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Stereoisomer Discrimination in Complexes of Halogen-Substituted Difuranes and Li or Na Cations

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The theoretical study of the stereoisomer discrimination of the 2:1 homo- and heterochiral complexes between chiral 5,5'-dihalogen bifuranes and lithium or sodium cations has been carried out using DFT methods. To understand the chiral effect produced by the introduction of a second bifurane molecule, the 1:1 complexes also have been calculated. All the 2:1 heterochiral complexes computed showed a nonplanar configuration around the metallic cation, but in the case of the homochiral complexes, the dibromo- and dichloro-bifurane systems around Na⁺ were quasi-planar. The nature of the interactions established between cations and bifurane systems has been analyzed by means of AIM and NBO, and correlations between the electron density topological parameters with the O...M distance and with the orbital interaction energy have been found. Stereodiscrimination is observed favoring the heterochiral complexes except for the Na⁺ complexes with chloro and bromo substituents in which the homochiral forms are more stable. Stereodiscrimination values correlate with the difference in electron density at the bond critical point and orbital interaction energy between homo- and heterochiral systems.

Introduction

In a recent issue of *Science* addressing the 125 scientific most important questions that have not yet been answered or that will drive research in the future years,¹ the authors identify the origin of homochirality in nature as one of those fundamental questions remaining to be solved. This is only an example of the significance of the topic considering that chirality is present not only in many biomolecules (amino acids are left-handed and sugars are right-handed) but also plays a fundamental role in many chemical processes and systems (enantioselective synthesis, chiral catalysts, chiral separation columns, or chiral recognition).

In general, the interaction between a particular enantiomer of one compound and the two enantiomers of another molecule to give a diastereomeric pair exhibiting differences in energy and physical properties is a manifestation of stereodiscrimination.² In some cases, though, metals can be used to bring together this chiral recognition. Covering this topic, Speranza has recently published a very complete review on ionic (including metal-bound complexes) and molecular chiral clusters in the gas phase, analyzing the forces involved as well as the experimental and theoretical data available on the structure, stability, and characterization of these clusters.³ In addition, Speranza and co-workers have presented another review that deals with chiral recognition in the gas phase through the application of laser resolved mass spectrometric techniques.⁴ Trying to deepen the understanding of these recognition processes, our group has recently published a review on the theoretical calculation of chiral discrimination.⁵

The area of chiral recognition in the coordination of olefins to chiral transition-metal moieties is of great interest, both for its role in metal-promoted enantioselective syntheses and because it provides simple procedures for the determination of enantiomeric excess or the resolution of racemic mixtures. Thus, some authors have used metal-coordination processes for colorimetric assessment of enantiopurity,⁶ whereas other authors have used chiral recognition in Ag(I)-olefin complexes with chiral diamines for the resolution of racemic alkenes and NMR discrimination of enantiomers.⁷ As well, chemists have taken advantage of metal-directed and metal-templated synthesis to prepare molecular and supramolecular complexes. Hence, by associating chiral labile [Fe(bipy or phen)₃]²⁺ complexes with tris(tetrachlorobenzenediolato)phosphate anions, a stereocontrol of the metal-centered chirality has been achieved by Lacour and co-workers.⁸

By means of DFT calculations, our group has recently studied the stereoisomer discrimination in binuclear square planar complexes of Ni, Pd, and Pt.⁹ In addition, we had previously explored the influence of different substituents on the discrimination of complexes with chiral bis(5*H*-pyrroles) or bis-(oxazolines) and lithium cation.¹⁰ Continuing with our studies on metal-induced stereodiscrimination, we have chosen for the present study more rigid chiral moieties such as (*R,R* or *S,S*) 5,5'-dihalogen-5*H*,5'*H*-[2,2']bifuranyldienes (halogen = fluorine, chlorine, and bromine) and different metallic cations such as lithium and sodium. The *R,S* form is a nonchiral *meso* system not relevant for the study. The results will be discussed in terms of geometric and electronic analysis based on the AIM and NBO methods.

Computational Methods

The geometries of all the compounds have been fully optimized with the programs *Gaussian 98*¹¹ and *Gaussian 03*¹² using the hybrid method Becke3LYP¹³ with the 6-31G* and

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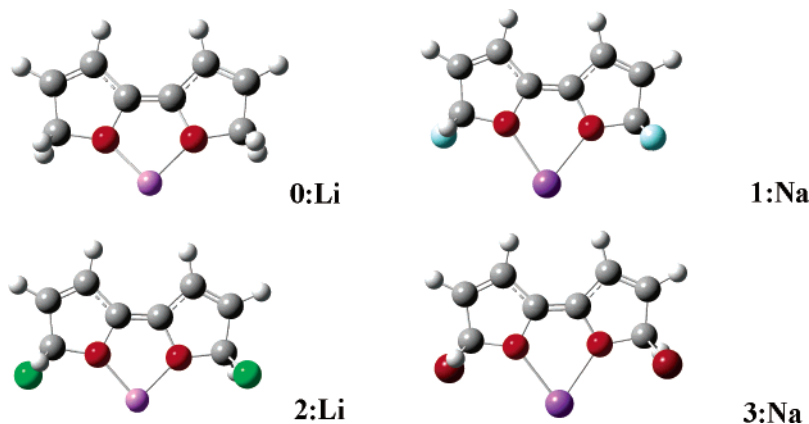


Figure 1. Some of the 1:1 complexes formed between bifurane derivatives and Li and Na cations. Color code: 0 = hydrogen, light gray; 1 = fluorine, light blue; 2 = chlorine, green; 3 = bromine, dark red; Li⁺, light purple; and Na⁺, dark purple.

