Asymmetric Cyclopropanation Using New Chiral Auxiliaries Derived from D-Fructose

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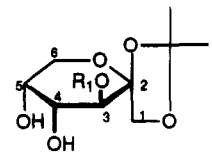
Acetals of α,β-unsaturated aldehydes with 3-O-alkylated derivatives of 1,2-*O*-isopropylidene-β-D-fructopyranose and 1,2-*O*-isopropylidene-β-D-psicopyranose, which are readily available from D-fructose, were cyclopropanated with Et_2Zn and CH_2I_2 with good diastereoselectivity. The effects of structure of the acetals on enantioselectivity were examined.

Introduction

The enantioselective methylenative cyclopropanation methods for prochiral alkenes are mainly classified into two categories: addition of a methylene group to a chiral alkene (*i.e.* alkenes with chiral auxiliaries)[1] and to an achiral alkene in the presence of chiral catalysts.[2] Although the latter method is highly appealing, its synthetic potential has not been fully developed to a synthetically useful level.

The chiral auxiliaries include oxazolidinones,[1a] oxazolidines,[1b] carbohydrates,[1c] phenylmenthyl alcohols,[1d] 1,4-di-*O*-benzyl-L-threitol,[1e] (*S,S*)-hydrobenzoin,[1f] and tartaric esters,[1g] etc. These reactions are carried out with the reagents prepared from Zn–Cu, Zn–Ag couple[1h] or Et_2Zn[1i] with CH_2X_2 (X = Br or I). Among the synthetic methods described, the most widely recognized methodology for the stereoselective generation of cyclopropanes are the Simmons–Smith reaction and its various modifications.[3]

Recent studies of asymmetric syntheses using carbohydrate derivative encouraged us to explore the possibility of the asymmetric Simmons–Smith reaction.[4] The design of a new chiral auxiliary for this reaction was based on the observation that oxygen atoms in a suitably substituted carbohydrate derivative proximal to the alkene could undergo prior coordination of the zinc atom by the reagent, which can direct the attack by the reagent.[5] In this paper, asymmetric cyclopropanation reactions of α,β-unsaturated carbonyl compound linked to new chiral auxiliaries, 3-*O*-alkylated derivatives of 1,2-*O*-isopropylidene-β-D-fructopyranose **1** and 1,2-*O*-isopropylidene-3-*O*-(*p*-phenylbenzyl)-β-D-psicopyranose **2**, which are readily available from D-fructose and reusable (*vide infra*), were attempted with the hope of stereoselective delivery of the reagent to only one side of the double bond.



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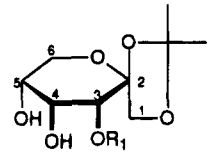

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Results and Discussion

Synthesis of Chiral Auxiliaries. The starting material 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**4**) was readily prepared from D-fructose (**3**) in acetone.[6] Alkylation of **4** with an excess of various alkyl halides, followed by treatment of the resulting mixture with 80% aqueous acetic acid at room temperature, gave 3-*O*-alkyl-protected diol **6** in good yield as shown in Scheme 1. The results with various alkyl halides are summarized in Table 1.

Also, its C-3 epimer **17** was prepared as described in Scheme 2. Oxidation of the alcohol **4** with pyridinium chlorochromate[7] gave the corresponding ketone in 65% yield. Subsequent reduction with $LiAlH_4$ at −78 °C provided the epimeric alcohol **16** {$[\alpha]_D$ −110.9° (*c* 0.24, acetone)} in 93% yield, O-alkylation of which with

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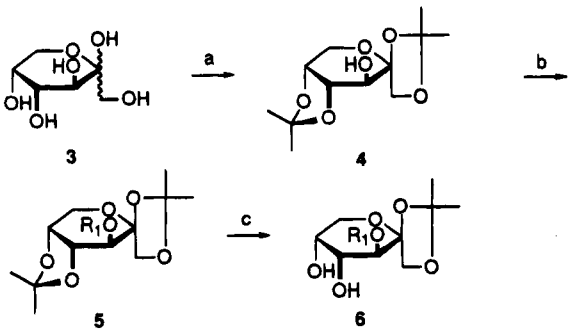
Scheme 1[a]



[a] Key: (a) 0.5% H_2SO_4/acetone, 2 h, rt, 45%; (b) NaH, R_1X, DMF, 1 h, rt; (c) 80% aqueous AcOH, 12 h, rt (or 3–4 h, 60 °C).

p-phenylbenzyl chloride followed by deacetalization with 80% aqueous acetic acid produced the diol **17** {$[\alpha]_D$ −80.9° (*c* 0.216, acetone)} in 79% yield for the two steps.

Synthesis of Aldehydes. Various *trans* aldehydes were synthesized as shown in Scheme 3. And the diethyl acetals were prepared from the corresponding enals by reaction with triethyl orthoformate in the presence of a catalytic amount of ammonium nitrate in ethanol.[8]

Synthesis of Chiral Acetal Derivatives. The acetal derivatives of β-D-fructopyranose (**27A** and **27B**) were obtained by transacetalization of the diethyl acetals of *trans* enals with the diol **6** in the presence of pyridinium tosylate as shown in Scheme 4.

Interestingly, the *endo* isomer **27A** was a major product in all cases, with the ratios of **27A** to **27B** being 1.1:1 to 1.8:1 as shown in Table 2. Fortunately, the mixture of **27A** and **27B** were easily separated by flash chromatography.

The relative configurations in the structure of the acetal **27** (*i.e.* **A** or **B**) were established by NOE experiments.[9] For example, in the case of the cinnamylidene-*O*-benzyl derivative **28**, the H_7 proton in the *endo* isomer (**A**) showed 2% NOE enhancement upon irradiation of the proton H_4, while no such effect was seen between the two protons in the *exo* isomer (**B**). Furthermore, upon irradiation of the proton H_7 in the *endo* (**A**) and *exo* (**B**) isomers of the acetal **28**, respectively, NOE enhancement for H_3 was detected only in the *exo* isomer (**B**) (Figure 1). These experiments unequivocally revealed that H_7 and H_4 in the *endo* isomer (**A**) and H_7 and H_3 in the *exo* isomer (**B**) were in close proximity, as depicted in Figure 1. The same analysis could be applied to the acetal **37** (Figure 1). Additionally, force field calculations have shown the most plausible conformation, which is consistent with these NMR data, as the one in which the *endo* acetal isomers adopt a chair conformation with the β-stryryl group stretching away from the concave space (Figure 1). More importantly, the β-styryl group in the *endo* acetal is approximately π-stacked with the *O*-benzyl group (R_1 in the structure of **27A**) in the conformer at the global minimum, while the two groups in the global minimum conformer of the *exo* acetal are quite independent of each other, which has some implication in why the *endo* acetals gave higher enantioselectivity than the *exo* acetals as we shall see later.

The acetal derivatives of β-D-psicopyranose (**41A** and **41B**) were prepared by the method shown in Scheme 5.

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After this reaction, the approximately 1:1 mixture of the *endo* and *exo* isomers was readily separated by flash chromatography {**41A**, $[\alpha]_D$ −160.6° (*c* 0.127, acetone); **41B**, $[\alpha]_D$ −60.0° (*c* 0.22, acetone)}. The stereochemistry of the acetal moiety in **41A** and **41B** was again confirmed by NOE measurements (Figure 2). Especially, upon irradiation of H_4 in each case, only the *endo* isomer **41A** showed NOE enhancement at H_7 by 7.1%. Supportive to this conclusion was the molecular modeling study, in which the global minimum structures of the pyranose moiety adopt boat conformations in which the severe 1,2-interaction of the *p*-phenylbenzyloxy group with the adjacent 1,3-dioxolane ring is more or less minimized by the ring deformation and placing the *p*-phenylbenzyl unit completely away from the sugar ring (Figure 2).

As shown in Scheme 6, the acetal derivatives of *cis* aldehydes with β-D-fructopyranose **43** were obtained by Lindlar reduction of the corresponding acetylenic aldehyde acetals with β-D-fructopyranose, which were prepared by treatment of the diol **6** with the diethyl acetals of the corresponding acetylenic aldehyde in the presence of pyridinium tosylate. The results are summarized in Table 3.

The *endo* nature of the acetal **45** was confirmed by 1.8% NOE enhancement of H_7 on irradiation of H_4 (Figure 3).

Cyclopropanation. Various conditions for cyclopropanation of *trans*-cinnamylidene-*O*-benzyl-β-D-fructopyranose (**28A**) as a model substrate using Et_2Zn/CH_2I_2 were examined in the Simmons–Smith type reaction (Scheme 7). The corresponding chloromethyl zinc reagent, which is known to afford a higher yield than the iodomethyl zinc analog because of better stability,[10] gave lower yields of cyclopropanation although it gave almost the same enantioselectivity. A samarium-based cyclopropanation[12] as an alternative was not successful (Table 4). For cyclopropanation, a 2:1 stoichiometry of diiodomethane to Et_2Zn was used throughout this study unless stated otherwise. This was followed by hydrolysis of the chiral auxiliary, which could be recovered in high yield without loss of chirality, and subsequent reduction of the aldehyde functionality to give cyclopropanemethanol, of which ee and absolute configurations were determined. The results are summarized in Table 4.

For cyclopropanation, 1,2-dichloroethane and toluene were found to be superior solvents for this reaction. The cyclopropanation in toluene or 1,2-dichloroethane gave similar results in terms of enantioselectivity. A cosolvent system (e.g., toluene–hexane or 1,2-dichloroethane–hexane) gave almost the same enantioselectivity but with lower yields. The failure of hexane to act as an efficient medium for cyclopropanation was apparently due to the insolubility of the starting material. In contrast, ethereal solvent (e.g., THF) was undesirable, since the rate of reaction dramatically decreased.

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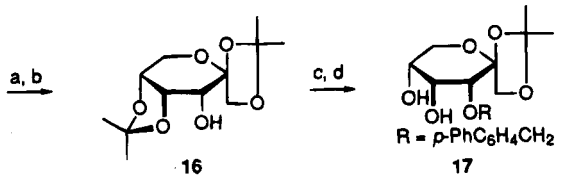
Table 1. Preparation of 1,2-*O*-Isopropylidene-3-*O*-alkyl-β-D-fructopyranose 6 from 4

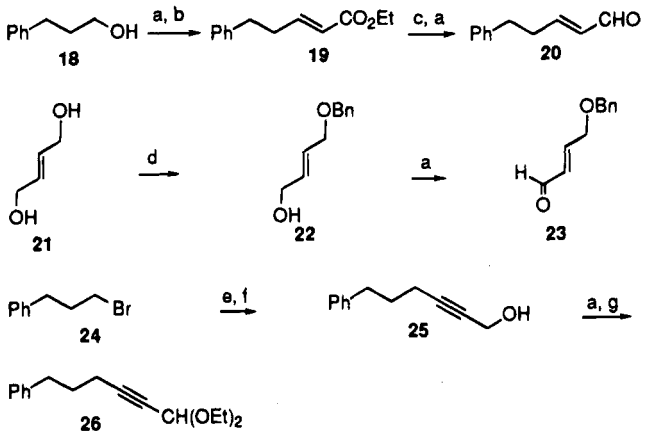
entry	R_1X	product (6, R_1)		yield(%)	$[\alpha]_D$
1	BnBr	Bn	**7**	89	−115.1° (*c* 1.52, $CHCl_3$)
2	CH_3I	CH_3	**8**	87	−96.2° (*c* 1.54, $CDCl_3$)
3	*o*-$MeC_6H_4CH_2Br$	*o*-$MeC_6H_4CH_2$	**9**	86	−79.5° (*c* 0.146, acetone)
4	*m*-$MeC_6H_4CH_2Br$	*m*-$MeC_6H_4CH_2$	**10**	88	−116.5° (*c* 0.103, acetone)
5	*p*-$MeC_6H_4CH_2Br$	*p*-$MeC_6H_4CH_2$	**11**	91	
6	*p*-$MeOC_6H_4CH_2Cl$	*p*-$MeOC_6H_4CH_2$	**12**	85	
7	*p*-*t*-$BuC_6H_4CH_2Br$	*p*-*t*-$BuC_6H_4CH_2$	**13**	93	−86.9° (*c* 0.107, acetone)
8	*p*-$PhC_6H_4CH_2Cl$	*p*-$PhC_6H_4CH_2$	**14**	85	−100° (*c* 0.143, acetone)
9	2-$NpCH_2Br$	2-$NpCH_2$	**15**	91	−94.4° (*c* 0.108, acetone)

Scheme 2[a]



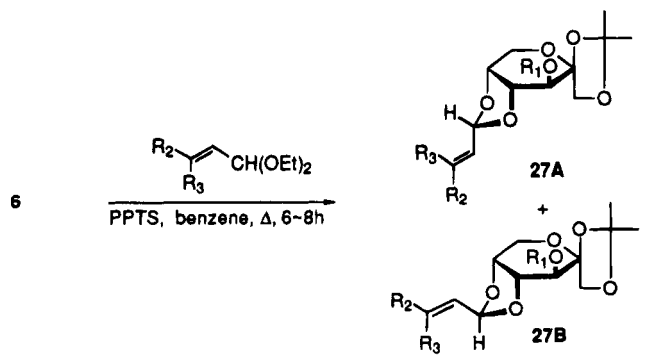
[a] Key: (a) PCC, CH_2Cl_2, 3 h, 65%; (b) $LiAlH_4$, THF, −78 °C, 1 h, 93%; (c) NaH, DMF, *p*-$PhC_6H_4CH_2Cl$, rt, 1 h; (d) 80% aqueous AcOH, rt, 12 h, 79%.

Scheme 3[a]



[a] Key: (a) PCC, CH_2Cl_2, rt, 80−85%; (b) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2, 1 h, 89%; (c) DIBAL, benzene, rt, 12 h, 81%; (d) NaH, BnBr, DMF, rt, 1 h, 38%; (e) $LiC{\equiv}CCH_2OTBDPS$, HMPA, −78 °C, rt, 5 h, 80%; (f) *n*-Bu_4NF, THF, rt, 1 h, 89%; (g) $HC(OEt)_3$, NH_4NO_3, EtOH, rt, 12 h.

Scheme 4



Lowering the reaction temperature dramatically enhanced the enantioselectivity in these reactions. Especially, the enantioselectivity improved to 90% in toluene at −15 °C. The enantiomeric excess of this reaction in 1,2-dichloroethane at −20 °C was 12% higher than at 0 °C in the same solvent, but at a sacrifice to the yield. Also, the reaction time affected the enantioselectivity: The shorter reaction time yielded higher enantioselectivity but resulted in lower yields as shown in Table 4. There may be some incompatibility of the starting materials with the reagent system. The direct evidence for this will be elaborated later.

Secondly, the face-blocking effect of R_1 in the chiral sugar moiety was examined (Scheme 8, Table 5): The alkyl group on the sugar moiety (R_1) dramatically affected enantioselectivity in these reactions: The size of R_1 was proportional to enantioselectivity (R_1 = Me ≪ Bn < *p*-$MeC_6H_4CH_2$ < *p*-$PhC_6H_4CH_2$). However, the alkyl substituents (X) on the phenyl ring of R_1 had virtually no effect on enantioselectivity with the order of *p*-$PhC_6H_4CH_2$ > Bn ≅ *m*-$MeC_6H_4CH_2$ > *o*-$MeC_6H_4CH_2$ ≅ *p*-*t*-$BuC_6H_4CH_2$ > 2-$NpCH_2$. This could be attributed to the steric repulsion between the bulky alkyl groups on the phenyl ring of the sugar moiety and the 5-membered acetal moiety. Consequently, the phenyl ring with the substituent X lies far from the oxygen atoms of the acetal moiety, minimizing the blocking chance of the benzyl group against either diastereotopic face of the double bond.

However, there is still the possibility that prior coordination of the reagent to the ethereal oxygen atom, especially the acetal oxygen atoms, precedes the cyclopropanation. Thus, as the size of the substituent X on the phenyl ring becomes larger, the possibility in which the Simmons−Smith reagent indiscriminately coordinates all of the acetal oxygen atoms increases, which would cause lower enantioselectivity. This is supported by the case of 3-*O*-(*p*-methoxybenzyl)-substituted auxiliary **33A**, with which the enantioselectivity was worse than expected, presumably due to the oxophilicity of the zinc reagent toward the methoxy oxygen. In other words, since the methoxy oxygen of the phenyl group would coordinate with the Simmons−Smith reagent, it would allow for transfer of the incipient carbenoid to either side of the double bond.

The fact that the enantioselectivity was higher in the case of *p*-phenylbenzyl-substituted derivatives **35A** can be attributed to π-stacking between the double bond and the phenyl group, as mentioned before. In other words, since one face was more efficiently blocked than other one, the facial selectivity increased (Scheme 8, Table 5).

As shown Scheme 9, with the *p*-phenylbenzyl group in the chiral auxiliary fixed, attention was focused on the general applicability of the reaction by varying the enals, *i.e.* the substituent (R_2) on the olefin, to determine the scope of the reaction as shown Table 6.

While almost the same high enantioselectivity was obtained when R_2 was phenyl or β-phenethyl, the enantioselectivity dramatically decreased in the case when R_2 was a benzyloxy group. This may be due to the oxophilicity of zinc atom toward the oxygen atom of the benzyloxy moiety via chelation, as mentioned before.

