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SYNTHESIS OF AMINO SUGARS VIA ISOXAZOLINES

DL- AND D-LIVIDOSAMINE (2-AMINO-2,3-DIDEOXY-*RIBO*-HEXOSE) DERIVATIVES FROM 4-VINYL-1,3-DIOXOLANES AND NITROACETALDEHYDE ACETALS[1,2]

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Abstract—1,3-Dipolar cycloaddition of nitrile oxides, generated from nitroethanol and nitroacetaldehyde derivatives **3**, **21** and **22**, respectively, and of benzonitrile oxide to 4-vinyldioxolanes **1**, **2** gave *ca* 4:1 *erythro*/*threo* mixtures of corresponding isoxazolines. LAH reduction of *erytho* isoxazolines proceeded with similar (*ca* 4:1) selectivity to furnish protected *ribo*-amino-polyols **11**, **15**, **19**, DL- and D-lividosamines **31** and **33**, respectively, as main products. The DL-lividosamine derivative **33** was obtained pure by crystallization. In the D-series, the corresponding *ribo*/*arabino* mixture D-**31**/D-**32** was transformed to the known α-methyl D-lividosaminide D-**37**.

A. BACKGROUND

1,3-Dipolar cycloaddition of nitrile oxides **B** to alkenes **A** allows for the construction of a variety of functionalized carbon skeletons.[5] The *in situ* generation of these dipoles from either hydroxamic acid chlorides (Huisgen's method[5,6]) or nitroalkanes (Mukaiyama's procedure[5,7]), in the presence of dipolarophiles, today is the most useful way to carry out these cycloadditions. The cycloadducts, isoxazolines **C**, may serve as precursors for various classes of compounds, provided that suitable ring cleavage reactions are at hand.[8,9] The general concept [eqn (a) in Scheme 1], outlined in 1976,[8] has proved very fruitful in our hands,[10] and in others,[10-12] and is increasingly used in natural products' synthesis.[10-12] Synthetic problems to assemble structures thus often may be solved by adding up [2 + 3], i.e. by proper choice of respective building blocks **A** and **B**.

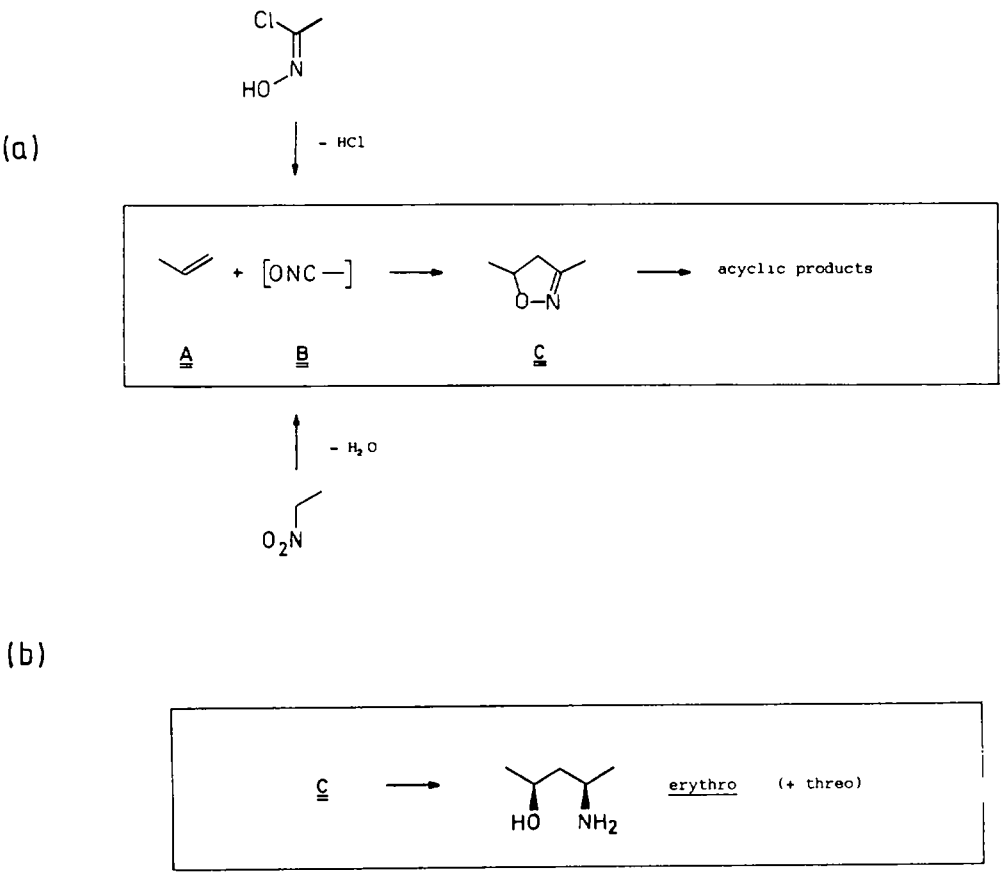
A particularly appealing conversion of the isoxazoline nucleus is complete reduction, to furnish γ-amino alcohols.[13] Our investigations of this process showed lithium aluminium hydride (LAH) in ether to be the most convenient reducing agent so far, both for preparative ease and what concerns asymmetric induction by (non-coordinating) ring substituents favouring "*erythro*" formation[14] [eqn (b) in Scheme 1]. The γ-amino alcohol unit is present in several natural product classes—e.g. amino polyols, amino sugars, and amino acids—many of these exhibiting notable physiological or pharmacological properties.[15] A long-term project was started therefore, to systematically elaborate solutions for the various structural and stereochemical problems associated with syntheses of these classes, based on the isoxazoline route.[8,10]

Requisite building blocks with protected hydroxymethyl and formyl groups in the nitrile oxide part, to be carried through the cycloaddition and LAH reduction step, have already been described.[16-18] A study of directing effects of groups bearing O-functionality[16a] has confirmed the additivity of ring substituent effects noted previously.[14] The following paper is concerned with two aspects of amino sugar synthesis via isoxazolines, the specific target being D-lividosamine (2-amino-2,3-dideoxy-D-*ribo*-hexose), constituent of aminoglycoside antibiotics lividomycin A and B.[19]

B. STRATEGY

A number of the synthetic problems that regio- and stereoselective access to various amino-desoxyaldoses and related products poses, may be simplified using isoxazoline precursors **D**–**H**[2,16c,20] (Scheme 2). For example, type **D** has been obtained by isoxazoline 4-anion hydroxylation;[16b] its highly selective reduction to 2,3,4-*ribo* aminodiols[16a] enabled a short route to phytosphingosine.[16b] *cis*-Oxygenated isoxazolines **E** and resulting 2,3,4-*xylo* derivatives are part of the amino polyol variety accessible via furan adducts **F**.[2,16c,20a,21] From **F** by hydroxylation furanoside **G**, a cyclic analog of **H**, is obtained also, to furnish *ido* derivatives on reduction, exemplified by the synthesis of 5-*epi*-nojirimycin derivatives.[16c] Stereoselective access to isoxazolines **H** of *erythro* configuration was part of our studies[3] bearing on π-facial selectivity in nitrile oxide cycloadditions to α-chiral olefins such as buten-3-ol (in collaboration with Prof. K. N. Houk and his group)[22] and 3-buten-1,2-diol and derivatives.[23] For the synthesis of lividosamine, 2-vinyl-1,3-dioxolanes (i.e. ketals of butenediol **I**) would serve as equivalents of **I** which had exhibited the highest (*ca* 4:1) diastereoselectivity in model cycloadditions.[23,24] As a suitable synthon for formyl nitrile oxide **J**, dialkyl acetals of nitroacetaldehyde[25] should be convenient, as the diethyl derivative[25d] in our hands had already served to this purpose in a satisfying manner.†[17,21] The main ques-

†In early experiments the dithiane derivative of nitroacetaldehyde[26] was used:[3a,21] the cycloaddition with **1** gave impure product in moderate yield (38%); the LAH reduction product could not be obtained pure.[3a] Fortunately, a convenient synthesis of nitroacetaldehyde dialkyl acetals, by René and Royer,[25d] appeared just in time.



