Aminoglycoside Antibiotics – Enantiomerically Pure Sporamine Building Blocks

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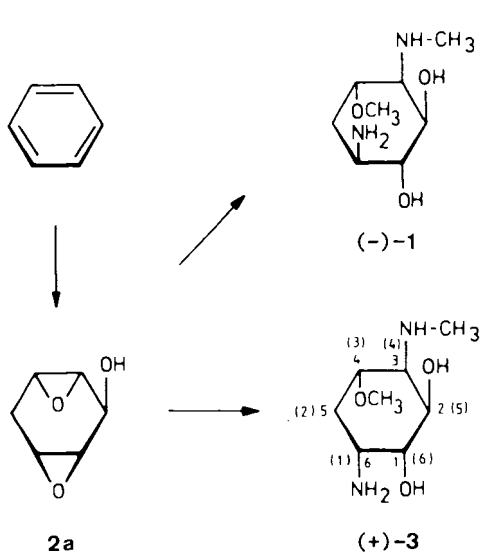
Starting from the 1,2:4,5-dianhydro-*epi*-deoxyinositol **2a** (available ultimately from benzene) an expedient total synthesis of *rac*-sporamine (*rac*-**3**) has been developed. Key steps are two regiospecific and quantitative epoxide openings, effected intramolecularly in the diepoxyurethane **2b** and intermolecularly by potassium iodide in the epoxyurethanes *rac*-**4**, and the equally uniform substitution in the iodide *rac*-**5d** by hexa(tetra)methylguanidinium azide. The separation of diastereomeric esters with (–)-camphanic acid (**19**/**19'**) opens the way to the pure enantiomers **3**/*ent*-**3**. The scheme allows chemical modifications and provides sporamine equivalents in which only the OH group to be ultimately glycosidated remains unprotected.

Aminoglycosid-Antibiotika – Enantiomerenreine Sporamin-Bausteine

Ausgehend vom 1,2:4,5-Dianhydro-*epi*-desoxyinosit **2a** (letztlich erhältlich aus Benzol) wurde eine leistungsfähige Synthese für *rac*-Sporamin (*rac*-**3**) entwickelt. Zentrale Schritte sind zwei regiospezifische, praktisch quantitative Epoxidöffnungen, intramolekular beim Diepoxyurethan **2b** und intermolekular mit Kaliumiodid bei den Epoxyurethanen *rac*-**4**, sowie eine gleichermaßen einheitliche Substitution in dem Iodid *rac*-**5d** durch Hexa(tetra)alkylguanidiniumazid. Die Trennung diastereomerer (–)-Camphansäureester (**19**/**19'**) eröffnet einen Zugang zu den reinen Enantiomeren **3**/*ent*-**3**. Der Syntheseweg erlaubt chemische Modifizierungen und führt zu Sporamin-Äquivalenten, in welchen nur die letztendlich zur Glycosidierung vorgesehene OH-Gruppe ungeschützt bleibt.

The synthesis of (+)/(–)sannamine (**1**/*ent*-**1**) presented in the preceding paper[1] starts ultimately from benzene; with the prochiral 1,2:4,5-dianhydro-*epi*-inositol **2a** as a readily available intermediate the construction of the five chiral centers is reduced to the regio- and stereospecific opening of the two epoxide rings (in a *trans*-diaxial manner) by suitable N-nucleophiles[1]. Sporamine (**3**) and de-*O*-methylsporamine, aglyca of the sporaricin antibiotics[2], differ from (de-*O*-methyl)sannamine (**1**) only in the configuration at C-6[3]. We demonstrate in this paper, how the above scheme may be applied to the preparation of racemic as well as enantiomerically pure sporamines and of derivatives thereof, which are suitably protected for direct glycosidation[4]. Syntheses of *rac*-**3**, of 3(4)-demethoxysporamine fluorinated in the 3(4)-position as well as of 3(4)-de-*O*-methylsporamine are subject of more recent publications by Knapp et al.[5] and by Japanese groups[6,7].



Our design for the synthesis of *rac*-**3**[8], depicted in Scheme 1, branches off from the sannamine route[1] after the cyclization of the prochiral methylurethane **2b** (catalyzed by an iminophosphorane base[9]) to yield uniformely bicyclic epoxyurethane *rac*-**4a**. Esterification (*rac*-**4b**) and etherification (*rac*-**4c,d**) of the latter are straightforward. Implied in this concept is a regiospecific opening of the epoxide ring in the *rac*-**4** compounds at C-1 by potentially good leaving groups – highly probable by earlier experience[10,11] – followed by substitution with inversion by N-nucleophiles selected according to the target molecules. This inversion of configuration was postponed till step **5** → **7** because of the earlier observation that in diepoxides **2** opening of one ring cannot be accomplished with sufficient selectivity. Selectivity is maintained, indeed, in the reaction of the tricycles *rac*-**4** – irrespective of the nature of the R group – with halogen nucleophiles (I^-, Br^-): The reactions of *rac*-**4a,b,d** with potassium iodide/acetic acid are fast at room temperature, of *rac*-**4c** with $MgSO_4$ catalysis at 40°C, and give, after crystallization, the racemic iodides **5a,c,e** with yields better than 90%. In some charges a very minor additional component was found (TLC, ^1H NMR) and separated in the case of *rac*-**5a** (after acetylation) and identified to be the 6α-isomer *rac*-**6b**, which stems from halogen substitution. With comparable selectivities and yields the bromides *rac*-**5h,j** are formed by treatment of *rac*-**4a,c** with potassium bromide in

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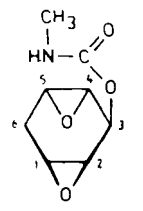
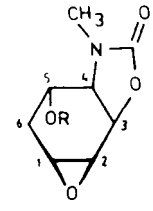
acetic acid/methanol (40 °C). For additional characterization the primary adducts were transformed into (di)acetates (*rac*-**5b,d,f,i,k**).

Scheme 1

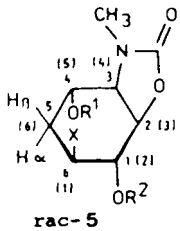


2b

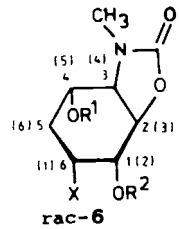


rac-**4**

	a	b	c	d
R	H	Ac	CH_3	MOM



rac-**5**



rac-**6**

5	a	b	c	d	e	f
X	I	I	I	I	I	I
R^1	H	Ac	CH_3	CH_3	MOM	MOM
R^2	H	Ac	H	Ac	H	Ac

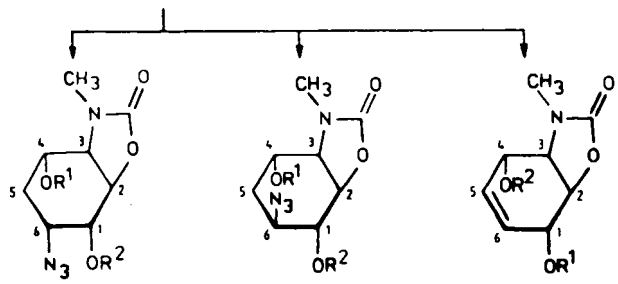
6	a	b	c
X	I	I	$OCOC(CH_3)_3$
R^1	H	Ac	CH_3
R^2	H	Ac	H

g	h	i	j	k	l
I	Br	Br	Br	Br	Br
CH_3	H	Ac	CH_3	CH_3	CH_3
$COC(CH_3)_3$	H	Ac	H	Ac	CO_2Ph

d	e
OH	$OCOC(CH_3)_3$
CH_3	CH_3
$COC(CH_3)_3$	$COC(CH_3)_3$

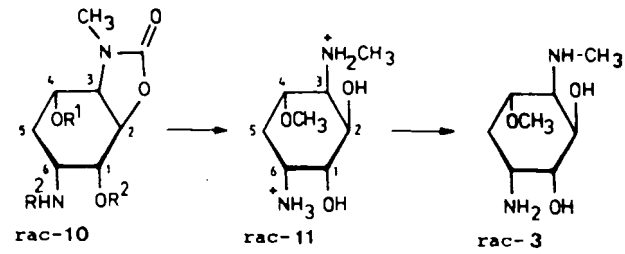
m	n	o	p
OSO_2CF_3	H	H	$OCOC(CH_3)_3$
CH_3	CH_3	CH_3	CH_3
H	H	$COC(CH_3)_3$	$COC(CH_3)_3$

f	g
OH	$SCH_2C_6H_5$
CH_3	CH_3
H	Ac



rac-**7** *rac*-**8** *rac*-**9**

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

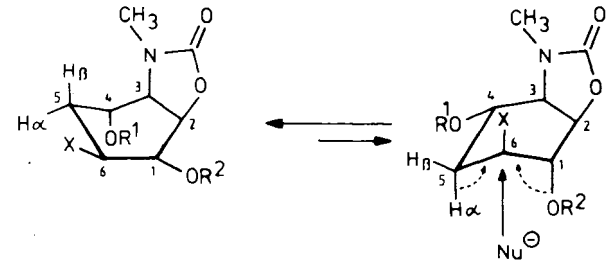


rac-**10** *rac*-**11** *rac*-**3**

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

MOM = CH_3OCH_2-

The (1α,2β,3β,4α,6β) configuration for the halides *rac*-**5a–k** is established by their ^{1}H- and (partly) ^{13}C-NMR spectra and especially by the comparison with those of analogues described earlier[1]. A strong preference for half-chair-like, mobile cyclohexane conformations with quasi-equatorial X- and OR^2 substituents and quasi-axial OR^1 substituent (**5***) is inferred from the sets of vicinal (and additionally long range) coupling constants (i.a. $J_{1,2} = J_{2,3} = 7.0-7.5$, $J_{3,4} = 3.0-3.8$, $J_{4,5\alpha} = 3.0-5.0$, $J_{4,5\beta} = 2.5-4.5$, $J_{5\alpha,5\beta} = 13.5-15.0$, $J_{5\alpha,6} = 3.5-4.0$, $J_{5\beta,6} = 10.5-12.5$, $J_{6,1} = 9.5-12.5$ Hz).



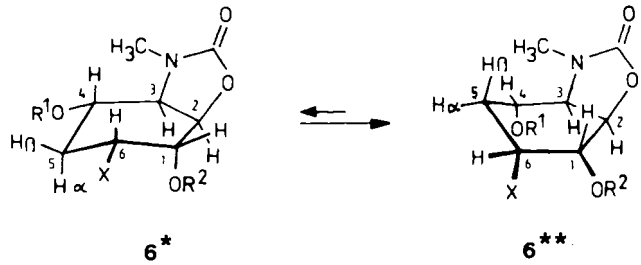
5* **5****

For the S_N2 substitution of the leaving groups X in the intermediates *rac*-**5** complications had to be reckoned with: With a quasi-axial alignment of the nucleofuge in the required thermodynamically unfavourable conformation **5**** HX elimination with participation of the 5α-hydrogen and neighbouring group participation of the likewise quasi-axial OR^2 substituent (OH or OCOR) are imminent competing processes. A model study with the azide nucleophile, used as hexamethylguanidinium salt, which is soluble in acetonitrile and was prepared especially for this study[12], made this complication evident: From the reaction with the hydroxy bromide *rac*-**5j** at room temperature the epoxide *rac*-**4c** results quantitatively. In case of the β-bromo acetate **5k** its acetoxonium ion is product determining: the raw material, formed nearly quantitatively, consists mainly (ca. 90%) of the 6β-azide *rac*-**8d** formed with retention and only ca. 10% of the 6α-azide *rac*-**7d**. In the iodides with their improved leaving group quality the S_N2 substitution prevails, as hoped for. From the β-hydroxy iodides *rac*-**5c** and *rac*-**5e** 88% of *rac*-**7c** and 73% of *rac*-**7e**, respectively, are isolated (besides traces of the olefins *rac*-**9c,e**, if any at all),

from the β-iodo acetate *rac*-**5b** 84% of *rac*-**7b** (besides ca. 10% of *rac*-**9b**) and from *rac*-**5d** almost quantitatively (96% after crystallization) *rac*-**7d**. When preparing *rac*-**7d** on a multi-gram scale, as educt for *rac*-sporamine, the hexamethylguanidinium salt can be replaced by the commercially available, but more basic tetramethyl salt without loss of selectivity. Yet, in the case of *rac*-**5c** and the latter salt, epoxide formation becomes somewhat more competitive again (ca. 30% *rac*-**4c**).

The azido group in the sporamine precursor *rac*-**7d** can be reduced under standard conditions (Pd/C, 0.5% hydrochloric acid in methanol, 12–24 h) without complications (98%, overall yield 80% based on **2**). The resulting amine *rac*-**10c** is additionally characterized as *rac*-**10d**. After hydrolysis [$Ba(OH)_2$, water/methanol 1:1, reflux] and addition of conc. sulfuric acid, the stable sporamine sulfate *rac*-**11** is isolated and identified inter alia by its known ^{1}H-NMR data[3,5]. The free sporamine base *rac*-**3** is set free by neutralization with $Ba(OH)_2$, separation of $BaSO_4$ by filtration, and concentration of the clear aqueous solution. From exploratory experiments, not totally analyzed and therefore not detailed here, it can safely be concluded that similarly *rac*-**7a(b)** and *rac*-**7c** can serve as precursors for the respective de-*O*-methyl-[4] and MOM-protected *rac*-sporamines[8].

