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Chiral Discrimination in Lithium Complexes of Bis(5*H*-pyrroles) and Bis(oxazolines)

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The 1:1 and 2:1 complexes of chiral bis(5*H*-pyrroles) and bis(oxazolines) with the lithium cation have been studied by means of DFT methods (B3LYP/6-31G* and B3LYP/6-311+G**). The energetic, geometric, electronic, and orbital properties of the complexes have been analyzed. The chiral discrimination in the 2:1 complexes (homo vs heterochiral ones) indicate that in all the cases the heterochiral complexes are more stable than the homochiral ones, except for the *tert*-butyl derivatives. The chiral discrimination energies will be discussed on the basis of different parameters related to the lithium atom such as the N−Li distance, the orbital interaction between the lone pair of the nitrogen and an empty orbital of the lithium, and its atomic contribution to the total energy of the complexes.

Introduction

The chiral discrimination is a process intimately related to biological molecular behavior. In addition, the presence of metal atoms in the structure of proteins plays, in many cases, an important role in the formation of selective complexes that have been described, for instance, in the selective oxidation of the cytochrome P450 proteins.[1] The interactions between the metal atoms and the heteroatoms are, in general, stronger than those formed by hydrogen bonds and confer a greater stability to the complex.

Several cases have been reported in the literature where the formation of homo- vs heterochiral complexes is due to the intervention of different metals. Probably, the most important one corresponds to the catalytic complexes used in reduction processes resulting in what is known as the nonlinear effect.[2] Theoretical work carried out by Noyori et al.[3] reported the different possible catalytic species in model systems.

The metals have been used to bring together chiral entities in the field of mass spectroscopy. Thus, Cooks et al. have used copper(II) attached to a chiral reference ligand to discriminate between D and L amino acid mixtures.[4] Speranza et al.[5] have studied the complexes of α-aminophosphonic acids with group I metallic cations. The complexes had the structures $[MA_SB_2]^+$ and $[MA_RB_2]^+$, where M = H, Li, Na, and K and A_S and A_R are the enantiomers of an acid A, while B is a reference α-aminophosphonic acid with a known configuration. After an induced fragmentation process, the abundance ratio between the species $[MAB]^+$ and $[MB_2]$, which depends on the ligand configuration, was studied and the different stabilities of the diastereomeric complexes in the gas phase were assigned. Molecular mechanics MM2 calculations were used as support. From the abundance ratio, the enantiodifferentiation energy of the clusters was obtained. Seven cases were found where the heterochiral complexes are more stable than the corresponding homochiral, but only four cases were found in which the homochiral complex is the most stable. A chiral recognition between −0.43 and +0.55 kcal/mol was found depending on the metallic center.[5]

Two recent reports have identified systems with axial chirality that tend to form selectively heterochiral dimers when complexed with square planar metals.[6,7] One of the systems selected for this study, the bis(oxazolines), is widely used as chiral catalyst associated with a variety of metals.[8−10]

In the present article, complexes in which a lithium cation has been used as linker between chiral bis(5*H*-pyrroles) and between chiral bis(oxazolines) have been studied by means of DFT calculations. The chiral discrimination results have been rationalized on the basis of the geometrical and electronic analysis of the complexes using AIM and NBO methods.

Methods

The geometries of the monomers, dimers, and trimers have been optimized with the B3LYP method[11,12] and the 6-31G* basis set[13] using the Gaussian-03 package.[14] The minimum nature of the structures has been confirmed by frequency calculations at the same computational level. A further geometry optimization has been carried out at the B3LYP/6-311+G** level.[15] The stabilization energy of the complexes has been corrected of the inherent basis set superposition error as defined by Boys and Bernardi.[16]

The electron density has been analyzed using the atoms in molecules (AIM) methodology[17] and the AIMPAC[18] and MORPHY[19] programs using the wave function obtained at the B3LYP/6-311+G** level. The atomic energy has been obtained by numerical integration within the atomic basin using the MORPHY program with the default parameters. As a measure of the integration quality, the value of the integrated Laplacian has been considered.[20] The largest value obtained for this parameter has been 0.3×10^{-3}, which indicates very accurate integrations.[20] Finally, the interactions between occupied and empty orbitals as well as charge transfer within the complexes have been studied with the NBO method.[21]

