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On the Thickness of Hydrophobic Bilayers

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Abstract: Disk micelles in lyotropic nematic phases have been synthesized with dodecylammonium chloride and with dodecyl-/undecyl-, dodecyl-/decyl-, dodecyl-/nonyl-, and dodecyl-/octylammonium chloride mixtures of relative mole fractions 4:1 in the bilayer micelles. In all these mesophases the head group is the same chemical identity, but the hydrocarbon chain lengths in the mixed micelles are different. A phenomenological model is introduced, which allows the use of degrees of order of C–D bonds in the chains to show that dilution with a shorter chain amphiphile decreases the bilayer thickness by increasing the defects in the all-trans arrangement of the dodecyl chain. The effect of removing each successive segment in the shorter chains is greater the shorter the chain. The model is based on filling the free volume that would be created by the vacancy between the bilayer center and the end of the short chains. The control of bilayer thickness by the mix of chain lengths of amphiphiles is an important aspect in the biological membrane where conformation to critical distances for protein inclusion is a factor.

Introduction

Disk-micelle nematic phases are derived from lamellar phases which have one degree of positional order.[1-4] The disk-bilayer micelles are large compared to molecular dimensions, and the nematic character of the system arises from the long-range orientational order of the micelle disks.[5] The bilayers in the large disk micelles behave in exactly the same manner as the bilayers in the lamellar phases.[2] The degree of order profiles of the aliphatic deuteriocarbon chains are affected at each segment by a constant factor which can be accounted for in the additional freedom of motion of the finite micelles, a motion not present in lamellar systems. Lamellar phases have proven to be excellent models for the biological membrane matrix and are widely used[6-9] for this purpose. Equally viable are the disk micelle mesophases, which can be regarded as planar bilayers, which range in size, depending on chemical content of the mesophase,[10] from $\approx$500 to 2000 Å or so in diameter.[5,10,11] One importnt aspect of bilayer chemistry, in the so-called fluid state,[12] is an estimate of the bilayer thickness. This is undoubtedly critical in the problem of conforming to protein inclusions, the study of which is still in its infancy.[13] The repetition in the positional order of multibilayered systems has been studied by low-angle X-ray diffraction,[14] and from this with a few minor assumptions the thickness can be determined for the hydrophobic plus head group region. The assumptions involve the density of material and how it varies within the repeat distance of the lamellar phase.[15] The low-angle X-ray studies of the disk-bilayer nematic systems give an estimation of the bilayer thickness including all that is adsorbed on the interface, such as counter- and co-ions as well as water.[5] The observed thickness of the bilayer in such measurements is much too large even for all-trans aliphatic chains,[6] and this implies an adsorbed layer. Seelig and co-workers[16] have used spin-labeled α,ω difunctional amphiphiles to detect a spanning conformation, and this information can be used to obtain the thickness of the hydrophobic part of the bilayer by counting segments. In later studies, this group estimated the bilayer thickness and its temperature dependence from the degree of order profile, obtained from deuterium magnetic resonance.[17] Reeves and co-workers[18] have used per- and α-deuterated α,ω difunctional amphiphiles to study the thickness of the hydrophobic part of the disk-micelle bilayers in the nematic systems.[18,19]

The present study follows a recent paper[20] in which changes in bilayer thickness were detected by their effect on the relative degree of order profile of a common amphiphile in the disk micelles of two nematic phases. The survey of many pairs of systems showed that this method was very sensitive to the hydrophobic bilayer thickness. The changes in thickness can be systematically studied by the synthesis of disk micelles from two or more amphiphiles which differ in chain length and their relative concentrations varied. At one extreme of concentration the bilayer thickness conforms to the longer chain and at the other, the shorter. In view of the important translation of these studies into biological terms, where thickness must conform to protein inclusions (such events as anesthesia result from membrane phenomena), this work encompasses a series of bilayers which have a common "head" group but differ only in chain length of the amphiphile. It is possible to derive a measure of the change in bilayer thickness provoked by chemical compositions in the micelle based on the accepted model of order profiles published by Seelig and coworkers.[17] An extension of the order profile model[17] can be addressed to the problem of bilayer thickness, and this study is directed to this end.

