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Stereoselective Syntheses of Aza, Amino and Imino Sugar Derivatives by Hydroboration of 3,6-Dihydro-2*H*-1,2-oxazines as Key Reaction

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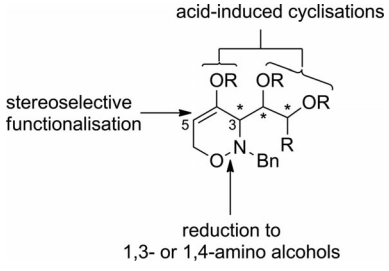
Starting from enantiopure 3,6-dihydro-2*H*-1,2-oxazines *syn*-**1** we introduced an additional hydroxy group in a stereoselective fashion by a standard hydroboration/oxidation protocol. Under "regular" conditions substrate control was sufficient to achieve a very high degree of stereoselectivity. However, a diastereomeric product was isolated when a partially "degraded" borane reagent was used. We could synthesise this new diastereomer on purpose by addition of alcohols to the "fresh" hydroboration reagent. The level of stereoinduction increased with the steric bulk of the added alcohol: MeOH < *n*BuOH < *i*PrOH < *t*BuOH. After a two-step oxidation/reduction sequence, another 5-hydroxy-1,2-oxazine epimer was accessible. The obtained 5-hydroxy-1,2-oxazine diastereomers **2** were used as versatile intermediates in a series of transformations leading to several amino polyol derivatives. Complete deprotection of both diastereomers without cleavage of the N–O bond led to the novel polyhydroxylated tetrahydro-2*H*-1,2-oxazines **3** and *epi*-**3**. By change of the deprotection conditions the open-chain amino polyol **4** with D-iditol configuration became accessible. In an alternative sequence 5-hydroxy-1,2-oxazines were utilised to synthesise imino sugars (polyhydroxylated pyrrolidines). Samarium diiodide induced cleavage of the 1,2-oxazine N–O bond furnished 1,4-amino alcohols, which were cyclised to give the corresponding pyrrolidine derivatives after activation by mesyl chloride. This sequence either led to a 3-methoxy-substituted trihydroxylated pyrrolidine derivative or to the related fully deprotected compound.

Introduction

Since our first synthesis of 3,6-dihydro-2*H*-1,2-oxazines utilising lithiated alkoxyallenes and carbohydrate-derived nitrones in a stepwise [3+3] cyclisation process[1] we are exploring the synthetic potential of this versatile class of compounds and still discover interesting and useful transformations. These 1,2-oxazines exhibit three characteristic reactive sites (Scheme 1): first, the N–O bond, which is susceptible to reductive ring opening processes leading to acyclic 1,3- and 1,4-amino alcohols as precursors for azetidine[2] or pyrrolidine derivatives;[3] second, the *O*-substituted side chain at C-3 proved to be essential in (Lewis) acid mediated interactions with the enol ether moiety furnishing a variety of heterocyclic skeletons, e.g. furans,[4] pyrans,[5] oxepanes;[6] finally, the double bond can also be exploited by reaction with external reagents for cyclopropanation[7] or bromination.[8] The stereochemical outcome of these processes is strongly influenced by the configuration of the existing stereogenic centre at C-3. An additional method to functionalise the double bond of 1,2-oxazines is the hydroboration. Since its discovery by Brown[9] a great variety of borane reagents were developed for this purpose addressing the needs for substrate-specific optimisation, regioselectivity issues or asymmetric syntheses,[10] 9-BBN[11] or Ipc_2BH[12] being some of the most notable among these.



Scheme 1. Reactive sites of 3,6-dihydro-2*H*-1,2-oxazines.

After the hydroboration, the newly generated organoboron species often exhibits a higher degree of stability compared to other organometallic compounds and gives entry to numerous functionalisation options at the negatively polarised carbon atom.[13] In particular, oxidative workup in the presence of hydrogen peroxide proved to be a reliable method to introduce a hydroxy group. Alkoxyboranes are regarded as weaker hydroborating agents mainly because of the diminished hydride character of the hydrogen atom. Even though there are examples for effective hydroborations with this class of compounds the substrate

