This article was downloaded by:
On: *29 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK

Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Synthesis of Chemical Modified β-cyclodextrin and its Inclusion Behavior in Alcohol/Water Mixed Solvents

Hongzhi Xie[a]; Shikang Wu[a]
[a] Chinese Academy of Sciences, Institute of Photographic Chemistry, Beijing, China

To cite this Article Xie, Hongzhi and Wu, Shikang(2001) 'Synthesis of Chemical Modified β-cyclodextrin and its Inclusion Behavior in Alcohol/Water Mixed Solvents', Supramolecular Chemistry, 13: 4, 545 — 556
To link to this Article: DOI: 10.1080/10610270108028301
URL: http://dx.doi.org/10.1080/10610270108028301

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SUPRAMOLECULAR CHEMISTRY, Vol. 13, pp. 545–556
Reprints available directly from the publisher
Photocopying permitted by license only

© 2001 OPA (Overseas Publishers Association) N.V.
Published by license under
the Gordon and Breach Science Publishers imprint,
a member of the Taylor & Francis Group.

Synthesis of Chemical Modified β-cyclodextrin and its Inclusion Behavior in Alcohol/Water Mixed Solvents

HONGZHI XIE and SHIKANG WU*

Institute of Photographic Chemistry, Chinese Academy of Sciences, Beijing 100101, China

(Received 25 January 2000)

Downloaded At: 15:29 29 January 2011

The chemical modified β-cyclodextrin(CD), which bears a fluorophore group – N,N-dimethylamino-chalcone (DMAC), was synthesized. The self-inclusion behavior of this compound in aqueous solution and in alcohol/water mixed solvents was investigated in detail, and compared with the inclusion system of non-modified CD with free DMAC molecule. The results showed that a deep self-inclusion complex was formed for this compound in aqueous solution and had the ability to recognize different organic molecules by two fully different modes: "in-out" and "co-inclusion" mechanisms. The inclusion behavior of these systems in various ratio of alcohol/water mixture as solvents was investigated. The results indicated that the self-inclusion complex has a higher stability in alcohol/water mixed solvents than that in the case of non-modified CD. The chalcone group appended at β-CD enabled the host as a sensitive probe to study the inclusion behavior of CD.

Keywords: Chemical modified β-cyclodextrin; N,N-Dimethylamino chalcone; Self-inclusion complex; Ternary complex; Molecular recognition

INTRODUCTION

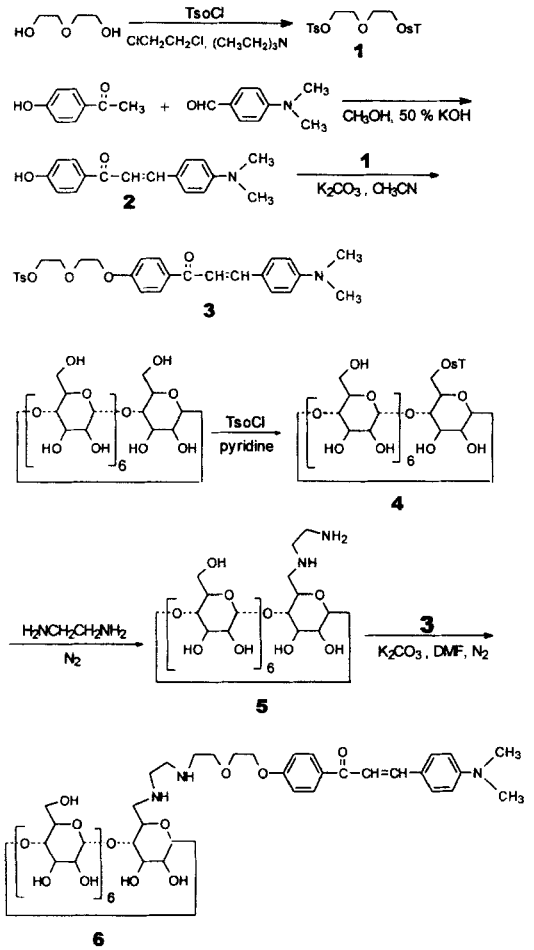
Cyclodextrins (CDs) are cyclic oligosaccharides that have the ability to form inclusion complexes by accommodating a variety of guest molecules into their cavities due to the hydrophobic interaction [1]. They have been received much attention as molecular receptors (hosts) used in molecular recognition of neutral molecules (guests) because they are able to discriminate between guests with different shapes and dimensions [2,3]. As CDs are basically inert with respect to optical spectroscopy, inclusion phenomena involving these molecules are usually studied with spectroscopically active guest molecules. Fortunately, CDs can be converted into spectroscopically active species by modified with chromophoric groups. Ueno [4,5] and Corradini [6,7] have prepared a number of cyclodextrin derivatives modified with the fluorophore, and the dansyl group has been widely used. This is based on the dansyl group has relatively weak fluorescence emission in a polar solvent, Such as water, whereas its emission intensity is higher and emission maximum wavelength is blue shift in non-polar solvent. The fluorophore attached to CD with adequate size as a pendant may form an

*Corresponding author.

intramolecular complex (self-inclusion) by being included into the cavity of CD moiety [4–8]. Upon guest addition, the modified CDs would exclude the fluorophore from inside to outside of the CDs cavity. Hence, CDs derivatives have been employed as fluorescent chemosensors (FCS) to detect certain chemical species inert in spectroscopy.

It is well known that most studies of CDs complex stability have been carried out in fully aqueous solution [9], but quite a few works investigated the CDs complex formation and dissociation in binary aqueous-organic solvent mixtures or even in pure organic solvents. Some investigators [10,11] employed the water-miscible solvents, usually with alcohols, DMSO, DMF, *etc.*, to study the stability of the CDs complex formed. However, the solvent effect on CDs complex stability was focused on by the addition of small amounts of organic cosolvents, usually no more than 1%(v/v). At this concentration, the alcohol does not significantly alter the bulk solvent polarity. It is obviously significant to design new kind of CD derivatives that bears a molecular probe which is sensitive to environment polarity and easily used to monitor the formation or dissociation of inclusion complex between probe and CDs.

We have prepared a new kind of intramolecular charge transfer (ICT) compounds, such as N,N-dimethylchalcone (DMAC), and investigated the photophysics of them in detail [12,13]. In present work, a novel chemical modified β-cyclodextrin was synthesized. We would like to study the inclusion complex behaviors of the chemical modified CD, compared with the non-modified one in the whole ratio of bulk alcohol/water mixed solvents. Hope to clarify the relationship of the formation and dissociation of multi-component inclusion complexes with the proportion of mixed solvents and learn the added alcohol molecules how to change the strength of host-guest associations. The fluorescence spectra are employed as sensitive monitor to follow and study this process, by comparing the stability of these complexes formed from the chemical modified CD and the non-modified one, so as to provide a general means of studying the stability of inclusion complex from CDs in mixed solvents.



