Pyrano[2,3-*b*]dioxanes through Bisacetalic Annulation of 2-Ketosugars to Glycol[‡]

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The utility of 2-ketohexosyl ("ulosyl") bromides has been extended to the straightforward generation of *cis*-fused pyrano[2,3-*b*]dioxanes (1,4,5-trioxadecalins) of type **11** and **13** by β-specific and α-selective glycosidation with glycol, and subsequent intramolecular hemiketalization. Mild basic conditions elicit highly stereoselective rearrangements to trioxadecalinones **22**–**25**, representing the structurally and configurationally correct framework of steroidal natural products in which the sugar portion is doubly glycosidically linked to the aglycon. Exposure of **11** or **13** to mineral acid results in an essentially stereospecific contraction of the pyranoid ring to yield trioxaspiro[4,5]decanes. Mechanistic considerations of the unusual rearrangements observed are discussed in light of available experimental facts and the scarce existing analogies.

Introduction

Glycos-2-ulosyl bromides of type **2** have recently become nearly as accessible as the usual glycosyl halides,[1] as they may be prepared in a straightforward one-step process from readily available[2] 2-hydroxyglycal esters (**1**); the conversion simply consists of reaction with *N*-bromosuccinimide or bromine in the presence of methanol[1] (Scheme 1). The ease with which the transformation **1** → **2** can be effected (30 min, room temperature) is as remarkable as the yields attainable (80−90%) and the feasibility with essentially any blocking group pattern.

Acylated ulosyl bromides[1,4] − unlike their reactive benzylated analogs[3] − are shelf-stable, crystalline substances with comparatively low anomeric reactivity, such that the tri-*O*-benzoyl derivative **2**, for example, may be recovered from a methanol solution at ambient temperature to react with cyanoborohydride by carbonyl addition to provide the 2-OH-free glucosyl bromide **3**.[5] Anomeric reactivity, though, can be substantially enhanced by either conversion into ulosyl iodides, e.g. **2** → **4**,[1] or by employing benzyl instead of acyl protecting groups.[3]

As the electron-withdrawing 2-keto group in ulosyl bromides strongly favors direct S_N2 displacement of the anomeric bromine by *O*-nucleophiles, Koenigs−Knorr type glycosidations proceed in an essentially β-specific manner,[1,3,4] e.g. **2** → **5**. Since reduction of the β-D-glycosiduloses formed is highly *manno*-selective,[3,6] the two-step-sequence, **2** → **5** → **6**, has evolved into an expedient procedure for the generation of β-D-mannosides, the "ulosyl donor approach", which has successfully been applied to the synthesis of β-D-mannose-oligosaccharides up to the hexasaccharide level,[3,7] as well as to the generation of β-L-rhamnosidic linkages.[8] A *gluco*-selective reduction may also be accomplished in a straightforward manner by using borane as the reductant, e.g. **5** → **7**, providing 2-OH-free β-D-glucosides.[6] As α-bromoketones, ulosyl bromides are also amenable to Reformatsky reactions, leading to *C*-glycosides on exposure to zinc and aldehydes (**2** → **8**).[9] Modest though is the α-selectivity attainable in glycosidations, which result in α,β-mixtures that require chromatographic separation, e.g. **2** → **9** (53%).[10]

An application of ulosyl bromides that has not been exploited is their reaction with vicinal diols for which pyranodioxanes of type **11** or **13** are to be expected, if glycoside formation with one glycol-OH is followed by ring closure with the other to a cyclic hemiacetal. As such products carry an OH group at the ring junction, they contain the structural and conformational elements of a series of cardioactive cardenolides such as asclepin, calotropin,[11] and its 7,8-dehydro analog humistratin,[12] for which the bisacetalic annulation of a 2-ketohexose to the steroid diol aglycon is all but synthetically solved.

To determine whether the "ulosyl donor approach" may be implemented to doubly link a hexosulose to a vicinal diol through an acetal (glycosidic) and a hemiketal bond, we have undertaken exploratory studies, which are the subject of this report. They have not only established the

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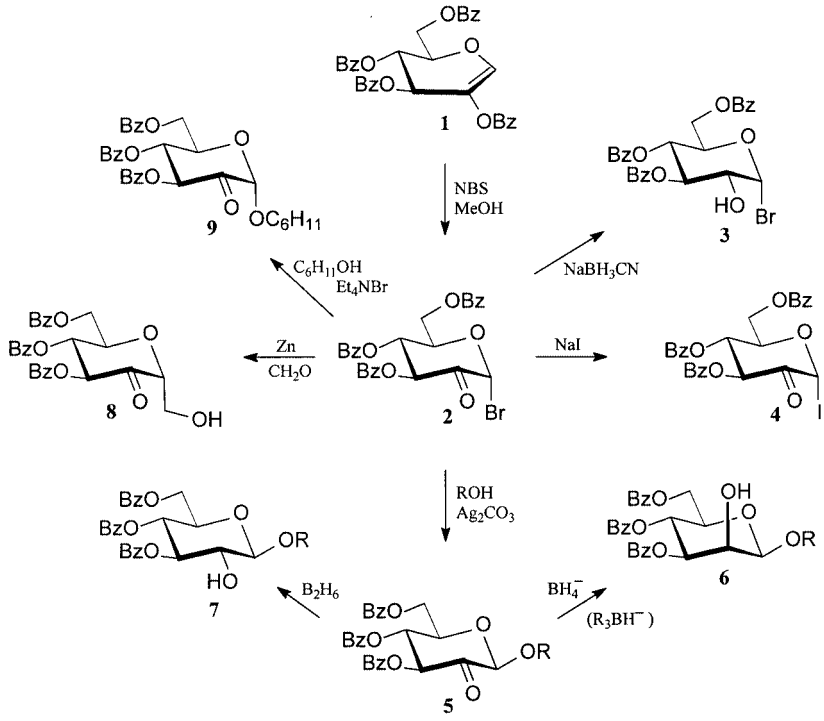


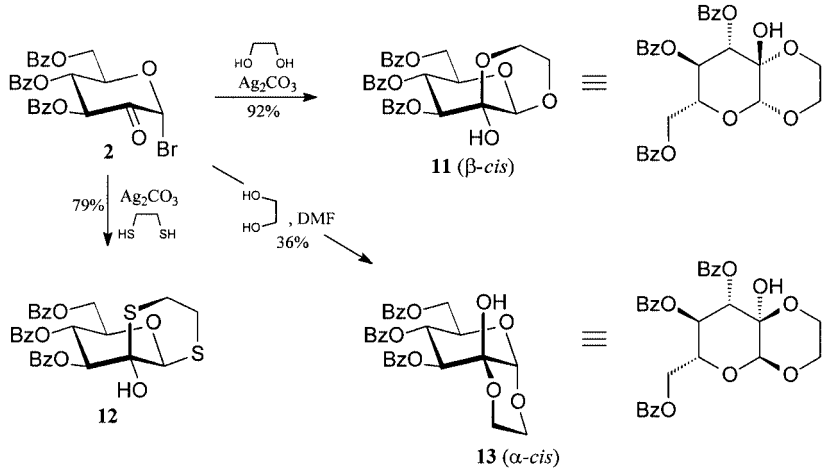
Scheme 1. Preparative utility of ulosyl bromides

feasibility of obtaining *cis*-fused pyrano[2,3-*b*]dioxanes in a concise fashion, but uncovered their exceptional proclivity of undergoing unique, stereospecific rearrangements.

Results and Discussion

When subjected to glycolysis with ethylene glycol in the presence of silver carbonate, the ulosyl bromide **2** smoothly gave the *cis*-fused trioxadecalin **11** in a nearly quantitative yield; the same reaction with 1,2-ethanedithiol provided the dithia-analog **12** (79%) as readily. Both products (**11** and **12**) were obtained in good crystalline form (Scheme 2). No *trans*-fused products could be detected by TLC or ^{1}H NMR spectroscopy in either mother liquor. Thus, in both cases, β-specific glycosidation was followed by addition of the second OH or SH group to the 2-carbonyl from the upper side to elaborate a *cis*-annulated dioxane or dithiane, respectively. Obviously, the *e,a*-linkup of these rings with the ring junction substituent (OH) in a diaxial disposition to the pyran ring oxygen is considerably more favored than an *e,e*-fusion with the OH group in a gauche arrangement relative to the pyranoid oxygen.

