Imidozirconium Complexes

Carboamination: Additions of Imine C=N Bonds Across Alkynes Catalyzed by Imidozirconium Complexes**

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The development of new reactions employing imidozirconium complexes or their derivatives as catalysts is an elusive goal in organometallic chemistry. To date, the imidozirconocene-catalyzed hydroamination of alkynes and allenes to yield new enamines (and, on tautomerization, imines) is the lone example of such a process.[1,2] We recently reported that aldehydes and electron-deficient imines insert into the carbon–zirconium bond of azazirconacyclobutene **1** to afford new six-membered ring metallacycles **2** and **3** (see Scheme 1). On heating, these expanded zirconacycles undergo a retro-[4+2] cycloaddition to afford α,β-unsaturated imine **4** and oxozirconium complex **5** or electron-poor imidozirconocene dimer **6**, both of which are unreactive (Scheme 1; EWG = electron-withdrawing group, Cp = C_5H_5).[3,4] We reasoned that insertion of an aldimine **7** with *N*-substitution identical to that of the nitrogen group in the metallacyclobutene, followed by subsequent retro-cycloaddition, would not only afford α,β-unsaturated imine **4** but would also generate imidozirconocene complex **8** previously used to prepare the starting azazirconacyclobutene (see Scheme 2).[5] Carrying out the reaction in the presence of the necessary alkyne would regenerate the starting metallacycle and close the catalytic cycle (Scheme 2).[6] This reaction is deemed a carboamination, because it results in the overall cleavage of an imine C=N bond and addition of the resulting C and N fragments across an alkyne, forming a new carbon–carbon double bond and a new ketimine carbon–nitrogen double bond.[7–9] Herein, we present the development of a novel, high-yielding imidozirconocene-catalyzed carboamination reaction that also represents the best method for preparing the highly arylated α,β-unsaturated imine co-products.

The most frequently studied imidozirconium complexes bear sterically bulky groups on the nitrogen atom to prevent competitive dimerization of the imido compound.[5] As such, *N*-2,6-dimethylphenyl- and *N*-*tert*-butyl-substituted azazirconacyclobutenes **1** and **9** (see Scheme 3) were explored in the desired insertion chemistry. Unfortunately, even at high concentrations of substrate and temperatures up to 165 °C, neither of these zirconium compounds was an effective catalyst as no imine insertion products were observed. In the case of metallacycle **1** and imine **10**, it appears that the combined steric bulk of the zirconacycle and imine *N*-substituents prohibits insertion; with metallacycle **9** and *N*-*tert*-butyl imine **11**, we began to observe C–D bond activation of the [D$_6$]benzene solvent. Presumably, this pathway arises from [2+2]-cycloreversion to afford the free imidozirconocene complex **12**, which had been shown to activate benzene C–H bonds at a minimum temperature of 75 °C (Scheme 3).[10]

While few obvious modifications can be made to the *N*-*tert*-butyl framework, we reasoned that a smaller *N*-aryl substituent would decrease the steric bulk of both the azazirconacyclobutene and the reacting imine to better facilitate insertion into the metallacycle Zr–C bond. $[\mathrm{Cp_2Zr{=}N}(p\text{-}\mathrm{C_6H_4CH_3})]$ (**13a**) undergoes irreversible dimerization in the absence of a trapping agent; however, imido complex **13a** will react preferentially with an alkyne to generate the *N*-tolyl metallacyclobutene **14a** (see Table 1).[5] This observation is particularly relevant to a potential catalytic system, since alkyne will be in substantial excess relative to **13a** for the majority of the reaction, further decreasing the likelihood of competitive dimerization. We

