

Reduction of alkynes into 1,2-dideuterioalkenes with hexamethyldisilane and deuterium oxide in the presence of a palladium catalyst†

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A combination of hexamethyldisilane and deuterium oxide was found to work as a deuterium transfer reagent for alkynes in the presence of a catalytic amount of a palladium complex to give (*E*)-1,2-dideuterioalkenes selectively through the corresponding (*Z*)-isomer.

Alkenes deuterated at their olefinic protons are an important class of compounds, which can be utilized for biological research and the elucidation of reaction mechanisms. Several efforts have been devoted to the development of the reduction of alkynes into 1,2-dideuterioalkenes with deuterium oxide, which is undoubtedly the most inexpensive and easy to handle deuterium source. Most of the previously reported methods, however, have failed to reconcile a high deuteration ratio with high stereoselectivity.^{1,2} On the other hand, combinations of a hydrosilane and a protic compound (ROH) in the presence of a palladium catalyst have been used for transfer hydrogenation of alkynes.³ However, both reagents have to be deuterated as D-Si and ROD to apply this method to the deuteration.⁴ No report has been available that disilanes instead of hydrosilanes work as reductants of alkynes, in spite that only deuterated proton sources are required there for deuteration. Here we report the palladium-catalyzed reduction of alkynes with hexamethyldisilane and deuterium oxide, which gives (*E*)-1,2-dideuterioalkenes selectively through the corresponding (*Z*)-derivatives.

Treatment of diphenylacetylene (**1a**) with hexamethyldisilane (**2**: 1.5 equiv.), D₂O (10 equiv.), [PdCl(η³-C₃H₅)₂] (5 mol% of Pd) and PPh₃ (10 mol%) in DMA at 80 °C for 24 h gave 99% yield of (*E*)-stilbene-*d*₂ (**3a**) in 99.1% deuterium ratio with high stereoselectivity (99.2% *E*) (eqn (1) and entry 1 in Table 1).⁵ Even a trace amount of an overreduced product, 1,2-diphenyl-1,1,2,2-tetradeuterioethane, was not detected in the reaction mixture. DMSO as a solvent showed comparable efficiency to DMA, whereas less polar solvents such as 1,4-dioxane and toluene were totally ineffective. The corresponding transfer hydrogenation using H₂O (2.5 equiv.) instead of D₂O gave hydrogenation product **4a**, (*E*)-stilbene, in 98% yield.

The deuteration with Me₃SiSiMe₃-D₂O was applied to various symmetrical and unsymmetrical internal alkynes, giving high yields of (*E*)-1,2-dideuterioalkenes with >97% deuterium ratios and >98% (*E*)-selectivities (Table 1). In addition to diphenylacetylene, those having one or two electron-withdrawing and/or -donating substituents accepted the addition of deuterium atoms (entries 2–8).

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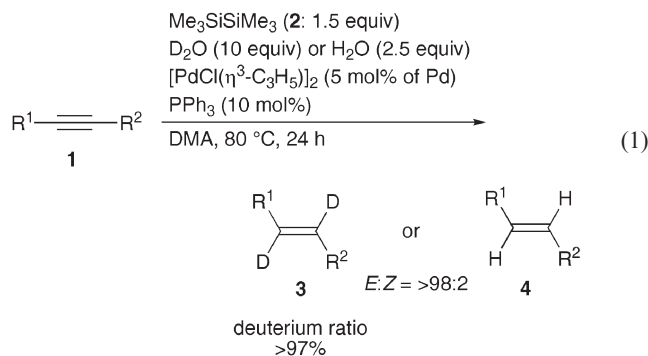


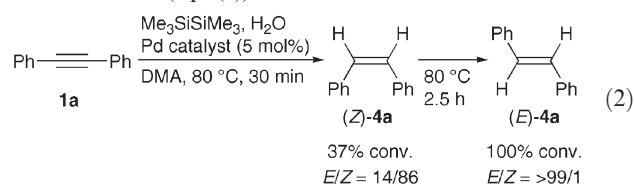
Table 1 Palladium-catalyzed reduction of alkynes into alkenes^a

