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Mild Niobium-Catalyzed [2 + 2 + 2] Cycloaddition of Sila-triynes: Easy Access to Polysubstituted Benzosilacyclobutenes

Cédric Simon, Muriel Amatore, Corinne Aubert, and Marc Petit*

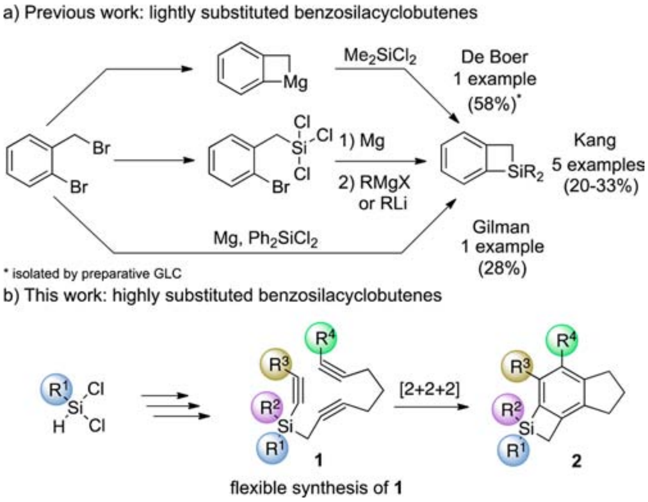
Sorbonne Universités, UPMC UNIV Paris 06, Institut Parisien de Chimie Moléculaire, UMR CNRS 8232, Case 229, 4 Place Jussieu, 75252 Paris Cedex 05, France

Supporting Information

ABSTRACT: A new and efficient synthesis of highly sensitive benzosilacyclobutenes has been developed. For the first time, these compounds can be synthesized in very high yields by a mild, unprecedented intramolecular niobium-catalyzed [2 + 2 + 2] cycloaddition of easily accessible tetrasubstituted sila-triynes. An easy access to highly functionalized benzosilacyclobutenes enlarging the number of potential applications in organic and material chemistry is described.

Silacycles have become an important class of molecules in materials chemistry and recent organic chemistry. They can be found in the literature as precursors for more elaborate silicon-containing molecules,[1] or they have direct applications because of their intrinsic optical properties.[2] Due to their ring strain and Lewis acidity, small silacycles have been used in a wide range of chemical transformations.[3] For instance, the more specific silacyclobutanes and benzosilacyclobutenes have been used in ring-opening polymerization (ROP) to afford polycarbosilane polymers[4] with interesting features. Silacyclobutanes and benzosilacyclobutenes have also been described in ring expansion chemistry by reaction with several transition metals such as Ni,[5] Pd,[6] Pt,[7] and Co[8] to afford larger silicon-containing cycles or rare polycyclic compounds bearing a silicon atom at the ring junction.[8] In each case, the same Si–C bond activation strategy has been employed to generate a metallacycle intermediate that can be trapped with different unsaturated molecules (carbonyls, alkynes, alkenes, etc.). However, the range of applications of the benzene-fused silacyclobutanes has been limited by the poor variability of the substitution on these molecules. Indeed, the downside of their high reactivity is unfortunately the low stability of these molecules during their synthesis.[9,10a] Thus, only a few synthetic approaches have been described in the literature. The most significant, by Gilman,[10a] Kang,[10b] and de Boer,[10c] all start with 2-bromobenzyl bromide derivatives in the presence of sensitive polyhalosilanes and magnesium yielding to the desired benzosilacyclobutenes in poor to moderate yields (Scheme 1a). To the best of our knowledge, until now, no modulation of the substitution on the aromatic moiety has been reported making the development of alternative and more practical synthetic routes highly desirable. In this paper, we propose to use the well-known [2 + 2 + 2] cycloaddition of newly synthesized sila-triynes to provide highly functionalized benzosilacyclobutenes (Scheme 1b).

Scheme 1. (a) Grignard Approaches to Benzosilacyclobutenes. (b) Proposed [2 + 2 + 2] Cycloaddition Approach



In the course of studying the reactivity of benzosilacyclobutenes toward cobalt,[8] we discovered that this sila-cycle could be generated as an intermediate by cycloaddition of the sila-triyne **1a**. However, an oxidative addition occurred immediately during the reaction and after ring expansion; the only compound formed is the sila-polycyclic compound **3a** in 41% yield (Scheme 2). Even if this proof of concept is very appealing, the [2 + 2 + 2] approach appears challenging.[11] Indeed, we have to find the right catalyst to allow efficient cyclotrimerization and preserve the integrity of the newly formed benzosilacyclobutene.

