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Synthesis of aza- and thia-spiroheterocycles and attempted synthesis of spiro sulfonium compounds related to salacinol

Wang Chen and B. Mario Pinto*

Department of Chemistry, Simon Fraser University, Burnaby, British Columbia, Canada V5A 1S6

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Abstract—The synthesis of aza- and thia-spiroheterocycles and the attempted synthesis of spiro sulfonium compounds related to salacinol are described. The binding of the nanomolar inhibitor swainsonine to *Drosophila* Golgi α-mannosidase II (dGMII) involves a large contribution of interactions between the six-membered ring of the inhibitor and the hydrophobic pocket within the enzyme active site. Salacinol, a naturally occurring sulfonium ion, is one of the active principles in the aqueous extracts of *Salacia reticulata* that are traditionally used in Sri Lanka and India for the treatment of diabetes. Spiro aza- and thia-heterocycles and a spiro analogue of salacinol were designed with the expectation that the hydrocarbon portions would make hydrophobic contributions to binding. The former sets of compounds were synthesized successfully but the salacinol analogue proved to be elusive. The stereochemistry of the final compounds was determined by means of 1D-NOESY experiments. The aza- and thia-heterocycles were not effective inhibitors of Golgi α-mannosidase II or human maltase glucoamylase.

Keywords: Glycosidase inhibitors; Salacinol; Aza- and thia-spiroheterocycles; Curtius rearrangement; Enolate of α-thio ketone; Enolate of α-amino ketone

1. Introduction

Glycosidases belong to a group of hydrolytic enzymes that are involved in a variety of biologically widespread process. Their inhibition can have profound effects on quality control, maturation, transport, and secretion of glycoproteins and can alter cell–cell or cell–virus recognition processes.[1] The transition-state structure in the enzyme-mediated hydrolysis of glycosides is believed to be the oxacarbenium ion with a distorted conformation. Thus, mimicking this distorted, positively charged species is one factor that could lead to a strong inhibitor of glycosidase enzymes.[2]

The α-glucosidase inhibitors salacinol **1** and kotalanol **2** (Fig. 1) have been isolated from *Salacia reticulata* WIGHT,[3,4] and *S. oblonga* and *S. chinensis*,[5] traditionally used in the Ayurvedic system of India and Sri Lanka for the treatment of diabetes.[6] Our group has reported the syntheses of compounds **3**[7] and **4**[8] (Fig. 1) related to salacinol that contain a carboxylate inner salt and heteroanalogues of salacinol containing nitrogen[9] or selenium[10] instead of sulfur, namely ghavamiol **5** and blintol **6**, respectively. Compounds **3**, **4**, and **6** inhibit recombinant human maltase glucoamylase (MGA),[11] one of the key intestinal enzymes involved in the breakdown of glucose oligosaccharides in the small intestine. We reasoned that the interaction of a permanent positive charge with active-site carboxylate residues would make a dominant contribution to the interaction energy.

In addition, compounds **1**, **3**, **5**, and **6** were found to inhibit *Drosophila* Golgi α-mannosidase II (dGMII), a key enzyme involved in *N*-glycan processing and thus a target in the development of anti-cancer therapies, with IC_{50} values in the low mM range.[7,12] The structure of dGMII in complex with the inhibitor swainsonine **7** (IC_{50} 20 nM, Figs. 2 and 3) has been published,[13] although the reason for the potency of swainsonine has not been clearly determined. The binding of the

* Corresponding author. Tel.: +1 604 291 4152; fax: +1 604 291 4860; e-mail: bpinto@sfu.ca

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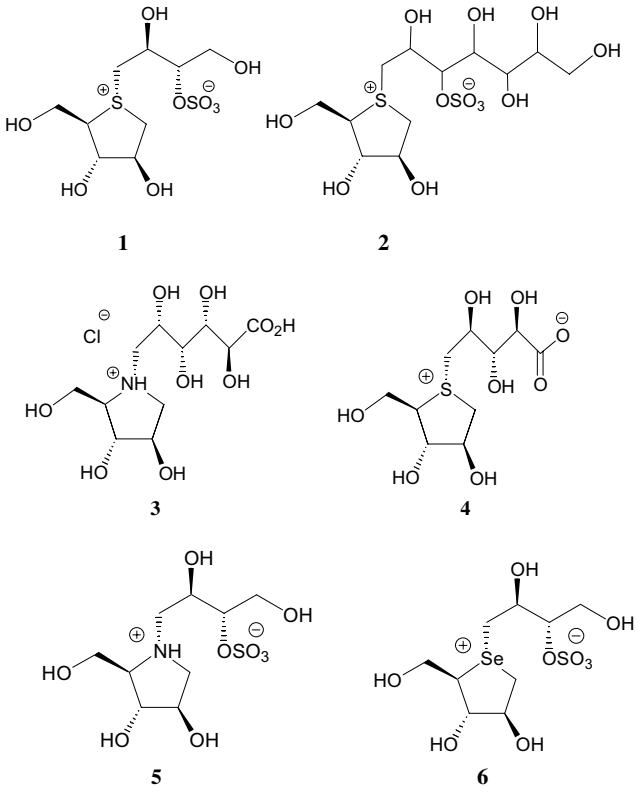


Figure 1. Structures of salacinol **1**, kotalanol **2**, compounds **3** and **4**, ghavamiol **5**, and blintol **6**.

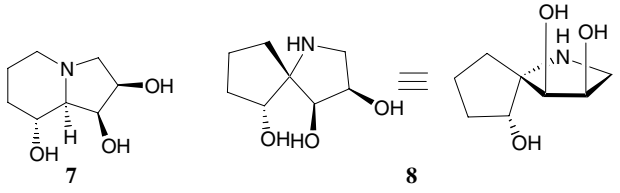


Figure 2. Structures of swainsonine **7** and the aza-spiroheterocycle **8**.

inhibitor involves a large contribution of hydrophobic interactions with aromatic residues Trp95, Phe206, and Tyr727. The plane of the six-membered ring is nearly parallel to Phe206 and approximately at 90° to Tyr727. Therefore, we now present the synthesis of the aza-spiroheterocycle, **8** (Fig. 2), the hydrocarbon portion of which is expected to interact with the hydrophobic pocket of Tyr727, Phe206, and Trp415.

Overlay of compounds bound in the active site of dGMII, obtained from X-ray crystallography, indicated that the position of the head groups of **3**, **5** and the diastereomer of salacinol **9** is similar (Figs. 4 and 5).[7] The positions of the nitrogen atoms and the positively charged sulfur atom, which are designed to mimic the positive charge on the oxacarbenium ion, are almost identical. However, it is the thiomethyl group of a nanomolar inhibitor *N*-benzyl mannostatin **10** (Figs. 4 and 5)

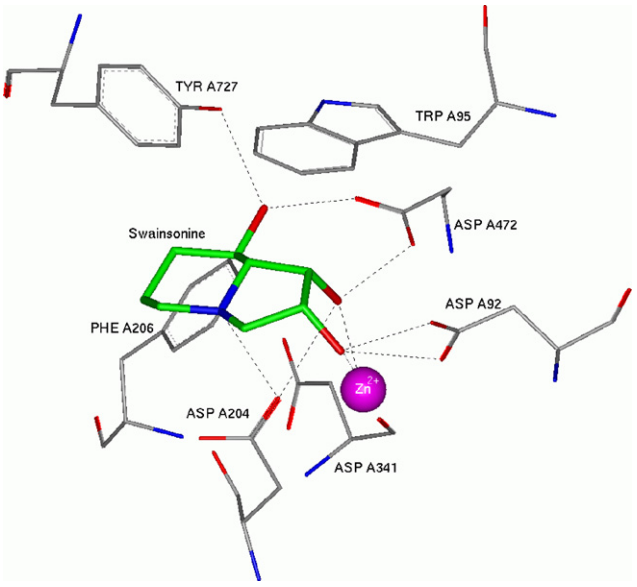


Figure 3. Structure of swainsonine **7** bound in the active site of dGMII (PDB 1HWW).

