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Chiral monometallic lanthanide(III) salt complexes are arrayed acid–base networks for enantioselective catalysis: a direct, nitroaldol (Henry) reaction

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Abstract—Shelf stable, but kinetically labile, highly symmetric, 3:1 complexes of 3,3′-bis-diethylaminomethyl-2,2′-dihydroxy-1,1′-dinaphthalene **1** ('binolam') with lanthanide(III) triflates are easily available compounds possessing an extended array of acid and base sites. The enantiopure lanthanum derivative is especially suited to catalyze the direct nitroaldol (Henry) reaction enantioselectively. Added non-aqueous base accelerates the reaction.

1. Introduction

Danishefsky was the first to assess the potential of chiral lanthanide(III) salts of type **A** [Ln(L-L)$_3$] to act as chiral Lewis acids (LA) (Fig. 1) in asymmetric catalysis.[1] More recently, Shibasaki et al. demonstrated the usefulness of bimetallic lanthanoate complexes of type **B** [Ln-(L-L)$_3$M$_3$] to work as Lewis acid–Lewis base (LALB) bifunctional catalysts.[2] Ionic complexes of type **C** [Ln(LH-LH)$_3$X$_3$] have not been discovered yet for enantioselective catalysis, although Kobayashi,[3] Markó,[4] Aspinall,[5] Jacobsen,[6] and Evans[7] pioneered the exploration of 1:1 or 2:1[5] chiral complexes of lanthanide(III) salts as Lewis acid (LA) catalysts. Type **C** complexes (LH-LH = binol derivative; binol = bis-2,2′-dihydroxy-1,1′-dinaphthalene) are the triple conjugate acids of the hitherto missing monometallic complexes of type **B** (i.e., Ln = lanthanide, M = H), of which the heterobimetallic congeners are the well-known Shibasaki's catalysts (Ln = lanthanide, M = alkali metal).[2] Provided we could remove XH from type **C** complexes with non-aqueous base, we expected the resulting **B** system (M = H) to be worth the analysis for enantioselective catalysis.

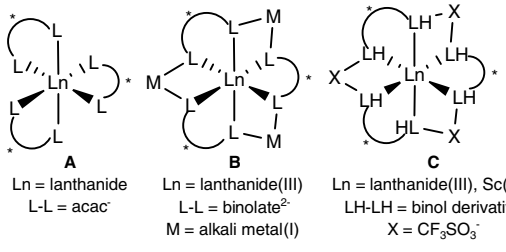

Figure 1. General structures for lanthanide 3:1 complexes.

2. Results and discussion

We set out to study a project aimed at finding chiral, thermodynamically stable, as well as highly symmetric and well-defined (for eventual easy fine tuning), complexes of lanthanide(III) salts (LnX$_3$) capable of operating in conventional as well as, if appropriately designed, non-conventional solvents.

We herein report on the straightforward formation of thermodynamically, shelf stable, though nevertheless kinetically labile, highly symmetric, type **C** complexes of 3,3′-bis-diethylaminomethyl-2,2′-dihydroxy-1,1′-dinaphthalene **1** ('binolam') with lanthanide(III) triflates,[8] which are armed with an array of acid and base sites (Lewis acid–Brönsted acid–Lewis base: LABALB) ideally suited to catalyze the direct nitroaldol (Henry) reaction[9] between nitromethane and aldehydes in an

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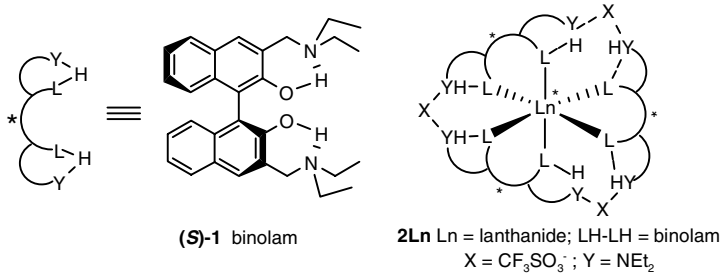


Figure 2. Type **C** lanthanide complexes of bifunctional 'binolam' (*S*)-**1**.

enantioselective manner,[10] either in the absence or presence of externally added amines, which accelerate the reaction.[11,12]

Type **C** complexes **2Ln** (Fig. 2) were obtained in quantitative yield by simply mixing the enantiomerically pure, bifunctional ligand (*S*)-**1** ('binolam', 3 equiv) with 1 equiv of the dried lanthanide(III) triflate (Ln = La, Pr, Nd, Sm, Eu, Gd, Yb, as well as Sc), in dry acetonitrile at room temperature, followed by evaporation to dryness. Titration experiments revealed a strong tendency of 'binolam' **1** to form stable 3:1 complexes.[13,14] Moreover, complexation of racemic (*RS*)-**1** with the triflates above, gave rise to the formation of a pair of enantiomers only, eventually recognized to be the Δ,*R*,*R*,*R* and Δ,*S*,*S*,*S* pair. No other diastereomeric species were noticed in the NMR spectra of the complexes resulting from racemic (*RS*)-**1**. All these compounds are shelf stable solids that can be conveniently stored for months without any special precaution.

