# (*R*)-2,3-Cyclohexylideneglyceraldehyde: A Potential Intermediate for Convenient Synthesis of 2-C-Branched 2-Deoxypentofuranoses

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Stereocontrol in C−C bond forming nucleophilic addition[1−3] of simple or functionalized organometallics to α- and/or *β*-alkoxy[1] or other heterosubstituted[2] carbonyl substrates has drawn considerable attraction during the last few decades. The resulting homochiral alcohols are generally exploited as building blocks for the synthesis of optically pure compounds via a chiron approach.[4] Consequently, there has been an increasing demand to perform such organometalations in aqueous medium[3] with a view to establishing their practical viability. Simultaneously, efforts are directed in understanding and controlling the stereoselectivity[1−3] for the organometalations of acyclic carbonyls, as a possibility exists in attaining stereochemical flexibility for such additions by changing the metal, solvent, stereochemistry of the nucleophiles, etc. Although a highly stereoselective organometalation of a carbonyl is always desirable from a synthetic viewpoint, a poor or moderately selective addition may prove advantageous if all the resulting diastereo alcohols are isolable in pure form from the reaction mixture without being derivatized, as this may not always be compatible with subsequent reactions protocol.

During our ongoing program on the synthesis of bioactive compounds, we have developed a practical synthesis[5a] of **1** of D-mannitol origin. We found **1** to be a good substrate for Zn-mediated (E)-crotylation[5b] in the presence of water under Luche's condition[6] to produce **2**, **3**, and **4**. Each of these crotylation products has three contiguous stereocenters, two of which are generated during organometalation. It is worth mentioning that crotylmetalation is a valuable alternative to conventional aldol condensation. However, the presence of a methyl group at C-3 blocks that branching for further elaboration. Hence with a view to introducing a hydroxymethyl group, the simplest functionalized C-branching at C-3 in the place of the methyl group, **1** was treated with bromide **7** (1 equiv) and excess (2.5 equiv) of Zn dust following a procedure similar to one done previously by us[5b] and was found to be totally reacted within 1.5 h. Compound **7** was prepared from commercially available (*Z*)-buten-1,4-diol (**5**) by sequential monobenzylation and bromination with an appreciable overall yield. This also provides us an opportunity to compare the stereoselection between Zn-mediated Barbier type (*E*)- and (*Z*)-allylmetalation of a chirally α-oxygenated aldehyde such as **1** under Luche's condition.[6] To our knowledge, this constitutes the first report of this type of study. The reaction between **1** and **7** has been effected with high regioselectivity in which C−C bond formation has exclusively taken place at the *γ*-position. This time the formation of all of the four possible isomers **8**−**11** of the product alcohol was evident from TLC (Scheme 1). However, column chromatography of the residue afforded total isolation of **10** and **11** and partial isolation of **9** that was formed. Some of the initial fractions were found to contain a mixture of **8** and **9**. On the basis of column chromatographic isolation, the formation of **8**/**9**, **10**, and **11** has been estimated to be in the ratio of 18.2:33.5:48.3. Because of the formation of a negligible amount of **8** and its $R_f$ close to that of **9**, its isolation by column chromatography has not been attempted seriously. The $^1$H NMR spectra of **9**, **10**, and **11** available in pure form show distinguishable patterns of signals in the region of $\delta$ 3.5−4.2 due to H-4, H-5, H-6, and $-CH_2OBn$. The stereochemistries of **9** and **10** could be identified by analyzing the signals in the aforementioned region of their $^1$H NMR spectra, which appear to be very much comparable with those of the reported ones[7] for the corresponding debenzylated and isopropylidene derivatives. The stereochemistry of **11** has been ascertained on the basis of our earlier observation[5b] that Zn-mediated allylation of **1** in the presence of water takes place via the Felkin−Ann model,[8] giving rise to the highly predominant formation of the anti alcohol with respect to the α-oxygenated carbon. It is worth noting that there has been an increase in, but not absolute formation of, *erythro* products **9** and **10** in the present case of the (Z)-allylmetalation of **1** compared to the (E)-crotylation of the same aldehyde, where the addition takes place with good *threo* selectivity.[5b] As the stereochemical purity of both crotyl bromide (Fluka) and **5** (Merck) is not absolute, it is not advisable to comment on the possible transition state for such Barbier-type allylmetalation of **1** under

