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Stereoselective Access to the Versatile 4-Aminohex-5-ene-1,2,3-triol Pattern

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We developed a stereocontrolled route allowing potential access to the eight isomers of 4-benzylaminohex-5-ene-1,2,3-triol in two or four steps and ca. 50% yield from readily available chiral nonracemic *cis*- or *trans*-α,*β*-epoxyimine precursors. A new $(NH_4)_2CO_3$-based carboxylation/intramolecular cyclization sequence allowed regio- and stereocontrolled C-3 epoxide opening while neat C-2 hydrolysis was ensured by simple aqueous acidic treatment.

Introduction

Aliphatic intermediates presenting the 4-amino-1,2,3-triol heading pattern have proven useful in the synthesis of various natural compounds, such as the linear amino acid portion of polyoxins[1] **1** and callipeltins[2] **2** (Figure 1).

This 4-amino-1,2,3-triol functional arrangement is also commonly encountered in synthetic precursors of nitrogenated heterocycles, accessible through 4- or 5-exo *tet* cyclization upon an activated hydroxyl group. Preparation of several azetidine,[3] pyrrolidine,[4] and indolizidines alkaloids[5] relies, for instance, on the use of such derivatives (Figure 2).

In the course of our ongoing research program directed toward iminosugars,[6] we developed a flexible and stereoselective approach to the 4-benzylaminohex-5-ene-1,2,3-triol intermediates in which the terminal vinyl group allows further oxidative manipulation toward various C_1- or C_2-oxygenated fragments and/or elongation by means of olefin metathesis. We wish to describe herein this work in details.

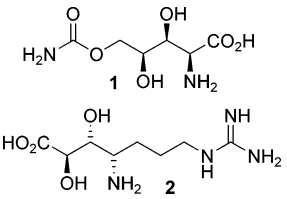

FIGURE 1. Amino acid moieties of polyoxines and callipeltins.

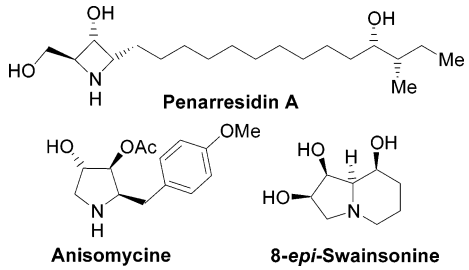

FIGURE 2. Alkaloids synthesized from a 4-amino-1,2,3-triol pattern-containing intermediate.

Results and Discussion

Our approach, starting from α,*β*-epoxyaldehydes of general structure **3**, was based on three key features: (1) optical series selection during the initial Sharpless epoxidation, (2) diastereocontrolled establishment of the C-4 amino group via Felkin−Anh type organometallic reagent addition to an intermediate α,*β*-epoxyimine, and (3) access to the four possible diastereoisomeric arrangements through a stereochemical manifold based on the combined choice of the C-2/C-3 epoxide opening site and the cis/trans epoxide geometry (the cis series giving rise to both 2,3-*syn* compounds and both 2,3-*anti* isomers coming from the trans series).[7]

Preparation of the starting *cis*- or *trans*-α,*β*-epoxyaldehydes (**3a** or **3b**) was readily accomplished from *cis*-but-2-ene-1,4-diol (in three steps and 78% yield or five steps and 67% yield, respectively) (not shown).[8] Noteworthy is the use of *o*-iodoxybenzoic acid (IBX) (1.5 equiv, standard grade DMSO, rt, 5 h) to accomplish oxidation

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(7) For matter of coherence the targeted aminotriol carbon numbering has been used throughout the article including for NMR peak assignments.

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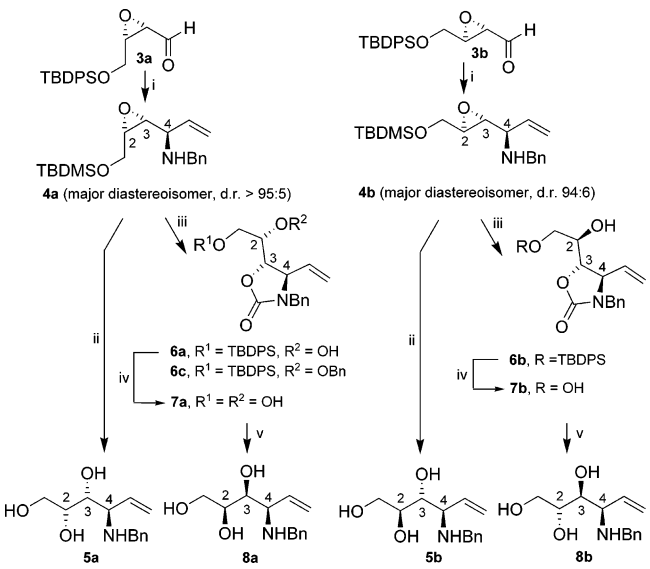
SCHEME 1[a]