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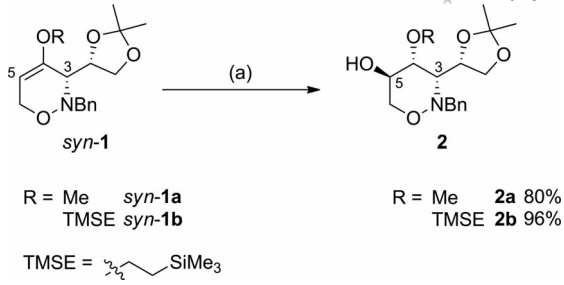
scope is rather limited compared to the typically used reagents, and more forcing conditions or catalytic activation are needed.[14] In this report we will supplement our earlier studies towards the hydroboration of 1,2-oxazines.[2,15] We demonstrate that the presence of alkoxyboranes can play a crucial role for the stereoselectivity of hydroboration reactions, although they are presumably not the active hydroborating species. Furthermore, we will present new short and efficient routes to polyhydroxylated 1,2-oxazines as well as to their analogous open-chain amino sugar derivatives. We complete the overview of accessible amino polyols by presenting the syntheses of pyrrolidine derivatives. All approaches to these target compounds depend on the stereoselective hydroboration of 1,2-oxazines.

Results and Discussion

Hydroboration Experiments

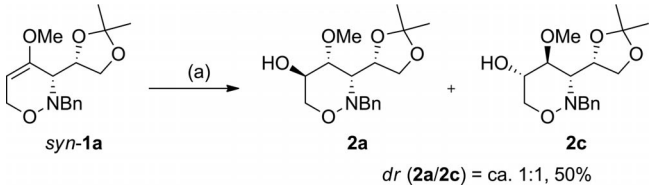
Our approach towards the syntheses of amino polyols utilises 3,6-dihydro-2*H*-1,2-oxazines as enantiopure precursors, which are readily accessible through stereoselective [3+3] cyclisation of in situ generated lithiated alkoxyallenes and chiral-pool-derived nitrones.[1] Precursors *syn*-**1a** and *syn*-**1b** were chosen to start off the respective synthetic routes allowing for the preparation of either fully deprotected amino polyols or their derivatives bearing one methoxy group. In order to install an oxygen substituent at C-5 of the 1,2-oxazine core hydroboration of the incorporated enol ether double bond followed by oxidative workup in the presence of hydrogen peroxide was an obvious choice. Treatment of 1,2-oxazines *syn*-**1a** and *syn*-**1b** with 4 equiv. of borane–THF complex and subsequent oxidation and hydrolysis of the respective organoboranes gave entry to 5-hydroxylated compound **2a** in 80% yield and to **2b** in 96% yield (Scheme 2). As expected for a substrate with an electron-rich double bond[16] excellent regio- and stereoselectivity were observed in both cases, forming the *trans*-4-alkoxy-5-hydroxy-1,2-oxazine derivatives. Substrate-induced stereoselectivity was controlled by the configuration of the stereogenic centre C-3, which led exclusively to 1,2-oxazine diastereomers **2** (Scheme 2). The relative configuration was confirmed by NOESY-NMR analyses.[15] As expected, the borane reagent attacks the C-4/C-5 double bond opposite to the (moderately) bulky 3-(1,3-dioxolan-2-yl) substituent. We also performed hydroboration experiments with the *anti* diastereomers of **1a** and **1b**, but here we observed that these reactions are considerably less efficient, providing the expected diastereomers of **2** in low yields.[2,15] One side-reaction diminishing the yield of the desired hydroboration product was the N–O bond cleavage by the borane reagent. These examples demonstrate again that the reactivity of 1,2-oxazines strongly depends on their relative configuration.

By chance we discovered that it was possible to influence the stereochemical outcome of the hydroboration process. When the used borane–THF complex was stored for a longer period and thus apparently being "degraded" to some extend, this reagent led to the formation of a mixture



Scheme 2. Hydroboration of 1,2-oxazines *syn*-**1**. (a) BH_3·THF, THF, –30 °C to r.t.; r.t., 3 h; NaOH, H_2O_2, –10 °C to r.t.; r.t., overnight.

of diastereomers **2a** and **2c** with a ratio of ca. 1:1 (Scheme 3). It was possible to isolate pure **2c** by HPLC separation and to prove the relative configuration of this unexpected product by X-ray crystal structure analysis (Figure 1).[17] Now the hydroboration reagent is less selective and attacks *syn*-**1a** also from the side that bears the C-3 side chain. The X-ray crystal structure also shows a chair-like conformation of the 1,2-oxazine skeleton, with the substituents at C-3, C-4 and C-5 in axial positions, whereas the bulky *N*-benzyl group prefers the equatorial position.



