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ALLYLIC ORGANOMETALLIC WAY TO CONTROL ACYCLIC STEREOCHEMISTRY AND ITS APPLICATION TO THE SYNTHESIS OF CARBOHYDRATES

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Summary

The Cram/anti-Cram selectivity in the reactions of allylmetals with aldehydes and the *erythro / threo* selectivity in the reactions of substituted allylic organometallic compounds with other aldehydes can be controlled by the metal (M). Based on both selectivities, we can predict the diastereofacial selectivity of more complex systems. Finally, 1-O-methyl-2,6-dideoxyhexose and 1-O,3-O-dimethyl-4,6-dideoxyhexose are prepared.

The reaction of allylic organometallic compounds with aldehydes is becoming increasingly important for the control of acyclic stereochemistry [1]. Representative reactions on the acyclic stereocontrol of two and three carbon units are summarized in Table 1 [2]. The diastereoface selectivity in the reactions of Table 1 depends on several factors, including the metal (M), the structure of the aldehydes, the geometry of the double bond, and the reaction conditions. In this paper, we report (i) that the stereoselectivity can be controlled by the choice of metal (M), (ii) the carbohydrate synthesis via eq. 7 and 8, and (iii) a method for predicting the stereoselectivity in the reaction of substituted allylic organometallic compounds with aldehydes having chiral centers.

Results and discussion

The Cram / anti-Cram selectivity (1,2- and 1,3-asymmetric induction)

One of the most fundamental problems in acyclic stereocontrol is how to enhance the Cram or anti-Cram selectivity. To clarify the metal effect on the Cram/anti-Cram selectivity, we examined the reactions of eq. 1–3. The results are summarized in Table 2. The Cram selectivity of **1** is not so high; the highest selectivity (84/16) is realized in the reaction of allylstannane in the presence of $AlCl_3$ (entry 6). The Cram

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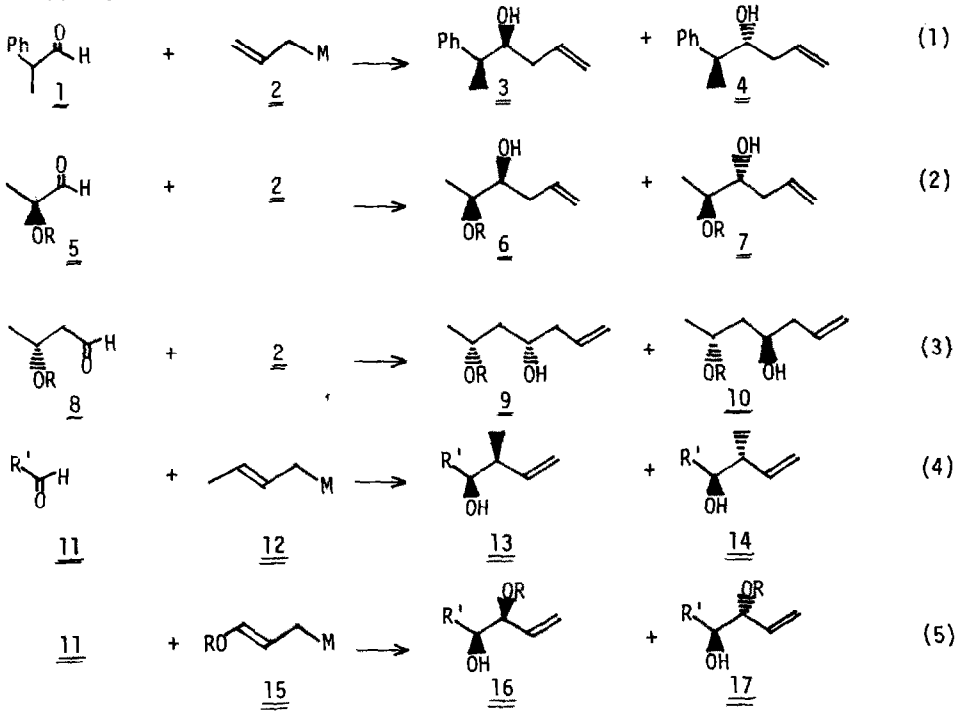
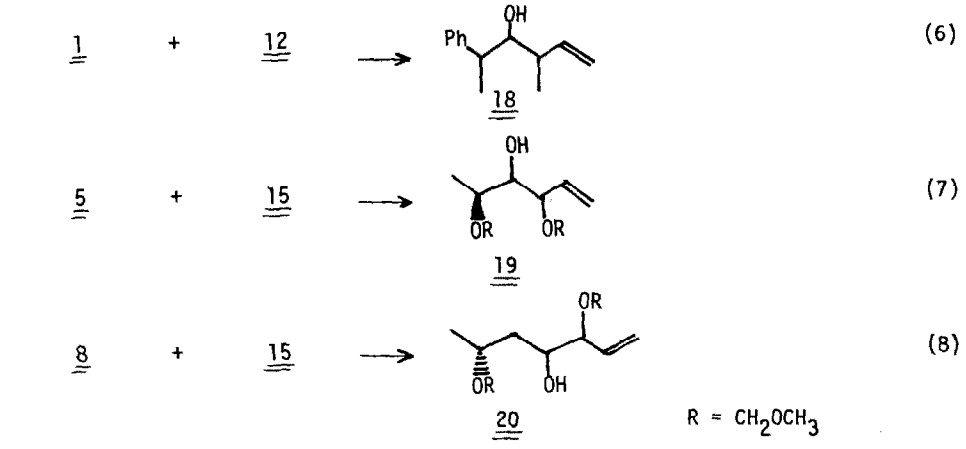
TABLE 1

