

DFT study of glucose based glycolipid crown ethers and their complexes with alkali metal cations Na⁺ and K⁺

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Abstract A theoretical study of a series of five glucose based glycolipid crown ethers and their complexes with Na⁺ and K⁺ was performed using the density functional theory with B3LYP/6-31 G* to obtain the optimized geometrical structures and electronic properties. The local nucleophilicity of the five molecules was investigated using Fukui function, while the global nucleophilicity was calculated from the ionization potential and electron affinity. The structures and coordination of the complexes were studied to identify the best match of the glycolipid crown ethers with cations. In general, it was found that the oxygen atoms pairs O2 and O3 (or O4 and O6) on the sugar ring are constrained from moving toward the cation, which results in a weaker O-cation coordination strength for the oxygen pair compared to the other oxygen atoms in the crown ether ring. The thermodynamic properties of the binding of the complexes and the exchange reaction in gas phase were evaluated. The cation selectivity pattern among the five molecules was in good agreement with the experiment.

Keywords Alkali metal cation · Cation selectivity · Crown ether · Density functional theory (DFT) · Glycolipids

Introduction

Glycolipids are surfactants, which consist of a hydrophilic carbohydrate head group and a hydrophobic alkyl tail. Thus, there are many types of glycolipids, which vary in terms of the sugar head group and the hydrophobic tails; some being

synthetic, while others are natural [1, 2]. In nature, glycolipids are found in cell membranes [3, 4], the basic building block of the organism on earth. Glycolipids exhibit an interesting behavior of self-organization in dry state as well as when solvated, where many different liquid crystal phases (both thermotropic and lyotropic) can be observed [5–7]. In addition to being biodegradable, non-toxic, the amphitropic [8] nature of glycolipids makes them interesting liquid crystal materials. This fact enables a wide range of possible applications, for example in cosmetics, pharmaceuticals and nanomaterials [9, 10].

Crown ethers were first discovered by Pederson in 1967 and have long been well known for their ion selection capability [11, 12]. Crown ethers ((CH₂CH₂O)_n, cyclic), with ether units act as hosts, able to trap the ionic species as guests. The various cavity sizes of the crown ethers make them possible for specific entrapment of guest particles, especially metal cations. One can also find this kind of host-guest chemistry in nature such as in cyclodextrins and macrocyclic polyether antibiotics [13]. Moreover, host-guest complexes interaction with surfaces is of a special interest to many researchers, since it has many applications, such as molecular recognition, ion sensing, heterogeneous catalysis or molecular switching [14–17].

The combination of the self-assembly behavior with the special functionality of some supramolecules has provided a way to scale up the specific function from molecular level to nano scale, offering new functionality to the self-assembly system [18]. These include incorporating cation selectivity capability of crown ether to the system of self-organization, which can be applied in creating a cation channel, which mimics the natural ion-channel protein for bio-membranes [19–21].

Recently, a series of new compounds has been prepared by Sabah et al. [22] which combined the self-organizing

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property of sugar-based glycolipids with the crown ethers (see Fig. 1). These compounds are a combination of glycolipid dodecyl- β -D-glucoside with crown ethers. The compounds 15-crown-5, 18-crown-6 and 21-crown-7 have their crown ethers attached to hydroxyl groups at O2 and O3 positions on the sugar ring of the dodecyl- β -D-glucoside to give G15C5, G18C6 and G21C7, see Fig. 1a–c respectively. Meanwhile different positions of the hydroxyl groups (O4 and O6) of the dodecyl- β -D-glucoside are chosen to attach the crown ethers of the 16-crown-5 and 19-crown-6 for G16C5 and G19C6 (Fig. 1d–e). These new functionalized glycolipids have significantly increased in the size of their hydrophilic heads due to the crown ethers. In terms of self-assembly packing, increase in the size of head group would result in higher packing parameters [23], which could prevent the formation of lamellar phase and induce the formation of non-lamellar curve phases such as micellar, hexagonal and even cubic phases. Besides this, the ion selectivity of the new compounds has also been studied and it was found that there is an overall tendency to favor sodium over potassium in solution [22].

In this work, we studied the properties of these compounds from a theoretical point of view. The electronic structure, molecular conformations and the thermodynamic properties of these compounds and their complexes with cation Na^+ and K^+ were obtained from the quantum chemistry calculation using Gaussian 09 W program.

