Comparison of Experimental and Theoretical study of Solvent effect on Interfacial head group and hydrocarbon chains of DPPC molecule.

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ABSTRACT

The bilayer's lipids head groups and hydrocarbon chains affect solvent transport activity.The dielectric constant of solvent can affect both of these interfacial regions. The present article will focus on the effects of solvents on DPPC, 1, 2 - dipalmito l- sn - glycero - 3- phosphatidylcholine, as an important component of lipid membrane and its head group. We could detect and effectively mimic a ten-dielectric model for conformational analysis, in which the obtained results on DPPC compared with its head group results. The effect of solvents on the conformation and disordering of DPPC molecule has been investigated with calculation at the Hatree-Fock level using the 6-31G basis set with Onsager continuum solution, Frequency and GIAO models. Furthermore, the simulated model in solvents was confirmed experimentally by solution nmr technique. Results show that some of the obtained results on DPPC and its head group were different obviously. On the other hand hydrophobic force in tail group caused most atoms to show ordinary constant behavior.And high disordering in main transition temperature was shown for head group region. Therefore, the hydrophobic interaction of solvent partitioning into DPPC is the predominant force involved in DPPC packaging and has the most effect on dielectric constant and also it's totally related to temperature.

INTRODUCTION

The solvents of biological media and interactions between solvents and phospholipids are applied to explain membrane structure. It is theoretically proved that mobility in lipid membranes can be modified by a dielectric environment[1].

This effect is often dictated by the mobility of charge carriers[2, 3]. Therefore, influences of solvents are far from negligible. Phospholipids are a particularly interesting group of molecules because they serve multiple purposes in living organisms responding selectively to solvents across membranes. The most common biological lipids one encounters in studies are glycerol-backbone lipids like DPPC which is predominantly found in animal cell membranes[4]. On DPPC molecular level it has been of interest to explore to what extent molecular conformations, lateral interactions and dielectric constant affect the properties and topology of the membrane surface. DPPC molecule can exist in different phases in membranes[5]. And transition from one phase to another can be detected by physical techniques as the temperature is increased. The most consistently observed of these phase transitions is the one occurring at the highest temperature when the membrane passes from a tightly ordered 'gel' or 'solid' phase, to a liquid-crystal phase at raised temperatures where the freedom of movement of individual molecules is higher [6]. Many techniques such as esr spectroscopy, x-ray diffraction, ir/raman spectroscopy have been used to study specific bilayer properties e.g. tail dihedral gauche-defects and phase transition studies by differential scanning calorimetry (DSC)[7]. In some phospholipid structures, however, studies are limited to measurement of the transition temperature and the effect of solvents. Therefore, studies on this model considers phospholipid function

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when exposed to different solvents and specifies selective solvents across membrane.

There are many studies on various factors that affect phospholipid headgroup[8] including temperature, pH and phospholipid concentration[9] which all affect the effective phospholipid shape or the phospholipid/water ratio and, thus, the geometry of the structure by which the alkyl chains become best removed from water[10]. These are based on changes in headgroup conformations and depend on the solvent character. But the most important characteristic of phospholipids can clearly be seen simply by looking at the molecular structure: it consists of a polar part and an apolar part. More importantly, the polar part is hydrophilic in nature whereas the apolar part is hydrophobic. Therefore, a combination of electrostatic and hydrophobic interactions is important in many other processes in (bio) chemistry. This study focuses on the localized structural changes induced by a series of solvents in DPPC headgroup compared with the whole molecule. Our goal in this study is to investigate the effect of hydrophobic force of hydrocarbon chains on alteration of conformation and ordering of DPPC molecule that lead to different behavior of headgroup of molecule during exposure to changing dielectric constant. Furthermore, Temperature has a strong effect on lipid structure and stability. In the present work we have extended our model to explore the effects of the polarity of the environment on the headgroup minimum energy conformations and relate the results with the temperature changes, enthalpy, entropy and Gibbs free energy. To this aim, we discuss the effects of dielectric constant of chemical solvents on DPPC by using *ab initio* method at constant pressure of one atmosphere. Recent enhancements in computing power and storage capacities, as well as in computational methods, have led to a rapid evolution in the field of *ab initio calculations*[11, 12]. The effect of solvents on the conformation and disordering of DPPC molecule has been investigated with calculation at the Hatree-Fock level using the 6-31G basis set with Onsager continuum solution, Frequency and GIAO models. The simulated model in solvents was confirmed experimentally by solution nmr technique.

