Strategies for protodesilylation of C-2 trialkylsilyl terminal alkenes

James C. Anderson* and Alice Flaherty

*School of Chemistry, University of Nottingham, Nottingham, UK NG7 2RD.*
E-mail: j.anderson@nottingham.ac.uk

The mild and high yielding protodesilylation of C-2 trialkylsilyl terminal alkenes can be effected *via* a hydroboration–Peterson elimination protocol or, in the case of the phenyldimethylsilyl analogues, a one pot procedure using *t*-BuOK–18-C-6–TBAF can be used.

During our work on the acyclic aza-[2,3]-Wittig sigmatropic rearrangement we found that for efficient stereocontrol the incorporation of a trialkylsilyl group at C-2 was necessary (Scheme 1).[1] Although the vinylsilane present in products **1** has
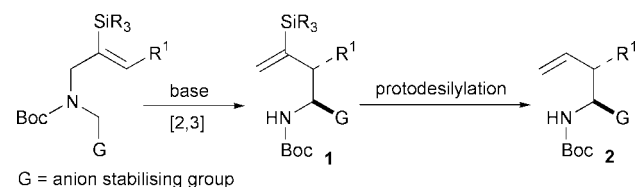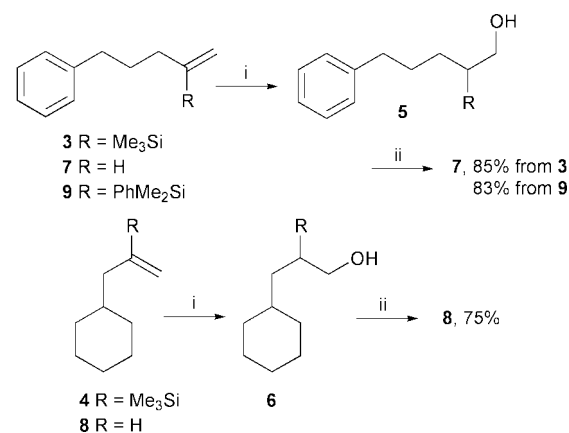
Scheme 1

its own rich chemistry,[2] in certain instances we desired the replacement of this group with a proton to give **2**. Protodesilylation of terminal vinylsilanes, where the silyl group is on C-2, under standard acidic conditions is known to be difficult, presumably because the accepted mechanism would require the formation of an incipient primary carbocation. All our attempts using standard literature conditions failed.[2] Following an isolated report that the phenyldimethylsilyl group could be removed from the C-2 position of a terminal alkene with TBAF,[3] we used this group to help facilitate the scope of the aza-[2,3]-Wittig rearrangement.[1] However, removal of the phenyldimethylsilyl group using this protocol from a number of rearrangement products gave yields consistently below 50% with considerable decomposition.

We therefore investigated an alternative approach which involved hydroboration of the vinylsilane and subsequent Peterson elimination to regenerate the alkene. It was expected that the bulky silyl substituent would control the regiochemistry of hydroboration *via* sterics.[4] Treatment of the C-2 trimethylsilyl terminal alkenes **3** and **4** with 9-BBN followed by basic peroxide work up gave the crude silanols **5** and **6**. Treatment with KH in anhydrous THF gave the desired alkenes **7**[5] and **8** in good overall yields (Scheme 2). The corresponding phenyldimethylsilyl compound **9** could also be protodesilylated using this protocol in 83% yield. Despite various modifications in the reaction conditions, subjecting the rearrangement products **1** to this protocol resulted in mixtures of hydroborated alkene and degraded protecting group in moderate yield. Although this was disappointing the method would still be useful for protodesilylation of C-2 trialkylsilyl terminal alkenes where other functional groups present in the molecule were resistant to hydroboration. In the case of substrates **1**, hydroboration of allylic secondary amines is known to be low yielding, which implies the free N–H bond may interfere with the reaction despite the nitrogen atom being attached to an electron with-

Scheme 2 *Reagents and conditions*: i, 9-BBN (2–3 equiv.), THF; NaOH–H₂O₂; ii, KH, THF.

drawing protecting group.[6] The reduction of amide like bonds with borane is also precedented.[7]

