Telomerization of Amines Mediated by Cationic *N*-Heterocyclic Carbene (NHC) Palladium Complexes

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*Summary: The synthesis and characterization of novel [(NHC)Pd(allyl)]X complexes (where NHC = N-heterocyclic carbene and X is a counteranion) are reported. The complexes with a general formula [(IPr)Pd(allyl)(S)]X (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, X = BF_4 (**1**) or PF_6 (**2**)) have been structurally characterized by single-crystal diffraction studies and adopt a distorted square-planar geometry and include a coordinated solvent molecule (S). These cationic complexes promote the rapid and selective combination of 1,3-butadiene and amine into telomers. The active complexes are conveniently prepared in situ and display activity even at very low catalyst loadings. Operating temperatures are mild and can be as low as room temperature. Both secondary and primary amines are cleanly converted to the corresponding telomers.*

Telomerization, the formation of short oligomers from dienes, is a very efficient organic transformation with an overall atom economy of 100%. Complexes of palladium are known to catalyze the reaction of dienes with a variety of nucleophiles.[1] Mechanistically, the reactions are thought to proceed by allyl coordination of two butadiene molecules to a palladium(0) center followed by the formation of a C−C bond. The eight-carbon chain is then attacked by a nucleophile at the terminal or at the 3 position. It is also known that the dimerization process of butadiene-type substrates can take place if a "naked" palladium center is the catalyst, leading to linear or cyclic products.[2] When ligands are appended to the reactive palladium center, the formation of octadiene is suppressed.[1] If a nucleophile is added to the diene under palladium-mediated telomerization conditions, this nucleophile acts as a reaction partner. The most commonly encountered ligands employed in telomerization reactions are tertiary phosphines.[1] A closer inspection of the proposed catalytic cycle and kinetic data[3] supports the hypothesis that only one ligand is required to promote and sustain the catalytic activity (Scheme 1).

When tertiary phosphine ligands are used, a mixture of products can be obtained due to the degradation[4] associated with this type of ligand (thermal P−C bond degradation). As a result, excess ligand is commonly used.[5] The full potential of this reaction is then limited due to slower rates associated with the use of excess ligand.

Recently, Beller and co-workers have reported a very active catalytic system for telomerization of butadiene and methanol.[6] The catalyst consists of an *N*-heterocyclic carbene (NHC) ligand bound to a palladium(0) center.

N-Heterocyclic carbenes have proven to be excellent ligands in numerous palladium-coupling reactions[7] and a very attractive alternative to tertiary phosphines in olefin metathesis.[8] The ability of this ligand family to strongly coordinate to most metal centers[9] facilitates catalyst design efforts, as ligand−metal ratios can be fully controlled.

Our first attempts to promote the telomerization of butadiene using morpholine as a nucleophile using neutral (NHC)Pd(allyl)Cl complexes failed. We presume this failure was due to the inefficient reduction of Pd(II) to Pd(0). Previous studies on this class of complexes revealed a reliable reduction of the metal center by nucleophilic attack of a base on the allyl fragment.[10] Adding NaO^tBu, in catalytic amount, to the reaction mixture enables the telomerization reaction to proceed with the neutral palladium complex, although at a very slow rate. We then chose to enhance the reactivity of the palladium metal center by replacing the chloride with a noncoordinating anion. Cationic complexes, bearing a more electrophilic center, should display an increased susceptibility to nucleophilic attack.[5]

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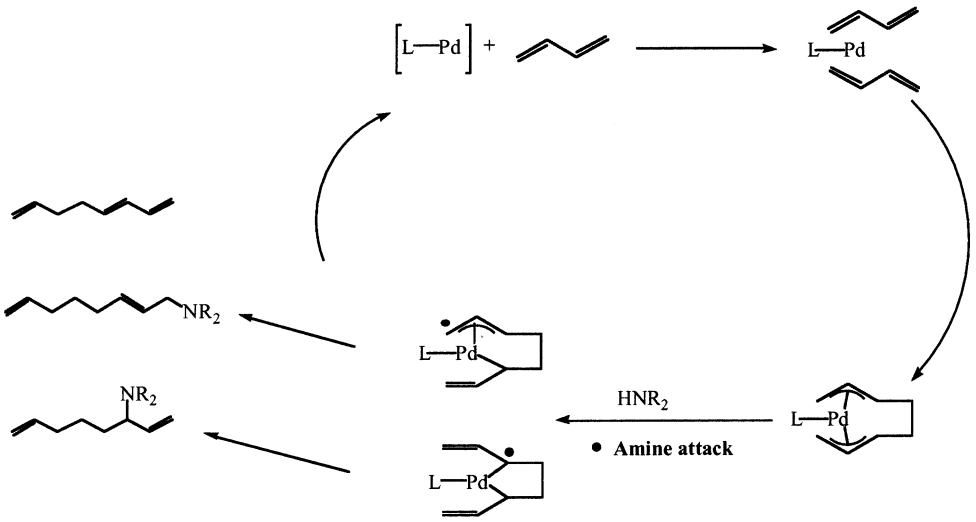
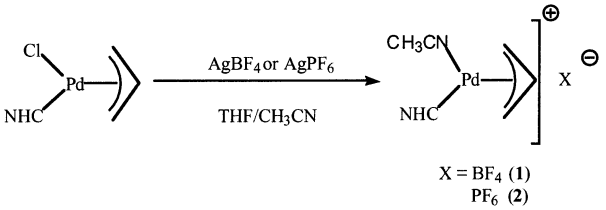
Scheme 1. Mechanism of Telomerization



