Tetrahedron 67 (2011) 8790–8799

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Heterobimetallic dianionic guanidinate complexes of lanthanide and lithium: highly efficient precatalysts for catalytic addition of amines to carbodiimides to synthesize guanidines

Xingmin Zhang[a], Chuanyong Wang[a], Cunwei Qian[a], Fubin Han[a], Fan Xu[a], Qi Shen[a,b,*]

[a] *College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, People's Republic of China*
[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, People's Republic of China*

ARTICLE INFO

Article history:
Received 24 June 2011
Received in revised form 19 August 2011
Accepted 26 August 2011
Available online 30 August 2011

Keywords:
Heterobimetallic complexes
Catalysis
Addition
Guanidines

ABSTRACT

A series of heterobimetallic dianionic guanidinate complexes of lanthanide and lithium, $[\mathrm{Li(THF)(DME)}]_3\mathrm{Ln}[\mu\text{-}\eta^2\eta^1(^i\mathrm{PrN})_2\mathrm{C(NC_6H_4}p\text{-R)}]_3$ [R=Cl, Ln=Nd (**I**), Y (**II**), La (**III**); R=H, Ln=Nd (**IV**)] were synthesized and fully characterized. These complexes were found to be highly efficient precatalysts for the addition of various primary and secondary amines, and aromatic and aliphatic diamines to carbodiimides to give the corresponding monoguanidine and biguanidine derivatives under mild condition (at 25–60 °C), which provides an efficient way for the synthesis of biguanidines compounds. The activity depends on the central metals and ligands: La>Nd>Y for the metals and $[(^i\mathrm{PrN})_2\mathrm{C(NC_6H_4}p\text{-Cl)}]^{2-} > [(^i\mathrm{PrN})_2\mathrm{C(NC_6H_5)}]^{2-}$ for the ligands were observed.

1. Introduction

The synthesis of guanidines is of significant importance in organic synthesis because guanidines are important structural motifs found in many biologically and pharmaceutically active compounds[1] and can serve as base catalysts in organic synthesis.[2] Besides, guanidines can also be used as ancillary ligands in the preparation of a variety of metal complexes, including those of the main, transition and lanthanides metals.[3] An addition of amine to carbodiimide provides a convenient and atom-economical approach to multisubstituted guanidines. However, the addition reaction without a catalyst requires harsh condition.[4] Recently, imido complexes of titanium and vanadium,[3k,5] were reported to be highly active catalysts for the addition of primary aromatic amines to carbodiimides, but not for that with secondary amines, as the active species in that process is an imido intermediate. Amide complexes of metals including $\mathrm{LiN(SiMe_3)_2}$,[6] lanthanide amides[7] and titanacarborane amide,[8] and alkyl complexes of metals, such as half-sandwich lanthanide alkyl complexes,[9] and commercial available alkyl metal complexes $\mathrm{ZnEt_2}$, $\mathrm{MgBu_2}$, *n*-BuLi,[10a] $\mathrm{AlR_3}$,[10b] and $\mathrm{Zn(OTf)_2}$[10c] were explored to be the efficient catalysts with a wide scope of amines including primary aromatic amines and aliphatic secondary amines. Divalent lanthanide complexes[11] and ytterbium triflate[12] are also found to be the efficient catalysts for addition of primary and secondary amines to carbodiimides. Nevertheless, the guanylation reactions with secondary aliphatic amines catalyzed by all these catalysts reported still need to elevate reaction temperature and/or prolong reaction time.[7–12] Because secondary amines are generally less active than primary amines toward carbodiimides.

Biguanidines could serve as useful templates for the construction of further larger molecules, or as ligands for the synthesis of metal complexes with constrained geometry.[13] However, the catalytic reaction of diamines with carbodiimides to multisubstituted biguanidines has been limited. Only a few examples were found in the literatures till now.[7b,8,9,13] The reaction of 1,3-diaminobenzene with 2 equiv of $^i\mathrm{PrN{=}C{=}N}^i\mathrm{Pr}$ was reported to give quantitatively the corresponding biguanidine compound with 1 mol % of a half-sandwich yttrium alkyl complex at 80 °C for 1 h.[9] The catalytic addition of 1,4-diaminobenzene to $^i\mathrm{PrN{=}C{=}N}^i\mathrm{Pr}$ catalyzed by 3–5 mol % of half-sandwich titanacarborane amide complex at 110 °C for 6 h[8] and by 1 mol % of lanthanide amide complex at 60 °C for 4 h,[7b] respectively, afforded the 1,4-diguanidinobenzene in excellent yield. Ethylenediamine could react with $^i\mathrm{PrN{=}C{=}N}^i\mathrm{Pr}$ at 100 °C in the absence of a catalyst, however, only 60% of the biguanidine was obtained after 18 h.[13] Thus, the design of efficient catalysts capable of promoting addition of secondary aliphatic amines and diamines including aromatic and aliphatic diamines to carbodiimides under mild conditions is still required. Recently, we have reported that the heterobimetallic lanthanide and lithium

