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New Routes to Regioselectively Mono-Protected 1,3-Diols from Allyl and Homoallyl Alcohols via Intramolecular Hydrosilation1),†

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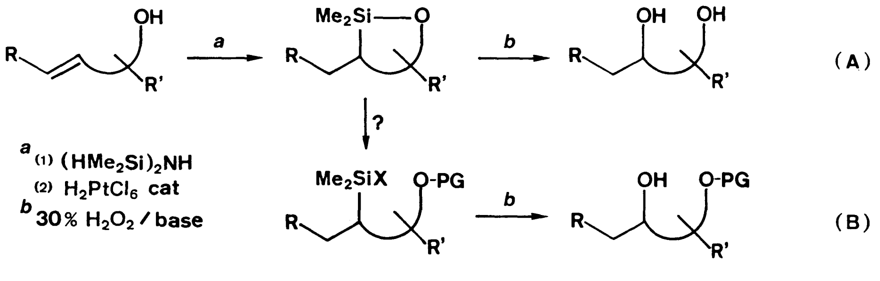
Allyl and homoallyl alcohols are transformed into 1,3-diol derivatives, in which only the originally present hydroxy groups are regioselectively protected, by a sequence of intramolecular hydrosilation, protection, and oxidative cleavage of the carbon-silicon bond. Stereochemical aspects are also described.

We have recently developed a new methodology for the highly regio- and stereo-selective transformation of allyl and homoallyl alcohols into 1,3-diols by a sequence of intramolecular hydrosilation and oxidative cleavage of the resulting carbon-silicon bond,1c,2) as shown by route (A) in Scheme 1. Synthetic utility of this method has already been demonstrated by a facile, stereoselective synthesis of polypropionate derivatives having five consecutive chiral centers.1c) In order to enhance the synthetic utility of the intramolecular hydrosilation, we have planned to open up routes to mono-protected 1,3-diols, in which only the originally present hydroxy group is protected, as shown by route (B) in Scheme 1. Such routes should be of synthetic value, in view of difficulties encountered in selective mono-protection of two free hydroxy groups.3)



Scheme 1.

For that purpose, it is necessary to develop such a cleavage reaction of the silicon-oxygen bond that introduces an appropriate protecting group to oxygen and at the same time to silicon a functional group suitable for the subsequent oxidative cleavage of the carbon-silicon bond.4) Two types of intramolecular hydrosilation products, primary alcohol derivative 1 and secondary alcohol derivative 2,1c,2) were used as model compounds. Results are summarized in Eqs. 1 - 9.

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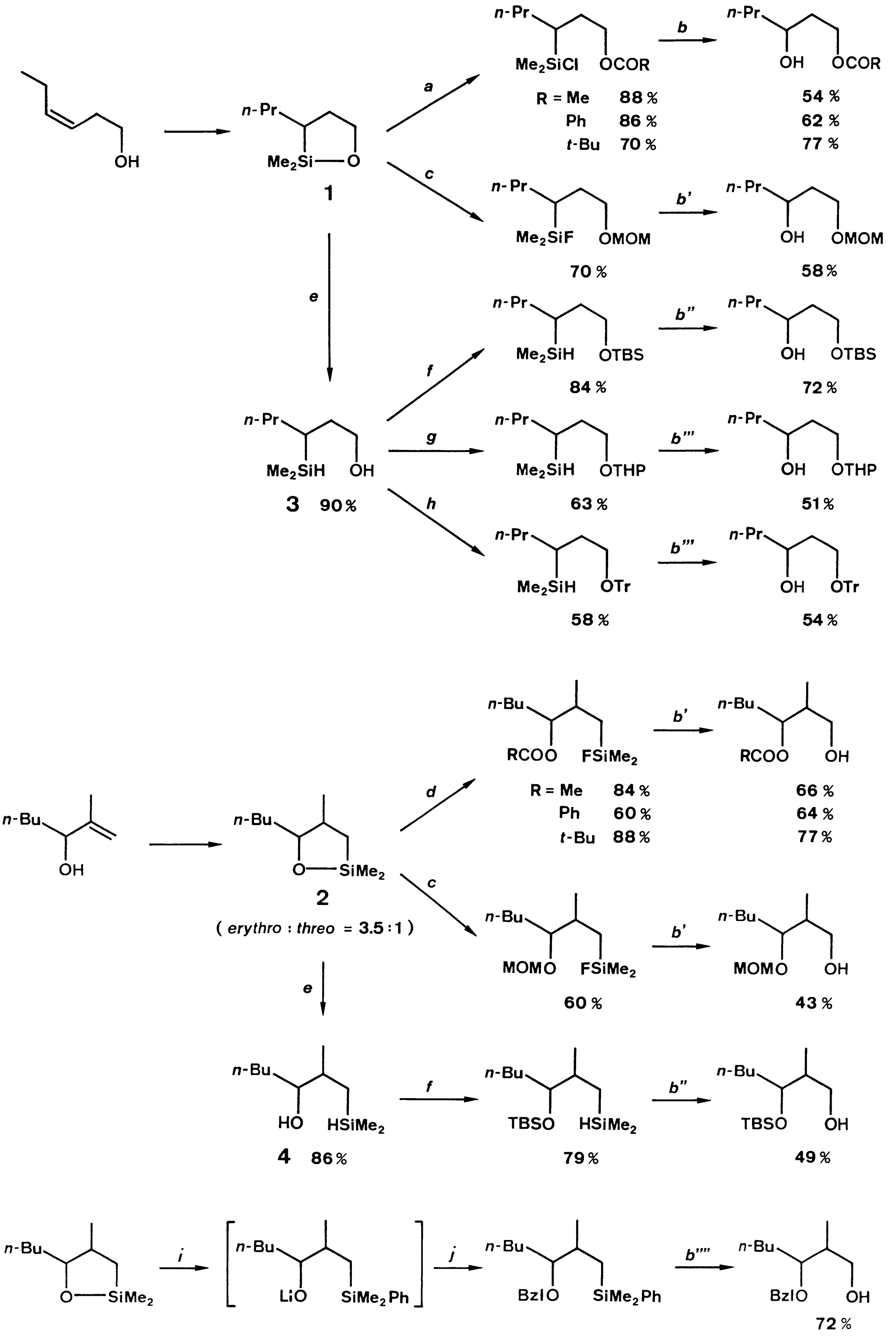
† Dedicated to Professor Teruaki Mukaiyama on the occasion of his 60th birthday.


