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Double Diastereoselective Glucosidation of Cyclic Hemiacetals: Synthesis of the 1,4-Benzoxazinone Acetal Glucosides GDIBOA and GDIMBOA from *Gramineae*

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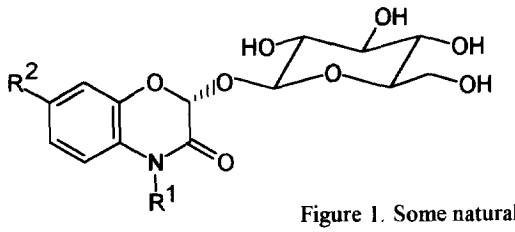
Abstract: A double diastereoselective glucosidation procedure giving rise in one step to the natural (2*R*)-2-β-configuration of **6** and, for the first time, **7**, benzoxazinoid acetal glucosides from *Gramineae* species, is described by reaction of *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) trichloroacetimidate **3** as glucosyl donor with 2,4-dihydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one **1** or its 7-methoxy derivative **2** as hemiacetalic glucosyl acceptors in the presence of excess borontrifluoride etherate as promoter without a need for a covalent protection of the cyclic hydroxamic acid unit in the aglucones.

INTRODUCTION

Almost 1000 natural products are known that due to their direct connection of two cyclic hemiacetals have to be regarded as hemiacetal ethers. The minority of such hemiacetal ethers arise from the combination of two sugar components, like α,α-trehalose[1] or α,β-galactobiose,[2] whereas the majority, the so called acetal glycosides, is represented by glycosidic derivatives of hemiacetals of a great structural diversity formed by metabolism. Nearly 100 acetal glycosides contain at least one nitrogen in the aglycone moiety. Usually, the nitrogen is part of rings annelated to the cyclic hemiacetal ring of the aglucone, as in *e.g.* xylostosidine,[3] pumiloside,[4] or alangiside.[5] Exceptionally, in the case of 2-β-D-glucosides of the 2-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one skeleton the N atom is part of the aglyconic hemiacetal ring (Figure 1).



R^1	R^2	compound
H	H	Blepharin
OH	H	**6**
OH	OMe	**7**
OMe	OMe	**11**

Figure 1. Some natural 1,4-benzoxazinone acetal glucosides.

Representatives of this class have been recently found to occur as allelo chemicals in various species of *Gramineae*,[6] *Acanthaceae*,[7] *Ranunculaceae*[8] and of *Scrophulariaceae*.[9] The biological function of such glucosides as possible endogeneous ligands in the plant cell is under investigation.[10] However, it has been

shown that the hemiacetalic aglucones exhibit high bioactivity as plant resistance factors in maize, rye and wheat against microbial diseases and insects,[11] phytotoxins of root exudates from the weed quackgrass,[12] and inhibitory agents towards prostate cancer cell lines.[13] Among the acetal glucosides isolated the hydroxamic acids (*2R*)-2-β-D-glucopyranosyloxy-4-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one **6** (GDIBOA),[14] its 7-methoxy derivative **7** (GDIMBOA)[15] and the 4,7-dimethoxy compound **11** (GHDIBOA)[16] are of most interest.

It is the aim of this paper to describe the first double diastereoselective total synthesis of **6** and **7** and the synthesis of the corresponding 4-methoxy derivatives.

