A New Approach to (±)-2-Amino-2-deoxytetritol Derivatives

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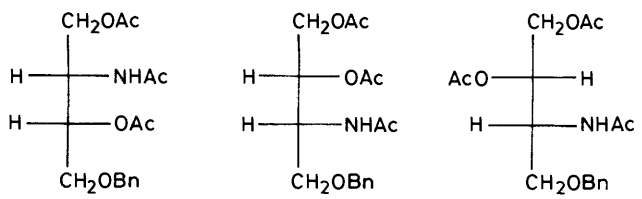
A new approach to the (±)-2-amino-2-deoxytetritol derivatives (**1**), (**2**) and (**3**) is described, starting either from the allylic trichloroacetimidate (**5**) or from the allylic trichloroacetamide (**11**). The 4,5-dihydro-oxazole (**6**), obtained by iodocyclization of the acetimidate (**5**), was hydrolysed to the corresponding amide (**7**) which, by treatment with CO_3^{2-} on a polymeric support, afforded the *cis*-4,5-dihydro-oxazole (**8**). Cleavage of compound (**8**) and acetylation gave the *erythro*-derivative (**1**). On the other hand, iodocyclization of the amide (**11**) led to the *trans*-4,5-dihydro-oxazole (**12a**) which, after hydrolysis and basic treatment, was converted into the *cis*-4,5-dihydro-oxazole (**14**). After hydrolysis and acetylation, the *erythro*-derivative (**2**) was obtained in good yield. Alternatively, after hydrolytic cleavage of the *trans*-4,5-dihydro-oxazole (**12a**), treatment with AcO^- on a polymeric support and acetylation gave the *threo*-derivative (**3**) in good yield.

The area of stereoselective synthesis of acyclic molecules has been expanding rapidly in recent years. Moreover the use of heterocyclic compounds as precursors of regio- and stereo-functionalized acyclic molecules has found an increasing number of successful applications. We recently reported on the synthesis of iodo-4,5-dihydro-oxazoles *via* iodocyclization either of allylic trichloroacetimidates[1] or allylic trichloro-acetamides.[2] These reactions proceed in high yields and under mild conditions to afford 2-amino-1,3-diols and 1-amino-2,3-diols, respectively.

This kind of reaction found an interesting application in the total synthesis of methyl glycosides of L-ristosamine[3] and L-daunosamine,[4] two bioactive amino sugars which constitute respectively the glycosidic residues of the antibiotics ristomycin and daunomycin.

Since we were interested in extending both processes to the synthesis of amino sugars, we report now on two different approaches to *erythro*- and *threo*-derivatives of (±)-2-amino-2-deoxytetritols, (**1**), (**2**) and (**3**).



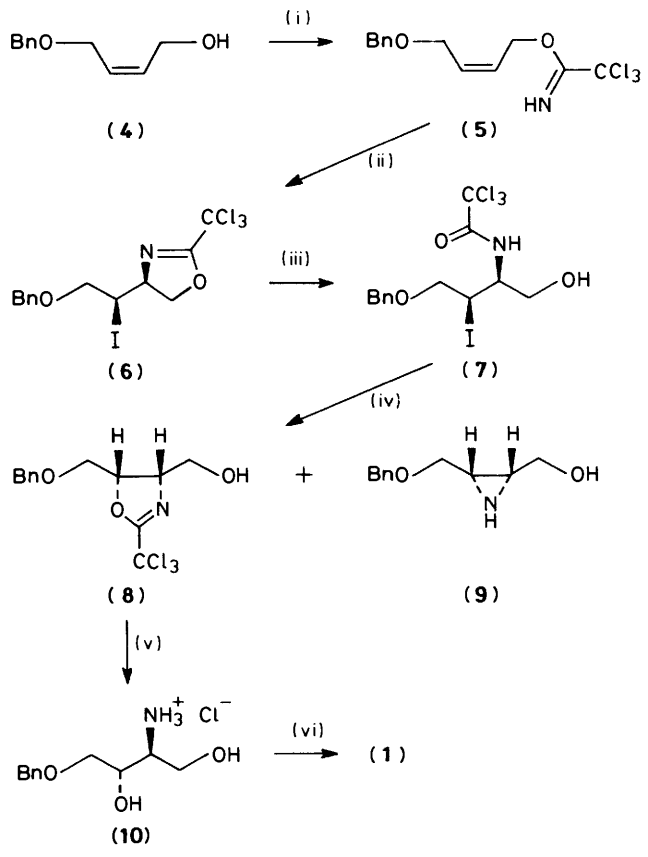
(**1**) (**2**) (**3**)

