

Unusual twisted intramolecular charge transfer processes of 4,4'-diaminodiphenylsulfone in β -cyclodextrin: a study by electronic spectra

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Analysis of the absorption and fluorescence characteristics of 4,4'-diaminodiphenylsulfone (4DADPS) in aqueous β -cyclodextrin (β -CDx) solution under different acidic conditions reveals that: (i) the twisted intramolecular charge transfer state (TICT) is more populated than the locally excited (LE) state of 4DADPS in β -CDx; and (ii) the protonation of the monocation of 4DADPS in the S_0 and S_1 states in β -CDx requires more acidic conditions than in the absence of β -CDx. The higher stabilisation of the TICT state compared to the LE state of 4DADPS in β -CDx inclusion complex is contrary to normal observation. This anomalous behaviour is explained by the geometry of the 1: 1 inclusion complex.

Keywords: 4,4'-diaminodiphenylsulfone, β -cyclodextrin, twisted intramolecular charge transfer, excited state acidity constants, photoprototropism.

Although 4,4'-diaminodiphenylsulfone(4DADPS) is well-known as an anti-leprosy and an antimalarial drug^{1,2} (named DAPSONE), recently it has been found to possess an added application as a safe and effective alternative to cotrimoxazole or pentamidine for prophylaxis for pneumocystis carinii pneumonia (PCP) in HIV-positive patients.^{3–5} For the detection and quantification of this pharmaceutically important drug, several analytical techniques have been employed.^{6–8}

4DADPS shows dual fluorescence in polar solvents and this is due to the TICT state of 4DADPS.⁹ Recently photophysical properties of molecules showing TICT behaviour have been studied in cyclodextrin–water environments.^{10,11} Cyclodextrins are cyclic oligosaccharides consisting of 6, 7 or 8 D(+)-glycopyranose units and they can form inclusion complexes with molecules of appropriate size. The fluorescence characteristics of TICT molecules are very sensitive to their environment. The changes observed in TICT and normal fluorescence bands depend upon the microenvironment provided by CDx to the guest molecule after encapsulation. The fluorescence enhancement of 4DADPS due to formation of a 1: 1 supramolecular complex with β -CDx in the presence of linear alcohols has been reported.¹² Its emission characteristics, prototropic behaviour and the structure of the complex have not been investigated in detail. The luminescence and the photoprototropic characteristics of 4DADPS in water have been reported from our laboratory.¹³ Recently we have investigated the inclusion complexation of some amino substituted biphenyls, fluorenes and sulfones in β -cyclodextrin.¹⁴ We now report the spectroscopic and photoprototropic characteristics of the 4DADPS- β -CDx inclusion complex and its structure.

Experimental

4,4'-Diaminodiphenylsulfone (Aldrich) and β -CDx (S.D. Fine chemicals) were used as received. The absorption spectra were

measured on a JASCO model 7800 spectrophotometer. Fluorescence spectra were recorded on a JASCO FP-770 spectrofluorimeter. Fluorescence lifetimes were determined using a time-correlated picosecond single photon counting spectrofluorimeter (Tsunami, Spectraphysics, USA). pH Values in the range of 2–6 were measured on an ELICO pH metre model LI-10T. A modified Hammett's acidity scale¹⁵ (using a H_2SO_4 – H_2O mixture) was used for making solutions below pH 1.5. The isosbestic wavelengths were used for measuring the fluorescence intensities for fluorimetric titration at any analytical wavelength.

Results and discussion

The absorption spectroscopic data of 4DADPS with various concentrations of β -CDx are compiled in Table 1.

The absorption maximum at 290.8 nm is red-shifted to 295.4 nm in 4.0×10^{-4} M β -CDx solution. Further increase in the concentration of β -CDx does not affect the maximum and the molar absorptivity significantly. A clear isosbestic point is observed at 292 nm. This may be due to the equilibrium between the free and the β -cyclodextrin-complexed forms of 4DADPS.