In solution these compounds are kinetically labile as demonstrated by both the exchange (slow on the NMR time scale) observed by ^{1}H NMR of a solution of **2La**, to which labeled ligand **1**-d_4 (deuterium instead of hydrogen at the benzylic carbons of **1**) was added, also by means of an EXSY NMR experiment.[15] Unfortunately, in solution, the addition of water caused hydrolysis (easier for those lanthanides having large, expansible coordination numbers). All compounds appear to be isostructural, D_3-symmetric, 6-coordinate 3:1 complexes according to their spectroscopic properties (^{1}H, ^{13}C, ^{45}Sc NMR, FAB-MS, ESI-MS). Moreover, variable temperature (−40 to +60 °C) NMR studies in CD_3CN showed them to be unique species in this temperature range (no change was observed, besides some freezing of the *N*-CH_2–CH_3 moiety at low temperature, and minute hydrolysis occurring at high temperature).

The DFT-optimized geometry for **m2La** (a somewhat simplified model of **2La** in which 'binolam' **1** was substituted by 'biphelam'[16]) obtained by computation using B3LYP/6-31G* for non-metal atoms, and the Stuttgart group pseudopotential (MWB) for the lanthanide atom,[17] attest to the chiral-at-metal[18] nature of these species, thus supporting the fact that complexation of racemic 'binolam' **1** leads to the formation of the Δ,*R*,*R*,*R* and Δ,*S*,*S*,*S* pair of enantiomers, only (Fig. 3). In addition, it shows its symmetric structure

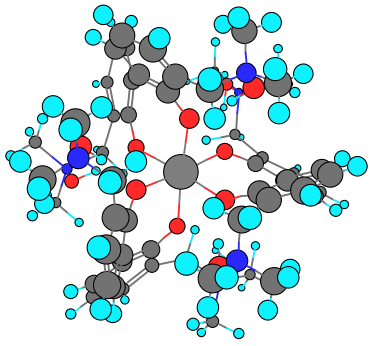
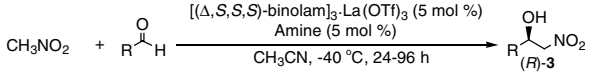


Figure 3. DFT-optimized structure for **m2La**.

characterized by an arrayed La–O–H–N acid–base network having average distances La–O = 2.548, O–H = 1.817, H–N = 1.049 Å, angles La–O–H = 127.8° and dihedrals La–O–N–H = −125.3°.

Initial exploration of complexes **2Ln** as catalysts for the direct, enantioselective nitroaldol condensation between nitromethane and hydrocinnamaldehyde, led us to select binolam-derived lanthanum complex **2La** as the most interesting candidate for development. Working with a polar solvent (CaH_2-dried acetonitrile was the best choice) and lowering the temperature down to −40 °C, led to a sound increase in enantioselectivity. At −40 °C, the lower limit for the catalyst load was fixed at 5 mol %. During isolation of the nitroaldol products **3a**–**i**, the valuable enantiomerically pure 'binolam' **1** could be recovered unaltered by acid–base extraction, as previously reported.[16] In striking contrast with expectations for a dissociative process, we found that the presence of excess 'binolam' **1** (up to 3 equiv) actually accelerated the direct nitroaldol condensation.[19] Indeed, our best results were found when carrying out the reaction in the presence of external strong bases (1 equiv with respect to catalyst) such as 1,1,3,3-tetramethylguanidine (TMG), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 2,8,9-trimethyl-2,5,8,9-tetraaza-1-phosphabicyclo[3,3,3]undecane (Verkade's base), or 1,8-bis(dimethylamino)naphthalene (proton sponge®), the last being the best choice. This surprising behavior is, however, not without precedent.[10a,10d] The payoff for working under these conditions is that care has to be taken to avoid water entering the reaction mixture as it immediately hydrolyzes the catalyst, thus stopping the reaction early.

Table 1. Enantioselective nitroaldol condensations[a]



Entry	R	Product	Yield (%)[b] DBU/ proton sponge®	ee (%)[c] DBU/ proton sponge®
1	$Ph(CH_2)_2$	**3a**	91/90	87/91
2	*c*-C_6H_{11}	**3b**	63/71	80/99
3	*t*-Bu	**3c**	91/91	92/83
4	*i*-Pr	**3d**	95/95	90/90
5	Ph	**3e**	88/96	65/80
6	*p*-$NO_2C_6H_4$	**3f**	98/73	31/28
7	*p*-CNC_6H_4	**3g**	79/75	64/76
8	*p*-FC_6H_4	**3h**	62/65	75/58
9	(*E*)-PhCH=CH	**3i**	56/98	72/72[d]

[a] 1 equiv of aldehyde (0.53 mmol) and 10 equiv of nitromethane were used.
[b] Isolated yields.
[c] Determined by HPLC (Daicel Chiralpak AD or Chiralcel OD columns); absolute configuration assigned on the basis of literature data.
[d] Absolute configuration not determined.

In exploring the scope of the reaction of nitromethane with aldehydes, we found that the reaction works well for aliphatic, aromatic, and α,β-unsaturated aldehydes, as illustrated in Table 1. We attributed the poor results obtained for *p*-nitro-benzaldehyde due to its ability to coordinate to the lanthanum core, thereby blocking further action at the core nucleus, thus facilitating external racemic condensation. This result also suggests that nitromethane likely coordinates to lanthanum prior to deprotonation (actually, no deprotonation was observed on mixing nitromethane and proton sponge® in CD_3CN).

