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The Aggregated Higher-Structure of 1,3 : 2,4-Di-*O*-benzylidene-D-sorbitol in Organic Gels

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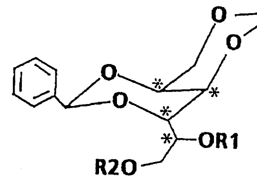
1,3 : 2,4-Di-*O*-benzylidene-D-sorbitol (D-DBS) can cause gelation of organic solvents of a wide range of polarity into a gel state. The aggregated structures of D-DBS/organic solvent systems were studied, mainly by using IR, UV, and circular dichroism (CD) spectroscopy. In the case of the racemate DL-DBS, no gel state was formed. In IR spectra of D-DBS and DL-DBS in the solid state, the intensities of νOH and νCO absorption in D-DBS were found to be larger than those in DL-DBS. It is assumed that the hydrogen bonding formed between an acetal oxygen and a hydroxyl group in the aggregation of D-DBS. From the changes in the IR spectra from solution into a gel state, we can conclude that the chirality and the hydrogen bonding of DBS molecules are essential for the formation of the gel. Comparing the gel-forming ability of D-DBS with its derivatives, 5- or 6-hydroxyl-group-blocked compounds by methyl group, the 6-hydroxyl group seems to be important in the formation of D-DBS aggregates. The results of UV spectra suggest that the benzene rings are ordered in a side by side arrangement. The molar ellipticities in CD spectra increased about 500 times during the change from the solution to the gel state. From these results, it is concluded that D-DBS forms a helical structure of thin fibrous crystals in the gel state.

In studying the chiral oil gelators 12-hydroxyoctadecanoic acid, 1,3 : 2,4-di-*O*-benzylidene-D-sorbitol (D-DBS), *N*,*N*-dibutyl-N^2-dodecanoyl-L-glutamine, and cholesteryl 4-(2-anthryloxy)butyrate (CAB), only D-DBS can convert organic solvents with a wide range of polarity, from heptane to glycerol/DMSO, into a gel form.[1,6,24] It was reported that the racemates of 12-hydroxyoctadecanoic acid and *N*,*N*-dibutyl-N^2-dodecanoyl-L-glutamine did not produce a gel form, but precipitated as crystals.[1,2,6] Tachibana et al. did the pioneering studies on 12-hydroxyoctadecanoic acid,[2—5] and showed that a new hydrogen bond, which could not be observed in the solution state, was formed, and a super-helical structure of 12-hydroxyoctadecanoic acid appeared. Honma demonstrated that the gelator having an amino acid residue formed hydrogen bonds in the gel state and the CD absorption in the gel state was greater than that in solution[1] Lin et al. demonstrated that the structures that CAB formed in the gel state were different depending upon the kinds of solvents, and helical twist structure was observed in a CAB/1-octanol gel.[6] The super-helical structure was believed to be characteristic of the gel state in chiral surfactant-water systems.[6—11] Kunitake et al. have shown that amphiphiles having amino acid residues form a super-helical structure below the gel–liquid crystalline phase transition temperature, *Tc*, and the CD intensities increase in these states.[7] Fuhrhop et al. demonstrated that the gluconamide molecules were aggregated in the super-helical structure using TEM simulation technique,[9,10] and Yanagawa et al. also showed the similar results with DNA derivatives by the same method.[11] The CAB molecules were stacked helically with the anthryl groups overlapping one another by the spectroscopic measurements.[13] In this paper, the aggregated structures of D-DBS molecules in nonaqueous solvents have been studied, mainly using the IR, UV, and CD spectral measurements.

