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$Ti(NMe_2)_4$ and $[HNMe_2Ph][B(C_6F_5)_4]$: A Convenient Blend for Effective Catalytic Carboamination of Alkynes

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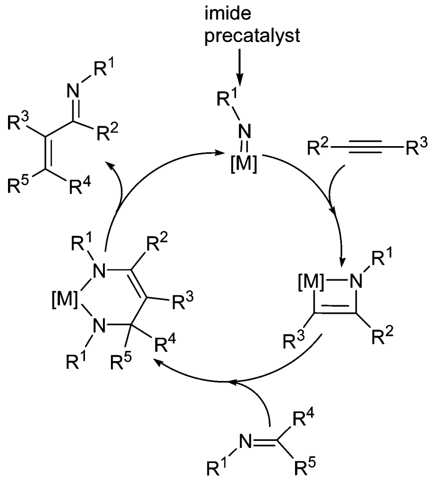
Summary: $Ti(NMe_2)_4$, when combined with $[HNMe_2Ph][B(C_6F_5)_4]$, catalyzes carboamination of alkynes with aldimines to form highly arylated α,β-unsaturated imines with exclusive (E,E)-configuration at the olefin and imine residues. Complexes $[Ti(NHMe_2)(NMe_2)_3][B(C_6F_5)_4]$ and $[Ti{=}NAr(NHMe_2)_3(NMe_2)][B(C_6F_5)_4]$ ($Ar = 2,6\text{-}^iPr_2C_6H_3$), isolated from stoichiometric reactions involving $Ti(NMe_2)_4/[HNMe_2Ph][B(C_6F_5)_4]$ and $Ti(NMe_2)_4/[HNMe_2Ph][B(C_6F_5)_4]/ArNH_2$, respectively, also catalyze carboamination with activity comparable to that of the $Ti(NMe_2)_4/[HNMe_2Ph][B(C_6F_5)_4]$ system.

The catalytic carboamination of alkynes with imines is an emerging field in organotransition metal chemistry allowing access to a new class of highly arylated organic archetypes.[1−3] Recently, the Bergman group reported imidozirconocene-catalyzed carboamination reactions involving aryl aldimines and diaryl alkynes to generate α,β-unsaturated imines.[1,2] Inspired by this work, in which new C═C and C═N bonds are formed, our group discovered that the latent low-coordinate titanium imide $[(nacnac)Ti{=}NAr(FC_6H_5)][B(C_6F_5)_4]$ ($nacnac^- = [ArNC(^tBu)]_2CH$, $Ar = 2,6\text{-}^iPr_2C_6H_3$) can also engage, efficiently, in catalytic carboamination reactions to produce α,β-unsaturated imines as well as triaryl-substituted quinolines.[3] In both titanium- and zirconium-catalyzed reactions, the first step in the catalytic cycle involves generation of an unsaturated metal imide $[M]{=}NR^1$. [2+2] Cycloaddition of the alkyne across the M═N linkage and subsequent insertion of aldimine into the M−C bond of the four-membered azametallacyclobutene forms a six-membered metallacycle. The latter readily undergoes a retro-[4+2] cycloaddition to extrude the α,β-unsaturated imine product and regenerate the corresponding imide (Scheme 1). In the catalytic reaction, the electron-deficient cation $[(nacnac)Ti{=}NAr(FC_6H_5)]^+$ was a precatalyst since it readily underwent imine metathesis in situ with the appropriate aldimine substrate to afford a sterically less hindered imide, which would then execute the catalytic cycle. Although the Ti(IV) fluorobenzene precatalyst was effective in performing these reactions, the exceedingly reactive nature of this complex limited our ability to manipulate this system under traces of donors as well as explore functional group tolerance.[3] Consequently, these limitations prompted us to seek other catalysts or precatalysts that not only would be facile to prepare and manipulate but would reduce reaction times and temperatures and expand the range of substrates.

Scheme 1. Mechanism for the Catalytic Carboamination of Alkynes with Imines



In this work, we wish to disclose that the combination of $Ti(NMe_2)_4$ and $[HNMe_2Ph][B(C_6F_5)_4]$[4] generates an efficient catalyst system for the carboamination of alkynes with aldimines. The commercial availability of the two reagents avoids multistep ligand and metal complex syntheses, allowing for the facile preparation of highly arylated α,β-unsaturated imines. Additionally, this catalyst system also tolerates a variety of functional groups and reduces both reaction times and temperatures. In the process of investigating the active species involved in the catalytic carboamination cycle we discovered two titanium salts, both of which appear to be precatalysts in the catalytic carboamination reaction.

