Use of Vanadium Complexes as Catalysts in the Synthesis of Guanidines: New Experimental Data and DFT Analysis of the Carbodiimide Interaction with the Catalyst

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The activity of several imido vanadium complexes as catalysts of the guanylation reaction was studied. Complex V(N-2,6-$^{i}Pr_2C_6H_3$)Cl_3, **1**, was found to be an efficient precatalyst for the reaction between carbodiimides and both primary and secondary aryl amines to give the corresponding guanidines **2**−**6**. Two possible pathways for the reaction were considered for a DFT study: (i) [2+2] carbodiimide addition to the vanadium−imido bond, a mechanism previously ascertained by Richeson and co-workers for the synthesis of guanidines catalyzed by titanium imido compounds (*J. Am. Chem. Soc.* **2003**, *125*, 8100); and, alternatively, (ii) carbodiimide insertion into the vanadium−amido bond, which would be formed in situ by the interaction of the amine reagent with **1**. First, the titanium-catalyzed reaction, using $\{(Me_2N)C(NMe)_2\}_2Ti(=NMe)$ (**A**) as a model complex, was studied. Second, two different vanadium model complexes, $V(=NMe)Cl_3$ (**B**) and $V(=NMe)(NMe_2)Cl_2$ (**C**), were considered for the guanylation. Noticeably, whereas for model **A** the [2+2] carbodiimide addition to the metal−imido bond was an exergonic process, for model **B** the same pathway was not exergonic and gave a much higher activation barrier than that computed for **A**. Finally, the two pathways were investigated with model **C**, containing both imido and amido functionalities. The results show that for vanadium-catalyzed guanylation reactions the carbodiimide insertion into the metal−amido bond is favorable with respect to the carbodiimide addition to the metal−imido bond, which is the mechanism operative for titanium.

Introduction

The guanidine core is present in a good number of chemicals with significant biological and pharmaceutical importance.[1] Additionally, neutral guanidines and guanidinate(1−) and guanidinate(2−) anions have recently attracted increased attention as versatile ligands in coordination chemistry.[2] Consequently, much effort has been directed toward efficient synthesis of this type of compounds.[3] Most synthetic methods involve the reaction of an amine with a guanylating reagent.[4] One of the guanylation reagents commonly employed is carbodiimide, and several processes are known to yield different substituted guanidines through direct reaction between amines and carbodiimides.[4,5] However, in some cases the participation of a metal complex, acting as active catalyst for the guanylation reaction, is necessary. For instance, Richeson et al. have recently shown the first example of transition metal-catalyzed guanylation of aromatic amines with carbodiimides.[6] The catalysts are imido titanium complexes, supported by guanidinate(1−) co-ligands, which are also active in other catalytic processes.[7]

Following our interest in the area of imido complexes of group 5,[8] we have extended our research on imido complexes of vanadium to the study of the assembling reaction between carbodiimides and aromatic amines. Here, we report the efficient synthesis of guanidines **2**−**6** by using the precatalyst V(N-2,6-$^{i}Pr_2C_6H_3$)Cl_3, **1**.[9] Additionally, we have theoretically studied the first steps of the guanylation reaction and compared the two different mechanisms of this reaction catalyzed with Ti and V imido compounds. To our knowledge, there is only one other related theoretical report concerning the investigation of the carbodiimide insertion into Al−N bonds.[10] Part of this work has been previously communicated.[11]

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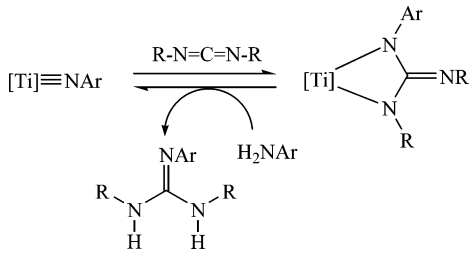
Scheme 1



Results and Discussion

Guanylation of Primary and Secondary Aryl Amines. Richeson et al. have recently shown that the guanylation of aromatic primary amines with carbodiimides is efficiently catalyzed by imido titanium complexes.[6] The proposed catalytic cycle begins with [2+2] addition of the carbodiimide to the titanium−imido moiety (Scheme 1). The resulting diazametallacyclobutane intermediate, for which exists experimental evidence,[6] reacts with the amine, affording the corresponding guanidine. The same diazametallacyclobutane species has been proposed as an intermediate in the catalytic cycle of carbodiimide metathesis reactions catalyzed by group 4[12] and group 5[7a,13] imido complexes.

Taking into consideration these results, we decided to study the reaction between carbodiimides and aromatic amines in the presence of imido vanadium derivatives. Among all the complexes studied (see below), compound V(N-2,6-$^{i}Pr_2C_6H_3$)-Cl_3, **1**, has revealed itself to be an efficient precatalyst for the guanylation of primary and secondary aryl amines (Scheme 2). The reactions were carried out in toluene at 105 °C with the addition of 2% of catalyst precursor **1** and are completed after approximately 24 h, giving good yields of the corresponding guanidines $(RHN)_2C(=NAr)$ **2**−**4** and (RHN)(MeArN)C(=NR) **5** and **6** (see Table 1 and Scheme 2). No reaction was observed under the same conditions in the absence of a catalyst. Furthermore, the guanidine yield was found to be strongly dependent on the temperature; no reaction was observed at room temperature between 2,4,6-trimethylaniline and diisopropylcarbodiimide in the presence of **1**.