The change in configuration at C-1(6) (the numerotation of compounds **6** changes with the X substituent) of the urethanes **6**, **7**, and **10** as compared with **5a–k** causes profound changes of the conformational situation with partially high preference of the 1e,4a,6e conformation **6****, as manifested inter alia by the vicinal coupling constants [$J_{1,2(2,3)}$ = 3.0–6.0, $J_{2,3(3,4)}$ = 7.0–8.0, $J_{3,4(4,5)}$ = 7.0–8.0, $J_{4,5\alpha(5,6\alpha)}$ = 9.5–14.0, $J_{4,5\beta(5,6\beta)}$ = 3.8–5.5, $J_{5\alpha,5\beta(6\alpha,6\beta)}$ = 12.0–13.5, $J_{5\alpha,6(6\alpha,1)}$ = 7.5–10.5, $J_{5\beta,6(6\beta,1)}$ = 3.8–5.5, $J_{6,1(1,2)}$ = 2.5–3.8 Hz] as well as NOE effects (e.g. from 5β- and 5α-H to 6-H and 4-H or of NCH_3 to 4-H in compounds **6b–e**). In the sporamine precursors *rac*-**7** and *rac*-**10** the 1-OH group, that to be glycosidated, shows generally quasi-axial orientation.

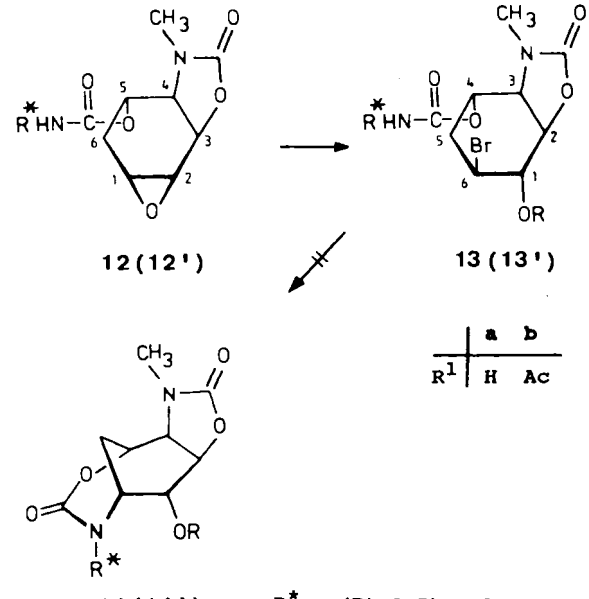


6* **6****

In the fortamine[10] and sannamine series[1] (*R*)- and (*S*)-1-phenylethylamine, resp., had proven as reagents of choice for separation of racemates at the stage of intermediates analogous to bicycles *rac*-**5**, the primary amino group introduced in this step being suitably protected. Unfortunately, no comparably clean S_N2 substitution in the hydroxy iodide *rac*-**5c** and the "protected" iodopivaloate *rac*-**5g** could be induced with these amines. Under repeatedly varied conditions only complex mixtures of products turned out. Even with the triflate *rac*-**5m**, which was prepared from *rac*-**4c** and trifluoromethanesulfonic acid in solution and characterized ^{1}H-NMR spectroscopically, the outcome was not better. Towards the same substrates (*rac*-**5c,g,m**) SAMP[12] (acetonitrile, 58°C) and 1,1-dimethylhydrazine (from *rac*-**5c** i.a. 80% *rac*-**4c**), too, are no efficient nucleophiles.

As attractive alternatives for economically combining the introduction of the (protected) primary amino group into *rac*-**5** halides with the separation of racemates routes via the diastereomeric bisurethanes **13** and **16** were examined. The cyclization **13** → **14** would also yield sporamine derivatives suitable for glycosidation without further protecting group manipulations; with **16** as intermediates, the phenylethyl group would have to be removed first by hydrogenolysis followed by a selective hydrolysis of the unsubstituted urethane ring – for which there are precedents[13]. Separation of diastereomers could be managed at any stage of the two routes.

The epoxybisurethanes **12/12′** required for the preparation of **13a/13a′** are formed nearly quantitatively in a boiling solution of *rac*-**4a** and (*R*)-1-phenylethyl isocyanate as a mixture of two rotamers, which can be distinguished at room temperature by ^{1}H NMR (rapidly converting at 55°C) and separated by TLC. It is noteworthy that in the recyclization of **13a/13a′** with the BEMP base only one of these rotamers is formed. Under conditions successfully applied to *rac*-**4a–c**, the addition of bromide ion to **12a/12a′** is slow and not selective; it proceeds much faster and highly selective, however, with tetraethylammonium bromide in the presence of BF_3–Et_2O: Besides 91% **13a/13a′** no regioisomer (cf. **8**) can be detected. Alternatively, **13a/13a′** is accessible via bromodiol *rac*-**5h** also with the remarkable feature that the isocyanate (1 equiv.) with up to ca. 65% conversion adds only to the 4-OH group. For ^{1}H-NMR analysis the oily **13a/13a′** was derivatized as acetate **13b/13b′**.

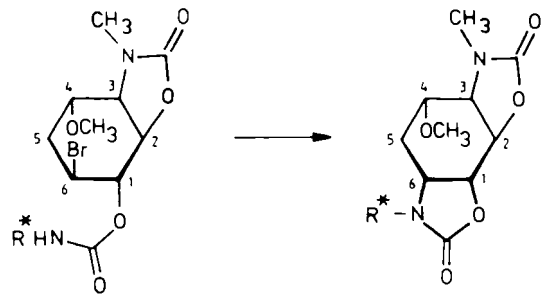


12(12′) **13(13′)**

	a	b
R^1	H	Ac

14(14′) R^* = (R)-1-Phenylethyl

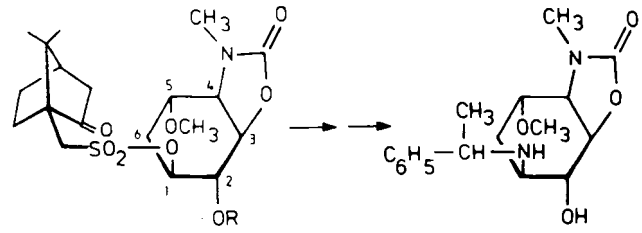
For transannular cyclization **13** → **14**, with the highly selective formation of oxanorbornanes in analogous 5α-hydroxy frameworks as models[14,15], the conformational prerequisites were a priori rather unfavourable. Moreover, in the a,e,a-conformation (**5****) of the starting material **13b**/**13b'**, necessary for the bridging substitution, the 1-acetate function can act as neighbouring group as in the case of the azide ring opening of *rac*-**5k**. And, indeed, this competition became heavily detracting: neither with partial deprotonation using iminophosphorane bases (e.g. BEMP, CH_3CN, 70°C, TDMIP)[9] nor with quantitative deprotonation using amide bases (potassium *N*-*tert*-butyl pivalamide or LDA in THF, 25°C) **14**/**14'** was formed. Besides decomposition products only the epoxides **12**/**12'** could be detected in variable amounts. When the reaction of *rac*-**5j** with chiral isocyanates to give **15a** turned out as problematical, the detour via phenyl carbonate *rac*-**5l**, which reacted with (*R*)-1-phenylethylamine uniformely, proved to be rewarding (93% **15a**/**15a'**). With an excess of BEMP base the course of the cyclization **15**/**15'** → **16**/**16'** is fast and uniform. With only 0.5 equivalents of base a slight kinetic differentiation leads to a diastereomer ratio of 1.6:1 (de = 23%, assignment by ^1H NMR). A satisfactory separation of **16**/**16'**, however, could not be attained, neither by crystallization nor by chromatography. It remains open whether easily accessible variations of the substituent at C-4 or (selective) modifications of the NH-oxazolidone ring allows the development of a preparatively acceptable separation procedure.



15(15') **16(16')**

R* = (R)-1-Phenylethyl-

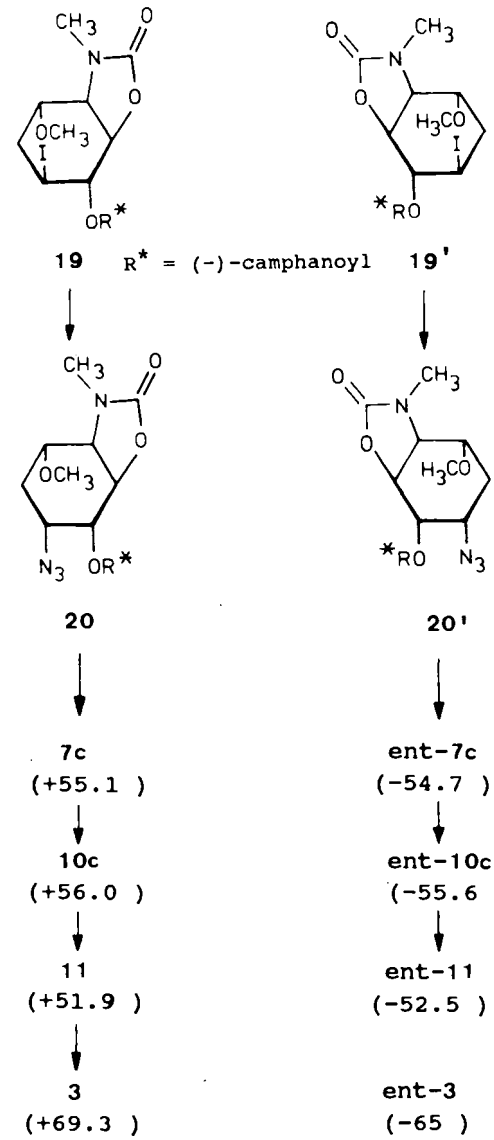
In view of the experiences in the sannamine series[1] and the unproblematical substitution **5** → **7**, diastereomeric 6(1α) esters of type **17** with good leaving groups were obvious candidates for this purpose. D-(+)-camphor-10-sulfonic acid adds to the epoxide *rac*-**4c** at room temperature (CH_2Cl_2). The preliminary yield (60–65%) of sulfonates **17a**/**17a'** was not optimized, however, when numerous separation experiments remained without preparatively useful results. Moreover, upon treatment of **17a**/**17a'** with (*R*)-1-phenylethylamine substitution occurred with retention via *rac*-**4c**; the isolated adduct **18**/**18'** (80%) was known from the sannamine series[1]. In the pivaloates **17c**/**17c'** again no selective substitution could be brought about by SAMP[12].



17(17') **18(18')**

	a	b	c
R	H	Ac	$COC(CH_3)_3$

Success, if only limited, was finally gained in a study with diastereomeric esters prepared from the halogenated alcohols *rac*-**5c,k**, and the azido alcohol *rac*-**7c**, resp., and (−)-camphanic acid or (+)-camphor-10-sulfonic acid[12,16]. Specifically the mixture **19**/**19'**, formed quantitatively from *rac*-**5c** and (−)-camphanoyl chloride in the presence of 2,6-bis-



(dimethylamino)pyridine, could be separated in gram quantities by continuous HPLC. Substitution by azide is performed preferably at this stage; under the conditions developed for *rac*-**7c** (tetramethylguanidinium azide), a practically quantitative yield of the diastereomeric azides **20/20′** (98% isolated as crystals) was achieved. Here the second carbamate ring enforces a more planarized half chair (i.a. $J_{1,2} = 4.5, J_{2,3} = J_{3,4} = 7.5, J_{5\alpha,5\beta} = 14.0, J_{5\alpha,6} = 8.0, J_{5\beta,6} = 4.5, J_{6,1} = 3.7$ Hz). After hydrolysis of the esters with KOH/methanol the enantiomeric azides **7c**/*ent*-**7c** ($[\alpha]_D = +55.1/-54.7$) were hydrogenated as in the *rac*-series to give the amides **10**/*ent*-**10** ($[\alpha]_D = +56.0/-55.6$) and the latter transformed via the sulfates **11**/*ent*-**11** ($+51.9/-52.5$) to the free bases sporamine (+)-**3** ($[\alpha]_D = +69.3$) and *ent*-sporamine (−)-*ent*-**3** ($[\alpha]_D = -65$). By comparison of the rotational values with natural (+)-sporamine ($[\alpha]_D = +75$)[3] the assignment is simultaneously ascertained for the precursors back to **19/19′**.