Recently, Sharpless reported an elegant synthesis of L-threitol and L-erythritol through the titanium-catalysed asymmetric epoxidation and selective ring-opening reaction of 2,3-epoxy alcohols,[5] and Kishi synthesized 2-amino-2-deoxypentitols through ring opening of oxiranes by carbamates.[6]

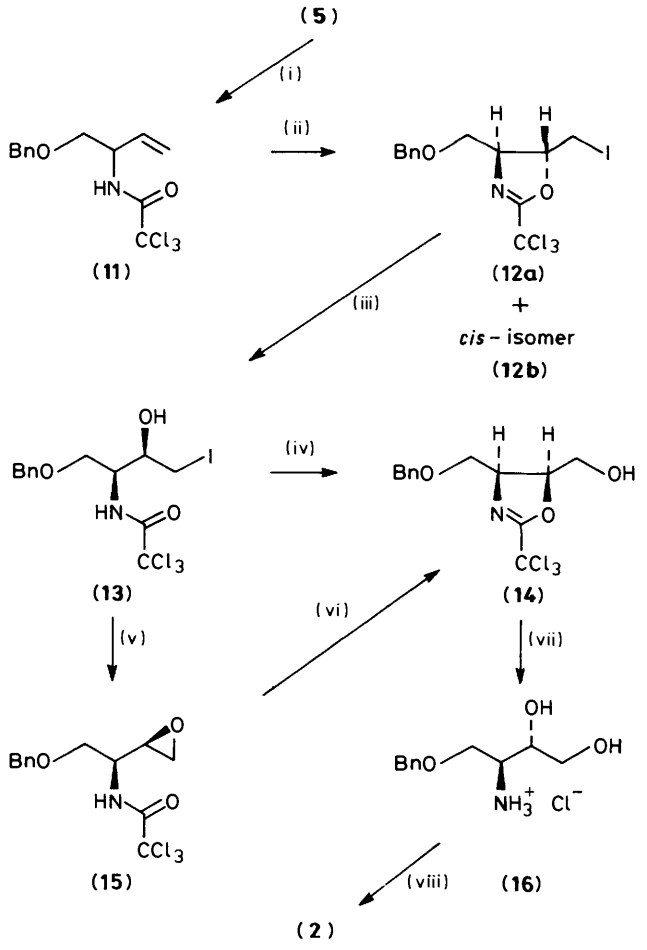
In our approach to the 2-amino-2-deoxyerythritol derivative (**1**), (*Z*)-4-benzyloxybut-2-en-1-ol (**4**), prepared as described in the literature,[7] was converted into the corresponding trichloroacetimidate (**5**) in 90% yield by treatment with a catalytic amount of NaH, followed by addition of trichloro-acetonitrile at 0 °C in THF.[8] The iodocyclization reaction of compound (**5**) to the 4,5-dihydro-oxazole (**6**) was performed in quantitative yield with *N*-iodosuccinimide (NIS) in $CHCl_3$ at room temperature. The hydrolytic cleavage of the heterocyclic ring was performed in water–methanol at reflux and the corresponding *threo*-iodoamide (**7**) was obtained in 82% yield. Treatment of compound (**7**) under basic conditions (Amberlyst A 26 in the CO_3^{2-} form, methanol) afforded the *cis*-4,5-dihydro-oxazole (**8**) in only 30% yield: the *cis*-configuration of the product (**8**) was determined through analysis of its ^1H n.m.r. spectrum, where $J_{4\text{-H},5\text{-H}} = 10$ Hz.[9] Actually, the major product, obtained in 63% yield, was the *cis*-aziridine (**9**). A variety of bases and solvents was investigated to improve the yield, but unfortunately a higher ratio (**8**):(**9**) could not be obtained, probably owing to the steric hindrance of the *threo*-amide (**7**). It is known that displacement of primary halide by the amido group leads mainly to 4,5-dihydro-oxazole ring formation,[10] while a similar displacement of a secondary halide affords a mixture of the 4,5-dihydro-oxazole and the azir-idine.[11] Moreover the propensity for aziridine formation to intervene in the basic treatment of α-halogenoamides has been noted previously.[12] The *cis*-4,5-dihydro-oxazole (**8**) was then converted into the corresponding salt (**10**) by treatment with 6M HCl in methanol. This compound in acetic anhydride–pyridine gave the triacetyl derivative (**1**) in 90% yield (Scheme 1).

