Synthesis of *N*-Substituted (3*S*,4*S*)- and (3*R*,4*R*)-Pyrrolidine-3,4-diols: Search for New Glycosidase Inhibitors

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N-Substituted (3*S*,4*S*)- and (3*R*,4*R*)-pyrrolidine-3,4-diols **9** and **10**, respectively, were derived from (+)-L- and (−)-D-tartaric acid, respectively. Compounds **9k**, **9l**, and **9m** with the *N*-substituents, $BnNH(CH_2)_2$, 4-$PhC_6H_4CH_2NH(CH_2)_2$ and 4-$ClC_6H_4CH_2NH(CH_2)_2$, respectively, showed modest inhibitory activities toward α-D-amyloglucosidases from *Aspergillus niger* and from *Rhizopus* mold (*Table 1*). Unexpectedly, several (3*R*,4*R*)-pyrrolidine-3,4-diols **10** showed inhibitory activities toward α-D-mannosidases from almonds and from jack bean (*Table 3*). *N*-Substitution by the $NH_2(CH_2)_2$ group, *i.e.*, **10g**, led to the highest potency.

Introduction. – Inhibitors of α-D-glucosidases [1][2] have manifested *in vitro* anti-HIV activities [3]. Among them, 1-deoxynojirimycin (**1**) [4][5] and *N*-butyl-1-deoxynojirimycin (**2**) [6] (*Fig. 1*) have shown promising results as they exhibit little toxicity.

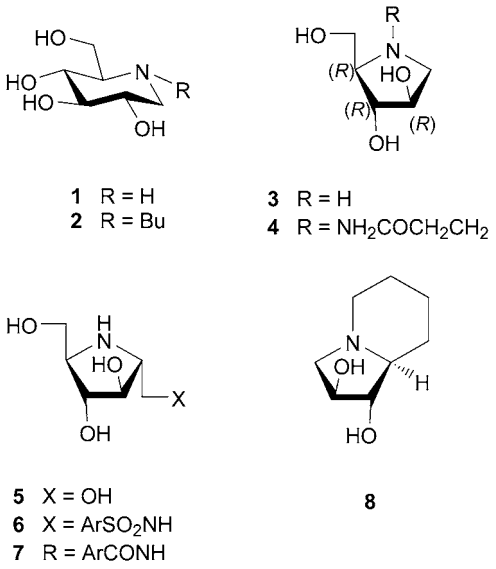


Fig. 1. *Inhibitors of α-D-glucosidases*

The polyhydroxyalkaloid **1** and derivatives have been isolated from mulberry trees (*Morus alba* L.) [7] and silkworms (*Bombyx mori* L.) [8] together with (2*R*,3*R*,4*R*)-2-

(hydroxymethyl)pyrrolidine-3,4-diol (**3**) and derivatives such as **4**. The latter alkaloids are also α-D-glucosidase inhibitors [8][9]. The crude drug 'Sohaku-hi', the root bark of mulberry trees, is used in some formulas of Japanese-Oriental (Kampo) medicine. Silk powder, silkworm powder, and mulberry leaves and fruits have been developed as natural functional food in Korea and Japan (antihyperglycemic effect) [8][10]. The (2*R*,3*R*,4*R*,5*R*)-2,5-bis(hydroxymethyl)pyrrolidine-3,4-diol (**5**) has been extracted from *Derris elliptica* (WALL) BENTH (leguminosal), and found to inhibit α-D-glucosidases, β-D-glucosidases, β-D-galactosidases, invertase (yeast), β-D-xylosidases, and trehalases [9][11]. Conjugation of **5** as arenesulfonamides **6** or carboxamides **7** constitute β-D-glucosidase inhibitors in the nanomolar range [12]. Fewer pyrrolidine-2,3-diols with the (3*S*,4*S*) configuration are known [1][9][13]. Among them (2*S*,3*S*,4*S*)-2-(hydroxymethyl)pyrrolidine-3,4-diol and lentiginosine (**8**) [14] are good inhibitors of α-D-glucosidases. Lentiginosine can be seen as an *N*-alkylated pyrrolidinediol derivative. There is an urgent need for new anti-HIV therapies. Orally active and inexpensive compounds should be found, and HIV-entry inhibition is one possible target for the discovery of new drugs (see, *e.g.*, [15]). As it is known that *N*-substitution of pyrrolidine derivatives can improve their glycosidase inhibitory activity, we envisioned that readily available (3*R*,4*R*)- and (3*S*,4*S*)-pyrrolidine-3,4-diol could generate useful compounds by *N*-substitution. Because they bear only two OH groups and a lipophilic moiety, they are expected to be compatible with the requirement of orally active drugs. Furthermore, we have demonstrated for (2*R*,3*R*,4*S*)- [16] and (2*S*,3*R*,4*S*)-2-(aminomethyl)pyrrolidine-3,4-diol [17] that *N*-substitution of their primary amine moiety leads to more-potent and more-selective α-D-mannosidase inhibitors. We report here the synthesis of (3*S*,4*S*)- and (3*R*,4*R*)-pyrrolidine-3,4-diol derivatives **9** and **10** and present preliminary results on their inhibitory activities toward several glycosidases.

9 **10**

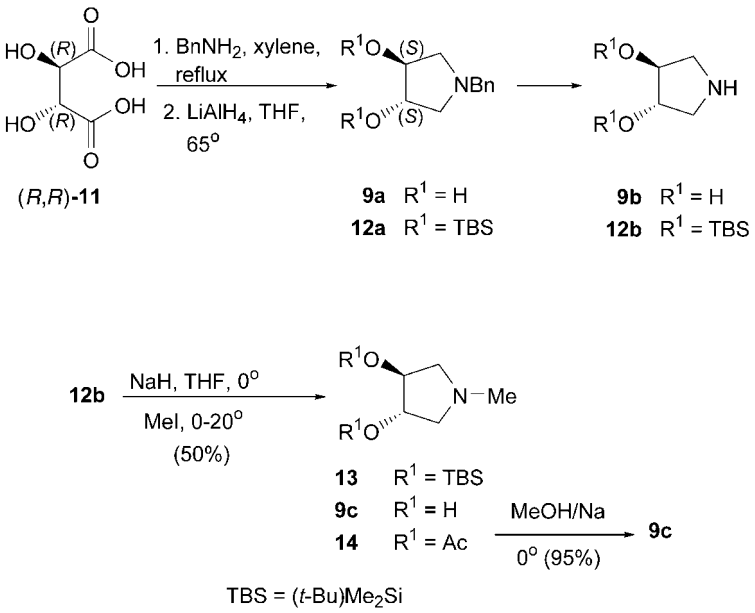
Fig. 2. *Pyrrolidine-3,4-diol derivatives* **9** *and* **10**

The best α-D-glucosidase (amyloglucosidase from *Aspergillus niger* and from *Rhizopus* mold) inhibitors happen to be compounds **9l** (R = 4-$PhC_6H_4CH_2NH(CH_2)_2$ and **9m** (R = 4-$ClC_6H_4CH_2NH(CH_2)_2$). Unfortunately these compounds are less potent α-D-glucosidase inhibitors than lentiginosine (**8**) or the more-polar polyhydroxypyrrolidine derivatives **3**–**7**.

Results and Discussion. – *Synthesis of New Pyrrolidine-3,4-diol Derivatives.* Our initial studies used (+)-L-tartaric acid ((*R*,*R*)-**11**) as starting material for the synthesis of (3*S*,4*S*)-pyrrolidine-3,4-diols. The known *N*-benzyl [18] and nonsubstituted [19][20] systems **9a** and **9b** were obtained readily applying published procedures (*Scheme 1*). The *O*-silylated derivatives **12a** and **12b** were also obtained under standard conditions

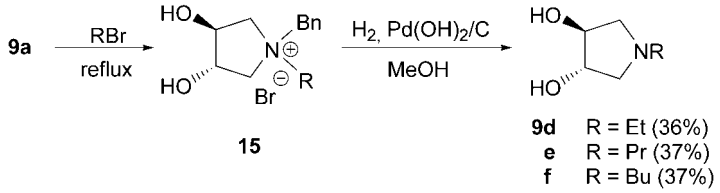
[18]. Direct *N*-methylation (NaH, THF, MeI) of **12b** produced derivative **13** in 50% yield. After desilylation with Bu_4NF in aqueous THF, impure **9c** (contaminated with Bu_4NF and Bu_3N) was obtained. The crude reaction mixture was then treated with Ac_2O/pyridine at 20°. This generated diacetate **14** (82%) that could be purified by flash chromatography (silica gel). Subsequent methanolysis under *Zemplen*'s conditions afforded pure **9c** (95%).

Scheme 1. *Synthesis of Derivative* **9c** *from (+)-*L*-Tartaric Acid*



The *N*-ethyl [13], *N*-propyl, and *N*-butyl derivatives **9d**–**f** were obtained on heating **9a** under reflux with EtBr, PrBr, and BuBr, respectively, without solvent (formation of the corresponding quaternary ammonium bromides **15**). Subsequent hydrogenolysis (20% $Pd(OH)_2$/C in MeOH, 20°, 5 days) produced **9d** (36%), **9e** (37%), and **9f** (37%)[1]), respectively, in moderate yields (*Scheme 2*). An alternative route was to heat

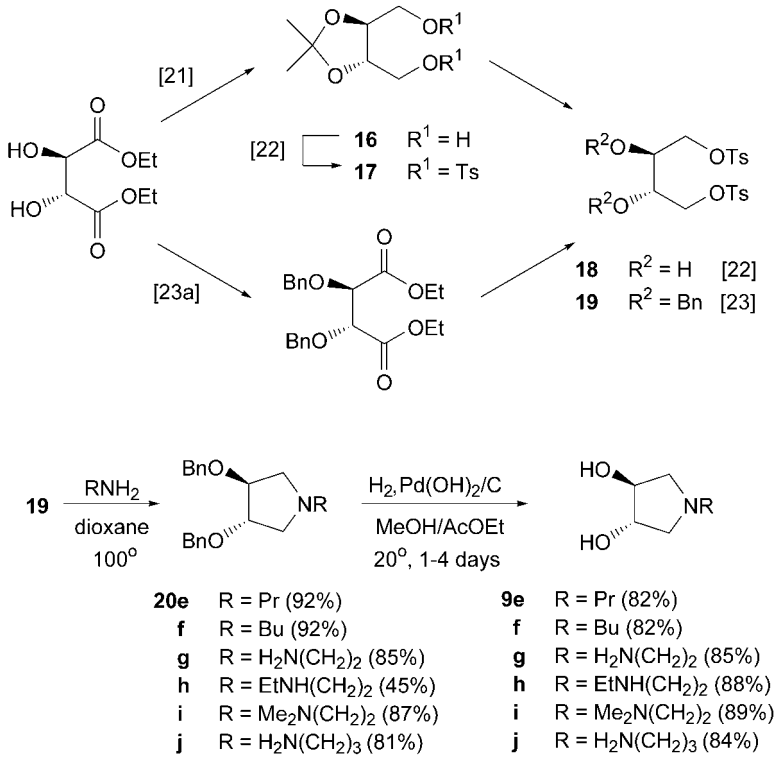
Scheme 2. *Synthesis of* N*-Alkylated Derivatives* **9d**–**f**



[1]) Compound **9f** was also obtained from (+)-L-tartaric acid and butanamine *via* (3*R*,4*R*)-1-butyl-3,4-dihydroxypyrrolidine-2,5-dione (see *Exper. Part*) and $LiAlH_4$ reduction of the latter (yield 28% over two steps; not shown).

the dihydroxy bis-tosylate **18** (obtained from (*R*,*R*)-**11** *via* **16** and **17** [21][22]) with the corresponding primary amines (*Scheme 3*). Unfortunately, yields were even poorer than those observed with reactions of *Scheme 2*.

