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Highly Atom Efficient Guanylation of both Aromatic and Secondary Amines Catalyzed by Simple Lanthanide Amides

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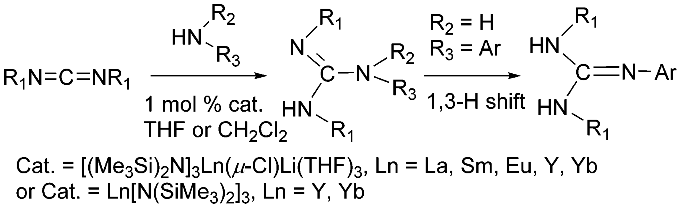

It is demonstrated that the cyclopentadienyl-free simple lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ (Ln = La, Sm, Eu, Y, Yb) and $Ln[N(SiMe_3)_2]_3$ (Ln = Y, Yb) are highly efficient catalysts for the guanylation of both aromatic and secondary amines with a high activity under mild conditions. It is found that these catalysts are compatible with a wide range of solvents and substrates.

Introduction

Catalytic formation of C−N bonds is an active subject in organic synthesis. Substituted guanidines are an important functionality in many biologically relevant compounds.[1] Guanidine derivatives have been widely used as ligands for the construction of a variety of organometallic catalysts containing early transition metals and lanthanides.[2] Aliphatic primary and some secondary amines can undergo direct guanylation with carbodiimides (RN═C═NR) to yield the corresponding *N*,*N*′,*N*″-trialkylguanidines.[3] To the best of our knowledge, only a few catalytic methods have been reported for the guanylation of either aromatic or secondary amines using a catalytic amount of the added bases. Guanylation of the aromatic amines catalyzed by lithium bis(trimethylsilyl) amide has been reported recently,[4] and the guanylation of both aromatic and secondary amines catalyzed by titanacarboranyl or transition-metal−imido complexes has been achieved.[5] The guanylation of secondary[6a] and aromatic[6b] amines with *N*,*N*′-dialkylcarbodiimides catalyzed by the half-sandwich yttrium alkyl compound $\{Me_2Si(C_5Me_4)(NPh)\}Y(CH_2SiMe_3)(THF)_2$ has been reported recently. We recently reported that the lanthanocene amides (EBI)LnN(TMS)$_2$ (EBI = ethylenebis(indenyl), TMS = trimethylsilyl) can be highly efficient catalysts for the addition of N−H bonds of amines and C−H bonds of terminal alkynes to carbodiimides.[6c] Guanylation of both aromatic and secondary amines catalyzed by cyclopentadienyl-free lanthanide amido complexes such as $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$[7] and $Ln[N(SiMe_3)_2]_3$[8] has not been reported so far.

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(1) (a) *Guanidines: Historical, Biological, Biochemical and Clinical Aspects of the Naturally Occurring Guanidino Compounds*; Mori, A., Cohen, B. D., Lowenthal, A., Eds.; Plenum Press: New York, 1985. (b) *Guanidines 2: Further Explorations of the Biological and Clinical Significance of Guanidino Compounds*; Mori, A., Cohen, B. D., Koide, H., Eds.; Plenum Press: New York, 1987.

(2) (a) Barker, J.; Kilner, M. *Coord. Chem. Rev.* **1994**, *133*, 219−300. (b) Rowley, C. N.; DiLabio, G. A.; Barry, S. T. *Inorg. Chem.* **2005**, *44*, 1983−1991 and references therein.

(3) (a) Tin, M. K. T.; Yap, G. P. A.; Richeson, D. S. *Inorg. Chem.* **1998**, *37*, 6728. (b) Molina, P.; Alajarín, M.; Sánchez-Andrada, P.; Sanz-Aparicio, J.; Martínez-Ripoll, M. *J. Org. Chem.* **1998**, *63*, 2922−2927. (c) Chinchilla, R.; Nájera, C.; Sánchez-Agulló, P. *Tetrahedron*: *Asymmetry* **1994**, *5*, 1393−1402.