Structural Modifications

With the intention to preparatively use the now conveniently available polyfunctionalized cyclohexanes of type **5** for the construction of (deoxy)inosamines with novel, biologically valuble substitution patterns, several alternatives for chemical modification have been pursued. Not very surprisingly, neither in the iodides *rac*-**5a/5g** nor in the triflate *rac*-**5m** could S_N2 substitution by fluoride ion[17] be effected. Tetrabutylammonium fluoride on silica[18] provoked quantitative epoxide formation (*rac*-**4c**) from *rac*-**5a/5m**, polymer-supported fluoride[19] quantitative elimination (*rac*-**9f**). In contrast, introduction of a thio functionality proved unproblematical: warming the solution of phenylmethanethiol and *rac*-**5a** in DMF produced uniformly *rac*-**6g**[20]. Searching for an attractive access to the aminoconduritol *rac*-**9d** starting from *rac*-**5d**, a delicate influence of the nature of the base involved became apparent. With potassium *tert*-butylate (CH_3CN, 25°C) the epoxide *rac*-**4c** was formed exclusively, with DBN (at least 3 equivalents) uniformely 4-methoxyphenol, with the BEMP iminophosphorane base[8], which is especially suitable for elimination reactions, yet 70% *rac*-**9d** (besides *rac*-**4c**, which could supposedly be avoided under optimized conditions). Reductive elimination of the iodine in *rac*-**5c** to give the dideoxy aglycon *rac*-**5n**, wanted for glycosidation experiments[21], is possible in 93% yield using $NaBH_4/NiCl_2$[22]. *rac*-**5n** was additionally characterized as pivaloate *rac*-**5o**. In *rac*-**5n,o** (i.a. $J_{1,2} = 5.3, J_{2,3} = J_{6,1} = 3.5$ Hz), as expected, the **5**** conformation makes a larger contribution than for *rac*-**5a**–**l**. Attempts to protect the 1-OH group of *rac*-**5m** as pivaloate by treating *rac*-**4c** with trifluoromethanesulfonic acid in the presence of pivalic anhydride (1.1 equivalents) led quickly to a mixture of mono-[*rac*-**6c** (17%)/*rac*-**6d** (76%)] and diesters [*rac*-**6e** (5%)/*rac*-**5p** (2%)]. After chromatographic separation hydrolysis of the fraction with *rac*-**6c,6d** led almost quantitatively to the corresponding diol *rac*-**6e**. In this way **2a** can also serve as expeditious starting material for the corresponding (1α,2α,3β,-4β,5α)-4-(methylamino)-6-deoxyinosamine[22].

Resumé

With the route to sporamine and de-*O*-methyl sporamine equivalents presented here the chemistry of (deoxy)inosadiamines, which is based on a pool of easily accessible dianhydro(deoxy)inositols, is further expanded. High selectivity and efficiency of the individual steps qualify the underlying schemes as equivalent if not superior to alternative procedures[5,7]. Still a less laborious way for optical resolution would be welcome. With respect to the envisaged total syntheses of antibiotics it is once more essential that chemical modifications can be effected in a straightforward manner at various stages. An obvious extension of this project encompasses the analogous transformation of suitably protected fortamine precursors (e.g. *rac*-**24** in ref.[11]) into fortamine equivalents epimeric at the position carrying NH_2. Our endeavours to exploit these modified aglyca for the total synthesis of non-natural aminoglycoside antibiotics will be detailed in a forthcoming paper[23].

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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. – ^1H 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. – HPLC: analytical: Waters 6000 A; columns: Bondapak C 18 (3.9 × 300 mm, Knauer LiChrosorb Merck Si 100, detector: PE LC-55-S). Preparative: PE 2-LC; columns: LiChrosorb RP-C18 (16 × 250 mm), LiChrosorb Si 100 (7 µ, 10 × 250 mm), detector: Waters 450. – 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 the appropriate alcohol, 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; yields 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.

DL-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-6-iodo-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5a**) *and DL-(1α,2β,3β,4α,6α)-1,4-Di-O-acetyl-2-O,3-N-carbonyl-6-iodo-3-(methylamino)-1,2,4-cyclohexanetriol* (*rac*-**6b**): A mixture of 925 mg (5.0 mmol) of *rac*-**4a** in 20 ml of acetic acid and 1.24 g (7.5 mmol) of potassium iodide was stirred at room temp. for 1 h (total conversion, TLC, $CHCl_3/CH_3OH$, 10:1, two components). The excess of potassium iodide was filtered off, the solution concentrated in vacuo, and the residue separated by column chromatography (silica, $CHCl_3/CH_3OH$, 10:1) to give

60 mg (4%, R_f = 0.34) of *rac*-**6a** and 1.46 g (94%, R_f = 0.27) of *rac*-**5a**; *rac*-**6a** was characterized as diacetate *rac*-**6b**.

rac-**5a**: Colorless crystals, m.p. 152–153°C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 3600–3300 cm^{-1}, 2900, 1755–1720, 1650, 1425, 1400, 1360, 1315, 1075, 1030, 1010, 980, 880, 795, 765, 660, 620. – ^1H NMR (CD_3OD): δ = 4.45 (t, 2-H), 4.28 (dt, 6-H), 3.98 (m, 4-H), 3.83 (ddd, 3-H), 3.68 (dd, 1-H), 2.82 (s, NCH_3), 2.49 (ddt, 5α-H), 2.27 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{3,5\alpha} \leqslant 1$, $J_{4,5\alpha} \approx J_{4,5\beta} = 4.5$, $J_{5\alpha,5\beta} = 14.5$, $J_{5\alpha,6} = 3.8$, $J_{5\beta,6} = J_{6,1} = 10.5$ Hz.

$C_8H_{12}INO_4$ (313.1) Calcd. C 30.69 H 3.86 N 4.47
Found C 30.34 H 3.86 N 4.70

rac-**6b**: Colorless crystals, m.p. 143–144°C. – IR (KBr): $\tilde{\nu}$ = 2920 cm^{-1}, 1780, 1745, 1435, 1395, 1380, 1365, 1280, 1220, 1110, 1065, 1020, 935, 890, 850, 830, 770, 760, 675. – ^1H NMR ($CDCl_3$): δ = 5.17 (t, 1-H), 4.98 (ddd, 4-H), 4.57 (dd, 2-H), 4.37 (ddd, 6-H), 3.75 (t, 3-H), 2.89 (s, NCH_3), 2.60 (ddt, 5α-H), 2.26 (ddd, 5β-H), 2.28, 2.10 (s, CH_3); $J_{1,2} = 4$, $J_{2,3} = J_{3,4} = 7$, $J_{4,5\alpha} = 12.5$, $J_{4,5\beta} = 4$, $J_{5\alpha,5\beta} = 13.5$, $J_{5\alpha,6} = 10.5$, $J_{5\beta,6} = 4$, $J_{6,1} = 3.5$ Hz.

$C_{12}H_{16}INO_6$ (397.2) Calcd. C 36.29 H 4.06 N 3.53
rac-**5b**: Found C 36.08 H 4.14 N 3.46
rac-**6b**: Found C 36.10 H 4.04 N 3.48

DL-(1α,2β,3β,4α,6β)-1,4-Di-O-acetyl-2-O,3-N-carbonyl-6-iodo-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5b**): 940 mg (3.0 mmol) of *rac*-**5a** was acetylated under standard conditions. After drying and concentrating in vacuo from $CHCl_3$/ether, 2:1, 1.15 g (97%) of colorless crystals were obtained, dec. > 177°C. – IR (KBr): 2980–2880 cm^{-1}, 1750, 1420, 1395, 1380, 1365, 1300, 1220, 1165, 1130, 1110, 1050, 1015, 975, 915, 885, 855, 815, 660, 635, 600. – ^1H NMR ($CDCl_3$): δ = 5.26 (dd, 1-H), 5.10 (q, 4-H), 4.53 (t, 2-H), 4.19 (dt, 6-H), 3.83 (ddd, 3-H), 2.87 (s, NCH_3), 2.60 (ddt, 5α-H), 2.42 (ddd, 5β-H), 2.15, 2.14 (s, CH_3); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{3,5\alpha} \leqslant 1.5$, $J_{4,5\alpha} = J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 15$, $J_{5\alpha,6} = 3.8$, $J_{5\beta,6} = J_{6,1} = 12$ Hz.

DL-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-6-iodo-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5c**): A mixture of 4.98 g (25.0 mmol) of *rac*-**4c**, 8.30 g (50.0 mmol) of potassium iodide, and 60 ml of acetic acid was stirred for 2.5 h at room temp. (total conversion, TLC, $CHCl_3/CH_3OH$, 10:1). After concentrating in vacuo the residue was dissolved in 300 ml of CH_2Cl_2 and the solution extracted 3 times with 75 ml of water. The organic layer was dried, concentrated in vacuo and the residue crystallized from ethyl acetate to give 7.97 g (97%) of colorless crystals, m.p. 160°C. – IR (KBr): $\tilde{\nu}$ = 3400 cm^{-1}, 2970, 2920, 2890, 2820, 1770–1740, 1475, 1455, 1435, 1400, 1360, 1340, 1300, 1240, 1200, 1165, 1095, 1060, 1030, 1015, 870, 810, 785, 770, 660, 620, 585, 500, 475. – ^1H NMR (CD_3OD): δ = 4.38 (t, 2-H), 4.15 (dt, 6-H), 3.94 (ddd, 3-H), 3.67 (dd, 1-H), 3.59 (m, 4-H), 3.39 (s, OCH_3), 2.82 (s, NCH_3), 2.63 (ddt, 5α-H), 2.21 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3$, $J_{3,5\alpha} \approx 1.5$, $J_{4,5\alpha} \approx 4$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14.5$, $J_{5\alpha,6} = 4$, $J_{5\beta,6} = J_{6,1} = 12$ Hz.

$C_9H_{14}INO_4$ (327.1) Calcd. C 33.05 H 4.31 N 4.28
Found C 33.10 H 4.29 N 4.38

DL-(1α,2β,3β,4α,6β)-1-O-Acetyl-2-O,3-N-carbonyl-6-iodo-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5d**): 4.90 g (15.0 mmol) of *rac*-**5c** was acetylated under standard conditions (15 h, room temp.). After concentrating in vacuo, the oily residue was dissolved in 250 ml CH_2Cl_2 and the solution extracted twice with 50 ml of 2 N H_2SO_4 and twice with 50 ml of water. The organic layer was dried, concentrated, the solid residue was crystallized from $CHCl_3$/ether, 5:1, to give 5.32 g (96%) of colorless crystals, m.p. 134°C. – IR (KBr): $\tilde{\nu}$ = 2875 cm^{-1}, 2835, 1770, 1450, 1395, 1375, 1305, 1270, 1215, 1110, 1085, 1015, 890, 810, 780, 765, 660, 640. – ^1H NMR ($CDCl_3$): δ = 5.26 (dd, 1-H), 4.49 (t, 2-H), 4.41 (dt, 6-H), 3.86 (ddd, 3-H), 3.53 (m, 4-H), 3.41 (s, OCH_3), 2.85 (s, NCH_3), 2.63 (ddt, 5α-H), 2.26 (dt, 5β-H), 2.14 (s, CH_3); $J_{1,2} = J_{2,3} = 7$, $J_{3,4} = 3$, $J_{3,5\alpha} \leqslant 1$, $J_{4,5\alpha} = 4$, $J_{4,5\beta} = 3$, $J_{5\alpha,5\beta} = 14.5$, $J_{5\alpha,6} = 3.5$, $J_{5\beta,6} = J_{6,1} = 11$ Hz.

$C_{11}H_{16}INO_5$ (369.1) Calcd. C 35.79 H 4.37 N 3.79
Found C 35.39 H 4.24 N 3.91

DL-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-6-iodo-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5e**): A solution of 1.80 g (8.0 mmol) of *rac*-**4d**, 1.40 g (12.0 mmol) of $MgSO_4$, 1.98 g (12.0 mmol) of potassium iodide, and 245 mg (4.0 mmol) of acetic acid in 20 ml of CH_3OH was heated at reflux for 5 h (total conversion, TLC, $CHCl_3/CH_3OH$, 25:1). It was concentrated in vacuo, the residue dissolved in 50 ml of H_2O and the solution extracted twice with 40 ml of CH_2Cl_2. The organic layer was dried, concentrated in vacuo and the solid residue crystallized from ethyl acetate to give 2.57 g (90%) of colorless crystals, m.p. 140°C. – IR (KBr): $\tilde{\nu}$ = 3440 cm^{-1}, 2910, 2850, 1775, 1425, 1400, 1325, 1255, 1150, 1085, 1025, 965, 890, 765, 475. – ^1H NMR ($CDCl_3$): δ = 4.65, 4.73 (OCH_2), 4.51 (t, 2-H), 4.27 (ddd, 6-H), 3.89–3.79 (m, 1-, 3-, 4-H), 3.40 (s, OCH_3), 3.21 (d, OH), 2.84 (s, NCH_3), 2.63 (ddt, 5β-H), 2.27 (ddd, 5α-H); $J_{CH_2} = 6.8$, $J_{1,2} = J_{2,3} = 7.5$, $J_{4,5\beta} = 2.2$, $J_{4,5\alpha} = J_{5\alpha,6} = 3.8$, $J_{5\alpha,5\beta} = 14$, $J_{5\beta,6} = 12.5$, $J_{6,1} = 11$, $J_{1,OH} = 3.7$ Hz.