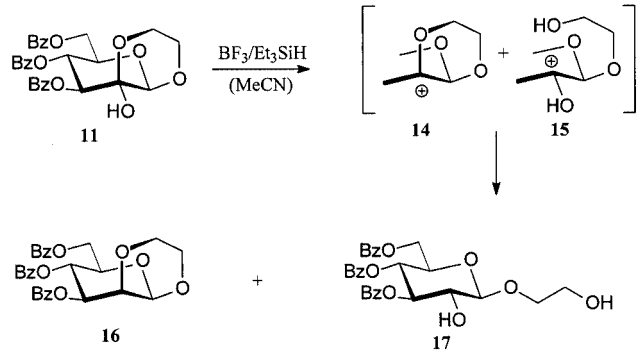
When the glycosidation of ulosyl bromide **2** with glycol was conducted in an α-selective manner, either with silver triflate in CH_2Cl_2 or, preparatively more advantageous, by stirring in dimethylformamide at ambient temperature, mixtures of β-*cis* (**11**) and α-*cis* isomers (**13**) were obtained



Scheme 2. Glycosidations of ulosyl bromide **2** with glycol and 1,2-ethanedithiol, and subsequent cyclo-hemiketal formation

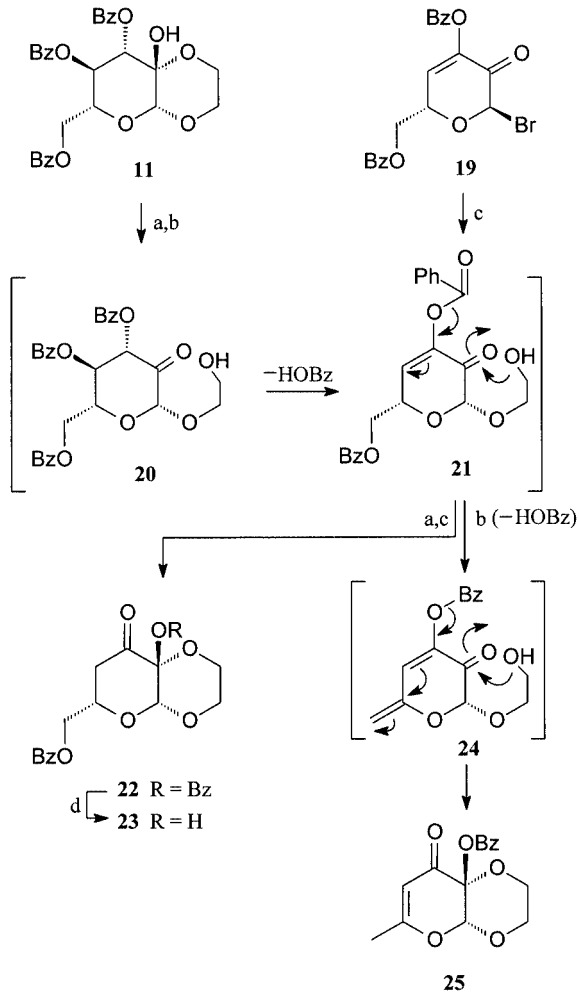
(Scheme 2), from which **13** could be separated by crystallization from diethyl ether in moderate yield (36%).

Whilst ^{1}H and ^{13}C NMR spectroscopic data for **11** and **13** are clearly consistent with their pyrano[2,3-*b*]dioxane structure, they are not sufficient for differentiating between *cis*- and *trans*-decalinoid annulation. Strong indications for the *cis*-fusion of the two rings, however, can be derived from force field calculations of the hemiketal formation enthalpies,[13] clearly revealing that the β-*cis* isomer is favored by more than 10 kcal/mol over the β-*trans*-annulated product. For the α-*cis* and α-*trans* isomers, the energy is even higher.[13] Experimental validation for the *cis*-fusion of the two rings in **11** was provided by its conversion into the 1,2-*O*-ethanediyl β-D-mannoside **16**, by removing the tertiary OH group through the established[14] hemiketal reduction with triethylsilane/BF_3-etherate (Scheme 3). This reaction, comprising hydride addition to the intermediate carboxonium ion generated by BF_3-mediated cleavage of the hemiketal C−O bond, proceeds in two directions: abstraction of the OH group through intermediate **14** to give **16**[15] and, alternatively, cleavage of the dioxane C−O bond to oxocarbonium ion **15**, which on hydride addition elaborates the hydroxyethyl β-D-glucoside **17**. The resulting mixture, 3:1 in favor of the mannoside, could readily be separated, and the configurations of the products could unambiguously be established by their pyranoid ring couplings.



Scheme 3

of an analogous product (with two methoxy groups instead of the annulated dioxane ring) on glycosidation with methanol (Scheme 4).



Scheme 4. Reagents and conditions: (a) Bu_4NOAc, CH_2Cl_2, 1.5 h, room temperature, → **22** (72%); (b) Bu_4NOAc, MeCN, 30 min, room temperature, → **22** (29%) and **25** (34%); (c) Ag_2CO_3, glycol, CH_2Cl_2, 2 h, room temperature, → **22** (82%); (d) K_2CO_3, MeOH, 15 min, room temperature, 75%

Pyranoid Ring Rearrangements

Whilst the *cis*-trioxadecalinols **11** and **13** are stable crystalline compounds, in solution though, notably under slightly basic conditions, the dioxanoid hemiketal link reveals a pronounced tendency to open (**11** ⇄ **20**), hence giving ensuing reactions via the free 2-carbonyl group. Accordingly, brief exposure of **11** at ambient temperature to tetrabutylammonium acetate in dichloromethane afforded the decalinone **22** (72%), obviously generated through elimination of benzoic acid (**20** → **21**) and subsequent migration of the enolic benzoyl group (arrows in **21**) thereby liberating the underlying carbonyl group. The same product could also be obtained by Ag_2CO_3-mediated glycosidation of glucose-derived[16] enolone bromide **19** (82%) − a course not unexpected in view of the previously observed[17] formation

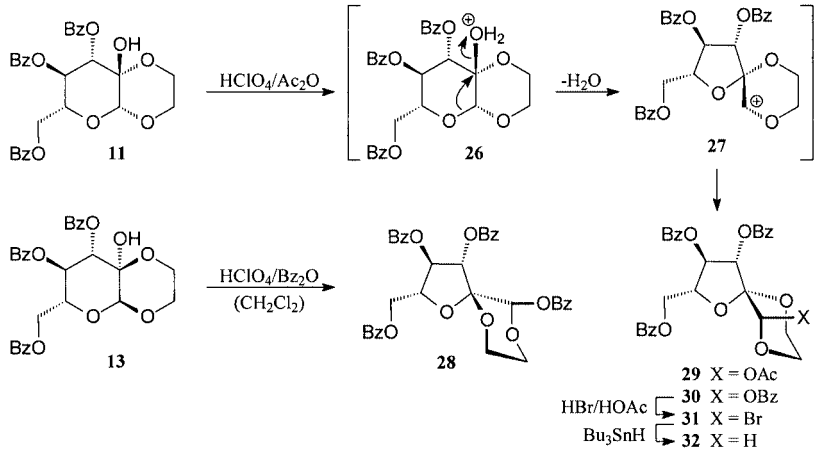
Surprisingly, when **11** was exposed to Bu_4NOAc in a more polar solvent such as acetonitrile (30 min, room temperature), the initial elimination of benzoic acid **20** → **21** was partially followed by a second one involving the terminal OBz group to give a dienolone ester (**21** → **24**), which on hemiketalization, *O*-8a → *O*-8-benzoyl shift, and protonation at the exocyclic double bond (arrows in **24**) led to the dihydropyranone **25**. De facto, an approximate 1:1 mixture of **22** and **25** was obtained, indicating that elimination of benzoic acid from the terminal positions in intermediate **21** was not complete under the conditions employed.

The *cis*-trioxadecalinones **22** and **25**, thus readily accessible, possess a unique array of three differently functionalized carbonyl groups, and, due to their close structural and configurational relationships to the sugar portion of the *Asclepiadaceae* cardenolides labriformidine[18] and

uscharidine,[11] and the antibiotic spectinomycin,[19] are deemed to be of particular value for the construction of these products in an enantiomerically pure form.

