Ligand Lability and Chirality Inversion in Yb Heterobimetallic Catalysts

Lorenzo Di Bari,[a] Moreno Lelli,[b] and Piero Salvadori*[a]

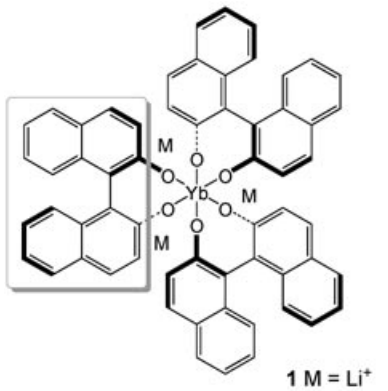
Abstract: We have investigated the exchange dynamics between the free and bound ligand in $K_3[Yb\{(R)\text{-binol}\}_3]$, the most active heterobimetallic lanthanoid catalyst for cyclic imine hydrophosphonylation; we found that the Yb–binol bond is labile. The rate constant for this exchange was determined through NMR saturation transfer experiments. Upon addition of (*S*)-binaphthol, ligand exchange leads to the formation of a small quantity of heterochiral complexes and, in the presence of a molar excess of (*S*)-binaphthol, to chirality inversion of the whole complex. This demonstrates that, in contrast to other analogous systems, $K_3[Yb(binol)_3]$ displays a strong chiral discrimination, with the overwhelming preference for ligands of the same configuration. The lability of Yb–binol bond in THF may suggest a ligand-to-substrate exchange as a key step in the catalytic process.

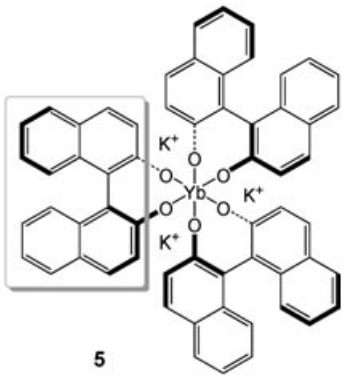
Keywords: chirality · circular dichroism · enantioselectivity · heterometallic complexes

Introduction

The recent widespread interest on the heterobimetallic lanthanoid complexes[1] (general formula $M_3[Ln(binol)_3]$)[2] led us to investigate the solution structure of the last members of the series, $M_3[Yb(binol)_3]$ (M = Li, Na, K).[3]

This study revealed two important points that shed new light on the catalytic mechanism: 1) all the three complexes $Li_3[Yb\{(R)\text{-binol}\}_3]$ (**1**), $Na_3[Yb\{(R)\text{-binol}\}_3]$ (**2**), and $K_3[Yb\{(R)\text{-binol}\}_3]$ (**3**) have the same solution structure and 2) ytterbium is only six coordinate and, in contrast to the complexes at the beginning of the lanthanide series (La, Nd, Eu), it does not coordinate H_2O even if free water is available in solution. The systems **1**–**3** catalyze the hydrophosphonylation of cyclic imines, following Scheme 1, with high *ee*, but only **3** produces high yields (90%), whereas in case of **2** and **1** the yield reduces to 56 and 39%, respectively.[4]





Gröger et al. demonstrated the interaction between the complex **3** and dimethylphosphite, by observing the lanthanide induced shift (LIS) in the ^{31}P NMR phosphite resonance after the addition of Yb (and Pr) heterobimetallic catalysts.[4–6] Starting from this observation, they proposed a mechanism in which Yb^{III} expands its coordination number in order to accommodate the substrate.[4,5] Unfortunately, this picture hardly reconciles with the fact that even in the presence of such a small and strong ligand as water, the complex remains six-coordinate. Therefore, we postulated that a ligand-to-substrate exchange might take place and, to

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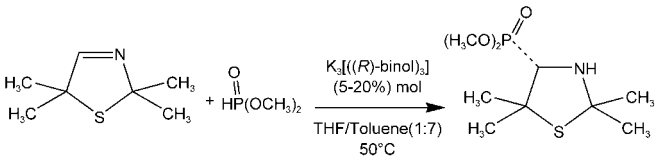
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author. EXSY spectrum of **3** after the addition of (*S*)-binol.