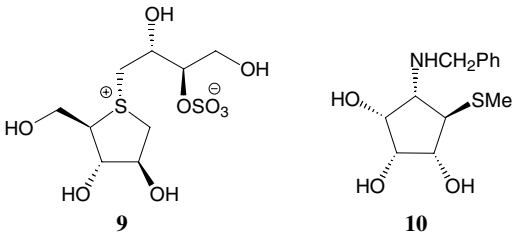


Figure 4. Structures of the diastereomer of salacinol, **9**, and *N*-benzyl mannostatin **10**.

and the hydrophobic hydrocarbon moiety of swainsonine **7** that occupy the hydrophobic region of the active site through which the hydrophilic C-5 hydroxyl groups of salacinol analogues pass. The thiomethyl group, which is critical for high affinity, is believed to make important nonpolar interactions with aromatic rings in the active site of dGMII.[14] Accordingly, we also present the attempted synthesis of spiro sulfonium compounds **11** and **12** (Fig. 6) related to salacinol but with more nonpolar moieties than salacinol analogues themselves.

2. Results and discussion

Paquette et al.[15,16] have synthesized a number of 4′-spiroalkylated nucleosides to impose conformational constraints that might have importance in modulation of the sugar-phosphate DNA backbone, and ultimately the secondary structure of DNA and base recognition.[17] Our synthesis takes advantage of the stereochemistry of (*R*)-isopropylidene glyceraldehyde and provides an alternative synthetic route to 4′-spiroalkylated compounds.

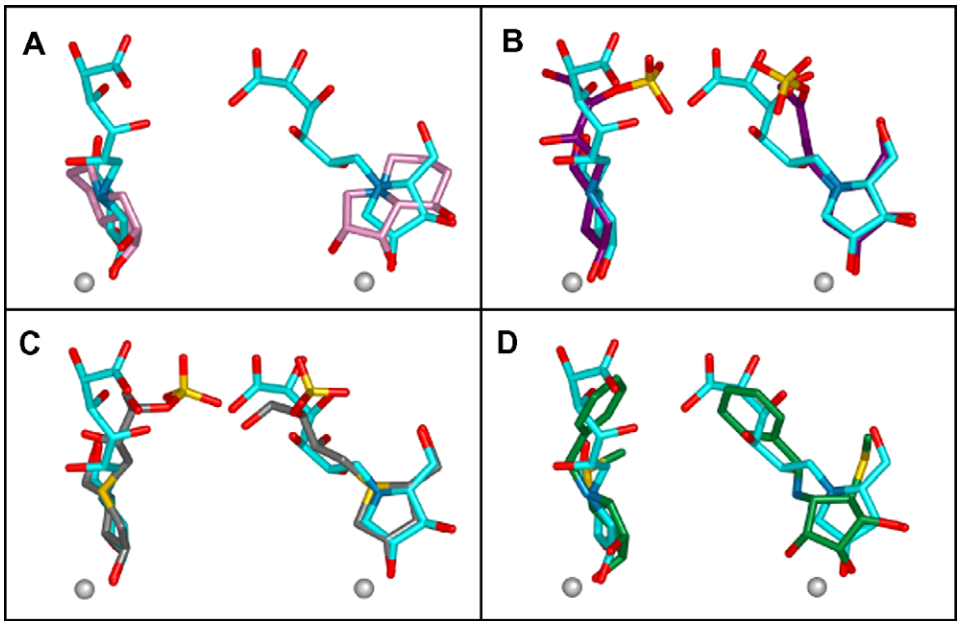


Figure 5. Overlay of compounds bound in the active site of dGMII. Compound **3** (cyan) is overlayed with **A**. Swainsonine **7** (pink, PDB 1HWW) **B**. Ghavamiol **5** (magenta, PDB 1TQU) **C**. Salacinol Diastereomer **9** (gray, PDB 1TQT) or **D**. *N*-Benzyl mannostatin **10** (green, PDB 2F7P). Reprinted with permission from Ref. 7.

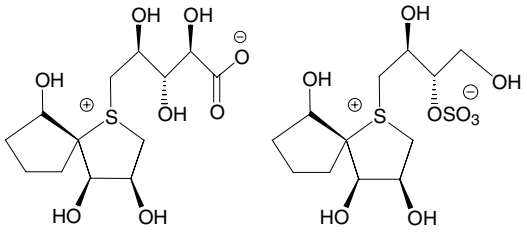
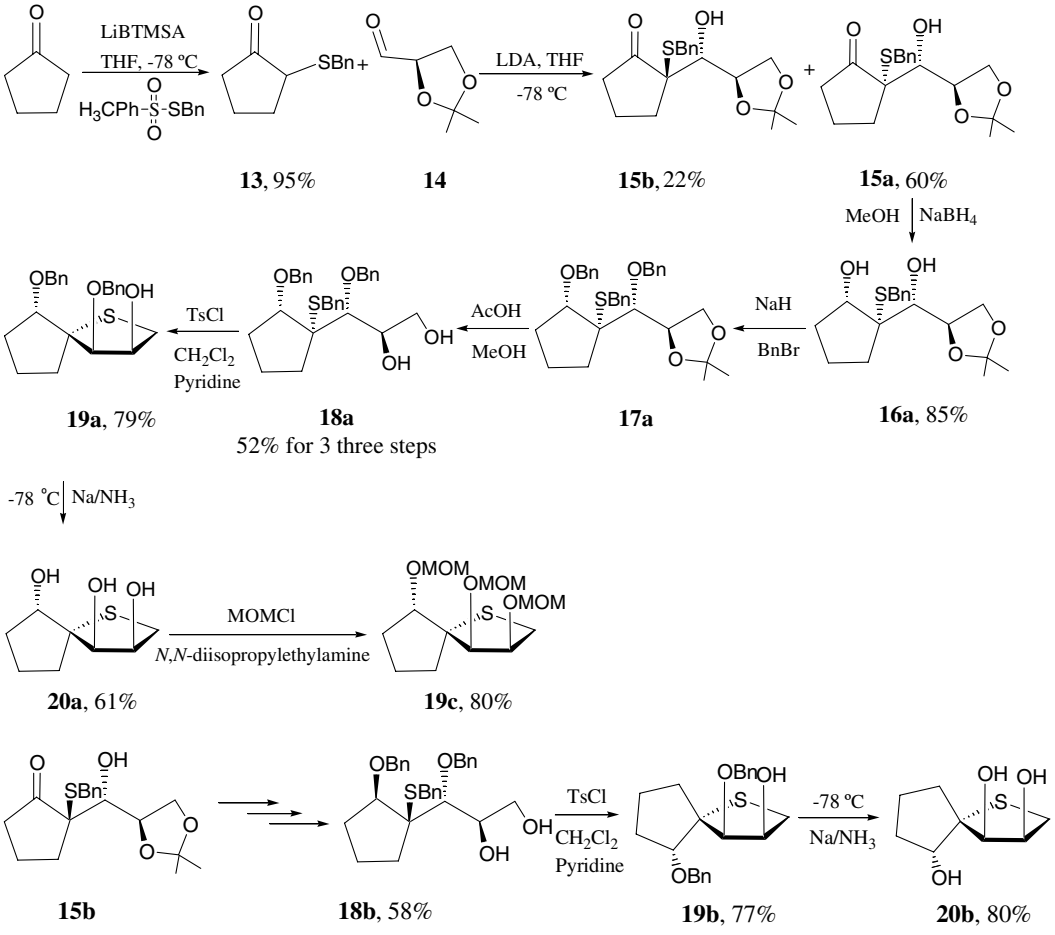


Figure 6. Structures of the spiro sulfonium compounds **11** and **12**.