Table 2. Preparation of the Acetals of *Trans* Enal 27 from 3-*O*-Alkyl-β-D-fructopyranose 6

products						[α]D in acetone	
R_1	R_2	R_3	no.	*endo*:*exo*	yield (%)[a]	*endo* (**A**)	*exo* (**B**)
Bn	Ph	H	**28**	1.8:1	90	−126.7° (*c* 0.105)	−65.9° (*c* 0.135)
CH_3	Ph	H	**29**	1.6:1	49[b]	−85.1° (*c* 0.047)	
o-$MeC_6H_4CH_2$	Ph	H	**30**	1.5:1	89	−112.7° (*c* 0.118)	−47.9° (*c* 0.192)
m-$MeC_6H_4CH_2$	Ph	H	**31**	1.5:1	93	−123.8° (*c* 0.084)	−49.5° (*c* 0.2)
p-$MeC_6H_4CH_2$	Ph	H	**32**	1.4:1	87	−132.0° (*c* 0.05)	−54.7° (*c* 0.137)
p-$MeOC_6H_4CH_2$	Ph	H	**33**	1.6:1	88	−119.2° (*c* 0.052)	−50.0° (*c* 0.112)
p-*t*-$BuC_6H_4CH_2$	Ph	H	**34**	1.2:1	90	−112.4° (*c* 0.121)	−54.4° (*c* 0.103)
p-$PhC_6H_4CH_2$	Ph	H	**35**	1.5:1	90	−128.6° (*c* 0.091)	−56.9° (*c* 0.065)
2-$NpCH_2$	Ph	H	**36**	1.4:1	88	−141.2° (*c* 0.102)	−60.0° (*c* 0.1)
p-$PhC_6H_4CH_2$	$PhCH_2CH_2$	H	**37**	1.5:1	88	−54.2° (*c* 0.059)	−38.5° (*c* 0.039)
p-$PhC_6H_4CH_2$	$BnOCH_2$	H	**38**	1.1:1	90	−94.5° (*c* 0.055)	−69.8° (*c* 0.263)
p-$PhC_6H_4CH_2$	CH_3	CH_3	**39**	1.7:1	80	−82.2° (*c* 0.107)	−99.7° (*c* 0.305)
p-$PhC_6H_4CH_2$	*n*-C_5H_{11}	H	**40**	1.4:1	87	−87.4° (*c* 0.154)	−76.9° (*c* 0.09)

[a] The combined yield of *endo* and *exo* isomers. [b] The yield of *endo* isomer only.

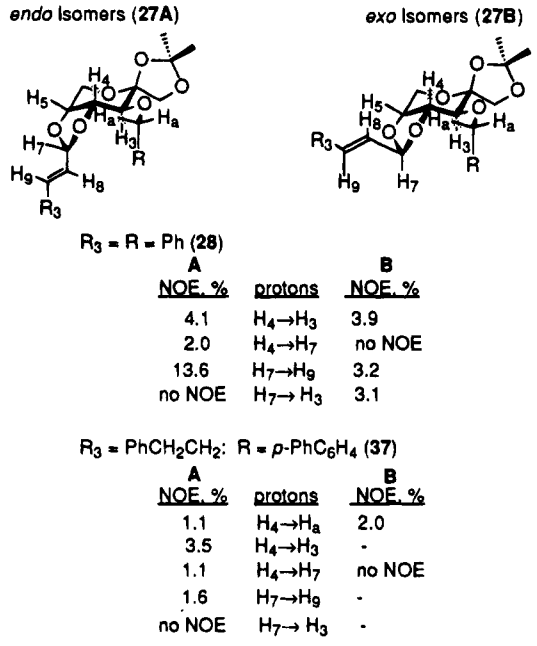


Figure 1.

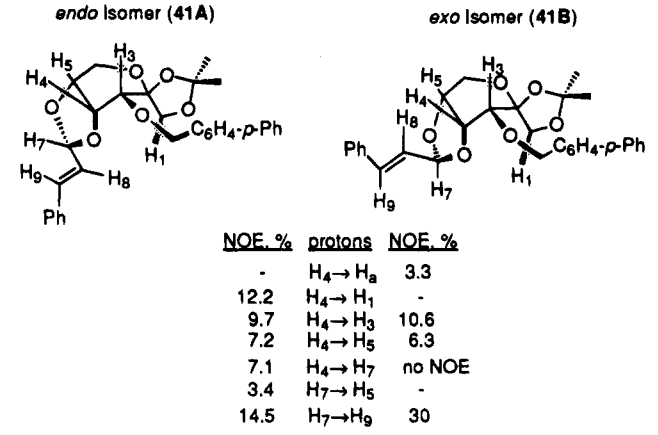
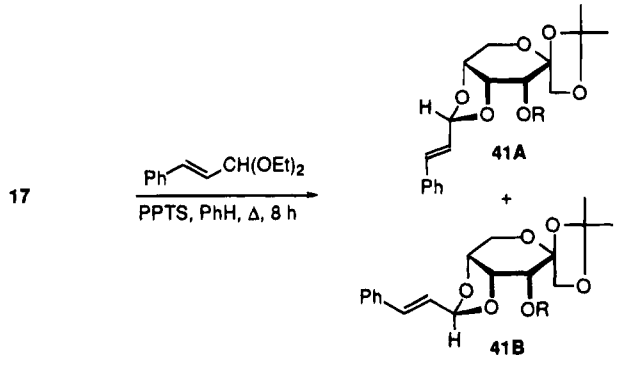


Figure 2.

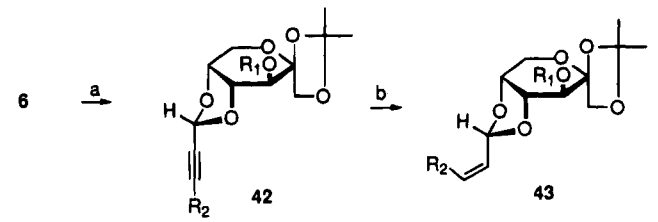
Scheme 5



Next, the reaction with the *exo* acetal isomers was examined (Scheme 10). In these cases, the blocking group (R_1) cannot effectively block either side of the double bond in contrast to the *endo* isomers. Consequently, the enantiomeric excess was lower than that in the case of the *endo* forms as expected, which is shown in Table 7.

Next, this Simmons–Smith reaction was applied to the *cis*-cinnamaldehyde *endo* acetal derivative (Scheme 11, Table 8). The cyclopropanation reaction of **43** (R_2 = Ph) with diethylzinc and diiodomethane at 0 °C surprisingly

Scheme 6[a]

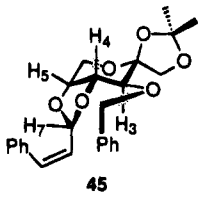


[a] Key: (a) $R_2C{\equiv}CCH(OEt)_2$, PPTS, benzene, Δ, 8 h; (b) Lindlar cat., H_2, MeOH.

gave a 2:1 mixture of an *endo* acetal of *cis*-cyclopropanecarboxaldehyde (**56**) and also an *exo* acetal of *trans*-cyclopropanecarboxaldehyde (**57**) (R_2 = Ph) in 96% yield. The ratio of products was determined from the integration of the benzylic methine protons (on the 3-membered rings) in ^1H NMR after isolation [*cis* δ 2.35 (m), *trans* δ 2.10 (m)]. Treatment of the mixture with 80% aqueous acetic acid gave a 2:1 mixture of *cis*- and *trans*-2-phenylcyclopropanecarboxaldehydes in 93% yield. Further reaction of the resulting mixture with sodium cyanide, manganese dioxide, acetic acid, and methanol at room temperature afforded (1*R*,2*S*)-methyl *cis*-2-phenylcyclopropanecarboxylate (55% yield) {$[\alpha]_D$ −29.7° (*c* 0.175, $CHCl_3$); lit.[13] *ent*-form $[\alpha]_D$ +32.8° (*c* 1.99, $CHCl_3$)} and (1*S*,2*S*)-methyl *trans*-2-phenylcyclopropanecarboxylate (28% yield) {$[\alpha]_D$ +173° (*c* 0.185, $CHCl_3$); lit.[13] $[\alpha]_D$ +324.7° (*c* 1.24, $CHCl_3$)} after flash chromatography. The absolute configuration of the esters was determined by the comparison of its specific rotation with a literature value.[13] The enantiomeric excess was determined after conversion of the esters with diisobutyl-

Table 3. Preparation of Acetals of *Cis* Enal 43 from 3-*O*-Alkyl-β-D-fructopyranose 6

R_1 in **6**	R_2 in acetal	product, **42** (yield, %)	product, **43** (yield, %)	product, **43** optical rotation
Bn	Ph	**44** (84)	**45** (82)	$[\alpha]_D$ −14.5° (*c* 0.069, acetone)
p-$PhC_6H_4CH_2$	$PhCH_2CH_2CH_2$	**46** (70)	**47** (79)	$[\alpha]_D$ −53.2° (*c* 0.062, acetone)

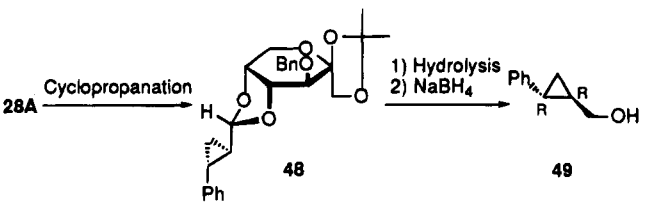


protons	NOE, %
$H_4 \rightarrow H_3$	4.1
$H_4 \rightarrow H_7$	1.8

45

Figure 3.

Scheme 7



aluminum hydride to (1*R*,2*S*)-*cis*- and (1*S*,2*S*)-*trans*-1-(hydroxymethyl)-2-phenylcyclopropane, respectively.

Since no isomerization was observed during the hydrolysis of the chiral auxiliary under various acidic conditions, the isomerization should only occur during cyclopropanation, during which period the coordinated starting material with Simmons–Smith reagent could isomerize via generation of an allylic cation which is further stabilized via resonance through the phenyl group. This is supported by the fact that the *cis*-cyclopropylfructopyranose **43** (R_2 = $PhCH_2CH_2CH_2$), which has no phenyl moiety at the allylic position, did not produce an isomerized product.

On the other hand, the *endo* and *exo* isomers of psicopyranose derivatives **41** (Scheme 12) gave lower enantiomeric excesses than those of the fructopyranose derivatives as shown in Table 9, which can be attributed to a reduced blocking effect of the *p*-phenylbenzyl group in the case of psicopyranose derivatives in contrast to fructopyranose derivatives (*vide supra*).

Conclusion. Among various isomeric compounds, the asymmetric cyclopropanation reaction provided good enantioselectivity (consistent attack on the same face) with high chemical yields especially with *endo* acetals of 1,2-*O*-isopropylidene-3-*O*-(*p*-phenylbenzyl)-β-D-fructopyranose. However, the observed diastereoselectivity was not perfect. One of the reasons for this may be the tendency of the *endo* acetals, which gave better diastereoselectivity, to isomerize to the less suitable *exo* acetals during the cyclopropanation. For example, the *trans-endo* acetal **35A** was cyclopropanated under standard conditions. Analysis of the resulting crude reaction mixture by NMR revealed it to be a diastereomeric mixture, which could be carefully separated into two fractions, each containing *endo* and *exo* acetals of cyclopropanated (*R*,*R*)-aldehydes, **51** and **65**, in an approximately 13:1 ratio (Scheme 13). The diastereomeric excess of the *endo* acetals was found to be 76% as judged from the NMR of the diastereomeric *endo* acetal mixture [δ 3.90 (d, *J* = 8.42 Hz) (minor) and δ 3.83 (d, *J* = 8.40 Hz) (major)]. This was further confirmed by the HPLC analysis of the (1*R*,2*R*)-*trans*-1-(hydroxymethyl)-2-phenylcyclopropane (**49**) (77% ee) obtained after hydrolysis of chiral auxiliary and subsequent reduction of the diastereomeric *endo* acetal mixture. However, the diastereomeric *exo* acetal mixture could neither be separated by HPLC analysis nor gave any discernible peak difference in NMR. Thus, direct hydrolysis of chiral auxiliary and subsequent reduction gave again (1*R*,2*R*)-*trans*-1-(hydroxymethyl)-2-phenylcyclopropane (**49**) only in 24% ee (HPLC) (Scheme 13). One important implication here is that although the amount of isomerization was small (*ca.* 7%), the *endo*-to-*exo* isomerization seemed to occur mainly after the cyclopropanation since the pure exo acetals **28B**, **37B**, and **40B** gave (1*S*,2*S*)-*trans*-1-(hydroxymethyl)-2-aryl(or alkyl)cyclopropane in 33–54% ee's.

Experimental Section

General. Nuclear magnetic resonance spectra were recorded on 200 and 300 MHz spectrometers. Chemical shifts are reported as δ values in parts per million (ppm) from tetramethylsilane (δ = 0) and reported as follows: chemical shifts, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad peaks), coupling constant, and integration or identified proton. Carbon-13 chemical shifts are reported in parts per million (ppm) from the center line of the chloroform-*d* triplet (77.0 ppm). Mass spectra were taken with an electron beam energy of 70 eV (EI) unless otherwise stated.

Chiral columns for gas chromatographic analyses were Chiraldex B-TA (30 m × 0.25 mm) and G-TA (30 m × 0.25 mm). Chiral HPLC columns used were Chiralcel OJ and OD. Melting points were uncorrected. Thin layer chromatographic analyses were performed on precoated the plates (silica gel 60 GF254, 0.25 mm thickness). For flash column chromatography was used silica gel Kieselgel 60. When necessary, solvents and reagents were dried prior to use as follows: tetrahydrofuran was distilled from sodium benzophenone ketyl; hexane, benzene, and toluene were distilled from calcium hydride. Unless otherwise stated, the reagents were purchased and used without further purification.

Molecular Modeling. Energy minimization of compounds was carried out on a SG Iris Crimson workstation using Discover software. Energy minimization with the CVFF force field was carried out until the change in energy was less than 0.001 kcal/mol between two successive iterations. Molecular dynamics simulations were performed by the method provided by Discover. To perform conformational searching to find the global minimum, dynamics annealing runs are employed. Thus, the structure was heated to 900 K and gradually cooled down to 300 K, and then the molecule was allowed to equilibrate for 5 ps. A dynamics simulation of 10 ps was performed using a time step of 1 fs. The conformations were sampled from the collection of all conformers during the course of simulation and were minimized.

Preparation of 1,2:4,5-Di-*O*-isopropylidene-β-D-fructopyranose (4). To a suspension of D-fructose (**3**, 30 g, 166.5 mmol) and acetone (600 mL) was added concd H_2SO_4 (2.916 mL). The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was cooled to 0 °C, and the reaction was quenched with NaOH (9.3 g) in H_2O (84 mL). After evaporation of the acetone, the residue was extracted with CH_2Cl_2. The organic phase was separated and washed with water and brine and then dried over $MgSO_4$. After filtration and removal of solvents under reduced pressure, the

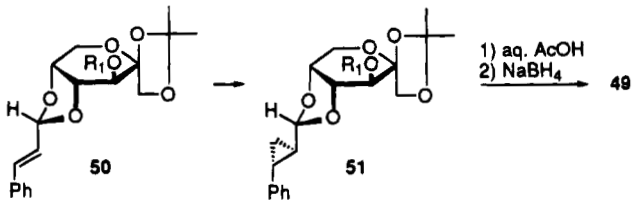
(13) Krieger, P. E.; Langrebe, J. A. *J. Org. Chem.* **1978**, *43*, 4447.

Table 4. Optimization of Cyclopropanation of Acetal of *trans*-Cinnamaldehyde 28A

cyclopropanation[a]			hydrolysis[c]		reduction[d]	
solvent	temp, °C (time, h)	yield[b] (%)	reagent	yield[b] (%)	yield[b] (%)	ee[e] (%)
hexane	−78 → 0 (20)	trace				
toluene	−40 → 0 (3)	33[f]	*p*-TsOH, aqueous EtOH	82	93	88
toluene	−40 → 0 (20)	72	80% aqueous AcOH		91[g]	75
toluene	−78 → 0 (48)	81	80% aqueous AcOH		80[g]	72
toluene[h]	−78 → −30 (24) → −15 (24)	50[f]	80% aqueous AcOH		86[g]	90
$(ClCH_2)_2$	−20 → 0 (3)	61[f]	*p*-TsOH, aqueous EtOH	81	90	82
$(ClCH_2)_2$	−20 → 0 (24)	85	80% aqueous AcOH		88[g]	71[i]
$(ClCH_2)_2$[h]	−30 → −20 (48)	54[f]	80% aqueous AcOH		86[g]	83
THF	−78 → 0 (24)	trace				
Tol:hex[j]	0 (65)	50[f]	80% aqueous AcOH		60[g]	76
$(ClCH_2)_2$:hex[k]	0 (42)	72[f]	80% aqueous AcOH		58[g]	74
$(ClCH_2)_2$[l]	0 (48)	23[f]	80% aqueous AcOH		62[g]	70
THF[m]	−78 → 0 (24)	trace				

[a] $Et_2Zn:CH_2I_2$ = 5 mmol:10 mmol unless noted otherwise. [b] Isolated yield by column chromatography unless noted otherwise. [c] The reaction time for hydrolysis of chiral auxiliary was 15 min with 80% AcOH/H_2O at 60 °C. Under this condition, the chiral auxiliary could be recovered in high yield without loss of chirality. [d] The reaction time of reduction was 1 h with $NaBH_4$ at room temperature. [e] The enantiomeric excess was based on HPLC analysis. (Daicel OJ, 10% *i*-PrOH in hexane). The absolute configuration (1*R*,2*R*) of *trans*-1-(hydroxymethyl)-2-phenylcyclopropane was determined by the reported specific rotation. Lit.[11] $[\alpha]^{24}_D$ −46.6° (*c* 2.64, EtOH as 51.3% ee). [f] The yields were based on ^1H NMR. [g] Yield for two steps (hydrolysis−reduction). [h] $Et_2Zn:CH_2I_2$ = 10 mmol:20 mmol. [i] $[\alpha]_D$ −64.7° (*c* 0.19, EtOH). [j] Toluene:hexane = 1:2. [k] 1,2-Dichloroethane:hexane = 1:2. [l] $Et_2Zn:ClCH_2I$ = 5 mmol:10 mmol. [m] Reaction with $Sm-CH_2I_2$.

