Aminoglycoside Antibiotics – Enantiomerically Pure Sannamine Building Blocks

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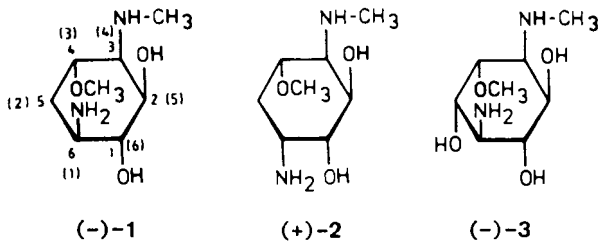
Starting from the prochiral dianhydrodeoxy-*epi*-inositol **9** a highly efficient synthesis for *rac*-sannamines (**1**, salts, derivatives) and *rac*-de-*O*-methylsannamine (**18**, salt) has been developed. Key steps are two regiospecific, practically quantitative epoxide opening reactions: intramolecularly in the diepoxyurethanes **11** and intermolecularly in the epoxyurethanes *rac*-**13**. With (*R*)-1-phenylethylamine as potential primary amino group in the second step separation of the corresponding diastereomers (**16**, **16'**) is achieved without significant loss of material. By this route enantiomerically pure (de-*O*-methyl)sannamines become available in which all functionalities are protected except that to be glycosidated. Attempts for an asymmetric realization of this synthesis resulted in only very small ee(de) values.

Aminoglycosid-Antibiotika – Enantiomerenreine Sannamin-Bausteine

Ausgehend vom prochiralen Dianhydrodesoxy-*epi*-inosit **9** wurde eine leistungsfähige Synthese für enantiomerenreine *rac*-Sannamine (**1**, Salze, Derivate) und *rac*-Des-*O*-methylsannamin (**18**, Salz) ausgearbeitet. Essentielle Schritte sind zwei regiospezifische, praktisch quantitative Epoxidöffnungen: Intramolekular in den Diepoxyurethanen **11** und intermolekular in den Epoxyurethanen *rac*-**13**. Mit (*R*)-1-Phenylethylamin als potentieller primärer Aminogruppe im zweiten Schritt gelingt die Diastereomerentrennung (**16**, **16'**) ohne signifikante Verluste. Es werden direkt enantiomerenreine (Des-*O*-methyl)Sannamin-Derivate gewonnen, in welchen alle Substituenten bis auf die zu glycosidierende OH-Gruppe geschützt sind. Versuche zur asymmetrischen Durchführung der Synthese brachten nur bescheidene ee(de)-Werte.

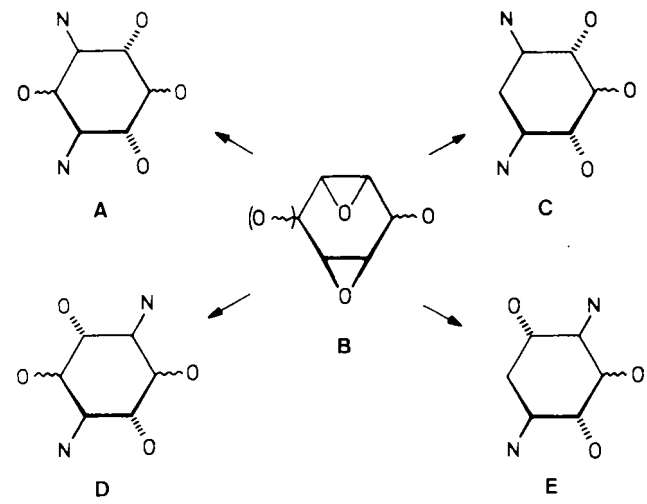
Sannamine (**1**) (2-deoxyfortamine) and sporamine (**2**) are the aglycon building blocks[1] of a new class of aminoglycoside antibiotics (sannamycins[2], istamycins[3], sporaricins[4]). Their structure is closely related to fortamine (**3**), the aglycon component of the fortimicins (astromicins)[5]. Reduced side effects and activity towards resistent strains of bacteria are characteristic of this group of antibiotics. A pecularity is their relatively simple pseudo disaccharide structure – with only one sugar (purpurosamine) and one non-sugar component, making synthetic activities in this area particularly attractive.



In recent years several total syntheses for the aglyca **1** – **3** (in brackets antibiotics numbering) starting from racemic or chiral material were published[6] – including the detailed protocol of our own access to enantiomerically pure (de-*O*-methyl)fortamines[1]. The paper presented here summarizes our activities in the sannamine area[7], the subsequent paper[8] the results of an investigation in the sporamine area. Thus a research program is continued (Scheme 1), which is based on a pool of anhydroconduritols and anhydro(deoxy)inositols **B** ultimately available from benzene. Other product families, which can be produced efficiently from these synthons and which are relevant in this context, are *cis*-1,3-(deoxy)inosadiamines (**B** → **A**, **B** → **C**) and *cis*-1,4-diamino analogues (**B** → **D**, **B** → **E**)[9,10].

Sannamine (**1**) is an **E** derivative. A limitation of our published approach to such polyfunctionalized cyclohexane de-

Scheme 1



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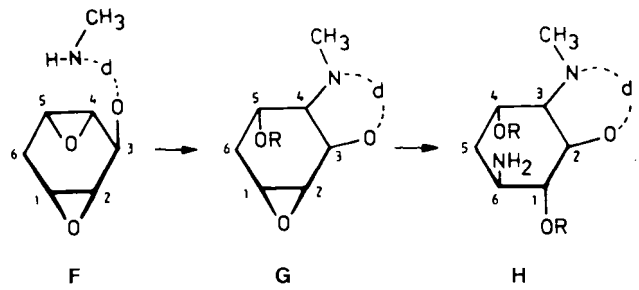
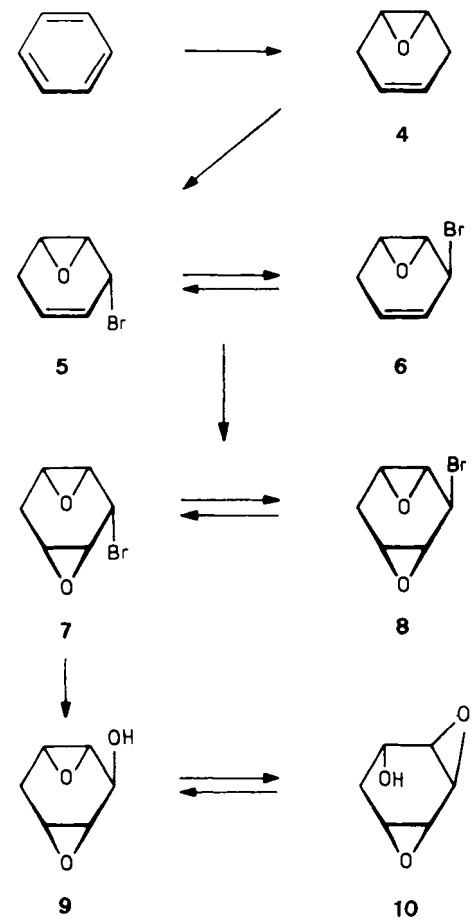
rivatives with different *N*-substituents arises from the low kinetic differentiation observed in the opening of the two epoxide rings in the dianhydroinositols **B**, as well as in the deoxy analogues, with various *N*-nucleophiles. The consequence is that it became virtually impossible to introduce stepwise two different N-residues with sufficient selectivity. Our finally successful access to **1**, patterned after the synthesis of **3**, principally circumvents this problem by following the reaction sequence **B** → **F** → **G** → **H** (Scheme 2): In the first step, the methylamino group, linked with the 3-O substituent of the prochiral educt **B**, is introduced intramolecularly. With an appropriate O – N distance (d) this should guarantee exclusive attack at the α-positions yielding **G** and *ent*-**G**, respectively. Moreover, in the 6-deoxy intermediates of type **G**, the interplay of steric and electronic effects should direct the attack of the second nucleophile, potentially the ultimate primary amino group, selectively to the 1-position. Several attractive features of this route are obvious: (i) Various steps in the procedure invite for the preparation of diastereomers suitable for a separation of racemates or for the application of stereoselective methodology. (ii) The reaction sequence may be directed in such a way that ultimately all functional groups are protected except the OH group to become glycosidated. (iii) The substituents in the 5-position of **G** and in the 4,6-positions of **H** can be widely modified.

Scheme 2



The experimentally realized route to diastereomeric intermediates of type **H** is depicted in Schemes 3/4. Starting material is (1α,2α,3β,4α,5α)-1,2:4,5-dianhydro-1,2,3,4,5-cyclohexane-pentol (**9**) [(1α,2α,3α,5α,7α)-4,8-dioxatricyclo-[5.1.0.0^{3,5}]octan-2-ol; 1,2:4,5-*epi*-dianhydrodeoxyinositol][11]. The published synthesis of **9**[10] consists of a selective allylic monobromination of epoxycyclohexene **4** derived from benzene giving a mixture of **5**/**6**, followed by epoxidation yielding a 1:9 mixture of epimeric diepoxy bromides **7**/**8**, equilibration with tetraethylammonium bromide in CH_3CN to a ca. 7:3 composition, separation of **7** by crystallization from methanol, substitution with tetraethylammonium acetate, and ammonolysis. When handling **9** one should be aware of the fact that epoxide migration to **10** is a relatively fast process; at room temperature in a 0.1 M $NaOCH_3/CH_3OH$ solution the equilibrium (≈ 5:4) is established within 15 min. Two modifications of the original procedure[1] were made in order to account for the sometimes rather erratic results: (i) the crude mixture of bromides **5**/**6** was not purified any more, since sporadically explosion-like decompositions occured and (ii) in step **7** → **8** the extremely hygroscopic tetraethylammonium acetate was replaced by the tetramethyl salt. The latter is obtainable as a dry microcrystalline powder in a reproducible quality. In this way more or less detracting side reactions (hydrolysis, epoxide → allyl alcohol rearrangement) can be avoided. Though the resulting tetramethylammonium bromide is more soluble in acetone than tetraethylammonium bromide – this was the primary reason for the use of the tetraethylammonium acetate – epoxide opening by bromide ion does not cause significant loss of material.

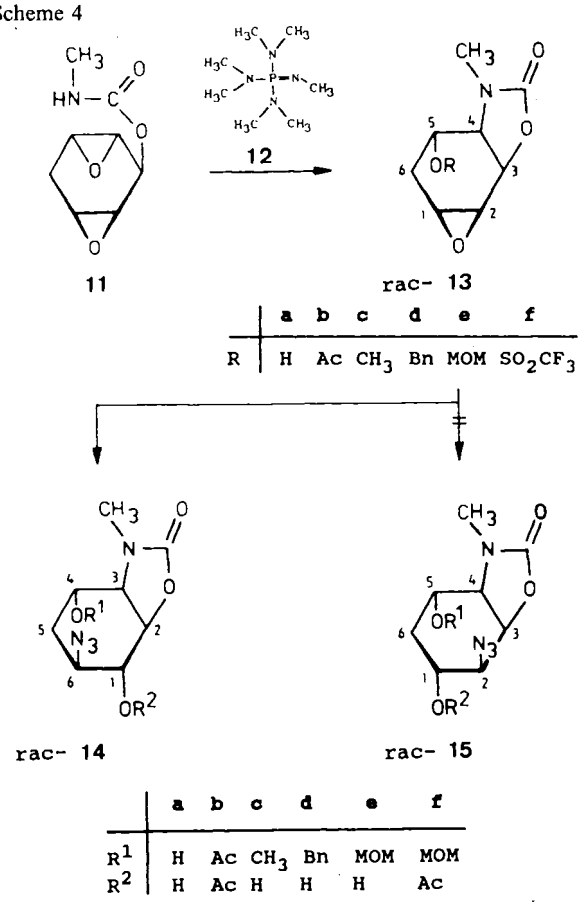
Scheme 3



Reaction of **9** with methyl isocyanate in boiling dioxane yields the urethane **11** nearly quantitatively, provided moisture and base are carefully excluded. For the cyclization **11** → *rac*-**13**, a stereoelectronically favoured 5-*exo* ring closure[12], under the aspects of competing N- and O-participation in the ambident anion[1] as well as direct and indirect epoxide opening reaction (deprotonation at C-6), the iminophosphorane base **12** [pK_a (CH_3CN) = 28[13]] proved once more first choice; it is sufficiently but not too strongly basic and only negligeably nucleophilic. Reaction of 0.27 mol of **11** with 7.5 mmol of base in pure acetonitrile under careful exclusion of moisture (dry box) yields after crystallization 93% *rac*-**13a** [DL-(1α,2α,3β,4β,5α-)-1,2-anhydro-3-

O,4-*N*-carbonyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol]. The structure of three minor by-products, detectable on thin layer chromatograms, was not elucidated. Specifically, the amount of the isomer resulting from β-attack (6-*endo*) must be smaller than 3% according to high-field ^{1}H-NMR analysis. Esterification of *rac*-**13a** to give *rac*-**13b** and etherification to give *rac*-**13c–e**, undertaken primarily with respect to glycosidation, were accomplished along standard procedures.

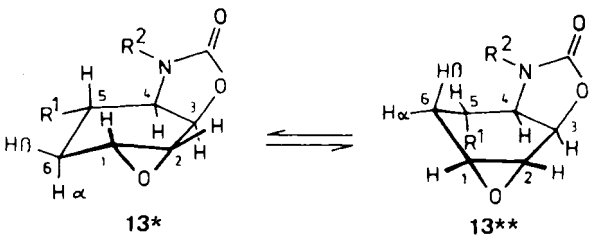
Scheme 4

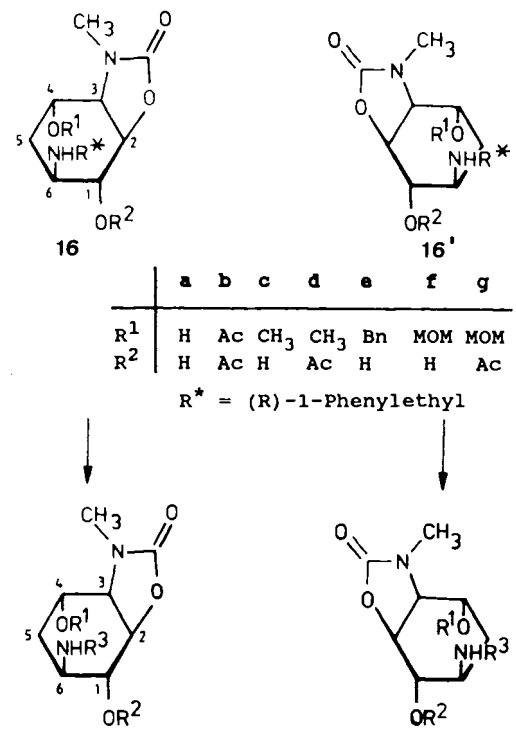


	a	b	c	d	e	f
R	H	Ac	CH_3	Bn	MOM	SO_2CF_3

	a	b	c	d	e	f
R^1	H	Ac	CH_3	Bn	MOM	MOM
R^2	H	Ac	H	H	H	Ac

The structures *rac*-**13a–f** are substantiated by fully analyzed ^{1}H-NMR spectra (Table 1) and in part by ^{13}C-NMR spectra. Typical details for the five-membered carbamate ring are the groups of signals at 4.77–5.00 (3-H) and 3.55–4.01 (4-H) with ^3J = 6.5–9.9 Hz, only slightly influenced by the R substituent. The vicinal H/H coupling constants – for **13a, c** determined also at –70°C – and the temperature dependance of the chemical shift especially of the 5-H signals, when compared i.a. with ^3J values calculated for the individual conformers, allow a rough evaluation of the conformational situation: in the case of alcohol *rac*-**13a** in an aprotic medium (CH_2Cl_2) the 5-axial conformation **13****, stabilized by the intramolecular hydrogen bond with the epoxide oxygen ($J_{5,OH}$ = 11 Hz, δ_{OH} and $J_{5,OH}$ are nearly temperature invariant) is preponderant. The ^{1}H-NMR spectrum of methyl ether **13c**, however, was found to be temperature dependend with mainly the chemical shift of 6α/6β-H being concerned; in addition, the significantly larger $J_{5,6}$ coupling constants indicate considerable participation of the 5-equatorial conformation **13***.





	a	b	c	d	e	f	g
R^1	H	Ac	CH_3	CH_3	Bn	MOM	MOM
R^2	H	Ac	H	Ac	H	H	Ac

R* = (R)-1-Phenylethyl

	a	b	c	d	e	f
R^1	H	Ac	CH_3	CH_3	MOM	MOM
R^2	H	Ac	H	Ac	H_2^+	Ac
R^3	H_2^+	Ac	H_2^+	Ac	H_2^{2+}	Ac

$[\alpha]_D$: **17**: -37 +111 +62.5 -82.4 -70.9 +80.7
ent-17: +40 -104 -62.4 +84.7 +75.6 -82.2

MOM = CH_3OCH_2

First information about the regiochemistry of epoxide opening in the tricycles **13** came from the reaction of *rac*-**13a** with sodium azide (excess NaN_3, $MgSO_4$, methanol, reflux) (Scheme 4). Continuous monitoring of the reaction progress (TLC, ^{1}H NMR) reveals only one product, which can be isolated after total conversion and crystallization with at least 95% yield and is identified as **14a** [DL-(1α,2β,3β,4α,6β)-6-azido-2-*O*,3-*N*-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol]. As judged by analysis of the respective crude product mixtures (TLC, ^{1}H NMR), the addition of azide proceeds also regiospecifically in the case of the ethers *rac*-**13c–e**

(97% *rac*-**14c**, 96% *rac*-**14d**, 80% *rac*-**14e** (the lower yield in the last case is presumably due to loss during work-up). *rac*-**14a** and *rac*-**14e** are characterized additionally as acetates *rac*-**14b**/**14f**. Taken this outcome for the epoxide openings, it seemed promising to pursue the separation of racemates by reaction with (*R*)- or (*S*)-1-phenylethylamine. In line with the lower nucleophilicity of these amines the addition of the *R*-enantiomer to *rac*-**13a** is relatively slow in boiling dioxane but somewhat faster in boiling 1-propanol. The only two products, formed in nearly equal amounts, are UV-active and can be separated cleanly by TLC. They are identified as diastereomers **16a** and **16a'**. In larger quantities (10 g) the chromatographic separation can be simplified (and made cheaper) by crystallization of the crude mixture from methanol providing the major part of one diastereomer [**16**, leading to natural sannamine (**1**)] rather pure; the remaining mixture can then be separated by rapid chromatography without significant loss. By this procedure a yield of 47% for **16a** and **16a'** can be reproduced on a multi-gram scale. On standing of solutions of **16a** or **16a'** in acetanhydride/pyridine only the two OH groups are transformed (**16b**, **16b'**). With the ethers *rac*-**13c**, **e** (*R*)-1-phenylethylamine reacts in boiling dioxane only in the presence of a Lewis acid catalyst, in boiling 1-propanol without catalyst. After similar work-up comparably good yields (44–47%) of **16c**, **e**/**16c'**, **e'** are achieved. Acetylation under standard conditions of **16c** leads to a diacetylated derivative besides the monoacetate **16d**, of **16c'** only to a diacetate, of **16f** and **16f'** to the monoacetates **16g** and **16g'**.