Experimental

Materials. 1,3 : 2,4-Di-*O*-benzylidene-D-sorbitol (D-DBS, **1** in Fig. 1) was purchased from Shin-Nihon-Rika Co., Ltd., and found to be more than 95% pure by NMR. (The main impurity was 1,3 : 2,4 : 5,6-tri-*O*-benzylidene-D-sorbitol.) The sample was used without further purification. The solvents (acetonitrile, 1,4-dioxane, and chloroform) used in this work were obtained from Dohjin-Kagaku Co., Ltd., and dried over molecular sieves. To synthesize DL-DBS (**2** in Fig. 1), L-sorbitol was added to a benzene solution of benzaldehyde (2 molar amounts) and toluenesulfonic acid as a catalyst, and dehydrated for 16 h in the azeotropic condition of benzene and water. After this was cooled down to room temperature, a gel-like product was filtered out and



D-DBS (**1**)	R1=R2=H
DL-DBS (**2**)	R1=R2=H
D-DBS-5-Me (**3**)	R1=Me, R2=H
D-DBS-6-Me (**4**)	R1=H,R2=Me

Fig. 1. Chemical structure of a D-DBS molecule and its derivatives. The signs, * denote the asymmetric carbon atoms.

washed with a 5% NaOH solution. Upon recrystallization from dioxane–hexane mixed solvent, 1,3 : 2,4-di-*O*-benzylidene-L-sorbitol was precipitated out as white powder (yield: 60.7%). The DL form was obtained by equimolar mixing of D- and L-forms. L-DBS: mp 220.1—221.1 °C; IR (KBr) ν 3250, 2872, 1407, 1098, 1050, 735, 696 cm^{-1}; ^{1}H NMR (90 MHz; DMSO-d_6) δ=3.40—3.70 (m, 2H), 3.70—3.98, 4.28 (m, 4H), 4.17 (bs, 3H), 4.43 (bs, 1H), 4.85 (bs, 1H), 5.62 (s, 2H), 7.30—7.55 (m, 10H). Found: *m*/*z* 358.1414. Calcd for $C_{20}H_{22}O_6$: M, 358.1417. To synthesize 5-*O*-methyl-1-1,3 : 2,4-di-*O*-benzylidene-D-sorbitol, L-glucono-1,5-lactone was added to 4 molar amounts of benzaldehyde dimethyl acetal and 0.6 molar amounts of hydrochloric acid, and the solution was stirred at room temperature for 12 h. The product was collected by filtration, and washed with ether and water (yield: 95.8%). To an NaH dispersion in THF, 3,5 : 4, 6-di-*O*-benzylidene-L-gluconic acid and methyl iodide were added dropwise, and the mixture was stirred at room temperature for 30 min. The solution was neutralized by aqueous NH_4Cl, and the product was extracted with $CHCl_3$. After evaporation of the solvent, the crude product of 3,5 : 4,6-di-*O*-benzylidene-L-glucono acid methyl ester was obtained. 3, 5 : 4, 6-di-*O*-benzylidene-L-glucono acid methyl ester was slowly added to a THF solution of $LiAlH_4$ and stirred for 30 min. The mixture was poured into water, and the product was filtered. 5-*O*-methyl-1,3 : 2,4-di-*O*-benzylidene-D-sorbitol (**3** in Fig. 1) was recrystallized from the mixed solvent of dioxane and benzene, and obtained as a while solid (yield: 45.1%). **3**: Mp 219—220 °C; IR (KBr) ν 3370, 2950, 1407, 1335, 1122, 1098, 1032, 735, 696 cm^{-1}; ^{1}H NMR (90 MHz; DMSO-d_6) δ=3.39 (s, 3H), 3.30—4.27 (m, 8H), 4.54 (bs, 3H), 5.67 (s, 1H), 5.72 (s, 1H), 7.30—7.55 (m, 10H). Found: *m*/*z* 372.1573. Calcd for $C_{21}H_{24}O_6$: M, 372.1572. 6-*O*-Methyl-1,3 : 2,4-di-*O*-benzylidene-D-sorbitol (**4** in Fig. 1) was synthesized by the following procedures. To a pyridine solution of 1, 3 : 2, 4-di-*O*-benzylidene-D-sorbitol, 1.1 molar amount of *p*-toluenesulfonyl chloride was added at 0 °C, and the mixed solution was stirred for 2 h. The reaction mixture was poured into water, and the crude product was extracted with $CHCl_3$. Silica-gel column chromatography of the residue afforded a white powder of 6-*O*-methyl-1,3 : 2,4-di-*O*-benzylidene-D-sorbitol (**4** in Fig. 1, yield: 49.3%). **4**: Mp 172.5—174.0 °C; IR (KBr) ν 3472, 2890, 1407, 1032, 741, 696 cm^{-1}; ^{1}H NMR (90 MHz; DMSO-d_6) δ=2.54 (d, 1H), 3.38 (s, 3H), 3.56—3.66 (m, 2H), 3.56—3.66 (m, 2H), 3.76—3.92 (m, 2H), 4.09—4.28 (m, 4H), 5.62 (s, 1H), 5.63 (s, 1H), 7.30—7.55 (m, 10H). Found: *m*/*z* 372.1576. Calcd for $C_{21}H_{24}O_6$: M, 372.1572.

