A New Glucose: Towards Conformationally Locked Hexoses through Annulation

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A new family of surface-modified carbohydrates with locked, *axial-rich* conformations and bipolarofacial architectures has been developed with the aid of carbocyclic ring annulation. These novel *trans*-decalin-based carbohydrates have been synthesized, from simple aromatic precursors such as tetralin, through the ozonolysis of an appropriately protected allylic alcohol, followed by a cascade of intramolecular acetalizations to generate the sugar pyran moiety. The stereoselective synthesis of (racemic) cyclohexane-annulated β-glucopyranoside and α-glucofuranoside from a common annulated *trans*-cyclohexadiene diol (*trans*-CHD) precursor underscores the versatility of our approach. The efficacy of the annulation stratagem in generating carbohydrate diversity has been demonstrated through the synthesis of two regioisomeric annulated gulose derivatives, which differ only in the site of ring annulation on the sugar moiety. The mapping of the MLP surface and solid-state architecture of the new sugar shows that cycloalkane annulation results in surface modification and fine-tuning of sugar hydrophilicity.

Introduction

Carbohydrates are ubiquitous and important biomolecules, endowed with vast functional and structural diversity. As components of glycoproteins, glycolipids and other conjugates, they have been implicated in the regulation of a wide variety of biological processes such as cell–cell communication, cell signalling and molecular and cellular targeting.[1] Carbohydrate recognition events are involved in the progression of a number of diseases, as the binding of many pathogens and biological toxins to host cell surface are carbohydrate-mediated. Despite their important role, the molecular details of many of these carbohydrate recognition events are only scantily understood, underscoring the need for de novo design of structural and functional group variants capable of serving as molecular probes and with potential as therapeutic agents.[1,2] Among the various strategies that have been developed in the quest for structurally modified carbohydrates, the approach involving conformationally constrained analogues offers interesting possibilities. It is quite well known, for example, that conformationally locked nucleic acids (LNAs) incorporating bridged bicyclic pentose sugars display promising therapeutic profiles.[3] However, in carbohydrate chemistry, conformational locking tactics capable of providing access to unnatural, less stable conformations have not received much attention. In particular, a conformational locking device that can dependably provide access to *axial-rich* hexose conformations remains a challenge.

The role of *axial-rich* hexose conformations in protein–carbohydrate interactions has been highlighted recently.[4–6] Yoshida et al. have shown that kifunensine and 1-deoxymannojirimycin, both inhibitors of Class I α-1,2-mannosidases, each adopt a nonstandard $^1C_4$ (*axial-rich*) conformation at the active site.[5] Bols et al. very recently observed that oligosaccharides containing glucose residues in $^1C_4$ conformations underwent selective hydrolysis or rearrangement at this site, thus making these conformationally restricted entities potential markers for oligosaccharide cleavage.[6] In the above examples, the unnatural *axial-rich* conformations were accessed through metal ion binding or internal locking through bridging. It occurred to us, in the light of our concurrent studies with inositols, that the tool of ring annulation offers a promising strategy to provide axial-rich conformations of hexoses in a predictable manner.

We have recently reported the successful syntheses of a range of cyclopentane and cyclohexane ring-annulated inositols (**1** and **2**, respectively) in which annulation was used as a predictable and effective tool to lock inositols in their *axial-rich "unnatural"* conformations (Figure 1).[7] While the natural *myo*-inositol **3**, for example, exits in a stable conformation with five of its hydroxy groups in equatorial dispositions (5eq/1ax), the cyclohexane-annulated *myo*-inositol **4** has been shown to exist in a locked conformation with a five axial/one equatorial (5ax/1eq) disposition of its hydroxy groups (Figure 1). Furthermore, the carbocyclic annulus in

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1 and **2** serves as a handle with which to fine-tune the hydrophobicity of the polar inositols and to achieve chemodifferentiation of the hydroxy groups. The synthesis of bicyclic inositols **1**–**2** began from simple, commercially available aromatics such as indane (**5**) and tetralin (**6**) through the intermediacy of annulated *trans*-cyclohexadiene diol (*trans*-CHD) derivatives **7** and **8**, respectively (Scheme 1).[7] These interesting efforts in the inositol area impelled us to extend the strategy of carbocyclic annulation to provide conformationally locked carbohydrates. Consequently, a new family of annulated carbohydrates **9a**–**d** functioning as new sugar variants was conceptualized (Figure 2). These decalin-based carbohydrates can be visualized as arising through annulation of a *trans*-fused cyclohexane ring on the carbohydrate moiety. The *trans* ring fusion in these entities ensures that the hexose moiety remains locked in an unnatural *axial-rich* conformation, an elusive feature among carbohydrates in their free states. For example, cyclohexane ring annulation to β-glucose (**10**), known to exist in a stable conformation with all equatorial substituents,[8] would give rise to a "*new sugar*" variant **11** with all the substituents in axial dispositions. It is reasonable to expect that cycloalkane ring fusion in hexose sugars would offer the possibility to fine-tune the hydrophobic–hydrophilic balance and to give them pronounced dipolarofacial (bifacial molecules with distinct hydrophilic–hydrophobic face separation) characters and thereby modulate their recognition and binding with proteins in a very subtle way. In addition, a ring annulation approach can also be viewed as an interesting means of generating carbohydrate diversity, arising through variation in the site of annulation with retention of the sugar configuration (vide infra). Structures **9a**–**d** duly demonstrate possibilities along these lines.

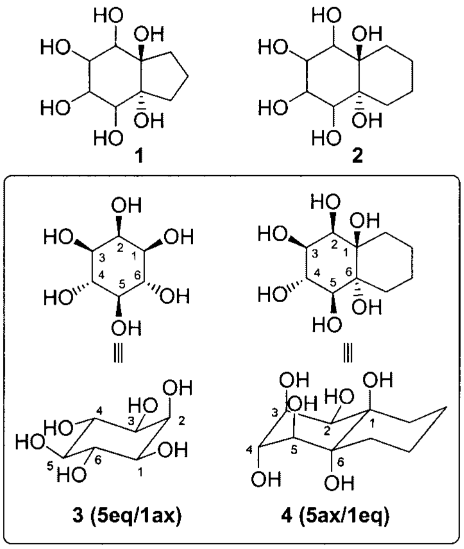
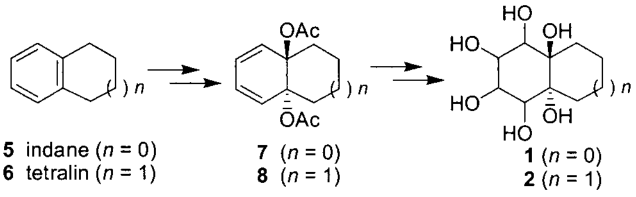


Figure 1. Conformationally locked, *axial-rich* annulated inositols **1** and **2**.



Scheme 1. General synthetic route to annulated inositols **1** and **2**.

β-Glucose (11)

A literature survey revealed that there have been relatively few attempts to synthesize annulated carbohydrates, and that these have mainly been directed towards exploitation of the chirality of the hexoses to generate chiral building blocks.[9] Among the notable examples of these efforts are Fraser-Reid's annulated furanoside **12** and pyranoside **13**,[9a–9c] Jenkins' annulated sugar entities **14** and **15**,[9d–9f,9k,9l] Ghosh's annulated furanose **16**[9i] and Nagarajan's cyclopropane-annulated glycal **17**[9g] (Figure 3).These "annulated" carbohydrates were synthesized through ring annulation on tactically protected sugar molecules, and none of these examples can be regarded as a truly annulated sugar, as they each lack the full complement of hydroxy groups on the pyran ring. In contrast, our conceptualization of the annulated carbohydrates **9a**–**d** has full complements of hydroxy functionalities on the sugar moieties, but they are still suited for conformational locking of their

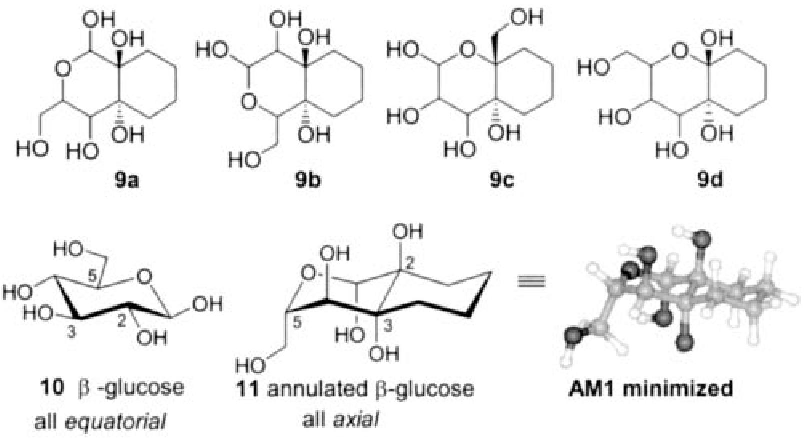


Figure 2. Annulated and conformationally locked *axial-rich* carbohydrates **9a**–**d**.

hexose components. Here we report the successful pursuit of a strategy that has for the first time provided access to novel, ring-annulated, conformationally locked, dipolarofacial hexose sugars.

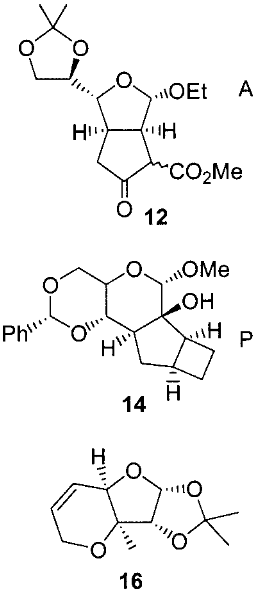
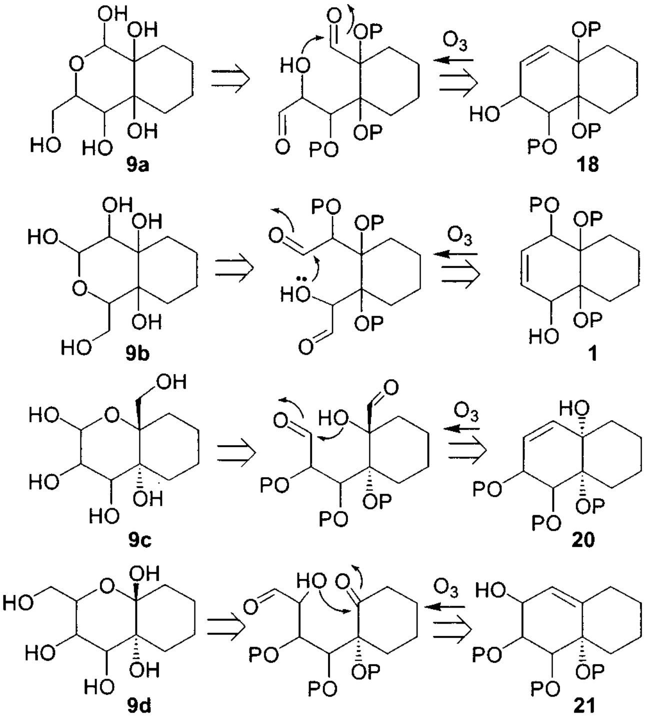


Figure 3. Annulated furanoses and pyranoses reported by Fraser-Reid, Ghosh, Jenkins and Nagarajan.[9]



(P = protecting group)

Scheme 2. Retrosynthetic analysis of annulated hexoses **9a–d**.

