Tetrahedron: *Asymmetry* 20 (2009) 1817–1823

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Regioselective synthesis and biological evaluation of spiro-sulfamidate glycosides from *exo*-glycals

Mahmoud Benltifa [a], Miklos De Kiss [b], Maria Isabel Garcia-Moreno [c], Carmen Ortiz Mellet [c], David Gueyrard [b,*], Anne Wadouachi [a,*]

[a] *Laboratoire des Glucides, UMR CNRS 6219, Université de Picardie Jules Verne, 33 Rue Saint-Leu, F-80039 Amiens, France*
[b] *Université de Lyon, ICBMS, Laboratoire de Chimie Organique 2-Glycochimie, UMR 5246, Université Claude Bernard Lyon 1-CNRS, Bâtiment 308(CPE), 43 Boulevard du 11 novembre 1918, F-69622 Villeurbanne, France*
[c] *Departamento de Química Orgánica, Facultad de Química, Universidad de Sevilla, C/ Profesor García González,1, E-41012 Sevilla, Spain*

ARTICLE INFO

Article history:
Received 9 June 2009
Accepted 7 July 2009
Available online 10 August 2009

ABSTRACT

We report the synthesis of spiro-sulfamidate glycosides from *exo*-glycals. This route is regioselective and furnishes an original class of spiro-hydantoin glycoside analogues. A biological evaluation of this family on a range of glycosidases shows that these compounds are weak but very selective inhibitors of α-glucosidase and amyloglucosidase.

1. Introduction

Glycosylidene-spiro-heterocycles are compounds of interest and have attracted considerable attention.[1] For example, the natural spiro-nucleoside (+)-hydantocidin **A**, isolated from a culture of *Streptomyces hygroscopicus,* exhibits non-toxically herbicidal and regulatory plant growth activities,[2] and an inhibitory activity of its 5′-phosphorylated metabolite against adenylosuccinate synthase has been observed.[3] Other sugar heterocycles related to hydantocidin **A** have been synthesized. Spiro-oxathiazole **B**,[4] spiroisoxazolines **C**,[5] spiro-hydantoin **D**,[6] and spiro-(thio)hydantoin **E**[7] glucosides have shown good inhibitory activities on glycogen phosphorylase (Fig. 1). More recently spiro-isoxazoline-C-disaccharides have shown inhibitions against α-amylase, and other α- and β-glucosidases.[8] The synthesis of spirobicyclic compounds requires regio- and stereoselective reactions that can be induced by the structure and the natural chirality of sugars. For example, intramolecular radical-based cyclization involving the anomeric center and the nucleobase of a modified nucleoside[9] or 1,3-dipolar cycloaddition of *exo*-glycals[5] has been studied for such transformation.

Intramolecular metal-catalyzed amination of the pseudo-anomeric C–H bond in C-glycoside carbamate and sulfamate esters has been used to synthesize spiro-oxazolidines and spiro-sulfamidates, respectively.[10] Whereas the cyclization of carbamoyloxymethyl glycosides gives the corresponding α- and β-spirooxazolidines, the analogous cyclization of sulfamoyloxymethyl glycosides was successful only in the case of the β-anomer, leading to the corresponding β-spiro-sulfamidates. Furthermore, these syntheses were only limited to 2-deoxysugar derivatives.

Considering the potential biological activities of spiro-heterocyclic glycosides, we focused our interest on the synthesis of spiro-sulfamidate glycosides via a synthetic pathway involving activation by the Burgess reagent of an intermediate diol obtained from methylene *exo*-glycals. This reagent is known as a mild and selective dehydrating agent of secondary and tertiary alcohols to afford the corresponding olefins.[11] It has been used in the synthesis of heterocyclic systems,[12] and as a source of heteroatoms in the synthesis of urethanes,[13] sulfamidates,[14] sulfamides,[15] and disulfides.[16]

Thus, *exo*-glycals,[17] which are useful intermediates for the synthesis of C-glycosides,[18] C-disaccharides,[19] and natural products,[2d] can be readily obtained using our recently reported methodology.[20] We recently developed the synthesis of methylene[20a] or substituted[20b] *exo*-glycals from sugar-derived lactones by employing Julia-Kocienski reagents.[21]

2. Results and discussion

The starting materials, hept-2-ulopyranoses **2a–c**[22] and hex-2-ulofuranoses **2d–e**, were prepared by a dihydroxylation reaction of the corresponding methylene *exo*-glycals **1a–e**, using a combination of OsO_4 and *N*-methylmorpholidine N-oxide (NMO) as co-oxidant (Scheme 1).[23]

The osmylation of the benzylated pyranosidic *exo*-glycals **1a** and **1c** was performed, the ^1H NMR and ^{13}C NMR indicate that the resulting products are α-epimers. In the case of acetylated *exo*-glucal **1b** and furanic *exo*-glycals **1d–e**, C-2 epimeric mixtures were obtained which could not been separated by chromatography. We first

* Corresponding authors. Tel.: +33 4 72 44 83 49; fax: +33 4 72 44 81 83 (D.G.); tel.: +33 3 22 82 75 27; fax: +33 3 22 82 75 60 (A.W.).
E-mail addresses: david.gueyrard@univ-lyon1.fr (D. Gueyrard), anne.wadouachi@u-picardie.fr (A. Wadouachi).

0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.07.012

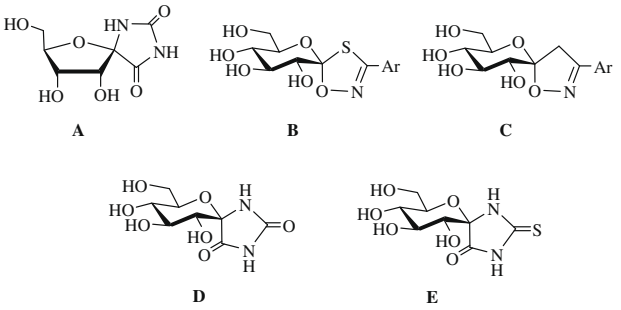
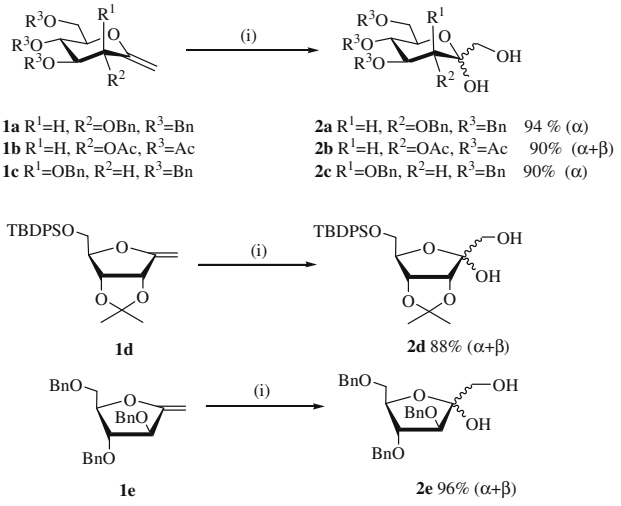


Figure 1.



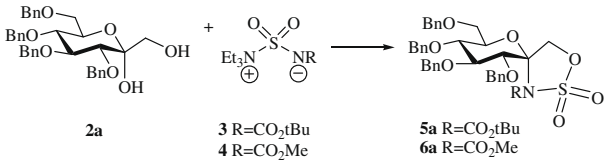
Scheme 1. Osmylation of *exo*-glycals. Reagents and condition: (i) OsO_4/NMO, acetone–H_2O (5/2), rt.

optimized the cyclic sulfamidation of the diol **2a** (Table 1) with *tert*-butyl and methyl *N*-(triethylammoniumsulfonyl)carbamates **3**[14a] and **4**, respectively.