Computational method and theory-

Ab initio calculations: the GAIO method and Solvent model

All the compound geometries were fully optimized at the RHF/6-31G level of the theory. This procedure was followed both in the gas-phase and solvent phases and also using the simple Onsager cavity solution model (SCRF). The solvent effect was calculated using SCRF model. According to this method, the total energy of solute and solvent, which depends on the dielectric constant, ε, is denoted as Es[12]. Only the electrostatic effects of solution are included in the Onsager model, while other forces such as cavity work, dispersion, or exchange repulsion effects are neglected[13], this is a reasonable approximation when zwitterions or strongly polar molecules are studied in polar solvents where the electrostatic effects of solution are expected to predominate. For computation the corresponding energies and nmr shielding were evaluated using the gauge-included atomic orbital (GIAO) method. Nuclear magnetic resonance (nmr) spectroscopy has become one of the more powerful methods for probing molecular structure in solution [14]. The isotropic part <σiso> of σ is measured by taking the average of σ with respect to the orientation of the magnetic field, i.e.

$$< \sigma iso >= \frac{\sigma_{11} + \sigma_{22} + \sigma_{33}}{3}$$

where σ_{xx}, σ_{yy} and σ_{zz} are principal axis values of σ.

The obtained result of calculated by using HF theory.

The anisotropy is

$$\Delta\sigma = |\sigma_{33} - < \sigma iso >|$$

And the asymmetry is

$$\eta = \frac{\sigma_{22} - \sigma_{33}}{\Delta\sigma}$$

Then, Partial atomic charges in a polar surrounding were calculated according to the CHELP charge partitioning scheme[15]. For phosphatidylcholine and its derivatives, the dipole moments calculated from the CHELP charges correspond closely with the dipole moment calculated from the wave function directly.

Thermochemistry

As standard *ab initio* methods, Geometries of the DPPC in each solvent and temperature have been optimized at 6-31G basis set and vibration frequencies obtained at the same levels. Enthalpies have been calculated as the energy differences of solvent and temperature for head group of DPPC, corrected for zero point energy and a thermal correction term, which was evaluated here by integration of theoretical Cp function. The partition function from any component can be used to determine the entropy contribution S from that component, using the relation [Eq. 1]:

$$\Delta S = \frac{\Delta H_{cal}}{T_m} \qquad [1]$$

Entropy has been evaluated by standard statistical thermodynamic methods[16]. Finally, Gibbs free energy of the reaction has been evaluated by using the expression [Eq. 2]:

$$\Delta G\,(T) = \Delta H\,(T) - T\Delta S\,(T) \qquad [2]$$

Furthermore, equilibrium constants were calculated as function of temperature at the different temperatures 4, 25, 36, 37, 41, 60, 70 °C and constant pressure (1 atm.).

All calculations were performed using the GAUSSIAN 03 program[17].

nmr sample preparation and experiment

DPPC was obtained from Avanti Polar Lipids. Pure lipid sample was prepared by mixing the lipid with de-ionized water (pH= 7) in a conical vial with a vortex mixer. This was followed by a minimum of 5 freeze-thaw cycles in dry ice and a warm water bath set at 300K (below the liquid crystalline phase transition for DPPC).

Thus, the samples in this study are large MLV's greater than ~ 1 µm in diameter. Samples containing lipid constituents were first combined and dissolved in chloroform followed by vacuum drying overnight to remove the solvent. The samples were than hydrated in chloroform, Benzene, Carbon Tetrachloride and methanol solvents with the above procedure.

All lipid samples were 33 wt% DPPC. Therefore a solution of 50 mg DPPC was prepared.

^{13}C-nmr spectra were recorded at 20 °C on a DRX 500 MHz spectrometer (Burker Analytische Messtechnik, Karlsruhe, FRG) with a B-VT-1000 heating unit. Natural abundance solution ^{13}C nmr spectra yielded cholin and glycerol resonances that are applied for conformational analysis. Reduced chemical shift anisotropies have been estimated for the cholin C_α, C_β, and C_γ carbons and for glycerol C1, C2 and C3 carbons (Fig.1)