Scheme 8



residue was recrystallized with ether/hexanes to afford the alcohol **4** (19.6 g, 45%) as a white solid: $[\alpha]^{28}_D$ −156.6° (*c* 1.00, acetone); mp 117.5−118 °C; ^1H NMR ($CDCl_3$) δ 1.37 (s, 3 H), 1.44 (s, 3 H), 1.51 (s, 3 H), 1.53 (s, 3 H), 2.29 (d, *J* = 8.25 Hz, 1H), 3.66 (dd, *J* = 6.74 Hz, *J* = 8.18 Hz, 1H), 3.93−4.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) 25.90, 26.23, 26.37, 27.90, 60.69, 70.34, 72.26, 73.29, 77.25, 104.49, 109.36, 111.80; IR 3460 cm^{-1}; MS (EI) *m/e* (relative intensity) 260 (M^+, 2), 245 (34), 144 (25), 127 (20), 117 (74), 100 (33), 85 (50), 59 (87), 43 (100). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.70; H, 7.84.

Preparation of 3-*O*-Benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (7). To a solution of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**4**, 4.0 g, 15.4 mmol) in DMF (23 mL) was added 60% sodium hydride (0.7 g, 17.5 mmol) at room temperature. After the solution was stirred for 0.5 h, benzyl bromide (1.92 mL, 16.2 mmol) was added to the above solution. The reaction mixture was stirred for 1 h at room temperature, diluted with water, and then extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:20 ethyl acetate−toluene to give 3-*O*-benzyl-1,2;4,5-di-*O*-isopropylidene-β-D-fructopyranose (**5**, 5.33 g, 99%) as a white oil: $[\alpha]^{22.5}_D$ −89.6° (*c* 2.22, $CHCl_3$); syrup; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3 H), 1.41 (s, 3 H), 1.50 (s, 3 H), 1.53 (s, 3 H), 3.50 (d, *J* = 7 Hz, 1 H), 3.87 (d, *J* = 8.5 Hz, 1 H), 3.99 (dd, *J* = 0.8 Hz, *J* = 13 Hz, 1 H), 4.08 (d, *J* = 8.5 Hz, 1 H), 4.14 (dd, *J* = 2.7 Hz, *J* = 13 Hz, 1 H), 4.22 (ddd, *J* = 5.5 Hz, *J* = 2.7 Hz, *J* = 0.8 Hz, 1 H), 4.38 (dd, *J* = 5.5 Hz, *J* = 7.0 Hz, 1 H), 4.66 (d, *J* = 12 Hz, 1 H), 4.97 (d, *J* = 12 Hz, 1 H), 7.29−7.40 (m, 5 H). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 65.37; H, 7.47.

A solution of the benzyl ether **5** (1.04 g, 2.97 mmol) in 80% acetic acid in H_2O (10 mL) was stirred overnight at room temperature. After evaporation of solvent, the residue was purified by flash chromatography on silica gel with 1:2 acetone−hexane to give the benzyl ether diol **7** (827 mg, 90%) as a white solid. As an alternative, the crude benzyl ether could be directly hydrolyzed with 80% acetic acid in H_2O to give the same product without lowering the yield: $[\alpha]_D$ −115.1° (*c* 1.52, chloroform); mp 99-101 °C; ^1H NMR ($CDCl_3$ + D_2O) δ 1.42 (s, 3 H), 1.48 (s, 3 H), 3.67 (d, *J* = 9.5 Hz, 1 H), 3.74 (dd, *J* = 1.5 Hz, *J* = 11.5 Hz, 1 H), 3.90−4.08 (m, 5 H), 4.71 (d, *J* = 11.5 Hz, 1 H), 4.82 (d, *J* = 11.5 Hz, 1 H), 7.3−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) 26.15, 26.81, 63.55, 69.69, 71.30, 71.82, 75.33, 76.52, 105.56, 111.95, 127.94, 128.09, 128.65; IR 3422 cm^{-1}; MS (CI) *m/e* (relative intensity) 311 (M + 1), 163 (10), 117 (18), 103 (40), 91 (100), 59 (33). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.14. Found: C, 62.12; H, 7.15.

Using the above reaction protocol, the compounds listed below were prepared.

1,2-*O*-Isopropylidene-3-*O*-methyl-β-D-fructopyranose (8): 87% as an oily solid; $[\alpha]_D$ −96.2° (*c* 1.52, $CDCl_3$); ^1H NMR ($CDCl_3$) δ 1.39 (s, 3 H), 1.46 (s, 3 H), 2.5 (b, 2 H), 3.39 (dm, *J* = 9.39 Hz, 1 H), 3.59 (s, 3 H), 3.73 (dd, *J* = 1.27 Hz, *J* = 12.7 Hz, 1 H), 3.89−4.01 (m, 3 H), 3.99 (d, *J* = 8.62 Hz, 1 H), 4.06 (d, *J* = 8.62 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 26.04, 26.78, 61.40, 63.59, 69.67, 71.23, 71.84, 78.3, 105.59; IR 3408 cm^{-1}; MS (CI) *m/e* (relative intensity) 235 (M + 1, 3), 217 (50), 177 (92), 159 (52), 145 (49), 127 (100), 99 (27), 74 (21). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.28; H, 7.74. Found: C, 50.99; H, 7.65.

1,2-*O*-Isopropylidene-3-*O*-(*o*-methylbenzyl)-β-D-fructopyranose (9): 86% as a white solid; $[\alpha]_D$ −79.5° (*c* 0.146, acetone); mp 92.9 °C; ^1H NMR ($CDCl_3$) δ 1.40 (s, 3 H), 1.46 (s, 3 H), 2.35 (s, 3 H), 3.68 (d, *J* = 9.29 Hz, 1 H), 3.74 (dd, *J* = 1.67 Hz, *J* = 12.84 Hz, 1 H), 3.89 (s, 2 H), 3.90−3.98 (m, 3 H), 4.70 (d, *J* = 11.77 Hz, 1 H), 4.82 (d, *J* = 11.77 Hz, 1 H), 7.17−7.33 (m, 4 H); ^{13}C NMR ($CDCl_3$) 18.84, 26.21, 26.76, 63.58, 69.77, 71.51, 71.90, 73.40, 76.44, 105.59, 111.90, 126.04, 128.21, 128.75, 130.44, 135.94, 136.45; IR 3402 cm^{-1}; MS (EI) *m/e* (relative intensity) 324 (M^+, 5), 177 (11), 117 (20), 105 (100), 59 (15). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 63.09; H, 7.55.

1,2-*O*-Isopropylidene-3-*O*-(*m*-methylbenzyl)-β-D-fructopyranose (10): 88% as a white solid; $[\alpha]_D$ −116.5° (*c* 0.103, acetone); mp 73.3 °C; ^1H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.47 (s, 3 H), 2.33 (s, 3 H), 2.36 (s, 1 H), 2.45 (s, 1 H), 3.65 (d, *J* = 9.05 Hz, 1 H), 3.74 (dd, *J* = 12.86 Hz, *J* = 1.60 Hz, 1 H), 3.90−4.06 (m, 5 H), 4.70 (s, 2 H), 7.16 (m, 4 H); ^{13}C NMR ($CDCl_3$) 21.34, 26.13, 26.84, 63.51, 69.63, 71.22, 71.80, 75.40, 76.52, 105.57, 111.93, 124.99, 128.59, 128.71, 128.85, 137.79; IR 3391 cm^{-1}; MS (EI) *m/e* (relative intensity) 324 (M^+, 3), 309 (2), 177 (16), 146 (9), 235 (2), 190 (6), 117 (24). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 63.22; H, 7.64.

1,2-*O*-Isopropylidene-3-*O*-(*p*-methylbenzyl)-β-D-fructopyranose (11): 93% as a white solid; ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.47 (s, 3 H), 2.30 (b, 2 H), 2.32 (s, 3 H), 3.64 (d, *J* = 8.87 Hz, 1 H), 3.73 (dd, *J* = 12.9 Hz, *J* = 1.3 Hz, 1 H), 3.89−4.04 (m, 5 H), 4.67 (d, *J* = 12.0 Hz, 1 H), 4.71 (d, *J* = 12.0 Hz, 1 H), 7.13−7.25 (m, 4 H).

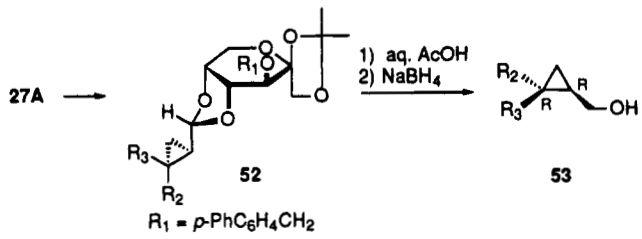
1,2-*O*-Isopropylidene-3-*O*-(*p*-methoxybenzyl)-β-D-fructopyranose (12): 85% as a white solid; ^1H NMR ($CDCl_3$) δ

Table 5. Effect of Alkyl Chain of β-D-Fructopyranose Auxiliary in Cyclopropanation

starting material		cyclopropanation				hydrolysis–reduction	
R_1 in **50**	no.	solvent	temp (°C)	time (h)	yield (%)[a]	yield (%)[a]	ee (**49**: %)[b]
Bn	**28A**	$(ClCH_2)_2$	−20 → 0	24	85	88	71
Bn	**28A**	$(ClCH_2)_2$	−30 → −20	48	54[c]	86	83
CH_3	**29A**	$(ClCH_2)_2$	−20 → 0	24	88	88	46
o-$MeC_6H_4CH_2$	**30A**	$(ClCH_2)_2$	−25 → 0	22	72[c]	86	68
m-$MeC_6H_4CH_2$	**31A**	$(ClCH_2)_2$	−25 → 0	22	87	89	72
p-$MeC_6H_4CH_2$	**32A**	toluene	−20 → 0	22	86	86	75
p-$MeC_6H_4CH_2$	**32A**	$(ClCH_2)_2$	−30 → −10	48	43[c]	90	82
p-$MeOC_6H_4CH_2$	**33A**	$(ClCH_2)_2$	−20 → 0	20	87	85	66
p-t-$BuC_6H_4CH_2$	**34A**	$(ClCH_2)_2$	−20 → 0	22	89	91	69
p-$PhC_6H_4CH_2$	**35A**	$(ClCH_2)_2$	−30 → 0	24	85	93	77
2-$NpCH_2$	**36A**	$(ClCH_2)_2$	−30 → 0	24	85	90	64

[a] Isolated yield unless noted otherwise. [b] The enantiomeric excess was determined by HPLC analysis (Daicel OJ, 10% *i*-PrOH in hexane). [c] Based on ^1H NMR.

Scheme 9



1.43 (s, 3 H), 1.49 (s, 3 H), 2.50 (b, 2 H), 3.67 (d, J = 8.99 Hz, 1 H), 3.80 (s, 3 H), 3.69–4.05 (m, 6 H), 4.67 (d, J = 12.0 Hz, 1 H), 4.72 (d, J = 12.0Hz, 1 H), 6.89 (d, J = 8.64 Hz, J = 8.66 Hz, 2 H), 7.29 (d, 2 H).

1,2-*O*-Isopropylidene-3-*O*-(*p*-*tert*-butylbenzyl)-β-D-fructopyranose (13): 93% as a white solid; $[\alpha]_D$ −86.9° (*c* 0.107, acetone); mp 92 °C; ^1H NMR ($CDCl_3$) δ 1.29 (s, 9 H), 1.42 (s, 3 H), 1.47 (s, 3 H), 3.67 (d, J = 9.18 Hz, 1 H), 3.75 (dd, J = 12.3 Hz, J = 1.5 Hz, 1 H), 3.86–4.16 (m, 5 H), 4.72 (d, J = 11 Hz, 1 H), 4.75 (d, J = 11 Hz, 1 H), 7.25 (d, J = 9.63 Hz, J = 8.39 Hz, 2 H), 7.36 (d, 2 H); ^{13}C NMR ($CDCl_3$) 26.18, 26.82, 32.31, 63.51, 69.63, 71.23, 71.80, 75.13, 77.45, 113.81, 125.59, 127.81; IR 3370 cm^{-1}; MS (EI) *m/e* (relative intensity) 366 (M^+), 351 (1), 219 (5), 147 (100), 132 (14), 117 (38), 103 (76), 59 (11). Anal. Calcd for $C_{20}H_{30}O_6$: C, 65.55; H, 8.25. Found: C, 65.17; H, 8.51.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-β-D-fructopyranose (14): 85% as a white solid; $[\alpha]_D$ −100° (*c* 0.143, acetone); mp 155.2 °C; ^1H NMR ($CDCl_3$) δ 1.44 (s, 3 H), 1.48 (s, 3 H), 2.20 (b, 2 H), 3.69 (d, J = 9.35 Hz, 1 H), 3.76 (dd, J = 1.87 Hz, J = 12.85 Hz, 1 H), 3.93–4.10 (m, 5 H), 4.80 (s, 2 H), 7.32–7.60 (m, 9 H); ^{13}C NMR ($CDCl_3$) 26.19, 26.79, 63.58, 69.72, 71.33, 71.86, 74.99, 76.56, 105.57, 111.96, 127.07, 127.34, 128.34, 128.77, 136.87, 140.64, 140.97; IR 3369 cm^{-1}; MS (EI) *m/e* (relative intensity) 386 (M^+), 371 (25), 300 (20), 239 (17), 167 (100), 117 (11), 103 (46), 59 (33). Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.68; H, 6.87.

1,2-*O*-Isopropylidene-3-*O*-(2-naphthylmethyl)-β-D-fructopyranose (15): 91% as a white solid; $[\alpha]_D$ −94.4° (*c* 0.108, acetone); mp 128.3 °C; ^1H NMR ($CDCl_3$) δ 1.45 (s, 3 H), 1.48 (s, 3 H), 2.15 (b, 2 H), 3.70 (d, J = 9.43 Hz, 1 H), 3.75 (dd, J = 12.87 Hz, J = 1.75 Hz, 1 H), 3.93–4.10 (m, 5 H), 4.88 (d, J = 12.03 Hz, 1 H), 4.94 (d, J = 12.03 Hz, 1 H), 7.44–7.45 (m, 3 H), 7.79–7.85 (m, 4 H); ^{13}C NMR ($CDCl_3$) 26.19, 26.81, 63.56, 69.73, 71.38, 71.88, 75.42, 76.59, 105.58, 111.98, 125.69, 126.12, 126.29, 126.76, 127.72, 127.94, 128.51; IR 3416 cm^{-1}; MS (EI) *m/e* (relative intensity) 360 (M^+), 213 (1), 167 (5), 141 (100), 103 (37), 59 (42), 43 (44). Anal. Calcd for $C_{19}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.96; H, 6.84.

Preparation of 1,2:4,5-Di-*O*-isopropylidene-β-D-psicopyranose (16). Pyridinium chlorochromate (9.7 g, 45 mmol) was added to 1,2;3,4-di-*O*-isopropylidene-β-D-fructopyranose (**4**, 7.8 g, 30 mmol) in CH_2Cl_2 (80 mL). The reaction mixture was well stirred for 3 h. When the oxidation was complete, the reaction mixture was diluted with diethyl ether and filtered through Florisil. Removal of the solvent gave 1,2:4,5-di-*O*-isopropylidene-β-D-*erythro*-2,3-hexadiulopyranose (5 g, 65%) as a colorless oil. To the resulting ketone (4.3 g, 16.6 mmol) in THF (150 mL) was added lithium aluminum hydride (1.27 g, 33.3 mmol) under nitrogen at −78 °C. The reaction mixture was stirred for 1 h at −78 °C. Workup was executed by the X−2X−X rule. That is, 1.27 mL of water was added dropwise followed by addition of 2.54 mL of 15% NaOH solution and finally 1.27 mL of water. The solution was filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with 2:1 ether–hexane to give 1,2:4,5-di-*O*-isopropylidene-β-D-psicopyranose (**16**, 4.03 g, 93%) as a white solid: $[\alpha]_D$ −110.9° (*c* 0.238, acetone); mp 65.8 °C; ^1H NMR ($CDCl_3$) δ 1.36 (s, 3 H), 1.38 (s, 3 H), 1.47 (s, 3 H), 1.53 (s, 3 H), 3.72 (d, J = 4.00 Hz, 1 H), 3.98 (m, 2 H), 4.02 (d, J = 9.29 Hz, 1 H), 4.21 (m, 1 H), 4.23 (d, J = 9.30 Hz, 1 H), 4.41 (dd, J = 3.99 Hz, J = 6.73 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 25.05, 25.99, 26.10, 26.46, 61.17, 68.73, 71.80, 72.08, 72.99, 104.86, 109.38, 111.07; IR 3470 cm^{-1}; MS (CI) *m/e* (relative intensity) 261 (M + 1, 8), 245 (10), 203 (100), 185 (26), 145 (21), 127 (38), 99 (13), 85 (17), 69 (12). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.50; H, 7.86.

