4.1. Abstract

Interactions of β-cyclodextrin (β-CD) with a few novel viologen linked acridine conjugates having rigid aromatic \(1a-c\) and flexible methylene \(2a-c\) spacer groups have been investigated through photophysical, chiroptical, electrochemical and atomic force microscopic (AFM) techniques. The dyads with \(para\)-tolyl \(1a\) and biphenyl \(1c\) spacer groups exhibited significantly decreased fluorescence quantum yields and lifetimes when complexed with β-CD, while negligible changes were observed for the \(ortho\)-isomer \(1b\). In contrast, the conjugates \(2a-c\) with flexible spacer units, in the presence of β-CD, showed spacer length dependent significantly increased fluorescence quantum yields and lifetimes. Association constants for the complexes formed between β-CD and various dyads have been calculated and the complexation was confirmed using AM1 calculations, competitive ligand displacement, circular dichroism (CD), cyclic voltammetry (CV), \(^1\)H NMR and AFM techniques. The intramolecular electron transfer rates \(k_{ET}\) have been estimated and are found to increase nearly 2-fold for
Chapter 4: Interactions of viologen linked acridines with β-CD

the dyads with para-tolyl and biphenyl spacer groups when complexed with β–CD, whereas significantly decreased \( k_{ET} \) values (ca. 15-fold) were observed for the dyads with flexible spacer group. These results demonstrate that the complexation of donor-acceptor conjugates having aromatic spacer group, with β–CD unusually leads to planarization of the conjugate resulting in enhanced electron transfer processes between the donor and acceptor moieties, while conformational unfolding of sandwich type of structure occurs in the dyads having flexible spacer groups.

4.2. Introduction

The study of interactions of cyclodextrins (CDs) with drugs and photoactive molecules has been an active area of research in recent years as they mimic the biological environment. Cyclodextrins are cyclic oligosaccharides consisting of six to nine glucose units and are called α–, β–, γ–, and δ–cyclodextrins, respectively. CDs are water soluble and have not only rigid, well-defined torus shape with relatively apolar interior, but also rotational symmetry with an asymmetric environment. These cyclic systems are known to form inclusion complexes with a variety of compounds, ranging from low molecular weight non-polar aliphatic molecules, polar amino acids to high molecular weight polymeric materials, depending on the size of CD cavity and the cross sectional area of the guest molecules. Because of these unique properties, CDs have found wide applications in pharmaceutical industry, catalysis,
separation technology, and recently in the design of biomimetic systems, supramolecular architectures and molecular machines. Moreover, the hydrophobic and spatial control of CD inclusion processes have been extensively exploited for not only using them as drug carriers, in catalysis and separation technology, but also in controlling the reactivity and in understanding the photochemical properties of a variety of functional molecules. Of these systems, the electron donor-acceptor conjugates have attracted great attention, since inclusion of such systems in CDs not only alter the interactions between the donor and acceptor moieties but also results in supramolecular architectures that are useful as molecular machines.

The rate of intramolecular electron transfer \( k_{ET} \) in a donor-acceptor conjugate is dependent on several parameters. These include, free energy change, the distance between the donor and acceptor units, nature and their orientation, and the intervening medium. Of these factors, the distance between the donor and acceptor, which also involves the nature of the spacer group is the most important factor, because of the approximately exponential decrease of the rates with increasing distance. Although the interactions of CDs with donor-acceptor molecules having flexible spacers have been reported, to the best of our knowledge, the systems with sterically bulky and rigid aromatic spacers have received less attention. This Chapter presents our results obtained through investigation of interactions of \( \beta \)-cyclodextrin (\( \beta \)-CD) with a few selected novel donor-acceptor dyads 1a–c and 2a–c (Figure 4.1), which are biologically
important and are efficient in cleaving DNA through the co-sensitization mechanism.\textsuperscript{17} Upon inclusion in $\beta$-CD, we observed reduced $k_{ET}$ for 2a–c with

![Diagram of viologen linked acridine derivatives and $\beta$-cyclodextrin](image)

**Figure 4.1.** Structures of the viologen linked acridine derivatives 1a-c and 2a-c and $\beta$-cyclodextrin ($\beta$-CD) used in the present study.

flexible spacer, negligible changes for 1b with sterically bulky spacer group but surprisingly enhanced $k_{ET}$ for 1a and 1c with rigid aromatic spacer. Results of these investigations demonstrate for the first time that inclusion of the donor-acceptor dyads with the rigid aromatic spacer in $\beta$-CD leads to planarization of the dyad and thereby facilitates an effective interaction between the donor and acceptor moieties present in it.
4.3. Results

4.3.1. Synthesis of a Few Viologen Linked Acridines

Synthesis of the viologen linked tolylacridines 1a and 1b was achieved as shown in Scheme 4.1. The ortho- and para-tolylacridines 3a and 3b, respectively were synthesized by the reaction of diphenylamine with the corresponding toluic acids in presence of anhydrous zinc chloride using a modified Bernthsen procedure.\(^\text{18}\) These derivatives were then converted to the corresponding bromo derivatives 4a (60%) and 4b (56%) by the reaction with N-bromosuccinimide. Finally, the synthesis of the viologen linked tolylacridine derivatives was achieved by the reaction of the corresponding bromotolylacridine derivative with 1-butyl-4,4'-bipyridinium bromide. Thus, for example, the reaction of the bromo derivative 4a with 1-butyl-4,4'-bipyridinium bromide yielded the viologen linked para-tolylacridine 1a in 77% yield.\(^\text{17a}\) Similarly, the reaction of 4b with 1-butyl-4,4'-bipyridinium bromide, gave the viologen linked ortho-tolylacridine derivatives 1b in quantitative yields.
Synthesis of the bromoalkylacridine 7 was achieved by a modified Bernthsen procedure (Scheme 4.2). The condensation reaction of diphenylamine with 4-methyl biphenylcarboxylic acid in presence of anhydrous zinc chloride gave 10% of the acridine derivative 7, which in turn was converted to 8 (54%) by the reaction with N-bromosuccinimide as shown in Scheme 4.2. Reaction of 8 with 1-butyl-4,4'-bipyridinium bromide gave the product, 1c, in 35% yield.
Synthesis of the viologen linked acridine conjugates 2a-c has been achieved as per the Scheme 4.3. $\text{S}_{\text{N}}2$ reaction of 1-butyl-4,4'-bipyridinium bromide with corresponding bromoalkylacridines 9-11 gave the viologen linked acridine conjugates 2a-c, in 65-77% yield.\textsuperscript{17b} All these compounds were purified through recrystallization and characterized on the basis of spectral data and analytical evidence. $^1\text{H}$ NMR spectrum of the viologen linked tolylacridine 1a in DMSO-$d_6$, for example, showed a peak corresponding to the methylene group between the phenyl and viologen moieties at $\delta$ 6.3 as a singlet, while the aromatic protons corresponding to the acridine and viologen moieties appeared as multiplets in the region between $\delta$ 7.5 and $\delta$ 9.85. In the case of the viologen linked ortho-tolyl derivative 1b, the methylene group between the phenyl and viologen moieties appeared at $\delta$ 5.6. On the other hand, viologen linked acridine 1c showed peak corresponding to the methylene group between biphenyl and acridine moieties at $\delta$ 6.30, whereas aromatic protons corresponding to the acridine, biphenyl and viologen moieties appeared as multiplets in the region between $\delta$ 6.3 and $\delta$ 9.85. In the case of viologen linked acridine 2a, the methylene group appeared at $\delta$ 7.16 as
a singlet, while the aromatic protons corresponding to the viologen and acridine moieties appeared as a multiplet at $\delta$ 7.79-9.37 (16H). $^1$HNMR spectra of 2b and 2c, in addition to the other peaks, showed peaks corresponding to the methylene groups at $\delta$ 4.60-4.90. The $^{13}$C spectrum of 1a showed five sp$^3$ carbons appearing at $\delta$ 13.33, 18.77, 32.70, 60.64, and 63.87 corresponding to the four carbons of n-butyl group and one methylene carbon. The other aromatic carbons appeared in the region between $\delta$ 124.2 and $\delta$ 149.2. The mass spectra of the derivatives 1a-c and 2a-c gave a molecular ion peak in each case corresponding to $M^+ Br^-$, indicating that one of the bromide ions is closely associated with the organic ligand ($M^+$).

