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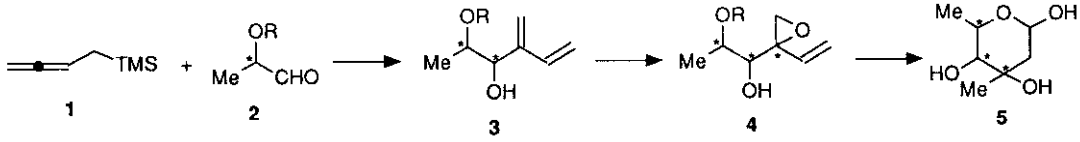
ENANTIO- AND STEREOCONTROLLED SYNTHESES OF BRANCHED-CHAIN SUGAR, L-ARCANOSE AND L-OLIVOMYCOSE BASED ON THE CHEMISTRY OF 1-TRIMETHYLSILYL-2,3-BUTADIENE

Susumi Hatakeyama, Kazutoshi Sugawara, and Seiichi Takano*
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan

Summary: Branched-chain sugars, L-arcanose and L-olivomycose, have been synthesized in a completely enantio- and stereocontrolled manner starting from Lewis acid mediated reaction of 1-trimethylsilyl-2,3-butadiene with (*S*)-2-benzyloxy-propanal.

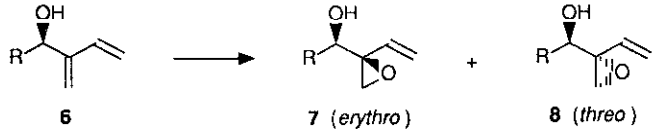
We have recently established an effective method for the preparation of either racemic or chiral alkyl(1,3-butadien-2-yl)methanol derivatives by use of Lewis acid mediated addition of 1-trimethylsilyl-2,3-butadiene to aldehydes or acetals.[1] For the purpose of exploring the synthetic utility of this method, we have this time been engaged in studies directed toward the enantio- and stereocontrolled synthesis of branched-chain sugars[2] based on a new strategy as outlined in Scheme 1. The crucial point of this strategy is whether these unprecedented transformations can be performed regio- and stereoselectivcly or not.



1 2 3 4 5

Scheme 1

Initially, the mono-epoxidation was tested using three racemic dienols **6a-c**[1] (Scheme 2). The results are given in Table 1.[3] It can be seen that the vanadium catalyzed epoxidation[4] proceeded with complete regio- and stereoselectivity to afford the *erythro* epoxy alcohol **7** exclusively and that the *m*CPBA epoxidation resulted in rather poor diastereoselection.



6 **7** (*erythro*) **8** (*threo*)

Scheme 2

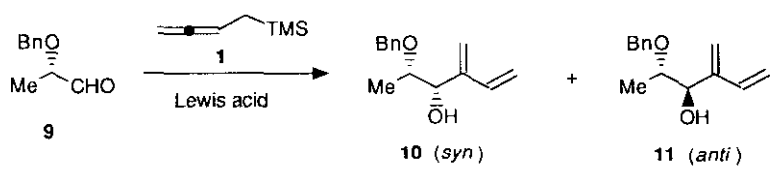
Table 1. Monoepoxidation of Dienols

	dienol **6** R	conditions method[a]	temp. (°C)	time (h)	**7** + **8** yield[b] (%)	ratio[c] **7**/**8**
(a)	$ph(CH_2)_2$–	A	–25	12	45	9/1
(a)	$ph(CH_2)_2$–	B	0	4	85	>98/1
(b)	$phCH_2$–	B	0	8	73	>98/1
(c)	c-C_6H_{11}	B	0	8	71	>98/1

a) method A : the reaction was carried out in CH_2Cl_2 using *m*CPBA (1.2 eq.) and $NaHCO_3$ (3.6 eq.); method B : the reaction was carried out in CH_2Cl_2 using $VO(acac)_2$ (8 mol%), and ^tBuOOH (1.5 eq.). b) isolate yield. c) determined by ^1H NMR (500 MHz).

