Cryptands
Криптанды

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Paper
Статья

Host−Guest Complexes of Two Isomeric 2,2′−Bioxazole Based {2}−Lehn−Type Cryptands. Prediction of Ion Selectivity by Quantum Chemical Calculations. Part XIV[§]

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Dedicated to the 75th birthday of our friend and teacher
Prof. Dr. Dr. h.c. mult. Rudi van Eldik

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*The two isomeric cryptands **1** (N,N'-bis(2,2'-bioxazole-5,5'-dimethyl)-2,2'-bioxazole-5,5'-bis(methylamine)) and **2** (N,N'-bis(2,2'-bioxazole-4,4'-dimethyl)-2,2'-bioxazole-4,4'-bis(methylamine)) were investigated by DFT-calculations (RB3LYP/LANL2DZp). Based on these structures and energies we have determined with model equations and by structural comparison with solvent complexes ([M(Furan)$_n$]$^{m+}$, [M(Pyridine)$_n$]$^{m+}$ and [M(NH$_3$)$_n$]$^{m+}$) the ion selectivity of **1** and **2**. **1** exhibits preferences for the sodium cation and the calcium dication, nearly equally with the strontium dication. Therefore, **1** has a cavity comparable to [phen.phen.phen]. In contrast, cryptand **2**, although it also shows a preference for the third-row sodium cation, for the third-row alkaline earth cation Mg^{2+}. Therefore, the cavity size must be similar to that of Bühl's cryptand dodeka(ethylene)octamine and [2.1.1]. We attribute this difference in selectivity to the longer M^{m+}-N-interactions in **2** compared to M^{m+}-O-interactions in **1**.*

Keywords: Selective ion complexation, cryptand, DFT-study.

Комплексы "хозяин−гость" двух изомерных {2}−криптандов Лена на основе 2,2′−биоксазола. Прогнозирование ионной селективности с помощью квантово−химических расчетов. Часть XIV[§]

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Two Isomeric 2,2'-Bioxazole Based {2}-Lehn-Type Cryptands

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*В работе методом DFT (RB3LYP/LANL2DZp) были изучены два изомерных криптанда: криптанд **1** (N,N'-бис(2,2'-биоксазол-5,5'-диметил)-2,2'-биоксазол-5,5'-бис(метиламин)) и криптанд **2** (N,N'-бис(2,2'-биоксазол-4,4'-диметил)-2,2'-биоксазол-4,4'-бис(метиламин)). Основываясь на их структурных и энергетических параметрах, при помощи модельных уравнений и сравнения со структурами комплексов, образованных с молекулами растворителей ([M(Furan)ₙ]ᵐ⁺, [M(Pyridine)ₙ]ᵐ⁺ и [M(NH₃)ₙ]ᵐ⁺), мы определили ионную селективность криптандов **1** и **2**. Криптанд **1** проявляет предпочтение к катионам натрия и кальция, почти наравне с катионами стронция. Следовательно, его полость сопоставима с полостью [phen.phen.phen]. Криптанд **2** имеет сродство не только к ионам натрия, но и к ионам щелочноземельного магния, что делает его полость сопоставимой с полостью криптандов додека(этилен)октамин (криптант Бюля) и [2.1.1]. Мы считаем, что эту разницу в селективности можно отнести на счет более длинных Mᵐ⁺-N связей в криптанде **2** по сравнению с Mᵐ⁺-O связями в криптанде **1**.*

Ключевые слова: Ионная селективность комплексообразования, криптанд, DFT расчеты.

Introduction

Selective ion complexation is closely connected to supramolecular chemistry since the first seminal manuscripts of Charles J. Pederson on crown ethers[1] and of Jean-Marie Lehn, Bernard Dietrich, and Jean Pierre Sauvague on 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane, well known today as [2.2.2] and traded as Kryptofix 222.[2,3] The potential of similar cage like compounds to selectively bind guests was recognized immediately. Those first publications paved a way for the development of more complex and refined structures of such cage like systems; some of them currently have potential applications in a selective complexation of radioactive or toxic ions in medicine,[4] in analysis[5] as a ligand for MRI contrast agents,[6] in catalysis[7] or in elementary research,[8] and as model compounds, *e.g.* for valinomycin and enzyme inhibitors.[9] Selective complexation of alkali and alkaline earth metal cations is an important topic in (bio-)inorganic supramolecular chemistry. Additional interest is emerging due to application in the synthesis and stabilization of organic electrides, which are of great interest for theories of electron-spin interactions and insulator-metal transitions.[10]

