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Oxidative cleavage of C–Si bonds in polyhydroxylated silacyclopentanes

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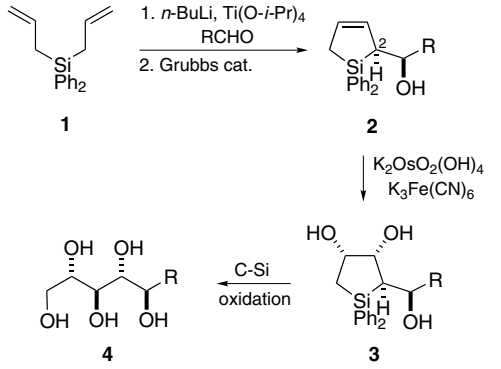
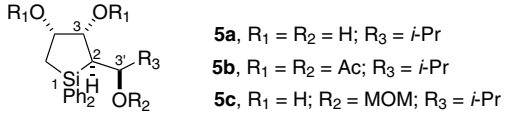
Abstract—Oxidative cleavage of C–Si bonds of polyhydroxylated silacyclopentanes under various conditions have led to both the desired polyols and to Peterson elimination products. Further studies on the reactivity of these silacycles, under acidic and basic conditions have been carried out, leading to unexpected results. Treatment of these silacycles under basic conditions thus provided various diols after the cleavage of C_{sp^3}–Si bonds. A mechanistic rationale has been proposed for each case.

The oxidative cleavage of carbon–silicon bonds, discovered independently by Kumada–Tamao and Fleming some twenty years ago now constitutes a useful tool in organic synthesis and has thus received considerable attention.[1] The unmasking of a silicon group into the corresponding hydroxy group occurs with retention of configuration. The use of a latent hydroxy group is very practical in total synthesis of natural products, as it avoids the sometimes tedious alcohol protection and deprotection sequences. Various organosilicon groups have thus been devised which allow the transformation to be carried out under mild conditions.

This oxidation has been the key-step in several strategies devised in our laboratory, en route to the total synthesis of various targets of biological interest.[2] In line with these studies, we recently reported a new preparation and stereocontrolled functionalisation of silacyclopentenes **2**.[3] The strategy relied on an hydroxy-alkylation of commercially available diallylsilane **1**, which upon ring-closing metathesis led to the parent silacyclopentenes **2** substituted at C2, in excellent overall yield (Scheme 1). Dihydroxylation of the latter afforded a diastereocontrolled access to polyhydroxylated silacyclopentane **3** that we envisioned to elaborate further. Amongst the transformation that we had envisaged,



Scheme 1.



Scheme 2.

the oxidation of both C–Si bonds of **3** appeared very attractive as it would offer a straightforward access to useful polyols such as **4**.[4]

We thus started our investigations, with the oxidation of readily available silacyclopentanes **5a**,**b**[3b] (Scheme 2)

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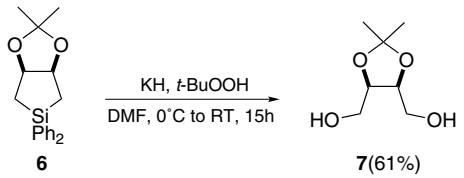
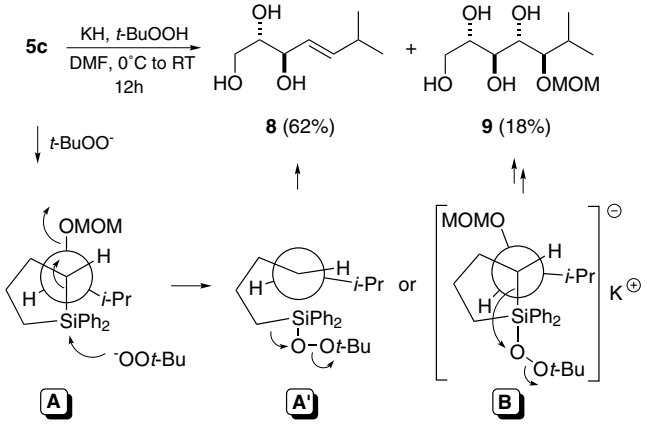


Scheme 3.

using classical Tamao conditions[1a,b] (KF, $KHCO_3$, H_2O_2, THF–MeOH 1:1). This unfortunately led essentially to recovered starting material. In contrast, the use of Fleming's electrophilic conditions[1c,d] (Br_2, AcOOH, AcONa) led to extensive decomposition.