Scheme 2. Synthesis of (IPr)Pd(η^3-allyl)]X



The cationic complexes were prepared in quantitative yields from neutral (NHC)Pd(allyl)Cl[9] with $AgBF_4$ (leading to **1**) or $AgPF_6$ (leading to **2**) (Scheme 2).

The reactions were performed initially in THF, but the complexes generated were unstable and decomposed upon workup. Changing the solvent to acetonitrile or MeCN/THF mixtures resulted in isolation of complexes stabilized by the more strongly coordinating acetonitrile solvent. The solvent molecule is presumably now occupying the free coordination site generated upon chloride abstraction. The halide abstraction reaction is very rapid and is confirmed by rapid precipitation of AgCl. The MeCN/THF solutions were evaporated at room temperature, and colorless crystals were obtained. These crystals were subjected to single-crystal diffraction studies (Figure 1).

In all cases, the complexes show a distorted square-planar geometry. The symmetry of the allyl group is affected by the presence of ligand, and all protons are magnetically inequivalent. The palladium to carbenic carbon distance is 2.066 Å for **1** and 2.050 Å for **2**, evidence for a stronger interaction between the palladium center and carbene supporting ligand when PF_6 is the counterion. All cationic complexes have Pd−$C_{carbenic}$ distances longer than their parent neutral complex (2.04 Å).[9a] In both complexes, **1** and **2**, the counterion (closest F to the Pd center) is located a considerable distance away from the central metal ion, 7.234 Å in **1** and 8.197 Å in **2**. The fourth coordination site is occupied by acetonitrile. Despite an electronically stable configuration around palladium, the complexes are moisture-sensitive. The enhanced electrophilicity of the metal ion may facilitate an indirect nucleophilic attack of water on the allyl moiety and subsequent catalyst decomposition.

In early experiments, the reaction between morpholine and butadiene mediated by [(IPr)Pd(allyl)]BF_4 was observed to lead to telomeric products. The reaction was found to reach completion in 3 h at 60 °C under 2 atm of butadiene with a catalyst loading of 0.2 mol %. The catalyst can be activated by coordination of diene or nucleophilic attack of amine. It is interesting to note that catalytic activity of palladium complexes is superior if they are generated in situ by reaction of (IPr)Pd(allyl)-Cl with sodium salts of the noncoordinating anions.[11] A possible explanation for this behavior is the formation of a vacant coordination site when the reaction is performed in weakly coordinating or noncoordinating

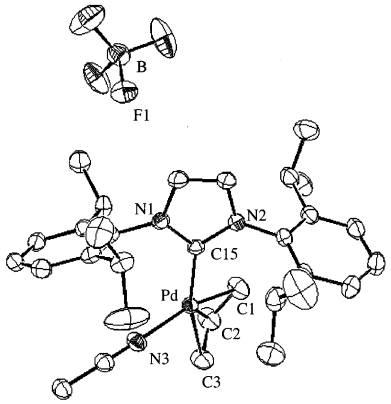


Figure 1. ORTEP of (IPr)Pd(allyl)BF_4 (**1**). Hydrogens have been omitted for clarity. Selected bond distances (Å) and angles (deg): Pd−C(15), 2.066; Pd−N(3), 2.086; Pd−F(1), 7.234; Pd−C(1), 2.081; Pd−C(2), 2.150; Pd−C(3), 2.199; Pd−C(15)−N(3), 100.05.

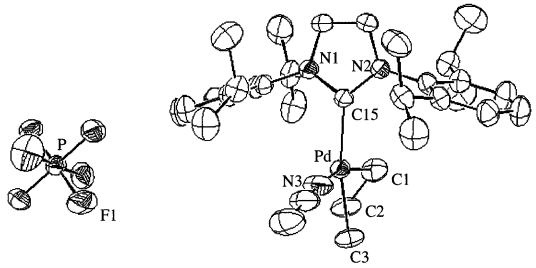
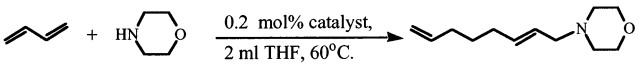


Figure 2. ORTEP of (IPr)Pd(allyl)PF_6 (**2**). Hydrogens have been omitted for clarity. Selected bond distances (Å) and angles (deg): Pd−C(15), 2.050; Pd−N(3), 2.082; Pd−F(1), 8.197; Pd−C(1), 2.149; Pd−C(2), 2.147; Pd−C(3), 2.178; Pd−C(15)−N(3), 101.27.

