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Synthesis of Oxepines and 2-Branched Pyranosides from a D-Glucal-Derived *gem*-Dibromo-1,2-cyclopropanated Sugar

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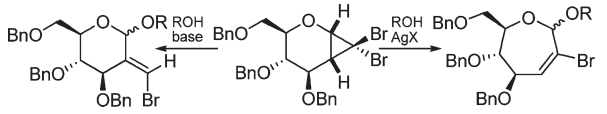
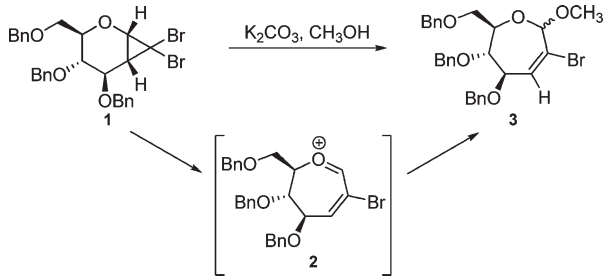


The conversion of cyclopropane-fused carbohydrates into oxepines is an attractive method for accessing diverse members of the septanoside family of carbohydrate mimetics. 2-Bromooxepines are obtained through silver(I)-promoted thermal ring expansion of a D-glucal-derived *gem*-dihalocyclopropanated sugar. In contrast, cyclopropane ring cleavage under basic conditions leads to 2-*C*-branched pyranosides, not the 2-bromooxepine structures assigned in an earlier report.

Oxepines (aka oxepenes) are seven-membered oxacycles with at least one double bond present in the ring.[1] Interest in the synthesis of substituted oxepines has been driven by their inclusion in a number of bioactive natural products[1] and the ability to convert them into a diverse range of septanosides.[2] These seven-membered-ring sugars have the potential to mimic the structures and functions of natural carbohydrates, while the conformations adopted by these homologues lead to their binding and interaction with biological targets.[3,4] Among the various strategies developed for the synthesis of oxepines and septanosides,[1,5,6] several methods have featured the homologation of pyranoses via cyclopropanes.[3,7−9] Specifically, the cyclopropanation of unsaturated carbohydrate scaffolds[10] and subsequent cyclopropane cleavage leads to ring expansion. Alternatively, branched cyclic products can instead be generated depending on the cyclopropane substituents and the reaction conditions.[8,11]

gem-Dihalocyclopropanes are readily synthesized by dihalocarbene addition to the corresponding alkenes[12] and have been used in numerous synthetic applications.[12,13] Nagarajan et al. described, inter alia, the conversion of several glycal-derived *gem*-dihalocyclopropanated sugars into 2-bromooxepines in the presence of methanol and potassium carbonate in 1997 (for example, Scheme 1).[8] Extension of this methodology by Ganesh and Jayaraman led to the synthesis of a number of septanosides from 2-oxyglycals.[9]

SCHEME 1. Reported Base-Promoted Reaction of Cyclopropane 1[8]



In an effort to prepare a variety of oxepines containing the 2-bromoalkene functionality for further manipulations to novel septanosides, we repeated the chemistry reported by

(1) (a) Snyder, N. L.; Haines, H. M.; Peczuh, M. W. *Tetrahedron*, **2006**, *62*, 9301−9320 and references cited therein. (b) Pakulski, Z. *Pol. J. Chem.* **2006**, *80*, 1293–1326.

(2) (a) Batchelor, R.; Harvey, J. E.; Northcote, P. T.; Teesdale-Spittle, P.; Hoberg, J. O. *J. Org. Chem.* **2009**, *74*, 7627–7632. (b) DeMatteo, M. P.; Snyder, N. L.; Morton, M.; Baldisseri, D. M.; Hadad, C. M.; Peczuh, M. W. *J. Org. Chem.* **2005**, *70*, 24–38.

(3) Sabatino, D.; Damha, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 8259–8270.

