ORGANIC
LETTERS

2013
Vol. 15, No. 23
6038–6041

Supported Gold Nanoparticle-Catalyzed *cis*-Selective Disilylation of Terminal Alkynes by σ Disilanes

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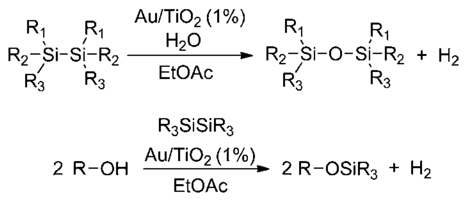
Received October 11, 2013

ABSTRACT

Supported gold nanoparticles on metal oxides (1 mol %) catalyze for the first time the *cis*-selective disilylation of terminal alkynes by 1,2-disilanes in isolated yields up to 94%. It is likely that the reaction proceeds through oxidative insertion of the σ Si–Si bond of disilanes on gold followed by 1,2-addition to the alkyne.

The isolobal analogy among the couples Au(I/III) and Pd(0/II) is currently triggering interest of organic chemists toward unraveling gold-catalyzed versions of C–C or C–heteroatom bond-forming reactions involving 2e redox catalysis. So far the progress is slow, and a few examples have been reported regarding the classical cross-coupling Suzuki[1] and Sonogashira[2] reactions. A specific case dealing with C–F activation in perfluoroarenes[3] has also been reported. The majority of those cases involve catalysis by supported gold nanoparticles.[4] From a mechanistic point of view, the Au-catalyzed Sonogashira reaction is controversial,[5] as the ability for oxidative insertion from the carbon halide bond to the metal is questioned. There is debate regarding the oxidation state of gold. It was recently shown that σ disilanes[6] or distannanes[7] undergo intramolecular oxidative insertion on Au(I) forming bis(silyl)- or stannylgold(III) complexes. In general, the activation of σ Si–Si bonds through oxidative insertion on metals is well established under catalysis by Pd, Pt, or Rh.[8] The observation of spontaneous intramolecular oxidative insertion of a

Scheme 1. Hydrolysis and Alcoholysis of 1,2-Disilanes Catalyzed by Au/TiO$_2$[9]



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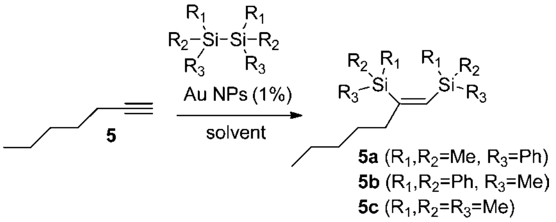
10.1021/ol402935x

Table 1. Reaction of 1-Heptyne (**5**) with 1,2-Disilanes **1**−**4** Catalyzed by Supported Au NPs



substituents	catalyst	solvent	time (h)/temp (°C)	isolated yield (%)
R_1, R_2, R_3 = Me (**1**)	Au/TiO_2	EtOAc	12/65	55
R_1, R_2, R_3 = Me (**1**)	Au/TiO_2	DCE	4/65	93
R_1, R_2 = Me, R_3 = Ph (**2**)	Au/TiO_2	EtOAc	6/65	48
R_1, R_2 = Me, R_3 = Ph (**2**)	Au/TiO_2	THF	5/65	40
R_1, R_2 = Me, R_3 = Ph (**2**)	Au/TiO_2	Toluene	5/65	34
R_1, R_2 = Me, R_3 = Ph (**2**)	Au/TiO_2	DCE	2/65	81
R_1, R_2 = Me, R_3 = Ph (**2**)	Au/ZnO	DCE	6/65	65
R_1, R_2 = Me, R_3 = Ph (**2**)	Au/Al_2O_3	DCE	5/65	67
R_1, R_2 = Ph, R_3 = Me (**3**)	Au/TiO_2	EtOAc	16/65	28
R_1, R_2 = Ph, R_3 = Me (**3**)	Au/TiO_2	DCE	10/65	72
R_1, R_2, R_3 = Ph (**4**)	Au/TiO_2	DCE	48/65	-

Si−Si functionality on gold(I) triggered the question by the authors[6a] on whether gold-catalyzed bis-silylation reactions on π systems by σ disilanes is feasible. Our initial exploration on the possible activation of 1,2-disilanes by gold revealed that supported Au nanoparticles (especially Au/TiO_2) readily catalyze their hydrolysis or alcoholysis with release of H_2 gas (Scheme 1).[9] A series of homogeneous Au(I) catalysts were proven significantly less reactive or even completely unreactive.

