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Facile Syntheses of α-Bromo-α-Silyl Ketones and α-Bromoacylsilanes from *tert*-Butyldimethylsilyldibromomethane and Carbonyl Compounds

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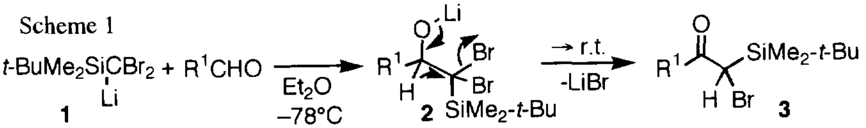
Abstract: An addition of benzaldehyde to an ethereal solution of *tert*-butyldimethylsilyldibromomethyllithium, derived from t-BuMe$_2$SiCHBr$_2$ and lithium diisopropylamide, provided α-bromo-α-silyl ketone. The use of ketone instead of aldehyde afforded α-bromoacylsilane via a bromo silyl epoxide intermediate. Further treatment of the α-bromo-α-silyl ketone with butyllithium afforded lithium enolate which provided β-hydroxy-α-silyl ketone upon treatment with aldehyde in ether. The enolate gave α,β-unsaturated ketone or monosilyl ether of 2-acyl-1,3-diol in THF instead of ether. The use of isopropylmagnesium bromide in place of butyllithium also resulted in a formation of the corresponding magnesium enolate. Copyright © 1996 Elsevier Science Ltd

In the last two decades, both α-silyl ketone[1] (β-ketosilane) and acylsilane[2] have been extensively explored in organic synthesis. In many cases, they are prepared through a multistep operation involving oxidation of the corresponding hydroxysilane. We report here a facile and non-oxidative method for formation of α-bromo-α-silyl ketones and α-bromoacylsilanes[3] from *tert*-butyldimethylsilyldibromomethyllithium and carbonyl compounds. We also describe the reductive formation of enolates from α-bromo-α-silyl ketones and their aldol-type reaction with aldehydes involving the 1,3-rearrangement of a silyl group (homo-Brook rearrangement) from carbon to oxygen.[4]

We have previously reported[5] that treatment of a THF solution of *tert*-butyldimethylsilyldihalomethyllithium with aldehyde (R^1CHO) followed by an addition of a second aldehyde (R^2CHO) and HMPA gave a monosilyl ether of 1,3-diol ($R^1CH(OSiMe_2\text{-}t\text{-}Bu)CX_2CH(OH)R^2$).. The use of ether instead of THF as a solvent has proved to change the reaction pathway dramatically and treatment of *tert*-butyldimethylsilyldibromomethyllithium (**1**) with aldehyde (R^1CHO) gave α-bromo-α-silyl ketone ($R^1COCHBrSiMe_2\text{-}t\text{-}Bu$). Furthermore, the reaction of **1** with ketone ($R^2{}_2CO$) under the same conditions afforded α-bromoacylsilane ($R^2{}_2CBrCOSiMe_2\text{-}t\text{-}Bu$).

Treatment of *tert*-butyldimethylsilyldibromomethyllithium (**1**), derived from t-BuMe$_2$SiCHBr$_2$ and lithium diisopropylamide, with benzaldehyde in ether at –78 °C provided α-bromo-α-silyl ketone **3a** in 76% yield upon warming the reaction mixture to room temperature. The representative results are shown in Scheme 1. Quenching the reaction mixture at –78 °C with dilute hydrochloric acid afforded a simple adduct ($PhCH(OH)CBr_2SiMe_2$-*t*-Bu) in 77 % yield.[5] Thus, the reaction obviously involves initial formation of adducts **2** followed by 1,2-migration of hydrogen[6] giving α-bromo-α-silyl ketones. The *tert*-butyldimethylsilyl group played a critical role in the formation of α-bromo-α-silyl ketones. Thus, the reaction of trimethylsilyldibromomethyllithium with benzaldehyde gave α-bromo-acetophenone and 2,2-dibromo-1-phenyl-2-trimethylsilylethanol in 29 % and 26 % yield, respectively and no α-bromo-α-silyl ketone was detected in the reaction mixture. The formation of α-bromoacetophenone might result from desilylation of α-bromo-α-trimethylsilylacetophenone during aqueous workup. The use of *tert*-butyldimethylsilyldichloromethyllithium resulted in a formation of complex mixtures.