4.3.2. Photophysical Properties in Presence of $\beta$-Cyclodextrin

The viologen linked acridine conjugates exhibited high solubility in aqueous medium and obeyed Beer’s law under experimental conditions. We observed no evidence for ground-state charge-transfer interaction between the acridine and viologen moieties present in these compounds under these conditions. Figure 4.2 shows the change in fluorescence spectra of 1a with the increase in addition of $\beta$-CD. Upon increasing $\beta$-CD concentration, the fluorescence emission spectra corresponding to the acridine chromophore showed a significant quenching (ca. 2-fold). Similar observations were made with the dyad 1c containing biphenyl spacer (Figure 4.3). In contrast, with the addition of $\beta$-CD,
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Figure 4.2. Effect of β–CD concentration on the fluorescence spectra of 1a (4.1 × 10⁻⁵ M) and [β–CD] a) 0, (b) 0.68, (c) 1.35, (c) 2.01, (d) 2.67, (e) 3.31, (f) 3.94, (g) 4.57, (h) 5.19, (i) 5.80 and (k) 6.40 mM in water. Inset show the corresponding Benesi–Hildebrand plot.

Negligible changes were observed in the absorption spectra of dyads 1a (Figure 4.4) and also in the absorption (inset of Figure 4.4) and fluorescence spectra of the dyad with ortho-tolyl spacer 1b (Figure 4.5). On the other hand, the donor-acceptor dyads 2a–c, with the flexible spacer groups (methylene units of n = 1, 3 and 11; Figures 4.6-4.8), exhibited spacer–length dependent increase in fluorescence intensity with increase in addition of β–CD. For example, in the case of the viologen linked acridine conjugate 2c, we observed ca. 15-fold enhancement in the fluorescence intensity with increase in concentration of β–CD.
Figure 4.3. Effect of β-CD concentration on the fluorescence spectra of \(1c\) \((9.1 \times 10^{-5} \text{ M})\) and \([\beta\text{-CD}]\) \(0\), \(0.29\), \(0.58\), \(0.87\), \(1.16\), \(1.44\), \(1.73\), and \(2.01 \text{ mM}\) in water. Excitation wavelength 360 nm. Insets show their corresponding Benesi-Hildebrand plots.

Benesi-Hildebrand analysis of the fluorescence changes (inset of Figures 4.2-4.3 and Figures 4.6-4.8), gave a 1:1 stoichiometry for the complexes formed between β-CD and the dyads \(1a, 1c\) and \(2a-c\). The \(1a-\beta\text{-CD}\) complex showed an association constant \((K_{\text{ass}})\) of 239 M\(^{-1}\) and the corresponding change in free energy value of -13.7 kJ M\(^{-1}\) (Table 4.1). In the case of the dyad with biphenyl spacer, \(1c-\beta\text{-CD}\) complex, we observed significantly higher association constant of 325 M\(^{-1}\) and change in free energy of -14.3 kJ M\(^{-1}\). On the other hand, \(2c\) with a flexible spacer length of \(n = 11\), exhibited nearly ca. 124-fold higher association constant \((K_{\text{ass}} = 29600 \text{ M}^{-1}\) and \(\Delta G = -25.7 \text{ kJ M}^{-1}\)), when compared to \(1a\) (Table 4.1).
However, the dyads 2a and 2b showed significantly reduced association constants of 36 and 219 M$^{-1}$, with the corresponding change in free energy of -8.9 and -13.4 kJ M$^{-1}$ respectively, when compared to 2c.

Table 4.1. Association constants ($K_{ass}$), free energy change ($\Delta G$) and fluorescence lifetimes ($\tau$) for the complexes formed between $\beta$–CD and the donor–acceptor conjugates 1a–c and 2a–c.$^a$

<table>
<thead>
<tr>
<th>Compound</th>
<th>$K_{ass}$, M$^{-1}$</th>
<th>$-\Delta G$, kJ M$^{-1}$</th>
<th>$\tau$, ns</th>
<th>$\tau_{\beta$–CD}, ns</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>239 ± 5$^d$</td>
<td>13.7 ± 0.1</td>
<td>5.4 (100 %)</td>
<td>5.4 (69 %)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.9 (31 %)</td>
</tr>
<tr>
<td>1b</td>
<td>Nil</td>
<td>Nil</td>
<td>10.6 (87 %)</td>
<td>e</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.40 (13 %)</td>
<td></td>
</tr>
<tr>
<td>1c</td>
<td>325 ± 6</td>
<td>14.3 ± 0.1</td>
<td>5.7 (100 %)</td>
<td>5.7 (40%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.4 (60%)</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>36 ± 2</td>
<td>8.9 ± 0.1</td>
<td>14.6 (100 %)</td>
<td>15.0 (100 %)</td>
</tr>
<tr>
<td>2b</td>
<td>219 ± 6$^d$</td>
<td>13.4 ± 0.1</td>
<td>13.6 (81 %)</td>
<td>15.5 (82 %)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.80 (19 %)</td>
<td>5.80 (18 %)</td>
</tr>
<tr>
<td>2c</td>
<td>29600 ± 100</td>
<td>25.7 ± 0.4</td>
<td>14.7 (82 %)</td>
<td>15.0 (82 %)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.70 (18 %)</td>
<td>8.30 (18 %)</td>
</tr>
</tbody>
</table>

$^a$ Average of more than two experiments. $^b$ $K_{ass}$ was calculated using Benesi–Hildebrand equation. $^c$ $\Delta G$ for the complexes was calculated using equation $-\Delta G = R T \ln K_{ass}$. $^d$ $^{1}H$ NMR titrations gave $K_{ass} = 337 \pm 9$ and 224 $\pm 12$ M$^{-1}$ for 1a and 2b, respectively. $^{e}$ Negligible changes were observed.

