ACS Catalysis

Research Article

pubs.acs.org/acscatalysis

Convenient Transfer Semihydrogenation Methodology for Alkynes Using a Pd^{II}-NHC Precatalyst

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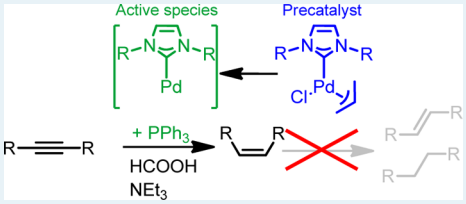
Supporting Information

ABSTRACT: A convenient and easy-to-use protocol for the *Z*-selective transfer semihydrogenation of alkynes was developed, using ammonium formate as the hydrogen source and the easily prepared and commercially available, highly stable complex $PdCl(\eta^3\text{-}C_3H_5)(IMes)$ (**1**) as the (pre)catalyst. Combined with triphenyl posphine as an additional ligand, this system provides a robust catalytic synthetic method that shows little to no over-reduction or isomerization after full substrate conversion. The system allows the direct use of solvents and reagents, as received from the supplier without drying or purification, thus providing a practical method for semihydrogenation of a broad range of alkynes. The mechanism behind these high and enhanced selectivities was determined through a set of kinetic experiments.



KEYWORDS: *alkyne reduction, palladium, N-heterocyclic carbene, NHC, transfer-hydrogenation*

INTRODUCTION

Catalysis is a research area of considerable activity, in which, frequently, new and improved catalysts are developed and reported. However, whether these catalysts are actually applied depends on more than their performance: generally, a convenient method is just as important, making applicability an integral aspect of catalyst design. *Z*-Alkenes are present in many biologically and pharmaceutically active compounds and are produced in several bulk and fine chemical processes.[1−4] Therefore, convenient methods for the synthesis of these compounds, especially at the laboratory scale, are intensively studied. Several methods for the synthesis of alkenes have been developed, such as the Wittig,[5−7] the Peterson[8] and Julia[9] olefination, olefin metathesis,[10,11] cross-coupling reactions,[12] and elimination[13] of halides from alkenyl halides. However, these methods suffer from the disadvantage that any preference for the formation of *E*- or *Z*-isomers is highly substrate dependent.[3] Another often applied route is the reduction of alkynes, which is the generally preferred methodology for two reasons: first, it is a reliable method to obtain *Z*-alkenes, and second, alkynes are versatile synthetic building blocks for, among others, Sonogashira,[14,15] Glaser,[16,17] and Cadiot−Chodkiewicz[13] reactions.[2,18,19] The catalytic semihydrogenation of alkynes has mainly focused on palladium as the active metal, using both particle and molecular catalysts.[3,20−30] However, catalysts based on other transition metals, such as Rh,[31] Ru,[32−34] Ni,[35,36] Nb,[37] Cr,[38] Cu,[39] and V[40] have also been reported. Although many processes have been developed, the improved Lindlar's catalyst (Pd black on $BaCO_3$ that is poisoned with PbOAc and quinoline) is still the benchmark.[3,20] However, this catalyst suffers from isomerization of the *Z*- to the *E*-alkene, migration of the double bond, and over-reduction of the substrate (see also Figure 1). Furthermore, leaching of the poisonous metals and poor reproducibility between batches of catalyst are additional issues in its application. When considering laboratory applications, it has another disadvantage: it uses molecular hydrogen as the reductant, which requires specific conditions for safe handling.[41] Yet, despite these drawbacks, Lindlar's catalyst is still widely applied because it is practical, it is cheap, commercially available, and does not require inert conditions.

The importance of the semihydrogenation reaction, especially at the laboratory scale, and the disadvantages of the benchmark catalyst system mentioned above have prompted the development of improved methodologies. To circumvent the use of molecular hydrogen and to develop a safer protocol that is more straightforwardly applicable, the transfer semihydrogenation reaction of alkynes has been developed. While sodium methanolate,[22] a combination of silanes and alkyl alcohols,[39] and Hantzsch ester 1,4-dihydropyridine[42,43] have also been applied as the hydrogen source, the majority of the applied systems use ammonium formate,[44−49] which may also be generated *in situ* by the decomposition of DMF.[34,50] Transfer hydrogenation, especially the protocols using ammonium formate, has greatly improved the applicability of alkyne semihydrogenation. Catalyst systems that tolerate a wide variety of functional groups have been developed, and when applying these, high selectivities are obtained for many

Received: December 5, 2013
Revised: March 14, 2014
Published: March 20, 2014

   dx.doi.org/10.1021/cs4011502 | ACS Catal. 2014, 4, 1349−1357

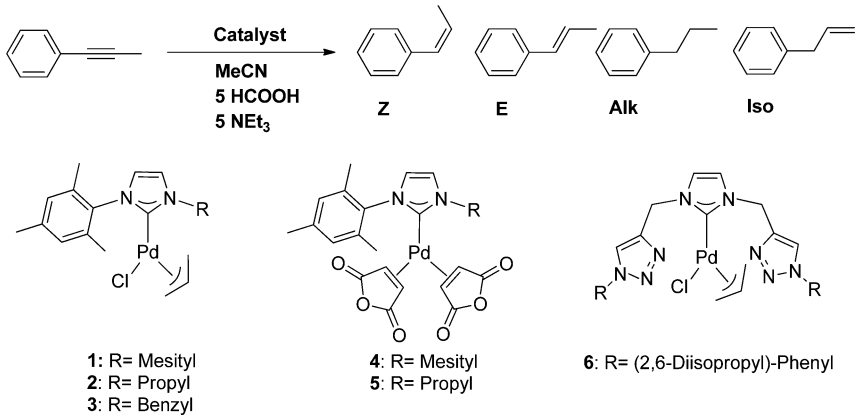


Figure 1. Transfer semihydrogenation of 1-phenyl-1-propyne, the catalysts applied, and the (expected) products of the reaction: *Z*-1-phenyl-1-propene (**Z**), *E*-1-phenyl-1-propene (**E**), 1-phenyl-propane (**Alk**), and 1-phenyl-2-propene (**Iso**).

substrates.[3] Currently, the main challenges are the prevention of over-reduction and isomerization at high degrees of conversion, selective conversion of (skipped) diynes, and achieving enhanced activities toward electron deficient 1,2-diaryl alkynes.