Scheme 1.

tions regarding the success of the projected lividosamine synthesis then concerned the extent of asymmetric induction in the LAH reduction step,—the O-substituents in the 5- and 3-side chain of the isoxazoline ring system might show a detrimental effect[16a] (*cf* Scheme 3); second, product isolation/purification after protective group manipulations was new territory, as all D-lividosamine syntheses known did constitute carbohydrate remodeling.[19b,c]

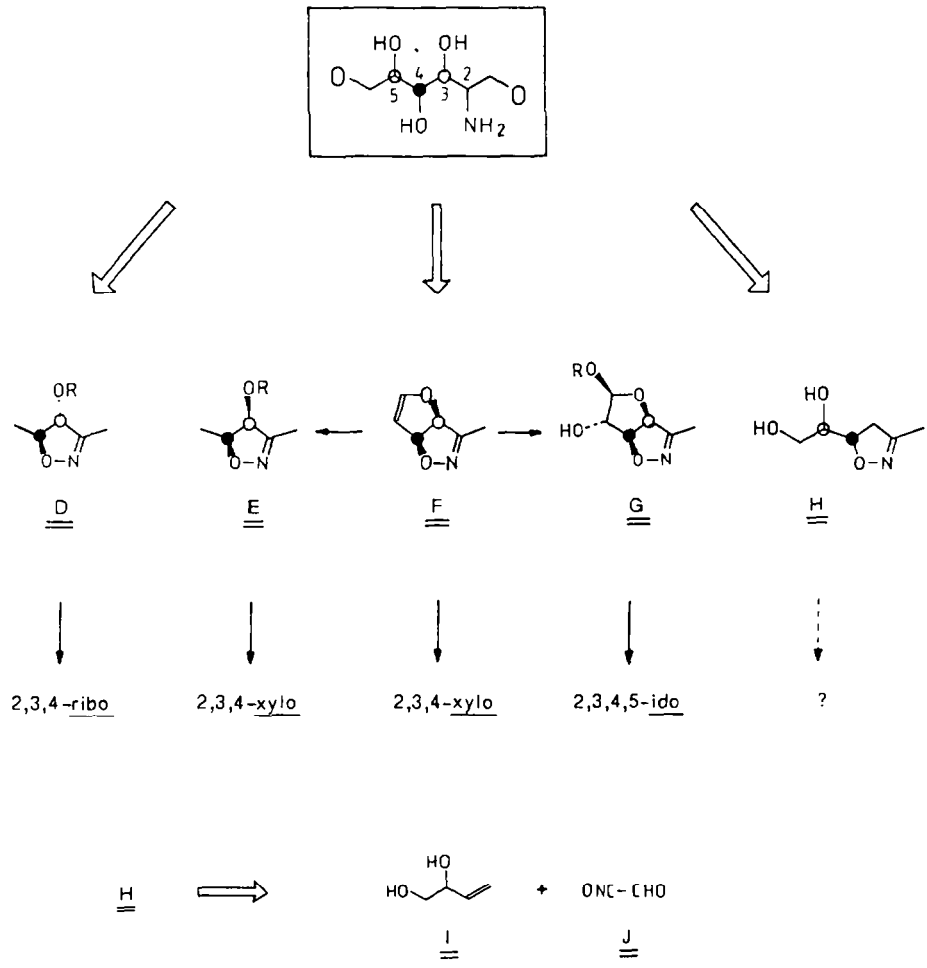
C. DIRECTIVE EFFECT OF THE DIOXOLAN-4-YL GROUP; 2-AMINO-2,3-DIDESOXYHEXITOLS AND 1-AMINO-1-PHENYL-3,4,5-PENTANETRIOLS

The *anti*-directing effect of a 5-alkyl group in isoxazoline reductions by LAH[14] is decreased slightly, both with tetrahydropyranyloxy groups present in the 5$^{\alpha}$- and 3$^{\alpha}$-position†[16a] (Scheme 3). The directing effect of the now necessary *dioxolanyl* 5-substituent was studied therefore with model isoxazolines **5–9**. The building blocks used were the vinyl dioxolans **1**,[27] **2**,[3a] and the nitrile oxide precursors **3**,[16] **4**[5] (Scheme 4). As expected,[23] *erythro/threo* mixtures of the corresponding isoxazolines were obtained in a $\approx 4:1$ ratio (Table in Scheme 4). The main product in each case was assigned the same configuration on the basis of very consistent ^{13}C NMR shift differences for each cycloadduct pair (Table 1). As **9** had been shown to belong to the *erythro* series by X-ray analysis,[23] this could be derived for **5** and **7** likewise. The minor isomers—**6**, **8**, and **10**—thus constituted *threo* compounds.

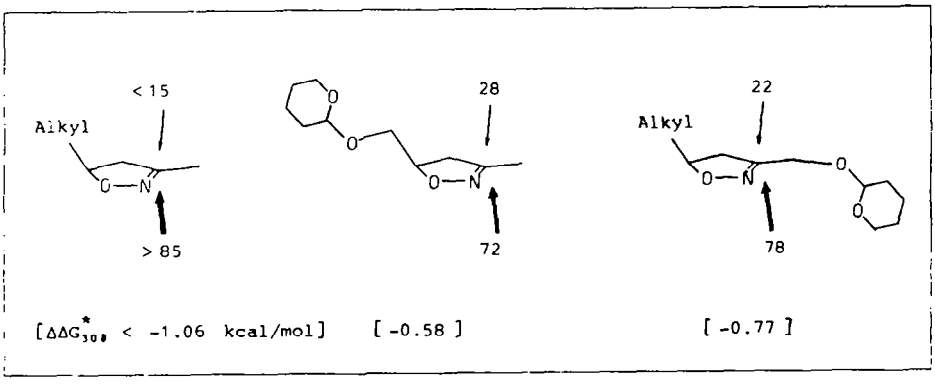
The isoxazolines **5/6**, without separation, were subjected to LAH reduction to produce, in quantitative yield, a mixture of 2-amino-2,3-dideoxyhexitol derivatives **11–14**. A ^{13}C NMR spectrum revealed that the four stereoisomers had been formed in a 63:17:13:7 ratio. Apparently, the *erythro* isoxazoline **5** had been transformed to **11** and **12**, again with *ca* 4:1 diastereoselectivity (*cf* Table in Scheme 4); **6** had furnished **13** and **14** with lower, i.e. *ca* 2:1, selectivity. Analyses of the ^{13}C NMR chemical shift differences, in particular of the C-2 and C-4 signal groups, could be effected on the basis of empirical rules derived from previous work on the determination of relative configurations and conformations of simple γ-amino alcohols;‡[10b,14] (Table 2). The main products of the two epimer pairs, **11** and

†LAH and similar reductions of isoxazolines proceed by (i) stereoselective hydride transfer to C=N guided by $Li^{\oplus}\ldots O$ coordination, (ii) N–O cleavage; in catalytic hydrogenation and sodium/protic solvent reductions by N–O cleavage first, *then* C=N hydrogenation of the resulting *acyclic* intermediate in a stereorandom fashion.[14]

‡This could be done due to intramolecular O–H ... NH_2 hydrogen bridges present in these amino alcohols, which therefore consistently show characteristics of six-membered species.[10b,14]



Scheme 2.

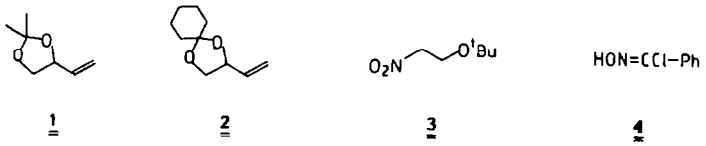


Scheme 3.

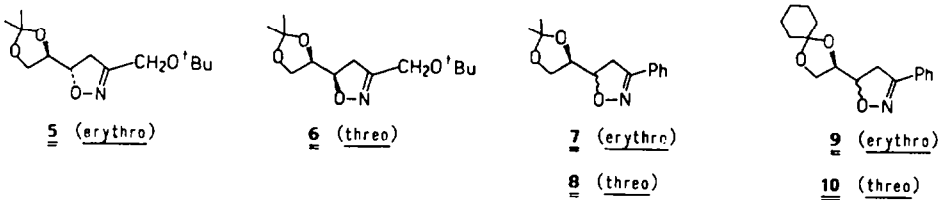
13 were assigned the same relative configuration concerning C-4/C-2 (*erythro*). With the C-5/C-4 relationship retained during the reduction, assignments then were made as depicted in Scheme 4, i.e. **11** ≡ *ribo*, **12** ≡ *arabino*, **13** ≡ *lyxo*, **14** ≡ *xylo*!

These considerations and conclusions were confirmed by the results obtained on reduction of enriched *erythro* (90:10) and *threo* (75:25) phenyl isoxazolines **7** and **8** to give **15/16** and **17/18** pairs, respectively, as the main isomers. Further, pure **9** was reduced to give **19/20** in a 85:15 ratio.

