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Intramolecular aldol cyclization of *C*-4-ulopyranosyl-2′-oxoalkanes controlled by steric effects. Asymmetric synthesis of substituted 8-oxabicyclo[3.2.1]octanones and -octenones and cyclopentenones

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Abstract—Whereas *C*-2- and 4-ulopyranosyl compounds (*C*-2- and *C*-4-ulosides) can be converted to cyclopentenones under base conditions through β-elimination and ring contraction, base-initiated β-elimination of *C*-glycosyl 2′-aldehydes and 2′-ketones results in the formation of acyclic α,β-unsaturated aldehydes or ketones. By combining both molecular features we synthesized 1-*C*-(4-ulopyranosyl)-2-oxoalkanes **6**, **13**, and **20** and investigated their reactions when they were treated with base. Both α- and β-anomers of *C*-(4-ulopyranosyl)acetaldehydes **6** and **13** underwent a fast intramolecular aldol reaction between the C-5 enolate and 2′-aldehyde to form optically pure 8-oxabicyclo[3.2.1]octanones, which further transformed to 8-oxabicyclo[3.2.1]octenones **14** and **15** by β-elimination. However, this aldol reaction did not occur when 1-*C*-(4-ulopyranosyl)propan-2-one **20** was treated with base because of steric hindrance exerted by the additional methyl group. Instead, an alternate C-3 enolization led to β-elimination and further electro-ring opening to form an acyclic enol, which was then converted through a disrotatory intramolecular aldol cyclization to a cis-substituted cyclopentenone **21**.

Keywords: Aldol reaction; β-Elimination; Cyclization; Asymmetric synthesis; Oxabicycles; Cyclopentenones

1. Introduction

Carbohydrates have long been considered versatile starting materials for natural product syntheses because of their inherent chirality and unique chemistry associated with their rigid conformations.[1] As synthetically useful intermediates to natural products[2] and herbicides,[3] 8-oxabicyclo[3.2.1] derivatives have been mainly prepared employing various [5+2] cycloadditions[4] and [3+4] allyl cation–furan cycloadditions.[5] Considering some of the natural products that can be derived from oxabicycles are functionalized with various substituents,[6] a carbohydrate approach to oxabicycles is an attractive and probably advantageous alternative over the existing methods. Herein, we describe a enantioselective synthesis of 8-oxabicyclo[3.2.1]octanones and -octenones from *C*-(4-ulopyranosyl)acetaldehydes by an intramolecular aldol cyclization between a C-5 enolate and the 2′-aldehydo group. Because of steric hindrance, the above aldol reaction was not possible in the case of 1-*C*-(4-ulopyranosyl)propan-2-one. Instead, an alternate C-3 enolization led to 2,3-β-elimination and further electro-ring opening to an enol derivative. An intramolecular aldol cyclization between C-1 and C-5 carbonyl then followed to provide racemic cis-substituted cyclopentenone derivatives.

2. Results and discussion

It is known that *C*-2- and *C*-4-ulosides can be converted by base treatment to cyclopentenones through a

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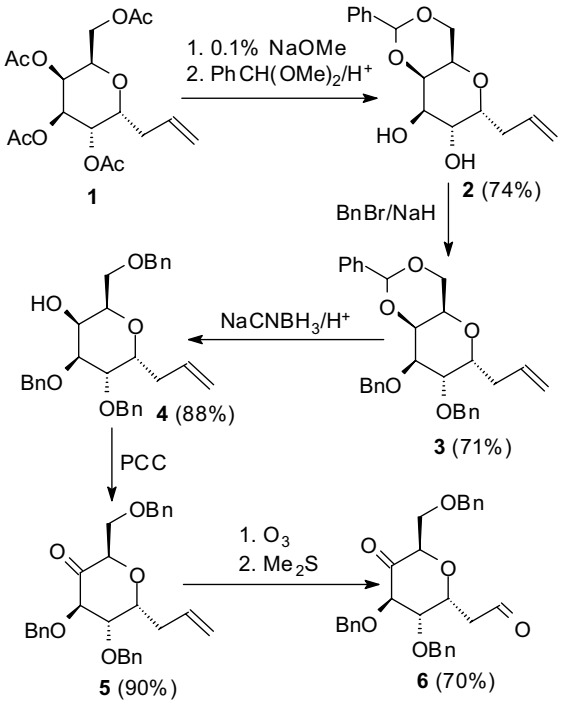
ring-contraction rearrangement,[7] and also that 2′-oxoalkyl *C*-glycosides can be converted to an acyclic α,β-unsaturated aldehyde (ketone) under basic conditions through C-1′ enolization and β-elimination.[8] However, it is not known what would occur when 1-*C*-(4-ulopyranosyl)-2′-oxoalkyl compounds [*C*-(2′-oxoalkyl)-4-ulosides], which combine both of the above structural features, are treated with base. Three reactions are possible upon base treatment of 1-*C*-(4-ulopyranosyl)-2′-oxoalkyl compounds: (1) formation of a C-3 enolate leading to β-elimination and further rearrangement to cis-substituted cyclopentenones[7] without the involvement of the 2′-carbonyl group; (2) formation of C-1′ and C-3 enolates resulting in double β-eliminations to yield acyclic 1,6-dioxo-2,4-dienes, which by an aldol cyclization could be converted to trans-substituted cyclopentenones;[9] and (3) deprotonation at C-3 or C-5, followed by an intramolecular aldol reaction to the 2′-carbonyl group to give oxabicycles. Thus we synthesized the α- and β-anomers of 1-*C*-(4-ulopyranosyl)acetaldehyde compounds **6** and **13**, as well as the 1-*C*-(4-ulopyranosyl)propan-2-one **20** to investigate reaction selectivities and mechanisms.



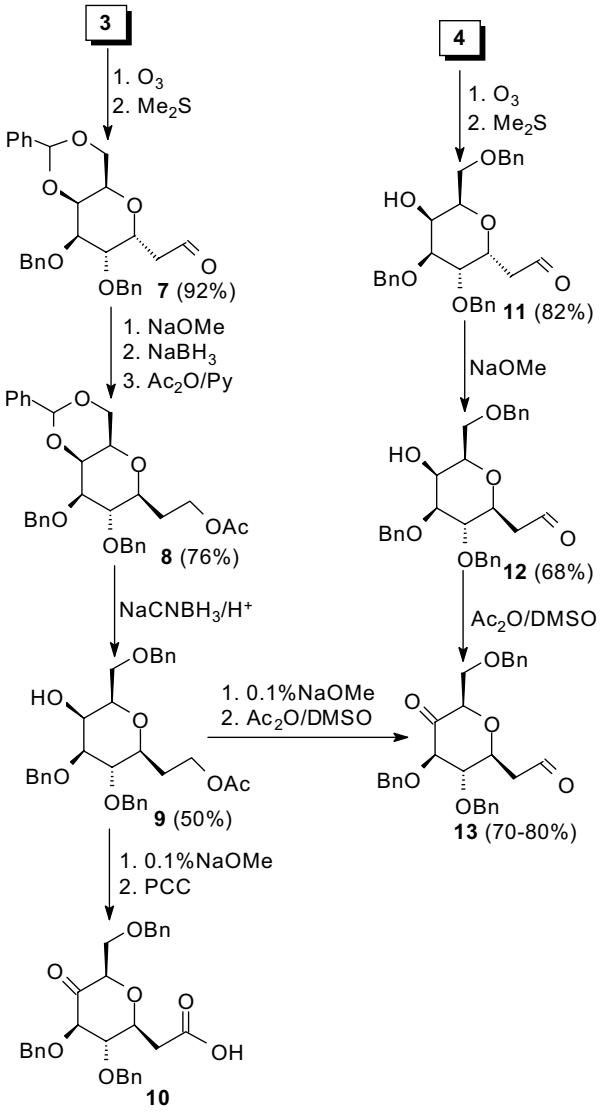
Scheme 1.

2.1. Synthesis of *C*-(2,3,6-tri-*O*-benzyl-α-D-*xylo*-hex-4-ulopyranosyl)acetaldehyde (6)

C-Allyl α-glycoside **1** was used as starting material as shown in Scheme 1. The synthesis of compound **4** from **1** followed previously described procedures,[8c] which included (1) removal of the Ac groups by treatment of **1** with 0.1% NaOMe; (2) benzylidenation using $PhCH(OMe)_2$ in MeCN to afford **2**; and (3) benzylation with BnBr–NaH in DMF to give 3-*C*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)propene (**3**). Both **2** and **3** were obtained in good yields by crystallization without column chromatography. Regioselective reductive-ring opening of the 4,6-*O*-benzylidene ring system of **3** with $NaCNBH_3$–HCl[10] produced **4** with a free 4-OH group. After oxidation of the 4-OH using PCC in CH_2Cl_2, *C*-allyl-4-uloside **5** was isolated in excellent yield. Finally, **6** was obtained from **5** by ozonolysis and subsequent treatment with Me_2S (see Scheme 1).

