Research Journal of Chemical Sciences _____ ISSN 2231-606X
Vol. **2(10),** 60-63, October **(2012)** *Res.J.Chem. Sci.*

FTIR, ^{1}H NMR Spectral, Powder X-ray diffraction and DSC studies of "β-cyclodextrin-para-chlorobenzonitrile" Inclusion Complex

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Available online at: www.isca.in
Received 19th June 2012, revised 26th June 2012, accepted 3rd July 2012

Abstract

By keeping in mind the application of nitriles, the inclusion complex of β-cyclodextrin-para-chlorobenzonitrile with 1:1 stoichiometric ratio has been prepared in aqueous media by co-precipitation method. The intermolecular interaction between β-cyclodextrin and para-chlorobenzonitrile are studied and confirmed by various physical measurements like FTIR, ^{1}H NMR, powder X-ray diffraction and differential scanning calorimetry.

Keywords: β-Cyclodextrin (*β-CD*), para-chlorobenzonitrile, inclusion complex, FTIR, ^{1}H NMR, X-ray diffraction, differential scanning calorimetry (DSC).

Introduction

There has been great interest for the aromatic nitriles in various fields like synthesis of a potent, orally bioavailable HIV-1 non-nucleoside reverse transcriptase inhibitor[1], arylation of oxazoles and benzoxazole[2] and poly ether amides[3]. Para-chlorobenzonitrile is also used for the purpose of N-arylation on benzimidazoles[4]. Nitriles are widely used for the transformation into amide, amines, esters, carboxylic acids, etc[5]. Hence they have been used as intermediate for the synthesis of fine chemicals such as agricultural chemicals, dyes and medicines[6]. Nitriles are found to be very useful starting for synthesis of various bioactive molecules[7]. Aryl chloronitriles are useful for synthesis of aromatic alkynes by Sonogashira cross coupling reaction[8].

β-Cyclodextrin ; figure 1(a) is a cyclic heptamer composed of seven glucose units jointed "head to tail" by α-1,4 glycosidic linkage and produce by the action of certain enzyme on starch[9]. Cyclodextrins has tendency to form inclusion complex with varieties of hydrophobic compounds[10-12]. It is widely accepted that the binding forces involving in the inclusion formation are Vander Waals interactions, hydrophobic interactions, hydrogen bonding and electrostatic interaction between *β*-cyclodextrin and guest molecule[13]. Cyclodextrins are widely used as molecular cages in the pharmaceutical, agrochemical, food and cosmetic industries[14] Cyclodextrin are also act as a potential candidate for the drug carrier because of their ability to alter physical, chemical and biological properties of the guest molecules through the formation of inclusion complex[15]. The use of cyclodextrins as microvessels to perform the chemical reactions has attracted the attention of chemist since the 1960s[16,17]. Taking into account the importance of nitriles and our work in continuation with *β-CD*[18-20], herein we have prepared and study inclusion complex of para-chlorobenzonitrile with *β-CD* and confirm by various physical measurements.

