Radical Addition of Silanes to Alkenes Followed by Oxidation

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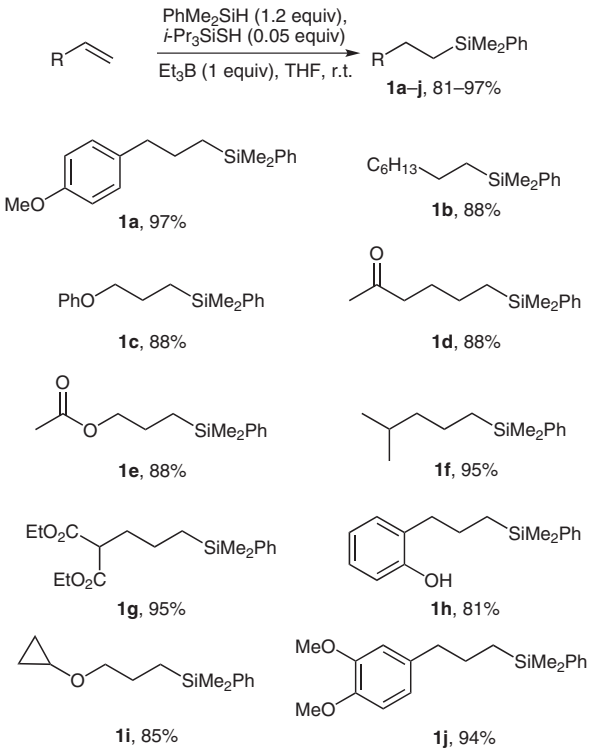
Abstract: Phenyldimethylsilane and trichlorosilane are shown to undergo efficient radical hydrosilylation reactions, on reaction with various alkenes, using triethylborane as the initiator. Adducts from the trichlorosilane reactions can be oxidised to afford alcohols in good yields. This two-step process leads to the anti-Markovnikov hydration of alkenes.

Key words: addition reaction, alcohol, alkene, radical reaction, silane

Organosilanes are useful intermediates in synthesis, and their reactivity has been exploited in synthetically important reactions including the Peterson olefination to form alkenes,[1] and the Fleming–Tamao or Tamao–Kumada oxidations to form alcohols.[2] One particularly mild synthetic approach to organosilanes involves the addition of silicon hydrides to alkenes, via regioselective addition of silyl radical intermediates to C=C bonds.[3] Although this radical hydrosilylation reaction has been reported in the literature, subsequent transformations of the organosilane adducts, to form useful synthetic targets, has rarely been exploited.[4] Consequently, this paper describes our novel results on the radical addition reactions of a range of silicon hydrides, to various alkenes under mild conditions, and their subsequent oxidation using different reagents to form alcohols. Overall, this method leads to the anti-Markovnikov hydration of a C=C bond and it complements the classical hydroboration followed by oxidation methodology.

Our initial studies focussed on the development of a mild and efficient method of hydrosilylation. Previous work by Roberts[5] had shown that, in conjunction with a thiol catalyst, alkyl- or arylsilanes efficiently add to C=C bonds, typically using di-*tert*-butyl hyponitrite as the initiator at 60 °C. To develop a milder method of hydrosilylation, our studies investigated the use of triethylborane as initiator at room temperature, and we explored the addition of phenyldimethylsilane (1.2 equiv) to alkenes (1 equiv) using triisopropylsilanethiol (0.05 equiv) as the catalyst. Optimisation studies showed that for efficient addition of the silane to the C=C bond, one equivalent of triethylborane (added in two equal portions) was required, as shown in Scheme 1. Under these conditions it was found that phenyldimethylsilane adds regioselectivity to electron-rich terminal C=C bonds, in the presence of a range of functional groups, to afford adducts **1a**–**j** in 81–97% yield after column chromatography.[6,7]