DOI: 10.1002/chem.200400302



Scheme 1.

ascertain this possibility, we investigated the lability of the binol–Yb^{III} bond, by means of ^{1}H NMR spectroscopy and CD, in the most active species **3**. Two-dimensional exchange spectroscopy (EXSY) and saturation transfer seemed completely adequate to follow the kinetic process and to determine its rate constant. In contrast, only chiroptical spectroscopy would provide information on a possible chirality inversion. In this paper we demonstrate that in the presence of free binol-H_2 complex **3** promptly exchanges the ligand and that, by adding the chiral ligand of opposite configuration, a total chirality inversion is obtained. These findings shed new light on the chemistry of these systems and provide useful information for rationalizing the mechanism and the chiral inductions of these catalysts.

Results and Discussion

To investigate the ligand lability in K_3[Yb{(*R*)-binol}$_3$] we studied the ligand exchange in the simplest case of a solution of **3** in presence of (*R*)-binol-H_2. The ^{1}H NMR spectrum of a mixture of (*R*)-binol-H_2 and **3**, is an exact superposition of the spectra of the two isolated compounds, with no appreciable modification in the line widths and shifts of the resonances. EXSY experiments demonstrate that free binol-H_2 and bound binaphtholate are in free exchange.[7] Resonance overlap for the free ligand prevents the correct application of direct analysis of the two-dimensional spectrum.[8] In contrast, from the quantitative analysis of build-up curves in ^{1}H NMR saturation transfer experiments between free and bound binaphthol, the kinetic constant k_1 for Equation (1) can be determined ($k_1 = 370 \pm 30\ \mathrm{mol^{-1}\,s^{-1}\,L}$):[9]

$$K_3[Yb\{(R)\text{-binol}\}_3] + (R)\text{-binol}^*\text{-}H_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} K_3[Yb\{(R)\text{-binol}\}_2(R)\text{-binol}^*] + (R)\text{-binol-}H_2 \quad (1)$$

This process [i.e., Eq. (1)] is the combination of at least two events: ligand replacement and a proton exchange. They might occur more or less concertedly or in sequence, possibly within a second coordination sphere. We deemed that the interplay of these events, without a clearer picture of relative rates, prevents any further insight into the process through speculation on the NMR data. Only the absence of dissociation of **3** demonstrated through NMR[4] and the low stability in THF, expected for charged dissociation fragments arising from Yb-binaphtholate, point toward a concerted mechanism for ligand exchange.

When the same equilibrium is studied with the ligand of opposite configuration (*S*)-binol-H_2, a more complicated system of equilibria can be envisaged, as represented in Scheme 2.

The exchange between bound and free ligand of opposite configuration would lead to heterochiral complexes, for example, with *R*,*R*,*S* configuration, which is diastereomeric with respect to the starting compound **3**. Analogous heterochiral systems were prepared for several combinations of Ln^{III} and alkali ions by using racemic binaphtholate in the synthesis of the heterobimetallic complexes, but no evidence of ligand exchange in solution has been provided so far.[10] Moreover, provided this process occurs, it may or may not lead to a complete shuffling of chiral ligands, leading to the formation of the enantiomeric *S*,*S*,*S* complex.

Clearcut evidence of the situation for **3** comes from near IR circular dichroism (NIR CD). This technique responds solely to the chiral environment of ytterbium and is insensitive to the organic ligand possibly present in solution in free form.[11] This aspect is particularly relevant, because as soon as one adds (*S*)-binol-H_2 to a solution of K_3[Yb{(*R*)-binol}$_3$], one would have the simultaneous presence of the two enantiomers of binaphthol; this leads to total band overlap and cancellation in UV CD. In fact, free and bound binaphthol give slightly different spectra,[12,3] but such a difference is too small for determining their relative proportion accurately. In contrast, Figure 1 demonstrates that the NIR CD spectrum of K_3[Yb{(*R*)-binol}$_3$] becomes exactly inverted (allowing for a scale factor) following the addition of 1.2 equivalents[13] of (*S*)-binol-H_2.