$C_{10}H_{16}NO_5$ (357.1) Calcd. C 33.63 H 4.52 N 3.92
Found C 33.30 H 4.54 N 3.82

DL-(1α,2β,3β,4α,6β)-1-O-Acetyl-2-O,3-N-carbonyl-6-iodo-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5f**): 1.80 g (5.0 mmol) of *rac*-**5e** was acetylated under standard conditions. The solution was filtered over a short pad of silica (ethyl acetate/cyclohexane, 1:2). Crystallization from $CHCl_3$/ether, 1:1, gave 1.85 g (93%) of colorless crystals, m.p. 127°C. – IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1}, 2950, 1775, 1420, 1390, 1375, 1310, 1300, 1265, 1215, 1165, 1045, 1030, 1015, 915, 775, 660, 645, 625. – ^1H NMR ($CDCl_3$): δ = 5.26 (dd, 1-H), 4.62, 4.68 (OCH_2), 4.53 (dd, 2-H), 4.27 (ddd, 6-H), 3.93–3.88 (m, 3-, 4-H), 3.41 (s, OCH_3), 2.84 (s, NCH_3), 2.63 (ddt, 5α-H), 2.32 (ddd, 5β-H), 2.14 (s, CH_3); $J_{CH_2} = 7.5$, $J_{1,2} = 7.5$, $J_{2,3} = 7$, $J_{4,5\alpha} = J_{5\alpha,6} = 3.8$, $J_{3,5\alpha} = 1.5$, $J_{4,5\beta} = 2.5$, $J_{5\alpha,5\beta} = 13.5$, $J_{5\beta,6} = J_{6,1} = 12$ Hz.

$C_{12}H_{18}INO_6$ (399.1) Calcd. C 36.11 H 4.55 N 3.51
Found C 36.15 H 4.64 N 3.39

DL-(1α,2β,3β,4α,6β)-6-Bromo-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5h**): A solution of 1.00 g (5.4 mmol) of *rac*-**4a** and 0.62 g (6.0 mmol) of sodium bromide in acetic acid was stirred for 2 h at 60°C (total conversion, TLC, chloroform/CH_3OH, 10:1). It was concentrated in vacuo and filtered through a short pad of silica (cyclohexane/ethyl acetate, 1:3). Crystallization from ethyl acetate gave 1.35 g (90%) colorless crystals, m.p. 142°C. – IR (KBr): $\tilde{\nu}$ = 3600–3200 cm^{-1}, 2895, 1700, 1480, 1425, 1395, 1365, 1335, 1305, 1250, 1135, 1115, 1100, 1085, 1050, 1030, 1010, 980, 875, 800, 765, 660, 645. – ^1H NMR ($CDCl_3$/[D_6]acetone 1:1): δ = 5.04 (d, OH), 4.59 (d, OH), 4.47 (dd, 2-H), 4.29 (ddd, 6-H), 4.24 (m, 4-H), 3.85 (ddd, 3-H), 3.79 (ddd, 1-H), 2.84 (s, NCH_3), 2.46 (dddd, 5α-H), 2.18 (ddd, 5β-H); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 3.0$, $J_{3,5\alpha} = 1.0$, $J_{4,5\alpha} = 4.5$, $J_{4,5\beta} = 3.0$, $J_{5\alpha,5\beta} = 14.0$, $J_{5\alpha,6} = 4.5$, $J_{5\beta,6} = 11.0$, $J_{1,6} = 9.5$, $J_{1,OH} = 5.3$, $J_{4,OH} = 3.8$ Hz.

$C_8H_{12}BrNO_4$ (265.9) Calcd. C 36.11 H 4.55 N 5.26
Found C 36.05 H 4.67 N 5.16

DL-(1α,2β,3β,4α,6β)-1,4-Di-O-acetyl-6-bromo-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5i**): *rac*-**5h** was acetylated under standard conditions to give *rac*-**5i**. From ethyl acetate colorless crystals, m.p. 157°C. – IR (KBr): $\tilde{\nu}$ = 3550–3300 cm^{-1}, 2980, 2930, 2890, 1765, 1735, 1460, 1415, 1385, 1370, 1355, 1305,

1295, 1260, 1215, 1130, 1105, 1090, 1045, 1010, 970, 910, 880, 860, 810, 770, 760, 660, 635. — ^{1}H NMR ($CDCl_3$): δ = 5.27 (m, 1-, 4-H), 4.55 (dd, 2-H), 4.14 (ddd, 6-H), 3.80 (m, 3-H), 2.90 (s, NCH_3), 2.52 (dddd, 5α-H), 2.31 (dddd, 5β-H), 2.17, 2.15 (s, $COCH_3$); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,5\alpha}$ = 1.0, $J_{4,5\alpha}$ = 4.5, $J_{4,5\beta}$ = 3.0, $J_{5\alpha,5\beta}$ = 14.0, $J_{5\alpha,6}$ = 4.5, $J_{5\beta,6}$ = 11.0, $J_{6,1}$ = 9.5 Hz. — MS (70 eV, CI, methane): *m/z* = 352, 350 (M^+), 212, 152, 108, 95, 75.

$C_{12}H_{16}BrNO_6$ (349.9) Calcd. C 41.16 H 4.61 N 4.00
Found C 41.06 H 4.57 N 3.97

DL-(1α,2β,3β,4α,6β)-6-Bromo-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5j**): A solution of 3.00 g (15.1 mmol) of *rac*-**4c** and 3.57 g (30.0 mmol) of potassium bromide in 40 ml of acetic acid was stirred for 8 h at 40°C (total conversion, TLC, $CHCl_3/CH_3OH$, 10:1). It was concentrated in vacuo, the residue dissolved in 250 ml of CH_2Cl_2 and the solution extracted twice with 60 ml of water. The organic layer was dried, concentrated in vacuo and the residue crystallized from ethyl acetate to give 3.74 g (89%) of colorless crystals, m.p. 185°C. — IR (KBr): $\tilde{\nu}$ = 3370 cm^{-1}, 2940, 2900, 1762, 1425, 1400, 1310, 1115, 1090, 1035, 1010, 880, 825, 795, 765, 680, 480. — ^{1}H NMR (CD_3OD): δ = 4.39 (t, 2-H), 3.97 (dt, 6-H), 3.88 (ddd, 3-H), 3.78 (m, 4-H), 3.59 (dd, 1-H), 3.41 (s, OCH_3), 2.81 (s, NCH_3), 2.39 (ddt, 5α-H), 1.94 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.8, $J_{3,5\alpha} \leqslant 1$, $J_{4,5\alpha}$ = 5, $J_{4,5\beta}$ = 2.5, $J_{5\alpha,5\beta}$ = 14, $J_{5\alpha,6}$ = 4, $J_{5\beta,6}$ = $J_{6,1}$ = 12 Hz.

$C_9H_{14}BrNO_4$ (280.1) Calcd. C 38.59 H 5.04 N 5.00
Found C 38.52 H 4.98 N 5.09

DL-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-bromo-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5k**): 280 mg (1.0 mmol) of *rac*-**5j** was acetylated under standard conditions. From $CHCl_3$/ether, 2:1, 315 mg (98%) of colorless crystals were obtained, m.p. 102°C. — IR (KBr): $\tilde{\nu}$ = 3520−3400 cm^{-1}, 2940, 2880, 1770, 1450, 1415, 1395, 1305, 1275, 1220, 1120, 1100, 1085, 1055, 1040, 1020, 840, 800, 765, 680. — ^{1}H NMR ($CDCl_3$): δ = 5.17 (dd, 1-H), 4.46 (t, 2-H), 4.05 (dt, 6-H), 3.75 (ddd, 3-H), 3.68 (m, 4-H), 3.38 (s, OCH_3), 2.81 (s, NCH_3), 2.40 (ddt, 5α-H), 2.11 (s, CH_3), 2.00 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.7, $J_{3,5\alpha} \approx 1.5$, $J_{4,5\alpha}$ = 4, $J_{4,5\beta}$ = 3, $J_{5\alpha,5\beta}$ = 14.2, $J_{5\alpha,6}$ = 3.8, $J_{5\beta,6}$ = $J_{6,1}$ = 10.5 Hz.

$C_{11}H_{16}BrNO_5$ (322.2) Calcd. C 41.01 H 5.00 N 4.35
Found C 41.27 H 4.89 N 4.31

DL-(1α,2β,3β,4α,6β)-6-Bromo-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1-O-(phenoxycarbonyl)-1,2,4-cyclohexanetriol (*rac*-**5l**): To a solution of 750 mg (2.7 mmol) of *rac*-**5j** and 330 mg (2.7 mmol) of DMAP in 20 ml of CH_2Cl_2 630 mg (4.1 mmol) of freshly distilled phenyl chloroformate was added by syringe. If after 6 h at room temp. starting material could still be detected, the reaction was completed by addition of a catalytical amount of pyridine. The solution was concentrated in vacuo, the residue dried at 10^{-2} Torr/40°C and dissolved in 100 ml of CH_2Cl_2. The solution was extracted with 2 N H_2SO_4 and buffer (pH 7), dried ($MgSO_4$), concentrated in vacuo and the residue crystallized from ethyl acetate to give 670 mg (63%) of colorless crystals, m.p. 163°C. — IR (KBr): $\tilde{\nu}$ = 3476 cm^{-1}, 2990, 1775, 1755, 1482, 1430, 1398, 1324, 1266, 1207, 1099, 1040, 989, 953, 779, 747, 713. — ^{1}H NMR ($CDCl_3$): δ = 7.39 (m, 2H), 7.24 (m, 3H), 5.11 (dd, 1-H), 4.64 (dd, 2-H), 4.26 (ddd, 6-H), 3.86 (ddd, 3-H), 3.66 (m, 4-H), 3.41 (s, OCH_3), 2.85 (s, NCH_3), 2.59 (dddd, 5α-H), 2.15 (ddd, 5β-H); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{1,6}$ = 10.5, $J_{3,4}$ = 3.0, $J_{3,5\alpha}$ = 0.8, $J_{4,5\alpha}$ = 3.7, $J_{4,5\beta}$ = 3.0, $J_{5\alpha,5\beta}$ = 14.3, $J_{5\alpha,6}$ = 3.7, $J_{5\beta,6}$ = 12.0 Hz.

$C_{16}H_{18}BrNO_6$ (400.2) Calcd. C 48.02 H 4.53 N 3.50
Found C 47.78 H 4.38 N 3.52

DL-(1α,2β,3α,4α,5β)-3-O,4-N-Carbonyl-5-O-methyl-4-(methylamino)-1-O-(trifluoromethylsulfonyloxy)-1,2,5-cyclohexanetriol (*rac*-**5m**): The labile *rac*-**5m** was characterized ^{1}H-NMR spectroscopically and used without further purification. — ^{1}H NMR (CD_2Cl_2): δ = 4.99 (ddd, 1-H), 4.54 (dd, 3-H), 3.91 (dd, 4-H), 3.85−3.77 (m, 2H, 2-, 5-H), 3.42 (s, OCH_3), 2.82 (s, NCH_3), 2.45 (dddd, 6β-H), 1.99 (ddd, 6α-H); $J_{1,2}$ = 10, $J_{2,3}$ = $J_{3,4}$ = 7, $J_{4,5}$ = 9, $J_{5,6\alpha}$ = 3, $J_{5,6\beta}$ = 5, $J_{6\alpha,6\beta}$ = 14, $J_{6\alpha,1}$ = 10, $J_{6\beta,1}$ = 5, $J_{4,6\beta}$ = 0.5 Hz.

DL-(1α,2β,3β,4α)-2-O,3-N-Carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**5n**): To a solution of 8 ml of CH_2Cl_2, 40 ml of CH_3OH, and 2.35 g of *rac*-**5c** (7.2 mmol) 2.40 g of nickel(II) chloride hexahydrate was added. The mixture was cooled to 0°C, and with vigorous stirring $NaBH_4$ was added in portions till no more starting material was detectable (TLC, CH_2Cl_2/CH_3OH, 15:1). 20 ml of water was added, the solution filtered and extracted 5 times with 25 ml each of CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The oily residue was identified spectroscopically and used for glycosidation without further purification. — IR (CCl_4): $\tilde{\nu}$ = 3818 cm^{-1}, 3426, 2936, 1751, 1429, 1393, 1304, 1256, 1233, 1207, 1097, 1027, 992, 940, 820, 798, 766, 671. — ^{1}H NMR ($CDCl_3$): δ = 4.44 (dd, 2-H), 3.97 (b, OH), 3.71 (dd, 3-H), 3.4 (m, 1-, 4-H), 3.35 (s, OCH_3), 2.90 (s, NCH_3), 1.75 (m, 5-, 6-H); $J_{1,2}$ = 5.25, $J_{2,3}$ = 6.5 Hz.

DL-(1α,2β,3β,4α)-2-O,3-N-Carbonyl-4-O-methyl-3-(methylamino)-1-O-pivaloyl-1,2,4-cyclohexanetriol (*rac*-**5o**): *rac*-**5n** was transformed into *rac*-**5o** with pivaloyl chloride/triethylamine/DMAP under standard conditions. After filtration over a short pad of silica (CH_2Cl_2/CH_3OH, 15:1) and crystallization from ethyl acetate colorless crystals were obtained, m.p. 94°C. — ^{1}H NMR ($CDCl_3$): δ = 5.02 (q, 1-H), 4.44 (dd, 2-H), 3.63 (t, 3-H), 3.44 (4-H), 3.39 (s, OCH_3), 2.92 (s, NCH_3), 1.90−1.57 (m, 5-, 6-H), 1.22 [s, $C(CH_3)_3$]; $J_{1,2}$ = $J_{1,6}$ = 5.25, $J_{2,3}$ = $J_{3,4}$ = 6.5 Hz.

