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Studies of Some Physicochemical Properties of Isatin

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Some physicochemical properties such as dissociation constant, acoustical parameters and thermal studies of isatin have been studied in methanol and 1,4-dioxane at 298.15 K. It is observed that pK^H value is slightly greater in methanol + water system. Acoustical properties have been evaluated from experimental data of density, viscosity and ultrasonic velocity. It is observed that in both the solvents, strong solute-solvent interactions exist for isatin. Further, degradation is single step process.

Keyword: Physico Chemical Properties, Dissociation Constant, Thermal Degradation

1. Introduction

Isatin and their derivatives are an important group of heterocyclic compounds which are biologically active and are of significant importance in medicinal chemistry.

A variety of biological activities are associated with isatin. Some of these are analgesic, anticonvulsant, antidepressant, anti-inflammatory, antimicrobial and CNS activities ^[1]. Further, physiological concentrations of isatin inhibit membrane bound natriuretic peptide receptor A guanylate cyclase ^[2,3], and soluble guanylate cyclase stimulated by sodium nitroprusside ^[4].

These applications of isatin prompted us to study their physicochemical properties such as dissociation constant and acoustical parameters in methanol and 1,4-dioxane at 298.15 K. Further, thermal analysis of isatin was also done to determine some kinetic parameters.

2. Experimental:

Isatin was purchased from Sigma Aldrich (CAS Number 91-56-5), which was recrystallized from methanol. The solvents; methanol and 1,4-dioxane used in the present study was of B.D.H Analar grade and were purified by standard procedure ^[5]. All the solutions were prepared using in Milli-Q water (Millipore Pvt. Lt. Bangalore-India). An electrical balance (Mettler Toledo AB204-S) with an accuracy of ± 0.1 mg was used for solution preparation.

2.1 Dissociation:

The dissociation constant of Isatin has been studied in methanol and 1,4 dioxane at 298.15 K by Calvin Bjerrum pH titration technique ^[6]. For this, following sets of mixtures were prepared:

(I) 2 ml HNO_3 (1.0M) + 4 ml water + 30 ml methanol / 1,4-dioxane + 4.0 ml NaNO_3 (1.0 M).

(ii) 2 ml HNO_3 (1.0M) + 4 ml water + 28 ml methanol / 1,4-dioxane + 2.0 ml isatin solution (0.1M) + 4.0 ml NaNO_3 (1.0 M).

These solutions were titrated against 0.5 M-sodium hydroxide and the corresponding pH was measured using Systronic pH meter (Model No. EQ 664). The glass electrode and a saturated calomel electrode were used as indicator and reference electrodes respectively. Before operation, the glass electrode was immersed in 0.1 M HCl for twenty minutes. Then, it was washed thoroughly with Milli-Q-water. The pH meter was calibrated with buffer solution of known pH.

2.2 Acoustical Properties:

The solutions of Isatin were prepared in methanol and 1,4-dioxane solvents over a wide range of concentrations. At 298.15 K, for each solution, density, ultrasonic velocity and viscosity were measured.

The densities (ρ) of pure solvents and their solutions were measured by using a single capillary pycnometer, made of borosil glass having a bulb capacity of 10 ml. The ultrasonic velocity (U) of pure solvents and their solutions were measured by using single crystal variable path ultrasonic interferometer operating at 2

MHz. The accuracy of density and velocity are $\pm 0.0001 \text{ g/cm}^3$ and $\pm 0.1\% \text{ cm/sec}$ respectively. The viscosity (η) of pure solvents and solutions were measured by an Ubbelohde viscometer with an accuracy of 0.05%. All the measurements were carried out at 298.15 K. The uncertainty of temperature is $\pm 0.1 \text{ K}$ and that of concentration is $0.0001 \text{ moles /dm}^3$.

2.3 Thermal Analysis:

Thermal analysis of isatin has been done by DSC and TGA techniques. Thermo gravimetric analysis (TGA) and Differential Scanning Calorimetry (DSC) measurements were made on the instrument "Pyris-1, Perkin Elmer Thermal Analysis" at the heating rate of $10 \text{ }^\circ\text{C /min}$ in nitrogen atmosphere.