Results and Discussion

The structure of chiral 2,2′-methylene-bis(5*H*-pyrrol-2-yl) (**1**) and 2,2′-methylenebis(oxazolin-2-yl) derivatives (**2**) considered in this article are shown in Chart 1. These ligands present C_2 symmetry and are able to form complexes with different metals

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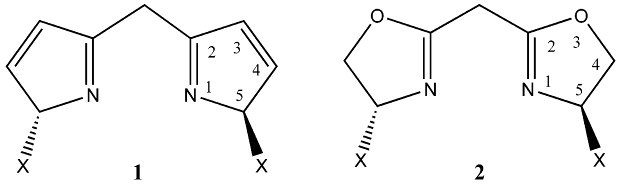
CHART 1



X = F, Cl, Br, CH_3, CF_3, CCH, $C(CH_3)_3$

TABLE 1: Stabilization Energy, E_{Sta} (kcal/mol), of the 1:1 Complexes of Li^+ and the Chelating Molecules (1 and 2)

	B3LYP/6-31G*		B3LYP/6-11+G**	
system	E_{Sta}	$E_{Sta+BSSE}$	E_{Sta}	$E_{Sta+BSSE}$
1(F)	−84.56	−77.74	−75.93	−74.97
1(Cl)	−81.87	−78.03	−76.81	−75.63
1(Br)	−94.12	−78.18	−77.35	−76.34
1(CH_3)	−88.82	−84.60	−83.22	−82.39
1(CF_3)	−90.60	−80.96	−76.48	−75.00
1(CCH)	−89.22	−84.46	−82.19	−81.30
1[$C(CH_3)_3$]	−95.00	−91.17	−85.74	−84.84
2(F)	−85.03	−73.89	−73.91	−72.89
2(Cl)	−72.98	−69.20	−74.60	−73.36
2(Br)	−94.70	−78.31	−74.59	−73.51
2(CH_3)	−86.92	−82.89	−81.36	−80.48
2(CF_3)	−88.76	−79.20	−73.99	−72.42
2(CCH)	−87.38	−82.94	−80.40	−79.49
2[$C(CH_3)_3$]	−88.92	−85.23	−83.16	−82.26

using their nitrogen atoms as chelating points. A search in the CSD[22] shows 56 crystal structures with bis(oxazolines) chelated with metals including two cases where two chiral molecules are associated to a unique metal atom.[23,24] The substituents chosen in the present study have been selected on the basis of their limited conformational profile and simultaneously for a broad range of steric and electronic characteristics.

As a first step, the 1:1 complexes between the Li^+ ion and the chelating molecules have been calculated. The complexes show C_2 symmetry (as an example, in Figure 1 is shown the corresponding complex of the methyl derivative of **2**), and the calculated stabilization energies have been gathered in Table 1. The effect of the BSSE correction is, in average, 6.9 kcal/mol for the smallest basis set but only 1.0 kcal/mol for the largest one. The corrected data show similar values at the two levels considered here. These values at the B3LYP/6-311+G** level range between −73.9 kcal/mol for the Li^+:**2**(F) and −84.9 kcal/mol for the Li^+:**1**[$C(CH_3)_3$] complexes. A linear correlation between the corrected stabilization energies of the two series, at the highest level calculated here, provides a square correlation coefficient, R^2, of 0.992. This result indicates a similar dependence of the interaction energies with the substituents in the two series. The effect of the substituents on the stabilization energy can be rationalized using some Taft parameters. The linear correlation with σ_I (inductive effect) (eqs 1 and 2) provides a correlation coefficient of 0.93 and 0.92 for the Li^+:**1** and Li^+:**2** series of complexes, respectively.

