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Diastereoselective alkylation and reduction of β-alkoxyacylsilanes: stereoselective construction of three contiguous stereogenic centers

Mitsunori Honda,* Naoto Ohkura, Shin-ichi Saisyo, Masahito Segi and Tadashi Nakajima

Department of Chemistry and Chemical Engineering, Faculty of Engineering, Kanazawa University, 2-40-20 Kodatsuno, Kanazawa 920-8667, Japan

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Abstract—The nucleophilic addition reaction to acylsilanes, having stereogenic centers at the α and β positions, derived from the aldol reaction of dimethyl acetals and acylsilane silyl enol ethers gives the corresponding α-silylalcohols in high yields with excellent diastereoselectivity. The protiodesilylation of α-silylalcohols proceeds with complete retention of the configuration. In addition, the reduction of acylsilanes having stereogenic centers at the α and β positions affords the corresponding α-silylalcohols in good yields with high diastereoselectivity similarly to the nucleophilic addition. And the treatment of acylsilanes having a phenyl group on silicon atom with fluoride ion results in the formation of phenyl carbinol derivatives via migration of the phenyl group with high diastereoselectivity.

1. Introduction

Acylsilanes are an useful class of compounds in organic synthesis,[1,2] and several procedures using acylsilanes have been developed for the asymmetric synthesis.[2,3] In particular, the important utility of acylsilanes is their ability to function as aldehyde equivalents in stereoselective nucleophilic addition reactions.[4,5] For these reasons, the stereocontrolled nucleophilic addition to α- or β-chiral acylsilanes has been studied.[4–6] The works of Ohno[4a,b] and Panek[4c] et al. on the reaction of α- or β-chiral acylsilanes with nucleophiles demonstrate the synthetic potential of 1,2- or 1,3-asymmetric induction in chiral acylsilanes. The stereochemistry of these reactions is respectively explained by open-chain pathway (Felkin-Anh-type) or Cram-type chelation model.

On the other hand, we recently found that $TiCl_4$ mediated aldol reaction of silyl enol ethers of simple acylsilanes with acetals gives the corresponding β-alkoxyacylsilanes which have two stereogenic centers at the α and β positions with high diastereoselectivity.[7] The stereoselectivity of the nucleophilic addition to acylsilanes having two stereogenic centers at the α and β positions has not been clarified. Thus, our interest focused on efficient and stereoselective formation of multiple stereogenic centers via reaction of above obtained acylsilanes with nucleophiles. The purpose of this paper is to report the results of our experiments on the nucleophilic addition reaction to the carbonyl group of the acylsilanes having stereogenic centers at the α and β positions and the subsequent protiodesilylation of the resulting silylcarbinols[8] to lead to the construction of three contiguous stereogenic centers.

Furthermore, the reduction[9,10] and the protiodesilylation[11–13] of acylsilanes having stereogenic centers at the α and β positions are also described in this article. The reduction of simple acylsilanes (e.g. acetylsilane and benzoylsilane) has already been published,[10] however, no other detailed study has been reported on the reduction of acylsilanes having stereogenic centers at the α and β positions. On the other hand, only a few reports have been published for the protiodesilylation of acylsilanes having stereogenic centers at the α and β positions.[12]

2. Results and discussion

2.1. Preparation of acylsilanes 1–4

Acylsilanes having stereogenic centers at the α and β positions **1**–**4** were employed in this study. α-Substituted-β-methoxyacylsilanes **1** and **2** were prepared by the aldol reaction of acylsilane silyl enol ethers with simple acetals in the presence of $TiCl_4$.[7,14] Aldol adducts containing three contiguous stereogenic centers **3** and **4** were obtained by

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* Corresponding author. Tel.: +81-76-234-4789; fax: +81-76-234-4800; e-mail: honda@t.kanazawa-u.ac.jp

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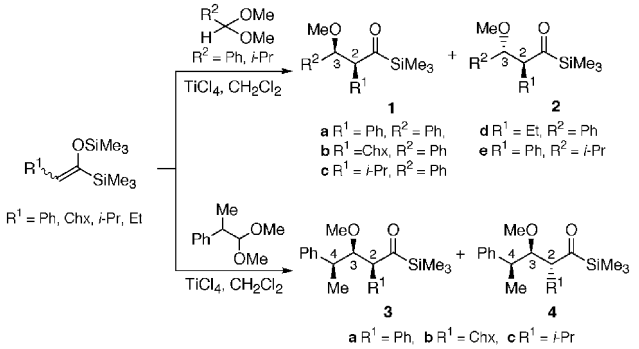
condensation of acylsilane silyl enol ethers with 2-phenylpropionaldehyde dimethyl acetal[15] in the presence of $TiCl_4$ (Scheme 1). In this reaction, it has been reported that the aldol adducts **3** and **4** are formed with complete Cram-type (3,4-*syn*) selectivity.[7]



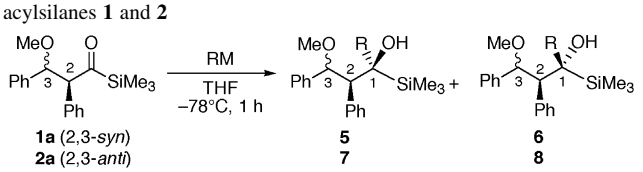
Scheme 1. Synthesis of β-methoxyacylsilane having stereogenic centers at the α and β positions.

The pure 2,3-*anti* and 2,3-*syn* isomers as a starting acylsilane are required to study the stereoselectivity of nucleophilic addition reaction or reduction, but the products obtained under the above conditions were a mixture of the 2,3-*anti* and 2,3-*syn* isomers in most cases. These diastereomers were separated completely by column chromatography on silica gel and then used.

2.2. Nucleophilic addition reaction to β-methoxyacylsilanes

Acylsilanes **1a** and **2a**, derived from benzaldehyde dimethyl acetal and silyl enol ether of benzyl silyl ketone, were treated with organolithium reagents or methylmagnesium bromide at −78°C in THF. The results are summarized in Table 1. In all cases, the reaction proceeded smoothly to afford the corresponding 1,2-*syn*-3-methoxysilylalcohols **5** and **7** (*syn* refers to the relationship between the phenyl group at β position and the hydroxy group on the zig zag main chain containing the silyl group) having the three contiguous stereogenic centers in high yields with excellent diastereoselectivity. This 1,2-*syn* stereoselectivity was independent of the relative configuration at the 2 and 3 positions of starting acylsilanes and of the kind of organometallic reagents.

Table 1. Nucleophilic addition of organometallic reagents to β-methoxyacylsilanes **1** and **2**

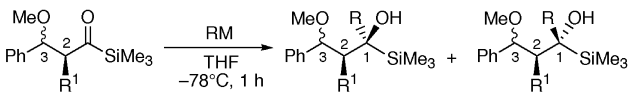


Entry	Substrate	RM	Product	Yield (%)[a]	1,2-*syn*/1,2-*anti*[b]
1	**1a**	MeLi	**5f**, **6f**	99	>99/1
2	**2a**	MeLi	**7f**, **8f**	95	>99/1
3	**2a**	MeMgBr	**7f**, **8f**	59	>99/1
4	**2a**	BuLi	**7g**, **8g**	99	>99/1
5	**2a**	*s*-BuLi	**7h**, **8h**	97	>99/1
6	**2a**	PhLi	**7i**, **8i**	74	>99/1

Molar ratio; **1a** or **2a**/RLi=1:2, **1a** or **2a**/MeMgBr=1:4.
[a] Isolated yield.
[b] Determined by ^{1}H NMR analysis.