3. Results and Discussion:

3.1 Dissociation:

Figure 1 shows that typical titrations curve of the acid in the absence and presence of Isatin at 298.15 K for methanol + water and 1,4-dioxane + water systems. It is evident that for the same volume of alkali added, the Isatin titration curves showed a lower pH value than the titration curve of free acid.

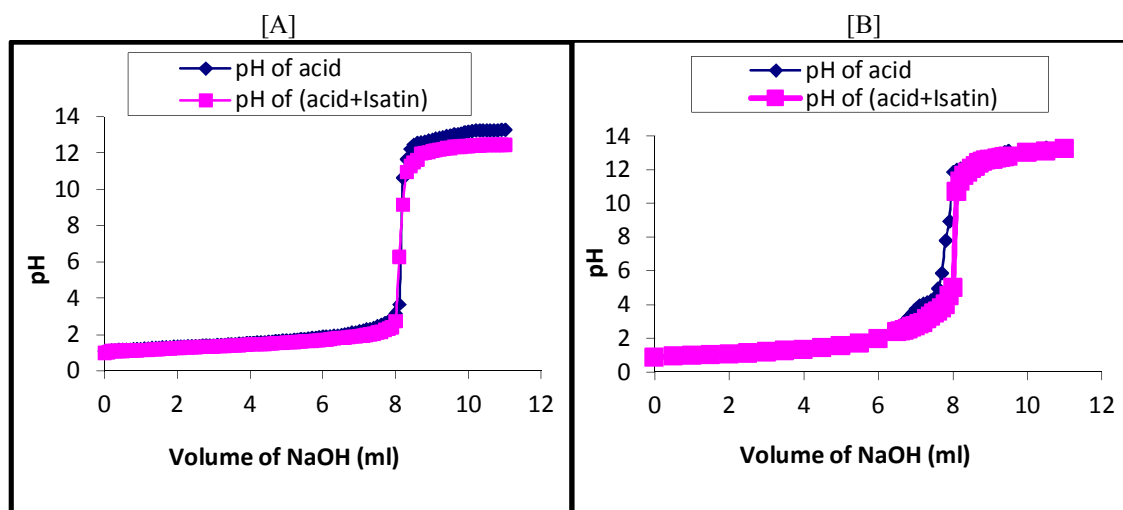


Fig 1: The plot of pH against volume of NaOH in [A] methanol + water and [B] 1,4-dioxane + water at 298.15K.

From these titration curves, the average number of protons associated with the isatin (\bar{n}_H) can be calculated by the following equation given by Irving and Rossotti [7].

$$\bar{n}_H = Y - \frac{\{(V'' - V') (N^0 + E^0)\}}{\{(V^0 + V') T_L^0\}}$$

where Y is the number of displaceable protons. V' and V'' are the volume of alkali required at the same pH for both acid and Isatin titration curves respectively. V^0 is the initial volume of the test solution. N^0 , E^0 and T_L^0 are the initial concentration of the alkali, acid and Isatin respectively.

The dissociation in both the solvent systems has been evaluated by half-integral and average methods.

It is observed that the value of \bar{n}_H are found to be between zero to one suggesting thereby that Isatin has one replaceable proton. In half-integral method, the pK^H value were evaluated at $\bar{n}_H = 0.5$.

In average method, for all the points below $\bar{n}_H = 1$, the following equation was used to determine pK^H

$$\log pK^H = pH + \log \frac{\bar{n}_H}{(\bar{n}_H - 1)}$$

From these evaluated various value of $\log pK^H$, average value of pK^H was calculated. Table 1 shows the dissociation constant of Isatin by both average and half-integral methods in methanol + water and 1,4-dioxane + water systems.

Table 1: The pK^H values for Isatin evaluated by Average and half-integral methods in methanol and 1,4-dioxane.

