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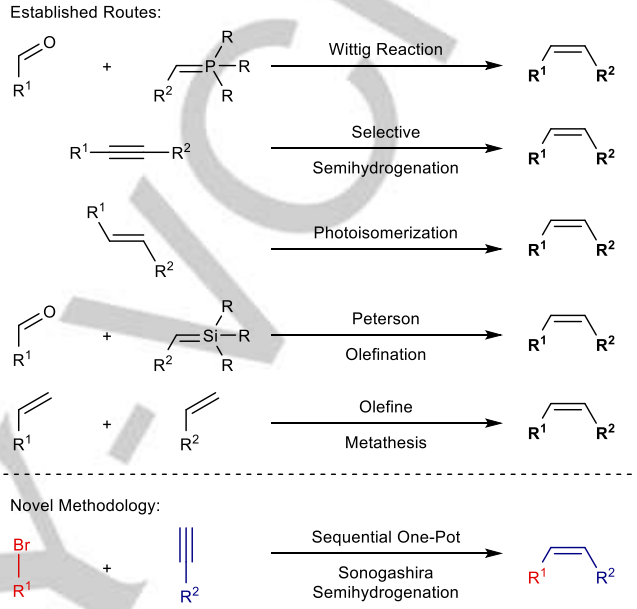
Development of a Novel Palladium-Catalyzed Process for the Synthesis of *Z*-Alkenes by Sequential Sonogashira-Hydrogenation-Reaction

Sören Hancker,[a] Helfried Neumann,[b] and Matthias Beller*[a]

Abstract: A novel and selective sequential one-pot protocol for the synthesis of *Z*-alkenes *via* Sonogashira-Semihydrogenation is reported. The efficiency of the methodology is increased by utilizing $PdCl_2$/$BuPAd_2$ as homogeneous catalyst for the Sonogashira coupling and subsequently transforming the transition metal complex into a heterogeneous Pd hydrogenation catalyst. This methodology represents one of the rare examples directly combining homogeneous and heterogeneous catalysis.

Introduction

Catalysis represents a key technology for efficient and sustainable production in the chemical industry. In addition, academic laboratories and life science industries benefit from this well-established tool box for the synthesis of biologically active compounds and fine chemicals. Due to their respective advantages and disadvantages, both homogeneous and heterogeneous catalysts are applied in the manufacturing of numerous daily products.[1] Traditionally, due to superior reusability and recyclability heterogeneous catalysts are favored for the synthesis of bulk chemicals. On the other hand, the demand for high selectivity and activity under mild conditions benefits the application of molecularly-defined homogeneous catalysts, specifically in the field of fine chemicals and specialties. However, in recent years there has been an increasing interest to develop more active and selective heterogeneous catalysts to overcome the conventional disadvantages of such materials while sustaining the benefits.[2] Among other approaches, we and other groups demonstrated that the pyrolysis of distinct molecular complexes adsorbed on inorganic materials generates doped metal centers embedded into the support as catalytically active sites, which constitute highly efficient heterogeneous catalysts.[3]
Interestingly, beside from this current approach, the methodology of utilizing a homogeneous complex for an initial chemical transformation prior to converting it into a heterogeneous material which is active in a sequential reaction step has been reported as early as 1994.[4] Notably, this strategy turned the synthesis of the agrochemical Prosulfuron into an economically feasible process.[5] Surprisingly, despite this success, this concept has rarely been applied in other areas.[6]
Inspired by all these reports, we present a new methodology for the selective synthesis of *Z*-alkenes including homogeneous and heterogeneous palladium catalyzed transformations. As an initial step, a Sonogashira reaction is performed followed by hydrogenation of the resulting alkyne catalyzed by a heterogeneous catalyst formed from the initially homogeneous metal complex. The resulting structural motif is found in various biologically active compounds and represents a valuable building block for organic syntheses.[7]



Scheme 1. Selected routes for the synthesis of *Z*-alkenes.

In general, *Z*-alkenes are synthesized sequentially from the corresponding internal acetylene by hydrogenation (Scheme 1). For this second step, specific hydrogenation catalysts such as the Lindlar catalyst are typically used.[8] In recent years other heterogeneous materials have been developed based on both noble metals,[9] and other transition metals.[10] More traditionally, starting from aldehydes and phosphonium ylides, the Wittig reaction constitutes a stoichiometric approach leading to almost exclusively *Z*-alkenes under optimized conditions.[11] The related Peterson olefination is another approach towards *Z*-alkenes.[12] Herein, aldehydes are reacted with α-silyl carbanions followed by an acidic or basic work-up which determines the stereoselectivity. Furthermore, *Z*-alkenes can be synthesized by photoisomerization of *E*-alkenes.[13] Finally, alkene metathesis provides access to *Z*-alkenes starting from easily available terminal olefins.[14] However, the selectivity of this C-C bond forming transformation remains challenging especially for intermolecular reactions.

