Homoleptic Lanthanide Alkyl and Amide Precatalysts Efficiently Mediate Intramolecular Hydrophosphination/Cyclization. Observations on Scope and Mechanism

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Summary: Homoleptic lanthanide alkyls of the form Ln[CH(SiMe$_3$)$_2$]$_3$ (Ln = La, Nd, Sm, Y, Lu) and amides of the form Ln[N(SiMe$_3$)$_2$]$_3$ (Ln = La, Nd, Sm, Y) serve as efficient precatalysts for intramolecular homogeneous hydrophosphination. Both phosphinoalkynes and phosphinoalkenes undergo cyclization to the corresponding heterocyclic structures.

Lanthanocene complexes of the composition Cp$^{‡}_2$LnR (Cp‡ = η^5-alkylcyclopentadienyl ligand; Ln = La, Nd, Sm, Y, Lu; R = N(SiMe$_3$)$_2$, CH(SiMe$_3$)$_2$) efficiently mediate the intramolecular hydroamination of a variety of substrates, including aminoolefins[1] and aminoalkynes.[2] Although metal-catalyzed carbon−phosphorus bond formation[3] is of great interest due to the importance of organophosphorus compounds in a variety of industries,[4] application of analogous hydrophosphination processes presents a significant challenge. Substantial differences in Ln−P and Ln−N bond enthalpies,[5] the softer nature of phosphorus vs nitrogen,[6] and the greater Brønsted acidity of primary phosphines vs amines[7] are all expected to lead to substantially different reactivity and selectivity trends. Recently, our group reported that lanthanocenes efficiently catalyze the intramolecular hydrophosphination of phosphinoalkenes and phosphinoalkynes in a regio- and diastereoselective manner.[8] However, the multistep syntheses of lanthanocene complexes are in general nontrivial.[9] For this reason, readily accessible homoleptic lanthanide bis(trimethylsilyl)alkyl (Ln[CH(SiMe$_3$)$_2$]$_3$) and bis(trimethylsilyl)amide (Ln[N(SiMe$_3$)$_2$]$_3$) complexes would, in principle, be attractive alternative precatalysts. Homoleptic lanthanide amides are known to catalyze the hydroamination of restricted classes of aminoalkenes[10] and more reactive aminoalkynes,[11] although at diminished rates versus lanthanocene catalysts. Herein we report that homoleptic lanthanide catalysts are competent for the hydrophosphination of phosphinoalkynes and phosphinoalkenes and show that rates and selectivities are generally comparable to those of analogous lanthanocene-catalyzed processes.[12]

Ln[CH(SiMe$_3$)$_2$]$_3$[13] (Ln = La (**1a**), Nd (**1b**), Sm (**1c**), Y (**1d**), Lu (**1e**)) and Ln[N(SiMe$_3$)$_2$]$_3$[14] (Ln = La (**2a**), Nd (**2b**), Sm (**2c**), Y (**2d**)) complexes were prepared and purified as reported elsewhere. Hydrophosphination reactions were carried out under rigorously anhydrous and anaerobic conditions and were monitored in situ by ^{1}H and ^{31}P NMR spectroscopy (see the Supporting Information). With regard to catalyst initiation, it is found that addition of substrate **5** to a solution of La[CH(SiMe$_3$)$_2$]$_3$ in benzene-d_6 (**1a**, 2.1 mol %) at 22 °C

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(2) Recent hydroamination of alkynes: (a) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 1757−1771. (b) Bürgstein, M. R.; Berberich, H.; Roesky, P. W. *Organometallics* **1998**, *17*, 1452−1454.

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(5) Bond enthalpy data: (a) Nolan, S. P.; Stern, D.; Hedden, D.; Marks, T. J. *ACS Symp. Ser.* **1990**, *No. 428*, 159−174. (b) Nolan, S. P.; Stern, D.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 7844−7853. (c) Skinner, H. A.; Pilcher, G. In *The Chemistry of the Metal−Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: Chichester, U.K., 1982; Vol. 1, Chapter 2. (d) Goldwhite, H. *Introduction to Phosphorus Chemistry*; Cambridge University Press: Cambridge, U.K., 1981.