The reaction of **1** or **2** having an aliphatic group at the α position with several nucleophiles was carried out under similar conditions as above. The results are shown in Table 2. In all cases, the corresponding diastereomeric mixture of 3-methoxysilylalcohols **5**–**8** was obtained in good yields with preference of 1,2-*syn* isomer **5** or **7**. It was found that the reaction of **1** with alkyllithium reagents (entries 1 and 3) exhibited higher diastereoselectivity than that of **2** (entries 2 and 6). The stereoselectivity increased with the bulkiness of the α-substituent of **1** or **2**. The reaction with Grignard reagent resulted in the selective formation of 1,2-*syn* isomer (entries 4 and 8).

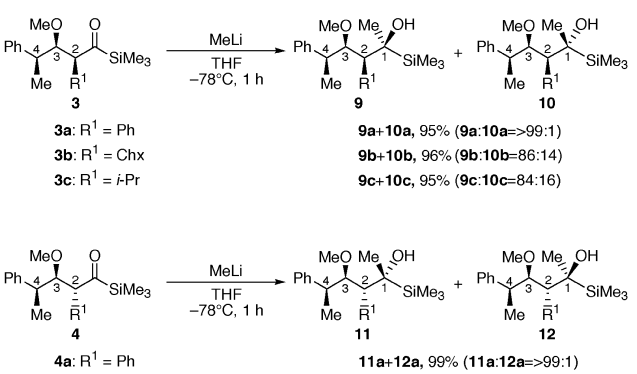
Table 2. Substituent effect of β-methoxyacylsilanes **1** and **2** in nucleophilic addition



Entry	Substrate	R^1	RM	Product	Yield (%)[a]	1,2-*syn*/1,2-*anti*[b]
1	**1b**	Chx[c]	MeLi	**5j**, **6j**	99	98/2
2	**2b**	Chx[c]	MeLi	**7j**, **8j**	97	74/26
3	**1c**	*i*-Pr	BuLi	**5k**, **6k**	98	88/12
4	**1c**	*i*-Pr	MeMgBr	**5l**, **6l**	79	>99/1
5	**2c**	*i*-Pr	MeLi	**7l**, **8l**	85	76/24
6	**2c**	*i*-Pr	BuLi	**7k**, **8k**	99	77/23
7	**2d**	Et	MeLi	**7m**, **8m**	84	67/33
8	**2d**	Et	MeMgBr	**7m**, **8m**	77	96/4

Molar ratio; **1** or **2**/RLi=1:2, **1** or **2**/MeMgBr=1:4.
[a] Isolated yield.
[b] Determined by ^{1}H NMR analysis.
[c] Chx=Cyclohexyl.

In order to examine the construction of the four contiguous stereogenic centers, β-methoxyacylsilanes **3** and **4** were also used as the substrate. The reaction with methyllithium proceeded smoothly to afford the corresponding 3-methoxysilylalcohols **9**–**12** in high yields (Scheme 2). As mentioned above, high 1,2-*syn* selectivity was observed in the reaction using acylsilanes **3a** and **4a** having a phenyl group at the α position, independent of the stereochemistry in C-2, C-3 and C-4 of the starting acylsilanes. However, the



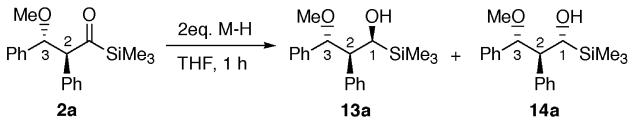
Scheme 2. Nucleophilic addition of methyllithium to β-methoxyacylsilanes **3** and **4**.

diastereoselectivity in the reaction of **3b** or **3c** having an aliphatic group at the α position was decreased.

2.3. Reduction of β-methoxyacylsilanes

The hydride reduction of **2a** with various reducing agents was carried out. In this study, lithium aluminum hydride, sodium borohydride, diisobutylaluminum hydride and borane were employed as reducing agents. The results are summarized in Table 3. Using lithium aluminum hydride as a reducing agent, the reaction proceeded smoothly to afford the corresponding two diastereomers of 3-methoxysilylalcohols **13a** and **14a** in quantitative yields with preference of **13a**. The diastereoselectivity in the reaction was increased with lowering the reaction temperature (entries 1–3). The reduction using sodium borohydride also gave the silylalcohols in excellent yields at 0°C (entry 5), but the stereoselectivity was low. In the reaction at −78°C (entry 4), the stereoselectivity was improved, but the product was obtained in low yield. The reduction using diisobutylaluminum hydride gave high yield, but the stereoselectivity was relatively low (entries 6 and 7). The reaction using borane as a reducing agent gave low yield and poor diastereoselectivity (entries 8 and 9). Since the mechanism of reaction with diisobutylaluminum hydride or borane is different from that of reaction with lithium aluminum hydride or sodium borohydride, the decrease in the diastereoselectivity was observed.[16] Among the reducing agents examined, best results were obtained by using lithium aluminum hydride at low temperature, and hence all of the following reductions were carried out using lithium aluminum hydride in THF at −78°C for 0.5 h.

Table 3. Reaction of β-methoxyacylsilane **2a** with various reducing agents



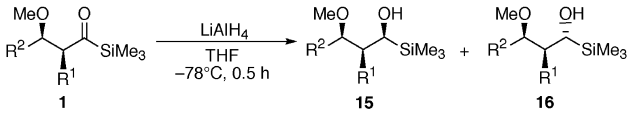
2a **13a** **14a**

Entry	M–H	Solvent	Temperature.(°C)	Product	
				Yield (%)[a]	**13a/14a**[b]
1	$LiAlH_4$	THF	−78	99	96/4
2			rt	99	76/24
3			Reflux	99	71/29
4	$NaBH_4$	MeOH	−78	13	89/11
5			0	99	81/19
6	DIBAL-H	Toluene	−78	91	61/39
7			Reflux	99	84/16
8	BH_3	THF	rt	13	53/47
9			Reflux	40	64/36

[a] Isolated yield of a mixture of **13** and **14**.
[b] Determined by ^{1}H NMR analysis.

The reduction of β-methoxyacylsilanes **1** and **2** having various substituent groups at the α and β positions using lithium aluminum hydride was carried out. The results of the reaction using **1** and **2** are, respectively, summarized in Tables 4 and 5. In all cases, the corresponding diastereomeric mixtures of 3-methoxysilylalcohols **13**–**16** were obtained quantitatively. In analogy with the reaction of **1** or **2** with organometallic reagents (Tables 1 and 2), the

Table 4. Reduction of 2,3-*syn*-3-methoxyacylsilanes **1** with $LiAlH_4$

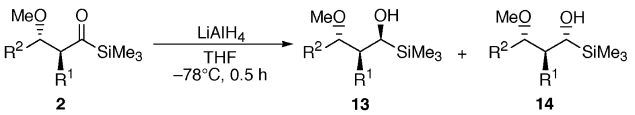


1 **15** **16**

Entry	Substrate	R^1	R^2	Product	Yield (%)[a]	**15/16**[b]
1	**1a**	Ph	Ph	**15a**, **16a**	89	>99/1
2	**1b**	Chx[c]	Ph	**15b**, **16b**	98	93/7
3	**1d**	Et	Ph	**15d**, **16d**	96	91/9
4	**1e**	Ph	*i*-Pr	**15e**, **16e**	99	>99/1

Molar ratio; **1**/$LiAlH_4$=1:0.5.
[a] Isolated yield of a mixture of **15** and **16**.
[b] Determined by ^{1}H NMR analysis.
[c] Chx=Cyclohexyl.