Experimental Section

New lyotropic nematic phases based on disk micelles were synthesized from dodecylammonium chloride. The decylammonium chloride mesophase has been well studied[21] and behaves macroscopically in every way similar to the nematic systems studied in this work. They are type II DM $\Delta\chi < 0$ and align rather rapidly in the magnetic field. The mesophases also spontaneously align in about 0.5 h in the absence of a magnetic field to give a dark field, which is independent of the angle of rotation of the stage of the polarizing microscope. The stable arrangement with respect

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Table I. Phase Compositions (moles)[a]

	phase				
	12 Acl	11 Acl	10 Acl	9 Acl	8 Acl
host					
12 Acl	0.711	0.712	0.711	0.698	0.708
12 Acl perd	0.088	0.089	0.088	0.087	0.088
guest					
12 Acl	0.021				
11 Acl		0.199			
10 Acl			0.201		
9 Acl				0.215	
8 Acl					0.204
NH_4Cl	0.091	0.180	0.360	0.672	1.311
H_2O	42.12	42.20	42.11	41.38	41.96

[a] The first column classifies the mesophase. The compositions are all quoted in moles of compound normalized to 1 mol of total detergents. 12 Acl and 12 Acl perd are dodecylammonium and perdeuterated decylammonium chloride, 11 Acl, 10 Acl, 9 Acl, and 8 Acl are the undecyl-, decyl-, nonyl-, and octylammonium chlorides. The total moles of detergents = 1, while the guest short chain ammonium chlorides are all close to 20 mol % in the bilayer of the disk micelles. The 100% dodecylammonium chloride based mesophase is separated as though 20 mol % of it was a guest in an identical host bilayer. The electrolyte content is adjusted successively higher with the short-chain guests, in order to preserve the integrity of the type II DM liquid crystal. The perdeuterated dodecyl chain was 44% deuterated in the α position and 25% in the rest of the chain. The pH of the H_2O was maintained by HCl to be 1, and 0.5% D_2O was added to give a clear water doublet in the deuterium spectra.

to a glass interface therefore occurs with the optic axis perpendicular to this interface and the process of achieving this state is greatly accelerated (in a few seconds) by applying a magnetic field of 14 kG in the plane of the microscope slide. These observations are proof that the new nematic systems are type II DM.[22,23]