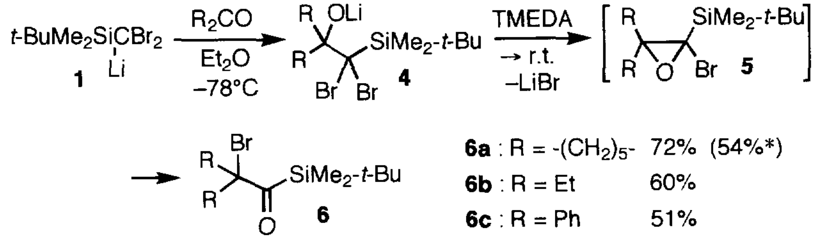
Scheme 1



R^1 = Ph **3a** : 76% R^1 = *c*-C_6H_{11} **3b** : 72%
R^1 = PhCH=CH **3c** : 62% R^1 = *t*-Bu **3d** : 49%
R^1 = *n*-C_6H_{13} **3e** : 42%

The reaction of **1** with ketone such as cyclohexanone in place of aldehyde gave α-bromoacylsilane. The representative results are shown in Scheme 2. An addition of TMEDA increased the yield of the product, for example, from 54 % to 72 % in the case of **6a**. Interestingly, the addition of TMEDA did not accelerate the 1,3-rearrangement of the silyl group from carbon to negatively charged oxygen. The effect of TMEDA is quite different from that of HMPA which does cause 1,3-rearrangement.[5] The reaction would proceed via bromo silyl epoxide which is so unstable as to rearrange into acylsilane.[3h] This mechanism was supported by

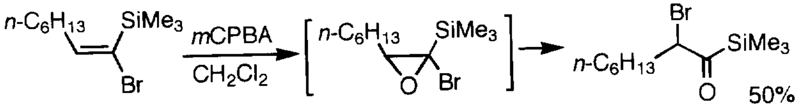
Scheme 2



6a : R = -$(CH_2)_5$- 72% (54%*)
6b : R = Et 60%
6c : R = Ph 51%
* in the absence of TMEDA

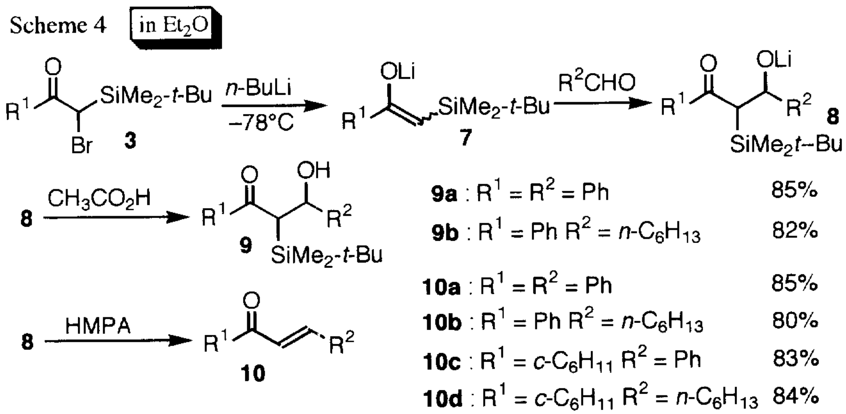
the following experiment (Scheme 3). Treatment of 1-bromo-1-trimethylsilyl-1-octene with *m*-chloroperoxybenzoic acid in dichloromethane afforded α-bromoacylsilane (n-$C_6H_{13}CHBrCOSiMe_3$) in 50% yield. In the case of aldehyde (*vide supra*), no corresponding α-bromoacylsilane could be observed. Thus, the 1,2-migration of hydrogen in the adduct **2** seems to be much faster than epoxide formation.

Scheme 3



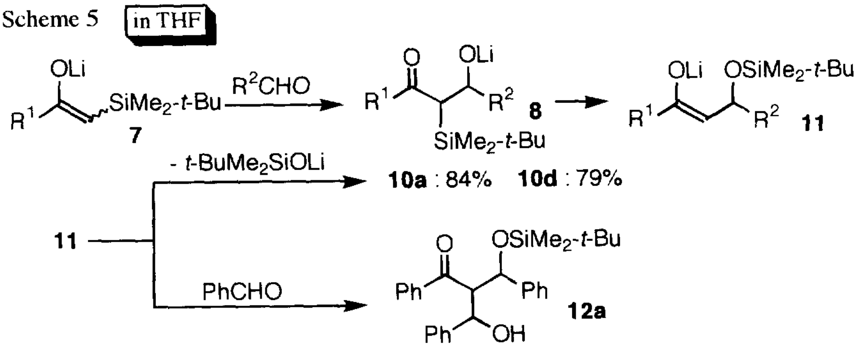
Then we turned our attention toward the reductive formation of enolate[7] from α-bromo-α-silyl ketone. An addition of butyllithium to an ether solution of α-bromo-α-silyl ketone **3** at –78 °C caused a lithium-bromine exchange to afford an enolate **7**[8] which was quenched with dilute hydrochloric acid to give α-silyl ketone ($R^1COCH_2SiMe_2$-*t*-Bu) quantitatively. The sequential treatment of the enolate **7** with aldehyde in ether followed by quenching with acetic acid yielded β-hydroxy-α-silyl ketone **9**. An addition of HMPA to the adduct **8** before quenching provided only (*E*)-α,β-unsaturated ketone **10** with high stereoselectivity in good yield. Six examples are shown below (Scheme 4).

