CHAPTER 2

NON-POLAR FACES IN SUGAR CHAINS
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2.0. INTRODUCTION

The existence of nonpolar surfaces in sugars appears counter-intuitive. Yet there are certain features in these molecules which suggest that the idea cannot be easily dismissed. Neal and Goring (1970) compared the models of maltose and cellobiose (α-1,4 linked and β-1,4 linked dimers of glucose respectively) and showed that maltose folds into a L-shaped conformation with the inner surface dotted with methine hydrogens while the outer face with all the OH groups. While the regular repetition of the α-1,4 linkage in the oligosaccharides of D-glucose would reinforce to form the hydrophobic surface, the β-1,4 linkage in the cellulosic oligosaccharides breaks this order. Suggett (1975) said that polysaccharides can generate apolar surfaces by adopting certain conformations and these apolar surfaces would be capable of entering into hydrophobic interactions with other nonpolar substances. Marsden (1977) also argued that while monomeric glucose as such does not possess hydrophobic character, a stable array of the nonpolar faces can occur when it is polymerised.

It is well known that α-amyllose, the higher molecular weight polymer of glucose predominantly linked by the α-1,4 linkage, folds into several helical forms (Rees, 1977). The inner cavity in these folded helices is relatively apolar which accommodates the stilbene-substituted fatty acids as inclusion complexes (Hui et al., 1983a and 1983b). This kind of hydrophobic binding and also the formation of
inclusion complexes of molecular iodine (I\(_2\)) with \(\alpha\)-amylose support the above argument that \(\alpha\)-1,4 linked oligosaccharides and polysaccharides tend to display amphiphilicity. Earlier Nakatani \textit{et al.} (1977) had reported that fluorescence probes such as TNS experience a hydrophobic environment upon binding to the linear \(\alpha\)-amyloses, resulting in the enhancement of its fluorescence intensity. In the present work we have used \(\alpha\)-1,4 linked linear oligomers of glucose up to a chain length of ten to estimate the extent of amphiphilicity. We have used three extrinsic fluorescence probes, namely 1-(anilino)-8-naphthalenesulfonic acid (ANSA), pyrene and a neutral dye 5-(dimethylamino)-1-naphthalenesulfonamide (or dansamide) in order to monitor the hydrophobic surface of dextrins and related saccharides.

Another important property of amphiphiles is the ability to solubilize lipophilic and nonpolar compounds in water. Some sugars display this ability. The free energy of transfer from water to the sugar solution is expressed as

\[
\Delta G_t = \Delta G_c + \Delta G_{pi} + \Delta G_{npi},
\]

where, \(\Delta G_c\) is the part due to cavity formation in the solvent to help accommodate the solute, and the second and third terms refer to the polar and nonpolar interactions between the solvent and solute. It is suggested that the \(\Delta G_t\) values are dominated by the "nonpolar interaction" term over the "cavity formation" term, and the polar interactions play a minor role. With the glucosides, the capacity to solubilize increases from glucose to maltose to maltodextrins. Sugars are conventionally thought to reduce the solubility of nonpolar compounds in water; the term "sugaring out" has been used in this connection (Lakshmi and Nandi, 1976), to emphasize the similarity with the salting out by chaotropic agents. Instead, what we are looking for is the "sugaring in" phenomenon, akin to the salting in by antichaotropic agents (e.g., KSCN, urea). We have studied such solubilization behavior of sugars with a variety of nonpolar compounds (Sivakama Sundari \textit{et al.}, 1991; Raman \textit{et al.}, 1992;
Balasubramanian et al., 1993). Already, the use of dextrins as carriers of drugs such as diazepam and prednisolone is being evaluated in the lyophilized, solid dispersion form (Te-Wierick et al., 1993).

In this chapter, we have explored the possibilities of the generation of amphiphilic surfaces, by first determining the free energy of interaction of the sugars with water followed by use of probes to estimate the polarity of the environment. We also present evidence that certain conformations in carbohydrates display amphiphilic tendencies by energy minimization calculations based on molecular modeling. The second order rate constant values for a Diels-Alder reaction in the presence of various sugars has been determined. All these results together suggest the existence of amphiphilic tendencies in linear dextrins.