SCHEME 1

EXPERIMENTAL

General

H'NMR, IR and MS spectra were recorded at a Varian GERMANA-300 MHz NMR, a Bio-RAD FTS spectrometers and a Finnigan 4021C GC/MS systems, respectively. Elemental analyses were

Downloaded At: 15:29 29 January 2011

Downloaded At: 15:29 29 January 2011

carried out on a Heiaeus CHN-Rapid instrument. Commercially available reagents were used as received unless otherwise noted. Such as β-cyclodextrin monohydrate (Aldrich Chemical Co.) was dried in vacuo for 48 h at 110°C. Pyridine was refluxed over Na for 15 h and then distilled. DMF was dried over CaH_2 for 2d, and then distilled under reduced pressure prior to use. Ethylenediamine was redistilled before use. The following materials – p-tosyl chloride, diethylene glycol, p-dimethyl-amino-benzaldehyde are all purchased from Beijing Chemical Co. Methanol (MeOH), Ethanol (EtOH), 1-Propanol (1-PrOH) and 2-Propanol (2-PrOH) were all AR regeants. 1-Adamentanecarboxylic acid (1-ACA, 99%) and stearyltrimethylammonium chloride (STAC) were purchased from Aldrich (USA) and Tokyo TCI kasei Co. (Japan), respectively. 4-hydroxy-acetophenone (98%), was obtained from Acros. TLC experiment was carried out on a precoated silica gel plates (60F-254) with solvent of EtoAc/2-propanol/concentration ammonia liquor/H_2O (7:7:5:4). A solution of diphenylamine (0.1 g), aniline (0.1 mL), and 85% phosphoric acid (1 mL) in acetone (10 mL) was used as a spray reagent to detect the parent and modified β-CD.

Synthesis of 1,5-ditosyloxy-3-oxapentane(1)

To a solution of 11.6 mL of dithylene glycol (0.110 mol) and 33.0 mL of triethylamine (0.176 mol) in 150 mL of 1,2-dichloroethane, 44.0 g of p-tosyl chloride(0.231) was added within 1h. After stirring for 12 h at room temperature, the reaction mixture was filtrated to remove the precipitate and the filtrate was concentrated to dryness. The residue was recrystallized from 95% ethanol and dried in vacuo to give 28.8 g of white crystals (yield, 64%). mp: 78 ~ 79°C, IR(KBr): 3022(PhC—H), 2887(HC—H), 1360 (S=O) cm^{-1}; ^{1}HNMR (300 MHz, $CDCl_3$): δ2.40 (6H, s), 3.58 ~ 3.61(4H, t, J = 4.5 Hz), 4.07 ~ 4.10 (4H, t, J = 4.5 Hz), 7.33 ~ 7.36(4H, d, J = 8.1 Hz), 7.76 ~ 7.79(4H, d, J = 8.2 Hz).

Synthesis of 4-hydroxy-4′-N,N-dimethylaminochalcone(2)

To a solution of 10 g of 4-hydroxy-acetophenone(73.4 mmol) and 11.6 g p-N,N-dimethylaminobenzadehyde (77.8 mmol) in 50 mL of methanol, 40 mL of 50% KOH aqueous solution was added. The mixture was stirred at 40°C for 48 h. After cooling, the reaction mixture was poured in 300 mL water containing 45 mL of acetic acid. The yellow precipitate were collected by filtration and washed with water. Recrystallization of the solid from 95% ethanol yields 15.0 g of yellow crystals (yield, 77%). mp: 212 ~ 214°C IR(KBr): 3318(PhO—H), 3022(PhC—H), 1637 (C=O), 1605, 1546(C=C) cm^{-1}; ^{1}HNMR (300 MHz, CD_3OD): δ3.04(6H, s), 6.75 ~ 6.78(2H, d, J = 8.9 Hz), 6.87 ~ 6.89(2H, d, J = 8.7), 7.48 ~ 7.53 (1H, d, J = 15.2), 7.58 ~ 7.61(2H, d, J = 10.1), 7.69 ~ 7.74(1H, d, J = 15.4), 7.96 – 7.99(2H, d, J = 8.9). MS(EI) m/e: 267 (M^+).

Synthesis of 1-Tosyloxy-5-(4″-N,N-dimethylaminochalcone-4′-oxy)-3-oxa-pentane(3)

A solution of **1** (3.34 g, 8.07 mmol) in 20 mL of acetonitrile was warmed up to 110°C, a solution of **2** (1.68 g, 6.29 mmol) in 60 mL of acetonitrile was added dropwise over 2h. Then the mixture was stirred for 10h at 110°C. After cooling, the reaction mixture was concentrated in vacuo and poured into water, causing immediate formation of a orange precipitate. The crude product was collected by filtration and washed with water. Silica gel column chromatography(petroleum ether(60 ~ 90°C)/ethyl acetate, 1:1) afforded 1.80g orange solid(yield, 55%). mp: 82 ~ 84°C. IR(KBr): 3022(PhC—H), 1653(C=O), 1605, 1540(C=C), 1350(S=O) cm^{-1}, ^{1}HNMR (300 MHz, D_6-DMSO): δ2.40(3H,s); 2.98(6H, s); 3.48 ~ 3.50(2H, t, J = 4.0 Hz); 3.63 ~ 3.66(2H, t, J = 4.0 Hz); 3.63 ~ 3.69(2H, t, J = 3.9); 4.02 ~ 4.04 (2H, t, J = 3.9 Hz); 6.72 ~ 6.74(2H,d, J = 8.5 Hz); 7.02 ~ 7.05(2H, d, J = 8.5 Hz); 7.40 ~ 7.46(3H,t,J_1 = 8.5 Hz;

$J_2 = 16.0$ Hz); 7.64 ~ 7.67(2H, d, 9.4 Hz); 7.70 ~ 7.75(1H, d, J = 15.0 Hz); 7.75 ~ 7.78(2H, d, J = 8.0 Hz); 8.09 ~ 8.12(2H, d, J = 8.5 Hz). MS(EI) m/e (rel. Intens.): 355(2); 155(18); 91(100).

