LIEBIGS ANNALEN DER CHEMIE

HERAUSGEGEBEN VON DER
GESELLSCHAFT DEUTSCHER CHEMIKER

JAHRGANG 1986 · HEFT 12 · SEITE 2009–2182

Dieses Heft wurde am 12. Dezember 1986 ausgegeben

VCH Verlagsgesellschaft

Aminoglycoside Antibiotics – Fortamine Aglyca Total Synthesis, Optical Resolution, Chemical Modifications

Jürgen Schubert, Reinhard Schwesinger, Lothar Knothe, and *Horst Prinzbach**

Institut für Organische Chemie und Biochemie, Universität Freiburg, Albertstraße 21, D-7800 Freiburg i. Br.

Received May 9, 1986

Starting from the dianhydro-*epi*-inositol **10** (available ultimately from benzene) an expedient total synthesis of enantiomerically pure (+)/(−)-de-*O*-methylfortamines (derivatives) has been developed. Key steps are the regiospecific epoxide openings which occur intramolecularly in the diepoxybis(urethane) **11** and intermolecularly by (+)-1-phenylethylamine in the epoxyurethanes *rac*-**13**. The diastereomeric adducts (**30, 32**) are quantitatively separated by crystallization/chromatography. Following hydrogenation, natural and nonnatural *cis*-1,4-inosadiamines are obtained optically pure [e.g. fortamine (−)-**1**, *ent*-fortamine (+)-**1**, 3-*O*-demethylfortamine (−)-**38**, *ent*-3-*O*-demethylfortamine (+)-**38**]. This approach, which was optimized by numerous model reactions, allows wide chemical modifications and leads among others to 3-*O*-demethylfortamine and *ent*-fortamine derivatives in which only the (6)4-OH-group, the one to be glycosidated, remains unprotected.

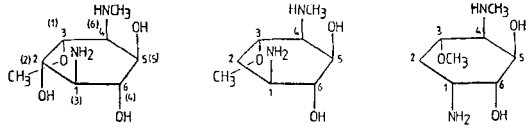
Aminoglycosid-Antibiotika – Fortamin-Aglyca
Totalsynthese, Racemattrennung, chemische Modifizierungen

Ausgehend vom Dianhydro-*epi*-inosit **10** (letztlich erhältlich aus Benzol) wurde eine leistungsfähige Synthese für enantiomerenreine (+)/(−)-Des-*O*-methylfortamine (Derivate) entwickelt. Zentrale Schritte sind die regiospezifischen Epoxidöffnungen, intramolekular beim Diepoxybis(urethan) **11** und intermolekular mit (+)-1-Phenylethylamin bei den Epoxyurethanen *rac*-**13**. Die diastereomeren Addukte (**30, 32**) können verlustfrei durch Kristallisation/Chromatographie getrennt werden. Nach hydrierender Spaltung werden natürliche und nichtnatürliche *cis*-1,4-Inosadiamine enantiomerenrein erhalten [z.B. Fortamin (−)-**1**, *ent*-Fortamin (+)-**1**, 3-*O*-Desmethylfortamin (−)-**38**, *ent*-3-*O*-Desmethylfortamin (+)-**38**)]. Der in zahlreichen Modellreaktionen optimierte Syntheseweg erlaubt breite che-

0170–2041/86/1212–2009 $ 02.50/0

mische Modifizierungen und führt u.a. zu 3-*O*-Desmethylfortamin- und *ent*-Fortamin-Derivaten, in denen nur die zur Glycosidierung gebrauchte (6)4-OH-Gruppe ungeschützt bleibt.

Fortamine (**1**)*), sannamine (**2**), and sporamine (**3**) are the aglycone components of a recently discovered family of aminoglycoside antibiotics, i.e. fortimicins[1-8] ("astromicins"[9]), sannamycins[10-13], istamycins[14-16], sporaricins[17-19], lysinomycins[20,21].



(−)-1 (1R) (−)-2 (−)-3

These structurally similar systems exhibit a broad activity spectrum against both Gram-negative and -positive bacteria[22] and are of additional interest on account of their reduced nephro- and ototoxicity as well as their activity against aminoglycoside-resistent strains[23].

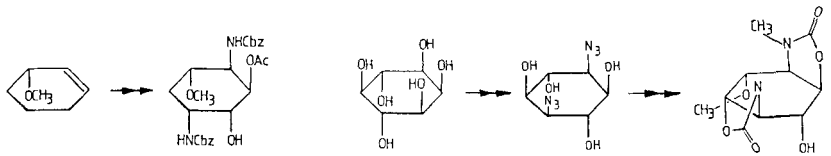
A peculiarity of this new class of antibiotics is their structural simplicity: They consist of only one monosaccharide (purpurosamine) and aglycone moiety. Information concerning structure – activity relationship, especially in fortimicins, can be summarized for the aglycone part in the following way:

1) The amino functions in 1,4-position (*cis*- or *trans*) and the 5-OH group[24] are essential. Absence of the 4-*N*-methyl group[25] and the 4-*N*-acyl group[11,14,17,26] nearly always results in entire loss of activity (except for lysinomycins). Alterations of the acyl group have positive effects only in a few cases[4,27].

2) The 2- and 3-positions can be modified in a wide range with favourable consequences on the antibacterial activity. To this group belong the 2-deoxy compounds (sannamycins, istamycins, sporaricins), the 3-*O*-demethyl derivatives[4,5,11,25], 3-demethoxy-3-fluoro-sporaricin[18], and 2-deoxy-3-demethoxyfortimicin A[6].

Several total syntheses of aglycones **1**–**3** from racemic or nonchiral precursors have been accomplished in the last few years (parallel to this work)[28a]. They have in common that, with mostly moderate yields, (unseparated) racemates are obtained. Enantiomerically pure aglycones have been accessible, so far, only from biological sources [e.g. fortamine (**1**) by hydrolysis of fortimicine B[28b]].

Hasegawa et al. (1980)[29] used 1-methoxycyclo-2-hexene (*rac*-**4**) for a lengthy synthesis (14 steps) with low overall yield of a (±)-sporamine derivative suitably protected for glycosidation (7% *rac*-**5**). *Honda* and *Suami* (1982)[30] transformed the diazide *rac*-**6** (or the cheap

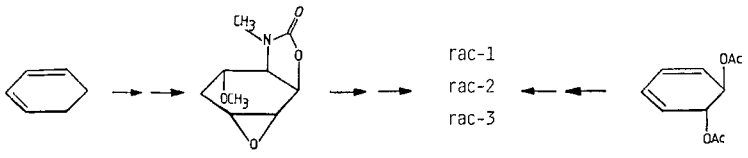


rac-4 rac-5 rac-6 rac-7

*) In this paper cyclohexane numbering (in parentheses) is used (cf. ref.[40]) – in variance to the numbering in the fortimicin literature.

myo-inositol, resp.) into *rac*-**7** (4%) (19 steps with elaborate protecting group manipulations). The latter was connected to purpurosamine yielding an α-glycoside (37%).

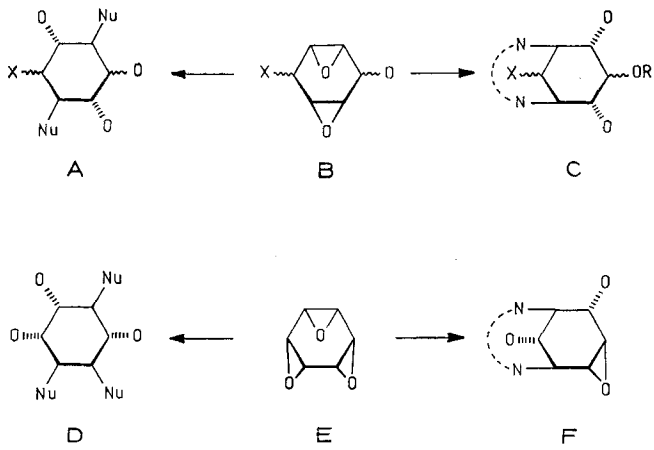
Knapp et al. (1983)[31] constructed the intermediate *rac*-**8** starting with 1,3-cyclohexadiene (7 steps, ca. 50%), from which (±)-fortamine (*rac*-**1**, ca. 50%), (±)-sannamine (*rac*-**2**) and (±)-sporamine (*rac*-**3**) were produced. *Kuo* and *Wendler* (1984)[32] synthesized (±)-fortamine, starting from the *trans*-glycol diacetate *rac*-**9**, in which the two amino groups were introduced via Diels-Alder addition of dimethyl azodicarboxylate[36].



rac-8 rac-9

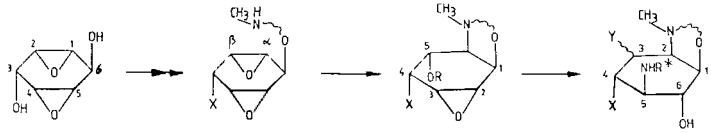
Aiming at a total synthesis of such pseudo-disaccharide antibiotics which would allow broad modifications in the sugar[36] as well as in the nonsugar part, we designed a route to the aglycone part which features several advantages – as exemplified in this paper with the 3-*O*-demethylfortamines.

From our earlier work we had at our disposal a pool of anhydro conduritols and anhydro(deoxy)inositols[37,38] that is derived from benzene. Their preparative value for the synthesis of polyfunctionalized cyclohexanes, especially of *cis*-1,4-(deoxy)inosadiamines (**B**→**A**)[39,40], *cis-chiro*-inosatriamines (**E**→**D**)[41], and of *cis*-1,3-diamino analogues (**B**→**C**, **E**→**F**)[41,42] has already been amply demonstrated. Early relevant examples are the achiral aglycones streptamine and 2-deoxystreptamine. With regard to the target substances **1**–**3**, a severe restriction is the poor kinetic differentiation between the opening of the individual epoxide rings in **B** and **E** with the consequence that two (or three) different monovalent N-nucleophiles cannot be introduced with sufficient selectivity.



The eventually successful strategy for the synthesis of (±)-fortamine and the individual enantiomers, resp., is generalized in Scheme 1: Starting material was the *trans*-diol **B** (≡**10**; 1,2:4,5-dianhydro-*epi*-inositol[37]). The methylamino group, attached to **10** (≡**G**), was introduced intramolecularly (**G**→**H**). The O−N spacer, simultaneously an *O,N*-protecting group, was designed to guarantee α-attack and to favour the C-3 addition of the second N-nucleophile in the intermediate **H**. In the latter, the X,O functionalities at C-4, C-5 are potential sites for chemical modifications. The primary amino group was introduced at C-3 in **H** by a chiral amine, the choice of which was based on its availability and suitability for the following manipulations (separation of the diastereomers, removal of the R* group). This procedure has the advantage that at the stage **I**, only the 6-OH group (after protection of the NHR* functionality), which is to be glycosidated, remains unprotected.

Scheme 1

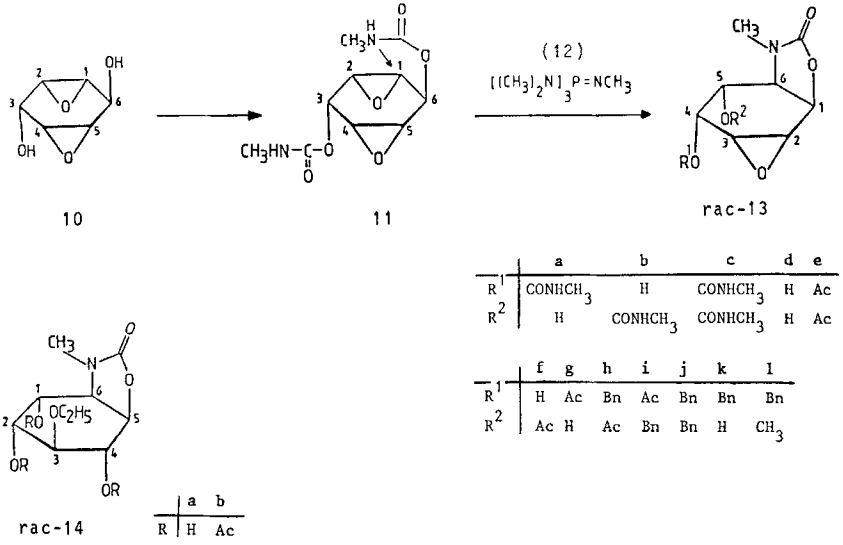


10 G H I

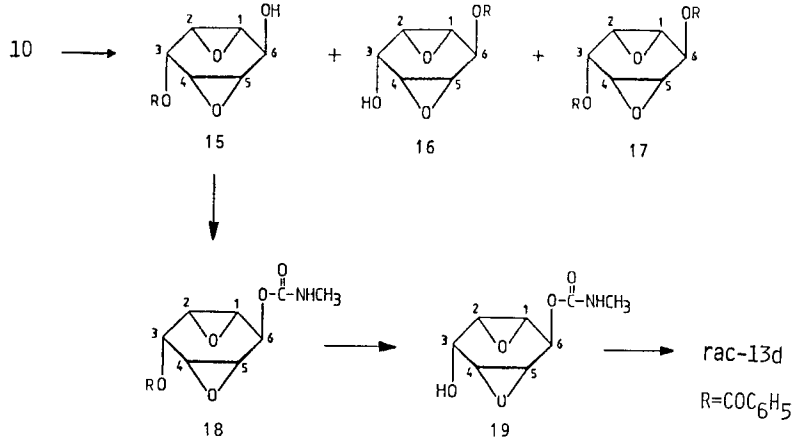
Cyclization G→H

The bis(urethane) **11**, accessible from the diepoxydiol **10** and methyl isocyanate without detraction by epoxide migration in nearly quantitative yield, seemed to fulfill all the prerequisites necessary for a selective transformation **G**→**H**. In (intramolecular) epoxide opening reactions with the ambident carbamoyl group, preferential *N*-attack[43] under S_N2 conditions (S_N1 conditions favour *O*-attack[44]) is observed. The substitution at C-1(5), a 5-*exo* process, should be very much faster than at C-2(4) (6-*endo*)[45], though exceptions to this rule are not uncommon. Typical base systems for such cyclizations[43,44,47] like *tert*-BuOK/THF, *tert*-BuOK/*tert*-BuOH, NaH/THF, pyridine, DBN/THF proved to be unsuitable, primarily because **11** is not sufficiently soluble in these solvents.

Deprotonation at C-3 and formation of the allylic alcohol is another plausible complication. Finally, a procedure was followed in which a saturated solution of **11** in extremely purified, absolute acetonitrile under an inert atmosphere (Ar, N_2) is treated at 60°C with 5 mol-% of the phosphorane base **12** [tris(dimethylamino)(methylimino)phosphorane][48]. After total conversion (4 h) a 7:2:3:3 equilibrium mixture (97% isolated; no olefinic component) consisting of the primary product *rac*-**13a**, the 4-hydroxy-5-carbamate *rac*-**13b**, the 4,5-bis(carbamate) *rac*-**13c**, and the diol *rac*-**13d** was formed. Obviously, cyclization was excessively accompanied by "transesterification". This complication could not be totally avoided by diluting the reaction mixture or by lowering the reaction temperature. Rather than to separate *rac*-**13a** (required for the selective installation of the



3-CH_3O group of **1**) and to recycle the remaining material, the synthesis was pursued with the 3-*O*-demethyl derivative of (−)-**1** as primary goal. To this end the crude 7:2:3:3 mixture was transformed into uniform diol *rac*-**13d** via alkaline hydrolysis. Unfortunately, this transformation was accompanied by competitive cleavage of the two hetero rings. These side reactions could not (yet) be suppressed by varying the base (methanol, ethanol, 2-propanol, alkoxides). In addition to *rac*-**13d** at least one by-product (4–6%) was identified (Table 3) in the case of the C_2H_5ONa/ethanol reaction as the ethyl ether *rac*-**14a** (derivative *rac*-**14b**). So far the best conditions (1:1 equiv. of C_2H_5ONa/ethanol, 60 °C, 1 h) give a reproducible yield of 71% *rac*-**13d** (derivative *rac*-**13e**). Carbamate cleavage via *N*-nitrosation

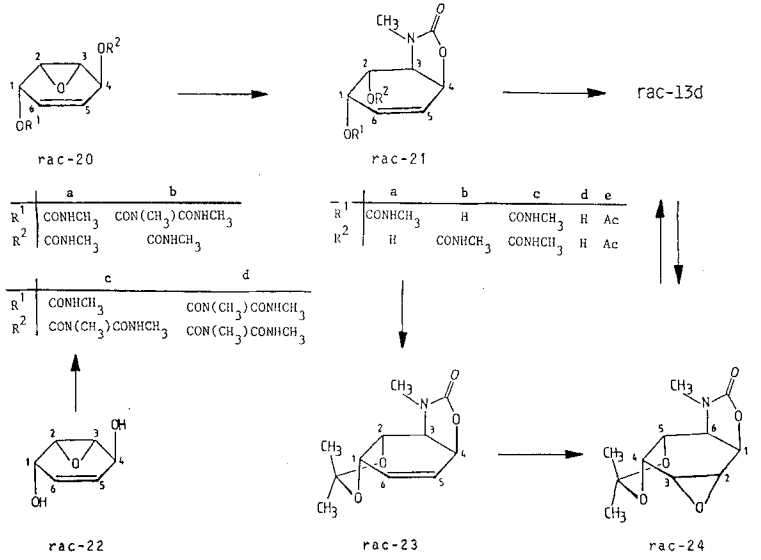


($HOAc/NaNO_2$)[49] required drastic conditions and was very unselective. In summary, although the intramolecular substitution in the bis(urethane) **11** is indeed regiospecific (>97%), the isolated yield of 65% *rac*-**13d** (based on **10**) was not considered satisfactory and for this reason two (finally futile) variations in the synthetic scheme were investigated. These are described briefly below.

The complications at the stage of *rac*-**13a** are caused by the carbamoylation at O-3 of **10**. As a consequence, we looked for a mono-*O* derivative of **10**, which could be formed as selective as possible with the use of a protecting group incapable of migration but readily removable under suitable conditions. It was considered feasible to acylate selectively the 3-OH group, which is capable of H-bridging to the neighbouring epoxide-O atoms[50]. Because benzoylation is often more sensitive to the different reactivities of hydroxy groups than e.g. acetylation, **10** was treated with 1.0 equiv. of benzoyl chloride in pyridine (10°C).

Chromatographic separation yielded in addition to 11% of remaining starting material **10** 14% of dibenzoate **17**, 2% of monobenzoate **16**, and 67% of the isomer **15**. On larger scale (0.1 mol) **15** could be isolated by fractional crystallization with recycling of the other benzoates in a yield of at least 85% based on conversion. It was transformed nearly quantitatively (92% isolated) into the carbamate **18** and this was cleaved to give **19** with comparable yield. The improvement up to this stage (ca. 75% based on **10**) was, however, allegated by some loss in the cyclization to *rac*-**13d** (max. yield 85%). By-products were, once again, *rac*-**13a–c**, the bis(urethane) **11**, and the diol **10**. Intermolecular "transesterification" is obviously rather detrimental, too.

In the second alternative *rac*-**13d** was aimed at via **20a**, the bis(urethane) of the well-available anhydroconduritol *rac*-**22**[37]. It was assumed that the mixture of products resulting from the cyclization *rac*-**20a**→*rac*-**21a** could be transformed

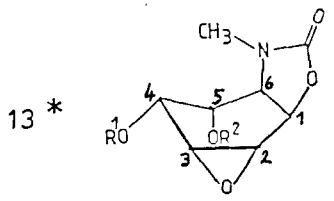


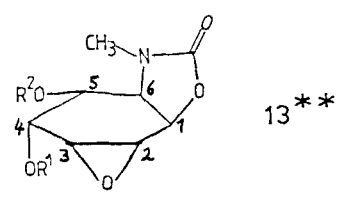
into uniform diol *rac*-**21d** without any loss, epoxide rings being absent. In the reaction with methyl isocyanate the production of *rac*-**20a** (86%) was accompanied by the formation of *rac*-**20b, c** (ca. 1:1, 6%). As expected, the cyclization of **20a** (base **12**, acetonitrile, 60°C, 4 h) yielded the mixture *rac*-**21a–d**, out of which 83% of *rac*-**21d** was obtained by treatment with 1.05 equiv. of CH_3ONa/ethanol (60°C, 2 h). This significantly higher yield, as compared with the 71% of *rac*-**13d**, indicated the epoxide ring for the latter case as a main source of the side reactions. This advantage, however, was cancelled by the extremely slow and unselective epoxidation (*m*-chloroperbenzoic acid, CF_3CO_3H) of *rac*-**21d** to *rac*-**13d**. Besides

Table 1. ^3J Coupling constants for the tricyclic structures **13**

	13a	13b	13c	13d	13e	13f	13g	13h	13i	13j	13k	13l
$J_{3,4}$	1.0	1.0	-	1.0	1.5	1.5	1.0	1.5		3.5	1.0	3.5
$J_{3,5}$	1.5	-	-	1.0	1.0	-	0.8	-		-	1.5	-
$J_{4,5}$	4.0	4.5	-	4.0	4.0	4.5	4.0	4.5		3.5	4.0	3.5
$J_{5,6}$	4.0	3.5	2.5	3.5	4.0	4.5	3.5	4.0		6.5	4.0	7.0
$J_{5,OH}$	11.0	-	-	-	-	-	11.0	-		-	10.5	-

Table 2. Estimated dihedral angles [°] and calculated ^3J coupling constants [Hz] in the half-chair conformations **13***/**13****





	13*		13**	
CH-X/CH-Y	Φ	Jx, y	Φ	Jx, y
CH-1/CH-2	80°	< 0.5	90°	0
CH-3/CH-4	60°	1.5	10°	5.0
CH-4/CH-5	40-50°	5.0-4.0	40°	5.0
CH-5/CH-6	50°	4.0	140°	6.5

rac-**13d** several additional components of significant proportions were manifested by ^{1}H-NMR control, but were not chemically identified. After acetal formation (*rac*-**23**, 92%) again a selective epoxidation leading to *rac*-**24** could not be achieved.

The structures *rac*-**13a**–**e** have been assigned in accordance with their ^{1}H-NMR spectra. Evidence for the 5-membered ring carbamate units is a doublet at δ = 4.9–5.15 (8.0 Hz) (1-H) and a double of doublets at δ = 3.95–4.15 (8.0, 2.5–4.0 Hz) (6-H). Including the derivatives *rac*-**13f**–**l** mentioned below, comparison of the measured ^3J values with those calculated[51] for the extreme conformations **13*/13**** (Tables 1, 2) demonstrates a general preponderance of the 4e,5a- rather than the 4a,5e-half-chair conformation with an H-bridge between 5-OH and epoxide O-atoms ($J_{5,OH}$ = 10.5–11 Hz) (*rac*-**13k, g**). This is manifested also by a further, long-range coupling $^4J_{3,5}$ = 0.8–1.5 Hz. Both, diol *rac*-**21d** ($J_{1,5}$ = 1.0, $J_{4,5}$ = 3.5, $J_{4,6}$ = 1.0, $J_{5,6}$ = 10.0, $J_{6,1}$ = 4.5 Hz) and its diacetate *rac*-**21e** ($J_{1,2}$ = 3.0, $J_{2,3}$ = 7.0, $J_{3,4}$ = 8.0, $J_{4,5}$ = 3.0, $J_{6,1}$ = 3.5 Hz) in $CDCl_3/CD_3OD$ (3:1) adopt a 1a,2e-half-chair conformation, whereas the acetal *rac*-**23** is more planar ($J_{1,2}$ = 5.0, $J_{1,4}$ = $J_{1,5}$ = 1.0, $J_{2,3}$ = 3.0, $J_{2,6}$ = 1.0, $J_{3,4}$ = 7.5, $J_{4,5}$ = 3.0, $J_{4,6}$ = 1.0, $J_{5,6}$ = 10.0, $J_{6,1}$ = 3.0 Hz). In the acetal *rac*-**24**, the threefold annulated 6-membered ring is probably nearly planar ($J_{3,4}$ = 2.5, $J_{3,5}$ = 0.5, $J_{4,5}$ = 6.5, $J_{5,6}$ = 2.0 Hz) as in [1.1.1]-tris-σ-homobenzenes[52].

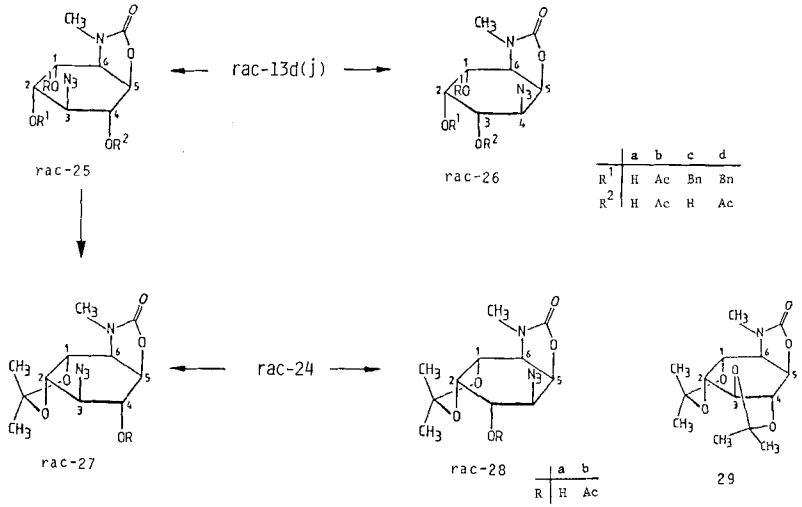
Table 3. Selected J values [Hz] of the bicyclic *chiro* compounds **14, 25,** and **34** ($CDCl_3$)

	14a	**14b**	**25a**	**25b**	**25c**	**25d**	**34a**	**34b**	**34c**	**34d**	**34e**
$J_{2,3}$	4.0	5.0	–	10.0	5.0	5.0	10.0	9.0	–	9.0	5.5
$J_{3,4}$	7.5	7.5	–	10.0	8.5	8.0	11.5	10.5	–	11.0	10.0
$J_{4,5}$	9.0	8.5	7.5	7.5	8.5	8.5	7.5	8.0	8.0	8.0	9.0
$J_{6,1}$	6.5	6.5	3.5	3.5	5.5	6.0	3.0	4.0	5.5	3.5	6.5

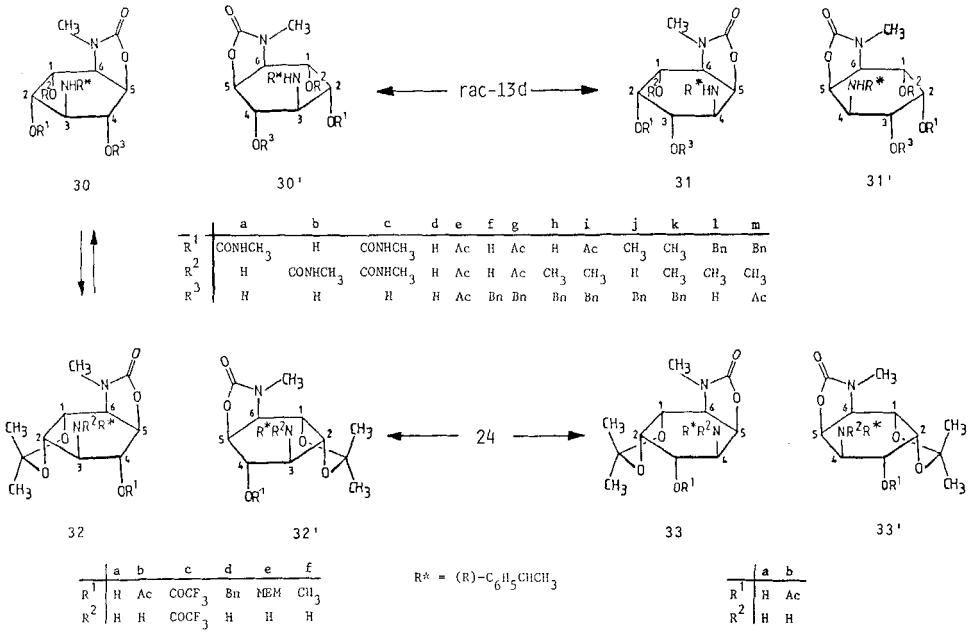
Epoxide Opening Reactions H→I

With the transformation of **11** into *rac*-**13d**, two intentions of the program had been realized. From nonchiral material, a racemate was produced, the methylamino group was introduced and, at the same time, the *cis*-vicinal 1-OH group was protected. Concerning the regioselectivity of the second epoxide ring opening reaction (**H→I**), any prediction based on the differential stereoelectronic effects seemed highly unreliable in view of the complex substitution pattern and mobile conformational situation. Specifically in the case of the diol *rac*-**13d**, however, the expectation was not unreasonable that, under S_N2-type conditions, the acyl-*O* functionality at C-1 should sterically and inductively hinder the attack on C-2 more than the 4-OH group an attack on C-3. Initial information on this was gained from experiments with sodium azide as nucleophile. Under conventional conditions (methanol, 3 equiv. of NaN_3, $MgSO_4$, reflux) *rac*-**13d** was completely consumed after 6 h (TLC) and only one product was formed. This, isolated in 85% yield, was identified as the desired azide *rac*-**25a** resulting from C-3 attack.