Concerning the entries 1−3 of Table 1, reactions carried out with primary aryl amines, our results are comparable to those described by Richeson with the Ti catalytic system, although the yields and the reaction times seem, respectively, somewhat lower and higher for vanadium than those reported for the titanium catalyst. Interestingly, we have extended with success the guanylation reaction to secondary alkyl,aryl amine reagents and obtained good isolated yields of guanidines **5** and **6** after 24 h of reaction (entries 4, 5). The direct reaction between secondary dialkyl amines and carbodiimides has been described,[14] but no examples are known, to our knowledge, of direct reaction of carbodiimide with secondary alkyl,aryl amines. Prior to this report, this reaction was known to be achievable only via a two-step process: reaction of the amine with BuLi and subsequent interaction with the carbodiimide.[15] While our work was in progress, Hou and co-workers have recently reported the catalytic addition of secondary alkyl amines to carbodiimides using an yttrium compound.[16]

Mechanistic Considerations of the Guanylation Reaction Catalyzed by Vanadium Complexes. Before the selection of **1** as precatalyst of the guanylation, we evaluated the activity of other known imido vanadium compounds, such as V(NAr)-Cl_3(dme)[8a] and V(NAr)(^{i}Pr-dtc)$_3$[8b] (Ar = 2,6-$^{i}Pr_2C_6H_3$). Additionally, we have also tested the new complex V(N-2,6-$^{i}Pr_2C_6H_3$)[$(OCH_2CH_2)_3N$], which was prepared by a reaction between V(N-2,6-$^{i}Pr_2C_6H_3$)Cl_3(dme) and $(HOCH_2CH_2)_3N$ in the presence of Et_3N and characterized straightforwardly by analytical and spectroscopic methods (see Scheme 3 and details in the Experimental Section).

Table 2 shows the results obtained in the preparation of guanidine **2**. Complex V(NAr)Cl_3(dme) was found to be an effective precatalyst. This result was not surprising in view of the complex's ability to lose the coordinated dimethoxyethane ligand at high temperature to produce the unsaturated complex **1**. By contrast, the other imido vanadium complexes, V(NAr)-(^{i}Pr-dtc)$_3$ and V(NAr)[$(OCH_2CH_2)_3N$], were found to be inactive for the process. The lack of activity in these complexes could be associated with the steric hindrance of the metal center or the difficulties associated with the chelated ligand to allow the formation of a vanadium−amido bond (see below the proposed alternative mechanism to the [2+2] carbodiimide addition, based on the insertion into a vanadium−amido bond).

In the communication of our preliminary results concerning the activity of complex **1**,[11] we assumed that the mechanism proposed by Richeson et al. for the guanylation of aromatic amines catalyzed by titanium imido complexes[6] could also be operative in our process. Concretely, a diazavanadacyclobutane, formed from the [2+2] addition of the carbodiimide to the V=NAr group, should be the implied intermediate in this process. The formation of this species is reasonable, and it has been previously proposed as an intermediate in the carbodiimide metathesis reactions catalyzed by vanadium−imido compounds.[13] However, one referee pointed out the possibility of an alternative mechanism involving carbodiimide insertion into the vanadium amido bond that would form by the reaction of the V(NAr)Cl_3 complex with the excess of amine under the reaction conditions. Carbodiimide insertion into the metal−amido bond is a well-known process, and also several recent literature results described such an insertion for different metals: block s and p metals for the synthesis of the corresponding guanidinates[17] and transition and lanthanide metals for the preparation of derivatives containing guanidinate ligands.[18]

With the aim to determine if a different mechanism could be operating in the vanadium-catalyzed guanylation reaction, we have performed a DFT analysis of the reaction of MeNCNMe with some vanadium and titanium model complexes at the B3LYP level using a triple-ζ quality basis set (see Computational Details). First, we have studied the proposed mechanism for the titanium-catalyzed reaction, using $\{(Me_2N)C(NMe)_2\}_2$-Ti(=NMe) (**A**) as a model of the Richeson catalyst, to establish

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Scheme 2

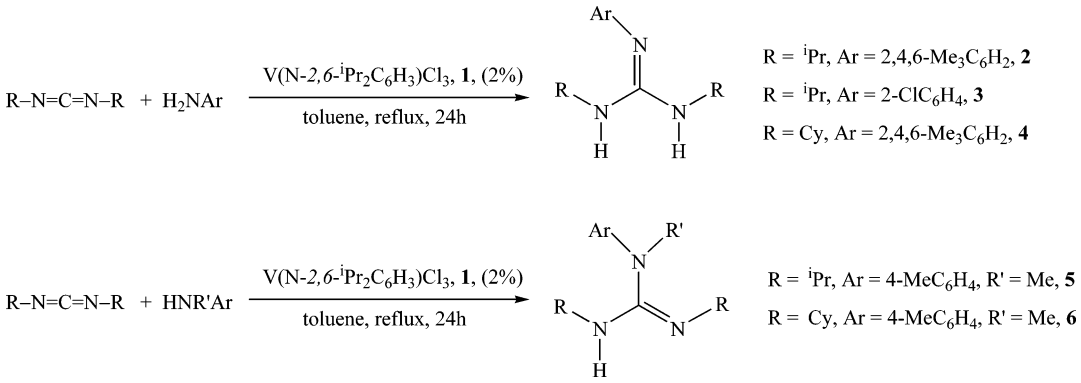

Table 1. Guanylation of Aromatic Amines Using V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$, 1, as Precatalyst[a]

entry	R group of carbodiimide	aryl amine	product	isolated yield (%)
1	^{i}Pr	2,4,6-Me$_3$C$_6$H$_2$NH$_2$	**2**	84
2	^{i}Pr	2-ClC$_6$H$_4$NH$_2$	**3**	88
3	Cy	2,4,6-Me$_3$C$_6$H$_2$NH$_2$	**4**	80
4	^{i}Pr	(4-MeC$_6$H$_4$)(Me)NH	**5**	68
5	Cy	(4-MeC$_6$H$_4$)(Me)NH	**6**	72

[a] Conditions: see Experimental Section.