Table 1. Selected ^{1}H-NMR data [δ; *J*(Hz)] of tricycles **13a–f** ($CDCl_3$, a: CD_2Cl_2)

	1-	2-	3-	4-	5-	6α-	6β-H
13a	3.43	3.33	4.97	3.83	3.84	2.35	2.10
b	3.36	-3.28	4.92	3.71	5.02	2.28	-2.15
c	3.35	3.28	4.88	3.60	3.43	1.96	2.30
d	3.35	-3.27	4.88	3.56	3.63	2.28	1.97
e	3.18	3.12	4.77	3.55	3.69	2.01*	2.12*
f	3.33	3.26	5.00	4.01	5.18	2.50	2.50

	$J_{1,2}$	2,3	3,4	4,5	5,6α	5,6β	6α,6β	6α,1	6β,1
13a	3.5	≈0	8.5	3.0	≈3	3.5	15.5	≈3	≈0[a]
b	-	-	8.0	4.5	4.5	4.5	-	-	-
c	4.0	≈0	8.0	7.0	7	4.5	15.0	4.0	2.0
d	4.0	<0.5	6.5		5.0	7.0	15.5	4.0	≈1.5
e	3.0	≈0	7.5	5.3	5.3	5.3	15.8	2.0	3.5
f	4.0	≈0	9.0	3.8	3.8	3.8	-	-	2.0

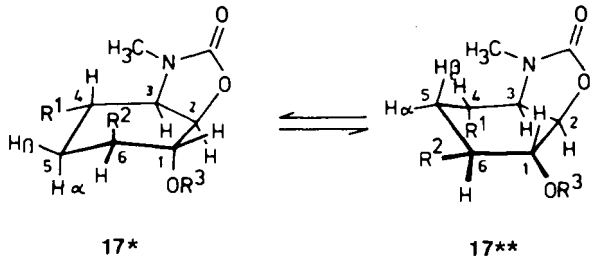
Hydrogenolytic elimination of the phenylethyl group from the diastereomers **16a**, **e**, **f** or **16a'**, **e'**, **f'** can be brought about without affecting the carbamate rings. The amines isolated in nearly quantitative yield as HCl/H_2SO_4 salts **17a**, **c**, **e** and *ent*-**17a**, **c**, **e** can be transformed into derivatives **17b**, **d**, **f** and *ent*-**17b**, **d**, **f** with acetanhydride/pyridine.

The ^{1}H-NMR differentiation (Table 2) of products **14**/**16**, and hence of **17**, from their regioisomers of type **15** is primarily based upon the vicinal H/H coupling and their in-

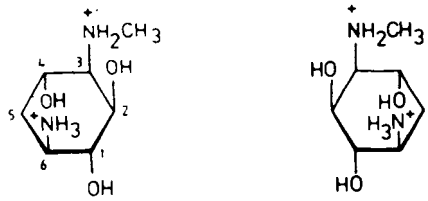
Table 2. Selected ^{1}H-NMR data [δ; *J*(Hz)] of bicycles **14a–f**, **16a–g**, **16a'–g'**, **17a–f**, **33a**, **b** and **34** [$CDCl_3$; a: $CDCl_3/CD_3OD$ (1:1); b: CD_3OD/D_2O; c: CD_3OD]

	1-	2-	3-	4-	5α-	5β-	6-H	$J_{1,2}$	2,3	3,4	4,5α	4,5β	5α,5β	5α,6	5β,6	6,1	3,5α
14a	3.56	4.48	3.79	4.19	2.01	1.62	3.72	7.5	7.5	3.0	5.0	3.0	13.0	5.0	10.0	10.0	<1
b	5.10	4.56	≈3.7	5.32	2.17	1.86	≈3.7	7.5	7.5	3.5	3.0	3.0	14.5	4.0	11.0	10.0	-
c	≈3.7	4.47	3.78	≈3.7	2.15	1.58	≈3.7	7.5	7.5	4.0	4.5	3.0	15.0	4.5	10.0	10.0	<1.5
d	3.60	3.87	3.79		2.11	1.61	3.72	7.0	7.0	3.0	5.0	3.0	14.0	4.0	10.0	10.0	<1[a]
e	≈3.7	4.50	≈3.7	4.08	2.14	1.61	≈3.7	7.5	7.5	3.0	3.0	3.0	14.3	4.0	10.5	7.5	-
f	5.07	4.63	≈3.8	4.13	2.20	1.75	≈3.8	7.5	7.5	6.8	3.0	3.0	14.2	4.5	10.5	10.5	-
16a	3.52	4.30	3.61	4.07	1.87	1.59	2.56	8.0	8.0	4.5	5.5	3.5	14.0	5.0	9.5	10.5[a]	
b	4.94	4.43	3.67	5.20	2.16	1.60	2.65	7.5	7.5	3.0	6.0	3.0	13.5	3.5	10.0	10.0	
c	3.55	4.29	≈3.65	≈3.65	2.12	1.42	2.55	7.5	7.5	-	4.5	3.0	13.5	4.5	10.0	10.0	
d	4.94	4.38	≈3.65	3.65	2.00	1.59	2.70	7.5	7.5	-	≈3	2.2	13.8	4.5	8.2	8.2	
e	3.58	4.33	3.67	3.85	2.18	1.46	2.67	7.5	7.5	3.5	4.5	3.5	13.5	4.5	10.0	10.5	
f	3.52	4.33	3.64	4.02	2.15	1.61	2.60	7.5	7.5	3.0	4.0	4.5	13.5	4.5	10.5	10.5	
g	4.93	4.42	3.69	4.04	2.07	1.55	2.75	7.5	7.5	3.8	5.2	3.0	14.2	3.8	9.0	9.0	
a'	3.51	4.46	3.69	4.04	1.77	1.31	2.97	8.0	8.0	4.0	5.5	3.5	14.0	5.0	9.5	9.5	
b'	5.06	4.52	3.66	5.14	1.84	1.59	2.77	7.0	7.0	3.0	5.0	3.0	15.0	≈4	9.8	9.8	
c'	-	4.41	3.66	-	1.68	1.24	2.79	7.5	7.5	3.5	4.5	3.0	14.0	4.5	10.5	10.5	
e'	3.49	4.44	3.65	3.65	1.74	1.22	2.88	7.5	7.5	3.5	4.0	3.0	14.0	4.0	10.5	11.0	
f'	3.83	4.44	3.79	4.08	2.01			7.5	7.5	2.3	3.8	3.0	14.5	3.8	12.0	11.3	
g'	5.00	4.68	3.65	3.94	1.80	1.48	2.85	7.5	7.5	3.7	4.5	≈3	15.0	4.5	9.8	9.8	
17a	3.71	4.58	3.90	4.35	2.22	1.88	3.47	7.5	7.5	3.0	4.5	3.0	14.5	4.5	11.0	11.0	-
b	4.94	4.66	3.84	5.31	2.09	1.83	4.31	7.5	7.5	3.0	3.0	3.0	14.0	3.0	12.0	10.0	≤1[a]
c	3.57	4.43	≈3.9	≈3.9	2.29	1.73	3.23	7.5	7.5	-	4.0	3.0	14.0	4.0	11.5	11.5	<1.5[b]
d	4.91	4.60	3.79	3.70	2.39	1.56	4.24	7.5	7.5	3.0	≈4	3.0	15.0	≈4	10.5	10.5	<1.5
e	3.52	4.45	3.93	4.21	2.20	1.75	3.22	7.5	7.5	3.0	3.8	3.0	14.3	3.8	11.2	10.5	≤1[c]
f	4.90	4.65	3.82	4.08	2.28	1.58	4.35	7.5	7.5	2.3	3.8	3.0	14.3	3.8	12.0	11.0	<1
33a	3.64	4.41	3.69	3.60	5.80	5.80	3.77	7	8	3.5	4	2.5	14	4	10	10	
b	4.91	4.56	3.78	3.70	5.08	5.08	4.00	7.5	7.5	3	3.5	2.5	13.5	3.5	11	11	
34	4.65	4.29	3.64	3.87	1.92	2.49	3.60	8.2	8.2	4.5	6	3	14	-	9	10.5	

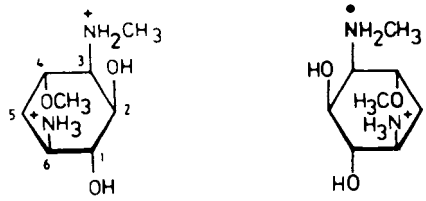
terconnectivity [for the 1e,2e,5e conformation of *rac*-**15** the calculated values for $J_{1,2}$ (≈ 10 Hz), $J_{1,6\beta}$ (≈ 10 Hz), and $J_{5,6\beta}$ (≈ 7 Hz) display especially large deviations]. In the case of the diastereomers **16**/**16'** the largest δ variations are observed for the 6-H signals, as expected. The preference for the 1e,4a,6e (**17****) conformation in the equilibrium with the 1a,4e,6a conformation (**17***) is confirmd i.a. by the generally large coupling constants $J_{5\beta,6}$ (9.5–12.0 Hz) and $J_{6,1}$ (7.5–11.2 Hz) and the long range coupling constants $J_{3,5\alpha}$ (1–3 Hz). Accordingly, the signals of equatorial 5α-H generally appear at lower field than those of axial 5β-H.



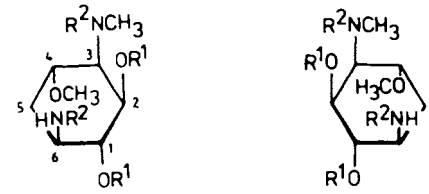
17* **17****



18 **ent - 18**



19 **ent - 19**

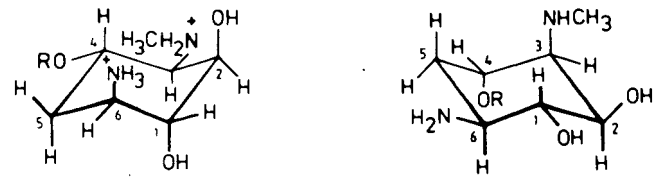


1,20a,b **ent- 1,20a,b**

	1	20a	20b
R^1	H	Ac	H
R^2	H	Ac	Ac
$[\alpha]_D$	-37.0	+49.9	+90.1

	ent-1	ent-20a	ent-20b
R^1	H	Ac	H
R^2	H	Ac	Ac
$[\alpha]_D$	+37.0	-50.0	-90.0

After hydrolysis of the carbamate ring in **17a**/*ent*-**17a** and **17c**/*ent*-**17c** [water/methanol, $Ba(OH_2)$] and acidification with conc. H_2SO_4 the sulfates **18**/*ent*-**18** and **19**/*ent*-**19** are obtained and, in the usual manner, from **19**/*ent*-**19** the free bases sannamine (**1**) and *ent*-sannamine (*ent*-**1**) as well as the tetraacetyl-(**20a**/*ent*-**20a**) and diacetyl derivatives **20b**/*ent*-**20b** are formed. As may be deduced from the ^{1}H-NMR spectra, especially from the coupling constants (Table 3), the salts **18** and **19** as well as the acetyl derivatives **20a**, **b** preferably populate the aaeea chair (**18***), the bases **1**, however, the eeaae chair (**1****). A comparison of the rotational values of **1** and **20b** with those published by the Japanese authors[3,14] allowed the assignments, i.e. the sannamine derived from diastereomer **16c** is the natural laevorotary product (**1**). By methylation of **16a** giving **16c** the assignments in the de-*O*-methyl series are confirmed.



18* **1****

Table 3. ^{1}H-NMR data [δ; *J*(Hz)] of sannamines **1**, **18**–**20** (D_2O) (a: rotamer-1, $CDCl_3$; b: rotamer-1, CD_3OD)

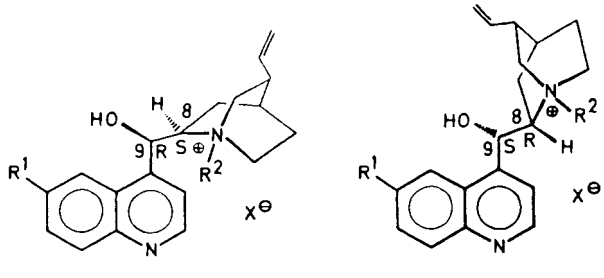
	1-	2-	3-	4-	5α-	5β-	6-H			
18	3.89	4.17	3.14	4.08	≈2	≈2	3.45			
19	4.10	4.35	3.41	3.95	2.08	2.42	3.66			
1		4.30	3.79	4.15	2.49	2.06	3.25			
20a[a]	4.90	5.43	4.78	3.80	1.98	2.34	4.40			
20b[b]		4.03	4.61	4.00	2.26	1.81	4.19			
	$J_{1,2}$	2,3	3,4	4,5α	4,5β	5α,5β	5α,6	5β,6	6,1	
18	5	5	9	9	≈5	14.0	≈5	≈5	≈5	
19	3.8	3.8	9.0	10.5	4.5	15.0	4.5	4.5	4.0	
1	9.0	4.5	3.0	4.0	3.5	14.5	4.5	11.0	10.0	

For completion it has been experimentally verified that the racemic salts of de-*O*-methylsannamine (*rac*-**18**) and of sannamine (*rac*-**19**) are accessible by practically quantitative catalytic hydrogenation of the racemic azides *rac*-**14a**, **c** to the racemic amines *rac*-**17a**, **c**.

Attempts Towards Enantioselective Reaction Control

The separation of diasteromers, as detailed above, could not be effected with the corresponding sporamine (**2**)[8] precursors – one of the motives to check the chances for an asymmetric performance of the sequences **F** → **G** → **H**. Enantioselective cyclization of prochiral diepoxy urethane

(F → G) was an obvious alternative, in which, however, an efficient differentiation between the pro-*R* and the pro-*S* hemisphere was a priori doubtful without additional manipulations of the structure. The results of extensive experimentation with substrate **11** and the chiral phase-transfer catalysts[15] **21**–**23**, the chiral base **24**, and the chiral phosphazene bases **25**/**26**[16,17], developed especially for this purpose, are summarized in Table 4: The yields of **13a** are generally high, the ee values – determined by ^{1}H NMR by addition of (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol (ATE) – consistently very low, however. The absolute configuration of the products as formulated in the Schemes is based upon ^{1}H-NMR analyses (Table 5, see also Table 1), with consideration of the anisotropic influence of the aromatic rings in the preferred 5a conformation (**13****), as judged from the ^3J values. "External" position of the phenyl ring (**28a**, *ent*-**28a**) is concluded from the ca. 0.5-ppm high-field shift of the 4-H signal, "internal" position (**28a'**, *ent*-**28a'**) from the ca. 0.4/0.7-ppm high-field shift of the 6α/6β-H signal. With the larger naphthyl group these effects are more pronounced (ca. 1 ppm for 4-H and ca. 1/1.9 ppm for 6α-/6β-H). Taken this assignment, (*S*)-configurated groups in **27** would lead preferentially into the non-natural *ent*-sannamine series.