$$E_{Sta+BSSE}(Li^+:\mathbf{1}) = 15.38\sigma_I - 83.08 \tag{1}$$

$$E_{Sta+BSSE}(Li^+:\mathbf{2}) = 15.63\sigma_I - 80.86 \tag{2}$$

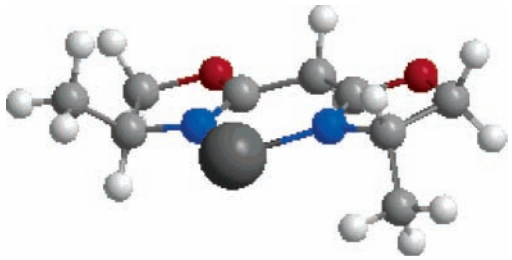


Figure 1. Li^+:**2**(X = CH_3) 1:1 complex obtained at the B3LYP/6-311+G** computational level.

TABLE 2: Calculated N−Li Interatomic Distances (Å) and N−Li−N Angles (deg)

	B3LYP/6-31G*		B3LYP/6-311+G**	
system	N−Li	N−Li−N	N−Li	N−Li−N
1(F)	1.953	95.3	1.938	97.6
1(Cl)	1.957	96.2	1.939	97.6
1(Br)	2.025	90.5	1.941	97.2
1(CH_3)	1.923	103.9	1.912	103.8
1(CF_3)	1.997	89.3	1.971	91.2
1(CCH)	1.947	97.0	1.928	99.0
1[$C(CH_3)_3$]	1.922	100.7	1.913	100.9
2(F)	2.102	90.6	1.943	98.8
2(Cl)	1.978	96.4	1.950	98.1
2(Br)	2.068	91.4	1.957	97.3
2(CH_3)	1.930	103.2	1.920	102.9
2(CF_3)	2.011	90.8	1.988	91.3
2(CCH)	1.949	97.8	1.934	99.0
2[$C(CH_3)_3$]	1.926	100.9	1.920	100.7

The most important geometrical characteristics of the N−Li interactions formed are reported in Table 2. For the same complexes, the B3LYP/6-31G* calculations provide longer N−Li distances than the ones obtained at the B3LYP/6-311+G** level. The largest difference found is 0.158 Å for the fluorine derivative of **2**, the average deviation being 0.036 Å.

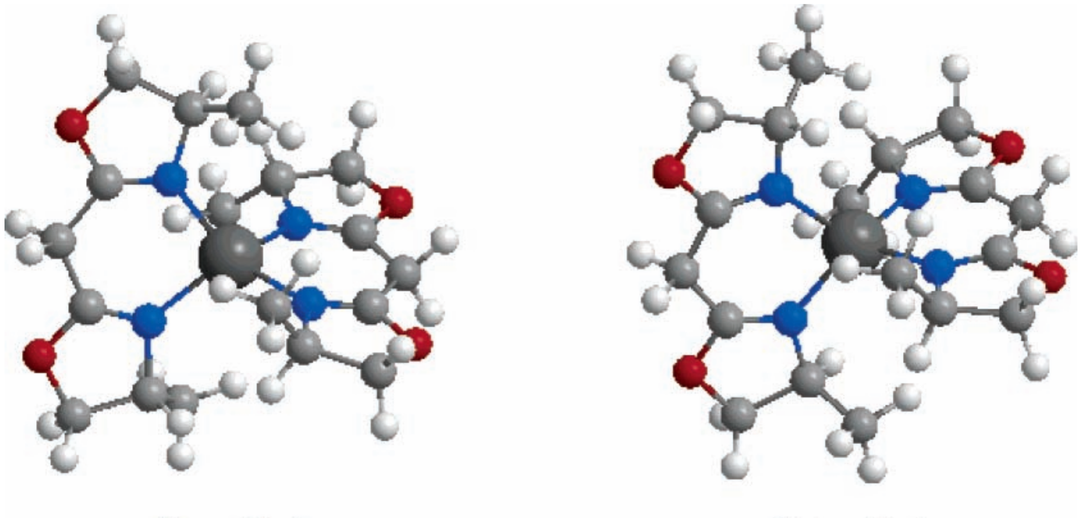
The N−Li−N angles are in most of the cases larger with the B3LYP/6-311+G** method than with the B3LYP/6-31G* one. This parameter compensates the differences in the Li−N distances to maintain the intramolecular N···N distances almost constant in both methods. In addition, the angle formed by the planes of the heterocyclic rings is larger with the small basis set than with the extended one.