The fluorescence spectrum of 4DADPS is more sensitive than the absorption spectrum when β -CDx is added to aqueous solution. The fluorescence spectra of 4DADPS without and with β -CDx are shown in Fig. 1 and the spectral maxima are given in Table 1. There are two emission maxima, one at 346 nm and another at 440 nm for 4DADPS in aqueous solution. 4DADPS is reported to show dual fluorescence in polar solvents due to the formation of the TICT state.⁹ The shorter wavelength emission is from the locally excited state (LE) and the longer wavelength emission is from the TICT state. The fluorescence emission from the TICT state is more intense than that from the LE state. On addition of β -CDx, the fluorescence intensities of both the emissions increase but the increase in the longer wavelength emission is much more than the increase in fluorescence intensity of the shorter wavelength emission. So the fluorescence

Table 1 Absorption and fluorescence spectral data of 4DADPS

Concentration of β -CDx/M	Absorption maximum $\lambda_{abs}/$ nm (log ϵ)	Fluorescence maximum $\lambda_{flu}/$ nm (Excitation wavelength = 260 nm)
0	256.6 (4.45), 290.8 (4.67)	346, 440
4.0×10^{-4}	258.6 (4.45), 295.4 (4.67)	432
8.0×10^{-4}	258.8 (4.41), 295.6 (4.66)	432
1.2×10^{-3}	259.0 (4.41), 295.6 (4.66)	432
1.6×10^{-3}	259.4 (4.40), 296.6 (4.64)	432
2.0×10^{-3}	260 (4.40), 297 (4.64)	432

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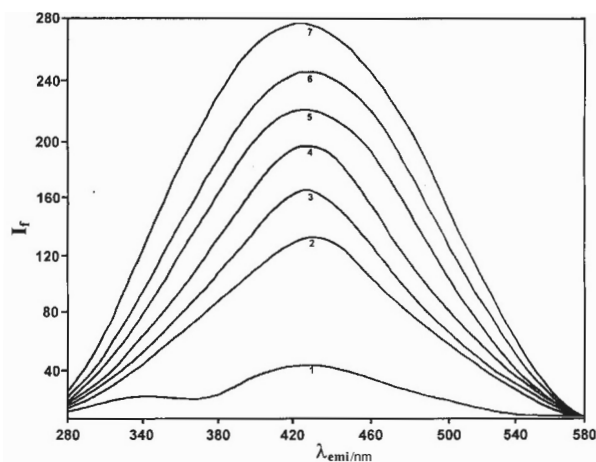


Fig. 1 Fluorescence emission spectra of 4DADPS at different concentrations of β -CDx (at pH 8). 1, 0 M β -CDx; 2, 2.0×10^{-4} M β -CDx; 3, 4.0×10^{-3} M β -CDx; 4, 8.0×10^{-3} M β -CDx; 5, 1.2×10^{-3} M β -CDx; 6, 1.6×10^{-3} M β -CDx; 7, 2.0×10^{-3} M β -CDx.

emission from the LE state is submerged in the broad absorption and could not be observed in the presence of β -CDx. A small blue shift is noticed in the TICT emission. Both the emissions coalesce to give a broad and intense fluorescence spectrum with β -CDx. The increase in intensity of the fluorescence at longer wavelength maximum is shown in Fig. 2. The blue shift and increase in intensity of the emission indicate the inclusion of 4DADPS in the hydrophobic cavity of β -CDx. Further, the larger increase in the longer wavelength emission indicates that the TICT state is more populated in the presence of β -CDx. The binding constant for the equilibrium between the free and the complexed forms of β -CDx using the Benesi-Hildebrand equation can be determined using the absorption and the fluorescence spectroscopic data. Since the change in absorbance is much less, the fluorescence data are preferred. The following Benesi-Hildebrand equation for the 1:1 inclusion complex was used for determination of the binding constant.

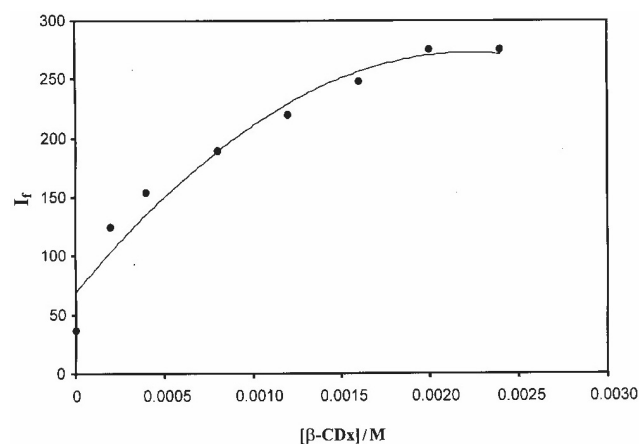


Fig. 2 Fluorescence intensities of 4DADPS at 440 nm with various concentrations of β -CDx at pH 8.