Even though we have not yet carried out a detailed kinetic analysis of the reaction, some mechanistic clues are worth noting: (i) we have found no significant NLE, thus suggesting the involvement of monomeric complexes, only;[20] (ii) working in the presence of excess 'binolam' **1** (up to 3 equiv), under the otherwise standard reaction conditions (i.e., no other external base added), we found an increase in rate, as expected for an associative process, likely an acid–base reaction (see part v below); (iii) working in the presence of external strong bases led to a significant increase in rate and enantioselectivity; (iv) reaction of the species resulting from mixing $La(OTf)_3$, enantiomerically pure, commercial (*S*)-binol [instead of 'binolam' (*S*)-**1**] and TMG in either 1:1:2 or 1:3:6 ratios led to the nitroaldol product **3a** in 0%, and 7% ee, thus suggesting that our lanthanum catalyst is likely providing its arrayed acid–base network for binding, activation of the reagents, and eventually catalyzing the direct nitroaldol condensation; (v) ESI-MS analysis of some **2Ln** complexes, including that of Sc, in the presence of either proton sponge®, or 'binolam' **1**, show that precatalysts **2Ln** actually lose three TfOH units (the parent ion shows-up at $m/z = [M-3TfOH+H^+]$), thereby giving rise to **4Ln** (Ln = La, Sm, Sc), that is, the Shibasaki's type **B** species having M = H (Fig. 1); the DFT-optimized (B3LYP/6-31G* and MWB) structure of model **m4La** (Fig. 4) shows that this species is in fact a 6-coordinate lanthanum triaryloxide derivative (La–O_{1-3} = 2.300, 2.305, 2.320 Å) having three extra HO_{4-6}–La bonding contacts

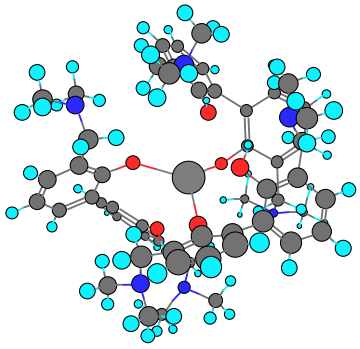


Figure 4. DFT-optimized structure for **m4La**.

(2.592, 2.688, 2.780 Å), the hydroxyl oxygen atoms being hydrogen-bonded to the nearby nitrogen atoms (O_4–HN = 1.029, O_4H–N = 1.647 Å, with angle O_4–H–N = 150°; O_5–HN = 1.025, O_5H–N = 1.485 Å, with angle O_5–H–N = 153°; O_6–HN = 1.008, O_6H–N = 1.788 Å, with angle O_6–H–N = 149.6°);[21] these data compared to that of the precursor **m2La** illustrate the existence of an active acid–base network system, which presumably facilitates the catalytic action; (vi) moreover, careful solution NMR studies upon **2Sc** and **2La** showed that titration with 1 equiv of proton sponge® leads to the full **2Sc** or partial **2La** removal of one hydrogen atom. Further addition of base does not change this situation (excess base is in slow equilibrium). As expected, this mixture has been proved to catalyze the condensation of added nitromethane and aldehyde.

On the basis of these grounds, we propose the following rationale for the mechanistic cycle of the direct nitroaldol coupling: monodeprotonation of precatalyst **2La** so as to produce locally, that is, at least at one single point, the corresponding monometallic type **B** complex (M = H) having an array of acid and base sites (La–O–H–N) for binding of both nitromethane and aldehyde, followed by deprotonation, coupling, and eventual recycling of the catalyst.[22]

3. Conclusions

In conclusion, the straightforward access to shelf stable, chiral-at-metal, ionic complexes of lanthanide(III) triflates (scandium included) of type **C**, is secured by using binaphthol derivatives having dialkylaminomethyl arms at C-3 and C-3′ as ligands. The lanthanum triflate complex **2La** is, at the moment, our best catalyst for the nitroaldol reaction between nitromethane and aldehydes of all kinds, in an enantioselective manner, either in the absence (slow reaction) or presence of externally added bases (fast reaction), proton sponge®, or DBU, being our best choices. The evidence provided (ESI-MS, NMR and DFT calculations) suggests the intermediacy of a monometallic type **B** complex (i.e., Ln = lanthanide, M = H). We expect that these complexes might be of further use for enantioselective catalysis.

