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(*R*)-2,3-*O*-Cyclohexylideneglyceraldehyde: a useful template for a simple entry into carbafuranose stereoisomers

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ABSTRACT

(*R*)-2,3-*O*-Cyclohexylideneglyceraldehyde **1** provides a simple route for the preparation of carbafuranoses. This has been exemplified by the preparation of **10c** and **10d**, the derivatives of carba D-xylofuranose and carba-L-arabinofuranose respectively, starting from homoallylic alcohol **2a** derived from **1**. The key step in this protocol was the intramolecular allylation of **9** promoted by several metals under wet conditions that resulted in the construction of the carbafuranose skeleton of **10**. The potential of several metals regarding the efficacy and stereoselectivity of this crucial intramolecular allylation reaction has been studied. The moderate stereoselectivity in all of the successful intramolecular allylations of **9** yielding both D-**10c** and L-**10d** as the major products contributed significantly in attaining stereo-divergence in this route. The utility of this route was due to the easy availability of **1**, and the operational simplicity as well as scalability of all of the reactions involved.

1. Introduction

Chiral polyoxygenated cyclopentanes are constituents of many bioactive compounds, such as glycosidase inhibitors,[1] carbocyclic nucleosides,[2] and prostaglandins.[3] They are also referred to as carbafuranoses and treated as analogues of monosaccharides in which the ring oxygen of a furanose has been replaced by a methylene (–CH_2–) group. This modification transforms the (hemi-) acetal anomeric center of a natural sugar unit into an ether (alcohol) group in the resulting carbasugar. The lack of an acetal moiety preserves the carbafuranoses from hydrolysis as compared to sugar derivatives. In addition, this modification has a positive effect on the conformational changes in their structures. Over the last few decades, the chemistry of carbafuranoses and other carbasugars has emerged as a topic of intense investigation in bioorganic research.[4] Interestingly, two carbafuranose nucleosides were identified in natural sources, neplanocin A[5a] and aristeromycin,[5b] which display antibiotic and antitumor activities but so far no carbafuranose sugar has been isolated as such in Nature. In view of this, since the first synthesis reported by Wilcox et al.[6a,b] considerable attention has been focused on the synthesis[6] of carbafuranoses and analogues in their different stereochemical forms in order to make them amenable for varied applications.

In our ongoing program on the synthesis of biologically active molecules, we have been exploiting easily accessible and highly stable (*R*)-2,3-*O*-cyclohexylideneglyceraldehyde **1**[7a] for the asymmetric construction of several structural units[7] that are present in our target molecules. Included among them was our recent work[7i] related to the synthesis of carbocycles. Herein we report another application of **1** to develop a simple and efficient route for the preparation of carbafuranose sugars in their different stereochemical forms. This is shown here by the synthesis of **10c** and **10d**, derivatives of two carbafuranose sugars.

2. Results and discussion

Retrosynthetic analysis (Fig. 1) of carbafuranose sugar skeleton, **X** suggested that it could be obtained from its olefinic precursor **Y**. Consequently, the C-3 and C-4 stereocenters of **Y** could simultaneously be constructed via intramolecular allylation of intermediate **Z**, which are accessible starting from either of the two homoallylic alcohols **2a**,**b** derived from **1**. For the present work we chose *anti*-**2a**[7b] to start with (Scheme 1). Silylation of both hydroxyl of groups diol **3a**, which was obtained from **2a**,[8] using 2 equiv of TBDMS chloride and imidazole produced **3b** in good overall yield. Ozonolysis of the olefin of **3b,** followed by PPh_3 reduction of the resulting ozonide in one-pot afforded aldehyde **4**. This was found to be unstable on standing, and so without further purification was quickly subjected to Wittig Horner olefination to obtain **5** in good yield. The DIBAL reduction of **5** afforded allylic alcohol **6** which was transformed into bromide **7b** in two steps [(a) mesylation; (b) treatment of mesylate **7a** with NaBr in acetone] in good overall yield. Next, the regioselective desilylation of **7b** was accomplished by stirring it in acidified $CHCl_3$ solution to afford **8** in good yield. The free hydroxyl of **8** was oxidized with