Computational details and theory

A series of glycolipid crown ethers was modeled using Avogadro software package [24]. Molecular mechanics of Merck Molecular force field (MMFF94) available within the software, was used to minimize the conformational energies for these models. Using these optimized conformations, glycolipid crown ether complexes with cations Na^+ or K^+ were prepared by bringing the cation close to the crown ether ring. Further MMFF94 minimizations were performed to obtain the optimized complexes so that all oxygen atoms on the crown ether ring were as close as possible to the cations. These optimized

structures and their complexes were studied using the density functional theory (DFT) at B3LYP/6–31 G* level. All the calculation was carried out using the Gaussian 09 program package [25]. The DFT method is an efficient method in the study of large molecules and has been widely used since it is capable of giving sufficiently accurate conformational analyses and thermodynamics properties. Meanwhile the B3LYP (Becke–Lee–Yang–Parr) version of DFT is the combination of Becke's three-parameter nonlocal hybrid functional of exchange terms [26] with the Lee, Yang and Parr correlation functional [27]. The basis set 6–31 G* contains a reasonable number of basis functions that are able to reproduce experimental data [28, 29]. Using the DFT method, the best minimum energy conformations were achieved by full geometry optimization of each crown ether glycolipid. In order to prove that each conformation is located at a stable minimum point of the potential energy surface, frequency calculations were carried out based on these optimized structures to subsequently obtain their vibrational frequencies. Furthermore, using the results obtained from the calculation, the structural and electronic properties such as charge distribution, ionization potentials (I), HOMO energies (ϵ_{HOMO}), LUMO energies (ϵ_{LUMO}), bond length, electron affinity (A) and condensed Fukui functions were investigated.

The local nucleophilicity and electrophilicity refer to the capability of a site in a particular molecule to donate and attract electron, respectively. Fukui function is one of the ways used to describe this local reactivity toward electron donors or acceptors. According to Parr and Yang [30], Fukui function $f(\vec{r})$, is written as follows:

$$f(\vec{r}) = \left(\frac{\partial \rho(\vec{r})}{\partial N} \right)_{v(\vec{r})} \quad (1)$$

where $\rho(\vec{r})$ is the electron density, N is the atomic charge of the system and $v(\vec{r})$ denotes the external potential of the system. A simple way to analyze Fukui function was proposed by Yang and Mortier [31] and called the condensed Fukui function. The condensed Fukui function calculations are based on the finite difference approximation and partitioning of the electron density $\rho(\vec{r})$ between atoms in a

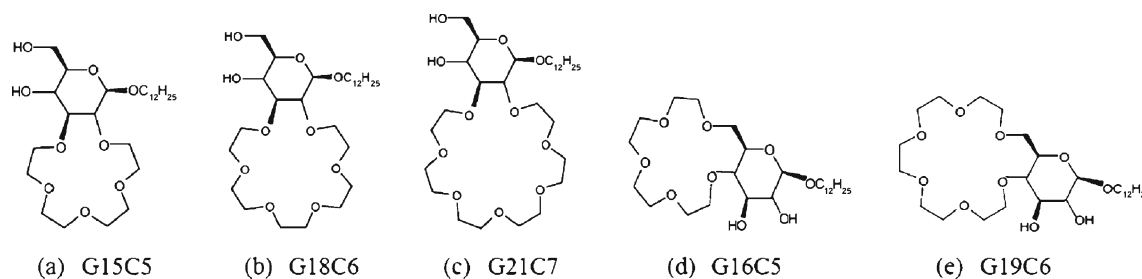


Fig. 1 Schematic drawing of the molecular structures of glycolipid ethers (a–e). Each contains a dodecyl- β -D-glucoside attached to crown ethers of various sizes and at different locations

molecular system. With the approximation, the Fukui function at the atom k , denoted as f_k^+ and f_k^- , can be estimated by using an atomic charge partitioning scheme, such as Mulliken population analysis, [32] where for nucleophilic attack,

$$f_k^+ = q_{N+1} - q_N \quad (2)$$

and for electrophilic attack,

$$f_k^- = q_N - q_{N-1} \quad (3)$$

Here, q_N , q_{N+1} and q_{N-1} denote the charges for atom k on the neutral, cation and anions species respectively. In this study of glycolipid crown ethers, since only interaction with cation is of interest, we calculated only the condensed Fukui function of the nucleophilic attack. While the condensed Fukui function gives the nucleophilicity locally at each atom, the overall or global nucleophilicity or electrophilicity [32] of the systems can be measured according to their ionization potential I and electron affinity A , which is calculated as

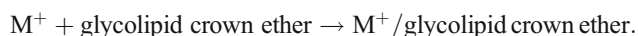
$$\begin{aligned} I &= E(N-1) - E(N) \\ A &= E(N) - E(N+1) \end{aligned} \quad (4)$$

where $E(N)$, $E(N-1)$ and $E(N+1)$ are the calculated total energies for the neutral, cationic and anionic states. There have been a number of quantitative indicators to describe the global nucleophilicity [32, 33]. Here, using the estimated I and A , we analyzed the global nucleophilicity according to the nucleophilicity index N defined as:

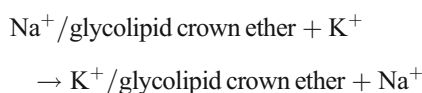
$$N = \left(\frac{(I+A)^2}{8(I-A)} \right)^{-1} \quad (5)$$

One of the key parameters to understanding the electronic structure is the difference between the energy of the lowest unoccupied molecular orbital and the highest occupied molecular orbital ($\Delta\varepsilon_{LUMO-HOMO} = \varepsilon_{LUMO} - \varepsilon_{HOMO}$) that is defined as the energy gap. The energy gap is related to the polarizability and chemical hardness of the molecules, where a higher energy gap means lower molecular polarizability and higher chemical hardness [34]. In fact according to Koopman theorem [35], the chemical hardness η is equal to the energy gap.

