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Design, Synthesis, and Biological Activities of Some Branched Carbasugars: Construction of a Substituted 6-Oxabicyclo[3.2.1]nonane Skeleton

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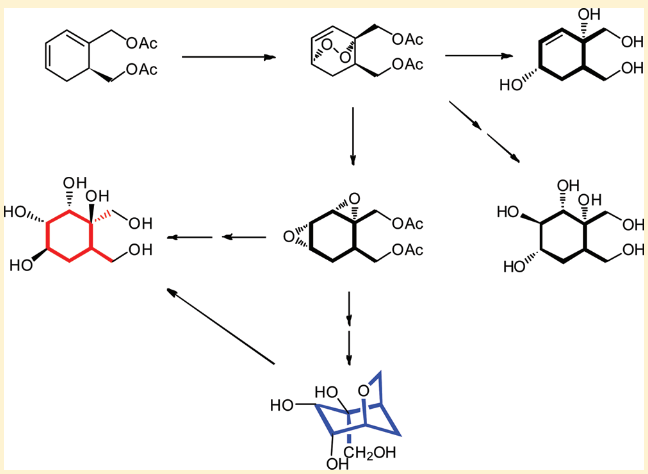
Supporting Information

ABSTRACT: Transformation of cyclohexa-2,4-diene-1,2-diylbis(methylene) diacetate to various carbasugars is described. Photooxygenation of a cyclohexadiene derivative gave a bicyclic endoperoxide, which was reduced with thiourea to [2-[(acetyloxy)-methyl]cyclohexa-2,4-dien-1-yl]methyl acetate. Epoxidation of the remaining double bond followed by epoxide ring-opening and hydrolysis of the acetate groups gave one of the target hexols. The bicyclic endoperoxide was rearranged to a diepoxide with CoTPP. The diepoxide was reacted with sulfamic acid in acetic anhydride, resulting in the formation of a new branched carbasugar as well as in the formation of cyclitols with a 6-oxabicyclo[3.2.1]nonane skeleton. The mechanism of the formation of the products is discussed. The inhibition activity of six cyclitol derivatives was tested against α-glycosidase.



INTRODUCTION

Glycosidases are a family of essential enzymes in the human body, and they catalyze the hydrolysis of glycosidic linkages to release smaller sugars.[1] Therefore, glycosidase inhibitors are generally regarded as promising candidates for new drug development. Inhibition of intestinal α-glycosidases can be used to treat diabetes through the lowering of blood glucose levels.[2] Carba-analogues of oligosaccharides (carbasugar) generated by replacing the endocyclic oxygen atom in monosaccharides[3] are thought to be more potent drug candidates than natural sugars, since they are hydrolytically stable.

The first carbahexopyranose **1** found in nature[5] was isolated as a weak antibiotic from the fermentation broth of *Streptomyces* species[6] and synthesized by McCasland et al.[7] Recently, we synthesized two new carbasugars, namely, 5a-carba-6-deoxy-α-DL-*galacto*-heptopyranose (**2**) and 5a-carba-6-deoxy-α-DL-*gluco*-heptopyranose (**3**) (Figure 1).[8] The pentol **2** showed inhibition of α-glycosidase and increased the activity of α-amylase, whereas **3** did not. Furthermore, we prepared various branched carbahexopyranose derivatives such as **4**, which showed high inhibition for α-glycosidase.[9] Vogel et al. synthesized some double-branched carbahexopyranose **5** and its amino derivatives.[10] After the pioneering work carried out by McCasland,[11] oxanorbornene derivatives were extensively used for the synthesis of carbasugars.[12] The microbial oxidation of benzene and its derivatives to cyclohexadiene has also been prevalent in carbasugar chemistry.[13−15]

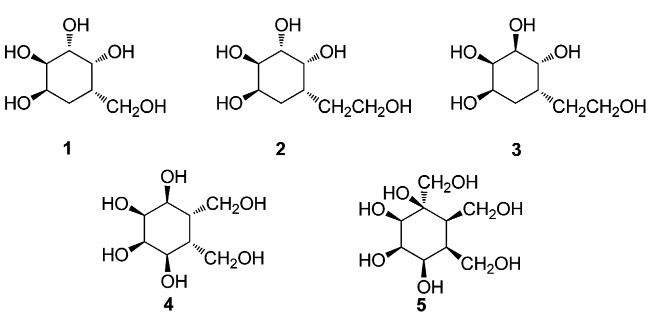


Figure 1. Representative cyclitols.

In the present paper, we describe the regio- and stereospecific synthesis of new branched carbasugars **6−8** starting from a cyclohexadiene derivative **13** (Figure 2). The applied synthetic strategy was based on the photooxygenation of **13** followed by transformation of the bicyclic endoperoxide formed.

RESULTS AND DISCUSSION

The starting material *rel*-(1*R*,2*S*)-cyclohex-4-ene-1,2-diylbis-(methylene) diacetate (**11**) was prepared in three steps starting with the addition of maleic anhydride to in situ generated butadiene.

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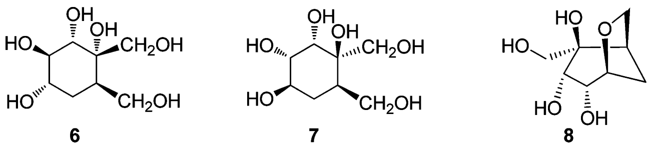
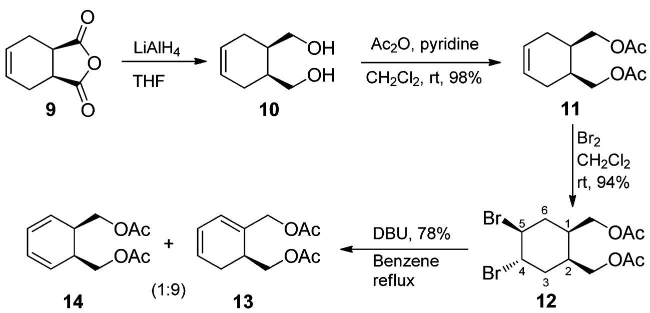


Figure 2. Target compounds.

The reduction of the anhydride functionality in **9**[16] followed by acetylation of diol **10**[17] afforded the desired diacetate **11**.[18] The resulting compound **11** was brominated at room temperature to give only the *trans*-dibromide **12** in high yield. The unsymmetrical structure, confirmed by ^{13}C NMR, was in agreement with the *trans*-addition of bromine to the double bond in **11**. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)-induced elimination furnished the unsymmetrical diene **13** and the symmetrical diene **14**[19] in a ratio of 9:1 (Scheme 1).

Scheme 1. Preparation of Diene 13 from Anhydride 9



The geometry-optimized (DFT, B3LYP at 6-31G** level) structure of the *trans*-dibromide **12** is given in Figure 3. We assume that the elimination of 2 mol of HBr takes place step by step. DBU, a non-nucleophilic base, can easily approach the *axial*-hydrogens H-6 in **12** since the proton H-3 is hindered because of the steric effect caused by the axial acetoxymethylene group in **12**. Therefore, the elimination of the first mole of HBr is chemoselective, and the *axial*-proton H-6 and bromine atom attached to C-5 are first eliminated to give **15**. The initially formed monobromide **15** can undergo two types of elimination, namely, 1,2- and 1,4-elimination,[20] to form **14** and **13**, respectively (Scheme 2). The geometry-optimized (DFT, B3LYP at 6-31+G* level) structure of the monobromide **15** (Figure 3) shows that the conformation of the proton attached to C-6 and the bromine atom is not suitable for *trans*-elimination to give **14**. However, allylic activation of the proton H-2 to be abstracted for 1,4-elimination significantly accelerates the base-induced elimination reaction. Therefore, **15** underwent *syn*-1,4-elimination, and the unsymmetrical diene **13** was formed as the major product. Furthermore, DFT calculations showed that the diene **13** is about 3.7 kcal/mol more stable than the symmetrical diene **14**.

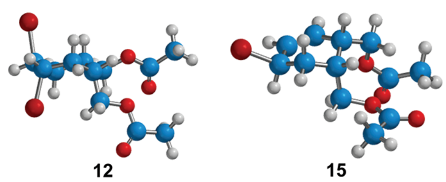


Figure 3. Geometry-optimized structures of **12** and **15**.

After the successful synthesis of diene **13**, the next step was functionalization of the diene unit. Photooxygenation[21] of **13** in methylene chloride (500 W, projection lamp) at room temperature using tetraphenylporphyrin as the sensitizer afforded the bicyclic endoperoxide **16** in a yield of 82%. The diene unit in **13** is not symmetric and can be attacked from both sides of the diene. The repulsive interaction[22] between the axial acetoxymethylene group in **13** and the singlet oxygen molecule is directing the singlet oxygen to approach the diene unit from the *anti* position.[4a,23] Exclusive formation of the *anti* product **16** was later supported by X-ray analysis.

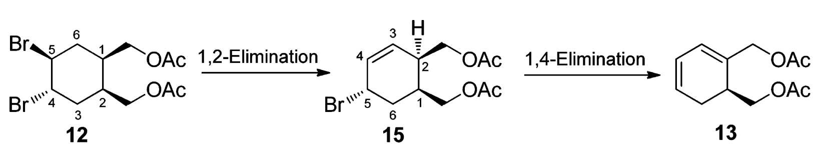
After the successful synthesis of the endoperoxide **16**, we turned our attention to the selective reduction of the peroxide linkage in **16**. Reaction of bicyclic endoperoxide **16** with thiourea[20,24] under very mild conditions followed by acetylation in pyridine at room temperature afforded the tetraacetate **19** (Scheme 3). For synthesis of cyclitols, the tetraacetate **19** was reacted with *m*-CPBA. Unfortunately, the desired epoxide **20** was not formed due to the steric crowdedness hindering the approach of *m*-CPBA.

After the failure of the epoxidation reaction, the diol **17** was submitted to the selective acetylation reaction with acetic anhydride in pyridine under milder reaction conditions. The triacetate **21** was isolated as the sole product, where only the secondary alcohol functionality was acetylated. In contrast to the tetraacetate **19**, the triacetate **21** reacted smoothly with *m*-CPBA in methylene chloride at room temperature to give a mixture of two separable epoxides **22** and **23** in 75% and 7% yields, respectively (Scheme 4). For further characterization, the major product **22** was transferred into the corresponding tetraacetate ***syn*-20** by reaction with acetic anhydride in the presence of a catalytic amount of H_2SO_4 (Scheme 5).

