International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Nano ZnO Catalyzed Synthesis of 2-(4-hydroxynaphthalen-1-yl)-N-methyl-2-Phenylacetamide and its Aggregation in Water

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Abstract: ***A novel organic compound, 2-(4-hydroxynaphthalen-1-yl)-N-methyl-2- phenylacetamide was synthesized by making use of non-toxic recyclable zinc oxide nanoparticles as catalyst and characterized using UV visible, FT-IR and ^1H NMR spectral techniques. Using conductometric method, its aggregation property in aqueous medium was studied at various temperatures. The thermodynamic analysis concludes that the driving force of aggregation is not enthalpic in nature.***

Keywords: Multi component reactions, ZnO nanoparticles, critical micelle concentration and aggregation

1. Introduction

Nano Science and technology is the pioneering field of 21st century in which an extensive research is going on[1]. Nano particles are characterized by its size below 100 nm and gained considerable importance compared to bulk counterparts. Among different nanoparticles, zinc oxide nanoparticles (ZnO NPs) are very much important due to their utilization in gas sensors, solar cell, cosmetics, drug-delivery systems and so forth [2,3].

Zinc oxide (ZnO) is a colourless, water insoluble inorganic compound used extensively as a catalyst due to its non-toxic recyclable property or an additive for various chemical reactions [4,5]. Multi-component reactions[6] are valuable device for assembling three or more reactants and converting them into higher molecular weight compounds. In recent years, such reactions[7,8] have become a powerful synthetic strategy and the synthetic applications of these protocols are further made more attractive when the reactions are carried out under solvent free conditions.

In the present work an attempt was made to prepare a novel organic compound 2-(4-hydroxynaphthalen-1-yl)-N-methyl-2-phenylace- tamide (HNMA) from 1-napthol, benzaldehyde and N-methylformamide by making use of ZnO NPs as a catalyst. The organic compound HNMA was characterized using UV visible, FT-IR and ^{1}H-NMR and spectroscopic techniques. Additionally the aggregating nature of HNMA in aqueous medium was studied conductometrically at different temperatures in order to study its driving force. In living systems, aggregation of protein is found to be the major cause of a wide variety of disease known as amyloidoses, including Alzheimer's, Parkinson's and prion diseases[9,10]. The mechanism of aggregation is to be studied in order to find drug for the above. In the present work, an attempt is been made to study aggregation of organic molecule which can mimic the aggregation of proteins.

2. Materials and Methods

2.1. Preparation of Zinc Oxide nanoparticles

ZnO NPs were prepared according to the literature method[11] with some modifications. Zinc acetate (0.05 mol) and oxalic acid (0.06 mol) were combined by grinding in a mortar for 2 hr at room temperature. Thus, formed $ZnC_2O_4.2H_2O$ nanoparticles were subjected to microwave (IFB-20BC4) irradiation at 150W microwave power for 30 min to produce ZnO nanoparticles[12].

2.2. Synthesis of 2-(4-hydroxynaphthalen-1-yl)-N-methyl-2-phenylacetamide (HNMA)

In a 50-ml beaker, a mixture of benzaldehyde (3.18 g, 30 mmol), N-Methyl formamide (1.86 g, 30 mmol) and 1-Naphthol (4.32 g, 30 mmol) were subjected to micro wave irradiation for 4 minutes, each pulse was of 30 seconds with intermittent time to avoid overheating. The reaction mixture was stirred with glass rod at regular interval. The progress of reaction was monitored by TLC (n-Hexane: Ethyl acetate (8:2)). After completion of reaction, the reaction mixture was cooled to room temperature and the compound 2-(4-hydroxynaphthalen-1-yl)-N-methyl-2-phenylacetamide (HNMA), was extracted using ethyl acetate as solvent. The insoluble ZnO catalyst was filtered off. The filtrate was collected, dried and the residue HNMA (Molecular formula, $C_{19}H_{17}NO_2$: Molecular Weight, 291.343: colour : Brown) was recrystallized from ethanol.

2.3 UV-Visible spectrophotometer

To locate the chromophoric absorption, UV visible spectrophotometer instrument SYSTRONICS model type 119 instrument was used at room temperature (302 K). The blank was calibrated using ethanol. The sample was scanned between 270 nm to 700 nm in ethanol medium.