Synthesis of mono-6-O-(p-tosyl)-6-β-cyclodextrin(CDoTs)(4)

A solution of p-tosyl chloride (7.5 g, 39.4 mmol) in 30 mL of dry pyridine was dropped to a solution of dry β-cyclodextrin (22.4 g, 19.8 mmol) in 225 mL of dry pyridine, with stirring at room temperature for 8 h under N_2. Then, the reaction mixture was concentrated in vacuo then poured into a large amount of acetone. The white precipitate were collected by filtration and washed with acetone for several times. The crude product was recrystallized three times from water and dried in vacuo to give pure white crystals 8.2 g (yield 32.2%, based on β-CD). The TLC of the product gave only a spot with $R_f = 0.6$ ($R_f = 0.28$ for β-CD). mp: 178 ~ 179°C (dec, rfs 179°C [14]), IR(KBr): 3400(O—H), 2930(PhC—H), 1630, 1320(S=O) cm^{-1}; ^{1}HNMR (300 MHz,D_6-DMSO): δ2.42(3H,s,$-CH_3$), 3.18 ~ 3.42(14H, m, C2, C4—H), 3.43 ~ 3.74(28H, m, C3—H, C5—H, C6a, C6b—H), 4.13 ~ 4.55 (6H, m, C6—OH]), 4.76 ~ 4.82(7H, s, C1—H), 5.58 ~ 5.87(14H, m, C2—OH, C3—OH), 7.40 ~ 7.45(2H, d, J = 15Hz, Ph—H), 7.72 ~ 7.77(2H, d, J = 15, Ph—H). Anal. Calcd. for $C_{49}H_{76}O_{37}S.3H_2O$: C, 43.81; H, 6.15; S, 2.39. found: C, 43.58; H, 6.21; S, 2.49.

Synthesis of mono-6-deoxy-(6-aminoethylamino)-β-cyclodextrin (5)

The dried β-CDoTs (1.5 g, mmol) was dissolved in 10 mL of dried anhydrous ethylenediamine and then stirring at 70°C for 3 h under N_2. The reaction mixture was poured into a large excess of ethanol and the precipitate was collected by filtration. The crude product was recrystalized from 70% ethanol, giving 0.7 g of white crystals (Yield, 51%, based on β-CDoTs), m.p. 248°C. IR(KBr): 3400 ~ 3500(O—H, N—H) cm^{-1}, ^{1}HNMR(300 MHz, D6-DMSO): 2.65(4H, m, N—CH_2), 3.40 ~ 3.55(14H, m, 2-H, 4-H), 3.60 ~ 3.90(28H, m, 3-H, 5-H, 6a, 6b-H), 4.90 ~ 4.93 (7H, d, 1-H), Anal. Calcd. for $C_{44}H_{76}O_{34}N_2.4H_2O$: C, 42.0; H, 6.81; S, 2.22. found: C, 41.65.; H, 6.05; S, 2.25.

Synthesis of mono-6-deoxy-6-[8-(4″-N,N-dimethylaminochalcone-4′-oxy)-3-amino-6-oxy-octa-1-amino]-β-Cyclodextrin(6)

5 (0.41 g, 0.35 mmol), **3** (0.21 g, 0.42 mmol) and 0.1 g of K_2CO_3 were dissolved in 10 mL of dry DMF and stirred for 24h at 70°C under N_2. The reaction mixture was cooled and poured into 50 mL of acetone, causing an immediate formation of a yellow precipitate. The precipitate was collected by suction filtration and washed with acetone. The crude product was purified by a column of Sephadex G-15 (1.5 × 40 cm bed) eluted with water. The yellow fraction was collected and assay by TLC. Fractions that gave only one spot with $R_f = 0.52$ were combined and evaporated to dryness by ice-drying (−40°C, 40 mbar,). A 0.33 g of yellow crystals were obtained (yield, 53.7%, Based on **5**). mp: 246 ~ 248°C(dec.), IR(KBr): 3405(O—H), 2929(PhC—H), 1631(C=O), 1650, 1570(C=C) cm^{-1}, ^{1}HNMR(300 MHz, D_6-DMSO): δ2.24(2H, t, N—CH_2), 2.34(2H, t, N—CH_2), 2.68(2H, t, N—CH_2), 2.74(2H, t, N—CH_2), 3.01(6H, s, N—CH_3), 3.20(2H, t, O—CH_2), 3.54(2H, t, O—CH_2), 3.64(2H, t, O—CH_2), 3.10 ~ 4.01(42H, m, CD—CH), 4.03 ~ 4.38 (6H, m, C6b-OH), 4.75 ~ 4.79(7H, d, C1—H), 5.72 ~ 6.60 (14H, m, C2—OH, C3—OH), 6.23 ~ 6.67(2H, d, J = 7.3Hz, Ph—H), 7.09 ~ 7.12 (2H, d, J = 7.2Hz, Ph—H), 7.45 ~ 7.47(2H, d, J = 8.0Hz, Ph-H), 7.64 ~ 7.72 (2H, q, J = 12Hz, —C=CH), 8.08 ~ 8.10 (2H, d, J = 8.0Hz, Ph-H); Anal. Calcd. for: $C_{65}H_{99}O_{37}N_3.H_2O$: C, 50.91; H, 6.60; N, 2.74. Found: C, 50.68; H, 6.54; N, 2.73.

Downloaded At: 15:29 29 January 2011

Fluorescence and UV Measurements

Fluorescence and UV spectra were measured by using a Hitachi MPF-4 Fluorescence and a Hitachi 300 spectrophotometers in a 1×1 cm quartz cell, respectively. The stock solutions of 5×10^{-4} mol.dm^{-3} of compound **6** (DMAC–CD) and **2** (DMAC) and 5×10^{-3} mol.dm^{-3} of β-CD were prepared in methanol, respectively. The experimental solutions of DMAC and DMAC–CD in mixed solvents were prepared by following procedure. Adding 1 mL of the stock solution of DMAC to each 10-mL flask and removing methanol in vacuo, each alcohol was added into the flask directly to give the solutions which were $0 \sim 100\%$ by volume in alcohols upon dilution to the mark with deionized water. The final concentration of fluorescence samples is at 5×10^{-5} mol.dm^{-3}. Each sample was shaken for 20 min with a KQ-50B ultrasonic shaker and allowed to equilibrate overnight.