Octyl-, nonyl-, decyl-, undecyl-, and dodecylammonium chlorides were prepared from the corresponding amines (Aldrich) by adding hydrochloric acid to an ethanolic solution of the amine. After removing the solvent on a Roto-Vac, the products were recrystallized several times from petroleum ether (60–80 °C)/chloroform mixtures in the case of the octyl and nonyl compound and petroleum ether (60–80 °C)/ethanol for the decyl, undecyl, and dodecyl compounds. Perdeuterated dodecylammonium chloride was synthesized from the laboratory stock of lauric-d_{23} acid.[24] The perdeuterated lauric acid was treated with thionyl chloride to yield the acyl chloride. The lauroyl chloride was then treated at 0 °C with a concentrated ammonia solution to yield lauramide.[25] The lauramide was then reduced to lauramine by treatment with lithium aluminum deuteride in ether.[26] The deuterated amine product was diluted with the protonated material and converted to dodecylammonium chloride as above. The preparations of nematic mesophases has been adequately described.[27] The first object of the study described here was to prepare and characterize a new series of type II DM nematic phases in which the disk micelles had a composition of 20 mol % short-chain amphiphile and 80 mol % of a host amphiphile (dodecylammonium ion). The guest-chain amphiphiles were of successively shorter length in the order: undecyl-, decyl-, nonyl-, and octylammonium ion. All the amphiphiles in the bilayer had a chemically identical head group, and consequently the interface region of the micelle remained chemically the same as that in a mesophase prepared from dodecylammonium chloride. In having chemical homogeneity at the micelle interface, such properties as the area of the head group remain constant in the mixed disk micelles. Some small adjustment of the electrolyte concentration was necessary in order to achieve the correct nematic type II DM structures. The effect of simple electrolytes is to cause a growth in the average micelle size,[11] but there is no change in the degree of order profiles of the aliphatic chains immersed inside the micelle,[10] indicating that area per surfactant head group does not alter. The compositions of the mesophases is listed in Table I. In each phase a small fraction of the host chains was perdeuterated and the degree of order profile of these chains was extracted from measurements of the quadrupole splitting of the deuterium magnetic resonance. The nuclear magnetic resonance spectra were obtained using the Bruker WH400 at the South West Ontario NMR facility. The probe temperature was 30 ± 1 °C. The concentration of deuterated chains was arranged so that good signal to noise was obtained in less than 15 min. Some aging of the samples for a day or so improved the quality of the spectra with respect to line widths; this process is not understood. Alignment in the 94-k G field of the spectrometer was rapid enough that only a minute or two was necessary before spectral information could be collected. Temperature is an important factor, leading to some frustrating journeys to the South West Ontario NMR Center, but this was overcome by checking that the phases did not go isotropic or separate into two phases, by changing either probe temperature to suit preparation lab temperature or the reverse. Samples were finally studied at a probe temperature of 30 °C.

Figure 1. Deuterium magnetic resonance spectrum of type II DM mesophase prepared from the pure host detergent dodecylammonium chloride. The mesophase composition is recorded in Table I. The high-field spectrum is assigned according to the carbon segment in the chain. Extensive overlap occurs for positions 2–8 because of a long plateau of order in the profile. Since the shortest guest added is the octyl chain, the positions which are important, 9–12, do show a clean resolution on the dodecyl chain. The sharp doublet at the center of the spectrum belongs to the DOH signal.

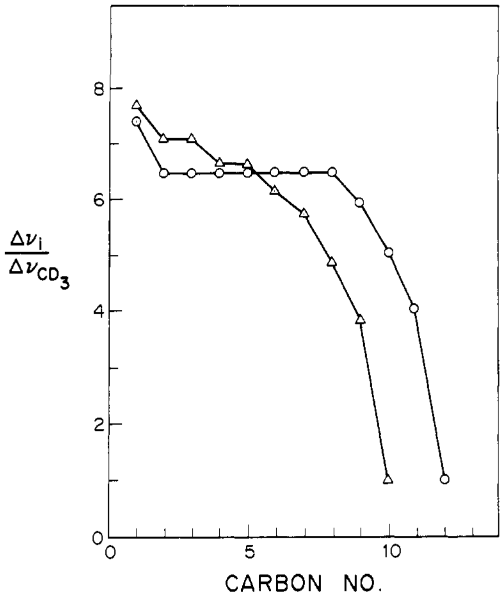

Figure 2. Comparison of the degree of order profile of decylammonium and dodecylammonium chains in type II DM mesophases. The decylammonium results were obtained earlier. The profiles are plotted according to the ratio method of eq 5 of the text, so as to enable the direct comparison of the trans/gauche intrachain motions.

Results

A typical deuterium magnetic resonance spectrum for the perdeuterated dodecyl chain in a nematic phase at 30 °C is reproduced in Figure 1. The assignments are found above each quadrupole doublet, and other details are given in the legend. In Figure 2 the relative degree of order profile of the dodecyl chain in disk micelles of an uncontaminated mesophase, prepared from 100% dodecyl detergent, is reproduced. The relative degree of order profile, expressed as ratios of deuterium quadrupole splittings of successive segments to the terminal methyl, are a means of

