stability of DMPCN is less and the energy of activation also less. Free energy is positive which indicates that the decomposition is non-spontaneous process. Since the activation energy values slightly varied with the conversion level, the average activation energy values were used to interpret decomposition model. The negative value of entropy indicates that the activated complex in these processes is in high ordered state than the reactant.

Acknowledgement

The authors thanks to IIT-Madras and Annamalai University, Annamalai Nagar, for recording IR & NMR and Mass spectra of synthesized compound.

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