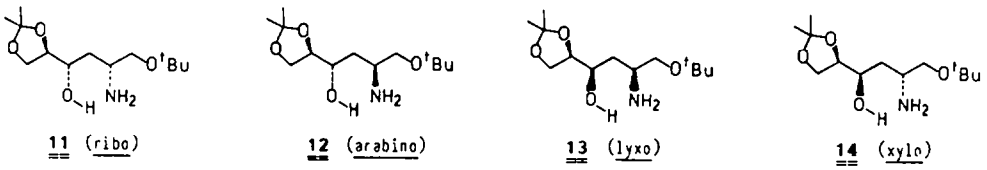
The above results with dioxolanyl substituents



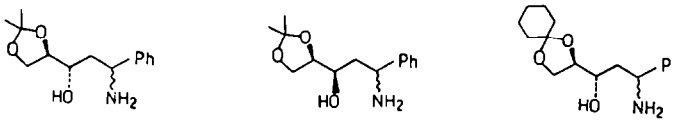
1 2 3 4



5 (erythro) 6 (threo) 7 (erythro) 8 (threo) 9 (erythro) 10 (threo)



11 (ribo) 12 (arabino) 13 (lyxo) 14 (xylo)



15 (ribo) 16 (arabino) 17 (lyxo) 18 (xylo) 19 (ribo) 20 (arabino)

Diastereomer ratios

Cycloaddition		LAH reduction	
1 + 3 → 5/6	78:22	5,6 (78:22) → 11/12/13/14	63:17:13:7
1 + 4 → 7/8	65:15	7,8 (90:10) → 15/16	81:19 **)
		7,8 (25:75) → 17/18	**) 66:34
2 + 4 → 9/10	81:19	9 → 19/20	85:15

Scheme 4 *).

*Racemic compounds; for clarity, the drawings show enantiomers of one series (see **1**, **2**) only.–**Not determined.

Scheme 4.

agree well with those of the THPO-methyl group[16a] (Scheme 3). It was hoped, that the acetal group in 3-position required for the entry to the aminohexose series, would not decrease this selectivity markedly.

D. DL-LIVIDOSAMINE DERIVATIVES

For the synthesis of the target amino sugar, D-**35**, a number of experiments was carried out to evaluate the suitability of protecting groups for the two basic components, the butendiol **I** and nitroacetaldehyde **J**. Vinyl dioxolanes **1** and **2** were opposed to nitroacetaldehyde diethyl acetal **21** (Mukaiyama conditions[7]) to furnish *erythro/threo* isoxazoline pairs **23/24** and **25/26** (Scheme 5). Again *ca* 4:1 diastereoselectivity was noted. At this stage, diethyl acetal protection caused some difficulties due to partial hydrolysis during chromatographic attempts to separate the *erythro/threo* pair **25/26**. Similarly, the amino alcohol mixture formed on reduction of **23/24** could not be obtained in an analytically pure form, so a more stable acetal protecting group was required.

Compound **21** therefore was converted to the nitromethyl dioxane **22**,[25b] on treatment with neopentyl glycol [28]/*p*-toluene sulfonic acid (catalyst) at 90° (87% yield). Cycloadditions of **22** with **1** and **2**, carried out as above, gave isoxazoline pairs **27/28** and **29/30** in near quantitative yield. The *erythro* isomers

Table 1. ^{13}C NMR chemical shifts of *erythro/threo* isoxazolines **5–10, 23–30** (in $CDCL_3$, δ in ppm)

Compound	OCH_2	OCH	C-5	C-4	C-3	C-1'
5 [a]	67.1	76.3	80.5	38.1	158.0	57.2
6 [a]	65.4	77.5	79.6	37.1	157.5	
7 [b]	67.2	76.1	81.3	37.7	156.6	129.4
8 [b]	65.4	76.4	80.5	36.6	156.4	
9 [c]	66.9	75.7	81.5	37.8	156.6	129.4
10 [c]	64.9	77.0	80.5			
23 [d]	66.8	76.1	80.6	35.1	157.2	97.4
24 [d]	65.3	76.6	79.8	34.5	156.9	
25 [e]	66.7	75.9	80.9	35.5	157.4	97.5
26 [e]	65.1	76.3	79.9	35.0		95.5
27 [f]	67.1	76.1	81.0	35.5	156.6	95.9
28 [f]	65.4	76.3	80.6	34.2	156.3	
29 [g]	66.9	75.9	81.2	34.8	156.6	96.0
30 [g]	65.0	76.0	80.7	34.3	156.4	95.9

a Acetonide part: 25.1 25.3 26.4, 26.7, 109.6, 109.9; t-Bu: 27.4, 74.2.

b Acetonide part: 25.1, 26.3, 26.8, 109.7, 109.9; phenyl: 126.8, 128.7.

c Cyclohexane part:23.7, 24.0, 25.1, 34.6, 36.6, 110.3; phenyl: 126.8 - 130.2.

d Acetonide part: 25.1, 25.3, 26.3, 26.6, 109.7, 109.9; OEt: 15.0, 63.0, 63.1, 63.2, 63.3.

e Cyclohexane part: 23.8, 24.0, 24.1, 25.2, 34.6, 34.8, 36.0, 36.5, 110.4; OEt: 15.1, 63.0, 63.1, 63.2, 63.2.

f Acetonide part: 25.2, 26.4, 26.7, 109.7, 110.1; dioxanyl part: 21.8, 22.8, 30.3, 30.5, 77.0.

g Cyclohexane part: 23.8, 24.0, 25.2, 35.6, 35.7, 36.4, 36.6, 110.3, 110.7; dioxanyl part: 21.8, 22.9, 30.3, 77.2, 77.3 (?).

27 and **29** were obtained pure ($\gtrsim$ 95:5 according to ^{13}C NMR) applying flash chromatography on silica, in 53 and 55% yield, respectively. LAH reductions went smoothly. With **27**, 89% of amino alcohols **31/32** (ratio 78:22) were isolated. One crystallization of this material from hexane gave a 64% fraction where the content of the desired *ribo* isomer **31** had increased to 89:11. This worked even better with the cyclohexanone derivative **29**: from the crude reduction product (quantitative yield; **33/34** = 79:21) *after one careful crystallization pure* DL-*lividosamine 5,6-acetonide acetal* **33** *was collected*†.

Exploratory experiments to remove both protecting groups from **31** and **33** gave the following informations: Organic acids such as 80% acetic acid did not give pure hydrolysis products, which we attribute to partial N-acylation; further, as expected,[28] both acetone and cyclohexanone ketals were cleaved more rapidly than the neopentyl glycol acetal. Complete deprotection, as evidenced by NMR, could be effected in the case of **33**, when treated with 6N HCl/1,2-dichloroethane. This system was devised to achieve complete separation of hydrolysis products neopentyl glycol/aminohexose hydrochloride, based on their contrasting solubility behaviour. However, no crystalline product could be isolated. As physical properties of racemic mixtures and pure enantiomers often differ considerably, subsequent derivatization to overcome this problem was deferred to efforts in the D series.

A summary of achievements in the D,L-series seems appropriate. The isoxazoline route makes accessible protected DL-lividosamines **31**and **33** in 2 steps only. Isoxazolines of the *erythro* series, such as **27** and **29**, were prepared in gram quantities, yields exceeding 50%. With the instrumentarium of isoxazoline modification reactions elaborated so far,[8,10,16b,29] we may easily predict these compounds to serve as starting points for diastereoselective syntheses of a number of acyclic derivatives, be it amino compounds, aldols or other target molecules. Similarly,

†The neopentyl glycol protecting group in several cases with related work in our group has shown some remarkable properties: (a) ease of acetal formation, stability towards hydrolysis; (b) high tendency to furnish crystalline products; (c) increased solubility of compounds with polar groups in hydrocarbon solvents; (d) NMR spectra less complicated than those of diethyl acetals, the methylene carbon signals appearing with $CHCl_3/CDCl_3$ peaks.