Different analogs of Lehn's [2.2.2] cryptand, where the bridging oxygen donor atoms have been replaced by sp^3-hybridized nitrogen in [N2N2N2][11] or [TriPip222],[12] and with sp^2-hybridized nitrogen donor atoms as in [bpy.bpy.bpy] or [phen.phen.phen][13] were extensively studied regarding their selective ion complexation abilities by means of computational chemistry. As a continuation of these studies we report herein a quantum chemical study on the selective alkali and alkaline earth metal cation complexation by [2.2.2]-type (Lehn type) cryptands in which the bridging ethylene glycol ether moieties were replaced by 2,2'-bioxazole units (Figure 1). This allowed us to examine the coordination affinities of different donor atoms (nitrogen and oxygen) included in the bridging units of two cryptand isomers, further noted as cryptand **1** (*N,N'*-bis(2,2'-bioxazole-5,5'-dimethyl)-2,2'-bioxazole-5,5'-bis(methylamine)) and **2** (*N,N'*-bis(2,2'-bioxazole-4,4'-dimethyl)-2,2'-bioxazole-4,4'-bis(methylamine)).

Quantum Chemical Method

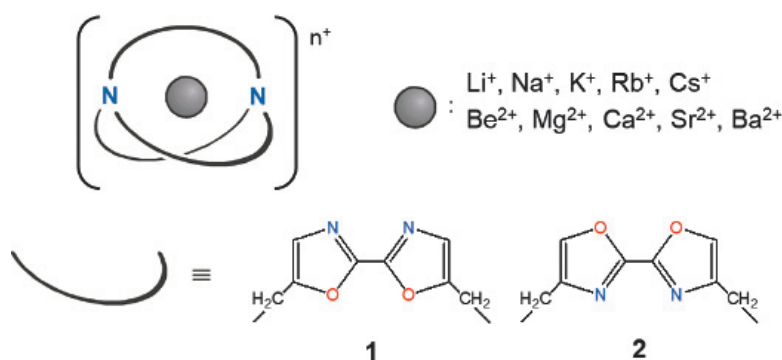Density functional calculations were performed using the hybrid B3LYP functional[14] in combination with the LAN-

Figure 1. Schematic presentation of the investigated isomeric cryptands **1** (*N,N'*-bis(2,2'-bioxazole-5,5'-dimethyl)-2,2'-bioxazole-5,5'-bis(methylamine)) and **2** (*N,N'*-bis(2,2'-bioxazole-4,4'-dimethyl)-2,2'-bioxazole-4,4'-bis(methylamine)).

L2DZ basis set with effective core potentials,[15] augmented with polarization functions on non-hydrogen atoms.[16] We selected that particular combination of functional and basis set (denoted as B3LYP/LANL2DZp), since in earlier studies on selective ion complexation and related topics we obtained results, that were consistent with experimental values. The success of calculations at this level has been documented,[17] and additionally permits comparison of the results of the current study with our earlier work. All calculations were performed without any implicit solvent model. Structures were characterized as minima on the potential energy surface by carrying out calculations of vibrational frequencies which resulted in no imaginary frequencies. Relative energies were corrected for zero-point vibrational energy. The calculations were performed using the GAUSSIAN suite of programs.[18]
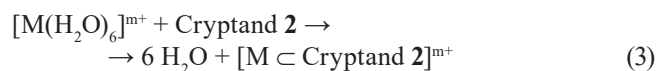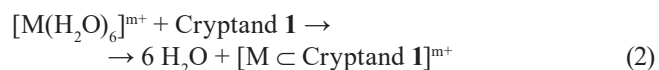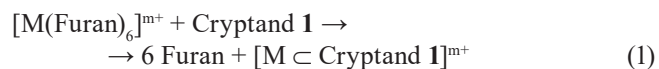
Results and Discussion

In the field of computational chemistry two criteria have proven to be reliable for the prediction of selective ion complexation.[19,20]

a) Comparison of the energy values obtained from the construction of model reactions.

b) Monitoring of the geometry and variations of it in the host-guest complexes, and comparison with appropriate references.

For the current investigation three different model equations have been constructed:

$$[M(Furan)_6]^{m+} + Cryptand\ 1 \rightarrow$$
$$\rightarrow 6\ Furan + [M \subset Cryptand\ 1]^{m+} \quad (1)$$

$$[M(H_2O)_6]^{m+} + Cryptand\ 1 \rightarrow$$
$$\rightarrow 6\ H_2O + [M \subset Cryptand\ 1]^{m+} \quad (2)$$

$$[M(H_2O)_6]^{m+} + Cryptand\ 2 \rightarrow$$
$$\rightarrow 6\ H_2O + [M \subset Cryptand\ 2]^{m+} \quad (3)$$