Ring Contractions to spiro-Trioxadecanes

When exposed to BF_3/triethylsilane in dichloromethane, **11** generated the carboxonium ion intermediate **14**, which was then trapped by the hydride ion to give β-D-mannoside **16** (Scheme 3). Under stronger acidic conditions such as 70% aqueous $HClO_4$ in acetic anhydride, or in dichloromethane containing benzoic anhydride, a highly stereoselective ring contraction to the spiro-trioxadecanes **29** and **30** was elicited, isolable in yields of 94 and 83%, respectively (Scheme 5). The sequence of reactions involved are thought to be initiated by protonation of the hemiketal-OH in **11**, the subsequent loss of water entailing the pyranoid ring oxygen to migrate (arrows in **26**), whereupon the oxygen-stabilized carbocation **27** is trapped by acetate or benzoate. Although an antiperiplanar *a*,*a*-disposition in **26** of the pyranoid oxygen and the water to be expelled favors the course of the reaction, it is not a stereochemical requirement, as the α-*cis*-analog **13**, with an *a*,*e*-arrangement of



Scheme 5. Acid-induced pyranoid ring contraction of trioxadecalins **11** and **13** to trioxaspiro[4,5]decanes

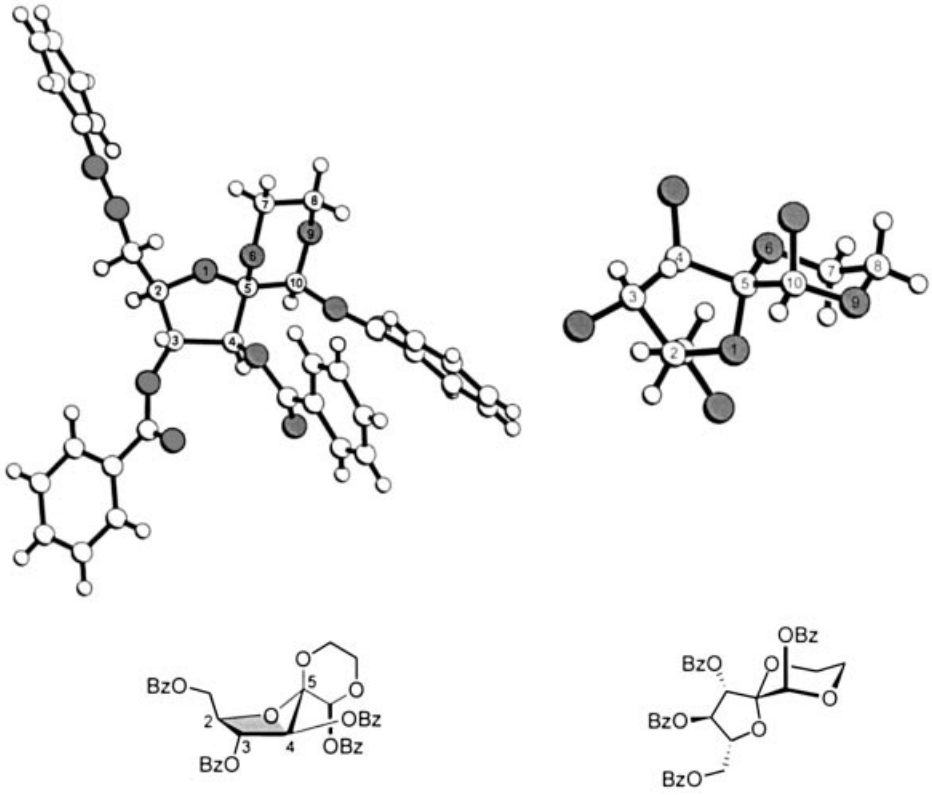


Figure 1. Perspective drawing and atomic numbering of 1,6,9-trioxaspiro[4,5]decane **30** as determined by X-ray crystallography; relevant dihedral angles around the spiro carbon (C-5): O1−C5−O6−C7 −63.6, O1−C5−C10−O9 +69.5, O1−C5−C10−O11 −167.7, O1−C5−C4−O40 −153.1[23]

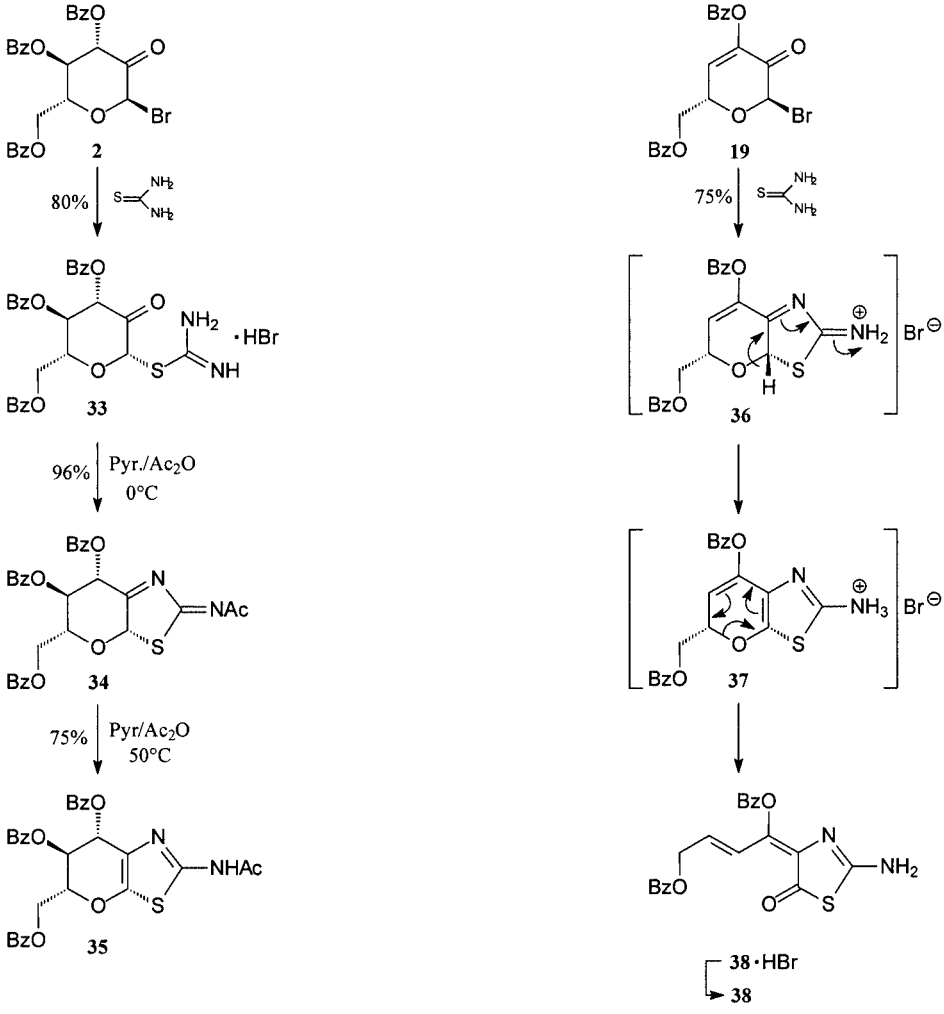
the groups involved in ring contraction, reacted as readily to form the isomeric spiro-trioxadecane **28** (84%).

This ring contraction, in the essentially stereospecific course observed, appears to be without precedence, albeit distantly related analogies exist in the formation of 2,5-anhydro-D-mannose on nitrous acid induced deamination of glucosamine[20] and in the solvolysis of methyl 2-*O*-(*p*-nitrophenylsulfonyl)-α-D-glucopyranoside in water containing sodium acetate.[21]

The configurations of the spiro compounds **28**−**30** could not be determined on the basis of ^{1}H and ^{13}C NMR spectroscopic data alone, as the orientation at the tertiary ring junction remained unresolved. Proof of its stereochemistry at the spiro carbon in **30**, however, could be secured chemically by conversion − through HBr/acetic acid treatment (→ **31**) and subsequent reductive debromination − into 1,2-*O*-ethanediyl β-D-fructofuranoside (**32**). It was unequivocally characterized as the β-anomer by its $J_{3,4}$ coupling constant of 6.6 Hz, which correlated well with those of a variety of β-fructofuranoses, yet was in distinct contrast to those of the α-furanoid anomers ($J_{3,4}$ = 1.7−2.2 Hz).[22] Further unequivocal proof for this assignment as well as for the configuration of the dioxane ring substituent, was provided by an X-ray structural analysis of tetrabenzoate **30** (Figure 1): the furanoid ring adopts a ^{5}E conformation with only slight distortions toward the $^5T_0$ form, whilst the dioxane portion, based on ring dihedral angles in the 52−59° range, assumes a standard chair conformation with the benzoyloxy group in an axial disposition. Another distinctive feature is represented by the fact that the furanoid ring oxygen and both of the benzoyloxy groups at C-4 and C-10 are in a near antiparallel arrangement, obviously a result of the operation of the "generalized anomeric effect"[24] in the formation of **30** from **11**, whereby intermediate **27** is captured by benzoate from the site opposite to the furanose oxygen.

Pyranothiazoles

As α-haloketones are known to readily react with thiourea to form aminothiazoles,[25] which are of interest as pharma-intermediates, ulosyl bromide **2** and the enolone analog **19** were exploited for the generation of enantiomerically pure pyrano-thiazolamines. Indeed, when equimolar parts of thiourea and **2** reacted in acetone solution at room temperature, the anomeric bromine was instantaneously displaced by sulfur to give the β-thioamidine, isolated as



Scheme 6

the hydrobromide **33** in 88% yield (Scheme 6). Removal of HBr by ion exchange resin left the β-glyosidulose intact (TLC), yet quantitative ring closure was effected on acetylation with pyridine/acetic anhydride (20 min, 0 °C) to yield the acetimido-thiazole **34** (91%), readily characterized structurally by its ^{1}H and ^{13}C NMR spectroscopic data. Only on more vigorous exposure to the acetylation conditions (5 h, 50 °C) did tautomerization take place to give the acetamido-thiazole **35**.

