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Diacetone Glucose Architecture as a Chirality Template. II.[1] Versatile Synthon for the Chiral Deuterium Labeling and Synthesis of All Diastereoisomers of Chirally Monodeuterated Glycerol

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Abstract: *Chirally deuterated ethylene oxide derivatives attached to a diacetone glucose template were developed as new versatile synthons for chiral deuterium labeling. All four diastereoisomers of chirally monodeuterated glycerol were also synthesized by chirality transcription from the same template.*

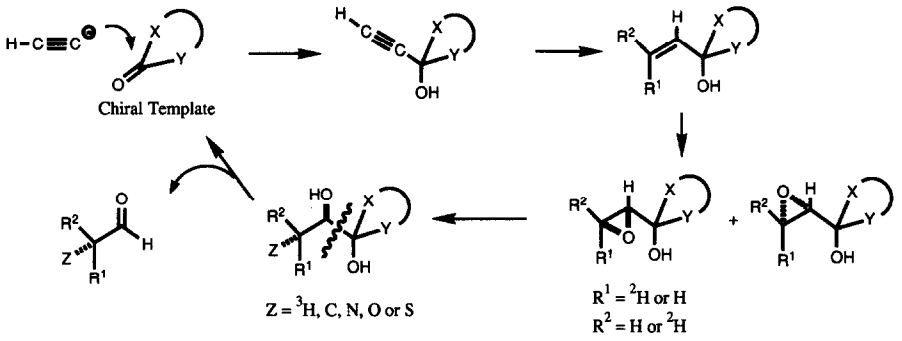
The mechanisms and stereochemistry of enzyme reactions are of current interest in bio-organic chemistry. Essential to the stereochemical investigations of organic reactions are suitable isotopically labeled substrates and appropriate analytical methods for the chirally labeled reaction products. A number of approaches have so far been described for the synthesis of various compounds having chirally labeled site(s) by the use of enzymatic and/or chemical reactions.[3] Nonetheless, highly versatile methodology is still strongly desired especially to create chirally labeled methylene groups substituted with a hetero-atom. It should also be pointed out that most of the chiral labeling methods so far described are conceptually unrelated to one another so that rather tedious works are required to correlate and to unambiguously determine the stereochemistry of each chiral center from one compound to another. Therefore, it is desirable to develop pivotal synthons which can be transformed into various compounds with chirally labeled sites, thereby allowing easy correlation of each absolute stereochemistry.

This paper describes a new preparative method of such versatile synthons with a chirally deuterated ethylene oxide function on the basis of a chirality transcription approach in detail.[4] Also described is an extension of this methodology to the synthesis of chirally monodeuterated glycerol and derivatives thereof.

Although ingenious Sharpless epoxidation of deuterated allyl alcohol systems can be widely applicable, it is not always suitable, especially for rather simple ones. Our approach is based on a concept of chirality transcription from a covalently bound chiral template which is derived readily from a carbohydrate.

Carbohydrates are important sources of chirality in organic synthesis, especially for the synthesis of physiologically significant natural products.[5] During our first synthesis of D-(6*R*)- and D-(6*S*)-(6-$^2H_1$)glucose,[6] we became aware of possible stereochemical control element to be exploited, that is, the intrinsic molecular architecture of carbohydrate may affect an important function as a template for chirality transcription irrespective of individual stereogenic centers. In this context, our attention was primarily focussed on utilization of the chirality of D-glucose, one of the major chiral resources today. A basic concept of the present approach is illustrated in Scheme 1. As can be seen, the chirality donor can conceptually be recovered and recycled as a template depending upon the final targets. Molecules with an ethynyl group seemed to be the

most suitable starting material having appropriate oxidation state for chemical manipulations to various functional groups with simultaneous introduction of hydrogen isotopes, as exemplified in the classical synthesis of chiral acetic acid by Cornforth *et al.*[7] An acetylenic carbanion can be readily added to a chiral carbonyl compound serving as a template. The stereoselectivity of this addition reaction is crucial in the present context. The ethynyl carbinol can be conveniently deuterated and stereospecifically reduced to a monodeuterated ethenyl carbinol. Epoxidation of the latter turns out to give chirally deuterated ethylene oxide derivatives, which are expected in principle to be used as a suitable acceptor of various nucleophiles through a well-defined stereochemical course at the labeled oxymethylene site. The resulting substituted glycol compound may then oxidatively be chopped off into two pieces, *i.e.* an aldehyde or an acid and the starting carbonyl template.

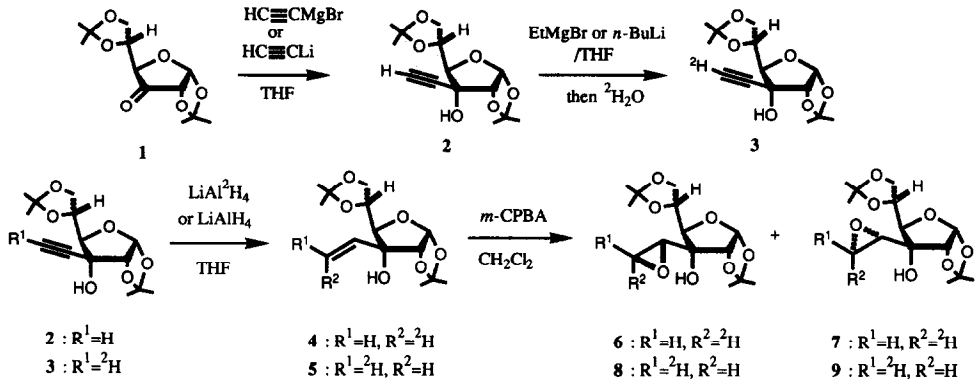


Scheme 1

A crucial feature was the selection of a suitable chiral template as mentioned above. An attempt to react 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-furanos-5-ulose with ethynylmagnesium bromide gave a diastereoisomeric mixture of 5-*C*-ethynyl derivatives. Although the mixture was chromatographically separable, both isomers were uncrystallized syrup. These preliminary results were not as desired, because tedious chromatographic separation was required to obtain each diastereoisomer in pure forms. Further exploitation with molecular models allowed us to choose 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-3-hexulofuranose (**1**) as a promising template (Scheme 2). Three features should be pointed out as to the reasons why we chose **1** as a chiral template. Firstly, the ketone **1** can be prepared easily in good yield from D-glucose in two steps. Secondly, the reaction of **1** with a nucleophile is known to give rise to a product with high stereoselectivity through an attack of the nucleophile from the top face of the furanulose ring because of the steric hindrance of the bulky 1,2-*O*-isopropylidene substituent. Thirdly, the diastereotopic faces of the derived ethenyl intermediate were expected to be differentiated conceptually due to the steric bulkiness of the dioxolane group on the C-4 position of the furanose ring. In other words, by taking advantage of this carbohydrate ketone, we can utilize the dual steric effects of each of the bulky protecting groups sequentially to control the stereochemical courses.

The reaction of acetylene with **1** *via* either the Grignard reagent or lithium acetylide exclusively afforded crystalline 3-*C*-ethynyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**2**) in an excellent yield.[1] The acetylenic hydrogen of **2** were able to be exchanged with a deuterium first by treatment with butyl lithium or ethylmagnesium bromide, followed by hydrolysis with deuterium oxide to give a deuterated acetylene **3**.

Stereospecific reduction of the triple bond of **2** with simultaneous regioselective introduction of a deuterium was readily affected in high yield by treatment of **2** with an excess amount of $LiAl^2H_4$ in tetrahydrofuran (THF) at 0 °C or at room temperature to yield (*Z*)-olefin **4**, δ_H: 5.37 ppm (d, *J*=10.5 Hz) and 5.82 ppm (d, *J*=10.5 Hz), δ_C: 116.3 ppm (t, *J*=24 Hz) and 134.7 ppm.[1] Treatment of **3** with $LiAlH_4$, followed by quenching with H_2O afforded stereospecifically γ-deuterated (*E*)-olefin **5**, δ_H: 5.56 ppm (d, *J*=17.6 Hz) and 5.82 ppm (d, *J*=17.9 Hz), δ_C: 116.3 ppm (t, *J*=24 Hz) and 134.6 ppm.