Recently, we discovered that the $[Co(R)(PMe_3)_4]$ family of cobalt complexes was able to catalyze the cycloaddition of triynes and enediynes at room temperature with a different reactivity compared to the $CpCo(L)_2$ type of complexes.[12] Thus, we decided to screen (Table 1) this family of

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Scheme 2. First Evidence of a Possible Synthesis of Benzosilacyclobutenes by [2 + 2 + 2] Cycloaddition

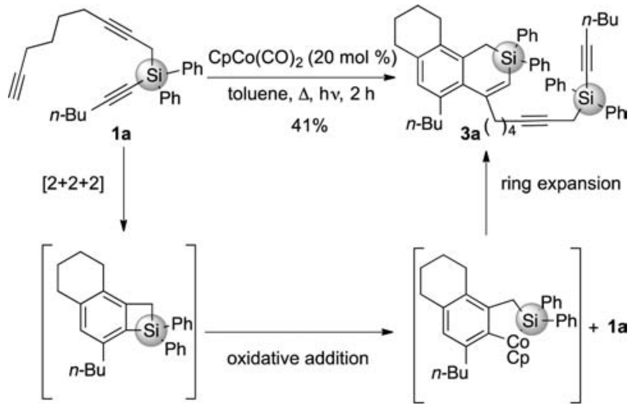
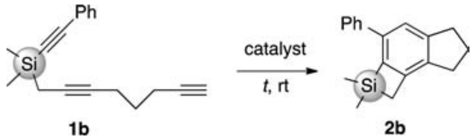


Table 1. Screening of [2 + 2 + 2] Cycloaddition Catalysts



entry	catalyst (mol %)	solvent	time (h)	conversion NMR[a]	yield of 2b[b] (%) (NMR yield, %)[a]
1	CoH(PMe$_3$)$_4$ (10 mol %)	toluene	12	NR	nd
2	CoMe(PMe$_3$)$_4$ (10 mol %)	toluene	12	NR	nd
3	CoCl(PMe$_3$)$_3$ (20 mol %)	DCE	20	22	10
4	CoCl(PPh$_3$)$_3$ (20 mo l%)	toluene	30	13	nd
5	Co(PMe)$_3$ (10 mol %)	toluene	12	50[c]	nd[d]
6	RhCl(PPh$_3$)$_3$ (20 mol %)	DCE	24	82	26 (61)[a]
7	[Rh(cod)$_2$]·BF$_4$ (20 mol %)	DCE	12	NR	nd
8	NbCl$_3$·DME (20 mol %)	DCE	2	76	28 (76)[a]

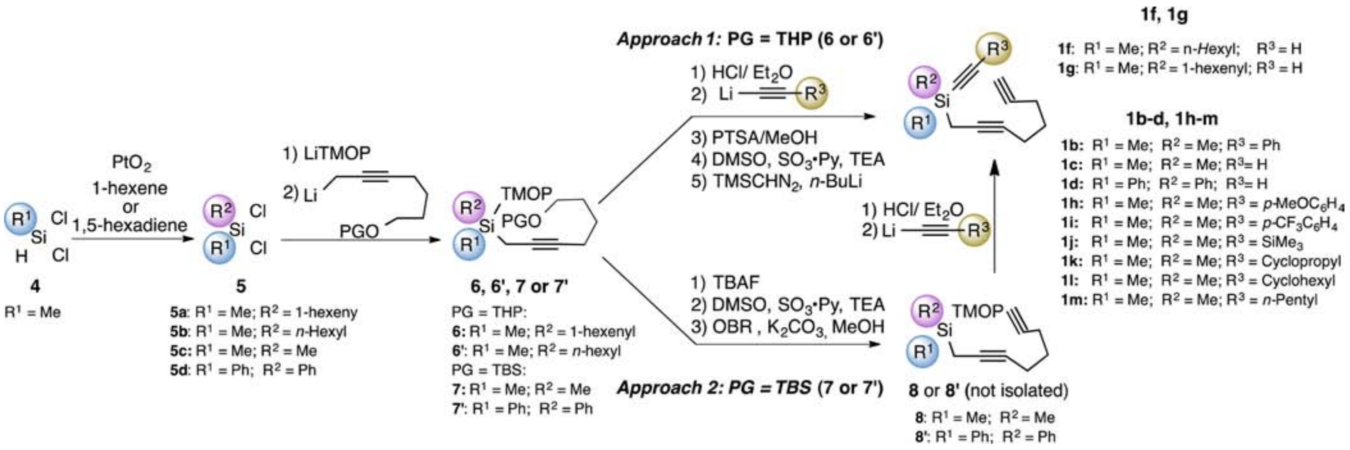
[a] Yield and conversion measured by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene as internal standard. [b] After chromatography on silica gel. [c] Several compounds were observed on the basis of the $(CH_3)_2Si$ resonances. [d] Compound obtained in a mixture of undetermined silicon compounds.