Scheme 4



Again, the reaction solvent played a critical role in the reaction of enolate **7** with aldehydes. In THF, the reaction of enolate **7** with aldehyde (1.1 equiv) provided (*E*)-α,β-unsaturated ketone **10** directly without an addition of HMPA (Scheme 5). For instance, the enolate **7a** (R^1 = Ph) or **7b** (R^1 = *c*-C_6H_{11}) gave α,β-unsaturated ketone **10a** or **10d** in 84% or 79% yield, respectively, upon treatment with benzaldehyde or heptanal. An addition of an excess of PhCHO[9] to **7a** gave monosilyl ether of 2-acyl-1,3-diol **12a** (R^1 = R^2 = Ph), derived from two molecules of aldehyde, in addition to α,β-unsaturated ketone **10a**. The yield of **12a** increased with increase of the amount of benzaldehyde employed and the use of four molar equivalents of benzaldehyde per one mol of enolate gave a mixture of **10a** and **12a** in 23% and 73% yields, respectively. Thus, the 1,3-rearrangement[10] of the silyl group (**8**→**11**) takes place readily in THF and an addition of **11** to the second molecule of aldehyde competes with elimination of *t*-BuMe$_2$SiOLi to give α,β-unsaturated ketone.

Scheme 5



In these reactions, α,β-unsaturated ketone does not arise from 1,2-elimination of silanoxide (Peterson elimination) from **8**. This was confirmed by the following experiment (Scheme 6). The reaction of magnesium enolate **13** with heptanal (*vide infra*) gave a diastereomeric mixture (56/44) of β-hydroxy-α-silyl ketone **9d**. It was anticipated that Peterson-type 1,2-elimination of silanoxide would proceed in *syn* fashion with high stereospecificity to afford a mixture of (*E*)- and (*Z*)-α,β-unsaturated ketone (*E*/*Z* = 56/44). However, treatment of the diastereomeric mixture **9d** with lithium diisopropylamide provided only (*E*)-α,β-unsaturated ketone **10d**.[11] Thus, stereoselective formation of (*E*)-α,β-unsaturated ketone could be explained by the relative stabilities of the rotamer **A** of the intermediate enolate **11** (R^1 = *c*-C$_6$H$_{11}$, R^2 = *n*-C$_6$H$_{13}$), which is more stable than **B** (Figure 1).[10]

Scheme 6

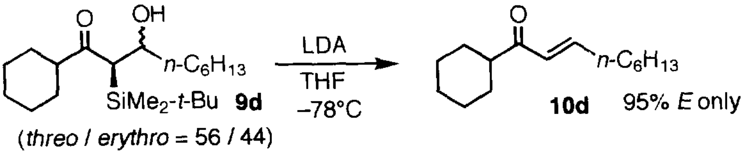
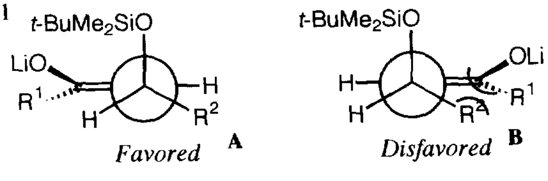
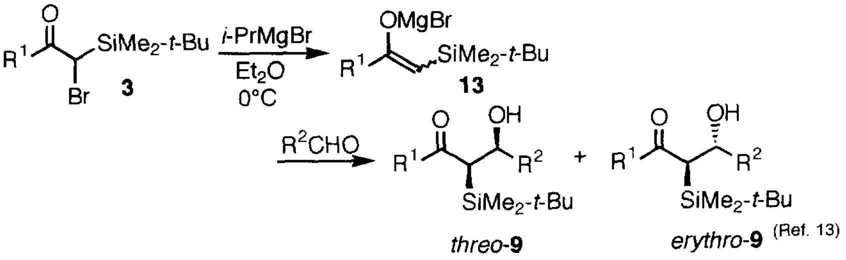


Figure 1



Treatment of α-bromo-α-silyl ketone **3** with isopropylmagnesium bromide in ether gave magnesium enolate **13** in good yields. The reaction of the magnesium enolate with aldehydes afforded β-hydroxy-α-silyl ketone **9**[12] selectively in good yields (Scheme 7). No trace of α,β-unsaturated ketone could be observed in the reaction mixture. 1,3-Rearrangement of the silyl group could not take place because of the lower nucleophilicity of magnesium alkoxide compared to lithium alkoxide.

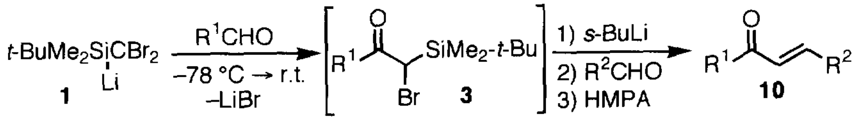
Scheme 7



9a : R^1 = Ph	R^2 = Ph	78%	(89 / 11)
9b : R^1 = Ph	R^2 = n-C_6H_{13}	78%	(88 / 12)
9c : R^1 = c-C_6H_{11}	R^2 = Ph	75%	(72 / 28)
9d : R^1 = c-C_6H_{11}	R^2 = n-C_6H_{13}	73%	(56 / 44)

Finally, one-pot synthesis of α,β-unsaturated ketone starting from *tert*-butyldimethylsilyldibromomethyllithium (**1**) was conducted. An addition of aldehyde to an ethereal solution of **1** gave α-bromo-α-silyl ketone which was further converted into lithium enolate with *sec*-BuLi[15] and then treated with second aldehyde and subsequently with HMPA to afford α,β-unsaturated ketone **10a** or **10b** in 59% or 57% yield, respectively (Scheme 8).