Most reactions in bio-related chemistry are in an aqueous medium. Therefore, for the purpose of constructing our model equations water was often chosen as the solvent

surrounding alkali and alkaline earth metals. For the sake of consistency, all calculations upon cations, in the case of Eqs. (1), (2) and (3), were based upon the cations being present in a six-fold coordination environment, furan in Eq.(1), whereas water in Eqs. (2) and (3).[21] In the case of cryptand **1**, the oxygen donor atom is part of an aromatic system, therefore Eq. (1) was constructed, where furan is used as a solvent, supposedly to mimic reliably the O-coordinating oxazolyl-moiety of cryptand **1**. This method was applied to maintain the donor atom coordinated to the metal ions similarly hybridized in the cryptand as well as in the reference system, in order to ensure coherence of the whole system. Results of the computed complexation energies obtained by applying the present model equations are shown in Table 1, and are plotted against the ionic radii[22] in Figure 2.

The calculated complexation energies obtained by applying model Eq. (1) with furan as the reference solvent result in significantly lower energies for all investigated guest cations compared to Eq. (2) and $[M(H_2O)_6]^{m+}$ as references. We attribute this observation to the sp^2-hybridization of the O-donor atom in furan in **1**. All equations applied here are model equations calculated in gas phase and they do not refer to experimentally measured values, therefore there is no point in discussing which value is more reliable or more correct. The most important observation when comparing results using Eqs. (1) and (2) is, that both equations exhibit an identical trend. This tends to show that in the case of the energetic criteria the precise hybridization in the reference solvent complex is not of major importance. The highest stabilities calculated by applying Eqs. (1) and (2) for cryptand **1** are found in the case of the alkali metal cations for the Na$^+$ encapsulation. In the case of the alkaline earth cations Sr^{2+} is preferred but barely significantly relative to Ca^{2+}. For cryptand **2**, the N-coordinating isomer, the picture is much less clear. Based on Eq. (3) the small alkali metal ions (Li$^+$ or Na$^+$) and alkaline earth (Be^{2+}and Mg^{2+}) ions seem to fit best. Taking the second criterion, the comparison of the ion-donor distances into account, the Na$^+$ ion may fit best as an alkali ion, while Mg^{2+} may be the most appropriate alkaline earth cation. Incorporation of the Be^{2+}

Table 1. Calculated (B3LYP/LANL2DZp) complexation energies for the systems presented in Figure 1 based on Eqs. (1–4) (Eq. (4) *vide infra*).

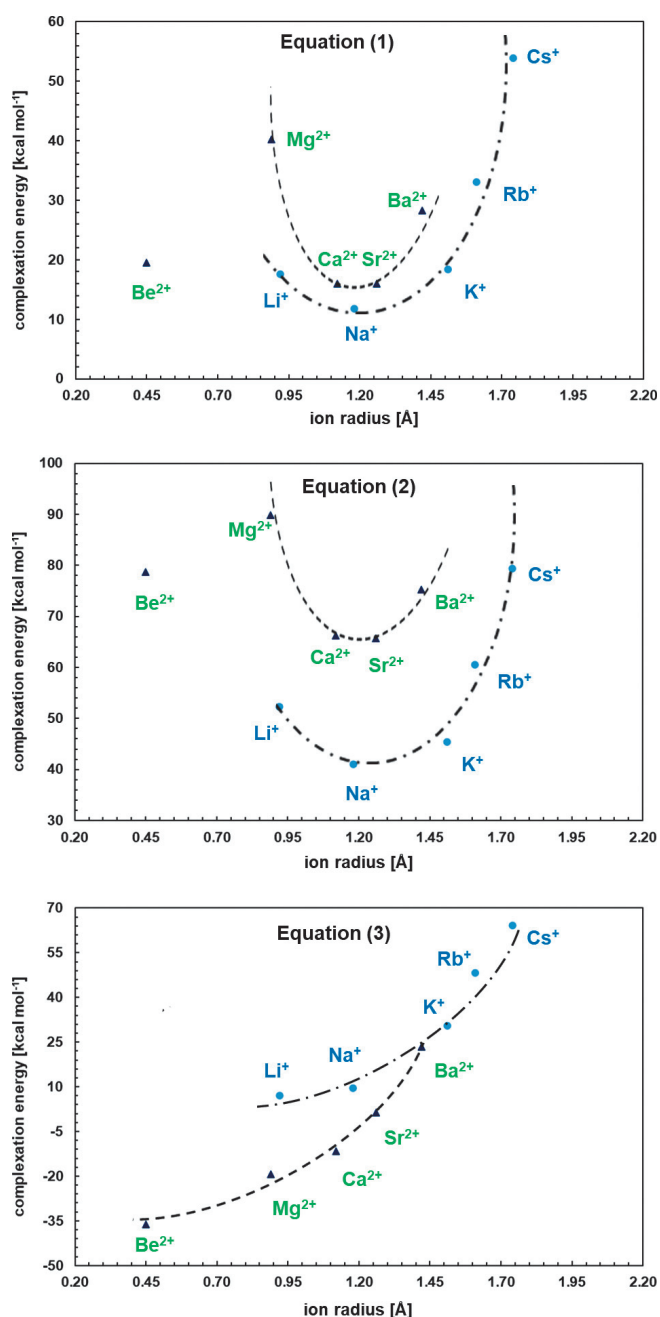| Metal ions	R [Å]	E_{com} [kcal mol^{-1}]			
		Equation (1)	Equation (2)	Equation (3)	Equation (4)
Li$^+$	0.92	17.64	52.25	7.17	−45.08
Na$^+$	1.18	11.77	41.08	9.46	−31.62
K$^+$	1.51	18.39	45.37	30.44	−14.92
Rb$^+$	1.61	33.05	60.58	48.21	−12.37
Cs$^+$	1.74	53.90	79.43	64.22	−15.21
Be^{2+}	0.45	19.56	78.72	−36.12	−114.84
Mg^{2+}	0.89	40.25	89.88	−19.44	−109.32
Ca^{2+}	1.12	16.06	66.28	−11.60	−77.88
Sr^{2+}	1.26	15.97	65.73	1.28	−64.45
Ba^{2+}	1.42	28.33	75.21	23.38	−51.83