(4) (a) Tauss, A.; Steiner, A. J.; Stütz, A. E.; Tarling, C. A.; Withers, S. G.; Wrodnigg, T. M. *Tetrahedron: Asymmetry* **2006**, *17*, 234–239. (b) Castro, S.; Duff, M.; Snyder, N. L.; Morton, M.; Kumar, C. V.; Peczuh, M. W. *Org. Biomol. Chem.* **2005**, *3*, 3869–3872.

(5) (a) Jadhav, V. H.; Bande, O. P.; Pinjari, R. V.; Gejji, S. P.; Puranik, V. G.; Dhavale, D. D. *J. Org. Chem.* **2009**, *74*, 6486–6494. (b) Alcázar, E.; Pletcher, J. M.; McDonald, F. E. *Org. Lett.* **2004**, *6*, 3877–3880. (c) Peczuh, M. W.; Snyder, N. L. *Tetrahedron Lett.* **2003**, *44*, 4057–4061. (d) Wong, J. C. Y.; Lacombe, P.; Sturino, C. F. *Tetrahedron Lett.* **1999**, *40*, 8751–8754. (e) Ovaa, H.; Leeuwenburgh, M. A.; Overkleeft, H. S.; van der Marel, G. A.; van Boom, J. H. *Tetrahedron Lett.* **1998**, *39*, 3025–3028.

(6) (a) Saha, J.; Peczuh, M. W. *Org. Lett.* **2009**, *11*, 4482–4484. (b) Pavlik, C.; Onorato, A.; Castro, S.; Morton, M.; Peczuh, M.; Smith, M. B. *Org. Lett.* **2009**, *11*, 3722–3725. (c) Kumaraswamy, G.; Sadaiah, K.; Ramakrishna, D. S.; Police, N.; Sridhar, B.; Bharatam, J. *Chem. Commun.* **2008**, 5324–5326. (d) Castro, S.; Fyvie, W. S.; Hatcher, S. A.; Peczuh, M. W. *Org. Lett.* **2005**, *7*, 4709–4712. (e) Contour, M.-O.; Fayet, C.; Gelas, J. *Carbohydr. Res.* **1990**, *201*, 150–152.

(7) (a) Batchelor, R.; Hoberg, J. O. *Tetrahedron Lett.* **2003**, *44*, 9043–9045. (b) Hoberg, J. O. *J. Org. Chem.* **1997**, *62*, 6615–6618.

(8) Ramana, C. V.; Murali, R.; Nagarajan, M. *J. Org. Chem.* **1997**, *62*, 7694–7703.

(9) (a) Ganesh, N. V.; Raghothama, S.; Sonti, R.; Jayaraman, N. *J. Org. Chem.* **2010**, *75*, 215–218. (b) Ganesh, N. V.; Jayaraman, N. *J. Org. Chem.* **2009**, *74*, 739–746. (c) Ganesh, N. V.; Jayaraman, N. *J. Org. Chem.* **2007**, *72*, 5500–5504.

(10) (a) Fraser−Reid, B; López, J. C. *Curr. Org. Chem.* **2009**, *13*, 532–553. (b) Hoberg, J. O.; Bozell, J. J. *Tetrahedron Lett.* **1995**, *36*, 6831–6834. (c) Brimacombe, J. S.; Evans, M. E.; Forbes, E. J.; Foster, A. B.; Webber, J. M. *Carbohydr. Res.* **1967**, *4*, 239–243.

(11) (a) Sridhar, P. R.; Kumar, P. V.; Seshadri, K.; Satyavathi, R. *Chem.—Eur. J.* **2009**, *15*, 7526–7529. (b) Gammon, D. W.; Kinfe, H. H.; De Vos, D. E.; Jacobs, P. A.; Sels, B. F. *J. Carbohydr. Chem.* **2007**, *26*, 141–157. (c) Banwell, M. G.; Phillis, A. T.; Willis, A. C. *Org. Lett.* **2006**, *8*, 5341–5344. (d) Shao, H.; Ekthawatchai, S.; Chen, C.-S.; Wu, S.-H.; Zou, W. *J. Org. Chem.* **2005**, *70*, 4726–4734. (e) Shao, H.; Ekthawatchai, S.; Wu, S.-H.; Zou, W. *Org. Lett.* **2004**, *6*, 3497–3499. (f) Henry, K. J. Jr.; Fraser-Reid, B. *Tetrahedron Lett.* **1995**, *36*, 8901–8904. (g) Banwell, M. G.; Gable, R. W.; Halton, B.; Phyland, J. R. *Aust. J. Chem.* **1994**, *47*, 1879–1884.