After esterification (excess acetic anhydride/pyridine) of the crude product (uniform by TLC, ^{1}H NMR) and acetalization (2,2-dimethoxypropane/*p*-toluenesulfonic acid), again no regio isomers (*rac*-**26b**/*rac*-**28a**), in addition to the triacetate *rac*-**25b** and the acetal *rac*-**27a**, resp., were detected. How serendipitous this selectivity of the C-3 opening was, became evident in the reactions of the dibenzyl ether *rac*-**13j** and the acetal *rac*-**24**, which were prepared from *rac*-**13d** along standard procedures. Under the conditions used for *rac*-**13d**, *rac*-**13j** yielded *rac*-**25c** (92%) and a small amount (4%) of *rac*-**26c**; *rac*-**24**, in a much slower reaction (total conversion after 3 d), produced *rac*-**27a** (60%) in addition to a comparable amount (40%) of *rac*-**28a**. After chromatographic separation, the individual components have been characterized also as the acetates *rac*-**25b**, *rac*-**26b** and *rac*-**27b**/*rac*-**28b**. In the preparation of *rac*-**24**, care must be taken that the *p*-toluenesulfonic acid catalyst is totally free of water, otherwise the bis(acetal) *rac*-**29** is formed via hydrolysis of *rac*-**13d** (or *rac*-**24**, resp.).



As a chiral amine which met our specifications, 1-phenylethylamine was introduced. Both enantiomers are available commercially and the alkyl group is removable via hydrogenation with Pd/C. With 2 equiv. of *R*-(+)-amine in boiling dioxane, after total conversion of *rac*-**13d** (7 h), a 1:1 mixture of products was formed (TLC, ^{1}H NMR) which was separated on silica (deactivated with triethylamine) practically without loss. The crystalline components are identified as the diastereomers **30d/30d'** (m.p. 76–78°C, 178–180°C). This specificity of C-2-attack was additionally substantiated after derivatization: On acetylation of the crude mixture in order to obtain the triacetates **30e/30e'** (m.p. 122°C/179–181°C), no traces of **31e/31e'** were found. Even with very large excess of reagent and long reaction time the NHR* group was not affected; the NHR* group in **30e/30e'** was resistent also against Cbz chloride under various conditions.



The loss of material caused mainly by competitive reactions of the epoxide ring during the transformation of the mixture *rac*-**13a–d** into uniform *rac*-**13d** was reason to postpone this manipulation until the stage of **30a–d/30a′–d′**. To this end, the pure components *rac*-**13a–d** were treated with (+)-phenylethylamine. *rac*-**13a, b** reacted stereospecifically like *rac*-**13d** (*rac*-**13b** more slowly) to yield the diastereomeric pairs **30a,b/30a′,b′**; *rac*-**13c** needed a Lewis acid or a protic solvent (ethanol, 1-propanol) in order to react with an acceptable rate, but it opened the ring with the same selectivity to give **30c/30c′**. In view of the general selectivity, it was surprising that, starting with the crude mixture *rac*-**13a–d** (in 1-propanol), after reaction with the amine and treatment with ethanolate, at best a 40% yield of **30d/30d′** could be achieved. This alternative therefore was not pursued further.

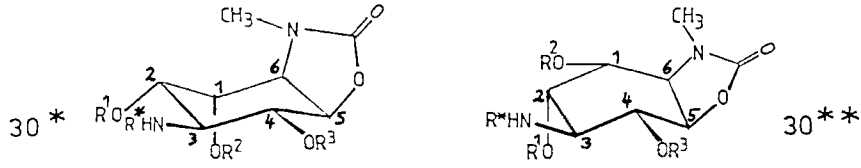
For glycosidation purposes (e.g. with the aglycone **30d/30d′**) the OH groups at C-1/C-2 had to be protected selectively from the one at C-4. Deactivation of the secondary amino function (–NHR*) at C-3 was deemed desirable as (strong) bases can interfere with glycosidation. Since the NHR* group in **30e/30e′** proved accessible only with difficulty, the following variations were considered: (i) protection of the vicinal *cis*-OH groups in **30d/30d′** as acetals, cleavage of the R* group, and protection of the primary amino group or (ii) cleavage of the R* group in **30d**, protection of the primary amino group, and acetal formation (next section).

Because from route (i) a pair of diastereomeric acetals is formed, which might be separated even more efficiently than the diols **30d/30d′**, it was pursued first. **30d** (**30d′**) reacts with 2,2-dimethoxypropane (pure or dimethylformamide solution) in the presence of more than 1 equiv. of TosOH (80 °C, 1 h, 1 equiv. of acid

is consumed to form the ammonium salts) to give nearly quantitatively **32a/32a′**. Fortunately, **32a′** (m.p. 191 °C) is only slightly soluble in chloroform/ether, whilst **32a** (m.p. 142 °C) is very soluble. 90% of **32a′** can therefore be separated by a single crystallization. A further simplification of the route to the acetals **32a/32a′** seemed feasible by altering the sequence **13**→**30**→**32** to **13**→**24**→**32**. Not surprisingly, however, in view of the behaviour of e.g. dibenzyl ether **13j**, the step **24**→**32** is not sufficiently regioselective. *rac*-**24** reacts with (+)-phenylethylamine as expected only slowly: with 10 equiv. of NH_2-R^* after 6 d in dioxane only ca. 30% were consumed, *chiro*-**32a/32a′** and *neo*-**33a/33a′** (ca. 1:4) being the exclusive products. By addition of Al_2O_3 the reaction can be accelerated (ca. 80% after 6 d), the *chiro/neo* ratio being raised to ca. 1:3, and in boiling 1-propanol the reaction rate is once more doubled, the share of **32a/32a′** being now ca. 35% (ca. 1:2) (Table 9, Experimental). The absolute configuration attributed to the two *neo* products **33** in the formula scheme is arbitrary. The first fraction **33a′** was assigned the (1*S*)-configuration in analogy to **30d/30d′**, where the first fraction **30d′** is the (1*S*)-isomer. For comparison with **32b/32b′**, **33a/33a′** were transformed into the acetates **33b/33b′**, whereby once more the NHR* group remained unaffected. Only with the highly reactive trifluoracetic anhydride (CH_2Cl_2, triethylamine, 0 °C, 10 min) a bis(trifluoracetyl) derivative (e.g. **32c′** from **32a′**) was readily formed (^{1}H NMR). All attempts to selectively saponify **32c′** to give the 4-OH-unprotected derivative were accompanied by partial *N*-deacetylation.

The ^{1}H-NMR differentiation between the *chiro/neo* products resulting from C-3(C-2) attack at **13** was, in most cases, straightforward. The O- and N-carbamoyl H-signals (5-/6-H) with $\delta = 4.25-4.7$ and $\delta = 3.5-4.1$, resp., each of them exhibiting two large couplings (7–10 Hz), are typical for the *chiro* configurations (Tables 4, 5). In the case of the diastereomeric pairs, the differences in δ values of 2-/3-H are significant. For instance in the pair

Table 4. Estimated dihedral angles [°] and ^3J values [Hz] for the conformers **30***/**30****



	30*		30**	
CH-X/CH-Y	φ	Jx, y	φ	Jx, y
CH-2/CH-3	160-180°	9.5-10.5	110-130°	2.5-5.5
CH-3/CH-4	160-180°	9.5-10.5	160-180°	9.5-10.5
CH-6/CH-1	50-60°	4.0-3.0	150-160°	8.0-9.0

30d/30d' $\delta_{2\text{-H}}$ is larger for the (1*R*)-isomer and $\delta_{3\text{-H}}$ smaller than for the (1*S*)-isomer. These δ values are only slightly influenced by the nature of the *O*-substituents of the stereoisomers and amount to 0.2–0.3 ppm for 2-H and to −0.3 to −0.4 ppm for 3-H. These are of reliable diagnostic value, especially when considering the vicinal coupling constants measured for 3-H. The difference $J_{3,4} - J_{2,3}$ lies generally (exception for **30f**) between 6.0 and 9.5 Hz for the (1*R*)- and between 2.5 and 5.0 Hz for the (1*S*)-compounds. On this basis it was possible to assign absolute configuration on the basis of the ^{1}H-NMR spectra, assuming, however, identical conformations.

Table 5. Selected NMR data ⟨δ values, *J*[Hz]⟩ of the *chiro* products **30** ($CDCl_3$, $CDCl_3/CD_3OD$*)

	30d	30d'	30e	30e'	30f *)	30g	30h	30i	30j	30k	30l	30l'	30m	30m'
δ2-H	3.76	3.55	5.20	4.95	3.38	3.70	5.22	3.87	5.34	3.35	3.51	3.74	3.45	3.72	3.40
δ3-H	2.51	2.80	2.60	2.93	2.93	2.62	2.64	2.72	2.51	2.67	2.66	2.74	3.02	2.65	3.01
$J_{2,3}$	3.0	4.0	2.0	5.0	8.5	3.0	3.0	4.0	1.5	2.0	-	1.0	2.0	1.0	1.0
$J_{3,4}$	10.0	9.0	8.0	7.5	9.5	10.5	9.0	10.0	9.0	8.0	8.0	8.0	6.5	10.5	6.0
$J_{6,1}$	7.0	7.0	7.5	6.0	3.5	8.0	7.5	7.5	8.5	7.0	8.0	7.5	7.5	8.0	7.5

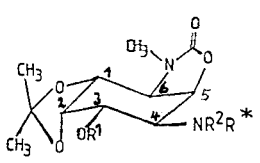
The regularities concerning the δ values of 2-/3-H observed for the diastereomeric pairs are also indicative of the isopropylidene derivatives in the *chiro* series (Table 6). As can be judged from the *J* values of 2-/3-H, the boat-conformational character is even more pronounced, the substituents being quasi equatorial.

Table 6. ^3J values [Hz] of the *chiro* acetals **27, 32,** and **36** ($CDCl_3$)

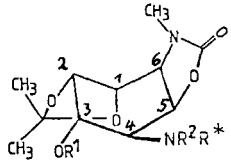
	27a	27b	32a	32a'	32b	32b'	32d	32e'	32f'	36a	36b	36c
$J_{1,2}$	7.0	-	7.5	7.0	7.0	7.0	7.5	-	-	7.5	7.0	-
$J_{2,3}$	7.5	7.5	7.0	6.0	7.0	7.0	6.5	5.0	6.0	8.0	8.0	7.5
$J_{3,4}$	12.0	12.0	12.0	12.0	12.5	12.0	12.0	12.0	12.0	12.5	12.0	12.0
$J_{4,5}$	7.5	8.0	8.0	7.5	8.5	8.5	7.0	8.0	7.5	8.5	8.0	7.0
$J_{5,6}$	9.0	9.5	10.0	9.5	9.5	9.5	9.5	9.5	10.0	9.5	9.5	9.5
$J_{6,1}$	6.0	6.0	8.0	7.5	8.0	7.0	6.5	-	7.5	6.0	7.0	7.5

For the *neo* products **26/31(31')** and the corresponding acetals **28/33(33')**, the chemical shifts of 4-H and 5-H are (in $CDCl_3$) significantly different (Tables 7, 8). The absolute configurations, here also derived from the behaviour in TLC, correlate with the facts that $\delta_{4\text{-H}}$ in (supposedly) (1*R*)-**31l** is smaller ($\Delta\delta = -0.23$), $\delta_{5\text{-H}}$ in contrast larger ($\Delta\delta = +0.5$) than in (1*S*)-**31l'**. The same is true in the case of the acetal pairs **33a/33a'** and **33b/33b'** (but not for 4-H in **33b**).

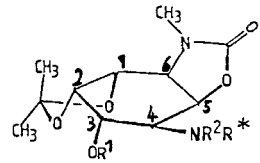
Table 7. Estimated dihedral angles [°] and ^3J values [Hz] of the conformers **33***, **33****, and **33*****



33*



33**



33***

	33*		33**		33***	
CH-X/CH-Y	Φ	Jx, y	Φ	Jx, y	Φ	Jx, y
CH-1/CH-2	10–20°	8.0–7.0	40–50°	5.0–4.0	0–10°	8.5–8.0
CH-2/CH-3	0–10°	8.5–8.0	40–50°	5.0–4.0	40–50°	5.0–4.0
CH-6/CH-1	70–80°	2.0–1.5	140–150°	6.5–8.0	110–120°	2.5–4.0

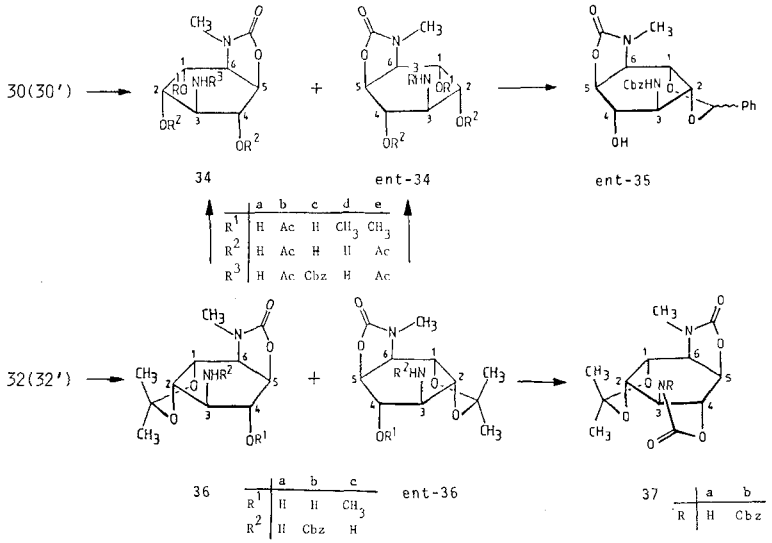
Table 8. Selected NMR data ⟨δ values, J[Hz]⟩ of the *neo* products **26/31** and **28/33** ($CDCl_3$)

	26c	26d	31e	31e'	28a	28b	33a	33a'	33b	33b'
δ4-H	–	–	3.05	3.28	–	–	2.94	3.14	3.20	3.20
δ5-H	4.70	4.73	4.72	4.22	4.99	4.93	4.92	4.38	4.92	4.62
$J_{1,2}$	2.0	2.0	2.5	2.5	7.5	7.5	7.5	7.5	7.5	8.0
$J_{2,3}$	2.0	5.0	1.5	1.5	4.5	4.5	3.5	3.0	4.0	4.5
$J_{3,4}$	–	8.0	10.5	10.5	8.0	10.5	11.0	9.5	10.5	8.5
$J_{4,5}$	3.5	8.5	4.5	4.5	4.5	4.0	4.0	4.5	4.0	4.5
$J_{5,6}$	6.5	9.0	6.5	6.5	10.0	10.0	9.5	9.5	9.5	10.0
$J_{6,1}$	8.0	6.0	8.0	8.0	4.0	3.0	2.0	4.0	3.0	4.5

(−)- and (+)-3-*O*-Demethylfortamines

In the acetals **32a/32a'**, the NHR* group could not be blocked in a way considered mandatory for glycoside formation. This blocking procedure had to be performed, after cleavage of the R* group, with the primary amine (variation ii).

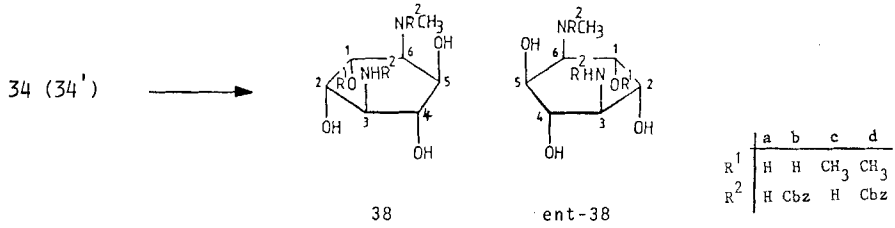
Catalytic hydrogenation with Pd/C is the standard procedure for this purpose[53]. After variation of solvent, acid, temperature, and the amount of catalyst in the experiments with the mixture **30a**/**30a'**, the pure diastereomers could be cleaved in methanol/sulfuric acid (Pd/C, 1 bar H_2, 20 °C, 24 h) cleanly yielding the sulfate salts of **34a**/*ent*-**34a**, which crystallize from ethanol/water and have the composition (**34a**)$_2$ · H_2SO_4 · H_2O ⟨m.p. 262–265 °C, $[\alpha]_D^{20}$ values of −92 (+93), 90–94% isolated⟩. For their tetraacetates **34b** (*ent*-**34b**) $[\alpha]_D^{20}$ values of −82 (+83) have been measured. Hydrogenation of the acetals **32a**/**32a'** in the presence of excess acid yielded, again quantitatively, the enantiomerically pure amines **34a**/*ent*-**34a**. With a smaller amount of acid [0.5 mol H_2SO_4 (no excess!) per 1 mol **32a**/**32a'**], the cleavage of the acetal can be completely prevented. The sulfate salts of **36a**/*ent*-**36a** (89–95%) crystallize from ethanol/water and have the composition (**36a**)$_2$ · H_2SO_4 · 2 H_2O, m.p. 235–240 °C.



For glycosidations with **36a** (*ent*-**36a**) the primary amino group had to be protected with respect to the planned manipulations, preferably with the Cbz group. In the reaction with Cbz–Cl in CH_2Cl_2/triethylamine, complications arose with the amine catalyzing the ring closure of the amide **36b** to **37a**(**37b**). **36b**/**37a** were easily separated by taking advantage of their very different solubilities in chloroform. In acetone/H_2O/Na_2CO_3 (0–20 °C) only **36b** is formed (82% isolated). In order to vary the steric demand of the protecting groups, as an example **36b** was cleaved to give the triol *ent*-**34c** (89%), and the latter was transformed into the acetal *ent*-**35** (87%) with benzaldehyde dimethyl acetal.

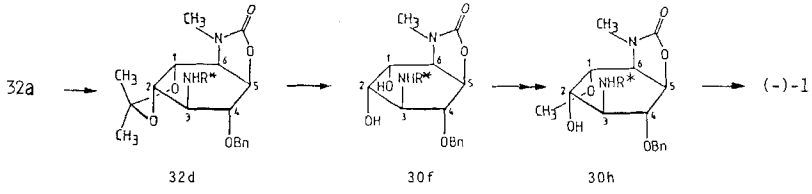
From **34a** (*ent*-**34a**), after heating with aqueous $Ba(OH)_2$ solution and subsequent addition of sulfuric acid, the *O*-demethylfortamines were obtained as sulfates (92–96% of **38a** · H_2SO_4 · H_2O; decomp. above 260 °C), and from these, with

equivalent amounts of $Ba(OH)_2$, the free bases **38a** (*ent*-**38a**). The latter are characterized by their optical rotation ⟨$[\alpha]_D^{20}$ = 75 (−74) (*c* = 1.0, CH_3OH)⟩ and as bis(Cbz) derivatives **38b** (*ent*-**38b**) ⟨m.p. 143°C, $[\alpha]_D^{20}$ = −56 (+56) (*c* = 1.0, CH_3OH)⟩. The absolute $[\alpha]_D^{20}$ values of **38a** and **38b** correspond with those of naturally occurring fortamine (−88) and its bis(Cbz) derivative (+47)[28]. Substances which differ only by an *O*- or *N*-alkyl group but prefer the same conformation have $[\alpha]_D^{20}$ values which differ only by 5–15 (deg · ml)/dm · g)[54]. Thus, preliminary assignment of the acetals **32a**/**32a'** could be made. This assignment was proven by the transformation of **32a** into the naturally occurring (−)-fortamine **1**.

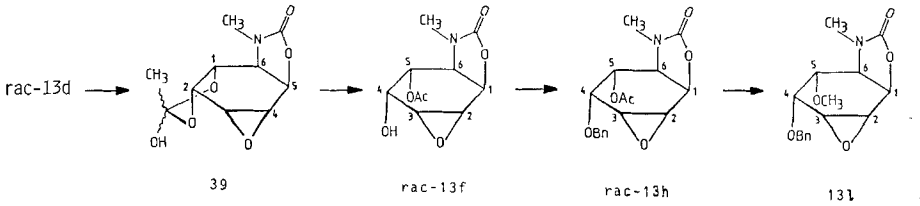


(−)- and (+)-Fortamines

The methylation of de-*O*-methylfortamine **32a** to form natural (−)-**1** was performed only for analytical purposes and was therefore not optimized. To this end, **32a** was transformed into **32d** [NaH, benzyl chloride, 60°C, 81% (no *N*-alkylation!)] and **32d** was cleaved by refluxing for several days in methanol/sulfuric acid to give **30f** (93%). After methylation (glyme, 2 NaH, 1 CH_3I, 20°C, 10 min, cf. Supplements) **30h** (12%) could be separated by chromatography from the mixture which consisted of remaining starting material (35%), **30j** (10%), and **30k** (36%). After hydrogenation the crude amine **34d** was converted nearly quantitatively into the triacetate **34e** ⟨m.p. 248°C, $[\alpha]_D^{20}$ = −65, (*c* = 1, $CHCl_3$)⟩. After alkaline hydrolysis, precipitation of $BaSO_4$, and titration with $Ba(OH)_2$ solution, the rotation of the resultant free amine confirms the configuration of (−)-fortamine (**1**). This assignment infers in the separation of the diastereomeric acetals **32f**/**32f'** that the "nonnatural" intermediate is less soluble and therefore easier to isolate. For the isolation of the "natural" product it would therefore be advantageous to separate *rac*-**13d** with (*S*)-(−)-1-phenylethylamine.



It was pointed out above that the "transesterification" in **13a** prohibited the straightforward modification of the 5-OH function (e.g. methylation) and therefore the expedient preparation of the fortamines along Scheme 1. One obvious solution might be the use of 3-*O*-protected urethanes **15** (R: base-stable groups like MOM, Bn, THP)[55]. Alternatively, the selective manipulation of the 5(4)-OH group in *rac*-**13d** was considered. A large repertoire of methods exists[56] for such a monoprotection of *cis*-1,2-diols. In carbohydrates the axial OH group can be selectively protected via acidic hydrolysis of ortho esters[57], the equatorial OH group via cleavage of dibutyl stannylen derivatives[58]. En route to the nonnatural (+)-fortamine (*ent*-**1**) some insight was gained from preliminary experiments with *rac*-**13d**. The ortho ester **39**, formed quantitatively in trimethyl orthoacetate (TosOH, reflux, 1 h), was rapidly hydrolyzed in 80% acetic acid: Within a few minutes besides 67% of the 5-acetate **13f** (m.p. 118–122°C), 27% of the 4-acetate *rac*-**13g** (m.p. 148–150°C) was present.

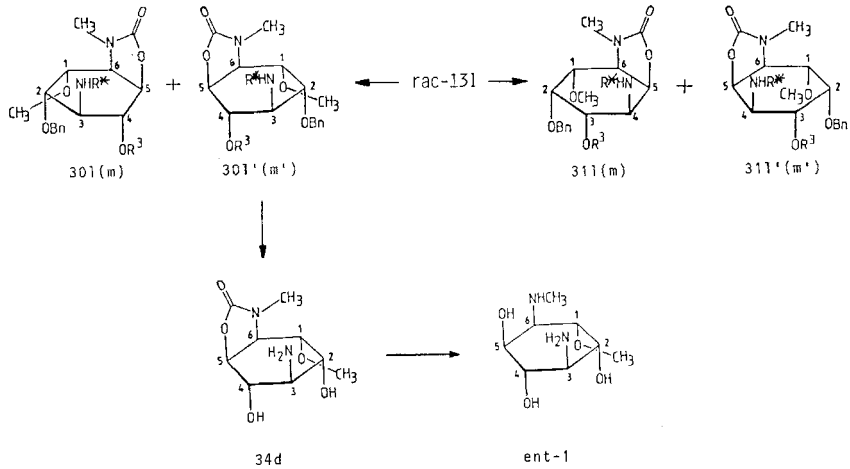


The selectivity was accordingly lower than hoped for. *rac*-**13f** could be isolated easily and without loss because it is very much less soluble in chloroform than *rac*-**13g** (intramolecular H-bridge). After one crystallization (60–70% **13f**) and recycling the mother liquor (via ammonolysis to give **13d**) the total yield of *rac*-**13f** based on conversion was better than 90%. The low selectivity of the cleavage of the ortho ester **39** (or the intermediate dioxolenium salt) could be due to an insufficient preponderance of the 4e,5a-conformation (cf. the situation in the acetal **24**).

The non-base-catalyzed protection of 4-OH in **13d** required a group which was stable against strong base (methylation of 5-OH) and suitable for the following manipulations. After the failure of the acidic MOM-etherification, acid-catalyzed benzyl ether formation with benzyl trichloroacetimidate (BTA, trifluoromethanesulfonic acid) was attempted[59]. Standard conditions, however, only led to a mixture of 50–55% of the 4-benzyl-5-acetate *rac*-**13h**, 5-benzyl-4-acetate *rac*-**13i**, dibenzyl ether *rac*-**13j**, and several decomposition products. Even after recycling the by-products and several variations of the reaction conditions, the yield of **13h** was only slightly improved (at best 60%). The ammonolysis to give *rac*-**13k** (90%) and its methylation to afford *rac*-**13l** (96%) posed no problems.

The reaction of *rac*-**13l** with an excess of (+)-1-phenylethylamine was very slow even in boiling 1-propanol and was interrupted after 80% conversion (3 d, the first by-products being visible). The crude mixture, which contained educt and two pairs of diastereomers, could be separated by column chromatography to

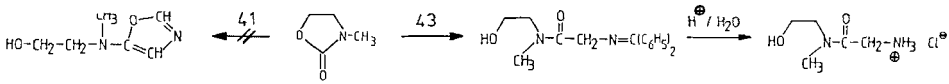
give **131** (18%), *chiro*-**301/301′** (36% each), and *neo*-**311/311′** (4%). This *chiro/neo* ratio is, as expected, only slightly different from the one observed for the dibenzyl ether **13j**. The pairs **301/301′** and the acetates **30m/30m′** display similar physical properties concerning behaviour in chromatography, melting points, and ^{1}H-NMR data (Table 5) compared with **30a/30a′** and **30b/30b′** (the diastereomer marked with ′ has the larger rotation and the higher melting point), and as a result **301** was provisionally assigned the natural fortamine configuration. This was subsequently confirmed. After hydrogenolysis and acetate formation starting with **301′** the triacetate *ent*-**34e** (93%, $[\alpha]_D^{20} = +63$) and after alkaline hydrolysis the nonnatural (+)-fortamine *ent*-**1** ($[\alpha]_D^{20} = +82$) was isolated.