Figure 2. Calculated complexation energies (RB3LYP/LANL2DZp) according to Eqs. (1), (2) and (3) plotted against the ionic radius of M^{m+} (the dashed lines illustrate the trend in the relevant properties in this and in Figures 4 and 5).

ion by cryptand **2** as the best regarding the energy criterion (see Table 1 and Figure 2) can be excluded by further examination of the geometric properties, precisely the coordination bond lengths, (see Table 3); where for cryptate complex $[Be \subset \mathbf{2}]^{2+}$ two different bond length values for both Be^{2+}-N_{oxazol} and Be^{2+}-N_{host}, were obtained which lead us to the conclusion that the smallest of all the investigated metal cations is occupying only one part of the cryptand cavity. The same can be observed for the encapsulation of the Li^+ and again for the Be^{2+} cation by cryptand **1**.

All studied alkaline earth metal cations demonstrated lower absolute complexation energies in comparison with the alkali metal cations. This is certainly an artifact of the method due to their dicationic nature. The charge receives extra stabilization in the large supramolecule, which six water molecules cannot provide. This is quite different in the case of Eq. (1), where larger furan molecules have been used as solvent molecules.

In order to compare the ion selectivity of cryptand **1** against the isomeric cryptand **2** by energies free of influences of solvents or reference complexes, a further much simpler model equation (4), can be constructed by formally subtracting Eq. (2) from Eq. (3):

$$[M \subset \text{Cryptand } \mathbf{1}]^{m+} + \text{Cryptand } \mathbf{2} \rightarrow$$
$$\rightarrow [M \subset \text{Cryptand } \mathbf{2}]^{m+} + \text{Cryptand } \mathbf{1} \qquad (4)$$

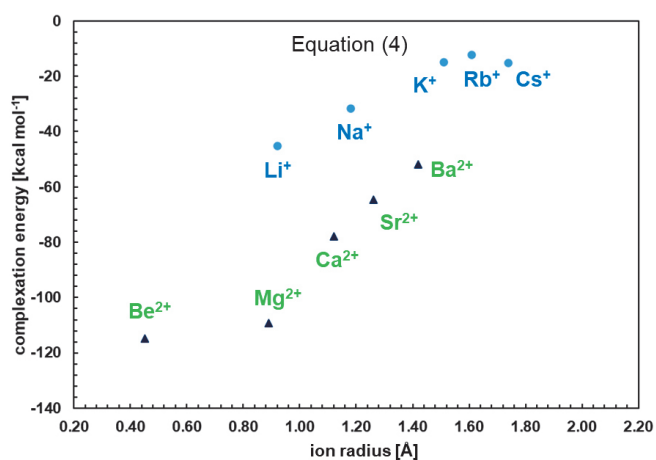Results obtained from Eq. (4) are presented in Table 1 and graphically displayed in Figure 3.

Figure 3. Calculated complexation energies (RB3LYP/LANL2DZp) according to Eq. (4), plotted against the ionic radius of M^{m+}.

