Design and Synthesis of the Next Generation of Crown Ethers for Waste Separations

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Purpose

Design, Synthesis, and Characterization of the Next Generation of Crown Ethers for Metal-Ion Separations

Target Separations

Fission Product Separations: Sr, Cs, Ra

Removal of Lithium from Groundwater

Separation Techniques

Solvent Extraction

Ion Exchange

Approach

Develop Detailed Basic Understanding of Structural and Thermodynamic Properties of Model and Actual Separation Systems

Use This Insight to Design and Synthesize New Extractants and Resins With Improved Separation Properties

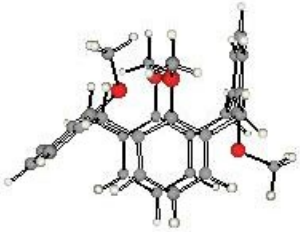
Evaluate New Materials for Desired Properties and Provide Feedback for Basic Design Efforts

Molecular Modeling

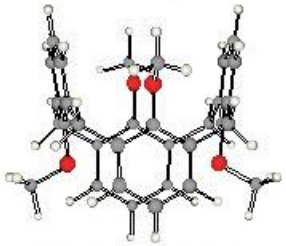
Computational Studies are Directed Towards Understanding the Role Conformation and π-Cation Interactions Play in Metal-Ion Binding by Calix[4]arenes and Calixarene Crown Ethers

Calix[4]arenes Adopt Four Main Conformers

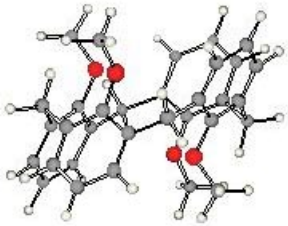
cone (C_{2v})



partial cone (C_s)



1,3 alternate (D_{2d})



1,2 alternate (C2h)

The various modes of cation binding to the different calixarene conformations differ with respect to the number of oxygens and arenes that serve as donor groups

CONFORMATIONAL ENERGIES FOR TETRAMETHOXYCALIX[4] ARENE

Numerous calculations of the relative energies of the four calix[4]arene conformers (see below) have been performed with a variety of molecular mechanics methods (AMBER, CHARMm, MM2, and MM3) and semi-empirical quantum mechanical methods (AM1 and PM3). A notable aspect of these earlier studies is the broad disagreement between the results obtained by the various computational approaches. The agreement between calculated "gas-phase" populations and measured solution phase populations in general has been poor.

Our goal is to obtain definitive geometries and relative energies for the four conformers of tetramethoxy-calix[4]arene. Recent advances on computational methodology implemented at our lab, along with large increases in computational power, have made possible calculations of these previously intractable systems. Each conformer has been optimized using density functional theory at both the BLYP/DZVP2 and at the B3LYP/DZVP2 levels of theory (see Table below). Single point MP2/aug-cc-TZVP calculations on the B3LYP/DZVP2 geometries are in progress to confirm the B3LYP/DZVP2 relative energies.

RELATIVE "GAS-PHASE" ENERGIES (KCAL/MOL) OF TETRAMETHOXY-CALIX[4]ARENE CONFORMERS AT VARIOUS LEVELS OF THEORY

Conformer	BLYP/ DZVP2	BL3YP/ DZVP2	MINDO/d	MM3(96) type 6 O	MM3(96) type 41 O	SYBYL	CHARMm	AMBER
cone	0.00	0.00	2.67	0.24	0.16	0.82	1.81	7.34
partial cone	0.10	0.20	0.69	0.00	0.00	0.00	0.00	2.99
1,3 alt	3.04	3.44	0.00	1.10	0.57	2.91	0.38	0.00
1,2 alt	5.23	5.85	3.36	4.05	5.25	3.33	5.51	4.29

MM3(92), type 6 oxygens. Relative energies are similar to those reported with MM3(92): cone, 0.27; partial cone, 0.00; 1,3 alternate, 1.50; 1,2 alternate, 4.10 kcal/mol (Harada, T.; Rudzinski, J. M.; Shinkai, S. *J. Chem. Soc. Perkin Trans. 2* **1992**, 2109).
MM3(96), type 41 oxygens Oxygen type 41 is recommended for conjugated ethers as described in Hay, B.P.; Yang, L.; Allinger, N.L.; Lii, J.-H. *J. Mol. Struct. (THEOCHEM)* **1998**, 428, 203. **SYBYL** as implemented in the MacSpartan Program.
CHARMm Using parameters and partial charges from a prior calixarene study (van Hoorn, W.P.; Briels, W.J.; van Duynhoven, J.P.M.; van Veggel, F.C.J.M.; Reinhoudt, D.N. *J. Org. Chem.* **1998**, *63*, 1299). Relative energies are comparable to those reported for the para t-butyl analogue: cone, 3.3; partial cone, 0.6; 1,3 alternate, 0.0; 1,2 alternate, 6.3 kcal/mol.
AMBER Using the default parameter set of AMBER4.1 with missing parameters and 6-31G* electrostatic potential charges from a prior calixarene study.(Grootenhuis, P. D. J.; Kollman, P.A.; Groenen, L.C.; Reinhoudt, D.N.; van Hummel, G.J.; Ugozzoli, F.; Andretti, G.D. *J. Am. Chem. Soc.* **1990**, *112*, 4165-4176). Relative energies are comparable to those reported for the para t-butyl analogue: cone, 9.3; partial cone, 4.2; 1,3 alternate, 0.0; 1,2 alternate, 4.2 kcal/mol.

