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A Practical Synthesis of Several Polyhydroxylated Chiral Building Blocks

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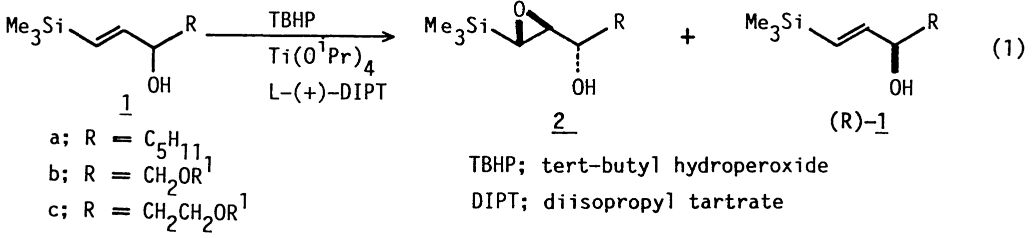
A practical method for the synthesis of several useful polyhydroxylated chiral building blocks has been developed. The key reaction is the kinetic resolution of (E)-1-trimethylsilyl-4-alkoxy-1-buten-3-ol or (E)-1-trimethylsilyl-5-alkoxy-1-penten-3-ol using the Sharpless asymmetric epoxidation reaction.

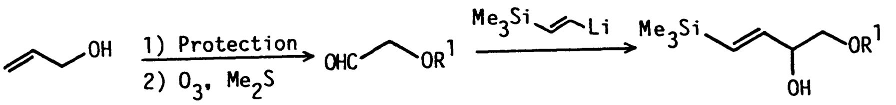
In relation to the synthesis of polyhydroxylated natural compounds such as ionophores and sugars by chiral building block method, much efforts have been directed to develop an efficient method for the synthesis of useful chiral building blocks.[1)] Thus far, these chiral building blocks have been prepared mainly by transformation of natural compounds such as sugars and tartaric acid.[2)] However, these methods often suffer from lengthy and troublesome synthetic sequence including protection and deprotection of the hydroxyl groups. In this paper, we wish to report an efficient method for the synthesis of several polyhydroxylated chiral building blocks including new one without using these natural compounds as starting materials.[3)]

Recently we have found that the kinetic resolution of γ-trimethylsilyl allylic alcohol 1a using the Sharpless asymmetric epoxidation reaction proceeds highly efficiently to afford the epoxy alcohol with more than 99% ee and the allylic alcohol with more than 99% ee, simultaneously (Eq. 1).[4)] With this result in hand, we were interested in the kinetic resolution of 1b or 1c (Eq. 1), since the resulting epoxy alcohols and the remaining allylic alcohols are expected to serve as good precursors for the synthesis of polyhydroxylated chiral building blocks. This communication describes the results of the kinetic resolution of 1b and 1c and the conversion of the resulting compounds into several chiral building blocks.



TBHP; tert-butyl hydroperoxide
DIPT; diisopropyl tartrate

The allylic alcohol 1b was readily prepared in multigram quantity by the procedure shown in Eq. 2. Thus, protection of the hydroxyl group of allyl alcohol followed by ozonolysis afforded the alkoxy acetaldehyde 3,[5] which was reacted with vinyllithium, prepared in situ from (E)-1-tributylstannyl-2-trimethylsilylethylene and ^{n}BuLi,[6] to afford 1b in high overall yield. Similarly, allylic alcohol 1c was prepared starting with cis-3-hexen-1-ol in 80% overall yield (Eq. 3).