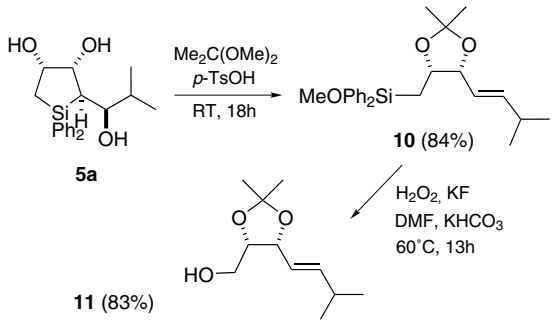
Surprised by the lack of reactivity of silacyclopentanes **5a**,**b**, under the mild Tamao conditions, it was decided to test different oxidation conditions on a simpler model **6**, lacking the chain at C2 (Scheme 3). Again, Tamao and Fleming's conditions failed to provide the desired polyols but we were pleased to find that more drastic Woerpel's conditions[5] led to the desired diol **7** in reasonable yield (Scheme 3).



Scheme 4.

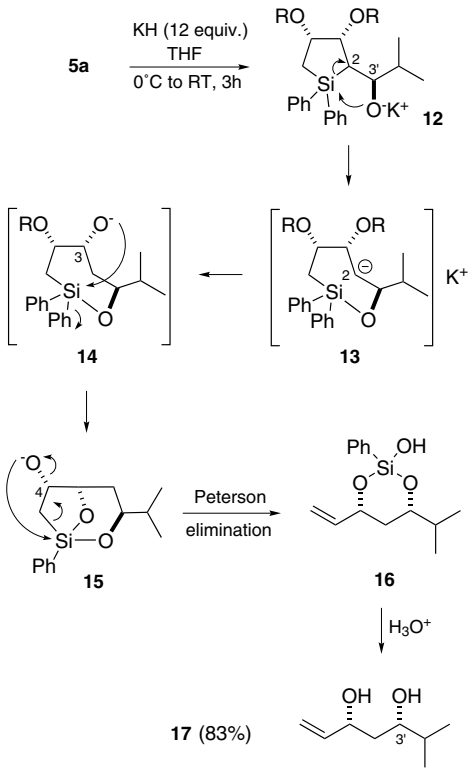
Encouraged by these results, Woerpel's conditions were then applied for the oxidation of diol **5c**[6] which afforded the desired tetrol **9**, albeit in low yield in the presence of a large amount of triol **8** and a third product which structure could not be determined (Scheme 4). The presence of a Peterson elimination product **8**, under such conditions is not unexpected.[7] Base-promoted Peterson elimination of β-hydroxysilanes is usually a *syn*-stereospecific process.[7d] Therefore, starting from an *anti*-β-hydroxysilane, one would expect the formation of a (*Z*)-olefin. As in **5c** the OH groups at C3′ is protected as a MOM ether, the oxyanion cannot be formed and the Hudrlik–Peterson elimination is thought to proceed instead through a preliminary attack of the nucleophilic species *t*-$BuOO^-$ onto the silicon centre,[7] following an *anti*-pathway[8] (i.e. **A**)[9] (Scheme 4). Elimination through **A** would generate an (*E*)-olefinic peroxysilane **A′**[9] rearranging to provide triol **8** after work-up.[1d,10] An alternative pathway, involving pentacoordination of silicon[11] as in **B**[12] may also be envisioned that would be followed by rearrangement through migration of the substituents on the silicon centre, leading to tetrol **9** after hydrolysis.[1a,b] In the absence of a leaving group at C3′ (i.e. MOM in **5c**), the reaction would only proceed through this route (**B**→**9**) as observed by Kozmin and co-workers[4c,d] for closely related silacyclopentanes lacking an OH group at C3′.