The fortamines **1**/*ent*-**1** and their *O*-demethyl derivatives **38a**/*ent*-**38a** are characterized as sulfates by their ^{1}H-NMR spectra. As for the free base (−)-**1**, for the bis(ammonium) salts the 1a,2e,3e,4e,5a,6a-conformation ("B-type") is confirmed[60].

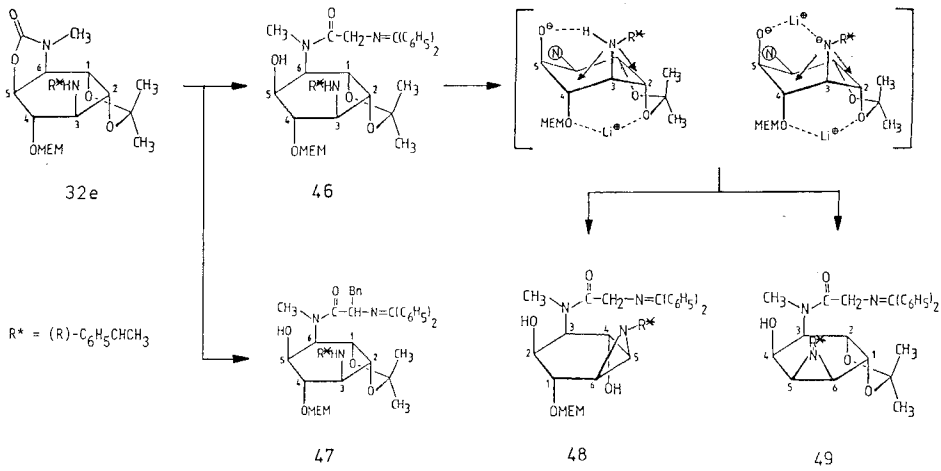
Supplements

The 4-*N*-glycyl substituent in the aglycone part of fortimicin A can be introduced using standard procedures[27,61]. It would mean an improvement on methodology and a real asset for our approach if the carbamate entity, also protecting the methylamino group, could be transformed directly into the glycyl rest. Some observations in this direction are reported here. Carbanionic candidates with masked amino group were metallated methyl isocyanide ($LiCH_2NC$, **41**) and metallated *N*-methylbenzophenone imine [$LiCH_2-N=C(C_6H_5)_2$, **43**][62].



40 42 44 45

Both were tested with *N*-methyloxazolidinone[63] (**42**) as substrate, since the reactivity of **41**/**43**[64] towards carbamates was to our knowledge not documented in the literature. Reaction of **41** with **42**, under various conditions, yielded no oxazol **40**[65]. In contrast **43**[66] provided (−50 to −10°C) ca. 50% of the adduct **44** or (after hydrolysis) of the glycine derivative **45**. Under similar low-temperature conditions **43** reacts with the 4-MEM/3-R*-protected carbamate **32e′**: After quenching with methanol and workup by chromatography the desired adduct **46** (73% based on conversion, not optimized) could be separated from remaining educt. After quenching with benzyl chloride the C- (**47**) and not the exprected 5-*O*-alkylated derivative was the main product.

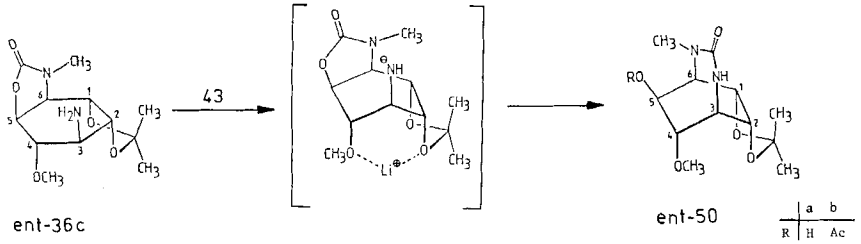


46 is sensitive under the strongly alkaline conditions of its preparation: When the reaction temperature was raised above 0°C, increasingly the formation of a pair of products (ca. 3:1) was observed, characterized as the aziridines **48**/**49**. They were formed in the same ratio in the reaction of LDA with **46** (0°C). This rather unusual acetal (ether) substitution by an N-nucleophile[67] might have been accelerated by complexation with Li cations favouring the 1e,2a,3a,4a,5a,6e-chairs **46***/**46****, Analogous acetal substitutions by carbanions occur frequently[68].

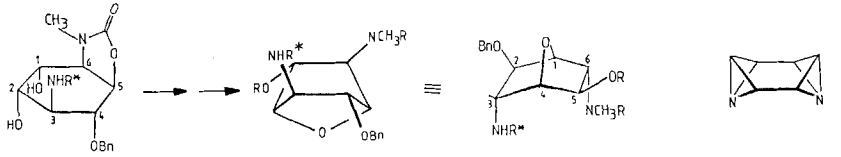
46, according to the ^{1}H-NMR analysis ($J_{1,2}$ = 6.0, $J_{2,3}$ = 5.5, $J_{3,4}$ = 4.5, $J_{4,5}$ = 3.5, $J_{5,6}$ = 1.5, $J_{6,1}$ = 10.0 Hz), prefers (in $CDCl_3$) a conformation somewhere between the boat with 2(3)-H *trans*-diaxial and the chair with these two hydrogens *trans*-diequatorial. The aziridine rings in **48**/**49** were recognized by their typical ^{1}H- and ^{13}C-NMR shifts and coupling constants[69]. For **48** (two rotamers) a half-chair conformation with quasi-e NCH_3R ($J_{3,4}$ = 10.0 Hz) and with quasi-a 2-OH group ($J_{2,OH}$ = 10.5 Hz, stabilized by a H-bridge of 2-OH to the aziridine nitrogen) is indicated.

For the glycylation **32e′**→**46** an effective protection of the 3-amino group was an essential prerequisite. This was exemplified by the reaction between **43** and the amino acetal *ent*-**36c**. As a consequence of a fast intramolecular migration of the

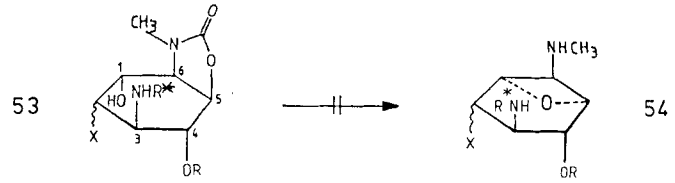
carbamoyl group, besides several minor uncharacterized components, the urea with bicyclo[3.2.2]nonane skeleton (*ent*-**50a**) was formed, presumably via an amide ion, whose conformation again might be fixed as a Li-complex. Lack of basicity, monoacetylation (**50b**), a slowly exchangeable proton (CD_3OD), a C=O absorption in the IR at 1635 cm^{-1} (1730 cm^{-1} for the carbamate **36c**) and the ^3J values around the cyclohexane ring ($J_{1,2}$ = 7.5, $J_{2,3}$ = 3.5, $J_{2,4}$ = $J_{3,4}$ = 1.0, $J_{4,5}$ = 6.0, $J_{5,6}$ = 3.5, $J_{6,1}$ = 2.0) are some of the criteria for assigning the structure **50**.



As a first resumee for the use of the Li-organyl **43** in the construction of a glycyl unit from carbamates: The specific reaction conditions invite competitive intramolecular reactions or prohibit the presence of a number of typical substituents. In addition, application to glycosides with a carbamate ring in the aglycone part and with unprotected NH_2 groups, glycyl migration as seen in the fortimicin–isofortimicin transposition[70] would become highly probable.

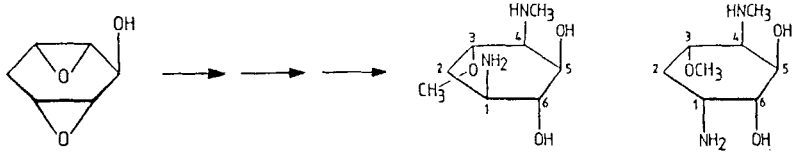


In this context, a transannular bond formation in the bicyclic diol **30f** deserves mentioning. In the presence of NaH (glyme) the 7-oxanorbornane **51a** very slowly at 20 °C but rapidly at 80 °C arises via substitution of the carbamoyl group[71] as the main product. With such highly functionalized oxanorbornanes being of considerable preparative interest – in our group for the synthesis of the diazaoctabisvalene **52**[72] – the scope of this approach with respect to variations of the substituents in positions 1, 3, and 4 of **30f** is being examined[73]. In 2-OH-protected **30f** or in the 2-deoxyanalogue **53**, the stereoelectronically unfavourable 1,3-cyclization to give the 7-oxabicyclo[3.3.1]heptanes **54** could not be realized[74].



Remarks

The reaction sequence of Scheme 1 allows the expedient preparation of *rac*-de-*O*-methylfortamines, of the individual enantiomers, and of derivatives (type **30** or **31**) in which only one OH group, the one to become glycosidated, is unprotected. The drastic influence of the OR substituents at C-4/C-5 upon the regioselectivity in the epoxide opening reaction **H**→**I** extends the potential of this route to *neo-cis*-1,3-inosadiamines (**32, 33**) and hence to enantiomerically pure 2,5-*diepi*-streptamine derivatives[75]. There are several restrictions concerning the preparation of fortamines **1**/*ent*-**1**; still the route via **32d**/**30h** could in principle be optimized at different stages. Rather broad manipulations, including epimerization (cf. lysinomycins[20,21]) at the C-2 (C-3,C-1) positions of **1**, appear possible at the 3-*N*/4-*O*-protected stage of the diol **34**. The step **G**→**H** offers the chance for an early optical induction though under the given steric circumstances the chances were not considered very promising. And, indeed, with the (few) chiral bases utilized so far, no significant induction was achieved.



55 (−)-2 (−)-3

The restrictions mentioned above for **1**/*ent*-**1** (derivatives), caused by the "trans-esterification" in **13a** are not valid when the sequence of the Scheme 1 is applied to the synthesis of the 2-deoxyfortamine (sannamine) family (**2**/*ent*-**2**), starting from the well-available dianhydro-deoxy-inositol **55**[74]. Details of this study[74,76] as well as of the glycosidation experiments[77] will be presented in forthcoming publications.

Financial support by the *Deutsche Forschungsgemeinschaft*, the *Fonds der Chemischen Industrie*, and the *BASF AG* is gratefully acknowledged.

Experimental

Melting points: Bock monoskope (uncorrected values). – IR: Perkin-Elmer PE 457. – ^{1}H NMR: Bruker WM 250, HX 400. – ^{13}C NMR: Bruker HX 400 (values marked with an asterisk* are interchangeable). – Optical rotation: PE 141 polarimeter. Specific rotation values are given in (deg · ml)/(dm · g).

General Procedure for Acetylations: The alcohol or amine was dissolved in a 1:1 mixture of pyridine/acetanhydride (1 ml/mmol OH/NH), 4-(dimethylamino)pyridine (50 mg) was added, and the solution was allowed to stand at 20°C for 1 d. After concentrating i. vac. (0.01 Torr) at 50°C, the residue was purified on silica (10 g/mmol product).

(−)-(1R)- and (+)-(1S)-(1α,2α,3β,4α,5β,6β)-3-Ammonio-1-O-methyl-6-(methylammonio)-1,2,4,5-cyclohexanetetrol Sulfate (Fortamine Sulfate) [**38c** · H_2SO_4/*ent*-**38c** · H_2SO_4

(≡*ent*-**1**)]: A mixture of the triacetate **34e** (160 mg, 0.45 mmol) and of $Ba(OH)_2 \cdot 8\ H_2O$ (630 mg, 2 mmol) in 10 ml of water was heated at reflux for 6 h. After acidification (pH ≈ 3) with dilute sulfuric acid, $BaSO_4$ was separated by centrifugation. The solution was concentrated i. vac. to afford crude fortamine sulfate (**1** · H_2SO_4, 130 mg, 96% yield) as a spectroscopically pure (^{1}H NMR) yellow oil; free base: $[\alpha]_D^{20} = -85$ ($c = 1.0$, H_2O).

1: ^{1}H NMR (D_2O): δ = 4.27 (dd, 2-H), 4.22 (dd, 5-H), 4.04 (dd, 1-H), 3.95 (t, 4-H), 3.78 (t, 6-H), 3.55 (s, OCH_3), 3.50 (t, 3-H), 2.90 (s, NCH_3); $J_{1,2} = 3.5$, $J_{2,3} = J_{3,4} = 8.5$, $J_{4,5} = 8.0$, $J_{5,6} = 4.5$, $J_{6,1} = 5.5$ Hz.

$C_8H_{18}N_2O_4 \cdot H_2SO_4$ (304.3)

ent-**38c** (*ent*-**1**): From **34e′**; 94%, free base: $[\alpha]_D^{20} = +82$ ($c = 1.0$, H_2O).

1,2:4,5-Dianhydro-3,6-bis-O-(methylcarbamoyl)epi-inositol (**11**): A suspension of the diol **10** (14.4 g, 100 mmol) in a mixture of methyl isocyanate (23.8 ml, 400 mmol) and dioxane (150 ml) was heated at reflux for 4 h. The product began to precipitate after about 2 h. After removing the excess of methyl isocyanate by distillation and on cooling (20°C) a first crop (60–65%) of **11** was isolated by filtration. The filtrate was concentrated i. vac. and the residue recrystallized from methanol; total yield of **11**: 24.3 g (94%) as colorless crystals, m.p. 203–205°C. — IR (KBr): 3330, 3070, 2945, 2810, 1700, 1545, 1420, 1310, 1260, 1150, 1130, 1010, 940, 915, 830, 775, 470 cm^{-1}. — ^{1}H NMR ($CDCl_3$): δ = 5.56 (t, 3-H), 5.48 (s, 1-H), 5.02 (br. s, NH), 4.83 (br. s, NH), 3.38 (m, 1-, 2-, 4-, 5-H), 2.86 (d, 2 NCH_3); $J_{2,3} = J_{3,4} = 2.5$, $J_{NH,CH_3} = 5.0$ Hz.

$C_{10}H_{14}N_2O_6$ (258.2) Calc. C 46.51 H 5.46 N 10.85 Gef. C 46.44 H 5.49 N 10.89

DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-1-O,6-N-carbonyl-6-(methylamino)-4-O-(methylcarbamoyl)-1,2,3,4,5-cyclohexanepentol (*rac*-**13a**), *DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-1-O,6-N-carbonyl-6-(methylamino)-5-O-(methylcarbamoyl)-1,2,3,4,5-cyclohexanepentol* (*rac*-**13b**), *DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-4,5-bis-O-(methylcarbamoyl)-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol* (*rac*-**13c**), and *DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol* (*rac*-**13d**): A suspension of the bis(carbamate) **11** (25.8 g, 100 mmol) and **12** (1.0 ml, 5 mmol) in absolute acetonitrile (100 ml) was heated under N_2 at 60°C for 4 h with vigorous stirring. The solution was cooled, then neutralized (acetic acid) and concentrated i. vac. to give a solid residue which was purified by column chromatography (50 g silica, $CHCl_3/CH_3OH$, 10:1). *rac*-**13a–d** (25.1 g, 97% yield) were obtained as a colorless powder. Column-chromatographic separation (silica, $CHCl_3/CH_3OH$, 25:1) of 2.58 g of the mixture *rac*-**13a–d** afforded successively *rac*-**13c** (590 mg, 19%), *rac*-**13a** (1.20 g, 46%), *rac*-**13b** (330 mg, 13%), and *rac*-**13d** (380 mg, 19%).

rac-**13a**: Colorless crystals, m.p. 175–176°C ($CHCl_3$/ether, 1:1). — IR (KBr): 3470, 3350, 3320, 3000, 2935, 1775, 1745, 1690, 1530, 1420, 1385, 1295, 1260, 1140, 1025, 945, 860, 775, 760, 660, 555, 515, 460 cm^{-1}. — ^{1}H NMR ($CDCl_3$): δ = 5.17 (d, 4-H), 5.03 (d, 1-H), 5.00 (br. s, NH), 4.22 (dtd, 5-H), 4.10 (dd, 6-H), 3.62 (br. d, 3-H), 3.57 (td, 2-H), 3.20 (d, OH), 2.90 (s, NCH_3), 2.86 (d, $NHCH_3$); $J_{1,2} = 1.0$, $J_{2,3} = 3.0$, $J_{2,6} = J_{3,4} = 1.0$, $J_{3,5} = 1.5$, $J_{4,5} = J_{5,6} = 4.0$, $J_{5,OH} = 11.0$, $J_{6,1} = 8.0$, $J_{NH,CH_3} = 5.0$ Hz.

$C_{10}H_{14}N_2O_6$ (258.2)	Calc.	C 46.51	H 5.46	N 10.85
rac-**13a**:	Found	C 46.24	H 5.49	N 10.83
rac-**13b**:	Found	C 46.35	H 5.43	N 10.83

rac-**13b**: Colorless crystals, m.p. 196–198°C ($CHCl_3$/ether, 1:1). — IR (KBr): 3450, 3320, 3010, 2945, 1750, 1725, 1695, 1525, 1445, 1265, 1120, 1085, 1035, 975, 870, 760, 685 cm^{-1}. — ^{1}H NMR ($CDCl_3/CD_3OD$, 1:1): δ = 5.12 (t, 5-H), 4.90 (d, 1-H), 4.24 (d, 4-H), 3.98 (dd,

6-H), 3.46 (m, 2-, 3-H), 2.93 (s, NCH_3), 2.77 (s, NCH_3); $J_{1,2}$ = 0.5, $J_{3,4}$ = 1.0, $J_{4,5}$ = 4.5, $J_{5,6}$ = 3.5, $J_{6,1}$ = 8.0 Hz.

rac-**13c**: Colorless crystals, m.p. 185–187°C ($CHCl_3$/ether, 1:1). – IR (KBr): 3360, 3000, 2940, 2810, 1750, 1725, 1530, 1430, 1265, 1150, 1120, 1030, 870, 760, 450 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.32 (br. s, 4-, 5-H), 5.02 (br. q, NH), 4.92 (br. q, NH), 4.88 (br. d, 1-H), 3.94 (dd, 6-H), 3.44 (br. s, 2-, 3-H), 2.95 (s, NCH_3), 2.86 (d, $NHCH_3$), 2.81 (d, $NHCH_3$); $J_{1,6}$ = 8.0, $J_{5,6}$ = 2.5, J_{NH,CH_3} = 4.5 Hz.

$C_{12}H_{17}N_3O_7$ (315.3) Calc. C 45.72 H 5.43 N 13.33 Found C 45.45 H 5.46 N 13.26

rac-**13d**: Colorless crystals, m.p. 152–155°C (CH_3OH). – IR (KBr): 3360, 3300, 2950, 2900, 1780, 1725, 1435, 1400, 1375, 1260, 1155, 1085, 1025, 895, 865, 800, 750, 655, 585, 525 cm^{-1}. – ^1H NMR (D_2O): δ = 5.14 (td, 1-H), 4.23 (dd, 4-H), 4.15 (dd, 6-H), 4.10 (dt, 5-H), 3.65 (s, 2-, 3-H), 2.84 (s, NCH_3); $J_{1,2}$ = $J_{1,3}$ = $J_{3,4}$ = $J_{3,5}$ = 1.0, $J_{4,5}$ = 4.0, $J_{5,6}$ = 3.5, $J_{6,1}$ = 8.0 Hz. – ^{13}C NMR (D_2O): δ = 160.1 (C=O), 69.4 (C-1), 66.5 (C-5), 64.5 (C-4), 61.0 (C-6), 65.3* (C-3), 53.9* (C-2), 30.0 (CH_3).

$C_8H_{11}N_1O_5$ (201.2) Calc. C 47.76 H 5.51 N 6.96 Found C 47.66 H 5.58 N 6.95

*Preparation of the Diol rac-***13d** *and DL-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-3-O-ethyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol (rac-***14a**) *from the Mixture rac-***13a–d**: A solution of the mixture *rac*-**13a–d** (25.8 g, 100 mmol) and $NaOC_2H_5$ (110 mmol) in ethanol (400 ml) was heated to 60°C for 1 h. The solution was cooled, then neutralized with dilute sulfuric acid, and concentrated i. vac. The crude product was purified by column chromatography (100 g silica, $CHCl_3/CH_3OH$, 25:1). *rac*-**13d** (13.5 g, 67%) was crystallized from methanol. The mother liquor was subjected to column chromatography (silica, $CHCl_3/CH_3OH$, 20:1) to afford *rac*-**13d** (800 mg, 4%) and the ethyl ether *rac*-**14a** (1.42 g, 5.5%).

rac-**14a**: Colorless crystals, m.p. 162°C ($CHCl_3/CH_3OH$, 50:1). – IR (KBr): 3510, 3360, 2975, 2930, 2895, 1755, 1430, 1385, 1300, 1260, 1110, 1075, 1020, 980, 940, 895, 815, 770, 755, 730, 665, 565 cm^{-1}. – ^1H NMR ($CDCl_3/CO_3OD$, 10:1): δ = 4.58 (t, 5-H), 3.97 (dd, 1-H), 3.86 (dd, 6-H), 3.80–3.68 (m, 2-, 4-H, CH_2), 3.41 (dd, 3-H), 2.94 (s, NCH_3), 1.23 (t, CH_3); $J_{1,2}$ = 2.5, $J_{2,3}$ = 4.0, $J_{3,4}$ = 7.5, $J_{4,5}$ = 9.0, $J_{5,6}$ = 8.5, $J_{6,1}$ = 6.5, $J_{CH_2CH_3}$ = 7.0 Hz.

$C_{10}H_{17}N_1O_6$ (247.3) Calc. C 48.58 H 6.93 N 5.66 Found C 48.36 H 6.79 N 5.66

DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol 4,5-Diacetate (*rac*-**13e**): By acetylation of **13d** (200 mg, 1.0 mmol): 270 mg (95%) of colorless crystals, m.p. 131–132°C ($CHCl_3$/ether, 1:1). – IR (KBr): 3000, 2970, 1775, 1760, 1745, 1435, 1405, 1395, 1370, 1295, 1250, 1225, 1155, 1120, 1060, 1040, 910, 865, 755, 600, 570, 440 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.42 (dt, 5-H), 5.38 (dd, 4-H), 4.95 (d, 1-H), 3.88 (ddd, 6-H), 3.47 (td, 2-H), 3.43 (qd, 3-H), 2.95 (s, NCH_3), 2.13, 2.11 (s, 2 OAc); $J_{1,2}$ = $J_{1,3}$ = 1.0, $J_{2,3}$ = 4.0, $J_{2,6}$ = 0.5, $J_{3,4}$ = 1.5, $J_{3,5}$ = 1.0, $J_{4,5}$ = $J_{5,6}$ = 4.0, $J_{6,1}$ = 8.0 Hz.

$C_{12}H_{15}N_1O_7$ (285.3) Calc. C 50.53 H 5.30 N 4.91 Found C 50.21 H 5.17 N 4.99

DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol 5-Acetate and 4-Acetate (*rac*-**13f**/*rac*-**13g**): A suspension of *rac*-**13d** (400 mg, 2 mmol) and *p*-toluenesulfonic acid monohydrate (35 mg, 0.2 mmol) in trimethyl orthoacetate (4 ml) was heated at reflux for 1 h. The solution was concentrated and 80% aqueous acetic acid (5 ml) was added. After concentrating i. vac. the crude product was extracted with $CHCl_3$. The monoacetate *rac*-**13f** (305 mg, 63%) remains as a colorless powder. Column-chromatographic separation (silica, $CHCl_3/CH_3OH$, 25:1) of the extract afforded successively *rac*-**13g** (130 mg, 27%) and *rac*-**13f** (20 mg, 4%).

rac-**13f**: Colorless crystals, m.p. 118–122°C ($CHCl_3$). – IR (KBr): 3480, 3025, 2990, 2930, 1760, 1435, 1405, 1375, 1225, 1155, 1075, 1045, 970, 865, 765, 740, 550 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.21 (t, 5-H), 4.89 (d, 1-H), 4.33 (dd, 4-H), 3.92 (dd, 6-H), 3.49 (s, 2-, 3-H), 2.95 (s, NCH_3), 2.40 (br. s, OH), 2.18 (s, OAc); $J_{1,2}$ = $J_{1,3}$ = 1.0, $J_{3,4}$ = 1.5, $J_{4,5}$ = $J_{5,6}$ = 4.5, $J_{6,1}$ = 8.0 Hz.

$C_{10}H_{13}N_1O_6$ (243.2)	Calc.	C 49.38	H 5.39	N 5.76
rac-**13f**:	Found	C 49.39	H 5.45	N 5.54
rac-**13g**:	Found	C 49.21	H 5.27	N 5.76

rac-**13g**: Colorless crystals, m.p. 148–150°C ($CHCl_3$/ether, 1:1). – IR (KBr): 3500, 3030, 2950, 2920, 1750, 1730, 1405, 1370, 1295, 1240, 1155, 1120, 1030, 935, 910, 865, 840, 765, 730, 640, 565, 460 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.23 (d, 4-H), 5.05 (d, 1-H), 4.21 (dt, 5-H), 4.09 (dd, 6-H), 3.59 (s, 2-, 3-H), 3.19 (d, OH), 2.89 (s, NCH_3), 2.23 (s, OAc); $J_{1,2}$ = $J_{1,3}$ = $J_{3,4}$ = $J_{3,5}$ = 0.8, $J_{4,5}$ = 4.0, $J_{5,6}$ = 3.5, $J_{5,OH}$ = 11.0, $J_{6,1}$ = 8.0 Hz.

DL-*(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-4-O-benzyl-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol 5-Acetate* (*rac*-**13h**): To a suspension of *rac*-**13f** (4.86 g, 20 mmol) and benzyltrichloroacetimidate (9.4 g, 40 mmol) in CH_2Cl_2 (100 ml, freshly distilled over P_2O_5) was added trifluoromethanesulfonic acid (0.1 ml, 1 mmol) at 20°C. The alcohol was completely dissolved after stirring for 10 min. After 1 h, the clear solution was washed with dilute $NaHCO_3$ solution (50 ml) and water (50 ml), then dried ($MgSO_4$) and concentrated. Column-chromatographic separation of the residue (silica, cyclohexane/ethyl acetate, 3:2) afforded successively trichloroacetamide, the benzyl ether *rac*-**13h** (3.47 g, 52%), fractions which contained *rac*-**13i**, *rac*-**13j** besides decomposition products (^1H NMR), and finally a mixture of *rac*-**13f/g** (750 mg, 15%).

rac-**13h**: Colorless crystals, m.p. 116–118°C ($CHCl_3$). – IR (KBr): 3030, 2950, 2890, 1755, 1740, 1425, 1390, 1375, 1235, 1090, 1050, 1035, 970, 775, 760, 740, 700 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.40–7.32 (m, 5H), 5.30 (t, 5-H), 4.90 (d, 1-H), 4.67 (m, CH_2), 4.00 (dd, 4-H), 3.85 (dd, 6-H), 3.41 (s, 2-, 3-H), 2.82 (s, NCH_3), 2.15 (s, OAc); $J_{3,4}$ = 1.5, $J_{4,5}$ = 4.5, $J_{5,6}$ = 4.0, $J_{6,1}$ = 8.0 Hz.