Entry	R ¹	R ²	Yield (%) ^b of 3	Yield (%) ^{b,c} of 4
1	Ph	Ph	99	98 ^d
2	4-CF ₃ C ₆ H ₄	4-CF ₃ C ₆ H ₄	94	91
3	4-CF ₃ C ₆ H ₄	Ph	93	—
4	4-MeOCOC ₆ H ₄	Ph	93	—
5	4-MeOC ₆ H ₄	Ph	99	—
6	4-MeC ₆ H ₄	Ph	96	—
7	4-MeOC ₆ H ₄	4-CF ₃ C ₆ H ₄	85	96
8	2-MeC ₆ H ₄	2-MeC ₆ H ₄	88	95
9	Ph	<i>t</i> -Bu	79	—
10	4- <i>n</i> -C ₅ H ₁₁ C ₆ H ₄	Me	64	—

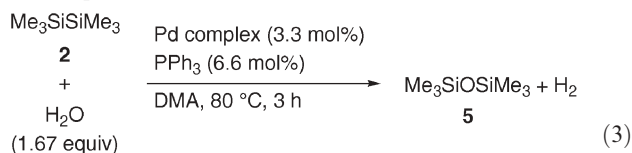
^a The reaction was carried out in DMA (0.5 mL) at 80 °C for 24 h using an alkyne (0.40 mmol), Me₃SiSiMe₃ (0.60 mmol) and D₂O (4.0 mmol) in the presence of [PdCl(η³-C₃H₅)₂] (10 μmol) and PPh₃ (40 μmol). ^b Isolated yield based on the alkyne. ^c H₂O (1.0 mmol) was used instead of D₂O. ^d Reaction time = 3 h.

Alkyl(aryl)acetylenes also participated in the deuteration (entries 9 and 10). The hydrogen transfer reaction from H₂O to some of the alkynes was conducted successfully (entries 1, 2, 7 and 8).

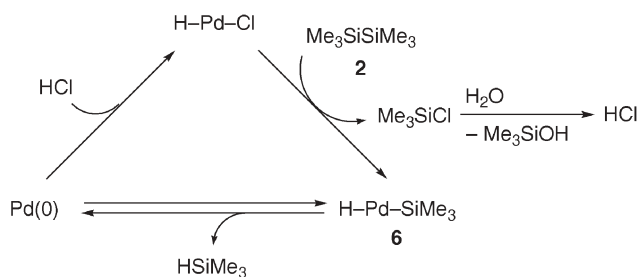
(*E*)-Isomers were found to be produced by isomerization of the initially formed (*Z*)-isomers. Thus, the reaction of diphenylacetylene (**1a**) with Me₃SiSiMe₃ (1.5 equiv.) and H₂O (2.5 equiv.) in the presence of [PdCl(η³-C₃H₅)₂]-PPh₃ (5 mol% of Pd, PPh₃/Pd = 2) at 80 °C for 30 min gave the (*Z*)-isomer predominantly (*E* : *Z* = 14 : 86) with 37% conversion, and heating the reaction mixture for another 2.5 h at 80 °C changed the *E* : *Z* ratio to >99 : 1 with full conversion of **1a** (eqn (2)).