(12) (a) Fedoryński, M. *Chem. Rev.* **2003**, *103*, 1099–1132. (b) Banwell, M. G.; Reum, M. E. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press Ltd: London, UK, 1991; Vol. 1, pp 19−64.

(13) (a) Halton, B.; Harvey, J. *Synlett* **2006**, 1975–2000. (b) Stanislawski, P. C.; Willis, A. C.; Banwell, M. G. *Chem. Asian J.* **2007**, *2*, 1127–1136.

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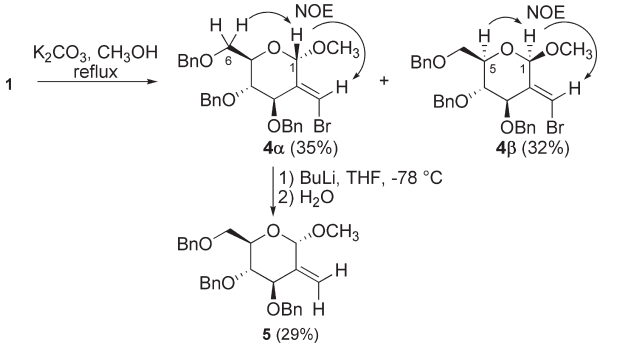
Nagarajan,[8] in which the D-glucal-derived *gem*-dibromocyclopropane **1** is treated with potassium carbonate in methanol and heated at reflux. This provided a separable pair of diastereoisomeric bromoalkenes in a 1.1:1 ratio and 67% combined yield, and with NMR spectral data that match those previously reported.[8] The expected ring-expansion mechanism would involve ejection of a bromide ion with concomitant electrocyclic opening to give the oxygen-stabilized allylic cation **2** (Scheme 1). Attack by methoxide at C1 of this oxonium ion would result in formation of the anomeric methyl 2-bromo-2,3-unsaturated oxepines **3** that were reported.[8] However, the absence of a significant coupling between the proton of the benzyl-protected allylic oxymethine and the alkene proton in both anomers cast doubt upon structure **3**. In addition, the chemical shifts of the olefinic protons (ca. 6.8 ppm) were surprisingly high for the alkene of structure **3**. Moreover, the observation of NOE correlations between the alkene and acetal protons indicated that the products were actually the 2-*C*-branched pyranosides **4α** and **4*β*** (Scheme 2), rather than the reported 2-bromooxepines.[8] The anomeric stereochemistry was tentatively assigned on the basis of small NOE enhancements between H-1 and H-5 in the minor (*β*-) anomer, and between H-1 and H-6 in the major (α-) anomer. More compelling evidence was obtained through derivatization, in which the major isomer was subjected to bromine-for-lithium exchange and a quench, generating the known 2-*C*-methylene α-pyranoside **5** (Scheme 2).[14] The spectroscopic data match those previously reported,[14] with the NMR spectra of the resulting product showing distinctive signals for an exocyclic methylene group, thus serving to confirm the revised structures.

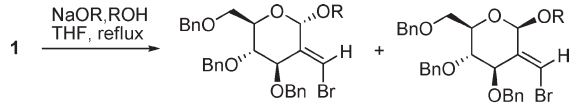
SCHEME 2. Revised Product Structures from Base-Promoted Reaction of Cyclopropane 1



The mode of cyclopropane ring-opening observed here is unusual, but related reactions in which *gem*-dichlorocyclopropanes are converted, using potassium *tert*-butoxide, to dienes incorporating a chloromethylidene branch have been reported by Banwell and co-authors.[11c,g] There are several possible mechanisms that would account for the course of these reactions. For example, a cyclopropene, formed from **1** by alkoxide-induced elimination of the elements of HBr,[12b,15] may ring open to provide, in a stereoselective manner, the observed branched products. Alternatively, direct opening of the cyclopropane to an exocyclic dibromomethyl anion,[11g] facilitated by formation of an oxonium ion, would produce a zwitterion that has the potential to convert to the products.[16]