2-Benzylsulfanylcyclopentanone **13** was prepared in one step from the enolate of cyclopentanone and the thiolating reagent *S*-benzyl 4-methylbenzenethiosulfonate (Scheme 1). The lithium-catalyzed aldol reaction of **13** with (*R*)-isopropylidene glyceraldehyde **14**[18] gave two products **15a** and **15b** in a ratio of 3:1 that were separated by chromatography. No other diastereomer was obtained. The reaction is believed to go through a six-membered ring transition state with the enolate generated toward the α-substituent (Fig. 7). Both products are predicted to arise by application of the Felkin-Anh model for asymmetric induction, assuming the alkoxyl group to be the 'large' group (Fig. 7).[19] The major product **15a** was reduced selectively by $NaBH_4$ to generate **16a**, suggesting that the β-hydroxyl group helps to deliver hydride from the *si*-face of the ketone. The hydroxyl groups of compound **16a** were benzylated and the isopropylidene protecting group was removed. Treatment of compound **18a** with tosyl chloride afforded the spiro compound **19a**, presumably formed by regioselective tosylation of the primary alcohol, followed by a benzyl sulfonium-ion intermediate. The hydroxyl groups of **19a** were deprotected by Birch reduction to furnish the thia-spiroheterocycle **20a**. In a similar way, the spiro compound **20b** was synthesized (Scheme 1). Compound **19a** was also transformed into its methoxymethyl derivative **19c** for future use (Scheme 1).

The stereochemistry of **20a** and **19b** was confirmed on the basis of NOE studies (Fig. 8). For example, the *syn* nature of H-2a, H-3, H-4, and H-9a in **20a** was made evident by the strong correlations observed between H-9a/H-4 and H-9a/H-3. A strong NOE with H-9a/H-6 was also observed, indicating the *syn* relationship of these two protons.

The synthesis of the aza-spiroheterocycle was examined next. Unlike the enolate of the α-thio ketone that formed toward the α-substituent predominantly, the enolates of the α-amino ketones **21** and **22** (Fig. 9) were not readily accessible by conventional enolization techniques.[20] Thus, the β-ketoester **23** was employed as a functional equivalent of **21** to react with the aldehyde **14** (Scheme 2). We reasoned that a Curtius rearrangement[21] would convert the carboxylate to an amine-derived functional group. Thus, aldol condensation of **23** with **14** gave, after acylation of the hydroxyl group, the four possible diastereomers **24a–d** in a ratio of 30:6:5:1 (based on weight and NMR spectroscopic analysis). No other product was obtained. The major product was presumably obtained through a six-membered ring transition state and the stereochemical course of



Scheme 1.

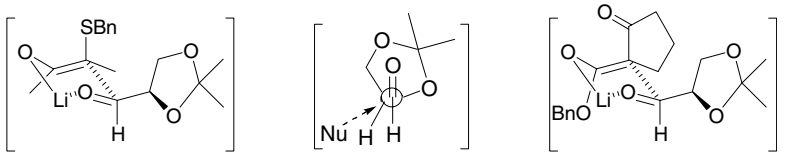


Figure 7. Putative transition states for the aldol reaction.

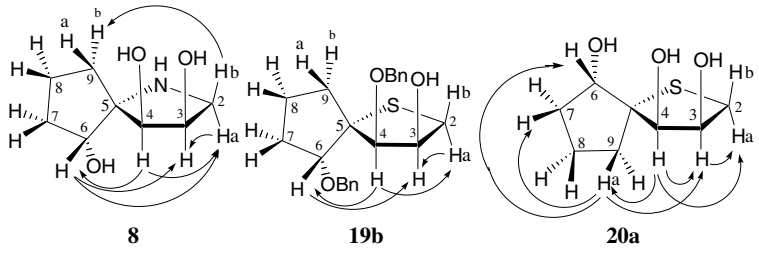
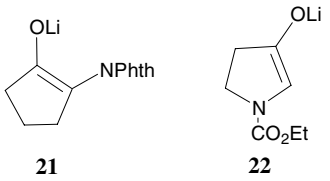


Figure 8. Observed NOE correlations for compounds **8**, **19b**, and **20a**.

this aldol reaction corresponds to that predicted by the Felkin-Anh model (Fig. 7).[19] The optically pure **24d** was isolated by silica chromatography from the mixture of its diastereomers **24a**–**c** which was inseparable. The ketone **24d** was reduced stereoselectively to the alcohol **25** which was acylated subsequently. Compound **25** was converted to the benzyl carbamate **26** by a Curtius rearrangement reaction. Deprotection of **26** and conver-

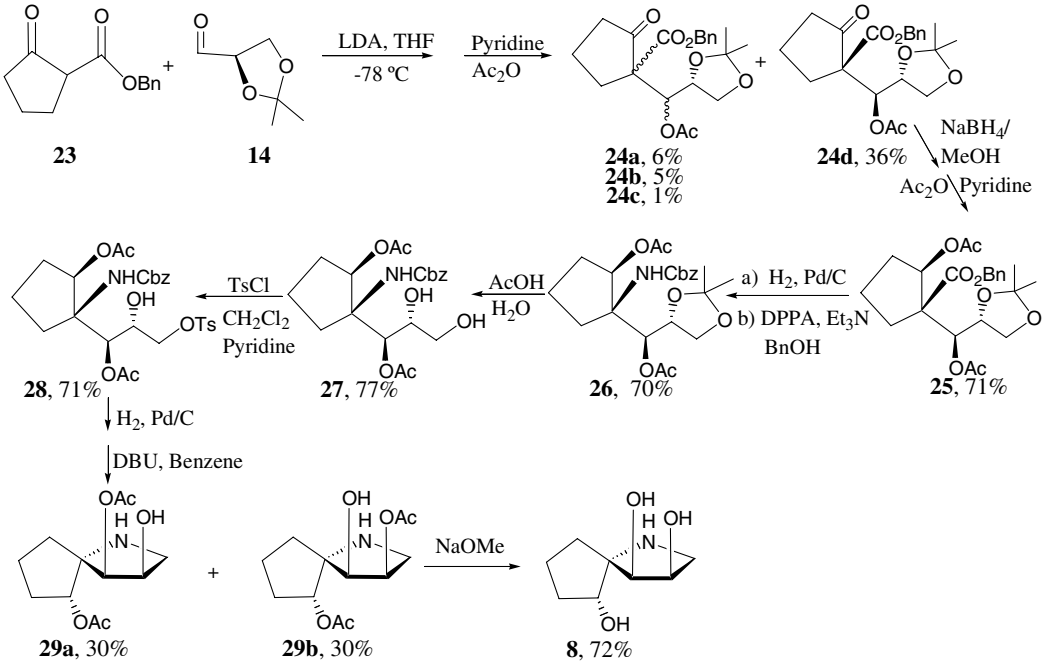


21 22

Figure 9. Structures of enolates **21** and **22**.

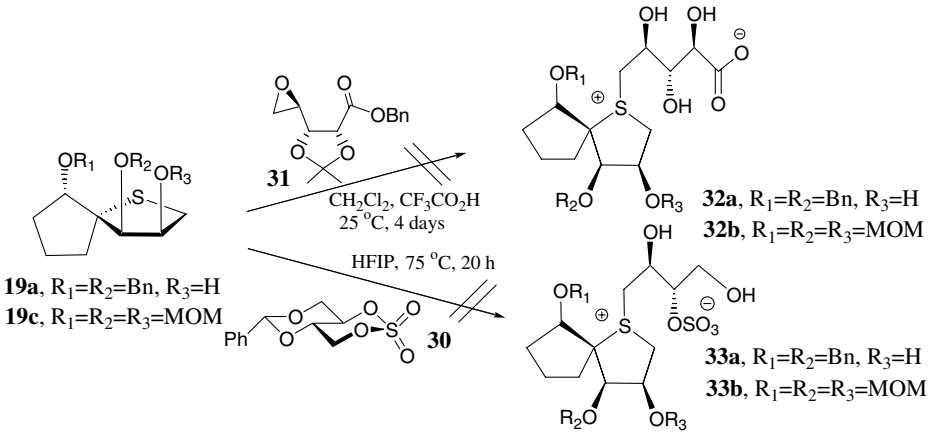
sion of the resulting alcohol **27** to the tosylate **28** utilized standard procedures. The amine in **28** was released and subsequently treated, without purification, with DBU to produce the desired spirocycles **29a** and **29b** as a 1:1 inseparable mixture that was subsequently deacylated to furnish the target compound **8**. As with compound **19b**, the stereochemistry at C-4, C-5, and C-6 in **8** was confirmed on the basis of NOE studies (Fig. 8) by the strong correlations observed between H-6/H-4 and H-6/H-3. A strong NOE between H-3/H-2a indicated a *syn* relationship of these two protons; a weak NOE was also observed between H-3 and H-2b, as usually observed in pyrrolidine derivatives.[22]

The synthesis of analogues of salacinol **1** was examined next. However, despite many attempts under a variety of conditions, the coupling reactions of the compounds **19a** or **19c** with the cyclic sulfate **30** or the epoxide **31** failed to yield the protected precursors of analogues of salacinol **1**, **32a**/**32b**, or **33a**/**33b** (Scheme 3).