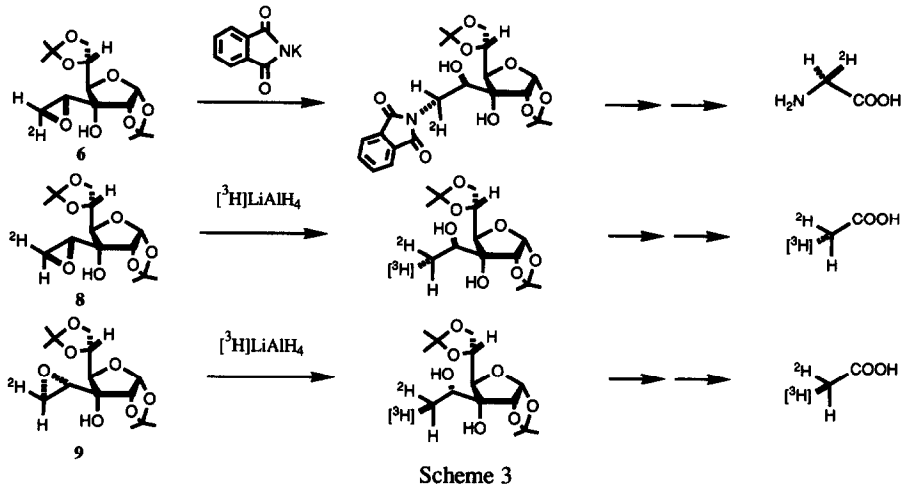
Scheme 2

The next crucial step was the oxidation of the deuterated allyl alcohols. As was anticipated from the relatively low electron density of the monosubstituted ethylene function, epoxidation of **4** with an excess amount (5.5 eq.) of *m*-CPBA required rather long reaction time for completion. After separation of the products by medium pressure chromatography on silica gel,[8] **6** and **7** were isolated in a ratio of ca. 3 : 1 to 5 : 1. The carbohydrate moiety was apparently significant as a chiral auxiliary for the separation of the diastereoisomers as well. The stereochemistries of the products, **6** and **7**, were first assigned by taking into account of the steric effect of the bulky dioxolane group on the C-4 position of the furanose ring *vide supra*. Thus, the major epoxide **6** was presumed to have (*R*) configurations both at the C-1' and C-2' positions in the side chain and the minor epoxide **7** being predicted to have (*S*) configurations at C-1' and C-2' positions.

Similarly, the stereoisomeric (*E*)-olefin **5** was epoxidized to a major epoxide **8** and a minor **9**. It should be pointed out that all the compounds described above are crystalline, which is quite important to obtain diastereoisomerically homogeneous products by repeating recrystallization.

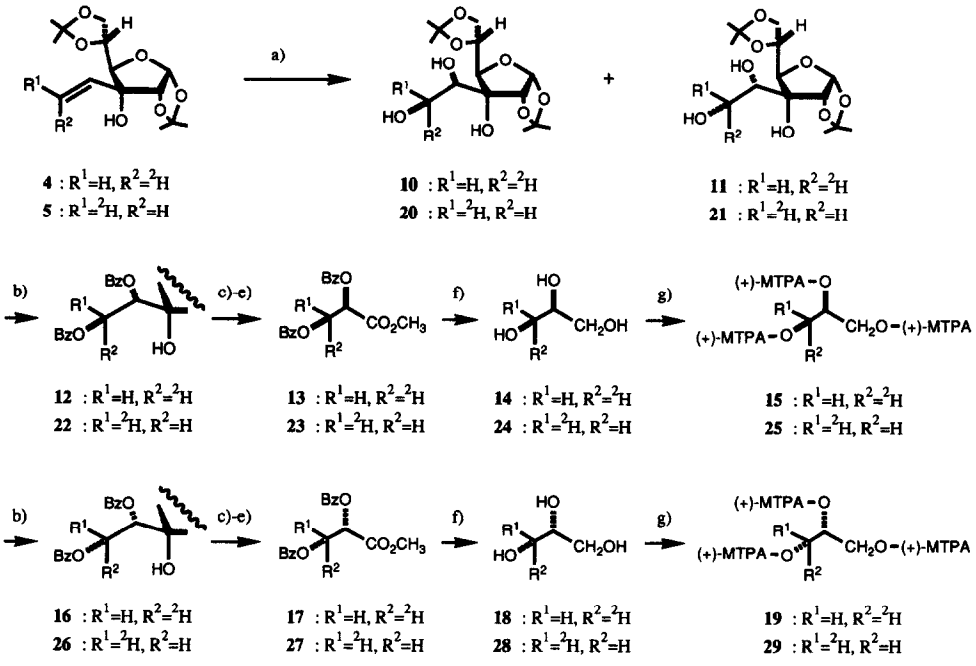
The absolute stereochemistry of each chirally deuterated ethylene oxide derivative was unambiguously determined by conversion to stereochemically known compounds as depicted in Scheme 3. Thus, **6** was transformed into (*S*)-(2-$^2H_1$)glycine through the nucleophilic opening with potassium phthalimide to a corresponding phthaloylaminodiol.[4] The stereoisomeric epoxides **8** and **9** were, on the other hand, converted into the known (*S*)- and (*R*)-[2-$^3H_1$](2-$^2H_1$)acetic acid, respectively, by reduction with tritiated lithium aluminium hydride.[9] In addition, Brimacombe *et al.* subsequently confirmed independently the absolute stereochemistry of the unlabeled phthalimide intermediate by means of the X-ray crystallographic analysis.[10] To be emphasized is that, as a consequence, these chirally deuterated epoxides **6**, **7**, **8** and **9** turned out to serve as crucial and unambiguous logical links between chiral glycines and chiral acetic acids on the basis of the absolute stereochemistry of D-glucose. It thus appears that these deuterated ethylene oxide derivatives **6**, **7**, **8** and **9** are versatile synthons with high chiral purity for various compounds stereospecifically labeled at a prochiral methylene center and may play pivotal key roles to correlate the stereochemistry of biologically important chirally deuterated compounds. Carbon- as well as other nucleophiles may be utilized for the transformation of these epoxides. For instance, we have recently synthesized a derivative of (2*S*,3*R*)-(3-$^2H_1$)-2-hydroxyisocaproic acid from the epoxide **6** for the studies of the stereochemistry of decarboxylation reaction by 3-isopropylmalate dehydrogenase.[11]

It seemed logical anticipation that the diastereotopic face of the monodeuterated olefins **4** and **5** can be differentiated with other oxidation reactions. Glycerol is a biologically ubiquitous molecule. It is an essential structural component of membrane lipids in any living cells. It is also an important starting material in the various metabolisms for production of cell constituents as well as of energy. Introduction of hydrogen isotopes to the glycerol molecule is therefore biologically significant to chase its fate in the living systems from the stereochemical viewpoints. Glycerol is quite intriguing because a single deuterium substitution to one of the



Scheme 3

hydroxymethyl groups of the achiral glycerol molecule simultaneously induces two chiral centers.[12,13] Thus, the synthesis of stereochemically defined monodeuterated glycerols requires special designs to pursue. Here, we demonstrate a rather simple synthesis of all four diastereoisomers of monodeuterated glycerol.