Scheme 8



10a : 59% **10b** : 57% **10c** : 56% **10d** : 53%

Experimental

Distillation of the products was performed by the use of Kugelrohr (Büchi), and boiling points are indicated by air-bath temperature without correction. Melting points were obtained on a Yanako MP-50929 melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were taken on a Varian GEMINI 300 spectrometer, $CDCl_3$ was used as a solvent, and chemical shifts being given in δ with tetramethylsilane as an internal standard. IR spectra were determined on a JASCO IR-810 spectrometer. The analyses were carried out at the Elemental Analysis Center of Kyoto University. Diethyl ether was dried over a slice of sodium. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl before use.

General Procedure for the Preparation of α-Bromo-α-silyl Ketones. An ethereal solution of *tert*-butyldimethyl(dibromomethyl)silane (0.29 g, 1.0 mmol) was added to a solution of lithium diisopropylamide (1.2 mmol) in ether (3 ml) at –78 °C under argon atmosphere. After being stirred for 1 h at –78 °C, benzaldehyde (0.13 g, 1.2 mmol) in Et_2O (1 ml) was added and the reaction mixture was allowed to warm to ambient temperature over 10 h with stirring. The mixture was poured into saturated aqueous ammonium chloride and extracted with hexane (20 ml × 3). The combined organic layer were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by silica-gel column chromatography gave 1-bromo-1-(*tert*-butyldimethylsilyl)-2-phenyl-2-ethanone (**3a**, 0.24 g) in 76% yield: Mp 55–56 °C; IR (neat) 2952, 2926, 2856, 1676, 1465, 1448, 1261, 832, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ –0.01 (s, 3H), 0.24 (s, 3H), 0.95 (s, 9H), 4.90 (s, 1H), 7.40–7.65 (m, 3H), 7.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –6.11, 5.67, 17.96, 27.03, 35.73, 128.49, 128.77, 133.37, 136.61, 196.32. Found: C, 53.37; H, 6.79%. Calcd for $C_{14}H_{21}BrOSi$: C, 53.67; H, 6.76%.

1-Bromo-1-(*tert*-butyldimethylsilyl)-2-cyclohexyl-2-ethanone (3b): Bp 85 °C (0.5 Torr); IR (neat) 2926, 2852, 1703, 1685, 1450, 1251, 1000, 840, 824 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.10 (s, 3H), 0.23 (s, 3H), 0.96 (s, 9H), 1.15–1.95 (m, 10H), 2.65 (tt, J = 11.0, 3.1 Hz, 1H), 3.95 (s, 1H); ^{13}C NMR ($CDCl_3$) δ –6.10, 17.78, 25.31, 25.69, 25.93, 26.99, 28.59, 29.71, 39.25, 50.05, 209.12. Found: C, 52.58; H, 8.67%. Calcd for $C_{14}H_{27}BrOSi$: C, 52.65; H, 8.52%.

1-Bromo-1-(*tert*-butyldimethylsilyl)-4-phenyl-3-buten-2-one (3c): Bp 100 °C (0.5 Torr); IR (neat) 2950, 2926, 2854, 1670, 1607, 1466, 1311, 1253, 1135, 1068, 980, 839, 823, 787 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 3H), 0.28 (s, 3H), 0.97 (s, 9H), 4.05 (s, 1H), 7.08 (d, J = 15.8 Hz, 1H), 7.35–7.60 (m, 5H), 7.66 (d, J = 15.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ –6.37, –5.97, 18.02, 26.85, 42.10, 122.95, 128.54, 128.95, 130.74, 134.29, 143.77, 194.70. Found: C, 56.46; H, 6.90%. Calcd for $C_{16}H_{23}BrOSi$: C, 56.63; H, 6.83%.

1-Bromo-1-(*tert*-butyldimethylsilyl)-3,3-dimethyl-2-butanone (3d): Bp 60 °C (0.5 Torr); IR (neat) 2958, 2856, 1698, 1465, 1366, 1251, 1209, 1053, 994, 842, 823, 779 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 3H), 0.32 (s, 3H), 0.97 (s, 9H), 1.22 (s, 9H), 4.18 (s, 1H); ^{13}C NMR ($CDCl_3$) δ –5.95, –5.74, 17.60, 26.97, 27.05, 28.84, 46.00, 212.16. Found: C, 49.40; H, 8.60%. Calcd for $C_{12}H_{25}BrOSi$: C, 49.14; H, 8.59%.