STEREOREGULATED SYNTHESIS OF ACYCLIC SYSTEMS VIA ALLYLIC ORGANOMETALS

Stereocontrol of two carbon units



Stereocontrol of three carbon units



selectivity with ordinary chiral aldehydes having no ability to be chelated is generally low, and this long-pending problem must await future investigation.

Fortunately, excellent selectivity has been realized in α- and β-alkoxy substituted aldehydes, in which chelation through the metal plays an important role for the

TABLE 2

DIASTEREOFACE SELECTIVE REACTIONS BETWEEN 2 AND ALDEHYDES

entry	aldehyde	allylmetal; condition	product ratio, syn : anti
	1	2 (M)	3 (Cram) : 4 (anti-Cram)
1		$SiMe_3$; $TiCl_4$	70 : 30
2		$SnCl_4$	73 : 27
3		$AlCl_3$ or BF_3	74 : 26
4		$SnMe_3$; $TiCl_4$	69 : 31
5		BF_3	80 : 20
6		$AlCl_3$	84 : 16
7		10 Kbar, 25°C	67 : 33
8			55 : 45
	5	2 (M)	6 (anti-Cram or chelation) : 7 (Cram or non-chelation)
9		$SnMe_3$; $TiCl_4$	~100 : -
10		10 Kbar, 25°C	39 : 61
11			52 : 48
12		MgCl	53 : 47
13		$^-AlEt_3\overset{+}{M}gCl$	58 : 42
14		$^-AlEt_3Li^+$	40 : 60
15		ZnBr	41 : 69
16		$Ti(O\text{-}i\text{-}Pr)_3$	45 : 55
	8	2 (M)	9 (Cram or non-chelation) : 10 (anti-Cram or chelation)
17		$SiMe_3$; $TiCl_4$	26 : 74
18		$SnMe_3$; $TiCl_4$	21 : 79
19		BF_3	30 : 70

continued

TABLE 2 (continued)

20	10 Kbar	29 : 71
21		49 : 51
22	$MgCl$	36 : 64
23	$^{-}AlEt_3{}^{+}MgCl$	58 : 42
24	$^{-}AlEt_3Li^{+}$	33 : 67
25	$ZnBr$	32 : 68
26	$Ti(O\text{-}i\text{-}Pr)_3$	53 : 47
27	$ZrCp_2Cl$	62 : 38

stereocontrol [3]. Here also, the high anti-Cram selectivity [4] is achieved in the reaction of allylstannane with **5** (entry 9). Other allylmetals (B, Mg, Al, Zn, and Ti) exhibit low selectivity. The high-pressure reaction of allylstannane produces **7** as a major isomer (entry 10) [5], indicating that $TiCl_4$ acts as a chelating agent, as well as an activator of the carbonyl group. It should be noted that the counter-ion of the aluminum ate complex exerts an influence on the stereoselection (entries 13 and 14); Mg^+ produces **6** predominantly, while Li^+ gives **7** preferentially.

The 1,3-asymmetric induction in our system (**8**) is not so high; the ratio of **9**/**10** is 21/79 at most (entry 18). Reetz and co-workers have reported very high 1,3-asymmetric induction in the reaction of allylsilane/$TiCl_4$ with 3-benzyloxybutanal [3c]. The discrepancy is presumably due to the substituent (OR): benzyl vs. methoxymethyl. Quite interestingly, the high-pressure reaction gives the anti-Cram product (**10**) predominantly (entry 20, cf. entry 10). We speculate that chelation between Sn and both oxygen atoms of **8** occurs easily, while such a chelation of **5** is difficult owing to the rigid five-membered chelate. Here again, the counter-ion of the aluminum ate complex play an important role in the stereoselection; Mg^+ favors the Cram product, while Li^+ favors the anti-Cram product.