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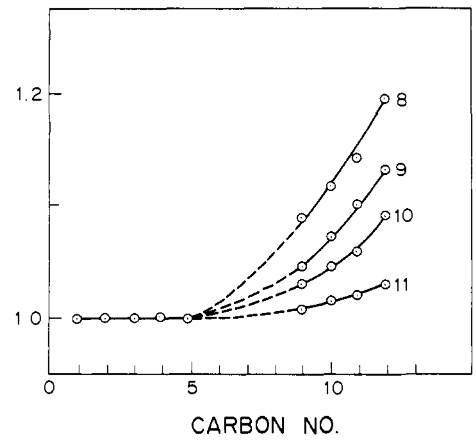

Figure 3. Comparison of the bilayer thickness for a mesophase with guests, with the mesophase prepared from pure dodecylammonium chloride according to the procedure of ref 20. The ordinate function is the normalized segment order ratios ($\Delta\nu_i^{\alpha}/K_{\alpha\beta}\Delta\nu_i^{\beta}$) for two phases α and β. $\Delta\nu_i^{\alpha}$ is the quadrupole splitting of segment $CD_2 = i$ in the pure dodecylammonium bilayer and $\Delta\nu_i^{\beta}$ is the same quadrupole splitting in the bilayer with 20% of a shorter chain guest. The four curves numbered 8, 9, 10, and 11 serve to identify the alkyl chain length of the alkylammonium guest. $K_{\alpha\beta}$ is the normalization factor[20] based on the ratio of quadrupole splittings in the first and unperturbed segment of the dodecyl chain in the same two phases. This corrects for such extraneous factors as the difference in micelle size in the two bilayers which are compared. The segment number i is plotted as the abscissa.

eliminating the effects of all whole-body chain motions which cancel in the ratio.[4,10,24] Figure 2 also shows, for comparative purposes, the degree of order profile ratios of the decyl chain in type II DM nematic systems prepared from the pure decylammonium chloride micelles.[21,28,29] The plateau region of uniform degree of order of the C–D bonds is much more developed in the dodecylammonium chain, which, also having a smaller ratio of order for the first five segments, is less defective in kinks, jogs, and single gauche rotations.[6,17] The long plateau of equal order from segments 2 to 8 creates, in principle, a problem in distinguishing very small changes in relative order in segments 6–8 which probably occur when shorter chain guests are added. The major changes in relative order occur in segments 9 to 12 when short-chain guests are added, and failure to detect the very small changes at positions 6–8 does not affect the conclusions of this paper. The recent study of relative changes in bilayer thickness in two disk-micelle systems[20] can be applied to the present results. Figure 3 gives the plot of normalized segment order ratios for the present investigation for each of the pairs of mesophases: 100 mol % dodecyl/20 mol % undecyl, 80 mol % dodecyl; 100 mol % dodecyl/20 mol % decyl, 80 mol % dodecyl; 100 mol % dodecyl/20 mol % nonyl, 80 mol % dodecyl; 100 mol % dodecyl/20 mol % octyl, 80 mol % dodecyl. The normalized segment order ratios have been defined[20] as:

$$\frac{(S_{\text{exptl}})_i^{\alpha}}{(S_{\text{exptl}})_i^{\beta}} \Big/ (K_{\alpha\beta})_i = \frac{(S_{\text{k/j}})_i^{\alpha}}{(S_{\text{k/j}})_i^{\beta}} \qquad (1)$$

$K_{\alpha\beta}$ is the ratio of degrees of order for the dodecyl chain in mesophase α and mesophase β, which are observed for the initial four or five segments and therefore unperturbed when the 20% shorter chain guests are added.[20] For the systems under study, the dodecyl chain profile does not allow a good determination of the above segment order ratios because of overlap of the quadrupole splittings in the segments 6 to 8, but the figure shows that these changes are quite small by interpolation. $(S_{\text{exptl}})_i^{\alpha}$ and $(S_{\text{exptl}})_i^{\beta}$ are the observed experimental quadrupole splittings in segments i for positions 8–12 in the chain in the standard phase α made from pure dodecyl chains and for β from the composite mesophases prepared from 80% dodecyl chains and 20% shorter chains in the micelles. The normalized segment order ratios are a measure of the relative degree of order arising from the trans/gauche rotations $(S_{\text{k/j}})_i^{\alpha}/(S_{\text{k/j}})_i^{\beta}$ of a given segment i on the same amphiphile in two mesophases, where the bilayer thickness may be different. This ratio is always 1 for all segments if the micelle composition is not changed between phase α and phase β, that is, if extra micellar components only are varied, such as alkali metal ions, co-ions, or water content.[10,20] The quadrupole splittings measured for the dodecyl chain in the mesophases studied here are given in Table II.