$C_{14}H_{23}NO_5$ (285.3) Calcd. C 58.93 H 8.12 N 4.91
Found C 58.88 H 8.13 N 4.83

DL-(1α,2α,3β,4β,5α)-3-O,4-N-Carbonyl-5-O-methyl-4-(methylamino)-1-O-pivaloyl-1,2,3,5-cyclohexanetetrol (*rac*-**6c**), *-2-O-pivaloyl-1,2,3,5-cyclohexanetetrol* (*rac*-**6d**), *and -1,2-di-O-pivaloyl-1,2,3,5-cyclohexanetetrol* (*rac*-**6e**): To a solution of 199 mg (1.0 mmol) of *rac*-**4c** and 205 mg (1.1 mmol) of pivalic anhydride in 5 ml of CH_2Cl_2 165 mg (1.1 mmol) of trifluoromethanesulfonic acid was added. After total conversion (5 min, TLC, cyclohexane/ethyl acetate, 1:3), the solution was concentrated in vacuo, and mono- and diester were separated by column chromatography (silica, cyclohexane/ethyl acetate, 1:3). The first fraction contained *rac*-**6e** (*rac*-**5p**) (5 and 2%, resp.), the second *rac*-**6c**/*rac*-**6d** (17 and 76%, resp.); they were characterized by ^{1}H/^{13}C NMR and mass spectra as mixtures. *rac*-**6c**: ^{1}H NMR ($CDCl_3$): δ = 5.13 (dd, 2-H), 4.62 (dd, 3-H), 4.10 (ddd, 1-H), 3.68 (dd, 4-H), 3.55 (ddd, 5-H), 3.42 (s, OCH_3), 2.95 (s, NCH_3), 2.20 (m, 6-H), 1.25 (s, 9H); $J_{1,2}$ = 3, $J_{2,3}$ = 5.5, $J_{5,6\beta}$ = 4.5, $J_{6\alpha,6\beta}$ = 14, $J_{1,6\beta}$ = 4.5 Hz. — ^{13}C NMR ($CDCl_3$): δ = 78.9 (C-5), 74.0 (C-3), 71.4 (C-2), 66.0 (C-1), 60.4 (C-4), 56.7 (OCH_3), 39.0 (C-9), 30.8 (NCH_3), 29.7 (C-6), 27.1 (3C). — *rac*-**6d**: ^{1}H NMR ($CDCl_3$): δ = 5.02 (ddd, 1-H), 4.62 (dd, 3-H), 4.16 (dd, 2-H), 3.68 (dd, 4-H), 3.49 (ddd, 5-H), 3.38 (s, OCH_3, 2.97 (s, NCH_3), 2.22 (ddd, 6β-H), 1.77 (ddd, 6α-H), 1.23 (s, 9H); $J_{1,2}$ = 3.5, $J_{2,3}$ = 4.5, $J_{3,4}$ = $J_{4,5}$ = 7.5, $J_{5,6\alpha}$ = 9.5, $J_{5,6\beta}$ = 5, $J_{6\alpha,6\beta}$ = 13.5, $J_{6\alpha,1}$ = 7.5, $J_{6\beta,1}$ = 5.5 Hz. — ^{13}C NMR: δ = 177.5 (CO), 157.4 (C-4), 78.2 (C-5), 75.9 (C-3), 68.9 (C-1), 67.3 (C-2), 59.8 (C-4), 55.5 (OCH_3), 38.9 (1C), 30.7 (NCH_3), 27.1 (3C), 27.1 (C-6). — MS (70 eV): *m/z* (%) = 301 (M^+, 1), 100 (100). — *rac*-**6e**: ^{1}H NMR ($CDCl_3$): δ = 5.25 (dd, 2-H), 5.16 (ddd, 1-H), 4.60 (dd, 3-H), 3.64 (dd, 4-H), 3.54 (ddd, 5-H), 3.37 (s, OCH_3), 3.00 (s, NCH_3), 2.39 (ddd, 6β-H), 1.70 (ddd, 6α-H), 1.23 (s, 9H), 1.20 (s, 9H); $J_{1,2}$ = 2.5, $J_{2,3}$ = 5.5, $J_{3,4}$ = $J_{4,5}$ = 8, $J_{5,6\alpha}$ = 9.5, $J_{5,6\beta}$ = 5.5, $J_{6\alpha,6\beta}$ = 13.5, $J_{6\alpha,1}$ = 7.5, $J_{6\beta,1}$ = 5 Hz. — ^{13}C NMR

($CDCl_3$): δ = 177.1, 176.8 (C-8, -8'), 157.2 (C-7), 78.5 (C-5), 73.6 (C-3), 68.7 (C-2), 67.1 (C-1), 60.4 (C-4), 56.5 (OCH_3), 38.9, 38.8 (C-9, -9'), 30.9 (NCH_3), 28.7 (C-6), 27.07, 27.05 (C-10')*. – MS (70 eV, NH_3): *m/z* (%) = 403 (MNH_4^+, 100), 301 (20).

DL-(1α,2α,3β,4β,5α)-3-O,4-N-Carbonyl-5-O-methyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (*rac*-**6f**): A solution of 110 mg (0.36 mmol) of *rac*-**6c**/**6d** in 1.5 ml of 3% methanolic sodium hydroxide solution was neutralized after 15 min with 2 N HCl, concentrated in vacuo, the residue dissolved in CH_2Cl_2, the solution dried ($MgSO_4$), concentrated in vacuo, and the residue crystallized from ethyl acetate: 74 mg (96%) of colorless crystals, m.p. 139°C. – ^{1}H NMR ($CDCl_3$): δ = 4.63 (dd, 3-H), 4.03 (ddd, 1-H), 3.98 (dd, 2-H), 3.71 (dd, 4-H), 3.48 (ddd, 5-H), 3.42 (s, OCH_3), 2.95 (s, NCH_3), 2.14 (ddd, 6β-H), 1.83 (ddd, 6α-H); $J_{1,2}$ = 3.75, $J_{2,3}$ = 4.5, $J_{3,4}$ = 7.5, $J_{4,5}$ = 6.75, $J_{5,6\alpha}$ = 9, $J_{5,6\beta}$ = 4.5, $J_{6\alpha,6\beta}$ = 13.5, $J_{6\alpha,1}$ = 7.5, $J_{6\beta,1}$ = 4.5 Hz.

$C_9H_{15}NO_5$ (217.2) Calcd. C 49.76 H 6.96
Found C 49.51 H 6.75

DL-(1α,2β,3β,4α,6α)-1-O-Acetyl-6-(benzylthio)-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**6g**): To a solution of 10.5 mg (0.084 mmol) of phenylmethanethiol in 3 ml of absol. DMF 2 mg of NaH was added. After stirring for 5 min the solution of 26 mg (0.07 mmol) of **5d** in 3 ml of absol. DMF is added. After warming to 60°C for 6 h (total conversion, TLC, cyclohexane/ethyl acetate, 2:1) the solution was concentrated in vacuo and the residue filtered over silica (cyclohexane/ethyl acetate, 2:1). 24 mg (96%) of colorless oil. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.3 (5H), 5.47 (dd, 1-H), 4.45 (dd, 2-H), 3.76 (s, CH_2), 3.43 (t, 3-H), 3.29 (s, OCH_3), 3.22 (ddd, 4-H), 2.95 (s, NCH_3), 2.84 (ddd, 6-H), 2.44 (s, CH_3), 1.95 (5β-H), 1.55 (5α-H); $J_{1,2}$ = 3, $J_{2,3}$ = 7, $J_{3,4}$ = 8, $J_{4,5\alpha}$ = 11, $J_{4,5\beta}$ = 5, $J_{5\alpha,5\beta}$ = 13, $J_{5\alpha,6}$ = 13, $J_{5\beta,6}$ = 3.5, $J_{6,1}$ ≈ 3 Hz. – ^{13}C NMR ($CDCl_3$): δ = 169.4 ($COCH_3$), 157.0 (NCO), 137.3–127.4 (6C), 81.6 (C-4), 74.7 (C-2), 67.0 (C-1), 60.2 (C-3), 56.0 (OCH_3), 38.9 (C-6), 35.6 (CH_2), 30.7 (NCH_3), 27.8 (C-5), 20.7 (CH_3).

$C_{17}H_{23}NO_5S$ (353.4) Calcd. C 57.77 H 6.56
Found C 57.51 H 6.38

DL-(1α,2β,3β,4α,6α)-1,4-Di-O-acetyl-6-azido-2-O,3-N-carbonyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**7b**): A solution of 100 mg (0.25 mmol) of *rac*-**5b** and 95 mg (0.5 mmol) of hexamethylguanidinium azide in 5 ml of dry acetonitrile was heated at reflux for 30 min (N_2, total conversion, TLC, $CHCl_3/CH_3OH$, 10:1). After concentration in vacuo the residue was separated from salts by column chromatography (silica, $CHCl_3/CH_3OH$, 10:1). The eluate consisted of 90% of *rac*-**7b** and 10% of *rac*-**9b** [DL-(1α,2β,3β,4α)-1,4-di-*O*-acetyl-2-*O*,3-*N*-carbonyl-3-(methylamino)-5-cyclohexene-1,2,4-triol] (^{1}H NMR, 250 MHz). From $CHCl_3$/ether, 3:1, 55 mg (70%, not optimized) colorless crystals were obtained, m.p. 112 to 113°C. – IR (KBr): ν̃ = 2110 cm^{-1}, 1780, 1735, 1420, 1400, 1370, 1330, 1290, 1230, 1100, 1085, 1050, 1020, 975, 765, 665. – ^{1}H NMR ($CDCl_3$): δ = 5.17 (dd, 1-H), 5.08 (ddd, 4-H), 4.71 (dd, 2-H), 4.03 (ddd, 6-H), 3.84 (dd, 3-H), 2.92 (s, NCH_3), 2.32 (dt, 5β-H), 2.16, 2.14 (s, CH_3), 1.96 (ddd, 5α-H); $J_{1,2}$ = 6.2, $J_{2,3}$ = 7.5, $J_{3,4}$ = 6, $J_{4,5\alpha}$ = 7.5, $J_{4,5\beta}$ = 5.2, $J_{5\alpha,5\beta}$ = 15, $J_{5\alpha,6}$ = 7.5, $J_{5\beta,6}$ = 5.2, $J_{6,1}$ = 3 Hz.

$C_{12}H_{16}N_4O_6$ (312.3) Calcd. C 46.15 H 5.16 N 17.94
Found C 46.12 H 5.10 N 17.82

DL-(1α,2β,3β,4α,6α)-6-Azido-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**7c**) (cf. *rac*-**7b**): 2.62 g (8.0 mmol) of *rac*-**5c**, 2.97 g (16.0 mmol) of hexamethylguanidinium azide, 50 ml of CH_3CN, 4 h, 40°C. From cyclohexane/ether, 10:1, 1.80 g (93%) colorless crystals, m.p. 94°C. – IR (KBr): ν̃ = 3600–3200 cm^{-1}, 2090, 1735, 1435, 1395, 1365, 1315, 1290, 1245, 1235, 1190, 1105, 1090, 1025, 1010, 920, 870, 835, 770, 675. – ^{1}H NMR ($CDCl_3$): δ = 4.48 (dd, 2-H), 4.16 (t, 1-H), 3.69 (ddd, 6-H), 3.63 (t, 3-H), 3.42 (ddd, 4-H), 3.42 (s, OCH_3), 2.97 (s, NCH_3), 2.82 (d, OH), 2.21 (dt, 5β-H), 1.84 (dt, 5α-H); $J_{1,2}$ = 3, $J_{2,3}$ = $J_{3,4}$ = 7.5, $J_{4,5\alpha}$ = 10, $J_{4,5\beta}$ = 5, $J_{5\alpha,5\beta}$ = 13, $J_{5\alpha,6}$ = 10, $J_{5\beta,6}$ = 5, $J_{6,1}$ = 3 Hz.

$C_9H_{14}N_4O_4$ (242.2) Calcd. C 44.63 H 5.82 N 23.13
Found C 44.29 H 5.81 N 22.97

DL-(1α,2β,3β,4α,6α)-1-O-Acetyl-6-azido-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**7d**) (cf. **7b**): 370 mg (1.0 mmol) of *rac*-**5d**, 372 mg (2.0 mmol) of hexamethylguanidinium azide, 10 ml of CH_3CN, 5 h, 40°C. Oil (<1% *rac*-**9d'**, ^{1}H NMR). From cyclohexane/ether, 5:1, 270 mg (96%) of colorless crystals were obtained, m.p. 87°C. – IR (KBr): ν̃ = 2100 cm^{-1}, 1770, 1745, 1425, 1400, 1375, 1290, 1240, 1220, 1105, 1075, 1025, 930, 830, 760, 680. – ^{1}H NMR ($CDCl_3$): δ = 5.28 (dd, 1-H), 4.58 (dd, 2-H), 3.79 (ddd, 6-H), 3.63 (t, 3-H), 3.46 (ddd, 4-H), 3.41 (s, OCH_3), 2.97 (s, NCH_3), 2.35 (dt, 5β-H), 2.15 (s, CH_3), 1.77 (ddd, 5α-H); $J_{1,2}$ = 5.2, $J_{2,3}$ = $J_{3,4}$ = 7.5, $J_{4,5\alpha}$ = 10.5, $J_{4,5\beta}$ = 5.2, $J_{5\alpha,5\beta}$ = 13.5, $J_{5\alpha,6}$ = 9, $J_{5\beta,6}$ = 5.2, $J_{6,1}$ = 3 Hz.