We earlier reported on a catalyst system that applies Pd^0-complexes with a bis-mesityl-imidazole-2-ylidene (IMes) ligand that is highly selective for some of the most challenging substrates reported.[47,51] This catalyst does not lead to any over-reduction nor isomerization of the *Z*-alkene product after consumption of the substrate. This feature, up to then, remained one of the main challenges in this research field, so alleviation of this serious problem renders this type of catalysts an ideal basis for the design of a convenient semihydrogenation protocol. However, a disadvantage of this system is that the active catalyst cannot be isolated and that the corresponding precatalyst is not shelf-stable. Therefore, the precatalyst must be generated shortly before using it, which requires specific know-how, hands-on experience with inorganic laboratory manipulations, and specialized equipment that allows synthetic manipulations under strict anaerobic conditions. As a result, this catalytic system is not very practical for many general synthetic applications. In order to improve the applicability of this catalytic methodology, we set out to develop a catalyst system that is based on a shelf-stable Pd(NHC) catalyst, and readily available additives may be employed for the enhancement of their selectivity and stability. The aim is to obtain a system that provides excellent selectivities in the semihydrogenation of several representative alkynes using commercially available analytical reagent (AR) grade solvents and reagents, as received from the suppliers. Such a methodology would provide a novel, easy to perform and straightforward synthetic protocol for the semihydrogenation of alkynes to *Z*-alkenes employing triethylammonium formate as the reducing agent. Since improvement of a method and optimization for individual substrates should, preferably, be achieved in a rational fashion, mechanistic research is an essential aspect in the development of a catalytic synthetic protocol. Hence, the mechanism of the precatalyst activation, the molecularity of the active catalyst, and, most noteworthy, the kinetic analysis of the product formation were elucidated. On the basis of these studies, a mechanism was proposed.

RESULTS AND DISCUSSION

The first requirement for the development of a hands-on and selective catalytic synthetic protocol is the availability of a suitable precatalyst. The stable $PdCl(\eta^3\text{-}C_3H_5)(NHC)$ complexes such as **1**−**3** were reasoned to be ideal precatalysts. Besides their high stability, they are straightforwardly synthesized in high yields, and some of them are even commercially available.[52−54] Another reason to choose this type of catalyst precursors was that they may be transformed directly into the required active Pd^0-species under the conditions of the transfer semihydrogenation, which was confirmed in initial studies (Scheme 1).[55,56] Complexes **1**−**3** and their Pd^0-analogues **4** and **5** were screened in the semihydrogenation of 1-phenyl-1-propyne (Figure 1 and Table 1). Since we focused on the prevention of over-reduction and isomerization, a 5-fold excess of triethylammonium formate was applied. This allowed the determination of the true selectivity of the catalyst

Table 1. Results of the Transfer Semihydrogenation of 1-Phenyl-1-propyne with Various Precatalysts

#	cat.; add.[a,b]	*Z*-yield (%)[c]	*Z*-sel[d] (conv) (%)	time to FC (h)[e]
1	**1**	91	93 (97)[f]	1.2
2	**2**	84	95 (90)[f]	3.1
3	**3**	88	92 (97)[f]	5.6
4	**4**	76	98 (77)	>24
5	**5**	43	99 (44)	>24
6	**6**[d]	61	94 (64)	>24
7	**1**+ 1 PPh_3	93	98 (95)	24
8	**1**+ 2 PPh_3	98	99 (98)	24
9	**1**+ 4 PPh_3[c]	17	99 (18)	>24
10	$Pd(PPh_3)_4$	62	99 (63)	>24
11	Lindlar[g]	78	93 (83)	>24

[a]1 mol % catalyst and 2.7 mmol 1-phenyl-1-propyne, 70 °C. Additives in equivalents with respect to the catalyst. [b]For a full table of tested precatalysts and additives. See Table S1, Supporting Information. [c]GC-yields given for the *Z*-alkene. [d]Selectivity toward the *Z*-alkene in % ([response factor corrected GC area of *Z*-alkene]/[response factor corrected GC area of the total products total product]·100%) at the corresponding conversion, given in brackets. [e]Time to reach full conversion of the substrate; experiments were stopped after 24 h. [f]Strong over-reduction and isomerization of the *Z*-alkene product was observed after full substrate conversion. [g]3 mol % of the catalyst was used.

dx.doi.org/10.1021/cs4011502 | ACS Catal. 2014, 4, 1349−1357

instead of a selectivity induced by the stoichiometry of the formic acid.

From the results shown in Table 1, it is clear that the ligand bearing two mesityl groups on the wing tips gives the highest activity. Furthermore, Pd^{II}-precatalysts **1** and **2** hydrogenate 1-phenyl-1-propyne significantly faster than their Pd^0 analogues **4** and **5**. However, these show a high degree of isomerization and over-reduction of the product after full conversion of the substrate (**1** in Figure 2A and B and **2** and **3** in Figure S2

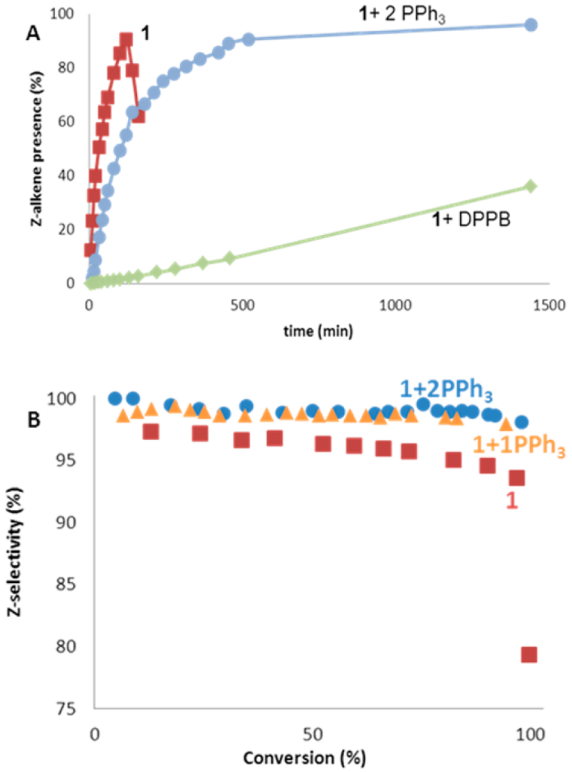


Figure 2. Effect of applying additives together with catalyst **1** in the semihydrogenation of 1-phenyl-1-propyne. (A) The yield in *Z*-alkene versus time is shown. (B) The influence of the phosphine additive on the selectivity throughout the reaction is shown (further over-reduction and isomerization by precatalyst **1** without additives is omitted for clarity).