RESULTS AND DISCUSSION

Studies of Self-inclusion Behavior and Recognition Mechanism of DMAC–CD

It is well known that the photophysical behaviors of the intra-molecular charge transfer (ICT) compounds in excited states strongly depends on the polarity of the environment surrounded [12, 15]. Among these compounds, the N,N-dimethylaminochalcone (DMAC) derivatives appear to be particularly susceptible to change the intensity of the fluorescence emission with the polarity of the solvent used, for instance, the fluorescence of this compound is very weak in water. In addition, the peak wavelength in the fluorescence spectrum of this compound will shift obviously to red, if the solvent polarity increases [12, 13]. So, this compound can be used as a suitable probe molecule for detecting the property of different environments. Figure 1 shows the fluorescence spectra of compound

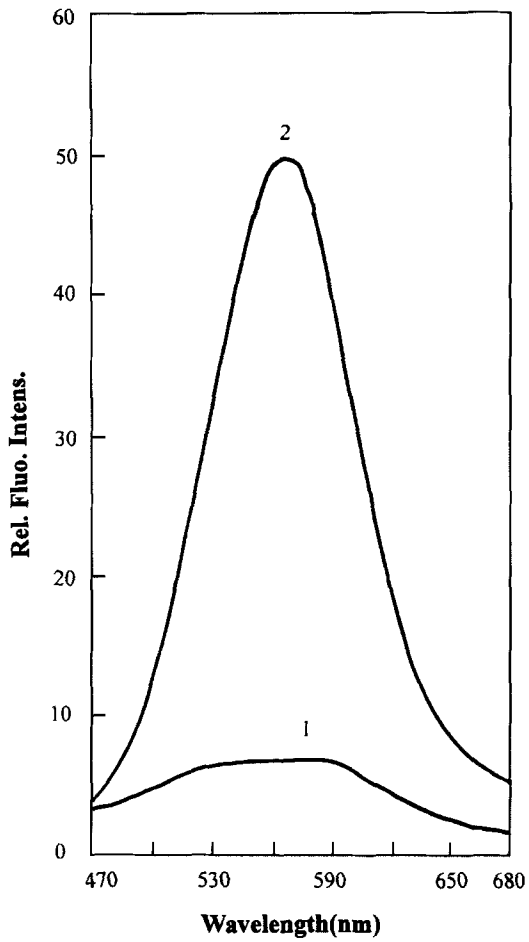


FIGURE 1 The fluorescence emission spectra of DMAC (1) and DMAC–CD (2) in the aqueous solution at pH = 7.0: excitation wavelength(λ_{ex}) was 435 nm. Each concentration was 5×10^{-5} mol · dm^{-3}.

DMAC–CD, DMAC, and DMAC mixed with β-CD (1:10, DMAC + CD) in aqueous solution. The fluorescence intensity of the DMAC–CD is much higher than that of the reference compound DMAC, and its peak wavelength is blue shift from 580 nm to 560 nm, similar as DMAC + CD system. This result demonstrates evidently that the chalcone moiety of DMAC–CD is located inside of the CD cavity and to form an intra-molecular complex (self-inclusion) due to the hydrophobic interaction. The fluorescence spectra of DMAC–CD in different organic solvents were examined too.

Downloaded At: 15:29 29 January 2011

In Figure 2, it can be found that the fluorescence peak wavelength (λ_{em}) is correlated linearly with the polarity parameter [E_t (30)] [16,17] of the media used. This result is well consistent with the fluorescence character of DMAC in same condition, suggesting that the chalcone moiety of DMAC–CD is located at the outside of CD cavity in organic solvents. The fluorescence intensities of DMAC–CD in various organic solvents, as shown in Figure 3, exhibit evidently "positive solvato-kinetic effect" [18],

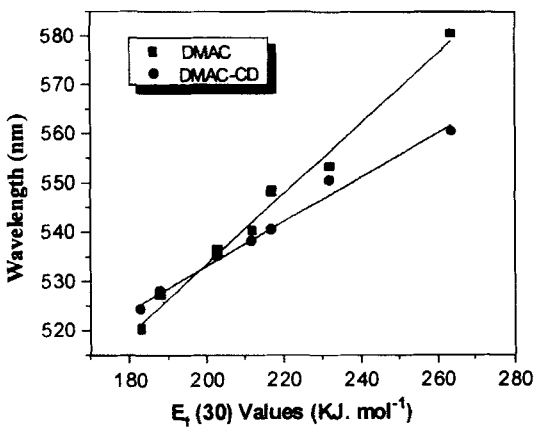


FIGURE 2 The change of fluorescence peak wavelength (λ_{em}(max.)) of compounds DMAC and DMAC–CD with the E_t (30) values function.

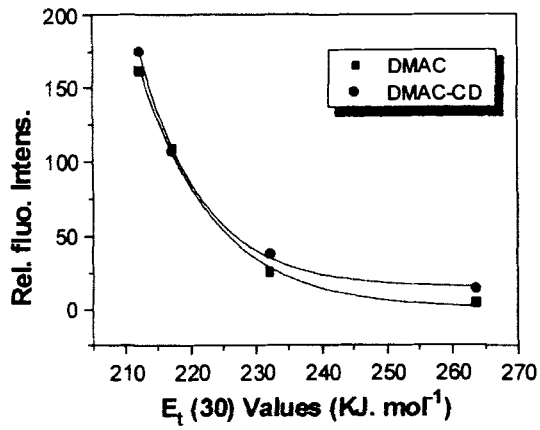


FIGURE 3 The change of fluorescence intensities (Rel. Fluo. Intens., I_f) of compounds DMAC and DMAC–CD at λ_{em}(max.) with the E_t (30) values function.

which is the fluorescence intensity increases with the decreasing of the polarity of solvent. These results give another evidence that the DMAC moiety of DMAC–CD was excluded from CD cavity in pure alcohols, resulting in same fluorescence behavior as that of DMAC.

Nelson *et al.* [19] have gathered more evidence for the formation of ternary complexes(CD/PAH/alcohol). Warner *et al.* [20] have also investigated the influence of various straight-chain and branched molecule of alcohols upon the β-CD/acridine complex and confirmed the existence of ternary inclusion complexes from β-CD. However, with regard to the multi-component complex of chemical modified CD, to the best of our knowledge, it has been not noted clearly in the literature so far. In the present studies, the addition of 1-ACA into the aqueous solution of DMAC–CD results in a decrease of emission intensity and a red shift of peak wavelength in fluorescence spectrum (from 560 to 580 nm). This demonstrates clearly that the DMAC moiety included in the cavity is excluded from the CD cavity to the bulk water environment with guest accommodation. But upon addition of STAC, a remarkable increase in the emission intensity of DMAC–CD was observed. To further confirm this phenomenon that was not from the micelle solubilization, the following experiment was done. In a mixed solution of modified CD and STAC, a certain amount of 1-ACA was added with ratio (host 5: 1-ACA = 1:40). The experiment showed that the fluorescence of the system decreases. It is just the formation of ternary complex that results in the increasing of the emission intensity when the hydrophobic alkyl chain of STAC molecule inserts into the cavity of CD causing an alteration of the polarity CD inner cavity. Hence, there are two different kinds of molecular recognition mode existing in here, and they are strongly depended on the shapes and dimensions of the guests. One of them is "in-out" mechanism and the other one is the "co-inclusion" mechanism. For "large dimension molecule", such as 1-ACA,