Apart from reporting the Au/TiO_2-catalyzed hydrolysis and alcoholysis of disilanes, our challenge was to explore the question raised by Bourissou and co-workers,[6a] thus providing the first example of a Au-catalyzed version of Si−Si 1,2-addition[10] to alkynes. Highly efficient dehydrogenative double silylation of alkynes has been recently achieved by our group with tethered 1,*n*-dihydrodisilanes, such as 1,1,3,3-tetramethyldisiloxane, in the presence of Au/TiO_2.[11] Notably, analogous attempts to perform double boronation of alkynes with bis(pinacolato)diboron in the presence of supported gold nanoparticles were unsuccessful[12] and achievable only under catalysis by Pt nanoparticles. Initially, we examined the reaction of a model alkyne (1-heptyne, **5**) with a series of symmetrical 1,2-disilanes, namely 1,1,1,2,2,2-hexamethyldisilane (**1**), 1,1,2,2-tetramethyl-1,2-diphenyldisilane (**2**), 1,2-dimethyl-1,1,2,2-tetraphenyldisilane (**3**), and 1,1,1,2,2,2-hexaphenyldisilane (**4**), varying the support of the Au catalyst,[13] its loading level, the solvent, and the temperature (Table 1). To our delight, disilanes **1**−**3** react smoothly with 1-heptyne in 1,2-dichloroethane (DCE) at 65 °C (1 mol % of Au) and provide the *cis*-1,2 addition products in good to excellent isolated yields. Other solvents provided either lower yield or slow reaction rates (ethyl acetate, THF, acetonitrile, toluene). Hexaphenyldisilane (**4**) is completely unreactive, more likely due to steric reasons. The preferable catalyst is Au/TiO_2, as Au/ZnO and Au/Al_2O_3, are less effective as also observed in the catalytic hydrolysis of disilanes by Au NPs.[9] The solvent should be dry; otherwise, an excess of disilane (typically 1.5−2.5 molar equiv) is required to compensate for its Au-catalyzed hydrolysis but also to avoid occasional formation of minor β-(*E*)-hydrosilylation side products.[14] The hydrosilylation products arise from the transient hydrosilanes generated during the gold nanoparticle-catalyzed hydrolysis of 1,2-disilanes.[9] Although no extended studies were performed, the catalyst (Au/TiO_2) was recovered by filtration after completion of the reaction among alkyne **5** and disilane **1** and reused in a separate experiment with a small deterioration of its activity. In addition, a series of homogeneous Au(I) catalysts such as $Ph_3PAuNTf_2$, [(2-biphenyl)di-*tert*-butylphosphine]$AuSbF_6$, or AuCl are completely inefficient.

These observations prompted us to study the scope and limitations of the 1,2-addition on a variety of alkynes, working with the reactive 1,2-disilanes **1**−**3** in DCE as solvent at 65 °C. The results are presented in Table 2.[15]

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(12) Grirrane, A.; Corma, A.; Garcia, H. *Chem.—Eur. J.* **2011**, *17*, 2467. Very recently, diboration of alkynes was achieved under catalysis by a nanoporous gold catalyst: Chen, Q.; Zhao, J.; Ishikawa, Y.; Asao, N.; Yamamoto, Y.; Jin, T. *Org. Lett.* **2013**, DOI: 10.1021/ol4028013.

(13) The screened catalysts Au/TiO_2, Au/Al_2O_3, and Au/ZnO (~1 wt % in Au) are commercially available and have an average gold crystallite size of ~2−3 nm.