(Supporting Information)). In previous mechanistic studies of the Pd^0-NHC catalyst, we found that maleic anhydride (MA) functions as a boomerang ligand that slows down the reaction but also enhances the selectivity of the catalyst.[51] As, under the applied catalytic conditions (Table 1,entry 1 and 2), a Pd^0-NHC species is generated in absence of stabilizing ligands such as MA, the formation of more reactive but less selective species is actually an expected observation.

Two approaches to improve these catalytic systems were investigated. First, complexes with hemilabile ligand functionalities were applied, which may prevent isomerization and over-reduction of the product through competition for the coordination site between the Z-alkene and the secondary donor group within the ligand. Complex **6**, that bears two hemilabile triazole moieties on its wingtips, was tested in the reaction and is highly selective. However, its activity was greatly diminished with respect to precatalyst **1** (and **4**); it does not reach full conversion in 24 h, presumably due to too strong an interaction between Pd and the triazole groups.

In a second approach to obtain better catalytic results, we investigated the influence of several additives. On the basis of our previous research, we first chose to use MA as an additive ligand (Table S1 (Supporting Information), entries 7 and 8). One equivalent of MA with respect to the catalyst showed little improvement, and two equivalents did improve the *Z*-selectivity of the reaction substantially. However, still some over-reduction of the product occurred after full conversion of the substrate. As an alternative, we tested triphenyl phosphine as an additive ligand because it is water-stable, easy to handle, and readily available (Figure 2).

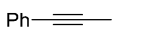
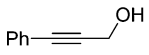
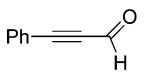
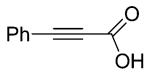
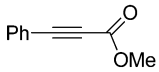
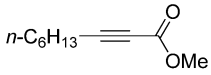
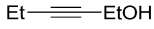
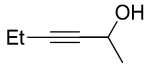
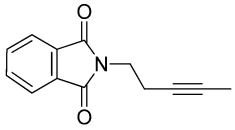
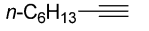
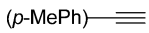
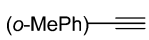
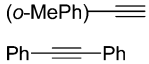
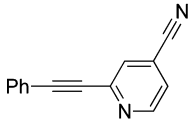
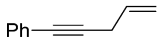
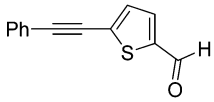
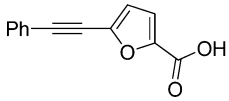
As mentioned above, applying catalyst **1** without any additives leads to fast reactions, but these reactions are associated with considerable over-reduction to the alkane and *Z*-alkene to *E*-alkene isomerization, especially when the reaction reaches full conversion of the alkyne (Table 1, entry 1 and Figure 2A and B). These problems can be circumvented by the addition of two equivalents of PPh_3. This leads to an increased selectivity of the catalyst throughout the reaction (Figure 2A and B), and most importantly, it virtually stops the alkene over-reduction and alkene isomerization reactions at full substrate conversion. Stronger coordinating additives, such as diphenylphosphinobutane (DPPB), are less beneficial (Figure 2A). Addition of one equivalent of DPPB reduces the activity several orders of magnitude, making the reactions too slow for practical application. The beneficial influence of the NHC-ligand was demonstrated through a control reaction with $Pd(PPh_3)_4$ (Table 1, entry 10). This complex is an order of magnitude slower than complex **1** with 2 equivalents of PPh_3. From this observation, we conclude that the NHC ligand forms a more active complex and is not substituted for a phosphine ligand during the reaction. The added value of applying this NHC ligand system was further demonstrated by testing $[Pd(\eta_3\text{-}C3H_5)Cl]_2$, a common Pd^{II} source, as a precatalyst. This simple Pd salt was significantly less selective and gave a strong over-reduction; applying this compound with two and four equivalents of PPh_3 led to severe deactivation of this catalyst (Table S1 (Supporting Information) entries 20−22). Among the above-described systems, complex **1** combined with 2 equivalents of PPh_3 proved to be the most robust and selective, without compromising the reaction rates too much. This finding allowed a significant simplification of the catalytic-synthetic protocol, where all commercial solvents and reagents can be used without additional purification and/or drying steps, in which all time-consuming preparative manipulations and Schlenk techniques can be omitted. Briefly bubbling an inert gas (Ar or N_2) through the reaction mixture of the reagents before introducing complex **1** and the PPh_3 additive suffices to obtain excellent catalytic results.

The substrate scope of this simplified and robust catalytic procedure was explored, using a range of alkynes with various electronic and steric properties, and containing different functional groups that can potentially interfere with the transfer semihydrogenation reaction. The results are summarized in Table 2.