In conclusion, the following problems remain to be solved; (i) enhancement of the Cram and/or anti-Cram selectivity in ordinary aldehydes; (ii) enhancement of the Cram selectivity in α- and β-alkoxy substituted aldehydes.

The erythro / threo (or syn / anti) selectivity

Another important problem in acyclic stereocontrol is to enhance the erythro/threo selectivity in eq. 4 and 5. The metal effect of the diastereofacial selectivity in eq. 4 has been extensively investigated [1]. We examined the metal effect in eq. 5. The results are summarized in Table 3. It is generally accepted that the Lewis acid mediated reaction of **12**, in which M = Sn and Si, produces **13** with very high diastereoselectivity (entry 1). Recently, it has been revealed that the *erythro*-selectivity in the presence of BF_3 is observed in a wide range of crotylorganometallic compounds, although the degree of stereoselectivity is variable (entries 2 and 3) [7,8]. Without BF_3, crotyl-Cr, B, Ti, Zr, and even Sn [5] produce the *threo*-isomer (**14**) either predominantly or exclusively (entry 4).

TABLE 3

DIASTEREOFACE MATCHING REACTIONS OF **12** AND **15**

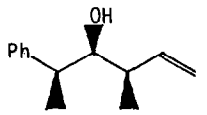
entry	aldehyde	allylmetal; condition	product ratio, syn : anti		ref.
	11	**12** (M)	**13** (erythro) : **14** (threo)		
1	R'CHO	$SnMe_3$, $SiMe_3$; Lewis acid	major	minor	1,6
2		Cp_2TiX; BF_3	>76 : <24		7
3		MgX , ZnX , Cu, ; BF_3	major	minor	8
		CdX, HgX, TlX,			
		$TiCp_2Cl$, $ZrCp_2Cl$,			
		VCp_2Cl			
4		BLn, $SnMe_3$, CrLn,	minor	major	1
		TiLn, $ZrCp_2Cl$			
	11	**15** (M)	**16** (erythro) : **17** (threo)		
5	PhCHO	$^-AlEt_3Li^+$	92 : 8		
6	EtCHO	$^-AlEt_3Li^+$	~100 : -		
7	Me_2CHCHO	$^-AlEt_3Li^+$	70 : 30		
8		$Ti(O\text{-}i\text{-}Pr)_3$	56 : 44		
9		ZnBr	14 : 86		
10	Me_2CHCH_2CHO	$^-AlEt_3Li^+$	71 : 29		
11		$Ti(O\text{-}i\text{-}Pr)_3$	59 : 41		
12		ZnBr	31 : 69		
13	PhCHO	$ZrCp_2Cl$	48 : 52		
14		$TiCp_2Cl$	17 : 83		

The reaction of **15** ($M = {}^-AlEt_3Li^+$) produces the *erythro*-isomer with very high stereoselectivity (entries 5 and 6) [9]. On the other hand, the *threo*-selectivity of **15** is not so high as shown in entries 9, and 12–14. The *erythro*-selectivity of the aluminum ate complex decreases with the branched aldehydes (entries 7 and 10). In conclusion, although we are now in a position to attain very high *erythro / threo* selectivity in a simple crotyl system, such selectivity in heteroatom substituted allylic systems like **15** must be enhanced in future studies.

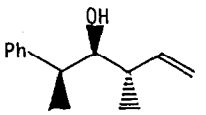
TABLE 4

DIASTEREOFACE SELECTIVE AND MATCHING REACTIONS [10] BETWEEN 1 AND 12

entry	12 (M)	product ratio				Cram / anti-Cram	erythro / threo
		18a	18b	18c	18d		
		Cram-erythro	Cram-threo	anti-Cram -erythro	anti-Cram -threo		
1	$SnBu_3$; BF_3	86	-	14	-	86/14	~100/ -
2	$SnBu_3$; 10 Kbar	18	52	14	16	70/30	32/68
3	$SnMe_3$; BF_3	88	-	12	-	88/12	~100/ -
4		26	40	6	28	66/34	32/68
5	MgCl	34	33	12	21	67/33	46/54
6	CrLn	-	67	-	33	67/33	- /~100
7	$ZrCp_2Cl$	-	73	-	27	73/27	- /~100
8	α-$SnMe_3$-substituted crotyl-9-BBN[2]	-	81	-	19	81/19	- /~100



18a



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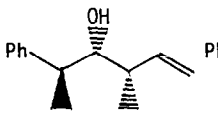