1-Bromo-1-(*tert*-butyldimethylsilyl)-2-octanone (3e): Bp 82 °C (0.5 Torr); IR (neat) 2928, 2856, 1693, 1467, 1253, 838, 824, 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (s, 3H), 0.24 (s, 3H), 0.87 (t, J = 7.5 Hz, 3H), 0.96 (s, 9H), 1.20–1.70 (br, 8H), 2.42 (ddd, *J* = 17.3, 8.2, 6.6 Hz, 1H), 2.78 (ddd, *J* = 17.3, 8.2, 6.6 Hz, 1H), 3.86 (s, 1H); ^{13}C NMR ($CDCl_3$) δ –6.30, –5.95, 14.02, 17.83, 22.48, 24.15, 26.82, 28.81, 31.56, 41.28, 41.84, 206.66. Found: C, 52.43; H, 9.38%. Calcd for $C_{14}H_{29}BrOSi$: C, 52.32; H, 9.10%.

General Procedure for the Preparation of α-Bromoacylsilanes. An ethereal solution of *tert*-butyldimethyl(dibromomethyl)silane (0.29 g, 1.0 mmol) was added to a solution of lithium diisopropylamide (1.2 mmol) in ether (3 ml) at –78 °C under argon atmosphere. After being stirred for 1 h at –78 °C, cyclohexanone (0.12 g, 1.2 mmol) in Et_2O (1 ml) and TMEDA (0.14 g, 1.2 mmol) were added and the reaction mixture was allowed to warm to ambient temperature over 10 h with stirring. The mixture was poured into saturated aqueous ammonium chloride and extracted with hexane (20 ml × 3). The combined organic layer were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by silica-gel column chromatography gave 1-bromocyclohexyl *tert*-butyldimethylsilyl ketone (**6a**, 0.22 g) in 72% yield: Bp 105 °C (1 Torr); IR (neat) 2928, 2854, 1633, 1464, 1448, 1249, 1112, 837, 774, 738, 674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.34 (s, 6H), 0.97 (s, 9H), 1.20–1.36 (m, 1H), 1.60–1.70 (m, 3H), 1.70–1.85 (m, 4H), 2.11 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –3.45, 17.34, 22.73, 25.18, 26.95, 34.31, 79.81, 233.34. Found: C, 51.06; H, 8.44%. Calcd for $C_{13}H_{25}BrOSi$: C, 51.14; H, 8.25%.

2-Bromo-1-(*tert*-butyldimethylsilyl)-2-ethyl-1-butanone (6b): Bp 98 °C (1 Torr); IR (neat) 2930, 2882, 2856, 1635, 1463, 1249, 1097, 1015, 936, 821, 775, 676 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.34 (s, 6H), 0.92 (t, *J* = 7.2 Hz, 6H), 0.97 (s, 9H), 2.00 (dq, *J* = 14.7, 7.2 Hz, 2H), 2.07 (dq, *J* = 14.7, 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ –3.42, 9.77, 17.45, 26.97, 28.72, 84.01, 235.53. Found: C, 49.37; H, 8.87%. Calcd for $C_{12}H_{25}BrOSi$: C, 49.14; H, 8.59%.

2-Bromo-1-(*tert*-butyldimethylsilyl)-2,2-diphenyl-1-ethanone (6c): Mp 148-149 °C; IR (neat) 1649, 1445, 1365, 1252, 1020, 834, 776, 701, 676 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ –0.03 (s, 6H), 0.99 (s, 9H), 7.20–7.30 (m, 4H), 7.30–7.40 (m, 6H); ^{13}C NMR ($CDCl_3$) δ –3.79, 17.70, 27.27, 81.02, 128.07, 128.44, 130.35, 137.70, 227.13. Found: C, 61.67; H, 6.42%. Calcd for $C_{20}H_{25}BrOSi$: C, 61.69; H, 6.47%.

Preparation of Lithium Enolate and its Aldol-type Reaction in THF. Under argon atmosphere, to a solution of 1-bromo-1-(*tert*-butyldimethylsilyl)-2-phenyl-2-ethanone **3a** (0.16 g, 0.5 mmol) in THF (5 ml) was added butyllithium in hexane (1.60 M, 0.34 ml, 0.55 mmol) dropwise at –78 °C. After being stirred for 30 min, benzaldehyde (0.06 g, 0.55 mmol) in THF was added and the whole reaction mixture was stirred for another 1 h. Extractive workup (saturated aqueous ammonium chloride and ethyl acetate) followed by purification by silica-gel column chromatography gave phenyl 2-phenylethenyl ketone (**10a**, 0.18 g) in 85% yield. The use of large excess (4.0 equiv) of benzaldehyde afforded 2-(1-*tert*-butyldimethylsiloxy)benzyl-3-hydroxy-1,3-diphenyl-1-propanone (**12a**, 0.16 g) in 73% yield. **12a**: (mixture of two diastereomers) IR (neat) 3466, 3084, 3055, 2952, 2926, 2854, 1655, 1598, 1450, 1363, 1253, 1206, 1066, 937, 863, 836, 777, 699, 550 cm^{-1}; Major product: ^{1}H NMR ($CDCl_3$) δ –0.36 (s, 3H), –0.23 (s, 3H), 0.51 (s, 9H), 4.11 (dd, *J* = 2.7, 9.7