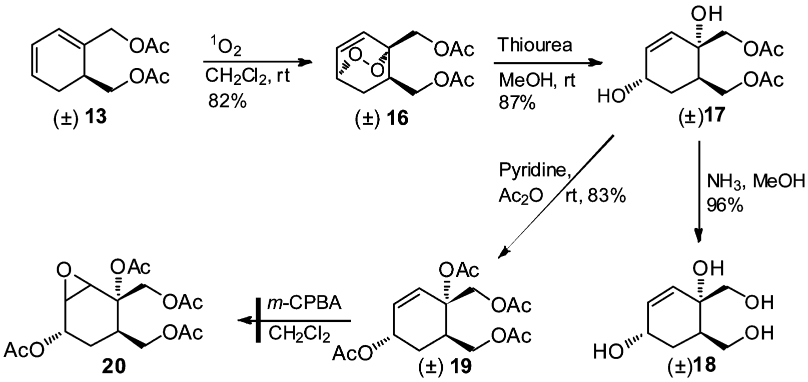
Geometry optimization calculations (DFT, B3LYP at 6-31+G* level) for *syn*- and *anti*-epoxides with respect to the hydroxyl group show dihedral angles of 52° and 105.5° between the vicinal protons H-5 and H-6 (Figure 4). We calculated the vicinal coupling constants[25] between the protons H-5 and H-6 by considering substituent electronegativities and found a value of 2.97 Hz for **22** and 0.81 Hz for **23**. The measured coupling constants 3.5 Hz for **22** and <1.0 Hz for **23** are in good agreement with our configurational assignments. It is well established that upon the treatment of cyclic allylic alcohols with *m*-CPBA the formation of epoxides occurs mainly on the same side as the hydroxyl group.[26]

After the successful synthesis of the epoxides **22** and **23**, we turned our attention to the ring-opening reaction of the major epoxide isomer **22**. *syn*-Epoxide **22** was subjected to the

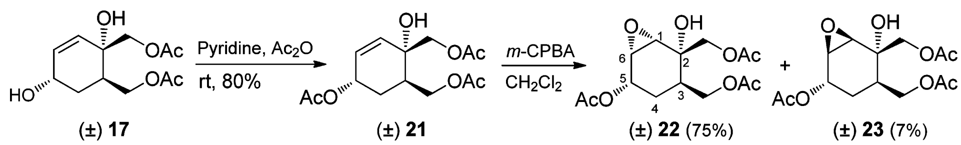
Scheme 2. Formation of Diene 13 from Dibromide 12



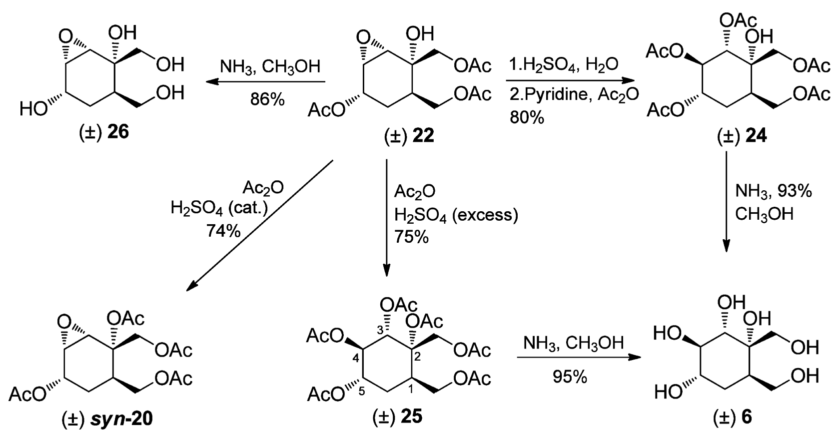
Scheme 3. Formation of Tetrol 18 from Diene 13



Scheme 4. Synthesis of Epoxides 22 and 23



Scheme 5. Synthesis of Hexol 6 and Tetrol 26



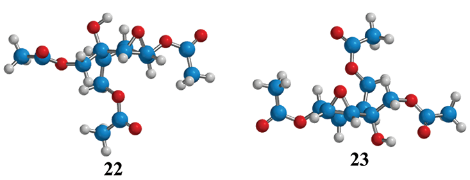


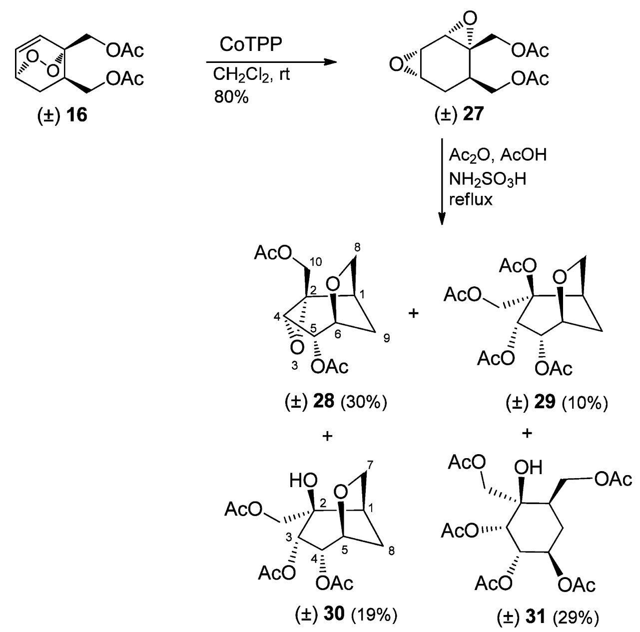
Figure 4. Geometry-optimized structures of **22** and **23**.

acid-catalyzed ring-opening reaction in the presence of H_2SO_4 followed by acetylation with acetic anhydride in pyridine resulting in the formation of a single isolable product, penta-acetate **24**. However, when the epoxide ring-opening reaction of **22** was carried out in acetic anhydride with H_2SO_4, the hexaacetate **25** was isolated as the sole product in 75% yield. The analysis of the NMR spectra of **24** and **25** showed that these compounds have the same configuration. The configuration of the three acetate groups attached directly to the cyclohexane ring in **24** was found to be *trans*–*trans*. The resonance signal of H-4 appears as a triplet at 5.32 ppm with a coupling constant of $J_{4,3} = J_{4,5} = 9.6$ Hz, which clearly supports the *trans* relation of protons H-4–H-5 as well as H-4–H-3. These configurational assignments showed that the epoxide-ring in **22** underwent a normal *trans*-ring-opening reaction. It was surprising to note that the neighboring acetoxyl group was not involved (no anchimeric assistance) in the ring-opening reaction. This can be attributed to the *cis*-configuration of the acetoxyl group.[9] Hydrolysis of **24** and **25** with ammonia in CH_3OH resulted in the formation of branched hexol **6** in 93% and 95% yields, respectively.

In the second part of this work, we turned our attention to the synthesis of other isomeric branched cyclitols starting from the bicyclic endoperoxide **16**. Unsaturated bicyclic endoperoxides can be easily converted to the corresponding diepoxides upon treatment with cobalt(II) tetraphenylporpyrin (CoTPP).[27,28] The reaction of the endoperoxide **16** with CoTPP in methylene chloride gave the expected diepoxide **27** with *syn*-configuration in 80% yield (Scheme 6).

Bisepoxide **27** was subjected to an acid-catalyzed ring-opening reaction in AcOH/Ac_2O in the presence of sulfamic acid[29] at reflux resulting in the formation of four separable products **28**–**31** in 30%, 10%, 19%, and 29% yields, respectively (Scheme 6). However, when the reaction was carried out in acetic anhydride in the presence of a catalytic amount of H_2SO_4, two products, **28** and **29**, were formed in 47% and 24% yields, respectively (Scheme 7). Moreover, the compound **28** was smoothly converted to **29** with a catalytic amount of H_2SO_4. When the acid concentration was increased, **28** was hydrolyzed to **30**.

Scheme 6. Synthesis of Bisepoxide 27 and Its Acid-Catalyzed Ring-Opening Reaction



Scheme 7. Reaction of Bisepoxide 27 in Ac_2O with a Catalytic Amount of H_2SO_4

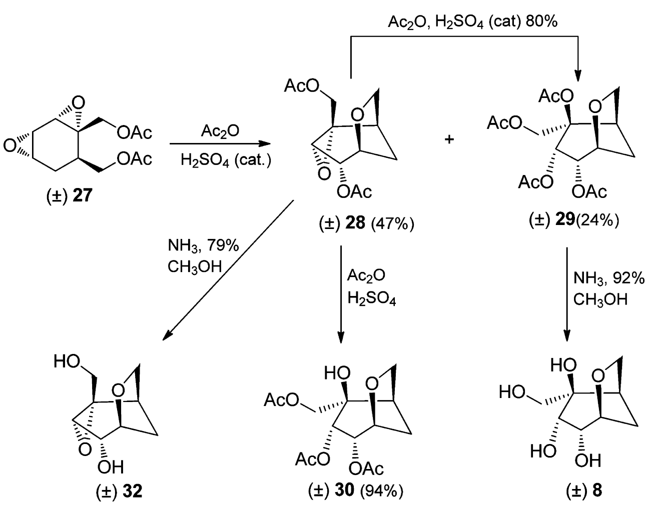
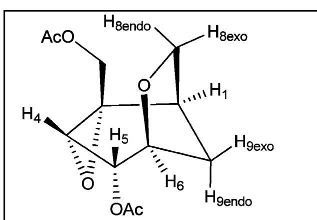
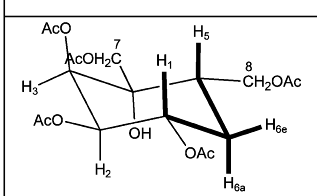


Table 1. Selected ^{1}H−^{1}H Coupling Constants in 28 and 31

 28	$J_{4,5}$ = 4,2 Hz $J_{5,6}$ = 2.8 Hz $J_{5,9exo}$ = 1.5 Hz $J_{6,9exo}$ = 6.1 Hz $J_{6,9endo}$ ≈ 0.0 Hz $J_{9exo,9endo}$ = 12.3 Hz $J_{1,8exo}$ = 4.1 Hz	$J_{1,8endo}$ ≈ 0.0 Hz $J_{1,9exo}$ = 4.1 Hz $J_{8exo,8endo}$ = 8.4 Hz $J_{1,9endo}$ ≈ 0.0 Hz
 31	$J_{3,2}$ = 3.1 Hz $J_{2,1}$ = 10.5 Hz $J_{1,6a}$ = 10.5 Hz $J_{1,6e}$ = 5.1 Hz $J_{6a,6e}$ = 12.3 Hz	$J_{7,7'}$ = 12.0 Hz $J_{8,8'}$ = 11.5 Hz $J_{5,8}$ = 6.4 Hz $J_{5,8'}$ = 5.9 Hz

After the successful separation of compounds **28**−**31**, we determined the constitution of **28** by using NMR spectroscopic data (COSY, HSQC, HMBC). The gated decoupled ^{13}C NMR spectrum of **28** clearly indicated that one of the epoxide rings, where the acetoxymethylene group is attached, was retained. The large coupling constant observed in the signal at 52.7 (d, ^1J = 184.0 Hz) indicated the presence of an epoxide ring, whereas the other coupling constants observed between ^{13}C and ^{1}H (157.0−128.8 Hz) lay within the expected ranges.[30] Further analysis of the HMBC spectrum of **28** showed that one of the acetyl groups present in the starting material **27** was removed during the ring-opening reaction, indicating that this group was involved in the ring-opening reaction. After careful analysis of all possible coupling constants, we assigned the *cis*-configuration to the epoxide ring and the acetoxyl group attached to C-5 (Table 1). This configuration was further proved later by comparison with the structure of **30**, which was obtained by single crystal X-ray analysis.

