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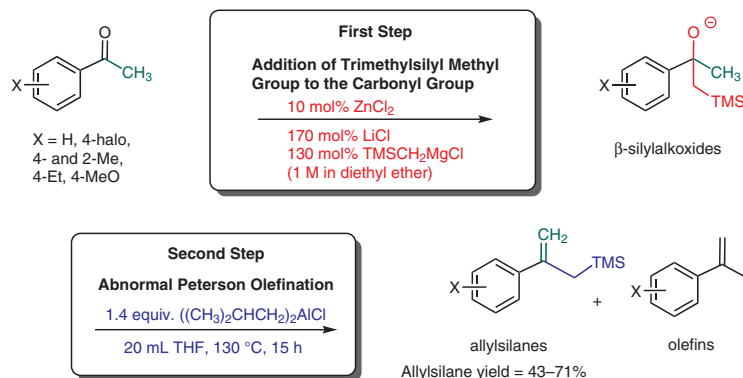SynOpen   M. L. D. Kwan et al.   THIEME OPEN ACCESS   Letter

Convenient One-Pot Synthesis of Allylsilanes from Enolizable Ketones

Man Lung D. Kwan* [ORCID]
Paul R. Challen
Quynh D.-D. Tran

Department of Chemistry, John Carroll University,
1 John Carroll Blvd, University Heights, OH 44118, USA
mlkwan@jcu.edu

First Step
Addition of Trimethylsilyl Methyl Group to the Carbonyl Group
10 mol% ZnCl$_2$
170 mol% LiCl
130 mol% TMSCH$_2$MgCl
(1 M in diethyl ether)

X = H, 4-halo, 4- and 2-Me, 4-Et, 4-MeO

β-silylalkoxides

Second Step
Abnormal Peterson Olefination
1.4 equiv. ((CH$_3$)$_2$CHCH$_2$)$_2$AlCl
20 mL THF, 130 °C, 15 h

allylsilanes   +   olefins

Allylsilane yield = 43–71%

Abstract A convenient one-pot synthesis of allylsilanes from enolizable methyl aryl ketones has been developed. The first step involves nucleophilic addition of the trimethylsilylmethyl group to ketones using the alkylation method developed by Ishihara with slight modification to generate the corresponding β-silylalkoxides. The second step entails addition of diisobutylaluminum chloride and heating at about 130 °C overnight to afford allylsilanes in fair yields.

Key words abnormal Peterson olefination, allylsilane, one-pot synthesis

Allylsilanes are versatile allylic anion equivalents.[1,2] Unlike most allyl organometallic species such as allylic Grignard reagents, allylic rearrangement is not a concern for allylsilanes. Formation of the new bond via electrophilic reaction occurs regiospecifically at the γ-position of the allylsilane (Scheme 1).[1e]


Scheme 1
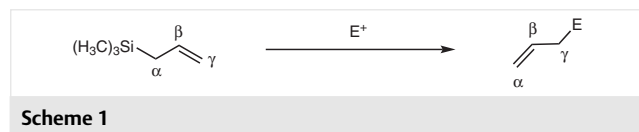
Many allylsilane syntheses were reported during the 1990s.[2] Most popular are transformations of alkenes; whereas transformations of carbonyl compounds into allylsilanes are scarce, although one obvious example utilizes the Wittig protocol to convert ketones or aldehydes.[2e] However, this method requires multiple synthetic steps starting from triphenylphosphine to furnish the corresponding allylsilane, and removing the triphenylphosphine oxide by-product is challenging (Scheme 2).[3]
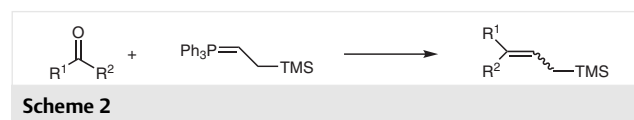
Scheme 2