Downloaded At: 15:29 29 January 2011

there exists a "in-out" movement of appended chalcone group for inclusion of the guest in CD cavity, so the interaction of host with guest is governed by the "in-out" mechanism. For long linear-chained molecule, such as STAC, it can insert into the CD cavity, as a spacer, to form ternary inclusion complexes with β-CD and the chalcone moieties. Obviously, the "co-inclusion" mechanism plays an important rule in here. The method of "continuous variation" [21] has been employed as a means of verifying the stoichiometry of CD/guest associations. But this method is not suitable to our case of the DMAC–CD system associating with guest. This is attributed the two of following facts. One is the lower solubility of guest such as 1-ACA in aqueous solution. Another is the case of highest concentration of guest such as STAC, which may form a micelle system resulting in an additional enhancement in fluorescence intensity. Another method to determine the stoichiometry of the association is the "Benesi-Hildebrand plots" method [20,22]. The basement of this method is that, to promise a 1:1 stoichiometry of DMAC–CD/guest association, Benesi-Hildebrand plots of the fluorescence data should result in linear relationship and be well consistent to following equation.

$$1/(I_f - I_0) = 1/(c[H]_0) + 1/(cK_b[H]_0) \cdot 1/[G]_t$$

in which I_0, I_f is the emission intensity in absence and presence of guest, K_b is the binding constant of host with guest, and $[H]_0$, $[G]_t$ are the total amount of host and guest, respectively. And c is instrument constant. As shown in Figure 4, the plots of $1/(I_f - I_0)$ as a function of $1/[G]_t$ are well linear relationship for both of 1-ACA (Fig. 4a) and STAC (Fig. 4b), suggesting that the most appropriate model for DMAC–CD and 1-ACA or STAC is 1:1 stoichiometry of the association. It is necessary to emphasize that this stoichiometry(1:1) is based on whole of the host and guest but the "ternary" called here is in an accordance with the each part of complex: CD moiety, chalcone group and guest. The binding constants (K_b) of them are 793 mol^{-1} for 1-ACA and 1270 mol^{-1} for STAC.

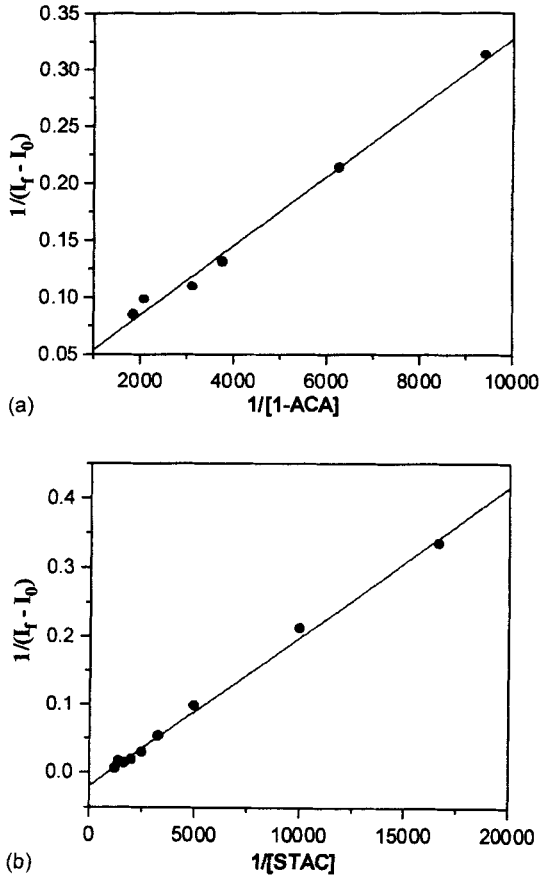


FIGURE 4 Benesi-Hildebrand plots for DMAC–CD host (5×10^{-5} mol · dm^{-3}) in 0.1 mol · dm^{-3} KH_2PO_4 buffer at pH = 7.0 (25°C) depicting with (a) 1:1 DMAC–CD/1-ACA and (b) 1:1 DMAC–CD/STAC stoichiometric fits. λ_{ex} = 435 nm, λ_{em} = 560 nm.

The Inclusion Behaviors of CD Systems in Alcohol/Water Mixed Solvents

Figure 5a shows the fluorescence peak wavelength (λ_{em}) of the above-mentioned three systems as a function of different percentages of methanol/water mixed solvents. It can be seen that the λ_{em} of DMAC in absence of β-CD is blue shift (from 580 nm to 560 nm) linear-likely with the increasing of methanol percentages in