The geometry-optimized (DFT, B3LYP at 6-31G** level) structure of **27** (Figure 5) shows that one of the acetoxyl groups

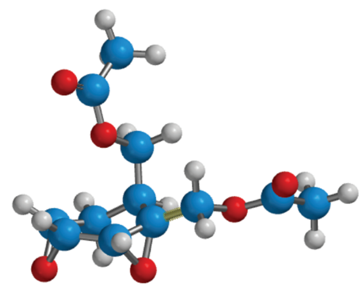
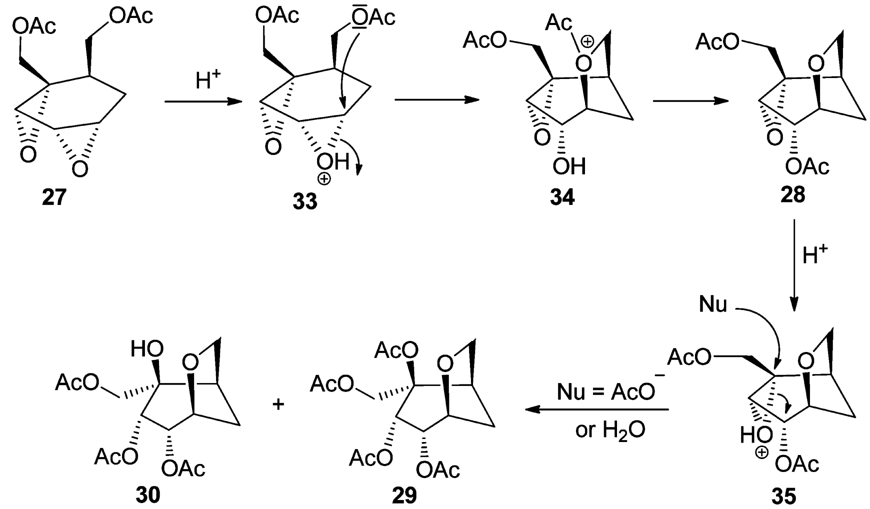


Figure 5. Geometry-optimized structure of **27**.

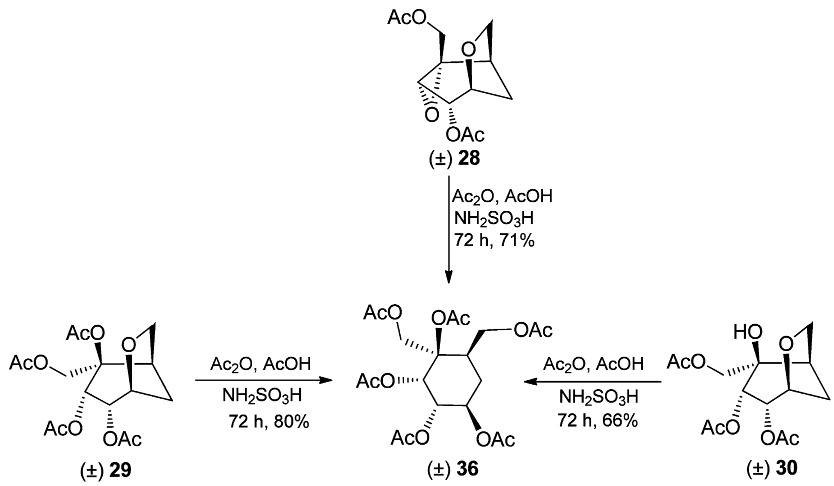
exists in a rigid conformation and is ideally aligned to effect neighboring group participation. Probably, the initially protonated epoxide ring **33** undergoes an attack by the ester oxygen atom to form the intermediate **34**. Removal of the acetoxyl group from **34** followed by acetylation of the epoxide oxygen provides the monoepoxide **28**.[31] This attack also explains the configurations of the acetate groups in **28**−**30** (Scheme 8).

The ring-opening reaction of **28** results in the formation of **29** and **30**. Protonation of the second epoxide ring forms the intermediate **35**, which can undergo two different ring-opening reactions. Since the configuration of the acetoxymethylene

Scheme 8. Mechanism of Formation of 28−30 by Hydrolysis of 27



Scheme 9. Synthesis of Hexaacetate 36 Starting from 28−30



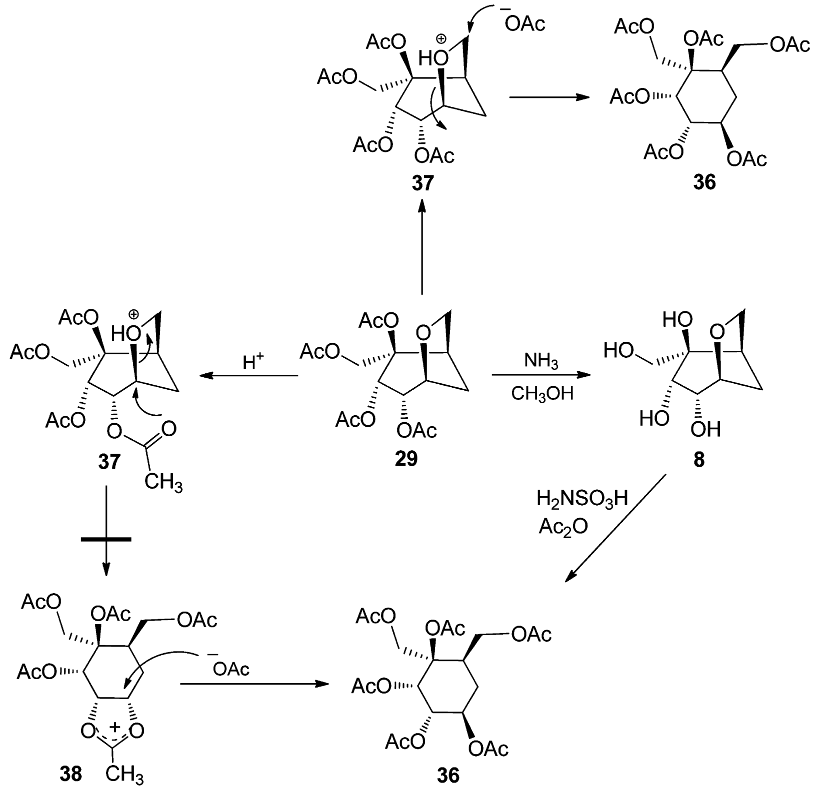
groups in **29** and **30** are inverted, we assumed that the more stable tertiary carbocation is formed during the epoxide ring-opening reaction, which is then attacked by water and acetate anion from the less crowded side to give **29** and **30**. Finally, X-ray analysis of **30** confirmed all structural findings in **30** as well as in **29** (Supporting Information).

Finally, the structure of the ring-opening product **31** was found to be *rel*-(1*S*,2*R*,3*R*,4*S*,5*S*)-4-hydroxy-4,5-bis(acetoxymethyl)-cyclohexane-1,2,3-triyl triacetate based on the analysis of NMR spectroscopic data (COSY, HSQC, HMBC). To determine the exact configuration of **31**, we analyzed the splitting pattern of the AB system arising from methylene protons H_{6a} and H_{6e} (Table 1). The diastereotopic methylene protons in **31** give rise to an AB system. The A part (H_{6e}) of this system is overlapped by methyl ester resonances, whereas the B part (H_{6a}) appears as a doublet of triplets at 1.69 ppm with coupling constants of J = 11.5 and 12.3 Hz. Doublet splitting (12.3 Hz) is due to the geminal coupling ($J_{6a,6e}$) of protons H_{6a} and H_{6e}. Triplet splitting (11.5 Hz) arises from the coupling between the methylene proton H_{6a} and the vicinal protons H_1 and H_5. The geminal coupling is within the expected range.[31] The large vicinal couplings indicate that the coupled protons (H_{6a}, H_1, and H_5) have an axial conformation; in other words, the substituents (OAc and CH_2OH) attached to the C-1 and C-5 carbon atoms have a *cis*-configuration. The coupling constant between the protons H_1 and H_2 (J = 10.5 Hz) indicates the *trans* configuration of these protons. On the other hand, the smaller coupling constant (J = 3.1 Hz) measured between the protons H_2 and H_3 shows the axial−equatorial orientation of the protons and the *cis*-configuration of the substituent. All these data confirm the proposed structural assignment of **31**.

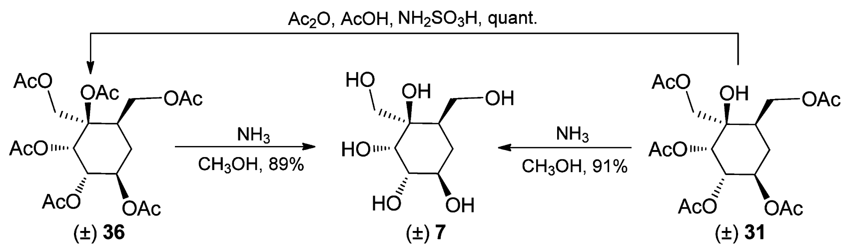
The formation of skeletons **28**−**30** is interesting. To synthesize cyclitols derived from this skeleton, the bicyclic compounds **28** and **29** were submitted to a hydrolysis reaction with ammonia in methanol. The obtained epoxydiol **32** and tetrol **8** were isolated, and their structures were determined unambiguously (Scheme 7).

We then extended this synthetic scheme to the preparation of the desired branched cyclitol **7** by cleavage of the oxomethylene bridges in **28**−**30** followed by hydrolysis of acetate groups. During the ring-opening reaction of **27** with sulfamic acid, **31** was formed in only 29% yield. We were not able to decide at this stage whether **31** was a primary product formed directly by ring-opening of diepoxide **27** or was formed by subsequent ring-opening of **28**−**30**. To address this question, isolated isomers **28**−**30** having oxomethylene bridges were submitted to a

Scheme 10. Mechanism of Formation of 36 from 28−30



Scheme 11. Synthesis of Hexol 7 Starting from 31 and 36



hydrolysis reaction with sulfamic acid in a mixture of Ac_2O/AcOH at reflux temperature. In all three cases, we observed the formation of the same hexaacetate **36** in high yields (Scheme 9). Acetylation of **31** also gave the same hexaacetate **36** (Scheme 11). Since the configuration in **31** during acetylation of the hydroxyl group will not change, we assigned the same configuration of the substituents in **31** to those in **36**.

The *cis*-opening of the oxomethylene bridge in **28−30** needs explanation. It is likely that neighboring group participation controls the mode of the reaction. The initially protonated bridge oxygen in **37** can be attacked by the adjacent acetoxy group to form cyclic oxolonium ion **38**, which then can undergo ring-opening by attack of the acetate anion. To determine the involvement of any neighboring group participation, the acetate groups in **29** were removed and the formed tetrol **8** was treated with sulfamic acid under the same reaction conditions as shown in Scheme 10. The formed hexaacetate **36** was identical to those obtained from the reaction of **28−30** with sulfamic acid. We concluded that the acetate group was not involved during the ring-opening reaction. For the opening of the oxomethylene bridge we suggest the following mechanism as shown in Scheme 10. The acetate anion attacks the protonated oxomethylene bridge in **37** from the back of methylene carbon so that the original configuration at the bridgeheads will be retained in the product.