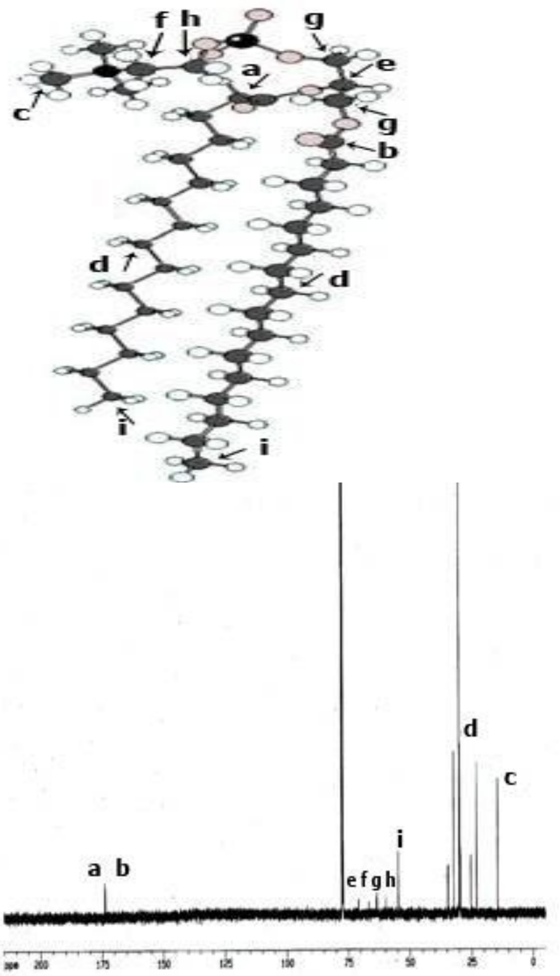


Fig. 1: a plot of the peak position of natural abundance 13C NMR spectra yielded choline and glycerol resonance in chloroform that is accessible to conformational analysis. Chemical shifts have been estimated for the choline C_α(h), C_β(f), and C_γ(c) carbons and for glycerol C1(g), C2(e), and C3(g) carbons and Sn2-CO (a) and Sn1-CO (b).

RESULTS AND DISCUSSION

The bilayer's lipid head groups and hydrocarbon chains affect solvent transport activity. This early observation has been refined into the “solubility-diffusion” model, which states that for substances of solvent to cross a lipid membrane they must partition into or dissolve in both of the interfacial region[19]. Therefore, we have considered the effects of solvents on both the whole of DPPC molecule and its head group. We could detect and effectively mimic a ten-dielectric model which compared the obtained results of DPPC with its head group results.

Solvent effects on geometry, stability and electronic parameters of DPPC structure

We have used an approximate model to describe the interactions between DPPC, an important component of lipid membrane, and solvents.

Aqueous solvent has noticeable effects on the equilibrium geometries and the relative energies as shown in Tables 1 and 2; the effect of dielectric constant of both the headgroup and whole DPPC molecule is also shown.

Initial geometry given from calculations compared well with nmr-determined structure (Figure 3). The obtained theoretical models were confirmed by the study of Hauser and co-workers which show that the PC headgroup has a distinct preferred conformation with α_4 in the range 150-160° and α_5 ± gauche, both in solution and in lipid aggregates[20]. Figure 2 also shows that the only θ_4 of the dihedral angles is only slightly affected by the polarity increase, changing from 54.456˚ (ε = 78.39) to 52.718˚ (ε = 1.92). Therefore the dihedral θ_4 of this model is little affected by polarity changes while the remaining geometry parameters are obviously affected. This confirms why the glycerol backbone is thought to be the most rigid part of the lipid headgroup. Generally the DPPC conformer in nonpolar system has the lower energy (Figure 4); however, at (ε = 78) the difference is only 7.1 kcal/mol. Dihedral angle α_2, α_3 and α_4 are more sensitive to the medium. Especially in methanol, ethanol and chloroform, these dihedral angles turn in the opposite direction.

Table 1: Dihedral Angles of the whole of the DPPC molecule (B) Optimized at εs using the Onsager Salvation Model at the 6-31 G.

Dielectric const	α2	α3	α4	α5
B				
78.39	-173.49	-49.11	-129.92	70.40
46.7	-173.39	-49.09	-129.90	70.39
32.63	-173.35	-49.07	-129.88	70.39
24.55	-173.27	-49.06	-129.85	70.38
20.7	-173.18	-49.04	-129.83	70.37
10.36	-172.85	-48.95	-129.73	70.33
4.9	-172.26	-48.78	-129.52	70.25
4.335	-172.16	-48.74	-129.48	70.23
2.379	-171.47	-48.52	-129.22	70.12
2.247	-171.41	-48.50	-129.19	70.11
C				
Gas phase	-170.46	-48.17	-128.75	49.76

Table 2, Dihedral Angles of the DPPC headgroup (A) Optimized at ε_s using the Onsager Salvation Model at the 6-31 G.

Dielectric const	α2	α3	α4	α5
A				
78.39	152.75	68.54	174.67	42.20
46.7	148.78	60.02	172.75	61.29
32.63	-171.46	-48.52	-129.22	70.12
24.55	-173.23	-49.06	-129.85	70.38
20.7	149.10	60.83	172.88	60.65
10.36	149.60	69.21	173.08	59.57
4.9	-172.28	-48.78	-129.52	70.25
4.335	151.04	64.89	173.74	57.46
2.379	152.75	67.54	174.67	42.20
2.247	152.97	67.84	174.80	55.25
C				
Gas phase	157.35	72.41	178.35	52.41

Alcoholic environments with chloroform have more effect on dihedral angle degree. θ_4 angle, has less variation compared with α_5, α_4, α_3 and α_2 and α_1 angles. Therefore headgroup of DPPC has more conformational changes when the molecule is treated with different dielectric constants. In contrast with the whole molecule, the variation of head group dihedral angles isn't related to dielectric constant when we consider studying head group model only.