The Burgess reagents **3** and **4** are oxidation and moisture sensitive.[24] Reactions were carried out at room temperature for very long time and furnished the corresponding spiro-sulfamidates **5a** and **6a** in very low yields (entries 1 and 4). In refluxing THF for 2 h, the yields increased and reached to 73% and 93%, respectively, with 4 equiv of Burgess reagents (entries 3 and 6). The sulfamidation of 3,4,5,7-tetra-*O*-benzyl-α-D-*gluco*-hept-2-ulopyranose **2a** was selective and gave only the corresponding α-spiro-sulfamidates. The heterocyclization involves a di-sulfonated intermediate **I** as shown in Scheme 2, which undergoes an intramolecular nucleophilic attack of the nitrogen anion on the more electrophilic center of the cyclic sulfamidate. The heterocyclization proceeds most likely by an S_N1-type mechanism, with the formation of an oxocarbenium ion **II**.

Under the above-mentioned optimal conditions, spiro-sulfamidate **6c** was synthesized in 66% yield as a separable mixture of α and β anomers (Scheme 2).

Table 1
Optimization of the synthesis of spiro-sulfamidates **5a** and **6a** from **2a**



2a — **3** R=CO_2tBu, **4** R=CO_2Me — **5a** R=CO_2tBu, **6a** R=CO_2Me

Entry	Burgess reagent	Equiv	T[a] (°C)	Time	Product (yield%)
1	**3**	2.5	rt	24	**5a** (10)
2	**3**	2.5	Reflux	2	**5a** (35)
3	**3**	4	Reflux	2	**5a** (73)
4	**4**	2.5	rt	24	**6a** (17)
5	**4**	2.5	Reflux	2	**6a** (41)
6	**4**	4	Reflux	2	**6a** (93)

[a] The reactions were conducted in THF.

Comparison of the ^{1}H NMR spectra of **6c**-**α** and **6c**-**β** revealed that the latter adopts a conformation of the pyranose ring from $^5C_8$, due to a probable equilibrium between the $^5H_4$ and $^4H_5$ half-chair conformations of oxocarbenium ions (Scheme 6). This change of conformation has already been reported in guanofosfocin analogues[25] and glycosylations of restricted mannuronate esters.[26] Glycosidation of heptulopyranose donors has been reported from benzylated compounds[27] and exclusively gave α-linked ketodisaccharide. The authors concluded that the stereochemical course of the glycosylation is neither governed by the type of promoter, nor by the nature of the leaving or protecting group at the C-2 and O-1 positions. They evaluated the effect of the ester group at C-3 and obtained an anomeric mixture. They proposed that these reactions proceed via an intermediate oxonium ion. The stereochemical outcome is mainly determined by the anomeric effect and steric factors.

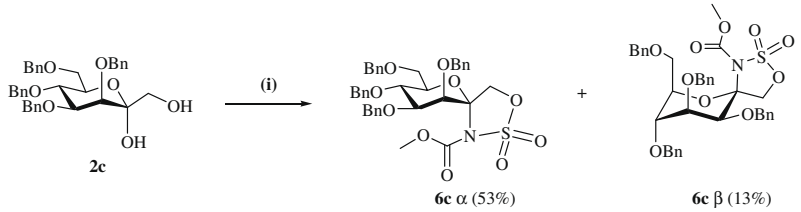
The acetylated hept-2-ulopyranose **2b** furnished a complex mixture when reacted with the Burgess-type reagent **3** or **4**.

The two hex-2-ulofuranose derivatives **2d** and **2e** also gave the corresponding spiro-sulfamidates as diastereoisomeric mixture (Scheme 3). The α,β mixture resulted in a nucleophilic attack by the nitrogen anion on a five-membered ring oxocarbenium ion which adopts a folded conformation[28] but showed no stereoselective nucleophilic substitution.

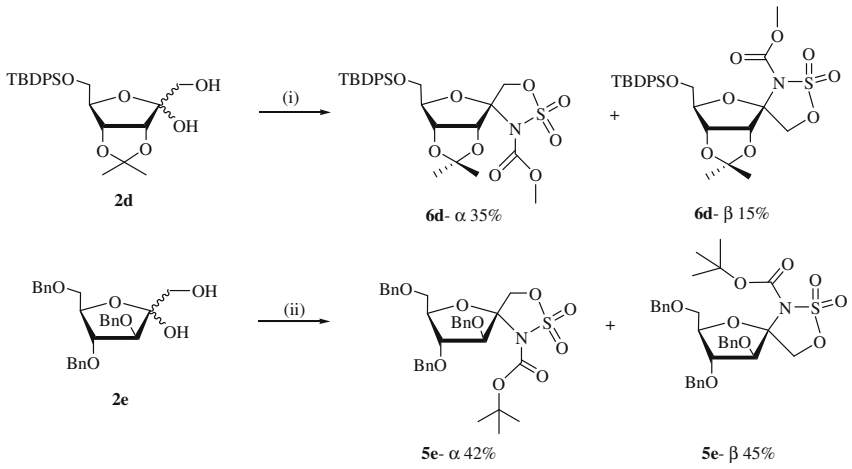
The full assignment of the protons has been performed using the combination of standard 2D experiments such as COSY, HSQC, and HMBC. Furthermore, the anomeric configuration has been determined by 2D NMR spectroscopy. For example, in the D-gluco series, NOESY experiment shows a correlation between H-1, H-1′ and H-3 which prove that the nitrogen atom is axial.

Similarly, the stereochemistry at the anomeric center has been proven by NOESY experiments for each series of compounds. NOESY correlations are listed in Figure 2.

From compound **5a**, deprotection of *N*-Boc with TFA in dichloromethane gave compound **7**, which was debenzylated by catalytic hydrogenation to afford the spiro-sulfamidate **8** in quantitative yield. The *N*-methoxycarbonyl protected spiro-sulfamidate **6a**



Scheme 2. Reagents: (i) **4** (4 equiv)/THF, reflux.



Scheme 3. Reagents: (i) **4** (4 equiv)/THF, reflux; (ii) **3** (4 equiv)/THF, reflux.

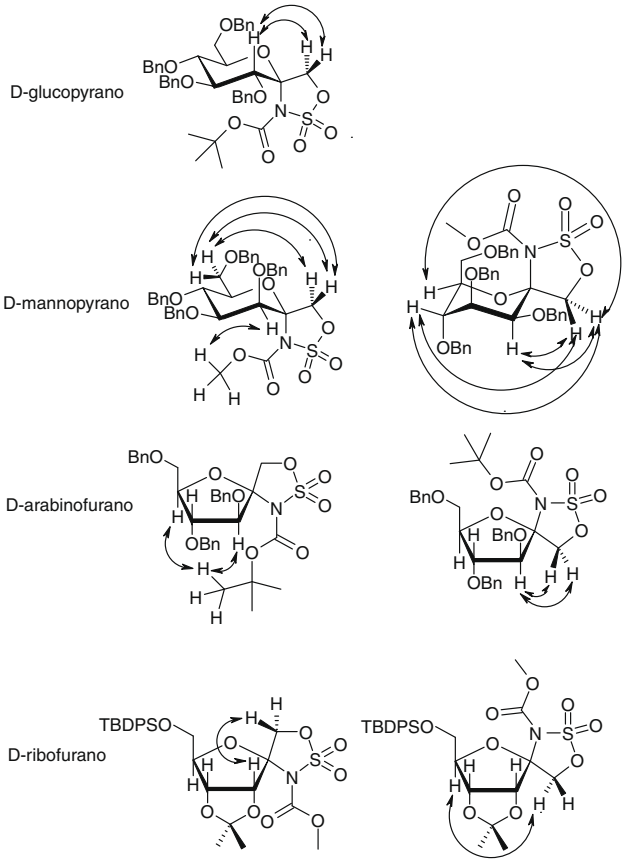


Figure 2. Noesy correlations of spiro-sulfamidates **5a**, **6c, 6d**, and **5e**.

was also debenzylated using the same conditions to furnish **9** in 93% yield (Scheme 4).