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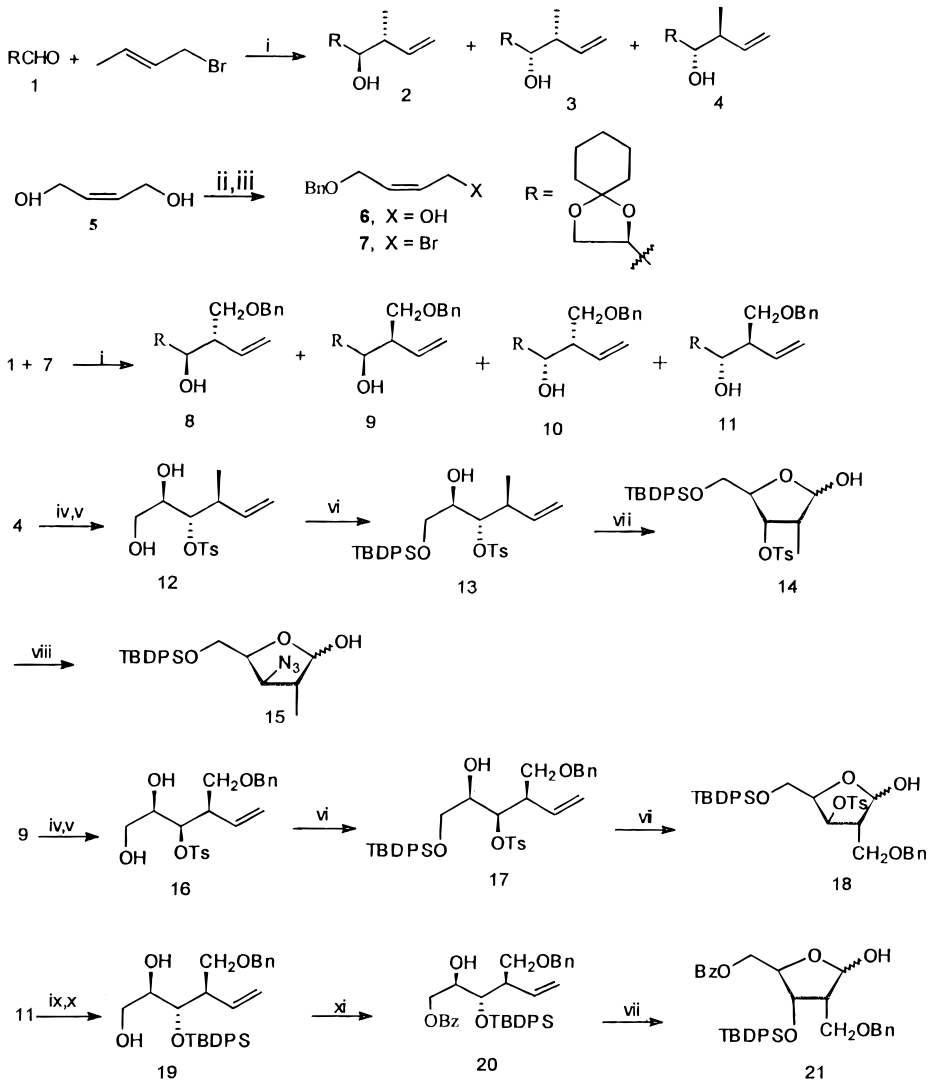
**Scheme 1**



(i) Zn,$NH_4Cl$ (aq); (ii) NaH, BnBr, (iii) $PPh_3$, $Br_2$; (iv) *p*-TsCl, Py; (v) Aq. $CF_3COOH$ (90%); (vi) TBDPSCl, Imidazole; (vii) a) $O_3$, $CH_2Cl_2$, - 78 $^0$C b) $PPh_3$; (viii) $NaN_3$, DMF; (ix) NaH, TBDPSCl; (x) Aq..$CF_3COOH$ (90%), $CH_2Cl_2$,/ THF (1:1), 15 $^0$C; (xi) TEA, BzCN.

Luche's condition. However, an acyclic linear transition state[9] suggests *erythro* selectivity with (*E*)-bromide and poor selectivity with (*Z*)-bromide, whereas the cyclic six-membered[10] transition state favors the formation of the *threo* isomer using (*E*)-bromide and the *erythro* isomer using (*Z*)-bromide.