The reaction of thiourea with the enolone bromide **19**, unexpectedly, took a different course: a thiouronium bromide was obtained in 75% yield, which was analyzed correctly to be the pyrano-thiazol structures **36** or **37**, yet was devoid of optical rotation and had NMR spectroscopic data, notably large olefinic couplings of 15.6 Hz, that were incompatible with **36** or **37**. Closer inspection of the ^{1}H and, in particular, the ^{13}C NMR spectra revealed the product to be the hydrobromide of aminothiazolone (**38**· HBr) instead. The mechanism involved in this multistep reaction sequence can be understood in terms of an initial *S*-glycosidation of **19** by thiourea, followed by cyclization to the pyrano-thiazolamine hydrobromide **36** and subsequent tautomerization to **37**, which − as a 2*H*-pyran lacking electron-withdrawing stabilizing substituents − undergoes ring opening by a cycloreversion process (arrows in **37**). Although being a unique example, the electrocyclic ring opening of destabilized 2*H*-pyrans has been observed previously;[26] there is even a hexose-derived 2-ethoxy-2*H*-pyran that underwent ring opening to a hexadienone in an analogous fashion.[27]

Conclusion

The chemistry detailed in this report describes the utilization of 2-ketohexosyl ("ulosyl") bromide **2** − conveniently accessible and already amenable to a variety of preparatively useful reactions such as the "ulosyl donor approach" to β-D-mannosides − for the straightforward generation of the *cis*-annulated pyrano-dioxanes (or 1,4,5-trioxadecalins) **11** and **13** by α- and β-selective glycosidations with glycol, followed spontaneously by cyclo-hemiketalization. Salient features of the ensuing chemistry of **11** comprise highly stereoselective rearrangements to spiro-trioxadecanes as well as to *cis*-trioxadecalinones, the latter comprising the structural and configurational framework of a variety of cardenolides in which the sugar portion is doubly annulated to the aglycon. This approach is thus deemed to be of particular relevance towards their synthesis.

Experimental Section

General: Melting points, determined with a Bock hot-stage microscope, are uncorrected. Optical rotations were measured with a Perkin−Elmer 241 polarimeter at 20 °C with a cell of 1 dm path length; concentration (*c*) in g/100 mL and solvent are given in parentheses. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-300 spectrometer in the solvents given. Mass spectra were acquired on Varian MAT 311 and MAT 212 spectrometers. Microanalyses were determined with a Perkin−Elmer 240 elemental analyzer. Analytical thin layer chromatography (TLC) was performed on precoated Merck plastic sheets (0.2 mm silica gel 60 F_{254}) with detection by UV (254 nm) and/or spraying with H_2SO_4 (50%) and heating. Column and flash chromatography was carried out on Fluka silica gel 60 (70−230 mesh) with the specified eluents.

1. *cis*-1,4,5-Trioxadecalins[28]

(4a*R*,6*R*,7*R*,8*S*,8a*S*)-7,8-Bis(benzoyloxy)-6-(benzoyloxymethyl)-8a-hydroxy-1,4,5-trioxa-*cis*-decalin (11): A mixture of Ag_2CO_3 (3.30 g, 12 mmol), ethylene glycol (0.75 g, 12 mmol), CH_2Cl_2 (100 mL), and molecular sieves (4 Å, 3 g) was stirred at ambient temperature for 15 min. Ulosyl bromide **2** (5.53 g, 10 mmol) was then added and stirring was continued for 5 h in the dark. Filtration through kieselguhr and evaporation of the filtrate in vacuo gave a crystalline residue, which was recrystallized from EtOAc to give 4.90 g (92%) of **11** as colorless crystals. M.p. 181−182 °C. $[\alpha]_D^{20} = -7.1$ (*c* = 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.57, 4.33 (two m, 2 H each, 2-H_2 and 3-H_2), 4.10 (ddd, 1 H, 6-H), 4.50, 4.67 (dd, 2 H, BzOCH_2), 4.85 (s, 1 H, 4a-H), 5.24 (d, 1 H, 8-H), 5.25 (s, 1 H, OH), 5.86 (dd, 1 H, 7-H), 7.3−8.1 (m, 15 H, 3 C_6H_5) ppm; $J_{6,7} = J_{7,8} = 10.0$, $J_{6,CH_2} = 2.9$ and 5.0, $J_{BzOCH_2gem} = 12.1$ Hz. ^{13}C NMR ($CDCl_3$): δ = 59.1, 59.4 (C-2, C-3), 63.2 (BzOCH_2), 67.9 (C-7), 71.8 (C-6), 79.1 (C-8), 90.9 (C-8a), 95.3 (C-4a), 128−134 (3 C_6H_5), 165.2, 166.2, 168.4 (3 C_6H_5CO) ppm; $J_{C\text{-}4a,H\text{-}4a} = 167.9$ Hz. MS (FD, 14 mA): *m*/*z* = 534 (100) [M^+]. $C_{29}H_{26}O_{10}$ (534.5): calcd. C 65.16, H 4.90; found C 64.89, H 4.91.

(4a*S*,6*R*,7*R*,8*S*,8a*S*)-7,8-Bis(benzoyloxy)-6-(benzoyloxymethyl)-8a-hydroxy-1,4-dithia-5-oxa-*cis*-decalin (12): To a suspension of Ag_2CO_3 (330 mg, 1.2 mmol) and molecular sieves (4 Å, 1 g) in CH_2Cl_2 (10 mL) was added consecutively ulosyl bromide **2** (555 mg, 1 mmol) and ethanedithiol, and the mixture was stirred for 1 h at ambient temperature. Filtration with suction and evaporation of the filtrate to dryness in vacuo left a crystalline residue, which was recrystallized from EtOAc to give 445 mg (79%) of **12** as colorless crystals. M.p. 198−199 °C. $[\alpha]_D^{20} = -29.5$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48, 2.74 and 3.32 (m, 2 H and one m, 2 H, 2-H_2, 3-H_2), 4.17 (ddd, 1 H, 6-H), 4.39 (s, 1 H, OH), 4.45 (s, 1 H, 4a-H), 4.47, 4.68 (dd, 2 H, CH_2OBz), 5.54 (d, 1 H, 8-H), 5.92 (dd, 1 H, 7-H), 7.3−8.1 (m, 15 H, 3 C_6H_5) ppm; $J_{6,7} = 10.0$, $J_{7,8} = 9.7$, $J_{6,CH_2} = 3.0$, 4.6 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.5, 25.4 (C-2, C-3), 63.4 (CH_2OBz), 68.7 (C-6), 77.5 (C-4a), 78.9 (C-8a), 79.0, 80.6 (C-7, C-8), 128−133 (C_6H_5), 165.2, 166.2, 166.8 (3 Bz*C*O) ppm. MS (FD, 10 mA): *m*/*z* = 567 [M^+]. $C_{29}H_{26}O_8S_2$ (566.7): calcd. C 61.46, H 4.63; found C 61.09, H 4.59.

(4a*S*,6*R*,7*R*,8*S*,8a*R*)-7,8-Bis(benzoyloxy)-6-(benzoyloxymethyl)-8a-hydroxy-1,4,5-trioxa-*cis*-decalin (13): Freshly desiccated molecular sieves (3 Å) and glycol (620 mg, 10 mmol) were added to a solution of ulosyl bromide **2** (555 mg, 1 mmol) in dry dimethylformamide (10 mL), and the mixture was stirred at ambient temperature for 24 h. Dilution with CH_2Cl_2 (100 mL), washing with water (3 × 30 mL), drying (Na_2SO_4), and removal of the solvents in vacuo gave a syrup, which was subjected to three preparative silica plates (20 × 20 cm) and developed with benzene/EtOAc (4:1). Extraction of the middle zone (R_f = 0.45) with CH_2Cl_2 and evaporation to dryness resulted in a syrup, which crystallized on trituration with diethyl ether. Collection of the crystals and recrystallization from diethyl ether gave 190 mg (36%) of **13**. M.p. 137−139 °C, $[\alpha]_D^{20}$ = +8.8 (*c* = 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72, 3.94, 4.07 (m, 3 H, 2-H_2, 3-H_e), 4.32 (ddd, 1 H, 3-H_a), 4.44 (dd, 1 H,

$BzOCH_A$), 4.60 (m, 2 H, 6-H, $BzOCH_B$), 4.80 (s, 1 H, 4a-H), 5.88 (dd, 1 H, 7-H), 6.20 (d, 1 H, 8-H) ppm, $J_{6,7}$ = 9.8, $J_{7,8}$ = 9.7, J_{6,CH_2} = 5.5 Hz; NOE: irradiation of the 8-H doublet at δ = 6.20 ppm amplifies signals at 4.32 (3-H_a) and 4.60 (6-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 62.5 (C-3), 63.0 (*C*OBz), 66.1 (C-2), 67.9 (C-7), 68.6 (C-8), 70.6 (C-6), 93.2 (C-8a) 97.7 (C-4a) ppm; $J_{C\text{-}4a,H\text{-}4a}$ = 170.0 Hz. MS (FD, 14 mA): *m*/*z* = 535 [M^+ + 1]. $C_{29}H_{26}O_{10}$ (534.5): calcd. C 65.16, H 4.90; found C 65.08, H 4.85.

