Synthesis and Glycosidase Inhibitory Activities of 5-(1′,4′-Dideoxy-1′,4′-imino-D-erythrosyl)-2-methyl-3-furoic Acid (= 5-[(3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylic Acid) Derivatives: New Leads as Selective α-L-Fucosidase and β-Galactosidase Inhibitors

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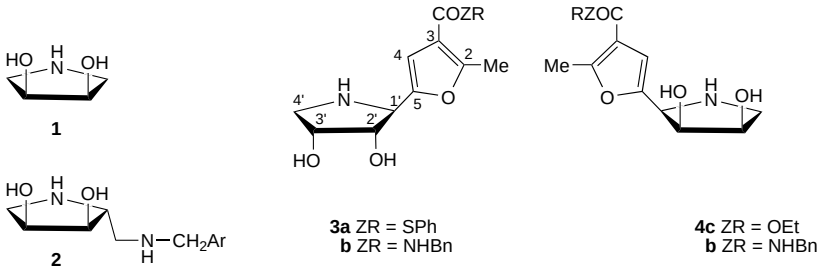
The *García-González* reaction of D-glucose and ethyl acetoacetate generated ethyl 5-[(1′*S*)-D-erythrosyl]-2-methyl-3-furoate (**5**), which was converted to ethyl 5-[(1′*R*)-1′,4′-dideoxy-1′,4′-imino-D-erythrosyl]-2-methyl-3-furoate (**3c**) and to ethyl 5-[(1′*S*)-1′,4′-dideoxy-1′,4′-imino-D-erythrosyl]-2-methyl-3-furoate (**4c**). Similar methods were developed to generate other carboxylic acid derivatives such as methyl (see **3e** and **4e**), isopropyl (see **3f**), and butyl esters (see **3g**), *S*-phenyl (see **3a**) and *S*-ethyl thioesters (see **3m**), *N*-benzylcarboxamides **3b** and **4b**, glycine-derived amide **3h**, and *N*-phenyl (see **3i**), *N*-isopropyl (see **3j** and **4j**), *N*,*N*-diethyl- (see **3k** and **4k**), and *N*-ethyl-carboxamides (see **3l**). All the new 5-(1′,4′-dideoxy-1′,4′-imino-D-erythrosyl)-3-furoic acid (= 5-[(3*S*,4*R*)-3,4-dihydroxypyrrolidin-2-yl)furan-3-carboxylic acid) derivatives **3** and **4** were assayed for inhibitory activity towards 25 commercially available glycosidases. Derivative **3a** with a *S*-phenyl thioester group is a good and selective α-L-fucosidase inhibitor ($K_i = 2-4$ μM), whereas **4b** (with a *N*-benzylcarboxamide group) is a good β-galactosidase inhibitor.

Introduction. – Derivatives of pyrrolidine-3,4-diols (= 1,4-dideoxy-1,4-iminoalditols) constitute an important class of glycosidase inhibitors [1] although, in some cases, there is a lack of selectivity due to the higher conformational flexibility compared to 1,5-dideoxy-1,5-iminoalditols and other imino-bicyclic structures. For instance, simple *meso*-pyrrolidine-3,4-diol (**1**) is a weak and nonselective inhibitor [2] that presents activity towards several glycosidases.



Approaches have been developed to increase selectivity in enzyme inhibition that consist of providing the dideoxy-iminosugar with some information about the shape and charge of the glycosyl moiety cleaved in the enzymatic hydrolysis and also that of

the aglycon itself. Dideoxy-imino-*C*-disaccharide mimetics fulfill these requirements, and several syntheses of this type of compounds have been reported [3]. Nevertheless, the use of these inhibitors present some inconveniences, such as critical reaction conditions and multiple-step sequences needed for their preparation. Furthermore, their preparation does not allow for the required molecular and configurational diversity needed for drug development.

To design more-active and more-specific enzyme inhibitors, we envisaged other alternatives like attaching to the pyrrolidine ring several moieties through hydrolytically stable C–C bonds, using easy and high-yielding reactions. We have found that pyrrolidinediols of type **2** with (benzylamino)methyl side chains [2] can be highly selective and competitive inhibitors of α-mannosidases, and we have presented a quick combinatorial approach for their preparation [4].

In a preliminary communication [5], we have reported that 5-[(1′*R*)-1′,4′-dideoxy-1′,4′-imino-D-erythrosyl]-2-methyl-3-furoic acid ester and amide derivatives[1]) (= 5-[(2*R*,3*S*,4*R*)-3,4-dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylic acid esters and -3-carboxamides) of type **3** are selective and competitive inhibitors of α-L-fucosidase from bovine epididymis and from human placenta. We have also found [6] that stereoisomeric derivatives of type **4** are specific inhibitors of various β-galactosidases. We describe here the details of the synthesis of these inhibitors that can be viewed as a new type of dideoxy-iminosugar-derived *C*-nucleoside analogue. We also prepared further derivatives and tested them for inhibitory activity towards 25 commercially available glycosidases. It appears that thioester **3a** and *N*-benzylcarboxamide **3b** are the most-potent α-L-fucosidase inhibitors found for this series ($K_i = 2-3$ μM) and **4b** and **4c** the most-potent β-galactosidase inhibitors ($K_i = 6-7$ μM). These compounds are leads in the search for better α-L-fucosidase and β-galactosidase inhibitors, a search that must probably involve changes of the furan-ring substitution and the introduction of a Me group at C(4′) of **3** generating (4′*S*) configuration and hydroxylated side chains at C(4′) of **4** if inhibitors as potent as deoxyfuconojirimycin and 1-deoxygalactonojirimycin (low nM range) are to be found [7].

Synthesis of the New Inhibitors. – For the synthesis of dideoxy-iminosugar-derived *C*-glycosides of heterocylces, we applied a methodology that implies a double functionalization of (polyhydroxyalkyl)-substituted heterocycles with appropriate leaving groups, followed by nucleophilic internal displacements. Thus, starting from the known furan derivative **5** obtained in a single step from D-glucose [8], selective tosylation of the primary-alcohol function (TsCl/pyridine, –15°, 2 h) provided tosyloxy derivative **6** in 57% yield (*Scheme 1*). Treatment of **6** with *N*-chlorosuccinimide (NCS) and dimethyl sulfide [9] (CH_2Cl_2, –20°) gave a mixture of chloro compounds **7** and **8** in a ratio of 1:1 that reacted with butylamine or benzylamine to give **9** or **10**, with the (1′*R*) (=β-D) configuration at the pseudoanomeric center, in 47% and 44% yield respectively. This result can be explained by the formation of an oxirane intermediate **11**

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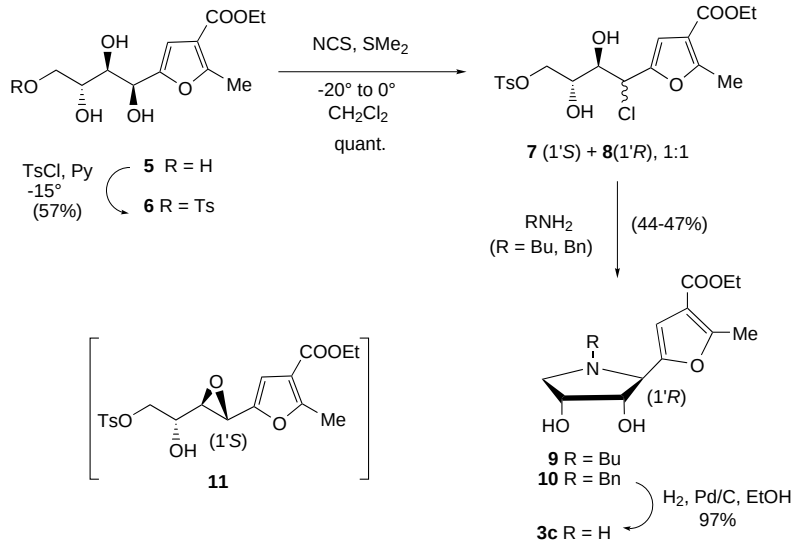
[1]) For convenience, *C*-glycoside names are used in the *General Part* and for the characterization of NMR spectra; for systematic names, see *Exper. Part*.

by 1,3-elimination of HCl. Debenzylation (H_2, Pd/C, EtOH) of **10** gave **3c** in 98% yield. Its structure was established by spectral data and confirmed by NOE experiments.

Scheme 1

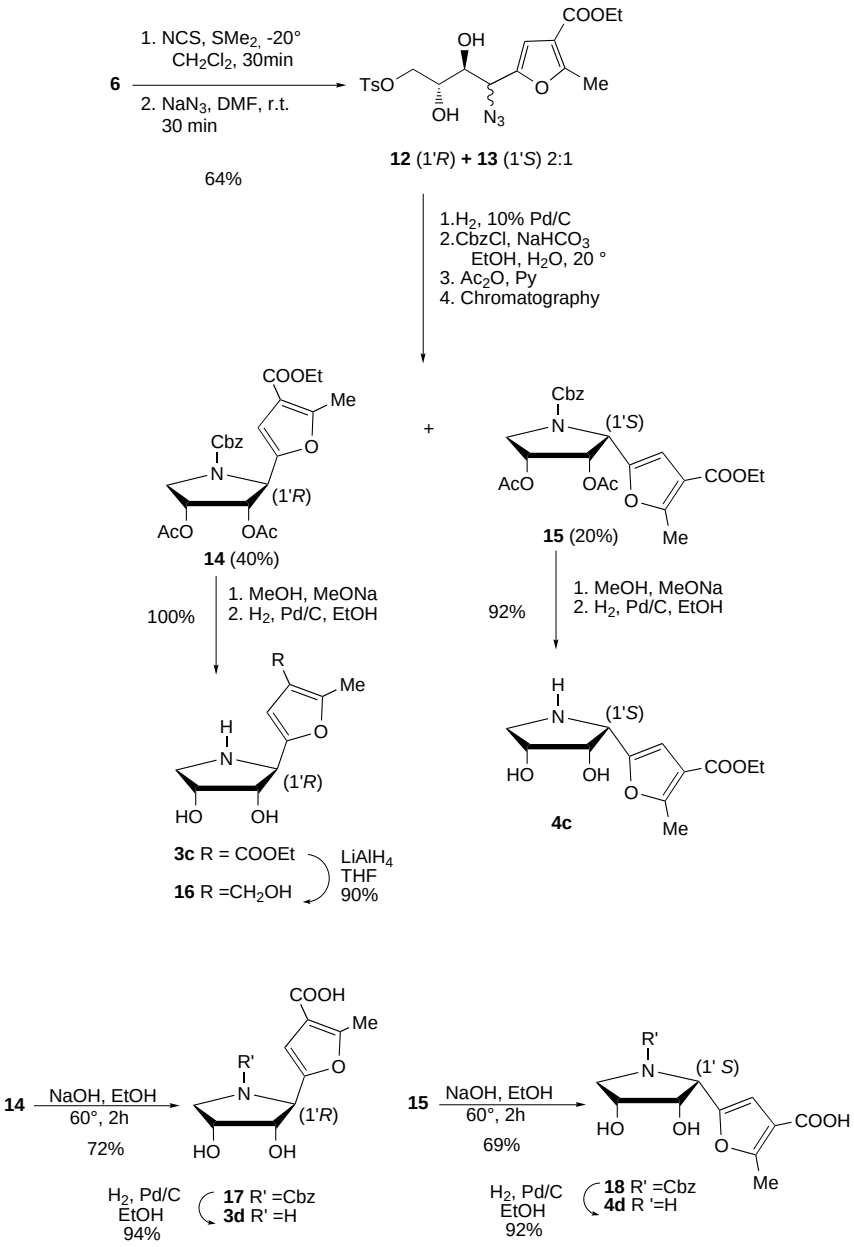


When azide anion was used as the nucleophile, a mixture **12**/**13** was obtained in 64% overall yield with a product ratio of 2:1 (*Scheme 2*). This result can be interpreted in terms of competing S_N1 and S_N2 azidolyses together with the intermediacy of oxirane **11**. Hydrogenation (H_2, Pd/C, EtOH, 20°) of **12**/**13** gave the corresponding primary-amine derivatives. The latter underwent displacement of the tosyloxy group furnishing a 2:1 mixture of (1′*R*)- and (1′*S*)-1′,4′-dideoxy-1′,4′-imino-D-erythrosyl derivatives (β-D and α-D configuration, resp.) that could be separated by chromatography on silica gel after protection of the amino group as benzyl carbamate (Cbz = (benzyloxy)carbonyl) and the OH groups as acetates. This provided **14** and **15** in 40 and 20% yield, respectively. Their structures were established by analytical and spectral data (see *Exper. Part*) and were confirmed by NOE experiments in their ^{1}H-NMR spectra.

Compound **15** showed a strong NOE (10%) between proton pairs H–C(1′) (δ 5.14)/H–C(2′) (δ 5.44) that was not observed for **14**, indicating (1′*R*) and (1′*S*) configuration in **14** and **15**, respectively. Noteworthy is the observation of coupling constants ^3J(1′,2′) for both *N*-protected compounds that are markedly different: ^3J(1′,2′) = 3.3 H for **14** and ^3J(1′,2′) = 7.2 Hz for **15**. In the case of the corresponding *N*-unprotected targets **3c** and **4c**, ^3J(1′,2′) = 7.5 and 4.3 Hz, respectively, were found. This is in accordance with the data reported for derivatives of dideoxy-imino-D-ribitols [10] and dideoxy-imino-L-lyxitols [11]. A modification in the average conformation of the pyrrolidine moiety explains this change.

Alkaline methanolysis of **14** and **15** followed by hydrogenolysis gave **3c** and **4c** in 100 and 92% yields, respectively (*Scheme 2*). Reduction of **3c** with $LiAlH_4$ afforded alcohol **16** in 90% yield. Saponification of **14** and **15** gave **17** and **18**, respectively, that, after hydrogenolysis on Pd/C, provided the corresponding *N*-unprotected furoic acids **3d** and **4d**, respectively, in good yields (*Scheme 2*).