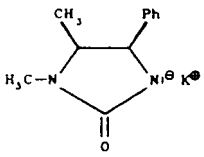


21

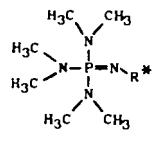
$R^1 = OCH_3$, $R^2 = CH_2C_6H_5$

22: R^1 = H, $R^2 = CH_2C_6H_5$

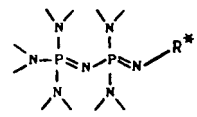
23: $R^1 = OCH_3$, $R^2 = CH_2C_6H_4NO_2$-(4)



24



25



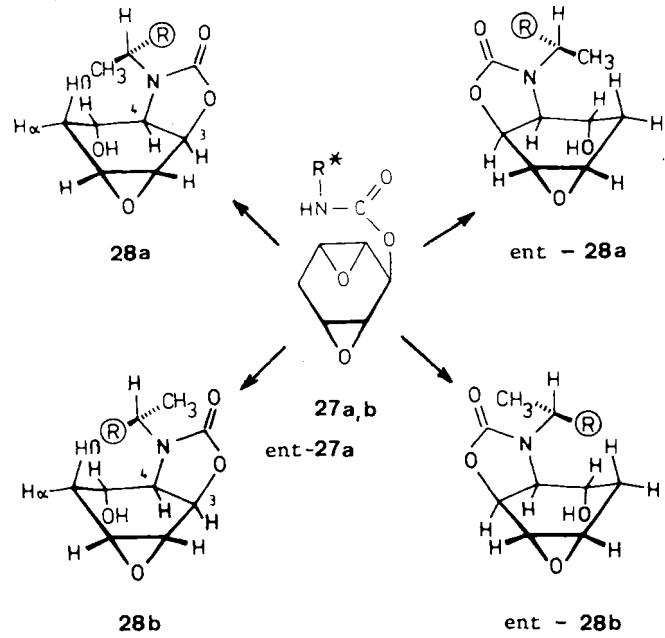
26

R* = (R)-1-Phenylethyl

Table 4. Cyclizations **11a** → **13a** with chiral phase-transfer catalysts (PTC) and chiral bases

Base	KOH[a]	KOH[a]	KOH[a]	**24**[b]	**25**[c]	**26**[c]
PTC	**21**	**22**	**23**			
yield	> 97	> 97	90	> 97	96	90
ee	8	14	11	6	6	4

[a] 10 mol-% of PTC and KOH, 23°C, dioxane. – [b] Excess base, –78°C, toluene. – [c] 10 mol-% of base, 23°C, CH_2Cl_2 or dioxane.



28a ent – **28a**

27a,b ent-**27a**

28b ent – **28b**

a: R* = (*R*)-1-Phenylethyl
ent-**a**: R* = (*S*)-1-Phenylethyl
b: R* = (*R*)-1-(1-Naphthyl)ethyl

Table 5. Selected ^{1}H-NMR data [δ; *J*(Hz)] of **28a**, **b** and **28a'**, **b'**

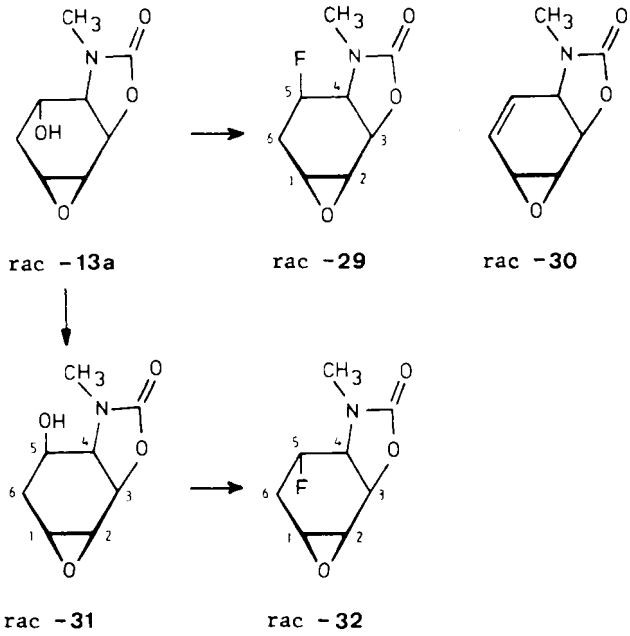
	1-	2-	3-	4-	5-	6α-	6β-H	
28a	3.44	3.38	4.92	3.70	3.87	2.34	2.15	
28a'	3.34	3.38	4.98	4.12	3.56	1.91	1.42	
28b	3.46	3.36	4.73	3.10	3.79	2.34	2.29	
28b'	3.01	3.27	4.94	4.17	3.10	1.38	0.55	
	$J_{1,2}$	2,3	3,4	4,5	5,6α	5,6β	6α,6β	6α,1	6β,1
28a	4.0	0.5	8.5	3.0	3.0	3.5	16.0	3.0	
28a'	4.0	0.5	8.5	3.0	3.0	3.5	16.0	3.0	
28b	3.5	1.0	9.0	2.5	2.5	3.5		≈2.5	1.0
28b'	3.5	–	8.5	3.0	2.5	3.5		≈2.5	1.0

Principally inadequate side diffentiation was also operative in cyclizations of the carbamates **27a**/*ent*-**27a** and **27b**, derived from **9a** and (*R*)/(*S*)-1-phenylethyl isocyanate and (*R*)-1-naphthylethyl isocyanate, respectively. Upon treatment with the BEMP base (CH_3CN, 22°C)[13] the pairs **28a**/**28a'**, *ent*-**28a**/*ent*-**28a'** (ratio 42:58, de = 16%), and **28b**/**28b'** (ratio 39:61, de = 22%) were isolated in nearly quantitative yields, but with only insignificantly better stereoselectivity[17].

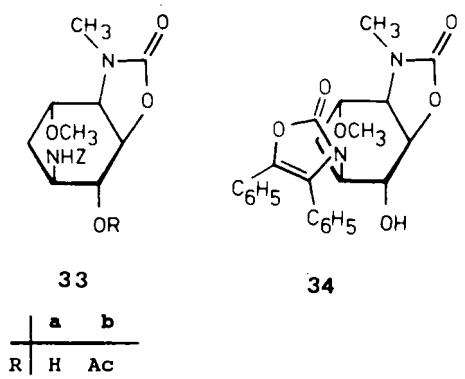
Supplements

A bonus of the reaction sequence F → G → H specified above implied the possibility for chemical modification specifically at the 5-position in the intermediates **G**. Of special relevance in the antibiotics field are fluorinated compounds[18]. In the reaction of 5α-alcohol *rac*-**13a** with (diethylamino)sulfur trifluoride (DAST)[19] substitution leading to 5β-fluoride *rac*-**29** (10%) was dominated by elimination to give *rac*-**30** (39%). With 5α-triflate *rac*-**13f** and water-free

tetrabutylammonium fluoride on silica[20] the yield of *rac*-**29** could be raised to ca. 40%; still, the olefin *rac*-**30** runs up to a comparable share[21]. With remarkable selectivity 5β-alcohol *rac*-**31**, prepared from *rac*-**13f**, reacts with DAST to yield 85% of 5α-fluoride *rac*-**32**. The adducts, formed stereospecifically and quantitatively from the latter and (*R*)-1-phenylethylamine, can be separated analogously to **16a**/**16a'**.



For glycosidation experiments the urethanes **17**/*ent*-**17** are first choice. In **17c**, **e**/*ent*-**17c**, **e** only the primary amino group needs to be protected in order to have solely the 1-OH free for connection with the sugar part. The Z- (**33a**, **b**/*ent*-**33a**, **b**) and the strongly fluorescent "ox"-protected derivatives (**34**/*ent*-**34**)[22] have been prepared from **17c**/*ent*-**17c** under standard conditions. They generally prefer conformations with the free OH group being quasi-equatorial oriented (**17****).



Resumé

With 80–85% over all yield of racemic (de-*O*-methyl) sannamine salts **18**/**19** for the five (six) operations starting from dianhydro-*epi*-inositol **9** and over all 90% for the three operations from epoxide **4** leading to **9**[10] the preparative value of this approach needs no further comment. Restrictions as noted for the analogous construction of the fortamines (**3**), especially for the preparation of 3-*O*-methyl compounds[1], are, as expected, not operative in the 5(2)-deoxy series. For both series, however, so far no significant enantioselective execution could be achieved. On the other hand, with both the natural as well as the non-natural enantiomers being available now by a highly efficient and strategically advantageous resolution procedure, their application for the total synthesis of novel aminoglycoside antibiotics is being intensively studied[23].

Financial support by the *Fonds der Chemischen Industrie*, the *Deutsche Forschungsgemeinschaft*, and the *BASF AG* is gratefully acknowledged. We thank Dr. *D. Hunkler* and Dr. *J. Wörth* for extensive NMR and MS measurements.

Experimental

Melting points: Monoskop IV (Fa. Bock), uncorrected values. – Elemental analyses: Analytische Abteilung des Chemischen Laboratoriums der Universität Freiburg i.Br. – IR: Perkin-Elmer 457. – ^{1}H NMR: Bruker WM 250, HX 400 (250 MHz, when not specified otherwise, values marked with an asterisk* are interchangeable). – ^{13}C NMR: Bruker HX 400. – Optical rotation: PE 141 polarimeter. Specific rotation values are given in (deg·ml)/(dm·g).

General Procedures. – Esterification of Acyl Chlorides: A solution of 1.0 mmol of an alkohol, 1.2 mmol of acyl chloride, and 1.2 mmol of 4-(dimethylamino)pyridine (DMAP) in 5 ml of CH_2Cl_2 is kept at room temp. for 1 d. After total conversion of the alcohol (TLC, chloroform/CH_3OH 10:1), CH_2Cl_2 (10 ml) is added and the solution extracted three times with 2 N H_2SO_4. The organic layer is dried ($MgSO_4$) and concentrated in vacuo. Crystallization from ethanol; 90–96%.

Ammonolysis of Esters: The solution of the ester in CH_3OH is saturated with ammonia (dried over KOH). After total conversion (TLC, chloroform/CH_3OH 10:1) the solution is concentrated in vacuo and the residue purified by column chromatography (silica, chloroform/CH_3OH 25:1). Generally quantitative yield.

(1α,2α,3β,4α,5α)-1,2;4,5-Dianhydro-3-O-(methylcarbamoyl)-1,2,3,4,5-cyclohexanepentol (**11**): A solution of 51.2 g (0.4 mol) of **9**[10] and 34.2 g (0.6 mol) of distilled methyl isocyanate in 200 ml of absolute dioxane (N_2) was heated at reflux for 6 h (total conversion, DC, $CHCl_3$/CH_3OH 25:1). The solution was concentrated in vacuo and the solid residue dried in vacuo (10^{-2} Torr) and crystallized from CH_3OH to give 71.8 g (97%) of colorless crystals, m.p. 138°C. – IR (KBr): $\tilde{\nu}$ = 3340 cm^{-1}, 2910, 1705, 1535, 1420, 1210, 1265, 1250, 1140, 1015, 1000, 940, 795. – ^{1}H NMR ($CDCl_3$): δ = 5.45 (br. s, 3-H), 4.91 (br., NH), 3.09–3.12 (m, 1-, 2-, 4-, 5-H), 2.87 (d, CH_3), 2.76 (br., d, 5α-H), 2.33 (dt, 5β-H); J_{NH,CH_3} = 3.5, $J_{5\alpha,5\beta}$ = 16.5, $J_{5\alpha,1} = J_{5\alpha,6} \leq 1$, $J_{1,5\beta} = J_{5\beta,6}$ = 2 Hz.

$C_8H_{11}NO_4$ (185.2) Calcd. C 51.89 H 5.99 N 7.56
Found C 51.57 H 5.89 N 7.87

DL-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (*rac*-**13a**): In a dry box (N_2) in a 500-ml round bottom flask with magnetic stirrer 50.0 g (270 mmol) of **11** was dissolved in 200 ml of acetonitrile distilled from $KMnO_4$ and dried with B_2O_3. Then 1.5 ml (7.5 mmol) of tris(dimethylamino)-*N*-methylphosphinimine (**12**) was added. The solution was stirred at 45°C to reach total conversion (6–7 h, TLC control, ethyl ac-

etate/CH_3OH 20:1) and concentrated in vacuo. The yellowish, oily raw material was separated by column chromatography (silica, $CHCl_3/CH_3OH$ 10:1, 30/4 cm) from the base. The solute was concentrated in vacuo and the residue crystallized from $CHCl_3$/ether (5:1) to give 46.5 g (93%) of colorless crystals, m.p. 97°C. – IR (KBr): $\tilde{\nu}$ = 3500 cm^{-1}, 3040, 2970, 2910, 1755, 1480, 1435, 1415, 1380, 1360, 1335, 1320, 1305, 1265, 1230, 1205, 1125, 1070, 1035, 975, 950, 900, 850, 820, 780, 755, 725, 665, 605, 550, 500, 410. – ^1H NMR (CD_2Cl_2): δ = 4.97 (dd, 3-H), ≈ 3.84 (dt, 5-H), ≈ 3.83 (dd, 4-H), 3.43 (ddd, 1-H), 3.33 (m, 2-H), 3.10 (d, OH), 2.35 (ddd, 6α-H), 2.10 (ddd, 6β-H); $J_{1,2}$ = 3.5, $J_{2,3}$ ≈ 0, $J_{3,4}$ = 8.5, $J_{4,5}$ = 3, $J_{5,6\alpha}$ ≈ 3, $J_{5,6\beta}$ ≈ 3.5, $J_{6\alpha,6\beta}$ = 15.5, $J_{6\alpha,1}$ ≈ 3, $J_{6\beta}$ = ≈ 0, $J_{5,OH}$ = 11 Hz. – ^{13}C NMR (CD_2Cl_2): δ = 68.5 (C-3), 63.4 (C-5), 58.6, (C-4), 53.0 (C-1), 51.8 (C-2), 29.8 (NCH_3), 25.3 (C-6).

$C_8H_{11}NO_4$ (185.2) Calcd. C 51.89 H 5.99 N 7.56
Found C 51.54 H 5.98 N 7.61

DL-(1α,2α,3β,4β,5α)-5-O-Acetyl-1,2-anhydro-3-O,4-N-carbonyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (*rac*-**13b**): 926 mg (5.0 mmol) of *rac*-**13a** was acetylated under standard conditions. From chloroform/ether (1:1) 1.08 g (95%) of colorless crystals, m.p. 115°C. – IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1}, 1750, 1480, 1440, 1400, 1370, 1310, 1230, 1120, 1045, 1025, 935, 835, 810, 780, 765, 710, 670. – ^1H NMR ($CDCl_3$): δ = 5.02 (q, 5-H), 4.92 (d, 3-H), 3.71 (dd, 4-H), 3.36–3.28 (m, 1-, 2-H), 2.90 (s, NCH_3), 2.28–2.15 (m, 6α-, 6β-H), 2.09 (s, CH_3); $J_{3,4}$ = 8, $J_{4,5}$ = $J_{5,6\alpha}$ = $J_{5,6\beta}$ = 4.5 Hz.

$C_{10}H_{14}NO_5$ (228.2) Calcd. C 52.63 H 6.18 N 6.14
Found C 52.54 H 5.98 N 6.61

DL-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-5-O-methyl-4-(methylamino-1,2,3,5-cyclohexanetetrol (*rac*-**13c**): To a solution of 23.0 g (125 mmol) of *rac*-**13a** in 60 ml of abs. DMF 4.56 g (190 mmol) of NaH was added at 0°C. The suspension was stirred, till no more gas evolved (30 min), then 26.9 g (190 mmol) of methyl iodide was added. After 1 h (total conversion, TLC, $CHCl_3/CH_3OH$ 25:1) the excess of NaH was destroyed with ca. 8 ml of *tert*-butyl alcohol (0°C). The solution was concentrated in vacuo (10^{-3} Torr), the oily residue dissolved in 500 ml of CH_2Cl_2, and the solution extracted twice with 75 ml of water. The organic phase was dried ($MgSO_4$), concentrated in vacuo and the oily residue crystallized from ether; 23.8 g (94%) of colorless crystals, m.p. 56°C. – IR (KBr): $\tilde{\nu}$ = 3000 cm^{-1}, 2940, 1760, 1745, 1440, 1425, 1390, 1360, 1335, 1300, 1240, 1210, 1100, 985, 930, 835, 820, 765, 710, 670, 570, 500. – ^1H NMR ($CDCl_3$): δ = 4.88 (d, 3-H), 3.60 (dd, 4-H), 3.43 (dt, 5-H), 3.39 (s, OCH_3), 3.35 (m, 1-H), 3.28 (d, 2-H), 2.93 (s, NCH_3), 2.30 (ddd, 6β-H), 1.96 (ddd, 6α-H); $J_{1,2}$ = 4, $J_{2,3}$ ≈ 0, $J_{3,4}$ = 8, $J_{4,5}$ = 7, $J_{5,6\alpha}$ = 7, $J_{5,6\beta}$ = 4.5, $J_{6\alpha,6\beta}$ = 15, $J_{6\alpha,1}$ = 4, $J_{6\beta,1}$ = 2 Hz. – ^{13}C NMR (CD_2Cl_2): δ = 157.6 (CO), 75.3 (C-5), 70.4 (C-3), 58.2 (C-4), 57.0 (OCH_3), 51.2 (C-1), 50.1 (C-2), 30.9 (NCH_3), 25.0 (C-6).

