Tetrahedron 72 (2016) 2293–2299

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Facile and highly selective silylation of vinylpyridines at the β-olefinic carbon by magnesium-promoted reduction

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ARTICLE INFO

Article history:
Received 26 February 2016
Received in revised form 8 March 2016
Accepted 9 March 2016
Available online 17 March 2016

Keywords:
Silylation
Vinylpyridine
Magnesium-promoted reduction

ABSTRACT

Magnesium-promoted reductive silylation of 2- and 4-vinylpyridines with chlorotrialkylsilanes in *N*-methylpyrrolidinone at room temperature led to the selective formation of a variety of the corresponding β-mono-silylated compounds at the terminal carbon atom in good to excellent yields, whereas silylation of 3-vinylpyridine under the same reduction conditions failed to give a complex mixture of silylated compounds. The difference of the results between 2- or 4-vinylpyridines and 3-vinylpyridine is attributed to that of the stabilizing effect to reaction intermediates by the resonance with the nitrogen atom of pyridine.

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1. Introduction

Organosilicons[1] are one of the most valuable synthetic intermediates, primarily because of their great versatility. For example, they are widely used as protecting groups,[2] especially, masking hydroxyl groups[3] and served as building blocks for many reactions, such as palladium-catalyzed Hiyama-coupling,[4] Tamao-Fleming oxidation[5] and Hosomi-Sakurai reaction.[6] The traditional synthetic method of organosilicon compounds sometimes involved the rigorous reaction conditions,[7] the use of expensive transition metal catalysts[8] or that of alkali metals such as lithium[9] and sodium.[10] Although Lewis acids such as aluminum chloride are widely used as a catalyst for hydrosilylation of alkenes or alkynes, recently,[11] the limitation of the applicable substrates is a troublesome problem. Therefore, regardless of these synthetic routes, further investigation on selective, efficient, and widely used methods in the preparation of organosilicon compounds has still been required.

In our previous studies, we developed umpoled syntheses of silicon-containing organic compounds by magnesium-promoted reductive silylation under the mild reaction conditions[12] and recently, we reported the synthesis of silylated allenes by the magnesium-promoted reduction at room temperature from aromatic conjugated ynones in high yields[13] (Scheme 1). In this study, we selected vinylpyridines as electrophilic compounds and tried a direct and simple silylation of vinylpyridines at room temperature with no use of transition metal catalysts. As a result, we explored a facile and efficient silylation of 2- and 4-vinylpyridines under the magnesium-promoted reduction conditions in *N*-methyl-2-pyrrolidinone (NMP), to give the corresponding β-mono-silylated products, most of which were not synthesized before, in good to excellent yield with high selectivity. The application of various kinds of silanes and vinylpyridines to this coupling reaction was investigated in detail under the optimized reaction conditions.

2. Results and discussion

As reported previously,[12–14] the magnesium-promoted reductive coupling reactions of aromatic carbonyl compounds usually required aprotic polar solvents such as *N*,*N*-dimethylformamide (DMF), NMP, and *N*,*N*-dimethylacetamide (DMAc). This research was initiated from the investigation on the solvent effects (Table 1), and 4-vinylpyridine **1a** in the presence of chlorotrimethylsilane (TMSCl) **2a** could be consumed only in those aprotic polar solvents, and the reaction in NMP gave **3aa** in 80% GC yield as a single product (Table 1, entry 3), while no reaction occurred in tetrahydrofuran (THF) and acetonitrile. This selective silylation of **1a** showed a great contrast with trifluoroacetylation of **1a**, in which an α-, β-double trifluoroacetylated product was obtained in part under any reaction conditions.[14d]

After the optimization of the equivalents of starting materials and reaction temperature (Table 2), the combination of 6 equiv of TMSCl **2a** and 3 equiv of magnesium at room temperature gave the best result (Table 2, entry 3). Lower temperature led to a decreased yield of **3aa** with the recovery of a small amount of starting materials (Table 2, entry 4).

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http://dx.doi.org/10.1016/j.tet.2016.03.042
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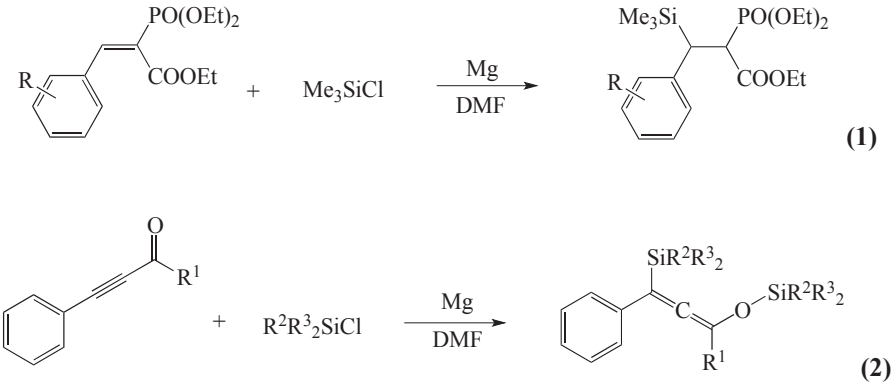
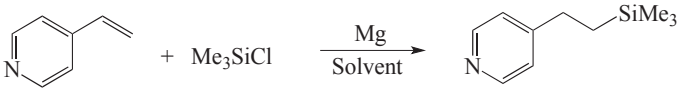


Scheme 1.