Reagents: a) OsO_4, NMO/ ^{t}BuOH-THF-water; b) PhCOCl/pyridine; c) ^+H; d) $NaIO_4$; e) CH_2N_2; f) $LiAlH_4$/THF; g) (*R*)-(+)-MTPACl/pyridine

Scheme 4

The OsO_4 oxidation of the (*Z*)-olefin **4** underwent smoothly either under the stoichiometric or under the catalytic conditions in the presence of *N*-methylmorpholine *N*-oxide to give, as being anticipated, a

diastereoisomeric mixture of *syn*-dihydroxylated products **10** and **11** in the ratio of 2.5 : 1 to 3 : 1. Because of the effective auxiliary ability of the carbohydrate moiety, the isomers were easily separated by conventional silica gel column chromatography.

The stereochemistry of the major triol **10** was tentatively assigned to be 1'-*R* configuration by prediction that the *re*-face of the ethylenic bond is stereochemically less congested as discussed above for epoxidation. The absolute stereochemistry of **10** was subsequently confirmed as an ester derivative of (2*R*)-glyceric acid *vide post.*

Although the following processes were somewhat apart from the above-mentioned template concept in that the original carbohydrate moiety was immolated, the chemistry involved in the transformation into the monodeuterated glycerols was rather straightforward. The triol **10** was treated first with benzoyl chloride in pyridine to give, as expected, a 1',2'-di-*O*-benzoyl derivative **12**. The unesterified tertiary hydroxyl group was essential for the oxidative cleavage of 1,2,3-triol system of **10** to derive a carboxylic acid function. The dibenzoate **12** was then hydrolyzed under acidic conditions to remove the isopropylidene groups. The resulting polyol di-*O*-benzoate intermediate was subjected, without purification, to an exhaustive oxidation with $NaIO_4$ to afford 2,3-di-*O*-benzoyl glyceric acid, which in turn converted with CH_2N_2 to its methyl ester **13**, $[\alpha]_D$ - 24.7 °.

The configuration at C-2 of **13** was determined to be *R* by comparison of the optical rotation with an authentic antipode with (2*S*)-configuration, $[\alpha]_D$ + 22.5 °, prepared from L-serine *via* diazotization, esterification,[14] and benzoylation. The ester dibenzoate **13** was totally reduced with $LiAlH_4$ to give, after removal of the resulting benzyl alcohol by solvent extraction and chromatographic purification, *sn*-(1*R*)-(1-$^2H_1$)glycerol **14** as a syrup. The characterization of **14** was carried out as its tri-*O*-(*R*)-(+)-α-methoxy-α-trifluoromethyl-phenylacetate (MTPA) derivative **15**. The minor triol **11** was transformed similarly *via* **17** to *sn*-(3*S*)-(3-$^2H_1$)glycerol **18**.

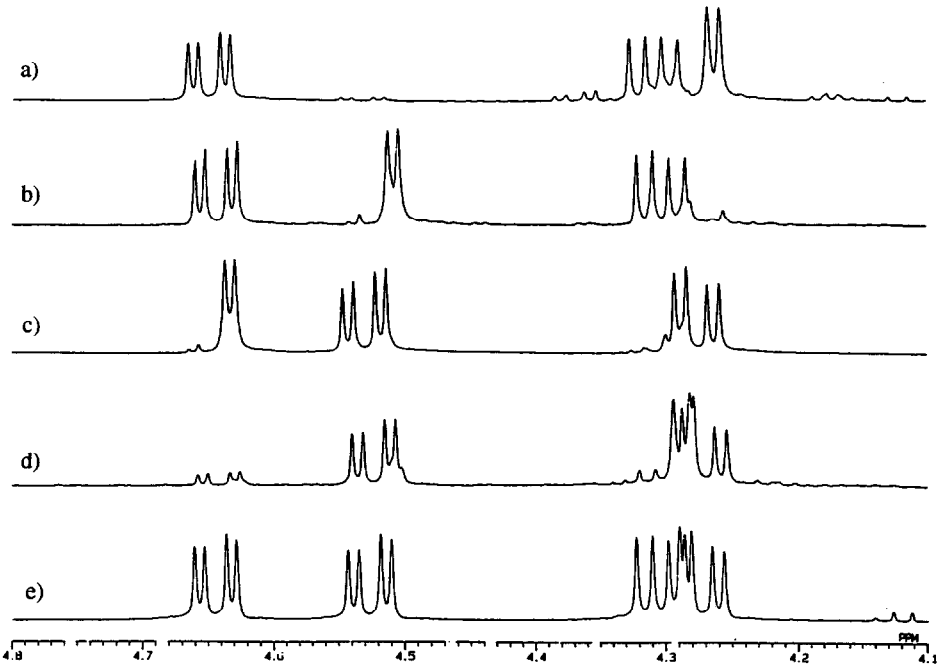


Figure 1. Pertinent region of 500 MHz ^1H NMR spectra of tri-(*R*)-(+)-MTPA ester derivatives of chirally monodeuterated glycerols : (a) *sn*-(1*S*)-**25**, (b) *sn*-(1*R*)-**15**, (c) *sn*-(3*S*)-**19**, (d) *sn*-(3*R*)-**29** and (e) non labeled control.

From the isomeric (*E*)-olefin **5**, *sn*-(1*S*)-(1-$^2H_1$)glycerol **24** and *sn*-(3*R*)-(3-$^2H_1$)glycerol **28** were prepared similarly. Thus, the present approach utilizing 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-3-hexulofuranose **1** offers an easy access to all four diastereoisomers of chirally monodeuterated glycerol. Fig. 1 illustrates the pertinent methylene regions of the 500 MHz ^1H NMR spectra of all four glycerol isotopomers in the forms of their tri-(*R*)-(+)-MTPA esters. Assignments for the non-deuterated glycerol tri-(*R*)-(+)-MTPA ester are as follows: δ 3.33 (3H, s, CH_3O-), 3.39 (3H, s, CH_3O-), 3.45 (3H, s, CH_3O-), 4.28 (1H, dd, *J*=4.6 and 12.1 Hz, *sn*-1 *pro-R*), 4.30 (1H, dd, *J*=4.0 and 12.1 Hz, *sn*-3 *pro-S*), 4.53 (1H, dd, *J*=4.1 and 12.1 Hz, *sn*-1 *pro-S*), 4.64 (1H, dd, *J*=4.0 and 12.1 Hz, *sn*-3 *pro-R*), 5.52 (1H, m, *sn*-2), and 7.30-7.50 (15H, aromatic).

In summary, the carbohydrate template approach described above appears to be quite useful. Simple acetylene molecule can be divergently converted into various chirally labeled molecules through the addition into and the oxidative cleavage from the template. Further, the derived chirally monodeuterated ethylene oxide derivatives **6**, **7**, **8** and **9** may be utilized as key synthons for the various chirally deuterated molecules.

Experimental

Melting points were measured on a Yanagimoto hot stage apparatus and are uncorrected. Infrared spectra were obtained with a Hitachi Model 260-10 grating spectrophotometer. Proton nuclear magnetic resonance spectra were recorded with either a JEOL PS-100, FX-100, FX-200, GSX-270, GX-400 or a GSX-500 spectrometer in a $CDCl_3$ solution using tetramethylsilane as an internal standard unless otherwise stated. Carbon-13 nuclear magnetic resonance spectra were recorded on a JEOL FX-100, FX-200, GSX-270 or a GX-400 spectrometer in a $CDCl_3$ solution using the central line of the solvent signal as the chemical shift standard (δ = 77.0 ppm). Optical rotations were measured using a JASCO DIP-360 digital polarimeter. Mass spectra were recorded on a Shimadzu LKB-9020DF spectrometer using a direct inlet system. HR-MS spectra were recorded on a Hitachi M-80A mass spectrometer with an acceleration voltage at 70 eV. HR-FAB-MS spectra were measured on a JEOL JMS-HX-110H spectrometer (FAB gun, Xe; matrix, glycerol). All reactions were carried out under inert argon or nitrogen atmosphere. Chromatographic separations were carried out with Merck Kieselgel 60, 70-230 mesh for atmospheric pressure columns and 230-400 mesh for medium pressure columns.