Scheme 3. Hydroboration of 1,2-oxazine *syn*-**1a** with partially "degraded" borane–THF complex. (a) "BH_3·THF", THF, –30 °C to r.t.; r.t., 3 h; NaOH, H_2O_2, –10 °C to r.t.; r.t., overnight.

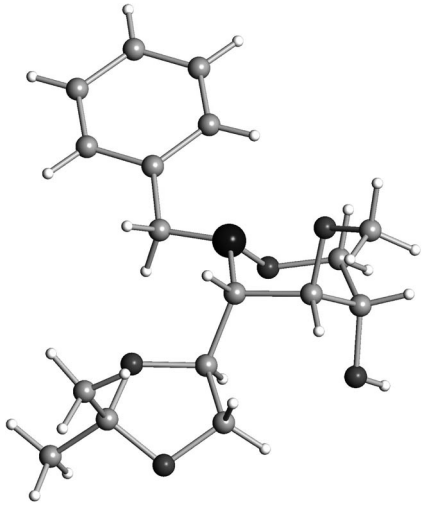


Figure 1. X-ray crystal structure of 1,2-oxazine **2c**.

Surprisingly, for the formation of diastereomer **2c** the addition of the borane reagent must have occurred to the sterically more hindered face of the double bond, a fact which we never observed before in hydroborations of this class of 1,2-oxazines. In order to understand the origin of this

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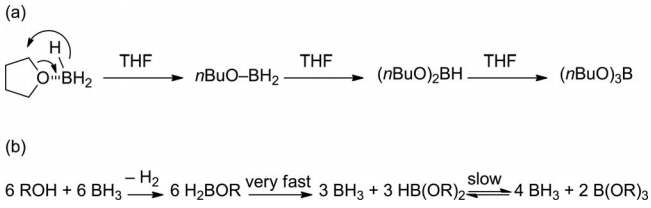
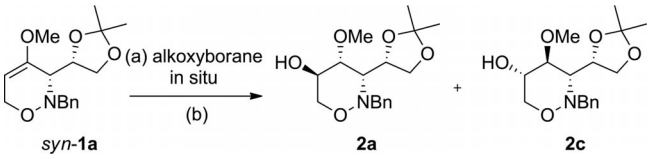
unexpected selectivity the assumed degradation of the borane–THF complex was further investigated. Although its degradation process is very complex and not entirely clear, it is known that at temperatures between 5 and 50 °C an initial reduction of the coordinating tetrahydrofuran occurs to provide a monoalkoxyborane.[18] At this point two possible subsequent pathways of the monoalkoxyborane include: (a) reduction of two solvent molecules with formation of a trialkoxyborane via a dialkoxyborane,[18] (b) reaction with a second monoalkoxyborane to regenerate borane itself and to form a dialkoxyborane and subsequently a trialkoxy species (Scheme 4).[19] Monoalkoxyboranes are unstable compounds and readily undergo further transformations; therefore, the newly formed species should mainly be dialkoxy- or trialkoxyboranes.



Scheme 4. Possible degradation processes of the borane–THF complex. (a) Degradation mode at 5–50 °C. (b) Decomposition of monoalkoxyboranes after in situ preparation with 1:1 mixtures of borane–THF complex and various alcohols.

To test our hypothesis that alkoxyboranes are responsible for the unexpected stereochemical outcome during the hydroboration of 3,6-dihydro-2*H*-1,2-oxazine *syn*-**1a** a series of control experiments was performed. Newly purchased "intact" borane–THF complex was treated with different alcohols to intentionally form alkoxyboranes before the substrate was added. Indeed, formation of the second diastereomer **2c** was now observed. The results indicate that an increase of the steric bulk of the alcohol shifts the ratio of **2a**/**2c** towards the latter diastereomer, but the conversion of starting material was also decreased (Scheme 5, Table 1). The biggest impact was achieved by using *tert*-butyl alcohol, which resulted in a nearly 1.3:1 ratio for diastereomeric 1,2-oxazines **2a**/**2c**. NMR spectra of the crude products before the oxidation step indicate that two diastereomers are already formed during the hydroboration and exclude the possibility that the oxidation conditions being somehow involved in the stereochemical outcome. Although we never obtained a 1:1 ratio as observed in the initial experiment with "degraded" borane–THF complex, our experiments clearly demonstrate that formation of alkoxyboranes is very likely the reason for the reduced stereoselectivity.