Eq. (4) does not illustrate any more clearly the ion selectivity as Eqs. (1–3) do, and favors clearly the cryptate complexes $[M \subset \text{Cryptand } \mathbf{2}]^{n+}$ as thermodynamically more stable. While Eq. (4) is free of the influences of the selected reference compounds it becomes severely hampered by the relative stability of **1** and **2**. The isomeric cryptand **1** is by 14 kcal mol^{-1} more stable than **2**. Keeping this 14 kcal mol^{-1} in mind the obvious thermodynamic preference of the cryptate complexes based on **2** becomes less absolute. As we have already proven in an earlier contribution, direct comparison of properties relating to isomeric cryptands is fraught with uncertainty and does not necessarily lead to definitive results.[23]

Geometric properties and structural changes according to the guest metal cation of the investigated cryptands **1** and **2** are shown in Table 2 and 3, and are graphically displayed in Figures 4, 5 and 6, respectively. A comparison of the bond distances between the donor atoms of the investigated cryptands and the endohedrally encapsulated metal cation, obtained in this work, with bond distances between the metal cations coordinated by solvent molecules in the reference systems $[M(\text{Furan})_n]^{m+}$, $[M(\text{Pyridine})_n]^{m+}$

Table 2. RB3LYP/LANL2DZp computed geometric parameters for [M $\subset$ Cryptand **1**]$^{m+}$ complex.

Metal ions	R [Å]	d(M-O$_{oxazol}$) [Å]	d(M-N$_{host}$) [Å]	d(M-O$_{furan}$) [Å]	d(M-N$_{NH3}$) [Å]	$\Phi(\alpha)^e$ [°]	$\Phi(\beta)^f$ [°]
Li$^+$	0.92	2.12[a]	2.26[c]	1.97	2.13	−10.1	70.0
Na$^+$	1.18	2.50	3.10	2.43	2.67	−12.8	66.6
K$^+$	1.51	2.63	3.07	2.81	3.01	−24.3	54.0
Rb$^+$	1.61	2.74	3.08	3.04	3.21	−39.7	45.2
Cs$^+$	1.74	3.01	3.26	3.30	3.45	−92.8	24.1
Be^{2+}	0.45	1.72[b]	1.75[d]	1.65	1.77	8.0	84.3
Mg^{2+}	0.89	2.32	3.08	2.14	2.29	0.1	90.7
Ca^{2+}	1.12	2.53	2.98	2.47	2.63	−10.0	68.1
Sr^{2+}	1.26	2.60	2.99	2.63	2.80	−15.0	58.8
Ba^{2+}	1.42	2.70	3.01	2.83	3.00	−25.2	48.2

[a]Longer d(Li-O$_{oxazol}$) is 2.99 [Å]
[b]Longer d(Be-O$_{oxazol}$) is 3.46 [Å]
[c]Longer d(Li- N$_{host}$) is 4.06 [Å]
[d]Longer d(Be- N$_{host}$) is 5.09 [Å]
[e]$\Phi(\alpha)$ refers to O$_{oxazol}$-C-C-O$_{oxazol}$ dihedral angle; for Cryptand **1** is −17.5°
[f]$\Phi(\beta)$ refers to C-N$\cdots$N-C$_O$ dihedral angle; for Cryptand **1** is 65.0°
Ionic radii R: taken from ref.[22]; d(M-N$_{NH3}$): taken from ref.[19]; d(M-O$_{furan}$): calculated at the same theory level (RB3LYP/LANL2DZp).

Table 3. RB3LYP/LANL2DZp computed geometric parameters for [M $\subset$ Cryptand **2**]$^{m+}$ complex.

Metal ions	R [Å]	d(M-N$_{oxazol}$) [Å]	d(M-N$_{host}$) [Å]	d(M-N$_{pyr}$) [Å]	d(M-N$_{NH3}$) [Å]	$\Phi(\alpha)^c$ [°]	$\Phi(\beta)^d$ [°]
Li$^+$	0.92	2.33	3.60	2.07	2.13	−10.1	61.9
Na$^+$	1.18	2.44	3.49	2.62	2.67	−16.5	51.8
K$^+$	1.51	2.66	3.33	2.95	3.01	−39.3	41.9
Rb$^+$	1.61	2.84	3.31	3.16	3.21	−64.4	34.4
Cs$^+$	1.74	3.07	3.35	3.39	3.45	−93.8	21.6
Be^{2+}	0.45	1.72[a]	1.87[b]	1.75	1.77	−10.5	60.1
Mg^{2+}	0.89	2.30	3.51	2.31	2.29	−3.5	69.7
Ca^{2+}	1.12	2.50	3.31	2.61	2.63	−10.1	51.3
Sr^{2+}	1.26	2.59	3.24	2.75	2.80	−16.3	45.8
Ba^{2+}	1.42	2.72	3.18	2.95	3.00	−29.6	40.3