Solvents	Half-integral method	Average method
Methanol	9.9153	9.9061
1,4-dioxane	8.2729	8.3080

It is observed that pK^H value is slightly greater in methanol + water. This suggests that dissociation decreases in methanol system. Further, comparison of pK^H value in the two solvents suggests that isatin is more acidic in 1,4-dioxane + water system. The values evaluated by two methods are in fair agreement.

3.2 Ultrasonic:

The density (ρ), viscosity (η), and sound velocity (U) of pure solvents and solutions of isatin in methanol and 1,4-dioxane are reported in Table 2. It is observed that all these values increase with concentration in both the solvents.

Table 2: Experimental values of density (ρ), viscosity (η), ultrasonic velocity (U) for Isatin in methanol and 1,4-dioxane at 298.15 K.

Conc. (mol/l)	Methanol			1,4-dioxane		
	ρ (g/cm ³)	U (cm/s)	η (poise)	ρ (g/cm ³)	U (cm/s)	η (poise)
0.00	0.7858	1.1100	5.4485	1.02891	1.3458	12.2937
0.01	0.7921	1.1104	5.6977	1.02923	1.3465	12.3321
0.02	0.7929	1.1116	5.8453	1.02931	1.3475	12.7543
0.04	0.7932	1.1122	5.9584	1.02939	1.3484	12.9096
0.06	0.7935	1.1136	6.0920	1.02945	1.3489	13.4031
0.08	0.7948	1.1141	6.2211	1.02957	1.3498	14.0310
0.10	0.7951	1.1147	6.3150	1.02969	1.3508	14.5393

From these experimental data, various acoustical parameters like specific acoustical impedance (Z), adiabatic compressibility (κ_s), intermolecular free length (L_f), Vander waal's constant (b),

relaxation strength (r), internal pressure (π), free volume (V_f) and solvation number (S_n), etc. were evaluated using equations reported earlier^[8]. Some of these values are given in Table 3.

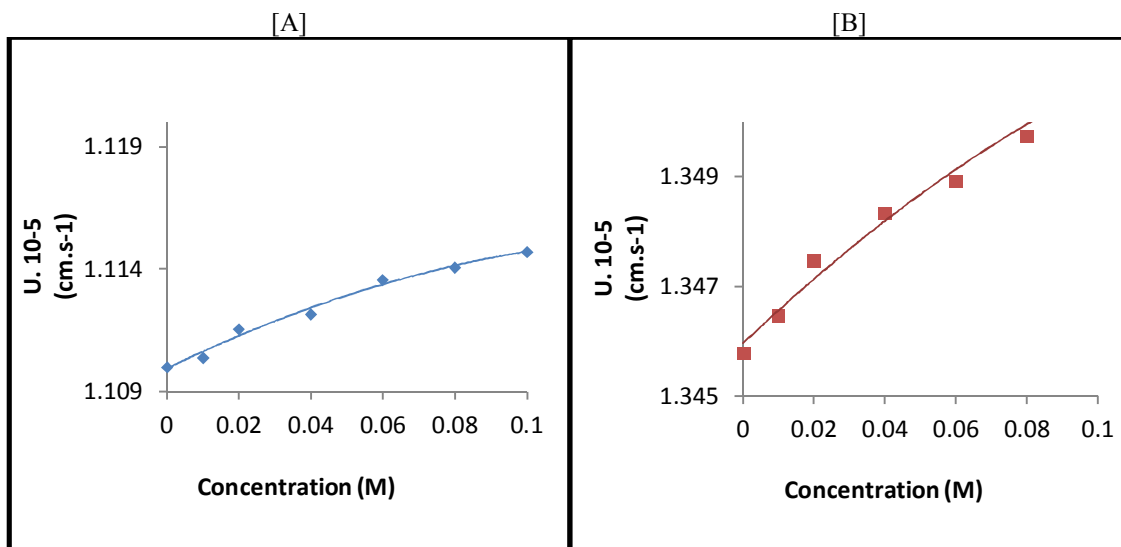


Fig 2: The variation of velocity (U) with concentration for Isatin in [A] methanol and [B] 1,4-dioxane.