2.4 FT-IR Infrared spectrophotometer

To locate the functional group and to characterize the molecular frame work, FT-IR spectrophotometer (ALPHA-BRUKER) was used at air-conditioned temperature (298 K). The method of sample preparation was a direct method without making use of potassium bromide. The presence of –OH group will arise at 3600-3200 cm^{-1}. The existence of carbonyl (C=O) will occur at 1750-1620 cm^{-1}. The N-H group will reflect at 3500-3300 cm^{-1}.

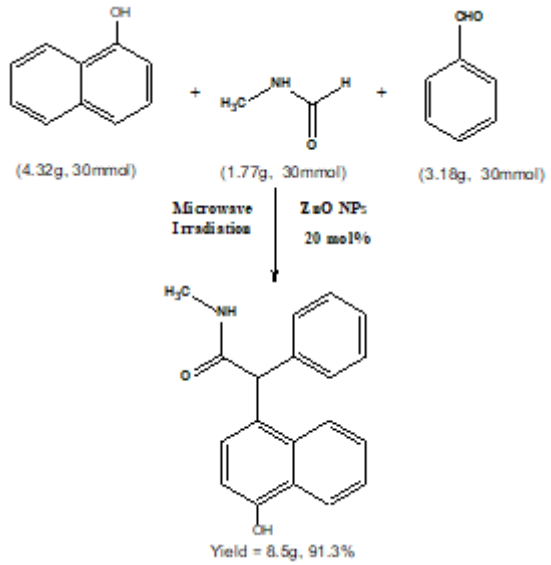
2.5. ^{1}H NMR spectrophotometer

To further characterize the molecular structure, ^{1}H NMR spectrum was recorded on Bruker FT-NMR spectrophotometer operating at 400 MHz. The solvent used was $CDCl_3$ and tetramethylsilane (TMS) as an internal reference.

2.6 Conductivity Measurements

The conductance of aqueous solution of HNMA was recorded using Systronics Digital Conductometer (model-304). A Fabricated double walled glass container (70 ml) was used which can circulate water at various temperatures connected with thermostat for thermodynamic work.

3. Results and Discussion



Scheme 1: Preparation of HNMA from 1-napthol, N-methyl formamide and benzaldehyde

The one pot preparation of HNMA from 1-napthol, N-methyl formamide and benzaldehyde under solvent from condition using ZnO Nps is shown in scheme 1. It consists of solvophobic aromatic rings and solvophilic hydroxyl group. The UV visible spectrum of HNMA is shown in the figure 1. It exhibits at two characteristic peaks at 310.2 nm and 369 nm, the absorption at 310.2 nm is due to $\pi \rightarrow \pi^*$ transition of aromatic C=C in the HNMA and the peak at 369 nm is due to the $n \rightarrow \pi^*$ transition of C=O present in amide group supporting the structure of HNMA.

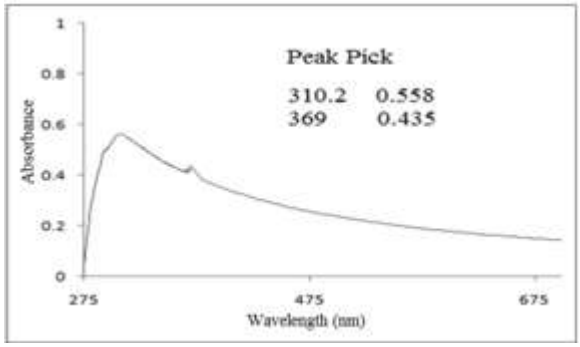


Figure 1: UV-visible Spectrum of HNMA

The FT-IR spectrum of HNMA is shown in the figure 2. It shows five major peaks at 1572 cm^{-1}, 1660 cm^{-1}, 3053 cm^{-1}, 3299 cm^{-1} and 3402 cm^{-1}. The peak appear at 1572 cm^{-1} due to aromatic C=C bending vibrations, the peak at 1660 cm^{-1} is due to the presence of C=O of amide, the peak at 3053 cm^{-1} is for C-H stretching of aromatic ring, the peak at 3299 cm^{-1} is for N-H stretching and the peak at 3402 cm^{-1} is due to O-H stretching. FT-IR spectrum supports the structure of HNMA.

To further study about the number and type of protons of HNMA, ^{1}H NMR is taken in $CDCl_3$. The ^{1}H NMR spectrum of HNMA is shown in the figure 3. The chemical shift at 7.0-8.4 is due to the aromatic protons of phenyl and naphthyl rings and 5.8 is due to the C-H methine proton connected to aromatic rings. The peak at 5.5 is due to O-H proton attached to naphthalene ring and the peak at 2.4 is due to methyl group attached to NH of amide.

