Synthesis and Reactions of 1,2-Cyclopropanated Sugars

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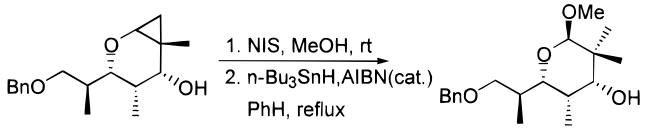
Diastereospecific cyclopropanation of glycals **1**, **2**, **3**, **4**, and **41** was carried out using either dihalocarbene addition or zinc-carbenoid addition to yield 1,2-cyclopropanated sugars. Dichloro- and dibromocarbenes added stereoselectively *anti* to the C_3 benzyloxy group, whereas (under Simmons−Smith conditions) the cyclopropanes were formed *syn* to the same substituent. The reactions of these 1,2-cyclopropanated sugars to provide either ring expanded glycosides or C_2-branched chain glycosides were explored. Solvolytic ring expansion of 1,2-dibromocyclopropanated sugars with K_2CO_3 in refluxing methanol yielded the corresponding chiral oxepins **20**−**22**. Electrophilic ring openings of parent cyclopropanes (**14** and **17** derived from glucal **1**) were carried out with different electrophiles to give functionalized 2-deoxy-2-C-branched chain glycosides. The ring openings of **14** in different solvents resulted in both α- and *β*-anomers, whereas **17** gave exclusively the α-anomer.

Introduction

1,2-Anhydrosugars are important synthetic intermediates for the synthesis of a variety of C-1 substituted sugars. A well-known example of this class of compounds is Brigl's anhydride, prepared more than 70 years ago.[1] Their high reactivity is attributed to the strained epoxide ring which is also part of an acetal. Recently, a straightforward route to 1,2-anhydrosugars was developed by Danishefsky, via expoxidation of glycals with dimethyldioxirane.[2a] He has also made extensive use of them in oligosaccharide synthesis.[2] However, comparatively little attention has been bestowed on 1,2-aziridino and 1,2-cyclopropanated sugars. Descotes[3] showed that a 1,2-aziridino sugar is the intermediate in the conversion of a glycosylamine derivative to a 2-aminoglycoside. Later Danishefsky exploited this concept by employing sulfonamidoglycosylation of glycals for rapid assembly of modified 2-amino-2-deoxy oligosaccharides.[4] In 1967, Brimacombe and co-workers described the synthesis of 3,4,6-tri-*O*-methyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-D-*gulo*-hexitol by addition of dichlorocarbene to trimethylglucal followed by dechlorination of the adduct with $LiAlH_4$.[5] The high reactivity of cyclopropanes and the absence of further work in this area prompted us to study the synthesis and reactions of 1,2-cyclopropanated sugars. A preliminary communication has appeared.[6] In this paper, we present a detailed account of our results. In the interim period, Fraser−Reid and Hoberg published preliminary accounts of their work on 1,2-cyclopropanated sugars and Heathcock reported a facile synthesis of 3,4,6-tri-*O*-benzyl-2-*C*-methyl-D-glucal from **17**.[7]

The unusual bonding and strain present in cyclopropanes as well as their ability to interact with adjacent *π*-electron systems and *p*-electron centers, enables them to undergo selective transformations. The chemical resemblance of cyclopropanes to that of double bonds[8] makes possible hydrogenation, halogenation, and acid and electrophilic additions accompanied by concomitant ring cleavage. In fact, the utility of such building blocks for organic synthesis has been well recognized.[9] Among the many applications of cyclopropane derivatives in organic synthesis are solvolytic one-carbon homologation, synthesis of allenes from double bonds *via* dihalocyclopropanes, solvolytic ring opening of cyclopropyl carbinols, ring enlargement (to five-membered rings) of vinyl cyclopropanes, and Cope rearrangement of *cis*-divinylic cyclopropanes for either synthesis or annelation of seven-membered rings.

Our interest in 1,2-cyclopropanated sugars, as shown in path A, Scheme 1, arose from the possibility that the solvolytic ring enlargement of dihalocyclopropanes would yield chiral oxepins, which, either alone or fused with other rings, are found in several complex natural products. However, there is a paucity of general methods for



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(1) Brigl, P. *Z. Physiol. Chem.* **1922**, *122*, 257.

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(3) (a) Lafont, D.; Descotes, G. *Carbohydr. Res.* **1987**, *166*, 195. (b) Lafont, D.; Descotes, G. *Carbohydr. Res.* **1988**, *175*, 35.

(4) (a) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 5811. (b) Park, T. K.; Kim, I. J.; Danishefsky, S. J. *Tetrahedron Lett.* **1995**, *36*, 9089. (c) Kim, I. J.; Park, T. K.; Hu, S.; Abrampah, K.; Zhang, S.; Livingston, P. O.; Danishefsky, S. J. *J. Org. Chem.* **1995**, *60*, 7716 (and references cited therein).

(5) Brimacombe, J. S.; Evans, M. E.; Forbes, E. J.; Foster, A. B.; Webber, J. M. *Carbohydr. Res.* **1967**, *4*, 239.

(6) Murali, R.; Ramana, C. V.; Nagarajan, M. *J. Chem. Soc., Chem. Commun.* **1995**, 217.

(7) (a) Hoberg, J. O.; Bozell, J. J. *Tetrahedron Lett.* **1995**, *36*, 6831. (b) Hoberg, J. O.; Claffey, D. J. *Tetrahedron Lett.* **1996**, *37*, 2533. (c) Henry, K. J., Jr.; Fraser-Reid, B. *Tetrahedron Lett.* **1995**, *36*, 8901. (d) Timmers, C. M.; Leeuwenburgh, M. A.; Verheijen, J. C; van der Marel, G. A.; van Boom, J. H. *Tetrahedron: Asymmetry* **1996**, *7*, 49. (e) Scott, R. W.; Heathcock, C. H. *Carbohydr. Res.* **1996**, *291*, 205. (f) Recently Danishefsky has used the glycal cyclopropane solvolysis strategy for the introduction of the *gem*-dimethyl group. Bertinato, P.; Sorensen, E. J.; Meng, D.; Danishefsky, S. J. *J. Org. Chem.* **1996**, *61*, 8000.

(8) de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 809 and references cited therein.

(9) For recent reviews covering this area, see: (a) Rappoport, Z. *The Chemistry of the Cyclopropyl Group*; Wiley-Interscience, New York, 1987. (b) de Meijere, A.; Wessjohann, L. *Synlett* **1990**, 20. (c) Wong, H. N. C. In *Rodds Chemistry of Carbon Compounds Vol II*^{a}/*II*^{b}, Chapter 2; Sainsbury, M., Ed.; Elsevier Science Publishers B.V.: Amsterdam, 1992, and references cited therein. (d) Nair, V. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. E., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, Chapter 4.7, p 999.

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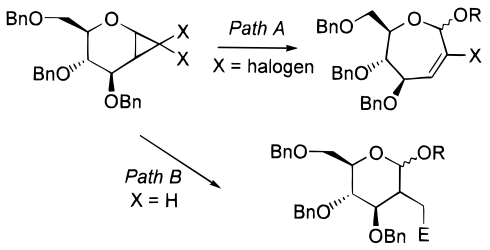
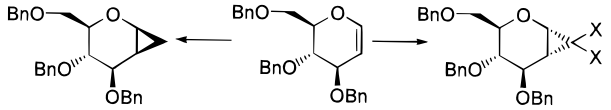
Scheme 1



Scheme 2



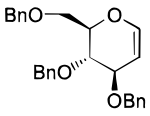
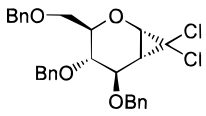
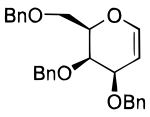
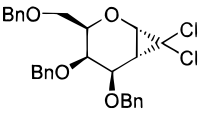
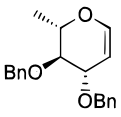
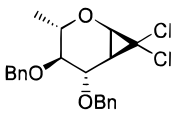
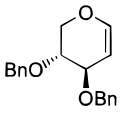
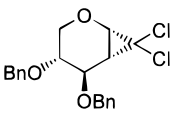
the synthesis of functionalized oxepanes/oxepins[10] and there are very few reports on the synthesis of chiral oxepins.[11] Another aspect of our interest in 1,2-cyclopropanated sugars is their potential ability to undergo, in presence of a protic solvent, an electrophilic ring opening[12] assisted by the pyranose oxygen to furnish a 2-deoxy-2-C-branched chain glycoside with defined C-2 stereochemistry, inherently present in the cyclopropane (Scheme 1, path B). A similar strategy is known with 3,4-dihydro-2*H*-pyran;[13] with glycals the products not only reveal the stereo- and regioselectivtiy aspects but also yield synthetically important intermediates.

In this context, we envisioned that a convenient face selective cyclopropanation of appropriately protected 1,2-unsaturated sugars or glycals is possible on the basis of the directing effect of the C-3 substituent. As shown in Scheme 2, the steric hindrance associated with the C-3 benzyloxy group is expected to direct a bulky dihalocarbene to the less hindered α-face of 3,4,6-tri-*O*-benzyl-D-glucal as reported earlier, by Brimacombe,[5] whereas the same C-3 benzyloxy group, by coordinating with zinc would result in a *β*-cyclopropanation under Simmons–Smith[14] conditions.

Results and Discussion

Gross and co-workers added dihalocarbenes generated by a phase transfer catalyzed procedure to unsaturated sugars.[15] We adopted a similar methodology with glycals. Thus, treatment of 3,4,6-tri-*O*-benzyl-D-glucal (**1**) dissolved in chloroform, with 50% aqueous sodium hydroxide in the presence of a catalytic amount of triethylbenzylammonium chloride, afforded the corresponding dichloro adduct **5** in 84% yield. This procedure was extended to 3,4,6-tri-*O*-benzyl-D-galactal (**2**), 3,4-di-*O*-benzyl-L-rhamnal (**3**), and 3,4-di-*O*-benzyl-D-xylal (**4**). All the glycal derivatives **1**–**4** gave single adducts with dichlorocarbene. The individual results are tabulated in Table 1.