BOLTZMANN POPULATIONS (%) at T = 243 K

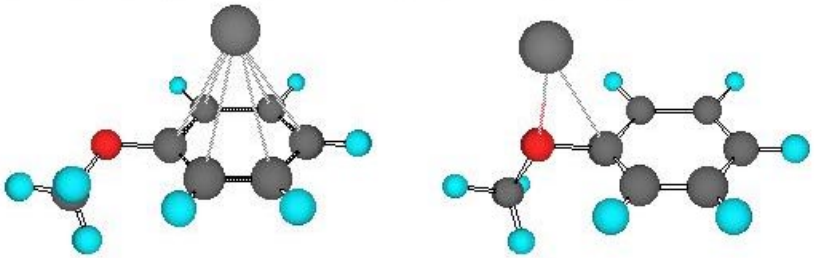
Method	Partial Cone	Cone	1,3 Alternate	1,2 Alternate
NMR CDCl3	73	27	n.d.	n.d
B3LYP/DZVP2	72.5	27.5	0.04	0.00001
BLYP/DZVP2	76.4	23.5	0.04	0.0001
MM3(96), O type 41	79.6	14.3	6.1	0.00001
MM3(96), O type 6	84.9	12.9	2.2	0.001
SYBYL	95.6	4.4	0.06	0.001
CHARMm	89.3	0.5	10.2	0.00001
MINDO/d	48.8	0.2	51.0	0.0001
AMBER	0.8	0.00002	99.2	0.003

Populations are calculated after correcting the energies for entropic terms arising from conformational and rotational degeneracies, i.e., G = E + RTln(s/n). Symmetry and s/n values were as follows: partial cone, Cs, 1/8; cone, C2v, 2/4; 1,3 alternate, D2d, 4/2; 1,2 alternate, C2h, 1/2.

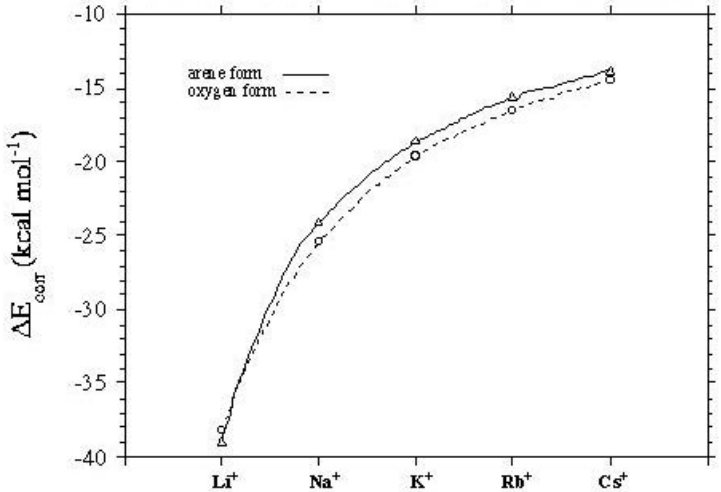
METHOXYBENZENE IS AN AMBIDENT LIGAND

Tetramethoxycalix[4]arene is composed of 4 methoxybenzene subunits linked with methylene spacers. We have completed high-level calculations on complexes of the alkali cations with methoxybenzene to better understand the energetics and geometries of the host-guest interactions present in calixarene-cation complexes. We find that methoxybenzene is an ambident ligand, i.e., it offers two binding sites to a cation.

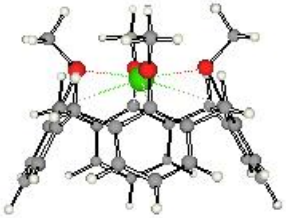
THE TWO STABLE GEOMETRIES FOR $[K(METHOXYBENZENE)]^+$



BINDING ENERGIES OF ARENE FORM AND OXYGEN FORM

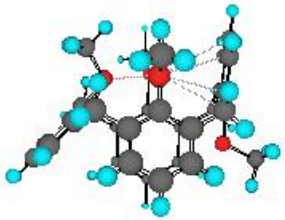


MINIMA LOCATED FOR SODIUM COMPLEXES

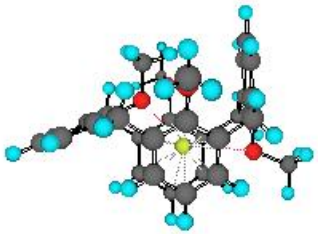


cone, 4 O (0.0 kcal/mol)