Scheme 2



Acid **17** was transformed into a small library of esters and amides (*Scheme 3*). Esterification with MeOH, ^{i}PrOH, or BuOH was achieved in the presence of 2,6-dichlorobenzoyl chloride as the activating agent that, after hydrogenolysis in MeOH or

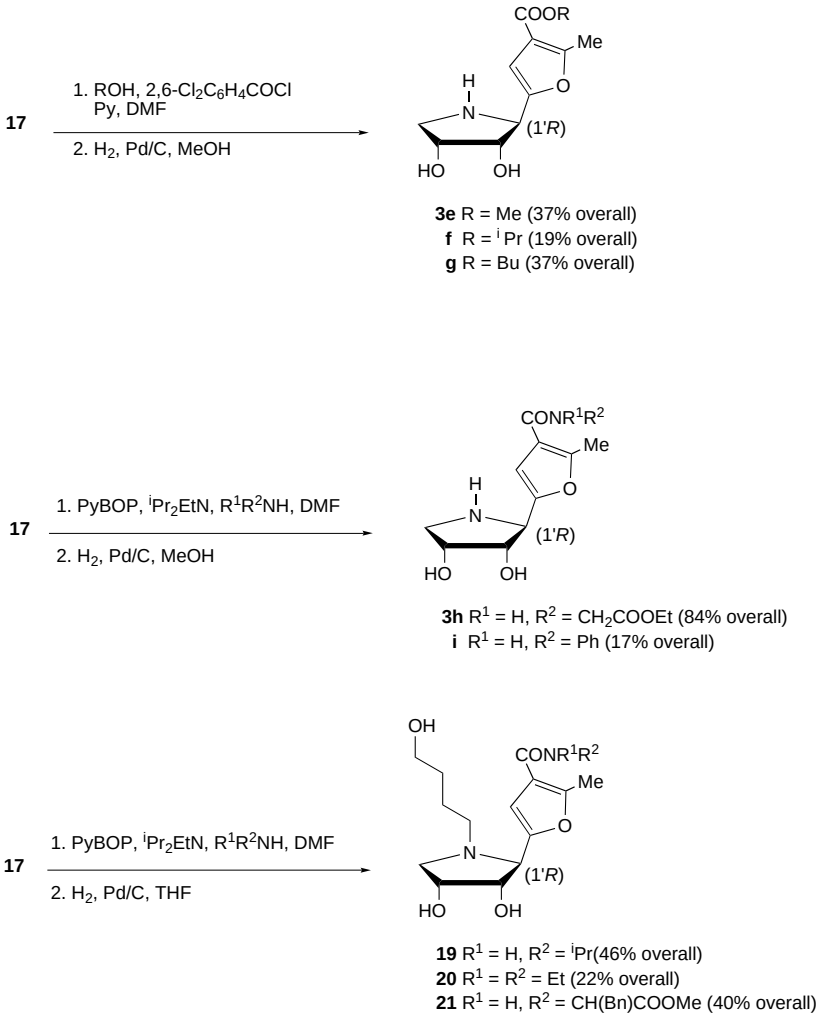
THF, gave esters **3e**–**g** in moderate yields. The formation of amides by reaction of **17** with glycine ethyl ester, aniline, isopropylamine, diethylamine, and L-phenylalanine methyl ester was performed by means of PyBOP and *Hünig*'s base ($^{i}Pr_2EtN$) as activating agents. Subsequent removal of the protecting *N*-[(benzyloxy)carbonyl] group was carried out in MeOH or THF. Hydrogenolysis in MeOH gave poor yields, except for compound **3h**, which was obtained in 84% overall yield under these conditions. Compound **3i** was obtained in 17% yield. The success of the hydrogenolysis in THF is strongly dependent on the nature of the substrate. While esters gave reasonable yields, in the case of amides, the pyrrolidine amino group, probably assisted by Pd, provoked the opening of the THF ring, and compounds **19**–**21** were obtained. There is only one recent precedent of this type of reaction in the literature reported by *Nicolaou* and co-workers [12] in the course of their total synthesis of balanol. As in the case of the latter synthesis, the presence of an amide moiety is required for this aminohydrogenolysis of tetrahydrofuran. Under similar conditions, pyrrolidinediol and pyrrolidine refused to react with THF.

With the goal in mind to avoid this side reaction during the deprotection step, another synthetic route was explored (*Scheme 4*). Saponification of mixture **3c**/**4c**, followed by silylation of the diol moieties with Me_3SiCl/pyridine, followed by treatment with FmocCl (9*H*-fluoren-9-ylmethyl carbonochloridate) and H_2O [13], provided a 2:1 mixture of carboxylic acids **22** and **23**, respectively, after aqueous workup. This mixture was directly submitted to the amidification conditions (PyBOP, $^{i}Pr_2EtN$) with isopropylamine, benzylamine, and diethylamine to give the corresponding amide mixtures, which were separated by chromatography (silica gel). Alkaline methanolysis and Fmoc deprotection with Et_2NH in DMF liberated pure *N*-deprotected furyol amides **3b**, **3j**, and **3k** derived from furoic acid **22** and **4b**, **4j**, and **4k** derived from furoic acid **23**. The same treatment (without acetylation) applied to **22** and ethylamine gave **3l** after Fmoc deprotection.

Finally the reaction of **22** and **23** with thiophenol in the presence of dicyclohexylcarbodiimide (DCC) and *N*,*N*-dimethylpyridin-4-amine (DMAP), followed by acetylation gave a mixture of thioesters **24** and **25** that were separated by chromatography and, independently, deprotected upon basic methanolysis and treatment with Et_2NH, to give pure *N*-unprotected furancarbathioic acid *S*-ester **3a** (*Scheme 5*). The products **3e** and **4e** resulting from a transesterification during the deprotection of **24** and **25** were also isolated (in the latter case, the *S*-ester **4a** (=(1′*S*)-epimer of **3a**) was not observed. Pure **3m** was obtained by a similar treatment applied to **22** and ethanethiol.

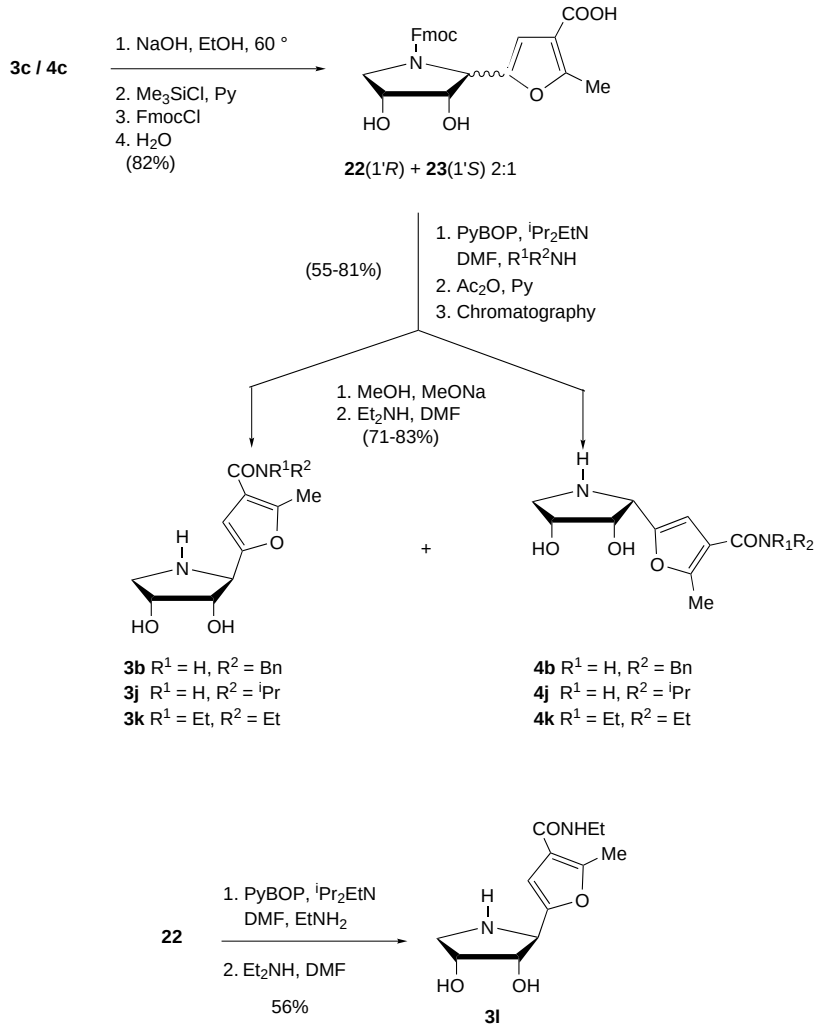
Inhibitory Studies Towards Glycosidases. – We assayed [14] all the new compounds **3**, **4**, and **19**–**21** as well as derivatives **9** and **1** towards two α-L-fucosidases (from bovine epididymis, human placenta), three α-galactosidases (from coffee beans, *Aspergillus niger, E. coli*), five β-galactosidases (from *E. coli*, bovine liver, *Aspergillus niger*, *Aspergillus oryzae*, jack beans), two α-glucosidases (from yeast, rice), one isomaltase (from bakers yeast), two amyloglucosidases (from *Aspergillus niger*, *Rhizopus mold*), two β-glucosidases (from almonds, *Caldocellum saccharolyticum*), two α-mannosidases (from jack beans, almonds), one β-mannosidase (from *Helix pomatia*), one β-xylosidase (from *Aspergillus niger*), one α-*N*-acetylgalactosaminidase (from chicken

Scheme 3



liver), and three *β-N*-acetylglucosaminidases (from jack beans, bovine epididymis A and B). At 1 mM concentration, no inhibition was observed by all these 1′,4′-dideoxy-1′,4′-imino-D-erythrosyl or dihydroxypyrrolidine derivatives for *α*-galactosidases from *Aspergillus niger* and from *E. coli*, for *α*-glucosidases from yeast and from rice, for *β*-mannosidases from *Helix pomatia*, for *β*-xylosidase from *Aspergillus niger*, and for *β-N*-acetylglucosaminidases from jack beans, and from bovine epididymis A and B. At 1 mM, the simple *meso*-pyrrolidine-2,3-diol (**1**) was also assayed and proved to be a weak inhibitor of the following enzymes: *α*-galactosidase from coffee beans (50%, $IC_{50} = 1$ mM), *β*-galactosidase from *E. coli* (41%), from bovine liver (25%), from *Aspergillus niger* (39%), from *Aspergillus oryzae* (53%, $IC_{50} = 790$ μM), and from jack

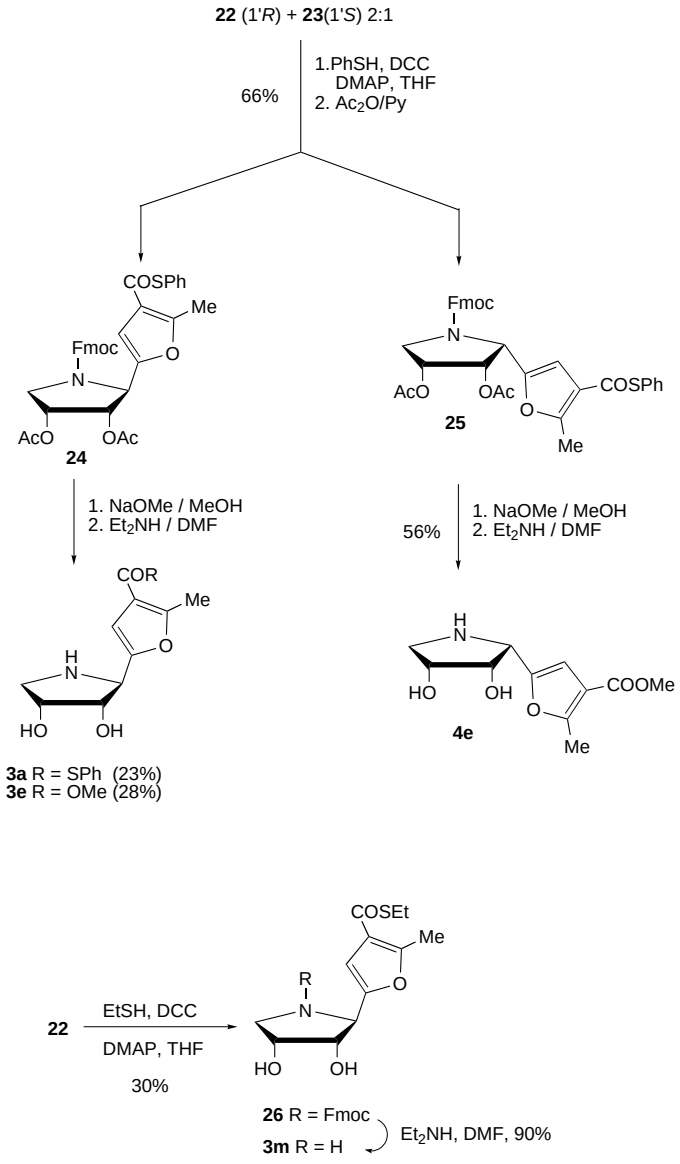
Scheme 4



beans (55%, $IC_{50} = 700$ μM), α-glucosidase (isomaltase) from bakers yeast (32%), amyloglucosidase from *Aspergillus niger* (24%), and from *Rhizopus mold* (47%), β-glucosidase from almonds (60%, $IC_{50} = 600$ μM), α-mannosidase from jack beans (70%, $IC_{50} = 400$ μM), and from almonds (44%), and α-*N*-acetylgalactosaminidase from chicken liver (63%, $IC_{50} = 500$ μM).

Coupling the pyrrolidine-2,3-diol moiety at C(5) of a 2-methyl-3-furoic acid moiety as in **3** and **4** generated more selective and more-potent glycosidase inhibitors. Most interesting is the observation that the [(1′*R*)-1′,4′-dideoxy-1′,4′-imino-D-erythrosyl]-furoic acid derivatives **3** are selective α-L-fucosidase inhibitors (see *Table 1*), whereas the corresponding (1′*S*)-epimers **4** are selective β-galactosidase inhibitors (see *Table 2*).