Finally, deacetylation of **31** and **36** with ammonia gave the same hexol **7**, which furthermore indicated that **31** and **36** have the same configuration (Scheme 11). The H_{6a} proton in **7** resonates as a doublet of triplets at 1.35 ppm with coupling constants of 13.5 Hz (geminal coupling) and 11.1 Hz (vicinal coupling). The large vicinal couplings between the protons H_{6a} and the protons H_1 and H_5 here also indicate the *cis*-configuration of the hydroxyl group and the hydroxymethyl group attached to C-1 and C-5 in **7**.

α-Glycosidase Inhibition Study. The inhibitory activities of compounds **18**, **26**, **6**, **32**, **8**, and **7** were screened against α-glycosidase. The results are summarized in Table 2. While the compounds **6**, **7**, **8**, **26**, and **32** were found to be weak inhibitors of α-glucosidase, the tetrol **18** turned out to be a stronger inhibitor toward α-glycosidase with an inhibition of 64.6 ± 2.2% for 30 μM concentration (IC_{50} = 24 μM). Although the activity of **18** is lower when compared to commercially available

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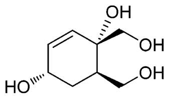
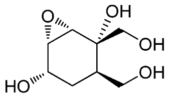
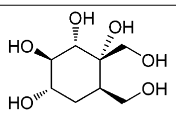
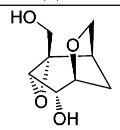
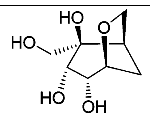
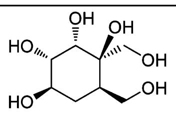
Table 2. Inhibition of α-Glycosidase by Racemic 18, 26, 6, 32, 8, and 7

Compound	Inhibition[a] (%)	IC_{50} (μM)[e]
 (±) **18**	64.6±2.2[a,b]	24
 (±) **26**	8.7±1.2[a,c]	NT[f]
 (±) **6**	3.0±2.0[a,d]	NT[f]
 (±) **32**	13.0±2.4[a,b]	NT[f]
 (±) **8**	12.3±6.6[a,c]	NT[f]
 (±) **7**	10.6±2.19[a,d]	NT[f]

[a]Four experiments were performed for all compounds in each experiment duplicated. [b]Inhibition by 30 μM compound. [c]Inhibition by 400 μM compound. [d]Inhibition by 40 μM compound. [e]Concentration required for 50% inhibition of the enzyme activity under the assay conditions. [f]NT = not tested.

antidiabetics such as miglitol (IC_{50} = 1.3 μM), voglibose (IC_{50} = 0.11 μM), and acarbose (IC_{50} = 0.35 μM),[32] the inhibitory activity of tetrol **18** against α-glycosidase is comparable with respect to newly synthesized carbasugars.[8,33,34]

■ CONCLUSION

The methodology detailed herein facilitated the convenient conversion of the diene **13** into various carbasugar derivatives. The oxygen functionalities were introduced by photooxygenation of the diene unit to give an unsaturated bicyclic endoperoxide. Cleavage of the oxygen−oxygen bond followed by epoxidation of the double bond and ring-opening of the formed epoxide resulted in the formation of **6**, **18**, and **26**. The rearrangement of the unsaturated bicyclic endoperoxide **16** to the corresponding diepoxide **28** with CoTPP followed by an epoxide-ring-opening reaction in the presence of sulfamic acid and removal of acetate groups gave bicylic carbasugars **32** and **8** and the monocyclic carbasugar **7**. This methodology also provides an entry to the synthesis of carbasugar derivatives as well as for aminocarbasugars. Six compounds, **6**, **7**, **8**, **18**, **26**, and **32**, were screened against α-glycosidase. The tetrol **18** showed comparable inhibition.

■ EXPERIMENTAL SECTION

***rel*-(4*R*,5*S*)-4,5-Bis(hydroxymethyl)cyclohexene (10).** Compound **10** was prepared according to the procedure described in the literature.[17]

***rel*-(1*R*,2*S*)-[2-[(Acetyloxy)methyl]cyclohex-4-en-1-yl]methyl Acetate (11).**[18] To a solution of diol **10** (40.0 g, 281.3 mmol), pyridine (68 mL), and dichloromethane (500 mL) was added acetyl chloride (42 mL, 2.1 equiv) dropwise. A colorless precipitate was formed, and the mixture was stirred at room temperature overnight. The mixture was washed with water, 1 N hydrochloric acid, and brine, dried, and concentrated to give **11** as a colorless oil (63.22 g, 98%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (bs, 2H, H-4 and H-5), 4.03 (dd, A part of AB system, *J* = 11.0, 6.5 Hz, 2H, OCH*H*), 3.93 (dd, B part of AB system, *J* = 11.0, 7.3 Hz, 2H, OC*H*H), 2.17−2.06 (m, 4H, 2CH and 2 CH*H*), 2.03 (s, 6H, CH_3), 1.86 (dd, B part of AB system, *J* = 16.4, 5.9 Hz, 2H, C*H*H); ^{13}C NMR (75 MHz, $CDCl_3$) 170.7, 125.0, 64.9, 33.6, 26.5, 20.8.

***rel*-((1*R*,2*S*,4*S*,5*S*)-[2-[(Acetyloxy)methyl]-4,5-dibromocyclohexyl]methyl Acetate (12).** Bromine (10.62 g, 66.6 mmol) in 100 mL of dichloromethane was added dropwise to a magnetically stirred solution of diacetate **11** (10.0 g, 44.2 mmol) in 200 mL of dry dichloromethane at room temperature over a period of 4 h. The mixture was then stirred at room temperature for 6 h. After removal of the solvent, the oily dibromodiacetate **12** (16.06 g, 94%) was used without purification for further reactions: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 (dt, *J* = 10.0, 4.0 Hz, 1H), 4.15−3.95 (m, 5H), 2.48 (dt, *J* = 14.3, 4.2 Hz, 1H), 2.44−2.37 (m, 1H), 2.30−2.25 (m, 1H), 2.18−2.10 (m, 1H), 2.03−1.94 (m, 2H), 2.02 (s, 3H, CH_3), 2.1 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 171.04, 170.99, 65.1, 62.8, 54.50, 53.4 (2C), 38.2, 35.2, 35.4, 21.2, 21.1; IR (KBr, cm^{-1}) 2954, 2899, 1732, 1446, 1367, 1222, 1033, 979, 910, 848, 788, 744, 684, 605. Anal. Calcd for $C_{12}H_{18}Br_2O_4$: C, 37.33; H, 4.70. Found: C, 37.57; H, 4.74.

[2-[(Acetyloxy)methyl]cyclohexa-2,4-dien-1-yl]methyl Acetate (13). To a magnetically stirred solution of dibromodiacetate **12** (20.0 g, 51.82 mmol) in 300 mL of dry benzene was added a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (19.72 g, 129.7 mmol) in 200 mL of dry benzene at room temperature. The resulting mixture was heated at the reflux temperature of benzene for 12 h and then cooled to room temperature. Water (200 mL) was added, and the organic phase washed with saturated aqueous sodium bicarbonate (3 × 250 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give a mixture of the dienes **13** and **14**[19] (9.1 g, 78%) in a ratio of 9:1 as a colorless liquid. An analytically pure sample of **13** was obtained by column chromatography over silica gel eluting with *n*-hexane/EtOAc (5:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.02 (bd, *J* = 5 Hz, 1H), 5.94−5.90 (m, 1H), 5.75−5.71 (m, 1H), 4.63 (AB system, *J* = 11.0 Hz, 2H), 4.09 (dd, A part of AB system, *J* = 10.5, 5.4 Hz, 1H, CH*H*), 3.98 (dd, B part of AB system, *J* = 10.5, 9.1 Hz, 1H, C*H*H), 2.53−2.49 (m, 1H), 2.38−2.34 (m, 2H), 2.09 (s, 3H, CH_3), 2.05 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.7, 126.2, 125.1, 124.4, 123.5, 66.6, 63.0, 32.8, 25.2, 20.9, 20.8; IR (KBr, cm^{-1}) 3043, 2947, 2829, 1735, 1367, 1220, 1070, 1026, 974; HRMS-ESI (*m*/*z*) $[M + H]^+$ calcd for $C_{12}H_{17}O_4$ 225.11268, found 225.10966.

***rel*-(1*R*,4*R*,5*R*)-[4-[(Acetyloxy)methyl]-2,3-dioxabicyclo-[2.2.2]oct-7-en-5-yl]methyl Acetate (16).** A stirred solution of diene **13** (10.0 g, 44.60 mmol) and 250 mg of tetraphenylporphyrin (TPP) in 250 mL of CH_2Cl_2 was irradiated with projection lamp (500 W) while oxygen gas passed through the solution. The reaction was completed after 12 h. The solvent was evaporated under reduced pressure. The residue (9.94 g, 87%) was crystallized from diethyl ether to give pure bicyclic endoperoxide **16** (9.37 g, 82%) as colorless crystals: mp 78−79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (dd, A part of AB system, $J_{7,8}$ = 8.5 Hz and $J_{7,1}$ = 5.9 Hz, 1H, H-7) 6.37 (d, B part of AB system, $J_{7,8}$ = 8.5, 1H, H-8), 4.75−4.70 (m, 1H, H-1)), 4.48 (d, A part of AB system, $J_{10,10'}$ = 12.9 Hz, 1H, H-10 or H-10′), 4.35 (d, B part of AB system, $J_{10,10'}$ = 12.9 Hz, 1H, H-10′ or H-10), 3.84 (dd, A part of AB system, $J_{9,9'}$ = 11.8 Hz and $J_{9,7(9',7)}$ = 5.9 Hz, 1H, H-9 or H-9′), 3.69 (dd, B part of AB- system $J_{9,9'}$ = 11.8 Hz and $J_{9,6(9',6)}$ = 8.5 Hz, 1H, H-9 or H-9′), 2.82 (m, 1H, H-6), 2.53 (ddd, $J_{5,5'}$ = 13.5 Hz, *J* = 9.4, 3.8 Hz, 1H, H-8 or H-8′), 2.14 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.09 (ddd, $J_{5,5'}$ = 13.5 Hz, *J* = 3.8, 2.0 Hz, 1H, H-8 or H-8′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (2C), 134.0, 129.1, 78.4, 70.9, 65.8, 63.8, 34.0, 27.1, 21.01, 20.97; IR (KBr, cm^{-1}) 3016, 2970, 2941, 1726, 1365, 1222, 1035, 987, 956, 902, 877. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 55.92; H, 6.35.