The efficacy of this approach lies in the formation and easy isolation of a substantial amount of **10** and **11** and an appreciable amount of **9** starting from an easily accessible aldehyde **1** and in the operational simplicity of the entire procedure. Compounds **9**−**11** are rich with functionalities of diverse nature and possess varied stereochemical combinations that should make them very useful chirons. This has been exemplified by exploiting two of them (**9** and **11**) and also **4**[5b] for the synthesis of pentofuranoses **18**, **21**, and **14** respectively, the precursors of 2′-C-branched 2′-deoxynucleosides, which are of considerable current attention as described below.

The continuing search for new antiviral compounds has recently led to the synthesis of a variety of sugar modified nucleosides.[11] This has been triggered by the finding that several 2′,3′-dideoxynucleosides such as AZT, ddC, ddI, etc. are potentially effective therapeutic agents for the treatment of AIDS.[11a,b] The synthetic nucleosidic analogues that are only minimally altered with respect to the corresponding natural nucleosides have become the topic of serious physiological and pharmaceutical interest. Incidentally, the cellular kinases are known to be more tolerant of various changes in the sugar moiety rather than within the base moiety of the nucleosides. One variety of modification of the sugar units is effected by the introduction of C-branching[12] at different positions

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of the basic pentofuranose unit of both 2′-deoxynucleosides and 2′,3′-dideoxynucleosides. So far several reports are available for the synthesis and relevant bioassays of nucleosides with branching at the 1′,[13] 2′,[14] 3′,[15] and 4′[16] positions. It is noteworthy that a number of 2′-deoxy 2′-C-branched ribonucleosides have displayed anticarcinogenic and antiviral properties and a few of them have shown significant therapeutic activity.[17] In a recent development it has been visualized that the substrate diversity of RNA enzymes (ribozymes) can be enhanced by introducing suitably functionalized C-branching at the 2′-position of the 2′-deoxynucleoside molecules.[18] To prepare a nucleosidic analogue, the convergent synthetic approach deals with the condensation of an appropriately functionalized pentofuranose intermediate with a nucleoside base. This has an inherent advantage as it is possible to carry out a desired modification of the sugar unit prior to its combination with the base. A report is available for the synthesis of several furanoside precursors[19a] and the subsequent convergent synthesis of 2′-C-branched 2′,3′-dideoxyribonucleosides.[19b] We feel that our synthesized 2-C-branched 2-deoxypentofuranoses **14**, **18**, and **21** have good prospects as useful precursors for the convergent synthesis of different types of 2′-C-branched 2′-deoxy nucleosides.

Compound **4** on tosylation and subsequent deketalization produced the diol **12**. Monosilylation of the primary hydroxyl of **12** with TBDPSCl gave **13** with good yield. This was successively subjected to ozololysis and reduction in situ with $PPh_3$ to produce the furanose **14**, which possesses a relatively stable OTBDPS at C-5, an easily leaving OTs at C-3, and a Me branching at C-2. The presence of OTs at C-3 makes it amenable for $SN_2$ substitution by various nucleophiles. As a representative example, **14** was treated with sodium azide to produce the *threo* isomer of the resulting 2-methyl-3-azido-dideoxypentofuranose **15**. The preparation of the corresponding *erythro* isomer, which is generally desired as the nucleoside analogue, is possible by an appropriate double inversion at C-3 following a reported procedure.[20] Thus, **14** is found to be a suitable precursor of 2′-C-methyl-2′,3′-dideoxynucleosides.

Compound **9** was tosylated and subsequently deketalized to get the diol **16**, which was monosilylated at the primary hydroxyl to produce **17**. This was then successively ozonolyzed and reduced ($PPh_3$) to give the furanose **18**, which has a stable OTBDPS at C-5, an easily displaceable OTs at C-3, and a protected hydroxymethyl branching $CH_2OBn$ at C-2. Hence, as a result of its having these versatilely protected hydroxyl functionalities, **18** is likely to be utilized as a useful precursor for 2′-C-branched 2′,3′-dideoxyribonucleosides following the substitution of OTs with nucleophiles. Here the presence of OTs at the $\beta$ position will lead to the introduction of an $SN_2$ substituent at the desired $\alpha$ position.

Compound **11** was silylated and subsequently deketalized to obtain the diol **19**. In this case, the deketalization has been effected by treating it in a solvent mixture of THF and dichloromethane (1:1) with trifluoroacetic acid at 15 °C to avoid desilylation. The progress of the reaction was monitored by TLC. The diol **19** was monobenzoylated at the primary hydroxyl to afford **20**. This was successsively ozonolyzed and reduced ($PPh_3$) in situ to afford the furanose **21**. Compound **21**, having a hydrolyzable OBz at C-5, a relatively stable OTBDPS at C-3, and $CH_2OBn$ at C-2, has potential as a useful precursor of 2′-C-branched 2′-deoxyribonucleosides. In this case, the versatile nature of protection of all of the hydroxyl functionalities makes all of them amenable for selective manipulation.

