1366 *Organometallics* **1999,** *18,* 1366−1368

# $Li_3[Ln(binol)_3]\cdot 6THF$: New Anhydrous Lithium Lanthanide Binaphtholates and Their Use in Enantioselective Alkyl Addition to Aldehydes

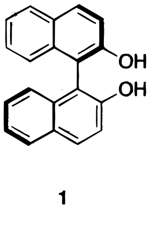
Helen C. Aspinall,* Jennifer L. M. Dwyer, Nicholas Greeves, and
Alexander Steiner

*Department of Chemistry, Donnan and Robert Robinson Laboratories, University of Liverpool,
Crown Street, Liverpool, L69 7ZD, U.K.*

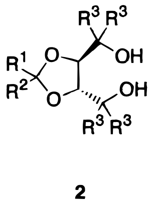
*Received December 10, 1998*

*Summary: Anhydrous lithium lanthanide binaphtholates have been prepared by reaction of lanthanide tris(silylamides) with 3 equiv of LiHbinol.* $Li_3[Y(R\text{-}binol)_3]\cdot 6THF$ *has been characterized by single-crystal X-ray diffraction, and* $Li_3[La(S\text{-}binol)_3]\cdot 6THF$ *has been shown to be an effective reagent for the enantioselective addition of MeLi to a range of aldehydes.*

The unique chemistry of the lanthanide metals, especially their combination of Lewis acidity and large ionic radius, has been exploited in the application of their complexes as reagents and catalysts for organic synthesis. One of the best established applications is the use of alkyl cerium(III) reagents in alkyl addition to carbonyls,[1] where the oxophilicity of the Ce and the reduced basicity of the alkyl species are crucial to their effectiveness. Organocerium reagents are generated by reaction of $CeX_3$ (X = halogen) with RLi in ethereal solvents, and although their structures are not known, their reactivity is distinctly different from that of the parent RLi, and it has been suggested by Denmark that they have the composition $Li_3CeCl_3R_3$.[2] These reagents may be modified by addition of chiral diols such as *R*-binaphthol **1** and TADDOLs ($\alpha,\alpha,\alpha',\alpha'$-tetraaryl-1,3-dioxolan-4,5-dimethanols) **2** to give reagents for enantioselective alkyl addition to carbonyls.[3a−d] In the case of the TADDOL-modified reagents, optimum enantioselectivity was achieved with 3 equiv of TADDOL per Ce.[3c]



**1**



**2**

Binaphthol has also been used to generate enantioselective lanthanide *catalysts*, the most spectacularly successful of which are Shibasaki's heterometallic complexes $M_3[Ln(H_2O)(binol)_3]$ (M = alkali metal; Ln = lanthanide; $H_2$binol = binaphthol), which have been fully characterized by X-ray diffraction for M = Na; Ln = La, Pr, Nd, Eu.[4] These complexes act as both Brønsted base and Lewis acid catalysts for a range of organic transformations.[5] We reasoned that the chiral diol modified organocerium reagents were structurally related to the Shibasaki heterometallic complexes and might be more easily generated from a soluble lanthanide binaphtholate complex than from $CeCl_3$. However, the presence of the acidic coordinated $H_2O$ in the Shibasaki complexes would be expected to be incompatible with the generation of an organolanthanide species. We therefore set out to prepare anhydrous analogues of Shibasaki's catalysts and to use them as precursors to enantioselective alkyl transfer reagents. In this communication we report the successful preparation of $Li_3[Ln(binol)_3]$ and their application in methyl addition to a range of aldehydes.

We chose lanthanide tris(silylamides) $[Ln\{N(SiMe_3)_2\}_3]$ as soluble, anhydrous, alkali metal- and halide-free precursors to binaphtholate complexes. Addition of 3 equiv of LiHbinol to a THF solution of $[Ln\{N(SiMe_3)_2\}_3]$ at 0 °C resulted in quantitative formation of the desired product as shown in reaction 1. The byproduct $HN(SiMe_3)_2$ is volatile and easily removed. The preparation has been carried out for Ln = La, Y, and Yb, and the product may be crystallized from THF/petroleum ether at −20 °C.[6] Single crystals of the La complex broke down by loss of solvent, but crystals of $Li_3[Y(R\text{-}binol)_3]\cdot 6THF$ were more robust and have been characterized by single-crystal X-ray diffraction.[7] An ORTEP plot of this complex is shown in Figure 1.

