Aminotroponate and Aminotroponiminate Calcium Amides as Catalysts for the Hydroamination/Cyclization Catalysis

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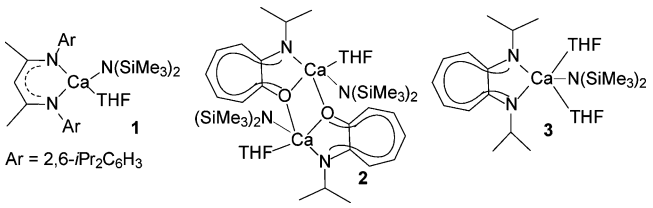
Summary: Reaction of [Ca{N(SiMe$_3$)$_2$}(THF)$_2$] with the neutral ligands (iPrAT)H and {(iPr)$_2$ATI}H resulted in the corresponding amido complexes [(iPrAT)Ca{N(SiMe$_3$)$_2$}(THF)]$_2$ (iPrAT = 2-(isopropylamino)troponate) and [{(iPr)$_2$ATI}Ca{N(SiMe$_3$)$_2$}-(THF)$_2$] ((iPr)$_2$ATI = N-isopropyl-2-(isopropylamino)troponiminate). The solid-state structures of both compounds were established by single-crystal X-ray diffraction. The latter compound showed a high reactivity as catalyst in the intramolecular hydroamination/cyclization reaction of nonactivated amino alkenes.

The catalytic addition of an organic amine N−H bond to alkenes or alkynes (hydroamination) to give nitrogen-containing molecules is of great interest to both academic and industrial researchers alike.[1] At the present time most amines are made in multistep syntheses, and as such, hydroamination offers an attractive alternative to give nitrogen-containing molecules that are important for fine chemicals and pharmaceuticals and as useful chiral building blocks. It has been shown that hydroamination can be catalyzed by d- and f-block transition metals[2] and alkali metals.[3] The scope of catalytic hydroamination has been reviewed recently.[1] Early transition metals are highly efficient catalysts for the hydroamination reaction of various C−C multiple bonds. In lanthanide chemistry it was shown by T. J. Marks et al. that amido and alkyl metallocene complexes are proved to be efficient catalysts for the hydroamination/cyclization of aminoalkenes, allenes, and alkynes.[1l] It is well-established that the reactivity and coordination behavior of the heavier alkaline earth metals (especially Ca and Sr) is somewhat similar to the divalent lanthanide metals.[4] This similarity is a result of the large ionic radii and the electropositive character of the cations. Thus, some similarities can also be seen between the trivalent lanthanide metals and the heavier alkaline earth metals. Whereas for the lanthanides a number of complexes being active for the hydroamination/cyclization were reported,[1b,2c−e] there is only one publication about the Ca-catalyzed hydroamination reaction, from M. S. Hill et al.,[5] in which the β-diketiminato calcium bis(trimethylsilyl)amide [{HC(C(Me)$_2$N-2,6-*i*Pr$_2$C$_6$H$_3$)$_2$}-Ca{N(SiMe$_3$)$_2$}(THF)] (**1**) was used as catalyst (Scheme 1). The low cost and availability of calcium offer significant commercial advantages. On the basis of these results we were interested in studying the influence of the ligand system on the catalytic activity of the calcium catalyst. Therefore, we wanted to synthesize other calcium catalysts for the hydroamination and compare them with the literature compound **1**. We used as ligand 2-(isopropylamino)tropone, (*i*PrAT)H, and *N*-isopropyl-2-(isopropylamino)troponimine, {(*i*Pr)$_2$ATI}H, a system that earlier has been successfully employed as ligand in rare earth[6] and zinc chemistry.[7] These complexes have proven to be highly active catalysts for the intramolecular hydroamination/cyclization reaction.

