DOI: 10.1002/ejoc.201000612

1-*exo*-Alkylidene-2,3-anhydrofuranoses: Valuable Synthons in the Preparation of Furanose-Based Templates

Ana M. Gómez,*[a] Ana Pedregosa,[a] Clara Uriel,[a] Serafín Valverde,[a] and J. Cristóbal López*[a]

Keywords: Carbohydrates / Glycals / Molecular diversity / Template synthesis / Epoxidation

Highly functionalized 1-*exo*-alkylidene-2,3-anhydro-, and 1′-halo-1-*exo*-alkylidene-2,3-anhydrofuranoses can be prepared in four or five steps, respectively, from D-mannose. These compounds feature a variety of functionalities, including a double bond, an oxirane, an allylic oxirane and (in the case of the 1′-halo derivative) an alkenyl halide. The reactivity of each functionality in these derivatives has been explored, and the usefulness of these substrates has been demonstrated with the preparation of furanose-based carbohydrate templates with up to four sites of molecular diversity.

Introduction

Diversity-oriented synthesis (DOS) is now recognized as a unique tool for the generation of many structurally diverse and complex molecules with application in biological studies.[1] The key elements of a successful DOS include: i) a reduced number of steps to build up the core scaffolds, and ii) the efficient use of chemical reactions to increase diversity and complexity in the development of the library. On the other hand, the design of novel molecular platforms that allow stereodetermined, three-dimensional orientations of pharmacophores remains an important goal in drug discovery[2] approachable through diversity-oriented synthesis (DOS). In this context, the successful use of carbohydrates as scaffolds in the area of peptidomimetics[3] has triggered a considerable research effort on the use of sugar derivatives as templates in bioactive compound discovery.[4] Carbohydrate templates have consequently been generated from pyranoses, furanoses, disaccharides and bicyclic sugar derivatives, with most of the strategies for their construction having been based on the stepwise derivatization of *orthogonally protected* carbohydrate derivatives.[5–7]

We have recently embarked on a project relating to the design of novel furanose-based scaffolds by chemoselective transformations of a core structure. With this in mind, we selected compound types **1** and **2** (Figure 1). These derivatives fulfil conditions i) and ii) described above for the successful implementation of DOS strategies. Compound types **1** and **2** are readily available from inexpensive D-mannose, in four and five steps, respectively, and can be subjected to simple chemical reactions that lead to diversified platforms

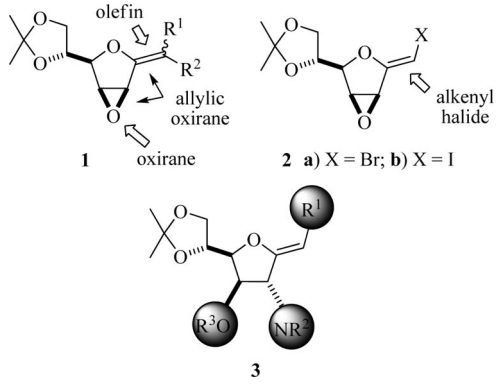


Figure 1. The epoxy-*exo*-glycals **1** and the halo epoxy-*exo*-glycals **2**, precursors of the furanose-based templates **3**.

(e.g., **3**) in which the (three) different substituents can be incorporated sequentially and in a completely stereocontrolled manner.

Compounds **1** each possess a variety of functionalities: an exocyclic double bond, an oxirane, and – if the two are combined – an allylic oxirane, amenable to a variety of chemical transformations. Compounds **2**, available by stereoselective halogenation of **1**, each incorporate an additional alkenyl halide component as well as the previously listed functionalities. We have been investigating the reactivity of derivatives **1** and **2** and in this manuscript we disclose in detail our studies directed towards: i) exploring the reactivity of the different functionalities, and ii) the development of stepwise transformations of **1** and **2** into furanose-based templates of type **3**.

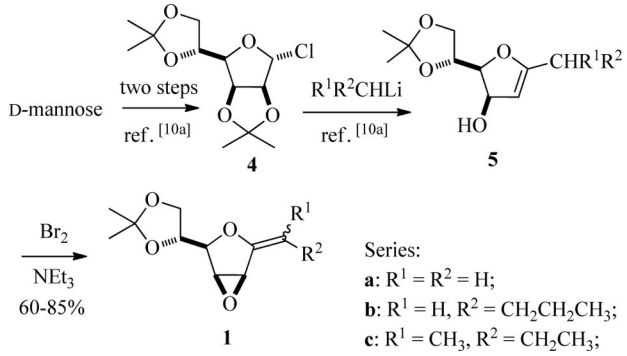
Results and Discussion

Synthesis of Epoxy-*exo*-glycals from D-Mannose

The synthetic strategy for epoxy-*exo*-glycals[8] (i.e., compounds **1**) takes advantage of the straightforward prepara-

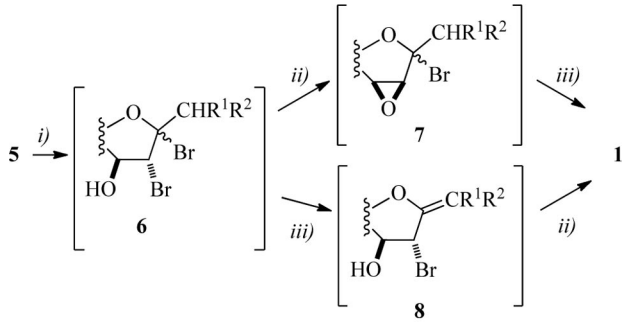
[a] Instituto de Química Orgánica General, CSIC,
Juan de la Cierva 3, 28006 Madrid, Spain
Fax: +34-915644853
E-mail: anagomez@iqog.csic.es
clopez@iqog.csic.es

tion of *C*-1 glycals such as compounds **5** (Scheme 1) from D-mannose through the transformation of intermediate glycosyl chlorides of type **4** with the aid of organolithium reagents[9] recently described by us.[10] Subsequent treatment of the *C*-1 glycals **5a**–**c** with bromine in triethylamine gave access to the epoxy-*exo*-glycals **1a**–**c**.[11]



Scheme 1. Strategies for the synthesis of substituted *exo*-glycals.

Remarkably, the one-pot process **5**→**1** (Scheme 1) involves three well-established transformations in carbohydrate chemistry: i) the bromination of glycals, pioneered by Lemieux and Fraser-Reid,[12] ii) the formation of epoxides from halohydrins,[13] and iii) the base-mediated elimination of anomeric halides[14] (Scheme 2). Two possible reaction pathways for this transformation, differing in the order in which steps ii) and iii) might take place, can accordingly be proposed.



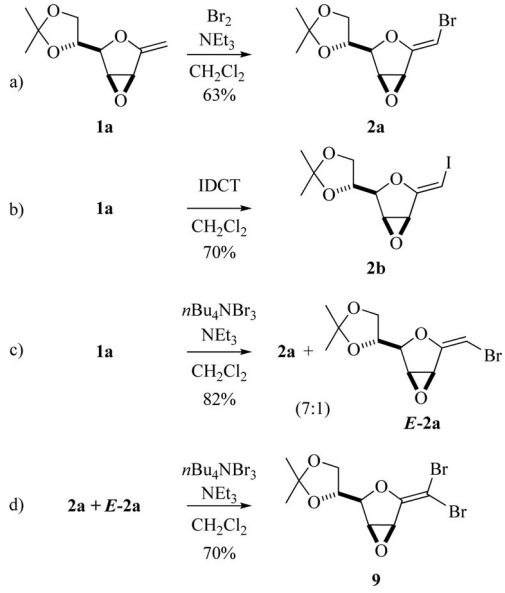
Steps: *i)* halogenation; *ii)* epoxide formation; *iii)* elimination

Scheme 2. One-pot transformation of the furanosidic *C*-1 glycals **5** into the epoxy-*exo*-glycals **1**.

In our opinion, the sequence will probably start with the stereoselective bromination of the electron-rich double bond[15] (step i, Scheme 2) to furnish the dibromide **6**. No reaction intermediate (**7** or **8**) has ever been observed (TLC) in these transformations, so a **6**→**8**→**1** pathway involving a reactive allylic bromide seems more likely.

Reactions at the Exocyclic Olefin

We have studied the reactivity of the enol ether double bond in the *exo*-glycal **1a** towards a number of halogenating agents: bromine, iodonium dicollidine triflate (IDCT)[16] and tetra-*n*-butylammonium tribromide (nBu_4NBr_3, TBAT).[17] Accordingly, treatment of **1a** with bromine and with IDCT gave the halo-*exo*-glycals **2a** and **2b** in a stereocontrolled manner and in 63% and 70% yields, respectively. The *Z* derivatives were obtained as the sole isomers (Scheme 3, a and b). On the other hand, treatment of **1a** with TBAT furnished a 7:1 mixture of isomeric (*Z*)- and (*E*)-**2a** (Scheme 3, c). This mixture could be efficiently transformed into the dibromo *exo*-glycal **9** by further treatment with TBAT (Scheme 3, d).



Scheme 3. Electrophilic halogenation of the *exo*-glycals **1a** and **2a**.

The stereochemical outcomes of these reactions have been interpreted previously.[18,19] In the formation of **2b**, the *s*-collidine released in situ could abstract a proton from a 1-iodomethyloxocarbenium ion, in which the bulky iodine atom would be located away from the oxirane ring (Figure 2, **A**). Likewise, a related preferred rotamer, in which the bromine atom is away from the epoxide, could experience NEt_3-induced HBr elimination leading to **2a** (Figure 2, **B**).

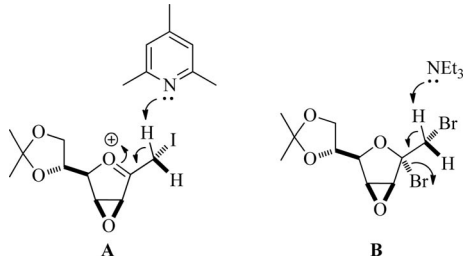
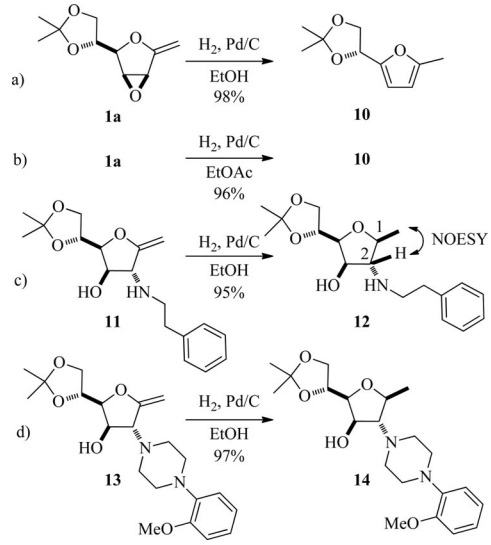


Figure 2. Proposed reaction pathways leading to **2b** and to **2a**.

We also studied the hydrogenation of the enol ether double bond. Treatment of **1a** under typical hydrogenation conditions (H_2, Pd/C, EtOH, 25 psi) led to the furan derivative **10** (Scheme 4, a). Additional hydrogenation attempts in the presence of different catalysts, such as $Pd(OH)_2$ or supported Pd,[20] gave similar results, which serves to illus-

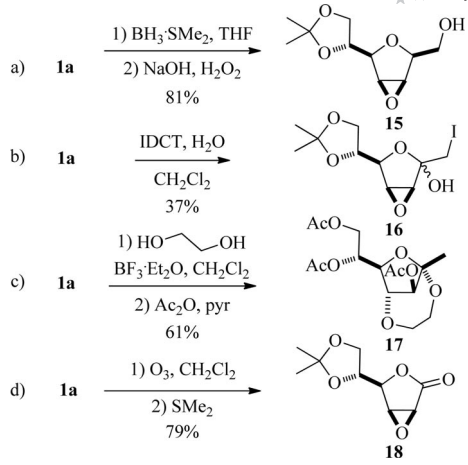
trate the ease with which aromatization takes place in these systems.[21] The use of EtOAc as solvent also gave similar results (Scheme 4, b).



Scheme 4. Hydrogenation of the exocyclic double bonds in *exo*-glycals.

Conversely, the absence of the oxirane ring in the molecule renders the hydrogenation process possible (Scheme 4, c and d). The stereochemistry at the newly created stereogenic centre in compound **12** was assigned through an observed NOESY between H_2 and the methyl group at C_1.

Hydroboration of **1a** with BH_3SMe_2, followed by oxidation (NaOH, H_2O_2), proved to be completely stereoselective, and furnished the *C*-1 glycal **15** in 81% yield (Scheme 5, a). Treatment of **1a** with IDCT in the presence of H_2O yielded the ketose **16** in moderate yield (37%, Scheme 5, b).[22] Treatment of **1a** with $BF_3{\cdot}Et_2O$ in the presence of ethylene glycol yielded a bicyclic derivative from which compound **17** could be obtained after acetylation (61% yield, Scheme 5, c). The formation of compound **17** involves three processes: i) acid-mediated glycosylation of the *exo*-glycal double bond,[23] most probably followed by ii) intramolecular acid-catalysed regioselective epoxide ring-opening, and iii) acetal deprotection, probably through ethylene-glycol-mediated transacetonation. Acetylation of the intermediate to afford **17** proved necessary for rigorous assignment of the location of the 2-OAc group. H-2 appeared as a doublet at δ = 5.08 ppm, whereas H-3 showed as a dd at δ = 3.65 ppm. Finally, ozonation of **1a** gave access to the epoxy-lactone **18**, in 79% yield (Scheme 5, d).



