

#### RESEARCH ARTICLE

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# A theoretical mechanistic study of $[K \subset [2.2.2]]^+$ enantiomerization

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## Abstract

Density functional calculations at three different levels of theory (B3LYP/LAN-L2DZp, B3LYP-GD3/LANL2DZp, and  $\omega$ B97XD/def2tzvp) were applied to different conformers of the Lehn-type macrobicyclic polyether cryptate complex  $[K \subset [2.2.2]]^+$  to construct the enantiomerization pathway and to compute the energy barrier for the change in symmetry. Changes in the conformation of the investigated complex are discussed in terms of energy and geometric criteria, where changes in the structures follow a trend of activation energies prohibiting the achiral pathways. The investigated  $D_3$ -symmetric cryptate  $[K \subset [2.2.2]]^+$  shows enantiomerization through an all chiral five step pathway with two local minima ( $C_2$  and  $C_2$ ) and three  $C_1$  transition states ending in the  $D_3$ '-symmetric cryptate [K  $\subset$  [2.2.2]]<sup>+</sup>, the mirror image of the starting structure. The potential achiral transition states are higher order saddle points with a minimum twice as high in energy as an all-chiral path. This study unambiguously accounts for Lehn's NMR data showing fluxionality of the studied complex. The obtained results were further rationalized by means of energy decomposition analysis (EDA) and natural bond orbital (NBO) calculations performed for the metal cation and the host in its different conformations.

#### KEYWORDS

cryptand, DFT study, EDA, enantiomerization, NBO

#### 1 INTRODUCTION

The three-dimensional extension of the diaza-derivate of 18-crown-6 was presented more than 50 years ago in 1969 by Jean-Marie Lehn, Bernard Dietrich, and Jean Pierre Sauvage as 4,7,13,16,21,24-(hexaoxa-1,10-diazabicyclo [8.8.8]hexacosane, today well known as [2.2.2] and traded as Kryptofix 222 (Figure 1).<sup>[1]</sup> For these developments, Lehn together with Pedersen and Cram received the Nobel Prize in 1987.<sup>[2]</sup> The outstanding potential of these

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This is dedicated to Dr. Manfred Ettlinger, a real friend and an outstanding ambassador for chemistry.



**FIGURE 1** Structural presentation of the investigated cryptand [2.2.2] (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane) with number labeling on relevant atoms

compounds especially in the field of selective binding of guests, in particular alkali and alkaline earth metal ions, was immediately recognized. Today, these classes of compounds are widely employed: in phase-transfer catalysis,<sup>[3]</sup> studies on Zintl phases,<sup>[4]</sup> selective complexation of radioactive or toxic ions in medicine,<sup>[5]</sup> and elsewhere,<sup>[6]</sup> as a ligand for magnetic resonance imaging (MRI) contrast agents,<sup>[7]</sup> and as models for carrier antibiotics such as valinomycin and enzyme inhibitors.<sup>[8]</sup>

While selective complexation of metal ions with Lehn-type cryptands has been quantum chemically studied in detail over the past years,<sup>[9–11]</sup> there are little data available concerning the energy profile for the process of enantiomerization of the Lehn-type cryptand with incorporated metal ion. In contrast, in metallo supramolecular systems, such enantiomerization processes were investigated in detail.<sup>[12]</sup> This is especially surprising since in the NMR spectra, Lehn and coworkers were able to observe temperature-dependent motions for cryptate complexes based on [2.2.2] already in the early 1970s<sup>[13]</sup> and for bipyridine and phenanthroline spaced systems again in the early 1980s.<sup>[14]</sup> Driven by the experimental observation of Lehn's team and our interest in cryptate complexes, we report in this density functional theory (DFT)-based mechanistic study of the enantiomerization process of  $[K \subset$ [2.2.2]<sup>+</sup> at three different levels of theory, as well as an investigation of the electron density distribution.