[a] Reagents and conditions: (i) 1.0 equiv of $BnNH_2$, 30% w/w 4 Å MS, Et_2O, overnight, then 1.3 equiv of $Et_2O{\cdot}BF_3$, −78 to −40 °C, 5 min, then 1.7 equiv of $CH_2CHMgBr$ as a commercial 1.0 M solution in THF, −78°C, 2 h; *cis*-epoxide **4a**, 67% (dr >95:5); *trans*-epoxide **4b** (3,4-*anti*)**/4c** (3,4-*syn*), 70% (dr 94:6); (ii) 2.7 equiv of H_2SO_4 as a 3 M aqueous solution, *p*-dioxane, reflux, 5 h; 2,3-*syn* **5a** 70% from *cis*-epoxide; 2,3-*anti* **5b** 80% from *trans*-epoxide; (iii) 8 equiv of $(NH_4)_2CO_3$, THF/H_2O (4:1), rt, 8−20 h, 2,3-*syn* **6a** 94% from *cis*-epoxide; 2,3-*anti* **6b** 93% from *trans*-epoxide; (iv) 1.9 equiv of TBAF on silica gel (1.25 mmol F^-/g), THF, rt, overnight; 2,3-*syn* **7a** and 2,3-*anti* **7b** 85%; (v) 6 equiv of $LiOH{\cdot}H_2O$, *p*-dioxane/H_2O (3:1), reflux, 8 h; 2,3-*syn* **8a** and 2,3-*anti* **8b** 95%. TBDPS = *tert*-butyldiphenylsilyl.

steps in a very convenient and efficient manner (>90% isolated yield in essentially pure material).[9] Installation of the allylic amine was then inspired from Procter's Grignard reagent addition to $Et_2O{\cdot}BF_3$-chelated in situ generated *cis*-α,*β*-epoxyimines.[10] The adapted procedure involving the simple benzylamine-derived imine allowed production of the desired *cis*-epoxyamine **4a** as a single detectable isomer (67% yield from **3a**) (Scheme 1). To our satisfaction, this route was extended to the *trans*-α,*β*-epoxyaldehyde **3b** affording the corresponding adduct **4b/4c** with high selectivity (dr 94:6) and comparable efficiency (66% yield in major diastereoisomer **4b** to which the 3,4-*anti* configuration was attributed by analogy with the cis series). The main byproducts isolated were the aziridines resulting from an aza-Payne type rearrangement occurring under acidic catalysis during the course of the reaction or the purification.[11] The *anti*-epoxyamine relationship, initially attributed on the basis of Procter's work, was further confirmed by means of chemical filiation and X-ray crystallography in the *trans*-epoxide series (vide infra).

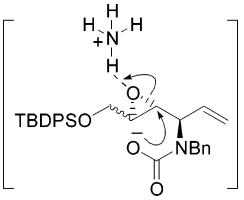


FIGURE 3. Proposed reaction intermediate for the carboxylation/intramolecular cyclization process.

Central to our approach was the regio- and diastereocontrolled opening of the oxirane moiety. Exclusive C-2 hydrolysis was accomplished by direct aqueous acidic treatment of the C-1 silylated *cis*- and *trans*-α,*β*-epoxyamines **4a** and **4b**. The resulting 2,3-*syn*-3,4-*anti* and *all-anti* aminotriols **5a** and **5b** were isolated in good yields (70 and 80%, respectively). No trace of other diastereoisomers was detected in the crude reaction mixtures (^1H NMR). Such site-selective opening could arise from the deactivation of the C-3 position by the adjacent protonated amino group.[12] Aminotriol **5a** was involved in a concise total synthesis of (−)-lentiginosine and a pyrrolizidinic analogue thereof.[6c]

Regiocontrolled C-3 opening relied on a carboxylation/intramolecular cyclization sequence using new conditions. Treatment of epoxyamines **4a** and **4b** by $(NH_4)_2CO_3$ in a THF/H_2O mixture at rt smoothly delivered oxazolidinones **6a** and **6b** respectively in excellent yields. From a mechanistic point of view, this transformation is believed to involve attack of the secondary amine onto the CO_2 slowly released by decomposition of the carbonate salt in the aqueous medium (Figure 3). Related formation of oxazolidinones from α,*β*-epoxyamine under CO_2 atmosphere (MeOH, rt) has been described.[13] The intermediate carbamic acid salt would then spontaneously cyclize into the oxazolidinone. Interestingly, the use of the ammonium cation revealed determinant for reaction progress, likely through electrophilic assistance of the oxirane opening. A study conducted with the desilylated derivative **7a** (vide infra) showed that, when $NaHCO_3$ or K_2CO_3 were used, the presence of a catalytic amount of pyridine was necessary to observe the desired carboxylation/intramolecular cyclization process.[14] It is worth emphasizing the experimental simplicity of this efficient and selective transformation.[15] Moreover, the identity of the *trans*-oxazolidinone in the *cis*-epoxide series was unambiguously determined by X-ray diffraction analysis of a single crystal of *ent*-**6a** and of the corresponding benzyl ether *ent*-**6c**, both derived from α,*β*-epoxyaldehyde *ent*-**3a** (see the Supporting Information). These X-ray structures allowed confirmation of the previously assigned relative and absolute configuration. If one assumes that this oxazolidinone arose from an S_N2 invert-

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(11) The proportion of rearranged product was found to depend on the aging of the opened commercial vinyl Grignard solution. For the same reason prolonged contact with silica gel should also be avoided.

(12) Bordwell, F. G.; Brannen Jr, W. T. *J. Am. Chem. Soc.* **1964**, *86*, 4645−4650.