The two spiro-sulfamidates **8** and **9** were assayed against a panel of glycosidases. The spiro-sulfamidate **8** behaved as a selective but weak competitive inhibitor of both α-glucosidase from yeast (maltase, K_i 190 μM) and amyloglucosidase from *Aspergillus Niger* (K_i 258 μM). No inhibition was observed against β-glucosidase (from almonds), β-glucosidase/β-galactosidase (from bovine liver, cytosolic), trehalase (from pig kidney), isomaltase (from yeast), α-galactosidase (from green coffee beans), α-mannosidase (from Jack beans), β-mannosidase (from *Helix pomatia*), or naringinase (β-glucosidase/α-L-rhamnosidase, *Penicillium decumbes*). These results confirm that compound **8** behaves as glucomimetic. This selectivity toward the α-glucosidases is in agreement with the linkage specificity previously encountered in spiro-glycosides.[29] Interestingly, the inhibition was totally abolished for the *N*-methoxycarbonyl derivative **9**, a strong influence of the presence of N-substituent on the biological activity was observed. This fact pointed out that the anomeric NH group can be establishing hydrogen bond interactions with complementary groups in the active site of glucosidases. On the other hand, the five-membered cyclic sulfamide group seems to be particularly well adapted for interacting with amino acids of proteins, which offers a possibility for further improvement of the molecular design (see Scheme 5).

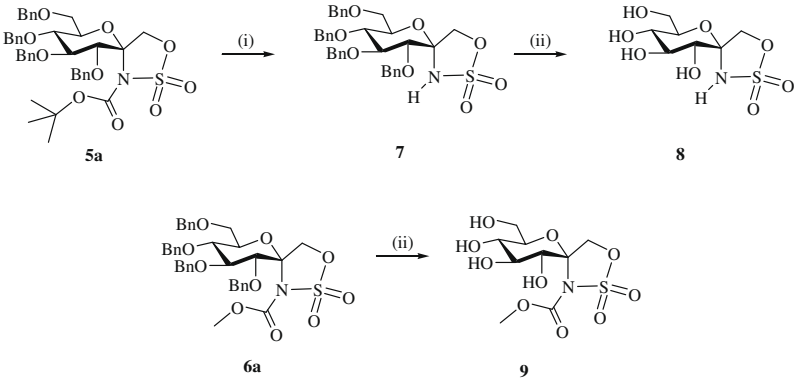
3. Conclusion

We have developed an original and regioselective route to spiro-sulfamidate glycosides from *exo*-glycals. This method was shown to occur with diverse sugar series (furanose and pyranose) and different types of protective groups, such as silyl and benzyl ethers and/or isopropylidene. In each case, the stereochemistry at the anomeric center has been determined by NMR experiments. Finally, two spiro-sulfamidates were tested on a range of glycosidases and they have shown a weak but very selective activity against α-glucosidase and amyloglucosidase.

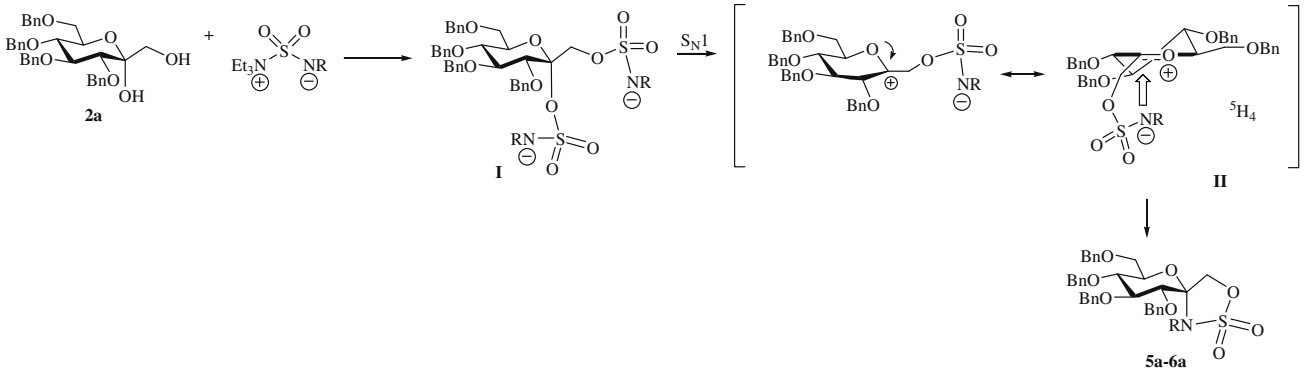
4. Experimental

4.1. General

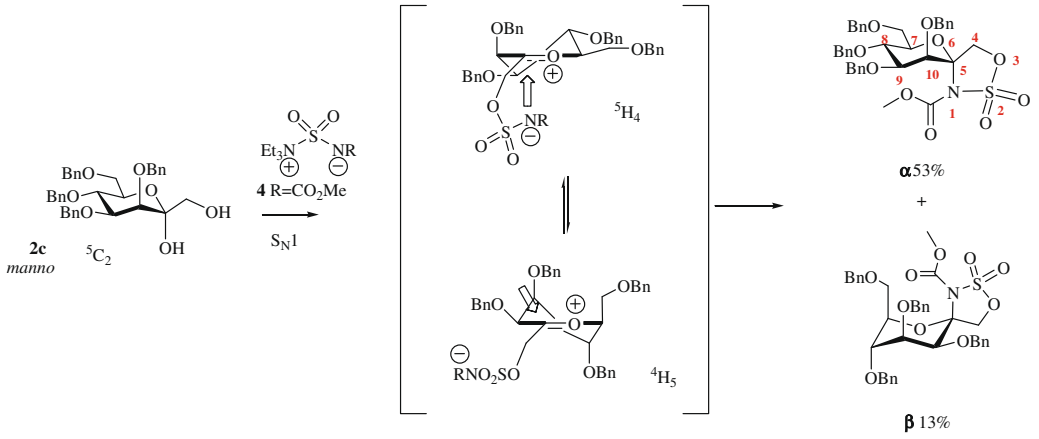
All chemicals were purchased from Aldrich or Acros (France). Thin-layer chromatography (TLC) was performed on Silica Gel 60 F_{254} (Merck) plates with visualization by UV light (254 nm) and/or charring with a vanillin-H_2SO_4 reagent. Preparative column chromatography was performed using 230–400 mesh Merck silica gel (purchased from Aldrich). Optical rotations were determined with a Jasco Dip 370 electronic micropolarimeter (10 cm cell). ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 WB spectrometer at 300 MHz and 75 MHz, respectively, and Noesy experiments were recorded using Bruker Avance DRX500. Chemical shifts are given as δ values with reference to tetramethylsilane (TMS). Low resolution electrospray mass spectra (ESI-MS) in the positive ion mode were obtained on a Waters-Micromass ZQ quadrupole instrument, equipped with an electrospray (Z-spray) ion source (Waters-Micromass, Manchester, UK). High resolution electrospray



Scheme 4. Reagents and conditions: (i) TFA–CH_2Cl_2 (1/3), rt, quant; (ii) H_2, Pd/C, MeOH, rt, quant.