Scheme 1



It was shown earlier that the reaction of [{(*i*Pr)$_2$ATI}-Li(THF)$_2$] with CaI$_2$ does result only in the ate-complex

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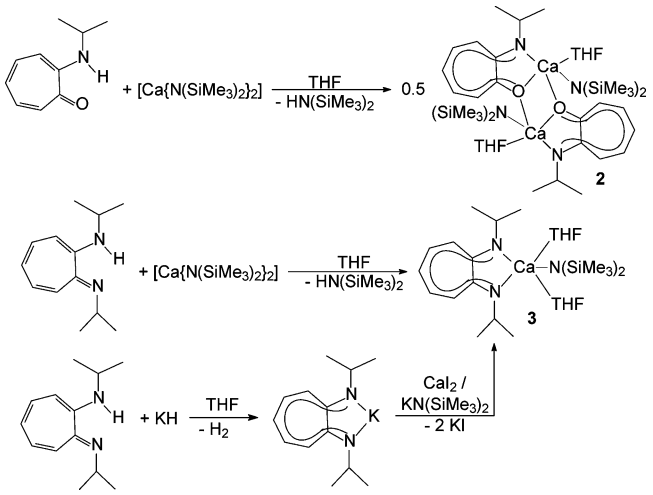
Scheme 2



[{(*i*Pr)$_2$ATI}Ca(THF)$_2$I$_2$Li$_2$(THF)$_2$].[8] Therefore, an amide elimination route was chosen first. Reaction of [Ca{N(SiMe$_3$)$_2$}(THF)$_2$] with the neutral ligands (*i*PrAT)H and {(*i*Pr)$_2$ATI}H resulted in the corresponding amido complexes [(*i*PrAT)Ca{N(SiMe$_3$)$_2$}(THF)]$_2$ (**2**) and [{(*i*Pr)$_2$ATI}Ca{N(SiMe$_3$)$_2$}(THF)$_2$] (**3**) (Schemes 1 and 2). Alternatively, compound **3** can also be obtained via a classical salt metathesis in a one-pot reaction from CaI$_2$ and the potassium salts KN(SiMe$_3$)$_2$ and [{(*i*Pr)$_2$ATI}K]. The new complexes have been characterized by standard analytical/spectroscopic techniques, and the solid-state structures of both compounds were established by single-crystal X-ray diffraction.[9]

The ^{1}H and ^{13}C{^{1}H} NMR spectra of both compounds show the expected set of signals for the organic groups. The solid-state compound **2** is a dimeric complex in which the metal centers are asymmetrically bridged by two μ-oxygen atoms (Ca1−O1 2.329(2) Å, Ca1−O1′ 2.3408(14) Å) (Figure 1). In the center of the Ca−O−Ca′−O′ plane, a crystallographic inversion center is observed. Besides the (*i*PrAT)$^-$ ligand, one N(SiMe$_3$)$_2^-$ group and one molecule of THF are attached to each calcium atom. The bite angle of the (*i*PrAT)$^-$ ligand is N1−Ca1−O1 66.13(6)°. As a result of the higher sterical demand of the {(*i*Pr)$_2$ATI}$^-$ ligand, compound **3** is, in contrast to **2**, monomeric in the solid state (Figure 2). The structure reveals a 5-fold coordination sphere of the ligands around the calcium atom, which consists of one {(*i*Pr)$_2$ATI}$^-$ ligand, one N(SiMe$_3$)$_2^-$ group, and two molecules of THF. The bond distances and angles are as expected. The bite angle of the {(*i*Pr)$_2$ATI}$^-$ ligand is N1−Ca−N2 68.03(6)°.

We have tested compounds **2** and **3** in the intramolecular hydroamination/cyclization reaction of terminal aminoalkenes and one aminoalkyne (Table 1). Our intention was to evaluate the catalytic activity of compounds **2** and **3** in comparison to the β-diketiminato complex **1**. In this context it should be mentioned that compound **1** shows a significantly higher activity than the diamido compound [Ca{N(SiMe$_3$)$_2$}(THF)$_2$].[5] In our substrate screening we focused on the challenging nonactivated aminoalkenes. The rigorously anaerobic reaction of the catalyst