Wojtkowski[19] had shown that 1:1 mixtures of alcohols and borane led to equilibria of dialkoxy- and trialkoxyborane species with values for the equilibrium constant K_c = 2.9–7 in favour of the trialkoxy species for sterically less demanding alcohols and K_c = 0.13–0.17 in favour of the dialkoxyborane species for *tert*-butyl alcohol. Given the facts, that monoalkoxyboranes are fairly unstable, that alkoxyboranes are significantly weaker reducing agents than



Scheme 5. Hydroboration in the presence of alcohols. (a) ROH/BH_3·THF (2:3), THF, 0 °C, 15–60 min. (b) Addition of 1,2-oxazine dissolved in THF at 0 °C, 1.5 h, r.t., 7 h; NaOH, H_2O_2, –10 °C to r.t.; r.t., overnight. R = Me, *n*Bu, *i*Pr, *t*Bu.

Table 1. Product ratios after hydroboration in the presence of alcohols.

Entry	Alcohol	**2a**/**2c**[a]
1	MeOH	only traces of **2c**[b]
2	*n*BuOH	2.7:1
3	*i*PrOH	2.2:1[b,c]
4	*t*BuOH	1.3:1[d]

[a] Ratios determined by integration of the signals of the methoxy group by ^{1}H NMR spectroscopy. [b] No purification performed. [c] 90% conversion. [d] 50% conversion.

borane itself, and that our hydroboration attempts with primary or secondary boranes such as thexylborane, disiamylborane, 9-BBN and catecholborane[14g] completely failed, we assume that in situ formed *dialkoxyboranes are the key for shifting the ratio of diastereomers, but are not the reducing agents*. Currently, we can only speculate on the exact mechanism. A coordination of the present dialkoxyborane to one of the 1,2-oxazine heteroatoms probably changes the reactive conformation of the substrate, and as a consequence the remaining borane–THF complex then adds in an unselective fashion by attacking the double bond from both sides.

Subsequent Reactions

The 5-hydroxy-1,2-oxazines **2a** and **2b** proved to be ideal intermediates en route to a variety of polyhydroxylated compounds. Short-time hydrogenolysis (20 min) of **2b** catalysed by palladium on charcoal led to the *N*-debenzylated 1,2-oxazine. Complete deprotection was achieved by cleavage of the ketal in the presence of acidic ion exchange resin DOWEX 50 to furnish tetrahydroxylated 1,2-oxazine **3** in 78% overall yield (Scheme 6). In order to synthesise its C-5 epimer, the hydroxy group in **2b** was first oxidised with Dess–Martin periodinane[20] to the corresponding ketone, which was achieved without epimerisation at C-4. Subsequent stereoselective reduction by L-Selectride provided *epi*-**2b** in an overall yield of 70% (Scheme 6). By applying the same deprotection sequence as for **2b** it was possible to prepare *epi*-**3** in a yield of 72% over both steps. Compounds of type **3** and *epi*-**3**, which we propose to name aza sugars since one carbon atom of the pyran ring of carbohydrates is replaced by a nitrogen atom, are very rare in literature.[21] Their potentially very interesting biological activity deserves more attention.[22]

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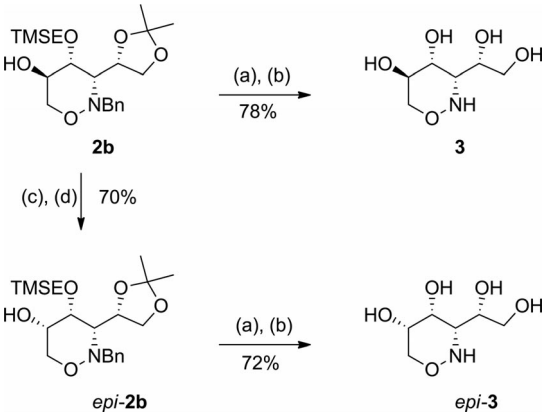
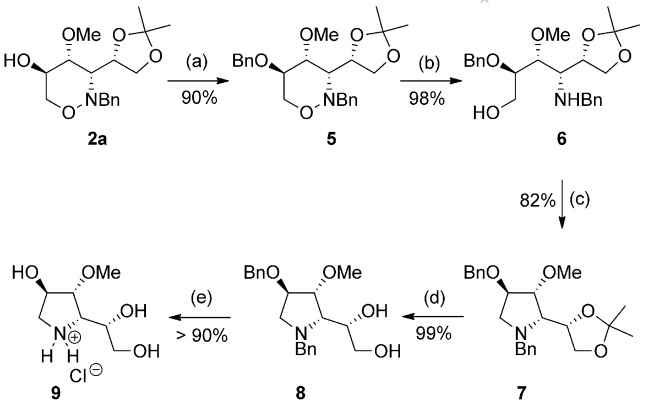
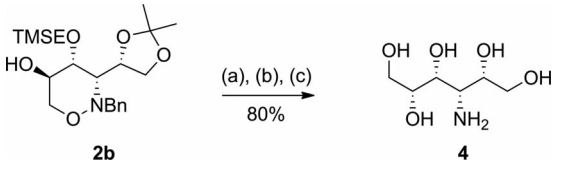