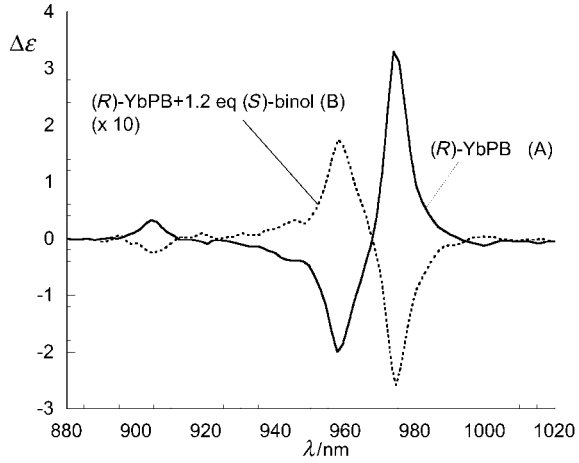
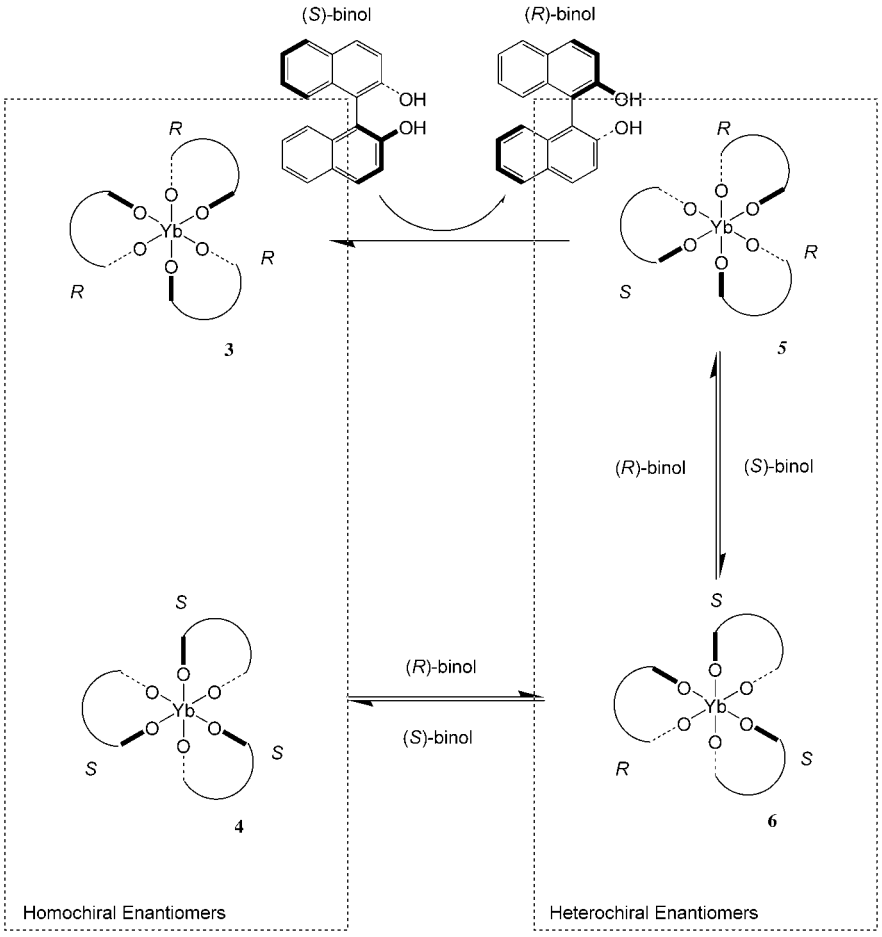


Figure 1. NIR-CD spectra of: A) the free compound **3** (18.0 мм); B) the same sample after the addition of 1.2 equivalents of (*S*)-binol-H_2. Notice the change of scale in curve B.

The presence of a diastereomeric form is not apparent through the NIR CD spectrum. The same sample, containing both enantiomers of binol was the subject of an NMR investigation, which showed the presence of three sets of signals (Figure 2): six signals of the free binol-H_2 ((*R*)-binol-H_2 + (*S*)-binol-H_2)), six signals of the homochiral species **3** and **4**, and a third set composed by six weak peaks indicating the presence of the heterochiral species K_3[Yb{(*R*)-



Scheme 2.

binol}$_2${(*S*)-binol}] (**5**) and its enantiomer K_3[Yb{(*S*)-binol}$_2${(*R*)-binol}] (**6**).[14]

EXSY reveals the ligand exchange between all the three sets; moreover, the free binol-H_2 resonances and those of **3** and **4** appear broader than in the case of the simple homochiral exchange [Eq. (1)]. Both NIR CD and NMR data confirm that the equilibria hypothesized in Scheme 2 are effective in solution, and operate a progressive one-by-one substitution of the (*R*)-binol with the (*S*)-ligand [Eqs. (2a)–2c)]. These equilibria flank the above described "homochiral exchange" [Eq. (1)] due to the simultaneous presence in solution of both (*R*)- and (*S*)-binol. This complicated interconnection of equilibria makes the determination of the rate constants k_a and k_b uneasy, and will be a matter of a further work.[15]