Another example uses the Peterson olefination[4] protocol to convert an ester into the desired allylsilane via loss of trimethylsilanol from the initial bis-adduct (Scheme 3).[2d]
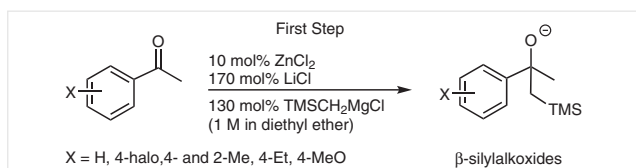

Scheme 3
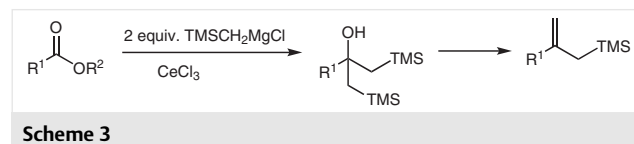
The standard Peterson olefination converts β-hydroxysilanes into desilylated olefins under either acidic or basic conditions. Battiste and Kwan reported the use of alumoxanes in vinylsilane synthesis.[5] The methodology employs a Peterson protocol to convert non-enolizable ketones into the corresponding vinylsilanes. Since the silyl group is intact during the elimination, these are referred to as abnormal Peterson olefinations. Doxsee and Kwan extended the vinylsilane synthesis, starting from non-enolizable aryl aldehydes via the abnormal Peterson olefination.[6] Instead of using alumoxanes as amphoteric reagents, Doxsee and Kwan used the Tebbe reagent for the elimination step. Kwan's subsequent work revealed that an additional Lewis acid such as the titanium in Tebbe's reagent assists the deoxygenation.[7] We report herein the use of the abnormal Peterson protocol to convert enolizable ketones into allylsilanes in a convenient two-step, one-pot reaction. Alkylating

enolizable ketones and aldehydes is often challenging because it can give undesired products such as self-aldol condensation products. Several synthetic methods have been developed to alkylate enolizable ketones and aldehydes effectively.[8] Recognizing the ability of Zn^{2+} to cleave carbon–oxygen bonds,[9] we have employed the alkylation method, using $ZnCl_2$, developed by Ishihara et al.[8d] for our first reaction step with slight modification.

In Ishihara's method, the $(CH_3)_3SiCH_2$ group (20 mol%) was used as a non-transferable ligand in the catalytic alkylzinc(II) ate complex and to enhance its catalytic efficacy in Grignard reactions (nucleophilic additions to carbonyl group). Reaction of excess $TMSCH_2MgCl$ (≥ 110 mol%) with acetophenone led to the formation of the corresponding β-hydroxysilane. We decided to examine the scope of the reaction of excess $TMSCH_2MgCl$ further with other aryl enolizable ketones to yield the corresponding β-silylalkoxides.

Enolizable aryl ketones were added to a heterogeneous mixture of 130 mol% trimethylsilylmethyl magnesium chloride (1 M in diethyl ether), 10 mol% $ZnCl_2$ and 170 mol% LiCl (Scheme 4). The original protocol called for the use of THF as solvent. Our preliminary study focused on the reaction with acetophenone by subjecting acetophenone to the reaction protocol with and without the use of THF as solvent. The reported protocol called for 2 hours stirring at 0 °C after dropwise addition of ketone also at 0 °C. Our results suggested that the reaction can be allowed to stir overnight (ca. 12 h) without significant formation of side-products, even in the absence of THF solvent. Diethyl ether from the (trimethylsilyl)methyl magnesium chloride solution (1 M) appears to suffice as solvent to facilitate the formation of β-silylalkoxides.