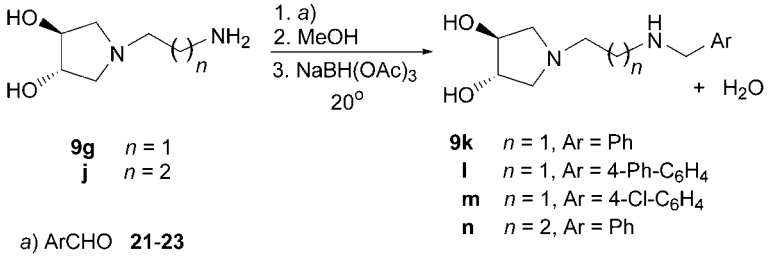
Scheme 3. *Synthesis of Derivatives* **9e**–**j**



The known dibenzyloxy bis-ditosylate **19** [23] reacted with propanamine and butanamine giving pyrrolidine-3,4-diols **20e** (92%) and **20f** (92%), respectively. Subsequent hydrogenolysis (H_2, $Pd(OH)_2$/C, MeOH, AcOEt) afforded **9e** (82%) and **9f** (82%), respectively (*Scheme 3*). With diamines $H_2N(CH_2)_2NH_2$, $H_2N(CH_2)_2NHEt$, $H_2N(CH_2)_2NMe_2$, and $H_2N(CH_2)_3NH_2$, bis-tosylate **19** yielded the corresponding pyrrolidine-3,4-diols **20g**–**j** that were debenzylated to the corresponding *N*-substituted (3*S*,4*S*)-pyrrolidine-3,4-diols **9g**–**j** in good yields. (Aminoethyl)pyrrolidinediol **9g** was also obtained by amidification of (2*R*,3*R*)-2,3-di-*O*-benzyltartaric acid [24] with $H_2N(CH_2)_2NH_2$ [25]. Amide reduction with $LiAlH_4$ (26%) and subsequent debenzylation (89%) under standard conditions produced **9g**.

Reductive amination of benzaldehyde (**21**), [1,1′-biphenyl]-4-carboxaldehyde (**22**), and 4-chlorobenzaldehyde (**23**) with (aminoethyl)pyrrolidinediol **9g** (MeOH, 20°; then $NaBH(OAc)_3$) [16] provided pyrrolidine-3,4-diols **9k** (73%), **9l** (73%), and **9m** (77%), respectively. Similarly, reductive amination of benzaldehyde (**21**) with (aminopropyl)-pyrrolidinediol **9j** gave pyrrolidine-3,4-diol **9n** (42%) (*Scheme 4*).

Scheme 4. *Synthesis of Derivatives* **9k – n**



All enantiomers of **9**, *i.e.*, pyrrolidine-3,4-diols **10**, were prepared in the same way starting from (−)-D-tartaric acid. The structures of all the new compounds were confirmed by their elemental analyses or high-resolution mass spectrometry and by their spectral data (see *Exper. Part*).

Glycosidase Inhibition Assays. Pyrrolidine-3,4-diols **9** and **10** were evaluated for their inhibitory activities toward 25 commercially available glycosidases at 1 mM concentration and under optimum pH conditions [13]. The following enzymes were not inhibited by any of the derivatives **9** and **10**: α-D-galactosidases from coffee beans, from *Aspergillus niger*, and from *Escherichia coli*; β-D-galactosidases from *E. coli*, from *A. niger*, from *A. orizae*, and jack beans; α-D-glucosidases from rice and from bakers yeast (isomaltase); β-D-mannosidase from *Helix pomatia*; β-D-xylosidase from *A. niger*; α-D-*N*-acetylgalactosaminidase from chicken liver; β-D-*N*-acetylglucosaminidase from jack bean and from bovine epididymis A and B.

None of compounds **9** and **10** inhibited α-D-glucosidase from yeast, except (3*R*,4*R*)-1-(3-aminopropyl)pyrrolidine-3,4-diol (**10j**). The latter enzyme was inhibited by 95% at 1 mM of **10j**. A $K_i = 2.8$ μM (noncompetitive) was evaluated (*Fig. 3*).

As shown in *Table 1*, α-D-amyloglucosidases from *A. niger* and from *Rhizopus* mold were inhibited weakly by the derivatives **9**. At first glance, the inhibitory activities of the corresponding enantiomers **10** were, in some cases, weaker (see **10b**,**c**,**h**,**l**,**m**,**j**) and in others stronger (see **10g**,**n**). These results are quite deceiving in comparison with the good inhibitory activities and selectivities toward α-D-mannosidases that were found by 'dressing up' the primary amino group of (2*R*,3*R*,4*S*)- and (2*S*,3*R*,4*S*)-2-(aminomethyl)pyrrolidine-3,4-diol by benzylic groups. From the comparison of the inhibitory activities of pyrrolidinediols **9b**,**c** with those of aminopyrrolidinediols **9g – n**, it can be stated that the introduction of a second amino function does not significantly improve the activity of (3*S*,4*S*)-pyrrolidine-3,4-diols. Improvement is the highest with the ([1,1′-biphenyl]-4-ylmethyl)amino and (4-chlorobenzyl)amino derivatives **9l** and **9m**, respectively (see *Table 1*).

A few derivatives **9** and **10** showed inhibitory activities toward β-D-glucosidases (*Table 2*). *A priori*, there is no structural element (α- or β-substituent at C(2)) that should make these compounds to be recognized better by α-D-glucosidases then by β-D-glucosidases. We observed that fewer derivatives of **9** and **10** inhibited β-D-glucosidases than α-D-glucosidases. The most-potent compound, (3*R*,4*R*)-1-(2-aminoethyl)pyrrolidine-3,4-diol (**10g**), inhibited β-D-glucosidase from *Caldocellum saccharolyticum* by 81% at 1 mM concentration.

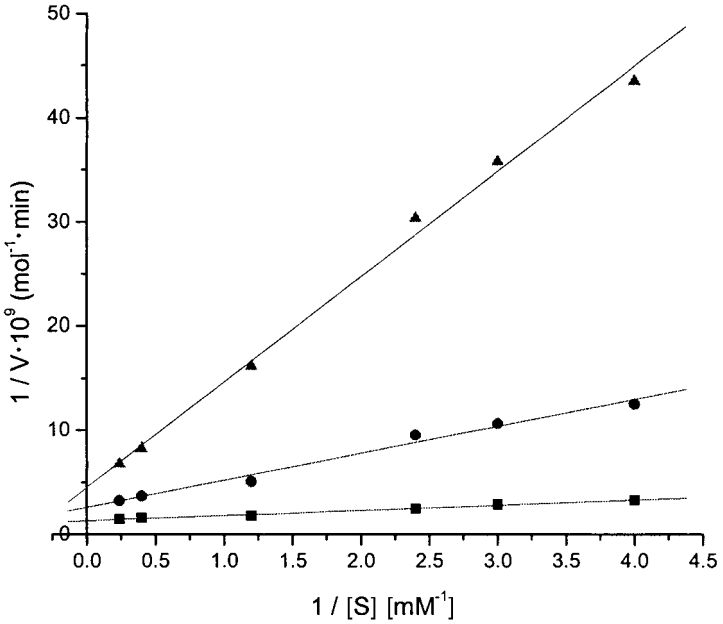


Fig. 3. Lineweaver-Burk *plots for the inhibition of* α-D-*glucosidase from jack bean* (pH 5.25°) *by (3*R,*4*R*)-1-(3-aminopropyl)pyrrolidine-3,4-diol* (**10j**). ■ = 0 μM (control), ● = 16 μM, △ = 32 μM.

Unexpectedly, several pyrrolidine-3,4-diols **10** inhibited α-D-mannosidases (*Table 3*). This was not the case with enantiomers **9**. The origin of this selectivity is not obvious at this moment. (2*R*,3*R*,4*S*)- and (2*S*,3*R*,4*S*)-2-(aminomethyl)pyrrolidine-3,4-diols are better α-D-mannosidase inhibitors than *cis*-pyrrolidine-3,4-diols [16]. Benzylation of the primary amino groups of the former compounds enhanced their inhibitory activities and selectivities toward these enzymes. It is thus not a surprise to find that **10k**–**n** are better α-D-mannosidase inhibitors than **10a**–**f**.

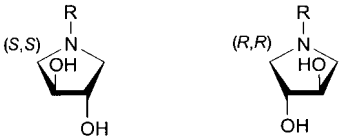
Compounds **9** and **10** were also tested for their inhibitory activities toward α-L-fucosidase from bovine epididymis. Only aminopyrrolidinediol **10g** was recognized by this enzyme. The inhibitory activity remained modest as at 1 mM concentration, 53% of inhibition was observed (IC_{50} *ca.* 400 μM).

Conclusions. – The (3*S*,4*S*)- and (3*R*,4*R*)-pyrrolidine-3,4-diol derivatives **9** and **10** were readily obtained from L- and D-tartaric acid, respectively. Contrary to the natural lentiginosine (**8**; *Fig. 1*), a potent inhibitor of α-D-amyloglucosidases with a (3*S*,4*S*)-1-alkylpyrrolidine-3,4-diol moiety, the monocyclic analogues **9a**,**c**,**f** are weak inhibitors of these enzymes. *N*-Substitution by a 2-aminoethyl (see **9g**) or 3-aminopropyl (see **9j**) group does not improve the inhibitory activities. Slight enhancements of the inhibitory activities toward α-D-amyloglucosidases are observed, however, when the primary amino group of **9g** is benzylated or alkylated by a [1,1′-biphenyl]-4-ylmethyl or a 4-chlorobenzyl group (**9l** and **9m**). This contrasts with the significant inhibitory and selectivity enhancements toward α-D-mannosidases observed with (2*R*,3*R*,4*S*)- and

Table 1. *Inhibitory Activity* (% of inhibition) *of Pyrrolidine-3,4-diols* **9** *and* **10** *toward* α-D-*Amyloglucosidases at 1 mM Concentration of the Inhibitor and Optimal pH*[a]). n.m. = not measured.

	R	**9a–e, g–n**		**10a–e, g–n**	
		α-D-Aminoglucosidase		α-D-Aminoglucosidase	
		Aspergillus niger	*Rhizopus* mold	*Aspergillus niger*	*Rhizopus* mold
9a	Bn	0	30% [13]	20%	31%
b	H	23%	0	0	0
c	Me	44%	72%	38%	53%
d	Et	0	53% [13]	33%	45%
e	Pr	48%	0	38%	36%
	$HO(CH_2)_2$	n.m.	0 [13]	n.m.	
	$HO(CH_2)_3$	n.m.	55% [13]	n.m.	
g	$H_2N(CH_2)_2$	0	0	48%	33%
h	$EtNH(CH_2)_2$	36%	38%	40%	32%
i	$Me_2N(CH_2)_2$	0	0	0	0
k	$BnNH(CH_2)_2$	47%	72%	0	32%
l	4-Ph–$C_6H_4CH_2NH(CH_2)_2$	58%	78%	46%	56%
m	4-Cl–$C_6H_4CH_2NH(CH_2)_2$	45%	69%	0	23%
j	$H_2N(CH_2)_3$	39%	45%	20%	23%
n	$BnNH(CH_2)_3$	0	0	51%	47%

[a])



9a–e, g–n **10a–e, g–n**

Table 2. *Inhibitory Activity* (% of inhibition) *of Some Pyrrolidine-3,4-diols* **9** *and* **10** *toward* β-D-*Glucosidases from Almonds and from* Caldocellum saccharolyticum *at 1 mM Concentration and optimal pH*[a])

	Almonds	*C. saccharol.*		Almonds	*C. saccharol.*	R
9a	30	0	**10a**	0	0	Bn
c	36	27	**c**	0	0	Me
e	0	0	**e**	23	0	Pr
f	36	0	**f**	72	0	Bu
g	0	0	**g**	0	81	$H_2N(CH_2)_2$
i	0	24	**i**	0	0	$Me_2N(CH_2)_2$
j	0	22	**j**	0	0	$H_2N(CH_2)_3$
k	0	0	**k**	0	0	$BnNH(CH_2)_2$
l	0	48	**l**	0	0	4-Ph–$C_6H_4CH_2NH(CH_2)_2$

[a]) All other derivatives **9** and **10** did not inhibit these enzymes.

