Stereoselective synthesis of dioxabicycles from 1-*C*-allyl-2-*O*-benzyl-glycosides — An intramolecular cyclization between 2-*O*-benzyl oxygen and the allyl double bond[1]

An-Tai Wu, Tian Yi, Huawu Shao, Shih-Hsiung Wu, and Wei Zou

Abstract: Addition of a proton to the double bond of 1-*C*-allyl-*O*-benzylglycosides gave a 2′-carbonium ion, which in turn reacted intramolecularly, in a regio- and diastereo-selective manner, with the nucleophilic oxygen of the 2-*O*-benzyl group to form an oxonium intermediate. Subsequent cleavage of the benzyl C—O bond led to dioxabicycles in moderate yields. Surprisingly, opposite diastereoselectivities were observed from 1-*C*-allylglycofuranosides and 1-*C*-allylglycopyranosides, which produced 2,2′-*trans*- and 2,2′-*cis*-dioxabicycles, respectively.

Key words: C-glycoside, olefin, cyclization, oxocarbonium, dioxabicycles.

Résumé : L'addition d'un proton sur la double liaison 1-*C*-allylglycosides de *O*-benzyle conduit à la formation d'un ion carbonium en 2′ qui réagit ensuite d'une façon intramoléculaire, régio- et diastéréosélective, avec l'oxygène nucléophile du groupe 2-*O*-benzyle pour conduire à la formation d'un intermédiaire oxonium. Un clivage subséquent de la liaison C—O du benzyle conduit à des dioxabicycles avec des rendements modérés. D'une façon surprenante, on a observé des diastéréosélectivités opposées les 1-*C*-allylglycofuranosides et les 1-*C*-allylglycopyranosides qui ont conduit respectivement aux 2,2′-*trans*- et 2,2′-*cis*-dioxabicycles.

Mots clés : C-glycoside, oléfine, cyclisation, oxocarbonium, dioxabicycles.

[Traduit par la Rédaction]

Introduction

The electrophile-promoted addition to an olefinic double bond is one of the most investigated reactions (1). The intermediate can be a carbonium ion or more often a bridged cation, which then reacts with a nucleophile, e.g., alcohol, acid, amine, and amide, to form an addition product. The stereoselectivity of the addition to a double bond can be achieved using selenium reagents (2), iodo complexes (3), mercury complexes (4), and Ru reagents (5). In certain cases, the stereochemistry may be guided by the asymmetric substrates (1).

Recently, during a large-scale preparation of 1-*C*-allyl-2,3,5-tri-*O*-benzyl-α-D-ribofuranoside (**2**) using ribofuranoside **1** and allyltrimethylsilane in the presence of TMSOTf, we also isolated 5-O-debenzylated **3** in 17% yield (Scheme 1), a useful intermediate obtained previously from **2** by regioselective 5-O-acetolysis followed by de-O-acetylation (6). This result prompted us to investigate if TMSOTf can selectively remove the 5-*O*-benzyl group from **2** (7). However, when compound **2** was treated with TMSOTf in acetonitrile, instead of the desired **3**, we obtained a dioxabicyclic compound as the only major product. Further studies using 1-*C*-allylglycofuranosides and 1-*C*-allylglycopyranosides as substrates revealed that the formation of dioxabicycles was both highly regioselective and diastereoselective. Here, we wish to describe this stereoselective intramolecular cyclization between 2-*O*-Bn and the allyl double bond.

Received 19 August 2005. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on 5 May 2006.

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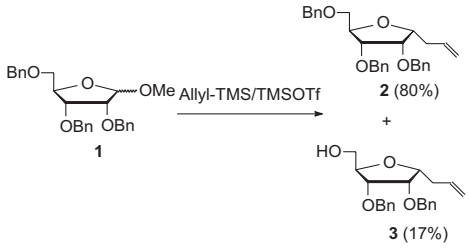
[4]Dr. Wei Zou was a postdoctoral fellow with Professor Walter Szarek (1990–1993).

