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STEREOSELECTIVE REDUCTION OF β-HYDROXYKETONES TO 1,3-DIOLS

HIGHLY SELECTIVE 1,3-ASYMMETRIC INDUCTION VIA BORON CHELATES

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Abstract—Highly selective asymmetric induction can be achieved in the reduction of acyclic β-hydroxyketones via boron chelates. Treatment of β-hydroxyketones (**1**) with tributyl or triisobutylborane and successively with sodium borohydride afforded *syn*-1,3-diols (**3**) in highly stereoselective manner. *Syn*-α-substituted-β-hydroxyketones (**8**) were also reduced to give *syn*, *syn*-1,3-diols (**9**) exclusively. The reaction was further applied to the convenient preparation of 3-deoxy-hexoses.

In recent years, many approaches to the asymmetric inductions in the reactions of acyclic precursors have been widely studied, and various useful and stereoselective methods have been developed.[1] For examples, directed aldol reactions, allylation using some allylic metals, sigmatropic rearrangements and nucleophilic addition to α-asymmetric carbonyl compounds have been explored and successfully applied to the syntheses of complex molecules such as macrolides and ionophore antibiotics. According to these methods, asymmetric induction in the relationship between adjacent C atoms, that is 1,2-relationship, is highly achieved. In contrast, asymmetric induction between more remote atoms such as 1,3-, 1,4-, --- relationships becomes more and more difficult. When we started this work, only few reactions were noted in which remote asymmetric inductions take place in highly selective manner. Reduction of γ,δ-epoxyketones[2] and OH-directed epoxidations of homo- and bishomoallylic alcohols[2,3] can be used effectively to introduce chiral centers with 1,3- or 1,4-asymmetric induction in acyclic systems. Also, remote asymmetric induction of dienes utilizing hydroboration was reported[4] at the same time of our preliminary report.[5]

Recently, stereoselective preparations of 1,3-diols have been strongly required, and some attempts have been made for the preparation of 1,3-diols from β-hydroxyketones accompanying 1,3-asymmetric induction.[6a-g] However, they are not highly stereoselective and have limited utility.

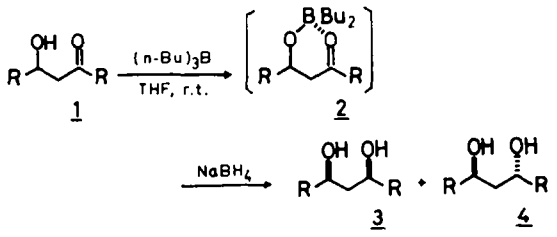
Nowadays, various β-hydroxyketones are readily prepared by directed aldol reactions in regio- and stereoselective manner.[7] Therefore, it was expected that the development of a new and general method for stereoselective reduction of β-hydroxyketones would afford an efficient preparative method for 1,3-diol synthesis, and we investigated the exploration of a new method for stereoselective reduction of acylic β-hydroxyketones.

In order to realize high stereoselectivity of the reduction, conformations of β-hydroxyketones have to be controlled. We expected that stable chelate complexes of β-hydroxyketones (**1**) with boron compounds would be sufficiently regid to control the approach of a reducing agent on the complexes. According to this consideration, we examined at first the reduction of 3-hydroxy-1,3-diphenylpropan-1-one (**1a**) via the corresponding dibutylborinic ester (**2a**).

To a tetrahydrofuran (THF) solution of tributylborane and **1a** was bubbled a cat. amount of air and the solution was stirred at room temperature. At this stage, the formation of dibutylborinic ester (boron chelate) was suggested by the NMR spectrum of the condensed reaction mixture, which showed the presence of phenyl and butyl groups in 1:1 ratio. Then the mixture was treated with an equimolar amount of sodium borohydride at −78°. After quenching with a mixture of 30% hydrogen peroxide, pH 7 buffer and methanol, *meso*-1,3-diphenyl-1,3-propanediol (**3a**) was obtained almost exclusively.

This method seemed to be available for the stereoselective reduction of β-hydroxyketones, therefore, the generality of the reaction was further examined using 7-hydroxyundecan-5-one (**1b**) and 1,3-dicyclohexyl-3-hydroxypropan-1-one (**1c**). The reduction of these ketones proceeded smoothly according to the above procedure. In some cases, isolation of the diols presented a problem as it was difficult to free the diol completely from boron. This problem was overcome by repeating several times the following procedure[8] on the extract of the quenched reaction mixture: To the condensed extract was added 1% conc. hydrochloric acid in methanol and evaporated *in vacuo* to decompose the small amount of remaining boric ester of a diol (**3**). The results were listed in Table 1, and it became apparent that the sodium borohydride reduction of β-hydroxyketones (**1**) via dibutylborinic esters proceeded stereoselectively to give *meso*-1,3-diols.