$C_9H_{13}NO_4$ (199.2) Calcd. C 54.26 H 6.57 N 7.03
Found C 53.88 H 6.72 N 6.98

DL-(1α,2α,3β,4β,5α)-1,2-Anhydro-5-O-benzyl-3-O,4-N-carbonyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (*rac*-**13d**): An anhydrous solution of 1.85 g (10.0 mmol) of *rac*-**13a** in 15 ml of glyme/DMF (3:1) was cooled to 0°C, 720 mg (30.0 mmol) of NaH was added and the solution stirred for 1 h at 0°C. To this suspension 1.90 g (15.0 mmol) of freshly distilled benzyl chloride was added. The solution was stirred for 1 h at room temp. (TLC control, ethyl acetate/cyclohexane 2:1), then the excess of NaH was destroyed with ca. 5 ml of *tert*-butyl alcohol and the solution concentrated at 10^{-2} Torr/ca. 30°C. The residue was dissolved in 100 ml of CH_2Cl_2, the solution extracted twice with 50 ml of water, dried, and concentrated in vacuo. The remaining yellow oil was purified by column chromatography (silica, 6/3 cm, ethyl acetate/cyclohexane 2:1). From $CHCl_3$/ether (5:1) 2.66 g (97%) of colorless crystals were obtained, m.p. 82°C. – IR (KBr): $\tilde{\nu}$ = 3000 cm^{-1}, 2980, 2850, 1755, 1500, 1480, 1435, 1400, 1375, 1355, 1315, 1300, 1275, 1255, 1240, 1210, 1165, 1145, 1100, 1060, 1030, 1020, 935, 840, 820, 765, 750, 700, 670. – ^1H NMR ($CDCl_3$): δ = 7.42–7.28 (m, 5H), 4.88 (d, 3-H), 4.66, 4.46 (d, CH_2), 3.63 (dt, 5-H), 3.56 (t, br. 4-H), 3.35–3.27 (m, 1-, 2-H), 2.86 (s, CH_3), 2.28 (dt, br. 6α-H), 1.97 (ddd, 6β-H); $J_{1,2}$ = 4, $J_{2,3}$ < 0.5, $J_{3,4}$ = 6.5, $J_{5,6\alpha}$ = 5, $J_{5,6\beta}$ = 7, $J_{6\alpha,6\beta}$ = 15.5, $J_{6\alpha,1}$ = 4, $J_{6\beta,1}$ ≈ 1.5, J_{CH_2} = 12 Hz.

$C_{15}H_{17}NO_4$ (275.3) Calcd. C 65.44 H 6.22 N 5.08
Found C 65.44 H 6.20 N 5.07

DL-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-5-O-(methoxymethyl)-4-(methylamino)-1,2,3,5-cyclohexanetetrol (*rac*-**13e**): To an anhydrous solution of 4.63 g (25.0 mmol) of *rac*-**13a** in 50 ml of glyme/DMF (3:1) 1.80 g (75.0 mmol) of NaH was added at 0°C. The suspension was stirred at that temperature for 1 h. To this suspension 3.02 g (37.5 mmol) of distilled (chloromethyl) methyl ether was added by syringe and the suspension stirred at room temp. for 1 h (TLC control, ethyl acetate/cyclohexane 2:1). In case that the conversion was not yet complete, 20% of the above amounts of NaH and (chloromethyl) methyl ether were added, and the suspension was stirred for another 1 h. Excess of NaH was destroyed with ca. 5 ml of *tert*-butyl alcohol, the solution concentrated at 10^{-2} Torr/30°C, and the distillate collected in a cooled trap with a solution of CH_3ONa/CH_3OH. To the residue 400 ml of CH_2Cl_2/H_2O (1:1) was added. The organic layer was extracted twice with 50 ml of water, dried, and concentrated in vacuo. The remaining yellow oil was purified by column chromatography (silica, 6/3 cm, ethyl acetate/cyclohexane 2:1): 5.16 g (90%) of colorless oil. – IR (film): $\tilde{\nu}$ = 2940 cm^{-1}, 2820, 1780–1740, 1435, 1400, 1335, 1295, 1265, 1210, 1150, 1060–1040, 910, 835, 815, 795, 765, 725, 665. – ^1H NMR ($CDCl_3$, 400 MHz): δ = 4.77 (d, 3-H), 4.61, 4.55 (d, CH_2), 3.69 (q, 5-H), 3.55 (dd, 4-H), 3.26 (s, OCH_3), 3.18 (m, 1-H), 3.12, (d, 2-H), 2.77 (s, NCH_3), 2.12* (ddd, 6α-H), 2.01* (ddd, 6β-H); $J_{1,2}$ = 3, $J_{2,3}$ ≈ 0, $J_{3,4}$ = 7.5, $J_{4,5}$ = $J_{5,6\alpha}$ = $J_{5,6\beta}$ = 5.3, $J_{6\alpha,6\beta}$ = 15.8, $J_{6\alpha,1}$ = 2, $J_{6\beta,1}$ = 3.5, J_{CH_2} = 7 Hz. – ^{13}C NMR ($CDCl_3$): δ = 157.2 (CO), 95.7 (CH_2), 69.9 (C-5), 69.3 (C-3), 57.4 (C-4), 55.4 (OCH_3), 50.1 (C-1), 49.2 (C-2), 30.1 (NCH_3), 25.3 (C-6).

$C_{10}H_{15}NO_5$ (229.3) Calcd. C 52.38 H 6.59 N 6.11
Found C 52.01 H 6.30 N 6.46

DL-(1α,2α,3β,4β,5β)-1,2-Anhydro-3-O,4-N-carbonyl-4-(methylamino)-5-O-(trifluoromethylsulfonyl)cyclohexane-1,2,3,5-tetrol (*rac*-**13f**): A solution of 2.0 g (10.8 mmol) of *rac*-**13a** and 3.96 g (14.1 mmol) of trifluormethanesulfonic anhydride in 20 ml of pyridine was stirred at −70°C (N_2) for 30 min. After addition of the anhydride a passing precipitate was formed, and the solution became red. Then 50 ml of cold (−10°C) 2 N H_2SO_4 was added and the solution extracted with 3 × 40 ml of CH_2Cl_2. The organic layer was dried ($MgSO_4$), concentrated in vacuo and the residue treated with CH_3OH (in which *rac*-**13f** is nearly insoluble): 2.8 g (81%) of *rac*-**13f**. The triflate is very labile and was used without further purification, m.p. 110°C. – IR (KBr): $\tilde{\nu}$ = 2925 cm^{-1}, 1780, 1470, 1458, 1432, 1405, 1400, 1338, 1301, 1242, 1228, 1212, 1145, 1040, 1015, 930, 901, 822, 793, 759, 750, 718, 662, 620, 605, 579, 562, 510, 469, 408. – ^1H NMR ($CDCl_3$): δ = 5.18 (ddd, 5-H), 5.00 (d, 3-H), 4.01 (dd, 4-H), 3.33 (m, 1-H), 3.26 (m, 2-H), 2.79 (NCH_3), 2.50 (m, 6α-, 6β-H); $J_{1,2}$ = 4.0, $J_{1,6\beta}$ = 2.0, $J_{2,3}$ ≈ 0, $J_{3,4}$ = 9.0, $J_{4,5}$ = $J_{5,6\alpha}$ = $J_{5,6\beta}$ = 3.8 Hz.

$C_9H_{10}F_3NO_6S$ (317.2) Calcd. C 34.08 H 3.18 N 4.42
Found C 33.79 H 3.17 N 4.57

DL-(1α,2β,3β,4α,6β)-6-Azido-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**14a**): A mixture of 1.00 g (5.4 mmol)

of *rac*-**13a**, 440 mg (6.75 mmol) of NaN_3, 1.09 g (6.75 mmol) of $ZnSO_4$, and 20 ml of CH_3OH was heated at reflux for 6 h (total conversion, TLC, $CHCl_3/CH_3OH$ 10:1). The mixture was filtered from the insoluble, the residue washed twice with 5 ml of CH_3OH and the organic layer concentrated in vacuo. The solid residue was purified by column chromatography (silica, 5/3 cm, $CHCl_3/CH_3OH$ 10:1). From ethyl acetate 1.17 g (95%) of colorless crystals were obtained, m.p. 92°C. – IR (KBr): $\tilde{\nu}$ = 3340 cm^{-1} (br.), 2950, 2100, 1725, 1445, 1400, 1330, 1310, 1270, 1140, 1105, 1090, 1060, 1035, 990, 910, 845, 765, 670. – ^1H NMR (CD_3OD): δ = 4.48 (t, 2-H), 4.19 (dt, 4-H), 3.79 (dd, 3-H), 3.72 (dt, 6-H), 3.56 (dd, 1-H), 2.83 (s, CH_3), 2.01 (ddt, 5α-H), 1.62 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{3,5\alpha} \leq 1$, $J_{4,5\alpha} = 5$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 13$, $J_{5\alpha,6} = 5$, $J_{5\beta,6} = 10$, $J_{6,1} = 10$ Hz.

$C_8H_{12}N_4O_4$ (228.2) Calcd. C 42.10 H 5.30 N 24.55
Found C 42.15 H 5.28 N 24.60

DL-(1α,2β,3β,4α,6β)-1,4-Di-O-acetyl-6-azido-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**14b**): *rac*-**13b** was acetylated under standard conditions. From chloroform/ether (5:1) colorless crystals, m.p. 109°C. – IR (KBr): $\tilde{\nu}$ = 2100, 1780, 1735, 1425, 1370, 1295, 1265, 1225, 1200, 1055, 1030, 1020, 970, 920, 910, 860, 770 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.32 (q, 4-H), 5.10 (dd, 1-H), 4.56 (t, 2-H), 3.73–3.68 (m, 3-, 6-H), 2.87 (s, NCH_3), 2.18 (s, CH_3), 2.17 (m, 5α-H), 2.14 (s, CH_3), 1.86 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3.5$, $J_{4,5\alpha} = J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14.5$, $J_{5\alpha,6} = 4$, $J_{5\beta,6} = 11$, $J_{6,1} = 10$ Hz.

$C_{12}H_{16}N_4O_6$ (312.3) Calcd. C 46.15 H 5.16
Found C 46.47 H 5.21

(1α,2β,3β,4α,6β)-6-Azido-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**14c**): A mixture of 1.00 g (5.0 mmol) of *rac*-**13c**, 0.65 g (10.0 mmol) of NaN_3, 1.2 g (10.0 mmol) of $MgSO_4$, and 30 ml of CH_3OH was heated at reflux for 4 h (only one product, TLC, $CHCl_3/CH_3OH$ 25:1). After filtering off the insoluble, the filtrate was concentrated in vacuo and the crystalline residue crystallized from ethyl acetate: 1.17 g (97%) of colorless crystals, m.p. 156°C. – IR (KBr): $\tilde{\nu}$ = 3390 cm^{-1}, 2990, 2470, 2100, 1430, 1405, 1385, 1360, 1260, 1200, 1115, 1080, 955, 885, 765, 665, 510, 495. – ^1H NMR ($CDCl_3$): δ = 4.47 (t, 2-H), 3.78 (ddd, 3-H), 3.74–3.62 (1,- 4-, 6-H), 3.40 (s, OCH_3), 2.84 (s, NCH_3), 2.15 (dt, 5α-H), 1.58 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} \approx 4$, $J_{4,5\alpha} = 4.5$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 15$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = 10$, $J_{3,5\alpha} = 1.5$, $J_{1,OH} = 3$ Hz.

$C_9H_{14}N_4O_4$ (242.2) Calcd. C 44.62 H 5.82 N 23.13
Found C 44.42 H 5.91 N 22.87

DL-(1α,2β,3β,4α,6β)-6-Azido-4-O-benzyl-3-O,4-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**14d**): A solution of 1.37 g (5.0 mmol) of *rac*-**13d**, 650 mg (10.0 mmol) of NaN_3, and 1.2 g (10.0 mmol) of $MgSO_4$ in methanol (30 ml) was heated at reflux for 6 h (total conversion, TLC, $CHCl_3/CH_3OH$ 20:1). The solution was filtered from $MgSO_4$, concentrated in vacuo and the residue purified by column chromatography (silica, 5/2 cm, $CHCl_3/CH_3OH$ 35:1); the eluate was concentrated in vacuo and the residue crystallized from $CHCl_3$ to give 1.52 g (96%) of colorless crystals, m.p. 134°C. – IR (KBr): $\tilde{\nu}$ = 3410 cm^{-1}, 3050, 2900, 2100, 1755, 1470, 1455, 1430, 1405, 1370, 1315, 1300, 1250, 1170, 960, 890, 815, 770, 750, 730, 705, 665, 640, 575, 560, 540, 510. – ^1H NMR ($CDCl_3/CD_3OD$ 1:1): δ = 7.30–7.42, 4.60, 4.57 (CH_2), 3.87 (t, 2-H), 3.79 (dd, 3-H), 3.72 (ddd, 6-H), 3.60 (dd, 1-H), 2.74 (s, CH_3), 2.11 (dt, 5α-H), 1.61 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7$, $J_{3,4} = 3$, $J_{4,5\alpha} = 5$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14$, $J_{5\alpha,6} = 4$, $J_{5\beta,6} = J_{6,1} = 10$, $J_{5\alpha,3} \leq 1$, $J_{CH_2} = 12.5$.

$C_{15}H_{18}N_4O_4$ (318.2) Calcd. C 56.57 H 5.70 N 17.61
Found C 56.37 H 3.66 N 17.42

DL-(1α,2β,3β,4α,6β)-6-Azido-2-O,3-N-carbonyl-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**14e**): A solution of 570 mg (2.5 mmol) of *rac*-**13e**, 325 mg (5.0 mmol) of NaN_3, and 870 mg (5.0 mmol) of $MgSO_4$ in methanol (15 ml) was heated at reflux for 6 h (total conversion, TLC, $CHCl_3/CH_3OH$ 20:1). The solution was filtered, concentrated in vacuo and the oily residue (only **14e**, ^1H NMR) purified by column chromatography (silica, 5/2 cm, $CHCl_3/CH_3OH$ 35:1). The eluate was concentrated in vacuo and the residue crystallized from $CHCl_3$ to give 545 mg (80%) of colorless crystals, m.p. 92°C. – IR (KBr): $\tilde{\nu}$ = 3370 cm^{-1}, 2960, 2900, 2100, 1755, 1480, 1425, 1405, 1400, 1360, 1250, 1155, 1095, 1025, 990, 970, 940, 915, 890, 815, 770, 670, 560, 515, 485. – ^1H NMR ($CDCl_3$): δ = 4.73, 4.67 (d, CH_2), 4.50 (t, 2-H), 4.08 (q, 4-H), 3.82–3.63 (m, 1-, 3-, 6-H), 3.42 (s, OCH_3), 2.80 (s, NCH_3), 2.14 (dt, 5α-H), 1.61 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = J_{4,5\alpha} = J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14.3$, $J_{5\alpha,6} = 4$, $J_{5\beta,6} = 10.5$, $J_{6,1} = 7.5$ Hz.

$C_{10}H_{16}N_4O_5$ (272.3) Calcd. C 44.12 H 5.92 N 20.58
Found C 44.51 H 6.10 N 20.19

DL-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-azido-2-O,3-N-carbonyl-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**14f**): The raw material obtained from 272 mg (1.0 mmol) of *rac*-**13e** and sodium azide (130 mg, 2.0 mmol) was acetylated; from $CHCl_3$/ether (1:2) 300 mg (96%) of colorless crystals were obtained, m.p. 177°C. – IR (KBr): $\tilde{\nu}$ = 2945 cm^{-1}, 2890, 2100, 1765, 1425, 1385, 1375, 1260, 1240, 1220, 1150, 1100, 1025, 965, 940, 915, 765. – ^1H NMR ($CDCl_3$): δ = 5.07 (dd, 1-H), 4.73, 4.67 (d, CH_2), 4.63 (t, 2-H), 4.13 (q, 4-H), 3.84–3.73 (m, 3-, 6-H), 3.41 (s, OCH_3), 2.83 (s, NCH_3), 2.20 (ddd, 5α-H), 2.15 (s, CH_3), 1.75 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 6.8$, $J_{4,5\alpha} = J_{4,5\beta} \approx 3$, $J_{5\alpha,5\beta} = 14.2$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = 10.5$, $J_{6,1} = 10.5$, $J_{CH_2} = 7$ Hz.

$C_{12}H_{18}N_4O_6$ (314.3) Calcd. C 45.86 H 5.77 N 17.83
Found C 45.65 H 5.99 N 17.63

(+)-(1R)- and (+)-(1S)-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-3-(methylamino)-6[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol (**16a**/**16a'**): A solution of 9.26 g (50.0 mmol) of *rac*-**13a** and 9.09 g (75.0 mmol, 9.6 ml) of (*R*)-1-phenylethylamine in 40 ml of absolute 1-propanol was heated at reflux for 5 h (N_2) (total conversion, two products, TLC, $CHCl_3/CH_3OH$ 10:1/1% triethylamine). The solution was concentrated and the excess of phenylethylamine recovered by distillation at 10^{-2} Torr/60°C. Crystallization of the crystalline residue (14.8 g, 97%) from ca. 25 ml of CH_3OH gave 6.1 g (42%) of **16a**. Two batches of 4.0 g of the mother liquor were separated by rapid chromatography (silica, 14/4 cm, ethylacetate/acetone 1:1/1% triethylamine) to give 6.95 g (47%, R_f = 0.35) of **16a'** and 1.10 g of **16a** (7%, totally 49%, R_f = 0.25).