[a]Longer d(Be-N$_{oxazol}$) is 3.55 [Å]
[b]Longer d(Be-N$_{host}$) is 5.42 [Å]
[c]$\Phi(\alpha)$ refers to N$_{oxazol}$-C-C-N$_{oxazol}$ dihedral angle; for Cryptand **2** is −134.2°
[d]$\Phi(\beta)$ refers to C-N$\cdots$N-C$_N$ dihedral angle; for Cryptand **2** is −6.4°
Ionic radii R: taken from ref.[22]; d(M-N$_{pyr}$) and d(M-N$_{NH3}$): ref.[19]

and [M(H$_2$O)$_n$]$^{m+}$ (n = 4 for Li$^+$ and Be^{2+} and n = 6 for all others) is depicted in Figures 4 and 5. The bisecting lines in the figures represent the cases in which coordination will fit most satisfactorily, where ions above the line are undoubtedly too small, whereas the ions below the line are too large for a proper coordination in the studied macromolecular cages.

Upon examining Figure 4 it is clear that the three metal ions Li$^+$, Be^{2+} and Mg^{2+} are of insufficient magnitude, whereas K$^+$, Rb$^+$, Cs$^+$ and Ba^{2+} can be put into a group of metal ions that are too large for incorporation by cryptand **1**. The metal ions Na$^+$, Ca^{2+} and Sr^{2+} are representative of those that may be termed "ideal". The metal ions Na$^+$ and Mg^{2+} can be revealed, from Figures 5, as those that are fit well into the cavity of cryptand **2**. The Li$^+$ and Be^{2+} ions seem to be too small, whereas K$^+$, Rb$^+$, Cs$^+$, Sr^{2+} and Ba^{2+} are too large to be hosted by cryptand **2**. These observations are consistent with the results obtained by applying adequate model equations (see Figure 2). All the cations investigated seem to form more ideal bonds with donor atoms located at the 2-(oxayole-2-yl)oxazole bridged moiety of the investigated cryptands (M-O$_{oxazol}$ and M-N$_{oxazol}$) in comparison to other donor atoms (M-N$_{host}$). This implies that the bridging components of the cryptands are more
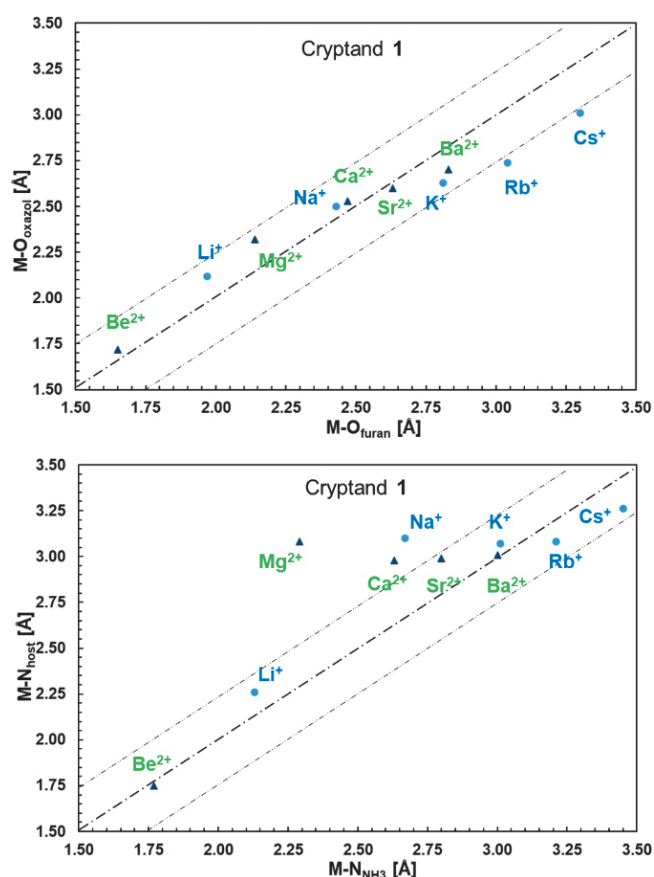
Figure 4. Calculated (RB3LYP/LANL2DZp) M-O$_{oxazol}$ and M-N$_{host}$ distances in [M $\subset$ Cryptand **1**]$^{m+}$ plotted against the calculated (RB3LYP/LANL2DZp) M-O$_{Furan}$ and M-NH$_3$ distances.

Figure 5. Calculated (RB3LYP/LANL2DZp) M-N$_{oxazol}$ and M-N$_{host}$ distances in [M $\subset$ Cryptand **2**]$^{m+}$ plotted against the calculated (RB3LYP/LANL2DZp) M-NH$_3$ and M-N$_{pyr}$ distances.

adaptable to the incorporation of metal ions and therefore more important with regard to successful hosting of them.