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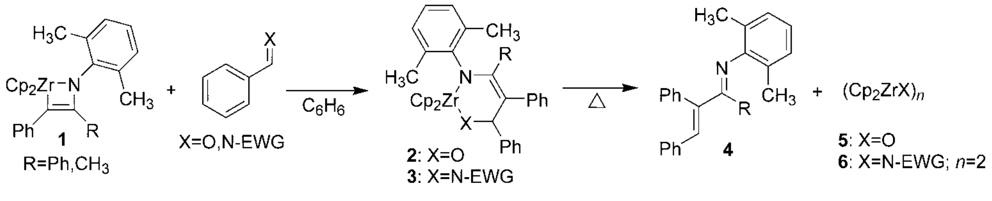
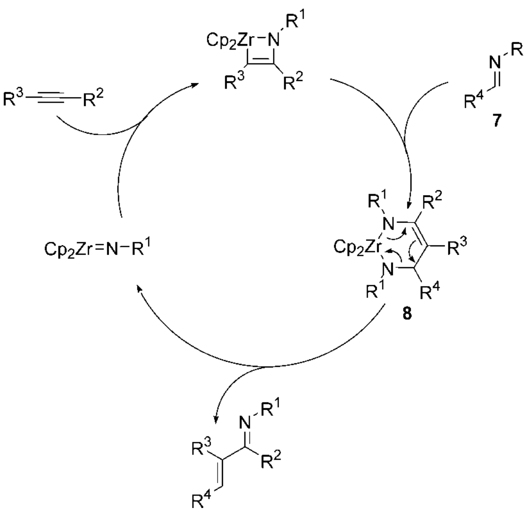
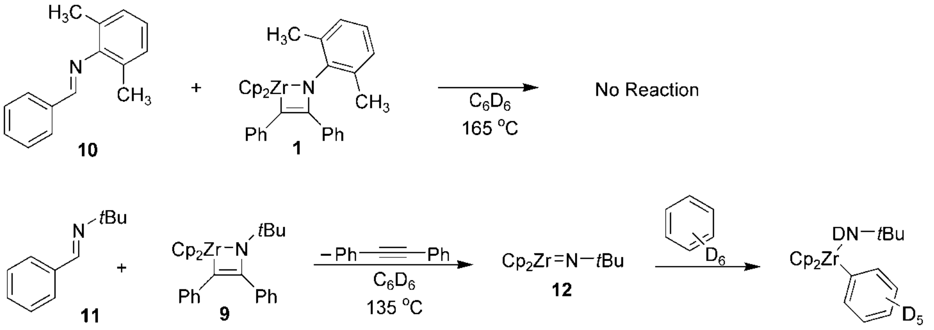


Scheme 1.



Scheme 2.



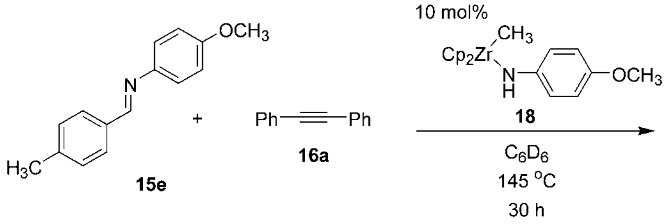
Scheme 3.

were pleased to find that one equivalent of azazirconacyclobutene **14a** reacted with four equivalents of both *N*-*p*-tolyl *p*-tolualdimine (**15a**) and diphenylacetylene (**16a**) at 135 °C (reactions carried out in sealed tubes, for full experimental details see the Supporting Information) to effect complete consumption of **15a** and generation of new α,β-unsaturated imine **17a**. No intermediate six-membered-ring metallacycle was observed during the course of the reaction, consistent with rate-determining imine insertion into the azametallacyclobutene Zr–C bond. Optimization of temperature, catalyst concentration, and concentration of reagents led to the development of a system that employs 10 mol% of **14a** and one equivalent each of imine and alkyne in benzene at 145 °C to afford a 71% yield of α,β-unsaturated imine **17a**. This catalytic carboamination reaction generates the (*E*)-imine and (*E*)-olefin stereoisomers exclusively and provides the only known synthesis of this product.

With optimized conditions in hand, we next sought to expand the scope of all components of the reaction. The more electron-rich substrates, *N*-*p*-tolyl *p*-anisaldimine (**15b**) and *N*-*p*-tolyl *p*-*N*,*N*-dimethylaminobenzaldimine (**15c**) were also competent in this chemistry (Table 1), whereas electron-poor *N*-*p*-tolyl *p*-trifluoromethylbenzaldimine failed to insert. These observations were somewhat surprising given the ease with which electron-deficient imines were shown to insert previously.[11] We have also been able to employ bis(*p*-methoxyphenyl)acetylene (**16b**) by preparing the requisite azazirconacyclobutene **14b**. This metallacycle catalyzed the carboamination of alkyne **16b** with imine **15a** in good yield at 160 °C.[12,13] The azazirconacyclobutene formed by reaction of imidozirconocene complex **13a** with 1-phenyl-1-propyne was unstable at the high temperatures required for insertion.[14] Finally, *N*-*p*-methoxyphenyl (PMP) azametallacyclobutene **14c** catalyzed the carboamination reaction between *N*-*p*-methoxyphenyl *p*-benzaldimine (**15d**) or *N*-*p*-methoxyphenyl *p*-tolualdimine (**15e**) and diphenylacetylene (**16a**).[15] *N*-*p*-Methoxyphenyl *m*-tolualdimine (**15f**) was also a competent substrate in this chemistry, while only approximately 30% of *N*-*p*-methoxyphenyl *o*-tolualdimine was converted into product. Use of the PMP group as a substituent on the nitrogen atom is particularly attractive, since nucleophilic addition to or reduction of the product PMP-imine provides a *p*-methoxyphenyl-protected primary amine, which may be liberated under mild oxidative conditions.[16]

