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Studies in silanol synthesis: internal nucleophiles and steric hindrance

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Abstract—As a model system for the synthesis of complex silanediols, *N*,*N*-dimethyl 3-(*tert*-butyldiphenylsilyl)propionamide was prepared and treated with triflic acid, resulting in the removal of one phenyl group and yielding a silanol. Even with a large excess of triflic acid, only a single phenyl group could be removed. This contrasts with a diphenylsilyl group flanked by a pair of amides, for which both phenyl groups are rapidly cleaved. A combination of steric hindrance by the *tert*-butyl group and lack of a second internal nucleophile appears to limit triflic acid-mediated phenyl hydrolysis from the silicon. © 2001 Published by Elsevier Science Ltd.

Nearly 100 dialkyl and aryl silanediols have been prepared and characterized.[1] Some of these, such as dimethylsilanediol **1**, are notoriously unstable toward dehydration and polymerization. Others have been found to be quite stable and unusual properties have been noted: diisobutylsilanediol **2** is a liquid crystal, self-assembling through strong intermolecular hydrogen bonding;[2] diphenylsilanediol **3** has been studied for its anti-epileptic properties.[3] Recently, we have reported the first silanediol-based protease inhibitor **4**, designed as a transition state analog of the tetrahedral intermediate of amide hydrolysis[4] (Fig. 1).

Most silanediols have been prepared by hydrolysis of dichlorosilanes.[5] In contrast, synthesis of silanediol **4** had, as its pivotal and ultimate step, acid-catalyzed hydrolysis of the corresponding diphenylsilane, employing the well known acidic cleavage of the aryl–silicon bond. As part of this investigation, we postulated that the amides surrounding the diphenylsilane would participate in this hydrolysis. We describe here an investigation of the triflic acid-mediated hydrolysis of a diphenylsilane bearing a single amide group. The results are consistent with cleavage of the silicon–carbon bond involving assistance of the internal amide nucleophile.

As the model substrate for this investigation, *N*,*N*-dimethyl amide **9** was prepared from the commercially available *tert*-butyldiphenylchlorosilane **5**, via the known allyl silane **6**.[6,7] Hydroboration of **6**[8] and oxidation with TPAP[9] followed by buffered potassium permanganate[10] gave acid **8**, which was coupled with dimethylamine to yield **9**[11] (Fig. 2).

As a reagent for cleavage of aryl–silicon bonds, triflic acid has been broadly applied,[12,13] in part because it can be rendered anhydrous, and the cleavage is an efficient method for generating silyl triflates.[14] In a number of cases, diphenylsilanes have been converted to silyl ditriflates.[15] Once formed, the highly electrophilic silyl triflates will react with a wide variety of electrophiles, including amide carbonyls.[14,16,17] In the case of **9**, conversion of an aryl–silicon bond to a silicon–triflate bond would be expected to rapidly *O*-

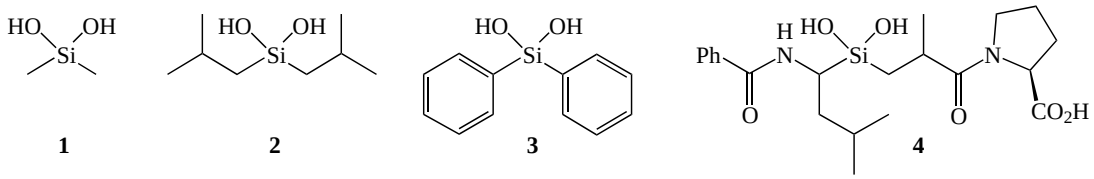

Figure 1. Representative silanediols.

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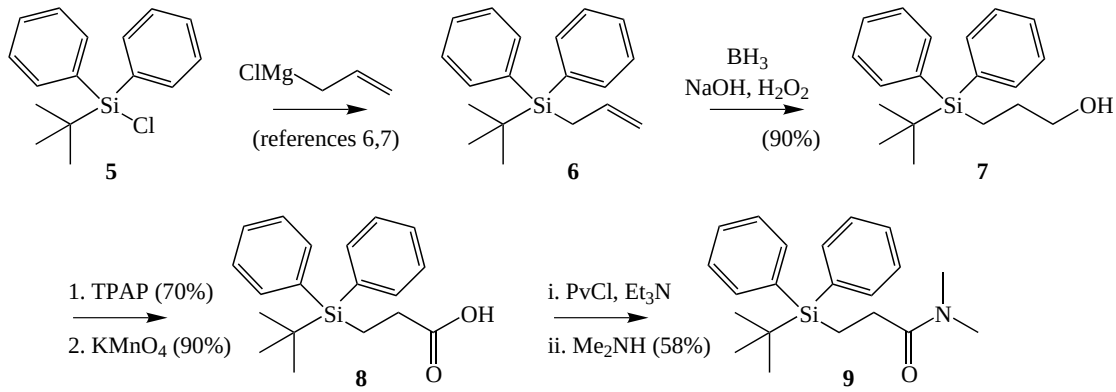

Figure 2. Synthesis of model substrate **9**.

silylate the nearby amide. Alternatively, formation of the silicon–amide bond could pre-empt a triflate intermediate (Fig. 3).

