# Chiral Organolanthanide Complexes for Enantioselective Olefin Hydrogenation

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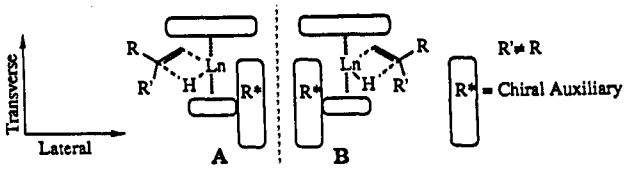
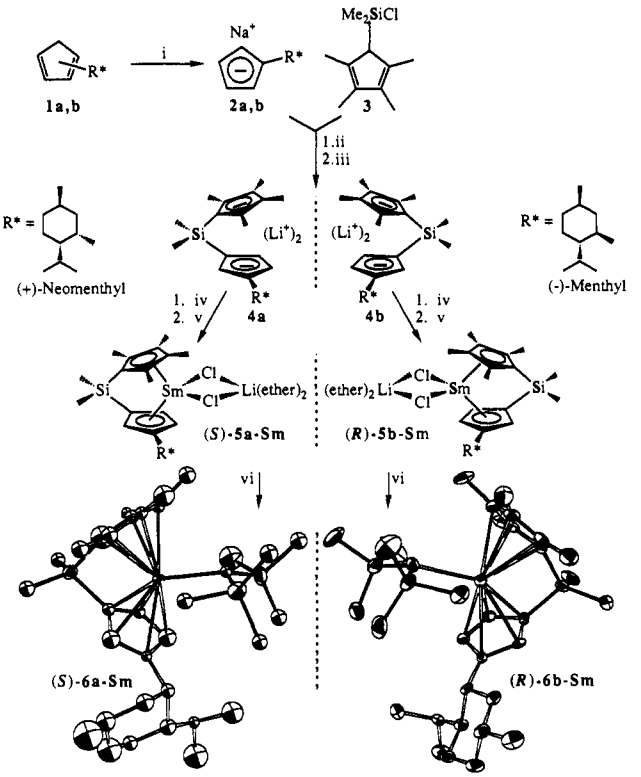
Organolanthanides with $Cp'_2Ln$, $R_2SiCp''_2Ln$, and $R_2SiCpCp''Ln$ supporting ligation ($Cp' = \eta^5$-$Me_5C_5$; R = alkyl; $Cp'' = \eta^5$-$Me_4C_5$)[1-4] catalyze diverse olefin transformations (hydrogenation,[1a,5] oligomerization/polymerization,[1,3] hydroamination,[6] hydrosilylation[7]) with rapidity and selectivity. These characteristics and their tunability with ionic radius and ancillary ligands[1,4,5b,6] raise the question of whether f-element coordination environments can be devised for *asymmetric* transformations.[8] We report here a chelating ligand system designed to preserve $Cp'_2Ln$ stereoelectronic properties while providing a rigid, chiral template for lateral/transverse substrate enantioface discrimination (A, B);[9] we discuss the properties of four related enantioselective organosamarium hydrogenation catalysts.




Ligand synthesis (Scheme I) employs chiral cyclopentadienes **1a,b**[10] and $HCp''SiMe_2Cl$ (**3**).[4,11] The enantiopure auxiliaries (R*) provide lateral steric discrimination and insure that the resulting organolanthanides are diastereomeric, hence potentially separable. Synthesis of pseudoenantiomorphous dichloro complexes (*S*)-**5a**-Sm and (*R*)-**5b**-Sm utilizes standard procedures[1,4,12,13] and proceeds with high initial diastereoselection (>80% by $^1H$ NMR), providing diastereomerically pure products after recrystallization. These complexes can be selectively epimerized

**Scheme I.** Synthesis of Chiral Organosamarium Hydrocarbyls[a]




[a] (i) NaH/THF; (ii) THF; (iii) $LiCH_2TMS$/pentane; (iv) $SmCl_3$/THF; (v) diethyl ether; (vi) $LiCH(TMS)_2$/toluene.

**Table I.** Product Enantiomeric Excess and Absolute Configuration Data for Hydrogenation of 2-Phenyl-1-butene and Deuteration of Styrene by Organosamarium Catalysts

| substrate | precatalyst | temp (°C) | % enantiomeric excess (sign) |
|---|---|---|---|
| 2-phenyl-1-butene | | | |
| 1 | (*R*)-**6a**-Sm | 25 | 71(−)[a,b] |
| 2 | | 0 | 61(−)[a,b] |
| 3 | (*S*)-**6a**-Sm | 25 | 19(+)[a,b] |
| 4 | | 0 | 17(+)[a,b] |
| 5 | 70/30 (*S*)/(*R*)-**6b**-Sm | 25 | 64(+)[a,b] |
| 6 | | 0 | 71(+)[a,b] |
| 7 | | −30 | 79(+)[a,b] |
| 8 | | −78 | 96(+)[a,b] |
| 9 | (*R*)-**6b**-Sm | 25 | 8(−)[a,b] |
| 10 | | 0 | 15(−)[a,b] |
| 11 | | −30 | 27(−)[a,b] |
| styrene | | | |
| 12 | 70/30 (*S*)/(*R*)-**6b**-Sm | 25 | 72(+)[c,d] |
| 13 | (*R*)-**6b**-Sm | 25 | 43(−)[c,d] |