Attention then turned to oxidative removal of the silyl group using oxidation conditions developed by Fleming[2] (Scheme 2). Cleavage of the Si–Ph bond of **1a**–**c** was efficiently accomplished using boron trifluoride acetic acid complex to form the fluorosilanes **2a**–**c** in 75–88% yield.[8] Subsequent oxidation using MCPBA and potassium fluoride gave the desired alcohols **3a**–**c**, but in our hands, in only moderate yields of 25–31%.[9] Unfortunately, when treating the phenyldimethylsilanes with MCPBA and potassium fluoride in alternative solvents to DMF, or using AcOOH/Et_3N as the oxidising agent, there was no improvement in the yields of the alcohols. In addition, a one-pot conversion of the phenyldimethylsilanes **1a**–**c** into alcohols **3a**–**c** was explored, using various oxidising conditions (including KBr, AcOOH, NaOAc, AcOH or Br_2, AcOOH, NaOAc, AcOH), but these also gave the alcohols in low yield (typically less than 10%).



Scheme 1

In an attempt to increase the efficiency of the transformation, the radical addition of ethoxysilanes and methoxy-

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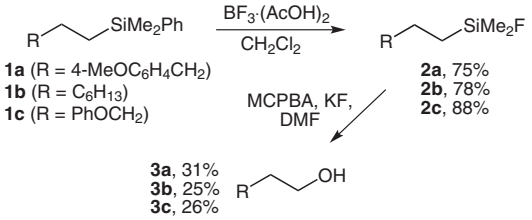
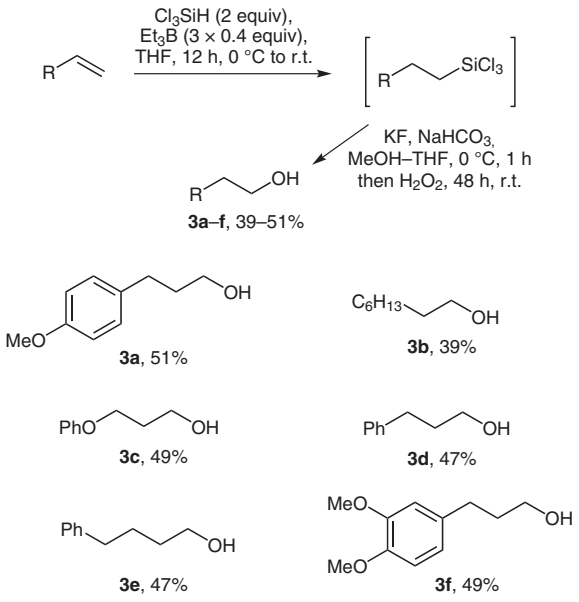
silanes [including $(EtO)_3SiH$, $(EtO)_2MeSiH$, $(MeO)_3SiH$, and $(MeO)_2MeSiH$] to alkenes, to give alkoxysilanes, which are precursors of the Tamao oxidation, were investigated. However, it was found that initiation using Et_3B and a thiol catalyst resulted in mainly recovered starting material. Even when using *t*-BuOO*t*-Bu as initiator, and heating in a sealed tube, only starting alkene was recovered.



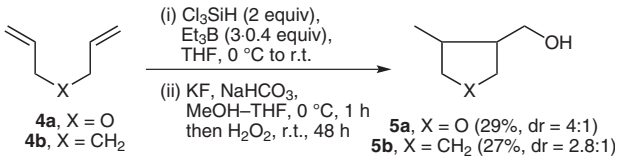
Scheme 2

It was then decided to investigate the radical addition of trichlorosilane to a C=C bond[10] using triethylborane as the initiator. Pleasingly, it was found that reaction of trichlorosilane (2 equiv) and triethylborane (3 × 0.4 equiv) with 1-allyl-4-methoxybenzene (1 equiv), in an ice-bath and in the absence of a thiol catalyst, resulted in complete conversion of the alkene into the trichlorosilane adduct (as indicated by the ^1H NMR spectrum of the unpurified reaction mixture).[11] Due to the high reactivity of the trichlorosilane adduct, isolation and purification was not straightforward and so the unpurified adduct was immediately treated under Tamao oxidation conditions, with potassium fluoride and sodium hydrogen carbonate, followed by the addition of hydrogen peroxide. This two-step sequence afforded the desired alcohol 3-(4-methoxyphenyl)propan-1-ol (**3a**) in 51% overall yield (Scheme 3).[12] This novel radical addition–oxidation sequence was successfully applied to the synthesis of alcohols **3b–f** in similar yields.