Preparation of 1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-β-D-psicopyranose (17). 1,2:3,4-Di-*O*-isopropylidene-β-D-psicopyranose (**16**, 2.95 g, 11.3 mmol) was treated with 80% sodium hydride (408 mg, 13.6 mmol) and *p*-phenylbenzyl chloride (2.53 g, 12.5 mmol) in *N,N*-dimethylformamide (35 mL), followed by treatment of the crude product with 80% acetic acid in H_2O (40 mL). After evaporation of the solvent, the residue was purified by flash chromatography on silica gel with 2:1 hexane–acetone to give the benzylated psicopyranose **17** (3.46 g, 79%) as a white solid: $[\alpha]_D$ −80.9° (*c* 0.216, acetone); mp 117.8 °C; ^1H NMR ($CDCl_3$) δ 1.35 (s, 3 H), 1.47 (s, 3 H), 3.70~4.0 (m, 6 H), 4.08 (d, J = 9.22 Hz, 1 H), 4.72 (d, J = 11.25 Hz, 1 H), 4.90 (d, J = 11.25 Hz, 1 H), 7.33–7.60 (m, 9 H); ^{13}C NMR ($CDCl_3$) 26.32, 26.72, 65.35, 67.38, 69.28, 73.41, 75.88, 81.27, 104.80, 112.14, 127.11, 127.41, 127.46, 128.51, 128.80, 136.06, 140.30, 141.10; IR 3408 cm^{-1}; MS (EI) *m/e* (relative intensity) 386 (M^+, 5), 325 (20), 282 (15), 239 (30), 167 (100), 117 (11), 103 (54), 59 (11). Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.51; H, 6.88.

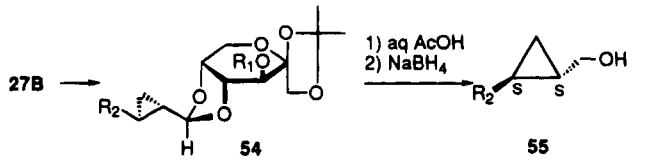
Preparation of *trans*-5-Phenyl-2-penten-1-al Diethyl Acetal. Pyridinium chlorochromate (2.85 g, 13.2 mmol) was added to 3-phenylpropan-1-ol (**18**, 1.2 g, 8.8 mmol) in dichloromethane (25 mL). The mixture was well stirred for 2 h. When the oxidation was complete, the reaction mixture was diluted with diethyl ether and filtered through Florisil. Removal of the solvent gave the pure 3-phenylpropanal (968 mg, 81.9%) as a colorless oil. Ethyl (triphenylphosphoranylidene)acetate (2.96 g, 8.5 mmol) was added to 3-phenylpropanal (950 mg, 7.1 mmol) in dichloromethane (20 mL) at room temperature. The mixture was stirred for 1 h at the same temperature. The mixture was diluted with H_2O and then extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:3 ether–hexane to give ethyl *trans*-5-phenyl-2-pentenoate (**19**, 1.29 g, 89%) as a

Table 6. Effect of Structure of Acetals on Cyclopropanation

	starting material			cyclopropanation			hydrolysis–reduction	
entry	R_2	R_3	no.	temp (°C)	time (h)	yield (%)	yield (%)	ee, % (config) of **53**
1	Ph	H	**35A**	−30 → 0	24	85	93	77[a] (1*R*,2*R*[e])
2	$PhCH_2CH_2$	H	**37A**	−30 → −10	48	45[j]	80	69[b] (1*R*,2*R*[f])
3	$PhCH_2CH_2$	H	**37A**	−30 → 0	35	87	88	52[b] (1*R*,2*R*[f])
4	$BnOCH_2$	H	**38A**	−30 → 0	24	90	89	21[a] (1*R*,2*R*[g])
5	CH_3	CH_3	**39A**	−15 → 0	24	81		60[c] (1*R*[h])
6	n-C_5H_{11}	H	**40A**	−30 → −5	35	69	82	81[d] (1*R*,2*R*[i])
7	n-C_5H_{11}	H	**40A**	−15 → 0	48	90	85	64[d] (1*R*,2*R*[i])

[a] HPLC analysis (Daicel OJ, 10% *i*-PrOH in hexane). [b] HPLC analysis (Daicel OD, 5% *i*-PrOH in hexane). [c] GC analysis of the corresponding amide with (*R*)-(+)-α-methylbenzylamine (Chiraldex B-PH GC column, 30 m, flow rate 1.01 mL/min, oven temp 150 °C). [d] GC analysis of the corresponding ester with (*R*)-(+)-MTPA (Chiraldex G-TA GC column, 30 m, flow rate 1.00 mL, oven temp 140 °C). [e] $[\alpha]_D$ −70.3° (*c* 0.26, EtOH) {lit.[11c] $[\alpha]_D$ −92° (*c* 1.23, EtOH)}. [f] $[\alpha]_D$ −17.1° (*c* 1.5, $CHCl_3$ as 52% ee) {lit.[17] $[\alpha]_D$ −24.6° (*c* 1.13, $CHCl_3$ as 80% ee)}. [g] $[\alpha]_D$ −3.05° (*c* 0.6, $CHCl_3$ as 21% ee) {lit.[11b] −6.0° (*c* 1.02, $CHCl_3$ as 35% ee)}. [h] The absolute configuration was determined by the comparison of its specific rotation with the literature value after transformation to the known (1*R*)-2,2-dimethylcyclopropanecarboxylic acid from pure cyclopropanated acetal **52** by the following sequence: (i) O_3/ethyl acetate, (ii) NaOH/EtOH. {$[\alpha]_D$ −85° (*c* 0.1, $CHCl_3$) lit.[14] *ent*-form $[\alpha]_D$ +142° (*c* 1.01, $CHCl_3$)}. [i] The absolute configuration was determined by the comparison of its specific rotation with the reported value after transformation to the known (1*R*,2*R*)-methyl *trans*-2-pentylcyclopropanecarboxylate from pure 2-pentylcyclopropanecarboxaldehyde by the following reaction: (i) MnO_2, NaCN, AcOH, MeOH {$[\alpha]_D$ −49.2° (*c* 0.1, $CHCl_3$ as 64% ee), lit.[15] *ent*-form $[\alpha]_D$ +71° (*c* 2.6, $CHCl_3$ as 92% ee)}. [j] The yield was based on ^1H NMR.

Scheme 10



colorless oil: [^1H NMR ($CDCl_3$) δ 1.26 (t, 3 H), 2.50 (m, 2 H), 2.76 (t, 2 H), 4.16 (q, 2 H), 5.82 (d, *J* = 15.68 Hz, 1 H), 6.99 (dt, 1 H), 7.14–7.31 (m, 5 H)]. A solution of 1.0 M diisobutylaluminum hydride in hexane (35.3 mL, 35.3 mmol) was added to a stirred solution of ethyl *trans*-5-phenyl-2-pentenoate (**19**, 1.2 g, 5.88 mmol) in benzene (15 mL) under nitrogen at 0 °C. After the solution was stirred overnight at room temperature, the reaction was stopped by addition of methanol (2.5 g) in benzene (5 mL) followed by water (0.15 g). The aluminum salts were filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography to give the corresponding alcohol (773 mg, 81.1%) as a colorless oil, to which a portion (740 mg, 4.6 mmol) in dichloromethane (15 mL) was added pyridinium chlorochromate (1.5 g, 6.9 mmol). The reaction mixture was well stirred for 1 h. When the oxidation was complete, the reaction mixture was diluted with diethyl ether and filtered through Florisil. The residue was purified by flash chromatography to give *trans*-5-phenyl-2-penten-1-al (**20**, 587 mg, 80%) as a colorless oil. A mixture of the aldehyde **20** (420 mg, 2.63 mmol), triethyl orthoformate (0.53 mL, 3.15 mmol), and a catalytic amount of ammonium nitrate (21 mg) in ethanol (26 mL) was stirred at room temperature until consumption of most of the starting aldehyde was completed (by TLC). After the solvents were evaporated, the residue was worked up with ethyl acetate and aqueous sodium bicarbonate. The organic layer was separated and dried over $MgSO_4$. Removal of the solvent left the corresponding diethyl acetal (584 mg, 95%), which was used for the next reaction without further purification: ^1H NMR ($CDCl_3$) δ 1.18 (t, 6 H), 2.40 (m, 2 H), 2.71 (t, 2 H), 3.54 (m, 4 H), 4.80 (d, *J* = 5.51 Hz, 1 H), 5.53 (dd, *J* = 5.62 Hz, *J* = 15.5 Hz, 1 H), 5.81 (dt, 1 H), 7.13–7.30 (m, 5 H).

Preparation of *trans*-4-(Benzyloxy)-2-buten-1-al Diethyl Acetal. To a solution of *trans*-2-butene-1,4-diol (**21**, 2.5 g, 28.4 mmol) in DMF (40 mL) was added 80% sodium hydride (426 mg, 14.2 mmol) at room temperature. After 0.5 h of stirring, benzyl bromide (1.7 mL, 14.2 mmol) was added to the above solution, which was stirred for 1 h at room temperature. The reaction mixture was diluted with water and then extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:2 ethyl acetate–hexane to give the monobenzylated alcohol **22** (1.9 g, 38%) as a colorless oil [^1H NMR ($CDCl_3$) δ 1.65 (b, OH), 4.03 (d, 2 H, *J* = 4.1 Hz), 4.14 (d, 2 H, *J* = 3.91 Hz), 4.52 (s, 2 H), 5.87 (m, 2 H), 7.31 (m, 5 H)]. Pyridinium chlorochromate (3.14 g, 14.6 mmol) was added to the monobenzylated alcohol **22** (1.3 g, 7.3 mmol) in dichloromethane (15 mL). The mixture was well stirred for 2 h. When the oxidation was complete, the reaction mixture was diluted diethyl ether and filtered through Florisil. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel with 1:4 ethyl acetate–hexane to give *trans*-4-(benzyloxy)-2-buten-1-al (**23**, 1.03 g, 80%) as a colorless oil [^1H NMR ($CDCl_3$) δ 4.27 (dd, *J* = 1.93 Hz, *J* = 4.0 Hz, 2 H), 4.58 (s, 2 H), 6.42 (ddt, *J* = 15.7 Hz, *J* = 7.86 Hz, 1 H), 6.84 (dt, *J* = 15.7 Hz, 1 H), 7.33 (m, 5 H), 9.57 (d, *J* = 7.96 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 68.58, 73.02, 127.67, 127.97, 128.53, 131.86, 137.40, 152.93, 173.8]. A mixture of the enal **23** (490 mg, 2.78 mmol), triethyl orthoformate (0.56 mL, 3.34 mmol), and a catalytic amount of ammonium nitrate (23 mg) in ethanol (30 mL) was stirred at room temperature until the consumption of the starting aldehyde was confirmed by TLC. After the solvents were evaporated, the residue was worked up with ethyl acetate and aqueous sodium bicarbonate. The organic layer was separated and dried over $MgSO_4$. Removal of the solvent left the corresponding diethyl acetal (656 mg, 94%), which was used for next reaction without further purification: ^1H NMR ($CDCl_3$) δ 1.20 (t, 6 H), 3.59 (m, 4 H), 4.04 (d, *J* = 5.24 Hz, 2 H), 4.51 (s, 2 H), 4.90 (d, *J* = 4.85 Hz, 1 H), 5.74 (dd, *J* = 4.74 Hz, *J* = 15.53 Hz, 1 H), 5.95 (dt, *J* = 15.53 Hz, 1 H), 7.31 (m, 5 H).

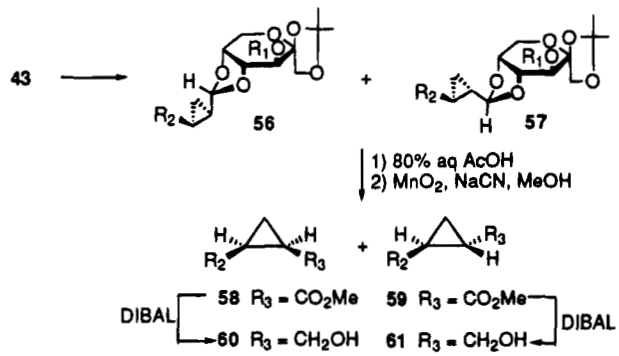
Preparation of 6-Phenyl-2-hexyn-1-al Diethyl Acetal (26). A solution of 1.6 M *n*-butyllithium in hexane (14.6 mL, 23.3 mmol) was added to a stirred solution of 3-((*tert*-butyldiphenylsilyl)oxy)propyne (6.25 g, 21.25 mmol) and hexamethylphosphoric triamide (11.1 mL, 63.8 mmol) in THF (50 mL) under nitrogen at −78 °C. The temperature was progressively raised to −15 °C and maintained for 40 min. 1-Bromo-3-phenylpropane (**24**, 4.44 g, 22.3 mmol) was added dropwise at −78 °C, and the resulting solution was stirred for 5 h at room temperature. The reaction mixture was washed with water and then extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:4 chloroform–hexane to give 1-((*tert*-butyldiphenylsilyl)oxy)-6-phenyl-2-hexyne (7.37 g, 80%) as a colorless oil [^1H NMR ($CDCl_3$) δ 1.2 (s, 9 H), 1.78 (m, 2 H), 2.19 (m, 2 H), 2.65 (t, 2 H), 4.35 (t, 2 H), 7.1–7.8 (m, 15 H)]. To a solution of 1-((*tert*-butyldiphenylsilyl)oxy)-6-phenyl-2-hexyne (7 g, 17 mmol) in THF (50 mL) was added tetrabutylammonium fluoride (6.7 g, 25.5 mmol) at room temperature. After 1 h, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give 6-phenyl-2-hexyn-1-ol (**25**, 2.6 g, 88%) as a colorless oil [^1H NMR ($CDCl_3$) δ 1.61 (b, OH), 1.83 (m, 2 H), 2.21 (m, 2 H), 2.70 (t, 2 H), 4.24 (s, 2 H), 7.24 (m, 5 H); IR 3346 cm^{-1}]. Pyridinium chlorochromate (2 g, 9.48

Table 7. Simmons–Smith Reaction of *Exo* Acetals

starting material			cyclopropanation			hydrolysis–reduction	
R_1	R_2	no.	temp (°C)	time (h)	yield (%)	yield (%)	ee, %[a] (config) of **55**
Bn	Ph	**28B**	−30 → 0	24	82	72	33[b] (1*S*,2*S*[e])
p-$PhC_6H_4CH_2$	$PhCH_2CH_2$	**37B**	−30 → −10	24	88	85	45[c] (1*S*,2*S*[f])
p-$PhC_6H_4CH_2$	*n*-C_5H_{11}	**40B**	−30 → −5	35	84	84	54[d] (1*S*,2*S*[g])

[a] The enantiomeric excess was determined by HPLC analysis. [b] Daicel OJ, 10% *i*-PrOH in hexane. [c] Daicel OD, 5% *i*-PrOH in hexane. [d] GC analysis of the corresponding ester with (*R*)-(+)-MTPA (Chiraldex G-TA GC column 30 m, flow rate 1.00 mL, oven temp 140 °C). [e] $[\alpha]_D$ +37.9° (*c* 0.14, EtOH) {lit.[11] *ent*-form $[\alpha]_D$ −92° (*c* 1.23, EtOH)}. [f] $[\alpha]_D$ +14.2° (*c* 0.7, $CHCl_3$ as 45% ee) {lit.[17] *ent*-form $[\alpha]_D$ −24.6° (*c* 1.13, $CHCl_3$ as 80% ee)}. [g] The absolute configuration was determined by the comparison of its specific rotation with a literature value after transformation to (1*S*,2*S*)-methyl *trans*-2-pentylcyclopropanecarboxylate: $[\alpha]_D$ +40.2° (*c* 1.9, $CHCl_3$) {lit.[15] $[\alpha]_D$ +71° (*c* 2.6, $CHCl_3$ as 92% ee)}.