Table II. Quadrupole Splitting ($\Delta\nu_D$, Hz) of Deuterium Measured for the Dodecyl Chain in Pure and Mixed Mesophases[a]

	phase				
	12 Acl	11 Acl	10 Acl	9 Acl	8 Acl
C_1	11556	10269	10719	9178	17326
C_{2-8}	10098	9048	9430	8026	15068
C_9	9239	8156	8316	7019	12695
C_{10}	7843	6866	6963	5798	10521
C_{11}	6324	5501	5547	4562	8285
C_{12}	1556	1343	1323	1091	1953

[a] The first column lists the carbon segment numbers in the chain, C_1 being the first $-CD_2-$ group and C_{12} being the last. The mesophases correspond to those whose compositions are listed in Table I.

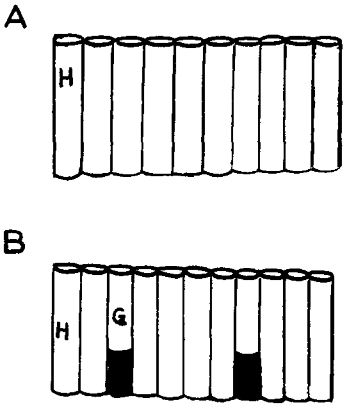

Figure 4. To illustrate the proposed model for decreases in bilayer thickness with the addition of shorter chain guests "G" to dilute the host "H". A is a representation of the homogeneous half-bilayer of a pure dodecyl chain mesophase. The chains are confined to a mean volume equal to the area of their head groups times their mean length. This is represented as a cylindrical shape. In B the host chains "H" of 12 carbons in length are diluted by guest chains "G" of different lengths. Should the bilayer of host chains not change, the black regions below the short chains will become empty volume. The area of all head groups (cross sections of cylinders) in the present experiment is the same for guest and host. The empty volume is filled by further increasing the defects of the dodecyl chain from the all trans arrangement which leads to a contraction of the half-bilayer distance.

Discussion

Prior studies of the degree of order profile for the same amphiphile in pairs of disk-micelle mesophases[20] were used to compare the bilayer thickness, but the other micelle components were not controlled so as to give a chemically homogeneous head group interface to the micelle entities. The present investigation rectifies this defect so that a more extensive model of the micelle interior can be employed. In 17 pairs of mesophases the normalized segment order ratios clearly showed the sensitivity of the terminal segments of the chain in the interior of the micelle to the accommodation in the bilayer thickness parameter.[20] A model is now developed to extend this concept to quantify this relative change in bilayer thickness. Figure 4 illustrates the proposed model. The surface area at the interface required by the ionic or polar head group is designated as A. If the guest amphiphile does not have a chemically identical head group, the guest and

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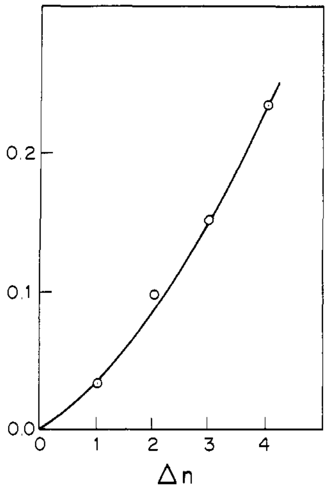