Scheme 4

A mixture of hexanes was also examined as a possible solvent. While no significant difference was observed in the first reaction step (converting the enolizable ketones into their corresponding β-silylalkoxides), the subsequent elimination reaction generally required longer reaction times and higher temperatures.
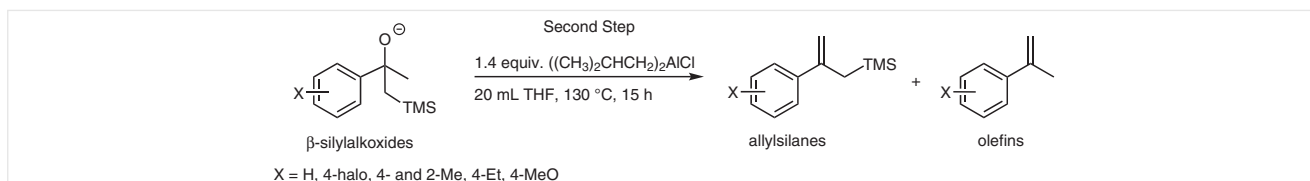
To carry out the abnormal Peterson reaction of the β-silylalkoxides, diisobutylaluminum chloride was added followed by THF. The resulting mixture was transferred by using a cannula into a sealed tube under argon and the mixture was heated at 130 °C for 15 hours (Scheme 5), followed by washing with saturated aqueous sodium tartrate and work-up. The results are summarized in Table 1.

**Table 1** Two Step, One-Pot Synthesis of Allylsilane from Aryl Methyl Ketones

Entry	Aryl methyl ketones	Yield (%)[a]	
		Allysilane	Olefin
1	X = 4-H	58[10]	8[11]
2	X = 4-F	71[10]	0[12]
3	X = 4-Cl	63[13]	0[14]
4	X = 4-Br	68[15]	0[12]
5	X = 4-OCH_3	43[16]	32[12]
6	X = 4-CH_3	43[16]	7[14]
7	X = 4-CH_2CH_3	64[16]	11[17]
8	X = 2-CH_3	multiple products: aldol products + allylsilane + olefin	

[a] References for ^1H NMR spectroscopic comparison.

The Ishihara study[8d] briefly examined the use of the trimethylsilylmethyl group $((CH_3)_3SiCH_2–)$ as the alkylating agent. We modified the reported protocol slightly and used it to alkylate substituted aryl methyl ketones in the first step, yielding the corresponding β-silylalkoxides. Heating the reaction mixture containing the silylalkoxide derived from acetophenone (Table 1, entry 1) reaction in THF (without adding diisobutylaluminum chloride) simply produced the corresponding β-hydroxysilane. This indicates that additional amphoteric reagent, diisobutylaluminum chloride, is required for the abnormal Peterson olefination to yield the corresponding allylsilanes. Diisobutylaluminum chloride was used rather than less bulky diethylaluminum chloride since, in the acetophenone reaction (entry 1), the latter yielded a greater amount of olefin product.

Scheme 5

p-Haloaryl methyl ketones afforded the corresponding allylsilanes in acceptable yields with high chemoselectivity. Reactions of electron-rich ketones (Table 1, entry 5–7) afforded a mixture of the corresponding allylsilanes and olefins. It is worth noting that the most electron-rich ketone (entry 5) produced the highest amount of the corresponding olefin. To determine in which step the corresponding olefin is produced in the two-step, one-pot synthesis, we ran a series of alkylation reactions to produce β-hydroxysilanes for each ketone. Reactions of electron-rich ketones yielded a mixture of β-silylalcohols and olefins while *p*-haloaryl methyl ketones yielded primarily β-silylalcohols. Alkylation of *o*-methylaryl methyl ketone gave multiple products such as aldol addition products, olefins, and β-silylalcohols.

Applying the developed protocol with 2-methylacetophenone afforded multiple products (Table 1, entry 8). To understand the system better, we applied Ishihara's protocol in attempts to convert 2-methyl-, 2-fluoro-, and 3-methylacetophenone into their corresponding β-hydroxysilanes (Scheme 6). Repeated reactions yielded multiple products from these three ketones. ^{1}H NMR spectroscopic and TLC analyses indicated a minimum of three components in the mixture: recovered ketone, self-aldol condensation product, and β-hydroxysilane. Thus, our attempts to prepare allylsilanes were ineffective with these three ketones. We also examined the developed protocol with 4-nitroacetophenone but, given the vulnerability of the nitro group to nucleophilic attack from the Grignard reagent, it is not surprising that the reaction failed to produce the corresponding allylsilane product.[18]