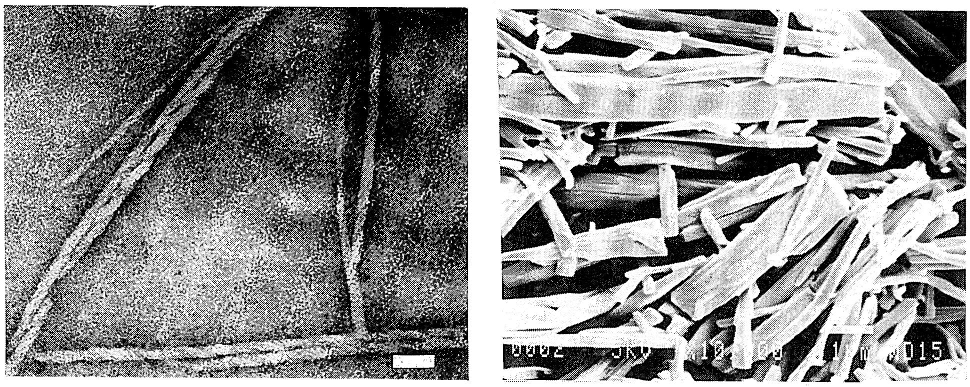
Preparation of Solutions and Gels of D-DBS and It's Derivatives. D-DBS was dissolved in chloroform or acetonitrile or dioxane at 60—100 °C in a concentrations range of 2×10^{-4}—3.0×10^{-1} M, and cooled down to room temperature. The gels were formed at concentrations more than 8.0×10^{-3} M (chloroform), 1.8×10^{-2} M (acetonitrile), and 2.8×10^{-2} M (dioxane). Below these critical concentration, the samples were easily flowable solution states. The D-DBS derivatives (**2**, **3**, and **4**) were dissolved into 1,4-dioxane at 100 °C to 3.5×10^{-2} M, and cooled down to room temperature.

Methods. The IR spectra were obtained by using a JASCO FT-IR 8000, using films between KBr plates for hexachloro-1,3-butadiene dispersion of solid samples and gel and solution samples. Scanning of wavenumber was made from 4000 to 1000 cm^{-1}. The detector was used TGS. The UV absorption measurements were done with a Shimadzu type UV 150-02. The path length of the quartz cell was 0.03 mm. The solvent used in the UV measurements was acetonitrile. The CD spectra were obtained using a JASCO type J-600. The path length of the quartz cells was 0.03 mm in the gel and the solution state. Scanning of wavelength was made from 400 to 200 nm at the speed of 20 nm min^{-1}. The aggregated molecular weight of D-DBS in chloroform and acetonitrile solutions at 2.7×10^{-4} M (below critical gel concentration) was measured by vapor pressure osmometry (VPO), using a Korona type 117 apparatus. The scanning electron microscopy was done with a JEOL type JMS-840. The dried crystals of DL-DBS were used as the SEM samples. Transmission electron microscopic (TEM) observation was done at room temperature on a Hitachi H-7100 electron microscope, operated at 75 kV. For the negative staining method, the dried specimen on a carbon-coated electron microscope grid was negatively stained with 0.7% uranyl acetate solution.