Scheme 3

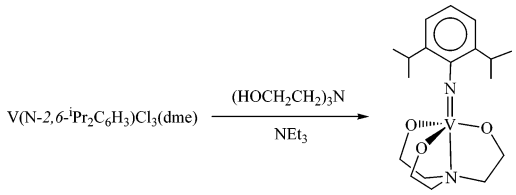

Table 2. Effect of the Catalyst in the Guanylation of Aryl Amines[a]

entry	catalyst	product	isolated yield (%)
1	none		no reaction
2	V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$	**2**	84
3	V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$(dme)	**2**	75
4	V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(^{i}Pr-dtc)$_3$		no reaction
5	V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)[(OCH$_2$CH$_2$)$_3$N]		no reaction

[a] Conditions: see Experimental Section.

the basis for the comparison with the vanadium-catalyzed reaction. Second, two different vanadium model complexes, V(=NMe)Cl$_3$ (**B**) and V(=NMe)(NMe$_2$)Cl$_2$ (**C**), have been considered for the guanylation reaction. For the latter, two possible mechanisms—(i) [2+2] carbodiimide addition to the imido group or (ii) carbodiimide insertion into the amido group—are possible, and we expect that DFT calculations will help us to discriminate between them. We have chosen symmetrical carbodiimide and amido ligands in order to avoid the existence of different isomers for the intermediates studied. To our knowledge, there is only one other related theoretical report concerning the investigation of the carbodiimide insertion into Al−N bonds.[10]

DFT Study of the Reaction of {(Me$_2$N)C(NMe)$_2$}$_2$Ti(=NMe) (A) with Carbodiimide MeNCNMe. Richeson et al. have reported that complex {(Me$_2$N)C(N^{i}Pr)$_2$}$_2$Ti(=NC$_6$F$_5$) reacts readily and reversibly with diisopropylcarbodiimide at room temperature to produce a diazametallacycle (see Scheme 1). The latter reacts with a primary amine to afford the corresponding guanidine. Here we have examined the energetic profile of the first steps of the guanylation using DFT calculations. To simplify the study of the proposed mechanism of carbodiimide addition to the metal−imido bond, a much simpler model for the titanium catalyst, namely, {(Me$_2$N)C(NMe)$_2$}$_2$-Ti(=NMe) (**A**), and carbodiimide MeNCNMe have been chosen.

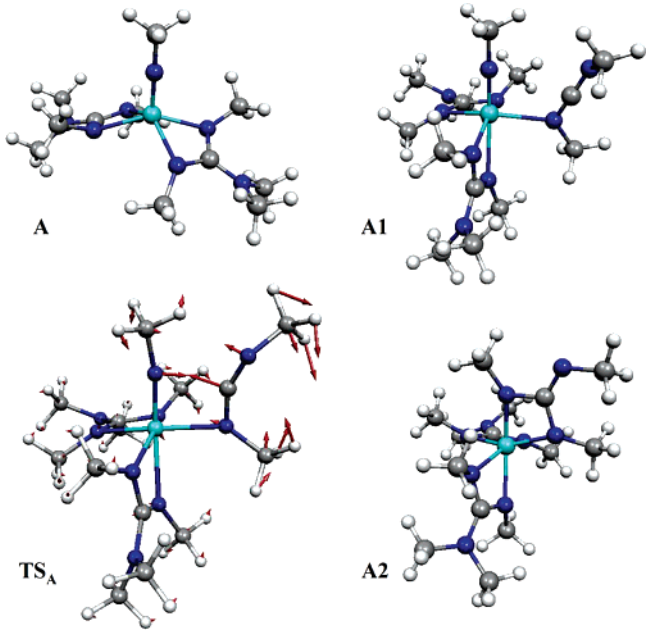

Figure 1. Optimized structures of the model titanium complexes **A**.

The starting model compound {(Me$_2$N)C(NMe)$_2$}$_2$Ti(=NMe) (**A**), as well as other considered intermediates, were optimized without symmetry restrictions. The resulting structures are displayed in Figure 1, while selected computed structural parameters are grouped in the Supporting Information. A good correlation with the experimental values of the related {(Me$_2$N)C(N^{i}Pr)$_2$}$_2$Ti(=NC$_6$F$_5$) complex was found for model **A** (see Table 3). Similarly to the mechanism postulated for the theoretically studied aluminum system,[10] we have consider that the first step for the reaction would be coordination of the carbodiimide via a dative bond to pentacoordinate complex **A**, to afford the pseudo-octahedral complex {(Me$_2$N)C(NMe)$_2$}$_2$-Ti(=NMe){N(Me)CNMe} (**A1**). From complex **A1** a [2+2] carbodiimide addition to the Ti−imido bond would afford the complex {(Me$_2$N)C(NMe)$_2$}$_2$Ti{κ^2-MeNC(=NMe)NMe} (**A2**), containing one bidentate guanidinate(2−) ligand. The calculated bond distances and angles for **A2** are in good agreement with those found for the complexes characterized by X-ray diffraction methods, {(Me$_2$N)C(N^{i}Pr)$_2$}$_2$Ti{κ^2-(C$_6$F$_5$)NC(=N^{i}Pr)N^{i}Pr}[6] and {(Me$_2$N)C(N^{i}Pr)$_2$}$_2$Ti{κ^2-(C$_6$F$_5$)NC(=NCy)NCy}[7a] (see Table 4). A transition state **TS$_A$** connecting **A1** and **A2** and characterized by a single imaginary frequency (210i cm^{-1}) has also been

Table 3. Comparison of the Computed Model Compound $\{(Me_2N)C(NMe)_2\}_2Ti(=NMe)$ (A) with the Experimental $\{(Me_2N)C(N^iPr)_2\}_2Ti(=NC_6F_5)$ Complex

bond distances (Å) and angles (deg)	A	$\{(Me_2N)C(N^iPr)_2\}_2Ti(=NC_6F_5)$
Ti−N (imido)	1.684	1.752(2)
Ti−N (guanidinate(1−))	2.126	2.090(1)
	2.128	2.107(2)
N−C (guanidinate(1−))	1.335	1.348(2)
	1.342	1.351(2)
N−C (guanidinate(1−), exo)	1.385	1.379(2)
Ti−N−C (imido)	179.9	180.0
N(imido)−Ti−N	115.5	101.90(4)
	107.1	122.26(4)
	115.8	
	106.9	

located. The reaction of **A2** with free amine (not yet theoretically studied) would lead to guanidine formation, closing the catalytic cycle.