Scheme 6
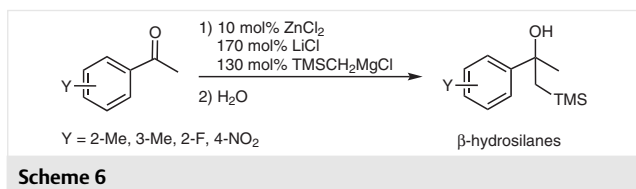
In conclusion, we have employed and slightly modified the method for alkylation of enolizable ketones developed by Ishihara to alkylate a series of methyl aryl ketones with a trimethylsilylmethyl ((CH_3)$_3$SiCH$_2$–) group to generate β-silylalkoxides as the first step of our one-pot allylsilane synthesis protocol. The second step entails addition of diisobutylaluminum chloride with heating, leading to the abnormal Peterson olefination reaction, affording allylsilanes in fair yield.[19] This one-pot synthesis works particularly well with *p*-haloaryl methyl ketones.

Funding Information

Supporting Information

References and Notes

(1) For examples of synthetic uses of allylsilanes, see: (a) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley: Chichester, **2000**. (b) Fleming, I.; Dunoguès, J.; Smithers, R. *Organic Reactions*; John Wiley & Sons, Inc: New York, **2004**, 57–575. (c) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, *5*, 941. (d) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (e) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. (f) Sakurai, H.; Hosomi, A.; Hayashi, J. *Org. Synth.* **1984**, *62*, 86. (g) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293. (h) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763.

(2) For examples of the preparation of allylsilanes, see: (a) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 12650. (b) Murakami, K.; Yorimitsu, H.; Oshima, K. *J. Org. Chem.* **2009**, *74*, 1415. (c) Bhushan, V.; Lohray, B. B.; Enders, D. *Tetrahedron Lett.* **1993**, *34*, 5067. (d) Bunnellem, W. H.; Narayanan, B. A. *Tetrahedron Lett.* **1987**, *28*, 6261. (e) Fleming, I.; Marchi, D. *Synthesis* **1981**, 560.

(3) Batesky, D. C.; Goldfogel, M. J.; Weix, D. J. *J. Org. Chem.* **2017**, *82*, 9931.

(4) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780.

(5) Kwan, M. L.; Battiste, M. A. *Tetrahedron Lett.* **2002**, *43*, 8765.

(6) Kwan, M. L.; Yeung, C. W.; Breno, K. L.; Doxsee, K. M. *Tetrahedron Lett.* **2001**, *42*, 1411.

(7) Elimination of the β-silyl alkoxides with alanes (not Tebbe's reagent) requires higher temperatures and prolonged reflux time (several days).

(8) (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392. (b) Krasovskiy, A.; Kopp, F.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 497. (c) Metzger, A.; Gavryushin, A.; Knochel, P. *Synlett* **2009**, 1433. (d) Hatano, M.; Ito, O.; Suzuki, S.; Ishihara, K. *J. Org. Chem.* **2010**, *75*, 5008.

(9) Lucas, H. J. *J. Am. Chem. Soc.* **1930**, *52*, 802.

(10) Mo, J.; Xu, L.; Xiao, J. *J. Am. Chem. Soc.* **2005**, *127*, 751.

(11) Pandey, S. K.; Greene, A. E.; Poisson, J. *J. Org. Chem.* **2007**, *72*, 7769.

(12) Fryszkowska, A.; Fisher, K.; Gardiner, J. M.; Stephens, G. M. *J. Org. Chem.* **2008**, *73*, 4295.

(13) Liu, J.; Chu, L.; Qing, F.-L. *Org. Lett.* **2013**, *15*, 894.

(14) Gupton, J. T.; Layman, W. J. *J. Org. Chem.* **1987**, *52*, 3683.

(15) Walkowiak, J.; Martinez del Campo, T.; Ameduri, B.; Gouverneur, V. *Synthesis* **2010**, 1883.

(16) Cai, G.; Zhou, Z.; Wu, W.; Yao, B.; Zhang, S.; Li, X. *Org. Biomol. Chem.* **2016**, *14*, 8702.

(17) Isagulyants, V. I.; Kustanovich, Z. D.; Dessuki, A. M. *Zh. Prikl. Khim.* **1967**, *40*, 1355.