In conclusion, **1** has been found to be a useful starting material to produce a series of homoallylic alcohols that can serve as chirons with versatile utility. Three (**4**, **9**, and **11**) of them have been exploited to prepare functionalized pentofuranoses **14**, **18**, and **21**, respectively, the probable precursors for the convergent synthesis of a wide array of 2′-C-branched 2′-deoxy nucleosides. Hopefully, following similar reactions protocols with the other isomers **3**[5b] and **10** which are also available in substantial amount, the stereochemical flexibility and functional diversity of the nucleosides can be achieved. In the present case, all of the pentofuranoses have been prepared as a mixture of $\alpha$ and $\beta$ anomers whose separation has not been attempted. However, reports are available[11a,b,21] for the successful conversion of the anomeric mixture of several pentofuranoses into the required $\beta$-anomer of the nucleoside following selective manipulation of the hydroxyl group at C-3 or C-5. Moreover, the ready availability of the enantiomer[22] of **1** is likely to generate more stereochemical flexibility in the resulting 2′-C-branched 2′-deoxynucleosides.

## Experimental Section

Chemicals used as starting materials are commercially available and are used without further purification unless otherwise mentioned. The IR spectra were recorded with a Perkin-Elmer spectrophotometer model 837. The PMR spectra were scanned with a Brucker Ac-200 (200 MHz) instrument in $CDCl_3$. The optical rotations were measured with a Jasco DIP-360 polarimeter. The organic extracts were desiccated over $Na_2SO_4$.

**4-Benzyloxy-(2*Z*)-buten-1-ol (6).** To a stirred suspension of NaH (4.8 g of 50% suspension in oil, 0.1 mole, washed with hexane) in THF (100 mL) was added dropwise (2*Z*)-buten-1,4-diol **5** (8.8 g, 0.1 mol) in THF (50 mL) over a period of 1.5 h. The mixture was gently heated to 50 °C for 1 h. Benzyl bromide (17.1 g, 0.1 mol) in THF (100 mL) was added dropwise to the stirred mixture at 50 °C over a period of 3 h. After stirring for 30 min

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more, the mixture was treated with water. Usual extraction, solvent removal, and column chromatography (silica gel, 0−10% EtOAc in petroleum ether) of the residue afforded pure monobenzyl ether **6** (13.5 g, 78%): bp 125−128 °C (0.6 mmHg), lit.[23a] bp 114−120 °C (0.4 mmHg); IR (film) 3397, 3063, 3028; $^1$H NMR ($CDCl_3$) $\delta$ 1.9 (bs, $D_2O$ exchangeable, 1H), 4.1−4.3 (m, 4H), 4.51 (m, 2H), 5.3−5.5 (m, 2H), 7.2−7.5 (m, 5H).

**4-Benzyloxy-1-bromo-(2*Z*)-butene (7).** To a stirred suspension of $PPh_3$ (18.9 g, 0.072 mol) in benzene (50 mL) was added $Br_2$ (14.2 mL of a 5 M solution in $CCl_4$, 0.071 mol). To the resulting suspension was added **6** (12.5 g, 0.07 mol) in benzene (50 mL) containing pyridine (5 mL) over a period of 1 h. Stirring was continued for 1 h. The solvent was evaporated, and the residue was chromatographed (silica gel, 0−10% ether in hexane) to afford **7** (14 g, 83%): bp 88−90 °C (0.3 mmHg), lit.[23b] bp 80 °C (0.13 mmHg); IR (film) 3063, 3030; $^1$H NMR ($CDCl_3$) $\delta$ 3.8−3.9 (m, 2H), 4.1−4.3 (m, 2H), 4.51 (s, 2H), 5.3−5.5 (m, 2H), 7.2−7.5 (m, 5H).