The variation of ultrasonic velocity with concentration is shown in Figure 2. It is observed from Figure 2 that ultrasonic velocity increases non-linearly with concentration. The velocity (U) depends on intermolecular free path length (L_f). Larger the intermolecular free path length, smaller will be the velocity and vice versa. It is evident from Figure 3 that intermolecular free path length decreases non-linearly with concentration. The increase of velocity and decrease of intermolecular free path length suggests close association between isatin molecules and solvent molecules.

Further, Table 3 shows that relaxation strength (r) decreases whereas Z increases with concentration. This again suggests that solute molecules interact strongly with solvent molecules.

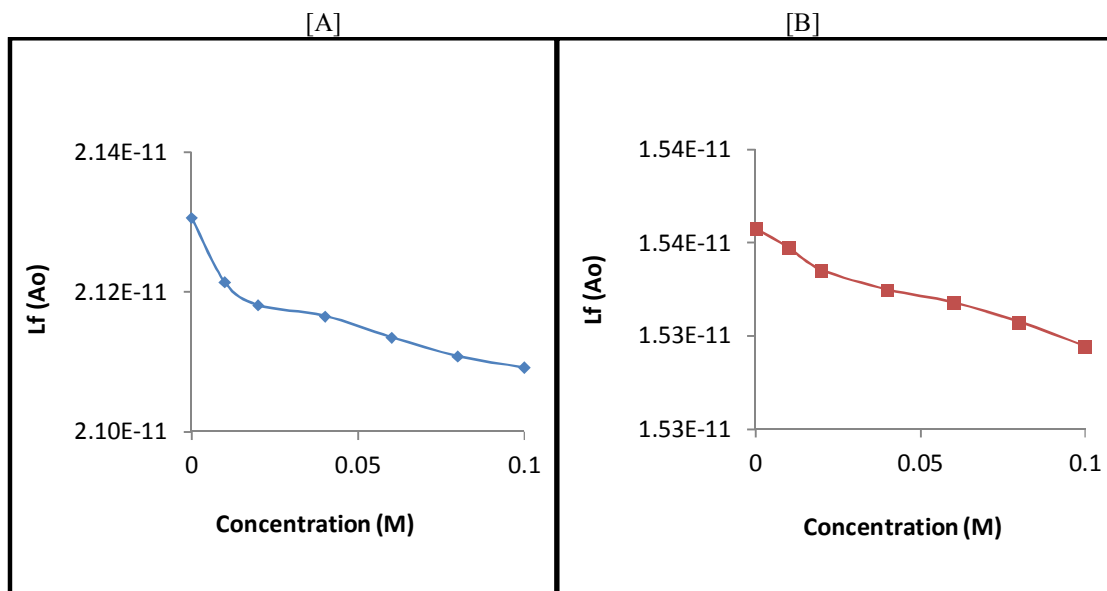
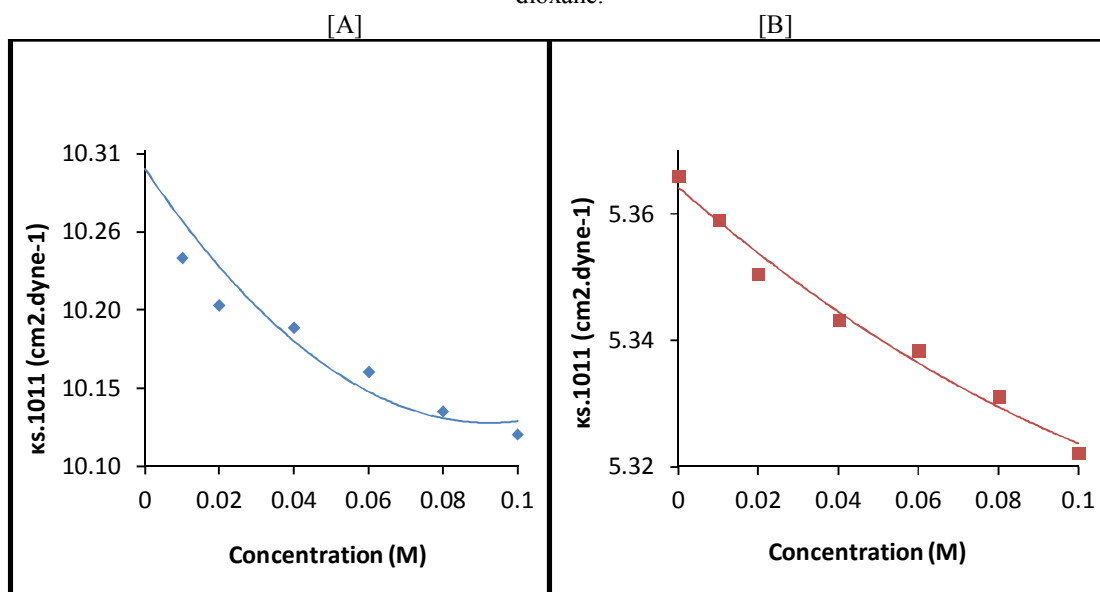
The variation of adiabatic compressibility with concentration is shown in Figure 4. It shows that adiabatic compressibility (κ_s) decreases with concentration for both the solvents. The decrease of κ_s further confirms close association between solute and solvent molecules in the studied systems [9].