Scheme 5



The enzyme selectivity depends on the nature of the carboxylic acid derivative (COZR). In the case of compounds **3**, all COZR are recognized by β-galactosidases from bovine liver, but not by the other β-galactosidases, except for **3c** with the COOEt group (see *Table 3*). A general trend is that esters, *i.e.*, **3c**, **3e**, **3f**, and **3g**, are less selective than the other derivatives as they all inhibit amyloglucosidases and α-mannosidases to some extent. The *S*-ethyl thioester **3m** has a behavior similar to that of

O-alkyl esters. Interestingly, the *S*-phenyl thioester **3a** is not only one of the most-potent α-L-fucosidase inhibitors (see K_i values in *Table 1*) but appears to be also the most selective. Amides **3b**, **3j**, **3k**, and **3l** are weak inhibitors of amyloglucosidase and α-mannosidases. The ethyl glycinate derivative **3h** is more selective than other amides but not as potent as α-L-fucosidase inhibitor.

Table 1. *Inhibitory Activities of [(1′R)-1′,4′-Dideoxy-1′,4′-imino-D-erythrosyl]furancarboxylic Acid Derivatives* **3** *and of* **16** *towards Two α-L-Fucosidases.* Percentage of inhibition at 1 mM, IC_{50} (in parenthesis), and K_i (bold and italic) in μM if measured. Optimal pH, 35°[a])[b])[c]).

	COZR	α-L-Fucosidase			
		from human placenta		from bovine epididymis	
3a	COSPh	89% (38)	***2.9***	90% (60)	***3.8***
3b	CONHBn	94% (28)	***2.2***	95% (43)	***3.4***
3c	COOEt	84% (200)	***9***	76% (300)	***15***
3d	COOH	n.i.		n.i.	
3e	COOMe	80% (100)	***6.5***	88% (150)	***13.8***
3f	COO-^{i}Pr	91% (50)	***4.9***	92% (160)	***8.6***
3g	COOBu	91% (35)	***4.1***	93% (75)	***4.2***
3h	$CONHCH_2COOEt$	72% (360)	***13***	73% (360)	***26***
3i	CONHPh	10%		51% (1000)	
3j	CONH^{i}Pr	94% (40)	***3***	93% (80)	***5.3***
3k	$CONEt_2$	85% (110)	***9.1***	86% (220)	***20***
3l	CONHEt	91% (40)	***3.2***	92% (80)	***4.8***
3m	COSEt	92% (44)	***3.1***	94% (120)	***5.7***
16		n.i.		n.i.	

[a]) For conditions of measurements, see [14]. [b]) All inhibitors showed competitive inhibition from *Lineweaver–Burk* plots. [c]) n.i. = no inhibition at 1 mM.

Table 2. *Inhibitory Activities of [(1′S)-1′,4′-Dideoxy-1′,4′-imino-D-erythrosyl]furancarboxylic Acid Derivatives* **4** *and of* **1** *towards β-Galactosidases.* Percentage of inhibition at 1 mM, IC_{50} (in parenthesis), and K_i (bold and italic) in μM if measured. Optimal pH, 35°[a])[b])[c]).

	COZR	*β-Galactosidase from*				
		E. coli	*Bovine liver*	*Aspergillus niger*	*Aspergillus oryzae*	Jack bean
4b	CONHBn	81% (150)	88% (120)	94% (50)	89% (20)	66% (420)
		7 (m.)	***20*** (c.)	***60*** (non-c.)	***20*** (c.)	
4c	COOEt	83% (90)	78% (250)	99% (7.5)	98% (12)	94% (12)
		74 (c.)	***35*** (m.)	***9.8*** (non-c.)	***6.6*** (m.)	***6.4*** (m.)
4d	COOH	n.i.	n.i.	n.i.	n.i.	n.i.
4e	COOMe	55% (750)	80% (200)	94% (50)	87% (90)	81% (240)
				47 (non-c.)	***27*** (c.)	
4j	CONH^{i}Pr	n.i.	49% (1000)	79% (250)	68% (500)	22%
4k	$CONEt_2$	33%	90% (42)	96% (28)	93% (65)	52% (1000)
			13 (c.)	***30*** (non-c.)	***13*** (m.)	
1		41%	25%	39%	53% (790)	55% (720)

[a]) For conditions of measurements, see [14]. [b]) c. = competitive, non-c. = non-competitive, m. = mixed type of inhibition, from *Lineweaver–Burk* plots. [c]) n.i. = no inhibition at 1 mM.

Table 3. *Inhibitory Activities of Compounds* **3** *towards Other Glycosidases than* α-L-*Fucosidases.* Percentage of inhibition at 1 mM and IC_{50} (in parenthesis, μM) if measured. Optimal pH, 35°[a])[b])[c]).

	3a (COZR = COSPh)	**3b** (COZR = CONHBn)	**3c** (COZR = COOEt)	**3e** (COZR = COOMe)	**3f** (COZR = COO^{i}Pr)	**3g** (COZR = COOBu)	**3h** (COZR = CONH–Gly–OEt)	**3j** (COZR = CONH^{i}Pr	**3k** (COZR = CONEt$_2$)	**3l** (COZR = CONHEt)	**3m** (COZR = COSEt)
α-Galactosidase:											
coffee bean	48%	n.i.	n.i.	42%	29%	43%	n.i.	n.i.	n.i.	n.i.	57% (650)
Isomaltase:											
bakers yeast	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.
Amyloglucosidase:											
Asp. niger	n.i.	52%	n.i.	23%	27%	38%	n.i.	23%	n.i.	n.i.	n.i.
Rhiz. mold	n.i.	71% (310)	25%	33%	44%	52%	n.i.	33%	25%	26%	33%
β-Glucosidase:											
almonds	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.
Caldoc. sacch.	n.i.	n.i.	n.i.	n.i.	n.i.	32%	n.i.	n.i.	n.i.	n.i.	n.i.
α-Mannosidase:											
jack bean	n.i.	n.i.	38%	23%	78% (250)[d])	71% (320)[c])	n.i.	n.i.	27%	29%	69% (390)
almonds	n.i.	n.i.	n.i.	36%	57%	52%	n.i.	29%	31%	32%	53%
α-*N*-Acetyl-galactosaminidase											
chicken liver	n.i.	n.i.	n.i.	48%	n.i.	27%	n.i.	n.i.	n.i.	n.i.	57% (690)
β-Galactosidase:											
bovine liver	67% (450)	43%	57%	54%	57%	76%	21%	38%	58%	52%	58%
Asp. niger	n.i.	n.i.[c])	80% (370)[c])	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.
Asp. oryzae	n.i.	n.i.	45%	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.
jack bean	n.i.	n.i.	42%	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.	n.i.

[a]) For conditions of measurements, see [14]. [b]) n.i. = no inhibition at 1 mM. [c]) K_i = 340 μM (m.). [d]) K_i = 85 μM (c.). [e]) K_i = 116 μM (c.).

N-Substitution at the imino moiety suppresses all inhibitory activity toward all the enzymes assayed as found for derivatives **19**–**21** and **9**.

The most-potent β-galactosidase inhibitor of (1′*S*)-series **4** is the *N*-benzylcarboxamide **4b**, which shows competitive inhibition of β-galactosidases from bovine liver and from *Aspergillus oryzae*, noncompetitive inhibition towards β-galactosidase from *Aspergillus niger*, and mixed-type inhibition towards β-galactosidase from *E. coli* (see *Table 2*). As in the case of carboxylic acid **3d**, the (1′*S*)-epimer **4d** is inactive towards all enzymes assayed. Except for *N*-isopropylcarboxamide **4j**, which is a moderate inhibitor of some of the β-galactosidases assayed, the other compounds **4b**, **4c**, **4e**, and **4h** are weak inhibitors of α-mannosidases. None of the (1′*S*)-epimers **4** that were tested is a specific inhibitor of other glycosidases than β-galactosidases (see *Table 4*).

Table 4. *Inhibition of Other Glycosidases than β-Galactosidases by* **4**. Percentage of inhibition at 1 mM and IC_{50} (in parenthesis, μM) if measured. Optimal pH, 35°[a])[b]).

	4b (COZR = CONHBn)	**4c** (COZR = COOEt)	**4e** (COZR = COOMe)	**4j** (COZR = CONH^{i}Pr)	**4k** (COZR = CONEt$_2$)
α-L-Fucosidase:					
from bovine epididymis	37%	n.i.	36%	22%	n.i.
from human placenta	56% (640)	n.i.	48%	39%	n.i.
α-Glucosidase (isomaltase):					
from baker yeast	43%	n.i.	n.i.	n.i.	n.i.
α-Mannosidase:					
from jack beans	37%	49%	22%	n.i.	37%
from almonds	40%	37%	34%	n.i.	38%
β-Glucosidase:					
from almonds	n.i.	38%	n.i.	n.i.	n.i.
Caldoc. sacch.	n.i.	36%	n.i.	n.i.	n.i.

[a]) For conditions of measurements, see [14]. [b]) n.i. = no inhibition at 1 mM.

Conclusions. – Efficient syntheses of [(1′*R*)-1′,4′-dideoxy-1′,4′-imino-D-erythrosyl]-furoic acid derivatives **3** and their (1′*S*)-epimers **4** were developed starting from D-glucose and ethyl acetoacetate. Whereas **3** are selective inhibitors of α-L-fucosidases, derivatives **4** are selective inhibitors of β-galactosidases. This work demonstrates that *meso*-pyrrolidine-3,4-diol (**1**), which is a weak inhibitor of a larger number of glycosidases, can be converted to potent and selective α-L-fucosidase or β-galactosidase inhibitors by linking its C(2) position to C(5) of a 2-methyl-3-furoic acid moiety. Whereas the 3-furoic acids do not inhibit any of the glycosidases assayed, their esters, thioesters, and amides are interesting inhibitors. They constitute new leads for the search of α-L-fucosidase and β-galactosidase inhibitors that possess not only polar (OH, NH) functions but also lipophilic moieties, which might be required for the development of orally active drugs. The inhibitory activities observed are still three orders of magnitude lower than those reported for 1-deoxy-L-fuconojirimycin and 1-deoxy-D-galactonojirimycin [1], but introduction of additional substituents at C(4′) of the 1′,4′-dideoxy-1′,4′-imino-D-erythrosyl moiety as well as modification of the furan ring by substituents (nature and position) leave the possibility to find better leads. It is possible

also that other heterocycles than furan attached at C(1′) of the 1′,4′-dideoxy-1′,4′-imino-D-erythrosyl moiety might generate new and better leads as glycosidase inhibitors.

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Experimental Part

General. Anh. solvents and reagents were freshly distilled under N_2 prior to use: THF from sodium and benzophenone, CH_2Cl_2 and $^iPr_2NEt$ from CaH_2. TLC: silica gel HF_{254} (*Merck*); detection by UV light and charring with H_2SO_4. Prep. chromatography (CC): silica gel *60* (*Merck*; 230 mesh). Optical rotations: at 25°; *Perkin-Elmer 241-MC* and *Jasco DIP-370* spectropolarimeters. IR Spectra: *FT-IR Bomem MB-120* instrument; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra[1]): *Bruker AMX-300*, *Bruker ARX-400*, and *Bruker AMX-500* spectrometers; $CDCl_3$, (D_6)DMSO, CD_3OD, and D_2O solns.; *J* values in Hz and δ in ppm. FAB-MS, EI-MS, and CI-MS: *Kratos MS-80-RFA* instrument; for HR-MS, *Micromass AutoSpeQ* instrument; in *m/z* (rel. %).

*Ethyl 2-Methyl-5-[(1*S*,2*R*,3*R*)-1,2,3,4-trihydroxybutyl]furan-3-carboxylate* (**6**). To a stirred soln. of **5** (4 g, 14.6 mmol) in dry pyridine (20 ml) at −15°, a soln. of TsCl (7 g, 36.7 mmol) in dry pyridine (10 ml) was added. The mixture was stirred for 2 h at −15°, then H_2O (2 ml) was added and the soln. stirred for 15 min at r.t. The solvent was evaporated, the residue dissolved in CH_2Cl_2, and the soln. washed with 1M HCl, sat. aq. $NaHCO_3$ soln., and brine, dried (Na_2SO_4), and evaporated, and the residue purified by CC (SiO_2, ether/petroleum ether 1:2 → 3:1): **6** (3.56 g, 57%). Hygroscopic solid. $[\alpha]_D^{25} = -15$ ($c = 3.3$, MeOH). IR: 3468 (OH), 2982, 2922, 1709 (CO), 1589, 1408, 1099, 980, 833. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.77 (*d*, $^3J(2'',3'') = {}^3J(5'',6'') = 8.3$, H−C(2″) and H−C(6″) of Ph); 7.33 (*d*, H−C(3″) and H−C(5″) of Ph); 6.59 (*s*, H−C(4)); 4.91 (*m*, H−C(1′)); 4.25 (*q*, ^3J(H,H) = 7.1, MeCH_2); 4.29–4.20 (*m*, H_a−C(4′)); 4.17 (*dd*, $^3J(3',4'b) = 5.8$, $^3J(4'a,4'b) = 10.5$, H_b−C(4′)); 3.98–3.93 (*m*, H−C(3′)); 3.85 (*dd*, $^3J(1',2') = 2.4$, $^3J(2',3') = 7.7$, H−C(2′)); 3.10 (*s*, Me of Ts); 2.51 (*s*, Me); 1.32 (*t*, ^3J(H,H) = 7.1, *Me*CH_2). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 163.9 (*C*OOEt); 158.9, 151.6 (C(2), C(5)); 145.1 (C(1″) of Ph), 132.2 (C(4″) of Ph); 129.9, 127.9 (2 C each, Ph); 114.1 (C(3)); 108.4 (C(4)); 72.0, 71.5 (C(2′), C(3′)); 69.6 (C(4′)); 66.3 (C(1′)); 60.2 (Me*C*H_2); 21.5 (Me of Ts), 14.2 (*Me*CH_2), 13.7 (Me). FAB-MS: 451 (100, $[M + Na]^+$). HR-FAB-MS: 451.1022 ($[C_{19}H_{24}O_9S + Na]^+$; calc. 451.1039). Anal. calc. for $C_{19}H_{24}O_9S$: C 57.27, H 6.07; found: C 57.10, H 5.90.