In order to continue our investigation along similar lines, we attempted to add a variety of oxygen nucleophiles to the alkene terminus, by analogy to the addition of carbanions in similar systems.[8] Ultimately we envisaged unmasking of an oxygen anion to perform a Peterson elimination. After a long study we found that treatment of **9** with a mixture of *t*-BuOK, 18-crown-6 and TBAF in THF–DMSO at room temperature furnished the protodesilylated material **7** in quantitative yield.† Although the cleavage of carbon–silicon bonds with *t*-BuOK in DMSO is known,[9] our result is an unusual transformation as nucleophilic protodesilylation of vinylsilanes is difficult unless the putative vinyl anion is stabilised.[10] ‡ Also comparative experiments suggest that although phenyl groups can be displaced from silicon with fluoride ion, vinyl groups are much more robust.[11] § Treatment of **9** with only *t*-BuOK and 18-crown-6 in DMSO or THF allowed the isolation of a crude mixture of silanol **10** and fully protodesilylated material **7** (4:1, Scheme 3). Formation of
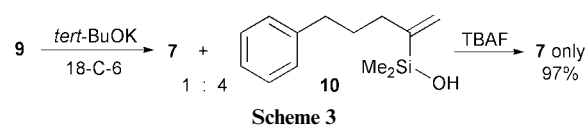
Scheme 3

silanols in this manner has been observed before, but the proposed mechanism requires DMSO,[12] which is not consistent with our observation. Treatment of the crude mixture with TBAF gave pure **7** as expected[3,13] in near quantitative yield. Use of TMSOK or AcOK did not lead to any products, KOMe was effective, but caused epimerisation with more complex substrates (*e.g.* **16**) and KOH gave a very slow reaction. Although it is difficult to obtain all the reagents in anhydrous form, we have noticed that rigorously dry conditions severely retard the reaction. The best protocol was to use undried THF with a drop of

water added. Use of water as a cosolvent was deleterious to the reaction.

Mechanistically it is known that hydroxide and alkoxide anions can form pentavalent anions with silicon,[11] even more so if at least one substituent is a phenyl group (Scheme 4).[14]

Scheme 4
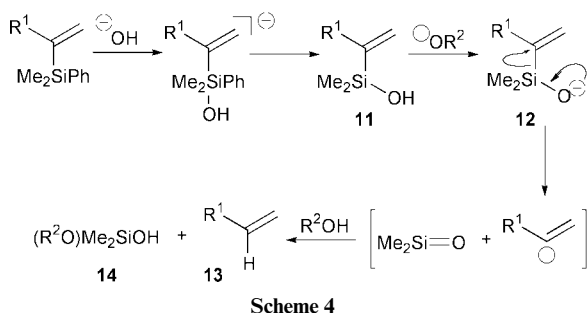
Collapse to give the neutral silanol **11** would occur *via* expulsion of phenyl anion, probably acquiring a proton from the solvent as it separates. There is no experimental evidence to suggest that hydroxide or alkoxide anion can displace the vinyl moiety.[11,15] The formation of protodesilylated material **13**, in the absence of TBAF, can conceivably arise from alkoxide attack on the silanol **11** or unimolecular decomposition from the silanoate anion **12**, the latter mechanism having some preference in the literature.[16] We do not invoke the expulsion of vinyl anion, but as is probable in the phenyl case, it acquires a proton from the reaction mixture as it leaves. We have no evidence for the formation of silyl ethers derived from alkoxide substitution of phenyl groups or the formation of silanols **14**. The former may not be stable under the reaction conditions.[16]

The one pot procedure proved useful in the protodesilylation of rearrangement products **15** and **16** to give **17** and **18** in 82% and 71% yield respectively (Scheme 5). The slightly lower yield

Scheme 5
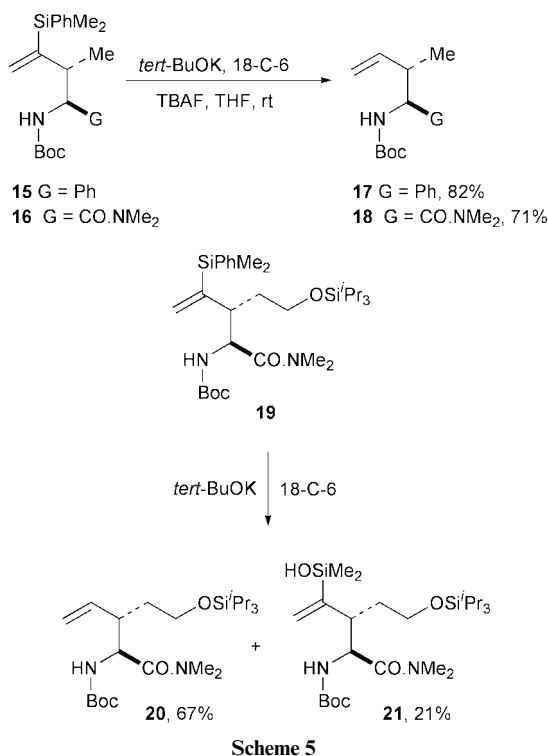
of **18** could be due to some amide hydrolysis.[17] It is noteworthy that no epimerisation of **18** was detected by ^{1}H NMR. Protodesilylation of **19**, where the TIPS protecting group precludes the use of the one pot procedure containing TBAF, was achieved by stirring with *t*-BuOK and 18-crown-6 in THF for 30 minutes to give desired **20** in 67% isolated yield along with silanol **21** (21%). Longer reaction times led to lower yields of