Downloaded At: 15:29 29 January 2011

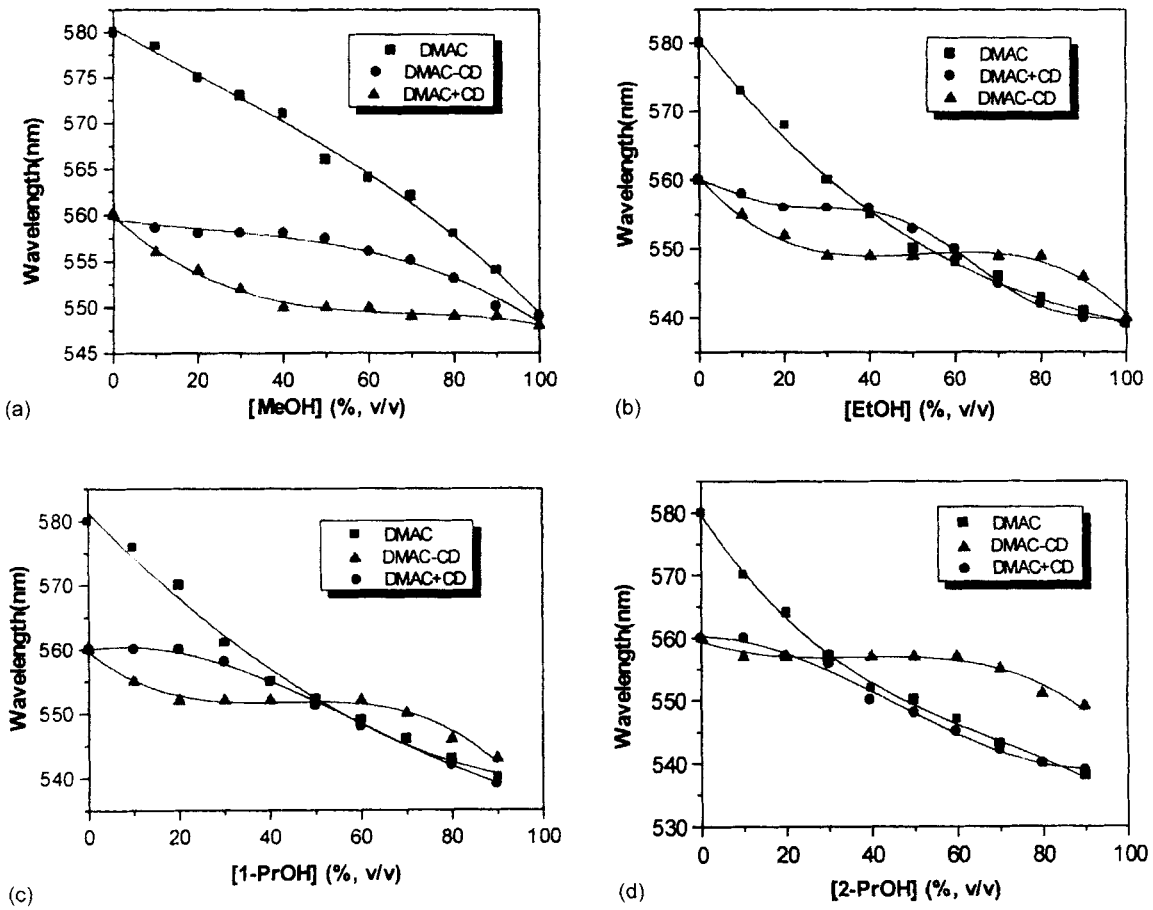


FIGURE 5 Fluorescence peak wavelength (λ_{em}(max.)) of DMAC, DMAC with β-CD (DMAC + CD, with the molar ratio DMAC : CD = 1 : 10), and DMAC–CD system as a function of alcohol content in aqueous solution (%, v/v): a, MeOH, b, EtOH, c, 1-PrOH, d,2-PrOH. Each concentration of DMAC with and without CD, and DMAC–CD was 4×10 mol · dm^{-3} · λ_{ex} was set at each maximum absorption wavelength.

aqueous solution, consistent with the decreasing in polarity of bulk mixed solvents. As for DMAC added CD system, the λ_{em} (560 nm) is much shorter than that of DMAC (580 nm) in fully aqueous solution, owing to the hydrophobic driving force to make the DMAC located at the inside of the β-CD. Then, a little blue shift plateau occurs with the increasing of the content of methanol in aqueous solution until 50%(v/v) methanol/water mixture arrived, after that the further blue shift appeared again with increasing of the percentage of methanol till 100%. But for the DMAC–CD system, a fully different result is observed. The λ_{em} of this system is blue shift continuously with increasing of the methanol until 40%(v/v) methanol contained and does not vary if further increasing concentration of methanol in solvent, as shown in Figure 5a. All of these results suggest that the formation and dissociation of inclusion complex between β-CD and DMAC are influenced or controlled by the hydrophobic driving force of bulk mixed solvents. At lower concentration of methanol, as the methanol does not significantly alter the bulk solvent hydrophobicity, the methanol molecule can insert into the CD cavity to form a multicomponent complex (CD/DMAC/MeOH$_n$), exhibiting a little blue shift in fluorescence

Downloaded At: 15:29 29 January 2011

spectrum. At 50% (v/v) methanol in water, an "inverse driving force" which is against the original hydrophobic interaction, occurs due to the decreasing of polarity of mixed solvent. This interaction extracts the DMAC molecule into the bulk phase eventually. But for DMAC−CD system, the movement of the chalcone group is limited by the linking chain and the hindrance existing in the narrower rim of the β-CD. So the self-inclusion complex of DMAC−CD shows itself the higher stability in methanol/water mixed solvents than the complexes from the free DMAC with β-CD.

Figure 5b shows the λ_{em} of three systems as a function of ethanol percentage in aqueous solution. The λ_{em} of DMAC−CD, is blue shift with increasing of ethanol content in water at about 0∼30%, and does not vary until the 70% of ethanol is contained, then is blue shift again if further increasing the content of ethanol. As for DMAC+CD system, the included DMAC molecule is extracted from the CD cavity in 40% (v/v) ethanol, similar as the case of methanol. However, an obvious difference was observed from the fluorescence behavior of DMAC−CD in methanol and ethanol, as shown in Figures 5a, 5b. This suggests that the size and polarity of alcohol play a important rule in affecting on the inclusion behavior of chemical modified CD. Since the molecular size of methanol is smaller than that of ethanol, the self-inclusion complex (DMAC−CD) leaves residual "void space" at each CD cavity opening for more methanol molecules to occupy, relative to ethanol. So it results in the average polarity of solvent-like environment of the CD cavity to be approximately that of methanol, exhibiting the same fluorescence behavior as that of DMAC in pure methanol. But for ethanol, the contribution for the changing of polarity of CD cavity by ethanol molecule is obviously less than for methanol owing to the fewer ethanol molecules included within the CD cavity. The others alcohol/water mixed solvents, such as 1-propanol/water and 2-propanol/water, were also examined to influence on inclusion behavior of these CD systems. The plots of λ_{em} of three above system as a function of percentage of 1-propanol/water and 2-propanol/water mixed solvents are presented in Figures 5c, 5d, respectively. The similar variation tendency was obtained, compared with ethanol/water mixed solvents. At lower concentration of alcohol in water, it is obviously favorable to the formation of multi-component complex. But at the higher percentage of alcohol in water, the inclusion complex was destroyed, owing to that the hydrophobic driving force of bulk solvents decreases with increasing the organic content of the aqueous mixture.