*Ethyl 5-[(2*R*,3*S*,4*R*)-1-Butyl-3,4-dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**9**) *and Ethyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxy-1-(phenylmethyl)pyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**10**). To a stirred soln. of *N*-chlorosuccinimide (NCS; 167 mg, 1.25 mmol) in dry CH_2Cl_2 (3 ml) cooled to 0°, Me_2S (97 µl, 1.25 mmol) was added under N_2. After 5 min, a soln. of **6** (0.41 g, 0.94 mmol) in dry CH_2Cl_2 (4 ml) at −20° was added under N_2. The mixture was allowed to warm to 5° and the solvent evaporated. The crude product containing *ethyl 5-((1*S*,2*R*,3*R*)- and (1*R*,2*R*,3*R*)-1-chloro-2,3-dihydroxy-4-[[(4-methylphenyl)sulfonyl]oxy}butyl)-2-methylfuran-3-carboxylate* (**7** and **8**, resp.) ((1*S*)/(1*R*) 1:1) was used without purification in the next step. ^{1}H-NMR (500 MHz, $CDCl_3$); epimer *a:* 7.75 (*d*, $^3J(2'',3'') = {}^3J(5'',6'') = 8.3$, H−C(2″) and H−C(6″) of Ph); 7.33 (*d*, H−C(3″) and H−C(5″) of Ph); 6.68 (*s*, H−C(4)); 5.36 (*d*, $^3J(1',2') = 2.2$, H−C(1′)); 4.28–4.14 (*m*, MeCH_2, H_a−C(4′), H_b−C(4′)); 3.97 (*dd*, $^3J(2',3') = 8.4$, H−C(2′)); 3.90–3.87 (*m*, H−C(3′)); 2.70 (*s*, Me of Ts); 2.41 (*s*, Me); 1.31–1.27 (*m*, *Me*CH_2); epimer *b:* 7.75 (*d*, $^3J(2'',3'') = {}^3J(5'',6'') = 8.3$, H−C(2″) and H−C(6″) of Ph); 7.33 (*d*, H−C(3″) and H−C(5″) of Ph); 6.69 (*s*, H−C(4)); 5.20 (*d*, $^3J(1',2') = 4.1$, H−C(1′)); 4.28–4.14 (*m*, MeCH_2, CH_2(4′)); 4.04 (*dd*, $^3J(2',3') = 8.4$, H−C(2′)); 3.75–3.72 (*m*, H−C(3′)); 2.72 (*s*, Me of Ts); 2.51 (*s*, Me); 1.31–1.27 (*m*, *Me*CH_2). ^{13}C-NMR (125.7 MHz, $CDCl_3$; mixture of epimers): 163.5, 163.4 (*C*OOEt(*a*), *C*OOEt(*b*)); 159.5, 159.3, 149.1, 147.4 (C(2)(*a*), C(5)(*a*), C(2)(*b*), C(5)(*b*)); 144.9 (C(1″) of Ph(*a*), C(1″) of Ph(*b*)); 132.2 (C(4″) of Ph(*a*), C(4″) of Ph(*b*)); 129.7, 127.8 (4 C each, C(2″), C(3″), C(5″), C(6″) of Ph(*a*) and Ph(*b*)); 114.3 (2 C, C(3)(*a*), C(3)(*b*)); 111.0, 110.0 (C(4)(*a*), C(4)(*b*)); 73.9, 72.0, 71.3, 71.3 (4 C, C(2′)(*a*), C(3′)(*a*), C(2′)(*b*), C(3′)(*b*)); 69.7 (C(4′)(*b*)); 69.5 (C(4′)(*a*)); 60.1 (2 C, Me*C*H_2(*a*), Me*C*H_2(*b*)); 56.0 (C(1′)(*a*)); 55.5 (C(1′)(*b*)); 21.4 (2 C, Me of Ts(*a*) and Ts(*b*)); 14.1 (2 C, *Me*CH_2(*a*), *Me*CH_2(*b*)); 13.7, 13.6 (Me(*a*), Me(*b*)).

The mixture **7**/**8** was dissolved in butylamine (6.5 ml; for **9**) or benzylamine (10 ml; for **10**) cooled at 0°. The soln. was allowed to warm to r.t. and stirred for 4 h (for **9**) or 12 h (for **10**). Then the solvent was evaporated and the residue purified by CC (SiO_2, Et_2O/petroleum ether, 1:1 → 3:1 (for **9**) or 1:3 → 1:1 (for **10**).

Data of **9**: 134.7 mg (47% overall from **6**). Syrup. $[\alpha]_D^{30} = +26$ ($c = 2$, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 6.53 (*s*, H–C(4)); 4.31–4.25 (*m*, H–C(3′)); 4.25 (*q*, ^3J(H,H) = 7.1, MeCH_2); 4.16 (*t*, $^3J(1',2') = {}^3J(2',3') = 6.5$, H–C(2′)); 3.53 (*dd*, $^3J(3',4'a) = 6.2$, $^3J(4'a,4'b) = 10.4$, H_a–C(4′)); 3.39 (*d*, H–C(1′)); 2.82 (br. *s*, 2 OH); 2.54 (*s*, CH_3); 2.57–2.20 (*m*, H_a–C(1″)); 2.38 (*dd*, $^3J(3',4'b) = 4.7$, H_b–C(4′)); 2.23–2.15 (*m*, H_b–C(1″)); 1.32 (*t*, ^3J(H,H) = 7.1, *Me*CH_2); 1.42–1.30 (*m*, 2 H–C(2″)); 1.26–1.18 (*m*, 2 H–C(3″)); 0.83 (*t*, ^3J(H,H) = 7.2, 3 H–C(4″)). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 164.0 (*C*OOEt); 159.2, 150.9 (C(2), C(5)); 113.9 (C(3)); 109.6 (C(4)); 74.7 (C(2′)); 68.7 (C(3′)); 67.2 (C(1′)); 60.0 (Me*C*H$_2$); 59.0 (C(4′)); 53.6 (C(1″)); 29.5 (C(2″)); 20.3 (C(3″)); 14.2 (*Me*CH$_2$); 13.8, 13.7 (2 C, C(4″), Me). FAB-MS: 334 (100, $[M + Na]^+$). EI-MS: 311 (100, $M^{+\bullet}$). HR-EI-MS: 311.1731 ($C_{16}H_{25}NO_5^+$; calc. 311.1732).

Data of **10**: 141 mg (44% overall from **6**). Syrup. $[\alpha]_D^{25} = +8$ ($c = 0.5$, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.33–7.21 (*m*, Ph); 6.61 (*s*, H–C(4)); 4.28 (*q*, ^3J(H,H) = 7.1, MeCH_2); 4.30–4.25 (*m*, H–C(3′)); 4.21 (*t*, $^3J(1',2') = {}^3J(2',3') = 6.3$, H–C(2′)); 3.85 (*d*, ^2J(H,H) = 13.0, PhC*H*); 3.54 (*d*, H–C(1′)); 3.38 (*dd*, $^3J(3',4'a) = 6.0$, $^3J(4'a,4'b) = 10.5$, H_a–C(4′)); 3.34 (*d*, PhC*H*), 2.58 (*s*, Me); 2.41 (*dd*, $^3J(3',4'b) = 4.7$, H_b–C(4′)); 1.34 (*t*, *Me*CH_2). ^{13}C-NMR (75.4 MHz, $CDCl_3$): 163.9 (*C*OOEt); 159.1, 150.8 (C(2), C(5)); 137.6 (C(1) of Ph); 128.7–127.0 (5 C, Ph); 114.0 (C(3)); 109.6 (C(4)); 75.0 (C(2′)); 68.6 (C(3′)); 66.6 (C(1′)); 60.0 (Me*C*H$_2$); 58.6 (C(4′)); 57.4 (Ph*C*H$_2$); 14.2 (*Me*CH$_2$); 13.7 (Me). FAB-MS: 368 (100, $[M + Na]^+$). EI-MS: 345 (100, $M^{+\bullet}$). HR-EI-MS: 345.1578 ($C_{19}H_{23}NO_5^+$; calc. 345.1576).

*Ethyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**3c**). *Procedure A*. A soln. of **10** (41 mg, 0.12 mmol) in MeOH (3 ml) was hydrogenated over 10% Pd/C (15 mg) at 1 atm for 1.5 h. Filtration of the catalyst and evaporation gave **3c** (30 mg, 98%). White solid.

Procedure B. To a soln. of **14** (92 mg, 0.19 mmol) in MeOH (5 ml), 1M MeONa/MeOH (3 drops) was added. The mixture was stirred at r.t. for 20 min, made neutral with *Amberlyst IR-120* (H^+), and filtered, and the resin washed with MeOH. The filtrate was hydrogenated over 10% Pd/C (20 mg) at 1 atm for 2 h. Filtration of the catalyst and evaporation gave **3c** (49 mg, 100%). White solid. $[\alpha]_D^{25} = -44$ ($c = 1.5$, MeOH). ^{1}H-NMR (300 MHz, CD_3OD): 6.55 (*s*, H–C(4)); 4.25 (*q*, ^3J(H,H) = 7.1, MeCH_2); 4.17–4.08 (*m*, H–C(2′), H–C(3′)); 3.99 (*d*, $^3J(1',2') = 7.5$, H–C(1′)); 3.27 (*dd*, $^3J(3',4'a) = 5.1$, $^3J(4'a,4'b) = 12.0$, H_a–C(4′)); 2.87 (*dd*, $^3J(3',4'b) = 3.0$, H_b–C(4′)); 2.54 (*s*, Me); 1.34 (*t*, *Me*CH_2). ^{13}C-NMR (75.4 MHz): 165.5 (*C*OOEt); 160.2, 153.7 (C(2), C(5)); 115.2 (C(3)); 108.8 (C(4)); 77.3 (C(2′)); 72.3 (C(3′)); 61.3 (Me*C*H$_2$); 60.3 (C(1′)); 52.5 (C(4′)); 14.6 (*Me*CH$_2$); 13.8 (Me). EI-MS: 255 (100, $M^{+\bullet}$). HR-EI-MS: 255.1105 ($C_{12}H_{17}NO_5^+$; calc. 255.1107). Anal. calc. for $C_{12}H_{17}NO_5$: C 56.49, H 6.72, N 5.49; found: C 56.45, H 6.61, N 5.81.

*Ethyl 5-{(1*R*,2*S*,3*R*)- and (1*S*,2*S*,3*R*)-1-Azido-2,3-dihydroxy-4-{[(4-methylphenyl)sulfonyl]oxy}butyl}-2-methylfuran-3-carboxylate* (**12** and **13**, resp.). Chlorination of **6** (1.17 mmol) with NCS (207.9 mg, 1.56 mmol) and Me_2S (120.7 µl, 1.17 mmol) as described above gave **7**/**8**, which were dissolved in dry DMF (2 ml), and NaN_3 (0.15 g, 2.3 mmol) was added. The mixture was stirred for 15 min at r.t., diluted with CH_2Cl_2 (60 ml), and washed with H_2O (40 ml) and brine. The org. layer was dried (Na_2SO_4) and evaporated, and the residue purified by CC (SiO_2, ether/petroleum ether 1:3 → 1:1): 2:1 mixture of epimers **12** and **13** (0.34 g, 64% overall from **6**). Syrup. IR (**12**/**13**): 3491 (OH), 2984, 2926, 2111 (N_3), 1705 (CO), 1358, 1175. ^{1}H-NMR (500 MHz, $CDCl_3$; **12**): 7.78 (*d*, $^3J(2'',3'') = {}^3J(5'',6'') = 8.3$, H–C(2′) and H–C(6″) of Ph); 7.35 (*d*, H–C(3″) and H–C(5″) of Ph); 6.73 (*s*, H–C(4)); 4.74 (*d*, $^3J(1',2') = 4.7$, H–C(1′)); 4.30–4.19 (*m*, MeCH_2, CH_2(4′)); 3.95 (*dd*, $^3J(2',3') = 7.7$, H–C(2′)); 3.74–3.72 (*m*, H–C(3′)); 2.56 (*s*, Me of Ts); 2.44 (*s*, Me); 1.34 (*t*, ^3J(H,H) = 7.1, *Me*CH_2). ^{1}H-NMR (500 MHz, $CDCl_3$; **13**): 7.78 (*d*, $^3J(2'',3'') = {}^3J(5'',6'') = 8.3$, H–C(2″) and H–C(6″) of Ph); 7.35 (*d*, H–C(3′) and H–C(5″) of Ph); 6.71 (*s*, H–C(4)); 4.82 (*d*, $^3J(1',2') = 1.1$, H–C(1′)); 4.30–4.19 (*m*, MeCH_2, CH_2(4′)); 3.91 (*m*, H–C(2′), H–C(3′)); 2.56 (*s*, Me of Ts); 2.44 (*s*, Me); 1.32 (*t*, ^3J(H,H) = 7.1, *Me*CH_2). ^{13}C-NMR (125.7 MHz, $CDCl_3$; **12**): 163.5 (*C*OOEt); 159.9, 146.2 (C(2), C(5)); 145.2 (C(1″) of Ph); 132.2 (C(4″) of Ph); 129.9 (2 C, C(3″) and C(5″) of Ph); 127.9 (2 C, C(2″) and C(6″) of Ph); 114.4 (C(3)); 111.4 (C(4)); 72.1 (C(2′)); 71.0 (C(4′)); 69.9 (C(3′)); 60.3 (Me*C*H$_2$); 59.5 (C(1′)); 21.5 (Me of Ts); 14.2 (*Me*CH$_2$); 13.8 (Me). ^{13}C-NMR (125.7 MHz, $CDCl_3$; **13**): 163.5 (*C*OOEt); 159.6, 147.7 (C(2), C(5)); 145.2 (C1″) of Ph); 132.2 (C(4″) of Ph); 129.9 (2 C, C(3″) and C(5″) of Ph); 127.9 (2 C, C(2″) and C(6″) of Ph); 114.4 (C(3)); 110.2 (C(4)); 72.0 (C(2′)); 71.1 (C(4′)); 69.5 (C(3′)); 60.3 (Me*C*H$_2$); 58.5 (C(1′)); 21.5 (Me of Ts); 14.2 (*Me*CH$_2$); 13.7 (Me). FAB-MS (**12**/**13**): 476 (100, $[M + Na]^+$). HR-FAB-MS: 476.1099 ($[C_{19}H_{23}N_3O_8S + Na]^+$); calc. 476.1103).