(13) Karikomi, M.; Yamazaki, T.; Toda, T. *Chem. Lett.* **1993**, 1965−1968.

(14) Participation of a pyridinium species in place of the ammonium cation might explain this observation.

(15) Similar reaction sequence has been achieved using the uncommon carbonate form of Amberlyst A-26 resin. Although it involved a reactive primary amine, this process was reported to be somewhat slower than ours (48 h at room temperature): Wood, J. L.; Jones, D. R.; Hirschmann, R.; Smith, A. M., III. *Tetrahedron Lett.* **1990**, *31*, 6329−6330.

ing process, its trans arrangement is in agreement with the proposed anti arrangement in the starting epoxyamine. Both oxazolidinones **6a** and **6b**, presenting three differentiated alcohol functions, constitute an interesting platform for further synthetic developments.

The targeted aminotriols were finally prepared from intermediates **6a** and **6b** by hydroxyl group desilylation, delivering primary alcohols **7a** and **7b** in 85% yield, followed by cyclic carbamate basic hydrolysis (95% yield). That way, the *all-syn* derivative **8a** and the 2,3-*anti*-3,4-*anti* isomer **8b** were readily obtained from the corresponding oxazolidinones in good overall yield. Access to derivative **6a** already allowed a total synthesis of 1,4-dideoxy-1,4-imino-glucitol.[6a]

Conclusion

In summary, we developed a stereocontrolled route offering potential access to the eight isomers of the 4-benzylaminohex-5-ene-1,2,3-triol in two or four steps (ca. 50% yield in both cases) from readily available chiral nonracemic *cis*- or *trans*-α,*β*-epoxyimine precursors. Noteworthy is the use of a practical and efficient carboxylation/intramolecular cyclization sequence involving the trivial $(NH_4)_2CO_3$ salt as reagent. Synthetic work further exemplifying the versatility of these highly substituted synthetic intermediates will be reported in due course.

Experimental Section

Compound 4a. Benzylamine (687 μL, 5.88 mmol) was added dropwise to a solution of α,*β*-*cis*-epoxyaldehyde **3a** (2.00 g, 5.88 mmol) in freshly distilled Et_2O (40 mL) containing powder activated 4 Å molecular sieves (30% w/w). The resulting mixture was vigorously stirred at room temperature until no starting material could be detected by IR analysis (ca. 3 h, disappearance of C=O bond 1729 cm^{-1} and appearance of C=N bond 1663 cm^{-1}). The solution was then cooled to −78 °C, and freshly distilled $BF_3{\cdot}Et_2O$ (950 μL, 7.64 mmol) was added dropwise at this temperature. The mixture was allowed to stir at −40 °C for 5 min before being cooled again to −78 °C. Vinylmagnesium bromide in THF (10.00 mL of a 1 M commercial solution, 10.00 mmol) was then added dropwise over 5 min, and the mixture was vigorously stirred at −78 °C for 2 h. The reaction was quenched by portionwise addition of a THF/saturated aqueous NH_4Cl mixture (20:80, 20 mL) over 1 h 30 at −78 °C with vigorous stirring before being allowed to warm to room temperature. The mixture was then filtered through Celite, and the solvents were evaporated off under reduced pressure. The resulting suspension was extracted with Et_2O (3 × 100 mL), and the combined extracts were successively washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The pale yellow oil thus obtained was first filtered through a plug of silica gel eluting with petroleum ether/EtOAc (90:10) to remove magnesium salt. Concentration of the filtrate to dryness under reduce pressure gave a crude product that was then purified by medium-pressure column chromatography on silica gel treated with 2.5% v/v Et_3N eluting with petroleum ether/EtOAc (gradient 95:5 to 80:20) to afford epoxyamine **4a** (1.8 g, 3.94 mmol, 67% yield): R_f = 0.21 (petroleum ether/EtOAc 87:12 under a saturated atmosphere of NH_4OH); $[\alpha]^{25}_D$ +6.5 (*c* 1.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.72−7.62 (m, 4H, Ph), 7.50−7.35 (m, 6H, Ph), 7.30−7.20 (m, 5H, Ph), 5.88 (ddd, $^3J_{H5H4}$ = 7.5 Hz, $^3J_{H5H6}$ = 10.3 Hz, and $^3J_{H5H6'}$ = 17.4 Hz, 1H, H-5), 5.31 (brd, $^3J_{H6H5}$ = 10.3 Hz, 1H, H-6), 5.27 (brd, $^3J_{H6'H5}$ = 17.2 Hz, 1H, H-6′), 3.83−3.80 (m, 2H, 2 × H-1), 3.76 (AB of an ABX, $^2J_{gem}$ = 13.4 Hz, Δ*δ*a−*δ*b = 62.9 Hz, 2H, NC*H*$_2$-Ph), 3.24−3.19 (m, 1H, H-4), 3.07 (dd, $^3J_{H3H4}$ = 3.93 Hz and $^3J_{H3H2}$ = 8.0 Hz, 1H, H-3), 3.00 (pseudot, $^3J_{H2H1}$ = $^3J_{H2H3}$ = 8.0 Hz, 1H, H-2), 1.07 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 140.00 (Cquat arom), 137.6 (C-5), 135.7, 135.6 (CH arom), 133.3, 133.1 (Cquat arom), 129.9, 128.4, 128.1, 127.9, 127.8, 127.0 (CH arom), 118.2 (C-6), 62.0 (C-1), 59.0 (C-4), 58.8 (C-3), 56.9 (C-2), 50.9 (N*C*H$_2$Ph), 26.9 (*C*H$_3$), 19.2 (*C*(CH$_3$)$_3$); IR (thin film) 3154 (N−H), 1633 (C=C), 1108 (C−O) cm^{-1} ; MS (DCI/NH_3) *m/z* 458 (MH^+, 100); HRMS (DCI/NH_3) *m/z* calcd for $C_{29}H_{36}NO_2Si$ 458.2515, found 458.2512.

