Simulating Stability Constants of Crown Ether-Ion Complexes

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INTRODUCTION

- Julius Rebek showed that biphenyl bis-crown ethers can exhibit allosteric binding of mercury ligands[1] – a property rarely seen in non-biological molecules.

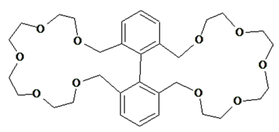


Figure 1: Crown ether biphenyl derivative studied by Julius Rebek.

- Molecular dynamics simulations (**MD**) with a simpler crown ether, **Benzo-15-Crown-5** (**B15C5**), were used in a first step to understand allosteric binding.

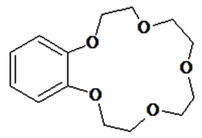
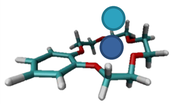


Figure 2: Benzo-15-crown-5 (B15C5) – simpler molecule studied in simulations.

SIMULATIONS



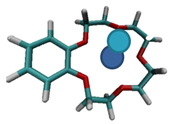


Figure 3: Two views of computer model of B15C5 crystal structure[2] with Na+ (purple) and counterion (blue)

- Each simulation began with one cation (**$Li^+ < Na^+ < K^+$**), one counterion, (**ClO_4^-**), and **B15C5.**
- Atom charge determined by quantum calculations in Gaussian03.
- Using Gromacs, the complex was solvated in **acetone**, **methanol**, and/or water.
- Experimental stability (**logKs**) values were compared to the **dissociation times** observed in MD:

$$cation^+ + crown \leftrightharpoons complex^+$$

RESULTS

Acetone **Methanol**

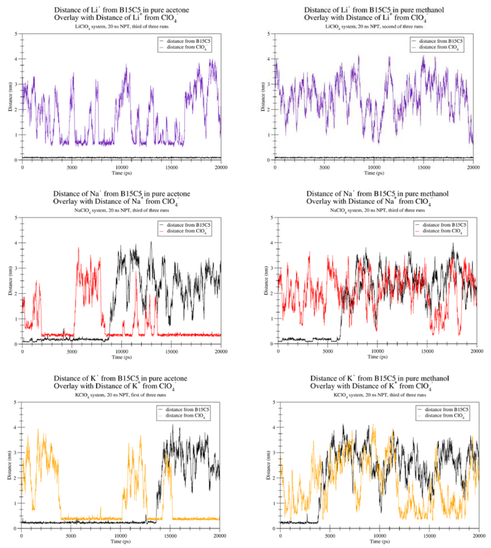
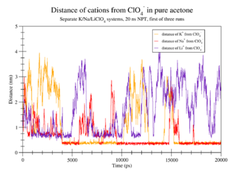


Figure 4: Distance between cation and B15C5 (black) and distance between cation and perchlorate (colors).

Acetone



Methanol

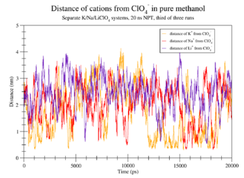


Figure 5: Cation-perchlorate pair distances.

Cation-B15C5 Dissociation Times (MD*) and $LogK_s$ Values (Experiment[4])

	Acetone			Methanol		
Ion	Li^+	Na^+	K^+	Li^+	Na^+	K^+
Average Dissociation Time (ns)	20**	8.7	17.9**	20**	3.7	3.2
$logK_s$[4]	3.2	3.7	3.7	1.1	3.0	3.2

*Triplicate 20-ns simulations at randomized temperatures. If the ion remained bound the dissociation time was taken as 20 ns**.

DISCUSSION

Summary of Results

	Acetone	Methanol
Computational	$Na^+ < K^+ < Li^+$	$K^+ \approx< Na^+ < Li^+$
Experimental	$Li^+ < Na^+ \approx K^+$	$Li^+ < Na^+ \approx< K^+$

Conclusion:
MD and experimental results do not agree. The model must be adjusted further to correlate with experiment, perhaps including quantum calculations to account for charge transfer.

Solvent composition and cationic radii affect the rate of dissociation as shown by both experiment and simulations.

ACKNOWLEDGMENTS

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