(2*S*,3*R*,4*S*)-2-(aminomethyl)pyrrolidine-3,4-diol upon *N*-benzylation of their primary amino group [16][17]. (3*R*,4*R*)-Pyrrolidine-3,4-diol and its *N*-alkyl and *N*-benzyl derivatives **10** are poorer inhibitors of α-D-amyloglucosidases than corresponding enantiomers **9**. Compound **10j**, (3*R*,4*R*)-1-(3-aminopropyl)pyrrolidine-3,4-diol, is

Table 3. *Inhibitory Activity* (% of inhibition) *of Some Pyrrolidine-3,4-diols* **9** *and* **10** *toward* α-D *Mannosidases from Almonds and from Jack Beans at 1 mM Concentration and Optimal pH*[a])

	Almonds	Jack beans		Almonds	Jack beans	R
9c	32	0	**10c**	46	36	Me
d	0	0	**d**	31	0	Et
e	0	0	**e**	27	0	Pr
g	0	0	**g**	32	81	$NH_2(CH_2)_2$
h	0	0	**h**	28	23	$EtNH(CH_2)_2$
k	0	0	**k**	53	65	$BnNH(CH_2)_2$
l	0	0	**l**	54	65	4-Ph−$C_6H_4CH_2NH(CH_2)_2$
m	0	0	**m**	54	70	4-Cl−$C_6H_4CH_2NH(CH_2)_2$
n	0	0	**n**	47	51	$BnNH(CH_2)_3$

[a]) All other derivatives **9** and **10** did not inhibit these enzymes.

exceptional as it is the unique derivative recognized by α-D-glucosidase from yeast as it inhibits this enzyme with $K_i = 2.8$ μM (mixed type). Unexpectedly, (3*R*,4*R*)-1-(2-aminoethyl)pyrrolidine-3,4-diol (**10g**) and its derivatives *N*-benzylated at the primary amino group inhibit α-D-mannosidases from almonds and jack beans.

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Experimental Part

General. All commercially available reagents (*Fluka*, *Aldrich*, *Acros Organics*) were used without further purification. Solvents were dried by standard methods. Light petroleum ether used refers to the fraction boiling between 40–60°. Solvents after reactions and extractions were evaporated in a rotatory evaporator. Liquid/solid flash chromatography (FC): silica gel *60* (*Merck* No. 9385, 240–400 mesh) or neutral alumina. TLC (reaction monitoring): *Merck* silica gel *60F*$_{254}$ plates; detection by UV light, *Pancaldi* reagent ($(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O), $KMnO_4$, or 1% ninhydrin in MeOH. Melting points: *Büchi SMP-20* apparatus; uncorrected. Optical rotations: at 25°; *Jasco DIP-370* polarimeter or *Jasco P-1020* polarimeter; $[\alpha]_D$ in 10^{-1} deg cm^2 g^{-1}. IR Spectra: *Perkin-Elmer 1420* spectrometer; in cm^{-1}. ^{1}H-NMR Spectra: *Bruker ARX-400* spectrometer (400 MHz); δ(H) in ppm rel. to the solvent's residual ^{1}H signal ($CDCl_3$, δ(H) 7.27; CD_3OD, δ(H) 3.31) as internal reference, *J* in Hz; all assignments were confirmed by 2D-COSY-45 and 2D-NOESY experiments. ^{13}C-NMR Spectra: same instrument as for ^{1}H (100.6 MHz); δ(C) in ppm rel. to the solvent's C-signal ($CDCl_3$, δ(C) 77.0; CD_3OD, δ(C) 49.0) as internal reference, *J* in Hz; all assignments were confirmed by 2D-HMQC. MS: *Nermag R-10-10c* spectrometer, chemical-ionization (NH_3) mode; *m*/*z* (% rel. to the base peak (=100%)). Elemental analyses: *Ilse Beetz*, D-96301 Kronach, Germany.

*(3*S*,4*S*)-1-Benzylpyrrolidine-3,4-diol* (**9a**). According to [18] from commercially available (+)-L-tartaric acid ((*R*,*R*)-**11**; *Fluka*): **9a** (31% in 2 steps). $[\alpha]_{589}^{25} = +7$, $[\alpha]_{577}^{25} = +8$, $[\alpha]_{546}^{25} = +10$, $[\alpha]_{535}^{25} = +15$, $[\alpha]_{405}^{25} = +17$ ($c = 1.1$, $CHCl_3$ ([18a]: $[\alpha]_D^{25} = +8.3$ ($c = 1.1$, $CHCl_3$)).

*(3*S*,4*S*)-Pyrrolidine-3,4-diol* (**9b**). According to [19][20], from **9a**: (97%). $[\alpha]_{589}^{25} = +13$, $[\alpha]_{577}^{25} = +14$, $[\alpha]_{546}^{25} = +15$, $[\alpha]_{535}^{25} = +23$, $[\alpha]_{405}^{25} = +27$ ($c = 1.4$, MeOH) ([19]: $[\alpha]_D^{25} = +12.4$ ($c = 2.4$, MeOH)).

*(3*S*,4*S*)-1-Benzyl-3,4-bis{[(*tert*-butyl)dimethylsilyl]oxy}pyrrolidine* (**12a**). According to [18a], from **9a**: **12a** (95%). $[\alpha]_{589}^{25} = +57$, $[\alpha]_{577}^{25} = +60$, $[\alpha]_{546}^{25} = +68$, $[\alpha]_{535}^{25} = +116$, $[\alpha]_{405}^{25} = +139$ ($c = 1.0$, $CHCl_3$) ([18a]: $[\alpha]_D^{25} = +58.3$ ($c = 1.0$, $CHCl_3$)).

*(3*S*,4*S*)-3,4-Bis{[(*tert*-butyl)dimethylsilyl]oxy}pyrrolidine* (**12b**). According to [18a], from **9a**: **12b** (85%). $[\alpha]_{589}^{25} = +33$, $[\alpha]_{577}^{25} = +34$, $[\alpha]_{546}^{25} = +40$, $[\alpha]_{535}^{25} = +64$, $[\alpha]_{405}^{25} = +75$ ($c = 1.0$, $CHCl_3$) ([18a]: $[\alpha]_D^{25} = +35.9$ ($c = 0.88$, $CHCl_3$)).

*(2*S*,3*S*)-Butane-1,4-diol Bis[4-methylbenzenesulfonate]* (**18**). According to [21][22], from diethyl (+)-L-tartrate (*Fluka*): **18** (36% in 4 steps). $[\alpha]_{589}^{25} = -4.9$ ($c = 2.1$, acetone) ([22]: $[\alpha]_D^{25} = -4.6$ ($c = 2.1$, acetone)).

*(2*S*,3*S*)-2,3-Bis(benzyloxy)butane-1,4-diol bis[4-Methylbenzenesulfonate]* (**19**). According to [23] from diethyl (+)-L-tartrate (*Fluka*): **19** (54% in 3 steps). $[\alpha]_{589}^{25} = +13$, $[\alpha]_{577}^{25} = +12$, $[\alpha]_{546}^{25} = +16$, $[\alpha]_{535}^{25} = +28$, $[\alpha]_{405}^{25} = +35$ ($c = 1.0$, $CHCl_3$) ([23b]: $[\alpha]_D^{25} = +14.58$ ($c = 4.8$, $CHCl_3$)).

*(3*S*,4*S*)-3,4-Bis{[(*tert*-butyl)dimethylsilyl]oxy}-1-methylpyrrolidine* (**13**). To a soln. of **12b** (1.0 g, 3.01 mmol) in dry THF (10 ml) cooled to 0°, 60% NaH dispersion in mineral oil (0.14 g, 3.62 mmol) was added. The suspension was stirred at 0° for 25 min prior to addition of MeI (0.16 ml, 2.56 mmol). The mixture was stirred at 0° for another 15 min and then at 20° for 45 min (TLC monitoring). Excess of NaH was destroyed by addition of MeOH. The mixture was evaporated and the residue submitted to FC (20–40% AcOEt/hexane): 0.52 g (50%) of **13**. Yellowish oil. $[\alpha]_{589}^{25} = +44$, $[\alpha]_{577}^{25} = +47$, $[\alpha]_{546}^{25} = +51$, $[\alpha]_{535}^{25} = +85$, $[\alpha]_{405}^{25} = +100$ ($c = 1.2$, $CHCl_3$). IR (film) 2955, 2929, 2857, 1472, 1256, 1104, 1069, 835, 776. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.10 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.6$, H–C(3), H–C(4)); 2.82 (*dd*, $^2J = 9.8$, $^3J(2b,3) = {}^3J(5b,4) = 5.8$, H_b–C(2), H_b–C(5); 2.39 (*dd*, $^2J = 9.8$, $^3J(2a,3) = {}^3J(5a,4) = 4.4$, H_a–C(2), H_a–C(5); 2.31 (*s*, Me–C(1)); 0.88 (*s*, 2 ^{t}Bu); 0.07, 0.05 (2*s*, 4 MeSi). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 80.6 (*d*, ^1J(C,H) = 147, C(3), C(4)); 63.3 (*t*, ^1J(C,H) = 137, C(2), C(5)); 42.9 (*q*, ^1J(C,H) = 133, *Me*–C(1)); 25.8 (3*q*, ^1J(C,H) = 125, 2 *Me*$_3$C); 18.0 (*s*, Me$_3$*C*); −4.6 (*q*, ^1J(C,H) = 119, 2 MeSi); −4.8 (*q*, ^1J(C,H) = 119, 2 MeSi). CI-MS (NH_3): 346 (100, $[M+H]^+$), 345 (20), 344 (3), 288 (9), 280 (2), 141 (2), 82 (1), 73 (1). HR-MALDI-TOF-MS: 346.2534 ($C_{17}H_{40}NO_2Si_2^+$, $[M+H]^+$; calc. 346.2589). Anal. calc. for $C_{17}H_{39}NO_2Si_2$ (345.252): C 59.07, H 11.37; found: C 58.99, H 11.20.

*(3*S*,4*S*)-1-Methylpyrrolidine-3,4-diol Diacetate* (**14**). A soln. of **9c** (0.048 g, 0.41 mmol) and *N*,*N*-dimethylpyridin-4-amine (DMAP, 0.01 g) in Ac_2O/pyridine 1:2 (2 ml) was stirred at 20° (TLC monitoring). After 1 h, the mixture was poured into H_2O, extracted with CH_2Cl_2 (3×), dried (Na_2SO_4), and evaporated. The residue was purified by FC (2–6% MeOH/CH_2Cl_2): 0.068 g (82%) of **14**. Light yellowish oil. $[\alpha]_{589}^{25} = +51$, $[\alpha]_{577}^{25} = +56$, $[\alpha]_{535}^{25} = +102$, $[\alpha]_{405}^{25} = +119$ ($c = 0.215$, $CHCl_3$). UV ($CHCl_3$): 241 (290), 226 (105), 207 (106). IR (film): 2967, 2942, 2785, 1737, 1454, 1372, 1232, 1158, 1048, 1021, 850. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.10 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.6$, H–C(3), H–C(4)); 3.06 (*dd*, $^2J = 10.5$, $^3J(2b,3) = {}^3J(5b,4) = 6.0$, H_b–C(2), H_b–C(5)); 2.51 (*dd*, $^2J = 10.5$, $^3J(2a,3) = {}^3J(5a,4) = 3.5$, H_a–C(2), H_a–C(5)); 2.36 (*s*, Me–C(1)); 2.07 (*s*, 2 Me-CO). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 170.3 (*s*, 2 Me*C*O); 78.3 (*d*, ^1J(C,H) = 156, C(3), C(4)); 60.6 (*t*, ^1J(C,H) = 139, C(2), C(5)); 41.9 (*q*, ^1J(C,H) = 134, *Me*–C(1)); 20.9 (*q*, ^1J(C,H) = 130, 2 *Me*CO). CI-MS (NH_3): 202 (10, $[M+H]^+$), 201 (3, M^+), 182 (12), 152 (11), 141 (87), 127 (14), 115 (52), 100 (9), 98 (100), 96 (5). HR-MALDI-TOF-MS: 224.0890 ($C_9H_{15}NO_4Na^+$, $[M+Na]^+$; calc. 224.0899).