Table 1
Solvent effects of magnesium promoted silylation



1a **2a** **3aa**

Entry	Solvent	GC yield (%)
1	DMF	30
2	DMAc	55
3	NMP	80 (73)[a]
4	THF	No reaction
5	CH_3CN	No reaction

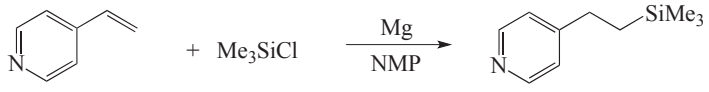
1a (5.0 mmol), **2a** (6 equiv), Mg (3 equiv), Solvent (30 mL), rt, 3 h, N_2 atmosphere.
[a] Isolated yield.

With the optimal reaction conditions in hand, the substrate scope with respect to the 4-vinylpyridines **1b**–**1m** was first explored (Table 3). It was found that the isolated yield decreased slightly to give 63% yield of **3ba** when a methyl group was substituted at the α-position of the vinyl group (Table 3, entry 1). On the contrary, the yield increased to 77–93% when the α-position was replaced by aromatic substituents with an electron-donating group at the *para*-position[15] (Table 3, entries 2–4). The product **3fa** was obtained in extremely low yield when a methyl group was introduced at the β-position (Table 3, entry 5).

This result was probably attributed to both the steric hindrance at the reacting point and the destabilizing electron-donating effect of the methyl group. On the other hand, reactions of TMSCl **2a** and 4-vinylpyridines **1** with an aromatic substituent at the β-position proceeded smoothly to afford silylated products **3ga**–**3ka** in good to excellent yields (Table 3, entries 6–10). It is noteworthy that a substituent at the *ortho*-position did not show the steric effect and **3ja** was obtained in 79% yield (Table 3, entry 9). Furthermore, a naphthyl substituent at the β-position gave only moderate yield of **3la**, which was more likely because the long conjugation system decreased the reactivity of the generated anionic species (Table 3, entry 11). Interestingly, when an aromatic substituent with an ester, an electron-withdrawing group, was replaced at β-position, a compound **4ma** was obtained as a main product with no silylation at the α-position or the β-position. Because the strong stabilizing effect to the generated anionic species by the ester group, made the β-position of the pyridine ring much more unreactive and the vinyl group was simply reduced.[14d] Then, the carbonyl group of ester was reduced to give the final compound **4ma**, partially.[16]

Attempts to extend this silylation to other chlorotrialkylsilanes were performed and several kinds of the corresponding β-monosilylated compounds **3ab**–**3ah** were obtained in moderate to good yields (Table 4). The coupling reactions with bulky silylating reagents showed the steric influence to silylation, remarkably. Namely, **3ac** was produced in 45% isolated yield, while more bulky *tert*-butyldimethylchlorosilane **2d** gave no formation of the desired compound **3**, instead, the dimeric compound of 4-vinylpyridine **1a**

Table 2
Optimization of reductive trimethylsilylation of **1a**

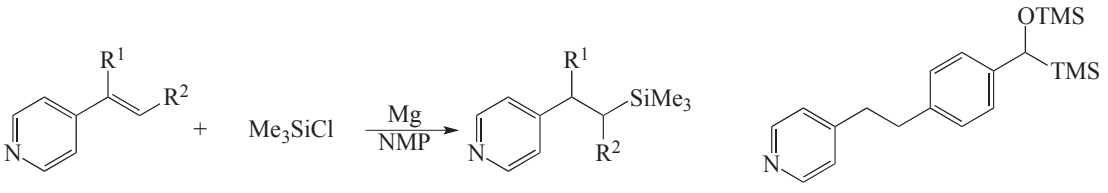


1a **2a** **3aa**

Entry	**2a** (equiv)	Mg (equiv)	GC yield (%)[a]
1	4	3	52
2	5	3	55
3	6	3	80 (73)[b]
4	6	3	65[c]
5	7	3	78
6	8	3	57
7	6	2	57
8	6	4	70

1a (5.0 mmol), NMP (30 mL), rt, 3 h, N_2 atmosphere.
[a] The starting material was consumed.
[b] Isolated yield.
[c] Reaction was performed at 0 °C.

Table 3
Mg-promoted silylation of 4-vinylpyridine derivatives

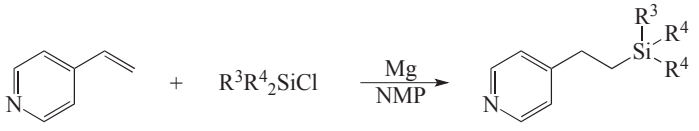


1 **2a** **3** **4ma**

Entry		R^1	R^2	Reduction potential (V)[a,b]		Isolated yield (%)[c]
1	**1b**	Me	H	−2.38	**3ba**	63
2	**1c**	Ph	H	−2.05	**3ca**	93
3	**1d**	4-$MeOC_6H_4$	H		**3da**	77
4	**1e**	4-MeC_6H_4	H		**3ea**	84
5	**1f**	H	Me	−2.36	**3fa**	18
6	**1g**	H	Ph	−1.94	**3ga**	91
7	**1h**	H	4-MeC_6H_4		**3ha**	90
8	**1i**	H	4-$MeOC_6H_4$	−2.02	**3ia**	72
9	**1j**	H	2-$MeOC_6H_4$	−1.96	**3ja**	79
10	**1k**	H	4-ClC_6H_4		**3ka**	70
11	**1l**	H	1-Naphthyl		**3la**	40
12	**1m**	H	4-$MeO_2CC_6H_4$			—[d]

1 (5.0 mmol), **2a** (6 equiv), Mg (3 equiv), NMP (30 mL), rt, 3 h, N_2 atmosphere.
[a] Working Electrode: Pt. Counter Electrode: Pt. Reference Electrode: Ag/AgCl. Solvent: NMP. Supporting Electrolyte: 1% n-Bu_4NClO_4. Scan Rate: 200 mV s^{-1}.
[b] The reduction potential of **1a** was −2.13 V under the same reduction conditions.
[c] The starting material was consumed.
[d] **4ma** was obtained in 29% yield, instead.