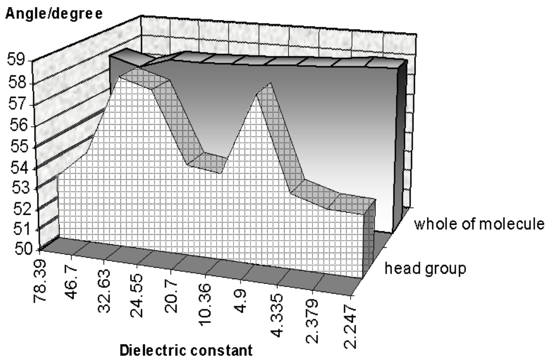


Fig. 2: A comparison of the variation of θ_4 dihedral angle degree, between DPPC head group and whole of the molecule.

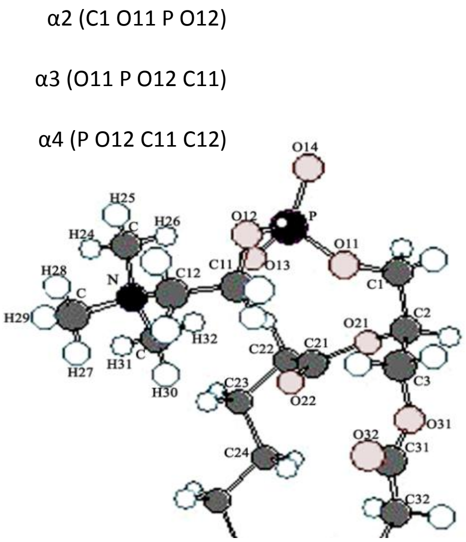


Fig. 3: Atom numbering and notation for torsion angles of DPPC headgroup region according to Sundaralingam[18].

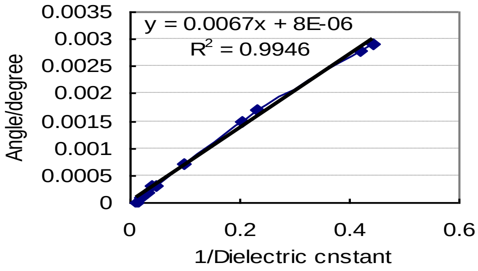


Fig. 4: A linear relationship between the Relative energy and 1/ε in DPPC.

There is a linear relationship between the variation of relative energy in whole of the DPPC and 1/dielectric constant (y=0.0067x+8E-06, R^2=0.9946). DPPC-solvent system increases polarity of molecule compared with DPPC-water system. On the other hand, the interaction of DPPC-solvent system is increased. Therefore, the relative energy will be more negative. According to obtained results in Figure 4, the relative energies of DPPC depend on the polarity of the environment. In all the solvents, the molecule conformer in Water (ε = 78) has lower energy compared with the others. Therefore, in consideration of conformational energy, water is the most suitable solvent. In polar medium a DPPC conformer becomes additionally stabilized by intermolecular ionic and hydrogen bond interactions with polar neighbouring molecules. Moreover, as the polarity of the medium increases, the conformational stability of this molecule increases faster than the stability of DPPC in nonpolar solvents.

Solvent effects on electronic parameters of DPPC

To develop electrostatic parameters for non-bonded interactions between DPPC and Solvents, the "CHELP" (charges from electrostatic potentials) was fitted to the electrostatic potential arising from the wave function of the molecule. This method has y become a widely used technique leading to charge-independent results. Therefore, in this investigation, CHELP charges were used to detect variation of charges of both head group region and whole molecule of DPPC in solvents (Figure 5) and also for detecting the effect of dielectric constant on charge (Figs. 5 and 6), here we have plotted the dielectric constant and relative charge of some critical atoms in both the headgroup and whole of the DPPC molecule. More variations of charge were observed in head group atoms.

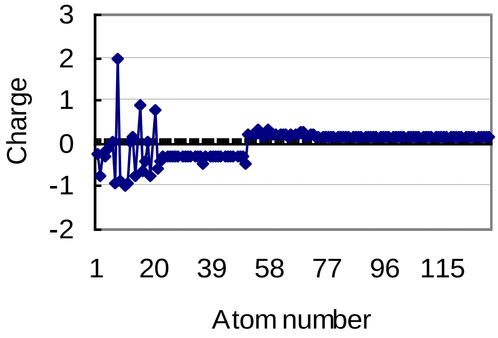


Fig. 5: The variations of charge parameter for DPPC atoms in Water (ε = 78.39).