Compound 4b. *trans*-α,*β*-Epoxyamine **4b** (2.22 g, 4.85 mmol, 66% yield) was prepared from α,*β*-*trans*-epoxyaldehyde **3b** (2.5 g, 7.35 mmol) using the procedure described for the preparation of compound **4a**: R_f = 0.24 (petroleum ether/EtOAc 90:10 under a saturated atmosphere of NH_4OH); $[\alpha]^{25}_D$ −0.6 (*c* = 1.94, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.80−7.70 (m, 5H, Ph), 7.50−7.28 (m, 10H, Ph), 5.81 (ddd, $^3J_{H5H4}$ = 7.8 Hz, $^3J_{H5H6'}$ = 10.2 Hz, and $^3J_{H5H6}$ = 17.3 Hz, 1H, H-5), 5.36 (brd, $^3J_{H6H5}$ = 17.3 Hz, 1H, H-6), 5.34 (brd, $^3J_{H6'H5}$ = 10.2 Hz, 1H, H-6′), 3.85 (AB_q, $^2J_{gem}$ = 13.3 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 57.0 Hz), 3.83 (AB of ABX, $^3J_{H1H2}$ = 3.5 Hz, $^3J_{H1'H2}$ = 4.6 Hz, and $^2J_{gem}$ = 11.8 Hz, 2H, 2 × H-1, Δ*δ*a-*δ*b = 33.0 Hz), 3.30 (dd, $^3J_{H4H3}$ = 4.8 Hz and $^3J_{H4H5}$ = 7.8 Hz, 1H, H-4), 3.26−3.22 (m, 1H, H-2), 3.04 (dd, $^3J_{H3H2}$ = 2.2 Hz and $^3J_{H3H4}$ = 4.8 Hz, 1H, H-3), 1.85−1.77 (m, 1H, N-*H*), 1.14 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 140.4 (Cquat arom), 137.0 (C-5), 135.8 (CH arom), 133.5 (Cquat arom), 130.0, 128.7, 128.4, 128.0, 127.2 (CH arom), 118.7 (C-6), 64.0 (C-1), 60.7 (C-4), 58.0 (C-3), 56.4 (C-2), 51.3 (N*C*H$_2$Ph), 27.1 (*C*H$_3$), 19.5 (*C*(CH$_3$)$_3$); IR (thin film) 2931 (N−H), 1588 (C=C), 1110 (C−O) cm^{-1}; MS (DCI/NH_3) *m/z* 458 (MH^+, 100); HRMS (DCI/NH_3) *m/z* calcd for $C_{29}H_{36}NO_2Si$ 458.2515, found 458.2514.

Compound 4c. In the course of the preparation of **4b** the 3,4-*syn* minor diastereoisomer **4c** was also isolated in 4% yield: R_f = 0.22 (petroleum ether/EtOAc 90:10 under a saturated atmosphere of NH_4OH); $[\alpha]^{25}_D$ −0.6 (*c* = 1.94, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.80−7.65 (m, 5H, Ph), 7.30−6.80 (m, 10H, Ph), 5.89−5.79 (m, 1H, H-5), 5,34−5,28 (m, 2H, 2 × H-6), 3.86 (AB_q, $^2J_{gem}$ = 13.3 Hz, 2H, NC*H*$_2$Ph) Δ*δ*a−*δ*b = 47.9 Hz, 3.82 (AB of ABX, $^3J_{H1H2}$ = 3.4 Hz, $^3J_{H1'H2}$ = 4.6 Hz, $^2J_{gem}$ = 11.9 Hz, 2H, 2 × H-1) Δ*δ*a−*δ*b = 38.5 Hz, 3.14 (m, 1H, H-2), 3.04−3.00 (m, 2H, H-3, H-4), 2.10−1.85 (m, 1H, N-*H*), 1.10 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 140.3 (Cquat arom), 136.5 (C-5), 135.8 (CH arom), 133.5 (Cquat arom), 130.0, 128.7, 128.4, 128.0, 127.2 (CH arom), 118.3 (C-6), 63.1 (C-1), 62.6 (C-4), 58.8 (C-3), 56.7 (C-2), 51.3 (N*C*H$_2$-Ph), 27.0 (*C*H$_3$), 19.5 (*C*(CH$_3$)$_3$); IR (thin film) 2931 (N−H), 1660 (C=C), 1110 (C−O) cm^{-1}; MS (DCI/NH_3) *m/z* 458 (MH^+, 100); HRMS (DCI/NH_3) *m/z* calcd for $C_{29}H_{36}NO_2$ Si 458.2515, found 458.2512.

