

Preparation of Alkyl Silyl Acetals from Carboxylic Esters with *tert*-Butyldimethylsilyldihalomethylithium. 1,3-Rearrangement of Silyl Group from Carbon to Oxygen

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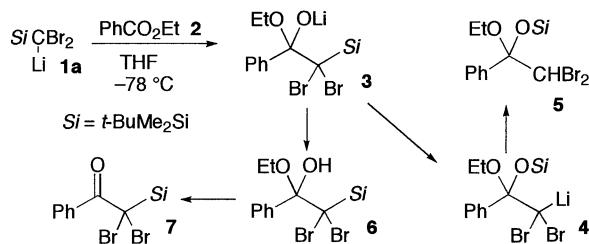
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Treatment of ethyl benzoate or isopropyl formate with *tert*-butyldimethylsilyldibromomethylithium gave alkyl silyl mixed acetal via 1,3-rearrangement of silyl group from carbon to oxygen. The reaction of the mixed acetals with allylsilane in the presence of Lewis acid afforded allylated ethers.

Recently, we have reported that one-pot synthesis of $R^1CH(OSiMe_2-t-Bu)CX_2CH(OH)R^2$ by successive addition of two different electrophiles has been achieved starting from *tert*-butyldimethylsilyldihalomethylithium **1**.¹ The reaction proceeds via 1,3-rearrangement of silyl group from carbon to oxygen. Here we wish to report further application of this type rearrangement to the synthesis of alkyl silyl acetals from carboxylic esters.

Ethyl benzoate **2** (0.18 g, 1.2 mmol) was added to a solution of *tert*-butyldimethylsilyldibromomethylithium (**1a**) in THF, prepared from *tert*-butyl(dibromomethyl)dimethylsilane (1.0 mmol) and LDA (1.2 mmol), at -78°C and the mixture was stirred for 20 min. Methanol was added to quench the reaction.² Workup followed by silica gel column chromatography gave ethyl *tert*-butyldimethylsilyl acetal **5**³ (0.41 g) in 94% yield. The use of acetic acid in place of methanol afforded hemiacetal **6** which decomposed to α -silyl ketone **7** after standing for three days in NMR tube (CDCl_3 solution). The formation of **5** is explained by 1,3-rearrangement of silyl group from carbon to oxygen in the intermediate β -oxido silane **3** (Scheme 1).

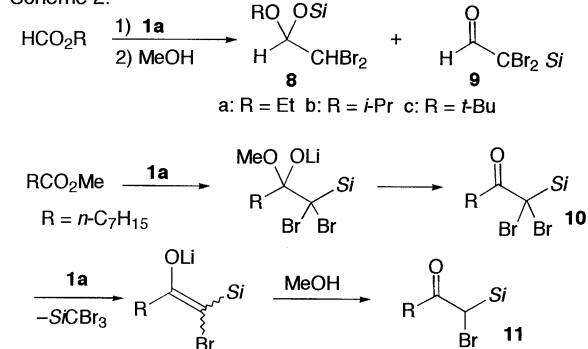
Scheme 1.



The facility of 1,3-rearrangement depends on the structure of substrate. Treatment of ethyl formate with **1a** gave ethyl silyl acetal **8a** in only 36% yield⁴ along with dibromo(*tert*-butyldimethylsilyl)acetaldehyde (**9**) (47%) which might be generated by elimination of ethoxide from β -oxido silane or rapid decomposition of hemiacetal after workup. The use of isopropyl formate instead of ethyl formate improved the yield of mixed acetal **8b** up to 80% and the formation of aldehyde **9** was reduced (5%). *tert*-Butyl formate was not so effective for the acetal formation compared to isopropyl formate. Thus, treatment of *tert*-butyl formate with **1a** gave *tert*-butyl silyl acetal **8c** in only 13% yield in addition to aldehyde **9** (28%).⁵ Methyl octanoate gave only bromo(*tert*-butyldimethylsilyl)methyl heptyl ketone (**11**) (38%) which might be produced by elimination of methoxide from β -oxido silane giving dibromo(*tert*-

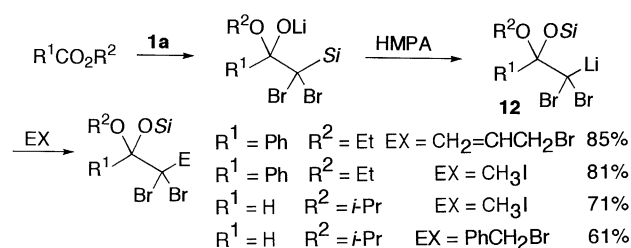
butyldimethyl-silyl)methyl heptyl ketone (**10**) followed by lithium-bromine exchange between **10** and lithium compound **1a** (Scheme 2).