(4) Ong, T.-G.; O'Brien, J. S.; Korobkov, I.; Richeson, D. S. *Organometallics* **2006**, *25*, 4728−4730.

(5) (a) Shen, H.; Chan, H.-S.; Xie, Z. *Organometallics* **2006**, *25*, 5515−5517. (b) Ong, T.-G.; Yap, G. P. A.; Richeson, D. S. *J. Am. Chem. Soc.* **2003**, *125*, 8100. (c) Montilla, F.; Pastor, A.; Galindo, A. *J. Organomet. Chem.* **2004**, *689*, 993.

(6) (a) Zhang, W.-X.; Nishiura, M.; Hou, Z. *Synlett* **2006**, *8*, 1213−1216. (b) Zhang, W.-X.; Nishiura, M.; Hou, Z. *Chem. Eur. J.* **2007**, *13*, 4037−4051. (c) Zhou, S.; Wang, S.; Yang, G.; Li, Q.; Zhang, L.; Yao, Z.; Zhou, Z.; Song, H. *Organometallics* **2007**, *26*, 3755.

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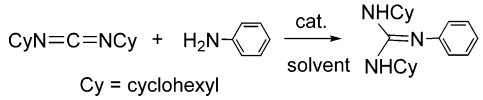
Lanthanide complexes have been shown to be catalysts or precatalysts for an efficient hydroamination of alkenes or alkynes, leading to the formation of new C−N bonds.[9] Since the pioneering work of Marks and co-workers on the catalytic activity of lanthanocene for intramolecular hydroaminations,[10] there has been a continuous interest in developing new catalytic systems to perform this sort of transformation.[11] This efficient process even has been used for the rapid synthesis of pharmaceutically active molecules by Molander and Pack.[12]

Lanthanide tris(silyl)amides, $Ln[N(TMS)_2]_3$, have been used for the first time by Livinghouse and co-workers[13] as nonmetallocene catalysts for the construction of C−N bonds for the cyclization of aminopentenes into pyrrolidines. Since this first report, a series of nonmetallocene catalysts have been developed and used for catalytic hydroamination reactions.[14] We have demonstrated that the lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-Cl})Li(THF)_3$ can initiate a Cannizzaro-type disproportionation of aromatic aldehydes to produce the corresponding amides and alcohols.[15]

In this paper, we will report that the lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-Cl})Li(THF)_3$[7] and $Ln[N(SiMe_3)_2]_3$[8] can be highly efficient catalysts for the guanylation of both aromatic and secondary amines with a high activity. These catalysts are compatible with a wide range of substrates and solvents.

TABLE 1. Reaction of Aniline with *N,N′*-Dicyclohexylcarbodiimide Catalyzed by $[(Me_3Si)_2N]_3Yb(\mu\text{-Cl})Li(THF)_3$[a]



entry	catalyst loading (mol %)	solvent	temp (°C)	time (h)	yield[b] (%)
1	10	THF	room temp	24	91
2	5	THF	room temp	24	92
3	3	THF	room temp	24	95
4	1	THF	room temp	24	95
5	0.5	THF	room temp	24	66
6	0	THF	0 or 60	24	0
7	1	toluene	room temp	24	97
8	1	Et_2O	room temp	24	96
9	1	*n*-hexane	room temp	24	96
10	1	CH_2Cl_2	room temp	24	99
11	1	THF	room temp	1	26
12	1	THF	room temp	2	61
13	1	THF	room temp	3	70
14	1	THF	room temp	6	97
15	1	THF	0	4	18
16	1	THF	30	4	92
17	1	THF	60	4	96

[a] The reaction was performed by treating 1 equiv of aniline with 1 equiv of *N,N′*-dicyclohexylcarbodiimide with $[(Me_3Si)_2N]_3Yb(\mu\text{-Cl})Li(THF)_3$ as the catalyst. [b] Isolated yield.