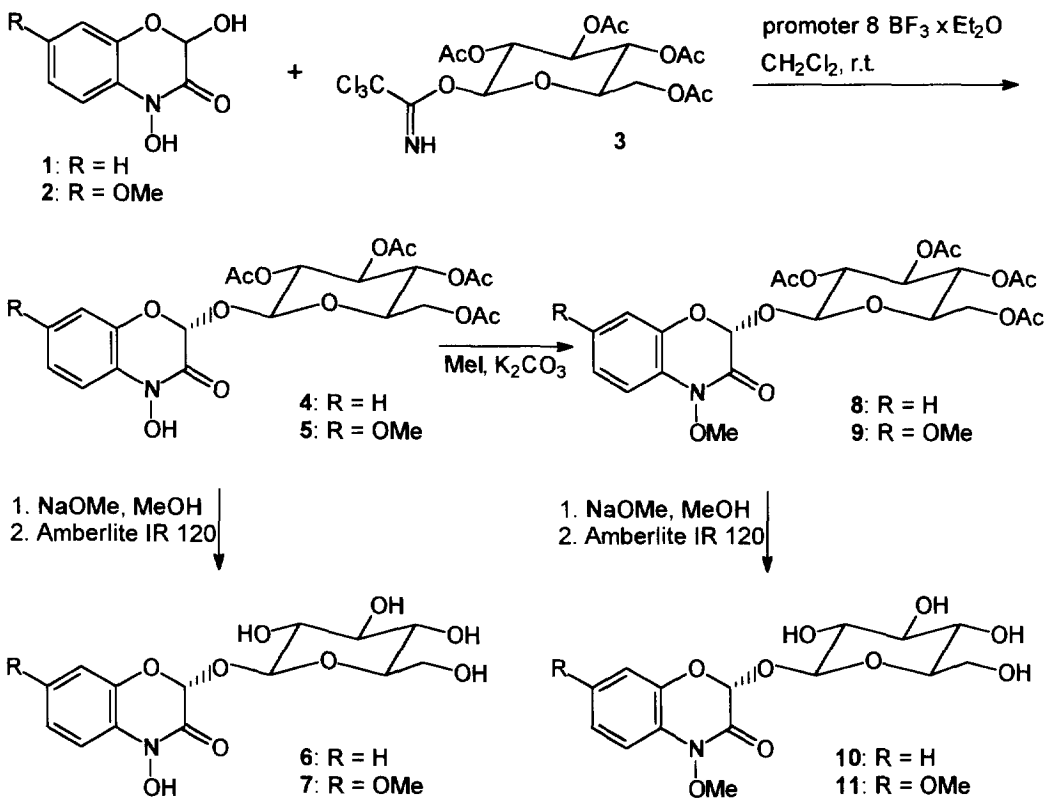
RESULTS AND DISCUSSION

Preparation of the starting glucosyl acceptors and the glucosyl donor. 2,4-Dihydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one **1** (DIBOA) was prepared from ethyl 2-nitrophenoxyacetate over three steps in 73% yield according to our procedure.[17] 2,4-Dihydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one **2** (DIMBOA) was obtained from ethyl 5-methoxy-2-nitrophenyl oxalate *with* reductive cyclisation to 4-hydroxy-7-methoxy-2,3-dioxo-1,4-benzoxazine[18] followed by diisobutylaluminum hydride reduction of this lactone to the lactol **2**[19] in two steps in 67% yield. Recently, we have also described an alternative access based upon an α-hydroxylation of 4-hydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one by a peroxide oxidation.[20] Alternatively, a procedure for the isolation of **2** from maize seedlings at the semigram scale has been described.[21] *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl) trichloroacetimidate **3** was synthesized following the Schmidt method.[22]

Stereoselectivity in the glycosidation of cyclic hemiacetals. A multitude of glycosidation methods have been described for alcohols or phenols. Stereochemically, the synthesis of such glycosides deals with the problem how to achieve a high single diastereoselectivity either for the formation of an α- or a β-linked glycoside, whereas the configuration of an alcoholic glycosyl acceptor is transferred unchanged to the product. In contrast, glycosidations of cyclic hemiacetals have been reported very seldom. Most likely, this is caused by the necessity to control now the two configurational possibilities that can be formed at the anomeric centers of both the glycosyl donor and acceptor. Therefore, in principle a set of four diastereomers is to be expected. Nevertheless, a total synthesis of a natural acetal glycoside with stereogenic centers in both the aglycone and the glycosidic unit can proceed with high diastereoselectivity due to the support by the asymmetric induction of both partners. An excellent example is the synthesis of iridoid glucosides, described by Tietze *et al.* using a trimethylsilyl β-glucopyranoside as glucosyl donor in the presence of catalytic amounts of trimethylsilyl triflate.[23]

The benzoxazinone glucosides of interest offer the same stereogenic challenge, but with a reduced kind of support because no asymmetric induction results from a 2-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one skeleton.