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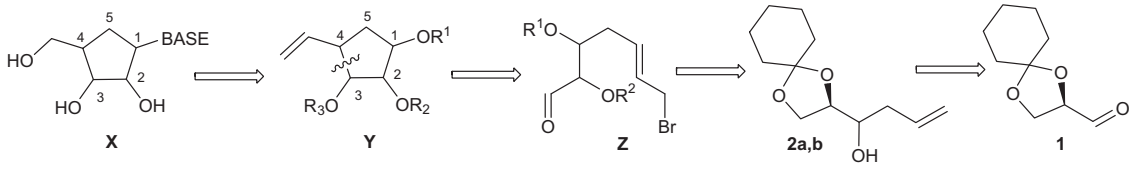
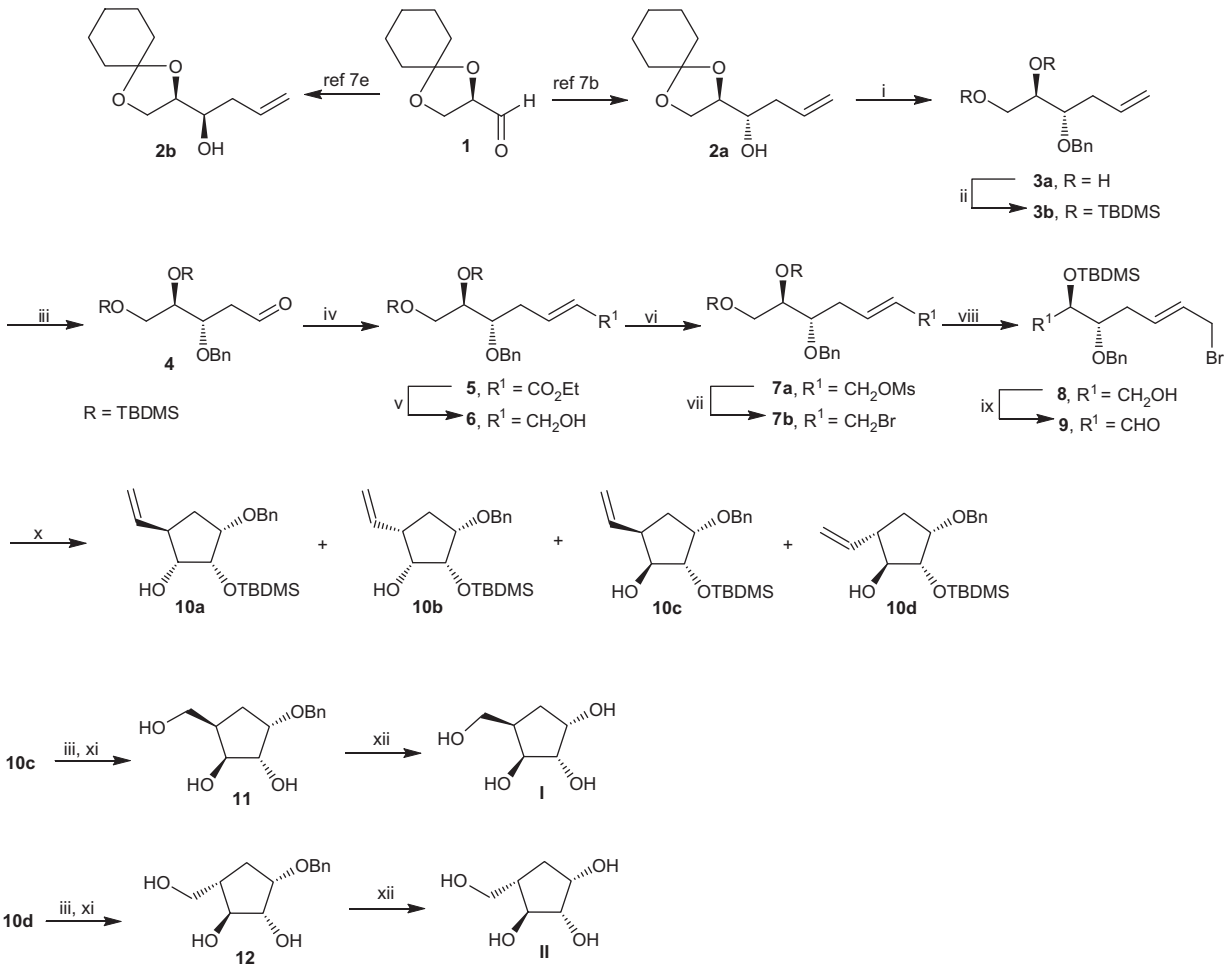


Figure 1. Retrosynthesis of carbafuranose.



Scheme 1. Synthesis of carbafuranose. Reagents and conditions: (i) Ref. 8; (ii) TBDMSCl, imidazole, DMAP, DMF, 94%; (iii) O_3, PPh_3, CH_2Cl_2, −78 °C, 86%; (iv) NaH, $C_2H_5COOCH_2P(O)(OC_2H_5)_2$, THF, 25 °C, 81%; (v) DIBAL-H, THF, −78 °C, 91%; (vi) MsCl, Et_3N, CH_2Cl_2, 0 °C; (vii) NaBr, $NaHCO_3$, Acetone, 25 °C, 90% (in two steps); (viii) $CHCl_3$ aq HCl, 91%; (ix) Dess Martin Periodinane, CH_2Cl_2, 91%; (x) (a) Zn/aq NH_4Cl, moist THF, 74%, (b) Zn/$FeCl_3$, moist THF, 68%, (c) Zn/$SnCl_2{\cdot}2H_2O$, moist THF, 88%, (d) Zn/$CuCl_2{\cdot}2H_2O$ moist THF, no reaction, (e) In/H_2O, no reaction; (xi) $LiAlH_4$, Et_2O; (xii) 10% Pd/C, H_2, EtOH, 94% from **11** to I, 90% from **12** to II.

Dess Martin periodinane to obtain aldehyde **9**, which was equivalent to **Z** in Figure 1. Since Compound **9** was relatively unstable on long standing, it was quickly subjected to intramolecular allylation resulting in construction of the carbafuranose unit of **10** (equivalent to intermediate **Y** in Fig. 1) with simultaneous generation of its two stereocenters at C-3 and C-4. With a view to determine its practical viability, this allylation reaction was performed under wet conditions in the presence of five different metal mediators viz Luche's zinc[9] and three low valent metals iron, copper, and tin,[10] and indium.[11] In order to ensure smooth progress, all of the heterogeneous metal mediated allylation reactions were performed using an excess of metal/metal salts. The efficacies of all these allylation reactions (step xi, Scheme 1) are summarized in Table 1.