Scheme 5. Reactivity of the double bond in the *exo*-glycal **1a**.

Reactions at the Oxirane Ring

Nucleophilic ring-opening reactions of furanose-derived 2,3-oxiranes are well documented. Lowary and co-workers studied the regiochemistry of the nucleophilic ring-opening of isomeric alkyl 2,3-epoxy furanosides,[24] whereas Hirota and co-workers studied the nucleophilic ring-opening of furanosidic allylic oxirane systems, more closely related to our derivatives.[25]

As already reported by us,[26] compound **1a** reacted with a series of amines in ethanol at reflux to give 2-deoxy-2-amino derivatives (**11**, **13** and **19**–**25**, Figure 3). Similarly, the epoxy-*exo*-glycals **1b** and **1c** underwent regioselective ring-opening to give amino alcohols such as **26** and **27** (Figure 3).

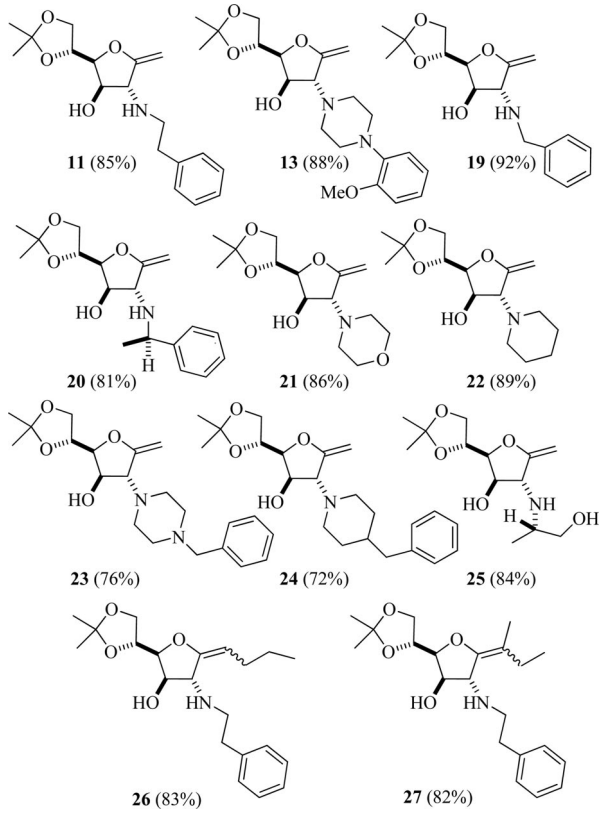


Figure 3. Amino alcohols prepared by nucleophilic ring-opening of the epoxy *exo*-glycals **1a**–**c**.

The behaviour of the 1′-bromo- and 1′-iodo-epoxy-*exo*-glycals **2a** and **2b**, respectively, towards amines proved to be similar, and their treatment with (primary or secondary) amines in ethanol at reflux led to the 2-deoxy-2-amino derivatives **28**–**30** without any effect on the anomeric alkenyl

halide moiety (Figure 4). Higher yields of amino alcohols were consistently observed for the bromo derivatives than for the iodine-containing compounds, probably due to the greater lability of the latter compound class.

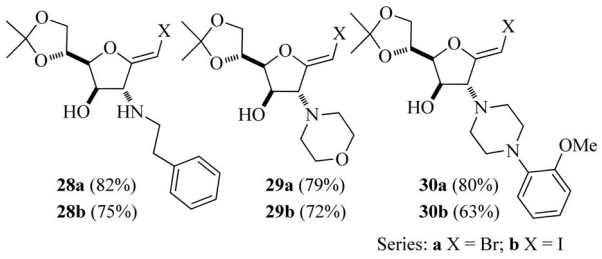


Figure 4. Amino alcohols obtained by nucleophilic ring-opening of the 1′-halo-*exo*-glycals **2a** and **2b**.

We next examined the nucleophilic ring-opening of the allylic oxiranes **1** and **2** with hydroxide anion, to provide allylic diol derivatives (e.g., **31**–**35**, Table 1). Two sets of conditions were examined, and the best results were obtained by treatment of the epoxides with nBu$_4$NOH in THF/H$_2$O (3:1) at reflux. Under such reaction conditions the corresponding diols (or their acetates) could be obtained in moderate yields.

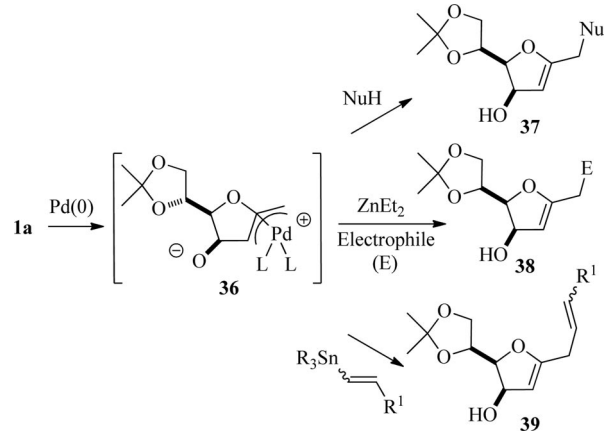
Table 1. Nucleophilic oxirane ring-opening of the allylic epoxides **1a**–**c** and **2a** and **2b** with H$_2$O.

Entry	Epoxide	Reaction conditions	Product	Yield (%)
i	**1a**	1[a]	**31**	57[b]
ii	**1a**	2[c]	**31**	49[b]
iii	**1b**	1	**32**	52
iv	**1c**	1	**33**	49
v	**2a**	1	**34**	59[d]
vi	**2b**	1	**35**	64[d]

[a] Bu$_4$NOH (2 equiv.), THF/H$_2$O (3:1) reflux. [b] Characterized as its diacetate. [c] KOH (5%, 3 mL mmol^{-1}), 40 °C. [d] Followed by acetylation: Ac$_2$O, pyridine.

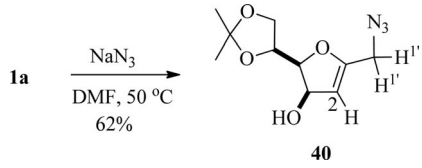
Reactions at the Allylic Oxirane Moiety

We had already evaluated the reactivity of the allylic epoxide moiety in **1a** towards palladium. Compound **1a** is able to react smoothly (through the π-allyl palladium complex **36**,[27] Scheme 6) with nucleophiles,[11] vinylstannanes[27,28] or, after treatment with ZnEt$_2$, with electrophiles[29] to give highly functionalized *C*-1 glycals[27,30] such as **37**–**39**.



Scheme 6. Pd^0-catalysed reactions of the vinyl oxirane **1a** with nucleophiles, electrophiles and vinylstannanes.

On the other hand, treatment of **1a** with sodium azide in DMF at 50 °C yielded the primary allylic azide **40** in 62% yield as the only isolated product (Scheme 7). Its structure was rigorously assigned by NMR spectroscopy. Two doublets, one at δ = 3.84 ppm (J = 2.6 Hz, 2 H) and the second at δ = 5.22 ppm (J = 2.6 Hz, 1 H), corresponding to H-1′ and H-2, respectively, were observed. Additionally, by ^{13}C NMR spectroscopy, signals were observed at δ = 102.3 and 157.4 ppm and at 47.1 ppm, corresponding to an endocyclic double bond and to CH_2N_3, respectively. Compound **40** should be the result of a formal S_N2' opening of the allylic epoxide, although a reaction pathway involving S_N2 opening of the oxirane followed by sigmatropic rearrangement of an intermediate allylic azide to the thermodynamically more stable **40** could not be ruled out on the basis of the reactivities found in related allylic epoxides by Pauls and Fraser-Reid.[31]



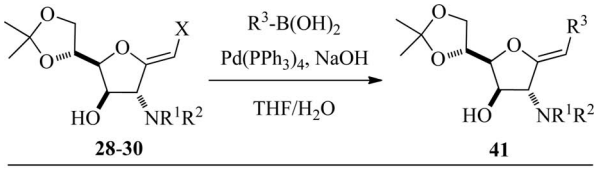
Scheme 7. Reaction of allylic epoxide **1a** with sodium azide.

Reactions at the Alkenyl Halide Component – Generation of Furanosidic Libraries with Two Sites of Diversity

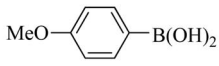
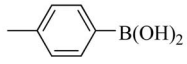
In order to generate a library of furanosidic derivatives each possessing two diversity points, we decided to exploit the reactivity of the vinyl halide moieties in the amino

alcohols **28**–**30**. We had previously shown that structurally related vinyl halides could be engaged in a variety of palladium-catalysed reactions,[32] including Suzuki cross-couplings,[33,34] leading to monosubstituted *exo*-glycals. We thus carried out Suzuki couplings between the vinyl halides **28**–**30** and the boronic acids **42**–**44** to give the allylic amines **41**, and our results are displayed in Table 2. Treatment of the vinyl halides **28**–**30** with the boronic acids **42**–**44** (1.3 equiv.) in the presence of $Pd(PPh_3)_4$ (5%) and NaOH (2 M, 2.7 equiv.) in THF/H_2O (4 mL mmol^{-1}) at reflux led to the allylic derivatives **41a**–**i** in moderate to good yields.

Table 2. Suzuki cross-couplings between the 1′-halo-*exo*-glycals **28**, **29** and **30** and the boronic acids **42**–**44**, catalysed by $Pd(PPh_3)_4$ in the presence of NaOH, in THF/H_2O as solvent at reflux.



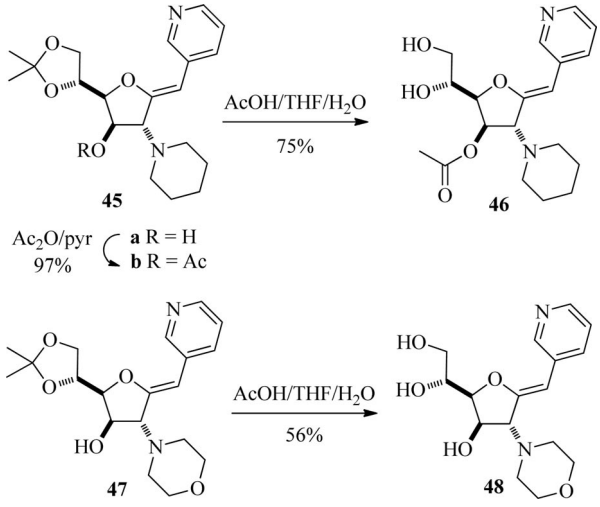
28-30 **41**

Entry	Alkenyl halide	Boronic acid R^3-$B(OH)_2$	Reaction time (h)	Product (yield)
i	**28a**	 **42**	24	**41a** (69%)
ii	**28a**	 **43**	48	**41b** (63%)
iii	**28a**	 **44**	72	**41c** (67%)
iv	**29a**	**42**	24	**41d** (86%)
v	**29a**	**43**	48	**41e** (75%)
vi	**29a**	**44**	48	**41f** (73%)
vii	**30a**	**42**	48	**41g** (72%)
viii	**30a**	**43**	24	**41h** (74%)
ix	**30a**	**44**	48	**41i** (66%)
x	**28b**	**42**	24	**41a** (72%)
xi	**28b**	**43**	48	**41b** (66%)
xii	**28b**	**44**	72	**41c** (64%)
xiii	**29b**	**42**	24	**41d** (93%)
xiv	**29b**	**43**	48	**41e** (86%)
xv	**29b**	**44**	48	**41f** (76%)
xvi	**30b**	**42**	24	**41g** (77%)
xvii	**30b**	**43**	24	**41h** (82%)
xviii	**30b**	**44**	48	**41i** (67%)

The observed reaction times varied from 24 to 72 h, and the isolated yields of allylic amines ranged from 60% to 90%.

Generation of Furanodisic Libraries Possessing Three – or More – Sites for Diversity

The derivatives **41a**–**i**, resulting from oxirane opening followed by palladium-catalysed cross-coupling, already each incorporate two substituents. Moreover, the presence of the 3-OH and the 5,6-*O*-isopropylidene acetal components makes further derivatization of these derivatives possible. To illustrate this point we performed the transformations of the amino alcohols **45a** and **47** into **45b**, **46** and **48** (Scheme 8), thus laying the foundations for syntheses of additional furanose-based libraries.



Scheme 8. Furanose derivatives **46** and **48**, each with more than three points of diversity.

Accordingly, acetylation of **45a** led to the acetate **45b**, possessing three points of diversity. Interestingly, the enol ether double bond in **45b** displayed an enhanced stability towards acid, and consequently the 5,6-*O*-isopropylidene group acetal could be removed without the anomeric functionality being affected, thus affording the diol **46**.