$C_{11}H_{16}N_4O_5$ (284.2) Calcd. C 46.47 H 5.67 N 19.71
Found C 46.21 H 5.67 N 19.44

DL-(1α,2β,3β,4α,6α)-6-Azido-2-O,3-N-carbonyl-4-O-(methoxymethyl)-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**7e**) (cf. *rac*-**7b**): 570 mg (1.60 mmol) of *rac*-**5e**, 590 mg (3.20 mmol) of hexamethylguanidium azide, 3 ml of acetonitrile, 6 h, 40°C. From ethyl acetate 550 mg (73%, not optimized) colorless crystals were obtained, m.p. 89°C. – IR (KBr): ν̃ = 3350 cm^{-1}, 2950, 2110, 1730, 1445, 1405, 1335, 1275, 1240, 1145, 1110, 1090, 1070, 1060, 1035, 990, 915, 845, 765, 670. – ^{1}H NMR ($CDCl_3$): δ = 4.71, 4.75 (CH_2), 4.61 (dd, 2-H), 4.15 (q, 1-H), 3.85–3.65 (m, 3-, 4-, 5-H), 3.41 (s, OCH_3), 3.22 (d, OH), 2.99 (s, NCH_3), 2.29 (dt, 5β-H), 1.95 (dt, 5α-H); J_{CH_2} = 6.5, $J_{1,2}$ = 4, $J_{2,3}$ = 7.5, $J_{4,5\alpha}$ = $J_{5\alpha,6}$ = 9.8, $J_{4,5\beta}$ = $J_{5\beta,6}$ = 4.5, $J_{5\alpha,5\beta}$ = 13.5, $J_{6,1}$ = $J_{1,OH}$ = 3.8 Hz.

$C_{10}H_{16}N_4O_5$ (272.3) Calcd. C 44.12 H 5.92 N 20.58
Found C 43.76 H 5.94 N 20.69

DL-(1α,2β,3β,4α)-2-O,3-N-Carbonyl-3-(methylamino)-4-O-methyl-5-cyclohexene-1,2,4-triol (*rac*-**9d**): In a dry box (N_2) a solution of 1.47 g (4.0 mmol) of *rac*-**5d** and 100 mg of 2-(*tert*-butylimino)-2-(diethylamino)hexahydro-1,3-dimethyl-1,3,2λ^5-diazaphosphorine (BEMP)[9] in 5 ml of dry CH_3CN ($KMnO_4$, B_2O_3) was stirred for 2 d at room temp. TLC ($CHCl_3/CH_3OH$ 25:1) showed two products besides a trace of starting material. 2 ml of acetic acid was added, the mixture dissolved in 10 ml of water, the solution extracted 5 times with 15 ml of ether each, dried ($MgSO_4$), concentrated in vacuo and the residue separated by column chromatography (silica, $CHCl_3/CH_3OH$, 25:1) to give 675 mg (70%) of olefin *rac*-**9d** (R_f = 0.42) and 160 mg (20%) of *rac*-**4c** (R_f = 0.35). – *rac*-**9d** crystallized from $CHCl_3$/ether as colorless needles, m.p. 120°C. – IR (KBr): ν̃ = 3000 cm^{-1}, 2960, 2830, 1760–1750, 1430, 1370, 1330, 1270, 1225, 1130, 1105, 1060, 1040, 1005, 960, 930, 890, 845, 750, 685, 625, 590, 510, 480, 460. – ^{1}H NMR ($CDCl_3$): δ = 5.98 (ddd, 6-H), 5.72 (dt, 5-H), 5.27 (ddt, 1-H), 4.58 (dd, 2-H), 3.82 (ddt, 4-H), 3.69 (dd, 3-H), 3.47 (s, OCH_3), 2.98 (s, NCH_3), 2.14 (s, CH_3); $J_{1,2}$ = $J_{3,4}$ = 6.8, $J_{2,3}$ = 10.2, $J_{4,5}$ = $J_{6,1}$ = $J_{4,1}$ = 2.2, $J_{5,6}$ = 10.5 Hz.

$C_{11}H_{15}NO_5$ (241.2) Calcd. C 54.77 H 6.26 N 5.81
Found C 54.71 H 6.33 N 5.69

DL-(1α,2β,3β,4α,6α)-6-Amino-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**10c**): A solution of 970 mg (4.0 mmol) of *rac*-**7c** in 40 ml of CH_3OH was hydrogenated

over 300 mg Pd/C (1 at H_2, 12 h, room temp., total conversion, TLC, $CHCl_3/CH_3OH$, 10:1). The catalyst was centrifugated off and the solution concentrated in vacuo. From CH_3OH/ether, 1:1, 850 mg (98%) colorless crystals were obtained, m.p. 160°C. – IR (KBr): $\tilde{\nu}$ = 3350 cm^{-1}, 3280, 2940–2900, 1795, 1595, 1435, 1390, 1365, 1300, 1270, 1230, 1200, 1110, 1075, 1025, 1000, 960, 830, 770, 765. – ^1H NMR ($CDCl_3/CD_3OD$, 1:1): δ = 4.49 (dd, 2-H), 3.91 (t, 1-H), 3.57 (dd, 3-H), 3.39 (ddd, 4-H), 3.38 (s, OCH_3), 2.93 (s, NCH_3), 2.98 (ddd, 6-H), 2.00 (dt, 5β-H), 1.51 (ddd, 5α-H); $J_{1,2}$ = 3.5, $J_{2,3}$ = 7, $J_{3,4}$ = 7.5, $J_{4,5\alpha}$ = 11, $J_{4,5\beta}$ = 4.5, $J_{5\alpha,5\beta}$ = 12, $J_{5\alpha,6}$ = 10.5, $J_{5\beta,6}$ = 4.5, $J_{6,1} \approx$ 3.5 Hz.

$C_9H_{16}N_2O_4$ (216.2) Calcd. C 49.99 H 7.46 N 12.94
Found C 49.43 H 7.77 N 12.59

DL-(1α,2β,3β,4α,6α)-1-O-Acetyl-6-(acetylamino)-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (*rac*-**10d**): 425 mg (2.0 mmol) of *rac*-**10c** was acetylated under standard conditions. From $CHCl_3$/ether, 1:5, 590 mg (98%) of colorless crystals were obtained, m.p. 204–205°C. – IR (KBr): $\tilde{\nu}$ = 3280 cm^{-1}, 3080, 2940, 1760–1750, 1640, 1550, 1435, 1400, 1375, 1300, 1230, 1120, 1100, 1065, 1045, 1025, 990, 830, 765, 590, 500. – ^1H NMR ($CDCl_3$): δ = 6.23 (d, NH), 5.04 (dd, 1-H), 4.54 (dd, 2-H), 4.49 (dt, 6-H), 3.71 (dd, 3-H), 3.61 (ddd, 4-H), 3.45 (s, OCH_3), 2.90 (s, NCH_3), 2.10 (s, CH_3), 2.05 (dt, 5β-H), 1.96 (s, CH_3), 1.82 (ddd, 5α-H); $J_{1,2}$ = 6, $J_{2,3}$ = 7, $J_{3,4}$ = 4.5, $J_{4,5\alpha}$ = 7, $J_{4,5\beta}$ = 3.8, $J_{5\alpha,5\beta}$ = 13.5, $J_{5\alpha,6}$ = 7.5, $J_{5\beta,6}$ = $J_{6,1}$ = 3.8 Hz.

$C_{13}H_{21}N_2O_6$ (301.3) Calcd. C 51.99 H 6.71 N 9.33
Found C 51.70 H 6.98 N 9.15

DL-(1α,2β,3β,4α,6α)-6-Ammonio-4-O-methyl-3-(methylammonio)-1,2,4-cyclohexanetriol Sulfate (rac-Sporamine Sulfate) (*rac*-**11**): To a solution of 540 mg (2.5 mmol) of *rac*-**10c** in 20 ml of water/CH_3OH, 1:1, 900 mg (3.0 mmol) of $Ba(OH)_2 \cdot 8\ H_2O$ was added and heated at reflux for 4 h. It was neutralized with ca. 0.01 ml of conc. H_2SO_4, the microcrystalline $BaSO_4$ centrifugated off, and the solution concentrated in vacuo. From water/CH_3OH/ether, 1:1:2, 670 mg (90%) of colorless cubes were obtained, dec. >300°C. – IR (KBr): $\tilde{\nu}$ = 3600–3380 cm^{-1}, 3240, 3100–2500, 2140, 1630, 1555, 1420, 1410, 1380, 1330, 1290, 1205, 1105, 1040, 970, 650, 615, 600. – ^1H NMR ($CDCl_3$): δ = 4.35 (t, 1-H), 4.16 (t, 2-H), 3.96–3.75 (m, 4-, 6-H), 3.46 (s, OCH_3), 3.22 (dd, 3-H), 2.76 (s, NCH_3), 2.46 (dt, 5β-H), 1.70 (ddd, 5α-H); $J_{1,2}$ = $J_{2,3}$ = 3, $J_{3,4}$ = $J_{4,5\alpha}$ = 10.5, $J_{4,5\beta}$ = 4.5, $J_{5\alpha,5\beta}$ = 12, $J_{5\alpha,6} \approx$ 11, $J_{5\beta,6} \approx$ 4.5, $J_{6,1}$ = 3 Hz.

$C_8H_{20}N_2O_3 \cdot SO_4 \cdot H_2O$ (297.2) Calcd. C 32.35 H 7.46 N 9.43
Found C 32.76 H 7.39 N 9.32

DL-(1α,2α,3β,4β,5α)-1,2-Anhydro-3-O,4-N-carbonyl-4-(methylamino)-5-O-[(R)-(1-phenylethyl)carbamoyl]-1,2,3,5-cyclohexanetetrol (**12/12'**): A solution of 1.08 g (5.8 mmol) of *rac*-**4a** and 1.65 g (11.6 mmol) of (*R*)-1-phenylethyl isocyanate in 50 ml of freshly dried dioxane was heated at reflux for 4 h. The solution was concentrated in vacuo and dried (0.01 Torr). The oily main component was separated from three UV-active unknown components (totally <5%) by rapid chromatography (silica, cyclohexane/ethyl acetate, 1:1) to give the diastereomers **12/12'** as a hard foam, 1.81 g (94%). The product was characterized by IR and ^1H-NMR spectra. – IR (KBr): $\tilde{\nu}$ = 3600–3200 cm^{-1}, 3080, 3055, 3020, 2960, 2920, 1770–1740, 1720–1700, 1520, 1445, 1420, 1395, 1370, 1295, 1235, 1115, 1060, 1050, 1030, 950, 910, 850, 810, 760, 700, 660. – ^1H NMR ($CDCl_3$, two rotamers): δ = 7.4–7.2 (m, 5H), 5.49 (dd, NH), 5.0–4.7 (m, 3-, 5-, 1'-H), 3.76 (dd, 4-H)*, 3.67 (dd, 4-H)*, 3.25 (m, 1-, 2-H), 2.87 (s, NCH_3)*, 2.83 (s, NCH_3)*, 2.3–2.1 (m, 6α-, 6β-H), 1.46 (d, CH_3). There is no better signal separation in [D_6]benzene or [D_3]acetonitrile. – ^1H NMR ($CDCl_3$, 55°C): δ = 7.4–7.2 (m, 5H), 5.30 (dd, NH), 4.92 (m, 5-H), 4.81 (d, 3-H), 4.76 (q, 1'-H), 3.64 (dd, 4-H), 3.22 (m, 1-, 2-H), 2.83 (s, NCH_3), 2.18 (m, 6α, 6β-H), 1.48 (d, CH_3)*, 1.45 (d, CH_3)*; $J_{3,4}$ = 8.2, $J_{4,5}$ = 4.5, J_{1',CH_3} = 7.0 Hz.