Results and Discussion

The catalytic activity of the lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-Cl})Li(THF)_3$ for the guanylation of aromatic amines was investigated by performing the reaction of the aniline with *N,N′*-dicyclohexylcarbodiimide using a catalytic amount of $[(Me_3Si)_2N]_3Yb(\mu\text{-Cl})Li(THF)_3$ in THF as a test reaction. The results are given in Table 1.

It is interesting to find that the guanylation reaction can proceed efficiently, and excellent yields (>90%) of the product were obtained using a catalyst loading ranging between 10 and 1 mol % (Table 1, entries 1−4). When the catalyst loading was 0.5 mol %, the yield of product decreased dramaticatlly from over 90% to 66% (Table 1, entry 5), and no guanylation product could be isolated in the absence of catalyst at both 0 and 60 °C (Table 1, entry 6). Therefore, a catalyst loading of 1 mol % was selected for the following experiments.

It is notable that the catalyst is compatible with a variety of solvents such as toluene, diethyl ether, *n*-hexane, and CH_2Cl_2, and high product yields (>95%; Table 1, entries 4 and 7−10) can be obtained using the ytterbium amide as a catalyst. The reaction temperature has a strong influence on the outcome of the reaction (experiments 14−16). Only an 18% isolated yield of product was obtained in 4 h when the reaction was performed at 0 °C (Table 1, entry 15), a 97% yield of product was obtained when the reaction was performed in THF for 6 h at room temperature (Table 1, entry 14), and a 96% yield of product was obtained in 4 h when the reaction temperature was raised to 60 °C (Table 1, entry 17). Thus, the following standard reaction conditions were used for carrying out the studies: 1 equiv of aniline was reacted with 1 equiv of carbodiimide in the presence of 1 mol % of catalyst in THF at 60 °C.

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(7) Zhou, S.; Wang, S.; Yang, G.; Liu, X.; Sheng, E.; Zhang, K.; Cheng, L.; Huang, Z. *Polyhedron* **2003**, *22*, 1019.

(8) (a) Schuetz, S. A.; Day, V. W.; Sommer, R. D.; Rheingold, A. L.; Belot, J. A. *Inorg. Chem.* **2001**, *40*, 5292−5295. (b) Bradley, D. C.; Ghotra, J. S.; Hart, F. A. *J. Chem. Soc., Dalton Trans.* **1973**, 1021−1023. (c) Alyea, E. C.; Bradley, D. C.; Copperthwaite, R. G. *J. Chem. Soc., Dalton Trans.* **1972**, 1580−1584.

(9) For general reviews on hydroamination reactions, see: (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675−703. (b) Nobis, M.; Driessen-Hölscher, B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3983−3985. (c) Brunet, J. J.; Neibecker, D. In *Catalytic Heterofunctionalization from Hydroamination to Hydrozirconation*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001; pp 91−141. (d) Roesky, P. W.; Müller, T. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 2708−2710. (e) Pohlki, F.; Doye, S. *Chem. Soc. Rev.* **2003**, *32*, 104−114. (f) Beller, M.; Tillack, A.; Seayad, J. In *Transition Metals for Organic Synthesis*, 2nd ed.; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 2, pp 403−414.

(10) (a) Gagné, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *118*, 275−294. (b) Zhao, J.; Marks, T. J. *Organometallics* **2006**, *25*, 4763−4772 and references therein.

(11) (a) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673−686. (b) Hultzsch, K. C. *Adv. Synth. Catal.* **2005**, *347*, 367−391. (c) Hultzsch, K. C.; Gribkov, D. V.; Hampel, F. *J. Organomet. Chem.* **2005**, *690*, 4441−4452. (d) Zhao, J.; Marks, T. J. *Organometallics* **2006**, *25*, 4763−4772. (e) Motta, A.; Fragalà, I. L.; Marks, T. J. *Organometallics* **2006**, *25*, 5533−5539 and references therein.

(12) Molander, G. A.; Pack, S. K. *J. Org. Chem.* **2003**, *68*, 9214−9220 and references therein.