2.2. Synthesis of *C*-(2,3,6-tri-*O*-benzyl-β-D-*xylo*-hex-4-ulopyranosyl)acetaldehyde (13)

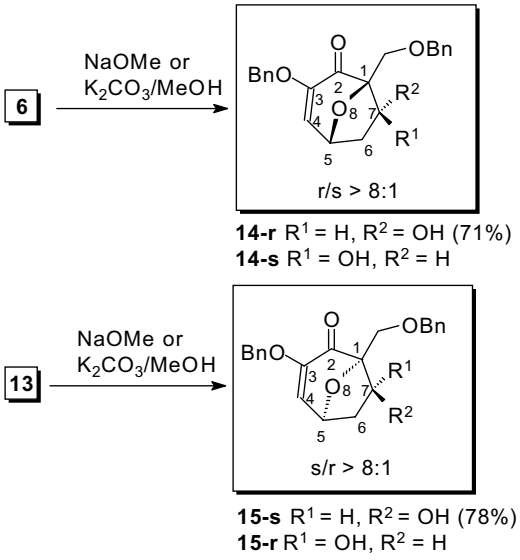
C-Allyl α-glycoside **3** was converted to the ozonide by bubbling O_3 into a solution of **3** in CH_2Cl_2. When this ozonide intermediate was treated with Me_2S overnight, 2′-oxoethyl compound **7** crystallized from the reaction mixture and was obtained in over 90% yield. Treatment of **7** with base (4% NaOMe or 1% K_2CO_3) effectively converted **7** to the more stable *C*-(2′-oxoethyl) β-glycoside through an anomeric epimerization.[8] The acetoxy derivative **8** was then isolated in good yield after $NaBH_4$ reduction and acetylation as shown in Scheme 2. Regioselective ring opening of the 4,6-*O*-benzylidene ring system of **8** afforded 4-OH *C*-glycoside **9** in moderate yield. Since both **8** and **9** have the same R_f on TLC in various solvent systems, we had difficulty monitoring the reaction progress. Therefore, aliquots of the reaction mixture were analyzed by ^1H NMR spectroscopy to verify the completion of the reaction by monitoring the disappearance of the benzylidene proton resonance at δ 5.49 ppm. Oxidation of the 2′,4-diols, obtained from **9** by *O*-deacetylation using PCC gave the 2′-carboxylic acid **10** as a major product and the desired 2′-aldehyde **13** as a minor product. DMSO–Ac_2O[11] was therefore used to oxidize both hydroxy groups to afford the *C*-(4-ulo-β-D-pyranosyl)acetaldehyde **13** in 71% yield. We also attempted an alternative approach for the synthesis of **13** in order to circumvent the ambiguity encountered in the reductive-ring opening of **8** to **9**. Thus, *C*-allyl glycoside **4**, which already had a free 4-OH, was first converted by ozonolysis to the 2′-aldehyde **11**, which in turn was epimerized with 4% NaOMe to its β-anomer **12**. Unlike compound **8**, 2′-aldehyde **12** was isolated without reduction and acetylation, and its 4-OH group was subsequently oxidized with DMSO–Ac_2O to give **13** in 80% yield. Apparently, the latter approach is more practical because of fewer steps involved and higher overall yield.



Scheme 2.

2.3. Intramolecular aldol cyclization to oxabicycles

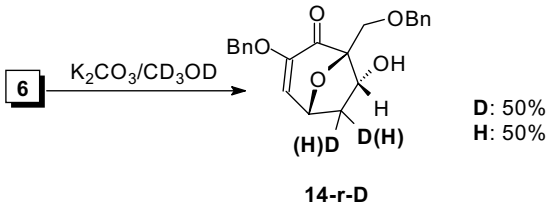
With both α- and β-anomers of the *C*-(4-ulopyranosyl)acetaldehydes in hand, we first treated the α-anomer **6** with base (4% NaOMe or 1% K_2CO_3 in MeOH), and after 2 days at room temperature, **6** was completely converted to a new spot with lower R_f on TLC (1:1 EtOAc–hexanes). After purification by silica gel chromatography, we obtained a mixture of two diasteromers (**14**-*r* and **14**-*s*) in 70–80% yield in a ratio of >8:1 based on ^{1}H NMR analysis (see Scheme 3). An attempt to separate the two diastereomers by chromatography resulted only in the isolation of pure **14**-*r* and a mixture of **14**-*r*/**14**-*s*. Both the diastereoselectivity of the reaction and the chemical yield were reproducible using different bases. In addition, when the reaction was performed under 1% K_2CO_3–CD_3OD conditions, we isolated oxabicyclic **14**-*r*-D. ^{1}H NMR analysis indicated that **14**-*r*-D had



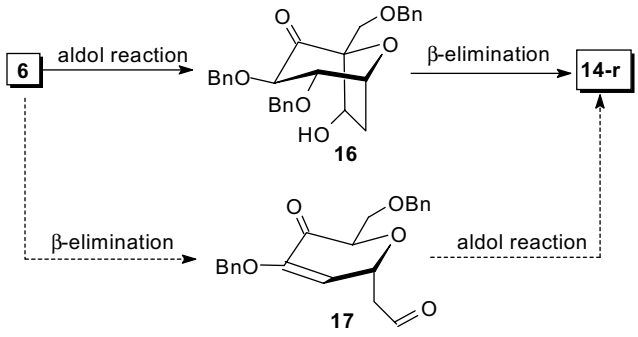
Scheme 3.

50% of the protons at C-6 (δ_H 1.80 and 2.59 ppm), the remainder having been replaced by deuterium (see Scheme 4). Although the pK_a values for the uloside ring protons are not available, the pK_a of the α-proton in cyclohexanone has a p$K_a \sim 10$–12.[12] Thus the significantly high acidity of H-3 and H-5 in comparison to the protons at C-1′ of the 2′-aldehydo compound **6** (p$K_a \sim 16$)[13] overwhelmingly favors the C-5 enolization leading to subsequent aldolization to the 2′-aldehydo group. β-Elimination of the C-1′ enolate to an acyclic conjugated aldehyde was negligible.

As expected, when the β-anomer of the *C*-(4-ulopyranosyl)acetaldehyde **13** was subjected to the same basic conditions, we obtained oxabicycles **15**-*r* and **15**-*s* in comparable yield and stereoselectivity (ds > 8:1) (see Scheme 3). Similarly, only pure **15**-*s* was obtained by chromatography. The ^{1}H and ^{13}C NMR spectra of **15**-*s* are identical to those of **14**-*r*, and the optical rotation analysis provided further evidence that they are enantiomers. The positive optical rotation of **15**-*s* ($[\alpha]_D$ +102, *c* 0.7) observed in chloroform is of the same magnitude but of opposite sign to that of **14**-*r* ($[\alpha]_D$ −102, *c* 0.2) suggesting that both **14** and **15** are optically pure. The results confirm that the limited C-1′ enolization in



Scheme 4.



Scheme 5.

C-(4-ulopyranosyl)acetaldehyde **6** did not result in β-elimination and epimerization at the anomeric center. Thus, this intramolecular aldol cyclization provides a method for the enantioselective synthesis of 8-oxabicyclo[3.2.1]octenones.

The low level of deuterium replacement at C-6 in **14**-*r*-D suggests a fast intramolecular aldol reaction in **6**. In fact, we were able to isolate oxabicycle **16** when the reaction was worked up before its completion. Based on the TLC analysis, compound **16** was indeed formed as an intermediate very quickly from **6** in the presence of base via an aldol reaction between the C-5 enolate and the 2′-aldehydo group, which was then converted slowly through β-elimination to **14**-*r* (see Scheme 5). It is known that the H-5 of a pyranoside is the most reactive under certain conditions,[14] and the fact that neither the elimination product **17** nor its rearrangement product (cyclopentenone) were obtained indicates that a C-5 enolization, and not a C-3 enolization, dominated. Thus, we were able to conclude that **17** is unlikely an intermediate to **14** unless a fast aldol reaction between its C-5 enolate and 2′-aldehyde occurs immediately following 2,3-β-elimination.