n-Pr
Me2Si—O
1
a
Me2SiCl OCOR
R = Me 88 %
Ph 86 %
t-Bu 70 %
b
OH OCOR
54 %
62 %
77 %
c
Me2SiF OMOM
70 %
b'
OH OMOM
58 %
e
f
Me2SiH OTBS
84 %
b''
OH OTBS
72 %
Me2SiH OH
3 90 %
g
Me2SiH OTHP
63 %
b'''
OH OTHP
51 %
h
Me2SiH OTr
58 %
b'''
OH OTr
54 %
n-Bu
OH
O—SiMe2
2
(erythro : threo = 3.5 : 1)
d
RCOO FSiMe2
R = Me 84 %
Ph 60 %
t-Bu 88 %
b'
RCOO OH
66 %
64 %
77 %
c
MOMO FSiMe2
60 %
b'
MOMO OH
43 %
e
HO HSiMe2
4 86 %
f
TBSO HSiMe2
79 %
b''
TBSO OH
49 %
i
LiO SiMe2Ph
j
BzlO SiMe2Ph
b''''
BzlO OH
72 %

(1)

(2)

(3)

(4)

(5)

(6)

(7)

(8)

(9)

[a] RCOCl (1.5 equiv.)/ $ZnCl_2$ (5 mol%)/ room temp/ 1-3 h. [b] (1) KF/ $KHCO_3$/ MeOH/ THF. (2) 30% H_2O_2/ room temp/ 6-10 h. [b'] 30% H_2O_2/ $KHCO_3$/ MeOH/ room temp-50 °C/ 10-24 h. [b''] 30% H_2O_2/ $NaHCO_3$/ MeOH/ THF/ 60 °C/ 1.5-2.5 d. [b'''] 30% H_2O_2/ KF/ $KHCO_3$/ MeOH/ THF/ 40-60 °C/ 28-42 h. [b''''] (1) $HBF_4 \cdot OEt_2$/ $CHCl_3$/ 0 °C/ 15 min. (2) 30% H_2O_2/ 15% KOH/ MeOH/ THF/ 50 °C/ 4 h. [c] $MeOCH_2Cl$ (3-4 equiv.)/ CsF or $PHCH_2NMe_3 \cdot BF_4(MeOH)_x$ (2 equiv.)/ MeCN/ room temp/ 6-10 h. [d] RCOCl (2.5 equiv.)/ $PhCH_2NMe_3 \cdot BF_4(MeOH)_x$ (1.2 equiv.)/ MeCN/ 80 °C/ 0.5-5 d. [e] (1) i-Bu_2AlH/ Et_2O/ 0-60 °C/ 3 h. (2) 1M HCl. [f] TBSCl/ Et_3N/ DMAP/ CH_2Cl_2/ room temp/ 4 h. [f'] TBSCl/ Et_3N/ DMAP/ DMF/ room temp/ 14 h. [g] Dihydropyran/ p-TsOH/ CH_2Cl_2/ room temp/ 4 h. [h] TrCl/ Et_3N/ DMAP/ CH_2Cl_2/ room temp/ 5.5 h. [i] PhLi/ Et_2O/ room temp/ 1 h. [j] $PhCH_2Br$/ HMPA/ room temp/ 8 h.