The catalyst system performs well for a wide range of alkynes and is compatible with a variety of functional groups. In the presence of an additional equivalent of NEt_3 (to ensure neutral conditions), the reaction is compatible with carboxylate functionalities generated *in situ* from substrates containing carboxylic acids (entries 4 and 17). The yields and selectivities are somewhat compromised when the carboxylate group is directly attached to the alkyne moiety of the substrate (entry

dx.doi.org/10.1021/cs4011502 | ACS Catal. 2014, 4, 1349−1357

Table 2. Transfer Semihydrogenation for a Selection of Substrates Using the Simplified and Robust Catalytic Procedure Based on Complex 1 and 2 Equivalents of PPh_3

#[a]	Substrate	*Z*-yield (%)[b]	*Z*-selectivity (conversion) (%)[c]	Time (h)[d]
1		92	99 (93)	24[e]
2		92	92 (99)	2
3		0	0 (99)	3[f]
4		45	71 (64)	48[g]
5		85	93 (92)	3
6		99	99 (99)	12
7		86	96 (90)	24
8		60	70 (85)	2[f]
9		85	85 (99)	12
10		95[h]	96 (99)	24
11		58[h]	60 (98)	2[f]
12		31[h]	31 (99)	4[f]
13		75	98 (77)	24[f]
14		21	99 (21)	48[f]
15		61	83 (74)	24[f]
16		99	99 (99)	12
17		96	96 (99)	6[g]

[a]All substrates were used as received; 1 mol % catalyst, 2 mol % PPh_3, 2.7 mmol of the selected substrate, 13.5 mmol of HCOOH, and 13.5 mmol of NEt_3 at 70 °C. [b]GC-yield for the *Z*-alkene except for entries 5 and 17, which are determined by NMR. [c]Selectivity toward the *Z*-alkene in % ([GC area of *Z*-alkene]/[internal standard corrected initial GC area of alkyne −GC area of alkyne]·100%) conversion within parentheses. [d]The time at which the sample was taken. The reaction was stopped after 48 h for entries 4 and 14 and after 24 h for entries 1, 7, and 13. [e]Addition of fresh substrate and formic acid shows that the catalyst is still active at full conversion. It was found that the reaction time is dependent on the grade of the formic acid while it does not affect the selectivity. [f]See text. [g]An additional equivalent of NEt_3 was added to ensure neutral conditions. [h]For entry 8, a mass balance of 74% was found. Entry 11 had a mass balance of 66%, and entry 12 had a mass balance of 77%.

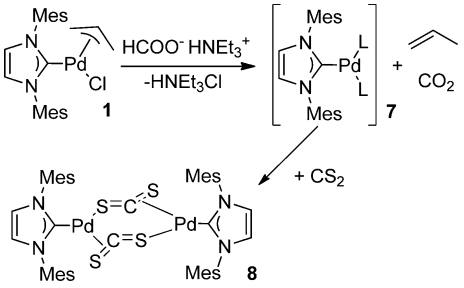
4). This may well be the result of simultaneous (chelate) binding of the alkyne and the carboxylate moieties of propargilic acid to the metal.[4] This hypothesis is supported by the smooth and selective conversion of the methyl esters shown in entries 5 and 6. The reaction in entry 5 does reach full conversion; however, after a prolonged reaction time (14 h), a yield of 85% of the *Z*-alkene was obtained, but a mass balance of 90% was found on GC. Presumably, hydrolysis of the ester takes place. The transfer semihydrogenation reaction does not seem compatible with aldehydes that are linked directly to the alkyne (entry 3). The substrate is fully converted within 3 h, but none of the expected products was observed on GC-MS. The NMR-spectrum of the crude reaction mixture did also not allow us to identify which species were formed. However, when a spacer is present between the aldehyde and the alkyne moieties, excellent yields and conversions are obtained, and the aldehyde functionality remains intact (entry 16). Primary alcohols (entry 2) and allylic alcohols (entries 7 and 8) are also hydrogenated efficiently. The results with the challenging allylic alcohols, that easily eliminate water to form ene-ynes, are noteworthy. Partial dehydration may still be the reason for the observed incomplete mass balance (74%) when using 3-hexyn-2-ol (entry 8). The selectivity toward the *Z*-alkene of this substrate is excellent since no isomerized or alkane compounds were observed. Several terminal alkenes were investigated (entries 10, 11, and 12). The alkyl substituted alkyne is converted neatly. However, the styrene products that are formed when phenyl acetylens (entries 11 and 12) are hydrogenated give rise to subsequent coupling reactions to another styrene or alkyne molecule, which are detected as side products in GC and GC-MS. Furthermore, the mass balances are low (66 and 77%) for these reactions. This may be caused by a side reaction, in which the styrene-like species are oligo- or polymerized. Diphenyl acetylene (entry 13) is known to be a difficult substrate in semihydrogenation reactions, but nonetheless, *Z*-stilbene is formed with high Z-selectivity at 77% conversion. After 24 h, the conversion is virtually halted. Possibly, improved results may be obtained by application of higher catalyst loadings. The nicotinitrile (entry 14) only reaches a conversion of 21%, but the selectivity is excellent, and most importantly, the nitrile functionality is not hydrogenated. 1-Phenyl-pentyn-4-ene (entry 15) is converted with a moderate selectivity and yield, but the results seem promising for this difficult type of substrate. The conversion continued after 24 h, but the selectivity decreased, and the determination of the exact conversion became difficult because a byproduct formed that was not separable on GC. Excellent results were further obtained for 5-(2-phenyleth-1-ynyl)thiophene-2-carbaldehyde (entry 16). This substrate is converted quickly and very selectively. This is noteworthy, considering the complex structure of this molecule that consists of multiple functionalities that are known to interact with Pd. The selective conversion of furoic acid (entry 17) is another example demonstrating the high functional group tolerance of the catalytic system. Furthermore, it should be noted that this procedure was optimized for the conversion of 1-phenyl-1-propyne, but given this wide variety of functionalies that are present in the tested substrates, improved results for several of these challenging entries may be obtained by tuning the reaction conditions and the concentration of the additive.

After the successful development of this convenient methodology and demonstrating that it has a broad substrate scope, we focused on the reaction mechanism behind these selective

dx.doi.org/10.1021/cs4011502 | ACS Catal. 2014, 4, 1349−1357

transfer semihydrogenation reactions. First, the mechanism of the *in situ* reduction of the precatalyst to the active Pd^0-species was studied. Mass analysis of the gas phase of the reaction was performed, and the formation of CO_2 and propene was detected confirming similar findings as reported by Nolan et al.[52,55] The presence of a Pd^0-IMes species was subsequently corroborated by a trapping experiment with CS_2, in which the dinuclear CS_2 bridged $[(Pd(IMes))_2\text{-}\mu(\kappa\text{-}S,\text{-}\eta^2\text{-}CS_2)]_2$ complex, **8**, was isolated and characterized. On the basis of these findings, we propose the mechanism for catalyst activation shown in Scheme 1.