To have a better understanding of fluorescence changes observed in presence of $\beta$–CD, we have analyzed the interaction of $\beta$–CD with the dyads 1a–c and 2a–c by picosecond time–resolved fluorescence technique. As shown in
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Figure 4.4. Effect of β-CD concentration on the absorption spectra of 1a (4.1 × 10⁻⁵ M) in water. [β-CD] (a) 0, (b) 0.68, (c) 1.35, (d) 2.01, (e) 2.67, (f) 3.31, (g) 3.94, (h) 4.57, (i) 5.19, (j) 5.80 and (k) 6.40 mM. Inset shows the effect of β-CD concentration on the absorption spectra of 1b under same conditions.

Figure 4.5. Effect of β-CD concentration on the fluorescence emission spectra of 1b (4.1 × 10⁻⁵ M) in water. [β-CD] (a) 0, (b) 0.68, (c) 1.35, (d) 2.01, (e) 2.67, (f) 3.31, (g) 3.94, (h) 4.57, (i) 5.19, (j) 5.80 and (k) 6.40 mM. Excitation wavelength 360 nm.
Figure 4.6. Effect of β-CD concentration on the fluorescence spectra of 2c (4.1 x 10^-5 M) and [β-CD] (a) 0, (b) 0.02, (e) 0.07, (g) 0.09 mM. Insets show their corresponding Benesi-Hildebrand plots.

Figure 4.7. Effect of β-CD concentration on the fluorescence emission spectra of 2b (1.23 x 10^-6 M) in water. [β-CD] (a) 0, (b) 0.12, (c) 0.38, (d) 0.63, (e) 0.89 and (f) 6.3 mM. Excitation wavelength, 360 nm. Inset shows Benesi-Hildebrand plot for the change in absorption for 2b with increasing concentration of β-CD.
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Figure 4.8. Effect of $\beta$-CD concentration on the fluorescence emission spectra of 2a (1.73 x $10^{-6}$ M) in water. $[\beta$-CD] (a) 0, (b) 0.12, (c) 0.38, (d) 0.63, (e) 0.89 and (f) 6.3 mM. Excitation wavelength, 360 nm. Inset shows Benesi-Hildebrand plot for the change in absorption for 2a with increasing concentration of $\beta$-CD.

Figure 4.9, the para-isomer 1a exhibited monoexponential decay with lifetime of 5.4 ns. In the presence of $\beta$–CD, this dyad showed biexponential decay with lifetimes of 0.9 ns (31%) and 5.4 ns (69%) (Table 4.1). Similar observations were made with the dyad 1c containing the biphenyl spacer group. The dyad 1c, which showed monoexponential decay with lifetime of 5.7 ns, exhibited biexponential decay with lifetimes of 1.4 ns (60%) and 5.7 ns (40%) in the presence of $\beta$–CD. On the other hand, negligible changes were observed in the presence of $\beta$–CD in the case of the ortho–isomer 1b, which showed biexponential decay with the
lifetimes of 10.6 ns and 0.4 ns (inset of Figure 4.9). In contrast, the dyads 2a–c with the flexible spacer groups showed enhancement in lifetimes in the presence of β-CD. For example, the dyad 2a showed monoexponential decay with a lifetime of 14.6 ns, but when complexed with β-CD, it exhibited a marginal enhancement in the lifetime (15 ns). The dyad 2b, on the other hand, exhibited enhanced lifetimes of 15.5 and 5.8 ns in the presence of β-CD, as compared to its

Figure 4.9. Fluorescence decay profiles of 1a (1.23 x 10^-6 M) in water (a) in the absence and (b) in the presence of β-CD. [β-CD] 6.40 mM. Inset shows the effect of β-CD concentration on the fluorescence decay profiles of 1b (1.23 x 10^-6 M) in water (a) in the absence and (b) in the presence of β-CD. [β-CD] 6.40 mM. Excitation and emission wavelengths are 360 and 485 nm, respectively.

lifetimes of 13.6 and 2.8 ns in the absence of β-CD. Similarly, the dyad 2c with a long flexible spacer length of n = 11, showed biexponential decay with lifetimes of
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14.7 and 1.7 ns. In the presence of β–CD, it exhibited significantly enhanced lifetimes of 15.0 and 8.3 ns. As indicated above, of the two lifetimes of the dyads 2b and 2e, only the short lived component exhibited significantly increased lifetimes (Table 4.1) in the presence of β–CD as compared to the long lived major component.

The values of $k_{ET}$ for the electron transfer\textsuperscript{17} for the dyads have been calculated using the fluorescence quantum yields and lifetimes. Unusually, $k_{ET}$ increased from $1.17 \times 10^{10}$ s\textsuperscript{-1} to $2.03 \times 10^{10}$ s\textsuperscript{-1} for the dyad with para–tolyl spacer 1a in the presence of β–CD. Similarly, ca. 2-fold enhancement was observed with the dyad containing biphenyl spacer group. In contrast to the dyads 1a and 1c, the dyad with flexible spacer group such as 2c (n = 11) ($k_{ET} = 0.6 \times 10^{9}$ s\textsuperscript{-1}) exhibited significantly reduced rate of electron transfer by one order, when bound to β–CD ($k_{ET} = 0.4 \times 10^{8}$ s\textsuperscript{-1}). To understand the contrasting behavior of the dyads with flexible and rigid spacer groups in the presence of β–CD, we have investigated the interaction of these dyads with an alternative microenvironment medium such as micelles. Interestingly, irrespective of the nature of spacer group, the viologen linked acridine derivatives showed enhancement in the fluorescence quantum yields in the presence of micelles. For example, 1a with rigid spacer and 2c with flexible spacer unit, exhibited enhancement in the fluorescence quantum yields ca. 16 and 2 fold, respectively (Figure 4.10) in the presence of sodium dodecyl sulphate micelles (SDS) as compared to the aqueous medium.
4.3.3. Characterization of β-Cyclodextrin Inclusion Complexes

Evidence for the interaction of the donor–acceptor dyads 1a, 1c and 2a–c with β-CD and formation of the stable inclusion complexes is obtained through time-resolved fluorescence anisotropy, competitive ligand displacement, \(^{19}\)\(^1\)H NMR, circular dichroism (CD) and cyclic voltammetry (CV) techniques.

**Figure 4.10.** Effect of SDS concentration on the fluorescence emission spectra of 1a (1.21 × 10\(^{-4}\) M) in water. [SDS] (a) 0, (b) 1.09, (c) 2.13, (d) 3.31, (e) 4.55 and (f) 6.57 mM; excitation wavelength 360 nm. Inset shows the effect of SDS concentration on the absorption spectra of 2c. [SDS] (a) 0, (b) 2.13, (c) 4.55 and (d) 6.57 mM; excitation wavelength 360 nm.