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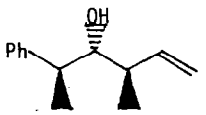


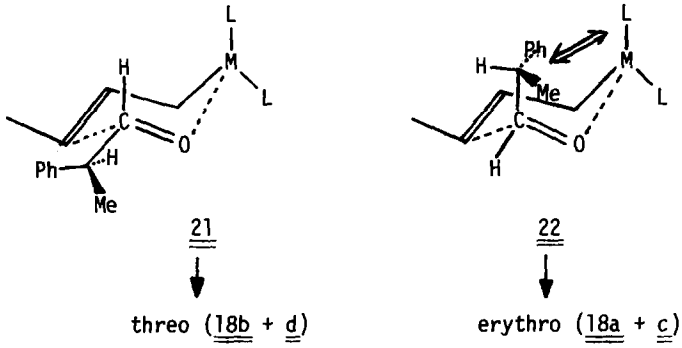
18d

Stereocontrol of three carbon units

(1) The simple system. Since the metal effect in the stereocontrol of two carbon units was established, we next examined the metal effect in the three carbon unit (eq. 6). The results are summarized in Table 4. The Cram/anti-Cram selectivity of **12** is greater than that of **2** irrespective of the metal (M) (cf. entries 1–4 of Table 4 vs. entries 4–8 of Table 2). The *erythro-* or *threo*-selectivity in the reaction of **12** with **1** is also greater than the selectivity in the reaction with simple aldehydes such as benzaldehyde and n-butyraldehyde (cf. entries 1, 3, 6, and 7 of Table 4 vs. entries 1 and 4 of Tables 3). Although both selectivities [10] are somewhat enhanced, the direction of the selectivities is identical to that of the selectivities of eq. 1 and 4 [11]. Accordingly, we can predict the diastereofacial selectivity of the three carbon unit from the stereochemical information on the corresponding two carbon units. For example, the Cram-*erythro* selectivity of Sn (entry 1, Table 4) can be predicted from the selectivity of entry 5 in Table 2 and of entry 1 in Table 3.

Quite interestingly, in the reaction of B and Mg (entries 4 and 5) the Cram/anti-Cram selectivity of the *erythro*-products is different from that of the *threo*-products. The former is greater than the latter; in the reaction of B the ratio is 26/6 for the

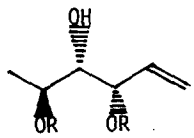
erythro and 40/28 for the *threo*; in the reaction of Mg it is 34/12 for the *erythro* and 33/21 for the *threo*. These observations indicate that the difference of the ratios is due to the difference of the transition states leading to both isomers, and can be explained as follows (Scheme 1). In the geometry of **21** leading to the *threo*-products,



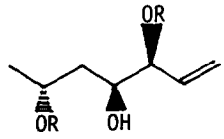
SCHEME 1

the Cram/anti-Cram selectivity is determined only by the steric factor at the chiral center. On the other hand, in **22** leading to the *erythro*-isomers, the chiral center goes to the axial position. The cumulative steric factor of the chiral center and ligand L must increase the Cram/anti-Cram selectivity. In fact, this type of stereoelectronic effect has been observed in the reaction of imines with **12**, in which very high Cram selectivity (up to 100/0) is realized [12].

(2) Carbohydrate synthesis. Since the fundamental selectivity and the metal effect on diastereoface selective and matching reactions (eq. 1–6) were established, we intended to synthesize certain carbohydrates via the allylic organometallic way [13]. If the stereoselectivity in eq. 7 can be divided into two components, diastereoface selective (the Cram/anti-Cram) and matching (*erythro/threo*) components, we can predict the metal effect in the stereoselectivity. Since $^{-}AlEt_3Li^{+}$ produces the Cram-isomer predominantly in eq. 2 (entry 14, Table 2) and the *erythro*-isomer preferentially in eqn. 5 (entry 7, Table 3), it should give the Cram-*erythro* isomer (**19a**) predominantly in eq. 7. Similarly, since $^{-}AlEt_3Li^{+}$ affords the anti-Cram-isomer predominantly in eq. 3 (entry 24, Table 2) and the *erythro*-product preferentially in eq. 5 (entry 10, Table 3), it must produce the anti-Cram-*erythro*-isomer (**20a**) as a major product among four isomers in eq. 8. We examined the reactions of eq. 7 and 8 via the aluminum ate complex, and the results are summarized in Table 5. The major isomer in eq. 7 was transformed into 1-O-methyl-2,6-dideoxyhexose