The thermodynamic properties such as binding energy, binding enthalpy and Gibbs free energies in gas phase of the complexes, formed by the combination of the glycolipid crown ethers with cation Na^+ and K^+ , were also studied. The calculations were based on the reaction scheme 1 as follows:



In addition, the exchange enthalpies and the Gibbs free energies were also calculated for the reaction scheme 2:



It was known that a finite basis set such as 6-31 G*, can give rise to the basis set superposition error (BSSE) in the DFT calculation involving interaction of two different fragments, which in our case is between a glycolipid crown ether and a cation. To remove this error, the counterpoise method [36, 37] was applied in the DFT calculation of the complexes.

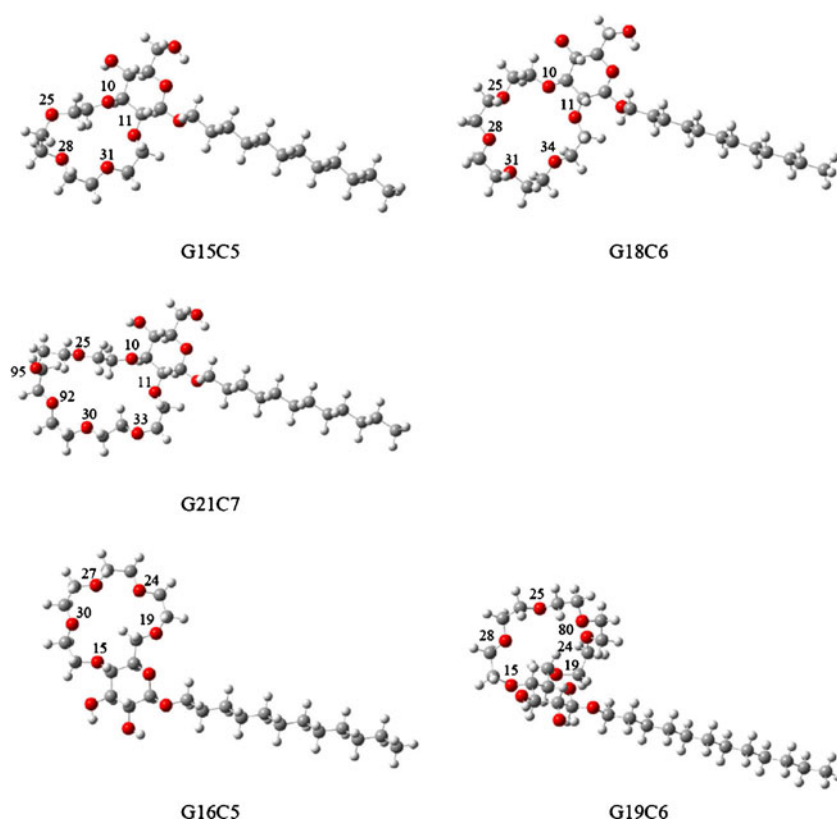
Results and discussion

Structure of glycolipid crown ethers and their nucleophilicity

Figure 2 shows the optimized structures of different glycolipid crown ethers calculated at B3LYP/6-31 G* level of DFT in ground state. From these structures we can see that the shape of crown ethers in G18C6 and the G16C5 is less deformed compared to the rest. The reactivity of the oxygen atoms around the crown ethers of the five molecules described using condensed Fukui function are given in Table 1. Positive values of the condensed Fukui function f_k^+ at site k mean that the particular atom is especially reactive to nucleophilic attacks. The higher the values of the f_k^+ on the site, the more reactive the particular site. From Table 1, we can see that not all the oxygen atoms in the crown ethers are reactive sites for nucleophilic attacks and the most reactive site of each molecule is located further away from the sugar ring, i.e., O31 in G15C5 and G18C6, O92 in G21C7, O24 in G16C5 and O80 in G19C6.

Table 2 gives the overall electronic properties of the optimized structures in terms of HOMO-LUMO energies, energy gaps, ionization energies, electron affinity and nucleophilicity index. The energy gaps $\Delta\varepsilon_{LUMO-HOMO}$ calculated show that they are more or less the same for the five glycolipid crown ethers. However, among them G16C5 has the highest energy gap, suggesting that G16C5 is chemically the hardest. The ionization potential of the five molecules gives values that are also rather close to one another, while their electron affinities are more sensitive to the difference in size of crown ethers. Relatively, the largest glycolipid crown ether G21C7 has the highest ionization potential and electron affinity. However, G19C6 is the lowest in both quantities, although it is not the smallest molecule. This is probably due to the optimized structure of the G19C6 being deformed in such a way that its cavity became as small as that of G15C5 (see Fig. 2). The trend for the global nucleophilicity index N of various glycolipid crown ethers is G19C6 > G15C5 > G16C5 > G18C6 > G21C7.