The flexibility of the investigated cryptands can be seen clearly in Figure 6 which illustrates the change of the selected dihedral angles upon coordination of the particular metal cations (see Table 2 and 3). Both angles, $\Phi(\alpha)$ and $\Phi(\beta)$, exhibit a trend of reduction upon coordination of bigger metal cations. In both studied cryptands, angle $\Phi(\alpha)$ goes from $\approx 0°$ for the smallest Be^{2+} to $\approx -95°$ for the largest one, Cs$^+$. The biggest changes of angle $\Phi(\beta)$ can be observed in cryptand **1** from $\approx 90°$ for Mg^{2+} to a $\approx 20°$ for Cs$^+$. In cryptand **2** $\Phi(\beta)$ decreases less, from $\approx 70°$ for Mg^{2+} to $\approx 20°$ for Cs$^+$. Dihedral angles gradually reduce with increasing ion radii of the investigated metal cations indicating the great flexibility and adaptability of the cryptands **1** and **2** as respective hosts.

Cryptands **1** and **2** offer the unique possibility and opportunity to compare nearly identical host systems, as only six donor atoms are changed. An initial, simplified consideration could lead to the idea that both cages will offer the same cavity and show the same selectivity, but **1** and **2** show significant differences. While **1** prefers Na$^+$ and Sr^{2+} only marginally more than Ca^{2+} it is comparable to [phen.phen.phen], **2** prefers the ions Na$^+$ and Mg^{2+} thus exhibiting a cavity comparable to that of dodeka(ethylene)octamine (Bühl's cryptand) and [2.1.1].[19] These observations can be easily rationalized by comparing the cation-
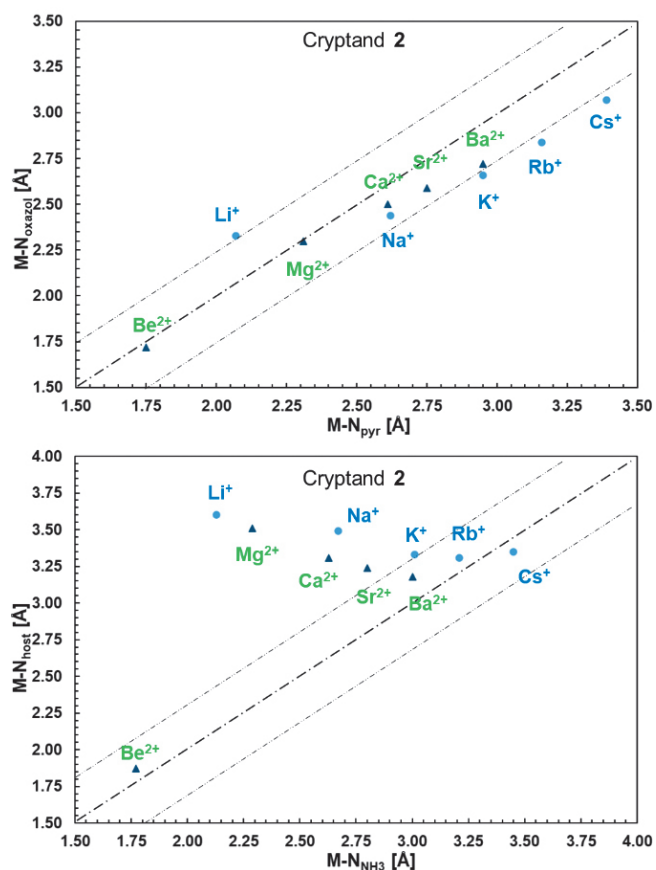
nitrogen and cation-oxygen interaction properties extant in our solvent complexes [M(Furan)$_n$]$^{m+}$, [M(Pyridine)$_n$]$^{m+}$, [M(NH$_3$)$_n$]$^{m+}$ (Tables 2, 3) and in the literature [M(H$_2$O)$_n$]$^{m+}$.[19] Comparing the bond lengths of a given cation with oxygen or a nitrogen donor of the same hybridizations, one obtains consequently longer M^{m+}-N interactions than M^{m+}-O interactions. This leads to the situation that a cavity that will select the same cation based on N-coordination as well as one based on O-coordination, has to be of greater magnitude.