The aggregate formation of any compound is usually determined by plotting any of its physical property as a function of its concentration and the point of intersection between two straight lines is taken as Critical Micelle Concentration (CMC)[13,14]. CMC is defined as the concentration of organic amphiphilic molecules above which micelles formation takes place in true solution[15].

In the present study CMC of HNMA was determined by plotting the conductance values at various concentrations measured using digital conductometer versus concentration. As per Arrhenius theory, one should get a straight line, but in the contrary, two lines of different slopes were obtained suggesting aggregation at that particular concentration which is called the critical micelle concentration (CMC) at that particular temperature in water as solvent. The existence of

CMC were determined at different temperatures 306 K, 311 K, 315 K and 319 K (figure 4). From the CMC value obtained from the graph, ln(CMC) was computed. Based on ln (CMC), the thermodynamic parameters ($\Delta G_m°$, $\Delta H_m°$, $\Delta S_m°$) are obtained using biphasic micellar model[13,15]. The standard free energy for aggregate formation, $\Delta G_m°$ of the HNMA has been calculated from the following equation (1).

$$\Delta G_m° = RT\ln (CMC) \quad (1)$$

$$\Delta G_m° = \Delta H_m° - T\Delta S_m° \quad (2)$$

The standard enthalpy change for micelle formation ($\Delta H_m°$) was calculated using the value obtained from the slope of the plot ln (CMC) versus temperature. The $\Delta H_m°$ was calculated using the equation (3).

The value of $\Delta S_m°$ was calculated from $\Delta G_m°$ and $\Delta H_m°$, using equation (2). The change in standard heat capacity at constant pressure $\Delta C_p°$ was obtained from the slope of the plot of $\Delta H_m°$ versus temperature.

$$\Delta H_m° = -RT^2 [d\ln (CMC)/dT] \quad (3)$$

$$\Delta C_p° = [d\Delta H_m°/dT] \quad (4)$$

The values of CMC determined conductometrically for HNMA in aqueous condition at various temperatures and their corresponding thermodynamic parameters determined using equations 1, 2, 3 and 4 are given in table 1. From the table 1, the CMC of the HNMA, increases with decrease in temperature, indicating the micelle formation is less favored with a rise in temperature. The variation of ln (CMC) with temperature for the HNMA is shown in figure 5.The thermodynamic parameters ($\Delta G_m°$, $\Delta H_m°$, $\Delta S_m°$) for the HNMA at various temperatures are also given in table 1. From the values of positive $\Delta H_m°$, it is clear that the driving