Results and Discussion

Retrosynthetic Analysis

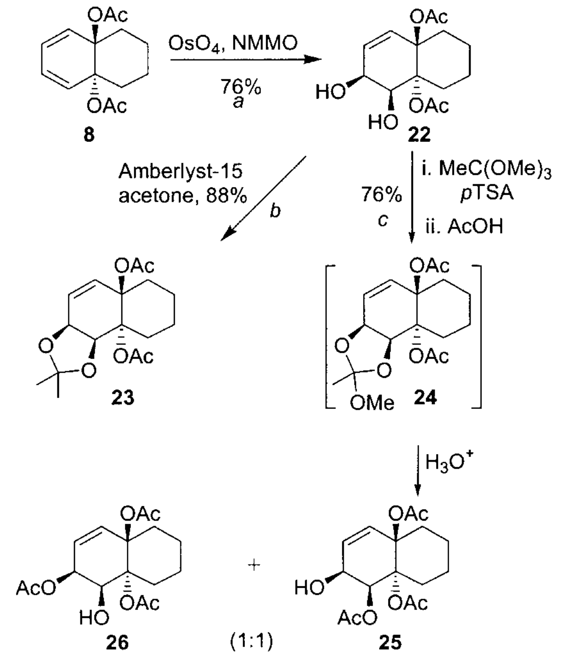
The key idea in our approach towards annulated hexoses was the generation of a cyclic acetal moiety (bearing the anomeric centre), a structural characteristic of sugars. It was sought to accomplish this through the ozonolytic cleavage and in situ intramolecular acetalization of an appropriately protected bicyclic allylic alcohol. Scheme 2 shows a generalized representation of this simple tactic for accessing annulated hexoses **9a–d** from the corresponding bicyclic allylic alcohols **18–21**, with ozonolysis planned to serve as the pivotal step to set up the cascade intramolecular acetalization. Acquisition of precursors **18–21** thus became our primary concern, and for this purpose the readily available and recently reported *trans*-CHD **8**[7] was identified as an appropriate starting point.

Synthesis of Annulated *rac*-β-Glucopyranose and *rac*-α-Glucofuranose

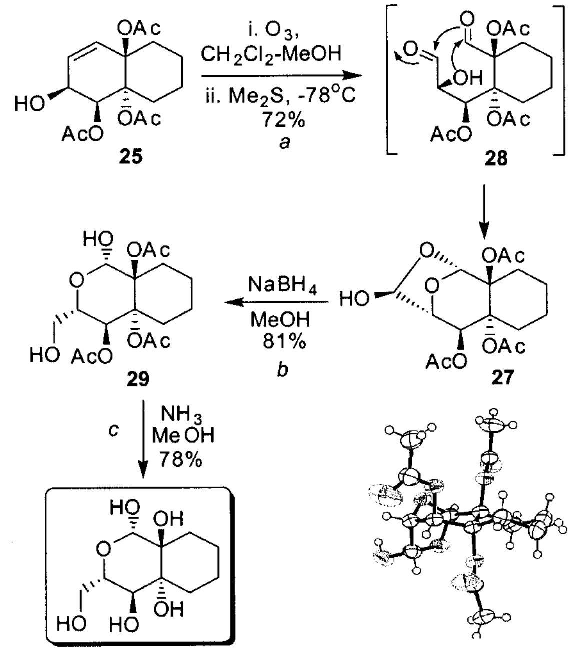
The annulated β-glucose **11** was chosen as our first target, and the synthetic approach commenced from the tetralin-derived C_2-symmetric annulated *trans*-cyclohexadiene diol (*trans*-CHD) derivative **8**. The bicyclic diene **8** was subjected to catalytic OsO$_4$-mediated dihydroxylation under controlled conditions to furnish the *cis*-diol **22** stereoselectively (Scheme 3). The stereostructure of the diol **22** was verified by the single-crystal X-ray structure determination of its acetonide derivative **23**. At this juncture it was necessary to monoprotect the hydroxy groups in diol **22** selectively, to generate the requisite allylic alcohol, and for this purpose it was first converted into the ortho ester derivative **24**, with subsequent hydrolysis under acidic conditions furnishing the regioisomeric alcohols **25** and **26** (1:1) (Scheme 3). The structural identities of **25** and **26** were secured through single-crystal X-ray structure analysis.[10] It was envisaged that ozonolysis of **25** and **26** and intramolecular acetalization should generate pyranose and furanose variants, respectively, of a hexose sugar.

To this end, ozonolysis of **25** and quenching with dimethyl sulfide exclusively furnished the annulated glucopyranose derivative **27** with complete regio- and stereocontrol (Scheme 4).[10,11] The origin of the bis-acetal moiety in **27** can be attributed to a cascade of intramolecular acetalizations in the intermediate dialdehyde **28** (Scheme 4). The stereoselectivity leading to **27** is noteworthy, though a precise reason for it is not obvious.

The structure of **27** was secured through single-crystal X-ray structure determination and, quite pleasingly, revealed the presence of five axially locked substituents, with glucose configuration, on the pyran ring.[10] The hemiacetal moiety in **27** was carefully disengaged by reduction to furnish **29**, an annulated β-glucopyranose derivative. Finally, deprotection of the acetates in **29** afforded the annulated β-glucopyranose **11** (Scheme 4). The energy-minimized structure of **11** clearly showed the glucose moiety to have all five substituents in the "*unnatural*" axial orientation (see Figure 2). In contrast, the most stable conformation of β-glucopyranose



Scheme 3. *Reagents and conditions*: a) OsO_4 (1 mol%), NMMO, Me_2CO/H_2O (4:1), 10 °C, 5 h, 76%. b) Amberlyst-15, acetone, 4-Å mol. sieves, room temp., 2 h, 95%. c) i. $MeC(OMe)_3$, *p*TSA, CH_2Cl_2, room temp., 3 h; ii. 50% AcOH, room temp., 1 h, 76% (2 steps) [NMMO = *N*-methylmorpholine *N*-oxide, *p*TSA = *para*-toluenesulfonic acid].

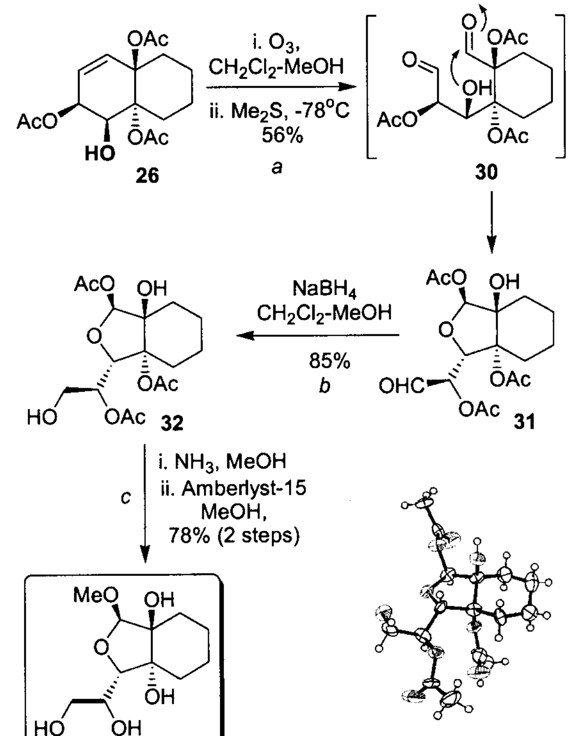


ORTEP diagram of 27 with 50% ellipsoidal probability

Scheme 4. *Reagents and conditions*: a) O_3, $CH_2Cl_2/MeOH$ (5:1), –40 °C; Me_2S, –78 °C, 30 min, 72%. b) $NaBH_4$, MeOH, 0 °C, 10 min, 81%. c) NH_3, MeOH, room temp., 4 h, 78%.

(**10**) as determined by single-crystal X-ray analysis shows all the substituents in equatorial orientations.[8] The β-glucopyranose **11** is thus the first example of an annulated *axial-rich* glucopyranoside (*new glucose*).

Attention was next turned to the bicyclic alcohol **26**, which on ozonolysis and quenching of the intermediate ozonide with dimethyl sulfide provided the intermediate dialdehyde **30** (Scheme 5).[11] A sequence of regio- and stereoselective intramolecular acetalization and concomitant migration of the tertiary acetate group to the anomeric centre exclusively furnished the aldehyde **31** (Scheme 5), and the aldehyde group in **31** was carefully reduced to furnish the annulated glucofuranose derivative **32**. The stereostructure of **32** was once again secured through X-ray crystal structure determination.[10] Finally, removal of the acetate groups in **32** and subsequent glycosylation[12] under acidic condition furnished the annulated methyl α-glucofuranoside **33** (Scheme 5). A notable feature of the synthesis of annulated glucose in pyranose (**11**) and furanose (**33**) forms is that they emanate from a common annulated *trans*-CHD precursor **8** and the stereoselectivity (i.e., the formation of the anomeric centres in **27** and **31**) observed in the key steps of ozonolysis and intramolecular acetalization is quite significant.



ORTEP diagram of 28 with 50% ellipsoidal probability

Scheme 5. *Reagents and conditions*: a) i. O_3, $CH_2Cl_2/MeOH$ (5:1), –40 °C; ii. Me_2S, –78 °C, 30 min, 56%. b) $NaBH_4$, $CH_2Cl_2/MeOH$ (3:1), 0 °C, 10 min, 85%. c) i. NH_3, MeOH, room temp., 5 h; ii. Amberlyst-15, MeOH, room temp., 12 h, 78% (2 steps).

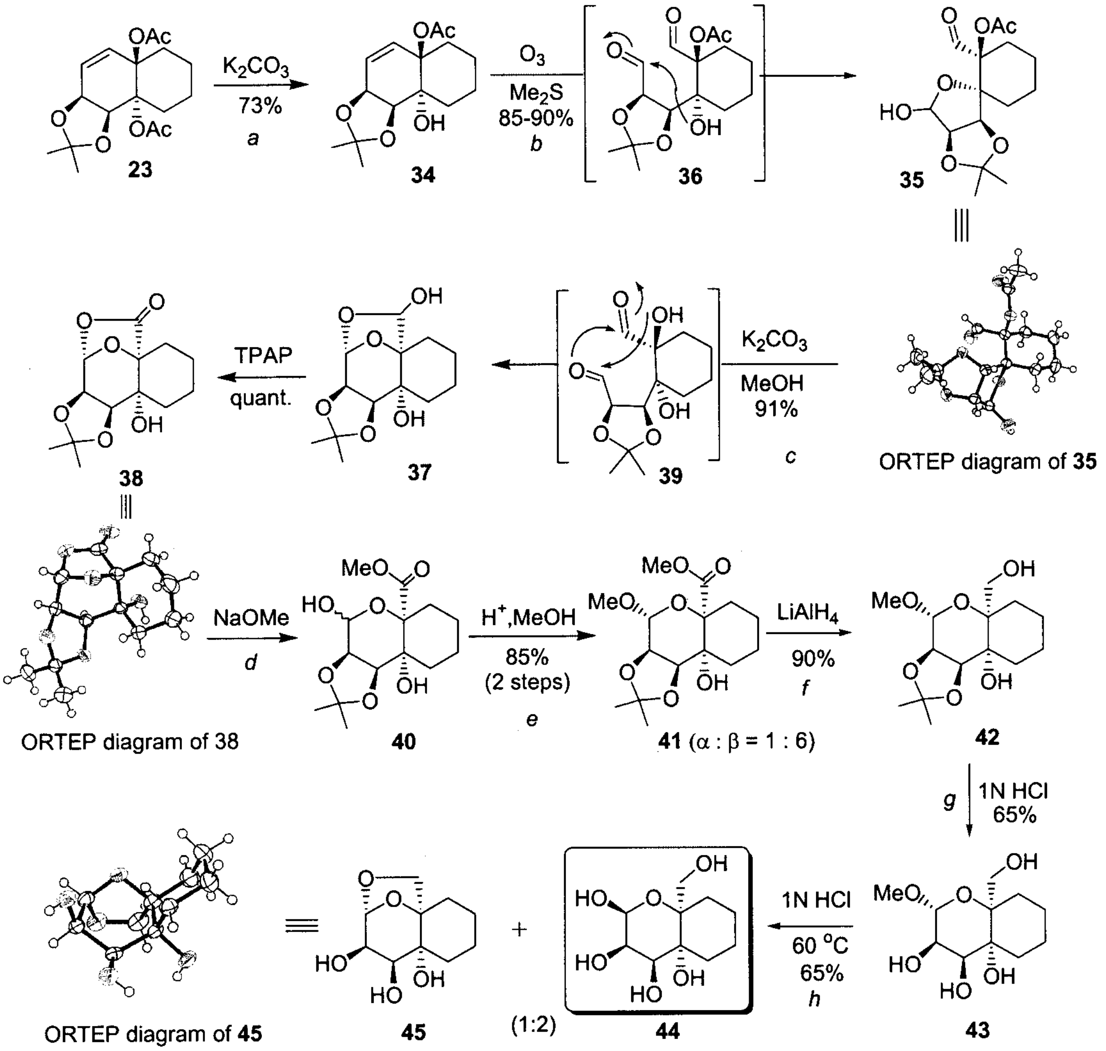
Carbohydrate Diversity–Synthesis of Annulated α- and β-Gulose

At this stage it was of interest to explore the tactic of carbocyclic annulation, effectively used to access conformationally locked sugars, for the generation of carbohydrate diversity. As already stated above, the premise for this was that a range of annulated hexoses might be generated by altering the site of annulation on the sugar moiety. We demonstrate this idea through the synthesis of two annulated gulose sugars.