## 2 | QUANTUM CHEMICAL METHOD

Quantum chemical calculations of the different complex structures were performed at three different levels of theory: (i)  $\omega$ B97XD<sup>[15]</sup> with the Ahlrichs basis set def2tzvp,<sup>[16]</sup> (ii) the hybrid density functional B3LYP<sup>[17]</sup> extended by Grimme's dispersion correction<sup>[18]</sup> (B3LYP-GD3), with the LANL2DZ basis set with effective core potentials augmented with polarization functions on nonhydrogen atoms (denoted as LANL2DZp),<sup>[19]</sup> and (iii) pure B3LYP<sup>[17]</sup> again with the LANL2DZp<sup>[20]</sup> basis set. Additionally, the influence of bulk solvent was evaluated via single-point calculations using the conductorlike polarizable continuum model (CPCM) formalism<sup>[21]</sup> on the  $\omega$ B97XD/def2tzvp theory level where water was used as a solvent. All the three computational methods were employed for geometry optimization and frequency calculations of all molecular structures along the proposed the enantiomerization pathway. The transition states and higher order saddle points were initially generated by following the negative frequencies associated with the  $D_{3h}$  structure, while the  $D_3$  ground state of [K  $\subset$ [2.2.2]]<sup>+</sup> is well-known since the first structural investigation and today text book knowledge.<sup>[9]</sup>

The obtained structures were characterized as minima, transition states, or saddle points of higher order by examining the vibrational frequencies at the same level. The three levels of theory were selected to increase our understanding of selective ion complexation<sup>[10]</sup> and to test the influence of dispersion. These calculations were performed using the GAUSSIAN09 program package.<sup>[22]</sup> Localized orbital energy decomposition analysis (EDA) method developed by Su and Li was employed.<sup>[23]</sup> The EDA interaction energy between two fragments (in our case K<sup>+</sup> cation and [2.2.2] cryptand) can be decomposed into electrostatic ( $\Delta E_{es}$ ), exchange ( $\Delta E_{ex}$ ), Pauli repulsion ( $\Delta E_{Pauli}$ ), polarization ( $\Delta E_{pol}$ ), and dispersion ( $\Delta E_{disp}$ ) components:

$$\Delta E_{\rm int} = \Delta E_{\rm es} + \Delta E_{\rm ex} + \Delta E_{\rm Pauli} + \Delta E_{\rm pol} + \Delta E_{\rm disp}$$

It should be noted that  $\Delta E_{int}$  is not the same as the bond dissociation energy (BDE), because the relaxation of the fragments is not considered.<sup>[24]</sup> The EDA was performed at the B3LYP/LANL2DZp level by means of the GAMESS program package.<sup>[25,26]</sup>

The bonding situation in the cryptate  $[K \subset [2.2.2]]^+$  was further investigated by means of natural bond orbital (NBO) analysis.<sup>[27]</sup> The electrostatic interactions in the studied system were rationalized by means of the NBO charge distribution. Furthermore, within the NBO method, delocalization effects can be assessed through the off-diagonal elements of the Fock matrix in the NBO basis. The extent of the delocalization interaction is quantified by means of the second order perturbation theory:

$$E^{(2)} = q_i \frac{F^2(i,j)}{E(j) - E(i)}$$

where  $q_i$  is the *i*th donor orbital occupancy, E(i) and E(j) are the diagonal elements (energies of the donor and acceptor orbitals), and F(i,j) are the off-diagonal elements of the NBO Fock matrix.

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## **3** | **RESULTS AND DISCUSSION**

For the explanation of the temperature-dependent NMR spectra in supramolecular complex chemistry, two possibilities can in general be considered. i) An equilibrium for complexation and decomplexation of metal cations, including bond breaking and bond formation, which is generally connected to high energy barriers, ii) or mechanisms that operate via distortion and twisting. Such processes can conserve all bonds and consequently show low energy barriers. The investigated cryptate  $[K \subset [2.2.2]]^+$ shows  $D_3$ -symmetry, a chiral point group, as there is no reason for chiral discrimination in solvated  $[K \subset$ [2.2.2]<sup>+</sup>, both enantiomers  $D_3$  and  $D_3'$  will be in solution and should be connected by a non-dissociative enantiomerization process with relative low energy barriers. Such non-dissociative pathways can either proceed via a fully chiral pathway, known as Mislow's Paradoxon,<sup>[28,29]</sup> or can proceed via a nonchiral transition state structure of higher symmetry. Both pathways were tested and are reported in this manuscript.