23 **14** **24a**, 6% **24b**, 5% **24c**, 1% **24d**, 36% **25**, 71% **26**, 70% **27**, 77% **28**, 71% **29a**, 30% **29b**, 30% **8**, 72%

Scheme 2.



19a, R_1=R_2=Bn, R_3=H
19c, R_1=R_2=R_3=MOM

32a, R_1=R_2=Bn, R_3=H
32b, R_1=R_2=R_3=MOM

33a, R_1=R_2=Bn, R_3=H
33b, R_1=R_2=R_3=MOM

Scheme 3.

Compounds **8**, **20a**, and **20b** were tested for inhibition of human maltase glucoamylase, a critical intestinal enzyme involved in the breakdown of maltooligosaccharides to glucose, as well as for inhibition of Golgi mannosidase II. These compounds did not show effective inhibition of either enzyme, presumably because of poor fit in the respective active sites.[23]

3. Experimental

3.1. (2*R*)-2-Benzylsulfanyl-2-[(*R*)-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-hydroxymethyl]-cyclopentanone (15b) and (2*S*)-2-benzylsulfanyl-2-[(*R*)-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-hydroxymethyl]-cyclopentanone (15a)

To a solution of diisopropylamine (0.74 mL) in dry THF (13.4 mL) was added 2.0 M *n*-BuLi (2.6 mL) at 0 °C. After 10 min, the solution was cooled to −70 °C, and 2-benzylsulfanylcyclopentanone (0.96 g, 4.65 mmol) was added over 3 min. After the mixture had been stirred for 2 h at −70 °C, isopropylidene-D-glyceraldehyde (0.604 g, 1.0 equiv) was slowly added and the mixture was stirred for 20 min. The reaction was quenched by the addition of a satd aq $NaHCO_3$, the mixture was extracted with ether, and the ether layer was concentrated. The crude product was purified by column chromatography (hexanes–EtOAc, 2:1) to afford **15a** (0.93 g, 60%) and **15b** (0.31 g, 22%) as colorless oils. Compound **15a** $[\alpha]_D$ −11 (*c* 0.02, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.34–7.22 (5H, m, Ar), 4.19 (1H, dd, $J_{4',5'a} = 6.4$ Hz, $J_{5'a,5'b} = 8.5$ Hz, H-5′a), 4.13 (1H, ddd, $J_{4',5'b} = 5.0$ Hz, H-4′), 3.97 (1H, dd, H-5′b), 3.91 (1H, d, $J_{A,B} = 12.2$ Hz, SCH_2Ph), 3.79 (1H, d, $J_{4',6'} = 8.1$ Hz, H-6′ C*H*OH), 3.68 (1H, d, SCH_2Ph), 2.58 (1H, dd, $J_{4a,5a} = 8.3$ Hz, $J_{5a,5b} = 18.7$ Hz, H-5a), 2.35 (1H, dd, $J_{4b,5b} = 9.1$ Hz, H-5b), 2.67 (1H, m, H-3a), 2.06 (1H, m, H-4a), 1.95 (1H, m, H-4b), 1.80 (1H, dd, $J_{3a,3b} = 14.1$ Hz, $J_{3a,4b} = 6.8$ Hz, H-3b), 1.34 (1H, s, CCH_3), 1.34 (1H, s, CCH_3). ^{13}C NMR ($CDCl_3$) δ: 211.87 (*C*=O), 137.25 (C_{ipso}), 129.34–127.65 ($5C_{Ar}$), 109.98 ($C(CH_3)_2$), 75.75 (C-4′), 73.35 (C-6′), 68.46 (C-5′), 60.40 (C-2), 36.89 (C-5), 33.66 (S*C*H$_2$Ph), 31.35 (C-3), 26.00, 25.53 (2*C*H$_3$), 18.00 (C-4). Anal. Calcd for $C_{18}H_{24}O_4S$: C, 64.26; H, 7.19. Found: C, 64.38; H, 7.09. Compound **15b** $[\alpha]_D$ +53 (*c* 0.03, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.34–7.22 (5H, m, Ar), 4.56 (1H, ddd, $J_{4',5'a} = 6.4$ Hz, $J_{4',5'b} = 8.2$ Hz, $J_{4',6'} = 2.6$ Hz, H-4′), 4.45 (1H, d, H-6′ C*H*OH), 3.90 (2H, m, H-5′a, H-5′b), 3.79 (1H, d, $J_{A,B} = 12.3$ Hz, SCH_2Ph), 3.66 (1H, d, SCH_2Ph), 2.63 (1H, dd, $J_{4a,5a} = 8.3$ Hz, $J_{5a,5b} = 18.8$ Hz, H-5a), 2.41 (1H, m, H-3a), 2.20 (1H, m, H-5b), 2.08 (1H, m, H-4a), 1.94 (1H, m, H-4b), 1.50 (1H, dd, $J_{3a,3b} = 13.4$ Hz, $J_{3a,4a} = 6.6$ Hz, H-3b), 1.41 (1H, s, CCH_3), 1.35 (1H, s, CCH_3). ^{13}C NMR ($CDCl_3$) δ: 211.71 (*C*=O), 136.97 (C_{ipso}), 129.37–127.54 ($5C_{Ar}$), 108.37 ($C(CH_3)_2$), 76.00 (C-4′), 67.86 (C-6′), 63.73 (C-5′), 57.71 (C-2), 36.18 (C-5), 33.66 (S*C*H$_2$PH), 29.24 (C-3), 26.61, 25.90 (2*C*H$_3$), 18.26 (C-4). Anal. Calcd for $C_{18}H_{24}O_4S$: C, 64.26; H, 7.19. Found: C, 64.58; H, 6.86.

3.2. (1*S*,2*R*)-2-Benzylsulfanyl-2-[(*R*)-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-hydroxymethyl]-cyclopentanol (16a)

To a solution of **15a** (200 mg, 0.595 mmol) in dry MeOH (20 mL) was added $NaBH_4$ (10 mg, 2.0 equiv) slowly at room temperature. When TLC showed the reaction to be complete, the solvent was removed. The residue was extracted with saturated NH_4Cl and CH_2Cl_2. The organic layer was concentrated to give **16a** as a colorless oil (170 mg, 85%). $[\alpha]_D$ −8 (*c* 0.02, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.39–7.22 (5H, m, Ar), 4.29 (1H, dt, $J_{1,OH} = 4.9$ Hz, $J_{1,5} = 8.1$ Hz, H-1), 4.25 (1H, m, H-4′), 4.23 (1H, m, H-5′a), 4.09 (1H, m, H-5′b), 3.99, 3.92 (2H, d, $J_{A,B} = 12.1$ Hz, 2SCH_2Ph), 3.67 (1H, dd, $J_{4',6'} = 6.4$ Hz, $J_{6',OH} = 5.9$ Hz, H-6′ C*H*OH), 1.98 (3H, m, H-5a, H-5b, H-3a), 1.78 (2H, m, H-3b, H-4b), 1.63 (1H, m, H-4a), 1.42 (3H, s, CCH_3), 1.37 (3H, s, CCH_3). ^{13}C NMR ($CDCl_3$) δ: 137.13 (C_{ipso}), 128.96–127.12 ($5C_{Ar}$), 109.11 ($C(CH_3)_2$), 81.30 (C-1), 73.35 (C-6′), 76.66 (C-4′), 67.49 (C-5′), 64.24 (C-2), 33.52 (S*C*H$_2$Ph), 32.02 (C-3), 30.66 (C-5), 26.65, 25.43 (2*C*H$_3$), 19.39 (C-4). Anal. Calcd for $C_{18}H_{26}O_4S$: C, 63.87; H, 7.74. Found: C, 63.58; H, 7.92.