Previous studies by Odom[5] and Schafer[6] have demonstrated that common reagents such as $Ti(NMe_2)_4$ can serve as competent precatalysts for the hydroamination[7,8] of alkynes and intramolecular hydroamination of amino alkenes, respectively. Unfortunately, $Ti(NMe_2)_4$ was not efficient in catalyzing carboamination reactions using di-*p*-tolylaldimine and PhCCPh in the presence or absence of *p*-toluidine (Table 1, entries 1, 2). Realizing that the carboamination precatalyst [(nacnac)Ti═NAr-

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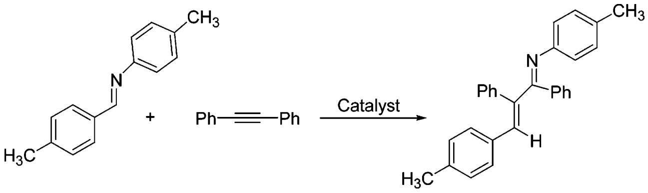
Table 1. Screening of Catalysts for the Carboamination Reaction[a]



entry	catalyst	time (h)	yield (%)
1	$Ti(NMe_2)_4$ (20 mol %)	120	traces
2	$Ti(NMe_2)_4$/4-$CH_3C_6H_4NH_2$ (20 mol % each)	120	traces
3	$Ti(NMe_2)_4$/4-$CH_3C_6H_4NH_2$/ $[HNMe_2Ph][B(C_6F_5)_4]$(10 mol % each)	16	80−90
4	$Ti(NMe_2)_4$/$[HNMe_2Ph][B(C_6F_5)_4]$ (10 mol % each)	16	80−90

[a] Reactions were carried out on a 0.25 mmol scale of aldimine using 10 mol % catalyst in C_6D_6 at 125 °C and % yield was assayed by ^1H NMR.

$(FC_6H_5)][B(C_6F_5)_4]$ is a salt-like, latent low-coordinate titanium imide reagent, we hypothesized whether acids such as $[HNMe_2Ph][B(C_6F_5)_4]$ could activate $Ti(NMe_2)_4$.

Gratifyingly, 1:1:1 C_6D_6 solutions of 10 mol % $Ti(NMe_2)_4$, $[HNMe_2Ph][B(C_6F_5)_4]$, and *p*-toluidine catalyzed carboamination reactions in considerably shorter reaction times (16 h) and lower temperatures (125 °C) when compared to the Cp_2Zr[2] and (nacnac)Ti-based[3] catalysts previously reported in the literature (Table 1, entry 3).[9] To our surprise, the same carboamination reaction also proceeded smoothly but in the absence of the aniline (Table 1, entry 4).[9] Since early transition metal imides have been proposed to be active intermediates along the carboamination cycle,[1−3] the absence of aniline in the latter reaction suggests that aldimine might be playing a role as an imide-transfer reagent.[10] The titanium reagent $Ti(NMe_2)_4$ is critical in these reactions since 10−20 mol % of $[HNMe_2Ph][B(C_6F_5)_4]$ alone failed to show any conversion to the α,*β*-unsaturated imine product.

On the basis of these preliminary experiments, reactions of a series of aldimines and alkynes were carried out according to the reaction conditions described in entry 4 of Table 1. Aldimines bearing electron-donating groups such as methyl, methoxy, and dimethylamino groups gave the corresponding α,*β*-unsaturated imine derivatives in good yields (Table 2a, entries 2−8), whereas aldimines bearing an electron-withdrawing trifluoromethyl group did not afford the product. Alkynes such as bis(*p*-methylphenyl)acetylene and bis(*p*-methoxyphenyl)acetylene containing electron-donating groups also gave the corresponding α,*β*-unsaturated imine derivatives in good yields (Table 2a, entries 9−12). The carboamination of bis(*p*-bromophenyl)acetylene afforded the corresponding dibromo-substituted α,*β*-unsaturated imine in 32% yield (Table 2a, entry 13). Unsymmetrical alkynes such as $PhCC(4\text{-}CH_3C_6H_4)$ did not exhibit regioselective carboamination. All the α,*β*-unsaturated imines generated from these carboamination reactions have exclusive (*E*,*E*)-configuration at the olefin and the imine residues (Table 2a, entries 1−13).[9] Most notably, the reaction times are dramatically reduced from 24−96 h to 16−24 h using this combination of ingredients.