[a] [Substrate]/[catalyst] = (100–500)/1; solvent = heptane; $P_{H_2}$ = 760 Torr; rapid stirring; 100% conversion by GLC and NMR. [b] Based upon $[\alpha]^{20}_D = +28.4°$ for (*S*)-(+)-2-phenylbutane ($c$ = 1.00, 95% EtOH, $l$ = 0.5 dm);[18] rotation confirmed by independent synthesis from (*S*)-(+)-2-phenylbutyric acid.[19] Reported ee's based upon lower $[\alpha]$ values must be adjusted downward accordingly. [c] [Substrate]/[catalyst] = 100/1; solvent = heptane; $P_{D_2}$ = 760 Torr; rapid stirring; 100% conversion by GLC and NMR. [d] Based upon $[\alpha]^{20}_D = +0.80°$ for (*S*)-(+)-phenylethane-1,2-$d_2$ (neat, $l$ = 0.5 dm);[20] regiospecificity confirmed by $^{13}C$ NMR.

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to the pseudoenantiomorphous counterparts (*R*)-**5a**-Sm and (*S*)-**5b**-Sm (the latter isolable as a 4/1 *S*/*R* mixture).[12] Absolute configurations follow from CD (pseudoenantiomers exhibit near-mirror-image spectra for $\lambda > 250$ nm)[12] and the crystal structure of (*R*)-**5a**-Sm.[14] Conversion of the diastereomeric chloro complexes to hydrocarbyl precatalysts proceeds with net retention of configuration as adduced from CD and X-ray diffraction (Scheme I).[12,15] The latter data reveal unexceptional metrical parameters[1,4] and unambiguously confirm that (*S*)-**6a**-Sm and (*R*)-**6b**-Sm are pseudoenantiomorphous. Alkylation[1,4] of the aforementioned (*R*)-**5a** and (*S*)/(*R*)-**5b** complexes similarly affords (*R*)-**6a**-Sm and a 70/30 (*S*)/(*R*)-**6b**-Sm mixture, respectively.[12]

In transformations doubtless mediated by the corresponding hydrides,[1,4,16] **6**-derived catalysts are capable of reducing traditionally challenging[7,17] unfunctionalized olefins such as 2-phenyl-1-butene (**7**)[18] and styrene (**8**)[19] with high activity (e.g., for **7**, $N_t$((*R*)-**6a**-Sm) = 20 000 $h^{-1}$ at 25 °C)[20] and moderate to unprecedently high enantioselectivity (Table I). Enantioselection exhibits appreciable (but not identical) temperature dependence, with the pseudoenantiomorphous catalysts yielding products of *opposite* absolute configurations (and *inequivalent* ee's). For **7**, product configurations suggest a stereodifferentiating insertion process in which R = Ph and R′ = Et in A and B or, more likely, an olefin approach occurring along the ring centroid–Sm–ring centroid bisector,[17a,d,21] with Sm–H bent back and R = Ph oriented away from Cp″ and R*. Kinetic measurements[22] on all four catalysts under non-mass-transport-limited conditions in $H_2$[5b] yield rate law 1, compatible with rapid, operationally irreversible olefin

$$v = k[\mathrm{Sm}]^{1/2}[\mathrm{H_2}]^1[\mathbf{7}]^0 \qquad (1)$$

addition,[5b] a rapid preequilibrium involving a dialkyl or alkyl hydride dimer, and turnover-limiting Sm–C hydrogenolysis.[5b] Both $k_{H_2}/k_{D_2}$ = 1.5–2.3 (25 °C)[23] and an increase in ee under non-mass-transport-limited conditions[24] (rapid hydrogenolytic interception of the Sm–alkyl intermediate) support this scenario.

In summary, these results demonstrate that organolanthanide coordination geometries can be constructed that effect, in a structurally understandable manner, asymmetric reductions of unfunctionalized olefins with high turnover frequencies and enantioselectivities. Extension to the organolanthanide-catalyzed hydroamination/cyclization of amino olefins[6] with high enantioselectivity is reported in a second communication.[25]

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**Supplementary Material Available:** Synthetic, spectroscopic, and analytical data, X-ray experimental details including tables of positional and anisotropic displacement parameters, and tables of bond lengths and angles (63 pages); listing of observed and calculated structure factor amplitudes for **6a**-Y and **6b**-Sm (70 pages). Ordering information is given on any current masthead page.