Scheme 1. Generation of the Pd^0 Species from Precatalyst 1 and Its Trapping with CS_2 Forming 8



First, the chloride ligand of **1** is exchanged for a formate ion, which upon liberation of CO_2 forms a hydride complex. Subsequent reductive elimination of propene gives the active Pd^0-catalyst **7**, which is likely to have two coordinating solvent and/or substrate molecules bound to the metal. The addition of CS_2 leads to the formation of the highly stable complex **8**, which was isolated. The structure of **8** was derived from mass spectrometry and the characteristic IR-vibrations for this rare type of palladium complexes as reported by Ferrar et al.[57]

Subsequently, the kinetic order in the precatalyst was determined by measuring the dependence of the reaction rate on the catalyst concentration, varying the concentration of the precatalyst between 0.7 and 2.3 mM. Using the differential rate method, an order of 0.98 in the precatalyst was found. This clearly indicated first order kinetics in the concentration of the catalyst, pointing to a mononuclear active species (Figure S3, Supporting Information).[58]

Cazin et al. recently reported a system that also consists of a Pd^0-NHC species with a phosphine ligand. This species is also highly active in the transfer semihydrogenation of alkynes using formic acid as the hydrogen source but without NEt_3.[46] At first glance, these systems seem similar. However, they operate via different mechanisms. The $Pd^0(NHC)(PCy_3)$ complex by Cazin et al. was found to generate molecular hydrogen under catalytic conditions and was proposed to involve a dihydride intermediate. For the currently discussed system, no dihydrogen was detected by mass spectrometry of the gas phase of the reaction. Apparently, the formation of hydrogen does not occur in the catalyst system presented here. Most likely, the currently reported reaction proceeds via an anionic $Pd^0(NHC)$(hydride) intermediate similar to that reported by Hauwert et al., which operates with two separate hydrogen donors (triethylammonium and formate).[51]

Having determined the kinetic order of the catalyst system and the mechanism for the generation of the active catalyst, the role of the additive was investigated. Comparing the selectivity against the conversion of the reactions with zero, one, or two equivalents of phosphine, we noted an increased *Z*-selectivity throughout the entire reaction (Figure 2B) when two equivalents of PPh_3 were applied. Subsequently, the influence of the phosphine concentration on the rate was measured using a catalyst concentration of 1.5 mM and a triphenylphosphine concentration ranging from 0 to 6.0 mM (Figure S4, Supporting Information). A strong inhibiting effect by the phosphine was observed; when **1** and PPh_3 are applied in a 1:1 ratio, the activity of the catalyst system is reduced by 80%, thus demonstrating that the phosphine-coordinated complex is either significantly less active or perhaps even in a dormant state.

The phosphine additive functions as an inhibitor and increases the selectivity of the reaction. Subsequently, a kinetic pseudo-first-order analysis of the product formation was performed that determined the mechanism behind these effects. This method allowed for the estimation of the rates of formation of the individual reaction products, through which the effects of phosphine on the rate of formation of each product were quantified (Figure S5 (Supporting Information) and Table 3).[59,60] The model of the reaction was simplified by

Table 3. Calculated Values of the Individual Rate Constants Quantifying the Influence of the Phosphine Additive on the Pathways to the Reaction Products

	1	**1** + 1 PPh_3	**1** + 2 PPh_3
k_1[a]	3×10^{-02}	7×10^{-03}	6×10^{-03}
k_2	1×10^{-03}	4×10^{-05}	1×10^{-07}
k_3	8×10^{-05}	6×10^{-05}	6×10^{-05}

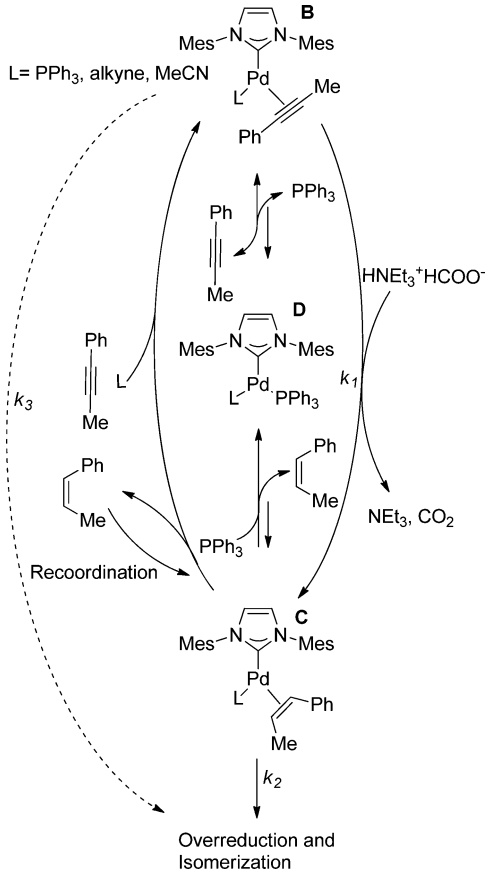
[a]*k*-Values were determined in min^{-1} at 70 °C.

treating the formation of the byproducts as a single reaction step (Scheme 2 and Scheme S2 (Supporting Information)). This not only greatly reduced the number of reaction constants that need to be calculated (which increases the accuracy of the fits) but also was in line with the proposed mechanism for the Pd^0-(Ar)BIAN (bis(aryl)acenaphthenequinonediimine) catalyzed semihydrogenation of 1-octyne, in which all byproduct formation proceeds via one common [Pd(hydrido)(BIAN)(*Z*-alkenyl)] intermediate.[4] With this (simplified) kinetic analysis, three rate constants were determined: (1) the rate of semihydrogenation of the alkyne to the *Z*-alkene (k_1), (2) the rate of isomerization and hydrogenation of the Z-alkene to the byproducts (k_2), and (3) the rate of direct conversion of the alkyne into the byproducts (k_3) (Scheme 2 and Figure S5 (Supporting Information)). Fitting the data and integration of the differential equations showed that for the catalyst without additive a stepwise mechanism ($k_1 + k_2$) is responsible for the formation of the byproducts (>90%), while the contribution of the direct isomerization pathway (k_3) is negligible. This was also proposed by Hauwert et al. and Kluwer et al.[4,51]

