

Synthetic Methods

How to cite: *Angew. Chem. Int. Ed.* **2021**, *60*, 4408–4410

International Edition: doi.org/10.1002/anie.202017157

German Edition: doi.org/10.1002/ange.202017157

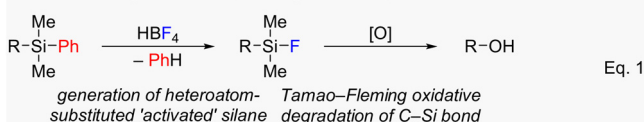
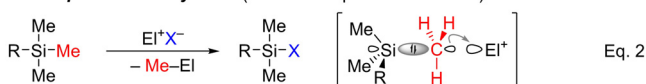
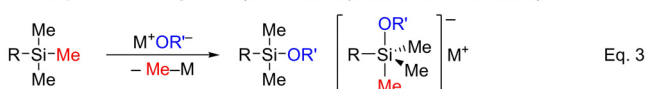
At Long Last: The Me₃Si Group as a Masked Alcohol

Avijit Roy and Martin Oestreich*

Keywords: alcohols · density functional calculations · hypervalent compounds · silicon · Tamao–Fleming oxidation

Silicon, carbon's closest neighbor in the periodic table, forms strong covalent bonds with carbon. Due to the more electropositive nature of silicon, carbon–silicon bonds are however more polarized and, hence, more vulnerable to nucleophilic and electrophilic attack, respectively, as compared to carbon–carbon bonds. Such fragility of carbon–silicon bonds had been realized a century ago for the first time by the pioneer of silicon chemistry, Frederick S. Kipping.^[1] His serendipitous discovery of the acid-mediated cleavage of C(sp³)–Si bonds in arylsilanes (=protodesilylation) was further advanced by Colin Eaborn,^[2] and eventually streamlined by Ian Fleming for the synthesis of alcohols from arylsilanes^[3] [Eq. 1]. The overall procedure is the now called Tamao–Fleming oxidation (gray box).^[4] Unactivated tetraalkylsilanes were found to be too unreactive though, and the oxidative degradation of trialkylsilyl groups, especially the Me₃Si group, as masked hydroxy groups is still elusive.^[5]

Tamao–Fleming oxidation (Fleming's method)

Electrophilic demethylation (Ei⁺ = electrophiles such as H⁺)Nucleophilic demethylation (Nu⁻ = nucleophiles such as alkoxides)

[*] A. Roy, Prof. Dr. M. Oestreich
Institut für Chemie, Technische Universität Berlin
Strasse des 17. Juni 115, 10623 Berlin (Germany)
E-mail: martin.oestreich@tu-berlin.de
Homepage: <http://www.organometallics.tu-berlin.de>

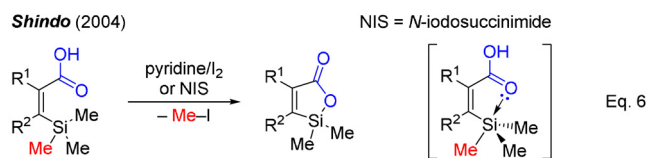
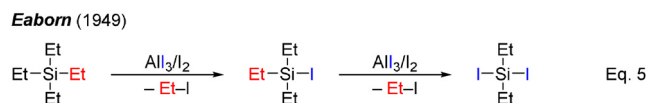
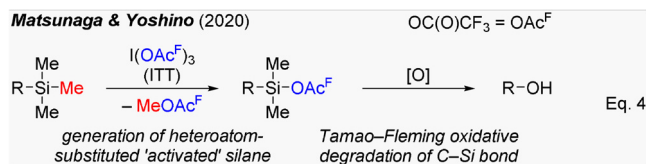
ORCID The ORCID identification number(s) for the author(s) of this article can be found under:
<https://doi.org/10.1002/anie.202017157>.

© 2021 The Authors. Angewandte Chemie International Edition published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

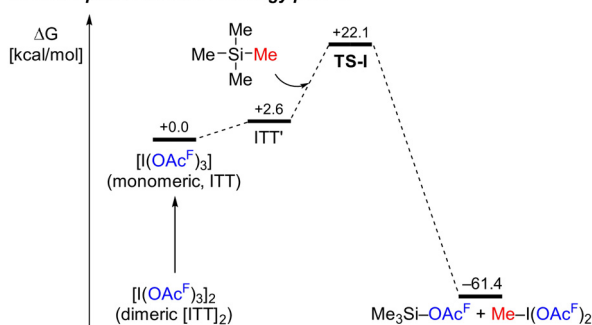
Following a similar strategy, several attempts have been made for the demethylation of trimethylsilane derivatives employing strong Brønsted acids [Eq. 2]. In 1953, Sommer and co-workers reported a concentrated sulfuric acid-aided synthesis of aliphatic organosiloxanes through the cleavage of one methyl group from the trimethylsilyl moiety.^[6a] Kinetic studies confirmed a pseudo-first order character of the reaction, involving an “electrophilic attack” on the carbon center followed by the formation of methane and a (at least formally) silylium-ion intermediate in the rate-determining step.^[6b] Later, a series of experiments was described by O'Brien on the stepwise protolytic cleavage of C(sp³)–Si bonds in tetra- and trialkylsilanes employing acid systems stronger than concentrated sulfuric acid, including HSO₃F/SbF₅/SO₂, HSO₃F/SO₂, and HSO₃F.^[7] The downside of these approaches is the difficulty of isolating the products from super acidic media. Independent reports by Olah^[8] and Demuth^[9] about the electrophilic demethylation overcame this problem. By using triflic acid, one of the methyl groups in tetramethylsilane is selectively protonated, affording trimethylsilyl triflate in almost quantitative yield. Our laboratory recently showed that Reed's carborane acids are also capable of performing selective protonation of one alkyl group, thereby providing access to various counteranion-stabilized silylium ions.^[10] As to nucleophilic demethylation, hard oxygen nucleophiles have been mostly employed^[11] but, unless intramolecular, modest substrate specificity has so far limited synthetic applications [Eq. 3].