Scheme 6. Syntheses of polyhydroxylated 1,2-oxazines. (a) H_2, Pd/C, MeOH, r.t., 20 min. (b) DOWEX 50, EtOH, 50 °C, 3 d. (c) Dess–Martin periodinane, CH_2Cl_2, r.t., 6 h. (d) L-Selectride, THF, –78 °C, 3 h.



Scheme 8. Synthesis of pyrrolidine hydrochloride **9**. (a) NaH, BnBr, DMF, r.t., overnight. (b) SmI_2, THF, r.t., 3.5 h. (c) MsCl, Et_3N, CH_2Cl_2, r.t., 15 h. (d) *p*TsOH, MeOH, r.t., 2 d. (e) H_2, Pd/C, MeOH/HCl, r.t., 22 h.

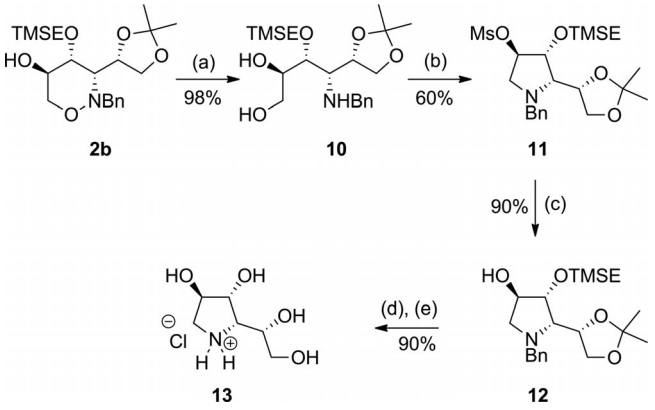
By a different deprotection sequence acyclic amino polyol **4** was accessible (Scheme 7). First desilylation of 1,2-oxazine **2b** was performed by using $BF_3{\cdot}OEt_2$ followed by ketal cleavage under aqueous acidic conditions at elevated temperature. Finally, reductive removal of the benzyl group and cleavage of the N–O bond provided 4-amino-4-deoxy-D-iditol **4** in a total yield of 80%. It should be emphasised here that the enantiomers of the precursor 1,2-oxazines *syn*-**1a** and *syn*-**1b** are also easily available.[4b,5d] As a consequence, the smooth preparation of enantiomers of all compounds mentioned in this report are possible.



Scheme 7. Conversion of 1,2-oxazine **2b** into amino polyol **4**. (a) $BF_3{\cdot}Et_2O$, CH_2Cl_2, r.t., 6 h. (b) aq. AcOH (60%), THF, 50 °C, overnight. (c) H_2, Pd/C, MeOH, r.t., 6 h.

The 1,2-oxazines **2a** and **2b** could also be successfully employed for the preparation of two differently substituted polyhydroxylated pyrrolidine derivatives (imino sugars). Our strategy is shown in Scheme 8 illustrating the synthesis of 5-methoxy-substituted pyrrolidinium salt **9**. To avoid side-product formation in the cyclisation step 1,2-oxazine **2a** was first *O*-benzylated in 90% yield to afford 1,2-oxazine derivative **5**. Then the N–O bond of this intermediate was quantitatively cleaved with samarium diiodide,[15,23] and the resulting amino alcohol **6** underwent cyclisation by treatment with mesyl chloride to furnish pyrrolidine **7** in 82% yield for both steps. Deprotection of the side-chain diol to give compound **8** was achieved with *p*-toluenesulfonic acid followed by hydrogenation in HCl-saturated methanol, which provided the desired pyrrolidine derivative as hydrochloride **9** in a yield of over 90% for the final two steps.