Having developed a method for the highly regio- and stereoselective transformation of dienols to *erythro* epoxy alcohols, we then started the synthesis of branched-chain sugars, L-arcanose (**17**)[5] and L-olivomycose (**23**).[6,7] Thus, (*S*)-2-benzyloxypropanal (**9**)[8] was allowed to react with 1-trimethylsilyl-2,3-butadiene (**1**) in the presence of Lewis acid under various conditions (Scheme 3). The results are summarized in Table 2.

It suggests that in the cases of $TiCl_4$ and $SnCl_4$ the reaction predominantly proceeded *via* a chelated transition state, while the $BF_3{\cdot}Et_2O$ mediated reaction took place *via* a non-chelated transition state. These stereochemical outcomes are exactly same as those observed in the reaction of allylsilanes.[9]

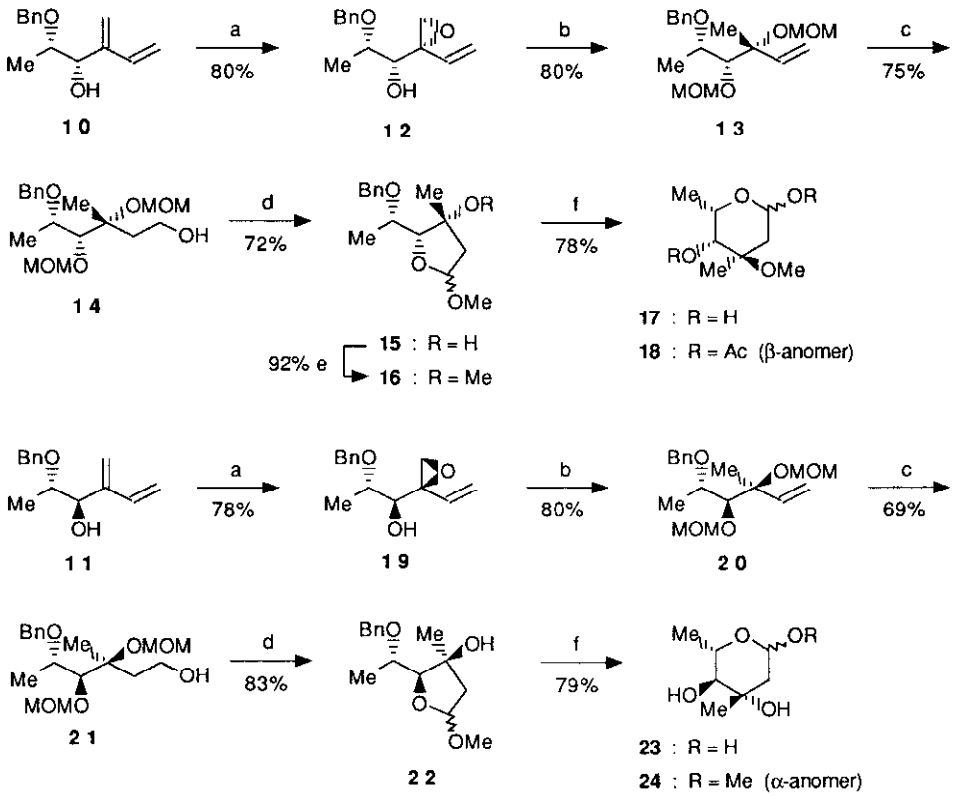


Scheme 3

Table 2. Lewis Acid Mediated Addition of 1-Trimethylsilyl-2,3-butadiene to (*S*)-2-Benzyloxypropanal

	conditions[a]		**10** + **11**	ratio[c]
Lewis acid	temp. (°C)	time (h)	yield[b] (%)	**10**/**11**
$TiCl_4$	–78	12	77	>98/1
$TiCl_4$	–90	12	61	>98/1
$SnCl_4$	–90	10	45	18/1
$BF_3{\cdot}Et_2O$	–78	24	79	1/3
$BF_3{\cdot}Et_2O$	–90	12	29	1/4

a) the reaction was carried out in CH_2Cl_2 using Lewis acid (1.1 eq.) and **1** (2.0 eq.). b) isolated yield. c) determined by ^1H NMR (500 MHz).