The structure and the stereochemistry of compounds **14**-*r*/**14**-*s*, **15**-*s*/**15**-*r*, and **16** were unambiguously determined based on various 2D NMR analyses. Strong NOEs in **14**-*r* were observed between H-4 (6.17 ppm) and H-6a (1.80 ppm), between H-6b (2.59 ppm) and H-7 (4.73 ppm), and between H-6b (2.59 ppm) and H-5 (4.84 ppm), among others as illustrated in Figure 1, suggesting an *R*-configuration at C-7. This assignment was further supported by the observation of additional NOEs between H-3 (4.45 ppm) and 7-OH (2.01 ppm) and between H-3 (4.45 ppm) and H-6a (2.22 ppm) in **16** (see Fig. 1). Because the minor diastereoisomers, **14**-*s* and **15**-*r*, were not obtained in their pure form, their proton chemical shifts and ^{1}H–^{1}H and ^{1}H–^{13}C correlations were therefore assigned based on selective 1D TOCSY in conjunction with other 2D NMR experiments (COSY, NOESY, and ROESY). The NOEs observed in **15**-*r* between H-5 (4.99 ppm) and H-6b (2.43 ppm) and between H-6a (2.07 ppm) and H-7 (4.49 ppm) (see Fig. 1) confirmed that its C-7 is in the *R*-configuration.

Oxabicyclo[3.2.1] ring systems such as those of compounds **14**, **15**, and **16** are useful intermediates. With the availability of selective bridgehead opening by transition-metal catalysts[15] and other reagents,[16] such molecules may be converted to other cyclic and acyclic compounds with multiple stereocenters.

Having successfully demonstrated *C*-(4-ulopyranosyl)acetaldehydes as versatile intermediates for the enantioselective synthesis of oxabicycles, we next attempted to extend the same chemistry to the 1-*C*-(4-ulopyranosyl)propane-2-one **20**.

2.4. Synthesis of 1-*C*-(2,3,6-tri-*O*-benzyl-α-D-*xylo*-hex-4-ulopyranosyl)propan-2-one (20) and its rearrangement

Treatment of the *C*-glycosyl acetaldehyde **7** with MeMgBr in a binary solvent (2:1 Et_2O–toluene) provided the 2′-alcohol **18** in 81% yield as a mixture of two diastereoisomers (see Scheme 6). The ratio of the diastereomers was 2:3 as indicated by the integration of the methyl group, a doublet at δ 1.23 ppm in the ^{1}H NMR spectrum. Although the two diastereoisomers were separable by column chromatography, their absolute stereochemistries were not determined. Instead, the mixture was used directly for the reductive-ring opening of the 4,6-*O*-benzylidene compound to obtain **19**, which was another mixture of two 2′,4-diols obtained in 60% yield. Further oxidation using PCC provided the 1-*C*-

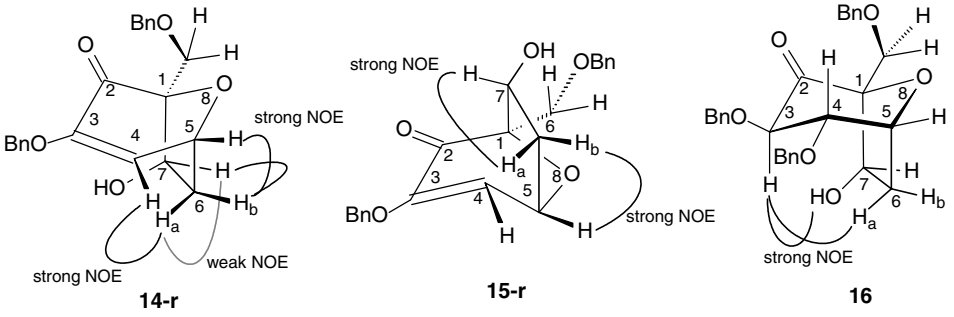
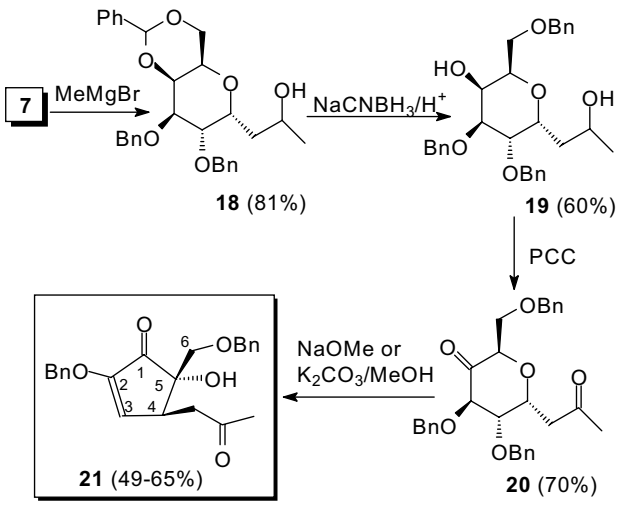


Figure 1. Some of NOEs observed in compounds **14**-*r*, **15**-*r*, and **16**.

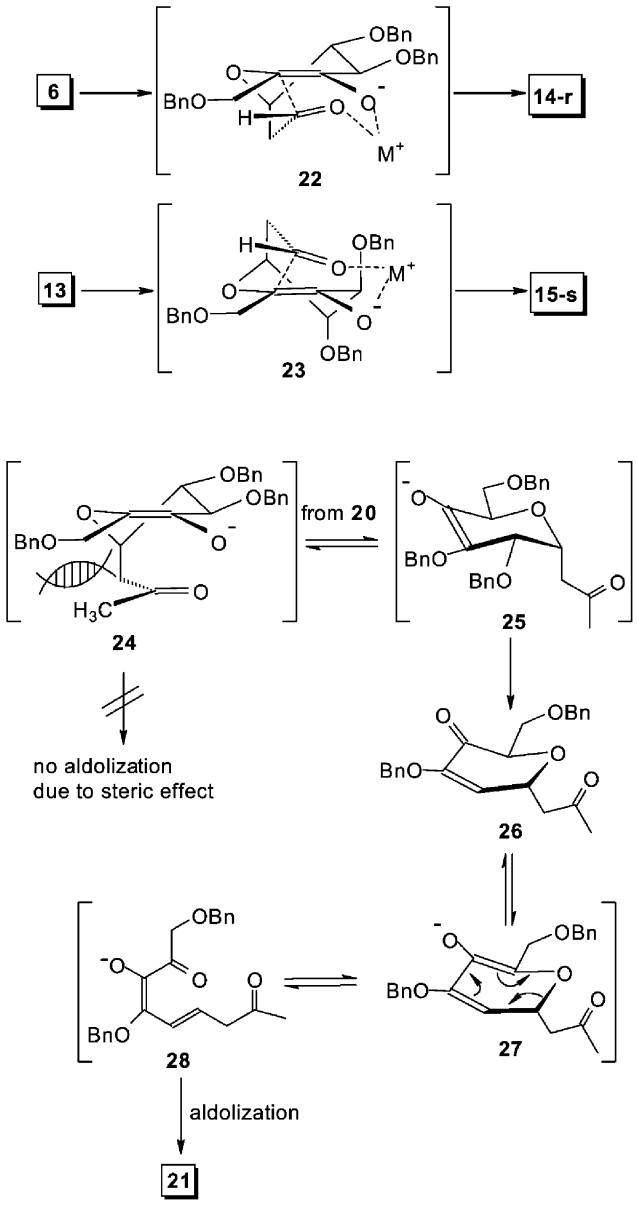


Scheme 6.

(4-ulopyranosyl)propan-2-one **20** in 70% yield. However, upon the treatment of **20** with base (4% NaOMe and 1% K_2CO_3–MeOH) at room temperature for 2 days, the major product with a lower R_f was cyclopentenone **21** (49–65% yield). No oxabicycle was isolated.

Steric effects are known to be critical to the stereochemistry of intramolecular aldol reactions in a pre-existing ring system.[17] In the aldol cyclization to **14** and **15**, the C-5 enolates **22** and **23** derived from **6** and **13**, respectively, adopt twisted chair conformations as shown in Scheme 7. Coordination between the C-5 enolate and the C-2′ aldehydo group can then occur, which in turn directs the stereochemistry of the aldol reaction. We assume that the C-5 enolization of **20** took place in a similar way to form **24**; however, due to steric hindrance exerted by the methyl group of the 2′-keto group, the distance and trajectory angle between the C-5 enolate and the 2′-keto group would not allow an aldol reaction to occur (see Scheme 7). Consequently, the equilibrium was tipped to the less favorable C-3 enolate **25**, followed by 2,3-β-elimination to **26** and further rearrangement to cyclopentenone **21**. This rearrangement is stereoselective, and both alkyl substituents on the cyclopentenone are always in *cis*-configurations regardless of the anomeric configuration of the starting *C*-ulosides.[7]

Three possible intermediates for a similar rearrangement of 4-ulosides were proposed by Caddick et al.[18] (see Chart 1). These intermediates are (1) an enol derivative from electro-ring opening, (2) a biradical from a 1,2-Wittig rearrangement, and (3) an epoxide from nucleophilic ring opening. We have evidence that the cyclopentenones were formed through an enol intermediate similar to **28** (see Scheme 7) initially formed via **27** by a electro-ring opening because (1) a migration of the allyl double bond occurred when *C*-allyl-2-ulosides were treated with base and (2) both α- and β-*C*-glycosides afforded the same cyclopentenone product.[7]



Scheme 7.