Blepharin, ((*2R*)-2-β-D-glucopyranosyloxy-2*H*-1,4-benzoxazin-3(4*H*)-one), a natural product found in *Blepharis edulis* Pers,[24] was the first benzoxazinone glucoside synthesized again by Tietze's group[25] by an inverse Koenigs-Knorr technique using the aglucone equipped with the bromine function. The glucosidation step yielded diastereoselectively two of the four isomers, *i.e.* the (*2R*)-2-β- and the (*2S*)-2-β- isomers (ratio 1:2) , which have been separated by chromatography. Inspired by this work, we have recently reported on the first synthesis of the hydroxamic acid glucoside **6** with full β-, but not (*2R/2S*)-diastereoselectivity[26] using *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) trichloroacetimidate catalysed by boron trifluoride etherate for a glucosidation of 4-benzyloxy-2*H*-1,4-benzoxazin-3(4*H*)-one[20] according to the Schmidt method. However, all attempts to use this methodology for the synthesis of **7** have failed due to the strong influence of the 7-methoxy group on the properties of the aglucone.



Scheme 1. Double diastereoselective glucosidation of cyclic hemiacetals to form natural acetal glucosides

A successful synthesis of **7** has to meet the following requirements: (i) The racemic aglucone has to undergo the reaction without a need for a preceeding covalent protection of the 4-position, because it was impossible to achieve a protection of **2** by a typical protecting group such as a benzyl or trimethylsilyl group.

This behaviour is obviously consistent with the 7-methoxy promoted ability to expel a substituent from the 4-position which is known for close analogues, for example derivatives of 4-hydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one.[27] (ii) A selective access should give rise to the natural (*2R*)-2-β-configuration, exclusively. (iii) The method should be applicable to the synthesis of other benzoxazinoid hydroxamic acid glucosides like **6**.

The essential feature of the new method of glucosidation (Scheme 1) consists in using an excess of boron trifluoride etherate. This Lewis acid accomplishes several functions. An interaction with the aglucone was proven by a comparison of the ^{1}H NMR spectra in DMSO-d_6 of **2** in the absence and in the presence of BF_3 x Et_2O. Both the signals for the 4-OH and for the 2-OH group disappeared on addition of BF_3 x Et_2O. Obviously, the anions of the hydroxamic acid unit and the hemiacetal unit of the aglucone are accepted as fourth ligands at boron atoms. For a further reaction with the glucosyl donor **3** the hemiacetalic function is clearly expected to be more nucleophilic than a hydroxamate ion which is stabilized by mesomerism. Thus, for the aglucones **1** and **2** interaction with BF_3 x Et_2O means a noncovalent protection of their hydroxamic acid unit and acts in the case of **2** as a tool to receive the enhanced electron density which is supplied to the N-substituent by the 7-MeO group. In contrast to many unsuccessful attempts to stabilise **2** by a covalent 4-protecting group, the ion pair formed by this Lewis acid interaction proved to be stable.

Acetyl-protected trichloroacetimidates like **3** have been shown to give exclusively β-glucosides due to neighboring group assistence of the acetyl groups.[28] Therefore, improving the diastereoselectivity of the glucosidation reaction meant finding a way to distinguish between the natural (*2R*)-2-β- and the diastereomeric (*2S*)-2-β-configuration. We have found, that changing from a catalytic amount (10%) of BF_3 x Et_2O hitherto used during glucosidation,[26] to an 8-fold excess, results in generating conditions which promote the glucosyl transfer and allow equilibration to the thermodynamically more stable diastereomer, which proved to be that with the natural configuration.