2.1. MATERIALS AND METHODS

Dextrin 10, Dextrin 20 and Dextran 4 were purchased from Serva, Heidelberg. L-tyrosine, pyrene, progesterone and β-estradiol were purchased from Sigma Chemical Company. Anthracene-9-carbinol was synthesized in the laboratory. Dipyrenylmethylene ether (DPME) and 3,12-bispyrenyl methyl cholate (BPCM) were kind gifts from Dr. Klass Zachariasse of the Max Planck Institute for Biophysical Chemistry, Göttingen, and Professor Uday Maitra of the Indian Institute of Science, Bangalore respectively. All other reagents were of analytical grade.

2.1.1. Solubilization Experiments

The candidate solubilizate was added to the various sugar solutions of increasing concentrations and incubated for 48 hours at room temperature (~298 K).
The residual solid was centrifuged and the supernatant filtered through a 0.45 μM Millipore filter. The concentration of the solubilized substance such as L-tyrosine, progesterone, β-estradiol and pyrene were determined from the absorbance values at 275 nm (ε =1370), at 249 nm (log ε = 4.23), at 280 nm (log ε =3.33) and 335 nm (log ε = 4.78) respectively. The free energy of transfer, ΔGtr, was calculated from the equation ΔGtr = -RT ln[Cs / Cw ], where Cs and Cw are the solubilities of the given compound in the chosen solution of the oligosaccharide and in water respectively.

2.1.2. Inclusion Complex Formation with I₂

A dilute solution of iodine was made in saturated KI and added to solutions of Dextrin 10% of increasing concentrations. The binding was monitored by measuring the absorbance values at the λabs max of 520 nm on a Cary spectrophotometer.

2.1.3. Fluorescence Studies

All fluorescence spectra were recorded with a Hitachi model F-4000 spectrofluorimeter. Estimation of the changes in the environment polarity was done using three probes, namely pyrene, ANSA (8-anilino-naphthalene-1-sulfonic acid) and (dimethylamino)-1-naphthalene sulfonamide (dansamide). Pyrene and ANSA were purchased from Sigma Chemical Company. The neutral probe dansamide, was synthesized in our laboratory. 10 mM stocks of these solutions were prepared in methanol. Small volumes of these stocks were added to aqueous solutions of the samples so that the effective concentration was a few μM. The excitation wavelengths for ANSA and dansamide were 365 nm and 323 nm respectively. The characteristic emission spectrum of pyrene (effective concentration 1 μM) was recorded by exciting at 335 nm. Pyrene excimer spectra were recorded upon the addition of millimolar amounts of the stock (upto 2% of the volume in solution).
2.1.4. Determination of Conformation by Energy Minimization Calculations

These calculations were done using the procedure of Rao (Rao et al., 1969; Yathindra and Rao, 1970) choosing the coordinates of Arnott and Scott (1972) for the sugar rings with the bond lengths and angles given for D-glucose in the \(4\text{C}_1\) form.

2.1.5. Diels-Alder Reaction

The cycloaddition reaction between anthracene-9-carbinol and N-ethylmaleimide was carried out as per the published method (Breslow et al., 1983). The reaction was conducted in the presence of the various additives, by monitoring the time dependent loss in the optical density of the carbinol at 385 nm for 60 min (which was adequate) at 318 K. The second order rate constants were calculated.