Scheme 5.



Scheme 6.

experiments (ESI-HRMS) were performed on a Waters-Micromass Q-TOF *Ultima Global* hybrid quadrupole time-of-flight instrument, equipped with an electrospray (Z-spray) ion source (Waters-Micromass, Manchester, UK). All solvents were distilled before use.

The glycosidases α-glucosidase (from yeast), β-glucosidase (from almonds), β-glucosidase/β-galactosidase (from bovine liver, cytosolic), trehalase (from pig kidney), isomaltase (from yeast), amyloglucosidase (from *A. Niger*), α-galactosidase (from green coffee beans), α-mannosidase (from Jack beans), β-mannosidase (from *H. pomatia*), and naringinase (*P. decumbes*) used in the inhibition studies, as well as in the corresponding *o*- and *p*-nitrophenyl glycoside substrates were purchased from Sigma Chemical Co. Inhibitory potencies were determined by spectrophotometrically measuring the residual hydrolytic activities of the glycosidases against the respective *o*- (for β-glucosidase/β-galactosidase from bovine liver) or *p*-nitrophenyl α- or β-D-glycopyranoside or α,α′-trehalose (for trehalase), in the presence of the corresponding spiro-sulfamidate derivative. Each assay was performed in phosphate buffer or phosphate-citrate buffer (for α- or β-mannosidase and amyloglucosidase) at the optimal pH for each enzyme. The K_m values for the different glycosidases used in the tests and the corresponding working pHs are listed herein: α-glucosidase (yeast), K_m = 0.35 mM (pH 6.8); isomaltase (yeast) K_m = 1.0 mM (pH 6.8), β-glucosidase (almonds), K_m = 3.5 mM (pH 7.3); β-glucosidase/β-galactosidase (bovine liver), K_m = 2.0 mM (pH 7.3); α-galactosidase (coffee beans), K_m = 2.0 mM (pH 6.8); trehalase (pig kidney), K_m = 4.0 mM (pH 6.2); amyloglucosidase (*A. niger*), K_m = 3.0 mM (pH 5.5); β-mannosidase (*H. pomatia*), K_m = 0.6 mM

(pH 5.5); α-mannosidase (jack bean), K_m = 2.0 mM (pH 5.5); naringinase (*P. decumbes*), K_m = 2.7 mM (pH 6.8). The reactions were initiated by the addition of the enzyme to a solution of the substrate in the absence or presence of various concentrations of the inhibitor. After the mixture was incubated for 10–30 min at 37 or 55 °C, the reaction was quenched by the addition of 1 M Na_2CO_3 or a solution of Glc-Trinder (Sigma, for trehalase). The absorbance of the resulting mixture was determined at 405 nm or 505 nm. The K_i value and enzyme inhibition mode were determined from the slope of Lineweaver–Burk plots and double reciprocal analysis using a Microsoft Office Excel 2003 program.

4.2. 2,4-*O*-Isopropylidene-6-*tert*-butyldiphenylsilyl-D-*ribo*-hex-2-ulofuranose 2d

Following the procedure of osmylation as described in Ref. 23b, compound **2d** was isolated with 88% yield as a mixture of anomers (522.6 mg from 550 mg of **1d**). Colorless amorphous solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78–7.65 (m, 4H, Ph), 7.53–7.38 (m, 6H, Ph), 4.91 (dd, 1H, *J* = 6.92 Hz, *J* = 4.1 Hz, H-4α), 4.86 (dd, 1H, *J* = 5.9 Hz, *J* = 1.1 Hz, H-4β), 4.80 (d, 1H, *J* = 6.95 Hz, H-3α), 4.67 (d, 1H, *J* = 5.9 Hz, H-3β), 4.32 (m, 1H, H-5α), 4.26 (m, 1H, H-5β), 3.93–3.68 (m, 8H, H1aα, H1bα, H1aβ, H1bβ, H6aα, H6bα, H6aβ, H6bβ), 1.64, 1.45 (2CH_3, α), 1.53, 1.36 ((2CH_3, β)), 1.15 (s, 9H, *t*Bu β), 1.15 (s, 9H, *t*Bu α). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.8–135.6 (C_{Ar}H), 132.0, 129.9 (C*ipso*), 128.0–127.9 (C_{Ar}H), 115.0 (C_{IV}α), 112.7 (C_{IV}β), 106.1 (C-2β), 103.1 (C-2α), 86.5 (C-3β), 86.2 (C-5β), 82.8 (C-4β), 81.2 (C-3α), 81.0 (C-4α), 65.8, 63.8 (C-1α, C-6α), 65.3, 64.5 (C-1β, C-6β), 26.9 (3 × CH_3 α,β), 26.7 (CH_3α, 26.4 (CH_3β, 25.1 (CH_3α, 24.9 (CH_3β. HRMS: $[M+Na]^+$ calcd for $C_{25}H_{34}NO_6NaSi$: 481.2022, found $[M+Na]^+$ *m/z* 481.2024.

4.3. (5*S*,7*R*,8*R*,9*S*,10*R*)-8,9,10-Tribenzyloxy-7-benzyloxymethyl-1-*tert*-butoxycarbonyl-3,6-dioxa-2-thia-1-azaspiro [4.5]decan-2,2-dioxide 5a

To a solution of 3,4,5,7-tetra-*O*-benzyl-α-D-*gluco*-hept-2-ulopyranose **2a** (127.7 mg, 0.22 mmol) in anhydrous THF (5 mL) was added *tert*-butyl *N*-(triethyl-ammoniumsulfonyl)carbamate **3**[22] (251 mg, 0.89 mmol) at room temperature in a single portion. The resulting solution was placed immediately in an oil bath at 75 °C and stirred for 2 h. Upon completion of the reaction, the solvent was removed under reduced pressure and the residue was diluted in CH_2Cl_2 (30 mL), then washed with saturated aqueous NH_4Cl (15 mL). The organic phase was dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate = 7:3) to afford **5a** (86 mg, 73%) as a colorless syrup: $[\alpha]_D$ = +30 (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.21 (m, 20H, H*arom*), 4.94 (d, 1H, *J* = 9.5 Hz, H-4a), 4.90–4.52 (m, 9H, 4 × C*H*$_2$Ph, H-10), 4.56 (d, 1H, *J* = 9.5 Hz, H-4b), 3.91–3.76 (m, 3H, CH_2OBn, H-8),3.57 (m, 1H, H-7), 3.46(t, 1H, *J* = 9.9 Hz, H-9) 1.59 (s, 9H, 3 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.6 (C=O (Boc)), 138.2, 138.1, 137.7, 137.2 (4 × C_{Ar}), 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7 (C_{Ar}H), 92.0 (C-5), 86.4 (C_{IV} (Boc)), 83.0 (C-9), 77.0 (C-10), 76.7 (C-8), 75.7, 75.7, 75.4 (3 × CH_2Ph), 75.1 (C-7), 72.6 (CH_2Ph), 68.0 (CH_2OBn), 67.3 (C-4), 27.9 (3 × CH_3(Boc)). HRMS: $[M+Na]^+$ calcd for $C_{40}H_{45}NO_{10}NaS$: 754.2662, found $[M+Na]^+$ *m/z* 754.2640.