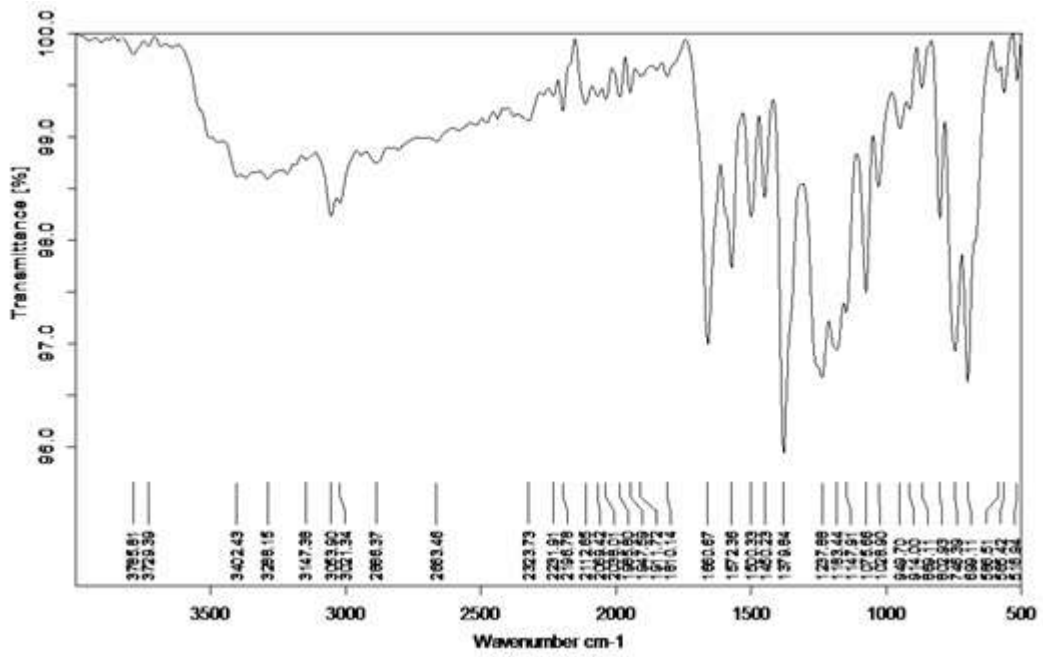


Figure 2: FT–IR Spectrum of HNMA

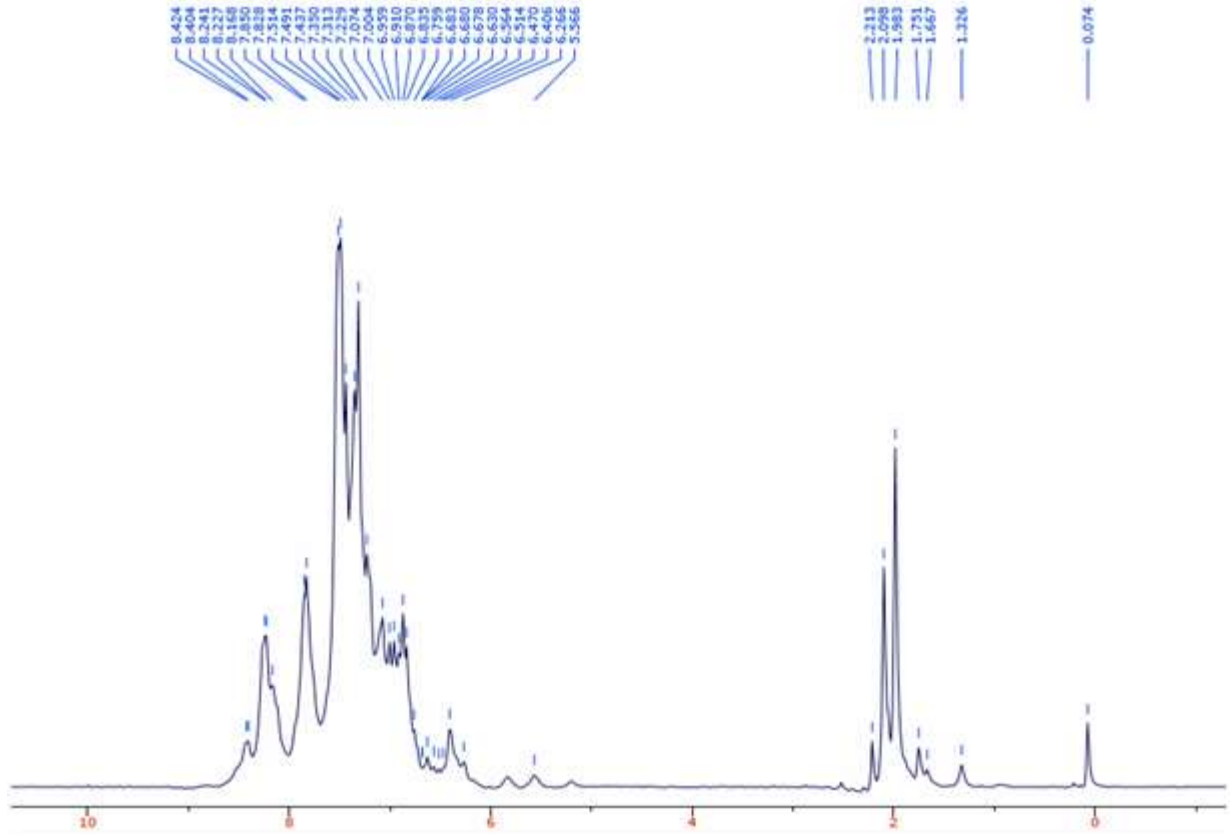


Figure 3: FT – NMR Spectrum of HNMA

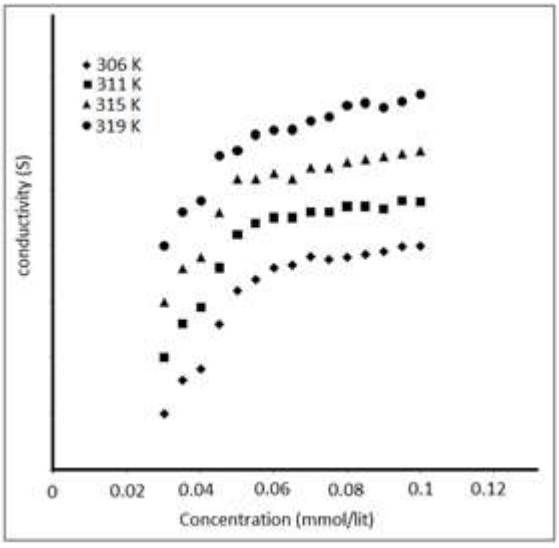


Figure 4: Plot of conductivities of various concentrations HNMA at different temperatures.