Results and discussion

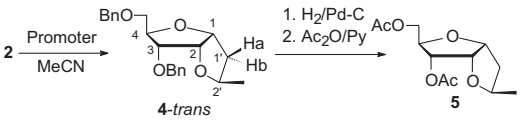
The dioxabicylic compound obtained by treatment of **2** with TMSOTf (1 equiv.) in acetonitrile was characterized as **4**-*trans* (Scheme 2). The newly formed ring and the stereochemistry at C2′ were established by NMR analysis. Because of the observation of NOE between H-1 and H-3, the cyclization must have occurred at the 2-O-position. In addition, the 2,2′-trans configuration was assigned on the basis of the NOE observed between H-2′ and H-4 and the lack of NOE between H-2′ and H-2/H-1. This stereochemistry was further confirmed by NMR analysis on acetylated derivative **5**, as we observed a downfield shift of the H-3 resonance from 3.85 to 4.87 ppm owing to acetylation, and the

 doi:10.1139/V06-046

Scheme 1. 1-C-Allylation promoted by TMSOTf.



Scheme 2. Regioselective cyclofunctionalization.



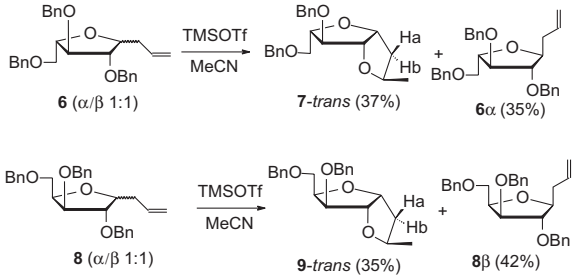
Promoter	*T/t*	*Isolated yield of* **4**-*trans*
TMSOTf (1equiv.)	0 °C-rt/16h	61%
TfOH (1equiv.)	0 °C/4h	41%
p-TsOH (1equiv.)	60 °C/24h	-
TfOH/p-TsOH (0.2/1 equiv.)	0 °C-rt/16h	53%

strong NOEs between H-1 and H-1′a and between H-2′ and H-1′b.

This regio- and diastereo-selective conversion of **2** to **4**-*trans* can also be promoted by TfOH (1 equiv.) at 0 °C, but with lower yield (see Scheme 2) because of the decomposition caused by nonselective de-O-benzylation. No significant transformation occurred when *p*-TsOH (1 equiv.) was used alone even at elevated temperature (60 °C, 24 h), but additional TfOH (0.2 equiv.) facilitated the formation of **4**-*trans*. Hence, this cyclization was likely acid-promoted. The proton source in the case of TMSOTf as a promoter might be the residual water from acetonitrile because when we performed the experiment under dry, but otherwise the same conditions, the reaction became very sluggish.[5] Additionally, acetonitrile as the proton source was excluded because when the reaction was performed in MeCN-d_3, no deuterium substitution on the methyl group of **4**-*trans* was detected by NMR and MS analyses.

The formation of a five-membered ring indicates that the reaction proceeded through a kinetic process. We were interested to know if six-membered ring products could also be formed under certain circumstances. For instance, using 1-*C*-allyl-L-arabinofuranoside (**6**), a mixture of two anomers (α/β, 1:1) as a substrate, we expected a similar cyclization occurred in **6β** because of its 1,2-cis configuration, but we were also interested to see if the 1-*C*-allyl group in the α anomer (**6α**) would react to the 3-*O*-Bn, which is sterically possible, to form a six-membered ring. Thus, a mixture of **6α/β** was treated with TMSOTf in acetonitrile under the aforementioned conditions. TLC analysis showed the formation of a new product, but a significant amount of starting material remained. After the separation, the newly formed product with a lower R_f was characterized as dioxabicyclic **7**-*trans* (37% yield based on total starting material), produced by the cyclization between the 2-*O*-Bn and the *cis*-1-*C*-β-allyl group (Scheme 3). Again, the 2,2′-trans configuration was assigned on the basis of NOE analysis. The remaining starting material (**6α**), contaminated only with very small amount of **6β**, was recovered, which did not produce a six-membered ring product.

Scheme 3.