Scheme 2.



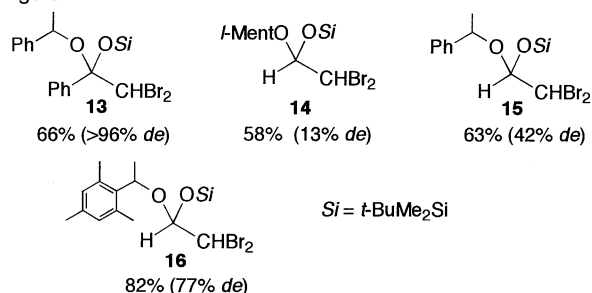
An addition of HMPA to the reaction mixture of ethyl benzoate or isopropyl formate and **1a** caused the rearrangement providing a carbanion **12** which reacted with various second electrophiles effectively (Scheme 3).

Scheme 3.



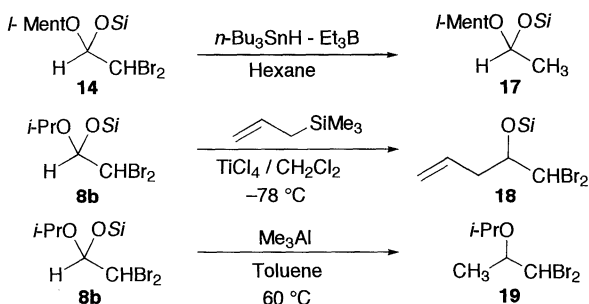
The reaction was successfully applied to the diastereoselective synthesis⁶ of mixed acetals starting from benzoates or formates prepared from chiral alcohols. For instance, treatment of α -phenethyl benzoate with **1a** gave **13**⁷ with high diastereoselectivity ($>96\%$ de) in 66% yield. Typical examples are shown below.

Figure 1.



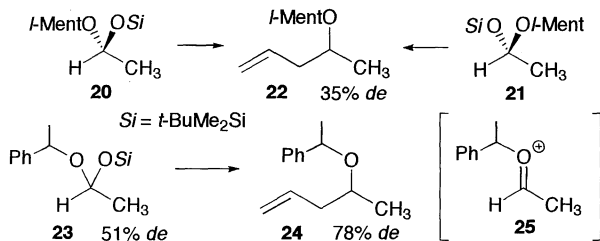
Then, several reactions of mixed acetals were examined. Triethylborane-induced reduction of **14** with *n*-Bu₃SnH afforded HC(*O*-*l*-menthyl)(OSiMe₂-*t*-Bu)CH₃ (**17**) quantitatively. Treatment of acetal **8b** with allyltrimethylsilane⁸ in the presence of BF₃·OEt₂, or TiCl₄ in CH₂Cl₂ at -78 °C gave allylated silyl ether **18** in 98% yield. In this case, isopropoxy group was substituted selectively. The nature of reagent affected which of alkoxy and silyloxy group will be replaced. Treatment of **8b** with Me₃Al⁹ in toluene at 60 °C gave CH₃CH(*O*-*i*-Pr)CHBr₂ **19** (41%) as a single product along with starting material. (Scheme 4).

Scheme 4.



Treatment of both diastereomers **20** and **21**, separated each other by silica gel column chromatography, with allyltrimethylsilane in the presence of BF₃·OEt₂ at -78 °C gave the same diastereomeric mixture **22** (35% de).¹⁰ An addition of allyltrimethylsilane to acetal **23** (51% de) in the presence of BF₃·OEt₂ gave phenethyl ether **24** (78% de) in 49% yield. These facts support that allylation reaction proceeds through cationic intermediate **25** (Scheme 5).^{11,12}

Scheme 5.