To get the structures traversed in both reaction pathways, the symmetry of the cryptand was changed by changing the orientation of the O–Et–O–bridges in the cryptate  $[K \subset [2.2.2]]^+$  (see Table 1). The  $D_3$  geometry of

 $[K \subset [2.2.2]]^+$  is clearly the most stable structure in terms of energy criteria at all applied levels of theory, as can be seen in Figure 2. The chiral enantiomerization pathway goes from the  $D_3$  structure through a first  $C_1$  transition state, a  $C_2$  local minimum, a second  $C_1$  transition state, reaching the "mirror images" local minima  $C_2'$ , transition state  $C_1'$ , and finally  $D_3'$ . Alternatively, the achiral pathway traversing the cryptate structures with  $D_{3h^-}$  or  $C_{3h^-}$ structures shows much higher energies and is associated with higher order saddle points on the energy hypersurface. By applying the CPCM water solvent model, we have the lowering of all energy barriers along the reaction path on the relevant theory level by ~30%. Optimized structures of the investigated complex for all applied symmetries are displayed in Figures 3 and 4.

As mentioned before, different  $[K \subset [2.2.2]]^+$ rotamers with structures of different symmetry were investigated by changing the orientation of the O–Et–O– bridge, and subsequently, the dihedral angle also changed. These changes are displayed in Tables 1–3 for all here applied theory levels. In addition, these changes lead to a change in bond lengths between the K<sup>+</sup> cation and the coordinated oxygen and nitrogen atoms. This lengthening/shortening of K<sup>+</sup>–N and K<sup>+</sup>–O bonds can be regarded as negligible in the case of the traversed reaction

TABLE 1	Geometric properties extracted from optimized structures at the $\omega$ B97XD/def2tzvp theory level for different symmetries of the
investigated co	omplex

Symmetry	$\Phi(\alpha)^{\mathrm{a}}$ (°)	$\varPhi(\beta)^{b}$ (°)	$\varPhi(\gamma)^{c}(^{\circ})$	$d(K^+-N_1)$ (Å)	$d(K^+-O_1)$ (Å)	d(K <sup>+</sup> -O <sub>2</sub> ) (Å)	d(K <sup>+</sup> -N <sub>2</sub> ) (Å)
$D_3$	66.6	-67.3	66.6	3.07	2.85	2.85	3.07
	66.6	-67.3	66.6		2.85	2.85	
	66.6	-67.3	66.6		2.85	2.85	
$C_{1}(ts1)$	-58.9	-2.8	-52.6	2.95	2.75	2.70	3.02
	60.4	-63.8	66.2		2.79	2.80	
	65.6	-63.6	63.4		2.73	2.77	
$C_2$	-59.0	71.7	-59.0	3.04	2.83	2.83	3.04
	65.3	-63.5	64.2		2.79	2.82	
	64.2	-63.5	65.3		2.82	2.79	
$C_{1}$ (ts2)	-60.2	71.1	-61.4	3.01	2.84	2.83	3.07
	60.0	-2.7	66.2		2.78	2.73	
	65.0	-65.0	64.2		2.77	2.81	
$C_{3h}$	-56.3	0.0	56.3	2.83	2.79	2.79	2.83
	-56.3	0.0	56.3		2.79	2.79	
	-56.3	0.0	56.3		2.79	2.79	
$D_{3h}$	0.0	0.0	0.0	3.33	2.72	2.72	3.33
	0.0	0.0	0.0		2.72	2.72	
	0.0	0.0	0.0		2.72	2.72	

<sup>a</sup> $\Phi(\alpha)$  refers to N<sub>1</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O<sub>1</sub> dihedral angle (see Figure 1).

 ${}^{b}\Phi(\beta)$  refers to O<sub>1</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O<sub>1</sub> dihedral angle (see Figure 1).

 ${}^{c}\Phi(\gamma)$  refers to O<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-N<sub>2</sub> dihedral angle (see Figure 1).