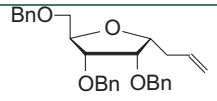
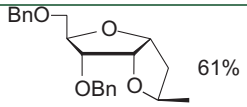
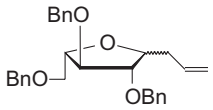
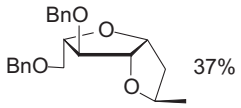
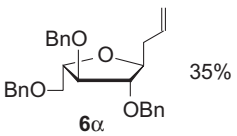
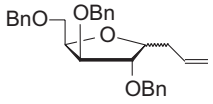
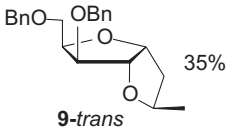
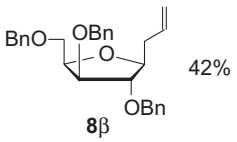
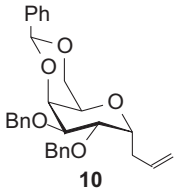
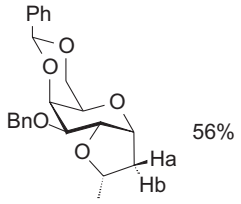
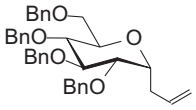
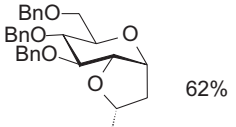
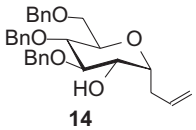
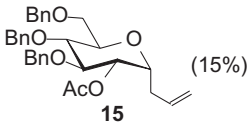
Because of the close distance between C2′ and C4 as indicated by the observation of NOE between H-2′ and H-4 in **4**-*trans*, one might speculate that the 2,2′-trans selectivity in **4**-*trans* and **7**-*trans* may have resulted from the steric hindrance exerted by 3-*O*-Bn in **2** or 5-*O*-Bn in **6**, which could prevent the methyl group at C2′ from adopting a cis configuration in the transition state. However, this argument was proven not true because 1-*C*-allyl-D-xylofuranoside (**8**), which lacks such steric effect, under the above conditions produced **9**-*trans* as the only major product (35%) and the recovery of its 1,2-trans starting material (**8β**) (42%) (see Scheme 3).

Besides the 1-*C*-allylglycofuranosides, the cyclization between the 1-*C*-allyl and the 2-*O*-Bn also occurred with 1-*C*-allylglycopyranosides under the above conditions. Remarkably, however, in contrast to the 2,2′-trans diastereoselectivity observed in 1-*C*-allylglycofuranosides, when 1-*C*-allylgalactoside (**10**) and 1-*C*-allylglucosides (**12**) were treated with TMSOTf in acetonitrile, we only obtained the respective products with the 2,2′-cis configurations, **11**-*cis* (56%) and **13**-*cis* (62%) (see Table 1). The cyclization also proceeded with 2-OH glucoside (**14**) to give **13**-*cis* (59%) as the major product and a 2-O-acetylated **15** (15%) as a minor one (8). The 2-O-acetylation resulted from the reaction between 2-OH and acetonitrile followed by hydrolysis. No cyclization occurred when **15** was used as a substrate because of the diminished 2-O-nucleophicility owing to the electron-withdrawing effect by 2-O-acetylation.

Although this acid-promoted cyclization was never reported, the iodonium-promoted cyclization between the olefin double bond and O-Bn are known. For example, Rychnovsky and Bartlett (9) prepared 2,5-cis disubstituted tetrahydrofurans by cyclizing olefinic ether in the presence of iodine and suggested that the 2,5-cis stereoselectivity was controlled by an oxonium ion intermediate with the 1,2-trans, 1,5-trans configurations. Nicotra and co-workers (10) also subjected 1-*C*-allyl-2-*O*-benzylglycoside to similar conditions to obtain a mixture of two diastereomers at C2′. The oxonium ion was also an intermediate in Fraser-Reid's glycosylation using *n*-pentenyl glycoside in which the formation of a bridged olefin halogenium ion was followed by

[5] Compound **2** and TMSOTf were separately dissolved in acetonitrile and dried over 3 Å molecular sieves. Equivalents of **2** and TMSOTf in acetonitrile were then mixed and kept at 0 °C overnight.

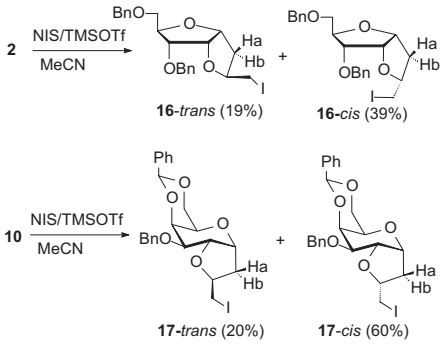
Table 1. Dioxabicycles from 1-*C*-allyl-*C*-glycosides.

Entry	Substrate	Product(s) (isolated yield)	
1	 **2**	 **4**-*trans* 61%	
2	 **6** (α/β 1:1)	 **7**-*trans* 37%	 **6**α 35%
3	 **8** (α/β 1:1)	 **9**-*trans* 35%	 **8**β 42%
4	 **10**	 **11**-*cis* 56%	
5	 **12**	 **13**-*cis* 62%	
6	 **14**	**13**-*cis* (59%)	 **15** (15%)
7	**15**	N/A	

nucleophilic attack from the glycosidic oxygen leading to a glycosyl oxocarbonium ion as a glycosyl donor and the concurrent formation of a tetrahydrofuran (11).