Figure 5. A plot of the summation term (ordinate) $\sum_i\{[(\Delta\nu_i)_{ng}/(\Delta\nu_1)_{ng}] - [(\Delta\nu_i)_{wg}/(\Delta\nu_1)_{wg}]\}$ vs. the value of Δn. See eq 15 of text.

host may have different areas A_2 and A_1. The model differs in no great respect if this is the case, but we shall proceed for the present case, where the areas are equal. The hydrocarbon chain is confined in the model, to a cylinder of cross section A and length L, where this is the pseudo-extended length to include the usual chain defects such as kinks, jogs, etc., up to the bilayer center. The chain is rotating rapidly about its long axis. The pure uncontaminated bilayer of dodecyl chains is changed by the insertion of shorter chains such as octyl → undecyl, depending on the case considered. There is now created in the bilayer vacant space between the end of the shorter chains and the bilayer center. This vacant space is now filled by increasing the chain defects in the host dodecyl chain, which as a consequence become shorter and cause a contraction of the bilayer thickness. The length of a pseudo-extended aliphatic chain in a bilayer has been given by Seelig[17] as:

$$\langle L\rangle = \sum_{i=1}^{n}\langle l_i\rangle = l\left(12 - 0.5\sum_{i=1}^{12}P_{Bi}\right) \qquad (2)$$

$\langle l_i\rangle$ is the mean length of the segment i in a pseudo-extended chain; l is the full length of an extended segment (1.25 Å); P_{Bi} is the probability that the segment i is inclined at an angle 60° to the pseudo-extended chain axis.[17] The factor 12 arises because of the 12 segments for the 12 carbons of the dodecyl chain. The value of P_{iB} is given by[17]

$$P_{Bi} = (1 - S_0S_i)/1.125 \qquad (3)$$

S_i is the degree of order along the chain axis of segment i. Seelig[17] has pointed out that the degree of order of all segments in a chain are uniformly reduced by a factor S_0, estimated for dipalmitoyl lecithin bilayers at 0.7 to 0.8 in lamellar systems.[6,30] When this factor is applied to S_i, the bilayer thickness calculated essentially agrees with X-ray diffraction values. In the present study a relative measure of bilayer thickness is sought; consequently, the factor S_0 is introduced, because it is unknown in the disk-micelle systems. In the type II DM systems, it has been shown that S_{exptl}, the measured degree of order at any segment i,[4,10,20] is given by:

$$(S_{exptl})_i = -\tfrac{1}{2}S_{diff}S_{MO}S_{CO}(S_{k/j})_i \qquad (4)$$

The experimental degree of order of i is given by a product of degrees of order associated with whole-chain diffusion S_{diff}, micelle oscillation S_{MO}, whole-chain oscillation S_{CO}, and the effect of trans/gauche motions at segment i. The important factor specific to segment i is the trans/gauche motion which is taken care of in (2) and (3), and we can identify $(S_{k/j})_i$ with S_i in eq 3. Since motions of the chain as a whole affect every segment equally within a given mesophase, we can write

$$(S_{exptl})_i/(S_{exptl})_j = S_i/S_j \qquad (5)$$

from (3) and (4) for two segments i andd j of the same chain. Equation 3 may be rearranged and taken as the ratio of degrees of order in two segments i and j.

$$\frac{S_i}{S_j} = \frac{1 - 1.125P_{Bi}}{1 - 1.125P_{Bi}} \qquad (6)$$

If $j = 1$ for the first segment of a dodecyl chain, then we assume that P_{B_1} has a constant value independent of the mesophase within the systems under study. Equation 6 takes the form:

$$\frac{S_i}{S_1} = \frac{1}{K}(1 - 1.125P_{Bi}) \qquad (7)$$

where K is a constant value. Within the situation of chemically homogeneous head groups, this added assumption is not an unreasonable one.