$C_{17}H_{19}N_1O_6$ (333.3) Calc. C 61.25 H 5.75 N 4.20 Found C 61.01 H 5:65 N 4.02

DL-*(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-4,5-di-O-benzyl-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol* (*rac*-**13j**): To a solution of *rac*-**13d** (2.0 g, 10 mmol) in DMF (20 ml) at 20°C was added NaH (750 mg, 30 mmol). After stirring for 15 min benzyl chloride (2.5 ml, 22 mmol) was added by syringe, and stirring was continued for 4 h. The mixture was neutralized with dilute acetic acid, diluted with water (200 ml), and extracted with CH_2Cl_2 (2 × 200 ml). The organic layer was washed with water (3 × 200 ml), dried ($MgSO_4$), and concentrated to give 3.35 g (88%) of colorless crystals, m.p. 60–62°C (CH_3OH). – IR (KBr): 3115, 2870, 1745, 1435, 1380, 1255, 1025, 870, 735, 690 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.42–7.28 (m, 10H), 4.88 (d, 1-H), 4.80, 4.71, 4.60, 4.49 (d, 2 CH_2), 4.00 (t, 4-H), 3.71 (dd, 6-H), 3.60 (dd, 5-H), 3.41 (t, 3-H), 3.39 (d, 2-H), 2.72 (s, NCH_3); $J_{1,2}$ = $J_{1,3}$ = 1.0, $J_{2,3}$ = $J_{3,4}$ = $J_{4,5}$ = 3.5, $J_{5,6}$ = 6.5, $J_{6,1}$ = 8.0, J_{CH_2} = 12.5 Hz.

$C_{22}H_{23}N_1O_5$ (381.4) Calc. C 69.28 H 6.08 N 3.67 Found C 67.98 H 6.07 N 3.57

DL-*(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-4-O-benzyl-1-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol* (*rac*-**13k**): Gaseous ammonia was passed through a solution of *rac*-**13h** (1.67 g, 5 mmol) in methanol (30 ml) at 20°C for 30 min. After 1 h, ammonia was again passed through the solution for 15 min. After standing for about 12 h at 20°C, the solution was concentrated and the product recrystallized from methanol to afford 1.35 g (93%) of colorless crystals, m.p. 134–136°C. – IR (KBr): 3540, 3480, 2930, 1760, 1750,

1640, 1425, 1385, 1295, 1265, 1150, 1110, 1070, 1030, 860, 770, 740, 700 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.42–7.30 (m, 5H), 4.98 (dt, 1-H), 4.80, 4.73 (d, CH_2), 4.07 (dtd, 5-H), 4.03 (ddd, 6-H), 3.83 (dd, 4-H), 3.54 (m, 3-H), 3.48 (dt, 2-H), 3.14 (d, OH), 2.68 (s, NCH_3); $J_{1,2}$ = $J_{1,3}$ = 1.0, $J_{2,3}$ = 4.0, $J_{2,6}$ = $J_{3,4}$ = 1:0, $J_{3,5}$ = 1.5, $J_{4,5}$ = $J_{5,6}$ = 4.0, $J_{5,OH}$ = 10.0, $J_{6,1}$ = 8.0, J_{CH_2} = 12.0 Hz.

$C_{15}H_{17}N_1O_5$ (291.3) Calc. C 61.85 H 5.88 N 4.81 Found C 61.69 H 5.88 N 4.66

DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-4-O-benzyl-1-O,6-N-carbonyl-5-O-methyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol (*rac*-**13l**): To a suspension of *rac*-**13k** (1.16 g, 4 mmol) in glyme (10 ml) was added NaH (170 mg, 7 mmol). After stirring for 15 min, CH_3I (0.44 ml, 7 mmol) was added by syringe, and the mixture was stirred at 20°C for 1 h. The reaction was quenched with ice and CH_2Cl_2 (100 ml) was added. The organic layer was washed with water (2 × 50 ml), dried ($MgSO_4$), and concentrated to give 1.17 g (96%) of a colorless oil. ^1H NMR ($CDCl_3$): δ = 7.44–7.32 (m, 5H), 4.87 (d, 1-H), 4.83, 4.65 (d, CH_2), 4.04 (t, 4-H), 3.81 (dd, 6-H), 3.57–3.33 (m, 2-, 3-, 5-H), 3.42 (s, OCH_3), 2.85 (s, NCH_3); $J_{3,4}$ = $J_{4,5}$ = 3.5, $J_{5,6}$ = 7.0, $J_{6,1}$ = 8.0, J_{CH_2} = 12.0 Hz.

DL-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-3-O-ethyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol 1,2,4-Triacetate (*rac*-**14b**): By acetylation of **14a** (245 mg, 1.0 mmol): 350 mg (94%) colorless crystals, m.p. 149°C ($CHCl_3$/ether, 1:2). – IR (KBr): 2970, 2910, 1765, 1740, 1430, 1375, 1225, 1100, 1040, 925, 885, 750 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.42 (dd, 1-H), 5.27 (dd, 4-H), 5.19 (dd, 2-H), 4.65 (t, 5-H), 3.97 (dd, 6-H), 3.71, 3.53 (dq, CH_2), 3.58 (dd, 3-H), 2.87 (s, NCH_3), 2.13 (s, 2 OAc), 2.12 (s, OAc), 1.17 (t, CH_3); $J_{1,2}$ = 2.5, $J_{2,3}$ = 5.0, $J_{3,4}$ = 7.5, $J_{4,5}$ = $J_{5,6}$ = 8.5, $J_{6,1}$ = 6.5, J_{CH_2,CH_3} = 7.0, J_{CH_2} = 9.5 Hz.

$C_{16}H_{23}N_1O_9$ (373.4) Calc. C 51.47 H 6.21 N 3.75 Found C 51.42 H 6.33 N 3.93

1,2:4,5-Dianhydro-3-O-benzoyl-epi-inositol (**15**), *1,2:4,5-Dianhydro-6-O-benzoyl-epi-inositol* (**16**), *and 1,2:4,5-Dianhydro-3,6-di-O-benzoyl-epi-inositol* (**17**): A solution of the diol **10** (4.32 g, 30 mmol) in pyridine (15 ml) was cooled to 0°C and a solution of benzoyl chloride (4.22 g, 30 mmol) in pyridine (5 ml) was added over 15 min with vigorous stirring. After 15 min at 0°C the solution was concentrated i. vac. and CH_2Cl_2 (200 ml) was added. The organic layer was washed with water (100 ml), dilute sulfuric acid (100 ml), and again with water (100 ml) [from the first water extract 470 mg (11%) of educt **10** was recovered]. The solvent was dried ($MgSO_4$), filtered, and concentrated to give a solid residue (6.7 g). Column chromatography on silica ($CHCl_3$/CH_3OH, 10:1) afforded successively **17** (1.48 g, 14%), **16** (140 mg, 2%), and **15** (5.01 g, 67%). Alternatively, the benzoate **15** could be separated from the reaction mixture by fractional crystallization. About 90% of the dibenzoate **17** crystallized from $CHCl_3$/ether (3:1), then about 80% of the benzoate **15** from $CHCl_3$/ether (1:1).

15: Colorless crystals, m.p. 134°C ($CHCl_3$/ether, 1:1). – IR (KBr): 3480, 3005, 1695, 1600, 1450, 1330, 1275, 1115, 1045, 980, 925, 890, 805, 755, 720, 475 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 8.17–7.49 (m, 5-H), 5.90 (t, 3-H), 4.70 (td, 6-H), 3.49 (dd, 2-, 4-H), 3.47 (dd, 1-, 5-H), 2.93 (d, OH); $J_{1,2}$ = 4.0, $J_{2,3}$ = $J_{3,4}$ = 2.5, $J_{4,5}$ = 4.0, $J_{5,6}$ = $J_{6,1}$ = 1.5, $J_{6,OH}$ = 7.0 Hz.

$C_{13}H_{12}O_5$ (248.2) Calc. C 62.90 H 4.87
15: Found C 62.91 H 4.80
16: Found C 62.88 H 4.60

16: Colorless crystals, m.p. 154–158°C ($CHCl_3$/ether, 1:1). – IR (KBr): 3450, 3070, 3005, 2930, 1725, 1600, 1460, 1415, 1325, 1275, 1180, 1110, 1060, 990, 900, 870, 745, 710 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 8.09–7.50 (m, 5H), 5.77 (s, 6-H), 4.48 (td, 3-H), 3.51 (dd, 1-, 5-H), 3.47 (t, 2-, 4-H), 2.90 (d, OH); $J_{1,2}$ = 3.5, $J_{2,3}$ = $J_{3,4}$ = 3.0, $J_{3,OH}$ = 11.5, $J_{4,5}$ = 3.5, $J_{5,6}$ = $J_{6,1}$ = 1.5 Hz.

17: Colorless crystals, m.p. 221°C (subl. at about 195°C) ($CHCl_3$/ether, 4:1). — ^1H NMR ($CDCl_3$): δ = 8.20–7.51 (m, 10H), 6.00 (t, 3-H), 5.86 (s, 6-H), 3.57 (t, 1-, 5-H), 3.52 (dd, 2-, 4-H); $J_{1,2}$ = 4.0, $J_{2,3}$ = $J_{3,4}$ = 3.0, $J_{4,5}$ = 4.0, $J_{5,6}$ = $J_{6,1}$ = 1.5 Hz.

$C_{20}H_{16}O_6$ (352.3) Calc. C 68.18 H 4.58 Found C 67.99 H 4.30

1,2:4,5-Dianhydro-3-O-benzoyl-6-O-(methylcarbamoyl)-epi-inositol (**18**): A solution of the monobenzoate **15a** (1.0 g, 4 mmol) and methyl isocyanate (1.0 ml, 16 mmol) in dioxane (5 ml) was heated at 100°C for 48 h. After distilling the excess methyl isocyanate and concentrating i. vac. the solid residue was extracted with $CHCl_3$/ether (1:5). The carbamate **18** (1.12 g, 92% yield) remains as a colorless powder, m.p. 207–210°C (subl. at about 175°C). — IR (KBr): 3360, 3025, 2990, 2930, 2820, 1720, 1695, 1600, 1540, 1455, 1425, 1330, 1260, 1175, 1155, 1065, 1005, 945, 920, 890, 810, 775, 755, 710, 640, 470, 380 cm^{-1}. — ^1H NMR ($CDCl_3$): δ = 8.19–7.47 (m, 5H), 5.88 (t, 3-H), 5.51 (s, 6-H), 4.84 (br. s, NH), 3.50 (dd, 2-, 4-H), 3.43 (t, 1-, 5-H), 2.88 (d, NCH_3); $J_{1,2}$ = 4.0, $J_{2,3}$ = $J_{3,4}$ = 2.5, $J_{4,5}$ = 4.0, $J_{5,6}$ = $J_{6,1}$ = 1.5, J_{NH,CH_3} = 5.5 Hz.

$C_{15}H_{15}N_1O_6$ (305.3) Calc. C 59.02 H 4.95 N 4.59 Found C 58.93 H 4.77 N 4.57

1,2:4,5-Dianhydro-6-O-(methylcarbamoyl)-epi-inositol (**19**): A solution of the carbamate **18** (915 mg, 3 mmol) and sodium methoxide (from 10 mg of Na, 0.4 mmol) in methanol (5 ml) was stirred at 20°C for 1 h. The mixture was neutralized with acetic acid, then concentrated, and purified by column chromatography (20 g silica, $CHCl_3/CH_3OH$, 20:1). The alcohol **19** (565 mg, 94% yield) was crystallized from $CHCl_3$ to give colorless crystals, m.p. 165–170°C. — IR (KBr): 3350, 2940, 1700, 1545, 1425, 1310, 1270, 1140, 1045, 1000, 940, 910, 825, 755, 465 cm^{-1}. — ^1H NMR ($CDCl_3$): δ = 5.40 (s, 6-H), 4.73 (br. s, NH), 4.34 (br. td, 3-H), 3.40 (m, 1-, 2-, 4-, 5-H), 2.85 (d, NCH_3), 2.42 (br. d, OH); $J_{2,3}$ = $J_{3,4}$ = 2.5, $J_{3,OH}$ = 11.5, J_{NH,CH_3} = 5.0 Hz.

$C_8H_{11}N_1O_5$ (201.2) Calc. C 47.76 H 5.51 N 6.96 Found C 47.48 H 5.51 N 6.88

DL-(1α,2α,3α,4β)-2,3-Anhydro-1,4-bis-O-(methylcarbamoyl)-5-cyclohexene-1,2,3,4-tetrol (*rac*-**20a**): A solution of *rac*-**22**[37] (3.84 g, 30 mmol) and methyl isocyanate (7.15 ml, 120 mmol) in dioxane (20 ml) was heated at 100°C for 10 h. After distilling the excess methyl isocyanate and on cooling (20°C) a first crop of product *rac*-**20a** (4.4 g) was isolated by filtration. The filtrate was concentrated i. vac. and the residue recrystallized from methanol; total yield of *rac*-**20a**: 6.1 g (84%) of colorless crystals, m.p. 201–203°C. — IR (KBr): 3320, 3060, 2940, 2920, 1690, 1550, 1420, 1400, 1320, 1265, 1140, 995, 935, 905, 835, 800, 775, 750, 680, 450 cm^{-1}. — ^1H NMR ($CDCl_3$) 25°C: δ = 5.80 (br. m, 6-H), 5.67 (br. d, 5-H), 5.65 (br. s, 4-H), 5.46 (br. d, 1-H), 4.85, 4.75, 4.60 (br. s, 2 NH), 3.58 (br. s, 3-H), 3.44 (br. s, 2-H), 2.84, 2.82 (d, 2 NCH_3); 56°C: δ = 5.78 (m, 6-H), 5.66 (m, 5-H), 5.63 (m, 4-H), 5.43 (d, 1-H), 4.75, 4.62 (br. s, 2 NH), 3.57 (m, 3-H), 3.42 (m, 2-H), 2.84, 2.82 (d, 2 NCH_3); $J_{1,2}$ = 2.0, $J_{2,3}$ = 3.5, $J_{2,6}$ = 2.0, $J_{4,6}$ = 3.0, $J_{5,6}$ = 10.5, $J_{6,1}$ = 4.5, J_{NH,CH_3} = 5.0 Hz.

$C_{10}H_{14}N_2O_5$ (242.2) Calc. C 49.59 H 5.83 N 11.56 Found C 49.55 H 6.03 N 11.64

By chromatography (silica, $CHCl_3$/methanol, 5:1) of the mother liquor ca. 100 mg (1%) of *rac*-**20d**, m.p. 214–217 (ether), 540 mg (6%) of a 1:1 mixture of *rac*-**20b/c**, and 150 mg (2%) of *rac*-**20a** are isolated.

20b, c:	$C_{12}H_{17}N_3O_6$ (299.3)	Calc.	C 48.16	H 5.73	N 14.04
		Found	C 47.67	H 5.76	N 13.90
20d:	$C_{14}H_{20}N_4O_7$ (356.3)	Calc.	C 47.19	H 5.66	N 15.72
		Found	C 46.49	H 5.36	N 15.13

DL-(1α,2α,3β,4β)-3-N,4-O-Carbonyl-3-(methylamino)-5-cyclohexene-1,2,4-triol (*rac*-**21d**): A solution of *rac*-**20a** (6.06 g, 25 mmol) and **12** (0.5 ml, 2.5 mmol) in acetonitrile (25 ml) was heated at 60°C for 4 h. Methanol (10 ml) was added, the brown solution concentrated, and purified by column chromatography (20 g silica, $CHCl_3/CH_3OH$, 10:1). The mixture *rac*-**21a–d** was dissolved in ethanol (10 ml) and a solution of $NaOC_2H_5$ [prepared from sodium (600 mg, 26 mmol) in ethanol (30 ml)] was added. This solution was heated at 60°C for 2 h and after cooling neutralized (acetic acid) and concentrated i. vac. The residue was purified by column chromatography (silica, $CHCl_3/CH_3OH$, 10:1) to give the diol *rac*-**21d** (3.85 g, 83% yield) as colorless crystals, m.p. 163°C (CH_3OH). – IR (KBr): 3380–3320, 2935, 2890, 1735, 1435, 1400, 1385, 1350, 1325, 1240, 1145, 1105, 1090, 1070, 1045, 1025, 905, 890, 855, 785, 760 cm^{-1}. – ^1H NMR ($CDCl_3/CD_3OD$, 3:1): δ = 6.08 (dd, 6-H), 5.90 (dd, 5-H), 5.02 (m, 4-H), 4.18 (m, 1-H), 3.96 (m, 2-, 3-H), 2.99 (s, NCH_3); $J_{1,5}$ = 1.0, $J_{4,5}$ = 3.5, $J_{4,6}$ = 1.0, $J_{5,6}$ = 10.0, $J_{6,1}$ = 4.5 Hz.

$C_8H_{11}N_1O_4$ (185.2) Calc. C 51.85 H 5.99 N 7.56 Found C 51.87 H 6.14 N 7.46

DL-(1α,2α,3β,4β)-3-N,4-O-Carbonyl-3-(methylamino)-5-cyclohexene-1,2,4-triol 1,2-Diacetate (*rac*-**21e**): By acetylation of *rac*-**21d** (185 mg, 1.40 mmol): 250 mg (93%) of colorless crystals, m.p. 125°C ($CHCl_3$/ether, 1:5). – IR (KBr): 2935, 1770, 1745, 1735, 1435, 1400, 1370, 1240 1145, 1060, 1035, 940, 910, 780, 760, 660, 605 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 6.05 (m, 5-, 6-H), 5.54 (m, 1-H), 5.31 (dd, 2-H), 5.06 (m, 4-H), 4.06 (t, 3-H), 2.96 (s, NCH_3), 2.11, 2.08 (s, 2 OAc); $J_{1,2}$ = 3.0, $J_{2,3}$ = 7.0, $J_{3,4}$ = 8.0, $J_{4,5}$ = 3.0, $J_{6,1}$ = 3.5 Hz.

$C_{12}H_{15}N_1O_6$ (269.2) Calc. C 53.53 H 5.62 N 5.20 Found C 53.18 H 5.60 N 5.05

DL-(1α,2α,3β,4β)-3-N,4-O-Carbonyl-1,2-O-isopropylidene-3-(methylamino)-5-cyclohexene-1,2,4-triol (*rac*-**23**): A suspension of *rac*-**21d** (930 mg, 5 mmol) and *p*-toluenesulfonic acid monohydrate (50 mg, 0.3 mmol) in 2,2-dimethoxypropane (10 ml) was heated at 60°C for 30 min. The solution was concentrated i. vac., and CH_2Cl_2 (100 ml) was added. The organic layer was washed with 0.5 M $NaHCO_3$ (50 ml) and with water (50 ml), dried ($MgSO_4$), and concentrated to give the acetal *rac*-**23** (1.04 g, 92% yield) as colorless crystals, m.p. 115°C (cyclohexane/ethyl acetate, 2:1). – IR (KBr): 2980, 2930, 2865, 1750, 1430, 1395, 1380, 1240, 1220, 1165, 1115, 1060, 1035, 1015, 1000, 950, 880, 865, 800, 770, 650 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.94 (tdd, 6-H), 5.82 (ddd, 5-H), 4.94 (tdd, 4-H), 4.53 (m, 1-H), 4.46 (ddd, 2-H), 4.16 (dd, 3-H), 2.94 (s, NCH_3), 1.40 (s, 2 CH_3); $J_{1,2}$ = 5.0, $J_{1,4}$ = $J_{1,5}$ = 1.0, $J_{2,3}$ = 3.0, $J_{2,6}$ = 1.0, $J_{3,4}$ = 7.5, $J_{4,5}$ = 3.0, $J_{4,6}$ = 1.0, $J_{5,6}$ = 10.5, $J_{6,1}$ = 3.0 Hz.

$C_{11}H_{15}N_1O_4$ (225.3) Calc. C 58.66 H 6.71 N 6.22 Found C 58.57 H 6.74 N 6.38

DL-(1α,2β,3β,4β,5β,6α)-2,3-Anhydro-1-O,6-N-carbonyl-4,5-O-isopropylidene-6-(methylamino)-1,2,3,4,5-cyclohexanepentol (*rac*-**24**): *rac*-**13d** (1.0 g, 5.0 mmol) and *p*-toluenesulfonic acid (35 mg, 0.2 mmol) were heated in 2,2-dimethoxypropane (5 ml) under reflux for 1 h. After concentration i. vac. the residue is dissolved in 30 ml of CH_2Cl_2. After workup 1.12 g (93%) of colorless crystals ($CHCl_3$/ether, 1:4) with m.p. 149–150°C (subl. at ca. 120°C) are obtained. – IR (KBr): 3020, 3010, 2980, 2965, 2940, 2895, 1775, 1755, 1425, 1395, 1380, 1370, 1340, 1310, 1290, 1255, 1240, 1220, 1175, 1140, 1100, 1060, 1035, 905, 885, 875, 835, 805, 780, 760, 660, 595, 520 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.00 (ddd, 1-H), 4.59 (dd, 4-H), 4.17 (ddd, 5-H), 4.02 (dd, 6-H), 3.57 (dd, 2-H), 3.43 (tdd, 3-H), 2.95 (s, NCH_3), 1.54, 1.40 (s, 2 CH_3); $J_{1,2}$ = 2.0, $J_{1,3}$ = 0.5, $J_{2,3}$ = 4.0, $J_{3,4}$ = 2.5, $J_{3,5}$ = 0.5, $J_{4,5}$ = 6.5, $J_{5,6}$ = 2.0, $J_{6,1}$ = 8.5 Hz.

$C_{11}H_{15}N_1O_5$ (241.2) Calc. C 54.77 H 6.27 N 5.81 Found C 54.97 H 6.39 N 5.84

DL-(1α,2α,3β,4α,5β,6β)-3-Azido-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol (*rac*-**25a**): A suspension of *rac*-**13d** (400 mg, 2.0 mmol), NaN_3 (390 mg, 6.0 mmol), and $MgSO_4$ (1.2 g, 10 mmol) in methanol (10 ml) was heated at reflux for 6 h. After cooling the

reaction mixture was filtered, concentrated i. vac., and purified by column chromatography (10 g of silica, $CHCl_3/CH_3OH$, 5:1): 380 mg (85%) of colorless crystals, m.p. 183–184°C (ethyl acetate). – IR (KBr): 3510, 3380, 2980, 2135, 1775, 1435, 1400, 1355, 1320, 1285, 1260, 1200, 1090, 1015, 970, 890, 765, 550 cm^{-1}. – ^1H NMR (D_2O): δ = 4.66 (m, 5-H), 4.28 (t, 1-H), 4.05 (dd, 6-H), 3.71 (m, 2-, 3-, 4-H), 2.83 (s, NCH_3); $J_{1,2}$ = 2.5, $J_{4,5}$ = $J_{5,6}$ = 7.5, $J_{6,1}$ = 3.5 Hz.

$C_8H_{12}N_4O_5$ (244.2) Calc. C 39.35 H 4.95 N 22.94 Found C 39.23 H 4.98 N 22.75

DL-(1α,2α,3β,4α,5β,6β)-3-Azido-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol 1,2,4-Triacetate (*rac*-**25b**): Acetylation of **25a** (245 mg, 1.0 mmol) gave 350 mg (95%) of colorless crystals (methanol), m.p. 78–80°C. – IR (KBr): 2940, 2100, 1745, 1420, 1370, 1210, 1025, 935, 895, 760, 600, 460, 440 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.58 (t, 1-H), 5.15 (dd, 4-H), 5.01 (dd, 2-H), 4.63 (t, 5-H), 3.92 (t, 3-H), 3.88 (dd, 6-H), 2.91 (s, NCH_3), 2.19, 2.18, 2.12 (s, 3 OAc); $J_{1,2}$ = 3.0, $J_{2,3}$ = $J_{3,4}$ = 10.0, $J_{4,5}$ = $J_{5,6}$ = 7.5, $J_{6,1}$ = 3.5 Hz.

$C_{14}H_{18}N_4O_8$ (370.3) Calc. C 45.41 H 4.90 N 15.13 Found C 44.50 H 4.86 N 14.83

DL-(1α,2α,3β,4α,5β,6β)-3-Azido-1,2-di-O-benzyl-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol (*rac*-**25c**) *and DL-(1α,2α,3α,4β,5β,6β)-4-Azido-1,2-di-O-benzyl-5-O,6-N-carbonyl-6-(methylamino)-1,2,3,5-cyclohexanetetrol* (*rac*-**26c**): A suspension of dibenzyl ether *rac*-**13j** (3.81 g, 10 mmol), NaN_3 (1.3 g, 20 mmol), and $MgSO_4$ (2.4 g, 20 mmol) in methanol (20 ml) was heated at reflux for 2 d. The mixture was concentrated i. vac., diluted with water (100 ml), and extracted with CH_2Cl_2 (3 × 80 ml). The extracts were dried ($MgSO_4$) and concentrated to give a colorless oil (4.2 g) which was crystallized from cyclohexane/ethyl acetate (2:1) to afford the 3-azide *rac*-**25c** (about 85%). Recrystallization of the mother liquor from cyclohexane/ethyl acetate (4:1) afforded pure 4-azide *rac*-**26c** (170 mg, 4%). Additional *rac*-**25c** was obtained by further crystallization (total yield: 3.92 g, 92%).

rac-**25c**: Colorless crystals, m.p. 126°C. – IR (KBr): 3370, 3030, 2920, 2100, 1750, 1455, 1430, 1405, 1375, 1250, 1235, 1100, 1070, 1030, 755, 700 cm $^{-1}$. – ^1H NMR ($CDCl_3$): δ = 7.40–7.25 (m, 10H), 4.75, 4.62, 4.56, 4.45 (d, 2 CH_2), 4.55 (t, 5-H), 3.87 (dd, 6-H), 3.82 (dd, 3-H), 3.72 (t, 4-H), 3.65 (dd, 1-H), 3.57 (dd, 2-H), 2.66 (s, NCH_3); $J_{1,2}$ = 2.0, $J_{2,3}$ = 5.0, $J_{3,4}$ = $J_{4,5}$ = $J_{5,6}$ = 8.5, $J_{6,1}$ = 5.5, J_{CH_2} = 12.0 Hz.

$C_{22}H_{24}N_4O_5$ (424.5)	Calc.	C 62.25	H 5.70	N 13.20
rac-**25c**:	Found	C 62.10	H 5.66	N 13.19
rac-**26c**:	Found	C 61.94	H 5.62	N 13.16

rac-**26c**: Colorless crystals, m.p. 194°C (dec.). – IR (KBr): 3340, 3025, 2860, 2100, 1755, 1455, 1440, 1405, 1340, 1265, 1215, 1150, 1100, 1070, 1025, 890, 760, 745, 700, 610 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.42–7.28 (m, 10H), 4.83, 4.73 (d, CH_2), 4.70 (m, 5-H), 4.63, 4.44 (d, CH_2), 4.16 (br. t, 2-H), 4.01 (m, 3-, 4-H), 3.82 (dd, 6-H), 3.65 (dd, 1-H), 3.31 (br. s, OH), 2.95 (s, NCH_3); $J_{1,2}$ = $J_{2,3}$ = 2.0, $J_{4,5}$ = 3.5, $J_{5,6}$ = 6.5, $J_{6,1}$ = 8.0, J_{CH_2} = 11.5 Hz.