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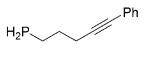
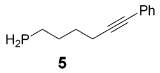
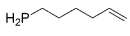
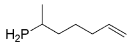
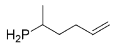
Table 1. Scope of Homoleptic Lanthanide-Catalyzed Hydrophosphination of Phosphinoalkynes and Phosphinoalkenes

entry	substrate	product	precatalyst[a] (mol%)	conditions[b]	conv %[c]
1.	 **3**	 **4**	**1a** (2.2)	4 h, 22 °C	85
			1b (1.9)	8 h, 22 °C	>95
			1c (2.4)	14 h, 22 °C	>95
			1d (2.5)	24 h, 22 °C	85
			2a (2.7)	6.5 h, 60 °C	>95
			2c (3.6)	9 h, 60 °C	>95
			2d (2.7)	14 h, 60 °C	>95
2.	 **5**	 **6**	**1a** (2.0)	11 h, 22 °C	85
			2a (2.3)	14 h, 60 °C	95
3.	 **7**	 **8**	**1d** (3.5)	24 h, 90 °C	53
			2d (2.9)	24 h, 90 °C	61
4.	 **9**	 **10**	**1d** (2.3)	24 h, 90 °C	82
			2d (2.2)	24 h, 90 °C	41
5.	 **11**	 **12**	**1d** (3.8)	24 h, 22 °C	35
			1e (3.6)	24 h, 22 °C	25

[a] 2.5−3.5 mg of precatalyst. [b] All reactions carried out in C_6D_6 or C_7D_8 with total of 1.0 mL of solution. [c] All reactions carried out to 100% completion but only monitored by ^1H and ^{31}P NMR until the percent conversion reported.

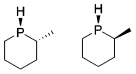
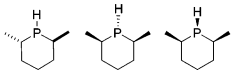
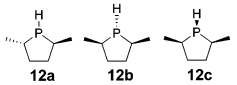
Table 2. Comparison of Lanthanocene and Homoleptic Lanthanide Precatalysts for Phosphinoalkyne Hydrophosphination

entry	substrate	product	precatalyst	N_t (h^{-1})[a]
1	**3**	**4**	$La[CH(SiMe_3)_2]_3$	18.3[b]
			$Cp'_2LaCH(SiMe_3)_2$	12.4
			$CGCSmN(SiMe_3)_2$	13.5
2	**5**	**6**	$La[CH(SiMe_3)_2]_3$	3.5[b]
			$Cp'_2LaCH(SiMe_3)_2$	4.4

[a] Reactions carried out in C_6D_6 at 22 °C. [b] N_t values are calculated from (TON)/time at 75% substrate consumption.

leads to complete La−$CH(SiMe_3)_2$ protonolysis within ∼15 min, as judged by ^1H NMR (see the Supporting Information). In the presence of the homoleptic Ln alkyl and amide complexes, phosphinoalkyne substrates **3** and **5** undergo clean, rapid, and quantitative cyclization to the corresponding, known[8] phosphorus heterocycles (Table 1).[15,16] Interestingly, turnover frequencies for cyclization of **3** and **5** using $La[CH(SiMe_3)_2]_3$ as the precatalyst are comparable to those observed using the most active lanthanocene catalysts (Table 2).[8] The homoleptic amide precatalysts mediate phosphinoalkyne cyclization somewhat more slowly than the homoleptic alkyls, presumably because initiation to form active Ln phosphido species is slower; thus, at 60 °C after 60 min reaction time, ≲30% of the La−$N(SiMe_3)_2$ groups undergo protonolysis in the reaction of $La[N(SiMe_3)_2]_3$ (**2a**, 3.0 mol %) with **5**, as judged by ^1H NMR. However, hydrophosphination of **5** proceeds smoothly at 60 °C to

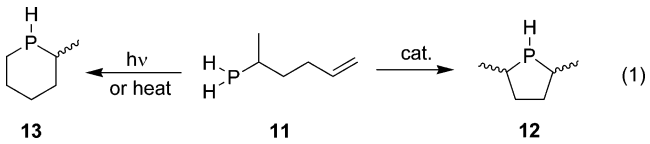
Table 3. Effect of Precatalyst Structure on Cis/Trans Selectivity of Hydrophosphination Processes

substrate	possible exocyclic products	precatalyst	conditions	distribution (%) a	b	c
7	 **8a** **8b**	**2d**	90 °C	70	22	-
		1d	90 °C	73	21	-
		Cp'_2Sm-	25 °C	89	11	-
9	 **10a** **10b** **10c**	**2c**	90 °C	51	43	7
		2d	90 °C	41	47	22
		1d	90 °C	40	37	9
		Cp'_2Sm-	25 °C	12	86	2
11	 **12a** **12b** **12c**	**1d**[a]	22 °C	41	10	trace
		1e[a]	22 °C	18	5	trace
		Cp'_2Sm-	25 °C	72	17	trace
		Cp'_2Lu-	25 °C	24	64	trace

[a] Endocyclic side product accounts for the remainder of the product mixture.