Similarly, treatment of the amino alcohol **47** with AcOH/THF/H_2O (4:2:1) under reflux yielded the triol **48**.

These compounds already each possess more than three sites for structural diversity.

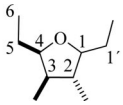
Conclusions

The highly functionalized *exo*-glycal **1a** is a useful synthetic intermediate for the preparation of furanose-based libraries. This compound contains an allylic epoxide moiety that can undergo chemoselective reactions variously at the double bond, at the epoxide or at the allylic oxirane system. Halogenation of the double bond gives rise to the synthetically useful 1′-halo-epoxy-*exo*-glycals **2**. Attempted hydrogenation of **1a** led to furan formation, but hydrogenation

of *exo*-glycals not containing the oxirane ring permits the hydrogenation to occur without aromatization. Additionally, this process takes place in a stereocontrolled manner, probably due to the presence of the bulky β-oriented 5,6-*O*-isopropylidene ring. The oxirane moiety undergoes ring-opening with nitrogen nucleophiles or hydroxide in a completely regioselective manner, thus leading to allylic amino alcohols and allylic diols, respectively. Nucleophilic ring-opening of the oxirane ring in a 1′-halo-epoxy-*exo*-glycal leaves the vinyl halide functionality unreacted, so that it can be engaged in Suzuki cross-coupling reactions with boronic acids, thus allowing the generation of a library of furanose-based allylic amines. These amines each still bear a C3–OH component and a 5,6-isopropylidene acetal unit suitable for further transformations. Acylation can then be performed at O-3, to incorporate a third substituent. Remarkably, these derivatives undergo acid-mediated chemoselective 5,6-*O*-isopropylidene ring-opening without aromatization to the corresponding furan derivatives.[21] Diols such as **46** and triols such as **48** can be readily prepared, ready for further derivatization. Additional transformations on these derivatives are under investigation and will be reported in due course.

Experimental Section

General Remarks: All reactions were performed in dry flasks fitted with glass stoppers or rubber septa under a positive pressure of Ar, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred by syringe or stainless steel cannula. Optical rotations were determined for solutions in chloroform. Flash column chromatography was performed with 230–400 mesh silica gel. Thin-layer chromatography was conducted with Kieselgel 60 F254 (Merck). Spots were observed first under UV irradiation (254 nm) and then by charring with a solution of 20% aqueous H_2SO_4 (200 mL) in AcOH (800 mL). Anhydrous $MgSO_4$ or Na_2SO_4 were used to dry organic solutions during workup, and evaporation of the solvents was performed under vacuum with a rotary evaporator. Solvents were dried and purified by standard methods. Unless otherwise noted ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 MHz and 50 MHz, respectively. Chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ = 7.25 ppm). The numbering pattern used for the ^1H NMR is illustrated below.



General Procedure for the Synthesis of Epoxy-*exo*-glycals (1): A solution of Br_2 (1.1 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise to a cooled (0 °C) solution of the corresponding *C*-1 alkyl glycal **5** (1 mmol) in CH_2Cl_2 (10 mL) containing Et_3N (2 mL). The mixture was stirred at room temperature overnight, after which the reaction mixture was diluted with CH_2Cl_2 and washed with aqueous sodium thiosulfate (10%) and water. The organic layer was then dried and concentrated and the residue was purified by flash chromatography.

(1*S*,2*R*,5*S*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-methylene-3,6-dioxabicyclo[3.1.0]hexane (1a): This compound was prepared from the *C*-methyl glycal **5a** (5.0 g, 25 mmol) by the General Procedure. Purification (hexane/EtOAc 95:5) afforded the oxirane **1a** (4.2 g, 85%): m.p. 41–42 °C, $[\alpha]_D^{25}$ = +56.2 (*c* = 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, Me), 1.40 (s, 3 H, Me), 3.87–4.16 (m, 6 H), 4.32 (d, *J* = 2.0 Hz, 1 H, 1′-H), 4.44 (d, *J* = 2.0 Hz, 1 H, 1′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0, 26.6, 55.2, 57.1, 66.9, 72.9, 79.9, 87.3, 109.3, 157.2 ppm. API-ES positive 199.1 $[M + H]^+$. $C_{10}H_{14}O_4$ (198.09): calcd. C 60.59, H 7.12; found C 60.37, H 7.03.

(1*S*,4*R*,5*S*)-2-Butylidene-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo[3.1.0]hexane (1b): This compound was prepared from the *C*-butyl glycal **5b** (150 mg, 0.6 mmol) by the General Procedure. Purification (hexane/EtOAc 95:5) afforded the oxirane **1b** as a mixture of isomers (96 mg, 65%). For the major isomer: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.3 Hz, 3 H, Me), 1.30 (m, 2 H, CH_2), 1.36 (s, 3 H, Me), 1.44 (s, 3 H, Me), 2.04 (m, 2 H, CH_2), 3.85 (br. s, 1 H, 2-H), 3.95–4.20 (m, 5 H), 4.71 (t, *J* = 7.3 Hz, 1 H, 1′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 22.8, 25.5, 27.0, 27.3, 56.1, 57.5, 67.3, 73.5, 79.8, 104.9, 109.7, 150.2 ppm. API-ES positive 241.1 $[M + H]^+$. $C_{13}H_{20}O_4$ (240.14): calcd. C 64.98, H 8.39; found C 64.81, H 8.19.

(1*S*,4*R*,5*S*)-2-(Butan-2-ylidene)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo[3.1.0]hexane (1c): This compound was prepared from the *C*-butyl glycal **5c** (150 mg, 0.6 mmol) by the General Procedure. Purification (hexane/EtOAc 95:5) afforded the oxirane **1c** as a mixture of isomers (89 mg, 60%). For the major isomer: ^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 7.3 Hz, 3 H, Me), 1.39 (s, 3 H, Me), 1.46 (s, 3 H, Me), 1.66 (s, 3 H, Me), 2.16 (q, *J* = 7.3 Hz, 2 H, CH_2), 4.0–4.26 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 14.0, 25.2, 25.8, 26.8, 52.9, 57.8, 67.2, 73.3, 78.9, 109.5, 114.7, 144.8 ppm. EI-MS 240.1 $[M]^+$. $C_{13}H_{20}O_4$ (240.14): calcd. C 64.98, H 8.39; found C 64.79, H 8.33.

(1*S*,4*R*,5*S*,*Z*)-2-(Bromomethylene)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo[3.1.0]hexane (2a): A solution of the oxirane **1a** (200 mg, 1.01 mmol) and Et_3N (2 mL) in dry CH_2Cl_2 (5 mL) was cooled to 0 °C under argon and a solution of Br_2 (52 μL, 161 mg, 1.1 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred overnight, after which the mixture was washed with aqueous sodium thiosulfate (10%) containing sodium hydrogen carbonate and then with water. The organic layer was dried and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc 95:5) to give the bromide **2a** (174 mg, 63%) followed by recovered starting material (58 mg, 29%). For (*Z*)-**2a**: m.p. 69–70 °C, $[\alpha]_D^{25}$ = +56.2 (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H, Me), 1.47 (s, 3 H, Me), 4.01–4.26 (m, 6 H), 5.43 (d, *J* = 2.0 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.1, 26.9, 55.3, 58.0, 67.1, 72.8, 79.7, 80.7, 109.7, 153.6 ppm. API-ES positive 299.0 $[M + Na]^+$, 301.0 $[M + Na + 2]^+$. $C_{10}H_{13}BrO_4$ (276.00): calcd. C 43.34, H 4.73; found C 43.41, H 4.59.

(1*S*,2*R*,5*S*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-(iodomethylene)-3,6-dioxabicyclo[3.1.0]hexane (2b): A solution of the oxirane **1a** (150 mg, 0.75 mmol) in dry CH_2Cl_2 (5 mL) was cooled to 0 °C under argon, activated molecular sieves (3 Å, 2 g) and IDCT (425 mg, 0.82 mmol) were added, and the reaction mixture was stirred for 15 min. After removal of the molecular sieves, the filtrate was washed with aqueous sodium thiosulfate (10%) containing sodium hydrogen carbonate and then with water. The organic layer was dried and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc 90:10) to give the iodide **2b** (70 mg, 70%). $[\alpha]_D^{25}$ = +57.0 (*c* = 0.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H, Me), 1.46 (s, 3 H, Me), 4.02–4.22 (m,

6 H), 5.28 (br. s, J = 2.0 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.4, 27.1, 48.1, 55.0, 58.6, 67.3, 73.1, 80.7, 110.0, 158.1 ppm. API-ES positive 325 $[M + H]^+$.

(1*S*,4*R*,5*S*,*E*)-2-(Bromomethylene)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo[3.1.0]hexane [(*E*)-2a]: A mixture of Br_2 (307 μL, 6.0 mmol) and nBu$_4$NBr (1.9 g, 6 mmol) in CH_2Cl_2 (10 mL) was added under argon to a solution of the epoxide **1a** (400 mg, 2.0 mmol) in CH_2Cl_2. The resulting solution was stirred for 10 min, after which Et_3N (836 μL, 6 mmol) was added. After the starting material had been consumed (10 min) the reaction mixture was washed with aqueous sodium thiosulfate (10%) containing sodium hydrogen carbonate and then with water. The organic layer was dried and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc 95:5) to give the oxirane **2a** (397 mg, 72%) followed by the oxirane (*E*)-**2a** (55 mg, 10%). For (*E*)-**2a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H, Me), 1.47 (s, 3 H, Me), 3.93 (dd, J = 9.0, 8.1 Hz, 1 H), 4.07–4.12 (m, 3 H), 4.19 (m, 1 H), 4.35 (m, 1 H), 5.67 (s, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.0, 26.7, 54.2, 56.8, 66.8, 72.9, 80.8, 83.1, 109.5, 154.2 ppm. API-ES positive 299.0 $[M + Na]^+$, 301.0 $[M + Na + 2]^+$. $C_{10}H_{13}BrO_4$ (275.9996): calcd. C 43.34, H 4.73; found C 43.27, H 4.62.

(1*S*,4*R*,5*S*)-2-(Dibromomethylene)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo[3.1.0]hexane (9): A mixture of Br_2 (160 μL, 3.0 mmol) and nBu$_4$NBr (950 mg, 3 mmol) in CH_2Cl_2 (5 mL) was added under argon to a solution of the epoxides **2a** and (*E*)-**2a** (277 mg, 1.0 mmol) in CH_2Cl_2. The resulting solution was stirred for 10 min, after which Et_3N (420 μL, 3 mmol) was added. After the starting material had been consumed (10 min) the reaction mixture was washed with aqueous sodium thiosulfate (10%) containing sodium hydrogen carbonate and then with water. The organic layer was dried and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc 95:5) to give the dibromide **9** (397 mg, 70%): $[a]_D^{25}$ = +60.4. (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H, Me), 1.46 (s, 3 H, Me), 3.99–4.04 (m, 1 H), 4.10–4.19 (m, 2 H), 4.22 (m, 2 H), 4.35 (d, J = 2.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.1, 26.9, 55.4, 58.0, 66.9, 68.3, 72.9, 81.4, 109.8, 152.3 ppm. API-ES positive 354.9 $[M - 2]^+$, 356.9 $[M]^+$, 358.9 $[M + 2]^+$.

General Procedure A. Pd/C-Catalysed Hydrogenation in a Parr Apparatus: Argon was passed through a solution of the compound (ca. 50–75 μmol) in EtOH (10 mL) for 5 min, after which a catalytic amount of Pd/C (20 mg, 10 wt.-% Pd on C) was added. The reaction vessel was placed under vacuum and subsequently ventilated with hydrogen gas. This cycle was repeated one more time, after which the vessel was placed under 25 psi of hydrogen gas and mechanically shaken for 1 h. The Pd/C was removed by filtration through a Celite path, followed by thorough rinsing of the filter cake with MeOH. The filtrate was concentrated under vacuum and the residue was purified by silica gel flash chromatography.

(*R*)-2,2-Dimethyl-4-(5-methylfuran-2-yl)-1,3-dioxolane (10): Compound **1a** (150 mg, 0.75 mmol) was subjected to General Procedure A to give compound **10** (139 mg, 98%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 95:5). $[a]_D^{25}$ = +68.0 (c = 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.46 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.30 (s, 3 H, Me), 4.10 (dd, J = 7.8, 8.0 Hz, 1 H, 6-H), 4.21 (dd, J = 6.3, 8.0 Hz, 1 H, 6-H), 5.04 (dd, J = 6.4, 7.8 Hz, 1 H, 5-H), 5.94 (d, J = 3.1 Hz, 1 H, 3-H), 6.25 (d, J = 3.0 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.9, 26.3, 28.2, 67.6, 71.3, 106.2, 109.1, 109.6, 149.3, 152.8 ppm. API-ES positive 183 $[M + H]^+$. $C_{10}H_{14}O_3$ (182.09): calcd. C 65.91, H 7.74; found C 65.70, H 7.83.