Fluorescence anisotropy gives a physical insight into the extent of restriction imposed by the microenvironment on the dynamics of the molecule and thus can
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be exploited for confirming the formation of stable inclusion complexes with β-CD. Figure 4.11 shows the time–resolved anisotropy studies of the para-isomer 1a–β-CD complex. We observed a monoexponential decay with rotational correlation time of 0.37 ns and $r_0$ value of 0.03–0.05. As expected, the ortho-isomer showed no anisotropic behavior under the same conditions, indicating its negligible interactions with β-CD. The calculated value for hydrodynamic radius of the 1:1 complex formed between 1a and β-CD using the rotational correlation time was found to be 7.2 ± 0.5 Å, which corresponds to a diameter of 14.4 ± 0.5 Å, indicating the formation of a tight complex between β-CD and the dyad 1a.

Figure 4.11. Time–resolved fluorescence anisotropy of 1a (1.23 μM) in the presence of β-CD (6.40 mM). Inset shows the circular dichroic (CD) spectra of derivative 1a (3.1 x 10^{-4} M) in the a) absence and b) presence of β–CD (6.40 mM).
having a diameter of 14.9 Å. These observations furthermore rules out the possibility of peripheral binding of β–CD with the dyad 1a, since the diameter obtained from the anisotropy measurements is in good agreement with the theoretically determined diameter for the dyad 1a.

Figure 4.12 shows the revival of the fluorescence intensity of the dyad 1a through ligand displacement technique. The addition of β–CD results in the decrease in fluorescence intensity of 1a followed by saturation at ca. 6.4 mM of β–CD. When AD–COOH, a known β–CD binding agent \( K_{\text{ass}} = 1.14 \times 10^3 \text{ M}^{-1} \),\(^{19} \) was gradually added to this 1a–β–CD complex, we observed the quantitative revival of the fluorescence intensity of 1a, confirming thereby the effective displacement of 1a by AD–COOH from the β–CD cavity. Figure 4.13 shows \(^1\text{H}

![Figure 4.12. Effect of β–CD concentration on emission spectra of 1a (4.1 x 10\(^{-5}\) M) in water. [β–CD] (a) 0, (d) 2.01, (g) 3.94, (k) 6.40 mM, followed by gradual addition of AD–COOH. [AD–COOH] (l) 0.12, (p) 0.61, (r) 0.85, (t) 1.21 mM.](image-url)
Figure 4.13. Effect of β-CD concentration on proton chemical shift of compound 1a (37.2 mM) in water. [β-CD] (a) 0, (b) 0.55, (c) 1.03, (d) 1.45, (e) 1.84, (f) 2.49 mM.

NMR spectra of 1a with the gradual addition of β-CD. In presence of β-CD, the dyad 1a showed significant changes in chemical shift (Δδ = 0.3), for the proton corresponding to the spacer phenyl group. Analysis of the chemical shift changes through Benesi–Hildebrand plot (Figure 4.14) gave an association constant of 337 ± 12 M⁻¹ for 1a, which is relatively higher than the value obtained by fluorescence titrations (Kₐₛₛ = 239 ± 5 M⁻¹). However, the NMR spectrum of the ortho-isomer 1b, as expected showed negligible changes in the presence of β-CD (Figure 4.15).

Electrochemical studies of redox active ligands are highly useful in probing the ligand-β-CD interactions. The complexation of a ligand within host molecule such as β-CD can reduce the mobility of the ligand thereby resulting in the decrease in the intensity of current. Moreover, ligands as such are also expected to
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Figure 4.14. Benesi–Hildebrand plot of change in chemical shift of proton $H_a$ of the dyad 1a (37.2 mM) with increasing in concentration of β-CD in D$_2$O.

Figure 4.15. Effect of β-CD concentration on proton chemical shift of compound 1c (35.6 mM) in water. [β-CD] (a) 0, (b) 2.49 mM.

exhibit significant changes in their redox properties when complexed with β-CD, depending on the nature of interactions involved. In this context, we examined the redox properties of the viologen linked acridines in presence of β-CD to
understand the nature of their complexation. Figure 4.16 shows the cyclic voltammograms of 1a, which exhibited two reversible one-electron reduction processes centered at \(-0.44\) and \(-0.73\) V, characteristic of the viologen moiety.\(^{21}\) With increase in addition of \(\beta\)-CD, we observed an increase in the reduction potentials by 66 and 10 mV, along with a decrease in current intensity of 35.7 \(\mu\)A (71\%) and 15.7 \(\mu\)A (61\%), respectively. The viologen linked acridine derivative 2b, on the other hand, is found to have one reversible one-electron reduction process centered at \(-0.54\) V.\(^{22}\) When \(\beta\)-CD was added, we observed a decrease in the reduction potentials by 38 mV (inset of Figure 4.16), along with a significant

**Figure 4.16.** Cyclic voltammograms of 1a (0.24 mM) in 24 mM NaCl with increasing concentrations of \(\beta\)-CD a) 0, b) 0.045, c) 0.09 and d) 0.18 mM. Scan rate, 100 mV/s. Inset shows cyclic voltammograms of 2b (0.17 mM) in 17 mM NaCl with increasing concentrations of \(\beta\)-CD a) 0, b) 0.09 and c) 0.18 mM. Scan rate, 100 mV/s.
decrease in current intensity of 6 µA (39%). These results indicate the formation of stable complexes between the dyads and β-CD and the importance of the spacer group on the current intensity of such complexes.

Circular dichroism studies are useful in understanding the complex formation of organic ligands with β-CD. Binding of an achiral molecule within a chiral environment, such as β-CD, can lead to the induced optical activity of the bound species. Inset of Figure 4.11 shows the CD spectral changes of 1a in the presence of β-CD. As shown in the inset of Figure 4.11, we observed induced CD signal corresponding to the acridine moiety of the dyad 1a at higher concentrations of β-CD. In contrast, the CD studies of the ortho-isomer 1b in the presence of β-CD, showed no induced CD signal, confirming its negligible interactions with β-CD.

Understanding the interaction of molecules at the atomic level is gaining much attention in the recent years. In contrast to the precision electron microscopes, atomic force microscopy is advantageous due to the non-invasive imaging of the materials. Particularly, tapping mode atomic force microscopy has been instrumental in imaging the soft materials such as organic molecules and biological samples. To understand how the viologen linked acridine conjugates interacts with β-CD, we have carried out tapping mode atomic force microscopic studies (TM AFM) of β-CD in the presence and absence of various representative ligands. β-Cyclodextrin alone showed a flaky, crystalline like structure with a height of 5 ± 1 nm, whereas in the presence of derivative 1a, we observed drastic
changes in the morphology of β-CD resulting in the loss of crystalline structure (Figure 4.17). As expected, we observed negligible changes in the morphology of the β-CD in the presence of the ortho-isomer 1b, which exhibits insignificant interactions with β-CD.