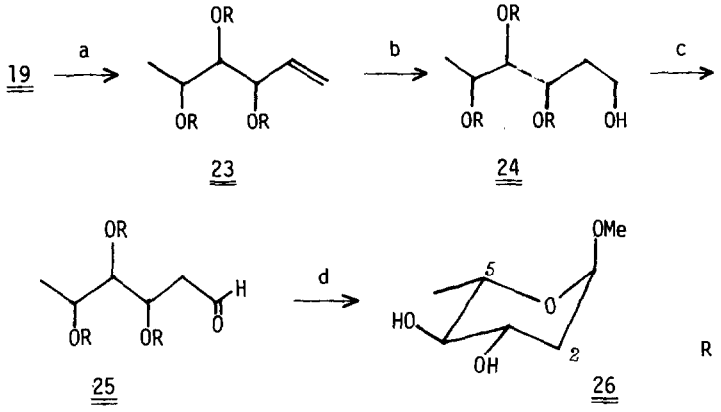
19a



20a

(**26**), as shown in eq. 9. The structure of **26** was confirmed by 400 MHz ^{1}H NMR analysis. Therefore, it is clear that the major isomer is **19a**, as predicted. The major isomer in eq. 8 was converted into 1-O,3-O-dimethyl-4,6-dideoxyhexose (**29**), as shown in eq. 10. The structure of **29** was confirmed by 400 MHz ^{1}H NMR analysis of **30**, indicating that the major isomer is **20a** as anticipated.

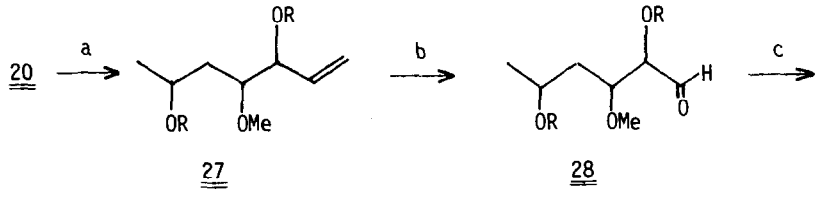
The ratio of the major isomer in the observed value is greater than that in the calculated value (entries 1 and 4). This tendency is also observed in the simple three carbon unit, as described above (eq. 6) (entries 1,3,6, and 7 of Table 4). In

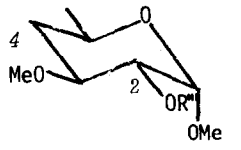


(9)

R = MOM = CH_2OCH_3

Reagents: a, MOMCl/DPEA; b, $BH_3 \cdot SMe_2$; H_2O_2/NaOH; c, $(COCl)_2$/DMSO/Et_3N; d, HCl/MeOH





(10)

R = CH_2OCH_3

29; R" = H

30; R" = COPh

Reagents: a, MeI/NaH; b, OsO_4/$NaIO_4$; c, HCl/MeOH

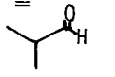
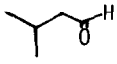
conclusion, the stereoselectivity of three carbon units can be predicted from information on the diastereofacial selectivities of two carbon units. This concept may be useful for the construction of acyclic systems having three or more consecutive chiral centers.

Experimental

General information concerning instrumentation and materials has been described previously [5,14].

TABLE 5

PREDICTION OF THE DIASTEREOFACIAL SELECTIVITY

entry	aldehyde	allylmetal M = $^{-}AlEt_3Li^{+}$	Observed isomer ratio	Calcd isomer ratio
1	5	15	66 : 18 : 11 : 5	42 : 28 : 18 : 12
2	5	2	Cram : anti-Cram = 60 : 40	
3		15	erythro : threo = 70 : 30	
4	8	15	50 : 30 : 11 : 9	48 : 23 : 19 : 10
5	8	2	Cram : anti-Cram = 33 : 67	
6		15	erythro : threo = 71 : 29	

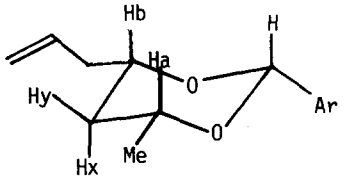
Reaction of 2 with 1, 5, and 8. All reactions were carried out on 1 mmol scale. In the reactions of Si, Sn, and B, CH_2Cl_2 was used as the solvent, while ether was used in the reactions of Mg, Al, Zn, Ti, and Zr. The Lewis acid dissolved in CH_2Cl_2 was added at −78°C. Allyl-ZnBr, $Ti(O\text{-}i\text{-}Pr)_3$, and $^{-}AlEt_3\overset{+}{M}gCl$ were prepared in situ by the addition of one equivalent of $ZnBr_2$ in THF, $ClTi(O\text{-}i\text{-}Pr)_3$ in hexane, and $AlEt_3$ in hexane to an ether solution of allylmagnesium chloride at −78°C. Allyl-$^{-}AlEt_3Li^{+}$ was prepared in situ by the addition of $AlEt_3$ in hexane to an ether solution of allyllithium at −78°C, which was prepared from allyltriphenyltin and phenyllithium [14]. The reactions in entries 1–6, 9, and 17–19 were quenched at −78°C, and the other reactions were quenched at 0°C except those in entries 7, 10 and 20. The product ratio was determined by GLPC (Carbowax 6000, 2 m) and ^1H NMR analysis. The total yield was in the range of 80–96%. The structures of **3** and **4** had been determined previously [5]. Structural determination of **6**, **7**, **9**, and **10** was carried out by comparison with authentic samples prepared via the reported procedure [3].