Fig. 2 The optimized structures of the series of glycolipid crown ethers with the level of theory B3LYP/6-31 G*. The oxygen atoms on the crown ethers are labeled



Geometrical structure of the complexes

The optimized structures of the complexes formed by the glycolipid crown ethers with the cations are given in Figs. 3 and 4. For each complex, the distances in Angstrom between the binding sites of oxygen atoms in the crown ethers to the cation Na^+ and K^+ have been worked out and presented in Table 2. From Fig. 3, the optimized structure of complexes $\text{Na}^+/\text{G15C5}$ and $\text{K}^+/\text{G15C5}$ shows that the cations are located on the mean planes formed by the crown ethers, where K^+ is slightly away from its crown ethers mean plane. This suggests that the cavity size for G15C5 is fit to accommodate Na^+ but too small for K^+ . For bigger sized crown ethers such as G18C6 and G21C7, the crown ethers cavity is big enough to encapsulate cation Na^+ by

distorting their structure from being planar to form $\text{Na}^+/\text{G18C6}$ and $\text{Na}^+/\text{G21C7}$ complexes. The cavity size of G18C6 matches the size of cation K^+ , such that the cation is located on the mean plane of the crown ethers in the $\text{K}^+/\text{G18C6}$ complex. Nevertheless, the cavity size of G21C7 is still bigger than that of cation K^+ . Therefore the crown ether of the structure of the complex $\text{K}^+/\text{G21C7}$ is distorted from planar.

On the other hand, glycolipid crown ethers G16C5 and G19C6, which have a different linkage to the sugar ring from the other three, form complexes with the two cations Na^+ and K^+ with their crown ethers in planar structure (see Fig. 4). G16C5 is shown to have the cavity size that matches well the size of the Na^+ since its optimized structure in Fig. 4 shows that the cation Na^+ is located at the mean plane

Table 1 Fukui function values for a nucleophilic for the different glycolipid crown ethers

G15C5		G18C6		G21C7		G16C5		G19C6	
Atom	f_k^+	Atom	f_k^+	Atom	f_k^+	Atom	f_k^+	Atom	f_k^+
O3	-0.0073	O3	-0.0266	O3	0.0022	O4	-0.0122	O4	0.0008
O25	-0.0033	O25	0.0027	O25	-0.0096	O30	0.0061	O28	-0.0025
O28	0.0041	O28	0.0055	O95	-0.0116	O27	0.0055	O25	0.0041
O31	0.0121	O31	0.0060	O92	0.0128	O24	0.0079	O80	0.0124
O2	-0.0008	O34	0.0011	O30	0.0064	O6	0.0047	O24	-0.0011
		O2	-0.0041	O33	-0.0138			O6	-0.0070
				O2	0.0037				

Table 2 HOMO and LUMO energies ε_{HOMO} and ε_{LUMO} , energy gaps $\Delta\varepsilon_{LUMO-HOMO}$, ionization potential I , electron affinity A and nucleophilicity index N for the glycolipid crown ethers

Molecule	ε_{HOMO} (eV)	ε_{LUMO} (eV)	$\Delta\varepsilon_{LUMO-HOMO}$ (eV)	I (eV)	A (eV)	N (eV)
G15C5	-6.372	1.559	7.889	7.385	-2.226	2.890
G18C6	-6.395	1.534	7.932	7.412	-1.713	2.247
G21C7	-6.565	1.397	7.962	7.534	-1.629	2.102
G16C5	-6.326	1.957	8.283	7.465	-1.906	2.425
G19C6	-6.032	1.881	7.913	7.346	-2.611	3.552

formed by the crown ether. Meanwhile the cation K^+ in the $K^+/G16C5$ complex is located at slightly above the mean plane of its crown ethers. The crown ether of G19C6 is expected to have a bigger cavity size than the crown ether in G15C5, G16C5 and G18C6. Surprisingly the optimized structure of the $Na^+/G19C6$ complex in Fig. 4 shows that the crown ether of G19C6 still forms a plane with its cation Na^+ in the middle of the plane. Comparing the top view of the structure of the $Na^+/K19C6$ complex with its side view, we can see that the mean plane is formed by five out of six of its oxygen binding sites. This can also be seen from the distribution of the Na^+-O distances for the complex in Table 2, where only five out of six oxygens are coordinated to the Na^+ . This makes up the five Na^+-O distances ranging from

2.367 Å to 2.507 Å, while a remaining Na^+-O distance of 3.568 Å. The crown ether of the $K^+/G19C6$ complex is also planar with the cation located in the middle of the plan. This time all six oxygen atoms are involved in forming the plane.