3.3. (2*R*,3*R*)-3-Benzyloxy-3-[(1*R*,2*S*)-2-benzyloxy-1-benzylsulfanylcyclopentyl]-propane-1,2-diol (18a) and (2*R*,3*R*)-3-benzyloxy-3-[(1*S*,2*R*)-2-benzyloxy-1-benzylsulfanylcyclopentyl]-propane-1,2-diol (18b)

To a solution of **15a** (200 mg, 0.595 mmol) in dry MeOH (20 mL) was added $NaBH_4$ (10 mg, 2.0 equiv) slowly at room temperature. When TLC showed the reaction to be complete, the solvent was removed. The residue was extracted with saturated NH_4Cl and CH_2Cl_2. The organic layer was concentrated to give a colorless oil. The resulting compound **16a** was dissolved in dry DMF (5 mL), NaH (55 mg, 2.0 equiv) was added slowly at 0 °C, and the solution was stirred for 3 h. BnBr (0.23 mL, 2.0 equiv) was added dropwise and the solution was stirred at room temperature for 2 h. The reaction was quenched by the addition of MeOH and the mixture was concentrated. The residue was extracted with CH_2Cl_2 and brine, and the organic layer was concentrated to give a colorless oil. The resulting compound **17a** was dissolved in 80% acetic acid and heated at reflux for 1 h, after which the solvent was removed. The crude product was purified by column chromatography (hexanes–EtOAc, 2:1) to afford **18a** as a colorless oil (0.147 g, 52%). Compound **18a** $[\alpha]_D$ −4 (*c* 0.04, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.41–7.26 (15H, m, Ar), 4.76 (1H, d, $J_{A,B} = 11.0$ Hz, OCH_2Ph), 4.58 (1H, d, $J_{A,B} =$

11.6 Hz, OCH_2Ph), 4.56 (1H, d, OCH_2Ph), 4.48 (1H, d, OCH_2Ph), 4.29 (1H, t, $J_{2',3'} = 7.7$ Hz, H-2′), 4.13 (1H, m, H-2), 3.84 (1H, d, $J_{A,B} = 11.8$ Hz, SCH_2Ph), 3.81 (1H, dd, $J_{1a,1b} = 11.5$ Hz, $J_{1a,2} = 3.0$ Hz, H-1a), 3.76 (1H, d, SCH_2Ph), 3.77 (1H, dd, $J_{1b,2} = 3.8$ Hz, H-1b), 3.70 (1H, d, $J_{2,3} = 7.9$ Hz, H-3), 2.16–1.87 (5H, m, H-3′a, H-5′a, H-3′b, H-4′a, H-5′b), 1.60 (1H, m, H-4′b). ^{13}C NMR ($CDCl_3$) δ: 138.20, 138.10, 137.73 (3C$_{ipso}$), 129.60–127.50 (15C$_{Ar}$), 81.82 (C-2′), 80.06 (C-3), 75.58 (OCH$_2$Ph), 73.73 (C-2), 72.00 (OCH$_2$Ph), 64.13 (C-1′), 62.82 (C-1), 33.09 (SCH$_2$Ph), 33.01 (C-3′), 29.50 (C-5′), 20.52 (C-4′). Anal. Calcd for $C_{29}H_{34}O_4S$: C, 72.77; H, 7.16. Found: C, 72.59; H, 7.39. Compound **18b** was synthesized from **15b** similarly in three steps (58%). Compound **18b** $[\alpha]_D$ −3 (*c* 0.02, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.40–7.20 (15H, m, Ar), 4.75 (1H, d, $J_{A,B} = 11.1$ Hz, OCH_2Ph), 4.64 (1H, d, $J_{A,B} = 11.3$ Hz, OCH_2Ph), 4.59 (1H, d, OCH_2Ph), 4.39 (1H, d, OCH_2Ph), 4.26 (1H, m, H-2), 4.14 (1H, d, $J_{A,B} = 11.7$ Hz, SCH_2Ph), 4.13 (1H, t, $J_{2',3'} = 8.9$ Hz, H-2′), 3.91 (1H, d, SCH_2Ph), 3.87 (2H, m, 2H-1), 3.73 (1H, d, $J_{2,3} = 7.9$ Hz, H-3), 2.17 (2H, m, 2H-3′), 2.07 (1H, m, H-5′a), 2.00 (1H, m, H-4′a), 1.95 (1H, m, H-5′b), 1.63 (1H, m, H-4′b). ^{13}C NMR ($CDCl_3$) δ: 138.60, 138.50, 137.45 (3C$_{ipso}$), 129.49-127.20 (15C$_{Ar}$), 85.19 (C-2′, C-3), 75.61 (OCH$_2$Ph), 73.42 (C-2), 72.12 (OCH$_2$Ph), 64.13 (C-1′), 63.88 (C-1), 34.04 (SCH$_2$Ph), 32.57 (C-5′), 28.54 (C-3′), 19.03 (C-4′). Anal. Calcd for $C_{29}H_{34}O_4S$: C, 72.77; H, 7.16. Found: C, 72.43; H, 6.84.

3.4. (3*R*,4*S*,5*R*,6*S*)-4,6-Bis-benzyloxy-1-thia-spiro[4.4]-nonan-3-ol (19a) and (3*R*,4*S*,5*S*,6*R*)-4,6-bis-benzyloxy-1-thia-spiro[4.4]nonan-3-ol (19b)

To a solution of **18a** (0.9 g, 1.88 mmol) in CH_2Cl_2 (40 mL) and pyridine (2 mL) was added TsCl (0.36 g, 1.0 equiv). The mixture was stirred for 4 days. TLC showed that the reaction was complete. The organic solution was extracted with brine, the organic layer was dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography (hexanes–EtOAc, 4:1) to afford **19a** as a colorless oil (0.55 g, 79%). Compound **19a** $[\alpha]_D$ −4 (*c* 0.02, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.42–7.22 (10H, m, Ar), 4.81 (1H, d, $J_{A,B} = 11.0$ Hz, OCH_2Ph), 4.71 (1H, d, $J_{A,B} = 11.9$ Hz, OCH_2Ph), 4.55 (1H, d, OCH_2Ph), 4.49 (1H, m, H-3), 4.45 (1H, d, OCH_2Ph), 4.16 (1H, dd, $J_{6,7a} = 9.5$ Hz, $J_{6,7b} = 7.4$ Hz, H-6), 3.76 (1H, d, $J_{3,4} = 3.9$ Hz, H-4), 3.04 (1H, dd, $J_{2a,2b} = 11.6$ Hz, $J_{2a,3} = 4.5$ Hz, H-2a), 2.84 (1H, d, H-2b), 2.10 (1H, m, H-9a), 1.96 (1H, m, H-7a), 1.79 (1H, m, H-9b), 1.71 (1H, m, H-8a), 1.63 (1H, m, H-7b), 1.59 (1H, m, H-8b). ^{13}C NMR ($CDCl_3$) δ: 138.12, 137.13 (2C$_{ipso}$), 128.45-126.93 (10C$_{Ar}$), 84.67 (C-4), 78.35 (C-6), 72.24 (OCH$_2$Ph), 71.87 (OCH$_2$Ph), 71.24 (C-3), 65.31 (C-5), 37.15 (C-9), 35.40 (C-2), 27.10 (C-7), 19.19 (C-8). Anal. Calcd for $C_{22}H_{26}O_3S$: C, 71.32; H, 7.07. Found: C, 71.21; H, 7.22. Compound **19b** was synthesized from **18b** by a similar procedure (77%). Compound **19b** $[\alpha]_D$ −97 (*c* 0.01, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.42–7.22 (10H, m, Ar), 4.63 (1H, d, $J_{A,B} = 12.3$ Hz, OCH_2Ph), 4.45 (1H, d, $J_{A,B} = 11.5$ Hz, OCH_2Ph), 4.44 (1H, m, H-3), 4.43 (1H, d, OCH_2Ph), 4.34 (1H, d, OCH_2Ph), 3.76 (1H, d, $J_{3,4} = 4.1$ Hz, H-4), 3.65 (1H, t, $J_{6,7} = 8.0$ Hz, H-6), 3.04 (1H, dd, $J_{2a,2b} = 11.6$ Hz, $J_{2a,3} = 5.3$ Hz, H-2a), 2.88 (1H, dd, $J_{2b,3} = 5.2$ Hz, H-2b), 2.15 (1H, m, H-9a), 1.94 (2H, m, H-7a, H-9b), 1.82 (1H, m, H-8a), 1.59 (1H, m, H-8b), 1.52 (1H, m, H-7b). ^{13}C NMR ($CDCl_3$) δ: 138.68, 137.79 (2C$_{ipso}$), 128.80–127.97 (10C$_{Ar}$), 84.85 (C-4), 81.77 (C-6), 73.92 (OCH$_2$Ph), 72.33 (OCH$_2$Ph), 71.90 (C-3), 65.94 (C-5), 33.71 (C-2), 33.25 (C-9), 28.55 (C-7), 19.70 (C-8). Anal. Calcd for $C_{22}H_{26}O_3S$: C, 71.32; H, 7.07. Found: C, 71.60; H, 7.30.