2.2. RESULTS AND DISCUSSION

2.2.1. Solubilization of Lipophiles by Sugars

We have measured the solubility of the aromatic amino acid L-tyrosine, the neutral lipophilic arene, pyrene and steroids such as progesterone and \(\beta\)-estradiol in aqueous solutions of dextrins, dextran, cellobiose and several other monomeric sugars. Figure 2.1 shows the effect of these sugars on the solubility of L-tyrosine in water. The activity coefficient \(f (f = c_\circ / c)\), where \(c_\circ\) is the solubility in water and \(c\) is the solubility in the presence of the added sugar) of L-tyrosine was decreased significantly by dextrins, since they enhance its solubility in water. Monomeric glucose, cellobiose (the \(\beta\)-1,4 linked dimer of glucose) and sucrose did not affect the activity coefficient. The \(\alpha\)-1,6 linked polymer dextran and another polymer xylan (at the accessible solution concentrations), behaved oppositely to the \(\alpha\)-1,4 linked dextrin. The free energies of transfer of tyrosine from water to dextrin solutions at
Figure 2.1. Solubilization of L-tyrosine by aqueous sugar solutions 298 K. Curve(1) is for sucrose, (2) for glucose, (3) for Dextrin 10, (4) for Dextrin 20, (5) for cellubiose, (6) for Dextran 4 and (7) for xylan. Activity coefficients were calculated as the ratio of the solubility in water to that in the additive test solution.
### Table 2.1. Free energies of transfer of L-tyrosine from water to aqueous sugar solutions at 298° K

<table>
<thead>
<tr>
<th>Solvent system</th>
<th>ΔG_{tr} (cal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 M Glucose</td>
<td>+25</td>
</tr>
<tr>
<td>1 M Maltose</td>
<td>+25</td>
</tr>
<tr>
<td>2 M Sucrose</td>
<td>+240</td>
</tr>
<tr>
<td>200 mM Dextrin 20</td>
<td>-380</td>
</tr>
<tr>
<td>150 mM Dextrin 10</td>
<td>-460</td>
</tr>
<tr>
<td>20 mM Dextran 4</td>
<td>+70</td>
</tr>
</tbody>
</table>

ΔG_{tr} = RT ln (1/a), where a is the activity coefficient
298 K were calculated (Table 2.1) and found to be -380 (cal / mol) for Dextrin 20 and -460 (cal / mol) for 150 mM Dextrin 10. Xylan (0.05%) and Dextran 4 (20 mM) were found to sugar out tyrosine in water with $\Delta G_{tr}$ values of +160 and +70 respectively. In the case of the smaller sugars the values were slightly positive (25 cal / mol for 2M glucose and 240 cal/mol for 2 M sucrose), indicating that they "sugar out" the tyrosine from water.

Next we measured the solubility of pyrene, a neutral lipophilic arene, in the various sugar solutions. Optical density at 335 nm ($\lambda_{abs} \text{ max}$) was used as a measure of the solubility in the different sugar solutions. A 300 mM Dextrin 20 solution seemed to increase the solubility of pyrene in water, by ten folds. The $\Delta G_{tr}$ of pyrene from water to 150 mM Dextrin 10 was found to be -2090 cal / mol indicating a favourable free energy of interaction (see Table 2.2).

The solubilizing ability of these saccharides can be utilized in systems wherein the solubility of sparingly soluble compounds such as drugs can be enhanced for practical purposes such as in drug formulations and as carriers in their delivery. We have attempted to solubilize steroid drugs such as progesterone and $\beta$-estradiol which are otherwise sparingly soluble in water. Figure 2.2 shows that maltooligosaccharides substantially increase the solubility of the two steroids in water. In contrast, Dextran 4 and several other mono- and disaccharides "sugar-out" the steroids. The values of the free energies of transfer ($\Delta G_{tr}$) of these compounds from water to the additives are given in Table 2.2. These results obtained with the steroids are in agreement with that obtained with L-tyrosine. Also dextrins have been reported to be biocompatible, nonpyrogenic and nonimmunogenic. They have been already used as carriers for drugs such as diazepam and prednisolone in the lyophilised, solid dispersion form (Te-Wierick et
Figure 2.2. Solubilization of Progesterone (P) and β-estradiol (E) by various sugars at 298 K.
Table 2.2. *Free energies of transfer of steroids and of pyrene from water to some oligosaccharides*  