The same 2-*C*-branched pyranosides **4α** and **4*β*** are also generated from cyclopropane **1** by the action of methanolic sodium methoxide in THF (Scheme 3). These conditions allow faster reaction while maintaining a good yield (71%) and have been adapted for the generation of allyl and benzyl glycosides as shown in Scheme 3. The ratios of anomers in the crude reaction mixtures range from 1.1:1 to 2.3:1, and the isolated yields reflect these ratios.

SCHEME 3. Conversion of Cyclopropane 1 into 2-*C*-Branched Pyranosides



R = CH_3	**4α** (49%)	**4β** (22%)
R = $CH_2CH{:}CH_2$	**6α** (49%)	**6β** (22%)
R = Bn	**7α** (30%)	**7β** (33%)

2-*C*-Methylene glycosides,[14,17] of which products **4**, **6**, and **7** are novel examples, are important modified sugars with potential for transformation into a diverse range of carbohydrate mimetics by functionalization at the anomeric position, the alkene, and, in this case, the bromide. Derivatizations of these 2-*C*-branched pyranosides are currently underway.

The use of silver(I) salts is widely favored in promoting ring expansion of *gem*-dihalocyclopropanes.[12,13] The resulting allylic cation can be trapped by the ejected halide ion, the silver counterion, or an intra- or intermolecular nucleophile.[12,13,18] However, we found that reaction of *gem*-dihalocyclopropane **1** with silver tetrafluoroborate or silver acetate in methanol at reflux was extremely sluggish. Nevertheless, acetal and alkenyl proton resonances were detected in the NMR spectrum after several days' reaction, and small quantities of the ring-expanded 2-bromooxepine anomers **3α** and **3*β*** were isolated in 11% and 4% yields, respectively (Scheme 4). The NMR spectra of these materials were distinctly different from those of the base-derived products. Specifically, the alkene protons were in the expected region (δ 6.44 and 6.33 for **3α** and **3*β***, respectively), and the expected homonuclear 3-bond couplings between the alkene (H3) and allylic (H4) protons were observed in the ^{1}H and COSY spectra of both anomers.

It appeared likely that the silver-promoted reaction would proceed more efficiently at a higher temperature.[19] The use of alternative nucleophiles and solvents would allow exploration of higher temperatures than methanol provides. In agreement with the results reported by Nagarajan et al., we found that reaction of cyclopropane **1** with silver acetate

(14) Booma, C.; Balasubramanian, K. K. *J. Chem. Soc., Chem. Commun.* **1993**, 1394–1395.

(15) Baird, M. S. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press Ltd: London, UK, 1991; Vol. 1, pp 65−116.

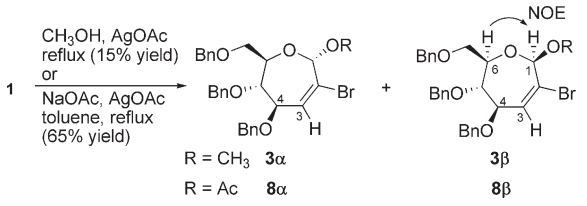
(16) The presence of a hydrogen atom at the 2-position is necessary for formation of the observed branched products by all of the plausible mechanistic pathways, and therefore the oxepine structures assigned by Ganesh and Jayaraman[9] in the more substituted 2-oxyglycal-derived systems are assumed to be correct.

(17) (a) Kashyap, S.; Vidadala, S. R.; Hotha, S. *Tetrahedron Lett.* **2007**, *48*, 8960−8962 and references cited therein. (b) Sato, K.; Sekiguchi, T.; Hozumi, T.; Yamazaki, T.; Akai, S. *Tetrahedron Lett.* **2002**, *43*, 3087–3090.