To isolate an active species involved in the carboamination reactions, we studied the products generated by various combinations of $Ti(NMe_2)_4$, $[HNMe_2Ph][B(C_6F_5)_4]$, diphenylacetylene, and *p*-tolylaldimine. Accordingly, reaction of $Ti(NMe_2)_4$ with 1 equiv of $[HNMe_2Ph][B(C_6F_5)_4]$ generated the trisamide monoamine salt $[Ti(NHMe_2)(NMe_2)_3][B(C_6F_5)_4]$ in 85% yield. ^1H, ^{13}C, ^{19}F, and ^{11}B NMR spectra of **1** are consistent with cation formation resulting from an amide being protonated, while the single-crystal X-ray structure confirms the ionic and monomeric nature of the four-coordinate titanium center (Figure 1).[9,11] Our hypothesis that aldimine might play a role as an imide transfer reagent in the catalytic cycle proved reasonable inasmuch as isolated samples of complex **1** catalyze carboamination reactions of alkynes with aldimines with similar catalytic activity (Table 2b, entries 14−17) to the $Ti(NMe_2)_4$/$[HNMe_2Ph][B(C_6F_5)_4]$ system reported in entries 2, 4, 6, and 7 of Table 2a (vide supra).[9] Multiple attempts to isolate a complex from the stoichiometric reaction mixtures containing $Ti(NMe_2)_4$, $[HNMe_2Ph][B(C_6F_5)_4]$, and *p*-tolylaldimine in the presence and absence of diphenylacetylene were unsuccessful.

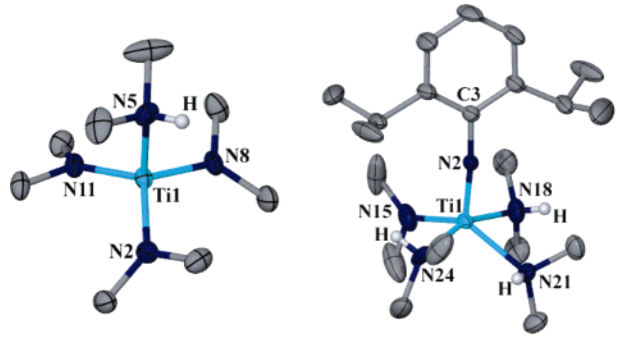


Figure 1. Molecular structure of cationic components of complexes **1** (left) and **2** (right) depicting thermal ellipsoids at the 50% probability level. Only α-hydrogens on the amines are depicted for the purpose of clarity. Selected bond lengths (Å) and angles (deg) for the cation of **1**: Ti1−N2, 1.857(2); Ti1−N8, 1.870(2); Ti1−N11, 1.876(2); Ti−N5, 2.188(2); N2−Ti1−N8, 108.96(5); N2−Ti1−N11, 111.12(5); N2−Ti1−N5, 110.71(5); N5−Ti1−N8, 102.72(5); N5−Ti1−N11, 110.16(5); N8−Ti1−N11, 112.87(5). For the cation of **2**: Ti1−N2, 1.714(2); Ti1−N15, 1.908(2); Ti1−N18, 2.234(2); Ti1−N24, 2.259(3); Ti1−N21, 2.295(2); N15−Ti1−N18, 91.2(1); N18−Ti1−N21, 85.11(9); N21−Ti1−N24, 81.49(9); N24−Ti1−N15, 93.1(1); N15−Ti1−N2, 105.9(1); N18−Ti1−N2, 99.2(1); N21−Ti1−N2, 109.1(1); N24−Ti1−N2, 96.2(1); Ti1−N2−C3, 173.4(9).