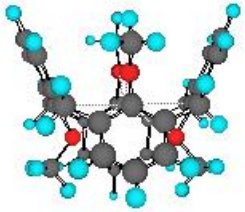
cone, 2 O + 2 arene (1.3 kcal/mol)



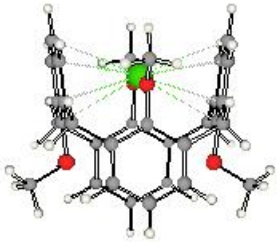
partial cone, 3 O + 1 arene (1.2 kcal/mol)



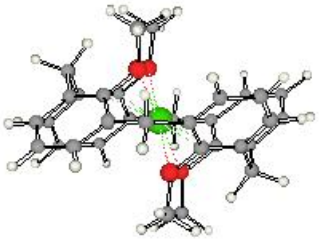
partial cone, 3 O + 1 arene (2.5 kcal/mol)



1,3 alternate, 4 O (2.8 kcal/mol)



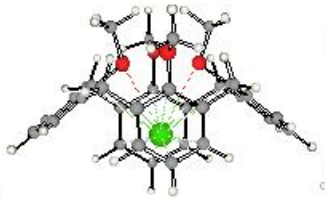
1,3 alternate, 2 O + 2 arene (4.3 kcal/mol)



1,2 alternate, 4 O (3.2 kcal/mol)

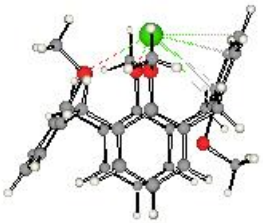
MINIMA LOCATED FOR CESIUM COMPLEXES

cone, 4 arene

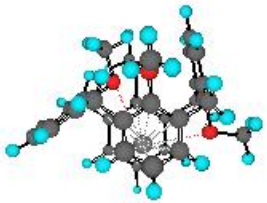


cone, 2 O + 2 arene

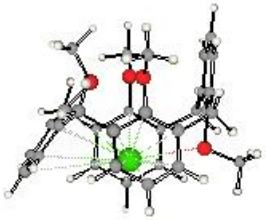
cone, 4 O



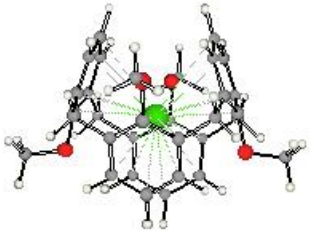
partial cone, 3 O + 1 arene



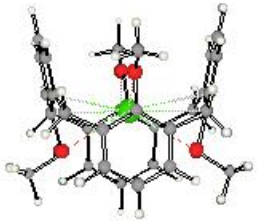
partial cone, 2 O + 2 arene



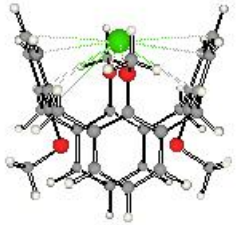
partial cone, 1 O + 3 arene



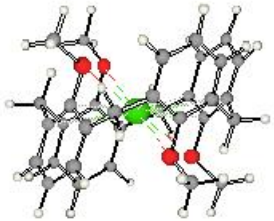
1,3 alternate, 4 arene



1,3 alternate, 4 O



1,3 alternate, 2 O + 2 arene



1,2 alternate, 4 O

1,2 alternate, 2 O + 2 arene

Next-Generation Calix[4]arene-Crown Ethers for Cesium Extraction

Goal

Design New Calix[4]arene Crown Ethers with improved Cesium/Potassium selectivity

Background

Calix[4]arene crown-6 ethers extract Cesium 10 -10 times more strongly than other crown ethers, with the highest Cs/Na selectivities (>10) known

Recent Studies Show

Cs/K selectivities are modest (10 -10)

Potassium competes with Cesium under extraction conditions simulating Hanford tank wastes

Molecular Modeling studies suggest that 1,3-deoxygenated calix[4]arene crown ethers may exhibit better complementarity for cation complexation

Approach

Synthesize new calix[4]arene crown ethers lacking ether oxygens on two of the four arene rings

Evaluate extraction behavior for alkali metal nitrate salts and compare to that of known calix[4]arene crown ethers

Investigate structural factors that influence binding strength and selectivity

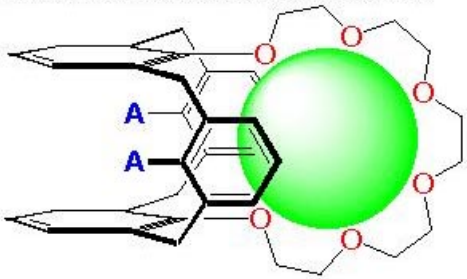
Molecular Mechanics Modeling of Calix[4]arene Crown Ethers

Calix[4]arene Crown-6 Ethers in the 1,3-alternate conformation are efficient and selective Cesium Extractants

When a cation is bound in the crown ether cavity, coordination to any or all of the six oxygens of the crown ether and two arenes of the calixarene is possible

It is reasonable to propose that varying the distance between the oxygens and/or arens of the calixarene will influence the complementarity of the cavity for cation binding

Molecular mechanics (MM3) calculations were performed to evaluate the role of substituents in position **A** of the calixarene in influencing ligand complementarity and π-cation interactions



Conformational analyses were performed on the Cs and K complexes of a model calix[4]arene crown ether to determine the most probable low-energy conformations of the crown ether portion of the molecule.