*Ethyl 5-[(2*R*,3*S*,4*R*)-3,4-Bis(acetyloxy)-1-[(phenylmethoxy)carbonyl]pyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**14**) *and Ethyl 5-[(2*S*,3*S*,4*R*)-3,4-Bis(acetyloxy)-1-[(phenylmethoxy)carbonyl]pyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**15**). The mixture **12**/**13** 2:1 (277 mg, 0.61 mmol) in abs. EtOH (7 ml) was hydrogenated over 10% Pd/C (30 mg) at 1 atm for 1 h. The catalyst was then removed by filtration and the solvent evaporated. The crude product was dissolved in EtOH/H_2O 1:1 (5 ml) and cooled to 0°. $NaHCO_3$ (168 mg, 2 mmol) and benzyl carbonochloridate (193 µl, 1.5 mmol) were added, and mixture was stirred at r.t. for 1.5 h. Then sat. aq.

$NaHCO_3$ soln. (1.5 ml) was added at 0° and the mixture stirred for 10 min. The solvent was evaporated and the residue conventionally acetylated with Ac_2O/pyridine for 6 h. The resulting residue was purified by CC (SiO_2, Et_2O/petroleum ether 1:2 → 2:1): **14** (115 mg, 40% overall) followed by **15** (56 mg, 20% overall). Colorless oils.

Data of **14**: $[\alpha]_D^{25} = -1$ ($c = 1$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO, 90°): 7.42–7.21 (*m*, arom. H of Cbz), 6.50 (*s*, H–C(4)); 5.42–5.37 (*m*, H–C(2′), H–C(3′)); 5.12, 5.01 (*d*, ^2J(H,H) = 12.7, CH_2 of Cbz); 4.84 (*d*, $^3J(1',2') = 3.3$, H–C(1′)); 4.23 (*q*, ^3J(H,H) = 7.1, MeCH_2); 3.94 (*dd*, $^3J(3',4'a) = 5.6$, $^3J(4'a,4'b) = 11.6$, H_a–C(4′)); 3.56 (*dd*, $^3J(3',4'b) = 5.1$, H_b–C(4′)); 2.47 (*s*, Me); 2.03, 2.02 (*s*, 2 MeCO); 1.23 (*t*, *Me*CH_2). ^{13}C-NMR (75.4 MHz, (D_6)DMSO, 90°): 168.9, 168.7 (2 Me*C*O); 162.3 (*C*OOEt); 157.6 (CO of Cbz); 153.4, 148.9 (C(2), C(5)); 136.0 (C(1) of Ph); 127.7–126.7 (5 C, arom. C of Cbz); 113.6 (C(3)); 107.8 (C(4)); 73.9, 69.0 (C(2′), C(3′)); 66.0 (CH_2 of Cbz); 59.3 (Me*C*H_2); 57.4 (C(1′)); 47.8 (C(4′)); 19.7 (2 *Me*CO); 13.6 (*Me*CH_2); 12.8 (Me).

Data for **15**: $[\alpha]_D^{25} = +40$ ($c = 0.6$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO, 90°): 7.32–7.16 (*m*, arom. H of Cbz); 6.30 (*s*, H–C(4)); 5.44 (*dd*, $^3J(1',2') = 7.2$, $^3J(2',3') = 4.8$, H–C(2′)); 5.39–5.34 (*m*, H–C(3′)); 5.14 (*d*, H–C(1′)); 5.07, 4.96 (*d*, ^2J(H,H) = 12.7,CH_2 of Cbz); 4.20 (*q*, ^3J(H,H) = 7.1, MeCH_2); 3.88 (*dd*, $^3J(3',4'a) = 5.8$, $^3J(4'a,4'b) = 11.8$, H_a–C(4′)); 3.54 (*dd*, $^3J(3',4'b) = 3.8$, H_b–C(4′)); 2.43 (*s*, Me); 1.93, 1.84 (*s*, 2 MeCO), 1.25 (*t*, *Me*CH_2). ^{13}C-NMR (75.4 MHz, (D_6)DMSO, 90°): 169.3, 168.9 (2 Me*C*O); 163.1 (*C*OOEt); 157.3 (CO of Cbz); 153.9, 149.3 (C(2), C(5)); 136.8 (C(1) of Ph); 128.2–127.3 (5 C, arom. C of Cbz); 113.9 (C(3)); 108.6 (C(4)); 71.4 (C(2′)); 69.9 (C(3′)); 66.4 (CH_2 of Cbz); 59.7 (Me*C*H_2); 55.3 (C(1′)); 49.2 (C(4′)); 20.2, 20.0 (2 *Me*CO); 14.1 (*Me*CH_2); 13.2 (Me). CI-MS: 474 (15, $[M+H]^+$). Anal. calc. for $C_{24}H_{27}NO_9$: C 60.88, H 5.75, N 2.96; found: C 60.71, H 5.99, N 2.58.

*Ethyl 5-[(2*S*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**4c**). To a soln. of **15** (95 mg, 0.20 mmol) in MeOH (5 ml), 1M NaMeO/MeOH (3 drops) was added. The mixture was stirred at r.t. for 20 min, made neutral with *Amberlyst IR-120* (H^+), and filtered, and the resin washed with MeOH. The filtrate was hydrogenated over 10% Pd/C (20 mg) at 1 atm for 2 h. The catalyst was removed by filtration and the solvent evaporated: **4c** (47 mg, 92%). Colorless oil. $[\alpha]_D^{25} = -33$ ($c = 1$, MeOH). IR: 3300–2780 (OH, NH); 1707 (CO), 1541, 1398, 1227, 1101. ^{1}H-NMR (300 MHz, CD_3OD): 6.62 (*s*, H–C(4)); 4.33–4.24 (*m*, H–C(3′)); 4.26 (*q*, ^3J(H,H) = 7.1, MeCH_2); 4.12 (*t*, $^3J(1',2') = {}^3J(2',3') = 4.3$, H–C(2′)); 4.07 (*d*, H–C(1′)); 3.07 (*dd*, $^3J(3',4'a) = 7.3$, $^2J(4'a,4'b) = 11.5$, H_a–C(4′)); 2.92 (*dd*, $^3J(3',4'b) = 6.1$, H_b–C(4′)); 2.53 (*s*, Me); 1.32 (*t*, *Me*CH_2). ^{13}C-NMR (75.4 MHz, CD_3OD): 165.7 (*C*OOEt); 159.7, 152.1 (C(2), C(5)); 115.2 (C(3)); 109.3 (C(4)); 74.0, 73.9 (C(2′), C(3′)); 61.2 (Me*C*H_2); 60.5 (C(1′)); 51.9 (C(4′)); 14.6 (*Me*CH_2); 13.7 (Me). CI-MS: 256 (10, $[M+H]^+$). HR-CI-MS: 256.1183 ($[C_{12}H_{17}NO_5+H]^+$; calc. 256.1185). Anal. calc. for $C_{12}H_{17}NO_5$: C 56.49, H 6.72, N 5.49; found: C 56.59; H 6.53, N 5.78.

*(2*R*,3*S*,4*R*)-2-[4-(Hydroxymethyl)-5-methylfuran-2-yl]pyrrolidine-3,4-diol* (**16**). To a suspension of $LiAlH_4$ (15 mg, 0.4 mmol) in dry THF (0.5 ml), a soln. of **3c** (51 mg, 0.2 mmol) in dry THF (2 ml) was added under N_2. The mixture was stirred for 15 min at r.t. The soln. was diluted with Et_2O (10 ml), and sat. aq. Na_2SO_4 soln. was added. The solid was filtered and washed with EtOH and the filtered soln. evaporated: **16** (38 mg, 90%). Colorless oil. $[\alpha]_D^{25} = -27$ ($c = 0.3$, MeOH). ^{1}H-NMR (300 MHz, CD_3OD)[1]): 6.58 (*s*, H–C(4)); 4.48–4.33 (*m*, H–C(2′), H–C(3′)); 4.39 (*s*, CH_2OH); 4.44 (*d*, $^3J(1',2') = 8.8$, H–C(1′)); 3.51 (*dd*, $^3J(3',4'a) = 3.5$, $^2J(4'a,4'b) = 12.5$, H_a–C(4′)); 3.21 (*dd*, $^3J(3',4'b) = 1.8$, H_b–C(4′)); 2.30 (*s*, Me). ^{13}C-NMR (75.4 MHz, CD_3OD)[1]): 152.3, 146.0 (C(2), C(5)); 121.9 (C(3)); 114.1 (C(4)); 75.5 (C(2′)); 71.1 (C(3′)); 58.6 (C(1′)); 56.1 (CH_2OH); 50.9 (C(4′)); 11.6 (Me). CI-MS: 214 (70, $[M+H]^+$), 196 (100, $[M-H_2O+H]^+$). HR-CI-MS: 214.1068 ($[C_{10}H_{15}NO_4+H]^+$; calc. 214.1079).

*5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxy-1-[(phenylmethoxy)carbonyl]pyrrolidin-2-yl]-2-methylfuran-3-carboxylic Acid* (**17**). A soln. of **14** (100 mg, 0.21 mmol) in EtOH/1N NaOH 2:1 (6 ml) was heated at 60° for 6 h. Then *Amberlyst IR-120* (H^+) was added until pH was reached. The mixture was filtered, the resin washed with EtOH, the filtrate evaporated, and the residue purified by CC (SiO_2, CH_2Cl_2/MeOH 40:1 → 15:1): **17** (53 mg, 72%). Colorless oil. $[\alpha]_D^{25} = +17$ ($c = 2$, MeOH). IR: 3579–2054 (OH, CO*OH*), 1688 (CO), 1425, 1356, 1227, 1101. ^{1}H-NMR (300 MHz, (D_6)DMSO, 90°): 7.34–7.18 (*m*, Ph); 6.35 (*s*, H–C(4)); 5.07, 4.98 (*d*, ^2J(H,H) = 12.8, CH_2 of Cbz); 4.56 (*d*, $^3J(1',2') = 4.1$, H–C(1′)); 4.18 (*m*, H–C(3′)); 4.04 (*t*, $^3J(2',3') = 4.1$, H–C(2′)); 3.60 (*dd*, $^3J(3',4'a) = 5.7$, $^2J(4'a,4'b) = 10.8$, H_a–C(4′)); 3.40 (*dd*, $^3J(3',4'b) = 5.3$, H_b–C(4′)); 2.45 (*s*, Me). ^{13}C-NMR (75.4 MHz, (D_6)DMSO, 90°): 163.9 (COOH); 156.5 (CO of Cbz); 153.9, 150.9 (C(2), C(5)); 136.4 (C(1) of Ph); 127.7–126.7 (5 C, Ph); 114.2 (C(3)); 107.1 (C(4)); 75.2 (C(2′)); 68.7 (C(3′)); 65.5 (CH_2 of Cbz); 59.9 (C(1′)); 50.4 (C(4′)); 12.7 (Me). CI-MS: 362 (65, $[M+H]^+$). HR-CI-MS: 362.1222 ($[C_{18}H_{19}NO_7+H]^+$; calc. 362.1239).

*5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylic Acid* (**3d**). A soln. of **17** (53 mg, 0.15 mmol) in MeOH/THF 3:1 (4 ml) was hydrogenated over 10% Pd/C (15 mg) as described above for **3c**/**3d** (34 mg, 94%). White solid. $[\alpha]_D^{25} = -77$ ($c = 2.7$, MeOH). IR: 3615–2117 (OH, NH, COO*OH*), 1615 (CO),

1582, 1443, 1103. ^{1}H-NMR (500 MHz, CD_3OD): 6.69 (*s*, H–C(4)); 4.44 (*dd*, $^3J(1',2')=8.6$, $^3J(2',3')=3.8$, H–C(2′)); 4.41 (*d*, H–C(1′)); 4.33–4.30 (*m*, H–C(3′)); 3.51 (*dd*, $^3J(3',4'a)=4.4$, $^2J(4'a,4'b)=12.5$, H_a–C(4′)); 3.21 (*dd*, $^3J(3',4'b)=1.9$, H_b–C(4′)); 2.51 (*s*, Me). ^{13}C-NMR (75.4 MHz, CD_3OD): 171.2 (COOH); 159.1, 145.9 (C(2), C(5)); 120.9 (C(3)); 113.8 (C(4)); 75.5 (C(2′)); 71.2 (C(3′)); 58.4 (C(1′)); 50.9 (C(4′)); 13.7 (Me). CI-MS: 228 (100, $[M+H]^+$). HR-CI-MS: 228.0869 ($[C_{10}H_{13}NO_5+H]^+$; calc. 228.0872).

*5-[(2*S*,3*S*,4*R*)-3,4-Dihydroxy-1-[(phenylmethoxy)carbonyl]pyrrolidin-2-yl]-2-methylfuran-3-carboxylic Acid* (**18**). A soln. of **15** (90 mg, 0.19 mmol) in EtOH/1M NaOH 2:1 (6 ml) was treated as described for **17**. Purification by CC (SiO_2, CH_2Cl_2/MeOH 40:1 → 15:1) gave **18** (46 mg, 69%). Colorless oil. $[\alpha]_D^{25}=-26$ (*c* = 1.8, CH_3OH). IR: 3580–2190 (OH, CO*OH*), 1686 (CO), 1422, 1356, 1227, 1101. ^{1}H-NMR (300 MHz, (D_6)DMSO, 90°): 7.32–7.19 (*m*, Ph); 6.37 (*s*, H–C(4)); 5.07, 4.95 (*d*, ^2J(H,H) = 12.8, CH_2 of Cbz); 4.83 (*d*, $^3J(1',2')=6.7$,H–C(1′)); 4.22 (*dd*, $^3J(2',3')=4.6$,H–C(2′)); 4.14 (*m*, H–C(3′)); 3.65 (*dd*, $^3J(3',4'a)=5.9$, $^2J(4'a,4'b)=11.1$, H_a–C(4′)); 3.38 (*dd*, $^3J(3',4'b)=4.6$, H_b–C(4′)); 2.42 (*s*, Me). ^{13}C-NMR (75.4 MHz, (D_6)DMSO, 90°): 164.2 (COOH); 155.8 (CO of Cbz); 153.8, 150.3 (C(2), C(5)); 136.4 (C(1) of Ph); 127.6–126.5 (5 C, Ph); 114.1 (C(3)); 107.9 (C(4)); 71.6 (C(2′)); 69.2 (C(3′)); 65.5 (CH_2 of Cbz); 57.2 (C(1′)); 51.0 (C(4′)); 12.7 (Me). CI-MS: 362 (4, $[M+H]^+$). HR-CI-MS: 362.1222 ($[C_{18}H_{19}NO_7+H]^+$; calc. 362.1239).

