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Diastereoselective Conversion of L-(S)-Erythrulose to 2-Amino-2-deoxy-L-erythritol

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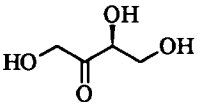
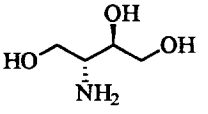
Abstract : L-(S)-Erythrulose (1) was converted into 2-amino-2-deoxy-L-erythritol (2) (six steps, overall yield 35%) through diastereoselective reduction of the bridged orthoester **21**, (1S,5S)-2,7,8-trioxabicyclo[3.2.1]octan-4-one-*O*-benzyloxime, with K-selectride® as the key process. Alternative methods, involving reduction of the imino group in acyclic *O*-benzyloxime derivatives of **1**, or reductive amination of the 2-ketone function, afforded various proportions of *erythro* and *threo* 2-amino diastereoisomers. The distribution of rotamers for the deprotected ammonium salts apparently is governed by hydrogen bonding between the ammonium group and the 3-hydroxyl oxygen, resulting in characteristic $^3J_{H\text{-}2,H\text{-}3}$ coupling constant values. Substitution of the bridged *O*-benzyloximes **21** and **22** *via* deprotonation of the α-methylene position was not successful.

INTRODUCTION

Optically active 2-aminoalditols are key intermediates in the synthesis of various natural products, e.g. sphingolipids,[1] oxazolidinones,[2] and L-*erythro*-ß-hydroxy-α-aminoacids.[3] However, for the smallest-chain chiral system, i.e. the C_4 compounds 2-amino-2-deoxy-L and D-erythritol and -threitol, none of the four isomers has been isolated as a pure substance. Apparently, a mixture of *threo* and *erythro* compounds was produced on hydrogenation of 'erythrulose' with ammonia and Raney nickel at high pressure.[4] In the present work we describe various routes for transformation of L-(S)-erythrulose (**1**),[5] a ketotriol chiral building block exhibiting a single stereogenic center, into chiral 2-aminoalditols e.g. 2-amino-2-deoxy-L-erythritol (**2**).



1



2

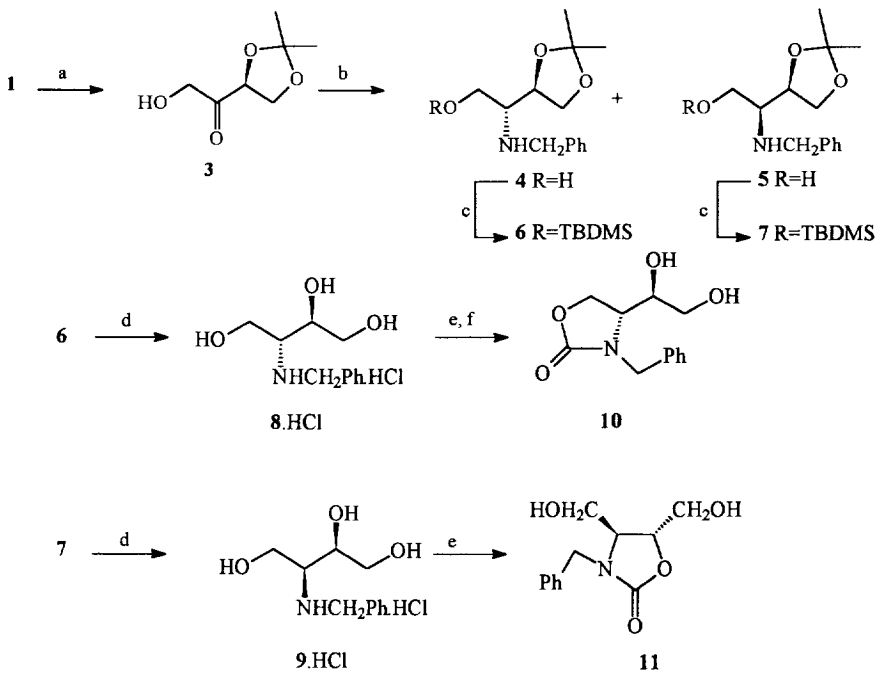
RESULTS AND DISCUSSION

Following protection (Scheme 1) of ketose **1** as the 3,4-*O*-isopropylidene derivative **3**,[6] reductive amination was attempted first under common conditions using benzylamine and $NaCNBH_3$ in methanol, to afford a 1:1 mixture of the *erythro* and *threo* amino compounds **4** and **5**. The isomers were separated as the 1-*O*-*tert*-butyldimethylsilyl derivatives **6** and **7**, and isolated in 16% and 21% yield calculated on **1**. Side products were due to dimerisation of the starting α-ketol compounds **1** and **3** (as known[7] for dihydroxyacetone), and to

competing reduction of the carbonyl function to form *meso*-erythritol and L-threitol. Deprotection of the diastereoisomers **6** and **7** using methanolic HCl afforded the corresponding aminotriol hydrochlorides **8**.HCl and **9**.HCl. Stereostructures were assigned to the hydrochlorides on basis of the $^3J_{H\text{-}2,H\text{-}3}$ coupling constant values (3.6 and 7.5 Hz) in the ^{1}H-NMR spectra (Table 1). Apparently, the distribution of rotamers for each isomer is governed by hydrogen bonding between the 2-ammonium group and the 3-hydroxyl oxygen (Figure 1). This bonding leads to preferred *gauche* conformations I and (probably to a lesser extent) II for the *erythro* isomer **8**.HCl ($^3J_{H\text{-}2,H\text{-}3}$ = 3.6 Hz), and to preferred rotamers III and IV for the *threo* isomer **9**.HCl ($^3J_{H\text{-}2,H\text{-}3}$ = 7.5 Hz). A similar hydrogen bonding control on conformational preferences has been used before to assign the stereoisomers of 1-amino-1-phenyl-2-propanol.[8]

Compounds **8** and **9** were differentiated also by their conversion to cyclic oxazolidinone derivatives. On treatment with phenyl chloroformate at pH 9 the *threo* isomer **9** was transformed smoothly into the *trans* disposed 4,5-bis(hydroxymethyl)oxazolidinone **11**, corresponding to cyclisation with the 3-OH group. By contrast, prolonged reaction with an excess of K_2CO_3 (pH 12) was required to convert the phenyl carbamate intermediate derived from the *erythro* isomer **8** into oxazolidinone **10**, the product of 1-OH cyclisation.

Scheme 1



a) $CH_3COCH_3/(CH_3)_2C(OCH_3)_2$ (9/1), cat. *p*TsOH, 30 min.; b) $PhCH_2NH_2$, $NaCNBH_3$, MeOH, pH 6; c) TBDMSCl, imidazole, DMF; d) 2N HCl/MeOH; e) PhOCOCl, MeOH-H_2O (1:1), K_2CO_3 (pH 9), 48 h; f) excess K_2CO_3 (pH 12), 24 h.

Figure 1 Preferred conformations for **8**.HCl (I,II) and **9**.HCl (III,IV)

