

The evaporation of Ibuprofen from Ibuprofen-starch mixtures using simultaneous TG-DTA

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Received 15 September 1998; accepted 25 March 1999

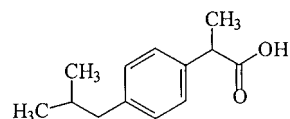
Abstract

The variation of the activation energy (E_{act}) is reported for the evaporation of Ibuprofen-starch binary mixtures in nitrogen atmosphere. It is shown that all the features of Ibuprofen and starch are still present in the mixtures. That is, the loss of water from the starch, melting of the Ibuprofen, the evaporation of the Ibuprofen, and the degradation of the starch, appearing in this order as the heating mode is progressed. The temperature range for the evaporation of Ibuprofen is moved to a higher temperature as the Ibuprofen content in the mixture is increased. This is reflected in the energy of evaporation associated with each binary mixture. The kinetic analysis of the starch degradation is also affected in that the temperature range for the degradation increases with the Ibuprofen content. This again is reflected in an analysis of the activation energy as a function of the original Ibuprofen content in the mixture. The cause of this effect is discussed in the paper. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Evaporation of mixtures; Ibuprofen and starch; Thermal analysis

1. Introduction

Ibuprofen, a nonsteroidal anti-inflammatory drug having analgesic and antipyretic activities, shows a melting point at 75–77°C [1] and in an open container will evaporate. In the thermogravimetric-differential thermal analysis (TG-DTA) unit, this evaporation will often exhaust the material before it reaches the normal boiling point. The earlier investigation [2] reported the evaporation process of Ibuprofen to be a zero order and the activation energy was found to be 81.8–87.0 kJ mol⁻¹. The degradation of starch, diluent and tablet binder, shows a loss of moisture followed by degradation to carbon at a higher temperature. The two materials are dissimilar. Ibuprofen has a formula:



while starch is a polymeric carbohydrate, made up of anhydroglucose units of amylose, α -D-(1→4) glucosidic linkages, and highly branched amylopectin, α -D-(1→4) glucosidic linkages plus α -D-(1→6) glucosidic linkages [3]. The degradation of starch in nitrogen atmosphere is complicated [4]. The end product is carbon. It is well established that heating starch to around 300°C produces dextrin. In the range from 250 to 400°C evolution of carbon dioxide and carbon monoxide is reported in the early stages followed by methane and unsaturated hydrocarbons in the higher temperature region [5]. Picon [6] found the yield of carbonaceous residue varied with the origin of starch from 4 to 18% at 1000°C. Shafizadeh and Chin

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[7] and Gardiner [8] reported the early production of levoglucosan from the heat treatment of starch indicating a similarity with the early stages of the degradation of cellulose. Bryce and Greenwood [9] reported the kinetics of the degradation based on the evolution of gaseous products. The thermal analysis data reported here is a single stage process but is obviously an overall kinetic process embodying many stages.

The Ibuprofen evaporation process from an open crucible would be expected to be a zero order as it is a surface phenomenon and in a straight sided crucible once the steady state has been reached, it would be expected that the interface between liquid and atmospheric nitrogen, would remain constant in area until the final fraction of the evaporation process when there is insufficient material to present this uniform area of interface. This picture has been shown to be the case in previous studies of the evaporation investigated by thermogravimetry (TGA) [10].

At any specified temperature, the rate of evaporation from a uniform surface will be a constant value. One can write:

$$\frac{dM}{dt} = k_T \quad (1)$$

where M is equal to mass of material in mg; t is time in mm; k coefficient of evaporation and T is equal to temperature in Kelvin. Hence, dM/dt represents the rate of loss of the liquid into the gaseous phase at each temperature T . The k_1 term is, thus, the coefficient of evaporation at that temperature. The rising temperature treatment of a zero order process is one of the easiest approaches to interpret using derivative thermogravimetry (DTG) curve. In such a case:

$$\frac{dM\beta}{dT} = \frac{dM}{dt} = k_T \quad (2)$$

where β is a heating rate. At each temperature T and by reading directly from the DTG signal, k_T can be determined. The shape of the zero order process is characteristic and can be recognized from the DTG plot [11]. The process is kinetically based and can be related to the temperature by the Arrhenius equation:

$$\ln k = \ln A - \frac{E_{\text{act}}}{RT} \quad (3)$$

where A is equal to pre-exponential parameter; E_{act} activation energy; R gas constant, hence, $\ln A$ and E_{act} can be calculated.