Shibasaki has reported a related complex tentatively characterized as $Li_3[Sm(R\text{-}binol)_3]\cdot 3THF$.[8] However the *R* factor for the X-ray structure determination of this complex was rather high (approximately 13%), and no

---

[1] Imamoto, T.; Kusomoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904−3912.

[2] Denmark, S. E.; Edwards, J. P.; Nicaise, O. *J. Org. Chem.* **1993**, *58*, 569−578.

[3] (a) Greeves, N.; Pease, J. E.; Bowden, M. C.; Brown, S. M. *Tetrahedron Lett.* **1996**, *37*, 2675−2678. (b) Chibale, K.; Greeves, N.; Lyford, L.; Pease, J. E. *Tetrahedron: Asymmetry* **1993**, *4*, 2407−2410. (c) Greeves, N.; Pease, J. E. *Tetrahedron Lett.* **1996**, *37*, 5821−5824. (d) Organocerium tris(binaphtholates) have been investigated. Greeves, N.; Mishir, Q. Unpublished work.

[4] Sasai, H.; Arai, T.; Satow, Y.; Houk, K. N.; Shibasaki, M. *J. Am. Chem. Soc.* **1995**, *117*, 6194−6198.

[5] Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1236−1256.

[6] Li[*R*-Hbinol] was prepared by addition of $Bu^nLi$ in hexane (1 equiv) to a solution of *R*-$H_2$binol (0.794 g, 2.77 mmol) in THF (10 $cm^3$) at 0 °C. To this solution was added a solution of $[Y\{N(SiMe_3)_2\}_3]$ (0.526 g, 0.923 mmol) in $Et_2O$ (15 $cm^3$). The reaction mixture was stirred at 0 °C until a clear solution had formed (ca. 10 min). Solvent was then removed in vacuo, and the resulting white solid was recrystallized from THF/petroleum ether at −20 °C to give product as colorless prisms. Yield = 0.741 g (57.5%). $^{13}C$ NMR (THF-$d_8$): 119.08, 120.95, 125.05, 126.71, 127.06, 128.58, 128.93, 136.42, 162.83 (aromatics). $Li_3[Ln(binol)_3]\cdot 6THF$ (Ln = La, Yb) were prepared in a similar manner. La complex: Anal. C, 69.24; H, 5.86; Li, 1.42. $C_{84}H_{84}Li_3O_{12}La$ requires: C, 69.81; H, 5.86; Li, 1.44. $^{13}C$ NMR (THF-$d_8$): 119.04, 120.39, 124.80, 126.84, 128.05, 128.37, 136.69, 163.41 (aromatics).

10.1021/om981011s CCC: $18.00

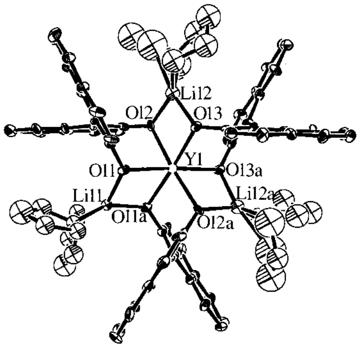


**Figure 1.** ORTEP plot (40% probability) of $Li_3[Y(R\text{-binol})_3]\cdot 6THF$. Selected bond lengths (Å) and angles (deg) are Y1−O11, 2.237(11); Y1−O12, 2.244(10); Y1−O13, 2.238(10); O11−Y1−O12, 80.7(3); O13−Y1−O13a, 81.5(5); O12−Li12−O13, 75.1(4); O11−Y1−O11a, 73.7(5). O11 and O11a, etc., are related by a $C_2$ rotation.