**1,2-*O*-Cyclohexylidene-4-benzyloxymethyl-5-hexen-1,2,3-triol.** To a well stirred mixture of **1** (8.16 g, 0.048 mol), **7** (12 g, 0.05 mol), and Zn dust (19.5 g, 0.3 mol) in THF (100 mL) was added saturated aqueous $NH_4Cl$ (10 mL) in portions over a period of 40 min. The reaction mixture was stirred for 1.5 h until the aldehyde **1** was found to disappear completely (TLC). The mixture was filtered and thoroughly washed with EtOAc. The combined organic layer was washed with 5% HCl to dissolve the suspended turbid material and then with water and brine and dried. Solvent removal and column chromatography (silica gel, 0−20% EtOAc in petroleum ether) of the residue sequentially isolated the mixture of **8** and **9** (430 mg, 3%), pure **9** (1.8 g, 11%), **10** (4.1 g, 26%), and **11** (5.9 g, 37%). The $R_f$ (20% EtOAc in hexane) values of **8**, **9**, **10** and **11** are 0.60, 0.57, 0.51, and 0.45, respectively.

**(2*R*,3*R*,4*S*)-isomer (9):** $[\alpha]^{22}_D$ +5.72 (*c* 1.9, $CHCl_3$); IR (film) 3400, 3063, 3030, 3005, 1650, 995, 920; $^1$H NMR ($CDCl_3$) $\delta$ 1.4−1.6 (m, 10H), 2.35 (m, 1H), 3.0 (bs, $D_2O$ exchangeable, 1H), 3.5−3.6 (m, 1H), 3.65−3.83 (m, 3H), 3.9−4.2 (m, 2H), 4.51 (m, 2H), 5.0−5.2 (m, 2H), 5.8−6.0 (m, 1H), 7.2−7.5 (m, 5H).

**(2*R*,3*S*,4*R*)-isomer (10):** $[\alpha]^{22}_D$ +20.72 (*c* 0.4, $CHCl_3$); IR (film) 3400, 3065, 3025, 3005, 1650, 995, 920; $^1$H NMR ($CDCl_3$) $\delta$ 1.4−1.6 (m, 10H), 2.45 (m, 1H), 3.0 (bs, $D_2O$ exchangeable, 1H), 3.62−3.7 (m, 1H), 3.75−3.85 (m, 2H), 3.9−4.02 (m, 2H), 4.05−4.1 (m, 1H), 4.51 (m, 2H), 5.0−5.2 (m, 2H), 5.8−6.0 (m, 1H), 7.2−7.5 (m, 5H).

**(2*R*,3*S*,4*S*)-isomer (11):** $[\alpha]^{22}_D$ −4.38 (*c* 2.6, $CHCl_3$); IR (film) 3400, 3065, 3025, 3005, 1650, 995, 920; $^1$H NMR ($CDCl_3$) $\delta$ 1.4−1.6 (m, 10H), 2.0 (bs, $D_2O$ exchangeable, 1H), 2.66 (m, 1H), 3.6−3.77 (m, 2H), 3.8−4.1 (m, 4H), 4.51 (m, 2H), 5.0−5.2 (m, 2H), 5.8−6.0 (m, 1H), 7.2−7.5 (m, 5H). Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.27; H, 8.57 for **9**; C, 72.38; H, 8.37 for **10**; C, 72.41; H, 8.33 for **11**.

**(2*R*,3*S*,4*S*)-3-Tosyloxy-4-methyl-5-hexene-1,2-diol (12).** To a cooled and well stirred solution of **4** (2.26 g, 0.01 mol) in pyridine (20 mL) was added *p*-toluenesulfonyl chloride (2.09 g, 0.011 mol). The mixture was stirred overnight at room temperature, treated with water, and extracted with ether. The organic extract was washed with dilute HCl, water, and brine and dried. Solvent removal under reduced pressure afforded the corresponding tosylate in almost quantitative yield. This was mixed with 90% aqueous trifluoroacetic acid (20 mL), stirred for 5 h at 0 °C, and diluted with water. The mixture was extracted with $CHCl_3$. The combined organic layer was washed with water to make it acid-free and then brine and dried. Solvent removal and chromatography of the residue (silica gel, 0−5% MeOH in $CHCl_3$) afforded pure **12** (2.44 g, 81%): $[\alpha]^{22}_D$ +10.32 (*c* 2.6, $CHCl_3$); IR (film) 3500, 3075, 3005, 1365, 1178, 995, 910; $^1$H NMR ($CDCl_3$) $\delta$ 1.03 (d, $J$ = 6.6 Hz, 3H), 2.3−2.45 (m, 1H), 2.43 (s, 3H), 2.56 (bs, $D_2O$ exchangeable, 2H), 3.5−3.8 (m, 3H), 4.6−4.8 (m, 1H), 5.0−5.2 (m, 2H), 5.5−5.7 (m, 1H), 7.34 (d, $J$ = 8.0 Hz, 2H), 7.78 (d, $J$ = 8.0 Hz, 2H). Anal. Calcd for $C_{14}H_{20}O_5S$: C, 55.98; H, 6.71. Found: C, 55.77; H, 6.87.