***rel*-(1*R*,2*S*,5*S*)-[2-[(acetyloxy)methyl]-2,5-dihydroxycyclohex-3-en-1-yl]methyl Acetate (17).** Bicyclic endoperoxide **16** (4.0 g, 15.62 mmol) was dissolved in absolute methanol (150 mL). Thiourea (1.43 g, 18.8 mmol) was added to the solution. After completion of the addition (ca. 15 min), the mixture was stirred for 24 h at room temperature. The solids were removed by filtration. After the removal of the solvent, the residue was filtered on a short silica gel column (25.0 g) eluting with dichloromethane to yield diol diacetate **17** (3.5 g, 87%). Crystallization from ethyl acetate gave white crystals: mp 108−110 °C (2.97 g, 74%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (ddd, A part of AB system, $J_{4,3}$ = 10.0 Hz, $J_{4,5}$ = 4.1 Hz, and $J_{4,6}$ = 1.0 Hz, 1H, H-4), 5.72 (dd, B part of AB system, $J_{3,4}$ = 10.0 Hz and $J_{3,5}$ = 0.6 Hz, 1H, H-3), 4.30 (dd, A part of AB system, $J_{8,8'}$ = 11.3 Hz and $J_{8,1(8',1)}$ = 6.0 Hz, 1H, H-8 or H-8′), 4.25 (q, $J_{5,4} = J_{5,4} = J_{5,6'}$ = 4.1 Hz, 1H, H-5), 4.09 (dd, B part of AB system, $J_{8,8'}$ = 11.3 Hz and $J_{8,1(8',1)}$ = 7.0 Hz, 1H, H-8 or H-8′), 4.11−4.04 (AB- system, $J_{7,7'}$ = 11.7 Hz, 2H, H-7 and H-7′), 3.3−2.9 (br s, 2H, −OH), 2.41 (m, 1H, H-1), 2.10 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 1.92 (ddt, A part of AB system, $J_{6,6'}$ = 14.3 Hz, $J_{6,5(6',5)}$ = 3.6 Hz, and $J_{6,4(6',4)}$ = 1.0 Hz, 1H, H-6 or H-6′), 1.82 (ddd, B part of AB system, $J_{6,6'}$ = 14.3 Hz, J = 11.1, 4.6 Hz, 1H, H-6 or H-6′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.33, 171.31, 133.2, 131.2, 71.4, 67.1, 64.3, 63.3, 38.9, 31.7, 21.2, 21.1; IR (KBr, cm^{-1}) 3387, 3279, 2958, 2926, 2897, 1728, 1462, 1440, 1381,1363, 1305, 1228, 1105, 1035, 1004, 977, 927, 912, 812. Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.73; H, 6.69.

General Procedure for Hydrolysis of Acetates. Synthesis of Cyclitols. Di-, tri-, or tetraacetates (3.0 mmol) were dissolved in 60 mL of absolute methanol. Dry NH_3(g) was passed through solution for 1 h. Then, the flask was closed with a stopper. The solution was stirred for 12 h at room temperature. Evaporation of the solvent and formed acetamide gave the corresponding cyclitols.

***rel*-(1*S*,4*S*,6*R*)-2,3-Bis(hydroxymethyl)cycloheptane-2,5-diol (18).** Diacetate **17** (4.0 g, 15.5 mmol) was hydrolyzed as described above to give tetrol **18** (2.62 g, 97%) as a colorless viscous oil: ^{1}H NMR (300 MHz, CD_3OD) δ 5.83 (ddd, 1H, A part of AB system, $J_{3,2}$ = 10.1 Hz, $J_{3,4}$ = 3.8 Hz and $J_{3,5}$ = 0.9 Hz, 1H, H-3), 5.63 (dd, B part of AB system, $J_{3,2}$ = 10.1 Hz, $J_{2,4}$ = 1.0 Hz, 1H, H-2), 4.9 (s, 4H, −OH), 4.17 (q, $J_{4,3} = J_{4,5} = J_{4,5'}$ = 3.8 Hz, 1H, H-4), 3.73 (dd, A part of AB system, $J_{7,7'}$ = 10.8 Hz and $J_{7,6(7',6)}$ = 5.8 Hz, 1H, H-7 or H-7′), 3.65 (dd, B part of AB system, $J_{7,7'}$ = 10.8 Hz and $J_{7,6(7',6)}$ = 5.8 Hz, 1H, H-7 or H-7′), 3.53−3.42 (AB system, $J_{8,8'}$ = 11.5 Hz, 2H, H-8 and H-8′), 2.17−2.09 (m, 1H, H-6), 1.92 (ddd, A part of AB system, J = 12.9, 10.8, 4.8 Hz, 1H, H-5 or H-5′), 1.82 (ddd, B part of AB system, J = 12.9, 3.8, 1.0 Hz, 1H, H-5 or H-5′); ^{13}C NMR (75 MHz, CD_3OD) δ 133.8, 130.7, 72.4, 65.0, 63.2, 61.5, 41.4, 31.3. IR (KBr, cm^{-1}) 3305, 2931, 1662, 1402, 1203.58, 1043, 999, 756. Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.34; H, 8.31.

***rel*-(1*S*,4*S*,5*R*)-4-(Acetyloxy)-4,5-bis[(acetyloxy)methyl]-cyclohex-2-en-1-yl Acetate (19).** Dihydroxy diacetate **17** (1.0 g, 3.87 mmol) was dissolved in pyridine (2.5 mL) and acetic anhydride Ac_2O (3 mL). The resulting mixture was stirred magnetically at room temperature for 72 h. The mixture was worked up as described above to yield tetraacetate **19** (1.1 g, 83%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.13 (dd, A part of AB system, $J_{3,2}$ = 10.3 Hz, $J_{3,1}$ = 0.9 Hz, 1H, H-3), 5.91 (dd, B part of AB system, $J_{2,3}$ = 10.3 Hz, $J_{2,1}$ = 4.1, 1H, H-2), 5.23 (bq, $J_{1,2} = J_{1,6} = J_{1,5'}$ = 4.1 Hz, 1H, H-1), 4.48 (d, A part of AB system, $J_{8,8'}$ = 12.1 Hz, 1H, H-8 or H-8′) 4.23 (dd, A part of AB system, $J_{7,7'}$ = 11.4 Hz, $J_{7,5}$ = 5.2 Hz, 1H, H-7 or H-7′), 4.11 (d, B part of AB system, $J_{8,8'}$ = 12.1 Hz and, 1H, H-8 or H-8′), 3.98 (dd, B part of AB system, $J_{7,7'}$ = 11.4 Hz and $J_{7,5}$ = 7.3 Hz, 1H, H-7 or H-7′), 2.92 (dq, J = 5.0, 7.1 Hz, 1H, H-5), 2.05 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.97 (dd, J = 7.0, 4.7 Hz, 2H, H-6 and H-6′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 170.9, 170.5, 170.0, 131.6, 128.6, 79.6, 65.6, 64.0, 63.0, 36.3, 28.4, 22.2, 21.5, 21.1, 21.0; IR (KBr, cm^{-1}) 2956, 1732, 1435, 1367, 1222, 1031, 1016, 972, 941, 858, 765, 638. Anal. Calcd for $C_{16}H_{22}O_8$: C, 56.13; H, 6.48. Found: C, 56.27; H, 6.40.

***rel*-[(1*R*,2*S*,5*S*)-5-(Acetyloxy)-2-[(acetyloxy)methyl]-2-hydroxy-cyclohex-3-en-1-yl]methyl Acetate (21).** Dihydroxy diacetate **17** (1.29 g, 5.0 mmol) was dissolved in pyridine (3 mL) and acetic anhydride (5 mL). The resulting mixture was stirred magnetically at room temperature for 6 h. The mixture was acidified with ice-cold HCl (100 mL, 5%) and washed with water (2 × 300 mL) and saturated $NaHCO_3$ (2 × 100 mL). The organic phase was dried (Na_2SO_4), and evaporation of the solvent gave triacetate **21** (1.2 g, 80%) as the sole product as a colorless viscous oil. An analytical pure sample was obtained by chromatography on a short silica gel column eluting with EtOAc/*n*-hexane (2:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddd, A part of AB system, $J_{4,3}$ = 10.3 Hz, $J_{4,5}$ = 4.1 Hz and $J_{4,6}$ = 1.2 Hz, 1H, H-4), 5.81 (dd, B part of AB system, $J_{3,4}$ = 10.3 Hz, $J_{3,5}$ = 0.6 Hz, 1H, H-3), 5.23 (bq, $J_{5,4} = J_{5,6} = J_{5,6'}$ = 4.1 Hz 1H, H-5), 4.26 (dd, A part of AB system, $J_{7,7'}$ = 11.4 Hz and $J_{(7,1')}$ = 6.2 Hz, 1H, H-7 or H-7′), 4.12 (dd, B part of AB system, $J_{7,7'}$ = 11.4 Hz and $J_{(7,1)}$ = 6.5 Hz, 1H, H-7 or H-7′), 4.08 (s, 2H, H-8 and H-8′), 2.42−2.34 (m, 1H, H-1), 2.28 (s, 1H, OH), 2.07 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.04 (s, 3H, 1.90 (ddd, A part of AB system, J = 14.6, 4.1, 1.2 Hz, 1H, H-6 or H-6′), 1.85 (ddd, J = 14.6, 11.4, 4.7 Hz, 1H, H-6 or H-6′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 171.1, 170.8, 135.4, 127.2, 71.4, 67.0, 65.7, 64.0, 39.2, 28,6, 21.5, 21.2, 21.1; IR (KBr, cm^{-1}) 3464, 3240, 3151, 2966, 1732, 1693, 1525, 1487, 1367,1230, 1211, 1020, 976. Anal. Calcd for $C_{14}H_{20}O_7$: C, 55.99; H, 6.71. Found: C, 55.81; H, 6.64.

Reaction of Triacetate 21 with *m*-Chloroperbenzoic Acid. Triacetate **21** (6.35 g, 21.14 mmol) was dissolved in 400 mL of dichloromethane and *m*-CPBA (10.95 g, 44.4 mmol, 70%) was added. The reaction mixture was stirred magnetically at room temperature for one week. After completion of the reaction, saturated $NaHSO_3$ (400 mL) was added and the mixture was stirred for 20 min. The organic layer was separated, washed with saturated $NaHCO_3$ (3 × 300 mL) and dried ($MgSO_4$). After removal of solvent, the residue was chromatographed on silica gel eluting with EtOAc/hexane (1:4) to give two separable fractions.