(2*S*,3*R*,4*R*,5*S*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-methyl-4-(phenethylamino)tetrahydrofuran-3-ol (12): Compound **11** (150 mg, 0.49 mmol) was subjected to General Procedure A to give compound **12** (149 mg, 95%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 2:8). $[a]_D^{25}$ = +25.0 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (d, J = 6.2 Hz, 3 H, Me), 1.33 (s, 3 H, Me), 1.40 (s, 3 H, Me), 2.85 (m, 3 H, CH_2 and 2-H), 2.96 (m, 2 H, CH_2), 3.64 (q, J = 6.2 Hz, 1 H, 1-H), 3.76 (dd, J = 4.6, 8.2 Hz, 1 H, 4-H), 3.91 (dd, J = 5.3, 8.4 Hz, 1 H, 6-H), 4.13 (dd, J = 6.2, 8.6 Hz, 1 H, 6-H), 4.18 (dd, J = 2.4, J = 4.6 Hz, 1 H, 3-H), 4.30 (ddd, J = 5.5, 6.1, 8.2 Hz, 1 H, 5-H), 7.18–7.47 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.1, 25.4, 26.9, 36.0, 49.5, 67.9, 73.0, 74.2, 78.4, 80.3, 81.9, 109.5, 126.5, 128.7 (×2), 128.8 (×2), 139.4 ppm. API-ES positive 322.3 $[M + H]^+$. $C_{18}H_{27}NO_4$ (321.19): calcd. C 67.26, H 8.47, N 4.36; found C 67.01, H 8.56, N 4.44.

(2*S*,3*R*,4*R*,5*S*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-[4-(2-methoxyphenyl)piperazin-1-yl]-5-methyltetrahydrofuran-3-ol (14): Compound **13** (150 mg, 0.38 mmol) was subjected to General Procedure A to give compound **14** (144 mg, 97%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 1:9). $[a]_D^{25}$ = +13.8 (c = 0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.40 (d, J = 6.1 Hz, 3 H, Me), 1.43 (s, 3 H, Me), 2.60 (dd, J = 2.2, 6.9 Hz, 1 H, 2-H), 2.73 (m, 2 H, CH_2–N), 2.86 (m, 2 H, CH_2–N), 3.10 (br. s, 4 H, 2× CH_2–N), 3.70 (dd, J = 4.5, 8.4 Hz, 1 H, 4-H), 3.86 (s, 3 H, OMe), 3.93 (q, J = 6.6 Hz, 1 H, 1-H), 3.96 (dd, J = 5.0, 8.4 Hz, 1 H, 6-H), 4.16 (dd, J = 6.2, 8.5 Hz, 1 H, 6-H), 4.32 (ddd, J = 5.1, 6.1, 8.4 Hz, 1 H, 5-H), 4.47 (dd, J = 2.2, 4.6 Hz, 1 H, 3-H), 6.94 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.1, 25.5, 27.1, 50.8 (×2), 51.8 (×2), 55.6, 68.1, 74.3, 75.6, 77.1, 80.9, 82.7, 109.6, 111.3, 118.4, 121.2, 123.3, 141.2, 152.4. API-ES positive 393.2 $[M + H]^+$. $C_{21}H_{32}N_2O_5$ (392.23): calcd. C 64.26, H 8.22, N 7.14; found C 64.35, H 8.13, N 7.23.

[(1*R*,2*S*,4*R*,5*R*)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo(3.1.0)hexan-2-yl]methanol (15): BH_3·SMe_2 (142 μL, 1.5 mmol, 3 equiv.) was slowly added to a cooled (0 °C) solution of the *exo*-glycal **1a** (100 mg, 0.5 mmol) in dry THF (5 mL). The resulting solution was allowed to warm to room temperature and was then stirred for two hours, after which it was recooled to 0 °C and treated with aqueous NaOH solution (10%, 5 mL) and hydrogen peroxide (30%, 5 mL). The reaction mixture was stirred overnight, diluted with diethyl ether and washed with NaCl. The aqueous phase was back-extracted with diethyl ether. The combined organic phases were concentrated and the residue was purified by flash chromatography (hexane/EtOAc 1:1) to give the alcohol **15** (87.5 mg, 81%) as a colourless oil. $[a]_D^{25}$ = +18.0 (c = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (s, 3 H, Me), 1.39 (s, 3 H, Me), 3.76 (m, 5 H), 3.86 (dd, J = 4.8, 8.3 Hz, 1 H, 6-H), 3.94 (t, J = 5.5 Hz, 1 H), 4.09 (m, 2 H, CH_2OH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.2, 26.8, 56.4, 56.8, 61.8, 67.2, 73.8, 78.1, 78.5, 109.3 ppm. API-ES positive 217 $[M + H]^+$, 234 $[M + NH_4]^+$, 239 $[M + Na]^+$. $C_{10}H_{16}O_5$ (216.10): calcd. C 55.55, H 7.46; found C 55.67, H 6.98.

(1*S*,4*R*,5*S*)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-(iodomethyl)-3,6-dioxabicyclo[3.1.0]hexan-2-ol (16): IDCT (427 mg, 0.82 mmol) was added to a well stirred CH_2Cl_2/H_2O (5 mL, 9:1, v/v) solution of the *exo*-glycal **1a** (150 mg, 0.75 mmol). After the mixture had been stirred for 15 min, TLC analysis showed complete disappearance of the starting material. The reaction mixture was quenched by addition of aq. $Na_2S_2O_3$ and subsequently extracted with CH_2Cl_2. The combined organic phases were dried and concentrated. The residue was purified by silica gel column chromatography (hexane/

EtOAc 9:1) to provide the ketose **16** (95 mg, 37%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 3 H, Me), 1.43 (s, 3 H, Me), 2.48 (s, 1 H, OH), 3.42 (m, 1 H, CH_2–I), 3.79 (d, J = 2.8 Hz, 1 H), 4.01 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 9.9, 25.5, 27.0, 56.8, 57.5, 67.2 73.9, 77.9, 100.6, 109.8 ppm. EI-MS 342.1 $[M]^+$.

1-[(1*R*,6*S*,8*R*,9*S*)-9-Acetoxy-6-methyl-2,5,7-trioxabicyclo(4.2.1)-nonan-8-yl]ethane-1,2-diyl Diacetate (17): Ethylene glycol (18 mg, 0.3 mmol.) and $BF_3{\cdot}OEt_2$ (18.5 μL, 0.15 mmol.) were successively added to a cooled (0 °C) solution of the *exo*-glycal **1a** (30 mg, 0.15 mmol) in anhydrous CH_2Cl_2 (3 mL). After the mixture had been stirred at 0 °C for 2 h, TLC analysis showed complete disappearance of the starting material. To facilitate the separation of the product, the reaction mixture was concentrated by coevaporation with toluene and subsequently dissolved in pyridine (5 mL) and treated with an excess of Ac_2O (300 μL). After the mixture had been stirred at room temperature for 10 h, the crude product was concentrated and the residue was purified by flash chromatography (hexane/EtOAc 6:4) to give the bicyclic derivative **17** (52 mg, 61%). $[\alpha]_D^{25}$ = –25.0 (c = 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.41 (s, 3 H, Me), 2.04 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.16 (s, 3 H, OAc), 3.57 (ddd, J = 3.3, 6.4, 9.8 Hz, 1 H), 3.66 (dd, J = 4.6, 9.0 Hz, 1 H, 3-H), 3.73 (ddd, J = 3.4, 5.9, 9.7 Hz, 1 H), 3. 79 (m, 1 H, 6-H), 3.89 (dd, J = 5.6, 8.2 Hz, 1 H, 6-H), 4.10 (m, 2 H), 4.59 (m, 1 H, 5-H), 5.07 (d, J = 9.0 Hz, 1 H, 2-H), 5.29 (dd, J = 2.4, J = 4.6 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1, 19.7, 20.8, 20.9, 63.4, 66.4, 68.5, 68.8, 75.2, 75.3, 75.8, 107.1, 169.9, 170.6, 170.8 ppm. EI-MS 346.6 $[M]^+$; ES-HRMS 347.1341 [M + H]$^+$, calcd. for $[C_{15}H_{22}O_9 + H]^+$ 347.1342.

(1*S*,4*R*,5*S*)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3,6-dioxabicyclo-[3.1.0]hexan-2-one (18): A flask containing a solution of the *exo*-glycal **1a** (150 mg, 0.75 mmol) in dry CH_2Cl_2 (10 mL) was placed in a dry ice/acetone bath at –78 °C. Ozone was then generated by passing an oxygen stream through an electrical discharge-type ozone generator and the O_2/O_3 mixture was bubbled through the cooled and stirred solution for 15 min. After this time, the contents of the flask were bubbled through with O_2 for about 20 min to remove free O_3 and then SMe_2 (1 mL) was added. The reaction mixture was allowed to warm to room temperature and then concentrated under reduced pressure in a rotary evaporator. The residue was purified by flash chromatography (hexane/EtOAc 8:2) to give the epoxy-lactone **18** (118 mg, 79%) as a white solid: m.p. 74–76 °C. $[\alpha]_D^{25}$ = –40.7 (c = 0.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (s, 3 H, Me), 1.46 (s, 3 H, Me), 3.83 (d, J = 2.5 Hz, 1 H, 2-H), 3.97 (dd, J = 3.6, 9.1 Hz, 1 H, 6-H), 4.11 (dd, J = 5.6, 9.1 Hz, 1 H, 6-H), 4.24–4.30 (m, 3 H, 3-H, 4-H and 5-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.1, 27.0, 50.6, 55.7, 67.0, 72.7, 78.2, 110.2, 169.7 ppm. EI-MS 200.0 $[M]^+$. ES-HRMS 201.0765 [M + H]$^+$, calcd. for $[C_9H_{12}O_5 + H]^+$ 201.0765.

General Procedure B. Nucleophilic Ring-Opening of Epoxy *exo*-Glycals with Amines: A solution of the appropriate epoxide in EtOH (10 mL mmol^{-1}) was treated with the appropriate amine (3 equiv.). The resulting mixture was heated to reflux until TLC showed that all the starting material had been consumed (usually 3–5 h). The reaction mixture was then allowed to cool to room temperature and concentrated in vacuo, and the residue was purified by flash chromatography.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-methylene-4-(phenethylamino)tetrahydrofuran-3-ol (11): Compound **1a** (150 mg, 0.75 mmol) and 2-phenylethylamine (284 μL, 2.25 mmol) were subjected to General Procedure B to give compound **11** (203 mg, 85%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 4:6). $[\alpha]_D^{25}$ = +9.2 (c = 0.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.43 (s, 3 H, Me), 2.80–2.88 (m, 2 H), 2.88–2.9 (m, 1 H), 2.9–3.09 (m, 1 H), 3.54 (s, 1 H, 2-H), 3.99 (m, 1 H, 6-H), 4.0 (s, 1 H, 1′-H), 4.2–4.15 (m, 2 H, 6-H, 3-H), 4.24 (dd, J = 3.4, 8.4 Hz, 1 H, 4-H), 4.33 (m, 1 H, 5-H), 4.37 (s, 1 H, 1′-H), 7.2–7.31 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.5, 27.0, 36.3, 49.2, 67.3, 67.7, 73.3, 75.2, 83.9, 84.3, 109.8, 126.5, 128.7 (× 2), 128.9 (× 2), 139.7, 163.2 ppm. EI-MS 319.1 $[M]^+$. $C_{18}H_{25}NO_4$ (319.18): calcd. C 67.69, H 7.89, N 4.39; found C 67.47, H 7.88, N 4.25.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-[4-(2-methoxyphenyl)piperazin-1-yl]-5-methylenetetrahydrofuran-3-ol (13): Compound **1a** (250 mg, 1.26 mmol) and 1-(2-methoxyphenyl)piperazine (726 mg, 3.78 mmol) were subjected to General Procedure B to give compound **13** (354 mg, 88%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 4:6). $[\alpha]_D^{25}$ = +23.0 (c = 0.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H, Me), 1.45 (s, 3 H, Me), 2.82 (m, 4 H), 3.07 (m, 4 H), 3.44 (s, 1 H, 2-H), 3.86 (s, 3 H, OMe), 4.02 (dd, J = 4.9, 8.7 Hz, 1 H, 6-H), 4.15 (s, 1 H, 1′-H), 4.17–4.23 (m, 2 H, 4-H and 6-H), 4.31–4.35 (m, 1 H, 5-H), 4.51 (d, J = 3.4 Hz, 1 H, 3-H), 4.54 (s, 1 H, 1′-H), 6.84–7.2 (4 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.1, 26.8, 50.6 (× 2), 50.7 (× 2), 55.2, 67.4, 71.9, 73.2, 74.0, 83.7, 86.7, 109.4, 110.9, 118.0, 120.8, 122.9, 140.9, 152.0, 159.4 ppm. EI-MS 391.1 $[M]^+$. $C_{21}H_{30}N_2O_5$ (390.2155): calcd. C 64.59, H 7.74, N 7.17; found C 67.66, H 7.81, N 6.95.