Table 1

Entry	Substrate	Time	Product	Yield %
1	 **1**	4h	 **5**	84
2	 **2**	24h	 **6**	92
3	 **3**	18h	 **7**	95
4	 **4**	18h	 **8**	55

When the reaction was performed replacing chloroform by bromoform under otherwise identical conditions, no product could be isolated. The reaction mixture turned black within a few minutes and also became very viscous. Decreasing the concentration of sodium hydroxide solution did not offer any useful results. This problem was overcome by employing a large excess of potassium fluoride and smaller amounts of alkali.[16] Under these conditions, the addition of dibromocarbene took place cleanly and the dibromocyclopropanes were obtained in good yields. Barring 3,4-di-*O*-benzyl-L-rhamnal (**3**) which gave two adducts **11** and **12** in a 7:1 ratio, the other glycals gave only single adducts. These results are presented in Table 2.

We established the stereochemistry of the products of addition of dihalocarbenes to glycals **1**, **2**, **3**, and **4** by ^{1}H NMR spectroscopy. The C-2 hydrogen, in all the adducts, resonated around 2.0 ppm and appeared as a doublet of doublets with the sole of exception of **12** in which it was an apparent triplet. The four-line pattern of the C-2 hydrogen had coupling constants around 8 and 4 Hz. The larger value was assigned to $J_{1,2}$ coupling as evidenced from the H-1 signal (a doublet with 8 Hz coupling constant). The smaller value of the coupling between C-2 and C-3 protons suggests a quasi axial–equatorial arrangement. In adduct **12**, the H-2 proton appeared as an apparent triplet with a coupling constant of 8 Hz. This is possible only if the concerned protons H-1, H-2, and H-3 are all on the same face of the molecule. Therefore,

(10) (a) Nakata, T.; Nomura, S.; Matsukura, H. *Tetrahedron Lett.* **1996**, *37*, 213. (b) Palazón, J. M.; Martín, V. S. *Tetrahedron Lett.* **1995**, *36*, 3549. (c) Nicolaou, K. C.; Theodorakis, E. A.; Rutges, F. P. J. T.; Tiebes, J.; Sato, M.; Untersteller, D.; Xiao, X.-Y. *J. Am. Chem. Soc.* **1995**, *117*, 1171. (d) Hishiyama, O. H.; Hirama, S. O. T. *Synlett* **1995**, 1252. (e) Kadota, I.; Matsukawa, Y.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1993**, 1638. (f) Ravelo, J. L.; Regueiro, A.; Martín, J. D. *Tetrahedron Lett.* **1992**, *33*, 3389. (g) Molander G. A.; Andrews, S. W. *J. Org. Chem.* **1989**, *54*, 3114.

(11) (a) Nicolaou, K. C.; Prasad, C. V. C.; Somers P. K.; Hwang, C. K. *J. Am. Chem. Soc.* **1989**, *111*, 5330 and 5335. (b) Moody, C. J.; Sie, E.-R. H. B.; Kulagowski, J. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 501. (c) Kadata, I.; Gevorgyan, V.; Yamada V.; Yamamoto, Y. *Synlett* **1991**, 823. (d) Soler, M. A.; Palazón J. M.; Martín, V. S. *Tetrahedron Lett.* **1993**, *34*, 5471. (e) Datta, S.; Chattopadhyay, P.; Mukhopadhyay, R.; Bhattacharjya, A. *Tetrahedron Lett.* **1993**, *34*, 3585. (f) Berger, D.; Overman, L. E.; Renhowe, P. A. *J. Am. Chem. Soc.* **1993**, *115*, 9305.

(12) Reissig, H. U. In *Topics in Current Chemistry 144* (Small Ring Compounds in Organic Synthesis); deMeijere, A., Ed.; Springer-Verlag: Berlin 1988; p 73 and references cited therein.

(13) Skattebøl, L. *J. Org. Chem.* **1970**, *35*, 3200.

(14) (a) Chan, J. H.; Rickborn, B. *J. Am. Chem. Soc.* **1968**, *90*, 6406. (b) Poulter, C. D.; Friedrich, E. C.; Winstein, S. *J. Am. Chem. Soc.* **1969**, *91*, 6892.

(15) Duchaussoy, P.; Cesare, P. D.; Gross, B. *Synthesis* **1979**, 198.

(16) Fedorynski M.; Makosza, M. *J. Organomet. Chem.* **1973**, *51*, 6406.

Table 2

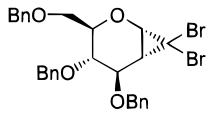
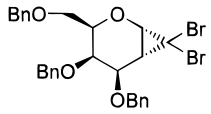
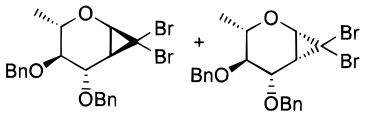
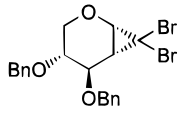
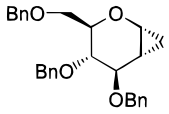
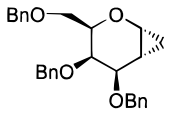
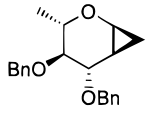
Entry	Substrate	Product(s)	Yield %
1	**1**	 **9**	84
2	**2**	 **10**	71
3	**3**	 **11** (7 : 1) **12**	81
4	**4**	 **13**	64

Table 3

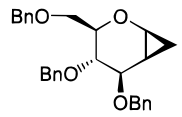
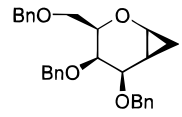
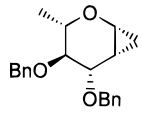
Entry	Substrate	Time	Product(s)	Yield %
1	**5**	2h	 **14**	78
2	**6**	8h	 **15**	71
3	**7**	4h	 **16**	67

it is reasonable to assume that $J_{2,3}$ is around 4 Hz when H-2 and H-3 are *trans* to one another and is around 8 Hz when they are *cis* to one another. This is in keeping with the report that in cyclopropanes[17] the 1,2-*cis* couplings are larger than the 1,2-*trans* couplings. Thus, the products of dihalocyclopropanation are either exclusively or predominantly formed on the face of the double bond away from the C-3 substituent, as expected on steric grounds.

Dehalogenation of these adducts with LAH in THF was next attempted. Our studies showed that the reductions of dichlorocyclopropanes were clean and economical compared to their dibromo counterparts. Table 3 summarizes the yields of these dehalogenation reactions.

In the ^{1}H NMR spectrum, the multicipity of the H-2 signal increased and also moved further upfield compared to both dichloro- and dibromocyclopropanes and lay centered at 0.9 ppm. The additional multiplets at 0.7 ppm integrating for two protons were assigned to the protons attached to C-7, thus confirming the complete reduction of dichloro adducts.

Table 4

Entry	Substrate	Product	Yield %
1	**1**	 **17**	89
2	**2**	 **18**	80
3	**3**	 **19**	87

In order to examine the validity of our assumption regarding the synthesis of the other diastereomeric cyclopropanes, we attempted to cyclopropanate glycals under Simmons−Smith conditions, where the reaction is known to proceed via an oxygen-directed pathway with allylic alcohols and ethers to yield products with the cyclopropane ring *syn* to the coordinating oxygen. The Friedrich-modified version of the Simmons−Smith reaction,[18] using acetyl chloride as an activator, was found to be convenient, and single diastereomers were obtained with glycals **1**−**3**. These results are summarized in Table 4.

It was immediately obvious from their ^{1}H NMR spectra that these cyclopropanes were different from the ones obtained by LAH reduction of the corresponding dichloro adducts **5**−**7**. The C-3 hydrogen, in all cases, appeared as an apparent triplet, suggesting that $J_{2,3}$ and $J_{3,4}$ are nearly equal. It is known in the case of glucose and rhamnose that the C-3 and C-4 hydrogens, which are *trans* diaxial to one another, have large couplings. This, taken together with the larger value of *cis* $J_{2,3}$ makes it clear that the products obtained have the stereochemistry as shown above (Table 4). Similar results have also been reported by Hoberg et al.[7a]

After identification of simple procedures for both diastereomers of 1,2-cyclopropanated sugars, efforts toward their utility in the synthesis of chiral oxepin derivatives through solvolytic ring expansion and functionalized 2-deoxy 2-branched chain sugars by electrophilic ring openings were initiated.

As shown in Scheme 3, we anticipated that the cyclopropyl cation resulting from the loss of *endo* halogen[19] would rearrange in such a way that the positive charge of the resultant allyl cation is placed at C-1, due to its stabilization by the adjacent oxygen atom. Capture by a nucleophilic solvent like methanol would then provide a seven-membered glycoside.

(17) (a) Graham, J. D.; Rogers, M. T. *J. Am. Chem. Soc.* **1962**, *84*, 2249. (b) Williamson, K. L.; Lanford, C. A.; Nicholson, C. R. *J. Am. Chem. Soc.* **1964**, *86*, 762. (c) Wiberg, K. B.; Barth, D. E.; Schertler, P. H. *J. Org. Chem.* **1973**, *38*, 378.

(18) Friedrich, E. C.; Lewis, E. J. *J. Org. Chem.* **1990**, *55*, 6892.

(19) (a) Skell, P. S; Sandler, S. R. *J. Am. Chem. Soc.* **1958**, *80*, 2024. (b) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

Scheme 3

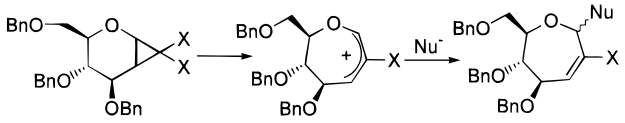
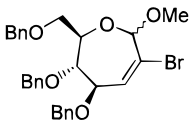
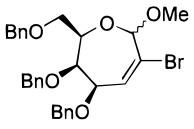
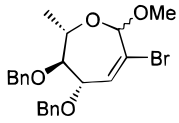


Table 5

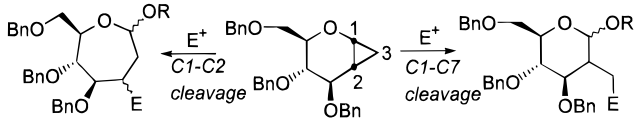
Entry	Substrate	Product	Yield %
1	**9**	 **20**	67
2	**10**	 **21**	55
3	**11**	 **22**	70

Solvolysis of the dichloro- and dibromocyclopropanes was attempted initially with silver ion and Lewis acid catalysis. No reaction was observed under mild conditions (stirring at room temperature in AcOH). Under more vigorous conditions (AcOH or 1,4-dioxane, reflux temperatures) the starting material was completely destroyed. However, when boiled with excess K_2CO_3 in methanol,[20] adducts **9**, **10**, and **11** underwent smooth solvolysis providing ring-expanded oxepins **20**−**22** as anomeric mixtures in good yields (Table 5). The anomers of **20** could be separated by column chromatography while those of **21** and **22** were inseparable. The product identities were established by extensive NMR studies as well as by analytical methods. The presence of narrow doublets at δ 5.17 and 6.80 in the ^{1}H NMR spectrum of **20** (major) confirmed that ring expansion had indeed taken place. These signals correspond to anomeric and olefinic protons (H-1 and H-3), respectively, as established by 2D NMR studies (COSY and HETCOR). The minor anomer of **20** also showed similar spectral features. Although the anomers of **21** and **22** were inseparable, their ^{1}H and ^{13}C NMR spectra indicated that they also have an oxepin skeleton.