The fluorescence intensity (I_f) of above three systems are plotted as a function of alcohol percentage in water in Figure 6. From Figure 6a, the results show that the emission intensity of DMAC in absence of CD increases in whole methanol concentration range, whereas that of DMAC−CD increases between 0∼40% and does not vary from 40 to 100% of methanol. But for the system of DMAC+CD mixture, its fluorescence intensity increases at low methanol concentration, then does not vary (nearly from 30 to 50%), and increases once again if further increasing the methanol concentration. The finial result is that the fluorescence intensities of three different systems are same in 100% methanol. All of these results are well fit with those in Figure 5a, giving another strong evidence to support the suggestion that the self-inclusion complex of chemical modified β-CD has a stronger stability in mixed methanol/water solvents than that of β-CD with free DMAC. It is also interesting to note that the I_f of DMAC−CD system in 50% methanol/water mixed solvent are approximately equal to those in 100% methanol, obviously different relative to the case of DMAC+CD system. This result is probably explained that there is a hydrophobic "capped" area formed at the narrower rim of DMAC−CD. This extended hydrophobic area may be caused to occupied more methanol molecules in, resulting in a less polar environment relative to the CD cavity – approximately

Downloaded At: 15:29 29 January 2011

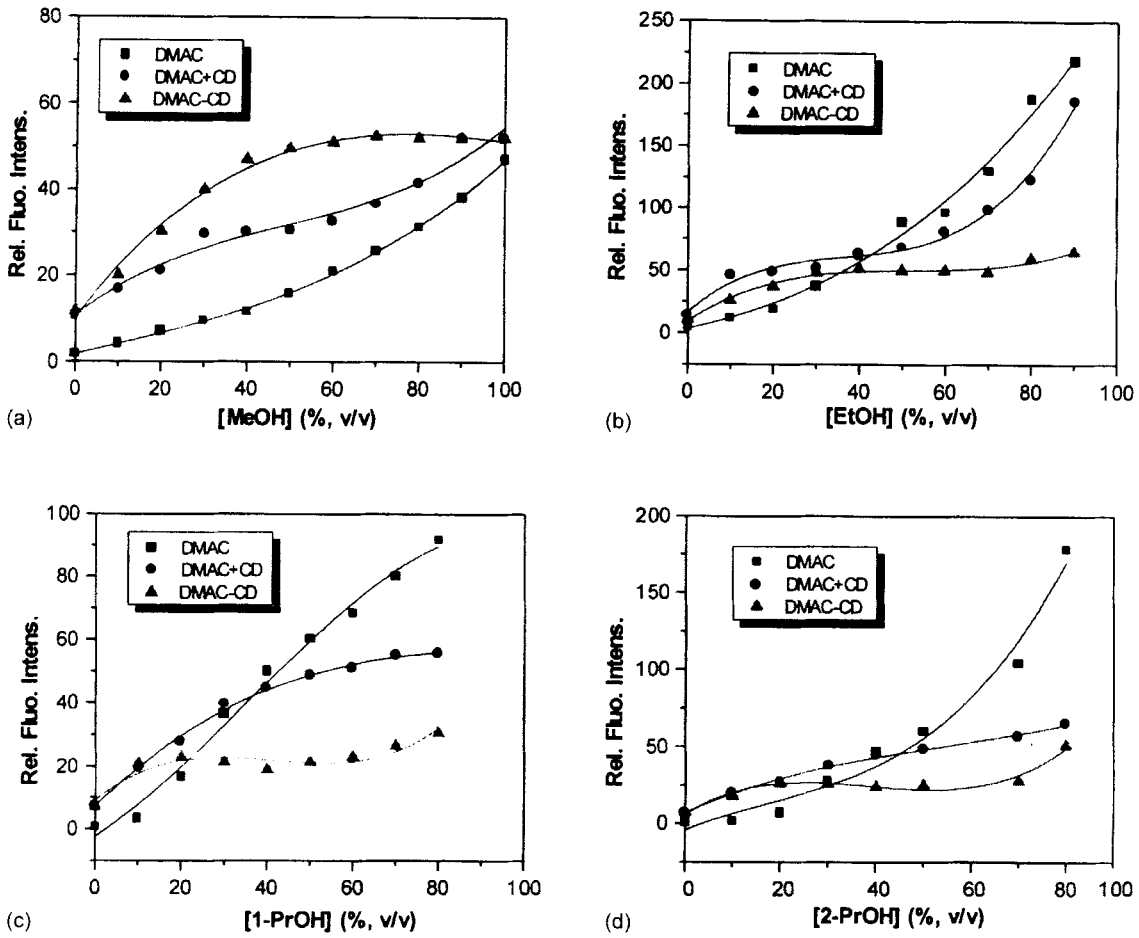


FIGURE 6 Fluorescence intensities (I_f) of DMAC, DMAC with β-CD (DMAC + CD, [DMAC]:[CD] = 1:10), and DMAC–CD system at λ_{em} as a function of alcohol content in aqueous solution (%, v/v): a, MeOH; b, EtOH; c, 1-PrOH; d, 2-PrOH. Other conditions were same as the case of Figure 5.

Downloaded At: 15:29 29 January 2011

equal to the polarity of pure methanol media. Therefore, the chalcone group is located in this situation exhibits similar fluorescence behavior as in pure methanol solvent. The variation of the fluorescence intensity of three systems with alcohol content, such as EtOH (Fig. 6b), 1-PrOH (Fig. 6c) and 2-PrOH (Fig. 6d), were examined too and the results are well consistent with the results from fluorescence wavelength. It is necessary to indicate here that the difference in fluorescence intensity among these systems at higher concentration of alcohol, arises from the reduction in the solubility of DMAC–CD in alcohol.

Five different hypotheses, such as "hydrophobic interaction" [23], "dispersion interaction" [24], "stoichiometic equilibrium" [25], "competitive substrate" [20] and "co-solvents" [9, 26] have been proposed to account for solvent effects on CD complex stability. In present work, the effect of different alcohol/water mixed solvents on the stability of self-inclusion complex formed from chemical modified β-CD and the complex from the non-modified β-CD with chalcone molecule were investigated in detail by fluorescence variation. The interested results are summarized in Table I. It can be seen that, in general, the polarity of CD cavity decreases as

TABLE I Difference of inclusion behavior between DMAC–CD and DMAC + CD systems in alcohol/water mixed solutions

Alcohol /water	Formation of multi-complex [ROH]/(%)[a] A	B	Dissociation of multi-complex [ROH]/(%) A	B	Formation of multi-complex λ_{em} (max)/nm A	B	DMAC in Pure alcohol λ_{em} (max)/nm	$\Delta\lambda$/nm A	B
MeOH	30	40	50	90	558	550	550	8	0
EtOH	10	30	40	70	556	549	540	16	9
l-PrOH	–	20	–	60	557	557	538	19	19
2-PrOH	–	10	–	60	560	552	531	29	21

[a] A = DMAC + CD system; B = DMAC–CD system.