4.4. (5*S*,7*R*,8*R*,9*S*,10*R*)-8,9,10-Tribenzyloxy-7-benzyloxymethyl-1-methoxycarbonyl-3,6-dioxa-2-thia-1-aza-spiro-[4.5]decan-2,2-dioxide 6a

Using the general procedure for preparing **5a** from 3,4,5,7-tetra-*O*-benzyl-α-D-*gluco*-hept-2-ulopyranose **2a** (158 mg, 0.27 mmol) and commercial methyl *N*-(triethylammoniumsulfonyl)carbamate **4** (264 mg, 1.1 mmol), 178.1 mg (93%) of **6a** was obtained as a colorless syrup: $[\alpha]_D$ = −8 (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.23 (m, 20H, H*arom*), 4.98 (d, 1H, *J* = 9.6 Hz, H-4a), 4.92–4.55 (m, 8H, 4 × C*H*$_2$Ph), 4.61 (d, 1H, *J* = 9.6 Hz, H-4b), 3.90–3.3 (m, 4H, CH_3O, CHOBn, H8), 3.77 (dd, 1H, *J* = 11.5 Hz, *J* = 1.5 Hz, CHOBn), 3.61 (m, 1H, H-7), 3.53 (t, 1H *J* = 9.7 Hz, H-9). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.3 (C=O (CO_2Me)), 138.2, 137.9, 137.7, 137.1 (4 × C_{Ar}), 128.5, 128.4, 128.2, 128.1, 128.0, 127.8, 127.7 (C_{Ar}H), 92.4 (C-5), 83.3 (C-9), 76.8 (C-8), 76.3 (C-10), 75.9, 75.5, 75.4 (3 × CH_2Ph), 75.2 (C-7), 73.6 (CH_2Ph), 68.2 (CH_2OBn), 67.7 (C-4), 54.5 (OCH_3). HRMS: $[M+Na]^+$ calcd for $C_{37}H_{39}NO_{10}NaS$: 712.2192, found $[M+Na]^+$ *m/z* 712.2193.

4.5. (5*S*,7*R*,8*R*,9*S*,10*S*)-8,9,10-Tribenzyloxy-7-benzyloxymethyl-3,6-dioxa-1-methoxycarbonyl-2-thia-1-azaspiro[4.5]decan-2,2-dioxide 6c-α and (5*R*,7*R*,8*R*,9*S*,10*S*)-8,9,10-tribenzyloxy-7-benzyloxymethyl-3,6-dioxa-1-methoxycarbonyl-2-thia-1-azaspiro-[4.5]decan-2,2-di oxide 6c-β

Using the general procedure for preparing **5a** from 3,4,5,7-tetra-*O*-benzyl-α-D-*manno*-hept-2-ulopyranose **2c** (130.7 mg, 0.23 mmol) and commercial methyl *N*-(triethylammoniumsulfonyl)carbamate **4** (218.3 mg, 0.91 mmol), 84.6 mg (53%) of the epimer **6c**-**α** and 20 mg (13%) of the epimer **6c**-**β** were obtained as colorless syrups: Compound **6c**-**α**: $[\alpha]_D$ = +36 (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23–7.43 (m, 20H, H*arom*), 5.35 (d, 1H, *J* = 9.8 Hz, H-4a), 4.96 (d, 1H, *J* = 2.4 Hz, H-10), 4.68–4.50 (m, 8H, H-4b, H-7, 3CH_2Ph), 4.39 (m, 2H, CH_2Ph), 3.95 (d, 1H *J* = 2.5 Hz, H-9), 3.82 (s, 3H, OCH_3), 3.80 (d, 1H, *J* = 8.6 Hz, H-8), 3.67 (dd, 1H, *J* = 11.5 Hz, *J* = 2.6 Hz, CHOBn), 3.60 (dd, 1H, *J* = 11.5 Hz, *J* = 4.5 Hz, CHOBn). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.7 (C=O (CO_2Me)), 138.3, 137.6, 137.5, 137.0 (4 × C_{Ar}), 128.6, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7 (C_{Ar}H), 93.7 (C-5), 76.4 (C-8), 75.6 (C-9), 75.2 (C-7), 74.9 (C-4), 73.2, 72.6, 72.5 (3 × CH_2Ph), 71.7 (C-10), 71.5 (CH_2Ph), 69.4 (CH_2OBn), 54.4 (OCH_3). HRMS: [M+Na] calcd for $C_{37}H_{39}NO_{10}NaS$: 712.2192, found [M+Na] *m/z* 712.2186. Compound **6c**-**β**: $[\alpha]_D$ = +12 (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.25 (m, 20H, H*arom*), 5.04 (d, 1H, *J* = 10.5 Hz, C*H*Ph), 4.93 (d, 1H, *J* = 10.7 Hz, C*H*Ph), 4.77–4.54 (m, 6H, 3C*H*$_2$Ph), 4.40 (2d, 2H, *J* = 9.5 Hz, H-4a, H-4b), 4.16 (m, 2H, H-8, H-10), 3.98 (dd, 1H, *J* = 11.5 Hz, *J* = 4.3 Hz, CHOBn), 3.77 (m, 2H, H-9, CHOBn) 3.53 (m, 1H, H-7), 3.41 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.2 (C=O (CO_2Me)), 138.3, 137.8, 137.4, 137.3 (4 × C_{Ar}), 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.6 (C_{Ar}H), 91.7 (C-5), 80.1 (C-9), 77.7 (C-8), 76.7 (C-7), 76.4, 75.3, 73.5, 73.3 (4 × CH_2Ph), 73.1 (C-10), 71.8 (C-4), 68.9 (CH_2OBn), 53.8 (OCH_3). HRMS: $[M+Na]^+$ calcd for $C_{37}H_{39}NO_{10}NaS$: 712.2192, found $[M+Na]^+$ *m/z* 712.2202.

4.6. (5*S*,7*R*,8*S*,9*S*)-8,9-Dimethylmethylenedioxy-7-tert-butyldiphenylsilyloxymethyl-3,6-dioxa-1-methoxycarbonyl-2-thia-1-aza-spiro[4.4]nonan-2,2-dioxide 6d-α and (5*R*,7*R*,8*S*,9*S*)-8,9-dimethyl-methylenedioxy-7-tert-butyldiphenylsilyloxymethyl-3,6-dioxa-1-methoxycarbonyl-2-thia-1-azaspiro[4.4]nonan-2,2-dioxide 6d-β

Using the general procedure for preparing **5a** from 3,4-*O*-isopropylidene-7-*O*-*tert*-butyldiphenylsilyl-D-*ribo*-hex-2-ulopyranose **2d** (239.3 mg, 0.52 mmol) and commercial methyl *N*-(triethylammoniumsulfonyl)carbamate **4** (497.4 mg, 2.08 mmol) in THF (10 mL), 112.8 mg (35%) of the epimer **6d**-**α** and 49 mg (15%) of the epimer **6d**-**β** were obtained as colorless syrups: Compound **6d**-**α**: $[\alpha]_D$ = −28 (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (m, 5H, Ph), 7.47 (m, 5H, Ph), 5.11 (dd, 1H, *J* = 7.2 Hz, *J* = 3.7 Hz, H-8), 4.84 (d, 1H, *J* = 7.2 Hz, H-9), 4.76 (m, 1H, H-7), 4.43 (d, 1H, *J* = 9.5 Hz, H-4a), 4.33 (d, 1H, *J* = 9.5 Hz, H-4b), 3.89 (m, 4H, CHOSi, OCH_3), 3.82 (dd, 1H, *J* = 1.9 Hz, *J* = 11.7 Hz, CHOSi), 1.57 (CH_3), 1.43