(18) Verhé, R.; De Kimpe, N. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; John Wiley & Sons: Chichester, UK, 1987; Vol. 1, pp 445−564.

(19) Reactions in a sealed vessel under microwave irradiation generate several new products, and will be discussed in a future publication.

SCHEME 4. Silver-Promoted Ring Expansions of Cyclopropane 1



in refluxing acetic acid caused extensive decomposition.[8] However, optimization of the reaction conditions provided the anomeric acetates **8α** and **8*β*** in 52% yield and a 3.5:1 ratio after treatment with silver(I) acetate in acetic acid at 100 °C (Scheme 4). Replacing the acetic acid with toluene and adding sodium acetate (5 equiv) to the reaction led to improved results (65% combined yield, 4.3:1 ratio of **8α** and **8*β***). The anomeric stereochemistries of the oxepines **8** were tentatively assigned on the basis of an NOE enhancement (ca. 5%) between H1 and H6 in the minor isomer. The presence of the anomeric acetate provides an opportunity for the formation of alternative glycosidic linkages. The alkenyl bromide moiety provides scope for further derivatizations to a range of septanosides.

In summary, several 2-*C*-branched pyranosides and septanoside precursors have been prepared. The product structures previously reported[8] for the reaction of D-glucal-derived cyclopropane **1** with potassium carbonate in methanol have been revised as 2-*C*-branched pyranose sugars. Additionally, conditions involving silver(I) salts that successfully produce 2-bromooxepines are provided.

Experimental Section

General Procedure for the Synthesis of 2-*C*-Branched Pyranosides. A solution of sodium alkoxide (ca. 1.5 equiv) in the corresponding alcohol (ca. 5 equiv), prepared by dissolution of metallic sodium in the alcohol, was diluted with THF (10 mL/mmol of cyclopropane). Cyclopropane **1** (1 equiv) was added and the resulting solution was refluxed until the starting material was consumed. The reaction mixture was then cooled, diluted with water, and extracted with dichloromethane. The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated. The crude products were separated with flash chromatography.

Methyl (2*E*)-3,4,6-Tri-*O*-benzyl-2-*C*-(bromomethylene)-2-deoxy-α-D-*arabino*-hexopyranoside (4α) and Methyl (2*E*)-3,4,6-Tri-*O*-benzyl-2-*C*-(bromomethylene)-2-deoxy-*β*-D-*arabino*-hexopyranoside (4*β*). Use of sodium (6.5 mg, 0.3 mmol), methanol (63 μL, 1.6 mmol), THF (1.7 mL), and cyclopropane **1** (100 mg, 0.17 mmol) as described above yielded a yellow oil after 75 min. Chromatography of this oil (silica, 1:9 EtOAc/hexanes) afforded compounds **4*β*** (20 mg, 22%) as a colorless oil and **4α** (45 mg, 49%) as a colorless oil.

4*β*: R_f 0.35 (1:9 EtOAc/hexanes); $[\alpha]^{17}_D$ +57 (*c* 1.0, $CHCl_3$) [lit.[8] $[\alpha]^{25}_D$ +69 (*c* 2, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.18 (complex m, 15H), 6.81 (d, *J* = 1.7 Hz, 1H), 5.19 (d, *J* = 1.7 Hz, 1H), 4.73 (d, *J* = 1.2 Hz, 1H), 4.64 (d, *J* = 12.2 Hz, 1H), 4.60 (d, *J* = 12.2 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.50 (d, *J* = 12.2 Hz, 1H), 4.43 (d, *J* = 12.2 Hz, 1H), 4.29 (d, *J* = 11.5 Hz, 1H), 3.74 (dd, *J* = 9.0, 1.5 Hz, 1H), 3.69 (ddd, *J* = 8.8, 5.1, 2.4 Hz, 1H), 3.65 (dd, *J* = 10.9, 2.5 Hz, 1H), 3.62 (dd, *J* = 10.9, 5.3 Hz, 1H), 3.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3 (C), 138.1 (C), 137.7 (C), 137.5 (C), 128.32 (CH), 128.27 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.72 (CH), 127.67 (CH), 127.5 (CH), 112.6 (CH), 98.9 (CH), 79.3 (CH), 76.1 (CH), 73.1 (CH_2), 71.5 (CH_2), 71.4 (CH), 70.8 (CH_2), 69.5 (CH_2), 55.2 (CH_3); IR (KBr) 3054, 3027, 2961, 2865, 1629, 1496, 1453, 1345, 1261, 1094, 1072, 802, 735, 697 cm^{-1}.