alcohol molecule is included in, resulting in a blue shift in the λ_{em} of chalcone moiety located in CD cavity due to its high sensitivity with the polarity of the surrounded environment. There are two main factors that influence the alcohol molecule accessing to the CD inner cavity. One is the hydrophobicity of alcohol, which increases with increasing the length of alkyl part of alcohol molecule resulting in the longer-chained alcohol such as 1-PrOH to interact more deeply within the cavity. Another is the contribution of the polarity of inner CD cavity by the alcohol molecules that decreases as the quantity of them included increases. This is obviously related to the size of the certain alcohol molecule and the hindrance existing in the entry of CD cavity. The data from Table I indicates that, the difference ($\Delta\lambda$) of λ_{em}, between the systems with CD at the alcohol concentration of which the multi-component complex is formed and the free DMAC in pure alcohol solvent, increases with increasing the size of alcohol molecule. The order is as follows: MeOH < EtOH < 1-PrOH < 2-PrOH. This result is consistent with the suggestion that the contribution of alcohol to polarity of CD cavity is related to the quantity of "co-solvent" molecules included in. On the other hand, from Table I, it also can be seen that the dissociation of the complexes of non-modified CD with free DMAC become easier as the polarity of alcohol decreases – with the order as following: MeOH < EtOH < 1-PrOH < 2-PrOH. So these factors result in the self-inclusion complex of DMAC–CD having a higher stability in mixed alcohol/water solvent, relative to DMAC + CD system.

CONCLUSION

The method described in this work for studying the formation and dissociation of inclusion complexes and the stability of them by regulating the proportion of alcohol/water mixed solvent is most useful for gaining a deep insight into the structure of these inclusion complexes. The self-inclusion and the multi-component inclusion behaviors of the fluorescent sensory system (DMAC–CD) with guest, clearly demonstrate that this system is a very sensitive chemosensor to detect organic guests with different shapes and dimensions. In alcohol/water mixed solvents, the multi-component complexes of this system with different alcohol molecules are formed at lower percentage of alcohol in water but dissociated at higher percentage, about 70%, of them. And the order of the ability to form or dissociate these inclusion complexes for different alcohols is as follows: MeOH < EtOH < 1-PrOH < 2-PrOH. The self-inclusion complex of DMAC–CD in alcohol/water mixed solvents has a higher stability and the ability to accommodate more methanol molecules in its CD cavity than that in the case of non-modified CD. This seems to attribute to the fact that the cavity of DMAC–CD molecule is only one entrance or exit relative to non-modified CD.

Downloaded At: 15:29 29 January 2011

Acknowledgment

We thank the Foundation of National Natural Science in China (Major Project, Grant No. 29733100) for financial support.

References

[1] Bender, M. L. and Komiyama, M., *Cyclodextrin Chemistry*, Springer-Verlag: New York, 1978.
[2] Saenger, W. (1980). *Angew. Chem. Int. Ed. Engl.*, **19**, 344–362.
[3] Easton, C. J. and Lincoln, S. F. (1996). *Chem. Soc. Rev.*, pp. 163–170.
[4] Ueno, A., Minato, S., Suzuki, I., Fukushima, M., Ohkubo, M., Osa, T., Hamada, F. and Murai, K. (1990). *Chem. Lett.*, pp. 605–608.
[5] Wang, Y., Ikeda, T., Ikeda, H., Ueno, A. and Toda, F. (1994). *Bull. Chem. Soc. Jpn.*, **67**, 1598–1607.
[6] Corradini, R., Dossena, A., Marchelli, R., Panagia, A., Sartor, G., Saviano, M., Lombardi, A. and Pavone, V. (1996). *Chem. Eur. J.*, **2**, 373–381.
[7] Corradini, R., Dossena, A., Galaverna, G., Marchelli, R., Panagia, A. and Sartor, G. (1997). *J. Org. Chem.*, **62**, 6283–6289.
[8] Ikeda, H., Nakamura, M., Ise, N., Oguma, N., Nakamura, A., Ikeda, T. Toda, F. and Ueno, A (1996). *J. Am. Chem. Soc.*, **118**, 10980–10988.
[9] Kenneth, A. C. (1997). *Chem. Rev.*, **97**, 1325–1357.
[10] Siegel, B. and Breslow, R. (1975). *J. Am. Chem. Soc.*, **97**, 6869–6870.
[11] Harada, A. and Takahashi, S. (1984). *Chem. Lett.*, 2089–2090.
[12] Wang, P. F. and Wu, S. K. (1994). *J. Photochem. Photobio. A: Chem.*, **77**, 127–131.
[13] Wang, P. F. and Wu, S. K. (1994). *J Luminescence*, **62**, 33–39.
[14] Petter, R. C., Salek, J. F., Sikorski, C. T., Kumaravel, G. and Lin, F. T. (1990). *J. Am. Chem. Soc.*, **112**, 3860–3868.
[15] Buncel, E. and Rajagopal, S. (1990). *Acc. Chem. Res.*, **23**, 226–231.
[16] Reichdt, C. (1979). *Angew. Chem. Int. Ed. Engl.*, **18**, 98–110.
[17] Marcus, Y. (1993). *Chem. Soc. Rev.*, pp. 409–416.
[18] Siebbrand, W. and Zgiershi, M. Z. (1980). *J. Chem. Phys.*, **72**, 1641–1646.
[19] Nelson, G., Patonay, G. and Warner, I. (1988). *M. Anal. Chem.*, **60**,274–279.
[20] Schuette, J. M., Ndou, T. T. Munoz de la, P. A., Mukundan, S. J. and Warner, J. (1993). *Am. Chem. Soc.*, **115**, 292–298.
[21] Munoz de la Pena, A., Ndou, T. T., Zung, J. B., Greene, K. L., Live, D. H. and Warner, I. M. (1991). *J. Am. Chem. Soc.*, **113**, 1572–1577.
[22] Schuette, J. M., Ndou, T. T., Munoz de la, P. A., Greene, K. L., Williamson, C. K. and Warner, I. M. (1991). *J. Phys. Chem.* **95**, 4897–4902.
[23] Okubo, T., Kitano, H. and Ise, N. (1976). *J. Phys. Chem.*, **80**, 2661–2664.
[24] Eftink, M. R. and Harrison, J. C. (1981). *Bioorg. Chem.*, **10**, 388.
[25] Irwin, P. L., King, G. and Hicks, K. B. (1996). *Carbohydr Res.*, **282**, 65.
[26] Bergmark, W. R., Davis, A., York, C., Macintosh, A. and Jones, G. (1990). *J. Phys. Chem.*, **94**, 5020–5022.

Downloaded At: 15:29 29 January 2011