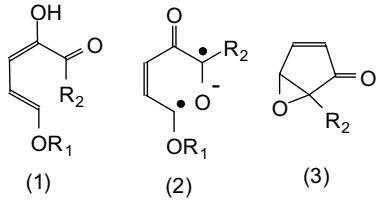


Chart 1. Possible intermediates proposed by Caddick et al.

Although this aldol cyclization is highly stereoselective, its origin and mechanism were not thoroughly investigated in previous reports.[7,18] Now it is clear to us that the stereoselectivity in the formation of racemic

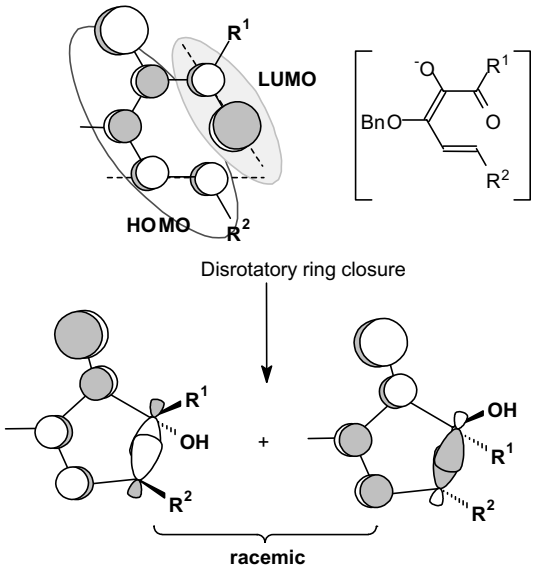


Figure 2. Orbital correlation for the ring contraction to cyclopentenones.

cis-substituted cyclopentenones is determined by the orbital symmetry between the LUMO of the carbonyl group and the HOMO of the enol as illustrated in Figure 2.[19] Thus, the new σ-bond can only be formed through a disrotatory ring closure between the HOMO and LUMO components of the intermediate **28** to afford product **21** with two alkyl substitutions on the same side. It is also expected, based on this analysis, that the electro-ring closure from **28** to **26** could take place (also see Scheme 7) through a conrotatory cyclization between the LUMO and HOMO π-orbitals. This was supported by the isolation of both anomers of the *C*-2-eno-4-uloside after base treatment of the *C*-4-uloside.[7]

In summary, we have described two intramolecular aldol cyclizations on 1-*C*-(4-ulopyranosyl)-2-oxoalkanes with high chemical and stereoselectivities. The C-5 enolate of *C*-(4-ulopyranosyl)acetaldehydes (2′-aldehydes) formed by base treatment attacked the 2′-aldehydo group to afford optically pure 8-oxabicycles, whereas this aldol reaction was not possible in the case of 1-*C*-(4-ulopyranosyl)propan-2-one (the 2′-ketones) because of the steric hindrance of the methyl group. Consequently, the alternative C-3 enolization led to 2,3-β-elimination, followed by an electro-ring opening to an enol intermediate. Subsequent intramolecular aldol cyclization between C-1 and C-5 carbonyl group resulted in the formation of a *cis*-substituted cyclopentenone.

3. Experimental section

3.1. General methods

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 400 and 100 MHz, respectively, with a Varian instrument at 293 K. Chemical shifts are given in ppm downfield from the signal of internal Me_4Si and were assigned on the basis of 2D ^{1}H COSY and ^{1}H–^{13}C chemical-shift correlated experiments. Melting points were measured without calibration. All chemicals were purchased from Aldrich Chemical Co. and used without further purification.

3.2. 3-*C*-(4,6-*O*-Benzylidene-α-D-galactopyranosyl)propene (2)

A solution of **1** (15 g, 40 mmol) in 0.1% NaOMe (200 mL) was kept at room temperature for 4 h and was neutralized by the addition of Dowex-50 (H^+). The filtrate was concentrated to a residue. To a suspension of the above residue in MeCN (100 mL) was added $PhCH(OMe)_2$ (10 mL, 66 mmol) and *p*-TsOH (0.3 g). The mixture was stirred at room temperature overnight. Crystals were collected by filtration and recrystallized from EtOAc to give **2** as needles (8.7 g, 74%) with mp 170–171 °C; $[\alpha]_D$ +79.2 (*c* 0.67, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.32–2.53 (m, 2H, CH_2–CH=CH_2), 3.58 (s, 1H, H-5), 3.77 (m, 1H, H-2), 4.04 (d, 1H, H-6a, *J* 12.4 Hz), 4.14 (dd, 1H, H-3, *J* 6.0, 9.2 Hz), 4.23–4.25 (m, 2H, H-4, 6b), 4.30 (m, 1H, H-1), 5.08–5.16 (m, 2H, CH=CH_2), 5.54 (s, 1H, CHPh), 5.85 (m, 1H, CH=CH_2), 7.37–7.50 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$): δ 28.8 (C-1′), 63.2 (C-5), 69.6 (C-3), 70.0 (C-6), 70.4 (C-2), 75.8 (C-1), 76.0 (C-4), 101.6 (*C*HPh), 117.0 (CH=*C*H_2), 126.5, 128.4, 129.4, 135.0 (*C*H=CH_2), 137.6; HRFABMS: calcd for $C_{16}H_{21}O_5$ (M+H) *m*/*z* 293.1389; found *m*/*z* 293.1438.

3.3. 3-*C*-(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)propene (3)

To a solution of **2** (5 g, 17 mmol) in DMF (100 mL) was added 60% NaH (2.0 g, 50 mmol), and the mixture was stirred for 30 min prior to the addition of BnBr (5 mL, 0.042 mol). After stirring overnight the mixture was diluted by the addition of 1:1 EtOAc–H_2O (300 mL). The organic phase was washed twice with water, dried, and concentrated to a syrup. Crystals were obtained upon addition of hexanes. Recrystallization from EtOAc–hexanes gave **3** as needles (5.7 g, 71%): mp 138 °C; $[\alpha]_D$ +99.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.37 and 2.51 (m and m, 2H, CH_2–CH=CH_2), 3.44 (s, 1H, H-5), 3.75 (dd, 1H, H-3, *J* 3.6, 9.2 Hz), 3.98 (d, 1H, H-6a, *J* 12.0 Hz), 4.17–4.25 (m, 3H, H-2, 4, 6b), 4.32 (m, 1H, H-1), 4.64 and 4.82 (d and d, 1H each, CH_2Ph, *J* 11.6 Hz), 4.77 (s, 2H, CH_2Ph), 5.05 and 5.09 (d and d, 1H each, CH_2–CH=CH_2, *J* 10.4, 17.2 Hz), 5.49 (s, 1H, C*H*Ph), 5.82 (m, 1H, CH_2–C*H*=CH_2), 7.26–7.55 (m, 15H, 3 × Ph); ^{13}C NMR ($CDCl_3$): δ 29.7 (C-1′), 63.2, 70.2, 71.8, 73.8, 74.8 (2), 75.9, 76.8, 101.4 (*C*HPh), 116.7 (CH=*C*H_2), 126.6, 127.7, 127.8, 128.3,

128.5, 129.0, 135.3 (*C*H=CH_2), 138.0, 138.8, 138.9; HRFABMS: calcd for $C_{30}H_{33}O_5$ (M+H) *m/z* 473.2328; found *m/z* 473.2599.