*5-[(2*S*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylic Acid* (**4d**). A soln. of **18** (46 mg, 0.13 mmol) in MeOH/THF 3:1 (4 ml) was hydrogenated as described for **3d**/**4d** (28 mg, 92%). Colorless oil. $[\alpha]_D^{25}=-10$ (*c* = 1, MeOH). IR: 3643–2141 (OH, NH, CO*OH*), 1692 (CO), 1580, 1425, 1227, 1103. ^{1}H-NMR (300 MHz, CD_3OD): 6.83 (*s*, H–C(4)); 4.56 (*d*, $^3J(1',2')=3.0$, H–C(1′)); 4.48 (*m*, H–C(3′)); 4.26 (*t*, $^3J(2',3')=3.5$, H–C(2′)); 3.48 (*dd*, $^3J(3',4'a)=8.0$, $^2J(4'a,4'b)=11.4$, H_a–C(4′)); 3.14 (*dd*, $^3J(3',4'b)=7.4$, H_b–C(4′)); 2.50 (*s*, Me). ^{13}C-NMR (75.4 MHz, CD_3OD): 171.3 (COOH); 158.2, 144.6 (C(2), C(5)); 120.9 (C(3)); 114.1 (C(4)); 72.7 (C(2′)); 72.2 (C(3′)); 59.7 (C(1′)); 49.0 (C(4′)); 13.6 (Me). FAB-MS: 228 (100, $[M+H]^+$). HR-CI-MS: 228.0872 ($[C_{10}H_{13}NO_5+H]^+$; calc. 228.0872).

Esters **3e**–**g**. *General Procedure*. To a soln. of ROH (*x* mmol) and 2,6-dichlorobenzoyl chloride (*y* mmol) in dry pyridine (*z* ml), a soln. of **17** (50 mg, 0.139 mmol) in dry DMF (0.9 ml) was added. The mixture was stirred for 5 h. Then the soln. was diluted with CH_2Cl_2 (50 ml) and washed with 1M HCl, sat. aq. $NaHCO_3$ soln., and brine. The org. layer wasdried (Na_2SO_4) and evaporated and the residue purified by CC (SiO_2, CH_2Cl_2/MeOH 80:1 → 60:1). The obtained protected alkyl ester was dissolved in MeOH or THF (4 ml) (see below) and hydrogenated over 10% Pd/C (20 mg) at 1 atm for 1 h. The catalyst was removed by filtration and the solvent evaporated. The following esters were prepared in this manner.

*Methyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**3e**): ROH = MeOH; *x* = 0.556 mmol; *y* = 0.60; *z* = 2 ml. Purification of the protected methyl ester by CC (SiO_2, CH_2Cl_2/MeOH 20:1 → 10:1) followed by hydrogenolysis (MeOH) gave **3e** (5.7 mg, 37% overall). White solid. $[\alpha]_D^{25}=-45$ (*c* = 0.3, MeOH). IR: 3412 (OH, NH); 2920, 1717 (CO), 1588, 1443, 1236, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.61 (*s*, H–C(4)); 4.21 (*m*, H–C(3′)); 4.15 (*dd*, $^3J(1',2')=7.6$, $^3J(2',3')=5.0$, H–C(2′)); 4.04 (*d*, H–C(1′)); 3.84 (*s*, COOMe); 3.33 (*dd*, $^3J(3',4'a)=5.2$, $^2J(4'a,4'b)=12.1$, H_a–C(4′)); 2.93 (*dd*, $^3J(3',4'b)=3.1$); 2.59 (*s*, Me). ^{13}C-NMR (100.5 MHz, CD_3OD): 165.9 (*C*OOMe); 160.4, 153.8 (C(2), C(5)); 114.7 (C(3)); 108.8 (C(4)); 77.3 (C(2′)); 72.3 (C(3′)); 60.2 (C(1′)); 52.5 (C(4′)); 13.7 (Me). CI-MS: 242 (8, $[M+H]^+$). EI-MS: 241 (7, $M^{+\cdot}$). HR-EI-MS: 241.0955 ($C_{11}H_{15}NO_5^+$; calc. 241.0950).

*1-Methylethyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**3f**). ROH = ^{i}PrOH; *x* = 12.7 mmol; *y* = 0.38 mmol; *z* = 0.8 ml. Purification of the protected 1-methylethyl ester by CC (SiO_2, CH_2Cl_2/MeOH 80:1 → 60:1) followed by hydrogenolysis in THF gave **3f** (6.3 mg, 19% overall). White solid. $[\alpha]_D^{25}=-32$ (*c* = 0.2, MeOH). IR: 3396 (OH, NH); 2922, 1731 (CO), 1588, 1406, 1105. ^{1}H-NMR (400 MHz, CD_3OD): 6.59 (*s*, H–C(4)); 5.16 (*sept.*, ^2J(H,H) = 6.2, Me_2CH), 4.20 (*td*, $^3J(3',4'b)=3.1$, $^3J(3',4'a)=^3J(3',2')=5.1$, H–C(3′)); 4.14 (*dd*, $^3J(1',2')=7.7$, H–C(2′)); 4.03 (*d*, H–C(1′)); 3.31 (*dd*, $^2J(4'a,4'b)=12.1$, H_a–C(4′)); 2.92 (*dd*, H_b–C(4′)); 2.58 (*s*, Me); 1.36 (*d*, Me_2CH). ^{13}C-NMR (100.5 MHz, CD_3OD): 165.1 (*C*OO^{i}Pr); 160.1, 153.6 (C(2), C(5)); 115.5 (C(3)); 108.8 (C(4)); 77.3 (C(2′)); 72.3 (C(3′)); 68.9 (Me_2CH), 60.3 (C(1′)); 52.5 (C(4′)); 22.2 (Me_2CH); 13.8 (Me). EI-MS: 269 (14, $M^{+\cdot}$). HR-EI-MS: 269.1260 ($C_{13}H_{19}NO_5^+$; calc. 269.1263).

*Butyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**3g**): ROH = BuOH; *x* = 0.27 mmol; *y* = 0.27 mmol; *z* = 1.2 ml. Purification of the protected butyl ester by CC (SiO_2, CH_2Cl_2/MeOH 80:1 → 60:1) followed by hydrogenolysis in THF gave **3g** (14.2 mg, 37% overall). Colorless oil. $[\alpha]_D^{25}=-30$ (*c* = 0.4, MeOH). IR: 3420 (OH, NH), 2926, 1719 (CO), 1588, 1406, 1103. ^{1}H-NMR (400 MHz, CD_3OD): 6.60 (*s*, H–C(4)); 4.27 (*t*, ^2J(H,H) = 7.4, CH_2 of Bu); 4.19 (*m*, H–C(3′)); 4.14 (*dd*, $^3J(1',2')=7.6$, $^3J(2',3')=5.0$, H–C(2′)); 4.03 (*d*, H–C(1′)); 3.31 (*dd*, $^3J(3',4'a)=5.2$, $^2J(4'a,4'b)=12.1$, H_a–C(4′)); 2.91 (*dd*, $^3J(3',4'b)=3.1$, H_b–C(4′)); 2.57 (*s*, Me), 1.74 (*m*, CH_2 of Bu), 1.51 (*m*, CH_2 of Bu), 1.02 (*t*, CH_2 of Bu). ^{13}C-NMR (100.5 MHz,

CD_3OD): 165.3 (*C*OOBu); 160.2, 153.9 (C(2), C(5)); 115.2 (C(3)); 108.7 (C(4)); 77.3 (C(2′)); 72.3 (C(3′)); 65.1 (CH_2 of Bu); 60.3 (C(1′)); 52.5 (C(4′)); 31.9 (CH_2 of Bu); 20.3 (CH_2 of Bu); 14.0 (Me of Bu); 13.8 (Me). CI-MS: 284 (17, $[M+H]^{+\cdot}$). EI-MS: 283 (12, $M^{+\cdot}$). HR-EI-MS: 283.1422 ($C_{14}H_{21}NO_5^+$; calc. 283.1420).

Amides **3h**,**i**: *General Procedure.* To a soln. of **17** (20 mg, 0.055 mmol) in dry DMF (0.75 ml), PyBOP (1*H*-benzotriazol-1-yloxy)tri(pyrrolidin-1-yl)phosphonium hexafluorophosphate; 34 mg, 0.06 mmol), ^{i}Pr_2Etn (24 µl, 0.14 mmol), and RNH_2 (0.06 mmol) were added. The mixture was stirred 30 min at r.t. and then evaporated. The residue was diluted with CH_2Cl_2 and washed with 1M HCl and brine. The org. layer was dried (Na_2SO_4) and evaporated. Purification of the residue by CC (SiO_2, CH_2Cl_2/MeOH 60:1 → 30:1) gave the protected amide derivative that was dissolved in MeOH (2 ml) and hydrogenated over 10% Pd/C (15 mg) at 1 atm for 1 h. The catalyst was removed by filtration, and the solvent was evaporated. The following amides were obtained in this manner.

N-*{[5-[(2*R,*3*S,*4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-yl}carbonyl}glycine Ethyl Ester* (**3h**): With RNH_2 = glycine ethyl ester hydrochloride, **3h** (15 mg, 84% overall) was obtained. Colorless oil. $[\alpha]_D^{25} = -44$ ($c = 0.7$, MeOH). IR: 3422 (OH, NH), 1732, 1651 (CO), 1539, 1404, 1223, 1103. ^{1}H-NMR (300 MHz, CD_3OD)[1]): 6.62 (*s*, H–C(4)); 4.22–4.12 (*m*, H–C(2′), H–C(3′), MeCH_2); 4.03 (*d*, ^3J(1′,2′) = 7.3, H–C(1′)); 4.01 (*s*, NHCH_2); 3.31 (*dd* (overlapped by MeOH), ^3J(3′,4′a) = 5.4, H_a–C(4′)); 2.91 (*dd*, ^3J(3′,4′b) = 2.8, ^2J(4′a,4′b) = 12.0, H_b–C(4′)); 2.52 (*s*, Me); 1.26 (*t*, ^3J(H,H) = 7.1, *Me*CH_2). ^{13}C-NMR (75.4 MHz, CD_3OD): 171.6 (*C*OOEt); 166.7 (CONH); 158.2, 153.0 (C(2), C(5)); 117.1 (C(3)); 107.6 (C(4)); 77.2 (C(2′)); 72.3 (C(3′)); 62.3 (Me*C*H_2); 60.4 (C(1′)); 52.4 (C(4′)); 42.0 (CH_2NH); 14.5 (*Me*CH_2). EI-MS: 312 (23, $M^{+\cdot}$). HR-EI-MS: 312.1318 ($C_{14}H_{20}N_2O_6^+$; calc. 312.1321).

*5-[(2*R,*3*S,*4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methyl*-N-*phenylfuran-3-carboxamide* (**3i**): With RNH_2 = Ph,NH_2 **3i** (2.8 mg, 17% overall) was obtained. Colorless oil. $[\alpha]_D^{22} = -46$ ($c = 0.7$, MeOH). ^{1}H-NMR (300 MHz, CD_3OD): 7.60 (*d*, ^3J(H,H) = 7.5, H–C(2) and H–C(6) of Ph); 7.32 (*t*, H–C(3) and H–C(5) of Ph); 7.11 (*t*, H–C(4) of Ph); 6.80 (*s*, H–C(4)); 4.22–4.15 (*m*, H–C(2′), H–C(3′)); 4.06 (*d*, ^3J(1′,2′) = 7.0, H–C(1′)); 3.35 (*m*, H_a–C(4′)); 2.93 (*dd*, ^3J(3′,4′b) = 2.8, ^2J(4′a,4′b) = 13.4, H_b–C(4′)); 2.57 (*s*, Me). ^{13}C-NMR (75.4 MHz, CD_3OD): 164.7 (CONH); 158.7, 153.5 (C(2), C(5)); 139.7 (C(1) of Ph); 129.9 (C2) and C(6) of Ph); 125.5 (C(4) of Ph); 122.4 (C(3) and C(5) of Ph); 118.1 (C(3)); 107.7 (C(4)); 77.3 (C(2′)); 72.3 (C(3′)); 60.6 (C(1′)); 52.5 (C(4′)); 13.7 (Me). CI-MS: 303 (100, $[M+H]^+$). HR-CI-MS: 303.1329 ($[C_{16}H_{18}N_2O_4+H]^+$; calc. 303.1345).

Amides **19**–**21**: *General Procedure.* To a soln. of **17** (0.1 mmol) in dry DMF (1 ml), PyBOP (1.2 equiv.), ^{i}Pr_2EtN (1.2 equiv.), and R^1R^2NH (1.2 equiv.) were added. The mixture was stirred for 30 min and then evaporated. The residue was diluted with CH_2Cl_2 and washed with 1M HCl and brine. The org. layer was dried (Na_2SO_4) and evaporated. Purification of the resulting residue by CC (SiO_2, CH_2Cl_2/MeOH 80:1 → 40:1) gave the protected amide derivative, which was dissolved in dry THF (4 ml) and hydrogenated over 10% Pd/C at 1 atm for 1 h. The catalyst was removed by filtration, the solvent evaporated, and the corresponding residue purified by CC (SiO_2, CH_2Cl_2/MeOH 25:1 → 6:1). The following compounds were prepared in this manner.