The selectivity was increased as the reduction was carried out at the lower (−100°) temperature (run 2, 3 and 4, 5). Furthermore, when triisobutylborane was



Scheme 1.

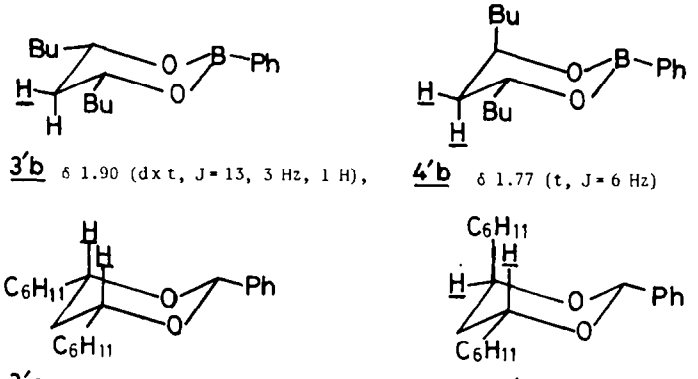
protons of C-1 and C-3; **3'c**, δ 3.44 (2H, dxdxd, J = 10.2, 6.6, 3.3 Hz); **4'c**, δ 3.87 ~ 3.53 (2H, m).

A simple application of this methodologies involves the synthesis of *syn*[10]-7-octene-2,4-diol (**6**), the synthetic intermediate of nonactic acid.[11] 2-Hydroxy-7-octen-4-one (**5**) which was prepared by aldol reaction of acetaldehyde with the kinetic lithium enolate of 5-hexen-2-one was treated with tributylborane and was then reduced with sodium borohydride at − 100°. The desired *syn*-diol (**6**, 88% yield)

Table 1.

Run	1,	R	Reaction temp. (reaction time)	Ratio of meso(3):dl(4) (Tatal yield)
1	1a	C_6H_5	-78°C (2 hr)	98 : 2 (94%)
2	1b	n-C_4H_9	-100°C (5 hr)	96 : 4 (74%)
3			-78°C (2 hr)	88 : 12 (73%)
4	1c	cyclo-C_6H_{11}	-100°C (6 hr)	84 : 16 (90%)
5			-78°C (6 hr)	73 : 27 (94%)
6			-78°C (36 hr)	88 : 12 (85%)

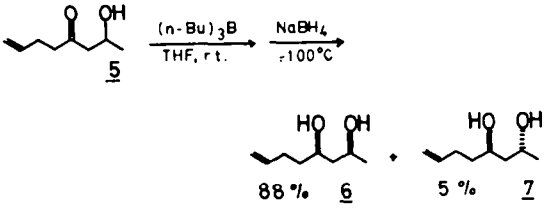
*$(iso\text{-}Bu)_3$ was used instead of $(n\text{-}Bu)_3B$.



Scheme 2.

employed instead of tributylborane in the reduction of **1c**, the selectivity was found to increase remarkably (run 4, 6). Some reducing agents such as lithium aluminiumhydride (LAH), lithium selectride and diborane were also employed, however, sodium borohydride gave the best selectivity.

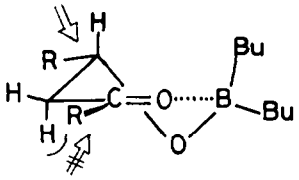
The structure of **3a** was determined by the comparison of NMR spectrum with the literature.[9] The diastereomers (**3b** and **4b**) were converted to phenylborinic esters (**3'b** and **4'b**) and the NMR analysis showed their relative stereochemistry: **3'b**; one of the methylene protons of C-6 appears at δ 1.90 (d × t, J = 13, 3 Hz); **4'b**; the two methylene protones of C-6 was observed at δ 1.77 as triplet (J = 6 Hz). Each isomer of 1,3-dicyclohexylpropane-1,3-diols (**3c** and **4c**) was treated with benzaldehyde in the presence of molecular sieve to form their cyclic acetals. From **3c** was expected the formation of two stereoisomers of cyclic acetals, however only one isomer was produced. The configurational assignment was confirmed by the coupling patterns of two methyne



Scheme 3.

was obtained in high selectivity along with a small amount (5% yield) of the *anti*-isomer (**7**).

