Communication

Guanylation of aromatic amines catalyzed by vanadium imido complexes

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Abstract

The reaction of formation of guanidines by coupling of carbodiimides and aromatic amines using imido vanadium complexes as catalyst have been investigated. Results demonstrate that the complex $V(N-2,6-^{i}Pr_2C_6H_3)Cl_3$ is an effective catalyst for this process.
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1. Introduction

Reactions involving imido complexes in which the imido moiety undergoes chemical transformations have experienced a remarkable growth in the last years due to the role they play in many important reactions [1,2]. Richeson et al. have recently showed that the guanylation [3] of aromatic amines with carbodiimides is catalyzed by imido titanium complexes [4]. 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 [4], reacts with the amine affording the corresponding guanidine.

On the other hand, recent works have described carbodiimide metathesis reactions catalyzed by group 4 [5] and group 5 [6] imido complexes. Particularly, compounds of the formula $V(NAr)X_3$ (X = Cl, OR) have been successfully employed in this reaction [7]. The proposed catalytic cycle for the process implies the formation of a diazametallacyclobutane intermediate

derived from the [2 + 2] cycloaddition between the metal-nitrogen double bond and the double bond of the unsaturated carbodiimide (Scheme 2).
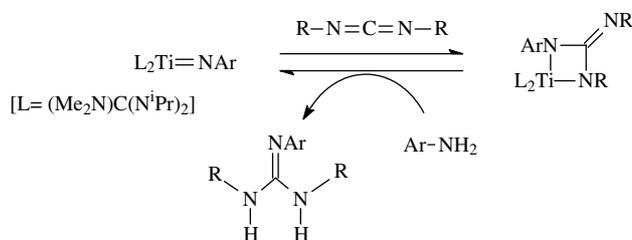

Scheme 1.
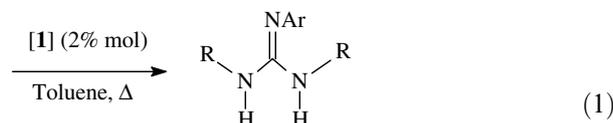
R = ^{i}Pr, Ar = 2,4,6-Me$_3$C$_6$H$_2$, **2**
R = ^{i}Pr, Ar = 2-ClC$_6$H$_4$, **3**
R = Cy, Ar = 2,4,6-Me$_3$C$_6$H$_2$, **4**

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$$X_3V=NR \xrightarrow{\quad R'-N=C=N-R' \quad} \begin{array}{c} RN \diagdown \quad \diagup NR' \\ | \qquad | \\ X_3V-NR' \end{array}$$

Scheme 2.
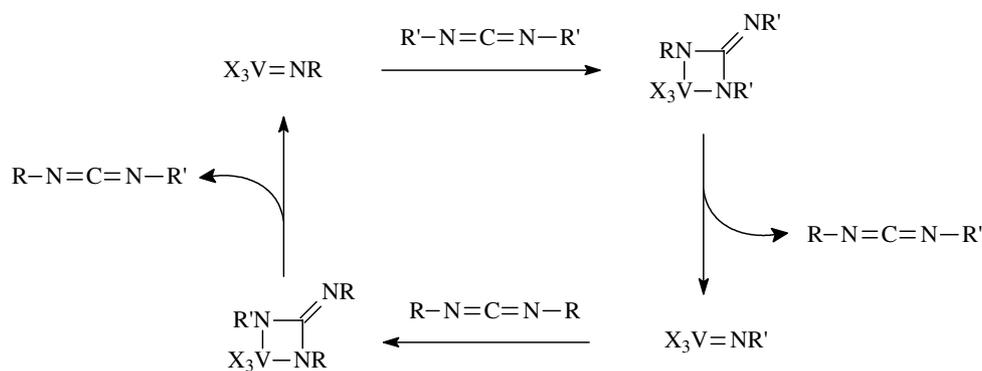
Taking into consideration the similarity of both intermediates and following our interest in the area of imido complexes of group 5 [8] and 6 metals [9], we have extended our results on imido complexes of vanadium to the study of the assembling reaction between carbodiimides and aromatic amines. To the best of our knowledge, this communication represents the first report of group 5 metal catalyzed guanylation of aromatic amines with carbodiimides.