The situation might be expected to change when solid particles are present in the liquid Ibuprofen. This is the probable description of the Ibuprofen-starch thermal analysis studies presented here.

After the evaporation process is completed, the starch will degrade to carbon [12]. The suspending medium (in this case Ibuprofen) might cause a change in the aggregation of the particles of starch remaining in the reaction crucible. In such circumstances this might be reflected in an alteration of the reaction kinetics of starch.

The alteration in the evaporation process of Ibuprofen and in the subsequent degradation of starch in a nitrogen atmosphere for binary mixtures of Ibuprofen-starch is the subject of the present study.

2. Experimental

2.1. Materials

Ibuprofen (Lot. # 1194F) was supplied by Pharmacia & Upjohn, and was a racemic compound [2]. Starch 1500[®], pregelatinized corn starch, (Lot # 4SE0110H) was obtained from Chelsea Labs.

2.2. Equipment and procedure

Simultaneous TG-DTA Model No. SDT 2960 from TA Instruments was used to study the Ibuprofen-starch mixtures. Data was collected in the temperature range from room temperature to 600°C. The equipment recorded TG and DTA data. The heating rate was 10°C mm⁻¹. Dry nitrogen was used as a purge gas at a flow rate of 200 ml min⁻¹. The sample mass varied from 7.73 to 10.21 mg. Two platinum crucibles were used (capacity 110 µl) and the reference crucible was left empty. The two components were mixed by grinding for 15 min in a 5 dram glass bottle with the aid of Burundum[®] grinding pebbles. Each compound and/or binary mixture were subjected to the heat treatment under the similar conditions three times. Reporting statistical data upon which the Arrhenius equation is employed is not advisable [13]. The purpose of performing