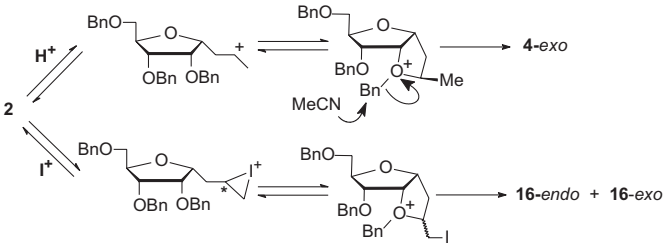
The poor stereoselection in the iodine-promoted cyclizations contrasts with those obtained from acid-promoted cyclization. Such a difference is not substrate dependent because when **2** and **10** were treated with NIS–TMSOTf in acetonitrile a mixture of diasteromers (**16**-*trans*/*cis* and **17**-*trans*/*cis*) were also obtained, respectively, in a 1:2 to 3 trans:cis ratio (Scheme 4). The NOE between H-2′ and H-4 in **16**-*trans*, similar to **4**-*trans*, was observed, but not between H-4 and CH_2I in **16**-*cis*.[6] The chemical shifts of H-1′a (cis to H-1) and H-1′b (trans to H-1) and the pattern of proton couplings were also similar to those observed in 2′-methyl dioxabicycles (**4**-*trans*, **7**-*trans*, **9**-*trans*, **11**-*cis*, and **13**-*cis*). The double doublet H-1′b resonance in the 2,2′-trans compounds always appears downfield (2.2–2.4 ppm) from that of the H-1′a resonance (1.5–2.0 ppm), and are reversed in the 2,2′-cis compounds likely because of the change of conformation from one envelope to another.

Scheme 4. Regioselective cyclization promoted by NIS–TMSOTf.



[6] Due to the overlap of the proton signals of H-2′ and H-4, this result was obtained from a TOCSY (H-5 to H-4) – NOESY (H-4) experiment.

Scheme 5. Stereoselective cyclization.



Unlike proton-promoted electrophilic addition, which follows Markovnikov's rule leading to a carbonium ion, the addition of an iodonium ion to a double bond can result in two bridged iodonium intermediates (Scheme 5). Consequently, the subsequent S_N2 displacement by 2-*O*-Bn produced two respective diastereoisomers (2,2′-cis and 2,2′-trans) (11) (see Scheme 4). Acetonitrile likely also plays a role by facilitating the cleavage of the O—Bn bond from the oxonium intermediate by forming a benzylacetonium ion (12) because the same reaction did not occur in dichloromethane.

The opposite stereochemistry obtained from 1-*C*-allyl-glycofuranosides and -glycopyranosides suggests two distinctive transition states. It is conceivable that the parent ring structure, the chair form in the pyranosides and the envelope form in the furanosides, may play a critical role in the stabilization of the respective oxonium ion transition states. It is also possible that the stereochemistry at C2′ may simply be predetermined by the orientation of the 2-*O*-Bn, which the 2′-carbonium ion must approach from the less-hindered side to form a 1,2-trans oxonium intermediate. Unfortunately, at this moment, we have no convincible explanation for those experimental results. Molecular modeling and calculation of the minimum energies of the possible oxonium transition states may provide the information on the most likely reaction pathway.

In summary, we described an intramolecular cyclization from 1-*C*-allyl-*O*-benzylglycosides in moderate to good yields. The allyl double bond was activated by electrophiles to generate a carbonium at C2′, which reacted with nucleophilic benzyl ether giving dioxabicyclic derivatives. The cyclization is highly regioselective in favor of five-membered products. The reaction is also highly diastereoselective to form 2,2′-cis and 2,2′-trans dioxabicycles from 1-*C*-pyranosides and 1-*C*-furanosides, respectively.[7]

Experimental section

General methods

^{1}H and ^{13}C NMR spectra were recorded 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 TMS and are assigned on the basis of 2D COSY, TOCSY, and ^{1}H–^{13}C chemical-shift correlated experiments. High-resolution fast atom bombardment mass spectrometry (HRFABMS) was carried out on a JEOL JMS-AX505H mass spectrometer using a 6 kV xenon beam at an accelerating voltage of 3 kV. *m*-Nitrobenzyl alcohol (*m*-NBA) was used as the matrix, and polyethylene glycol (PEG) was the internal calibrant. All chemicals were purchased from the Sigma-Aldrich Chemical Co. and used without further purification.