Table 5. Reduction of 2,3-*anti*-3-methoxyacylsilanes **2** with $LiAlH_4$



2 **13** **14**

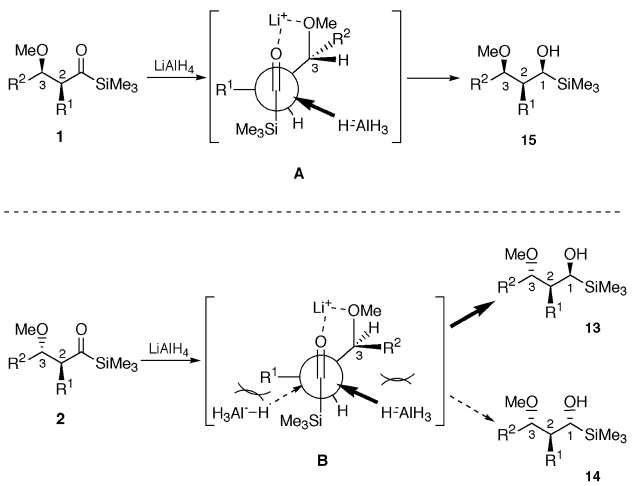
Entry	Substrate	R^1	R^2	Product	Yield (%)[a]	**13/14**[b]
1	**2a**	Ph	Ph	**13a**, **14a**	99	96/4
2	**2b**	Chx[c]	Ph	**13b**, **14b**	98	77/23
3	**2d**	Et	Ph	**13d**, **14d**	96	45/55
4	**2e**	Ph	*i*-Pr	**13e**, **14e**	96	92/8

Molar ratio; **2**/$LiAlH_4$=1:0.5.
[a] Isolated yield of a mixture of **13** and **14**.
[b] Determined by ^{1}H NMR analysis.
[c] Chx=Cyclohexyl.

diastereoselectivity of the reduction was influenced by the stereochemistry of the starting acylsilanes and the bulkiness of α-substituent (R^1). In the reaction of **1**, high stereoselectivity was observed in most cases independent of the bulkiness of R^1 (Table 4). On the other hand, high diastereoselectivity was observed when acylsilanes **2** having a phenyl group at the α position were employed (Table 5, entries 1 and 4), while lower selectivity was observed when the α-substituent was a cyclohexyl or an ethyl group (entries 2 and 3). In other words, the stereoselectivity in the reaction of **2** increased with increasing the bulkiness of R^1.

2.4. Mechanistic considerations

In general, the stereoselection of reduction of carbonyl compounds having a β-methoxy group is understood by assuming the Cram-chelate model.[17] Thus, the following mechanism for the reduction of **1** or **2** is proposed (Scheme 3). First, the metal ion coordinates to two oxygen atoms of carbonyl group and methoxy group to give chelation models **A** (from **1**) and **B** (from **2**). The illustrated two models are favorable as the steric interaction between a bulky silyl group and R^1. In the reaction of **1**, the attack of hydride occurs from the less-hindered site in **A**, giving the 1,2-*syn* products **15**. On the other hand, the stereochemical outcome for the hydride reduction of **2** depended on the bulkiness of R^1 (Table 5). That is, when R^1 is a bulky group in chelating model **B**, the attack of hydride occurs preferentially from the opposite side of the R^1 to avoid the steric repulsion between incoming hydride and R^1 leading to

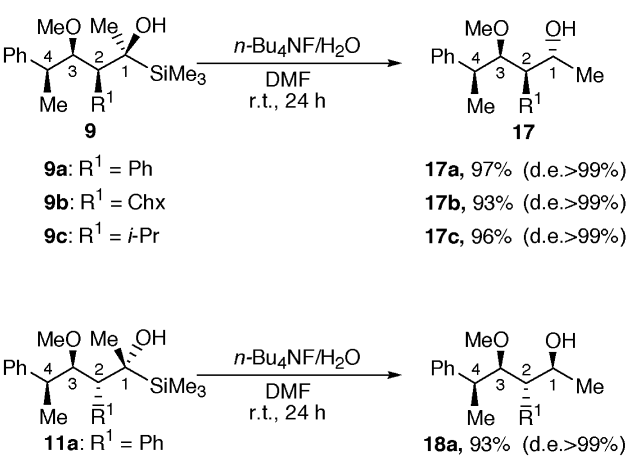


Scheme 3.

the 1,2-*syn* products **13**. On the other hand, when R^1 is a small group such as ethyl group, due to the steric repulsion between R^2 at C-3 and incoming hydride, the attack of hydride from the same side of R^1 to lead to the 1,2-*anti* products **14** also becomes a significant route (dotted arrow in **B**), which results in a low stereoselectivity. In addition, the stereoselectivity of the nucleophilic addition reaction of organometallic reagents to **1** or **2** would also be explained according to similar models as above.

2.5. Protiodesilylation of 3-methoxysilylalcohols

The protiodesilylation of α-silylalcohols proceeds with complete retention of the configuration.[8] Treatment of 3-methoxysilylalcohols **9** or **11** with tetrabutylammonium fluoride (TBAF) at room temperature for 24 h in *N*,*N*-dimethylformamide (DMF) gave the corresponding protiodesilylated compounds **17** or **18**, respectively. The results are shown in Scheme 4. In all cases the products **17** and **18** having the four contiguous stereogenic centers were quantitatively obtained with a high diastereomeric purity independent of the stereochemistry of the starting silylalcohols and the kind of β-substituent.

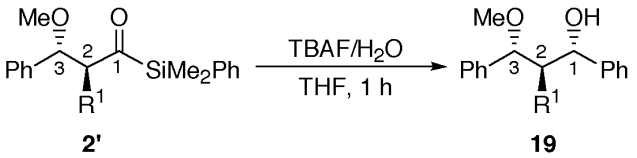


Scheme 4. Protiodesilylation of 3-methoxysilylalcohols **9** and **11**.

2.6. Treatment of β-methoxyacylsilanes with tetrabutylammonium fluoride (TBAF)

It has been reported that the treatment of acylsilane having one or more phenyl groups on silicon atom with base such as alkoxide or fluoride ion gives phenyl carbinol derivative via migration of a phenyl group.[12,13] The aldol adducts **2′** having a dimethylphenylsilyl group were prepared, and then the reaction with TBAF in THF was examined. The reaction proceeded smoothly at room temperature to afford the corresponding phenyl carbinols **19** having the three contiguous stereogenic centers with excellent 1,2-*anti* selectivity. The results are summarized in Table 6. When the α-substituent of **2′** was an aliphatic group, the reaction with TBAF afforded the products **19** in good yields regardless of amounts of TBAF or reaction temperature (entries1–4). Indeed, the reaction proceeded efficiently for 1 h even at −30°C with 0.2 equiv. of TBAF (entry 3). However, in the reaction of **2′** having a phenyl group as the α-substituent, the yield was lowered and stilbene was formed as the byproduct (entry 5).

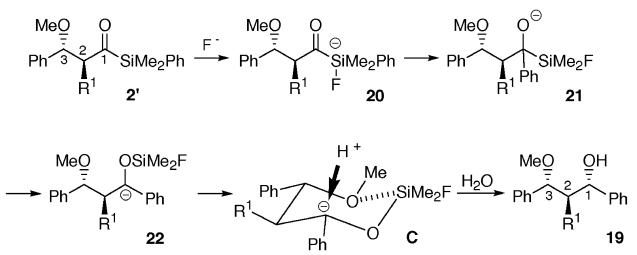
Table 6. Treatment of β-methoxyacylsilanes **2′** with TBAF



Entry	Substrate	R^1	TBAF (equiv.)	Temperature (°C)	Product	Yield (%)[a]	d.e. (%)[b]
1	**2′d**	Et	1	rt	**19d**	99	>99
2	**2′d**	Et	0.2	rt	**19d**	99	>99
3	**2′d**	Et	0.2	−30	**19d**	99	>99
4	**2′c**	*i*-Pr	0.2	rt	**19c**	78	>99
5	**2′a**	Ph	0.2	rt	**19a**	20[c]	>99

[a] Isolated yield.
[b] Determined by ^{1}H NMR analysis.
[c] Stilbene was formed as the byproduct.