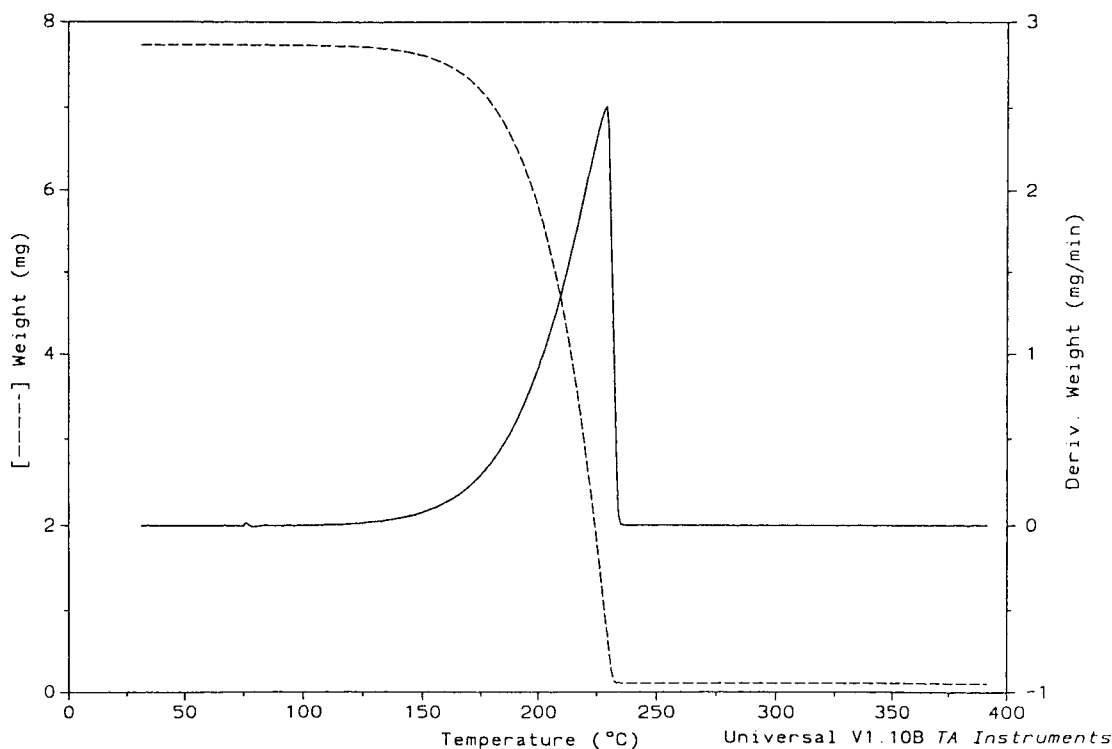


Fig. 1. TG-DTG plots of Ibuprofen in N_2 atmosphere.

triplicate runs is only to ensure the repeatability of the experiments.

3. Results and discussion

TG-DTG plots for Ibuprofen alone in the nitrogen atmosphere is shown in Fig. 1. The shape of this plot is characteristic of a zero order [10]. Fig. 2 represents a typical TG-DTG plots for a 50:50% by mass Ibuprofen-starch mixture.

A plot of $\ln k$ versus $1/T$ according to Eq. (3) for the evaporation process of Ibuprofen present in the binary mixture is given in Fig. 3 as an example. The slope of this plot enables E_{act} to be calculated and the intercept is equal to $\ln A$. Table 1 summarizes the Arrhenius parameters for Ibuprofen evaporation obtained for Ibuprofen per sec and for all the binary mixtures. In this Table, R^2 is the linear regression coefficient.

It can be seen from Table 1 that the Arrhenius parameters, E_{act} and $\ln A$, for Ibuprofen evaporation

process in the mixtures tends to increase when the Ibuprofen content rises. However, the change is minute (75.2 – 81.9 kJ mol^{-1} for E_{act} , and 19.0 – 20.7 for $\ln A$) over the range of 25–100% Ibuprofen. This suggests that the starch particles are inert towards the evaporation process which is occurring from a constant area interface in each experiment.

A plot of $\ln A$ versus E_{act} for Ibuprofen in the mixture is shown in Fig. 4. This linear relationship between the two parameters is called the compensation effect in which the influence of changes in A on reaction rate is offset to a certain extent by a similar alteration in E_{act} . There are several literature discussions on this topic but no definitive opinion can be drawn [14–22] except to observe that an alteration in the slope of a line of plots of $\ln k$ versus $1/T$ is going to have a related effect on the intercept.

It might be expected that the subsequent degradation of the starch (in the mixtures) to carbon in a nitrogen atmosphere would be identical to that of starch alone with respect to Arrhenius kinetic

