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Desilylation versus elimination reactions of β-hydroxysilanes: effect of substituents on silicon

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Abstract— β -Hydroxy(trimethyl)silanes undergo stereospecific desilylation reactions to give alcohols using KOt-Bu in DMSO:H₂O, but the reactions are very slow. In this work, desilylation reactions are facilitated using β -hydroxysilanes with (*i*-PrO)Me₂Si, HMe₂Si, or HOMe₂Si groups (e.g. $9 \rightarrow 11$). The (HO)Me₂Si compound (10) (or alkoxide) was shown to be an intermediate, and undergoes β elimination less readily than the Me₃Si compound (7). © 2003 Elsevier Science Ltd. All rights reserved.

Silicon compounds are widely used in organic synthesis, partly because of the stability of many types of organosilicon compounds to a variety of reagents, enabling the silicon group to be carried through a multi-step synthesis, and because of the availability of conditions to remove the silicon group when it is no longer needed. For example, arylsilanes, vinylsilanes, and epoxysilanes are easily desilylated, and these reactions have been widely used. In some cases, however, removal of silicon is not easy. For example, β -functional organosilicon compounds readily undergo elimination reactions, but desilylation (without elimination) is difficult.¹ In this work, we find that desilylation of β -hydroxysilanes is greatly facilitated by changing the silyl group.



Keywords: desilylation; elimination; β-hydroxysilane.

A number of methods for preparing β -hydroxysilanes exist,² some with impressive stereochemical control. The olefin-forming β -elimination reactions of β -hydroxysilanes are stereospecific, and take place under mild conditions and in high yield, so have been useful for the synthesis of olefins and heteroatom-substituted olefins of defined stereochemistry.³ Some time ago we showed that β -hydroxy(trimethyl)silanes undergo desilylation reactions to give simple alcohols (e.g. $1 \rightarrow 2$),⁴ that the reactions were stereospecific,⁴ and could be used for introduction of deuterium.^{4b} However, the reactions were very slow in unactivated compounds unless the silicon was at a primary carbon. For example, treatment of β -hydroxysilane 7 with 5% KOt-Bu in 19:1 DMSO- d_6 :D₂O containing 18-crown-6 at rt gave a 2:3 mixture of starting material (7) and product (cis-2-deuteriocyclohexanol) after 15 days.4b

These reactions are believed to take place via a pathway that can be considered as a homo-Brook rearrangement⁵ followed by hydrolysis (see Scheme 1). An anionic four-membered ring species was proposed (such as that generally accepted for the β -elimination reactions,^{2d,6} which are normally carried out under anhydrous conditions such as KH/THF).

If these reactions are to be useful, they need to be made faster. (The reactions can be made faster by decreasing the water concentration, but this is accompanied by increasing amounts of olefin from β -elimination.) We have therefore studied the effect of substituents on the silicon on the course of the reaction. Initially we attempted to facilitate the desilylation reactions by replacing the Me₃Si group by PhMe₂Si or Ph₂MeSi groups. [Phenyl groups on silicon have been shown to

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Scheme 1.



Scheme 2. Reagents and conditions: (a) MeLi/CuCN (2:1), ether, -70° C for 4 h, warm to rt (84%); (b) From 14: Li powder, naphthalene, THF, -78° C for 40 min; add 14, -78° C for 4 h, add ClMe₂SiH, -78° C for 10 h (54%). From 15: *t*-BuLi, THF–ether–hexane, -105 to -80° C, 45 min, then ClMe₂SiH, allow to warm to 0°C (82%); (c) MCPBA, Na₂HPO₄, CH₂Cl₂, 0°C, 6 h (65% of 17); (d) LiAlH₄, THF, rt, 8 h (78%); (e) NaO*i*-Pr, *i*-PrOH, rt, 3 h (37% of 9 and 23% of 10); (f) *i*-PrOH, H₂PtCl₆, 0°C, 2 h (43%); (g) MCPBA, CH₂Cl₂, 0°C to rt, 18 h; (h) LiAlH₄, THF, rt, 5 h (62%); (i) *i*-PrOH, H₂PtCl₆, 0°C, 4 h (30%).

accelerate the Brook rearrangement,⁷ presumably by stabilizing an anionic pentacoordinated intermediate.] Unfortunately, preliminary experiments showed the PhMe₂Si and Ph₂MeSi groups facilitate both desilylation and elimination reactions.⁸

We have now found that the desilylations of β -hydroxysilanes having the silicon at a secondary carbon can be carried out effectively if the (*i*-PrO)Me₂Si, HMe₂Si, or (HO)Me₂Si groups are used (i.e. $4 \rightarrow 5$; **8**, **9**, or $10 \rightarrow 11$). Furthermore, β -hydroxysilanes **10** and **7**, having the (HO)Me₂Si and Me₃Si groups, respectively, undergo a dramatic change in relative reactivity at low water concentrations.