![AFM images](image-url)

**Figure 4.17.** AFM images; A: β-CD (0.11 mM) alone, B: β-CD (0.11 mM) in the presence of 1a (0.11 mM) and C: β-CD (0.11 mM) in the presence of 1b (0.11 mM).

### 4.3.4. Molecular Modeling Studies

With a view to understand various photophysical properties of the viologen linked acridine derivatives in the presence and absence of β-CD, we have carried out semi-empirical AM1 calculations to find out the possible stable conformers for the dyads 1a–c and 2a–c. All the calculations have been carried out at AM1 level using a suite of Gaussian 03W programs. We obtained minimum energy conformers for the dyads 1a–c and 2a–c by geometry optimization of several conformers. Figure 4.18 shows structures of the energy-minimized conformations of the viologen linked acridine conjugates 1a–c and 2a–c. AM1 calculations show...
that the viologen linked acridine derivatives 1a, 1c and 2a exist in one extended form as the minimum energy conformer, while, the dyads 1b, 2b and 2c have two minimum energy conformers. In agreement with the observation of various conformers through AM1 calculations, we obtained monoexponential fluorescence decay in the case of the dyads 1a, 1c and 2a whereas the biexponential decay was observed for the dyads 1b, 2b and 2c. From the orientation of the donor acridine chromophore with respect to the acceptor viologen moiety, we assign the major component (80–90%) with long lifetime to the lowest energy minimum conformer i.e. the extended form, while the minor (10–20%) and short lived species as that of

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**Figure 4.18.** Minimum energy conformers of the viologen linked acridine derivatives 1a–c and 2a–c, obtained through AM1 calculations.
the folded conformer. However, in all these cases, the difference in the enthalpy of formation of these two conformations is marginal. Thus, the extended form is found to be slightly more stable than the folded one by 0.18–0.2 kcal mol\(^{-1}\).

To understand the nature of the encapsulation of the viologen linked acridine containing para-tolyl spacer 1a with \(\beta\)-CD, AMI calculations have been carried out. Figure 4.19 shows the energy-minimized space-filling representation of the dyad 1a-\(\beta\)-CD inclusion complex. It is apparent from this figure that the \(\beta\)-CD cavity fits neatly over the phenyl spacer group and should greatly restrict the rotational motions of the tolyl moiety. Evidence for such a complexation is obtained from the fluorescence anisotropy and \(^1\)H NMR experiments, where we observed significant changes in chemical shifts of the spacer phenyl group when complexed with \(\beta\)-CD.

![Figure 4.19. Minimum energy conformation for the complex 1a-\(\beta\)-CD, obtained by the AMI calculations.](image)
4.4. Discussion

For compounds in which a donor and an acceptor are separated by flexible or rigid spacer groups, the distance dependence of electron transfer reactions are well documented in the literature. In such systems, both through-bond and through-space interactions play a key role in determining their photophysical properties. In the case of the dyads 1a and 1c, the observed decrease in fluorescence quantum yields (Fluorescence 'OFF', Figure 4.20) and the lifetimes in the presence of β-CD could be attributed to the increase in the rate of electron transfer from the excited state of the acridine chromophore to viologen moiety. This is evident, from the negligible changes in fluorescence quantum yields and the lifetimes observed for the dyad 1b, which showed negligible interactions with

Figure 4.20. Schematic illustration of interactions between β-CD and (A) the dyad 1a having rigid aromatic spacer and (B) the dyad 2c consisting of flexible methylene spacer group (n = 11).
β–CD. On the other hand, the spacer length dependent enhancement in the fluorescence quantum yields and the lifetimes of the dyads 2a–c was observed when complexed with β–CD (Fluorescence ‘ON’, Figure 4.20). This could be attributed to the decrease in the rate of electron transfer from the excited state of the acridine chromophore to viologen moiety in these cases. However, all these dyads 1a-c and 2a-c exhibited similar fluorescence enhancement in the presence of micelles. These results demonstrate that microencapsulation of all these derivatives occurs in micelles, whereas unusual planarization of the rigid spacer takes place in the β–CD cavity, particularly in the case of the dyads 1a and 1c. Further support for such planarization was obtained through electrochemical studies. We observed increase in the reduction potentials of the dyad 1a corresponding to the viologen moiety in the presence of β–CD, whereas decreased values were observed for the dyad 2b under similar conditions. This indicates the enhanced interactions between the donor and the acceptor moieties in the former case through planarization of the rigid spacer when complexed with β–CD.

As evident from the photophysical, electrochemical and chiroptical studies, all the dyads 1a and 1c (rigid), and 2a-c (flexible), spacer groups undergo stable 1:1 complex formation with β-CD. Our results clearly demonstrate that the dyads 1a and 1c form tight complexes with β–CD through the inclusion of aryl spacer groups in the hydrophobic β–CD cavity, while the dyads 2a-c through involvement of polymethylene spacer groups. This is based on the following facts:
i) observation of induced CD signal, ii) hydrodynamic radius of 14.4 ± 0.4 Å from the anisotropy measurements as compared to the theoretically calculated molecular length of 14.9 Å, iii) competitive displacement of the dyad 1a from the 1a-β-CD complex by AD-COOH, iv) change in chemical shift of the phenyl spacer group when complexed with β-CD, and v) observation of distinct AFM morphological changes of β-CD, when complexed with the dyad 1a.

Inclusion of the para-tolyl moiety of the dyad 1a in β-CD cavity obtained through AM1 calculations can be further understood as follows. Though the acridine unit can undergo interactions with β-CD along the long molecular axis (radius = 9.19 Å), the substitution at the 9th position in the dyads 1a, 1c and 2a–c, prevents it from such interactions due to steric reasons (Figure 4.20). Therefore, β-CD binds to the dyads through the viologen unit leading to a less stable transition state and then finally the complexed state, where β-CD is located on the spacer group. The para-tolyl moiety in 1a with a length of 5.84 Å and width of 4.30 Å undergoes an effective encapsulation while 1b with the ortho-tolyl spacer fails to interact with β-CD (Figure 4.20) due to steric constraints. This hypothesis is confirmed by the fact that the derivative 1c with biphenyl moiety as a spacer unit has a length of 9.49 Å and width of 4.30 Å. As expected, the dyad 1c is found to undergo an effective interaction with β-CD compared to 1a, resulting in the formation of relatively a stable complex. Free energy changes observed during the β-CD complexation are found to be favorable for 1a and 1c, while in
the case of 2a–c, it increases with the increase in methylene spacer length (Table 4.1). This could be attributed to the increase in entropy due to the displacement of water molecules from the β-CD cavity by the guest molecules. The observed spacer length dependent increase in the association constants of the dyads 2a-c with flexible spacer groups with β-CD confirm the involvement of the flexible methylene groups in the formation of stable inclusion complexes from these cases.