Efforts in this direction began from the acetonide derivative **23** (vide supra). As indicated in the retrosynthetic plan, it was necessary to remove one of the acetate groups selectively to generate the required allylic alcohol. However, selective deprotection in **23** gave only **34**, a non-allylic alcohol, but this too was recognized as serviceable and was carried forward (Scheme 6). Ozonolysis of the double bond in **34** and quenching with dimethyl sulfide gave the aldehyde **35**, a spiro-annulated gulofuranose derivative (Scheme 6).[11] The generation of this interesting architecture could be ascribed to an in situ intramolecular acetalization in the intermediate dialdehyde **36** formed during ozonolysis (Scheme 6). Recourse was once again made to single-crystal X-ray crystallography to settle the formulation of **35** unambiguously.[10]

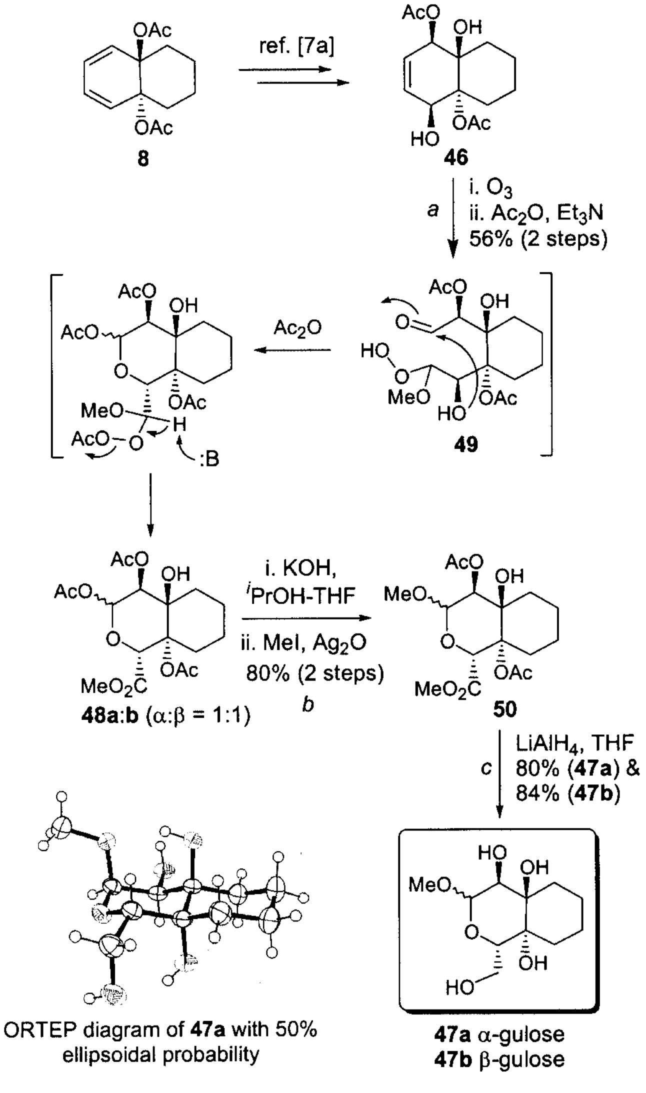
The lactol-aldehyde **35** on treatment with base under carefully controlled conditions, underwent a deep-seated restructuring process to deliver an intermediate bis-lactol **37**, which was immediately oxidized with TPAP[13] to furnish the γ-lactone **38** (Scheme 6). The stereostructure of **38** was unequivocally established from its single-crystal X-ray structure, and the compound was found to be a C_4C_5 annulated 1,6-gulonolactone derivative, its formation being visualizable through a cascade of intramolecular acetalizations in the intermediate dialdehyde diol **39** (Scheme 6).[10]

Methanolysis of the γ-lactone **38**, under controlled conditions, was smooth and exclusively furnished an annulated methyl β-gulopyranouronate **40** (Scheme 6). The reactive anomeric hydroxy group in **40** was protected as its methyl



Scheme 6. *Reagents and conditions*: a) K_2CO_3, MeOH, room temp., 2 h, 73%. b) i. O_3, CH_2Cl_2/MeOH (5:1), –40 °C; ii. Me_2S, –78 °C, 85–90%. c) i. K_2CO_3, MeOH, room temp., 30 min; ii. TPAP, NMMO, CH_2Cl_2, room temp., 6 h, 91% (2 steps). d) NaOMe, MeOH, room temp., 10 min. e) Amberlyst-15, MeOH, $Me_2C(OMe)_2$, room temp., 16 h, 85% (2 steps). f) $LiAlH_4$, THF, room temp., 90%. g) 1 N HCl, room temp., 2 h, 65%. h) 1 N HCl, 50 °C, 60%. [TPAP = tetrapropylammonium perruthenate]

ether under standard glycosylation conditions to furnish the methyl β-gulopyranoside derivative **40** (β/*a* = 6:1), along with the minor α-isomer. The ester functionality in the dominant β-isomer **41** was reduced with $LiAlH_4$ to furnish the corresponding alcohol **42** (Scheme 6). Controlled acid hydrolysis of the acetonide protecting group in **42** provided the annulated methyl β-gulopyranoside **43** and, after further acidic hydrolysis, the target C_4C_5 annulated α-gulopyranose **44** and the annulated 1,6-anhydrogulopyranose or *gulosan* **45** (Scheme 6). While the structure of **44** followed from its spectroscopic data, that of its sibling **45** was established through single-crystal X-ray structure determination. Concurrent formation of **45** can be ascribed to intramolecular glycosylation with participation of the primary hydroxy group.



Scheme 7. *Reagents and conditions*: a) i. O_3, CH_2Cl_2/MeOH (5:1), –40 °C; ii. Ac_2O, Et_3N, room temp., 2 h, 56%, [*α*:*β* = 1:1]. b) i. KOH, *i*PrOH/THF (1:1), 0 °C, 5 min; ii. MeI, Ag_2O, room temp., 80% (2 steps). c) $LiAlH_4$, THF, room temp., 1 h, 80% (**47a**) and 84% (**48b**).

In another structural variation, the annulated 1,4-*cis*-diol diacetate **46**, obtained from the *trans*-CHD derivative **8** as described by us recently,[7a] was recognized as an appropriate starting material towards the production of annulated gulose **47**. Ozonolysis of the double bond in **46**, followed by dimethyl sulfide quench, resulted in a disappointing reaction profile. However, ozonolytic cleavage of the double bond in **46** by Schreiber's ozonolysis procedure,[14] giving chemodifferentiated termini, resulted in a improved reaction profile and gave an anomeric mixture of C_3C_4 annulated methyl gulopyranouranoate derivatives **48a** and **48b** (1:1) through treatment of the intermediate hydroperoxide aldehyde **49** in an Ac_2O/Et_3N milieu (Scheme 7). After this modified ozonolysis procedure the aldehyde group in the intermediate **49** undergoes in situ intramolecular acetalization to generate the pyran ring of the hexose derivative **48**. The anomers **48a** and **48b** were chromatographically separable and were individually deacetylated selectively at the anomeric centre[15] and immediately reprotected as the corresponding methyl ethers to furnish the methyl gulopyranosides **50a** and **50b**, respectively (Scheme 7). The ester functionalities in the anomers **50a** and **50b** were reduced with $LiAlH_4$ to furnish the C_3C_4 annulated methyl α- and β-gulopyranosides **47a** and **47b**, respectively (Scheme 7). The stereochemical architecture of **47a** was confirmed by its single-crystal X-ray structure determination, which in turn also confirmed the structure of its sibling **47b**.

The two annulated gulose derivatives **44** and **47** are regioisomeric, deriving from the same precursor bicyclic *trans*-cyclohexadiene diol derivative **8** and differing only in the site of ring annulation on the sugar moiety. By this principle, there could exist four regioisomeric annulated gulose variants (C_1C_2, C_2C_3, C_3C_4, C_4C_5 ring fusion), all conformationally constrained, underscoring the efficacy of the annulation stratagem in generating carbohydrate diversity.

Solid State Architectures of Annulated Hexoses

We indicated above that ring annulation on the hexose moiety might be expected to impart dipolarofacial character on the emerging new entities and also to fine-tune the hydrophilic/hydrophobic balance in them. In this context, in order to gauge the effect of the hydrophobic cyclohexane ring appendage on the hydrophilicity of the parent sugar, the MLP (Molecular Lipophilic Potential)[16] surface of the annulated methyl α-gulopyranoside **47a** was probed. The modulation of the hydrophilic character of the sugar moiety is apparent from the MLP surface of the annulated methyl α-gulopyranoside **47a** shown in Figure 4 (PSA = 132.3 Å^2, apolar surface = 276.7 Å^2).

The structural manifestation of the attachment of a hydrophobic moiety on a hydrophilic sugar molecule is profoundly reflected in the packing of molecules in the crystal of **47a**. The annulated methyl α-gulopyranoside **47a** displays bipolarofacial character as anticipated. In the solid state, the molecules are arranged in columns with the O–H···O hydrogen bonds defining a channel-like motif formed

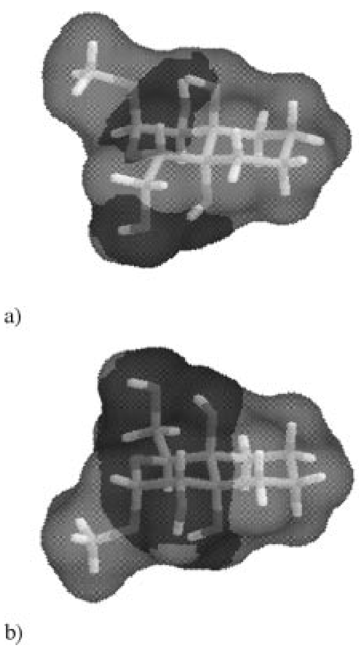


Figure 4. Molecular surface of annulated methyl α-gulopyranoside **47a**, showing the dominance of the hydrophobic surface (lighter shade) over the hydrophilic surface (polar surface area = 132.3 Å^2, apolar surface = 276.7 Å^2). a) Front view. b) Rear view.

by a hydrophilic interior (sugar moiety) and a hydrophobic exterior (cyclohexane annulus) (Figure 5).[17]

Conclusions

In short, by employing simple aromatic precursors such as tetralin, we have for the first time accomplished the synthesis of several annulated hexose sugars locked in unnatural conformations and with biplarofacial architectures. The synthesis of the annulated β-glucopyranose (new glucose) locked in the unnatural, *axial-rich* conformation is noteworthy. In addition, the synthesis of regioisomeric variants of annulated gulopyranoses highlights the efficacy of the ring fusion strategy for generating carbohydrate-like diversity. Although the novel sugar entities described here are racemic, efforts to develop chiral versions of the annulated hexose syntheses and to deploy them for the construction of a new class of oligosaccharides are currently underway.