*(3*S*,4*S*)-1-Methylpyrrolidine-3,4-diol* (**9c**). To a soln. of **13** (0.28 g, 0.81 mmol) in THF (5 ml), $Bu_4NF \cdot H_2O$ (0.25 g, 0.81 mmol) was added. The mixture was stirred at 20° for 3 h (TLC control), the solvent evaporated, and the crude product separated by FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:19:1): 0.086 g (*ca*. 90%) of **9c**. Acetylation of crude **9c** (Ac_2O/pyridine 2:1, 20°, 1 h; 82% yield) and deacetylation (Na/MeOH, 0°, 15 min; yield 95%) gave pure **9c**. White solid. M.p. 55–57°. $[\alpha]_{589}^{25} = +22$, $[\alpha]_{577}^{25} = +25$, $[\alpha]_{535}^{25} = +46$, $[\alpha]_{405}^{25} = +54$ ($c =$ 0.28, MeOH). IR (KBr): 3367, 2940, 1595, 1471, 1340, 1280, 1079, 998, 851, 674. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.14 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.2$, H–C(3), H–C(4)); 3.00 (*dd*, $^2J = 10.4$, $^3J(2b,3) = {}^3J(5b,4) = 5.9$, H_b–C(2), H_b–C(5)); 2.53 (*dd*, $^2J = 10.4$, $^3J(2a,3) = {}^3J(5a,4) = 3.6$, H_a–C(2), H_a–C(5); 2.36 (*s*, Me–C(1)). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 78.9 (*d*, ^1J(C,H) = 148, C(3), C(4)); 62.5 (*t*, ^1J(C,H) = 138, C(2), C(5)); 42.4 (*q*, ^1J(C,H) = 134, *Me*–C(1)). CI-MS (NH_3): 118 (91, $[M+H]^+$), 117 (100, M^+), 116 (11), 100 (10), 97 (8), 85 (24), 83 (37), 73 (7), 70 (6). HR-MALDI-TOF-MS: 118.5853 ($C_5H_{12}NO_2^+$, $[M+H]^+$; calc. 118.0868).

*(3*S*,4*S*)*-N-*Alkylpyrrolidine-3,4-diols* **9d**–**f** by Method A: *General Procedure.* A soln. of **9a** (0.43 g, 2.22 mmol) in bromoethane (6 ml) (or PrBr, BuBr) was heated under reflux for 6 h. After evaporation, the residue was dissolved in MeOH (10 ml) and stirred under H_2 for 5 days in the presence of 20% $Pd(OH)_2$/C (0.27 g). The mixture was then filtered through *Celite*, the filtrate evaporated, and the residue purified by FC (CH_2Cl_2/MeOH/30% NH_3 aq. soln. 38:11:1).

*(3*S*,4*S*)-1-Ethylpyrrolidine-3,4-diol* (**9d**). By *Method A:* 0.104 g (36%) of **9d**. White solid. $[\alpha]_{589}^{25} = +23$, $[\alpha]_{577}^{25} = +23$, $[\alpha]_{535}^{25} = +43$, $[\alpha]_{405}^{25} = +51$ ($c = 0.52$, MeOH). ([13]: $[\alpha]_D^{26} = +36.5$ ($c = 0.43$, MeOH). HR-MALDI-TOF-MS: 132.1034 ($C_6H_{14}NO_2^+$, $[M+H]^+$; calc. 132.1025).

*(3*S*,4*S*)*-N-*Alkylpyrrolidine-3,4-diols* **9e** *and* **9f** *by* Method B: *General Procedure*. Propanamine (0.38 ml, 4.58 mmol) and 1,4-di-*O*-tosyl-L-treitol **19** (0.7 g, 1.15 mmol) were reacted in 1,4-dioxane (4 ml) under reflux and stirring for *ca*. 14 h, under Ar (TLC control). The mixture was evaporated. The crude product was washed with H_2O and extracted with $CHCl_3$ (3×). The residue was purified by FC (25–40% AcOEt/hexane): 0.34 g (92%) of **20e** as pale yellow oil. The oil **20e** (0.275 g, 0.84 mmol) was dissolved in MeOH/AcOEt 1:1 (15 ml) and stirred under H_2 for *ca*. 2 days (TLC control) in the presence of 20% $Pd(OH)_2$/C (0.1 g). The soln. was filtered through a pad of *Celite*, the filtrate evaporated, and the residue purified by FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln.): 38:11:1): 0.1 g (82%) of **9e**. White solid.

(3S,4S)-3,4-Bis(benzyloxy)-1-propylpyrrolidine (**20e**). $[\alpha]_{589}^{25} = +24$, $[\alpha]_{577}^{25} = +27$, $[\alpha]_{546}^{25} = +28$, $[\alpha]_{535}^{25} = +47$, $[\alpha]_{405}^{25} = +52$ ($c = 0.41$, $CHCl_3$). IR (film) 3030, 2958, 2931, 2874, 2791, 1497, 1454, 1334, 1111, 1028, 735, 697. UV (MeCN): 217 (5382), 206 (4733), 189 (833). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38–7.26 (*m*, 10 arom. H); 4.55 (br. *d*, $^3J = 11.9$, 1 PhCH_2O); 4.51 (br. *d*, $^3J = 11.9$, 1 PhCH_2O); 4.07 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.7$, H–C(3), H–C(4)); 2.91 (*dd*, $^2J = 10.0$, $^3J(2b,3) = {}^3J(5b,4) = 6.0$, H_b–C(2), H_b–C(5)); 2.61 (*dd*, $^2J = 10.0$, $^3J(2a,3) = {}^3J(5a,4) = 4.0$, H_a–C(2), H_a–C(5)); 2.47–2.32 (*m*, 2 H–C(1′)); 1.53 (*sext.*, $^3J(2',1') = {}^3J(2',3') = 7.4$, 2 H–C(2′)); 0.92 (*t*, $^3J(3',2') = 7.3$, Me(3′)). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 138.2 (*s*, 2 arom. C); 128.4 (*d*, ^1J(C,H) = 160, 4 arom. C); 127.8 (*d*, ^1J(C,H) = 159, 4 arom. C); 127.7 (*d*, ^1J(C,H) = 159, 2 arom. C); 83.5 (*d*, ^1J(C,H) = 146, C(3), C(4)); 71.4 (*t*, ^1J(C,H) = 141, 2 PhCH_2O); 58.7 (*t*, ^1J(C,H) = 141, C(2), C(5)); 58.5 (*t*, ^1J(C,H) = 130, C(1′)); 21.5 (*t*, ^1J(C,H) = 130, C(2′)); 12.00 (*q*, ^1J(C,H) = 125, C(3′)). CI-MS (NH_3): 326 (100, $[M+H]^+$), 296 (11), 219 (6), 112 (10), 108 (5), 91 (38), 84 (7), 72 (13). HR-MALDI-TOF-MS: 326.0772 ($C_{21}H_{28}NO_2^+$, $[M+H]^+$; calc. 326.2120).

(3S,4S)-1-Propylpyrrolidine-3,4-diol (**9e**). By *Method A* 37% and by *Method B* 82% of **9e**. White solid. M.p. 72–75°. $[\alpha]_{589}^{25} = +5$, $[\alpha]_{577}^{25} = +7$, $[\alpha]_{546}^{25} = +6$, $[\alpha]_{535}^{25} = +6$, $[\alpha]_{405}^{25} = +8$ ($c = 0.32$, $CHCl_3$). IR (KBr) 3308, 2972, 2720, 1635, 1437, 1337, 1227, 1085, 1019, 975, 752. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.15 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.4$, H–C(3), H–C(4)); 3.00 (*dd*, $^2J = 10.3$, $^3J(2b,3) = {}^3J(5b,4) = 6.0$, H_b–C(2), H_b–C(5)); 2.55 (*dd*, $^2J = 10.3$, $^3J(2a,3) = {}^3J(5a,4) = 3.8$, H_a–C(2), H_a–C(5)); 2.50–2.35 (*m*, 2 H–C(1′)); 1.52 (*sext.*, $^3J(2',1') = {}^3J(2',3') = 7.4$, 2 H–C(2′)); 0.90 (*t*, $^3J(3',2') = 7.3$, Me(3′)). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 78.2 (*d*, ^1J(C,H) = 148, C(3), C(4)); 60.5 (*t*, ^1J(C,H) = 138, C(2), C(5)); 58.7 (*t*, ^1J(C,H) = 130, C(1′)); 21.0 (*t*, ^1J(C,H) = 126, C(2′)); 11.9 (*q*, ^1J(C,H) = 125, C(3′)). CI-MS (NH_3): 146 (100, $[M+H]^+$), 145 (4, M^+), 116 (35), 84 (3), 72 (3). HR-MALDI-TOF-MS: 146.1167 ($C_7H_{16}NO_2^+$, $[M+H]^+$; calc. 146.1181). Anal. calc. for $C_7H_{15}NO_2$ (145.110): C 57.90, H 10.41, N 9.65; found: C 58.17, H 10.26, N 9.64.

(3S,4S)-3,4-Bis(benzyloxy)-1-butylpyrrolidine (**20f**). By *Method B*, after FC (AcOEt/hexane 1:4): **20f** (92%). Pale yellow oil. $[\alpha]_{589}^{25} = +23$, $[\alpha]_{577}^{25} = +24$, $[\alpha]_{546}^{25} = +29$, $[\alpha]_{535}^{25} = +48$, $[\alpha]_{405}^{25} = +58$ ($c = 0.32$, $CHCl_3$). IR (film) 3031, 2955, 2928, 2861, 2791, 1497, 1455, 1334, 1111, 1028, 735, 697. UV (MeCN): 215 (5218), 200 (3762), 189 (639). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.27 (*m*, 10 arom. H); 4.55 (br. *d*, $^3J = 11.9$, 1 PhCH_2O); 4.51 (br. *d*, $^3J = 11.9$, 1 PhCH_2O); 4.06 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.6$, H–C(3), H–C(4)); 2.91 (*dd*, $^2J = 10.0$, $^3J(2b,3) = {}^3J(5b,4) = 6.0$, H_b–C(2), H_b–C(5); 2.62 (*dd*, $^2J = 10.0$, $^3J(2a,3) = {}^3J(5a,4) = 4.0$, H_a–C(2), H_a–C(5)); 2.51–2.35 (*m*, 2 H–C(1′)); 1.54–1.44 (*m*, 2 H–C(2′)); 1.34 (*sext.*, $^3J(3',2') = {}^3J(3',4') = 7.4$, 2 H–C(3′)); 0.92 (*t*, $^3J(4',3') = 7.3$, Me(4′)). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 138.1 (*s*, 2 arom. C); 128.4 (*d*, ^1J(C,H) = 160, 4 arom. C); 127.8 (*d*, ^1J(C,H) = 160, 4 arom. C); 127.7 (*d*, ^1J(C,H) = 160, 2 arom. C); 83.4 (*d*, ^1J(C,H) = 147, C(3), C(4)); 71.4 (*t*, ^1J(C,H) = 141, 2 PhCH_2O); 58.7 (*t*, ^1J(C,H) = 137, C(2), C(5)); 56.4 (*t*, ^1J(C,H) = 131, C(1′)); 30.4 (*t*, ^1J(C,H) = 121, C(2′)); 20.7 (*t*, ^1J(C,H) = 121, C(3′)); 14.0 (*q*, ^1J(C,H) = 125, C(4′)). CI-MS (NH_3): 340 (100, $[M+H]^+$), 296 (13), 248 (3), 233 (5), 126 (12), 108 (6), 91 (37), 98 (4), 86 (13), 82 (2). HR-MALDI-TOF-MS: 340.2256 ($C_{22}H_{30}NO_2^+$, $[M+H]^+$; calc. 340.2277).