General procedure for cyclization

To a solution of substrate (50–100 mg) in CH_3CN (2 mL) was added dropwise TMSOTf (1 equiv.) at 0 °C. The mixture was stirred and allowed to warm to room temperature overnight. The reaction was quenched by the addition of Et_3N and the solvent was removed under reduced pressure. Product purification was performed by silica gel column chromatography (hexane–EtOAc, 3:1).

1-*C*-(*R*-Propan-2′-ol)-3,5-di-*O*-benzyl-2,2′-anhydro-α-D-ribofuranoside (4-*trans*)

This compound was obtained as an oil in 61% yield. $[\alpha]_D$ +79.4° (*c* 7.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 4.80 (d, *J* = 12 Hz, 1H, $PhCH_2$), 4.77 (dd, *J* = 4.8, 4.8 Hz, 1H, H-1), 4.60 (dd, *J* = 4.8, 4.8 Hz, 1H, H-2), 4.54–4.50 (m, 3H, $PhCH_2$), 4.29 (m, 1H, H-2′), 4.00 (ddd, *J* = 8.4, 5.2, 2.4 Hz, 1H, H-7), 3.83 (dd, *J* = 8.4, 5.2 Hz, 1H, H-3), 3.66 (dd, *J* = 10.8, 2.4 Hz, 1H, H-5a), 3.45 (dd, *J* = 10.8, 5.2 Hz, 1H, H-5b), 2.23 (dd, *J* = 13.2, 4.8 Hz, 1H, H-1′b), 1.58 (ddd, *J* = 13.2, 10.4, 4.8 Hz, 1H, H-1′a), 1.30 (d, *J* = 6.0 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 83.6 (C-2), 80.8 (C-3), 80.5 (C-4), 79.9 (C-1), 77.0 (C-2′), 73.4 ($PhCH_2$), 72.0 ($PhCH_2$), 70.1 (C-5), 43.2 (C-1′), 20.7 (CH_3). HRFABMS calcd. for $C_{22}H_{27}O_4$ *m/z*: 355.1831 (MH^+); found: 355.2230. Starting material **2** (10 mg, 10%) was also recovered.

1-*C*-(*R*-Propan-2′-ol)-3,5-di-*O*-acetyl-2,2′-anhydro-α-D-ribofuranoside (5)

A solution of compound **4**-*trans* (120 mg, 0.33 mmol) in methanol (15 mL) was hydrogenated with 10% Pd/C (50 mg) under 50 psi (1 psi = 6.894 757 kPa) overnight. The filtrate was concentrated to a residue. To a solution of this residue in CH_2Cl_2 (10 mL) was added TEA (1 mL) and acetic anhydride (210 mg, 2.11 mmol), and the mixture was stirred overnight. Work-up and purification by chromatography gave **5** (60 mg, 68%). $[\alpha]_D$ +113.9° (*c* 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 4.87 (dd, 1H, *J* = 4.8, 7.6 Hz), 4.81 (dd, 1H, *J* = 4.8 Hz), 4.76 (dd, 1H, *J* = 4.8 Hz), 4.28 (dd, 1H, *J* = 11.6, 2.8 Hz), 4.20 (m, 1H), 4.14 (m, 1H), 4.05 (dd, 1H, *J* = 11.6, 5.6 Hz), 2.23 (dd, 1H, *J* = 13.2, 4.8 Hz), 2.13 (s, 3H), 2.09 (s, 3H), 1.59 (m, 1H), 1.28 (d, 3H, *J* = 6.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 170.8, 170.4, 84.0, 80.6, 78.7, 77.3, 75.2, 64.0, 42.9, 20.9, 20.8, 20.6. ESMS: 259.2 (MH^+).

1-*C*-(*R*-Propan-2′-ol)-3,5-di-*O*-benzyl-2,2′-anhydro-β-L-arabinofuranoside (7-*trans*)

Under the same conditions, **7**-*trans* (37%) and **6α** (35%) were obtained from **6** (α:β, 1:1).

For **7**-*trans*: $[\alpha]_D$ –44.0° (*c* 1.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 7.37–7.24 (m, 10H), 4.72 (m, 1H), 4.71 (d, 1H, *J* = 11.6 Hz), 4.63 (dd, 1H, *J* = 4.8, 1.6 Hz), 4.56 (s, 2H),

[7] Supplementary data for this article are available on the journal Web site (http://canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 5025. For more information on obtaining material refer to http://cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml.