Table 3 clearly shows the role of the additive: it decreases the alkene isomerization and over-reduction rate of the Z-alkene, k_2, by 4 orders of magnitude, while affecting the alkyne semihydrogenation rate only by a factor of 5. The direct over-reduction and isomerization pathway k_3 is hardly affected by PPh_3. In fact, in the presence of two equivalents of PPh_3, the k_2 isomerization and over-reduction pathway gets blocked kinetically, while the k_1 alkyne semihydrogenation pathway remains clearly competitive over the intrinsically slow direct isomerization pathway k_3 (k_1 remaining 2 orders of magnitude larger than k_3). The additive effect is most likely a result of

dx.doi.org/10.1021/cs4011502 | *ACS Catal.* 2014, 4, 1349−1357

Scheme 2. Proposed Role of the Additive on the Reaction Pathways in the Catalytic Cycle



competition between the phosphine, the alkyne, and the *Z*-alkene for coordination to the complex, with the improved selectivities being a direct result of the relative coordination strengths to palladium. The phosphine binds much stronger than the *Z*-alkene, and hence, the additive slows down the over-reduction and isomerization steps (k_2) by substituting the alkene and preventing its recoordination. The semihydrogenation steps (k_1) are also slowed down but to a lesser extent because the binding affinity of the alkyne and PPh_3 are competitive. This implies that the selectivity of the semihydrogenation of alkynes to *Z*-alkenes may be optimized for specific substrates by variation of the phosphine ligand and its concentration.

The combined mechanistic data led to the proposed mechanism in Scheme 2, where the active species has the form of a Pd(IMes)L_2 complex (Scheme 2, **B**) that forms the *Z*-alkene with a high initial selectivity (k_1, **C**). The phosphine additive rapidly removes intermediate **C**, thus slowing down over-reduction and isomerization, and provides an alternative pathway via species **D** back to **B**, leading to enhanced selectivities.

CONCLUSIONS

We have developed a convenient and easy-to-use catalytic-synthetic protocol for selective transfer semihydrogenation of alkynes into *Z*-alkenes using ammonium formate as the hydrogen source and the easily prepared and commercially available complex [PdCl(η^3-C_3H_5)(IMes)] (**1**) as the precatalyst. Combining the robust and air-stable (pre)catalyst with two equivalents of PPh_3 allows selective transformation of a variety alkynes, differing in electronic and steric properties and containing various functional groups, without the need for strict solvent or reagent purification or the use of time-consuming glovebox or Schlenk techniques. The PPh_3 additive substantially slows down over-reduction and isomerization of the obtained *Z*-alkenes at high conversions. The detailed kinetic analysis of the catalytic system provided a plausible mechanistic rationale for the enhanced selectivities induced by PPh_3.

EXPERIMENTAL SECTION

Complex synthesis was performed using Schlenk techniques under dry nitrogen. Solvents were dried according to standard procedures and distilled prior to use,[61] unless stated otherwise. Maleic anhydride was crystallized from hot DCM. [Pd(Cl(η^3-C_3H_5)]$_2$, triethyl amine, formic acid, potassium *tert*-butoxide, and triphenylphosphine were purchased from Sigma Aldrich. A Pd-DVTMS (1,3-divinyl-1,1,3,3-tetramethyl-disiloxane palladium^0) solution was generously provided by Umicore. Compounds **1**,[62] **3**,[63] **4**,[64] and [1-mesityl-3-propyl-imidazolium] bromide[65] were synthesized according to literature procedures. NMR spectra were recorded on Bruker AV 400 MHz, Bruker DRX 300 MHz, and Varian Mercury 300 MHz spectrometers. HR mass spectrometry was performed on a Bruker MicrO-TOF-Q machine using ESI, and elemental analyses were performed by Mikroanalytisches Laboratorium Kolbe, Mülheim an der Ruhr, Germany.

((1-Mesityl)-3-(propyl)-imidazolylidene)palladium(η^3-allyl)chloride (2). The corresponding imidazolium salt (0.20 g, 0.65 mmol) was stripped three times with toluene and suspended in 40 mL of THF. Subsequently, [PdCl(η^3-C_3H_5)]$_2$ (0.12 g, 0.32 mmol) was added, and the solution was cooled in dry ice in EtOH solution to approximately −60 °C. Upon addition of KO^{t}Bu, the suspension turned into a pale yellow solution. The solution was allowed to warm to 20 °C and stirred overnight. The solvent was removed *in vacuo*, and the crude product was suspended in toluene, which was filtered in air over Celite. The solvent was removed and stripped with DCM three times yielding 0.23 g (84%) of an off-white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (d, J = 1.8 Hz, 1H, Im-bb), 6.95 (s, 1H, Im-bb), 6.90 (d, J = 1.8 Hz, 2H, Ar), 5.13−4.80 (m, 1H, allyl), 4.46 (ABX, J = 14.3, 6.9 Hz, 1H, $ImCH_2$), 4.29 (ABX, J = 13.8, 6.8 Hz, 1H, $ImCH_2$), 4.10 (dd, J = 7.5, 2.2 Hz, 1H, allyl), 3.39−3.25 (m, 1H, allyl), 3.03−2.84 (m, 1H, allyl), 2.31 (s, 3H, $ArCH_3$), 2.20 (s, 3H, $ArCH_3$), 2.03 (s, 3H, $ArCH_3$),1.90 (m, 3H, $ImCH_2CH_2CH_3$+ allyl), 0.93 (t, J = 7.4 Hz, 3H, $ImCH_2CH_2CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.03 (NCN), 138.88 (Ar), 136.54 (Ar), 136.07 (Ar), 135.33 (Ar), 129.24 (Ar), 128.799 (Ar), 122.36 (Im-bb), 121.36 (Im-bb), 114.25 (allyl), 71.81 (allyl), 52.96 (allyl), 51.53 (CH_2), 24.33 (CH_2), 21.21 (Mes-CH_3), 18.81 (Mes-CH_3), 18.22 (Mes-CH_3), 11.20 (CH_3). MS ESI-TOF calculated for $C_{18}H_{25}N_2Pd$ (MH^+-Cl) 375.1054; found, 375.1071.