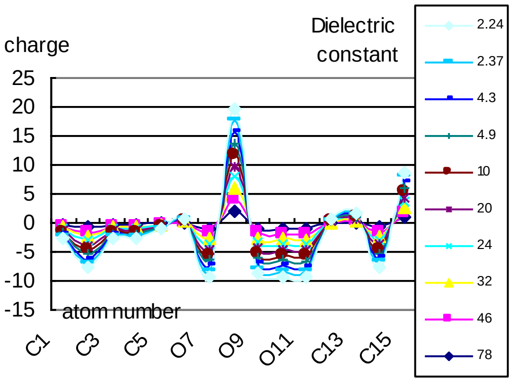


Figure 6, differential charge distribution of DPPC head group atoms in different dielectric constant.

The largest variation is related to Sn2-CO, Sn1-CO and phosphorus. The phosphorus atom (atom number in Figure 6 = 8) has more charge in water; but atom O7 is less charged. There is linear relation only between phosphorus and carbonyl atoms and 1/dielectric constant (data wasn't shown). This was confirmed by ab *initio* calculations showing that without influence from a polar environment, i.e. in the gas phase, the positively-charged ammonium or choline group of the PC headgroup interacts intermolecularly with one of the unspecified phosphate oxygen[21]. Moreover, recent study has shown that in the head group region, water molecules are ordered by phosphate, choline, and carbonyl groups. Instead, they form a clathrate structure around the choline methyl group, because there is a linear relation between only phosphorus and carbonyl groups and 1/dielectric constant. According to CHELP study, mainly due to the orienting effect of the larger variation of charge of these parts of molecule indicate that the carbonyl plane and phosphorus adopt a preferred orientation near to the solvent. And also the largest variation of charge occurs in headgroup and totally depends on polarity of the environment. Furthermore, the favorable solute-water interactions are attributed to the increase in polarizability of solvents. Therefore, the polarizability effect for aliphatic hydrocarbons is less important.

It seems that the variation of charge electrostatic potential is related to dielectric constant because the maximum value of charge was shown in nonpolar solvent. According to these results, the different effect of dielectric constant on the behavior of dihedral angles in the headgroup is not related to electrostatic forces because DPPC has less charge in polar solution like water (ε = 78) than in nonpolar solutions and it totally depends on polarity of environment.

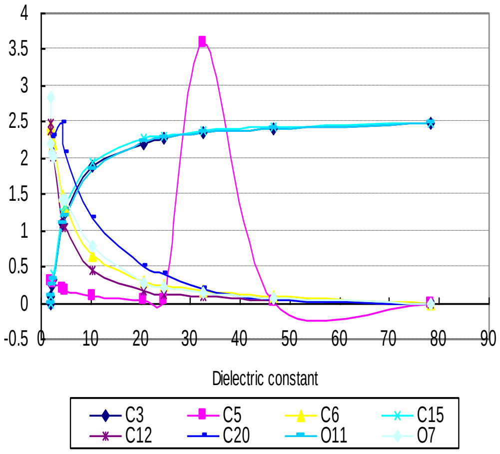
Calculation of nmr parameters in Solvent model

In previous sections, the effect of dielectric constant on dihedral angles of headgroup and relative charge were totally different. For detecting this , the CHELP method was used.

But when the variation of the whole of the DPPC was considered, it was shown that dielectric constant effects on dihedral angles ordinary. And there was a linear related to dielectric constant. For evolution of these variation of shifts on some atoms were involved in critical dihedral angles, the NMR shielding tensors were calculated for them.

The chemical shielding tensors calculated with the GAUSSIAN 03 program. At each dielectric constant, the nuclear shielding was calculated each geometrical structures (Table 1 & 2). These dates were compared with the result obtained from ^{13}C NMR of DPPC in chloroform, Methanol and Benzene solutions and also for more conforming initial DPPC conformer in ab initio model, the results were compared to the obtained results of ^{13}C NMR of DPPC in Methanol, Chloroform, Benzene (see 4.4) and also egg yolk phosphatidylcholine which were done by ytryr et al (data wasn't shown) [22].

For whole of DPPC molecule, the changes in σiso was related to dielectric constant as well as the variation of changes , Dihedral angles (α1, α2, α3, α4, α5, θ4) and Conformational energies which were studied. But there isn't any relation between dielectric constant and C5(12) for head group region of DPPC. The effect of alcohols on σiso was found more than the other solvents (Figure 7).