Results

Solution Behaviors of D-DBS, DL-DBS, and Their Derivatives. The D-DBS/organic solvent systems formed gels, but the racemic ones did not show any gelating phenomena and their crystals were precipitated from the solutions. The electron micrographs of the D-DBS gel and DL-DBS crystals in dioxane and shown in Fig. 2. As seen from the figure, the fiber is a rope-like helical structure. The helical sense is right handled. The diameter and helical pitch were about 3.2 and 11.0 nm respectively. The DL-DBS, on the other hand, did not make fibers, but formed platelet-like crystals. The gelating abilities of the 5-methoxy-(**3**), and 6-methoxy-derivatives (**4**) were checked in acetonitrile and dioxane. The 5-methoxy derivative made these solvents into gels, but the 6-methoxy one did not. It formed platelet crystals, as the racemic form did.

IR Spectra. In the infrared spectra of the chiral (D-DBS) and the racemic form of DBS in the crystalline state (Fig. 3), the OH stretching bands were observed at 3350 and 3450 cm^{-1} in the racemate, and at 3250 and 3350 cm^{-1} as a shoulder in the enantiomer. The bands shift to lower wavenumbers in D-DBS from those



D-DBS (1) **DL-DBS (2)**

Fig. 2. Electron micrographs of the D-DBS gel (bar; 10 nm) and DL-DBS crystals (bar; 1 µm) in the solid state.

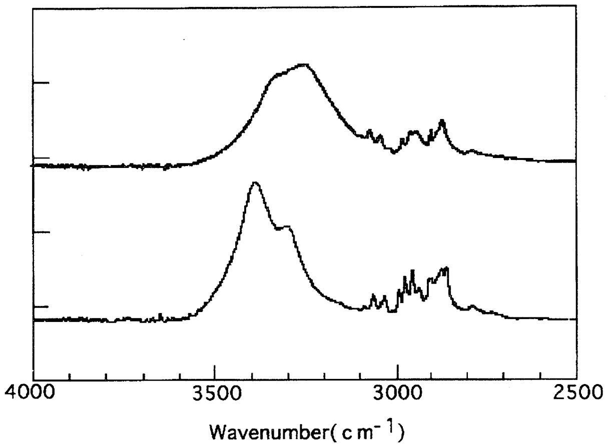


Fig. 3. IR spectra of D-DBS (upper) and DL-DBS (lower).

in DL-DBS. This may indicate that the hydrogen bond is stronger in D-DBS crystals than that in DL-DBS, and then the bond distance of O–H in DL-DBS is longer in D-DBS.[14] Next we evaluated the absorption intensities of νOH and νCO. They are listed in Table 1, and compared in the chiral (D-form) and racemic form of DBS. The data were normalized by the absorption of CH stretching. The intensities of νOH and νCO of D-DBS were stronger than those of DL-DBS. The aggregated structure of D-DBS must be very different from that of DL-DBS. The difference in IR intensities between D-DBS and DL-DBS crystals is, therefore, due to the difference of the dipole moment of these stretching modes in intermolecular coordinates.[19—23] It is considered that the vectors of C–O and OH stretching mode in the D-DBS system, were ordered in linear array more than those in the racemate. The OH and C–O functional groups may be regularly ordered in the enantiomer.[9,12] The IR spectra of D-DBS in the solution state of acetonitrile were taken to give the absorption band of the hydroxyl group, which was detected at around 3600 cm^{-1}, which suggested weak hydrogen bonding between D-DBS and the solvent molecules[2] (Fig. 4). In the gelation process, new absorption band appeared at around 3270 cm^{-1}. This band at 3270 cm^{-1} can be assigned to the hydrogen bonding between D-DBS molecules with each other, because it was observed also in the crystalline form. Roughly speaking, we can see two νOH bands in the gel state. The higher wavenumber can be assigned to the hydrogen bonding between D-DBS and the solvent and the lower one to the D-DBS molecules with each other.