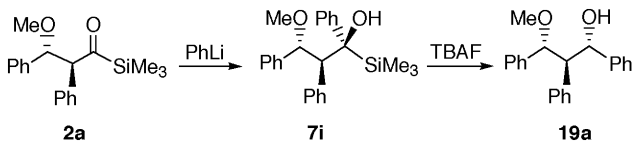
The following mechanism for the stereoselective formation of **19** is proposed (Scheme 5). At the first step of the reaction, fluoride ion attacks silicon atom of acylsilane **2′** to generate a pentacoordinate silicon anionic intermediate **20**. The migration of phenyl group from silicon to carbonyl carbon may occur to produce an alkoxide ion **21**, subsequent Brook rearrangement of silyl group from carbon to oxygen affords a carbanion intermediate **22**. The conformational structure of **22** would be pseudo six-membered ring (**C**) by the coordination of silicon atom to methoxy group at C-3 owing to Lewis acidity of silicon group. In this chelating model **C**, the attack of proton from the less-hindered side of



Scheme 5.

carbanion gives (3-methoxypropoxy)silane derivatives, followed by hydrolysis, could ultimately result in formation of rearranged 1,2-*anti* alcohol **19** with a high selectivity.

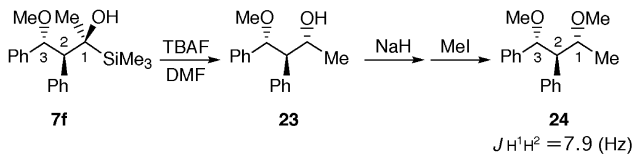
Additionally, the product **19a** derived from the reaction of **2′a** with TBAF was identical with the one obtained from the nucleophilic addition reaction of phenyllithium to **2a** followed by treatment of TBAF (Scheme 6).



Scheme 6.

2.7. Stereochemical assignment

Stereochemical assignment of the resulting 3-methoxysilylalcohol **7f** was performed by conversion into the corresponding dimethoxypropane derivative (Scheme 7). The protiodesilylation of **7f** with TBAF in DMF gave the corresponding 3-methoxyalcohol derivative **23** with retention of the configuration[8] as mentioned above. Treatment of **23** with sodium hydride followed by methylation with iodomethane gave dimethoxypropane derivative **24**. The stereochemistry of **24** has already been reported,[18] and the vicinal coupling constant of 7.9 Hz observed between the protons on C-1 and C-2 in the ^{1}H NMR spectrum indicates the 1,2-*anti* configuration, which is correlated to the 1,2-*syn* configuration in 3-methoxysilylalcohol **7f**.



Scheme 7.

Thus, the stereochemistry of other silylalcohols **5**–**12** was predicted by comparing with the chemical shift and $^3J(H^2,H^3)$ coupling constant of **7f**. On the other hand, the stereochemistry of silylalcohols **13**–**16** derived from the reduction of β-methoxyacylsilanes **1** and **2** was considered in a similar manner as above.

3. Conclusion

In summary, stereoselective construction of multiple stereogenic centers using β-methoxyacylsilanes derived from the aldol reaction of dimethyl acetals and acylsilane silyl enol ethers has been described. The acylsilanes having stereogenic centers at the α and β positions were treated with organometallic reagents such as alkyllithium, phenyllithium or methylmagnesium bromide to afford the corresponding silylalcohols in high yields with an excellent diastereoselectivity. The stereoselectivity was influenced by bulkiness of substituent at the α position of acylsilanes. The protiodesilylation of above obtained α-silylalcohols proceeded with complete retention of the configuration. Therefore, we could obtain the protiodesilylated compounds having three or four contiguous stereogenic centers with high diastereomeric purity. In addition, reduction of the acylsilanes afforded the corresponding α-silylalcohols in high yields with a high diastereoselectivity similarly to the nucleophilic reaction. Treatment of the acylsilanes having a dimethylphenylsilyl group with fluoride ion resulted in the formation of the corresponding phenyl carbinol derivatives via migration of a phenyl group in a high stereoselectivity. Further application and the efficient stereoselective construction of multiple stereogenic centers using these reactions are now in progress. The results will be reported in due course.

4. Experimental

4.1. General

IR spectra were recorded on a JASCO A-202 or SHIMADZU FTIR-8300 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM FX-100s, EX-270 or LA-400 spectrometer, and tetramethylsilane (TMS) served as the internal standard. Mass spectra were recorded on a JEOL JMS-SX102A, JMS-AM50 or Hitachi M-80 mass spectrometer.

Thin layer chromatography and flash column chromatography were performed by the use of silica gel 60F 254 (Merck) and silica gel BW-127ZH (Fuji Silysia), respectively.

All the solvents were distilled and stored over a drying agent. *n*-Buthyllithium (1.6 M solution in hexane) was purchased from Aldrich Chemical Co., Inc.

All reactions were carried out under an argon atmosphere in dried glassware.

Acylsilanes were prepared according to the literature procedures.[1]

4.2. A typical procedure for the preparation of β-methoxyacylsilane (1–4)[7]

A 300 ml, four-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, thermometer, drop funnel and magnetic stirring bar was charged with 50 ml of dichloromethane and 5 mmol of titanium tetrachloride. This solution was cooled to −78°C and acetal solution (5 mmol in 10 ml of dichloromethane) was added dropwise to the stirred solution. After 5 min, a solution of acylsilane silyl enol ether (5 mmol in 1 ml of dichloromethane) was added to the mixture. After completion of the reaction monitered by GC (usually after being stirred for 1 h at −78°C). A saturated NaCl solution was then added, and the resulting mixture was separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with a saturated NaCl solution, and dried over Na_2SO_4, filtered, concentrated. The crude product was purified and the diastereomers of β-methoxyacylsilane were separated by column chromatography (silica gel, benzene) to afford the pure 2,3-*anti* and 2,3-*syn* isomers as pale yellow oils.

4.3. Reaction of β-methoxyacylsilane with nucleophile

A 30 ml, three-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, thermometer and magnetic stirring bar was charged with 5 ml of THF and 0.5 mmol of β-methoxyacylsilane. This solution was cooled to −78°C and either organolithium reagent solution (1 mmol in hexane) or Grignard reagent solution (2 mmol in THF) was added slowly via syringe. After completion of the reaction monitered by GC (usually after being stirred for 5 min at −78°C), 5 ml of methanol was added to quench, and the resulting mixture was partitioned between H_2O and diethyl ether. The aqueous layer was extracted with diethyl ether. The combined organic phases were washed with a saturated NaCl solution, and dried over Na_2SO_4, filtered, concentrated. Column chromatography on silica gel afforded α-silylalcohol as pale yellow oils.

4.3.1. 4-Methoxy-3,4-diphenyl-2-trimethylsilyl-2-butanol (5f, 7f). *Compound* **5f**. IR (neat) 3470, 3055, 3040, 2955, 2900, 2810, 1600, 1495, 1455, 1245, 1105, 1085, 875, 835 cm^{-1}.

HRMS calcd for $C_{19}H_{24}OSi$ ($[M-CH_3OH]^+$) 296.1596, found 296.1603.

^1H NMR ($CDCl_3$) δ 7.49–6.72 (m, 10H), 5.23 (d, J=3.1 Hz, 1H), 4.10 (s, 1H), 3.31 (s, 3H), 2.63 (d, J=3.1 Hz, 1H), 1.62 (s, 3H), −0.29 (s, 9H).