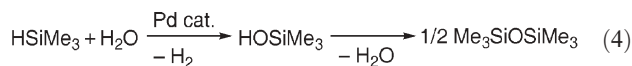
As described so far, $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2\text{-PPh}_3$ is an effective catalyst for the reduction of alkynes. In contrast, the present reaction was not catalyzed by $\text{Pd}(\text{PPh}_3)_4$ or $\text{Pd}(\text{PPh}_3)_2$ generated from $\text{PdCp}(\eta^3\text{-C}_3\text{H}_5)$ and PPh_3 (1 : 2). However, addition of HCl to the $\text{PdCp}(\eta^3\text{-C}_3\text{H}_5)\text{-PPh}_3$ system activated the catalyst and the hydrogenation was completed within 1 h. From these observations, a combination of a palladium(0) complex and HCl seems to be important, giving a species like H-Pd-Cl .⁶ Actually, $\text{PdH}(\text{Cl})(\text{PPh}_3)_2$ was found to be as effective as $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2\text{-PPh}_3$ as a catalyst for the reduction. The high activity of the H-Pd-Cl species was found to be ascribed to the ability to cleave Si-Si bonds.⁷ Thus, 85% of hexamethyldisilane (**2**) was converted to hexamethyldisiloxane (**5**) on treatment with $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2\text{-PPh}_3$ and H_2O at 80 °C for 3 h in the absence of an alkyne, whereas $\text{PdCp}(\eta^3\text{-C}_3\text{H}_5)\text{-PPh}_3$ did not catalyze the reaction at all (eqn (3)). A plausible catalytic cycle of the cleavage of the Si-Si bond is shown in Scheme 1. σ -Bond metathesis between H-Pd-Cl and disilane **2** cleaves the Si-Si bond to give Me_3SiCl and H-Pd-SiMe_3 **6**. Reductive elimination from **6** gives Me_3SiH and a palladium(0) complex. Then oxidative addition of HCl, generated by the reaction of Me_3SiCl with H_2O , to the palladium(0) complex regenerates H-Pd-Cl . Me_3SiH generated here should undergo the dehydrogenative coupling with H_2O in the absence of an alkyne to give Me_3SiOH ,⁸ which is dehydrated into **5** (eqn (4)).



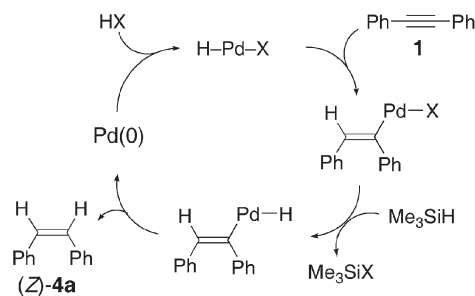
Pd complex	conv. (%)
$[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2$	85
$\text{PdCp}(\eta^3\text{-C}_3\text{H}_5)$	0



Scheme 1



With a H-Pd-Cl complex and Me_3SiH in our hands, it is most likely that the reduction of alkynes with $\text{Me}_3\text{SiSiMe}_3\text{-D}_2\text{O}$ follows essentially the same catalytic cycle (Scheme 2, exemplified by the reduction of diphenylacetylene) as proposed by Trost for the palladium-catalyzed reduction of alkynes with a hydrosilane and acetic acid.^{3a} Anionic ligand X stands for OAc for Trost or Cl for us. Initially formed (*Z*)-**4a** should insert into the H-Pd bond of the



Scheme 2

H-Pd-Cl complex, and the following β -hydride elimination gives the thermodynamically more stable (*E*)-isomer.⁹

In conclusion, we have disclosed that (*E*)-1,2-dideuterioalkenes are selectively obtained from alkynes using the most inexpensive deuterium source, D_2O , and hexamethyldisilane with the aid of a palladium catalyst.

Notes and references

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- A $\text{Ph}_2\text{SiD}_2\text{-MeOD}$ system was reported to transform diphenylacetylene into (*Z*)-stilbene-*d*₂ in 89% deuterium ratio. See reference 3b.
- Deuterium ratio and stereoselectivity were determined by ^1H NMR and GC/GC-MS, respectively.
- $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_5)]_2\text{-PPh}_3$ must be reduced to a palladium(0) complex by $\text{Me}_3\text{SiSiMe}_3$, leaving Me_3SiCl as a by-product, which gives Me_3SiOH (then $\text{Me}_3\text{SiOSiMe}_3$) and HCl on reaction with H_2O . For the reaction of π -allylpalladium complexes with disilanes, see: Y. Tsuji, M. Funato, M. Ozawa, H. Ogiyama, S. Kajita and T. Kawamura, *J. Org. Chem.*, 1996, **61**, 5779–5787. For a review, see: Y. Tsuji, in *Handbook of Organopalladium Chemistry for Organic Synthesis*, ed. E. Negishi, Wiley, New York, 2002, pp. 1913–1916.
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