***rel*-((1*R*,2*S*,3*R*,5*S*,6*R*)-5-Acetoxy-2-hydroxy-7-oxabicyclo-[4.1.0]heptane-2,3-diyl)bis(methylene) diacetate (23).** Compound **23** was isolated as the first fraction: colorless oil (470 mg, 1.48 mmol 7%); TLC (hexane/EtOAc, 1:1) R_f = 0.52; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.15 (ddd, $J_{5,4}$ = 11.0 Hz, $J_{5,4'}$ = 5.7 Hz and $J_{5,6}$ = 1.6 Hz, 1H, H-5), 4.25 (d, A part of AB system, $J_{7,7'}$ =11.6 Hz, 1H, H-7 or H-7′), 4.27 (dd, A part of AB system, $J_{8,8'}$ =11.4 Hz and $J_{8,3}$ = 5.7 Hz, 1H, H-8 or H-8′), 4.17 (dd, B part of AB system, $J_{7,7'}$ = 11.6 Hz, 1H, H-7 or H-7′), 3.91 (dd, B part of AB system, $J_{8,8'}$ = 11.4 Hz and $J_{8',3}$ = 7.0 Hz, H-8 or H-8′), 3.53 (bdt, $J_{6,1}$ = 4.0, and $J_{6,5} = J_{6,4}$ = 1.6 Hz, 1H, H-6), 3.36 (d, $J_{1,6}$ = 4.0 Hz, 1H, H-1), 2.70 (bs, 1H, −OH), 2.10 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.84−1.65 (m, 2H), 1.56 (dd, $J_{4,4'}$ = 12.7 Hz and $J_{4,5}$ = 11.0 Hz, 1H, H-4 or H-4′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 170.9, 170.7, 70.2, 68.4, 67.0, 63.8, 59.4, 56.3, 38.4, 22.8, 21.3, 21.2, 21.1; IR (KBr, cm^{-1}) 3466, 2947, 1732, 1433, 1367, 1226, 1028, 979, 912, 815, 734, 702. Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 53.20; H, 6.25.

***rel*-((1*S*,2*S*,3*R*,5*S*,6*S*)-5-Acetoxy-2-hydroxy-7-oxabicyclo-[4.1.0]heptane-2,3-diyl)bis(methylene) Diacetate (22).** Compound **22** was isolated as the second fraction: colorless oil (5.01 g, 75%); TLC (hexane/EtOAc, 1:1) R_f = 0.38; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.18 (dt, J = 5.0 and 3.6 Hz,1H, H-5), 4.25 (dd, A part of AB system, $J_{8,8'}$ = 11.4 Hz and $J_{8,3}$ = 5.2 Hz, 1H, H-8 or H-8′), 4.23 (d, A part of AB system, $J_{7,7'}$ = 11.6 Hz, 1H, H-7 or H-7′), 4.21 (AB system, $J_{7,7'}$ = 12.0 Hz, 2H, H-7 and H-7′), 4.02 (dd, B part of AB system, $J_{8,8'}$ = 11.4 Hz and $J_{8',3}$ = 6.7 Hz, H-8 or H-8′), 3.61 (t, $J_{6,1} = J_{6,5}$ = 4.1, 1H, H-6), 3.31 (d, $J_{1,6}$ = 4.1 Hz, 1H, H-1), 2.70−2.80 (bs, 1H, −OH), 2.33−2.24 (m, 1H, H-3), 2.12 (s, 3H, CH_3), 2.119 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 1.84−1.65 (m, 2H, H-4 and H-4′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.94, 170.90, 70.9, 66.4, 65.9, 63.3, 57.6, 55.3, 37.7, 27.4, 21.2, 21.15, 21.1; IR (KBr, cm^{-1}) 3468, 2958, 1732, 1433, 1369, 1226, 1028, 910, 875. Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 53.58; H, 6.31.

***rel*-(1*S*,2*S*,3*R*,5*S*,6*S*)-2,5-Acetoxy-7-oxabicyclo[4.1.0]-heptane-2,3-diyl)bis(methylene) Diacetate (*syn*-20).** To a stirred solution of monoepoxide **22** (1.2 g, 3.80 mmol) in Ac_2O (5 mL) was added a catalytic amount of H_2SO_4 (one drop). The solution was stirred for 12 h at room temperature, and then CH_2Cl_2 (300 mL) was added. The organic phase was extracted with saturated $NaHCO_3$ (2 × 150 mL) and then with water (3 × 300 mL), dried over $MgSO_4$, and filtered. The solution was evaporated under reduced pressure to give the tetraacetate ***syn*-20** (1.0 g, 74%), which was crystallized from EtOAc to give colorless prisms: mp 85−88 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.20 (dt, $J_{5,4}$ = $J_{5,4'}$ = 7.3 Hz and $J_{5,6}$ = 2.9, 1H, H-5), 4.97 (d, A part of AB system, $J_{7,7'}$ = 12.3 Hz, 1H, H-7 or H-7′), 4.18 (dd, A part of AB system, $J_{8,8'}$ = 11.4 Hz and $J_{8,3}$ = 5.3 Hz, 1H, H-8 or H-8′), 4.16 (d, B part of AB system, $J_{7,7'}$ = 12.3 Hz, 1H, H-7 or H-7′), 3.97 (dd, B part of AB system, $J_{8,8'}$ = 11.4 Hz and $J_{8',3}$ = 7.9 Hz, 1H, H-8 or H-8′), 3.67 (d, $J_{1,6}$ = 3.5 Hz, 1H, H-1), 3.54 (dd $J_{6,1}$ = 3.5 Hz and $J_{6,5}$ = 2.9 Hz, 1H, H-6), 2.41−2.49 (m, 1H, H-3), 2.11 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.76−1.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (2C), 170.3 (2C), 78.2, 67.1, 62.6, 62.4, 54.7, 54.5, 37.5, 24.3, 21.7, 21.3, 21.1, 21.0; IR (KBr, cm^{-1}) 2947, 2852, 1733, 1435, 1367, 1222, 1031, 906, 873, 815, 734. Anal. Calcd for $C_{16}H_{22}O_9$: C, 53.63; H, 6.19. Found: C, 53.58, H, 5.96.

***rel*-(1*S*,2*S*,3*R*,4*S*,6*R*)-1,6-Bis(acetoxymethyl)cyclohexane-1,2,3,4-tetrayl Tetraacetate (25).** Epoxy triacetate **22** (3.0 g, 9.49 mmol) was dissolved in Ac_2O (15 mL), and H_2SO_4 (12 drops) was added. The reaction was carried out as reported in the synthesis of ***syn*-20**. A dark residue was formed that was chromatographed on silica (50 g), eluting with hexane/ethyl acetate (4/1) to give **25** (3.28 g, 75%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (d, $J_{3,4}$ = 9.9 Hz, 1H, H-3), 5.40 (t, $J_{4,3}$ = $J_{4,5}$ = 9.9 Hz, 1H, H-4), 5.20 (ddd, $J_{5,6}$ = 11.7 Hz, $J_{5,4}$ = 9.9 Hz, and $J_{5,6'}$ = 5.3 Hz, 1H, H-5), 4.65 (d, A part of AB system, $J_{8,8'}$ = 11.7 Hz, 1H, H-8 or H-8′), 4.56, (d, B part of AB system, $J_{8,8'}$ = 11.7 Hz, 1H, H-8 or H-8′), 4.33 (dd, A part of AB system, $J_{7,7'}$ = 12.0 Hz and $J_{7,1}$ = 5.9 Hz, 1H, H-7 or H-7′), 4.20 (dd, B part of AB system, $J_{7,7'}$ =12.0 Hz and $J_{7',1}$ = 5.0 Hz, 1H, H-7 or H-7′), 3.27 (m, 1H, H-1), 2.16 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 2.16−2.08 (m, 1H, H-6 or H-6′), 1.87−1.75 (m, 1H, H-6 or H-6′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.28, 170.23, 169.9 (2C), 169.8, 84.2, 72.6, 70.0, 69.8, 63.4, 63.1, 37.0, 28.7, 21.9, 21.1 (2C), 20.9, 20.83, 20.76; IR (KBr, cm^{-1}) 2970, 1737, 1433, 1367, 1217, 1029, 952, 898, 864, 734 700, 640. Anal. Calcd for $C_{20}H_{28}O_{12}$: C, 52.17; H, 6.13. Found: C, 52.12, H, 6.08.

***rel*-(1*S*,2*R*,3*S*,4*S*,5*R*)-4,5-Bis(acetoxymethyl)-4-hydroxycyclohexane-1,2,3-triyl Triacetate (24).** To a suspension of epoxy acetate **22** (570 mg, 1.8 mmol) in water (20 mL) was added H_2SO_4 (2 mL), and the resulting mixture was stirred for 24 h at room temperature. After neutralization of the solution with saturated $NaHCO_3$, the water was evaporated, the residue was dissolved in MeOH, and the solid was filtered off. MeOH was evaporated, and without any purification, pyridine (1.5 mL) and acetic anhydride (2 mL) were added to the residue. The mixture was stirred for 12 h, and ethyl acetate (150 mL) was added. The mixture was hydrolyzed with ice-cooled HCl (100 mL, 5%), neutralized with saturated $NaHCO_3$ solution, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (10.0 g) eluting with hexane/ethylacetate (6:1) to yield pentaacetate **24** (600 mg, 80%), which was crystallized from hexane/EtOAc to give colorless crystals: mp 132−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.32 (t, A part of AB system, $J_{4,3}$ = $J_{4,5}$ = 9.6 Hz, 1H, H-4), 5.17 (d, B part of AB system, $J_{3,4}$ = 9.6, 1H, H-3), 5.03 (ddd, $J_{5,6}$ = 11.7 Hz, $J_{5,4}$ = 9.6 Hz, and $J_{5,6'}$ = 5.3 Hz, 1H, H-5), 4.14 (dd, A part of AB system, $J_{7,7'}$ =11.9 Hz and $J_{7,1}$ = 6.2 Hz, 1H, H-7 or H-7′), 4.08 (dd, B part of AB system, $J_{7,7'}$ = 11.9 Hz and $J_{7,7'}$ = 4.9 Hz, 1H, H-7 or H-7′), 3.97 (bs, 2H, H-8 and H-8′), 2.24−2.27 (m, 1H, H-1), 2.20−1.57 (m, 2H, H-6 and H-6′), 2.03 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 1.89 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 170.7, 170.4, 170.3, 169.9, 74.6, 72.7, 72.2, 70.0, 66.0, 63.6, 40.0, 28.0, 21.1(2C), 20.9 (2C), 20.7; IR (KBr, cm^{-1}) 3493, 2949, 1726, 1456, 1367, 1220, 1029, 983, 881. Anal. Calcd for $C_{18}H_{26}O_{11}$: C, 51.67; H, 6.26. Found: C, 52.11; H, 6.53.

***rel*-(1*S*,2*S*,3*R*,4*S*,6*R*)-1,6-Bis(hydroxymethyl)cyclohexane-1,2,3,4-tetraol (6).** Pentaacetate **24** (1.0 g, 2.39 mmol) was dissolved in 50 mL of absolute methanol and hydrolyzed with dry $NH_{3(g)}$ for 3 h as described above. Evaporation of methanol and formed acetamide gave hexol **6** (0.47 g, 93%) as colorless plates from ethanol/*n*-hexane (1:1): mp 195−198 °C; ^{1}H NMR (300 MHz, D_2O) δ 4.65 (bs, 6H, OH), 3.59−3.22 (m, 7H), 1.93 (m, 1H, H-5), 1.79 (ddd, 1H, $J_{6,6'}$ = 12.2 Hz, J = 5.3, 2.8 Hz, 1H, H-6 or H-6′), 1.59 (dt, $J_{6,6'}$ = 12.2 Hz and J = 4.4 Hz, 1H, H-6 or H-6′); ^{13}C NMR (75 MHz, D_2O) δ 76.3, 76.1, 72.9, 69.2, 64.8, 60.3, 41.3, 28.6; IR (KBr, cm^{-1}) 3446, 3342, 3155, 2956, 2927, 2893, 1384, 1363, 1327,1151, 1089, 1058, 1033, 1014, 975, 941. Anal. Calcd for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 46.01; H, 7.78.