1,2-*O*-(1,2-Ethanediyl) 3,4,6-Tri-*O*-benzoyl-β-D-mannopyranoside (16) and 2-Hydroxyethyl 3,4,6-Tri-*O*-benzoyl-β-D-glucopyranoside (17): Boron trifluoride etherate (0.25 mL, 2 mmol) was added to a stirred suspension of *cis*-trioxadecalin **11** (535 mg, 1 mmol) in a mixture of acetonitrile (10 mL) and CH_2Cl_2 (2 mL); this was followed by the addition of triethylsilane (0.32 mL, 2 mmol) and stirring at ambient temperature overnight. The then clear solution was quenched by adding solid Na_2CO_3 (250 mg) and stirring for 15 min, diluted with CH_2Cl_2 (100 mL), washed with water (20 mL), and dried (Na_2SO_4), and the solvents were evaporated to dryness in vacuo. The resulting syrup consisted of an approximate 3:1 mixture of mannoside **16** (R_f = 0.33 in 10:1 toluene/EtOAc) and glucoside **17** (R_f = 0.05) that was separated by elution from a silica gel column (2.5 × 30 cm) with toluene/EtOAc (10:1). The fraction eluted first gave a syrup on removal of the solvents in vacuo, which crystallized on trituration with diethyl ether/*n*-hexane to give 275 mg (53%) of **16**. M.p. 152−153 °C. $[\alpha]_D^{20}$ = −17.3 (*c* = 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.52 (dd, 1 H, 1′-H_2 and 2′-H_2), 3.75 and 4.29 (ddd, 1 H) with $J_{1',1'}$ = 11.5, $J_{1',2'}$ = 3.0, 11.5, and 12.0, $J_{2',2'}$ = 11.9 Hz, pyranoid H: 4.06 (ddd, 1 H, 5-H), 4.23 (dd, 1 H, 2-H), 4.49, 4.67 (dd, 2 H, 6-H_2), 4.97 (d, 1 H, 1-H), 5.37 (dd, 1 H, 3-H), 5.96 (dd, 1 H, 4-H), 7.3−8.1 (m, 15 H, 3 C_6H_5) ppm; $J_{1,2}$ = 0.9, $J_{2,3}$ = 3.3, $J_{3,4}$ = 10.2, $J_{4,5}$ = 10.0, $J_{5,6}$ = 3.0, 5.0 Hz. MS (FD, 12 mA): *m*/*z* = 518 [M^+]. $C_{29}H_{26}O_9$ (518.6): calcd. C 67.17, H 5.06; found C 67.23, H 4.93.

Evaporation in vacuo of the fraction eluted second gave 95 mg (18%) of **17** as a colorless syrup. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (dd, 1 H, 2-H), 4.12 (ddd, 1 H, 5-H), 4.44, 4.61 (dd, 2 H, 6-H_2), 4.65 (d, 1 H, 1-H), 5.46 (dd, 1 H, 4-H), 5.67 (dd, 1 H, 3-H), $J_{1,2}$ = 7.9, $J_{2,3}$ = $J_{3,4}$ = $J_{4,5}$ = 9.5, $J_{5,6}$ = 3.1, 5.5, $J_{6,6}$ = 12.2 Hz; ethylene-H_2: δ = 3.70 (m, 3 H) and 3.98 (m, 1 H) ppm. MS (FD, 12 mA): *m*/*z* = 537 [M^+], 538 [M^+ +1].

(4a*R*,6*S*,8a*S*)-8a-Benzoyloxy-6-benzoyloxymethyl-1,4,5-trioxa-*cis*-decalin-8-one (22)

A. Glycosidation of Enolone Bromide 19 with Glycol: To a stirred slurry of Ag_2CO_3 (605 mg, 2.2 mmol) and molecular sieves (4 Å, 1 g) in CH_2Cl_2 (10 mL) was added consecutively (2*R*,6*S*)-4-benzoyloxy-6-(benzoyloxymethyl)-2-bromo-2*H*-pyran-3(6*H*)-one (**19**)[16] (860 mg, 2 mmol) and ethylene glycol (1.1 mL, 20 mmol), and stirring was continued for 2 h at ambient temperature with the exclusion of light. The mixture was then filtered through kieselguhr, and the filtrate was evaporated to dryness in vacuo to leave a syrup which crystallized on trituration with methanol to give 675 mg (82%) of **22** as colorless crystals. M.p. 136−138 °C, $[\alpha]_D^{20}$ = +16.3 (*c* = 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.75, 2.85 (dd, 2 H, 7 H_2), 3.63, 3.81 (m, 2 H, 2-H_e, 3-H_e), 4.40 (m, 3 H, 2-H_a, 3-H_a, 6-H), 4.50 (m, 2 H, $BzOCH_2$), 5.43 (s, 1 H, 4a-H), 7.4−8.1 (m, 10 H, 2 C_6H_5) ppm; $J_{6,7e}$ = 3.5, $J_{6,7a}$ = 10.5, $J_{7,7}$ = 16.5 Hz. ^{13}C NMR ($CDCl_3$): δ = 40.8 (C-7), 58.7, 61.5 (C-1, C-2), 65.6 ($BzOCH_2$), 68.9 (C-6), 93.5 (C-4a), 94.7 (C-8a), 128.5−134.0 (2 C_6H_5), 166.0, 166.2 (2 C_6H_5CO), 195.3 (C-8) ppm. MS (FD, 12 mA): *m*/*z*: 412 [M^+]. $C_{22}H_{20}O_8 \cdot CH_3OH$ (444.4): calcd. C 62.16, H 5.44; found C 62.09, H 5.36.

B. From Uloside 11 by Bu_4NOAc-Promoted Elimination of Benzoic Acid and *O*-8 → *O*-8a-Benzoyl Shift: Tetrabutylammonium acetate (900 mg, 3 mmol) was added to a solution of **11** in CH_2Cl_2 (25 mL), and the mixture was stirred for 1.5 h at room temperature. Subsequent dilution with CH_2Cl_2 (150 mL), washing with water (3 × 50 mL), drying (Na_2SO_4), and removal of the solvent in vacuo gave a syrup, which crystallized spontaneously. Recrystallization from methanol gave 295 mg (72%) of **22**, whose physical properties are identical with those of the product described under A.

(4a*R*,6*S*,8a*R*)-6-(Benzoyloxymethyl)-8a-hydroxy-1,4,5-trioxa-*cis*-decalin-8-one (23): Solid K_2CO_3 (140 mg, 1 mmol) was added to a solution of dibenzoate **22** (412 mg, 1 mmol) in dry methanol (20 mL), and the mixture was stirred at ambient temperature for 15 min. Subsequent dilution with CH_2Cl_2 (50 mL), washing with water (3 × 20 mL), drying (Na_2SO_4), and removal of the solvent in vacuo left a syrup, which crystallized on trituration with methanol to give 230 mg (75%) of **23** as colorless crystals. M.p. 107−108 °C. $[\alpha]_D^{20}$ = +3.2 (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.60, 3.06 (dd, 2 H, 7-H_2), 3.61, 3.65 (m, 2 H, 1-H_e, 2-H_e), 4.03 (m, 1 H, 6-H), 4.40 (m, 3 H, 1-H_a, 2-H_a, OH), 4.54 (m, 2 H, $BzOCH_2$), 4.67 (s, 1 H, 4a-H), 7.3−8.1 (m, 5 H, C_6H_5) ppm; $J_{6,7e}$ = 2.1, $J_{6,7a}$ = 12.2, $J_{7,7}$ = 14.3 Hz. ^{13}C NMR ($CDCl_3$): δ = 39.9 (C-7), 59.4, 59.7 (C-1, C-2), 65.8 ($BzOCH_2$), 69.3 (C-6), 90.4 (C-8a), 96.4 (C-4a), 128−133 (C_6H_5), 166.0 (C_6H_5CO), 201.0 (C-8) ppm. MS (FD, 5 mA): *m*/*z* = 308 [M^+]. $C_{15}H_{16}O_7$ (308.3): calcd. C 58.44; H 5.23; found C 58.64; H 5.28.