95% completion in 6.5 h. With both the homoleptic alkyls and amides, the cyclizations of **3** and **5** exhibit increasing cyclization rates with increasing Ln ionic radius (La > Nd > Sm >Y; Table 1, entry 1).

Hydrophosphination of phosphinoalkene substrates **7**, **9,** and **11** is also mediated by the homoleptic Ln alkyls and amides to yield the known[8] heterocycles (Table 1). In comparison to the high activities achieved using lanthanocene catalysts,[8] diminished rates are observed in phosphinoalkene cyclizations using the homoleptic catalysts.[17] Upon synthesis, purification, and storage of substrate **11**, ∼5−20% yield of phosphorinane **13** is detected (eq 1).[18] The formation of the noncatalytic six-



13 **11** **12** (1)

membered endocyclic product **13** is accelerated by heat and light,[19] and therefore, cyclization of **11** is not clean at higher temperatures. There is literature precedent for the endocyclic addition of P−H bonds to olefins to form phosphorus heterocycles, which is thought to be radical in nature.[16b−e,20] Addition of substrate **11** to a solution of AIBN in C_6D_6 (∼10 mol %) at 22 °C results in the formation of phosphorinane **13** in 88% yield with a <1% yield of phospholane **12** over 24 h. This observation provides evidence that the endocyclic side product **13** is formed via a radical pathway.

With respect to hydrophosphination stereoselectivity, processes mediated by the homoleptic Ln catalysts are somewhat less selective than can be achieved with lanthanocene catalysts (Table 3). Diastereoselectivities are found to be independent of conversion under the above reaction conditions.[21] Interestingly, using homoleptic Ln catalysts, phospholane-forming diastereoselectivities appear to be invariant with starting ligands and Ln metal.

(15) As observed with lanthanocene catalysts,[8] while heterocycles **4** and **6** can be detected by in situ NMR, they undergo dimerization.

(16) For alternative syntheses of phosphorus heterocycles, see: (a) Soulier, E.; Clément, J.; Yaouanc, J.; des Abbayes, H. *Tetrahedron Lett.* **1998**, *39*, 4291−4294. (b) Hackney, M. L.; Schubert, D. M.; Brandt, P. F.; Haltiwanger, R. C.; Norman, A. D. *Inorg. Chem.* **1997**, *36*, 1867−1872. (c) Brandt, P. F.; Schubert, D. M.; Norman, A. D. *Inorg. Chem.* **1997**, *36*, 1728−1731. (d) Field, L. D.; Thomas, I. P. *Inorg. Chem.* **1996**, *35*, 2546−2548. (e) Davies, J. H.; Downer, J. D.; Kirby, P. *J. Chem. Soc. C* **1966**, 245−257.

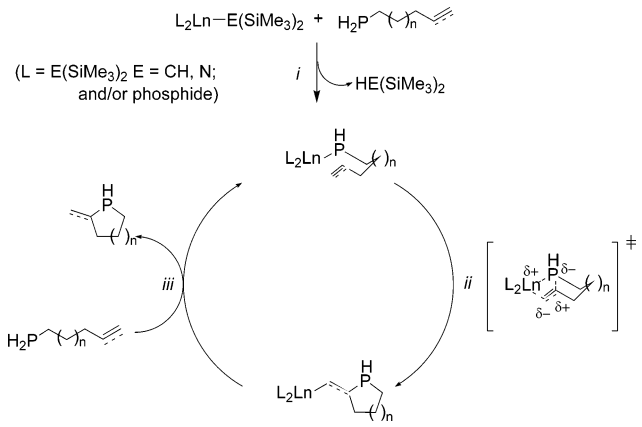
(17) No reaction is observed when substrate **11** is reacted with 13 mol % $KN(SiMe_3)_2$ in C_6D_6 at room temperature for 7 days, which argues against a base-catalyzed pathway.

(18) Telomer formation is not observed during catalytic reactions or upon storage of the substrate solution at room temperature for months.