Hz, 1H), 4.43 (dd, *J* = 2.7, 10.4 Hz, 1H), 4.88 (d, *J* = 10.4 Hz, 1H), 5.37 (d, *J* = 9.7 Hz. 1H), 6.95-7.75 (m. 15H); ^{13}C NMR ($CDCl_3$) δ -5.74, -4.84, 17.69, 25.31, 60.00, 72.72, 76.50, 124.90, 126.81, 127.00, 128.02, 128.45, 128.45, 128.52, 133.12, 138.67, 142.43, 142.49. Minor one: ^{1}H NMR ($CDCl_3$) δ -0.16 (s, 3H), 0.17 (s, 3H), 0.92 (s, 9H), 4.08 (dd, *J* = 9.5, 3.3 Hz, 1H), 4.61 (d, *J* = 9.5 Hz, 1H), 5.24 (d, *J* = 9.1 Hz, 1H), 5.46 (dd, *J* = 9.1, 3.3 Hz, 1H), 6.95-7.50 (m, 15H); ^{13}C NMR ($CDCl_3$) δ -5.21, -4.63, 18.19, 25.79, 62.04, 72.14, 74.20, 125.14, 126.70, 126.81, 127.51, 127.67, 128.02, 132.62, 137.93, 142.17, 142.98. Found: C, 75.06; H, 7.80%. Calcd for $C_{28}H_{34}O_3Si$: C, 75.29; H, 7.67%.

Preparation of Magnesium Enolate and its Aldol-type Reaction. Under argon atmosphere, to a solution of 1-bromo-1-(*tert*-butyldimethylsilyl)-2-phenyl-2-ethanone **3a** (0.16 g, 0.5 mmol) in ether (5 ml) was added isopropylmagnesium bromide in ether (0.98 M, 0.61 ml, 0.6 mmol) dropwise at 0 °C. After being stirred for 1 h, the resulting purple solution was cooled to -78 °C and benzaldehyde (0.06 g, 0.6 mmol) in ether was added and the whole reaction mixture was stirred for another 1 h. Extractive workup (saturated aqueous ammonium chloride and ethyl acetate) followed by purification by silica-gel column chromatography gave 2-(*tert*-butyldimethylsilyl)-3-hydroxy-1,3-diphenyl-1-propanone (**9a**, 0.13 mg, 89:11 diastereomeric mixture) in 78% yield. **9a**: IR (neat) 3430, 2952, 2926, 2854, 1636, 1597, 1449, 1339, 1251, 1202, 1051, 1002, 840, 823, 789, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ -0.14 (s, 0.33H), -0.05 (s, 2.67H), 0.22 (s, 0.33H), 0.32 (s, 2.67H), 0.89 (s, 8.01H), 0.91 (s, 0.99H), 2.35 (bs, 0.11H), 3.91 (d, *J* = 2.4 Hz, 0.89H), 4.02 (d, *J* = 9.3 Hz, 0.11H), 5.23 (dd, *J* = 2.4, 9.6 Hz, 0.89H), 5.36 (d, *J* = 9.6 Hz, 0.89H), 5.39 (d, *J* = 9.3 Hz, 0.11H), 7.13 (m, 1H), 7.20-7.35 (m, 6H), 7.46 (m, 1H), 7.54 (m, 2H); ^{13}C NMR ($CDCl_3$, *threo* isomer) δ -5.81, -5.27, 17.81, 26.83, 46.66, 74.13, 124.96, 126.95, 128.09, 128.33, 128.51, 132.99, 139.33, 145.78, 207.39. Found: C, 73.83; H, 8.36%. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29%.

2-(*tert*-Butyldimethylsilyl)-3-hydroxy-1-phenyl-1-nonanone (9b, 88:12 diastereomeric mixture): IR (neat) 3464, 2928, 2854, 1637, 1467, 1414, 1345, 1251, 1199, 1002, 822, 725, 688 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ -0.13 (s, 0.36H), -0.11 (s, 2.64H), 0.20 (s, 0.36H), 0.23 (s, 2.64H), 0.84 (t, *J* = 6.3 Hz, 3H), 0.86 (s, 7.92H), 0.88 (s, 1.08H), 1.20-1.40 (m, 6H), 1.40-1.64 (m, 4H), 2.08 (d, *J* = 4.5 Hz, 0.12H), 3.640 (d, *J* = 2.4 Hz, 0.88H), 3.641 (d, *J* = 7.8 Hz, 0.12H), 3.99 (m, 0.88H), 4.30 (m, 0.12H), 4.32 (d, *J* = 10.5 Hz, 0.88H), 7.47 (m, 2H), 7.58 (m, 1H), 7.87 (m, 2H); ^{13}C NMR ($CDCl_3$, *threo* isomer) δ -5.78, -5.15, 13.91, 17.81, 22.43, 26.56, 26.88, 29.02, 31.67, 38.98, 44.08, 73.01, 128.30, 128.76, 133.21, 139.51, 207.59. Found: C, 72.46; H, 10.40%. Calcd for $C_{21}H_{36}O_2Si$: C, 72.36; H, 10.41%.