4.5. Conclusions

In conclusion, the viologen linked acridine derivatives under investigation form stable complexes depending on the nature and length of the spacer group. Our results demonstrate the contrasting effects of the flexible and rigid spacer groups in the electron donor–acceptor dyads, when bound to β-CD. Upon β-CD complexation, the electron transfer process between the donor and acceptor moieties is inhibited in the dyads with flexible spacer groups, but significantly enhanced rate of electron transfer processes were observed with systems having the rigid aromatic spacer group. In the presence of β-CD, the viologen linked acridines containing flexible spacer group undergoes unfolding of the sandwich like folded structure, which results in the decrease in the interaction between the donor and acceptor moiety. In contrast, the enhanced electron transfer rates observed with systems having rigid spacer is attributed to the unusual planarization of the molecule, when encapsulated in the β-CD cavity. The results
of these investigations are important in understanding the interaction between donor-acceptor dyads, unusual effects of the organized media such as β-CD and also in the design of supramolecular drug delivery systems and molecular machines.

4.6. Experimental Section

4.6.1. General Techniques

All the molecular geometries were optimized at the semi-empirical level by using AM1 method as implemented in the Gaussian 03W suite of programs. All melting points are uncorrected and were determined on a Mel-Temp II melting point apparatus. An Elico pH meter was used for pH measurements. The electronic absorption spectra were recorded on a Shimadzu UV-VIS-NIR spectrophotometer. Fluorescence spectra were recorded on a SPEX-Fluorolog F112X spectrofluorimeter. The fluorescence quantum yields were determined by using optically matching solutions. 9-Aminoacridine in methanol (Φf = 0.99) was used as the standard. The quantum yields of fluorescence were calculated using the equation 4.1, where, \( A_s \) and \( A_u \) are the absorbance of standard and unknown,

\[
\Phi_u = \frac{A_s F_u n_u^2}{A_u F_s n_s^2} \Phi_s \quad (4.1)
\]

respectively. \( F_s \) and \( F_u \) are the areas of fluorescence peaks of the standard and unknown and \( n_s \) and \( n_u \) are the refractive indices of the standard and unknown
solvents, respectively. $\Phi_s$ and $\Phi_u$ are the fluorescence quantum yields of the standard and unknown compound. Fluorescence lifetimes and anisotropy were measured using an IBH Picosecond single photon counting system. Fluorescence lifetimes and anisotropy were determined by deconvoluting the instrumental function with mono or biexponential decay and minimizing the $\chi^2$ values of the fit to $1 \pm 0.1$. The quenching rate constant $k_q$ was calculated by employing Equations (4.2) and (4.3), where $I_0$ and $I$ are the fluorescence intensities in the absence and presence of quencher (Q), $K_{sv}$ the Stern–Volmer constant, and $\tau_0$ the singlet lifetime of $para$–tolylacridine in the absence of quencher.

$$\frac{I_0}{I} = 1 + K_{sv}[Q] \quad (4.2)$$
$$K_{sv} = K_q \times \tau_0 \quad (4.3)$$

From the relative fluorescence quantum yields of the viologen–linked acridine derivatives and fluorescence lifetime of the model derivative $para$–tolylacridine, an estimate of the rate constant of electron transfer process $k_{ET}$ can be made by using Equation 4.4, where $\Phi_{ref}$ and $\Phi$ are the relative fluorescence quantum yields of the model derivative $para$–tolylacridine and the viologen linked acridine derivative, respectively,

$$k_{ET} = \left(\frac{[\Phi_{ref} / \Phi] - 1}{\tau_{ref}}\right) \tau_{ref} \quad (4.4)$$

and $\tau_{ref}$ is the fluorescence lifetime of the model compound $para$–tolylacridine. Cyclic voltammetry was performed on a BAS CV50W Cyclic Voltammeter with potassium nitrate as supporting electrolyte in water. A standard three–electrode
configuration was used with a glassy carbon working electrode, a platinum auxiliary electrode, and a Ag/AgCl (3 M NaCl) reference electrode. The potentials were calibrated against the standard calomel electrode (SCE). $^1$H and $^{13}$C NMR were measured on a 300 MHz Bruker advanced DPX spectrometer. Circular dichroism spectra were recorded on Jasco Corporation, J-810 spectropolarimeter. NMR studies were performed with a Bruker 300 MHz system in D$_2$O at 298 ± 1 K. Association constants were determined using Benesi–Hildebrand equation for a 1:1 stoichiometric complex using equation 4.5, where $K_{ass}$ is the association constant, $\Phi_f$ is the quantum yield of emission of a free viologen linked acridine,

$$1 / (\Phi_f - \Phi_{ob}) = 1 / (\Phi_f - \Phi_{ob}) + 1 / K_{ass}(\Phi_f - \Phi_{ob})[\beta-CD] \quad (4.5)$$

$\Phi_{ob}$ is the observed quantum yield in the presence of β-CD and $\Phi_f$ is the quantum yield of emission of β–CD complex. The linear dependence of $1 / (\Phi_f - \Phi_{ob})$ on the reciprocal of β–CD concentration indicates the formation of 1:1 molecular complex between β–CD and viologen linked acridine. Change in free energy ($\Delta G$) associated with the complexation between viologen linked acridine derivatives and β–CD, was determined using the equation 4.6,$^{27a}$ where $K_{ass}$ is the

$$\Delta G = -RT \ln K_{ass} \quad (4.6)$$

binding constant. Doubly distilled water was used in all the studies. All experiments were carried out at room temperature (25 ± 1 °C), unless otherwise mentioned. Hydrodynamic radius ($r_h$) of the complex is related to rotational correlation time
\( \tau_R \) as in the equation 4.7, where \( \eta \) is the viscosity of water, \( K \) is Boltzmann's constant and \( T \) is the temperature.

\[
r_h = \sqrt{\frac{3KT\tau_R}{4\pi\eta}} \quad (4.7)
\]

**Atomic force microscopy (AFM).** Samples for the imaging were prepared by drop casting the \( \beta \)-CD solution in the absence and presence of viologen linked acridine derivatives on freshly cleaved mica at the required concentrations. AFM images were recorded under ambient conditions using a Digital Instrument Multimode Nanoscope IV operating in the tapping mode regime. Micro-fabricated silicon cantilever tips (MPP-11100-10) with a resonance frequency of 299 kHz and a spring constant of 20–80 Nm\(^{-1}\) were used. The scan rate varied from 0.5 to 1.5 Hz. AFM section analysis was done offline.

### 4.6.2. Spectrophotometric and Spectrofluorimetric Titrations

The linearity of absorbance vs. concentrations was determined in the concentration range of \((10^{-4}-10^{-6} \text{ M})\) for all the derivatives. The sample concentrations were taken between \(0.1-10 \times 10^{-5} \text{ M}\), where it obeyed Beer’s law and formed no aggregation of the solute in the aqueous solutions. The linearity of the fluorescence emission vs. concentrations was also checked in the same concentration range used. The absorbance of the excitation wavelength was maintained lower than 0.15. Titrations of \( \beta \)-cyclodextrin with donor-acceptor dyads were carried out in aqueous medium. 3 mL of these dyads were taken in a quartz
cuvette with a concentration ranging 0.1–10 x 10⁻⁵ M. Subsequently, a 0.090 M stock solution of β-cyclodextrin were added in 20 µl – 200 µl volume to 3 mL solution of these dyads. A series of ¹H NMR spectra were recorded upon addition of 50 µl of 8.7 mM stock solution of β-cyclodextrin to 0.75 mL of dyads.