3.4. 3-*C*-(2,3,6-Tri-*O*-benzyl-α-D-galactopyranosyl)propene (4)

To a mixture of **3** (2.5 g, 5.3 mmol), 3 Å molecular sieves (3 g), $NaCNBH_3$ (2.5 g, 39.7 mmol), and a few crystals of methyl orange in THF (50 mL) was added satd HCl–Et_2O at 0 °C until a pink color persisted. After 2 h the reaction mixture was filtered, and the filtrate was washed subsequently with water, aq $NaHCO_3$ and water, dried, and concentrated. Purification by chromatography (1:1 EtOAc–hexanes) afforded **4** as a syrup (2.2 g, 88%): $[\alpha]_D$ +51.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.42 (dd, 2H, C*H*$_2$–CH=CH_2, *J* 6.8, 8.0 Hz), 2.63 (d, 1H, 4-OH, *J* 2.0 Hz), 3.63–3.69 (m, 2H, H-3, 6a), 3.75–3.82 (m, 2H, H-5, 6b), 3.97 (dd, 1H, H-2, *J* 5.6, 8.8 Hz), 3.99–4.14 (m, 2H, H-1, 4), 4.54 and 4.57 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.61 and 4.72 (d and d, 1H each, C*H*$_2$Ph, *J* 11.6 Hz), 4.71 (s, 2H, C*H*$_2$Ph), 5.04–5.13 (m, 2H, CH$_2$–CH=C*H*$_2$), 5.82 (m, 1H, CH$_2$–C*H*=CH$_2$), 7.25–7.37 (m, 15H, 3 × Ph); ^{13}C NMR ($CDCl_3$): δ 30.2 (C-1′), 67.8 (C-4), 69.6 (C-6), 69.8 (C-5), 72.5 (*C*H$_2$Ph), 73.5 (*C*H$_2$Ph), 73.8 (2) (C-1, *C*H$_2$Ph), 75.9 (C-2), 78.0 (C-3), 117.1 (CH=*C*H$_2$), 127.9, 128.0, 128.6, 128.7, 135.1 (*C*H=CH$_2$), 138.3 (2), 138.6; HRFABMS: calcd for $C_{30}H_{35}O_5$ (M+H) *m/z* 475.2484; found *m/z* 475.2444.

3.5. 3-*C*-(2,3,6-Tri-*O*-benzyl-α-D-*xylo*-hex-4-ulopyranosyl)propene (5)

To a solution of **4** (1.0 g, 2.11 mmol) in CH_2Cl_2 (20 mL) was added 4 Å molecular sieves (2.0 g), NaOAc (0.5 g), and PCC (1.0 g, 4.64 mmol). The mixture was stirred at room temperature for 3 h and filtered through Celite. The combined filtrate was washed with water, $NaHCO_3$ and water, dried, and concentrated. Purification by chromatography afforded **5** as crystals (0.9 g, 90%). Recrystallization from EtOAc–hexanes gave mp 97–98 °C (needles); $[\alpha]_D$ +69.8 (*c* 0.53, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.45 (m, 2H, C*H*$_2$–CH=CH_2), 3.81–3.84 (m, 3H, H-2, 6a, 6b), 4.15–4.20 (m, 2H, H-1, 3), 4.34 (dd, 1H, H-5, *J* 5.0, 5.0 Hz), 4.50 and 4.81 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.52 and 4.71 (d and d, 1H each, C*H*$_2$Ph, *J* 11.6 Hz), 4.55 and 4.56 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 5.05–5.13 (m, 2H, CH=C*H*$_2$), 5.81 (m, 1H, C*H*=CH$_2$), 7.22–7.36 (m, 15H, 3 × Ph); ^{13}C NMR ($CDCl_3$): δ 33.1 (C-1′), 68.6 (C-6), 73.29 (*C*H$_2$Ph), 73.34 (*C*H$_2$Ph), 73.6 (*C*H$_2$Ph), 74.0 (C-1), 78.6 (C-5), 80.6 (C-2), 81.9 (C-3), 117.6 (CH=*C*H$_2$), 127.8, 128.1, 128.2, 128.3, 128.5, 128.6, 134.4 (*C*H=CH$_2$), 137.3, 137.8, 138.2, 205.1 (C-4); HRFABMS: calcd for $C_{30}H_{33}O_5$ (M+H) *m/z* 473.2328; found *m/z* 473.2236.

3.6. *C*-(2,3,6-Tri-*O*-benzyl-α-D-*xylo*-hex-4-ulopyranosyl)acetaldehyde (6)

To a solution of **5** (100 mg, 0.212 mmol) in CH_2Cl_2 (15 mL) was bubbled with O_3 at −72 °C until the starting material was disappeared (30 min). The solution was concentrated, and the residue was treated with Me_2S (1 mL) overnight at room temperature. After evaporation of the solvent under vacuum, the residue was subjected to column chromatography (1:2 EtOAc–hexane) to afford product **6** as crystals (70 mg, 70%). Recrystallization from EtOAc–hexane gave mp 97–98 °C (needles); $[\alpha]_D$ +49.3 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.71 (dd, 1H, C*H*$_2$–CH=O, *J* 6.0, 17.2 Hz), 2.77 (ddd, 1H, C*H*$_2$–CH=O, *J* 2.0, 7.0, 17.2 Hz), 3.79 (dd, 1H, H-6a, *J* 4.0, 10.8 Hz), 3.86–3.91 (m, 2H, H-2, 6b), 4.24 (d, 1H, H-3, *J* 5.6 Hz), 4.34 (dd, 1H, H-5, *J* 4.0, 5.6 Hz), 4.43 and 4.68 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.49 and 4.81 (d and d, 1H each, C*H*$_2$Ph, *J* 11.6 Hz), 4.54 (s, 2H, C*H*$_2$Ph), 4.72 (m, 1H, H-1), 7.22–7.36 (m, 15H, 3 × Ph), 9.72 (s, 1H, CHO);^{13}C NMR ($CDCl_3$): δ 43.9 (C-1′), 68.6, 70.2, 73.4, 73.5, 73.8, 80.0, 80.3, 82.2, 128.0, 128.4, 128.8, 137.5, 137.9, 138.2, 200.1 (C=O), 205.1 (C-4); HRFABMS: calcd for $C_{29}H_{31}O_6$ (M+H) *m/z* 475.2121; found *m/z* 475.2345.

3.7. *C*-(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)acetaldehyde (7)

To a solution of **3** (7 g, 14.8 mmol) in CH_2Cl_2 (150 mL) was bubbled with O_3 at −72 °C for 1 h. The residue obtained after removal of solvent was treated with Me_2S (20 mL) overnight at room temperature. The crystals from the reaction mixture were collected and washed with hexanes to afford **7** (6.5 g, 92%). Recrystallization from EtOAc gave mp 169–170 °C (needles); $[\alpha]_D$ +58.5 (*c* 1.72, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.61 (ddd, 1H, C*H*$_2$–CH=O, *J* 4.0, 9.6, 16.0 Hz), 2.85 (dd, 1H, C*H*$_2$–CH=O, *J* 4.8, 16.0 Hz), 3.43 (s, 1H, H-5), 3.68 (dd, 1H, H-3, *J* 3.2, 10.0 Hz), 3.97 (br d, 1H, H-6a, *J* 12.4 Hz), 4.15 (d, 1H, H-6b, *J* 12.4 Hz), 4.22 (d, 1H, H-4, *J* 3.2 Hz), 4.27 (dd, 1H, H-2, *J* 6.0, 9.6 Hz), 4.64 and 4.85 (d and d, 1H each, C*H*$_2$Ph, *J* 11.6 Hz), 4.75 (s, 2H, C*H*$_2$Ph), 4.89 (m, 1H, H-1), 5.48 (s, 1H, C*H*Ph), 7.26–7.53 (m, 15H, 3 × Ph), 9.68 (d, 1H, CHO, *J* 3.2 Hz); ^{13}C NMR ($CDCl_3$): δ 41.4 (C-1′), 64.1 (C-5), 70.0 (C-6), 71.0 (C-1), 71.8 (CH$_2$Ph), 74.2 (CH$_2$Ph), 74.4 (C-4), 74.9 (C-2), 77.0 (C-3), 101.3 (*C*HPh), 126.5, 127.9, 128.0, 128.3, 128.6, 129.1, 137.8, 138.4, 200.5 (CHO); HRFABMS: calcd for $C_{29}H_{31}O_6$ (M+H) *m/z* 475.2121; found *m/z* 475.2133.