4.52 (d, 1H, *J* = 11.6 Hz), 4.15 (m, 1H), 3.95 (dt, 1H, *J* = 3.2, 6.4 Hz), 3.78 (dd, 1H, *J* = 7.2, 2.0 Hz), 3.65 (dd, 1H, *J* = 10.4, 3.2 Hz), 3.56 (dd, 1H, *J* = 10.8, 6.4 Hz), 2.17 (dd, 1H, *J* = 13.2, 4.4 Hz), 1.42 (m, 1H), 1.27 (d, 3H, *J* = 6.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 138.2, 137.8, 128.5, 128.4, 127.9, 127.7, 88.5, 85.9, 83.8, 82.6, 74.7, 73.5, 72.1, 70.2, 41.0, 19.9. ESMS: 355.3 (MH^+).

For **6α**: $[\alpha]_D$ –19.5° (*c* 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 7.37–7.22 (m, 15H), 5.58 (m, 1H), 5.10 (m, 2H), 4.50 (m, 6H), 4.21 (m, 1H), 4.07 (m, 1H), 4.06 (dd, 1H, *J* = 3.2 Hz), 3.87 (dd, 1H, *J* = 4.4, 2.8 Hz), 3.57 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 138.4, 138.0, 134.4, 128.5, 128.4, 128.3, 127.8, 127.7, 87.0, 85.4, 82.0, 81.6, 73.4–71.9, 70.3, 37.7. ESMS: 445.2 (MH^+).

1-*C*-(*R*-Propan-2′-ol)-3,5-di-*O*-benzyl-2,2′-anhydro-α-D-xylofuranoside (9-*trans*)

Under the same conditions, **9**-*trans* (35%) and **8β** (42%) were obtained from **8** (α:β, 1:1).

For **9**-*trans*: $[\alpha]_D$ –44.0° (*c* 1.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 7.37–7.24 (m, 10H), 4.87 (dd, 1H, *J* = 4.4 Hz), 4.67 (d, 1H, *J* = 12.0 Hz), 4.63 (d, 1H, *J* = 11.6 Hz), 4.59 (m, 1H), 4.52 (d, 1H, *J* = 6.4 Hz), 4.49 (d, 1H, *J* = 6.4 Hz), 4.18 (m, 1H), 4.12 (m,1H), 3.97 (d, 1H, *J* = 4.0 Hz), 3.68 (d, 2H, *J* = 5.6 Hz), 2.25 (dd, 1H, *J* = 13.6 Hz, 5.2 Hz), 1.50 (m, 1H), 1.24 (d, 3H, *J* = 6.4 Hz). ^{13}C NMR ($CDCl_3$) δ: 128.5, 128.4, 127.9, 127.7, 85.9, 83.8, 83.5, 81.3, 75.9, 73.6, 72.2, 68.9, 42.5, 20.6. ESIMS: 355.3 (MH^+).

For **8β**: $[\alpha]_D$ –19.5° (*c* 1.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 7.37–7.22 (m, 15H), 5.80 (m, 1H), 5.08 (m, 2H), 4.63–4.44 (m, 6H), 4.20 (dt, 1H, *J* = 1.6, 4.4 Hz), 3.96 (d, 1H, *J* = 3.6 Hz), 3.90 (dt, 1H, *J* = 3.6, 6.8 Hz), 3.79 (dd, 1H, *J* = 9.6, 5.6 Hz), 3.76 (m, 1H), 3.73 (dd, 1H, *J* = 9.6, 6.0 Hz), 2.49–2.32 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 138.4, 138.0, 134.4, 128.5, 128.4, 127.9, 127.8, 127.7, 87.0, 85.4, 82.0, 81.6, 73.4–71.9, 70.3, 37.7. ESMS: 455.3 (MH^+).