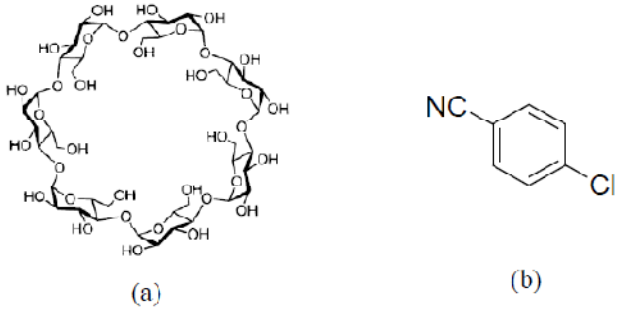

Figure1
Chemical structure of (a) *β-CD* and (b) para-chlorobenzonitrile

Material and Methods

β-Cyclodextrin (Sigma-Aldrich), para-chlorobenzonitrile (From S. D. Fine) were purchased and used without further purifications. Infrared (IR) spectra were obtained with FTIR spectroscopy (Shimadzu IRAffinity-1 model) using KBr. ^{1}H NMR was recorded on a Bruker Avance II spectrophotometer operating at 500 MHz. Powder X-ray diffraction patterns were obtained using a Rigaku miniflex diffractometer using Cu source. Differential scanning calorimetry (DSC) analyses were carried out in the temperature range from 30 to 300^{0}C in a stream of nitrogen atmosphere on DSC-50 Thermal Analyzer (Shimadzu, Japan). During experiments, aluminium crucibles were used. The heating rate was 10^{0}C/min, and the flow rate of nitrogen atmosphere was 50 mL/min.

Procedure for preparation of inclusion complex of para-chlorobenzonitrile with *β-CD*: The complex of *β-CD* and para-chlorobenzonitrile has been prepared by coprecipitating

method[18] from aqueous ethanol solution. *β-CD* (3.405 gm, 3 mmol) dissolve in water (25 mL) under warm condition till clear solution obtained. To this clear solution, para-chlorobenzonitrile (0.411 gm, 3 mmol) previously dissolved in ethanol (2 mL) added dropwise with stirring at room temperature and allow to stir it for 24 h and freeze to overnight. The resulting white precipitate was filtered and washed with cold water and allow drying for 24 h at room temperature yielding white crystalline powder.

Procedure for preparation of physical mixture: A physical mixture of para-chlorobenzonitrile and *β-CD* (molar ratio 1:1) was prepared by simple mixing in ceramic mortar.

Results and Discussion

The complex of *β-CD* and para-chlorobenzonitrile has been studied by various physical measurements.

FTIR study of complex: The formation of inclusion complex of *β-CD* and a guest substance is accompanied by changes in their IR spectra as compared with the individual components[21,22]. Figure 2 shows the IR spectra of *β-CD*, para-chlorobenzonitrile, inclusion complex and physical mixture in solid state. Significance difference in OH, CH and CN vibration modes are found. Peaks are not only shifted after complex formation, but the shapes of peaks are also change. The broad peak of OH in *β-CD* becomes sharp and intense in inclusion complex. The aliphatic CH of cyclodextrin 2926 cm^{-1} and CN peak in individual para-chlorobenzonitrile 2225 cm^{-1} shifted to 2924 cm^{-1} and 2227 cm^{-1} respectively. This is not observed in physical mixture suggesting an interaction between para-chlorobenzonitrile and *β-CD*. The absorption band at 827 cm^{-1} of disubstituted benzene in individual 4-chlorobenzonitrile shifted to 829 cm^{-1} in inclusion complex, which was unaffected in physical mixture indicating phenyl ring interaction with *β-CD*. Though the shift difference occurs is small, this might be owing to the effect of inner microenvironment and non-covalent interaction of *β-CD* hydroxyls on para-chlorobenzonitrile.

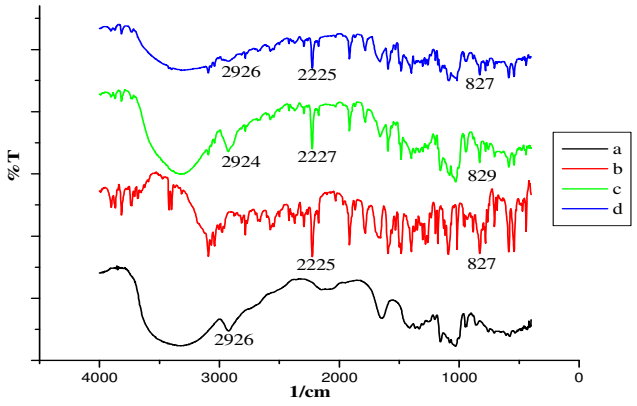

Figure-2
FTIR of (a) *β-CD*, (b) para-chlorobenzonitrile, (c) *β-CD*-para-chlorobenzonitrile complex and (d) physical mixture