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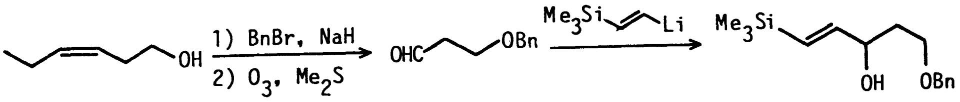
1b

R^1=benzyl(Bn); 68% yield from allyl alcohol
R^1=$^{t}BuMe_2Si$(TBS); 77% yield



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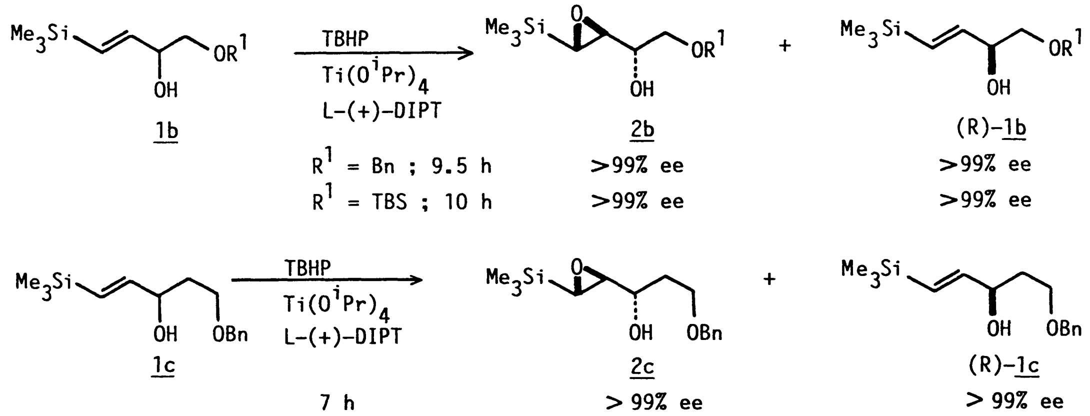
1c (80% yield from cis-3-hexen-1-ol)

The kinetic resolution of 1b or 1c using 1.0 equiv. of $Ti(O^{i}Pr)_4$, 1.2 equiv. of L-(+)-DIPT, and 1.5 equiv. of TBHP (-21 °C) was found to proceed with similar large rate difference for the two enantiomers as 1a to afford the corresponding epoxy alcohols 2 with more than 99% ee and the allylic alcohols (R)-1 with more than 99% ee (Eq. 4).[7] The yields, R_f values (TLC on silica gel), $[\alpha]_D$ values, and partial ^1H NMR data of the resulting epoxy alcohols and the remaining allylic alcohols are summarized in Table 1.

Table 1. The yields, R_f values (TLC on silica gel), $[\alpha]_D$ values, and ^1H NMR data of the epoxy alcohols 2 and the allylic alcohols (R)-1

Compd.	Yield /%	R_f (hexane:ether)	$[\alpha]_D^{25}/°$ (c in $CHCl_3$)	^1H NMR (CCl_4, D_2O)
2b (R^1=Bn)	48	0.28 (1:1)	-2.2 (1.2)	δ 2.17(d, J=3.6 Hz, 1H, $\underline{H}C\overset{O}{-}CHC$), 2.78(dd, J=3.6, 4.2 Hz, 1H, $HC\overset{O}{-}C\underline{H}C$).
(R)-1b (R^1=Bn)	43	0.38 (1:1)	-1.9 (1.1)	δ 3.32(dd, J=7.8, 10.3 Hz, 1H, $\underline{H}CHO$), 3.42(dd, J=4.1, 10.3 Hz, 1H, $\underline{H}CHO$), 5.95-6.10(m, 2H, HC=CH).
2b (R^1=TBS)	48	0.24 (3:1)	-4.3 (1.0)	δ 2.16(d, J=3.6 Hz, 1H, $\underline{H}C\overset{O}{-}CHC$), 2.77(dd, J=3.6, 4.7 Hz, 1H, $HC\overset{O}{-}C\underline{H}C$).
(R)-1b (R^1=TBS)	46	0.36 (3:1)	+3.4 (1.2)	δ 3.36(dd, J=7.4, 10 Hz, 1H, $\underline{H}CHO$), 3.49(dd, J=4.6, 10 Hz, 1H, $\underline{H}CHO$), 5.83-5.93(m, 2H, HC=CH).
2c	45	0.23 (1:1)	-10.1 (0.97)	δ 2.13(d, J=3.6 Hz, 1H, $\underline{H}C\overset{O}{-}CHC$), 2.68(t, J=3.6 Hz, 1H, $HC\overset{O}{-}C\underline{H}C$).
(R)-1c	43	0.32 (1:1)	-3.2 (1.0)	δ 3.53(dt, J=2.5, 6.1 Hz, 2H, CH_2O), 5.80(d, J=19.9 Hz, 1H, $\underline{H}C=CHC$), 5.91 (dd, J=4.0, 19.9 Hz, 1H, $HC=C\underline{H}C$).