From the geometrical parameters in Table 3, in general, within a complex, the cation Na^+ can bind with the donor oxygen more closely than the K^+ . Moreover, the distribution of the cation-O distances within each complex in Table 3 implies that the majority of the complexes have all their oxygen atoms in the crown ethers coordinated to the cations. The complexes that do not have their oxygen atoms in crown ethers fully coordinated to the cations are $Na^+/G18C6$, $Na^+/G19C6$, $Na^+/G21C7$ and $K^+/G21C7$. In these four complexes, the oxygen atoms in the crown ether rings

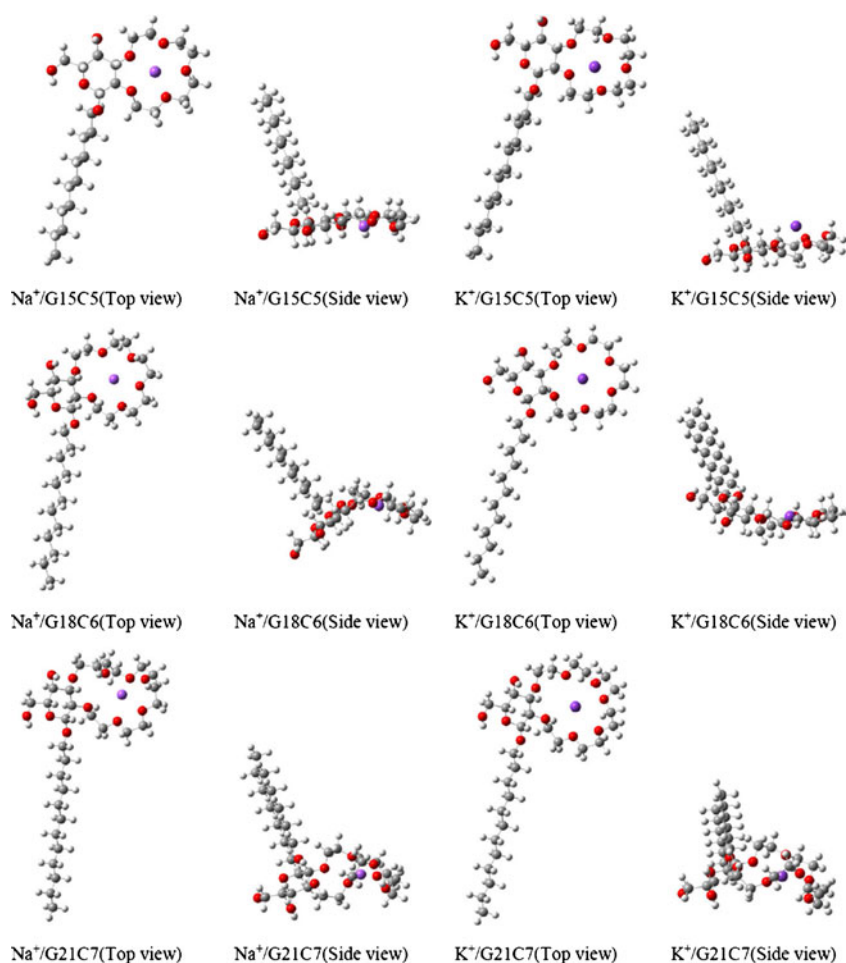
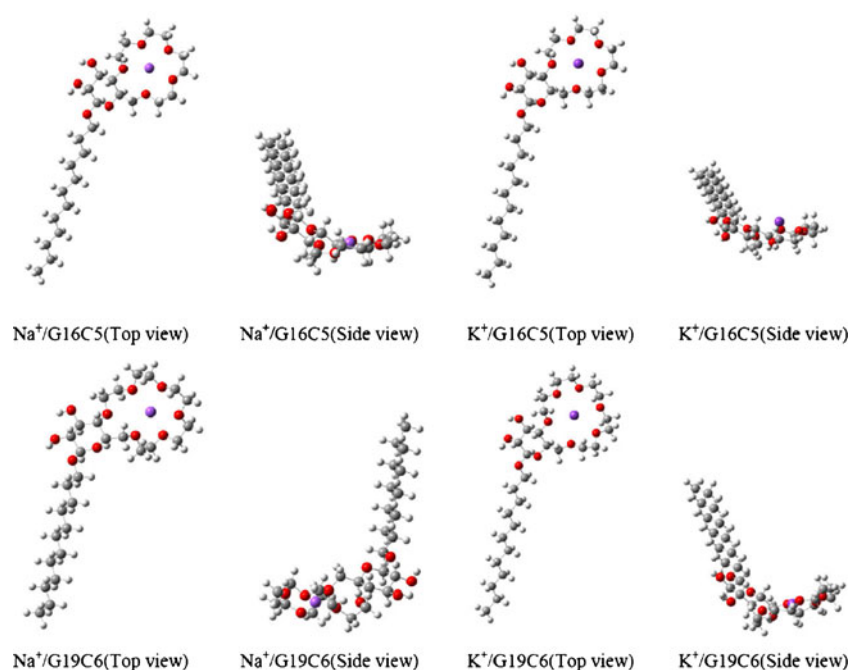
Fig. 3 Optimized structures of complexes $M^+/G15C5$, $M^+/G18C6$ and $M^+/G21C7$ at the level of theory B3LYP/6-31 G* where M^+ represent the cations Na^+ and K^+ 