^{13}C NMR ($CDCl_3$) δ 140.2, 138.3, 131.8, 127.7, 127.6, 127.5, 127.3, 126.5, 87.2, 69.7, 63.7, 55.9, 24.8.

Anal. calcd for $C_{20}H_{28}O_2Si$: C, 73.12; H, 8.59. Found: C, 73.27; H, 8.47.

Compound **7f**. HRMS calcd for $C_{19}H_{24}OSi$ ($[M-CH_3OH]^+$) 296.1596, found 296.1592.

^1H NMR ($CDCl_3$) δ 7.18–6.88 (m, 10H), 6.71 (d, J=10.5 Hz, 1H), 3.52 (s, 1H), 3.24 (d, J=10.5 Hz, 1H), 3.14 (s, 3H), 1.16 (s, 3H), 0.14 (s, 9H).

4.3.2. 7-Methoxy-6,7-diphenyl-5-trimethylsilyl-5-heptanol (7g). IR (neat) 3470, 3080, 3065, 3045, 2960, 2910, 2880, 1605, 1595, 1465, 1455, 1377, 1355, 1255, 1200, 1100, 980, 885, 835 cm^{-1}.

HRMS calcd for $C_{22}H_{30}OSi$ ($[M-CH_3OH]^+$) 338.2066, found 338.2066.

^1H NMR ($CDCl_3$) δ 7.39–6.68 (m, 10H), 4.70 (d, J=10.3 Hz, 1H), 3.42 (d, J=10.3 Hz, 1H), 3.30 (s, 1H), 3.14 (s, 3H), 1.79–1.05 (m, 6H), 0.86 (t, J=6.1 Hz, 3H), 0.16 (s, 9H).

4.3.3. 6-Methoxy-2-methyl-5,6-diphenyl-4-trimethylsilyl-4-hexanol (7h). IR (neat) 3455, 3055, 3030, 2955, 2900, 1495, 1450,1245, 1095, 840 cm^{-1}.

HRMS calcd for $C_{22}H_{30}OSi$ ($[M-CH_3OH]^+$) 338.2066, found 338.2050.

^1H NMR ($CDCl_3$) δ 7.49–6.79 (m, 10H), 4.73 (d, J=10.4 Hz, 1H), 4.65 (s, 1H), 3.48 (d, J=10.4 Hz, 1H), 3.12 (s, 1H), 1.63–1.32 (m, 1H), 1.03 (d, J=6.8 Hz, 3H), 0.87–0.70 (m, 2H), 0.65 (t, J=6.8 Hz, 3H), 0.28 (s, 9H).

4.3.4. 3-Methoxy-1,2,3-triphenyl-1-silyl-1-propanol (7i). IR (neat) 3450, 3095, 3060, 3045, 2960, 2910, 2835, 1605, 1495, 1455, 1445, 1340, 1245, 1100, 1075, 835 cm^{-1}.

HRMS calcd for $C_{25}H_{30}O_2Si$ (M^+) 390.2015, found 390.2035.

^1H NMR ($CDCl_3$) δ 7.43–6.65 (m, 15H), 5.04 (s, 1H), 4.37 (d, J=10.5 Hz, 1H), 3.78 (d, J=10.5 Hz, 1H), 3.06 (s, 1H), −0.13 (s, 9H).

4.3.5. 3-Cyclohexyl-4-methoxy-4-phenyl-2-trimethylsilyl-2-butanol (5j, 7j and 8j). *Compound* **5j**. IR (neat) 3450, 3040, 2940, 2850, 1445, 1365, 1245, 1095, 1075, 865, 840 cm^{-1}.

HRMS calcd for $C_{19}H_{30}OSi$ ($[M-CH_3OH]^+$) 302.2066, found 302.2065.

^1H NMR ($CDCl_3$) δ 7.62–7.08 (m, 5H), 4.55 (d, J=4.6 Hz, 1H), 4.26 (br, 1H), 3.25 (s, 3H), 2.22–0.57 (m, 12H), 1.18 (s, 3H), 0.08 (s, 9H).

Compound **7j**. HRMS calcd for $C_{19}H_{30}OSi$ ($[M-CH_3OH]^+$) 302.2066, found 302.2062.

^1H NMR ($CDCl_3$) δ 7.54–7.02 (m, 5H), 4.61 (d, J=6.6 Hz, 1H), 3.14 (s, 3H), 2.01–0.62 (m, 12H), 1.35 (s, 3H), 0.10 (s, 9H).

Compound **8j**. ^1H NMR ($CDCl_3$) δ 4.99 (d, J=3.4 Hz, 1H), 3.38 (s, 3H), 0.14 (s, 9H).

4.3.6. 6-Isopropyl-7-methoxy-7-phenyl-5-trimethylsilyl-5-heptanol (5k, 6k, 7k and 8k). *Compound* **5k**. IR (neat) 3570, 3500, 3070, 3030, 2960, 2880, 1455, 1365, 1250, 1090, 1075, 835 cm^{-1}.

HRMS calcd for $C_{19}H_{32}OSi$ ($[M-CH_3OH]^+$) 304.2222, found 304.2229.

^1H NMR ($CDCl_3$) δ 7.45–7.08 (m, 5H), 4.58 (d, J=2.5 Hz, 1H), 4.38 (br, 1H), 3.36 (s, 3H), 1.20 (d, J=6.8 Hz, 3H), 1.03 (d, J=6.8 Hz, 3H), 2.40–0.60 (m, 11H), 0.08 (s, 9H).

Compound **6k**. ^1H NMR ($CDCl_3$) δ 3.01 (s, 3H), 0.13 (s, 9H).

Compound **7k**. HRMS calcd for $C_{19}H_{32}OSi$ ($[M-CH_3OH]^+$) 304.2222, found 304.2219.

^1H NMR ($CDCl_3$) δ 7.55–7.10 (m, 5H), 4.79 (d, J=4.6 Hz, 1H), 3.25 (s 1H), 2.85 (br, 1H), 2.24–0.93 (m, 8H), 1.26 (d, J=7.1 Hz, 3H), 1.11 (d, J=7.3 Hz, 3H), 0.84 (t, J=7.3 Hz, 3H), 0.19 (s, 9H).

Compound **8k**. ^1H NMR ($CDCl_3$) δ 4.94 (d, J=3.7 Hz, 1H), 3.39 (s, 3H), 0.13 (s, 9H).

4.3.7. 3-Isopropyl-4-methoxy-4-phenyl-2-trimethylsilyl-2-butanol (5l, 7l, 8l). *Compound* **5l**. IR (neat) 3595, 3500,

3105, 3090, 3045, 2980, 2910, 2840, 1500, 1455, 1375, 1255, 1205, 1105, 1085, 1065, 860, 835 cm^{-1}.

HRMS calcd for $C_{16}H_{26}OSi$ ($[M-CH_3OH]^+$) 262.1753, found 262.1753.

^1H NMR ($CDCl_3$) δ 7.54–7.07 (m, 5H), 4.50 (d, J=4.6 Hz, 1H), 3.26 (s, 3H), 2.23–2.02 (m, 1H), 1.88 (dd, J=4.6 Hz, 1.6 Hz, 1H), 1.19 (s, 3H), 1.11 (d, J=7.1 Hz, 3H), 0.88 (d, J=7.1 Hz, 3H), 0.07 (s, 9H).

Compound **7l**. HRMS calcd for $C_{16}H_{26}OSi$ ($[M-CH_3OH]^+$) 262.1753, found 262.1742.