3.8. 1-Acetoxy-2-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)ethane (8)

A solution of **7** (0.3 g, 0.633 mmol) in 4% NaOMe (5 mL) was stirred at room temperature overnight. $NaBH_4$ (40 mg) was added, the solution was evaporated after 0.5 h, and the residue was extracted with EtOAc (3×10 mL). After evaporation of the solvent under vacuum, the residue was acetylated in 1:1 Ac_2O–pyridine (10 mL) to obtain crystalline **8** (0.25 g, 76%) after chromatography (1:1 EtOAc–hexanes). Recrystallization from EtOAc–hexanes gave mp 114–115 °C; $[\alpha]_D$ +56.7 (*c* 0.46, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.88 and 2.26 (m and m, 1H each, C*H*$_2$–CH$_2$O), 2.02 (s, 3H, Ac), 3.29 (s, 1H, H-5), 3.37 (ddd, 1H, H-1, *J* 2.0, 9.2, 9.2 Hz), 3.63 (dd, 1H, H-3, *J* 3.2, 8.8 Hz), 3.72 (dd, 1H, H-2, *J* 8.8, 9.6 Hz), 3.97 (br d, 1H, H-6a, *J* 12.4 Hz), 4.20 (d, 1H, H-4, *J* 3.2 Hz), 4.21–4.30 (m, 3H, H-6b, C*H*$_2$OAc), 4.65 and 4.99 (d and d, 1H each, C*H*$_2$Ph, *J* 10.8 Hz), 4.72 and 4.77 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 5.49 (s, 1H, C*H*Ph), 7.26–7.55 (m, 15H, $3 \times$ Ph); ^{13}C NMR ($CDCl_3$): δ 21.3 (Ac), 31.1 (C-1′), 61.5, 69.7, 69.9, 71.3, 74.1, 75.7, 76.0, 78.0, 82.0, 101.4 (*C*HPh), 126.6, 128.0, 128.3, 128.4, 128.6, 129.1, 138.1, 138.6 (2), 171.4 (C=O); HRFABMS: calcd for $C_{31}H_{35}O_7$ (M+H) *m*/*z* 519.2383; found *m*/*z* 519.2439.

3.9. 1-Acetoxy-2-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)ethane (9)

To a solution of **8** (0.2 g, 0.386 mmol), 3 Å molecular sieves (0.5 g), $NaCNBH_3$ (0.25 g, 3.97 mmol), and a few crystals of methyl orange in THF (10 mL) was added satd HCl–Et_2O at 0 °C until a pink color persisted. After 2 h the reaction mixture was filtered, and the filtrate was washed subsequently with water, aq $NaHCO_3$ and water, dried, and concentrated. Purification by chromatography (1:1 EtOAc–hexanes) afforded **9** as an amorphous solid (0.1 g, 50%): $[\alpha]_D$ +2.0 (*c* 4.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.78 and 2.18 (m and m, 1H each, C*H*$_2$–CH$_2$O), 2.01 (s, 3H, Ac), 2.61 (d, 1H, 4-OH, *J* 1.2 Hz), 3.33 (ddd, 1H, H-1, *J* 2.0, 8.8, 9.2 Hz), 3.51–3.57 (m, 3H, H-2, 3, 5), 3.67 (dd, 1H, H-6a, *J* 5.6, 10.0 Hz), 3.74 (dd, 1H, H-6b, *J* 6.0, 10.0 Hz), 4.13 (br s, 1H, H-4), 4.15–4.30 (m, 2H, C*H*$_2$OAc), 4.57 (s, 2H, C*H*$_2$Ph), 4.65 and 4.92 (d and d, 1H each, C*H*$_2$Ph, *J* 10.8 Hz), 4.66 and 4.74 (d and d, 1H each, C*H*$_2$Ph, *J* 11.2 Hz), 7.28–7.35 (m, 15H, $3 \times$ Ph); ^{13}C NMR ($CDCl_3$): δ 21.2 (Ac), 31.2 (C-1′), 61.3 (*C*H$_2$OAc), 67.0 (C-4), 69.5 (C-6), 71.7 (*C*H$_2$Ph), 73.9 (*C*H$_2$Ph), 75.6 (*C*H$_2$Ph), 76.2 (C-1), 76.7 (C-5), 78.3 (C-2), 83.2 (C-3), 128.0, 128.1, 128.2, 128.3, 128.6, 128.7, 137.9, 138.0, 138.2, 171.3 (Ac); HRFABMS: calcd for $C_{31}H_{37}O_7$ (M+H) *m*/*z* 521.2539; found *m*/*z* 521.2567.

3.10. 2-*C*-(2,3,6-Tri-*O*-benzyl-β-D-*xylo*-hex-4-ulopyranosyl)acetic acid (10)

A solution of **9** (95 mg) in 0.1% NaOMe (5 mL) was kept at room temperature for 2 h and neutralized by the addition of Dowex-50 (H^+). The filtrate was concentrated to a residue. To a solution of above residue in CH_2Cl_2 (10 mL) was added NaOAc (0.2 g) and PCC (0.5 g). The mixture was stirred overnight at room temperature and filtered through Celite. The filtrate was concentrated to a residue. Purification by chromatography (2:1–10:1 EtOAc–hexanes gradient) afforded **10** as a syrup (51 mg, 57%) and a small amount of **13**: $[\alpha]_D$ +35.9 (*c* 1.54, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.50 (dd, 1H each, C*H*$_2$–CO$_2$H, *J* 8.0, 16.0 Hz), 2.81 (dd, 1H each, C*H*$_2$–CO$_2$H, *J* 3.2, 16.0 Hz), 3.59–3.65 (m, 2H, H-2, 6a), 3.92 (dd, 1H, H-6b, *J* 3.6, 10.8 Hz), 4.06–4.10 (m, 2H, H-1, 5), 4.18 (d, 1H, H-3, *J* 8.8 Hz), 4.52 and 4.61 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.55 and 4.90 (d and d, 1H each, C*H*$_2$Ph, *J* 11.2 Hz), 4.58 and 4.99 (d and d, 1H each, C*H*$_2$Ph, *J* 11.2 Hz), 7.23–7.41 (m, 15H, $3 \times$ Ph); ^{13}C NMR ($CDCl_3$): δ 37.4 (C-1′), 67.6, 73.8, 74.1, 75.2, 75.7, 80.7, 82.4, 86.7, 127.9, 128.0, 128.3, 128.4, 128.5, 128.6, 128.7, 137.5, 137.6, 138.0, 175.9 (CO_2H), 201.3 (C=O); HRFABMS: calcd for $C_{29}H_{31}O_7$ (M+H) *m*/*z* 491.2070; found *m*/*z* 491.2179.

3.11. *C*-(2,3,6-Tri-*O*-benzyl-α-D-galactopyranosyl)acetaldehyde (11)

To a solution of **4** (1.0 g, 2.11 mmol) in CH_2Cl_2 (30 mL) was bubbled with O_3 at −72 °C for 1 h. The residue obtained after removal of solvent was treated with Me_2S (2 mL) overnight at room temperature. The solvent was evaporated under vacuum, and the residue was subjected to a column chromatography (1:2 EtOAc–hexanes) to afford **11** (0.82 g, 82%): $[\alpha]_D$ +30.7 (*c* 0.56, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.62 (d, 1H, 4-OH, *J* 2.0 Hz), 2.63 (ddd, 1H, C*H*$_2$–CHO, *J* 2.8, 8.4, 16.0 Hz), 2.79 (ddd, 1H, C*H*$_2$–CHO, *J* 1.2, 6.0, 16.0 Hz), 3.61 (dd, 1H, H-3, *J* 3.2, 8.4 Hz), 3.64 (dd, 1H, H-6a, *J* 8.0, 12.4 Hz), 3.72–3.75 (m, 2H, H-5, 6b), 4.00 (dd, H-2, *J* 6.0, 8.8 Hz), 4.12 (br s, 1H, H-4), 4.53 (s, 2H, C*H*$_2$Ph), 4.58 (d, 1H, C*H*$_2$Ph, *J* 11.6 Hz), 4.67–4.73 (m, 4H, H-1, $1.5 \times$ C*H*$_2$Ph), 7.25–7.35 (m, 15H, $3 \times$ Ph), 9.68 (dd, 1H, CHO, *J* 1.6, 1.6 Hz); ^{13}C NMR ($CDCl_3$): δ 41.7 (C-1′), 67.5, 69.4, 69.7, 70.9, 72.5, 73.9, 74.0, 75.1, 78.0, 128.0, 128.2, 128.7, 128.8, 138.0 (3), 200.2 (C=O); HRFABMS: calcd for $C_{29}H_{33}O_6$ (M+H) *m*/*z* 477.2277; found *m*/*z* 477.2296.