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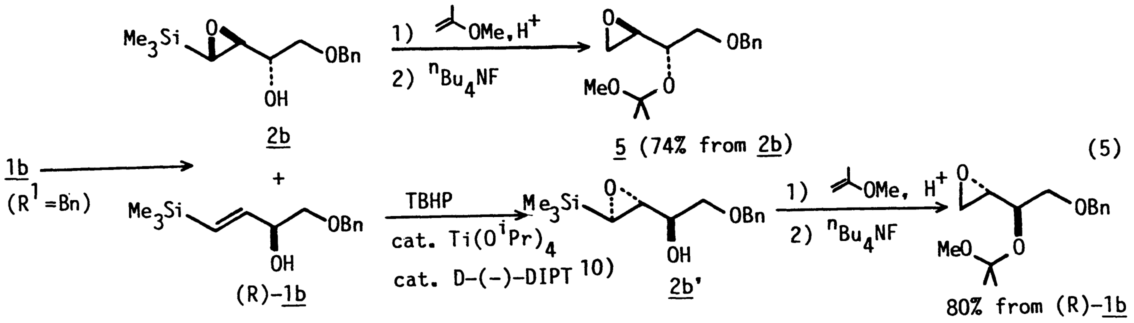
With these optically pure epoxy alcohols and the allylic alcohols in hand, we turned our attention to the conversion of these compounds into useful polyhydroxylated chiral building blocks. Recently Seebach and co-workers reported the synthesis of the diol epoxide 5 and its enantiomer starting with D-(-)- and L-(+)- diethyl tartrate, respectively, and showed their usefulness as chiral building blocks for the synthesis of sugars.[2b,8] The compound 5 and its enantiomer were found to be readily prepared from 2b (R^1 = Bn) and (R)-1b (R^1 = Bn), respectively, according to the procedure shown in Eq. 5. Thus, treatment of 2b (R^1 = Bn) with ^{n}Bu$_4$NF after protection of the hydroxyl group as 1-methyl-1-methoxyethyl ether resulted in protiodesilylation to afford 5[9] ($[\alpha]_D^{25}$ +21.5° (c 0.994, CHCl$_3$), lit.[8] $[\alpha]_D^{25}$ +20° (c 0.785, CHCl$_3$)) in 74% yield (based on 2b), while the allylic alcohol (R)-1b (R^1 = Bn) was changed into the enantiomer of 5[9] ($[\alpha]_D^{25}$ -21.2° (c 1.04, CHCl$_3$)) by the same method after converting into the epoxy alcohol 2b' (80% based on (R)-1b).



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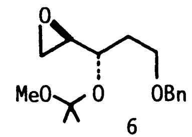
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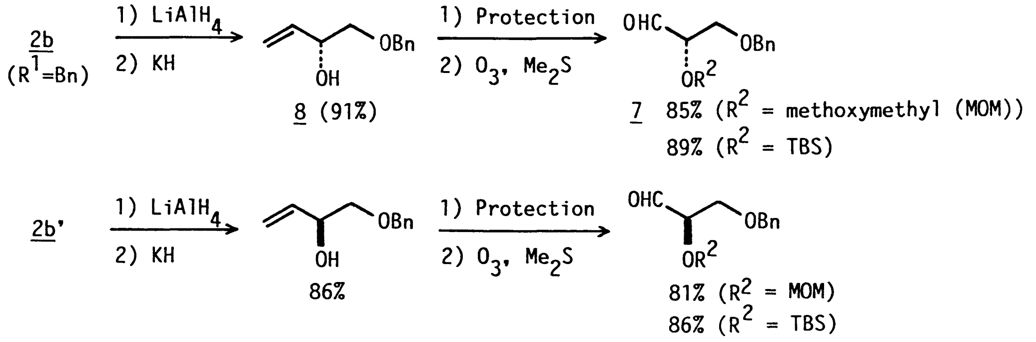
In the same manner, 2c and (R)-1c were converted into diol epoxide 6 (85%) and its enantiomer (78%), respectively. The compounds thus prepared must be useful chiral building blocks for the synthesis of deoxy sugars.