(4a*R*,8a*S*)-8a-Benzoyloxy-6,7-dehydro-6-methyl-1,4,5-trioxa-*cis*-decalin-8-one (25): Tetrabutylammonium acetate (900 mg, 3 mmol) was added to a solution of glycol-uloside **11** (535 mg, 1 mmol) in dry acetonitrile (50 mL), and the mixture was stirred for 30 min at ambient temperature. Workup by dilution with CH_2Cl_2 (150 mL), washing with water (3 × 50 mL), drying (Na_2SO_4), and removal of the solvents in vacuo gave a brownish syrup, consisting of an approximate 1:1 mixture (TLC in benzene/EtOAc, 4:1) of enone **25** (R_f = 0.47) and monobenzoate **23** (R_f = 0.10), aside from small amounts of dibenzoate **22** (R_f = 0.53). Separation was effected by flash chromatography (2 × 15 cm column, toluene/EtOAc, 8:1) to afford, after a minor fraction (**22**), the enone **25** as a colorless foam on evaporation to dryness, which then crystallized on trituration with methanol to give 98 mg (34%). M.p. 152−153 °C. $[\alpha]_D^{20}$ = −8.7 (*c* = 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 2.15 (d, 3 H, CH_3), 3.80 (m, 2 H, 2-He, 3-He), 4.50 (m, 2 H, 2-Ha, 3-Ha), 5.52 (d, 1 H, 7-H), 6.02 (s, 1 H, 4a-H), 7.3−8.1 (m, 5 H, C_6H_5) ppm; J_{7CH_3} = 0.7 Hz. ^{13}C NMR ($CDCl_3$): δ = 21.2 (CH_3), 59.3, 60.7 (C-2, C-3), 92.7 (C-8a), 94.9 (C-4a), 103.3 (C-7), 128.5−131.7 (C_6H_5), 165.0 (C_6H_5CO), 172.7 (C-6), 183.4 (C-8) ppm. $C_{15}H_{14}O_6$ (290.3): calcd. C 62.06; H 4.86; found C 61.81; H 4.83.

The third fraction contained monobenzoate **23** and gave, on removal of the solvents in vacuo and crystallization from methanol, 90 mg (29%). M.p. 107−108 C, identical in all respects with the product obtained by mono-debenzoylation of **22** (see above).

2. 1,6,9-Trioxaspiro[4,5]decanes

(2*R*,3*R*,4*S*,5*R*,10*R*)-3,4,10-Tris(benzoyloxy)-2-(benzoyloxymethyl)-1,6,9-trioxaspiro[4,5]decane (28): A solution of pyrano-dioxane **13** (300 mg, 0.56 mmol), benzoic anhydride (1.35 g, 6 mmol), and 70% aqueous $HClO_4$ (50 mL, 0.6 mmol) in CH_2Cl_2 (10 mL) was stirred at ambient temperature for 15 min. Dilution with CH_2Cl_2 (70 mL), washing with water, saturated $NaHCO_3$ solution, and water again (2 × 10 mL each), drying (Na_2SO_4), removal of the solvent, and purification of the residue by flash chromatography (*n*-hexane/

diethyl ether, 1:1) gave 298 mg (84%) of **28** as a colorless, amorphous solid (R_f = 0.29, diethyl ether/*n*-hexane, 2:1). $[\alpha]_D^{20}$ = +27.8 (c = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.69 (dd, 1 H, 7-H_e), 3.78 (dd, 1 H, 8-H_e), 4.27 (ddd, 1 H, 7-H_a), 4.45 (ddd, 1 H, 8-H_a), 4.62 (ddd, 1 H, 2-H), 4.79, 4.89 (dd, 2 H, CH_2OBz), 5.51 (dd, 1 H, 3-H), 5.76 (d, 1 H, 4-H), 6.38 (s, 1 H, 10-H), 7.1−8.3 (m, 20 H, 4 C_6H_5) ppm; J_{2,CH_2} = 3.2, 4.2, $J_{2,3}$ = 4.4, $J_{3,4}$ = 0.4, $J_{7,7}$ = 11.6, $J_{7a,8a}$ = 12.2, $J_{7a,8e}$ = 2.7, $J_{7e,8a}$ = 2.9, $J_{7e,8e}$ = 0, $J_{8,8}$ = 11.5 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 59.5, 59.6 (C-7, C-8), 63.5 (*C*H_2OBz), 78.6 (C-3), 81.1 (C-4), 82.1 (C-2), 88.2 (C-10), 102.8 (C-5) ppm. MS (FD, 20 mA): *m*/*z* (%) = 637 (40) [M^+ − 1], 533 (100) [M^+ − C_6H_5CO]. $C_{36}H_{30}O_{11}$ (638.6): calcd. C 67.71, H 4.73; found C 67.89, H 4.58.

(2*R*,3*R*,4*S*,5*S*,10*S*)-10-Acetoxy-3,4-bis(benzoyloxy)-2-(benzoyloxymethyl)-1,6,9-trioxaspiro[4.5]decane (29): Acetic anhydride (1.89 mL, 20 mmol) and 70% aqueous $HClO_4$ (0.1 mL) was stirred into a cooled (0 °C) solution of pyranodioxane **11** (1.07 g, 2 mmol) in CH_2Cl_2 (25 mL); this was followed by removal of the ice-bath. After stirring for another 5 min, the mixture was diluted with CH_2Cl_2 (200 mL) and washed consecutively with water (2 × 50 mL), saturated $NaHCO_3$ solution (2 × 30 mL), and water (2 × 30 mL). Drying (Na_2SO_4), evaporation to dryness in vacuo left a syrup, which was purified by elution from a short silica gel column with toluene/EtOAc (4:1) to give 1.09 g (94%) of **29** a colorless foam (R_f = 0.54, toluene/EtOAc, 4:1). $[\alpha]_D^{20}$ = −124.7 (c = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, AcH_3), 3.55 (dd, 1 H, 7-H_e), 3.67 (dd, 1 H, 8-H_e), 4.12 (ddd, 1 H, 7-H_a), 4.46 (ddd, 1 H, 8-H_a), 4.59 (ddd, 1 H, 2-H), 4.70, 4.81 (dd, 2 H, CH_2OBz), 5.91 (m, 2 H, 3-H and 4-H), 5.99 (s, 1 H, 10-H), 7.3−8.2 (m, 15 H, 3 C_6H_5) ppm; $J_{2,3}$ = 5.5, J_{2,CH_2} = 4.1, 6.0, $J_{7,7}$ = 11.8, $J_{7e,8e}$ = 0, $J_{7a,8e}$ = 2.9, $J_{7e,8a}$ = 3.0, $J_{7a,8a}$ = 12.1, $J_{8,8}$ = 11.6 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 59.1 (C-7), 60.8 (C-8), 65.1 (*C*H_2OBz), 75.5 (C-4), 77.1 (C-3), 79.0 (C-2), 89.5 (C-10), 98.6 (C-5) ppm. MS (FD): *m*/*z* = 576 (100) [M^+]. $C_{31}H_{28}O_{11}$ (576.6): calcd. C 64.58, H 4.89; found C 64.51, H 4.78.

Replacement of $HClO_4$ by BF_3−diethyl ether (1 mmol) in otherwise identical conditions similarly induced the rearrangement **11** → **29**; yield 88%.

(2*R*,3*R*,4*S*,5*S*,10*S*)-3,4,10-Tris(benzoyloxy)-2-(benzoyloxymethyl)-1,6,9-trioxaspiro[4,5]decane (30): To a CH_2Cl_2 solution of pyranodioxane **11** (2.3 g, 4.3 mmol in 25 mL) was added benzoic anhydride (9.7 g, 43 mmol) and 70% aqueous $HClO_4$ (250 µL, 2.9 mmol); this was followed by stirring of the mixture at room temperature for 10 min. Workup by dilution with CH_2Cl_2 (200 mL), washing with water, saturated $NaHCO_3$ solution, and water again (2 × 25 mL each), removal of the solvent, and purification of the resulting syrup by elution from a silica gel column (2 × 15 cm) first with *n*-hexane/diethyl ether (10:1) to remove impurities, then followed by diethyl ether, afforded a residue, which crystallized from diethyl ether/*i*PrOH to give 1.97 g (83%) of **30** as colorless crystals. M.p. 124−125 °C. $[\alpha]_D^{20}$ = −108.6 (c = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.61 (dd, 1 H, 7-H_e), 3.75 (dd, 1 H, 8-H_e), 4.23 (ddd, 1 H, 7-H_a), 4.49 (ddd, 1 H, 8-H_a), 4.63 (ddd, 1 H, 2-H), 4.73, 4.85 (two 1H-dd, CH_2OBz), 5.94 (dd, 1 H, 3-H), 6.02 (d, 1 H, 4-H), 6.23 (s, 1 H, 10-H), 6.9−8.2 (m, 20 H, 4 C_6H_5) ppm; J_{2,CH_2OBz} = 4.0 and 6.1, J_{BzOCH_2gem} = 11.8, $J_{2,3}$ = 5.5, $J_{3,4}$ = 7.1, $J_{7,7}$ = 11.8, $J_{7a,8a}$ = 12.0, $J_{7a,8e}$ = 2.8, $J_{7e,8a}$ = 3.0, $J_{7e,8e}$ = 0, $J_{8,8}$ = 11.7 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 59.4 (C-7), 60.1 (C-8), 65.2 (CH_2OBz), 75.5 (C-4), 77.1 (C-3), 79.1 (C-2), 89.9 (C-10), 99.1 (C-5) ppm. MS (FD): *m*/*z* = 638 (100) [M^+]. $C_{36}H_{30}O_{11}$ (638.65): calcd. C 67.71, H 4.73; found C 67.75, H 4.74.