With these results in hand, we then realised that elimination products such as triol **8** might be useful intermediates for organic synthesis and decided to focus on their synthesis starting from precursors **5a**–**c**. Protection of diol **5a** as an acetonide under standard conditions gave the acetonide **10** as a result of a stereospecific acid-catalysed Peterson elimination occurring during the protection of the diol. Methanol formed in situ attacks the silicon centre and thus assists the elimination of water to form the unsaturated methoxysilane **10**. Oxidation of **10** under Tamao's conditions[1a,b] finally led to the desired alcohol **11**[13] in good overall yield (70%, two steps) (Scheme 5).

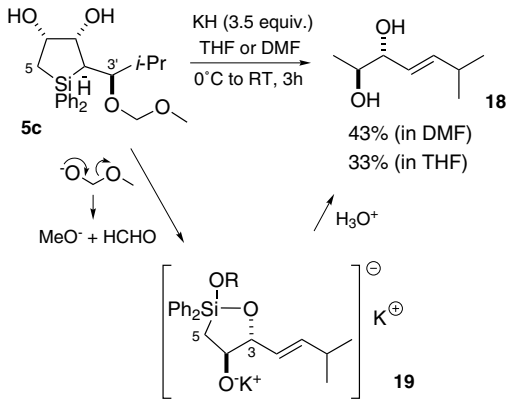


Scheme 5.

In order to get an access to the corresponding (*Z*)-isomer of **11**, we then studied the base-catalysed Peterson elimination of **5a**, having the requisite OH group at C3′. Treatment of **5a** using an excess of KH surprisingly led to the diol **17** in excellent yield. The formation of such a diol shows that the Peterson olefination has taken place with complete regiocontrol and surprisingly without elimination of the OH group at C3′. It also implies that a C_{sp^3}–Si bond has been cleaved under basic conditions, which is rather unusual.[14] The regiocontrol and the cleavage of this C–Si bond during formation of **17** may be rationalised as depicted below (Scheme 6). The OH group at C3′ is not eliminated and thus likely attacks the silicon centre to generate a pentacoordinated species,[7b,c] possessing a strongly polarised C_{sp^3}–Si.[7,15] The rapid cleavage of this very labile C2–Si bond would generate a carbanion at C2 (i.e. **13**[16]) reacting further with any proton source in the medium (solvent), forming the seven-membered ring intermediate **14**.[17] Although the mechanism of the Peterson elimination is presently not clear,[7b,c] recent studies indicate that it is likely to proceed through a stepwise mechanism, involving intermediates such as **13**.[18] Attack of the C3 oxyanion of **14** onto the silicon centre would then lead to



Scheme 6.



Scheme 7.

siloxane **15** and the removal of a phenyl group.[19] The remaining oxyanion at C4 would then attack the silicon centre, to provide regioselectively the olefinic moiety through a Peterson elimination. Such a pathway thus rationalises the regioselectivity of the Peterson elimination, which is the consequence of the formation of the more stable bicyclic siloxane system **15**. The likely formation of such a species, yet not isolated, is supported by the isolation of the silaketal **16** (obtained in a separate experiment in 33% yield before acidic work-up) which upon hydrolysis leads to **17**. The formation of **17**[20] and **16**[21] and the cascade of events illustrated below would thus support the hypothesis made by several authors that Peterson elimination follows a stepwise and not a concerted mechanism.[7c,18] To our knowledge, this is the first observation of an attack of an oxyanion, β- to a silicon centre, leading to the isolation of a siloxane intermediate (i.e. **16**) instead of the normal elimination product. The reasons why carbanion **13** does not eliminate (i.e. as in step **ii** → **iii**)[18] remain presently unclear. The conformation of the seven-membered ring in **13** may not be favourable for the elimination process, which requires the alignment between the carbanion orbital and the σ_{C-O} bond. Protonation of **13** would then be faster than elimination, leading to **14** instead of the expected olefin.