16a: colorless needles, m.p. 209°C ($CHCl_3$/ether 1:1), $[\alpha]_D$ = +17.0 (*c* = 1, CH_3OH). – IR (KBr): $\tilde{\nu}$ = 3370 cm^{-1}, 2890, 1740, 1495, 1465, 1450, 1430, 1400, 1285, 1355, 1330, 1320, 1295, 1230, 1210, 1185, 1115, 1095, 1070, 1030, 1000, 930, 895, 870, 765, 705, 660, 520. – ^1H NMR (CD_3OD): δ = 7.4–7.2 (m, 5H), 4.30 (t, 2-H), 4.07 (ddd, 4-H), 3.89 (q, 1'-H), 3.61 (dd, 3-H), 3.52 (dd, 1-H), 2.87 (s, NCH_3), 2.56 (ddd, 6-H), 1.87 (m, 5α-H), 1.59 (ddd, 5β-H), 1.40 (d, 2'-H); $J_{1,2} = J_{2,3} = 8$, $J_{3,4} = 4.5$, $J_{4,5\alpha} = 5.5$, $J_{4,5\beta} = 3.5$, $J_{5\alpha,5\beta} = 14$, $J_{5\alpha,6} = 5$, $J_{5\beta,6} = 9.5$, $J_{6,1} = 10.5$, $J_{3,5\alpha} \leq 1$, $J_{1',2'} = 4.5$ Hz. – ^{13}C NMR (CD_3OD): δ = 160.9 (CO), 145.6 (C_s), 129.7 (C_m), 128.1 (C_p), 127.7 (C_o), 79.9 (C-2), 74.6 (C-1), 66.3 (C-4), 65.2 (C-3), 55.3 (C-1'), 51.1 (C-6), 33.0 (C-5), 30.6 (NCH_3), 24.7 (C-2').

16a': colorless crystals, m.p. 190–191°C ($CHCl_3$/ether 1:1). $[\alpha]_D$ = +4.0 (*c* = 1, CH_3OH). – IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1}, 3280, 3060, 2980, 2920, 1765, 1470, 1450, 1440, 1425, 1390, 1365, 1340, 1315, 1285, 1260, 1245, 1220, 1190, 1095, 1065, 1030, 985, 940, 920,

860, 760, 705, 660, 550, 510. – ^{1}H NMR ($CDCl_3$): δ = 7.4–7.3 (m, 5H), 4.46 (t, 2-H), 4.04 (m, 4-H), 3.98 (q, 1′-H), 3.69 (dd, 3-H), 3.51 (dd, 1-H), 3.05 (s, NCH_3), 2.97 (ddd, 6-H), 1.77 (dt, 5α-H), 1.53 (d, 2′-H), 1.31 (m, 5β-H); $J_{1,2} = J_{2,3} = 8$, $J_{3,4} = 4$, $J_{4,5\alpha} = 5.5$, $J_{4,5\beta} = 3.5$, $J_{5\alpha,5\beta} = 14$, $J_{5\alpha,6} = 5$, $J_{5\beta,6} = J_{6,1} = 9.5$, $J_{3,5\alpha} \leq 1$, $J_{1',2'} = 4.5$ Hz. – ^{13}C NMR ($CDCl_3$): δ = 160.9 (CO), 147.2 (C_s), 129.5 (C_m), 128.0 (C_p), 127.7 (C_o), 80.1 (C-2), 75.1 (C-1), 66.1 (C-4), 64.2 (C-3), 57.5 (C-1′), 53.1 (C-6), 34.2 (C-5), 30.4 (NCH_3), 23.8 (C-2′).

$C_{16}H_{22}N_2O_4$ (306.4)	Calcd.	C 62.73	H 7.23 N 9.14
16a :	Found	C 62.42	H 7.19 N 8.94
16a′:	Found	C 62.49	H 7.36 N 9.06

(+)-(1R)- and (+)-(1S)-(1α,2β,3β,4α,6β)-1,4-Di-O-acetyl-2-O,3-N-carbonyl-3-(methylamino)-6-[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol (**16b**/**16b′**): The crude material obtained from 926 mg (5.0 mmol) of *rac*-**13a**, 910 mg (7.5 mmol) of (R)-(1-)-phenylethylamine, and 5 ml of 1-propanol (1.91 g, 98%) was acetylated under standard conditions with 5 ml of acetic anhydride/5 ml pyridine (two products, TLC, $CHCl_3/CH_3OH$ 10:1). The acetates were separated by column chromatography (silica, 10/3 cm, $CHCl_3/CH_3OH$ 10:1/1% triethylamine) to give 920 mg (47%, R_f = 0.37) of **16b′** and 940 mg (48%, R_f = 0.29) of **16b**. – **16b**: Colorless crystals, m.p. 126°C (chloroform/ether 5:1), $[\alpha]_D$ = +11 (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 2970 cm^{-1}, 1760, 1735, 1475, 1440, 1390, 1370, 1320, 1310, 1270, 1235, 1115, 1020, 960, 910, 885, 720, 700, 600, 520. – ^{1}H NMR ($CDCl_3$): δ = 7.4–7.2 (m, 5-H), 5.20 (dt, 4-H), 4.94 (dd, 1-H), 4.43 (t, 2-H), 3.86 (q, 1′-H), 3.67 (dd, 3-H), 2.85 (s, NCH_3), 2.65 (dt, 6-H), 2.16 (m, 5α-H), 2.14, 1.92 (s, CH_3), 1.60 (ddd, 5β-H), 1.39 (br, NH), 1.29 (d, 1′, 2′-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{4,5\alpha} = 6$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 13.5$, $J_{5\alpha,6} = 3.5$, $J_{5\beta,6} = J_{6,1} = 10$, $J_{1',2'} = 7$ Hz. – **16b′**: Colorless crystals, m.p. 115°C (chloroform/ether 5:1), $[\alpha]_D$ = +2 (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1}, 2960, 1750, 1430, 1370, 1305, 1235, 1120, 1030, 1010, 960, 920, 880, 770, 700, 525. – ^{1}H NMR ($CDCl_3$): δ = 7.3–7.1 (m, 5H), 5.14 (dt, 4-H), 5.06 (dd, 1-H), 4.52 (t, 2-H), 3.87 (q, 1′-H), 3.66 (dd, 3-H), 2.84 (s, NCH_3), 2.77 (dt, 6-H), 2.18, 1.91 (s, CH_3), 1.84 (m, 5α-H), 1.71 (br, NH), 1.59 (ddd, 5β-H), 1.26 (d, 2′-H); $J_{1,2} = J_{2,3} = 7$, $J_{3,4} = 3$, $J_{4,5\alpha} = 5$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 15$, $J_{5\alpha,6} \approx 4$, $J_{5\beta,6} = J_{6,1} = 9.8$, $J_{5\alpha,3} \leq 1$, $J_{1',2'} = 7$ Hz.

$C_{20}H_{26}N_2O_6$ (390.4)	Calcd.	C 61.52	H 6.71 N 7.17
16b :	Found	C 61.11	H 6.77 N 7.03
16b′:	Found	C 61.09	H 6.75 N 7.10

(+)-(1R)- and (+)-(1S)-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-4-O-methyl-3-(methylamino)-6-[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol (**16c**/**16c′**): Analogously to **13a** a solution of 10.0 g (50.0 mmol) of *rac*-**13c** and 9.09 g (75.0 mmol) of (*R*)- 1-phenylethylamine in 50 ml of abs. 1-propanol was heated at reflux (N_2) for 12 h (two products, TLC, $CHCl_3/CH_3OH$ 10:1/1% triethylamine). After concentration in vacuo excess of phenylethylamine was distilled off (10^{-2} Torr, bath 60°C) and the remaining light yellow oil crystallized from ethyl acetate/cyclohexane (1:1) (15.2 g, 95%). The mother liquor consisted only of **16c′**/**16c** (TLC); from ethyl acetate/ether (1:1) 6.5 g (41%) of **16c′** was obtained by crystallization. The mother liquor was separated by rapid chromatography (silica, $CHCl_3/CH_3OH$ 10:1/1% triethylamine) to give 7.20 g (45%, R_f = 0.33) of **16c′** and 960 mg (6%, totally 47%, R_f = 0.22) of **16c**. – **16c**: Colorless crystals, m.p. 125°C (ethyl acetate/cyclohexane 1:1), $[\alpha]_D$ = +4 (*c* = 1, CH_3OH). – IR (KBr): $\tilde{\nu}$ = 3600–3200 cm^{-1}, 2880, 1760, 1450, 1425, 1390, 1365, 1290, 1270, 1235, 1210, 1200, 1110, 1075, 1035, 1000, 939, 895, 870, 760, 700. – ^{1}H NMR ($CDCl_3$): δ = 4.29 (t, 2-H), 3.95 (q, 1′-H), 3.7–3.6 (m, 3-, 4-H), 3.55 (dd, 1-H), 3.20 (s, OCH_3), 2.80 (s, NCH_3), 2.55 (dt, 6-H), 2.12 (dt, 5α-H), 1.42 (ddd, 5β-H), 1.41 (d, 2′-H); $J_{1,2} = J_{2,3} =$ 7.5, $J_{4,5\alpha} = 4.5$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 13.5$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = J_{6,1} = 10$, $J_{1',2'} = 6$ Hz. – ^{13}C-NMR ($CDCl_3$): δ = 158.8 (CO), 144.3 (C_s), 128.6 (C_m), 127.2 (C_p), 126.5 (C_o), 78.1 (C-2), 74.6 (C-4)*, 73.8 (C-1)*, 61.1 (C-3), 56.2 (OCH_3), 54.5 (C-1′), 49.5 (C-6), 30.3 (NCH_3), 27.7 (C-5), 25.1 (C-2′). – **16c′**: Colorless crystals, m.p. 95°C (ethyl acetate/cyclohexane 1:1), $[\alpha]_D$ = +10 (*c* = 1, CH_3OH). – IR (KBr): $\tilde{\nu}$ = 3600–3300 cm^{-1}, 2970, 2920, 2840, 1775, 1740, 1480, 1430, 1405, 1345, 1335, 1260, 1200, 1130, 1100, 1080, 1045, 965, 760, 700. – ^{1}H NMR ($CDCl_3$): δ = 4.41 (t, 2-H), 3.89 (q, 1′-H), 3.66 (dd, 3-H), 3.56–3.45 (m, 1, 4-H), 3.06 (s, OCH_3), 2.79 (dt, 6-H), 2.76 (s, NCH_3), 1.68 (dt, 5α-H), 1.38 (d, 2′-H), 1.24 (ddd, 5β-H); $J_{1,2} = J_{2,3} =$ 7.5, $J_{3,4} = 3.5$, $J_{4,5\alpha} = 4.5$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = J_{6,1} = 10.5$, $J_{1',2'} = 6$ Hz. – ^{13}C NMR ($CDCl_3$): δ = 158.7 (CO), 146.4 (C_s), 128.5 (C_m), 127.1 (C_p), 126.6 (C_o), 78.7 (C-2), 74.6 (C-4)*, 74.4 (C-1)*, 61.0 (C-3), 57.5 (C-1′), 56.3 (OCH_3), 52.5 (C-6), 30.3 (NCH_3), 29.1 (C-5), 24.4 (C-2′).

$C_{17}H_{24}N_2O_4$ (320.4)	Calcd.	C 63.73	H 7.55 N 8.74
16c :	Found	C 63.95	H 7.62 N 8.66
16c′:	Found	C 63.69	H 7.87 N 8.43

(−)-(1R)-(1α,2β,3β,4α,6β)-1-O-Acetyl-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-6-[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol(**16d**)*and (−)-(1R)-(1α,2β,3β,4α,6β)-6-N,1-O-Diacetyl-6-O,3-N-carbonyl-6-[(R)-(1-phenylethyl)amino]-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol:* 320 mg (1.0 mmol) of **16c** was acetylated under standard conditions. The solution containing two products (TLC, $CHCl_3/CH_3OH$ 10:1) was concentrated in vacuo and separated by column chromatography (silica, 8/2 cm, $CHCl_3/CH_3OH$ 25:1) to give 65 mg (18%, R_f = 0.27) of **16d** and 275 mg (68%, R_f = 0.41) of the 6-*N*-acetyl derivative. – **16d** was identified only by ^{1}H NMR ($CDCl_3$): δ = 7.4–7.2 (m, 5H), 4.94 (dd, 1-H), 4.38 (t, 2-H), 3.84 (q, 1′-H), 3.7–3.6 (m, 3-, 4-H), 3.25 (s, OCH_3), 2.84 (s, NCH_3), 2.70 (ddd, 6-H), 2.10 (s, CH_3), 2.00 (m, 5α-H), 1.59 (dd, 5β-H), 1.52 (br., NH), 1.31 (s, CH_3); $J_{1,2} = J_{2,3} = 7.5$, $J_{4,5\alpha} \approx 3$, $J_{4,5\beta} = 2.2$, $J_{5\alpha,5\beta} = 13.8$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = J_{6,1} = 8.2$, $J_{1',2'} = 6.8$ Hz. – *O,N*-Diacetyl derivative: colorless crystals, m.p. 154°C ($CHCl_3$/ether 1:1), $[\alpha]_D$ = −35.5 (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 2990 cm^{-1}, 2970, 2940, 2880, 1760, 1640, 1495, 1450, 1425, 1385, 1335, 1310, 1285, 1225, 1170, 1115, 1100, 1085, 1030, 1010, 985, 970, 905, 885, 800, 775, 745, 710, 660, 630, 505. – ^{1}H NMR ($CDCl_3$): δ = 7.5–7.2 (m, 5H), 6.00 (br. t, 1-H), 5.08 (q, 1′-H), 4.36 (t, 2-H), 3.79 (m, 4-H), 3.52 (dd, 3-H), 3.0 (br. m, 6-H) 2.86 (s, OCH_3), 2.80 (s, NCH_3), 2.28 (s, CH_3), 2.12 (s, CH_3), 1.52 (d, 2′-H), 1.10 (m, 5β-H); $J_{1,2} = J_{2,3} = 8.7$, $J_{3,4} = 5$, $J_{6,1} = 9.6$ Hz.

$C_{21}H_{28}N_2O_6$ (404.5)	Calcd.	C 62.35	H 6.98 N 6.93
	Found	C 62.21	H 6.77 N 7.00

(+)-(1R)- and (+)-(1S)-(1α,2β,3β,4α,6β)-4-O-Benzyl-2-O,3-N-carbonyl-3-(methylamino)-6-[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol (**16e** and **16e′**): A solution of 2.35 g (9.0 mmol) of *rac*-**13d** and 1.41 g (12.0 mmol) of (*R*)-(1)-phenylethylamine in 10 ml of 1-propanol was heated at reflux for 12 h (N_2). The solution was concentrated in vacuo to give 3.50 g (98%) of a light yellow oil. This was dissolved in little $CHCl_3$/ether (1:5), and the solution was shortly warmed to give 3.42 g (96%) of colorless crystals (two components, TLC, $CHCl_3/CH_3OH$ 25:1). By crystallization from $CHCl_3$/ether (1:1) 1.46 g (41%) of **16e** (R_f = 0.33) was obtained. The mother liquor was separated by rapid chromatography (silica, $CHCl_3/CH_3OH$ 25:1/1% triethylamine) go give 1.57 (44%) of **16e′** (R_f = 0.45) and 180 mg (5%, totally 46%) of **16e**. – **16e**: Colorless crystals, m.p. 119°C ($CHCl_3$/ether 1:1), $[\alpha]_D$ = +16 (*c* = 1, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 4.33 (t, 2-H), 3.85 (m, 4-H), 3.67 (dd, 3-H), 3.58 (dd, 1-H), 3.14 (s, OCH_3), 2.76 (s, NCH_3), 2.67 (dt, 6-H), 2.18 (m, 5α-H), 1.46 (5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3.5$, $J_{4,5\alpha} =$

4.5, $J_{4,5\beta}$ = 3.5, $J_{5\alpha,5\beta}$ = 13.5, $J_{5\alpha,6}$ = 4.5, $J_{5\beta,6}$ = 10.0, $J_{6,1}$ = 10.5 Hz. — **16e'**: Colorless crystals, m.p. 85°C ($CHCl_3$/ether 1:2), $[\alpha]_D$ = +8 (*c* = 1, $CHCl_3$). — ^1H NMR ($CDCl_3$): δ = 4.44 (t, 2-H), 3.7–3.6 (m, 3-, 4-H), 3.49 (dd, 1-H), 3.05 (s, OCH_3), 2.88 (dt, 6-H), 2.69 (s, NCH_3), 1.74 (m, 5α-H), 1.22 (m, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.5, $J_{4,5\alpha}$ = 4.0, $J_{4,5\beta}$ = 3.0, $J_{5\alpha,5\beta}$ = 14, $J_{5\alpha,6}$ = 4.0, $J_{5\beta,6}$ = 10.5, $J_{6,1}$ = 10.5 Hz.