Three crown ether conformations were used in the subsequent modeling of the calixarene part of the molecule

Results show that varying the substituents at **A** influences the complementarity for cation binding

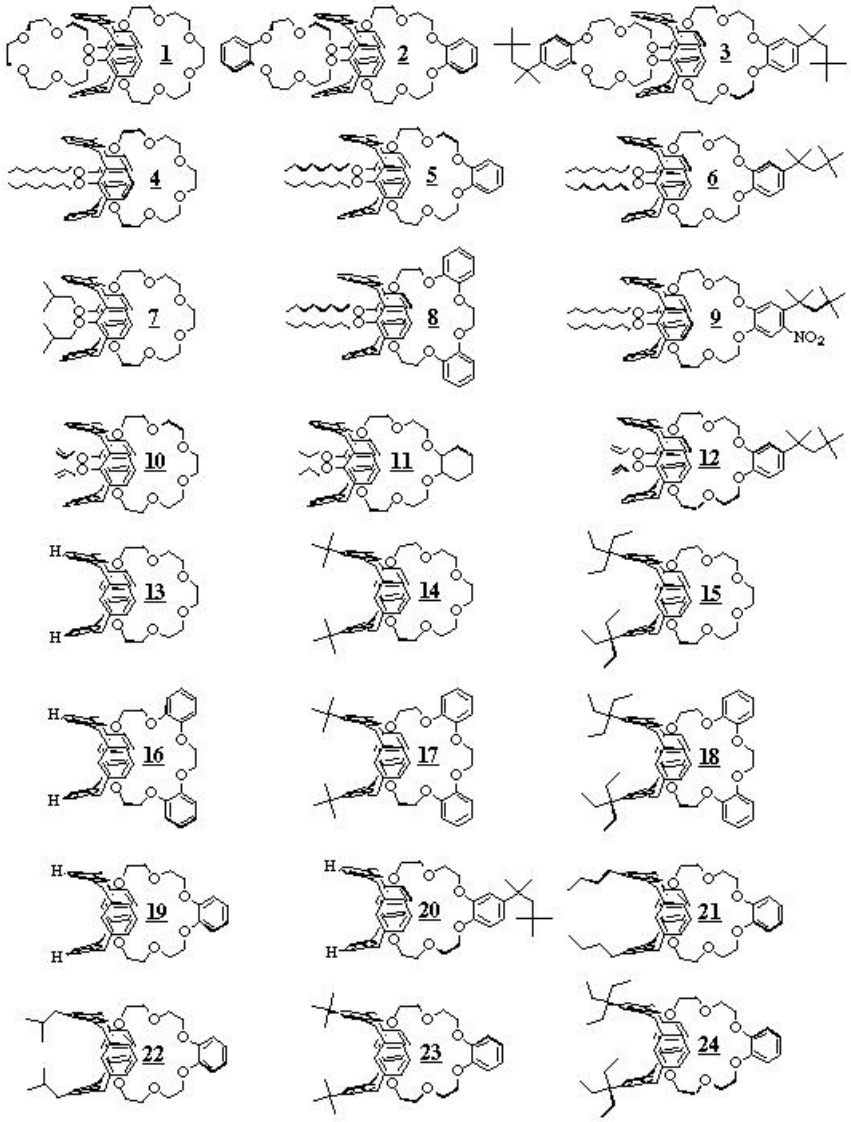
Lower values for $\Delta U_{comp} + E_{\pi}$ = Sum represent higher binding site complementarity.

Best Complementarity occurs for **A** = **-H**,

∴ a series of new calix[4]arene crown ethers were synthesized bearing **-H** at position **A**

	Conformer #1			Conformer #2			Conformer #3		
A	ΔU_{comp}	E_{π}	**Sum**	ΔU_{comp}	E_{π}	**Sum**	ΔU_{comp}	E_{π}	**Sum**
K									
-H	6.88	-8.96	**-2.08**	7.94	-8.69	**-.075**			
$-OCH_3$	7.64	-8.23	-.058	8.61	-8.11	0.51			
$-OC(CH_3)_3$	7.44	-7.48	-.004	7.93	-7.35	0.58			
Cs									
-H	5.93	-5.04	**0.89**	3.36	-4.85	**-1.49**	2.89	-4.94	**-2.05**
$-OCH_3$	7.18	-4.30	2.88	4.87	-3.97	0.90	4.86	-4.06	0.80
$-OC(CH_3)_3$	6.99	-3.90	3.09	4.64	-3.54	1.10	4.96	-3.62	1.34