The energetic profile of the process has also been calculated. Solvent effects (toluene) were taken into account using the PCM method with the 6-311+G(2d,p) basis set (see Computational Details). At this level of theory BSSEs are small (1−2 kcal·mol^{-1}) and have not been taken into account. The carbodiimide addition to the imido bond is calculated to be an exergonic process in toluene (relative free energy, −4.5 kcal·mol^{-1}) with a barrier of 8.3 kcal·mol^{-1} between the intermediate **A1** and the transition state $\mathbf{TS}_A$. These values are in good agreement with the experimental observation that $\{(Me_2N)C(N^iPr)_2\}_2Ti(=NC_6F_5)$ reacts readily and reversibly with diisopropylcarbodiimide at room temperature.[6]

DFT Study of the Reaction of $V(=NMe)Cl_3$ (B) with Carbodiimide MeNCNMe. To contrast the same mechanism with vanadium, we have studied the reaction of $V(=NMe)Cl_3$ (**B**), a simple model of $V(N\text{-}2,6\text{-}^iPr_2C_6H_3)Cl_3$, **1**, with carbodiimide MeNCNMe. All the compounds considered were optimized without symmetry restrictions. The resulting structures are displayed in Figure 2, while selected computed structural parameters are collected in the Supporting Information. A good correlation was found for model **B** with respect to the experimental values of the related $V(NSiMe_3)Cl_3$ complex[19] (see Table 5).

Similar to the titanium compound, we also consider that the first step for the reaction would be the adduct formation, namely, coordination of the carbodiimide via a dative bond to tetracoordinate complex **B**, to afford the pentacoordinate complex $V(=NMe)Cl_3\{N(Me)CNMe\}$ (**B1**). Then, a [2+2] carbodiimide addition to the vanadium−imido bond would afford the complex $VCl_3\{\kappa^2\text{-}MeNC(=NMe)NMe\}$ (**B2**). This addition goes through

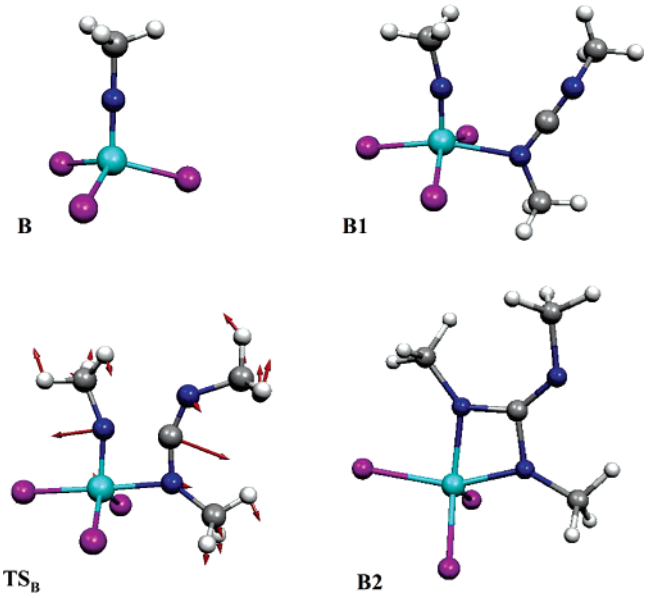

Figure 2. Optimized structures of the model vanadium complexes **B**.

Table 5. Comparison between the Computed Model Compound $V(NMe)Cl_3$ (B) and the Experimental $V(NSiMe_3)Cl_3$ Complex

bond distances (Å) and angles (deg)	B	$V(NSiMe_3)Cl_3$
V−N	1.596	1.59(1)
V−Cl	2.166	2.145(5)
		2.147(3)
		2.147(3)
Cl−V−Cl	112.5	111.4(1)
	112.5	112.8(1)
	112.6	112.8(1)
N−V−Cl	106.1	106.9(4)
		106.2(2)
		106.2(2)

the transition state $\mathbf{TS}_B$, characterized by a single imaginary frequency (435i cm^{-1}). Complex **B2** contains a bidentate guanidinate(2−) ligand, for which there are some structurally characterized examples of tantalum. The computed bond distances and angles for this ligand (C−N lengths: 1.396, 1.405, and 1.265 Å) fit quite well with those found in compounds $Ta\{(^iPrN)_2C{=}N^iPr\}(NMe_2)\{(Me_2NC{=}N(2,6\text{-}Me_2C_6H_3)\}_2$[20] (C−N lengths: 1.385(8), 1.431(7), and 1.278(8) Å), $Ta\{(CyN)_2C{=}NCy\}(NMe_2)_3$[21] (C−N lengths: 1.40(2), 1.44(2), and 1.28(2) Å), and $Ta\{(^iPrN)_2C{=}N^iPr\}(NMe_2)_3$[18e] (C−N lengths: 1.372-(10), 1.421(10), and 1.276(10) Å).

Table 4. Comparison of the Computed Model Compound $\{(Me_2N)C(NMe)_2\}_2Ti\{\kappa^2\text{-}MeNC(=NMe)NMe\}$ (A2) with the Experimental $\{(Me_2N)C(N^iPr)_2\}_2Ti\{\kappa^2\text{-}(C_6F_5)NC(=N^iPr)N^iPr\}$ and $\{(Me_2N)C(N^iPr)_2\}_2Ti\{\kappa^2\text{-}(C_6F_5)NC(=NCy)NCy\}$ Complexes

bond distances (Å)	A2	$\{(Me_2N)C(N^iPr)_2\}_2Ti\{\kappa^2\text{-}(C_6F_5)NC(=N^iPr)N^iPr\}$	$\{(Me_2N)C(N^iPr)_2\}_2Ti\{\kappa^2\text{-}(C_6F_5)NC(=NCy)NCy\}$
Ti−N (guanidinate(1−))	2.140	2.071(3)	2.061(3)
	2.114	2.078(3)	2.081(3)
	2.139	2.104(3)	2.127(3)
	2.091	2,123(3)	2.132(3)
Ti−N (guanidinate(2−))	1.969	1.947(3)	1.962(3)
	1.948	2.060(3)	2.061(3)
N−C (guanidinate(1−))	1.336	1.331(5)	1.359(4)
	1.340	1.352(5)	1.330(4)
	1.338	1.335(5)	1.355(5)
	1.339	1.341(4)	1.335(4)
N−C (guanidinate(1−), exo)	1.382	1.381(5)	1.387(4)
	1.380	1.389(5)	1.384(5)
N−C (guanidinate(2−))	1.403	1.412(4)	1.411(4)
	1.406	1.416(4)	1.402(4)
N−C (guanidinate(2−), exo)	1.282	1.268(5)	1.289(5)