***rel*-(1*S*,2*S*,3*R*,5*S*,6*S*)-2,3-Bis(hydroxymethyl)-7-oxabicyclo-[4.1.0]heptane-2,5-diol (26).** Epoxy triacetate **22** (0.30 g, 0.95 mmol) was hydrolyzed with $NH_{3(g)}$ as described above to give epoxy tetrol **26** (0.15 g, 86%) as a colorless viscous oil: ^{1}H NMR (300 MHz, D_2O) δ 4.06 (m, 1H), 3.57−3.39 (m, 3H), 3.34 (t, J = 3.3 Hz, 1H, H-6), 3.24 (dd, B part of AB system, J = 11.0, 8.0 Hz, 1H, H-8 or H-8′), 3.15 (d, 1H, J = 4.0 Hz, 1H, H-1), 1.70−1.60 (m, 1H, H-3), 1.59−1.45 (m, 1H, H-4 or H-4′), 1.42−1.37 (m, 1H, H-4 or H-4′); ^{13}C NMR (75 MHz, D_2O) δ 72.6, 62.9 (2C), 60.5, 58.5, 57.2, 38.7, 29.5; IR (KBr, cm^{-1}) 3331, 3298, 3286, 2933, 1406, 1332, 1257, 1031. Anal. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.16; H, 7.07.

Deacetylation of Hexaacetate with $NH_{3(g)}$ in MeOH. Hexaacetate **25** (1.0 g, 2.17 mmol) was hydrolyzed with MeOH in the presence of $NH_{3(g)}$ as described above to give hexol **6** (0.43 g, 95%) as colorless crystals. The spectral data of this compound was the same as the compound, which was obtained by hydrolysis of **24** with ammonia.

***rel*-(1*S*,2*S*,4*S*,5*R*,7*S*)-[4-[(Acetyloxy)methyl]-3,8-dioxatricyclo-[5.1.0.0^{2,4}]oct-5-yl]methyl Acetate (27).** To a magnetically stirred solution of bicyclic endoperoxide **16** (5.0 g, 19.5 mmol) in 150 mL of CH_2Cl_2 was added a solution of cobalt *meso*-tetraphenylporphyrin (180 mg) in 25 mL of CH_2Cl_2 at 0 °C. After complete addition (20 min), the mixture was allowed to stir for 30 min at room temperature. Removal of solvent and chromatography of the residue on 50 g silica gel eluting with hexane/EtOAc (5:1) gave bisepoxide **27** (4.0 g, 80%) as colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (d, $J_{7,7'}$ = 12.6 Hz, 1H, H-8 or H-8′), 4.24 (dd, A part of AB system, $J_{7,7'}$ =11.6 Hz and $J_{7,6}$ = 5.8 Hz, 1H, H-7 or H-7′), 4.17 (dd, B part of AB system, $J_{7,7'}$ =11.6 Hz and $J_{7,6}$ = 5.3 Hz, 1H, H-7 or H-7′), 3.94 (d, $J_{8,8'}$ = 12.6 Hz, 1H, H-8 or H-8′), 3.39 (d, A part of AB system, $J_{2,3}$ = 2.6 Hz, 1H, H-2), 3.31 (dd, B part of AB system $J_{3,4}$ = 4.1 Hz and $J_{3,2}$ = 2.6 Hz, 1H, H-3), 3.03 (dt, 1H, J = 5.6, 3.8 Hz, 1H, H-5), 2.5−2.42 (m, 1H, H-6), 2.08 (s, 3H, CH_3), 2.07 (s,3H, CH_3), 1.94−1.88 (m, 2H, H-5 and H-5′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.7, 65.3, 64.5, 57.3, 51.6, 48.0, 46.3, 33.1, 24.5, 21.2, 21.0; IR (KBr, cm^{-1}) 2956, 1735, 1431, 1365, 1224, 1103, 1029, 975. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.27; H, 6.40.

Ring Opening of Bisepoxide 27 with Sulfamic Acid. Bisepoxide **27** (3.0 g,11.71 mmol) was dissolved in 10 mL of Ac_2O/AcOH (1:1), and then sulfamic acid (100 mg) was added. The resulting solution was heated at reflux temperature for 12 h. After the mixture was cooled to room temperature, ice-cooled HCl solution (150 mL, 5%) was added, and the solution was extracted with methylene chloride (3 × 75 mL). The organic phase was washed with water and dried ($MgSO_4$). After removal of the solvent under reduced pressure, the residue was chromatographed on a silica gel column (120 g) eluting with hexane/EtOAc (4:1). Four compounds **28**, **29**, **30**, and **31** were isolated in the following order:

***rel*-((1*R*,2*S*,4*S*,5*S*,6*R*)-5-Acetoxy-3,7-dioxatricyclo[4.2.1.0^{2,4}]-nonan-2-yl)methyl acetate (28):** 0.9 g, 30% as colorless needles from ether; mp 92−94 °C; TLC (hexane/EtOAc, 1:1) R_f = 0.84, ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.73 (ddd, J = 4.2, 2.8, 1.5 Hz, 1H, H-5), 4.53 (d, A part of AB system, J = 12.5 Hz, 1H, H-10), 4.06 (dt, J = 6.2, 2.1 Hz, 1H, H-6), 3.98 (dd, A part of AB system, J = 8.4, 0.9 Hz, 1H, H-8$_{endo}$), 3.96 (d, B part of AB system, J = 12.5 Hz, 1H, H-10′), 3.80 (dd, B part of AB system, J = 8.4, 3.9 Hz, 1H, H-8$_{exo}$), 3.33 (ddd, J = 4.1, 1.9, 0.6 Hz, 1H, H-4), 2.74 (bt, J = 4.1 Hz, 1H, H-1), 2.31 (d, J = 12.1 Hz, 1H, H-9$_{endo}$), 1.58 (dddd, J = 12.1, 6.1, 4.4, 1.5 Hz, 1H, H-9$_{exo}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 170.3, 74.5, 70.0, 69.9, 64.1, 60.0, 52.7, 35.6, 27.4, 21.0, 20.96; gated decoupled ^{13}C NMR (75 MHz, $CDCl_3$) only one bond C−H couplings are given δ 170.8 (s), 170.3 (s), 74.5 (t, ^1J = 157.0 Hz), 70.0 (d, ^1J = 150.0 Hz), 69.9 (t, ^1J = 149.0 Hz), 64.1 (t, ^1J = 148.0 Hz), 60.0 (s), 52.7 (d, ^1J = 184.0 Hz), 35.6 (d, ^1J = 141.0 Hz), 27.4 (t, ^1J = 136.2 Hz), 21.0 (q, ^1J = 129.8 Hz), 20.96 (q, ^1J = 128.8 Hz); IR (KBr, cm^{-1}) 3001, 2962, 2949, 2879, 1745, 1726, 1433, 1367, 1232, 1220, 1197, 1095, 1031, 1006, 974, 883. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.08; H, 6.35.

***rel*-(1*R*,2*S*,3*S*,4*S*,5*R*)-2-(Acetoxymethyl)-6-oxabicyclo[3.2.1]-octane-2,3,4-triyl triacetate (29):** 0.42 g, 10% as colorless crystals from EtOAc/*n*-hexane; mp 97−99 °C; TLC (hexane/EtOAc, 1:1) R_f = 0.64; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (d, *J* = 5.2 Hz, 1H, H-3), 5.27 (dt, *J* = 5.0, 1.2 Hz, 1H, H-4), 5.17 (d, A part of AB system, *J* = 12.7 Hz, 1H, H-9), 4.56 (d, B part of AB system, *J* = 12.7 Hz, 1H, H-9′), 4.27 (t, *J* = 5.1 Hz, 1H, H-5), 4.11 (bd, A part of AB system, *J* = 9.1, 1H, H-7_{endo}), 3.77 (dd, B part of AB system, *J* = 9.1, 4.5 Hz, 1H, H-7_{exo}), 3.31 (bt, *J* = 4.5 Hz, 1H, H-1), 2.22 (bd, A part of AB system, *J* = 13.2 Hz, 1H, H-8_{endo}), 2.13 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.85 (ddt, *J* = 13.2, 5.1, 1.2 Hz, 1H, H-8_{exo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 169.9, 169.8, 169.5, 84.3, 74.1, 71.7, 70.2, 68.7, 62.4, 40.3, 28.6, 22.2, 21.11, 21.07, 20.8; IR (KBr, cm^{-1}) 2970, 2893, 1737, 1456, 1435, 1367, 1218, 1055, 1039, 952, 894, 813, 777, 734, 705, 638. Anal. Calcd for $C_{16}H_{22}O_9$: C, 53.63; H, 6.19. Found: C, 53.79; H, 6.34.

***rel*-(1*R*,2*S*,3*S*,4*S*,5*R*)-2-(Acetoxymethyl)-2-hydroxy-6-oxabicyclo[3.2.1]octane-3,4-diyl Diacetate (30):** 0.71 g, 19% as colorless crystals from ether; mp 174−176 °C; TLC (hexane/EtOAc, 1:1) R_f = 0.51, ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.25 (dt, *J* = 5.2, 1.2 Hz, 1H, H_4), 5.15 (d, J = 5.2 Hz, 1H, H-3), 4.45 (d, A part of AB system *J* = 12.3 Hz, 1H, H-9), 4.35 (d, B part of AB system, *J* = 12.3 Hz, 1H, H-9′), 4.27 (t, *J* = 5.2 Hz, 1H, H-5), 4.23 (bd, *J* = 8.8 Hz, 1H, H-7_{endo}), 3.75 (dd, *J* = 8.8, 4.4 Hz, 1H, H-7_{exo}), 3.4−3.0 (1H, −OH), 2.55 (bt, *J* = 4.4 Hz, 1H, H-1), 2.15 (bd, A part of AB system, *J* = 13.0 Hz, 1H, H-8_{endo}) 2.13 (s, 3H, CH_3), 2.09 (s, 3H, CH_3). 2.04 (s, 3H, CH_3), 1.81 (dddd, *J* = 13.0, 5.2, 4.4, 1.2 Hz, 1H, H-8_{exo}); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 171.0, 169.7, 75.2, 74.6, 74.2, 70.0, 68.7, 66.5, 42.1, 28.9, 21.1, (2C), 21.0; IR (KBr, cm^{-1}) 3481, 2972, 2900, 1735, 1716, 1373, 1232, 1217, 1195,1134, 1056, 1037, 883. Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 53.49; H, 6.31.