(3R,4R)-1-Butyl-3,4-dihydroxypyrrolidine-2,5-dione. (+)-(2*R*,3*R*)-Tartaric acid (20 g, 133.2 mmol) was added to xylene (mixture of isomers, *Fluka*; 120 ml) in a flask fitted with a water separator and condensor. To the vigorously stirred and refluxing xylene soln. was added butanamine (13.4 ml, 133.25 mmol) within 20 min. Heating under reflux was continued for *ca.* 4 h. The soln. was cooled in an ice bath, and the crystalline product was filtered off and washed with cold hexane (3×). Recrystallization from AcOEt gave 14.9 g (60%) of the pyrrolidinedione. Pale yellow powder. M.p. 118–120° (from AcOEt). $[\alpha]_{589}^{25} = +111$, $[\alpha]_{577}^{25} = +118$, $[\alpha]_{546}^{25} = +135$, $[\alpha]_{535}^{25} = +226$, $[\alpha]_{405}^{25} = +236$ ($c = 1.25$, MeOH). UV (MeOH): 216 (1739). IR (film): 3412, 2957, 2874, 1786, 1680, 1450, 1403, 1340, 1194, 1091, 995, 819, 650. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.41 (br. *s*, H–C(3), H–C(4)); 3.58–3.45 (*m*, 2 H–C(1′)); 1.58 (*quint.*, $^3J(2',1') = {}^3J(2',3') = 7.3$, 2 H–C(2′)); 1.34 (*sext.*, $^3J(3',2') = {}^3J(3',4') = 7.4$, 2 H–C(3′)); 0.96 (*t*, $^3J(4',3') = 7.3$, Me(4′)). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 176.1 (*s*, C(3), C(4)); 76.1 (*t*, ^1J(C,H) = 145, C(2), C(5)); 39.2 (*t*, ^1J(C,H) = 141, C(1′)); 30.7 (*t*, ^1J(C,H) = 127, C(2′)); 20.9 (*t*, ^1J(C,H) = 121, C(3′)); 13.9 (*q*, ^1J(C,H) = 125, C(4′)). CI-MS (NH_3): 187 (100, $[M+H]^+$), 176 (2), 164 (4), 146 (2), 108 (4), 105 (2), 91 (27), 71 (2). HR-MALDI-TOF-MS: 226.0485 ($C_8H_{13}KNO_4^+$, $[M+K]^+$; calc. 226.0482).

(3S,4S)-1-Butylpyrrolidine-3,4-diol (**9f**). By *Method A*, after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:19:1): **9f** (37%). White solid. *Method B*, from **20f**: **9f** (82%). White solid. M.p. 35–37°. $[\alpha]_{589}^{25} = +5$, $[\alpha]_{577}^{25} = +5$, $[\alpha]_{546}^{25} = +8$, $[\alpha]_{535}^{25} = +10$, $[\alpha]_{405}^{25} = +10$ ($c = 0.5$, $CHCl_3$). IR (film) 3358, 3125, 2957, 2810, 1474, 1391, 1335, 1278, 1150, 1094, 1031, 848. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.14 (*t*, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.4$, H–C(3), H–C(4)); 2.99 (*dd*, $^2J = 10.2$, $^3J(2b,3) = {}^3J(5b,4) = 5.9$, H_b–C(2), H_b–C(5)); 2.51 (*dd*, $^2J = 10.2$, $^3J(2a,3) = {}^3J(5a,4) = 3.6$, H_a–C(2), H_a–C(5)); 2.51–2.39 (*m*, 2 H–C(1′)); 1.52–1.44 (*m*, 2 H–C(2′)); 1.33 (*sext.*, $^3J(3',2') = {}^3J(3',4') = 7.3$, 2 H–C(3′)); 0.93 (*t*, $^3J(4',3') = 7.3$, Me(4′)). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 77.7 (*d*, ^1J(C,H) = 150, C(3), C(4)); 60.4 (*t*, ^1J(C,H) = 138, C(2), C(5)); 56.5 (*t*, ^1J(C,H) = 132, C(1′)); 29.8

(t, ^1J(C,H) = 124, C(2′)); 20.6 (t, ^1J(C,H) = 124, C(3′)); 13.9 (q, ^1J(C,H) = 125, C(4′)). CI-MS (NH_3): 160 (100, $[M+H]^+$), 159 (5, M^+), 117 (5), 116 (57), 98 (3), 86 (4). HR-MALDI-TOF-MS: 160.1339 ($C_8H_{18}NO_2^+$, $[M+H]^+$; calc. 160.1338). Anal. calc. for $C_8H_{17}NO_2$ (159.126): C 60.35, H 10.76, N 8.80; found: C 60.76, H 10.68, N 8.60.

(3S,4S)-3,4-Bis(benzyloxy)pyrrolidine-1-ethanamine (**20g**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 95:5:2): **20g** (85%). Pale yellow oil. $[\alpha]_{589}^{25} = +25$, $[\alpha]_{577}^{25} = +26$, $[\alpha]_{546}^{25} = +28$, $[\alpha]_{535}^{25} = +46$, $[\alpha]_{405}^{25} = +54$ ($c = 0.78$, $CHCl_3$). UV (MeCN): 260 (522), 215 (6308), 190 (1110). IR (film): 3366, 3030, 2928, 2797, 1586, 1496, 1454, 1334, 1206, 1104, 1028, 737, 698. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.14–7.04 (m, 10 arom. H); 4.31 (br. d, $^3J = 12.6$, 1 PhCH_2O); 4.27 (br. d, $^3J = 11.9$, 1 PhCH_2O); 3.83 (t, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.7$, H–C(3), H–C(4)); 2.68 (dd, $^2J = 9.9$, ^3J(2b,3) = ^3J(5b,4) = 6.0, H_b–C(2), H_b–C(5)); 2.55 (t, $^3J(\alpha,\beta) = 6.2$, 2 H–C(α)); 2.38 (dd, $^2J = 9.9$, ^3J(2a,3) = ^3J(5a,4) = 4.0, H_a–C(2), H_a–C(5)); 2.35–2.21 (m, 2 H–C(β)); 1.49 (br. s, NH_2). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 138.0 (s, 2 arom. C); 128.4 (d, ^1J(C,H) = 160, 4 arom. C); 127.8 (d, ^1J(C,H) = 160, 4 arom. C); 127.7 (d, ^1J(C,H) = 159, 2 arom. C); 83.5 (d, ^1J(C,H) = 146, C(3), C(4)); 71.5 (t, ^1J(C,H) = 141, 2 PhCH_2O); 59.2 (t, ^1J(C,H) = 131, C(β)); 58.7 (t, ^1J(C,H) = 137, C(2), C(5)); 40.3 (t, ^1J(C,H) = 134, C(α)). CI-MS (NH_3): 327 (100, $[M+H]^+$), 297 (8), 296 (29), 237 (2), 112 (2), 108 (6), 91 (27), 82 (3). HR-MALDI-TOF-MS: 327.2079 ($C_{20}H_{27}N_2O_2^+$, $[M+H]^+$; calc. 327.2073).

(3S,4S)-3,4-Bis(benzyloxy)-N-*ethylpyrrolidine-1-ethanamine* (**20h**). FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1) gave **20h** (45%). Pale yellow oil. $[\alpha]_{589}^{25} = +27$, $[\alpha]_{577}^{25} = +27$, $[\alpha]_{546}^{25} = +29$, $[\alpha]_{535}^{25} = +48$, $[\alpha]_{405}^{25} = +57$ ($c = 0.48$, $CHCl_3$). UV (MeCN): 217 (5100), 201 (3829), 187 (504). IR (film): 3312, 3030, 2928, 2890, 2805, 1496, 1454, 1334, 1205, 1114, 1028, 737, 698. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.27 (m, 10 arom. H); 4.54 (br. d, ^3J = 12.1, 1 PhCH_2O); 4.50 (br. d, $^3J = 12.1$, 1 PhCH_2O); 4.06 (t, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.7$, H–C(3), H–C(4)); 2.92 (dd, $^2J = 9.7$, ^3J(2b,3) = ^3J(5b,4) = 6.0, H_b–C(2), H_b–C(5)); 2.73–2.52 (m, H_a–C(2), H_a–C(5), 2 H–C(α)), 2 H–C(β), MeCH_2); 2.00 (br. s, NH); 1.12 (t, $^3J = 7.2$, *Me*CH_2). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 138.0 (s, 2 arom. C); 128.4 (d, ^1J(C,H) = 160, 4 arom. C); 127.8 (d, ^1J(C,H) = 160, arom. C); 127.7 (d, ^1J(C,H) = 158, arom. C); 83.5 (d, ^1J(C,H) = 147, C(3), C(4)); 71.5 (t, ^1J(C,H) = 141, 2 PhCH_2O); 58.7 (t, ^1J(C,H) = 137, C(2), C(5)); 55.9 (t, ^1J(C,H) = 131, C(β)); 47.7 (t, ^1J(C,H) = 132, C(α)); 44.2 (t, ^1J(C,H) = 133, MeCH_2); 15.2 (q, ^1J(C,H) = 126, *Me*CH_2). CI-MS (NH_3): 355 (3, $[M+H]^+$), 298 (2), 297 (17), 296 (68), 160 (3), 138 (3), 105 (2), 91 (100), 84 (6), 82 (5), 72 (3). HR-MALDI-TOF-MS: 355.2381 ($C_{22}H_{31}N_2O_2^+$, $[M+H]^+$; calc. 355.2386). Anal. calc. for $C_{22}H_{30}N_2O_2$ (354.231): C 74.54, H 8.53, N 7.90; found: C 74.55, H 8.60, N 7.80.

(3S,4S)-3,4-Bis(benzyloxy)-N,N-*dimethylpyrrolidine-1-ethanamine* (**20i**). FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 90:9:1) gave **20i** (87%). Pale yellow oil. $[\alpha]_{589}^{25} = +19$, $[\alpha]_{577}^{25} = +20$, $[\alpha]_{546}^{25} = +22$, $[\alpha]_{535}^{25} = +36$, $[\alpha]_{405}^{25} = +44$ ($c = 56$, $CHCl_3$). UV (MeCN): 260 (470), 217 (5470), 203 (4385), 187 (612). IR (film): 2942, 2814, 2769, 1496, 1455, 1336, 1264, 1205, 1153, 1099, 736, 698. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.27 (m, 10 arom. H); 4.53 (br. d, $^3J = 11.9$, 1 PhCH_2O); 4.50 (br. d, $^3J = 11.9$, 1 PhCH_2O); 4.05 (t, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.4$, H–C(3), H–C(4)); 2.94 (dd, $^2J = 9.8$, ^3J(2a,3) = ^3J(5a,4) = 6.0, H_b–C(2), H_b–C(5); 2.69–2.45 (m, 2 H–C(α), 2 H–C(β)); 2.63 (dd, $^2J = 9.8$, ^3J(2b,3) = ^3J(5b,4) = 4.1, H_a–C(2), H_a–C(5)); 2.29 (br. s, 2 MeN). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 138.0 (s, 2 arom. C), 128.4 (d, ^1J(C,H) = 160, 4 arom. C); 127.8 (d, ^1J(C,H) = 160, 4 arom. C); 127.7 (d, ^1J(C,H) = 159, 2 arom. C); 83.3 (d, ^1J(C,H) = 146, C(3), C(4)); 71.5 (t, ^1J(C,H) = 141, 2 PhCH_2O); 59.00 (t, ^1J(C,H) = 137, C(2), C(5)); 57.7, 54.1 (2t, ^1J(C,H) ≈ 134, C(α), C(β)); 45.7 (q, ^1J(C,H) = 133, 2 MeN). CI-MS (NH_3): 355 (100, $[M+H]^+$), 297 (4), 296 (15), 244 (2), 243 (11), 108 (3), 91 (12), 72 (2). HR-MALDI-TOF-MS: 355.2336 ($C_{22}H_{31}N_2O_2^+$, $[M+H]^+$; calc. 355.2386). Anal. calc. for $C_{22}H_{30}N_2O_2$ (354.231): C 74.54, H 8.53, N 7.90; found: 74.48, H 8.51, N 7.88.