(2*S*,3*R*,4*R*)-4-(Benzylamino)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-5-methylenetetrahydrofuran-3-ol (19): Compound **1a** (150 mg, 0.75 mmol) and benzylamine (245 μL, 2.25 mmol) were subjected to General Procedure B to give compound **19** (211 mg, 92%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 4:6). $[\alpha]_D^{25}$ = +3.7 (c = 1.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.43 (s, 3 H, Me), 3.59 (s, 1 H, 2-H), 3.85 (d, J = 13.2 Hz, 1 H, CH_2), 3.94 (d, J = 13.2 Hz, 1 H, CH_2), 4.02 (dd, J = 4.0, 8.8 Hz, 1 H, 6-H), 4.05 (d, J = 1.9 Hz, 1 H, 1′-H), 4.18 (m, 2 H, 3-H and 6-H), 4.31 (m, 2 H, 4-H and 5-H), 4.41 (d, J = 1.9 Hz, 1 H, 1′-H), 7.36 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.6, 27.2, 52.1, 67.1, 67.7, 73.5, 75.1, 84.2, 84.6, 109.9, 127.6, 128.1, 128.5, 128.9, 129.1, 140.0, 163.4 ppm. API-ES positive 306.3 $[M + H]^+$. $C_{17}H_{23}NO_4$ (305.16): calcd. C 66.86, H 7.59, N 4.59; found C 66.93, H 7.45, N 4.63.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-methylene-4-[(*R*)-1-phenylethylamino]tetrahydrofuran-3-ol (20): Compound **1a** (250 mg, 1.26 mmol) and (*R*)-1-phenylethylamine (482 μL, 3.78 mmol) were subjected to General Procedure B to give compound **20** (322 mg, 81%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 4:6). $[\alpha]_D^{25}$ = +15.1 (c = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (d, J = 6.6 Hz, 3 H, Me), 1.37 (s, 3 H, Me), 1.45 (s, 3 H, Me), 3.39 (s, 1 H, 2-H), 3.93 (q, J = 6.6 Hz, 1 H, CH), 3.94 (d, J = 1.8 Hz, 1 H, 1′-H), 3.99 (dd, J = 4.4, 8.4 Hz, 1 H, 6-H), 4.17 (dd, J = 5.5, 8.5 Hz, 1 H, 6-H), 4.27 (m, 1 H, 3-H), 4.32 (m, 2 H, 4-H and 5-H), 4.33 (d, J = 1.8 Hz, 1 H, 1′-H), 7.30 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 24.3, 25.1, 26.7, 56.1, 64.4, 67.6, 73.2, 75.3, 83.2, 83.5, 109.3, 126.4, 127.2 (× 2), 128.7 (× 2), 144.9, 164.1 ppm. EI-MS 319.1 $[M]^+$. $C_{18}H_{25}NO_4$ (319.18): calcd. C 67.69, H 7.89, N 4.39; found C 67.50, H 7.87, N 4.29.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-methylene-4-morpholinotetrahydrofuran-3-ol (21): Compound **1a** (250 mg, 1.26 mmol) and morpholine (328 μL, 3.78 mmol) were subjected to General Procedure B to give compound **21** (309 mg, 86%) as white solid after silica gel column chromatography (hexane/EtOAc 3:7). m.p. 97–99 °C. $[\alpha]_D^{25}$ = –17.1 (c = 1.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$,

300 MHz): δ = 1.36 (s, 3 H, Me), 1.45 (s, 3 H, Me), 2.61 (t, J = 4.6 Hz, 4 H, 2× CH_2–N), 3.31 (d, J = 0.6 Hz, 1 H, 2-H), 3.69 (t, J = 4.6 Hz, 4 H, 2× CH_2–O), 3.99 (dd, J = 4.8, 8.8 Hz, 1 H, 6-H), 4.11 (dd, J = 0.8, 1.7 Hz, 1 H, 1′-H), 4.15–4.22 (m, 2 H, 4-H and 6-H), 4.28–4.35 (m, 1 H, 5-H), 4.42 (m, 1 H, 3-H), 4.53 (dd, J = 0.8, 1.7 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.1, 26.8, 51.1 (×2), 67.0, 67.4 (×2), 72.0, 73.1, 74.1, 83.6, 87.1, 109.5, 158.8 ppm. API-ES positive 286.2 $[M + H]^+$. $C_{14}H_{23}NO_5$ (285.16): calcd. C 58.93, H 8.12, N 4.91; found C 58.87, H 8.25, N 4.93.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-methylene-4-(piperidin-1-yl)tetrahydrofuran-3-ol (22): Compound **1a** (250 mg, 1.26 mmol) and piperidine (373 μL, 3.78 mmol) were subjected to General Procedure B to give compound **22** (318 mg, 89%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 3:7). $[a]_D^{25}$ = +10.9 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (s, 3 H, Me), 1.38 (m, 2 H, CH_2) 1.40 (s, 3 H, Me), 1.52 (m, 4 H, 2× CH_2), 2.50 (m, 4 H, 2× CH_2–N), 3.32 (s, 1 H, 2-H), 3.94 (dd, J = 5.1, 8.5 Hz, 1 H, 6-H), 4.03 (d, J = 0.7 Hz, 1 H, 1′-H), 4.11 (dd, J = 6.3, 8.5 Hz, 1 H, 6-H), 4.13 (dd, J = 4.1, 8.3 Hz, 1 H, 4-H), 4.30 (m, 1 H, 5-H), 4.38 (br. d, J = 3.1 Hz, 1 H, 3-H), 4.45 (d, J = 0.7 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.3, 24.5, 25.4, 26.3 (×2), 51.8 (×2), 67.5, 72.5, 73.6, 75.1, 84.0, 86.4, 109.6, 159.8 ppm. API-ES positive 284.2 $[M + H]^+$. $C_{15}H_{25}NO_4$ (283.18): calcd. C 63.58, H 8.89, N 4.94; found C 63.23, H 8.75, N 4.87.

(2*S*,3*R*,4*R*)-4-(4-Benzylpiperazin-1-yl)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-5-methylenetetrahydrofuran-3-ol (23): Compound **1a** (200 mg, 1.01 mmol) and 1-benzylpiperazine (527 μL, 3.03 mmol) were subjected to General Procedure B to give compound **23** (287 mg, 76%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 3:7). $[a]_D^{25}$ = +8.2 (c = 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.44 (s, 3 H, Me), 2.50 (br. s, 4 H, 2× CH_2–N), 2.63 (br. s, 4 H, 2× CH_2–N), 3.36 (s, 1 H, 2-H), 3.53 (s, 2 H, CH_2–N), 3.98 (dd, J = 5.0, 8.6 Hz, 1 H, 6-H), 4.09 (d, J = 0.8 Hz, 1 H, 1′-H), 4.16 (m, 2 H, 4-H and 6-H), 4.31 (m, 1 H, 5-H), 4.43 (br. d, J = 3.6 Hz, 1 H, 3-H), 4.50 (d, J = 0.8 Hz, 1 H, 1′-H), 7.31 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.4, 27.1, 50.6 (×2), 53.4 (×2), 63.2, 67.8, 72.4, 73.6, 74.2, 83.9, 86.9, 109.8, 127.3, 128.4 (×2), 129.5 (×2), 138.1, 159.8 ppm. API-ES positive 375.2 $[M + H]^+$. $C_{21}H_{30}N_2O_4$ (374.22): calcd. C 67.35, H 8.07, N 7.48; found C 58.87, H 8.25, N 4.93.

(2*S*,3*R*,4*R*)-4-(4-Benzylpiperidin-1-yl)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-5-methylenetetrahydrofuran-3-ol (24): Compound **1a** (250 mg, 1.26 mmol) and 4-benzylpiperidine (664 μL, 3.78 mmol) were subjected to General Procedure B to give compound **24** (339 mg, 72%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 3:7). $[a]_D^{25}$ = +15.3 (c = 0.4, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.26 (td, J = 3.9, 12.6 Hz, 2 H, CH_2), 1.36 (s, 3 H, Me), 1.44 (s, 3 H, Me), 1.53 (m, 1 H, CH), 1.64 (td, J = 3.6, 10.2 Hz, 2 H, CH_2), 2.15 (m, 2 H, CH_2), 2.52 (d, J = 5.7 Hz, 2 H, CH_2), 2.94 (m, 2 H, CH_2), 3.38 (s, 1 H, 2-H), 3.98 (dd, J = 5.1, 8.7 Hz, 1 H, 6-H), 4.08 (d, J = 1.2 Hz, 1 H, 1′-H), 4.16 (dd, J = 5.7, 8.7 Hz, 1 H, 6-H), 4.15 (m, 1 H, 4-H), 4.30 (m, 1 H, 5-H), 4.42 (d, J = 4.2 Hz, 1 H, 3-H), 4.48 (s, 1 H, 1′-H), 7.26 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.1, 26.8, 32.3 (×2), 37.8, 43.0, 50.8, 50.9, 67.4, 72.3, 73.4, 74.4, 83.7, 86.2, 109.4, 125.7, 128.1 (×2), 129.0 (×2), 140.5, 159.6 ppm. API-ES positive 374.2 $[M + H]^+$. $C_{22}H_{31}NO_4$ (373.23): calcd. C 70.75, H 8.37, N 3.75; found C 70.81, H 8.21, N 3.86.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-[(*S*)-1-hydroxypropan-2-ylamino]-5-methylenetetrahydrofuran-3-ol (25): Compound **1a** (200 mg, 0.73 mmol) and L-alaninol (207 μL, 2.89 mmol, 3 equiv.) were subjected to General Procedure B to give compound **25** (167.6 mg, 84%) as a colourless oil after silica gel column chromatography (hexane/EtOAc 1:9). $[a]_D^{25}$ = +34.0 (c = 0.44, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.06 (d, J = 6.6 Hz, 3 H, CH_3–CH–), 1.35 (s, 3 H, Me), 1.43 (s, 3 H, Me), 3.01–3.07 (m, 1 H, CH_3-*CH*-CH_2-), 3.31 (dd, J = 7.6, 10.7 Hz, 1 H, *CH*$_2$–OH), 3.6 (dd, J = 3.9, 10.7 Hz, 1 H, *CH*$_2$–OH), 3.65 (s, 1 H, 2-H), 4.0 (dd, J = 4.7, 8.6 Hz, 1 H, 6-H), 4.05 (d, J = 1.8 Hz, 1 H, 1′-H), 4.15 (m, 2 H, 3-H and 6′-H), 4.25 (dd, J = 3.5, 8.3 Hz, 1 H, 4-H), 4.3–4.38 (m, 1 H, 5-H), 4.39 (d, J = 1.8 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 17.4, 25.4, 27.0, 52.2, 64.3, 66.3, 67.7, 73.4, 76.6, 83.4, 84.8, 109.9, 162.7 ppm. API-ES positive 274.1 $[M + H]^+$. $C_{13}H_{23}NO_5$ (273.1576): calcd. C 57.13, H 8.48, N 5.12; found C 56.98, H 8.40, N 4.97.

(2*S*,3*R*,4*R*)-5-Butylidene-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-(phenethylamino)tetrahydrofuran-3-ol (26): Compound **1b** (200 mg, 0.83 mmol) and 2-phenylethylamine (314 μL, 2.49 mmol) were subjected to General Procedure B to give compound **26** (249 mg, 83%) as a 3:1 mixture of isomers after silica gel column chromatography (hexane/EtOAc 3:7). For the major isomer $[a]_D^{25}$ = +12.3 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.89 (t, J = 7.1 Hz, 3 H, Me), 1.2–1.45 (m, 2 H, CH_2–CH_2–), 1.38 (s, 3 H, Me), 1.45 (s, 3 H, Me), 2.0 (m, 2 H, CH_2), 2.77–3.11 (m, 4 H, CH_2–CH_2–N), 3.47 (s, 1 H, 2-H), 4.0 (dd, J = 4.9, 8.4 Hz, 1 H, 6-H), 4.13–4.38 (m, 4 H), 7.2–7.3 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.7, 22.9, 25.3, 26.8, 27.0, 36.2, 48.9, 67.0, 67.7, 73.5, 75.3, 83.1, 101.0, 110.0, 126.2, 128.5 (×2), 128.7 (×2), 139.7, 155.3 ppm. API-ES positive 362.2 $[M + H]^+$. $C_{21}H_{31}NO_4$ (361.23): calcd. C 69.78, H 8.64, N 3.87; found C 69.81, H 8.53, N 3.76.

(2*S*,3*R*,4*R*)-5-(Butan-2-ylidene)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-(phenethylamino)tetrahydrofuran-3-ol (27): Compound **1c** (200 mg, 0.83 mmol) and 2-phenylethylamine (314 μL, 2.49 mmol) were subjected to General Procedure B to give compound **27** (246 mg, 82%) as a mixture of isomers after silica gel column chromatography (hexane/EtOAc 3:7). Selected peaks for the major isomer: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.8 (t, J = 7.3 Hz, 3 H Me), 1.37 (s, 3 H, Me), 1.44 (s, 3 H, Me), 1.57 (s, 3 H, Me), 1.90 (m, 2 H, CH_2–Me), 2.7–3.0 (m, 4 H, CH_2–CH_2–N), 3.6 (s, 1 H, 2-H), 4.0 (dd, J = 5.3, 7.8 Hz, 1 H, 6-H), 4.10–4.22 (m, 3 H), 4.3 (m, 1 H, 5-H), 7.19–7.3 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.5, 13.7, 25.4, 26.0, 26.9, 36.3, 49.7, 65.1, 67.8, 73.6, 75.0, 82.6, 109.3, 109.5, 126.4, 128.6 (×2), 128.7 (×2), 139.6, 150.5 ppm. API-ES positive 362.2 $[M + H]^+$. $C_{21}H_{31}NO_4$ (361.23): calcd. C 69.78, H 8.64, N 3.87; found C 69.70, H 8.59, N 3.68.