Fig. 4 Optimized structures of complexes $M^+/G16C5$ and $M^+/G18C5$ at the level of theory B3LYP/6-31 G^* where M^+ represents the cations Na^+ and K^+



that are not coordinated to the cation are those from the glucose ring, namely, O3 for $Na^+/G18C6$, O4 for $Na^+/G19C6$, O2 and O3 for $Na^+/G21C7$, and O3 for $K^+/G21C7$ (see Table 3). Furthermore, from Table 3, one can see that the pairs of oxygen atoms in the crown ether rings that belong to the sugar rings are most likely to be further away from the cation compared to other oxygen atoms in the crown ether. This indicates that some constraint is imposed by the glucose ring on the O2 and O3 or O4 and O6, resulting in the latter to be less involved in the coordination with the cation compared to the other oxygen atoms from the crown ether. This restriction from the sugar ring can be

seen in all the complexes except $Na^+/G15C5$, $Na^+/G16C5$ and $K^+/G16C5$. The cavity size in G15C5 and G16C5 fit for Na^+ cation. Therefore, the O- Na^+ coordination distances do not vary much in the cases of $Na^+/G15C5$ and $Na^+/G16C$. On the other hand, K^+ is too big to be fully contained within the cavities of G15C5 and G16C5. For $K^+/G15C5$, the constrained sugar ring causes the O2 not to be as close to the cation as that of the O3, which has similar cation coordination distance as the other oxygen atoms. Meanwhile, both O4 and O6 in $K^+/G16C5$ have similar coordination distances to the cation. This is because, unlike the O2 in $K^+/G15C5$, the O6 has one C-C bond away from it sugar

Table 3 Geometrical parameters of different glycolipid crown ethers complexes with Na^+ or K^+ optimized at the level of theory B3LYP/6-31 G^* (Å)

Cation	Parameter	G15C5	Parameter	G18C6	Parameter	G21C7	parameter	G16C5	parameter	G19C6
Na^+	r_{Na-O3}	2.371	r_{Na-O3}	3.487	r_{Na-O3}	4.502	r_{Na-O4}	2.365	r_{Na-O4}	3.568
	r_{Na-O25}	2.300	r_{Na-O25}	2.628	r_{Na-O72}	2.367	r_{Na-O30}	2.321	r_{Na-O28}	2.347
	r_{Na-O28}	2.388	r_{Na-O28}	2.451	r_{Na-O69}	2.423	r_{Na-O27}	2.409	r_{Na-O25}	2.406
	r_{Na-O31}	2.293	r_{Na-O31}	2.572	r_{Na-O66}	2.485	r_{Na-O24}	2.357	r_{Na-O80}	2.447
	r_{Na-O2}	2.351	r_{Na-O34}	2.471	r_{Na-O63}	2.448	r_{Na-O6}	2.341	r_{Na-O24}	2.399
			r_{Na-O2}	2.511	r_{Na-O60}	2.388			r_{Na-O6}	2.356
K^+				r_{Na-O2}	3.162					
	r_{K-O3}	2.732	r_{K-O3}	2.796	r_{K-O3}	3.852	r_{K-O4}	2.701	r_{K-O4}	2.802
	r_{K-O25}	2.705	r_{K-O25}	2.722	r_{K-O72}	2.826	r_{K-O30}	2.684	r_{K-O28}	2.794
	r_{K-O28}	2.756	r_{K-O28}	2.851	r_{K-O69}	2.811	r_{K-O27}	2.768	r_{K-O25}	2.854
	r_{K-O31}	2.739	r_{K-O31}	2.813	r_{K-O66}	2.867	r_{K-O24}	2.715	r_{K-O80}	2.864
	r_{K-O2}	2.938	r_{K-O34}	2.724	r_{K-O63}	2.887	r_{K-O6}	2.704	r_{K-O24}	2.755
			r_{K-O2}	2.972	r_{K-O60}	2.801			r_{K-O6}	2.908
					r_{K-O2}	2.874				

ring, therefore it has a greater flexibility. One way for the pairs of O2 and O3 or O4 and O6 to minimize the coordination distances with the cation, is by reducing their dihedral angles O2-C-C-O3 for G15C5, G18C6 and G21C7, and O4-C-C-C for the G16C5 and G19C6, where the -C-C- belongs to the sugar rings (see Fig. 2). This can be verified by comparing the dihedral angles of the free crown ethers and those of the complexes. The comparison is given in Tables 4 and 5.

From Tables 4 and 5, we can see that these dihedral angles of the glycolipid crown ethers generally become smaller when the complexes are formed due to the interaction of the oxygen binding sites with the cation. As for the other dihedral angles O-C-C-O, around each crown ethers beside the O2-C-C-O3, the optimized structures in Fig. 2 show that G18C6, G16C5 and G19C6 all have their dihedral angles of O-C-C-O in their crown ethers, either in the state of gauche+ ($0^\circ \leq \varnothing < 120^\circ$) or gauche- ($120^\circ \leq \varnothing < 0^\circ$). Besides the gauche+ and gauche- states, the G15C5 has one of its O-C-C-O in the trans state ($120^\circ \leq \varnothing$ and $\varnothing < -120^\circ$), while G21C7 has two trans states. However, all the trans states are transformed to the gauche states when the optimum coordination of oxygen atoms to the cations was considered.