All energies in kcal/mol.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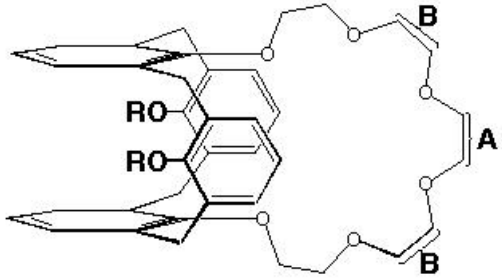
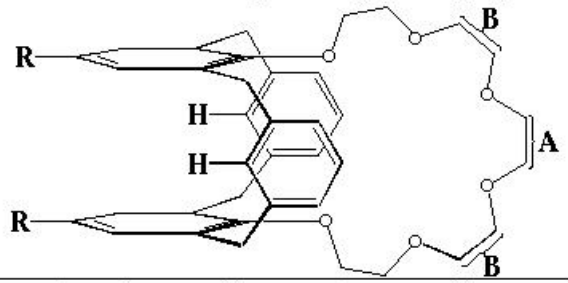
Extraction of Alkali Metal Nitrates by Calix[4]arene Crown-6 Ethers Derived from Tetrahydroxy Calix[4]Arene



Compound	D_{Cs}	$S_{Cs/Li}$	$S_{Cs/Na}$	$S_{Cs/K}$	$S_{Cs/Rb}$
1	4.402	116786	10042	237	15
duplicate	4.680	119063	10542	249	16
2	4.488E	264904	58226	227	17
duplicate	4.591	382974	55943	245	18
3	4.324	235972	41366	223	17
duplicate	4.120	316374	41098	225	17
4	3.761	117376	16555	238	20
duplicate	3.550	128327	16728	242	20
5	3.856	304127	101094	263	18
duplicate	4.219	600046	104780	311	20
6	4.979	732178	105126	334	15
duplicate	4.946	780246	111039	342	16
7	5.689	241952	18118	353	19
duplicate	5.269	216640	17371	333	18
8	1.583	107311	632000	119	9
duplicate	1.644	347970	656435	140	10
9	2.186	220501	621878	253	18
duplicate	2.402	694806	472873	308	20
10	6.436	997196	105808	427	18
duplicate	6.357	1103027	113248	427	18
11	1.227	32464	8643	184	17
duplicate	1.149	30389	8067	187	17
12	5.119	250932	18521	285	18
duplicate	4.693	192981	16173	255	16

Extraction of Alkali Metal Nitrates by Calix[4]arene Crown-6 Ethers Derived from Dihydroxy Calix[4]Arene

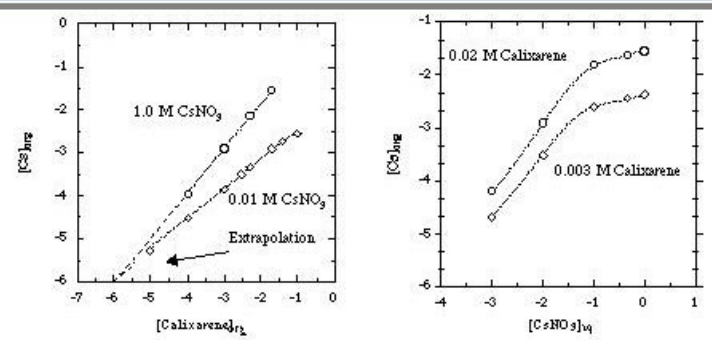


Compound	D_{Cs}	$S_{Cs/Li}$	$S_{Cs/Na}$	$S_{Cs/K}$	$S_{Cs/Rb}$
13	0.3899	13008	12517	>4000	>39
duplicate	0.4156	51514	33455	>4300	>42
14	0.7191	37582	26594	1337	>72
duplicate	0.7919	52051	20706	1513	>79
15	0.3672	14286	8441	416	>37
duplicate	0.3429	15822	6679	452	>34
16	0.1165	>20000	>46000	>1200	>12
duplicate	0.1163	>20000	>46000	>1200	>12
17	0.2414	>400000	>96000	>2500	>24
duplicate	0.2400	>400000	>95000	>2500	>24
18	0.1071	12064	>42000	1111	>11
duplicate	0.1036	42806	>41000	1075	>10
19	0.3865	>600000	>150000	>4000	>39
duplicate	0.3799	>600000	>150000	>4000	>38
20	0.4840	>800000	>190000	2842	>48
duplicate	0.5273	>900000	>210000	2518	>53
21	0.7707	>1300000	>300000	2787	>77
duplicate	0.7384	>1200000	>290000	2701	>74
22	0.7127	>1200000	>280000	1420	>71
duplicate	0.7108	>1200000	>280000	1663	>71
23	0.9222	>1500000	>360000	1232	72
duplicate	0.9128	>1500000	>360000	1215	76
24	0.3235	32640	>130000	273	>32
duplicate	0.3209	79539	>130000	338	>32