(19) Formation of the seven-membered endocyclic ring is thermodynamically and kinetically unfavorable.

(20) Storage of substrate **11** with the common radical inhibitor hydroquinone does not significantly inhibit the formation of **13**.[8]

Scheme 1. Simplified Catalytic Cycle for Homoleptic Lanthanide-Mediated Hydrophosphination



As a function of metal ionic radius, $Cp'_2LnCH(SiMe_3)_2$-mediated hydrophosphination of phosphinoalkenes exhibits the highest turnover frequencies for intermediate-sized Ln = Y, followed by larger and smaller sized ions (Y > Sm > Lu > La).[8] In addition, more open $Me_2Si(Me_4C_5)(^tBuN)LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ precatalysts exhibit depressed rates for phosphinoalkene cyclization. Therefore, the diminished rates observed with the present homoleptic catalysts support the idea that the "fit" among ancillary ligands, metal, and substrate is not optimal[8] and that larger metal ions and more open coordination spheres may permit the coordination of excess phosphine moieties, which may in turn block sites for phosphinoalkene hydrophosphination/cyclization.

While a pathway similar to that proposed for lanthanocene-catalyzed hydrophosphination is likely operative in the present homoleptic systems, it is clear that there are also significant differences. Homoleptic Ln-catalyzed hydrophosphination should occur via initial $Ln-CH(SiMe_3)_2$ protonolysis to generate a Ln−P bond, followed by intramolecular insertion of the C−C unsaturation into the Ln−P bond and finally Ln−C protonolysis to release the heterocyclic product and complete the catalytic cycle (Scheme 1).

In the presence of diamagnetic $La[CH(SiMe_3)_2]_3$ (**1a**, 2.1 mol %), the cyclization of phosphinoalkyne **5** can be monitored as a function of time by ^1H NMR. A nonlinear [substrate]:[catalyst] vs time plot is obtained (see the Supporting Information), suggesting that the reaction rate is not zero-order in [substrate]. Interestingly, when the data are plotted as 1/([substrate]:[catalyst]) vs time, a linear plot is obtained which suggests an unusual second-order dependence on [substrate] (Figure 1). This result stands in contrast to lanthanocene systems, where a typical [substrate]:[catalyst] plot is linear over 2 half-lives, implying zero-order dependence of rate on [substrate].[8] With the current system, the apparent second-order behavior may arise from other factors: multiple active catalyst species, severe product inhibition, and/or catalyst decomposition. One, two, or three $Ln-E(SiMe_3)_2$ (E = CH, N) linkages can in principle undergo protonolysis by substrate or product, leading to numerous active species and doubtless a complex manifold of catalytic cycles. The possible coordination of one or more phosphines adds greater complexity. Therefore, more detailed kinetic and mechanistic studies are in progress.

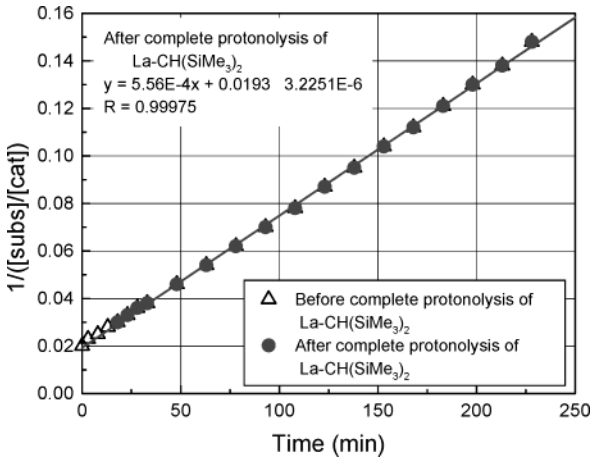


Figure 1. Kinetics of the hydrophosphination of 5-phenyl-4-pentynylphosphine (**5** → **6**) mediated by **1a** in C_6D_6 at 22 °C: inverse ratio of [substrate]:[lanthanide] as a function of time. The line represents the least-squares fit.

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Supporting Information Available: Text giving detailed synthetic procedures for compounds **1**−**11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) After cyclization of substrate **11** by $Y[CH(SiMe_3)_2]_3$, the diastereomeric product mixture was heated at 60 °C for 3 days in both the presence and absence of catalyst. There was no discernible change in the ratio of product diastereomers.