Compound 5a. A 3 M aqueous H_2SO_4 solution (2.91 mL, 8.72 mmol) was added to a solution of *cis*-α,*β*-epoxyamine **4a** (500 mg, 1.09 mmol) in *p*-dioxane (10 mL). The mixture was refluxed for 5 h and allowed to cool before neutralization with a 3 M aqueous NaOH solution (6 mL, 18.00 mmol) followed by solid $NaHCO_3$. *p*-Dioxane was then evaporated off under reduced pressure and the resulting aqueous phase extracted with CH_2Cl_2 (3 × 100 mL) and with EtOAc (2 × 50 mL). The combined organic phases were successively washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on deactivated silica gel (treated with 2.5% v/v Et_3N) eluting with EtOAc/Et_2O/MeOH (gradient 85:10:5 to 75:10:15) to afford aminotriol **5a** (180 mg, 0.76 mmol, 70% yield): R_f = 0.17 (EtOAc/Et_2O/MeOH, 80:10:10 under a saturated atmosphere of NH_4OH); $[\alpha]^{25}_D$ +1.0 (*c* 6.00, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) *δ* 7.38−7.25 (m, 5H, Ph), 5.87−5.77 (m, 1H, H-5), 5.36 (brd, $^3J_{H6H5}$ = 11.9 Hz, 1H, H-6), 5.32 (brd, $^3J_{H6'H5}$ = 18.1 Hz, 1H, H-6′), 3.85−3.82 (m, 1H, H-1), 3.81−3.78 (m, 1H, H-1′), 3.76 (m, 1H, H-2), 3.75−3.72 (m, 1H, H-3), 3.73 (AB_q, $^2J_{gem}$ = 13.0 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 112.2 Hz), 3.49 (brdd, $^3J_{H4H3}$ = 4.8 Hz and $^3J_{H4H5}$ = 8.4 Hz, 1H, H-4); ^{13}C NMR (63 MHz, $CDCl_3$) *δ* 139.5 (Cquat arom), 136.4 (C-5),

128.7, 128.5, 127.4 (CH arom), 119.8 (C-6), 75.1 (C-3), 70.8 (C-2), 65.4 (C-1), 64.3 (C-4), 51.2 (N*C*H$_2$Ph); IR (thin film) 3421 (O−H), 1636 (C=C), 1060 (C−O) cm^{-1}; MS (DCI/NH$_3$) *m/z* 238 (MH$^+$, 100); HRMS (DCI/NH$_3$) *m/z* calcd for $C_{13}H_{20}NO_3$ 238.1443, found 238.1446.

Compound 5b. By applying to *trans*-α,*β*-epoxyamine **4b** (400 mg, 0.87 mmol) the procedure described for the preparation of compound **5a,** aminotriol **5b** was obtained (165 mg, 0.70 mmol, 80% yield): R_f = 0.18 (EtOAc/Et$_2$O/MeOH, 80:10:10 under a saturated atmosphere of NH$_4$OH); $[\alpha]^{25}_D$ −11.9 (*c* 0.80, CH$_3$OH); ^{1}H NMR (400 MHz, CD$_3$OD /D$_2$O) *δ* 7.40−7.20 (m, 5H, Ph), 5.80 (ddd, $^3J_{H5H4}$ = 8.9 Hz, $^3J_{H5H6}$ = 10.3 Hz, and $^3J_{H5H6'}$ = 17.2 Hz, 1H, H-5), 5.38 (dd, $^2J_{gem}$ = 1.9 Hz and $^3J_{H6H5}$ = 10.2 Hz, 1H, H-6), 5.28 (ddd, $^4J_{H6'H4}$ = 0.6 Hz, $^2J_{gem}$ = 1.9 Hz, and $^3J_{H6'H5}$ = 17.3 Hz, 1H, H-6′), 3.76 (AB$_q$, $^2J_{gem}$ = 12.9 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 86.6 Hz), 3.75 (dd, $^3J_{H1H2}$ = 3.6 Hz and $^2J_{gem}$ = 11.4 Hz, 1H, H-1), 3.61 (dd, $^3J_{H3H2}$ = 3.0 Hz and $^3J_{H3H4}$ = 5.0 Hz, 1H, H-3), 3.60 (dd, $^3J_{H1'H2}$ = 5.2 Hz and $^2J_{gem}$ = 11.4 Hz, 1H, H-1′), 3.57−3.51 (m, 1H, H-2), 3.38 (brdd, $^3J_{H4H3}$ = 5.0 Hz and $^3J_{H4H5}$ = 8.9 Hz, 1H, H-4); ^{13}C NMR (100 MHz, CD$_3$OD /D$_2$O) *δ* 139.1 (Cquat arom), 135.5 (C-5), 128.5, 128.4, 127.1 (CH arom), 118.9 (C-6), 73.5 (C-3), 72.3 (C-2), 63.6 (C-4), 63.4 (C-1), 50.3 (N*C*H$_2$Ph); IR (thin film) 3365 (O−H), 1661 (C=C), 1025 (C−O); MS (DCI/NH$_3$) *m/z* 238 (MH$^+$, 100); HRMS (DCI/NH$_3$) *m/z* calcd for $C_{13}H_{19}NO_3$ 238.1443, found 238.1443.