$C_{15}H_{27}NO_4$ Calcd. C 67.26 H 8.46 N 4.36
16e: Found C 67.18 H 8.23 N 4.30
16e': Found C 67.35 H 8.39 N 4.23

(+)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-4-O-(methoxymethyl)-3-(methylamino)-6-[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol (**16f** and **16f'**): A solution of 6.88 g (30.0 mmol) of *rac*-**13e** and 5.45 g (45 mmol) of (*R*)-(1)-phenylethylamine in 40 ml of abs. 1-propanol was heated at reflux (N_2) for 7 h (two products, TLC, $CHCl_3$/CH_3OH 10:1/1% triethylamine). The solution was concentrated in vacuo and the excess of phenylethylamine recovered by distillation (10^{-2} Torr, 60°C bath). The residue (10.5 g, 100%, light yellow oil) crystallized from ethyl acetate (≈ 25 ml) to give 3.78 g (36%) of **16f**. The mother liquor was separated by rapid chromatography (silica, 14/4 cm, $CHCl_3$/CH_3OH 50:1/1% triethylamine) to give 4.73 g (45%, R_f = 0.37) of **16f'** and 1.15 g (11%, totally 47%, R_f = 0.32) of **16f**; 800 mg (7%) mixture. — **16f**: Colorless crystals, m.p. 132°C, $[\alpha]_D$ = +30 (*c* = 1, $CHCl_3$). — IR (KBr): $\tilde{\nu}$ = 3300 cm^{-1}, 3460–3200, 2920, 2880, 1770, 1450, 1420, 1395, 1360, 1285, 1265, 1210, 1140, 1110, 1100, 1070, 1050, 1035, 1025, 910, 895, 870, 760, 700. — ^1H NMR ($CDCl_3$): δ = 7.4–7.2 (m, 5H), 4.54, 4.48 (d, CH_2), 4.33 (t, 2-H), 4.02 (ddd, 4-H), 3.96 (q, 1'-H), 3.64 (dd, 3-H), 3.52 (dd, 1-H), 3.28 (s, OCH_3), 2.80 (s, NCH_3), 2.60 (dt, 6-H), 2.15 (dt, 5α-H), 1.61 (dt, 5β-H), 1.38 (d, 2'-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 3, $J_{4,5\alpha}$ = 4, $J_{4,5\beta}$ = 4.5, $J_{5\alpha,5\beta}$ = 13.5, $J_{5\alpha,6}$ = 4.5, $J_{5\beta,6}$ = $J_{6,1}$ = 10.5, $J_{1',2'}$ = 6.8, J_{CH_2} = 6.8 Hz. — **16f'**: Colorless crystals, m.p. 224°C, $[\alpha]_D$ = +48.4 (*c* = 1, $CHCl_3$). — IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1}, 3250, 2950, 2930, 2850, 2820, 1760, 1755, 1590, 1580, 1450, 1420, 1385, 1360, 1280, 1255, 1235, 1210, 1155, 1135, 1100, 1065, 1025, 980, 915, 760, 700. — ^1H NMR ($CDCl_3$): δ = 7.6–7.4 (m, 5H), 4.44, 4.39 (d, CH_2), 4.44 (t, 2-H), 4.08 (ddd, 4-H), 3.83 (dd, 1-H), 3.79 (dd, 3-H), 3.17 (s, OCH_3), 2.80 (s, NCH_3), 2.01 (dt, 5α-H), 1.74 (d, 2'-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 2.3, $J_{4,5\alpha}$ = 3.8, $J_{4,5\beta}$ = 3, $J_{5\alpha,5\beta}$ = 14.5, $J_{5\alpha,6}$ = 3.8, $J_{5\beta,6}$ = 12, $J_{6,1}$ = 11.3, $J_{1',2'}$ = 6.8, J_{CH_2} = 6.8 Hz.

$C_{18}H_{26}N_2O_6$ (350.4) Calcd. C 61.65 H 7.48 N 8.00
16f: Found C 61.28 H 7.57 N 7.81
16f': Found C 61.36 H 7.25 N 7.85

(−)-(1R)- and (−)-(1S)-(1α,2β,3β,4α,6β)-1-O-Acetyl-2-O,3-N-carbonyl-4-O-(methoxymethyl)-3-(methylamino)-6-[(R)-(1-phenylethyl)amino]-1,2,4-cyclohexanetriol (**16g** and **16g'**): 350 mg (1.0 mmol) of **16f** and **16f'** was acetylated by standard conditions. **16g**: from $CHCl_3$/ether (1:1), 380 mg (97%) of colorless crystals, m.p. 116°C, $[\alpha]_D$ = −33.4 (*c* = 1, $CHCl_3$). — IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1}, 3320, 2960, 2890, 1770, 1750, 1730, 1440, 1430, 1395, 1365, 1275, 1245, 1240, 1145, 1090, 1035–1025, 910, 770, 700. — ^1H NMR ($CDCl_3$): δ = 7.3–7.1 (m, 5H), 4.93 (dd, 1-H), 4.59, 4.53 (d, CH_2), 4.42 (t, 2-H), 4.04 (ddd, 4-H), 3.86 (q, 1'-H), 3.69 (dd, 3-H), 3.31 (s, OCH_3), 2.85 (s, NCH_3), 2.75 (dt, 6-H), 2.13 (s, CH_3), 2.07 (ddd, 5α-H), 1.55 (ddd, 5β-H), 1.29 (d, 2'-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.8, $J_{4,5\alpha}$ = 5.2, $J_{4,5\beta}$ = 3, $J_{5\alpha,5\beta}$ = 14.2, $J_{5\alpha,6}$ = 3.8, $J_{5\beta,6}$ = $J_{6,1}$ = 9, J_{CH_2} = 7.5, $J_{1',2'}$ = 6.5 Hz. — **16g'**: 360 mg (96%) of colorless oil, $[\alpha]_D$ = −44 (*c* = 1, $CHCl_3$). — ^1H NMR ($CDCl_3$): δ = 7.4–7.2 (m, 5H), 5.00 (dd, 1-H), 4.68 (t, 2-H), 4.43, 4.39 (d, CH_2), 3.94 (m, 4-H), 3.84 (q, 1'-H), 3.65 (dd, 3-H), 3.21 (s, OCH_3), 2.85 (ddd, 6-H), 2.81 (s, NCH_3), 2.14 (s, CH_3), 1.80 (dt, 5α-H), 1.50 (br, NH), 1.48 (ddd, 5β-H), 1.25 (d, 2'-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.7, $J_{4,5\alpha}$ = 4.5, $J_{4,5\beta}$ ≈ 3, $J_{5\alpha,5\beta}$ = 15, $J_{5\alpha,6}$ = 4.5, $J_{5\beta,6}$ = $J_{6,1}$ = 9.8, J_{CH_2} = 6, $J_{1',2'}$ = 6.8 Hz.

$C_{20}H_{28}N_2O_6$ (392.5) Calcd. C 61.21 H 7.19 N 7.14
16g: Found C 61.27 H 7.25 N 6.93

(−)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-6-Ammonio-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol Chloride (**17a** and *ent*-**17a**): A solution of 6.13 g (20.0 mmol) of **16a** (**16a'**) in 20 ml of CH_3OH p.a., containing ca. 1.0 ml of conc. HCl, was hydrogenated over 500 mg Pd/C (1 at H_2, room temp., 8 h, total conversion, TLC, $CHCl_3$/CH_3OH 10:1). The catalyst was centrifugated off and the solution concentrated in vacuo. The colorless oily residue (5.0 g, 98%) was uniform (^1H NMR) and crystallized from $CHCl_3$/ether (1:1) to give **17a** (*ent*-**17a**) as its hydrochlorides with one mol of crystal water, m.p. 201–202°C, $[\alpha]_D$ = −37 (*ent*-**17a**: $[\alpha]_D$ = +40) (*c* = 1, CH_3OH). — ^1H NMR ($CDCl_3$): δ = 4.58 (t, 2-H), 4.35 (dt, 4-H), 3.90 (dd, 3-H), 3.71 (dd, 1-H), 3.47 (dt, 6-H), 2.85 (s, NCH_3), 2.22 (dt, 5α-H), 1.88 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = $J_{4,5\beta}$ = 3, $J_{4,5\alpha}$ = 4.5, $J_{5\alpha,5\beta}$ = 14.5, $J_{5\alpha,6}$ = 4.5, $J_{5\beta,6}$ = $J_{6,1}$ = 11 Hz.

$C_8H_{15}ClN_2O_4 \cdot H_2O$ (256.7) Calcd. C 37.49 H 6.67 N 10.93
Found C 37.17 H 6.36 N 10.95

(+)-(1R) and (−)-(1S)-(1α,2β,3β,4α,6β)-1,4-Di-O-acetyl-6-(acetylamino)-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (**17b** and *ent*-**17b**): 510 mg (2.0 mmol) of **17a** (*ent*-**17a**) was acetylated under standard conditions. From $CHCl_3$/ether (1:1) 640 mg (98%) of colorless crystals were obtained, m.p. 210°C, $[\alpha]_D$ = +111 (*ent*-**17b**: $[\alpha]_D$ = −104) (*c* = 1, $CHCl_3$). — IR (KBr): $\tilde{\nu}$ = 1755–1735 cm^{-1}, 1645, 1560, 1425, 1370, 1305, 1275, 1225, 1120, 1020, 910, 770. — ^1H NMR ($CDCl_3$/CD_3OD 1:1): δ = 6.00 (d, NH), 5.31 (q, 4-H), 4.94 (dd, 1-H), 4.66 (t, 2-H), 4.31 (dt, 6-H), 3.84 (ddd, 3-H), 2.89 (s, NCH_3), 2.15 (s, $COCH_3$), 2.11 (s, $COCH_3$), 2.09 (ddt, 5α-H), 1.92 (s, $COCH_3$), 1.83 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = $J_{4,5\alpha}$ = $J_{4,5\beta}$ = 3, $J_{5\alpha,5\beta}$ = 14, $J_{5\alpha,6}$ = 3, $J_{5\beta,6}$ = 12, $J_{6,1}$ = 10, $J_{6,NH}$ = 9, $J_{3,5\alpha}$ ≤ 1 Hz.

$C_{14}H_{20}N_2O_7$ (328.3) Calcd. C 50.21 H 6.16 N 8.53
Found C 50.42 H 6.13 N 8.32

(+)-(1R) and (−)-(1S)-(1α,2β,3β,4α,6β)-6-Ammonio-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol Chloride (**17c** and *ent*-**17c**): A solution of 6.41 g (20.0 mmol) of **16c** (**16c'**) in 20 ml of CH_3OH p.a. containing ca. 0.5 ml of conc. H_2SO_4 was hydrogenated over 500 mg of Pd/C (1 at H_2, 6 h, room temp., total conversion, TLC, $CHCl_3$/CH_3OH 10:1). The catalyst was removed and the solution concentrated in vacuo. The remaining foam was crystallized from methanol/2 N HCl to give 4.85 g (96%) of colorless crystals, dec. above ca. 240°C, $[\alpha]_D$ = +62.5 (*ent*-**17c**: $[\alpha]_D$ = −62.4) (*c* = 1, CH_3OH). — IR (KBr): $\tilde{\nu}$ = 3310 cm^{-1}, 2900–2800, 1620, 1595, 1515, 1425, 1395, 1300, 1280, 1240, 1195, 1160, 1085, 1070, 1000, 875, 810, 765, 655. — ^1H NMR (CD_3OD/D_2O): δ = 4.43 (t, 2-H), 3.96–3.86 (m, 3-, 4-H), 3.57 (dd, 1-H), 3.44 (s, OCH_3), 3.23 (dt, 6-H), 2.81 (s, NCH_3), 2.29 (ddt, 5α-H), 1.73 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{4,5\alpha}$ = 4, $J_{4,5\beta}$ = 3, $J_{5\alpha,5\beta}$ = 14, $J_{5\alpha,6}$ = 4, $J_{5\beta,6}$ = $J_{6,1}$ = 11.5, $J_{3,5\alpha}$ ≤ 1.5 Hz. — *Free base*: ^1H-NMR (CD_3OD): δ = 4.33 (t, 2-H), 3.85 (ddd, 3-H), 3.77 (br. q, 4-H), 3.40 (s, OCH_3), 3.30 (dd, 1-H), 2.84 (dt, 6-H), 2.80 (s, NCH_3), 2.09 (ddt, 5α-H), 1.48 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{4,5\alpha}$ ≈ $J_{4,5\beta}$ ≈ $J_{5\alpha,6}$ ≈ 4, $J_{5\alpha,5\beta}$ = 14, $J_{5\beta,6}$ = $J_{6,1}$ = 11.5, $J_{3,5\alpha}$ = 1 Hz.

$C_9H_{17}N_2O_4$ (252.7) Calcd. C 42.77 H 6.78 N 11.08
Found C 42.44 H 7.01 N 10.97

(−)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-(acetylamino)-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**17d** and *ent*-**17d**): 250 mg (1.0 mmol) of **17c** (*ent*-

17c) was acetylated under standard conditions. After concentration, purification by column chromatography, and crystallization from $CHCl_3$/ether (5:1) 285 mg (96%) of colorless crystals were obtained, m.p. 202–204°C; $[\alpha]_D = -82.4$ (*ent*-**17d**: $[\alpha]_D = +84.7$) ($c = 1$, $CHCl_3$). – IR (KBr): $\tilde{\nu} = 3270\ cm^{-1}$, 2870, 1755, 1730, 1640, 1535, 1425, 1380, 1370, 1355, 1290, 1230, 1020, 950, 910, 875, 765, 715, 600. – ^1H NMR ($CDCl_3$): $\delta = 6.03$ (d, NH), 4.91 (dd, 1-H), 4.60 (t, 2-H), 4.24 (ddt, 6-H), 3.79 (ddd, 3-H), 3.70 (m, 4-H), 3.43 (s, OCH_3), 2.83 (s, NCH_3), 2.39 (ddt, 5α-H), 2.11 (s, 2 CH_3), 1.92 (s, CH_3), 1.56 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{4,5\alpha} \approx J_{5\alpha,6} \approx 4$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 15$, $J_{5\beta,6} = J_{6,1} = 10.5$, $J_{6,NH} = 7.5$, $J_{3,5\alpha} \leq 1.5$ Hz.

$C_{13}H_{20}N_2O_6$ (300.3) Calcd. C 51.99 H 6.71 N 9.52
Found C 51.35 H 6.77 N 9.33

(–)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-6-Ammonio-2-O,3-N-carbonyl-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol Chloride (**17e** and *ent*-**17e**): A solution of 2.45 g (7.0 mmol) of **16f** (**16f'**) in 30 ml of CH_3OH p.a. containing 0.5 equiv. of conc. HCl (0.34 g, 3.5 mmol) was hydrogenated over 240 mg of Pd/C (1 at H_2, 18 h, room temp). Pd/C is centrifugated off and the solution concentrated in vacuo. The remaining colorless oil (1.65 g, 96%) was uniform (TLC, $CHCl_3/CH_3OH$ 10:1). $[\alpha]_D = -70.9$ (*ent*-**17e**: $[\alpha]_D = +75.6$) ($c = 1$, $CHCl_3$). – ^1H NMR (CD_3OD): $\delta = 4.61$, 4.59 (d, CH_2), 4.45 (t, 2-H), 4.21 (m, 4-H), 3.93 (ddd, 3-H), 3.52 (dd, 1-H), 3.40 (s, OCH_3), 3.22 (dt, 6-H), 2.81 (s, NCH_3), 2.20 (ddt, 5α-H), 1.75 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{3,5\alpha} \leq 1$, $J_{4,5\alpha} = 3.8$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14.3$, $J_{5\alpha,6} = 3.8$, $J_{5\beta,6} = 11.2$, $J_{6,1} = 10.5$, $J_{CH_2} = 6.5$ Hz.

$C_{16}H_{15}ClN_2O_5$ (314.3·HCl, analyzed as **17f**)

(+)-(1R) and (–)-(1S)-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-(acetylamino)-2-O,3-N-carbonyl-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol (**17f** and *ent*-**17f**): 250 mg (1.0 mmol) of **17e** (*ent*-**17e**) was acetylated under standard conditions. The product was crystallized from $CHCl_3$/ether (1:1); colorless crystals, m.p. 163–164°C, $[\alpha]_D = +80.7$ (*ent*-**17f**: $[\alpha]_C = -82.2$) ($c = 1$, $CHCl_3$). – IR (KBr): $\tilde{\nu} = 3320\ cm^{-1}$, 2950, 2905, 1745, 1675, 1545, 1425, 1375, 1295, 1245, 1230, 1150, 1100, 1085, 1030, 1010, 950, 910, 885, 775, 660, 600. – ^1H NMR ($CDCl_3$): $\delta = 5.82$ (d, NH), 4.90 (dd, 1-H), 4.76, 4.70 (d, CH_2), 4.65 (t, 2-H), 4.35 (ddd, 6-H), 4.08 (ddd, 4-H), 3.82 (dd, 3-H), 3.43 (s, OCH_3), 2.83 (s, NCH_3), 2.28 (ddt, 5α-H), 2.12 (s, $COCH_3$), 1.92 (s, $COCH_3$), 1.58 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 2.3$, $J_{3,5\alpha} \leq 1$, $J_{4,5\alpha} = 3.8$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14.3$, $J_{5\alpha,6} = 3.8$, $J_{5\beta,6} = 12$, $J_{6,1} = 11$, $J_{6,NH} = 8.3$, $J_{CH_2} = 6.5$ Hz.

$C_{14}H_{22}N_2O_7$ (330.4) Calcd. C 50.90 H 6.71 N 8.48
Found C 50.39 H 6.70 N 8.41

(+)-(1R) and (–)-(1S)-(1α,2β,3β,4α,6β)-6-Ammonio-3-(methylammonio)-1,2,4-cyclohexanetriol Sulfate (**18** and *ent*-**18**): A solution of 4.5 g (17.5 mmol) of **17a** (*ent*-**17a**) and 8.25 g (26.0 mmol) of barium hydroxide in 25 ml of CH_3OH/water (1:1) was heated at reflux for 5 h. The solution was acidified with sulfuric acid (pH 3–4), the microcrystalline barium sulfate centrifugated off, and the solution concentrated in vacuo. The remaining colorless oil (4.54 g, 99%) was uniform (^1H NMR) and crystallized from CH_3OH/H_2O (1:1), m.p. 205°C $[\alpha]_D = 23.5$ (*ent*-**18**: $[\alpha]_D = -27.0$) ($c = 1$, H_2O). – ^1H NMR (D_2O): $\delta = 4.17$ (br. t, 2-H), 4.08 (dt, 4-H), 3.89 (t, 1-H), 3.45 (q, 6-H), 3.14 (dd, 3-H), 2.58 (s, CH_3), 2.05–1.93 (m, 5α-, 5β-H); $J_{1,2} = J_{2,3} = 5$, $J_{3,4} = J_{4,5\alpha} = 9$, $J_{4,5\beta} \approx J_{5\alpha,6} \approx J_{5\beta,6} \approx J_{6,1} \approx 5$ Hz.