Scheme 3

Following the successful addition of trichlorosilane to terminal alkenes, the cyclisation of 1,6-dienes, followed by oxidation, was attempted (Scheme 4). It was found that, under the standard conditions used for the terminal alkenes, the radical addition of trichlorosilane to diallyl ether **4a** or hepta-1,6-diene **4b** resulted in polymerisation. However, efficient cyclisation was found to occur under increased dilution to afford the corresponding trichlorosilyl adducts in reasonable yields. Subsequent oxidation of the unpurified cyclic adducts resulted in the isolation of the expected alcohols **5a**,**b** (as predominantly the *cis* diastereomers).



Scheme 4

In conclusion, this paper has shown that phenyldimethylsilane adds efficiently to a range of terminal alkenes under mild conditions using triethylborane as the radical initiator in the presence of triisopropylsilanethiol. Oxidative removal of the phenyldimethylsilyl group from the adducts was then examined, and although efficient conversion to the fluorosilanes was possible, subsequent oxidation gave the desired alcohols in only low yields.

Pleasingly, it was also found that trichlorosilane adds efficiently to terminal C=C bonds in the presence of triethylborane as radical initiator (but in the absence of a thiol catalyst). The unpurified adducts were then subjected to the Tamao oxidation conditions to afford the desired alcohols in good yields. A combined radical addition–cyclisation–oxidation sequence is also possible.

Acknowledgment

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References and Notes

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(6) All new compounds gave spectroscopic and HRMS data in accord with their structures.

(7) **Typical Procedure for the Addition of Phenyldimethylsilane to Alkenes**

To a stirred solution of the alkene (10 mmol, 1 equiv), phenyldimethylsilane (2.0 g, 15 mmol, 1.5 equiv) in THF (3 mL) was added Et_3B in THF (0.5 mL, 1 M solution, 5 mmol, 0.5 equiv) and, shortly after, triisopropylsilane thiol (105 μL, 0.5 mmol, 5 mol%, care required due to noxious smell). After stirring at r.t. for 1 h, a further portion of Et_3B in THF (0.5 mL, 1 M solution 5 mmol, 0.5 equiv) was added and the mixture was left stirring overnight. Removal of the solvent under reduced pressure afforded the crude product which was purified by flash silica chromatography (elution gradient PE to PE–EtOAc = 5:1) to afford the silane addition products **1a–j** (81–97%).

Representative Analytical Data

[3-(4-Methoxyphenyl)propyl]dimethyl(phenyl)silane (1a)

R_f = 0.45 (PE–EtOAc = 10:1). IR (thin film): ν_{max} = 3010 (w), 2988 (w), 2959 (w), 2837 (w), 1743 (m), 1503 (w), 1512 (s), 1466 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.53 (2 H, m, ^{Ar}CH), 7.42–7.38 (3 H, m, ^{Ar}CH), 7.11 (2 H, app dd, *J* = 8.6, 2.1 Hz, ^{Ar}CH), 6.87 (2 H, app dd, *J* = 8.6, 2.1 Hz, ^{Ar}CH), 3.81 (3 H, s, OCH_3), 2.61 (2 H, t, *J* = 7.7 Hz, $^{Ar}CH_2$), 1.71–1.63 (2 H, m, CH_2), 0.86–0.79 (2 H, m, $SiCH_2$), 0.29 [6 H, s, $Si(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9 (^{Ar}CO), 139.6 (^{Ar}C), 134.4 (^{Ar}C), 133.7 (2 × ^{Ar}CH), 129.5 (2 × ^{Ar}CH), 128.9 (^{Ar}CH), 127.9 (2 × ^{Ar}CH), 113.7 (2 × ^{Ar}CH), 55.0 (OCH_3), 38.5 ($^{Ar}CH_2$), 25.8 (CH_2), 15.0 ($SiCH_2$), –3.5 [2 × $Si(CH_3)_2$]. ESI-MS: *m/z* (%) = 285 (20), 284 (100) [M^+], 207 (10).