Luche's allylation[9] of **9** produced **10** in good yield (74.7%, Table 1, entry a) containing a mixture of its all four possible diastereomers **10a–d**. Among them, **10c** and **10d** were obtained as the major products of which **10d** was produced with better selectivity. Both **10c** and **10d** could easily be isolated by column chromatography of the reaction product to obtain each in pure form. The other two stereoisomers **10a** and **10b** were obtained in much smaller amounts and could be isolated as a mixture of chromatographically inseparable compounds.[12]

The low valent iron mediated reaction[10a] produced **10**, albeit in a lower yield (68.2%, Table 1, entry b) compared to Luche's reaction. This reaction also afforded **10c** and **10d** as the major products and the mixture of **10a/b** as the minor product. Similar to Luche's allylation, the iron mediated reaction produced **10d** with better stereoselectivity than that of **10c**. The low valent tin mediated[10c] reaction was found to be more efficient compared to the previous ones that was evident from the improved yield of **10** (87.5%,

Table 1
Intramolecular allylation of aldehyde **9**

Entry	Metal/salt or metal salt/metal	Solvent	Time (h)	Overall yield of **10** (%)	**10a and 10b**:**10c**:**10d**[a]
a	Zn/NH_4Cl	THF	18	74.7	8.7: 20.8: 70.5
b	$FeCl_3/Zn$	THF	18	68.2	10.2: 23.2: 66.6
c	$SnCl_2$, $2H_2O/Zn$	THF	18	87.5	11.4: 62.7: 25.9
d	$CuCl_2$, $2H_2O/Zn$	THF	18	NR	—
e	In	H_2O/THF	48	NR	—

NR: No reaction.
[a] The relative ratio of the chromatographically separable components of the reaction product.

Table 1, entry c). In this case, the reaction yielded **10a,b** in a minor amount while the other two were obtained as the major products. However, contrary to the previous two cases, this reaction yielded **10c** with better stereoselectivity than that of **10d**. However, our attempts to perform the same intramolecular allylation of **9**, in the presence of either low valent copper[10a] or indium[12] as mediators were unsuccessful, as no reaction took place in either case even when stirring the reaction mixture for longer (Table 1, entries d and e). The stereochemical differentiations of the aforementioned successful allylation reactions could be assessed from the isolable amount of all of the chromatographically separable components of **10** and the results are summarized in Table 1.

The stereochemistry of **10c** could be established by transforming it into the known carba α-D-xylofuranose **I**[6d] following Scheme 1, which involves only functional manipulation and so does not affect any of its stereocenters. Accordingly, **10c** was subjected to a series of reactions viz (a) ozololysis, (b) in situ PPh_3 reduction of the resulting ozonide; and (c) $LiAlH_4$ reduction of the crude aldehyde thus obtained (this took place with concomitant desilylation) to afford **11**. This upon catalytic hydrogenation afforded **I** whose specific rotation and spectroscopic data were in good agreement with the reported values.[6d] Following the same reaction protocol, **10d** was transformed into carba-β-L-arabinofuranose **II** via intermediate **12**. The specific rotation and spectroscopic data of synthetic **II** were in good agreement with the reported values.[6k]

The preferential formation of **10c,d** in the three successful intramolecular metal mediated allylations (Table 1, entries a–c) suggested that all of these reactions took place via a Felkin-Anh model[13] (Fig. 2). Simultaneously, the formation of the same two major products with a reversal in stereochemistry at the C-4 position [(4*R*) in **10c** and (4*S*) in **10d**] in the intramolecular addition reactions of *E*-allylic bromide **9** suggested that there could be an isomerization between the initially formed *E*-crotylmetal *E*-**M** (from **9**) and *Z*-crotylmetal *Z*-**M** (step (i) Fig. 3).[10c] This was followed by the intramolecular allylation of the aldehyde functionality through the corresponding Zimmerman–Traxler transition states (steps (ii) and (iii), Fig. 3).[14] Thus, the relative ratio between the two Felkin-Anh products **10c** and **10d** obtained in each of the successful reactions (Table 1, entries a–c) largely depended on the degree of isomerization between the corresponding *E*-**M** and *Z*-**M** of the crotylmetal.

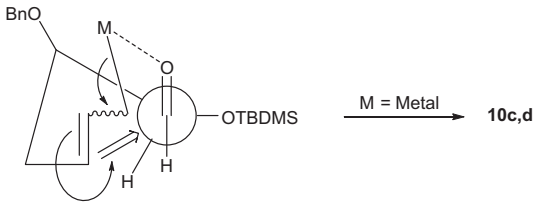


Figure 2. Felkin-Anh model for metal mediated intramolecular allylation of 9.

3. Conclusion

In conclusion, compound **1** has been exploited as a useful chiral template to develop a simple route to obtain carbafuranose sugars. This has been shown by the preparation of **10c** and **10d**, derivatives of carba α-D-xylofuranose and carba-β-L-arabinofuranose respectively, from **2a** in turn obtained from **1**. The efficacy of this protocol was due to the easy availability of **2a** from **1** on a multigram scale,[7a] the low cost and operational simplicity of all of the reactions involved. Due to all of these advantages, the overall route could be scalable. The novel feature in the structures of both **10c,d** was due to the presence of differently hydroxyl protected substituents at three centers (C-1, C-2, and C-3), which could allow selective chemical and stereo chemical manipulation. Understandably, the presence of a vinyl unit at the C-4 position in both compounds could be advantageous because of its amenability to be converted into different functionalities through suitable chemical transformation. It is worth mentioning that there is precedent for the preparation of 4-vinyl substituted carbafuranoses that are relevant to the synthesis of modified carbocycles.[6d,t] The availability of homochiral **10c** and **10d** in substantial amounts could provide an opportunity for their versatile applications in different synthetic objectives. The formation of both D- and L-carbasugars **10c** and **10d** respectively as the major products in all of these successful metal mediated intramolecular allylation (Table 1) reactions of **9** could be of considerable importance with regard to achieving stereo divergence *ivian* this route. This was facilitated by the moderate stereoselectivity that is found in all of these allylation reactions. The preparation of L-**10d** could be relevant due to the recent interest in the application of L-carbanucleosides in anti viral chemotherapy.[15] There is also scope to apply the present protocol with **2b**,[7e] or the homoallylic alcohols corresponding to **2a,b**, which could be derived from (−)-**1**,[16] and explore their efficacies as well as stereoselectivities to gain access to other stereoisomers of **10,** the derivatives of the corresponding carbafuranoses.