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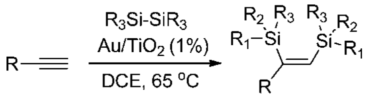
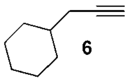
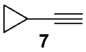
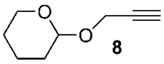
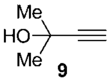
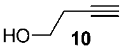
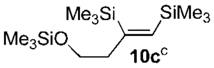
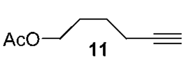
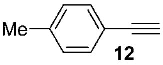
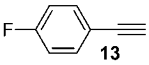
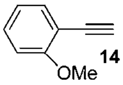
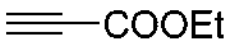
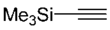
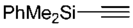
Table 2. 1,2-Disilylation of Terminal Alkynes by 1,2-Disilanes Catalyzed by Au/TiO_2



reactants	products	yield[a]/time
 **6**	**6a** (R_1=R_2=Me, R_3=Ph) **6b** (R_1=R_2=Ph, R_3=Me)	83%/2 h 76%/10 h
 **7**	**7a** (R_1=R_2=Me, R_3=Ph) **7b** (R_1=R_2=Ph, R_3=Me)[a] **7c** (R_1=R_2=R_3=Me)[b]	90%/3 h 66%/10 h 86%/4 h
 **8**	**8a** (R_1=R_2=Me, R_3=Ph) **8c** (R_1=R_2=R_3=Me)	80%/2 h 91%/4 h
 **9**	**9a** (R_1=R_2=Me, R_3=Ph) **9b** (R_1=R_2=Ph, R_3=Me)	91%/2 h 60%/12 h
 **10**	 **10c**[c]	75%/3 h
 **11**	**11a** (R_1=R_2=Me, R_3=Ph) **11b** (R_1=R_2=Ph, R_3=Me)[d] **11c** (R_1=R_2=R_3=Me)	74%/4 h 62%/14 h 79%/8 h
 **12**	**12a** (R_1=R_2=Me, R_3=Ph) **12c** (R_1=R_2=R_3=Me)	77%/4 h 93%/5 h
 **13**	**13a** (R_1=R_2=Me, R_3=Ph) **13c** (R_1=R_2=R_3=Me)	80%/2 h 83%/3 h
 **14**	**14a** (R_1=R_2=Me, R_3=Ph) **14b** (R_1=R_2=Ph, R_3=Me)[e] **14c** (R_1=R_2=R_3=Me)[f]	70%/3 h 76%/12 h 94%/5 h
 **15**	**15a** (R_1=R_2=Me, R_3=Ph) **15c** (R_1=R_2=R_3=Me)[g]	76%/2 h 38%/14 h
 **16**	**16a** (R_1=R_2=Me, R_3=Ph)[h] **16b** (R_1=R_2=Ph, R_3=Me)[i] **16c** (R_1=R_2=R_3=Me)	83%/0.5 h 76%/4 h 92%/2 h
 **17**	**17a** (R_1=R_2=Me, R_3=Ph) **17c** (R_1=R_2=R_3=Me)[j]	84%/0.5 h 81%/2 h

[a] Z/E = 68/32. [b] Z/E = 89/11. [c] 2 equiv of hexamethyldisilane was used. [d] Z/E = 94/6. [e] Z/E = 81/19. [f] Z/E = 93/7. On standing in $CDCl_3$, **14c** gradually isomerized into the E isomer (after 1 day Z/E = 68/32). [g] Only the E isomer was isolated; however, it derives from the initially formed Z isomer which was detected and isolated at the initial stages of reaction. [h] Z/E = 34/66. [i] Z/E = 23/77. [j] Z/E = 42/58.