References and Notes

- H. Shinokubo, K. Miura, K. Oshima, and K. Utimoto, *Tetrahedron Lett.*, **34**, 1951 (1993).
- An addition of methanol to **3** gave an equilibrium mixture of **3** and **6**. The rearrangement of silyl group (**3** to **4**) could be promoted because of an increased polarity of the solvent. Protonolysis of **4** with methanol provided **5** which was irreversible (Scheme 6).
- 5**: Bp 109–110 °C (bath temp, 0.5 Torr); IR (neat) 2928, 2854, 1472, 1448, 1391, 1257, 1157, 1062, 873, 837, 778, 701 cm⁻¹; ¹H NMR (CDCl₃) δ 0.16 (s, 3H), 0.35 (s, 3H), 1.03 (s, 9H), 1.20 (t, *J* = 7.0 Hz, 3H), 3.39 (dq, *J* = 7.0, 9.0 Hz, 1H), 3.58 (dq, *J* = 7.0, 9.0 Hz, 1H), 5.83 (s, 1H), 7.35–7.45 (m, 3H), 7.55–7.65 (m, 2H); ¹³C NMR (CDCl₃) δ -2.95, -2.11, 14.97, 19.14, 26.13, 53.22, 59.70, 100.80, 127.68, 128.21, 128.76, 138.60. Found: C, 44.10; H, 5.90%. Calcd for C₁₆H₂₆Br₂O₂Si: C, 43.85; H, 5.98%.
- An addition of HMPA facilitated the rearrangement of silyl group. For instance, an addition of benzyl bromide and HMPA to a mixture derived from ethyl formate and **1a** provided HC(OEt)(OSiMe₂-*t*-Bu)CBr₂CH₂Ph in 70% yield.
- The structure of silyldihalomethylthium also affected the distribution of the products. The use of *t*-BuMe₂SiC(Li)Cl₂ (**1b**) in the reaction with PhCO₂Et provided the corresponding mixed acetal in 76% yield. However, treatment of isopropyl formate with **1b** gave acetal HC(*O*-*i*-Pr)(OSiMe₂-*t*-Bu)CHCl₂ in only 7% yield along with α-silylaldehyde *t*-BuMe₂SiCCl₂CHO (63%).
- Diastereoselective formation of *l*-menthyl trimethylsilyl acetal has been performed by the reduction of *l*-menthyl carboxylate with *i*-Bu₂AlH followed by stirring with trimethylsilyl triflate. S. Kiyooka, M. Shirouchi, and Y. Kaneko, *Tetrahedron Lett.*, **34**, 1491 (1993).
- 13**: Bp 150–153 °C (bath temp, 0.5 Torr); IR (neat) 3058, 3024, 2954, 2926, 2884, 2854, 1449, 1257, 1201, 1154, 1027, 873, 836, 778, 696 cm⁻¹; ¹H NMR (CDCl₃) δ 0.29 (s, 3H), 0.32 (s, 3H), 1.04 (s, 9H), 1.43 (d, *J* = 6.5 Hz, 3H), 4.65 (q, *J* = 6.5 Hz, 1H), 5.88 (s, 1H), 7.10–7.30 (m, 8H), 7.30–7.35 (m, 2H); ¹³C NMR (CDCl₃) δ -2.05, -1.50, 19.11, 26.03, 26.20, 53.16, 73.95, 101.78, 125.86, 126.99, 127.41, 127.79, 128.08, 128.66, 137.96, 144.82. Found: C, 51.20; H, 5.89%. Calcd for C₂₂H₃₀Br₂O₂Si: C, 51.37; H, 5.88%.
- A. Hosomi, M. Endo, and H. Sakurai, *Chem. Lett.*, **1976**, 941; T. Mukaiyama and M. Murakami, *Synthesis*, **1987**, 1043; P. A. Bartlett, W. S. Johnson, and J. D. Elliott, *J. Am. Chem. Soc.*, **105**, 2088 (1983).
- K. Ishihara, N. Hanaki, and H. Yamamoto, *J. Am. Chem. Soc.*, **113**, 7074 (1991).
- In contrast, treatment of **14** with allyltrimethylsilane in the presence of TiCl₄ gave allylated silyl ether.
- Diastereoselective formation of ether from aldehyde, secondary alcohol silyl ether, and allyltrimethylsilane in the presence of a catalytic amount of Ph₂BOTf has been reported. T. Mukaiyama, M. Ohshima, and N. Miyoshi, *Chem. Lett.*, **1987**, 1121.
- T. Sammakia and R. S. Smith, *J. Am. Chem. Soc.*, **116**, 7915 (1994).