complexes together with other metals able to catalyze the cycloaddition of triynes at room temperature in order to avoid a subsequent nondesired oxidative addition and degradation of the very sensitive benzosilacyclobutenes.

We initially chose the substrate **1b** as model substrate, and using the above family of cobalt(I) catalysts, no desired compound or only a small amount was formed (Table 1, entries 1−3). In the case of ClCo(PR$_3$)$_3$, changing the trimethylphosphine to triphenylphosphine did not improve the conversion (Table 1, entry 4). Finally, the cobalt(0) catalyst Co(PMe$_3$)$_4$ allows the observation of the desired compound in 50% yield by NMR analysis, but it could never be obtained in a pure form (Table 1, entry 5). Extensive screening of room temperature-reactive nickel and ruthenium catalysts did not allow the formation of compound **2b**. By using Wilkinson's catalyst, a conversion of 82% and a yield of 61% could be measured by NMR monitoring but due to its high sensitivity to acidic medium, compound **2b** could be isolated after silica gel chromatography only with a moderate yield of 26% (Table 1, entry 6). In this transformation, the cationic rhodium was also not efficient, and no conversion was observed (Table 1, entry 7).[13] Finally, the less known and rarely used low-valent niobium catalyst NbCl$_3$·DME was the most efficient of all catalysts in the trial with both a conversion and a NMR yield of 76% (Table 1, entry 8).[14] However, once again, the corresponding benzosilacyclobutene was isolated in a poor 28% yield, justifying an optimization of the reaction and purification conditions. With this promising result in hand, we next focused on developing a more efficient niobium-catalyzed process to reach full conversion in order to avoid complicated chromatography. Optimizations of the workup, degassing procedures, catalyst loading, and concentration led us to the optimal conditions of 5 mol % catalyst in 2 h with a concentration of 0.8 M. Pure product can be isolated after a simple filtration on an alumina pad, with an excellent 97% yield (see the Supporting Information).

To establish that our methodology is a real breakthrough in the synthesis of highly functionalized benzosilacyclobutenes, we wish to demonstrate that the substitution on the silicon atom but also on the aromatic moiety could be easily modulated. Thus, we had to develop an efficient synthesis of the acyclic starting sila-triynes incorporating a tri- or tetrasubstituted silicon atom. We first thought of using our previously published strategy on the synthesis of dissymmetric silicon tethers.[15] However, the use of THF to generate some of the requisite lithiated nucleophiles was not compatible with the formation of the bromosilane in the presence of NBS. Therefore, we decided to use the 2,4,6-trimethoxyphenyl (TMOP) as protecting group for chlorosilane in order to develop a flexible synthesis of the sila-triynes.[16] Thus, precursors **1b**−**m** owning tri- or tetrasubstituted silanes can be prepared using that approach (Scheme 3). The hydrosilylation of 1-hexene and 1,5-hexadiene with the commercially available methyldichlorosilane **4** delivers the corresponding dissymmetric disubstituted dichlorosilanes **5**. Next, two successive monosubstitutions were performed using first the bulky Li-TMOP reagent and then the requisite lithium derivatives giving selectively compounds **6** or **7**. From compounds **6** or **7** ,two approaches were developed for the introduction of the other triple bonds. The first one using a THP as protecting group allowed the formation of compounds **1f,g** after a sequence: deprotection of TMOP (in the presence of nonaqueous HCl), nucleophilic substitution, alcohol deprotection, Parikh−Doering oxidation, and Colvin homologation.[17,18] With the removal of the TMOP group at the very beginning, this strategy allows the purification of each in termediate. However, introduction of the R^3 group on the silylacetylene moiety is done at the beginning of the synthesis, and varying this group requires all of the steps to be repeated. Thus, a second approach has then been developed and centered on the use of TBS as protecting group. Therefore, the alcohol can be deprotected in the first step using TBAF, followed by an oxidation and homologation with Ohira−Bestmamnn reagent (OBR) allowing the formation of a common intermediate **8**.[19] Then, introduction of the last alkyne moiety can be carried out after TMOP replacement by a chlorine atom. This strategy is more divergent; however, due to the low stability of the Si-TMOP bond toward acidic medium all the sequence starting from the