Table 1. IR Intensities of D-DBS and DL-DBS

ν/νOH	D-DBS	DL-DBS	Ratios of increase (%)
νOH/νCH	8.86	3.12	26.9
νC–O/νCH	6.89	2.71	15.1

νOH, νCH, and νC–O denote the absorptions of OH (3270 cm^{-1}), CH (2850 cm^{-1}), and CO (1050 cm^{-1}) stretching respectively.

UV Spectra. UV spectra of the D-DBS solution showed the La transition of benzene ring at 206 nm and the Lb transition at 255 nm.[25] In the gal state, however, the La transition was observed at 206 and 220 nm (Fig. 5). Figure 6 shows the extinction coefficient

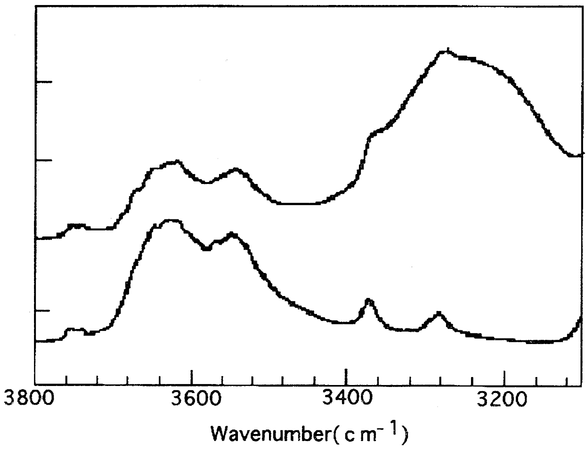


Fig. 4. IR spectra of D-DBS in the solution (lower) and gel state (upper).

at 206 and 220 nm against the D-DBS concentration in acetonitrile. The absorption at 206 nm decreased and that at 220 nm increased during the process of gelation. Once a gel is formed at 1.8×10^{-2} M, the absorption at 220 nm decreased with increasing D-DBS concentration. In the D-DBS/acetonitrile system, the La absorption was red-shifted on gelation and showed hypochromism after gelation.

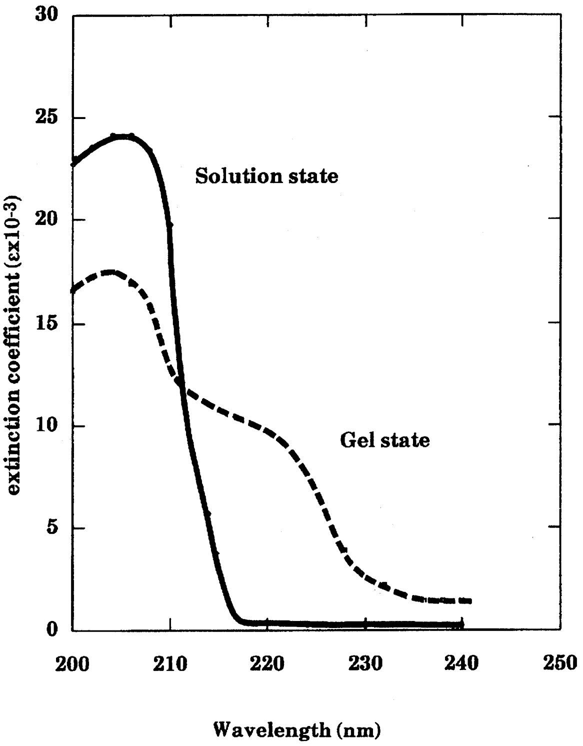


Fig. 5. UV spectra of D-DBS in the solution and gel state.