6-311+G**¹⁴ basis sets. In all the cases, the nature of the compounds as a potential energy minimum has been established at the B3LYP/6-31G* level, by verifying that all the corresponding frequencies were real.

Stabilization energies, E_{Sta} s, have been calculated as the difference of the total energy of the complex and the sum of that of the isolated monomers. They have been corrected of the inherent basis set superposition error (BSSE) using the Boys–Bernardi counterpoise technique.¹⁵

The topological properties of the electron charge density [electron density at the bond critical point, $\rho(\text{BCP})$, and its Laplacian, $\nabla^2\rho(\text{BCP})$] have been studied using the atoms in molecules methodology (AIM) with the *AIMPAC*¹⁶ and *MORPHY98*¹⁷ programs using the wave function obtained at the B3LYP/6-311+G** level. The atomic energy and charge have been obtained by numerical integration within the atomic basin using the *MORPHY98* program. Following the criteria established in a previous study,¹⁸ the value of the integrated Laplacian has been considered as a measure of the integration quality. Thus, the largest value obtained for this parameter has been 1×10^{-3} , indicating very accurate integrations.

The natural bond orbital (NBO) analysis was used to determine the nature of the interactions in the formation of the complexes. These calculations were performed with the NBO code¹⁹ implemented in *Gaussian 98* and *Gaussian 03*.

We will use the terms “homochiral” for a [RR]–M–[RR] or [SS]–M–[SS] complex and “heterochiral” for a [RR]–M–[SS] or [SS]–M–[RR] complex. The 1:1 studied complexes between one unit of dihalogen–bifurane and one metallic cation (Li⁺ or Na⁺) with fluorine atoms will be named **1:M**, those with chlorine substituents will be named **2:M**, and those with bromine will be named **3:M**, where **M** = Li or Na cations. In the case of the 2:1 complexes (two units of dihalogen–bifurane), those complexes with fluorine will be named **1:M:1**, with chlorine **2:M:2** and with bromine **3:M:3** (homochiral or heterochiral in each case depending on the substitution of the chiral centers) and where **M** could be Li or Na cations. To estimate the influence of the halogen substituents, the 1:1 and 2:1 complexes of the corresponding unsubstituted bifurane were also computed as a reference and will be named **0:M** and **0:M:0**, respectively.

Results and Discussion

Study of the 1:1 Complexes. First, the 1:1 complexes between each bifurane derivative and the Li and the Na cations were computed and analyzed. Some of the optimized dimers are shown in Figure 1. All the optimized complexes with

TABLE 1: BSSE Corrected Stabilization Energy (kcal mol^{−1}) and Oxygen–Metal Distances (Å) of Bifuranes 0–3 Complexed to Li⁺ and Na⁺ Cations (1:1) Calculated at B3LYP/6-311+G Level**

system	$E_{\text{Sta}} + \text{BSSE}$	$d(\text{O} \cdots \text{M})$
0:Li	−63.91	1.87
1:Li	−54.05	1.91
2:Li	−53.32	1.91
3:Li	−52.44	1.91
0:Na	−44.85	2.25
1:Na	−38.03	2.29
2:Na	−37.55	2.29
3:Na	−36.99	2.30

TABLE 2: Electron Density and Laplacian (au) at BCP of Oxygen···Metal Interaction Calculated at B3LYP/6-311+G Level for All 1:1 Bifurane–Metal Complexes Studied**

system	O···M	
	$\rho(\text{BCP})$	$\nabla^2\rho(\text{BCP})$
0:Li	0.0332	0.2541
1:Li	0.0302	0.2265
2:Li	0.0301	0.2253
3:Li	0.0299	0.2235
0:Na	0.0244	0.1631
1:Na	0.0220	0.1442
2:Na	0.0218	0.1423
3:Na	0.0214	0.1395

substituted bifuranes (**1:Li/Na**, **2:Li/Na**, and **3:Li/Na**) show C_2 symmetry, whereas both unsubstituted complexes (**0:Li/Na**) have C_{2v} symmetry.

The stabilization energy was calculated at the B3LYP/6-311+G** level and BSSE corrected (BSSE values obtained between 1.17 and 1.44 kcal mol^{−1}). The energy values and the O···M distances are presented in Table 1. It can be observed that, in all the cases, the stabilization of the 1:1 complexes diminishes according to the size of the substituent increase (from H to Br) and that Li⁺ complexes are more stable than the Na⁺ ones. In the same way, the O···M distance becomes larger with the size of both the bifurane substituents and the cation. Accordingly, when the repulsion between the substituents and the metal increases, the dimers are less stable.