(13) (a) Kim, Y. K.; Livinghouse, T.; Bercaw, J. E. *Tetrahedron Lett.* **2001**, *42*, 2933−2935. (b) Kim, Y. K.; Livinghouse, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 3645−3647.

(14) (a) Riegert, D.; Collin, J.; Meddour, A.; Schulz, E.; Trifonov, A. *J. Org. Chem.* **2006**, *71*, 2514−2517. (b) Kim, J. Y.; Livinghouse, T. *Org. Lett.* **2005**, *7*, 4391. (c) Kim, J. Y.; Livinghouse, T. *Org. Lett.* **2005**, *7*, 1737. (d) Kim, Y. K.; Livinghouse, T.; Horino, Y. *J. Am. Chem. Soc.* **2003**, *125*, 9560. (e) Kim, H.; Livinghouse, T.; Shim, J. H.; Lee, S. G.; Lee, P. *Adv. Synth. Catal.* **2006**, *348*, 701−704. (f) O'Shaughnessy, P. N.; Scott, P. *Tetrahedron: Asymmetry* **2003**, *14*, 1979−1983. (g) O'Shaughnessy, P. N.; Knight, P. D.; Morton, C.; Gillepsie, K. M.; Scott, P. *Chem. Commun.* **2003**, 1770−1771. (h) O'Shaughnessy, P. N.; Gillepsie, K. M.; Knight, P. D.; Munslow, I.; Scott, P. *Dalton Trans.* **2004**, 2251−2256. (i) Knight, P. D.; Munslow, I.; O'Shaughnessy, P. N.; Scott, P. *Chem. Commun.* **2004**, 894−895. (j) Hong, S.; Tian, S.; Metz, M. V.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 14768−14783. (k) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *Chem. Eur. J.* **2003**, *9*, 4796−4810. (l) Gribkov, D. V.; Hultzsch, K. C. *Chem. Commun.* **2004**, 730−731. (m) Gribkov, D. V.; Hampel, F.; Hultzsch, K. C. *Eur. J. Inorg. Chem.* **2004**, 4091−4101. (n) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748−3759.

(15) Zhang, L.; Wang, S.; Zhou, S.; Yang, G.; Sheng, E. *J. Org. Chem.* **2006**, *71*, 3149.

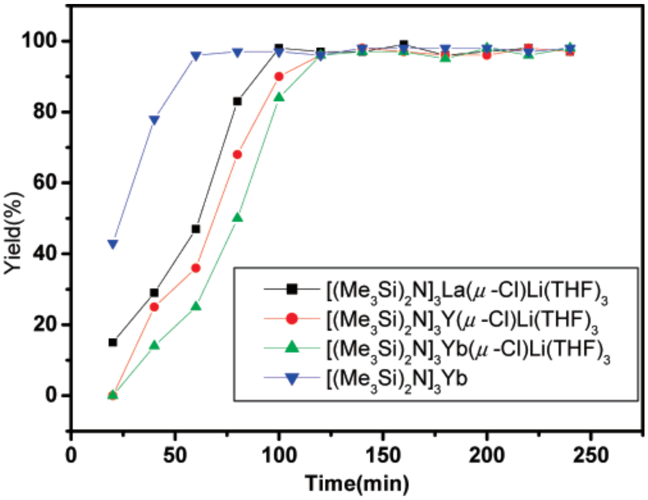


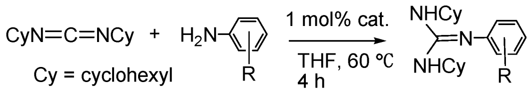
FIGURE 1. Plot of the yield of guanidine versus reaction time. The reaction was performed by treating 1 equiv of aniline with 1 equiv of *N,N′*-dicyclohexylcarbodiimide.