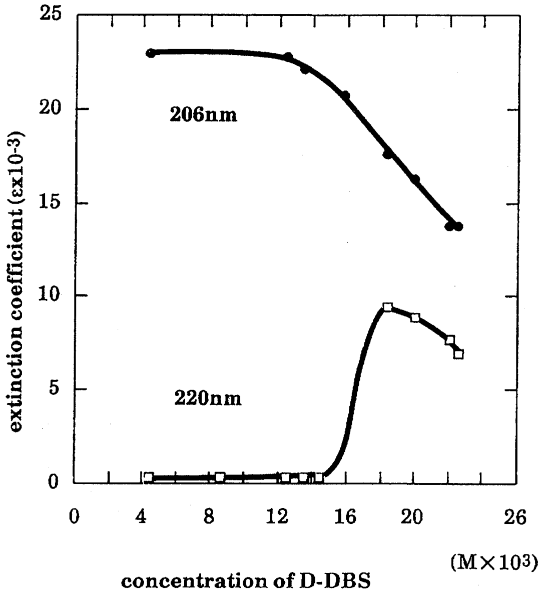


Fig. 6. Molar extinction coefficients of UV absorption at 206 and 220 nm plotted against the D-DBS concentration.

CD Spectra. The CD spectroscopy is one of the most suitable techniques to analyze gel formation and the phase transition from gel to solution in chiral amphiphile/water systems.[17,18] The D-DBS/acetonitrile gel was isotropic between crossed polarizers. The CD spectra observed at 6.6×10^{-3} M and 1.8×10^{-2} M are shown in Fig. 7a and b, respectively. Figure 7a shows the spectrum of the solution state, and Fig. 7b shows those of the gel state. A positive Cotton effect was observed in all the spectra. The wavelength at the absorption maximum shown in Fig. 7a agreed with that in the UV spectra of the solution. In Fig. 7b, the red-shifted La transition reflected at longer wavelengths than 206 nm was observed. The molar ellipticity values $[\theta]_{260}$ are plotted against D-DBS concentration in Fig. 8. $[\theta]_{260}$ values increased dramatically upon the transition from the solution to the gel state. Similar changes were also observed in the chloroform and 1,4-dioxane systems.

Discussion

The Solution State of D-DBS. The molecular weight of D-DBS at the concentration of 2.7×10^{-3} M in acetonitrile was 3.6×10^{2} by a VPO method. This result indicates that the D-DBS is molecularly dispersed in the solution state of acetonitrile. The IR absorption of the hydroxyl group of D-DBS was detected at 3600 cm^{-1}.

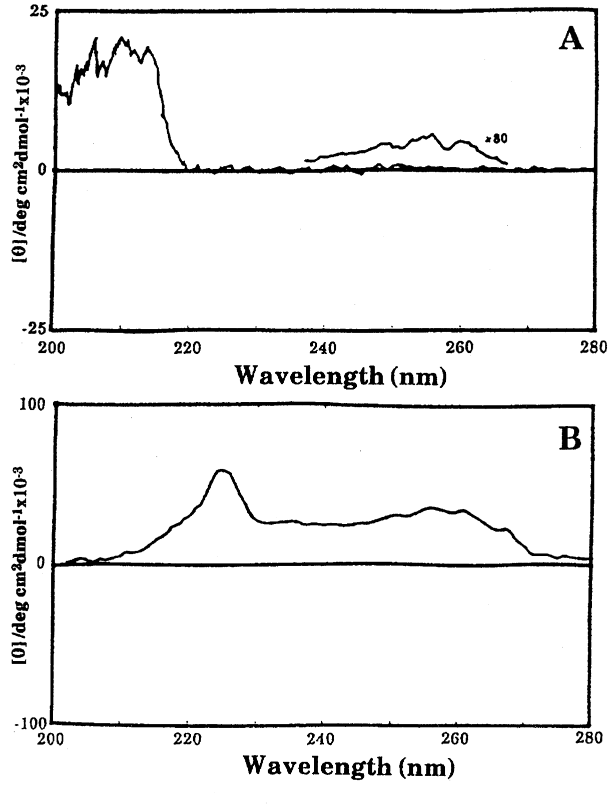


Fig. 7. The CD spectra of D-DBS in the solution (A) and gel state (B).