(CH_3), 1.12 (s, 9H, *t*Bu). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.3 (C=O), 132.8, 132.5 (2 × C_{Ar}), 130.2, 130.1, 128.03, 128.0 ($C_{Ar}H$), 116.2 (C_{IV}), 98.9 (C-5), 88.8 (C_{IV} *t*Bu), 88.2 (C-7), 84.9 (C-9), 80.8 (C-8), 74.0 (C-4), 63.7 (CH_2OSi), 54.2 (OCH_3), 27.0 (3 × CH_3), 25.3, 24.6 (2 × CH_3). HRMS: $[M+Na]^+$ calcd for $C_{27}H_{35}NO_9NaSSi$: 600.1700, found $[M+Na]^+$ *m/z* 600.1706. Compound **6d-β**: $[\alpha]_D = -56$ (*c* 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.69 (m, 5H, Ph), 7.44 (m, 5H, Ph), 5.14 (d, 1H, *J* = 6.2 Hz, H-9), 4.93 (m, 2H, H-8, H-4a), 4.57 (d, 1H, *J* = 10.3 Hz, H-4b), 4.31 (dd, 1H, *J* = 5.2 Hz, *J* = 11.3 Hz, H-7), 3.77 (m, 2H, CH_2OSi), 3.77 (OCH_3), 1.55 (CH_3), 1.38 (CH_3), 1.09 (s, 9H, *t*Bu). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.3 (C=O), 135.7, 133.2 (2 × C_{Ar}), 129.7–127.7 ($C_{Ar}H$), 114.3 (C_{IV}), 98.1 (C-5), 88.8 (C-7), 86.8 (C_{IV} *t*Bu), 84.4 (C-9), 81.5 (C-8), 73.5 (C-4), 64.1 (CH_2O-Si), 54.6 (OCH_3), 26.8 (4 × CH_3), 25.3 (CH_3). HRMS: $[M+Na]^+$ calcd for $C_{27}H_{35}NO_9NaSSi$: 600.1700, found $[M+Na]^+$ *m/z* 600.1683.

4.7. (5*S*,7*R*,8*S*,9*R*)-8,9-Dibenzyloxy-7-benzyloxymethyl-1-*tert*-butoxycarbonyl-3,6-dioxa-2-thia-1-azaspiro[4.4]nonan-2,2-dioxide 5e-α and (5*S*,7*R*,8*S*,9*R*)-8,9-dibenzyloxy-7-benzyloxymethyl-1-*tert*-butoxycarbonyl-3,6-di-oxa-2-thia-1-azaspiro[4.4]nonan-2,2-dioxide 5e-β

Using the general procedure for preparing **5a** from 3,4,6-tri-*O*-benzyl-D-*arabino*-hex-2-ulopyranose **2e** (206 mg, 0.46 mmol) and *tert*-butyl *N*-(triethyl-ammoniumsulfonyl)carbamate **3**[22] (511.8 mg, 1.83 mmol) in THF (10 mL), 117.6 mg (42%) of the epimer **5e-α** and 126 mg (45%) of the epimer **5e-β** were obtained as a colorless syrup: Compound **5e-α**: $[\alpha]_D = +36$ (*c* 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.36 (m, 15H, H*arom*), 5.13 (d, 1H, *J* = 8.1 Hz, H-9), 4.94 (d, 1H, *J* = 9.6 Hz, H-4a), 4.82–4.44 (m, 6H, 3 × CH_2Ph), 4.38 (m, 2H, H-4b, H-7), 4.19 (dd, 1H, *J* = 8.1 Hz, *J* = 8.8 Hz, H-8), 3.67 (dd, 1H, *J* = 2.0 Hz, *J* = 11.2 Hz, CHOBn), 3.46 (dd, 1H, *J* = 2.6 Hz, *J* = 11.2 Hz, CHOBn), 1.61 (s, 9H, 3 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.7 (C=O), 138.9, 138.8, 136.7 (3 × C_{Ar}), 128.7, 128.5, 128.4, 128.4, 128.0, 127.8, 127.7 ($C_{Ar}H$), 95.9 (C-5), 86.2 (C_{IV} Boc), 83.3 (C-9), 79.8 (C-7), 79.4 (C-8), 73.6, 73.4, 72.9 (3 × CH_2Ph), 71.8 (C-4), 60.0 (CH_2OBn), 28.1 (3 × CH_3). HRMS: $[M+Na]^+$ calcd for $C_{32}H_{37}NO_9NaS$: 643.2087, found $[M+Na]^+$ *m/z* 634.2075. Compound **5e-β**: $[\alpha]_D = +12$ (*c* 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.34 (m, 15H, H*arom*), 4.83 (d, 1H, *J* = 11.2 Hz, C*H*Ph), 4.68–4.52 (m, 7H, H-4a, H-8, *CH*$_2$Bn), 4.42 (d, 1H, *J* = 9.1 Hz, H-4b), 4.13 (m, 2H, H-7, H-9), 3.86 (dd, 1H, *J* = 7.3 Hz, *J* = 10.6 Hz, CHOBn), 3.73 (dd, 1H, *J* = 3.6 Hz, *J* = 10.6 Hz, CHOBn), 1.56 (s, 9H, 3 × CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.5 (C=O), 137.9, 137.7, 136.8 (3 × C_{Ar}), 128.5, 128.4, 128.3, 128.2, 127.8, 127.7 ($C_{Ar}H$), 94.8 (C-5), 86.4 (C-9), 85.6 (C_{IV} Boc), 83.4 (C-8), 80.9 (C-7), 74.8 (C-4), 73.4, 73.2, 72.9 (3 × CH_2Ph), 70.7 (CH_2OBn), 27.9 (3 × CH_3). HRMS: $[M+Na]^+$ calcd for $C_{32}H_{37}NO_9NaS$: 643.2087, found $[M+Na]^+$ *m/z* 634. 2103.

4.8. (5*S*,7*R*,8*R*,9*S*,10*R*)-8,9,10-Tribenzyloxy-7-benzyl-oxymethyl-3,6-dioxa-2-thia-1-azaspiro[4.5]decan-2,2-di-oxide 7

Spiro-sulfamidate **5a** (57 mg, 0.08 mmol) was treated with TFA-CH_2Cl_2 (3 mL, 3:1) at rt for 2 h, then concentrated under reduced pressure and chromatographed on silica gel (cyclohexane/ethyl acetate = 7:3) to afford **7** (49 mg, quant.) as a colorless syrup: $[\alpha]_D = -18$ (*c* 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.39–7.21 (m, 20H, H*arom*), 5.18 (s, 1H, NH), 5.01–4.49 (m, 8H, 4 × C*H*$_2$Ph), 4.32 (d, 1H, *J* = 8.8 Hz, H-4a), 4.05 (d, 1H, *J* = 8.8 Hz, H-4b), 3.97 (m, 1H, H-7), 3.86 (m, 2H, H-8, CHOBn), 3.73 (m, 2H, H-9, CHOBn), 3.55 (d, 1H, *J* 9.1 Hz, H-10). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 137.7, 136.2 (4 × C_{Ar}), 128.9, 128.7, 128.6, 128.5, 128.1, 128.0, 127.9, 127.8 ($C_{Ar}H$), 92.8 (C-5), 84.5 (C-9), 77.3 (C-8), 77.0 (C-4), 76.3 (C-10), 75.9, 75.3, 75.0, 73.7 (4 × CH_2Ph), 73.0 (C-7), 67.8 (CH_2OBn). HRMS: $[M+Na]^+$ calcd for $C_{35}H_{37}NO_8NaS$: 654.2138, found $[M+Na]^+$ *m/z* 654.2159.