Experimental Section

General: Melting points were recorded on a Büchi B-540 apparatus and are uncorrected. Infrared spectra were recorded on JASCO FT-IR 410 spectrometer. 1H NMR spectra were recorded on JEOL JNM-LA 300 or Bruker AMX 400 or Bruker DRX 500 instruments in $CDCl_3$ solutions and at 21 °C, unless otherwise stated. Chemical shifts are reported with respect to tetramethylsilane (Me_4Si) as the internal standard (for ^1H NMR) and the central line (δ = 77.0 ppm) of $CDCl_3$ (for ^{13}C NMR). The chemical shifts are expressed in parts per million (δ) downfield from Me_4Si. The standard abbreviations s, d, t, q and m refer to singlet, doublet, triplet, quartet and multiplet, respectively. Coupling constants (J), whenever discernible, have been reported in Hz. Low-Resolution Mass Spectra (LRMS) were recorded either on a Shimadzu GCMS-QP 5050A spectrometer (EI or CI mode) or on a Q-TOF Micromass mass spectrometer. High Resolution Mass Spectra (HRMS) were recorded on a Q-TOF Micromass mass spectrometer. Elemental analyses were obtained on a Carlo–Erba 1106 CHN analyzer. Commercial Acme silica gel (100–200 mesh particle size) was used for column chromatography. All moisture- and air-sensitive reactions were performed under argon with dry, freshly distilled solvents under anhydrous conditions by standard syringe–septum techniques. Reported yields are of isolated materials judged homogeneous by thin layer chromatography (TLC) and NMR spectroscopy. All solvent extracts were washed with water/brine as appropriate and were dried over anhydrous Na_2SO_4 before removal of the solvent in a rotary evaporator under reduced pressure.

(4a*R,5*S**,6*S**,8a*R**)-8a-Acetoxy-5,6-dihydroxy-1,2,3,4,4a,5,6,8a-octahydro-4-naphthalenyl Acetate (22):** OsO_4 (0.5 mg, 1 mol-%) and NMMO (50% aq., 51 µL, 0.22 mmol) were added at 0 °C to a solution of diene **8** (55 mg, 0.22 mmol) in acetone/water (4:1, 5 mL), and the resulting pale yellow reaction mixture was stirred at 10 °C for 6 h, before quenching with solid $NaHSO_3$. The resulting mixture was diluted with ethyl acetate (20 mL) and filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was subjected to silica gel column chromatography (50% ethyl acetate/hexane) to afford the diol **22** (48 mg, 76%), m.p. 158.7 °C (melts with charring). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.17 (d, J = 10.2 Hz, 1 H, C=C*H*), 5.81 (dd, J = 10.5, 3.9 Hz, 1 H, C=C*H*), 4.72 (br. s, 1 H, C*H*OH), 4.12 (br. s, 1 H, C*H*OH), 3.22

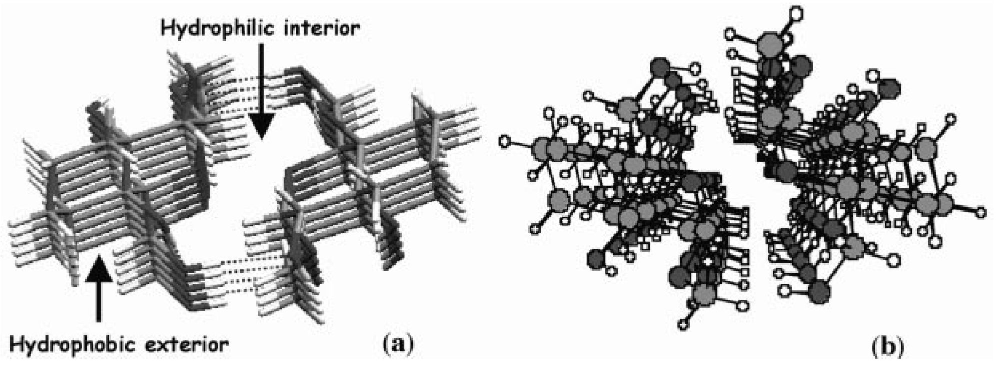
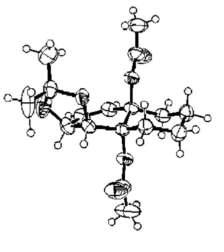


Figure 5. a) Solid-state architecture of annulated methyl α-gulopyranoside **47a** exhibiting bilayer arrangement with hydrophilic interior and hydrophobic exterior. b) Perspective view showing the channel-type motif in the solid-state architecture of **47a**.

(d, J = 10.2 Hz, 1 H), 2.92 (br. s, 1 H), 2.69 (d, J = 15.6 Hz, 1 H), 2.60 (d, J = 13.5 Hz, 1 H), 2.25 (dt, J = 13.5, 4.7 Hz, 1 H), 1.87–1.86 (m, 1 H), 1.64–1.39 (m, 3 H), 2.08 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9 ($C{=}O_{acetate}$), 167.3 ($C{=}O_{acetate}$), 132.3 ($C{=}CH$), 127.5 ($C{=}CH$), 82.5 (C_q), 81.5 (C_q), 68.8 (CHOH), 66.4 (CHOH), 27.0 (CH_2), 24.7 (CH_2), 22.1 ($COCH_3$), 21.8 ($COCH_3$), 20.0 (CH_2), 19.6 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ = 3360 cm^{-1}. LRMS (70 eV, EI) m/z 284 $[M]^+$: $C_{14}H_{20}O_6$ [284]: C 59.14, H 7.09; found C 59.96, H 7.10.

(3a*S,5a*R**,9a*R**,9b*S**)-5a-Acetoxy-2,2-dimethyl-3a,5a,6,7,8,9,9a,9b-octahydronaphtho[1,2-*d*][1,3]dioxol-9-yl Acetate (23):** Amberlyst 15 (≈ 10 mg) and molecular sieves (4 Å, 60 mg) were added to a solution of diol **22** (30 mg, 0.105 mmol) in dry acetone (5 mL). The resulting mixture was stirred at room temperature for 2 h, after which all the starting material was consumed (TLC). The reaction mixture was filtered through a small pad of celite and the filtrate was concentrated in vacuo. The residue obtained was chromatographed over a silica gel column (30% ethyl acetate/hexane eluent) to yield **23** (32 mg, 95%), m.p. 156.2–156.8 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.21 (d, J = 10.2 Hz, 1 H, C=CH), 5.81 (dd, J = 10.5, 3.9 Hz, 1 H, C=CH), 5.01 (d, J = 6.3 Hz, 1 H, $H_{acetonide}$), 4.54 (dd, J = 6.3, 4.2 Hz, 1 H, $H_{acetonide}$), 2.76 (d, J = 14.4 Hz, 1 H), 2.51 (d, J = 14.4 Hz, 1 H), 2.26 (dt, J = 14.4, 4.5 Hz, 1 H), 2.02 (s, 6 H, $COCH_3$), 1.17 (dt, J = 13.5, 4.5 Hz, 1 H), 1.54–1.25 (m, 4 H), 1.39 (s, 3 H, $CH_{3\,acetonide}$), 1.36 (s, 3 H, $CH_{3\,acetonide}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4 ($C{=}O_{acetate}$), 168.7 ($C{=}O_{acetate}$), 130.9 ($C{=}CH$), 127.4 ($C{=}CH$), 110.3 (C_q), 83.9 (2C, C_q), 73.4 ($C_{acetonide}$), 71.6 ($C_{acetonide}$), 28.3 (CH_2), 27.5 ($CH_{3\,acetonide}$), 25.5 ($CH_{3\,acetonide}$), 24.9 (CH_2), 22.2 ($COCH_3$), 21.9 ($COCH_3$), 20.1 (CH_2), 20.0 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 1732, 1367 cm^{-1}. LRMS (70eV, EI) m/z 325 $[M + 1]^+$; $C_{17}H_{24}O_6$ [324]: C 62.95, H 7.46; found C 62.93, H 7.50

Crystal Data for 23: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: $P2_1/c$, cell parameters: a = 7.8512(7) Å, b = 12.500(1) Å, c = 17.529(2) Å, β = 99.339(2)°, V = 1697.52 Å^3, Z = 4, ρ(calcd.) = 1.27 $g\,cm^{-3}$, $F(000)$ = 659.9, μ = 0.096 mm^{-1}, λ = 0.71 Å. R_1 = 0.0497 for 1850 $F_o > 4\sigma(F_o)$ and 0.0908 for all 2987 data wR_2 = 0.1086, GooF = 0.969, Restrained GooF = 0.969 for all data. An ORTEP drawing of compound **23** with 50% ellipsoidal probability level is shown below.



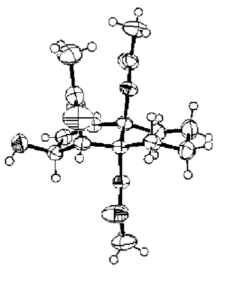
ORTEP diagram of compound **23**

(1*S,2*S**,4a*R**,8a*R**)-4a,8a-Diacetoxy-2-hydroxy-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl Acetate (25) and (1*S**,2*S**,4a*R**,8a*R**)-4a,8a-Diacetoxy-1-hydroxy-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl Acetate (26):** A slight excess of $MeC(OMe)_3$ (250 µL,1.99 mmol) and a catalytic amount of *p*TSA (10 mg) were added to a stirred solution of the *vic*-diol **22** (380 mg, 1.33 mmol) in dry CH_2Cl_2 (25 mL), cooled to 0 °C. The resulting reaction mixture was stirred at room temperature for 3 h, after which all the starting material was consumed (TLC). AcOH (30%, 150 µL) was added to this reaction mixture, and the resulting solution was stirred at room temperature for a further 1 h. The usual workup gave a residue, which on chromatographic purification over a silica gel column (30% ethyl acetate/hexane) furnished the regioisomeric (1:1) triacetates **25** (164 mg) and **26** (165 mg) in 76% overall yield.

Compound 25: M.p. 186.5–188 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.26 (dd, J = 10.5, 2.4 Hz, 1 H, C=CH), 6.13 (d, J = 4.5 Hz, 1 H, CHOAc), 5.75 (ddd, J = 10.5, 2.4, 1.5 Hz, 1 H, C=CH), 4.38–4.34 (m, 1 H, CHOH), 2.54 (m, 2 H), 2.13 (s, 3 H, $COCH_3$), 2.05 (s, 3 H, $COCH_3$), 2.02 (s, 3 H, $COCH_3$), 2.06–1.23 (series of m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6 ($C{=}O_{acetate}$), 169.0 ($C{=}O_{acetate}$), 168.3 ($C{=}O_{acetate}$), 130.1 ($C{=}CH$), 129.1 ($C{=}CH$), 83.0 (C_q), 77.7 (C_q), 68.5 (CHOAc), 65.6 (CHOH), 27.3 (CH_2), 24.8 (CH_2), 22.1 ($COCH_3$), 21.8 ($COCH_3$) 21.0 ($COCH_3$), 19.9 (CH_2), 19.7 (CH_2) ppm. IR (KBr): $\tilde{\nu}$ 3427, 1733 cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{22}O_8Na$ $[M + Na]^+$: 349.1263; found 349.1293.