For the synthesis of fully deprotected pyrrolidine derivative **13** we started from 1,2-oxazine derivative **2b** bearing the smoothly removable 2-(trimethylsilyl)ethoxy group (Scheme 9). Here, we first cleaved the N–O bond by treatment with samarium diiodide, which led to amino diol **10** in excellent yield. This intermediate was converted into the dimesylate by using an excess of mesyl chloride. The presence of triethylamine rapidly induced the S_N2 displacement of the primary mesylate, thus leading to the desired pyrrolidine derivative **11** in 60% yield. The corresponding azetidine derivative involving the secondary mesylate was also formed, hence explaining the moderate yield for the pyrrolidine. Compound **11** was converted into the free alcohol **12** by treatment with LDA[24] in a yield of 90%. Finally, stepwise deprotection by Lewis acid induced desilylation and hydrogenolysis led to pyrrolidinium salt **13** with 90% yield over both steps. Overall, this synthesis established a very efficient approach to compound **13**,[25] which is known as moderate inhibitor of α-L-fucosidase.[26] The enantiomer of **13**, which is a potent inhibitor of α-D-galactosidase and a



Scheme 9. Synthesis of pyrrolidine hydrochloride **13**. (a) SmI_2, THF, r.t., 3 h. (b) MsCl, Et_3N, THF, r.t., 1 d. (c) LDA, THF, –78 °C to r.t., 7 h. (d) $BF_3{\cdot}Et_2O$, CH_2Cl_2, r.t., 6 h. (e) H_2, Pd/C, MeOH/HCl, r.t., 1 d.

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weak inhibitor of α-D-arabinosidase,[26] should also be accessible by our route due to the simple availability of the enantiomer *ent*-*syn*-**1b**.[4b,5d] The high synthetic value of our route to similar glycosidase inhibitors is evident.[27]

Conclusions

3,6-Dihydro-2*H*-1,2-oxazines proved to be versatile precursors for the syntheses of aza, amino and imino sugars, which mimic natural carbohydrates. An additional hydroxy group was readily installed by hydroboration in a highly stereoselective process when "fresh" borane–THF complex was used and the standard oxidative workup was employed. The unexpected finding of a second diastereomeric 5-hydroxy-1,2-oxazine revealed an interesting and new opportunity to alter the stereochemical outcome of the hydroboration of 1,2-oxazines. Further investigations are necessary to prove that dialkoxyboranes play indeed an integral role in influencing the hydroboration mechanism, but our observations may have general significance. Starting from 5-hydroxy-substituted 1,2-oxazines and by careful control of the subsequent steps we could prepare unusual aza sugar derivatives, amino polyols and polyhydroxylated pyrrolidine derivatives.[28] All these compounds are of interest due to their known or expected biological activity. Again it should be emphasised that both enantiomers of the compounds presented in this report are easily available by the methods developed.

Experimental Section

General: If not differently stated all reactions were carried out under Ar. The solvents used were purified by distillation using common drying agents and procedures and were transferred under Ar. Flash chromatography: Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded with AC 500 (Bruker), ECP 500 and ECX 400 (Jeol) spectrometers in the solvents indicated; chemical shifts (δ) are given in ppm relative to residual solvent peaks; coupling constants (J) are given in Hz. IR: Nicolet-FT-IR spectrometer 5 SXC: wavenumbers are given in cm^{-1}. MS, HRMS: MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV), CH5DF (FAB, 3 kV) (all Finnigan), Ionspec QFT-7 (ESI-FT ICRMS) (Varian) und Agilent 6210 (ESI-TOF, 4 μL/min, 1.0 bar, 4 kV). Melting points: Thermovar (Reichert) melting point apparatus (not corrected). Elemental analyses: Elemental Analyzer (Perkin–Elmer), Vario EL elemental analysis system. All commercially available compounds (Acros, Lancaster, Fluka, Aldrich, TCI Europe) were used as received unless stated otherwise. Dess–Martin periodinane was prepared according to a previously described procedure.[20]