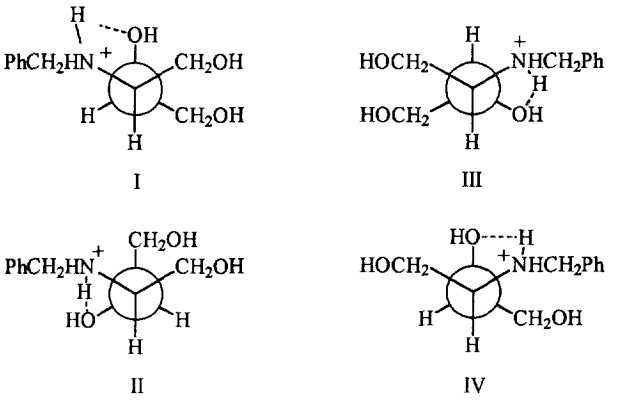


Table 1: ^{1}H NMR spectra of **8**.HCl, **9**.HCl and **2**.HCl

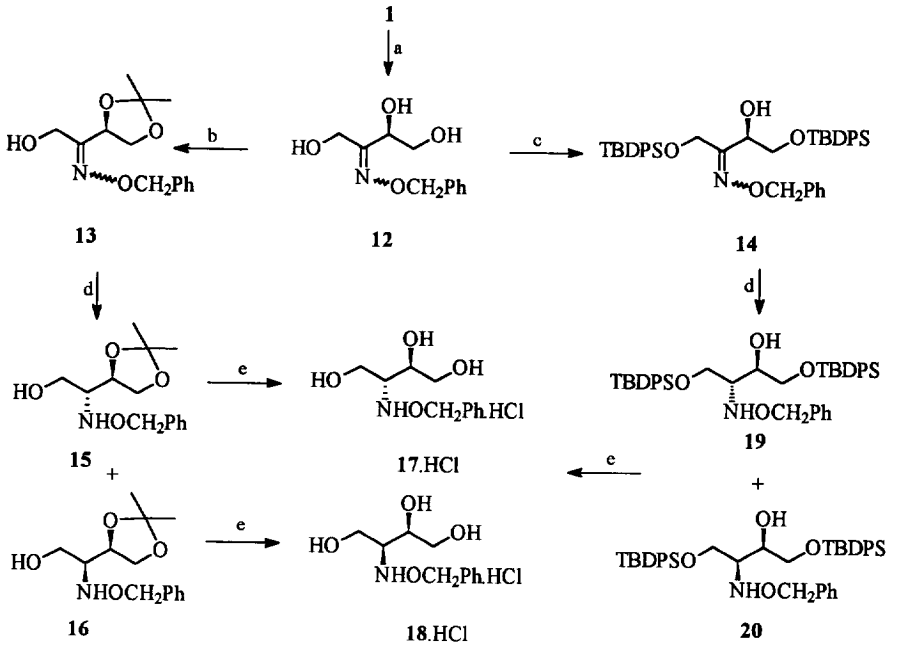
Proton	**8**.HCl δ(ppm), mutiplicity, *J*(Hz)[a]	**9**.HCl δ(ppm), multiplicity, *J*(Hz)[a]	**2**.HCl δ(ppm), multiplicity, *J*(Hz)[b]
H-2	3.53, ddd, ^3J=6.5, 4.5, 3.6	3.42, ddd, ^3J=7.5, 5.5, 4	3.37, m, , ΣJ=18
H-4	3.71, dd, ^2J=12, ^3J=5.7	3.71, dd, ^2J=12, ^3J=4.5	3.60, dd, ^2J=11, ^3J=6
H-4'	3.84, dd, ^2J=12, ^3J=5.7	3.84, dd, ^2J=12, ^3J=3	3.67, dd, ^2J=11, ^3J=5
H-1	3.95, dd, ^2J=12.5, ^3J=6.5	3.93, dd, ^2J=12.5, ^3J=5.5	3.75, dd, ^2J=11, ^3J=5
H-1'	4.01, dd, ^2J=12.5, ^3J=4.5	4.03, dd, ^2J=12.5, ^3J=4	3.85, dd, ^2J=11, ^3J=8
H-3	4.22, td, ^3J=5.7, 5.7, 3.6	4.05, ddd, ^3J=7.5, 4.5, 3	3.87, m, ΣJ=16

[a] 250 MHz, D_2O; [b]400MHz, CD_3OD

To avoid the above side reactions, i.e. dimerisation and competitive reduction, ketose **1** was transformed (Scheme 2) into the stable *O*-benzyloxime **12** (68%), characterized as a 3:2 mixture of *anti* and *syn* isomers.[9] Selective protection of the 3,4-diol and the primary hydroxyl groups afforded the 3,4-*O*-isopropylidene and 1,4-di-*O*-*tert*-butyldiphenylsilyl compounds **13** and **14**, ready for face-selective reduction of the oxime function. Such reduction could proceed through complexation of the α-hydroxyimine moiety with $ZnBH_4$, similar to that reported for the analogous α-hydroxyketones.[10,11] As indicated in Figure 2, *threo* selectivity might be expected for the 1-hydroxyoxime **13** according to the Felkin-Anh model, whereas the Cram chelate model predicts *erythro* selectivity for the Zn^{2+}-chelated 3-hydroxyoxime **14**.[12] The latter prediction was borne out by the experiment, which provided a 3:1 mixture of the *erythro* and *threo* *N*-benzyloxyamines **19** and **20**. The isomeric components were assigned following acid hydrolysis by comparing the ^{1}H-NMR spectrum of the mixture to the spectra for the single compounds **17**.HCl and **18**.HCl described below.

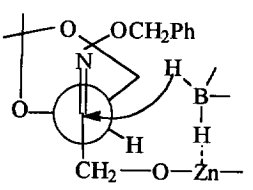
In contrast to the reduction of the 3-hydroxyoxime **14**, no stereoselection was observed on treatment of the 1-hydroxyoxime **13** with $ZnBH_4$. The resulting 1:1 mixture of *erythro* and *threo* isomers was separated through HPLC, and the *N*-benzyloxyamines **15** and **16** were deprotected with HCl in methanol to afford the

Scheme 2

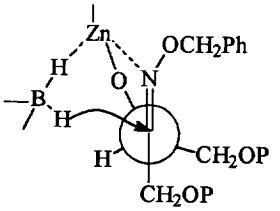


a) $PhCH_2ONH_2$.HCl, NaOAc, MeOH; b) $CH_3COCH_3/(CH_3)_2C(OCH_3)_2$ (9/1), cat. *p*TsOH, 2 h; c) TBDPSCl, imidazole, DMF; d) $ZnBH_4$, Et_2O, -78°C; e) 2N HCl/MeOH.

Figure 2



Felkin-Anh model for **13**



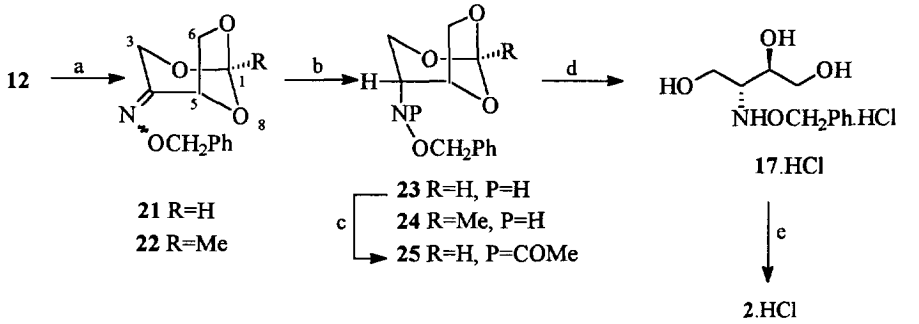
Cram chelate model for **14**

corresponding hydrochlorides **17**.HCl and **18**.HCl. For the 3-OH protected compounds **15** and **16**, a non-biased distribution of rotamers was revealed by similar coupling constant values ($^3J_{H\text{-}2,H\text{-}3}$ = 6.5 Hz). The small value (4 Hz) observed for the deprotected *erythro* compound **17**.HCl appears to be consistent with the hydrogen bonding proposed (Figure 1) for the 3-hydroxyamines **8**.HCl and **9**.HCl. However, owing to coinciding signals in the spectrum of the L-threitol isomer **18**.HCl, definite assignment of the isomeric pairs **15**,**16** and **17**.HCl, **18**.HCl finally rested on the stereospecific synthesis of *N*-benzyloxyamino-L-erythritol (**17**.HCl) described below (Scheme 3).

Since acyclic derivatives of L-erythrulose-*O*-benzyloxime **12** failed to induce a diastereospecific reduction, we sought to enhance asymmetric expression at C-3 by tying up the triol system, i.e. 3-OH and the primary hydroxyl groups, as the bridged orthesters **21** and **22**. The desired conversions (**12**→**21**) and (**12**→**22**) proceeded through reaction of **12** with trimethyl orthoformate and triethyl orthoacetate (Scheme 3); forcing conditions were required to shift the equilibrium from the monocyclic 3,4-*O*-methoxymethyl intermediate to the bicyclic orthoester **21**.