4. Experimental

4.1. General

Commercial (Sigma–Aldrich Co.) scandium(III) and lanthanide(III) triflates of the highest quality available were dried under vacuum for 96 h at 220 °C in a Büchi Glass Oven B-580 and stored in a desiccator. Prior to use in the nitroaldol reaction, they were dried under vacuum for an extra 2 h at 220 °C. Aldehydes, obtained from commercial sources, were distilled prior to use, except for 4-nitrobenzaldehyde and 4-cyanobenzaldehyde, which were used as received. Nitromethane was used as received. Commercial grade solvents were boiled with the appropriate drying agent[23] and eventually distilled prior to use. Analytical thin layer chromatography was performed on Macherey-Nagel Polygram Sil G/UV_{254} plates, whose visualization was accomplished under UV light or under iodine vapors. Purification of reaction products was carried out by flash chromatography using Merck silica gel 60 (70–230 mesh). Melting points were measured on a Büchi Dr. Tottoli apparatus and are uncorrected. Optical rotations were measured on a Perkin Elmer 341 LC polarimeter provided with a sodium lamp and are reported as follows: $[\alpha]_{\lambda}^{T\,(^{\circ}C)}$ (c = g/100 mL, solvent). Infrared spectra were recorded on a FT-IR Bruker IFS 66 spectrometer and are reported in wavenumbers (cm^{-1}). Enantiomeric excesses were determined by HPLC analysis using a Waters 600E chromatograph provided with Daicel Chiralpak AD or Chiralcel OD columns (see products for further details). ^1H NMR spectra were recorded on a Bruker AMX-300 (300 MHz) spectrometer and are reported in parts per million using solvent as internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hertz, integration. Proton-decoupled ^{13}C NMR spectra were recorded on a Bruker AMX-300 (75.5 MHz) spectrometer and are reported in parts per million using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). Proton-decoupled ^{45}Sc NMR were recorded on a Bruker AMX-300 (73 MHz) spectrometer and are reported in parts per million using a solution of $ScCl_3$ 1 M in D_2O as external reference calibrated at 0 ppm. Low-resolution mass spectra by use of electronic impact ionization (EI^+) were obtained on a (GC–MS) Shimadzu QP-5000. Low- and high-resolution mass spectra by use of electrospray ionization (ESI^+) were obtained on a Micromass Autospect 3000 spectrometer. Low- and high-resolution mass spectra by use of fast atom bombardment ionization (FAB^+) were obtained on a Kratos MS80-RFA spectrometer using *p*-nitrobenzyl alcohol (NBA) as matrix, unless otherwise indicated.

4.1.1. (*S*)-3,3′-Bis(diethylaminomethyl)-2,2′-dihydroxy-1,1′-dinaphthalene [(*S*)-binolam] ((*S*)-1. Obtained, as reported by Katsuki,[24] by reduction of the precursory amide with $LiAlH_4$. A pale yellow solid. (53.6% yield). Mp: 139–140 °C. $[\alpha]_{589}^{25} = -140.8$ (c 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 11.9 (br s, 2H), 7.77 (d, $J = 7.9$ Hz, 2H), 7.63 (s, 2H), 7.28–7.18 (m, 6H), 4.19 (d, $J = 13.7$ Hz, 2H), 3.93 (d, $J = 13.7$ Hz, 2H), 2.80–2.60 (m, 8H), 1.10 (t, $J = 7.2$ Hz, 12H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 154.7, 134.3, 128.8, 128.2, 128.1, 126.3, 125.6, 125.4, 123.3, 117.1, 58.2, 46.9, 11.7 ppm. IR (KBr) ν: 2973, 2825, 2680, 1625, 1430, 1250, 880, 750 cm^{-1}. MS (EI^+) m/z (%): 456 $[M]^+$ (79), 427 (66), 385 (86), 354 (100), 312 (84). HRMS (EI^+): Exact mass calcd for $C_{30}H_{36}O_2N_2$ $[M]^+$: 456.277679, found: 456.277010. Elemental analysis calcd for $C_{30}H_{36}O_2N_2$: C, 78.91; H, 7.95; N, 6.13. Found: C, 79.09; H, 7.92; N, 5.81. The enantiomeric purity of **1** (>96% ee) was determined by HPLC with a Daicel Chiralpak AD column (using a 90:10 hexane/isopropanol solvent mixture, at a flow rate of 1 mL/min, and UV detection at $\lambda = 254$ nm), the major enantiomer having $t_r = 5.7$ min, whereas the minor one showed $t_r = 6.6$ min. The absolute configuration of the major enantiomer was assigned on the basis of literature data.[24]

4.1.2. (*RS*)-3,3′-Bis(diethylaminodideuteromethyl)-2,2′-dihydroxy-1,1′-dinaphthalene [(*RS*)-binolam-d_4] 1-d_4. Obtained, as above, by reduction of the precursor amide with $LiAlD_4$. A pale yellow solid. (60% yield). Mp: 139–140 °C. ^1H NMR (300 MHz, $CDCl_3$) δ: 11.9 (br s, 2H), 7.77 (d, $J = 6.9$ Hz, 2H), 7.62 (s, 2H), 7.27–7.18 (m, 6H), 2.77–2.61 (m, 8H), 1.09 (t, $J = 7.2$ Hz, 12H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 154.7, 134.3, 128.8, 128.2, 128.1, 126.3, 125.6, 125.4, 123.3, 117.1, 46.9, 11.7 ppm. MS (EI^+) m/z (%): 460 $[M]^+$ (74), 431 (50), 389 (100), 358 (70), 316 (83). HRMS (EI^+) Exact mass calcd for $C_{30}H_{32}D_4N_2O_2$ $[M]^+$: 460.302786, found: 460.302841.

4.2. P1. General procedure for the preparation of scandium(III) and lanthanide(III) salt complexes 2Ln

Dried scandium(III) or lanthanide(III) triflates (0.085 mmol, 1 equiv) and (*S*)-binolam ((*S*)-**1** (0.255 mmol, 3 equiv) were put in a flame-dried 5 mL round-bottomed flask containing a stirring bar. Freshly distilled (CaH_2) acetonitrile (1.5 mL) was added and the mixture stirred under an argon atmosphere for 1 h. Then, the solvent was removed under reduced pressure, thereby affording complexes **2Ln** in quantitative yield.