^{1}H NMR study of the complex: Direct evidence for the formation of inclusion complex can be obtained from ^{1}H NMR spectroscopy. The values of chemical shift, δ for different protons in *β-CD*, *β-CD*-para-chlorobenzonitrile complex and pure para-chlorobenzonitrile were listed in table 1 and table 2. It can be seen from ^{1}H NMR that in inclusion complex, a variation in chemical shift of protons of *β-CD* as well as para-chlorobenzonitrile was observed. In addition, the upfield in signal of H3 and H5 of *β-CD* was observed which lies on inner side of cavity indicating the penetration of guest molecule inside the cavity. On the other hand, as shown in figure 3b, when para-chlorobenzonitrile form complex with *β-CD*, the change in micro-environment leaded phenyl ring proton signals splits.

Table-1
500 MHz ^{1}H chemical shift of *β-CD* protons in free and complex state in D_2O[a]

Proton	H1	H2	H3	H4	H5	H6ab
β-CD	4.911	3.490	3.805	3.427	3.695	3.720
Complex	4.954	3.532	3.787	3.474	3.685	3.770
Δδ	0.043	0.042	-0.018	0.047	-0.010	0.050

[a]Chemical shifts expressed in ppm

Table-2
500 MHz ^{1}H chemical shift of para-chlorobenzonitrile in free and complex state[b]

Proton	H_{ortho}	H_{meta}
4-Chlorobenzonitrile	7.613	7.468
Complex	7.655	7.503
Δδ	0.042	0.035

[b] Chemical shifts expressed in ppm.

Powder X-ray diffraction study of complex: True inclusion complexes have its diffraction pattern altered from those of pure components[23]. The powder X-ray pattern for individual components, complex and physical mixture is shown in figure 4. The diffraction pattern of complex was found to be different than diffraction pattern of pure *β-CD* and para-chlorobenzonitrile. Comparing the pattern for *β-CD*-para-chlorobenzonitrile complex with that of physical mixture reveals mark differences. In complex the new peaks were found and shift in peak position also found where as the physical mixture has peaks which are superimposition of two individuals. The intensity of certain peaks in the complex are also enhanced thereby confirming complex formation[24].

Differential scanning calorimetry (DSC) study of complex: The DSC thermogram for *β-CD*, para-chlorobenzonitrile, *β-CD*-para-chlorobenzonitrile complex and physical mixture (keeping the mass constant) are represented in figure 5. The thermogram of para-chlorobenzonitrile shows a characteristic endothermic peak at 92.53^{0}C, corresponding to its fusion peak. The *β-CD* exhibited a characteristic broad peak associated with water loss from 60-120^{0}C.[25] As regards the analysis of *β-CD*-para-chlorobenzonitrile complex, the peak of para-chlorobenzonitrile

found at 92.94^{0}C with strongly reduced in intensity. Where as in physical mixture, the peak of para-chlorobenzonitrile was found at 92.52^{0}C without significant reduction in intensity clearly indicating an interaction between both *β-CD* and para-chlorobenzonitrile molecules.