Compound 6a. To a solution of *cis*-α,*β*-epoxyamine **4a** (400 mg, 0.87 mmol) in THF/water 4:1 (20 mL) was added (NH$_4$)$_2$CO$_3$ (670 mg, 7.00 mmol), and the heterogeneous mixture was vigorously stirred at room temperature until TLC analysis showed no remaining starting material (ca. 20 h). The THF was then evaporated off under reduced pressure and the resulting aqueous phase extracted with Et$_2$O (3 × 50 mL). The combined organic phases were successively washed with water and brine, dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel eluting with petroleum ether/EtOAc (80:20) to afford oxazolidinone **6a** (410 mg, 0.82 mmol, 94% yield): R_f = 0.25 (petroleum ether/EtOAc 80:20); $[\alpha]^{25}_D$ +30.2 (*c* 1.06, CHCl$_3$); ^{1}H NMR (250 MHz, CDCl$_3$) *δ* 7.63−7.59 (m, 5H, Ph), 7.43−7.26 (m, 10H, Ph), 5.67 (ddd, $^3J_{H5H4}$ = 8.9 Hz, $^3J_{H5H6}$ = 9.9 Hz, and $^3J_{H5H6'}$ = 16.8 Hz, 1H, H-5), 5.33 (d, $^3J_{H6H5}$ = 9.3 Hz, 1H, H-6), 5.22 (d, $^3J_{H6'H5}$ = 16.8 Hz, 1H, H-6′), 4.39 (AB$_q$, $^2J_{gem}$ = 15.1 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 181.0 Hz), 4.25 (dd, $^3J_{H3H2}$ = 2.3 Hz and $^3J_{H3H4}$ = 7.1 Hz, 1H, H-3), 4.05 (dd, $^3J_{H4H3}$ = 6.9 Hz and $^3J_{H4H5}$ = 9.1 Hz, 1H, H-4), 3.82−3.55 (m, 3H, 2 × H-1 and H-2), 2.39−2.21 (m, 1H, O−H), 1.04 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (63 MHz, CDCl$_3$) *δ* 157.5 (C=O), 135.6 (Cquat arom), 135.6 (C-5), 135.5 (CH arom), 134.6 (Cquat arom), 132.9, 132.8 (Cquat arom), 130.0, 128.7, 128.3, 127.9 (CH arom), 122.9 (C-6), 78.0 (C-3), 70.8 (C-2), 64.1 (C-1), 60.0 (C-4), 46.0 (N*C*H$_2$Ph), 27.0 (*C*H$_3$), 19.2 (*C*(CH$_3$)$_3$); IR (thin film) 3405 (O−H), 1726 (C=O), 1635 (C=C), 1064 (C−O) cm^{-1}; MS (DCI/NH$_3$) *m/z* 519 (MNH$_4^+$, 100); HRMS (DCI/NH$_3$) *m/z* calcd for $C_{30}H_{36}NO_4Si$ 502.2414, found 502.2415.

Compound 6b. Oxazolidinone **6b** (508 mg, 1.01 mmol, 93% yield) was prepared from *trans*-α,*β*-epoxyamine **4b** (500 mg, 1.09 mmol) using the procedure described for the preparation of compound **6a**: R_f = 0.23 (petroleum ether/EtOAc 88:12); $[\alpha]^{25}_D$ +38.8 (*c* 1.19, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.70−7.60 (m, 5H, Ph), 7.50−7.20 (m, 10H, Ph), 5.74 (ddd, $^3J_{H5H4}$ = 8.8 Hz, $^3J_{H5H6}$ = 10.0 Hz, and $^3J_{H5H6'}$ = 17.1 Hz, 1H, H-5), 5.34 (1H, d, $^3J_{H6H5}$ = 10.0 Hz, H-6), 5.24 (d, $^3J_{H6'H5}$ = 17.0 Hz, 1H, H-6′), 4.41 (AB$_q$, $^2J_{gem}$ = 15.1 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 314.8 Hz), 4.27 (pseudot, $^3J_{H3H2}$ = $^3J_{H3H4}$ = 5.8 Hz, 1H, H-3), 4.12 (dd, $^3J_{H4H3}$ = 5.7 Hz and $^3J_{H4H5}$ = 8.6 Hz, 1H, H-4), 3.85−3.69 (m, 3H, 2 × H-1 and H-2), 2.71 (d, $^3J_{OH-H2}$ = 4.7 Hz, 1H, O-*H*), 1.08 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 157.5 (C=O), 135.9 (Cquat arom), 135.7 (CH arom), 135.3 (C-5), 132.9, 132.8 (Cquat arom), 130.2, 128.9, 128.5, 128.2, 128.1, 128.0 (CH arom), 121.2 (C-6), 78.3 (C-3), 71.9 (C-2), 63.6 (C-1), 59.7 (C-4), 45.9 (N*C*H$_2$Ph), 27.1 (*C*H$_3$), 19.5 (*C*(CH$_3$)$_3$); IR (thin film) 3421 (O−H), 1741 (C=O), 1638 (C=C), 1109 (C−O) cm^{-1}; MS (DCI/NH$_3$) *m/z* 519 (MNH$_4^+$, 100); HRMS (DCI/NH$_3$) *m/z* calcd for $C_{30}H_{37}NO_4Si$ 502.2414, found 502.2411