3.12. *C*-(2,3,6-Tri-*O*-benzyl-β-D-galactopyranosyl)acetaldehyde (12)

A solution of **11** (0.5 g) in 4% NaOMe (10 mL) was kept overnight at room temperature, diluted by the addition

of EtOAc (50 mL), washed with water, dried, and concentrated to a residue. Purification by chromatography (1:2 EtOAc–hexanes) afforded **12** (0.34 g, 68%): $[\alpha]_D$ +2.0 (*c* 0.26, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.56 (br s, 1H, 4-OH), 2.60 (br dd, 1H, C*H*$_2$–CHO, *J* 7.2, 16.0 Hz), 2.73 (br d, 1H, C*H*$_2$–CHO, *J* 16.0 Hz), 3.53–3.80 (m, 6H, H-1, 2, 3, 5, 6a, 6b), 4.15 (br s, 1H, H-4), 4.56 (s, 2H, C*H*$_2$Ph), 4.58 and 4.91 (d and d, 1H each, C*H*$_2$Ph, *J* 10.4 Hz), 4.67 and 4.75 (d and d, 1H each, C*H*$_2$Ph, *J* 11.6 Hz), 7.25–7.35 (m, 15H, 3 × Ph), 9.70 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$): δ 46.5 (C-1′), 67.1, 69.5, 71.8, 73.9, 74.7, 75.4, 77.1, 77.6, 83.2, 128.0, 128.1, 128.2, 128.3, 128.5, 128.7, 128.9, 137.7, 138.0 (2), 200.4 (C=O); HRFABMS: calcd for $C_{29}H_{33}O_6$ (M+H) *m*/*z* 477.2277; found *m*/*z* 477.2366.

3.13. *C*-(2,3,6-Tri-*O*-benzyl-β-D-*xylo*-hex-4-ulopyranosyl)acetaldehyde (13)

A solution of **12** (0.1 g) in 2:1 Me_2SO–Ac_2O (2 mL) was kept overnight at room temperature. The solution was diluted by the addition of EtOAc (30 mL) and washed subsequently with water, aq $NaHCO_3$, and water dried, and concentrated. Purification by chromatography (1:2 EtOAc–hexanes) afforded **13** as a syrup (80 mg, 80%): $[\alpha]_D$ +25.2 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.60 (ddd, 1H, C*H*$_2$–CH=O, *J* 2.4, 8.0, and 16.8 Hz), 2.77 (ddd, 1H, C*H*$_2$–CH=O, *J* 2.0, 4.4, and 16.8 Hz), 3.57–3.65 (m, 2H, H-2, 6a), 3.92 (dd, 1H, H-6b, *J* 4.0 and 10.8 Hz), 4.08 (dd, 1H, H-5, *J* 4.0, 5.6 Hz), 4.17 (m, 1H, H-1), 4.19 (d, 1H, H-3, *J* 8.4 Hz), 4.52 and 4.58 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.58 and 4.88 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.58 and 4.99 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 7.22–7.36 (m, 15H, 3 × Ph), 9.71 (dd, 1H, CHO, *J* 2.0, 2.0 Hz);^{13}C NMR ($CDCl_3$): δ 46.2 (C-1′), 67.7, 73.9, 74.1, 74.4, 75.2, 80.6, 82.7, 86.7, 128.1, 128.3, 128.4, 128.5, 128.6, 128.8, 137.4, 138.0 (2), 199.4, 200.2; HRFABMS: calcd for $C_{29}H_{31}O_6$ (M+H) *m*/*z* 475.2121; found *m*/*z* 475.2592.

3.14. 3-Benzyloxy-1-benzyloxymethyl-7-hydroxy-(1*s*,5*r*,7*r*)-8-oxabicyclo[3.2.1]-3-octen-2-one (14-*r*)

A solution of **6** (20 mg, 0.042 mmol) in 1% K_2CO_3–MeOH (1 mL) was kept at room temperature for 2 days, at the end of which time the starting material had disappeared as determined by TLC, and a major polar product was indicated. The solution was diluted by the addition of EtOAc (15 mL), washed with water, dried, and concentrated to a residue. Purification by chromatography (1:2–1:1 EtOAc–hexanes gradient) afforded a mixture of **14**-*r* and **14**-*s* as a syrup (>8:1, 11 mg, 71%) with $[\alpha]_D$ −61 (*c* 0.6, $CHCl_3$); for pure **14**-*r*: $[\alpha]_D$ −102 (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.80 (dd, 1H, H-6a, *J* 1.6, 12.8 Hz), 1.85 (br s, 1H, 7-OH), 2.59 (ddd, 1H, H-6b, *J* 2.0, 6.8, 12.8 Hz), 3.89 and 4.00 (d and d, 1H each, C*H*$_2$OBn, *J* 10.8 Hz), 4.62 and 4.66 (d and d, 1H each, C*H*$_2$Ph, *J* 12.0 Hz), 4.73 (dm, 1H, H-7, *J* 9.6 Hz), 4.84 (m, 1H, H-5), 4.87 (s, 2H, C*H*$_2$Ph), 6.17 (d, 1H, H-4, *J* 5.2 Hz), 7.27–7.36 (m, 10H, 2 × Ph); ^{13}C NMR ($CDCl_3$): δ 39.2 (C-6), 68.4 (*C*$_2$OBn), 70.1 (*C*H$_2$Ph), 71.7 (C-7), 73.5 (C-5), 74.2 (*C*H$_2$Ph), 90.7 (C-1), 120.6 (C-4), 127.5, 127.9, 128.1, 128.2, 128.4, 128.6, 128.7, 135.8, 137.9, 149.9 (C-3), 190.9 (C-2); HRFABMS: calcd for $C_{22}H_{22}O_5$ (M) *m*/*z* 366.1467; found *m*/*z* 366.1563. For **14**-*s* (data extracted from a mixture of **14**-*r*/**14**-*s*): ^1H NMR ($CDCl_3$): δ 2.07 (ddd, 1H, H-6a, *J* 2.8, 7.6, 12.8 Hz), 2.43 (dd, 1H, H-6b, *J* 7.6, 12.8 Hz), 3.31 (d, 1H, 7-OH, *J* 6.8 Hz), 4.00 and 4.14 (d and d, 1H each, C*H*$_2$OBn, *J* 10.8 Hz), 4.49 (m, 1H, H-7), 4.99 (m, 1H, H-5), 6.06 (d, 1H, H-4, *J* 5.2 Hz).

3.15. 3-Benzyloxy-1-benzyloxymethyl-7-hydroxy-(1*r*,5*s*,7*s*)-8-oxabicyclo[3.2.1]-3-octen-2-one (15-*s*)

A solution of **13** (20 mg) in 4% MeOH (2 mL) or 1% K_2CO_3–MeOH (2 mL) were kept at room temperature for 2 days, at the end of which time TLC indicated completion of the reaction. The same workup as that for compound **14** afforded **15**-*s*/**15**-*r* as a syrup (>8:1, 12.0 mg, 78%), $[\alpha]_D$ +67 (*c* 0.2, $CHCl_3$); for pure **15**-*s*: $[\alpha]_D$ +102 (*c* 0.7, $CHCl_3$); ^1H and ^{13}C NMR spectra of **15**-*s* were identical to those of compound **14**-*r*.

3.16. 3-Benzyloxy-1-benzyloxymethyl-7-hydroxy-(1*s*,3*r*,4*s*,5*r*,7*r*)-8-oxabicyclo[3.2.1]-octan-2-one (16)

A syrup with $[\alpha]_D$ +30.0 (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.01 (d, 1H, 7-OH, *J* 2.1 Hz), 2.22 (dd, 1H, H-6a, *J* 3.6, 14.0 Hz), 2.49 (m, 1H, H-6b), 3.52 and 4.01 (d and d, 1H each, C*H*$_2$OBn, *J* 10.0 Hz), 3.96 (dd, 1H, H-4, *J* 3.2, 8.8 Hz), 4.38 (m, 1H, H-5), 4.45 (d, 1H, H-3, *J* 8.8 Hz), 4.58–4.59 (m, 5H, H-7, 2 × C*H*$_2$Ph), 4.78 (d, 1H, C*H*$_2$Ph, *J* 11.6 Hz), 5.04 (d, 1H, C*H*$_2$Ph, *J* 11.6 Hz), 7.29–7.44 (m, 15H, 3 × Ph); ^{13}C NMR ($CDCl_3$): δ 32.9 (C-6), 68.3 (*C*$_2$OBn), 73.4, 74.3 (C-7), 74.4, 74.6, 76.3 (C-5), 83.5 (C-4), 84.7 (C-3), 86.6 (C-1), 127.9, 128.0, 128.1, 128.4, 128.6, 128.8, 137.9, 138.4, 201.3 (C-2); HRFABMS: calcd for $C_{29}H_{29}O_6$ (M−H) *m*/*z* 473.1964; found *m*/*z* 473.2393.