Table 3: Some evaluated acoustical parameters for solution of Isatin in methanol and 1,4-dioxane at 298.15 K.

Conc. (mol/l)	Z ($\text{gm}^2.\text{s}^{-1}$)	r	$\pi * 10^{-8}$	b $\text{cm}^3.\text{mol}^{-1}$
Methanol				
0.00	0.8722	0.5187	1073.1799	40.7210
0.01	0.8795	0.5184	1094.5677	40.6671
0.02	0.8814	0.5174	1100.3155	40.8952
0.04	0.8822	0.5168	1094.0652	41.4180
0.06	0.8836	0.5156	1089.3241	41.9400
0.08	0.8855	0.5152	1085.5909	42.4050
0.10	0.8863	0.5146	1077.8279	42.9241
1,4-dioxane				
0.00	1.3847	0.2925	537.5308	85.6324
0.01	1.3858	0.2918	537.7435	85.6877
0.02	1.3870	0.2907	546.0884	85.7630
0.04	1.3880	0.2898	548.0291	85.9202
0.06	1.3886	0.2892	557.0717	86.0791
0.08	1.3897	0.2883	568.5760	86.2328
0.10	1.3909	0.2872	577.3179	86.3865

Table 4: Some kinetic parameters of decomposition reaction of isatin.

n	E. kJ.mol ⁻¹	A. sec ⁻¹	ΔS° J.mol ⁻¹ .K ⁻¹
0.589	162.954	1.375X10 ³⁰	332.877

**Fig 3:** The variation of intermolecular free path length (L_f) against concentration for Isatin in [A] Methanol and [B] 1,4-dioxane.**Fig 4:** The variation of adiabatic compressibility (κ_s) against concentration for Isatin in [A] Methanol and [B] 1,4-dioxane

The internal pressure π is a measure of cohesive forces which is found to increase with concentration (Table 3). This confirms the existence of solute-solvent interactions in the solutions of isatin in both the solvents. Figure 5 shows the variation of free volume with concentration. It is observed that for both

the solvents free volume decreases non-linearly with concentration. As discussed above, increase of internal pressure means increase of cohesive forces. This causes decrease in free volume due to compression^[10]. Thus, internal pressure is reverse of free volume.