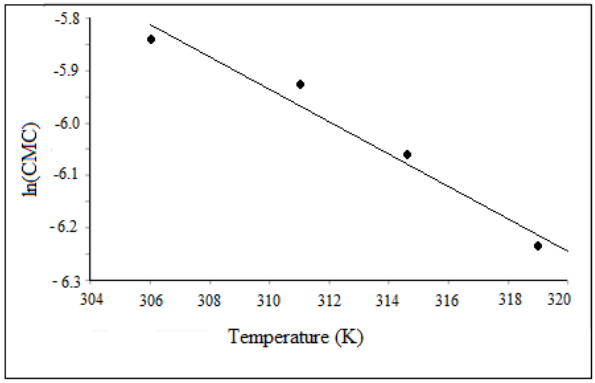


Figure 5: Plot of ln (CMC) versus temperature for HNMA

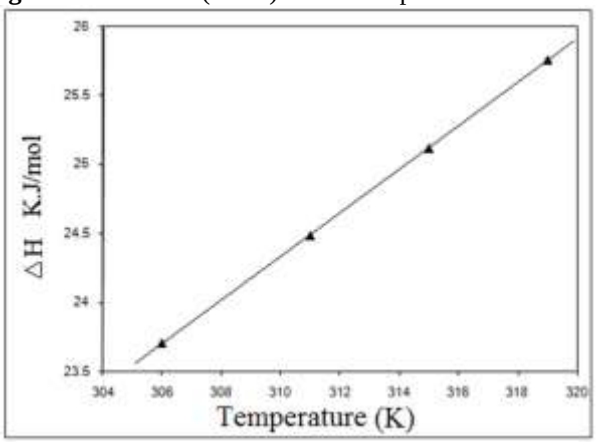


Figure 6: Plot of $\Delta H_m°$ versus temperature for HNMA

force for HNMA aggregation is not enthalpic in nature over the temperature range under investigation. When HNMA aggregates, the solvophilic groups (the hydroxyl groups) are 'clustered' together, resulting in a fairly close approach of the hydrophobic groups. This result

Table 1: Thermodynamic parameters of HNMA at various temperatures

Temp (K)	*CMC (mmol/lit)*	*In (CMC)*	ΔG_m°	ΔH_m°	ΔS_m°	ΔC_p°
306	2.913	-5.84	-14.9	23.7	126.0	158.1837
311	2.676	-5.92	-15.3	24.5	128.0	
315	2.439	-6.02	-15.8	25.2	129.7	
319	1.961	-6.23	-16.5	25.8	132.6	

in electrostatic destabilization due to unfavorable dipole-dipole interactions. However, such unfavorable interaction could be compensated by solvation of the hydrophilic groups with water molecules. On increasing the temperature, both ΔH_m° and ΔS_m° increases, indicating that less solvent molecules are accessible to the complex, resulting in more "structured" HNMA molecules.

The standard heat capacity change for micellization (ΔC_p°) is obtained from the slope of ΔH_m° versus temperature (figure 6; table 1). The positive ΔC_p° signifies that the structure of complex is unaffected by the solvent water. Comparing the results of thermodynamic experiments on model organic compounds, it is apparent that the heat capacity changes play a central role in characterizing the solvophobic interactions. The positive heat capacity can be attributed to the ordering of solvent molecules around the exposed solvophilic groups i.e., on increasing the temperature; we get more tightly packed larger micelle like structures. The positive entropic contribution leads to the aggregate stabilization at higher temperature.

4. Conclusion

Using ZnO NPs, a novel organic compound HNMA was prepared using 1-napthol, N-methyl formamide and benzaldehyde. The compound was characterized using various spectral techniques. In aqueous medium, its aggregation behaviour was studied along with its thermodynamic parameters. The results conclude that the driving force of aggregation is not enthalpic in nature. During aggregation less solvent molecules are accessible which can be inferred from ΔH_m° and ΔS_m° values at different temperatures. The positive standard heat capacity change for micellization (ΔC_p°) signifies that the structure of aggregate is unaffected by the solvent water.

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