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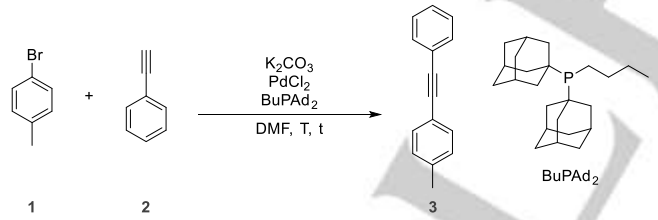
Results and Discussion

For our initial investigations, the reaction of 4-bromotoluene (**1**) and phenylacetylene (**2**) to give phenyl-p-tolyl-acetylene (**3**) was chosen as model system. Previously, it was shown that the combination of $PdCl_2$/$BuPAd_2$ with K_2CO_3 in DMF catalyzes Sonogashira reactions without the need of further additives (Cu salts, amines).[15] Initially, the influence of the reaction temperature was evaluated applying this system. Even at room temperature, the reaction reached 68% conversion and 65% yield. However, 4 days were required and significant amounts of both starting materials remained unconverted (Table 1, entry 1).

Simply increasing the temperature to 40 °C led to full conversion of the aryl bromide and 82% of **3** were obtained after 24 hours (entry 2). At 60 °C, complete conversion was achieved after only 4 hours while the reaction provided 78% of the desired compound (entry 3). Despite the decreased selectivity, the ongoing optimization was conducted at 60 °C due to the increased reaction rate and the desire to further lower the catalyst loading. Furthermore, the effect of the acetylene concentration was investigated since the complete consumption of **2** was observed in several experiments. Noteworthy, the yield further declined to 67% when 3 equivalents of phenylacetylene were employed (entry 4).

The selectivity remained at 80% compared to entries 2 and 3 when 1.2 equivalents were applied by adding the reagent continuously over a period of two hours (entry 5). However, significant amounts of the aryl bromide were detected while **2** was completely converted after the reaction. Upon reducing the catalyst and ligand loading to 2 mol%, 84% of the desired product was obtained (entry 6). Notably, the selectivity towards the internal acetylene was improved when lower catalyst loadings were applied (entries 6-13). Accordingly, the selectivity

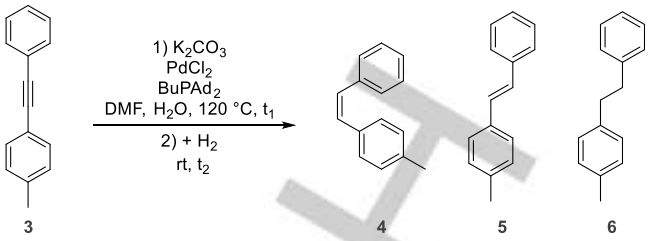
Table 1. Optimization of the copper- and amine-free Sonogashira reaction.



Entry[a]	**2** [mmol]	Pd:L [mol%]	T [°C]	t [h]	Conversion[b,c] [%]	Yield[c] [%]
1	1	4:6	25	96	68	65
2	1	4:6	40	24	>99	82
3	1	4:6	60	4	>99	78
4	1.5	4:6	60	4	>99	67
5[d]	0.6	4:6	60	6	88[e]	70
6	1	2:2	60	16	>99	84
7	**1**	**1:1**	**60**	**16**	**>99**	**88**
8[d]	0.6	1:1	60	16	67[e]	61
9	1	1:1	60	8	90	80
10	1	0.5:0.5	60	16	90	81
11	1	0.1:0.1	60	16	66	60
12	1	0:1	60	16	<1	<1
13	1	1:0	60	16	<1	<1

[a] Standard conditions (Entry 7): 0.5 mmol **1**, 1 mmol **2**, 1 mmol K_2CO_3, 1 mol% $PdCl_2$, 1 mol% $BuPAd_2$, 2 mL DMF at 60 °C for 16 hours. [b] Regarding **1**. [c] Determined by GC with hexadecane as internal standard. [d] **2** was dissolved in 1 mL DMF and added continuously over the first 2 hours of the experiment. [e] Conversion of **2**: >99%.

