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An efficient one-pot protocol for the synthesis of phenyl substituted 3-silatetrahydropyrans

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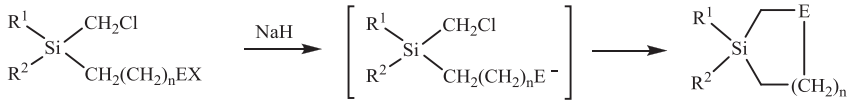
ABSTRACT

A new facile and efficient one-pot procedure for the synthesis of 3-phenyl-3-silatetrahydropyrans with an easily functionalized Si–Ph bond was developed. The method is based on the intramolecular cyclization of chloromethyl(3-hydroxypropyl)phenylsilanes using the n-Bu_4NBr/*i*-Pr_2NEt combination. As an example of functionalization, the synthesis of the first 3-silatetrahydropyran with an exocyclic RO–Si bond is reported.

1. Introduction

Intramolecular cyclization of α,ω-haloalcohols and α,ω-halothiols has remained one of the most simple and efficient approaches to cyclic ethers and sulfides. The method is also applicable to the synthesis of silaheterocycles containing the Si–CH_2–Het motif in the ring.[1] Earlier we reported a base-promoted ring closure reaction of chloromethyl(mercaptoalkyl)silanes. For example, the sulfide anion generated from *S*-protected[2–4] thiols with NaH[2,3] or $LiAlH_4$[4] undergoes intramolecular cyclization, giving rise to the corresponding 3-silathiophane[5] and 3-silathiane[2–4] derivatives in good yields (Scheme 1).



E = **S**; X=$COCH_3$; R^1=R^2=Me, n=1; R^1=H, R^2=Me, Ph; R^1=Me, R^2=Me, Ph; n=2;
E = **O**, X=H; R^1=R =Me; n=1.

Scheme 1. Synthetic route to 3-silaheterocycles.

However, in the case of Si,O-heterocycles, this procedure can be used only for the synthesis of 3,3-dimethyl-3-tetrahydrofuran (E=O, R^1=R^2=Me, *n*=1) from chloromethyl(2-hydroxyethyl)-dimethylsilane and sodium hydride.[6] Hudrlik et al. showed that treatment of chloromethyl(3-hydroxypropyl)dimethylsilane with various base/solvent combinations (NaH/THF, NaH/DME, KH/hexane, KH/THF, NaH/ether) gave exclusively 2-methyl-2-ethyl-2-silatetrahydrofuran. This result may be attributed to the high oxophilicity of silicon, which undergoes intramolecular nucleophilic attack by the intermediate oxyanion followed by migration of an organic group from silicon to the α-carbon.[7] The expected 3,3-dimethyl-3-silatetrahydropyran was prepared by using *n*-BuLi/THF system in a yield as low as 3%. All attempts to synthesize the corresponding PhSi-substituted heterocycles failed.[7]

An efficient method to prepare 3,3-dimethyl-3-silatrahydropyran and its 6-alkyl derivatives was first described by Fessenden et al. in 1964.[8] In the slightly modified procedure, these compounds were also obtained in 50–80% yield by heating the corresponding chloromethyl(3-hydroxyalkyl)dimethylsilanes with Na_2CO_3 at high temperatures (>200 °C).[9]

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Later on, some new methods based on using (hydroxymethyl) alkenylsilanes as starting compounds were developed. Thus, Yoshida et al. described the electrophile-induced route to 3,5-dimethyl-3-phenyl-3-silatetrahydrofuran, whose formation is dictated by the ability of silyl groups to stabilize a neighboring β-carbocation determining the regioselectivity of the electrophilic addition in the first step.[10] Later on, the procedure was modified that resulted in an increased yield of the final product (Scheme 2).[11]

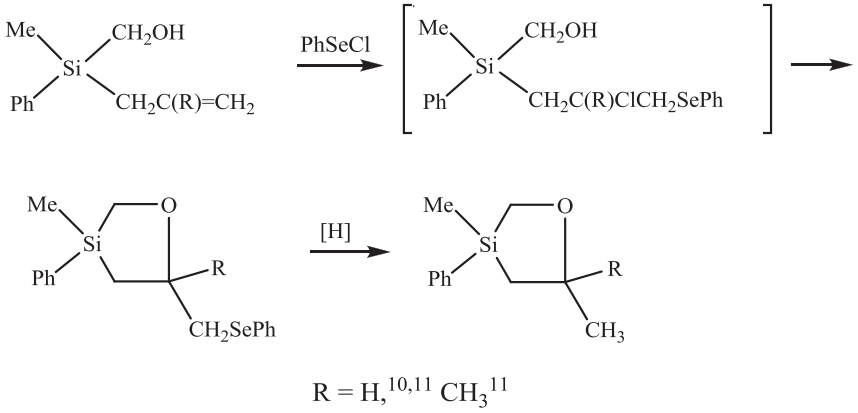
Recently, Tacke et al. reported the first $Al(OTf)_3$-catalyzed intramolecular electrophilic cyclization of (hydroxymethyl)alkenylmethylphenylsilanes to afford the Ph–Si-containing oxasilacycloalkanes in low yield (Scheme 3).[11] Note the different regioselectivity of cyclization for R=H and Me, reflecting different polarization of the $SiCH_2CH{=}CH_2$ and $SiCH_2CH{=}CMe_2$ groups.