Table 2. ^{13}C NMR chemical shifts of amino alcohols **11–20, 31–34** (in $CDCl_3$, δ in ppm)

Compound	C-6	C-5	C-4	C-3	C-2	C-1
11 [a]	67.2	79.3	74.0	35.9	52.6	67.8
12 [a]	66.8	79.0	70.9	34.8	49.2	
13 [a]	65.6	78.5	72.9	35.3	52.3	
14 [a]	66.0	79.6	69.1	36.4	48.9	
31 [b]	67.0	79.2	73.9	33.7	55.1	102.6
32 [b]		77.9	70.4	32.7	51.3	102.7
33 [c]	66.9	79.0	74.3	34.2	55.3	103.0
34 [c]	66.8	77.8	71.0	33.2	51.7	103.2
	C-5	**C-4**	**C-3**	**C-2**	**C-1**	**C-1'**
15 [d]	66.5	78.9	73.2	40.4	56.1	146.3
16 [d]	66.4	78.2	69.9	40.1	52.7	145.4
17 [e]	65.6	78.9	72.4	40.2	56.1	146.1
18 [e]	65.9	79.3	69.3	41.4	52.8	145.3
19 [f]	66.7	79.6	71.7	42.7	54.8	146.1
20 [f]		79.4	70.3	43.2	52.9	146.3

a Acetonide part: 25.4, 25.5, 26.6, 26.8, 109.3; t-Bu: 27.6, 72.9.

b Acetonide part: 25.3, 26.6, 108.9; dioxane part: 21.6, 22.8, 29.4, 76.8.

c Cyclohexane part: 23.9, 24.1, 25.4, 35.1, 36.5, 36.6, 109.7; dioxane part: 21.8, 23.0, 30.0, 30.2, 30.3, 30.8, 77.1, 77.3.

d Acetonide part: 25.1, 26.4, 108.8; phenyl: 125.4, 125.6, 126.8, 126.9, 128.3, 128.5.

e Acetonide part: 25.2, 26.5 (?), 109.3; phenyl: 125.8 - 128.8.

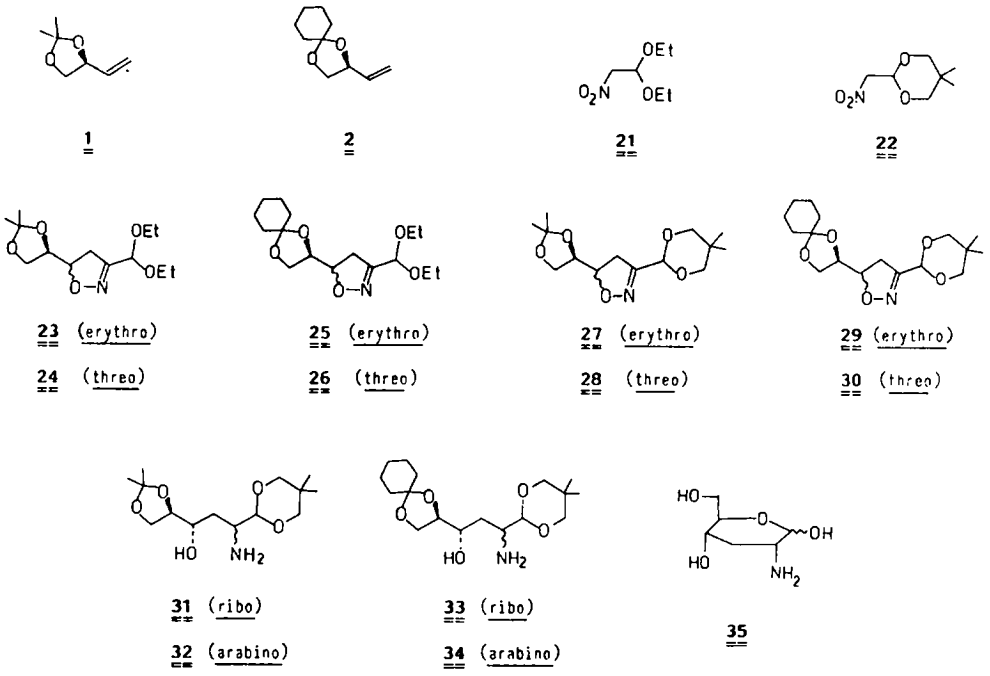
f Cyclohexane part: 24.4, 24.6, 25.8, 35.5, 37.0, 110.4, 110.5; phenyl: 126.8, 127.2, 127.5, 127.8, 129.2. Spectrum recorded in $CD_3OD/CDCl_3$ 9:1.

this should be valid with optically active derivatives as evident from the results in the D-series given below.

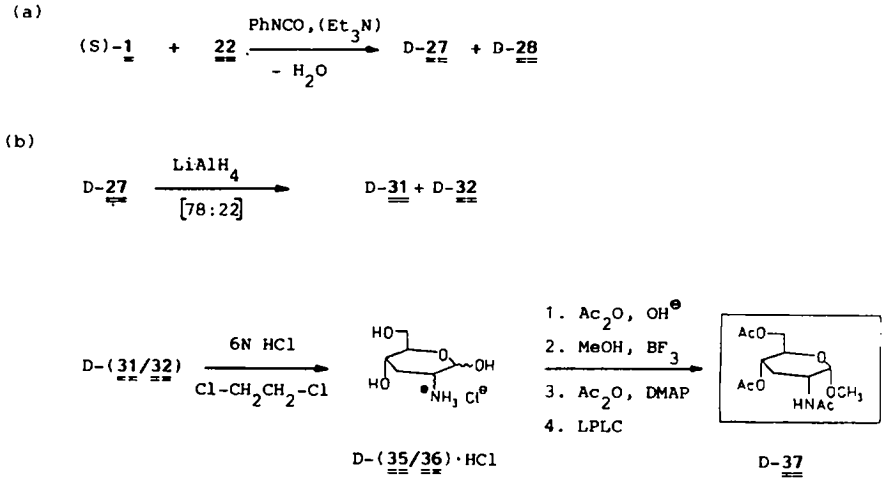
E. D-LIVIDOSAMINE; METHYL N-ACETYL-4,6-DI-O-ACETYL-α-D-LIVIDOSAMINIDE D-37

The synthesis of D-lividosamine was started with the (*S*)-vinyl dioxolane (*S*)-**1**, obtained from D-glyceraldehyde acetonide as described by Crawford *et al.*[30] and acetal **22** as above (Scheme 6). Pure *erythro* adduct D-**27** was isolated in 58% yield after low pressure liquid chromatography (LPLC) on silica. LAH reduction of D-**27** again proceeded in high yield (94%). In contrast to the results in the D,L-series, repeated crystallization produced only 78:22 *ribo/arabino* fractions of protected amino-dideoxyhexoses D-**31**/D-**32**, that is epimer separation by this way was ineffective in the D-series! The mixture of D-**31**/D-**32** therefore was hydrolyzed directly by means of the 6N HCl/1,2-dichloroethane two-phase system (16 hr at reflux). The hexosamine hydrochloride mixture of (D-**35**/D-**36**)·HCl was obtained in 87% crude yield as a foam. This consisted of > 2 compounds, according to ^{13}C NMR absorptions in the 90–100 ppm region, where C-1 pyranose signals were expected;[31] this was interpreted with *two pairs* of anomers being present. Fortunately, Oda *et al.*, in the course of their structure elucidation of lividomycin A, already described the conversion of D-lividosamine hydrochloride to a configurationally homogeneous, crystalline compound, the N,O,O-triacetyl glycoside D-37 (3 steps, 24% yield).[19a] Following this route with the mixture of (D-**35**/D-**36**)·HCl (Scheme 6) we obtained a mixture of triacetyl derivatives, which, finally, did not resist separation attempts. LPLC of this material on silica gave colourless needles, in 16% from D-**31**/D-**32**. The spectral (Experimental) and physical data of this product agreed well with the published data of authentic D-lividosaminide D-**37**: m.p. 139° as opposed to the literature value of 134 ~ 135° (dec.),[19a] and $\alpha_D^{26} + 90.2°$ (*c*, 0.6, MeOH) found here, the literature value being + 90° (*c*, 0.12, MeOH).[19a]

The sequence described constitutes a short alternative access to lividosamine and derivatives, as compared to partial syntheses from glucosamine or glucose derivatives.[19] More efficient separation technique, not available in the course of this study, should permit an essentially three-step approach (6 steps, when counted from D-mannitol, which serves as the actual D-glyceraldehyde acetonide source). Efficient syntheses of these and similar amino compounds, e.g. of higher/lower or branched amino sugars, by modification of key intermediates or building blocks, are conceivable via isoxazolines now, almost as easily as adding up [3 + 2].



Scheme 5.



Scheme 6.

EXPERIMENTAL

For general remarks concerning solvents, diastereomer ratio (d.r.) determinations, general procedures for cycloadditions, LAH reductions and handling of γ-amino alcohols see Ref. 14*b*,29. M.ps (Tottoli apparatus) and b.ps are not corrected; if not stated otherwise, the latter refer to air bath temp in Kugelrohr distillations. IR spectra: Perkin–Elmer 157 G and Beckman Acculab 4; ^{1}H NMR spectra: Varian EM 360, 390, and Bruker WM 400; ^{13}C NMR spectra: Bruker WH 90 and WM 400, for both with TMS as internal standard, $\delta_{TMS} = 0$ ppm; α: Perkin–Elmer 241 MC. Flash chromatography was done on silica (Woelm, 32–63 μm), LPLC on Merck Lobar silica columns. High-precision, pressure-equalizing dropping funnels (Normag) or syringes were used throughout to add solns to reaction mixtures.