Scheme 11



mmol) was added to the alcohol **25** (1.1 g, 6.32 mmol) in dichloromethane (15 mL). The mixture was well stirred for 2 h. When the oxidation was complete, the reaction mixture was diluted with diethyl ether and filtered through Florisil. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel with 1:2 ether–hexane to give 6-phenyl-2-hexyn-1-al (931 mg, 86%) as a colorless oil [^{1}H NMR ($CDCl_3$) δ 1.87 (m, 2 H), 2.39 (m, 2 H), 2.73 (t, 3 H), 7.25 (m, 5 H), 9.17 (s, 1 H); IR 2201, 1666 cm^{-1}]. A mixture of 6-phenyl-2-hexyn-1-al (800 mg, 4.65 mmol), triethyl orthoformate (0.93 mL, 5.58 mmol), and a catalytic amount of ammonium nitrate (37 mg) in ethanol (50 mL) was stirred at room temperature until the consumption of the starting aldehyde was complete (TLC). After the solvent was evaporated, the residue was worked up with ethyl acetate and aqueous sodium bicarbonate. The organic layer was separated and dried over $MgSO_4$. Removal of the solvent left the corresponding diethyl acetal **26** (1.03 g, 90%), which was used for next reaction without further purification: ^{1}H NMR ($CDCl_3$) δ 1.21 (m, 6 H), 1.84 (m, 2 H), 2.25 (m, 2 H), 2.72 (m, 2 H), 3.57 (m, 4 H), 5.25 (t, 1 H), 7.25 (m, 5 H).

General Procedure for Acetalization of α,β-Unsaturated Aldehyde Diethyl Acetal with Sugar Diol: Preparation of 3-*O*-Benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1′*R*) (and (1′*S*))-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (28A and 28B). A mixture of the *trans*-cinnamaldehyde (10 mL, 79.3 mmol), triethyl orthoformate (15.8 mL, 95.2 mmol), and a catalytic amount of ammonium nitrate (7.9 mmol, 635 mg) in ethanol (80 mL) was stirred at room temperature until the consumption of the starting aldehyde was confirmed by TLC. The solvent was evaporated, and the residue was worked up with ethyl acetate and aqueous sodium bicarbonate. The organic layer was separated and dried over anhydrous sodium sulfate. Removal of the solvent left the corresponding diethyl acetal, which was used for the next reaction without further purification. A mixture of the *trans*-cinnamaldehyde diethyl acetal (725 mg, 3.5 mmol), a catalytic amount of pyridinium tosylate (25 mg), and 3-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (**7**, 1.2 g, 3.87 mmol) in 30 mL of benzene was heated for 24 h. After the solvent was evaporated, the residue was purified by flash chromatography (ether:hexane:chloroform = 1:6:2) on silica gel to give white solids of 3-*O*-benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (**28A**, 888 mg, 58%) and of 3-*O*-benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (**28B**, 492 mg, 32%).

3-*O*-Benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (28A): $[\alpha]_D$ −126.7° (*c* 0.105, acetone); mp 97.6 °C; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.49 (s, 3 H), 3.49 (d, *J* = 7.12 Hz, 1 H), 3.86 (d, *J* = 8.45 Hz, 1 H), 4.07–4.21 (m, 4 H), 4.44 (dd, *J* = 5.77 Hz, *J* = 7.01 Hz 1 H), 4.68 (d, *J* = 12.04 Hz, 1 H), 4.93 (d, *J* = 12.04 Hz, 1 H) 5.52 (d, *J* = 6.62 Hz, 1 H), 6.12 (dd, *J* = 6.57 Hz, *J* = 15.98 Hz, 1 H), 6.79 (d, *J* = 15.99 Hz, 1 H), 7.24–7.44 (m, 10 H); ^{13}C NMR ($CDCl_3$) 26.02, 26.90, 59.80, 71.80, 72.66, 75.88, 76.36, 77.37, 104.38, 112.29, 125.65, 127.02, 127.65, 128.00, 128.28, 128.60, 135.53, 135.64; IR 3030, 1658 cm^{-1}; MS (CI) *m/e* (relative intensity) 425 (M + 1, 34), 367 (22), 349 (9), 303 (9), 259 (6), 213 (9), 185 (12), 133 (19), 117 (28), 91 (100), 69 (12). Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.69; H, 6.59.

3-*O*-Benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (28B): $[\alpha]_D$ −65.9° (*c* 0.135, acetone); mp 87.2 °C; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.49 (s, 3 H), 3.52 (d, *J* = 7.5 Hz, 1 H), 3.88 (d, *J* = 8.38 Hz, 1 H), 4.05–4.19 (m, 4 H), 4.58 (dd, *J* = 5.31 Hz, *J* = 7.42 Hz, 1 H), 4.71 (d, *J* = 11.85 Hz, 1 H), 4.97 (d, *J* = 11.85 Hz, 1 H), 5.69 (d, *J* = 6.09 Hz, 1 H), 6.14 (dd, *J* = 15.89 Hz, *J* = 6.12 Hz, 1 H), 6.73 (d, *J* = 15.99 Hz, 1 H), 7.24–7.43 (m, 10 H); ^{13}C NMR ($CDCl_3$) 26.03, 26.91, 60.16, 71.78, 72.79, 73.08, 73.75, 78.53, 103.13, 104.36, 112.41, 125.59, 126.95, 127.77, 128.01, 128.38, 128.44, 128.60, 134.34, 135.64, 137.88; IR 3032, 2993, 2935, 1655 cm^{-1}; MS (CI) *m/e* (relative intensity) 425 (M + 1), 367 (19), 349 (6), 321 (6), 259 (5), 213 (7), 185 (10), 173 (8), 133 (26), 117 (29), 91 (100), 69 (13). Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.50; H, 6.74.

Using the procedure given above, the following compounds were prepared.

1,2-*O*-Isopropylidene-3-*O*-methyl-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (29A): 49% as a white solid; $[\alpha]_D$ −85.1° (*c* 0.047, acetone); mp 111.9 °C; ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.49 (s, 3 H), 3.28 (d, *J* = 7.26 Hz, 1 H), 3.57 (s, 3 H), 3.95 (d, *J* = 8.4 Hz, 1 H), 4.01–4.2 (m, 4 H), 4.34 (dd, *J* = 5.47 Hz, *J* = 7.15 Hz, 1 H), 5.51 (d, *J* = 6.31 Hz, 1 H), 6.19 (dd, *J* = 6.33 Hz, *J* = 15.93 Hz, 1 H), 6.79 (d, *J* = 15.90 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 25.99, 26.83, 59.89, 60.05, 71.90, 75.97, 77.09, 79.29, 104.21, 104.30, 125.57, 126.98, 128.54, 128.62, 135.59; IR 2901, 1662 cm^{-1}; MS (EI) *m/e* (relative intensity) 348 (M^+, 3), 333 (3), 232 (11), 205 (15), 159 (29), 131 (89), 115 (59), 104 (100), 87 (62), 84 (46), 59 (33), 43 (46). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.76; H, 7.06.

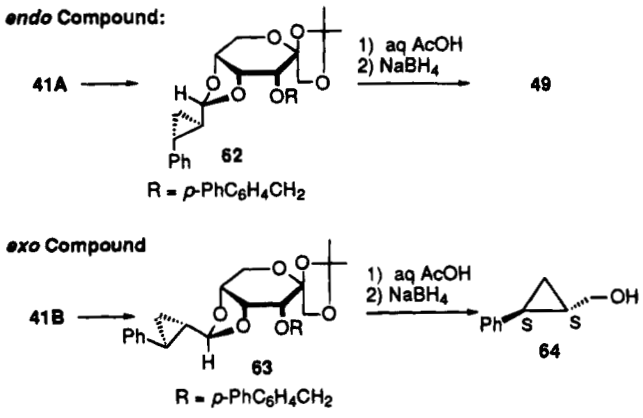
1,2-*O*-Isopropylidene-3-*O*-(*o*-methylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (30A): 53% as a white solid; $[\alpha]_D$ −112.7° (*c* 0.118, acetone); mp 96.8 °C; ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 3 H), 1.48 (s, 3 H), 2.33 (s, 3 H), 3.51 (d, *J* = 7.22 Hz, 1 H), 3.82 (d, *J* = 8.38 Hz, 1 H), 3.93 (d, *J* = 8.38 Hz, 1 H), 4.05–4.21 (m, 3 H), 4.44 (dd, *J* = 5.63 Hz, *J* = 6.97 Hz, 1 H), 4.65 (d, *J* = 12.06 Hz, 1 H), 4.96 (d, *J* = 12.06 Hz, 1 H), 5.54 (d, *J* = 6.34 Hz, 1 H), 6.20 (dd, *J* = 6.38 Hz, *J* = 15.93 Hz, 1 H), 6.82 (d, *J* = 15.90 Hz, 1 H), 7.10–7.45 (m, 9 H); ^{13}C NMR ($CDCl_3$) 18.77, 26.08, 26.63, 59.86, 71.12, 71.96, 76.03, 76.08, 77.46, 104.27, 104.38, 112.26, 125.59, 125.64, 126.99, 127.89, 128.57, 128.64, 129.01, 130.23, 135.53, 135.83, 136.79; IR 3028, 1658 cm^{-1}; MS (EI) *m/e* (relative intensity) 438 (M^+, 2), 318 (2), 229 (16), 194 (20), 171 (44),

Table 8. Simmons–Smith Reactions of *Cis* Enal Acetals

starting material			cyclopropanation			hydrol	oxidn	reduction		
R_1	R_2	no.	temp (Time, h)	yield[b] (%)	**56**:**57**[a]	yield[b] (%)	no. (yield, %)[b]	no.	yield[b] (%)	ee (%)
Bn	Ph	**45**	−20 → 0 °C (20)	96	2:1	93	**58** (55)[c]	**60**	89[d]	82[e]
							59 (28)[c]	**61**	90[f]	58[e]
p-$PhC_6H_4CH_2$	$Ph(CH_2)_3$	**47**	−30 → 0 °C (24)	89	**56** only			**60**	88[g]	80[h]

[a] The ratio was determined by ^1H NMR. [b] Isolated yield. [c] **58**: $[\alpha]_D$ −29.7° (*c* 0.175, $CHCl_3$) {lit.[13] *ent*-form $[\alpha]_D$ +32.8° (*c* 1.99, $CHCl_3$)}. **59**: $[\alpha]_D$ +173° (*c* 0.185, $CHCl_3$) {lit.[13] $[\alpha]_D$ +324.7° (*c* 1.24, $CHCl_3$)}. [d] Yield from the pure *cis*-methyl ester **58**. [e] HPLC analysis (Daicel OJ, 10% *i*-PrOH in hexane). [f] Yield from the pure *trans*-methyl ester **59**. [g] Yield for two steps (hydrolysis, reduction) from the isolated *cis* acetal of **56**. [h] HPLC analysis of the corresponding urethane with (*R*)-(+)-α-methylbenzyl isocyanate (Daicel OD, 10% *i*-PrOH in hexane). The absolute configuration of (1*R*,2*S*)-*cis*-1-(hydroxymethyl)-2-(3′-phenylpropyl)-cyclopropane was determined by the comparison of its specific rotation with a literature value. {$[\alpha]_D$ +18.2° (*c* 0.77, EtOH), lit.[11a] $[\alpha]_D$ +19° (*c* 0.7, EtOH as 81% ee)}.

Scheme 12



131 (31), 115 (26), 105 (100). Anal. Cacld for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 71.56; H, 7.01.

1,2-*O*-Isopropylidene-3-*O*-(*o*-methylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-1′-propen-1′-yl]-β-D-fructopyranose (30B): 35% as a white solid; $[\alpha]_D$ −47.90° (*c* 0.192, acetone); mp 109.2 °C; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.49 (s, 3 H), 2.38 (s, 3 H), 3.56 (d, *J* = 7.25 Hz, 1 H), 3.84–4.20 (m, 5 H), 4.59 (dd, *J* = 5.48 Hz, *J* = 7.21 Hz, 1 H), 4.69 (d, *J* = 11.97 Hz, 1 H), 5.00 (d, *J* = 11.97 Hz, 1 H), 5.75 (d, *J* = 5.99 Hz, 1 H), 6.18 (dd, *J* = 15.9 Hz, *J* = 5.72 Hz, 1 H), 6.75 (d, *J* = 15.9 Hz, 1 H), 7.20–7.44 (m, 9 H); ^{13}C NMR ($CDCl_3$) 18.85, 26.08, 26.86, 60.19, 71.52, 71.69, 72.95, 73.76, 78.61, 103.12, 104.38, 112.36, 125.64, 125.68, 126.96, 128.02, 128.44, 128.61, 129.05, 130.31, 134.30, 135.64, 135.75, 136.92; IR 3059, 1653, 1604 cm^{-1}; MS (EI) *m/e* (relative intensity) 438 (M^+, 2), 217 (9), 171 (17), 131 (30), 115 (19), 105 (100), 91 (5), 69 (7). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 70.97; H, 6.93.

1,2-*O*-Isopropylidene-3-*O*-(*m*-methylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (31A): 56% as a white solid; $[\alpha]_D$ −123.8° (*c* 0.084, acetone); mp 87.1 °C; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.49 (s, 3 H), 2.25 (s, 3 H), 3.48 (d, *J* = 7.03 Hz, 1 H), 3.86 (d, *J* = 8.38 Hz, 1 H), 4.04–4.20 (m, 4 H), 4.43 (dd, *J* = 5.83 Hz, *J* = 7.01 Hz, 1 H), 4.65 (d, *J* = 12.04 Hz, 1 H), 4.90 (d, *J* = 12.04 Hz, 1 H), 5.51 (d, *J* = 6.64 Hz, 1 H), 6.11 (dd, *J* = 6.69 Hz, *J* = 15.9 Hz, 1 H), 6.80 (d, *J* = 15.98 Hz, 1 H), 7.06–7.43 (m, 9 H); ^{13}C NMR ($CDCl_3$) 21.32, 26.01, 26.94, 59.82, 71.82, 72.76, 75.89, 76.04, 77.42, 104.40, 112.50, 125.07, 125.63, 127.04, 128.20, 128.38, 128.61, 128.67, 135.71, 138.10; IR 3030, 1657 cm^{-1}; MS (EI) *m/e* (relative intensity) 438 (M^+, 7), 333 (10), 260 (21), 229 (5), 194 (10), 171 (25), 131 (20), 105 (100), 91 (8), 77 (7). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 71.47; H, 7.02.

1,2-*O*-Isopropylidene-3-*O*-(*m*-methylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (31B): 37% as a white solid; $[\alpha]_D$ −49.5° (*c* 0.2, acetone); mp 82.4 °C; ^1H NMR ($CDCl_3$) δ 1.44 (s, 3 H), 1.50 (s, 3 H), 2.35 (s, 3 H), 3.52 (d, *J* = 7.47 Hz, 1 H), 3.89 (d, *J* = 8.40 Hz, 1 H), 3.99–4.19 (m, 4 H), 4.59 (dd, *J* = 5.25 Hz, *J* = 7.48 Hz, 1 H), 4.69 (d, *J* = 11.82 Hz, 1 H), 4.96 (d, *J* = 11.82 Hz, 1 H), 5.67 (d, *J* = 6.10 Hz, 1 H), 6.15 (dd, *J* = 6.10 Hz, *J* = 15.85 Hz, 1 H), 6.73 (d, *J* = 15.85 Hz, 1 H), 7.05–7.4 (m, 9 H); ^{13}C NMR ($CDCl_3$) 21.40, 26.02, 26.93, 60.17, 71.78, 72.54, 73.07, 73.78, 78.56, 103.15, 104.39, 112.40, 125.13, 125.63, 126.95, 128.29, 128.44, 128.49, 128.60, 128.86, 134.36, 135.65, 137.77; IR 2987, 1658 cm^{-1}; MS (EI) *m/e* (relative intensity) 438 (M^+, 13), 423 (11). 217 (4), 194 (4), 171 (13), 145 (6), 131 (24), 115 (15), 105 (100), 77 (6), 69 (8). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 70.97; H, 6.93.

1,2-*O*-Isopropylidene-3-*O*-(*p*-methylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (32A): 51% as a white solid; $[\alpha]_D$ −132° (*c* 0.05, acetone); mp 122.1 °C; ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.47 (s, 3 H), 2.31 (s, 3 H), 3.47 (d, *J* = 7.14 Hz, 1 H), 3.84 (d, *J* = 8.46 Hz, 1 H), 4.03–4.19 (m, 4 H), 4.42 (dd, *J* = 5.75 Hz, *J* = 7.05 Hz, 1 H), 4.65 (d, *J* = 11.9 Hz, 1 H), 4.89 (d, *J* = 11.9 Hz, 1 H), 5.51 (d, *J* = 6.58 Hz, 1 H), 6.10 (dd, *J* = 6.61 Hz, *J* = 15.94 Hz, 1 H), 6.78 (d, *J* = 15.94 Hz, 1 H), 7.03–7.43 (m, 9 H); ^{13}C NMR: 21.13, 26.02, 26.94, 59.82, 71.82, 72.50, 75.49, 76.06, 77.44, 104.41, 112.28, 125.79, 127.05, 128.22, 128.61, 128.98, 134.83, 135.61, 137.35; IR 2994 cm^{-1}; MS (EI) *m/e* (relative intensity) 438 (M^+, 1), 260 (4), 194 (19), 171 (29), 131 (22), 105 (100), 91 (5), 77 (4). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 71.22; H, 6.94.