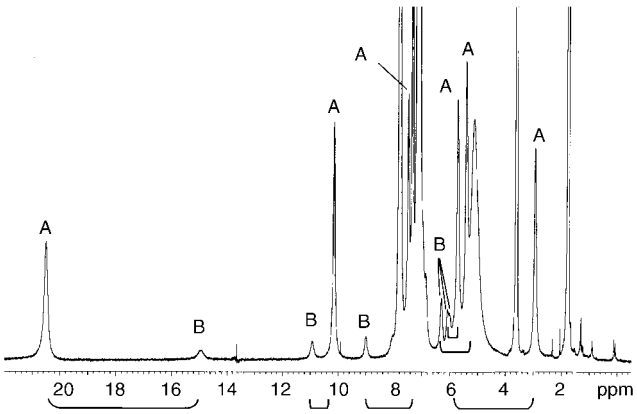


Figure 2. ^{1}H NMR spectrum of K_3[Yb{(*R*)-binol}$_3$] (**3**) (11.0 mM) in the presence of 1.0 equivalents of (*S*)-binol-H_2 in [D_8]THF. $T = 298$ K. The square brackets indicate exchanges between the resonances of the homochiral species (A) and those of the heterochiral species (B), as found through EXSY.

$$K_3[Yb\{(R)\text{-binol}\}_3] + (S)\text{-binol-}H_2 \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} K_3[Yb\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}] + (R)\text{-binol-}H_2 \quad (2a)$$

$$K_3[Yb\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}] + (S)\text{-binol-}H_2 \underset{k_{-b}}{\overset{k_b}{\rightleftharpoons}} K_3[Yb\{(S)\text{-binol}\}_2\{(R)\text{-binol}\}] + (R)\text{-binol-}H_2 \quad (2b)$$

$$K_3[Yb\{(S)\text{-binol}\}_2\{(R)\text{-binol}\}] + (S)\text{-binol-}H_2 \underset{k_{-c}}{\overset{k_c}{\rightleftharpoons}} K_3[Yb\{(S)\text{-binol}\}_3] + (R)\text{-binol-}H_2 \quad (2c)$$

The six resonances assigned to the heterochiral species **5** and **6**, do not imply a true D_3 symmetry of the complex (as we demonstrated for **3** and **4**);[3] this is prevented, because the presence of two configurationally different ligands ((*R*)- and (*S*)-binol) exclude a C_3 axis. Indeed, the analogous heterochiral species Li_3[Yb{(*R*)-binol}$_2${(*S*)-binol}] and

$Na_3[Yb\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}]$[16] have eighteen ^1H NMR resonances, in agreement with both C_2 symmetry and with the C_2-symmetric crystallographic structure of $Li_3[Y\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}]$.[10] Thus, the presence of only six peaks in our case can be explained by invoking a fast exchange regime for the equilibrium given in Equation (2b). In such a case, each nucleus experiences all the possible (nonequivalent) positions around the metal and, ultimately, the fast exchange destroys most of the structural information that might be used to refine the solution geometry of this species.

From the analysis of the signal integrals of the homo- and heterochiral forms, one can roughly estimate the equilibrium constant for Equation (2a) as $K_a = 0.13 \pm 0.01$. It is interesting to observe that when $Li_3[Yb(binol)_3]$ is synthetized from racemic binol, $Li_3[Yb\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}]$ and its enantiomer are the prevalent species (that means $K_a \gg 1$); in contrast, in the sodium complex, homochiral species are favored over the heterochiral ones, with a relative ratio of 3:1 ($K_a \approx 0.33$). The value of K_a relative to the potassium system indicates that by increasing the alkali metal radius, the heterochiral forms become less stable with respect to the corresponding homochiral ones.