Concerning the 1,3-asymmetric induction in addition reactions to CO groups, some models for asymmetric inductions were discussed,[6b,h] and the achievement of the present high 1,3-asymmetric induction might be explained by assuming the following cyclic model. A dibutylborinic ester of β-hydroxyketone exists in a chair-like conformation and the axial H of α-C prevents the approach of a reducing agent from



Scheme 4.

the bottom side. Hence, sodium borohydride attacks preferentially from the top side and *syn*-isomers were resulted selectively.

Next, the reduction of two diastereomeric α-substituted-β-hydroxyketones were examined. When α,β-*syn*-β-hydroxyketones (**8a, b, c**) reacted with tributylborane and was reduced with sodium borohydride at −100°, only all *syn*-isomers (**9a, b, c**) were obtained exclusively and none of the isomer (**10**) was detected.

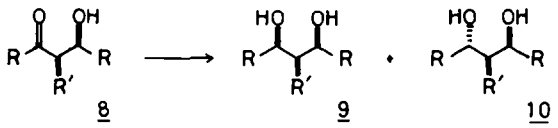
Although the stereospecificity was exhibited in the reduction of *syn*-isomers (**8**) with complete stereoselection, the reduction of *anti*-isomers (**11**) proceeded stereoselectively but not in specific manner. When the substituent (R′) was Me group, the *anti, anti*-isomer (**12**) was obtained predominantly. On the other hand, in case of the substituent (R′) was Et or Bu group, the *syn, anti*-isomer (**10b, c**) was yielded selectively. Thus the selectivity was observed, however, the specificity was not observed in the reduction of *anti*-isomers (**11**).

The relative stereochemistry of the products was determined as follows. Treatment of *syn*- or *anti*-α-substituted hydroxyketone (**8** or **11**) only with sodium borohydride in methanol at room temperature afforded two diastereomers of 1,3-diols (**9** and **10**) or (**10** and **12**), respectively. One of the each reduction products of *syn*- and *anti*-isomers was identical by TLC analysis, which should be the *syn, anti*-isomer (**10**). Consequently, the structure of the remaining ones were corresponding to the symmetrical 1,3-diols (**9** and **12**). These structures were also confirmed by transformation of the products to 6-membered cyclic silyl acetals by treating diols (**9, 10, 12**) with dimethylsilyl chloride and pyridine in benzene (Experimental).

The observed selectivity allows the following consideration about the stereochemistry of the nucleophilic attack on dibutylborinic esters of **8** and **11**. The boron chelate for **8** is expected to exist in a chair-like conformation (**A**) if the equatorial preference of the substituted R group is taken into account. The approach of sodium borohydride from the bottom side is effectively hindered by steric effect of the axial α-substituent (R′) to exhibit the complete asymmetric induction.

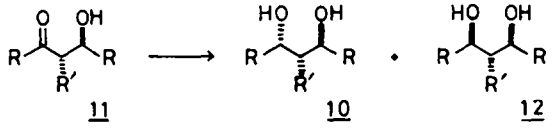
On the contrary, borinic esters of *anti*-isomers (**11**) are considered to exist between two possible chair-like conformations (**B, C**). The conformation (**B**) causes eclipsing interactions involving the substituents R, R′ and R of acyl group. In the conformation (**C**), these eclipsing interactions are relieved, however, 1,3-diaxial interaction between R and Bu group generates. Therefore, the selectivity is largely depend on the substituents (R and R′), hence the specificity was not observed in the reduction of *anti*-isomers (**11**).

The utility of the present reaction was further demonstrated in the convenient preparation of



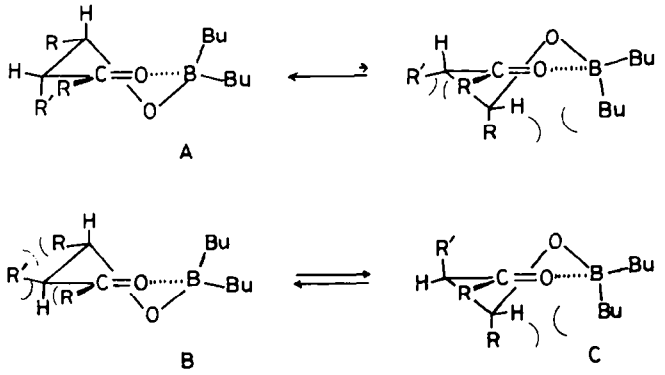
8	R	R′	9 : 10	Yield(%)
8 a	isoPr	Me	100 : 0	95
8 b	Ph	n-Bu	100 : 0	93
8 c	n-Pr	Et	100 : 0	94

Scheme 5.