(3S,4S)-3,4-Bis(benzyloxy)pyrrolidine-1-propanamine (**20j**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 95:5:2): **20j** (81%). Pale yellow oil. $[\alpha]_{589}^{25} = +23$, $[\alpha]_{577}^{25} = +27$, $[\alpha]_{546}^{25} = +26$, $[\alpha]_{535}^{25} = +42$, $[\alpha]_{405}^{25} = +52$ ($c = 0.52$, $CHCl_3$). UV (MeCN): 260 (448), 216 (4589), 199 (3207), 188 (521). IR (film): 3362, 3030, 2931, 2796, 1586, 1496, 1454, 1391, 1335, 1309, 1205, 1103, 1028, 847, 737, 698. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.38–7.27 (m, 10 arom. H); 4.54 (br. d, $^3J = 11.9$, 1 PhCH_2O); 4.50 (br. d, $^3J = 11.9$, 1 PhCH_2O); 4.05 (t, $^3J(2,3) = {}^3J(3,4) = {}^3J(4,5) = 4.6$, H–C(3), H–C(4)); 2.90 (dd, $^2J = 9.9$, ^3J(2b,3) = ^3J(5b,4) = 6.0, H_b–C(2), H_b–C(5)); 2.75 (t, $^3J(\alpha,\beta) = 6.7$, 2 H–C(α)); 2.60 (dd, $^2J = 9.9$, ^3J(2a,3) = ^3J(5a,4) = 4.1, H_a–C(2), H_a–C(5)); 2.54–2.41 (m, 2 H–C(γ)); 1.65 (*quint.*, $^3J(\beta,\gamma) = {}^3J(\beta,\alpha) = 7.1$, 2 H–C($\beta$)); 1.51 (br. s, NH_2). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 138.1 (s, 2 arom. C); 128.4 (d, ^1J(C,H) = 160, 4 arom. C); 127.8 (d, ^1J(C,H) = 160, 4 arom. C); 127.7 (d, ^1J(C,H) = 159, 2 arom. C); 83.5 (d, ^1J(C,H) = 147, C(3), C(4)); 71.4 (t, ^1J(C,H) = 141, 2 PhCH_2O); 58.8 (t, ^1J(C,H) = 137, C(2), C(5)); 54.2 (t, ^1J(C,H) = 130, C(γ)); 40.7 (t, ^1J(C,H) = 136, C(α)); 32.0 (t, ^1J(C,H) = 125, C(β)). CI-MS (NH_3): 341 (100, $[M+H]^+$), 340 (2, M^+), 296 (2), 284 (3), 125 (4), 124 (7), 108 (5), 91 (19), 82 (3), 81 (11). HR-MALDI-TOF-MS: 341.2226 ($C_{21}H_{29}N_2O_2^+$, $[M+H]^+$; calc. 341.2229). Anal. calc. for $C_{21}H_{28}N_2O_2$ (340.459): C 74.08, H 8.29; found: C 73.88, H 8.01.

(3S,4S)-1-(2-Aminoethyl)pyrrolidine-3,4-diol (**9g**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 20:3:2): **9g** (85%). Colorless oil. $[\alpha]_{589}^{25}=+30$, $[\alpha]_{577}^{25}=+32$, $[\alpha]_{546}^{25}=+37$, $[\alpha]_{535}^{25}=+59$, $[\alpha]_{405}^{25}=+67$ ($c=0.52$, MeOH). IR (film): 3343, 2938, 1578, 1474, 1333, 1237, 1150, 1093, 1043, 874. ^{1}H-NMR (400 MHz, CD_3OD): 4.05 (t, $^3J(2,3)=^3J(3,4)=^3J(4,5)=3.8$, H–C(3), H–C(4)); 2.97 (dd, $^2J=10.1$, $^3J(2b,3)=^3J(5b,4)=5.5$, H_b–C(2), H_b–C(5)); 2.77 (t, $^3J(2',1')=6.3$, 2 H–C(2′)); 2.67–2.53 (m, 2 H–C(1′)); 2.51 (dd, $^2J=10.1$, $^3J(2a,3)=^3J(5a,4)=3.1$, H_a–C(2), H_a–C(5)). ^{13}C-NMR (100.6 MHz, CD_3OD): 79.0 (d, ^1J(C,H) = 148, C(3), C(4)); 61.6 (t, ^1J(C,H) = 137, C(2), C(5)); 59.0 (t, ^1J(C,H) = 131, C(1′)); 40.5 (t, ^1J(C,H) = 136, C(2′)). CI-MS (NH_3): 147 (100, $[M+H]^+$), 146 (3, M^+), 145 (17), 127 (2), 121 (2), 116 (20), 104 (20), 85 (2), 75 (4). HR-MALDI-TOF-MS: 147.1934 ($C_6H_{15}N_2O_2^+$, $[M+H]^+$; calc. 147.1134). Anal. calc. for $C_6H_{14}N_2O_2$ (146.188): C 49.30, H 9.65; found: C 49.43, H 9.26.

(3S,4S)-1-[(2-Ethylamino)ethyl]pyrrolidine-3,4-diol (**9h**). By *Method B*, after FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1): **9h** (88%). Pale yellow oil. $[\alpha]_{589}^{25}=+15$, $[\alpha]_{577}^{25}=+18$, $[\alpha]_{546}^{25}=+23$, $[\alpha]_{535}^{25}=+31$, $[\alpha]_{405}^{25}=+48$ ($c=0.38$, MeOH). IR (film): 3283, 2930, 2815, 1668, 1471, 1454, 1332, 1119, 1093, 1041, 844. ^{1}H-NMR (400 MHz, CD_3OD): 4.05 (t, $^3J(2,3)=^3J(3,4)=^3J(4,5)=3.9$, H–C(3), H–C(4)); 2.98 (dd, $^2J=10.1$, $^3J(2b,3)=^3J(5b,4)=5.4$, H_b–C(2), H_b–C(5)); 2.80–2.61 (m, 2 H–C(1′), 2 H–C(2′), 2 H–C(1″)); 2.52 (dd, $^2J=10.1$, $^3J(2a,3)=^3J(5a,4)=3.2$, H_a–C(2), H_a–C(5)); 1.19 (t, $^3J(2'',1'')=7.2$, Me(2″)). ^{13}C-NMR (100.6 MHz, CD_3OD): 79.0 (d, ^1J(C,H) = 149, C(3), C(4)); 61.5 (t, ^1J(C,H) = 137, C(2), C(5)); 55.5 (t, ^1J(C,H) = 133, C(1′)); 47.9 (t, ^1J(C,H) = 137, C(2′)); 44.5 (t, ^1J(C,H) = 136, C(1″)); 14.0 (q, ^1J(C,H) = 126, C(2″)). CI-MS (NH_3): 175 (2, $[M+H]^+$), 130 (6), 117 (13), 116 (100), 99 (6), 98 (3), 82 (2), 72 (7). HR-MALDI-TOF-MS: 175.1417 ($C_8H_{19}N_2O_2^+$, $[M+H]^+$; calc. 175.1447).

(3S,4S)-1-[2-(Dimethylamino)ethyl]pyrrolidine-3,4-diol (**9i**). By *Method B* (89%), after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:9:1): **9i** (87%). White crystals. M.p. 63–65° (from THF): $[\alpha]_{589}^{25}=+4$, $[\alpha]_{577}^{25}=+6$, $[\alpha]_{546}^{25}=+5$, $[\alpha]_{535}^{25}=+7$, $[\alpha]_{405}^{25}=+13$ ($c=0.9$, $CHCl_3$) ([24]: $[\alpha]_D=+2.9$ ($c=0.90$, $CHCl_3$). IR (KBr): 3332, 2953, 2815, 1466, 1313, 1039, 850, 686. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.03 (t, $^3J(2,3)=^3J(3,4)=^3J(4,5)=3.7$, H–C(3), H–C(4)); 2.99 (dd, $^2J=10.0$, $^3J(2b,3)=^3J(5b,4)=5.5$, H_b–C(2), H_b–C(5); 2.77–2.49 (m, H_a–C(2), H_a–C(5), 2 H–C(1′), 2 H–C(2′)); 2.21 (br. s, 2 MeN). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 79.0 (d, ^1J(C,H) = 148, C(3), C(4)); 61.7 (t, ^1J(C,H) = 137, C(2), C(5)); 58.4, 54.9 (2t, ^1J(C,H) ≈ 133, C(1′), C(2′)); 45.7 (q, ^1J(C,H) = 134, 2 MeN). CI-MS (NH_3): 175 (2, $[M+H]^+$), 130 (3), 117 (12), 116 (100), 98 (2), 72 (9), 70 (3). HR-MALDI-TOF-MS. 175.2410 ($C_8H_{19}O_2O_2^+$, $[M+H]^+$; calc. 175.1447).

(3S,4S)-1-(3-Aminopropyl)pyrrolidine-3,4-diol (**9j**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 20:3:2): **9j** (84%). Pale yellow oil. $[\alpha]_{589}^{25}=+27$, $[\alpha]_{577}^{25}=+22$, $[\alpha]_{546}^{25}=+28$, $[\alpha]_{535}^{25}=+48$, $[\alpha]_{405}^{25}=+55$ ($c=0.52$, MeOH). IR (film): 3346, 3288, 2933, 2807, 1599, 1470, 1453, 1392, 1334, 1149, 1093, 1044. ^{1}H-NMR (400 MHz, CD_3OD): 4.05 (t, $^3J(2,3)=^3J(3,4)=^3J(4,5)=4.0$, H–C(3), H–C(4)); 2.95 (dd, $^2J=10.0$, $^3J(2b,3)=^3J(5b,4)=5.6$, H_b–C(2), H_b–C(5)); 2.70 (t, $^3J(3',2')=7.0$, 2 H–C(3′)); 2.56–2.45 (m, H_a–C(2), H_a–C(5), 2 H–C(1′)); 1.68 (*sext.*, $^3J(2',1')=^3J(2',3')=7.2$, 2 H–C(2′)). ^{13}C-NMR (100.6 MHz, CD_3OD): 78.9 (d, ^1J(C,H) = 148, C(3), C(4)); 61.7 (t, ^1J(C,H) = 137, C(2), C(5)); 55.7 (t, ^1J(C,H) = 132, C(1′)); 41.0 (t, ^1J(C,H) = 134, C(3′)); 32.2 (t, ^1J(C,H) = 126, C(2′)). CI-MS (NH_3): 161 (6, $[M+H]^+$), 144 (4), 117 (13), 116 (100), 104 (9), 99 (5), 98 (7), 94 (4), 87 (4), 82 (10), 81 (72), 80 (4),70 (8). HR-MALDI-TOF-MS: 161.1204 ($C_7H_{17}N_2O_2^+$, $[M+H]^+$; calc. 161.1212). Anal. calc. for $C_7H_{16}N_2O_2$ (160.121): C 52.48, H 10.07, N 17.49; found: 52.98, H 10.16, N 17.67.

Reductive Aminations with **9g** *and* **9j**: *General Procedure*. $NaBH(OAc)_3$ (1.4 equiv.) was added portionwise to a stirred soln. of **9g** or **9j** (0.4 mmol) and an appropriate aldehyde (0.4 mmol; PhCHO (**21**), 4-PhC_6H_4CHO (**22**), 4-ClC_6H_4CHO (**23**)) in abs. MeOH (2 ml) at 20°. After complete disappearance of **9g** or **9j** (TLC control), the solvent was evaporated and the residue subjected to FC (hexane/AcOEt 3:7, then pure AcOEt, then MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1).