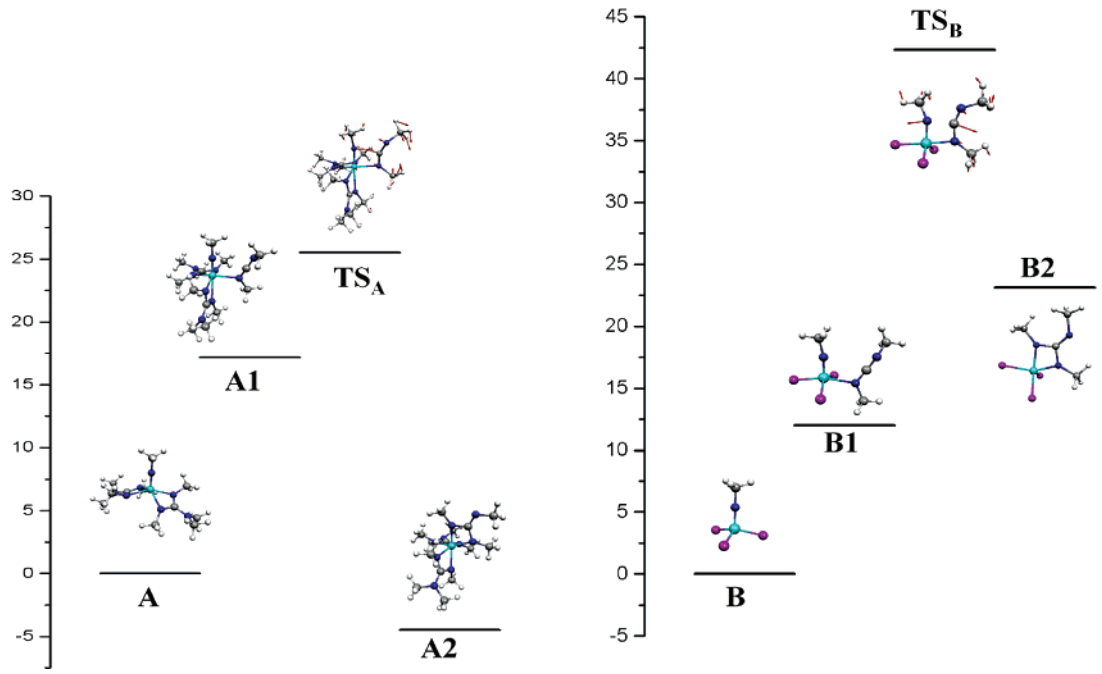

Figure 3. Comparison of the relative free energy (kcal·mol^{-1}) profile for the carbodiimide addition to the metal−imido bond for titanium (**A** compounds, left side) and vanadium (**B** compounds, right side) in toluene.

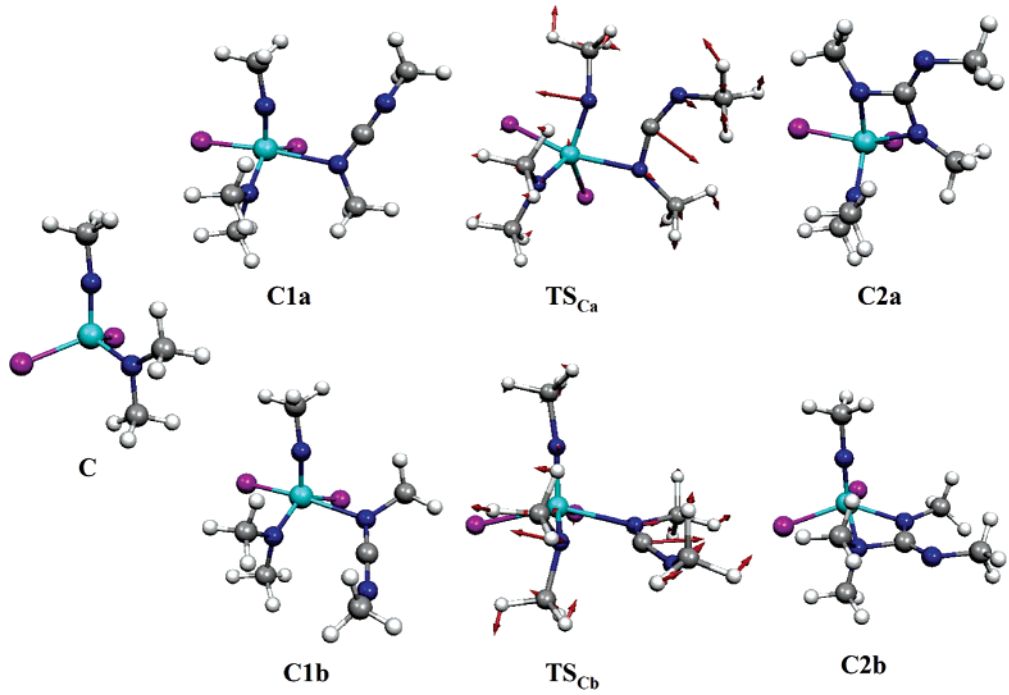

Figure 4. Optimized structures of the model vanadium complexes **C**.