11	R	R′	10 : 12	Yield(%)
11 a	isoPr	Me	27 : 73	90
11 b	Ph	n-Bu	87 : 13	91
11 c	n-Pr	Et	100 : 0	93

Scheme 6.



Scheme 7.

3-deoxyhexoses from 2,3-O-isopropylidene-D-glyceraldehyde. Aldol reaction between kinetic enolate of methylglyoxal dimethylacetal and 2,3-O-isopropylidene-D-glyceraldehyde gave the 4,5-*anti*-adduct (**13**) predominantly.[11] Heathcock *et al.* had also reported the predominant formation of *anti*-isomers in the aldol reaction of 2,3-O-isopropylidene-D-glyceraldehyde.[12] The *anti*-adduct (**13**) was then submitted for reduction using tributylborane and sodium borohydride to afford the 2,4-*syn*-diol (**15**) and the 2,4-*anti*-diol (**16**) in the ratio of 86:14. Because the stereoselectivity was not sufficiently high, the effects of chelating reagents such as alkylboranes, alkyllithium and Grignard reagent was investigated (Table 2).

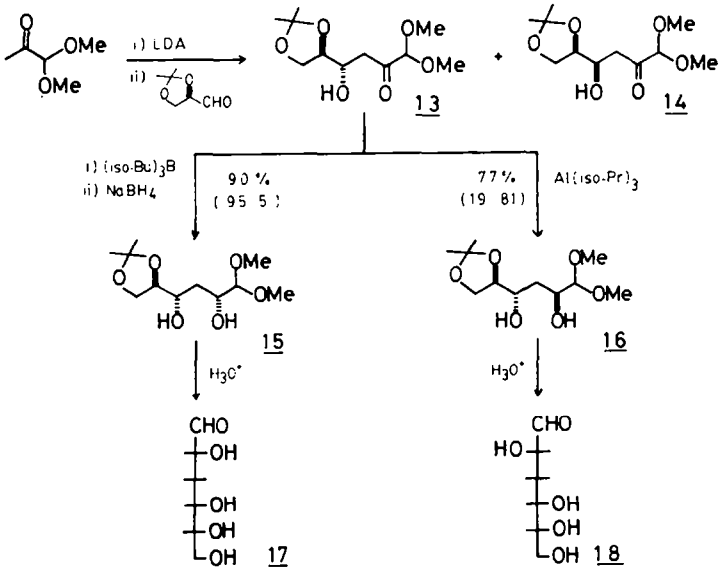
Lithium and magnesium chelates had no effect on the stereoselection, and when tri(sec-butyl)borane was employed, the reduction products were little detected in spite of the long reaction time. Of these metal compounds examined, triisobutylborane was found to be most effective for 1,3-asymmetric induction, and remarkably high stereoselectivity was obtained, (**15**:**16** = 95:5). Deprotection of the *syn*-diol (**15**) by acid hydrolysis afforded 3-deoxy-D-*ribo*-hexose (**17**).

As postulated above, it was noted that β-hydroxyketones are stereoselectively reduced to *syn*-1,3-diols with sodium borohydride via dibutyl or diisobutylborinic esters. Next, we investigated the development of an alternative method which generates *anti*-1,3-diols from β-hydroxyketones. And the Meerwein–Ponndorf reduction was found to give the *anti*-diol predominantly. When hydroxyketone (**13**) was treated with an equimolar amount of aluminium triisopropoxide in toluene at 0°, the 2,4-*anti*-diol (**16**) was obtained in 62% yields along with 15% yield of the *syn*-diol (**15**). The *anti*-isomer (**16**) was successively converted to 3-deoxy-D-*arabino*-hexose (**18**).

In conclusion, it was noted that β-hydroxyketones were reduced stereoselectively with sodium borohydride via borinic esters. Further, this method was found to have wide generality for the preparation of various acyclic 1,3-diols.

Table 2.

Chelating reagent	Reducing reagent	Syn(15):Anti(16)	Yield(%)
$(i\text{-Bu})_3B$	$NaBH_4$	95: 5	90
$(n\text{-Bu})_3B$	"	86:14	87
$(s\text{-Bu})_3B$	"	reduction did not proceed	
9-BBN	"	33:67	81
BH_3	BH_3	40:60	84
n-BuLi	$NaBH_4$	50:50	79
n-BuMgBr	$NaBH_4$	50:50	76



Scheme 8.

EXPERIMENTAL

All m.p. were determined on a Büchi apparatus and are uncorrected. NMR spectra were recorded on a Hitachi R-24B or Varian EM-390 using TMS as the internal standard. IR spectra were measured on Hitachi 260-30. THF was freshly distilled over LAH.