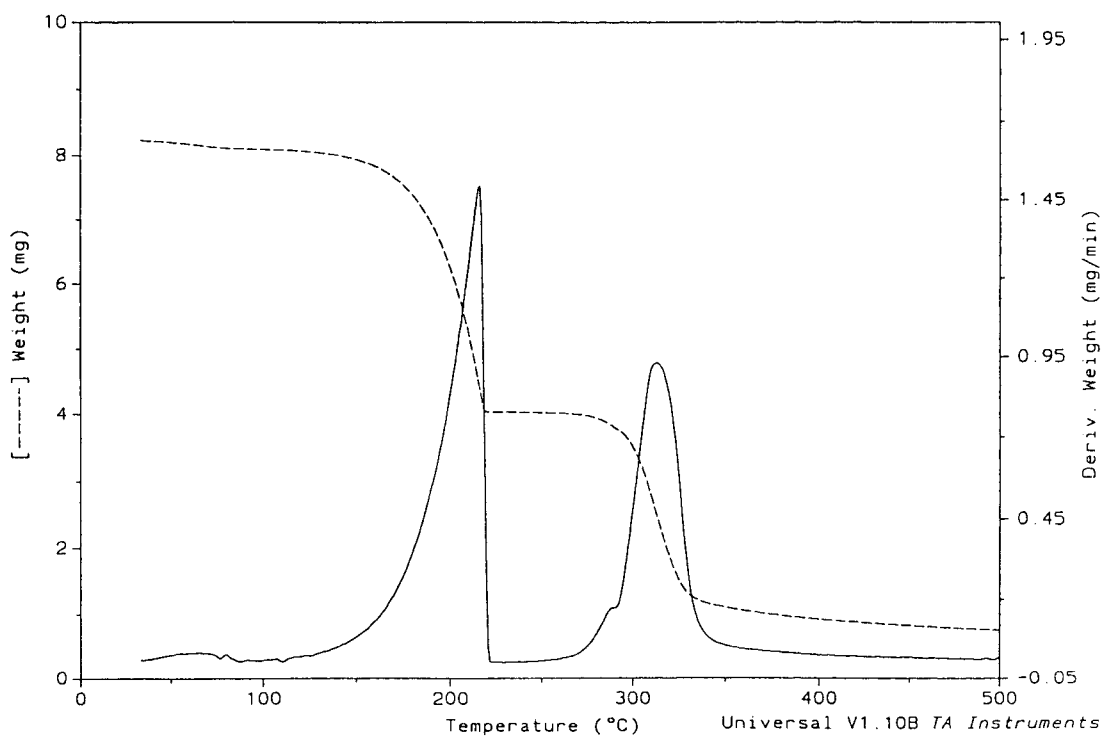


Fig. 2. TG-DTG plots for Ibuprofen-starch mixture (50:50% by mass).

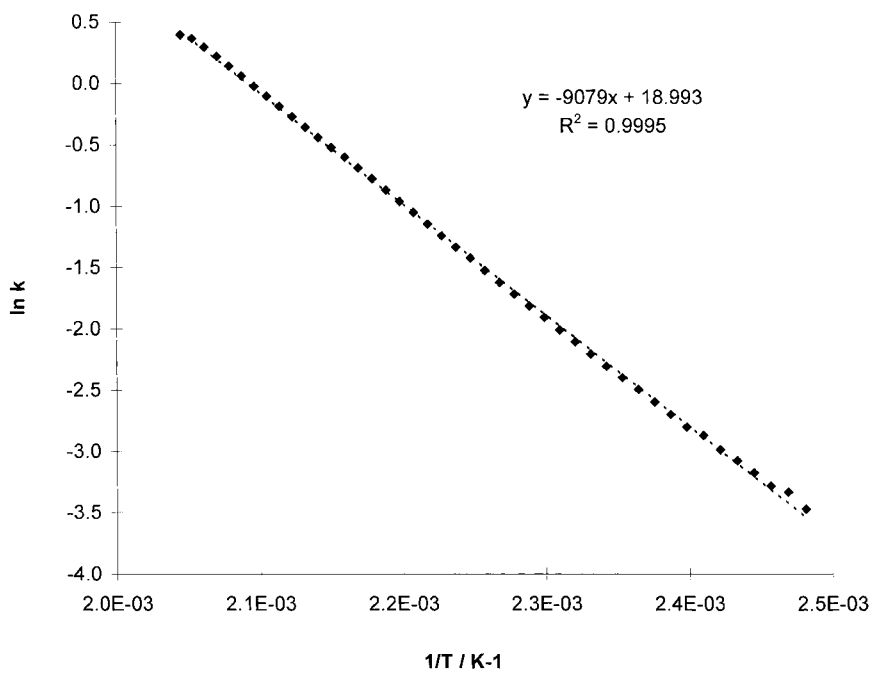
Fig. 3. A plot of $\ln k$ versus $1/T$ for Ibuprofen in Ibuprofen-starch mixture (50:50% by mass).