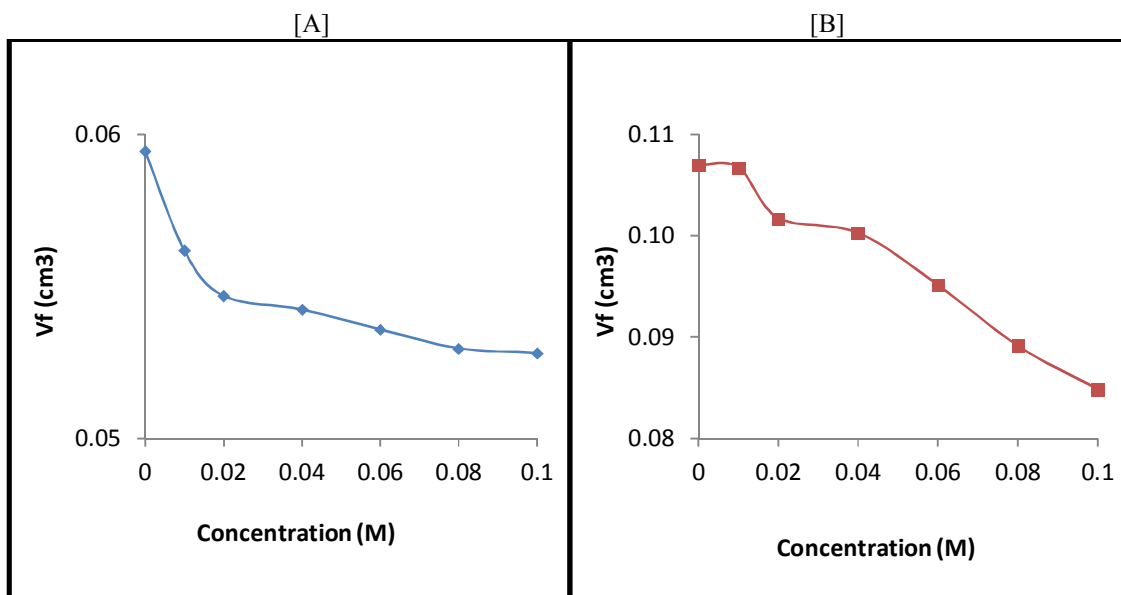


Fig 5: The variation of free volume (V_f) against concentration for Isatin in [A] Methanol and [B] 1,4-dioxane.

The type of interactions in a solution can also be confirmed by the solvation number, which is a measure of structure forming or structure breaking tendency of a solute in a solution. Figure 6 shows that for the studied compound, solvation number (S_n) increases with concentration. Further, these S_n values

are positive in both the solvents. The positive S_n values suggest structure forming tendency of isatin in solutions. This further confirms that there exist strong solute-solvent interactions in the studied solutions. Thus, it is concluded that in both the solvents, strong solute-solvent interactions exists for isatin.

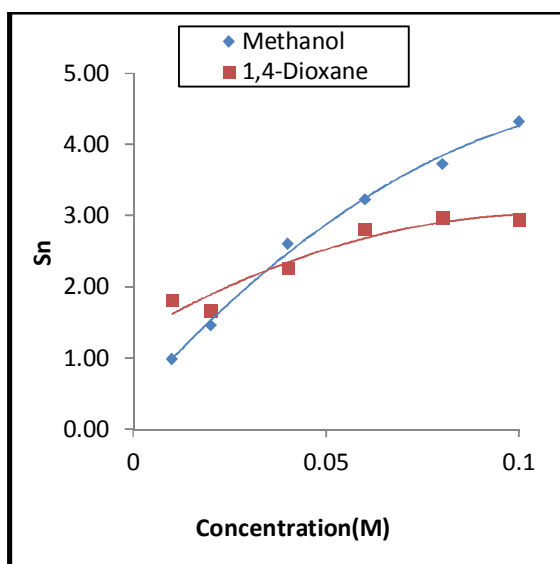


Fig 6: The variation of S_n against concentration for Isatin in Methanol and 1,4-dioxane.

3.2 Thermal:

The TGA thermo gram of isatin is given in Figure 7, which shows that degradation is single step process. The decomposition temperature range is

found to be approximately from 210-300 °C and the maximum degradation temperature is 270.32 °C.