4.6.3. Materials

Diphenylamine, β-cyclodextrin (β-CD) and 1-adamantanecarboxylic acid (AD-COOH) were purchased from Aldrich and were used without further purification. The synthesis of 9-(4-methylphenyl)acridine (3a), mp 188-189 °C (lit. mp 189 °C) and 9-(2-methylphenyl)acridine (3b), mp 212-213 °C (lit. mp 214 ºC) was achieved as per reported procedures. 4-Methyl-4'-biphenylcarboxylic acid (6) mp 168-189 °C (lit. mp 169 ºC) was prepared by modification of the reported procedures. The starting materials, 9-bromomethylacridine (9), mp 162-163 ºC (lit. mp 160-161 ºC), 3-(acridin-9-yl)-1-bromopropane (10), mp 104-105 ºC (lit. mp 103-104 ºC), 11-(acridin-9-yl)-1-bromoundecane (11), 58-59 °C (lit. mp 58-59 °C), were prepared by modification of the reported procedures. 1-Butyl-4,4'-bipyridinium bromide was obtained in a 95% yield by the reaction of 4,4'-bipyridine with 1-bromobutane in the molar ratio of 3:1 in dry acetonitrile.

4.6.4. Synthesis of the viologen linked tolylacridines (1a and 1b)

A solution of 9-(4-methylphenyl)acridine (3a, 1 mmol), N-bromosuccinimide (NBS, 1 mmol) and benzoyl peroxide (20 mg) in dry CCl₄ (20 mL) was
refluxed for 8 h. The reaction mixture was cooled and filtered. The filtrate was concentrated to give a residue, which was chromatographed over silica gel column. Elution of the column with a mixture (1:4) of ethyl acetate and petroleum ether gave 9-(4-bromomethylphenyl)acridine 4a in 60% yield, mp 203-204 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 4.7 (2H, s), 7.3-8.05 (8H, m), 8.25-8.50 (4H, m); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 148.60, 146.28, 137.95, 136.04, 130.85, 129.96, 129.54, 129.06, 126.52, 125.69, 125.69, 124.92, 32.88; (HRMS-ESI) Calcd for C\(_{29}\)H\(_{15}\)NBr 348.0388. Found 348.0384.

Similar reaction of 9-(2-methylphenyl)acridine (3b) with NBS in dry CCl\(_4\) in presence of benzoyl peroxide yielded 9-(2-bromomethylphenyl)acridine 4b in 56% yield, mp 136-137 °C; \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 4.05 (2H, s), 7.10-7.90 (10H, m), 8.15-8.45 (2H, m); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 148.46, 144.04, 136.49, 135.30, 130.62, 129.75, 129.54, 129.07, 128.26, 126.23, 125.63, 124.96, 30.34; (HRMS-ESI) Calcd for C\(_{29}\)H\(_{15}\)NBr 348.0388. Found 348.0394.

A solution of 9-(4-bromomethylphenyl)acridine (4a, 1 mmol) and 1-butyl-4,4'-bipyridinium bromide (2 mmol) in dry acetonitrile (30 mL) was stirred at 30 °C for 12 h. The precipitated solid was filtered, washed with dry acetonitrile and dichloromethane to remove the unreacted starting materials. The solid was further purified by Soxhlet extraction with dichloromethane and recrystallization from a mixture (4:1) of ethyl acetate and acetonitrile to give 77% of 1a, mp 268-269 °C; \(^1\)H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 0.85-1.05 (3H, t, \(J = 2.89 \) Hz), 1.15-1.55 (2H,
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m), 1.80-2.20 (2H, m), 4.70-4.90 (2H, t, $J = 2.80$ Hz), 6.3 (2H, s), 7.50-8.40 (12H, m), 8.75-9.05 (4H, m), 9.42-9.60 (2H, m), 9.70-9.85 (2H, m); $^{13}$C NMR (DMSO-$d_6$, 75 MHz) $\delta$ 149.23, 1483.61, 147.74, 146.19, 146.00, 145.76, 136.21, 134.42, 131.09, 130.64, 129.36, 128.94, 127.26, 126.79, 126.38, 126.21, 124.23, 63.87, 60.64, 32.70, 18.77, 13.33; MS m/z 561 ($M^{+}Br^-$, 5), 481 ($M^+$, 100), 424 (10); Anal. Calcd for C$_{34}$H$_{31}$Br$_2$N$_3$: C, 63.66; H, 4.87; N, 6.55. Found: C, 63.81; H, 5.09; N, 6.42.

Similar reaction of 9-(2-bromomethylphenyl)acridine (4b, 1 mmol) with 1-butyl-4,4'-bipyridinium bromide (2 mmol) in dry acetonitrile and purification as in the earlier case gave 75% of 1b, mp 224-225 °C; $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 0.80-1.00 (3H, t, $J = 2.89$ Hz), 1.05-1.50 (2H, m), 1.70-2.10 (2H, m), 4.65-4.90 (2H, t, $J = 2.85$ Hz), 5.60 (2H, s), 7.15-8.70 (16H, m), 9.30-9.55 (4H, m); $^{13}$C NMR (DMSO-$d_6$, 75 MHz) $\delta$ 148.50, 147.80, 145.82, 145.27, 142.77, 135.64, 132.08, 131.90, 131.36, 130.55, 130.44, 129.98, 129.47, 127.08, 126.68, 126.49, 125.95, 125.34, 124.24, 62.02, 60.64, 32.68, 18.78, 13.35; MS m/z 561 ($M^{+}Br^-$, 7), 481 ($M^+$, 100), 424 (7); Anal. Calcd for C$_{34}$H$_{31}$Br$_2$N$_3$: C, 63.66; H, 4.87; N, 6.55. Found: C, 63.69; H, 5.06; N, 6.46.

4.6.5. Synthesis of viologen linked 9-(biphenyl-4-methyl)acridine (1c)

A mixture of 4-methyl-4'-biphenylcarboxylic acid (1.42 mmol), diphenylamine (1.42 mmol) and anhydrous ZnCl$_2$ (14 mmol) was heated at 230 °C
for 24 h. To the reaction mixture 20% H₂SO₄ (20 mL) was added and refluxed for 4 h. It was then cooled and neutralized with 25% aqueous NH₃ solution and the solid product thus obtained was chromatographed over silica gel. Elution of the column with a mixture of (1:1) of ethyl acetate and hexane gave 9-(biphenylyl 4-methyl)acridine (10%), mp 267–269 °C: ¹H NMR (CDCl₃, 300 MHz) δ 2.42 (3H, s), 7.31–8.17 (16H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 21.1, 126.4, 127.4, 128.9, 129.8, 130.5, 131.1, 134.9, 135.9, 136.7, 138.2, 140.4, 143.3, 143.8; HRMS (ESI) Calcd for C₂₆H₁₉N: 345.4358. Found: 345.4367.