***rel*-(1*R*,2*S*,3*S*,4*R*,5*R*)-4,5-Bis(acetoxymethyl)-4-hydroxycyclohexane-1,2,3-triyl Triacetate (31):** 1.41 g, 29% as colorless crystals from ether; mp 138−140 °C; TLC (hexane/EtOAc, 1:1) R_f = 0.25, ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.33 (bd, A part of AB system, *J* = 3.1 Hz, 1H, H-3), 5.26 (bdd, B part of AB system *J* = 10.5, 3.2 Hz, 1H, H-2), 5.08 (b dt, *J* = 10.5 and 5.1 Hz, H-1), 4.21 (dd, A part of AB system, *J* = 11.5 and 6.4 Hz, 1H, CHCH*H*O), 4.17 (d, A part of AB system *J* = 12.0 Hz, 1H, OCH*H*), 4.14 (d, B part of AB system, *J* = 12.0 Hz, 1H, OC*H*H), 3.98 (dd, B part of AB system, *J* = 11.5, 5.9 Hz, 1H, HCC*H*HO), 3.41 (bs, 1H, OH), 2.25−2.15 (m, 1H, H-5), 2.12−1.98 (m, 1H, CH*H*), 2.05 (s, 3H, CH_3), 2.03 (s, 2 × CH_3), 2.00 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 1.69 (q, B part of AB system, *J* = 12.3 Hz, 1H, C*H*H); ^{13}CNMR (75 MHz, $CDCl_3$) δ 171.6, 170.9, 170.8, 170.7, 169.7, 73.9, 71.1, 70.3, 69.2, 67.0, 63.5, 36.9, 28.4, 21.3, 21.2, 21.0, 20.99, 20.9; IR (KBr, cm^{-1}) 3462 3441, 2966, 1730, 1456, 1433, 1365, 1220, 1178, 1076, 1028, 987. Anal. Calcd for $C_{18}H_{26}O_{11}$: C, 51.67; H, 6.26. Found: C, 51.98; H, 6.55.

Ring-Opening Reaction of the Bisepoxide 27 in Acetic Anhydride with a Catalytic Amount of H_2SO_4. To a stirred solution of bisepoxide **27** (3.0 g, 11.71 mmol) in 10 mL of acetic anhydride was added H_2SO_4 (4 drops), and then the mixture was stirred for 12 h at room temperature. After completion of the reaction, dichloromethane (350 mL) was added. The solution was extracted first with HCl (100 mL, 5%), then with saturated $NaHCO_3$ (2 × 350 mL), and next with water (4 × 350 mL) and then dried ($MgSO_4$). The solvent was evaporated, and the residue was chromatographed on silica gel (60 g), eluting with hexane and ethyl acetate (1/3) to give the monoepoxide **28** (1.4 g, 47%) as the first fraction. The second fraction was identified as the tetraacetate **29** (1.02 g, 24%).

Ring-Opening Reaction of the Monoepoxide 28 in Acetic Anhydride with H_2SO_4: Synthesis of 30. To a stirred solution of **28** (0.75 g, 2.93 mmol) in 8 mL of acetic anhydride was added H_2SO_4 (8 drops) and the mixture stirred for 12 h at room temperature. The same workup was applied as described above. After column chromatography over silica gel, the hydroxytriacetate **30** (0.87 g, 94%) was isolated as the sole product.

Ring-Opening Reaction of the Monoepoxide 28 in Acetic Anhydride with a Catalytic Amount of H_2SO_4: Synthesis of 29. To a stirred solution of **28** (0.8 g, 3.12 mmol) in 8 mL of acetic anhydride was added a catalytic amount of H_2SO_4 (one drop), and the mixture was stirred for 12 h at room temperature. The same workup was applied as described above. After column chromatography over silica gel, the tetraacetate **29** (0.9 g, 80%) was isolated as the sole product.

***rel*-(1*R*,2*S*,4*S*,5*S*,6*R*)-2-(Hydroxymethyl)-3,7-dioxatricyclo-[4.2.1.0^{2,4}]nonan-5-ol (32).** Epoxy diacetate **28** (0.27 g, 1.05 mmol) was hydrolyzed with $NH_{3(g)}$ as described above to give epoxy tetrol **32** (0.14 g, 79%) as a colorless viscous oil after column chromatography eluting with EtOAc: ^{1}H NMR (300 MHz, D_2O) δ 3.84−3.75 (m, 3H), 3.58 (m, 2H), 3.35 (d, *J* = 13.1 Hz1H,), 3.09 (m, 1H), 2.62 (t, *J* = 3.8 Hz, 1H,), 1.97 (bd, *J* = 12.3 Hz, 1H), 1.41−1.34 (m, 1H); ^{13}C NMR (75 MHz, D_2O) δ 76.6, 69.5, 67.6, 63.3, 61.4, 54.7, 34.5, 26.1; IR (KBr, cm^{-1}) 3327, 3313, 3300, 2941, 2883, 1558, 1435, 1332, 1288, 1253, 1116, 1097, 1045, 1024, 993. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02; Found: C, 55.39; H, 6.57.

***rel*-(1*R*,2*R*,3*S*,4*R*,5*R*)-2-(Hydroxymethyl)-6-oxabicyclo[3.2.1]-octane-2,3,4-triol (8).** Tetraacetate **29** (0.33 g 0.92 mmol) was hydrolyzed with $NH_{3(g)}$ as described above to give tetrol **8** (0.18 g, 92%) as a colorless powder: mp 256−258 °C from ethanol; ^{1}H NMR (300 MHz, D_2O) δ 4.6 (bs, 4H, OH), 4.09 (t, *J* = 5.0 Hz, 1H, H-4), 3.83 (d, *J* = 8.5 Hz, 1H, H-4), 3.72 (m, 2H), 3.53 (m, 3H), 2.35 (t, *J* = 4.7 Hz, 1H, H-1), 1.98 (bd, *J* = 12.9 Hz, 1H, H-8), 1.53 (dt, *J* = 12.9, 5.3 Hz, 1H, H-8′); ^{13}C NMR (75 MHz, D_2O) δ 77.1, 76.7, 73.3, 70.5, 68.2, 63.4, 40.3, 27.5; IR (KBr, cm^{-1}) 3334, 3213, 2937, 2893, 1392, 1350, 1323, 1251, 1060, 1033, 977. Anal. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.16; H, 7.33.

General Procedure for Ring-Opening of Bicyclic Acetates 28−30. To a stirred solution of tetraacetate **29** (1.0 g, 2.79 mmol) in Ac_2O/AcOH (7 mL, 1:1) was added sulfamic acid (70 mg) at room temperature, followed by heating at reflux for 72 h. After the mixture was cooled to room temperature, HCl was added (50 mL, 5%), and the mixture was extracted with EtOAc (3 × 100 mL). The organic phase was washed with saturated $NaHCO_3$ (2 × 100 mL) and then with water (2 × 100 mL) and dried ($MgSO_4$). The organic phase was concentrated, and the residue was chromatographed on silica gel (50.0 g) eluting with hexane/ethyl acetate 4:1 to afford hexaacetate **36**.

***rel*-(1*R*,2*S*,3*S*,4*R*,6*R*)-1,6-Bis(acetoxymethyl)cyclohexane-1,2,3,4-tetrayl tetraacetate (36):** 1.02 g, 80% as colorless liquid; ^{1}H NMR ($CDCl_3$, 300 MHz) 5.97 (d, *J* = 2.0 Hz, 1H, H-2), 5.2−5.03 (m, 2H, H-3 and H-4), 4.78 (d, A part of AB system, *J* = 12.3 Hz, 1H, OC*H*H), 4.34 (d, B part of AB system, *J* = 12.3 Hz, 1H, OCH*H*), 4.26 (dd, A part of AB system, *J* = 11.4, 5.3 Hz, 1H, HCCH*H*O), 3.96 (dd, B part of AB system, *J* = 11.4, 8.0 Hz, 1H, HCC*H*HO), 2.56−2.40 (m, 1H, H-6), 2.19−2.1 (H-5), 2.12 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.96 (s, 3H, CH_3), 1.64−1.50 (m, 1H, H-5′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.91, 170.6, 170.19, 170.15, 169.3, 169.27, 81.7, 70.4, 69.25, 68.9, 63.5, 63.3, 37.9, 28.6, 21.8, 21.3, 21.1, 20.95, 20.9, 20.86; IR (KBr, cm^{-1}) 2966, 1737, 1367, 1209, 1078, 1031, 902. Anal. Calcd for $C_{20}H_{28}O_{12}$: C, 52.17; H, 6.13. Found: C, 52.19; H, 6.25.

Ring Opening of 28. Epoxy diacetate **28** (1.0 g 3.90 mmol) was hydrolyzed, acetylated, and chromatographed as described above for **29** to give **36**. The hexaacetate **36** was isolated as a colorless liquid (1.28 g, 71%).

Ring Opening of 30. Compound **30** (1.0 g 3.17 mmol) was hydrolyzed, acetylated, and chromatographed as described above to give **36** as colorless liquid (0.96 g, 66%).

Acetylation of Pentaacetate 32 with $Ac_2O/AcOH/H_2NSO_3H$. Pentaacetate **31** (1.0 g, 2.39 mmol) was dissolved in Ac_2O/AcOH (8 mL, 1:1), and H_2NSO_3H (20 mg) was added. The mixture was stirred at reflux temperature for 12 h at room temperature. Dichloromethane (200 mL) was added, and then ice-cooled HCl (50 mL, 5%) was added. The organic phase was washed with saturated $NaHCO_3$ solution (2 × 100 mL) and water (3 × 100 mL) and then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave hexaacetate **36** almost in quantitative yield (1100 mg).

***rel*-(1*R*,2*S*,3*S*,4*R*,6*R*)-1,6-Bis(hydroxymethyl)cyclohexane-1,2,3,4-tetraol (7).** Hexaacetate **36** (1.5 g 3.26 mmol) was dissolved in absolute methanol (60 mL), and dry $NH_{3(g)}$ was passed through the solution for 45 min. NH_3 gas streaming was stopped, and the mixture was stirred additionally for 6 h. Evaporation of the solvent and formed acetamide gave hexol **7** (0.60 g, 89%) as a colorless powder from EtOH/*n*-hexane (5:3): mp 176−179 °C.

Pentaacetate **31** (1 g, 2.39 mmol) was hydrolyzed with dry $NH_{3(g)}$ in MeOH as described above. The hexol **7** (0.45 g, 91%) was obtained as a colorless powder: ^{1}H NMR (300 MHz, D_2O) δ 4.67 (s, 6H, OH), 3.72 (d, J = 3.2 Hz, 1H, H-2), 3.67−3.49 (m, 5H), 3.39 (dd, J = 11.4, 6.2 Hz, 1H, CHCHHOH), 1.79−1.70 (m, 2H), 1.35 (dt, J = 13.5, 11.1 Hz, 1H, H-6); ^{13}C NMR (75 MHz, D_2O) δ 110.0, 76.2, 73.0, 69.2, 65.0, 61.5, 37.6, 31.0; IR (KBr, cm^{-1}) 3296, 2935, 2899, 1643, 1415, 1301, 1244, 1060, 1028. Anal. Calcd for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 46.11; H, 7.77.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra (^{1}H and ^{13}C) for all new compounds and X-ray structure and CIF of **30**, experimental details for the glycosidase inhibition assay, and tables of atom coordinates and absolute energies of the calculated compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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