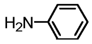
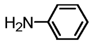
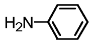
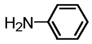
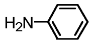
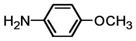
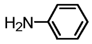
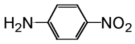
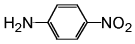
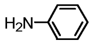
Figure 1 shows the yields of guanidine product from the reaction of aniline with *N,N′*-dicyclohexylcarbodiimide versus reaction time catalyzed by different lanthanide amides (Table 4 in the Supporting Information gives the detailed results). From the figure, we can see that both $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ (Ln = La, Y, Yb) and $[(Me_3Si)_2N]_3Yb$ can catalyze the reaction with high efficiency. Product yields of 98% and 96% could be isolated in 100 or 120 min when the lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ (Ln = La, Y, Yb) were used as catalysts, indicating that the ionic radii of the lanthanide metals have little influence on the guanylation reaction. When $[(Me_3Si)_2N]_3Yb$ was used as the catalyst, a 96% yield of product was obtained in 60 min. Considering the different electronic and steric effects of the substrates, the standard reaction time was selected as 4 h for the following studies for comparison.

Examination of the catalytic activity of another lanthanide amide, $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ (Table 2), on the reactions of aniline with *N,N′*-dicyclohexylcarbodiimide under the selected standard conditions also showed high isolated yields of products, indicating that the ionic radii of the rare-earth metals have little influence on the catalytic activity of the catalysts. Examination of the catalytic activity of $Yb[N(SiMe_3)_2]_3$ or $Y[N(SiMe_3)_2]_3$, the sublimate of their corresponding amides $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$, on the reaction of anilines with electron-donating substituents or with electron-withdrawing substituents such as 4-methoxyaniline, aniline, and 4-nitroaniline with *N,N′*-dicyclohexylcarbodiimide under standard conditions produced the corresponding guanidines in 96%, 98%, and 93% isolated yields (Table 2, entries 6−8), suggesting that the sublimates obtained from the lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ can be highly efficient catalysts for the guanylation reaction. The catalytic activities of lanthanide amides on the guanylation is comparable to that of the lithium amide $LiN(TMS)_2$ (Table 2, entry 10).[4]

The ionic radii of the lanthanides used as catalysts and the types of the lanthanide amides have little influence on the outcome of the guanylation reaction. The more easily available complex $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$, with the smallest ionic radius of the metal, was selected as the catalyst of choice for the following experiments to study the steric effects of the substrates and the scope of the guanylation reaction. A variety of aromatic amines and secondary amines were evaluated under the optimized reaction conditions. The results are presented in Table 3. In general, the reactions proceed smoothly to afford the guanylation products with excellent isolated yields both in THF and in CH_2Cl_2, regardless of the electronic nature or steric effects of the substituents on the aryl groups. The catalyst is compatible with a wide range of substituents on the phenyl ring. These substituents can be electron-donating groups, for example, CH_3O, CH_3, and *i*-Pr, or elelctron-withdrawing groups, for example, Cl, Br, and O_2N. The catalytic activity of the ytterbium amide is comparable to that of the half-sandwich yttrium alkyl complex.[6a,6b] The steric bulk of the amines has a great influence on the catalytic reaction; for example, reactions of 4-isopropylaniline with carbodiimides produced almost quantitative amounts of the product in 4 h using either THF or CH_2Cl_2 as a solvent (Table 3, entries 10 and 11). The interactions of 2,6-diisopropylaniline with carbodiimides gave only 62% and 71% yields of the corresponding products, even after 12 h (Table 3, entries 21 and 22). The reactions required 24 h for completion (Table 3, entries 21 and 22). These results showed that the cyclopentadienyl-free lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ exhibited a higher catalytic activity toward the guanylation reaction than the lanthanocene amides $(EBI)Ln(TMS)_2$. The reactions catalyzed by the lanthanocene amides $(EBI)Ln(TMS)_2$ gave only 81−85% yields of product, even at 110 °C for 24 h.[6c] The above observation is also in accordance with the results obtained for the reactions of 2-nitroaniline or 4-nitroaniline with carbodiimides (Table 3, entries 28−31). The reactions of 4-nitroaniline with carbodiimides required 4 h, while the reaction of 2-nitroaniline with carbodiimides required 24 h to be finished.