By this means, it was possible for the first time to obtain in a generally applicable glucosidation the tetraacetates **4** and **5** as the only reaction products. Therefore, a chromatographic separation of diastereomers was no longer necessary. Finally, the precursors **4** and **5** were deprotected to give rise to the acetal glucosides **6** and, for the first time, to synthetic **7**. Furthermore, **4** and **5** were methylated with methyl iodide in acetonitrile in the presence of K_2CO_3 to afford the 4-methoxy derivatives **8** and **9**. Deprotection of **8** and **9** liberated the 4-methylated hydroxamic acid acetal glucosides **10** and **11**, respectively. Whereas **10** is an artefact which has not been described as a natural product yet, **11** is a known constituent of some *Gramineae* species. Compound **11** is of a special interest, because its aglucone, 2-hydroxy-4,7-dimethoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (HDIBOA), is expected to show a very high bioactivity due to the ease of formation of a reactive electrophile that should be possible by extrusion of a methylate ion from the 4-position.[16b] Hitherto, this aglucone could neither be isolated nor prepared, however, **11** seems to be a promising precursor.

The structures of the closely related compounds **4-11** were established by spectroscopic means. The β-configuration of the glucosidic bond could be assigned from the value of the coupling constant, J, at about 8 Hz for the H-1′-H-2′ interaction. The (*2R*)-configuration could be proven by means of CD spectra, showing a positive Cotton effect at about 230 nm and a negative one at about 280 nm. This behavour is analogous with the CD spectrum of natural GHMBOA,[6c] (*2R*)-2-β-D-glucopyranosyloxy-4-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one, the only benzoxazinoid glucoside for which an X-ray structure exists. Furthermore, Tietze′s rule for acetal glucosides,[29] recently applied for the determination of configurations during the synthesis of Blepharin and 1′-Epiblepharin,[25] also gives evidence for the (*2R*) configuration. In accordance with this rule, the chemical shift value δ of H-2 of glucosides with the natural configuration is slightly (ca. 0.1 ppm) high field shifted in comparison to that of the (*2S*)-diastereomer. For acetal glucosides of 4-hydroxy-substituted 1,4-benzoxazinones it is expected at around 5.76 ppm, as we have recently shown during our first synthesis of **6**.[26] The corresponding shift values for H-2 from the spectra of **4-11** are in accordance with this rule.

CONCLUSION

In summary, a double diastereoselective glucosidation of the racemic hemiacetals **1** and **2** with glucosyl donor **3** has been developed giving rise in one step exclusively to the natural (*2R*)-2-β-configuration of **6** and, for the first time, to **7**. The main feature of the new glucosidation method consists in using an excess of boron trifluoride etherate, which accomplishes functions as a noncovalent protecting group for the aglucone and a promoter for the glucosyl transfer and a reagent ensuring an equilibration into the thermodynamically most stable diastereomer with the natural configuration. Finally, **7** was used as a precursor for the synthesis of the natural product **11**.

EXPERIMENTAL

General. Melting points were determined on a Boetius melting point apparatus and are corrected. ^{1}H and ^{13}C NMR spectra were recorded at 199.975 MHz and 50.289 MHz, respectively, using a Varian Gemini 200 spectrometer and hexamethyldisiloxane as internal reference. Infrared spectra were obtained on a Carl Zeiss Jena spectrometer M80. FAB mass spectra were determined with a VG ZAB-HSQ spectrometer from a 3-nitrobenzyl alcohol matrix. HRMS measurements were made at an AMD-402 mass spectrometer with 70 eV E.I. ionisation. CD-spectra were run at a JASCO J-710 spectrometer. The optical rotation was measured on a semiautomatic polarimeter Polartronic D (Schmidt & Haensch) using the Na-D line.