20, presumably due to amide hydrolysis.[17] Treatment of **21** with methoxide gave a very slow protodesilylation unfortunately accompanied by epimerisation. The fact that no TBAF was required in this particular reaction suggests that protodesilylation is assisted by the β-amido group in much the same way as analogous β-hydroxy examples.[18]

In summary we have demonstrated two complementary and mild methods for the protodesilylation of C-2 trialkylsilyl terminal alkenes. The hydroboration–Peterson elimination protocol should be applicable to a wide range of trialkylsilyl groups where other functional groups are resistant to hydroboration and the one pot *t*-BuOK–18-C-6–TBAF protocol serves as a valuable alternative for the phenyldimethylsilyl congeners. These protocols are useful in our own research, in providing stereochemically pure amino acid building blocks from the aza-[2,3]-Wittig sigmatropic rearrangement, and we hope will also be for others engaged in synthesis.

Experimental

General details

Our general experimental details have been reported.[1a] Representative protodesilylations are given for the hydroboration–Peterson elimination protocol **3** to **7** and the one pot *t*-BuOK–18-C-6–TBAF **15** to **17**.

5-Phenylpent-1-ene (7)

Neat alkene **3** (90 mg, 0.413 mmol) was treated with a solution of 9-BBN in THF (2.48 mL of a 0.5 M solution, 1.24 mmol, 3.0 equiv.) at rt and then warmed to 70 °C until **3** had disappeared by TLC analysis. After 5 h the reaction was cooled to 0 °C, treated with EtOH (1 mL), NaOH (1 mL of a 2 M aq. solution), H_2O_2 (30%, 1 mL) and after 5 min warmed to 50 °C for 30 min. The reaction was then diluted with Et_2O, separated and extracted with Et_2O. The combined ethereal layers were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude β-hydroxysilane (169 mg).

The crude product in THF (0.4 mL + 0.4 mL wash) was added to a suspension of KH (276 mg of a 30% dispersion in mineral oil, prewashed with dry hexane, 2.07 mmol, 5.0 equiv.) in THF (0.4 mL) at 0 °C, warmed to rt and stirred for 2.5 h. The reaction mixture was cooled to 0 °C, quenched by the addition of saturated aq. NH_4Cl (0.5 mL), and extracted with Et_2O. The combined ethereals were washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a crude oil which was purified by flash column chromatography (hexane) to give **7** (85%) as a clear oil which possessed identical analytical data to that prepared in the literature.[5]

(1S*,2R*)-N-*tert*-Butoxycarbonyl-2-methyl-1-phenylbut-3-enylamine (17)

To a stirred solution of **15** (83 mg, 0.21 mmol) in DMSO (2 mL) was added TBAF (1.05 mL of a 1 M THF solution, 5 equiv.) dropwise. The resulting mixture was cooled to 0 °C and treated with potassium *tert*-butoxide (27 mg, 0.24 mmol, 1.1 equiv.), 18-crown-6 (10 mg, 0.038 mmol, 0.2 equiv.). After 1 h the mixture was warmed to rt and stirred for 36 h after which time MeOH (0.02 mL, 2 equiv.) was added. The mixture was washed with H_2O (2 × 10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash-column chromatography (5% EtOAc–light petroleum) gave **17** (45 mg, 82%) as a white solid which possessed identical analytical data to the sample prepared previously.[1a]

Notes and references

† Stirring with TBAF alone for 5 days at rt gave only recovered starting material (90%).

‡ Compare protodesilylation conditions for the series of vinylsilanes included in ref. 9

§ See ref. 3*b*, footnote 8.

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