3.5. (3*R*,4*S*,5*R*,6*S*)-1-Thia-spiro[4.4]nonane-3,4,6-triol (20a) and (3*R*,4*S*,5*S*,6*R*)-1-thia-spiro[4.4]nonane-3,4,6-triol (20b)

NH_3 was condensed into a two-neck round bottom flask at −78 °C, and lithium (1 cm wire) was added slowly. To the resulting blue solution, **19a** (190 mg, 0.51 mmol) in dry ether (5 mL) was added dropwise. The mixture was stirred for 0.5 h and then allowed to warm to room temperature to allow NH_3 to evaporate. At −78 °C, the reaction was quenched by the addition of MeOH. The mixture was concentrated and the crude product was purified by column chromatography (CH_2Cl_2–MeOH, 10:1) to afford **20a** as a colorless oil (61 mg, 61%). Compound **20a** $[\alpha]_D$ −16 (*c* 0.06, MeOH). ^{1}H NMR (CD_3OD) δ: 4.25 (1H, ddd, H-3), 4.20 (1H, t, $J_{6,7} = 7.1$ Hz, H-6), 3.86 (1H, d, $J_{3,4} = 3.8$ Hz, H-4), 2.97 (1H, dd, $J_{2a,2b} = 11.0$ Hz, $J_{2a,3} = 5.7$ Hz, H-2a), 2.70 (1H, dd, $J_{2b,3} = 4.4$ Hz, H-2b), 2.02 (1H, m, H-9a), 1.91 (1H, m, H-7a), 1.86 (1H, m, H-9b), 1.65 (1H, m, H-8a), 1.59 (1H, m, H-7b), 1.56 (1H, m, H-8b). ^{13}C NMR (CD_3OD) δ: 78.84 (C-4), 74.44 (C-3), 72.42 (C-6), 66.74 (C-5), 37.23 (C-9), 33.00 (C-2), 30.91 (C-7), 19.58 (C-8). Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42. Found: C, 50.84; H, 7.56. Compound **20b** was obtained from **19b** by a similar procedure (80%). Compound **20b** $[\alpha]_D$ −77 (*c* 0.01, MeOH). ^{1}H NMR (CD_3OD) δ: 4.36 (1H, ddd, $J_{2a,3} = 6.5$ Hz, $J_{2b,3} = 7.6$ Hz, $J_{3,4} = 3.5$ Hz, H-3), 3.74 (1H, t, $J_{6,7} = 6.7$ Hz, H-6), 3.73 (1H, d, H-4), 2.87 (1H, dd, $J_{2a,2b} = 10.2$ Hz, H-2a), 2.83 (1H, dd, H-2b), 2.26 (1H, m, H-9a), 1.95 (1H, m, H-7a), 1.85 (1H, m, H-9b), 1.65 (1H, m, H-8a), 1.56 (1H, m, H-8b), 1.52 (1H, m, H-7b). ^{13}C NMR (CD_3OD) δ: 78.22 (C-4), 76.95 (C-6), 74.95 (C-3), 68.10 (C-5), 32.53 (C-9, C-2), 32.09 (C-7), 19.29 (C-8). Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42. Found: C, 50.39; H, 7.29.

3.6. (1*R*)-1-[(*S*)-Acetoxy-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-methyl]-2-oxocyclopentane-carboxylic acid benzyl ester (24d) and its diastereomers (24a–c)

To a solution of diisopropylamine (0.68 mL) in dry THF (12.4 mL) at 0 °C was added 2 M *n*-BuLi in pentane (2.37 mL). After 10 min, the solution was cooled to −78 °C, and 2-oxocyclopentanecarboxylic acid benzyl ester (0.9 g, 4.13 mmol) was added over 3 min. After the solution had been stirred for 2 h at −78 °C, 2,3-*O*-isopropylidene-D-glyceraldehyde (0.536 g, 1.0 equiv) was added. The mixture was stirred for 30 min and then quenched by the addition of a satd aq $NaHCO_3$. The reaction mixture was extracted with ether twice. The organic layer was concentrated, the residue was redissolved in CH_2Cl_2 (5 mL), and Ac_2O (0.84 g, 2.0 equiv) and pyridine (0.65 g, 2.0 equiv) were added to the solution, and the mixture was stirred overnight. The reaction mixture was concentrated and the crude product was purified by column chromatography (hexanes–EtOAc, 3:1) to afford a mixture of **24a**, **24b** and **24c** (0.19 g, 6%, 5%, 1%) and **24d** (0.57 g, 36%) as colorless oils. Compound **24d** $[\alpha]_D$ −18 (*c* 0.03, MeOH). ^{1}H NMR ($CDCl_3$) δ: 7.38–7.28 (5H, m, Ar), 5.82 (1H, d, $J_{4',6'} = 6.7$ Hz, H-6′ AcOC*H*), 5.20 (1H, d, $J_{A,B} = 12.6$ Hz, OCH_2Ph), 5.04 (1H, d, OCH_2Ph), 3.97 (2H, m, H-4′, H-5′a), 3.86 (1H, m, H-5′b), 2.74 (1H, m, H-5a), 2.36 (1H, m, H-3a), 2.18 (2H, m, H-3b, H-5b), 2.02 (2H, m, 2H-4), 1.97 (3H, s, OCCH_3), 1.25, 1.26 (6H, s, C(CH_3)$_2$). ^{13}C NMR ($CDCl_3$) δ: 210.87 (CH_2*C*OC), 169.33, 166.74 (2*C*O_2), 135.56 (C_{ipso}), 128.77, 128.41, 127.95 (5C_{Ar}), 109.59 (*C*(CH_3)$_2$), 75.77 (C-4′), 74.34 (C-6′), 67.65 (O*C*H_2Ph), 67.50 (C-5′), 64.16 (C-1), 38.42 (C-3), 28.26 (C-5), 26.00, 25.59 (C(*C*H_3)$_2$), 20.89 (CO*C*H_3), 19.92 (C-4). Anal. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.35; H, 6.75. Compound **24a**–**c** Anal. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.29; H, 6.85.