A mixture of 9-(biphenylyl-4-methyl)acridine (0.1 mmol), N-bromosuccinimide (0.1 mmol) and AIBN in 10 mL dry CCl₄ was refluxed for 12 h. The reaction mixture was cooled and filtered. The filtrate was concentrated to give a residue, which was chromatographed over silica gel column. Elution of the column with a mixture (1:4) of ethyl acetate and petroleum ether gave the bromo derivative 8 (54%), mp 285–286 °C: ¹H NMR (CDCl₃, 300 MHz) δ 4.56 (2H, s), 7.52–8.05 (16H, m); ¹³C NMR (CDCl₃, 75 MHz) δ 33.7, 126.7, 127.4, 128.5, 129.9, 130.5, 131.1, 134.9, 135.9, 138.2, 139.9, 142.1, 144.2, 145.8; HRMS (ESI) Calcd for C₂₆H₁₈BrN: 424.3319. Found: 424.3337.

To a solution of 9-(4-bromomethylbiphenyl)acridine (0.1 mmol) in dry acetonitrile (50 mL), 1-butyl-4,4'-bipyridinium bromide (0.1 mmol) was added and stirred at room temperature for 12 h. Precipitated product was filtered and dried to give 1c, which was recrystallised from a mixture (7:3) of methanol and
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ethylacetate. 35% yield, mp 291–293 °C: \(^1^H\) NMR (DMsol-d\(_6\), 300 MHz) \(\delta\) 0.93–0.97 (3H, t, \(J = 7.4\) Hz), 1.35–1.38 (2H, m), 1.99–2.02 (2H, m), 4.79 (2H, t, \(J = 7.1\) Hz), 6.30 (2H, s), 7.37–8.27 (9H, m), 8.93–9.85 (8H, m); \(^1^3^C\) NMR (DMsol-d\(_6\), 75 MHz) \(\delta\) 13.4, 18.8, 32.7, 60.6, 62.8, 109.1, 124.2, 126.2, 126.4, 126.8, 127.3, 128.3, 129.1, 129.3, 130.5, 131.1, 134.5, 136.2, 145.8, 146.0, 147.9, 148.6, 149.2; HRMS (ESI) Calcd for C\(_{40}\)H\(_{35}\)BrN\(_3\): 637.6301. Found: 637.6301. Anal. Calcd for C\(_{40}\)H\(_{35}\)Br\(_2\)N\(_3\): C, 66.96; H, 4.92; N, 5.86. Found: C, 66.74; H, 5.01; N, 5.96.

4.6.5. Synthesis of the viologen linked acridines (2a-c)

A solution of \(\omega\)-(acidin-9-yI)-\(\alpha\)-bromoalkanes (1 mmol) and 1-alkyl-4,4'-bipyridinium bromide (1 mmol) in dry acetonitrile (30 mL) was stirred at 30 °C for 12 h. The precipitated solid thus obtained was filtered, washed with dry acetonitrile and dichloromethane to remove any unreacted starting materials. The solid was further purified by soxhlet extraction with dichloromethane to gave 2a-c in quantitative to moderate yields.

2a (67%; obtained by the reaction of 9 with 1-alkyl-4,4'-bipyridinium bromide, was recrystallized from a mixture (1:4) of methanol-acetonitrile): mp 260-261 °C; \(^1^H\) NMR (DMSO-d\(_6\)) \(\delta\) 0.94 (3H, t, \(J = 2.9\) Hz), 1.30-1.37 (2H, m), 1.93-1.98 (2H, m), 4.70 (2H, t, \(J = 2.8\) Hz), 7.16 (2H, s), 7.79-8.36 (4H, m), 8.51-8.72 (8H, m), 9.20-9.37 (4H, m); \(^1^3^C\) NMR (DMSO-d\(_6\)) \(\delta\) 149.78, 148.91, 146.02,
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145.69, 131.43, 130.97, 130.22, 128.70, 127.13, 126.92, 126.02, 124.36, 121.42, 61.02, 55.45, 33.01, 19.10, 13.67; (HRMS-ESI) Calcd for C$_{28}$H$_{27}$Br$_2$N$_3$: 484.1388. Found: 484.1372. Anal. Calcd for C$_{28}$H$_{27}$Br$_2$N$_3$: C, 59.49; H, 4.81; N, 7.43. Found: C, 59.28; H, 4.98; N, 7.31.

2b (71%: obtained by the reaction of 10 with 1-alkyl-4,4'-bipyridinium bromide, was purified by washing several times with a mixture (1:4) of methanol-acetonitrile): mp 253-254 °C; $^1$H NMR (DMSO-$d_6$) δ 0.90 (3H, t, J = 2.7 Hz), 1.10-1.60 (2H, m), 1.70-2.20 (2H, m), 2.20-2.70 (2H, m), 4.75 (4H, t, J = 3.6 Hz), 7.60-8.30 (6H, m), 8.50-9.00 (6H, m), 9.30-9.75 (4H, m); $^{13}$C NMR (DMSO-$d_6$) δ 149.45, 149.35, 146.18, 145.40, 133.29, 127.49, 127.19, 125.91, 124.96, 61.12, 60.73, 33.21, 33.05, 24.89, 19.28, 13.85; MS (FAB): m/z (%) 433 (M$^+$, 10), 408 (1), 376 (3), 347 (1). Anal. Calcd for C$_{30}$H$_{31}$Br$_2$N$_3$: C, 60.72; H, 5.27; N, 7.08. Found: C, 60.51; H, 5.21; N, 7.27.

2c (65%: obtained by the reaction of 11 with 1-alkyl-4,4'-bipyridinium bromide, was recrystallised from acetonitrile): mp 248 -249 °C; IR $\nu_{\text{max}}$ (KBr) 3032, 2933, 2859 (C-H), 1648 (C=N), 1559 (C=C) cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) δ 0.90-2.3 (27H, m), 4.7-4.9 (4H, t, J = 3.6 Hz), 7.50-8.00 (6H, m), 8.05-8.60 (6H, m), 8.70-9.30 (2H, m), 9.20-9.30 (2H, m); $^{13}$C NMR (DMSO-$d_6$) 148.98, 148.35, 147.65, 146.09, 130.49, 130.09, 127.02, 126.20, 125.15, 124.71, 61.25, 61.04, 33.07, 31.64, 31.15, 29.68, 29.26, 29.14, 28.76, 27.13, 25.80, 19.16, 13.72; MS
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(FAB) m/z (%) 545 (M⁺, 10), 488 (2), 429 (1), 323 (2), 270 (6). Anal. Calcd for C₃₈H₄₇Br₂N₃: C, 64.68; H, 6.71; N, 5.98. Found: C, 64.42; H, 6.44; N, 5.72.

4.7. References


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