<table>
<thead>
<tr>
<th>solute</th>
<th>medium</th>
<th>$\Delta G_{tr}$ (cal / mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>progesterone</td>
<td>100 mM Dextrin 10</td>
<td>-1440</td>
</tr>
<tr>
<td></td>
<td>400 mM Dextrin 20</td>
<td>-1450</td>
</tr>
<tr>
<td></td>
<td>18 mM Dextran 4</td>
<td>+540</td>
</tr>
<tr>
<td>$\beta$-Estradiol</td>
<td>150 mM Dextrin 10</td>
<td>-1680</td>
</tr>
<tr>
<td></td>
<td>400 mM Dextrin 20</td>
<td>-1560</td>
</tr>
<tr>
<td></td>
<td>18 mM Dextran 4</td>
<td>+1470</td>
</tr>
<tr>
<td>pyrene</td>
<td>150 mM Dextrin 10</td>
<td>-2090</td>
</tr>
</tbody>
</table>

* All measurements were made using 10 mM sodium phosphate pH 7.2 buffer; concentrations measured using absorbance values, as given in Materials and Methods; temperature 298 K; $\Delta G_{tr}$ values were calculated from the equation $\Delta G_{tr} = -RT \ln (1 / a)$, where $a = $ activity coefficient ($= C_w / C_m$, where $C_w$ and $C_m$ are solubilities in buffer and in the oligosaccharide solution).
Therefore we believe that dextrins can be used as efficient solubilizers and bioavailability agents in drug formulations. Their cyclic analogs namely the cyclodextrins, solubilize by forming inclusion complexes, restricting thereby the solubilization generally to a 1:1 mole ratio (or occasionally a 2:1 or 1:2 ratio), whereas higher ratios are possible using linear maltodextrin polymers. Also unlike the cyclodextrins that need derivatisation to enhance the solubility in water, linear dextrins are more soluble in water (upto a few hundred millimolar concentrations).

2.2.2. Binding of Molecular Iodine

The inclusion complex of molecular iodine with α-amylose is the best classical example for the hydrophobic interaction of polysaccharides, wherein it imparts deep blue color to the solution, upon complexation. When similar studies were carried out in the presence of Dextrin 10, the solution turned dark red upon complexation (which is otherwise orange in water). Figure 2.3 shows the progressive increase in the absorbance of I₂ at 520 nm, as the concentration of Dextrin 10 is increased, reaching a limit value beyond 60 mM. This is perhaps due to the non-specific binding of the I₂ to the short chain linear dextrins; also the chain length may not be sufficient to induce formation of helical folds as seen in the case of α-amylose.

2.2.3. Estimation of the Polarity using Fluorescence Probes

The results shown in sections 2.2.1 and 2.2.2 suggest that maltodextrin chains are able to offer a nonpolar surface for the binding of lipophiles. An estimation of the hydrophobicity (or the polarity) can be made by comparing it to that of water-dioxan mixtures, or in terms of the polarity parameter Eₐ (30), defined by Reichardt (1992) on the basis of the transition energy needed for a polarity-sensitive dye to absorb light and be excited to a higher electronic state; he
Figure 2.3. Binding of molecular iodine to Dextrin 10
has also provided a table of $E_T (30)$ values for various solvents and solvent mixtures.

The naphthalenesulfonate class of fluorophores are excellent monitors of the polarity of the medium they are placed in (more precisely the microenvironment, or the cybotactic zone that immediately surrounds the probe molecule) (Kosower et al., 1978; Detoma and Brand, 1977; Cardamone and Puri, 1992). We have used two of the probes, namely 1-(anilino)-8-naphthalenesulfonic acid (ANSA) and a neutral dye 5-(dimethylamino)-1-naphthalenesulfonamide (or dansamide) in order to monitor the hydrophobic surface of dextrins and related saccharides. Figure 2.4 shows that the dextrins blue-shift the emission band of ANSA by as much as 25 nm and enhance its fluorescence intensity six-fold. The other polarity probe dansamide also shows a similar behaviour. Figure 2.5 compares the blue shifts in dansamide effected by maltohexaose, and by water: dioxan mixtures. The polarity experienced by the probe in the maltodextrin is roughly comparable to that of 30% dioxan. Figure 2.5 also shows that the other sugars dextran, cellobiose, maltose itself, glucose, sucrose and xylan (not shown) offer a medium polarity that is not very different from that of water.