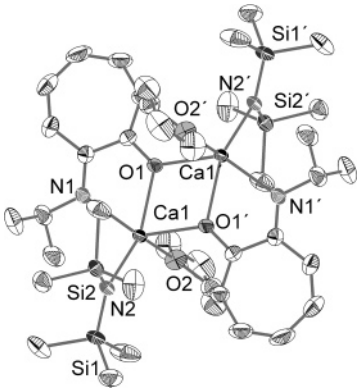


Figure 1. Perspective ORTEP view of the molecular structure of **2**. Thermal ellipsoids are drawn to encompass 50% probability. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): Ca1−N1 2.458(2), Ca1−N2 2.336(2), Ca1−O1 2.329(2), Ca1−O1′ 2.3408(14), Ca1−O2 2.382(2); Ca1′−O1−Ca1 106.39(6), N1−Ca1−N2 106.02(6), N1−Ca1−O1 66.13(6), N1−Ca1−O2 103.54(6), N2−Ca1−O1 145.18(6), N2−Ca1−O1′ 103.83(6), N2−Ca1−O2 113.18(7), O1−Ca1−O1′ 73.61(6), O1−Ca1−O2 101.57(6), O1−Ca1′−O2′ 89.09(6).

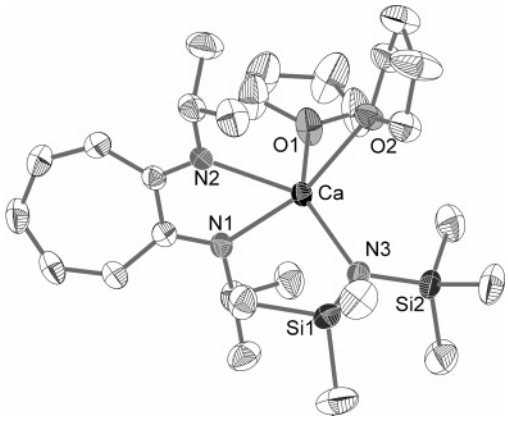


Figure 2. Perspective ORTEP view of the molecular structure of **3**. Thermal ellipsoids are drawn to encompass 50% probability. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): Ca−N1 2.408(2), Ca−N2 2.422(2), Ca−N3 2.336(2), Ca−O1 2.418(2), Ca−O2 2.438(2); N1−Ca−N2 68.03(6), N1−Ca−N3 103.92(7), N2−Ca−N3 127.46(7), N3−Ca−O1 137.90(7), O1−Ca−O2 80.96(6).

with dry, degassed aminoalkenes proceeds regiospecifically. It turned out that all substrates are converted to the cyclic product at mild reaction conditions. Using compound **3** as catalyst all substrates leading to five-membered rings (entries 1−5) could be cyclized in high yields with low catalyst loadings of 2 mol %. Substrates bearing bulky geminal substituents in the β-position to the amino group (Thorpe−Ingold effect)[10] could be cyclized within a few minutes (entries 1−3 and 6). Compound **2** shows a good catalytic activity for the less challenging substrates (entry 1) but clearly is significantly less active then **3**. We suggest that the dimeric compound **2** does not completely dissociate in solution, and thus the calcium atom is partly blocked. Most interesting is a comparison of **3** with the published compound **1**. It should be mentioned that only few catalytic results were reported for **1**. Since for compound **1** a 10 mol % loading of catalyst was reported, we first used a

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(9) Crystal data for **2** and **3**: **2**: space group $P\bar{1}$ (No. 2), a = 10.0537(6) Å, b = 12.5300(8) Å, c = 21.2668(12) Å, α = 86.150(5)°, β = 89.693(5)°, γ = 70.709(5)°, V = 2522.5(3) Å^3, T = 200 K, Z = 2, 18 565 reflections collected, 8825 independent reflections (R_{int} = 0.0290), R_1 = 0.0390 and wR_2 = 0.0983. **3**: space group $P2_1$ (No. 4), a = 9.9551(11) Å, b = 14.6826(13) Å, c = 11.242(2) Å, β = 96.457(11)°, V = 1632.6(4) Å^3, T = 200 K, Z = 2, 8379 reflections collected, 5041 independent reflections (R_{int} = 0.0253), R_1 = 0.0318 and wR_2 = 0.0717.