3-*C*-Ethynyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (2)

Purified and dried acetylene gas was slowly introduced at room temperature for 1 hr into 650 ml of dry tetrahydrofuran (THF) in a 2-l three-necked flask equipped with a mechanical stirrer. While acetylene gas was continuously introduced, 100 ml of ethylmagnesium bromide (3 *M* solution in ether) was added portionwise over a period of 5 hr. After completion of the addition, stirring was continued for another 1 hr. A solution of 23.4 g (90.7 mmol) of the ketone **1**, prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose by a literature procedure,[15] in 100 ml of THF was added dropwise to the reaction mixture in 40 min and stirring was continued for 1 hr. The reaction mixture was concentrated to *ca.* 200 ml under reduced pressure and then 300 ml of saturated aqueous NH_4Cl solution was added. Organic solvent was further removed under reduced pressure and the residual aqueous mixture was extracted 4 times with 200-ml portions of ether. The combined extract was washed with 1*N* HCl, saturated aqueous $NaHCO_3$ and brine, and then dried over anhydrous $MgSO_4$. Filtration and removal of solvent under reduced pressure provided a crude crystalline residue, which was recrystallized from *n*-hexane-ether to give 25.0 g of **2** as colorless rods (88 %). m.p. 105 °C; IR ($CHCl_3$): 3560, 3320, 3020-2900, 2125, 1380, 1225, 1120, 1070, 1040, 1000, 870, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.37 (6H, s), 1.47 (3H, s), 1.60 (3H, s), 2.68 (1H, s), 3.13 (1H, br. s), 3.86 (1H, d, *J*=8.1 Hz), 4.04 (1H, dd, *J*=4.6 and 8.8 Hz), 4.15 (1H, dd, *J*=6.1 and 8.8 Hz), 4.44 (1H, ddd, *J*=4.6, 6.1 and 8.1 Hz), 4.62 (1H, d, *J*=3.4 Hz), 5.82 (1H, d, *J*=3.4 Hz); ^{13}C NMR (67.5 MHz, CD_3OD): δ 26.24, 27.55, 27.63, 27.77, 67.68, 76.57, 77.01, 79.38, 83.26, 83.37, 86.70, 106.61, 110.89, 115.29; EI-MS: m/z 269 (M^+-CH_3). *Anal.* Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.28; H, 7.23.

(2'-$^2H_1$)-3-*C*-Ethynyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (3)

To a solution of 20.7 g (72.8 mmol) of **2** in 400 ml of dry THF in an iced water bath was added dropwise 80 ml of ethylmagnesium bromide (3 *M* solution in ether) and the mixture was stirred overnight at room temperature. To the mixture was added 20 ml of ^2H_2O (99.8 Atom %, Aldrich) and stirring was continued for 1 hr. The reaction was quenched by adding 600 ml of ether and 200 ml of saturated aqueous NH_4Cl solution. The aqueous solution was extracted 4 times with 200-ml portions of ether. The organic extracts were combined and washed with 1*N* HCl, saturated $NaHCO_3$ and brine, and then dried over anhydrous $MgSO_4$. Filtration and evaporation of solvent under reduced pressure provided a crude crystalline residue, which was recrystallized from ether-pet. ether to give 16.4 g of **3** as colorless rods (80 %). m.p. 104-105 °C; IR ($CHCl_3$): 3560, 3020-2900, 2590, 1985, 1380, 1225, 1120, 1070, 1040, 1000, 870, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.37 (6H, s), 1.46 (3H, s), 1.59 (3H, s), 3.11 (1H, br. s), 3.86 (1H, d, *J*=8.1 Hz), 4.05 (1H, dd, *J*=4.6 and 8.8 Hz), 4.14 (1H, dd, *J*=6.1 and 8.8 Hz), 4.44 (1H, ddd, *J*=4.6, 6.1 and 8.1 Hz), 4.62 (1H, d, *J*=3.4 Hz), 5.82 (1H, d, *J*=3.4 Hz); EI-MS (70 eV): *m/z* 270 (M^+-CH_3). *Anal.* Calcd for $C_{14}H_{19}{}^2H_1O_6$: C, 58.94; H+^{2}H 7.07. Found: C,59.01; H+^{2}H, 7.02.

(*Z*)-(2'-$^2H_1$)-3-*C*-Ethenyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (4)

To a suspension of 4.0 g (95.3 mmol) of $LiAl^2H_4$ in 30 ml of dry THF was added dropwise a solution of 2.0 g (6.9 mmol) of **2** dissolved in 5 ml of THF at 0 °C and the resulting mixture was stirred for 2 hr at room temperature. The reaction mixture was diluted with ether and aqueous saturated sodium potassium tartarate was added. Layers were separated and the aqueous layer was further extracted with ether. Combined organic extract was washed with brine and dried over anhydrous Na_2SO_4. Filtration and evaporation of solvent afforded a crude product, which was recrystallized from n-hexane to give 1.6 g of the (*Z*)-olefin **4** (80 %). m.p. 72 °C; IR ($CHCl_3$): 3350, 2998, 1384, 1378 cm^{-1}; ^1H NMR (200 MHz): δ 1.33 (3H, s), 1.36 (3H, s), 1.45 (3H, s), 1.62 (3H, s), 2.80 (1H, s), 3.88-4.17 (4H, m), 4.28 (1H, d, *J*=3.5 Hz), 5.37 (1H, d, *J*=10.5 Hz), 5.79 (1H, d, *J*=3.5 Hz), 5.82 (1H, d, *J*=10.5 Hz); ^{13}C NMR (50 MHz): δ 25.2, 26.4, 26.56, 26.62, 66.9, 73.7, 80.2, 81.4, 83.6, 103.7, 109.2, 112.9, 116.3, 134.7; EI-MS: *m/z* 272 (M^+-CH_3). *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_6$: C, 58.52; H+^{2}H, 7.72. Found: C, 58.43; H+^{2}H, 8.01.

(*E*)-(2'-$^2H_1$)-3-*C*-Ethenyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (5)

Treatment of 9.8 g of **3** with $LiAlH_4$ instead of $LiAl^2H_4$ as described for the preparation of **4** afforded 8.6 g of **5** (87 %). m.p. 61-62 °C; ^1H NMR (200 MHz): δ 1.33 (3H, s), 1.36 (3H, s), 1.44 (3H, s), 1.62 (3H, s), 3.88-4.16 (4H, m), 4.39 (1H, d, *J*=3.9 Hz), 5.56 (1H, d, *J*=17.6 Hz), 5.78 (1H, d, *J*=3.9 Hz), 5.82 (1H, d, *J*=17.9 Hz); ^{13}C NMR (50 MHz): δ 25.2, 26.4, 26.56, 26.62, 66.8, 73.7, 80.1, 81.3, 83.5, 103.6, 109.1, 112.9, 116.3, 134.6. *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_6$: C, 58.52; H+^{2}H, 7.72. Found: C, 58.46; H+^{2}H, 7.95.