The AIM analysis shows symmetric bond critical points (bcp) between the cation and the O atoms with identical electron density properties (see Table 2) and a ring critical point in the

TABLE 3: Atomic Energy Difference (kcal mol⁻¹) with Respect to Isolated Cation and Atomic Charges (e) of Metal Cations for All Complexes Calculated at B3LYP/6-311+G Level Using Both AIM and NBO Approaches**

system	Δ (atomic energy) (AIM)	atomic charge (AIM)	atomic charge (NBO)
0:Li	-32.72	0.9338	0.9601
1:Li	-23.24	0.9405	0.9673
2:Li	-20.05	0.9405	0.9562
3:Li	-12.98	0.9404	0.9543
0:Na	-146.79	0.9434	0.9769
1:Na	-100.52	0.9502	0.9784
2:Na	-50.95	0.9494	0.9733
0:Li	92.19	0.9476	0.9713

plane formed by the O=C=C=O of the bifurane moiety and the metal. According to the $\rho(\text{bcp})$ and $\nabla^2\rho(\text{bcp})$ values, all the interactions established between the different bifuranes and the metal cations correspond to ionic bonds.

As well, using the AIM approach, the atomic energy of the metal cation was computed for each complex with integrated Laplacian values smaller than 0.00014 au in all cases. The difference in atomic energy with respect to the uncomplexed cation (Li⁺: -7.2849178 au and Na⁺: -162.087568 au) is presented in Table 3 together with the atomic charges calculated both with the AIM and with the NBO approaches. In the Li complexes, the Li metal always becomes more stable upon complexation with the bifurane system, and this stabilization decreases according to the size of the bifurane substituent increase. In the case of the Na complexes, the stabilization of

the Na cation within the complex also diminishes with the size of the substituents until the point that in the corresponding bromine-substituted complex (**3:Na**), Na⁺ is less stable than the uncomplexed cation.

The calculated atomic charge of the cations, independent of the method used, is smaller in the unsubstituted complexes (**0:Li** and **0:Na**) than in those with halogen substituents, and among these, it diminishes with the size of the halogen.

Analysis of Structure and Energy of the 2:1 Complexes. The chiral 2:1 complexes formed between two units of dihalogen-bifurane and a metallic cation (Li⁺ or Na⁺) show different symmetries when optimized. In all cases, the two bifurane moieties are in a more or less perpendicular disposition to each other (angles ranging between 90, 62.5, and 52.3°), except for the **2:Na:2** and **3:Na:3** homochiral complexes where the bifurane monomers and the sodium cation lies approximately in the same plane in a square planar coordination.

Thus, in the case of both the optimized Li⁺ and the optimized Na⁺ complexes, all the homochiral complexes present *D*₂ symmetry, whereas in the case of the heterochiral complexes, all exhibit *S*₄ symmetry as represented in Figures 2 and 3.

Both the homo- and the heterochiral optimized Li⁺ systems seem to prefer a nonplanar approach for the complexation. However, in the optimized Na⁺ complexes, while the heterochiral complexes exhibit a perpendicular approach, that is not the case for all the homochiral ones since two of them, **2:Na:2** and **3:Na:3**, are almost planar (see Figure 3).