Table 4
Mg-promoted silylation of 4-vinylpyridine with various silylating agents



1a **2** **3**

Entry		R^3	R^4		Isolated yield (%)
1	**2b**	Et	Me	**3ab**	74[a]
2	**2c**	n-Bu	Me	**3ac**	45[a]
3	**2d**	t-Bu	Me		0
4	**2e**	Et	Et	**3ae**	61[a]
5	**2f**	CH_2Cl	Me	**3af**	46[a]
6	**2g**	Cl	Me		0
7	**2h**	Ph	Me	**3ah**	41[a]

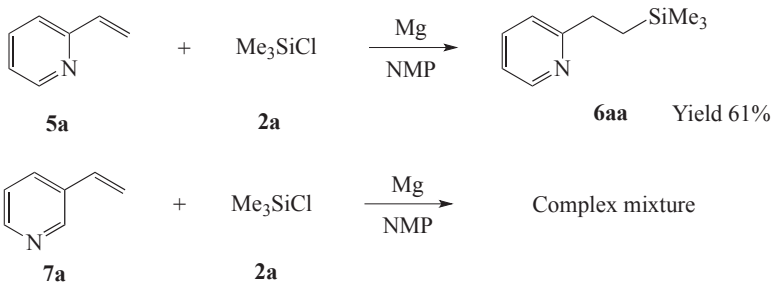
1a (5.0 mmol), **2** (6 equiv), Mg (3 equiv), NMP (30 mL), rt, 3 h, N_2 atmosphere.
[a] The starting material was consumed.

was detected by gas chromatography (Table 4, entries 2 and 3). Furthermore, a silane bearing two chlorine atoms (entry 5) gave the normal product **3af** in 46% yield, while no desired product **3** from dichlorodimethylsilane **2g** was detected as shown in entry 6, which would be explained by the higher reactivity of **2g**. The application of aromatic chlorodimethylphenylsilane **2h** to this coupling reaction also gave **3ah** in 41% isolated yield, successfully (Table 4, entry 7).

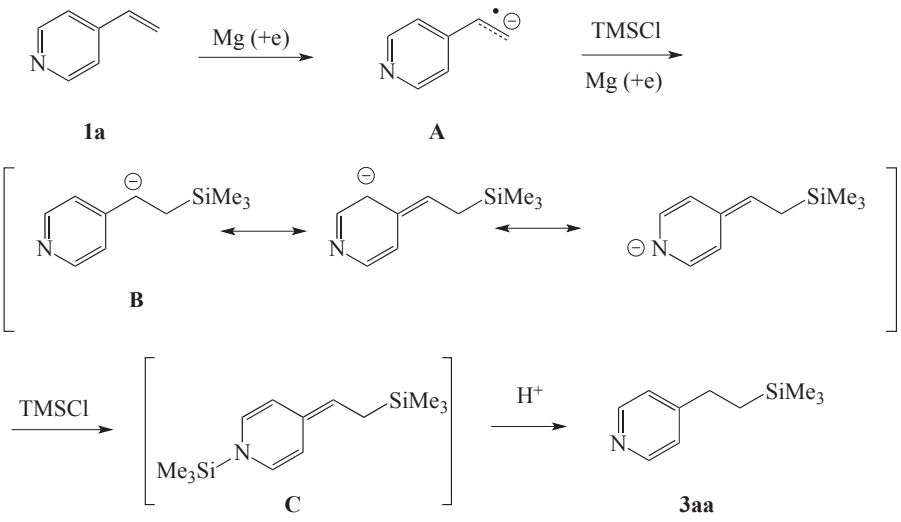
Silylation of 2-vinylpyridine **5a** and 3-vinylpyridine **7a** was performed under similar reaction conditions (Scheme 2). As a result, the reaction of 2-vinylpyridine **5a** gave the corresponding β-mono-silylated product **6aa** in 61% isolated yield. However, a complex mixture including α-mono, β-mono- and double-silylated products was obtained with no selectivity when 3-vinylpyridine **7a** was reductively silylated. This result may be mainly based on the different conjugation system between 3-vinylpyridine and 4-vinylpyridine, that is, the nitrogen atom will be involved in the stabilization of the generated anionic species by the resonance for 4-vinylpyridine or 2-vinylpyridine, whereas there is no stabilizing effect by the nitrogen atom in the case of 3-vinylpyridine.[17]

As shown in Table 3, the reduction potential of typical starting materials was measured by cyclic voltammetry, which suggested that all vinylpyridines would be reduced under the magnesium-promoted reduction conditions,[14d] whereas chlorotrimethylsilane **2a** showed no significant reduction peak in the field of the appropriate range. Therefore, this reaction can be initiated by a single electron transfer from magnesium to 4-vinylpyridine.

A proposed reaction mechanism for this magnesium-promoted silylation of 4-vinylpyridine is shown in Scheme 3. First, a single electron transfer from magnesium metal to 4-vinylpyridine **1a** will give an anion radical species **A**, which is attacked by **2a** and a β-silylated intermediate **B** will be formed through the second electron transfer at the same time. The intermediate **B** is stabilized by the resonance with the pyridine ring, especially with the nitrogen



Scheme 2.