Reduction of **21** and **22** with K-Selectride® (potassium tri-*sec*-butylborohydride), followed by oxidative workup using hydrogen peroxide and sodium hydroxide, exclusively afforded the axial amines **23** and **24**. The axial orientation of the amino group was demonstrated by the small coupling constant values for the equatorial proton H-4 and its neighbouring protons H-3_{ax} and H-3_{eq} in the 400 MHz ^{1}H-NMR spectra. It should be noticed that this assignment rests on the assumption of a chair-like conformation, which appears to be characteristic of the six-membered ring in analogous bicyclooctane compounds.[13] Alternative disposition of the axial amino group in a boat derived from the C-4 epimers of **23** and **24** can be excluded in the present case, since this would lead to severe eclipsing with the axial CH_2O bridge. The axial amines probably form through an equatorial attack of the bulky hydride reagent, similar to that producing axial alcohols from 4-methyl- or 4-*tert*-butylcyclohexanone, and K- or L-Selectride®.[14,15] Interestingly, no reduction at all was observed when the acyclic oxime **13** and the 1-*O*-*tert*-butyldimethylsilyl derivative of **13** were treated with K-Selectride®. This result probably reflects a relief of ring strain for the bridged bicyclic system in going (**21**,**22**→**23**,**24**) from a planar sp^2 to a tetrahedral sp^3 C-4 atom, since a less flattened[16] six-membered ring may facilitate accommodation of the 1,3-diaxial CH_2O bridge.

Scheme 3



a) (**12**→**21**) $(MeO)_3CH$, LiBr, PPTS; ClPh, reflux or (**12**→**22**) $(EtO)_3CMe$, PPTS, MeCN; b) i) K-Selectride, THF ii) H_2O_2, NaOH; c) Ac_2O, pyridine, d) 2N HCl/MeOH; e) Pd/C, H_2, MeOH

The (1S,5S)-2,7,8-trioxabicyclo[3.2.1]octan-4-one-*O*-benzyloximes **21** and **22** represent an interesting chiral system. Bridging of the original stereogenic position at C-5 and the newly formed center at C-1 leads to a clearcut differentiation, not only for the diastereotopic faces of the imino group but also for its two α-positions. In contrast to the proton located at the C-5 bridgehead position, appreciable acidity might be expected for the α-methylene protons at C-3. Generation of the anion therefore could result in stereoselective equatorial substitution, similar to the asymmetric α- and α'-alkylation reported for a chiral hydrazone derived from

O-isopropylidene protected dihydroxyacetone.[17] Unfortunately, treatment of orthoester **21** with lithium diisopropylamide (LDA) in tetrahydrofuran only gave rise to decomposition products, for which disappearance of the orthoformate proton was indicated by the ^{1}H-NMR spectra. Orthoacetate **22**, as opposed to orthoformate **21**, was left unchanged on treatment with either LDA or *tert*-butyllithium : on workup with deuterium oxide no trace of deuterium incorporation into **22** was detected in the chemical ionisation mass spectrum. From this result it appears that, in line with the facilitated reduction of the imino group of **21** and **22**, the already strained bicyclic system is unable to accommodate any further ring strain imposed by incorporation of the planar imine α-anion moiety.

Amine **23** was transformed readily into the target compound 2-amino-2-deoxy-L-erythritol isolated as the hydrochloride **2**.HCl. This conversion proceeded *via* *N*-acetylation to form the more easily purified *N*-acetyl derivative **24**, acid hydrolysis using 2N HCl in methanol affording the pure stereoisomer **17**.HCl referred to above, and final hydrogenation of **17**.HCl with palladium on charcoal in methanol. The ^{1}H-NMR data for aminoalditol **2**.HCl are assembled in Table 1. Selective ^{13}C-{^{1}H} decoupling was performed to assign absorptions for protons H-1 and H-4.

CONCLUSION

In this work we developed a diastereoselective route for conversion of L-(S)-erythrulose **1** into 2-amino-2-deoxy-L-erythritol **2**; this proceeded in six steps with an overall yield of 35%. Compound **2** as well as several selectively protected amino intermediates are suited for further transformation into more complex target structures. This holds true, in particular, for the *N*-(benzyloxy)amine **23** derived from (1S,5S)-2,7,8-trioxabicyclo[3.2.1]octan-4-one-*O*-benzyloxime, and for the readily separated pairs of diastereomeric amines **6** and **7** and *N*-(benzyloxy)amines **15** and **16**.

EXPERIMENTAL SECTION

General methods

The optical rotations were measured on a Propol polarimeter fitted with a 7 cm cell. IR spectra were recorded as thin films between NaCl plates on a Perkin-Elmer 297 grating IR spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker AMX 400 and WM 250 instruments operating at 400 and 250 MHz for ^{1}H and 100 and 62.9 MHz for ^{13}C. Chemical shifts are reported in ppm relative to tetramethylsilane as an internal reference. Mass spectra were run on Kratos MS50 and Hewlett-Packed 5989A instruments; the ion source temperature was 150-250°C as required. Exact masses were measured at a resolution of 10,000. Analytical and preparative thin layer chromatography was carried out using Merck silica gel 60 PF-224. Column chromatography was carried out using 70-230 mesh silica gel 60 (E. M. Merck). Dry solvents were freshly distilled. Solutions were dried over $MgSO_4$. L-(S)-Erythrulose was supplied by Cerestar.

3,4-*O*-Isopropylidene-L-erythrulose (3). L-(S)-erythrulose **1** (87% mixture with water, 13.8 g, 0.10 mol) was dissolved in acetic acid (11 ml). The solvent was removed by co-evaporation with toluene (22 ml). The residue was dissolved in a 9:1 mixture of acetone/2,2-dimethoxypropane (30 ml) containing a catalytic amount of *p*-toluenesulfonic acid (1.9 g, 10 mmol). The mixture was stirred at room temperature for 30 minutes. After

addition of sodium acetate (1.6 g, 20 mmol), the mixture was filtered and the residue chromatographed on silica gel (EtOAc/hexanes : 3/7) to afford 8.0 g (50%) of 3,4-*O*-isopropylidene-L-erythrulose as an oil: $[\alpha]_D^{20}$ = -56.0° (c=1.87, THF); IR (NaCl) cm^{-1} : 3440, 2960-2850, 1730, 1390; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.39 (s , 3 H, CH_3), 1.45 (s , 3 H, CH_3), 4.05(dd , 1 H, H-4, ^2J=8.5 , ^3J=5), 4.27 (dd , 1 H, H-4', ^2J=8.5 , ^3J=7.5), 4.52 (s, 1 H, H-1), 4.53 (s, 1 H, H-1'), 4.60(dd, 1 H, H-3, ^3J=7.5, ^3J=5); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 24.8 (CH_3), 25.9 (CH_3), 66.4 (C-1), 66.8 (C-4), 78.8 (C-3), 111.3 ($C(CH_3)_2$), 169.2 (C=O); HRMS : Calcd. for $C_7H_{14}O_3$ 160.0736, found 160.0748.

2-(*N*-Benzyl)amino-2-deoxy-3,4-*O*-isopropylidene-L-erythritol (4) and 2-(*N*-benzyl)amino-2-deoxy-3,4-*O*-isopropylidene-L-threitol (5). To a solution of 3,4-*O*-isopropylidene-L-erythrulose (16 g, 0.1 mol) in methanol (100 ml) were added benzylamine (21.4 ml, 0.2 mol) and $NaCNBH_3$ (18.8 g, 0.3 mol). The mixture was adjusted to pH=6 with acetic acid and stirred at room temperature for 6 hours. After evaporation of the solvent, the residue was dissolved in water and the solution was made alkaline with aq. K_2CO_3 to pH=9 and extracted with CH_2Cl_2. The organic phase was dried and evaporated. The residue was purified by column chromatography (MeOH/$CHCl_3$: 3/47) to afford 14 g of a 1:1 mixture of compounds **4** and **5** (55%) as an oil: IR (NaCl) cm^{-1} : 3440, 3060, 2960-2850, 1390; ^{1}H-NMR (250 MHz, $CDCl_3$) δ isomer **1** : 2.72 (ddd, 1 H, H-2, ^3J=6, ^3J=4, ^3J=4), 3.61 (dd, 1 H, H-1, ^2J=11, ^3J=4), 3.72 (dd, 1 H, H-1', ^2J=11, ^3J=4), 4.13 (t, 1 H, H-3, ^3J=6) isomer **2** : 2.67 (ddd, 1 H, H-2, ^3J=7.2, ^3J=4.2, ^3J=3.3), 3.38 (dd, 1 H, H-1, ^2J=11, ^3J=3.3), 3.61 (dd, 1 H, H-1', ^2J=11, ^3J=4.2), 4.17 (t, 1 H, H-3, ^3J=7.2); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ isomer **1** : 24.6 (CH_3), 26.1 (CH_3), 46.8 ($PhCH_2N$), 55.8 (C-2), 63.4, 65.8 (C-1,C-4), 74.1 (C-3), 109.9 ($C(CH_3)_2$), 128.0-128.9 (C-Ar), isomer **2** : 24.6 (CH_3), 26.3 (CH_3), 47.3 ($PhCH_2N$), 56.4 (C-2), 63.3, 65.1 (C-1,C-4), 76.6 (C-3), 109.9 ($C(CH_3)_2$), 128.0-128.9 (C-Ar); HRMS Calcd. for $C_{14}H_{21}O_3N$ 251.1521, found 251.1521.