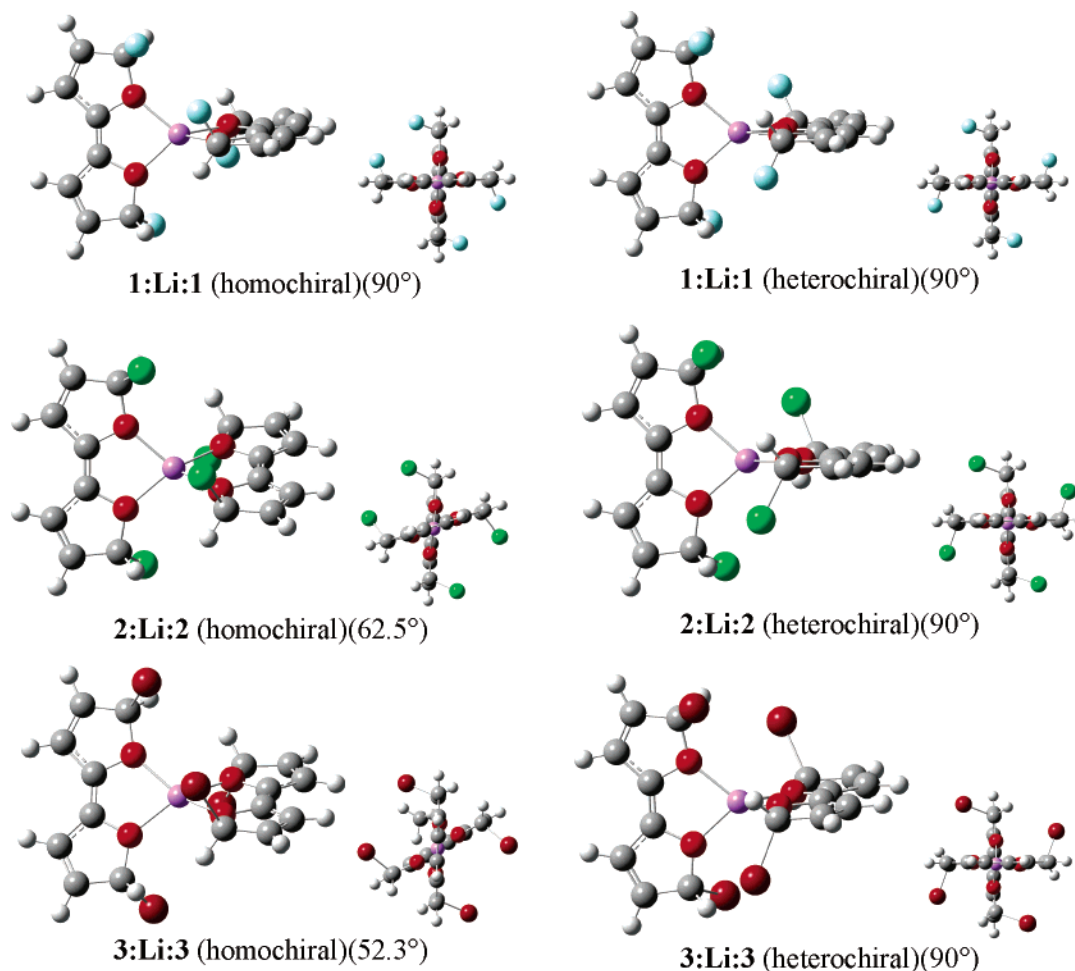


Figure 2. Two views of the chiral 2:1 complexes with Li⁺ of the different di-halogen (**1** = fluoro, light blue; **2** = chloro, green; and **3** = bromo, dark red) substituted bifuranes.

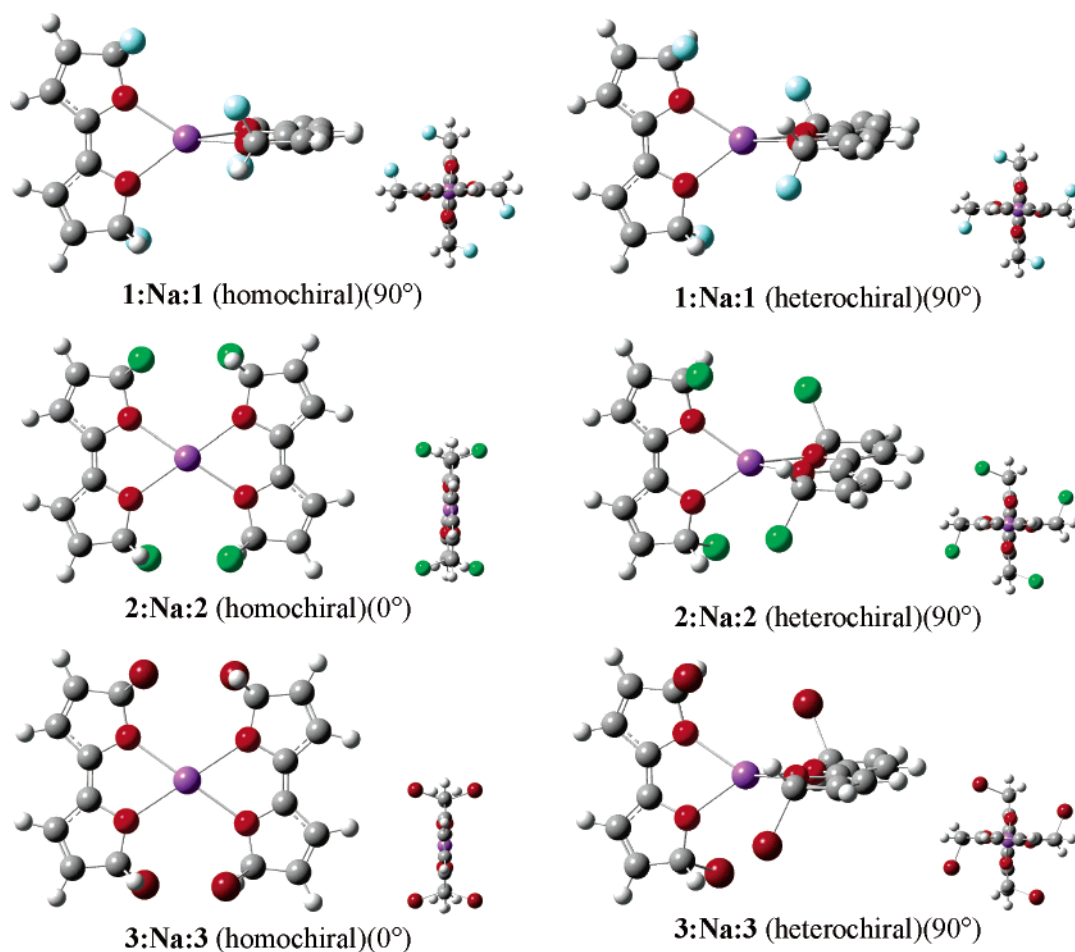


Figure 3. Two views of the chiral 2:1 complexes with Na^+ of the different di-halogen (**1** = fluoro, light blue; **2** = chloro, green; and **3** = bromo, dark red) substituted bifuranes.