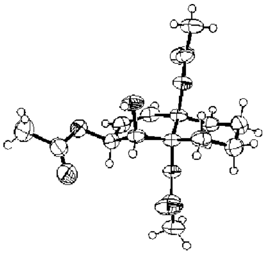
Compound 26: M.p. 169.0–170.5 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.32 (dd, J = 10.8, 2.4 Hz, 1 H, C=CH), 5.71 (ddd, J = 10.5, 2.1, 1.5 Hz, 1 H, C=CH), 5.32 (dt, J = 5.1, 2.4 Hz, 1 H, CHOAc), 4.88 (dd, J = 9.9, 4.5 Hz, 1 H, CHOH), 2.86 (d, J = 10.5 Hz, 1 H), 2.68 (m, 2 H), 2.29 (br. td, J = 13.8, 4.5 Hz, 1 H), 2.14 (s, 3 H, $COCH_3$), 2.07 (s, 6 H, $COCH_3$), 1.88–1.79 (m, 1 H), 1.67–1.58 (m, 2 H), 1.48–1.23 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2 ($C{=}O_{acetate}$), 168.9 ($C{=}O_{acetate}$), 167.6 ($C{=}O_{acetate}$), 130.1 ($C{=}CH$), 127.5 ($C{=}CH$), 82.9 (C_q), 80.4 (Cq), 69.7 (CHOH), 67.5 (CHOAc), 27.0 (CH_2), 24.4 (CH_2), 22.1 ($COCH_3$), 21.9 ($COCH_3$), 21.1 ($COCH_3$), 20.0 (CH_2), 19.6 (CH_2) ppm. IR (KBr): $\tilde{\nu}$ 3513, 1737 cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{22}O_8Na$ $[M + Na]^+$: 349.1263; found 349.1293.

Crystal Data for 25: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: $P2_1/c$, cell parameters: a = 12.929(6) Å, b = 8.354(4) Å, c = 15.487(7) Å, β = 106.230(2)°, V = 1606.0 (4) Å^3, Z = 4, ρ(calcd.) = 1.35 $g\,cm^{-3}$, $F(000)$ = 659.9, μ = 0.106 mm^{-1}, λ = 0.71 Å. R_1 = 0.041 for 2618 $F_o > 4\sigma(F_o)$ and 0.0466 for all 2990 data wR_2 = 0.1105, GooF = 1.084, Restrained GooF = 1.084 for all data. An ORTEP drawing of compound 25 with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **25**

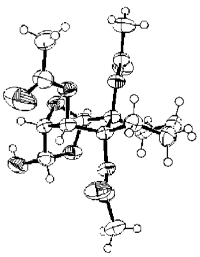
Crystal Data for 26: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: $P2_1/c$, cell parameters: a = 15.787(3) Å, b = 8.035(2) Å, c = 14.279(3) Å, β = 116.479(3)°, V = 1621(3) Å^3, Z = 4, ρ(calcd.) = 1.34 $g\,cm^{-3}$, $F(000)$ = 695.9, μ = 0.105 mm^{-1}, λ = 0.71 Å. R_1 = 0.044 for 2727 $F_o > 4\sigma(F_o)$ and 0.052 for all 3244 data, wR_2 = 0.120, GooF = 1.096, Restrained GooF = 1.096 for all data. An ORTEP drawing of compound **26** with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **26**

(1*R,2*S**,7*R**,8*S**,9*R**,10*S**)-2,7-Diacetoxy-10-hydroxy-11,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-8-yl Acetate (27):** A pre-cooled stream of O_3/O_2 was bubbled through a stirred solution of allylic alcohol **25** (80 mg, 0.245 mmol) in CH_2Cl_2/MeOH (5:1, 2 mL), maintained at –40 °C, and was continued until the pale blue colour (indicating excess ozone) persisted. A stream of oxygen was bubbled through the solution to remove the excess ozone (blue colour of solution disappears). The solution was placed under inert atmosphere, cooled to –78 °C and quenched by cautious addition of excess dimethyl sulfide (35 µL, 0.49 mmol). The reaction mixture was stirred at 0 °C for a further 3 h. The volatiles were removed under reduced pressure and the residue obtained was chromatographed on a silica gel column (50% ethyl acetate/hexane) to furnish the lactol **27** (63 mg, 72%), m.p. 198.5–200 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.29 (s, 1 H), 5.61 (d, J = 1.8 Hz, 1 H), 5.30 (d, J = 10.2 Hz, 1 H), 4.35 (d, J = 1.8 Hz, 1 H), 3.03 (d, J = 10.2 Hz, OH), 2.43–2.31 (m, 2 H), 2.15 (s, 3 H), 2.14 (s, 3 H), 2.13 (s, 3 H), 2.10–1.92 (m, 3 H), 1.64–1.53 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.7 ($C=O_{acetate}$), 169.0 ($C=O_{acetate}$), 168.8 ($C=O_{acetate}$), 101.1 (CH), 95.5 (CH), 81.3 (2C, C_q and CH), 79.3 (C_q), 65.5 (CH_2), 23.1 (CH_2), 22.6 (CH_2), 22.3 ($COCH_3$), 21.8 ($COCH_3$), 20.8 ($COCH_3$), 19.4 (CH_2), 19.2 (CH_2) ppm. IR (KBr): $\tilde{\nu}$ 3510, 1740 cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{22}O_9Na$ $[M + Na]^+$: 381.1162; found 381.1190.

Crystal Data for 27: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: triclinic, space group: $P\bar{1}$, cell parameters: a = 8.439(6) Å, b = 8.594(6) Å, c = 12.452(8) Å, α = 106.051(9)°, β = 91.740(1)°, γ = 102.364(9)° V = 843.8(3) Å^3, Z = 2, ρ (calcd.) = 1.41 g cm^{-3}, F(000) = 380.0, μ = 0.116 mm^{-1}, λ = 0.71 Å, R_1 = 0.054 for 2520 $F_o > 4\sigma(F_o)$ and 0.063 for all 3044 data, wR_2 = 0.146, GooF = 1.069, Restrained GooF = 1.069 for all data. An ORTEP drawing of compound **27** with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **27**

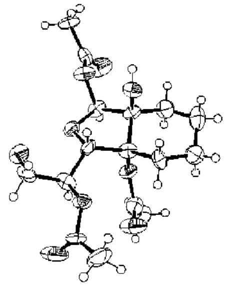
(1*S,3*S**,4*S**,4a*R**,8a*S**)-4a,8a-Diacetoxy-1-hydroxy-3-(hydroxymethyl)perhydro-4-isochromenyl Acetate (29):** $NaBH_4$ (11 mg, 0.294 mmol) was added under inert atmosphere to an ice-cooled solution of the lactol **27** (35 mg, 0.098 mmol) in dry MeOH (2 mL). The reaction mixture was stirred at the same temperature for a further 10 min. The reaction was quenched by addition of saturated NH_4Cl and subjected to usual workup. Chromatographic purification of the residue on silica gel (60% ethyl acetate/hexane) afforded the diol **29** (28 mg, 81%), m.p. decomposes (126–127 °C) before melting. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.89 (s, 1 H), 5.56 (d, J = 4.8 Hz, 1 H), 4.22 (m, 1 H), 3.86 (dd, J = 12, 9 Hz, 1 H), 3.60 (dd, J = 12, 3 Hz, 1 H), 2.68 (s, OH), 2.17 (s, 3 H), 2.14 (s, 3 H), 2.11 (s, 3 H), 2.05–1.95 (m, 1 H), 1.72–1.58 (m, 7 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 ($C=O_{acetate}$), 169.3 ($C=O_{acetate}$), 168.8 ($C=O_{acetate}$), 90.6 ($CH_{anomeric}$), 82.4 (Cq), 76.7 (CH), 71.0 (C_q), 66.8 (CH), 60.6 (CH_2), 28.9 (CH_2), 23.5 (CH_2), 22.2 ($COCH_3$), 21.1 ($COCH_3$), 20.8 ($COCH_3$), 19.8 (CH_2), 19.3 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3479, 3372, 1746 cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{24}O_9Na$ $[M + Na]^+$: 383.1318; found 383.1313.

C_2C_3-Cyclohexano-Annulated β-Glucopyranose (11): The diol **29** (28 mg, 0.078 mmol) in MeOH (500 µL) was added to a solution of ammonia in MeOH (1 mL, prepared by bubbling ammonia through MeOH maintained at 0 °C for 10–15 min) and the resulting reaction mixture was stirred at room temperature for 4 h. The volatiles were removed under reduced pressure, and the obtained residue was washed with ice-cooled ethyl acetate (1 mL) and dried to furnish the annulated glucopyranose **11** (14 mg, 78%). ^{1}H NMR (300 MHz, D_2O): δ = 4.77 (s, 1 H, $H_{anomeric}$), 3.92–3.89 (m, 1 H), 3.76 (dd, J = 12.3, 8.1 Hz, 1 H), 3.67–3.61 (m, 1 H), 3.59–3.50 (m, 1 H), 2.00–1.65 (series of m, 8 H) ppm. ^{13}C NMR (75 MHz, D_2O): δ = 92.7 ($CH_{anomeric}$), 79.8 (CH), 73.5 (C_q), 73.3 (C_q), 72.6 (CH), 62.3 (CH_2), 29.8 (CH_2), 29.3 (CH_2), 20.2 (CH_2), 19.7 (CH_2) ppm. HRMS (ES): calcd. for $C_{10}H_{18}O_6Na$ $[M + Na]^+$: 257.1001; found 257.0995.

(1*S)-1-[(1*S**,3*R**,3a*R**,7a*R**)-3-Acetoxy-3a,7a-dihydroxyperhydro-1-indenyl]-2-oxoethyl Acetate (31):** A slow stream of pre-cooled O_3/O_2 was bubbled through the solution of the alcohol **26** (100 mg, 0.31 mmol) in CH_2Cl_2/MeOH (5:1, 3 mL), cooled to –40 °C, until the solution had become a pale blue colour, indicating the presence of excess ozone. A stream of oxygen was bubbled through the solution to remove the excess ozone (blue colour of solution disappears). The reaction mixture was cooled to –78 °C and quenched by cautious addition of excess Me_2S (45 µL, 0.62 mmol). The reaction mixture was stirred at the same temperature for 30 min, prior to removal of the volatiles under reduced pressure. The residue obtained was subjected to silica gel column chromatography (40% ethyl acetate/hexane) to deliver the aldehyde **31** (62 mg, 56%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.61 (s, 1 H, HC=O), 6.19 (s, 1 H, $CH_{anomeric}$), 5.11 (d, J = 9.0 Hz, 1 H, CHOAc), 4.66 (d, J = 9 Hz, 1 H), 2.17–1.52 (series of m, 8 H), 2.17 (s, 3 H, $COCH_3$), 2.16 (s, 3 H, $COCH_3$), 2.15 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.6 ($C=O_{aldehyde}$), 169.4 ($C=O_{acetate}$), 169.1 ($C=O_{acetate}$), 169.0 ($C=O_{acetate}$), 98.3 ($CH_{anomeric}$), 90.0 (C_q), 81.8 (CH), 78.0 (C_q), 75.0 (CH), 26.9 (CH_2), 22.8 (CH_2), 22.0 ($COCH_3$), 21.1 ($COCH_3$), 20.4 ($COCH_3$), 19.6 (CH_2), 18.6 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3488, 1747, 1716 cm^{-1}.