Equilibrium Analysis of KNO_3 and $CsNO_3$ Extraction by BOBCalix4C6 Revealed Species Stoichiometry and Elucidated Selectivity Factors

- BOBCalix4C6 extracts 1 or 2 Cs^+ Ions
- The 2nd Cs^+ ion is two orders of magnitude more weakly bonded than the 1st
- SXLSQI analysis for extraction into 1,2Dichloroethane at 25 °C gave the following:

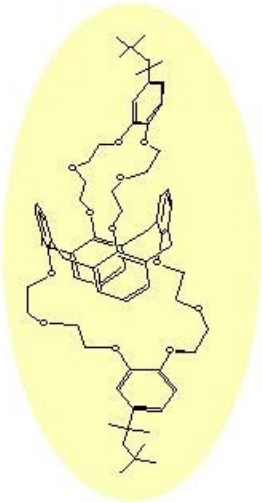
	$\log K_{ex,1}$	$\log K_{ex\pm,1}$	$\log K_{ex,2}$	$\log K_{ex\pm,2}$
$CsNO_3$	2.77 ± 0.02	-0.93 ± 0.02	3.54 ± 0.04	< -0.4
KNO_3	0.18 ± 0.06	-4.03 ± 0.15		



Investigating Thermodynamic Properties in the Solvent Extraction of $CsNO_3$ and KNO_3 by BOBCalix4C6 in 1,2-Dichloroethane

Partitioning of BOBCalix4C6

$CsNO_3$ mol L^{-1}	log P_B
0	> 5.12
1E-06	4.61 ± 0.06
1E-05	4.74 ± 0.80
1E-04	4.80 ± 0.24
1E-03	5.12 ± 0.12
1E-02	5.03 ± 0.46
1E-01	> 5.12

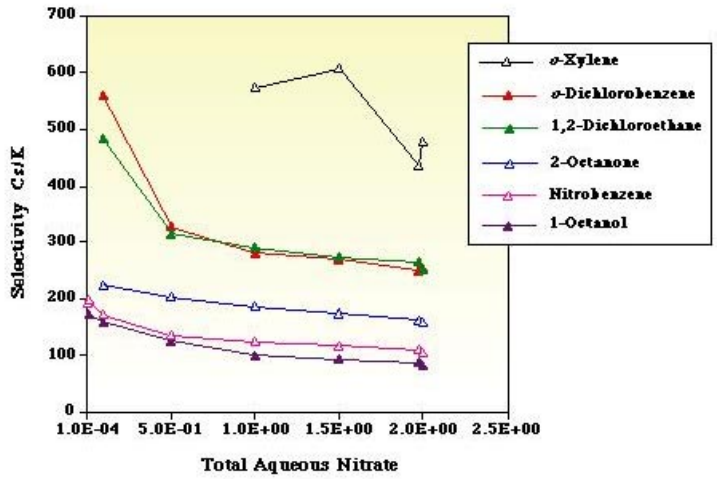


Extraction Takes Place by:

$$nM^+ + nX^- + B_{org} \xrightarrow{\log K_{ex,n}} M_nBX_{n,org}$$

$$nM^+ + nX^- + B_{org} \xrightarrow{\log K_{ex\pm,n}} MBX^+_{n-1,org} + X^-$$

Selectivity of Cesium over Potassium in Competitive Extractions is Dependent upon Potassium Concentration and Diluent Type



Conditions:
Equal volumes at 25 °C for 1 hour; 5 mM BOBCalix4C6 in 1,2-DCE
Variable KNO_3 0.001 M - 2.0 M; $CsNO_3$ constant at 5×10^{-5} M

SXLSQI modeling results for 1,2-DCE showed that the decrease in $S_{Cs/K}$ as loading of KNO_3 increases is due to increased ion-pairing in the solvent phase.

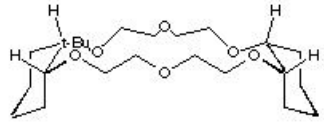
Next Generation Solvent Extraction Systems Employing Crown Compounds

Introduction

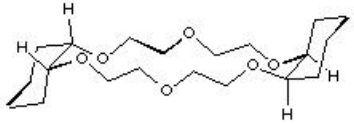
Synergistic solvent extraction systems employ *two different ligands* to effect partitioning of a solute that is *greater than that observed when either extractant is used alone*. Such systems show promise in the development of extraction processes of *improved efficiency and selectivity* because the *unfavorable thermodynamic requirements* of co-ion transport and dehydration *are diminished* by the cation-exchange and solvating abilities of the two extractants. To date, no systematic investigations of synergism using crown ethers and dialkyl phosphoric acids have been reported. An understanding of how these classes of extractants interact to synergize the partitioning of cations is important if such systems are to see more widespread application.