DL-(1α,2α,3β,4α,5β,6β)-3-Azido-1,2-di-O-benzyl-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol 4-Acetate (*rac*-**25d**): Acetylation of *rac*-**25c** (105 mg, 0.25 mmol) gave 105 mg (90%) of a colorless oil. – ^1H NMR ($CDCl_3$): δ = 7.42–7.25 (m, 10H), 5.06 (t, 4-H), 4.79, 4.69, 4.59, 4.51 (d, 2 CH_2), 4.58 (t, 5-H), 3.88 (dd, 6-H), 3.82 (dd, 3-H), 3.69 (dd, 2-H), 3.62 (dd, 1-H), 2.58 (s, NCH_3), 2.12 (s, OAc); $J_{1,2}$ = 2.0, $J_{2,3}$ = 5.0, $J_{3,4}$ = 8.0, $J_{4,5}$ = 8.5, $J_{5,6}$ = 9.0, $J_{6,1}$ = 6.0, J_{CH_2} = 12.0 Hz.

$C_{24}H_{26}N_4O_6$ (466.5)

DL-(1α,2α,3α,4β,5β,6β)-4-Azido-1,2-di-O-benzyl-5-O,6-N-carbonyl-6-(methylamino)-1,2,3,5-cyclohexanetetrol 3-Acetate (*rac*-**26d**): Acetylation of *rac*-**26c** (85 mg, 0.20 mmol) yielded 85 mg (91%) of colorless crystals, m.p. 114°C (cyclohexane/ethyl acetate, 4:1). – IR (KBr): 3025, 2900, 2100, 1770, 1750, 1495, 1450, 1430, 1375, 1245, 1230, 1145, 1105, 1040, 915, 765, 745, 700, 650 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.42–7.26 (m, 10H), 5.05 (dd, 3-H), 4.73 (dd, 5-H), 4.73, 4.65, 4.63, 4.45 (d, 2 CH_2), 4.24 (t, 2-H), 4.21 (dd, 4-H), 3.83 (dd, 6-H), 3.65 (dd, 1-H), 2.96 (s, NCH_3), 2.11 (s, OAc); $J_{1,2}$ = $J_{2,3}$ = 2.0, $J_{3,4}$ = 11.0, $J_{4,5}$ = 5.0, $J_{5,6}$ = 6.5, $J_{6,1}$ = 8.0, J_{CH_2} = 11.5 Hz.

$C_{24}H_{26}N_4O_6$ (466.5) Calc. C 61.79 H 5.62 N 12.01 Found C 61.60 H 5.56 N 12.01

DL-(1α,2α,3β,4α,5β,6β)-3-Azido-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,4,5-cyclohexanetetrol (*rac*-**27a**) *and DL-(1α,2α,3α,4β,5β,6β)-4-Azido-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,3,5-cyclohexanetetrol* (*rac*-**28a**): A suspension of *rac*-**24** (480 mg, 2.0 mmol), NaN_3 (390 mg, 6.0 mmol), and $MgSO_4$ (720 mg, 6.0 mmol) in methanol (10 ml) was heated at reflux for 3 d. After filtration and concentration i. vac. the solid residue was chromatographed (silica, cyclohexane/ethyl acetate 1:1) to give 335 mg (59%) of *rac*-**27a**, then 180 mg (32%) of *rac*-**28a**.

rac-**27a**: Colorless crystals, m.p. 138°C ($CHCl_3$/ether, 1:5). – IR (KBr): 3350, 2985, 2910, 2890, 2105, 1720, 1485, 1440, 1405, 1380, 1255, 1220, 1060, 1030, 950, 865, 765, 665, 580 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 4.60 (dd, 5-H), 4.23 (t, 1-H), 4.18 (t, 2-H), 3.97 (s, OH), 3.81 (dd, 6-H), 3.78 (dd, 4-H), 3.52 (dd, 3-H), 2.95 (s, NCH_3), 1.54, 1.36 (s, 2 CH_3); $J_{1,2}$ = 7.0, $J_{2,3}$ = 7.5, $J_{3,4}$ = 12.0, $J_{4,5}$ = 7.5, $J_{5,6}$ = 9.0, $J_{6,1}$ = 6.0 Hz.

$C_{11}H_{16}N_4O_5$ (284.3)	Calc.	C 46.48	H 5.67	N 19.71
rac-**27a**:	Found	C 46.13	H 5.79	N 19.51
rac-**28a**:	Found	C 46.25	H 5.66	N 19.58

rac-**28a**: Colorless crystals, m.p. 119°C (methanol). – IR (KBr): 3360, 2975, 2920, 2115, 1745, 1445, 1410, 1380, 1375, 1250, 1205, 1160, 1040, 985, 920, 750, 670 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 4.99 (dd, 5-H), 4.48 (dd, 2-H), 4.38 (dd, 1-H), 4.22 (dt, 3-H), 4.11 (dd, 4-H), 3.92 (dd, 6-H), 2.97 (s, NCH_3), 2.70 (d, OH), 1.53, 1.40 (s, 2 CH_3); $J_{1,2}$ = 7.5, $J_{2,3}$ = 4.5, $J_{3,4}$ = 8.0, $J_{3,OH}$ = $J_{4,5}$ = 4.5, $J_{5,6}$ = 10.0, $J_{6,1}$ = 4.0 Hz.

DL-(1α,2α,3β,4α,5β,6β)-3-Azido-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,4,5-cyclohexanetetrol 4-Acetate (*rac*-**27b**): Acetylation of *rac*-**27a** (140 mg, 0.5 mmol) gave 150 mg (93%) of colorless crystals, m.p. 147–149°C (cyclohexane/ethyl acetate, 4:1). – IR (KBr): 2980, 2940, 2095, 1750, 1440, 1385, 1265, 1210, 1165, 1025, 885, 865, 755, 665, 600 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.13 (dd, 4-H), 4.68 (dd, 5-H), 4.32–4.23 (m, 1-, 2-H), 3.83 (m, 6-H), 3.62 (m, 3-H), 2.97 (s, NCH_3), 2.19 (s, OAc), 1.54, 1.37 (s, 2 CH_3); $J_{2,3}$ = 7.5, $J_{3,4}$ = 12.0, $J_{4,5}$ = 8.0, $J_{5,6}$ = 9.5, $J_{6,1}$ = 6.0 Hz.

$C_{13}H_{18}N_4O_6$ (326.3) Calc. C 47.85 H 5.56 N 17.17 Found C 47.70 H 5.69 N 16.47

DL-(1α,2α,3α,4β,5β,6β)-4-Azido-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,3,5-cyclohexanetetrol 3-Acetate (*rac*-**28b**): Acetylation of *rac*-**28a** (140 mg, 0.5 mmol) gave 145 mg (89%) of colorless crystals, m.p. 139–140°C (cyclohexane/ethyl acetate, 4:1). – IR (KBr): 2940, 2100, 1770, 1740, 1430, 1375, 1295, 1235, 1160, 1120, 1095, 1040, 910, 875, 780, 755, 515, 420 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.15 (dd, 3-H), 4.93 (dd, 5-H), 4.70 (dd, 2-H), 4.44 (dd, 1-H), 4.12 (dd, 4-H), 4.00 (dd, 6-H), 2.96 (s, NCH_3), 2.18 (s, OAc), 1.51, 1.35 (s, 2 CH_3); $J_{1,2}$ = 7.5, $J_{2,3}$ = 4.5, $J_{3,4}$ = 10.5, $J_{4,5}$ = 4.0, $J_{5,6}$ = 10.0, $J_{6,1}$ = 3.0 Hz.

$C_{13}H_{18}N_4O_6$ (326.3) Calc. C 47.85 H 5.56 N 17.17 Found C 47.42 H 5.58 N 16.49

DL-(1α,2α,3β,4α,5β,6β)-1,2:3,4-Di-O-isopropylidene-5-O,6-N-carbonyl-6-(methylamino)-1,2,3,4,5-cyclohexanepentol (*rac*-**29**): If in the preparation of *rac*-**24** the *p*-toluenesulfonic acid contains much water, after crystallization of *rac*-**24** the mother liquor contains up to 5% of *rac*-**29**, isolated by chromatography (cyclohexane/ethyl acetate, 2:1); colorless crystals, m.p. 240°C (ether, subl. at ca. 170°C). — IR (KBr): 2980, 2930, 1740, 1440, 1370, 1275, 1230, 1210, 1145, 1035, 845, 800, 755, 695, 660, 505 cm^{-1}. — ^1H NMR ($CDCl_3$): δ = 4.70 (dd, 5-H), 4.49 (t, 2-H), 4.30 (t, 1-H), 3.81 (dd, 4-H), 3.79 (dd, 6-H), 3.71 (dd, 3-H), 2.98 (s, NCH_3), 1.52, 1.35 (s, 2 CH_3), 1.46 (s, 2 CH_3); $J_{1,2} = J_{2,3} = 7.5$, $J_{3,4} = 11.0$, $J_{4,5} = 7.5$, $J_{5,6} = 9.5$, $J_{6,1} = 8.0$ Hz.

$C_{14}H_{21}N_1O_6$ (299.3) Calc. C 56.18 H 7.07 N 4.68 Found C 55.65 H 7.23 N 4.49

(+)-(1R)- and (+)-(1S)-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**30d**/**30d′**): A solution of *rac*-**13d** (2.0 g, 10 mmol) and (*R*)-(+)-1-phenylethylamine (2.6 ml, 20 mmol) in 1-propanol (10 ml) was heated at reflux for 4 h. After concentrating i. vac. and adding of $CHCl_3/CH_3OH$ (25:1, about 2 ml) the oily residue crystallized. The excess of (*R*)-(+)-1-phenylethylamine was removed i. vak. (0.01 Torr) at 60°C. Column-chromatographic separation [silica, $CHCl_3/CH_3OH/N(C_{12}H_5)_3$, 25:1:1] of the diastereomeric adducts afforded **30d′** (1.50 g, 46.5%) and **30d** (1.48 g, 46%).

30d: Colorless crystals, m.p. 76—78°C (CH_3OH): $[\alpha]_D^{20} = +4$ (*c* = 1.0, CH_3OH). — IR (KBr): 3610, 3320, 3060, 3025, 2955, 2865, 1755, 1630, 1600, 1430, 1395, 1320, 1245, 1145, 1125, 1055, 760, 695 cm^{-1}. — ^1H NMR ($CDCl_3/CD_3OD$, 1:1): δ = 7.37—7.20 (m, 5H), 4.40 (t, 5-H), 4.05 (q, *CH*CH_3), 3.93 (dd, 1-H), 3.85 (dd, 6-H), 3.76 (t, 2-H), 3.53 (t, 4-H), 2.95 (s, NCH_3), 2.51 (dd, 3-H), 1.41 (d, CH*CH*$_3$); $J_{1,2} = 2.5$, $J_{2,3} = 3.0$, $J_{3,4} = 10.0$, $J_{4,5} = J_{5,6} = 9.0$, $J_{6,1} = J_{CH,CH_3} = 7.0$ Hz.

$C_{16}H_{22}N_2O_5$ (322.4) Calc. C 59.62 H 6.88 N 8.69
30d: Found C 59.14 H 6.90 N 8.64
30d′: Found C 59.41 H 7.00 N 8.60

30d′: Colorless crystals, m.p. 178—181 °C (CH_3OH): $[\alpha]_D^{20} = +55$ (*c* = 1.0, CH_3OH). — IR (KBr): 3550, 3400, 3320, 3020, 2970, 2930, 2890, 1775, 1430, 1400, 1285, 1260, 1200, 1105, 1065, 1010, 890, 760, 700, 645 cm^{-1}. — ^1H NMR ($CDCl_3/CD_3OD$, 1:1): δ = 7.40—7.20 (m, 5H), 4.55 (t, 5-H), 4.09 (q, *CH*CH_3), 3.92 (dd, 1-H), 3.87 (dd, 6-H), 3.59 (t, 4-H), 3.55 (dd, 2-H), 2.93 (s, NCH_3), 2.80 (dd, 3-H), 1.42 (d, CH*CH*$_3$); $J_{1,2} = 2.5$, $J_{2,3} = 4.0$, $J_{3,4} = 9.0$, $J_{4,5} = 8.5$, $J_{5,6} = 8.0$, $J_{6,1} = J_{CH,CH_3} = 7.0$ Hz.

(+)-(1R)- and (−)-(1S)-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol 1,2,4-Triacetate (**30e**/**30e′**): Acetylation of **30d** (**30d′**) (320 mg, 1.0 mmol) yielded 420—425 mg (94—95%) of product.

30e: Colorless crystals, m.p. 122°C (ether); $[\alpha]_D^{20} = +10$ (*c* = 1.0, $CHCl_3$). — IR (KBr): 3320, 3030, 2970, 2930, 2880, 1750, 1430, 1370, 1225, 1115, 1040, 885, 755, 705, 605, 530, 480 cm^{-1}. — ^1H NMR ($CDCl_3$): δ = 7.34—7.13 (m, 5H), 5.38 (dd, 1-H), 5.20 (t, 2-H), 4.93 (dd, 4-H), 4.61 (t, 5-H), 4.07 (dd, 6-H), 3.89 (q, *CH*CH_3), 2.83 (s, NCH_3), 2.60 (dd, 3-H), 2.13, 2.08, 1.99 (s, 3 OAc), 2.03 (br. s, NH), 1.35 (d, CH*CH*$_3$), $J_{1,2} = J_{2,3} = 2.0$, $J_{3,4} = 8.0$, $J_{4,5} = 10.0$, $J_{5,6} = 9.5$, $J_{6,1} = 7.5$, $J_{CH,CH_3} = 6.5$ Hz.

$C_{22}H_{28}N_2O_8$ (448.5) Calc. C 58.92 H 6.29 N 6.26
30e: Found C 59.29 H 6.18 N 6.16
30e′: Found C 58.55 H 6.05 N 5.99

30e′: Colorless crystals, m.p. 179—181 °C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20} = +32$ (*c* = 1.0, $CHCl_3$). — IR (KBr): 2975, 2950, 2890, 1780, 1750, 1430, 1370, 1220, 1040, 945, 885, 765,

700, 660, 600, 585 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.33–7.19 (m, 5H), 5.37 (dd, 1-H), 5.11 (t, 4-H), 4.95 (dd, 2-H), 4.67 (t, 5-H), 3.95 (dd, 6-H), 3.92 (q, *CH*CH_3), 2.93 (dd, 3-H), 2.85 (s, NCH_3), 2.14, 2.02, 2.01 (s, 3 OAc), 2.00 (br. s, NH), 1.30 (s, CH*CH*$_3$); $J_{1,2}$ = 2.0, $J_{2,3}$ = 5.0, $J_{3,4}$ = 7.5, $J_{4,5}$ = $J_{5,6}$ = 8.5, $J_{6,1}$ = 6.0, J_{CH,CH_3} = 6.5 Hz.

(–)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**30f**): A solution of the acetal **32d** (1.81 g, 4 mmol) and 96-% sulfuric acid (500 mg, 5 mmol) in methanol (20 ml) was heated at reflux for 5 d. The solution was neutralized with $NaOCH_3$, concentrated i. vac., and the residue was purified by column chromatography (20 g of silica, ethyl acetate) to give 1.54 g (93%) of colorless crystals, m.p. 53–57°C (cyclohexane/ethyl acetate, 1:1); $[\alpha]_D^{20}$ = –25 (*c* = 1.0, CH_3OH). – IR (KBr): 3510, 3470, 3300, 3060, 3025, 2965, 2920, 2865, 1745, 1435, 1405, 1250, 1210, 1145, 1070, 1045, 1025, 975, 915, 840, 755, 695, 525 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.35–7.20 (m, 10H), 4.88, 4.58 (d, CH_2), 4.71 (dd, 5-H), 4.18 (t, 1-H), 4.07 (q, *CH*CH_3), 3.88 (dd, 6-H), 3.55 (br. s, OH), 3.53 (dd, 4-H), 3.38 (dd, 2-H), 2.93 (dd, 3-H), 2.90 (br. s, OH), 2.86 (s, NCH_3), 1.75 (br. s, NH), 1.29 (d, CH*CH*$_3$); $J_{1,2}$ = 3.0, $J_{2,3}$ = 8.5, $J_{3,4}$ = 9.5, $J_{4,5}$ = 7.0, $J_{5,6}$ = 8.0, $J_{6,1}$ = 3.5, J_{CH,CH_3} = 6.5, J_{CH_2} = 11.5 Hz. – ^1H NMR ($CDCl_3/CD_3OD$, 1:1): δ = 7.40–7.18 (m, 10H), 4.89, 4.56 (d, CH_2), 4.63 (t, 5-H), 3.93 (q, *CH*CH_3), 3.93 (dd, 1-H), 3.87 (t, 6-H), 3.70 (t, 2-H), 3.47 (t, 4-H), 2.96 (s, NCH_3), 2.62 (dd, 3-H), 1.30 (d, CH*CH*$_3$); $J_{1,2}$ = $J_{2,3}$ = 3.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 8.5, $J_{5,6}$ = 9.0, $J_{6,1}$ = 8.0, J_{CH,CH_3} = 6.5, J_{CH_2} = 2.0 Hz.

$C_{23}H_{28}N_2O_5$ (412.5) Calc. C 66.97 H 6.84 N 6.79 Found C 66.62 H 6.98 N 6.87

(+)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol 1,2-Diacetate (**30g**): Acetylation of **30f** (250 mg, 0.5 mmol) gave 230 mg (92%) of colorless crystals, m.p. 142°C (cyclohexane/ethyl acetate, 3:1); $[\alpha]_D^{20}$ = +12 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3325, 3030, 2980, 1755, 1740, 1430, 1395, 1370, 1240, 1215, 1105, 1040, 770, 755, 740, 705, 695 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.43–7.10 (m, 10H), 5.27 (dd, 1-H), 5.22 (t, 2-H), 4.98, 4.60 (d, CH_2), 4.65 (t, 5-H), 3.97 (dd, 6-H), 3.91 (q, *CH*CH_3), 3.54 (t, 4-H), 2.85 (s, NCH_3), 2.64 (dd, 3-H), 2.06, 2.01 (s, 2 OAc), 1.68 (br. s, NH), 1.28 (d, CH*CH*$_3$); $J_{1,2}$ = 2.5, $J_{2,3}$ = 3.0, $J_{3,4}$ = $J_{4,5}$ = $J_{5,6}$ = 9.0, $J_{6,1}$ = 7.5, J_{CH,CH_3} = 6.5, J_{CH_2} = 11.5 Hz.

$C_{27}H_{32}N_2O_7$ (496.6) Calc. C 65.31 H 6.50 N 5.64 Found C 65.07 H 6.40 N 5.63

(+)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-1,2-di-O-methyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**30k**), *(–)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-2-O-methyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol* (**30j**), *and (+)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-1-O-methyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]1,2,4,5-cyclohexane-tetrol* (**30h**): To a solution of **30f** (1.24 g, 3 mmol) in glyme (5 ml) was added NaH (140 mg, 6 mmol). The mixture was stirred at 20°C for 10 min, then CH_3I (0.19 ml, 3 mmol) was added. After 10 min at 20°C the solution was hydrolyzed with ice, diluted with water (50 ml), and extracted with CH_2Cl_2 (3 × 100 ml). The organic layer was washed with water (40 ml), dried ($MgSO_4$), and concentrated. The oily residue (1.3 g) was separated by column chromatography (silica, $CHCl_3/CH_3OH$, 25:1) to afford successively the bis(ether) **30k** (475 mg, 35%), 1-methyl ether **30h** (155 mg, 12%), 2-methyl ether **30j** (125 mg, 10%), and educt **30f** (435 mg, 35%).

30h: Colorless crystals, m.p. 108°C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20}$ = +3 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3400, 3025, 2965, 2895, 1745, 1425, 1395, 1270, 1100, 1080, 1025, 755, 700 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.40–7.20 (m, 10H), 4.92, 4.56 (d, CH_2), 4.60 (t, 5-H), 3.92 (q, *CH*CH_3), 3.87 (t, 2-H), 3.82 (dd, 6-H), 3.57 (dd, 1-H), 3.50 (dd, 4-H), 3.48 (s, OCH_3), 2.90 (s,

NCH_3), 2.72 (dd, 3-H), 2.65 (br. s, OH), 1.87 (br. s, NH), 1.31 (d, $CHCH_3$); $J_{1,2}$ = 3.0, $J_{2,3}$ = 4.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 8.0, $J_{5,6}$ = 9.0, $J_{6,1}$ = 7.5, J_{CH,CH_3} = 6.5, J_{CH_2} = 12.0 Hz.

30j: Colorless crystals, m.p. 138°C ($CHCl_3$/ether, 1:3); $[\alpha]_{20}^{D}$ = −14 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3430, 3310, 3020, 2960, 2900, 2825, 1755, 1450, 1420, 1390, 1365, 1270, 1240, 1210, 1110, 1080, 1055, 1020, 790, 755 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.45–7.15 (m, 10H), 4.93, 4.58 (d, CH_2), 4.59 (t, 5-H), 3.98 (br. s, 1-H), 3.88 (q, $CHCH_3$), 3.78 (dd, 6-H), 3.44 (dd, 4-H), 3.35 (t, 2-H), 3.19 (s, OCH_3), 2.96 (s, NCH_3), 2.67 (dd, 3-H), 2.54 (br. d, OH), 1.73 (br. s, NH), 1.24 (d, $CHCH_3$); $J_{1,2}$ = 2.5, $J_{1,OH}$ = 6.0, $J_{2,3}$ = 2.0, $J_{3,4}$ = 8.0, $J_{4,5}$ = 9.5, $J_{5,6}$ = 9.0, $J_{6,1}$ = 7.0, J_{CH,CH_3} = 6.5, J_{CH_2} = 11.5 Hz.

$C_{24}H_{30}N_2O_5$ (426.5)	Calc.	C 67.59	H 7.09 N 6.57
30j:	Found	C 67.26	H 7.09 N 6.52
30h:	Found	C 67.04	H 7.05 N 6.52

30k: Colorless crystals, m.p. 165°C ($CHCl_3$/ether, 1:3); $[\alpha]_D^{20}$ = +14 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3300, 3060, 3020, 2975, 2925, 2890, 2820, 1740, 1450, 1390, 1355, 1260, 1090, 1020, 795, 760, 755, 735, 695 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.45–7.15 (m, 10H), 4.96, 4.59 (d, CH_2), 4.62 (t, 5-H), 3.89 (dd, 6-H), 3.85 (q, $CHCH_3$), 3.51 (s, 2-H), 3.49 (dd, 1-H), 3.43 (s, OCH_3), 3.38 (dd, 4-H), 3.21 (s, OCH_3), 2.92 (s, NCH_3), 2.66 (d, 3-H), 1.9–1.3 (br. s, NH), 1.25 (d, $CHCH_3$); $J_{1,2}$ = 1.5, $J_{3,4}$ = 8.0, $J_{4,5}$ = $J_{5,6}$ = 9.5, $J_{6,1}$ = 8.0, J_{CH,CH_3} = 6.5, J_{CH_2} = 12.0 Hz.

$C_{25}H_{32}N_2O_5$ (440.5) Calc. C 68.16 H 7.32 N 6.36 Found C 67.49 H 7.33 N 6.24

(+)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-1-O-methyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol 2-Acetate (**30i**): Acetylation of **30h** (40 mg, 0.1 mmol) gave 40 mg (88%) of colorless crystals, m.p. 204–206°C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20}$ = +30 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3310, 3060, 3025, 2975, 2925, 2870, 1740, 1450, 1430, 1395, 1355, 1230, 1095, 1050, 1020, 950, 740, 700 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.45–7.05 (m, 10H), 5.34 (br. t, 2-H), 4.94, 4.56 (d, CH_2), 4.59 (t, 5-H), 3.94 (q, $CHCH_3$), 3.83 (dd, 6-H), 3.57 (dd, 1-H), 3.45 (t, 4-H), 3.39 (s, OCH_3), 2.92 (s, NCH_3), 2.51 (dd, 3-H), 1.98 (s, OAc), 1.64 (br. s, NH), 1.28 (d, $CHCH_3$); $J_{1,2}$ = 2.0, $J_{2,3}$ = 1.5, $J_{3,4}$ = $J_{4,5}$ = 9.0, $J_{5,6}$ = 9.5, $J_{6,1}$ = 8.5, J_{CH,CH_3} = 6.5, J_{CH_2} = 12.0 Hz.

$C_{26}H_{32}N_2O_6$ (468.6) Calc. C 66.65 H 6.88 N 5.98 Found C 66.47 H 6.93 N 6.02

(+)-(1R)-, (+)-(1S)-(1α,2α,3β,4α,5β,6β)-2-O-Benzyl-5-O,6-N-carbonyl-1-O-methyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**30l/30l'**), *(1R)*- and (1S)*-(1α,2α,3α,4β,5β,6β)-2-O-Benzyl-5-O,6-N-carbonyl-1-O-methyl-6-(methylamino)-4-[(R)-(1-phenylethyl)amino]-1,2,3,5-cyclohexanetetrol* (**31l/31l'**): A solution of *rac*-**13l** (915 mg, 3 mmol) and (*R*)-(+)-1-phenylethylamine (1.95 ml, 15 mmol) in 1-propanol (10 ml) was heated at reflux for 3 d (N_2). The yellow solution was concentrated i. vac. (0.01 Torr) at 60°C and the oily residue subjected to column chromatography [silica, cyclohexane/ethyl acetate/$N(C_2H_5)_3$, 10:5:1] to afford successively a mixture of *rac*-**13l** (165 mg, 18%) and **31l/31l'** (50 mg, 4%), **30l'** (460 mg, 36%) and **30l** (445 mg, 35%).

30l: Colorless oil; $[\alpha]_D^{20}$ = +54 (*c* = 1.0, $CHCl_3$). – ^1H NMR ($CDCl_3$): δ = 7.40–7.20 (m, 10H), 4.47 (t, 5-H), 4.44, 4.39 (d, CH_2), 3.94 (dd, 6-H), 3.89 (q, $CHCH_3$), 3.74 (t, 2-H), 3.63 (dd, 4-H), 3.57 (dd, 1-H), 3.33 (s, OCH_3), 2.89 (s, NCH_3), 2.74 (dd, 3-H), 1.35 (d, $CHCH_3$); $J_{1,2}$ = 1.5, $J_{2,3}$ = 1.0, $J_{3,4}$ = 8.0, $J_{4,5}$ = 9.5, $J_{5,6}$ = 9.0, $J_{6,1}$ = 7.5, J_{CH,CH_3} = 6.5, J_{CH_2} = 12.0 Hz.

30l': Colorless crystals, m.p. 173–176°C ($CHCl_3$/ether, 1:4); $[\alpha]_D^{20}$ = +26 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3400, 3060, 3020, 2960, 2920, 2860, 1745, 1495, 1480, 1430, 1400, 1350,

1270, 1250, 1135, 1090, 1040, 790, 760, 730, 705, 510 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.35–7.15 (m, 10H), 4.60 (t, 5-H), 4.32 (s, CH_2), 3.87 (t, 6-H), 3.85 (q, $CHCH_3$), 3.69 (t, 4-H), 3.45 (m, 1-, 2-H), 3.06 (s, OCH_3), 3.02 (dd, 3-H), 2.88 (s, NCH_3), 1.68 (br. s, OH, NH), 1.37 (d, $CHCH_3$); $J_{2,3}$ = 2.0, $J_{3,4}$ = 6.5, $J_{4,5}$ = $J_{5,6}$ = 8.5, $J_{6,1}$ = 7.5, J_{CH,CH_3} = 6.5 Hz.

$C_{24}H_{30}N_2O_5$ (426.5)	Calc.	C 67.59	H 7.09 N 6.57
30l':	Found	C 67.27	H 7.09 N 6.88
31l/31l':	Found	C 65.73	H 6.90 N 6.50

The starting material *rac*-**13l** was separated from an acidic solution (H_2SO_4) of *rac*-**13l/31l/31l'** with ether. The amines **31l/31l'** could not be separated sufficiently (chromatography, crystallization).