Binding and exchange enthalpies and gibbs free energies

The thermodynamics properties of the five molecules calculated at the B3LYP levels of theory using 6-31 G* basis set are given in Table 6. All the results in Table 6 have been corrected for their BSSE using the counterpoise method. The table shows that the binding energies, ΔE^b , of the molecules to smaller cation Na^+ are lower than the binding energies to the cation K^+ which are higher. This is consistent with previous experimental and theoretical studies of other crown ethers systems [38, 39] and crytand [40] systems in gas phase which have shown that the binding energies are lower for small size alkali cations. This is because smaller size cations can have higher charge density and are able to bond with the coordination oxygens in crown ethers. Hence, Na^+ /glycolipid crown ethers complex are more stable than

Table 4 Dihedral angle O2-C-C-O3 for optimized structures of molecules G15C5, G18C6 and G21C7 and their complexes with cations Na^+ and K^+

M (glycolipid crown ether)	Dihedral angles of O2-C-C-O3(°)		
	M	Complex Na^+/M	Complex K^+/M
G15C5	71.047	61.831	61.855
G18C6	74.375	61.141	64.613
G21C7	69.845	68.067	67.362

Table 5 Dihedral angle O4-C-C-C for optimized structures of molecules G16C5 and G19C6 and their complexes with cations Na^+ and K^+

M (glycolipid crown ether)	Dihedral angles of O4-C-C-C(°)		
	M	Complex Na^+/M	Complex K^+/M
G16C5	65.158	59.809	63.114
G19C6	68.018	62.116	58.571

their counterpart complex of K^+ /glycolipid crown ethers, as shown in their binding enthalpies (Table 6). Furthermore, the feasibility of the complex formation is given by the Gibbs free energy. The Gibbs free energies calculated are negative values, indicating that all the complexes formation in gas phase considered here are chemically feasible.

Comparing the Na^+ complexes, our results show that the trend of the binding energies, binding enthalpies and the Gibbs free energies is in the order of $\text{G21C7} < \text{G19C6} < \text{G18C6} < \text{G16C5} < \text{G15C5}$. For the K^+ complexes, the trend is slightly different and is given as $\text{G21C7} < \text{G18C6} < \text{G19C6} < \text{G16C5} < \text{G15C5}$. From this comparison, we may deduce that, in gas phase, the glycolipid crown ether G21C7 is the most reactive in forming the stable complex with both the cations Na^+ and K^+ , while G15C5 is the least reactive. The sequence of the complex binding energies indicates that the higher the number of oxygen atoms in the crown ether ring, the more reactive is the formation of the complex with a cation. When comparing G16C5 and G15C5, both of which have the same number of oxygen atoms in their crown ether rings, suggests that the additional flexibility in G16C5 makes it more reactive than G15C5 toward the formation of the complex. On the other hand, while Na^+ is small compared to the cavities of G18C6 and G19C6, the additional flexibility of the latter, enable it to encapsulate Na^+ better than the former. However, the formation of the $\text{K}^+/\text{G18C6}$ complex is more reactive than that of $\text{K}^+/\text{G19C6}$,

Table 6 The binding energies ΔE^b , binding enthalpies ΔH^b , and Gibbs free energies ΔG^b , in the gas phase for the complexes at 298 K

Molecule	Metal cation	ΔE^b (kcal/mol)	ΔH^b (kcal/mol)	ΔG^b (kcal/mol)
G15C5	Na^+	-79.4503	-80.0433	-69.2432
	K^+	-50.3658	-50.9582	-41.0366
G18C6	Na^+	-83.6138	-84.2074	-74.8544
	K^+	-69.0568	-69.6498	-59.9580
G21C7	Na^+	-90.3181	-90.9118	-80.0107
	K^+	-69.3405	-69.9335	-59.1654
G16C5	Na^+	-81.7037	-82.2967	-73.0679
	K^+	-52.8257	-53.4180	-44.3599
G19C6	Na^+	-84.0154	-84.6084	-75.9036
	K^+	-64.4974	-65.0897	-56.7369

which seems to suggest that the cavity of G18C6 fits better for K^+ compared to the cavity of G19C6.