**(2*R*,3*S*,4*S*)-1-[(*tert*- Butyldiphenylsyl)oxy]-3-tosyloxy-4-methyl-5-hexen-2-ol (13).** To a stirred and cooled (10 °C) solution of **12** (2.1 g, 7 mmol) in DMF (30 mL) containing imidazole (1.2 g, 1.5 mmol) was added dropwise a solution of *tert*-butyldiphenylsilyl chloride (1.92 g, 7 mmol) in DMF (30 mL) over a period of 8 h. The mixture was stirred for 1 h, treated with water, and extracted with ether. The organic extract was washed with water and then brine and dried. Solvent removal and column chromatography of the residue (silica gel, 0−10% EtOAc in petroleum ether) afforded **13** (2.8 g, 75%): $[\alpha]^{22}_D$ +12.24 (*c* 2.1, $CHCl_3$); IR (film) 3545, 3073, 3047, 3012, 2855, 1369, 1177, 995, 906; $^1$H NMR ($CDCl_3$) $\delta$ 1.03 (d, $J$ = 6.6 Hz, 3H), 1.07 (s, 9H), 1.7 (bs, $D_2O$ exchangeable, 1H), 2.3−2.5 (m, 1H), 2.43 (s, 3H), 3.5−3.8 (m, 3H), 4.6−4.8 (m, 1H), 5.0−5.2 (m, 2H), 5.5−5.7 (m, 1H), 7.1−7.8 (m, 14H). Anal. Calcd for $C_{30}H_{38}O_5SSi$: C, 66.88; H, 7.11. Found: C, 66.97; H, 6.97.

**5-*O*-*tert*-Butyldiphenylsilyl-3-*O*-tosyl-2-*C*-methyl-2-deoxy-D-ribofuranose (14).** Through a stirred and cooled (−78 °C) solution of **13** (1.08 g, 0.002 mol) in $CH_2Cl_2$ (100 mL) was bubbled ozone until a blue color persisted. The excess ozone was removed by flushing with argon. $PPh_3$ (550 mg, 0.0021 mol) was added to the mixture. The blue color disappeared immediately. The solution was brought to room temperature, stirred for 5 h more, and concentrated under reduced pressure. The residue was chromatographed (silica gel, 0−25% EtOAc in petroleum ether) to afford **14** (816 mg, 75%) as a colorless oil as a mixture of $\alpha$ and $\beta$ anomers. The tosylate gradually darkens in color on long standing, possibly as a result of decomposition, and hence was immediately used for the next reaction. $[\alpha]^{22}_D$ +12.70 (*c* 3.18, $CHCl_3$); IR (film) 3518, 3071, 3050, 3014, 2858, 1369, 1177; $^1$H NMR ($CDCl_3$) $\delta$ 1.03, 1.06 (2s, 9H), 1.0−1.09 (m, 3H), 2.37 and 2.40 (2s, 3H), 2.2−2.6 (m, 1H), 2.7 (bs, $D_2O$ exchangeable, 1H), 3.5−3.8 (m, 2H), 4.0−4.3 (m, 1H), 4.9−5.2 (m, 1H), 5.4 (m, 1H), 7.1−7.8 (m, 14H). Anal. Calcd for $C_{29}H_{36}O_6SSi$: C, 64.41; H, 6.71. Found: C, 64.57; H, 6.95.