2. Results and discussion

Compound V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$ (**1**) [10] has revealed to be an efficient catalyst for the guanylation of aryl amines (Eq. (1)). The reactions were carried out in toluene at 105 °C with the addition of 2% of catalyst precursor **1**, giving good yields of the corresponding new guanidines **2**–**4** (Table 1). The guanidine yield was found to be strongly dependent on the temperature. At room temperature, no reaction of 2,4,6-trimethylaniline with diisopropylcarbodiimide was observed. Conversely, at 105 °C, the conversion to guanidine **2** was complete after approximately 24 h (see Section 3).

We assumed that the proposed mechanism for the guanylation reaction catalyzed by titanium imido complexes (Scheme 1) is also operative in our process [11].

Consequently, a diazavanadacyclobutane, formed from the [2 + 2] addition of the carbodiimide to the V = NAr group should be the intermediate implied in this process. However, the resulting diazavanadacyclobutane is a coordinatively unsaturated species and the efforts to isolate it by reaction of **1** with one equivalent of carbodiimide have been unproductive because the reaction yields a mixture of products. Attempts to isolate a related species by trapping it with a donor co-ligand are currently in progress.

We have also evaluated the activity of other imido and oxo vanadium compounds, such as V(NAr)Cl$_3$(dme) [8a], V(NAr)(^{i}Pr-dtc)$_3$ [8b], V(NAr)[(OCH$_2$CH$_2$)$_3$N] [12] (Ar = 2,6-^{i}Pr$_2$C$_6$H$_3$), V$_2$O$_5$ and VO(acac)$_2$. Table 2 collects the results obtained in the preparation of guanidine **2**. Complex V(NAr)Cl$_3$(dme) was found to be an effective catalyst. This result was not surprising in view of the capacity of this complex to lose the coordinated dimethoxyethane ligand at high temperature to afford the unsaturated complex **1**. By contrast, other imido vanadium complexes, such as V(NAr)(^{i}Pr-dtc)$_3$ and V(NAr)[(OCH$_2$CH$_2$)$_3$N], were found to be inactive for the process. The lack of activity observed for the seven-coordinate complex V(NAr)(^{i}Pr-dtc)$_3$ may be associated with the difficulty in reaching the diazametallacyclobutane intermediate due to the overcrowded vanadium environment [8b]. The lack of activity observed for complex

Table 1
Guanylation of aromatic amines using V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$ as catalyst[a]

Entry	R group of carbodiimide	Amine aryl group	Product	Conversion (%)[b]
1	^{i}Pr	2,4,6-Me$_3$C$_6$H$_2$	**2**	84
2	^{i}Pr	2-ClC$_6$H$_4$	**3**	88
3	Cy	2,4,6-Me$_3$C$_6$H$_2$	**4**	80

[a] Conditions: ratio carbodiimide:aniline:catalyst = 1:1:0.02, t = 24 h, T = 105 °C, solvent = toluene.
[b] Isolated yields.

Table 2
Effect of the catalyst in the guanylation of arylamines[a]

Entry	Catalyst	Product	Conversion (%)[b]
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
6	V$_2$O$_5$	–	No reaction
7	VO(acac)$_2$	**2**	44

[a] See conditions in Section 3.
[b] Isolated yields.

V(NAr)[(OCH$_2$CH$_2$)$_3$N] is clearly related with the high inertness of this species [12].