Epoxidation of (*Z*)-olefin (4)

To a solution of 3.32 g (19.2 mmol, 4.2 eq.) of *m*-CPBA in 30 ml of dry CH_2Cl_2, 1.32 g (4.6 mmol) of (*Z*)-olefin (**4**) in 5 ml of dry CH_2Cl_2 was added, and the mixture was stirred at room temperature for 5 hr. After 1.02 g (5.9 mmol) of *m*-CPBA was further added, the mixture was stirred for 22 hr. This mixture was diluted with ether, aqueous 0.5 *N* NaOH-saturated NaCl solution was added and the whole mixture was filtered. The filtrate was extracted with ether. The organic layer was washed with saturated aqueous Na_2CO_3 and brine, and then dried over Na_2SO_4. After filtration and evaporation, the residue was purified by flash chromatography (n-hexane:ether, 1 : 3) to afford 882 mg of (1'*R*, 2'*R*)-(2'-$^2H_1$)-3-*C*-1',2'-epoxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **6** (63 %) and 280 mg of (1'*S*, 2'*S*)-(2'-$^2H_1$)-3-*C*-1',2'-epoxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **7** (20 %). **6**; m.p. 92-93 °C; IR ($CHCl_3$): 3544, 3025, 2998, 1387, 1380 cm^{-1}; ^1H-NMR (200 MHz): δ 1.36 (3H, s), 1.38 (3H, s), 1.45 (3H, s), 1.61 (3H, s), 2.63 (1H, s), 2.87 (1H, d, *J*=4.0 Hz), 3.07 (1H, d, *J*=4.0 Hz), 3.96 (1H, d, *J*=7.8 Hz), 3.97 (1H, dd, *J*=5.8 and 8.6 Hz), 4.11 (1H, dd, *J*=6.1 and 8.6 Hz), 4.29 (1H, ddd, *J*=5.9, 6.1 and 8.6 Hz), 4.50 (1H, d, *J*=3.7 Hz), 5.86 (1H, d, *J*= 3.7 Hz). *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_7$: C, 55.45; H+^{2}H, 7.31, Found: C, 55.59; H+^{2}H, 7.49. **7**; m.p. 97 °C; IR ($CHCl_3$):

3540, 3026, 2993, 1388, 1380 cm^{-1}; ^1H NMR (200 MHz): δ 1.36 (3H, s), 1.46 (3H, s), 1.59 (3H, s), 1.63 (3H, s), 2.80 (1H, d, *J*= 4.2 Hz), 3.11 (1H, d, *J*= 4.2 Hz), 3.95 (1H, d, *J*= 8.6 Hz), 4.01 (1H, dd, *J*= 6.1 and 8.5 Hz), 4.14 (1H, dd, *J*= 6.1 and 8.6 Hz), 4.31 (1H, m), 4.34 (1H, d, *J*= 3.7 Hz), 5.78 (1H, d, *J*= 3.7 Hz); EI-MS: *m/z* 288 (M^+-CH_3). *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_7$: C, 55.45; H+^{2}H, 7.31. Found: C, 55.59; H+^{2}H, 7.49.

Epoxidation of (*E*)-olefin (5)

By the procedure described for the preparation of **6** and **7**, epoxidation of 5.0 g of (*E*)-olefin **5** was carried out to afford 2.43 g of (1'*R*, 2'*S*)-(2'-^{2}H)-3-*C*-1',2'-epoxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **8** (46 %) and 0.70 g of (1'*S*, 2'*R*)-(2'-^{2}H)-3-*C*-1',2'-epoxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **9** (13 %). **8**; m.p. 96-97 °C; ^1H NMR (200 MHz): δ 1.36 (3H, s), 1.38 (3H, s), 1.44 (3H, s), 1.61 (3H, s), 2.61 (1H, s), 3.07 (1H, d, *J*=2.4 Hz), 3.08 (1H, d, *J*=2.4 Hz), 3.94 (1H, dd, *J*=5.9 and 8.3 Hz), 3.96 (1H, d, *J*=7.8 Hz), 4.11 (1H, dd, *J*=5.9 and 8.3 Hz), 4.28 (1H, dt, *J*=5.9 and 7.8 Hz), 4.50 (1H, d, *J*=3.9 Hz), 5.86 (1H, d, *J*=3.9 Hz). *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_7$: C, 55.45; H+^{2}H, 7.31. Found: C, 55.52; H+^{2}H, 7.30. **9**; m.p. 83-84 °C; ^1H NMR (200 MHz): δ 1.36 (3H, s), 1.38 (3H, s), 1.46 (3H, s), 1.62 (3H, s), 2.90 (1H, d, *J*=2.4 Hz), 3.11 (1H, d, *J*=2.4 Hz), 3.95 (1H, d, *J*=8.3 Hz), 4.01 (1H, dd, *J*=4.9 and 8.8 Hz), 4.14 (1H, dd, *J*=5.9 and 8.8 Hz), 4.34 (1H, d, *J*=3.9 Hz), 4.38 (1H, m), 5.86 (1H, d, *J*= 3.9 Hz). *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_7$: C, 55.45; H+^{2}H, 7.31. Found: C, 55.60; H+^{2}H, 7.54.

Dihydroxylation of (*Z*)-olefin (4)

To a solution of 9.23 g (32.1 mmol) of (*Z*)-olefin **4** and 5.46 g (46.6 mmol, 1.5 eq.) of *N*-methylmorpholine *N*-oxide in 56 ml of ^{t}BuOH-THF-H_2O (10 : 3 : 1) were added unweighed catalytic amount of OsO_4 and 1 drop of pyridine at room temperature, and the mixture was stirred for 20 hr at room temperature. Aqueous $NaHSO_3$ solution was added to the reaction mixture, and stirring was continued for 30 min. The precipitate was filtered and washed with ether. The layers of the filtrate were separated and the aqueous layer was extracted repeatedly with ether. The combined organic extract was washed with 1*N* HCl, saturated aqueous $NaHCO_3$ and brine, and then dried over anhydrous Na_2SO_4. After filtration, the solvent was removed by evaporation to yield 10.9 g of a syrupy triol-mixture. The mixture was purified with silica gel column chromatography (ether) to afford 6.04 g of (1'*R*, 2'*R*)-(2'-$^2H_1$)-3-*C*-1',2'-dihydroxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **10** (59 %). m.p. 139-140 °C; $[\alpha]_D^{20}$ + 25.6° (*c*=1.21, $CHCl_3$); IR ($CHCl_3$): 3500, 2970, 1370, 1220, 1140, 1060, 1000, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.38 (3H, s), 1.49 (3H, s), 1.58 (6H, s), 2.24 (1H, d, *J*=6.8 Hz), 3.01 (1H, s), 3.14 (1H, d, *J*=3.9 Hz), 3.88 (1H, d, *J*=6.8 Hz), 3.95 (1H, br. t, *J*=5.9 Hz), 4.09 (1H, dd, *J*=6.8 and 8.3 Hz), 4.13 (1H, dd, *J*=6.8 and 8.3 Hz), 4.21 (1H, dd, *J*=4.1 and 6.8 Hz), 4.52 (1H, q, *J*=6.8 Hz), 4.69 (1H, d, *J*=3.9 Hz), 5.80 (1H, d, *J*=3.8 Hz); ^{13}C NMR (50 MHz): δ 24.7, 26.2, 26.5, 26.7, 62.6 (t, *J*=22.8 Hz), 66.4, 70.5, 73.2, 79.7, 80.5, 83.1, 104.5, 110.0, 112.4. *Anal.* Calcd for $C_{14}H_{23}{}^2H_1O_8$: C, 52.33; H+^{2}H, 7.53. Found, C 52.14; H+^{2}H, 7.77.

Further elution of the column afforded 2.16 g of (1'*S*, 2'*S*)-(2'-$^2H_1$)-3-*C*-1',2'-dihydroxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **11** (21 %). m.p. 97-98 °C; $[\alpha]_D^{20}$ + 12.8° (*c*=1.20, $CHCl_3$); IR ($CHCl_3$): 3500, 2960, 1380, 1230, 1070, 1010, 870, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.37 (6H, s), 1.46 (3H, s), 1.60 (3H, s), 2.34 (1H, d, *J*=6.4 Hz), 3.17 (1H, s), 3.21 (1H, d, *J*=2.9 Hz), 3.83 (1H, d, *J*=8.8 Hz), 3.84 (1H, m), 3.93 (1H, dd, *J*=5.4 and 8.8 Hz), 4.03 (1H, br. t, *J*= 2.9 Hz), 4.14 (1H, dd, *J*=6.0 and 8.7 Hz), 4.26 (1H, ddd, *J*=5.4, 5.9 and 8.8 Hz), 4.62 (1H, d, *J*=3.9 Hz), 5.74 (1H, d, *J*=3.9 Hz); ^{13}C NMR (50 MHz): δ 25.2, 26.4, 26.5, 26.7, 61.6 (t, *J*=22.0 Hz), 68.2, 70.7, 72.9, 76.5, 79.4, 81.0, 81.8, 103.8, 110.0, 112.7. *Anal.* Calcd for $C_{14}H_{21}{}^2H_1O_6$: C, 52.33; H+^{2}H 7.53. Found: C 52.50; H+^{2}H, 7.69.