(3S,4S)-1-[2-(Benzylamino)ethyl]pyrrolidine-3,4-diol (**9k**). Oil (73%). $[\alpha]_{589}^{25}=+15$, $[\alpha]_{577}^{25}=+15$, $[\alpha]_{535}^{25}=+29$, $[\alpha]_{405}^{25}=+34$ ($c=0.27$, MeOH). IR (KBr): 3328, 2929, 2826, 1566, 1470, 1453, 1407, 1334, 1150, 1098, 749. UV (MeOH): 260 (282), 216 (3008), 212 (2657). ^{1}H-NMR (400 MHz, CD_3OD): 7.39–7.27 (m, 5 arom. H); 4.02 (t, $^3J(2,3)=^3J(3,4)=^3J(4,5)=3.7$, H–C(3), H–C(4)); 3.83 (br. s, $PhCH_2N$); 2.94 (dd, $^2J=10.1$, $^3J(2b,3)=^3J(5b,4)=5.4$, H_b–C(2), H_b–C(5)); 2.77–2.53 (m, 2 H–C(2′), 2 H–C(1′)); 2.94 (dd, $^2J=10.1$, $^3J(2a,3)=^3J(5a,4)=3.3$, H_a–C(2), H_a–C(5)). ^{13}C-NMR (100.6 MHz, CD_3OD): 139.6 (s, 1 arom. C); 129.7 (d, ^1J(C,H) = 158, 1 arom. C; 129.6 (d, ^1J(C,H) = 160, 2 arom. C); 128.5 (d, ^1J(C,H) = 160, 2 arom. C); 78.8 (d, ^1J(C,H) = 149, C(3), C(4)); 61.4 (t, ^1J(C,H) = 137, C(2), C(5)); 55.8 (t, ^1J(C,H) = 134, C(1′)); 54.0 (t, ^1J(C,H) = 135, $PhCH_2N$); 47.4 (t, ^1J(C,H) = 136, C(2′)). CI-MS (NH_3): 219 (1), 133 (2), 120 (26), 117 (99), 116 (100), 106 (9), 99 (20), 91 (82), 89 (6), 83 (9), 79 (4), 70 (4). HR-MALDI-TOF-MS: 259.1428 ($C_{13}H_{20}N_2NaO_2^+$, $[M+Na]^+$; calc. 259.1422).

(3S,4S)-1-[2-[([1,1′-Biphenyl-4-yl]methyl)amino]ethyl]pyrrolidine-3,4-diol (**9l**). Oil (73%). $[\alpha]_{589}^{25}=+7$, $[\alpha]_{577}^{25}=+8$, $[\alpha]_{535}^{25}=+12$, $[\alpha]_{405}^{25}=+12$ ($c=0.27$, MeOH). IR (KBr): 3355, 2934, 2818, 1570, 1487, 1411, 1338, 1154, 1093, 763. UV (MeOH): 272 (5682), 218 (4704), 214 (4358), 199 (943). ^{1}H-NMR (400 MHz, CD_3OD): 7.71–7.63 (*m*, 4 arom. H); 7.56 (*m*, 2 arom. H); 7.49–7.45 (*m*, 2 arom. H); 7.39–7.35 (*m*, 1 arom. H); 4.13 (br. *s*, ArCH_2N); 4.05 (*m*, H–C(3), H–C(4)); 3.07 (*dd*, $^2J=10.3$, ^3J(2b,3) = ^3J(5b,4) = 5.0, H_b–C(2), H_b–C(5)); 3.03 (*t*, ^3J(2′,1′) = 6.1, 2 H–C(2′)); 2.92–2.81 (*m*, 2 H–C(1′)); 2.61 (*dd*, $^2J=10.3$, ^3J(2a,3) = ^3J(5a,4) = 2.7, H_a–C(2), H_a–C(5)). ^{13}C-NMR (100.6 MHz, CD_3OD): 142.8 (*s*, 1 arom. C); 141.6 (*s*, 1 arom. C); 134.7 (*s*, 1 arom. C); 131.0 (*d*, ^1J(C,H) = 159, 2 arom. C); 129.9 (*d*, ^1J(C,H) = 161, 2 arom. C); 128.7 (*d*, ^1J(C,H) = 161, 1 arom. C); 128.5 (*d*, ^1J(C,H) = 160, 2 arom. C); 128.0 (*d*, ^1J(C,H) = 159, 2 arom. C); 78.8 (*d*, ^1J(C,H) = 151, C(3), C(4)); 61.4 (*t*, ^1J(C,H) = 139, C(2), C(5)); 55.8 (*t*, ^1J(C,H) = 135, C(1′)); 54.0 (*t*, ^1J(C,H) = 140, ArCH_2N); 47.4 (*t*, ^1J(C,H) = 140, C(2′)). CI-MS (NH_3): 250 (1), 197 (7), 182 (16), 167 (88), 164 (8), 153 (23), 141 (2), 139 (5), 129 (7), 117 (90), 116 (100), 107 (12), 99 (20), 91 (12), 83 (15), 80 (10), 70 (9). HR-MALDI-TOF-MS: 335.1709 ($C_{19}H_{24}N_2NaO_2^+$, $[M+Na]^+$; calc. 335.1735).

(3S,4S)-1-[2-[(4-Chlorobenzyl)amino]ethyl]pyrrolidine-3,4-diol (**9m**). Oil (77%). $[\alpha]_{589}^{25}=+11$, $[\alpha]_{577}^{25}=+10$, $[\alpha]_{535}^{25}=+20$, $[\alpha]_{405}^{25}=+23$ ($c=0.35$, MeOH). IR (KBr): 3381, 2929, 2817, 1560, 1491, 1472, 1407, 1334, 1151, 1090, 1015, 805. UV (MeOH): 267 (391), 225 (3499), 212 (2560). ^{1}H-NMR (400 MHz, CD_3OD): 7.39–7.34 (*m*, 4 arom. H); 4.03 (*t*, ^3J(2,3) = ^3J(3,4) = ^3J(4,5) = 3.9, H–C(3), H–C(4)); 3.80 (br. *s*, ArCH_2N); 2.95 (*dd*, $^2J=10.1$, ^3J(2b,3) = ^3J(5b,4) = 5.5, H_b–C(2), H_b–C(5)); 2.73–2.63 (*m*, 2 H–C(2′), 2 H–C(1′)); 2.50 (*dd*, $^2J=10.1$, ^3J(2a,3) = ^3J(5a,4) = 3.5, H_a–C(2), H_a–C(5)). ^{13}C-NMR (100.6 MHz, CD_3OD): 138.9 (*s*, 1 arom. C); 134.1 (*s*, 1 arom. C); 131.3 (*d*, ^1J(C,H) = 160, 2 arom. C); 129.5 (*d*, ^1J(C,H) = 166, 2 arom. C); 78.8 (*d*, ^1J(C,H) = 148, C(3), C(4)); 61.4 (*t*, ^1J(C,H) = 138, C(2), C(5)); 56.0 (*t*, ^1J(C,H) = 135, C(1′)); 53.4 (*t*, ^1J(C,H) = 135, ArCH_2N); 47.4 (*t*, ^1J(C,H) = 135, C(2′)). CI-MS (NH_3): 155 (3), 140 (2), 127 (8), 125 (24), 116 (100), 106 (2), 99 (8), 89 (8), 84 (3), 81 (4), 75 (5), 70 (3). HR-MALDI-TOF-MS: 270.1109 ($C_{13}H_{19}ClN_2O_2^+$, M^+; calc. 270.1135).

(3S,4S)-1-[3-(Benzylamino)propyl]pyrrolidine-3,4-diol (**9n**). Oil (42%). $[\alpha]_{589}^{25}=+13$, $[\alpha]_{577}^{25}=+15$, $[\alpha]_{535}^{25}=+27$, $[\alpha]_{405}^{25}=+31$ ($c=0.27$, MeOH). IR (KBr): 3387, 2925, 2826, 1560, 1452, 1409, 1336, 1148, 1096, 746, 702. UV (MeOH): 216 (2965), 206 (1626). ^{1}H-NMR (400 MHz, CD_3OD): 7.41–7.31 (*m*, 5 arom. H); 4.06 (*t*, ^3J(2,3) = ^3J(3,4) = ^3J(4,5) = 3.2, H–C(3), H–C(4)); 3.92 (br. *d*, $^3J=13.3$, 1 H, PhCH_2N); 3.87 (br. *d*, $^3J=13.3$, 1 H, PhCH_2N); 3.00 (*dd*, $^2J=10.3$, ^3J(2b,3) = ^3J(5b,4) = 5.3, H_b–C(2), H_b–C(5)); 2.82 (*t*, ^3J(3′,2′) = 6.8, 2 H–C(3′)); 2.71–2.59 (*m*, 2 H–C(1′)); 2.60 (*dd*, $^2J=10.3$, ^3J(2a,3) = ^3J(5a,4) = 2.7, H_a–C(2), H_a–C(5)); 1.79 (*quint.*, ^3J(2′,1′) = ^3J(2′,3′) = 6.9, 2 H–C(2′)). ^{13}C-NMR (100.6 MHz, CD_3OD): 138.0 (*s*, 1 arom. C); 130.0 (*d*, ^1J(C,H) = 158, 2 arom. C); 129.7 (*d*, ^1J(C,H) = 160, 2 arom. C); 129.0 (*d*, ^1J(C,H) = 161, 1 arom. C); 78.5 (*d*, ^1J(C,H) = 149, C(3), C(4)); 61.4 (*t*, ^1J(C,H) = 138, C(2), C(5)); 56.3 (*t*, ^1J(C,H) = 129, C(1′)); 53.6 (*t*, ^1J(C,H) = 137, PhCH_2N); 49.6 (*t*, ^1J(C,H) = 134, C(3′)); 27.1 (*t*, ^1J(C,H) = 135, C(2′)). CI-MS (NH_3): 151 (1, $[M+H]^+$), 215 (2), 147 (5), 132 (8), 126 (8), 117 (61), 107 (33), 106 (40), 95 (7), 91 (100), 81 (39), 77 (5), 72 (8), 70 (25). HR-MALDI-TOF-MS: 250.1609 ($C_{14}H_{22}N_2O_2^+$; M^+; calc. 250.1681).

(3R,4R)-1-Benzylpyrrolidine-3,4-diol (**10a**). According to [18][26], from commercially available (−)-D-tartaric acid (*S,S*)-**11**; *Fluka*): **10a** (35% in 2 steps). $[\alpha]_{589}^{25}=-7$, $[\alpha]_{577}^{25}=-10$, $[\alpha]_{546}^{25}=-10$, $[\alpha]_{535}^{25}=-15$, $[\alpha]_{405}^{25}=-17$ ($c=1.0$, $CHCl_3$): $[\alpha]_{589}^{25}=-34$, $[\alpha]_{577}^{25}=-36$, $[\alpha]_{546}^{25}=-39$, $[\alpha]_{535}^{25}=-66$, $[\alpha]_{405}^{25}=-80$ ($c=1.0$, MeOH) ([26]: $[\alpha]_D^{25}=-32.5$ ($c=1.0$, MeOH)).

(3R,4R)-Pyrrolidine-3,4-diol (**10b**). According to [19][20], from **10a**: **10b** (87%). $[\alpha]_{589}^{25}=-13$, $[\alpha]_{577}^{25}=-14$, $[\alpha]_{546}^{25}=-14$, $[\alpha]_{535}^{25}=-22$, $[\alpha]_{405}^{25}=-25$ ($c=2.0$, MeOH). CI-MS (NH_3): 104 (100, $[M+H]^+$), 103 (5), 85 (3).

*(3R,4R)-1-Benzyl-3,4-bis[[(*tert*-butyl)dimethylsilyl]oxy}pyrrolidine* (*ent*-**12a**). According to [18a], from **10a**: *ent*-**12a** (91%). $[\alpha]_{589}^{25}=-57$, $[\alpha]_{577}^{25}=-58$, $[\alpha]_{546}^{25}=-67$, $[\alpha]_{535}^{25}=-114$, $[\alpha]_{405}^{25}=-132$ ($c=1.0$, $CHCl_3$).

*(3R,4R)-3,4-Bis{[(*tert*-butyl)dimethylsilyl]oxy}pyrrolidine* (*ent*-**12b**). According to [18a], from *ent*-**12a**: *ent*-**12b** (82%). $[\alpha]_{589}^{25}=-33$, $[\alpha]_{577}^{25}=-36$, $[\alpha]_{546}^{25}=-40$, $[\alpha]_{535}^{25}=-63$, $[\alpha]_{405}^{25}=-74$ ($c=1.0$, $CHCl_3$). HR-MALDI-TOF-MS: 331.2369 ($C_{17}H_{40}NO_2Si_2^+$, M^+; calc. 331.2363).