The presence of a free hydroxy group (C3′) able to displace a substituent on the silicon centre is responsible for the results described above. We thus studied the behaviour, under similar reaction conditions, of the analogue **5c** having a MOM protective group at C3′. The reaction carried out in THF and in DMF led surprisingly to the diol **18** in moderate yield, whatever the solvent (Scheme 7). This diol may be formed through the sequence depicted below. As above for **5a**, the Peterson elimination is regioselective, but involves the OR group on the side chain (C3′). This elimination is probably initiated by traces of OH^- present in the medium. Elimination of the MOM group then releases MeO^- which can continue the elimination process. Similarly to the process illustrated in Scheme 4 (**5c** → **A** → **A**′), elimination is antiperiplanar, leading exclusively to the (*E*)-olefin.[8] The subsequent loss of the silicon group is likely to occur through the pentacoordinated species **19**, formed by coordination of the C3 oxyanion to silicon.[11] Interestingly, the presence of an oxyanion on the adjacent carbon centre does not lead to a second Peterson elimination due to ring strain. The C5–Si in **19** is strongly polarised and is instead cleaved during work-up, to provide **18**.

In summary, we reported here a study on the unusual reactivity of polyhydroxylated silacyclopentanes in the presence of bases and under oxidative conditions. The unexpected formation of diols such as **17** and **18** under these conditions, due to the activation of strong C–Si bonds through pentacoordination, is of particular interest as it shows that reactivity of 'isolated' C_{sp^3}–Si bonds may be enhanced by simple coordination of suitably disposed chelating groups.[14,17] In the case of the formation of diol **17**, this observation further supports the hypothesis of a stepwise mechanism for the Peterson elimination.[7,18] Finally, as functionalised silacycles **5a–c** are easily prepared in three steps from commercially available material, these transformations may also be useful for the preparation of diastereomerically pure polyols, having contiguous (i.e. **9**, **11** and **18**) or non contiguous (i.e. **17**) stereogenic centres.

Acknowledgements

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6. Compound **5c** was prepared through the following sequence:[3b] hydroxy-alkylation of diallylsilane **1** (*n*-BuLi, Ti(*O*-*i*-Pr)$_4$, *i*-PrCHO, 83%), followed by protection of the OH group at C3′ (MOMCl, *i*-Pr$_2$NEt, 99%), ring-closing metathesis (Grubbs-I cat., benzene, reflux, 17 h, 70%) and treatment of the silacyclopent-3-ene with AD-mix® (94%). Dihydroxylation led to a separable 78:22 mixture of **5c** and its diastereomer.
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12. Compound **9** is probably formed through a conformation close to **B** in which a staggered rather than an *anti*-arrangement between SiR_3 and OMOM is operating.
13. Compound **11**: to a solution of KF (59.4 mg, 1.02 mmol) and $KHCO_3$ (107.3 mg, 1.02 mmol) in DMF (2 mL) was added successively, at 0 C, a 35% solution of H_2O_2 (0.37 mL, 4.2 mmol), then **10** (135.1 mg, 3.41 mmol) in DMF (4 mL). The reaction mixture was heated at 60 °C for 13 h, then quenched with sodium thiosulfite (507 mg) and the aqueous layer was extracted with diethyl ether. The combined extracts were washed with brine, dried over $MgSO_4$ and the solvents evaporated under vacuum. Purification by column chromatography over silica gel (petroleum ether–EtOAc 9:1) gave **11** (56.4 mg, 83%, R_f = 0.20). IR ($CHCl_3$): ν_{max} 3423, 2963, 2935, 1666, 1466, 1382, 1254, 1216, 1165, 1101, 1068, 1032, 977, 912, 738, 650 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.80 (dd, J = 15.6; 6.7 Hz, 1H), 5.42 (dd, J = 15.6; 8.2 Hz, 1H), 4.62 (t, J = 7.5 Hz, 1H), 4.20 (dd, J = 11.7; 5.8 Hz, 1H), 3.52 (d, J = 5.8 Hz, 2H), 2.34 (d, J = 6.7 Hz, 1H), 1.51 (s, 3H), 1.38 (s, 3H), 1.00 (d, J = 6.7 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 143.8, 121.3, 108.6, 78.4, 78.3, 62.3, 30.9, 27.9, 25.2, 22.2, 22.1.
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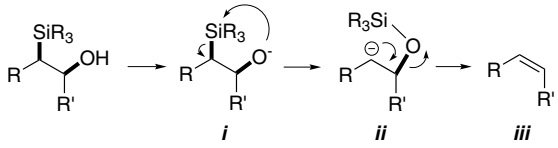
16. Attempts to trap the putative carbanion **13** with other electrophiles than proton however failed.
17. Anionic migration of silicon from carbon to oxygen with the conversion of an oxyanion into a carbanion is known as the Brook rearrangement. [1,3]- or Homo-Brook rearrangement, which is in competition with the Peterson elimination, is rare and occurs mainly when the resulting carbanion is stabilised by heteroatoms (Br, Cl, S). See: Shinokubo, H.; Miura, K.; Oshima, K.; Utimoto, K. *Tetrahedron* **1996**, *52*, 503–514, and references cited therein.
18. A stepwise mechanism would proceed through betaine **i**, followed by formation of the carbanion **ii** (as **13** in Scheme 6), evolving with the elimination of R_3SiO^- to form the olefin **iii**.[15] The strong polarisation of the C–Si bond in oxasiletanide would disfavour a concerted pathway proceeding through a four-membered ring transition state (as in Wittig reaction)