4.9. (5*S*,7*R*,8*R*,9*S*,10*R*)-3,6-Dioxa-8,9,10-trihydro-xy-7-hydroxymethyl-2-thia-1-azaspiro[4.5]decan-2,2-dioxide 8

A solution of **7** (49 mg, 0.07 mmol) in MeOH (7 mL) was hydrogenated at atmospheric pressure for 18 h using Pd/C (10 mg) as a catalyst. The suspension was filtered through Celite and concentrated. The residual syrup was purified by flash column chromatography (ethyl acetate/methanol 4:1) to afford **8** as a colorless syrup (20 mg, quant.): $[\alpha]_D = +26$ (*c* 0.1, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 4.66 (d, 1H, *J* 8.8 Hz, H-4b), 4.49 (d, 1H, *J* 8.8 Hz, H-4a), 3.80 (m, 2H, CH_2OH), 3.65 (m, 1H, H-7), 3.44 (m, 3H, H-10, H-9, H-2). ^{13}C NMR (75 MHz, CD_3OD): δ 92.9 (C-5), 76.7, 74.8 (C-9, C-10), 74.3 (C-7), 70.7 (C-8), 69.1 (C-4), 60.4 (CH_2OH). HRMS: $[M+Na]^+$ calcd for $C_7H_{13}NO_8NaS$: 294.0260, found $[M+Na]^+$ *m/z* 294.0268.

4.10. (5*S*,7*R*,8*R*,9*S*,10*R*)-8,9,10-Trihydroxy-7-hydroxymethyl-3,6-dioxa-1-methoxycarbonyl-2-thia-1-azaspiro[4.5]decan-2,2-dioxide 9

Using the general procedure for preparing **8** from **6a** (54.3 mg, 0.07 mmol), 34 mg of **9** was obtained as a colorless syrup: $[\alpha]_D = +19$ (*c* 0.1, MeOH). ^1H NMR (300 MHz, CD_3OD): δ 4.87 (m, 2H, H-4a et H-4b), 3.90 (s, 3H, CH_3), 4.45 (d, 1H, *J* = 9.8 Hz, H-10), 3.86 (dd, 1H, *J* = 2.1 Hz, *J* = 12.2 Hz, CHOH), 3.71 (dd, 1H, *J* = 5.2 Hz, *J* = 12.2 Hz, CHOH), 3.51 (ddd, 1H, *J* = 9.6 Hz, *J* = 5.2 Hz, *J* = 2.1 Hz, H-7), 3.38 (m, 1H, H-8), 3.32 (m, 1H, H-9). ^{13}C NMR (75 MHz, CD_3OD): δ 151.8 (C=O), 95.8(C-5), 78.6 (C-7), 76.0 (C-9), 71.5 (C-8), 70.9 (C-10), 69.6 (C-4), 63.4 (CH_2OH), 55.5 (OCH_3). HRMS: $[M+Na]^+$ calcd for $C_9H_{15}NO_{10}NaS$: 352.0314, found $[M+Na]^+$ *m/z* 352.0316.

Acknowledgments

The authors would like to thank Dr. B. Fenet for NMR experiments and Professor A. Vasella for his helpful discussion about *manno*-conformers

References

1. (a) Gasch, C.; Pradera, M. A.; Salameh, B. A. B.; Molina, J. L.; Fuentes, J. *Tetrahedron: Asymmetry* **2001**, *12*, 1267–1277; (b) Chang, C. F.; Yang, W. B.; Chang, C. C.; Lin, C. H. *Tetrahedron Lett.* **2002**, *43*, 6515–6519; (c) Sayago, F. J.; Pradera, M. A.; Gasch, C.; Fuentes, J. *Tetrahedron* **2006**, *62*, 915–921; (d) Taylor, R. J. K.; McAllister, G. D.; Franck, R. W. *Carbohydr. Res.* **2006**, *341*, 1298–1311; (e) Li, X.; Wang, R.; Wang, Y.; Chen, H.; Li, Z.; Ba, C.; Zhang, J. *Tetrahedron* **2008**, *64*, 9911–9920; (f) Somsak, L.; Nagy, V.; Hadady, Z.; Felfödi, N.; Docsa, T.; Gergely, P. *Front. Med. Chem.* **2005**, *2*, 253–272.
2. (a) Haruyama, H.; Takayama, T.; Kinoshita, T.; Kondo, M.; Nakajima, M.; Haneishi, T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1637–1640; (b) Nakajima, M.; Itoi, K.; Takamatsu, Y.; Kinoshita, T.; Okazaki, T.; Kawakubo, K.; Shindo, M.; Honma, T.; Tohjigamori, M.; Haneishi, T. *J. Antibiot.* **1991**, *44*, 293–300.
3. (a) Heim, D. R.; Cseke, C.; Gerwick, B. C.; Murdoch, M. G.; Green, S. B. *Pestic. Biochem. Physiol.* **1995**, *53*, 138–145; (b) Poland, B. W.; Lee, S. F.; Subramanian, M. V.; Siehl, D. L.; Anderson, R. J.; Fromm, H. J.; Honzatko, R. B. *Biochemistry* **1996**, *35*, 15753–15759.
4. (a) Praly, J. P.; Boyé, S.; Joseph, B.; Rollin, P. *Tetrahedron Lett.* **1993**, *34*, 3419–3420; (b) Praly, J. P.; Faure, R.; Joseph, B.; Kiss, L.; Rollin, P. *Tetrahedron* **1994**, *50*, 6559–6568; (c) Elek, R.; Kiss, L.; Praly, J. P.; Somsak, L. *Carbohydr. Res.* **2005**, *340*, 1397–1402; (d) Somsak, L.; Nagy, V.; Vidal, S.; Czifrak, K.; Berzsenyi, E.; Praly, J. P. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5680–5683.
5. Benltifa, M.; Vidal, S.; Gueyrard, D.; Goekjian, P. G.; Msaddek, M.; Praly, J. P. *Tetrahedron Lett.* **2006**, *47*, 6143–6147.
6. (a) Bichard, C. J. F.; Mitchell, E. P.; Wormald, M. R.; Watson, K. A.; Johnson, L. N.; Zographos, S. E.; Koutra, D. D.; Oikonomakos, N. G.; Fleet, G. W. J. *Tetrahedron Lett.* **1995**, *36*, 2145–2148; (b) Watson, K. A.; Chrysina, E. D.; Tsitsanou, K. E.; Zographos, S. E.; Archontis, G.; Fleet, G. W. J.; Oikonomakos, N. G. *Proteins: Struct. Funct. Bioinform.* **2005**, *61*, 966–983; (c) Archontis, G.; Watson, K. A.; Xie, Q.; Andreou, G.; Chrysina, E. D.; Zographos, S. E.; Oikonomakos, N. G.; Karplus, M. *Proteins: Struct. Funct. Bioinform.* **2005**, *61*, 984–998; (d) Gregoriou, M.; Noble, M. E. M.; Watson, K. A.; Garman, E. F.; Krulle, T. M.; De La Fuente, C.; Fleet, G. W. J.; Oikonomakos, N. G.; Johnson, L. N. *Protein Sci.* **1998**, *7*, 915–927.
7. (a) Somsak, L.; Kovacs, L.; Toth, M.; Osz, E.; Szilagyi, L.; Gyorgydeak, Z.; Dinya, Z.; Docsa, T.; Toth, B.; Gergely, P. *J. Med. Chem.* **2001**, *44*, 2843–2848; (b)