The objectives of this research are to study the synergistic extraction of Ca^{2+}, Sr^{2+}, and Ba^{2+} by a series of *dicyclohexano-18-crown-6* (*DCH18C6*) isomers and *dialkyl phosphoric acids* of increasing steric bulk, and to determine if the magnitude of the observed synergistic effects can be *predicted from macrocyclic ligand strain energies calculated by molecular mechanics*. These results will ultimately be employed to develop a new series of synergistic metal ion sorbents for alkali and alkaline earth cations.

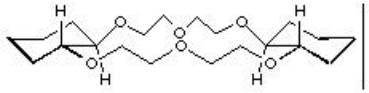
Isomers of Dicyclohexano-18-Crown-6



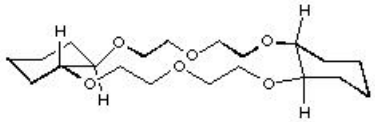
A : cis-syn-cis



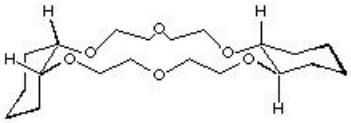
B : cis-anti-cis



C : trans-syn-trans

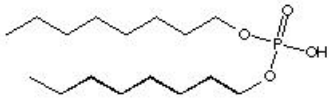


D: trans-anti-trans

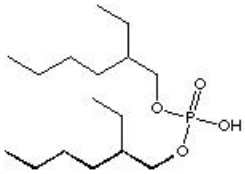


E : cis-anti-trans

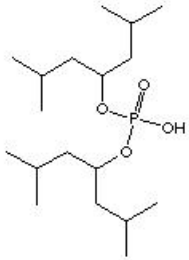
Dialkyl Phosphoric Acids Used in This Study



Di-n-Octyl phosphoric Acid : HDOP



Di-2-ethylhexyl phosphoric Acid : HDEHP



Di(di-isobutylmethyl) phosphoric Acid : HD(DiBM)P

General Equilibria

Osmometric and infrared spectroscopic evidence show that there is no interaction between DCH18C6 and the dialkyl phosphoric acids (HA) in toluene. The extraction equilibria can therefore be generalized as:

$$M^{2+} + DCH18C6 + 2(HA)_2 \underset{\text{toluene}}{\overset{K_{ex}}{\rightleftharpoons}} M(DCH18C6)(HA_2)_2 + 2H^+$$

$$K_{ex} = \frac{[M(DCH18C6)(HA_2)_2][H^+]^2}{[M^{2+}][DCH18C6][(HA)_2]^2}$$

D_M is defined here as:

$$D_M = \frac{[M(DCH18C6)(HA_2)_2]}{[M^{2+}]}$$

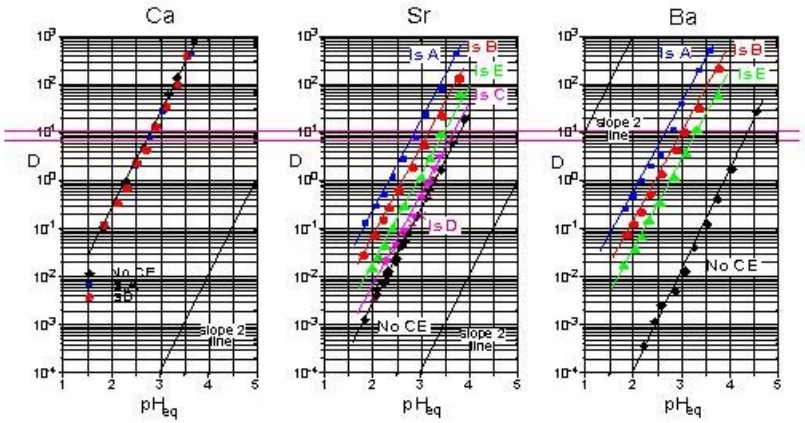
After substitution of D_M into the equation for K_{ex} and rearrangement:

$$\log D_M = \log K_{ex} + 2pH + \log[DCH18C6] + 2\log[(HA)_2]$$

Systematic variation of the pH, [DCH18C6], and $[(HA_2)]$ terms and their combinations are required to fully characterize the synergistic extraction equilibria.

Acid Dependencies in the Presence of DCH18C6

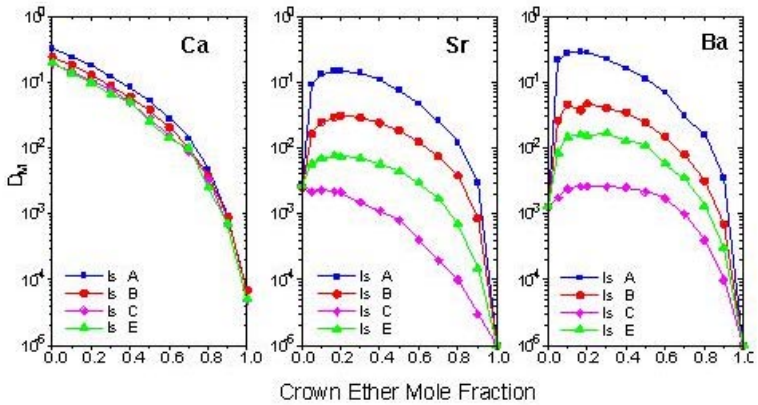
[HDOP] = 0.1M in toluene, [DCH18C6] = 0.025M, [M(NO3)2] = 0.001M