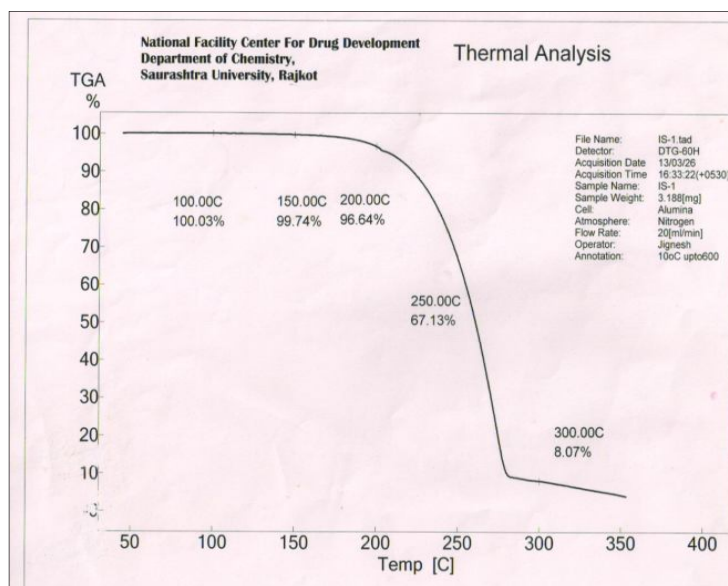


Fig 7: The Thermogram of Isatin

From the thermogram, various kinetic parameters, such as order of the degradation (n), energy of activation (E), frequency factor (A) and entropy change (ΔS) have also been calculated using Anderson-Freeman ^[11] and are reported in Table 3. The order of decomposition reaction is less than one whereas energy of activation (E) and frequency factor (A) values are quite high.

The positive change in entropy (ΔS) indicates that the transition state is less ordered than the original compound ^[12].

Figure 8 shows DSC of Isatin. From DSC, melting points is found to be 201.45 °C which is in agreement with the literature value, 200 °C^[13]. The enthalpy change is found to be 167.05 J/g.

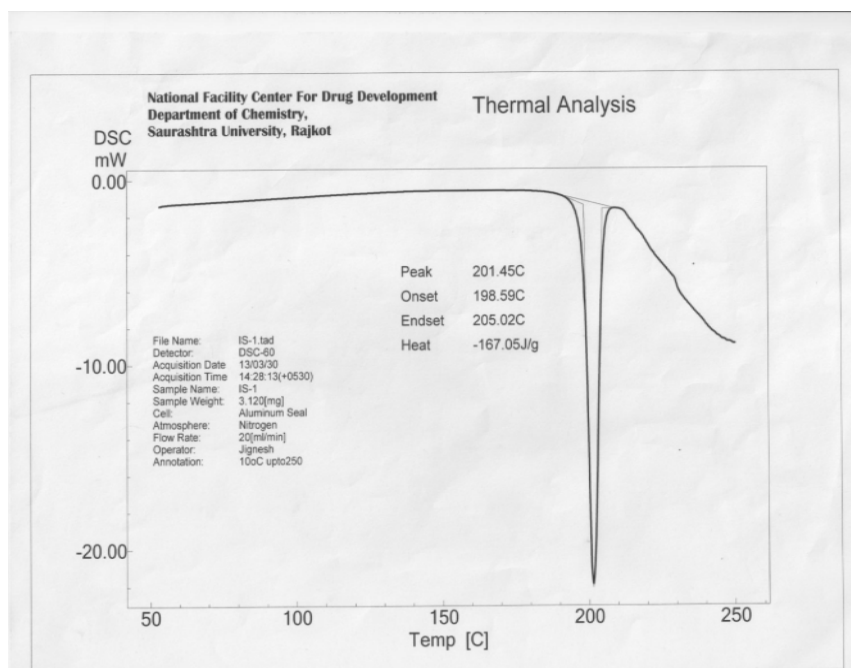


Fig 8: DSC of Isatin

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