Preparation of starting materials. The β-hydroxysilanes were prepared as shown in Scheme 2. The reaction conditions were not optimized. All the reaction pathways take advantage of the fact that α ,β-epoxysilanes generally undergo ring opening at the α position.^{2b,c,3} To prepare β-hydroxysilane **4**, we treated the (*i*-PrO)Me₂Si epoxysilane **13**⁹ with MeLi/CuCN (2:1). [Tamao and co-workers⁹ earlier found that **13** underwent the normal α opening characteristic of reactions of epoxysilanes with organocopper reagents^{2b} without affecting the *i*-PrO group.]

The most direct pathway to the cyclic β -hydroxysilanes **8–10** involved epoxidation of vinylsilane **16** followed by ring opening of the epoxide with LiAlH₄. Treatment of 16 with MCPBA resulted in oxidation of the Si-H as well as the double bond: Epoxysilane 17 was isolated (after chromatography) in 65% yield. [Epoxysilane 18 was obtained (24% yield) in less pure form, but was identified by GC/MS (171 (M⁺-H, 6), 157 (M⁺-Me, 8), 129 (17), 77 (60), 75 (Me₂SiOH⁺, 100)) and by ¹H NMR (includes δ 0.158 (s), 3.11 (appears as d, J=3 Hz).] Treatment of 17 with LiAlH₄ resulted in the HMe₂Si β -hydroxysilane 8, the expected product of α opening. [A more efficient way to 8, which we intend to explore, might be LiAlH₄ reduction of the crude product from the epoxidation.] Small scale reactions of the HMe₂Si β -hydroxysilane 8 with NaO*i*-Pr in *i*-PrOH appeared to give fairly pure (*i*-PrO)Me₂Si β -hydroxysilane 9, with only small amounts of hydrolysis product, silanol 10. However, in a larger scale reaction 37% of 9 and 23% of 10 were isolated after chromatography.

As an alternative entry to the cyclic β -hydroxysilanes **9** and **10**, we also looked at reduction of the (*i*-PrO)Me₂Si epoxysilane **20**. Compound **20** was prepared by treatment of vinylsilane **16** with *i*-PrOH/H₂PtCl₆ to give vinylsilane **19**, followed by treatment with MCPBA. Epoxide **20** was normally used in crude form, although some was chromatographed for spectra. Reaction of epoxide **20** with LiAlH₄ gave HMe₂Si β -hydroxysilane **8**, product of both α opening of the epoxide and reduction of the *i*-PrO group, even when the reaction was carried out at low temperature (-78°C). The (*i*-PrO)Me₂Si β -hydroxysilane **9** was prepared in 30% yield by treatment of **8** with H₂PtCl₆ in *i*-PrOH.

Desilylation reactions. For the desilylations we used 5% KO*t*-Bu (5% by weight of the DMSO) in varying ratios of DMSO/H₂O with 5 mol% of 18-crown-6 at rt. We initially studied the (*i*-PrO)Me₂Si β -hydroxysilane 4 and found that it undergoes desilylation using 50:1

DMSO:H₂O (20 h, rt) to form 3-nonanol (5) and 2-nonene (6) in a GC ratio of 92:8.¹⁰ The 2-nonene was identified by GC/MS, and the stereochemistry was not determined; the 3-nonanol was isolated by chromatography in 76% yield.

In agreement with our earlier work,⁴ for β -hydroxysilanes having the silicon at a secondary center, we found the cyclic system to be more sluggish than the acyclic. The (*i*-PrO)Me₂Si β -hydroxysilane **9** however, underwent smooth desilylation using 200:1 DMSO:H₂O (20 h, rt) to form cyclohexanol (**11**) with cyclohexene (**12**) in 74 and 9.5% GC yields, respectively (using butylbenzene as internal standard). In a preparative experiment, 67% yield of cyclohexanol (**11**) was isolated. When the above reactions were followed by GC analysis (with aqueous work-up) of aliquots, the (*i*-PrO)Me₂Si β hydroxysilanes (**4** and **9**) were found to disappear by the first aliquot (within 5–10 min at rt) with formation of a lower retention time compound, believed to be the corresponding silanol (e.g. **10** from **9**).

We also carried out a series of experiments in which the ratios of DMSO:H₂O were varied from 96:4 to 100:0.¹¹ The (*i*-PrO)Me₂Si β -hydroxysilane (9) was initially used as a substrate. GC yields (and % remaining starting material) were determined using butylbenzene as an internal standard. The results are summarized in Table 1.