31l/31l': Colorless crystals, m.p. 148–149°C (ether). – ^1H NMR ($CDCl_3$) **31l**: δ = 7.45–7.05 (m, 10H), 4.72 (dd, 5-H), 4.63, 4.52 (d, CH_2), 4.13 (t, 2-H), 4.07 (q, $CHCH_3$), 3.58 (dd, 6-H), 3.47 (dd, 3-H), 3.27 (s, OCH_3), 3.17 (dd, 1-H), 3.05 (dd, 4-H), 2.96 (s, NCH_3), 1.90 (br. s, NH), 1.40 (d, $CHCH_3$); $J_{1,2}$ = 2.5, $J_{2,3}$ = 1.5, $J_{3,4}$ = 10.5, $J_{4,5}$ = 4.5, $J_{5,6}$ = 6.5, $J_{6,1}$ = 8.0, J_{CH,CH_3} = 6.5, J_{CH_2} = 11.5 Hz. – **31l'**: δ = 7.45–7.20 (m, 10H), 4.90, 4.78 (d, CH_2), 4.22 (dd, 5-H), 4.21 (t, 2-H), 3.92 (q, $CHCH_3$), 3.60 (dd, 6-H), 3.44 (dd, 3-H), 3.28 (dd, 4-H), 3.25 (s, OCH_3), 3.15 (dd, 1-H), 2.91 (s, NCH_3), 1.90 (br. s, NH), 1.39 (d, $CHCH_3$); coupling constants as for **31l**.

(+)-(1R)- and (–)-(1S)-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-1,2-O-isopropylidene-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**32a/32a'**). – a): A solution of **30a(30a')** (1.61 g, 5 mmol), *p*-toluenesulfonic acid monohydrate (1.03 g, 6 mmol) and 2,2-dimethoxypropane (2.2 ml, 25 mmol) in DMF (10 ml) was heated at 80°C for 2 h. After distilling off excess of 2,2-dimethoxypropane, the solution was concentrated i. vac. (0.01 Torr) at 60°C. CH_2Cl_2 (50 ml) was added and the organic layer was washed with saturated $NaHCO_3$ solution (50 ml) and with water (50 ml), dried, and concentrated to give the acetal **32a** (**32a'**) (1.72–1.78 g, 95–98%).

b): A suspension of the crude product **30a/30a'** (obtained from *rac*-**13d** (20.1 g, 100 mmol)) and *p*-toluenesulfonic acid monohydrate (20.6 g, 120 mmol) in 2,2-dimethoxypropane (40 ml) was heated at reflux. When the triols had dissolved completely (5 min) the solution was cooled and worked up as described above. The mixture of acetals **32a/32a'** was separated by fractional crystallization. The (1*S*)-acetal **32a'** (80–90%) crystallized from $CHCl_3$/ether (1:5). The residue from the mother liquor was recrystallized from ethyl acetate to give the pure (1*R*)-acetal **32a**. Alternatively, the mother liquor could be purified by column chromatography [silica, ethyl acetate/petroleum ether/$N(C_2H_5)_3$, 30:20:1]; total yield of **32a/32a'**: 90–95% (based on epoxide *rac*-**13d**).

32a: Colorless crystals, m.p. 142°C (ether); $[\alpha]_D^{20}$ = +114 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3400, 3055, 3020, 2920, 2830, 1730, 1600, 1440, 1380, 1265, 1240, 1205, 1130, 1025, 955, 865, 755, 695, 660, 550, 530, 380 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.37–7.21 (m, 5H), 4.55 (br. s, OH), 4.29 (dd, 5-H), 4.25 (t, 2-H), 4.21 (q, $CHCH_3$), 4.15 (t, 1-H), 3.60 (dd, 4-H), 3.53 (dd, 6-H), 2.90 (s, NCH_3), 2.42 (dd, 3-H), 2.16 (br. s, NH), 1.46 (s, CH_3), 1.40 (d, $CHCH_3$), 1.38 (s, CH_3); $J_{1,2}$ = 7.5, $J_{2,3}$ = 7.0, $J_{3,4}$ = 12.0, $J_{4,5}$ = 8.0, $J_{5,6}$ = 10.0, $J_{6,1}$ = 8.0, J_{CH,CH_3} = 6.5 Hz. – ^{13}C NMR ($CDCl_3$): δ = 157.4 (C=O), 144.5 (C-s), 128.4 (C-*m*), 126.9 (C-*p*), 126.9 (C-*o*), 110.2 (OCO), 81.2* (C-1), 77.9 (C-5), 76.6* (C-2), 68.9 (C-4), 60.3 (C-6), 55.9 (C-3), 55.1 ($CHCH_3$), 29.9 (NCH_3), 27.5, 25.2 (2 CH_3), 25.1 ($CHCH_3$).

$C_{19}H_{26}N_2O_5$ (362.4)	Calc.	C 62.97	H 7.23 N 7.73
32a:	Found	C 62.86	H 7.42 N 7.60
32a':	Found	C 62.80	H 7.25 N 7.71

32a': Colorless crystals, m.p. 191 °C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20} = -13$ ($c = 1.0$, $CHCl_3$). – IR (KBr): 3400, 3025, 2990, 2970, 2930, 2810, 1740, 1600, 1440, 1410, 1370, 1350, 1265, 1240, 1215, 1140, 1045, 960, 865, 815, 760, 695, 660, 560, 520 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.40–7.21 (m, 5H), 4.51 (dd, 5-H), 4.20–4.05 (br. s, OH), 4.13 (q, $CHCH_3$), 4.10 (t, 2-H), 4.05 (t, 1-H), 3.67 (dd, 6-H), 3.53 (dd, 4-H), 2.94 (s, NCH_3), 2.80 (dd, 3-H), 1.78 (br. s, NH), 1.45 (s, CH_3), 1.38 (d, $CHCH_3$), 1.18 (s, CH_3); $J_{1,2} = 7.0$, $J_{2,3} = 6.0$, $J_{3,4} = 12.0$, $J_{4,5} = 7.5$, $J_{5,6} = 9.5$, $J_{6,1} = 7.5$, $J_{CH,CH_3} = 6.5$ Hz. – ^{13}C NMR ($CDCl_3$): δ = 157.4 (C=O), 146.0 (C-s), 128.3 (C-*m*), 127.0 (C-*p*), 126.6 (C-*o*), 110.0 (OCO), 80.1* (C-1), 77.8 (C-5), 76.4* (C-2), 69.5 (C-4), 60.2 (C-6), 57.4 (C-3), 56.0 ($CHCH_3$), 30.0 (NCH_3), 27.6, 24.8 (2 CH_3), 23.4 ($CHCH_3$).

(+)-(1R)- and (–)-(1S)-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-1,2-O-isopropylidene-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol 4-Acetate (**32b/32b'**): Acetylation of **32a**(**32a'**) (360 mg, 1.0 mmol) gave 380–385 mg (94–95%) of colorless crystals, m.p. 133 °C (ether); $[\alpha]_D^{20} + 39$ ($c = 1.0$, $CHCl_3$). – IR (KBr): 3360, 3030, 2980, 2965, 2925, 1755, 1440, 1370, 1265, 1235, 1205, 1040, 1020, 865, 755, 695 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.35–7.20 (m, 5H), 5.02 (dd, 4-H), 4.47 (dd, 5-H), 4.28 (t, 2-H), 4.19 (t, 1-H), 4.17 (q, $CHCH_3$), 3.57 (dd, 6-H), 2.92 (s, NCH_3), 2.59 (dd, 3-H), 2.17 (s, OAc), 1.45, 1.36 (s, 2 CH_3), 1.33 (br. s, NH), 1.31 (d, $CHCH_3$); $J_{1,2} = J_{2,3} = 7.0$, $J_{3,4} = 12.5$, $J_{4,5} = 8.5$, $J_{5,6} = 9.5$, $J_{6,1} = 8.0$, $J_{CH,CH_3} = 6.5$ Hz.

$C_{21}H_{28}N_2O_6$ (404.5)	Calc.	C 62.36	H 6.98	N 6.93
32b:	Found	C 62.25	H 6.89	N 6.90
32b':	Found	C 62.32	H 6.86	N 6.85

32b': Colorless crystals m.p. 136 °C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20} = +45$ ($c = 1.0$, $CHCl_3$). – IR (KBr): 3355, 3030, 2980, 2935, 1750, 1435, 1370, 1210, 1135, 1045, 1025, 865, 755, 695, 665 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.36–7.19 (m, 5H), 5.06 (dd, 4-H), 4.58 (dd, 5-H), 4.19 (t, 1-H), 4.14 (t, 2-H), 4.03 (q, $CHCH_3$), 3.68 (dd, 6-H), 2.93 (s, CH_3), 2.77 (dd, 3-H), 2.20 (s, OAc), 1.47 (br. s, NH), 1.35 (s, CH_3), 1.30 (d, $CHCH_3$), 1.23 (s, CH_3); $J_{1,2} = J_{2,3} = 7.0$, $J_{3,4} = 12.0$, $J_{4,5} = 8.5$, $J_{5,6} = 9.5$, $J_{6,1} = 7.0$, $J_{CH,CH_3} = 6.5$ Hz.

(+)-(1R)-(1α,2α,3β,4α,5β,6β)-4-O-Benzyl-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**32d**): A suspension of the alcohol **32a** (1.81 g, 5 mmol) and NaH (170 mg, 7 mmol) in glyme (15 ml) was stirred at 20 °C for 15 min. Benzylchloride (1.26 g, 10 mmol) was added by syringe, and the mixture was heated at 60 °C for 2 h. On cooling the reaction was quenched with ice and extracted with CH_2Cl_2 (100 ml). The organic layer was washed with water (2 × 50 ml), dried ($MgSO_4$), and concentrated to give a residue which was purified by column chromatography (silica, cyclohexane/ethyl acetate, 2:1) to give 1.84 g (81%) of colorless crystals, m.p. 171 °C (ethyl acetate); $[\alpha]_D^{20} = +56$. ($c = 1.0$, $CHCl_3$). – IR (KBr): 3345, 2990, 2960, 2935, 2890, 1765, 1430, 1400, 1380, 1235, 1215, 1135, 1120, 1065, 1040, 990, 875, 735, 705, 670 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.42–7.18 (m, 10H), 4.94, 4.59 (d, CH_2), 4.45 (dd, 5-H), 4.26 (t, 2-H), 4.08 (dd, 1-H), 4.07 (q, $CHCH_3$), 3.59 (dd, 4-H), 3.53 (t, 6-H), 2.93 (s, NCH_3), 2.60 (br. s, NH), 2.57 (dd, 3-H), 1.44, 1.33 (s, 2 CH_3), 1.34 (d, $CHCH_3$); $J_{1,2} = 7.5$, $J_{2,3} = 6.5$, $J_{3,4} = 12.0$, $J_{4,5} = 7.0$, $J_{5,6} = 9.5$, $J_{6,1} = 9.0$, $J_{CH,CH_3} = 6.5$, $J_{CH_2} = 12.0$ Hz.

$C_{26}H_{32}N_2O_5$ (452.6) Calc. C 69.01 H 7.13 N 6.19 Found C 68.74 H 6.96 N 6.21

(–)-(1S)-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-1,2-O-isopropylidene-4-O-[(2-methoxyethoxy)methyl]-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**32e'**): To a suspension of **32a'** (725 mg, 2.0 mmol) in glyme (10 ml, NaH (75 mg, 3.0 mmol) was added. The suspension was stirred vigorously for 15 min at 20 °C. Then (2-methoxyethoxy)methyl chloride (0.25 ml, 2.2 mmol) was added by syringe. After 1 h the mixture was

hydrolyzed with ice and concentrated i. vac. The residue was dissolved in CH_2Cl_2 (40 ml), washed twice with water (20 ml), dried, and concentrated i. vac.: 830 mg (92%) of colorless crystals, m.p. 58 °C (ether/*n*-hexane, 1:2); $[\alpha]_D^{20} = -28$ (c = 1.0, $CHCl_3$). – IR (KBr): 3340, 2900, 1745, 1440, 1385, 1265, 1215, 1040, 1015, 865, 760, 700, 520 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.40–7.18 (m, 5H), 4.99, 4.95 (d, CH_2), 4.51 (dd, 5-H), 4.07 (q, $CHCH_3$), 4.07–4.00 (m, 1-, 2-H), 3.86–3.75* (m, 2′-CH_2), 3.75 (dd, 4-H), 3.65–3.53* (m, 6-H, 1′-CH_2), 3.40 (s, OCH_3), 2.92 (s, NCH_3), 2.86 (ddd, 3-H), 1.98 (br. s, NH), 1.39, 1.05 (s, 2 CH_3), 1.37 (d, $CHCH_3$); $J_{2,3}$ = 5.0, $J_{3,4}$ = 12.0, $J_{4,5}$ = 8.0, $J_{5,6}$ = 9.5, $J_{CH_2} = J_{CH_2} = J_{CH,CH_3}$ = 6.5 Hz.

$C_{23}H_{34}N_2O_7$ (450.5) Calc. C 61.32 H 7.61 N 6.22 Found C 61.34 H 7.88 N 6.24

(–)-(1S)-(1α,2α,3β,4α,5β,6β)-5-O,6-N-Carbonyl-1,2-O-isopropylidene-4-O-methyl-6-(methylamino)-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**32f′**): To a suspension of **32a′** (1.81 g, 5.0 mmol) in glyme (15 ml) NaH (170 mg, 7.0 mmol) is added. After stirring for 15 min at 20 °C methyl iodide (0.44 ml, 7.0 mmol) was added by syringe. After 30 min the mixture was hydrolyzed with ice, concentrated i. vac., dissolved in water (30 ml), and extracted with CH_2Cl_2 (3 × 50 ml). The organic layer was washed with water (50 ml), dried, and evaporated i. vac. to give 1.67 g (89%) of colorless crystals, m.p. 138 °C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20} = -36$ (c = 1.0, $CHCl_3$). – IR (KBr): 3340, 2970, 2920, 2840, 1745, 1430, 1400, 1370, 1265, 1240, 1215, 1120, 1025, 970, 865, 810, 755, 695, 665, 520 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.40–7.17 (m, 5H), 4.50 (dd, 5-H), 4.02 (m, 1-, 2-H, $CHCH_3$), 3.61 (m, 6-H), 3.58 (s, OCH_3), 3.33 (dd, 4-H), 2.95 (s, NCH_3), 2.89 (m, 3-H), 2.15 (br. s, NH), 1.40, 1.02 (s, 2 CH_3), 1.38 (d, $CHCH_3$); $J_{2,3}$ = 6.0, $J_{3,4}$ = 12.0, $J_{4,5}$ = 7.5, $J_{5,6}$ = 10.0, $J_{6,1}$ = 7.5, J_{CH,CH_3} = 6.5 Hz.

$C_{20}H_{28}N_2O_5$ (376.5) Calc. C 63.81 H 7.55 N 7.44 Found C 63.65 H 7.66 N 7.49

(+)-(1R)- and (–)-(1S*)-(1α,2α,3α,4β,5β,6β)-5-O,6-N-Carbonyl-1,2-O-isopropylidene-6-(methylamino)-4-[(R)-(1-phenylethyl)amino]-1,2,3,5-cyclohexanetetrol* (**33a/33a′**): A solution of *rac*-**24** (240 mg, 1 mmol) and (*R*)-(+)-1-phenylethylamine (1.3 ml, 10 mmol) in 3 ml of solvent [and Al_2O_3 (1.0 g) as in entries of Tab. 9] was heated at reflux (N_2) for 6 d. When TLC showed decomposition products, the reaction mixture was cooled, the Al_2O_3 filtered off, and the solution concentrated i. vac. (0.01 Torr) at 60 °C. The oily residue consisted of two product pairs (TLC: $CHCl_3/CH_3OH$, 25:1) as well as starting material. The molar composition was determined by ^1H NMR (250 MHz). Column chromatography on silica ($CHCl_3/CH_3OH$, 100:1) afforded successively the educt *rac*-**24**, *neo*-amines **33a/33a′**, *chiro*-amines **32a′** and **32a** (total yield ca. 90%).

Table 9. Reaction conditions and rel. composition of the product mixtures (**33a/33a′**:**32a/32a′** = *X*:*Y*)

Entry	Solvent	Temp.	Time	% Conversion	*X*:*Y*
1	Ethanol	78 °C	4 d	90	2:1
2	1-Propanol	100 °C	3 d	95	2:1
3	Acetonitrile	80 °C	8 d	65	4:1
4	Dioxane	101 °C	6 d	30	4:1
5	Dioxane/Al_2O_3 (basic)	101 °C	6 d	80	3:1
6	Dioxane/Al_2O_3 (neutral)	101 °C	6 d	80	3:1
7	Dioxane/Al_2O_3 (acidic)	101 °C	6 d	80	3:1

33a: Colorless crystals, m.p. 170°C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20} = +195$ ($c = 1.0$, $CHCl_3$). — IR (KBr): 3430, 3290, 3025, 2930, 1760, 1740, 1430, 1400, 1380, 1250, 1205, 1120, 1100, 1065, 1040, 1000, 970, 885, 760, 700, 660, 510 cm^{-1}. — ^1H NMR ($CDCl_3$): $\delta = 7.37-7.21$ (m, 5H), 4.92 (dd, 5-H), 4.50 (dd, 2-H), 4.40 (dd, 1-H), 4.05 (q, *CH*CH_3), 3.97 (dd, 6-H), 3.65 (br. s, OH), 3.58 (dd, 3-H), 2.94 (dd, 4-H), 2.90 (s, NCH_3), 1.90 (br. s, NH), 1.41 (d, $CHCH_3$), 1.25, 0.95 (s, 2 CH_3); $J_{1,2} = 7.5$, $J_{2,3} = 3.5$, $J_{3,4} = 11.0$, $J_{4,5} = 4.0$, $J_{5,6} = 9.5$, $J_{6,1} = 2.0$, $J_{CH,CH_3} = 6.5$ Hz.

$C_{19}H_{26}N_2O_5$ (362.4)	Calc.	C 62.97	H 7.23 N 7.73
33a:	Found	C 62.83	H 7.23 N 7.71
33a':	Found	C 62.51	H 7.31 N 7.89

33a': Colorless crystals, m.p. 126°C (ether); $[\alpha]_D^{20} = -92$ ($c = 1.0$, $CHCl_3$). — IR (KBr): 3370, 3305, 3060, 3025, 2980, 2930, 1760, 1730, 1430, 1405, 1380, 1270, 1250, 1160, 1125, 1110, 1060, 1035, 970, 920, 880, 760, 700, 675, 655, 545, 510 cm^{-1}. — ^1H NMR ($CDCl_3$): $\delta = 7.40-7.22$ (m, 5H), 4.60 (dd, 1-H), 4.41 (dd, 2-H), 4.38 (dd, 5-H), 3.87 (q, *CH*CH_3), 3.79 (dd, 3-H), 3.78 (br. s, 6-H), 3.52 (br. s, OH), 3.14 (dd, 4-H), 2.88 (s, NCH_3), 1.87 (br. s, NH), 1.45, 1.37 (s, 2 CH_3), 1.39 (d, CH*CH*$_3$); $J_{1,2} = 7.5$, $J_{2,3} = 3.0$, $J_{3,4} = 9.5$, $J_{4,5} = 4.5$, $J_{5,6} = 9.5$, $J_{6,1} = 4.0$, $J_{CH,CH_3} = 6.5$ Hz.

(+)-(1R)- and (−)-(1S*)-1α,2α,3α,4β,5β,6β)-5-O,6-N-Carbonyl-1,2-O-isopropylidene-6-(methylamino)-4-[(R)-(1-phenylethyl)amino]-1,2,3,5-cyclohexanetetrol 3-Acetate* (**33b**/**33b'**): Acetylation of **33a**(**33a'**) (180 mg, 0.5 mmol) gave 175–180 mg (86–89%) of product.

33b: Colorless crystals, m.p. 157°C ($CHCl_3$/ether 1:4); $[\alpha]_D^{20} = +84$ ($c = 1.0$, $CHCl_3$). — IR (KBr): 3440, 2970, 2930, 1755, 1430, 1380, 1240, 1145, 1065, 1040, 760, 700 cm^{-1}. — ^1H NMR ($CDCl_3$): $\delta = 7.36-7.20$ (m, 5H), 5.02 (dd, 3-H), 4.92 (dd, 5-H), 4.46 (dd, 2-H), 4.39 (dd, 1-H), 3.98 (q, *CH*CH_3), 3.90 (dd, 6-H), 3.20 (dd, 4-H), 2.92 (s, NCH_3), 2.20 (s, OAc), 1.70 (br. s, NH), 1.32 (d, CH*CH*$_3$), 1.25, 1.06 (s, 2 CH_3); $J_{1,2} = 7.5$, $J_{2,3} = 4.0$, $J_{3,4} = 10.5$, $J_{4,5} = 4.0$, $J_{5,6} = 9.5$, $J_{6,1} = 3.0$, $J_{CH,CH_3} = 6.5$ Hz.

$C_{21}H_{28}N_2O_6$ (404.5)	Calc.	C 62.36	H 6.98 N 6.93
33b:	Found	C 62.37	H 7.01 N 6.86
33b':	Found	C 62.24	H 6.92 N 7.05

33b': Colorless crystals, m.p. 156°C ($CHCl_3$/ether, 1:4); $[\alpha]_D^{20} = -41$ ($c = 1.0$, $CHCl_3$). — IR (KBr): 3330, 3030, 2980, 2930, 1770, 1430, 1410, 1385, 1365, 1250, 1215, 1145, 1040, 880, 760, 705 cm^{-1}. — ^1H NMR ($CDCl_3$): $\delta = 7.37-7.22$ (m, 5H), 5.35 (dd, 3-H), 4.62 (dd, 5-H), 4.61 (dd, 2-H), 4.41 (dd, 1-H), 3.94 (q, *CH*CH_3), 3.80 (dd, 6-H), 3.20 (dd, 4-H), 2.95 (s, NCH_3), 2.12 (s, OAc), 1.80 (s, NH), 1.33 (s, 2 CH_3), 1.32 (d, CH*CH*$_3$); $J_{1,2} = 8.0$, $J_{2,3} = 4.5$, $J_{3,4} = 8.5$, $J_{4,5} = 5.0$, $J_{5,6} = 10.0$, $J_{6,1} = 4.5$, $J_{CH,CH_3} = 6.5$ Hz.

(−)-(1R)- and (+)-(1S)-Bis[(1α,2α,3β,4α,5β,6β)-3-ammonio-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol] Sulfate Monohydrate [(**34a**)$_2$ · H_2SO_4 · H_2O/*ent*-(**34a**)$_2$ · H_2SO_4 · H_2O]: A solution of **32a** (1.81 g, 5 mmol) in methanol (30 ml) containing 96-% sulfuric acid (300 mg, 3 mmol) was hydrogenated (1 at H_2) over 10-% Pd/C (200 mg) at 20°C for 24 h. The catalyst was filtered off and the clear solution was concentrated and recrystallized from water/ethanol (1:3) to give the amine **34a** as its sulfate (1.25–1.30 g, 90–94%).

(**34a**)$_2$ · H_2SO_4 · H_2O: Colorless crystals, m.p. 262–265°C (dec.); $[\alpha]_D^{20} = -92$ ($c = 1.0$, H_2O). — IR (KBr): 3500–2900, 1755, 1635, 1520, 1430, 1405, 1385, 1355, 1335, 1310, 1250, 1150–1030, 855, 770, 760, 620 cm^{-1}. — ^1H NMR (D_2O): $\delta = 4.68$ (t, 5-H), 4.34 (t, 1-H),

4.09 (dd, 6-H), 3.93 (dd, 2-H), 3.87 (dd, 4-H), 3.43 (t, 3-H), 2.85 (s, NCH_3); $J_{1,2}$ = 3.0, $J_{2,3}$ = 10.0, $J_{3,4}$ = 11.5, $J_{4,5}$ = 7.5, $J_{5,6}$ = 8.0, $J_{6,1}$ = 3.0 Hz.

$C_{16}H_{30}N_4O_{14}S_1 \cdot H_2O$ (552.5) Calc. C 34.78 H 5.84 N 10.14
Found C 34.67 H 6.05 N 10.17

ent-(**34a**)$_2 \cdot H_2SO_4 \cdot H_2O$: $[\alpha]_D^{20}$ = +93.

(−)-(1R)- and (+)-(1R)-1α,2α,3β,4α,5β,6β)-3-(Acetylamino)-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol 1,2,4-Triacetate (**34b**/*ent*-**34b**): Acetylation of **34a** (*ent*-**34a**) gave 355−365 mg (92−94%) of colorless crystals, m.p. 193 °C ($CHCl_3$/ether, 1:5); **34b**: $[\alpha]_D^{20}$ = −82 (*c* = 1.0, $CHCl_3$). − IR (KBr): 3380, 2990, 2940, 1750, 1670, 1535, 1420, 1375, 1300, 1210, 1025, 930, 890, 770, 590, 435 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 6.02 (d, NH), 5.52 (dd, 1-H), 5.15 (dd, 5-H), 5.12 (dd, 2-H), 4.70 (t, 5-H), 4.53 (td, 3-H), 3.91 (dd, 6-H), 2.91 (s, NCH_3), 2.17, 2.11, 2.07 (s, 3 OAc), 1.94 (s, NAc); $J_{1,2}$ = 3.0, $J_{2,3}$ = 9.0, $J_{3,4}$ = 10.5, $J_{3,NH}$ = 9.0, $J_{4,5}$ = $J_{5,6}$ = 8.0, $J_{6,1}$ = 4.0 Hz.

$C_{16}H_{22}N_2O_9$ (386.4) Calc. C 49.74 H 5.74 N 7.25 Found C 49.54 H 5.73 N 7.24

ent-**34b**: $[\alpha]_D^{20}$ = +83 (*c* = 1.0, $CHCl_3$).

(+)-(1S)-(1α,2α,3β,4α,5β,6β)-3-[(Benzyloxycarbonyl)amino]-5-O,6-N-carbonyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol (*ent*-**36c**). − a): A solution of *ent*-**36b** (1.96 g, 5 mmol) and 96-% sulfuric acid (100 mg, 1 mmol) in methanol (50 ml) was heated at reflux for 2 h. After cooling the mixture was neutralized with $NaOCH_3$ and concentrated. The residue was purified by column chromatography (silica, $CHCl_3/CH_3OH$, 3:1) to give 1.57 g (89%) of colorless crystals, m.p. 209−211 °C ($CHCl_3/CH_3OH$, 5:1).

b): A solution of *ent*-(**34a**)$_2 \cdot H_2SO_4 \cdot H_2O$ (550 mg, 1 mmol) and Na_2CO_3 (330 mg, 4 mmol) in water/acetone (1:1, 10 ml) was cooled to 0 °C. Benzyloxycarbonyl chloride (0.43 ml, 3 mmol) was added and the mixture was stirred for 30 min. After 30 min at 20 °C the solution was concentrated and the residue was extracted with hot methanol (3 × 30 ml). The extracts were concentrated and the product was purified by column chromatography (silica, $CHCl_3/CH_3OH$, 3:1) to give 610 mg (86%) of *ent*-**34c**; $[\alpha]_D^{20}$ = +55 (*c* = 1.0, CH_3OH). − IR (KBr): 3350, 3070, 2930, 1720, 1690, 1530, 1430, 1400, 1290, 1245, 1025, 735, 690 cm^{-1}. − ^1H NMR ($CDCl_3/CD_3OD$, 1:1): δ = 7.40−7.30 (m, 5H), 5.11 (s, CH_2), 4.59 (t, 5-H), 4.04 (dd, 1-H), 3.92 (dd, 6-H), 3.74−3.65 (m, 2-, 3-, 4-H), 2.90 (s, NCH_3); $J_{1,2}$ = 2.5, $J_{4,5}$ = 8.0, $J_{5,6}$ = 9.0, $J_{6,1}$ = 5.5 Hz.