Table 2. Optimization of the selective semihydrogenation.



Entry[a]	t_1 [h]	t_2 [min]	Conversion[b,c] [%]	Yield[c] [%]	**4** *Z*:*E*-Ratio[c] [%:%]	*Z*-Selectivity[d] [%]	Yield[c] **6** [%]
1	8	150	>99	<1	<1:9	<1	88
2	8	80	>99	33	33:9	33	55
3	8	40	>99	80	80:8	80	11
4	**8**	**20**	**>99**	**91**	**91:6**	**91**	**3**
5	8	10	60	51	51:5	85	3
6	4	20	46	38	38:4	83	2
7	2	20	21	14	14:3	67	2

[a] Standard conditions (Entry 4): 0.5 mmol **3**, 1 mmol K_2CO_3, 1 mol% $PdCl_2$, 1 mol% $BuPAd_2$, 2 mL DMF, 0.2 mL H_2O at 120 °C for 8 hours. Subsequently, hydrogen gas was bubbled through the solution at 25 °C for 20 min at 0.5 mL/s gas flow. [b] Regarding **3**. [c] Determined by GC with hexadecane as internal standard. [d] Referring to the ratio of yield to conversion.

improved to 88% at full conversion when 1 mol% of the catalyst was utilized (entry 7). Attempts to decrease the necessary concentration of **2** resulted in lower product yields (entries 5 and 8). As expected lower catalyst loadings require longer reaction times since a conversion of 90% was observed after 8 hours (entry 9). The necessity for longer reaction times under low catalyst loadings was emphasized by experiments applying 0.5 mol% or 0.1 mol% catalyst (entries 10 and 11). While the selectivity remained high, the conversion decreased to 90% and 66%, respectively. The control experiments proved that the palladium salt as well as the ligand is required for a successful reaction since the absence of either one of these compounds prevented the formation of the product.

Next, different hydrogen sources were tested for the selective hydrogenation of **3**. Applying our catalytic system, hydrides, formic acid and alcohols failed to generate the product, whereas hydrogen gas afforded full conversion of the internal acetylene **3**. For the implementation of hydrogen, the reaction mixture was heated to 120 °C for 8 hours before the solution was allowed to cool down to room temperature. Subsequently, hydrogen gas was bubbled through the reaction mixture for a specific time at 25 °C. The reaction provided full conversion, but no *Z*-alkene was detected after 150 min (Table 2, entry 1). Instead, quantitative amounts of the alkane (**6**) emerged as the reaction product. After a hydrogenation time of 80 min, 33% of the desired product **4** was obtained, but the *Z*-selectivity and *Z*:*E*-ratio remained at low levels (entry 2). These parameters were further improved as the reaction time was decreased to 40 min (entry 3). Herein, the *Z*-selectivity was increased to 80% at complete conversion and *Z*:*E*-ratio of 80:8. However, a hydrogenation period of 20 min gave the best result including 91% overall yield at *Z*:*E*-ratio of 91:6 (entry 4). Experiments to further decrease the reaction time proved that the generation of the desired *Z*-alkene remained uncompleted as only 60% of the desired *Z*-alkene was obtained (entry 5). Noteworthy, modifying the initial reaction step led to a decrease in the hydrogenation activity. In this case, the yields dropped to 38% and 14% after 20 min of hydrogenation when the first phase was reduced to 4