Scheme 3.

atom on the pyridine ring. Therefore, the intermediate **B** is unreactive and may exist as a magnesium salt in situ or be transformed into an *N*-silylated intermediate **C** with no silylation at the α-olefinic carbon. After quenching and hydrolysis, the β-mono-silylated product **3aa** will be formed as a single product with high selectivity.

3. Conclusions

The magnesium-promoted reductive silylation of 2- and 4-vinylpyridine brought about the selective formation of the corresponding β-mono-silylated compounds in good yields. This selective silylation at the terminal carbon atom of the vinyl group is controlled by the resonance effect of the nitrogen atom on the pyridine ring. Various silylating agents and 4-vinylpyridine derivatives can be applied to this coupling reaction with high selectivity. Further studies on the related reactions and substrates are currently in progress.

4. Experimental section

4.1. General

All reactions were carried out under nitrogen atmosphere and solvents were purified and dried by the standard procedures unless otherwise noted. Solvents, silylating reagents and starting materials 4-vinylpyridine **1a**, 2-vinylpyridine **5a** are commercially available, and compounds **1b**,[18] **1c**,[19] **1d**,[20] **1e**,[20] **1f**,[18] **1g**,[21] **1h**,[22] **1i**,[23] **1j**,[22] **1k**,[24] **1l**,[25] **1m**[26] and **7a**[27] were synthesized by the reported procedures. Magnesium for Grignard reagent is commercially available and was used with no pre-treatment. Products were purified by column chromatography on neutral silica gel (60N, spherical, 63–210 mesh, Kanto Chemical) using standard techniques. For thin-layer chromatography (TLC) analysis, Merck precoated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) were used. ^{1}H NMR and ^{13}C NMR spectra were measured on a JEOL JNM AL-400 (400 MHz) spectrometer. Chemical shifts (δ) in parts per million (ppm) are reported relative to the residual signal of chloroform (7.26 ppm), and coupling constants are reported in hertz (Hz). Carbon chemical shifts were referenced to the carbon signal of $CDCl_3$ at 77.00 ppm. Multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), and m (multiplet). IR spectra were recorded on a JASCO 470Plus FTIR spectrometer, and peaks are reported in wavenumber (cm^{-1}). Mass spectra and high-resolution mass spectra were recorded on a Shimadzu GCMS-QP2010plus spectrometer or a JEOL JMS-600H spectrometer. Melting point (mp) determinations were performed by using a Yanaco MP-J3 instrument and are uncorrected. Cyclic voltammograms were measured by ALS model 600. Cyclic voltammetry was carried out with a three-electrode system using a platinum working electrode, a platinum counter electrode, and Ag/AgCl as a reference electrode with sweeping rate of 200 mV s^{-1} in 1% tetrabutylammonium perchlorate/NMP.

4.2. General procedure for reductive silylation of vinylpyridines

Under the nitrogen atmosphere, to a 100 mL-four-necked flask charged with Mg turnings (0.36 g, 15 mmol) for Grignard reaction without pre-treatment, chlorotrialkylsilane (30 mmol) and dry

NMP (20 mL), vinylpyridine (5 mmol) in NMP (10 mL) was added dropwise at 25 °C within 30 min and the reaction mixture was stirred for 3 h at room temperature. Subsequently, the mixture was carefully poured into a mixture of diethyl ether (50 mL) and saturated sodium bicarbonate solution (200 mL), and stirring was continued for 10 min. Then, the product was extracted with diethyl ether three times and the combined organic layer was washed with brine, dried over anhydrous magnesium sulfate overnight. Next, the solvent was evaporated under reduced pressure and the residue was finally purified by column chromatography.

*4.2.1. 4-(2-Trimethylsilylethyl)pyridine (**3aa**).*[28] Hexane/ethyl acetate 4:1, 80% yield (0.72 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.01 (9H, s), 0.84 (2H, t, J=8.8 Hz), 2.59 (2H, t, J=8.8 Hz), 7.11 (2H, d, J=5.4 Hz), 8.45 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −1.87, 17.44, 29.45, 123.25, 149.55, 154.09; IR (neat): 3068, 3023, 2953, 1601, 1414, 1250, 992, 832 cm^{-1}; MS (EI) m/z: 179 [M$^+$]; HRMS (EI) calcd for $C_{10}H_{17}NSi$: 179.1130, found 179.1095.

*4.2.2. 4-(1-Methyl-2-trimethylsilylethyl)pyridine (**3ba**).* Hexane/ethyl acetate 3:1, 63% yield (0.61 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.11 (9H, s), 0.84 (1H, dd, J=7.6 Hz, J=14.6 Hz), 0.92 (1H, dd, J=7.6 Hz, J=14.6 Hz), 1.22 (3H, d, J=7.6 Hz), 2.81 (1H, sext, J=7.6 Hz), 7.09 (2H, d, J=5.4 Hz), 8.44 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −0.26, 26.04, 26.83, 36.62, 122.85, 150.45, 159.41; IR (neat): 3068, 3024, 2957, 2898, 1597, 1414, 1249, 992, 841 cm^{-1}; MS (EI) m/z: 193 [M$^+$]; HRMS (EI) calcd for $C_{11}H_{19}NSi$: 193.1287, found 193.1293.