As shown in Scheme 4, in the electrophilic ring opening of a 1,2-cyclopropanated sugar, although the competitive formation of a septanoside is possible, it is less likely due to preferential edge selection of the C1−C7 bond by the incoming electrophile on the basis of steric considerations.

In this context, the α- and β-cyclopropanes **14** and **17**, respectively, derived from 3,4,6-tri-*O*-benzyl-D-glucal (**1**) were chosen to investigate the ring opening. Our initial attempts using a proton as an electrophile to carry out the ring opening of cyclopropanes **14** and **17** were unsuccessful with hydrochloric acid, acetic acid, and perchloric acid as the proton source (all the reactions

Scheme 4



were carried with 1.5 equiv of acid in MeOH at rt). Later when the reaction was performed in refluxing methanol containing 1.5 equiv of HCl for 15 days, we were able to obtain about 40% conversion (70% yield) in case of the α-cyclopropane **14** giving methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-methyl-β-D-glucopyranoside (**23**) exclusively. Under similar conditions β-cyclopropane **17** was unreactive and increasing the amount of HCl caused its decomposition.

When α-cyclopropane **14** was treated with *N*-bromosuccinimide in methanol (8 h), it gave rise to two ring-opened products **24** and **25** (α- and β-anomers) in a 20:80 ratio (72%). Under similar conditions, the β-cyclopropane **17** reacted at a much slower rate (24 h) but with higher selectivity giving only the α-anomer **26** (62%). When *N*-iodosuccinimide was used as a source of I^+ (in MeOH) α-cyclopropane **14** reacted within 12 h giving both α- and β-anomers (**27** and **28**) in a 20:80 ratio, whereas the reaction with β-cyclopropane **17** gave only 10% conversion. When *N*-iodosuccinimide was replaced by iodonium di(*s*-collidine) perchlorate, the reaction with α-cyclopropane **14** was over within 6 h giving both α- and β-anomers (**27** and **28**, 15:85) in 86% yield. Again, the reaction was incomplete with β-cyclopropane **17** (36 h, 45% conversion) giving only the α-anomer (**29**) in about 70% yield.

All the above products were readily characterized from their spectral and analytical data. The ^{13}C NMR spectra of all three diastereomeric bromo and iodo derivatives showed only 11 lines in addition to the aromatic signals. The high-field signals around 31 and 47 ppm in **24** and **25** were assigned to C_7 and C_2, respectively. The DEPT-135 spectra of these substrates showed that the carbon attached to bromine or iodine was a methylene and not a methine, thus establishing the preference for ring opening over ring expansion. The larger coupling constant (J = 8.5 Hz) for the anomeric proton of **25**, when compared to **24** (J = 2.6 Hz) and also that of **28** (J = 8.6 Hz) to **27** (J = 3 Hz), shows that **25** and **28** are β-anomers.[21] In the ^{13}C NMR spectra, C_1 of **24** resonates at 102.3 ppm and that of **25** at 99.23 ppm, once again confirming the anomeric assignment.[21] Finally, the optical rotations of these anomers were also found to be in accord with Hudson's rule.[22]

Encouraged by this, and to further examine the generality of this method, the ring-opening reactions of **14** and **17** were carried out in different alcohols and the results are summarized in the Tables 6 and 7. As can be seen from the alcohols chosen, the glycosides formed from them can be hydrolyzed to the free sugars under acidic or neutral conditions, imparting flexibility to the method, if needed.

The reaction of cyclopropane **14** in 2-chloroethanol with NBS as an activator was complete in 4 h, giving **30** (α-anomer) and **31** (β-anomer) in a 35:65 ratio, whereas cyclopropane **17** took 12 h to go to completion yielding only the α-anomer **32**. In 2,2,2-trichloroethanol, the

(20) Banwell, M. G.; Corbett, M.; Gulbis, J.; Mackay, M. F.; Reum, M. E. *J. Chem. Soc., Perkin Trans. 1* **1993**, 945.

(21) Bundle, D. R.; Lemieux, R. U. *Methods Carbohydr. Chem.* **1976**, *7*, 79.

(22) Hudson, C. S. *J. Am. Chem. Soc.* **1909**, *31*, 66.

Table 6

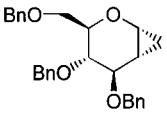
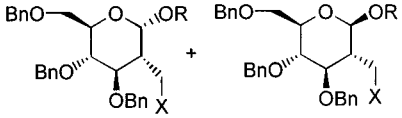
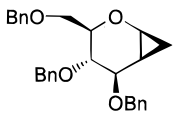
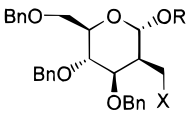
Entry	Substrate	Reagent\solvent\time	Product(s)	Yield %
	 **14**			
1		HCl\MeOH\15d	R = CH_3, X = H **23**	70
2		NBS\MeOH\8h	R = CH_3, X = Br **24** (20 : 80) **25**	72
3		NIS\MeOH\12h	R = CH_3, X = I **27** (20 : 80) **28**	86
4		IDCP\MeOH\6h	R = CH_3, X = I **27** (15 :85) **28**	86
5		NBS\$ClCH_2CH_2OH$\4h	R = CH_2CH_2Cl, X = Br **30** (35 :65) **31**	91
6		NBS\Cl_3CCH_2OH\1h	R = CH_2CCl_3, X = Br **33** (50 :50) **34**	89
7		NBS\$PhCH_2OH$\36h	R = CH_2Ph, X =Br **36** (35 : 65) **37**	91
8		NBS\H_2O\8h	R = H, X = Br **39**	66

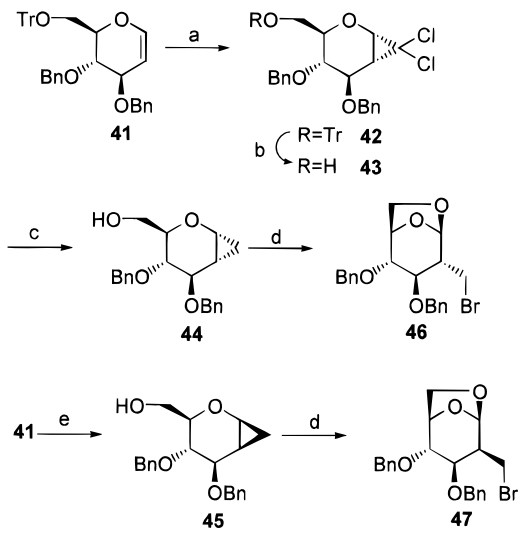
Table 7

Entry	Substrate	Reagent\solvent\time	Product	Yield %
	 **17**			
1		NBS\MeOH\24h	R = CH_3, X = Br **26**	62
2		IDCP\MeOH\36h	R = CH_3, X = I **29**	70
3		NBS\$ClCH_2CH_2OH$\12h	R = CH_2CH_2Cl, X = Br **32**	71
4		NBS\Cl_3CCH_2OH\8h	R = CH_2CCl_3, X = Br **35**	72
5		NBS\$PhCH_2OH$\4d	R = CH_2Ph, X =Br **38**	40
6		NBS\H_2O\8h	R = H, X = Br **40**	61

reaction was fast with α-cyclopropane **14** (1 h, **33** and **34** were obtained in 1:1 ratio) and took nearly 8 h with β-cyclopropane **17**, yielding only α-anomer **35**. Surprisingly, the opening of **14** with benzyl alcohol was sluggish, taking 36 h. The corresponding α- and β-anomers **36** and **37** were obtained in a 35:65 ratio. Under similar conditions, even after 4 days, only 20% conversion (40% yield) was observed with **17**. This clearly indicates the higher reactivity of α-cyclopropane **14** over β-cyclopropane **17**. The openings of α- and β-cyclopropanes with water as nucleophile were carried out in a 1:2 mixture of water and 1,4-dioxane. These reactions did not show much difference in reactivity. In all the above cases, the α- and β-anomers of the glucopyranoside products from **14** were easily separable by chromatography and the ratios determined from ^1H NMR spectra matched with those obtained from the separated products.

These experiments clearly reveal that the reactions with β-cyclopropane **17** are slower and display higher anomeric selectivity when compared to those of α-cyclopropane **14**. This is interesting because the ring openings of α-cyclopropane **14**, with all nucleophiles, give both

Scheme 5[a]



[a] Reagents and Conditions: (a) $CHCl_3$, 50% aqueous NaOH, 24 h; (b) HCO_2H:ether (1:2), 1 h; (c) LAH, THF, 24 h; (d) NBS, CH_3CN, 4 Å molecular sieves, 5 or 36 h; (e) Zn-CuCl, AcCl, CH_2I_2, ether, reflux, 2 h.

inversion and retention, but those of β-cyclopropane **17** proceed with complete inversion. The greater reactivity of cyclopropane **14** when compared to cyclopropane **17** can be accounted for by the increased steric hindrance to the approach of the electrophile to the three-membered ring in the latter compound. Exclusive formation of the α-glycoside from cyclopropane **17** is then a consequence of an elctrophile-activated S_N2 type ring opening of the cyclopropane by the external nucleophile. With the α-cyclopropane **14**, the β-glycoside is formed predominantly by the same route, while simultaneous formation of the α-anomer in this case points to the possible involvement of an S_N1 pathway. It may be noted in both instances that the α-glycoside is the one favored by the anomeric effect.