2. Results and discussion

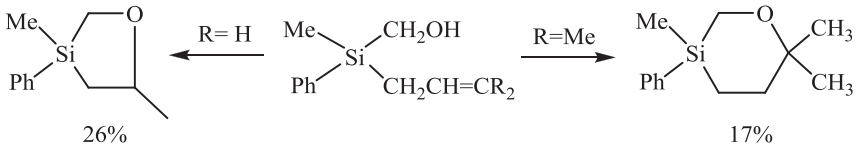
The starting silanes **1a** and **1b** were prepared by the H_2PtCl_6-catalyzed hydrosilylation of the corresponding (allyloxy)trimethylsilanes followed by acidic hydrolysis, as was described for compound **1a** earlier[21] (Scheme 4).

To optimize the cyclization conditions, we have studied the effect of temperature, solvent, the base nature, and the ratio of the reactants on the yield of the target heterocycles (Table 1).

For the initial screening, silane **1a** was chosen as a model substrate. Toluene was found to be an appropriate solvent because no cyclization of **1a** occurred at lower temperatures (Table 1, entry 1). DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and diisopropylamine (Hünig's base) were tested as strong non-nucleophilic organic ba-

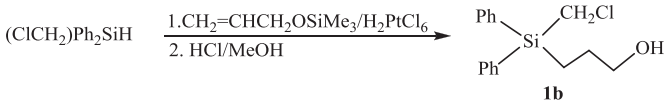


Scheme 2. Synthesis of 3-silaheterocycles from (hydroxymethyl)alkenylsilanes.



Scheme 3. Electrophilic cyclization of (hydroxymethyl)alkenylmethylphenylsilanes.

Most of the above protocols suffer from tedious procedures, narrow substrate scopes and/or low efficiency. For these reasons, the development of new reliable and efficient methods for the synthesis of 3-silatetrahydropyrans, especially with a Ph–Si group, is still a challenging task in synthetic organosilicon chemistry. A special emphasis on the Ar–Si compounds is made because they are valuable and versatile intermediates of great synthetic potential. Their advantages are, on the one hand, stability to air and moisture, which allows an easy handling in the synthesis and column purification steps. On the other hand, the high reactivity of the Ar–Si bond to electrophiles opens the way to a wide variety of silaheterocycles with a labile X–Si bond (X=H, Hal, HO, RO) such as silacyclohexanes,[12–15] disilacyclohexanes,[12] 1,3-silapiperidine[16] and 1,4-silapiperidines.[17–20] With our continuing interest in the chemistry and conformational properties of organosilicon heterocycles, we reported previously the preparation of Si-functionalized silacyclohexane and 3-silathianes via the Ph–Si bond cleavage.[15] Here we describe a new efficient protocol for the synthesis of phenyl substituted 3-silatetrahydropyrans **2a** and **2b** and the use of **2a** for the preparation of the first Si,O heterocycle **4a** with a labile RO–Si bond.



Scheme 4. Synthesis of chloromethyl(3-hydroxypropyl)diphenylsilane **1b**.

ses, and K_2CO_3 as an inorganic base. Among them, only DBU showed some efficiency to give **2a** in a low yield (Table 1, entry 2).

However, the ^1H and ^{13}C NMR spectra of the reaction mixture before the acidic workup revealed the lack of characteristic signals of the starting compound **1a** indicating its full consumption. The presence of a number of signals of the MeSi groups in the ^1H and ^{29}Si NMR spectra can be attributed to a mixture of unidentified oligomeric/polymeric decomposition products. Previously we found that DBU readily reacted with chloromethyltrimethylsilane to form quaternary ammonium salt $[DBU{\cdot}CH_2SiMe_3]^+ Cl^-$ at room temperature. No products of the $ClCH_2$–Si bond splitting were observed.[22] On the other hand, it is known that α-silyl ammonium salts can be desilylated by the attack of external nucleophiles, like amines or alkoxides.[23] The signals of the $SiCH_2N$ fragment in the NMR spectra of pure salt $[DBU{\cdot}CH_2SiMe_3]^+ Cl^-$ appear at 3.24 ppm