(2*S*,3*R*,4*R*,*Z*)-5-(Bromomethylene)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-(phenethylamino)tetrahydrofuran-3-ol (28a): Compound **2a** (250 mg, 0.90 mmol) and 2-phenylethylamine (340 mg, 2.7 mmol) were subjected to General Procedure B to give compound **28a** (294 mg, 82%) after silica gel column chromatography (hexane/EtOAc 4:6). $[a]_D^{25}$ = +62.3 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 3 H, Me), 1.43 (s, 3 H, Me), 2.89 (m, 4 H, 2× CH_2), 3.54 (s, 1 H, 2-H), 4.03 (dd, J = 4.5, 8.8 Hz, 1 H, 6-H), 4.20 (m, 2 H), 4.36 (m, 2 H), 5.06 (s, 1 H, 1′-H), 7.25 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.2, 26.8, 36.1, 48.6, 67.2, 67.5, 73.0, 75.7, 76.3, 84.5, 109.7, 126.4, 128.6 (×2), 128.7 (×2), 139.3, 158.5 API-ES positive 398.2 $[M]^+$. 400.2 $[M + 2]^+$. $C_{18}H_{24}BrNO_4$ (397.09): calcd. C 54.28, H 6.07, N 3.52; found C 53.98, H 6.12, N 3.48.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(iodomethylene)-4-(phenethylamino)tetrahydrofuran-3-ol (28b): Compound **2b** (250 mg, 0.77 mmol) and 2-phenylethylamine (291 mg, 2.31 mmol) were subjected to General Procedure B to give compound **28b**

(257 mg, 75%) after silica gel column chromatography (hexane/EtOAc 4:6). $[a]_D^{25}$ = +26.2 (c = 0.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H, Me), 1.44 (s, 3 H, Me), 2.94 (m, 4 H, 2× CH_2), 3.65 (s, 1 H, 2-H), 4.05 (dd, J = 4.0, 8.3 Hz, 1 H, 6-H), 4.21 (dd, J = 5.2, 8.2 Hz, 1 H, 6-H), 4.30 (m, 1 H, 3-H), 4.40 (m, 2 H, 4-H and 5-H), 4.85 (s, 1 H, 1′-H), 7.28 (m, 5 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.3, 26.9, 36.1, 49.1, 67.9 (×2), 73.1, 76.1, 76.4, 84.3, 109.8, 124.5, 127.2 (×4), 139.7, 162.3 ppm. API-ES positive 446.0 $[M + H]^+$. $C_{18}H_{24}INO_4$ (445.08): calcd. C 48.55, H 5.43, N 3.15; found C 48.38, H 5.32, N 3.28.

(2*S*,3*R*,4*R*,*Z*)-5-(Bromomethylene)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-morpholinotetrahydrofuran-3-ol (29a): Compound **2a** (250 mg, 0.90 mmol) and morpholine (234 μL, 2.7 mmol) were subjected to General Procedure B to give compound **29a** (268 mg, 82%) after silica gel column chromatography (hexane/EtOAc 4:6). $[a]_D^{25}$ = +13.1 (c = 1.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.44 (s, 3 H, Me), 2.57 (t, J = 4.6 Hz, 4 H, 2× CH_2–N), 3.40 (s, 1 H, 2-H), 3.67 (t, J = 4.6 Hz, 4 H, 2× CH_2–O), 4.07 (dd, J = 4.1, 8.7 Hz, 1 H, 6-H), 4.20 (dd, J = 5.6, 8.7 Hz, 1 H, 6-H), 4.32 (m, 2 H, 3-H, 4-H), 4.51 (m, 1 H, 5-H), 5.14 (s, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.6, 27.3, 51.4, 51.6, 67.4 (×2), 67.8, 72.9, 73.6, 74.9, 78.8, 85.1, 110.1, 155.5 ppm. API-ES positive 364.1 $[M + H]^+$, 366.1 $[M + 3]^+$. $C_{14}H_{22}BrNO_5$ (363.07): calcd. C 46.17, H 6.09, N 3.85; found C 46.38, H 6.10, N 3.78.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(iodomethylene)-4-morpholinotetrahydrofuran-3-ol (29b): Compound **2b** (250 mg, 0.77 mmol) and morpholine (202 mg, 2.31 mmol) were subjected to General Procedure B to give compound **29b** (228 mg, 72%) after silica gel column chromatography (hexane/EtOAc 4:6). $[a]_D^{25}$ = +37.1 (c = 1.9, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.45 (s, 3 H, Me), 2.56 (m, 4 H, 2× CH_2–N), 3.45 (s, 1 H, 2-H), 3.67 (m, 4 H, 2× CH_2–O), 4.08 (dd, J = 4.4, 8.8 Hz, 1 H, 6-H), 4.20 (dd, J = 5.8, 8.8 Hz, 1 H, 6-H), 4.33 (m, 2 H, 4-H and 5-H), 4.55 (s, 1 H, 3-H), 4.93 (s, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.3, 27.0, 46.3, 51.0 (×2), 67.1 (×2), 67.6, 73.0, 73.3, 74.7, 84.4, 109.9, 159.3 ppm. API-ES positive 412.2 $[M + H]^+$. $C_{14}H_{22}INO_5$ (411.05): calcd. C 40.89, H 5.39, N 3.41; found C 40.78, H 5.28, N 3.38.

(2*S*,3*R*,4*R*,*Z*)-5-(Bromomethylene)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-[4-(2-methoxyphenyl)piperazin-1-yl]tetrahydrofuran-3-ol (30a): Compound **2a** (250 mg, 0.90 mmol) and 1-(2-methoxyphenyl)piperazine (474 μL, 2.7 mmol) were subjected to General Procedure B to give compound **30a** (338 mg, 80%) after silica gel column chromatography (hexane/EtOAc 4:6). $[a]_D^{25}$ = +17.1 (c = 0.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H, Me), 1.46 (s, 3 H, Me), 2.78 (m, 4 H, 2× CH_2–N), 3.06 (m, 4 H, 2× CH_2–N), 3.60 (s, 1 H, 2-H), 3.86 (s, 3 H, OMe), 4.10 (m, 2 H, 2×6-H), 4.35 (m, 2 H, 4-H and 5-H), 4.61 (s, 1 H, 3-H), 5.20 (s, 1 H, 1′-H), 6.91 (4 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.4, 27.0, 50.6 (×2), 55.4 (×3), 67.5, 72.6, 73.4, 74.6, 78.3, 84.9, 109.8, 111.3, 118.3, 121.1, 123.2, 141.1, 152.3, 155.8 ppm. API-ES positive 468.1 $[M]^+$, 470.1 $[M + 2]^+$. $C_{21}H_{29}BrN_2O_5$ (468.13): calcd. C 53.74, H 6.28, N 5.97; found C 53.88, H 6.16, N 5.81.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(iodomethylene)-4-[4-(2-methoxyphenyl)piperazin-1-yl]tetrahydrofuran-3-ol (30b): Compound **2b** (250 mg, 0.77 mmol) and 1-(2-methoxyphenyl)piperazine (405 mg, 2.31 mmol) were subjected to General Procedure B to give compound **30b** (250 mg, 63%) after silica gel column chromatography (hexane/EtOAc 4:6). $[a]_D^{25}$ = +13.4 (c = 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.78 (m, 4 H, 2× CH_2–N), 3.06 (m, 4 H, 2× CH_2–N), 3.60 (s, 1 H, 2-H), 3.86 (s, 3 H, OMe), 4.10 (dd, J = 4.4, 8.8 Hz, 1 H, 6-H), 4.23 (dd, J = 5.8, 8.8 Hz, 1 H, 6-H), 4.35 (m, 2 H, 4-H and 5-H), 4.66 (s, 1 H, 3-H), 4.98 (s, 1 H, 1′-H), 7.10 (m, 4 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.5, 27.2, 46.2, 50.7 (×2), 51.0 (×2), 55.5, 67.7, 73.2, 73.6, 74.8, 84.7, 110.0, 111.3, 118.4, 121.2, 123.3, 141.2, 152.4, 160.0 ppm. API-ES positive 517.3 $[M]^+$. $C_{21}H_{29}IN_2O_5$ (516.1121): calcd. C 48.85, H 5.66, N 5.43; found C 48.70, H 5.57, N 5.29.

General Procedure C. Nucleophilic Ring-opening of Epoxy *exo*-Glycals with Ion Hydroxide

Method C1: A solution of the appropriate epoxide in THF/H_2O (3:1, 3 mL mmol^{-1}) was treated with Bu_4NOH (2 equiv.). The resulting mixture was heated to reflux until tlc showed that all the starting material had been consumed. The reaction mixture was then diluted with EtOAc and washed with water. The organic layer was then dried and concentrated.

Method C2: A solution of the appropriate epoxide in THF was treated with KOH (5%, 2 equiv.). The resulting mixture was heated to 40 °C and stirred at that temperature until TLC showed that all the starting material had been consumed. The reaction mixture was concentrated.

(2*S*,3*R*,4*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-methylenetetrahydrofuran-3,4-diol (31): This compound was prepared from **1a** (100 mg, 0.54 mmol) by General Procedure C1 and/or C2 to produce diol **31** (66 mg, 57% and 52 mg, 49%, respectively). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H, Me), 1.45 (s, 3 H, Me), 4.03 (dd, J = 4.5, 8.7 Hz, 1 H, 6-H), 4.18 (dd, J = 5.8, 8.7 Hz, 1 H, 6-H), 4.24 (d, J = 2.0 Hz, 1 H, 1′-H), 4.27 (m, 1 H, 3-H), 4.33 (m, 2 H, 4-H and 5-H), 4.42 (s, 1 H, 2-H), 4.45 (d, J = 2.0 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.4, 27.0, 67.7, 73.3, 75.8, 77.2, 83.5, 85.6, 110.0, 163.5 ppm.

This diol was subjected to acetylation and characterized as its diacetate as follows: the reaction mixture was concentrated by co-evaporation with toluene and subsequently dissolved in pyridine (5 mL) and treated with an excess of Ac_2O (300 μL). After the mixture had been stirred at room temperature for 10 h, the crude product was concentrated and the residue was purified by chromatography to yield the corresponding diacetate. $[a]_D^{25}$ = +30.2 (c = 0.6, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (s, 3 H, Me), 1.41 (s, 3 H, Me), 2.08 (s, 3 H, Me), 2.10 (s, 3 H, Me), 4.02 (dd, J = 4.8, 8.6 Hz, 1 H, 6-H), 4.10 (dd, J = 5.7, 8.8 Hz, 1 H, 6-H), 4.24 (ddd, J = 4.9, 5.7, 7.9 Hz, 1 H, 5-H), 4.35 (dd, J = 3.7, 8.0 Hz, 1 H, 4-H), 4.35 (d, J = 2.1 Hz, 1 H, 1′-H), 4.52 (d, J = 2.1 Hz, 1 H, 1′-H), 5.29 (d, J = 3.6 Hz, 1 H, 3-H), 5.47 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.7, 20.9, 25.2, 26.8, 66.9, 72.3, 74.3, 74.7, 81.8, 88.4, 109.5, 158.4, 169.1, 169.3 ppm. EI-MS 300.1 $[M]^+$. $C_{14}H_{20}O_7$ (300.12): calcd. C 55.99, H, 6.71; found C, 55.88; H, 6.62.

(3*R*,4*R*,5*S*)-2-(Butan-2-ylidene)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-tetrahydrofuran-3,4-diol (32): Compound **1b** (125 mg, 0.48 mmol) was subjected to General Procedure C1 to give compound **32** (64 mg, 52%) as a mixture of isomers after silica gel column chromatography (EtOAc). Selected peaks for the major isomer: ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.04 (t, J = 7.3 Hz, 3 H, Me), 1.38 (s, 3 H, Me), 1.45 (s, 3 H, Me), 2.05 (s, 3 H, Me), 2.1 (q, J = 7.3 Hz, 2 H, CH_2), 4.01–4.32 (m, 5 H), 4.62 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.9, 14.2, 25.3, 26.1, 26.8, 60.4, 67.5, 73.3, 74.2, 82.0, 109.6, 112.4, 150.5 ppm. API-ES positive 259.3 $[M + H]^+$. $C_{13}H_{22}O_5$ (258.15): calcd. C 60.45, H 8.58; found C 60.19, H 8.47.