General Procedure for the Glucosidation to form the Acetal Glucoside Tetraacetates 4 and 5

To a stirred suspension of 0.5 mmol of the corresponding cyclic hemiacetal (91 mg of 2,4-dihydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one (**1**) for **4**; 105 mg of 2,4-dihydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (**2**) for **5**) and 492 mg (1.0 mmol) *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) trichloroacetimidate (**3**) in 20 ml of absolute CH_2Cl_2 was added 0.5 ml (4.0 mmol) BF_3 x Et_2O with a syringe at 20 °C. Immediately, the suspension turned into a light yellow solution. The mixture was stirred at room temperature in an argon atmosphere until completeness of the reaction was monitored by TLC (Kieselgel 60, Merck, eluent: ethyl acetate/toluene 3:1 (v:v) for **4**, and 2:1 (v:v) for **5**, respectively). 20 ml of water was added and after 5 min, the organic layer was separated, dried and evaporated *in vacuo*. The remaining oil was dissolved in diethyl ether from which the product crystallised.

(2*R*)-2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-4-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one (4)

Recrystallisation of the crude product thus obtained from aqueous ethanol yielded 182 mg (71 %) of pure (**4**) as colourless needles. Mp: 222-224 °C, lit.[26] mp: 223-224 °C. All spectroscopic and chiroptic data were in agreement with those of previously described.[26]

(2*R*)-2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-4-hydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (5)

Recrystallisation of the crude product thus obtained from aqueous ethanol yielded 195 mg (72 %) of pure (**5**) as colourless needles. Mp: 191-193 °C. IR (KBr): 1755, 1670, 1515, 1370, 1230 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.95 (3H, s, C*H*$_3$CO), 1.96 (3H, s, C*H*$_3$CO), 1.99 (3H, s, C*H*$_3$CO), 2.07 (3H, s, C*H*$_3$CO), 3.70 (1H, ddd, $J_{5',4'}$ = 9.8 Hz, $J_{5',6b'}$ = 4.1 Hz, $J_{5',6a'}$ = 2.1 Hz, C5′-H), 3.75 (3H, s, C*H*$_3$O), 4.19 (1H, dd, $J_{6b',5'}$ = 4.1 Hz, ^2J= 12.3 Hz,C6′-Hb), 4.20 (1H, dd, $J_{6a',5'}$ = 2.1 Hz, ^2J= 12.4 Hz, C6′-Ha), 4.86 (1H, dd, $J_{2',1'}$ = 7.9 Hz, $J_{2',3'}$ = 9.2 Hz, C2′-H), 4.92 (1H, d, $J_{1',2'}$ = 7.9 Hz, C1′-H), 5.01 (1H, dd, $J_{4',5'}$ = 9.8 Hz, $J_{4',3'}$ = 9.7 Hz, C4′-H), 5.18 (1H, dd, $J_{3',4'}$ = 9.7 Hz, $J_{3',2'}$ = 9.2 Hz, C3′-H), 5.77 (1H, s, C2-H), 6.61 (1H, d, $J_{6,8}$ = 2.8 Hz , C8-H), 6.64 (1H, dd, $J_{6,8}$ = 2.8 Hz, $J_{6,5}$ = 8.8 Hz, C6-H), 7.27 (1H, d, $J_{5,6}$ = 8.8 Hz, C5-H), 9.33 (1H, s, NOH). ^{13}C-NMR ($CDCl_3$) δ: 20.5, 20.6, 20.8 (4 x CH_3CO), 55.7 (*C*H$_3$O), 61.8 (C6′), 68.1 (C4′), 71.0 (C2′), 72.5 (C5′), 72.6 (C3′), 97.3 (C2), 100.6 (C1′), 103.9 (C8), 108.9 (C6), 114.4 (C5), 120.0 (C4a), 141.4 (C8a), 154.1 (C3), 157.6 (C7), 169.4 (CH_3CO), 169.6 (CH_3CO), 170.3 (CH_3CO), 170.8 (CH_3CO). FABMS m/z (rel. Int.) 541 ($[M]^+$,40), 331 (65), 194 (90), 169 (100), 154 (30), 109 (53). $[\alpha]_{589}^{21}$ = + 37° ($CHCl_3$; c 0.75). CD $\Delta\varepsilon_{236}$ +3.25, $\Delta\varepsilon_{287}$ -0.54 (CH_3OH; c 0.1).