Starting materials

2,2-Dimethyl-4-vinyl-1,3-dioxolane[27] (**1**) was prepared from 3-butene-1,2-diol (BASF) and acetone/2,2-dimethoxypropane/*p*-TsOH (cat.) in benzene, azeotropic removal of methanol; 70%, b.p. 45–47°/40 torr (lit[27] 121–123°/760 torr).

(*S*) – **1**: According to Crawford *et al.*[30]

2,2-Pentamethylene-4-vinyl-1,3-dioxolane **2**: Obtained similarly to **1**, 84%, b.p. 82–84°/16 torr.

2-t-Butoxymethyl-1-nitroethane **3**:[16b] From 9.1 g (0.1 mol) of 2-nitro-ethanol, 100 ml of isobutene, 4 ml of conc. H_2SO_4 in 250 ml of CH_2Cl_2, mixed at −5° and left for 5 hr at room temp. in a pressure flask; yield of almost pure (NMR) **3**: quantitative; b.p. (analytical sample) 30–35°/0.05 torr with partial decomposition; for cycloadditions use of "crude" **3** was preferred; similar results were obtained with

$F_3B{\cdot}OEt_2$/85% H_3PO_4 (1:1, 3–4 ml) for 0.385 mmol of nitroethanol 40 ml of isobutene in 280 ml of CH_2Cl_2.

Benzhydroximoyl chloride **4**[5] was prepared from benzaldoxime and N-chloro succinimide adapting a procedure of Liu *et al.*,[32] yield 75%, m.p. 48–49° (in agreement with Ref. 33).

Nitroacetaldehyde diethyl acetal **21** was obtained according to Ref. 25*d*.

5,5-*Dimethyl*-2-*nitromethyl*-1,3-*dioxane* **22: 21** (16.3 g, 0.10 mol), neopentyl glycol (10.6 g; 0.10 mol), benzene (150 ml) and *p*-TsOH (0.5 g) were mixed and, by use of a 40cm-Vigreux column, the benzene/ethanol azeotropic mixture was distilled off slowly (at *ca* 75°). The residue was taken up in CH_2Cl_2 (10 ml), filtered, neutralized by stirring with dry ion exchange resin (Lewatit M 600 G 3, with indicator; $^-$OH form) for 30 min. After filtration and fractional distillation **22** [15.2 g, 87%, b.p. 69°/0.5 torr (lit 67°/0.5 torr[25b])] was collected as a colourless liquid. IR (film): 1550, 1468, 1095, 1057 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.73 [s, 3H, CH_3(e)]; 1.20 [s, 3H, CH_3(a)]; 3.58 (AB, $J \approx 10$ Hz, 4H, ring-CH_2); 4.53 (d, $J = 5$ Hz, 2H, CH_2NO_2), 5.13 (t, 1H, CH).

3-t-Butoxymethyl- and 3-phenylisoxazolines (**5–10**), *aminotetrol and aminotriol derivatives* (**11–20**)

Erythro/threo-3-*t-butoxymethyl*-5-(2,2-*dimethyl*-1,3-*dioxolan*-4-*yl*)-*isoxazolines* **5/6**: According to the procedure of Mukaiyama and Hoshino[7] **1** (1.00 g, 7.8 mmol), **3** (1.47 g, 10 mmol), phenyl isocyanate (4.4 ml, 40 mmol), and triethylamine (0.3 ml) in cyclohexane (25 ml) were refluxed (72 hr). 20 ml of conc. aqueous ammonia were added at room temp. and the mixture stirred for 2 d. Insolubles were filtered off and washed with cyclohexane. The water phase, after saturation with NaCl, was extracted with cyclohexane (3 times 20 ml), then all organic solutes were combined and washed with water (10 ml). The soln was dried (Na_2SO_4), evaporated and distilled (Kugelrohr) to afford **5/6** (78:22; 1.32 g, 66%; b.p. 125°/0.01 torr) as an analytically pure, light-brown oil. In another experiment 1.1 equiv of **1** were used and gave 76% of **5/6**. ^1H NMR ($CDCl_3$): δ 1.03 [s, $C(CH_3)_3$]; 1.33 (s) and 1.39 (s) [$C(CH_3)_2$]; 2.9–3.4 (m, 2H, 4-H); 3.7–4.8 (m of other protons). ^{13}C NMR see Table 1. (Found: C 60.74, H 8.92, N 5.48. Calc. for $C_{13}H_{23}NO_4$ (257.3): C 60.69, H 9.01, N 5.45%).

Erythro/threo-5′-(2,2-*dimethyl*-1,3-*dioxolan*-4-*yl*)-3-*phenylisoxazolines* **7/8**: According to the general procedure given by Huisgen *et al.*[34] triethylamine (3.07 ml, 22 mmol) in ether (20 ml) was added slowly (4 drops/min) to a soln of **1** (2.56 g, 20 mmol) and **4** (3.11 g, 20 mmol) in ether (50 ml), kept at 0°. The mixture was allowed to warm up overnight then the ppt was dissolved by addition of water (20 ml) and MeOH (1 ml). Ether extraction (3 times 20 ml each) of the aqueous phase, after separation, followed by treatment of combined ether solns with 2 × 10 ml of 0.1 N HCl at 0°, 10 ml of water, 10 ml of sat. $NaHCO_3$ soln and 10 ml of brine gave, after drying (Na_2SO_4) and solvent removal, crude **7/8** (4.34 g, 88%) as an oil. Diastereomer ratio (from the crude product of a similar run) 85:15. From the above material fractions enriched in **7** and **8**, resp., were obtained as follows: Crystallization from t-butyl methyl ether (TBME)/hexane, after charcoal treatment, gave a solid product which was washed cautiously with hexane to leave 2.79 g (57%) of colourless crystals, m.p. 52°; from the m.l. another 403 mg (8%, m.p. 53–54°) were crystallized. The first fraction (735 mg) was subjected to LPLC (Lobar, type B, TBME/pet ether (30/75)/NEt_3 30:70:0.1) and produced a 90:10 fraction of **7/8** (527 mg, 41%, m.p. 70–71.5°) and a sample enriched in the *threo* isomer (d.r. 25:75, 110 mg, 8%, m.p. 80–81°), from both of which spectral and analytical data were determined. ^1H NMR of **7** and **8** see Table 3. (Found for the **7/8** = 90:10 fraction: C, 68.16; H, 6.87, N, 5.80. Found for the **7/8** = 25:75 fraction: C, 67.95; H, 6.90; N, 5.73. Calc for $C_{14}H_{17}NO_3$ (247.3): C, 68.00; H, 6.93; N, 5.67%.)

Erythro/threo-5-(2,2-*pentamethylene*-1,3-*dioxolan*-4-*yl*)-3-*phenylisoxazolines* **9/10**: Procedure as above; **2** (1.22 g, 7.3 mmol), **4** (1.03 g, 6.6 mmol), triethylamine (0.67 g, 6.6 mmol), addition at 0° during 4 hr; 1.92 g (quant.) of crude product as a slowly crystallizing oil, d.r. **9/10** 81:19. Enrichment of the *erythro* isomer **9** was achieved by crystallization from ether/pentane, e.g. from the above product a 87:13 fraction (analytical sample) was collected (759 mg, 40%, m.p. 65–68°). Pure **9**: from 11.8 g of a **9/10** mixture obtained as above, after five crystallizations 0.96 g of product with constant m.p. of 73.5°, d.r. > 95:5 by ^{13}C NMR, were obtained. Another crystallization from heptane gave material suitable for X-ray analysis.[23] ^1H NMR (sample with m.p. 65–68°; $CDCl_3$): δ 1.3–1.7 [bs, $(CH_2)_5$]; 3.2–3.6 (m, 4-H); 3.7–4.2 (m, OCH_2CHO), 4.5–4.9 (m, 5-H), 7.2–7.8 (m, C_6H_5). 400 MHz ^1H NMR of **9** see Table 3; ^{13}C NMR of **9/10** see Table 1. (Found for the **9/10** = 87:13 fraction: C, 70.67; H, 7.38; N, 4.86. Found for **9**: C, 71.12; H, 7.40; N, 4.97. Calc for $C_{17}H_{21}NO_3$ (287.3): C, 71.06, H, 7.37; N, 4.88%.)