1,2-*O*-Isopropylidene-3-*O*-(*p*-methylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (32B): 36% as a white solid; $[\alpha]_D$ −54.7° (*c* 0.137, acetone); mp 75 °C; ^1H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.49 (s, 3 H), 2.33 (s, 3 H), 3.50 (d, *J* = 7.44 Hz, 1 H), 3.86 (d, *J* = 8.54 Hz, 1 H), 3.97–4.18 (m, 4 H), 4.57 (dd, *J* = 5.27 Hz, *J* = 7.47 Hz, 1 H), 4.69 (d, *J* = 11.73 Hz, 1 H), 4.92 (d, *J* = 11.73 Hz, 1 H), 5.66 (d, *J* = 6.1 Hz, 1 H), 6.14 (dd, *J* = 6.19 Hz, *J* = 15.89 Hz, 1 H), 6.72 (d, *J* = 15.90 Hz, 1 H), 7.12–7.43 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 21.16, 26.01, 26.92, 60.14, 71.73, 72.33, 72.92, 73.76, 78.57, 103.10, 104.38, 112.36, 125.62, 126.95, 128.22, 128.42, 128.59, 129.04, 134.32, 134.76, 135.64; IR 2987, 1657 cm^{-1}; MS (EI) *m/e* (relative intensity) 438 (M^+, 1), 277 (1), 217 (6), 171 (14), 131 (20), 115 (12), 105 (100), 69 (14), 43 (25). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 71.29; H, 6.91.

1,2-*O*-Isopropylidene-3-*O*-(*p*-methoxybenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (33A): 54% as a white solid; $[\alpha]_D$ −119.2° (*c* 0.052, acetone); mp 93.5 °C; ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.48 (s, 3 H), 3.46 (d, *J* = 7.18 Hz, 1 H), 3.74 (s, 3 H), 3.79–4.16 (m, 5 H), 4.43 (dd, *J* = 5.79 Hz, *J* = 7.17 Hz, 1 H), 4.63 (d, *J* = 11.78 Hz, 1 H), 4.85 (d, *J* = 11.78 Hz, 1 H), 5.52 (d, *J* = 6.74 Hz, 1 H), 6.13 (dd, *J* = 6.70 Hz, *J* = 15.98 Hz, 1 H), 6.80 (d, *J* = 15.98 Hz, 1 H), 6.78 (d, *J* = 8.68 Hz, 2 H), 7.22–7.43 (m, 7 H); ^{13}C NMR ($CDCl_3$) 26.03, 26.92, 55.21, 59.93, 71.83, 72.27, 75.29, 76.08, 77.49, 104.38, 104.43, 112.28, 113.71, 125.81, 126.97, 127.04, 128.59, 128.64, 129.74, 129.96, 135.59; IR 3034, 1612 cm^{-1}; MS (EI) *m/e* (relative intensity) 454 (M^+, 1), 260 (10), 171 (18), 121 (100), 115 (9), 91 (3), 77 (3). Anal. Calcd for $C_{26}H_{30}O_7$: C, 68.71; H, 6.65. Found: C, 68.58; H, 6.81.

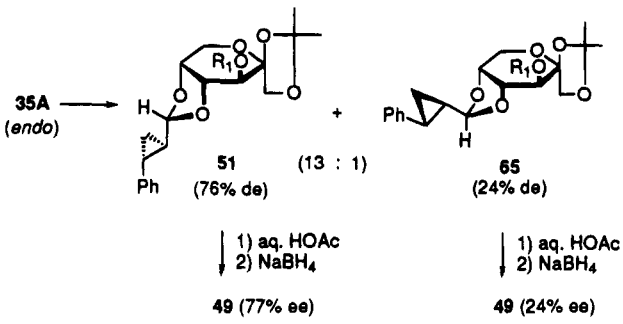
1,2-*O*-Isopropylidene-3-*O*-(*p*-methoxybenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (33B): 34% as a white solid; $[\alpha]_D$ −50° (*c* 0.112, acetone); mp 82.5 °C; ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.48 (s, 3 H), 3.49 (d, *J* = 7.43 Hz, 1 H), 3.79 (s, 3 H), 3.77–4.18 (m, 5 H), 4.56 (dd, *J* = 5.20 Hz, *J* = 7.50 Hz, 1 H), 4.66 (d, *J* = 11.62 Hz, 1 H), 4.88 (d, *J* = 11.62 Hz, 1 H), 5.64 (d, *J* = 6.09 Hz, 1 H), 6.14 (dd, *J* = 6.15 Hz, *J* = 15.93 Hz, 1 H), 6.72 (d, *J* = 15.93 Hz, 1 H), 6.86 (d, *J* = 8.69 Hz, 2 H), 7.24–7.43 (m, 7 H); ^{13}C NMR ($CDCl_3$) 25.99, 26.89, 55.25, 60.13, 71.71, 72.09, 72.73, 73.76, 78.55, 103.09, 104.39, 112.35, 113.77, 125.59,

Table 9. Simmons–Smith Reactions of Psicopyranose Derivatives

starting material	cyclopropanation temp (°C)	cyclopropanation time (h)	cyclopropanation yield (%)	hydrol–redn yield (%)	product ee (%)[a]	product config[b]
endo isomer **41A**	−30 → 0	48	82	90	48	(1*R*,2*R*)
exo isomer **41B**	−30 → 0	48	64	82	20	(1*S*,2*S*)

[a] HPLC analysis (Daicel OJ, 10% *i*-PrOH in hexane). [b] **49**: $[\alpha]_D$ −41.7° (*c* 0.42, EtOH) {lit.[11c] $[\alpha]_D$ −92° (*c* 1.23, EtOH)}. **64**: $[\alpha]_D$ +19° (*c* 0.1, EtOH).

Scheme 13



126.94, 128.43, 128.59, 129.74, 129.85, 134.35, 135.62, 159.31; IR 3034, 1613 cm^{-1}; MS (EI) *m/e* (relative intensity) 454 (M^+, 1), 318 (1), 260 (2), 217 (8), 171 (15), 148 (10), 131 (22), 121 (120), 104 (5), 69 (5). Anal. Calcd for $C_{26}H_{30}O_7$: C, 68.71; H, 6.65. Found: C, 68.31; H, 6.79.

1,2-Isopropylidene-3-*O*-(*p*-*tert*-butylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (34A): 49% as a white solid; $[\alpha]_D$ −112.4° (*c* 0.121, acetone); mp 116.3 °C; ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 9 H), 1.44 (s, 3 H), 1.49 (s, 3 H), 3.48 (d, *J* = 7.13 Hz, 1 H), 3.84 (d, *J* = 8.41 Hz, 1 H), 4.05–4.20 (m, 4 H), 4.45 (dd, *J* = 6.67 Hz, *J* = 7.11 Hz, 1 H), 4.68 (d, *J* = 11.99 Hz, 1 H), 4.89 (d, *J* = 11.99 Hz, 1 H), 5.52 (d, *J* = 6.61 Hz, 1 H), 6.18 (dd, *J* = 6.60 Hz, *J* = 15.93 Hz, 1 H), 6.80 (d, *J* = 15.95 Hz, 1 H), 7.24–7.44 (m, 9 H); ^{13}C NMR ($CDCl_3$) 26.08, 26.92, 31.34, 59.82, 71.82, 72.33, 75.42, 76.08, 77.52, 104.45, 112.28, 125.19, 125.73, 127.05, 127.98, 128.65, 134.83, 135.70; IR 2962, 1653 cm^{-1}; MS (EI) *m/e* (relative intensity) 480 (M^+, 17), 318 (15), 236 (11), 171 (31), 147 (100), 131 (26), 115 (22), 91 (14), 69 (8), 59 (15). Anal. Calcd for $C_{29}H_{36}O_6$: C, 72.48; H, 7.55. Found: C, 72.44; H, 7.56.

1,2-Isopropylidene-3-*O*-(*p*-*tert*-butylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (34B): 41% as a white solid; $[\alpha]_D$ −54.4° (*c* 0.103, acetone); mp 75.6 °C; ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 9 H), 1.45 (s, 3 H), 1.51 (s, 3 H), 3.53 (d, *J* = 7.61 Hz, 1 H), 3.88 (d, *J* = 8.92 Hz, 1 H), 4.01–4.21 (m, 4 H), 4.60 (dd, *J* = 6.23 Hz, *J* = 7.60 Hz, 1 H), 4.73 (d, *J* = 11.85 Hz, 1 H), 4.95 (d, *J* = 11.85 Hz, 1 H), 5.68 (d, *J* = 6.06 Hz, 1 H), 6.20 (dd, *J* = 6.03 Hz, *J* = 15.89 Hz, 1 H), 6.74 (d, *J* = 15.90 Hz, 1 H), 7.28–7.45 (m, 9 Hz); ^{13}C NMR ($CDCl_3$) 26.06, 26.89, 31.35, 60.15, 71.75, 72.37, 72.81, 73.76, 78.57, 103.09, 104.40, 112.37, 125.28, 125.60, 126.95, 127.86, 128.31, 128.42, 128.59, 128.93, 134.32, 134.76; IR 3030, 1676, 1628 cm^{-1}; MS (EI) *m/e* (relative intensity) 480 (M^+, 2), 465 (1), 333 (1), 260 (1), 217 (12), 171 (23), 147 (100), 131 (35), 115 (20), 91 (9), 69 (12). Anal. Calcd for $C_{29}H_{36}O_6$: C, 72.48; H, 7.55. Found: C, 72.66; H, 7.41.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (35A): 55% as a white solid; $[\alpha]_D$ −128.6° (*c* 0.091, acetone); mp 121.8 °C; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 3 H), 1.50 (s, 3 H), 3.52 (d, *J* = 7.22 Hz, 1 H), 3.90 (d, *J* = 8.47 Hz, 1 H), 4.05–4.22 (m, 4 H), 4.46 (dd, *J* = 5.86 Hz, *J* = 6.97 Hz, 1 H), 4.75 (d, *J* = 12.14 Hz, 1 H), 4.98 (d, *J* = 12.14 Hz, 1 H), 5.53 (d, *J* = 6.60 Hz, 1 H), 6.12 (dd, *J* = 6.66 Hz, *J* = 15.95 Hz, 1 H), 6.79 (d, *J* = 15.94 Hz, 1 H), 7.24–7.57 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.72, 27.55, 60.48, 72.52, 72.90, 76.72, 78.03, 78.27. 105.08, 112.99, 126.35, 127.66, 129.18, 129.25, 129.38, 136.31, 137.55; IR 3030, 1655 cm^{-1}; MS (EI) *m/e* (relative intensity) 500 (M^+, 18), 318 (11), 300 (20), 260 (8), 167 (100), 131 (14), 115 (14), 104 (5), 69 (5). Anal. Calcd for $C_{31}H_{32}O_6$: C, 74.38; H, 6.44. Found: C, 74.34; H, 6.49.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (35B): 35% as a white solid; $[\alpha]_D$ −56.9° (*c* 0.065, acetone); mp 100.8 °C; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 3 H), 1.50 (s, 3 H), 3.56 (d, *J* = 7.63 Hz, 1 H), 3.93 (d, *J* = 8.42 Hz, 1 H), 4.06–4.20 (m, 4 H), 4.59 (dd, *J* = 5.11 Hz, *J* = 7.53 Hz, 1 H), 4.78 (d, *J* = 11.99 Hz, 1 H), 5.01 (d, *J* = 11.99 Hz, 1 H), 5.68 (d, *J* = 6.05 Hz, 1 H), 6.15 (dd, *J* = 6.25 Hz, *J* = 15.87 Hz, 1 H), 6.71 (d, *J* = 15.87 Hz, 1 H), 7.24–7.61 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.06, 26.89, 60.17, 71.82, 72.81, 73.76, 78.47, 103.15, 104.39, 112.43, 125.55, 126.95, 127.09, 127.30, 128.49, 128.58, 128.77, 134.37, 135.59, 136.87; IR 3030, 1653 cm^{-1}; MS (EI) *m/e* (relative intensity) 500 (M^+, 1), 260 (2), 217 (6), 167 (100), 152 (8), 131 (4), 115 (14), 104 (5), 69 (8), 43 (5). Anal. Calcd for $C_{31}H_{32}O_6$: C, 74.38; H, 6.44. Found: C, 74.33; H, 6.51.

1,2-*O*-Isopropylidene-3-*O*-(2-naphthylmethyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (36A): 51% as a white solid; $[\alpha]_D$ −141.2° (*c* 0.102, acetone); mp 146.8 °C; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 3 H), 1.50 (s, 3 H), 3.52 (d, *J* = 7.14 Hz, 1 H), 3.84 (d, *J* = 8.47 Hz, 1 H), 4.04–4.21 (m, 4 H), 4.49 (dd, *J* = 6.63 Hz, *J* = 7.04 Hz, 1 H), 4.88 (d, *J* = 12.14 Hz, 1 H), 5.08 (d, *J* = 12.14 Hz, 1 H), 5.54 (d, *J* = 6.54 Hz, 1 H), 6.11 (dd, *J* = 6.57 Hz, *J* = 15.96 Hz, 1 H), 6.81 (d, *J* = 15.96 Hz, 1 H), 7.30–7.79 (m, 12 H); ^{13}C NMR ($CDCl_3$) 26.07, 26.93, 59.81, 71.89, 72.59, 75.60, 76.06, 77.50, 104.36, 104.47, 112.36, 125.63, 125.91, 126.06, 127.11, 127.63, 127.96, 128.13, 128.59, 128.66, 132.96, 133.11, 135.26, 135.55, 135.81; IR 3055, 1662 cm^{-1}; MS (EI) *m/e* (relative intensity) 474 (M^+, 2), 260 (8), 171 (22), 141 (100), 115 (26), 104 (6), 91 (5), 69 (6), 43 (10). Anal. Calcd for $C_{29}H_{30}O_6$: C, 73.40; H, 6.37. Found: C, 73.38; H, 6.43.

1,2-*O*-Isopropylidene-3-*O*-(2-naphthylmethyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (36B): 37% as a white solid; $[\alpha]_D$ −60° (*c* 0.1, acetone); mp 87.3 °C; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 3 H), 1.50 (s, 3 H), 3.55 (d, *J* = 7.54 Hz, 1 H), 3.89 (d, *J* = 8.41 Hz, 1 H), 4.0–4.19 (m, 4 H), 4.61 (dd, *J* = 5.29 Hz, *J* = 7.45 Hz, 1 H), 4.90 (d, *J* = 12.0 Hz, 1 H), 5.11 (d, *J* = 12.0 Hz, 1 H), 5.59 (d, *J* = 6.19 Hz, 1 H), 6.14 (dd, *J* = 6.24 Hz, *J* = 15.85 Hz, 1 H), 6.63 (d, *J* = 15.84 Hz, 1 H), 7.24–7.79 (m, 12 H); ^{13}C NMR ($CDCl_3$) 26.06, 26.91, 60.17, 71.80, 72.40, 73.13, 73.78, 78.50, 103.19, 104.38, 112.43, 125.46, 126.04, 126.17, 126.97, 127.13, 127.72, 127.88, 128.21, 128.45, 128.60, 133.03, 133.16, 134.48, 135.20, 135.60; IR 3053, 1657 cm^{-1}; MS (EI) *m/e* (relative intensity) 474 (M^+, 2), 217 (4), 141 (100), 131 (15), 115 (25), 91 (5), 69 (18), 43 (25). Anal. Calcd for $C_{29}H_{30}O_6$: C, 73.40; H, 6.37. Found: C, 73.41; H, 6.49.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-5′-phenyl-2′-penten-1′-yl]-β-D-fructopyranose (37A): 53% as a white solid; $[\alpha]_D$ −54.2° (*c* 0.059, acetone); mp 104.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.49 (s, 3 H), 2.42 (m, 2 H), 2.74 (t, 2 H), 3.45 (d, *J* = 7.12 Hz, 1 H), 3.88 (d, *J* = 8.5 Hz, 1 H), 4.08–4.14 (m, 4 H), 4.40 (dd, *J* = 6.91 Hz, *J* = 7.08 Hz, 1 H), 4.67 (d, *J* = 12.05 Hz, 1 H), 4.95 (d, *J* = 12.05 Hz, 1 H), 5.32 (d, *J* = 6.90 Hz, 1 H), 5.52 (dd, *J* = 6.88 Hz, *J* = 15.9 Hz, 1 H), 6.02 (dt, *J* = 15.95 Hz, 1 H), 7.14–7.59 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.07, 26.91, 33.77, 34.95, 59.87, 71.69, 72.50, 75.84, 76.31, 77.22, 104.37, 104.51, 112.30, 125.99, 127.02, 127.06, 127.26, 127.58, 128.36, 128.75, 137.13, 137.48, 140.58, 140.82, 141.28; IR 3026, 1674 cm^{-1}; MS (EI) *m/e* (relative intensity) 528 (M^+), 288 (5), 199 (10), 181 (4), 167 (100), 117 (16), 91 (75), 69 (10), 43 (18). Anal. Calcd for $C_{33}H_{36}O_6$: C, 75.0; H, 6.86. Found: C, 75.09; H, 7.04.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-5′-phenyl-2′-penten-1′-yl]-β-D-fructopyranose (37B): 35% as an oily solid; $[\alpha]$ −38.5° (*c* 0.039, acetone); ^{1}H NMR