(3*S*,4*R*,5*R*,4′*S*)-2-Benzyl-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-5-hydroxy-4-methoxy-3,4,5,6-tetrahydro-2*H*-1,2-oxazine (2a): To a solution of *syn*-**1a** (1.08 g, 3.54 mmol) in THF (70 mL) BH_3·THF (1 M in THF; 14.1 mL, 14.1 mmol) was added at –30 °C. The solution was warmed to room temp. and stirred for 3 h, then cooled to –10 °C, and NaOH solution (2 M; 21.2 mL) and H_2O_2 (30%; 7.1 mL) were added. Stirring was continued at room temp. overnight. After addition of $Na_2S_2O_3$ solution (satd.), the organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined extracts were dried with $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel; hexane/EtOAc, 1:1) to yield **2a** as colourless oil (0.914 g, 80%). $[\alpha]_D^{20}$ = +9.8 ($CHCl_3$, c = 0.99). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38, 1.41 (2 s, 3 H each, Me), 2.40 (br. s, 1 H, OH), 3.30 (dd, J = 3.3, 7.8 Hz, 1 H, 3-H), 3.37 (m_c, 1 H, 4-H), 3.41 (s, 3 H, OMe), 3.63 (dd, J = 6.0, 11.4 Hz, 1 H, 6-H_A), 3.67–3.72 (m, 2 H, 5-H, 5′-H_A), 3.85, 4.42 (2 d, J = 15.1 Hz, 1 H each, CH_2Ph), 4.08–4.14 (m, 2 H, 5′-H_B, 6-H_B), 4.47 (br. dt, J = 5.8, 7.8 Hz, 1 H, 4′-H), 7.21–7.39 (m, 5 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.2, 26.7 (2 q, Me), 58.0 (q, OMe), 60.3 (t, CH_2Ph), 64.9 (d, C-3), 65.1 (d, C-5), 66.7 (t, C-5′), 71.1 (t, C-6), 74.0 (d, C-4′), 81.6 (d, C-4), 108.4 (s, C-2′), 126.7, 128.0, 128.4, 138.8 (3 d, s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3460 (OH), 2980–2930 (CH) cm^{-1}. MS (EI): m/z (%) = 323 (7) [M^+], 308 (4) [M^+ – Me], 222 (100) [$M^+ - C_5H_9O_2$], 101 (3) [$C_5H_9O_2^+$], 91 (78) [Bn^+]. $C_{17}H_{25}NO_5$ (323.4): calcd. C 63.14, H 7.79, N 4.33; found C 61.65, H 7.53, N 4.02.

(3*S*,4*S*,5*S*,4′*S*)-2-Benzyl-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-5-hydroxy-4-methoxy-3,4,5,6-tetrahydro-2*H*-1,2-oxazine (2c)

Procedure for Using Intact BH_3·THF Complex in the Presence of *n*BuOH: To a solution of BH_3·THF (1 M in THF; 492 μL, 0.492 mmol) in THF (1 mL) *n*BuOH (30.1 μL, 0.329 mmol) was added at 0 °C, and the mixture was stirred for 15 min. Then **1a** (50 mg, 0.164 mmol) dissolved in THF (1 mL) was added dropwise. The solution was warmed to room temp. and stirred for 3 h, then NaOH solution (2 M; 740 μL) and H_2O_2 (30%; 250 μL) were added. Stirring was continued at room temp. overnight. After addition of $Na_2S_2O_3$ solution (satd.), the layers were separated, and the aqueous layer was extracted with Et_2O. The combined extracts were dried with $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel; hexane/EtOAc gradient 4:1, 2:1, 1:1) to yield a mixture of **2a**/**2c** (2.7:1) as a colourless oil (34 mg, 65%).