Although the results presented above constituted a useful application of the iodocyclization of allylic trichloroacet-imidates, the low yield obtained for the *erythro*-isomer (**1**) prompted us to develop an alternative route to both dia-stereoisomeric derivatives (**2**) and (**3**). For this approach, the trichloroacetamide (**11**), easily obtained in 88% yield by thermal rearrangement of the acetimidate (**5**),[8] was iodocyclized with NIS in $CHCl_3$, leading, in 96% yield, to the 4,5-dihydro-oxazole (**12a** and **b**) in a diastereoisomeric *trans*:*cis* ratio 8:2, as independently determined by g.l.c. analysis and ^{13}C n.m.r. spectroscopy. The assignment of diastereoisomeric structures was made by analogy with the greater shielding observed for *cis*-vicinal carbon atoms in the ^{13}C n.m.r. spectrum, as reported for five-membered rings [*trans*-isomer, δ_C 6.4 (CH_2I) and 70.4 (CH_2OBn); *cis*-isomer, δ_C −0.9 (CH_2I) and 67.1 (CH_2OBn)].[13] The major isomer (**12a**) was obtained in 70% yield by fractional crystallization of the crude mixture. The minor isomer (**12b**) remained as an oil. For (**12a**) the coupling constant $J_{4\text{-H},5\text{-H}}$ 6 Hz was fully consistent with the trans-configuration of the 4,5-dihydro-oxazole ring.[9]

When the *trans*-oxazoline (**12a**) underwent hydrolytic cleavage in refluxing methanol–water, the corresponding *threo*-amide (**13**) was obtained in 83% yield. By treatment of the amide (**13**) with MeONa–CH_2Cl_2, the *cis*-4,5-dihydro-oxazole (**14**) was



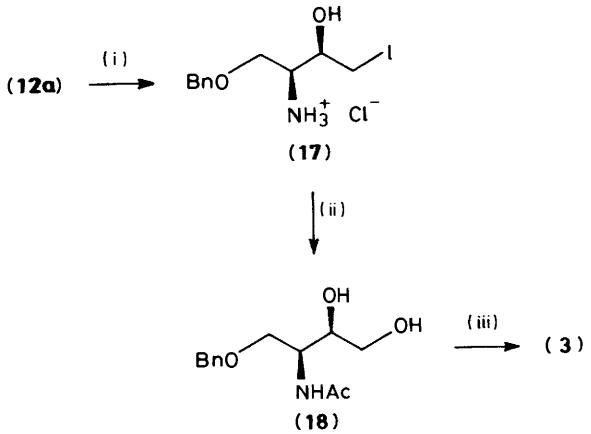
Scheme 1. *Reagents and conditions:* (i) NaH catalyst, THF, CCl_3CN; (ii) NIS, $CHCl_3$; (iii) MeOH–H_2O, reflux; (iv) Amberlyst A 26 (CO_3^{2-} form), MeOH; (v) 6M HCl–MeOH; (vi) Ac_2O, pyridine



Scheme 2. *Reagents and conditions:* (i) heat; (ii) NIS, $CHCl_3$; (iii) MeOH–water, reflux; (iv) MeONa, CH_2Cl_2; (v) Bu^{t}OK, THF; (vi) MeONa, CH_2Cl_2; (vii) 6M HCl–MeOH; (viii) Ac_2O, pyridine

obtained in 81% yield. The coupling constant $J_{4\text{-H},5\text{-H}}$ 10 Hz in the ^{1}H n.m.r. spectrum defined its configuration as a *cis*-4,5-system.[9] The reaction proceeded through the intermediate epoxide (**15**), which could be isolated when the reaction was carried out with Bu^{t}OK.[14] Further treatment of this epoxide (**15**) with MeONa–CH_2Cl_2 afforded the oxazoline (**14**) in 81% yield. Hydrolytic cleavage of compound (**14**) with 6M HCl in methanol gave quantitatively the salt (**16**), which was then acetylated in acetic anhydride–pyridine to give the *erythro*-triacetate (**2**) in 92% yield (Scheme 2).

The *trans*-3,4-dihydro-oxazole (**12a**) was studied also as the precursor of the 2-amino-2-deoxythreitol derivative (**3**). After hydrolysis of (**12a**) with 6M HCl in methanol, the corresponding *threo*-salt (**17**) was obtained in quantitative yield. By treatment with Amberlyst A 26 (AcO^- form) in refluxing methanol, the salt (**17**) was converted into the amide (**18**) which was directly acetylated to give the *threo*-derivative (**3**) in 95% yield (Scheme 3).