Compound 7a. TBAF on silica gel (0.89 g at ca. 1.25 mole of fluoride/g, ca. 0.71 mmol) was added to a solution of silyl ether **6a** (300 mg, 0.59 mmol) in anhydrous THF (20 mL). The reaction mixture was vigorously stirred until TLC analysis showed no remaining starting material (ca. 20 h) and then filtered. Silica gel was rinsed several times with ethyl acetate (3 × 70 mL), and the combined filtrates were concentrated in vacuo. The resulting crude product was purified by flash column chromatography on silica gel eluting with CH$_2$Cl$_2$/MeOH (gradient 100:0 to 95:5) to afford primary alcohol **7a** (133 mg, 0.51 mmol, 85% yield): R_f = 0.20 (CH$_2$Cl$_2$/MeOH 95:5); $[\alpha]^{25}_D$ +71.6 (*c* 0.55, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.27−7.18 (m, 5H, Ph), 5.61 (ddd, $^3J_{H5H4}$ = 8.9 Hz, $^3J_{H5H6}$ = 9.9 Hz, and $^3J_{H5H6'}$ = 16.9 Hz, 1H, H-5), 5.27 (d, $^3J_{H6H5}$ = 10.0 Hz, 1H, H-6), 5.20 (d, $^3J_{H6'H5}$ = 17.0 Hz, 1H, H-6′), 4.32 (AB$_q$, $^2J_{gem}$ = 15.3 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 245.5 Hz), 4.17 (dd, $^3J_{H3H2}$ = 2.6 Hz and $^3J_{H3H4}$ = 7.1 Hz, 1H, H-3), 4.05 (dd, $^3J_{H4H3}$ = 7.1 Hz and $^3J_{H4H5}$ = 8.9 Hz, 1H, H-4), 3.69−3.56 (m, 4H, 2 × H-1, H-2 and O-*H*); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 158.1 (C=O), 135.6 (Cquat arom), 134.5 (C-5), 128.8, 128.3, 127.9 (CH arom), 122.2 (C-6), 79.4 (C-3), 71.1 (C-2), 63.2 (C-1), 60.5 (C-4), 46.1 (N*C*H$_2$Ph); IR (thin film) 3346 (O−H), 1729 (C=O), 1440 (C=C), 1079 (C−O) cm^{-1} ; MS (DCI/NH$_3$) *m/z* 281 (MNH$_4^+$, 100); HRMS (DCI/NH$_3$) *m/z* calcd for $C_{14}H_{18}NO_4$ 264.1236, found 264.1235

Compound 7b. By applying to silyl ether **6b** (452 mg, 0.90 mmol) the procedure described for the preparation of compound **7a,** alcohol **7b** (210 mg, 0.80 mmol, 85% yield) was obtained: R_f = 0.22 (CH$_2$Cl$_2$/MeOH 95:5); $[\alpha]^{25}_D$ +82.0 (*c* 1.22, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$/D$_2$O) *δ* 7.40−7.20 (m, 5H, Ph), 5.69 (ddd, $^3J_{H5H4}$ = 8.8 Hz, $^3J_{H5H6}$ = 10.0 Hz, and $^3J_{H5H6'}$ = 17.0 Hz, 1H, H-5), 5.32 (d, $^3J_{H6H5}$ = 10.0 Hz, 1H, H-6), 5.26 (d, $^3J_{H6'H5}$ = 17.0 Hz, 1H, H-6′), 4.36 (AB$_q$, $^2J_{gem}$ = 15.2 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 290.1 Hz), 4.19 (pseudot, $^3J_{H3H2}$ = $^3J_{H3H4}$ = 5.6 Hz, 1H, H-3), 4.11 (dd, $^3J_{H4H3}$ = 5.9 Hz and $^3J_{H4H5}$ = 8.6 Hz, 1H, H-4), 3.84−3.78 (m, 1H, H-2), 3.63−3.52 (m, 2H, 2 × H-1); ^{13}C NMR (100 MHz, CDCl$_3$/D$_2$O) *δ* 158.0 (C=O), 135.7 (Cquat arom), 135.0 (C-5), 129.0, 128.4, 128.1 (CH arom), 121.6 (C-6), 80.0 (C-3), 71.9 (C-2), 62.2 (C-1), 59.7 (C-4), 46.0 (N*C*H$_2$-Ph); IR (thin film) 3429 (O−H), 1723 (C=O), 1634 (C=C), 1060 (C−O) cm^{-1} ; MS (DCI/NH$_3$) *m/z* 281 (MNH$_4^+$, 100); HRMS (DCI/NH$_3$) *m/z* calcd for $C_{14}H_{18}NO_4$ 264.1236, found 264.1239.