4. Experimental

4.1. General

Chemicals used as starting materials were commercially available and used without further purification. All solvents used for extraction and chromatography were distilled twice at atmospheric pressure prior to use. The organic extracts were desiccated over dry Na_2SO_4.

4.2. (4*S*,5*R*)-4-*O*-Benzyl-5,6-*O*-*tert*-butyldimethylsilyl-4,5,6-trihydroxy-hex-1-ene 3b

To a cooled (0 °C) solution of **3a**[9] (1.77 g, 8 mmol) in dry DMF (30 ml) containing DMAP (100 mg) was added imidazole (1.4 g, 20.5 mol), followed by the addition of *tert*-butyldimethylsilyl chloride (2.5 g, 16.6 mmol). The solution was stirred at room temperature overnight until completion of the reaction (confirmed by TLC).

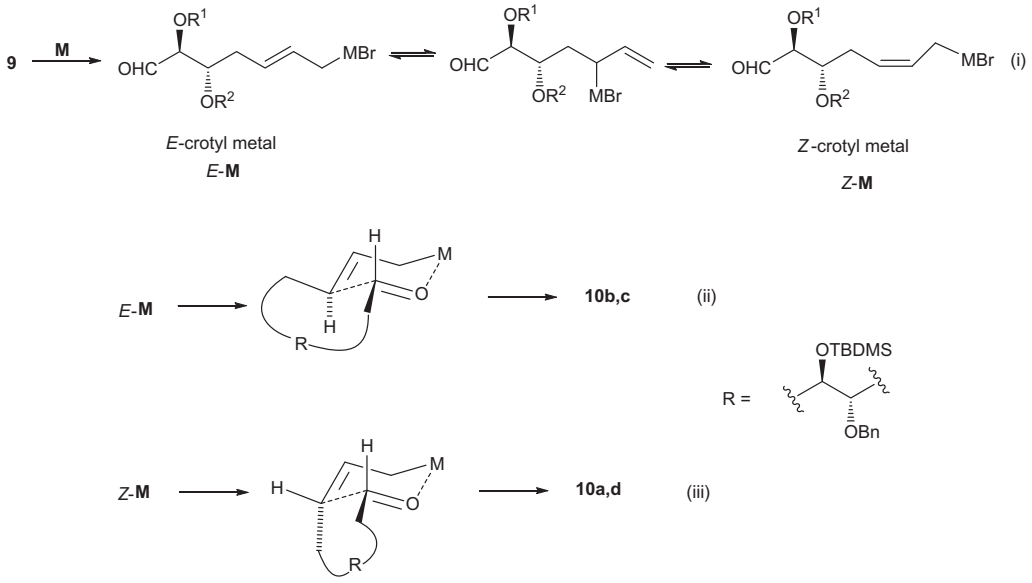


Figure 3. Zimmermann–Traxler model for the metal mediated intramolecular allylation of 9.

The mixture was treated with water and extracted with EtOAc. The combined organic extract was washed with water, brine and dried over Na_2SO_4. Solvent removal under reduced pressure, and column chromatography (silica gel, 0–10% EtOAc in hexane) of the residue afforded pure **3b** (3.38 g, 93.8%) as a colorless oil. $[\alpha]_D^2 6 = -17.9$ (*c* 1.06, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.05 (2s, 6H each), 0.90 (br s, 18H), 2.34 (t, *J* = 6.8 Hz, 2H), 3.55–3.64 (m, 3H), 3.79–3.82 (m, 1H), 4.52, 4.64 (AB q, *J* = 11.6 Hz, 2H), 5.05 (m, 2H), 5.7–5.9 (m, 1H), 7.2–7.4 (m, 5H). ^{13}C NMR (50 MHz $CDCl_3$): −5.38, −5.35, −4.7, −4.4, 18.1, 18.3, 25.92, 25.98, 34.9, 64.6, 72.3, 74.8, 80.2, 116.5, 127.4, 127.8, 128.2, 135.9, 138.9. Anal. Calcd for $C_{25}H_{46}O_3Si_2$: C, 66.61; H, 10.29. Found: C, 66.48; H, 10.52.

4.3. (3*S*,4*R*)-3-*O*-Benzyl-4,5-*O*-di *tert*-butyldimethylsilyl-3,4,5-trihydroxypent-1-al 4

Ozone was bubbled through a cooled (−78 °C) solution of **3b** (4.8 g, 10.65 mmol) in CH_2Cl_2 (40 ml) until the solution turned blue. After stirring the reaction mixture for another 10 min, Ph_3P (4.2 g, 15.97 mmol) was added in portions and the mixture was gradually brought to room temperature and stirred for 1 h, after which it was concentrated under reduced pressure to afford an oily residue, which was quickly purified by passing through a short pad of silica gel, eluting with 10% hexane: in EtOAc to obtain aldehyde **4** (4.14 g, 85.9%) as a colorless oil. The aldehyde was found to be unstable on long standing and hence a major portion of it was immediately used for the next step. A small portion was used for spectroscopic characterization. ^{1}H NMR (200 MHz $CDCl_3$): δ 0.04, 0.08 (2s, 6H each), 0.88 (s, 18H), 2.59–2.67 (m, 2H), 3.49–3.58 (m, 2H), 3.91–3.95 (m, 1H), 4.08–4.11 (m, 1H), 4.53, 4.66 (ABq, *J* = 11.5 Hz, 2H), 7.17–7.40 (m, 5H), 9.77 (t, *J* = 1.9 Hz, 1H); ^{13}C NMR (50 MHz $CDCl_3$): −5.5, −4.7, 18.1, 18.2, 25.8, 25.9, 43.9, 64.4, 71.9, 74.0, 75.6, 127.6, 127.3 128.8, 138.2, 201.5.