Preparation of 5. According to the literature [15], (*S*)-ethyllactate (from Aldrich Chemical Co.) is converted into (*S*)-ethyl-O-methoxymethyllactate on treatment with diisopropylethylamine (DPEA) and methoxymethyl chloride (MOMCl); b.p. 77–80°C/20 Torr, 89% yield, $[\alpha]_D^{23.5°}$ −45.015° (5 cm cell, neat); ^1H NMR (CCl_4) δ 1.11 (t, 3, *J* 7.5 Hz), 1.20 (d, 3, *J* 7.0 Hz), 3.21 (s, 3), 4.09 (quartet, 2, *J* 7.5 Hz), 4.20 (q, 1, *J* 7.5 Hz), 4.56 (s, 2). The MOM protected ester was reduced with a 0.6 equivalent amount of $LiAlH_4$ in ether at 0°C to produce (*S*)-2-(methoxy)methoxypropanol; bp 73–75°C/20 Torr, 86% yield, $[\alpha]_D^{24°} = +5.364°$ (5 cm cell, neat); ^1H NMR (CCl_4) δ 1.11 (d, 3, *J* 7.0 Hz), 3.34 (s, 3), 3.3–4.1 (m, 4), 4.68 (s, 2). Swern oxidation of this alcohol by the reported procedure [16] gave (*S*)-2-(methoxy)methoxypropanal (**5**) in 60% yield; bp 45–47°C/20 Torr, $[\alpha]_D^{24°} = -23.103°$ (5 cm cell, neat); ^1H NMR (CCl_4) δ 1.25 (d, 3, *J* 8.0 Hz), 3.43 (s, 3), 4.05

(qd, 1, J 7.5 and 2.0 Hz), 4.80 (s, 2), 9.72 (d, 1, J 2.0 Hz); IR (CCl_4) 1730 cm^{-1}; MS: m/e (M^+) 118.

Preparation of ***8.*** (R)-Methyl 3-hydroxybutyrate (from Wako Chemical Ind.) was converted into (R)-methyl 3-(methoxy)methoxybutyrate as described above; bp 82–83°C/20 Torr, 97% yield, $[\alpha]_D^{26.5°} = -7.653°$ (5 cm cell, neat); ^1H NMR (CCl_4) δ 1.16 (d, 3, J 6.5 Hz), 2.28 (dd, 1, J 16.0 and 6.5 Hz), 2.52 (dd, 1, J 15.0 and 7.0 Hz), 3.28 (s, 3), 3.66 (s, 3), 4.13 (m, 1), 4.64 (s, 2). The MOM protected ester was reduced similarly with $LiAlH_4$ to produce (R)-3-(methoxy)methoxy-1-butanol; bp 54–56°C/1 Torr, 94% yield, $[\alpha]_D^{25.5°} = -16.976°$ (5 cm cell, neat); ^1H NMR (CCl_4) δ 1.20 (d, 3, J 7.0 Hz), 1.73 (q, 2, J 7.0 Hz), 3.24 (bs, 1), 3.42 (s, 3), 3.6–4.4 (m, 3), 4.72 (AB pattern, 2). Swern oxidation gave (R)-3-(methoxy)methoxybutanal (**8**) in 96% yield; bp 65–68°C/20 Torr, $[\alpha]_D^{25.5°} = -9.394°$ (5 cm cell, neat); ^1H NMR (CCl_4) δ 1.23 (d, 3, J 7.0 Hz), 2.3–2.8 (m, 2), 3.34 (s, 3), 4.0–4.4 (m, 1), 4.65 (AB pattern, 2), 9.87 (t, 1, J 2.0 Hz); IR (CCl_4) 1730 cm^{-1}; MS: m/e (M^+) 132.