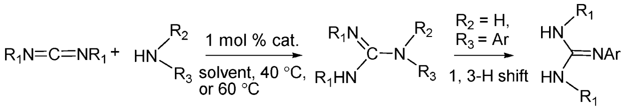
TABLE 2. Reaction of Aniline with *N,N′*-Dicyclohexylcarbodiimide Catalyzed by Different Lanthanide Amides[a]

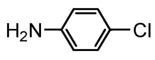
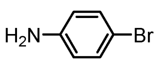
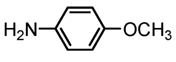
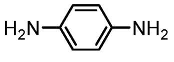
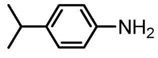
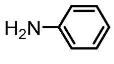
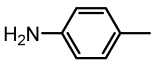
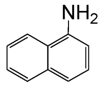
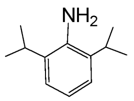
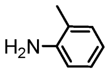
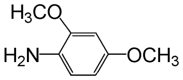
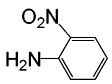
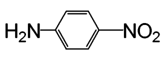
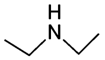
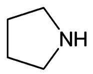
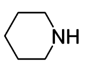
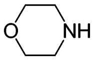


entry	catalyst	ArNH2	yield[b]
1	$[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$		98
2	$[(Me_3Si)_2N]_3Y(\mu\text{-}Cl)Li(THF)_3$		97
3	$[(Me_3Si)_2N]_3Eu(\mu\text{-}Cl)Li(THF)_3$		96
4	$[(Me_3Si)_2N]_3Sm(\mu\text{-}Cl)Li(THF)_3$		98
5	$[(Me_3Si)_2N]_3La(\mu\text{-}Cl)Li(THF)_3$		97
6	$[(Me_3Si)_2N]_3Yb$		96
7	$[(Me_3Si)_2N]_3Yb$		98
8	$[(Me_3Si)_2N]_3Yb$		93
9	$[(Me_3Si)_2N]_3Y$		89
10	$(Me_3Si)_2NLi$		97[c]

[a] The reaction was performed by treating 1 equiv of anilines with 1 equiv of *N,N′*-dicyclohexylcarbodiimide under the given conditions. [b] Isolated yield. [c] The reaction was run in CH_2Cl_2 at 40 °C.

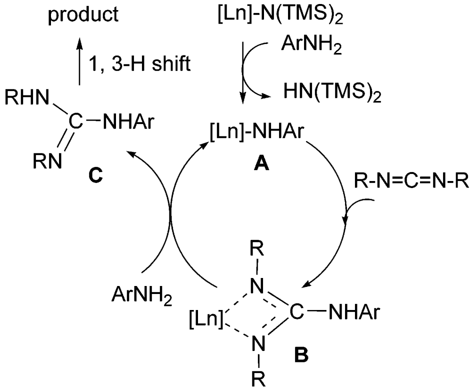
TABLE 3. Results of Reactions of Different Anilines with Carbodiimides Catalyzed by $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$