Table 2 Fluorescence lifetime data for 4DADPS

Excitation wavelength = 280 nm, detection wavelength = 443 nm

Concentration of β -CDx/M	Lifetime/s	Amplitude	χ^2	Standard deviation/s
0	1.02×10^{-10}	100	1.17	5.10×10^{-11}
8.0×10^{-4}	8.38×10^{-10}	100	0.96	2.89×10^{-11}
1.6×10^{-3}	8.66×10^{-10}	100	0.98	2.99×10^{-11}
2.4×10^{-3}	9.13×10^{-10}	100	1.21	2.67×10^{-11}

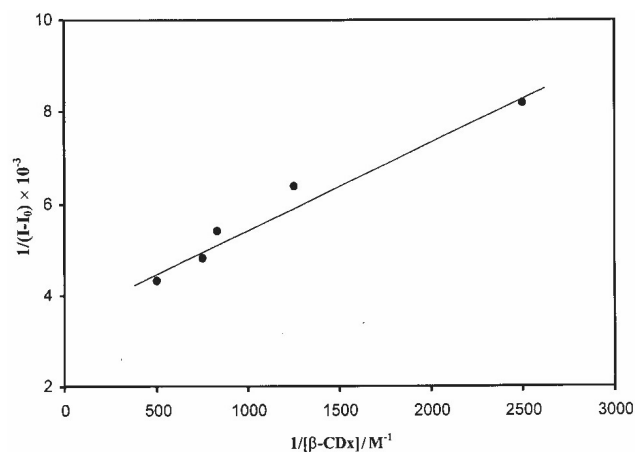


Fig. 3 Benesi-Hildebrand plot for 1:1 complexation of 4DADPS with β -CDx.

$$\frac{1}{I-I_0} = \frac{1}{I'-I_0} + \frac{1}{(I'-I_0)K[\beta\text{-CDx}]}$$

where I_0 and I' are the intensities of fluorescence of 4DADPS without CDx and with 2.0×10^{-3} M β -CDx respectively. I is the intensity of fluorescence at each concentration of β -CDx, and K is the binding constant. The linearity of the plot of $\frac{1}{I-I_0}$ vs $\frac{1}{[\beta\text{-CDx}]}$ (Fig. 3) suggests the formation of a 1:1 inclusion complex between 4DADPS and β -CDx. The binding constant K is calculated to be $1.5 \times 10^3 \text{ M}^{-1}$.

The fluorescence lifetime data for 4DADPS without and with β -CDx are compiled in Table 2.

The lifetime of the neutral species of 4DADPS increases with increase in concentration of β -CDx. This is due to the complexation of 4DADPS in β -CDx. The lifetime of the complexed form is more than that of free 4DADPS. This may be due to the restricted vibrational relaxation of 4DADPS in the complexed form.

Effect of acidity

The absorption and fluorescence characteristics of 4DADPS have been studied in the H_0 /pH range of -2.5 to 8.0 in 0.002 M β -CDx solution. The absorption spectra of different prototropic species are shown in Fig. 4.

The absorption maxima of the neutral form at pH 8 are 297 and 260 nm. Decrease of pH below 3 shows a blue shift in the longer wavelength maximum due to the formation of the monocation. At pH 1.5 the absorption spectrum with the maxima at 259.8 nm and 292.6 nm are due to the formation of the monocation. The shifts as well as the change in optical density are not large. Further decrease of pH below 1 results in decrease in absorption at 292.6 nm and 260 nm and a new absorption maximum appears around 235 nm at $H_0 + 0.44$. There is no proper isosbestic point in the pH range of 2.5 to 1.0. The new absorption spectrum with the maximum at 235 nm resembles the absorption spectrum of diphenylsulfone (DPS).

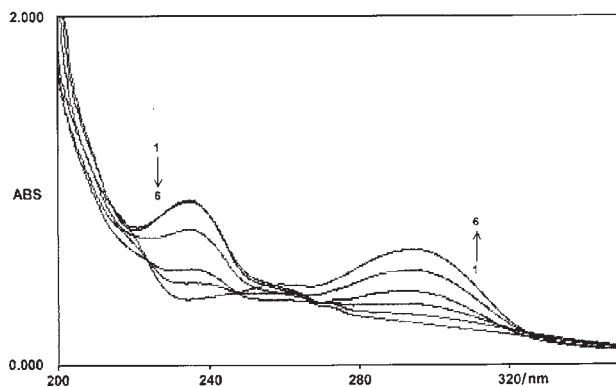


Fig. 4 Absorption spectra of 4DADPS with β -CDx at different H_0 /pH values: 1, H_0 -1.12; 2, H_0 -0.56; 3, H_0 -0.26; 4, H_0 + 0.44; 5, H_0 + 0.83; 6, pH 1.0.