Octyl(dimethyl)(phenyl)silane (1b)

R_f = 0.80 (PE). IR (thin film): ν_{max} = 3058 (w), 2918 (s), 2857 (s), 2120 (w), 1470 (m), 1431 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.45 (2 H, m, ^{Ar}CH), 7.38–7.30 (3 H, m, ^{Ar}CH), 1.33–1.20 (12 H, m, CH_2), 0.91 (3 H, t, *J* = 7.0 Hz, CH_3), 0.77 (2 H, t, *J* = 8.1 Hz, $SiCH_2$), 0.29 [6 H, s, $Si(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.7 (^{Ar}C), 133.5 (2 × ^{Ar}CH), 128.7 (^{Ar}CH), 127.7 (2 × ^{Ar}CH), 33.6 (CH_2), 31.9 (CH_2), 29.3 (2 × CH_2), 23.8 (CH_2), 22.6 (CH_2), 18.2 (CH_2), 15.7 (CH_2), 14.1 (CH_3), –3.0 [$Si(CH_3)_2$]. ESI-MS: *m/z* (%) = 250 (20), 249 (100) [MH^+], 233 (30), 171 (20)

[3-(3,4-Dimethoxyphenyl)propyl]dimethyl(phenyl)-silane (1j)

R_f = 0.30 (PE–EtOAc = 10:1). IR (thin film): ν_{max} = 3004 (w), 2990 (w), 2952 (w), 2929 (w), 2833 (w), 1739 (m), 1509 (w), 1514 (s), 1464 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.44 (2 H, m, ^{Ar}CH), 7.37–7.34 (3 H, m, ^{Ar}CH), 6.79 (1 H, d, *J* = 8.0 Hz, ^{Ar}CH), 6.69 (1 H, dd, *J* = 8.0, 1.9 Hz, ^{Ar}CH), 6.66 (1 H, d, *J* = 1.9 Hz, ^{Ar}CH), 3.86 (6 H, s, OCH_3), 2.57 (2 H, t, *J* = 7.6 Hz, $^{Ar}CH_2$), 1.68–1.56 (2 H, m, CH_2), 0.83–0.77 (2 H, m, $SiCH_2$), 0.26 [6 H, s, $Si(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.7 (^{Ar}CO), 147.1 (^{Ar}CO), 139.3 (^{Ar}C), 135.3 (^{Ar}C), 133.7 (2 × ^{Ar}CH), 128.9 (^{Ar}CH), 127.8 (2 × ^{Ar}CH), 120.4 (^{Ar}CH), 111.7 (^{Ar}CH), 111.1 (^{Ar}CH), 56.0 (OCH_3), 55.9 (OCH_3), 39.3 ($^{Ar}CH_2$), 26.1 (CH_2), 15.4 ($SiCH_2$), –3.0 [2 × $Si(CH_3)_2$]. ESI-MS: *m/z* (%) = 315 (20), 314 (100) [M^+], 283 (30), 237 (15).

(8) **Typical Procedure for the Oxidation of Phenyldimethylsilanes 1a–c**

To a stirred solution of the dimethylphenylsilane **1a–c** (5.0 mmol, 1 equiv) in dry CH_2Cl_2 (15 mL) at r.t. was added BF_3–AcOH complex (1.4 mL, 10.0 mmol, 2 equiv), and the resulting solution was stirred for 6 h, during which time the solution turned orange. The reaction mixture was quenched by being poured slowly into a stirred solution of 1 M $NaHCO_3$ (100 mL), the aqueous layer was extracted with CH_2Cl_2 (2 × 75 mL), the combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to afford the fluorosilanes **2a–c** as a pale yellow oil (0.71–0.93 g, 75–88%). No further purification was carried out, and the resulting oil was subjected to the oxidation conditions.