Table 1
The Arrhenius parameters (E_{act} and $\ln A$) for Ibuprofen evaporation in the binary mixtures of Ibuprofen-starch

Ibuprofen (%)	E_{act} (kJ mol ⁻¹)	E_{act} (mean value)/kJ mol ⁻¹	$\ln A$	$\ln A$ (mean value)	R^2	Temp. range (K)
25	75.6		19.0		0.9972	403–469
25	75.8	75.7	19.1	19.0	0.9975	403–471
25	75.7		19.0		0.9973	403–469
50	74.9		19.0		0.9996	403–489
50	75.5	75.2	19.0	19.0	0.9995	403–489
50	75.2		18.9		0.9988	403–489
75	77.5		19.6		0.9994	403–497
75	77.7	77.1	19.6	19.5	0.9994	403–497
75	76.0		19.2		0.9985	403–497
80	79.7		20.1		0.9997	403–499
80	79.3	79.5	20.0	20.1	0.9997	403–499
80	79.6		20.1		0.9998	403–499
85	80.5		20.4		0.9997	403–499
85	80.2	80.4	20.2	20.3	0.9998	403–499
85	80.4		20.3		0.9998	403–499
90	80.7		20.4		0.9997	403–501
90	80.7	80.7	20.4	20.4	0.9997	403–501
90	80.8		20.4		0.9997	403–501
95	78.4		19.8		0.9994	403–501
95	79.1	79.6	20.0	20.1	0.9995	403–501
95	81.2		20.5		0.9997	403–501
100	82.0		20.8		0.9990	393–503
100	81.9	81.9	20.7	20.7	0.9985	393–503
100	81.7		20.6		0.9990	393–503

parameters as by the time the starch degrades the Ibuprofen has already vaporized completely away from the system. It can be seen however that the prior evaporation of the Ibuprofen has the effect of raising the temperature range of the degradation from 537 to 591°C for pure starch to 543–607°C for 5% starch in the original mixture. The shape of the DTG plot suggests a first order process on the basis of the earlier selection method outlined by Dollimore et al [23]. In view of the fact that Bryce and Greenwood [9] also found a first order kinetic relationship for the low temperature degradation, the first order analysis was attempted here with moderate success as shown by the value of the linear regression coefficient.

In differential form, the first order plot may be represented by:

$$\frac{(d\alpha)\beta}{dT} = \frac{d\alpha}{dt} = k_T(1 - \alpha) \quad (4)$$

or

$$k_T = \frac{(d\alpha/dT)\beta}{1 - \alpha} \quad (5)$$

where α is a fraction decomposed. k_T can, therefore, be calculated for every temperature for each binary mixture with regard to the starch degradation in nitrogen. Then, $\ln k$ versus $1/T$ (Eq. (3)) for the degradation process of starch in each mixture can be generated. Table 2 summarizes the Arrhenius parameters calculated for starch degradation.

A plot of E_{act} versus % starch in the mixtures is delineated in Fig. 5 and this can be shown to have a logarithmic relationship. Its equation and the R^2 value are included in the plot. The E_{act} for starch degraded in the mixtures increases when the amount of starch rises, in other words, as the Ibuprofen content in the mixtures drops. However, the temperature range where the starch decomposes is narrower when larger