To further understand the selectivity of these molecules toward Na^+ we calculated the exchange enthalpies and exchange free energy given by the chemical reaction scheme 2. The results are tabulated in Table 7. The exchange enthalpies and Gibbs free energies for these molecules can be arranged in the following order $G15C5 > G16C5 > G21C7 > G19C6 > G18C6$. The exchange enthalpies for G15C5 and G16C5 are significantly higher than G21C6, G19C7 and G18C6, which implies two of the former show much higher selectivity toward Na^+ against K^+ . Although these results were obtained based on the gas phase condition, it is qualitatively similar to the experimental cation selectivity performed in an aqueous solution with an equimolar ratio of cations Na^+ and K^+ [22], where the measurements were done using electrospray ionization method. The significantly higher ion selectivity of the two compounds G16C5 and G15C5 to the Na^+ over K^+ than the others was also confirmed by the experiment [22]. However, G21C7 was shown experimentally to have a slightly higher affinity toward K^+ , in contradiction to the theoretical result obtained in the gas phase. Nevertheless, the selectivity patterns of the five molecules over Na^+ and K^+ were similar to those of crown ethers with a similar number of oxygen atoms in the crown in gas phase as measured in the experiment [41].

It is well known that the preference of the crown ether binding with a cation in the gas phase would shift toward a bigger cation in the aqueous solution [42, 43]. The crown ether 18 C6 is known to bond more strongly with Na^+ than K^+ in the gas phase, while in the aqueous solution it shifts toward a stronger bond with K^+ than Na^+ . Two reasons have been suggested for this change of ion selectivity [38, 44, 45]. Firstly, the stronger solvation effect on the smaller cation Na^+ than K^+ , to some extent, make the complexation of $K^+/18$ C6 preferable toward $Na^+/18$ C6. Secondly the stronger solvation of the complexes with a bigger cation K^+ adds to the extra stability of the solvated complexes of $K^+/18$ C6 compared to $Na^+/18$ C6. On the other hand, the glucose based crown ethers of 18 C6 equivalent, studied by Bako et al. [46] in an experiment, shows that it prefers Na^+ over K^+ in an aqueous solution. The same effects on the

glycolipid crown ethers can be expected, thus in aqueous condition these prefer Na^+ over K^+ , especially G18C6 and G19C6, which are the equivalent of 18 C6. The solvation effect on the glycolipid crown ethers is undoubtedly interesting to the behavior of these molecules in aqueous solution as well as when they are dissolved in other solvents. This is currently under investigation and will be reported in the near future.

Conclusions

The geometrical and electronic structures of a series of five glycolipid crown ethers and their complexes with Na^+ and K^+ cations were studied using the B3LYP with the 6-31 G* basis set. The condensed Fukui functions were evaluated to give the local reactivity of the oxygen atoms on the crown ethers of each molecule to the nucleophilic attacks. It was found that these oxygen atoms were partially reactive, while the most reactive sites of each molecule tend to be located a distance away from the sugar ring. The calculated global nucleophilicity index revealed that upon optimization, smaller crown ethers size generally gave higher nucleophilicity. The five molecules give the energy gaps, which are close to one another. Among them, G16C5 has the highest energy gap, which means it has the highest chemical hardness. These molecules also have rather similar ionization potential but their electron affinities are sensitive to the difference in the geometrical size of their crown ethers. The lowest electron affinity is given by G16C5.

From the optimized structures of the glycolipid crown ethers, it was found that the cavity size of G15C5 is the best match with the Na^+ cation. The cavity size of G18C6 and G19C6 fits with K^+ better than other glycolipid crown ethers, where the cation is located at the mean plane of the crown ethers with all the oxygen coordinated to the encapsulated cation. On the other hands, there are a few cases, where the cavity sizes of the crown ether rings are too big such that some oxygen atoms are not coordinated to the cation. Furthermore, we observed that the sugar oxygen atoms O2, O3, O4 and O6 in their respective glycolipid crown ethers are in most cases further away from the cation compare to other oxygen atoms in their respective crown ether rings. Constrained by the sugar ring, these sugars' oxygen atoms are hindered from getting nearer to the cation. These oxygen atoms move toward the cation by lowering their dihedral angles of O2-C-C-O3 or O4-C-C-C from their initial optimized structures.

The calculated binding energies, enthalpies and Gibbs energies in the gas phase at temperature 298 K showed that all five molecules bound more strongly with cation Na^+ than K^+ . Based on this, the molecular binding stability with Na^+ could be arranged in the order of $G21C7 > G19C6 > G18C6 > G16C5 > G15C5$, while that with K^+ was in the order of $G21C7 >$

Table 7 Exchange enthalpies ΔH and Gibbs free energies ΔG for the cation exchange in the gas phase at 298 K

Molecule	ΔH (kcal/mol)	ΔG (kcal/mol)
G15C5	29.0851	28.2066
G18C6	14.5576	14.8965
G21C7	20.9783	20.8453
G16C5	28.8786	28.7080
G19C6	19.5187	19.1667

G18C6 > G19C6 > G16C5 > G15C5. The exchange enthalpies and Gibbs energies for the reaction scheme 2 calculated showed that the ion selective capability toward Na⁺ over K⁺ of these molecules was in the order of G15C5 > G16C5 > G21C7 > G19C6 > G18C6. Among them, the exchange enthalpy of G16C5 was close to G15C5 and both were significantly higher than the others. This was similar to the selectivity pattern found in the experiment in aqueous solution of equimolar cation Na⁺ and K⁺, [23] except for the G21C7, which might be due to the effect of the solvation of the water.

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