General Procedure for the Methylation to form the N-Methoxy Acetal Glucoside Tetraacetates 8 and 9

To a solution of 0.1 mmol of the corresponding acetal glucoside tetraacetate (51 mg of (*2R*)-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-4-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one **(4)** for product **8**; 54 mg of (*2R*)-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-4-hydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one **(5)** for **9**) in 10 ml of absolute acetone were added 14 mg (0.1 mmol) potassium carbonate and 28 mg (0.2 mmol, 12.5 µl) methyl iodide with a syringe. The mixture was stirred at room temperature in an argon atmosphere until completeness of the reaction was monitored by TLC with ethyl acetate/toluene 2:1 (v:v). After filtration the solvent was removed *in vacuo*. The remaining residue was washed with diethyl ether and dried.

(*2R*)-2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-4-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (8)

52 mg (99%) of pure **(8)** were obtained as pale yellow crystals. Mp: 156-158 °C. IR (KBr): 1755, 1707, 1494, 1377, 1226 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.95 (3H, s, C*H*$_3$CO), 1.99 (3H, s, C*H*$_3$CO), 2.00 (3H, s, C*H*$_3$CO), 2.07 (3H, s, C*H*$_3$CO), 3.75 (1H, ddd, $J_{5',4'}$ = 10 Hz, $J_{5',6b'}$ = 4 Hz, $J_{5',6a'}$ = 2.4 H, C5′-H), 3.94 (3H, s, C*H*$_3$O), 4.16 (1H,dd, $J_{6b',5'}$ = 4 Hz, ^{2}J= 12.4 Hz, C6′-Hb), 4.20 (1H, dd, $J_{6a',5'}$ = 2.4 Hz, ^{2}J= 12.4 Hz, C6′-Ha), 4.87 (1H, dd, $J_{2',1'}$ = 8 Hz, $J_{2',3'}$ = 8.4 Hz, C2′-H), 4.92 (1H, d, $J_{1',2'}$ = 8 Hz, C1′-H), 5.02 (1H, dd , $J_{4',5'}$ = 9.2 Hz, $J_{4',3'}$ = 9.3 Hz, C4′-H), 5.17 (1H, dd, $J_{3',4'}$ = 9.3 Hz, $J_{3',2'}$ = 8.4 Hz, C3′-H), 5.66 (1H, s, C2-H), 7.04-7.25 (4H, m, arom.). ^{13}C-NMR ($CDCl_3$) δ: 20.5, 20.6, 20.8 (4 x CH_3CO), 61.9 (C6′), 62.9 (*C*H$_3$O), 68.1 (C4′), 70.9 (C2′), 72.5 (C5′,C3′), 98.0 (C2), 101.2 (C1′), 112.7 (C5), 118.1 (C8), 123.8 (C7), 125.0 (C6), 126.0 (C4a), 140.4 (C8a), 154.6 (C3), 169.3 (CH_3CO), 169.4 (CH_3CO), 170.3 (CH_3CO), 170.7 (CH_3CO). FABMS m/z (rel. Int.) 525 ($[M]^+$,20), 331 (30), 311 (35), 178 (28), 169 (100), 109 (36). $[\alpha]_{589}^{21}$ = + 37° ($CHCl_3$, c 1.0). CD $\Delta\varepsilon_{231}$ +18.7, $\Delta\varepsilon_{279}$ -0.45 (CH_3OH; c 0.1).