To better understand the processes taking place, we prepared the α- and β-cyclopropanes **44** and **45** with a free 6-OH group as outlined below. 3,4-Di-*O*-benzyl-6-*O*-trityl-D-glucal (**41**)[23b] on dichlorocarbene addition followed by detritylation using 2:1 ether/formic acid[23c] gave **43**, which on dehalogenation with LAH in THF yielded the corresponding α-cyclopropane **44** in 45% overall yield. Suprisingly, under Simmon−Smith cyclopropanation conditions, **41** directly yielded the required 6-OH β-cyclopropane **45** in 70% yield (Scheme 5).

The ring opening of these cyclopropanes with an electrophile in an aprotic solvent will result in the intramolecular attack of 6-OH at C-1, giving a levoglycosan derivative. This should be particularly favorable for the cyclopropane **44**, where the 6-OH group and cyclopropane are well set to react in an S_N2 type process. In cyclopropane **45** the S_N2 type process can be ruled out, but formation of a levoglycosan derivative is possible by an S_N1 pathway.

The intramolecular ring opening of α-cyclopropane **44** in acetonitrile with NBS as an activator in the presence of 4 Å molecular sieves took place smoothly within 5 h giving the levoglucosan derivative **46** in 71% yield. On the other hand, under similar conditions, the reaction with β-cyclopropane **45** was incomplete and yielded the levomannosan **47** derivative in 35% yield after 36 h. These results clearly indicate that the lower reactivity of the β-cyclopropane **45**, when compared to **44**, is due to steric hindrance to the approach of the electrophile. While α-cyclopropane **44** reacts clearly and rapidly by an S_N2 type process to give the levoglucosan derivative **46** in 71% yield, the β-cyclopropane **45**, with no such option available, forms the levomannosan derivative **47** in a much lower yield, probably through an S_N1 mechanism.

In conclusion, we have developed convenient procedures for the synthesis of 1,2-cyclopropanted sugars in both diastereomeric forms. These cyclopropanated sugars can be readily converted to chiral oxepin derivatives as well as to 2-C-branched sugars of defined stereochemistry. Applications of these results to the synthesis of oxepane-containing compounds and branched disaccharides are in progress.

Experimental Section

Materials. Unless specified otherwise, reagent grade reactants and solvents were used as received from chemical suppliers. Solvents were dried by appropriate methods wherever needed. Glycals **1**−**4** and **41** were prepared according to available literature methods.[23a,b] All organic extracts were dried over anhydrous magnesium sulfate. Acme silica gel 100−200 mesh was used for column chromatography.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dichloromethylene)-D-*glycero*-D-*gulo*-hexitol (5). Aqueous sodium hydroxide (5.0 g in 10 mL) was added to a vigorously stirred solution of tribenzyl-D-glucal (**1**) (1.60 g, 3.84 mmol) in chloroform (10 mL) containing benzyltriethylammonium chloride (20 mg). The reaction mixture was stirred at 35 °C for 4 h and then diluted with water (25 mL) and extracted with dichloromethane. The combined extracts were dried and concentrated, and the residue was purified by chromatography to furnish **5** (1.60 g, 84%) as a colorless solid (hexane): mp = 62−63 °C; $[\alpha]^{25}_D = +78$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.40−7.25 (m, 15H), 4.92−4.40 (m, 6H), 3.91−3.87 (d, J = 7.9 Hz, 1H), 3.81−3.74 (m, 3H), 3.55−3.53 (m, 2H), 1.81−1.75 (dd, J = 4.4, 7.9 Hz, 1H); ^{13}C NMR δ 138.34, 138.09, 128.51, 128.43, 128.20, 127.81, 127.18, 127.73, 80.01, 77.53, 75.33, 74.63, 73.44, 71.96, 70.30, 61.62, 59.05, 34.41. Anal. Calcd for $C_{28}H_{28}Cl_2O_4$: C, 67.33; H, 5.65. Found: C, 67.13; H, 5.66.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dichloromethylene)-D-*glycero*-L-*manno*-hexitol (6). Reaction of 3,4,6-tri-*O*-benzyl-D-galactal (**2**) under the same conditions as **1** for 24 h gave **6** in 92% yield: syrup; $[\alpha]^{25}_D = +13.5$ (*c* 1.2, $CHCl_3$); ^{1}H NMR δ 7.38−7.25 (m, 15H) 4.96−4.39 (m, 6H), 3.91−3.79 (m, 3H), 3.64−3.52 (m, 3H), 1.99−1.93 (dd, J = 8.9, 4.2 Hz, 1H); ^{13}C NMR δ 138.68, 138.0, 137.65, 128.63, 128.50, 128.38, 127.98, 127.86, 127.72, 78.05, 75.32, 74.58, 73.55, 71.70, 71.21, 69.16, 61.81, 58.69, 31.09. Anal. Calcd for $C_{28}H_{28}Cl_2O_4$: C, 67.33; H, 5.65. Found: C, 67.06; H, 5.67.

3,4-Di-*O*-benzyl-1,5-anhydro-2,6-dideoxy-1,2-*C*-(dichloromethylene)-L-*glycero*-L-*gulo*-hexitol (7). Under identical conditions 3,4-di-*O*-benzyl-L-rhamnal (**3**) gave **7** in 95% yield after a reaction time of 18 h: colorless syrup, $[\alpha]^{25}_D = -40$ (*c* 1.2, $CHCl_3$); ^{1}H NMR δ 7.32−7.25 (m, 10H), 4.94−4.57 (m, 4H), 3.95−3.72 (m, 3H), 3.29 (t, J = 7.4 Hz, 1H), 1.84−1.78 (dd, J = 8.2, 4.2 Hz, 1H), 1.30−1.27 (d, J = 6.4 Hz, 3H); ^{13}C NMR δ 138.33, 137.73, 128.52, 128.36, 127.99, 127.92, 127.75, 81.07, 77.04, 76.06, 74.49, 71.99, 61.42, 57.86, 33.92, 19.84. Anal. Calcd for $C_{21}H_{22}Cl_2O_3$: C, 64.13; H, 5.64. Found: C, 63.92; H, 5.62.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dichloromethylene)-D-*gulo*-pentitol (8). Aqueous sodium hydroxide (500 mg in 1 mL) was added to a vigorously stirred solution of 3,4-di-*O*-benzyl-D-xylal (**4**) (45 mg, 0.15 mmol) in chloroform (1 mL) containing benzyltriethylammonium chloride (5 mg). The biphasic reaction mixture was stirred at room temperature

(23) (a) Chmielewski, M.; Fokt, I.; Grodner, J.; Grynkiewicz, G.; Szeja, W. *J. Carbohydr. Chem.* **1989**, *8*, 735. (b) Esswein, A.; Rembold, H.; Schmidt, R. R. *Carbohydr. Res.* **1990**, *200*, 287. (c) Bessodes, M.; Komiotis, D.; Antonakis, K. *Tetrahedron Lett.* **1986**, *27*, 579.

for 18 h, diluted with water (10 mL), and worked up. **8** was obtained as a syrup after chromatographic purification (31 mg, 55%): $[\alpha]^{25}_D = +17.3$ (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 7.36−7.20 (m, 10H), 4.91−4.59 (m, 4H), 3.99−3.64 (m, 5H), 1.88−1.77 (dd, *J* = 7.9, 3.8 Hz, 1H); ^{13}C NMR δ 138.20, 137.64, 128.60, 128.46, 128.01, 127.78, 76.04, 75.39, 72.83, 72.02, 68.98, 60.87, 59.86, 33.08. Anal. Calcd for $C_{20}H_{20}Cl_2O_3$: C, 63.33; H, 5.32. Found: C, 63.25; H, 5.29.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dibromomethylene)-D-*glycero*-D-*gulo*-hexitol (9). A solution of sodium hydroxide (2.0 g) and potassium fluoride (15.0 g) in water (15 mL) was added to a vigorously stirred solution of **1** (2.50 g, 6 mmol) in bromoform (10 mL) containing benzyltriethylammonium chloride (20 mg). The biphasic mixture was stirred for 2 days at room temperature and then diluted with water (40 mL) and extracted with ether. The combined ether extracts were washed with brine, dried, and concentrated. The residue was purified by chromatography followed by crystallization from methanol−ethyl acetate to give 2.80 g (79%) of **9**: mp = 58−60 °C; $[\alpha]^{25}_D = +72$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.40−7.25 (m, 15H), 4.85−4.40 (m, 6H), 3.98−3.94 (d, *J* = 7.8 Hz, 1H), 3.91−3.68 (m, 3H), 3.56−3.53 (m, 2H), 1.91−1.85 (dd, *J* = 4.56, 7.8 Hz, 1H); ^{13}C NMR δ 138.18, 137.89, 137.71, 128.36, 128.24, 128.07, 127.77, 127.59, 80.06, 79.71, 74.83, 74.30, 73.06, 71.53, 70.0, 59.06, 35.0, 34.06. Anal. Calcd for $C_{28}H_{28}Br_2O_4$: C, 57.16; H, 4.80. Found: C, 57.0; H, 4.73.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dibromomethylene)-D-*glycero*-L-*manno*-hexitol (10). Reaction of 3,4,6-tri-*O*-benzyl-D-galactal (**2**) under the same conditions as **1** for 48 h gave **6** in 71% yield: pale yellow syrup; $[\alpha]^{25}_D = +20$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.38−7.25 (m, 15H), 4.97−4.44 (m, 6H), 3.99−3.95 (d, *J* = 8.8 Hz, 1H), 3.90−3.87 (m, 2H), 3.61−3.51 (m, 3H), 2.10−2.04 (dd, *J* = 8.8, 4.0 Hz, 1H); ^{13}C NMR δ 138.62, 137.93, 137.63, 129.23, 128.61, 128.47, 128.35, 127.85, 127.69, 78.50, 77.70, 74.61, 73.52, 71.89, 71.13, 69.08, 59.13, 35.15, 32.16; HRMS calcd for $C_{28}H_{28}Br_2O_4$ $(M - H)^+$ 589.0415, found 589.0414.