So this is due to the formation of the dication. There are two isosbestic points one at 247nm and the other at 267nm. This shows the presence of two equilibria in this pH range of 1.0 to -1.12. The presence of an isosbestic point at 267nm in the pH range of -1.12 to + 0.44 is due to the equilibrium between the dication and the monocation. The ground state pK_a for this equilibrium was determined using the following equation.

$$pK_a = pH + \log C_1/C_2; \text{ 1-dication species, 2-monocation species}$$

The value is found to be -0.3 ± 0.02 . In aqueous solution the pK_a values reported for monocation-neutral and dication-monocation equilibria are 1.97 and 0.52 respectively.¹³ The spectroscopic changes due to monocation formation are not significant in β -CDx solution. Hence we could not determine the pK_a for the monocation-neutral equilibrium in β -CDx. The pK_a value of -0.3 ± 0.02 is for the dication monocation equilibrium. This value is less than the value of 0.52 reported for the same equilibrium in aqueous solution. This reveals that higher acidity is required for the protonation of the monocation in β -CDx solution.

The fluorescence spectra of 4DADPS with various H_0 /pH values are given in Fig. 5. The fluorescence intensity at 430 nm decreases on decrease of pH from 2.5. At pH 0.5 the blue shift in the maximum is less. When the H_0 value is -0.26 there are two fluorescence maxima one at 390 nm and the other at 295 nm. With further increase of acidity a simultaneous

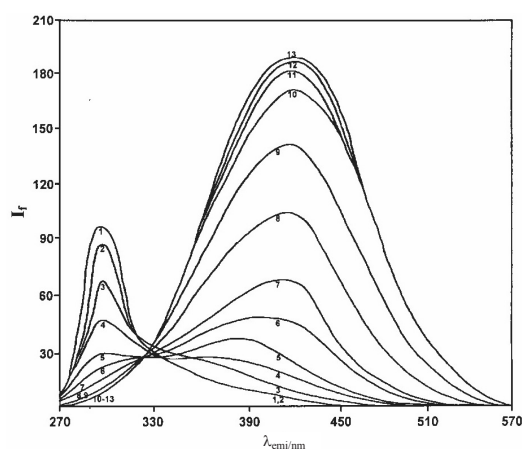


Fig. 5 Fluorescence spectra of 4DADPS with β -CDx at different H_0 /pH values: 1, H_0 -2.06 \times 5; 2, H_0 -1.62 \times 5; 3, H_0 -1.12 \times 5; 4, H_0 -0.56 \times 5; 5, H_0 -0.26 \times 5; 6, H_0 + 0.13 \times 5; 7, H_0 + 0.44 \times 5; 8, H_0 + 0.83 \times 5; 9, pH 1.00; 10, pH 1.36; 11, pH 1.75; 12, pH 2.15; 13, pH 2.50.

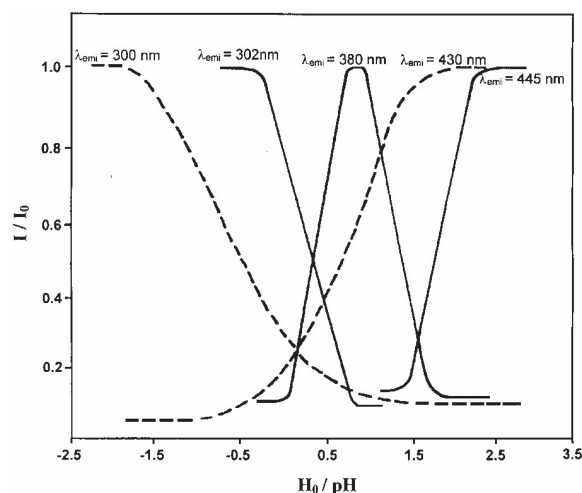


Fig. 6 Fluorimetric titration curves for 4DADPS without and with β -CDx —without β -CDx, --- with β -CDx.