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(15) (*R*)-**6b**-Sm: $C_{66}H_{118}Si_6Sm_2$, space group *P*1; $a$ = 8.993 (3) Å, $b$ = 12.738 (2) Å, $c$ = 16.549 (4) Å; $\alpha$ = 86.04 (2)°, $\beta$ = 82.81 (2)°, $\gamma$ = 72.91 (2)° (−120 °C); $V$ = 1797 (2) Å$^3$, $Z$ = 1. Structure solved by direct methods and refined to $R(F)$ = 0.026, $R_w(F)$ = 0.030 ($R_w(F)$ = 0.041 for the *S* configuration), for 8327 reflections having $I > 3\sigma(I)$. The two independent molecules differ slightly in orientation of the R* functionality. **6a**-Sm: diffraction-quality crystals only obtained for a 1/1 *R*/*S* mixed crystal; data collected on the isostructural Y analogue. $C_{33}H_{54}Si_3Y$, space group $P2_1$, $a$ = 19.178 (4) Å, $b$ = 8.736 (1) Å, $c$ = 21.391 Å, $\beta$ = 97.62 (2)° (−120 °C); $V$ = 3552 (2) Å$^3$, $Z$ = 4. Structure solved by direct methods and refined to $R(F)$ = 0.071, $R_w(F)$ = 0.083, for 3514 reflections having $I > 3\sigma(I)$.

(16) (a) Hydrides isolated after catalytic runs correspond spectroscopically to the independently prepared[16b] materials. (b) Conticello, V. P.; Brard, L.; Giardello, M. A.; Marks, T. J. Unpublished results.

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(20) [Catalyst] = 0.97 mM; [olefin] = 1.51 M; $P_{H_2}$ = 755 Torr. Catalytic reactions were carried out under rigorously anhydrous anaerobic conditions.[1,4] Hydrogenation products were isolated by vacuum transfer followed by fractionation at reduced pressure, and purity was verified by $^1$H NMR. Optical rotations were measured on an Optical Activity Ltd. AA-100 polarimeter using conditions identical to those reported in the literature.

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(22) [Catalyst] = 0.51–8.04 mM; $P_{H_2}$ = 75–755 Torr; [olefin] = 0.75–3.4 M.

(23) Lin, Z.; Marks, T. J. *J. Am. Chem. Soc.* **1987**, *109*, 7979–7985.

(24) For Table I entries 5 and 9, vortex mixing[5b] increases ee's to 80% and 16%, respectively.

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## Common Origin of Clavulanic Acid and Other Clavam Metabolites in *Streptomyces*

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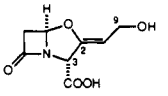
The potent β-lactamase inhibitor clavulanic acid (**1**)[1] co-occurs in *Streptomyces clavuligerus* with the clavam metabolites **2**–**5**.[2] The hydroxyethyl clavam **6** is known from an allied species, *S. antibioticus*.[3] These clavams share a common side chain configuration at C-2 and, importantly, lack the C-3 carboxyl and have the opposite ring fusion configuration to that in clavulanic acid.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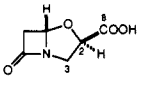
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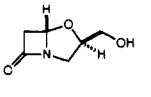
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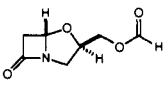
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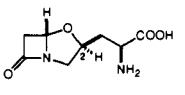
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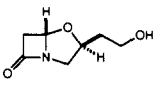
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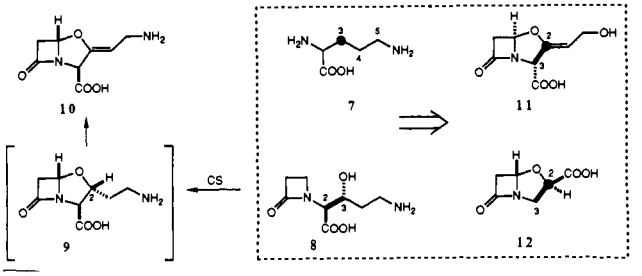
The structure of alanylclavam (**5**), from which the formation of **2**–**4**, **6**, and the dimeric clavamycins[4] could be easily rationalized, suggests that the biosynthetic origin of these clavams derives from utilization of L-ornithine (**7**) in the opposite regiochemical sense to that established for clavulanic acid (**1**),[5,6] i.e., such that the terminal nitrogen appears in the β-lactam ring rather than the α-amine. Moreover, a metabolic intermediate of **1**, dihydroclavaminic acid (**9**)[7,8] transiently involved in the oxidative cyclization/desaturation catalyzed by clavaminate synthase (CS),

**Scheme I**

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