(*2R*)-2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyloxy)-4,7-dimethoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (9)

54 mg (97%) of pure **(9)** were obtained as pale yellow crystals. Mp: 71-73 °C. IR (KBr): 1756, 1706, 1507, 1369, 1231 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.95 (3H, s, C*H*$_3$CO), 1.99 (3H, s, C*H*$_3$CO), 2.00 (3H, s, C*H*$_3$CO), 2.08 (3H, s, C*H*$_3$CO), 3.75 (3H, s, C*H*$_3$O), 3.76 (1H, m, C5′-H), 3.92 (1H, s, C*H*$_3$ON), 4.16 (1H, dd, $J_{6a',5'}$ = 2 Hz, ^{2}J= 12 Hz, C6′-Ha), 4.21 (1H, dd, $J_{6b',5'}$ = 4.8 Hz, ^{2}J= 12 Hz, C6′-Hb), 4.85 (1H, d, $J_{1',2'}$ = 8.2 Hz, C1′-H), 4.92 (1H, dd, $J_{2',1'}$ = 8.2 Hz, $J_{2',3'}$ = 9 Hz, C2′-H), 5.02 (1H, dd, $J_{4',5'}$ = 9.6 Hz, $J_{4',3'}$ = 9.6 Hz, C4′-H), 5.17 (1H,dd, $J_{3',4'}$ = 9.6 Hz, $J_{3',2'}$ = 9.2 Hz, C3′-H), 5.64 (1H, s, C2-H), 6.62 (1H, d, $J_{6,8}$ = 2.4 Hz ,C8-H), 6.64 (1H, dd, $J_{6,8}$ = 2.4 Hz, $J_{6,5}$ = 8.8 Hz, C6-H), 7.09 (1H, d, $J_{5,6}$ = 8.8 Hz, C5-H). ^{13}C-NMR ($CDCl_3$) δ: 20.5, 20.6, 20.8 (4 x CH_3CO), 55.7 (*C*H$_3$O), 61.9 (C6′), 62.8 (*C*H$_3$ON), 68.1 (C4′), 70.9 (C2′), 72.5 (C5′), 72.6 (C3′), 98.3 (C2), 101.2 (C1′), 104.4 (C8), 109.0 (C6), 113.4 (C5), 119.5 (C4a), 141.4 (C8a), 154.0 (C3), 157.4 (C7), 169.3 (CH_3CO), 169.4 (CH_3CO), 170.2 (CH_3CO), 170.7 (CH_3CO). FABMS m/z (rel. Int.) 555

([M]$^+$,25), 331 (55), 169 (100), 109 (45). $[\alpha]_{589}^{21}$ = + 50° ($CHCl_3$; c 0.4). CD $\Delta\varepsilon_{234}$ +6.54, $\Delta\varepsilon_{287}$ -1.99 (CH_3OH; c 0.1).

General Procedure for the Deprotection to form the Acetal Glucosides 6, 7, 10, and 11: To a solution of 0.1 mmol of the corresponding tetraacetate (51 mg of **4** for product **6**; 54 mg of **5** for **7**; 53 mg of **8** for **10**; 56 mg of **9** for **11**) in 10 ml of absolute MeOH was added 5 mg (0.09 mmol) sodium methoxide. After stirring the mixture for 30 min at room temperature the solution was neutralised by the addition of an ion exchange resin (Amberlite IR 120 (H^+)). The resin was filtered off and the solvent removed *in vacuo*. The residue was chromatographed over silica gel (Kieselgel 60, 60-200 µm, Merck) with chloroform / methanol (3:2 (v:v) for **6** and **7**; 3:1(v:v) for **10**; 4:1 (v:v) for **11**).

(*2R*)-2-β-D-Glucopyranosyloxy-4-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one (6)

The residue thus obtained was washed with diethyl ether to yield 27 mg (80%) of pure (**6**) as colourless crystals. Mp: 255-257 °C (dec.), lit.[14b] mp: 256-257 °C (dec.). All spectroscopic and chiroptic data were in agreement with those of previously described.[14b]

(*2R*)-2-β-D-Glucopyranosyloxy-4-hydroxy-7-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (7)

The residue thus obtained was washed with diethyl ether to yield 28 mg (75%) of pure (**7**) as colourless crystals. Mp: 168-170 °C (dec.), lit.[15b] mp: 170-172 °C (dec.). All spectroscopic and chiroptic data were in agreement with those of previously described.[15b]

(*2R*)-2-β-D-Glucopyranosyloxy-4-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (10)