Under all the reaction conditions, the $(i-PrO)Me_2Si$ β -hydroxysilane 9 disappeared by the first aliquot (within 5–10 min) with appearance (after aqueous work-up) of the corresponding silanol (10) (identified by GC/MS). Silanol 10 disappeared more slowly to form cyclohexanol (11) as the major product. Very little cyclohexene (12) was observed until the ratio of DMSO:H₂O reached 100:0. The reactions became somewhat faster as the water concentration decreased. We also subjected HMe₂Si β -hydroxysilane **8** and silanol **10** to the above desilylation conditions. Compound **8** disappeared by the first aliquot (within 5–10 min) to form silanol **10**; subsequent reactions were comparable to those above.

We were interested to compare the reactivity of the Me₃Si compound 7 with that of silanol 10 (or its precursors). The comparison could only be approximate for the following reasons: The possible formation of disiloxane or oligomers from 10 means that reactivity comparisons represent an upper limit for the reactivity of 10. In addition, because of the small amounts of water used, the conditions were difficult to reproduce exactly, and small amounts of water made a large difference in the reactivity, especially with 7. However, several comparisons were carried out on a mixture of the (*i*-PrO)Me₂Si compound 9 and the Me₃Si compound 7.

The Me₃Si compound 7 and silanol **10** (from hydrolysis of 9) disappeared at comparable rates under conditions with higher water concentrations, but under conditions with very little water, 7 disappeared much more quickly than 10, forming predominately cyclohexene (while 10 formed predominantly cyclohexanol). At the ratio of 96:4 DMSO: H_2O , the Me₃Si compound 7 and silanol 10 disappeared at comparable rates: after 48 h, about 60% of each remained. At the ratio of 98:2 DMSO:H₂O, the Me₃Si compound 7 disappeared a little more quickly: after 24 h, 46% of 10 and 15-20% of 7 remained. At the ratio of 99.5:0.5 DMSO:H₂O, the Me₃Si compound 7 was completely gone within 5–10 min, and the product was predominantly cyclohexene (12). For comparison, 61% of silanol 10 remained after 3 h under these conditions, and the major product was cyclohexanol (11) (see Table 1).

DMSO:H ₂ O	Time (h)	% silanol 10 ^a	GC yield of 11 (%)	GC yield of 12 (%)
96:4	2	98	1	b
96:4	120	55	49	b
97:3	9	76	20	b
97:3	45	32	53	b
97:3	120	ь	77	ь
98:2	2	88	9	b
98:2	9	60	36	b
98:2	48	13	74	ь
98:2	120	ь	88	b
99.5:0.5	3	61	25	1
99.5:0.5	6.5	37	42	2
99.5:0.5	12	24	53	2
99.5:0.5	36	7	55	2
100:0	3	32	27	44
100:0	12	10	48	33
100:0	21	0	53	37

Table 1. Reaction of the (*i*-PrO)Me₂Si compound 9 with KOt-Bu in DMSO:H₂O

^a The percentage remaining **10** was taken to be 100% at the first aliquot (5–10 min). (It should be noted that silanol **10** may have been accompanied by the corresponding disiloxane or oligomers, which might not have been detected under our GC conditions.) ^b Little or none.

Discussion. With all silvl groups studied, when the water concentration was sufficiently high, the reactions of β -hydroxysilanes with KOt-Bu in DMSO/ H₂O gave mostly alcohol from desilylation, with little or no olefin from β elimination. However, in some cases the reactions are too slow to be practical. Under the reaction conditions, the (i-PrO)Me₂Si and HMe₂Si groups were quickly converted to the (HO)Me₂Si group, and the (HO)Me₂Si compound was more slowly converted to the products. As the water concentration was decreased, both the Me₃Si and (HO)Me₂Si compounds disappeared more quickly, and the percentage of olefin in the product mixtures increased slightly. At very low water concentrations $(\sim 0.5\%)$, the Me₃Si compound disappeared very quickly, giving mainly olefin from β elimination. The (HO)Me₂Si compound disappeared more slowly, giving mainly alcohol from desilylation.

The difference between the Me₃Si and (HO)Me₂Si compounds at low water concentrations is remarkable. Under the same conditions (with 0.5% H₂O), the Me₃Si compound undergoes rapid elimination (e.g. $7\rightarrow 12$) while the (HO)Me₂Si compound undergoes slow desilylation (e.g. $10\rightarrow 11$). The presence of an OH group on the silicon, which may exist as O⁻ in the presence of base, seems to slow down the elimination reaction compared to that with the analogous silyl group having a Me in place of the OH. The low reactivity of the (HO)Me₂Si compounds may possibly result from the formation of dianions under basic conditions.

This work suggests that β -hydroxysilanes could find use as precursors to alcohols if the silicon has a ligand which will be converted to OH (or O⁻) under the reaction conditions, and that it should be possible to fine-tune the reaction conditions to suit the substrate by adjusting the water concentration.¹²

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