(1'*R*, 2'*R*)-(2'-$^2H_1$)-3-*C*-1',2'-Benzoyloxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (12)

To a solution of 1.17 g (3.6 mmol) of **10** in 4.2 ml of pyridine was added 1.5 ml (12.9 mmol, 3.2 eq.) of benzoyl chloride and 20 mg of 4-dimethylaminopyridine (DMAP), and the mixture was stirred for 10 hr at room temperature. The reaction mixture was diluted with ether and water was added. Layers were separated

and the aqueous layer was extracted several times with ether. Combined organic extract was washed with 1*N* HCl, saturated aqueous $NaHCO_3$ and brine, and then dried over anhydrous Na_2SO_4. After filtration and evaporation of solvent, the residue was purified by silica gel column chromatography (n-hexane:ethyl acetate, 3 : 1 to 2 : 1) to give 1.80 g of white crystalline **12** (93 %). m.p. 130-131 °C; $[\alpha]_D^{20}$ + 6.38° (*c*=1.41, $CHCl_3$); IR ($CHCl_3$): 3530, 1720, 1600, 1450, 1370, 1270, 1100, 1010, 870, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.40 (6H, s), 1.49 (3H, s), 1.62 (3H, s), 3.33 (1H, s), 3.86 (1H, dd, *J* = 6.0 and 8.5 Hz), 3.94 (1H, d, *J*=9.6 Hz), 4.11 (1H, dd, *J*=5.9 and 8.5 Hz), 4.27 (1H, ddd, *J*=5.9, 6.0 and 9.6 Hz), 4.98 (1H, d, *J*=4.0 Hz), 5.02 (1H, d, *J*=2.7 Hz), 5.88 (1H, d, *J*=3.9 Hz), 6.07 (1H, d, *J*=2.9 Hz), 7.29-7.60 (6H, m), 7.90-8.00 (4H, m). *Anal.* Calcd for $C_{28}H_{31}{}^2H_1O_{10}$: C, 63.51; H+^{2}H, 6.09. Found: C, 63.63; H+^{2}H, 6.06.

Methyl (2*R*, 3*R*)-2,3-di-*O*-benzoyl-(3-$^2H_1$)glycerate (13)

To a solution of 1.80 g (3.4 mmol) of **12** in 15 ml of THF was added 15 ml of 1*N* H_2SO_4, and the mixture was stirred at 70 °C for 18 hr. After being cooled to room temperature, the organic materials were repeatedly extracted with ether. Combined organic extract was washed with 1*N* HCl and brine, and then dried over anhydrous Na_2SO_4. Filtration, followed by evaporation of the solvent, afforded 1.33 g of a crude product. To a solution of 1.32 g (2.9 mmol) of the crude product in 30 ml of MeOH was added a solution of 6.0 g (28.0 mmol, 10 eq.) of $NaIO_4$ in 30 ml of water and the mixture was stirred at room temperature for 4 hr. The mixture was then extracted repeatedly with ether. The combined organic extract was washed with 1*N* HCl and brine, and then dried over Na_2SO_4. After filtration and evaporation, the residue was treated with ethereal diazomethane to give, after chromatographic purification, 654 mg of crystalline product **13** (82 %). m.p. 49-58 °C; $[\alpha]_D^{25}$ - 24.7 (*c*=2.18, MeOH); IR ($CHCl_3$): 3020, 2960, 1730, 1600, 1450, 1260, 1120 cm^{-1}; ^1H NMR (200 MHz): δ 3.84 (3H, s), 4.87 (1H, br. d, *J*=5.7 Hz), 5.70 (1H, d, *J*=5.7 Hz), 7.40-7.62 (6H, m), 8.00-8.12 (4H, m); HR-MS: Calcd for $C_{18}H_{15}{}^2H_1O_6$ 329.1008: Found 329.0997. *Anal.* Calcd for $C_{18}H_{15}{}^2H_1O_6$: C, 65.65; H+^{2}H 4.90. Found: C 65.52; H+^{2}H 4.90.

Methyl (2*S*)-2,3-di-*O*-benzoylglycerate

Methyl (2*S*)-glycerate was prepared according to the reported method.[14] To a solution of 175 mg (1.45 mmol) of methyl glycerate in 1 ml of pyridine was added 20 mg of DMAP and 500 μl (4.3 mmol, 3.0 eq.) of benzoyl chloride, and the mixture was stirred for 1 hr. The reaction mixture was diluted with ether and water was added. Layers were separated and the aqueous layer was extracted several times with ether. Combined organic extract was washed with 1*N* HCl, saturated aqueous $NaHCO_3$ and brine, and then dried over anhydrous Na_2SO_4. After filtration and evaporation of solvent, products were purified by silica gel column chromatography (n-hexane:ethyl acetate, 7 : 1 to 5 : 1) to yield 290 mg of methyl (2*S*)-2,3-di-*O*-benzoylglycerate. m.p. 46-51 °C; $[\alpha]_D^{25}$ + 22.5° (*c*=1.01, MeOH); IR ($CHCl_3$): 3050, 1725, 1600, 1455, 1265, 1105 cm^{-1}; ^1H NMR (200 MHz): δ 3.82 (3H, s), 4.85 (1H, dd, *J*=5.1 and 12.0 Hz), 4.87 (1H, dd, *J*=3.4 and 12.0 Hz), 5.70 (1H, dd, *J*=3.4 and 5.1 Hz); ^{13}C NMR (50 MHz): δ 52.8, 63.2, 70.9, 128.4, 128.5, 129.7, 130.1, 133.3, 133.5, 133.6, 165.5, 165.7, 167.7. *Anal.* Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.88; H, 4.61.

***sn*-(1*R*)-(1-$^2H_1$)Glycerol (14)**

To a suspension of 42 mg (1.12 mmol) of $LiAlH_4$ in 1.5 ml of ether was added dropwise a solution of 129 mg (0.39 mmol) of the ester **13** in 1 ml of ether at 0 °C. The mixture was warmed to room temperature and stirring was continued for 30 min. Then, a small amount of water was added to the reaction mixture and the whole was filtered by suction. The filtrate was extracted with ether to remove benzyl alcohol, and the residual aqueous layer was separated and evaporated. Inorganic salts were removed by column chromatography with Amberlite IR 120B (H^+), to give, after evaporation, 18 mg of colorless syrup **14** (48 %). ^1H NMR (200 MHz, D_2O, δ_{HDO} =4.75): δ 3.41 (1H, dd, *J*=6.5 and 12 Hz), 3.47 (1H, br), 3.49 (1H, dd, *J*=4.5

and 12 Hz), 3.62 (1H, br. dt, *J*=4.5 and 6.6 Hz); HR-FAB-MS: Calcd. for $C_3H_8{}^2H_1O_3$ (M^++H), 94.0614; Found 94.0602; Calcd for $C_3H_7{}^2H_1O_3Na$ (M^++Na), 116.0434; Found 116.0428.