β-Hydroxyketones **1a-c** were prepared by aldol reaction of lithium enolate of the corresponding methylketones with aldehydes, and purified by column chromatography on silica gel. Further details of the reaction procedure are described in the preparation of **5**.

Preparation of 1,3-*diols* **3a-c**. The typical experimental procedure was shown in the preparation of **3b**. To a THF (3.5 ml) soln of tributylborane (1.1 mmol) and **1b** (1.0 mmol) was bubbled a small amount of air (3 ml) and the soln was stirred for 2 hr at room temp under an argon atmosphere. Then the soln was cooled to −100°, and solid $NaBH_4$ (1.1 mmol) was added in one portion. The mixture was stirred for 6 hr, and quenched with a mixture of 30% H_2O_2 (5 ml), pH 7 buffer (10 ml) and MeOH (15 ml). Almost all the organic solvent was evaporated under reduced pressure and the residual water soln was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and condensed *in vacuo*. To the residue was added 4 ml of 1% conc HCl in MeOH and evaporated.[8] This procedure was repeated 5 times to completely decompose the remaining boric acid ester of diols. Then the resulting oily substance was chromatographed on silica gel (hexane–ether = 6:1 mixture as eluent) to give *meso*- **3b** (136 mg, 72%) and *dl*- **4b** (3.5 mg, 2%).

meso-1,3-*Diphenylpropane*-1,3-*diol* **3a**, m.p. 106–107° (recrystallized from benzene), lit. 106–107°;[3a,9] NMR spectrum of crude product was identical with that of the lit,[9] (δ, $CDCl_3$) 1.72–2.41 (m, 2H), 3.73 (br s, 2H), 4.85 (d × d, J = 9, 4 Hz, 2H), 7.23 (s, 10H); The isomer ratio was determined by GLPC analysis (PEG-20M).

meso-*Undecane*-5,7-*diol* **3b** and *dl-undecane*-5,7-*diol* **4b**:**3b**, b.p. 125°/1 mmHg (bath temp); (Found: C, 70.04, H, 12.85. Calc for $C_{11}H_{24}O_2$: C, 70.16, H, 12.85%); NMR (δ, $CDCl_3$) 0.72–1.83 (m, 21H), 3.51–4.05 (m, 2H + 0H); IR (neat) 3350 cm^{-1}. **4b**, m.p. 76–78° (recrystallized from hexane–benzene); (Found: C, 70.34, H, 13.15. Calc for $C_{11}H_{24}O_2$: C, 70.16, H, 12.85%); NMR (δ, $CDCl_3$) 0.72–1.83 (m, 21H), 2.41 (br s, 1H), 3.65–4.01 (m, 2H); IR (KBr disk) 3300 cm^{-1}.

meso-1,3-*Dicyclohexylpropane*-1,3-*diol* **3c** *and the* dl-*diol* **4c**: **3c**, m.p. 109–110° (recrystallized from benzene-hexane); (Found: C, 75.00, H, 11.84. Calc for $C_{15}H_{28}O_2$: C, 74.95, H, 11.74%): NMR (δ, $CDCl_3$) 1.03–2.04 (m, 24H), 3.51–3.72 (m, 4H); IR (KBr disk) 3410 cm^{-1}. **4c**, m.p. 148–150° (recrystallized from benzene-hexane); (Found: C, 74.96, H, 11.86. Calc for $C_{15}H_{28}O_2$: C, 74.95, H, 11.74%; NMR (δ, $CDCl_3$) 1.03–2.04 (m, 24H), 2.30 (s, 2H), 3.63 (m, 2H); IR (KBr disk) 3420 cm^{-1}.

Phenylboronic esters **3'b** *and* **4'b**; A mixture of **3b** and 1.1 equimolar amount of phenylboronic acid in CH_2Cl_2 was stirred overnight in the presence of molecular sieve. Molecular sieve was filtered off and the condensed filtrate was chromatographed on silica gel (hexane-EtOAc = 6:1) to afford the boronic ester (**3'b**). The *dl*-isomer (**4'b**) was also prepared according to the above procedure, and NMR spectra of these esters are mentioned in the text.

Cyclic acetals **3'c** *and* **4'c**; To a CH_2Cl_2 soln of *meso*-diol (**3c**) or *dl*-diol (**4c**) was added a CH_2Cl_2 soln of 1.1 equimolar amount of benzaldehyde and stirred overnight at room temp in the presence of molecular sieve. Chromatographic purification (hexane–ether = 3:1) gave the corresponding cyclic acetal (**3'c** or **4'c**, NMR; see in the text).