Conclusions

The two isomeric cryptands **1** (*N,N*'-bis(2,2'-bioxazole-5,5'-dimethyl)-2,2'-bioxazole-5,5'-bis(methylamine)) and **2** (*N,N*'-bis(2,2'-bioxazole-4,4'-dimethyl)-2,2'-bioxazole-4,4'-bis(methylamine)) were investigated with quantum chemical methods: By application of well-established energetic and structural criteria we determined that **1** exhibits a preference for the alkaline cation Na$^+$ and the alkaline earth cation Sr^{2+} slightly in excess of its affinity for Ca^{2+}. This leads to the conclusion that **1** has a cavity comparable to [phen.phen.phen]. The cryptand **2** prefers again the alkali cation Na$^+$, but also Mg^{2+}, an alkaline earth cation and is therefore in this context comparable to the cryptands dodeka(ethylene)octamine (Bühl's cryptand) or [2.1.1]. The
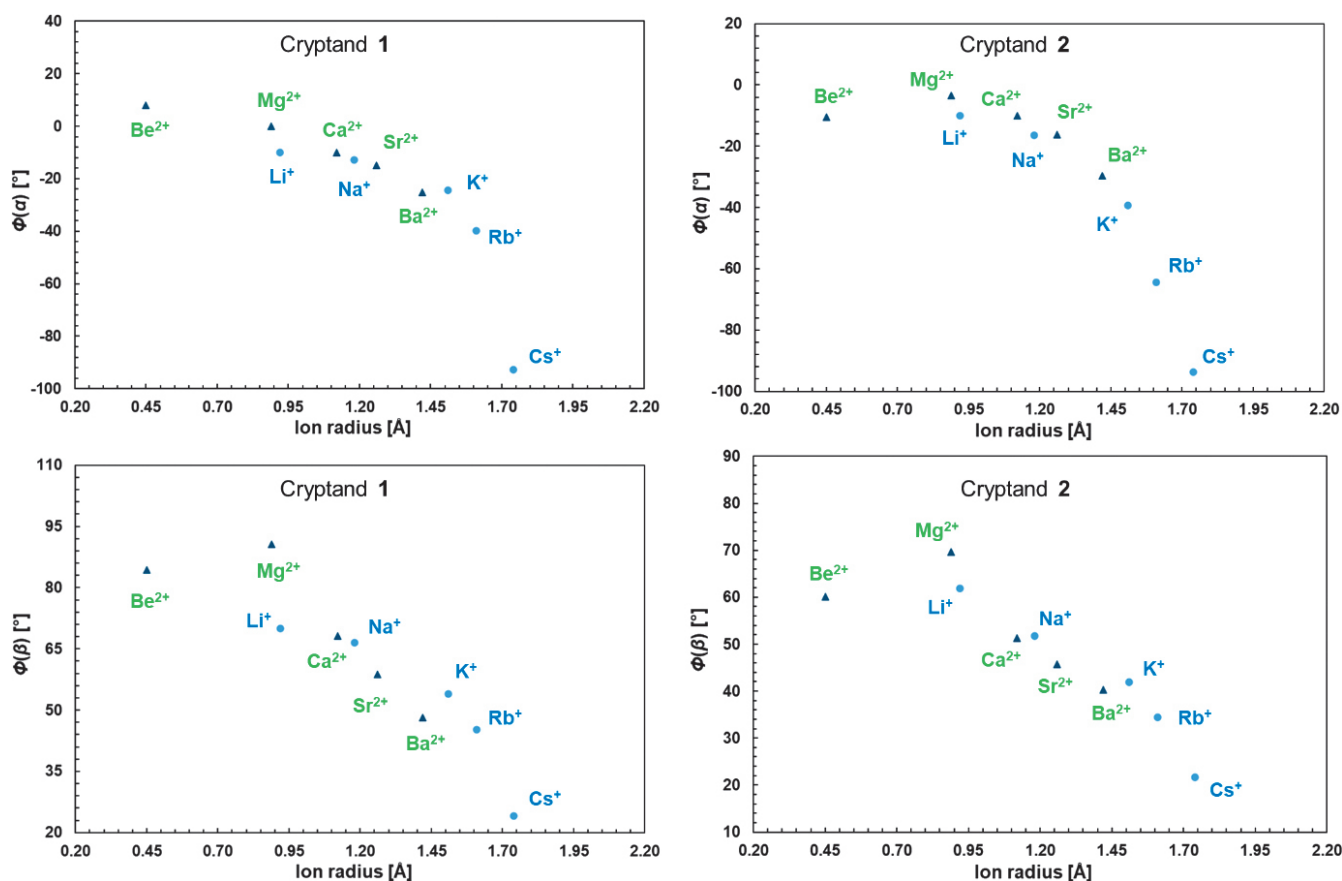
Figure 6. Calculated (RB3LYP/LANL2DZp) dihedral angles $\Phi(\alpha)$ and $\Phi(\beta)$ of cryptands **1** and **2** in [M ⊂ Cryptand **1**]^m+ and [M ⊂ Cryptand **2**]^m+ complexes, plotted against the ionic radius of M^m+ (see Tables 2 and 3, respectively).

origin of the different selectivity of **1** and **2** can be attributed to the longer M^m+-N interactions compared to M^m+-O interactions.

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