Interestingly, the energetic profile of the carbodiimide addition for vanadium is different from that observed for titanium. The reaction is not exergonic (relative free energy in toluene, 23.1 kcal·mol^{-1}), and the calculated barrier of 30.3 kcal·mol^{-1} (between **B1** and **TS**$_B$) is considerably higher for this vanadium complex than the associated barrier computed for the titanium model (see Figure 3). These results are compatible with our experimental observations: when a solution of complex V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$, **1**, was treated solely with carbodiimide under the same reaction conditions of Table 1, no color change was observed. In contrast, when a solution of complex V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$, **1**, was treated solely with the appropriate amine H$_2$NAr, the color change was similar to that observed in the guanylation reactions. Consequently, we can presume that the [2+2] addition pathway was not operative for the guanylation reaction catalyzed by vanadium complexes, and we therefore postulate the formation of amido−imido compounds of formula V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(NHAr)$_x$(Cl)$_{3-x}$, due to the interaction of excess amine with complex **1**. An analogous reaction has been reported for the trichloroimidovanadium complex V(N^{t}Bu)Cl$_3$ with HN^{i}Pr$_2$ that yields the amido−imido derivative V(N^{t}Bu)-

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Table 6. Comparison between the Computed Model Compound V(NMe)Cl$_2$(NMe$_2$) (C) and the Experimental V(N^{t}Bu)Cl$_2$(N^{i}Pr$_2$) Complex

bond distances (Å) and angles (deg)	C	V(N^{t}Bu)Cl$_2$(N^{i}Pr$_2$)
V−N (imido)	1.608	1.626(4)
V−N (amido)	1.805	1.795(4)
V−Cl	2.210	2.211(2)
		2.223(2)
Cl−V−Cl	114.9	114.0(1)
N−V−N	104.1	106.1(2)

(N^{i}Pr$_2$)Cl$_2$.[22] Once the amido−imido compound is formed, the reaction may continue with the interaction of this species and the carbodiimide reagent.

DFT Study of the Reaction of V(═NMe)(NMe$_2$)Cl$_2$ (C) with Carbodiimide MeNCNMe. With the aim to confirm the possible existence of an alternative pathway for the vanadium catalyst, with respect to that established by Richeson for the titanium catalyst, we have performed a DFT analysis of the reaction of carbodiimide MeCNCMe with the vanadium model complex V(NMe)(NMe$_2$)Cl$_2$ (**C**), which displays one imido ligand and one amido ligand. The resulting structures, which are displayed in Figure 4, correspond to the two pathways studied. Selected computed structural parameters are collected in the Supporting Information. A fairly good correlation with the experimental values of the related V(N^{t}Bu)Cl$_2$(N^{i}Pr$_2$) complex[22] was found for model **C** (see Table 6).

Starting with model **C**, following the adduct formation through coordination of the carbodiimide to the vanadium center (models **C1a** and **C1b**), two possible pathways were studied: (i) carbodiimide addition to the vanadium−imido bond, through the transition state **TS**$_{Ca}$ (with a single imaginary frequency, 419i cm^{-1}), to yield VCl$_2$(NMe$_2$){κ^2-MeNC(═NMe)NMe} (**C2a**), containing a guanidinate(2−) ligand; and, alternatively, (ii) carbodiimide insertion into the vanadium−amido bond, through the transition state **TS**$_{Cb}$ (with a single imaginary frequency, 349i cm^{-1}), affording V(═NMe)Cl$_2${κ^2-Me$_2$NC-(NMe)NMe} (**C2b**), containing an asymmetric guanidinate(1−) ligand. The symmetric guanidinate(1−) ligand, observed experimentally in other systems,[17,18] can be obtained by simple rotation around the C−N bond.

The most interesting result found is the comparison between the thermodynamic profiles of both pathways in toluene (shown in Figure 5). There are two notable differences: (a) the relative free energy from **C** to **C2a** or to **C2b** is favorable for the latter process by 12.3 kcal·mol^{-1}; (b) the barrier of 34.4 kcal·mol^{-1} computed between **C** and **TS**$_{Cb}$ is significantly lower than that found between **C** and **TS**$_{Ca}$ (45.8 kcal·mol^{-1}). On the basis of these data, the preferred thermodynamic pathway is the carbodiimide insertion into the amido bond, and consequently, we proposed this pathway as a valid alternative to that proposed by Richeson. This route is consistent with the recent work of Fischer and co-workers.[23] In fact, they reported the selective insertion of carbodiimide into the metal−amido bond in a tantalum complex that contains both imido and amido functionalities. This insertion affords a guanidinate(1−) ligand coordinated to the metal. Furthermore, the catalytic formation of guanidines, just reported by Hou and co-workers, makes use of an amido complex of yttrium as the catalyst.[16]

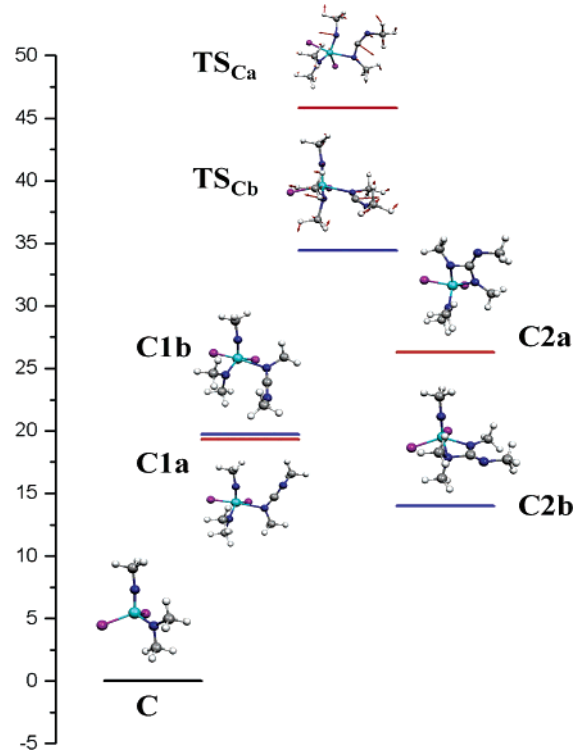

Figure 5. Comparison between the relative free energy (kcal·mol^{-1}) profile for the carbodiimide addition to the V−imido bond (red) and the carbodiimide insertion into the V−amido bond (blue) in toluene.