2-(*tert*-Butyldimethylsilyl)-1-cyclohexyl-3-hydroxy-3-phenyl-1-propanone (9c, 72:28 diastereomeric mixture): IR (neat) 3422, 2924, 2854, 1662, 1452, 1337, 1251, 1114, 1048, 1003, 947, 839, 772, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ -0.05 (s, 0.84H), 0.05 (s, 2.16H), 0.22 (s, 0.84H), 0.34 (s, 2.16H), 0.98 (s, 2.52H), 1.04 (s, 6.48H), 1.20-1.80 (m, 10H), 2.03 (tt, *J* = 11.4, 3.3 Hz, 1H), 2.23 (d, *J* = 2.7 Hz, 0.28H), 3.07 (d, *J* = 1.8 Hz, 0.72H), 3.18 (d, *J* = 9.3 Hz, 0.28H), 5.17 (dd, *J* = 9.3, 2.7 Hz, 0.28H), 5.59 (d, *J* = 10.2

Hz, 0.72H), 7.17–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, *threo* isomer) δ –5.68, –5.12, 17.86, 24.82, 25.48, 26.06, 26.11, 26.87, 27.38, 50.71, 52.76, 73.90, 125.09, 126.88, 128.14, 146.14, 219.83. Found: C, 72.56; H, 9.84%. Calcd for $C_{21}H_{34}O_2Si$: C, 72.78; H, 9.89%.

2-(*tert*-Butyldimethylsilyl)-1-cyclohexyl-3-hydroxy-1-nonanone (9d, 56:44 diastereomeric mixture): IR (neat) 3458, 2926, 2854, 1665, 1466, 1451, 1251, 1145, 1096, 1003, 839, 824cm^{-1}; ^{1}H NMR ($CDCl_3$) δ –0.05 (s, 1.32H), 0.01 (s, 1.68H), 0.21 (s, 1.32H), 0.22 (s, 1.68H), 0.86 (t, *J* = 6.6 Hz, 3H), 0.97 (s, 9H), 1.10-2.00 (m, 20H), 2.26 (tt, *J* = 11.4, 3.3 Hz, 1H), 2.34 (m, 0.44H), 2.82 (d, *J* = 2.1 Hz, 0.56H), 2.85 (d, *J* = 6.9 Hz, 0.44H), 3.76 (m, 0.56H), 4.04 (m, 0.44H), 4.42 (d, *J* = 10.2 Hz, 0.56H); ^{13}C NMR ($CDCl_3$, *threo* isomer) δ –5.60, –5.01, 13.93, 17.81, 22.47, 24.96, 25.70, 26.30, 26.43, 26.62, 26.85, 29.09 29.62, 31.73, 39.32, 48.07, 52.76, 72.63, 220.84. Found: C, 71.39; H, 11.69%. Calcd for $C_{21}H_{42}O_2Si$: C, 71.12; H, 11.94%.

General Procedure for One-pot Synthesis of α,β-Unsaturated Ketones. An ethereal solution of *tert*-butyldimethyl(dibromomethyl)silane (0.29 g, 1.0 mmol) was added to a solution of lithium diisopropylamide (1.2 mmol) in ether (3 ml) at –78 °C under argon atmosphere. After being stirred for 1 h at –78 °C, benzaldehyde (0.13 g, 1.2 mmol) in Et_2O (1 ml) was added and the reaction mixture was allowed to warm to ambient temperature over 10 h to provide **3a**. The reaction mixture was cooled to –78 °C and *sec*-butyllithium (2.5 mmol) was added. After the reaction mixture was stirred at –78 °C for 1 h, benzaldehyde (3.0 mmol) was added. The mixture was stirred for another 30 min and then HMPA (2.5 mmol) was added. The resulting mixture was stirred at –78 °C for 1 h, then at 0 °C for 10 min and poured into saturated ammonium chloride. Extractive workup followed by silica-gel column chromatography gave phenyl 2-phenylethenyl ketone (**10a**, 0.12 g) in 59% yield.