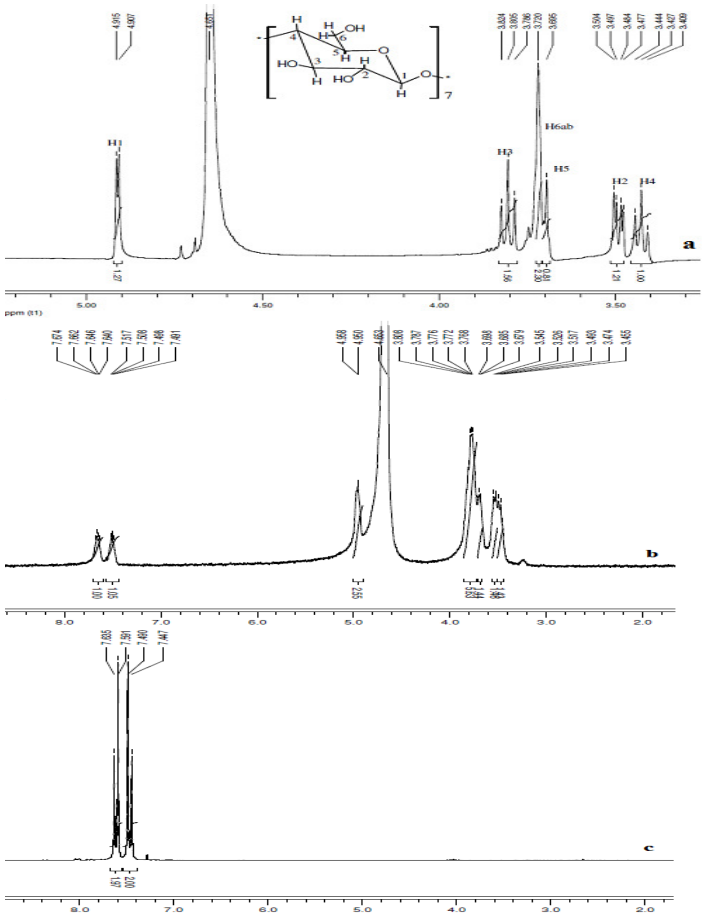

Figure-3
^{1}H NMR of (a) *β-CD*, (b) *β-CD*-para-chlorobenzonitrile complex and (c) para-chlorobenzonitrile

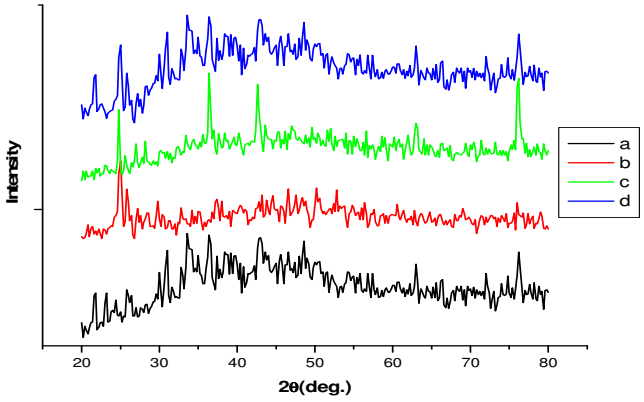

Figure-4
Powder X-ray diffraction patterns of (a) *β-CD*, (b) para-chlorobenzonitrile, (c) *β-CD*-para-chlorobenzonitrile complex and (d) physical mixture

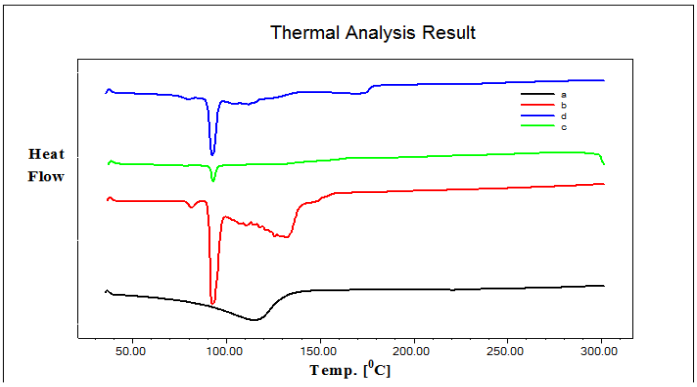

Figure-5
DSC of (a) *β-CD*, (b) para-chlorobenzonitrile, (c) *β-CD*-para-chlorobenzonitrile complex and (d) physical mixture

Conclusions

In this work, the 1:1 inclusion complex of para-chlorobenzonitrile and *β-CD* has been prepared in aqueous media and intermolecular interactions between them studied. The significant difference in FTIR, ^{1}H NMR, powder X-ray diffraction pattern and DCS thermogram of complex confirms the molecular interactions. In addition, the observed upfield chemical shift of H3 and H5 proton of *β-CD* suggest that para-chlorobenzonitrile interacts with internal protons of *β-CD* and reveal clear evidence for inclusion phenomena.

Acknowledgement

The authors are thankful to Department of Science and Technology and University Grant Commission, New Delhi, India for financial support of this work.

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