The glyceraldehyde derivatives have been widely used for the synthesis of various kinds of natural compounds.[11] We have found that the epoxy alcohol 2b (R^1 = Bn) and its enantiomer 2b' can also be readily converted into glyceraldehyde derivative 7 and its enantiomer, respectively, by using a simple sequence of conventional reactions (Eq. 6). Thus, regiospecific epoxide ring opening of 2b with LiAlH$_4$ followed by Peterson olefination with KH afforded the allylic alcohol 8, which was converted into 7 by ozonolysis after protection of



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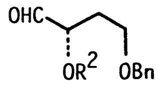
the hydroxyl group. Similarly, the enantiomer of 7 was prepared from 2b'. It is clear that the present reaction provides a general method for the preparation of the glyceraldehyde derivatives having two different hydroxyl protecting groups, some of which are not necessarily easy to prepare.12) α,γ-Dialkoxy aldehyde 9 and its enantiomer, which are also expected to be useful building blocks for the synthesis of deoxy sugars, were prepared similarly from 2c and (R)-1c, respectively.



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In summary, we developed a practical method for the synthesis of polyhydroxylated chiral building blocks 5, 6, 7, and 9. Natural product synthesis using these compounds is in progress in our laboratory.

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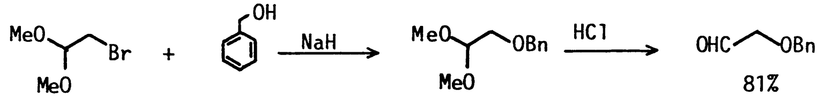
References
1) For recent reviews see: J. W. Scott, "Asymmetric Synthesis," ed by J. D. Morrison, Academic Press, New York (1984), Vol. 4, Chap. 1.
2) a) A. Vasella, "Modern Synthetic Method," ed by R. Scheffold, Otto Salle Verlag, Frankfurt am Main (1980), Vol. 2, p. 173; b) D. Seebach and E. Hungerbühler, ibid., p. 91.
3) For the synthesis of the polyhydroxylated chiral building blocks without using sugars or tartaric acid, see; R. Annunziata, M. Cinquini, F. Cozzi, L. Raimondi, and S. Stefanelli, Tetrahedron Lett., 28, 3139 (1987); T. Katsuki, A. W. M. Lee, P. Ma, V. S. Martin, S. Masamune, K. B. Sharpless, D. Tuddenham, and F. J. Walker, J. Org. Chem., 47, 1373 (1982).
4) Y. Kitano, T. Matsumoto, and F. Sato, J. Chem. Soc., Chem. Commun., 1986 1323.
5) Alkoxy acetaldehyde 3 (R^1 = Bn) was also prepared in multigram quantity according to the following scheme; M. Julia and G. Tchernoff, Bull. Soc. Chim. Fr., 20, 479 (1953).



6) E. J. Corey and R.H. Wollenberg, J. Am. Chem. Soc., 96, 5581 (1974).
7) Optical purity of the epoxy alcohols and the allylic alcohols were checked by ^1H NMR analysis of the corresponding MTPA esters.
8) E. Hungerbühler and D. Seebach, Helv. Chim. Acta, 64, 687 (1981).
9) ^1H NMR data were in accord with values reported by Seebach.8)
10) R. M. Hanson and K. B. Sharpless, J. Org. Chem., 51, 1922 (1986).
11) G. J. McGarvey, M. Kimura, T. Oh, and J. M. Williams, J. Carbohydr. Chem., 3, 125 (1984).
12) Recently, Reetz and co-workers reported the synthesis of glyceraldehyde derivative having two different hydroxyl protecting groups starting with D-mannitol. M. T. Reetz and K. Kesseler, J. Org. Chem., 50, 5434 (1985).

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