FIGURE 2 Calculated enantiomerization pathway for the  $[K \subset [2.2.2]]^+$  molecule. Energies of different symmetries at different theory levels relative to the  $D_3$  geometry of a  $[K \subset [2.2.2]]^+$  are graphically displayed and summarized in Table 5. Geometric structures with  $D_3$  and  $C_2$  symmetry are considered as local minima, where all other structures possess at least one imaginary frequency (Table 5) and can be regarded as transition states or a higher order saddle point on the energy hypersurface



FIGURE 3 Optimized structures at the  $\omega$ B97XD/def2tzvp level of theory with selected bond lengths for  $D_3$  and  $C_2$  symmetries as a ground states of the investigated  $[K \subset [2.2.2]]^+$  complex





pathway, as the variation in the K<sup>+</sup>–N bonds is around 0.1 and 0.15 Å for K<sup>+</sup>–O bonds (see Table 1). Clearly, higher deviations are found in  $C_{3h}$  and  $D_{3h}$  with a range between 2.83 and 3.33 Å for K<sup>+</sup>–N bonds and a range between 2.70 and 2.85 Å for K<sup>+</sup>–O bonds. The larger change in the structures goes parallel with high activation energies that prohibit the achiral pathways.

EDA was performed in order to investigate the nature of bonding interactions between the  $K^+$  metal cation and the host. The results of this investigation are presented in Table 5 and graphically displayed in Figure 5. The data

given in Table 5 show that the EDA-obtained  $\Delta E_{int}$  values are very close to the BDE values. It should be noted that unlike the  $\Delta E_{int}$ , the BDE values given in Table 5 include the geometry relaxation effects of the [2.2.2] cryptand. Based on  $\Delta E_{int}$  and BDE values, the most intensive bonding between the K<sup>+</sup> ion and the host is found for the  $D_{3h}$ geometry of [K  $\subset$  [2.2.2]]<sup>+</sup>, which is far less thermodynamically stable than other geometries (Figure 2). It can be seen that there is no relation between the thermodynamic stability of the studied molecular geometries, measured through the relative energies given in Table 4

Symmetry	$\Phi(\alpha)^{\mathrm{a}} (^{\circ})$	$\Phi(\beta)^{b}$ (°)	$\Phi(\gamma)^{c}$ (°)	$d(K^+-N_1)$ (Å)	$d(K^+-O_1)$ (Å)	d(K <sup>+</sup> -O <sub>2</sub> ) (Å)	$d(K^+-N_2)$ (Å)
$D_3$	67.2	-68.1	67.2	3.09	2.89	2.89	3.09
	67.2	-68.1	67.2		2.89	2.89	
	67.2	-68.1	67.2		2.89	2.89	
$C_1$ (ts1)	-52.8	-1.7	-59.7	3.05	2.82	2.77	2.98
	64.3	-64.7	66.5		2.75	2.77	
	67.1	-64.9	60.9		2.83	2.83	
$C_2$	66.7	-64.7	65.2	3.07	2.83	2.86	3.07
	65.2	-64.7	66.7		2.86	2.83	
	-59.4	72.4	-59.4		2.89	2.89	
$C_1$ (ts2)	66.4	-65.9	65.5	3.02	2.81	2.84	3.08
	60.0	-2.0	66.4		2.82	2.76	
	-61.2	71.8	-61.4		2.89	2.89	
$C_{3h}$	-57.0	0.0	57.0	2.87	2.83	2.83	2.87
	-57.0	0.0	57.0		2.83	2.83	
	-57.0	0.0	57.0		2.83	2.83	
$D_{3h}$	0.0	0.0	0.0	3.35	2.75	2.75	3.35
	0.0	0.0	0.0		2.75	2.75	
	0.0	0.0	0.0		2.75	2.75	

**TABLE 2** Geometric properties extracted from optimized structures at the B3LYP-GD3/LANL2DZp theory level for different symmetries of the investigated complex

 $^a\varPhi(\alpha)$  refers to N1-CH2-CH2-O1 dihedral angle (see Figure 1).

 ${}^{b}\varPhi(\beta)$  refers to O<sub>1</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O<sub>1</sub> dihedral angle (see Figure 1).

 $^{c}\varPhi(\gamma)$  refers to O\_2–CH2–CH2–N2 dihedral angle (see Figure 1).