entry	R_1[a]	R_2R_3NH	product	yield (%)[b]
1	*i*-Pr		**1**	93
2	Cy		**2**	98
3	*t*-Bu		**3**	95
4	*i*-Pr		**4**	89 (88[c])
5	Cy		**5**	93 (98[c])
6	*i*-Pr		**6**	91 (91[c])
7	Cy		**7**	94 (97[c])
8	*i*-Pr		**8**	97[d]
9	Cy		**9**	96[d]
10	*i*-Pr		**10**	98 (92[c])
11	Cy		**11**	95 (99[c])
12	*i*-Pr		**12**	95 (97[c])
13	Cy		**13**	96 (85[c])
14	*t*-Bu		**14**	93
15	*i*-Pr		**15**	99
16	Cy		**16**	87
17	*t*-Bu		**17**	95
18	4-MeC_6H_4		**18**	86
19	*i*-Pr		**19**	95[e]
20	Cy		**20**	96[e]
21	*i*-Pr		**21**	62[e] (98[f])
22	Cy		**22**	71[e] (99[f])
23	*t*-Bu			0
24	*i*-Pr		**23**	96
25	Cy		**24**	85
26	*i*-Pr		**25**	98
27	Cy		**26**	96
28	*i*-Pr		**27**	62[e] (85[f])
29	Cy		**28**	76[e] (90[f])
30	*i*-Pr		**29**	90
31	Cy		**30**	94
32	*i*-Pr		**31**	60 (96[g])
33	Cy		**32**	85 (97[g])
34	*i*-Pr		**33**	99
35	Cy		**34**	96
36	*i*-Pr		**35**	96
37	Cy		**36**	95
38	*i*-Pr		**37**	95
39	Cy		**38**	90

[a] Legend: Cy = cyclohexyl, *i*-Pr = isopropyl, *t*-Bu = *tert*-butyl. [b] Isolated yield; the reaction was run in THF at 60 °C for 4 h unless otherwise noted. [c] The reaction was run in CH_2Cl_2 at 40 °C for 4 h. [d] Isolated as the bis-guanylation product. [e] The reactions were run in THF at 60 °C for 12 h. [f] The reactions were run in THF at 60 °C for 24 h. [g] Isolated yield by running the reaction in THF at 60 °C for 6 h.

SCHEME 1. Proposed Mechanism for the Guanylation Reaction



The evidence that the ytterbium amide $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$ can catalyze the reactions of 2-nitroaniline and 4-nitroaniline with carbodiimides further suggested that cyclopentadienyl-free lanthanide amides are more active than the lanthanocene amides $(EBI)Ln(TMS)_2$, as the latter cannot catalyze those reactions.[6c] The steric bulk of the substituents on the carbodiimides has little influence on the outcome of the reaction: treatment of the sterically more hindered *N*,*N*′-di-*tert*-butylcarbodiimide with 4-chloroaniline, aniline, and 4-methylaniline produced the corresponding products in high isolated yields (Table 3, entries 3, 14, and 17). However, when the sterically more hindered 2,6-diisopropylaniline reacted with the sterically more hindered *N*,*N*′-di-*tert*-butylcarbodiimides, no product could be isolated, even after running the reaction in THF at 60 °C for 24 h (Table 3, entry 23), indicating that the combined steric effect of both substrates has a strong influence on the result of the reaction.

From Table 3, we can see that electronic effects have little influence on the reaction. Comparing the influence of electron-withdrawing groups such as Cl, Br, and O_2N shows only a minor influence on the outcome of the reaction. High yields of products can be isolated from the reactions of 4-chloroaniline, 4-bromoaniline, and 4-nitroaniline with carbodiimides in 4 h (Table 3, entries 1−5, 30, 31). The fact that reactions of 1-naphthylamine with carbodiimides (Table 3, entries 19 and 20) required reaction times longer than those of reactions of aniline with carbodiimides (Table 3, entries 12 and 13) may be due to the combined steric and electronic effects. Treatment of 4-methylaniline with *N*,*N*′-bis(4-methylphenyl)carbodiimide gave a satisfactory yield of the product (Table 3, entry 18).

From Table 2 (entries 6−8), Figure 1, and Table 3 (entries 7, 13, and 31), we can see that the catalytic activity of $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$ is comparable with that of its sublimate $Yb[N(SiMe_3)_2]_3$. These results suggest that either the ate complexes $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ or the sublimates of their neutral complexes $Ln[(N(SiMe_3)_2]_3$ can be highly efficient catalysts for the guanylation reaction.