4.2.1. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Sc(OTf)$_3$ 2Sc. Complex **2Sc** was prepared according to the general procedure P1. An orange solid. Mp: >300 °C. $[\alpha]_{589}^{25} = +139.2$ (*c* 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 9.00 (br s, 6H), 7.91 (d, $J = 8.1$ Hz, 6H), 7.51 (s, 6H), 7.28–7.23 (m, 6H), 7.09–7.04 (m, 6H), 6.81 (d, $J = 8.4$ Hz, 6H), 2.81 (d, $J = 13.2$ Hz, 6H), 2.81–2.38 (m, 24H), 2.48 (d, $J = 14.1$ Hz, 6H), 1.03 (t, $J = 7.1$ Hz, 18H), 0.61 (t, $J = 7.2$ Hz, 18H) ppm. ^{13}C NMR (75.5 MHz, CD_3CN) δ: 161.8, 136.6, 130.2, 129.1, 128.2, 126.9, 125.4, 122.9, 120.0, 55.4, 47.4, 46.0, 9.6, 8.0. ^{45}Sc NMR (73 MHz, CD_3CN) δ: 103 ppm. MS (FAB$^+$) *m*/*z* (%): 1861 $[M+H]^+$ (2.3×10^{-3}), 1712 $[M-TfOH+H]^+$ (13.1), 1256 (33.2), 799 (58), 457 (80.1), 384 (88.2), 311 (100). HRMS (FAB$^+$) Exact mass calcd for $C_{92}H_{108}F_6N_6O_{12}S_2Sc$ $[M-TfOH+H]^+$: 1711.693001, found: 1711.691898.

4.2.2. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·La(OTf)$_3$ 2La. Complex **2La** was prepared according to the general procedure P1. An orange solid. Mp: 258–259 °C. $[\alpha]_{589}^{25} = +25$ (*c* 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 9.1 (br s, 6H), 8.04 (d, $J = 8.1$ Hz, 6H), 7.80 (s, 6H), 7.29–7.24 (m, 6H), 7.10–7.04 (m, 6H), 6.65 (d, $J = 8.4$ Hz, 6H), 2.95 (d, $J = 13.5$ Hz, 6H), 2.90–2.67 (m, 24H), 2.42 (d, $J = 13.2$ Hz, 6H), 0.84 (t, $J = 7.2$ Hz, 18H), 0.24 (t, $J = 7.2$ Hz, 18H) ppm. ^{13}C NMR (75.5 MHz, CD_3CN) δ: 158.3, 135.8, 130.3, 128.0, 127.0, 126.3, 124.8, 123.7, 122.0, 118.6, 55.9, 47.6, 45.7, 9.5, 5.4. MS (FAB$^+$) *m*/*z* (%): 1806 $[M-TfOH+H]^+$, 1350 (32.8), 457 (100), 384 (68.9), 311 (61.1). HRMS (FAB$^+$) Exact mass calcd for $C_{92}H_{108}F_6N_6O_{12}S_2La$ $[M-TfOH+H]^+$: 1805.643442, found: 1805.648186.

4.2.3. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Pr(OTf)$_3$ 2Pr. Complex **2Pr** was prepared according to the general procedure P1. An orange solid. Mp: 254–255 °C. $[\alpha]_{589}^{25} = +58.3$ (*c* 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 11.45 (br s, 6H), 7.47 (d, $J = 7.8$ Hz, 6H), 6.98–6.86 (m, 18H), 5.98 (d, $J = 8.4$ Hz, 6H), 4.80–4.76 (br m, 6H), 4.45–4.43 (br m, 6H), 3.34–3.14 (m, 12H), 1.84 (br d, $J = 12.6$ Hz, 6H), 1.39 (t, $J = 3.6$ Hz, 18H), 0.95 (t, $J = 3.6$ Hz, 18H), 0.5 (br d, $J = 12.6$ Hz, 6H). ^{13}C NMR (75.5 MHz, CD_3CN) δ: 139.7, 133.8, 129.4, 129.1, 128.4, 127.9, 126.6, 126.0, 123.5, 117.5, 55.4, 50.3, 47.4, 11.1, 7.6. MS (ESI$^+$) *m*/*z* (%): 1807.6498 $[M-TfOH+H]^+$. HRMS (FAB$^+$) Exact mass calcd for $C_{92}H_{108}F_6N_6O_{12}S_2Pr$ $[M-TfOH+H]^+$: 1807.644744, found: 1807.627701.

4.2.4. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Nd(OTf)$_3$ 2Nd. Complex **2Nd** was prepared according to the general procedure P1. An orange solid. Mp: 258–259 °C. $[\alpha]_{589}^{25} = +48.8$ (*c* 0.25, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 8.80 (s, 6H), 8.44 (d, $J = 7.8$ Hz, 6H), 7.71 (d, $J = 8.1$ Hz, 6H), 7.55–7.43 (m, 12H), 3.49 (br s, 6H), 3.17 (br s, 6H), 2.45 (br m, 6H), 2.22 (br m, 6H), 1.13 (br s, 6H), 0.59 (br s, 6H), 0.14 (br s, 18H), −0.26 (br s, 18H). ^{13}C NMR (75.5 MHz, CD_3CN) δ: 142.9, 136.2, 135.6, 131.9, 130.9, 129.1, 128.2, 127.8, 127.4, 124.5, 57.3, 47.5, 46.1, 9.8, 6.3. MS (ESI$^+$) *m*/*z* (%): 1808.6449 $[M-TfOH+H]^+$. HRMS (FAB$^+$) Exact mass calcd for $C_{92}H_{108}F_6N_6O_{12}S_2Nd$ $[M-TfOH+H]^+$: 1808.644818, found: 1808.632528.