TABLE 3	Geometric properties extracted from optimized structures at the B3LYP/LANL2DZp theory level for different symmetries of
the investigate	ed complex

Symmetry	$\Phi(\alpha)^{\mathrm{a}} (^{\circ})$	$\Phi(\beta)^{b}$ (°)	$\Phi(\gamma)^{c}(^{\circ})$	d(K <sup>+</sup> -N <sub>1</sub> ) (Å)	d(K <sup>+</sup> -O <sub>1</sub> ) (Å)	d(K <sup>+</sup> -O <sub>2</sub> ) (Å)	$d(K^+-N_2)$ (Å)
$D_3$	65.5	-66.1	65.5	3.09	2.88	2.88	3.09
	65.5	-66.1	65.5		2.88	2.88	
	65.5	-66.1	65.5		2.88	2.88	
$C_{1}$ (ts1)	67.7	-64.6	62.24	3.01	2.78	2.84	3.10
	-58.9	-0.7	-56.96		2.79	2.74	
	61.0	-65.0	66.88		2.85	2.84	
$C_2$	64.3	-63.9	66.2	3.09	2.87	2.83	3.09
	66.2	-63.9	64.3		2.83	2.87	
	-58.9	70.2	-58.98		2.86	2.86	
$C_1$ (ts2)	65.6	0.5	62.2	3.09	2.77	2.83	3.03
	65.1	-66.6	66.0		2.87	2.87	
	65.9	-66.7	65.7		2.86	2.83	
$C_{3h}$	-57.0	0	57.0	2.89	2.83	2.83	2.89
	-57.0	0	57.0		2.83	2.83	
	-57.0	0	57.0		2.83	2.83	
$D_{3h}$	0.0	0.0	0.0	3.36	2.75	2.75	3.36
	0.0	0.0	0.0		2.75	2.75	
	0.0	0.0	0.0		2.75	2.75	

 ${}^{a}\varPhi(\alpha)$  refers to N<sub>1</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O<sub>1</sub> dihedral angle (see Figure 1).

 ${}^{b}{\varPhi}(\beta)$  refers to  $O_{1}\text{-}CH_{2}\text{-}CH_{2}\text{-}O_{1}$  dihedral angle (see Figure 1).

 ${}^c\varPhi(\gamma)$  refers to  $O_2\text{-}CH_2\text{-}CH_2\text{-}N_2$  dihedral angle (see Figure 1).



**FIGURE 5** Changes of different energy components along the symmetric path of  $[K \subset [2.2.2]]^+$  relative to  $D_3$ -symmetry (for a clear view see colored version)

TABLE 4 Cal	lculated energies :	relative to the D	3 symmetry a	nd number	of imaginary	/ frequencies o	on three differen	t levels of theory
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	Theory level									
	ωB97XD/def2tzvp			B3LYP-GD3/LA	NL2DZp	B3LYP/LANL2DZp				
Symmetry	$\Delta E$ (kcal/mol)	Nimag	ωB97XD (CPCM) <sup>a</sup>	$\Delta E$ (kcal/mol)	Nimag	$\Delta E$ (kcal/mol)	Nimag			
$D_3$	0	0	0	0	0	0	0			
$C_1$ (ts1)	12.49	1	8.86	13.63	1	13.81	1			
$C_2$	4.61	0	3.50	5.04	0	5.38	0			
$C_1$ (ts2)	13.12	1	9.21	13.86	1	9.16	1			
$C_{3h}$	22.86	3	15.93	24.32	3	22.89	3			
$D_{3h}$	110.42	13	79.64	111.05	13	102.82	13			

<sup>a</sup> $\omega$ B97XD(CPCM): R $\omega$ B97XD(CPCM)/def2tzvp//and R $\omega$ B97XD/def2tzvp + ZPE ( $\omega$ B97XD/def2tzvp).

and Figure 2, and  $\Delta E_{int}$  and BDE values, which quantify the bonding interaction between the K<sup>+</sup> ion and the hosts. This implies that the bonding interactions between the central metal ion and host are only secondary effects in the overall complex stability, which turns out to be mainly determined by the conformation features of the cryptand. As can be seen, the bonding between K<sup>+</sup> and [2.2.2] cryptand in all geometrical forms is dominated by the  $\Delta E_{es}$ component, which emerges from the classical electrostatic interaction between the fragments.