2-*Amino*-1-0-*t-butyl*-2,3-*dideoxyhexitol* 5,6-*acetonides* **11–14**: According to the general procedure given earlier[14b] a 78:22 mixture of **5/6** (536 mg, 2.08 mmol) was reduced with LAH (160 mg, 4.22 mmol) in ether, reaction time 15 hr at room temp. The usual work-up[14b] gave "crude" (analytically pure) amino compounds **11–14** (541 mg, quant., m.p. 68.5–71°), d.r. 63:17:13:7 (from ^{13}C NMR, *cf* Table 1). Recrystallization of a sample, obtained similarly, from ether/pentane gave a first fraction (42%, m.p. 82–85°), which was N-acetylated (Ac_2O, 3 N NaOH, 73%, m.p. 107–117°) and analyzed by ^{13}C NMR (d.r. 68:11:12:19).

IR (CCl_4) of "crude" **11–14**: 3380, 3280, 1582, 1380, 1360, 1065 cm^{-1}. ^1H NMR of "crude" **11–14** ($CDCl_3$): δ 1.18 [s, $C(CH_3)_3$]; 1.37 (s) and 1.41 (s) [$C(CH_3)_2$]; 1.3–1.8 (m, 3-H), 2.6–4.2 (m, other protons) with 2.9 (b s, exchanged with D_2O; OH, NH_2). ^{13}C NMR see Table 2. (Found: C, 59.61; H, 10.37; N, 5.56. Calc for $C_{13}H_{27}NO_4$ (261.3): C, 59.75; H, 10.41; N, 5.36%). N-Acetyl derivatives: IR (KBr) 3270, 1653, 1638, 1560 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.2 [s, $C(CH_3)_3$]; 1.33 (s) and 1.38 (s) [$C(CH_3)_2$]; 1.4–2.2 (m, 3-H) with 1.97 (s, $NCOCH_3$); 3.4 (m, 1-H); 3.5–4.5 (m, 2-H, 4-H, 5-H, 6-H, OH); 6.1 (b d, NHAc). (Found: C, 59.67; H, 9.51; N, 4.51. Calc for $C_{15}H_{29}NO_5$ (303.4): C, 59.38; H, 9.63; N, 4.62%.)

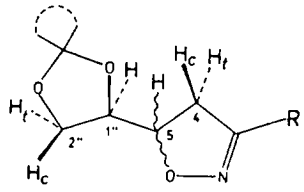
Ribo/arabino-5-*amino*-5-*phenyl*-1,2,3-*pentanetriol* 1,2-*acetonide* **15/16**: By reduction of **7/8** (248 mg, 1.0 mmol, d.r. 90:10) with LAH_4 (95 mg, 2.5 mmol) in ether (4.5 ml) for 6 hr at room temp.; after work-up colourless crystals of **15/16** (247 mg, 98%, m.p. 94–97°, analytically pure; d.r. 81:19); absorptions of **17/18**, supposedly present in $\leqslant$ 5%, could not be identified unambiguously. IR (CCl_4): 3280, 1378, 1365, 1063 cm^{-1}. ^1H NMR ($CDCl_3$, 400.1 MHz), *ribo* isomer **15**: δ 1.31 (s) and 1.36 (s) [$C(CH_3)_2$], 1.63 (2-H_a); 2.01 (2-H_e); 3.79 (3-H); 3.90 (4-H), 3.94 [5-H(trans)]; 4.03 (1-H); 4.07 [5-H(cis)]; 7.20–7.35 (m, C_6H_5). OH, NH_2 not observed. Coupling constants: $J_{1a} = 10.5$, $J_{1e} = 3.5$, $J_{2a3} = 10.5$, $J_{2e3} = 2.0$, $J_{22} = 14.0$, $J_{34} = 6.8$, $J_{45(trans)} = 6.0$, $J_{45(cis)} = 6.0$, $J_{55} = 8.0$ Hz. Signals of *arabino* isomer **16** (as far as not hidden by absorptions of main component **15**); δ 1.83 (2-H_a), 1.90 (2-H_e); $J_{1a} = 8.0$, $J_{1e} = 3.2$, $J_{2a3} = 3.5$, $J_{2e3} = 8.0$, $J_{22} = 14.5$ Hz. ^{13}C NMR see Table 2. (Found: C, 66.89; H, 8.35; N, 5.51. Calc for $C_{14}H_{21}NO_3$ (251.3): C, 66.91; H, 8.42; N, 5.57%.)

Lyxo/xylo *compounds* **17/18**: Reduction of **7/8** (39 mg, 0.16 mmol, d.r. 25:75) by LAH (24 mg, 0.63 mmol) in ether (1.5 ml) for 3 d at room temp. gave 40 mg of a colourless syrup with amino compounds **17/18** as major constituents (d.r. 66:34); besides, the ^{13}C NMR spectrum showed several unidentified peaks in the 30–40 ppm region. ^{13}C NMR data see Table 2.

Ribo/arabino *cyclohexanone ketals* **19/20**: Pure *erythro* isoxazoline **9** (150 mg, 0.5 mmol) with LAH (91 mg, 2.4 mmol) in ether (4 ml) at room temp. for 16 h gave **19/20** as a slowly crystallizing oil (130 mg, 89%, m.p. 76–78°), d.r.

Table 3. ^{1}H NMR data of isoxazolines **7–9, 27–30** (400 MHz, $CDCl_3$, δ in ppm, J in Hz)

Numbering scheme:



Compound	2"-H_c	2"-H_t	1"-H	5-H	4-H_c	4-H_t	Others	
	Chemical Shifts δ							
7	3.97	4.15	4.09	4.66	3.36	3.44	1.36, 1.44 [$C(CH_3)_2$]	R[a]
8	3.90	4.09	4.34	4.81	3.26	3.34	1.36, 1.46 "	
9	3.94	4.12	4.07	4.63	3.37	3.43	1.3 - 1.7 [$(CH_2)_5$]	R[a]
27	3.90	4.11	4.04	4.56	3.11	3.24	1.34, 1.43 [$C(CH_3)_2$]	R[b]
28	3.79	4.05	4.26	4.69	2.96	3.17	1.36, 1.45 "	R[b]
29	3.87	4.07	4.01	4.52	3.13	3.21	1.3 - 1.7 [$(CH_2)_5$]	R[c]
30	3.78	4.04	4.25	4.68	2.99	3.15		

7	2"-2" (gem)	2"$_c$-1" (trans)	2"$_t$-1" (cis)	1"-5	5-4$_c$ (trans)	5-4$_t$ (cis)	4-4 (gem)	
	Coupling Constants J							
7	8.3	4.7	6.2	7.8	6.8	10.3	16.8	
8	8.6	6.5	6.5	4.5	7.8	11.2	16.8	
9	8.0	4.5	6.3	7.8	6.8	10.0	17.0	
27	8.5	4.5	6.5	7.4	6.7	10.8	17.7	R[b]
28	8.8	6.3	6.5	5.3	8.3	11.0	17.5	
29	8.7	4.5	6.0	7.3	6.9	10.3	17.6	R[c]
30	8.5	6.5	6.5	5.3	8.3	11.1	17.6	

a C_6H_5: 7.3 (3H), 7.8 (2H).

b Dioxane part: δ 0.77 [4-CH_3(e)], 1.22 [4-CH_3(a)]; 3.55 (4-, 6-H_a) and 3.68 (4-, 6-H_e), $J_{gem} \simeq 11$ Hz; 5.30 (2-H).

c Dioxane part: δ 0.73 and 0.76 [4-CH_3(e)], 1.22 [4-CH_3(a)]; 3.53 (4-, 6-H_a) and 3.67 (4-, 6-H_e), $J_{gem} \simeq 10.5$ Hz; 5.28 and 5.29 (2-H).

85:15. IR (CCl_4): 3580 (w), 3385, 3310, 1102 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.2–2.1 [m, 2-H and $(CH_2)_5$], 2.9 (b s, OH, NH_2; disappears on D_2O treatment), 3.7–4.2 (1-H, 3-H, 4-H, 5-H), 7.4 (b s, C_6H_5). ^{13}C NMR see Table 2. (Found: C, 69.93; H, 8.56; N, 4.72; Calc for $C_{17}H_{25}NO_3$ (291.4): C, 70.08; H, 8.65; N, 4.81%.)