4α: R_f 0.25 (1:9 EtOAc/hexanes); $[\alpha]^{17}_D$ +18 (*c* 1.0, $CHCl_3$) [lit.[8] $[\alpha]^{25}_D$ +26.7 (*c* 1, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.24 (complex m, 15H), 6.78 (s, 1H), 5.05 (s, 1H), 4.71 (d, *J* = 11.5 Hz, 1H), 4.69 (d, *J* = 3.7 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.52 (complex m, 2H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 3.91 (dd, *J* = 5.0, 3.8 Hz, 1H), 3.85 (m, 1H), 3.83 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.77 (dd, *J* = 10.0, 5.1 Hz, 1H), 3.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4 (C), 138.3 (C), 137.8 (C), 137.0 (C), 128.4 (CH), 128.33 (CH), 128.25 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.56 (CH), 127.55 (CH), 114.7 (CH), 101.1 (CH), 76.0 (CH), 74.9 (CH), 74.6 (CH), 73.3 (CH_2), 72.2 (CH_2), 70.9 (CH_2), 70.6 (CH_2), 55.8 (CH_3); IR (KBr) 3060, 3030, 2912, 2865, 1629, 1496, 1453, 1363, 1303, 1205, 1097, 1072, 1027, 818, 735, 697 cm^{-1}; HRMS *m*/*z* $C_{29}H_{31}O_5{}^{79}BrK$ $[M + K]^+$ calcd 577.0992, found 577.0988.

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-methylene-α-D-*arabino*-hexopyranoside (5). A solution of bromide **4α** (20 mg, 0.037 mmol) in THF (0.5 mL) was cooled to −78 °C and treated with *n*-butyllithium (50 μL, 1.6 M in hexanes) and then stirred at this temperature for 1 h. The reaction mixture was then treated with water (50 μL), and immediately allowed to warm to room temperature. After 30 min of additional stirring, the reaction mixture was diluted with water, then extracted with diethyl ether. The ethereal fractions were combined, dried, and concentrated to provide a colorless oil, which was purified by flash chromatography (1:9 EtOAc/hexanes) to provide known alkene **5**[14] (5 mg, 29% yield) as a colorless oil: R_f 0.25 (1:9 EtOAc/hexanes); $[\alpha]^{17}_D$ +13 (*c* 0.3, $CHCl_3$) [lit.[14] $[\alpha]^{25}_D$ +32 (*c* 1, CH_2Cl_2)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.15 (complex m, 15H), 5.30 (s, 1H), 5.16 (s, 1H), 5.06 (s, 1H), 4.87 (d, *J* = 10.7 Hz, 1H), 4.76 (d, *J* = 11.2 Hz, 1H), 4.70 (d, *J* = 11.2 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.2 Hz, 1H), 4.49 (d, *J* = 10.7 Hz, 1H), 4.42 (dd, *J* = 9.0, 2.0 Hz, 1H), 3.92 (ddd, *J* = 9.9, 3.8, 1.9 Hz, 1H), 3.75 (dd, *J* = 10.6, 3.9 Hz, 1H), 3.69 (dd, *J* = 10.6, 1.9 Hz, 1H), 3.60 (t, *J* = 9.4 Hz, 1H), 3.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3 (C), 138.32 (C), 138.27 (C), 138.1 (C), 128.4 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.63 (CH), 127.61 (CH), 110.7 (CH_2), 102.4 (CH), 81.2 (CH), 79.9 (CH), 74.9 (CH_2), 73.5 (CH_2), 73.4 (CH_2), 71.5 (CH), 68.8 (CH_2), 54.5 (CH_3); IR (KBr) 3029, 2907, 1496, 1454, 1359, 1102, 1067, 1026, 968, 736, 697 cm^{-1}; HRMS *m*/*z* $C_{29}H_{32}O_5Na$ $[M + Na]^+$ calcd 483.2147, found 483.2145.