4.4. (5*S*,6*R*)-Ethyl-5-*O*-benzyl-6,7-*O*-di *tert*-butyl-dimethylsilyl-5,6,7-trihydroxy-hept-2*E*-enoate 5

To a cooled (0 °C) suspension of sodium hydride (0.47 g, 50% suspension in oil, 9.8 mmol, washed twice with dry hexane) and dry THF (20 ml), triethyl phosphonoacetate (2.21 g, 9.86 mmol) in dry THF (10 ml) was added dropwise over a period of 30 min under an argon atmosphere. After the addition, the reaction mixture was gradually brought to room temperature and stirred until the reaction mixture became clear. The mixture was again cooled to 0 °C and to it a solution of **4** (4.06 g, 8.97 mmol) in dry THF (20 ml) was added dropwise over a period of 45 min. The mixture was gradually brought to room temperature and stirred for 4 h until completion of reaction (confirmed from TLC). After cooling the reaction mixture to 0 °C, it was treated with water and with 2% aqueous dilute HCl to make it neutral. The mixture was then extracted with EtOAc. The combined organic layer was washed with water, brine and dried over Na_2SO_4. Solvent removal under reduced pressure and column chromatography (silica gel, 0–15% EtOAc in hexane) of the residue afforded pure **5** (3.79 g, 80.8%) as a colorless oil. $[\alpha]_D^{27} = -25.0$ (*c* 1.24, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.04, 0.09 (2s, 6H each), 0.88 (br s, 18H), 1.28 (t, *J* = 7.1 Hz 3H), 2.46 (t, *J* = 6.5 Hz 2H), 3.56–3.68 (m, 3H), 3.80–3.84 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.47, 4.62 (ABq, *J* = 11.5 Hz, 2H), 5.86 (d, *J* = 15.6 Hz, 1H), 7.02(dt, *J* = 15.6 Hz, 7.2 Hz, 1H) 7.25–7.32 (m, 5H); ^{13}C NMR (50 MHz $CDCl_3$): −5.4, −4.8, −4.5, 14.2, 18.1, 18.2, 25.8, 25.9, 32.9, 60.0, 64.4, 72.1, 74.3, 78.8, 122.9, 127.5, 127.8, 128.2, 138.3, 146.7, 166.4; Anal. Calcd for $C_{28}H_{50}O_5Si_2$: C, 64.32; H, 9.64. Found: C, 64.48; H, 9.55.

4.5. (5*S*,6*R*)-5-*O*-Benzyl-6,7-*O*-di-*tert*-butyl-dimethylsilyl-1,5,6,7-tetrahydroxy-hept-2E-ene 6

To a cooled (−78 °C) solution of **5** (3.7 g, 7.07 mmol) in THF, DIBAL-H (14.3 ml, 1.0 M solution in hexane, 14.3 mmol) was added dropwise over a period of 30 min. The mixture was then stirred for another hour at the same temperature until completion of the reaction (confirmed from TLC). To the mixture, methanol (15 ml) was added. The mixture was stirred at room temperature for 2 h and the resulting solid was filtered through a Celite pad. Solvent removal under reduced pressure and column chromatography (silica gel, 0–20% EtOAc in hexane) of the residue afforded pure **6** (3.1 g, 91.1%) as a colorless oil. $[\alpha]_D^{24} = -21.7$ (*c* 0.92, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.04, 0.07 (2s, 12H), 0.89 (br s, 18H), 1.44 (br s, 1H), 2.31 (t, *J* = 5.6 Hz, 2H), 3.50–3.65 (m, 3H), 3.80(dd, *J* = 9.1 Hz, 5.1 Hz 1H), 4.04 (d, *J* = 3.5 Hz, 2H), 4.52, 4.64 (AB q, *J* = 5.6 Hz, 2H), 5.66–5.75 (m, 2H), 7.25–7.32 (m, 5H); ^{13}C NMR (50 MHz $CDCl_3$): −5.4, −4.7, −4.4, 18.1, 18.3, 26.0, 25.9, 33.0, 63.5, 64.5, 72.2, 74.6, 79.9,

127.4, 127.9, 128.1, 129.8, 131.0, 138.7; Anal. Calcd for $C_{26}H_{48}O_4Si_2$; C, 64.95; H, 10.06; Found: C, 65.08; H, 10.19.

4.6. (5*S*,6*R*)-1-Bromo-5-*O*-benzyl-6,7-*O*-di *tert*-butyl-dimethylsilyl-5,6,7-trihydroxy-hept-2E-ene 7b

To the cooled (0 °C) solution of **6** (3.0 g, 6.24 mmol) in dry DCM (25 ml), triethylamine (1.07 g, 10.60 mmol) was added dropwise over a period of 15 min followed by the addition of methylsulfonyl chloride (0.93 g, 8.11 mmol) dropwise at the same temperature. The mixture was slowly brought to room temperature and stirred for 3 h until completion of the reaction (confirmed from TLC). The mixture was washed with water for neutrality and extracted with chloroform. The combined organic layer was washed with brine and dried over Na_2SO_4. Solvent removal under reduced pressure afforded a yellow oily liquid containing the crude mesylate **7a** product, which was used in the next reaction without further purification.