Assuming that the N−Li distance represents the interaction energy between both moieties, we have plotted the stabilization energy against the N−Li distance. Although a trend is observed (when the N−Li distance increases, the stabilization energy decreases), it is clear that other effects are responsible for the final stabilization energies. This fact is especially clear in the case of the CF_3 derivatives that show stabilization energies larger than the expected for the corresponding N−Li distances obtained in these complexes.

The AIM analysis shows bond critical points (BCP) between the lithium atom and the two nitrogen atoms and the corresponding ring critical point (Table 3). The small values of the electron density at the BCPs (between 0.030 and 0.038 au) and the positive and small value of the Laplacian of the electron density (between 0.248 and 0.196 au) are typical of ionic bonds. In the cases studied here, no critical points have been found between the lithium atom and the X substituents.

The strongest orbital interaction identified by the NBO method corresponds to the lone pair of the nitrogen with one of the empty orbitals of the lithium atom (Table 3). Some additional significant interactions can be found between the lithium and the X substituents, but their values are much smaller than the N−Li interaction except for the case of the CF_3 group where the interaction is larger than 5 kcal/mol.

On the basis of the NBO charges, the amount of charge transferred from the ligands to the lithium atom ranges from



Homochiral Heterochiral

Figure 2. Optimized geometries of the homo- and heterochiral complexes of the methyl derivatives of **2** obtained at the B3LYP/6-311++G** level.

TABLE 3: Electron Density and Laplacian (au) at the N−Li Interaction and the Most Important Orbital Interactions (kcal/mol) between the Li Atom and the Rest of the System Calculated at the B3LYP/6-311+G Level**

	N−Li interactn		NBO analysis ($E(2)$)	
system	ρ_{BCP}	$-{}^2\rho_{\mathrm{BCP}}$	N(lp)−Li$^+$	X−Li$^+$
1(F)	0.035	0.228	10.07	
1(Cl)	0.035	0.228	10.18	1.21
1(Br)	0.035	0.227	10.22	2.12
1(CH_3)	0.038	0.248	10.78	
1(CF_3)	0.032	0.208	11.51	5.52
1(CCH)	0.036	0.236	10.33	
1[$C(CH_3)_3$]	0.038	0.248	12.66	2.22
2(F)	0.034	0.224	10.01	
2(Cl)	0.034	0.220	10.08	1.05
2(Br)	0.033	0.215	10.14	2.08
2(CH_3)	0.037	0.240	10.83	
2(CF_3)	0.030	0.196	11.83	5.84
2(CCH)	0.035	0.231	10.27	
2[$C(CH_3)_3$]	0.037	0.241	11.48	1.95

0.091 e in the Li$^+$:**1**[$C(CH_3)_3$] complex to 0.061 e in the Li$^+$:**2**(CCH) one.

2:1 Complexes. The calculated 2:1 complexes show D_2 and S_4 symmetry for the corresponding homochiral and heterochiral complexes (Figure 2), respectively. The X groups of the two molecules in the homochiral complexes are disposed, in pairs, one opposite to the other while in the heterochiral case they are arranged as a gear. Due to the similarity of most of the results obtained with both basis sets considered here, only those obtained with the larger one will be commented on in this section.