The second important bonding component is the  $\Delta E_{\text{pol}}$  term. This component comes from the orbital relaxation effects, which can be related to charge transfer and orbital polarization effects (interaction between occupied orbitals on one fragment and unoccupied orbitals on the

other). The obtained EDA results are in line with those obtained with the NBO method. The strong electrostatic interactions (Table 5) are in agreement with a significant charge separation between the K<sup>+</sup> metal cation and O and N atoms of the host (Table 6). The NBO analysis shows that there are no formal bonds between the K<sup>+</sup> ion and host atoms. The second-order perturbation treatment within the NBO approach revealed a significant electron transfer from the lone pairs on the O and N atoms of the [2.2.2] cryptand (donor) to the empty orbitals of the K<sup>+</sup> ion (acceptor). The obtained NBO results are illustrated for the  $D_3$  geometry of [K  $\subset$  [2.2.2]]<sup>+</sup>. The donor NBO on the O atoms of the [2.2.2] cryptand are lone pairs that are the *sp* hybrids with 44% *s* and 56% *p* mixing (Figure 6A). These orbitals donate

	Symmetry								
Energy (kcal/mol)	$D_3$	C <sub>1</sub> (ts1)	<i>C</i> <sub>2</sub>	C <sub>1</sub> (ts2)	$C_{3h}$	D <sub>3h</sub>			
$\Delta E_{\mathrm{es}}$	-86.76	-92.23	-87.00	-89.27	-98.15	-100.27			
$\Delta E_{\rm ex}$	-4.65	-7.43	-5.57	-6.20	-7.3	-6.39			
$\Delta E_{\mathrm{Pauli}}$	32.13	43.46	36.01	38.58	43.13	39.02			
$\Delta E_{\mathrm{pol}}$	-17.79	-19.51	-18.56	-18.87	-19.8	-18.99			
$\Delta E_{ m disp}$	-12.55	-14.38	-13.26	-13.64	-14.23	-13.41			
$\Delta E_{ m int}$	-89.62	-90.10	-88.37	-89.40	-96.35	-100.04			
BDE	87.61	79.73	87.42	87.80	95.08	95.61			

	NBO charge distribution									
Atom	$\overline{D_3}$	C <sub>1</sub> (ts1)	<i>C</i> <sub>2</sub>	C <sub>1</sub> (ts2)	$C_{3h}$	D <sub>3h</sub>				
Κ	0.885	0.884	0.880	0.886	0.903	0.917				
N1	-0.448	-0.456	-0.455	-0.456	-0.447	-0.431				
N2	-0.448	-0.452	-0.455	-0.452	-0.447	-0.431				
01	-0.529	-0.533	-0.532	-0.532	-0.518	-0.512				
O2	-0.529	-0.529	-0.529	-0.530	-0.518	-0.512				

TABLE 6 Results of NBO analysis calculated at the  $\omega$  B97XD/def2tzvp level of theory

Abbreviation: NBO, natural bond orbital.



**FIGURE 6** Orbitals of the  $D_3$  geometry of  $[K \subset [2.2.2]]^+$  obtained from natural bond orbital (NBO) analysis: (A) lone pairs on O (donors) and formally "empty" orbitals on K ion (acceptor); (B) lone pairs on N (donors) and formally "empty" orbitals on K ion (acceptor)

electron charge to the empty orbital on the K ion (Figure 6A). These two acceptor orbitals are the hybrids with 34% *d* and 66% *p* mixing. On the other hand, the donating orbital on the N atoms has dominant *p* character, with 16% *s* mixing. The charge transfer from such lone pairs on the N atoms (Figure 6B) goes to the orbital on the K<sup>+</sup>, which has predominant *d* character (98%).