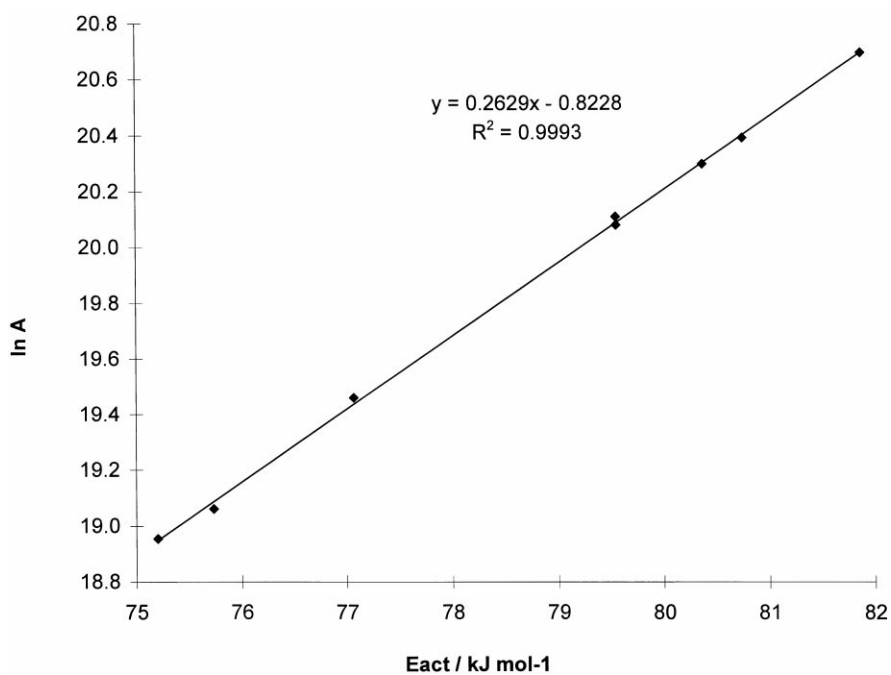


Fig. 4. A plot of $\ln A$ versus E_{act} for Ibuprofen in the mixture showing the compensation effect.

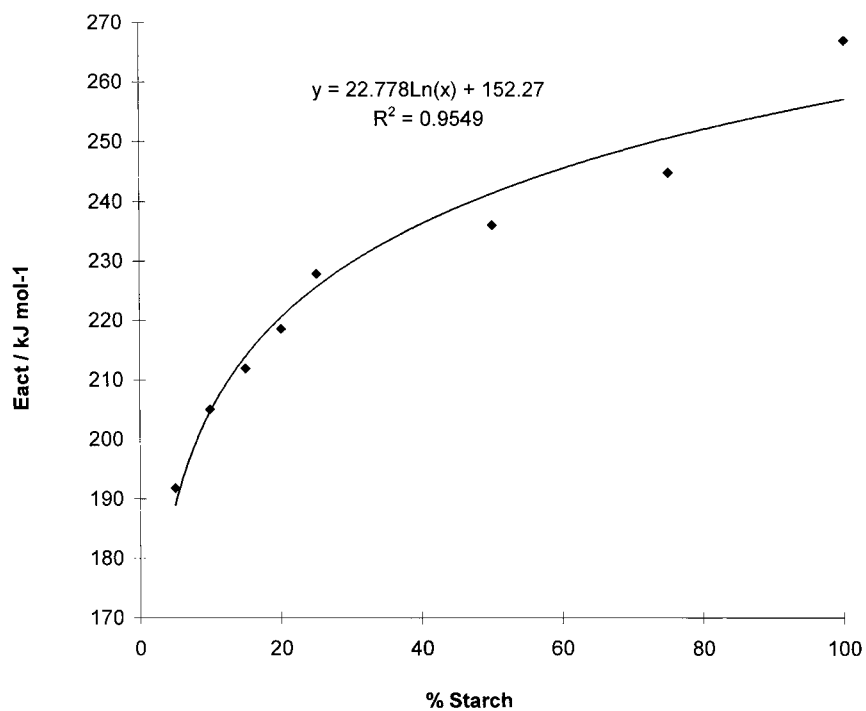


Fig. 5. A plot of E_{act} versus $\% \text{ starch}$ in the mixture.

Table 2
The Arrhenius parameters (E_{act} and $\ln A$) for starch degradation in the binary mixtures of Ibuprofen-starch

Starch (%)	E_{act} (kJ mol ⁻¹)	E_{act} (mean value)/kJ mol ⁻¹	$\ln A$	$\ln A$ (mean value)	R^2	Temp. range (K)
5	186.7		37.3		0.9881	543–607
5	195.3	191.8	39.1	38.4	0.9899	543–605
5	193.4		38.7		0.9848	543–607
10	204.3		41.0		0.9890	543–603
10	206.8	205.1	41.6	41.2	0.9905	543–603
10	204.2		41.0		0.9889	543–603
15	211.3		42.5		0.9896	543–601
15	212.9	211.9	42.9	42.7	0.9901	543–601
15	211.6		42.6		0.9868	543–601
20	218.2		44.0		0.9897	537–607
20	217.9	218.5	43.9	44.1	0.9905	537–601
20	219.5		44.3		0.9915	537–601
25	229.0		46.2		0.9915	537–599
25	226.8	227.8	45.8	46.0	0.9919	537–599
25	227.6		46.0		0.9885	537–599
50	238.4		48.4		0.9877	537–595
50	235.3	236.1	47.7	47.9	0.9900	537–597
50	234.5		47.5		0.9896	537–597
75	243.4		49.5		0.9908	537–593
75	246.2	244.8	50.0	49.8	0.9871	537–593
75	244.8		49.8		0.9881	537–593
100	269.2		55.1		0.9764	537–591
100	267.2	267.0	54.7	54.7	0.9758	537–591
100	264.6		54.2		0.9766	537–591

