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Efficient and multi-function compatible click-reaction of organosilanes

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Abstract

The synthesis of organotriethoxysilanes by click chemistry was studied using the recyclable, multidentate catalyst [Cu(C₁₈tren)]Br. For the evaluation, alkyne precursors containing some of the more common organic functions were reacted with a triethoxy silyl group containing azide. The procedure allowed the isolation of the desired products in high yields and high purity. Especially remarkable is the facility of the catalyst removal by simple filtration and evaporation. The catalyst is concluded to be ideal for the synthesis of moisture sensitive organotriethoxysilanes.

Keywords: click chemistry, copper(I)-tren catalyst, organosilane

Introduction

In many sectors, “Click”-Chemistry, as defined by Sharpless *et al.*¹, constitutes an important tool for the customization of organic compounds. An exemplary reaction is the Copper(I)-catalyzed Alkyne Azide Cycloaddition (CuAAC) that leads to the selective formation of 1,4-substituted 1,2,3-triazols by the 1,3-dipolar cycloaddition of alkynes to azides.²⁻⁴ This reaction bears the advantage of being strongly exothermic towards the desired product while the required functional groups (alkyne, azide) are inert to side reactions with other functionalities.⁵ Therefore, it is compatible with the delicacy that is required to prevent side-product formation in the synthesis of organosilanes. Possible applications of the resulting products include the processing to silica hybrid materials that have applications in many fields such as extraction⁶, medicine⁷ or catalysis⁸. However, the purification of the highly moisture sensitive trialkoxy silyl groups is often challenging especially if the synthesized precursors are non-distillable and non-crystallizable.

The most commonly used methodology for the CuAAC reaction is based on a CuSO₄/sodium ascorbate system which is not suitable for organosilane synthesis since it is carried out in a water/tert-butanol mixture. Wong Chi Man *et al.*⁹ proposed the use of bromotris(triphenylphosphine)copper(I) catalyst [Cu(PPh₃)₃]Br, in order to resolve this issue. They illustrated the effective use of this water- and alcohol-free CuAAC reaction for the synthesis of a large scope of functional groups in good yields. However, the reproduction of their reactions indicated copper residues in the purified products.

The present contribution aims at increasing the purity and the yield of the desired products by using the recyclable catalyst [Cu(C₁₈tren)]Br and, therefore, simplifying the purification step which is often critical for moisture-sensitive compounds such as organosilanes.

Results and discussion

Given the limitations explained earlier, to synthesize sol-gel precursors, the CuAAC was performed under anhydrous conditions which is consistent with the moisture-sensitive alkoxyethyl groups and a multitude of functional groups.

The organosilane synthesis *via* CuAAC was studied by comparing two different catalysts, a readily soluble tris-triphenylphosphane copper bromide ($[\text{Cu}(\text{PPh}_3)_3]\text{Br}$, **C1**), and a hydrophobic and recyclable catalyst tris(2-dioctadecylaminoethyl)amine copper bromide ($[\text{Cu}(\text{C18tren})]\text{Br}$, **C2**).

The choice of the latter catalyst was motivated by the work from Candelon *et al*¹⁰ which highlight that such a copper(I) complex is a highly reactive and recyclable catalyst for the Huisgen cycloaddition of azides with terminal alkynes.

In a first approach, the required catalyst loading to efficiently perform the click reaction with $[\text{Cu}(\text{C18tren})]\text{Br}$, (**C2**) in conditions similar to those for $[\text{Cu}(\text{PPh}_3)_3]\text{Br}$ was determined by following the reactant conversion *via* GC-MS with dodecane as internal standard (see ESI).