19. Such removal of a phenyl group at silicon in a basic medium has been reported in closely related γ-hydroxysilane systems which are able to form 5-membered ring siloxanes: Harada, T.; Imanaka, S.; Ohyama, Y.; Matsuda, Y.; Oku, A. *Tetrahedron Lett.* **1992**, *33*, 5807–5810.
20. Compound **17**: to a cooled solution (0 °C) of KH (116.5 mg, 2.9 mmol) in THF (5 mL) was added dropwise, a solution of **5a** (83 mg, 0.24 mmol) in THF (5 mL). The reaction mixture was then allowed to warm to room temperature. After completion of the reaction (3 h, TLC) and aqueous work-up (NH_4Cl, extraction with ether, brine, $MgSO_4$), the solvents were removed in vacuo and the resulting mixture purified by column chromatography through silica gel (petroleum ether–EtOAc 7:3) to afford **17** (29 mg, 83%, R_f = 0.62). IR ($CHCl_3$): ν_{max} 3489, 3441, 2966, 1643, 1862, 1422, 1251, 1116 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.86 (ddd, J = 17.2; 10.3; 5.9 Hz, 1H), 5.23 (dt, J = 17.2; 1.4 Hz, 1H), 5.08 (dt, J = 10.3; 1.4 Hz, 1H), 4.32 (m, 1H), 3.64 (ddd, J = 7.6; 4.9; 2.8 Hz, 1H), 3.33 (br s, 1H), 3.08 (br s, 1H), 1.67 (dd, J = 6.8; 1.5 Hz, 1H), 1.62 (m, 2H), 0.90 (d, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 140.8, 114.4, 77.4, 74.0, 39.4, 34.1, 18.2, 17.5.
21. **16**. Treatment of **5a** as above, but without acidic work-up, led to **16** after purification by chromatography through

silica gel (33%, $R_f = 0.60$). IR ($CHCl_3$): ν_{max} 3426, 2984, 2923, 1645, 1453, 1426, 1252, 1115, 1086 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.52–7.28 (m, 5H), 5.88 (ddd, $J = 17.2$; 10.4; 6.1 Hz, 1H), 5.25 (dtd, $J = 17.1$; 1.5; 0.6 Hz, 1H), 5.10 (dt, $J = 10.4$; 1.5 Hz, 1H), 4.34 (m, 1H), 3.64 (ddd, $J = 7.6$; 4.9; 2.8 Hz, 1H), 1.67 (dd, $J = 6.8$; 1.5 Hz, 1H), 1.62 (m, 2H), 0.90 (d, $J = 6.8$ Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 140.8, 114.4, 77.4, 74.0, 39.4, 34.1, 18.2, 17.5.