1-*C*-(*S*-Propan-2′-ol)-3-*O*-benzyl-4,6-*O*-benzylidene-2,2′-anhydro-α-D-galactopyranoside (11-*cis*)

This compound was obtained from **10** as an oil in 56% yield. $[\alpha]_D$ +44.8° (*c* 0.67, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 5.47 (s, 1H, PhCH), 5.07 (m, 1H, H-1), 4.87 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.73 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.39 (bd, *J* = 2.4 Hz, 1H, H-4), 4.33 (d, *J* = 12.4 Hz, 1H, H-6a), 4.08–4.03 (m, 2H, H-6b, H-2), 3.92 (m, 1H, H-2, 3.71 (dd, *J* = 5.6, 2.0 Hz, 1H, H-3), 3.58 (bs, 1H, H-5), 2.38 (m, 1H, H-1), 1.82 (ddd, *J* = 13.6, 8.4, 3.2 Hz, 1H, H-1), 1.34 (d, *J* = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 100.5 (PhCH), 82.8 (C-2), 79.5 (C-3), 78.0 (C-1), 74.2 (C-2′), 73.3 (C-4), 72.6 (C-6), 71.1 ($PhCH_2$), 67.5 (C-5), 40.8 (C-1′), 21.0 (CH_3). HRFABMS calcd. for $C_{23}H_{27}O_5$ *m/z*: 383.1780 (MH^+); found: 383.2146.

1-*C*-(*S*-Propan-2′-ol)-3,4,6-tri-*O*-benzyl-2,2′-anhydro-α-D-glucopyranoside (13-*cis*)

This compound was obtained from **12** as an oil in 62% yield. $[\alpha]_D$ +76° (*c* 0.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 7.18–7.40 (m, 15H, 3 × Ph), 4.90 (d, 1H, CH_2Ph, *J* = 11.6 Hz), 4.83 (d, 1H, CH_2Ph, *J* = 11.2 Hz), 4.73 (d, 1H, CH_2Ph, *J* = 11.6 Hz), 4.59 (d, 1H, H-1), 4.53 (d, 1H, CH_2Ph, *J* = 12.4 Hz), 4.46 (d, 1H, CH_2Ph, *J* = 11.2 Hz), 4.43 (d, 1H, CH_2Ph, *J* = 12.4 Hz), 3.95 (m, 1H, H-2′), 3.77–3.85 (m, 3H, H-2, H-3, H-5), 3.55–3.67 (m, 3H, H-4, H-6, 6′), 2.25 (m, 1H, H-1′a), 1.62 (m, 1H, H-1′b), 1.34 (d, 3H, H-3′, *J* = 6.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 138.9, 138.7, 138.4 (Ph), 128.6, 128.4, 127.9, 127.8, 127.6 (Ph), 83.4 (C-3), 83.3 (C-2), 76.1 (C-1), 75.5 (C-4), 75.2 (C-5), 74.7 (C-2′), 74.6 (CH_2Ph), 73.5 (CH_2Ph), 73.0 (CH_2Ph), 70.1 (C-6), 39.4 (C-1′), 21.6 (C-3′). ESMS: 475.3 (MH^+).

1-*C*-(3′-Iodo-*R/S*-propan-2′-ol)-3,5-di-*O*-benzyl-2,2′-anhydro-α-D-ribofuranoside (16-*trans* and 16-*cis*)

Compounds **16**-*trans* (19%) and **16**-*cis* (39%) obtained from **2** were separated by chromatography.

For **16**-*trans*: oil. $[\alpha]_D$ +51.7° (*c* 0.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 4.79–4.76 (m, 2H, $PhCH_2$, H-1), 4.66 (dd, *J* = 4.0, 4.0 Hz, 1H, H-2), 4.57–4.49 (m, 3H, $PhCH_2$), 4.17 (m, 1H, H-2′), 4.02 (m, 1H, H-4), 3.86 (dd, *J* = 8.0, 4.4 Hz, 1H, H-3), 3.66 (dd, *J* = 10.4, 1.6 Hz, 1H, H-5a), 3.46 (dd, *J* = 10.4, 4.8 Hz, 1H, H-5b), 3.38–3.30 (m, 2H, CH_2I), 2.37 (dd, *J* = 13.6, 5.2 Hz, 1H, H-1′b), 1.79 (ddd, *J* = 13.6, 10.0, 5.2 Hz, 1H, H-1′a). ^{13}C NMR ($CDCl_3$) δ: 83.1 (C-2), 81.9 (C-3), 80.7 (C-4), 80.1 (C-1), 79.5 (C-2′), 73.5 ($PhCH_2$), 72.2 ($PhCH_2$), 70.0 (C-5), 41.9 (C-1′), 10.2 (CH_2-I). HRFABMS calcd. for $C_{22}H_{25}IO_4$ *m/z*: 480.0797 (M^+); found: 479.0749.