(18) For examples of reactions of Grignard reagents with nitro-compounds, see: (a) Gilman, H.; McCracker, R. *J. Am. Chem. Soc.* **1929**, *51*, 821. (b) Bartoli, G.; Bosco, M.; Dalpozzo, R. *Tetrahedron Lett.* **1985**, *26*, 115. (c) Sapountzis, I.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 1610.

(19) **Allylsilane Synthesis; General Procedure**
To a 100 mL Schlenk flask, ZnCl$_2$ (10 mol%) was added and melt-dried with a heat gun under reduced pressure (5 Torr, 5 min). LiCl (170 mol%) was then added, followed by heating with a

heat gun under reduced pressure (5 Torr, 5 min). After cooling back to room temperature, trimethylsilylmethyl magnesium chloride (1 M in diethyl ether; 130 mol%) was added to the mixed dried salts under argon. The resulting heterogeneous mixture was allowed to stir for 15 min at room temperature followed by cooling to 0 °C. The requisite aryl methyl ketone (500 mg) was added dropwise by using a syringe to the heterogeneous mixture over 1 h at 0 °C and the resulting mixture was allowed to stir for an additional 2 h at 0 °C. Diisobutylaluminum chloride (140 mol%) and anhydrous THF (20 mL) were then added to the mixture at 0 °C. This mixture was then transferred by using a cannula from the 100 mL Schlenk flask to a 150 mL pressure flask. The pressure flask was capped and heated at 130 °C for 15 h. The reaction was quenched by washing the mixture with 10% sodium tartrate solution and the mixture was extracted with diethyl ether. The ether extract was dried over $MgSO_4$. Gravity filtration followed by solvent evaporation gave oily allyl silane products.

[(2-Phenyl)allyl]trimethylsilane (1): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.42–7.20 (m, 5 H), 5.14 (d, J = 1.8 Hz, 1 H), 4.88 (d, J = 1.8 Hz, 1 H), 2.03 (d, J = 1.2 Hz, 2 H), –0.09 (s, 9 H).

[2-(4-Fluorophenyl)allyl]trimethylsilane (2): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.34–7.30 (m, 2 H), 7.00–6.85 (m, 2 H), 5.05 (d, J = 1.8 Hz, 1 H), 4.83 (s, 1 H), 1.97 (d, J = 0.9 Hz, 2 H), –0.12 (s, 9 H).

[2-(4-Chlorophenyl)allyl]trimethylsilane (3): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.35–7.28 (m, 4 H), 5.11 (d, J = 1.5 Hz, 1 H), 4.87 (d, J = 0.9 Hz, 1 H), 1.98 (d, J = 0.9 Hz, 2 H), 0.10 (s, 9 H).

[2-(4-Bromophenyl)allyl]trimethylsilane (4): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.47–7.26 (m, 4 H), 5.12 (d, J = 1.8 Hz, 1 H), 4.89 (d, J = 1.5 Hz, 1 H), 1.98 (d, J = 0.9 Hz, 2 H), –0.08 (s, 9 H).

[2-(4-Methoxyphenyl)allyl]trimethylsilane (5): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.44–7.26 (m, 2 H), 6.90–6.80 (m, 2 H), 5.10 (s, 1 H), 4.79 (s, 1 H), 3.80 (s, 3 H), 1.98 (s, 2 H), –0.08 (s, 9 H).

[2-(4-Methylphenyl)allyl]trimethylsilane (6): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.44–7.11 (m, 4 H), 5.13 (d, J = 1.8 Hz, 1 H), 4.84 (s, 1 H), 3.56 (s, 3 H), 1.98 (s, 2 H), –0.08 (s, 9 H).

[2-(4-Ethylphenyl)allyl]trimethylsilane (7): ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.44–7.11 (m, 4 H), 5.12 (d, J = 1.5 Hz, 1 H), 4.84 (d, J = 0.9 Hz, 1 H), 2,65 (m, 2 H), 2.08 (s, 2 H), 1.25 (m, 3 H), –0.08 (s, 9 H).