(1*S)-1-[(1*S**,3*R**,3a*R**,7a*R**)-3-Acetoxy-3a,7a-dihydroxyperhydro-1-indenyl]-2-hydroxyethyl Acetate (32):** $NaBH_4$ (14 mg, 0.378 mmol) was added at 0 °C under an inert atmosphere to a magnetically stirred solution of the aldehyde **31** (45 mg, 0.126 mmol) in CH_2Cl_2/MeOH (3:1, 4 mL). The resulting homogeneous solution was stirred for 10 min at the same temperature, after which the starting material was completely consumed. The residue obtained after usual workup and evaporation of the solvent was chromatographed on a silica gel column (50% ethyl acetate/hexane) to furnish the diol **32** (38 mg, 85%), m.p. 186.0–188.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.09 (s, 1 H, $H_{anomeric}$), 4.67 (m, 2 H), 3.94 (br. d, J = 12.0 Hz, 1 H, CH_2OH), 3.79 (br. dd, J = 12.0, 3.0 Hz, 1 H, CH_2OH), 2.21–1.50 (series of m, 8 H), 2.17 (s, 3 H, $COCH_3$), 2.10 (s, 6 H, 2 $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8 ($COCH_3$), 169.2 ($COCH_3$), 168.9 ($COCH_3$), 98.2 ($CH_{anomeric}$), 90.2 (C_q), 81.3 (CHOAc), 78.6 (C_q), 72.8 (–CHO–), 62.9 (CH_2OH), 27.1 (CH_2), 23.1 (CH_2), 22.0 ($COCH_3$), 21.2 ($COCH_3$), 21.1 ($COCH_3$), 19.8 (CH_2), 18.7 (CH_2) ppm. IR (thin film): ṽ 3469, 1746, 1735 cm^{-1}. LRMS (ES, 70 eV) 384 $[M + Na + 1]^+$. HRMS (ES): calcd. for $C_{16}H_{24}O_9Na$ $[M + Na]^+$: 383.1318; found 383.1323.

Crystal Data for 32: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: Pc, cell parameters: a = 25.90(2) Å, b = 7.144(5) Å, c = 19.14(1) Å, β = 90.07(1)°, V = 3543.3(4) Å^3, Z = 8, ρ(calcd.) = 1.35 g cm^{-3}, F(000) = 1535.8, μ = 0.111 mm^{-1}, λ = 0.71 Å. R_1 = 0.098 for 3383 $F_o > 4\sigma(F_o)$ and 0.145 for all 6588 data, wR_2 = 0.210, GooF = 1.031, Restrained GooF = 1.031 for all data. An ORTEP drawing of compound **32** with 50% ellipsoidal probability level is shown below.



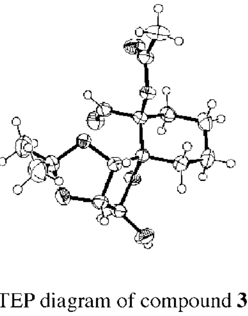
ORTEP diagram of compound **32**

(1*S,3*R**,3a*R**,7a*R**)-1-[(1*S*)-1,2-Dihydroxyethyl]-3-methoxyperhydroindene-3a,7a-diol (33):** The triacetate **32** (20 mg, 0.056 mmol) in MeOH (500 µL) was added to solution of ammonia in MeOH (500 µL) (prepared by bubbling ammonia into MeOH maintained at 0 °C for 10 min), and the resulting homogeneous solution was stirred at room temperature for 5 h, after which the starting material was completely consumed. The volatiles were removed under reduced pressure, the obtained residue was taken up in dry MeOH (300 µL), and Amberlyst-15 (≈ 5 mg) was added. The resulting suspension was stirred at room temperature for 12 h, prior to filtration of the reaction medium through a cotton plug. The filtrate was concentrated under reduced pressure to give a residue, which was rapidly chromatographed on a silica gel column (10% ethyl acetate/methanol) to furnish the annulated methyl α-glucofuranoside **33** (10 mg, 75%). ^{1}H NMR (300 MHz, CD_3OD): δ = 4.58 (s, 1 H, $H_{anomeric}$), 3.85 (m, 1 H), 3.82 (dd, J = 13.5, 3 Hz, 1 H), 3.77 (br. d, J = 3 Hz, 1 H), 3.59 (dd, J = 12.0, 4.8 Hz, 1 H), 3.36 (s, 3 H, OCH_3), 2.09–1.10 (series of m, 8 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 110.4 ($CH_{anomeric}$), 85.2 (CH), 80.4 (C_q), 79.5 (Cq), 72.3 (CH), 65.9 (CH_2), 55.9 (OCH_3), 28.8 (CH_2), 26.8 (CH_2), 20.7 (CH_2), 20.2 (CH_2) ppm. HRMS (ES): calcd. for $C_{11}H_{20}O_6Na$ $[M + Na]^+$: 271.1158; found 271.1178.

(3a*S,5a*R**,9a*R**,9b*S**)-9a-Hydroxy-2,2-dimethyl-3a,5a,6,7,8,9,9a,9b-octahydronaphtho[1,2-*d*][1,3]dioxol-5-yl Acetate (34):** Solid K_2CO_3 (168 mg, 1.223 mmol) was added to a stirred solution of the diacetate **23** (264 mg, 0.815 mmol) in MeOH (15 mL), and the resulting solution was stirred at room temperature for 2 h. Upon complete consumption of the starting material (TLC), the reaction mixture was diluted with ethyl acetate (15 mL). Usual workup gave a residue, which was purified over silica gel column (25% ethyl acetate/hexane) to furnish the monoacetate alcohol **34** (168 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.27 (d, J = 10.2 Hz, 1 H, C=CH), 5.91 (dd, J = 10.2, 4.2 Hz, 1 H, C=CH), 4.71 (dd, J = 6.6, 4.2 Hz, 1 H, $H_{acetonide}$), 4.08 (d, J = 6.6 Hz, 1 H, $H_{acetonide}$), 2.45 (d, J = 14 Hz, 1 H), 2.32 (dt, J = 13.5, 4.5 HZ, 1 H), 1.98 (s, 3 H, $COCH_3$), 1.80–1.43 (series of m, 6 H), 1.38 (s, 3 H, $CH_{3\ acetonide}$), 1.34 (s, 3 H, $CH_{3\ acetonide}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1 ($C=O_{acetate}$), 132.0 (C=CH), 127.89 (C=CH), 110.1 ($C_{q\ acetonide}$), 79.7 ($CH_{acetonide}$), 77.8 (C_q), 72.5 (C_q), 71.4 ($CH_{acetonide}$), 29.9 (CH_2), 28.4 (CH_2), 27.3 ($CH_{3\ acetonide}$), 24.9 ($CH_{3\ acetonide}$), 21.8 ($COCH_3$), 20.3 (CH_2), 19.3 (CH_2) ppm. IR (thin film): ṽ 3464, 1728 cm^{-1}. HRMS (ES): calcd. for $C_{15}H_{22}O_5Na$ $[M + Na]^+$: 305.1365; found 305.1392.

(2*S,3a′*S**,1′*R**,6′*R**,6a′*R**)-2-Formyl-6′-hydroxy-2′,2′-dimethylspiro[cyclohexane-1,4′-perhydrofuro[3,4-*d*][1,3]dioxol]-2-yl Acetate (35):** The alcohol **34** (100 mg, 0.355 mmol) was subjected to ozonolysis in CH_2Cl_2/MeOH (5:1, 4 mL) and subsequent quenching with Me_2S (52 µL, 0.71 mmol) by the procedure described for ozonolysis of **25**. Chromatographic purification of the residue over a silica gel delivered the lactol aldehyde **35** (100 mg, 90%), m.p.179.0–180.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.67 (s, 1 H, -CHO), 5.42 (s, 1 H, $H_{anomeric}$), 4.70 (½ ABq, J = 5.7 Hz, 1 H, $H_{acetonide}$), 4.54 (½ Abq, J = 5.7 Hz, 1 H, $H_{acetonide}$), 3.62 (s, OH), 2.38 (d, J = 14.4 Hz, 1 H), 2.21 (s, 3 H, $COCH_3$), 2.21–1.25 (series of m, 7 H), 1.41 (s, 3 H, $CH_{3\ acetonide}$), 1.29 (s, 3 H, $CH_{3\ acetonide}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.3 ($C=O_{aldehyde}$), 169.8 ($C=O_{acetate}$), 113.1 ($C_{q\ acetonide}$), 103.7 ($CH_{anomeric}$), 91.2 (C_q), 86.7 ($CH_{acetonide}$), 86.1 (C_q), 85.0 ($CH_{acetonide}$), 32.3 (CH_2), 26.2 (CH_2), 25.7 ($CH_{3\ acetonide}$), 24.8 ($CH_{3\ acetonide}$), 21.3 ($COCH_3$), 19.9 (CH_2), 19.7 (CH_2) ppm. IR (thin film): ṽ 3439, 1732 cm^{-1}. HRMS (ES): Calcd. for $C_{15}H_{22}O_7Na$ $[M + Na]^+$: 337.1263; found: 337.1258. $C_{15}H_{22}O_7$ [314]: C 57.316, H 7.054; found: C 56.964, H 7.024.

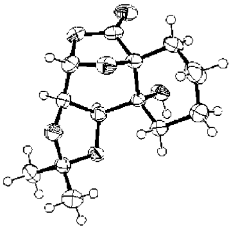
Crystal Data for 35: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: $P2_1/c$, cell parameters: a = 14.361(3) Å, b = 7.749(2) Å, c = 15.041(3) Å, β = 113.144(4)°, V = 1539.1(3) Å^3, Z = 4, ρ(calcd.) = 1.36 g cm^{-3}, F(000) = 671.9, μ = 0.107 mm^{-1}, λ = 0.71 Å. R_1 = 0.042 for 2623 $F_o > 4\sigma(F_o)$ and 0.054 for all 3341 data, wR_2 = 0.109, GooF = 0.971, Restrained GooF = 0.971 for all data. An ORTEP drawing of compound **35** with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **35**

(1*S,6*R**,7*S**,11*R**,12*S**)-6-Hydroxy-9,9-dimethyl-8,10,13,15-tetraoxatetracyclo[10.2.1.0^{1,6}.0^{7,11}]pentadecan-14-one (38):** Solid K_2CO_3 (184 mg, 1.338 mmol) was added at 0 °C to solution of lactol aldehyde **35** (140 mg, 0.446 mmol) in MeOH (10 mL) and the resulting suspension was stirred at room temperature for 30 min. Upon complete consumption of the starting material (TLC), the reaction mixture was diluted with ethyl acetate (10 mL) and was subjected to the usual workup. The obtained residue (**37**) was taken up in dry CH_2Cl_2 (15 mL), and a catalytic amount of TPAP (3 mg, 0.0089 mmol, 2 mol%) and solid NMMO (104 mg, 0.892 mmol) were added sequentially under inert atmosphere. The resulting black solution was stirred at room temperature for 6 h to ensure completion of the reaction. The residue obtained after dilution of the reaction mixture and the usual workup was chromatographed on silica gel (20% ethyl acetate/hexane) to furnish the lactone **38** (109 mg, 91%), m.p. 216–217.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.02 (s, 1 H, $H_{anomeric}$), 4.36 (½ ABq, J = 6.6 Hz, 2 H, $H_{acetonide}$), 2.26–2.14 (m, 2 H), 1.87 (½ ABq, J = 13.5 Hz, 1 H), 1.77–1.56 (m, 5 H), 1.56 (s, 3 H, $CH_{3\ acetonide}$), 1.36 (s, 3 H, $CH_{3\ acetonide}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.2 ($C{=}O_{lactone}$), 111.7 ($C_{qacetonide}$), 99.5 ($CH_{anomeric}$), 81.1 ($CH_{acetonide}$), 78.4 (C_q), 73.5 ($CH_{acetonide}$), 71.7 (C_q), 30.8 (CH_2), 26.3 (CH_2), 25.7 ($CH_{3\ acetonide}$), 25.0 ($CH_{3\ acetonide}$), 20.0 (CH_2), 19.4 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3439, 1803 cm^{-1}. HRMS (ES) calcd. for $C_{13}H_{18}O_6Na$ [M + Na]$^+$: 293.1001; found 293.1031. $C_{13}H_{18}O_6$ [270]: C 57.77, H 6.71. Found C 57.95, H 6.75.