For **16**-*cis*: oil. $[\alpha]_D$ +79.5° (*c* 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 4.79–4.73 (m, 2H, $PhCH_2$, H-1), 4.57–4.49 (m, 3H, $PhCH_2$), 4.45 (dd, *J* = 4.4, 4.4 Hz, 1H, H-2), 4.20–4.15 (m, 2H, H-2 H-4), 3.89 (dd, *J* = 8.4, 4.4 Hz, 1H, H-3), 3.67 (dd, *J* = 10.8, 1.6 Hz, 1H, H-5a), 3.50 (dd, *J* = 10.8, 4.8 Hz, 1H, H-5b), 3.41 (dd, *J* = 10.0, 5.2 Hz, 1H, CH_2I), 3.32 (dd, *J* = 9.2, 8.4 Hz, 1H, CH_2I), 2.42 (dt, *J* = 14.0, 6.8 Hz, 1H, H-1), 1.99 (ddd, *J* = 14.0, 6.8, 2.4 Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$) δ: 82.9 (C-1), 82.2 (C-2), 80.8 (C-2′), 79.2 (C-3), 79.0 (C-4), 73.4 ($PhCH_2$), 72.1 ($PhCH_2$), 69.6 (C-5), 40.2 (C-1′), 8.5 (CH_2I). HRFABMS calcd. for $C_{22}H_{25}IO_4$ *m/z*: 480.0797 (M^+); found: 479.0711.

1-*C*-(3′-Iodo-*R/S*-propan-2′-ol)-3-*O*-benzyl-4,6-*O*-benzylidene-2,2′-anhydro-α-D-galactopyranoside (17-*trans* and 17-*cis*)

Compounds **17**-*trans* (20%) and **17**-*cis* (60%) obtained from **10** were separated by chromatography.

For **17**-*trans*: oil. $[\alpha]_D$ –8° (*c* 5.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 5.48 (s, 1H, PhCH), 5.20 (dd, *J* = 8.8, 4.4 Hz, 1H, H-1), 4.86 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.73 (d, *J* = 12.8 Hz, 1H, CH_2Ph), 4.48 (dd, *J* = 9.2, 4.4 Hz, 1H, H-2), 4.40 (bs, 1H, H-4), 4.33 (d, *J* = 12.4 Hz, 1H, H-6a), 4.23 (m, 1H, H-2, 4.05 (d, *J* = 12.8 Hz, 1H, H-6b), 3.63 (d, *J* = 5.2 Hz, 1H, H-3), 3.56 (bs, 1H, H-5), 3.34–3.25 (m, 2H, CH_2I), 2.23 (dd, *J* = 13.6, 5.6 Hz, 1H, H-1), 1.82 (ddd, *J* = 13.6, 9.2, 5.6 Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$) δ: 100.5 (PhCH), 84.0 (C-2), 79.2 (C-3), 78.1 (C-1), 77.7 (C-2′), 73.5 (C-4), 72.6 (C-6), 70.8 ($PhCH_2$), 67.4 (C-5), 39.8 (C-1′), 10.1 (CH_2I). HRFABMS calcd. for $C_{23}H_{25}IO_5$ *m/z*: 508.0747 (M^+); found: 507.0730.

For **17**-*cis*: oil. $[\alpha]_D$ +6.8° (*c* 9.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 5.48 (s, 1H, PhCH), 5.15 (m, 1H, H-1), 4.86 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.73 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.39 (bs, 1H, H-4), 4.33 (d, *J* = 12.4 Hz, 1H, OCH_2), 4.25 (dd, *J* = 9.6, 4.8 Hz, 1H, H-2), 4.23 (m, 1H, H-2′), 4.05 (d, *J* = 12.4 Hz, 1H, H-6a), 3.66 (bd, *J* = 5.2 Hz, 1H, H-3), 3.57

(bs, 1H, H-5), 3.34–3.25 (m, 2H, CH_2I), 2.23 (m, 1H, H-1′a), 1.82 (dd, J = 14, 5.6 Hz, 1H, H-1′b). ^{13}C NMR ($CDCl_3$) δ: 100.5 (PhCH), 84.2 (C-2), 79.7 (C-3), 78.8 (C-2′), 77.6 (C-1), 73.4 (C-4), 72.5 (C-6), 70.9 ($PHCH_2$), 67.4 (C-5), 38.3 (C-1), 9.8 (CH_2I). HRFABMS calcd. for $C_{23}H_{25}IO_5$ *m/z*: 508.0747 (M^+); found: 507.0781.

Acknowledgments

This is NRCC publication No. 42508. The authors thank Ms. Milan Bhasin for technical assistance, Dr. Jean-Robert Brisson for assistance in NMR analysis, and Lisa Morrison and Dr. Jianjun Li for MS analysis.

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