(1'*S*, 2'*S*)-(2'-$^2H_1$)-3-*C*-1',2'-Benzoyloxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (16)

By the procedure described for the preparation of **12**, 141 mg (0.37 mmol) of **11** was benzoylated to give 111 mg of **16** (48 %). m.p. 148-149 °C; $[\alpha]_D^{20}$ - 15.6° (*c*=1.41, $CHCl_3$); IR ($CHCl_3$): 3540, 2980, 1720, 1600, 1450, 1380, 1260, 1100, 1020, 870, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.28 (3H, s), 1.39 (3H,s), 1.46 (3H, s), 1.61 (3H,s), 3.16 (1H, s), 3.95 (1H, d, *J*=9.1 Hz), 3.97 (1H, dd, *J*=5.9 and 8.8 Hz), 4.16 (1H, dd, *J*=6.1 and 9.6 Hz), 4.43 (1H, dt, *J*=5.9 and 8.7 Hz), 4.76 (1H, d, *J*=3.9 Hz), 4.90 (1H, d, *J*=2.9 Hz), 5.79 (1H, d, *J*=3.9 Hz), 5.96 (1H, d, *J*=2.9 Hz), 7.27-7.60 (6H, m), 7.94 (2H, br. d, *J*=7.1 Hz), 8.06 (2H, br. d, *J*=7.0 Hz). *Anal.* Calcd for $C_{28}H_{31}{}^2H_1O_{10}$: C, 63.51; H+^{2}H, 6.09. Found: C, 63.48; H+^{2}H, 5.79.

Methyl (2*S*, 3*S*)-2,3-di-*O*-benzoyl-(3-$^2H_1$)glycerate (17)

By the procedure described for the preparation of **13**, 111 mg (0.21 mmol) of **16** was converted to 51 mg of the glyceric acid ester derivative **17** (78 %). m.p. 48-55 °C; $[\alpha]_D^{25}$ + 27.5 ° (*c*=1.86, MeOH); IR ($CHCl_3$): 3000, 1730, 1600, 1440, 1260, 1120 cm^{-1}; ^1H NMR (200 MHz): δ 3.84 (3H, s), 4.87 (1H, br. d, *J*=5.7 Hz), 5.70 (1H, d, *J*=5.7 Hz), 7.40-7.62 (6H, m), 8.00-8.12 (4H, m); HR-MS: Calcd for $C_{18}H_{15}{}^2H_1O_6$ 329.1008: Found 329.1010. *Anal.* Calcd for $C_{18}H_{15}{}^2H_1O_6$, C, 65.65, H+^{2}H; 4.94: Found C, 65.49, H+^{2}H; 4.90.

***sn*-(3*S*)-(1-$^2H_1$)Glycerol (18)**

By the procedure described for the preparation of **14**, 91 mg (0.28 mmol) of **17** was reduced to give 19 mg of **18** (74 %). ^1H NMR (200 MHz, D_2O, δ_{HDO} = 4.75): δ 3.40 (1H, dd, *J*=6.5 and 12 Hz), 3.46 (1H, br), 3.49 (1H, dd, *J*=4.5 and 12 Hz), 3.61 (1H, br. dt, *J*=4.5 and 6.6 Hz); HR-FAB-MS: Calcd. for $C_3H_8{}^2H_1O_3$ (M^++H), 94.0614; Found 94.0596; Calcd for $C_3H_7{}^2H_1O_3Na$ (M^++Na), 116.0434; Found 116.0419.

Dihydroxylation of (*E*)-olefin (5)

According to the procedure described for the preparation of **10** and **11**, 2.0 g (7.00 mmol) of (*E*)-olefin **5** was oxidized to give 1.24 g of (1'*S*, 2'*R*)-(2'-$^2H_1$)-3-*C*-1',2'-dihydroxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **20** (55 %) and 0.60 g of (1'*R*, 2'*S*)-(2'-$^2H_1$)-3-*C*-1',2'-dihydroxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **21** (27 %). **20**; $[\alpha]_D^{20}$ + 26.3° (*c*=1.30, $CHCl_3$); IR ($CHCl_3$): 3500, 2980, 1330, 1240, 1220, 1140, 1060, 1000, 860 cm^{-1}; ^1H NMR (500 MHz): δ 1.38 (3H, s), 1.39 (3H, s), 1.50 (3H, s), 1.58 (3H, s), 2.24 (1H, br. d, *J*=5.5 Hz), 3.01 (1H, s), 3.16 (1H, d, *J*=3.9 Hz), 3.80 (1H, br. dd, *J*=5.0 and 6.7 Hz), 3.88 (1H, d, *J*=6.5 Hz), 4.11 (1H, dd, *J*=6.9 and 8.5 Hz), 4.12 (1H, dd, *J*=6.8 and 8.5 Hz), 4.21 (1H, dd, *J*=3.9 and 6.7 Hz), 4.51 (1H, q, *J*=6.7 Hz), 4.69 (1H, d, *J*=4.0 Hz), 5.81 (1H, d, *J*=4.0 Hz). *Anal.* Calcd for $C_{14}H_{23}{}^2H_1O_8$: C, 52.33, H+^{2}H, 7.53. Found: C, 52.37; H+^{2}H, 7.46. **21**; $[\alpha]_D^{20}$ + 14.6° (*c*=1.40, $CHCl_3$); IR ($CHCl_3$): 3500, 2980, 1360, 1240, 1220, 1140, 1060, 1000, 860 cm^{-1}; ^1H NMR (500 MHz): δ 1.37 (6H, s), 1.46 (3H, s), 1.60 (3H, s), 2.29 (1H, d, *J*=4.9 Hz), 3.15 (1H, s), 3.18 (1H, d, *J*=2.8 Hz), 3.66 (1H, br. t, *J*=4.9 Hz), 3.83 (1H, d, *J*=9.0 Hz), 3.93 (1H, dd, *J*=5.5 and 8.7 Hz), 4.04 (1H, dd, *J*=2.8 and 4.8 Hz), 4.14 (1H, dd, *J*=6.1 and 8.9 Hz), 4.25 (1H, ddd, *J*=5.5, 6.1 and 8.9 Hz), 4.62 (1H, d, *J*=3.9 Hz), 5.75 (1H, d, *J*=3.9 Hz). *Anal.* Calcd for $C_{14}H_{23}{}^2H_1O_8$: C, 52.33; H+^{2}H, 7.53: Found: C, 52.50; H+^{2}H, 7.69.

(1'*S*, 2'*R*)-(2'-$^2H_1$)-3-*C*-1',2'-Benzoyloxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (22)

By the procedure described for the preparation of **12**, 972 mg (3.03 mmol) of **20** was benzoylated to give 1.45 g of **22** (91 %). m.p. 130-131 °C; $[\alpha]_D^{20}$ + 3.51° (*c*=7.00, $CHCl_3$); IR ($CHCl_3$): 3540, 2950, 1740, 1590, 1445, 1370, 1315, 1260, 1200, 1065, 1015, 870, 840 cm^{-1}; ^1H NMR (200 MHz): δ 1.41 (3H, s), 1.42

(3H, s), 1.49 (3H, s), 1.63 (3H, s), 3.28 (1H, s), 3.88 (1H, dd, *J*=6.0 and 8.5 Hz), 3.93 (1H, d, *J*=9.8 Hz), 4.15 (1H, dd, *J*=6.0 and 8.5 Hz), 4.28 (1H, dt, *J*=6.0 and 9.8 Hz), 4.79 (1H, d, *J*=7.3 Hz), 4.97 (1H, d, *J*=3.9 Hz), 5.87 (1H, d, *J*=3.9 Hz), 6.06 (1H, d, *J*=7.4 Hz), 7.28-7.60 (6H, m), 7.92-7,99 (4H, m). *Anal.* Calcd for $C_{28}H_{31}{}^2H_1O_{10}$: C, 63.51; H+^{2}H, 6.09. Found: C, 63.67; H+^{2}H, 6.36.