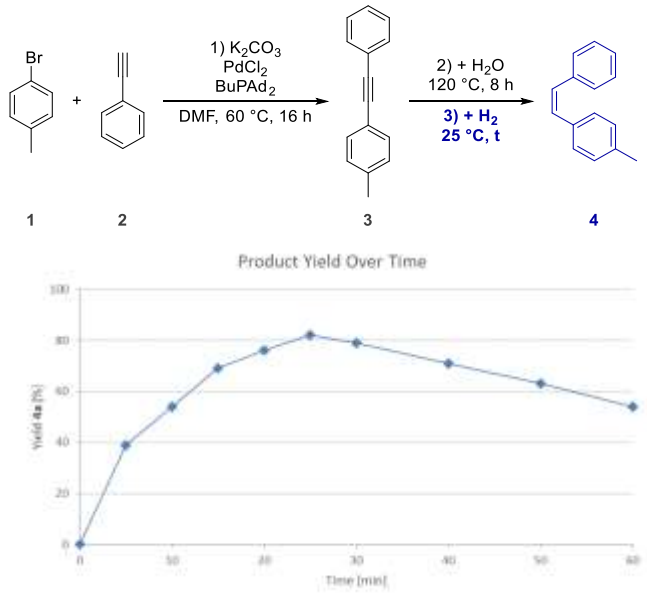


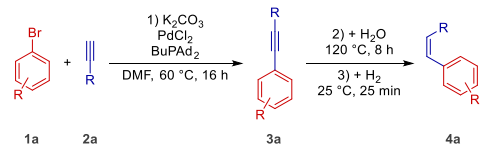
Figure 1. Product yield over time of the hydrogenation step in the sequential one-pot methodology.
Conditions: 0.5 mmol **1**, 1 mmol **2**, 1 mmol K_2CO_3, 1 mol% $PdCl_2$, 1 mol% $BuPAd_2$, 2 mL DMF at 60 °C for 16 hours. Subsequently, 0.2 mL H_2O was added at room temperature after which the solution was heated to 120 °C for 8 hours. Finally, H_2 was bubbled through the reaction mixture at 25 °C for 25 min. Yield determined by GC with hexadecane as internal standard.

and 2 hours, respectively (entries 6 and 7). *It is important to note that without heterogenization of the initially applied homogeneous Pd complex, no hydrogenation occurred.*

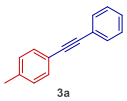
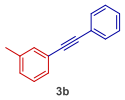
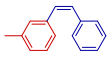
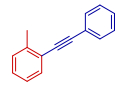
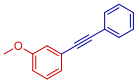
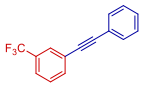
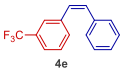
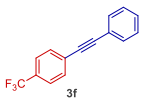
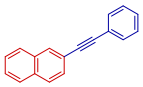
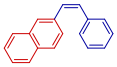
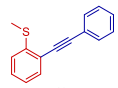
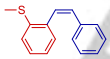
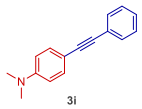
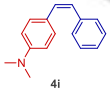
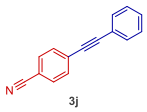
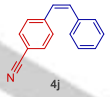
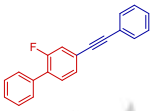
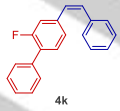
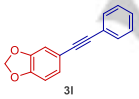
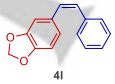
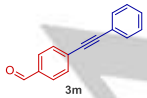
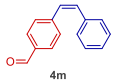
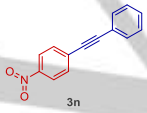
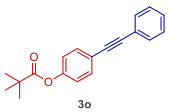
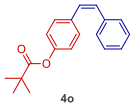
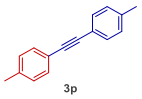
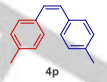
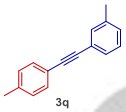
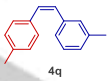
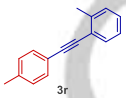
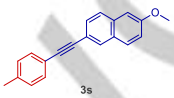
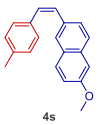
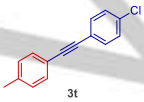
Finally, the separate reaction steps were combined to a sequential one-pot process. Therefore, the transformation was executed with the conditions developed in the optimization of the Sonogashira reaction (Table 1). Subsequently, water was added into the reaction mixture at room temperature before the solution was heated to 120 °C for 8 hours. In order to determine the optimal duration for the hydrogenation reaction, samples were prepared in specific intervals and analyzed for their composition. The results are depicted in Figure 1. The optimal duration was identified at 25 min of hydrogen flow and therefore slightly differing from the optimization results for the semihydrogenation step (Table 2).