---

[*] Corresponding author. E-mail address: qshen@suda.edu.cn (Q. Shen).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.08.072

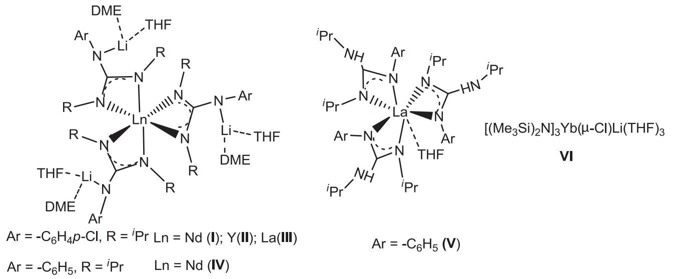


Fig. 1. Lanthanide complexes **I**–**VI**.

complexes supported by dianionic guanidinate ligands are highly efficient catalysts for addition of amines to aldehydes under mild conditions,[14] and the activity is much higher than that of the corresponding monometallic triguanidinate lanthanide complexes.[15] In continuation of our study on the reactivity of these heterobimetallic complexes, we have found that the complexes are extremely high active precatalysts for addition of amines to carbodiimides. The reactions with secondary amines can be carried out at 25 °C even with 0.5% catalyst loading. The catalytic double addition of aromatic diamines to carbodiimides afforded the corresponding biguanidines in almost quantitative yield at 25 °C, and the reactions with aliphatic diamines can proceed at 40–60 °C to give the corresponding biguanidines in excellent yield. Here we report the results.

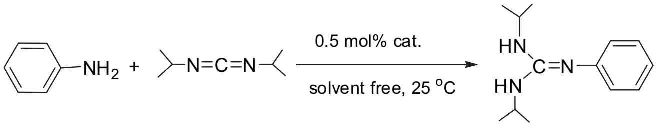
2. Results and discussion

Complexes **I**–**VI** (Fig. 1) were synthesized by the reported procedure.[14,15] New complexes **III** and **IV** were fully characterized including single-crystal structure analysis. Their molecular structures were quite similar to that of the analogous **I** reported previously.[14]

With these complexes in hand the reaction of $PhNH_2$ with $^{i}Pr_2N{=}C{=}N^{i}Pr_2$ was examined as model reaction at 25 °C under solvent-free condition. We were pleased to see that an addition of 0.5 mol % of **I** led to rapid addition of aniline to $^{i}PrN{=}C{=}N^{i}Pr$ to give **1** quantitatively after 30 min (Table 1, entry 3). In contrast, the same addition reaction did not occur without the presence of a catalyst (Table 1, entry 12). The other heterobimetallic complexes **II**–**IV** were also effective in this reaction to give **1** quantitatively (Table 1, entries 4–6). The reaction with these precatalysts could still proceed smoothly even when the catalyst loading decreased to 0.1 mol % (Table 1, entries 7–10). However, the differences in activity among them were observed. The active sequence is Y<Nd<La for the center metals (Table 1, entries 7–9), which is consistent with the order of the ionic radius, and $[(^{i}PrN)_2C(NC_6H_5)]^{2-} < [(^{i}PrN)_2C(NC_6H_4p\text{-}Cl)]^{2-}$ for the ligands (Table 1, entries 7 and 10). In comparison, the same reaction with monometallic trisguanidinate lanthanum complex was tested. As shown in Table 1 (entry 11), **V** could serve as a precatalyst to afford **1** in 75% yield after 30 min, when the catalyst loading increased to 2 mol %. Obviously, the activity of monometallic guanidinate complex is much lower than those of heterobimetallic complexes.