Methyl 4,5,7-Tri-*O*-benzyl-2-bromo-2,3-dideoxy-α-D-*arabino*-hept-2-enoseptanoside (3α) and Methyl 4,5,7-Tri-*O*-benzyl-2-bromo-2,3-dideoxy-*β*-D-*arabino*-hept-2-enoseptanoside (3*β*). A solution of cyclopropane **1** (104 mg, 0.177 mmol) in methanol (1.7 mL) was treated with silver acetate (37 mg, 0.22 mmol) and refluxed for 5 days in the dark. The reaction mixture was then diluted with diethyl ether, and filtered through a pad of Celite, then the ethereal filtrate was washed with water. The aqueous wash was further extracted with diethyl ether, then the ethereal solutions were combined, dried ($MgSO_4$), filtered, and concentrated to provide a pale-yellow oil. Purification of this crude product by column chromatography (silica, 1:9 EtOAc/hexanes) delivered recovered starting material **1** (63 mg, 61%), plus oxepines **3*β*** (4 mg, 4%) as a colorless oil and **3α** (11 mg, 11%) as a colorless oil.

3*β*: R_f 0.30 (1:9 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.15 (complex m, 15H), 6.33 (d, *J* = 5.1 Hz, 1H), 5.14 (s, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 11.2 Hz, 1H), 4.59 (d, *J* = 11.7 Hz, 1H), 4.59 (d, *J* = 12.2 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 4.17−4.14 (complex m, 2H), 3.77 (dd, *J* = 8.9, 5.7 Hz, 1H), 3.70 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.61 (dd, *J* = 10.5, 2.7 Hz, 1H), 3.46 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2 (C), 138.1 (C), 137.9 (C), 132.1 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.90 (CH), 127.87 (CH), 127.85 (CH), 127.76 (CH), 127.71 (CH), 127.6 (CH), 124.7 (C), 102.1 (CH), 80.5 (CH), 78.9 (CH), 73.7 (CH_2), 73.2 (CH_2), 72.1 (CH_2), 71.5 (CH), 70.4 (CH_2), 56.5 (CH_3).

3α: R_f 0.25 (1:9 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.14 (complex m, 15H), 6.44 (dd, J = 7.1, 1.0 Hz, 1H), 5.05 (s, 1H), 4.68 (d, J = 12.2 Hz, 1H), 4.57−4.56 (complex m, 2H), 4.51 (d, J = 12.4 Hz, 1H), 4.49 (d, J = 12.2 Hz, 1H), 4.33 (d, J = 11.5 Hz, 1H), 4.09 (dd, J = 7.1, 1.2 Hz, 1H), 3.70−3.69 (complex m, 2H), 3.65−3.63 (complex m, 2H), 3.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2 (C), 137.9 (C), 137.4 (C), 132.2 (CH), 128.5 (CH), 128.42 (CH), 128.37 (CH), 128.0 (CH), 127.93 (CH), 127.85 (CH), 127.7 (CH), 127.6 (CH), 123.5 (C), 104.2 (CH), 80.0 (CH), 77.4 (CH), 75.3 (CH), 73.3 (CH_2), 72.7 (CH_2), 71.3 (CH_2), 71.0 (CH_2), 55.8 (CH_3); HRMS m/z $C_{29}H_{31}O_5{}^{79}$BrNa $[M + Na]^+$ calcd 561.1253, found 561.1256.