References and Notes

1. (a) Colvin, E. W. *Silicon Reagents in Organic Synthesis*, Academic Press: London, 1988: pp. 77-79. (b) Hudrlik, P. F.; Peterson, D. *Tetrahedron Lett.* **1972**, 1785-1786. *Idem J. Am. Chem. Soc* . **1975**, *97*, 1464-1468. (c) Utimoto, K.; Obayashi, M. Nozaki, H. *J. Org. Chem.* **1976**, *41*, 2940-2941. (d) Obayashi, M.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1978**, 1383-1386; *Idem Bull. Chem. Soc. Jpn.* **1979**, *52*, 2646-2652. (e) Hudrlik, P. F.; Misra, R. N.; Withers, G. P.; Hudrlik, A. M.; Rona, R. J.; Arcoleo, J. P. *Tetrahedron Lett.* **1976**, 1453-1456. (f) Sato, S.; Okada, H.; Matsuda, I.; Izumi, Y. *Ibid.* **1984**, *25*, 769-770 (g) Larson, G. L.; Hernandez, D.; de Lopez-Cepero, I. M.; Torres, L. E. *J. Org. Chem.* **1985**, *50*, 5260-5267 (h) Corey, E. J.; Rücker, C. *Tetrahedron Lett* . **1984**, *25*, 4345-4348. (i) Yamamoto, Y. Ohdoi, K.; Nakatani, M.; Akiba, K. *Chem Lett.* **1984**, 1967-1968. (j) Fürstner, A.; Kollegger, G.; Weidmann, H. *J. Organomet. Chem.* **1991**, *414*, 295-305. (k) Enders, D.; Nakai, S. *Chem. Ber.* **1991**, *124*, 219-226. (l) Enders, D.; Ward, D.; Adam, J.; Raade, G.; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 981-984.

2. For recent reviews on acylsilane, see: (a) Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem, Soc, Rev.* **1990**, *19*, 147-195. (b) Ricci, A.; Degl'Innocent, A. *Synthesis*. **1989**, 647-660. (c) Cirillio, P. F.; Panek, J. S. *Org. Prep. Proc. Int.* **1992**, *24*, 553-582.
3. (a) Kuwajima, I.; Abe, T.; Minami, N. *Chem. Lett.* **1976**, 993-994. (b) Nowick, J. S.; Danheiser, R. L. *J. Org. Chem.* **1989**, *54*, 2798-2802. (c) Page, P. C. B.; Rosenthal, S. *Tetrahedron Lett.* **1986**, *27*, 5421-5422; *Idem Tetrahedron* **1990**, *46*, 2573-2586. (d) Hewkin, C. T.; Jackson, R. F. W. *J. Chem. Soc. Perkin Trans. I*, **1991**, 3103-3111. (e) Kuwajima, I.; Matsumoto, K.; *Tetrahedron Lett.* **1979**, *20*, 4095-4098. (f) Kuwajima, I.; Matsumoto, K.; Inoue, T. *Chem. Lett.* **1979**, 41-42. (g) Kuwajima, I.; Matsumoto, K.; Sugahara, S. *Ibid.* **1980**, 525-528. (h) Horiuchi, Y.; Taniguchi, M.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1995**, *36*, 5353-5356. (i) Morihata, K.; Horiuchi, Y.; Taniguchi, M.; Oshima, K.; Utimoto, K. *Ibid.* **1995**, *36*, 5555-5558.
4. A part of this work was published in a communication. Shinokubo, H.; K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1994**, *35*, 3741-3744.
5. Shinokubo, H.; Miura, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1993**, *34*, 1951-1954; *Idem Tetrahedron* **1996**, *52*, 503-514.
6. Rickborn, B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Pattenden, G. Eds.; Pergamon Press: New York, 1991; Vol. 3, Chapter 3.3 pp. 733-775. Similar 1,2-migration of hydrogen has been reported. See ref. 1d and 1e.
7. For a reductive formation of enolate from α-haloketone with various organometallic compounds, see: Aoki, Y.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1995**, 463-464.
8. A regioselective enolate formation from trimethylsilylmethyl ketones has been reported. Matsuda, I.; Okada, H.; Sato, S.; Izumi, Y. *Tetrahedron Lett.* **1984**, 25, 3879-3882.
9. The use of heptanal in place of benzaldehyde afforded a trace amount of the corresponding monosilyl ether of 2-acyl-1,3-diol.
10. Yamamoto, K.; Tomo, Y.; Suzuki, S.; *Tetrahedron Lett.* **1980**, *21*, 2861-2864; Larcheveque, M.; Debal, A. *J. Chem. Soc. Chem. Commun.* **1981**, 877-878; Larson, G. L.; de Kaifer, C. F.; Seda, R.; Torres, L. E.; Ramirez, J. R. *J. Org. Chem.* **1984**, *49*, 3385-3386.
11. Treatment of the diastereomeric mixture **9d** with BF_3•OEt_2 also gave only (*E*)-**10d** in 90 % yield. The exclusive formation of (*E*)-isomer might be attributed to the isomerization of (*Z*)-isomer into (*E*)-isomer under the acidic reaction conditions.
12. Stereochemistry of products was determined based on the observed vicinal coupling constants for the C_α–C_β protons.[14]
13. For the nomenclature of *threo* and *erythro*, see: Noyori; R; Nishida, H. J. *Am. Chem. Soc.* **1981**, *103*, 2106-2108.
14. House, H. O.; Crumrine. D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310-3324.
15. Butyllithium was not so effective as *sec*-BuLi for the formation of enolate in one-pot procedure.

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