Scheme 3. *Reagents and conditions:* (i) 6M HCl–MeOH; (ii) Amberlyst A 26 (AcO^- form), refluxing MeOH; (iii) Ac_2O, pyridine

Experimental

General Methods.—Tetrahydrofuran (THF) was distilled from $LiAlH_4$ or sodium–benzophenone immediately prior to use. All reactions involving organometallic reagents were carried out under an argon atmosphere. M.p.s (Pyrex capillary) were determined on a Buchi 510 hot-stage apparatus and are uncorrected. I.r. spectra were obtained with a Perkin-Elmer Model 682 spectrophotometer either on films or, for solids, on Nujol mulls. ^{1}H N.m.r. spectra were recorded on either a Perkin-Elmer R 12B (60 MHz), a Varian XL-100 (100 MHz), or a Bruker WH 300 (300 MHz) spectrometer for solutions in deuteriochloroform (tetramethylsilane as internal reference), unless otherwise reported. ^{13}C N.m.r. spectra (25 MHz) were recorded using a Varian FT 80-A spectrometer. All chemical shifts were measured relative to tetramethylsilane δ_C 0. Mass spectra were obtained with a double-focusing Varian MAT 112

instrument at an ionizing voltage of 70 eV. Mass spectral data are tabulated as *m/z* values. Analytical g.l.c. was carried out on a Carlo Erba capillary gas chromatograph (Fractovap 4160) equipped with a SE-52 flexible glass capillary column (25 m × 0.3 mm i.d.; carrier gas He, p_{He} 0.6 kg cm^{-2}). Chromatograms, peak areas, and retention times were obtained by using a Perkin-Elmer Sigma 10 data processor. T.l.c. and column chromatography were carried out on Kieselgel GF_{254} (Merck). Solvent ratios are in volumes before mixing. Solutions were dried over anhydrous magnesium sulphate.

(Z)-1-*Benzyloxy*-4-*trichloroacetimidoxybut*-2-*ene* (**5**).—A solution of the butenol (**4**) (7.1 g, 40 mmol) in dry THF (50 ml) under argon was added at 0 °C to a stirred suspension of NaH (50% in mineral oil; 400 mg, 8 mmol; previously washed with dry pentane) in dry THF (30 ml). After 1 h the resulting mixture was added dropwise at 0 °C to a solution of trichloroacetonitrile (6.4 g, 44 mmol) in dry THF (30 ml). The solution was stirred for 1.5 h at room temperature and then concentrated under reduced pressure. Pentane (70 ml) containing methanol (4 ml) was added to the stirred mixture. Successive filtration, evaporation of the solvent, and silica gel chromatography of the residue using cyclohexane–EtOAc (9:1) as eluant gave the acetimidate (**5**) (11.5 g, 90%) as an oil, $\nu_{max.}$ 3 330 and 1 650 cm^{-1}; δ_H 4.15 (2 H, m, CH_2OBn), 4.5 (2 H, s, PhCH_2O), 4.85 [2 H, m, CH_2OC(CCl$_3$)=NH], 5.85 (2 H, m, CH=CH), 7.3 (5 H, m, Ph), and 8.3 (1 H, br s, C=NH); δ_C 65.0, 65.8, 72.3, 125.7, 127.7, 128.4, 128.7, 131.6, and 137.2.

4-(2-*Benzyloxy*-1-*iodoethyl*)-2-*trichloromethyl*-4,5-*dihydro-oxazole* (**6**).—To a stirred solution of the acetimidate (**5**) (6.4 g, 20 mmol) in $CHCl_3$ (100 ml) was added NIS (4.9 g, 22 mmol) at room temperature. After 6 h the reaction mixture was diluted with $CHCl_3$ (100 ml), washed successively with 10% aqueous $Na_2S_2O_3$ and water, and the organic layer was dried. The solvent was removed under reduced pressure to afford the oxazoline (**6**) practically pure in quantitative yield as a low melting solid, $\nu_{max.}$ 1 650 cm^{-1}; δ_H 3.7—4.0 (2 H, m, CH_2OBn), 4.0—4.65 [6 H, m, CHN, CHI, CH_2OC(CCl$_3$)=N–, and PhCH_2O), and 7.3 (5 H, m, Ph); δ_C 35.3, 67.4, 72.6, 73.2, 76.0, 127.7, 127.8, 128.4, and 137.6.