Under identical conditions, 3,4-di-*O*-benzyl-L-rhamnal (**3**) gave **11** and **12** in 81% yield.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dibromomethylene)-L-*glycero*-L-*gulo*-hexitol (11): 69%, syrup; $[\alpha]^{25}_D = -49$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.43−7.26 (m, 10H), 4.95−4.60 (m, 4H), 3.98−3.82 (m, 2H), 3.74−3.66 (dd, *J* = 9.1, 4.3 Hz, 1H), 3.30 (dd, *J* = 9.1, 7.3 Hz, 1H), 1.93−1.87 (dd, *J* = 7.9, 4.2 Hz, 1H), 1.31−1.27 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR δ 138.34, 137.86, 128.60, 128.43, 128.08, 127.97, 127.83, 81.13, 79.66, 76.66, 74.58, 72.02, 58.33, 35.11, 33.73, 20.06; HRMS calcd for $C_{21}H_{22}Br_2O_3$ $(M - H)^+$ 480.9838, found 480.9842.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dibromomethylene)-L-*glycero*-L-*talo*-hexitol (12): 12%, white solid; mp = 104−106 °C (MeOH); $[\alpha]^{25}_D = +48$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.36−7.26 (m, 10H), 4.96−4.85 (dd, *J* = 9.8, 11.7 Hz, 2H), 4.73−4.59 (dd, *J* = 11.7, 17.7 Hz, 2H), 4.20−4.12 (dd, *J* = 8.2, 7.2, 1H), 4.02−3.99 (d, *J* = 7.9 Hz, 1H), 3.62−3.52 (dd, *J* = 7.2, 9.9 Hz, 1H), 3.49 3.36 (m, 1H), 2.55−2.45 (t, *J* = 8 Hz, 1H), 1.32−1.29 (d, *J* = 6 Hz, 3H); ^{13}C NMR δ 138.38, 137.95, 128.65, 128.42, 128.13, 128.01, 127.79, 81.43, 78.46, 74.95, 74.86, 71.03, 62.68, 33.92, 31.19, 17.61. Anal. Calcd for $C_{21}H_{22}Br_2O_3$: C, 52.30; H, 4.60. Found: C, 52.30; H, 4.59.

3,4-Di-*O*-benzyl-2-deoxy-1,2-*C*-(dibromomethylene)-D-*gulo*-pentitol (13): 64%, pale yellow syrup; $[\alpha]^{25}_D = +13.7$ (*c* 0.7, $CHCl_3$); ^{1}H NMR δ 7.42−7.26 (m, 10H), 4.90−4.60 (m, 4H), 4.0−3.70 (m, 5H), 1.92−1.86 (dd, *J* = 7.8, 3.8 Hz, 1H); ^{13}C NMR δ 138.24, 137.72, 128.58, 128.46, 128.22, 128.04, 127.78, 78.71, 75.40, 72.91, 71.97, 69.47, 60.37, 34.06, 32.81; mass spectral data *m*/*z* 467 (M − 1), 377, 325, 263, 182, 101, 91.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-D-*gulo*-hexitol (14). To a stirred suspension of lithium aluminum hydride (277 mg, 7.29 mmol) in dry tetrahydrofuran (4 mL) was added a solution of the dichlorocyclopropane **5** (400 mg, 0.80 mmol) in tetrahydrofuran (10 mL). After being stirred for 2 h at room temperature, the reaction mixture was cooled in ice and quenched by careful addition of saturated aqueous sodium sulfate. The salts were filtered and washed several times with hot ethyl acetate. The filtrate was dried and concentrated. The residue on chromatographic purification furnished **14** as a colorless syrup (270 mg, 78%): $[\alpha]^{25}_D = +62$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.37−7.25 (m, 15H), 4.82−4.53 (m, 6H), 3.72−3.55 (m, 6H), 1.0−0.80 (m, 1H), 0.75−0.67 (m, 2H); ^{13}C NMR δ 138.71, 138.55, 138.41, 128.45, 128.0, 127.76, 127.66, 80.17, 77.17, 76.90, 73.51, 73.36, 71.20, 70.21, 49.73, 14.93, 11.60. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 78.0; H, 7.05.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-L-*manno*-hexitol (15). This was obtained in 71% yield from the LAH reduction of dichloro adduct **10** for 8 h: $[\alpha]^{25}_D = +13.6$ (*c* 1.15, $CHCl_3$); ^{1}H-NMR δ 7.35−7.28 (m, 15H), 4.88−4.52 (m, 6H), 3.81−3.52 (m, 6H), 1.28−1.10 (m, 1H), 0.80−0.68 (m 1H), 0.40−0.31 (m, 1H); ^{13}C NMR δ 138.96, 138.71, 138.49, 128.65, 128.42, 128.34, 127.89, 127.58, 127.53, 77.17, 74.98, 73.70, 73.42, 73.35, 71.37, 69.35, 48.93, 14.47, 11.04. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 78.20; H, 7.06.

3,4-Di-*O*-benzyl-1,5-anhydro-2,6-dideoxy-1,2-*C*-methylene-L-*glycero* -L-*gulo*-hexitol (16). On carrying out the LAH reduction on dichlorocyclopropane **7** as mentioned above for 4 h, **16** was obtained as a colorless syrup after chromatography (67%): $[\alpha]^{25}_D = -11$ (*c* 1, $CHCl_3$); ^{1}H-NMR δ 7.36−7.15 (m, 10H), 4.82−4.74 (d, 2H), 4.55−4.48 (m, 2H), 3.69−3.59 (m, 2H), 3.57−3.49 (m, 1H), 3.36−3.17 (t, *J* = 6.6 Hz, 1H), 1.29−1.26 (d, *J* = 6.5 Hz, 3H), 1.05−0.92 (m, 1H), 0.76−0.65 (m, 2H); ^{13}C NMR δ 138.74, 138.57, 128.42, 128.29, 127.96, 127.79, 127.68, 81.83, 79.93, 73.63, 71.99, 71.21, 49.34, 18.91, 14.33, 10.15. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.56; H, 7.50.

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-D-*talo*-hexitol (17). To a stirred suspension of zinc dust (765 mg, 11.7 mmol) and cuprous chloride (250 mg, 2.5 mmol) in dry ether (1 mL) at room temperature was added 1 equiv of diiodomethane. After 5 min, acetyl chloride (20 μL) was added and the mixture was heated for 5 min at 40 °C. A solution of tribenzylglucal **1** (1.10 g, 2.65 mmol) in ether (4 mL) was then added. Five minutes later, an additional 2 equiv of diiodomethane was added and the heating was continued for 90 min. The reaction mixture was diluted with ether and washed with 5% sodium hydroxide solution, brine, and dried. The residue, after solvent evaporation, was purified by chromatography to furnish **17** as a low-melting solid, 1.0 g (89%).

3,4,6-Tri-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-L-*allo*-hexitol (18). The procedure described for **17** was followed. **18** was obtained from 2 as a colorless syrup (80%): $[\alpha]^{25}_D = -73.3$ (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 7.31 (m, 15H), 4.99−4.41 (m, 6H), 4.07−4.01 (t, *J* = 5.5 Hz, 1H), 3.90−3.82 (m, 2H), 3.51−3.45 (m, 3H), 1.60−1.40 (m, 1H), 1.30−1.20 (m, 1H), 0.80−0.60 (m, 1H); ^{13}C NMR δ 138.83, 138.66, 137.91, 128.25, 127.99, 127.93, 127.77, 127.55, 127.28, 76.01, 74.59, 74.24, 73.76, 73.31, 69.54, 69.26, 53.90, 14.13, 12.09. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 77.97; H, 7.10.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-L-*glycero*-L-*talo*-hexitol (19). Using the procedure described for **17**, **19** was obtained from **3** as a colorless syrup (87%): $[\alpha]^{25}_D = +89$ (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 7.32−7.18 (m, 10H), 4.89−4.81 (dd, *J* = 11.6, 5.5 Hz, 2H), 4.65−4.57 (dd, *J* = 11.2, 3.3 Hz, 2H), 4.17−4.11 (t, *J* = 6.9 Hz, 1H), 3.82−3.73 (m, 1H), 3.45−3.30 (m, 1H), 3.08−2.98 (dd, *J* = 9.7, 7.0 Hz, 1H), 1.40−1.27 (m, 1H), 1.23−1.20 (d, *J* = 6.6 Hz, 3H), 0.80−0.75 (m, 2H); ^{13}C NMR δ 138.41, 127.95, 127.86, 127.41, 127.11, 83.06, 78.24, 73.82, 73.63, 69.26, 54.42, 17.51, 15.30, 11.61. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.79; H, 7.48.

Solvolysis Experiments with Dibromocyclopropanes 9, 10, and 11 under Basic Conditions. The reaction mixture containing the dibromocyclopropane (1 equiv) and anhydrous potassium carbonate (6 equiv) in methanol (10 mL/mmol of substrate) was refluxed for 12 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature, diluted with water, and extracted with dichloromethane. The combined organic extracts were dried and concentrated under reduced pressure, and the products were

separated by chromatography. The dibromocyclopropane **9** gave the following products:

Major product of 20: yield 38.4%; $[\alpha]^{25}_D = +69$ (*c* 2, $CHCl_3$); ^{1}H NMR δ 7.34−7.14 (m, 15H, ArH), 6.79 (s, 1H, H-3), 5.17 (s, 1H, H-1), 4.73 (s, 1H, H-4), 4.66−4.25 (m, 6H, OCH_2Ph), 3.72−3.59 (m, 4H, H-5, H-6, H-7, H-7'), 3.45 (s, 3H, OCH_3); ^{13}C NMR δ 138.44, 138.20, 137.78, 137.64 (C-2), 128.37, 128.06, 127.91, 127.73, 127.53, 112.56 (C-3), 98.98 (C-1), 79.42 (C-5), 76.30 (C-4), 73.21 (OCH_2Ph), 71.60 (OCH_2Ph, C-6), 70.86 (OCH_2Ph), 69.73 (C-7) 55.19 (OCH_3). Anal. Calcd for $C_{29}H_{31}BrO_5$: C, 64.56; H, 5.79. Found: C, 64.75; H, 5.84.