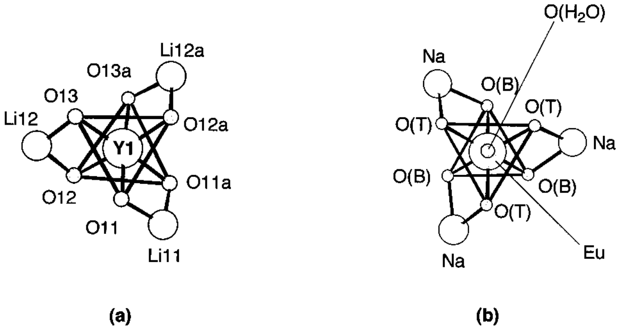
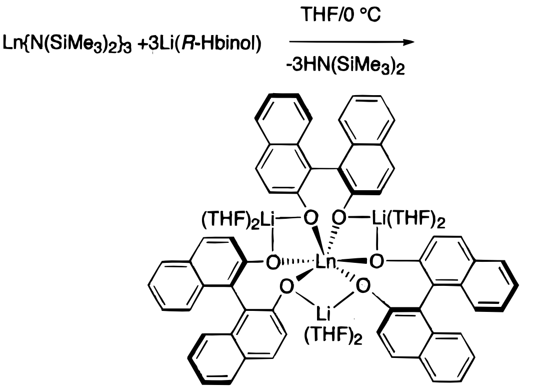


**Figure 2.** (a) $Li_3YO_6$ core of $Li_3[Y(R\text{-binol})_3]\cdot 6THF$. (b) $Na_3EuO_7$ core of $Na_3[Eu(S\text{-binol})_3(H_2O)]\cdot 6THF$.

crystal data were reported. The addition of 1 equiv of $H_2O$ during the preparation of "$Li_3[Sm(R\text{-binol})_3]\cdot 3THF$" suggests that it is unlikely to be an anhydrous complex.



(1)

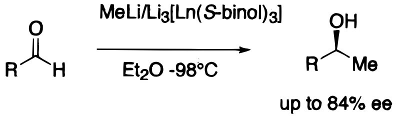
The $Li_3YO_6$ core of $Li_3[Y(R\text{-binol})_3]\cdot 6THF$ is shown in Figure 2a. The coordination geometry can be considered as an approximate trigonal antiprism derived by trigonal compression of an octahedron. The three Li atoms and the Y atom are coplanar, and the top triangular face of the antiprism, described by O11, O12a, and O13, is related to the bottom triangular face by a $C_2$ rotation about Li11−Y1. The top and bottom faces of the antiprism are not quite equilateral triangles: the O13−O12a, O12a−O11, and O11−O13 distances are 3.467, 3.526, and 3.487 Å, respectively. The closest analogue of $Li_3[Y(R\text{-binol})_3]\cdot 6THF$ for which crystallographic data are available is $Na_3[Eu(S\text{-binol})_3(H_2O)]\cdot 6THF$; the $Na_3YO_7$ core of this complex is shown in Figure 2b. $Na_3[Eu(S\text{-binol})_3(H_2O)]\cdot 6THF$ has $C_3$ symmetry, and the $EuO_7$ unit can be considered as a trigonally compressed capped (by $H_2O$) octahedron. The capped (or "top") face, described by the O(T) atoms, has edges of 3.804 Å, and the opposite ("bottom") face, described by the O(B) atoms, has edges of 3.274 Å. The Eu atom is 0.387 Å above the $Na_3$ plane. The coordination of $H_2O$ has thus led to a smaller binding site at the "bottom" face of the Eu complex than the binding sites in the Y complex. This effect could have implications for fine-tuning of enantioselectivity in reactions mediated by these complexes.

**Table 1. Effect of Ln on Enantioselective Addition of Me to Benzaldehyde**[a]

| Ln | ee/% | isolated yield/% |
|---|---|---|
| La | 69 | 72[b] |
| Y | 11 | not determined |
| Yb | 3 | 50 |

[a] 2 equiv of MeLi. [b] Basic workup.