3.17. 1-*C*-(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-2-propanol (18)

To a solution of **7** (0.6 g, 1.27 mmol) in Et_2O (20 mL) and toluene (10 mL) was added 3 M MeMgBr in Et_2O (3.0 mL, 9 mmol) at −72 °C. The mixture was stirred for 5 h at room temperature and diluted by the addition of 1:1 0.1 M HCl–EtOAc (100 mL). The organic phase was washed with brine, dried, and concentrated to give crystals. Recrystallization with EtOAc–hexanes gave

18 (0.5 g, 81%) as a mixture of two diastereoisomers in a ratio of 3:2, which were separated by column chromatography (1:1 EtOAc–hexanes). The major diastereoisomer with high R_f gave mp 131 °C; $[\alpha]_D$ +86.5 (*c* 0.43, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.23 (d, 3H, CH-3, *J* 6.4 Hz), 1.82 (m, 2H, 1′-CH_2), 2.38 (d, 1H, 2′-OH, *J* 4.8 Hz), 3.47 (s, 1H, H-5), 3.74 (dd, 1H, H-3, *J* 3.2, 9.6 Hz), 3.96 (m, 1H, 2′-C*H*), 4.01 and 4.19 (d and d, 1H each, H-6a, 6b, *J* 12.0 Hz), 4.22 (d, 1H, H-4, *J* 3.2 Hz), 4.26 (dd, 1H, H-2, *J* 6.0, 10.0 Hz), 4.51 (dt, 1H, H-1, *J* 6.4, 7.6 Hz), 4.67 and 4.84 (d and d, 1H each, CH_2Ph, *J* 11.6 Hz), 4.75 and 4.79 (d and d, 1H each, CH_2Ph, *J* 12.4 Hz), 5.49 (s, 1H, C*H*Ph), 7.26–7.55 (m, 15H, 3 × Ph);^{13}C NMR ($CDCl_3$): δ 23.8 (Me), 34.7 (C-1′), 63.9 (C-5), 65.5 (C-2′), 70.2 (C-6), 71.9 (*C*H_2Ph), 72.8 (C-1), 74.2 (*C*H_2Ph), 74.7 (C-4), 75.4 (C-2), 77.0 (C-3), 101.4 (*C*HPh), 126.5, 127.8, 127.9, 128.1, 128.3, 128.6, 129.1, 137.9, 138.7; HRFABMS: calcd for $C_{30}H_{35}O_6$ (M+H) *m*/*z* 491.2434; found *m*/*z* 491.2515.

3.18. 1-*C*-(2,3,6-Tri-*O*-benzyl-α-D-galactopyranosyl)-2-propanol (19)

To a solution of **18** (0.5 g, 1.02 mmol), 3 Å molecular sieves (1.5 g), $NaCNBH_3$ (0.7 g, 11.1 mmol), and a few crystals of methyl orange in THF (20 mL) was added satd HCl–Et_2O at 0 °C until a pink color persisted. Usual workup and purification by chromatography (1:1 EtOAc–hexanes) afforded **19** as a syrup (0.3 g, 60%). When the pure diastereoisomer with high R_f was used as starting material, a single product was obtained with $[\alpha]_D$ +25.6 (*c* 5.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.22 (d, 3H, CH-3, *J* 6.4 Hz), 1.65 and 1.87 (ddd and ddd, 1H each, 1′-CH_2), 2.51 (br s, 1H, 4-OH), 2.67 (br s, 1H, 2′-OH), 3.64–3.69 (m, 2H, H-3, 6a), 3.74 (dd, 1H, H-6b, *J* 6.8, 10.0 Hz), 3.85 (m, 1H, H-5), 3.93 (dd, 1H, H-2, *J* 5.2, 8.4 Hz), 3.97 (m, 1H, 2′-CH), 4.06 (br s, 1H, H-4), 4.34 (m, 1H, H-1), 4.53 and 4.57 (d and d, 1H each, CH_2Ph, *J* 12.0 Hz), 4.61 and 4.70 (d and d, 1H each, CH_2Ph, *J* 11.6 Hz), 4.64 and 4.71 (d and d, 1H each, CH_2Ph, *J* 12.0 Hz), 7.26–7.36 (m, 15H, 3 × Ph); ^{13}C NMR ($CDCl_3$): δ 23.4 (Me), 34.8 (C-1′), 65.1 (C-2′), 67.7 (C-4), 69.3 (C-6), 70.6 (C-1, 5), 72.7 (*C*H_2Ph), 73.7 (*C*H_2Ph), 73.8 (*C*H_2Ph), 75.6 (C-2), 77.9 (C-3), 127.9, 128.0, 128.1, 128.5, 128.6, 128.7, 138.0 (2), 138.0; HRFABMS: calcd for $C_{30}H_{37}O_6$ (M+H) *m*/*z* 493.2590; found *m*/*z* 493.2700.

3.19. 1-*C*-(2,3,6-Tri-*O*-benzyl-α-D-*xylo*-hex-4-ulopyranosyl)propan-2-one (20)

Compound **19** (0.25 g, 0.51 mmol) was oxidized by PCC to afford **20** as a wax (0.17 g, 70%) after purification by chromatography (1:2 EtOAc–hexanes); $[\alpha]_D$ +55.0 (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.08 (s, 3H, Ac), 2.76 (dd, 1H, $CH_2C{=}O$, *J* 7.2, 16.8 Hz), 2.81 (dd, 1H, $CH_2C{=}O$, *J* 7.2, 16.8 Hz), 3.81 (dd, 1H, H-6a, *J* 4.0, 11.2 Hz), 3.84 (dd, 1H, H-6b, *J* 6.0, 11.2 Hz), 3.91 (dd, 1H, H-2, *J* 4.4, 5.6 Hz), 4.24 (d, 1H, H-3, *J* 5.6 Hz), 4.34 (dd, 1H, H-5, *J* 4.0, 6.0 Hz), 4.39 and 4.68 (d and d, 1H each, CH_2Ph, *J* 11.6 Hz), 4.48 and 4.81 (d and d, 1H each, CH_2Ph, *J* 11.6 Hz), 4.52 and 4.56 (d and d, 1H each, CH_2Ph, *J* 11.6 Hz), 4.63 (m, 1H, H-1), 7.26–7.37 (m, 15H, 3 × Ph); ^{13}C NMR ($CDCl_3$): δ 30.8 (Me), 43.5 (C-1′), 68.4, 70.8, 73.2, 73.6, 73.7, 80.1, 80.4, 82.3, 128.0, 128.2, 128.3, 128.4, 128.6, 128.7, 137.3, 137.7, 138.0, 205.7 (C=O), 206.3 (C=O); HRFABMS: calcd for $C_{30}H_{32}O_6$ (M+H) *m*/*z* 488.2199; found *m*/*z* 488.2145.

3.20. 2-Benzyloxy-5-benzyloxymethyl-5-hydroxy-4-(2-oxopropyl)-4,5-*cis*-cyclopent-2-enone (21)

A solution of **20** (60 mg, 0.164 mmol) in 4% NaOMe (5 mL) was stirred at room temperature for 2 days. The solution was diluted by the addition of EtOAc (30 mL), and washed with water, dried, and concentrated to a residue. Purification by chromatography (1:1 EtOAc–hexanes) afforded **21** as a syrup (31 mg, 65%);^1H NMR ($CDCl_3$): δ 2.06 (s, 3H, COC*H*-3), 2.63 (dd, 1H, CH_2C=O, *J* 6.8, 18.0 Hz), 2.96 (dd, 1H, CH_2C=O, *J* 8.0, 18.0 Hz), 3.21 (m, 1H, H-4), 3.36 (s, 1H, 5-OH), 3.40 (d, 1H, H-6a, *J* 9.6 Hz), 3.51 (d, 1H, H-6b, *J* 9.6 Hz), 4.42 and 4.46 (d and d, 1H each, 6-CH_2Ph, *J* 12.0 Hz), 4.96 (s, 2H, 2-CH_2Ph), 6.21 (d, 1H, H-3, *J* 2.4 Hz), 7.26–7.37 (m, 10H, 2 × Ph); ^{13}C NMR ($CDCl_3$): δ 30.0 (O=C*C*H-3), 42.0 (C-4), 43.5 (*C*H_2C=O), 71.7 (2-*C*H_2Ph), 72.6 (C-6), 74.1 (6-*C*H_2Ph), 77.9 (C-5), 127.2, 127.7, 127.9, 128.0, 128.1, 128.2, 128.5, 128.7, 128.8, 129.3 (C-3), 135.6, 137.4, 154.6 (C-2), 201.0 (C-1), 208.5 (O=*C*CH-3); HRFABMS: calcd for $C_{23}H_{25}O_5$ (M+H) *m*/*z* 381.1702; found *m*/*z* 381.1729.

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