^1H NMR ($CDCl_3$) δ 7.50–7.09 (m, 5H), 4.65 (d, J=6.1 Hz, 1H), 3.16 (s, 3H), 2.08 (dd, J=6.1 Hz, 1.2 Hz, 1H), 1.83–1.56 (m, 1H), 1.35 (s, 3H), 1.05 (d, J=7.1 Hz, 3H), 1.03 (d, J=7.1 Hz, 3H), 0.10 (s, 9H).

Compound **8l**. ^1H NMR ($CDCl_3$) δ4.99 (d, J=4.1 Hz, 1H), 3.37 (s, 3H), 0.12 (s, 9H).

4.3.8. 3-Ethyl-4-methoxy-4-phenyl-2-trimethylsilyl-2-butanol (7m, 8m). *Compound* **7m**. IR (neat) 3465, 3060, 3025, 2950, 2865, 1495, 1455, 1250, 1080, 835 cm^{-1}.

HRMS calcd for $C_{15}H_{24}OSi$ ($[M-CH_3OH]^+$) 248.1596, found 248.1587.

^1H NMR ($CDCl_3$) δ 7.49–7.12 (m, 5H), 4.85 (br, 1H), 4.15 (d, J=10.5 Hz, 1H), 3.03 (s, 3H), 1.83–0.68 (m, 6H), 1.25 (t, J=7.3 Hz, 3H), 0.15 (s, 9H).

Compound **8m**. ^1H NMR ($CDCl_3$) δ 5.39 (br, 1H), 4.34 (d, J=10.0 Hz, 1H), 3.10 (s, 3H), 0.10 (s, 9H).

4.3.9. 4-Methoxy-3,5-diphenyl-2-trimethylsilyl-2-hexanol (9a, 11a). *Compound* **9a**. IR (neat) 3412, 3061, 3028, 2932, 2833, 1709, 1493, 1452, 1248, 1096, 1063 cm^{-1}.

HRMS calcd for $C_{21}H_{28}OSi$ ($[M-CH_3OH]^+$) 324.1909, found 324.1922.

^1H NMR ($CDCl_3$) δ 7.56–6.88 (m, 10H), 4.26 (dd, J=9.5, 2.4 Hz, 1H), 3.73 (s, 3H), 3.47 (br, 1H), 2.54 (dq, J=7.1, 2.4 Hz, 1H), 2.40 (d, J=2.4 Hz, 1H), 1.39 (s, 3H), 1.20 (d, J=7.1 Hz, 3H), −0.42 (s, 9H).

Anal. calcd for $C_{22}H_{32}O_2Si$: C, 74.10; H, 9.05. Found: C, 74.31; H, 8.97.

Compound **11a**. HRMS calcd for $C_{21}H_{28}OSi$ ($[M-CH_3OH]^+$) 324.1909, found 324.1905.

^1H NMR ($CDCl_3$) δ 7.48–6.85 (m, 10H), 4.06 (dd, J=8.3, 3.9 Hz, 1H), 3.17 (s, 3H), 2.96 (d, J=8.3 Hz, 1H), 2.86 (m, 1H), 1.60 (br, 1H), 1.31 (s, 3H), 1.27 (d, J=8.1 Hz, 3H), −0.12 (s, 9H).

4.3.10. 3-Cyclohexyl-4-methoxy-5-phenyl-2-trimethylsilyl-2-hexanol (9b). IR (neat) 3515, 3450, 3090, 3060, 3035, 2970, 2905, 2840, 1495, 1455, 1385, 1365, 1250, 1110, 1085, 860, 840 cm^{-1}.

HRMS calcd for $C_{21}H_{34}OSi$ ($[M-CH_3OH]^+$) 330.2379, found 330.2370.

^1H NMR ($CDCl_3$) δ 7.48–6.98 (m, 5H), 3.70 (dd, J=8.1, 2.1 Hz, 1H), 3.50 (s, 3H), 3.32–3.09 (m, 1H), 1.98–0.71 (m, 12H), 1.38 (d, J=7.1 Hz, 3H), 1.16 (s, 3H), −0.12 (s, 9H).

4.3.11. 3-Isopropyl-4-methoxy-5-phenyl-2-trimethylsilyl-2-hexanol (9c). IR (neat) 3510, 3470, 3080, 3025, 2935, 2835, 1495, 1455, 1250, 1100, 1080, 840 cm^{-1}.

HRMS calcd for $C_{18}H_{30}OSi$ ($[M-CH_3OH]^+$) 290.2066, found 290.2057.

^1H NMR ($CDCl_3$) δ 7.42–6.96 (m, 5H), 3.71 (dd, J=8.0, 2.0 Hz, 1H), 3.48 (s, 3H), 3.26–3.04 (m, 1H), 2.54–2.35 (m, 1H), 1.67–1.48 (m, 1H), 1.38 (d, J=7.1 Hz, 3H), 1.24 (d, J=7.1 Hz, 3H), 1.19 (d, J=7.1 Hz, 3H), 1.13 (s, 3H), −0.13 (s, 9H).

4.4. Reduction of β-methoxyacylsilanes with lithium aluminum hydride

A 30 ml, three-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, thermometer and magnetic stirring bar was charged with 5 ml of THF and 0.5 mmol of β-methoxyacylsilane. This solution was cooled to −78°C and lithium aluminum hydride solution (2 mmol in THF) was added slowly via syringe. After completion of the reaction monitered by GC (usually after being stirred for 30 min at −78°C), 5 ml of methanol was added to quench, and the resulting mixture was partitioned between H_2O and diethyl ether. The aqueous layer was extracted with diethyl ether. The combined organic phases were washed with a saturated NaCl solution, and dried over Na_2SO_4, filtered, concentrated. Column chromatography on silica gel afforded α-silylalcohol as pale yellow oils.

4.4.1. 3-Methoxy-2,3-diphenyl-1-trimethylsilylpropanol (13a–15a). *Compound* **13a**. IR (neat) 3460, 3090, 3070, 3045, 2960, 2910, 2825, 1495, 1455, 1250, 1105, 865, 840 cm^{-1}.

HRMS calcd for $C_{18}H_{22}OSi$ ($[M-CH_3OH]^+$) 282.1440, found 282.1440.

^1H NMR ($CDCl_3$) δ 7.33–6.84 (m, 10H), 4.63 (d, J=8.1 Hz, 1H), 4.23 (br, 1H), 3.24 (s, 3H), 2.84 (dd, J=8.1, 2.8 Hz, 1H), 2.36 (br, 1H), −0.25 (s, 9H).

^{13}C NMR ($CDCl_3$) δ 140.5, 140.4, 129.8, 127.9, 127.8, 127.2, 127.1, 126.5, 85.8, 65.2, 57.0, 55.6, −3.4.

Anal. calcd for $C_{19}H_{26}O_2Si$: C, 72.56; H, 8.33. Found: C, 72.40; H, 8.34.

Compound **14a**. ^1H NMR ($CDCl_3$) δ 7.25–6.83 (m, 10H), 5.13 (s, 1H), 4.62 (d, J=9.5 Hz, 1H), 4.05 (dd, J=10.6, 1.1 Hz, 1H), 3.23 (s, 3H), 3.14 (dd, J=10.6, 9.5 Hz, 1H), −0.29 (s, 9H).

Compound **15a**. HRMS calcd for $C_{18}H_{22}OSi$ ($[M-CH_3OH]^+$) 282.1440, found 282.1436.

^{1}H NMR ($CDCl_3$) δ 7.37–6.85 (m, 10H), 4.77 (d, J=6.7 Hz, 1H), 3.65 (d, J=3.3 Hz, 1H), 3.13 (s, 3H), 2.87 (dd, J=6.7, 3.3 Hz, 1H), −0.25 (s, 9H).