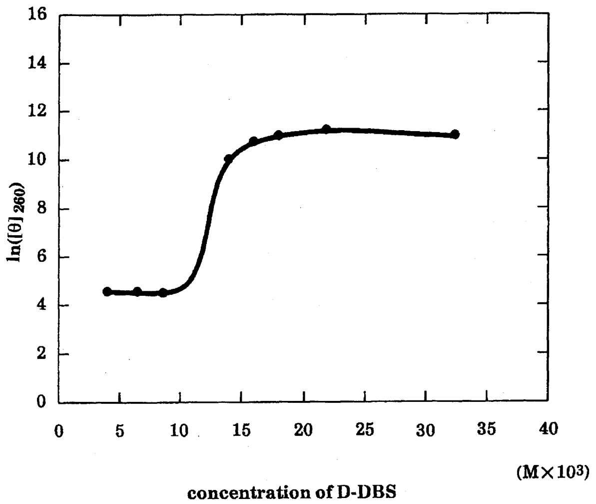


Fig. 8. Plot of the logarithm of the molar ellipticity value at 260 nm ($\ln[\theta]_{260}$) against D-DBS concentration.

The D-DBS molecules make weak hydrogen bonds to the solvent molecules in the molecularly dispersed solutions.

The Formation of Gels. From our experimental results mentioned previously, the following is essential to make the gels in organic solvents: (a) the gelator must be a chiral compound, because D-DBS forms a gel but DL-DBS does not, (b) a 6-hydroxyl group in the D-DBS molecule is essential to form gels, because the 5-methoxy derivative can form a gel, but the 6-methoxy one can't, and (c) the shape of aggregates is very important, because D-DBS formed a helical fiber but DL-DBS did a plate-like crystal. The 6-hydroxyl group in D-DBS molecule must be essential to form the helical aggregates of D-DBS, while the 5-hydroxyl group may just interact with the solvent molecules. When the gelation proceeds, new νOH absorption in IR spectrum appears at 3270 cm^{-1}. This absorption band was similar to that in the solid state, so that the 6-hydroxyl group of D-DBS in the acetonitrile gel may be in a similar hydrogen bonding state to that of the solid state.

The Molecular Assembly of D-DBS in the Gel State. We tried to make clear the aggregated structure of D-DBS molecules in the gel state. We took the following experimental results and the conditions into consideration to construct the structural model of aggregated D-DBS molecules. (a) The helical sense of the fiber observed in TEM measurements, may agree with the sense of the molecular arrangement of D-DBS and the $[\theta]_{260}$ value increased dramatically upon gelation. (b) The 6-hydroxyl group of the D-DBS molecule must be hydrogen-bonded with the acetal oxygen, since the IR absorption due to these two groups changed considerably on gelation. (c) The phenyl groups are ordered in the side by side type arrangement around the axis of the aggregates, because hypochromism was observed in UV absorption.[15,16] The structural model of D-DBS aggregates in the gel state has been obtained after repeated examination, and are shown in Fig. 9. We can reasonably understand from this model that (a) the hydrogen bonding of the 5-hydroxyl group with solvent molecules gave the IR absorption at 3600 cm^{-1} rather than 3270 cm^{-1}, (b) the large enhancement in CD spectra at 260 nm is caused by the formation of the helical structure of the fiber, (c) the red-shift of the La transition occurs because of the breaking of the intramolecular stacking of the benzene rings present in the solution state. We can not say this is the only one correct model, but believe it is the best model that is consistent with all the experimental results.

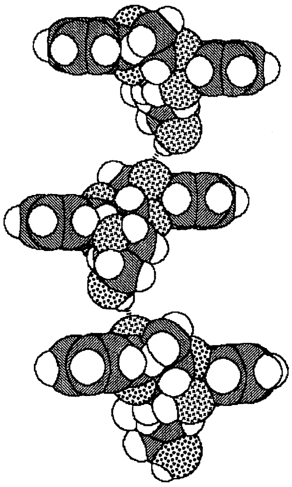


Fig. 9. The structural model of D-DBS aggregates in the gel state.

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