2-(*N*-Benzyl)amino-2-deoxy-3,4-*O*-isopropylidene-1-*O*-*tert*-butyldimethylsilyl-L-erythritol (6) and 2-(*N*-benzyl)amino-2-deoxy-3,4-*O*-isopropylidene-1-*O*-*tert*-butyldimethylsilyl-L-threitol (7). To a solution of the 1:1 mixture of compounds **4** and **5** (0.5 g, 2.0 mmol) in dry DMF were added *t*$BuMe_2SiCl$ (0.33 g, 2.2 mmol) and imidazole (0.34 g, 5.0 mmol). The mixture was stirred at room temperature for 12 hours. After evaporation of the solvent, the residue was distributed between CH_2Cl_2/hexane (5/95) and water. The organic phase was evaporated and the residue was purified by preparative TLC (EtOAc/CH_2Cl_2 : 1/4) to afford 0.20 g (55.4%) of compound **6** and 0.15 g (42.5%) of compound **7** as oils.

6: $[\alpha]_D^{20}$ = -14.5° (c=2.11, $CHCl_3$); IR (NaCl) cm^{-1} : 3500-3300, 3100-3000, 2960-2850, 1390; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 0.10 (s, 6 H, 2xCH_3), 0.90 (s, 9 H, *t*Bu), 1.30 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.80 (br s, 1 H, NH), 2.64 (m, 1 H, H-2, ^3J=7, ^3J=3.8, ^3J=3.8), 3.72 (dd, 1 H, H-1, ^2J=10.5, ^3J=3.8), 3.75 (dd, 1 H, CH-Ar, ^2J=12.5), 3.81 (dd, 1 H, H-1', ^2J=10.5, ^3J=3.8), 3.87 (d, 1 H, CH-Ar, ^2J=12.5), 3.90 (m, 1 H, H-4), 4.08 (m, 1 H, H-3, ^3J=7), 4.12 (m, 1 H, H-4'), 7.32 (s, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ -5.5 (2xCH_3), 18.2 ($C(CH_3)_3$), 25.3 (CH_3), 25.9 (3xCH_3), 26.7 (CH_3), 51.8 (C-Ar), 60.7 (C-1), 60.8 (C-2), 67.7 (C-4), 75.7 (C-3), 108.6 ($C(CH_3)_2$), 126.9 (C_p-arom), 128.1 (C_o-arom), 128.3 (C_m-arom), 140.7 (C_i-arom); HRMS : Calcd. for $C_{19}H_{32}O_3NSi$ (M -CH_3) 350.2151, found 350.2130.

7 :$[\alpha]_D^{20}$= +3.0° (c=2.15, $CHCl_3$); IR (NaCl) cm^{-1} : 3500-3300, 3100-3000, 2960-2850, 1390; ^{1}H-NMR (250

MHz, $CDCl_3$) δ 0.07 (s, 6 H, 2xCH_3), 0.9 (s, 9 H, *t*Bu), 1.35 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 2.05 (br s, 1 H, NH), 2.73 (m, 1 H, H-2, ^3J=6.6, ^3J=6.4, ^3J=5), 3.55 (dd, 1 H, H-1, ^2J=10.5, ^3J=6.6), 3.68 (dd, 1 H, H-1', ^2J=10.5, ^3J= 5), 3.83 (d, 1 H, CH-Ar, ^2J=13), 3.83 (m, 1 H, H-4, ^2J=8, ^3J=7.2), 3.93 (d, 1 H, CH-Ar, ^2J=13), 4.00 (m, 1 H, H-4', ^2J=8, ^3J=6.4), 4.13 (m, 1 H, H-3, ^3J=7.2, ^3J=6.4, ^3J=6.4), 7.36 (s, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ -5.5 (2xCH_3), 18.2 ($C(CH_3)_3$), 25.4 (CH_3), 25.9 (3xCH_3), 26.6 (CH_3), 52.2 (C-Ar), 60.7 (C-2), 62.9 (C-1), 67.0 (C-4), 77.3 (C-3), 108.5 ($C(CH_3)_2$), 126.9 (C_p-arom), 128.1 (C_o-arom), 128.3 (C_m-arom), 140.6 (C_i-arom); HRMS : Calcd. for $C_{19}H_{32}O_3NSi$ (M -CH_3) 350.2151, found 350.2134.

2-(*N*-Benzyl)amino-2-deoxy-L-erythritol (8.HCl) and 2-(*N*-benzyl)amino-2-deoxy-L-threitol (9.HCl). Compound **6** (0.18 g, 0.5 mmol) was dissolved in methanol (5 ml). The solution was acidified (pH=1) with 0.5N HCl, and stirred for 2 hours at room temperature. After evaporation of the solvent, compound **8** was obtained as the oily HCl-salt (0.100 g, 95%).

Similar acid treatment of **7** (0.18 g, 0.5 mmol) afforded the HCl-salt of compound **9** (0.100 g, 95%).

8.HCl : $[\alpha]_D^{20}$= +9.6° (c=1.9, H_2O); IR (NaCl) cm^{-1} : 3600-2850, 1605; ^{1}H-NMR (250 MHz, D_2O) see Table 1, 4.44 (s, CH-Ar), 4.44 (s, CH-Ar), 7.60 (s, Ar-H); ^{13}C-NMR (62.5 MHz, D_2O) δ 48.4 (C-Ar), 55.7 (C-1), 59.0 (C-2), 61.3 (C-4), 67.2 (C-3), 128.6 (C_o-arom), 129.0 (C_p-arom), 129.1 (C_m-arom), 129.7 (C_i-arom); HRMS : Calcd. for $C_{10}H_{14}O_2N$ (M -CH_2OH) 180.1025, found 180.1025.

9.HCl :$[\alpha]_D^{20}$= +42.4° (c=0.4, H_2O); IR (NaCl) cm^{-1} : 3600-2850, 1605; ^{1}H-NMR (250 MHz, D_2O) see Table 1, 4.32 (d, CH-Ar, ^2J=13), 4.44 (d, CH-Ar, ^2J=13), 7.60 (s, Ar-H); ^{13}C-NMR (62.5 MHz, D_2O) δ 48.1 (C-Ar), 56.0 (C-1), 59.1 (C-2), 62.1 (C-4), 66.8 (C-3), 128.5 (C_o-arom), 128.8 (C_p-arom), 129.0 (C_m-arom), 129.8 (C_i-arom); HRMS : Calcd. for $C_{10}H_{14}O_2N$ (M -CH_2OH) 180.1025, found 180.1026.

(4R,1'R)-3-Benzyl-4-[(1',2'-dihydroxy)ethyl]-2-oxazolidinone (10). Compound **8** (1.05 g, 5 mmol) was dissolved in water/methanol (1/1, 5 ml). To the cold (0°C) solution was added slowly phenyl chloroformate (6.3 ml, 0.05 mol) by syringe. The solution was adjusted to pH=8-9 with K_2CO_3. The mixture was stirred at room temperature for 2 days, and made alkaline (pH 12) with K_2CO_3/methanol. The mixture was stirred for one day, then evaporated. The residue was extracted with ethyl acetate. The organic phase was dried and evaporated. The residue was purified by column chromatography (MeOH/$CHCl_3$: 1/4). Compound **10** was isolated as an oil (0.20 g, 16%).