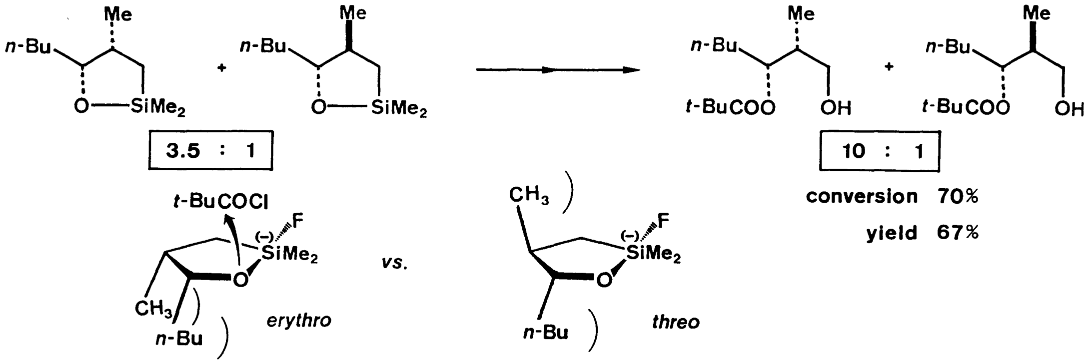
Ester groups were introduced in one step, as shown in Eqs. 1 and 6. Primary alcohol derivative **1** readily reacted with acyl chlorides in the presence of a catalytic amount of dried zinc chloride at room temperature to form acyloxychlorosilanes. The mono-acylated 1,3-diols were obtained in one-pot by the direct oxidation of the reaction mixture without isolation of the intermediates. The pivaloyl group may be most suitable for the mono protection, since the acetate and the benzoate underwent partial deprotection under the weakly basic oxidation conditions. The zinc chloride-catalyzed acylation was not applicable to the secondary alcohol derivative **2**, a complex mixture of products being formed. Instead, fluoride ion-induced acylation[5)] was found to be useful for **2**, as shown in Eq. 6. Benzyltrimethylammonium tetrafluoroborate[6)] was more effective than cesium fluoride. Mono-acylated diols were obtained by the direct oxidation of the reaction mixture in high overall yields, while the intermediate acyloxyfluorosilanes could also be isolated. All three ester groups examined were reasonably stable to the oxidation conditions.

The **methoxymethyl (MOM)** group could also be introduced directly to **1** and **2** by similar fluoride ion-induced reaction with chloromethyl methyl ether in acetonitrile under nitrogen atmosphere (Eqs. 2 and 7). The reaction proceeded rather slowly and required several days at room temperature: heating resulted in the formation of by-products.

Tert-**butyldimethylsilyl (TBS)**, **tetrahydropyranyl (THP)**, and/or **trityl (Tr)** groups could be introduced not directly to **1** or **2** but indirectly via the hydride reduction products **3** and **4**, as shown in Eqs. 3, 4, 5, and 8. Reduction of **1** and **2** with i-Bu_2AlH (or $LiAlH_4$) followed by acidic hydrolysis gave free alcohols having a hydrosilyl group. These hydrosilyl alcohols showed a great tendency to cyclize back to **1** or **2** under weakly basic conditions with evolution of hydrogen, but could endure the reaction conditions for the above three protections. In the case of TBS protection, the subsequent oxidative cleavage reactions were carried out in the absence of fluoride sources to avoid the concomitant deprotection.

A **benzyl group (Bzl)** was introduced only after phenylation of the hydrosilation product, as exemplified by Eq. 9. Thus, **2** was treated with phenyllithium followed by benzyl bromide in the presence of HMPA to form O-benzylated product; transformtion of the $PhMe_2Si$ group to the OH group was performed as reported previously,[4)] except the use of $HBF_4 \cdot OEt_2$ in the first protio-desilylation step.[7)] One of advantages of this stepwise mono-protection resides in that since the $PhMe_2Si$ group is tolerable to a variety of reaction conditions, the final oxidation step can be preserved, if necessary, until transformation of other parts of molecules has been performed.

Finally, it should be noted that two diastereoisomers, erythro- and threo-2, showed different reactivities toward the fluoride-induced acylation: the erythro isomer reacted much faster than the threo. Accordingly, the mono-protection made possible the stereochemical enrichment of the diastereoisomers. Thus, at the 70% conversion the 3.5 : 1 mixture gave, after oxidation, a 10 : 1 mixture of half-pivaloyl esters of diol, as shown in Eq. 10. Mechanistically, the stereochemical aspects imply that the acylation may proceed not after cleavage of the silicon-oxygen bond, but through five-coordinate silicon intermediates, on which acyl halide attacks to cleave the silicon-oxygen bond; the acylation may occur most favorably at the least hindered side in the erythro isomer, as shown below.



(10)

Coupled with the highly regio- and stereo-selective transformation of allyl and homoallyl alcohols into 1,3-diols, the regioselective mono-protection thus far mentioned should make the intramolecular hydrosilation much more synthetically useful. Such an ideal transformation has not readily been achieved by the traditional hydroboration.

References

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6) Prepared by mixing $PhCH_2NMe_3OH$ in methanol (Triton B) with tetrafluoroboric acid as low hygroscopic white needles.

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