Minor product of 20: yield 29.3%; $[\alpha]^{25}_D = +26.7$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.34−7.27 (m, 15H, ArH), 6.80 (s, 1H, H-3), 5.09 (s, 1H, H-1), 4.80−4.50 (m, 7H, OCH_2Ph, H-4), 4.0−3.85 (m, 4H, H-5, H-6, H-7, H-7'), 3.52 (s, 3H, OCH_3); ^{13}C NMR δ 138.46, 138.37, 137.87, 137.10 (C-2), 128.48, 128.41, 128.32, 128.0, 127.79, 127.63, 114.70 (C-3), 101.20 (C-1), 76.11 (C-5), 74.97 (C-6), 74.73 (C-4), 73.35, 72.25, 70.95, 70.65 (C-7), 55.80 (OCH_3). Anal. Calcd for $C_{29}H_{31}BrO_5$: C, 64.56; H, 5.79. Found: C, 64.45; H, 5.75.

Solvolysis of the dibromocyclopropane **10** gave an inseparable mixture of products **21** in 55% yield: ^{1}H NMR δ 7.41−7.32 (m, 15H), 6.67 (s, 1H, H-3), 4.86 (s, 1H, H-1), 4.90−4.70 (m, 8H), 3.79−3.70 (m, 3H), 3.49 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3); ^{13}C NMR δ 138.69, 138.35, 138.27, 138.19, 137.96, 137.16, 137.03, 128.32, 128.17, 128.06, 127.77, 127.63, 127.31, 112.65, 107.53, 101.52, 100.26, 75.95, 74.67, 73.47, 73.39, 73.28, 72.66, 72.23, 71.39, 70.76, 70.69, 68.46, 55.70, 55.56. Anal. Calcd for $C_{29}H_{31}BrO_5$: C, 64.56; H, 5.79. Found: C, 64.52; H, 5.78.

Solvolysis of the dibromocyclopropane **11** gave the corresponding products **22**: 60% yield; ^{1}H NMR δ 7.43−7.30 (m, 10H, ArH), 6.81 (s, 1H, H-3), 5.06 (s, 1H, H-1), 4.80−4.50 (m, 4H, OCH_2Ph), 3.80−3.52 (m, 3H), 3.50 (s, 3H, OCH_3), 1.43 (d, *J* = 6.3 Hz, 3H, H-7); ^{13}C NMR δ 138.46, 137.88, 137.68, 128.77, 128.40, 128.25, 127.92, 127.79, 127.54, 127.18, 114.02, 101.49, 81.66, 76.04, 72.43, 71.33, 70.97, 55.57, 19.35. Anal. Calcd for $C_{22}H_{25}BrO_4$: C, 60.97; H, 5.81. Found: C, 61.05; H, 5.82.

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-methyl-*β*-D-glucopyranoside (23). A solution of cyclopropane **14** (165 mg, 0.38 mmol) and acetyl chloride (0.38 mL) in methanol (5 mL) was heated at 80 °C for 15 days. The reaction mixture was diluted with dichloromethane, treated with solid sodium bicarbonate, and concentrated. On purification by column chromatography unreacted **14** eluted first (98 mg) followed by **23** (49 mg, 70% with respect the recovered cyclopropane) which was obtained as a colorless solid: mp = 104 −105 °C (ether/hexane); $[\alpha]^{25}_D = +4.5$ (*c* 0.2, $CHCl_3$); ^{1}H NMR δ 7.35−7.26 (m, 15H), 5.0−4.50 (m, 6H), 4.04−3.99 (d, *J* = 8.0 Hz, 1H), 3.80−3.40 (m, 7H), 3.27−3.24 (t, 1H), 1.85−1.75 (m, 1H); 1.06−1.03 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR δ 138.42, 128.49, 128.20, 127.96, 127.87, 127.71, 105.68, 85.37, 79.55, 75.32, 75.23, 74.83, 73.62, 70.75, 56.85, 42.79, 12.62. Anal. Calcd for $C_{29}H_{34}O_5$: C, 75.29; H, 7.41. Found: C, 75.31; H, 7.45.

General Procedure for NBS-Activated Ring-Opening Reactions of Cyclopropane 14 and Cyclopropane 17 with Different Solvents. To a stirred solution of the cyclopropane (215 mg, 0.5 mmol) in 5 mL of solvent at 0 °C, under nitrogen, was added 107 mg (0.6 mmol) of NBS, and the stirring was continued until the reaction mixture showed the absence of starting material on TLC. Except with benzyl alcohol, where the reaction mixture was concentrated by distilling out the benzyl alcohol under reduced pressure, in general, the reaction mixture was coevaporated with toluene in vacuo. An aqueous workup in all the above reactions was found to be less efficient. Chromatographic purifications were carried out using 5% ethyl acetate in hexane. Yields are based on the amount of pure material obtained. The anomeric ratios were calculated by ^{1}H NMR (for crude reaction mixture) as well as using chromatographically separated products.

Ring Opening of Cyclopropane 14 with NBS/MeOH. As described above, stirring cyclopropane **14** (290 mg, 0.67 mmol) with NBS (145 mg, 0.81 mmol) in MeOH (6 mL) for 8 h and purification of the reaction mixture gave the anomers **24** and **25** in a 20:80 ratio (263 mg, 72%).

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-glucopyranoside (24): colorless syrup, $[\alpha]^{25}_D = +87.3$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.36−7.16 (m, 15H), 5.0−4.99 (d, *J* = 2.6 Hz, 1H), 4.92−4.53 (m, 6H), 3.85−3.57 (m, 6H), 3.40 (s, 3H), 3.35−3.25 (t, 1H), 2.17−2.34 (m, 1H); ^{13}C NMR δ 138.22, 138.09, 128.52, 128.40, 127.86, 127.72, 99.23, 80.35, 79.48, 75.27, 74.79, 73.61, 70.96, 68.79, 55.26, 48.51, 30.60. Anal. Calcd for $C_{29}H_{33}O_5Br$: C, 64.32; H, 6.14. Found: C, 64.30; H, 6.35.

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-*β*-D-glucopyranoside (25): colorless syrup, $[\alpha]^{25}_D = +22$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.34−7.19 (m, 15H), 5.0−4.58 (m, 6H), 4.45−4.40 (d, *J* = 8.5 Hz, 1H), 3.87−3.46 (m, 10H), 2.20−1.81 (m, 1H); ^{13}C NMR δ 138.44, 138.30, 138.11, 128.52, 128.42, 127.86, 102.29, 80.01, 79.85, 75.58, 75.14, 74.84, 73.62, 69.04, 57.25, 47.70, 31.60. Anal. Calcd for $C_{29}H_{33}O_5Br$: C, 64.32; H, 6.14. Found: C, 64.25; H, 6.18.

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-mannopyranoside (26). Stirring cyclopropane **17** (215 mg, 0.5 mmol) with NBS (108 mg, 0.6 mmol) in MeOH (5 mL) for 24 h and purification yielded the ring-opened product **26** (170 mg, 62%) as a colorless syrup: $[\alpha]^{25}_D = +36$ (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 7.39−7.22 (m, 15H), 5.03 (s, 1H), 4.83−4.40 (m, 6H), 4.07−4.0 (dd, *J* = 9.4 Hz, 1H), 3.85−3.40 (m, 6H), 3.38 (s, 3H), 2.69−2.58 (m, 1H); ^{13}C NMR δ 138.34, 138.26, 138.15, 128.51, 128.39, 127.91, 127.79, 99.71, 79.57, 74.88, 74.33, 73.53, 71.92, 71.11, 68.99, 55.03, 46.24, 29.57. Anal. Calcd for $C_{29}H_{33}O_5Br$: C, 64.32; H, 6.14. Found: C, 64.25; H, 6.0.

Ring Opening of Cyclopropane 14 with NIS/MeOH. As mentioned above for NBS, after cyclopropane **14** was stirred for 12 h with NIS (1.2 equiv) in MeOH and purification of the reaction mixture, the anomers **27**and **28** were obtained in a 20:80 ratio (86%).

Ring Opening of Cyclopropane 14 with BCIP/MeOH. To a stirred solution of cyclopropane **14** (207 mg, 0.48 mmol) in methanol (5 mL) was added BCIP (325 mg, 0.69 mmol). After 6 h, the reaction mixture was concentrated in vacuo and the crude product was dissolved in 15 mL of dichloromethane, washed with 15 mL of saturated sodium bisulfite and 15 mL of brine, and purified by column chromatography. The anomers **27** and **28** were obtained in a 15:85 ratio (245 mg, 86%).

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(iodomethyl)-α-D-glucopyranoside (27): colorless syrup, $[\alpha]^{25}_D = +69.2$ (*c* 0.4, $CHCl_3$); ^{1}H NMR δ 7.36−7.15 (m, 15H), 4.96−4.94 (d, *J* = 3.0 Hz, 1H), 4.93−4.51 (m, 6H), 3.82−2.97 (m, 10H), 2.24−2.08 (m, 1H); ^{13}C NMR δ 138.40, 128.57, 128.47, 127.89, 127.77, 101.07, 81.29, 79.16, 75.45, 74.84, 73.66, 71.09, 68.79, 55.38, 48.46, 3.05. Anal. Calcd for $C_{29}H_{33}O_5I$: C, 59.19; H, 5.65. Found: C, 59.22; H, 5.68.

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(iodomethyl)-*β*-D-glucopyranoside (28): low-melting solid, $[\alpha]^{25}_D = +53.2$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 7.36−7.19 (m, 15H), 4.97−4.58 (m, 6H), 4.32−4.27 (d, *J* = 8.6 Hz, 1H), 3.78−3.49 (m, 10H), 1.35−1.21 (m, 1H); ^{13}C NMR δ 138.45, 138.24, 138.08, 129.79, 128.59, 128.54, 128.44, 127.89, 127.70, 104.39, 81.65, 79.75, 75.63, 75.13, 74.80, 73.61, 68.96, 57.34, 46.32, 6.97. Anal. Calcd for $C_{29}H_{33}O_5I$: C, 59.19; H, 5.65. Found: C, 59.45; H, 5.72.