The calculated BSSE-corrected stabilization energy and the chiral discrimination values are reported in Table 4. As in the case of the 1:1 complexes, a linear correlation is found between the stabilization energies obtained for the complexes of **1** and **2**, in this case with a square correlation coefficient of 0.94. Using the stabilization energies between the monomers with a lithium cation as a reference (1:1 complexes), the stabilization energy increases an average of −36.6 kcal/mol in the case of the heterochiral complexes of the 2:1 systems, ranging between −20.9 to −44.4 kcal/mol. The smaller increments in each series correspond to the $C(CH_3)_3$ derivatives as indication of the strong repulsion between the X groups in the complexes formed.

TABLE 4: Calculated Corrected Stabilization and Chiral Discrimination Energies (kcal/mol) of the Dimers Bonded by a Li$^+$ Atom (2:1) at the B3LYP/6-311+G Level**

	$E_{\mathrm{Sta+BSSE}}$		
system	homochiral	heterochiral	chiral discriminatn[a]
1(F)	−111.84	−114.94	−2.97
1(Cl)	−108.47	−114.32	−4.30
1(Br)	−107.51	−112.44	−4.94
1(CH_3)	−118.83	−119.15	−0.37
1(CF_3)	−104.05	−108.51	−4.59
1(CCH)	−114.97	−118.49	−3.48
1[$C(CH_3)_3$]	−108.13	−105.75	2.50
2(F)	−108.79	−113.48	−4.76
2(Cl)	−106.62	−112.65	−6.15
2(Br)	−105.06	−111.83	−6.93
2(CH_3)	−118.17	−118.55	−0.42
2(CF_3)	−102.65	−107.50	−4.58
2(CCH)	−114.83	−117.49	−2.54
2[$C(CH_3)_3$]	−108.72	−106.83	1.92

[a] Negative values indicate that the heterochiral complex is more stable than the homochiral one.

Regarding the chiral discrimination, all the compounds studied here show a preference for the heterochiral dimers, up to 6.9 kcal/mol, with the exception of the *tert*-butyl derivatives that show, in both cases, the opposite trend. In the series of the halogen derivatives, the increment of the atom size produces a larger discrimination as indication of the importance of steric factors in the chiral discrimination energy of these complexes. The larger discriminations are found for the bromine derivatives of **2** (−6.93 kcal/mol). A comparison between the complexes of **1** and **2** shows, in general, that the inclusion of the oxygen atom favored the heterochiral complexes as indicated by the more negative values obtained for the chiral discrimination.

The calculated Li−N distances at the B3LYP/6-311+G** level are reported in Table 5. The distances obtained for the 2:1 complexes are slightly longer, 0.12 Å on average, than those obtained for the 1:1 ones. Additionally, in all the cases the heterochiral distance is shorter than the homochiral one, except in the *tert*-butyl derivatives where the opposite happens. A graphical representation of the N−Li interatomic distance difference vs the corresponding chiral discrimination (Figure 3) shows a linear correlation between these two parameters with a square correlation coefficient, R^2, of 0.94.

Like in the case of the 1:1 complexes, BCP's between the Li and the N atoms were found for all the 2:1 complexes with small values of the electron density and positive values of the

TABLE 5: Li···N Distance (Å) in the 2:1 Complexes at the B3LYP/6-311+G Computational Level**

system	homochiral	heterochiral	system	homochiral	heterochiral
1(F)	2.043	2.031	**2**(F)	2.060	2.031
1(Cl)	2.058	2.038	**2**(Cl)	2.073	2.038
1(Br)	2.067	2.042	**2**(Br)	2.084	2.042
1(CH_3)	2.051	2.051	**2**(CH_3)	2.056	2.051
1(CF_3)	2.077	2.053	**2**(CF_3)	2.077	2.053
1(CN)	2.042	2.040	**2**(CN)	2.044	2.040
1(CCH)	2.055	2.031	**2**(CCH)	2.056	2.031
1($C(CH_3)_3$)	2.128	2.142	**2**($C(CH_3)_3$)	2.126	2.142