Palladium^0((1-mesityl)-3-(propyl)-imidazolylidene)-(maleic anhydride)$_2$ (5). The synthesis was performed in manner similar to that for **2** using Pd(DVTMS)$_2$ in DVTMS solution with a Pd content of 7.66 mass % by AES. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.39 (d, J = 1.8 Hz, 1H, Im-bb), 7.17 (d, J = 1.8 Hz, 1H, Im-bb), 7.00 (s, 2H, CH-Ar), 4.69 (s, 2H, MA), 4.41 (s, 2H, MA), 3.98 (t, J = 7.3 Hz, 2H, $ImCH_2$), 2.34 (s, 3H, CH_3−Ar), 2.07 (s, 6H, CH_3−Ar), 1.85 (h, J = 7.4 Hz, 2H, $ImCH_2CH_2CH_3$), 0.94 (t, J = 7.4 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_2$) δ 176.58 (NCN),167.29 (MA), 166.85

dx.doi.org/10.1021/cs4011502 | *ACS Catal.* 2014, 4, 1349−1357

(MA), 139.51 (Ar), 135.29 (Ar), 134.87(Ar_{CH}), 129.19 (Ar), 125.27 (Im-bb), 122.35 (Im-bb), 66.29 (MA), 65.88 (MA), 24.07 (Im-CH_2), 20.63 (ImCH$_2$*CH$_2$*), 17.32 ($ArCH_3$), 17.24 ($ArCH_3$) 10.53 (CH_3). MS ESI-TOF calculated for $C_{19}H_{22}N_2NaO_3Pd$ (M-Na^+-MA) 455.5065; observed, 455.5075; calculated for $C_{18}H_{22}N_2NaO_2Pd$ (M-Na^+-MA-CO) 427.0614; observed, 427.0643. Also observed: 471.06 (MH^+-CO_2), 441.04 (MH^+-2CO_2).

[1,3-Di((4−2,6-diisopropylphenyl)-1*H*-1,2,3-triazolyl)-methylene-imidazolium] Bromide. Bisethynyl imidazolium bromide[66] (1.00 g, 4.44 mmol) was dissolved in a solution of 150 mL of water and 100 mL of ^{t}BuOH. First, the DiPP azide[11] (2.00 g, 9.3 mmol) was added, followed by sodium ascorbate (0.35 g, 1.3 mmol), and finally $CuSO_4{\cdot}5H_2O$ (0.22 g, 0.88 mmol). The resulting suspension was heated to 60 °C and stirred for seven days, during which time an orange suspension formed. All solvents were removed *in vacuo*, and the solid was dissolved in 100 mL of DCM and washed with a saturated NH_4Br solution (25 mL 3×). The organic layer was separated, dried over $MgSO_4$, filtered over a glass filter, and removed *in vacuo*. The obtained oil was suspended in 25 mL of toluene, filtered over Celite, and layered with pentane for recrystallization. The solid was dissolved in a minimum of DCM and precipitated with pentane. The obtained solid (1.85 g) was then purified by column chromatography (40/45/5 acetone/DCM/MeOH, nondry solvents, in air) to yield 0.99 g (62%) of a white powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.75 (s, 1H, Im-bb), 8.28 (s, 2H, Trz), 7.76 (s, 2H, Im-bb), 7.49 (t, J = 7.8 Hz, 2H, Ar), 7.27 (d, J = 7.8 Hz, 4H, Ar), 5.91 (s, 4H, CH_2), 2.10 (dt, J = 13.5, 6.8 Hz, 4H, ^{i}Pr-CH), 1.10 (d, J = 6.6 Hz, 24H, Me).^{13}C NMR (101 MHz, MeOD) δ 140.49, 136.40, 135.04, 128.66, 128.31, 127.94, 124.58, 122.65, 53.73, 43.89. MS (FAB-TOF) calculated for $C_{33}H_{43}N_8$ (M^+-Br) 551.3611; found, 551.3607.

Palladium(η^3-allyl)chlorido(1,3-di-((4−2,6-diisopropyl-phenyl)-1*H*-1,2,3-triazolyl)methylene-imidazol-ylidene) (6). The ligand (see procedure above) (0.24 g, 0.36 mmol) was stripped three times with toluene (3 mL) and dissolved in 7 mL of THF. Allylpalladium chloride dimer (0.066 g 0.18 mmol) and KO^{t}Bu (0.056 g, 0.47 mmol) were suspended in 5 mL of THF. The solution containing the ligand was added dropwise to the suspension over 10 min. The solution was stirred overnight and filtered over Celite in air, and the solvent was removed. The complex was purified by column chromatography (in air, nondry solvents) using 40:45:5 acetone, DCM, MeOH eluents yielding 0.182 g of a white powder (64% yield). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.98 (s, 2H, Trz), 7.53 (t, J = 7.8 Hz, 2H, Ar), 7.32 (d, J = 7.8 Hz, 4H, Ar), 7.28 (s, 2H, Im-bb), 5.67 (d, J = 2.3 Hz, 4H, CH_2), 5.50 − 5.38 (m, 1H, $allyl_{C2}$), 4.31 (d, J = 9.1 Hz, 1H, allyl), 3.74 (d, J = 7.0 Hz, 1H, allyl), 3.28 (d, J = 13.5 Hz, 1H, allyl), 2.63 (d, J = 11.6 Hz, 1H, allyl), 2.17 (dt, J = 13.7, 7.0 Hz, 4H, ^{i}Pr-CH), 1.13 (d, J = 6.8 Hz, 12H, ^{i}Pr-CH_3), 1.09 (d, J = 6.9 Hz, 12H, ^{i}Pr-CH_3). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 180.32 (NCN), 145.82 (Ar), 142.90 (Ar), 132.90 (Ar), 130.74 (Ar), 126.44 (Im-bb), 123.70 (Im-bb), 121.54 (C-triazole), 115.06 (allyl), 71.45 (CH_2), 51,22 (allyl), 46.26 (CH-trz), 28.25 (^{i}Pr-CH), 23.75 (^{i}Pr-CH_3), 23.57(^{i}Pr-CH_3). MS (FAB-TOF) calculated for $C_{36}H_{47}N_8Pd$ (M^+-Cl) 697.2972; found, 697.2969.