The possibility of a titanium imide playing a role in these carboamination reactions motivated us to prepare a terminal imide using an alternative method. Treatment of **1** with the hindered aniline H_2NAr (Ar = 2,6-$^iPr_2C_6H_3$) afforded the five-coordinate titanium imide $[Ti{=}NAr(NHMe_2)_3(NMe_2)][B(C_6F_5)_4]$ (**2**) in excellent yield. NMR spectra, as well as the single-crystal X-ray structure, confirmed a cationic, five-coordinate titanium center possessing a terminal imide motif (Figure 1).[9,12] More specifically, the molecular structure of **2** clearly depicts a square pyramidal Ti(IV) center containing a terminal arylimide functionality in the axial position, while three pyramidalized dimethylamines and one planar dimethylamide occupy the equatorial sites. Complex **2** also catalyzes carboamination reactions comparable to that of the in situ-generated catalyst

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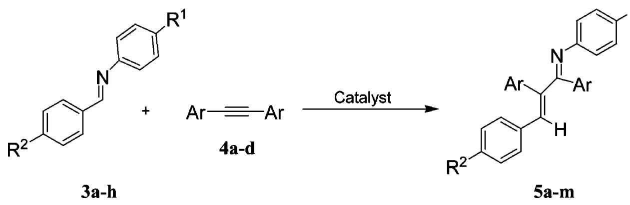
(9) See Supporting Information for complete experimental details.

(10) Gomez-Sal, P.; Martin, A.; Mena, M.; Morales, M. C.; Santamaria, C. *Chem Commun*. **1999**, 1839−1840.

(11) Crystal data for **1**: $C_{32}H_{25}BF_{20}N_4Ti$, 904.27 g/mol, triclinic, $P\bar{1}$, yellow prism, $a = 14.4540(17)$ Å, $b = 17.392(2)$ Å, $c = 17.702(2)$ Å, $\alpha = 109.676(3)°$, $\beta = 108.043(3)°$, $\gamma = 106.675(3)°$, $V = 3583.7(7)$ Å^3, $T = 127(2)$ K, $Z = 4$, $R(F$, observed data$) = 0.0371$, $S = 1.014$. Data were collected on a Bruker three-circle diffractometer with a SMART 6000 detector. The structure was solved by direct methods (SHELXS) and refined via full-matrix least-squares (SHELXL). Hydrogen atoms were placed in idealized positions and refined isotropically; non-hydrogen atoms were refined anisotropically.

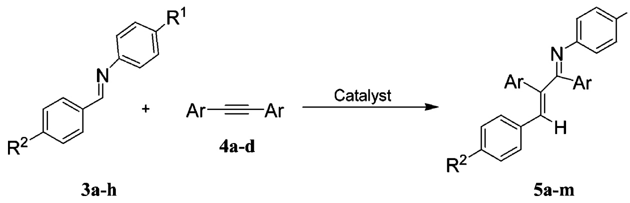
Table 2a. Carboamination Reactions Catalyzed by a $Ti(NMe_2)_4/[HNMe_2Ph][B(C_6F_5)_4]$ Mixture[a]



entry	aldimine	alkyne	product	yield (%)
1[b]	**3a**; $R^1 = R^2 = H$	**4a**; Ar = Ph	**5a**	71
2[b]	**3b**; $R^1 = R^2 = CH_3$	**4a**; Ar = Ph	**5b**	69
3	**3c**; $R^1 = CH_3$, $R^2 = OCH_3$	**4a**; Ar = Ph	**5c**	70
4[b]	**3d**; $R^1 = OCH_3$, $R^2 = CH_3$	**4a**; Ar = Ph	**5d**	68
5	**3e**; $R^1 = NMe_2$, $R^2 = OCH_3$	**4a**; Ar = Ph	**5e**	70
6	**3f**; $R^1 = R^2 = OCH_3$	**4a**; Ar = Ph	**5f**	68
7	**3g**; $R^1 = OCH_3$, $R^2 = NMe_2$	**4a**; Ar = Ph	**5g**	75
8	**3h**; $R^1 = CH_3$, $R^2 = NMe_2$	**4a**; Ar = Ph	**5h**	72
9	**3g**; $R^1 = OCH_3$, $R^2 = NMe_2$	4b; Ar = 4-$CH_3C_6H_4$	**5i**	72
10	**3h**; $R^1 = CH_3$, $R^2 = NMe_2$	**4c**; Ar = 4-$OCH_3C_6H_4$	**5j**	76
11	**3f**; $R^1 = R^2 = OCH_3$	**4b**; Ar = 4-$CH_3C_6H_4$	**5k**	62
12	**3d**; $R^1 = OCH_3$, $R^2 = CH_3$	**4c**; Ar = 4-$OCH_3C_6H_4$	**5l**	64
13[c]	**3h**; $R^1 = CH_3$, $R^2 = NMe_2$	**4d**; Ar = 4-BrC_6H_4	**5m**	32