To the solution of above crude product in dry acetone (20 ml), dry NaBr (0.78 g, 7.5 mmol) and a catalytic amount of $NaHCO_3$ was added and stirred overnight. The reaction mixture was concentrated under reduced pressure to remove the acetone, washed with dilute HCl (2%), and extracted with chloroform. The combined organic layer was washed with brine and dried over Na_2SO_4. Solvent removal under reduced pressure and column chromatography (silica gel, 0–10% EtOAc in hexane) of the residue afforded pure **7b** (3.06 g, 90.26%) as a colorless oil. $[\alpha]_D^{24} = -11.9$ (c 0.95, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.04, 0.06 (2s, 6H each), 0.94 (br s, 18H), 2.33 (t, J = 5.9 Hz 2H), 3.50–3.62 (m, 3H), 3.80 (dd, J_1 = 9.4 Hz, 5.1 Hz 1H), 3.91 (d J = 6.2 Hz, 1H), 4.01 (d, J = 6.2 Hz, 1H), 4.48, 4.62 (AB q, J = 11.58 Hz, 2H), 5.61–5.87 (m, 2H), 7.25–7.31 (m, 5H); ^{13}C NMR (175 MHz $CDCl_3$): −5.4, −5.3, −4.7, −4.4, 18.2, 18.3, 25.9, 26.0, 33.0, 45.3, 64.6, 72.3. 74.7, 79.7, 127.5, 127.7, 127.9, 128.2, 133.2, 138.7; Anal. Calcd for $C_{26}H_{47}BrO_3Si_2$; C, 57.43; H, 8.71; Found: C, 57.66; H, 8.61.

4.7. (5*S*,6*R*)-1-Bromo-5-*O*-benzyl-6-*O*-*tert*-butyl-dimethylsilyl-5,6,7-trihydroxy-hept-2*E*-ene 8

Compound **7b** (2.5 g, 4.59 mmol) was dissolved in acidified chloroform (15 ml) [prior to its use chloroform had been shaken with aqueous concentrated HCl (2 ml) and then separated]. The solution of **7b** was stirred at room temperature for 36 h until the completion of the reaction (confirmed by TLC). The organic layer was washed successively with water to remove HCl, brine and then dried over Na_2SO_4. Solvent removal under reduced pressure and column chromatography (silica gel, 0–20% EtOAc in hexane) of the residue afforded pure **8** (1.8 g, 6.44 mmol, 91.2%) as a pale yellow oil. $[\alpha]_D^{24} = -0.7$ (c 1.00, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.06 (s, 6H), 0.90 (br s, 9H), 1.88 (br s, 1H), 2.35–2.43 (m, 2H), 3.55–3.78 (m, 4H), 4.03 (d, J = 5.9 Hz,2H), 4.62 (bm, 2H), 5.70–5.82 (m, 2H), 7.25–7.32 (m, 5H); ^{13}C NMR (50 MHz $CDCl_3$): −4.6, −4.4, 18.0, 25.8, 33.7, 45.2, 63.8, 72.8, 73.7, 79.7, 127.8, 128.0, 128.4, 131.9, 137.9; Anal. Calcd for $C_{20}H_{33}BrO_3Si$; C, 55.93; H, 7.75; Found: C, 56.21; H, 7.82.

4.8. (2*R*,3*S*)-2-*O*-*tert*-Butyl-dimethylsilyl-3-*O*-benzyl-7-bromo-2,3-dihydroxy-hept-5*E*-enal 9

To a cooled (0 °C) solution of **8** (1.5 g, 3.50 mmol) in dry DCM (35 ml), Dess Martin periodinane (2.23 g, 5.25 mmol) was added portionwise. The reaction mixture was stirred for 30 min at 0 °C, and then gradually brought to room temperature and stirred until completion of the reaction (confirmed from TLC), after which it was diluted with chloroform (30 ml). The solution was poured into saturated aqueous $NaHCO_3$ (20 ml) containing a sevenfold excess of $Na_2S_2O_3$. The mixture was stirred to dissolve the solid. The organic layer was separated and the aqueous layer was extracted with chloroform. The combined organic layer was washed with water, brine and dried over Na_2SO_4. Solvent removal under reduced pressure gave an oily residue which was passed through a short pad of silica gel eluting with 10% EtOAc in hexane to obtain pure **9** (1.36 g, 91.4%) as a colorless oil. This was found to be unstable on long standing and hence a major part of it was immediately used for the next step. A small portion was used for tentative characterization. $[\alpha]_D^{25} = -25.0$ (c 0.92, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.07 (s, 6H), 0.94 (br s, 9H), 2.35–2.41 (m, 2H), 3.69–3.75 (m, 1H), 4.00 (d, J = 5.4 Hz, 2H), 4.12 (dd, J_1 = 3.6 Hz, J_2 = 1.5 Hz, 1H), 4.54, 4.64 (AB q, J = 11.72 Hz 2H), 5.65–5.72 (m, 2H), 7.25–7.35 (m, 5H), 9.6 (d, J = 1.5 Hz, 1H); ^{13}C NMR (50 MHz $CDCl_3$): −4.8, 18.1, 25.7, 33.1, 44.8, 72.2, 78.8, 80.6, 127.8, 128.3, 129.4, 130.9, 137.7, 203.4.

4.9. Luche's intramolecular allylation of 9

To a well stirred mixture of aldehyde **9** (1 g, 2.5 mmol) and Zn dust (520 mg, 8 mmol) in THF (30 ml), was added a saturated aqueous NH_4Cl solution (1.5 mL) dropwise over a period of 20 min. The reaction mixture was then stirred overnight after which the starting material disappeared 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, brine and dried. Solvent removal under reduced pressure and column chromatography (silica gel, 0–20% EtOAc in Hexane) of the residue afforded **10a**/**10b** (53 mg) as an inseparable mixture of compounds which eluted first, followed by **10c** (127 mg) and **10d** (430 mg) which eluted successively to obtain each in pure form.