*4.2.3. 4-(1-Phenyl-2-trimethylsilylethyl)pyridine (**3ca**).* Hexane/ethyl acetate 3:2, 93% yield (1.19 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.15 (9H, s), 1.36 (1H, dd, J=7.1 Hz, J=14.6 Hz), 1.45 (1H, dd, J=7.1 Hz, J=14.6 Hz), 4.06 (1H, t, J=7.1 Hz), 7.19–7.31 (7H, m), 8.48 (2H, d, J=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −1.25, 23.40, 46.83, 122.80, 126.63, 127.65, 128.59, 144.90, 149.65, 156.15; IR (neat): 3027, 2952, 1594, 1415, 1248, 993, 858, 835 cm^{-1}; MS (EI) m/z: 255 [M$^+$]; HRMS (EI) calcd for $C_{16}H_{21}NSi$: 255.1443, found 255.1424.

*4.2.4. 4-[1-(4-Methoxyphenyl)-2-trimethylsilylethyl]pyridine (**3da**).* Hexane/ethyl acetate 2:1, 77% yield (1.10 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.16 (9H, s), 1.31 (1H, dd, J=7.1 Hz, J=14.6 Hz), 1.39 (1H, dd, J=7.1 Hz, J=14.6 Hz), 3.77 (3H, s), 3.98 (1H, t, J=7.1 Hz), 6.82 (2H, d, J=8.3 Hz), 7.15 (2H, d, J=8.3 Hz), 7.18 (2H, d, J=5.4 Hz), 8.45 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −1.21, 23.51, 45.98, 55.19, 113.92, 122.72, 128.58, 136.94, 149.55, 156.74, 158.26; IR (neat): 3030, 2952, 1596, 1511, 1249, 861, 836 cm^{-1}; MS (EI) m/z: 285 [M$^+$]; HRMS (EI) calcd for $C_{17}H_{23}NOSi$: 285.1549, found 285.1520.

*4.2.5. 4-[1-(4-Methylphenyl)-2-trimethylsilylethyl]pyridine (**3ea**).* Hexane/ethyl acetate 2:1, 84% yield (1.13 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.16 (9H, s), 1.33 (1H, dd, J=7.3 Hz, J=14.6 Hz), 1.41 (1H, dd, J=7.3 Hz, J=14.6 Hz), 2.29 (3H, s), 4.00 (1H, t, J=7.3 Hz), 7.09 (2H, d, J=8.0 Hz), 7.14 (2H, d, J=8.0 Hz), 7.19 (2H, d, J=4.6 Hz), 8.46 (2H, d, J=4.6 Hz); ^{13}C NMR (100 MHz, CDCl3) δ (ppm): −0.26, 21.87, 24.37, 47.38, 123.68, 128.43, 130.18, 137.10, 142.90, 150.65, 157.32; IR (neat): 3022, 2952, 2893, 1596, 1512, 1247, 993, 859, 756 cm^{-1}; MS (EI) m/z: 269 [M$^+$]; HRMS (EI) calcd for $C_{17}H_{23}NSi$: 269.1600, found 269.1600.

*4.2.6. 4-(2-Trimethylsilylpropyl)pyridine (**3fa**).* Hexane/ethyl acetate 2:1, 18% yield (0.17 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.00 (9H, s), 0.80 (3H, d, J=7.1 Hz), 0.93–0.96 (1H, m) 2.21 (1H, t, J=13.7 Hz), 2.82 (1H, dd, J=3.8 Hz, J=13.7 Hz), 7.08 (2H, d, J=5.5 Hz), 8.45 (2H, d, J=5.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −3.49, 13.40, 21.44, 37.35, 124.30, 149.30, 151.91; IR (neat): 3026, 2955, 1600, 1414, 1250, 841 cm^{-1}; MS (EI) m/z: 193 [M$^+$]; HRMS (EI) calcd for $C_{11}H_{19}NSi$: 193.1287, found 193.1328.

*4.2.7. 4-(2-Phenyl-2-trimethylsilylethyl)pyridine (**3ga**).* Hexane/ethyl acetate 2:1, 91% yield (1.16 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.00 (9H, s), 2.37 (1H, dd, J=6.6 Hz, J=7.8 Hz), 3.05–3.07 (2H, m), 6.96–6.97 (4H, m), 7.05 (1H, t, J=7.6 Hz), 7.18 (2H, d, J=5.4 Hz), 8.33 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −2.94, 35.06, 37.76, 123.90, 124.79, 127.71, 128.18, 141.92, 149.27, 151.40; IR (neat): 3025, 2952, 1601, 1417, 1250, 993, 850, 704 cm^{-1}; MS (EI) m/z: 255 [M$^+$]; HRMS (EI) calcd for $C_{16}H_{21}NSi$: 255.1443, found 255.1422.

*4.2.8. 4-[2-(4-Methylphenyl)-2-trimethylsilylethyl]pyridine (**3ha**).* Hexane/ethyl acetate 2:1, 90% yield (1.21 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.01 (9H, s), 2.25 (3H, s), 2.34 (1H, t, J=7.8 Hz), 3.03 (2H, d, J=7.8 Hz), 6.85 (2H, d, J=7.8 Hz), 6.97 (4H, m), 8.34 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −2.93, 20.87, 35.06, 37.11, 123.99, 127.55, 128.90, 134.08, 138.58, 149.09, 151.74; IR (neat): 3020, 2953, 2859, 1600, 1511, 1249, 993, 867, 841 cm^{-1}; MS (EI) m/z: 269 [M$^+$]; HRMS (EI) calcd for $C_{17}H_{23}NSi$: 269.1600, found 269.1630.