Another fluorescence probe that reports on the polarity of its cybotactic region is the neutral arene, pyrene. Nakajima (1976), and Dong and Winnick (1982) have utilized the fact that the intensity ratio of the vibronic bands (in particular that of band 3 to band 1 or $I_3/I_1$) of the fluorescence spectrum of pyrene, called the Ham ratio, is particularly useful in this regard. Dong and Winnick (1982) have tabulated the values of the Ham ratio in a large number of solvents of varying polarity.

In addition, pyrene molecule also forms an intermolecular complex called the excimer, wherein the homodimeric complex is formed only at the electronically
Figure 2.4: Variation in the emission band maximum (Panel a) and intensity (Panel b) of the probe ANSA in water upon the addition of increasing concentrations of: (1) Glucose, (2) Dextrin 20, (3) Dextrin 10, (4) maltose, (5) Dextran 4 (MW 4000-6000), (b) cellobiose and (7) xylan. Excitation at 365 nm.
Figure 2.5: (Panel a): Variation in the emission band of the neutral probe dansamidine in water: dioxane mixtures. (Panel b): in solutions of glucose and of Dextrin 20. Excitation at 323 nm.
excited state (Fürster, 1969; Zachariasse et al., 1982; Maitra et al., 1998). Since pyrene is a hydrophobic molecule, its excimer formation would be promoted in nonpolar media, and inhibited in media where hydrophobic association is weakened.

In an effort to assess the amphiphilic character of sugars, we have studied on the one hand the Ham ratio, and the excimer formation of pyrene in aqueous sugar solutions.

The Ham ratio of pyrene of 0.58 in water, is seen to increase to 0.67 in 300 mM Dextrin 20 reflecting the decrease in the polarity of the medium; this may be compared with the value of 0.74 seen in Triton X-100 micelles. In contrast, dextran and other sugars did not change the intensity ratio from what was seen in water.

2.2.4. Excimer Formation

2.2.4.1. Formation of Intermolecular Excimers of Pyrene

Forster (1969) had shown the generation of excimers of polyaromatic hydrocarbons in organic solvents as a consequence of increase in their concentration in solution. Illustrated in Figure 2.6 are the fluorescence spectra of pyrene in the presence of 10 mM β-cyclodextrin (panel a), and 100 mM Dextrin 10 (panel b) for two different concentrations of pyrene; panel c is a plot of $I_e / I_m$ (ratio of the emission intensity of the excimer and the monomer) value with respect to concentration of pyrene added into the test solution. While there is a monotonic increase of the $I_e / I_m$ ratio in the case of the cyclodextrins, indicating that the dimerization is facilitated by inclusion of pyrene monomers in their apolar cavities, the ratio increases marginally up to a value of about 0.5 in the presence of linear
Figure 2.6. Intermolecular excimer formation of pyrene in sugars. Emission spectrum of (...) 15 μM and ( ___ ) 180 μM pyrene in (a) 10 mM β-cyclodextrin and (b) in 100 mM Dextrin 10. (c) Effect of the sugars on the excimer formation.
dextrins suggesting that the excimerization is inhibited due to the binding of the pyrene monomers to the apolar surfaces of the sugar chains.