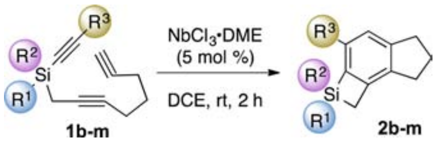
Scheme 3. Synthesis of Sila-triyne Precursors



silanes **4** or **5** has to be done without any purification for overall better yields.[20]

Having in hand a straightforward synthesis[21] of precursors and an efficient cycloaddition, we next tested all our substrates under the optimal conditions (Table 2). Variations on the silicon atom do not affect the reactivity, and even with bulky isopropyl substituents a very good yield is obtained (Table 2, entries 1−3). Silicon atom with four different substituents can be employed in this process, and introduction of an alkene moiety does not interfere in the cyclotrimerization of the sila-triyne (Table 2, entry 5). The substitution on the silylated alkyne was also studied and appeared to have no significant influence on the cycloaddition. Aromatic groups bearing electron-donating or electron-withdrawing groups (Table 2, entries 7 and 8), as well alkyl groups (Table 2, entries 10−12) and even a trimethylsilyl group, can be added on this position (Table 2, entry 9).

Table 2. Scope

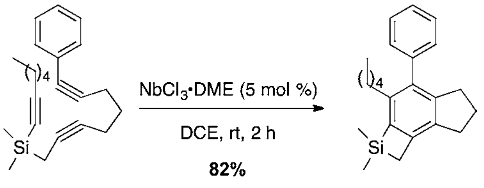


entry	1	R^1	R^2	R^3	isolated yield (%)
1	**1c**	Me	Me	H	84
2	**Id**	Ph	Ph	H	78
3	**1e**	*i*-Pr	*i*-Pr	H	94[a]
4	**1f**	Me	hexyl	H	85
5	**1g**	Me	1 -hexene	H	77
6	**1b**	Me	Me	Ph	97
7	**1h**	Me	Me	*p*-MeOC$_6$H$_4$	63
8	**1i**	Me	Me	*p*-CF$_3$C$_6$H$_4$	65
9	**1j**	Me	Me	SiMe$_3$	80
10	**1k**	Me	Me	cyclopropyl	72
11	**1l**	Me	Me	cyclohexyl	96
12	**1m**	Me	Me	*n*-pentyl	89

[a] Reaction was run for 3 h.

The fully substituted sila-triyne **1n** was finally obtained from substrate **1m** after a Sonogashira coupling. The latter submitted to our optimal conditions of [2 + 2 + 2] cycloaddition allows the unprecedented formation of a fully substituted benzosilacyclobutene **2n** in a very good 82% yield (Scheme 4).

Scheme 4. Synthesis of Fully Substituted Benzosilacyclobutene



1n **2n**

In summary, we have developed a versatile synthesis of the very sensitive benzosilacyclobutenes that features ease of operation, good yields, and a large scope of substrates. Indeed, this approach allows for the first time the formation of highly functionalized benzosilacyclobutenes in high yields (63−97%) compared to the few reported syntheses (20−58%). This new and efficient access to strained sila-cycles from new acyclic sila-triynes demonstrates the high potential of the scarcely used niobium-catalyzed [2 + 2+2] cycloaddition. Work toward the use of these new substituted sila-cycles to reach more complex sila-molecules with biological relevance is under investigation and will be reported in due course.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and physical properties of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: marc.petit@upmc.fr.

Notes

The authors declare no competing financial interest.

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(20) Free TMOP can be observed by NMR analysis if intermediates are purified by chromatography on silica gel.

(21) Because of steric hindrance, the use of TMOP was impossible with diisopropyldichlorosilane as starting silane; see the Supporting Information for the synthesis of **1e**.