SHORT PAPER

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A mechanistic study concerning the carbon-silicon bond cleavage in acylsilane bioreductions†

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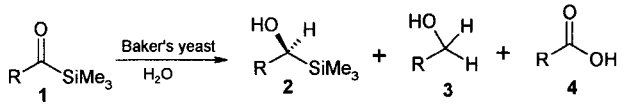
Some mechanistic proposals are made for the competitive desilylation reactions affording the corresponding primary alcohol and carboxylic acid that frequently occur in the bioreduction of acylsilanes.

The research in biotransformation of organosilicon compounds probably began with the first studies by Tacke[1] that applied microorganisms in acylsilane reductions to afford optically active silyl alcohols.[2] The scope of organosilane biotransformations is growing and has been of great applicability in many organic synthetic routes such as racemate resolution,[3] enantioselective esterifications[4] and oxidation of silyl alcohols.[5] Nevertheless, the necessary long period of incubation confers a great problem due to the side reactions of desilylation. For example, the baker's yeast reduction of acylsilanes **1** afforded optically active α-silyl alcohols in 20–70% yield with 43–88% ee and also the corresponding primary alcohols **3** and carboxylic acids **4**,[6] as outlined in Scheme 1. In this work we propose some mechanisms for these undesirable desilylation reactions, which have not yet been delineated.



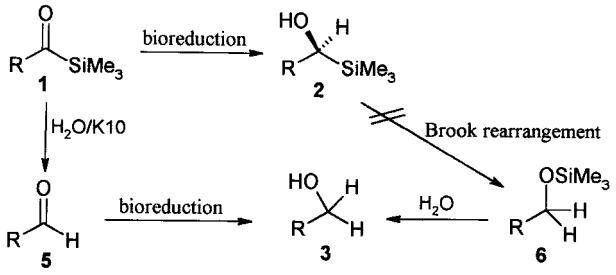
R = C_6H_5; 4-ClC_6H_4; 2-, 3- and 4-$MeOC_6H_4$; 3,4-$(MeO)_2C_6H_3$; 3,4-$(OCH_2O)C_6H_3$

Scheme 1

Results and Discussion

The formation of the alcohols **3** (5–30%) as principal by-products was observed in the acylsilane bioreduction[6] and specially when R = aryl (aroylsilanes) we observed also the production of carboxylic acids **4** (5–15%). Moreover, the highest amount of by-products **4** was observed when aroylsilanes having electron-donating groups attached to the aromatic ring were used. On the other hand the alkanoylsilanes incubation practically did not afford **3** or **4**.

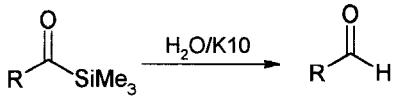
It has been suggested[7] that the alcohol **3** (R = Ph) could be produced by Brook rearrangement[8] through the corresponding α-hydroxysilane **2** (R = Ph). However, we observed that the α-hydroxysilanes **2** are stable when subjected to the same conditions that was used in the baker's yeast reaction mixture. In fact, the Brook rearrangement through a α-silyl alcohol needs vigorous conditions.[9,10] On the other hand, it is known that acylsilanes are cleaved by diluted alkaline solutions to give aldehydes and other more complex rearrangement products.[11] Although free cells of *Saccharomyces cerevisiae* can promote by themselves the formation of alcohols **3** from acylsilane, we investigated the influence of the montmorillonite K10 in the bioreduction of acylsilanes because we have frequently used this support to avoid the arduous work up when free cells are used.[12] We observed that aroylsilanes and alkenoylsilanes could undergo cleavage in water, to a greater extent when in the presence of montmorillonite K10, to give the corresponding aldehydes **5** after a long period (Table 1). These aldehydes may be reduced to the corresponding arylcarbinols **3** by NADH/NADPH-enzyme of baker's yeast (Scheme 2).

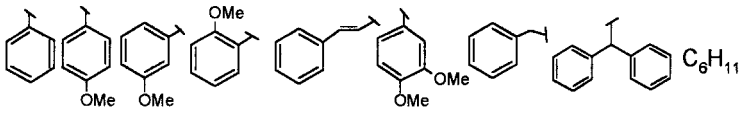


Scheme 2

As in the bioreduction, the formation of carboxylic acids **4** (5–20% yields) was also observed when acylsilanes **1** were treated with water/K10. The by-product yields increased when

Table 1 C–Si bond cleavage in acysilanes mediated by water in presence of montmorillonite K10 at 35°C



R group									
Reaction time (h)	60	60	72	72	90	72	60	72	60
Aldehyde yield (%)	10	18	20	25	25	10	–	–	–