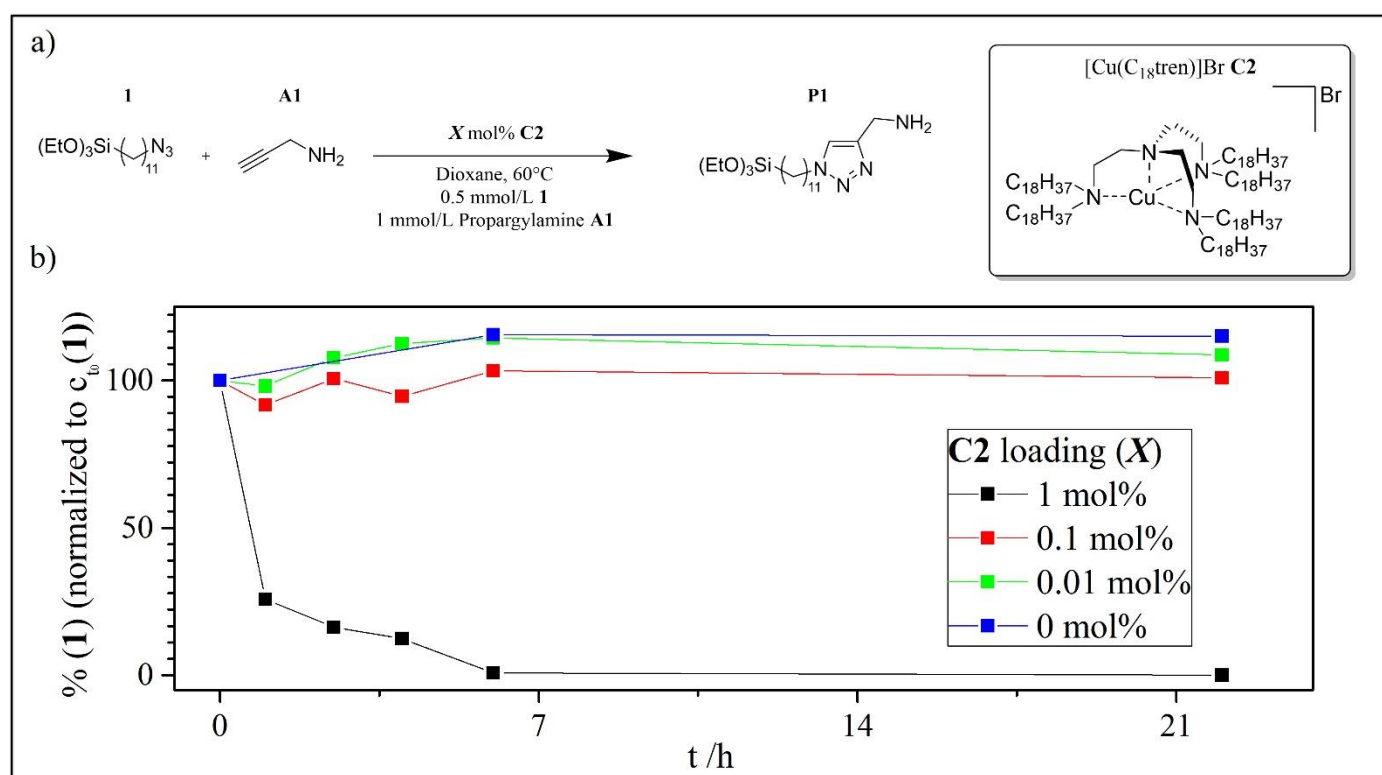
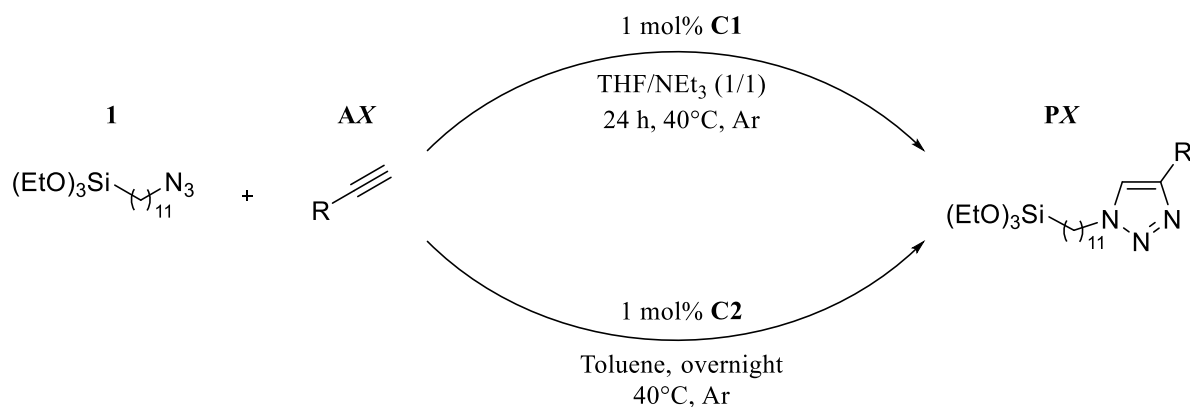


Figure 1. a) Synthesis of organosilane **P1** catalyzed by $[\text{Cu}(\text{C18tren})]\text{Br}$ (**C2**). b) Reaction progress determined by the remaining quantity of the starting product **1** at different points during the reaction of the samples without catalyst (0 mol%) and 0.01, 0.1 or 1 mol% **C2**.

The reaction was performed under argon atmosphere at 60°C in dry dioxane using two equivalents of propargylamine (**A1**) to one equivalent of 11-azidoundecyl triethoxysilane (Synthesis in literature¹¹, **1**) without catalyst and 0.01, 0.1, and 1 mol% of copper catalyst loading (**Figure 1 a**).

Under the observed conditions, the starting reagent **1** reacted only in presence of a catalyst loading of 1 mol% and the largest part was consumed after 7 h (**Figure 1 b**). Indeed, no coupling was observed when less than 1 mol% catalyst is involved in the click reaction.