4.2.5. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Sm(OTf)$_3$ 2Sm. Complex **2Sm** was prepared according to the general procedure P1. An orange solid. Mp: 254–255 °C. $[\alpha]_{589}^{25} = +70$ (*c* 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 8.24 (d, $J = 8.1$ Hz, 6H), 8.12 (s, 6H), 7.55–7.43 (m, 6H), 7.28–7.20 (m, 12H), 3.49 (br d, $J = 12.6$ Hz, 6H), 3.21 (br d, $J = 12.9$ Hz, 6H), 0.45 (t, $J = 7.4$ Hz, 18H), 0.015 (t, $J = 7.4$ Hz, 18H). ^{13}C NMR (75.5 MHz, CD_3CN) δ: 167.1, 138.3, 132.1, 129.6, 128.5, 127.8, 126.6, 125.2, 123.2, 122.0, 57.3, 47.9, 46.6, 10.1, 6.5. MS (ESI$^+$) *m*/*z* (%): 1818.6898 $[M-TfOH+H]^+$.

4.2.6. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Eu(OTf)$_3$ 2Eu. Complex **2Eu** was prepared according to the general procedure P1. An orange solid. Mp: 256–257 °C. $[\alpha]_{589}^{25} = +96.7$ (*c* 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 15.75 (br s, 6H), 7.24 (br d, $J = 7.5$ Hz, 6H), 7.07 (br s, 6H), 6.61 (br s, 6H), 5.77 (br s, 6H), 5.69 (br d, $J = 8.1$ Hz, 6H), 5.09 (br s, 6H), 4.82 (br s, 6H), 2.23 (br s, $J = 8.1$ Hz, 6H), 1.80 (br s, 18H), 1.38–1.27 (br m, 6H), 0.82 (br s, 18H), −0.12 (br s, 6H). ^{13}C NMR (75.5 MHz, CD_3CN) δ: 186.3, 139.6, 128.8, 127.8, 127.0, 125.5, 124.7, 122.4, 118.9, 107.3, 55.9, 49.7, 48.3, 11.5, 7.3. MS (ESI$^+$) *m*/*z* (%): 1819.6525 $[M-TfOH+H]^+$. HRMS (FAB$^+$) Exact mass calcd for $C_{92}H_{108}F_6N_6O_{12}S_2Eu$ $[M-OTf]^+$: 1819.658330, found: 1819.633972.

4.2.7. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Gd(OTf)$_3$ 2Gd. Complex **2Gd** was prepared according to the general procedure P1. An orange solid. Mp: 260–261 °C. $[\alpha]_{589}^{25} = +125$ (*c* 0.12, CH_2Cl_2). MS (FAB$^+$) *m*/*z* (%): 1825 $[M-TfOH+H]^+$ (14.43). HRMS (FAB$^+$) Exact mass calcd for $C_{92}H_{108}F_6N_6O_{12}S_2Gd$ $[M-TfOH+H]^+$: 1824.661198, found: 1824.643657.

4.2.8. [(Δ,*S*,*S*,*S*)-Binolam]$_3$·Yb(OTf)$_3$ 2Yb. Complex **2Yb** was prepared according to the general procedure P1. An orange solid. Mp: >300 °C. $[\alpha]_{589}^{25} = +175.8$ (*c* 0.12, CH_2Cl_2). ^{1}H NMR (300 MHz, CD_3CN) δ: 34.1 (br s), 12.55 (br s), 11.8 (br s), 7.38 (br s), 7.02 (br s), 5.82 (br s), 5.30 (br s), 3.36 (br s), 2.91 (br s), 1.36 (br s), −0.55 (br s), −6.30 (br s). ^{13}C NMR (75.5 MHz, CD_3CN) δ: 128.5, 124.4, 123.6, 123.3, 122.6, 122.0, 122.0, 121.7, 109.0, 56.1, 51.9, 51.1, 14.9, 10.8. MS (ESI$^+$) *m*/*z* (%): 1838.6671 $[M-TfOH+H]^+$.

4.3. P2. General procedure for the catalytic asymmetric nitroaldol reaction

Complex **2Ln** (0.0265 mmol, 5 mol %) was added to a flame-dried 10 mL Schlenk tube containing a stirring bar. Freshly distilled (CaH_2) acetonitrile (2 mL) was added. To the stirred mixture a solution of either proton sponge® (95 μL, 280 mM in dry acetonitrile, 0.0265 mmol, 5 mol %), or DBU (4 μL, 0.0265 mmol, 5 mol %) was added and cooled to −40 °C. Aldehyde (0.53 mmol, 1 equiv) and nitromethane (5.3 mmol, 10 equiv) were added and the resulting mixture stirred at −40 °C under an argon atmosphere for 24–96 h.

The reaction was quenched by adding aqueous 5% HCl solution (10 mL) and the resulting mixture partitioned with CH_2Cl_2 (10 mL). The organic phase was washed with aqueous 5% HCl solution (2 × 10 mL), then dried over Na_2SO_4, and filtered. After evaporation of the solvent, the residue was purified by column chromatography to afford the nitroaldol product **3a–3i**.