*4.2.9. 4-[2-(4-Methoxyphenyl)-2-trimethylsilylethyl]pyridine (**3ia**).* Hexane/ethyl acetate 2:1, 72% yield (1.03 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.01 (9H, s), 2.29 (1H, dd, J=4.9 Hz, J=11.0 Hz), 2.94–3.05 (2H, m), 3.73 (3H, s), 6.72 (2H, d, J=4.3 Hz), 6.87 (2H, d, J=4.3 Hz), 6.94 (2H, dd, J=1.5 Hz, J=4.4 Hz), 8.33 (2H, dd, J=1.5 Hz, J=4.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −2.97, 35.24, 36.61, 55.02, 113.58, 123.92, 128.47, 133.68, 149.15, 151.53, 156.87; IR (neat): 3025, 2953, 2834, 1599, 1490, 1414, 1240, 837, 751 cm^{-1}; MS (EI) m/z: 285 [M$^+$]; HRMS (EI) calcd for $C_{17}H_{23}NOSi$: 285.1549, found 285.1557.

*4.2.10. 4-[2-(2-Methoxyphenyl)-2-trimethylsilylethyl]pyridine (**3ja**).* Hexane/ethyl acetate 2:1, 79% yield (1.13 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.03 (9H, s), 2.98–3.11 (3H, m), 3.72 (3H, s), 6.75 (1H, d, J=7.6 Hz), 6.80 (1H, t, J=7.6 Hz), 6.97–6.98 (3H, m), 7.02 (1H, t, 7.6 Hz), 8.33 (2H, dd, J=1.7 Hz, J=4.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −2.79, 34.44(×2), 54.98, 110.13, 120.29, 123.83, 125.44, 127.55, 130.63. 149.23, 151.57, 156.67; IR (neat): 3025, 2953, 2834, 1599, 1490, 1414, 1240, 837, 751 cm^{-1}; MS (EI) m/z: 285 [M$^+$]; HRMS (EI) calcd for $C_{17}H_{23}NOSi$: 285.1549, found 285.1504.

*4.2.11. 4-[2-(4-Chlorophenyl)-2-trimethylsilylethyl]pyridine (**3ka**).* Hexane/ethyl acetate 2:1, 70% yield (1.01 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.01 (9H, s), 2.36 (1H, dd, J=4.4 Hz, J=11.4 Hz), 2.94–3.07 (2H, m), 6.88 (2H, d, J=8.3 Hz), 6.93 (2H, d, J=5.7 Hz), 7.13 (2H, d, J=8.3 Hz), 8.34 (2H, d, J=5.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −3.06, 34.90, 37.26, 123.86, 128.33, 128.86, 130.32, 140.46, 149.23, 151.06; IR (neat): 3024, 2954, 1600, 1489, 1250, 1414, 1250, 1012, 841 cm^{-1}; MS (EI) m/z: 289 [M$^+$]; HRMS (EI) calcd for $C_{16}H_{20}NSiCl$: 289.1054, found 289.1023.

*4.2.12. 4-[2-(1-Naphthyl)-2-trimethylsilylethyl)pyridine (**3la**).* Hexane/ethyl acetate 2:1, 40% yield (0.61 g). White solid, melting point 147.6–150.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.01 (9H, s), 3.23–3.33 (2H, m), 3.47 (1H, dd, J=5.8 Hz, J=9.7 Hz), 7.00 (2H, d, J=5.1 Hz), 7.31 (1H, d, 7.1 Hz), 7.38–7.46 (3H, m), 7.59 (1H, d, J=8.0 Hz), 7.79 (1H, d, J=7.1 Hz), 8.00 (1H, d, J=8.0 Hz), 8.27

(2H, d, J=5.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −2.67, 29.92, 35.61, 123.13, 123.22, 123.64, 125.17, 125.21, 125.37, 128.88, 132.11, 133.90, 138.77, 149.35, 151.04; IR (KBr): 3045, 2950, 1600, 1414, 1248, 871, 841, 782 cm^{-1}; MS (EI) m/z: 305 [M$^+$]; HRMS (EI) calcd for $C_{20}H_{23}NSi$: 305.1600, found 305.1632.

*4.2.13. 4-{2-[4-(Trimethylsilyltrimethylsilyloxymethyl)phenyl]ethyl} pyridine (**4ma**).* Hexane/ethyl acetate 2:1, 29% yield (0.52 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): −0.07 (9H, s), 0.00 (9H, s), 2.90 (4H, s), 4.40 (1H, s), 6.96–7.04 (6H, m), 8.44 (2H, d, J=4.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −4.15, 0.00, 36.29, 37.24, 70.04, 124.25, 124.95, 127.79, 136.98, 142.37, 148.87, 151.42; IR (neat): 3021, 2956, 1601, 1414, 1247, 871, 841 cm^{-1}; MS (EI) m/z: 357 [M$^+$]; HRMS (EI) calcd for $C_{20}H_{31}NOSi_2$: 357.1944, found 357.1947.

*4.2.14. 4-(2-Ethyldimethylsilylethyl)pyridine (**3ab**).* Hexane/ethyl acetate 1:1, 74% yield (0.71 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.00 (6H, s), 0.52 (2H, q, J=7.9 Hz), 0.86 (2H, t, J=8.8 Hz), 0.94 (3H, t, J=7.9 Hz), 2.60 (2H, t, J=8.8 Hz), 7.14 (2H, d, J=6.0 Hz), 8.47 (2H, d, J=6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −4.05, 6.70, 7.24, 15.72, 29.52, 123.37, 149.28, 154.61; IR (neat): 3025, 2953, 1601, 1414, 1250, 831 cm^{-1}; MS (EI) m/z: 193 [M$^+$]; HRMS (EI) calcd for $C_{11}H_{19}NSi$: 193.1287, found 193.1300.