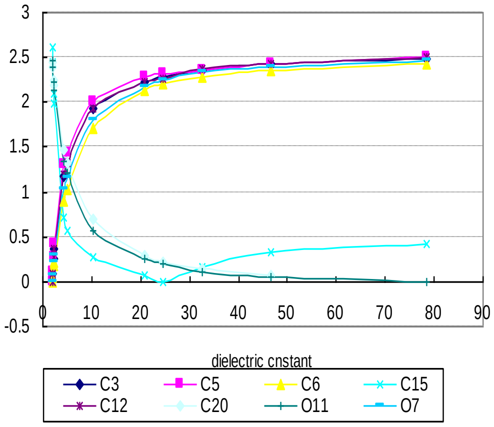


Figure 7, the average of isotropic values σiso (left-hand scale) variations for ^{13}C in ppm for some critical atoms in DPPC head group region, (a) the whole of molecule (b) head group study lonely as a function of the dielectric constant characterizing the polarity environment.

The locate of this carbon is in α5 and α4 dihedral angles, therefore, the Alcohols have the more effect on the choline region in compared with the other part of molecule. But when we have considered the whole of DPPC molecule it is shown that there is a linear relation between variation of iso and 1/dielectric constant (data wasn't shown). These results confirmed the pervious obtained results.

We reproduce in Table 3, a comparison of our theoretical data and the experimental data of DPPC molecule in different solutions all chemical shifts being referenced to Tetramethylsilane. For comparison, calculated chemical shift values (δ) were considered with the results obtained from GIAO calculations and both were similar. The ab initio quantum chemical results are fragmentary in that a large molecule like DPPC was typically not studied.

Table 3, Comparison between calculated and experimental ^{13}C isotropic shift values for DPPC in Chloroform, Methanol and Benzene solution.

	Isotropic value in ppm					
	$CDCl_3$		CD_3OD		C_6H_6	
Atom[a]	calculated[b]	experiment	calculated[b]	experiment	calculated[b]	experiment
i	54.7	48.7	50.3	48.8	48.8	48.7
h	59.7	51.6	50.5	52.0	48.9	51.3
g1	63.4	61.1	50.6	61.2	49.1	60.9
g2	63.7	61.9	50.8	61.9	49.3	62.0
f	66.7	63.4	66.5	52.0	69.1	63.1
e	70.9	82.5	51.0	82.6	49.4	82.6
a	173.9	240.2	176.6	239.7	173.5	231.6
b	173.6	231.6	176.2	231.7	173.7	240.7

[a] The numbering corresponds to the atom numbers given in Figure 1.

[b] Value obtained for the minimum energy conformation at 6-31G level and standard; TMS: Isotropic carbon shielding tensor=208.2102,

Dielectric constant dependence of the temperature parameters of DPPC headgroup.

In a previous section, we showed that most of the changes occur in the headgroup region.

It was important to consider the main temperature which has the strongest effect on the headgroup. So the effects of dielectric constant on the transition temperatures of DPPC on head group region was considered. Generally, transition is considered to be a melting of the hydrocarbon chains. However, the molecular interactions in the headgroup region are more complex than in the acyl chain region. The phase transition is mainly induced by the increasing mobility of the acyl chain (chain melting) which causes a sudden increase of the gauche conformers in the molecular arrangement.

For determining the effects of solvent and temperature on thermodynamic parameters of DPPC headgroup region, the temperature range was chosen around 4-60°C. 60ºC was chosen for the fluid-crystalline phase (Lα) and 25°C for the gel phase (Lβ'), 37°C for the prippled gel phase (Pβ'), 4°C for the crystalline phase (Lc) and 42°C for the main transition phase[23]. According to previous results, water was the most suitable solvent for both the headgroup area and the hydrophobic acyls of DPPC molecule. Therefore, the main thermochemical parameter chosen in water as a reference was Gibbs free energy. For DPPC in each solvent, the variation of Gibbs free energy was compared with DPPC-Water system. (Figure 8).

A typical dependence is shown in Table 4. The results obtained from thermochemical study of DPPC headgroup show that, at most of the dielectric constants, a similar qualitative change in Gibbs free energy and enthalpy with the temperature variation is apparent for our model. This model also indicates that the effect of solvent on enthalpy and Gibbs free energy values are largely unaffected by changes of the dielectric constant alone.

Table 5, Thermochemical parameters like the Gibbs energies, enthalpies and entropies in different solvents for DPPC headgroup at ten temperatures.