The volume occupied by the dodecyl chains is the head group area of the NH_3^+ group times the average length $\langle L\rangle$ of the chains. The change in length of the dodecyl chain, which is the host amphiphile, may be taken as the change in the half-bilayer thickness. Let us call this $\langle\Delta L\rangle$:

$$\langle\Delta L\rangle = \langle L\rangle_{ng} - \langle L\rangle_{wg} \qquad (8)$$

where $\langle L\rangle_{ng}$ is the length of the chain with no guest in the micelle and $\langle L\rangle_{wg}$ is the length of the dodecyl chain with a 20 mol % inclusion of a shorter chain ammonium chloride in the micelle. Using expressions 2, 3, and 5 with $S_j = S_1 = 1$, we obtain:

$$\langle L\rangle_{ng} = l\left\{12 - \frac{0.5}{1.125}\sum_i\left[1 - K\left(\frac{S_i}{S_1}\right)_{ng}\right]\right\} \qquad (9)$$

where $(S_i/S_1)_{ng}$ is the relative degree of order of segment i compared to S_1 in a dodecyl chain embedded in a pure dodecyl chain bilayer micelle. Correspondingly

$$\langle L\rangle_{wg} = l\left\{12 - \frac{0.5}{1.125}\sum_i\left[1 - K\left(\frac{S_i}{S_1}\right)_{wg}\right]\right\} \qquad (10)$$

where $(S_i/S_1)_{wg}$ is the relative degree of order of the ith to first segment in a dodecyl chain for a micelle bilayer with a short chain guest at a concentration of 20 mol %. It is presumed that the value of P_{B1} for the dodecyl chain is the same whether it be in the pure dodecylammonium bilayer or in a bilayer with 20 mol % of a shorter chain alkylammonium guest. This presumption is justified by the result in the previous studies, where different bilayers of different composition are compared using a common amphiphile.[20] The value of K is therefore the same in eq 9 and 10. Thus, now:

$$\langle\Delta L\rangle = \frac{lK}{2.25}\sum_i\left[\left(\frac{S_i}{S_1}\right)_{ng} - \left(\frac{S_i}{S_1}\right)_{wg}\right] \qquad (11)$$

The ratio of experimental degrees of order may be replaced with ratios of corresponding quadrupole splittings observed in the experiments.

$$\langle\Delta L\rangle = \frac{lK}{2.25}\left\{\sum_i\left[\frac{(\Delta\nu_i)_{ng}}{(\Delta\nu_1)_{ng}} - \frac{(\Delta\nu_i)_{wg}}{(\Delta\nu_1)_{wg}}\right]\right\} \qquad (12)$$

If we assume there is no change in the volume occupied by 1 mol of dodecyl chains in the pure and contaminated bilayers, then:

$\langle\Delta L\rangle A$ = volume of the vacant space created at the end of the 0.2 mol fraction short chains (13)

Since free volume is an odious aspect of fluid systems, this assumption has a general application. The solution in the micelle will no doubt behave as an ideal solution where there is no volume change on mixing (for long-chain hydrocarbons). The volume of vacant space, which is filled by creating more defects in the dodecyl chains, can be approximated as the moles of short chain per mole of dodecyl times the same head group area times the

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(30) J. Seelig and W. Neiderberger, *J. Am. Chem. Soc.*, **96**, 2069 (1974).

shortage of length to fill the space or:

$$x_g A(\Delta n)l = \text{volume vacant space} \qquad (14)$$

x_g is the number of moles of guest per mole of dodecyl chain; $\Delta n = (12 - n)$, where n is the number of carbons in the guest chain length. Using (11) and (12) with (10), we obtain:

$$\frac{K}{2.25}\left\{\sum_i\left[\frac{(\Delta\nu_i)_{ng}}{(\Delta\nu_1)_{ng}} - \frac{(\Delta\nu_i)_{wg}}{(\Delta\nu_1)_{wg}}\right]\right\} = \Delta n x_g \qquad (15)$$

Δn does not contain information about the defects in the shorter chain, which is also not an all-trans chain. A satisfactory plot (Figure 5) of the summation term on the left-hand side of eq 15 against the assumed Δn reveals that the basic model of avoidance of free volume in bilayers is a determining factor in the resultant bilayer thickness. The simple proportionality of eq 15 is not precisely followed because Δn is not really an integer as we have assumed. It is evident, however, that the shortening by one segment has the smallest relative effect as would be expected. The decrease in bilayer thickness increases with the shorter and shorter guest chains.