We examined a series of terminal alkynes and found that the reaction is smooth and proceeds in good to excellent yield with aliphatic and arylacetylenes but also tolerates a variety of functional groups on the side chains. Internal alkynes are unreactive. Regarding experimental details, under strictly dry conditions 1.2 molar equiv of disilanes were used to drive the reaction to completion, yet nondried DCE can also be used, requiring an excess of disilane. In this case, chromatographic purification is necessary to remove hydrolysis side products (silanols or 1,3-disiloxanes), while upon use of hexamethyldisilane its hydrolysis products are volatile and no further purification is often required. For the vast majority of products, the stereochemistry is Z as proven by NOE experiments (see the Supporting Information). In certain cases, however, E isomers are also seen in minor amounts, as a result of a gradual Z to E isomerization during the progress of reaction, a well-known effect in metal-catalyzed disilylation reactions.[16] Surprisingly, the bis-trimethylsilyl adducts have a higher tendency to isomerize, even on standing in $CDCl_3$, e.g., disilylation products of **14** (see the Supporting Information). Of particular interest is butynol **10**, which provides in the presence of 2 equiv of **1** trisilylated **10c** in high yield, featuring the double activation of the hydroxyl group (silyl protection[9]) and the triple bond (disilylation). In the case of ethyl propiolate (**15**), while disilane **2** provides the Z-adduct **15a**, hexamethyldisilane (**1**) led to the E-adduct **15c** in relatively low yield. By monitoring the progress of the reaction among **15** and **1** by ^{1}H NMR and GC–MS, we found that initially the Z-isomer is formed and under the reaction conditions gradually isomerizes into the thermodynamically more stable E. We were able to isolate **15c-Z** by careful column chromatography at the initial stages of reaction (see the Supporting Information). In the meantime, as the reaction of ethyl propiolate with **1** is slow, the alkyne undergoes partial Au-catalyzed trimerization[17] forming triethyl benzene-1,3,5-tricarboxylate and triethyl benzene-1,2,4-tricarboxylate in a relative ratio ~1/1 and ~25% relative yield (see the Supporting Information). Silyl-substituted acetylenes **16** and **17** are surprisingly more reactive than all acetylenes tested herein and provide disilylation adducts in excellent yields, yet unselectively. Both alkynes lead to the predominant formation of the thermodynamically more stable adducts (verified by NOE experiments). Furthermore, we found that there is no essential E/Z isomerization of disilylation products from **16** or **17** (e.g., **16b-Z** to **16b-E**) under the reaction conditions. The peculiar stereochemistry of these substrates in their disilylation reaction is analyzed in the accompanying mechanistic analysis.

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(15) General procedure for the Au/TiO_2-catalyzed disilylation: To a dry vial containing the alkyne (0.2 mmol), the disilane (0.24 mmol), and 1 mL of dry DCE were added 40 mg of Au/TiO_2 (~1.0 mol% in Au). When nondried solvent was used, an appropriate excess of disilane was added (typically 1.5–2.5 fold molar excess) to compensate for its competing hydrolytic destruction. After a certain period of time (see Table 2) at 65 °C, the reaction was complete (TLC, GC–MS). The slurry was filtered with the aid of 3 mL of DCM under low pressure through a short pad of silica gel or celite, and the filtrate was evaporated to afford the disilylation products. Chromatographic purification was performed, if necessary. The reaction is heterogeneous in nature, as leaching of gold into the solution under of the reaction conditions in the specific solvent is negligible (far below ppm level). See also: Efe, C.; Lykakis, I. N.; Stratakis, M. *Chem. Commun.* **2011**, *47*, 803.

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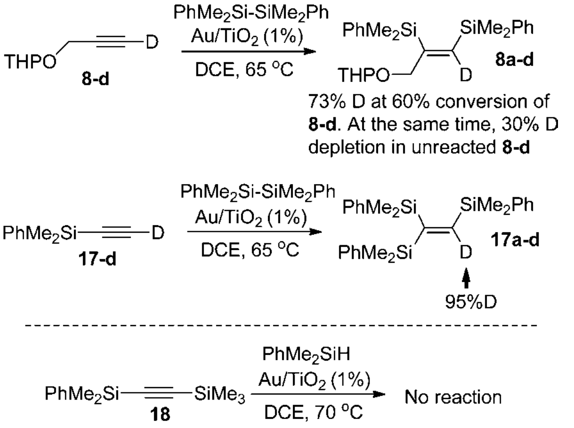
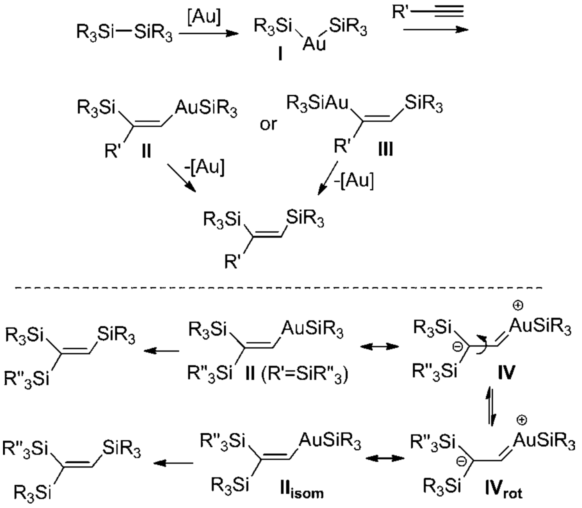
(17) The Au/TiO_2-catalyzed trimerization of ethyl propiolate (**15**) was recently established: Leyva-Perez, A.; Oliver-Meseguer, J.; Cabrero-Antonino, J. R.; Rubio-Marques, P.; Serna, P.; Al-Resayes, S. I.; Corma, A. *ACS Catal.* **2013**, *3*, 1865.