## 4 | CONCLUSIONS

In this study, we investigated the enantiomerization process of the  $D_3$ -symmetric  $[K \subset [2.2.2]]^+$  cryptate complex by quantum chemical methods. This process was first observed experimentally by the team of Lehn in their NMR spectra.<sup>[13,14]</sup> By calculating the achiral and chiral pathways, we were able to rule out the achiral pathway, because both structures that could be suggested as potential transition states  $(D_{3h} \text{ and } C_{3h})$  are much too high in energy. Therefore, the most reasonable pathway is an allchiral one that starts from the most stable rotamer  $D_3$ , traverses a  $C_1$  transition state, and leads to the intermediate  $C_2$  rotamer. This rotamer is connected via a second  $C_1$ transition state to the mirrored structures  $C_2'$ , followed by the mirrored transition state  $C_1$  and the final rotamer  $D_3'$ . The maximum activation energy along this path is with approximately 13 kcal/mol, only 50% of the lowest along the achiral pathway, which is surely not traversed. Our findings indicate that the bonding interactions between the central metal ion  $K^+$  and host cryptand are only secondary effects in the overall complex stability, which turn out to be mainly determined by the conformation features of the cryptand.

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### **CONFLICT OF INTEREST**

The authors declare that they have no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data are available on request from the authors.

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## REFERENCES

- a) B. Dietrich, J. M. Lehn, J. P. Sauvage, *Tetrahedron Lett.* **1969**, *34*, 2,889; b) M. Galle, R. Puchta, N. J. R. van Eikema Hommes, R. van Eldik, *Z. Phys. Chem.* **2006**, *220*, 511.
- [2] a) C. J. Pedersen, Angew. Chem. 1988, 100, 1053; b) C. J. Pedersen, Angew. Chem. Int. Ed. Engl. 1988, 27, 1,021; c) D. J. Cram, Angew. Chem. 1988, 100, 1,041; d) D. J. Cram, Angew. Chem. Int. Ed. Engl. 1988, 27, 1009; e) J.-M. Lehn, Angew. Chem. 1988, 100, 91; f) J.-M. Lehn, Angew. Chem. Int. Ed. Engl. 1988, 27, 89.
- [3] J.-H. Li, J.-S. Shih, J. Chin. Chem. Soc. 1999, 46, 885.
- [4] C. E. Housecroft, Clusterverbindungen von Hauptgruppenelementen, Weinheim, VCH 1994.
- [5] J. M. Lehn, M. Kirch, Angew. Chem. 1975, 87, 542.
- [6] H. S. Ajgaonkar, S. M. Khopkar, Chem. Anal. 1999, 44, 61.
- [7] L. Burai, R. Scopelliti, E. Toth, Chem. Commun. 2002, 43, 2366.
- [8] M. Farahbakhsh, H. Schmidt, D. Rehder, Chem. Ber. 1997, 130, 1123.
- [9] R. Puchta, S. Begel, R. van Eldik, Adv. Inorg. Chem. 2019, 73, 445.
- [10] N. Dehghani, B. Ghalami-Choobar, M. Arabieh, H. Dezhampanah, *Struct. Chem.* 2019, *30*, 1437.
- [11] T. A. Young, V. Martí-Centelles, J. Wang, P. J. Lusby, F. Duarte, J. Am. Chem. Soc. 2020, 142, 1300.
- [12] a) R. W. Saalfrank, B. Demleitner, H. Glaser, H. Maid, D. Bathelt, F. Hampel, W. Bauer, M. Teichert, *Chem. Eur. J.* 2002, *8*, 2679; b) R. W. Saalfrank, C. Deutscher, H. Maid, A. M. Ako, S. Sperner, T. Nakajima, W. Bauer, F. Hampel, B. A. Heß, N. J. R. van Eikema Hommes, R. Puchta, F. W. Heinemann, *Chem. Eur. J.* 2004, *10*, 1899; c) R. W. Saalfrank, H. Maid, A. Scheurer, R. Puchta, W. Bauer, *Eur. J. Inorg. Chem.* 2010, *19*, 2903; d) W. Meng, T. K. Ronson, J. R. Nitschke, *Proc. Natl. Acad. Sci. U. S. a.* 2013, *110*, 10531.
- [13] B. Dietrich, J. M. Lehn, J. P. Sauvage, J. Blanzat, *Tetrahedron Lett.* **1973**, *29*, 1,629.
- [14] J.-C. Rodriguez-Ubis, B. Alpha, D. Plancherel, J. M. Lehn, *Helv. Chim. Acta* 1984, 67, 2264.
- [15] J.-D. Chai, M. Head-Gordon, Phys. Chem. Chem. Phys. 2008, 10, 6615.
- [16] a) F. Weigend, M. Häser, H. Patzelt, R. Ahlrichs, *Chem. Phys. Lett.* 1998, 294, 143; b) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* 2005, 7, 3297.
- [17] a) A. D. Becke, J. Chem. Phys. 1993, 98, 5,648; b) C. Lee, W. Yang, R. G. Parr, Phys. Rev. B: Condens. Matter Mater. Phys. 1988, 37, 785; c) P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. Frisch, J. Phys. Chem. 1994, 98, 11623.
- [18] S. Grimme, J. Antony, S. Ehrlich, H. Krieg, J. Chem. Phys. 2010, 132, 154104.