Next, we examined the reactivity of different aryl bromides and terminal acetylenes to form preferentially Z-alkenes using this novel methodology (Table 3). Initially, we applied the previously optimized conditions to the reaction of methyl-substituted bromobenzenes such as *ortho*-, *meta*- and *para*-methyl-bromobenzene with phenylacetylene in order to study the effect of the substitution position. As shown in Table 3, entries 1-3, the corresponding intermediates **3a**, **3b** and **3c** were isolated with 85%, 87% and 84% overall yield. Thus, no significant effect on the yield of the coupling reaction was observed. However, the semihydrogenation only provided the products in comparable yields 75% (**4a**), 75% (**4b**) and 72% (**4c**) when the duration of the hydrogenation was adjusted. Herein, the *ortho*-substituted methyl-bromobenzene required longer reaction times presumably caused by steric hindrance of the methyl group. Due to the steric proximity of the *ortho*-substituent, the access of the catalysts surface to the internal acetylene is impeded. Therefore, the position of the substituent affects the semihydrogenation reaction, while the Sonogashira coupling displayed insignificant deviation based on the substituent position. Furthermore, the influence of the electron-withdrawing or -donating nature of the substituent was investigated. Accordingly, 3-methoxy-bromobenzene (**1d**) as well as 3-trifluoromethyl-bromobenzene (**1e**) was evaluated for the productivity in the Sonogashira-semihydrogenation (entries 4 and 5). In agreement with literature findings, the electron-withdrawing group promotes the coupling reaction as 93% of **3e** was formed. Conversely, only 72% of intermediate **3d** was obtained suggesting that electron-donating groups decrease the reactivity of the aryl bromide. The complete reaction of **1d** and **1e** to the corresponding *Z*-alkenes revealed an additional influence of the substituent on the hydrogenation result. The hydrogenation period had to be extended for substrate **1d** in order to achieve full conversion (68% yield) while the internal alkyne **3e** was completely hydrogenated after 25 min (83% yield). The tendency of (strongly) coordinating functional groups to require prolonged hydrogenation periods was observed in several cases during the exploration of the substrate scope (entries 4, 8, 9, 12, 19). Based on the steric and electronic properties of the substrate, the optimal hydrogenation time varies for every reaction. Continuing our studies, we examined the reactivity of 4-trifluoromethyl-bromobenzene (**1f**) for both reaction steps (entry 6). Applying this starting material afforded 88% of the intermediate **3f** and 79% of the corresponding final product **4f**. When 2-bromonaphthalene was tested, the internal alkyne **3g** of the conversion with phenylacetylene was provided with 82% overall yield while the hydrogenation gave 72% of the *Z*-alkene **4g** (entry 7). 2-Methylthio-bromobenzene was successfully converted to the intermediate **3h** with an overall yield of 69% despite the sulfur-containing functional group (entry 8). Albeit, the hydrogenation had to be extended to 3 hours, the process yielded 35% of the *Z*-alkene **4h**. Nevertheless, a significant amount of the first-step product remained unconverted in the crude mixture despite the prolonged reaction time. Therefore, the methylthio-moiety displays a rather drastic example of the functional group effect on the hydrogenation. The transformation of 4-dimethylamino-bromobenzene (**1i**) offered 70% of the intermediate product **3i** while the hydrogenation provided *Z*-alkene **4i** in 41% overall yield (entry 9). However, the resulting product additionally contained 15% *E*-alkene which could not be removed by preparative methods. Therefore, this substrate resulted in the most unfavorable *Z*:*E*-ratio (85:15). The aromatic nitrile **1j** was converted successfully to the corresponding intermediate **3j** in 98% yield (entry 10). Subsequently, the hydrogenation afforded 84% of the target *Z*-alkene **4j**. Furthermore, this result confirms the tendency of electron-withdrawing substituents to increase the reactivity of the aryl bromide in the coupling reaction. Next, we examined starting material **1k** in the transformation to the corresponding products and found both targets to be generated in 96% (**3k**) and 86% yield (**4k**), respectively (entry 11). Extending the list of different aryl bromides, intermediate **3l** was isolated in 68% yield while the associated final product was obtained in 64% (entry 12). Notably, also few functionalized substrates prevented the successful conversion to the desired products. In this respect, aldehyde- and nitro-containing substrates **1m** and **1n** smoothly converted to the corresponding intermediates in 87% and 83% yield; however, the hydrogenation led to a mixture of products including alkanes, alkenes and alkynes with either reduced or non-reduced aldehyde- or nitro-functional group (entries 13 and 14).

Table 3. Substrate scope for the Sonogashira-semihydrogenation.



1a 2a 3a 4a

Entry[a]	Intermediate	Yield[b] [%]	*Z*-Alkene	Yield[b] [%]
1	 3a	85	 4a	75
2	 3b	87	 4b	75
3[c]	 3c	84	 4c	72
4[d]	 3d	72	 4d	68
5	 3e	93	 4e	83
6	 3f	88	 4f	79
7	 3g	82	 4g	72
8[e]	 3h	69	 4h	35[f]
9[d]	 3i	70	 4i	41[g]
10	 3j	98	 4j	84
11	 3k	96	 4k	86
12[h]	 3l	68	 4l	64
13	 3m	87	 4m	0[i]
14	 3n	83	 4n	0[i]
15	 3o	86	 4o	0[i]
16	 3p	82	 4p	76
17	 3q	84	 4q	76
18[c]	 3r	80	 4r	71
19[c]	 3s	90	 4s	85
20	 3t	80	4t	0[j]
21[k]	3u	75	4u	52
22[l]	3v	69	4v	34