From the crystallographic structure of $Li_3[Y\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}]$, the geometry of the homochiral fragment $[Y\{(R)\text{-binol}\}_2]$ does not differ much from the same fragment in the structure of $Li_3[Y\{(R)\text{-binol}\}_3]$,[10] whereas the (*S*)-binol unit coordinates the metal with an orientation quite different with respect to (*R*)-binol. The progressive change in the K_a values indicates that changing the alkali metal from Li to K, the fragments $M_3[Yb\{(R)\text{-binol}\}_2]$ lead to different environments that reduce the possibility of a stable hosting of (*S*)-binol ligand.[17]

The lability of the binaphtholate ligand in the heterobimetallic $K_3[Yb\{(R)\text{-binol}\}_3]$ complex suggests a ligand-to-substrate exchange for explaining catalysis and chiral induction. During the first step, the substrate (e.g., dimethylphosphonate) would replace at least one of the binaphtholate oxygen atoms in the metal coordination sphere, while a proton migrates from the P–H of the phosphonate to binol, yielding binol-H;[18] in this view, the different basicity of the binaphtholate moiety (ROLi < RONa < ROK) would modulate the catalytic activity.[5] The hypothesis of ligand-to-substrate exchange dynamics would also introduce a different role for the alkali metal, because it might imply different exchange rates.

Conclusion

In summary, by means of EXSY and of NIR-CD measurements, we demonstrated the ligand exchange occurring in mixtures of heterobimetallic lanthanoidic catalysts and free ligand, and we proposed a ligand-to-substrate exchange as a possible alternative to the associative mechanism previously put forward. This is in agreement with the lower coordination numbers observed for the heterobimetallic Yb complexes and sheds new light on the role of the alkali metal. The dynamic process should be investigated also for heterobimetallic complexes of other lanthanides.

Experimental Section

General procedures, instruments, and materials: NMR spectra were recorded on a Varian VXR 300 spectrometer operating at 7 T. Standard pulse sequences were used. All spectra were recorded at 298 K dissolving the samples in commercial $[D_8]$THF stored over molecular sieves 4 Å.

The NMR determination of the homochiral exchange between $K_3[Yb\{(R)\text{-binol}\}_3]$ and (*R*)-binol-H_2 (EXSY, build-up, and other one-dimensional experiments) was performed on a sample $K_3[Yb\{(R)\text{-binol}\}_3]$ (1.83 mM) and (*R*)-binol-H_2 (6.8 mM) in dry $[D_8]$THF (0.5 mL).

The NMR determination of the heterochiral exchange between $K_3[Yb\{(R)\text{-binol}\}_3]$ and (*S*)-binol-H_2 (EXSY and other one-dimensional experiments) was performed on a sample $K_3[Yb\{(R)\text{-binol}\}_3]$ (11.0 mM) and (*S*)-binol-H_2 (33.0 mM) in dry $[D_8]$THF (0.5 mL).

CD-NIR spectra were recorded on a JASCO 200 D spectropolarimeter, operating between 750 and 1350 nm, modified with a tandem Si/InGaAs detector with dual photomultiplier amplifier. The bandwidth was 2.4 nm and further narrowing of slit did not improve the resolution. The spectra were recorded at room temperature with 8 acquisitions at 50 nm min^{-1} with a 0.5 s time constant; a 1 cm quartz cell (previously stored in a dessicator) was used.

The NIR-CD spectra were recorded on a sample of $K_3[Yb\{(R)\text{-binol}\}_3]$ (18.0 mM) in dry THF (0.5 mL). The inversion was observed after addition of solid (*S*)-binol-H_2 to this sample.

All the NIR-CD spectra were recorded dissolving the sample in dry THF, obtained by distilling the commercial product (BAKER) under N_2, over Na-K alloy. (*R*)- and (*S*)-1,1′-bis(2-naphthol) was resolved from the commercial FLUKA racemate following the literature procedure.[19] The potassium complex $K_3[Yb\{(R)\text{-binol}\}_3]$ was produced following the same procedure described in literature.[3]

^{1}H NMR saturation transfer build-up experiment: The saturation transfer experiments were conducted through continuous-wave saturation of a proton resonance of the complex **3** and observing the magnetization transfer to the resonance for the same nucleus in binol-H_2. This experiment was performed with saturation delay from 0.1 to 5 s and separately for several nuclei. The integrals of the observed peaks were plotted against the saturation delay and fitted through the function given in Equation (3), in which m and n are fitting constants, y is the observed integral and t is the saturation delay.

$$y = m(1-e^{-nt}) \quad (3)$$

In the case of a simple exchange (as in our case), the kinetics constant k_1 was $k_1 = mn/c$, in which c is the complex concentration.

Acknowledgments

Financial support from MIUR-COFIN 2003 (Project "Stereoselezione in Sintesi Organica) is kindly acknowledged.