DL-*Lividosamine series*

Erythro/threo-3-*diethoxymethyl*-5-(2,2-*dimethyl*-1,3-*dioxolan*-4-*yl*)-*isoxazolines* **23/24:** A soln of **21** (2.94 g, 18 mmol) and Et_3N (0.1 ml, 0.7 mmol) in benzene (10 ml) was added to **1** (2.69 g, 21 mmol)/phenyl isocyanate (4.1 ml, 37 mmol)/Et_3N (0.5 ml, 3.6 mmol), dissolved in benzene (20 ml), at room temp within 6.5 hr. Isocyanate (1.0 ml, 9.1 mmol) and Et_3N (0.1 ml, 0.7 mmol) were added then and the mixture was refluxed for 3 hr. After work-up (as described for **5/6**) crude isoxazolines **23/24** (4.07 g, 80%) were obtained as a yellow oil; Kugelrohr distillation afforded analytically pure product (3.07 g, 61%, b.p. 130–150°/0.1 torr); d.r. 80:20 (from ^{13}C NMR). IR (film): 1375, 1363, 1060 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.24 (t, CH_3 of Et), 1.34 (s) and 1.42 (s) [$C(CH_3)_2$], 3.3 (m, 4-H), 3.4–4.2 (m, 6-H, 7-H and CH_2 of Et), 4.6 (m, 5-H), 5.5 [s, $CH(OEt)_2$]. ^{13}C NMR see Table 1. (Found: C, 57.08; H, 8.44; N, 5.44. Calc for $C_{13}H_{23}NO_5$ (273.3): C, 57.12; H, 8.48; N, 5.13%.)

Erythro/threo-*isoxazolines* **25/26:** To a soln of **2** (3.30 g, 20 mmol), phenyl isocyanate (5.1 ml, 40 mmol) and Et_3N (0.5 ml, 3.6 mmol) in benzene (25 ml) was added **21** (3.02 g, 18.5 mmol) with Et_3N (0.1 ml, 0.7 mmol), dissolved in benzene (20 ml), at room temp within 30 hr. After 2 d more isocyanate (1.63 ml, 15 mmol) was added and the mixture was refluxed for 3 hr, then kept at room temp for another 5 d. Work-up as above gave **25/26** (2.58 g, 45%, b.p. 110°/0.05 torr) as a viscous yellow oil still containing *ca* 12% of furoxane; d.r. 81/19. LPLC did not produce analytically pure material. ^{13}C NMR see Table 1.

Erythro/threo-3-(5,5-*di-methyl*-1,3-*dioxan*-2-*yl*)-5-(2,2-*dimethyl*-1,3-*dioxolan*-4-*yl*)-*isoxazolines* **27/28** and **27**: To **1** (1.22 g, 9.5 mmol), phenyl isocyanate (1.8 ml, 16.4 mmol), and Et_3N (0.1 ml, 0.7 mmol) in benzene (30 ml) was added **22** (1.40 g, 8.0 mmol) in 30 ml of benzene at room temp within 5 hr; after 24 and another 30 hr two more 0.5 ml portions of isocyanate were introduced. After the usual work-up the crude product—in order to remove diphenyl urea—in benzene soln was filtered through basic alumina, and left, after evaporation, **27/28** (1.22 g, 53%; d.r. 77:23) as a pale yellow oil, which solidified after several weeks. An analytical sample (25%, m.p. 75.5–77°, d.r. 91:9) was provided by crystallization from TBME–ligroin 3:1 after passage through a small silica column. IR (CCl_4): 1379, 1372, 1108, 1056, 1008 cm^{-1}. ^{1}H NMR (400 MHz) see Table 3;

^{13}C NMR see Table 1. (Found: C, 59.05; H, 8.06; N, 5.17. Calc for $C_{14}H_{23}NO_5$ (285.4): C, 58.93; H, 8.12; N, 4.91%.)

Pure *erythro* compound **27** was obtained in a similar run (from **22**, 5.0 mmol), starting with 10 mmol of isocyanate and adding *ca* 2 mmol each on four consecutive days. Work-up after 13 d gave 1.8 g of crude product, which on flash chromatography [60 g of Woelm silica, 32–63 μm; TBME/p.e. (30–75°), Et_3N 20:80:0.2] in two runs gave **27** [742 mg, 53%, m.p. 76–78°; d.r. > 95:5 from ^1H NMR with 0.2 equiv of Eu(fod)$_3$·d_{27}] and a **27/28** mixture [440 mg, 31%, m.p. 68–71°].

Erythro *isoxazoline* **29** *and* threo *isoxazoline* **30:** In a dilution set-up (Normag) **22** (10.0 g, 57 mmol) in benzene (40 ml) at 80° during 32 hr was dropped to a mixture of **2** (10.9 g, 65 mmol), 4-chlorophenyl isocyanate (18.4 g, 120 mmol) and Et_3N (0.3 ml, 2.2 mol) in 100 ml of benzene. A portion (9.00 g, 59 mmol) of isocyanate was added after 2 d. Work-up after 8 d at reflux temp was done, after dilution with TBME (250 ml), as usual and gave impure crude product (23.8 g, red-brown oil, d.r. 76:24). Attempted crystallization from TBME/p.e. (65–95°) again afforded a red-brown oil (8.47 g) and a yellow paste (11.74 g). Portions of these were submitted to flash chromatography as above, elution done with TBME/p.e. (30–75°)/Et_3N 30:70:0.1. Collected material: 335 mg (19%; m.p. 75–77°; pure *erythro isomer* **29**) and 143 mg (8%, m.p. 86–89°; *threo* isomer **30** with 8% of **29**); 1.74 g (36%, m.p. 76.5–77.5; pure *erythro* **29**) and 674 mg (14%, m.p. 88.5–90.0°; pure *threo* **30**). Total yield: 55.5% of **29**, and *ca* 22% of **30**. IR spectra of **29** and **30** showed no significant differences (CCl_4): 1228, 1098, 1027, 1011 cm^{-1}. ^1H NMR and ^{13}C NMR data see Tables 3, 1. (Found for **29**: C, 62.81; H, 8.28; N, 4.60. Found for **30**: C, 62.59; H, 8.33; N, 4.58. Calc for $C_{17}H_{27}NO_5$ (325.4): C, 62.75; H, 8.36; N, 4.31%.)

Ribo/arabino-2-*amino*-2,3-*dideoxy*-5,6-0-*isopropyliden*-*hexose neopentyl glycol acetal* **31/32:** From **27** (400 mg, 1.4 mmol) with LAH (170 mg, 4.5 mmol) in ether (5 ml), 1 hr at room temp. Diastereomer ratio of crude product (361 mg, 89%, waxy solid) 78:22; crystallization (206 mg of the above material) from hexane gave analytically pure **31/32** (147 mg of colourless plates, 64%, m.p. 69–75°, d.r. 89:11). IR (CCl_4): 3390, 3310, 1373, 1360, 1188, 1070 cm^{-1}. ^1H NMR ($CDCl_3$, 400.1 MHz): *ribo* isomer **31** δ 1.33 (3-H_a), 1.90 (3-H_e), 2.98 (2-H), 3.74 (4-H), 3.87 (5-H), 3.95 [6-H(trans)], 4.09 [6-H(cis)], 4.23 (1-H); coupling constants: $J_{12} = 2.8$, $J_{23a} = 11.3$, $J_{23e} = 2.5$, $J_{3a4} = 10.5$, $J_{3e4} = 2.0$, $J_{33} = 14.5$, $J_{45} = 7.1$, $J_{56trans} = 6.0$, $J_{56cis} = 6.0$, $J_{66} = 8.3$ Hz; *arabino* isomer **32** δ 1.67 (3-H_a), 1.73 (3-H_e), 3.18 (2-H), 3.81 (4-H), 3.96 [6-H(trans)], 4.00 (5-H), ≈4.1 [6-H(cis)]; 4.30 (1-H); cpupling constants: $J_{12} = 3.5$, $J_{23a} = 9.5$, $J_{23e} = 3.5$, $J_{3a4} = 3.9$, $J_{3e4} = 6.8$, $J_{33} = 14.5$, $J_{45} = 7.0$, $J_{56trans} = 5.5$, $J_{56cis} = 5.5$, $J_{66} = 7.3$ Hz; coinciding signals: δ 0.73 (s) and 1.16 (s) [CH_3(e) and CH_3(a) of dioxane ring]; 1.34 (s) and 1.40 (s) [$C(CH_3)_2$ of acetonide], 3.3 (br s, OH, NH_2); 3.42, 3.44, 3.60, and 3.62 (H_a, H_b of CH_2 in dioxane ring; $J_{gem} = 11.5$ Hz, $^4J_{ae} = 2.8$ Hz). ^{13}C NMR see Table 2. (Found: C, 58.45; H, 9.41; N, 4.91. Calc for $C_{14}H_{27}NO_5$ (289.4): C, 58.11, H, 9.40; N, 4.84%.)

Ribo/arabino *compounds* **33/34** *and pure* ribo *compound* **34**: From **29** (1.10 g, 3.3 mmol) on reduction with LAH (416 mg, 11 mmol) in 5 ml of ether for 2.5 hr; the usual work-up afforded an analytically pure **33/34** mixture (1.13 g quant.; colourless oil solidifying, m.p. 68–75°). IR ($CHCl_3$): 3400, 3250, 1133 cm^{-1}. (Found: C, 62.14; H, 9.58; N, 4.62. Calc for $C_{17}H_{31}NO_5$ (329.4): C, 61.98; H, 9.49; N, 4.25%.)