*5-[(2*R,*3*S,*4*R*)-3,4-Dihydroxy-1-(4-hydroxybutyl)pyrrolidin-2-yl]-2-methyl*-N-*(1-methylethyl)furan-3-carboxamide* (**19**): With $R^1R^2NH = {}^i$PrNH_2, **19** (15 mg, 46% overall) was obtained. Colorless oil. $[\alpha]_D^{25} = +10$ (c = 0.7, MeOH). IR: 3324 (OH, NH), 2936, 1634 (CO), 1588, 1530, 1406, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.67 (*s*, H–C(4)); 4.22 (*m*, H–C(3)); 4.20 (*m*, Me_2CH); 4.13 (*dd*, ^3J(2′,3′) = 5.9, ^3J(1′,2′) = 7.1, H–C(2′)); 3.56–3.50 (*m*, H_a–C(4′), CH_2(4″)); 3.48 (*d*, H–C(1′)); 2.70 (*m*, H_a–C(1′)); 2.56 (*s*, Me); 2.44 (*dd*, ^3J(4′b,3′) = 4.9, ^2J(4′a,4′b) = 10.4, H_b–C(4′)); 2.36 (*m*, H_b–C(1″)); 1.55–1.50 (*m*, CH_2(2″), CH_2(3″)); 1.25 (*d*, ^3J(H,H) = 6.6, Me_2CH). ^{13}C-NMR (100.5 MHz, CD_3OD): 165.6 (*C*ONH^{i}Pr); 157.6, 152.6 (C(2), C(5)); 117.7 (C(3)); 108.9 (C(4)); 76.1 (C(2′)); 70.1 (C(3′)); 68.5 (C(1′)); 62.7 (C(4″)); 59.8 (C(4′)); 55.9 (C(1″)); 42.4 (Me_2*C*H); 31.6, 25.4 (C(2″), C(3″)); 22.6 (*Me*$_2$CH); 13.7 (Me). EI-MS: 340 (22, $M^{+\cdot}$). HR-EI-MS: 340.2003 ($C_{17}H_{28}N_2O_5^+$; calc. 340.1998).

*5-[(2*R,*3*S,*4*R*)-3,4-Dihydroxy-1-(4-hydroxybutyl)pyrrolidin-2-yl]*-N,N-*diethyl-2-methylfuran-3-carboxamide* (**20**). With $R^1R^2NH = Et_2NH$, **20** (18 mg, 22% overall) was obtained. Colorless oil. $[\alpha]_D^{25} = +11$ (c = 0.7, MeOH). IR: 3391 (OH), 2934, 1666–1603 (CO), 1443, 1221, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.40 (*s*, H–C(4)); 4.23 (*m*, H–C(3′)); 4.13 (*dd*, ^3J(2′,3′) = 5.9, ^3J(1′,2′) = 7.0, H–C(2′)); 3.55–3.50 (*m*, H–C(1′), H_a–C(4′), CH_2(4″), 2 MeCH_2); 2.70 (*m*, H_a–C(1″)); 2.44 (*dd*, ^3J(4′b,3′) = 4.9, ^2J(4′a,4′b) = 10.4, H_b–C(4′)); 2.40 (*m*, H_b–C(1″)); 2.36 (*s*, Me); 1.58–1.49 (*m*, CH_2(″), CH_2(3″)); 1.23 (br. *s*, 2 *Me*CH_2). ^{13}C-NMR (100.5 MHz, CD_3OD): 168.1 (*C*ONHEt_2); 153.6, 153.2 (C(2), C(5)); 118.1 (C(3)); 109.5 (C(4)); 76.3 (C(2′)); 70.1 (C(3′)); 68.4 (C(1′)); 62.8 (C(4″)); 59.9 (C(4′)); 55.9 (C(1″)); 44.6, 40.9 (2 MeCH_2); 31.6, 25.4 (C(2″), C(3″)); 14.6, 13.2 (2 *Me*CH_2); 12.8 (Me). EI-MS: 354 (22, $M^{+\cdot}$). HR-EI-MS: 354.2157 ($C_{18}H_{30}N_2O_5^+$; calc. 354.2155).

N-*{[5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxy-1-(4-hydroxybutyl)pyrrolidin-2-yl]-2-methylfuran-3-yl}carbonyl}*-L-*phenylalanine Methyl Ester* (**21**). With $R^1R^2NH = H_2N-Phe-OMe$ **21** (18 mg, 39% overall) was obtained. Colorless oil. $[\alpha]_D^{25} = -21$ ($c = 0.8$, MeOH). IR: 3367 (OH, NH); 2934, 2857, 1736 (CO), 1642 (CO), 1528, 1443, 1227, 1101, 849, 700. ^{1}H-NMR (400 MHz, CD_3OD)[1]): 7.31–7.24 (*m*, Ph); 6.64 (*s*, H–C(4′)); 4.82 (*dd*, ^3J(H,H$_a$ of Bn) = 5.4, ^3J(H,H$_b$ of Bn) = 9.4, HNC*H*COOMe), 4.22 (*m*, H–C(3′)); 4.12 (*dd*, ^3J(2′,3′) = 5.9, ^3J(1′,2′) = 7.0, H–C(2′)); 3.76 (*s*, COOMe); 3.57–3.51 (*m*, H$_a$–C(4′), CH$_2$(4″)); 3.49 (*d*, H–C(1′)); 3.29 (*dd*, ^2J(H,H) = 13.8, PhC*H*); 3.11 (*dd*, PhC*H*); 2.70 (*m*, H$_a$–C(1″)); 2.47 (*s*, Me); 2.45 (*dd*, ^3J(4′b,3′) = 4.9, ^2J(4′a,4′b) = 10.4, H$_b$–C(4′)); 2.37 (*m*, H$_b$–C(1″)); 1.59–1.48 (*m*, CH$_2$(2″), CH$_2$(3″)). ^{13}C-NMR (100.5 MHz, CD_3OD)[1]): 173.8 (*C*OOMe); 166.2 (*C*ONH); 158.1, 152.8 (C(2), C(5′)); 138.5 (C(1) of Ph); 130.2, 129.5, 127.8 (Ph); 117.0 (C(3)); 108.9 (C(4)); 76.1 (C(2′)); 70.1 (C(3′)); 68.5 (C(1′)); 62.8 (C(4″)); 59.8 (C(4′)); 55.9 (C(1″)); 55.3 (Ph*C*H$_2$); 52.8 (COO*Me*); 38.1 (CH of HN–Phe–OMe); 31.6, 25.4 (C(2″), C(3″)); 13.6 (Me). EI-MS: (30, $M^{+\bullet}$). HR-EI-MS: 460.2208 ($C_{24}H_{32}N_2O_5^+$; calc. 460.2209).

*5-[(2*R*,3*S*,4*R*)- and (2*S*,3*S*,4*R*)-1-[(9*H*-Fluoren-9-ylmethoxy)carbonyl]-3,4-dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylic Acid* (**22** and **23**, resp.). The mixture **3c**/**4c** 2:1 (0.77 g, 3.01 mmol) was dissolved in EtOH/1M NaOH (80 ml) and heated for 6 h at 60°. The mixture was then neutralized with *Amberlyst IR-120* (H^+), filtered, and evaporated. The residue was dissolved in dry pyridine (2 ml) and cooled to 0°. Chlorotrimethylsilane (2.3 ml, 18.24 mmol) was added dropwise. The mixture was allowed to warm to r.t. and stirred for 45 min. The soln. was then cooled to 0° and 9*H*-fluoren-9-ylmethyl carbonochloridate (1.19 g, 4.46 mmol) was added. The mixture was warmed to r.t. and stirred for 1.5 h. Then, the soln. was cooled again to 0°, H_2O (6 ml) was added, and the soln. stirred for 1 h at r.t. Finally, the solvent was evaporated and the residue purified by CC (SiO_2, CH_2Cl_2/MeOH 15:1 → 8:1): **22**/**23** 2:1 (1.11 g, 82% overall). White solid. IR: 3600–2350 (OH, CO*OH*)), 1690 (CO), 1418, 1223, 1103, 1024, 743. ^{1}H-NMR (300 MHz, CD_3OD; mixture of conformers of **22**/**23**): 7.75–7.23 (*m*, arom. H of Fmoc); 6.37, 6.28 (br. *s*, each, H–C(4)); 4.40–4.08 (*m*, CH and CH$_2$ of Fmoc, H–C(1′), H–C(2′), H–C(3′), H–C(4′)); 3.75–3.40 (*m*, H–C(4′)); 2.49, 2.47 (*s*, each, Me). ^{13}C-NMR (75.4 MHz, CD_3OD; mixture of conformers of **22**/**23**): 167.3 (COOH); 159.8, 159.7, 152.2 (C(2), C(5)); 145.2, 142.6, 128.7, 128.1, 125.9, 120.9 (arom. C of Fmoc); 116.1 (C(3)); 110.0, 109.0 (C(4)); 77.6, 70.6, 62.2, 59.1, 51.7 (C(1′), C(2′), C(3′), C(4′)); 68.5 (CH$_2$ of Fmoc); 49.9–48.2 (CH of Fmoc); 13.7 (Me). FAB-MS: 472 (33, $[M + Na]^+$), 494 (15, $[M - 1 + 2Na]^{+\bullet}$). HR-FAB-MS: 472.1377 ($[C_{25}H_{23}NO_7 + Na]^+$; calc. 472.1372).

Amides (**3b**,**j**,**k** *and* **4b**,**j**,**k**): *General Procedure.* To a soln. of **22**/**23** 2:1 (0.1 mmol) in dry DMF (1 ml), PyBOP (1.2 equiv.), ^{i}Pr$_2$EtN (1.2 equiv.), and R^1R^2NH (1.2 equiv.) was added. The mixture was stirred for 30 min and then evaporated. The residue was diluted with CH_2Cl_2 and washed with 1M HCl and brine. The org. layer was dried (Na_2SO_4) and evaporated and the residue acylated conventionally with Ac_2O/pyridine. The resulting residue was purified by CC (SiO_2, Et$_2$O/petroleum ether 1:2 → 5:1) to give, separately, the two *O*-acetylated 1′-epimeric[1]) amides that were, independently, dissolved in MeOH (2 ml). Then 1M NaOMe/MeOH (4 drops) was added and the mixture stirred at r.t. for 20 min. The solvent was evaporated and the residue dissolved in DMF (2 ml) and treated with Et$_2$NH (30 equiv.). The mixture was stirred for 15 min and then evaporated, and the resulting residue purified by CC (SiO_2, CH_2Cl_2/MeOH 20:1 → 6:1). The following compounds were prepared in this manner.

*5-[(2*R*,3*S*,4*R*)- and (2*S*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methyl*-N-*(phenylmethyl)furan-3-carboxamide* (**3b** and **4b**): With $R^1R^2NH = PhCH_2NH_2$, **3b** (9.8 mg, 46% overall) and **4b** (3.8 mg, 36% overall) were obtained. Colorless oils.

Data of **3b**: $[\alpha]_D^{25} = -55$ ($c = 0.8$, MeOH). IR: 3388 (NH, OH), 2917, 2830, 1640 (CO), 1404, 1221, 1103, 739. ^{1}H-NMR (400 MHz, CD_3OD): 7.36–7.23 (*m*, Ph); 6.73 (*s*, H–C(4)); 4.53 (*s*, CH$_2$ of Bn); 4.26–4.22 (*m*, H–C(2′), H–C(3′)); 4.15 (*d*, ^3J(1′,2′) = 7.3, H–C(1′)); 3.38 (*dd* (overlapped by MeOH), H$_a$–C(4′)); 3.01 (*dd*, ^3J(3′,4′b) = 2.3, ^2J(4′a,4′b) = 12.0, H$_b$–C(4′)); 2.58 (*s*, Me). ^{13}C-NMR (100.5 MHz, CD_3OD): 166.1 (*C*ONHBn); 158.3, 151.9 (C(2), C(5)); 140.3, 129.5, 128.5, 128.1 (6 C, Ph); 117.6 (C(3)); 108.3 (C(4)); 76.9 (C(2′)); 72.1 (C(3′)); 60.0 (C(1′)); 52.2 (C(4′)); 43.9 (Ph*C*H$_2$); 13.7 (Me). EI-MS: 316 (13, $M^{+\bullet}$). HR-EI-MS: 316.1415 ($C_{17}H_{20}N_2O_4^+$; calc. 316.1423).

Data of **4b**: $[\alpha]_D^{25} = -22$ ($c = 0.6$, MeOH). IR: 3388 (NH, OH), 2917, 2830, 1640 (CO), 1404, 1103, 1028, 739. ^{1}H-NMR (400 MHz, CD_3OD): 7.34–7.25 (*m*, Ph); 6.73 (*s*, H–C(4′)); 4.52 (*s*, PhC*H*$_2$); 4.37 (*m*, H–C(3′)); 4.23 (*d*, ^3J(1′,2′) = 3.9, H–C(1′)); 4.19 (*t*, ^3J(2′,3′) = 4.1, H–C(2′)); 3.20 (*dd*, ^3J(3′,4′a) = 7.5, ^2J(4′a,4′b) = 11.5, H$_a$–C(4′)); 2.99 (*dd*, ^3J(3′,4′b) = 6.3, H$_b$–C(4′)); 2.55 (*s*, Me). ^{13}C-NMR (100.5 MHz, CD_3OD): 166.3 (*C*ONHBn); 157.5, 150.6 (C(2), C(5)); 140.4, 129.5, 128.4, 128.1 (6 C, Ph); 117.6 (C(3)); 108.5 (C(4)); 73.7, 73.5 (C(2′), C(3′)); 60.3 (C(1′)); 51.3 (C(4′)); 43.8 (Ph*C*H$_2$); 13.6 (Me). EI-MS: 316 (4, $M^{+\bullet}$). HR-EI-MS: 316.1435 ($C_{17}H_{20}N_2O_4^+$; calc. 316.1423).

*5-[(2*R*,3*S*,4*R*)- and (2*S*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methyl*-N-*(1-methylethyl)furan-3-carboxamide* (**3j** and **4j**, resp.): With $R^1R^2NH = {}^iPrNH_2$, **3j** (7.5 mg, 41% overall) and **4j** (2.9 mg, 35% overall) were obtained. Colorless oils.