*4.2.15. 4-(2-Butyldimethylsilylethyl)pyridine (**3ac**).* Hexane/ethyl acetate 1:1, 45% yield (0.50 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.00 (6H, s), 0.52 (2H, t, J=8.5 Hz), 0.82–0.90 (5H, m), 1.23–1.35 (4H, m), 2.59 (2H, t, J=8.5 Hz), 7.12 (2H, d, J=6.1 Hz), 8.46 (2H, d, J=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −3.53, 13.76, 14.74, 16.17, 26.03, 26.54, 29.51, 123.30, 149.51, 154.33; IR (neat): 3025, 2955, 2872, 1600, 1494, 1414, 1249, 831 cm^{-1}; MS (EI) m/z: 221 [M$^+$]; HRMS (EI) calcd for $C_{13}H_{23}NSi$: 221.1600, found 221.1560.

*4.2.16. 4-(2-Triethylsilylethyl)pyridine (**3ae**).*[29] Hexane/ethyl acetate 1:1, 61% yield (0.67 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.56 (6H, q, J=7.9 Hz), 0.85–0.89 (2H, m), 0.96 (9H, t, J=7.9 Hz), 2.60 (2H, t, J=8.8 Hz), 7.15 (2H, d, J=6.1 Hz), 8.48 (2H, d, J=6.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 3.14, 6.37, 6.76, 7.37, 12.45, 29.51, 123.30, 149.29, 154.74; IR (neat): 3068, 2954, 1601, 1415, 1238, 797, 738 cm^{-1}; MS (EI) m/z: 221 [M$^+$]; HRMS (EI) calcd for $C_{13}H_{23}NSi$: 221.1600, found 221.1583.

*4.2.17. 4-(2-Chloromethyldimethylsilylethyl)pyridine (**3af**).* Hexane/ethyl acetate 1:1, 46% yield (0.49 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.15 (6H, s), 1.02 (2H, t, J=8.7 Hz), 2.66 (2H, t, J=8.7 Hz), 2.79 (2H, s), 7.15 (2H, d, J=5.4 Hz), 8.48 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −4.66, 14.44, 29.08, 29.85, 123.33, 149.36, 153.74; IR (neat): 3068, 3027, 2960, 1601, 1414, 1256, 844 cm^{-1}; MS (EI) m/z: 213 [M$^+$]; HRMS (EI) calcd for $C_{10}H_{16}NSiCl$: 213.0741, found 213.0719.

*4.2.18. 4-(2-Phenyldimethylsilylethyl)pyridine (**3ah**).* Hexane/ethyl acetate 1:1, 41% yield (0.49 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.32 (6H, s), 1.11 (2H, t, J=8.8 Hz), 2.61 (2H, t, J=8.8 Hz), 7.10 (2H, d, J=5.4 Hz), 7.37–7.39 (3H, m), 7.51–7.54 (2H, m), 8.46 (2H, d, J=5.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −3.23, 16.56, 29.42, 123.34, 127.88, 129.12, 133.50, 138.30, 149.26, 154.18; IR (neat): 3068, 3021, 2954, 1600, 1414, 1249, 816 cm^{-1}; MS (EI) m/z: 241 [M$^+$]; HRMS (EI) calcd for $C_{15}H_{19}NSi$: 241.1287, found 241.1247.

*4.2.19. 2-(2-Trimethylsilylethyl)pyridine (**6aa**).*[30] Hexane/ethyl acetate 5:1, 61% yield (0.55 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.02 (9H, s), 0.95 (2H, t, J=8.8 Hz), 2.79 (2H, t, J=8.8 Hz), 7.06–7.10 (1H, m), 7.17 (1H, d, J=8.2 Hz), 7.58 (1H, t, J=8.2 Hz), 8.50 (1H, d, J=4.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): −1.82, 16.99, 32.55, 120.79, 122.02, 136.50, 148.88, 164.00; IR (neat): 3068, 2953, 1591, 1434, 1248, 862 cm^{-1}; MS (EI) m/z: 179 [M$^+$]; HRMS (EI) calcd for $C_{10}H_{17}NSi$: 179.1130, found 179.1121.

Acknowledgments

This work was supported by Japan Society for the Promotion of Science KAKENHI Grant Number 22605003 and 25410110.

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016.03.042.