DL-(1α,2β,3β,4α,6β)-6-Bromo-2-O,3-N-carbonyl-3-(methylamino)-4-O-[(R)-(1-phenylethyl)carbamoyl]-1,2,4-cyclohexanetriol (**13a/13a'**)

a) To a solution of 0.60 g (1.8 mmol) of **12/12'** in 20 ml of CH_2Cl_2 0.42 g (2.0 mmol) of tetraethylammonium bromide and a catalytic amount of Et_2O-BF_3 were added at 0°C. After 30 min the reaction was complete (TLC, chloroform/CH_3OH 10:1; R_f = 0.45). Filtration over a short pad of silica (ethyl acetate) gave 0.68 g (91%) of **13a/13a'** as colorless oil.

b) A solution of 200 mg (0.75 mmol) of *rac*-**5h** and 111 mg (0.78 mmol) of (*R*)-1-phenylethyl isocyanate in 10 ml of freshly dried dioxane was heated at reflux for 2 h. The solution was concentrated in vacuo and the residue separated by column chromatography (silica, cyclohexane/ethyl acetate, 1:1, incomplete conversion) to give 190 mg (61%, based on conversion) of **13a/13a'** besides 70 mg (35%) of unreacted *rac*-**5h**. – IR (KBr): $\tilde{\nu}$ = 3402 cm^{-1}, 2974, 1763, 1695, 1530, 1451, 1427, 1402, 1371, 1350, 1320, 1298, 1254, 1102, 1089, 1076, 1055, 1016, 878, 824, 765, 704, 661. – ^1H NMR ($CDCl_3$, two rotamers): δ = 7.45–7.15 (m, 5H), 6.08, 5.83 (d, NH), 5.07, 4.96 (br. s, 4-H), 4.82 (OH), 4.78 (dq, 1'-H), 4.48 (dd, 2-H), 4.11 (m, 3-H), 3.74 (m, 1-, 6-H), 2.77 (s, NCH_3), 2.52 (m, 5α-H), 2.15 (m, 5β-H), 1.48 (d, CH_3). – MS (70 eV, CI, NH_3): *m/z* = 432, 430 (MNH_4^+), 350 (–HBr), 333, 291, 246, 203, 185, 149, 126, 104.

$C_{17}H_{21}BrN_2O_5$ (413.3)

DL-(1α,2β,3β,4α,6β)-1-O-Acetyl-6-bromo-2-O,3-N-carbonyl-3-(methylamino)-4-O-[(R)-(1-phenylethyl)carbamoyl]-1,2,4-cyclohexanetriol (**13b/13b'**): 206 mg (0.5 mmol) of the mixture of **13a/13a'** was acetylated under standard conditions; 211 mg (93%), colorless crystals. – IR (KBr): $\tilde{\nu}$ = 3342 cm^{-1}, 3058, 2848, 1995, 1872, 1782, 1522, 1448, 1316, 1235, 1136, 1110, 1055, 906, 886, 866, 823, 765, 697, 659, 636. – ^1H NMR ($CDCl_3$): δ = 7.45–7.22 (m, 5H), 5.48 (d, NH), 5.38 (d, NH), 5.24, 5.05 (dd, 1-H), 5.14 (br. s, 4-H), 4.82 (m, 1'-H), 4.52 (m, 2-H), 4.13 (m, 3-H), 3.89, 3.80 (d, 6-H), 2.88, 2.84 (s, NCH_3), 2.53 (m, 5α-H), 2.25 (m, 5β-H), 2.14 (s, $COCH_3$), 1.50 (d, CH_3); $J_{1,2}$ = $J_{2,3}$ = $J_{1',NH}$ = J_{1',CH_3} = 7.0, $J_{1,6}$ = 10.5 Hz. – MS (70 eV, CI, NH_3): *m/z* = 474, 472 (MNH_4^+), 327, 325, 247, 245, 187, 170, 124, 108.

$C_{19}H_{23}BrN_2O_6$ (455.3)

DL-(1α,2β,3β,4α,6β)-6-Bromo-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1-O-[(R)-1-(phenylethyl)carbamoyl]-1,2,4-cyclohexanetriol (**15/15'**): A solution of 470 mg (1.17 mmol) of *rac*-**5l** in 2 ml (*R*)-1-phenylethylamine was stirred for 45 min at 30°C (total conversion, TLC, chloroform/CH_3OH, 10:1). The excess of the amine was distilled off (0.01 Torr), the residue dissolved in 50 ml of CH_2Cl_2 and extracted twice with 2 N H_2SO_4 in order to remove remaining amine. The organic layer was dried ($MgSO_4$) and concentrated in vacuo to give 470 mg (93%) of colorless crystals. – IR (KBr): $\tilde{\nu}$ = 3398 cm^{-1}, 3348, 3052, 2968, 1799, 1762, 1526, 1448, 1388, 1299, 1241, 1145, 1109, 1079, 1024, 881, 770, 697, 659. – ^1H NMR ($CDCl_3$, 50°C): δ = 7.4–7.2 (m, 5H), 5.18 (d, NH), 5.07 (dd, 1-H), 4.97 (m, 1'-H), 4.48 (dd, 2-H), 4.17 (ddd, 6-H), 3.70 (m, 3-H), 3.63 (m, 4-H), 3.36 (s, OCH_3), 2.84 (s, NCH_3), 2.40 (m, 5α-H), 2.14 (ddd, 5β-H), 1.49 (d, CH_3); $J_{1,2}$ = $J_{2,3}$ = 6.8, $J_{3,4}$ = $J_{4,5\alpha}$ = 3.8, $J_{4,5\beta}$ = 3.0, $J_{5\alpha,5\beta}$ = 14.2, $J_{5\alpha,6}$ = 3.8, $J_{5\beta,6}$ = 9.8, $J_{1,6}$ = 9.0, $J_{1',NH}$ = 7.5 Hz.

DL-(1α,2β,3β,4α,6α)-2-O,3-N;1-O,6-N-Dicarbonyl-4-O-methyl-3-(methylamino)-6-[(R)-1-(phenylethyl)amino]-1,2,4-cyclohexane-triol (**16/16'**): A solution of 84 mg (0.2 mmol) of **15/15'** and 25 mg (0.1 mmol) of BEMP in 1 ml of acetonitrile was stirred for

12 h at room temp. (ca. 50% conversion) and concentrated in vacuo. Starting material and base were separated by column chromatography (silica, cyclohexane/ethyl acetate, 1:3) to give **16** and **16'** in a ratio of 1:1.6 (^{1}H-NMR) as hard foam (de = 23%). With equimolar amount of base the conversion is quantitative, the ratio of products hence 1:1. – IR (KBr): $\tilde{\nu}$ = 3568 cm^{-1}, 3472, 2974, 1765, 1734, 1514, 1492, 1448, 1423, 1294, 1271, 1187, 1122, 1101, 1061, 1035, 966, 830, 800, 786, 754, 712, 696, 636. – **16**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.45–7.30 (m, 5H), 5.17 (q, 1'-H), 4.82 (dd, 2-H), 4.52 (dd, 1-H), 3.78 (dd, 3-H), 3.61 (dddd, 6-H), 3.33 (s, OCH_3), 3.23 (ddd, 4-H), 2.91 (s, OCH_3), 1.82 (d, 5α-H)*, 1.72 (d, 5β-H)*, 1.70 (d, CH_3); $J_{1,2}$ = 4.0, $J_{2,3}$ = 9.0, $J_{3,4}$ = 5.0, $J_{4,5\alpha}$ = 2.5, $J_{4,5\beta}$ = 8.5, $J_{5\alpha,6}$ = 6.0, $J_{5\beta,6}$ = 6.5, $J_{1,6}$ = 8.5, J_{1',CH_3} = 7.0, $J_{5\alpha,5\beta}$ = 14.0 Hz. – ^{13}C NMR ($CDCl_3$): δ = 156.1 (CO), 138.9 (C_s), 128.9 (C_o), 128.3 (C_p), 127.2 (C_m), 75.3 (C-4), 71.9 (C-2), 71.0 (C-1), 58.3 (C-3), 56.9 (OCH_3), 53.1 (C-1'), 50.2 (C-6), 30.2 (NCH_3), 25.6 (C-5), 18.5 (CH_3). – **16'**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.4–7.3 (m, 5-H), 5.02 (q, 1'-H), 4.81 (dd, 2-H), 4.64 (dd, 1-H), 3.97 (dddd, 6-H), 3.70 (dd, 3-H), 3.17 (s, OCH_3), 3.14 (ddd, 4-H), 2.88 (s, OCH_3), 1.72 (d, CH_3), 1.42 (d, 5α-H)*, 1.18 (d, 5β-H)*; $J_{1,2}$ = 4.0, $J_{2,3}$ = 9.0, $J_{3,4}$ = 5.0, $J_{4,5\alpha}$ = 2.5, $J_{4,5\beta}$ = 8.5, $J_{5\alpha,6}$ = 6.0, $J_{5\beta,6}$ = 6.5, $J_{1,6}$ = 8.5, J_{1',CH_3} = 7.0, $J_{5\alpha,5\beta}$ = 14.0 Hz. – ^{13}C NMR ($CDCl_3$): δ = 156.4 (CO), 140.5 (C_s), 128.7 (C_o), 128.2 (C_p), 127.4 (C_m), 75.1 (C-4), 71.7 (C-2), 70.9 (C-1), 58.3 (C-3), 56.6 (OCH_3), 52.6 (C-1'), 49.9 (C-6), 30.1 (NCH_3), 25.5 (C-5), 17.4 (CH_3).

$C_{18}H_{22}N_2O_5$ (346.4)

DL-(1α,2β,3α,4α,5β)-3-O,4-N-Carbonyl-1-O-[(1S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-ylmethylsulfonyl]-5-O-methyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (**17a/17a'**): A suspension of 1.16 g (5.0 mmol) of D-(+)-camphor-10-sulfonic acid in 10 ml of CH_2Cl_2 was added in portions to a solution of 660 mg (3.3 mmol) of *rac*-**4c** in 10 ml CH_2Cl_2. The solution became clear. After 2 h at room temp. it was concentrated in vacuo, the residue filtered over a short pad of silica (cyclohexane/ethyl acetate, 1:3) and crystallized from ethyl acetate to give 870 mg (61%) of colorless crystals. – IR (KBr): ν = 3338 cm^{-1}, 2962, 1748, 1449, 1427, 1392, 1342, 1288, 1194, 1158, 1094, 1046, 970, 905, 886, 845, 806, 779, 766, 660. – ^{1}H NMR ($CDCl_3$): δ = 4.84, 4.82 (dd, 1-H), 4.53 (dd, 3-H), 3.94–3.70 (m, 2-, 4-, 5-H), 3.75, 3.60 (d, 10'-H), 3.50 (d, OH), 3.43, 3.42 (s, OCH_3), 3.13, 3.10 (d, 10'-H), 2.85, 2.84 (s, NCH_3), 2.53–2.32 (m, 5'eq-, 3'eq-, 6β-H), 2.19–2.00 (m, 4'-, 5'ax-H), 1.98, 1.96 (d, 3'ax-H), 2.00 to 1.70 (m, 6α-, 6'eq-H), 1.48 (ddd, 6'ax-H), 1.10 (s, CH_3), 1.08 (s, CH_3), 0.90 (s, CH_3), 0.87 (s, CH_3); $J_{1,2}$ = 9.0, $J_{2,3}$ = 6.8, $J_{3,4}$ = 6.8, $J_{10',10'}$ = 15.0, $J_{3'ax,4'}$ = 18.0 Hz.

$C_{19}H_{29}NO_8S$ (431.5) Calcd. C 52.89 H 6.77 N 3.25
Found C 52.76 H 6.75 N 3.23

DL-(1α,2β,3α,4α,5β)-2-O-Acetyl-3-O,4-N-carbonyl-1-O[(1S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-ylmethylsulfonyl]-5-O-methyl-4-(methylamino)-1,2,3,5-cyclohexanetetrol (**17b/17b'**): The mixture **17a/17a'** was acetylated under standard conditions. Colorless crystals. – IR (KBr): $\tilde{\nu}$ = 3438 cm^{-1}, 2954, 1765, 1626, 1447, 1423, 1361, 1284, 1221, 1170, 1099, 1048, 966, 915, 846, 800, 763, 656. – ^{1}H NMR ($CDCl_3$): δ = 5.22, 5.21 (dd, 2-H), 4.93, 4.88 (ddd, 1-H), 4.55, 4.53 (dd, 3-H), 3.75 (m, 4-, 5-H), 3.57, 3.55 (d, 10'-H), 3.41 (s, OCH_3), 3.04, 2.96 (d, 10'-H), 2.84 (s, NCH_3), 2.46–2.28 (m, 5'eq-, 3'eq-, 6β-H), 2.11 (s, $COCH_3$), 2.14–1.94 (m, 4'-, 5'ax-, 6α-H), 1.94 (d, 3'ax-H)*, 1.92 (d, 3'ax-H)*, 1.66 (ddd, 6'eq-H), 1.43 (ddd, 6'ax-H), 1.08 (s, CH_3), 1.07 (s, CH_3), 0.87 (s, CH_3), 0.85 (s, CH_3); $J_{1,2}$ = 9.0, $J_{2,3}$ = 6.8, $J_{3,4}$ = 6.8, $J_{10',10'}$ = 15.0, $J_{3'ax,4'}$ = 18.0 Hz.