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-(iodomethyl)-α-D-mannopyranoside (29). As described above, after cyclopropane **17** (310 mg, 072 mmol) was stirred for 36 h with BCIP (405 mg, 0.87 mmol) in MeOH (6 mL), followed by the usual workup and chromatographic purification of the reaction mixture, 134 mg (70%, based on recovered **17**) of the corresponding ring-opened product **29** was obtained as a colorless syrup: $[\alpha]^{25}_D = +32.3$ (*c* 0.3, $CHCl_3$); ^{1}H NMR δ 7.35−7.14 (m, 15H), 4.96 (s, 1H), 4.85−4.43 (m, 6H), 3.98−3.91 (m, 1H), 3.81−3.65 (m, 5H), 3.42 (s, 3H), 3.22−3.11 (t, 1H), 2.69−2.58 (m, 1H); ^{13}C-NMR δ 138.41, 138.30, 138.21, 128.51, 128.38, 127.90, 127.76, 127.66, 100.92, 80.16, 74.81, 74.11, 73.53, 71.90, 71.38, 69.07, 55.0, 46.77, 2.0. Anal. Calcd for $C_{29}H_{33}O_5I$: C, 59.19; H, 5.65. Found: C, 59.29; H, 5.70.

On further elution, unreacted **17** was obtained (173 mg).

Ring Opening of Cyclopropane 14 with NBS/$ClCH_2CH_2OH$. After cyclopropane **14** (110 mg, 0.25 mmol) was stirred with NBS (50 mg, 0.28 mmol) in 2-chloroethanol (3 mL) for 4 h, TLC showed clearly the disappearance of starting

compound and the formation of two close spots, which were separated and identified as **30** and **31** (35:65 ratio, 137 mg, 91% yield).

2′-Chloroethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-glucopyranoside (30): colorless syrup, $[\alpha]^{25}_D = +78.9$ (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 7.34−7.12 (m, 15H), 5.16−5.14 (d, *J* = 3.4 Hz, 1H), 4.94−4.49 (m, 6H), 3.93−3.60 (m, 10H), 3.41−3.30 (t, 1H), 2.36−2.19 (m, 1H); ^{13}C NMR δ 138.0, 128.56, 128.45, 127.94, 127.82, 98.48, 80.22, 79.29, 75.40, 74.91, 73.59, 71.38, 68.57, 68.33, 48.44, 42.83, 30.53. Anal. Calcd for $C_{30}H_{34}O_5BrCl$: C, 61.08; H, 5.83. Found: C, 61.0; H, 5.85.

2′-Chloroethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-β-D-glucopyranoside (31): low-melting solid, $[\alpha]^{25}_D = +22.5$ (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 7.34−7.18 (m, 15H), 4.94−4.53 (m, 7H), 4.21−4.07 (m, 1H), 3.86−3.66 (m, 9H), 3.51−3.41 (m, 1H), 1.97−1.84 (m, 1H); ^{13}C NMR δ 138.34, 138.14, 138.04, 128.49, 128.43, 127.84, 101.35, 79.86, 79.59, 75.54, 75.10, 74.83, 73.56, 69.84, 68.89, 47.54, 42.62, 31.49. Anal. Calcd for $C_{30}H_{34}O_5BrCl$: C, 61.08; H, 5.83. Found: C, 61.22; H, 5.82.

Ring Opening of Cyclopropane 17 with NBS/$ClCH_2$-CH_2OH. The reaction took 12 h for completion and yielded the corresponding ring-opened product **32** in 71% yield (as a colorless syrup).

2′-Chloroethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-mannopyranoside (32): $[\alpha]^{25}_D = +38.4$ (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 7.36−7.17 (m, 15H), 5.13 (s, 1H), 4.82−4.41 (m, 6H), 4.11−4.04 (dd, *J* = 5.2, 9.3 Hz, 1H), 3.95−3.50 (m, 9H), 3.48−3.38 (t, *J* = 11 Hz, 1H), 2.71−2.65 (m, 1H); ^{13}C NMR δ 138.09, 128.25, 127.80, 127.59, 98.89, 79.09, 74.61, 74.09, 73.33, 71.83, 71.45, 68.80, 67.92, 46.06, 42.62, 29.40. Anal. Calcd for $C_{30}H_{34}O_5BrCl$: C, 61.08; H, 5.83. Found: C, 61.25; H, 5.91.

Ring Opening of Cyclopropane 14 with NBS/Cl_3C-CH_2OH. The ring opening of **14** (85 mg, 0.197 mmol) with NBS (44 mg) in 2,2,2-trichloroethanol was complete within 1 h and yielded both α- and β-anomers in equal amounts (116 mg, 89% yield).

2′,2′,2′-Trichloroethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-glucopyranoside (33): colorless syrup, $[\alpha]^{25}_D = +70$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 7.38−7.21 (m, 15H), 5.35−5.34 (d, *J* = 2.9 Hz, 1H), 4.96−4.51 (m, 6H), 4.29−4.07 (m, 2H), 3.86−3.66 (m, 6H), 3.47−3.35 (t, 1H), 2.42−2.24 (m, 1H); ^{13}C NMR δ 137.92, 128.49, 127.91, 98.83, 96.01, 79.91, 79.57, 79.16, 75.49, 75.07, 73.65, 72.42, 68.02, 48.72, 29.94. Anal. Calcd for $C_{30}H_{32}O_5BrCl_3$: C, 54.69; H, 4.89. Found: C, 54.75; H, 4.91.

2′,2′,2′-Trichloroethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-β-D-glucopyranoside (34): colorless syrup, $[\alpha]^{25}_D = +24$ (*c* 0.2, $CHCl_3$); ^{1}H NMR δ 7.38−7.21 (m, 15H), 5.01−4.54 (m, 6H), 4.52−4.46 (d, *J* = 12.6 Hz, 1H), 4.20−4.11 (d, *J* = 11.7, 1H), 3.97−3.45 (m, 8H), 2.10−1.97 (m, 1H); ^{13}C NMR δ 138.35, 137.99, 128.50, 127.85, 101.40, 96.03, 80.73, 79.78, 79.41, 75.54, 75.26, 74.86, 73.61, 68.74, 48.57, 31.15. Anal. Calcd for $C_{30}H_{32}O_5BrCl_3$: C, 54.69; H, 4.89. Found: C, 54.65; H, 4.91.

Ring Opening of Cyclopropane 17 with NBS/Cl_3C-CH_2OH. The ring opening of **17** (375 mg, 0.87 mmol) with NBS (186 mg, 1.05 mmol) in 2,2,2-trichloroethanol took 8 h for completion and yielded the corresponding ring-opened product **35** (350 mg, 89% yield) as a pale yellow syrup.

2′,2′,2′-Trichloroethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-mannopyranoside (35): $[\alpha]^{25}_D = +51.3$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.35−7.13 (m, 15H), 5.33 (s, 1H), 4.81−4.41 (m, 6H), 4.26−4.08 (m, 3H), 3.86−3.61 (m, 5H), 3.48−3.37 (t, 1H), 2.79−2.68 (m, 1H); ^{13}C NMR δ 138.27, 138.0, 128.57, 128.47, 127.97, 127.79, 100.03, 96.64, 79.44, 78.79, 74.75, 74.14, 73.60, 72.50, 72.27, 68.97,46.09, 29.21. Anal. Calcd for $C_{30}H_{32}O_5BrCl_3$: C, 54.69; H, 4.89. Found: C, 54.32; H, 4.88.

Ring Opening of Cyclopropane 14 with NBS/$PhCH_2OH$. Cyclopropane **14** (295 mg, 0.69 mmol) was treated with benzyl alcohol and NBS (193 mg, mmol). After 36 h benzyl alcohol was distilled from the reaction mixture and the crude product was purified. Products **36** and **37** were obtained in a 35:65 ratio (383 mg, 91% yield).

Benzyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-glucopyranoside (36): colorless syrup, $[\alpha]^{25}_D = +85.5$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.38−7.14 (m, 20H), 5.25−5.23 (d, *J* = 3.2 Hz, 1H), 4.92−4.49 (m, 8H), 3.83−3.64 (m, 6H), 3.42−3.32 (t, 1H), 2.38−2.22 (m, 1H); ^{13}C-NMR δ 138.23, 137.66, 128.61, 128.52, 127.90, 98.03, 80.57, 79.63, 75.41, 74.99, 73.71, 71.48, 70.06, 68.85, 48.73, 30.66. Anal. Calcd for $C_{35}H_{37}O_5Br$: C, 68.07; H, 6.04. Found: C, 68.10; H, 6.10.

Benzyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-β-D-glucopyranoside (37): colorless solid, mp = 91−93 °C (ether/hexane); $[\alpha]^{25}_D = -7.5$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.38−7.12 (m, 20H), 4.99−4.59 (m, 9H), 3.92−3.69 (m, 6H), 3.54−3.45 (m, 1H), 2.02−1.89 (m, 1H); ^{13}C NMR δ 138.48, 138.38, 138.24, 128.49, 128.35, 127.88, 100.47, 80.09, 79.87, 75.57, 75.23, 74.85, 73.64, 71.44, 69.07, 47.73, 31.61. Anal. Calcd for $C_{35}H_{37}O_5Br$: C, 68.07; H, 6.04. Found: C, 67.98; H, 6.11.

Ring Opening of Cyclopropane 17 with NBS/$PhCH_2OH$. The reaction was incomplete even after 4 days. Distillation followed by purification afforded **38** in 40% yield (with respect to the cyclopropane recovered) as colorless syrup.

Benzyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-α-D-manno pyranoside (38): $[\alpha]^{25}_D = +59.8$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 7.35−7.18 (m, 20H), 5.21 (s, 1H), 4.82−4.41 (m, 8H), 4.14−4.07 (dd, *J* = 5.4, 9.2 Hz, 1H), 3.86−3.58 (m, 5H), 3.49−3.33 (t, 1H), 2.77−2.64 (m, 1H); ^{13}C NMR δ 138.27, 137.52, 128.38, 127.94, 127.75, 126.98, 98.33, 79.50, 74.86, 74.43, 73.52, 71.99, 71.51, 69.55, 68.97, 46.39, 29.55. Anal. Calcd for $C_{35}H_{37}O_5Br$: C, 68.07; H, 6.04. Found: C, 67.96; H, 6.08.

Ring Opening of Cyclopropane 14 with NBS/H_2O. To a solution of cyclopropane **14** (250 mg, 0.58 mmol) in dioxane/water (6 mL, 2:1) was added NBS (125 mg, 0.70 mmol), and the stirring was continued for 8 h. The reaction mixture was then concentrated to half its volume in vacuo and extracted with dichloromethane. The combined extracts were dried and concentrated. Purification by chromatography and recrystallization from ether/hexane yielded **39** (198 mg, 66% yield) as a colorless solid.