threo-4-*Benzyloxy*-3-*iodo*-2-*trichloroacetamidobutan*-1-*ol* (**7**)—To a stirred solution of the oxazoline (**6**) (8.9 g, 20 mmol) in methanol (70 ml) was added water (8 ml) and the mixture was heated at reflux for 20 h. After removal of the solvent under reduced pressure, the residue was chromatographed through silica gel using cyclohexane–EtOAc (7:3) as eluant to afford compound (**7**) (7.6 g, 82%) as a clear oil, $\nu_{max.}$ 3 400, 1 715, and 1 510 cm^{-1}; δ_H 2.9 (1 H, br s, OH), 3.5—4.2 (5 H, m, CH_2OH, CHI, and CH_2OBn), 4.3—4.7 (1 H, m, CHNH), 4.55 (2 H, s, PhCH_2O), 7.0 (1 H, d, *J* 10 Hz, NH), and 7.3 (5 H, m, Ph); δ_C 31.3, 54.3, 63.3, 72.5, 73.5, 128.0, 128.4, 136.8, and 161.9.

cis-5-*Benzyloxymethyl*-4-*hydroxymethyl*-2-*trichloromethyl*-4,5-*dihydro-oxazole* (**8**).—To a solution of the amide (**7**) (7.0 g, 15 mmol) in methanol (50 ml) was added Amberlyst A 26 (Rohm and Haas) (CO_3^{2-}) (12 g, *ca.* 3.8 mol equiv. g^{-1}) and the suspension was stirred at 0 °C for 0.5 h. The resin was then filtered off and removal of the solvent under reduced pressure gave an oil which was chromatographed through silica gel using cyclohexane–EtOAc (6:4) as eluant to give compound (**8**) (1.5 g, 30%) as an oil, $\nu_{max.}$ 3 400 and 1 650 cm^{-1}; δ_H 3.05 (1 H, br s, OH), 3.85 (4 H, m, CH_2OH and CH_2OBn), 4.5 (3 H, m, CHN and PhCH_2O), 5.1 (1 H, dt, *J* 10 and 5 Hz, CHO), and 7.3 (5 H, m, Ph); δ_C 60.5, 67.3, 69.6, 73.7, 84.1, 127.8, 128.0, 128.5, 137.0, and 161.8. Further elution using cyclohexane–EtOAc (1:1) afforded 1.8 g of *cis*-2-benzyloxymethyl-3-hydroxymethyl-aziridine (**9**) (63%) as a viscous oil, $\nu_{max.}$ 3 300 and 1 450 cm^{-1}; δ_H 2.1—2.4 (2 H, m, CH–CH), 2.65 (2 H, br s, OH and NH), 3.2—3.8 (4 H, m, CH_2OH and CH_2OBn), 4.5 (2 H, s, PhCH_2O), and 7.3 (5 H, m, Ph); δ_C 33.2, 35.2, 61.2, 69.6, 73.3, 127.9, 128.5, and 137.2.

erythro-2-*Amino*-4-*benzyloxybutane*-1,3-*diol Hydrochloride* (**10**).—To a solution of the oxazoline (**8**) (0.67 g, 2 mmol) in methanol (30 ml) at room temperature was added 6M HCl (1 ml) and the mixture was stirred for 24 h. The solvent was then removed under reduced pressure and after extraction of the residue with EtOAc, the insoluble salt (**10**) was obtained in quantitative yield as a viscous oil, $\nu_{max.}$ 3 300 cm^{-1}; δ_H(CD$_3$OD) 3.3—4.1 (6 H, m, CH_2OH, CH_2OBn, CHO, and CHN), 4.65 (2 H, s, PhCH_2O), 4.85 (5 H, br s, 2 OH and NH_3^+), and 7.5 (5 H, m, Ph).

erythro-2-*Acetamido*-1,3-*diacetoxy*-4-*benzyloxybutane* (**1**).—To a solution of the salt (**10**) (0.5 g, 2 mmol) in pyridine (2 ml) was added acetic anhydride (2 ml) at room temperature and the mixture was stirred for 24 h. After removal of the excess of both pyridine and acetic anhydride, the residue was chromatographed through silica gel using EtOAc as eluant to give compound (**1**) (0.6 g, 90%) as a white solid, m.p. 44 °C; $\nu_{max.}$ 3 300, 1 750, 1 660, and 1 550 cm^{-1}; δ_H 2.0, 2.05 and 2.1 (9 H, 3 × s, MeCO) 3.65 (2 H, d, *J* 4Hz, CH_2OBn), 4.2 (2 H, dd, *J* 4 and 5 Hz, CH_2OAc), 4.55 (3 H, m, CHN and PhCH_2O), 5.1 (1 H, q, *J* 6 Hz, CHOAc), 6.7 (1 H, d, *J* 8 Hz, NH), and 7.3 (5 H, m, Ph); δ_C 20.7, 20.9, 23.1, 49.0, 62.8, 69.3, 71.0, 73.5, 127.8, 127.9, 128.5, 137.7, 170.1, 170.2, and 170.7; *m/z* 337 (M^+, 3%), 232 (8), 231 (11), 204 (13), 172 (42), 171 (37), 111 (31), and 91 (100) (Found: C, 60.5; H, 6.85. $C_{17}H_{23}NO_6$ requires C, 60.52; H, 6.87%).