References and notes

1. (a) Colvin, E. W. *Silicon reagents in organic synthesis*; Academic Press: London, UK, 1988; (b) Sakurai, H. *Organosilicon and bioorganosilicon chemistry: structure, bonding, reactivity and synthetic application*; Ellis Horwood: Chichester, UK, 1985.
2. (a) Wuts, P. G. M. *Greene's protective groups in organic synthesis*, 5th ed.; John Wiley & Sons: New York, NY, 2014; (b) Kocienski, P. J. *Protective groups*; Thieme: New York, NY, 2000.
3. Fleming, I. *Chemtracts: Org. Chem.* **1996**, *9*, 1.
4. (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918; (b) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616; (c) Denmark, S. E.; Ober, M. H. *Aldrichimica Acta* **2003**, *36*, 75.
5. (a) Tamao, K.; Ishida, N. *Tetrahedron Lett.* **1984**, *25*, 4249; (b) Jensen, J. F.; Svendsen, B. Y.; Cour, T. V.; Pedersen, H. L.; Johannsen, M. *J. Am. Chem. Soc.* **2002**, *124*, 4558; (c) Sunderhaus, J. D.; Lam, H.; Dudley, G. B. *Org. Lett.* **2003**, *5*, 4571.
6. (a) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, *17*, 1295; (b) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 14556.
7. (a) Boeckman, R. K., Jr.; Blum, D. M.; Ganem, B.; Halvey, N. *Org. Synth.* **1978**, *58*, 152; (b) Cunico, R. F.; Kuan, C. P. *J. Org. Chem.* **1985**, *50*, 5410; (c) Desponds, O.; Franzini, I.; Schlosser, M. *Synthesis* **1997**, 150.
8. (a) Onopchenko, A.; Sabourin, E. T. *J. Org. Chem.* **1987**, *52*, 4118; (b) Takeuchi, R.; Nitta, S.; Watanabe, D. *J. Org. Chem.* **1995**, *60*, 3045; (c) Motoda, D.; Shinokubo, H.; Oshima, K. *Synlett* **2002**, 1529; (d) Ibrahem, I.; Santoro, S.; Himo, F.; Córdova, A. *Adv. Synth. Catal.* **2011**, *353*, 245; (e) Brunner, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 2749.
9. Yus, M.; Martínez, P.; Guijanrro, D. *Tetrahedron* **2001**, *57*, 10119.
10. Fleming, I.; Newton, T. W. *J. Chem. Soc. Perkin Trans. I* **1984**, 1805.
11. (a) Asao, N.; Sudo, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 7654; (b) Sudo, T.; Asao, N.; Gevorgyan, V.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2494; (c) Pérez, M.; Hounjet, L. J.; Caputo, C. B.; Dobrovetsky, R.; Stephan, D. W. *J. Am. Chem. Soc.* **2013**, *135*, 18308; (d) Simonneau, A.; Oestreich, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 11905.
12. (a) Kyoda, M.; Yokoyama, T.; Kuwahara, T.; Maekawa, H.; Nishiguchi, I. *Chem. Lett.* **2002**, *31*, 228; (b) Maekawa, H.; Sakai, M.; Uchida, T.; Kita, Y.; Nishiguchi, I. *Tetrahedron Lett.* **2004**, *45*, 607; (c) Maekawa, H.; Nagakubo, K.; Nishi, M.; Nishimura, M.; Nagahara, D. *Bull. Chem. Soc. Jpn.* **2013**, *86*, 1183.
13. Maekawa, H.; Takano, A.; Watanabe, M. *Tetrahedron Lett.* **2014**, *55*, 6208.
14. (a) Uchida, T.; Kita, Y.; Maekawa, H.; Nishiguchi, I. *Tetrahedron* **2006**, *62*, 3103; (b) Maekawa, H.; Kudo, M.; Nishiyama, Y.; Shimizu, K.; Abe, M. *Tetrahedron* **2014**, *70*, 2081; (c) Zhang, T.; Takano, A.; Nishiyama, Y.; Maekawa, H. *Tetrahedron* **2015**, *71*, 2629; (d) Maekawa, H.; Nishiyama, Y. *Tetrahedron* **2015**, *71*, 6694.
15. Preparation of α-aryl-4-vinylpyridines with an electron withdrawing group at the aromatic ring was unsuccessful.
16. Picard, J.-P.; Calas, R.; Dunoguès, J.; Duffaut, N.; Gerval, J.; Lapouyade, P. *J. Org. Chem.* **1979**, *44*, 420.
17. (a) Settambolo, R.; Scamuzzi, S.; Caiazzo, A.; Lazzaroni, R. *Organometallics* **1998**, *17*, 2127; (b) Caiazzo, A.; Settambolo, R.; Pontorno, L.; Lazzaroni, R. *J. Organomet. Chem.* **2000**, *599*, 298.
18. Eisch, J. J.; Gopal, H.; Russo, D. A. *J. Org. Chem.* **1974**, *39*, 3110.
19. Hansen, A. L.; Ebran, J.-P.; Gøgsig, T. M.; Skrydstrup, T. *Chem. Commun.* **2006**, 4137.
20. Kobayashi, K.; Kozuki, T.; Suzuki, T. *Helv. Chim. Acta* **2012**, *95*, 556.
21. Zhang, Z.; Wang, Z. *J. Org. Chem.* **2006**, *71*, 7485.
22. Hauser, S. A.; Korinth, V.; Herdtweck, E.; Cokoja, M.; Herrmann, W. A.; Kuhn, F. E. *Eur. J. Inorg. Chem.* **2010**, 4083.
23. Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Pipko, S. E.; Shivanyuk, A. N.; Tolmachev, A. A. *J. Comb. Chem.* **2007**, *9*, 1073.
24. Percino, M. J.; Chapela, V. M.; Montiel, L.-F.; Pérez-Gutiérrez, E.; Maldonado, J. L. *Chem. Pap.* **2010**, *64*, 360.
25. Efange, S. M. N.; Michelson, R. H.; Tan, A. K.; Krueger, M. J.; Singers, T. P. *J. Med. Chem.* **1993**, *36*, 1278.

26. Elacqua, E.; Kaushik, P.; Groeneman, R. H.; Sumrak, J. C.; Bučar, D.-K.; MacGillivray, L. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 1037.
27. Alunni, S.; Laureti, V.; Ottavi, L.; Ruzziconi, R. *J. Org. Chem.* **2003**, *68*, 718.
28. Nakao, Y.; Yamada, Y.; Kashihara, N.; Hiyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 13666.
29. Nametkin, N. S.; Lyashenko, I. N.; Chernysheva, T. I.; Borisov, S. N.; Pestunovich, V. A. *Dokl. Akad. Nauk. SSSR* **1967**, *174*, 1105.
30. Tilley, J. W.; Zawoiski, S. *J. Org. Chem.* **1988**, *53*, 386.