Crystal Data for 38: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: $P2_1/c$, cell parameters: a = 12.909(2) Å, b = 9.914(1) Å, c = 21.603(3) Å, β = 106.699(3)°, V = 2648.3(3) Å^3, Z = 8, ρ(calcd.) = 1.36 gcm^{-3}, F(000) = 1151.9, μ = 0.107 mm^{-1}, λ = 0.71 Å. R_1 = 0.052 for 3452 $F_o > 4\sigma(F_o)$ and 0.097 for all 5767 data, wR_2 = 0.116, GooF = 0.917, Restrained GooF = 0.917 for all data. An ORTEP drawing of compound **38** with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **38**

(3a*R,4*R**,5a*S**,9a*R**,9b*S**)-4,9a-Dihydroxy-2,2-dimethylperhydro-[1,3]dioxolo[4,5-*c*]chromene-5a-carboxylic Acid (40):** An ice-cooled solution of the lactone **38** (85 mg, 0.315 mmol) in dry MeOH (5 mL) was treated with NaOMe (20 mg, 0.378 mmol) under inert atmosphere, and the resulting pale yellow solution was stirred at the same temperature for 10 min. The reaction mixture was diluted with ethyl acetate (20 mL) and quenched with saturated NH_4Cl (500 µL). The residue obtained after the usual workup was chromatographed on a silica gel column to furnish the ester lactol **40** (84 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.51 (br. s, 1 H, $H_{anomeric}$), 4.64 (½ ABq, J = 6 Hz, 1 H, $H_{acetonide}$), 4.53 (½ ABq, J = 6 Hz, 1 H, $H_{acetonide}$), 3.76 (s, 3 H, CO_2CH_3), 2.03–1.42 (series of m, 8 H), 1.36 (s, 3 H, $CH_{3\ acetonide}$), 1.26 (s, 3 H, $CH_{3\ acetonide}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.5 ($C{=}O_{ester}$), 112.5 (C_q), 104.1 ($CH_{anomeric}$), 89.2 (C_q), 86.2 ($CH_{acetonide}$), 85.5 ($CH_{acetonide}$), 74.3 (C_q), 52.8 (OCH_3), 34.4 (CH_2), 32.7 (CH_2), 25.9 ($CH_{3\ acetonide}$), 24.5 ($CH_{3\ acetonide}$), 20.1 (CH_2), 19.9 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3489, 1723 cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{22}O_7Na$ [M + Na]$^+$: 325.1263; found 325.1276.

(3a*R,4*R**,5a*S**,9a*R**,9b*S**)-9a-Hydroxy-4-methoxy-2,2-dimethylperhydro[1,3]dioxolo[4,5-*c*]chromene-5a-carboxylic Acid (41):** Amberlyst-15 (acidic resin, ca. 5 mg) and 2,2-dimethoxypropane (22 µL, 0.182 mmol) were added sequentially to a solution of ester lactol **40** (55 mg, 0.182 mmol) in dry MeOH (4 mL). The resulting suspension was stirred at room temperature for 16 h. The reaction mixture was filtered through a cotton plug to remove the resin, and the filtrate was concentrated under reduced pressure. The residue obtained was subjected to silica gel column chromatography (20% ethyl acetate/hexane) to furnish the epimeric annulated methyl β-gulopyranouronate derivative **41** (50 mg, 0.158 mmol) and the corresponding α-isomer (8 mg, 0.025 mmol) in a ratio of 6:1 and 95% overall yield, m.p. 188–189.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.97 (s, 1 H, $H_{anomeric}$), 4.58 (½ ABq, J = 6.0 Hz, 1 H, $H_{acetonide}$), 4.47 (½ ABq, J = 6.0 Hz, 1 H, $H_{acetonide}$), 3.77 (s, 3 H, CO_2CH_3), 3.43 (s, 3 H, OCH_3), 2.07–1.52 (series of m, 8 H), 1.36 (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.8 ($C{=}O_{ester}$), 112.3 ($C_{q(acetonide)}$), 110.3 ($CH_{anomeric}$), 89.1(C_q), 85.7 ($CH_{acetonide}$), 84.8 ($CH_{acetonide)}$), 74.4 (C_q), 55.9 (CO_2CH_3), 52.7 (OCH_3), 34.3 (CH_2), 32.6 (CH_2), 25.6 ($CH_{3\ acetonide}$), 24.2 ($CH_{3\ acetonide}$), 20.3 (CH_2), 20.1 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3484, 1721 cm^{-1}. HRMS (ES): calcd. for $C_{15}H_{24}O_7Na$ [M + Na]$^+$: 339.1420; found 339.1434.

(3a*R,4*R**,5a*R**,9a*R**,9b*S**)-5a-(Hydroxymethyl)-4-methoxy-2,2-dimethylperhydro[1,3]dioxolo[4,5-c]chromen-9a-ol (42):** $LiAlH_4$ (8 mg, 0.213 mmol) was added to a solution of the ester **41** (45 mg, 0.142 mmol) in dry THF (5 mL) and the resulting suspension was stirred at room temperature for 40 min. The reaction mixture was cooled to 0 °C and diluted by careful addition of ethyl acetate (15 mL), followed by cold saturated aqueous Na_2SO_4 solution. The resulting suspension was filtered through a celite pad and repeatedly washed with ethyl acetate. The usual workup gave a solid residue that on chromatographic purification on a silica gel column (40% ethyl acetate/hexane) furnished the annulated methyl β-gulopyranoside **42** (36 mg, 90%), m.p. 210–211.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.96 (s, 1 H, $H_{anomeric}$), 4.70 (½ ABq, J = 6.0 Hz, 1 H, $H_{acetonide}$), 4.62 (½ ABq, J = 6.0 Hz, 1 H, $H_{acetonide}$), 4.06 (d, J = 10.5 Hz, 1 H), 3.81 (br. s, OH), 3.38 (s, 3 H, OCH_3), 3.30 (ABq, J = 10.5 Hz, 2 H, CH_2OH), 1.84–1.42 (series of m, 8 H), 1.54 (s, 3 H, $COCH_3$), 1.34 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.9 ($C_{q(acetonide)}$), 109.6 ($CH_{anomeric}$), 89.7 (C_q), 86.7 ($CH_{acetonide}$), 85.3 ($CH_{acetonide}$), 72.8 (C_q), 64.6 (CH_2OH), 55.8 (OCH_3), 34.7 (CH_2), 33.1 (CH_2), 26.0 ($CH_{3\ acetonide}$), 24.4 ($CH_{3\ acetonide}$), 21.5 (CH_2), 21.3 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3474 cm^{-1}. HRMS (ES): calcd. for $C_{14}H_{24}O_6Na$ [M + Na]$^+$: 311.1471; found 311.1497.

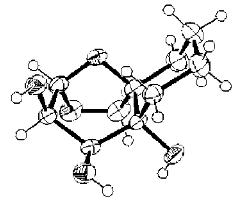
(2*R,3*R**,4*S**,4a*R**,8a*R**)-8a-(Hydroxymethyl)-2-methoxyperhydrochromene-3,4,4a-triol (43):** A suspension of the diol acetonide **42** (20 mg, 0.069 mmol) in HCl (1 N, 800 µL) was stirred vigorously at room temperature for 2 h, after which the starting material was completely hydrolysed. The solvent was removed under reduced pressure to furnish a residue, which was washed with cold diethyl ether (2×500 µL) to give the annulated methyl β-gulopyranoside **43** (11 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.82 (s, 1 H, $CH_{anomeric}$), 4.34 (m, 1 H), 4.22 (d, J = 11.7 Hz, 1 H, CH_2OH), 4.05 (br. d, J = 4.8 Hz, 2 H), 3.87 (br. s, OH) 3.41 (d, J = 11.7 Hz, 1 H, CH_2OH), 3.33 (s, 3 H, OCH_3), 2.13–2.05 (m, 1 H), 1.87–1.45 (m, 7 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 107.7 ($CH_{anomeric}$), 87.9 (C_q), 79.7 (CHOH), 75.9 (CHOH), 75.6 (C_q), 66.4 (CH_2OH), 54.9 (OCH_3), 38.2 (CH_2), 33.1 (CH_2), 22.7 (CH_2), 22.1 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3469 cm^{-1}. HRMS (ES): calcd. for $C_{11}H_{20}O_6Na$ [M + Na]$^+$: 271.1158; found 271.1187.

(2*S,3*R**,4*S**,4a*R**,8a*R**)-8a-(Hydroxymethyl)perhydrochromene-2,3,4,4a-tetraol (44) and (1*R**,6*R**,7*S**,8*R**,9*R**)-10,12-Dioxatricyclo[7.2.1.0^{1,6}]dodecane-6,7,8-triol (45):** A suspension of the tetrol **43** (11 mg, 0.044 mmol) in HCl (1 N, 500 µL) was stirred at 50 °C for 30 min, after which all the starting material was consumed. The solvent was removed under reduced pressure to give a residue, which was chromatographed on a silica gel column (1% methanol/ethyl acetate) to furnish the annulated α-gulopyranose **44** (3 mg, 0.0147 mmol) and the annulated β-1,6-anhydro gulopyranoside **45** (6 mg, 0.0293 mmol).

Compound 44: ^1H NMR (300 MHz, CD_3OD): δ = 5.06 (d, J = 4.2 Hz, 1 H, $H_{anomeric}$), 4.13–4.07 (m, 2 H), 3.86 (d, J = 9.6 Hz, 1 H, CH_2OH), 3.29 (d, J = 9.0 Hz, 1 H, CH_2OH), 2.21 (dt, J = 12.6, 4.8 Hz, 2 H), 1.77–1.28 (series of m, 6 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 99.1 ($CH_{anomeric}$), 82.2 (C_q), 76.3 (CH), 72.8 (CH_2), 70.4 (CH), 69.5 (C_q), 33.9 (CH_2), 31.9 (CH_2), 22.2 (CH_2), 21.4 (CH_2) ppm. IR (Nujol): $\tilde{\nu}$ 3450 cm^{-1}. HRMS (ES): calcd. for $C_{10}H_{18}O_6Na$ [M + Na]$^+$: 257.1001; found 257.0980.

Compound 45: ^1H NMR (300 MHz, CD_3OD): δ = 5.26 (s, 1 H, $H_{anomeric}$), 4.09 (d, J = 7.2 Hz, 1 H, CH_2OH), 3.75–3.71 (m, 2 H), 3.05 (d, J = 7.2 Hz, 1 H, CH_2OH), 1.96–1.28 (series of m, 8 H) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 103.5 ($CH_{anomeric}$), 82.8 (C_q), 74.4 (C_q), 73.6 (CH), 72.3 (CH), 70.6 (CH_2), 28.9 (2C, CH_2), 22.7 (CH_2), 20.7 (CH_2) ppm. IR (KBr): $\tilde{\nu}$ = 3470 cm^{-1}. HRMS (ES): calcd. for $C_{10}H_{16}O_5Na$ [M + Na]$^+$: 239.0895; found 239.0918.

Crystal Data for 45: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: triclinic, space group: $P\bar{1}$, cell parameters: a = 5.813(4) Å, b = 6.752(5) Å, c = 14.301(10) Å, α = 82.774(8)°, β = 82.539(8)°, γ = 72.144(8)°, V = 527.6(2) Å^3, Z = 2, ρ(calcd.) = 1.36 gcm^{-3}, F(000) = 232.0, μ = 0.109 mm^{-1}, λ = 0.71 Å. R_1 = 0.036 for 1643 $F_o > 4\sigma(F_o)$ and 0.043 for all 1903 data, wR_2 = 0.094, GooF = 1.062, Restrained GooF = 1.062 for all data. An ORTEP drawing of compound **45** with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **45**

Methyl (1*R,3*S**,4*S**,4a*R**,8a*R**)-3,4,8a-Triacetoxy-4a-hydroxyperhydroisochromene-1-carboxylate (48a) and Methyl (1*R**,3*R**,4*S**,4a*R**,8a*R**)-3,4,8a-Triacetoxy-4a-hydroxyperhydroisochromene-1-carboxylate (48b):** A pre-cooled stream of O_3/O_2 was bubbled through a well stirred solution of allylic alcohol **46** (120 mg, 0.422 mmol) in CH_2Cl_2/MeOH (5:1, 4 mL), cooled to –40 °C, and this was continued until the pale blue colour of excess O_3 persisted. A stream of oxygen was bubbled through the solution to remove the excess ozone (blue colour of solution disappeared). The solvent was removed under reduced pressure at 0 °C and the resulting residue was taken up in dry CH_2Cl_2 (5 mL). Ac_2O (60 µL, 0.633 mmol) and Et_3N (120 µL, 0.861 mmol) were sequentially added to this solution. After the reaction mixture had been stirred at room temperature for 2 h, it was diluted with CH_2Cl_2 (10 mL). The usual workup gave a residue, which was chromatographed on a silica gel column (20% ethyl acetate/hexane) to furnish the epimeric triacetates **48a** (47 mg, 0.121 mmol) and **48b** (46 mg, 0.119 mmol) in 1:1 ratio and in 56% overall yield.