**5-*O*-*tert*-Butyldiphenylsilyl-3-azido-2-*C*-methyl-2,3-dideoxy-D-xylofuranose (15).** Compound **14** (540 mg, 1 mmol) was heated in DMF (20 mL) with an excess of $NaN_3$ (137 mg, 2.1 mmol) at 80 °C for 6 h. The solvent was removed in vacuo. The crude product was dissolved in dry ether, and the insoluble salt was filtered off. Solvent removal and column chromatography of the residue (silica gel, 0−20% ether in petroleum ether) furnished pure **15** (254 mg, 62%) as clear oil: $[\alpha]^{22}_D$ −30.19 (*c* 1.4, $CHCl_3$); IR (film) 3448, 3071, 3050, 2858, 2103, 1605; $^1$H NMR ($CDCl_3$) $\delta$ 1.03, 1.06 (2s, 9H), 1.0−1.1 (m, 3H), 1.7 (bs, $D_2O$ exchangeable, 1H), 2.4−2.7 (m, 1H), 3.5−3.8 (m, 2H), 3.9−4.3 (m, 2H), 5.3−5.5 (m, 1H), 7.1−7.8 (m, 10H). Anal. Calcd for $C_{22}H_{29}O_3N_3Si$: C, 64.20; H, 7.10; N, 10.21. Found: C, 64.45; H, 7.19; N, 10.35.

**(2*R*,3*R*,4*S*)-3-Tosyloxy-4-benzyloxymethyl-5-hexene-1,2-diol (16).** Compound **9** (1.65 g, 5 mmol) was tosylated with *p*-tosyl chloride (1 g, 5.1 mmol) in pyridine (20 mL). The resulting tosylate was treated with 90% aqueous trifluoroacetic acid (15 mL) at 0 °C for 5 h to obtain the diol **16** (1.7 g, 84%): $[\alpha]^{23}_D$ +7.37 (*c* 3.8, $CHCl_3$); IR (film) 3500, 3075, 3005, 1605, 1365, 1178, 995, 910; $^1$H NMR ($CDCl_3$) $\delta$ 2.3−2.5 (m, 1H), 2.43 (s, 3H), 2.8 (bs, $D_2O$ exchangeable, 2H), 3.5−3.8 (m, 5H), 4.50 (m, 2H), 4.6−4.8 (m, 1H), 5.0−5.2 (m, 2H), 5.5−5.7 (m, 1H), 7.3−7.5 (m, 7H), 7.77 (d, $J$ = 8 Hz, 2H). Anal. Calcd for $C_{21}H_{26}O_6S$: C, 62.05; H, 6.45. Found: C, 62.19; H, 6.27.

**5-*O*-*tert*-Butyldiphenylsilyl-3-*O*-tosyl-2-*C*-benzyloxymethyl-2-deoxy-D-xylofuranose (18).** Following a similar procedure as for the preparation of **13**, **16** (1.62 g, 4 mmol) was monosilylated in DMF (30 mL) with TBDPSCl (1.1.g, 4 mmol) in the presence of imidazole (680 mg, 0.01 mol) to obtain **17** (2.08 g, 81%) after purification by column chromatography. A part of this (1 g) was dissolved in $CH_2Cl_2$ (50 mL) and subjected to ozonolysis at −78 °C followed by reduction with $PPh_3$ (410 mg) in situ following a similar procedure as for the preparation of **14**. Solvent removal under reduced pressure and column chromatography (silica gel, 0−30% EtOAc in petroleum ether) of the residue afforded **18** (750 mg, 75%) as a colorless oil as a mixture of $\alpha$ and $\beta$ anomers. The tosylate gradually darkened in color, possibly as a result of decomposition on long standing. $[\alpha]^{22}_D$ +10.47 (*c* 2.4, $CHCl_3$); IR (film) 3518, 3071, 3050, 2858, 1369, 1177; $^1$H NMR ($CDCl_3$) $\delta$ 1.04, 1.07 (2s, 9H), 2.36 and 2.38 (2s, 3H), 2.3−2.6 (m, 1H), 2.8 (bs, $D_2O$ exchangeable, 1H), 3.5−3.8 (m, 4H), 4.1−4.5 (m, 1H), 4.55 and 4.58 (2s, 2H), 5.0−5.3 (m,

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1H), 5.4−5.6 (m, 1H), 7.1−7.8 (m, 19H). Anal. Calcd for $C_{36}H_{42}O_7SSi$: C, 66.84; H, 6.55. Found: C, 66.68; H, 6.69.