The residue thus obtained was washed with diethyl ether to yield 28 mg (78%) of pure (**10**) as colourless crystals. Mp: 188-190 °C (dec.). IR (KBr): 1700, 1653, 1495, 1122 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.17 (1H, dd, $J_{1',2'}$ = 7.9 Hz, C2′-H), 3.36 (1H, dd, $J_{3',4'}$ = 9.3 Hz, C4′-H), 3.45 (1H, m, C5′-H), 3.50 (1H, dd, $J_{3',4'}$ = 9.3 Hz, C3′-H), 3.68 (1H, dd, ^{2}J = 12 Hz, C6′-Hb), 3.86 (1H, dd, ^{2}J = 12 Hz, C6′-Hb), 3.97 (3H, s, C*H*$_3$ON), 4.68 (1H, d, $J_{1',2'}$ = 7.9 Hz, C1′-H), 5.92 (1H, s, C2-H), 7.14-7.28 (4H, m, arom.). ^{13}C-NMR (CD_3OD) δ: 62.8 (C6′), 63.8 (*C*H$_3$O), 71.4 (C4′), 75.0 (C2′), 78.2 (C5′), 78.8 (C3′), 98.2 (C2), 104.2 (C1′), 113.9 (C5), 119.6 (C8), 124.8 (C7), 126.5 (C6), 127.5 (C4a), 142.7 (C8a), 157.7 (C3). HRMS m/z: 357.1043 [M]$^+$ (calcd. for $C_{15}H_{19}NO_9$ = 357.106). $[\alpha]_{589}^{21}$ = + 76° (H_2O; c 0.5). CD $\Delta\varepsilon_{230}$ +44.1, $\Delta\varepsilon_{276}$ -11.8 (H_2O; c 0.876).

(*2R*)-2-β-D-Glucopyranosyloxy-4,7-dimethoxy-2*H*-1,4-benzoxazin-3(4*H*)-one (11)

The residue thus obtained was washed with diethyl ether to yield 37 mg (95%) of pure (**11**) as pale yellow crystals. Mp. 143-145 °C (dec.), lit. [16a] 142-144 °C, lit. [6c] 91-93 °C. IR (KBr): 1696, 1624, 1508, 1075 cm^{-1}.

^{1}H-NMR (CD_3OD) δ: 3.12-3.45 (4H, m, C2′-H, C3′-H, C4′-H, C5′-H), 3.68 (1H, m, C6′-Ha), 3.79 (3H, s, CH_3O), 3.85 (1H, m, C6′-Hb), 3.95 (3H, s, CH_3ON), 4.68 (1H, d, $J_{1',2'}$ = 7.7 Hz, C1′-H), 5.89 (1H, s, C2-H), 6.73 (1H, dd, $J_{6,8}$ = 2.5 Hz, $J_{6,5}$ = 8.8 Hz, C6-H), 6.79 (1H, d, $J_{6,8}$ = 2.5 Hz, C8-H), 7.19 (1H, d, $J_{6,5}$ = 8.8 Hz, C5-H). ^{13}C-NMR (CD_3OD) δ: 56.5 (CH_3O), 62.9 (C6′), 63.7 (CH_3ON), 71.4 (C4′), 75.0 (C2′), 78.2 (C5′), 78.8 (C3′), 98.7 (C2), 104.4 (C1′), 105.6 (C8), 110.4 (C6), 114.8 (C5), 120.9 (C4a), 143.8 (C8a), 157.1 (C3), 159.4 (C7). HRMS m/z: 387.1186 $[M]^+$ (calcd. for $C_{16}H_{21}NO_{10}$ = 387.1165). $[\alpha]_{589}^{21}$ = + 22° (H_2O; c 0.25). CD $\Delta\varepsilon_{231}$ +25.9 , $\Delta\varepsilon_{282}$ -11.9 (H_2O; c 0.776).

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Dedicated to Professor Rolf Borsdorf on the occasion of his 65th birthday

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