[a] Reactions were carried out with 10 mol % $Ti(NMe_2)_4/[HNMe_2Ph][B(C_6F_5)_4]$ in C_6D_6 at 125 °C for 24 h. Reaction times were not minimized. Yield of the isolated product after column chromatography. [b] Reactions also proceeded to completion with 5 mol % catalyst mixture. [c] 15 mol % $Ti(NMe_2)_4/[HNMe_2Ph][B(C_6F_5)_4]$ was used.

Table 2b. Carboamination Reactions Catalyzed by Isolated Samples of Compound 1 or 2[d]



entry	catalyst	aldimine	alkyne	product	yield (%)
14	**1**	**3b**; $R^1 = R^2 = CH_3$	**4a**; Ar = Ph	**5b**	80−90[e]
15	**1**	**3d**; R1 = OCH_3, $R^2 = CH_3$	**4a**; Ar = Ph	**5d**	64[f]
16	**1**	**3f**; $R^1 = R^2 = OCH_3$	**4a**; Ar = Ph	**5f**	66[f]
17	**1**	**3g**; $R^1 = OCH_3$, $R^2 = NMe_2$	**4a**; Ar = Ph	**5g**	71[f]
18	**2**	**3b**; $R^1 = R^2 = CH_3$	**4a**; Ar = Ph	**5b**	80−90[e]
19	**2**	**3d**; $R^1 = OCH_3$, $R^2 = CH_3$	**4a**; Ar = Ph	**5d**	65[f]
20	**2**	**3f**; $R^1 = R^2 = OCH_3$	**4a**; Ar = Ph	**5f**	69[f]
21	**2**	**3g**; $R^1 = OCH_3$, $R^2 = NMe_2$	**4a**; Ar = Ph	**5g**	73[f]

[d] Reactions were carried out on a 0.25 mmol scale of aldimine using 10 mol % of catalyst in C_6D_6 at 125 °C for 24 h. Reaction times were not minimized. [e] The percent yield was assayed by ^1H NMR spectroscopy. [f] The percent yield was obtained after column chromatography.

system (Table 2b, entries 18−21), thereby hinting that **2** might also be a precatalyst.

In conclusion, we have shown that $[HNMe_2Ph][B(C_6F_5)_4]$ can transform a commercially available starting material such as $Ti(NMe_2)_4$ into an efficient catalyst for carboamination of alkynes, therefore providing a facile protocol for the synthesis of highly arylated α,β-unsaturated imines. The fact that complex **1** catalyzes carboamination reactions of alkynes with aldimines in the absence of aniline suggests tantalizingly that aldimine might be playing a role as an imide transfer reagent. We are currently exploring the mechanism of this reaction and the role of $[HNMe_2Ph][B(C_6F_5)_4]$ with other common reagents of titanium.

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Supporting Information Available: Complete experimental preparation (**1** and **2**, and organic products **3**−**5**) and crystallographic data (**1** and **2**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Crystal data for **2**: $C_{44}H_{44}BF_{20}N_5Ti$, 1081.55 g/mol, triclinic, $P\bar{1}$, yellow prism, $a = 11.516(2)$ Å, $b = 13.155(3)$ Å, $c = 16.474(3)$ Å, $\alpha = 88.869(5)°$, $\beta = 73.304(5)°$, $\gamma = 86.209(5)°$, $V = 2385.4(8)$ Å^3, $T = 124(2)$ K, $Z = 2$, $R(F$, observed data) = 0.0474, $S = 0.860$. Data were collected on a Bruker three-circle diffractometer with a SMART 6000 detector. The structure was solved by direct methods (SHELXS) and refined via full-matrix least-squares (SHELXL). Hydrogen atoms were placed in idealized positions and refined isotropically; non-hydrogen atoms were refined anisotropically.