Oikonomakos, N. G.; Skamnaki, V. T.; Osz, E.; Szilagyi, L.; Somsak, L.; Docsa, T.; Toth, B.; Gergely, P. *Bioorg. Med. Chem.* **2002**, *10*, 261–268.
8. Zhang, P. Z.; Li, X. L.; Chen, H.; Li, Y. N.; Wang, R. *Tetrahedron Lett.* **2007**, *48*, 7813–7816.
9. (a) Gimisis, T.; Chatgilialoglu, C. *J. Org. Chem.* **1996**, *61*, 1908–1909; (b) Kittaka, A.; Tanaka, H.; Kato, H.; Nonaka, Y.; Nakamura, K. T.; Miyasaka, T. *Tetrahedron Lett.* **1997**, *38*, 6421–6424; (c) Gimisis, T.; Chatgilialoglu, C.; Castellari, C. *Chem. Commun.* **1997**, 2089–2090; (d) Kittaka, A.; Kato, H.; Tanaka, H.; Nonaka, Y.; Amano, M.; Nakamura, K. T.; Miyasaka, T. *Tetrahedron* **1999**, *55*, 5319–5344; (e) Chatgilialoglu, C.; Gimisis, T.; Spada, G. P. *Chem. Eur. J.* **1999**, *5*, 2866–2876; (f) Chatgilialoglu, C. *Farmaco* **1999**, *54*, 321–325.
10. Toumieux, S.; Compain, P.; Martin, O. R. *Tetrahedron Lett.* **2005**, *46*, 4731–4735.
11. Burgess, E. M.; Penton, H. R.; Taylor, E. A. *J. Am. Chem. Soc.* **1970**, *92*, 5224–5226.
12. (a) Brain, C. T.; Hallett, A.; Ko, S. Y. *Tetrahedron Lett.* **1998**, *39*, 127–130; (b) Hua, G.; Liu, D.; Xie, F.; Zhang, W. *Tetrahedron Lett.* **2007**, *48*, 385–399; (c) Li, J. J.; Li, J. J.; Li, J.; Trehan, A. K.; Wong, H. S.; Krishnananthan, S.; Kennedy, L. J.; Gao, Q.; Ng, A.; Robl, J. A.; Balasubramanian, B.; Chen, B. C. *Org. Lett.* **2008**, *10*, 2897–2900.
13. (a) Wood, M. R.; Kim, J. Y.; Books, K. M. *Tetrahedron Lett.* **2002**, *43*, 3887–3890; (b) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26–31; (c) Atkins, G. M.; Burgess, E. M. *J. Am. Chem. Soc.* **1972**, *94*, 6135–6141.
14. (a) Rinner, U.; Adams, D. R.; dos Santos, M. L.; Abboud, K. A.; Hudlicky, T. *Synlett* **2003**, 1247–1252; (b) Leisch, H.; Saxon, R.; Sullivan, B.; Hudlicky, T. *Synlett* **2006**, 445–449; (c) Nicolaou, K. C.; Huang, X.; Snyder, S. A.; Rao, P. B.; Bella, M.; Reddy, M. V. *Angew. Chem., Int. Ed.* **2002**, *41*, 834–838.
15. Nicolaou, K. C.; Longbottom, D. A.; Snyder, S. A.; Nalbanadian, A. Z.; Huang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 3866–3870.
16. Banfield, S. C.; Omori, A. T.; Leisch, H.; Hudlicky, T. *J. Org. Chem.* **2007**, *72*, 4989–4992.
17. Taillefumier, C.; Chapleur, Y. *Chem. Rev.* **2004**, *104*, 263–292.
18. (a) Nicotra, F.; Panza, L.; Russo, G. *Tetrahedron Lett.* **1991**, *32*, 4035–4038; (b) Faivre-Buet, V.; Eynard, I.; Nga, H. N.; Descotes, G.; Grouiller, A. *J. Carbohydr. Chem.* **1993**, *12*, 349–356; (c) Gervay, J.; Flaherty, T. M.; Holmes, D. *Tetrahedron* **1997**, *53*, 16355–16364.
19. (a) Rajanbabu, T. V.; Reddy, G. S. *J. Org. Chem.* **1986**, *51*, 5458–5461; (b) Lay, L.; Nicotra, F.; Panza, L.; Russo, G.; Caneva, E. *J. Org. Chem.* **1992**, *57*, 1304–1306; (c) Rubinstenn, G.; Mallet, J. M.; Sinaÿ, P. *Tetrahedron Lett.* **1998**, *39*, 3697–3700.
20. (a) Gueyrard, D.; Haddoub, R.; Salem, A.; Said Bacar, N.; Goekjian, P. G. *Synlett* **2005**, 520–522; (b) Bourdon, B.; Corbet, M.; Fontaine, P.; Goekjian, P. G.; Gueyrard, D. *Tetrahedron Lett.* **2008**, *49*, 747–749.
21. (a) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Tetrahedron Lett.* **1991**, *32*, 1175–1178; (b) Baudin, J. B.; Hareau, G.; Julia, S. A.; Lorne, R.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 856–878.
22. References for known compounds **2a**, **2c**: see Ref. 23 for **2e**: Yamanoi, T.; Misawa, N.; Matsuda, S.; Watanabe, M. *Carbohydr. Res.* **2008**, *343*, 1366–1372.
23. (a) Aebischer, B.; Bieri, J. H.; Prewo, R.; Vasella, A. *Helv. Chim. Acta* **1982**, *65*, 2251–2272; (b) Li, X.; Takahashi, H.; Ohtake, H.; Shiro, M.; Ikegami, S. *Tetrahedron* **2001**, *57*, 8053–8066.
24. Wipf, P.; Venkatraman, S. *Tetrahedron Lett.* **1996**, *37*, 4659–4662.
25. (a) Sugimura, H.; Natsui, Y. *Tetrahedron Lett.* **2003**, *44*, 4729–4732; (b) George, T. G.; Szolcsanyi, P.; Koenig, S. G.; Paterson, D. E.; Isshiki, Y.; Vasella, A. *Helv. Chim. Acta* **2004**, *87*, 1287–1298.
26. Codée, J. D. C.; de Jong, A. R.; Dinkelaar, J.; Overkleeft, H. S.; van der Marel, G. A. *Tetrahedron* **2009**, *65*, 3780–3788.
27. Heskamp, B. M.; van der Marel, G. A.; van Boom, J. H. *Synlett* **1992**, 713–715.
28. Hernadez-Garcia, L.; Quintero, L.; Höpfl, H.; Sosa, M.; Sartillo-Piscil, F. *Tetrahedron* **2009**, *65*, 139–144.
29. (a) Kapferer, P.; Birault, V.; Poisson, J. F.; Vasella, A. *Helv. Chim. Acta* **2003**, *86*, 2210–2227; (b) Gonzalez-Bello, C.; Castedo, L.; Canada, F. J. *Eur. J. Org. Chem.* **2006**, *4*, 1002–1011.