$[\alpha]_D^{20}$= -6.6° (c=0.4,$CHCl_3$); IR (NaCl) cm^{-1} : 3400-3300, 3100-3090, 2960-2850, 1740; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 3.46 (dd, 1 H, H-4, ^2J=11.5, ^3J=6), 3.60 (dd, 1 H, H-4', ^2J=11.5, ^3J=4), 3.70 (ddd, 1 H, H-2, ^3J=8.5, ^3J=6.2, ^3J=2), 3.97 (ddd, 1 H, H-3, 36, ^3J=4, ^3J=2), 4.23 (t, 1 H, H-1, ^2J=9, ^3J=8.5), 4.23 (d, 1 H, CH-Ar, ^2J=15.5), 4.45 (dd, 1H, H-1', ^2J=9, ^3J=6.2), 4.79 (d, 1 H, CH-Ar, ^2J=15.5), 7.25-7.45(m, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 46.4(C-Ar), 57.1(C-2), 62.8(C-4), 63.2(C-1), 68.3(C-3), 128.0(C_o-arom), 128.1(C_p-arom), 129.0(C_m-arom), 135.9(C_i-arom), 159.3(C=O); HRMS : Calcd. for $C_{12}H_{15}O_4N$ 237.1001, found 237.0999.

(4S,5R)-3-Benzyl-4,5-bis(hydroxymethyl)-2-oxazolidinone (11). Compound **9** (1.1 g, 5 mmol) was dissolved in water/methanol (1/1, 5 ml). To the cold (0°C) solution was added slowly phenyl chloroformate

(6.3 ml, 0.05 mol) by syringe. The solution was adjusted to pH=8-9 with K_2CO_3. The mixture was stirred at room temperature for 2 days and evaporated. The residue was extracted with ethyl acetate. The organic phase was dried and evaporated. The residue was purified by column chromatography (MeOH/$CHCl_3$: 3/22). Compound **11** was isolated as an oil (0.60 g, 50%): $[\alpha]_D^{20}$= -23.6° (c=0.5,$CHCl_3$); IR (NaCl) cm-1 : 3400-3300, 3100-3090, 2960-2850, 1740; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 3.56-3.74 (m, 4 H, H-1, H-1', H-4, H-4'), 3.95 (m, 1 H, H-2), 4.34 (d, 1 H, CH-Ar), 4.64 (m, 1 H, H-3), 4.80 (d, 1 H, CH-Ar), 7.40-7.60 (m, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 45.6(C-Ar), 57.6(C-2), 59.2, 61.9(C-1,C-4), 77.5(C-3), 128.0(C_o-arom), 128.2(C_m-arom), 129.0(C_p-arom), 135.0(C_i-arom), 160.0(C=O); HRMS : Calcd. for $C_{12}H_{15}O_4N$ 237.1001, found 237.0996.

L-Erythrulose-*O*-benzyloxime (12). To a solution of dried L-(S)-erythrulose (10 g, 0.083 mol) in methanol (140 ml) were added *O*-benzylhydroxylamine hydrochloride (14.6 g, 0.092 mol) and sodium acetate (16 g, 0.183 mol). The mixture was stirred at room temperature for 2 hours. After addition of dichloromethane the mixture was filtered and the residue chromatographed on silica gel (EtOAc/hexanes : 4/1) to give 18 g (68% yield) of oily oxime **12**: $[\alpha]_D^{20}$= -33° (c=2.84, CH_3OH); IR (NaCl) cm^{-1}: 3350, 3090, 2950, 1690; ^{1}H-NMR (250 MHz, DMSO) δ *anti*-isomer 3.50-3.60 (m, 2 H, H-4, H-4', ^3J=5, ^3J=5), 3.94 (dd, 1 H, H-1, ^2J=13, ^3J=5), 4.20 (dd, 1 H, H-1', ^2J=13, ^3J=5), 4.55 (t, 1 H, OH (C-4), ^3J=5, ^3J=5), 4.68 (t, 1 H, OH (C-1), ^3J=5, ^3J=5), 4.85 (m, 1 H, H-3), 4.85 (m, 1 H, OH (C-3)), 5.04 (s, 2 H, CH_2-Ar), 7.47 (s, 5 H, Ar-H), *syn*-isomer 3.50-3.60(m, 2 H, H-4, H-4', ^3J=5, ^3J=5), 4.25 (dd, 1 H, H-1, ^2J=15, ^3J=5), 4.33 (dd, 1 H, H-1', ^2J=15, ^3J=5), 4.75 (t, 1 H, OH (C-4), ^3J=5, ^3J=5), 4.85 (m, 1 H, H-3), 4.90 (m, 1 H, OH (C-1)), 5.04 (s, 2 H, CH_2-Ar), 5.14 (d, 1 H, OH (C-3)), 7.47 (s, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, DMSO) δ *anti*-isomer 57.0 (C-1), 64.4 (C-4), 71.0 (C-3), 76.3 (CH_2-Ar), 128.0, 128.1, 128.4 (C-arom), 137.1 (C_i-arom), 159.2 (C-2), *syn*-isomer 60.6 (C-1), 63.3 (C-4), 69.0 (C-3), 76.3 (CH_2-Ar), 128.0, 128.1, 128.4 (C-arom), 137.0 (C_i-arom), 159.3 (C-2); HRMS : Calcd. for $C_{11}H_{13}O_3N$ (M -H_2O) 207.0895, found 207.0894.

3,4-*O*-Isopropylidene-L-erythrulose-*O*-benzyloxime (13). L-erythrulose-*O*-benzyloxime (10 g, 0.044 mol) was dissolved in a 9:1 mixture of acetone/2,2-dimethoxypropane (80 ml) with a catalytic amount of *p*-toluenesulfonic acid (0.84 g, 4.4 mmol). The mixture was stirred at room temperature for 2 hours, made alkaline with aq. K_2CO_3 and extracted with dichloromethane. The organic layer was dried and evaporated. The residue was purified by column chromatography (EtOAc/$CHCl_3$: 3/47) to afford 6.6 g of the 3/2 *syn/anti* mixture of compounds **12** (60% yield) as an oil: $[\alpha]_D^{20}$= -49° (c=2.25, $CHCl_3$); IR (NaCl) cm^{-1} : 3460, 3100-3000, 2960-2850, 1640, 1380; ^{1}H-NMR (250 MHz, $CDCl_3$) δ *anti*-isomer 1.36 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 2.85 (t, 1 H, OH, ^3J=6), 4.10 (dd, 1 H, H-4, ^2J=9, ^3J=7), 4.14 (dd, 1 H, H-4', ^2J=9, ^3J=7), 4.44 (dd, 2 H, H-1, H-1', ^2J=12, ^3J=6, ^3J=6), 4.75 (t, 1 H, H-3, ^3J=7, ^3J=7), 5.12 (s, 2 H, CH_2-Ar), 7.35 (s, 5 H, Ar-H), *syn*-isomer 1.36 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 2.70 (t, 1 H, OH, ^3J=7, ^3J=7), 3.72 (dd, 1 H, H-4, ^2J=9, ^3J=7), 4.30 (dd, 1 H, H-1', ^2J=14.5, ^3J=7), 4.34 (dd, 1 H, H-1', ^2J=14.5, ^3J=7), 4.39 (dd, 1 H, H-4', ^2J=9, ^3J=7), 5.08 (s, 2 H, CH_2-Ar), 5.15 (t, 1 H, H-3, ^3J=7, ^3J=7), 7.35 (s, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ *anti*-isomer 25.1 (CH_3), 26.2 (CH_3), 56.9 (C-1), 66.4 (C-4), 75.1 (C-3), 76.5 (CH_2-Ar), 109.6 ($C(CH_3)_2$), 128.0-128.4 (C-arom), 137.0 (C_i-arom), 157.3 (C=N), *syn*-isomer 24.8 (CH_3), 25.8 (CH_3), 60.8 (C-1), 68.0 (C-4),

72.2 (C-3), 76.5 (CH_2-Ar), 110.0 ($C(CH_3)_2$), 128.0-128.4 (C-arom), 137.0 (C_i-arom), 158.7 (C=N); HRMS : Calcd. for $C_{13}H_{16}O_4N$ (M -CH_3) 250.1079, found 250.1087.