Finally, we have also investigated the activity of some oxo vanadium compounds. V$_2$O$_5$ displayed not catalytic activity, while VO(acac)$_2$ shows some activity in the guanylation. The inactivity of the former can be attributed to the low solubility of the vanadium compound in the reaction media. The moderate activity of VO(acac)$_2$ was not unexpected considering this complex was an efficient catalyst for carbodiimide metathesis [7].

In conclusion, we have shown that vanadium imido complexes are efficient catalysts for the guanylation of carbodiimides using aromatic amines. Further studies are in progress in order to confirm the mechanism proposed for the process.

3. Experimental

All preparations and other operations were carried out under dry oxygen-free nitrogen atmosphere following conventional Schlenk techniques. Solvents were dried and degassed before use. Carbodiimides and anilines were purchased from Aldrich and they were used as supplied. Compounds V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$ (1) [10], V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$(dme) [8a], V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(^{i}Pr-dtc)$_3$ [8b] were prepared as previously reported. V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)[(OCH$_2$CH$_2$)$_3$N] was prepared by reaction of V(N-2,6-^{i}Pr$_2$C$_6$H$_3$)Cl$_3$(dme) and (HOCH$_2$CH$_2$)$_3$N in the presence of Et$_3$N [12]. Infrared spectra were recorded on Perkin–Elmer Model 883 spectrophotometer. ^{1}H and ^{13}C NMR spectra were run on Bruker AMX-300 spectrometer. Microanalyses (C, H, N) were carried out by the Microanalytical Service of the University of Sevilla. Mass spectra were recorded on Kratos MS80-RFA FAB technique using thioglycerol as a matrix.

3.1. Influence of the temperature

Reactions at different temperatures were monitored by NMR spectroscopy. 1 equivalent of vanadium complex 1 and 50 equivalent for both diisopropylcarbodiimide and 2,4,6-trimethylaniline were mixed in deuterated toluene. (Me$_3$Si)$_2$O was added as an internal standard and the NMR tube was heated at the required temperature for 17 h. Conversions to guanidine 2 were determined by ^{1}H-NMR integration relative to standard O(SiMe$_3$)$_2$. The reaction does not proceed at a reasonable rate below 105 °C.

3.2. Guanylation reaction

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 10 ml of toluene was heated in a thick-walled glass vessel with Teflon stopcock at 105 °C

for 24 h. The 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 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$_6$H$_2$). ^{13}C{^{1}H}-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, 148.0 (s, C$_6$H$_2$), quaternary carbon >C=N– not observed. Anal. Calc. for C$_{16}$H$_{27}$N$_3$(261.22): C, 73.51; H, 10.41; N, 16.07. Found: C, 72.79; H, 10.26; N, 15.62%.

Following a similar procedure were obtained guanidines 3 and 4. *N*-2-chlorophenyl,*N'*,*N''*-diisopropylguanidine (3). 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$_6$H$_4$), 7.11 (t, 1H, 6.6 Hz, C$_6$H$_4$), 7.32 (t, 1H, 7.8 Hz, C$_6$H$_4$). ^{13}C{^{1}H}-NMR (CDCl$_3$): δ 23.4 (s, CH$_3$, ^{i}Pr), 43.3 (s, CH, ^{i}Pr), 122.4, 125.2, 127.5, 129.9 (s, C$_6$H$_4$), 146.9, 149.9 (s, C$_6$H$_4$), quaternary carbon >C=N– not observed. Anal. Calc. for C$_{13}$H$_{20}$N$_3$Cl(253.13): C, 61.53; H, 7.94, N, 16.56. Found: C, 61.49; H, 7.98; N, 16.01%.

N-2,4,6-trimethylphenyl,*N'*,*N''*-dicyclohexylguanidine (4). 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$_6$H$_2$). ^{13}C{^{1}H}-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, 130.5, 143.4, 147.7 (s, C$_6$H$_2$), quaternary carbon >C=N– not observed. Anal. Calc. for C$_{22}$H$_{35}$N$_3$(341.28): C, 77.37; H, 10.33, N, 12.30. Found: C, 76.64; H, 11.31; N, 12.06%.