Most organocerium reagents (and all previous enantioselective variants) have been generated from heterogeneous reaction media, by addition of RLi to a slurry of $CeX_3$ (X = Cl, Br) in $Et_2O$ or THF.[3] We generated chiral organo Ln reagents from a homogeneous reaction medium: $Li_3[Ln(binol)_3]$ was dissolved in $Et_2O$ and cooled to −78 °C, 1 equiv of MeLi in $Et_2O$ was added, and the resulting solution was aged at −78 °C for 1 h. In our initial alkylation experiments, an $Et_2O$ solution of 1 equiv of benzaldehyde was added to the organolanthanide solution at −98 °C over a period of 2 h.



(2)

In any metal-mediated enantioselective reaction the precise geometry of the chiral binding site at the metal is likely to have a significant effect on the enantioselectivity of the process. The steady decrease in ionic radius on traversing the lanthanide series is therefore expected to lead to variation in enantioselectivity on changing Ln. The effect of Ln on enantioselectivity of our alkylation reactions is summarized in Table 1, where it can be seen that enantioselectivity decreases with decreasing ionic radius from La through Y to Yb. In every case the organolanthanide reagent derived from *S*-binol resulted in alcohol product of *S*-stereochemistry, as shown in reaction 2.

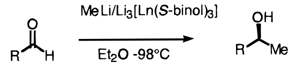
Following the success of the $Li_3[La(binol)_3]$-derived reagent in the addition of Me to benzaldehyde, we investigated the scope of this reaction in additions to other aldehydes, and our results are summarized in

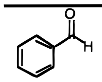
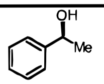
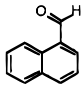
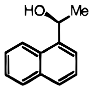
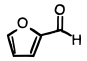
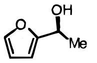
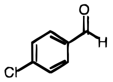
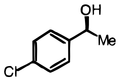
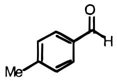
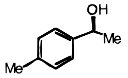
---

(7) Colorless prisms of $Li_3[Y(R\text{-binol})_3]\cdot 6THF$ suitable for X-ray diffraction were grown from THF/$Et_2O$. Crystal data: $C_{84}H_{84}Li_3O_{12}Y$; colorless prism (0.30 × 0.25 × 0.25 mm) monoclinic, C2; $a = 25.737(5)$ Å, $b = 14.854(3)$ Å, $c = 22.562(5)$ Å, $\beta = 120.61(3)°$, $V = 7423(3)$ Å$^3$, $Z = 4$, $D_{calc} = 1.248$ g cm$^{-3}$, $F(000) = 2928$, $\mu$(Mo Kα) = 0.847 mm$^{-1}$, $T = -120$ °C. A total of 10 141 reflections were measured (8301 unique) ($2.54° < \theta < 22.52°$). The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares on $F^2$ (SHELXL-97) to a final R1 = 0.0892 (5146 reflections with $I > 2\sigma(I)$), wR2 = 0.2321; goodness-of-fit on $F^2 = 1.065$. Residual density in a final Fourier map was 0.758 and −0.543 e A$^{-3}$.

(8) Takaoka, E.; Yoshikawa, N.; Yamada, Y. M. A.; Sasai, H.; Shibasaki, M. *Heterocycles* **1997**, *46*, 157−163.

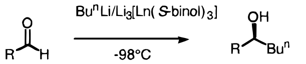
**Table 2. Enantioselective Addition of Me to Aldehydes Mediated by Li$_3$[La(binol)$_3$]**



| Substrate | Product | equiv of MeLi | ee/%$^a$ | isolated yield/% |
|---|---|---|---|---|
|  |  | 1 equiv | 84 | 46$^b$ |
| | | 2 equiv | 69 | 72$^b$ |
|  |  | 1 equiv | 67 | 60 |
| | | 2 equiv | 74 | 93 |
|  |  | 1 equiv | 68 | 31 |
| | | 2 equiv | 70 | 40 |
|  |  | 1 equiv | 28 | 71 |
| | | 2 equiv | 33 | 78 |
|  |  | 2 equiv | 62 | 56 |

$^a$ Determined by GC analysis of Mosher's ester. $^b$ Basic workup. See ref 8.