2-*Hydroxy*-7-*octen*-4-*one* **5**; To a THF (15 ml) soln of LDA prepared from diisopropylamine (1.14 g, 11 mmol) and BuLi (hexane soln 7.05 ml, 11 mmol) was added a THF soln (4 ml) of 5-hexen-2-one (0.99 g, 10 mmol) at −78° under an argon atmosphere. After stirring for 10 min, a THF (3 ml) soln of acetaldehyde (0.56 ml, 10 mmol) was added in one portion. The mixture was stirred for 20 min at −78° and quenched with sat NH_4Cl aq. The mixture was extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and condensed under reduced pressure. The residue was chromatographed on silica gel to give **5** in 71% yield (1.0 g). **5**, NMR (δ, $CDCl_3$) 1.10 (d, 3H), 2.13–2.72 (m, 6H), 3.62 (br s, 1H), 3.92–4.40 (m, 1H), 4.85–5.22 (m, 2H), 5.40–6.12 (m, 1H), IR (neat) 3450 cm^{-1}.

syn-7-*Octene*-2,4-*diol* **6** *and* anti-*isomer* **7**; The reduction of **5** was carried out as mentioned in the preparation of **3b**. Physical properties of **6** and **7** are as follows. **6**, b.p. 115/1.8 mmHg (oven temp); (Found: C, 75.00, H, 11.84. Calc for $C_8H_{16}O_2$: C, 74.95, H, 11.74%); NMR (δ, $CDCl_3$) 1.15 (d, J = 6 Hz, 3H), 1.31–1.82 (m, 4H), 1.92–2.33 (m, 2H), 3.27 (br s, 2H), 3.90 (m, 2H), 4.85–5.22 (m, 2H), 5.40–6.12 (m, 1H); IR (neat) 3365 cm^{-1}. **7**, oil; (Found: C, 74.96, H, 11.86. Calc for $C_8H_{16}O_2$: C, 74.95, H, 11.74%); NMR (δ, $CDCl_3$) 1.22 (d, J = 6 Hz, 3H), 1.41–1.83 (m, 4H), 1.92–2.40 (m, 2H), 3.30 (br s, 2H), 3.90 (br m, 2H), 4.85–5.22 (m, 2H), 5.40–6.12 (m, 1H); IR (neat) 3370 cm^{-1}. The relative configuration was determined by comparison with authentic samples by TLC analysis.[13]

Preparation of syn- *and* anti-α-*substituted*-β-*hydroxyketones* **8** *and* **11**: The *syn*- and *anti*-diastereomers (**8b** and **11b**) were prepared according to the lit.[14] The other hydroxyketones (**8a, c** and **11a, c**) was synthesized by aldol reaction of lithium enolates (**8b** and **11b** from 2-methylpentan-2-one and isobutyraldehyde; **8c** and **8b** from heptan-4-one and butyraldehyde) and the isomers were separated by column chromatography. The structure of the diastereomers (**8a, 11a**) and (**8b, 11b**) was determined by comparison of ^1H and ^{13}C NMR spectrum with those of lit.[14,15] The comparison of ^{13}C NMR spectrum of **8c** and **11c** suggested that the spectrum in which upfield shifts of C-6 (carbinol C) and methylene C of Et group were observed[15] corresponded to the *syn*-isomer (**8c**); ^{13}C NMR of **8c**, 71.601 ppm (>ÇHO–), 20.956 (–ÇH$_2$–CH$_3$); **11c**, 72.186 ppm (>ÇHO–), 22.286 (–ÇH$_2$–CH$_3$). *Reduction of* **8** and **11**; The reduction of these hydroxyketones (**8** and **11**) were carried out according to the preparation of **3b**, and the diastereomers were separated by column chromatography.

Compound **9a**; b.p. 140°/3 mmHg (oven temp), NMR (δ, $CDCl_3$) 0.81 (m, 15H), 1.75 (m, 3H), 3.22 (d, J = 9 Hz, 2H), 4.00 (br s, 2H). IR (KBr disk) 3330 cm^{-1}.

Compound **10a**; solid, NMR (δ, $CDCl_3$) 0.7–1.1 (m, 15H), 1.43–2.05 (m, 3H), 3.07 (d × d, J = 8, 3.6 Hz, 1H), 3.40 (d, J = 9 Hz, 1H), 3.68 (br s, 2H); IR (KBr disk) 3250 cm^{-1}.