($CDCl_3$) δ 1.44 (s, 3 H), 1.49 (s, 3 H), 2.41 (m, 2 H), 2.71 (t, 2 H), 3.50 (d, J = 7.54 Hz, 1 H), 3.89 (d, J = 8.59 Hz, 1 H), 4.01–4.16 (m, 4 H), 4.54 (dd, J = 5.16 Hz, J = 7.53 Hz, 1 H), 4.73 (d, J = 11.99 Hz, 1 H), 4.98 (d, J = 11.99 Hz, 1 H), 5.45 (d, J = 6.5 Hz, 1 H), 5.53 (dd, J = 14.46 Hz, 1 H), 5.94 (dt, J = 14.47 Hz, 1 H), 7.14–7.60 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.08, 26.90, 33.73, 35.03, 60.23, 71.83, 72.53, 72.73, 73.68, 78.43, 103.34, 104.36, 112.41, 125.98, 127.09, 127.31, 127.38, 128.37, 128.49, 128.76, 136.25, 136.89; IR 3059, 1672 cm^{-1}; MS (EI) *m/e* (relative intensity) 528 (M^+), 320 (1), 245 (4), 167 (100), 115 (24), 91 (54), 69 (11), 43 (14). Anal. Calcd for $C_{33}H_{36}O_6$: C, 75.0; H, 6.86. Found: C, 74.77; H, 6.93.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-4′-(benzyloxy)-2′-buten-1′-yl]-β-D-fructopyranose (38A): 47% as a white solid; $[\alpha]_D$ −94.5° (*c* 0.055, acetone); mp 75.2 °C; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.49 (s, 3 H), 3.47 (d, J = 7.17 Hz, 1 H), 3.87 (d, J = 8.53 Hz, 1 H), 4.09 (m, 6 H), 4.42 (dd, J = 5.74 Hz, J = 7.08 Hz, 1 H), 4.45 (s, 2 H), 4.69 (d, J = 11.99 Hz, 1 H), 4.97 (d, J = 11.99 Hz, 1 H), 5.39 (d, J = 6.42 Hz, 1 H), 5.84 (ddt, J = 6.40 Hz, J = 15.58 Hz, 1 H), 6.09 (dt, J = 15.59 Hz, 1 H), 7.23–7.58 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.07, 26.90, 59.86, 69.29, 71.87, 72.48, 72.63, 75.97, 76.37, 77.32, 103.74, 104.36, 112.32, 127.04, 127.26, 127.65, 127.68, 128.32, 128.42, 128.66, 128.74, 133.71; IR 2934, 1601 cm^{-1}; MS (EI) *m/e* (relative intensity) 544 (M^+), 436 (1), 254 (2), 167 (74), 91 (100), 69 (10). Anal. Calcd for $C_{33}H_{36}O_7$: C, 72.77; H, 6.66. Found: C, 72.42; H, 6.75.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-4′-(benzyloxy)-2′-buten-1′-yl]-β-D-fructopyranose (38B): 43% as an oily solid; $[\alpha]_D$ −68.8° (*c* 0.236, acetone); ^1H NMR ($CDCl_3$) δ 1.45 (s, 3 H), 1.50 (s, 3 H), 3.52 (d, J = 7.48 Hz, 1 H), 3.90 (d, J = 8.52 Hz, 1 H), 4.08 (m, 6 H), 4.55 (s, 2 H), 4.56 (m, 1 H), 4.75 (d, J = 11.96 Hz, 1 H), 5.00 (d, J = 11.96 Hz, 1 H), 5.58 (d, J = 5.92 Hz, 1 H), 5.77 (dd, J = 5.98 Hz, J = 15 Hz, 1 H), 6.02 (dt, J = 15 Hz, 1 H), 7.30–7.61 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.06, 26.89, 60.14, 69.28, 71.82, 72.52, 72.76, 72.84, 73.68, 78.43, 102.53, 104.36, 112.41, 127.08, 127.29, 127.68, 128.41, 128.75, 132.16; IR 2930, 1689 cm^{-1}; MS (EI) *m/e* (relative intensity) 544 (M^+), 436 (2), 362 (0.2), 309 (0.2), 273 (0.4), 167 (100), 91 (89), 69 (29). Anal. Calcd for $C_{33}H_{36}O_7$: C, 72.77; H, 6.66. Found; C, 73.08; H, 6.95.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-3′-methyl-2′-buten-1′-yl]-β-D-fructopyranose (39A): 50% as a white solid; $[\alpha]_D$ −82.2° (*c* 0.107, acetone); mp 104.2 °C; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.49 (s, 3 H), 1.78 (s, 6 H), 3.47 (d, J = 7.06 Hz, H_3), 3.87 (d, J = 8.47 Hz, 1 H), 4.01–4.13 (m, 4 H), 4.39 (t, J = 6.78 Hz, 1 H), 4.70 (d, J = 12.05 Hz, 1 H), 4.96 (d, J = 12.05 Hz, 1 H), 5.27 (dm, 1 H), 5.67 (d, J = 7.6 Hz, 1 H), 7.32–7.60(m, 9 H); ^{13}C NMR ($CDCl_3$) 18.37, 25.95, 26.08, 26.91, 59.92, 71.91, 72.53, 75.74, 76.43, 78.43, 100.63, 104.38, 112.25, 122.23, 127.01, 127.07, 127.24, 128.38, 128.74, 137.20, 140.89, 141.68; IR 2991 cm^{-1}; MS (EI) *m/e* (relative intensity) 452 (M^+, 10) 252 (2), 212 (11), 167 (100), 123 (22), 85 (11), 69 (10). Anal. Calcd for $C_{27}H_{32}O_6$: C, 71.66; H, 7.13. Found: C, 71.69; H, 6.59.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-3′-methyl-2′-buten-1′-yl]-β-D-fructopyranose (39B): 28% as a white solid; $[\alpha]_D$ −99.7° (*c* 0.305, acetone); mp 54.2 °C; ^1H NMR ($CDCl_3$) δ 1.44 (s, 3 H), 1.49 (s, 3 H), 1.78 (s, 6 H), 3.53 (d, J = 7.63 Hz, 1 H), 3.90 (d, J = 8.37 Hz, 1 H), 3.95–4.17 (m, 4 H), 4.56 (dd, J = 5.19 Hz, J = 7.49 Hz, 1 H), 4.76 (d, J = 12.02 Hz, 1 H), 4.99 (d, J = 12.02 Hz, 1 H), 5.25 (dm, J = 7.82 Hz, 1 H), 5.84 (d, J = 7.85 Hz, 1 H), 7.33–7.60 (m, 9 H); ^{13}C NMR ($CDCl_3$) 18.24, 25.97, 26.09, 26.90, 60.37, 71.87, 72.14, 72.57, 73.71, 78.45, 99.51, 104.38, 112.20, 122.24, 127.10, 127.13, 127.32, 128.53, 128.77, 136.91; IR 2978 cm^{-1}; MS (EI) *m/e* (relative intensity) 452 (M^+, 5), 225 (3), 217 (12), 212 (12), 167 (100), 123 (17), 105 (20), 83 (9), 69 (5). Anal. Calcd for $C_{27}H_{32}O_6$: C, 71.66; H, 7.13. Found: C, 71.85; H, 7.37.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-2′-octen-1′-yl]-β-D-fructopyranose (40A): 51% as a white solid; $[\alpha]_D$ −87.4° (*c* 0.154, acetone); mp 74.1 °C; ^1H NMR ($CDCl_3$) δ 0.86 (t, 3 H), 1.25–1.55 (m, 6 H), 1.43 (s, 3 H), 1.50 (s 3 H), 2.09 (m, 2 H), 3.47 (d, J = 7.09 Hz, 1 H), 3.88 (d, J = 8.5 Hz, 1 H), 4.09 (m, 4 H), 4.39 (t, J = 7.08 Hz, 1 H), 4.70 (d, J = 11.8 Hz, 1 H), 4.97 (d, J = 11.8 Hz, 1 H), 5.32 (d, J = 7.05 Hz, 1 H), 5.48 (ddt, J = 7.01 Hz, J = 15 Hz, 1 H), 5.98 (dt, J = 15.24 Hz, 1 H), 7.32–7.60 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 14.01, 22.49, 26.09, 26.91, 28.37, 31.40, 32.03, 59.91, 71.92, 72.54, 75.85, 77.19, 104.40, 104.82, 112.30, 126.86, 127.04, 127.08, 127.28, 128.40, 128.76, 137.17, 138.87, 140.61; IR 2987 cm^{-1}; MS (EI) *m/e* (relative intensity) 494 (M^+), 254 (13), 211 (5), 167 (100), 109 (3), 95 (12), 69 (15), 43 (27). Anal. Calcd for $C_{30}H_{38}O_6$: C, 72.85; H, 7.74. Found: C, 73.02; H, 7.86.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-2′-octen-1′-yl]-β-D-fructopyranose (40B): 36% as an oily solid; $[\alpha]_D$ −76.9° (*c* 0.09, acetone); ^1H NMR ($CDCl_3$) δ 0.87 (t, 3 H), 1.23–1.49 (m, 6 H), 1.43 (s, 3 H), 1.49 (s 3 H), 3.50 (d, J = 7.54 Hz, 1 H), 3.89 (d, J = 8.36 Hz, 1 H), 4.09 (m, 4 H), 4.54 (dd, J = 5.13 Hz, J = 7.51 Hz, 1 H), 4.73 (d, J = 11.96 Hz, 1 H), 4.98 (d, J = 11.96 Hz, 1 H), 5.47 (m, 2 H), 5.85 (m, 1 H), 7.32–7.60 (m, 9 H); ^{13}C NMR ($CDCl_3$) 13.98, 22.46, 26.08, 26.89, 28.27, 31.39, 31.90, 60.27, 71.83, 72.56, 72.74, 73.65, 78.41, 103.59, 104.37, 112.39, 126.66, 127.09, 127.30, 128.48, 128.75, 136.93, 137.57; IR 2926 cm^{-1}; MS (EI) *m/e* (relative intensity) 494 (M^+), 312 (0.7), 282 (0.9), 254 (3), 211 (14), 167 (100), 125 (8), 69 (23). Anal. Calcd for $C_{30}H_{38}O_6$: C, 72.85; H, 7.74. Found: C, 73.13; H, 7.68.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-psicopyranose (41A): 38% as an oily solid; $[\alpha]_D$ −160.6° (*c* 0.127, acetone); ^1H NMR ($CDCl_3$) δ 1.46 (s, 3 H), 1.51 (s, 3 H), 3.75 (d, J = 3.04 Hz, 1 H), 3.87 (m, 2 H), 4.04 (d, J = 9.22 Hz, 1 H), 4.20 (dm, J = 7.36 Hz, 1 H), 4.38 (d, J = 9.22 Hz, 1 H), 4.45 (dd, J = 3.18 Hz, J = 7.36 Hz, 1 H), 4.83 (s, 2 H), 5.42 (d, J = 6.79 Hz, 1 H), 6.17 (dd, J = 6.62 Hz, J = 15.97 Hz, 1 H), 6.75 (d, J = 16.04 Hz, 1 H), 7.23–7.60 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.26, 26.55, 61.84, 72.39, 73.58, 73.72, 73.93, 74.79, 104.83, 105.52, 110.15, 124.51, 126.99, 127.02, 127.15, 127.30, 128.41, 128.49, 128.75, 135.58, 136.16, 136.65, 140.76; IR 2989, 1662 cm^{-1}; MS (EI) *m/e* (relative intensity) 500 (M^+), 333 (7), 256 (4), 167 (100), 131 (23), 91 (5), 72 (11), 43 (12). Anal. Calcd for $C_{31}H_{32}O_6$: C, 74.38; H, 6.44. Found: C, 74.11; H, 6.32.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*S*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-psicopyranose (41B): 36% as a white solid; $[\alpha]_D$ −60.0° (*c* 0.22, acetone); mp 95.3 °C; ^1H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.49 (s, 3 H), 3.72 (d, J = 3.1 Hz, 1 H), 3.96 (m, 2 H), 4.01 (d, J = 9.24 Hz, 1 H), 4.24 (d, J = 9.23 Hz, 1 H), 4.29 (dm, 1 H), 4.54 (dd, J = 3.29 Hz, J = 6.68 Hz, 1 H), 4.83 (s, 2 H), 5.86 (d, J = 5.93 Hz, 1 H), 6.10 (dd, J = 5.91 Hz, J = 15.85 Hz, 1 H), 6.70 (d, J = 15.85 Hz, 1 H), 7.24–7.60 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.36, 26.51, 62.32, 72.40, 73.31, 73.43, 73.67, 75.36, 105.22, 105.47, 110.60, 125.95, 126.92, 127.09, 127.21, 127.35, 128.31, 128.56, 128.77, 134.08, 135.76, 136.56, 140.75, 140.95; IR 2989, 1655 cm^{-1}; MS (EI) *m/e* (relative intensity) 500 (M^+), 333 (4), 256 (6), 217 (2), 167 (100), 131 (18), 91 (5), 72 (8), 43 (10). Anal. Calcd for $C_{31}H_{32}O_6$: C, 74.38; H, 6.44. Found: C, 74.15; H, 6.50.

1,2-*O*-Isopropylidene-3-*O*-benzyl-4,5-*O*-[3′-phenyl-2′-propyn-1′-yl]-β-D-fructopyranose (44): 84% as colorless oil (*endo*:*exo* = 10:1 based on ^1H NMR); ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.48 (s, 3 H), 3.80 (d, J = 7.43 Hz, 1 H), 3.84 (d, J = 8.59 Hz, 1 H), 4.10 (d, J = 8.59 Hz, 1 H), 4.13 (s, 2 H), 4.12 (m, 1 H), 4.49 (dd, J = 5.1 Hz, J = 7.50 Hz 1 H), 4.73 (d, J = 11.97 Hz, 1 H), 5.02 (d, J = 11.97 Hz, 1 H), 5.91 (s, 1 H), 7.21–7.51 (m, 10 H).

1,2-*O*-Isopropylidene-3-*O*-benzyl-4,5-*O*-[(1′*R*)-*cis*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (45). To a solution of the alkynal acetal **44** (*endo*:*exo* = 10:1, 350 mg, 0.83 mmol) in methanol (8 mL) was added Lindlar catalyst (35 mg, 5% $Pd/CaCO_3$. PbO). Then, a toy balloon filled with hydrogen was attached to the flask. The reaction mixture was stirred overnight at room temperature and then filtered through Celite. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel with 1:6:2 ether–hexane–chloroform to afford the *cis*-alkenal acetal **45** (287 mg, 82%) as a white solid: $[\alpha]_D$ −14.5° (*c* 0.069, acetone); mp 79.7 °C; ^1H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.49 (s, 3 H), 3.49 (d, J = 7.22 Hz, 1 H), 3.87 (d, J = 8.41 Hz, 1 H), 4.07–4.14 (m, 4 H), 4.41 (dd, J = 5.98 Hz, J = 7.19 Hz, 1 H),

4.68 (d, J = 12.04 Hz, 1 H), 4.95 (d, J = 12.04 Hz, 1 H), 5.63 (d, J = 7.69 Hz, 1 H), 5.70 (dd, J = 7.65 Hz, J = 10.54 Hz, 1 H), 6.85 (d, J = 10.7 Hz, 1 H), 7.24–7.38 (m, 10 H); ^{13}C NMR ($CDCl_3$) 26.04, 26.92, 59.88, 71.85, 72.93, 76.04, 76.40, 77.37, 99.92, 104.38, 112.4, 127.63, 127.92, 128.22, 128.27, 128.98, 135.5, 136.15, 138; IR 3032, 1649 cm^{-1}; MS (EI) *m/e* (relative intensity) 424 (M^+, 10), 333 (11), 260 (10), 217 (4), 180 (7), 171 (21), 131 (22), 115 (23), 91 (100), 69 (7), 59 (12). Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.68; H, 6.71.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[6′-phenyl-2′-hexyn-1′-yl]-β-D-fructopyranose (46): 65% as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.48 (s, 3 H), 1.86 (m, 2 H), 2.29 (m, 2 H), 2.71 (t, 2 H), 3.77 (d, J = 7.46 Hz, 1 H), 3.88 (d, J = 8.42 Hz, 1 H), 4.06 (m, 4 H), 4.44 (dd, J = 5.08 Hz, J = 7.49 Hz, 1 H), 4.73 (d, J = 12.03 Hz, 1 H), 5.04 (d, J = 12.03 Hz, 1 H), 5.69 (t, 1 H), 7.12–7.58 (m, 14 H); ^{13}C NMR ($CDCl_3$) 18.18, 26.06, 29.91, 29.70, 34.79, 59.56, 71.73, 73.27, 75.33, 76.04, 77.86, 87.78, 93.25, 104.49, 112.34, 126.01, 127.04, 127.07, 127.26, 128.22, 128.41, 128.44, 128.75, 137.29, 140.53, 140.88, 141.15; IR 2932 cm^{-1}.