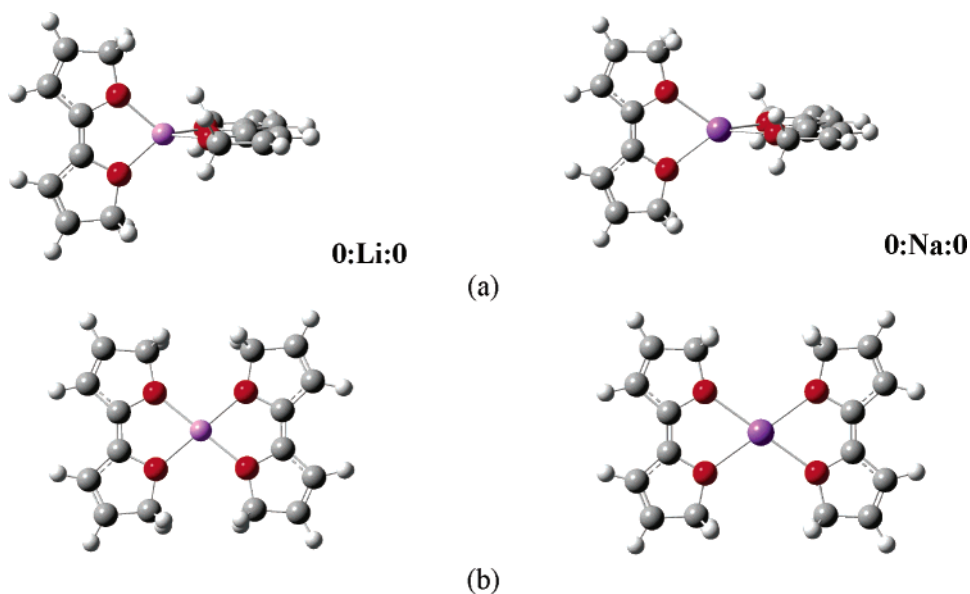
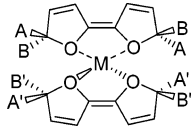


Figure 4. Nonchiral 2:1 complexes of the unsubstituted bifurane with Li^+ and Na^+ in (a) perpendicular (more stable) and (b) planar approximations optimized at the B3LYP/6-311+G** level.

The nonchiral 2:1 complexes formed between the unsubstituted bifurane and the Li and Na cations (**0:Li:0** and **0:Na:0**) have been also computed for the sake of comparison, and both optimized structures show D_{2d} symmetry (see Figure 4a).

The interaction energy and corrected stabilization energy are presented in Table 4. As compared to the 1:1 complexes, the introduction of a second bifurane moiety results in an increment

of the overall stability of the 2:1 complexes of approximately 25 kcal mol^{-1} . In the lithium complexes, the heterochiral systems are always more stable than the homochiral ones. It is interesting that in the 2:1 complexes with sodium, the heterochiral system is only more stable than the homochiral one in the case of the fluoro derivatives, those with the most electronegative and smaller substituents and with a perpendicular

TABLE 4: BSSE Corrected Stabilization Energy and Stereodiscrimination Energies (kcal mol⁻¹) of Bifuranes 0–3 Complexed to Li⁺ and Na⁺ Cations (2:1) Calculated at B3LYP/6-311+G Level**


1 (A= H, B= F, A'= H or F, B'= F or H)
 2 (A= H, B= Cl, A'= H or Cl, B'= Cl or H)
 3 (A= H, B= Br, A'= H or Br, B'= Br or H)
 M= Li⁺, Na⁺

system	$E_{\text{Sta+BSSE}}$		$\Delta E_{\text{Sta+BSSE}}$ stereodiscrimination ^a
	homochiral	heterochiral	
0:Li:0		−102.92	
1:Li:1	−87.36	−89.96	−2.60
2:Li:2	−84.28	−87.24	−2.96
3:Li:3	−81.78	−85.44	−3.65
0:Na:0		−77.57	
1:Na:1	−65.55	−67.13	−1.59
2:Na:2	−66.05	−65.34	0.71
3:Na:3	−64.77	−63.77	1.00

^a Negative value indicates that the heterochiral form is more stable than the homochiral one.

configuration in both chiral forms. In all cases, as compared to the E_{Sta} of the unsubstituted complexes (**0:Li:0** and **0:Na:0**), the introduction of halogens in positions 5 and 5' decreases the stabilization of the 2:1 complexes by 13 and 10 kcal mol⁻¹ with respect to the most stable **1:Li:1** and **1:Na:1** heterochiral systems, respectively (Table 4).

To understand the different behavior of the homochiral sodium complexes **2:Na:2** and **3:Na:3**, we calculated the planar (D_{2h}) complexes with Li⁺ and Na⁺ of the unsubstituted bifurane and compared them to the perpendicular, D_{2d} complexes (**0:Li:0** and **0:Na:0**). When optimized at the B3LYP/6-311+G** level (Figure 4), the energy difference between the most stable perpendicular forms and the planar ones was of 4.6 and 1.4 kcal mol⁻¹, respectively, always in favor of the perpendicular forms. Additionally, for the Li⁺ and Na⁺ complexes, the planar forms were determined to be transition structures showing one imaginary frequency. It is clear from these calculations that the difference between the planar and the perpendicular forms in the Na⁺ complexes is very small, and this barrier could be easily overcome when introducing large halogen substituents in the bifurane system, justifying the quasi-planar configuration of the complexes **2:Na:2** and **3:Na:3**.