Acetyl 4,5,7-Tri-*O*-benzyl-2-bromo-2,3-dideoxy-α-D-*arabino*-hept-2-enoseptanoside (8α) and Acetyl 4,5,7-Tri-*O*-benzyl-2-bromo-2,3-dideoxy-β-D-*arabino*-hept-2-enoseptanoside (8β). Method A: A solution of cyclopropane **1** (101 mg, 0.17 mmol) in acetic acid (1.7 mL) was treated with silver acetate (39 mg, 0.23 mmol) and then stirred at 100 °C for 25 h. The resulting cooled solution was diluted with dichloromethane and filtered through a pad of Celite, then the filtrate was washed with water. The aqueous phase was extracted further with dichloromethane, then the organic fractions were combined, dried ($MgSO_4$), filtered, and concentrated to provide a mixture of compounds **8α** and **8β** (3.5:1 ratio) as a light-yellow oil. Purification by column chromatography (1:14 EtOAc/hexanes) yielded the major oxepine **8α** (14 mg, 14%) as a clear, colorless oil, and a mixture of **8α** and **8β** (37 mg, 38% yield).

8α: R_f 0.15 (1:9 EtOAc/hexanes); $[\alpha]^{19}{}_D$ −23 (c 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.16 (complex m, 15H), 6.57 (s, 1H), 6.46 (dd, J = 6.3, 1.2 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 11.2 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.51 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 4.38 (d, J = 11.2 Hz, 1H), 4.17−4.14 (complex m, 2H), 3.74 (dd, J = 9.1, 4.2 Hz, 1H), 3.61 (dd, J = 10.5, 2.4 Hz, 1H), 3.54 (dd, J = 10.5, 7.1 Hz, 1H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3 (C), 138.0 (C), 137.8 (C), 137.5 (C), 133.5 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.95 (CH), 127.93 (CH), 127.88 (CH), 127.8 (CH), 127.6 (CH), 123.9 (C), 93.4 (CH), 81.1 (CH), 77.2 (CH), 74.4 (CH), 73.4 (CH_2), 73.2 (CH_2), 71.7 (CH_2), 70.3 (CH_2), 20.7 (CH_3); IR (KBr) 3086 3058, 3030, 2863, 1753, 1639, 1496, 1454, 1368, 1221, 1071, 1005, 952, 737, 698 cm^{-1}; HRMS m/z $C_{30}H_{31}O_6{}^{79}$BrNa $[M + Na]^+$ calcd 589.1202, found 589.1202.

The following data were obtained for **8β** by subtracting the NMR signals for **8α** from those of the mixture obtained. **8β**: R_f 0.15 (1:9 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.14 (complex m, 15H), 6.45 (m, 1H), 6.33 (s, 1H), 4.69−4.37 (complex m, 6H), 4.15 (m, 1H), 3.92 (dd, J = 11.0, 5.9 Hz, 1H), 3.80 (dd, J = 6.3, 4.4 Hz, 1H), 3.67−3.52 (complex m, 2H), 2.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0 (C), 138.1 (C), 137.8 (C), 137.5 (C), 133.4 (CH), 128.45 (CH), 128.40 (CH), 128.33 (CH), 127.93 (CH), 127.88 (CH), 127.81 (CH), 125.6 (C), 94.4 (CH), 79.2 (CH), 78.6 (CH), 75.4 (CH), 73.3 (CH_2), 72.7 (CH_2), 71.6 (CH_2), 70.4 (CH_2), 20.9 (CH_3).

Method B: A solution of cyclopropane **1** (102 mg, 0.173 mmol) in toluene (1.7 mL) was treated with sodium acetate (72 mg, 0.88 mmol) and silver acetate (41 mg, 0.25 mmol) and then stirred at reflux for 28 h. The resulting cooled solution was filtered through a pad of silica gel, further eluted with dichloromethane, then the fractions were combined, dried ($MgSO_4$), filtered, and concentrated to provide a mixture of compounds **8α** and **8β** (4.3:1 ratio) as a colorless oil. Purification by column chromatography (1:14 EtOAc/hexanes) yielded a mixture of **8α** and **8β** (64 mg, 65% combined yield).

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Supporting Information Available: General experimental methods, experimental procedures, and compound characterization data for all products (**3**−**8**), copies of ^{1}H and ^{13}C NMR spectra for **3**−**8**, copies of NOE spectra for **4**, and copies of COSY spectra for **3**, **4**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.