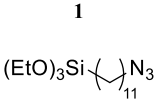
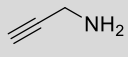
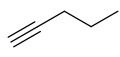
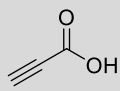
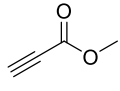
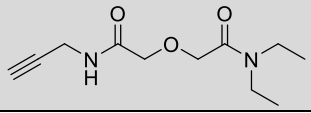
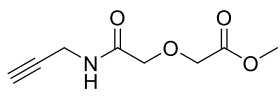
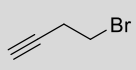
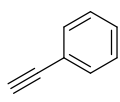
A second set of experiments was performed in order to compare the catalytic performance of **C2** to that of **C1** at the reaction of **1** with a selection of alkyne derivative (**AX**). An overview of the reaction conditions is given in **Scheme 1**.



Scheme 1. Reaction conditions of the investigated CuAAC.

For comparison, both protocols were carried out using 1 mol% of catalyst at 40 °C affording the corresponding 1,4-disubstituted-1,2,3-triazoles **PX**. In order to assure complete conversion, the reactions are left overnight when **C2** is used in the click reaction whereas 24 h are necessary using **C1** at 40°C. Tetrahydrofuran (THF) was used for the reaction involving the catalyst **C1** which requires the addition of triethylamine to increase the reactivity and induce the formation of the copper acetylide intermediate whereas a low polarity solvent such as toluene was chosen for **C2** to solubilize both the reactant and the catalyst. **Table 1** displays the resulting yields of **PX** starting from **1** and different alkynes **AX**.

Table 1. Substrate scope of the investigated CuAAC reaction using 1 mol% of [Cu(C₁₈tren)]Br or 1 mol% of [Cu(PPh₃)₃]Br in the conditions shown in Scheme 1. The yields were calculated from the isolated products.

Azide	Alkyne	Yield	
		C1	C2
1 	A1 	81%	97%
	A2 	74%	89%
	A3a 	0%	0%
	A3b 	62%	90%
	A4 	50%	99%
	A5 	28%	76%
	A6 	66%	82%
A7 	31%	73%	

Among the alkynes, unfunctionalized (**A2**) and phenyl derivatives (**A7**) were chosen to prove the concept. Taking into consideration further applications, alkynes bearing functional and reactive groups such as an amine (**A1**) and a bromide (**A6**) were evaluated. The CuAAC using an acid functionality (**A3a**) was unsuccessful and the methylated derivative (**A3b**) was used as an alternative. To avoid post-functionalization of the introduced amine group in a potential silica hybrid material, the diglycolic acid derivatives (**A4** & **A5**) have been evaluated.

The reactions carried out with the catalyst [Cu(C₁₈tren)]Br (**C2**) afford the desired product in good to excellent yields and in all cases significantly superior to those obtained with **C1**.

This can have several reasons. Toluene is less likely to contain large amounts of trace water than THF or triethylamine. Traces of water can induce the hydrolysis and condensation of the alkoxy silane which will be removed as precipitate during the filtration step. A temperature of 40 °C accelerates this process. Also, side-products such as triphenylphosphine oxide are observed when [Cu(PPh₃)₃]Br is used.⁹ This degradation of the catalyst by the oxidation of the phosphines may reduce the activity.¹²

Finally, the work up of reactions using **C2** is easier and does not involve filtration using hygroscopic celite®. Because of its solubility properties **C2** can be efficiently separated from the products *via* simple filtration after cooling the reaction mixture. In the present case, the catalyst precipitation was induced at low temperature in the polar solvent ethanol. This minimizes the risk of introducing water traces during the work up that would degrade the product. On another note, products synthesized with **C2** appear to contain fewer copper traces than those synthesized with **C1**.

The products are generally of an almost colorless aspect while those synthesized with **C1** are slightly green which is characteristic of a contamination by copper. This is especially remarkable with products that have complexing properties such as amine or diglycolic groups. This is not the case when **C2** is used, because the copper is caged inside a strongly coordinating *tren* ligand. Indeed, polydentate ligands form more stable complexes than their monodentate counterparts. The polydentate character of *tren*-ligands could explain the inferior copper contamination by an easier elimination of the Cu-complex during the filtration stage thanks to its solubility properties.

Therefore the higher purity in addition to higher yield make the catalyst [Cu(C₁₈tren)]Br (**C2**) the better choice for the synthesis of the required sol-gel precursors through a click reaction.

Conclusion

The experiments conducted show the effectiveness of the [Cu(C₁₈tren)]Br catalyst for the CuAAC of organosilylated compounds. The click reactions were carried out using 1 mol% of catalyst at 40 °C affording various silylated 1,4-disubstituted-1,2,3-triazoles compounds. Better yields were obtained in comparison to the previously employed [Cu(PPh₃)₃]Br as well as higher purity without traces of side product such as triphenylphosphine oxide and lower copper contamination due to the chelating and solubility properties of the [Cu(C₁₈tren)]Br. Also, the purification of these moisture sensitive compounds is often a critical step, this is made simpler with the use of [Cu(C₁₈tren)]Br. All of these reasons make this catalyst a convenient tool in order to perform efficiently the synthesis of organosilane through click chemistry especially those with chelating functional group.

Conflict of interest

The authors have no conflict of interest to declare.

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