**Table 3. Enantioselective Addition of Bu$^n$ to Aldehydes Mediated by Li$_3$[La(binol)$_3$]**



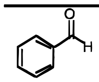
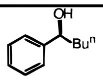
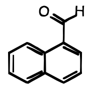
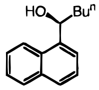
| Substrate | Product | equiv of Bu$^n$Li | Solvent for Bu$^n$Li | ee/% | Isolated yield/% |
|---|---|---|---|---|---|
|  |  | 1 equiv | hexanes | | 0 |
| | | 2 equiv | hexanes | 63 | 74 |
| | | 1 equiv | Et$_2$O | 39 | 40 |
| | | 2 equiv | Et$_2$O | 67 | 58 |
|  |  | 2 equiv | hexanes | 67 | 33 |
| | | 2 equiv | Et$_2$O | 56 | 52 |

Table 2.[9] The use of 1 or 2 equiv of MeLi was also investigated; there was generally a slight increase in both yield and % ee on using 2 equiv of MeLi, demonstrating that 2 equiv of MeLi is bound by the chiral Ln complex.

We have also made a preliminary investigation of the enantioselective addition of Bu$^n$Li to aldehydes. The results summarized in Table 3 show an important solvent effect: if only 1 equiv of Bu$^n$Li is used, it must be dissolved in Et$_2$O, not hexanes, to form an active alkylating reagent with Li$_3$[La(binol)$_3$]. As with Me addition, the best enantioselectivities were achieved using 2 equiv of RLi.

In summary, we have prepared and characterized a series of *anhydrous* lithium lanthanide binaphtholates. These complexes react with MeLi to give effective reagents for the enantioselective alkylation of a range of aldehydes. The ionic radius of the lanthanide is crucial in determining both the reactivity and the enantioselectivity of the reagents, with La giving the best results and Yb giving the worst. We are currently investigating the extension of this reaction to addition of other nucleophiles, as well as the preparation and use of other M$_3$[Ln(binol)$_3$] complexes.

**Acknowledgment.** We are grateful to EPSRC for financial support (studentship to J.L.M.D.), to Rhône-Poulenc for a gift of rare earth oxides, and to Mr. S. Apter for elemental analyses.

**Supporting Information Available:** Experimental details of X-ray data collection, tables of crystal data, positional and thermal parameters, and bond distances and angles for Li$_3$[Y($R$-binol)$_3$]·6THF. This material is available free of charge via the Internet at http://pubs.acs.org.

OM981011S

---

(9) Experimental details for a typical reaction are described. Li$_3$[La($S$-binol)$_3$]·6THF (0.312 g, 0.216 mmol) was dissolved in Et$_2$O (20 cm$^3$), and the solution was cooled to −78 °C (acetone/CO$_2$ slush bath). MeLi in Et$_2$O (0.26 cm$^3$, 0.432 mmol) was added, and the solution was stirred for 1 h. The solution was then cooled to −98 °C (Et$_2$O/CO$_2$ slush bath), and a solution of naphthaldehyde (29 mL, 0.216 mmol) in Et$_2$O was added by syringe pump over a period of 2 h. Stirring at −98 °C was continued for a further 2 h. The reaction was quenched by addition of saturated aqueous NaF (15 cm$^3$), and the reaction mixture was allowed to warm to room temperature. The precipitated LaF$_3$ was removed by filtration. The alcohol product was extracted into Et$_2$O ($4 \times 20$ cm$^3$), dried over MgSO$_4$, and concentrated in vacuo to give an off-white solid, which consisted of a mixture of product and H$_2$binol. Product was isolated by distillation at 150 °C/1 mmHg (Kugelrohr). Yield = 35 mg (93%); ee = 74% ($S$-enantiomer). A modification of the workup procedure was subsequently found to improve isolated yields. The Et$_2$O extract was washed with 1 M aqueous NaOH (25 cm$^3$) to remove H$_2$binol before drying. Concentration of the resulting Et$_2$O extract gave crude product, which was further purified by vacuum distillation. Enantiomeric excess for alcohol products was determined by GC and NMR analysis of Mosher's esters. The Mosher's esters were prepared by reaction of a CH$_2$Cl$_2$ solution of the alcohol with a slight excess of ($R$)-(−)-Mosher's acid chloride (($R$)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride) in the presence of 4-(dimethylamino)pyridine and triethylamine.