The same procedure was employed in the catalyst assays (Table 2) with different vanadium complexes using the same reaction conditions (ratio ^{i}PrN=C=N^{i}Pr:2,4,6-Me$_3$C$_6$H$_2$NH$_2$:catalyst = 1:1:0.02, *T* = 105 °C, *t* = 24 h, solvent = toluene).

References

[1] (a) D. Wigley, Prog. Inorg. Chem. 42 (1994) 239;
(b) W.A. Nugent, J.M. Mayer, Metal-Ligand Multiple Bonds, Wiley Interscience, New York, 1988.

[2] (a) R.A. Eikey, M.M. Abu-Omar, Coord. Chem. Rev. 243 (2003) 83;
(b) L.H. Gade, P. Mountford, Coord. Chem. Rev. 216–217 (2001) 65.

[3] For a recent paper devoted to synthesis of guanidines see for example: D.A. Powell, P.D. Ramsden, R.A. Batey, J. Org. Chem. 68 (2003) 2300 (references therein).

[4] (a) T.-G. Ong, G.P.A. Yap, D.S. Richeson, J. Am. Chem. Soc. 125 (2003) 8100;
(b) P. Royo, J. Sánchez-Nieves, J. Organomet. Chem. 597 (2000) 67.

[5] (a) R.L. Zuckerman, R.G. Bergman, Organometallics 20 (2001) 1792;
(b) R.L. Zuckerman, R.G. Bergman, Organometallics 19 (2000) 4795.

[6] T.-G. Ong, G.P.A. Yap, D.S. Richeson, Chem. Commun. (2003) 2612.

[7] K.R. Birdwhistell, J. Lanza, J. Pasos, J. Organomet. Chem. 584 (1999) 200.

[8] (a) F. Montilla, A. Monge, E. Gutiérrez-Puebla, A. Pastor, D. del Río, N.C. Hernández;, J. Fernández Sanz, A. Galindo, Inorg. Chem. 38 (1999) 4462;
(b) F. Montilla, A. Pastor, A. Monge, E. Gutiérrez-Puebla, A. Galindo, J. Chem. Soc., Dalton Trans. (1999) 2893;

(c) F. Montilla, N.C. Hernández, D. del Río, J. Fernández Sanz, A. Pastor, A. Galindo, Organometallics 19 (2000) 304.

[9] (a) A. Galindo, F. Montilla, A. Pastor, E. Carmona, E. Gutiérrez-Puebla, A. Monge, C. Ruiz, Inorg. Chem. 36 (1997) 2379;
(b) F. Montilla, A. Galindo, E. Carmona, E. Gutiérrez-Puebla, A. Monge, J. Chem. Soc., Dalton Trans. (1998) 1299;
(c) F. Montilla, A. Pastor, A. Galindo, J. Organomet. Chem. 590 (1999) 202;
(d) D. del Río, F. Montilla, A. Pastor, A. Galindo, A. Monge, E. Gutiérrez-Puebla, J. Chem. Soc., Dalton Trans. (2000) 2433.

[10] (a) S. Scheuer, J. Fischer, J. Kress, Organometallics 14 (1995) 2627;
(b) J.-K.F. Buijink, J.H. Teuben, H. Kooijman, A.L. Spek, Organometallics 13 (1994) 2922;
(c) D.D. Devore, J.D. Lichtenhan, F. Takusagawa, E.A. Maatta, J. Am. Chem. Soc. 109 (1987) 7408.

[11] One referee suggested the possibility of formation of $V(NAr)(NHAr)_x(Cl)_{3-x}$ species due to the presence of an excess of amine as both a reagent and base. In this case, an alternative mechanism involving carbodiimide insertion into the vanadium amido bond followed by protonation with free amine would also lead to guanidine formation.

[12] A. Pastor, F. Montilla, A. Galindo (unpublished).