$C_6H_{18}N_2O_7S$ (262.3) Calcd. C 27.47 H 6.91 N 10.68
Found C 27.42 H 6.88 N 10.59

(+)-(1R) and (–)-(1S)-(1α,2β,3β,4α,6β)-6-Ammonio-4-O-methyl-3-(methylammonio)-1,2,4-cyclohexanetriol Sulfate (**19** and *ent*-**19**): A solution of 5.05 g (20.0 mmol) of **17c** (*ent*-**17c**) and 9.0 g (30.0 mmol) of $Ba(OH)_2 \cdot 8\ H_2O$ in 50 ml of water was heated at reflux for 6 h. The salts were filtered off, the solution was neutralized with conc. H_2SO_4, the $BaSO_4$ centrifugated off, and the solution concentrated in vacuo. The light yellow oil (5.70 g, 99%) was uniform (^1H NMR) and crystallized when purged with methanol. From CH_3OH/H_2O (1:1) 5.56 g (97%) of colorless crystals, dec. above 285°C; **19**: $[\alpha]_D = +55.2$ (free base **1**: $[\alpha]_D = -37.0$); *ent*-**19**: $[\alpha]_D = -57.2$ (free base *ent*-**1**: $[\alpha]_D = +37.0$) ($c = 1$, H_2O). – IR (KBr): $\tilde{\nu} = 3420-3200\ cm^{-1}$, 3000–2860, 1585, 1460, 1380, 1100, 610. – ^1H NMR (D_2O): $\delta = 4.35$ (br. t, 2-H), 4.10 (br. t, 1-H), 3.95 (br. dt, 4-H), 3.66 (q, 6-H), 3.44 (s, OCH_3), 3.41 (dd, 3-H), 2.78 (s, NCH_3), 2.42 (dt, 5β-H), 2.08 (ddd, 5α-H); $J_{1,2} = J_{2,3} = 3.8$, $J_{3,4} = 9$, $J_{4,5\alpha} = 10.5$, $J_{4,5\beta} = 4.5$, $J_{5\alpha,5\beta} = 15$, $J_{5\alpha,6} = J_{5\beta,6} = 4.5$, $J_{5\beta,1} \leq 1$, $J_{6,1} = 4$ Hz. – Free base **1**: ^1H NMR (D_2O): $\delta = 4.30$ (dd, 2-H), 4.15 (t, br. 4-H), 3.79 (dd, 3-H), 3.81 (s, OCH_3), 3.25 (ddd, 6-H), 2.80 (s, NCH_3), 2.49 (dt, br. 5α-H), 2.06 (ddd, 5β-H); $J_{1,2} = 9.0$, $J_{2,3} = 4.5$, $J_{3,4} = 3$, $J_{4,5\alpha} = 4$, $J_{4,5\beta} = 3.5$, $J_{5\alpha,5\beta} = 14.5$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = 11$, $J_{6,1} = 10$ Hz.

$C_8H_{20}N_2O_7S \cdot H_2O$ (306.3) Calcd. C 31.36 H 7.23 N 9.14
Found C 31.35 H 7.61 N 9.09

(+)-(1R) and (–)-(1S)-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-(acetylamino)-3-(acetylmethylamino)-4-O-methyl-1,2,4-cyclohexanetriol (**20a** and *ent*-**20a**): 615 mg (2.0 mmol) of **19** (*ent*-**19**) was neutralized with $Ba(OH)_2$ and separated from $BaSO_4$. After acetylation (room temp., 12 h) and crystallization from ether 685 mg (97%) of colorless crystals, m.p. 253°C, $[\alpha]_D = +49.9$ (*ent*-**20a**: $[\alpha]_D = -50.0$) ($c = 1$, $CHCl_3$). – IR (KBr): $\tilde{\nu} = 3390\ cm^{-1}$, 3310, 2940, 1750, 1670, 1635–1610, 1350, 1410, 1385, 1240–1220, 1160, 1095, 980, 935, 915, 900, 890, 810, 800, 685, 630, 600, 560, 535, 430. – ^1H NMR ($CDCl_3$, 400 MHz, 253 K): $\delta_{rotamer\text{-}1} = 6.19$ (br. NH), 5.44 (m, 2-H), 4.88 (t, 1-H), 4.80 (dd, 3-H), 4.40 (m, 6-H), 3.79 (m, 4-H), 3.36 (s, OCH_3), 2.97 (s, NCH_3), 2.38 (m, 5β-H), 2.18, 2.15, 2.11, 2.04 (s, 4-CH_3), 1.85 (m, 5α-H); $J_{1,2} \approx J_{6,1} \approx 3$, $J_{2,3} = 3$, $J_{3,4} = 10$ Hz. – $\delta_{rotamer\text{-}2} = 6.11$ (br. NH), 5.29 m (2-H), 4.96 (t, 1-H), 4.07 (dd, 3-H), 4.40 (m, 6-H), 3.76 (m, 4-H), 3.38 (s, OCH_3), 2.93 (s, NCH_3), 2.32 (m, 5β-H), 2.14, 2.00 (s, 4-CH_3), 1.87 (m, 5α-H). – ^1H NMR ($CDCl_3$, 400 MHz, 295 K): $\delta_{rotamer\text{-}1} = 6.10$ (br. NH), 5.43 (m, 2-H), 4.90 (t, 1-H), 4.78 (dd, 3-H), 4.40 (m, 6-H), 3.80 (m, 4-H), 3.38 (s, OCH_3), 2.97 (s, NCH_3), 2.34 (m, 5β-H), 2.14, 2.13, 2.00 (s, 4-CH_3), 1.98 (m, 5α-H). – $\delta_{rotamer\text{-}2} = 5.98$ (br. NH), 5.29 (m, 2-H), 4.99 (t, 1-H), 4.10 (dd, 3-H), 4.39 (m, 6-H), 3.72 (m, 4-H), 3.37 (s, OCH_3), 2.92 (s, NCH_3), 2.09 (s, 4-CH_3), ≈ 1.9 (5α-H).

$C_{16}H_{26}N_2O_7$ (358.4) Calcd. C 53.62 H 7.31 N 7.82
Found C 53.89 H 7.60 N 7.53

(+)-(1R) and (–)-(1S)-(1α,2β,3β,4α,6β)-6-(Acetylamino)-3-(acetylmethylamino)-4-O-methyl-1,2,4-cyclohexanetriol (**20b** and *ent*-**20b**): A solution of 540 mg (1.5 mmol) of **20a** (*ent*-**20a**) in 10 ml CH_3OH was saturated with NH_3, kept at room temp. for 10 h and concentrated in vacuo. The oily residue was separated from acetamide by column chromatography (silica 5/1 cm, $CHCl_3/CH_3OH$ 10:1): 400 mg (98%) of colorless oil, $[\alpha]_D = +79.3$ (*ent*-**20b**: $[\alpha]_D = -80.2$) ($c = 1$, $CHCl_3$). $[\alpha]_D = +90.1$ (*ent*-**20b**: $[\alpha]_D = -90.0$), ($c = 1$, H_2O). – IR (KBr): $\tilde{\nu} = 3400\ cm^{-1}$, 2930, 1655, 1620, 1525, 1380, 1310, 1190, 1150, 1100, 1050, 1020, 970, 945, 840, 750. – ^1H NMR (CD_3OD, 400 MHz): $\delta_{rotamer\text{-}1} = 4.61$ (m, 3-H), 4.19 (m, 6-H), 4.03 (m, 2-H), 4.00 (m, 4-H), 3.32 (br. s, CH_3), 3.15 (br. s, NCH_3), 2.26 (m, 5α-H), 2.13 (br. s, CH_3), 1.97 (br. s, CH_3), 1.81 (m, 5β-H). – $\delta_{rotamer\text{-}2} = 4.19$ (m, 6-H), 4.03 (m, 2-H), 4.00 (m, 4-H), 3.94 (m, 3-H), 3.35 (s, OCH_3), 3.15 (s, NCH_3), 2.22 (m, 5α-H), 2.09, 1.98 (br, CH_3), 1.78 (m, 5β-H).

(1α,2α,3β,4α,5α)-1,2;4,5-Dianhydro-3-O-[(R)-(1-phenylethyl)-carbamoyl]-1,2,3,4,5-cyclohexanepentol (**27a**) *and (1α,2α,3β,4α,5α)-1,2;4,5-Dianhydro-3-O-[(S)-(1-phenylethyl)carbamoyl]-1,2,3,4,5-cyclohexanepentol* (*ent*-**27a**): A solution of 300 mg (2.3 mmol) of **9a** and 383 mg (2.6 mmol) of (*R*)-1-phenylethyl isocyanate [(*S*)-1-phenylethyl isocyanate] in 5 ml of dioxane was heated at reflux for 10 h. The solution was concentrated in vacuo, the solid residue washed with little CH_3OH and dried in vacuo; 480 mg (76%) of **27a** [*ent*-**27a**] as hard foam. – IR (KBr): $\tilde{\nu}$ = 3350 cm^{-1}, 3060, 3020, 2995, 2080, 2025, 1690, 1530, 1490, 1465, 1445, 1425, 1370, 1360, 1310, 1290, 1255, 1245, 1215, 1150, 1120, 1090, 1065, 1110, 1000, 970, 920, 885, 795, 755, 695, 535. – ^{1}H NMR ($CDCl_3$): δ = 7.4–7.2 (m, 5H), 5.45 (s, 3-H), 5.17 (d, NH), 4.88 (m, 1′-H), 3.2–3.1 (m, 1-, 2-, 4-, 5-H), 2.74 (d, 6α-H), 2.29 (d, 6β-H), 1.53 (d, CH_3); $J_{6\alpha,6\beta}$ = 17.5, J_{1',CH_3} = $J_{1',NH}$ = 7.0 Hz.

$C_{15}H_{17}NO_4$ (275.0) Calcd. C 65.41 H 6.18 N 5.09
Found C 65.23 H 6.20 N 5.07

(1α,2α,3β,4α,5α)-1,2;4,5-Dianhydro-3-O-[(R)-(1-naphthylethyl)-carbamoyl]-1,2,3,4,5-cyclohexanepentol (**27b**): A solution of 200 mg (1.56 mmol) of **9a** and 385 mg (1.95 mmol) of (*R*)-1-naphthylethyl isocyanate in 5 ml of dioxane was heated at reflux for 8 h. Besides **27b** an urea derived from the isocyanate was formed. Excess of isocyanate was distilled off and the solution concentrated in vacuo. The two products are only slightly soluble in various solvents; neither by crystallization nor by chromatography (e.g. ethyl acetate and CH_3OH) an efficient separation was possible. Small amounts of pure **27b** were obtained as colorless crystals from ethyl acetate, m.p. 182°C. – IR (KBr): $\tilde{\nu}$ = 3600–3200 cm^{-1}, 3325, 3060, 3000, 2965, 2920, 1685, 1540, 1450, 1440, 1430, 1380, 1370, 1360, 1335, 1255, 1105, 1060, 1010, 995, 970, 915, 800, 775. – ^{1}H NMR ($CDCl_3$): δ = 8.13, 7.88, 7.81, 7.52 (m, 7H), 5.70 (m, 1′-H), 5.50 (s, 3-H), 5.15 (d, NH), 3.15–3.1 (m, 1-, 2-, 4-, 5-H), 2.74 (d, 6α-H), 2.26 (d, 6β-H), 1.72 (d, CH_3); $J_{6\alpha,6\beta}$ = 17.5, J_{1',CH_3} = 8.0, $J_{1',NH}$ = 7.0 Hz.

(1R) and (1S)-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-4-[(R)-(1-phenylethyl)amino]-1,2,3,5-cyclohexanetetrol (**28a** and **28a′**): To a solution of 200 mg (0.73 mmol) of **27a** in 5 ml of absolute acetonitrile a catalytic amount of 2-(*tert*-butylimino)-2-(diethylamino)hexahydro-1,3-dimethyl-1,3,2λ^5-diazaphosphorine (BEMP) was added. After total conversion (1 h, TLC ethyl acetate/CH_3OH 20:1, R_F-values: **27a** = 0.66, **28a**/**28a′** = 0.62) the solution was concentrated in vacuo and the raw material filtered through silica (ethyl acetate) to remove the base. The yield was quantitative and the ratio of diastereomeric carbamates **28a′** (non-natural series)/**28a** was 58:42. – **28a**: ^{1}H NMR ($CDCl_3$): δ = 7.43–7.29 (m, 5H), 5.07 (q, 1′-H), 4.92 (d, 3-H), 3.87 (dddd, 5-H), 3.70 (dd, 4-H), 3.44 (dd, 1-H), 3.38 (m, 2-H), 3.21 (d, OH), 2.34 (ddd, 6α-H), 2.15 (dd, 6β-H), 1.67 (d, CH_3); $J_{1,2}$ = 4.0, $J_{2,3}$ = 0.5, $J_{3,4}$ = 8.5, $J_{4,5}$ = 3.0, $J_{5,OH}$ = 11.0, $J_{5,6\alpha}$ = 3.0, $J_{5,6\beta}$ = 3.5, $J_{6\alpha,6\beta}$ = 16.0, $J_{6\alpha,1}$ = 3.0, J_{1',CH_3} = 7.5 Hz. – **28a′**: IR (KBr): $\tilde{\nu}$ = 3480 cm^{-1}, 3460, 3080, 3055, 3025, 3000, 2975, 2940, 2920, 1750, 1735, 1600, 1580, 1480, 1450, 1425, 1400, 1380, 1375, 1360, 1315, 1290, 1250, 1235, 1215, 1205, 1125, 1075, 1050, 1040, 1035, 1010, 980, 945, 905, 855, 785, 755, 695, 640. – ^{1}H-NMR ($CDCl_3$): δ = 7.43–7.29 (m, 5H), 5.17 (q, 1′-H), 4.98 (d, 3-H), 4.12 (dd, 4-H), 3.56 (dddd, 5-H), 3.38 (m, 2-H), 3.34 (dd, 1-H), 3.12 (d, OH), 1.91 (ddd, 6α-H), 1.72 (d, CH_3), 1.42 (dd, 6β-H); $J_{1,2}$ = 4.0, $J_{2,3}$ = 0.5, $J_{3,4}$ = 8.5, $J_{4,5}$ = 3.0, $J_{5,OH}$ = 11.0, $J_{5,6\alpha}$ = 3.0, $J_{5,6\beta}$ = 3.5, $J_{6\alpha,6\beta}$ = 16.0, $J_{6\alpha,1}$ = 3.0, J_{1',CH_3} = 7.5 Hz.

$C_{15}H_{17}NO_4$ (275.3) Calcd. C 65.44 H 6.22 N 5.09
Found C 65.16 H 6.24 N 5.04

ent-**28a**/*ent*-**28a′** were prepared analogously starting from *ent*-**27a**.

(1R) and (1S)-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-4-{(R)-[1-(1-naphthyl)ethyl]amino}-1,2,3,5-cyclohexanetetrol (**28b** and **28b′**): Cf. **28a**/**28a′**, ratio 40:60. – IR (KBr): $\tilde{\nu}$ = 3452 cm^{-1}, 2918, 1742, 1506, 1447, 1399, 1232, 1116, 1064, 851, 800, 777, 635. – MS (70 eV): *m/z* = 325 (M^+), 198, 155, 129. – **28b**: ^{1}H NMR ($CDCl_3$): δ = 8.23, 7.95–7.82, 7.62–7.35 (m, 7H), 5.85 (q, 1′-H), 4.73 (d, 3-H), 3.10 (dd, 4-H), 3.36 (dd, 2-H), 3.79 (m, 5-H), 3.46 (m, 1-H), 1.79 (d, CH_3), 2.34 (dddd, 6α-H), 2.29 (ddd, 6β-H); $J_{1,2}$ = 3.5, $J_{2,3}$ = 1.0, $J_{3,4}$ = 9.0, $J_{4,5}$ = 2.5, $J_{5,6\alpha}$ = 2.5, $J_{5,6\beta}$ = 3.5, $J_{6\alpha,1}$ = 2.5, $J_{6\beta,1}$ = 1.0 Hz. – ^{13}C NMR ($CDCl_3$): δ = 67.8 (C-3), 64.4 (C-5), 56.2 (C-4), 52.2 (C-1)*, 51.6 (C-2)*, 50.0 (C-1′), 19.9 (CH_3). – **28b′**: ^{1}H NMR ($CDCl_3$): δ = 8.23, 7.93–7.82, 7.62–7.35 (m, 7H), 6.02 (q, 1′-H), 4.94 (d, 3-H), 4.17 (dd, 4-H), 3.27 (d, 2-H), 3.10 (dd, 5-H), 3.01 (m, 1-H), 1.81 (d, CH_3), 1.38 (dddd, 6α-H), 0.55 (ddd, 6β-H); $J_{1,2}$ = 3.5, $J_{3,4}$ = 8.5, $J_{4,5}$ = 3.0, $J_{5,6\alpha}$ = 2.5, $J_{5,6\beta}$ = 3.5, $J_{6\alpha,1}$ = 2.5, $J_{6\beta,1}$ = 1.0 Hz. – ^{13}C NMR ($CDCl_3$): δ = 67.6 (C-3), 62.9 (C-5), 54.8 (C-4), 52.4 (C-1)*, 51.5 (C-2)*, 49.7 (C-1′), 14.9 (CH_3).