Scheme 4. (a) $VO(acac)_2$ (catalyst), ^tBuOOH, CH_2Cl_2, 0 °C; (b) (i) $LiAlH_4$, THF, 0 °C, (ii) $MeOCH_2Cl$, $^iPr_2NEt$, CH_2Cl_2, reflux; (c) thexylborane, THF, 0 °C then 3N NaOH, 30% H_2O_2, 0 °C; (d) (i) $(COCl)_2$, DMSO, CH_2Cl_2, –60 °C then Et_3N, 0 °C, (ii) *p*-TsOH·H_2O (catalyst), MeOH; (e) KH, MeI, THF; (f) (i) H_2, 10% Pd-C (catalyst), 0.2% $HClO_4$-MeOH, (ii) 1N H_2SO_4-THF (1:1).

For the synthesis of L-arcanose (**17**), the *syn* dienol **10**, $[\alpha]_D^{27}$ +74.3° (*c* 0.70, $CHCl_3$), was converted to the epoxy alcohol **12**, $[\alpha]_D^{23}$ +122.2° (*c* 1.04, $CHCl_3$), in a completely diastereoselective manner[10] by the vanadium catalyzed epoxidation. LAH reduction followed by methoxymethylation gave the olefin **13**, $[\alpha]_D^{29}$ +19.1° (*c* 0.91, $CHCl_3$) which was then transformed into the primary alcohol **14**, $[\alpha]_D^{28}$ +23.2° (*c* 0.92, $CHCl_3$), by hydroboration-oxidation. Upon sequential Swern oxidation, acetalization, and methylation, the methyl ether **16** was obtained as a 2:1 anomeric mixture. Without separation of the anomers, **16** was subjected to debenzylation and acid hydrolysis to furnish L-arcanose (**17**), mp 107.5~108.5 °C, $[\alpha]_D^{23}$ –23.0° (*c* 1.19, EtOH, equilibrated) (lit.[11] mp 96-98 °C, $[\alpha]_D$ –20.9° (*c* 4.56, EtOH, equilibrated). Further identity of the synthesis of **17** was established by the fact that 1,4-di-*O*-acetyl-arcanose (**18**), $[\alpha]_D^{29}$ –31.6° (*c* 1.21, EtOH), derived from **17** exhibited spectral properties (^1H NMR, IR) in accord with those reported.[11,12]

Similarly, the *anti* alcohol **11** was transformed into L-olivomycose (**23**) via **19**, $[\alpha]_D^{28}$ +0.8° (*c* 0.98, $CHCl_3$), **20**, $[\alpha]_D^{26}$ +51.0° (*c* 0.96, $CHCl_3$), **21**, $[\alpha]_D^{27}$ +37.2° (*c* 1.07, $CHCl_3$), and **22** (3:1 anomeric mixture). It is worthy of note that the vanadium catalyzed epoxidation of **11** took place also with excellent diastereoselectivity[10] leading to exclusive formation of **19**. The synthesis of **23**, mp 104 °C, $[\alpha]^{29}$ –22.2° (*c* 1.04, H_2O, equilibrated) (lit.[7a] mp 102~103 °C, $[\alpha]_D$ –22.2° (*c* 1.0, H_2O, equilibrated), was confirmed by converting **23** to methyl L-α-olivomycoside (**24**). The synthetic **24**, $[\alpha]_D^{30}$ –150.8° (*c* 1.40, EtOH) (lit.[7d] $[\alpha]_D^{25}$ –145° (EtOH)), showed spectral properties (^1H NMR, IR) in accord with those reported.[7b]

References and Notes

1. See the preceding paper.
2. For the synthesis of carbohydrates and other polyhydroxylated materials from acyclic precursors, see: In *Trends in Synthetic Carbohydrate Chemistry*; Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium Series 386; Washington D. C., 1989.
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10. The corresponding *threo* isomer was not detected in the ^1H NMR (500 MIIz) spectrum of the reaction product.
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