°C	ε	ΔG*	ΔH*	ΔS*	ε	ΔG*	ΔH*	ΔS*
4	**78.4**	-1500.432486	-1500.508116	171.33	**4.9**	-1500.432486	-1500.508112	171.322
25		-1500.429425	-1500.513962	178.013		-1500.429424	-1500.513958	178.005
36		-1500.427757	-1500.517113	181.462		-1500.427756	-1500.517108	181.454
37		-1500.427603	-1500.517402	181.774		-1500.427602	-1500.517398	181.766
41		-1500.426984	-1500.518565	183.019		-1500.426983	-1500.51856	183.011
42		-1500.516617	-1500.424474	183.557		-1500.518852	-1500.426828	183.321
46		-1500.426202	-1500.520029	184.569		-1500.426202	1500.520025	184.561
51		-1500.425411	-1500.521506	186.113		-1500.42541	-1500.521501	186.105
60		-1500.423964	-1500.524195	188.878		-1500.423963	-1500.52419	188.87
70		-1500.422321	-1500.527229	191.928		-1500.42232	-1500.527225	191.92
4	**46.7**	-1500.432487	-1500.508111	171.319	**4.335**	-1500.432486	-1500.50811	171.319
25		-1500.429425	-1500.513957	178.002		-1500.429424	-1500.513956	178.002
36		-1500.427757	-1500.517107	181.45		-1500.42775	-1500.517107	181.451

						6		
37		-1500.427603	-1500.517397	181.762		-1500.427602	-1500.517396	181.763
41		-1500.426984	-1500.518559	183.007		-1500.426983	-1500.518559	183.008
42		-1500.516699	-1500.424568	183.534		-1500.51885	-1500.427825	183.318
46		-1500.426202	-1500.520024	184.558		-1500.426201	-1500.520023	184.558
51		-1500.425411	-1500.521501	186.102		-1500.42541	-1500.5215	186.102
60		-1500.423964	-1500.52419	188.866		-1500.423963	-1500.524189	188.867
70		-1500.422321	-1500.527224	191.916		-1500.42232	-1500.527223	191.917
4	**32.6**	-1500.432487	-1500.508108	171.311	**2.379**	-1500.432485	-1500.508114	171.327
25		-1500.429425	-1500.513953	177.994		-1500.429424	-1500.51396	178.01
36		-1500.427757	-1500.517104	181.443		-1500.427756	-1500.51711	181.459
37		-1500.427603	-1500.517393	181.755		-1500.427602	-1500.5174	181.77
41		-1500.426984	-1500.518556	182.999		-1500.426983	-1500.518562	183.015
		-1500.518848	-1500.426829	183.31		-1500.518458	-1500.426501	183.187
46		-1500.426202	-1500.52002	184.55		-1500.426201	-1500.520027	184.566

51		-1500.425411	-1500.521497	186.094		-1500.42541	-1500.521504	186.11
60		-1500.423964	-1500.524186	188.859		-1500.423963	-1500.524193	188.875
70		-1500.422321	-1500.52722	191.909		-1500.42232	-1500.527227	191.924
4	**24.6**	-1500.432486	-1500.508109	171.315	**2.247**	-1500.432485	-1500.508114	171.328
25		-1500.429425	-1500.513955	177.998		-1500.429424	-1500.51396	178.011
36		-1500.427757	-1500.517105	181.447		-1500.427756	-1500.517111	181.459
37		-1500.427603	-1500.517394	181.759		-1500.427602	-1500.5174	181.771
41		-1500.426984	-1500.518557	183.003		-1500.426983	-1500.518563	183.016
42		-1500.518848	-1500.426828	183.312		-1500.518855	-1500.426828	183.327
46		-1500.426202	-1500.520021	184.554		-1500.426201	-1500.520027	184.566
51		-1500.425411	-1500.521498	186.098		-1500.42541	-1500.521504	186.111
60		-1500.423963	-1500.524187	188.862		-1500.423963	-1500.524193	188.875
70		-1500.422321	-1500.527221	191.912		-1500.42232	-1500.527227	191.925
4	**20.7**	-1500.432486	-1500.508113	171.325	**10.4**	-1500.432485	-1500.508112	171.323
25		-1500.429424	-1500.513959	178.008		-1500.42942	-1500.513958	178.006

						4		
36		-1500.427756	-1500.51711	181.457		-1500.427756	-1500.517108	181.455
37		-1500.427602	-1500.517399	181.769		-1500.427602	-1500.517398	181.766
41		-1500.426983	-1500.518562	183.014		-1500.426983	-1500.51856	183.011
42		-1500.516931	-1500.42483	183.474		-1500.518852	-1500.426828	183.322
46		-1500.426201	-1500.520026	184.564		-1500.426201	-1500.520025	184.562
51		-1500.42541	-1500.521503	186.108		-1500.42541	-1500.521502	186.106
60		-1500.423963	-1500.524192	188.873		-1500.423963	-1500.524191	188.87
70		-1500.42232	-1500.527226	191.923		-1500.42232	-1500.527225	191.92

* ΔS (CAL/MOL-KELVIN), *ΔH and *ΔG (Hartree/Particle)