Methyl (2*R*, 3*S*)-2,3-di-*O*-benzoyl-(3-$^2H_1$)glycerate (23)

By the procedure described for the preparation of **13**, 886 mg (1.67 mmol) of **22** was converted to 654 mg of **23** (82 %). m.p. 53-58 °C; $[\alpha]_D^{25}$ - 23.8° (*c*=1.63, MeOH); IR ($CHCl_3$): 3250, 1735, 1615, 1460, 1260, 1120 cm^{-1}; ^{1}H NMR (200 MHz): δ 3.82 (3H, s), 4.80 (1H, br. d, *J*=6.8 Hz), 5.68 (1H, d, *J*=6.8 Hz), 7.30-7.60 (6H, m), 7.90-8.10 (4H, m); ^{13}C NMR (50 MHz): δ 52.7, 62.8 (t, *J*=23.5 Hz), 70.8, 128.2, 128.3, 128.4, 128.8, 129.2, 129.4, 129.7, 129.9, 133.1, 133.3, 133.3, 133.4, 165.4, 165.7, 167.5; HR-MS: Calcd for $C_{18}H_{15}{}^2H_1O_6$ 329.1008: Found 329.1007. *Anal.* Calcd for $C_{18}H_{15}{}^2H_1O_6$: C, 65.65; H+^{2}H, 4.90. Found: C, 65.39; H+^{2}H, 4.90.

***sn*-(1*S*)-(1-$^2H_1$)Glycerol (24)**

By the procedure described for the preparation of **14**, 129 mg (0.41 mmol) of **23** was reduced to give 41 mg of **24** (81 %). ^{1}H NMR (200 MHz, D_2O, δ_{HDO} = 4.75): δ 3.40 (1H, br. d, *J*=6.5 Hz), 3.42 (1H, dd, *J*=6.5 and 11.5 Hz), 3.51 (1H, dd, *J*=4.5 and 11.5 Hz), 3.64 (1H, dt, *J*=4.5 and 6.5 Hz); HR-FAB-MS: Calcd. for $C_3H_8{}^2H_1O_3$ (M^++H), 94.0614; Found 94.0607; Calcd for $C_3H_7{}^2H_1O_3Na$ (M^++Na), 116.0434; Found 116.0428.

(1'*R*, 2'*S*)-(2'-$^2H_1$)-3-*C*-1',2'-Benzoyloxyethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (26)

By the procedure described for the preparation of **12**, 120 mg (0.37 mmol) of **21** was benzoylated to give 173 mg of **26** (88 %). m.p. 148-149 °C; $[\alpha]_D^{20}$ - 23.8° (*c*=1.35, $CHCl_3$) ; IR ($CHCl_3$): 2950, 1715, 1590, 1370, 1260, 1080, 1060, 1010 cm^{-1}; ^{1}H NMR (200 MHz): δ 1.28 (3H, s), 1.39 (3H, s), 1.47 (3H, s), 1.62 (3H, s), 3.17 (1H, s), 3.98 (2H, m), 4.16 (1H, dd, *J*=6.3 and 8.5 Hz), 4.44 (1H, m), 4.60 (1H, d, *J*=8.3 Hz), 4.77 (1H, d, *J*=3.6 Hz), 5.80 (1H, d, *J*=3.6 Hz), 5.97 (1H, d, *J*=8.3 Hz), 7.25-7.60 (6H, m), 7.95 (2H, br. d, *J*=7.5 Hz), 8.07 (2H, br. d, *J*=7.5 Hz). *Anal.* Calcd for $C_{28}H_{31}{}^2H_1O_{10}$: C, 63.51; H+^{2}H, 6.09. Found: C, 63.25; H+^{2}H, 6.05.

Methyl (2*S*, 3*R*)-2,3-di-*O*-benzoyl-(3-$^2H_1$)glycerate (27)

By the procedure described for the preparation of **13**, 111 mg (0.21 mmol) of **26** was converted to 45 mg of **27** (69 %). m.p. 53-58 °C; $[\alpha]_D^{25}$ + 23.5° (*c*=1.25, MeOH); IR ($CHCl_3$): 3020, 2960, 1730, 1600, 1450, 1260, 1120 cm^{-1}; ^{1}H NMR (200 MHz): δ 3.82 (3H, s), 4.80 (1H, br. d, *J*=6.8 Hz), 5.70 (1H, d, *J*=6.8 Hz), 7.38-7.60 (6H, m), 8.00-8.10 (4H, m), HR-MS: Calcd for $C_{18}H_{15}{}^2H_1O_6$ 329.1008: Found 329.0981. *Anal.* Calcd for $C_{18}H_{15}{}^2H_1O_6$: C, 65.65; H+^{2}H, 4.90. Found: C, 65.56; H+^{2}H, 4.88.

***sn*-(3*R*)-(3-$^2H_1$)Glycerol (28)**

By the procedure described for the preparation of **14**, 33 mg (0.10 mmol) of **27** was reduced to give 7.5 mg of **28** (77 %), ^{1}H NMR (200 MHz, D_2O, δ_{HDO}=4.75): δ 3.41 (1H, br. d, *J*=6.5 Hz), 3.43 (1H, dd, *J*=6.5 and 12.0 Hz), 3.51 (1H, dd, *J*=4.5 and 12.0 Hz), 3.63 (1H, dt, *J*=4.5 and 6.5 Hz), HR-FAB-MS: Calcd. for $C_3H_8{}^2H_1O_3$ (M^++H), 94.0614; Found 94.0603; Calcd for $C_3H_7{}^2H_1O_3Na$ (M^++Na), 116.0434; Found 116.0430.

Typical procedure for the preparation of glycerol tri-(*R*)-(+)-MTPA esters

To a solution of 7.5 mg (0.13 mmol) of a labeled glycerol in 2 ml of pyridine was added 100 μl of (*R*)-(+)-MTPA-Cl and an unweighed catalytic amount of DMAP, and the mixture was stirred overnight at room

temperature. Water was added to the mixture and the whole was extracted with ether. The organic layer was washed with 1*N* HCl, saturated aqueous $NaHCO_3$ and brine, and then dried over Na_2SO_4. Filtration and evaporation of solvent yielded 23 mg of MTPA ester. **15;** ^1H NMR (500 MHz): δ 3.35 (3H, s), 3.38 (3H, s), 3.46 (3H, s), 4.30 (1H, dd, *J*=6.0 and 12.0 Hz), 4.50 (1H, d, *J*=4.0 Hz), 4.64 (1H, dd, *J*=3.0 and 12.0 Hz), 5.52 (1H, m), 7.30-7.50 (m); HR-FAB-MS: Calcd for $C_{36}H_{37}{}^2H_1O_{12}F_9$ (M^++glycerol+H), 834.2282; Found, 834.2272, **19;** ^1H NMR (500 MHz): δ 3.35 (3H, s), 3.38 (3H, s), 3.46 (3H, s), 4.28 (1H, dd, *J*=4.5 and 12.5 Hz), 4.53 (1H, dd, *J*=4.0 and 12.0 Hz), 4.63 (1H, d, *J*=3.5 Hz), 5.52 (1H, m), 7.30-7.50 (m); HR-FAB-MS: Calcd for $C_{36}H_{37}{}^2H_1O_{12}F_9$ (M^++glycerol+H), 834.2282; Found, 834.2281, **25;** ^1H NMR (500 MHz): δ 3.35 (3H, s), 3.38 (3H, s), 3.46 (3H, s), 4.26 (1H, d, *J*=4.5 Hz), 4.31 (1H, dd, *J*=5.0 and 12.0 Hz), 4.64 (1H, dd, *J*=12.0 and 4.0 Hz), 5.52 (1H, m), 7.30-7.50 (m), HR-FAB-MS: Calcd for $C_{36}H_{37}{}^2H_1O_{12}F_9$ (M^++glycerol+H), 834.2282; Found, 834.2280, **29;** ^1H NMR (500 MHz): δ 3.35 (3H, s), 3.38 (3H, s), 3.46 (3H, s), 4.27 (1H, dd, *J*=4.5 and 12.0 Hz) 4.29 (1H, d, *J*=6.0 Hz), 4.57 (1H, dd, *J*=12.0 and 4.0 Hz), 5.52 (1H, m), 7.30-7.50 (m); HR-FAB-MS: Calcd for $C_{36}H_{37}{}^2H_1O_{12}F_9$ (M^++glycerol+H), 834.2282; Found, 834.2291.

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