Compound **12a**; solid, NMR (δ, $CDCl_3$) 0.72 (d, J = 6.4 Hz, 3H), 0.87 (t, J = 6.6 Hz, 12H), 1.77 (m, 2H), 3.32 (d × d, J = 8.6, 2.2 Hz, 2H), 4.70 (br s, 2H); IR (KBr disk) 3330 cm^{-1}.

Compound **9b**; oil, (Found: C, 80.19, H, 8.74. Calc for $C_{19}H_{24}O_2$: C, 80.24, H, 8.51%) NMR (δ, $CDCl_3$) 0.51–1.05 (m, 7H), 1.1–1.6 (m, 2H), 1.83 (m, 1H), 3.61 (br s, 2H), 4.95 (d, J = 2.5 Hz, 2H) 7.20 (br s, 10H); IR (neat) 3350 cm^{-1}.

Compound **10b**; m.p. 99–100° (recrystallized from hexane–ether); (Found: C, 80.04, H, 8.60. Calc for $C_{19}H_{24}O_2$: C, 80.24, H, 8.51%) NMR (δ, $CDCl_3$) 0.55–1.65 (m, 9H), 1.77 (br t, 1H), 4.07 (br s, 2H), 4.73 (br s, 2H), 7.05 (br s, 5H), 7.20 (br s, 5H); IR (KBr disk) 3300 cm^{-1}.

Compound **12b**; m.p. 88–90° (recrystallized from cyclohexane); (Found: C, 80.26, H, 8.51. Calc for $C_{19}H_{24}O_2$: C, 80.24, H, 8.51%); NMR (δ, $CDCl_3$) 0.54–2.20 (m, 10H), 3.95 (br s, 2H), 4.70 (d, J = 8 Hz, 2H), 7.19 (br s, 10H); IR (KBr disk) 3160 cm^{-1}.

Compound **9c**; b.p. 110°/0.2 mmHg (oven temp); (Found: C, 69.93, H, 12.97. Calc for $C_{11}H_{24}O_2$: C, 70.16, H, 12.85%; NMR (δ, $CDCl_3$) 0.82–2.00 (m, 20H), 3.26 (br s, 2H), 3.75 (br s, 1H), 3.83 (br s, 1H). IR (neat) 3350 cm^{-1}.

Compound **10c**; b.p. 150°/1 mmHg (oven temp); (Found: C 69.88, H, 12.80. Calc for $C_{11}H_{24}O_2$: C, 70.16, H, 12.85%); NMR (δ, $CDCl_3$) 0.81–1.19 (m, 20H), 3.30 (br s, 2H), 3.55–4.12 (m, 2H); IR (neat) 3340 cm^{-1}.

Dimethylsilylacetals of **9**, **10** *and* **12**; The benzene (2 ml) soln of a diol (0.27 mmol), pyridine (0.1 ml) and dimeth-

yldichlorosilane (0.8 mmol) was stirred for 1 hr at room temp under an argon atmosphere.[16] The mixture was condensed *in vacuo* and dry ether was added. The resulting ppt was filtered off, and filtrate was distilled by Kugelrohr to afford pure silyl acetals.

Silylacetals of **9a**, ^{13}C NMR ($CDCl_3$) 38.106 ppm ($-\underline{C}HMe_2$); **10a**, 32.156, 33.781 ppm; 12a, 38.656 ppm.

Silylacetals of **9b**, NMR (δ, $CDCl_3$) 5.53 (d, J = 1.8 Hz, 2H, carbinol methyne H); 10b, 5.22 (d × d, J = 2.5, 1.7 Hz, 2H); 12b, 5.00 (d, J = 10 Hz, 2H).

Silylacetals of **9c**, ^{13}C NMR ($CDCl_3$) 37.557 ppm ($\underline{C}H_2CH_2CH_3$); **10c**, 34.576, 37.336 ($\underline{C}H_2CH_2CH_3$).