4.10. General procedure for the intramolecular allylation of 9 employing a bimetal redox strategy

To a cooled (15 °C) solution of aldehyde **9** (1 g, 2.5 mmol) in THF (30 ml) was added metal salt [$FeCl_3$ (1.29 g, 8.0 mmol) or $SnCl_2.2H_2O$ (1.8 g, 8.0 mmol) or $CuCl_2.2H_2O$ (1.36 g, 8.0 mmol)]. The mixture was stirred for 5 min. To this stirred suspension, Zn dust (650 mg, 10 mmol) was added in portions over a period of 20 min. The reaction mixture was gradually brought to ambient temperature and stirred for the period as mentioned in Table 1. Low valent iron and tin mediated reactions showed the total disappearance of starting material **9** and the formation of product **10** (while monitored by TLC). However, no reaction was found to take place in the case of low valent copper mediated reactions. Finally, in both of the successful reactions (iron and tin mediated reactions), the reaction mixture was treated successively with diethyl ether (50 mL) and water (25 mL) and then stirred for 10 min and filtered. The filtrate was treated with 2% aqueous HCl to dissolve a small amount of suspended particles. The organic layer was separated and the aqueous layer extracted with EtOAc. The combined organic extract was washed with water, brine and then dried. Solvent removal under reduced pressure and column chromatography (silica gel, 0-20% EtOAc/Hexane) of the residue gave **10a**/**10b** as an inseparable mixture of compounds, and **10c** and **10d** in pure form. Thus, chromatography of low valent iron mediated reaction gave 57 mg of **10a**/**10b,** 129 mg of **10c**, and 370 mg of **10d**. Similarly, low valent tin mediated reaction gave 81 mg **of 0a**/**10b**, 447 mg of **10c**, and 185 mg pf **10d**.

4.11. Indium mediated intramolecular allylation of 9 in H_2O/THF

To a magnetically stirred solution of **9** (1 g, 2.5 mmol) in a 1:1 solvent mixture of water and THF (8 mL) was added indium

(99.99% pure ingot, Alfa Aesar, 632 mg, 5.5 mmol). The reaction mixture was stirred for 48 h. No reaction took place (TLC).

4.12. (1*S*,2*S*,3*R*,4*R*)-1-*O*-Benzyl-2-O-*tert*-butyldimethylsilyl-4-vinyl-cyclopentane-1,2,3-triol 10a and (1*S*,2*S*,3*R*,4*S*)-1-*O*-benzyl-2-O-*tert*-butyldimethylsilyl-4-vinyl-cyclopentane-1,2,3-triol 10b

^{1}H NMR (200 MHz $CDCl_3$): δ 0.06 (br s, 6H), 0.93 (br s, 9H), 1.61–1.64 (m, 1H), 2.1–2.5 (m, 2H, overlapped with a br s, 1H), 3.65–3.70 (m, 1H), 3.81–3.84 (m, 1H), 4.0 (m, 1H), 4.53–4.65 (m, 2H), 4.9–5.1 (m, 2H), 5.73–5.86 (m, 1H), 7.25–7.34 (m, 5H); ^{13}C NMR (50 MHz $CDCl_3$): −4.9, −4.6, 18.3, 25.9, 32.8, 48.1, 71.7, 72.1, 75.1, 75.9, 77.2, 77.6, 78.9, 79.2, 113.9, 127.4, 127.5, 128.2 138.5, 138.6, 140.6.

4.13. (1*S*,2*S*,3*S*,4*R*)-1-*O*-Benzyl-2-*O*-*tert*-butyldimethylsilyl-4-vinyl-cyclopentane-1,2,3-triol 10c

$[\alpha]_D^{24} = +3.8$ (*c* 0.51, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.09 (br s, 6H), 0.91 (br s, 9H), 1.6–2.1 (m, 2H, overlapped with a br s, 1H), 3.10 (m, 1H), 3.94–4.06 (m, 3H), 4.53, 4.64 (AB q, *J* = 12.0 Hz, 2H), 5.1–5.2 (m, 2H), 5.7–5.9 (m, 1H), 7.2–7.4 (m, 5H); ^{13}C NMR (50 MHz $CDCl_3$): −4.8, −4.7, 18.2, 25.8, 32.2, 42.8, 71.7, 78.2, 79.1, 79.2, 116.8, 127.2, 127.5, 127.6 128.1, 129.6, 134.7, 137.7, 138.9 Anal. Calcd for $C_{20}H_{32}O_3Si$; C, 68.92; H, 9.25; Found: C, 68.71; H, 9.15.

4.14. (1*S*,2*S*,3*S*,4*S*)-1-*O*-Benzyl-2-*O*-*tert*-butyldimethylsilyl-4-vinyl-cyclopentane-1,2,3-triol 10d

$[\alpha]_D^{25} = +12.95$ (*c* 1.39, $CHCl_3$); ^{1}H NMR (200 MHz $CDCl_3$): δ 0.10 (br s, 6H), 0.94 (br s, 9H), 1.62–1.69 (m, 1H, overlapped with a br s, 1H), 2.16–2.26 (m, 2H), 3.74–3.93 (m, 3H), 4.59 (d, *J* = 5.5 Hz, 2H), 4.97–5.11 (m, 2H), 5.72–5.91 (m, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (50 MHz $CDCl_3$): −4.68, −4.63, 18.2, 25.8, 33.2, 45.2, 71.4, 77.2, 79.6, 80.5, 114.8, 127.3, 127.6, 128.2, 138.7, 140.9; Anal. Calcd for $C_{20}H_{32}O_3Si$;C, 68.92; H, 9.25; Found: C, 68.65; H, 9.08.