From a similar run ^1H NMR and ^{13}C NMR spectra (Table 2) were recorded, d.r. 79:21. ^1H NMR (400.1 MHz, $CDCl_3$): *ribo* isomer, δ 1.32 (3-H_a), 1.80 (3-H_e), 2.96 (2-H), 3.73 (4-H), 3.86 (5-H), 3.94 [6-H(trans)], 4.08 [6-H(cis)], 4.23 (1-H); coupling constants: $J_{12} = 2.6$, $J_{23a} = 11.0$, $J_{23e} = 2.4$, $J_{3a4} = 10.6$, $J_{3e4} = 2.4$, $J_{33} = 14.1$, $J_{45} = 7.3$, $J_{56trans} = 5.9$, $J_{56cis} = 6.1$, $J_{66} = 8.3$ Hz; *arabino* isomer (not all signals expected could be identified due to overlap or too low concentration): δ 1.70 (3-H_e), 3.17 (2-H), 3.80 (4-H), 3.94 [6-H(trans)], 4.00 (5-H), 4.09 [6-H(cis)], 4.29 (1-H); coupling constants: $J_{12} = 3.5$, $J_{23a} = 9.0$, $J_{23e} = 4.4$, $J_{3a4} = 3.8$, $J_{3e4} = 6.1$, $J_{33} = 14.3$, $J_{45} = 7.4$, $J_{56trans} = 5.8$, $J_{56cis} = 5.9$, $J_{66} = 7.6$ Hz. Coinciding absorptions: δ 0.70 (s) and 1.14 (s) [$C(CH_3)_2$], 1.4–1.7 [m, $(CH_2)_5$]; 3.42, 3.44, 3.61, 3.62 (H_a, H_e of CH_2 in dioxane ring; $J_{gem} = 11.0$ Hz, $^4J_{ae} = 2.5$ Hz); OH, NH_2 not observed.

Ribo *isomer isolation*: 1.08 g of crude product was recrystallized from hexane to afford fractions with m.p. 82–84° (715 mg, 68%, **33/34** = 70/30) and with m.p. 66–67° (320 mg, 30%, pure **33** by ^{13}C NMR). From a similar run with 1.95 mmol of **29** the crude product, crystallized carefully from hexane, gave 146 mg (23%, m.p. 84–85°) and 439 mg (68%, m.p. 64.5–66.5°; supposedly pure *erythro* by DC and m.p. comparison).

D-*Lividosamine*

Compounds D-**27**/D-**28** *and* erythro *isomer* D-**27**: The cycloaddition of (*S*)-**1**[30] (850 mg of a sample of *ca* 90% GC purity, *ca* 5.9 mmol) with **22** (701 mg, 4.0 mmol) was carried out as described in the D,L-case, except for isocyanate being added in 7 portions (0.5 ml; total of 32 mmol) in the course of 13 d. Usual work-up gave colourless material, partially crystalline (1.09 g, 95%), of which 1.044 g were subjected to LPLC [silica, Merck Lobar type C; TBME/p.e. (30–75°)/Et_3N 30:70:0.1] to yield fractions of pure D-**27** [629 mg, 58%, m.p. 93.5–95°; purity > 95:5 from ^1H NMR with Eu(fod)$_3$·d_{27} added; $\alpha_D^{24} = +77.4°$ and $\alpha_{365}^{24} = +260.5°$ ($c = 1.01$ in $CHCl_3$)] and of D-**28** (260 mg, still containing urea contaminations). IR (KBr): 1390, 1375, 1108, 1057, 1013, 888 cm^{-1}. ^1H-NMR identical to that from the D,L sample, *cf.* Table 3. (Found: C, 59.22; H, 8.03; N, 5.19. Calc for $C_{14}H_{23}NO_5$ (285.4); C, 58.93; H, 8.12; N, 4.91%.)

Reduction of D-**27**, ribo/arabino *compounds* D-**31**/D-**32**: Carried out as described for D,L-**27**, with 1.6 mmol of D-**27**; yield of analytically pure D-**31**/D-**32** 439 mg (94%; 78:22 mixture) of light-brown oil, that was used for the synthesis of D-**37**. IR, ^1H and ^{13}C NMR data were identical with those from D,L-**31/32**. $\alpha_D^{24} = -2.11°$ ($c = 0.57$ in $CHCl_3$). (Found: C, 58.29; H, 9.64; N, 4.81. Calc for $C_{14}H_{27}NO_5$ (289.4): C, 58.11; H, 9.40; N, 4.84%.)

Methyl N-*acetyl*-4,6-*di*-O-*acetyl*-α-D-*lividosaminide* D-**37**: D-**31**/D-**32** (432 mg, 1.5 mmol) was refluxed in a vigorously stirred two-phase system of 6 N HCl (40 ml) and 1,2-dichloroethane (300 ml) for 15 hr. The organic layer was separated, washed with water and the combined aqueous phases extracted with ether (twice). The aqueous soln was concentrated under reduced pressure (temp kept below 35°) to leave a brown syrup, which was taken up in 10 ml of water. The soln then was neutralized with ion exchange resin (Lewatit MP 62, weakly basic, $OH^\ominus$ form). Strongly acidic ion exchange resin (Lewatit S 100 G1, $H^\oplus$ form, 25 ml, *ca* 28 mval) was added after filtration, the mixture shaken for 20 hr, decanted and the resin washed with 150 ml of water in a small column. Hydrochlorides of D-**35**/D-**36** next were eluted with 0.2 N HCl (1 l) and the soln evaporated as above. The remainders on drying (P_4O_{10}, 0.1 torr) formed a pale yellow foam [258 mg; NMR spectra were indicative of absence of CH_3 groups, but otherwise gave little information except ^{13}C signals at δ 100.8 (?), 100.6 (major) and 99.4, 95.0, 88.5 (minor)]. 209 mg of this foam were converted to methyl triacetyl glycosides, essentially as described by Oda *et al.*[19a] via N-acetyl methyl glycosides (158 mg, m.p. 152–178°; lit[19a] 206–209° for pure α-D-*ribo*). 136 mg of this material were carried on, as described,[19a] except for O-acetylation, with DMAP (cat.) added. Crude methyl triacetyl glycosides were taken up in acetone, filtered through silica (1.5 g), evaporated and dried to give 263 mg of a semisolid material. Some impurities, as a brown oil (50 mg), separated from a dimethoxyethane/hexane solution of this product, when kept at −20°. Removal of the solvent gave 182 mg of a solidifying syrup, which on LPLC (silica, Merck Lobar type B; acetone–TBME 1:4) gave a crystalline 51 mg fraction. This, on recrystallization from acetone–TBME 1:15, pro-

duced clusters of colourless needles [49 mg, 16% from D-31/D-32, m.p. 139° lit[19a] 134–135° (dec.)]. IR (KBr): 3325, 1745, 1648, 1545, 1255, 1050 cm^{-1}. ^{1}H-NMR (400.1 MHz, $CDCl_3$): δ 1.66 (3-H_a), 1.98 ($NCOCH_3$), 2.03 and 2.09 (4- and 6-$OCOCH_3$), 2.25 (3-H_e), 3.42 (OCH_3), 3.83 (5-H), 4.15 and 4.22 (6-H), 4.28 (2-H), 4.61 (1-H), 5.60 (NH); coupling constants: $J_{12} = 3.5$, $J_{23a} = 12.5$, $J_{23e} = 4.8$, $J_{2,NH} = 9.1$, $J_{33} = 11.6$, $J_{3a4} = 11.3$, $J_{3e4} = 5.0$, $J_{45} = 10.3$, $J_{56} = 2.3$ and 5.0, $J_{66} = 12.0$ Hz. All data in agreement with literature values from 100 MHz recording.[19a] ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 20.7 and 20.9 (CH_3 of 4- and 6-OAc), 23.3 (CH_3 of NAc), 30.7 (C-3), 46.7 (C-2), 55.0 (OCH_3), 62.7 (C-6), 66.2 and 68.1 (C-4, C-5), 97.4 (C-1), 169.1, 169.3 and 170.7 (OCO and NCO). $\alpha_D^{26} = +90.2°$ and $\alpha_{365}^{26} = +250.8°$ ($c = 0.6$ in CH_3OH), lit[19a] $\alpha_D^{26} = +90°$ ($c = 0.12$ in CH_3OH). (Found: C, 51.44; H, 6.93; N, 4.60. Calc for $C_{13}H_{21}NO_7$ (303.3): C, 51.45; H, 6.93; N, 4.43%.)

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