4.3.1. (*R*)-1-Nitro-4-phenylbutan-2-ol 3a. Compound **3a**[10e] was prepared according to the general procedure P2 and purified by column chromatography (20% EtOAc/hexanes) to give a white solid. (90% yield with Proton sponge® as additive, 91% yield with DBU as additive). Mp: 102–103 °C. ^{1}H NMR (300 MHz, CD_2Cl_2) δ: 7.33–7.20 (m, 5H), 4.41–3.38 (m, 2H), 4.34–4.28 (m, 1H), 2.89–2.65 (m, 3H), 1.80 (m, 2H) ppm. ^{13}C NMR (75.5 MHz, CD_2Cl_2) δ: 141.3, 128.8, 128.7, 126.5, 81.1, 68.3, 35.6, 31.6 ppm. MS (EI$^+$) *m*/*z* (%): 195, 177, 135, 105, 90, 60. The enantiomeric purity of **3a** (91% ee with Proton sponge® as additive, 87% ee with DBU as additive) was determined by HPLC with a Daicel Chiralpak AD column (using a 90:10 hexane/isopropanol solvent mixture, at flow rate of 1 mL/min and UV detection at $\lambda = 254$ nm); the major enantiomer having $t_r = 13.7$ min whereas the minor one showed $t_r = 16.6$ min. The absolute configuration of the major enantiomer was assigned on the basis of the literature data.[10e]

4.3.2. (*R*)-1-Cyclohexyl-2-nitroethanol 3b. Compound **3b**[10e] was prepared according to the general procedure P2 and purified by column chromatography (15% EtOAc/hexanes) to give a pale yellow oil. (80% yield with Proton sponge® as additive, 63% yield with DBU as additive). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.55–4.35 (m, 2H), 4.09–4.03 (m, 1H), 2.82 (br s, 1H), 1.82–1.62 (m, 5H), 1.50–1.39 (m, 1H), 1.28–1.01 (m, 5H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 79.5, 73.0, 41.6, 28.9, 28.0, 26.2, 26.0, 25.8 ppm. MS (EI$^+$) *m*/*z* (%): 127, 95, 75, 67, 45. The enantiomeric purity of **3b** (99% ee with Proton sponge® as additive, 80% ee with DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 97:3 hexane/isopropanol solvent mixture, at flow rate 1 mL/min and UV detection at $\lambda = 230$ nm); the major enantiomer having $t_r = 20.2$ min, whereas the minor one showed $t_r = 21.2$ min. The absolute configuration of the major enantiomer was assigned on the basis of literature data.[10e]

4.3.3. (*R*)-3,3′-Dimethyl-1-nitrobutan-2-ol 3c. Compound **3c**[10e] was prepared according to the general procedure P2 and purified by column chromatography (5% EtOAc/hexanes) to give a colorless oil. (91% yield with Proton sponge® or DBU as additive). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.48 (dd, $J = 12.6$, 2.2 Hz), 4.32 (dd, $J = 12.6$, 10.2 Hz, 1H), 3.97 (d, $J = 9.9$ Hz, 1H), 2.94 (br s, 1H), 0.91 (s, 9H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 78.4, 76.3, 34.3, 25.5 ppm. MS (EI$^+$) *m*/*z* (%): 87, 71, 57. The enantiomeric purity of **3c** (83% ee with Proton sponge® as additive, 92% ee with DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 95:5 hexane/isopropanol solvent mixture, at flow rate 1 mL/min and UV detection at $\lambda = 230$ nm); the major enantiomer $t_r = 10.9$ min, minor enantiomer $t_r = 12.2$ min. The absolute configuration of the major enantiomer was assigned on the basis of literature data.[10e]

4.3.4. (*R*)-3-Methyl-2-nitrobutan-2-ol 3d. Compound **3d**[10e] was prepared according to the general procedure P2 and purified by column chromatography (15% EtOAc/hexanes) to give a colorless oil. (95% yield with Proton sponge® or DBU as additive). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.44–4.29 (m, 2H), 4.03–3.99 (m, 1H), 3.22 (br s, 1H), 1.74–1.65 (m, 1H), 0.91 (d, $J = 4.5$ Hz, 3H), 0.88 (d, $J = 4.5$ Hz, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 79.4, 73.4, 31.7, 18.2, 17.3 ppm. MS (EI$^+$) *m*/*z* (%): 92, 86, 73, 55. The enantiomeric purity of **3d** (90% ee with either Proton sponge® or DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 95:5 hexane/isopropanol solvent mixture, at flow rate 1 mL/min, and UV detection at $\lambda = 230$ nm); the major enantiomer having $t_r = 12.5$ min, whereas the minor one showed $t_r = 13.5$ min. The absolute configuration of the major enantiomer was assigned on the basis of literature data.[10e]

4.3.5. (*R*)-2-Nitro-1-phenylethanol 3e. Compound **3e**[10e] was prepared according to the general procedure P2 and purified by column chromatography (15% EtOAc/hexanes) to give a pale yellow oil. (96% yield with Proton sponge® as additive, 88% yield with DBU as additive). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40–7.32 (m, 5H), 5.42 (dd, $J = 6$, 3.3 Hz, 1H), 4.62–4.45 (m, 2H), 3.37 (br s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 138.3, 129.0, 128.9, 126.0, 81.3, 71.0. MS (EI$^+$) *m*/*z* (%): 167, 149, 134, 120, 105, 77, 51. The enantiomeric purity of **3e** (80% ee with Proton sponge® as additive, 65% ee with DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 90:10 hexane/isopropanol solvent mixture, at flow rate 1 mL/min, and UV detection at $\lambda = 254$ nm); the major enantiomer having $t_r = 18.1$ min, whereas the minor one showed $t_r = 22.3$ min. The absolute configuration of the major enantiomer was assigned on the basis of literature data.[10e]