This different behavior of the Na⁺ complexes showing different configurations around the cation has precedents in the literature. Hence, the case of crown ethers containing four O atoms that form planar complexes with Na⁺ is well-known.²⁰ Recently, an experimental and theoretical study of the structure and vibrational spectra of 12-crown-4 complexes with Na⁺ has been carried out by El-Azhary et al.,²¹ showing that the minimum energy conformation of these complexes has C_4 symmetry. As well, the hydration of Na⁺ has been computationally studied by Kim et al.²² using Hartree–Fock and Moller–Plesset perturbation (MP2) calculations and by Lopez et al.²³ using DFT methods. Both groups found that the most stable configuration of four water molecules around the cation is that in which the four O atoms surround Na⁺ in a tetrahedral arrangement.

The stereoisomer discrimination between homo- and heterochiral complexes is presented in Table 4. In the case of the Li⁺ complexes, the heterochiral forms are always more stable, and the values of stereodiscrimination become less negative with the electronegativity of the halogens in the 5 and 5' positions. When increasing the size of the metal cation (i.e., Na⁺

TABLE 5: Atomic Energy (hartree) and Relative Energy (kcal mol⁻¹) of Metal Cation in All Complexes Optimized at B3LYP/6-311+G Calculated within AIM Methodology**

complex	homo	hetero	relative atomic energy
0:Li:0		−7.34783	
1:Li:1	−7.34783	−7.35215	2.71
2:Li:2	−7.33893	−7.34474	3.65
3:Li:3	−7.32495	−7.33273	4.88
0:Na:0		−162.29691	
1:Na:1	−162.29691	−162.30253	3.53
2:Na:2	−162.21134	−162.21106	−0.18
3:Na:3	−161.97133	−161.97614	3.02

complexes), the order is inverted, and the stereoisomer discrimination becomes more negative with the electronegativity of the substituents.

We found a certain trend between stereodiscrimination and electronegativity of the substituents and metals using the χ Pauling values for electronegativity recalculated by Allred.²⁴ The electronegativity values of the halogens are between 3.98 and 2.96, and the values for the metals are 0.98 and 0.93 for Li and Na, respectively. When representing stereoisomer discrimination values versus χ for halogens, we observed that the slope for the Li complexes was positive, whereas that for the Na complexes was negative. Hence, there is some correlation between the difference in energy stabilization and the electron-withdrawing and electron-donating properties of the metals and halogen substituents of the 2:1 complexes studied.

As well, it seems that the size of the central metal and the size and electronegativity of the 5,5'-halogen substituents of the bifurane moieties play an important role in inverting the chiral recognition. However, the bromine complexes are always the ones showing stronger discrimination in absolute value, within each series.

Analyses of Atomic Energy and Charges of the Cations.

The atomic energy of the metal cation in each of the optimized 2:1 complexes has been calculated by using AIM methodology, and the values are shown in Table 5. In all cases, the atomic energy of Li⁺ or Na⁺ is larger in the heterochiral complexes than in the homochiral ones, except for the homochiral and planar **2:Na:2**. Thus, for the Li⁺ systems, the complexes with larger atomic energy in the metal are those with a larger stabilization energy (i.e., heterochiral complexes).

However, for the Na⁺ systems, no clear relation can be established. The more stable chiral forms for complexes **1:Na:1** and **2:Na:2** are the hetero- and homochiral forms, respectively, in agreement with the atomic energy values obtained since the atomic energy of Na in the fluoro system is larger for the heterochiral form, whereas for the chloro complex, it is larger for the homochiral form. However, the **3:Na:3** homochiral complex shows a more stable homochiral configuration, but the larger atomic energy corresponds to the heterochiral form (see Tables 4 and 5).

Additionally, the atomic charges of the metal cation for each 2:1 complex were calculated with both AIM and NBO methodologies, and the results are shown in Table 6. These atomic charges follow different patterns depending on the method used for the computation, and they do not follow the same order as the stabilization energy. However, in all cases, the heterochiral charges are smaller than the homochiral ones. The resulting charges for the Li⁺ complexes are smaller when calculated with the NBO methodology than with the AIM approach; however, the differences in charge between hetero- and homochiral complexes were very similar in both analyses. Results were not as consistent in the Na⁺ complexes as in the Li⁺ ones, and both AIM and NBO charges in Na⁺ are very similar. Additionally,

TABLE 6: Atomic Charge (e) of Metal Ion in All Complexes Calculated within AIM and NBO Methodologies Optimized at B3LYP/6-311+G, Respectively**

complex	AIM			NBO		
	homo	hetero	difference in charge	homo	hetero	difference in charge
0:Li:0		0.9095			0.8869	
1:Li:1	0.9155	0.9136	0.0019	0.8869	0.8853	0.0017
2:Li:2	0.9171	0.9147	0.0024	0.8783	0.8746	0.0037
3:Li:3	0.9199	0.9152	0.0047	0.8782	0.8738	0.0044
0:Na:0		0.9145			0.9340	
1:Na:1	0.9224	0.9211	0.0013	0.9338	0.9331	0.0008
2:Na:2	0.9235	0.9221	0.0014	0.9265	0.9210	0.0055
3:Na:3	0.9254	0.9221	0.0033	0.9210	0.9139	0.0071