**(2*R*,3*S*,4*S*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-4-benzyloxymethyl-5-hexene-1,2-diol (19).** To a stirred suspension of NaH (360 mg of 50% suspension in oil, 7.5 mmol, washed with hexane) in THF (100 mL) was added dropwise **11** (2.5 g, 7.5 mmol) in THF (30 mL) over a period of 30 min. The mixture was gently heated to 50 °C for 1 h. TBDPS-chloride (2.1 g, 7.7 mmol) in THF (30 mL) was added dropwise to the stirred mixture at 50 °C. After stirring for 30 min more, the mixture was treated with water. Usual extraction and solvent removal afforded the O-silylated compound in almost quantitative yield. This was dissolved in a solvent mixture (40 mL) of THF and $CH_2Cl_2$ in 1:1 ratio. To it was added 90% aqueous trifluoro acetic acid (10 mL). The mixture was stirred at 15 °C for 6 h when almost all of the silylated compound was found to have disappeared (TLC). The mixture was then extracted with $CHCl_3$. The combined organic extract was washed with 10% aqueous $NaHCO_3$, water, and brine. Solvent removal under reduced pressure followed by column chromatography of the residue (silica gel, 0−5% MeOH in $CHCl_3$ ) afforded pure **19** (2.84 g, 77%): $[\alpha]^{22}_D$ +8.47 (*c* 3.4, $CHCl_3$); IR (film) 3500, 3075, 3005, 2855, 1650, 995, 915; $^1$H NMR ($CDCl_3$) $\delta$ 1.04 (s, 9H), 2.0 (bs, $D_2O$ exchangeable, 2H), 2.3−2.5 (m, 1H), 3.3−3.8 (m, 6H), 4.45 (m, 2H), 5.0−5.2 (m, 2H), 5.5−5.7 (m, 1H), 7.2−7.9 (m, 15H). Anal. Calcd for $C_{30}H_{38}O_4Si$: C, 73.43; H, 7.80. FoundT C, 73.63; H, 7.59.

**(2*R*,3*S*,4*S*)-1-*O*-Benzoyl-3-*O*-*tert*-butyldiphenylsilyl-4-benzyloxymethyl-5-hexene-1,2,3-triol (20).** To a cooled (0 °C) solution of **19** (2.45 g, 5 mmol) and triethylamine (0.3 mL, 2 mmol) in $CH_2Cl_2$ (40 mL) was added a solution of benzoyl cyanide (0.6 mL, 5.1 mmol) in $CH_2Cl_2$ (10 mL) dropwise over a period of 30 min. The mixture was stirred for an additional hr at 0 °C and treated with water. The organic layer was separated and washed with water and then brine. Solvent removal followed by column chromatography (silica gel, 0−20% EtOAc in petroleum ether) of the residue afforded the monobenzoate **20** (2.43 g, 82%): $[\alpha]^{22}_D$ +18.09 (*c* 3.6, $CHCl_3$); IR (film) 3500, 3005, 2855, 1715, 1650, 995, 920; $^1$H NMR ($CDCl_3$) $\delta$ 1.04 (s, 9H), 2.0 (bs, $D_2O$ exchangeable, 1H), 2.3−2.5 (m, 1H), 3.5−3.9 (m, 4H), 4.1−4.3 (m, 2H), 4.51 (m, 2H), 5.0−5.2 (m, 2H), 5.5−5.7 (m, 1H), 7.3−8.2 (m, 20H). Anal. Calcd for $C_{37}H_{42}O_5Si$: C, 74.71; H, 7.12. Found: C, 74.63; H, 7.29.

**5-*O*-Benzoyl-3-*O*-*tert*-butyldiphenylsilyl-2-*C*-benzyloxymethyl-2-deoxy-D-ribofuranose (21).** Following a similar procedure as for the preparation of **14**, **20** (594 mg, 1 mmol) in $CH_2Cl_2$ (50 mL) was subjected to ozonolysis at −78 °C followed by reduction with $PPh_3$ (288 mg, 1.1 mmol) in situ. Solvent removal under reduced pressure and column chromatography (silica gel, 0−30% EtOAc in petroleum ether) of the residue afforded **21** (440 mg, 74%) as a mixture of $\alpha$ and $\beta$ anomers: $[\alpha]^{22}_D$ +17.47 (*c* 1.8, $CHCl_3$); IR (film) 3440, 3071, 2855, 1715, 1597; $^1$H NMR ($CDCl_3$) $\delta$ 1.04, 1.07 (2s, 9H), 2.4−2.7 (m, 1H), 2.9 (bs, $D_2O$ exchangeable, 1H), 3.5−3.9 (m, 2H), 4.1−4.3 (m, 2H), 4.4−4.6 (m, 2H), 4.51 and 4.53 (2s, 2H), 5.4 (m, 1H), 7.3−8.2 (m, 20H). Anal. Calcd for $C_{36}H_{40}O_6Si$: C, 72.45; H, 6.77. Found: C, 72.63; H, 6.59.

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