[1] a) M. Shibasaki, N. Yoshikawa, *Chem. Rev.* **2002**, *102*, 2187–2209; b) H. C. Aspinall, J. L. M. Dwyer, N. Greeves, A. Steiner, *Organometallics* **1999**, *18*, 1366–1368.

[2] M is an alkali metal (usually Li, Na, K), Ln a trivalent lanthanide and binol is the chiral enantiopure 1,1′-bis(2-naphtholate) ion, thus free binaphthol is represented by binol-H_2.

[3] L. Di Bari, M. Lelli, G. Pintacuda, G. Pescitelli, F. Marchetti, P. Salvadori, *J. Am. Chem. Soc.* **2003**, *125*, 5549–5558.

[4] H. Gröger, Y. Saida, H. Sasai, K. Yamaguchi, J. Martens, M. Shibasaki, *J. Am. Chem. Soc.* **1998**, *120*, 3089–3103.

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[6] The addition of Yb and Pr complexes to the phosphonate solution produces a small (a few ppm), but significant, deplacement of the ^{31}P resonance of the phosphonate. It may a surprise that Yb and Pr systems produce LIS of the same sign (as observed by Gröger

et al.[4]); however, one should take into account that LIS is a global effect, containing the sum of the pseudocontact shift (that are surely of opposite sign in Yb and Pr), but also of the contact term and of a diamagnetic coordination shift. The bulk term can be essentially neglected, by referring to an internal standard. The diamagnetic contribution should be accounted for by evaluating the shift induced by the coordination of $K_3[La\{(R)\text{-binol}\}_3]$ or $K_3[Lu\{(R)\text{-binol}\}_3]$; this may be especially relevant for ^{31}P, which displays a very large chemical shift range. Moreover, owing to the very short through-bond distance, the contact term may be dominant, as previously demonstrated in the case Yb and Pr β-diketonates (F. S. Mandel, R. H. Cox, R. C. Taylor, *J. Magn. Reson.* **1974**, *14*, 235–240 and T. A. Gerken, W. M. Ritchey, *J. Magn. Reson.* **1976**, *24*, 155–164). For these reasons, the observed LIS provide no reliable indication about the structure of the formed adduct.

[7] EXSY spectra is reported in the Supporting Information of reference [3].

[8] a) C. L. Perrin, R. K. Gipe, *J. Am. Chem. Soc.* **1984**, *106*, 4036–4038; b) L. Di Bari, G. Pintacuda, P. Salvadori, *Eur. J. Inorg. Chem.* **2000**, 75–82.

[9] The NMR exchange experiment "labels" one of the free or bound binaphthols, allowing one to follow the exchange between these two forms. This is rendered here by the asterisk labeling one ligand.

[10] H. C. Aspinall, J. F. Bickley, J. L. M. Dwyer, N. Greeves, R. V. Kelly, A. Steiner, *Organometallics* **2000**, *19*, 5416–5423.

[11] L. Di Bari, G. Pintacuda, P. Salvadori, *J. Am. Chem. Soc.* **2000**, *122*, 5557–5562.

[12] L. Di Bari, G. Pescitelli, P. Salvadori, *J. Am. Chem. Soc.* **1999**, *121*, 7998–8004.

[13] The equivalents are measured with respect to binol, so to add 1.2 equivalents of (*S*)-binol-H_2, 3.6 mmol of (*S*)-binol-H_2 must be added for each mmol of complex.

[14] Such a small amount of heterochiral species is not observed in the NIR CD spectra, because it is overlapped with the more intense spectra of the prevalent homochiral species.

[15] As enantiomers have the same chemical potential, the following relations can be directly derived: $K_a \cdot K_b \cdot K_c = 1$; $K_b = 1$; $k_a = k_c^{-1} \neq k_{-c}$.

[16] As these samples are prepared from racemic binol, each heterochiral and homochiral species is present with its enantiomer, which, of course, has the same NMR spectrum.

[17] Aspinall et al. proposed that a weak "edge-to-face" attractive interaction between the C–H of the (*S*)-binol and the π ring of the (*R*)-binol of $Li_3[Y\{(R)\text{-binol}\}_2\{(S)\text{-binol}\}]$ is responsible for the favored formation of the heterochiral form. The alkali metal ion radius, combined to the nature of the lanthanide should be determinant in favoring this interaction (ref. [10]).

[18] The proton exchange between the phosphonate and the binol is necessary to get a nucleophilic phosphite (refs. [4,5]).

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Received: February 2, 2004
Published online: August 2, 2004