This result has important consequences in biological bilayers since lipids such as cholesterol have not only a stiffer backbone, a point previously discussed, but also a shorter length than most other lipids. This, along with other heterogeneities in length of lipid chains in the biological mix, can be a useful factor in accommodation to the required conformation to local protein inclusions of the bilayer thickness.

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Electron-Transfer Reactions and Associated Conformational Changes. Electrochemical Reduction of Some Vicinal Dibromides

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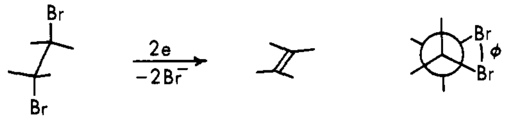
Abstract: The effect of molecular conformation on the electrochemical reduction of derivatives of *trans*-1,2-dibromocyclohexane (**1–4**) and substituted 1,2-dibromoethanes (**5–8**) has been investigated by low-temperature cyclic voltammetry. Reduction via conformations with antiperiplanar bromine atoms is preferred and conformational interconversion prior to electron transfer was observed in *trans*-1,2-dibromocyclohexane (**1**), 1,1-dimethyl-*trans*-3,4-dibromocyclohexane (**2**), *meso*- and *dl*-1,2-dibromo-1,2-diphenylethane (*meso*-**5** and *dl*-**5**), and 2,3-dibromo-2,3-dimethylbutane (**8**). Digital simulation of the low-temperature voltammetric data has provided thermodynamic and kinetic information on the conformational interconversion in **1**, **2**, **5**, and **8**. The energy barriers to conformational interconversion in *meso*- and *dl*-2,3-dibromobutane (*meso*-**6** and *dl*-**6**) are quite small, and conformational effects in the electrochemical reduction of **6** could not be detected at temperatures as low as −135 °C. 1-Methyl-*cis*-3,*trans*-4-dibromocyclohexane (**3**), 1-methyl-*trans*-3,*cis*-4-dibromocyclohexane (**4**), and *meso*- and *dl*-3,4-dibromo-2,5-dimethylhexane (*meso*-**7** and *dl*-**7**) exist almost entirely in a single conformation. Voltammetric peak potentials of **3**, **4**, *meso*-**7**, and *dl*-**7** reflect the geometry of their principal conformation.

In the past 10 years, direct experimental evidence has indicated that in certain cases there is a distinct structural arrangement of either the product or reactant which is preferred in an electrode reaction. Conformational effects may be manifested prior to electron transfer, following electron transfer, concurrently with electron transfer, or some combination of all three. If these effects are to be observed by modern electrochemical methods, the electrode reactions of different conformers (or isomers) must occur at potentials different enough to be resolved by these methods. This dissimilarity in potential can have a thermodynamic basis or be caused by differences in rate constants for the heterogeneous electron-transfer reactions or coupled chemical reactions of the conformers.

Examples of structural rearrangement prior to electron transfer have been found in cases where two different conformations react at an electrode at distinctly different potentials.[1,2] The electrochemical reaction will proceed via the more readily reduced (or oxidized) conformer. The most prevalent cause of different molecular conformations exhibiting separate electron-transfer processes is an acceleration in the rate of the electron-transfer reaction for a particular geometry.

Scheme I



Conformational changes have also been observed to occur following electron transfer. Most commonly reaction of a principal conformation (or isomer) at the electrode produces a short-lived intermediate which undergoes structural rearrangement to a preferred geometry. Many examples of electrochemically induced isomerizations have been reported for activated olefins[3] and or-

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