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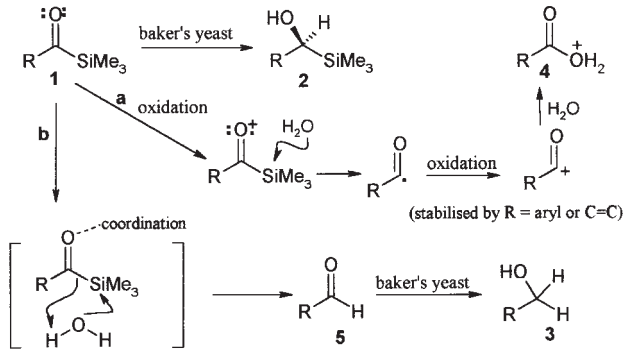
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

a methoxy group was attached to the aromatic ring. However, alkanoylsilanes are not susceptible to Si–C(O) bond cleavage in the bioreduction mediated by baker's yeast/water/K10 and also in the treatment with water/K10. On the other hand, the formation of 4-methoxybenzoic acid was considerably decreased when the acylsilane **1** (R = 4-MeOC$_6$H$_4$) was treated with water/K10/radical inhibitors (see Table 2). These observations led us to conclude that acylsilanes transfer electrons to acceptors, such as K10 or to enzymatic residues during the incubation period, by a mechanism similar to that proposed for electrochemical oxidation[13] where a carbocation intermediate should be stabilised by the aromatic ring (Scheme 3, pathway a). The oxidation of acylsilanes to carboxylic acids is well known to occur by light activation, high temperatures[14] and by treatment with peroxide,[15] ozone[16] and Fe(NO)$_3$.[17]



Scheme 3

Table 2 also shows that aldehyde yields were not decreased by the presence of radical inhibitors. Therefore, the aldehyde probably is produced by a mechanism that does not involve radical formation. Presumably one way is that a coordination group (which may be present in the Lewis acid montmorillonite K10[18] and in the enzymatic residues[19]) coordinates with the carbonyl group while the silicon is attacked by water promoting the C-Si bond cleavage to form the aldehydes **5** (Scheme 3, pathway b). In fact, the aldehyde formation was observed when acylsilanes were treated with aqueous solutions of Fe(NO$_3$)$_3$ and Al$_2$(SO$_4$)$_3$ but not with H$_2$SO$_4$ or HNO$_3$.[17] In contrast to acylsilane cleavage by fluoride ion,[20] it is possible that this mechanism occurs without arylcarbanion formation, because the cleavage ratio didn't diminish with the aromatic ring having a methoxy as substitute group.

Table 2 Radical inhibitor effect in reaction of 4-methoxybenzoyltrimethylsilane with water/ethanol (80:20) in presence of montmorillonite K10 at 35°C.

Reaction time (h)	Inhibitor	Acid + ester yield (%)	Aldehyde yield (%)
90	–	20	18
90	BHT[a]	03	15
90	DNB[b]	05	16

[a]BHT (2,6-di-tert-butyl-4-methyl-phenol); [b]DNB (1,3-dinitrobenzene)

In summary, the main by-products **3** and **4** produced in the bioreduction of acylsilanes **1** are provided from two different pathways, as presented in Scheme 3. The Si–C bond cleavage of acylsilanes **1** (probably promoted by coordination groups present in montmorillonite K10 and in the enzymatic residues) afford the aldehydes **5** that are subsequently reduced by NADH/NADPH-enzyme of baker's yeast to primary alcohols **3**. In another pathway, a radical oxidation of acylsilanes **1** takes place giving the carboxylic acids **4**.

Experimental

The acylsilanes were prepared following dithiane route[21] and the spectral data are described elsewhere[6,22]. Gas chromatography analyses of reaction products were performed on a QP 5000 - SHIMADZU gas chromatograph/mass spectrometer with a capillary column Simplicity 1 SUPELCO^{TM} (ID 0.25 mm, 30 m length) using helium as carrier gas (1.5 ml/min) and the column pressure at 100 kPa. The injector temperature was 230 °C and the oven temperature was maintained at 80 °C for 3 min and then raised at a rate of 10 °C/min up to 280 °C.

General procedure for acylsilane cleavage: 20 mg of acylsilane dissolved in 20 cm^3 of water/ethanol (9:1) was stirred with 1 g of montmorillonite K10 during a period indicated in Table 1. The products were extracted with 20 cm^3 of ethyl acetate and analysed by GC/MS.

Radical inhibitor test: 20 mg of 4-methoxybenzoyltrimethylsilane dissolved in 20 cm^3 of water/ethanol (9:1) was stirred with 1 g of K10 during 90 h. This procedure was repeated with addition of 0.5 equiv. of BHT (2,6-di-*tert*-butyl-4-methyl-phenol) and in another experiment with addition of 0.5 equiv. of DNB (1,3-dinitrobenzene). The products were extracted with 20 cm^3 of ethyl acetate and analysed by GC/MS (Table 2).

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