Preparation of syn- *and* anti-5,6-O-*isopropylidene*-4,5,6-*trihydroxy*-1,1-*dimethoxyhexan*-2-*one* **13** *and* **14**; To a THF (15 ml) soln of diisopropylamine (0.86 g, 8.30 mmol) was added a hexane soln (4.8 ml, 7.6 mmol) at −78° under argon. After stirring for 20 min, a THF (6 ml) soln of methylglyoxal dimethylacetal (0.81 g, 6.92 mmol) was added and the mixture was stirred for 10 min. Then a THF (6 ml) soln of 2,3-O-isopropylidene-D-glyceraldehyde[17] was added dropwise and stirred at −78° for 20 min. The mixture was quenched with sat NH_4Cl aq and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and condensed *in vacuo*. The residue was purified by column chromatography on silica gel (hexane–acetone = 6:1) to give 4,5-*anti*-5,6-O-isopropylidene-4,5,6-trihydroxy-1, 1-dimethoxyhexan-2-one (**13**, 0.91 g, 53% yield) and the crude 4,5-*syn*-isomer (**14**, less polar than 13). The 4,5-*syn*-isomer was contaminated with small amount of by-product and the ratio of **13**:**14** was about 5:1 ~ 6:1. 13, NMR (δ, $CDCl_3$) 1.32 (s, 3H), 1.37 (s, 3H), 2.66–2.95 (m, 2H), 3.00 (br s, 1H), 3.40 (s, 6H), 3.83–4.20 (m, 4H), 4.43 (s, 1H); IR (neat) 3450, 1720 cm^{-1}; $[\alpha]_D^{25}$ −20.87° (*c* 1.61, $CHCl_3$).

Preparation of 2,4-syn-*diol* **15**; To a THF (0.5 ml) soln of triisobutylborane (0.186 ml, 0.81 mmol) was added a THF (3 ml) soln of **13** (155 mg, 0.62 mmol), and 1 ml of air was bubbled. The mixture was stirred for 2 hr at room temp, and cooled to −78°. $NaBH_4$ was then added and the mixture was stirred for 4 days at −78°. The mixture was quenched with pH 7 buffer (10 ml), 30% H_2O_2 and MeOH (5 ml), then followed by extraction with CH_2Cl_2. The extract was dried with Na_2SO_4 and condensed *in vacuo*. Purification by column chromatography on silica gel (hexane–acetone = 5:1) afforded 2,4-*syn*-diol (**15**, 135 mg, 86% yield) and 2,4-*anti*-diol (**16**, 6 mg, 4% yield). 15; oil; NMR (δ, CCl_4) 1.29 (s, 3H), 1.34 (s, 3H), 1.35–2.05 (m, 2H), 3.40 (s, 6H), 3.50–4.00 (m, 5H + 20H), 4.06 (d, J = 6 Hz, 1H); IR (neat) 3450 cm^{-1}; $[\alpha]_D^{25}$ +17.98° (*c* 1.357, $CHCl_3$).

3-*Deoxy*-D-*ribo*-*hexose* **17**; A soln of 2,4-*syn*-diol (**15**) in 0.5 N H_2SO_4 was heated at 50° for 5 hr, then acid was removed through the column packed with ion exchange resin (IRA-400, CO_2 form). The eluent was condensed to give pure **17**. **17**; m.p. 105° (from EtOH), NMR (δ, D_2O, $C_6H_9O_4NaO_2Si$ as an internal standard) the spectrum of anomeric proton appeared at δ 4.55 (d, J = 7.8 Hz, β-pyranose), 5.11 (d, J = 3.5, α-pyranose), 5.23 (br s, J = < 1, β-furanose), 5.30 (d, J = 3.9 Hz, α-furanose) was identical with the lit[18]; $[\alpha]_D^{20}$ +32.0° (*c* 2.47, H_2O) lit. $[\alpha]_D^{20}$ +31.8° (*c* 1.0, H_2O)[19].

Preparation of 2,4-anti-*diol* **16** *and* 3-*deoxy*-D-*arabino*-*hexose* **18**; To a toluene (1.2 ml) soln of aluminium triisopropoxide (0.51 mmol) was added a toluene (3 ml) soln of 4,5-*anti*-hydroxyketone (**13**, 126 mg, 0.51 mmol), and the mixture was stirred 1.5 days at 0° under argon. The mixture was quenched with water and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was chromatographed on silica gel (hexane–acetone = 5:1) afford 2,4-*anti*-diol (**16**, more polar, 79 mg, 62% yield) and 2,4-*syn*-diol (**15**, 18 mg, 15% yield). **16**; NMR (δ, CCl_4) 1.27 (s, 3H), 1.33 (s, 3H), 1.53 (t, J = 5 Hz, 2H), 3.00 (br s, 2H) 3.35 (s, 3H), 3.40 (s, 3H), 3.60–3.97 (m, 5H), 4.08 (d, J = 6 Hz, 1H); IR (neat) 3450 cm^{-1}; $[\alpha]_D^{25}$ −3.12° (c 1.855, $CHCl_3$). The acid treatment of **16** afforded **18**; **18**; $[\alpha]_D^{25}$ +46.0° (*c* 2.05, H_2O), lit $[\alpha]_D^{20}$ +46.8° (*c* 0.96, H_2O).[19]

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