HDOP - CE Continuous Variation Study

[HDOP] + [CE] = 0.1M

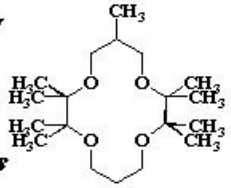
[HNO3] = 0.01M; [M(NO3)2] = 0.001M



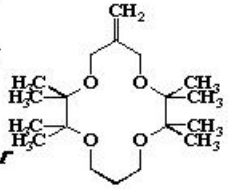
Polymer Immobilized Crown Ethers for Lithium Adsorption

Lithium leaching from burial sites at the Oak Ridge Y-12 Pla poses potential long-term environmental hazard.

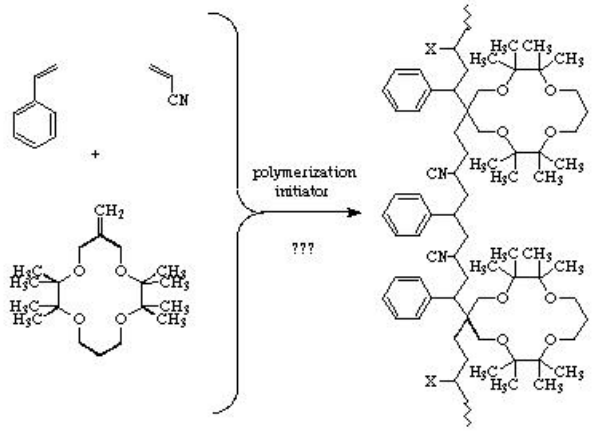
14-Crown-4 Ether bearing methyl groups on the ethylene bridges has been shown to a selective extractantfor Lithium salts



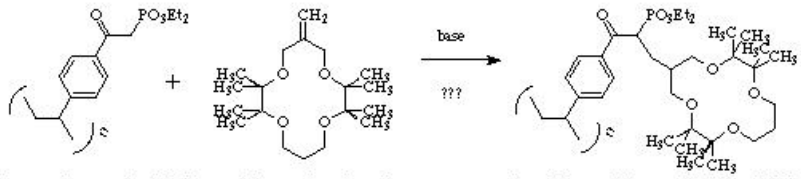
Precursor crown ether has olefinicfunctionality potentially suitable for incorporation into polymer network



Direct Incorporation of Crown Ether Into Polymer Network is Synthetically Attracti

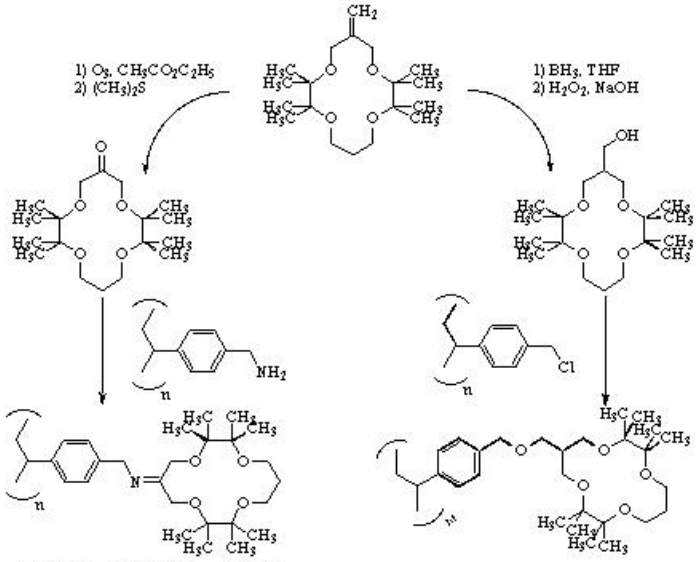


Low Incorporation of Crown Ether (as determ: by Li^+ uptake) Encourages Alternative Approa



Now, Low Lithium Uptake is Accompanied by Non-Selectivity

New Effort Involves Chemical Modification Crown Ether; Allows Potential Alternative Chemistries for Immobilization



No Measureable Lithium Uptake
Imine Linkage May Be Unstable

Conclusions

Development of high-level Molecular Modeling is leading to new insights into the binding modes of metal cations by calixarenes and providing input useful in the design of new calixarene crown ethers

Detailed SX studies and speciation modeling are leading to better understanding of structure and speciation in the extraction of alkali and alkaline earth cations by calixarene crown ethers and by crown ether-phosphoric acid synergistic systems

New calixarene crown ethers exhibit improved cesium selectivities for potassium (and rubidium) and help provide insight into the role substituents play in determining conformational preferences and preorganization of calix[4]arene crown ethers

Acknowledgements

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