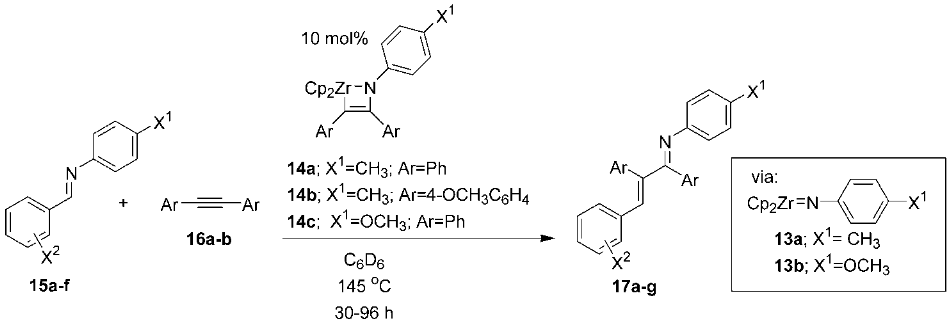
We have employed methylzirconocene (*p*-methoxyphenyl)amide (**18**) as the catalyst in the carboamination reaction between imine **15e** and alkyne **16a** to generate α,β-unsaturated imine product **17e** in 75% yield (Scheme 4).[17] This yield is comparable to that obtained with azazirconacyclobutene **14c** as catalyst (Table 1, entry 5). From a practical standpoint, this development allows the chemist to by-pass the additional step of azazirconacyclobutene formation, while also eliminating the necessity of preparing a different azazirconacyclobutene catalyst for each new alkyne considered. From a mechanistic standpoint, this result supports the intermediacy of imidozirconium compound **13b** (generated in situ on elimination of methane from **18**) along the proposed catalytic cycle.

In summary, we have succeeded in developing a novel imidozirconocene-catalyzed carboamination reaction that adds an imine C=N bond across an alkyne to generate



Scheme 4.

Table 1: Carboamination reactions catalyzed by imidozirconocenes **14**. [a]



Entry	Starting Imine	Alkyne	Catalyst	Product	Yield [%][b]
1	**15a**; $X^1 = CH_3$; $X^2 = 4\text{-}CH_3$	**16a**; Ar = Ph	**14a**	**17a**	71
2	**15b**; $X^1 = CH_3$; $X^2 = 4\text{-}OCH_3$	**16a**; Ar = Ph	**14a**	**17b**	71
3	**15c**; $X^1 = CH_3$; $X^2 = 4\text{-}N(CH_3)_2$	**16a**; Ar = Ph	**14a**	**17c**	82
4	**15d**; $X^1 = OCH_3$; $X^2 = H$	**16a**; Ar = Ph	**14c**	**17d**	80
5	**15e**; $X^1 = OCH_3$; $X^2 = 4\text{-}CH_3$	**16a**; Ar = Ph	**14c**	**17e**	80
6	**15f**; $X^1 = OCH_3$; $X^2 = 3\text{-}CH_3$	**16a**; Ar = Ph	**14c**	**17f**	85
7[c]	**15a**; $X^1 = CH_3$; $X^2 = 4\text{-}CH_3$	**16b**; Ar = 4-$OCH_3C_6H_4$	**14b**	**17g**	58

[a] Reaction is conducted with 10 mol% azazirconacyclobutene **14** (with appropriate X^1 and Ar substitution) as catalyst and imine **15** and alkyne **16** at 0.5 M in C_6D_6. [b] Yield of isolated product after chromatography. [c] Reaction was conducted at 160°C using a 3:1 mixture of **14c**:**16b**.

synthetically interesting α,β-unsaturated imine products. While the substrate scope of the transformation is, at present, limited to all-aryl substitution, the products generated have not been accessed by alternative means. We will continue to develop this chemistry with the goal of expanding the substrate scope to include new imines and alkynes. Full experimental details can be found in the Supporting Information. A related paper that reports the insertion of *N*-acylamines into azazirconacyclobutenes also appears in this issue.[18]

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[11] See ref. [4]. This observation implicates an alternative effect, speculatively pre-coordination of the electron-withdrawing group oxygen atom to zirconium, in the previously reported chemistry.

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