2.2.4.2. Formation of Intramolecular Excimers of Pyrene

Studies on the excimer fluorescence of pyrene, formed by dipyrenyl probe molecules such as (dipyrenyl)-methyl ether (DPME) and 3,12-bispyrenyl carboxy methyl cholate (BPCM) provided interesting results. These probes display the Ham effect in its emission around 370-400 nm due to the monomer, and also form an intramolecular excimer whose emission is a broad band around 450 nm. The efficiency of excimer formation is governed by the polarity of the medium. In the present instance, DPME was placed in solutions of Dextran 4, Dextrin 10, Dextrin 20 and β-cyclodextrin and the emission spectrum recorded. A plot of I_e / I_m (ratio of the emission intensity of the excimer and the monomer) versus concentration of the sugar is shown in Figure 2.7, which reflects the population of the pyrene molecules that exist in the form of dimer in the excited state. The ratio of I_e / I_m which is 6 in water, seems to drop to a value less than 1 in the presence of increasing concentrations of linear dextrins. This result suggests that the hydrophobic crowding of the two pyrene moieties that occur in water (and a concomitant increase in the excimer emission) is inhibited by the dextrins, due to the strong nonpolar interactions between the monomeric pyrene moieties with the apolar surfaces of present on the sugar chain. In the case of β-cyclodextrin, the I_e / I_m value of 12 in lower concentrations drops to a value of around 6; it also seems to saturate around 10 mM. This is indicative of formation of inclusion complexes with increase in availability of apolar cavities of β-cyclodextrin rather than the excimerization. Whereas in Dextran 4, the excimer population seems to predominate as the I_e / I_m value remains high.
Figure 2.7 Formation of DPME intramolecular excimers
Figure 2.8. Formation of intramolecular excimers of 3,12-bispyrenyl cholic acid methyl ester (BPCM)
A similar trend was observed for BPCM. As seen in Figure 2.8, there was a steady decrease of the $I_e / I_m$ ratio in the presence of linear dextrins and β-cyclodextrin indicating that these sugars hinder the hydrophobic crowding in solution. Also, the ratio almost remains constant in the presence of increasing amounts of Dextran 4 suggesting that the α-1,6 linked sugar does not enter into nonpolar interactions with the pyrene moieties.

These results suggest that these polarity probes bind to the dextrin chains in a manner such that they experience a local environment that is less polar than the bulk water medium. Such binding can be envisaged only if the dextrin chains were to have a nonpolar surface, which is possible due to the alignment of the CH groups on one side of the molecule leaving all the hydroxyls to line-up on the other side. These would make linear dextrins amphiphilic ribbons or sheets. Homopolysaccharides are known to adopt the extended ribbon (Type A), the flexible helix (Type B), the crumpled ribbon (Type C) and the flexible coil (Type D) conformations (see Figure 1.2), depending on their glycosidic chain linkage types (Rees, 1977; Kennedy, 1988). Out of the three forms of the Type B conformations known, cyclodextrin is thought to be one turn of one of these called the V form (Rees 1977; Brisson et al., 1991). The α-1,4 linked linear dextrins can adopt only the Type B or the helical conformation.

2.2.5. Deceleration of Diels-Alder Reaction by Dextrins

Breslow and his group have reported that rates of several bimolecular organic reactions are remarkably modified by salting-in and salting-out agents (Rideout and Breslow, 1980; Breslow et al., 1983; Breslow, 1991). They have studied the rates of the cycloaddition reaction between anthracene-9-carbinol and N-ethylmaleimide(NEM), in different solvent media in order to see the alterations in
Table 2.3. Second order rate constants of the reaction between anthracene-9-carbinol and N-ethylmaleimide*

<table>
<thead>
<tr>
<th>medium</th>
<th>$k_2 \times 10^3$ M$^{-1}$s$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>220</td>
</tr>
<tr>
<td>200 mM Dextran 4</td>
<td>210</td>
</tr>
<tr>
<td>200 mM cellobiose</td>
<td>210</td>
</tr>
<tr>
<td>2M D-glucose</td>
<td>280</td>
</tr>
<tr>
<td>4 M LiCl</td>
<td>460</td>
</tr>
<tr>
<td>500 mM maltose</td>
<td>200</td>
</tr>
<tr>
<td>100 mM maltotriose</td>
<td>190</td>
</tr>
<tr>
<td>100 mM Dextrin 20</td>
<td>150</td>
</tr>
<tr>
<td>50 mM Dextrin 10</td>
<td>140</td>
</tr>
<tr>
<td>100 mM Dextrin 10</td>
<td>130</td>
</tr>
<tr>
<td>100 mM Dextrin 10+ 4 M LiCl</td>
<td>280</td>
</tr>
</tbody>
</table>