2-(*N*-Benzyloxy)amino-2-deoxy-3,4-*O*-isopropylidene-L-erythritol (15) and -L-threitol (16). To a solution of 3,4-*O*-isopropylidene-L-erythrulose-*O*-benzyloxime (0.65 g, 2.4 mmol) in dry Et_2O (10 ml) at -78°C, was added $ZnBH_4$ (0.19M in Et_2O, 48 ml). The mixture was stirred for 12 hours (-78°C→room temperature) after which time it was distributed between EtOAc and water. The organic phase was dried and evaporated. The residue was purified by column chromatography (EtOAc/hexanes : 1/1), followed by HPLC (EtOAc/hexanes : 3/7). Compounds **15** and **16** were isolated as oils in 30% (0.20 g) and 28% (0.18 g) yield, respectively.

15 : $[\alpha]_D^{20}$= -6.2° (c=0.76, $CHCl_3$); IR (NaCl) cm^{-1} : 3550-3400, 3100-3050, 2960-2850, 1395, 1365; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 3.00 (m, 1 H, H-2, Σ^3J=16.6), 3.70 (dd, 1 H, H-1, ^2J=11.5, ^3J=7), 3.82 (m, 1 H, H-1'), 3.82 (m, 1 H, H-4), 4.02 (dd, 1 H, H-4', ^2J=9, ^3J=7), 4.10 (dd, 1 H, H-3, ^3J=7, ^3J=7, ^3J=6.5), 4.65 (s, 2 H, CH_2-Ar), 7.28-7.40 (m, 5 H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.3 (CH_3), 26.6 (CH_3), 60.6 (C-1), 63.7 (C-2), 67.7 (C-4), 74.9 (C-3), 76.9 (CH_2-Ar), 109.0 ($C(CH_3)_2$), 128.1, 128.5, 128.6 (C-arom), 137.4 (C_i-arom); HRMS : Calcd. for $C_{13}H_{18}O_4N$ (M -CH_3) 252.1236, found 252.1236.

16 : $[\alpha]_D^{20}$= -0.9° (c=0.83, $CHCl_3$); IR (NaCl) cm^{-1} : 3550-3400, 3100-3050, 2960-2850, 1395, 1365; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 2.97 (m, 1 H, Σ^3J=16), 3.52 (dd, 1 H, H-1, ^2J=13.3, ^3J=6), 3.67 (m, 1 H, H-1', ^2J=13.3, ^3J=4), 3.80 (m, 1 H, H-4, ^2J=8, ^3J=7), 4.04 (dd, 1 H, H-4', ^2J=8, ^3J=7), 4.27 (dd, 1 H, H-3, ^3J=7, ^3J=7, ^3J=6), 4.70 (s, 2 H, CH_2-Ar), 7.28-7.40 (m, 5 H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.4 (CH_3), 26.7 (CH_3), 60.5 (C-1), 64.2 (C-2), 66.8 (C-4), 73.6 (C-3), 76.7 (CH_2-Ar), 109.3 ($C(CH_3)_2$), 128.2, 128.5, 128.7 (C-arom), 137.3 (C_i-arom); HRMS : Calcd. for $C_{13}H_{18}O_4N$ (M -CH_3) 252.1236, found 252.1231.

1,4-Di-*O*-*tert*-butyldiphenylsilyl-L-erythrulose-*O*-benzyloxime (14). To a solution of L-erythrulose-*O*-benzyloxime **12** (0.29 g, 1.3 mmol) in dry DMF were added *t*$BuPh_2SiCl$ (0.75 ml, 2.9 mmol) and imidazole (0.39 g, 2.9 mmol). The mixture was stirred at room temperature for 2 hours. After evaporation of the solvent, the residue was distributed between CH_2Cl_2/hexane (5/95) and water. The organic phase was evaporated and the residue was purified by preparative TLC ($CHCl_3$) to afford the *syn/anti* mixture of **14** in 67% yield (0.60 g) : $[\alpha]_D^{20}$= -3.16° (c=0.6, $CHCl_3$); IR (NaCl) cm-1 : 3450, 3050, 2960-2850, 1395,1365; ^{1}H-NMR (400 MHz, $CDCl_3$) δ *anti*-isomer 0.95 (s, 9 H, *t*Bu), 1.05 (s, 9 H, *t*Bu), 3.31 (d, 1 H, OH, ^3J=5), 3.84 (dd, 1 H, H-4, ^2J=10, ^3J=7), 3.91 (dd, 1 H, H-4', ^2J=10, ^3J=4), 4.42 (d, 1 H, H-1, ^2J=12), 4.33 (d, 1 H, H-1', ^2J=12), 4.97 (s, 2 H, CH_2-Ar), 5.08 (m, 1 H, H-3, ^3J=7, ^3J=5, ^3J=4), 7.15-7.20 (m, 20 H, 4xAr-H), *syn*-isomer 0.95 (s, 9 H, *t*Bu), 1.05 (s, 9 H, *t*Bu), 3.38 (d, 1 H, OH, ^3J=8), 4.05 (m, 2 H, H-4, H-4', ^2J=10, ^3J=5, ^3J=5), 4.41 (d, 1 H, H-1, ^2J=16), 4.70 (d, 1 H, H-1', ^2J=16), 4.81 (m, 1 H, H-3, ^3J=8, ^3J=5, ^3J=4), 5.01 (s, 2 H, CH_2-Ar), 7.15-7.20 (m, 20 H, 4xAr-H); ^{13}C-NMR (100 MHz,$CDCl_3$) δ *anti*-isomer 19.1 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), 26.7 (6xCH_3), 63.4 (C-1), 65.4 (C-3), 69.8 (C-4), 127.3-135.6 (4xC-arom), 157.9 (C=N), *syn*-isomer 19.1 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), 26.7 (6xCH_3), 59.1 (C-1), 66.0 (C-4), 71.0 (C-3), 127.3-135.6 (4xC-arom), 157.7 (C=N); MS (m/z) 701(M,<1%), 644(M -*t*Bu,32%), 626(M -*t*Bu,-H_2O,0.6%), 566(M -135,19%), 388(M -*t*Bu, -*t*BDPSiOH,3%), 199(Ph_2Si=OH,50%),, 91(C_7H_7,100%).

2-(*N*-Benzyloxy)amino-2-deoxy-1,4-di-*O*-*tert*-butyldiphenylsilyl-L-erythritol (19) and -L-threitol (20). To a solution of **14** (0.47 g, 0.7 mmol) in dry Et_2O (10 ml) at -78°C, was added $ZnBH_4$ (0.19M in Et_2O, 25 ml). The mixture was stirred for 12 hours (-78°C→room temperature). Water was added and the solution was extracted with EtOAc. The organic phase was dried and evaporated. The residue was purified by column chromatography ($CHCl_3$). Compounds **19** and **20** were obtained as a 3:1 oily mixture in 70% yield (0.33 g).
19 : ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.95-1.05 (4xs, *t*Bu), 2.86 (br d, OH), 3.19 (m, H-2), 3.67-3.97 (m, H-1, H-1', H-3, H-4, H-4'), 4.60 (s, CH_2-Ar), 7.32 (m, Ar-H), 7.60 (m, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.3 ($C(CH_3)_2$, 26.8 (CH_3), 60.6 (C-4), 63.1 (C-1), 65.7 (C-2), 70.6 (C-3), 127.7-137.7 (C-arom)
20 : ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.95-1.05 (4xs, *t*Bu), 3.06 (br s, OH), 3.26 (m, H-2), 3.67-3.97 (m, H-1, H-1', H-3, H-4, H-4'), 4.65 (s, CH_2-Ar), 7.32 (m, Ar-H), 7.60 (m, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.3 ($C(CH_3)_2$, 26.8 (CH_3), 61.4 (C-4), 63.0 (C-1), 65.5 (C-2), 70.8 (C-3), 127.7-137.7 (C-arom); IR (NaCl) cm^{-1} : 3450, 3050, 2960-2850, 1395,1360; MS (m/z) 704(MH,6%), 646(M -*t*Bu,1%), 568(M -135,2%), 199(Ph_2Si=OH,50%), 91(C_7H_7,100%).