Treatment of **9** with triflic acid would be expected to initially protonate the amide carbonyl. Cleavage of the aryl–silicon bond would be initiated by *ipso* protonation of the aromatic ring (**10**, Fig. 3).[14] Cleavage of the C–Si bond would then occur, during or following attack of a nucleophile. With the silicon beta to an amide, the reversibly protonated oxygen can act as an intramolecular nucleophile, forming a five-membered intermediate, **11**. Hydrolysis of the five-membered silyl ether ring of **11** would be facilitated by ring strain.[18]

Cleavage of the remaining phenyl group of **11** would also require *ipso* protonation to give **14**. Without a second internal nucleophile, loss of the phenyl group would require displacement of the phenyl by triflate. This may not be possible with the *tert*-butyl group shielding the silicon from this weak nucleophile.[19]

In the event, treatment of **9** with 5 equiv. of triflic acid in methylene chloride at −78°C for 30 min led to the isolation of a single product, silanol **12**.[20] Raising the temperature to 25°C and increasing the triflic acid to 100 equiv. failed to alter the outcome. Higher temperatures led to decomposition. In addition to loss of one aromatic ring, the presence of a stereogenic center in product **12** was indicated by the diastereotopicity of the four methylene protons. Also notable is the coalescence of the amide methyl groups of **12**, possibly indicating an interaction of the amide carbonyl with the silanol.[21]

The reticence of **9** to lose both aryl groups is somewhat surprising. Ditriflates have been prepared by triflic acid substitution of two phenyl groups to make dimethylsilyl,[15b] diphenylsilyl[15e] and divinylsilyl[15g] ditriflates. The very hindered di-*tert*-butylsilyl ditriflate has been prepared using triflic acid, albeit by replacement of chlorine and hydrogen and not phenyl groups.[22,23] Both sterics and electronics can play a role in triflic acid-mediated substitution of phenyl and other groups, with electron withdrawing groups on silicon attenuating the cleavage rate.[14,24]

The *tert*-butyl group in **9**, incorporated to ensure that the desired silanediol product would be stable, subverted the second hydrolytic step. This result indicates that alternative synthesis strategies may be required for the construction of complex silanediols.[25]

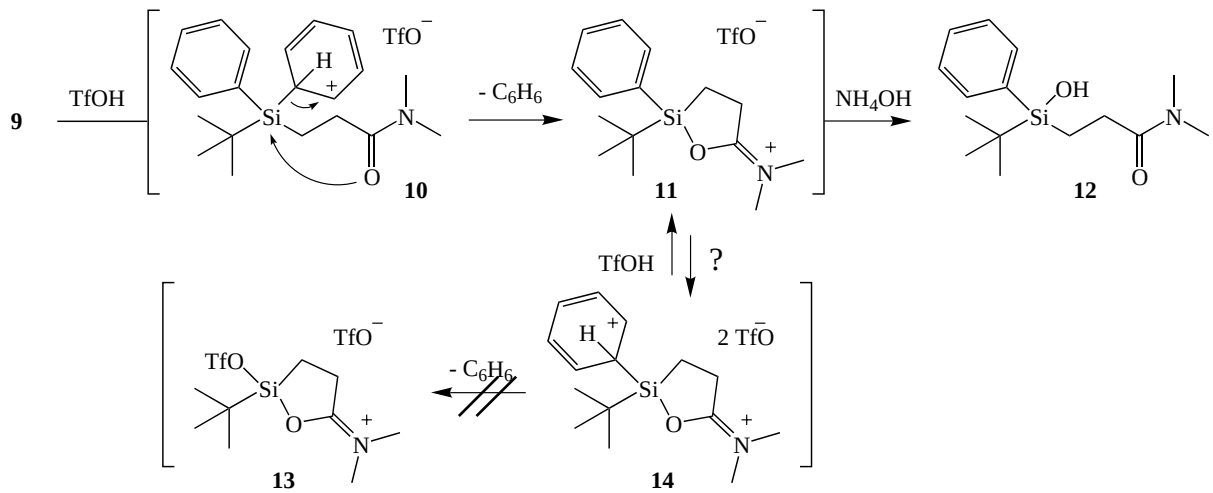

Figure 3. Treatment of **9** with excess triflic acid yields only silanol **12**.

Acknowledgements

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