4.3.6. (*R*)-2-Nitro-1-(4-nitrophenyl)ethanol 3f. Compound **3f**[10g] was prepared according to the general procedure P2 and purified by column chromatography (10–20% EtOAc/hexanes) to give a yellow solid. (73% yield with Proton sponge® as additive, 98% yield with DBU as additive). Mp: 83–85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.29–8.24 (m, 2H), 7.65–7.60 (m, 2H), 5.63–5.58 (m, 1H), 4.65–4.55 (m, 2H), 3.13 (d, $J = 3$ Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 148.0, 145.1, 127.1, 124.3, 80.7, 70.1. MS (EI$^+$) *m*/*z* (%): 151, 135, 120, 105, 77, 51. The enantiomeric purity of **3f** (28% ee with Proton sponge® as additive, 31% ee with DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 90:10 hexane/isopropanol solvent mixture, at flow rate 1 mL/min, and UV detection at $\lambda = 254$ nm); the major enantiomer having $t_r = 34.4$ min, whereas the minor one showed $t_r = 42.5$ min.

The absolute configuration of the major enantiomer was assigned on the basis of literature data.[10g]

4.3.7. (*R*)-4-(1-Hydroxy-2-nitroethyl)benzonitrile 3g. Compound **3g** was prepared according to the general procedure P2 and purified by column chromatography (30% EtOAc/hexanes) to give a pale brown solid. (75% yield with Proton sponge® as additive, 79% yield with DBU as additive). Mp: 80–81 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.70 (d, $J = 4.8$ Hz, 2H), 7.55 (d, $J = 6.6$ Hz, 2H), 5.56–5.52 (m, 1H) 4.62–4.51 (m, 2H), 3.35 (br s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 143.5, 132.9, 126.9, 118.3, 80.8, 70.3. MS (EI^+) m/z (%): 130, 102, 76, 50. The enantiomeric purity of **3g** (76% ee with Proton sponge® as additive, 64% ee with DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 90:10 hexane/isopropanol solvent mixture, at flow rate 1 mL/min, and UV detection at $\lambda = 254$ nm); the major enantiomer having $t_r = 4.0$ min, whereas the minor one showed $t_r = 9.0$ min. The absolute configuration of the major enantiomer was assigned by analogy and is supported by the consistent order of elution during chiral stationary phase HPLC.

4.3.8. (*R*)-1-(4-Fluorophenyl)-2-nitroethanol 3h. Compound **3h**[10g] was prepared according to the general procedure P2 and purified by column chromatography (20% EtOAc/hexanes) to give a colorless oil. (65% yield with Proton sponge® as additive, 62% yield with DBU as additive). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.36–7.31 (m, 2H), 7.07–7.02 (m, 2H), 5.41–5.37 (m, 1H), 4.58–4.42 (m, 2H), 3.45 (br s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 164.5, 161.2, 134.1, 127.9, 116.1, 115.8, 81.1, 70.3. MS (EI^+) m/z (%): 185 $[M]^+$, 138, 123, 109, 95, 91, 75, 50. The enantiomeric purity of **3h** (58% ee with Proton sponge® as additive, 75% ee with DBU as additive) was determined by HPLC with a Chiralcel OD column (using a 90:10 hexane/isopropanol solvent mixture, at flow rate 1 mL/min, and UV detection at $\lambda = 254$ nm); the major enantiomer having $t_r = 15.3$ min, whereas the minor one showed $t_r = 17.8$ min. The absolute configuration of the major enantiomer was assigned on the basis of literature data.[10g]

4.3.9. 1-Nitro-4-phenylbut-3-en-2-ol 3i. Compound **3i**[10h] was prepared according to the general procedure P2 and purified by column chromatography (20% EtOAc/hexanes) to give a yellow solid. (98% yield with Proton sponge® as additive, 56% yield with DBU as additive). Mp: 60–61 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45–7.29 (m, 5H), 6.77 (d, $J = 15.9$ Hz, 1H), 6.14 (dd, $J = 17.2$, 6.3 Hz, 1H), 5.06–5.02 (m, 1H), 4.51 (d, $J = 6$ Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 133.7, 128.8, 128.7, 128.6, 126.8, 125.2, 80.0, 69.7. MS (EI^+) m/z (%): 131, 103, 77, 51. The enantiomeric purity of **3i** (72% ee with either Proton sponge® or DBU as additive, 72% ee with DBU as additive) was determined by HPLC with a Daicel Chiralcel OD column (using a 90:10 hexane/isopropanol solvent mixture, at flow rate 1 mL/min, and UV detection at $\lambda = 254$ nm); the major enantiomer showed $t_r = 55.0$ min, whereas the minor one showed $t_r = 46.9$ min. The absolute configuration of the major enantiomer was not determined.

4.4. Computational details

Ground state geometries of **m2La** and **m4La** were fully optimized using gradient techniques at the DFT (B3LYP) level of theory, using split-valence d-polarized 6-31G* basis set for H, C, N, and O, and the Sttutgarts's group effective core potential MWB for lanthanum(III),[17] as implemented in Gaussian 98.[25] Stationary points were fully characterized as minima (all frequencies real) by vibrational analysis. The zero-point vibrational energies (ZPVE) were computed at the same level and were not scaled.

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