Conclusion

We have shown that vanadium imido complex V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$, **1**, is an efficient precatalyst for the guanylation of carbodiimides using both primary and secondary aromatic amines. DFT calculations, supported by experimental results, suggest that the [2+2] carbodiimide addition to the vanadium−imido bond, a mechanism demonstrated by Richeson et al.[6] for an imido−titanium complex, is not operative in this case and that carbodiimide insertion into the vanadium−amido bond of an intermediate, with formula V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(NHAr)$_x$(Cl)$_{3-x}$, is a more favorable mechanism for the guanylation reaction catalyzed by vanadium complexes.

Experimental Section

All preparations and other operations were carried out under a dry, oxygen-free nitrogen atmosphere following conventional Schlenk techniques. Solvents were dried and degassed before use. Carbodiimides and anilines were purchased from Aldrich and were used as supplied. Compounds V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$ (**1**),[9] V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$(dme),[8a] and V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(^{i}Pr-dtc)$_3$[8b] were prepared as previously reported. Infrared spectra were recorded on a Perkin-Elmer Model 883 spectrophotometer. ^{1}H and ^{13}C NMR spectra were run on a Bruker AMX-300 spectrometer. Microanalyses (C, H, N) were carried out by the Microanalytical Service of the University of Sevilla (CITIUS). Mass spectra were recorded on a Kratos MS80-RFA, FAB technique, with thioglycerol as a matrix.

Guanylation Reactions with the Precatalyst 1. The guanylation reactions for the synthesis of **2**−**6** were carried out at 105 °C for 24 h following a similar experimental procedure (ratio carbodiimide:aniline:catalyst = 1:1:0.02). The preparation of **2** and **5** is described here as representative.

A solution of **1** (0.064 mmol), 2,4,6-trimethylaniline (0.42 mL, 3.2 mmol), and diisopropylcarbodiimide (0.50 mL, 3.2 mmol) in

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10 mL of toluene was heated in a thick-walled glass vessel with a Teflon stopcock at 105 °C for 24 h. The reaction was cooled to room temperature, volatiles were removed, and the residue was extracted with diethyl ether. Cooling to −20 °C gave a white solid of *N*-2,4,6-trimethylphenyl,*N*′,*N*″-diisopropylguanidine (**2**), which was isolated by filtration and dried in a vacuum. Yield: 84%. MS (*m*/*z*): 262 $(M + H)^+$. ^{1}H NMR ($CDCl_3$): δ 0.89−1.21 (br, CH_3, ^{i}Pr), 2.27 (s, 6H, *o*-CH_3), 2.30 (s, 3H, *p*-CH_3), 3.39 (br, 2H, NH), 4.10 (br, CH, ^{i}Pr), 6.92 (s, 2H, C_6H_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 18.1 (s, *o*-CH_3), 20.7 (s, *p*-CH_3), 23.5 (CH_3, ^{i}Pr), 43.1 (br, CH, ^{i}Pr), 128.7, 130.7, 143.3 (s, C_6H_2), 148.0 (s, C_6H_2), quaternary carbon >C=N− not observed. Anal. Calc for $C_{16}H_{27}N_3$: C, 73.56; H, 10.34; N, 16.09. Found: C, 72.79; H, 10.26; N 15.62.

***N*-2-Chlorophenyl,*N*′,*N*″-diisopropylguanidine (3):** white solid. Yield: 88%. MS (*m*/*z*): 254 $(M + H)^+$. ^{1}H NMR ($CDCl_3$): δ 1.15 (d, 12H, 6.4 Hz, CH_3, ^{i}Pr), 3.46 (br, 2H, NH), 3.76 (br, 2H, CH, ^{i}Pr), 6.87 (m, 2H, C_6H_4), 7.11 (t, 1H, 6.6 Hz, C_6H_4), 7.32 (t, 1H, 7.8 Hz, C_6H_4). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 23.4 (s, CH_3, ^{i}Pr), 43.3 (s, CH, ^{i}Pr), 122.4, 125.2, 127.5, 128.3, 129.9 (s, C_6H_4), 146.9 (s, C_6H_4), 149.9 (s, C_6H_4), quaternary carbon >C=N− not observed. Anal. Calc for $C_{13}H_{20}N_3Cl$: C, 61.54; H, 7.89, N, 16.57. Found: C, 61.49; H, 7.98; N 16.01.

***N*-2,4,6-Trimethylphenyl,*N*′,*N*″-dicyclohexylguanidine (4):** white solid. Yield: 80%. MS (*m*/*z*): 342 $(M + H)^+$. ^{1}H NMR ($CDCl_3$): δ 1.06−1.61 (br, 22H, CH_2 and CH on cyclohexyl), 2.02 (s, 6H, *o*-CH_3), 2.16 (s, 3H, *p*-CH_3), 3.41 (br, 2H, NH), 6.74 (s, 2H, C_6H_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 18.0 (s, *o*-CH_3), 20.6 (s, *p*-CH_3), 24.9, 25.4, 34.1 (s, CH_2 on cyclohexyl), 49.8 (br, CH on cyclohexyl), 128.1, 130.4, 130.6, 143.4, 147.7 (s, C_6H_2), quaternary carbon >C=N− not observed. Anal. Calc for $C_{22}H_{35}N_3$: C, 77.42; H, 10.26, N, 12.32. Found: C, 76.64; H, 11.31; N 12.06.