decrease in the intensity of fluorescence at 390 nm and an increase in intensity at 295 nm occur. The fluorescence spectrum with the maximum at 390 nm is due to the formation of the monocation as it is similar to the monocation fluorescence reported in aqueous solution. The fluorescence spectrum with the maximum at 295 nm resembles the fluorescence of DPS and is due to the formation of the dication. The intensity of fluorescence of the monocation is much less than the neutral form. The fluorimetric titrations were carried out and FT curves are shown in Fig. 6. Since the fluorescence intensity of the monocation is less and submerged in the fluorescence spectrum of the neutral form, the fluorescence intensity at 390 nm could not be monitored. Hence the decrease of fluorescence intensity at 430 nm represents the protonation of the neutral form as well as the monocation. But the increase of fluorescence intensity at 295 nm represents only the formation of dication. So the mid point of this formation curve can be taken as the pK_a^* value for the dication-monocation equilibrium. This value is found to be -0.65. In this case the fluorimetric titration curves do not meet at the centre because the fluorescence intensity of the monocation is much less and cannot be monitored. The fluorescence intensity decrease at 430 nm represents the fluorescence quenching due to the protonation of the neutral form and the monocation. The ground and excited state pK_a values of 4DADPS in aqueous solution with and without β -CDx are given in Table 3.

Though 4DADPS is symmetrical it forms only 1 : 1 inclusion complex as revealed by the Benesi-Hildebrand plot and this is also confirmed by lifetime measurements. In 4DADPS, the two aromatic moieties are close to each other. As reported earlier for linear alcohols¹² the formation of 1 : 2 complex is prevented by the steric hindrance produced by the first β -CDx molecule in the 1 : 1 complex. In β -CDx solution,

Table 3 Ground and excited state pK_a values of 4DADPS

Equilibrium	Ground state pK_a	Excited state pK_a
Monocation \rightleftharpoons Neutral		
Without CDx	1.97	1.50
With β -CDx	—	—
Dication \rightleftharpoons Monocation		
Without CDx	0.52	-0.30
With β -CDx	-0.30	-0.65

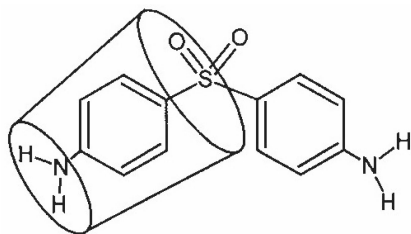


Fig. 7 Schematic diagram of the inclusion complex (1:1) of 4DADPS with β -CDx.

one of the amino groups of 4DADPS is in an aqueous environment and gets protonated immediately. As discussed earlier, the ground and excited state pK_a values for neutral–monocation equilibrium could not be determined. The ground and excited state pK_a values for dication–monocation equilibrium are less than those in aqueous solution. The decrease in the pK_a values observed for the protonation of the monocation in the S_0 and S_1 states are consistent with the fact that the protonation of the included NH_2 group is hindered by the hydrophobic cavity of β -CDx. This requires more acidic conditions in β -CDx than in aqueous solution.

Fluorimetric behaviour of 4DADPS in β -CDx shows that the population of the TICT state increases in β -CDx. In general, the population of the TICT state decreases in β -CDx as the twisting of a part of the molecule is restricted on inclusion complexation. The abnormal behaviour of 4DADPS in β -CDx is due to the following: (i) in 4DADPS one of the anilino groups is in an aqueous environment, as the TICT occurs there is no restriction for the twisting of this anilino group; and (ii) the other anilino group inside the hydrophobic cavity of β -CDx does not fit tightly as the size of the anilino group is less than the size of the hydrophobic cavity. In the anilino group the distance between H_3 and H_6 is 4.3 Å and

the diameter of NH_2 group is around 1.67 Å.¹⁴ Both distances are small when compared to the cavity diameter of 5.6 Å. The loose fitting of 4DADPS in β -CDx is also supported by a report of the inclusion of the dimethylanilino group in β -CDx.^{16,17} Based on these observations the structure of the 4DADPS- β -CDx complex could be as shown below (Fig. 7).

We thank the University Grants Commission for their financial assistance (Project No. 200.F.49) and to the National Centre for Ultrafast Processes, University of Madras, Chennai for help in taking fluorescence lifetime measurements.

Received 12 October 2005; accepted 2 February 2006
Paper 05/3542

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