Compound 8a. LiOH·H$_2$O (485 mg, 11.4 mmol) was added to a solution of oxazolidinone **7a** (500 mg, 1.90 mmol) in *p*-dioxane/water 3:1 (20 mL). The mixture was refluxed until TLC showed no remaining starting material (ca. 8 h) and allowed to cool before neutralization by solid NaHCO$_3$. *p*-Dioxane was then evaporated off under reduced pressure and the resulting aqueous phase extracted with CH$_2$Cl$_2$ (3 × 70 mL) and with EtOAc (2 × 50 mL). The combined organic phases were successively washed with water and brine, dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on deactivated silica gel (treated with 2.5% v/v Et$_3$N) eluting with EtOAc/Et$_2$O/MeOH (90:10:0 to 75:10:15) to afford aminotriol **8a** (428 mg, 1.81 mmol, 95% yield): R_f = 0.22 (EtOAc/Et$_2$O/MeOH, 85:10:5 under a saturated atmosphere of NH$_4$OH); $[\alpha]^{25}_D$ −20.0 (*c* 2.75, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$/D$_2$O) *δ* 7.40−7.24 (m, 5H, Ph), 5.79 (ddd, $^3J_{H5H4}$ = 8.5 Hz, $^3J_{H5H6}$ = 10.3 Hz and $^3J_{H5H6'}$ = 17.2 Hz, 1H, H-5), 5.35 (ddd, $^4J_{H6H4}$ = 0.5 Hz, $^2J_{gem}$ = 1.5 Hz and $^3J_{H6H5}$ = 10.3 Hz, 1H, H-6), 5.24 (ddd, $^4J_{H6'H4}$ = 0.8 Hz, $^2J_{gem}$ = 1.5 Hz, and $^3J_{H6'H5}$ = 17.2 Hz,1H, H-6′), 3.75 (AB$_q$, $^2J_{gem}$ = 12.8 Hz, 2H, NC*H*$_2$Ph, Δ*δ*a−*δ*b = 107.7 Hz), 3.75−3.73 (m, 2H, 2 × H-1), 3.72 (dd, $^3J_{H2H3}$ = 1.3 Hz and $^3J_{H2H1}$ = 3.3 Hz, 1H, H-2), 3.62 (dd, $^3J_{H3H2}$ = 1.3 Hz and $^3J_{H3H4}$ = 4.7 Hz, 1H, H-3), 3.22 (dd, $^3J_{H4H3}$ = 4.7 Hz and $^3J_{H4H5}$ = 8.5 Hz, 1H, H-4); ^{13}C NMR (100 MHz, CDCl$_3$/D$_2$O) *δ* 139.2 (Cquat arom), 136.3 (C-5), 128.8, 128.6, 127.6 (CH arom), 118.9 (C-6), 74.1 (C-3), 72.4 (C-2), 65.4

(C-1), 63.7 (C-4), 50.5 (N*C*H_2Ph); IR (thin film) 3453 (O−H), 1638 (C=C), 1066 (C−O) cm^{-1} ; MS (DCI/NH_3) *m/z* 238 (MH^+, 100); HRMS (DCI/NH_3) *m/z* calcd for $C_{13}H_{19}NO_3$ 238.1443, found 238.1449.

Compound 8b. Aminotriol **8b** (214 mg, 0.90 mmol, 95% yield) was prepared from oxazolidinone **7b** (250 mg, 0.95 mmol) using the procedure described for the preparation of compound **8a**: R_f = 0.22 (EtOAc/Et_2O/MeOH 80:10:10 under a saturated atmosphere of NH_4OH); $[\alpha]^{25}_D$ −5.8 (*c* 1.38, CH_3OH); ^{1}H NMR (400 MHz, $CDCl_3/D_2O$) δ 7.35−7.15 (m, 5H, Ph), 5.75 (ddd, $^3J_{H5H4}$ = 8.7 Hz, $^3J_{H5H6}$ = 10.2 Hz, and $^3J_{H5H6'}$ = 17.2 Hz, 1H, H-5), 5.27 (dd, $^2J_{gem}$ = 1.4 Hz and $^3J_{H6H5}$ = 10.3 Hz, 1H, H-6), 5.18 (d, $^3J_{H6'H5}$ = 17.2 Hz, 1H, H-6′), 3.65 (AB_q, $^2J_{gem}$ = 12.7 Hz, 2H, NCH_2Ph, $\Delta\delta a-\delta b$ = 108.9 Hz), 3.68−3.50 (m, 4H, 2 × H-1, H-2 and H-3), 3.15 (dd, $^3J_{H4H3}$ = 4.9 Hz and $^3J_{H4H5}$ = 8.7 Hz, 1H, H-4); ^{13}C NMR (100 MHz, $CDCl_3/D_2O$) δ 139.1 (Cquat arom), 136.4 (C-5), 128.7, 128.6, 127.5 (CH arom), 119.2 (C-6), 73.7 (C-3), 73.5 (C-2), 62.8 (C-4), 62.7 (C-1), 50.6 (N*C*H_2-Ph); IR (thin film) 3426 (O−H), 2920 (N−H), 1637 (C=C), 1061 (C−O); (DCI/NH_3) *m/z* 238 (MH^+, 100); HRMS (DCI/NH_3) *m/z* calcd for $C_{13}H_{20}NO_3$ 238.1443, found 238.1444.

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Supporting Information Available: General experimental methods. X-ray structure of the *trans*-oxazolidinone *ent*-**6a**. CIFs for compounds *ent*-**6a** and *ent*-**6c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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