4.4.2. 2-Cyclohexyl-3-methoxy-3-phenyl-1-trimethylsilyl-propanol (13b–16b). *Compound* **15b**. IR (neat) 3450, 3040, 2940, 2850, 1445, 1365, 1245, 1095, 1075, 865, 840 cm^{-1}.

HRMS calcd for $C_{18}H_{28}OSi$ ($[M-CH_3OH]^+$) 288.1909, found 280.1904.

^{1}H NMR ($CDCl_3$) δ 7.37–7.23 (m, 5H), 4.66 (d, J=1.6 Hz, 1H), 3.82 (s, 1H), 3.46 (d, J=1.6 Hz, 1H), 3.25 (s, 3H), 2.29–1.17 (m, 12H), −0.07 (s, 9H).

Compound **16b**. ^{1}H NMR ($CDCl_3$) δ 4.33 (dd, J=10.0, 2.7 Hz, 1H), 3.05 (s, 3H).

Compound **13b**. HRMS calcd for $C_{18}H_{28}OSi$ ($[M-CH_3OH]^+$) 288.1909, found 280.1905.

^{1}H NMR ($CDCl_3$) δ 7.39–7.25 (m, 5H), 4.41 (d, J=9.3 Hz, 1H), 3.13 (s, 3H), 3.10 (s, 1H), 1.99 (d, J=12.4 Hz, 1H), 1.79–0.90 (m, 12H), −0.02 (s, 9H).

Compound **14b**. ^{1}H NMR ($CDCl_3$) δ 4.76 (d, J=2.7 Hz, 1H), 3.81 (dd, J=5.3, 2.7 Hz, 1H), 3.53 (d, J=5.3 Hz, 1H), 3.24 (s, 3H), 2.19 (d, J=12.2 Hz, 1H), 0.15 (s, 9H).

4.4.3. 2-Ethyl-3-methoxy-3-phenyl-1-trimethylsilyl-propanol (13d–16d). *Compound* **15d**. IR (neat) 3450, 3040, 2940, 2850, 1445, 1365, 1245, 1095, 1075, 865, 840 cm^{-1}.

HRMS calcd for $C_{14}H_{22}OSi$ ($[M-CH_3OH]^+$) 234.1440, found 234.1436.

^{1}H NMR ($CDCl_3$) δ 7.38–7.23 (m, 5H), 4.63 (d, J=2.0 Hz, 1H), 3.84 (br, 1H), 3.38 (br, 1H), 3.26 (s, 3H), 1.65–1.37 (m, 2H), 0.60 (t, J=7.1 Hz, 3H), 0.06 (s, 9H).

Compound **16d**. ^{1}H NMR ($CDCl_3$) 0.17 (s, 9H).

Compound **13d**. HRMS calcd for $C_{14}H_{22}OSi$ ($[M-CH_3OH]^+$) 234.1440, found 234.1452.

^{1}H NMR ($CDCl_3$) δ δ 7.38–7.26 (m, 5H), 4.20 (d, J=9.5 Hz, 1H), 3.66–3.61 (m, 1H), 3.30–3.20 (m, 1H), 3.09 (s, 3H), 1.95–1.91 (m, 1H), 1.26–1.01 (m, 2H), 0.67 (t, J=7.6 Hz, 3H), 0.00 (s, 9H).

Compound **14d**. ^{1}H NMR ($CDCl_3$) δ 3.23 (s, 3H), 0.12 (s, 9H).

4.4.4. 3-Methoxy-4-methyl-2-phenyl-1-trimethylsilyl-propanol (13e, 15e). *Compound* **15e**. IR (neat) 3460, 3090, 3070, 3045, 2960, 2910, 2825, 1495, 1455, 1250, 1105, 865, 840 cm^{-1}.

HRMS calcd for $C_{15}H_{24}OSi$ ($[M-CH_3OH]^+$) 248.1596, found s248.1594.

^{1}H NMR ($CDCl_3$) δ 7.41–7.20 (m, 5H), 3.82 (dd, J=3.6, 3.4 Hz, 1H), 3.48 (dd, J=5.9, 5.9 Hz, 1H), 3.30 (s, 3H), 2.85 (dd, J=5.9, 3.4 Hz, 1H), 2.60 (d, J=3.6 Hz, 1H), 1.91–1.83 (m, 1H), 0.92 (d, J=6.8 Hz, 3H), 0.85 (d, J=6.8 Hz, 3H), −0.19 (s, 9H).

Compound **13e**. HRMS calcd for $C_{15}H_{24}OSi$ ($[M-CH_3OH]^+$) 248.1596, found s248.1584.

^{1}H NMR ($CDCl_3$) δ 7.41–7.21 (m, 5H), 4.03 (dd, J=6.6, 2.2 Hz, 1H), 3.54 (s, 3H), 3.52 (dd, J=8.3, 4.4 Hz, 1H), 2.72 (dd, J=8.3, 2.2 Hz, 1H), 1.97 (d, J=6.6 Hz, 1H), 1.63–1.56 (m, 1H), 0.95 (d, J=6.8 Hz, 3H), 0.83 (d, J=6.6 Hz, 3H), −0.25 (s, 9H).

4.5. Protiodesilylation of α-silylalcohol

A 30 ml, three-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, thermometer and magnetic stirring bar was placed in a water bath (30°C) and charged with 10 ml of DMF, 0.5 mmol of α-silylalcohol and tetrabuthylammonium fluoride solution (2.5 mmol in DMF). After 24 h, a saturated NaCl solution was added, and the resulting mixture was partitioned between H_2O and diethyl ether. The aqueous layer was extracted with diethyl ether. The combined organic phases were washed with a saturated NaCl solution, and dried over Na_2SO_4, filtered, and concentrated. Column chromatography on silica gel afforded the corresponding alcohols as pale yellow oils.

4.5.1. 4-Methoxy-3,5-diphenyl-2-hexanol (17a, 18a). *Compound* **17a**. IR (neat) 3474, 3061, 3026, 2970, 2930, 2882, 2837, 1493, 1452, 1408, 0369, 1136, 1086 cm^{-1}.

HRMS calcd for $C_{19}H_{24}O_2$ (M^+) 284.1776, found 284.1783.

^{1}H NMR ($CDCl_3$) δ 7.56–6.91 (m, 10H), 4.20 (dq, J=9.8, 6.1 Hz, 1H), 4.08 (dd, J=10.1, 2.5 Hz, 1H), 3.73 (s, 3H), 2.45 (dq, J=10.1, 6.8 Hz, 1H), 2.24 (dd, J=9.8, 2.5 Hz, 1H), 1.58 (br, 1H), 1.26 (d, J=6.8 Hz, 3H), 0.87 (d, J=6.1 Hz, 3H).

^{13}C NMR ($CDCl_3$) δ 145.0, 140.8, 128.8, 128.4, 128.2, 127.7, 126.9, 126.1, 93.4, 71.3, 61.2, 56.8, 40.9, 21.8, 11.7.

Anal. calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.38; H, 8.59.

Compound **18a**. HRMS calcd for $C_{19}H_{24}O_2$ (M^+) 284.1776, found 284.1777.

^{1}H NMR ($CDCl_3$) δ 7.54–6.84 (m, 10H), 4.63 (br, 1H), 4.18 (dq, J=8.6, 6.1 Hz, 1H), 3.85 (dd, J=9.8, 2.5 Hz, 1H), 3.14 (s, 3H), 2.76 (dd, J=9.8, 8.6 Hz, 1H), 2.69 (dq, J=7.2, 2.5 Hz, 1H), 1.29 (d, J=7.2 Hz, 3H), 0.84 (d, J=6.1 Hz, 3H).