General remark: For the isolated yields, the experiment was conducted twice. The first experiment was stopped after the Sonogashira step and the alkyne was isolated. The second experiment was conducted as described without purification of the intermediate and the *Z*-alkene was isolated. Therefore, the overall yield for the *Z*-alkene is obtained from **1** and **2** directly when the reaction is run without the isolation of **3**. [a] Standard conditions: 0.5 mmol **1**, 1 mmol **2**, 1 mmol K_2CO_3, 1 mol% $PdCl_2$, 1 mol% $BuPAd_2$, 2 mL DMF at 60 °C for 16 hours. Subsequently, 0.2 mL H_2O was added at room temperature followed by heating to 120 °C for 8 hours. Finally, H_2 was bubbled through the reaction mixture at 25 °C for 25 min. [b] Isolated yield. [c] 30 min hydrogenation. [d] 35 min hydrogenation. [e] 180 min hydrogenation. [f] Significant amounts of the intermediate remained unconverted. [g] The isolated product contained significant amounts of the corresponding *E*-alkene which could not be removed by preparative methods. [h] 40 min hydrogenation. [i] The resulting complex mixture was not further isolated. [j] Despite prolonged hydrogenation, only insignificant amounts of the corresponding product were detected and not further isolated. [k] 80 min hydrogenation with 25 mol% 3,6-dithia-1,8-octanediol (DTOD) at 0 °C. [l] 20 min hydrogenation at 0 °C.

Using the ester-containing compound **1o**, provided the intermediate **3o** in 86% yield (entry 15). Unfortunately, during heterogenization of the catalyst, the product was partially hydrolyzed in basic aqueous medium at 120 °C. Thus, a mixture of numerous compounds was obtained.

Moreover, we investigated the reactivity of different acetylenes in the one-pot Sonogashira-semihydrogenation process. To identify position effects, we compared the overall yields applying compounds **2p**, **2q** and **2r** (entries 16-18). The results indicate a marginal effect for the coupling reaction as all three corresponding intermediates were isolated in 82%, 84% and 80% overall yield. Regarding the final product, the tendency of *ortho*-substituents inhibiting the hydrogenation was observed as well. While the compounds **4p**-**4r** were obtained in similar quantities (76%, 76% and 71%), the duration of the hydrogenation had to be extended in the case of *ortho*-methylphenylacetylene (**2r**) to 25 min in order to achieve complete conversion. Continuing our substrate scope, the conversion of aryl bromide **1a** and terminal acetylene **2s** provided the

corresponding coupling product **3s** in 90% and the semihydrogenation product **4s** in 85% overall yield (entry 19). Unfortunately, the attempt to include 4-chloro-phenylacetylene in the list of convertible substrates failed although the intermediate **3t** was isolated in 80% yield (entry 20). Here, various attempts to hydrogenate the C-C triple bond ended unsuccessful. To our delight, the transformation of **1a** with 1-octyne (**2u**) afforded the intermediate in 75% yield (entry 21). Nevertheless, the initial hydrogenation results proved to be unsatisfactory/unsatisfying although promising. While the target was in fact formed and identified, the *Z*-selectivity accounted for only 58%. The remaining starting material was already converted to the corresponding alkane. To increase the chemoselectivity, this reaction was performed in the presence of 3,6-dithia-1,8-octanediol (DTOD), also known as Lindlar Catalyst Poison.[8a] Indeed, we discovered a positive effect of this additive for the hydrogenation of the intermediate **3u**. The results of the experiments with and without the additive are displayed in Figure 2.

Eventually, the final product **4u** was formed with 80% *Z*-selectivity and an isolated yield of 52% when the reaction was conducted with 25 mol% DTOD at 0°C for 80 min (Table 3, entry 21). Consequently, alkyl-substituted acetylenes can be converted by aid of the additive with our methodology as well.