2-(*N*-Benzyloxy)amino-2-deoxy-L-erythritol (17.HCl) and 2-(*N*-benzyloxy)amino-2-deoxy-L-threitol (18.HCl). Compound **15** (40 mg, 0.16 mmol) was dissolved in 2N HCl/MeOH (5 ml). The mixture was stirred at room temperature for 3 hours, evaporated, and the residue co-evaporated with methanol. The HCl-salt of **17** was isolated as an oil in 92% yield (31 mg).
Similar acid treatment of **16** (40 mg, 0.16 mmol) afforded the HCl-salt of compound **18** (31 mg, 92% yield).
17.HCl : $[\alpha]_D^{20}$= +13.2° (c=0.8, CH_3OH); IR (NaCl) cm^{-1} : 3500-3400, 3090, 2950; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.59 (dd, 1 H, H-4, ^2J=11, ^3J=6), 3.68 (dd, 1 H, H-4', ^2J=11, ^3J=6), 3.73 (m, 1 H, H-2, ^3J=6.5, ^3J=4.5, ^3J=4), 3.91 (dd, 1 H, H-1, ^2J=12, ^3J=6.5), 3.99 (dd, 1 H, H-1', ^2J=12, ^3J=4.5), 4.14 (m, 1 H, H-3, ^3J=6, ^3J=6, ^3J=4), 5.16 (dd, 2 H, CH_2-Ar), 7.35 (m, 5 H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 56.6 (C-1), 63.9 (C-4), 65.8 (C-2), 68.1 (C-3), 77.5 (CH_2-Ar), 129.9-134.2 (C-Ar); HRMS : Calcd. for $C_{10}H_{14}O_3N$ (M -CH_2OH) 196.0974, found 196.0974.
18.HCl : $[\alpha]_D^{20}$= +12.0° (c=0.5, CH_3OH); IR (NaCl) cm^{-1} : 3500-3400, 3090, 2950; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.64 (m, 1 H, H-2), 3.64 (dd, 1 H, H-4, ^2J=12, ^3J=4), 3.72 (dd, 1 H, H-4', ^2J=12, ^3J=4), 3.80 (dd, 1 H, H-1, ^2J=12, ^3J=6), 3.94 (dd, 1 H, H-1', ^2J=12, ^3J=4.5), 3.95 (m, 1 H, H-3), 5.18 (dd, 2 H, CH_2-Ar), 7.35 (m, 5 H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 56.7 (C-1), 65.6 (C-2), 64.5 (C-4), 68.1 (C-3), 77.8 (CH_2-Ar), 129.2-130.7 (C-Ar); HRMS : Calcd. for $C_{10}H_{14}O_3N$ (M -CH_2OH) 196.0974, found 196.0971.

(1S,5S)-2,7,8-Trioxabicyclo[3.2.1]octan-4-one-*O*-benzyloxime (21). To a solution of L-erythrulose-*O*-benzyloxime **12** (10 g, 0.044 mol) in trimethyl orthoformate (35.6 ml, 0.32 mol) were added lithium bromide (0.12 g, 1 mmol) and pyridinium tosylate (0.22 g, 0.8 mmol). The solution was heated (55°C) for 40 minutes. After addition of chlorobenzene (20 ml), the mixture was evaporated and the residue dissolved in chlorobenzene (20 ml). The mixture was stirred at 120°C for 2 hours. After co-evaporation of chlorobenzene with toluene, the residue was purified by column chromatography (EtOAc/$CHCl_3$: 1/19) to afford compound **21** as a mixture of *syn/anti* isomers in 72% yield (7.5 g) : $[\alpha]_D^{20}$ = +21.3° (c=3.1, $CHCl_3$); IR (NaCl) cm^{-1} :

3050, 2950, 1150,1070; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 3.89 (dd, 1 H, H-6_{endo}, ^2J=7.5, ^3J=4.5), 4.05 (d, 1 H, H-6_{exo}, ^2J=7.5, $^3J\approx0$), 4.40 (br d, 1 H, H-3_{eq}, ^2J=16.5, ^3J=1.5), 4.77 (d, 1 H, H-3_{ax}, ^2J=16.5), 4.92 (br d, 1 H, H-5, ^3J=4.5, $^3J\approx0$, ^4J=1.5), 5.08 (s, 2 H, CH_2-Ar), 6.13 (br s, 1 H, ^4J=1.5), 7.37 (s, 5 H, Ar-H), *syn*-isomer 3.82 (dd, 1 H, H-6_{endo}, ^2J=7.5, ^3J=4.5), 3.97 (d, 1 H, H-6_{exo}, ^2J=7.5, $^3J\approx0$), 4.22 (s, 1 H, H-3_{eq}), 4.22 (s, 1 H, H-3_{ax}), 5.60 (br d, 1 H, H-5, ^3J=4.5, $^3J\approx0$, ^4J=1.5), 5.08 (s, 2 H, CH_2-Ar), 6.17 (br s, 1 H, ^4J=1.5), 7.37 (s, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ *anti*-isomer 56.8 (C-3), 69.0 (C-6), 72.8 (C-5), 76.5 (CH_2-Ar), 111.1 (C-1), 128.1-128.5 (C-arom), 137.1 (C_i-arom), 151.2 (C-4), *syn*-isomer 58.7 (C-3), 67.4 (C-6), 69.1 (C-5), 76.5 (CH_2-Ar), 111.2 (C-1), 128.1-128.5 (C-arom), 137.1 (C_i-arom), 151.2 (C-4); HRMS : Calcd. for $C_{12}H_{13}O_4N$ 235.0845, found 235.0844.

(1S,5S)-1-Methyl-2,7,8-trioxabicyclo[3.2.1]octan-4-one-*O*-benzyloxime (22). To a solution of L-erythrulose-*O*-benzyloxime **12** (10 g, 0.044 mol) in dry acetonitrile (100 ml), were added triethyl orthoacetate (12 ml, 0.066 mol) and a catalytic amount of pyridinium tosylate (0.552 g, 2 mmol). The solution was stirred for 6 hours at room temperature, made alkaline with aq. K_2CO_3, and extracted with CH_2Cl_2. The organic phase was dried and evaporated. The residue was purified by column chromatography (EtOAc/$CHCl_3$: 1/19) to afford an oily mixture of *syn/anti* isomers (4/3) (6.5 g, 60%): $[\alpha]_D^{20}$= +17.1° (c=6.02, $CHCl_3$); IR (NaCl) cm^{-1} : 3100-3000, 2960-2850, 1640, 1150,1070; ^{1}H-NMR (400 MHz, $CDCl_3$) δ *anti*-isomer 1.70 (s, 3 H, CH_3), 3.98 (d, 1 H, H-6_{endo}, ^2J=8, ^3J<1), 4.03 (dd, 1 H, H-6_{exo}, ^2J=8, ^3J=5), 4.38 (d, 1 H, H-3, ^2J=16), 4.78 (d, 1 H, H-3', ^2J=16), 4.90 (br d, 1 H, H-5, ^3J=5, ^3J<1), 5.10 (s, 2 H, CH_2-Ar), 7.35 (s, 5 H, Ar-H), *syn*-isomer 1.70 (s, 3 H, CH_3), 3.90 (m, 1 H, H-6_{endo}, ^2J=8, ^3J=1), 3.90 (m, 1 H, H-6_{exo}, ^2J=8, ^3J=4), 4.25 (d, 1 H, H-3, ^2J=12), 4.26 (d, 1 H, H-3', ^2J=12), 5.10 (s, 2 H, CH_2-Ar), 5.60 (dd, 1 H, H-5, ^3J=1, ^3J=4), 7.35 (s, 5 H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ *anti*-isomer 21.8 (CH_3), 57.6 (C-3), 69.9 (C-6), 74.4 (C-5), 76.5 (CH_2-Ar), 119.7 (C-1), 128.1-128.5 (C-arom), 137.1 (C_i-arom), 151.0 (C-4), *syn*-isomer 21.9 (CH_3), 59.8 (C-3), 68.2 (C-6), 70.3 (C-5), 76.5 (CH_2-Ar), 119.7 (C-1), 128.1-128.5 (C-arom), 137.1 (C_i-arom), 153.9 (C-4); HRMS : Calcd. for $C_{13}H_{15}O_4N$ 249.1001, found 249.1021.