$C_{21}H_{31}NO_9S$ (473.5) Calcd. C 53.27 H 6.60 N 2.96
Found C 52.94 H 6.61 N 2.96

DL-(1α,2β,3α,4α,5β)-3-O,4-N-Carbonyl-1-O-[(1S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-ylmethylsulfonyl]-5-O-methyl-4-(methylamino)-2-O-pivaloyl-1,2,3,5-cyclohexanetetrol (**17c/17c'**): To a solution of 432 mg (1.0 mmol) of **17a/17a'** in 10 ml of CH_2Cl_2 204.8 mg (1.1 mmol) of pivalic anhydride, 0.5 ml of triethylamine, and a catalytical amount of DMAP were added at 0°C, the solution stirred for 1 h at room temp., extracted with 2 N H_2SO_4 and buffer solution (pH 7) and concentrated in vacuo. The oily residue was crystallized from ethyl acetate/ether, 1:1, to give 450 mg (87%) of colorless needles. – IR (KBr): $\tilde{\nu}$ = 3448 cm^{-1}, 2964, 1773, 1740, 1623, 1476, 1422, 1389, 1356, 1338, 1280, 1250, 1196, 1170, 1139, 1100, 1027, 971, 959, 892, 842, 807, 789, 750, 672, 654. – ^{1}H NMR ($CDCl_3$): δ = 5.24, 5.23 (dd, 2-H), 4.95, 4.94 (ddd, 1-H), 4.55 (dd, 3-H), 3.83–3.69 (m, 4-, 5-H), 3.60, 3.58 (d, 10'-H), 3.45 (s, OCH_3)*, 3.44 (s, OCH_3)*, 3.05 (d, 10'-H)*, 3.03 (d, 10'-H)*, 2.95 (s, NCH_3)*, 2.94 (s, NCH_3)*, 2.46–2.32 (m, 5'eq-, 3'eq-, 6β-H), 2.15–2.00 (m, 4'-, 5'ax-, 6α-H), 1.70 (ddd, 6'eq-H), 1.45 (ddd, 6'ax-H), 1.23 [s, $C(CH_3)_3$], 1.10 (s, CH_3)*, 1.09 (s, CH_3)*, 0.87 (s, CH_3)*, 0.86 (s, CH_3)*; $J_{1,2}$ = 9.0, $J_{2,3}$ = 6.8, $J_{3,4}$ = 6.8, $J_{10',10'}$ = 15.0, $J_{3'ax,4'}$ = 18.0 Hz.

$C_{24}H_{37}NO_9S$ (515.6) Calcd. C 55.91 H 7.23 N 2.72
Found C 55.71 H 7.29 N 2.66

(–)-(1'S) and (+)-(1'R)-(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-1-O-(–)-camphanoyl-6-iodo-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**19** and **19'**): Preparation as usual (5.0 mmol). **19/19'** cannot be distinguished by TLC (cyclohexane/ethyl acetate; CH_2Cl_2/acetone; chloroform/CH_3OH) or separated by normal or flash chromatography. Separation by HPLC: cyclohexane/ethyl acetate, 1.5:1; prepacked column (Bischoff), Merck LiChrosorb 100, 60 mg per injection, R_f (cyclohexane/ethyl acetate, 1.5:1) = 0.1. – **19**: colorless crystals, m.p. 169–173°C; $[\alpha]_D$ = –101 (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 3818 cm^{-1}, 3502, 2952, 1780, 1738, 1456, 1425, 1396, 1337, 1312, 1265, 1199, 1162, 1122, 1094, 1060, 1046, 1019, 987, 953, 927, 894, 820, 777, 754, 731, 659. – ^{1}H NMR ($CDCl_3$): δ = 5.38 (dd, 1-H), 4.55 (dd, 2-H), 4.28 (ddd, 6-H), 3.88 (dd, 3-H), 3.51 (m, 4-H), 3.41 (s, OCH_3), 2.85 (s, NCH_3), 2.70 (dddd, 5α-H), 2.49 (m, 6'eq-H), 2.27 (dddd, 5β-H), 2.11 (m, 5'eq-H), 1.95 (m, 6'ax-H), 1.70 (m, 5'ax-H), 1.14–1.0 (s, 7'-, 4'-CH_3); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,5\alpha}$ = 1.0, $J_{4,5\alpha}$ = 3.8, $J_{4,5\beta}$ = 2.3, $J_{5\alpha,5\beta}$ = 14.5, $J_{5\alpha,6}$ = 3.8, $J_{5\beta,6}$ = $J_{6,1}$ = 11.3 Hz. – **19'**: colorless crystals, m.p. 181–185°C; $[\alpha]_D$ = 81 (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 3476 cm^{-1}, 2960, 1775, 1631, 1466, 1423, 1401, 1332, 1315, 1259, 1165, 1107, 1062, 1034, 955, 928, 884, 777, 660. – ^{1}H NMR ($CDCl_3$): δ = 5.41 (dd, 1-H), 4.56 (dd, 2-H), 4.24 (ddd, 6-H), 3.88 (dd, 3-H), 3.51 (m, 4-H), 3.41 (s, OCH_3), 2.85 (s, NCH_3), 2.70 (dddd, 5α-H), 2.49 (m, 6'eq-H), 2.27 (dddd, 5β-H), 2.11 (m, 5'eq-H), 1.95 (m, 6'ax-H), 1.70 (m, 5'ax-H), 1.2–1.0 (3s, 3 CH_3); $J_{1,2}$ = $J_{2,3}$ = 7.5, $J_{3,5\alpha}$ = 1.0, $J_{4,5\alpha}$ = 3.8, $J_{4,5\beta}$ = 2.3, $J_{5\alpha,5\beta}$ = 14.5, $J_{5\alpha,6}$ = 3.8, $J_{5\beta,6}$ = $J_{6,1}$ = 11.3 Hz.

$C_{19}H_{26}INO_7$ (507.3) Calcd. C 44.98 H 5.17 N 2.76
Found C 45.11 H 5.20 N 2.80

(+)-(1'S) and (–)-(1'R)-(1α,2β,3β,4α,6α)-6-Azido-1-O-(–)-camphanoyl-2-O,3-N-carbonyl-4-O-metyl-3-(methylamino)-1,2,4-cyclohexanetriol (**20** and **20'**): 746 mg (4.72 mmol) of tetramethylguanidinium azide were ground under Ar, dried in vacuo (0.01 Torr) and added to a solution of 1.2 g (2.36 mmol) of **19** (**19'**) in 15 ml of dry acetonitrile (molecular sieve, 3 Å). After 1 d at 50°C the conversion was complete (TLC, ethyl acetate/CH_3OH, 20:1; **19**(**19'**) R_f = 0.55; **20**(**20'**) R_f = 0.5). The molecular sieve was filtered off, the solution concentrated in vacuo and filtered through a short pad of silica (ethyl acetate) in order to remove the salts. Crystallization from ethyl acetate gave 980 mg (98%). – **20**: Colorless crystals, m.p. 135°C; $[\alpha]_D$ = 9 ± 1 (*c* = 1, $CHCl_3$). – IR (KBr): 3626 cm^{-1}, 3522, 2962, 2098, 1776, 1634, 1445, 1392, 1257, 1194,

1165, 1101, 1064, 928, 760, 731, 674, 627. – ^{1}H NMR ($CDCl_3$): δ = 5.44 (dd, 1-H), 4.55 (dd, 2-H), 3.88 (ddd, 6-H), 3.60 (t, 3-H), 3.48 (ddd, 4-H), 3.42 (s, OCH_3), 2.99 (s, NCH_3), 2.43 (ddd, 6'eq-H), 2.36 (ddd, 5β-H), 2.2 – 1.6 (m, 5α-, 5'-, 6'-H), 1.13 (s, CH_3)*, 1.10 (s, CH_3)*, 1.00 (s, CH_3)*; $J_{1,2}$ = 4.5, $J_{2,3}$ = $J_{3,4}$ = 7.5, $J_{5\alpha,5\beta}$ = 14.0, $J_{5\alpha,6}$ = 8.0, $J_{5\beta,6}$ = 4.5, $J_{6,1}$ = 3.7 Hz. – **20'**: Colorless crystals, m.p. 105°C, $[\alpha]_D$ = −18 ± 1 (*c* = 1, $CHCl_3$). – IR (KBr): $\tilde{\nu}$ = 3480 cm^{-1}, 2960, 2098, 1773, 1464, 1394, 1265, 1195, 1166, 1105, 1059, 954, 930, 778, 673. – ^{1}H NMR ($CDCl_3$): δ = 5.45 (dd, 1-H), 4.59 (dd, 2-H), 3.93 (ddd, 6-H), 3.64 (t, 3-H), 3.48 (ddd, 4-H), 3.41 (s, OCH_3), 2.99 (s, NCH_3), 2.49 (ddd, 6'eq-H), 2.33 (ddd, 5β-H), 2.2 – 1.6 (m, 5α-, 5'-, 6'-H), 1.13 (s, CH_3)*, 1.08 (s, CH_3)*, 1.01 (s, CH_3)*; $J_{1,2}$ = 4.5, $J_{2,3}$ = $J_{3,4}$ = 7.5, $J_{5\alpha,6}$ = 8.0, $J_{5\beta,6}$ = 4.5, $J_{6,1}$ = 3.7 Hz.

(+)-(1S)- and (−)-(1R)-(1α,2β,3β,4α,6α)-6-Azido-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**7c** and *ent*-**7c**): Treatment of 1.09 g (2.56 mmol) of **20**(**20'**) with NaOH in methanol gave 580 mg (93%) of **7c** (*ent*-**7c**). – **7c**: $[\alpha]_D$ = 55.1; *ent*-**7c**: $[\alpha]_D$ = −54.7 (*c* = 1, $CHCl_3$).

(+)-(1S)- and (−)-(1R)-(1α,2β,3β,4α,6α)-6-Amino-2-O,3-N-carbonyl-4-O-methyl-3-(methylamino)-1,2,4-cyclohexanetriol (**10c** and *ent*-**10c**): 200 mg (0.80 mmol) of **7c** (*ent*-**7c**) was hydrogenated as described for *rac*-**10c**. – **10c**: $[\alpha]_D$ = +56.0; *ent*-**10c**: $[\alpha]_D$ = −55.6 (*c* = 1, $CHCl_3$).

(+)-(1S) and (−)-(1R)-(1α,2β,3β,4α,6α)-6-Ammonio-4-O-methyl-3-(methylammonio)-1,2,4-cyclohexanetriol Sulfate (**11** and *ent*-**11**) (cf. *rac*-**11**): **11**: $[\alpha]_D$ = +51.9. *ent*-**11**: −52.5 (*c* = 1, H_2O). **3** (*ent*-**3**) was obtained from **11** (*ent*-**11**) by neutralization with $Ba(OH)_2$. After filtration the clear solution was used for the rotation measurements. – **3**: $[\alpha]_D$ = +69.3 (ref.[3] +75). *ent*-**3**: $[\alpha]_D$ = −65 (*c* = 1, H_2O).

CAS Registry Numbers

3: 70580-80-2 / *ent*-**3**: 121916-71-0 / *rac*-**4a**: 94592-12-8 / *rac*-**4c**: 121916-52-7 / *rac*-**4d**: 121916-53-8 / *rac*-**5a**: 121811-35-6 / *rac*-**5b**: 121811-37-8 / *rac*-**5c**: 121811-38-9 / *rac*-**5d**: 121811-39-0 / *rac*-**5e**: 121811-40-3 / *rac*-**5f**: 121811-41-4 / *rac*-**5h**: 121811-42-5 / *rac*-**5i**: 121811-43-6 / *rac*-**5j**: 121811-44-7 / *rac*-**5k**: 121811-45-8 / *rac*-**5l**: 121811-46-9 / *rac*-**5m**: 121844-96-0 / *rac*-**5n**: 121811-47-0 / *rac*-**5o**: 121811-48-1 / *rac*-**6a**: 121811-34-5 / *rac*-**6b**: 121811-36-7 / *rac*-**6c**: 121811-49-2 / *rac*-**6d**: 121811-50-5 / *rac*-**6e**: 121811-51-6 / *rac*-**6f**: 121811-52-7 / *rac*-**6g**: 121811-53-8 / *rac*-**7b**: 121916-54-9 / **7c**: 121916-63-0 / *rac*-**7c**: 121958-01-8 / *ent*-**7c**: 121916-64-1 / *rac*-**7d**: 121811-55-0 / *rac*-**7e**: 121811-56-1 / *rac*-**9b**: 121811-54-9 / *rac*-**9d**: 121811-57-2 / **10c**: 121916-65-2 / *rac*-**10c**: 121916-55-0 / *ent*-**10c**: 121916-66-3 / *rac*-**10d**: 121916-56-1 **11**: 121916-68-5 / *rac*-**11**: 121916-57-2 / *ent*-**11**: 121916-70-9 / **12**: 121811-58-3 / **12'**: 121916-58-3 / **13a**: 121811-59-4 / **13a'**: 121811-60-7 / **13b**: 121811-61-8 / **13b'**: 121811-62-9 / **15**: 121844-69-7 / **15'**: 121844-97-1 / **16**: 121811-63-0 / **16'**: 121916-59-4 / **17a**: 121811-64-1 / **17a'**: 121916-60-7 / **17b**: 121811-65-2 / **17b'**: 121916-61-8 / **17c**: 121917-62-2 / **17c'**: 121811-66-3 / **19**: 121811-67-4 / **19'**: 121916-62-9 / **20**: 121811-68-5 / **20'**: 121811-69-6 / (R)-1-phenylethylamine: 3886-69-9 / (R)-1-phenylethyl isocyanate: 33375-06-3 / (+)-camphor-10-sulfonic acid: 3144-16-9

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