3.7. (1*S*,2*R*)-2-Acetoxy-1-[(*S*)-acetoxy-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl]cyclopentane carboxylic acid benzyl ester (25)

To a solution of **24d** (0.67 g, 1.72 mmol) in MeOH (50 mL) was added $NaBH_4$ (130 mg, 2.0 equiv) slowly. When TLC showed that the reduction was complete, MeOH was removed. The residue was extracted with CH_2Cl_2 and saturated NH_4Cl. The organic layer was concentrated. CH_2Cl_2 (10 mL) and Ac_2O (0.35 g, 2.0 equiv) were added, and the resulting mixture was stirred overnight. The mixture was concentrated and the crude product was purified by column chromatography (hexanes–EtOAc, 3:1) to afford **25** as a colorless oil (0.53 g, 71%). Compound **25** $[\alpha]_D$ +5 (*c* 0.06, MeOH). ^{1}H NMR ($CDCl_3$) δ: 7.38–7.31 (5H, m, Ar), 5.53 (1H, d, $J_{4',6'} = 6.1$ Hz, H-6′), 5.45 (1H, t, $J_{2,3} = 5.2$ Hz, H-2), 5.18, 5.08 (2H, d, $J_{A,B} = 12.2$ Hz, OCH_2Ph), 4.10 (1H, ddd, H-4′), 3.88 (1H, dd, $J_{4',5'a} = 6.39$ Hz, $J_{5'a,5'b} = 8.20$ Hz, H-5′a), 3.69 (1H, dd, $J_{4',5'b} = 7.32$ Hz, H-5′b), 2.39 (1H, m, H-5a), 1.94 (2H, m, H-5b, H-3a), 1.77 (1H, m, H-4a), 1.63 (1H, m, H-3b), 1.55 (1H, m, H-4b). ^{13}C NMR ($CDCl_3$) δ: 172.37, 170.23, 169.87 (3*C*=O), 135.50 (C_{ipso}), 128.80–128.49 (5C_{Ar}), 109.37 (*C*(CH_3)$_2$), 79.01 (C-2), 75.44 (C-4′), 74.11 (C-6′), 67.42 (*C*H_2Ph), 66.55 (C-5′), 59.43 (C-1), 32.49 (C-5), 30.26 (C-3), 26.32, 26.34 (C(*C*H_3)$_2$), 21.34 (C-4), 21.25 21.05 (2CO*C*H_3). Anal. Calcd for $C_{23}H_{30}O_8$: C, 63.58; H, 6.96. Found: C, 63.42; H, 7.04.

3.8. [(1*S*,2*R*)-2-Acetoxy-1-[(*S*)-acetoxy-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-methyl]cyclopentyl]-carbamic acid benzyl ester (26)

A mixture of **25** (200 mg, 0.46 mmol) and Pd/C (10 mg) in MeOH (10 mL) was stirred at room temperature under an atmosphere of H_2 for 10 h. The catalyst was filtered and the solvent was removed. The residue was dissolved in toluene (10 mL), and Et_3N (48 mg, 1.0 equiv) was added, followed by the addition of DPPA (308 mg, 1.0 equiv). After the mixture had been heated at reflux for 2 h, BnOH (50 mg, 1.0 equiv) was added. The mixture was heated at reflux for 12 h. The solvent was removed and the crude product was purified by column chromatography (hexanes–EtOAc, 3:1) to afford **26** as a colorless oil (140 mg, 70%). Compound **26** $[\alpha]_D$ +58 (*c* 0.01, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.38–7.30 (5H, m, Ar), 5.48 (1H, m, H-2), 5.40 (1H, d, $J_{4',6'} = 6.0$ Hz, H-6′), 5.06 (2H, s, OCH_2Ph), 4.26 (1H, dt, $J_{4',5'} = 6.47$ Hz, H-4′), 3.97 (1H, dd, $J_{5'a,5'b} = 8.10$ Hz, H-5′a), 3.79 (1H, dd, H-5′b), 2.18 (2H, m, H-3a, H-5a), 2.07 (7H, m, H-3b, 2COCH_3), 1.78 (1H, m, H-4a), 1.68 (2H, m, H-5b, H-4b), 1.31, 1.30 (6H, s, C(CH_3)$_2$). ^{13}C NMR ($CDCl_3$) δ: 170.43, 169.91 (2O*C*OCH_3), 154.89 (NH*C*O_2Bn), 136.54 (C_{ipso}), 128.75, 128.42, 128.33 (5C_{Ar}), 109.36 (*C*(CH_3)$_2$), 80.03 (C-1), 74.99 (C-4′), 74.17 (C-6′), 67.31 (O*C*H_2Ph), 66.75 (C-2), 66.45 (C-5′), 33.64 (C-3), 31.89 (C-5), 26.39, 25.44 (C(*C*H_3)$_2$), 21.40, 21.17 (2CO*C*H_3), 20.31 (C-4). Anal. Calcd for $C_{23}H_{31}NO_8$: C, 61.46; H, 6.95, N, 3.12. Found: C, 61.13; H, 7.25, N, 3.33.

3.9. [(1*S*,2*R*)-2-Acetoxy-1-[(1*S*,2*R*)-1-acetoxy-2,3-dihydroxypropyl]cyclopentyl]-carbamic acid benzyl ester (27)

A mixture of **26** (1.7 g, 3.78 mmol) in 80% acetic acid was heated at reflux for 10 min. The solution was concentrated under high vacuum. The crude product was purified by column chromatography (hexanes–EtOAc, 1:1) to afford **27** as a colorless oil (1.2 g, 77%). Compound **27** $[\alpha]_D$ +41 (*c* 0.12, acetone). ^{1}H NMR ($CDCl_3$) δ: 7.41–7.32 (5H, m, Ar), 5.48 (1H, d, $J_{1',2'} = 9.5$ Hz,

H-1′), 5.10, 5.07 (2H, d, $J_{A,B} = 12.3$ Hz, OCH_2Ph), 4.94 (1H, m, H-2), 3.67 (1H, ddd, $J_{2',3'a} = 2.89$ Hz, $J_{2',3'b} = 5.99$ Hz, H-2′), 3.54 (1H, dd, $J_{3'a,3'b} = 11.6$ Hz, H-3′a), 3.43 (1H, dd, H-3′b), 2.18 (1H, m, H-5a), 2.08 (6H, s, 2COCH_3), 2.03 (1H, m, H-3a), 1.77 (3H, m, H-3b, H-5b, H-4a), 1.70 (1H, m, H-4b). ^{13}C NMR ($CDCl_3$) δ: 173.00, 171.01 (2OCOCH$_3$), 156.20 (NHCO$_2$Bn), 136.10 (C_{ipso}), 128.75, 128.45, 128.13 (5C_{Ar}), 77.9 (C-2), 74.10 (C-1′), 70.50 (C-2′), 68.30 (C-1), 67.50 (CH$_2$Ph), 63.80 (C-3′), 36.04 (C-5), 32.00 (C-3), 21.40, 21.37 (2COCH$_3$), 19.95 (C-4). Anal. Calcd for $C_{20}H_{27}NO_8$: C, 58.67; H, 6.65, N, 3.42. Found: C, 58.85; H, 6.71, N, 3.46.

3.10. [(1*S*,2*R*)-2-Acetoxy-1-[(1*S*,2*R*)-1-acetoxy-2-hydroxy-3-(toluene-4-sulfonyloxy)propyl]cyclopentyl]-carbamic acid benzyl ester (28)

To a solution of **27** (200 mg, 0.489 mmol) in pyridine–CH_2Cl_2 (10 mL, 20:1) was added TsCl (94 mg, 1.0 equiv). The mixture was stirred for 4 days. When TLC showed the reaction to be complete, the mixture was extracted with a saturated NH_4Cl solution three times. The organic layer was concentrated and the crude product was purified by column chromatography (hexanes–EtOAc, 1:1) to afford **28** as a colorless oil (190 mg, 71%). Compound **28** $[\alpha]_D$ +21 (*c* 0.01, MeOH). ^{1}H NMR ($CDCl_3$) δ: 7.78 (2H, d, 2Ar), 7.35 (5H, m, Ar), 5.26 (1H, d, $J_{1',2'} = 9.0$ Hz, H-1′), 5.10, 5.06 (2H, d, $J_{A,B} = 12.1$ Hz, OCH_2Ph), 4.78 (1H, m, H-1), 4.00 (1H, dd, $J_{2',3'a} = 2.8$ Hz, $J_{3'a,3'b} = 9.8$ Hz, H-3′a), 3.92 (1H, dd, $J_{2',3'b} = 5.34$ Hz, H-3′b), 3.89 (1H, ddd, H-2′), 2.45 (3H, s, PhCH_3), 2.15 (2H, m, H-3a, H-5a), 2.05, 2.08 (6H, s, 2COCH_3), 1.78 (3H, m, H-3b, H-5b, H-4a), 1.65 (1H, m, H-4b). ^{13}C NMR ($CDCl_3$) δ: 170.30, 170.11 (2OCOCH$_3$), 156.45 (NHCO$_2$Bn), 145.10 (C_{ipso}-(SO_3Ph)), 136.09 (C_{ipso}(CH_2Ph)), 132.78 (C_{ipso}(PhCH$_3$)), 130.01–128.27 (9C_{Ar}), 77.3 (C-2), 73.70 (C-1′), 71.1 (C-2′), 68.74 (C-1), 68.7 (CH$_2$Ph), 67.4 (C-3′), 35.9 (C-3), 31.8 (C-5), 21.8 (PhCH$_3$), 21.24, 21.00 (2COCH$_3$), 19.23 (C-4). Anal. Calcd for $C_{27}H_{33}NO_{10}S$: C, 57.54; H, 5.90, N, 2.49. Found: C, 57.41; H, 6.07, N, 2.65.