(3*R*,4*R*,5*S*)-2-Butylidene-5-(2,2-dimethyl-1,3-dioxolan-4-yl)tetrahydrofuran-3,4-diol (33): Compound **1c** (100 mg, 0.38 mmol) was

subjected to General Procedure C1 to give compound **33** (48 mg, 49%) as a mixture of isomers after silica gel column chromatography (EtOAc). Selected peaks for the major isomer: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (t, J = 7.3 Hz, 3 H, Me), 1.38 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.39 (m, 2 H, CH_2), 2.0 (m, 2 H, CH_2), 4.05 (dd, J = 4.7, 8.5 Hz, 1 H, 6-H), 4.19 (dd, J = 5.8, 8.6 Hz, 1 H, 6-H), 4.32 (m, 4 H), 4.61 (t, J = 7.3 Hz, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.7, 22.7, 25.2, 26.7, 27.0, 67.5, 73.3, 75.6, 77.1, 82.8, 102.6, 109.6, 156.1 ppm. API-ES positive 259.3 [M + H]$^+$. $C_{13}H_{22}O_5$ (258.1467): calcd. C 60.45, H 8.58; found C 60.21, H 8.39.

(3*R*,4*S*,5*R*,*Z*)-2-(Bromomethylene)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)tetrahydrofuran-3,4-diyl Diacetate (34): This compound was prepared from **2a** (125 mg, 0.45 mmol) by General Procedure C1. To facilitate the purification of the product, the reaction mixture was subsequently dissolved in pyridine (5 mL) and treated with an excess of Ac_2O (300 μL). After the mixture had been stirred at room temperature for 10 h, the crude product was concentrated and the residue was purified by chromatography (hexane/EtOAc 8:2) to give compound **34** (101 mg, 59%). $[a]_D^{25}$ = +55.7 (c = 1.14, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.31 (s, 3 H, Me), 1.40 (s, 3 H, Me), 2.06 (s, 3 H, Me), 2.09 (s, 3 H, Me), 4.13 (m, 2 H, 6-H), 4.29 (m, 1 H, 5-H), 4.47 (dd, J = 3.6, 8.0 Hz, 1 H, 4-H), 5.35 (dd, J = 0.9, 3.6 Hz, 1 H, 3-H), 5.41 (d, J = 0.9 Hz, 1 H, 2-H), 5.52 (s, 1 H, 1′-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.7, 20.8, 25.3, 26.8, 66.9, 72.2, 74.4, 74.7, 82.3, 82.8, 109.7, 154.6, 169.0, 169.2 ppm. API-ES positive 379.0 [M + H]$^+$, 402 [M + Na]$^+$. $C_{14}H_{19}BrO_7$ (378.03): calcd. C 44.34, H 5.05; found C 44.26, H 5.12.

(2*R*,3*S*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(iodomethylene)-tetrahydrofuran-3,4-diyl Diacetate (35): This compound was prepared from **2b** (125 mg, 0.38 mmol) by General Procedure C1. To facilitate the purification of the product, the crude reaction mixture was dissolved in pyridine (5 mL) and treated with an excess of Ac_2O (300 μL). After the mixture had been stirred at room temperature for 10 h, the crude product was concentrated and the residue was purified by chromatography (hexane/EtOAc 8:2) to yield compound **35** (104 mg, 64%). $[a]_D^{25}$ = +56.6 (c = 1.06, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.33 (s, 3 H, Me), 1.43 (s, 3 H, Me), 2.08 (s, 3 H, Me), 2.10 (s, 3 H, Me), 4.10 (dd, J = 5.1, 8.9 Hz, 1 H, 6-H), 4.13 (dd, J = 5.8, 8.8 Hz, 1 H, 6-H), 4.29 (ddd, J = 5.1, 5.8, 7.8 Hz, 1 H, 5-H), 4.52 (dd, J = 3.7, 7.7 Hz, 1 H, 4-H), 5.38 (s, 1 H, 1′-H), 5.41 (dd, J = 1.3, 3.7 Hz, 1 H, 3-H), 5.48 (d, J = 1.3 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.7, 20.8, 25.2, 26.7, 50.7, 66.7, 72.1, 73.9, 75.1, 82.3, 109.6, 158.5, 169.0, 169.2 ppm. API-ES positive 427.1 [M + H]$^+$, 449.1 [M + Na]$^+$. $C_{14}H_{19}IO_7$ (426.02): calcd. C 39.45, H 4.49; found C 39.33, H 4.52.

(2*S*,3*R*)-5-(Azidomethyl)-2-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3-dihydrofuran-3-ol (40): A suspension of **1a** (150 mg, 0.75 mmol) and sodium azide (244 mg, 3.75 mmol) in DMF (5 mL) was heated at 50 °C for 4 h. The reaction mixture was concentrated and the residue was purified by silica gel column chromatography (hexane/EtOAc 6:4) to give the azide **40** (112 mg, 62%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.39 (s, 3 H, Me), 1.46 (s, 3 H, Me), 3.84 (d, J = 2.6 Hz, 2 H, CH_2–), 4.02 (dd, J = 5.0, 8.7 Hz, 1 H, 6-H), 4.17 (dd, J = 6.2, 8.8 Hz, 1 H, 6-H), 4.26 (dd, J = 6.5, 8.0 Hz, 1 H, 4-H), 4.49 (ddd, J = 5.0, 6.2, 8.0 Hz, 1 H, 5-H), 4.96 (dd, J = 2.6, J = 6.5 Hz, 1 H, 3-H), 5.22 (d, J = 2.6 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.1, 26.8, 47.1, 66.9, 72.7, 73.3, 85.6, 102.3, 109.4, 157.4 ppm. EI-MS 241.1 [M]$^+$.

General Procedure D. Suzuki Cross-Couplings between 1′-Halo-*exo*-glycals and Boronic Acids: NaOH (2 N, 3 mmol) was added to a mixture of the appropriate alkenyl halide (**28**–**30**, 1 mmol) and the appropriate arylboronic acid (1.3 mmol) in THF (5 mL). The resulting solution was degassed under argon for 10 min and then $Pd(PPh_3)_4$ (0.05 mmol) was added. The ensuing suspension was heated under argon to 60 °C and stirred at that temperature. After the starting materials had been consumed, the mixture was diluted with EtOAc and washed with brine. The organic layer was dried, concentrated and subjected to silica gel column chromatography.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-(phenethylamino)-5-(thiophen-3-ylmethylene)tetrahydrofuran-3-ol (41a): This compound was prepared from the bromide **28a** (100 mg, 0.25 mmol) or the iodide **28b** (111 mg, 0.25 mmol) and thiophene-3-boronic acid (42 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41a** (69 mg, 69% and 72 mg, 72%, respectively). $[a]_D^{25}$ = +8.5 (c = 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.39 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.84 (m, 2 H, CH_2–Ph), 3.03 (m, 2 H, CH_2N), 3.65 (s, 1 H, 2-H), 4.12 (dd, J = 4.6, 8.5 Hz, 1 H, 6-H), 4.20 (d, J = 2.2 Hz, 1 H, 3-H), 4.25 (dd, J = 5.6, 9.0 Hz, 1 H, 6-H), 4.44 (m, 2 H, 4-H and 5-H), 5.44 (s, 1 H, 1′-H), 7.18–7.60 (m, 8 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 23.6, 25.3, 34.5, 47.1, 65.6, 66.7, 71.6, 73.1, 82.9, 94.6, 108.1, 119.1, 124.7, 126.5, 127.0 (×2), 127.1, 127.2 (×2), 134.8, 137.9, 154.2 ppm. API-ES positive 402.1 [M + 1]$^+$. $C_{22}H_{27}NO_4S$ (401.17): calcd. C 65.81, H 6.78, N 3.49; found C 65.79, H 6.57, N 3.53.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(4-methoxybenzylidene)-4-(phenethylamino)tetrahydrofuran-3-ol (41b): This compound was prepared from the bromide **28a** (100 mg, 0.25 mmol) or the iodide **28b** (111 mg, 0.25 mmol) and *p*-methoxyphenylboronic acid (49 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41b** (66 mg, 63% and 70 mg, 66%, respectively). $[a]_D^{25}$ = +60.7 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H, Me), 1.46 (s, 3 H, Me), 2.80 (m, 2 H, CH_2–Ph), 3.01 (m, 2 H, CH_2N), 3.63 (s, 1 H, 2-H), 3.78 (s, 3 H, OMe), 4.10 (dd, J = 4.6, 8.8 Hz, 1 H, 6-H), 4.16 (m, 1 H, 3-H), 4.22 (dd, J = 5.6, 8.8 Hz, 1 H, 6-H), 4.39 (m, 2 H, 4-H and 5-H), 5.25 (s, 1 H, 1′-H), 6.82 (d, J = 9.0 Hz, 2 H, H_{arom}), 7.26 (m, 5 H, H_{arom}), 7.42 (d, J = 9.0 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.3, 26.8, 36.1, 48.9, 55.2, 67.5, 68.7, 73.2, 74.2, 84.8, 100.9, 109.6, 113.6 (×2), 126.3, 128.5 (2), 128.7 (×4), 130.2, 139.4, 154.8, 157.4 ppm. EI-MS 425.3 [M]$^+$. $C_{25}H_{31}NO_5$ (425.22): calcd. C 70.57, H 7.34, N 3.29; found C 70.53, H 7.27, N 3.33.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(4-methylbenzylidene)-4-(phenethylamino)tetrahydrofuran-3-ol (41c): This compound was prepared from the bromide **28a** (100 mg, 0.25 mmol) or the iodide **28b** (111 mg, 0.25 mmol) and *p*-methylphenylboronic acid (44 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41c** (68 mg, 67% and 65 mg, 64%, respectively). $[a]_D^{25}$ = +32.1 (c = 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.39 (s, 3 H, Me), 1.47 (s, 3 H, Me), 2.31 (s, 3 H, Me), 2.79 (m, 2 H, CH_2–Ph), 3.01 (m, 2 H, CH_2–N), 3.66 (s, 1 H, 2-H), 4.12 (dd, J = 4.9, 8.8 Hz, 1 H, 6-H), 4.18 (d, J = 3.2 Hz, 1 H, 3-H), 4.25 (dd, J = 5.9, 8.8 Hz, 1 H, 6-H), 4.45 (m, 2 H, 4-H and 5-H), 5.29 (s, 1 H, 1′-H), 7.09 (d, J = 7.8 Hz, 2 H, H_{arom}), 7.26 (m, 5 H, H_{arom}), 7.38 (d, J = 8.0 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.4, 25.5, 27.1, 36.5, 49.2, 67.8, 69.1, 73.5, 74.7, 85.2, 101.5, 109.9, 126.6, 127.9 (×2), 128.8 (×2), 128.9 (×2), 129.1 (×2), 133.1, 135.4, 139.8, 156.2 ppm. EI-MS 409.2 [M]$^+$. $C_{25}H_{31}NO_4$ (409.23): calcd. C 73.32, H 7.63, N 3.42; found C 73.39, H 7.57, N 3.36.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-morpholino-5-(thiophen-3-ylmethylene)tetrahydrofuran-3-ol (41d): This compound