4.15. (1*S*,2*S*,3*S*,4*R*)-1-*O*-Benzyl-4-hydroxymethyl-cyclopentane-1,2,3-triol 11

To a cooled (−78 °C) solution of **10c** (348 mg, 1.0 mmol) in CH_2Cl_2 (25 ml) was bubbled ozone gas until a blue color persisted. To it was added PPh_3 (300 mg, 1.15 mmol), and the blue color disappeared immediately. The solution was brought to room temperature and stirred for 40 min the solvent was removed from the reaction mixture under reduced pressure. The residue was passed through a short (2″) silica gel column and quickly eluted with 0–25% EtOAc in hexane to obtain an unstable aldehyde, which was taken in THF (25 ml). This solution was slowly added to a stirred suspension of $LiAlH_4$ (77 mg, 2.0 mmol) in THF (20 ml) at 10 °C. The mixture was stirred for 1 h at 10 °C and then at room temperature overnight. It was then cooled with ice water. The excess hydride was decomposed by the dropwise addition of a saturated aqueous solution of Na_2SO_4. The white precipitate formed was filtered and washed with dry diethyl ether. The solvent was removed from the combined washing under reduced pressure and the residue was passed through a short (2″) silica gel column and quickly eluted with 0–10% MeOH/$CHCl_3$ to obtain **11** (174 mg, 73.1%) as a colorless oil, which was used as such for the next reaction. A portion of the residue was subjected to spectral analysis for its characterization. $[\alpha]_D^{27} = +22.0$ (*c* 1.09, CH_2Cl_2); ^{1}H NMR (700 MHz $CDCl_3$): δ 1.77 (dt, *J* = 12.0 Hz, 6.0 Hz, 1H), 1.89 (m, 1H), 2.50 (m, 1H), 2.97(br s, 2H), 3.46 (br s, 1H), 3.63–3.65 (m, 1H), 3.76–3.77 (m, 1H), 3.94 (m, 1H), 4.03(m, 1H), 4.25 (t, *J* = 5.6 Hz, 1H), 4.48, 4.59 (AB q, *J* = 11.9 Hz, 2H), 7.26–7.35 (m, 5H); ^{13}C NMR (175 MHz $CDCl_3$): 29.2, 39.5, 62.9, 71.7, 78.6, 78.7, 78.8, 127.8, 127.9, 128.5, 137.8; Anal. Calcd for $C_{13}H_{18}O_4$; C, 65.53; H, 7.61; Found: C, 65.70; H, 7.45.

4.16. (1*S*,2*S*,3*S*,4*R*)-4-Hydroxymethyl)-cyclopentane-1,2,3-triol 11a [Carba-α-D-xylofuranose I]

A solution of **11** (125 mg) in EtOH (20 ml) was treated with 10% Pd-C (20 mg). The mixture was stirred under H_2 atmosphere for 10hr until the reaction was complete (monitored by TLC). The mixture was filtered through a Celite pad and solvent was removed under reduced pressure. The residue was chromatographed to afford pure **I** (73 mg, 93.9%) as a colorless oil. $[\alpha]_D^{26} = +12.7$ (*c* 1.0, MeOH) [lit.,[6d] $[\alpha]_D^{20} = +12.1$ (*c* 0.7, MeOH)]; ^{1}H NMR (600 MHz D_2O): δ 1.61 (m, 2H), 2.28–2.31 (m, 1H), 3.36 (dd, *J* = 7.2 Hz, 10.2 Hz, 1H), 3.53(dd, *J* = 7.2 Hz, 10.2 Hz, 1H), 3.72(m, 1H), 3.99 (m, 2H); ^{13}C NMR (150 MHz, D_2O): 34.7, 41.8, 64.3, 73.3, 78.5, 81.1.

4.17. (1*S*,2*S*,3*S*,4*S*)-1-*O*-Benzyl-4-hydroxymethyl-cyclopentane-1,2,3-triol 12

Following the same reactions protocol as carried out for the preparation of **11**, compound **10d** (348 mg, 1.0 mmol) was transformed into **12** (179 mg, 75.3%) as a colorless oil. $[\alpha]_D^{27} = +29.2$ (*c* 2.16, CH_2Cl_2); ^{1}H NMR (700 MHz $CDCl_3$): δ 1.48 (m, 1H), 1.64 (br s, 1H), 1.92(m, 1H), 2.06 (m, 1H), 3.57 (m, 1H), 3.63–3.70 (m, 1H, overlapped with a br s, 2H), 3.82(m, 1H), 3.88–3.90 (m, 1H), 3.93 (t, *J* = 7 Hz, 1H), 4.47 (d, *J* = 11.9 Hz, 1H), 4.574 (dd, *J* = 11.9 Hz, 5.6 Hz, 1H), 7.26–7.34 (m, 5H); ^{13}C NMR (175 MHz $CDCl_3$): 29.4, 43.3, 62.6, 71.6, 77.49, 78.6, 79.6, 127.8, 127.9, 128.5, 137.8; Anal. Calcd for $C_{13}H_{18}O_4$; C, 65.53; H, 7.61; Found: C, 65.41; H, 7.79.

4.18. (1*S*,2*S*,3*S*,4*S*)-4-Hydroxymethyl-cyclopentane-1,2,3-triol [Carba-α-L-arabinofuranose] II

Following the same procedure as carried out for the preparation of **I, 12** (125 mg) was hydrogenated to afford pure **II** (70 mg, 90%) as a thick oil. $[\alpha]_D^{24} = -8.6$ (*c* 1.4, MeOH) {lit.,[6k] $[\alpha]_D^{20} = -7.9$ (*c* 1.2, MeOH)}; ^{1}H NMR (600 MHz D_2O): δ 1.22–1.26 (m, 1H), 1.73–1.79 (m, 1H), 2.07–2.12 (m, 1H), 3.39–3.42 (m, 1H), 3.54–3.57 (m, 1H), 3.60–3.65 (m, 2H), 3.92–3.95 (m, 1H); ^{13}C NMR (150 MHz D_2O): 34.2, 45.3, 66.7, 72.5, 79.8, 80.9.

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12. Our attempts to separate **10a** from **10b** from each other by column chromatography using several solvent mixtures as eluents were unsuccessful. Incidentally these two diastereoisomers were consistently produced together in minor amounts. Herein the relative ratios of their combined yields with respect to those of other two separable stereoisomers **10c** and **10d** in all of the successful intramolecular allylation reactions of **9** were given (Table 1, entries a–c). Also representative spectroscopic data of the mixture of **10a** and **10b** are presented in the Experimental.
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