Table 1

Catalytic addition of aniline to *N,N′*-diisopropylcarbodiimide by complexes **I**–**V**[a]



Entry	Cat.	Catalyst loading (mol %)	Time (min)	Yield[b] (%)
1	**I**	2	30	>99
2	**I**	1	30	>99
3	**I**	0.5	30	>99
4	**II**	0.5	30	>99
5	**III**	0.5	30	>99
6	**IV**	0.5	30	98
7	**I**	0.1	10	90
8	**II**	0.1	10	85
9	**III**	0.1	10	93
10	**IV**	0.1	10	70
11	**V**	2	30	75
12	—	—	30	—

[a] The reaction was performed by treating 1 equiv of amine with 1 equiv of carbodiimide.

[b] Isolated yields.

Complex **III** was then chosen as a precatalyst for the addition reaction of various aromatic primary amines to carbodiimides. Representative results are summarized in Table 2. As shown in Table 2, **III** is a very robust and efficient precatalyst, which showed good functional group tolerance. The reaction was not influenced by either electron-withdrawing or electron-donating substituents or the position of the substituents at the phenyl ring (Table 2, entries 1–14). Aromatic C–F and C–Cl bond at the phenyl ring remained unchanged in the present reactions (Table 2, entries 3–6 and 12). The reaction with a steric bulky amine also went smoothly at 25 °C. For example, in the presence of 0.5 mol % of **III**, the addition reaction of 2,6-diisopropylaniline to $^{i}PrN{=}C{=}N^{i}Pr$ gave the guanidine compound **14** in 85% yield at 25 °C and in 97% yield at 50 °C for 5 h (Table 2, entry 14). Even the less reactive $n\text{-}BuNH_2$ could also add to $^{i}PrN{=}C{=}N^{i}Pr$ using 0.5 mol % of **III** to yield the desired product **15** in good yield at 25 °C for 5 h and in excellent yield at 50 °C for 5 h (Table 2, entry 15).

Secondary amines are well-known to be less reactive than primary amines toward carbodiimides. However, in the presence of 0.5 mol % of **III**, various cyclic secondary amines could react with $^{i}PrN{=}C{=}N^{i}Pr$ and CyN=C=NCy at 25 °C affording the corresponding tetrasubstituted guanidines in good to excellent yields after 2 h, depending on the amines (Table 2, entries 16–18 and 20–22). The yields can be improved when the same addition reactions were carried out at 50 °C (Table 2, entries 16, 17, 20, and 22). The addition reaction of methylbenzylamine to $^{i}PrN{=}C{=}N^{i}Pr$ could also give the guanidine compound **22** in 89% yield at 25 °C and in 97% yield at 50 °C for 2 h (Table 2, entry 23). In comparison, the addition reaction of piperidine to $^{i}PrN{=}C{=}N^{i}Pr$ with ytterbium amide complex **VI** was conducted and the reaction went sluggishly under the same conditions (Table 2, entry 19) indicating the activity of bimetallic complex **III** is much higher than that of the monometallic lanthanide amide complex **VI**.

A double catalytic addition reaction of diamines to 2 equiv of carbodiimides is a direct method to biguanidines. To explore the application of the present complexes in the synthesis of biguanidines compounds, the addition of 1,4-diaminobenzene with 2 equiv of $^{i}PrN{=}C{=}N^{i}Pr$ was then tried using 0.5 mol % of **III** at 25 °C, as the same reaction was reported to proceed under heating condition (at 60 °C using 1 mol % of lanthanide amide $[(Me_3Si)_2N]_3Yb(\mu\text{-}Cl)Li(THF)_3$[7b] and at 110 °C with 3–5 mol % of half-sandwich titanacarborane amide complex).[8] The reaction went smoothly and was completed for 2 h to afford quantitatively the corresponding biguanidine compound **23** (Table 3, entry 1). The result promoted us to examine the scope of diamines. As shown in Table 3 various aromatic diamines can be applied in the double addition reaction. The activity is not influenced by the position of the two amino groups on the phenyl ring. For example, all the addition reactions of diaminobenzene to $^{i}PrN{=}C{=}N^{i}Pr$, including 1,4-diaminobenzene, 1,3-diaminobenzene, and 1,2-diaminobenzene, could be carried out at 25 °C and was completed within 2 h to afford the corresponding biguanidines compounds **23**, **25**, and **27** in almost quantitative yields with a catalyst loading of 0.5 mol % (Table 3, entries 1, 3, and 5).