percentages of starch are present in the mixtures. The compensation effect is also noticed as can be seen from a plot of $\ln A$ versus E_{act} of starch in the mixtures in Fig. 6.

The use of a first order expression in these circumstances over a range between 264 and 334°C where very complex reactions are occurring both consecutively and simultaneously must be regarded as an approximation, nevertheless it demonstrates the remarkable ‘ghost’ effect of the prior presence of Ibuprofen.

4. Conclusions

The coefficients of evaporation in nitrogen for Ibuprofen in Ibuprofen-starch mixtures are affected by the % starch present and are accompanied by a

temperature shift in the range over which evaporation is observed. Starch present in the mixtures not only lowers the E_{act} but also narrows the temperature range of Ibuprofen evaporation process. This is due to the increasing surface area of evaporation as starch particles behave like a stationary phase or supporting media for liquid Ibuprofen to vaporize. On the other hand, liquid Ibuprofen acting as a suspending media for starch lowers the E_{act} by separating the starch particles hence reducing the energy barrier of starch degradation process. However, Ibuprofen present in the mixtures extends the temperature range of starch decomposition. This is a ‘ghost’ effect since when the starch degradation occurs all the Ibuprofen has already evaporated. It can be speculated that this effect is due to aggregation of starch particle brought about by surface tension of the evaporating Ibuprofen liquid in the mixture.

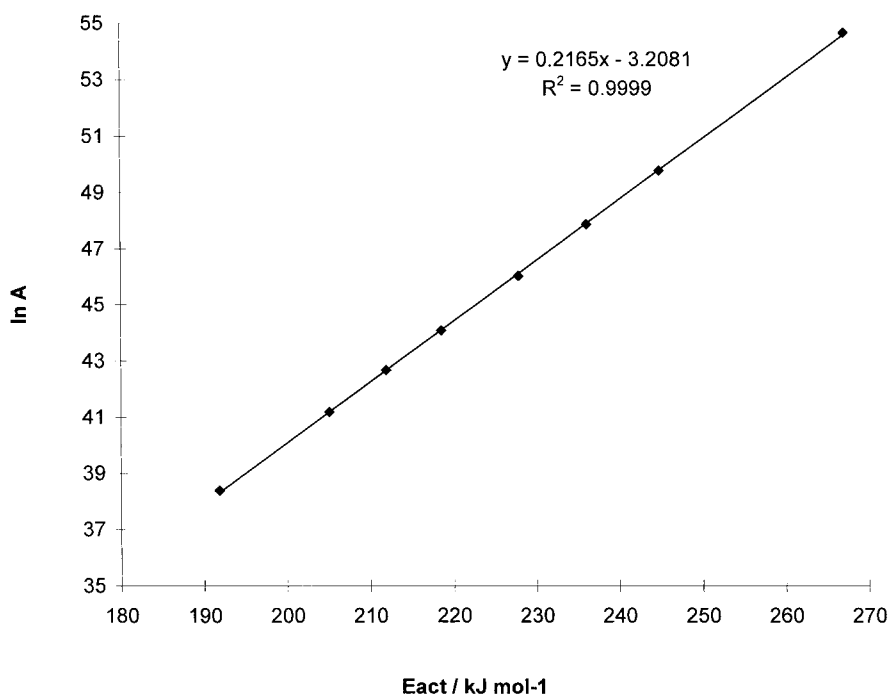


Fig. 6. A plot of $\ln A$ versus E_{act} for starch in the mixture showing the compensation effect.

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