Data of **3j**: $[\alpha]_D^{25} = -70$ ($c = 0.6$, MeOH). IR: 3356 (NH, OH), 1634 (CO), 1534, 1400, 1103. ^{1}H-NMR (400 MHz, CD_3OD): 6.67 (*s*, H–C(4)); 4.24–4.12 (*m*, H–C(2′), H–C(3′), Me_2CH); 4.06 (*d*, $^3J(1',2') = 7.5$, H–C(1′)); 3.33 (*dd*, H_a–C(4′)); 2.95 (*dd*, $^3J(3',4'b) = 3.0$, $^2J(4'a,4'b) = 12.1$, H_b–C(4′)); 2.56 (*s*, Me); 1.25 (*d*, $^3J(H,H) = 6.6$, Me_2CH). ^{13}C-NMR (100.5 MHz, CD_3OD): 165.5 ($CONH^iPr$); 157.6, 152.7 (C(2), C(5)); 117.8 (C(3)); 107.7 (C(4)); 77.2 (C(2′)); 72.3 (C(3′)); 60.4 (C(1′)); 52.4 (C(4′)); 42.4 (Me_2CH); 22.6 (Me_2CH); 13.6 (Me). EI-MS: 268 (18, $M^{+\bullet}$). HR-EI-MS: 268.1425 ($C_{13}H_{20}N_2O_4^+$; calc. 268.1423).

Data of **4j**: $[\alpha]_D^{25} = -10$ ($c = 0.3$, MeOH). IR: 3325 (NH, OH), 2930, 1634 (CO), 1588, 1402, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.88 (*s*, H–C(4)); 4.50–4.45 (*m*, H–C(1′), H–C(3′)); 4.29 (*t*, $^3J(1',2') = {}^3J(2',3') = 3.9$, H–C(2′)); 4.18 (*sept.*, $^3J(H,H) = 6.6$, Me_2CH); 3.38 (*dd* (overlapped by MeOH), H_a–C(4′)); 3.15 (*dd*, $^3J(3',4'b) = 6.8$, $^2J(4'a,4'b) = 11.6$, H_b–C(4′)); 2.55 (*s*, Me); 1.25 (*d*, $^3J(H,H) = 6.6$, Me_2CH). ^{13}C-NMR (100.5 MHz, CD_3OD): 165.3 ($CONH^iPr$); 157.7, 147.9 (C(2), C(5)); 118.2 (C(3)); 110.1 (C(4)); 73.2, 72.8 (C(2′), C(3′)); 59.9 (C(1′)); 50.2 (C(4′)); 42.5 (Me_2CH), 22.6 (Me_2CH); 13.5 (Me). CI-MS: 269 (8, $[M+H]^+$). EI-MS: (8, $M^{+\bullet}$). HR-EI-MS: 268.1429 ($C_{13}H_{20}N_2O_4^+$; calc. 268.1423).

*5-[(2*R*,3*S*,4*R*)- and (2*S*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-*N,N-*diethyl-2-methylfuran-3-carboxamide* (**3k** and **4k**): With $R^1R^2NH = Et_2NH$, **3k** (7.3 mg, 39% overall) and **4k** (3.1 mg, 36% overall) were obtained. Colorless oils.

Data of **3k**: $[\alpha]_D^{25} = -50$ ($c = 0.3$, MeOH). IR: 3412 (NH, OH), 2922, 1595–1700 (CO), 1443, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.42 (*s*, H–C(4)); 4.24–4.18 (*m*, H–C(2′), H–C(3′)); 4.10 (*d*, $^3J(1',2') = 7.5$, H–C(1′)); 3.52 (br. *s*, 2 $MeCH_2$); 3.38 (*dd* (overlapped by MeOH), H_a–C(4′)); 2.97 (*dd*, $^3J(3',4'b) = 2.5$, $^2J(4'a,4'b) = 12.0$, H_b–C(4′)); 2.36 (*s*, Me); 1.22 (br. *s*, 2 $MeCH_2$). ^{13}C-NMR (100.5 MHz, CD_3OD): 168.0 ($CONEt_2$); 153.7, 152.9 (C(2), C(5)); 118.2 (C(3)); 108.5 (C(4)); 77.2 (C(2′)); 72.2 (C(3′)); 60.2 (C(1′)); 52.3 (C(4′)); 44.6, 40.9 ($MeCH_2$); 14.6, 13.1 ($MeCH_2$); 12.8 (Me). EI-MS: 282 (14, $M^{+\bullet}$). HR-EI-MS: 282.1577 ($C_{14}H_{22}N_2O_4^+$; calc. 282.1579).

Data of **4k**: $[\alpha]_D^{25} = -13$ ($c = 0.3$, MeOH). IR: 3404 (NH, OH), 2974, 2932, 1661–1542 (CO), 1443, 1383, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.55 (*s*, H–C(4)); 4.44–4.39 (*m*, H–C(3′)); 4.31 (*d*, $^3J(1',2') = 3.9$, H–C(1′)); 4.23 (*t*, $^3J(2',3') = 3.9$, H–C(2′)); 3.52 (br. *s*, 2 $MeCH_2$); 3.26 (*dd*, $^3J(3',4'a) = 7.5$, $^2J(4'a,4'b) = 11.5$, H_a–C(4′)); 3.04 (*dd*, $^3J(3',4'b) = 6.4$, H_b–C(4′)); 2.36 (*s*, Me); 1.23 (*d*, 2 $MeCH_2$). ^{13}C-NMR (100.5 MHz, CD_3OD): 168.1 ($CONEt_2$); 153.5, 150.2 (C(2), C(5)); 118.3 (C(3)); 109.6 (C(4)); 73.5, 73.3 (C(2′), C(3′)); 60.2 (C(1′)); 51.0 (C(4′)); 44.6, 40.9 ($MeCH_2$); 14.6, 13.2, ($MeCH_2$); 12.8 (Me). EI-MS: 282 (15, $M^{+\bullet}$). HR-EI-MS: 282.1584 ($C_{14}H_{22}N_2O_4^+$; calc. 282.1579).

*5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-*N-*ethyl-2-methylfuran-3-carboxamide* (**3l**). As described for **3b**,**j**,**k**, with **22** (46 mg, 0.1 mmol) and $EtNH_2$ but omitting acetylation and deacetylation with 1M NaOMe/MeOH. Fmoc Deprotection gave **3l** (14.2 mg, 56% overall). Colorless oil. $[\alpha]_D^{25} = -51$ ($c = 0.5$, MeOH). IR: 3347 (NH, OH), 2928, 1634 (CO), 1588, 1445, 1101, 856, 748. ^{1}H-NMR (400 MHz, CD_3OD): 6.67 (*s*, H–C(4)); 4.25–4.21 (*m*, H–C(2′), H–C(3′)); 4.13 (*d*, $J(1',2') = 7.1$, H–C(1′)); 3.39–3.34 (*m* (overlapped by MeOH), H_a–C(4′), $MeCH_2$); 3.00 (*dd*, $^3J(3',4'b) = 2.5$, $^2J(4'a,4'b) = 12.1$, H_b–C(4′)); 2.57 (*s*, Me); 1.23 (*t*, $^3J(H,H) = 7.3$, $MeCH_2$). ^{13}C-NMR (100.5 MHz, CD_3OD): 166.1 ($CONHEt$); 157.9, 151.9 (C(2), C(5)); 117.7 (C(3)); 108.2 (C(4)); 76.9 (C(2′)); 72.1 (C(3′)); 60.1 (C(1′)); 52.2 (C(4′)); 35.2 ($MeCH_2$); 15.0 ($MeCH_2$); 13.6 (Me). CI-MS: 255 (23, $[M+H]^+$). EI-MS: 254 (12, $M^{+\bullet}$). HR-EI-MS: 254.1262 ($C_{12}H_{18}N_2O_4^+$; calc. 254.1267).

S-*Phenyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carbothioate* (**3a**) *and Methyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate* (**3e**). To a soln. of **22**/**23** (104 mg, 0.23 mmol) in dry THF (1.3 ml), thiophenol (30 µl, 0.3 mmol), DCC (63 mg, 0.3 mmol), and DMAP (3 mg) were added. The mixture was stirred for 2 h and evaporated and the residue acetylated conventionally with Ac_2O/pyridine. Purification of the residue by CC (SiO_2, Et_2O/petroleum ether 1:2 → 2:1) gave **24** (69 mg, 48%) and **25** (26 mg, 18%).

Diasteroisomer **24** was dissolved in MeOH (2 ml), and 1M NaMeO/MeOH was added until a basic pH was reached. The mixture was left to stand at r.t. for 20 min, then made neutral with *Amberlyst IR-120* (H^+), filtered, and evaporated. The residue was dissolved in DMF (2 ml), Et_2NH (30 equiv.) was added, the mixture stirred for 15 min at r.t. and then evaporated, and the residue purified by CC (SiO_2, CH_2Cl_2/MeOH 20:1 → 6:1): **3a** (8 mg, 23%) as colorless oil followed by **3e** (7 mg, 28%; see above). **3a**: $[\alpha]_D^{25} = -34$ ($c = 0.3$; MeOH). IR: 3375 (NH, OH), 2922, 1721 (CO), 1665, 1589, 1406, 1105. ^{1}H-NMR (400 MHz, CD_3OD); 7.54–7.48 (*m*, Ph); 6.81 (*s*, H–C(4)); 4.24–4.17 (*m*, H–C(2′), H–C(3′)); 4.10 (*d*, $^3J(1',2') = 7.5$, H–C(1′)); 3.35 (*dd* (overlapped by MeOH), H_a–C(4′)); 2.96 (*dd*, $^3J(3',4'b) = 2.8$, $^2J(4'a,4'b) = 12.0$, H_b–C(4′)); 2.59 (*s*, Me). ^{13}C-NMR

(100.5 MHz, CD_3OD): 185.6 (*C*OSEt); 158.5, 154.5 (C(2), C(5)); 136.2, 130.6, 130.3 (5 C, Ph); 128.5 (C(1) of Ph); 121.7 (C(3)); 107.6 (C(4)); 77.4 (C(2′)); 72.3 (C(3′)); 60.2 (C(1′)); 52.5 (C(4′)); 14.2 (Me). CI-MS: 320 (83, $[M+H]^+$). EI-MS: 319 (5, $M^{+\bullet}$). HR-EI-MS: 319.0884 ($C_{16}H_{17}NO_4S^+$; calc. 319.0878).

Methyl 5-[(2S,3S,4R)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate (**4e**). As described for **3a**/**3e**, with diastereoisomer **25** (see above; 26 mg, 0.041 mmol) in MeOH (3 ml), 1M NaOMe/MeOH, and Et_2NH/DMF: **4e** (5.5 mg, 56%) (the (1′*S*)-epimer[1]) **4a** of **3a** was not observed). Colorless oil. $[\alpha]_D^{25} = -27$ ($c = 0.3$, MeOH). IR: 3375 (NH, OH), 1719 (CO), 1589, 1406, 1101. ^{1}H-NMR (400 MHz, CD_3OD): 6.70 (*s*, H–C(4)); 4.36 (*m*, H–C(3′)); 4.20–4.48 (*m*, H–C(2′), H–C(1′)); 3.84 (*s*, COO*Me*); 3.18 (*dd*, $^3J(3',4'a) = 7.4$, $^2J(4'a,4'b) = 11.5$, H_a–C(4′)); 3.00 (*dd*, $^3J(3',4'b) = 6.2$, H_b–C(4′)); 2.58 (*s*, Me). ^{13}C-NMR (100.5 MHz, CD_3OD): 170.4 (*C*OOMe); 159.9, 151.6 (C(2), C(5)); 114.7 (C(3)); 109.7 (C(4)); 73.8, 73.7 (C(2′), C(3′)); 60.3 (C(1′)); 51.8 (COOMe); 51.6 (C(4′)); 13.7 (Me). CI-MS: 242 (14, $[M+H]^{+\bullet}$). EI-MS: 241 (8, $M^{+\bullet}$). HR-EI-MS: 241.0945 ($C_{11}H_{15}NO_5^+$; calc. 241.0950).

S-*Ethyl 5-[(2R,3S,4R)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carbothioate* (**3m**). To a soln. of **22** (40 mg, 0.09 mmol) in dry THF (1.5 ml), ethanethiol (14 µl, 0.18 mmol), DCC (38 mg, 0.18 mmol), and DMAP (3 mg) were added. The mixture was stirred for 2 h at r.t. and then evaporated. Purification of the residue by CC (SiO_2, CH_2Cl_2/MeOH 80:1 → 65:1) gave the protected thioester **26** (13 mg, 0.026 mmol), which was dissolved in DMF (1.5 ml). Et_2NH (30 equiv.) was added and the soln. stirred for 15 min at r.t. The solvent was evaporated and the resulting residue purified by CC (SiO_2, CH_2Cl_2/MeOH 20.1 → 6:1): **3m** (5.3 mg, 27% overall). Colorless oil. $[\alpha]_D^{25} = -70$ ($c = 0.4$, MeOH). IR: 3359 (NH, OH), 2928, 1651 (CO), 1570, 1406, 1103, 878. ^{1}H-NMR (400 MHz, CD_3OD): 6.71 (*s*, H–C(4)); 4.24–4.18 (*m*, H–C(2′), H–C(3′)); 4.10 (*d*, $^3J(1',2') = 7.4$, H–C(1′)); 3.36 (*dd* (overlapped by MeOH), H_a–C(4′)); 3.04 (*q*, $^3J(H,H) = 7.4$, MeCH_2); 2.97 (*dd*, $^3J(3',4'b) = 2.6$, $^2J(4'a,4'b) = 12.0$, H_b–C(4′)); 2.60 (*s*, Me); 1.33 (*t*, *MeCH*$_2$). ^{13}C-NMR (100.5 MHz, CD_3OD): 187.5 (*C*OSEt); 157.7, 153.4 (C(2′), C(5)); 122.6 (C(3)); 108.1 (C(4)); 77.2 (C(2′)); 72.2 (C(3′)); 60.0 (C(1′)); 52.3 (C(4′)); 23.7 (Me*C*H$_2$); 15.4 (*Me*CH$_2$); 14.2 (Me). EI-MS: 271 (13, $M^{+\bullet}$). HR-EI-MS: 271.0875 ($C_{12}H_{17}NO_4S^+$; calc. 271.0878).

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