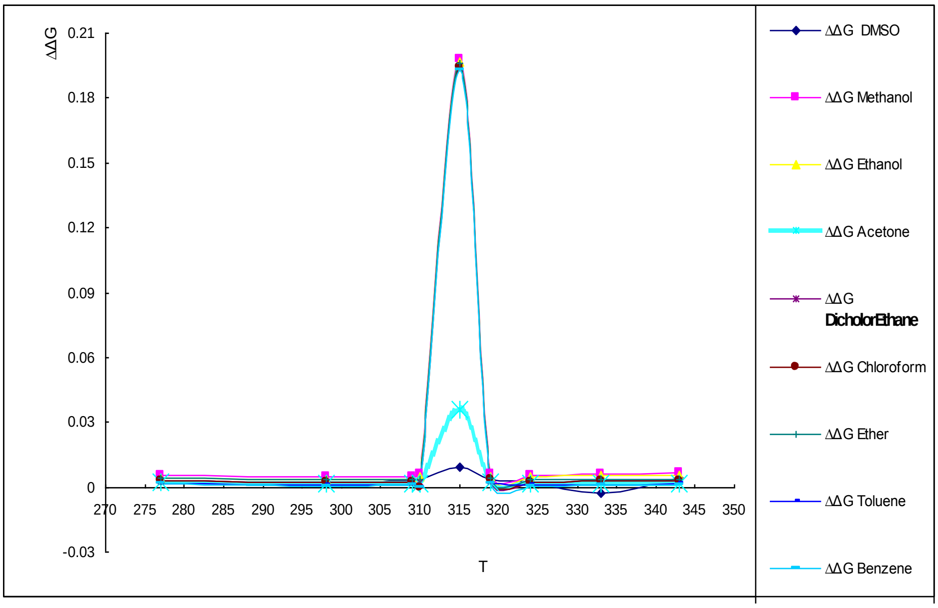


Figure 8: Thermochemical parameter ΔΔG for DPPC-solvent system.

However, when solvent and temperature are considered together, differences exist as fluctuation driven phenomena. However, there are large differences in enthalpy and Gibbs free energy at Tc for DPPC-solvent systems compared to the DPPC-water system.

At the transition temperature the influence of methanol and ethanol on DPPC head group properties is strikingly different from that of some other polar solvents. For instance, lower values of Gibbs were observed in water, DMSO and acetone.

Apparently, when compared with DPPC-water system, there is the same variation of thermodynamic parameters at the main transition in all the non polar solvents and alcohol DPPC headgroup-system. At Tm the headgroup has lower stability in water, DMSO, acetone and benzene. These results are confirmed by our previous results. Furthermore, the changes in enthalpy are related to the van der Waals interactions and hydrogen bonding while entropy change is an indication of hydrophobic effect. In all cases, entropy value variation for all the temperatures in different solvents is higher than the other thermo chemical parameters. This model then indicates that hydrophobic effects play a stronger role on DPPC ordering.

Hydrophobic effect on the other forces

We found that some obtained results of DPPC and its headgroup were deviant obviously. For DPPC, the results of geometries and variation of dihedral angles showed that the most variable in some dihedral angle degrees and nmr isotropic shift occurred at lower dielectric constant ($\varepsilon = 2.247$); therefore, these variations are related to dielectric constant. The headgroup region had different results in some polar solvents compared with nonpolar solvents that it has shown at dielectric constants of 32.63, 24.55 and 4.9. This could arise from small variations in the bulk headgroup radii compared with the total size of DPPC molecule in the solvent. Also, the solubility index of DPPC in the test solvents (methanol, ethanol and chloroform) could cause the observed disparities. From the results obtained on the geometries of DPPC headgroup alone, hydrogen bonding, electrostatic and dipolar forces are also important. However, the most important reason relates to hydrophobic forces in the hydrocarbon chains in the tail group.This is understood as the area of this molecule describes the two–dimensional packing density of the headgroup and the tail. Hydrophobic interaction plays an important role in solvent partitioning into DPPC.

This investigation has shown that the hydrophobic interaction of solvent partitioning into DPPC is the predominant force while other types of interactions such as hydrogen and dipolar bonding also play important roles. The closer the alkyl tails are packed, the more they are ordered and affect the other forces which are involved in DPPC packaging. Moreover, when the whole DPPC molecule is considered, a linear relationship occurs between most of the geometry dihedral angles of the headgroup and dielectric constant in our study model. On the other hand, hydrophobic force in the tail group causes most atoms to show constant and ordinary behavior. Therefore solvents influence DPPC headgroup and the whole molecule differently and this effect is totally related to temperature. It is at Tm that solvents show the largest variation compared with water. All the results confirmed that water is the most suitable solvent.

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