4-*Benzyloxy*-3-*trichloroacetamidobut*-1-*ene* (**11**).—A solution of the acetimidate (**5**) (9.6 g, 30 mmol) in decahydronaphthalene (50 ml) was refluxed for 12 h. The mixture was directly chromatographed through silica gel, using cyclohexane as eluant to remove decahydronaphthalene, and then with cyclohexane–EtOAc (95 : 5), to afford the butene (**11**) (8.5 g, 88%) as a clear oil, $\nu_{max.}$ 3 420, 3 340, 1 710, 1 505, and 925 cm^{-1}; δ_H 3.6 (2 H, d, *J* 6 Hz, CH_2OBn), 4.2—4.7 (1 H, m, CHNH), 4.55 (2 H, s, PhCH_2O), 5.0—6.0 (3 H, m, CH=CH_2), and 7.35 (6 H, m, Ph + NH).

trans-4-*Benzyloxymethyl*-5-*iodomethyl*-2-*trichloromethyl*-4,5-*dihydro-oxazole* (**12a**).—To a stirred solution of the butene (**11**) (8.0 g, 25 mmol) in $CHCl_3$ (100 ml) was added NIS (6.0 g, 27 mmol) at room temperature. After 8 h the reaction mixture was diluted with $CHCl_3$ (150 ml) and successively washed with 10% aqueous $Na_2S_2O_3$ and water, and then dried. The solvent was removed under reduced pressure to afford the crude mixture of oxazolines (**12a** and **b**) (10.7 g, 96%) as a low melting solid in a diastereoisomeric ratio *trans*:*cis* 8:2 (determined by the ^{13}C spectrum and g.l.c. analysis of the mixture). On recrystallization (from methanol), the *trans*-isomer (**12a**) was obtained (7.8 g, 70%) as a white solid, m.p. 81—83 °C; $\nu_{max.}$ 1 660 cm^{-1}; δ_H 3.35 (2 H, d, *J* 6 Hz, CH_2I), 3.6 (2 H, m, CH_2OBn), 4.2 (1 H, m, CHN), 4.55 (2 H, s, PhCH_2O), 4.8 (1 H, q, *J* 6 Hz, CHO), and 7.3 (5 H, m, Ph); δ_C 6.4, 70.4, 72.4, 73.4, 84.0, 127.5, 127.7, 128.4, 137.6, and 162.2. From the mother liquors the *cis*-isomer (**12b**) was obtained as a yellow oil (1.9 g, 17%), $\nu_{max.}$ 1 660 cm^{-1}; δ_H 3.3—4.0 (4 H, m, CH_2I and CH_2OBn), 4.0—4.5 (1 H, m, CHN), 4.55 (2 H, s, PhCH_2O), 5.3 (1 H, dt, *J* 4 and 10 Hz, CHO), and 7.35 (5 H, m, Ph); δ_C −0.9, 67.1, 68.0, 73.7, 85.9, 127.9, 128.7, 137.6, and 162.2.

threo-4-*Benzyloxy*-1-*iodo*-3-*trichloroacetamidobutan*-2-*ol* (**13**).—To a stirred solution of the *trans*-oxazoline (**12a**) (6.7 g, 15

mmol) in methanol (55 ml) was added water (5 ml) and the mixture was refluxed for 24 h. The solvent was then removed under reduced pressure and the residue was chromatographed through silica gel using cyclohexane–EtOAc (7:3) as eluant to afford the acetamide (**13**) (5.8 g, 83%) as a clear oil, $\nu_{max.}$ 3 400, 1 710, and 1 500 cm^{-1}; δ_H 3.2 (2 H, d, *J* 7 Hz, CH_2I), 3.65 (2 H, d, *J* 5 Hz, CH_2OBn), 3.9—4.4 (2 H, m, CHO and CHN), 4.5 (2 H, s, $PhCH_2O$), 4.9 (1 H, br s, OH), and 7.3 (6 H, m, Ph + NH); δ_C 8.3, 53.5, 69.9, 71.4, 73.6, 127.8, 128.1, 128.6, and 137.1.