Recrystallization of **30** from acetone/*i*PrOH afforded well-formed, colorless prisms suitable for X-ray structural analysis (Figure 1).[23]

Table 1. Crystallographic data for the crystal structure determination of trioxaspiro[4,5]decane **30**

Empirical formula	$C_{36}H_{30}O_{11}$
Molecular mass	638.65
Temperature (K)	293(2) K
Wavelength (Å)	0.71069 Å
Crystal system, space group	orthorhombic, $P2_12_12_1$
Unit cell dimensions	
a (Å)	8.844(1)
b (Å)	10.343(1)
c (Å)	34.116(4)
α (°)	90
β (°)	90
γ (°)	90
Volume (Å^3)	3120.7(6)
Z	4
Calculated density (Mg·m^{-3})	1.359
Absorption coefficient (mm^{-1})	0.101
F(000)	1360
Crystal size (mm)	0.6 × 0.2 × 0.1
$\theta_{max.}$ (°) for data collection	22.97
Reflections collected	3324
Independent reflections [R_{int}]	2505 [0.0541]
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	2505/0/424
Goodness-of-fit on F^2	1.106
final R indices [$I > 2\sigma(I)$]	R_1 = 0.0336, wR_2 = 0.0813
R indices (all data)	R_1 = 0.0452, wR_2 = 0.0883
Largest diff. peak and hole (e·Å^{-3})	0.190 and −0.172

(2*R*,3*R*,4*S*,5*S*,10*S*)-3,4-Bis(benzoyloxy)-2-(benzoyloxymethyl)-10-bromo-1,6,9-trioxaspiro[4.5]decane (31): A 33% HBr solution in glacial acetic acid (5.3 mL, 30 mmol) was added to a CH_2Cl_2 solution (30 mL) of either acetate **29** (1.15 g, 2 mmol) or tetrabenzoate **30** (1.28 g, 2 mmol), and the mixture was stirred at ambient temperature for 10 min. Workup by dilution with CH_2Cl_2 (150 mL), washing with ice-water (2 × 30 mL), saturated $NaHCO_3$ solution (1 × 30 mL) and water, drying (Na_2SO_4), and removal of the solvent in vacuo left bromide **31** as a chromatographically uniform, colorless syrup (R_f = 0.48, *n*-hexane/diethyl ether, 1:1). $[\alpha]_D^{20}$ = −210.2 (c = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.67 (dd, 1 H, 7-H_e), 3.76 (dd, 1 H, 8-H_e), 4.30 (ddd, 1 H, 7-H_a), 4.45 (ddd, 1 H, 8-H_a), 4.46, 4.79 (dd, 2 H, CH_2OBz), 4.59 (m, 1 H, 2-H), 5.79 (dd, 1 H, 3-H), 5.89 (d, 1 H, 4-H), 6.28 (s, 1 H, 10-H), 7.1−8.2 (m, 15 H, 3 C_6H_5) ppm; J_{2,CH_2OBz} = 3.8 and 6.0, J_{BzOCH_2gem} = 11.8, $J_{2,3}$ = 5.4, $J_{3,4}$ = 6.5, $J_{7,7}$ = 11.9, $J_{7a,8a}$ = 12.1, $J_{7a,8e}$ = 2.9, $J_{7e,8a}$ = 2.8, $J_{7e,8e}$ = 0, $J_{8,8}$ = 11.5 Hz. MS (FD, 20 mA): *m*/*z* = 517 (100) [M^+ − Br]. $C_{29}H_{25}BrO_9$ (597.4): calcd. C 58.30, H 4.22, Br 24.10; found C 58.38, H 4.31, Br 24.01.

1,2-*O*-(1,2-Ethanediyl) 3,4,6-Tri-*O*-benzoyl-β-D-fructofuranoside {(2*R*,3*R*,4*S*,5*R*)-3,4-Bis(benzoyloxy)-2-(benzoyloxymethyl)-1,6,9-trioxaspiro[4.5]decane} (32): AIBN (50 mg, 0.3 mmol) and Bu_3SnH (700 µL, 2.65 mmol) were added to a solution of bromide **23** (500 mg, 0.84 mmol) in toluene (25 mL), and the mixture was refluxed for 1 h. Subsequent dilution with acetonitrile (200 mL), washing with *n*-hexane (3 × 50 mL), and removal of the solvent in vacuo left a syrup, which was then subjected to elution from a silica gel column (2 × 10 cm) with *n*-hexane/Et_2O (1:1). The residue obtained on evaporation of the product-carrying eluates crystallized from diethyl ether/*i*PrOH to give 414 mg (96%) of **32** as colorless crystals. M.p. 95−96 °C. $[\alpha]_D^{20}$ = −89.8 (c = 0.9, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.61 (dd, 1 H, 1′-H_e), 3.70 (ddd,

1 H, 2′-H_a), 3.75 (dd, 1 H, 2′-H_e), 4.28 (ddd, 1 H, 1′-H_a) ppm; $J_{1',1'}$ = 10.0, $J_{1'e,2'a}$ = 2.7, $J_{1'e,2'e}$ = 0, $J_{1'a,2'e}$ = 4.0, $J_{1'a,2'a}$ = $J_{2',2'}$ = 12.0 Hz (2 ethylene-H_2); δ = 3.81, 3.91 (d, 2 H, 1-H_2), 4.59 (ddd, 1 H, 5-H), 4.70, 4.78 (d, 2 H, 6-H_2), 5.57 (d, 1 H, 3-H), 5.97 (dd, 1 H, 4-H) ppm; $J_{1,1}$ = 11.9, $J_{3,4}$ = 0.6, $J_{4,5}$ = 5.0, $J_{5,6}$ = 4.8, 6.5, $J_{6,6}$ = 11.6 Hz (fructose protons). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 61.3 (C-7), 65.6 (BzO*C*H_2), 66.1 (C-3), 70.1 (C-10), 77.2 (C-4), 77.5 (C-3), 79.3 (C-2), 101.1 (C-5) ppm. MS (FD, 20 mA): *m*/*z*= 518 (95) [M^+]. $C_{25}H_{26}O_9$ (518.5): calcd. C 67.17, H 5.05; found C 67.06, H 5.03.

3. Pyranothiazoles

3,4,6-Tri-*O*-benzoyl-β-D-*arabino*-hexopyrano-2-ulosyl Thiouronium Bromide (33): Thiourea (0.76 g, 10 mmol) was added to a solution of ulosyl bromide **2** (5.55 g, 10 mmol) in acetone (150 mL), the mixture was stirred at room temperature for 15 min, and was subsequently evaporated to dryness in vacuo. The residue crystallized from hot EtOAc to give 4.33 g (88%) of **33**. M.p. 174−175 °C (dec.). $[\alpha]_D^{20}$ = −4.6 (*c* = 1.1, acetone). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 4.43, 4.52 (dd, 2 H, 6-H_2), 4.68 (ddd, 1 H, 5-H), 5.40 (dd, 1 H, 4-H), 5.84 (s, 1 H, H-1), 6.09 (d, 1 H, 3-H), 7.4−8.2 (m, 16 H, 3 C_6H_5, NH), 9.24, 10.38, 10.84 (3 broad 1H-s, 3 NH) ppm; $J_{3,4}$ = $J_{4,5}$ = 10.0, $J_{5,6}$ = 2, 6, 4.4, $J_{6,6}$ = 12.5 Hz. ^{13}C NMR (75.5 MHz, [D_6]DMSO): δ = 62.5 (C-6), 67.8, 73.6, 74.3 (C-3, C-4, C-5), 88.4 (C-1), 92.6 [$SC(NH_2)_2$], 128−133 (3 C_6H_5), 164.7, 164.9, 165.3 (3 *C*OC_6H_5), 174.0 (C-2) ppm. MS (FD, 10 mA): *m*/*z* = 549 [M^+ − Br]. $C_{28}H_{25}BrN_2O_8S$ (629.5): calcd. C 53.42, H 4.01, N 4.45; found C 53.46, H 3.87, N 4.38.