Table 1. Effects of Catalyst Counterion on Telomerization of Amines with Butadiene



catalyst	time (h)	yield (%)[a]
(IPr)Pd(allyl)PF_6	0.25	100
(IPr)Pd(allyl)BF_4	2	100
(IPr)Pd(allyl)BAr'_6[b]	6	96
(IPr)Pd(allyl)BPh_4	6	45
(IPr)Pd(allyl)Cl	6	4

[a] GC yields. [b] Ar′ = 3,5-$(CF_3)_2C_6H_3$.

solvents such as THF and toluene. We chose to generate the catalysts in situ as a standard procedure based of the ease of handling and reaction rates.

A survey of solvent effects on the reaction profile supports the idea of solvent polarity/binding affinity contributions. THF and toluene led to the fastest rates for the standard morpholine/butadiene reaction. Despite the similarities between THF and dioxane, the latter shows both incomplete conversion and slow rates.

The choice of counterion was shown to have a dramatic effect on the telomerization of amines. $NaPF_6$ was found to be the most effective reagent. The standard morpholine/butadiene reaction can be efficiently performed in the presence of $NaBAr'_4$ (Ar′ = 3,5-$(CF_3)_2C_6H_3$) or $NaBPh_4$. Under these conditions, however, slight decomposition of the catalyst was observed.

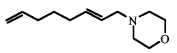
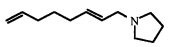
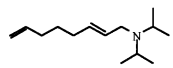
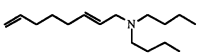
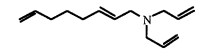
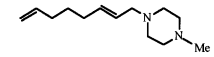
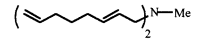
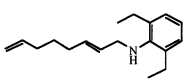
The nature and influence of the supporting NHC ligand was found to be less important than solvent or counterion selection. Ligands bearing bulky substituents on the NHC nitrogens (IPr) have been shown to have an accelerating effect on the elimination of the final product from the palladium center in palladium-mediated cross-coupling chemistry.[12]

Having the important parameters (ligand, solvent, and counterion) optimized, we investigated the scope of the reaction as a function of amine substrates.

Secondary amines, both cyclic and linear, led to octadienylamines in quantitative yields with a catalyst loading of only 0.2 mol %. The standard reaction of morpholine with butadiene is complete in 15 min at 60 °C. The reaction is selective and complete at temperatures as low as room temperature (in 4 h). The catalyst loading can be decreased at least 1 order of magnitude (0.02 mol % and 60 °C), but the time required to reach complete conversion then becomes 20 h. The presence of donor atoms such as oxygen (morpholine) or nitrogen (1-methylpiperazine) has no detrimental effect on catalyst stability. Slower reaction rates were observed when sterically demanding amines such as diisopropylamine were employed. The use of diallylamine leads to the formation of interesting telomers having three terminal and an internal double bond. The required reaction time for this reaction is longer but can be explained by facile competitive coordination of a number of allyl groups to the catalyst center (Table 2).

The order of amine reactivity in these telomerization reactions was found to be secondary > primary > ammonia. Previous studies showed that once the primary amines are converted into secondary amines, these will react further with butadiene to form dioctylalkylamines.[13] In the present system, a substantial size dependence of the final product was observed when primary amines are used as coupling partners. Methylamine leads exclusively to the corresponding tertiary amine acting as a nucleophile on two separate telomers. Larger amines (i.e., mesitylamine) take part in a simple telomerization leading to secondary amines. We suspect sterically demanding nucleophiles (amines) may have limited access to the metal center in a sterically congested transition state. Ongoing work examining mechanistic issues and applications to target specific synthesis is ongoing and will be reported shortly.

Table 2. Various Amines Reacting with Butadiene[a]

amine	product	time(h)	yield (%)[a]
		0.25 20 (0.02mol% cat) 4 (RT)	94 91 91
		0.5	98
		6	95
		0.5	89
		2	54
		1	95
		3	92
		1	70

[a] Conditions: 0.2 mol % (IPr)Pd(allyl)PF6, 1 mmol amine, THF 2 mL, 60 °C, excess butadiene, isolated yields are the average of two runs.

In summary, we have synthesized and fully characterized a number of cationic palladium/NHC complexes. The well-defined complexes as well as the in situ generated catalysts were used successfully in the telomerization of butadiene in the presence of various amines acting as nucleophiles. The strong coordination properties of NHC ligands prevent catalyst decomposition during the catalytic cycle. The stability of the catalyst minimizes the formation of byproducts in favor of terminal C8 telomers. We are currently expanding on these initial observations and examining various telomerization and related reactions.

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Supporting Information Available: Experimental details describing the synthesis of [(NHC)Pd(allyl)]X complexes, catalysis protocol, and product isolation as well as crystallographic tables are available free of charge via the Internet at http://pubs.acs.org.

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(11) The standard reaction of morpholine and butadiene is completed in 2 h for in situ generated [(IPr)Pd(allyl)]BF_4 compared to 3 h for well-defined catalyst, all other conditions being the same.

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