TABLE 6: Atomic (hartree) and Relative (kcal/mol) Energy of the Li Atom in the 2:1 Complexes Calculated within the AIM Methodology

	tot. energy		
system	homochiral complex	heterochiral complex	rel energy[a]
1(F)	−7.380 05	−7.385 27	−3.27
1(Cl)	−7.370 57	−7.377 87	−4.58
1(Br)	−7.356 36	−7.365 55	−5.77
1(CH_3)	−7.389 01	−7.389 04	−0.01
1(CF_3)	−7.367 50	−7.376 47	−5.63
1(CCH)	−7.382 68	−7.391 66	−5.64
1[$C(CH_3)_3$]	−7.368 45	−7.364 84	2.27
2(F)	−7.371 87	−7.380 13	−5.18
2(Cl)	−7.362 77	−7.374 13	−7.13
2(Br)	−7.348 53	−7.362 84	−8.98
2(CH_3)	−7.381 57	−7.382 07	−0.31
2(CF_3)	−7.363 92	−7.372 89	−5.62
2(CCH)	−7.377 28	−7.384 77	−4.70
2[$C(CH_3)_3$]	−7.364 00	−7.361 83	1.36

[a] Negative values indicate that the atom within the heterochiral complex is more stable than in the homochiral one.

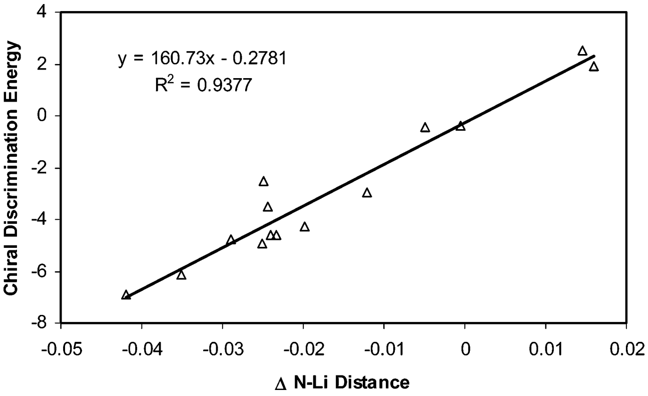


Figure 3. Chiral discrimination energy (kcal/mol) vs the difference of the N−Li distance (Å) in the homo-and heterochiral complexes. The fitted linear correlation is shown with the corresponding square correlation coefficient, R^2.

Laplacian. The values of the electron density and the Laplacian for all the N−Li interactions found in the present article have been plotted vs the corresponding interatomic distances (Figure 4). A good exponential relationship has been obtained in both cases, in agreement with other closed-shell interactions described in the literature that show a similar behavior.[25−27]

In agreement with the correlations found for the electron density vs the N−Li distance and the chiral discrimination vs the relative N−Li distance, a good linear relationship is found between the chiral discrimination vs the relative electron density at the bond critical point (square correlation coefficient, R^2, of 0.97).

The highly congested structure of these complexes is clearly proven by the presence of additional intermolecular BCP's between the substituents in position 5 and 5′ of the heterocyclic units, except for the heterochiral fluoro derivatives where none was found between those groups.

Since the differences in the N−Li distances show a good correlation with the chiral discrimination energy, the atomic contribution of the lithium atom to the total energy of the systems has been calculated with the AIM methodology (Table 6). It is significant that the relative atomic energies of the Li atom in the homo- vs the heterochiral complexes present values similar to those obtained for the chiral discrimination and that both parameters are highly correlated (square correlation coefficient $R^2 = 0.96$). It looks as if the information on the Li atoms is able to explain the relative characteristic of the whole molecules.