cis-4-*Benzyloxymethyl*-5-*hydroxymethyl*-2-*trichloromethyl*-4,5-*dihydro-oxazole* (**14**).—(a) *From the acetamide* (**13**). Freshly prepared sodium methoxide solution [from sodium metal (0.23 g) dissolved in dry methanol (20 ml)] was added dropwise under argon to a stirred solution of the acetamide (**13**) (4.6 g, 10 mmol) in dry methylene dichloride (25 ml) and the mixture was stirred for 2 h at room temperature. The reaction was quenched with water, the mixture was extracted with EtOAc, the extract was dried, and the solvent was removed under reduced pressure. The residue was chromatographed through silica gel, using cyclohexane–EtOAc (7:3) as eluant, to afford the oxazoline (**14**) (2.6 g, 80%) as a clear oil, $\nu_{max.}$ 3 400 and 1 655 cm^{-1}; δ_H 3.04 (1 H, br s, OH), 3.80 (2 H, m, CH_2OBn), 3.93 (2 H, m, *J* 3.5 Hz, CH_2OH), 4.60 (3 H, m, CHN and $PhCH_2O$), 5.00 (1 H, dt, *J* 5 and 10 Hz, CHO), and 7.32 (5 H, m, Ph); δ_C 60.2, 67.3, 67.6, 73.9, 85.9, 127.9, 128.2, 128.6, and 136.8.

threo-1-*Benzyloxy*-3,4-*epoxy*-2-*trichloroacetamidobutane* (**15**).—To a stirred solution of the iodohydrin (**13**) (5.6 g, 12 mmol) in dry THF (30 ml) under argon was added dropwise a solution of Bu^{t}OK (1.36 g, 12 mmol) in dry THF (15 ml) at room temperature. After 0.5 h the reaction mixture was poured into ice–water, extracted with EtOAc, and the organic phase was dried. Removal of the solvent under reduced pressure gave a residue which was chromatographed through silica gel using cyclohexane–EtOAc (7:3) as eluant to afford the epoxide (**15**) (3.8 g, 95%) as a clear oil, $\nu_{max.}$ 3 400, 3 330, 1 710, and 1 510 cm^{-1}; δ_H 2.5—2.9 (2 H, m, 4-H_2), 3.3 (1 H, m, 3-H), 3.65 (2 H, d, *J* 6 Hz, CH_2OBn), 4.2 (1 H, m, CHNH), 4.55 (2 H, s, $PhCH_2O$), 6.9 (1 H, d, *J* 8 Hz, NH), 7.3 (5 H, m, Ph); δ_C 43.7, 49.7, 50.8, 69.2, 73.4, 127.7, 127.9, 128.5, 137.4, and 162.0.

cis-4-*Benzyloxymethyl*-5-*hydroxymethyl*-2-*trichloromethyl*-4,5-*dihydro-oxazole* (**14**).—(b) *From the acetamide* (**15**). To a solution of the acetamide (**15**) (3.4 g, 10 mmol) in dry methylene dichloride (25 ml) under argon was added dropwise a freshly prepared sodium methoxide solution [from sodium metal (0.23 g) in dry methanol (20 ml)]. After being stirred at room temperature for 2 h, the mixture was diluted with water and extracted with EtOAc. After removal of the solvent under reduced pressure, the residue was chromatographed through silica gel using cyclohexane–EtOAc (7 : 3) as eluant to afford the oxazoline (**14**) (2.7 g, 81%) as a clear oil.

erythro-3-*Amino*-4-*benzyloxybutane*-1,2-*diol Hydrochloride* (**16**).—A stirred solution of the oxazoline (**14**) (3.4 g, 10 mmol) in methanol (5 ml) was treated with 6M HCl (3 ml) and stirred for 24 h at room temperature. After removal of the solvent under reduced pressure, the residue was washed with ether and the salt (**16**) was obtained in quantitative yield as a viscous oil, $\nu_{max.}$ 3 400 cm^{-1}; $\delta_H(CD_3OD)$ 3.3—4.1 (6 H, m, CH_2OH, CH_2OBn, CHN, and CHO), 4.55 (2 H, s, $PhCH_2O$), 4.85 (5 H, br s, 2 OH and NH_3^+), and 7.4 (5 H, m, Ph).