Structural determination of ***6, 7, 9, and 10.*** Although discrimination between **6** and **7** by 100 MHz NMR spectroscopy was difficult, 400 MHz ^1H NMR spectroscopy clearly differentiated both isomers. ^1H NMR of **6** ($CDCl_3$) δ 1.20 (d, 3, J 6.4 Hz), 2.20 (bs, 1), 2.22 (m, 2), 3.40 (s, 3), 3.57–3.60 (m, 2), 4.68–4.73 (AB, 2), 5.11 (m, 2), 5.90 (m, 1). ^1H NMR of **7** ($CDCl_3$) δ 1.18 (d, 3, J 7.3 Hz), 2.21–2.24 (m, 3), 3.39 (s, 3), 3.57–3.60 (m, 2), 4.68–4.73 (AB, 2), 5.12 (m, 2), 5.91 (m, 1). The retention time of **6** in Carbowax 6000 was shorter than that of **7**. Both isomers were compared with authentic samples [3]. Similarly, **9** and **10** were distinguished by the chemial shifts of the methyl protons. ^1H NMR of **9** ($CDCl_3$) δ 1.2069 (d, 3, J 6.1 Hz), 3.3885 (s, 3). ^1H NMR of **10** ($CDCl_3$) δ 1.2160 (d, 3, J 6.1 Hz), 3.3901 (s, 3). The retention time of **10** in Carbowax 6000 was shorter than that of **9**. Both isomers were compared with authentic samples [3]. Further, **9** and **10** were hydrolyzed with HCl/MeOH to produce the corresponding diols. These diols were converted into the 1,3-dioxane derivatives with p-nitrobenzaldehyde according to the reported procedure [17]. The coupling constants of **31** derived from **9** were as follows: $J_{a\text{-}x}$ 11.60 and $J_{a\text{-}y}$ 2.14 Hz. Another isomer from **10** exhibited the coupling constants $J_{a\text{-}x}$ 2.17 and $J_{a\text{-}y}$ 5.37 Hz.



31; Ar = p-NO_2-C_6H_4

Reaction of ***15.*** The MOM-allyllithium (**15**, M = Li) was prepared as described previously [9]. To this solution was added at −78°C an equivalent amount of $AlEt_3$ in hexane, $TiCl(O\text{-}i\text{-}Pr)_3$ in hexane, $ZnBr_2$ in THF, $ZrCp_2Cl_2$ in THF, or $TiCp_2Cl_2$ in THF. Then, the aldehyde was added at −78°C and the reaction was quenched with H_2O at 0°C. The product ratio was determined by GLPC (Carbowax 6000) and ^1H NMR spectroscopy. The structures of **16** and **17** were determined as described in ref. 9.

Reaction of ***12*** *with* ***1.*** The product ratio and structures of the isomers were determined as reported previously [5]. In entry 8, the reaction products, the alken-

ylstannane derivatives [2], were destannylated, and the resulting compound **18** was analysed.

Synthesis of methyl 2,6-dideoxy-α-L-arabino-hexopyranoside (26). The reaction of **15** with **5** was carried out as described above (10 mmol scale). Usual work-up and distillation through Kugelrohr produced **19** in 84% yield; b.p. 130°C/3 Torr. The isomer ratio was determined by GLPC (Tetrahydroxyethyl ethylene diamine (THEED) from Wako Chem. Ind., 10%, 3 m). The major isomer was separated through a column of silica gel (hexane/ether 10/1); ^{1}H NMR (CCl_4) δ 1.20 (d, 3, J 6.5 Hz), 2.34 (bs, 1), 3.35 (s, 3), 3.37 (s, 3), 3.66 (m, 1), 4.16 (m, 1), 4.66 (AB, 2), 4.70 (m, 1), 5.20–5.40 (m, 2), 5.65–6.10 (m, 1); MS: m/e (M^+) 200. The MOM-protected derivative (**23**) was prepared by a procedure similar to that described above; b.p. 140°C/3 Torr (Kugelrohr), 89% yield; ^{1}H NMR (CCl_4) δ 1.12 (d, 3, J 6.5 Hz), 3.31 (s, 9), 3.60–3.80 (m, 2), 4.01 (t, 1, J 7.5 Hz), 4.50–4.80 (m, 6), 5.22–5.40 (m, 2), 5.60–6.00 (m, 1); MS: m/e (M^+) 264. Usual hydroboration of **23** with $BH_3 \cdot SMe_2$ followed by oxidation with H_2O_2/NaOH produced **24** in 89% yield; b.p. 140°/2 Torr (Kugelrohr); ^{1}H NMR (CCl_4) δ 1.22 (d, 3, J 7.0 Hz), 1.75–1.92 (m, 2), 3.00 (bs, 1), 3.44 (s, 3), 3.50 (s, 6), 3.82 (m, 5), 4.70–4.95 (m, 6); MS: m/e (M^+) 282. Swern oxidation of **24** was carried out as described above, and the reaction product was purified through a column of silica gel (hexane/ether 4/1). Further purification through Kugelrohr distillation gave **25** in 60% yield; b.p. 90°C/0.1 Torr; ^{1}H NMR ($CDCl_3$) δ 1.25 (d, 3, J 7.0 Hz), 2.75 (m, 2), 3.39 (s, 3), 3.42 (s, 6), 3.74 (m, 1), 4.00 (m, 1), 4.30 (m, 1), 4.78 (m, 6), 9.90 (t, 1, J 2.0 Hz); IR (CCl_4) 1720 cm^{-1}; MS: m/e (M^+) 280. A few drops of conc. HCl were added to a methanol solution of **25** and the resulting mixture was refluxed for 1 h. The mixture was neutralized with saturated $NaHCO_3$ solution. Ether was added and the organic layer was separated, dried with $MgSO_4$, and condensed. Distillation through Kugelrohr gave **26** in 60% yield; b.p. 100°C/0.1 Torr, $[\alpha]_D^{25°}$ −130.15° (c 1.1, $CHCl_3$)(lit. [18a], $[\alpha]_D^{25}$ − 142.21° (c 1.3607, $CHCl_3$)). Other spectroscopic data were in good agreement with the reported values [18a]. The structure of **26** was established by the coupling constants: $J_{1\text{-}2ax} = 3.0$, $J_{1\text{-}2eq}$ 0, J_{2gem} 12.6, $J_{2ax\text{-}3ax}$ 12.5, $J_{2eq\text{-}3ax}$ 5.34, $J_{3ax\text{-}4ax}$ 9.15, $J_{4ax\text{-}5ax}$ 9.15 Hz.