Compound 48a: M.p. 215–216.7 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.43 (d, J = 3.0 Hz, 1 H, $H_{anomeric}$), 6.31 (d, J = 3.0 Hz, 1 H, CHOAc), 4.88 (s, 1 H, –CHO–), 3.78 (s, 3 H, CO_2CH_3), 2.80 (d, J = 14.4 Hz, 1 H), 2.73 (s, 1 H), 2.14 (s, 3 H, $COCH_3$), 2.12 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 1.90–1.52 (series of m, 7 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4 (C=O), 169.1 (C=O), 168.4 (C=O), 167.9 (C=O), 89.8 ($CH_{anomeric}$), 83.2 (C_q), 72.0 (Cq), 70.0 (CH), 67.9 (CH), 52.3 (CO_2CH_3), 29.1 (CH_2), 22.8 (CH_2), 21.8 ($COCH_3$), 21.0 ($COCH_3$), 20.5 ($COCH_3$), 20.0 (CH_2), 18.9 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 3450, 1748 cm^{-1}. HRMS (ES): calcd. for $C_{17}H_{24}O_{10}Na$ [M + Na]$^+$: 411.1267; found 411.1253.

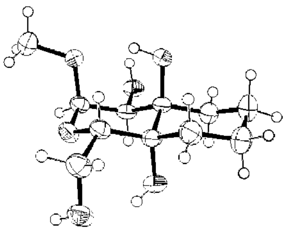
Compound 48b: M.p. 196.3–197.5 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.06 (d, J = 8.4 Hz, 1 H, $H_{anomeric}$), 5.24 (d, J = 8.4 Hz, 1 H, CHOAc), 4.72 (s, 1 H, –CHO–), 3.76 (s, 3 H, CO_2CH_3), 2.83 (br. d, J = 15 Hz, 1 H), 2.14 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 2.05–1.17 (series of m, 7 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4 (C=$O_{acetate}$), 169.3 (C=$O_{acetate}$), 169.0 (C=$O_{acetate}$), 167.3 (C=O_{ester}), 91.1 ($CH_{anomeric}$), 82.7 (C_q), 74.5 (CH), 73.7 (C_q), 71.4 (CH), 52.2 (CO_2CH_3), 29.5 (CH_2), 22.7 (CH_2), 21.8 ($COCH_3$), 21.0 ($COCH_3$), 20.6 ($COCH_3$), 19.9 (CH_2), 19.0 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 1746 cm^{-1}. HRMS (ES): calcd. for $C_{17}H_{24}O_{10}Na$ [M + Na]$^+$: 411.1267; found 411.1248.

Methyl (1*R,3*S**,4*S**,4a*R**,8a*R**)-4,8a-Diacetoxy-4a-hydroxy-3-methoxyperhydroisochrome-1- carboxylate (50a):** Solid KOH (8 mg, 0.145 mmol) was added to an ice-cooled solution of the annulated α-gulopyranouronate triacetate **48a** (47 mg, 0.121 mmol) in *i*PrOH/THF (1:1, 3 mL), and the reaction was allowed to continue further at the same temperature for 5 min. The reaction mixture was diluted with ethyl acetate and quenched by addition of ice-cooled water (1 mL). The resulting solution was worked up in the usual manner to give a solid residue. The obtained residue was taken up in MeI (3 mL) and stirred in the presence of Ag_2O (28 mg, 0.121 mmol) at room temperature for 2 h. The reaction mixture was diluted with ethyl acetate and filtered through a celite pad to remove silver salts. The filtrate was concentrated under reduced pressure to give a residue, which on purification by silica gel column chromatography (30% ethyl acetate/hexane) furnished the methyl α-gulopyranoside derivative **50a** (35 mg, 80%), m.p. 181–182 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.12 (br. s, 1 H, $H_{anomeric}$), 5.09 (br. s, 1 H, CHOAc), 4.63 (s, 1 H, –CHO–), 4.08 (s, OH), 3.79 (s, 3 H, CO_2CH_3), 3.44 (s, 3 H, OCH_3), 2.76 (d, J = 14.7 Hz, 1 H), 2.14 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 1.94–1.49 (series of m, 7 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4 (C=O), 169.4 (C=O), 168.5 (C=O), 98.4 ($CH_{anomeric}$), 84.2 (C_q), 72.6 (C_q), 69.1 (CH), 68.2 (CH), 56.5 (CO_2CH_3), 52.3 (OCH_3), 28.7 (CH_2), 22.9 (CH_2), 21.8 ($COCH_3$), 20.8 ($COCH_3$), 20.1 (CH_2), 18.9 (CH_2) ppm. IR (thin film): $\tilde{\nu}$ 1750 cm^{-1}. HRMS (ES): calcd. for $C_{16}H_{24}O_9Na$ [M + Na]$^+$: 383.1318; found 383.1324.

Methyl (1*R,3*R**,4*S**,4a*R**,8a*R**)-4,8a-Diacetoxy-4a-hydroxy-3-methoxyperhydroisochromene-1-carboxylate (50b):** The annulated β-gulopyranouronate triacetate **48b** (46 mg, 0.119 mmol) was converted into this methyl glycoside **50b** (34 mg, 80%) by the procedure used for the conversion of **48a** to **50a**. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 5.11 (d, J = 7.8 Hz, 1 H, H$_{anomeric}$), 4.70 (d, J = 7.8 Hz, 1 H, CHOAc), 4.59 (s, 1 H, –CHO–), 3.80 (s, 3 H, CO$_2$CH$_3$), 3.52 (s, 3 H, OCH$_3$), 2.80 (d, J = 14.4 Hz, 1 H), 2.14 (s, 3 H, COCH$_3$), 2.12 (s, 3 H, COCH$_3$), 1.86–1.60 (series of m, 8 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 169.4 (C=O), 169.2 (C=O), 168.0 (C=O), 100.6 (CH$_{anomeric}$), 82.9 (C$_q$), 73.8 (CH), 73.7 (C$_q$), 72.2 (CH), 57.1 (CO$_2$CH$_3$), 52.1 (OCH$_3$), 29.5 (CH$_2$), 22.8 (CH$_2$), 21.9 (CH$_2$), 20.9 (CH$_2$), 20.0 (CH$_2$), 19.1 (CH$_2$) ppm. IR (thin film): ṽ 3440, 1748 cm^{-1}. HRMS (ES): calcd. for C$_{16}$H$_{24}$O$_9$Na [M + Na]$^+$: 383.1318; found 383.1324.

(1*S,3*S**,4*S**,4a*R**,8a*R**)-1-(Hydroxymethyl)-3-methoxyperhydroisochromene-4,4a,8a-triol (47a):** LiAlH$_4$ (10 mg, 0.28 mmol) was cautiously added under inert atmosphere to a solution of the ester **50a** (20 mg, 0.056 mmol) in dry THF (6 mL), maintained at 0 °C. The resulting suspension was stirred at room temperature for 1 h, prior to quenching of the excess reagent by addition of ethyl acetate (10 mL) and saturated NH$_4$Cl (1 mL). The resulting suspension was filtered thorough a celite pad, which was repeatedly washed with ethyl acetate, and the filtrate was concentrated under reduced pressure to give a residue, which on chromatographic purification on a silica gel column (90% ethyl acetate/hexane) furnished the annulated methyl α-gulopyranoside **47a** (11 mg, 80%), m.p. 159.0–160 °C. ^{1}H NMR (300 MHz, CD$_3$OD): δ = 4.76 (d, J = 3.9 Hz, 1 H, H$_{anomeric}$), 3.85 (m, 1 H), 3.80 (d, J = 4.2 Hz, 1 H), 3.74 (m, 2 H), 3.45 (s, 3 H, OCH$_3$), 1.70–1.58 (m, 6 H), 1.41–1.36 (m, 2 H) ppm. ^{13}C NMR (75 MHz, CD$_3$OD): δ = 102.3 (CH$_{anomeric}$), 74.8 (C$_q$), 74.7 (C$_q$), 71.6 (CH), 69.5 (CH), 62.0 (CH$_2$), 56.1 (OCH$_3$), 28.9 (CH$_2$), 28.7 (CH$_2$), 20.9 (CH$_2$), 20.4 (CH$_2$) ppm. HRMS (ES): calcd. for C$_{11}$H$_{20}$O$_6$Na [M + Na]$^+$. 271.1158; found: 271.0639.

Crystal Data for 47a: The structure was solved by direct methods (SIR92). Refinement was by full-matrix, least-squares procedures on F^2 by use of SHELXL-97. Crystal system: monoclinic, space group: $C2/c$, cell parameters: a = 17.56(1) Å, b = 7.332(5) Å, c = 18.86(1) Å, β = 93.63(1)°, V = 2427.9(4) Å^3, Z = 8, ρ(calcd.) = 1.36 g cm^{-3}, F(000) = 1071.9, μ = 0.110 mm^{-1}, λ = 0.71 Å. R_1 = 0.046 for 1680 $F_o > 4\sigma(F_o)$ and 0.067 for all 2264 data, wR_2 = 0.107, GooF = 1.051, Restrained GooF = 1.051 for all data. An ORTEP drawing of compound **47a** with 50% ellipsoidal probability level is shown below.



ORTEP diagram of compound **47a**

(1*S,3*R**,4*S**,4a*R**,8a*R**)-1-(Hydroxymethyl)-3-methoxyperhydroisochromene-4,4a,8a-triol (47b):** The ester diacetate **50b** (22 mg, 0.061 mmol) was reduced with LiAlH$_4$ (11 mg, 0.305 mmol) by the procedure adopted for the conversion of **50a** into **47a**, to afford the annulated methyl β-gulopyranoside **47b** (12 mg, 84%). ^{1}H NMR (300 MHz, CD$_3$OD): δ = 4.52 (d, J = 8.1 Hz, 1 H, H$_{anomeric}$), 3.81 (m, 1 H), 3.73–3.67 (m, 2 H), 3.52 (s, 3 H, OCH$_3$), 3.42 (d, J = 8.1 Hz, 1 H), 1.77–1.63 (m, 5 H), 1.44–1.37 (m, 3 H) ppm. ^{13}C NMR (75 MHz, CD$_3$OD): δ = 104.4 (CH$_{anomeric}$), 77.5 (CH), 74.7 (C$_q$), 74.3 (C$_q$), 73.0 (CH), 62.0 (CH$_2$), 57.1 (OCH$_3$), 29.1 (CH$_2$), 28.9 (CH$_2$), 20.9 (CH$_2$), 20.6 (CH$_2$) ppm. HRMS (ES): calcd. for C$_{11}$H$_{20}$O$_6$Na [M + Na]$^+$: 271.1158; found 271.1127

Crystallographic Data: CCDC-243800 (for **23**), -246798 (for **25**), -246797 (for **26**), -243806 (for **27**), -243805 (for **32**), -243801 (for **35**), -243802 (for **38**), -243803 (for **45**) and -243804 (for **47a**) contain the crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.

Supporting Information (see also the footnote on the first page of this article): ^{13}C NMR spectra of all the new compounds reported here.

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