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- [19] a) T. H. Dunning Jr., P. J. Hay, in *In Modern Theoretical Chemistry*, (Ed: H. F. Schaefer III), Plenum Press, New York **1976** 1;
  b) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270; c) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* **1985**, *82*, 284; d) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299; e) S. Huzinaga, *Gaussian Basis Sets for Molecular Calculations*, Elsevier, Amsterdam, Netherlands **1984**.
- [20] a) O. Shyshov, R. C. Brachvogel, T. Bachmann, R. Srikantharajah, D. Segets, F. Hampel, R. Puchta, M. von Delius, Angew. Chem., Int. Ed. 2017, 56, 776; b) S. Begel, A. Scheurer, R. Puchta, R. van Eldik, Z. Anorg. Allg. Chem. 2016, 642, 395; c) S. Begel, A. Scheurer, R. Puchta, J. Coord. Chem. 2015, 68, 3374; d) S. Begel, R. Puchta, R. van Eldik, J. Mol. Model. 2014, 20, 2200; e) S. Begel, R. Puchta, R. van Eldik, Beilstein J. Org. Chem. 2013, 9, 1252; f) M. Schmeisser, P. Illner, R. Puchta, A. Zahl, R. van Eldik, Chem. - Eur. J. 2012, 18, 10969; g) R. Puchta, R. Meier, N. J. R. van Eikema Hommes, R. van Eldik, Eur. J. Inorg. Chem. 2006, 4063; h) A. Scheurer, H. Maid, F. Hampel, R. W. Saalfrank, L. Toupet, P. Mosset, R. Puchta, N. J. R. van Eikema Hommes, Eur. J. Org. Chem. 2005, 2566; i) P. Illner, A. Zahl, R. Puchta, N. J. R. van Eikema Hommes, P. Wasserscheid, R. van Eldik, J. Organomet. Chem. 2005, 690, 3567; j) C. F. Weber, R. Puchta, N. J. R. van Eikema Hommes, P. Wasserscheid, R. van Eldik, Angew. Chem., Int. Ed. 2005, 44, 6033.
- [21] a) V. Barone, M. Cossi, J. Phys. Chem. A 1998, 102, 1995; b) M.
   Cossi, N. Rega, G. Scalmani, V. Barone, J. Comput. Chem.
   2003, 24, 669.
- [22] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin,

V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Revision B.01, Gaussian Inc., Wallingford, CT, 2009.

- [23] P. Su, H. Li, J. Chem. Phys. 2009, 131, 14090.
- [24] S. Radenković, M. Antić, N. D. Savić, D. B. Glišić, New J. Chem. 2017, 41, 12407.
- [25] M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, J. A. Montgomery, *J. Comput. Chem.* **1993**, *14*, 1347.
- [26] M. S. Gordon, M. W. Schmidt, in *Theory and Applications of Computational Chemistry: The First Forty Years*, (Eds: C. E. Dykstra, G. Frenking, K. S. Kim, G. E. Scuseria), Elsevier, Amsterdam 2005 1167.
- [27] A. E. Reed, L. E. Curtiss, F. Weinhold, *Chem. Rev.* **1988**, *88*, 899.
- [28] a) K. Mislow, Science 1954, 120, 232; b) K. Mislow, R. Bolstad, J. Am. Chem. Soc. 1955, 77, 6,712.
- [29] a) M. Mauksch, P. v. R. Schleyer, Angew. Chem., Int. Ed. 1997, 36, 1856; b) M. Mauksch, P. v. R. Schleyer, Angew. Chem. 1997, 109, 1976.

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