Synthesis of methyl 4,6-dideoxy-3-O-methyl-α-D-xylo-hexopyranoside (29). The reaction of **15** with **8** was carried out similarly. **20** was obtained in 95% yield; b.p. 140°C/2 Torr (Kugelrohr). The major isomer was separated through a column of silica gel (hexane/ether = 10/1); ^{1}H NMR (CCl_4) δ 1.16 (d, 3, J 6.5 Hz), 1.40–1.75 (m, 2), 3.33 (s, 3), 3.35 (s, 3), 3.66–4.00 (m, 3), 4.50–4.70 (m, 4), 5.20–5.40 (m, 2), 5.56–6.00 (m, 1); MS: m/e (M^+) 234. Usual methylation with MeI and NaH gave **27** in 83% yield; bp 110°C/2 Torr (Kugelrohr); ^{1}H NMR (CCl_4) δ 1.12 (d, 3, J 6.5 Hz), 1.30–1.60 (m, 2), 3.30 (s, 6), 3.38 (s, 3), 3.60–3.80 (m, 2), 4.10–4.20 (m, 1), 4.50–4.70 (m, 4), 5.15–5.34 (m, 2), 5.60–6.00 (m, 1); MS: m/e (M^+) 248. Lemieux–Johnson oxidation of **27** with $OsO_4/NaIO_4$ in dioxane/H_2O (3/1) was carried out according to the reported procedure [19]. The product was purified through a column of silica gel (hexane : ether = 4 : 1) and distilled via Kugelrohr, giving **28** in 60% yield; bp 100°C/1 Torr; ^{1}H NMR (CCl_4) δ 1.16 (d, 3, J 7.0 Hz), 1.46–1.72 (m, 2), 3.32 (s, 3), 3.38 (s, 6), 3.60–4.10 (m, 3). 4.50–4.75 (m, 4), 9.78 (m, 1); IR (CCl_4) 1720 cm^{-1}; MS: m/e (M^+) 250. A few drops of conc. HCl were added to a methanol solution of **28** and the resulting mixture was refluxed for 30 min. The reaction mixture was neutralized, extracted with ether, dried with $MgSO_4$,

and condensed. The residue was purified through a column of silica gel (CH_2Cl_2/EtOH 20/1), giving **29** in 62% yield. The spectroscopic data were compared with those reported previously [20]. Further, to confirm the structure of **29**, it was converted to **30** with benzoyl chloride/pyridine. The coupling constants of **30** were in good agreement with its stereochemistry: $J_{1eq\text{-}2ax}$ 7.04, $J_{2ax-3ax}$ 9.46, $J_{3ax\text{-}4ax}$ 11.59, $J_{3ax\text{-}4eq}$ 5.19, J_{4gem} 13.12, $J_{4ax\text{-}5ax}$ 10–12, $J_{4eq\text{-}5ax}$ 1.83 Hz.

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