* Temperature 318 K; the concentrations of the carbinol and N-ethylmaleimide were 30 mM and 1 mM respectively, and the rates were measured as given in Breslow et al., 1983.
the second order rate constants, due to the hydrophobic effect. The reaction between the two organic (lipophilic) reactants would be accelerated in water, as they are brought into close proximity due to the hydrophobic effect, favouring the formation of the activated complex with great ease. On the other hand, the reaction rates are slower in organic solvents as the solvent molecules would also compete with the reactant molecules, thereby hindering the formation of the activated complex during the cycloaddition. Likewise in aqueous solution, an additive such as LiCl or smaller sugars like glucose, which promote hydrophobic interactions, is expected to accelerate the reaction, whereas additives that weaken them would retard the rate. We have looked at the effect of some sugars on the reaction between the carbinol and NEM. The rate constants of the reaction are given in Table 2.3. While the rate at 45° C in water (without any additive) is $220 \times 10^{-3} \text{M}^{-1} \text{s}^{-1}$, we observe that upon the addition of dextrins the reaction between anthracene-9-carbinol and N-ethylmaleimide is slackened to $<150 \times 10^{-3} \text{M}^{-1} \text{s}^{-1}$. If we suppose $k_{rel} = 1$ with no additive, the values of $k_{rel}$ are estimated as 0.86, 0.68 and 0.60 in 100 mM maltotriose, Dextrin 20 and Dextrin 10 respectively. The rate is unaffected by Dextran 4 and accelerated by 2 M glucose ($k_{rel} = 1.27$) and 4 M LiCl ($k_{rel} = 2.1$). It was also observed that reaction rate for a solution containing both 4 M LiCl and 100 mM Dextrin 10 was in between ($k_{rel} = 1.27$), when compared to the values obtained when the two additives were present separately. This reflects the mutually opposing effects of the two additives clearly. These results suggest that the dextrin chains might weaken the hydrophobic association between the reactant molecules by binding them at its amphiphilic surface, and inhibiting their mutual approach.

2.2.6. Molecular Models of Sugars

The three dimensional structure of polysaccharides is constrained by the glycosidic link geometry and the spatial disposition (axial or equatorial) of the
groups. For sugars that exist in the usual $^{4}C_1$ chair form, the following possibilities have been listed by Atkins (1986). The 1e, 4e-linked chains exist as two- or three-fold extended chains, with polar groups occupying the surface. This would make the 1e, 4e-linked sugars (cellulose, 1e, 4e- or β-D-mannan) simply hydrophilic and not amphiphilic. We have generated the energy minimized conformations of cellotriose on the computer, using the procedure of Rao and associates (Rao et al., 1969; Yathindra and Rao, 1970), using the bond lengths and angles given for D-glucose in the $^{4}C_1$ form (Arnott and Scott, 1972), and find the above feature to be true. Similar calculations on the dextran trimer yield a two-fold crankshaft-like structure which is again not amphiphilic. The 1e, 3e- and 1a, 4e-linked glucosides, on the other hand, are seen to form helical structures with the outer surface different from the inner. We illustrate the structures of the 1e, 4e cellotriose, dextran trimer and dextrin trimer (maltotriose) generated by this procedure in Figure 2.9. The amphiphilic features of the dextran chain are clearly seen. The 1e, 3e-chains from triple helices with a rather inaccessible interior, while the outer face is solvated (Atkins, 1986).

We may conclude that, in general, those chains that can adopt the Type B structure in solution may show amphiphilic character, while those than can adopt Type A, C and D may not. However, in interacting with small molecules, some saccharide chains that adopt the flexible coil form (Type D) may be able to present small or limited regions or subregions of nonpolarity with which lipophilic substrates may interact. It would thus appear that oligosaccharides that can adopt incipient helical structures, particularly of Type B, might display amphiphilicity. This property would be relevant in biochemistry and cell biology to the processes of intermolecular recognition on cell surfaces (between sugars and lipids, glycolipids, proteolipids and proteins at the peripheral and integral regions of membranes), lectin-sugar binding, antigen-antibody interactions, and might be manifested more in
Figure 2.9 The energy minimized conformation of (a) cellulose trimer, (b) dextran trimer and (c) dextrin trimer.
heteromolecular recognition event than as homomolecular self-aggregation; given the sheet-like nonpolar surface in dextrin, once a dimer is formed, the outer surface becomes hydrophilic (dotted with OH groups) and further aggregation would be inhibited by the equally attractive process of hydrogen bonding with solvent water. Homo-aggregation of oligodextrins may thus proceed, not beyond dimers.