was prepared from the bromide **29a** (91 mg, 0.25 mmol) or the iodide **29b** (103 mg, 0.25 mmol) and thiophene-3-boronic acid (41 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41d** (79 mg, 86% and 85 mg, 93%, respectively) $[\alpha]_D^{25}$ = +29.7 (*c* = 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.39 (s, 3 H, Me), 1.48 (s, 3 H, Me), 2.63 (m, 4 H, 2× CH_2–N), 3.43 (s, 1 H, 2-H), 3.69 (m, 4 H, 2× CH_2–O), 4.13 (dd, *J* = 4.1, 8.2 Hz, 1 H, 6-H), 4.24 (dd, *J* = 4.7, 7.8 Hz, 1 H, 6-H), 4.48 (m, 3 H, 3-H, 4-H, 5-H), 5.50 (s, 1 H, 1′-H), 7.27 (m, 3 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.2, 26.9, 51.2 (×2), 67.1 (×2), 67.5, 71.5, 73.3, 75.3, 84.8, 98.8, 109.7, 120.9, 124.6, 128.1, 136.2, 152.1 ppm. API-ES positive 368.0 $[M + 1]^+$. $C_{18}H_{25}NO_5S$ (367.15): calcd. C 58.83, H 6.86, N 3.81; found C 58.71, H 6.69, N 3.67.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(4-methoxybenzylidene)-4-morpholinotetrahydrofuran-3-ol (41e): This compound was prepared from the bromide **29a** (91 mg, 0.25 mmol) or the iodide **29b** (103 mg, 0.25 mmol) and *p*-methoxyphenylboronic acid (49 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41e** (73 mg, 75% and 84 mg, 86%, respectively) $[\alpha]_D^{25}$ = +38.6 (*c* = 0.6, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H, Me), 1.46 (s, 3 H, Me), 2.62 (m, 4 H, 2× CH_2–N), 3.42 (s, 1 H, 2-H), 3.69 (m, 4 H, 2× CH_2–O), 3.79 (s, 3 H, OMe), 4.08 (dd, *J* = 4.3, 8.6 Hz, 1 H, 6-H), 4.20 (dd, *J* = 5.6, 8.5 Hz, 1 H, 6-H), 4.41 (m, 3 H, 3-H, 4-H and 5-H), 5.38 (s, 1 H, 1′-H), 6.84 (d, *J* = 8.8 Hz, 2 H, H_{arom}), 7.46 (d, *J* = 8.8 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.6, 27.2, 51.6 (×2), 55.7, 67.6 (×2), 71.5, 73.9, 74.7, 76.4, 85.5, 103.9, 109.7, 114.1 (×2), 129.4 (×2), 133.5, 152.0, 157.9 ppm. API-ES positive 392.1 $[M + 1]^+$. $C_{21}H_{29}NO_6$ (391.20): calcd. C 64.43, H 7.47, N 3.58; found C 64.25, H 7.31, N 3.49.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(4-methylbenzylidene)-4-morpholinotetrahydrofuran-3-ol (41f): This compound was prepared from the bromide **29a** (91 mg, 0.25 mmol) or the iodide **29b** (103 mg, 0.25 mmol) and *p*-methylphenylboronic acid (44 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41f** (68 mg, 73% and 71 mg, 76%, respectively). $[\alpha]_D^{25}$ = +63.1 (*c* = 0.4, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.39 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.32 (s, 3 H, Me), 2.65 (m, 4 H, 2× CH_2–N), 3.44 (s, 1 H, 2-H), 3.70 (m, 4 H, 2× CH_2–O), 4.12 (dd, *J* = 4.4, 9.0 Hz, 1 H, 6-H), 4.25 (dd, *J* = 5.6, 8.5 Hz, 1 H, 6-H), 4.41 (m, 3 H, 3-H, 4-H, 5-H), 5.41 (s, 1 H, 1′-H), 7.10 (d, *J* = 8.0 Hz, 2 H, H_{arom}), 7.42 (d, *J* = 8.0 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.6, 25.6, 27.3, 51.6 (×2), 67.6 (×2), 67.9, 71.7, 73.8, 76.3, 85.4, 104.4, 110.1, 129.0 (×2), 132.3 (×2), 133.1, 135.8, 152.6 ppm. API-ES positive 376.1 $[M + 1]^+$. $C_{21}H_{29}NO_5$ (375.20): calcd. C 67.18, H 7.79, N 3.73; found C 66.94, H 7.65, N 3.58.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-[4-(2-methoxyphenyl)piperazin-1-yl]-5-(thiophen-3-ylmethylene)tetrahydrofuran-3-ol (41g): This compound was prepared from the bromide **30a** (117 mg, 0.25 mmol) or the iodide **30b** (130 mg, 0.25 mmol) and thiophene-3-boronic acid (42 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41g** (85 mg, 72% and 91 mg, 77%, respectively) $[\alpha]_D^{25}$ = +36.6 (*c* = 0.7, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.39 (s, 3 H, Me), 1.49 (s, 3 H, Me), 2.86 (m, 4 H, 2× CH_2–N), 3.09 (m, 4 H, 2× CH_2–N), 3.59 (s, 1 H, 2-H), 3.89 (s, 3 H, OMe), 4.16 (dd, *J* = 4.9, 8.7 Hz, 1 H, 6-H), 4.27 (dd, *J* = 6.2, 8.1 Hz, 1 H, 6-H), 4.44 (m, 2 H, 4-H and 5-H), 4.59 (s, 1 H, 3-H), 5.59 (s, 1 H, 1′-H), 6.96 (m, 4 H, H_{arom}), 7.25 (m, 2 H, H_{arom}), 7.33 (m, 1 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.5, 27.2, 50.9 (×2), 51.1 (×2), 55.6, 67.7, 71.6, 73.6, 75.5, 85.3, 98.7, 109.9, 111.3, 118.4, 121.0, 121.2, 123.3, 124.8, 128.4, 136.7, 141.3, 152.4, 153.1 ppm. EI-MS 472.0 $[M]^+$. $C_{25}H_{32}N_2O_5S$ (472.20): calcd. C 63.54, H 6.82, N 5.93; found C 63.61, H 6.60, N 5.78.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(4-methoxybenzylidene)-4-[4-(2-methoxyphenyl)piperazin-1-yl]tetrahydrofuran-3-ol (41h): This compound was prepared from the bromide **30a** (117 mg, 0.25 mmol) or the iodide **30b** (130 mg, 0.25 mmol) and *p*-methoxyphenylboronic acid (49 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41h** (92 mg, 74% and 102 mg, 82%, respectively) $[\alpha]_D^{25}$ = +54.9 (*c* = 0.6, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.42 (s, 3 H, Me), 1.52 (s, 3 H, Me), 2.86 (m, 4 H, 2× CH_2–N), 3.10 (m, 4 H, 2× CH_2–N), 3.59 (s, 1 H, 2-H), 3.83 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 4.15 (dd, *J* = 4.3, 8.6 Hz, 1 H, 6-H), 4.29 (dd, *J* = 5.9, 8.9 Hz, 1 H, 6-H), 4.49 (m, 2 H, 4-H and 5-H), 4.50 (s, 1 H, 3-H), 5.50 (s, 1 H, 1′-H), 6.92 (m, 6 H, H_{arom}), 7.52 (d, *J* = 8.8 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 25.6, 27.3, 51.1 (×2), 55.7 (×2), 59.5, 67.9, 71.6, 73.8, 76.2, 85.5, 103.7, 110.0, 111.5, 114.1, 118.6, 121.4, 123.4, 129.1 (×2), 129.5 (×2), 141.5, 152.6, 157.9 ppm. API-ES positive 497.3 $[M + H]^+$. $C_{28}H_{36}N_2O_6$ (496.26): calcd. C 67.72, H 7.31, N 5.64; found C 67.68, H 7.16, N 5.41.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-[4-(2-methoxyphenyl)piperazin-1-yl]-5-(4-methylbenzylidene)tetrahydrofuran-3-ol (41i): This compound was prepared from the bromide **30a** (117 mg, 0.25 mmol) or the iodide **30b** (130 mg, 0.25 mmol) and *p*-methylphenylboronic acid (44 mg, 0.32 mmol) by General Procedure D followed by silica gel column chromatography (hexane/EtOAc 3:7). Compound **41i** (79 mg, 66% and 81 mg, 67%, respectively). $[\alpha]_D^{25}$ = +39.8 (*c* = 1.6, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H, Me), 1.46 (s, 3 H, Me), 2.32 (s, 3 H, Me), 2.82 (m, 4 H, 2× CH_2–N), 3.08 (m, 4 H, 2× CH_2–N), 3.57 (s, 1 H, 2-H), 3.86 (s, 3 H, OMe), 4.10 (m, 2 H, 4-H and 6-H), 4.23 (dd, *J* = 4.9, 8.5 Hz, 1 H, 6-H), 4.38 (m, 1 H, 5-H), 4.60 (s, 1 H, 3-H), 5.46 (s, 1 H, 1′-H), 6.86 (d, *J* = 8.0 Hz, 2 H, H_{arom}), 7.01 (m, 4 H, H_{arom}), 7.45 (d, *J* = 8.0 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.1, 25.3, 26.9, 50.5 (×2), 50.8 (×2), 55.3, 67.5, 72.5, 73.3, 74.4, 84.8, 103.6, 109.7, 111.1, 118.2, 120.9, 123.1, 127.8 (×2), 128.9 (×2), 132.9, 135.2, 140.9, 152.2, 155.6 ppm. EI-MS 480.2 $[M]^+$. $C_{28}H_{36}N_2O_5$ (480.26): calcd. C 69.98, H 7.55, N 5.83; found C 69.73, H 7.37, N 5.61.

(2*S*,3*R*,4*R*,*Z*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-(piperidin-1-yl)-5-(pyridin-3-ylmethylene)tetrahydrofuran-3-yl acetate (45b): A solution of compound **45a** (50 mg, 0.14 mmol) in pyridine (5 mL) was treated with an excess of Ac_2O (500 μL). After the mixture had been stirred at room temperature for 10 h, the crude product was concentrated and the residue was purified by chromatography (hexane/EtOAc 1:1) to give the acetyl derivative **45b** (54.5 mg, 97%). $[\alpha]_D^{25}$ = +18.7 (*c* = 0.6, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 3 H, Me), 1.47 (s, 3 H, Me), 1.56 (m, 6 H), 2.05 (s, 3 H, Me), 2.54 (m, 2 H), 2.67 (m, 2 H), 3.57 (s, 1 H, 2-H), 4.13 (m, 2 H, 4-H and 6-H), 4.32 (dd, *J* = 5.8, 12.8 Hz, 1 H, 6-H), 4.64 (dd, *J* = 4.7, 7.3 Hz, 1 H, 5-H), 5.41 (d, *J* = 1.8 Hz, 1 H, 3-H), 5.49 (dd, *J* = 1.8, 4.4 Hz, 1 H, 1′-H), 7.42 (dd, *J* = 4.7, 8.3 Hz, 1 H), 8.06 (d, *J* = 8.1 Hz, 1 H), 8.34 (dd, *J* = 1.3, 4.7 Hz, 1 H), 8.70 (d, *J* = 1.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.2, 25.3, 27.1, 51.6 (×2), 66.7, 67.2 (×2), 72.4, 72.9, 74.1, 77.4, 84.5, 98.6, 109.9, 125.0, 133.9, 136.9, 143.9, 146.7, 157.5, 169.9 ppm. API-ES positive 403.3 $[M + H]^+$. $C_{22}H_{30}N_2O_5$ (402.22): calcd. C 65.65, H 7.51, N 6.96; found C 65.48, H 7.38, N 6.83.

General Procedure E. Cleavage of the Isopropylidene Acetal Units in Compounds 45b and 47: A solution of the corresponding compound

(0.12 mmol) in a THF/H_2O mixture (3 mL, 2:1, v/v) was acidified with AcOH (2 mL). The reaction mixture was heated at 75 °C for 10 h, after which it was concentrated and the residue was purified by flash chromatography.

(2*R*,3*R*,4*R*,*Z*)-2-(1,2-Dihydroxyethyl)-4-(piperidin-1-yl)-5-(pyridin-3-ylmethylene)tetrahydrofuran-3-yl Acetate (46): This compound was prepared from the acetonide **45a** (50 mg, 0.12 mmol) by General Procedure E, giving compound **46** (32 mg, 75%) after silica gel column chromatography (EtOAc/MeOH 8:2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.42 (m, 2 H), 1.58 (m, 4 H), 2.10 (s, 3 H), 2.59 (m, 4 H), 3.59 (s, 1 H), 4.34 (m, 2 H), 4.48 (m, 2 H), 4.61 (dd, J = 1.5, 4.4 Hz, 1 H), 5.34 (s, 1 H), 7.44 (dd, J = 4.6, 8.2 Hz, 1 H), 8.16 (d, J = 8.1 Hz, 1 H), 8.35 (dd, J = 1.2, 4.6 Hz, 1 H), 8.76 (d, J = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.2, 24.5, 26.3 (×2), 51.9 (×2), 66.4, 69.2, 71.8, 77.1, 83.9, 99.5, 123.6, 132.4, 134.9, 145.4, 148.5, 156.8, 171.8 ppm. API-ES positive 363.5 $[M + H]^+$. $C_{19}H_{26}N_2O_5$ (362.18): calcd. C 62.97, H 7.23, N 7.73; found C 62.81, H 7.17, N 7.82.

1-[(2*S*,3*R*,4*R*,*Z*)-3-Hydroxy-4-morpholino-5-(pyridin-3-ylmethylene)tetrahydrofuran-2-yl]ethane-1,2-diol (48): This compound was prepared from the acetonide **47** (50 mg, 0.12 mmol) by General Procedure E, giving compound **46** (21 mg, 56%) after silica gel column chromatography (EtOAc/MeOH 8:2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.40 (m, 4 H), 3.51 (s, 1 H, 2-H), 3.56 (m, 4 H), 3.75 (dd, J = 6.6, 11.6 Hz, 1 H), 3.99 (d, J = 3.3 Hz, 1 H), 4.25 (m, 2 H), 4.62 (dd, J = 3.3, 8.3 Hz, 1 H, 1 H), 5.59 (s, 1 H), 7.40 (dd, J = 4.9, 8.0 Hz, 1 H), 8.15 (d, J = 8.3 Hz, 1 H), 8.30 (dd, J = 1.5, 4.9 Hz, 1 H), 8.74 (d, J = 1.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 51.6 (×2), 63.9, 66.9 (×2), 69.2, 70.6, 76.8, 84.8, 99.2, 123.7, 133.2, 135.3, 144.9, 147.8, 157.2 ppm. API-ES positive 323.2 $[M + H]^+$. $C_{16}H_{22}N_2O_5$ (322.15): calcd. C 59.61, H 6.88, N 8.69; found C 59.70, H 6.97, N 8.83.

Acknowledgments

This research was supported with funds from the Ministerio de Ciencia e Innovación (MICINN) (Grants CTQ2006-15279-C03-02 and CTQ2009-10343), the Comunidad de Madrid (Grant S2009/PPQ-1752), and Janssen-Cilag SA. A. P. is thankful to Janssen-Cilag SA for financial support. We are grateful to Ms. Marina Rodriguez for skilful technical assistance and to Dr. Aitor Barrio for the preparation of compound **9**.

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Received: May 3, 2010
Published Online: August 24, 2010