(9) **Typical Procedure for the Oxidation of Fluorosilanes 2a–c**

To a stirred solution of the unpurified fluorosilane **2a–c** (3.4–4.0 mmol, 1 equiv) and anhyd KF (0.39–0.46 g, 6.8–8.0 mmol, 2 equiv) in dry DMF (5 mL) at r.t. was added dropwise a solution of MCPBA (1.38–1.62 g, 85%, 6.8–8.0 mmol, 2 equiv) in dry DMF (10 mL). The resulting solution was stirred for 4 h at r.t. The reaction mixture was diluted with CH_2Cl_2 (75 mL) and washed successively with aq $Na_2S_2O_3$ (2 × 50 mL), aq Na_2CO_3 (2 × 50 mL), brine (50 mL), then dried over $MgSO_4$ and purified by flash chromatography (PE–Et_2O = 10:1) to afford alcohols **3a–c** as colourless oils (0.11–0.18 g, 25–31%).

(10) For the addition of trichlorosilane to alkenes using a peroxide initiator see, for example: (a) Speier, J. L.; Webster, J. A. *J. Org. Chem.* **1956**, *21*, 1044. (b) Sommer, L. H.; Pietrusza, E. W.; Whitmore, F. C. *J. Am. Chem. Soc.* **1947**, *69*, 188.

(11) **Typical Procedure for the Addition of Trichlorosilane to Alkenes 1a–c**

To a stirred solution of the alkene (5.0 mmol, 1 equiv) in THF (5 mL) at 0 °C, under air, was added Cl_3SiH (1.0 mL, 10.0 mmol, 2 equiv) followed by the slow dropwise addition of Et_3B (2.0 mL, 1 M solution in THF, 2.0 mmol, 0.4 equiv). The resulting solution was stirred at 0 °C for 1 h, after which a further portion of Et_3B (2.0 mL, 1 M solution in THF, 2.0 mmol, 0.4 equiv) was added, and the mixture was stirred for a further 1 h at 0 °C followed by addition of a further portion of Et_3B (2.0 mL, 1 M solution in THF, 2.0 mmol, 0.4 equiv). The resulting solution was stirred at 0 °C for 1 h then warmed to r.t. and stirred for a further 4 h. Removal of the solvent under reduced pressure afforded the crude trichlorosilane addition product, as an oil.

(12) **Typical Procedure for the Oxidation of Trichlorosilanes to Give Alcohols 3a–f**

The crude trichlorosilane addition product was taken up in THF (75 mL), and the solution was stirred at r.t. (under air) while MeOH (75 mL) was slowly added, after which KF (2.6 g, 45.0 mmol, 9 equiv) and $KHCO_3$ (9.00 g, 90.0 mmol 18 equiv) were added, and the suspension was stirred for 1 h. To the resulting white suspension was added H_2O_2 (5.1 mL, 30% solution, 45.0 mmol, 9 equiv), and the reaction mixture was vigorously stirred for 24 h; after which $Na_2S_2O_3·5H_2O$ (7.4 g, 30.0 mmol, 6 equiv) was added, and the mixture was stirred for 1 h. The mixture was filtered through a Celite plug, and the filter cake was rinsed with Et_2O (50 mL). The

filtrate was concentrated under vacuum, the resulting residue was dissolved in CH_2Cl_2 (50 mL), dried over $MgSO_4$, and the solvent was removed in vacuo to afford the crude product. This was purified by flash silica chromatography (elution gradient PE to PE–EtOAc = 2:1) to afford alcohols **3a–f** (39–51%).