erythro-2-*Acetamido*-3,4-*diacetoxy*-1-*benzyloxybutane* (**2**).—Acetic anhydride (4 ml) was added at room temperature to a solution of the salt (**16**) (2.5 g, 10 mmol) in pyridine (4 ml). After 24 h excess of both pyridine and acetic anhydride were evaporated off under reduced pressure and the residue was chromatographed through silica gel, using EtOAc as eluant, to afford *compound* (**2**) (3.1 g, 92%) as an oil, $\nu_{max.}$ 3 280, 1 745, 1 650, and 1 535 cm^{-1}; δ_H 2.0 (9 H, br s, 3 CH_3CO), 3.5 (2 H, m, CH_2OBn), 4.2 (2 H, m, CH_2OAc), 4.5 (2 H, s, $PhCH_2O$), 4.5 (1 H, m, CHNH), 5.2 (1 H, m, CHOAc), 6.95 (1 H, d, *J* 10 Hz, NH), and 7.3 (5 H, m, Ph); δ_C 20.7, 20.8, 23.0, 48.2, 63.0, 68.2, 70.3, 73.2, 127.9, 128.4, 137.7, 170.1, and 170.7; *m/z* 337 (M^+, 2%), 262 (10), 250 (8), 188 (13), 170 (15), 114 (31), and 91 (100) (Found: C, 60.5; H, 6.85. $C_{17}H_{23}NO_6$ requires C, 60.52; H, 6.87%).

threo-3-*Amino*-4-*benzyloxy*-1-*iodobutan*-2-*ol Hydrochloride* (**17**).—A solution of the *trans*-oxazoline (**12a**) (6.7 g, 15 mmol) in methanol (40 ml) was treated with 6M HCl (5 ml) and stirred at room temperature for 24 h. After removal of the solvent under reduced pressure, the residue was washed with ether to afford the salt (**17**) in quantitative yield as a viscous oil, $\nu_{max.}$ 3 350 cm^{-1}; $\delta_H(CD_3OD)$ 2.8 (4 H, br s, OH and NH_3^+), 3.2—3.5 (2 H, m, CH_2I), 3.5—4.0 (4 H, m, CH_2OBn, CHO, and CHN), 4.6 (2 H, s, $PhCH_2O$), and 7.4 (5 H, m, Ph).

threo-3-*Acetamido*-4-*benzyloxybutane*-1,2-*diol* (**18**).—To a stirred solution of the salt (**17**) (3.5 g, 10 mmol) in methanol (40 ml) was added Amberlyst A 26 (Rohn and Haas) (AcO^-) (10 g, *ca.* 3.8 mol equiv. g^{-1}) and the suspension was refluxed for 4 h before being cooled and the resin filtered off; the solvent was removed under reduced pressure and the diol (**18**) was obtained in quantitative yield as an oil, $\nu_{max.}$ 3 300, 1 640, and 1 560 cm^{-1}; δ_H 1.97 (3 H, s, CH_3CO), 3.1—4.1 (5 H, m, CH_2OH, CH_2OBn, and CHO), 4.1—4.4 (1 H, m, CHNH), 4.5 (2 H, s, $PhCH_2O$), 5.1 (3 H, br s, 2OH and NH), and 7.35 (5 H, m, Ph); δ_C 22.6, 51.4, 64.2, 70.4, 71.6, 73.8, 128.6, 129.2, 139.3, and 173.5.

threo-2-*Acetamido*-3,4-*diacetoxy*-1-*benzyloxybutane* (**3**).—To a solution of the diol (**18**) (2.5 g, 10 mmol) in pyridine (4 ml) was added acetic anhydride (3 ml) and the mixture was stirred for 24 h at room temperature. Excess of both pyridine and acetic anhydride was then removed under reduced pressure and the residue was chromatographed through silica gel using EtOAc as eluant to afford *compound* (**3**) (3.2 g, 95%) as a clear oil, $\nu_{max.}$ 3 300, 1 740, 1 555, and 1 535 cm^{-1}; δ_H 1.97 (3 H, s, CH_3CO), 2.0 (3 H, s, CH_3CO), 2.03 (3 H, s, CH_3CO), 3.55 (2 H, m, CH_2OBn), 4.2 (2 H, m, CH_2OAc), 4.5 (2 H, s, $PhCH_2O$), 4.5 (1 H, m, CHNH), 5.4 (1 H, m, CHOAc), 6.2 (1 H, d, *J* 10 Hz, NH), and 7.3 (5 H, m, Ph); δ_C 20.7, 20.8, 23.2, 48.7, 62.9, 69.3, 70.7, 73.4, 127.9, 128.5, 137.5, 169.9, and 170.2; *m/z* 337 (M^+, 3%), 262 (11), 250 (7), 246 (5), 188 (9), 170 (18), 114 (35), and 91 (100) (Found: C, 60.5; H, 6.85. $C_{17}H_{23}NO_6$ requires C, 60.52; H, 6.87%).

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