Bis-[palladium^0(1,3-dimesityl-imidazolylidene)-μ(κ-S,η^2)-carbon Disulfide] (8). Compound **1** (0.050 g, 0.1 mmol) was added to a degassed solution of formic acid (21 μL, 0.5 mmol) and triethylamine (0.07 mL, 0.5 mmol) in MeCN (5 mL). The solution was stirred for 3 min, and 0.25 mL (1.0 mmol) of a 5 M CS_2 solution in THF was added. After another 10 min of stirring, the solvent was removed. The crude product was purified by column chromatography (DCM with 1% 5 M CS_2 in THF, in air, nondry solvents) yielding 0.02 g of an intensely yellow compound (45% yield). ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.11 (s, 2H, Im-bb), 7.01 (s, 4H, Ar), 2.37 (s, 6H, p-CH_3Ar), 2.14 (s, 12H, o-CH_3Ar). ^{13}C NMR (75 MHz, $CDCl_3$) δ (CS_2 ^{13}C not observed), 188.19 (NCN), 139.57 (p-C(Ar)), 136.54 (i-C(Ar)), 135.77 (o-C(Ar)), 129.66 (m-C(Ar)), 123.51(Im-bb), 21.64 (p-CH_3Ar), 18.33 (o-CH_3(Ar)). IR: 1119 cm^{-1} CS (s), 716 (s). MS ESI-TOF calculated for $C_{44}H_{48}KN_4Pd_2S_4$ ($M+K^+$) 1013.0473; found, 1013.0493. Elemental Analysis calculated for $C_{44}H_{48}N_4Pd_2S_4$: C, 54.26; H, 4.97; N, 5.75; Pd, 21.85; S, 13.17. Elemental analysis observed: % C 52.54, % H 4.80, % N 5.57, % S 13.51.

Catalytic Transfer Semihydrogenation of Alkynes. *General Procedure.* A Radleys' twelve-place reaction station with integrated heating and cooling setup was used for all catalytic experiments. Samples were taken at regular time intervals by filtering aliquots of the reaction mixture over short silica columns and eluting with DCM. Samples were analyzed on a Thermo Scientific Trace GC Ultra equipped with a R-Rxi 5 ms column (30 m, ID 0.25 mm) and quantified using the response factor corrected GC-area with respect to the internal standard. Samples were further analyzed by NMR-spectroscopy on a Bruker 400 MHz spectrometer.

Standard Catalytic Experiment (Using 1-Phenyl-1-propyne). A stock solution was prepared adding in their respective order acetonitrile (320 mL, 250.3 g,) 1-phenyl-1-propyne (6.4 g, 55 mmol), *p*-xylene (internal standard, 5.68 g, 54 mmol), triethylamine (27.00 g, 267 mmol), and formic acid (11.48 g, 267 mmol), which was saturated with nitrogen gas by gently bubbling N_2 through the solution for 20 min. From the stock solution, 20 mL was taken by a syringe and added to one of the 12 reaction vessels. The exact amount of added stock solution was determined by weighing; for this reason, molar and weight percentages were applied to determine quantities and further calculations. The Radleys' station was heated to 70 °C, after which the appropriate amount of catalyst and additive was added in aluminum weighing trays. Reaction rates were determined by taking the first order derivative of the conversion at 15%.

Catalytic Semihydrogenation Using All Components as Received. A stock solution was prepared with AR-Grade MeCN with a water content of >200 ppm, 99% formic acid, and 99% triethyl amine and *p*-xylene. The stock solution was degassed for 10 min with argon, and 20 mL was added to the reaction station. Subsequently, 2.7 mmol of the corresponding substrate was added (used as received), and the reaction was heated to 70 °C, at which point (t = 0) 1 mol % catalyst and 2 mol % PPh_3 were added. Reactions were monitored by GC and GC-MS (Jeol Accutof 4G GCv with a HP-5 MS capillary column (30 m, 0.25 mmID)). When the reaction products were not commercially available or products that are incompatible with GC were expected, NMR (128 scans, d1 = 20 s) was also used to follow the reaction over time. After 48 h, the reactions were worked up to allow for a more detailed NMR analysis. For entries (Table 2) 2, 3, 4, 5, 6, 8, 16, and 17, the reaction mixture was poured on a 200 mL 2 M $NaHSO_4$ aqueous solution. For the other entries, demi-water was used. If the substrate contained alkylic moieties, pentane was used for the extraction, and if aryl moieties were present in the molecule, Et_2O was

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used. The reaction products were extracted twice with 20 mL of the appropriate organic solvent, and the combined organic layers were washed twice with 20 mL of the aqueous medium that was initially used as well. The organic layer was then collected, dried over $MgSO_4$, and filtered, and the solvent was removed on a rotary film evaporation device. The obtained, worked up samples were analyzed by ^{1}H- and ^{13}C NMR spectroscopy and GC-MS, and the main peaks were cross-checked for identification. The determination of the stereochemistry of the alkene was performed on the basis of ^{1}H NMR by comparison to literature spectra (Entry 1,[47] Entry 2,[42] Entry 4,[67] Entry 5,[68] Entry 6,[69] Entry 7,[63] Entry 8,[70] Entry 9 S6.1, Entry 10,[71] Entry 11,[72] Entry 12,[73] Entry 13,[68] Entry 14 S6.2, Entry 15,[74] Entry 16,[75] Entry 17 S6.3). In cases where the literature did not provide coupling constants, the *Z*-configuration was assigned if the $^2J_{H-H}$ coupling was 10−14 Hz, and the *E*-configuration was assigned if the $^2J_{H-H}$ coupling was 15−18 Hz.

■ ASSOCIATED CONTENT

Supporting Information

Full results of the catalytic reactions, conversion versus selectivity graphs, data and graphs obtained from kinetic experiments, the derivation of the equations used for pseudo-first-order kinetics to determine the relative reaction constants, and the corresponding fitted data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was funded by the National Research School Combination Catalysis (project no. 2009-2013-UVA-Elsevier-02/03). We thank Umicore for providing the Pd-DVTMS solution, Elwin Janssen for assistance with mass measurements, and Dr. Santiago Gomez-Quero for his help with pseudo-first-order kinetic product analysis.

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