By clever combination of those electro- and nucleophilic activation strategies, Matsunaga, Yoshino, and co-workers accomplished the chemoselective C(sp³)–Si bond cleavage in tetraalkylsilanes using iodine tris(trifluoroacetate) (ITT) and merged their new method with the aforementioned oxidative degradation of the heteroatom-substituted silicon intermediate [Eq. 4].^[12] That two-step sequence is reminiscent of the original report on the Fleming oxidation.^[3a] The use of an electrophilic iodine reagent is a judicious choice for such transformation as evidenced by an early work from Eaborn^[13] [Eq. 5] and an unexpected finding by Shindo and co-workers^[14] [Eq. 6].

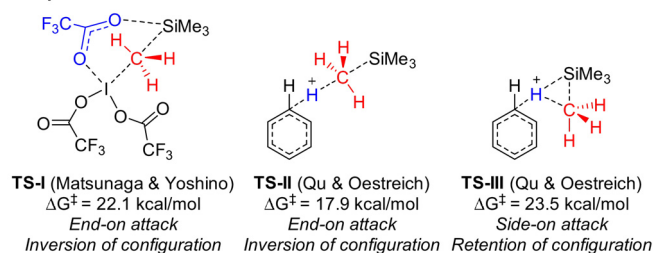
As outlined in Scheme 1 (top), the computed mechanism of the demethylation step reveals that in solution the dimeric ITT complex [ITT]₂ first converts into more reactive monomeric forms, that is the conformers ITT and ITT'. These then interact with the tetraalkylated silyl group. A concerted methyl group transfer from the silicon atom to the iodine(III)



DFT-computed Gibbs free energy profile



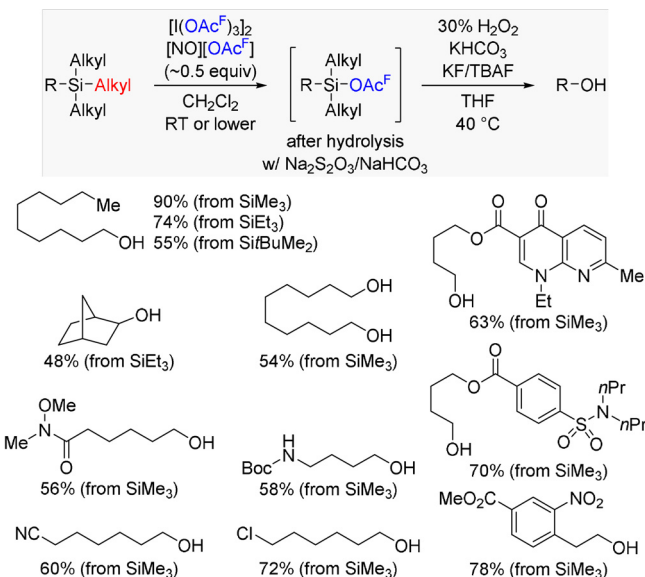
Computed transition states



Scheme 1. Concerted nucleophile-assisted electrophilic demethylation of a silicon atom by an electrophilic iodine reagent and, for comparison, protonation of a C(sp³)–Si bond.

center and formation of a silicon–oxygen bond leads to the generation of a silyl trifluoroacetate derivative (**TS-I**, bottom). For Me₃Si, the quantum-chemical calculations demonstrate an end-on interaction between the highly electrophilic iodine(III) center and one of the methyl groups. The same mechanistic picture had recently been drawn by Qu and Oestreich for the protolytic demethylation of Me₄Si.^[10] The end-on interaction of the proton with the back lobe of the $\sigma(\text{C–Si})$ orbital in **TS-II** was found to be energetically more favorable than a side-on interaction with the inner lobe as in **TS-III** ($\Delta\Delta G^\ddagger = 5.6$ kcal mol^{–1}, bottom).