The NBO analysis (Table 7) shows strong interaction between the lone pairs of the nitrogen atoms and the lithium cation. It is interesting to notice, excluding the *tert*-butyl derivatives, that the value of the orbital interaction is larger in the 2:1 complexes than in the case of the 1:1 even though the N−Li distance is shorter in the latter case. This interaction energy for the heterochiral complexes is, in all the cases, larger than the ones obtained for the homochiral ones except for the *tert*-butyl derivatives in agreement with the values obtained for the chiral discrimination energy. The additional interactions observed in the 1:1 complexes between the X group and the lithium atom are greatly reduced probably due to the longer distance between

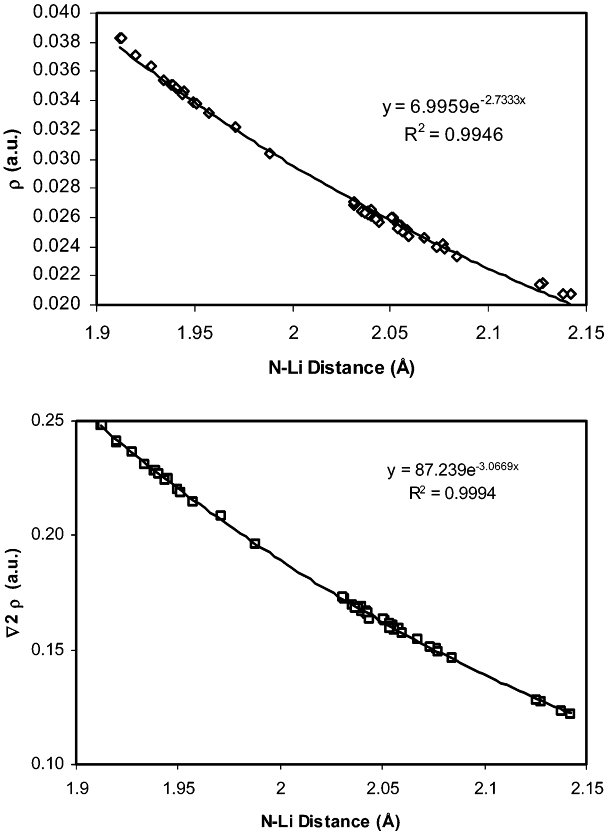


Figure 4. Electron density and its Laplacian at the N−Li bond critical point vs the N−Li distance. The equation and square correlation coefficient of the fitted curve are shown.

TABLE 7: NBO Analysis of the Orbital Interaction, *E*(2) (kcal/mol), between the Lone Pair on the Nitrogen and an Empty Orbital of the Lithium Cation Calculated at the B3LYP/6-311+G Level**

system	homochiral	heterochiral	system	homochiral	heterochiral
1(F)	19.02	19.58	**2**(F)	18.15	20.11
1(Cl)	17.25	18.02	**2**(Cl)	17.58	18.88
1(Br)	15.95	17.04	**2**(Br)	16.37	18.06
1(CH_3)	16.99	16.99	**2**(CH_3)	18.1	18.23
1(CF_3)	16.39	17.16	**2**(CF_3)	17.53	18.33
1(CCH)	16.92	17.98	**2**(CCH)	18.25	19.11
1[$C(CH_3)_3$]	7.54	6.64	**2**[$C(CH_3)_3$]	8.16	7.37

the cation atom and these groups. The larger value obtained is 2.0 kcal/mol for the complex Li^+:[**2**(CF_3)].

Finally, the special case of the *tert*-butyl derivatives whose behavior is the opposite to that of the rest of the systems will be discussed in more detail. In the heterochiral complex the disposition of the nitrogen around the Li atom is tetrahedral, but in the homochiral case the angle formed by the two planes defined by N−Li−N, where the two N's belong to the same molecule, is 72° while in an ideal situation it should be 90° as occurs for the heterochiral complexes. The disposition in the homochiral case is adopted to minimize the interaction between the *tert*-butyl moieties of different molecules, and simultaneously, one of the hydrogen atoms of this moiety became closer to the lithium atom in the homochiral complex than in the heterochiral one. A bond critical point can be located in the electron density maps. This extra stabilization interaction could slightly favor the homo- compared with the heterochiral complex. In addition, the rest of the parameters studied here (differences of N−Li distances, orbital interaction of the nitrogen lone pair with a empty orbital of the lithium, and atomic energy of the lithium atom) indicate a different behavior of the *tert*-butyl derivatives vs the remaining substituents.