4.5.2. 3-Cyclohexyl-4-methoxy-5-phenyl-2-hexanol (17b). IR (neat) 3449, 3061, 3026, 2926, 2851, 1493, 1450, 1375, 1094 cm^{-1}.

HRMS calcd for $C_{19}H_{30}O_2$ (M^+) 290.2246, found 290.2253.

^{1}H NMR ($CDCl_3$) δ 7.57–6.92 (m, 5H), 4.11–3.91 (m, 1H), 3.71 (dd, J=8.1, 2.2 Hz, 1H), 3.49 (s, 3H), 3.17–2.95 (m, 1H), 2.06–0.72 (m, 12H), 1.38 (d, J=6.8 Hz, 3H), 1.03 (d, J=6.4 Hz, 3H).

4.5.3. 3-Isopropyl-4-methoxy-5-phenyl-2-hexanol (17c). IR (neat) 3450, 3061, 3026, 2963, 2932, 2876, 2831, 1495, 1454, 1371, 1092, 1020 cm^{-1}.

HRMS calcd for $C_{16}H_{26}O_2$ (M^+) 250.1933, found 250.1936.

^{1}H NMR ($CDCl_3$) δ 7.57–6.93 (m, 5H), 4.13–3.89 (m, 1H), 3.72 (dd, J=8.1, 2.0 Hz, 1H), 3.50 (s, 3H), 3.14–2.99 (m, 1H), 2.07–2.01 (m, 1H), 1.39 (d, J=6.8 Hz, 3H), 1.37–1.32 (m, 1H), 1.03 (d, J=6.4 Hz, 6H), 0.85 (d, J=7.1 Hz, 3H).

4.5.4. 4-Methoxy-3,4-diphenyl-2-butanol (23). According to the general procedure, the protiodesililation of **7f** afforded **23** in 94% yield. IR (neat) 3490, 3100, 3080, 3060, 2960, 2940, 2840, 1500, 1460, 1420, 1375, 1295, 1135, 1090, 1035, 975 cm^{-1}.

HRMS calcd for $C_{16}H_{16}O$ ($[M-CH_3OH]^+$) 224.1201, found 224.1205.

^{1}H NMR ($CDCl_3$) δ 7.28–6.80 (m, 10H), 5.07 (s, 1H), 4.56 (d, J=10.1 Hz, 1H), 4.41 (dq, J=9.1, 6.1 Hz, 1H), 3.23 (s, 3H), 2.86 (dd, J=10.1, 9.1 Hz, 1H), 0.92 (d, J=6.1 Hz, 3H).

^{13}C NMR ($CDCl_3$) δ 139.6, 139.2, 128.8, 128.0, 127.7, 127.4, 127.3, 126.3, 90.3, 71.8, 60.3, 56.4, 21.9.

Anal. calcd for $C_{17}H_{20}O_2$: C, 79.59; H, 7.86. Found: C, 79.65; H, 7.98.

4.6. Treatment of β-methoxyacylsilane 2′ with tetrabutylammonium fluoride (TBAF)

A 30 ml, three-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, thermometer and magnetic stirring bar was placed in a water bath (25°C) and charged with 10 ml of THF, 0.5 mmol of acylsilane and tetrabuthylammonium fluoride solution (0.1 mmol in THF). After 1 h, a saturated NaCl solution was added, and the resulting mixture was partitioned between H_2O and diethyl ether. The aqueous layer was extracted with diethyl ether. The combined organic phases were washed with a saturated NaCl solution, and dried over Na_2SO_4, filtered, concentrated. Column chromatography on silica gel afforded the corresponding alcohols as pale yellow oils.

4.6.1. 3-Methoxy-1,2,3-triphenyl-1-propanol (19a). IR (neat) 3450, 3095, 3070, 3040, 2945, 2825, 1495, 1450, 1100, 1085, 1060, 1025 cm^{-1}.

HRMS calcd for $C_{21}H_{18}O$ ($[M-CH_3OH]^+$) 286.1358, found 286.1359.

^{1}H NMR ($CDCl_3$) δ 7.58–6.77 (m, 15H), 5.38 (d, J=2.7 Hz, 1H), 4.71 (d, J=7.7 Hz, 1H), 3.32 (s, 3H), 3.27 (dd, J=7.7, 2.7 Hz, 1H).

Anal. calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.96. Found: C, 82.95; H, 6.87.

4.6.2. 2-(Methoxyphenylmethyl)-3-methyl-1-phenyl-1-butanol (19c). IR (neat) 3430, 3080, 3070, 3015, 2945, 2830, 1220 cm^{-1}.

HRMS calcd for $C_{18}H_{20}O$ ($[M-CH_3OH]^+$) 252.1514, found 252.1509.

^{1}H NMR ($CDCl_3$) δ 7.47–7.14 (m, 10H), 4.93 (d, J=7.1 Hz, 1H), 4.45 (d, J=7.3 Hz, 1H), 4.45–4.19 (m, 1H), 3.20 (s, 3H), 2.25 (ddd, J=7.2, 6.8, 2.5 Hz, 1H), 1.60–1.35 (m, 1H), 0.75 (d, J=7.1 Hz, 3H), 0.75 (d, J=7.1 Hz, 3H).

4.6.3. 2-(Methoxyphenylmethyl)-1-phenyl-1-butanol (19d). IR (neat) 3440, 3085, 3065, 3040, 2970, 2935, 2880, 2830, 1085 cm^{-1}.

HRMS calcd for $C_{17}H_{18}O$ ($[M-CH_3OH]^+$) 238.1358, found 238.1357.

^{1}H NMR ($CDCl_3$) δ 7.41–7.19 (m, 10H), 4.98 (br, 1H), 4.29 (br, 1H), 4.28 (d, J=5.5 Hz, 1H), 3.29 (s, 3H), 1.90–1.84 (m, 1H), 1.36–1.29 (m, 1H), 1.27–1.18 (m, 1H), 0.84 (t, J=7.5 Hz, 3H).

4.6.4. 1,3-Dimethoxy-1,2-diphenylbutane (24). A 30 ml, three-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, reflux condenser and magnetic stirring bar was placed and charged with 15 ml of THF, 1.4 mmol of 4-methoxy-3,4-diphenyl-2-butanol **23** and sodium hydride (2.8 mmol). Then iodomethane (11.2 mmol) was added slowly via syringe. This mixture was stirred under reflux. After 6 h, water was added, and the resulting mixture was partitioned between H_2O and diethyl ether. The aqueous layer was extracted with diethyl ether. The combined organic phases were washed with a saturated NaCl solution, and dried over Na_2SO_4, filtered, concentrated. Column chromatography on silica gel afforded the corresponding dimethoxybutane **24** in 87% yield.

IR (neat) 3090, 3070, 3040, 2985, 2940, 2910, 2820, 1490, 1455, 1370, 1185, 1145, 1095, 1075 cm^{-1}.

HRMS calcd for $C_{18}H_{22}O_2$ (M^+) 270.1620, found 270.1617.

^{1}H NMR ($CDCl_3$) δ 7.25–6.81 (m, 10H), 4.76 (d, J=6.1 Hz, 1H), 3.67 (dq, J=7.9, 6.1 Hz, 1H), 3.41 (s, 3H), 3.29 (dd, J=7.9, 6.1 Hz, 1H), 3.22 (s, 3H), 1.03 (d, J=6.1 Hz, 3H).

^{13}C NMR ($CDCl_3$) δ 139.4, 138.2, 130.2, 128.0, 127.5, 127.3, 127.2, 126.3, 83.5, 76.6, 57.0, 56.7, 55.7, 16.4.

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