1,2-*O*-Isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-*cis*-6′-phenyl-2′-hexen-1′-yl]-β-D-fructopyranose (47). To a solution of the acetylenic acetal **46** (800 mg, 1.48 mmol) in methanol (20 mL) was added Lindlar catalyst (80 mg, 5% Pd/$CaCO_3$·PbO). Then, a toy balloon filled with hydrogen was attached to the flask. The reaction mixture was stirred overnight at room temperature and then filtered through Celite. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel with 1:2 ether–hexane to afford the *endo* acetal **47** (632 mg, 79%) as a white solid: $[\alpha]_D$ −53.2° (*c* 0.062, acetone); mp 90.8 °C; ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.49 (s, 3 H), 1.75 (m, 2 H), 2.22 (m, 2 H), 2.63 (t, 2 H), 3.45 (d, J = 7.09 Hz, 1 H), 3.87 (d, J = 8.45 Hz, 1 H), 4.08 (m, 4 H), 4.38 (dd, J = 5.61 Hz, J = 7.14 Hz 1 H), 4.68 (d, J = 12.06 Hz, 1 H), 4.96 (d, J = 12.06 Hz, 1 H), 5.48 (ddt, J = 8.02 Hz, J = 10.69 Hz, 1 H), 5.66 (d, J = 8.02 Hz, 1 H), 5.82 (dt, J = 10.65 Hz, 1 H), 7.14–7.59 (m, 14 H); ^{13}C NMR ($CDCl_3$) 26.08, 26.91, 27.32, 31.04, 35.27, 59.90, 71.88, 72.67, 75.92, 76.56, 77.10, 99.37, 104.38, 112.27, 125.79, 127.03, 127.08, 127.25, 128.34, 128.44, 128.74, 137.17, 137.51, 141.98; IR 2930 cm^{-1}; MS (EI) *m/e* (relative intensity) 542 (M^+, 2), 360 (5), 302 (2), 167 (100), 131 (20), 117 (11), 91 (48), 81 (15). Anal. Calcd for $C_{34}H_{38}O_6$: C, 75.25; H, 7.06. Found: C, 75.47; H, 7.24.

General Procedure for Cyclopropanation of Acetals of α,β-Unsaturated Aldehyde with Sugar Diol: Preparation of (1*R*,2*R*)-*trans*-1-(Hydroxymethyl)-2-phenylcyclopropane from 3-*O*-Benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1′*R*)-*trans*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyranose (28A). To a solution of the *trans*-cinnamaldehyde acetal **28A** (150 mg, 0.35 mmol) in 1,2-dichloroethane (10 mL) were added 1.0 M diethylzinc in hexane (1.77 mL, 1.77 mmol) and diiodomethane (0.29 mL, 3.5 mmol) at −20 °C. The reaction mixture was stirred for 24 h at 0 °C, the reaction was quenched with saturated ammonium chloride solution, and then the solution was extracted with ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and evaporated. The resulting residue was purified by flash chromatography on silica gel with 1:6:2 ether–hexane–chloroform to give the cyclopropanated acetal (131 mg, 84.8%) as a colorless oil. A solution of the acetal (130 mg, 0.3 mmol) in 80% acetic acid in H_2O (3 mL) was stirred for 15 min at 60 °C and then cooled to room temperature. The pH of the solution was adjusted to 7.5 with saturated $NaHCO_3$, and then the solution was extracted with ethyl acetate. The organic layer was washed with water and saturated NaCl solution, dried over magnesium sulfate, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:7 ethyl acetate–hexane to give (1*R*,2*R*)-*trans*-2-phenylcyclopropanecarboxaldehyde (40.3 mg, 93%) as a colorless oil. Further elution with 1:2 acetone–hexane gave the chiral auxiliary 3-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (74 mg, 80.3%) as a white solid. To a solution of the aldehyde (40 mg, 0.27 mmol) in ethanol (3 mL) was added sodium borohydride (15.5 mg, 0.41 mmol) at room temperature. The reaction mixture was stirred for 1 h at room temperature, and the reaction was quenched with saturated NH_4Cl solution. After evaporation of the solvent, the solution was diluted with water and ether. The organic layer was washed with water and saturated NaCl solution, dried over magnesium sulfate, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:4 ethyl acetate–hexane to give (1*R*,2*R*)-*trans*-1-(hydroxymethyl)-2-phenylcyclopropane (38.5 mg, 95%) as a colorless oil: $[\alpha]_D$ −64.7° (*c* 0.19, EtOH as 71.3% ee) {lit.[11c] $[\alpha]_D$ −92° (*c* 1.23, EtOH)}; TLC (20% ethyl acetate/hexane) R_f 0.11; ^{1}H NMR ($CDCl_3$) δ 0.92 (m, 2 H), 1.45 (m, 1 H), 1.83 (m, 1 H), 2.08 (b, OH), 3.60 (dd, J = 6.71 Hz, J = 2.24 Hz, 2 H), 7.16 (m, 5 H); ^{13}C NMR ($CDCl_3$); 13.77, 21.27, 25.25, 66.51, 125.63, 125.81, 128.32, 142.38; IR 3350 cm^{-1}; MS (EI) *m/e* (relative intensity) 148 (M^+, 22), 130 (21), 117 (100), 104 (44), 91 (32), 77 (8), 51 (8).

The results with other sugar derivatives are summarized in Tables 4, 5, 6, and 9. The properties of pertinent compounds are listed below.

(1*R*,2*R*)-*trans*-2-((Benzyloxy)methyl)-1-(hydroxymethyl)cyclopropane: a colorless oil; $[\alpha]_D$ −3.05° (*c* 0.6, $CHCl_3$ as 21% ee) {lit.[11b] $[\alpha]_D$ −6.0° (*c* 1.02, $CHCl_3$ as 35% ee)}; TLC (33% ethyl acetate/hexane) R_f 0.15; ^{1}H NMR ($CDCl_3$) 0.43 (t, 2 H), 0.99 (m, 2 H), 1.64 (b, 1 H), 3.38 (m, 4 H), 4.51 (s, 2 H), 7.30 (m, 5 H); ^{13}C NMR ($CDCl_3$) 7.99, 16.75, 19.78, 66.20, 72.59, 73.46, 127.59, 127.68, 128.36, 141.10; IR 3401 cm^{-1}; MS (EI) *m/e* (relative intensity) 192 (M^+), 161, 129 (2), 107 (40), 91-(100), 68(13).

(1*R*,2*R*)-*trans*-1-(Hydroxymethyl)-2-(2′-phenethyl)cyclopropane: a colorless oil; $[\alpha]_D$ −17.1° (*c* 1.5 as 52% ee) lit.[17] $[\alpha]_D$ −24.6° (*c* 1.3, $CHCl_3$ as 80% ee); TLC (25% ethyl acetate/hexane) R_f 0.2; ^{1}H NMR ($CDCl_3$) 0.34 (m, 2 H), 0.59 (m, 1 H), 1.20 (b, 1 H), 1.52 (m, 2 H), 2.69 (m, 2 H), 3.38 (m, 2 H), 7.20 (m, 5 H); ^{13}C NMR ($CDCl_3$) 9.76, 16.80, 21.38, 35.27, 35.82, 66.97, 125.73, 128.77, 128.42, 142.15; IR 3402 cm^{-1}; MS (EI) *m/e* (relative intensity) 176 (M^+), 158 (3), 129 (34), 104 (21), 91 (100), 65 (10).

(1*R*,2*R*)-*trans*-1-(Hydroxymethyl)-2-pentylcyclopropane: a colorless oil, $[\alpha]_D$ −24° (*c* 0.1, $CHCl_3$ as 64% ee); TLC (20% ethyl acetate/hexane) R_f 0.25; ^{1}H NMR ($CDCl_3$) δ 0.30 (m, 2 H), 0.58 (m, 1 H), 0.85 (m, 4 H), 1.24 (m, 9 H), 3.40 (dd, 2 H); ^{13}C NMR ($CDCl_3$) 9.91, 14.06, 17.21, 21.22, 22.65, 29.27, 31.65, 33.55, 67.26; IR 3354 cm^{-1}.

(1*R*)-2,2-Dimethylcyclopropanecarboxylic Acid. To a solution of 1,2-*O*-isopropylidene-3-*O*-(*p*-phenylbenzyl)-4,5-*O*-[(1′*R*)-3′-methyl-2′-buten-1′-yl]-β-D-fructopyranose (**39A**, 330 mg, 0.73 mmol) were added 1.0 M diethylzinc in hexane (3.65 mL, 3.65 mmol) and diiodomethane (0.61 mL, 7.3 mmol) at −15 °C. The reaction mixture was then stirred for 24 h at 0 °C. The reaction was quenched with saturated aqueous NH_4-Cl, and the mixture was extracted with ethyl acetate. The organic layer was dried over $MgSO_4$, filtered, and evaporated. The resulting residue was purified by flash chromatography on silica gel with 1:6:2 ether–hexane–chloroform to give pure cyclopropanated acetal (274 mg, 81%) as a colorless oil, to which (200 mg, 0.43 mmol) in ethyl acetate (20 mL) at −78 °C ozone gas was passed. After the solution was stirred for 1 h at 23 °C, excess ozone was removed by flushing the system with nitrogen. The solvent was removed by evaporation, and the residue was purified to give pure 1,2-*O*-isopropylidene-3-*O*-(*p*-phenylbenzoyl)-5-*O*-((2′,2′-dimethylcyclopropyl)carbonyl)-β-D-fructopyranose (169 mg, 79%) as a colorless oil after flash chromatography on silica gel with 1:3 ethyl acetate–hexane. To a solution of the ester fructopyranose (150 mg, 0.3 mmol) in ethanol (2 mL) was added aqueous 2 N NaOH (0.6 mL) at

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(17) The $[\alpha]_D$ value of (1*R*,2*R*)-*trans*-1-(hydroxymethyl)-2-(2′-phenethyl)cyclopropane, which was cited in ref 32b, was obtained from Dr. Kobayashi at Sagami Chemical Research Center.

rt, and the mixture was stirred for 1 h at rt. After evaporation of solvent, the pH of the solution was adjusted to 3 with dilute HCl and then extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. To the residue was added isopropyl ether. After filtration of resulting solid, the filtrate was evaporated to give 2,2-dimethylcyclopropanecarboxylic acid (17.5 mg, 51%) as a colorless oil: $[\alpha]_D$ −85° (*c* 0.1, $CHCl_3$ as 60% ee) {lit.[14] *ent*-form $[\alpha]_D$ +142° (*c* 1.01, $CHCl_3$)}; ^1H NMR ($CDCl_3$) δ 0.95 (dd, J = 5.47 Hz, J = 8.95 Hz, 1 H), 1.04 (t, 1 H), 1.15 (s, 3 H), 1.23 (s, 3 H), 1.45 (dd, J = 5.48 Hz, J = 8.95 Hz, 1 H); ^{13}C NMR ($CDCl_3$); 18.72, 22.86, 24.35, 26.74, 27.00, 179.62; IR 3051, 1692 cm^{-1}.

Methyl (1*R*,2*S*)-*cis*- and (1*S*,2*S*)-*trans*-2-Phenylcyclopropanecarboxylates. According to the general procedure, a solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-4,5-*O*-[(1*R*)-*cis*-3′-phenyl-2′-propen-1′-yl]-β-D-fructopyanose (**45**, 280 mg, 0.66 mmol), 1.0 M diethylzinc in hexane (3.3 mL, 3.3 mmol), diiodomethane (0.55 mL, 6.6 mmol), and 1,2-dichloroethane (17 mL) was stirred for 20 h at 0 °C. After the usual workup, the resulting residue was purified by flash chromatography on silica gel with 1:6:2 ether−hexane−chloroform to give a mixture of 2:1 of cyclopropanated *cis*-**56** and *trans*-**57** compounds (276 mg 96%) as a colorless oil (based on ^1H NMR, *cis* H_9, δ 2.35; *trans* H_9, δ 2.10). To a mixture of **56** and **57** (250 mg, 0.57 mmol) was added 80% AcOH in H_2O (5 mL). The reaction mixture was stirred for 1 h at 60 °C and cooled to room temperature. The pH of the solution was adjusted to 7.5 with saturated $NaHCO_3$ solution, and then the solution was extracted with ether. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with 1:7 ethyl acetate−hexane to give a mixture of 2:1 of (1*R*,2*S*)-*cis*- and (1*S*,2*S*)-*trans*-2-phenylcyclopropanal (77.8 mg 93%) as a colorless oil (*cis* aldehyde δ 8.64, *trans* aldehyde δ 9.30). To a mixture solution of (1*R*,2*S*)-*cis*- and (1*S*,2*S*)-*trans*-2-phenylcyclopropanal (75 mg, 0.51 mmol), sodium cyanide (252 mg, 5.1 mmol), acetic acid (0.12 mL, 2.1 mmol), and methanol (10 mL) was added manganese(IV) oxide (1.79 g, 20.5 mmol) at room temperature. The reaction mixture was stirred for 48 h at room temperature and then filtered through Celite. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel with 1:5 ether−hexane to give colorless oils of (1*R*,2*S*)-*cis* product (50.1 mg, 55%) **58** and (1*S*,2*S*)-*trans* product (25 mg, 28%) **59**, respectively.

Methyl (1*R*,2*S*)-*cis*-2-phenylcyclopropanecarboxylate: a colorless oil; $[\alpha]_D$ −29.7° (*c* 0.175, $CHCl_3$ as 82% ee) {lit.[13] *ent*-form $[\alpha]_D$ +32.8° (*c* 1.99, $CHCl_3$)}; TLC (17% ethyl acetate/hexane) R_f 0.23; ^1H NMR ($CDCl_3$) δ 1.31 (m, 1 H), 1.69 (m, 1 H), 2.07 (m, 1 H), 2.56 (q, 1 H), 3.41 (s, 3 H), 7.21 (m, 5 H); MS (EI) *m/e* (relative intensity) 176 (M^+, 14), 144 (22), 115 (100), 91 (43), 77 (14), 63 (15).

Methyl (1*S*,2*S*)-*trans*-2-phenylcyclopropanecarboxylate: a colorless oil; $[\alpha]_D$ +173° (*c* 0.185, $CHCl_3$ as 58% ee) {lit.[13] $[\alpha]_D$ +324.7° (*c* 1.24, $CHCl_3$)}; TLC (17% ethyl acetate/hexane) R_f 0.28; ^1H NMR ($CDCl_3$) δ 1.30 (m, 1 H), 1.57 (m, 1 H), 1.89 (m, 1 H), 2.51 (m, 1 H), 3.70 (s, 3 H), 7.20 (m, 5 H); ^{13}C NMR ($CDCl_3$) 16.99, 23.92, 26.26, 51.89, 126.21, 126.51, 128.47; IR 1728 cm^{-1}; MS (EI) *m/e* (relative intensity) 176 (M^+, 43), 144 (38), 117 (100), 91 (20), 59 (5).

(1*R*,2*S*)-*cis*-1-(Hydroxymethyl)-2-phenylcyclopropane. To a mixture of (1*R*,2*S*)-methyl *cis*-2-phenylcyclopropanecarboxylate (17.6 mg, 0.1 mmol) in dried ether (1 mL) was added 1.0 M diisobutylaluminum hydride in hexane (0.4 mL, 0.4 mmol) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then poured onto water and ether. The organic layer was separated, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with 1:4 ethyl acetate−hexane to afford (1*R*,2*S*)-*cis*-1-(hydroxymethyl)-2-phenylcyclopropane (**60**, 13.2 mg, 89%) as a colorless oil: $[\alpha]_D$ −60.8° (*c* 0.09 $CHCl_3$ as 82% ee) {lit.[16] *ent*-form $[\alpha]_D$ +39° (*c* 2.42 $CHCl_3$ as 50% ee), lit.[11a] $[\alpha]_D$ −52° (*c* 1.3, EtOH as 70% ee)}; TLC (20% ethyl acetate/hexane) R_f 0.15; ^1H NMR ($CDCl_3$) δ 0.87 (q, 1 H), 1.04 (m, 1 H), 1.41 (b, 1 H), 1.47 (m, 1 H), 2.27 (m, 1 H), 3.24 (dd, J = 8.39 Hz, 1 H), 3.46 (dd, J = 11.66 Hz, 1 H), 7.21 (m, 5 H); ^{13}C NMR ($CDCl_3$); 7.66, 20.69, 20.82, 62.90, 126.19, 128.27, 128.61, 138.20; IR 3370 cm^{-1}; MS (EI) *m/e* (relative intensity) 148 (M^+, 31), 130 (34), 117 (100), 91 (61), 65 (15), 51 (20).

(1*R*,2*S*)-*cis*-1-(Hydroxymethyl)-2-(3′-phenylpropyl)cyclopropane: a colorless oil; $[\alpha]_D$ +18.2° (*c* 0.77, EtOH as 80.1% ee) {lit.[11a] $[\alpha]_D$ +19° (*c* 0.7, EtOH as 81% ee)}; TLC (20% ethyl acetate/hexane) R_f 0.18; ^1H NMR ($CDCl_3$) δ −0.05 (m, 1 H), 0.75 (m, 1 H), 0.89 (m, 1 H), 1.12 (m, 1 H), 1.14 (b, OH), 1.28 (m, 1 H), 1.50 (m, 1 H), 1.77 (m, 1 H), 2.63 (m, 1 H), 3.59 (m, 1 H), 7.25 (m, 5 H); ^{13}C NMR ($CDCl_3$) 9.46, 15.99, 18.17, 28.14, 31.83, 35.75, 63.27, 125.67, 128.28, 128.36; IR 3402 cm^{-1}; MS (EI) *m/e* (relative intensity) 190 (M^+, 1), 159 (5), 131 (32), 104 (56), 91 (100), 77 (10).

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Supplementary Material Available: Global minimum structures of acetals **28A**, **28B**, **35A**, **35B**, **41A**, **41B**, and **45**, obtained by force field calculation (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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