$C_{16}H_{20}N_2O_7$ (352.3) Calc. C 54.54 H 5.72 N 7.95 Found C 54.22 H 5.42 N 7.53

(−)-(1R)-(1α,2α,3β,4α,5β,6β)-3-(Acetylamino)-5-O,6-N-carbonyl-1-O-methyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol 2,4-Diacetate (**34e**): A solution of **30h** (or **30k**) (210 mg, 0.5 mmol) and 96-% sulfuric acid (25 mg, 0.25 mmol) in methanol (15 ml) was hydrogenated (1 at H_2) over 10-% Pd/C (100 mg) at 20 °C for 24 h. The catalyst was filtered off, the clear solution was concentrated to give the pure (^1H NMR) sulfate **34d**. − ^1H NMR (D_2O): δ = 4.64 (t, 5-H), 4.21 (dd, 6-H), 4.02 (dd, 2-H), 3.95 (t, 1-H), 3.86 (dd, 4-H), 3.52 (s, OCH_3), 3.38 (dd, 3-H), 2.85 (s, NCH_3); $J_{1,2}$ = 3.0, $J_{2,3}$ = 9.0, $J_{3,4}$ = 11.0, $J_{4,5}$ = 8.0, $J_{5,6}$ = 7.5, $J_{6,1}$ = 3.5 Hz.

The crude product was acetylated and purified by column chromatography (silica, ethyl acetate) to give 165 mg (93%) of colorless crystals, m.p. 248 °C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20}$ = −65 (*c* = 1.0, $CHCl_3$). − IR (KBr): 3330, 3060, 2935, 1750, 1735, 1685, 1550, 1450, 1405, 1375, 1260, 1225, 1145, 1095, 1040, 990, 955, 900, 755, 485 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 6.13 (d, NH), 5.24 (dd, 2-H), 5.18 (dd, 4-H), 4.68 (t, 5-H), 4.18 (ddd, 3-H), 3.93 (dd, 6-H), 3.88

(dd, 1-H), 3.47 (s, OCH_3), 2.91 (s, NCH_3), 2.13, 2.10 (s, 2 OAc), 1.95 (s, NAc); $J_{1,2}$ = 2.5, $J_{2,3}$ = 5.5, $J_{3,4}$ = 10.0, $J_{3,NH}$ = 8.5, $J_{4,5}$ = 9.0, $J_{5,6}$ = 8.0, $J_{6,1}$ = 6.5 Hz.

$C_{15}H_{22}N_2O_8$ (358.4) Calc. C 50.28 H 6.19 N 7.82 Found C 49.85 H 6.26 N 7.97

(+)-(1S)-(1α,2α,3β,4α,5β,6β)-3-(Acetylamino)-5-O,6-N-carbonyl-1-O-methyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol 2,4-Diacetate (*ent*-**34e**): A solution of **30l'** (210 mg, 0.5 mmol) was hydrogenated and acetylated to give 165 mg (93%) of colorless crystals, m.p. 243 °C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20}$ = +63 (*c* = 1.0, $CHCl_3$).

(+)-(1S)-(1α,2α,3β,4α,5β,6β)-1,2-O-Benzylidene-3-[(benzyloxycarbonyl)amino]-6-methylamino)-1,2,4,5-cyclohexanetetrol (*ent*-**35**): A suspension of *ent*-**34c** (1.06 g, 3 mmol), α,α-dimethoxytoluene (1.52 g, 10 mmol), and *p*-toluenesulfonic acid monohydrate (60 mg, 0.3 mmol) in CH_2Cl_2 (10 ml) was heated at reflux for 2 h. CH_2Cl_2 (50 ml) was added and the organic layer was washed with saturated $NaHCO_3$ solution (50 ml) and water (50 ml), dried ($MgSO_4$), and concentrated. The oily residue was purified by column chromatography (silica, cyclohexane/ethyl acetate, 1:2) to give 1.15 g (87%) of colorless crystals, m.p. 215–217 °C ($CHCl_3$); $[\alpha]_D^{20}$ = +16 (*c* = 1.0, CH_3OH). – IR (KBr): 3410, 3360, 2930, 1740, 1690, 1540, 1410, 1310, 1275, 1230, 1090–1020, 975, 915, 760, 700, 665 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.6–7.2 (m, 5H), 6.13, 5.77 (s, CH), 5.64, 5.54 (d, NH), 5.1 (s, CH_2), 4.8–3.6 (m, 1-, 2-, 3-, 4-, 5-, 6-H, OH), 2.95–2.83 (m, NCH_3).

$C_{23}H_{24}N_2O_7$ (440.5) Calc. C 62.72 H 5.49 N 6.36 Found C 62.27 H 5.43 N 6.24

(−)-(1R)-Bis[(1α,2α,3β,4α,5β,6β)-3-ammonio-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,4,5-cyclohexanetetrol] Sulfate Dihydrate [(**36a**)$_2$ · H_2SO_4 · 2 H_2O]: A solution of **32a** (3.62 g, 10 mmol) in methanol (100 ml) containing 96-% sulfuric acid (300 mg, 3 mmol) was hydrogenated (1 at H_2) over 10-% Pd/C (300 mg) at 20 °C for 24 h. Water was added to dissolve the precipitate and the catalyst was filtered off. The clear solution was concentrated i. vac. and the residue was treated with dilute sulfuric acid (1.8–1.9 mmol). Recrystallization from water/ethanol (1:5) afforded **36a** as its sulfate (2.9–3.1 g, 89–95%).

(**36a**)$_2$ · H_2SO_4 · 2 H_2O: Colorless crystals, m.p. 235–240 °C (dec.); $[\alpha]_D^{20}$ = −14 (*c* = 1.0, H_2O). – IR (KBr): 3500–2850, 1760–1720, 1620, 1520, 1430, 1375, 1240, 1215, 1150–1020, 860, 755, 610, 400 cm^{-1}. – ^1H NMR (D_2O): δ = 4.75 (t, 5-H), 4.64 (t, 1-H), 4.56 (t, 2-H), 4.20 (dd, 6-H), 3.99 (dd, 4-H), 3.41 (dd, 3-H), 2.92 (s, NCH_3), 1.56, 1.42 (s, 2 CH_3); $J_{1,2}$ = 7.5, $J_{2,3}$ = 8.0, $J_{3,4}$ = 12.5, $J_{4,5}$ = 8.5, $J_{5,6}$ = 9.5, $J_{6,1}$ = 6.0 Hz.

$C_{22}H_{38}N_4O_{14}S_1$ · 2 H_2O (650.7) Calc. C 40.61 H 6.51 N 8.61
Found C 41.00 H 6.19 N 8.62

(−)-(1R)-(1α,2α,3β,4α,5β,6β)-3-[(Benzyloxycarbonyl)amino]-5-O,6-N-carbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,4,5-cyclohexanetetrol (**36b**): A solution of (**36a**)$_2$ · H_2SO_4 · 2 H_2O (6.5 g, 10 mmol) and Na_2CO_3 (3.3 g, 40 mmol) in water/acetone (1:1, 50 ml) was cooled to 0 °C. Benzyloxycarbonyl chloride (3.55 ml, 25 mmol) was added and the mixture was allowed to warm to room temperature over 1 h. Water (50 ml) was added and the suspension was extracted with CH_2Cl_2 (3 × 100 ml). The organic layer was dried ($MgSO_4$) and concentrated to give an oily residue which was purified by column chromatography (silica, cyclohexane/ethyl acetate, 2:1) to give 6.45 g (82%) of colorless crystals, m.p. 93–95 °C (cyclohexane/ethyl acetate, 1:1); $[\alpha]_D^{20}$ = −6 (*c* = 1.0, CH_3OH). – IR (KBr): 3400–3320, 2980, 2930, 1750–1700, 1530, 1435, 1405, 1380, 1235, 1165, 1110, 1030, 860, 755, 695, 665 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.39–7.30 (m, 5H), 5.56 (d, NH), 5.11 (s, CH_2), 4.51 (dd, 5-H), 4.28 (br. t, 2-H), 4.13 (t, 1-H), 4.01 (br. s, OH), 3.80 (br. s, 4-H), 3.68 (dd, 6-H), 3.61 (td, 3-H), 2.91 (s, NCH_3), 1.51, 1.33 (s, 2 CH_3); $J_{1,2}$ = 7.0, $J_{2,3}$ = 8.0, $J_{3,4}$ = 12.0, $J_{3,NH}$ = 8.5, $J_{4,5}$ = 8.0, $J_{5,6}$ = 9.5, $J_{6,1}$ = 7.0 Hz. – ^{13}C NMR ($CDCl_3$): δ = 157.4

(C=O), 157.0 (C=O–Cbz), 136.3, 128.5, 128.0, 127.9 (6 Phenyl-C), 110.3 (OCO), 77.6 (C-2, -5), 75.9 (C-1), 69.3 (C-4), 67.0 (CH_2), 60.1 (C-6), 54.1 (C-3), 29.9 (NCH_3), 27.5, 25.1 (2 CH_3).

$C_{19}H_{24}N_2O_7$ (392.4) Calc. C 58.16 H 6.16 N 7.14 Found C 57.66 H 6.13 N 7.00

*(−)-(1S)-(1α,2α,3β,4α,5β,6β)-3-Amino-5-O,6-N-carbonyl-1,2-O-isopropylidene-4-O-methyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol (ent-***36c**): A solution of **32f'** (1.88 g, 5.0 mmol) in methanol [20 ml/96-% sulfuric acid (150 mg, 1.5 mmol)] was hydrogenated (1 at H_2) over 10-% Pd/C (150 mg) at 20°C for 24 h. After filtration and concentration CH_2Cl_2 (100 ml) was added. After washing with $NaHCO_3$ solution (50 ml) and H_2O, drying ($MgSO_4$), and concentration 1.17 g (86%) of colorless crystals were obtained; m.p. 153°C ($CHCl_3$/ether, 1:5); $[\alpha]_D^{20} = -57$ (c = 1.0, $CHCl_3$). – IR (KBr): 3380, 3320, 2980, 2935, 1730, 1575, 1430, 1380, 1295, 1240, 1210, 1145, 1030, 960, 865, 750, 665, 600, 510, 475 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 4.51 (dd, 5-H), 4.14 (m, 1-, 2-H), 3.70 (m, 6-H), 3.56 (s, OCH_3), 3.20 (dd, 4-H), 2.98 (s, NCH_3), 2.93 (m, 3-H), 1.75 (s, NH_2), 1.51, 1.35 (s, 2 CH_3); $J_{2,3}$ = 7.5, $J_{3,4}$ = 12.0, $J_{4,5}$ = 7.0, $J_{5,6}$ = 9.5, $J_{6,1}$ = 7.5 Hz.

$C_{12}H_{20}N_2O_5$ (272.3) Calc. C 52.93 H 7.40 N 10.29 Found C 52.76 H 7.60 N 10.08

*(−)-(1R)-(1α,2α,3β,4α,5β,6β)-3-Amino-3-N,4-O:5-O,6-N-dicarbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,4,5-cyclohexanetetrol (***37a**): To a solution of (**36a**)$_2$ · H_2SO_4 · 2 H_2O (650 mg, 1.0 mmol) and triethylamine (0.5 ml) in CH_2Cl_2 (5 ml) at 0°C benzyloxycarbonyl chloride (0.35 ml, 2.5 mmol) was added. After 30 min of stirring at 0°C, then at 20°C, the solution was washed (H_2O) and concentrated i. vac. The solid residue was chromatographed (silica, cyclohexane/ethyl acetate, 1:2). After concentration the solid was extracted twice with boiling $CHCl_3$ (10 ml each). The extract contained 440 mg (56%) of **36b**, the rest was practically pure **37a**, 150 mg (25%) of colorless crystals, m.p. 325°C ($CHCl_3$/methanol, 10:1, subl. at 280°C); $[\alpha]_D^{20} = -92$ (c = 1.0, CH_3OH). – IR (KBr): 3420, 3370, 2990, 2930, 2900, 1775, 1750, 1440, 1410, 1380, 1260, 1240, 1215, 1160, 1050, 1015, 930, 920, 875, 765, 755, 750, 665, 550, 525 cm^{-1}. – ^1H NMR ($CDCl_3$/CD_3OD, 5:1): δ = 4.91 (dd, 5-H), 4.45 (t, 2-H), 4.33 (t, 1-H), 4.24 (dd, 4-H), 3.91 (dd, 6-H), 3.58 (dd, 3-H), 2.98 (s, NCH_3), 1.52, 1.36 (s, 2 CH_3); $J_{1,2}$ = $J_{2,3}$ = 8.0, $J_{3,4}$ = 13.0, $J_{4,5}$ = 8.5, $J_{5,6}$ = 10.0, $J_{6,1}$ = 7.5 Hz. – ^1H NMR ([D_6]DMSO): δ = 8.44 (s, NH), 4.96 (t, 5-H), 4.41 (m, 1-, 2-H), 4.34 (dd, 4-H), 3.94 (m, 6-H), 3.65 (m, 3-H), 2.80 (s, NCH_3), 1.45, 1.30 (s, 2 CH_3); $J_{2,3}$ = 7.5, $J_{3,4}$ = 12.5, $J_{4,5}$ = 8.5, $J_{5,6}$ = 9.0, $J_{6,1}$ = 6.5 Hz.

$C_{12}H_{16}N_2O_6$ (284.3) Calc. C 50.70 H 5.67 N 9.85 Found C 50.50 H 5.81 N 9.85

*(+)-(1R)-(1α,2α,3β,4α,5β,6β)-3-[(Benzyloxycarbonyl)amino]-3-N,4-O:5-O,6-N-dicarbonyl-1,2-O-isopropylidene-6-(methylamino)-1,2,4,5-cyclohexanetetrol (***37b**): In the above reaction – especially with a greater excess of reagent – **37b** can be formed and can be found as the first-eluted compound in the chromatographic separation; colorless crystals, m.p. 218–220°C (ether); $[\alpha]_D^{20} = +25$ (c = 1.0, $CHCl_3$). – IR (KBr): 3030, 2985, 2930, 1835, 1765, 1435, 1405, 1385, 1320, 1300, 1275, 1240, 1210, 1165, 1115, 1080, 1045, 1020, 870, 750, 695, 665 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 7.47–7.32 (m, 5H), 5.37, 5.26 (d, CH_2), 4.80 (t, 5-H), 4.61 (t, 2-H), 4.31 (dd, 1-H), 4.23 (dd, 4-H), 3.98 (dd, 3-H), 3.80 (t, 6-H), 2.98 (s, NCH_3), 1.46, 1.23 (s, 2 CH_3); $J_{1,2}$ = 7.0, $J_{2,3}$ = 7.5, $J_{3,4}$ = 13.0, $J_{4,5}$ = 8.5, $J_{5,6}$ = 9.5, $J_{6,1}$ = 9.0, J_{CH_2} = 12.0 Hz.

$C_{20}H_{22}N_2O_8$ (418.4) Calc. C 57.41 H 5.30 N 6.70 Found C 57.89 H 5.06 N 7.10

*(−)-(1R)- and (+)-(1S)-(1α,2α,3β,4α,5β,6β)-3-Ammonio-6-(methylammonio)-1,2,4,5-cyclohexanetetrol Sulfate Monohydrate (De-O-methylfortamine Sulfate) (***38a** · H_2SO_4 · H_2O/*ent-***38a** · H_2SO_4 · H_2O): A suspension of (**34a**)$_2$ · H_2SO_4 · H_2O (550 mg, 1 mmol) and

$Ba(OH)_2 \cdot 8\ H_2O$ (1.26 g, 4 mmol) in water (50 ml) was heated at reflux for 2 h (N_2). The mixture was filtered and acidified (pH = 2) with 2 N H_2SO_4. Then $BaSO_4$ was separated by centrifugation, and the clear solution was concentrated i. vac. The diamine **38a** crystallized from water/ethanol (1:3) as sulfate monohydrate (565–590 mg, 92–96% yield); colorless crystals, dec. at 260°C; $[\alpha]_D^{20} = -16$ (c = 1.0, H_2O). – IR (KBr): 3400–3280, 3160, 1750, 1610, 1520, 1460, 1375, 1240, 1100–1030, 600 cm^{-1}. – ^{1} NMR (D_2O): δ = 4.40 (t, 1-H), 4.21 (dd, 5-H), 4.12 (dd, 2-H), 3.87 (t, 4-H), 3.61 (t, 6-H), 3.45 (t, 3-H), 2.86 (s, NCH_3); $J_{1,2}$ = 3.0, $J_{2,3} = J_{3,4}$ = 9.0, $J_{4,5}$ = 8.5, $J_{5,6}$ = 5.0, $J_{6,1}$ = 4.5 Hz. – ^{13}C NMR (D_2O): δ = 69.4 (C-4), 68.3 (C-5), 67.6 (C-2), 66.5 (C-1), 61.9 (C-6), 54.7 (C-3), 33.8 (CH_3); free base: 74.5 (C-4), 72.2 (C-5), 71.4 (C-2), 70.4 (C-1), 65.2 (C-6), 55.2 (C-3), 35.7 (CH_3).

$C_7H_{18}N_2O_8S_1 \cdot H_2O$ (308.3) Calc. C 27.27 H 6.54 N 9.09 Found C 27.13 H 6.63 N 9.05

ent-**38a** $\cdot H_2SO_4 \cdot H_2O$: $[\alpha]_D^{20} = +16$ (c = 1.0, H_2O).

(+)-(1R)- and (–)-(1S)-(1α,2α,3β,4α,5β,6β)-3-[(Benzyloxycarboyl)amino]-6-[(benzyloxycarbonyl)(methyl)amino]-1,2,4,5-cyclohexanetetrol (**38b**/*ent*-**38b**): A solution of **38a**(*ent*-**38a**) $\cdot H_2SO_4 \cdot H_2O$ (155 mg, 0.5 mmol) and Na_2CO_3 (250 mg, 3 mmol) in water/acetone (1:1, 6 ml) was cooled to 0°C. Benzyloxycarbonyl chloride (0.28 ml, 2 mmol) was added and the mixture was stirred at 0°C for 30 min. After 30 min at 20°C the solution was concenrated i. vac., diluted with water (20 ml, and extracted with ether (3 × 30 ml). The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by column chromatography (silica, $CHCl_3/CH_3OH$, 10:1) to give 175 mg (76%) of colorless crystals, m.p. 143°C (ether); $[\alpha]_D^{20} = +56$ (c = 1.0, CH_3OH). – IR (KBr): 3400, 3060, 3030, 2920, 1670, 1500, 1450, 1400, 1340, 1225, 1155, 1015, 750, 690 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 7.32 (s, 10H), 6.42 (br. d, NH), 5.10, 5.02 (s, 2 CH_2), 4.62 (br. s, 2H), 4.43 (br. t, 1H), 4.24 (br. s, 1H), 4.18 (br. s, 2H), 4.05 (br. d, OH), 3.89 (br. s, 1H), 3.34 (br. d, OH), 3.09 (s, NCH_3), 2.20 (s, OH); $J_{3,NH}$ = 7.5.

$C_{23}H_{28}N_2O_8$ (460.5) Calc. C 59.99 H 6.13 N 6.08 Found C 59.44 H 6.11 N 6.02

ent-**38b**: $[\alpha]_D^{20} = -52$ (c = 1.0, CH_3OH).

(1S)-(1α,2α,3β,4α,5β,6β)-6-⟨[N-(Diphenylmethylen)glycyl](methyl)amino⟩-1,2-O-isopropylidene-4-O-[(2-methoxyethoxy)methyl]-3-[(R)-(1-phenylethyl)amino]-1,2,4,5-cyclohexanetetrol (**46**): To a solution of diisopropylamine (0.56 ml, 4.0 mmol) in tetrahydrofuran (freshly distilled over sodium, 3 ml) a solution of *n*-butyllithium in *n*-hexane (2 M, 2.0 ml, 4.0 mmol) was added at 0°C by syringe. After 10 min the solution was cooled to –78°C and *N*-methylbenzophenone imine (780 mg, 4.0 mmol, dissolved in 1 ml of THF) was added slowly. The color of the solution changed slowly from yellow to dark red. After 20 min **32e'** (450 mg, 1.0 mmol, dissolved in 2 ml of THF) was added by syringe. After 10 min methanol (10 ml) was added, the solution diluted with CH_2Cl_2 (50 ml), the organic layer washed with water (30 ml), dried, and concentrated. The residue was separated by chromatography (silica, cyclohexane/ethyl acetate/triethylamine, 25:25:1) to yield in the following order reagent and products thereof (^{1}H NMR): 185 mg of **32e'** (41%) and 275 mg of **46** (43%, 73% based on conversion), colorless oil. – ^{1}H NMR ($CDCl_3$): δ = 7.70–7.15 (m, 15H), 4.78, 4.75 (d, OCH_2O), 4.74 (dd, 1-H), 4.32, 4.27 (d, NCH_2), 4.28 (t, 2-H), 4.12 (m, 5-H), 4.12–4.05 (br. s, OH), 4.08 (q, $CHCH_3$), 3.95 (dd, 6-H), 3.85 (t, 4-H), 3.74, 3.65 (dt, 1'-CH_2), 3.51 (t, 2'-CH_2), 3.35 (s, OCH_3), 3.15 (s, NCH_3), 2.92 (t, 3-H), 1.36, 1.28 (s, 2 CH_3), 1.34 (d, $CHCH_3$); $J_{1,2}$ = 6.0, $J_{2,3}$ = 5.5, $J_{3,4}$ = 4.5, $J_{4,5}$ = 3.5, $J_{5,6}$ = 1.5, $J_{6,1}$ = 10.0, $J_{1',2'}$ = 4.5, $J_{1'\text{-}CH_2}$ = 11.5, J_{OCH_2O} = 7.0, J_{NCH_2} = 15.5, J_{CH,CH_3} = 6.5 Hz.

(1S)-(1α,2α,3β,4α,5β,6β)-6-⟨[2-(Diphenylmethylen)amino-3-phenylpropionyl](methyl)-amino⟩-1,2-O-isopropylidene-4-O-[(2-methoxyethoxy)methyl]-3-[(R)-(1-phenylethyl)-

amino]-1,2,4,5-cyclohexanetetrol (**47**): To the reaction mixture for the preparation of **46**, before the addition of methanol, benzyl chloride (250 mg, 2.0 mmol) was added by syringe. After 1 h at 0°C **47** was isolated by chromatography (silica, cyclohexane/ethyl acetate/triethylamine, 25:25:1, R_f between **32e'** and **46**): colorless oil, not totally pure. – ^{1}H NMR ($CDCl_3$): δ = 7.70–6.85 (m, 20H), 6.20 (br. s, OH), 4.77, 4.72 (d, OCH_2O), 4.75 (dd, 1-H), 4.47 (t, NCH), 4.27 (t, 2-H), 4.08 (q, $CHCH_3$), 4.02 (br. dd, 5-H), 3.83 (t, 4-H), 3.77 (br. s, 6-H), 3.73, 3.63 (dt, 1'-CH_2), 3.48 (t, 2'-CH_2), 3.34, 3.16 (dd, CH_2Ph), 3.32 (s, OCH_3), 2.87 (t, 3-H), 2.67 (s, NCH_3), 2.05 (br. s, NH), 1.35, 1.28 (s, 2 CH_3), 1.34 (d, $CHCH_3$); $J_{1,2}$ = 6.0, $J_{2,3}$ = 5,5, $J_{3,4}$ = 4.5, $J_{4,5}$ = 3.5, $J_{5,6}$ = 1.5, $J_{6,1}$ = 9.5, $J_{1',2'}$ = 4.5, $J_{1'\text{-}CH_2}$ = 11.5, J_{CH_2O} = J_{CH,CH_2} = 6.5, J_{CH_2Ph} = 13.0 Hz.

(1S)-(1α,2β,3β,4α,5β,6β)-3-⟨[N-(Diphenylmethylen)glycyl](methyl)amino⟩-1-O-[(2-methoxyethoxy)methyl]-5,6-[(R)-(1-phenylethyl)imino]-1,2,4-cyclohexanetriol (**48**) *and (1R)-(1α,2α,3β,4β,5β,6β)-3-([N-(Diphenylmethylen)glycyl](methyl)amino)-1,2-O-isopropylidene-5,6-[(R)-(1-phenylethyl)imino]-1,2,4-cyclohexanetriol* (**49**): When the reaction mixture for the synthesis of **46** was kept at 0°C for 1–2 h before the addition of methanol, two other main products were formed in a ratio of 3:1. Several by-products were isolated by chromatography (silica, cyclohexane/ethyl acetate/triethylamine, 50:25:2), sequence of products: **49**, **32e'**, **48**, **46**). Both, **48** and **49**, are colorless oils, not totally pure, characterized by NMR. In the solution of **48** two rotamers (I and II, ca. 3:1) are present.

48: ^{1}H NMR ($CDCl_3$, 400 MHz) of I: δ = 7.70–7.15 (m, 15H), 5.29 (d, 4-OH), 4.85 (s, OCH_2O), 4.39, 4.02 (d, NCH_2), 4.23 (t, 1-H), 4.21 (dd, 3-H), 4.16 (d, 4-H), 3.85 (m, 2-H), 3.75, 3.65 (m, 1'-CH_2), 3.55 (t, 2'-CH_2), 3.35 (s, OCH_3), 3.15 (s, NCH_3), 2.65 (q, $CHCH_3$), 2.30 (m, 6-H), 2.18 (d, 5-H), 1.42 (d, $CHCH_3$); $J_{1,2}$ = 3.0, $J_{2,3}$ = $J_{2,6}$ = 2.0, $J_{2,OH}$ = 10.5, $J_{3,4}$ = 10.0, $J_{4,5}$ = 0, $J_{5,6}$ = 5.0, $J_{6,1}$ = 3.0, $J_{1',2'}$ = 4.5, J_{CH,CH_3} = 6.5, J_{NCH_2} = 14.0 Hz. – Of II: δ = 7.70–7.15 (m, 15H), 5.29 (d, OH), 4.85 (s, OCH_2O), 4.67 (dd, 3-H), 4.23 (t, 1-H), 4.20 (s, NCH_2), 4.16 (d, 4-H), 3.90 (m, 2-H), 3.70 (m, 1'-CH_2), 3.56 (t, 2'-CH_2), 3.35 (s, OCH_3), 3.20 (s, NCH_3), 2.65 (q, $CHCH_3$), 2.30 (m, 6-H), 2.14 (d, 5-H), 1.42 (d, $CHCH_3$); coupling constants as in I.

^{13}C NMR ($CDCl_3$) of I: δ = 95.4 (OCH_2O), 74.0 (C-2), 73.7 (C-1), 71.6 (CH_2-2'), 68.8 ($CHCH_3$), 67.3 (CH_2-1'), 64.5 (C-4), 59.3 (C-3), 57.6 (NCH_2), 54.0 (OCH_3), 45.1 (C-5), 41.3 (C-6), 29.8 (NCH_3), 23.2 ($CHCH_3$). – Of II: δ = 95.4 (OCH_2O), 73.8 (C-1), 72.0 (C-2), 71.6 (CH_2-2'), 68.8 ($CHCH_3$), 67.4 (CH_2-1'), 67.2 (C-4), 59.0 (OCH_3), 56.7 (NCH_2), 56.0 (C-3), 44.4 (C-5), 41.6 (C-6), 32.0 (NCH_3), 23.0 ($CHCH_3$).