(1S,4R,5S)-4-(*N*-Benzyloxy)amino-2,7,8-trioxabicyclo[3.2.1]octane (23). The crude product **21** prepared from **12** (10 g, 0.044 mol) was co-evaporated with toluene, the residue was dissolved in dry THF and the solution transferred to a three-necked flask. K-Selectride® (1M in THF, 123 ml, 0.12 mol) was added by syringe. The mixture was stirred overnight under a N_2 atmosphere, and diluted with THF (50 ml). H_2O_2 (30%, 150 ml) and 3M NaOH (20 ml) were added to destroy the borane addition complex. The mixture was stirred at 0°C for 30 minutes. Water was added and the solution extracted with dichloromethane. The organic phase was dried and evaporated. The residue was purified by column chromatography (EtOAc/$CHCl_3$: 1/21) to afford the oily **23** (3.3 g, 32%): $[\alpha]_D^{20}$= +61.3° (c=1.07, $CHCl_3$); IR (NaCl) cm^{-1} : 3550-3300, 3050, 2950, 1150, 1070; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.82 (br s, 1H, H-4,), 3.76 (dd, 1H, H-3_{ax}, ^2J=12.5, ^3J=2), 3.88 (dd, 1H, H-6_{exo}, ^2J=8, ^3J=5), 4.00 (d, 1H, H-3_{eq}, ^2J=12.5, $^3J\approx0$), 4.01 (d, 1H, H-6_{endo}, ^2J=8, $^3J\approx0$), 4.72 (s, 2H, CH_2-Ar), 4.77 (d, 1H, H-5, ^3J=5), 5.93 (s, 1H, H-1), 6.40(br s, 1H, NH), 7.30 (m, 5H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 56.9 (C-4), 59.1 (C-3), 67.1 (C-6), 71.6 (C-5), 76.0 (CH_2-Ar), 111.6 (C-1), 127.8-128.8 (C-arom), 137.6 (C_i-arom); HRMS : Calcd. $C_{12}H_{15}O_4N$ 237.1001, found 237.0981.

(1S,4R,5S)-1-Methyl-4-(*N*-benzyloxy)amino-2,7,8-trioxabicyclo[3.2.1]octane (24). The crude product **22** prepared from **12** (10 g, 0.044 mol) was dissolved in dry THF and the solution transferred to a three-necked flask. K-Selectride® (170 ml, 0.17 mol, 1M in THF) was added using a syringe. The mixture was stirred overnight under a N_2 atmosfere, and diluted with THF (50 ml). H_2O_2 (30%, 150 ml) and 3M NaOH (20 ml) were added to destroy the borane addition complex. The mixture was stirred at 0°C for 30 minutes. Water was added and the solution extracted with dichloromethane. The organic phase was dried and evaporated. The residue was purified by column chromatography (EtOAc/$CHCl_3$: 1/21) to afford **24** in 49% yield (5.5 g) : $[\alpha]_D^{20}$= +49.6° (c=1.39, $CHCl_3$); IR (NaCl) cm^{-1} : 3550-3300, 3050, 2950, 1150-1070; ^{1}H-NMR : (400 MHz, $CDCl_3$) δ 1.60 (s, 3 H, CH_3), 2.80 (br s, 1 H, H-4), 3.82 (dd, 1 H, H-3_{eq}, ^2J=12.5, ^3J=2), 3.98 (dd, 1 H, H-6_{exo}, ^2J=8, ^3J=4.5), 4.01 (d, 1 H, H-6_{endo}, ^2J=8, ^3J=2), 4.04 (dd, 1 H, H-3_{ax}, ^2J=12.5, ^3J=4), 4.76 (s, 2 H, CH_2-Ar), 4.78 (m, 1 H, H-5, ^3J=4.5, ^3J=2), 6.40 (br s, 1 H, NH), 7.35 (m, 5 H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.7 (CH_3), 56.0 (C-4), 60.2 (C-3), 67.9 (C-6), 68.7 (C-5), 76.0 (CH_2-Ar), 127.5-128.9 (C-arom), 137.7 (C_i-arom); HRMS : Calcd. for $C_{13}H_{17}O_4N$ 251.1158, found 251.1148.

(1S,4R,5S)-4-(*N*-Acetylbenzyloxy)amino-2,7,8-trioxabicyclo[3.2.1]octane (25). The crude product **23** prepared from **21** (0.5 g, 2 mmol) was dissolved in a 1:1 mixture of pyridine and acetic anhydride (5 ml). After one hour, water was added and the solution was extracted with dichloromethane. The organic phase was dried and evaporated. The residue was purified by column chromatography (EtOAc/hexanes : 1/4) to afford **25** in 53% yield (0.3 g) : $[\alpha]_D^{20}$= +38.2° (c=2.08, $CHCl_3$); IR (NaCl) cm^{-1} : 3050, 2950, 1730, 1140, 1070; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 3.45 (dd, 1 H, H-6_{exo}, ^2J=8, ^3J=5), 3.60 (br d, 1 H, H-6_{endo}, ^2J=8, ^3J<1), 3.87 (m, 1 H, H-4_{eq}, Σ^3J=8.5), 3.95 (m, 2 H, H-3_{ax}, H-3_{eq}, ^2J=12.5), 4.55 (dd, 1 H, H-4_{eq}, ^3J=5, ^3J<1), 4.88 (d, 1 H, CH-Ar, ^2J=10), 5.27 (d, 1 H, CH-Ar, ^2J=10), 6.05 (d, H-1_{eq}, ΣJ=2), 7.35 (m, 5 H, Ar-H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 20.4 (CH_3), 55.6 (C-4), 57.8 (C-3), 66.8 (C-6), 73.4 (C-5), 78.7 (CH_2-Ar), 111.5 (C-1), 128.6-129.6 (C-arom), 134.5 (C_i-arom), 173.7 (C=O); HRMS : Calcd. for $C_{14}H_{16}O_4N$ (M -OH) 262.1079, found 262.1080.

2-(*N*-Benzyloxy)amino-2-deoxy-L-erythritol (17.HCl). Compound **25** (50 mg, 0.18 mmol) was dissolved in 2N HCl/MeOH (10 ml). The mixture was stirred at room temperature for 4 hours, evaporated, and the residue co-evaporated with toluene. Compound **17**.HCl was obtained as an oil (35 mg, 98%).
The ^{1}H-NMR spectral data were identical to that for compound **17**.HCl described above.

2-Amino-2-deoxy-L-erythritol (2.HCl). Compound **25** (90 mg, 0.32 mmol) was dissolved in 2N HCl/MeOH (10 ml). The mixture was stirred at room temperature for 4 hours, evaporated, and the residue co-evaporated with toluene. The residue was dissolved in methanol and Pd/C 10% (20 mg) was added. The mixture was hydrogenated in a Parr apparatus (35 Psi) for 8 hours. The catalyst was removed by filtration through a layer of Celite, and the filtrate was evaporated. Compound **2**.HCl was isolated in 97% yield (38 mg) : $[\alpha]_D^{20}$= +14.3° (c=0.9, CH_3OH); IR (NaCl) cm^{-1} : 3500-3400, 2950; ^{1}H-NMR (400 MHz, CD_3OD) see Table 1; ^{13}C-NMR (100 MHz, CD_3OD) δ 56.6 (C-2), 63.9 (C-1), 65.8 (C-4), 68.1 (C-3); HRMS : Calcd. for $C_3H_8O_2N$ (M - CH_2OH) 90.0555, found 90.0559.

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