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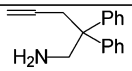
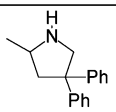
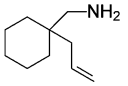
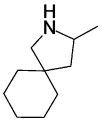
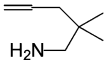
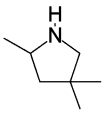
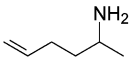
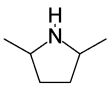
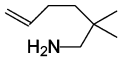
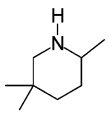
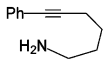
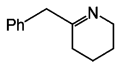
Table 1. Hydroamination/Cyclization Reaction of Terminal Aminoalkenes and Alkynes Catalyzed by 1−3[a]

Entry	Substrate	Product	Cat	mol% Cat	t	Yield
					h	%[b]
1			**1**	10	0.25	99[d]
			2	5	1	99
			3	10	0.25	99[c]
				2	1	99[c]
2			**2**	3	8	99
			3	2	0.6	99[c]
						93[e]
3			**1**	10	0.25	99[d]
			2	4	144	80
			3	10	3	99[c]
				2	3.5	>95[c]
4			**2**	8	48	30
					9	>90[f,g]
			3	8	35	>95[c,h]
				2	24	>90[h]
5			**1**	10	21	99[d]
			2	7	10	>80[i]
			3	10	40	>90[c]
				2	40	30
					9	>80[f]
6			**1**	20	6	86[d,f]
				10	72	85[d,f]
			2	10	48	>90[i]
			3	8	47	20[c]
					6	70[c,f]
					15	>90[c,f]
7			**3**	4	22	>90

[a] Reaction at room temperature in 0.7−0.8 mL of C_6D_6. [b]Calculated by ^{1}H NMR. [c]Ferrocene as additional internal standard. [d]Data taken from ref 5. [e]Isolated yield. [f]Reaction at 60 °C. [g]*cis*:*trans* ratio 3:7. [h]*cis*:*trans* ratio 1:4. [i]Reaction at 110 °C.

similar catalyst loading (entries 1, 3, 5, and 6). For both compounds **1** and **3** high rates were observed. For a 10 mol % loading of catalyst within the error range roughly the same turnover frequencies are observed for **1** and **3** using 1-amino-2,2-diphenylpent-4-ene (entry 1). By using less bulky substituents in the β-positions lower rates are observed for **3** in comparison to **1** (entries 3 and 5). Then, we lowered the catalyst concentration to 2 mol % for the cyclization of five-membered rings. Even under these conditions a slower but (almost) complete conversion was observed. By using the more challenging substrate 2,2-dimethyl-1-aminohex-5-ene (entry 6) a faster conversion is now observed for catalysts **3**. For compound **1** no reaction is seen at room temperature, and 6 h are need for 86% conversation at 60 °C using a catalyst loading of 20 mol %. By using a 10 mol % catalyst loading 72 h are needed to obtain 85% yield.[5] In contrast, by using compound **3** the reaction gives low yields at room temperature but more than 90% yield in 15 h at 60 °C by using only 8 mol % of catalyst loading, which is at least 5 times faster than the values reported for compound **1**. In contrast to previous reports on the catalytic intramolecular hydroamination/cyclization the conversion of aminoalkynes to the corresponding Schiff base was not as fast as expected (entry 7). Reaction yields were undertaken by *in situ* ^{1}H NMR spectroscopy. For some measurements ferrocene was used as internal standard. It could be shown that HN(SiMe$_3$)$_2$ was formed in stoichiometric ratios. We anticipate that the N(SiMe$_3$)$_2^-$ group of catalysts is protonated by the substrate in the initial step, forming a catalytically active species in which the substrate is bound as an amido group onto the Ca atom.

Unfortunately, only few data for the catalytic activity of compound **1** are available in the literature.[5] So far we believe that the difference in rate of compounds **1** and **3** is substrate dependent. Whereas compound **1** seems to be more active for the cyclization of some five-membered rings, compound **3** might be the more active catalyst for the cyclization of six-membered rings. In general it can be emphasized that calcium is, compared to other metal catalysts used for the hydroamination (especially platinum metals), inexpensive and nontoxic and thus offers potentially significant commercial advantages.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

Supporting Information Available: Experimental details and X-ray crystallographic files in CIF format for the structure determinations of **2** and **3** are available free of charge via the Internet at http://pubs.acs.org.

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