Conclusion

A theoretical study of the chiral discrimination of the 1:2 homo- and heterochiral complexes between the lithium cation and chiral bis(5*H*-pyrroles) and bis(oxazolines) has been carried out using DFT methods. To perform such a study, we have calculated first the isolated molecules and the 1:1 complexes.

The chiral discrimination energies show that, in all the cases, the heterochiral complexes are more stable than the homochiral ones, except for the *tert*-butyl derivatives where the opposite happens. These energetic results have been found to correlate with the relative N−Li distances, the orbital interaction between the lone pair of the N and an empty orbital of the lithium atom, and the atomic energy of the lithium atom within the complexes.

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References and Notes

(1) Harris, D.; Loew, G. *J. Am. Chem. Soc.* **1995**, *117*, 2738−2746.

(2) Girard, C.; Kagan, H. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 2923−2959.

(3) Yamakawa, M.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 6327−6335.

(4) Tao, W. A.; Zhang, D. X.; Nikolaev, E. N.; Cooks, R. G. *J. Am. Chem. Soc.* **2000**, *122*, 10598−10609.

(5) Paladini, A.; Calcagni, C.; Di Palma, T.; Speranza, M.; Lagana, A.; Fago, G.; Filippi, A.; Satta, M.; Guidoni, A. G. *Chirality* **2001**, *13*, 707−711.

(6) Kim, T. W.; Lah, M. S.; Hong, J. I. *Chem. Commun.* **2001**, 743−744.

(7) Claessens, C. G.; Torres, T. *J. Am. Chem. Soc.* **2002**, *124*, 14522−14523.

(8) Kobayashi, S.; Jørgensen, K. A. *Cycloaddition Reactions in Organic Synthesis*; Wiley-VCH Verlag GmbH: Weinheim, Germany, 2002.

(9) Fringuelli, F.; Tatichi, A. *The Diels−Alder Reaction: Selected Practical Methods*; John Wiley & Sons: New York, 2002.

(10) Lin, G.-Q.; Li, Y.-M.; Chan, A. S. C. *Principles and Applications of Asymmetric Synthesis*; John Wiley & Sons: New York, 2001.

(11) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

(12) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789.

(13) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213−222.

(14) Frisch, M. J. T.; et al. *Gaussian-03*; Gaussian: Wallingford, CT, 2003.

(15) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265−3269.

(16) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.

(17) Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Clarendon Press: Oxford, U.K., 1990.

(18) Bieglerkonig, F. W.; Bader, R. F. W.; Tang, T. H. *J. Comput. Chem.* **1982**, *3*, 317−328.

(19) Popelier, P. L. A. with a contribution from: Bone, R. G. A. *MORPHY98, a topological analysis program*; UMIST: Manchester, U.K., EU, 1999.

(20) Alkorta, I.; Picazo, O. *Arkivoc* **2005**, *ix*, 305−320.

(21) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899−926.

(22) Allen, F. H.; Davies, J. E.; Galloy, J. J.; Johnson, O.; Kennard, O.; Macrae, C. F.; Mitchell, E. M.; Mitchell, G. F.; Smith, J. M.; Watson, D. G. *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 187−204.

(23) Takacs, J. M.; Reddy, D. S.; Moteki, S. A.; Wu, D.; Palencia, H. *J. Am. Chem. Soc.* **2004**, *126*, 4494−4495.

(24) Crosignani, S.; Desimoni, G.; Faita, G.; Filippone, S.; Mortoni, A.; Righetti, P. P.; Zema, M. *Tetrahedron Lett.* **1999**, *40*, 7007−7010.

(25) Alkorta, I.; Rozas, I.; Elguero, J. *Struct. Chem.* **1998**, *9*, 243−247.

(26) Espinosa, E.; Alkorta, I.; Elguero, J.; Molins, E. *J. Chem. Phys.* **2002**, *117*, 5529−5542.

(27) Knop, O.; Boyd, R. J.; Choi, S. C. *J. Am. Chem. Soc.* **1988**, *110*, 7299−7301.