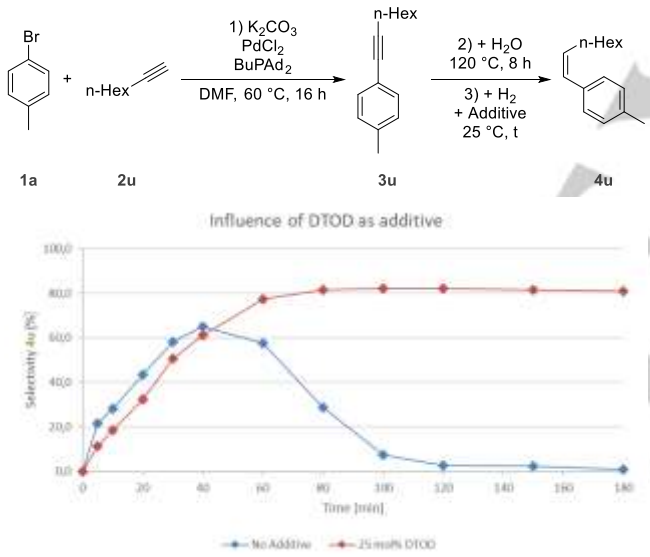
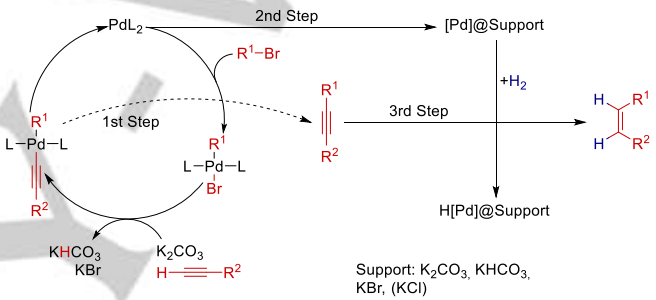


Figure 2. Influence of DTOD in the semihydrogenation step of internal acetylene **3u**.
Conditions: 0.5 mmol **1a**, 1 mmol **2u**, 1 mmol K_2CO_3, 1 mol% $PdCl_2$, 1 mol% $BuPAd_2$, 2 mL DMF at 60 °C for 16 hours. Subsequently, 0.2 mL H_2O was added at room temperature after which the solution was heated to 120 °C for 8 hours. Finally, the additive was added and H_2 was bubbled through the reaction mixture at 0 °C for 25 min. Yield determined by GC with hexadecane as internal standard.

Nonetheless, when tert-butyl-acetylene (**2v**) was applied in combination with aryl bromide **1l**, the hydrogenation was prevented almost entirely in the presence of DTOD. Without the additive, the corresponding *Z*-alkene **4v** was obtained in 34% yield when the reaction was conducted at 0°C (entry 22).

To improve our understanding of the process, we analyzed the heterogeneous material and the reaction solution after each step for its palladium content by ICP-OES analysis. The results indicate that the palladium remains homogeneously dissolved after the Sonogashira reaction since no palladium was observed in the isolated particles. Overall 94% of the originally applied palladium was detected in the homogeneous solution. In contrast, samples obtained after the heterogenization of the molecular catalyst as well as after the hydrogenation reaction contained detectable amounts of palladium. Herein, the homogeneous phase contained 69% while the heterogeneous material incorporated 26% of the employed transition metal. Obviously, the catalyst is not entirely heterogenized after the second reaction phase. To investigate the heterogeneous material XRD- and XPS-analysis were conducted. As expected, the material mainly consists of a K_2CO_3-$KHCO_3$ mixture containing additional KBr and residual amounts of KCl. Unfortunately, the palladium content in the substance was too low (<1%) to get a defined understanding of the catalyst nature. XPS-analysis confirmed the composition of the material by O, C, K, Br and Cl. Herein, the chloride is presumably present as KCl stemming from $PdCl_2$ and K_2CO_3.

Based on our findings, we postulate the mechanism depicted in Scheme 2 for the formation of *Z*-alkenes in the Sonogashira-semihydrogenation.



Scheme 2. Postulated mechanism for the sequential Sonogashira-semihydrogenation.

Initially, the synthesis of the internal acetylene is accomplished according to the generally accepted catalytic cycle for the Sonogashira reaction (first step).[16] Herein, the active palladium complex undergoes oxidative addition with the aryl bromide. Next, the bromide ion is exchanged with the terminal acetylene through abstraction with K_2CO_3. Aside from the formation of the aryl palladium acetylene complex, KBr and $KHCO_3$ are generated. Following the reductive elimination of the desired internal acetylene, the active palladium complex is regenerated and initiates a new catalytic cycle. During the partial heterogenization of the molecular Pd catalyst (second step), the generated intermediate remains unconverted in the reaction mixture. Finally, the resulting heterogeneous palladium catalyst is activated by reduction with hydrogen. Hereupon, a palladium hydride surface is generated which serves as the active hydrogenation catalyst. Due to the specific surface, the selectivity of the catalyst allows for the hydrogenation of the internal acetylene towards the desired *Z*-alkene.