Comparing the reactivities of different secondary amines with carbodiimides catalyzed by the ytterbium amide $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$ did not show any influence on the outcome of the experiments (Table 3, entries 32−39), indicating that the catalyst is compatible with a wide range of substrates of amines. The reactions of secondary amines with carbodiimides catalyzed by the lanthanocene amides required at least 24 h at 110 °C for completion.[6c] These results also showed the advantages of the simple lanthanide amides over the lanthanocene amides.

We propose the following reaction mechanism (Scheme 1). Reaction of the amines or anilines with the lanthanide amides gave the new amido intermediate **A** through an acid−base reaction.[8] The postulated intermediate **A** reacts with the carbodiimides, producing the metal guanidinate species **B** through an insertion process.[6,16] Interaction of the guanidinate intermediate **B** with the amines[3] afforded the guanylation products and the re-formed amido intermediate **A**, closing the catalytic cycle.

Conclusions

In summary, we have developed a new, highly efficient method for the synthesis of guanidines having different substituents using the cyclopentadienyl-free simple lanthanide amides $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ and $Ln[(N(SiMe_3)_2]_3$ as catalysts. This methodology has the advantages of easy availability of the catalysts, low catalyst loading, high conversion of reactants to products, mild reaction conditions, and compatibility with a wide range of solvents and substrates. Results indicated that the electronic and steric effects of the substituents have only a minor influence on the outcome of the reactions. Extensive studies are now in progress in our laboratory.

Experimental Section

General Procedure for the Direct Synthesis of Guanidines from the Reaction of Aromatic Amines with Carbodiimides Catalyzed by $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ (12 as an Example). A 30 mL Schlenk tube under dried argon was charged with the ytterbium amide $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$ (0.087 g, 0.095 mmol). To the flask were added *N*,*N*′-diisopropylcarbodiimide (1.200 g, 9.5 mmol), aniline (0.885 g, 9.5 mmol), and the solvent (5 mL). The resulting mixture was stirred at 60 °C for a fixed interval. The reaction mixture was then hydrolyzed with water (1 mL) and extracted with dichloromethane (3 × 10 mL), and the extracts were dried over anhydrous Na_2SO_4 and filtered. After the solvent was removed under reduced pressure, the final product could be obtained by washing the crude product with 10 mL of diethyl ether. ^{1}H NMR ($CDCl_3$): δ 7.18 (m, 2H), 6.87 (m, 1H), 6.80 (d, J = 7.6 Hz, 2H), 3.71 (br, 2H), 3.53 (br, 2H), 1.11 (d, J = 6.2 Hz, 12H). ^{13}C NMR ($CDCl_3$): δ 149.9, 149.8, 128.9, 123.2, 121.0, 42.8, 23.0.

General Procedure for the Direct Synthesis of Guanidines from Reaction of Secondary Amines with Carbodiimides Catalyzed by $[(Me_3Si)_2N]_3Ln(\mu\text{-}Cl)Li(THF)_3$ (34 as an Example). A 30 mL Schlenk tube was charged with the ytterbium amide $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$ (0.065 g, 0.071 mmol) under dried argon. To the flask were added *N*,*N*′-dicyclohexylcarbodiimide (1.465 g, 7.1 mmol), pyrrolidine (0.505 g, 7.1 mmol), and THF (5 mL). The resulting mixture was stirred at 60 °C for a fixed interval. After the solvent was removed under reduced pressure, the residue was extracted with hexane (3 × 15 mL) and the extracts were filtered to give a clean solution. After the solvent was removed under vacuum, the final product was obtained. ^{1}H NMR ($CDCl_3$): δ 3.19 (br, 4H), 2.90 (br, 2H), 1.74−1.18 (m, 24H). ^{13}C NMR ($CDCl_3$): δ 153.1, 54.5, 47.5, 34.8, 25.4, 25.2, 24.8.

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Supporting Information Available: Text and figures giving general methods, data, and spectra of the corresponding compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[16] The stoichiometric insertion of carbodiimides into the Ln−N bond has been reported. See: Zhang, J.; Cai, R.; Weng, L.; Zhou, X. *Organometallics* **2004**, *23*, 3303−3308.