The methodology introduced by the Matsunaga laboratory shows tremendous functional group tolerance, ranging from any type of carbonyl functionalities to various heterocycles (Scheme 2). Several densely functionalized molecules are compatible with both the demethylation and the oxidative



Scheme 2. Selected examples of the chemoselective cleavage of a C(sp³)–Si bond in unactivated tetraalkylsilanes with ITT followed by oxidative degradation of another C(sp³)–Si bond. TBAF = tetra-*n*-butylammonium fluoride, Boc = *tert*-butoxycarbonyl.

degradation steps. Aside from Me₃Si, the work also includes examples of Et₃Si and *t*BuMe₂Si; their dealkylation proceeds with lower yields.

Matsunaga, Yoshino, and co-workers have solved a long-standing challenge in synthetic methodology, that is, the oxidative degradation of a carbon–silicon bond in unactivated fully alkylated silanes. This brings the “unpopular” Me₃Si group back to life,^[5] thereby significantly expanding the selection of masked hydroxy groups beyond Me₂PhSi and heteroatom-substituted Tamao-type silyl groups. This work is complementary to the traditional protolysis approach but with unprecedented functional group tolerance. Although this methodology is currently limited to tetraalkylsilanes, it will be exciting to see future advances towards the chemoselective cleavage of C(sp³)–Si over C(sp²)–Si and C(sp)–Si bonds.

Acknowledgements

A.R. gratefully acknowledges the Berlin Graduate School of Natural Sciences and Engineering for a predoctoral fellowship (2018–2021). M.O. is indebted to the Einstein Foundation Berlin for an endowed professorship. Open access funding enabled and organized by Projekt DEAL.

Conflict of interest

The authors declare no conflict of interest.

[1] a) F. S. Kipping, L. L. Lloyd, *J. Chem. Soc. Trans.* **1901**, 79, 449–459; b) F. S. Kipping, *J. Chem. Soc. Trans.* **1907**, 91, 209–240.

- [2] a) C. Eaborn, *Pure Appl. Chem.* **1969**, *19*, 375–388 and cited references; for an authoritative review on electrophilic substitution reactions of mainly arylsilanes, see: b) T. H. Chan, I. Fleming, *Synthesis* **1979**, 761–786.
- [3] a) I. Fleming, R. Henning, H. Plaut, *J. Chem. Soc. Chem. Commun.* **1984**, 29–31; for oxidative degradation of heteroatom-substituted and as such activated silanes, see: b) K. Tamao, M. Akita, M. Kumada, *Organometallics* **1983**, *2*, 1694–1698; c) K. Tamao, T. Kakui, M. Akita, T. Iwahara, R. Kanatani, J. Yoshida, M. Kumada, *Tetrahedron* **1983**, *39*, 983–990.
- [4] G. R. Jones, Y. Landais, *Tetrahedron* **1996**, *52*, 7599–7662.
- [5] For a multi-step sequence, see: T. Torigoe, T. Ohmura, M. Sugimoto, *J. Org. Chem.* **2017**, *82*, 2943–2956.
- [6] a) L. H. Sommer, R. P. Pioch, N. S. Marans, G. M. Goldberg, J. Rockett, J. Kerlin, *J. Am. Chem. Soc.* **1953**, *75*, 2932–2934; b) L. H. Sommer, W. P. Barie, J. R. Gould, *J. Am. Chem. Soc.* **1953**, *75*, 3765–3768.
- [7] a) D. H. O'Brien, C. M. Harbordt, *J. Organomet. Chem.* **1970**, *21*, 321–328; b) D. D. Hopf, D. H. O'Brien, *J. Organomet. Chem.* **1976**, *111*, 161–169 and cited references.
- [8] G. A. Olah, A. Husain, B. G. B. Gupta, G. F. Salem, S. C. Narang, *J. Org. Chem.* **1981**, *46*, 5212–5214.
- [9] M. Demuth, G. Mikhail, *Synthesis* **1982**, 827.
- [10] Q. Wu, Z.-W. Qu, L. Omann, E. Irran, H. F. T. Klare, M. Oestreich, *Angew. Chem. Int. Ed.* **2018**, *57*, 9176–9179; *Angew. Chem.* **2018**, *130*, 9317–9320.
- [11] a) C. C. Price, J. R. Sowa, *J. Org. Chem.* **1967**, *32*, 4126–4127; see also: b) J. H. Smitrovich, K. A. Woerpel, *J. Org. Chem.* **1996**, *61*, 6044–6046.
- [12] K. Matsuoka, N. Komami, M. Kojima, T. Mita, K. Suzuki, S. Maeda, T. Yoshino, S. Matsunaga, *J. Am. Chem. Soc.* **2021**, *143*, 103–108.
- [13] C. Eaborn, *J. Chem. Soc.* **1949**, 2755–2764.
- [14] M. Shindo, K. Matsumoto, K. Shishido, *Angew. Chem. Int. Ed.* **2004**, *43*, 104–106; *Angew. Chem.* **2004**, *116*, 106–108 and cited references on demethylation.

Manuscript received: December 25, 2020

Version of record online: January 26, 2021