(3R,4R)-Bis(benzyloxy)butane-1,4-diol Bis[4-methylbenzenesulfonate] (*ent*-**19**). According to [23], from diethyl (−)-D-tartrate (*Fluka*): *ent*-**19** (54% in 3 steps). $[\alpha]_{589}^{25}=-14$, $[\alpha]_{577}^{25}=-11$, $[\alpha]_{546}^{25}=-18$, $[\alpha]_{535}^{25}=-28$, $[\alpha]_{405}^{25}=-34$ ($c=1.0$, $CHCl_3$) ([23b]: $[\alpha]_D^{25}=+14.74$ ($c=4.8$, $CHCl_3$)).

*(3R,4R)-3,4-Bis{[(*tert*-butyl)dimethylsilyl]oxy}-1-methylpyrrolidine* (*ent*-**13**). As described for **13**: *ent*-**13** (79%). Yellowish oil. $[\alpha]_{589}^{25}=-45$, $[\alpha]_{577}^{25}=-47$, $[\alpha]_{546}^{25}=-54$, $[\alpha]_{535}^{25}=-92$, $[\alpha]_{405}^{25}=-124$ ($c=1.2$, $CHCl_3$). HR-MALDI-TOF-MS: 345.2516 ($C_{17}H_{39}NO_2Si_2^+$, $[M+H]^+$; calc. 345.2519).

(3R,4R)-1-Methylpyrrolidine-3,4-diol Diacetate (*ent*-**14**). As described for **14**: *ent*-**14**: (75%). Light yellowish oil. $[\alpha]_{589}^{25}=-50$, $[\alpha]_{577}^{25}=-53$, $[\alpha]_{535}^{25}=-99$, $[\alpha]_{405}^{25}=-120$ ($c=0.22$, $CHCl_3$). HR-MALDI-TOF-MS: 224.0827 ($C_9H_{15}NaO_4^+$, $[M+Na]^+$; calc. 224.0899).

*(3*R*,4*R*)-1-Methylpyrrolidine-3,4-diol* (**10c**). FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:19:1) gave a white solid. M.p. 55–57°. $[\alpha]_{589}^{25} = -22$, $[\alpha]_{577}^{25} = -25$, $[\alpha]_{535}^{25} = -47$, $[\alpha]_{405}^{25} = -54$ ($c = 0.28$, MeOH). HR-MALDI-TOF-MS: 117.0790 ($C_5H_{12}NO_2^+$, $M+H]^+$; calc. 117.0790).

*(3*R*,4*R*)-1-Ethylpyrrolidine-3,4-diol* (**10d**). By *Method A*, after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 38:11:1): **10d** (36%). White solid. $[\alpha]_{589}^{25} = -23$, $[\alpha]_{577}^{25} = -23$, $[\alpha]_{535}^{25} = -43$, $[\alpha]_{405}^{25} = -51$ ($c = 0.51$, MeOH). HR-MALDI-TOF-MS: 132.1098 ($C_6H_{14}NO_2^+$, $[M+H]^+$; calc. 132.1025).

*(3*R*,4*R*)-1-Propylpyrrolidine-3,4-diol* (**10e**). By *Method A*, after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:19:1): **10e** (37%). White solid. $[\alpha]_{589}^{25} = -5$, $[\alpha]_{577}^{25} = -6$, $[\alpha]_{546}^{25} = -7$, $[\alpha]_{535}^{25} = -9$, $[\alpha]_{405}^{25} = -10$ ($c = 0.35$, MeOH). HR-MALDI-TOF-MS: 146.1183 ($C_7H_{16}NO_2^+$, $[M+H]^+$; calc. 146.1181).

*(3*R*,4*R*)-1-Butylpyrrolidine-3,4-diol* (**10f**). By *Method A*, after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:19:1): **10f** (37%). White solid. M.p. 35–37°. $[\alpha]_{589}^{25} = -5$, $[\alpha]_{577}^{25} = -4$, $[\alpha]_{546}^{25} = -6$, $[\alpha]_{535}^{25} = -10$, $[\alpha]_{405}^{25} = -11$ ($c = 0.42$, MeOH). HR-MALDI-TOF-MS: 182.1187 ($C_8H_{17}NNaO_2^+$, $[M+H]^+$; calc. 182.1157).

*(3*R*,4*R*)-3,4-Bis(benzyloxy)pyrrolidine-1-ethanamine* (*ent*-**20g**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 95:5:2): *ent*-**20g** (86%). Pale yellow oil. $[\alpha]_{589}^{25} = -23$, $[\alpha]_{577}^{25} = -26$, $[\alpha]_{546}^{25} = -28$, $[\alpha]_{535}^{25} = -46$, $[\alpha]_{405}^{25} = -53$ ($c = 0.73$, $CHCl_3$). HR-MALDI-TOF-MS: 327.2012 ($C_{20}H_{27}N_2O_2^+$, $[M+H]^+$; calc. 327.2073).

*(3*R*,4*R*)-3,4-Bis(benzyloxy)*-N-*ethylpyrrolidine-1-ethanamine* (*ent*-**20h**). By *Method B*, after FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1): *ent*-**20h** (83%). Pale yellow oil. $[\alpha]_{589}^{25} = -25$, $[\alpha]_{577}^{25} = -23$, $[\alpha]_{546}^{25} = -28$, $[\alpha]_{535}^{25} = -48$, $[\alpha]_{405}^{25} = -55$ ($c = 0.67$, $CHCl_3$). HR-MALDI-TOF-MS: 355.2712 ($C_{22}H_{31}N_2O_2^+$, $[M+H]^+$; calc. 355.2386).

*(3*R*,4*R*)-3,4-Bis(benzyloxy)*-N,N-*dimethylpyrrolidine-1-ethanamine* (*ent*-**20i**). By *Method B*, after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 90:9:1): *ent*-**20i** (74%). Pale yellow oil. $[\alpha]_{589}^{25} = -18$, $[\alpha]_{577}^{25} = -22$, $[\alpha]_{546}^{25} = -23$, $[\alpha]_{535}^{25} = -39$, $[\alpha]_{405}^{25} = -48$ ($c = 0.54$, $CHCl_3$). HR-MALDI-TOF-MS: 355.4912 ($C_{22}H_{31}N_2O_2^+$, $[M+H]^+$; calc. 355.2386).

*(3*R*,4*R*)-3,4-Bis(benzyloxy)pyrrolidine-1-propanamine* (*ent*-**20j**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 95:5:2): *ent*-**20j** (81%). Pale yellow oil. $[\alpha]_{589}^{25} = -23$, $[\alpha]_{577}^{25} = -25$, $[\alpha]_{546}^{25} = -29$, $[\alpha]_{535}^{25} = -47$, $[\alpha]_{405}^{25} = -52$ ($c = 0.61$, $CHCl_3$). HR-MALDI-TOF-MS: 363.2047 ($C_{21}H_{29}N_2O_2^+$, $[M+Na]^+$; calc. 363.2048).

*(3*R*,4*R*)-1-(2-Aminoethyl)pyrrolidine-3,4-diol* (**10g**). By *Method B*, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 20:3:2): **10g** (88%). Colorless oil. $[\alpha]_{589}^{25} = -30$, $[\alpha]_{577}^{25} = -33$, $[\alpha]_{546}^{25} = -38$, $[\alpha]_{535}^{25} = -54$, $[\alpha]_{405}^{25} = -82$ ($c = 0.52$, MeOH). HR-MALDI-TOF-MS: 147.1138 ($C_6H_{15}N_2O_2^+$, $[M+H]^+$; calc. 147.1134).

*(3*R*,4*R*)-1-[(2-Ethylamino)ethyl]pyrrolidine-3,4-diol* (**10h**). By *Method B*, after FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 90:9:1): **10h** (97%). Colorless oil. $[\alpha]_{589}^{25} = -16$, $[\alpha]_{577}^{25} = -24$, $[\alpha]_{546}^{25} = -23$, $[\alpha]_{535}^{25} = -39$, $[\alpha]_{405}^{25} = -53$ ($c = 0.47$, MeOH). HR-MALDI-TOF-MS: 175.1449 ($C_8H_{19}N_2O_2^+$, $[M+H]^+$; calc. 175.1447).

*(3*R*,4*R*)-1-[2(Dimethylamino)ethyl]pyrrolidine-3,4-diol* (**10i**). By *Method B*, after FC (CH_2Cl_2/MeOH/30% aq. NH_3 soln. 30:9:1): **10i** (77%). White crystals. M.p. 63–65°. $[\alpha]_{589}^{25} = -4$, $[\alpha]_{577}^{25} = -6$, $[\alpha]_{546}^{25} = -5$, $[\alpha]_{535}^{25} = -8$, $[\alpha]_{405}^{25} = -15$ ($c = 0.91$, $CHCl_3$). HR-MALDI-TOF-MS: 175.1441 ($C_8H_{19}N_2O_2^+$, $[M+H]^+$; calc. 175.1447).

*(3*R*,4*R*)-1-(3-Aminopropyl)pyrrolidine-3,4-diol* (**10j**). FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 20:3:2): **10j** (92%). Colorless oil. $[\alpha]_{589}^{25} = -25$, $[\alpha]_{577}^{25} = -26$, $[\alpha]_{546}^{25} = -28$, $[\alpha]_{535}^{25} = -46$, $[\alpha]_{405}^{25} = -55$ ($c = 0.52$, MeOH). HR-MALDI-TOF-MS: 161.1203 ($C_7H_{17}N_2O_2^+$, $[M+H]^+$; calc. 161.1290).

*(3*R*,4*R*)-1-[2-(Benzylamino)ethyl]pyrrolidine-3,4-diol* (**10k**). As described for **9k**–**n**, after FC (MeOH/$CHCl_3$/30% aq. NH_3 soln. 20:3:2): **10k** (55%). Colorless oil. $[\alpha]_{589}^{25} = -15$, $[\alpha]_{577}^{25} = -14$, $[\alpha]_{535}^{25} = -26$, $[\alpha]_{405}^{25} = -27$ ($c = 0.27$, MeOH). HR-MALDI-TOF-MS: 237.1607 ($C_{13}H_{21}N_2O_2^+$, $[M+H]^+$; calc. 237.1603).

*(3*R*,4*R*)-1-[2-[([1,1′-Biphenyl]-4-ylmethyl)amino]ethyl]pyrrolidine-3,4-diol* (**10l**). FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1) gave **10l** (68%). Colorless oil. $[\alpha]_{589}^{25} = -8$, $[\alpha]_{577}^{25} = -6$, $[\alpha]_{535}^{25} = -11$, $[\alpha]_{405}^{25} = -11$ ($c = 0.265$, MeOH). HR-MALDI-TOF-MS: 313.0366 ($C_{19}H_{25}N_2O_2^+$, $[M+H]^+$; calc. 313.1916).

*(3*R*,4*R*)-1-[2-[(4-Chlorobenzyl)amino]ethyl]pyrrolidine-3,4-diol* (**10m**). FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1) gave **10m** (62%). Colorless oil. $[\alpha]_{589}^{25} = -9$, $[\alpha]_{577}^{25} = -8$, $[\alpha]_{535}^{25} = -14$, $[\alpha]_{405}^{25} = -14$ ($c = 0.25$, MeOH). HR-MALDI-TOF-MS: 271.2422 ($C_{13}H_{20}ClN_2O_2^+$, $[M+H]^+$; calc. 271.1213).

*(3*R*,4*R*)-1-[3(Benzylamino)propyl]pyrrolidine-3,4-diol* (**10n**). FC (MeOH/CH_2Cl_2/30% aq. NH_3 soln. 30:19:1) gave **10n** (38%). Colorless oil. $[\alpha]_{589}^{25} = -15$, $[\alpha]_{577}^{25} = -15$, $[\alpha]_{535}^{25} = -26$, $[\alpha]_{405}^{25} = -27$ ($c = 0.27$, MeOH). HR-MALDI-TOF-MS: 251.1336 ($C_{14}H_{23}N_2O_2^+$, $[M+H]^+$; calc. 251.1336).

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