3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-D-glucopyranose (39): mp = 110−112 °C; $[\alpha]^{25}_D = +61.2$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.34−7.18 (m, 15H), 5.54−5.51 (bs) and 4.92−4.56 (m, together 7H), 4.14−3.26 (m, 8H), 2.33−2.17 and 1.89−1.72 (2m's, together 1H); ^{13}C NMR δ 138.07, 137.92, 128.49, 128.08, 127.93, 95.46, 92.43, 79.83, 79.67, 75.54, 75.39, 74.91, 74.73, 73.59, 70.91, 68.98, 48.71, 48.62, 30.92. Anal. Calcd for $C_{28}H_{31}O_5Br$: C, 63.75; H, 5.93. Found: C, 64.09; H, 6.07.

Ring Opening of Cyclopropane 17 with NBS/H_2O. When the reaction was carreid out under conditions similar to those described above, cyclopropane **17** (294 mg, 0.68 mmol) provided the corresponding ring-opened product **40** (210 mg, 61%) as a colorless solid.

3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-D-mannopyranose (40): mp = 90−91 °C (ether/hexane); $[\alpha]^{25}_D = +23.9$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.34−7.14 (m, 15H), 5.5 (s, 1H), 4.82−4.41 (m, 6H), 4.16−4.02 (m, 2H), 3.84−3.35 (m, 5H), 3.12 (b, 1H), 2.69−2.57 (m, 1H); ^{13}C-NMR δ 138.27, 138.16, 137.95, 128.53, 128.49, 128.01, 127.80, 93.16, 78.98, 74.72, 74.63, 73.45, 71.98, 71.03, 69.35, 46.39, 29.74. Anal. Calcd for $C_{28}H_{31}O_5Br$: C, 63.75; H, 5.93. Found: C, 63.84; H, 6.09.

3,4-Di-*O*-benzyl-6-*O*-(triphenylcarbinyl)-1,5-anhydro-2-deoxy-1,2-*C*-(dichloromethylene)-D-*glycero*-D-*gulo*-hexitol (42). Aqueous sodium hydroxide (4.0 g in 8 mL) was added to a vigorously stirred solution of the glucal **41** (1.88 g, 3.31 mmol) in chloroform (8 mL) containing benzyltriethylammonium chloride (20 mg). The reaction mixture was stirred at rt for 36 h and then diluted with water (25 mL) and extracted with dichloromethane. The combined extracts were dried and concentrated, and the residue was purified by chromatography to furnish **42** (1.58 g, 73%) as a colorless syrup: $[\alpha]^{25}_D = +42.3$ (*c* 1, $CHCl_3$); ^{1}H NMR δ 7.50−7.0 (m, 25H), 4.84−4.68 (m, 4H), 4.29−4.24 (d, *J* = 10.7 Hz, 1H), 4.08−4.05 (d, *J* = 7.8 Hz, 1H), 3.90 (m, 3H) 3.52−3.47 (d, *J* = 10 Hz, 1H), 1.93 (dd, *J* = 4.1, 7.8 Hz, 1H); ^{13}C NMR δ 143.90,

138.28, 137.81, 128.85, 128.61, 128.30, 128.01, 127.67, 127.25, 86.99, 80.54, 77.61, 76.09, 74.79, 72.18, 63.95, 61.82, 59.26, 34.77. Anal. Calcd for $C_{40}H_{36}Cl_2O_4$: C, 73.73; H, 5.57. Found: C, 73.65; H, 5.55.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-(dichloromethylene)-D-*glycero*-D-*gulo*-hexitol (43).[23c] To a solution of **42** (1.41 g, 2.164 mmol) in ether (6 mL) was added 5 mL of formic acid, and the solution was stirred at rt for 1 h. The reaction mixture was concentrated in vacuo and the residue diluted with dichloromethane. The dichloromethane layer was washed with saturated bicarbonate solution and brine, dried, and concentrated. Purification of the crude product by column chromatography using initially 5% ethyl acetate in hexane to elute triphenylcarbinol and then with 25% ethyl acetate yielded the detritylated product (**43**) as a colorless solid (650 mg, 74%): mp = 83−84 °C; $[\alpha]^{25}_D = +74.2$ (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 7.42−7.31 (m, 10H), 5.00−4.66 (m, 4H), 3.91- 3.87 (d, J = 8.7 Hz, 1H), 3.85−3.80 (dd, J = 9.8, 3.9 Hz, 1H), 3.78−3.60 (m, 4H), 1.98 (bs, 1H), 1.89−1.80 (dd, J = 3.9, 8.7 Hz, 1H); ^{13}C NMR δ 138.11, 137.58, 128.59, 128.17, 128.06, 79.77, 77.14, 74.97, 74.79, 72.11, 62.76, 61.04, 58.81, 33.90. Anal. Calcd for $C_{21}H_{22}Cl_2O_4$: C, 61.62; H, 5.42. Found: C, 61.68; H, 5.42.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-D-*gulo*-hexitol (44). To a stirred suspension of lithium aluminum hydride (455 mg, 12 mmol) in dry tetrahydrofuran (4 mL) was added a solution of the dichlorocyclopropane **43** (330 mg, 0.80 mmol) in tetrahydrofuran (10 mL). After 24 h of stirring at rt, the reaction mixture was cooled in ice and quenched with a saturated aqueous sodium sulfate. The usual workup and purification yielded **44** (228 mg, 84%) as a colorless low-melting solid: $[\alpha]^{25}_D = +24.5$ (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 7.35−7.29 (m, 10H), 4.89−4.62 (m, 4H), 3.87- 3.40 (m, 6H), 2.11 (b, 1H), 1.08−0.93 (m, 1H), 0.81−0.69 (m, 2H); ^{13}C NMR δ 138.49, 138.35, 128.51, 128.0, 127.79, 126.98, 79.61, 76.91, 76.53, 73.61, 71.25, 62.58, 49.98, 14.43, 10.29; HRMS calcd for $(M - Bn)^+$ $C_{14}H_{17}O_4$ 249.1127, found 249.1128.

3,4-Di-*O*-benzyl-1,5-anhydro-2-deoxy-1,2-*C*-methylene-D-*glycero*-D-*talo*-hexitol (45). To a stirred suspension of zinc dust (330 mg, 5.03 mmol) and cuprous chloride (108 mg, 1.08 mmol) in dry ether (1 mL) was added diiodomethane (327 mg, 1.12 mmol). After 5 min, acetyl chloride (20 μL) was added and the mixture was heated for 5 min at 40 °C. A solution of glucal **41** (670 mg, 1.12 mmol) in ether (3 mL) was then added. Five minutes after the addition of the glucal, an additional amount (2 equiv) of diiodomethane was added and the heating was continued for 2 h. Usual workup and purification by chromatography furnished **45** as a pale yellow syrup (282 mg, 70%): $[\alpha]^{25}_D = -70.1$ (*c* 1, $CHCl_3$); ^{1}H-NMR δ 7.39−7.21 (m, 10H), 4.89−4.58 (m, 4H), 4.24−4.16 (m, 1H), 3.85−3.74 (m, 2H), 3.69−3.54 (m, 1H), 3.38−3.32 (m, 2H), 1.98 (b, 1H), 1.50−1.25 (m, 1H), 0.88−0.73 (m, 2H); ^{13}C NMR δ 138.54, 138.42, 128.43, 128.03, 127.87, 127.74, 127.57, 78.74, 78.55, 77.92, 74.21,70.0, 62.52, 55.10, 15.69, 11.98. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.98; H, 7.09.

3,4-Di-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-1,6-anhydro-β-D-glucopyranose (46). To a solution of the substrate **44** (70 mg, 0.21 mmol) in acetonitrile (5 mL) was added 140 mg of 4 Å molecular sieves, and the contents were stirred for 30 min. To this NBS (44 mg, 0.25 mmol) was added, and the stirring was continued for 5 h. The reaction mixture was diluted with toluene, filtered, and concentrated in vacuo, and the crude product was purified chromatographically without any aqueous workup to yield the levoglucosan derivative **46** (61 mg, 70%) as a colorless syrup: $[\alpha]^{25}_D = -70.8$ (*c* 0.75, $CHCl_3$); ^{1}H-NMR δ 7.38−7.26 (m, 10H), 5.58 (s, 1H), 4.64−4.51 (m, 5H), 4.17−4.14 (d, J = 6.9 Hz, 1H), 3.77−3.68 (m, 2H), 3.54−3.40 (m, 3H), 2.31−2.23 (t, 1H); ^{13}C NMR δ 137.99, 137.67, 128.56, 128.49, 127.97, 127.78, 101.55, 76.46, 74.80, 74.56, 71.49, 71.32, 64.92, 45.56, 31.70. Anal. Calcd for $C_{21}H_{23}BrO_4$: C, 60.15; H, 5.53. Found: C, 60.07; H, 5.61.

3,4-Di-*O*-benzyl-2-deoxy-2-*C*-(bromomethyl)-1,6-anhydro-β-D-mannopyranose (47). To a solution of **45** (110 mg, 0.32 mmol) in acetonitrile (7 mL) was added 220 mg of 4 Å molecular sieves, and it was stirred for 30 min. NBS (70 mg, 0.39 mmol) was added and the stirring continued. The reaction was found to be incomplete even after 36 h. It was diluted with toluene and filtered. It was then concentrated in vacuo, and the crude product was purified as described above to yield the levomannosan derivative **47** (47 mg, 35%) as a colorless syrup: $[\alpha]^{25}_D = -12.4$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 7.38−7.25 (m, 10H), 5.50 (s, 1H), 4.64 (s, 2H), 4.59−4.57 (m, 1H), 4.46−4.45 (d, J = 1.65 Hz, 2H), 4.14−4.11 (d, J = 6.9 Hz, 1H), 3.77−3.66 (m, 2H), 3.52−3.44 (m, 3H), 2.43−3.32 (m, 1H); ^{13}C NMR δ 137.69, 128.63, 128.51, 128.10, 127.87, 101.12, 75.0, 73.91, 73.74, 73.17, 71.35, 64.74, 44.41, 30.38; calcd for $(M - Br)^+$ $C_{21}H_{23}O_4$ 339.1596, found 339.1615.

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