49: ^{1}H NMR ($CDCl_3$): δ = 7.70–7.10 (m, 15H), 4.50–4.10 (m, 1-, 2-, 3-, 4-H), 3.12 (s, NCH_3), 2.75 (q, $CHCH_3$), 2.48 (t, 5-H), 2.34 (d, 6-H), 1.42 (d, $CHCH_3$), 1.39, 1.28 (s, 2 CH_3); $J_{4,5}$ = 6.5, $J_{5,6}$ = 5.5, J_{CH,CH_3} = 6.5 Hz.

(+)-(1S)-1α,2α,3β,4α,5β,6β)-3-Amino-3,6-N-carbonyl-1,2-O-isopropylidene-4-O-methyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol (*ent*-**50a**): To a solution of diisopropylamine (0.30 ml, 3.0 mmol) in glyme (5 ml) a solution of *n*-butyllithium in *n*-hexane (1.6 M, 2.0 ml, 3.2 mmol) was added at 0°C by syringe. After 10 min *ent*-**36c** (270 mg, 1.0 mmol) was added in one portion as a fine powder. After stirring for 30 min at 0°C and for 30 min at 20°C, methanol (10 ml) was added, the reaction mixture was neutralized with acetic acid and concentrated i. vac. The crude product (250 mg) was separated from by-products by chromatography (silica, $CHCl_3$/methanol, 25:1), 195 mg (72%) of colorless crystals, m.p. 194°C ($CHCl_3$/methanol, 20:1); $[\alpha]_D^{20}$ = +75 (*c* = 1.0, methanol). – IR (KBr): 3350, 3300, 2980, 2910, 1635, 1580, 1505, 1405, 1370, 1260, 1210, 1155, 1090, 1055, 930, 880, 760 cm^{-1}. – ^{1}H NMR ($CDCl_3$/CD_3OD, 3:1): δ = 4.59 (dd, 2-H), 4.54 (dd, 1-H), 4.25 (dd, 5-H), 3.62 (dt,

4-H), 3.58 (d, 3-H), 3.50 (s, OCH_3), 3.32 (dd, 6-H), 3.08 (s, NCH_3), 1.50, 1.32 (s, 2 CH_3); $J_{1,2}$ = 7.5, $J_{2,3}$ = 3.5, $J_{2,4}$ = $J_{3,4}$ = 1.0, $J_{4,5}$ = 6.0, $J_{5,6}$ = 3.5, $J_{6,1}$ = 2.0 Hz.

$C_{12}H_{20}N_2O_5$ (272.3) Calc. C 52.93 H 7.40 N 10.29 Found C 52.55 H 7.73 N 10.03

(+)-(1S)-(1α,2α,3β,4α,5β,6β)-3-Amino-3,6-N-carbonyl-1,2-O-isopropylidene-4-O-methyl-6-(methylamino)-1,2,4,5-cyclohexanetetrol 5-Acetate (*ent*-**50b**): After acetylation of **50a** (135 mg, 0.5 mmol): 145 mg (92%) of colorless crystals, m.p. 239 °C ($CHCl_3$/ether, 1:3); $[\alpha]_D^{20}$ = +73 (*c* = 1.0, $CHCl_3$). – IR (KBr): 3300, 2980, 2930, 2910, 1735, 1660, 1610, 1495, 1455, 1410, 1375, 1260, 1230, 1125, 1110, 1055, 1035, 1000, 865, 810, 785, 760, 740, 610, 525, 510 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 5.75 (d, NH), 5.43 (dd, 5-H), 4.63 (ddd, 2-H), 4.55 (dd, 1-H), 3.82 (dt, 4-H), 3.64 (ddd, 3-H), 3.50 (dd, 6-H), 3.39 (s, OCH_3), 3.10 (s, NCH_3), 2.14 (s, OAc), 1.57, 1.33 (s, 2 CH_3); $J_{1,2}$ = 7.0, $J_{2,3}$ = 4.0, $J_{2,4}$ = $J_{3,4}$ = 1.0, $J_{3,NH}$ = 8.0, $J_{4,5}$ = 6.0, $J_{5,6}$ = 3.0, $J_{6,1}$ = 2.5 Hz.

$C_{14}H_{22}N_2O_6$ (314.3) Calc. C 53.49 H 7.05 N 8.91 Found C 53.47 H 7.31 N 8.77

CAS Registry Numbers

1: 73610-92-1 / *ent*-**1**: 104641-37-4 / **1** · H_2SO_4: 79951-95-4 / **10**: 50473-98-8 / **11**: 88563-84-2 / **12**: 49778-04-3 / *rac*-**13a**: 104641-38-5 / *rac*-**13b**: 88563-86-4 / *rac*-**13c**: 88563-87-5 / *rac*-**13d**: 88563-88-6 / *rac*-**13e**: 104600-51-3 / *rac*-**13f**: 104600-52-4 / *rac*-**13g**: 104600-53-5 / *rac*-**13h**: 104600-54-6 / *rac*-**13i**: 104600-55-7 / *rqc*-**13j**: 104600-56-8 / *rac*-**13k**: 104600-57-9 / *rac*-**13l**: 104600-58-0 / *rac*-**14a**: 104600-50-2 / *rac*-**14b**: 104600-59-1 / **15**: 104600-60-4 / **16**: 104641-39-6 / **17**: 104600-61-5 / **18**: 104600-62-6 / **19**: 104600-j63-7 / *rac*-**20a**: 104600-64-8 / *rac*-**20b**: 104600-65-9 / *rac*-**20c**: 104712-80-3 / *rac*-**20d**: 104600-66-0 / *rac*-**21d**: 104600-67-1 / *rac*-**21e**: 104600-68-2 / *rac*-**22**: 104641-40-9 / *rac*-**23**: 104600-69-3 / *rac*-**24**: 88563-89-7 / *rac*-**25a**: 104600-70-6 / *rac*-**25b**: 104600-71-7 / *rac*-**25c**: 104600-72-8 / *rac*-**25d**: 104600-74-0 / *rac*-**26c**: 104600-73-9 / *rac*-**26d**: 104600-75-1 / *rac*-**27a**: 104600-76-2 / *rac*-**27b**: 104600-78-4 / *rac*-**28a**: 104600-77-3 / *rac*-**28b**: 104600-79-5 / *rac*-**29**: 104600-80-8 / **30a**: 104619-30-9 / **30a′**: 104713-72-6 / **30d**: 88563-90-0 / **30d′**: 88642-98-2 / **30e**: 88563-91-1 / **30e′**: 88642-99-3 / **30f**: 104619-22-9 / **30g**: 104619-23-0 / **30h**: 104619-26-3 / **30i**: 104619-27-4 / **30j**: 104619-25-2 / **30k**: 104619-24-1 / **30l**: 104619-29-6 / **30l′**: 104712-72-3 / **31l**: 104619-28-5 / **31l′**: 104712-71-2 / **32a**: 88563-92-2 / **32a′**: 88643-00-9 / **32b**: 88563-93-3 / **32b′**: 88643-01-0 / **32d**: 104619-31-0 / **32e′**: 104619-32-1 / **32f′**: 104619-33-2 / **33a**: 104619-34-3 / **33a′**: 104712-73-4 / **33b**: 104619-35-4 / **33b′**: 104712-74-5 / **34a** · 0.5 H_2SO_4: 104619-37-6 / *ent*-**34a** · 0.5 H_2SO_4: 104713-74-8 / **34b**: 104619-38-7 / *ent*-**34b**: 104712-75-6 / *ent*-**34c**: 104619-39-8 / **34d**: 104712-76-7 / **34e**: 104600-49-9 / **34e′**: 104641-36-3 / *ent*-**35**: 104619-40-1 / **36a**: 104712-77-8 / **36b**: 88563-95-5 / *ent*-**36b**: 88643-02-1 / *ent*-**36c**: 104619-41-2 / **37a**: 104619-42-3 / **37b**: 104619-43-4 / **38a** · H_2SO_4: 104712-78-9 / *ent*-**38a** · H_2SO_4: 104712-79-0 / **38b**: 88563-97-7 / *ent*-**38b**: 88643-04-3 / **46**: 104619-44-5 / **47**: 104619-45-6 / **48**: 104619-46-7 / **49**: 104619-47-8 / *ent*-**50a**: 104619-48-9 / *ent*-**50b**: 104619-49-0 / *N*-methylbenzophenoneimine: 13280-16-5 / (*R*)-(+)-1-phenylethylamine: 3886-69-9 / methyl isocyanate: 624-83-9

[1] *R. S. Egan, R. S. Stanaszek, M. Cirovic, S. L. Mueller, J. Tadanier, J. R. Martin, P. Collum, A. W. Goldstein, R. L. DeVault, A. C. Sinclair, E. E. Fager*, and *L. A. Mitscher*, J. Antibiot. **30**, 552 (1977).

[2] *M. Sugimoto, S. Ishii, R. Okachi*, and *T. Nara*, J. Antibiot. **32**, 868 (1979).

[3] *T. Iida, M. Sato, I. Matsubara, Y. Mori*, and *K. Shirahata*, J. Antibiot. **32**, 1273 (1979).

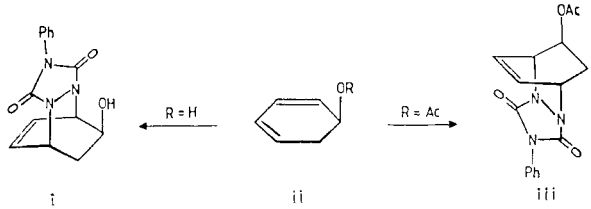
[4] *J. R. Martin, P. Johnson, J. Tadanier*, and *A. Goldstein*, Antimicrob. Agents Chemother. **18**, 761 (1980).

[5] *J. Tadanier, R. Hallas, J. Holms, L. A. Freiberg*, and *D. Bacino*, J. Antibiot. **36**, 267 (1983).

[6] *J. Tadanier* and *R. Hallas*, J. Antibiot. **35**, 688 (1982).

[7] *S. Inouve, K. Ohba, T. Shomura, M. Kojima, T. Tsuruoka, J. Yoshida, N. Kato, M. Ito, S. Amano, S. Omoto, N. Ezaki, T. Ito*, and *T. Niida*, J. Antibiot. **32**, 1354 (1979); *T. Shomura, M. Kojima, J. Yoshida, M. Ito, S. Amano, K. Totsugawa, T. Niwa, S. Inouve, T. Ito*, and

T. Niida, ibid. **33**, 924 (1980); *K. Ohba, T. Tsuruoka, K. Mizutani, N. Kato, S. Omoto, N. Ezaki, S. Inouye*, and *T. Niida*, ibid. **34**, 1090 (1981).
[8] *H. Paulsen* and *H. Schmidt-Lewerkuhne*, Liebigs Ann. Chem. **1985**, 959.
[9] *S. Itoh, Y. Odakura, H. Kase, S. Satoh, K. Takahashi, T. Iida, K. Shirahata*, and *K. Nakayama*, J. Antibiot. **37**, 1664 (1984); *Y. Odakura, H. Kase, S. Itoh, S. Satoh, S. Taksawa, K. Takahashi, K. Shirahata*, and *K. Nakayama*, ibid. **37**, 1670 (1984).
[10] *Y. Okami, K. Hotta, M. Yoshida, D. Ikeda, S. Kondo*, and *H. Umezawa*, J. Antibiot. **32**, 1354 (1979).
[11] *T. Deushi, A. Iwasaki, K. Kamiya, T. Mizoguchi, M. Nakayama, H. Itoh*, and *T. Mori*, J. Antibiot. **32**, 1061 (1979); *I. Watanabe, T. Deushi, T. Yamaguchi, K. Kamiya, M. Nakayama*, and *T. Mori*, ibid. **32**, 1066 (1979).
[12] *Y. Horiuchi, D. Ikeda, S. Kondo*, and *H. Umezawa*, J. Antibiot. **33**, 1577 (1980).
[13] *T. Deushi, T. Yamaguchi, K. Kamiya, A. Iwasaki, T. Mizoguchi, M. Nakayama, I. Watanabe, H. Itoh*, and *T. Mori*, J. Antibot. **33**, 1274 (1980).
[14] *D. Ikeda, Y. Horiuchi, M. Yoshida, T. Miyasaka, S. Kondo*, and *H. Umezawa*, Carbohydr. Res. **109**, 33 (1982).
[15] World Pharmaceutical News, June 23, 1982, p. 15.
[16] *Y. Horiuchi, D. Ikeda, S. Gomi, S. Kondo*, and *H. Umezawa*, Carbohydr. Res. **109**, 25 (1982).
[17] *T. Deushi, A. Iwasaki, K. Kamiya, T. Kunieda, T. Mizoguchi, M. Nakayama, H. Itoh, T. Mori*, and *T. Oda*, J. Antibiot. **32**, 173 (1979); *A. Iwasaki, H. Itoh*, and *T. Mori*, ibid. **32**, 180 (1979); *T. Deushi, M. Nakayama, I. Watanabe, T. Mori, H. Naganawa*, and *H. Umezawa*, ibid. **32**, 187 (1979).
[18] *T. Tsuchiya, T. Torii, S. Umezawa*, and *H. Umezawa*, J. Antibiot. **35**, 1245 (1982); *T. Tsuchiya, T. Torii, Y. Suzuki*, and *S. Umezawa*, Carbohydr. Res. **116**, 277 (1983).
[19] *T. Deushi, I. Watanabe, A. Iwasaki, K. Kamiya, K. Mizoguchi, M. Nakayama, M. Okuchi, H. Itoh*, and *T. Mori*, J. Antibiot. **34**, 811 (1981); *A. Iwasaki, T. Deushi, I. Watanabe, M. Okuchi, H. Itoh*, and *T. Mori*, ibid. **35**, 517 (1982); *N. Yasuda, K. Matsuda, H. Tsutsumi*, and *T. Takaya*, ibid. **38**, 1512 (1985).
[20] *P. Kurath, W. Rosenbrook, Jr., D. A. Dunnigan, J. B. McAlpine, R. S. Egan, R. S. Stanaszek, M. Cirovic, S. L. Mueller*, and *W. H. Washburn*, J. Antibiot. **37**, 1130 (1984).
[21] *P. Kurath, R. S. Stanaszek*, and *M. Cirovic*, J. Antibiot. **35**, 1338 (1982).
[22] *T. Nara, M. Yamamoto, I. Kawamoto, K. Takayama, R. Okachi, S. Takasawa, T. Sato*, and *S. Sato*, J. Antibiot. **30**, 533 (1977); *Y. Ohashi, H. Kawabe, K. Sato, N. Nakamura, S. Kurashige*, and *S. Mitsuhashi*, Antimicrob. Agents Chemother. **17**, 138 (1980); *C. Thornsberry, A. L. Barry, R. N. Jones, C. N. Baker, R. E. Badal*, and *R. R. Packer*, ibid. **19**, 122 (1981).
[23] *K. Yamashita, H. Kawabe*, and *S. Mitsuhashi*, Antimicrob. Agents Chemother. **20**, 33 (1981).
[24] *J. Tadanier, R. Hallas, J. R. Martin, M. Cirovic*, and *R. S. Stanaszek*, Carbohydr. Res. **92**, 207 (1981); *T. Suami, J.-I. Tadano*, and *K. Matsuzawa*, J. Antibiot. **33**, 1289 (1980); *T. Torii, T. Tsuchiya*, and *S. Umezawa*, Carbohydr. Res. **116**, 289 (1983).
[25] *P. Kurath, J. Tadanier, P. Johnson, D. Grampovnik, R. S. Egan, R. S. Stanaszek, M. Cirovic, W. H. Washburn*, and *J. E. Leonard*, J. Antibiot. **34**, 691 (1981); *D. Ikeda, Y. Horiuchi, S. Kondo*, and *H. Umezawa*, ibid. **33**, 1281 (1980).
[26] *T. Nara, M. Yamamoto, I. Kawamoto, K. Takayama, R. Okachi, S. Takasawa, T. Sato*, and *S. Sato*, J. Antibiot. **30**, 533 (1977).
[27] *J. Tadanier, J. R. Martin, P. Kurath, A. W. Goldstein*, and *P. Johnson*, Carbohydr. Res. **79**, 91 (1980); *J. Tadanier* und *R. Hallas*, J. Antibiot. **34**, 403 (1981).
[28] [28a] Preliminary communication: *J. Schubert, R. Schwesinger*, and *H. Prinzbach*, Angew. Chem. **96**, 162 (1984), Angew. Chem., Int. Ed. Engl. **23**, 167 (1984). – [28b] *H. Sano, T. Sakaguchi*, and *Y. Mori*, Bull. Chem. Soc. Jpn. **52**, 2727 (1979); *W. Rosenbrook, Jr.* and *J. S. Fairgrieve*, J. Antibiot. **34**, 681 (1981).
[29] *M. Kiso, H. Hibino, M. Tanaka*, and *A. Hasegawa*, Agric. Biol. Chem. **29**, 938 (1951).
[30] *Y. Honda* und *T. Suami*, Bull. Chem. Soc. Jpn. **55**, 1156 (1982).
[31] *S. Knapp, M. J. Sebastian*, and *H. Ramanathan*, J. Org. Chem. **48**, 4786 (1983).
[32] *C. H. Kuo* and *N. L. Wendler*, Tetrahedron Lett. **25**, 2291 (1984).
[33] Similarly we had pursued an access to deoxyfortamines via **i**/**iii**, which were selectively obtained by [4+2] addition of *N*-phenyltriazolinedione to benzene hydrate (**ii**) or its acetate[34]. This route was, however, given up in favour of a more promising approach (see remarks)[35].



i ii iii

[34] *J. Staroscik* and *B. Rickborn*, J. Am. Chem. Soc. **93**, 3046 (1971).
[35] *R. Kühlmeyer*, Diplomarbeit, Univ. Freiburg 1981.
[36] *B. Schwesinger, R. Schwesinger*, and *H. Prinzbach*, Tetrahedron Lett. **25**, 1979 (1984).
[37] *R. Keller, R. Schwesinger, W. Fritsche, H.-W. Schneider, D. Hunkler*, and *H. Prinzbach*, Chem. Ber. **112**, 3347 (1979).
[38] *S. Ogawa, S. Oki*, and *T. Suami*, Bull. Chem. Soc. Jpn. **52**, 1095 (1979).
[39] *D. Ikeda, Y. Horiuchi, S. Kondo*, and *H. Umezawa*, J. Antibiot. **33**, 1281 (1980).
[40] *R. Kühlmeyer, R. Keller, R. Schwesinger, Th. Netscher, H. Fritz*, and *H. Prinzbach*, Chem. Ber. **117**, 1765 (1984).
[41] *R. Schwesinger, W. Fritsche*, and *H. Prinzbach*, Chem. Ber. **115**, 946 (1982).
[42] *W. Fritsche-Lang, P. Wilharm, E. Hädicke, H. Fritz*, and *H. Prinzbach*, Chem. Ber. **118**, 2044 (1985).
[43] *N. Minami, S. S. Ko*, and *Y. Kishi*, J. Am. Chem. Soc. **104**, 1109 (1982); *W. R. Roush* and *R. J. Brown*, J. Org. Chem. **47**, 1371 (1982); *W. R. Roush, R. J. Brown*, and *M. DiMare*, ibid. **48**, 5083 (1983); *W. R. Roush* and *R. J. Brown*, ibid. **48**, 5093 (1983); *E. J. Corey, P. B. Hopkins, J. E. Munroe, A. Marfat*, and *S. Hashimoto*, J. Am. Chem. Soc. **102**, 7986 (1980); *M. Cerny, H. Vecerkova, I. Cerny*, and *J. Pacak*, Collect. Czech. Chem. Commun. **45**, 1837 (1980).
[44] *L. Goodman*, Adv. Carbohydr. Chem. **22**, 109 (1967).
[45] *J. E. Baldwin*, J. Chem. Soc., Chem. Commun. **1976**, 734; *J. E. Baldwin*, and *L. I. Kruse*, ibid. **1977**, 233; *J. E. Baldwin, R. C. Thomas, L. I. Kruse*, and *L. Silberman*, J. Org. Chem. **42**, 3846 (1977).
[46] *B. Bernet* and *A. Vasella*, Tetrahedron Lett. **24**, 5491 (1983); *D. H. R. Barton*, J. Chem. Soc. **1951**, 2988; *G. Stork, L. D. Cama*, and *D. R. Coulson*, J. Am. Chem. Soc. **96**, 5268 (1974); *G. Stork* and *F. Cohen*, ibid. **96**, 5270 (1974).
[47] *W. J. Farrissey, Jr.* and *A. M. Nashu*, J. Heterocycl. Chem. **1970**, 331; *Y. Iwakura* and *Y. Taneda*, J. Org. Chem. **24**, 1992 (1959).
[48] *R. Schwesinger*, Chimia **39**, 269 (1985).
[49] *W. R. Benson* and *R. J. Gajan*, J. Org. Chem. **31**, 2498 (1966).
[50] *A. H. Haines*, Adv. Carbohydr. Chem. Biochem. **33**, 11 (1976).
[51] *P. L. Durette* and *D. Horton*, Org. Magn. Reson. **3**, 417 (1971); *K. Tori, T. Kameno*, and *T. Nakagawa*, J. Org. Chem. **29**, 1136 (1964).
[52] *W. Littke* and *U. Drück*, Angew. Chem., **86**, 557 (1974), Angew. Chem. Int. Ed. Engl. **13**, 539 (1974); *U. Drück* and *W. Littke*, Acta Crystallogr., Sect. B, **35**, 1905 (1979); *R. Schwesinger, K. Piontek, W. Littke*, and *H. Prinzbach*, Angew. Chem. **97**, 344 (1985); Angew. Chem., Int. Ed. Engl. **24**, 318 (1985).
[53] e.g. *A. W. Frahm* and *G. Knupp*, Tetrahedron Lett. **22**, 2633 (1981).
[54] *J. Tadanier, D. A. Dunnigan, J. R. Martin, L. Freiberg*, and *M. Cirovic*, J. Antibiot.**34**, 193 (1981); *T. Yamaguchi, Y. Kyotani, I. Watanabe, S. Sato, Y. Takahashi, M. Nagakura*, and *T. Mori*, ibid. **32**, 1137 (1979).
[55] *Th. W. Greene*, Protective Groups in Organic Synthesis, Wiley-Interscience 1981.
[56] *R. Eby* and *C. Schuerch*, Carbohydr. Res. **100**, C41 (1982); *R. Toman, J. Rosik*, and *M. Zikmund*, ibid. **103**, 165 (1982); *T. Ogawa, T. Nukada*, and *M. Matsui*, ibid. **101**, 263 (1982); *J. Gelas*, Adv. Carbohydr. Chem. Biochem. **39**, 71 (1981); *P. J. Garegg* and *H. Hultberg*, Carbohydr. Res. **93**, C10 (1981).
[57] *R. U. Lemieux* and *H. Driguez*, J. Am. Chem. Soc. **97**, 4069 (1975); *H. Paulsen* and *D. Schnell*, Chem. Ber. **114**, 333 (1981); *J. F. King* and *A. D. Allbutt*, Can. J. Chem. **48**, 1754 (1970); *P. Deslongchamps, P. Atlani, D. Frehel*, and *A. Malaval*, Can. J. Chem. **50**, 3405 (1972).
[58] *M. A. Nashed* and *L. Anderson*, Carbohydr. Res. **56**, 419 (1977); *C. Auge, S. David*, and *A. Veyrieres*, J. Chem. Soc., Chem. Commun. **1976**, 375; *M. A. Nashed*, Carbohydr. Res. **60**, 200 (1978).

[59] *F. Cramer, K. Pawelzik,* and *H. J. Baldauf,* Chem. Ber. **91**, 1049 (1958); *T. Iversen* and *D. R. Bundle,* J. Chem. Soc., Chem. Commun. **1981**, 1240.
[60] *P. Kurath, J. Tadanier, P. Johnson, D. Grampovnik, R. S. Egan, R. S. Stanaszek, M. Cirovic, W. H. Washburn,* and *J. E. Leonard,* J. Antibiot. **34**, 691 (1981); *N. Hirayama, K. Shirahata, Y. Ohashi,* and *Y. Sasada,* Bull. Chem. Soc. Jpn. **54**, 2624 (1981); *N. Hirayama, K. Shirahata, Y. Ohashi,* and *Y. Sasada,* ibid. **53**, 1514 (1980).
[61] *M. Sato* and *Y. Mori,* J. Antibiot. **32**, 371 (1979).
[62] *D. Seebach* and *D. Enders,* Angew. Chem. **87**, 1 (1975), Angew. Chem., Int. Ed. Engl. **14**, 15 (1975).
[63] *M. S. Newman* and *A. Kutner,* J. Am. Chem. Soc. **73**, 4199 (1951).
[64] *D. Hoppe,* Angew. Chem. **86**, 878 (1974), Angew. Chem., Int. Ed. Engl. **13**, 789 (1974); *U. Schöllkopf,* Angew. Chem. **89**, 351 (1977), Angew. Chem., Int. Ed. Engl. **16**, 339 (1977).
[65] We thank cand. rer. nat. *M. Janes* for these experiments.
[66] *I. Moretti* and *G. Torre,* Synthesis **1970**, 141; *T. Kauffmann, E. Köppelmann,* and *H. Berg,* Angew. Chem. **82**, 138 (1970), Angew. Chem., Int. Ed. Engl. **9**, 163 (1970); *L. Hu, B. Mauze,* and *L. Miginiac,* C. R. Acad. Sci., Ser. C, **284**, 195 (1977).
[67] *M. Yamada, K. Tachibana,* and *T. Kuroda,* Carbohydr. Res. **112**, 189 (1983).
[68] *R. A. Mallory, S. Rovinski, F. Kohen,* and *I. Scheer,* J. Org. Chem. **32**, 1417 (1967); cit. lit.: *G. Jung* and *A. Klemer,* Chem. Ber. **114**, 740 (1981); *A. Klemer* and *G. Jung,* ibid. **114**, 1192 (1981); *K. K. Weinhardt,* Tetrahedron Lett. **25**, 1761 (1984).
[69] *R. Schwesinger, M. Breuninger, B. Gallenkamp, K.-H. Müller, D. Hunkler,* and *H. Prinzbach,* Chem. Ber. **113**, 3127 (1980), and cit. lit.
[70] *J. Tadanier, J. R. Martin, P. Johnson, A. W. Goldstein,* and *R. Hallas,* Carbohydr. Res. **85**, 61 (1980).
[71] *S. Karady, T. Y. Cheng, S. H. Pines,* and *M. Sletzinger,* Tetrahedron Lett. **1974**, 2625; *L. Capuano, R. Zander,* and *A. Bolourtschi,* Chem. Ber. **104**, 3750 (1971).
[72] *Ch. Rücker, H. Prinzbach, H. Irngartinger, R. Jahn,* and *H. Rodewald,* Tetrahedron Lett., in press.
[73] *G. Lutz,* Diplomarbeit, Univ. Freiburg 1986.
[74] *R. Kühlmeyer, R. Schwesinger,* and *H. Prinzbach,* Tetrahedron Lett. **25**, 3429 (1984).
[75] *J. R. Martin, P. Johnson, J. Tadanier, M. Cirovic,* and *R. S. Stanaszek,* J. Antibiot. **35**, 46 (1982); *N. Kurihara, K. Hayashi,* and *N. Nakajima,* Agric. Biol. Chem. **33**, 256 (1969).
[76] *R. Kühlmeyer, R. Schwesinger, H. Fritz, D. Hunkler,* and *H. Prinzbach,* publication in preparation.
[77] *B. Schwesinger, R. Schwesinger, Th. Weller, B. Seitz,* and *H. Prinzbach,* publication in preparation.

[132/86]