TABLE 7: Electron Density and Laplacian (au) at BCP of Metal...Oxygen Interaction and Metal...Oxygen Distances (Å) Calculated at B3LYP/6-311+G Level for All Bifurane–Metal Complexes Studied**

system	M...O		
	$\rho(\text{BCP})$	$\nabla^2\rho(\text{BCP})$	distance
0:Li:0	0.0248	0.1793	1.97
1:Li:1 homo	0.0232	0.1647	2.00
1:Li:1 hetero	0.0241	0.1730	1.99
2:Li:2 homo	0.0224	0.1584	2.01
2:Li:2 hetero	0.0236	0.1690	1.99
3:Li:3 homo	0.0218	0.1530	2.02
3:Li:3 hetero	0.0234	0.1671	2.00
0:Na:0	0.0206	0.1316	2.31
1:Na:1 homo	0.0187	0.1179	2.35
1:Na:1 hetero	0.0193	0.1221	2.34
2:Na:2 homo	0.0191	0.1217	2.34
2:Na:2 hetero	0.0188	0.1188	2.35
3:Na:3 homo	0.0180	0.1130	2.36
3:Na:3 hetero	0.0185	0.1168	2.35

the difference in charge in the Na cation is larger when calculations were performed with the NBO approach for **2:Na:2** and **3:Na:3**.

Again, for the Li⁺ complexes, a relation is found between atomic charges calculated with both approaches and the order of energy stabilization. Hence, those complexes with smaller atomic charge in the metal are those with a larger stabilization energy (i.e., heterochiral complexes). As before, no agreement was found for the Na⁺ systems. Heterochiral complex **1:Na:1** is more stable than the homochiral one, whereas the opposite happened for **2:Na:2** and **3:Na:3** (see Table 4), but the atomic charge is always larger in the homochiral forms.

Analysis of the Ligand...Metal Cation Interactions in the 2:1 Complexes. The analyses of the interactions established between bifurane moieties and metal cation have been performed by applying the AIM methodology on the study of the topology of the electron density of each system. Thus, for each complex, four bond critical points (bcp) were found around the cation corresponding to the four M⁺...O interactions with both bifurane moieties. The values of the computed electron density and Laplacian of the electron density at those bcp ($\rho(\text{bcp})$ and $\nabla^2\rho(\text{bcp})$) are presented in Table 7 and are in agreement with closed-shell interactions. In all cases, the interactions of the bifurane moieties with the Li⁺ are stronger than those with Na⁺ as indicated by the larger $\rho(\text{bcp})$ values.

Different exponential correlations between $\rho(\text{bcp})$ and $\nabla^2\rho(\text{bcp})$ and the M⁺...O distance were explored since relations among these parameters had been previously found.²⁵ When all the values for all the complexes (2:1 and 1:1) were considered, poor regression coefficients were found. However, it was possible to observe that different correlation clusters were forming. Thus, the values corresponding to the Li⁺ complexes gave very good

TABLE 8: Most Important Orbital Interactions (kcal mol⁻¹) between Metal Cation (Li⁺ and Na⁺) and Bifurane Moieties Calculated at B3LYP/6-311+G**

system	E(2)	
	O(lp)···M ⁺	X(lp)···M ⁺
0:Li:0	12.11	
1:Li:1 homo	11.17	
1:Li:1 hetero	11.54	
2:Li:2 homo	8.78	1.08
2:Li:2 hetero	9.31	1.06
3:Li:3 homo	7.06	1.88
3:Li:3 hetero	7.76	1.76
0:Na:0	5.69	
1:Na:1 homo	4.50	
1:Na:1 hetero	4.68	
2:Na:2 homo	2.92	1.66
2:Na:2 hetero	3.08	1.67
3:Na:3 homo	2.64	2.37
3:Na:3 hetero	2.93	2.35

exponential correlations: $\rho(\text{bcp}) = 7.3137 \text{ e}^{[-2.8783d(\text{Li}+\cdots\text{O})]}$, $R^2 = 0.9999$, $n = 11$ and $\nabla^2\rho(\text{bcp}) = 162.99 \text{ e}^{[-3.44491d(\text{Li}+\cdots\text{O})]}$, $R^2 = 0.9999$, $n = 11$. The Na⁺ complexes data provided good correlations as well: $\rho(\text{bcp}) = 8.9295 \text{ e}^{[-2.6268d(\text{Na}+\cdots\text{O})]}$, $R^2 = 0.9996$, $n = 11$ and $\nabla^2\rho(\text{bcp}) = 207.49 \text{ e}^{[-3.1818d(\text{Na}+\cdots\text{O})]}$, $R^2 = 0.9997$, $n = 11$. We explored other possible relationships between electron density at the bcp and other properties such as atomic energy and atomic charge at the metal cation, but no clear correlation was found.