(D,L)-(1α,2α,3β,4β,5β)-1,2-Anhydro-3-O,4-N-carbonyl-5-fluoro-4-(methylamino)-1,2,3-cyclohexanetriol (*rac*-**29**) *and (D,L)-(1α,2α,-3β,4β)-1,2-Anhydro-3-O,4-N-carbonyl-4-(methylamino)-5-cyclohexene-1,2,3-triol* (*rac*-**30**):

a) To a solution of 230 mg (0.73 mmol) of $NBu_4F \cdot 3H_2O$, dried at 10^{-2} Torr, in 15 ml of CH_2Cl_2 a solution of 201 mg (0.73 mmol) of *rac*-**13f** in 10 ml of CH_2Cl_2 was added by syringe. The mixture was kept at room temp. for 12 h, extracted with water (3x, 0°C), dried ($MgSO_4$), and purified by column chromatography (silica, cyclohexane/ethyl acetate 1:3) to give 68 mg (39%) of *rac*-**29** and 61 mg (39%) of *rac*-**30**.

b) To a solution of 266 mg (1.65 mmol) of (diethylamino)sulfur trifluoride (DAST) in 5 ml of CH_2Cl_2 at –70°C 200 mg (1.1 mmol) of *rac*-**13a** was added and the solution slowly warmed to 0°C. After 2 h the solution was cooled to –70°C and 1 ml (29.4 mmol) of CH_3OH was added. The solution was kept at 20°C for 1 h, concentrated in vacuo and the oily residue separated by column chromatography (silica, cyclohexane/ethyl acetate 1:3). The first fraction contained a DAST derivative active in the UV, the second a small amount of impure *rac*-**30**, the third 20 mg (10%) of the desired *rac*-**29** and the following a mixture of polar products, presumably phenols. In spite of broad variation of reaction conditions (temperature, excess of DAST, Na_2HPO_4 buffer) and workup (CH_3OH at –20°C, water/ice, instantaneous chromatography, silica dried over P_2O_5) the yields of *rac*-**29**/*rac*-**30** could not be improved. – *rac*-**29**: colorless crystals, m.p. 109°C. – IR (KBr): $\tilde{\nu}$ = 3600–3300 cm^{-1}, 2960, 2920, 1750, 1515, 1480, 1460, 1435, 1405, 1370, 1330, 1315, 1265, 1245, 1230, 1185, 1130, 1095, 1030, 995, 945, 855, 820, 775, 755, 720, 690, 665, 600, 560, 530, 440. – ^{1}H NMR ($CDCl_3$): δ = 4.93 (dddd, 5-H), 4.90 (d, 3-H), 4.00 (m, 4-H), 3.41 (m, 1-H), 3.22 (m, 2-H), 2.95 (s, NCH_3), 2.52 (dddd, 6β-H), 2.27 (dddd, 6α-H); $J_{1,2}$ = 4.0, $J_{1,6\alpha}$ = 1.8, $J_{1,6\beta}$ = 3.0, $J_{2,3} \approx 0$, $J_{3,4}$ = 8.5, $J_{4,5}$ = 2.5, $J_{4,6\beta}$ = 1.0, $J_{5,6\alpha}$ = 10.0, $J_{5,6\beta}$ = 4.5, $J_{6\alpha,6\beta}$ = 14.5, $J_{4,F}$ = 11.0, $J_{5,F}$ = 46.5, $J_{6\alpha,F}$ = 9.0, $J_{6\beta,F}$ = 10.0, $J_{NCH_3,F}$ = 2.0 Hz.

$C_8H_{10}FNO_3$ (187.2) Calcd. C 51.34 H 5.39 N 7.48
Found C 50.98 H 5.73 N 7.16

rac-**30**: ^{1}H NMR ($CDCl_3$): δ = 6.26 (dd, 6-H), 5.86 (dd, 5-H), 5.08 (d, 3-H), 4.01 (dd, 4-H), 3.61 (m, 1-H), 3.39 (m, 2-H), 2.92 (s, NCH_3); $J_{3,4}$ = 8.5, $J_{5,6}$ = 10.5 Hz.

$C_8H_9NO_3$ (167.1) Calcd. C 57.48 H 5.43
Found C 57.38 H 5.55

(D,L)-(1α,2α,3β,4β,5β)-1,2-Anhydro-3-O,4-N-carbonyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (*rac*-**31**): A solution of 317 mg (1.0 mmol) of *rac*-**13f** in 10 ml of DMF was stirred at room temp. for 30 min. and then concentrated in vacuo (80°C). The residue (formate, ^{1}H NMR) was dissolved in CH_3OH and the solution

saturated with ammonia (gas) to cleave the formates to give *rac*-**31**. After concentrating in vacuo column chromatography (silica, chloroform/CH_3OH 10:1) and crystallization from ethyl acetate gave 180 mg (97%) of colorless crystals, m.p. 141°C. – IR (KBr): $\tilde{\nu}$ = 3400 cm^{-1}, 2920, 1740, 1720, 1640, 1485, 1440, 1405, 1350, 1285, 1255, 1225, 1165, 1120, 1080, 1030, 975, 940, 910, 880, 845, 815, 790, 760, 725, 680, 640, 570, 520, 455, 410. – ^{1}H NMR ($CDCl_3$): δ = 4.82 (d, 3-H), 4.15 (m, 5-H), 3.63 (dd, 4-H), 3.36 (m, 1-H), 3.20 (m, 2-H), 3.00 (s, NCH_3), 2.28 (ddd, 6α-H), 2.14 (dddd, 6β-H), 2.0–2.5 (br., OH); $J_{1,2}$ = 3.8, $J_{1,6\alpha}$ = 3.0, $J_{1,6\beta}$ = 2.3, $J_{2,3} \approx 0$, $J_{3,4}$ = 8.3, $J_{4,5}$ = 2.3, $J_{5,6\beta}$ = 9.8, $J_{6\alpha,6\beta}$ = 15.0 Hz.

(D,L)-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-5-fluoro-4-(methylamino)-1,2,3-cyclohexanetriol (*rac*-**32**): To a solution of 1.2 g (6.5 mmol) of *rac*-**31f** at –78°C 4.1 g (26.0 mmol) of DAST in 30 ml of CH_2Cl_2 was added. After total conversion (3 h, TLC) the solution was stirred for 30 min and then extracted twice with 10 ml of water (0°C). The organic layer was dried ($MgSO_4$) and concentrated in vacuo and the yellowish oil purified by column chromatography (silica, cyclohexan/ethyl acetate 1:3); the first fraction contained 30 mg of a UV active DAST derivative, the second 500 mg (85%, based on conversion) of *rac*-**32**, the third 200 mg of *rac*-**31f**. – *rac*-**32**: colorless crystals, m.p. 91°C. – IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1}, 3010, 2980, 2935, 2920, 1750, 1525, 1475, 1430, 1410, 1385, 1360, 1355, 1315, 1295, 1260, 1250, 1160, 1145, 1125, 1080, 1060, 1035, 975, 950, 910, 850, 815, 790, 760, 725, 665, 600, 550, 490. – ^{1}H NMR ($CDCl_3$): δ = 4.98 (dd, 3-H), 4.73 (m, 5-H), 3.78 (m, 4-H), 3.35 (m, 1-, 2-H), 2.93 (s, NCH_3), 2.36 (m, 6β-H), 2.30 (m, 6α-H); $J_{1,6\alpha}$ = 2.0, $J_{1,6\beta}$ = 3.0, $J_{2,3} \approx 1.0$, $J_{3,4}$ = 8.0, $J_{4,5}$ = 5.5, $J_{5,6\alpha}$ = 6.0, $J_{5,6\beta}$ = 5.0, $J_{6\alpha,6\beta}$ = 16.0, $J_{4,F}$ = 8.0, $J_{5,F}$ = 46.5, $J_{6\alpha,F}$ = 15.2, $J_{6\beta,F}$ = 25.8, $J_{NCH_3,F}$ = 1.0 Hz.

$C_8H_{10}FNO_3$ (187.2) Calcd. C 51.34 H 5.39 N 7.48
Found C 51.63 H 5.50 N 7.42

(–)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-6-[(Benzyloxycarbonyl)amino]-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**33a** and *ent*-**33a**): The solution of 3.80 g (15.0 mmol) of **17a** (*ent*-**17a**) in 80 ml methanol/H_2O (1:1) is neutralized by addition of Na_2CO_3. At 0°C 3.66 g (30.0 mmol) of Na_2CO_3 and 5.12 g (30.0 mmol) of benzyloxycarbonyl chloride are added. After total conversion (45 min at 0°C, 30 min at room temp.) the suspension was concentrated in vacuo and, after addition of 250 ml of CH_2Cl_2, washed twice with 50 ml of water. After usual workup and filtration over a short silica column 5.1 g (97%) of a colorless uniform oil (DC; ^{1}H NMR) was obtained, $[\alpha]_D$ = –45.6 (*ent*-**33a**: +47) (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 3660–3300 cm^{-1}, 2950, 2880, 1750, 1720–1700, 1530, 1450, 1425, 1395, 1290, 1100, 1030, 770, 730, 695. – ^{1}H NMR ($CDCl_3$, 400 MHz, 50°C): δ = 7.31–7.25 (m, 5H), 5.08 (d, CH_2), 4.41 (dd, 2-H), 3.77 (ddt, 6-H), 3.69 (dd, 3-H), 3.64 (dd, 1-H), 3.60 (ddd, 4-H), 3.36 (br. s, OCH_3), 2.77 (s, NCH_3), 2.23 (ddd, 5α-H), 1.57 (ddd, 5β-H); $J_{1,2}$ = 7, $J_{2,3}$ = 8, $J_{3,4}$ = 3.5, $J_{4,5\alpha}$ = 4, $J_{4,5\beta}$ = 2.5, $J_{5\alpha,5\beta}$ = 14, $J_{5\alpha,6}$ = 4.5, $J_{5\beta,6}$ = $J_{6,1}$ = 10, $J_{6,NH}$ = 7 Hz. – ^{13}C NMR ($CDCl_3$, 50°C): δ = 158.9 (CO), 156.8 (CO), 136.7 (C_i), 128.6 (C_o), 128.1 (C_p, C_m), 78.5 (C-2), 74.5 (C-1)*, 73.4 (C-4)*, 66.9 (CH_2), 61.1 (C-3), 56.6 (OCH_3), 48.2 (C-6), 30.2 (NCH_3), 29.0 (C-5).

(–)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-[(Benzyloxycarbonyl)amino]-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**33b** and *ent*-**33b**): 450 mg (1.0 mmol) of **33a**/*ent*-**33a** was acetylated under standard conditions. 376 mg (96%) of colorless crystals (from $CHCl_3$/ether 3:1), m.p. 132°C, $[\alpha]_D$ = –55.8 (*ent*-**33b**: + 54.5) (*c* = 1, $CHCl_3$). – IR (KBr): 3360 cm^{-1}, 2950, 1755, 1740, 1720, 1520, 1425, 1395, 1375, 1290, 1240, 1150, 1105, 1035, 1010, 770, 750, 695. – ^{1}H NMR ($CDCl_3$): δ = 7.41–7.29 (m, 5H), 5.24 (d, NH), 5.08 (d, CH_2), 4.91 (dd, 1-H), 4.56 (t, 2-H), 4.00 (m, 6-H), 3.78 (dd, 3-H), 3.70 (m, 4-H), 3.42 (s, OCH_3), 2.82 (s, NCH_3), 2.32 (dt, 5α-H), 2.01 (s, CH_3), 1.63 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4} \approx 3$, $J_{4,5\alpha} \approx J_{5\alpha,6} \approx 3.5$, $J_{4,5\beta} \approx 2.5$, $J_{5\alpha,5\beta}$ = 13.5, $J_{5\beta,6}$ = $J_{6,1}$ = 11 Hz.

$C_{19}H_{24}N_2O_7$ (392.4) Calcd. C 58.16 H 6.16 N 7.14
Found C 58.14 H 6.28 N 7.13

(–)-(1R) and (+)-(1S)-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-6-(2,3-dihydro-2-oxo-4,5-diphenyl-3-oxazolyl)-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**34a** and *ent*-**34a**): To a solution of 2.53 g (10.0 mmol) of **17a**/*ent*-**17a**) in 50 ml of DMF, neutralized with 1.06 g (10.0 mmol) of Na_2CO_3, 2.4 g (10.0 mmol) of benzoin carbonate (4,5-diphenyl-1,3-dioxol-2-one) was added and warmed to 60°C for 6 h (total conversion, DC). After concentration in vacuo the oily residue was dissolved in 300 ml of CH_2Cl_2, washed with 60 ml of 0.5 N HCl and water. After workup the yellowish foam was treated with 10 ml of CF_3CO_2H for 1.5 h at room temp. After workup 4.15 g (95%) of colorless crystals were obtained, m.p. 129°C, $[\alpha]_D$ = –2.4 (*ent*-**34a**: +2.8) (*c* = 1, $CHCl_3$). – IR (KBr): ν = 3600–3400 cm^{-1}, 2930, 2880, 1770–1730, 1600, 1500, 1435, 1425, 1350, 1255, 1200, 1150, 1095, 1025, 995, 985, 880, 770, 755, 705, 695, 660. – ^{1}H NMR ($CDCl_3$): δ = 7.58–7.42, 7.25–7.14 (m, 5H), 4.65 (dd, 1-H), 4.29 (t, 2-H), 3.87 (m, 4-H), 3.64 (dd, 3-H), 3.60 (dd, 6-H), 3.20 (s, OCH_3), 2.80 (s, NCH_3), 2.49 (ddd, 5β-H), 1.92 (dt, 5α-H); $J_{1,2}$ = $J_{2,3}$ = 8.2, $J_{3,4}$ = 4.5, $J_{4,5\alpha}$ = 6, $J_{4,5\beta}$ = 3, $J_{5\alpha,5\beta}$ = 14, $J_{5\beta,6}$ = 9, $J_{6,1}$ = 10.5 Hz.

$C_{24}H_{24}N_2O_6$ (436.5) Calcd. C 66.05 H 5.54 N 7.71
Found C 66.24 H 5.50 N 7.79

CAS Registry Numbers

9: 55990-89-1 / **11**: 94592-11-7 / **12**: 49778-04-3 / *rac*-**13a**: 94592-12-8 / *rac*-**13b**: 94592-13-9 / *rac*-**13c**: 87902-30-5 / *rac*-**13d**: 94592-14-0 / *rac*-**13e**: 121393-84-8 / *rac*-**13f**: 121393-85-9 / *rac*-**14a**: 121467-79-6 / *rac*-**14b**: 121393-86-0 / *rac*-**14c**: 87902-31-6 / *rac*-**14d**: 121467-80-9 / *rac*-**14e**: 121393-87-1 / *rac*-**14f**: 121393-88-2 / **16a**: 121467-81-0 / **16a'**: 121467-82-1 / **16b**: 121393-89-3 / **16b'**: 121393-90-6 / **16c**: 121521-08-2 / **16c'**: 121521-30-0 / **16d**: 121393-91-7 / **16d**-*O,N*-diacetate: 121393-92-8 / **16e**: 121521-09-3 / **16e'**: 121521-10-6 / **16f**: 121424-87-1 / **16f'**: 121393-93-9 / **16g**: 121393-94-0 / **16g'**: 121393-95-1 / **17a**· HCl: 121521-31-1 / *ent*-**17a**· HCl: 121521-11-7 / **17b**: 121521-12-8 / *ent*-**17b**: 121521-13-9 / **17c**· HCl: 121467-83-2 / **17c**: 121467-84-3 / *ent*-**17c**· HCl: 121569-37-7 / **17d**: 121521-14-0 / *ent*-**17d**: 121467-85-4 / **17e**· HCl: 121393-96-2 / *ent*-**17e**· HCl: 121393-97-3 / **17f**: 121393-98-4 / *ent*-**17f**: 121393-99-5 / **18**· sulfate: 94668-89-0 / *ent*-**18**· sulfate: 94729-19-8 / **19**· sulfate: 94729-20-1 / *ent*-**19**· sulfate: 94729-21-2 / **20a**: 121467-86-5 / *ent*-**20a**: 121467-87-6 / **20b**: 72504-04-2 / *ent*-**20b**: 121467-88-7 / **27a**: 121394-00-1 / *ent*-**27a**: 121467-89-8 / **27b**: 121394-01-2 / **28a**: 121394-02-3 / **28a'**: 121394-03-4 / **28b**: 121424-88-2 / **28b'**: 121470-47-1 / *rac*-**29**: 121394-04-5 / *rac*-**30**: 121394-05-6 / *rac*-**31**: 121467-90-1 / *rac*-**32**: 121467-91-2 / **33a**: 121467-92-3 / *ent*-**33a**: 121467-93-4 / **33b**: 121394-06-7 / *ent*-**33b**: 121467-94-5 / **34**: 121394-07-8 / *ent*-**34a**: 121424-89-3 / methyl isocyanate: 624-83-9 / (*R*)-1-phenylethylamine: 3886-69-9 / (*R*)-1-phenylethyl isocyanate: 33375-06-3 / (*S*)-1-phenylethyl isocyanate: 14649-03-7 / (*R*)-1-naphthylethyl isocyanate: 88442-63-1 / 4,5-diphenyl-1,3-dioxol-2-one: 21240-34-6

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