(2*R*,3*R*,4*R*,7a*S*)-6-Acetimido-3,4-bis(benzoyloxy)-2-(benzoyloxymethyl)-3,4-dihydro-2*H*,7a*H*-pyrano[5,6-*d*]thiazoline (34): A mixture of **33** (2.50 g, 4 mmol), pyridine (20 mL), and Ac_2O (0.4 mL) was stirred at 0 °C for 20 min, whereby a colorless precipitate formed. The mixture was subsequently poured into ice-water (50 mL), stirred for 1 h, and the crystals formed were collected by filtration to give 2.08 g (91%) of **34**. M.p. 108−109 °C. $[\alpha]_D^{20}$ = +16.0 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, NAc), 4.16 (ddd, 1 H, 2-H), 4.44 and 4.56 (dd, 2 H, CH_2OBz), 5.31 (s, 1 H, 7a-H), 5.50 (dd, 1 H, 3-H), 5.89 (d, 1 H, 4-H), 7.2−8.0 (m, 15 H, 3 C_6H_5) ppm; J_{2,CH_2} = 3.4, 6.6, $J_{2,3}$ = 9.6, $J_{3,4}$ = 9.3 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 23.9 (Ac*C*H_3), 64.1 (CH_2), 68.9, 74.7, 76.8 (C-2, C-3, C-4), 90.0 (C-7a), 96.7, 96.9 (C-4a, C-6), 128.3−133.8 (3 C_6H_5), 166.9, 166.1, 165.3, 165.0 ($COCH_3$, 3 COC_6H_5) ppm. MS (FD): *m*/*z* = 572 [M^+], 450 [M − HOBz]. $C_{30}H_{24}N_2O_9S$ (572.6): calcd. C 62.92, H 4.23, N 4.89; found C 62.88, H 4.22, N 4.84.

(2*R*,3*R*,4*R*)-6-Acetamido-3,4-bis(benzoyloxy)-2-(benzoyloxymethyl)-3,4-dihydro-2*H*-pyrano[5,6-*d*]thiazole (35): A mixture of thiuronium bromide **33** (1.25 g, 2 mmol) in pyridine (10 mL) and Ac_2O (650 mg, 6.4 mmol) was stirred at ambient temperature for 2 h, resulting in a mixture of **34** (R_f = 0.12 in CH_2Cl_2/EtOAc, 20:1) and **35** (R_f = 0.30); this was followed by heating to 50 °C for 5 h, after which conversion into **35** was complete (TLC). The mixture was subsequently stirred with ice-water. The precipitate was collected and purified by elution from a silica gel column (3 × 30 cm) with CH_2Cl_2/EtOAc (20:1). Evaporation of the solvent in vacuo gave 580 mg (75%) of **35** as a yellowish, amorphous product. $[\alpha]_D^{20}$ = +5.3 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 3 H, NAc), 4.66 and 4.89 (dd, 2 H, CH_2OBz), 5.08 (ddd, 1 H, 2-H), 5.85 (dd, 1 H, H-3), 6.31 (dd, 1 H, 4-H), 9.38 (broad s, 1 H, NH) ppm; J_{2,CH_2} = 4.7 and 7.5, $J_{2,3}$ = 3.6, $J_{2,4}$ = 1.1, $J_{3,4}$ = 3.4, J_{C,H_2gem} = 12.1 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 22.8 (*C*H_3), 61.7 (CH_2OBz), 66.1, 68.6, 77.5 (C-2, C-3, C-4), 128.5−133.6 (m, 3 C_6H_5), 128.8, 147.5, 150.9 (C-4a, C-6, C-7a), 165.1, 165.7, 166.1, 167.9 (3 *C*OC_6H_5, *C*OCH_3) ppm. $C_{30}H_{24}N_2O_8S$ (572.6): calcd. C 62.92, H 4.23, N 4.89; found C 62.72, H 3.99, N 4.83.

2-Amino-4-[1′,4′-bis(benzoyloxy)but-2′-enylidene]thiazolin-5(4*H*)-one Hydrobromide (38·HBr): A solution of bromo-enolone **19**[17] (1.0 g, 2.3 mmol) and thiourea (200 mg, 0.6 mmol) in dry acetone (10 mL) was gently refluxed for 30 min. The crystalline product that separated on cooling was filtered off, washed with acetone, and dried to give 900 mg (79%) of the hydrobromide of **38**. M.p. 176−178 °C. $[\alpha]_D^{20}$ = 0.00 (*c* = 2, $CHCl_3$). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 5.02 (dd, 2 H, 4′-H_2), 6.39 (dt, 1 H, 3′-H), 7.2−8.2 (m, 11 H, 2′-H, 2 C_6H_5) ppm; $J_{2',3'}$ = 15.6, $J_{2',4'}$ = 1.6, $J_{3',4'}$ = 6.9 Hz. $C_{21}H_{17}BrN_2O_5S$ (489.34): calcd. C 51.54, H 3.50, N 5.72; found C 51.44, H 3.45, N 5.80.

2-Amino-4-[1′,4′-bis(benzoyloxy)but-2′-enylidene]thiazolin-5(4*H*)-one (38): A suspension of **38·HBr** (245 mg, 0.5 mmol) and solid $NaHCO_3$ (100 mg) in moist methanol was stirred for 30 min at room temperature; this was followed by evaporation to dryness in vacuo. The residue was extracted with hot *i*PrOH (3 × 5 mL) from which **38** crystallized on cooling. Collection and recrystallization gave 157 mg (77%). M.p. 160−162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.99 (dd, 2 H, 4′-H2), 5.45 (bs, 2 H, NH_2), 6.40 (dt, 1 H, 3′-H), 7.25−7.74 (m, 7 H, 2′-H, 6 ArH), 8.10 (dd, 2 H, 2 ArH), 8.25 (dd, 2 H, 2 ArH) ppm; $J_{2',3'}$ = 15.6, $J_{2',4'}$ = 1.6, $J_{3',4'}$ = 5.8 Hz. MS (FD, 14 mA): *m*/*z* = 408 [M^+]. $C_{21}H_{16}N_2O_5S$ (408.43): calcd. C 61.76, H 3.95, N 6.86; found C 61.61, H 3.88, N 6.81.

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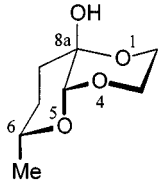

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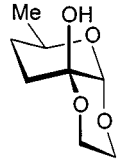

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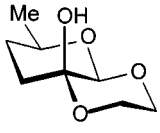
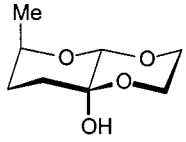


β-*trans* (11.2)



α-*trans* (21.7)

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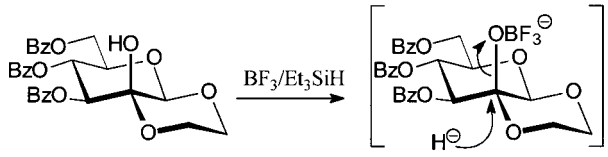
[15] In principle, the β-D-mannoside **16** could be conceived to also result from the C-2-isomeric, β-*trans*-annulated product I by S_N2 displacement of the F_3BO^- leaving group with the hydride ion, as indicated in II. Such an inversion at C-2, however, entails the transient adoption of the $^1C_4$ conformation of the pyranoid ring, i.e. II → III, most unlikely due to four axially disposed substituents in III and their multiple 1,3-diaxial interactions.



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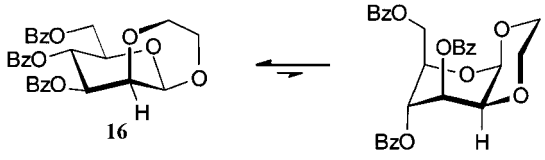

III

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[23] CCDC-242772 contains the supplementary crystallographic data for **30**. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223/336−033; E-mail: deposit@ccdc.cam.ac.uk].

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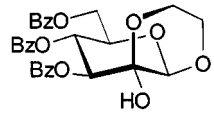
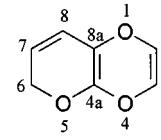
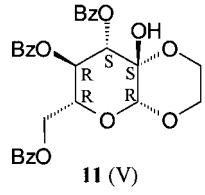
[28] Nomenclature: The divergence in naming and numbering heterodecalins of type **11**−**13** and **22**−**25** can be exasperating. Based on carbohydrate nomenclature, **11** is a 1,2-*O*-(ethane-1,2-diyl) 3,4,6-tri-*O*-benzoyl-2-hydroxy-β-D-mannopyranoside, whilst heterocyclic notations require its delineation from 6*H*-pyrano[2,3-*b*]-1,4-dioxine (IV), hence the designation (4a*R*,6*R*,7*R*,8*S*,8a*S*)-7,8-bis(benzoyloxy)-6-benzoyloxymethyl-8a-hydroxy-hexahydro-6*H*-pyrano[2,3-*b*]-1,4-dioxine(V). As the basic bicyclic skeleton of **11** constitutes a 1,4,5-trioxa-*cis*-decalin, which we consider mnemonically a more descriptive designation, it is employed in this paper in place of hexahydro-6*H*-pyrano[2,3-*b*]-1,4-dioxine.



11



IV



11 (V)

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