3.11. (3*S*,4*R*,5*R*,6*R*)-Acetic acid 3-acetoxy-4-hydroxy-1-aza-spiro[4.4]non-6-yl ester (29a) and (3*S*,4*R*,5*S*,6*R*)-acetic acid 4-acetoxy-3-hydroxy-1-aza-spiro[4.4]non-6-yl ester (29b)

A mixture of **28** (100 mg, 0.177 mmol) and Pd/C (10 mg) in acetic acid (5 mL) was stirred under an atmosphere of H_2 for 10 h. When TLC showed the reaction to be complete, the catalyst was filtered and the solvent was removed under high vacuum. Benzene (10 mL) and DBU (54 mg, 2.0 equiv) were added and the mixture was heated at reflux for 3 h. The mixture was concentrated and the crude product was purified by column chromatography (hexanes–EtOAc, 1:1) to afford a 1:1 mixture of **29a** and **29b** as a white solid (27 mg, 60%). Compound **29a** ^{1}H NMR (CD_3OD) δ: 5.09 (1H, ddd, $J_{2a,3} = 6.2$ Hz, $J_{2b,3} = 4.4$ Hz, $J_{3,4} = 5.3$ Hz, H-3), 4.86 (1H, m, H-6), 4.2 (1H, d, H-4), 3.10 (1H, dd, $J_{2a,2b} = 12.6$ Hz, H-2a), 2.90 (1H, dd, H-2b), 2.20 (1H, m, H-7a), 2.18 (1H, m, H-9a), 2.07, 2.05 (2COCH_3), 1.73 (1H, m, H-8a), 1.72 (1H, m, H-7b), 1.65 (1H, m, H-8b), 1.62 (1H, m, H-9b). ^{13}C NMR (CD_3OD) δ: 171.32, 171.07 (2OCOCH$_3$), 80.73 (C-6), 75.24 (C-3), 73.22 (C-5), 72.21 (C-4), 47.82 (C-2), 31.57 (C-7), 30.32 (C-9), 20.17 (C-8), 19.91, 19.73 (2COCH_3). Compound **29b** ^{1}H NMR (CD_3OD) δ: 5.10 (1H, d, $J_{3,4} = 5.1$ Hz, H-4), 4.86 (1H, m, H-6), 4.30 (1H, ddd, H-3), 3.08 (1H, dd, $J_{2a,2b} = 11.8$ Hz, $J_{2a,3} = 6.0$ Hz, H-2a), 2.84 (1H, dd, $J_{2b,3} = 5.3$ Hz, H-2b), 2.34 (1H, m, H-9a), 2.12 (COCH_3), 2.08 (1H, m, H-7a), 2.00 (COCH_3) 1.73 (1H, m, H-8a), 1.65 (1H, m, H-8b), 1.64 (1H, m, H-7b), 1.5 (1H, m, H-9b). ^{13}C NMR (CD_3OD) δ: 171.28, 170.92 (2OCOCH$_3$), 80.65 (C-6), 75.39 (C-4), 72.52 (C-5), 70.91 (C-3), 50.24 (C-2), 31.68 (C-7), 30.63 (C-9), 20.17 (C-8), 19.91, 19.67 (2COCH_3). Anal. Calcd for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44, N, 5.44. Found: C, 55.78; H, 7.65, N, 5.76.

3.12. (3*S*,4*R*,5*S*,6*R*)-1-Aza-spiro[4.4]nonane-3,4,6-triol (8)

A mixture of **29a** and **29b** (25.7 mg, 0.1 mmol) was dissolved in dry MeOH (2 mL) and 1 M sodium methoxide (2 mL) was added. The mixture was stirred for 1 h at room temperature and the solvent was removed. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 1:1) to afford **8** as a colorless oil (13 mg, 72%). $[\alpha]_D$ −4.5 (*c* 0.02, MeOH). ^{1}H NMR (CD_3OD) δ: 4.22 (1H, ddd, H-3), 4.12 (1H, d, $J_{3,4} = 5.2$ Hz, H-4), 3.77 (1H, t, $J_{6,7} = 5.2$ Hz, H-6), 3.02 (1H, dd, $J_{2a,2b} = 11.9$ Hz, $J_{2a,3} = 6.2$ Hz, H-2a), 2.77 (1H, dd, $J_{2b,3} = 4.9$ Hz, H-2b), 2.19 (1H, ddd, $J_{8a,9a} = 7.2$ Hz, $J_{8b,9a} = 9.4$ Hz, $J_{9a,9b} = 13.5$ Hz, H-9a), 2.04 (1H, m, H-7a), 1.75 (1H, m, H-8a), 1.63 (2H, m, H-7b, H-8b), 1.49 (1H, ddd, $J_{8a,9b} = 5.0$ Hz, $J_{8b,9b} = 8.5$ Hz, H-9b). ^{13}C NMR (CD_3OD) δ: 77.98 (C-6), 74.67 (C-5), 72.78 (C-4), 72.34 (C-3), 50.12 (C-2), 32.52 (C-7), 30.37 (C-9), 19.65 (C-8). HRMS Calcd for $C_8H_{16}NO_3$ (M+H): 174.1125. Found: 174.1120.

3.13. 3,4,6-Tris-methoxymethoxy-1-thia-spiro[4.4]nonane (19c)

To a solution of compound **20a** (30 mg, 0.158 mmol) and *N*,*N*-diisopropylethylamine (0.4 mL) in DMF (1 mL) was added chloromethyl methyl ether (75 mg, 2.0 equiv) at room temperature. The mixture was stirred for 18 h and the solvent was removed. The residue was purified by column chromatography (hexanes–EtOAc,

5:1) to afford **19c** as a colorless oil (40 mg, 80%). Compound **19c** $[\alpha]_D$ −18 (*c* 0.06, MeOH). ^{1}H NMR ($CDCl_3$) δ: 4.95 (1H, d, $J_{A,B} = 7.1$ Hz, OCH_2O), 4.79 (1H, d, $J_{A,B} = 6.8$ Hz, OCH_2O), 4.70 (1H, d, OCH_2O), 4.69 (1H, d, $J_{A,B} = 6.7$ Hz, OCH_2O), 4.65 (1H, d, OCH_2O), 4.64 (1H, d, OCH_2O), 4.35 (1H, ddd, $J_{2a,3} = 7.2$ Hz, $J_{2b,3} = 9.8$ Hz, $J_{3,4} = 2.8$ Hz, H-3), 4.28 (1H, d, H-4), 3.43 (3H, s, CH_3), 3.43 (3H, s, CH_3), 3.38 (3H, s, CH_3), 2.98 (1H, dd, $J_{2a,2b} = 10.0$ Hz, H-2a), 2.95 (1H, dd, H-2b), 2.10 (1H, m, H-8a), 1.89 (3H, m, H-7a, H-7b, H-9a), 1.80 (1H, m, H-8b), 1.68 (1H, m, H-9b). ^{13}C NMR ($CDCl_3$) δ: 97.42, 96.12, 95.98 ($3OCH_2O$), 82.09 (C-6), 81.93 (C-4), 80.46 (C-3), 64.91 (C-5), 56.70, 55.90, 55.79 ($3CH_3$), 40.83 (C-8), 30.32 (C-2), 30.11 (C-7), 21.89 (C-9). HRMS Calcd for $C_{14}H_{26}O_6S$: 322.1452. Found: 322.1442.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2007.07.003.

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