One of the objectives of the present study is to explain the stereodiscrimination of these 2:1 complexes of chiral bifuranes over metallic cations; therefore, a potential relation between the $\rho(\text{bcp})$ in the M⁺...O interactions established in these complexes and the stereoisomer discrimination (as calculated in Table 1) was investigated. Hence, we calculate the difference of $\rho(\text{bcp})$ for each homochiral–heterochiral pair, and we found an acceptable correlation with the stereodiscrimination values after removing the data corresponding to **3:Na:3**: [stereodiscrimination] = $-0.143 + 2343.2\Delta[\rho(\text{bcp})]$, $R^2 = 0.982$, $n = 5$. The fact that the values corresponding to the dibromo–bifurane complexes with Na⁺ do not fit into the equation could be explained because the homochiral complex is planar and more stable than the heterochiral one, possibly because in the planar form, there is some attractive interaction between the Br atoms of a bifurane molecule and the H(C) atoms of the other. The corresponding homochiral dichloro–bifurane complex (**2:Na:2**) is also planar and more stable than the heterochiral configuration, but no attractive interaction seems to be present between Cl and H atoms. Thus, by looking at the van der Waals radii of H (1.2 Å), Br (1.95 Å), and Cl (1.80 Å),²⁶ we found that the distance between a Br of one molecule and the H of the other in the homochiral **3:Na:3** is 3.17 Å, almost the sum of the corresponding van der Waals radii (3.15 Å), whereas the distance between Cl and H in the homochiral **2:Na:2** is 3.14 Å, longer than the corresponding van der Waals radii sum (3.00 Å).

This correlation is very interesting because it establishes a direct link between the nature of the interactions found within each complex (given by the electron density at the bcp) and the energetic preference of one of the chiral systems over the other (given by the stereodiscrimination values calculated as the difference between the stabilization energy).

Finally, the Natural Bond Orbital theory was used to analyze the orbital nature of the different interactions established within these 2:1 complexes, and the results are shown in Table 8. In

all the complexes, donations from the lone pairs of the O atoms of the bifurane systems to empty orbitals of the cation metals were found.

In addition, in all 2:1 complexes where the bifurane was substituted with chlorine or bromine, interactions between the halogens' lone pairs and metal empty orbitals were found. In all cases, the orbital interaction energy in the $O(lp) \cdots M^+$ interactions were found to be larger in the unsubstituted complexes than in the dihalogen ones, larger in the heterochiral complexes than in the homochiral, and stronger for the Li^+ complexes than for the Na^+ ones. This result is in agreement with the stabilization energy values obtained. In general, these $E(2)$ values diminish as the electronegativity of the halogen substituents decreases.

The orbital interaction energy found for the $X(lp) \cdots M^+$ interactions is larger for the bromine containing complexes than for the chlorine ones, and they are larger for the Na^+ complexes than for the Li^+ ones. In the case of the heterochiral **3:Na:3** complex, it is interesting that the $E(2)$ values of these $X(lp) \cdots M^+$ interactions are very similar to those considered to be primary interactions, $O(lp) \cdots M^+$.

As in previous studies,²⁷ we found a good correlation between the orbital interaction energy ($[E(2)]_{O \cdots M}$) and the electron density at the bcp ($\rho(bcp)$ at $O \cdots M$) of all 2:1 complexes studied (**0-3:M:0-3**): $[E(2)]_{O \cdots M} = -22.225 + 1367.9\rho(bcp)$, $R^2 = 0.925$, $n = 14$.

To understand the chiral recognition based on the nature of the interactions established within the complexes, linear regressions were investigated between the stereodiscrimination values (Table 4) and the difference between the $E(2)$ values for each chiral pair both for $O(lp) \cdots M^+$ ($\Delta[E(2)]_{O \cdots M}$) and $X(lp) \cdots M^+$ ($\Delta[E(2)]_{X \cdots M}$) interactions. However, only a correlation was found between the stereoisomer discrimination values and the $\Delta[E(2)]_{O \cdots M}$ for the nonplanar complexes **1:Li:1**, **2:Li:2**, **3:Li:3**, and **1:Na:1**: [stereodiscrimination] = $-0.9993 + 3.8217\Delta[E(2)]_{O \cdots M}$, $R^2 = 0.978$, $n = 4$. Again, it is possible to understand the discrimination in the nonplanar complexes, but in those, quasi-planar secondary interactions prevent simple explanations.

Conclusion

The theoretical study of the stereoisomer discrimination of the 2:1 homo- and heterochiral complexes between chiral 5,5'-dihalogen bifuranes and lithium and sodium cations has been carried out using DFT methods. To understand the chiral effect produced by the introduction of a second bifurane molecule, we have first calculated the 1:1 complexes. Additionally, and for a better comprehension of the effect of the halogens in 5,5' and the different configuration around the Na cation (square planar or tetrahedral), the unsubstituted 1:1 and 2:1 complexes have also been computed. All the 2:1 heterochiral complexes computed showed a nonplanar configuration around the metallic cation. In the case of the homochiral complexes, there was more a variety of configurations and, thus, the dibromo- and dichloro-bifurane systems around Na^+ were quasi-planar.

The nature of the interactions established between metal cations and bifurane systems has been analyzed by means of AIM and NBO methodologies, finding in all cases that these connections correspond to medium strength closed-shell interactions and that they are formed between the lone pairs of the O atoms and an empty orbital of the metallic cations. The usual

correlations between $\nabla^2\rho(bcp)$ and $\rho(bcp)$ with the $O \cdots M$ distance and $\rho(bcp)$ with $E(2)$ have been found.

In many of the cases studied, a stereodiscrimination is observed favoring the heterochiral complexes that are more stable than the homochiral ones except for the Na^+ complexes with chloro and bromo substituents in which the homochiral forms are favored. These stereoisomer discrimination values have been found to correlate with the difference in $\rho(bcp)$ and $E(2)$ between homo- and heterochiral systems.

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Supporting Information Available: Full references for the Gaussian program suites and all graphical representations of the regressions presented in the article. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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