Scheme 2. Mechanistic Studies in the Au-Catalyzed Disilylation



Useful mechanistic information was acquired upon studying the Au-catalyzed addition of disilane **2** to the deuterium labeled alkynes **8-d** (95% D) and **17-d** (97% D).[18] At ~60% conversion, in product **8a−d** the D content was 73% (Scheme 2). Yet, recovered alkyne **8−d** also showed ~30% isotopic depletion in accordance to previous observations with other deuterium-labeled terminal alkynes under treatment with Au/TiO_2 at elevated temperatures.[19] Additionally, labeled **17-d** reacts very fast (20−30 min) with **2**, without undergoing essential isotopic depletion during the reaction and provided product **17a−d** with ~95% D content. These results exclude the formation of gold acetylides as intermediates. In addition, the lack of Au/TiO_2-catalyzed hydrosilylation of internal disilyl alkyne **18**[20] with $PhMe_2SiH$, excludes the possibility of a pathway involving cross coupling among the terminal alkyne and disilane (e.g., **16** with **2** forming **18** and $PhMe_2SiH$) followed by hydrosilylation of **18** from the produced hydrosilane. In Scheme 3 we propose oxidized gold nanoclusters/nanoparticles as the reactive catalytic sites on Au/TiO_2, capable of undergoing insertion from the Si−Si bond of disilanes as proposed earlier[9] (intermediate **I**). There is a growing number of reports postulating ionic gold being the catalytically active sites in metal oxide supported gold nanoparticles.[21]

Scheme 3. Proposed Mechanism for the Au-Catalyzed 1,2-Disilylation of Alkynes



Intermediate **I** then undergoes addition to the alkyne forming either **II** or **III**. A similar stereoselective *syn* insertion of $Ph_3PAu\text{-}SiR_3$ to alkynes has been recently documented.[22] It is possible that for the reactions of silyl acetylenes **16-17**, the corresponding intermediate **II** is stabilized through charge transfer from gold to the double bond forming the silicon-stabilized dipole **IV**, capable of undergoing bond rotation, thus forming the isomerized adduct $\mathbf{II_{isom}}$. This concept nicely explains the formation of *E*/*Z* adducts **16a−b** and **17c** in thermodynamic ratios. An analogous mechanistic argument has been postulated in the Pd(0)-catalyzed silylstannylation of an alkyne.[23]

In conclusion, we have presented herein the first example of the Au-catalyzed disilylation of alkynes by σ 1,2-disilanes, thus expanding the ability of gold to catalyze reactions so far feasible with Pd, Pt, and other late transition metals. As typical homogeneous ionic gold catalysts are ineffective, this work provides an additional example of the powerful nature of supported Au nanoparticles in catalysis.

Acknowledgment. This work was supported by the project "IRAKLEITOS II - University of Crete" of the Operational Programme for Education and Lifelong Learning 2007-2013 (EPEDVM) of the NSRF (2007-2013), which is cofunded by the European Union (European Social Fund) and National Resources.

Supporting Information Available. Copies of ^1H and ^{13}C NMR of all products and selected NOE experiments for key compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Labeled alkynes **8-d** (95% D) and **17-d** (97% D) were prepared by treatment of **8** and **17**, respectively, with *n*-BuLi (THF, 0 °C, 30 min) followed by quench with D_2O.

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The authors declare no competing financial interest.