***N*-Methyl,4-methylphenyl,*N*′,*N*″-diisopropylguanidine (5).** A mixture of **1** (0.064 mmol), *N*-methyl-*p*-toluidine (0.42 mL, 3.2 mmol), and diisopropylcarbodiimide (0.50 mL, 3.2 mmol) in 10 mL of toluene was heated in a thick-walled glass vessel with a Teflon stopcock at 105 °C for 24 h. The reaction was cooled to room temperature, the volatiles were removed, and the residue was extracted with diethyl ether. The solvent was completely removed under vacuum to afford guanidine **5** as a colorless oil. Yield: 68%. MS (*m*/*z*): 248 $(M + H)^+$. ^{1}H NMR (DMSO-d_6, 363 K): δ 1.03 (d, J_{HH} = 6.2 Hz, 12H CH_3, ^{i}Pr), 2.22 (s, 3H, *p*-CH_3), 2.99 (s, 3H, N-CH_3), 3.55 (hp, J_{HH} = 6.2 Hz, 2H, CH, ^{i}Pr), 5.00 (br, CH, NH), 6.48, 7.00 (d, J_{HH} = 8.3 Hz, 2H, C_6H_4). ^{1}H NMR ($CDCl_3$, 293 K): δ 1.11 (br, CH_3, ^{i}Pr), 2.29 (s, 3H, *p*-CH_3), 3.10 (br, N-CH_3), 3.64 (br, CH, ^{i}Pr), 6.70 (br, C_6H_4), 7.07 (d, J_{HH} = 8.2 Hz, 2H, C_6H_4). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 293 K): δ 18.5 (s, *p*-CH_3), 23.9 (CH_3, ^{i}Pr), 37.1 (br, NCH_3), 45.5 (br, CH, ^{i}Pr), 112.6, 129.6 (s, C_6H_4), 144.2 (br, C_6H_4), 149.9 (br, >C=N−). Anal. Calc for $C_{15}H_{25}N_3$: C, 71.67; H, 10.17; N, 16.64. Found: C, 72.83; H, 10.19; N 16.99.

***N*-Methyl,4-methylphenyl,*N*′,*N*″-dicyclohexylguanidine (6):** white solid. This compound contains, even after crystallization, a small amount of the free amine as impurities, which makes it difficult to obtain a good microanalysis. Yield: 72%. MS (*m*/*z*): 328 $(M + H)^+$. ^{1}H NMR ($CDCl_3$, 293 K): δ 1.25−1.97 (br, 22H, CH_2 and CH on cyclohexyl), 2.26 (s, 3H, *p*-CH_3), 3.12 (br, N-CH_3), 6.75 (br, C_6H_4), 7.07 (d, J_{HH} = 8.1 Hz, 2H, C_6H_4). Anal. Calc for $C_{21}H_{33}N_3$: C, 71.01; H, 10.16; N, 12.83. Found: C, 69.85; H, 10.81; N 12.66.

Preparation of V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)[(OCH$_2$CH$_2$)$_3$N]. A solution of V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl_3(dme) (1.4 g, 3.3 mmol) in CH_2Cl_2 (30 mL) was treated at −60 °C with 1 equiv of $N(CH_2CH_2OH)_3$ (8.2 mL of a 0.4 M solution in CH_2Cl_2) and 3 equiv of NEt_3, and the resulting mixture was stirred for 30 min at −60 °C. It was allowed to warm to room temperature and then stirred overnight. The resulting solution was taken to dryness, and the residue was extracted with dme (40 mL). Centrifugation, partial evaporation of the solvent, and cooling at −20 °C afforded red crystals of the complex V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)[(OCH$_2$CH$_2$)$_3$N] (0.6 g, 50% yield). ^{1}H NMR (C_6D_6): δ 1.49 (d, 6.8 Hz, 12H, CH(CH_3)$_2$), 2.16 (t, 5.6 Hz, 6H, CH_2CH$_2$), 4.35 (t, 5.6 Hz, 6H, CH$_2$CH_2), 4.79 (h, 6.8 Hz, 2H, CH(CH$_3$)$_2$), 6.86 (t, 7.7 Hz, 1H, CH, Ph), 7.02 (d, 7.7 Hz, 2H, CH, Ph). $^{13}C\{^1H\}$ NMR (C_6D_6): δ 24.2 (s, CH_3), 28.6 (s, CH), 53.5 (s, CH_2), 72.0 (s, CH_2), 122.0, 126.4, 148.2 (s, phenyl ring, one signal was obscured by C_6D_6, confirmed by the GATED experiment). $^{51}V\{^1H\}$ NMR (C_6D_6, 78.86 MHz, ppm respect to $VOCl_3$): δ −316 (br, $\Delta\nu_{1/2}$ = 670 Hz). Anal. Calc for $C_{18}H_{29}N_2O_3V$: C, 58.06; H, 7.85; N, 7.52. Found: C, 58.18; H, 7.53; N 7.66.

Catalyst Effect in the Guanylation Reaction. The same experimental procedure was employed in the catalyst assays, collected in Table 2, with different vanadium complexes. Summary of the reaction conditions: reactions carried out in toluene at 105 °C, for 24 h, with a ratio ^{i}PrN=C=N^{i}Pr:2,4,6-Me$_3$C$_6$H$_2$NH$_2$:catalyst of 1:1:0.02.

Computational Details. The electronic structure and geometries of the model complexes were computed within the density functional theory at the B3LYP[24,25] level. In the case of the vanadium model a triple-ζ quality basis set (6-311G*) was used for all atoms. For the titanium model a mixed basis set was employed, by using 6-311G* for the Ti atom, the N atom of the carbodiimide and those bonded to the metal, and the central C atoms of the carbodiimide and the guanidinate(1−) ligands, along with 6-31G* for all other atoms. All the optimized geometries were characterized as local energy minima (NImag=0) or maxima (NImag=1) by diagonalization of the analytically computed Hessian (vibrational frequency calculations). To determine the reaction energies, single-point calculations on the optimized structures of reactants, products, and intermediates were carried out with the 6-311G+(2d, p) basis set. At this theory level BSSEs are insignificant (1−2 kcal·mol^{-1}), and therefore they have not been taken into account. Solvent effects (toluene) were taken into consideration by use of the PCM method. The DFT calculations were performed using the Gaussian 03 suite of programs.[26] Figures were drawn using Molekel.[27] Cartesian coordinates for the optimized molecules are available from the authors upon request.

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Supporting Information Available: Selected structural parameters of calculated titanium, **A**, and vanadium complexes, **B** and **C** (3 tables). This material is available free of charge via the Internet at http://pubs.acs.org.

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