Conclusions

In summary, we developed a novel protocol for the synthesis of *Z*-alkenes making use of palladium twice, once as homogeneous complex and once as heterogenized hydrogenation catalyst. This methodology consists of three steps: 1. homogenous Sonogashira reaction, 2. heterogenization of the homogeneous palladium complex and 3. selective

semihydrogenation. It represents one of the rare examples in which a catalyst is transformed into a new form sequentially enabling an additional reaction. The synthesized *Z*-alkenes are an interesting substance class for fine chemical syntheses and life sciences. We further demonstrated the application on various substrates containing different functional groups and indicated the limitations regarding functional group tolerance.

Experimental Section

General Information: All manipulations were conducted under argon with exclusion of moisture and oxygen by using standard techniques for the manipulation of air sensitive compounds. Reaction temperatures refer to silicon oil in an additional pressure tube within the heated aluminium block. NMR data were recorded on Bruker ARX 300, Bruker ARX 400 and Bruker Fourier 300 spectrometers. ^{13}C and ^{1}H NMR spectra are given in ppm and referenced to signals of deuterated solvents and residual protonated solvents, respectively (Acetone-d_6: ^{1}H: 2.050 ppm, ^{13}C: 29.840 ppm; CD_2Cl_2: ^{1}H: 5.320 ppm, ^{13}C: 54.000 ppm). The assignment of the carbon atoms was accomplished by aid of DEPT spectra. Gas chromatography analysis was performed on an Agilent HP-5890 instrument with a FID detector and HP-5 capillary column using argon as carrier gas. Gas chromatography-mass analysis was carried out on an Agilent HP-5890 instrument with an Agilent HP-5973 Mass Selective Detector (EI) and HP-5 capillary column using helium carrier gas. TOF HR-MS measurements were performed on an Agilent 1200/6210 Time-of-Flight LC-MS. Flash chromatography was performed on a Teledyne Isco CombiFlash Rf 200 system. Chemicals were purchased from Sigma Aldrich, Alfar Aesar, TCI or Strem and were used as received. DMF was dried by a SPS from Innovative Technology while H2O was flushed with argon for one hour. Solvents were stored in Aldrich Sure/store flasks under argon.

General Procedure for the Sonogashira-Semihydrogenation towards Z-Alkenes: In general, all steps are conducted subsequently without any intermediate work-up. Additives or solvents are only added after each step when indicated. In a glass pressure tube under argon, 4-bromotoluene (0.5 mmol, 63.5 µL), phenylacetylene (1 mmol, 110 µL) and DMF (2 mL) were added to the already present solids $PdCl_2$ (1 mol%, 0.9 mg), $BuPAd_2$ (1 mol%, 1.8 mg) and K_2CO_3 (1 mmol, 138 mg). The pressure tube was closed and the mixture was stirred in an aluminium block at 60 °C for 16 hours. Afterwards, 0.2 mL H_2O was added to reaction mixture under argon counter flow. The tube was closed again and heated to 120 °C for 8 hours. Unless otherwise noted, hydrogen gas was passed through the reaction mixture at 0.5 mL/s gas flow at room temperature (25 °C) for a specific time without further additives. Afterwards, argon was passed through the solution for 10 minutes to remove dissolved hydrogen gas. For work-up, the product was purified by flash chromatography after initial extraction to give 73 mg (75%) of **4a**. Detailed information can be obtained from the provided Supporting Information.

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Keywords: Catalysis • Palladium • Z-Alkenes • Sonogashira Coupling • Hydrogenation

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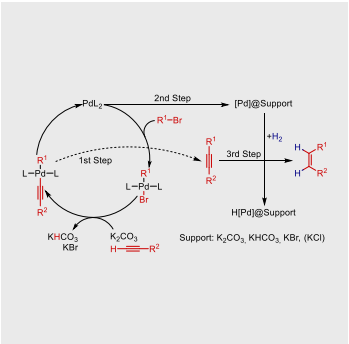
Entry for the Table of Contents

FULL PAPER

A selective one-pot protocol for the synthesis of Z-alkenes via Sonogashira-Semihydrogenation is reported. In this process the original homogeneous palladium catalyst is transformed into an active heterogeneous material.



From Homogenous to Heterogeneous Catalysis

*Sören Hancker, Helfried Neumann, Matthias Beller**

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