Procedure for Using Partially Degraded BH_3·THF Complex: By a procedure similar to that for **2a**, **1a** (2.70 g, 8.85 mmol) was treated with BH_3·THF (1 M in THF; 35.4 mL, 35.4 mmol), NaOH solution (2 M; 53 mL) and H_2O_2 (30%; 18 mL). Chromatography of the crude product (silica gel, hexane/EtOAc, 2:1) and subsequent purification by HPLC yielded pure **2c** (531 mg, 19%) as colourless crystals and a mixture of **2a**/**2c** (ca. 2:1) (907 mg) as a colourless oil. M.p. 61–63 °C. $[\alpha]_D^{20}$ = +13.0 ($CHCl_3$, c = 0.72). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.39, 1.43 (2 s, 3 H each, Me), 2.87 (br. s, 1 H, OH), 3.01 (dd, J = 3.7, 6.4 Hz, 1 H, 3-H), 3.17 (t, J = 3.7 Hz, 1 H, 4-H), 3.46 (s, 3 H, OMe), 3.62 (dd, J = 3.6, 11.8 Hz, 1 H, 6-H_A), 3.69 (m_c, 1 H, 5-H), 3.77 (br. t, $J \approx$ 8.1 Hz, 1 H, 5′-H_A), 3.96, 4.40 (2 d, J = 13.8 Hz, 1 H each, NCH_2), 4.07 (dd, J = 6.4, 8.1 Hz, 1 H, 5′-H_B), 4.19 (dd, J = 2.8, 11.8 Hz, 1 H, 6-H_B), 4.51 (td, J = 6.4, 8.1 Hz, 1 H, 4′-H), 7.20–7.50 (m, 5 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.0, 26.4 (2 q, Me), 58.1 (q, OMe), 59.3 (t, NCH_2), 65.0 (d, C-3), 66.6 (d, C-5), 67.3 (t, C-5′), 69.6 (t, C-6), 74.2 (d, C-4′), 79.2 (d, C-4), 109.0 (s, C-2′), 126.8, 128.0, 128.5, 138.3 (3 d, s, Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3435 (OH), 2985–2830 (CH) cm^{-1}. MS (EI): m/z (%) = 323 (6) [M^+], 308 (5) [$M^+ - CH_3$], 222 (85) [$M^+ - C_5H_9O_2$], 91 (100) [$C_7H_7^+$], 43 (47). $C_{17}H_{25}NO_5$ (323.2): calcd. C 63.14, H 7.79, N 4.33; found C 63.03, H 7.72, N 4.19.

(3*S*,4*R*,5*R*,4′*S*)-2-Benzyl-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-5-hydroxy-4-[(2′′-trimethylsilyl)ethoxy]-3,4,5,6-tetrahydro-2*H*-1,2-oxazine (2b): A stirred solution of 1,2-oxazine **1b** (500 mg, 1.28 mmol) in dry THF (25 mL) was cooled to –30 °C. To this solution was added dropwise a solution of the BH_3·THF complex (1 M in THF;

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5.1 mL, 5.10 mmol). The mixture was stirred at –30 °C for 0.5 h and then warmed up slowly to room temp. After 3 h at room temp., the mixture was cooled to –10 °C and then treated successively with NaOH (2 M; 7.68 mL) and H_2O_2 (30%; 2.56 mL) and stirred at this temperature for 0.5 h, then warmed to room temp. and stirred overnight. NH_4Cl solution (satd.; 10 mL) was added, and the mixture was extracted with CH_2Cl_2, dried with Na_2SO_4 and concentrated. The crude product was subjected to column chromatography (silica gel; hexane/EtOAc, 2:1). The pure product **2b** was obtained as colourless crystals (503 mg, 96%). M.p. 82–85 °C. $[\alpha]_D^{20}$ = –14.2 ($CHCl_3$, c = 0.23). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 9 H, $SiMe_3$), 0.87, 1.04 (2 m_c, 1 H each, CH_2Si), 1.38, 1.39 (2 s, 3 H each, Me), 2.32 (br. s, 1 H, OH), 3.28 (dd, J = 3.4, 7.7 Hz, 1 H, 3-H), 3.47 (br. s, 1 H, 4-H), 3.57 (m_c, 1 H, 6-H_A), 3.62 (m_c, 2 H, OCH_2), 3.68 (m_c, 1 H, 5′-H_A), 3.70 (m_c, 1 H, 5-H), 3.85, 4.39 (2 d, J = 15.1 Hz, 1 H each, NCH_2Ph), 4.10 (dd, J = 2.5, 10.8 Hz, 1 H, 6-H_B), 4.13 (dd, J = 5.6, 8.3 Hz, 1 H, 5′-H_B), 4.50 (br. s, 1 H, 4′-H), 7.21–7.38 (m, 5 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = –2.0 (q, $SiMe_3$), 18.7 (t, CH_2Si), 26.4, 26.8 (2 q, Me), 60.2 (t, NCH_2Ph), 64.8 (d, C-3), 66.4 (d, C-5), 67.7 (t, OCH_2), 71.1 (t, C-6), 73.8 (d, C-4′), 81.4 (d, C-4), 108.2 (s, C-2′), 126.8, 128.1, 128.4, 138.9 (3 d, s, Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3430 (OH), 3080–3030 (=CH), 2990–2890 (CH) cm^{-1}. MS (EI): m/z (%) = 409 (5) [M^+], 394 (1) [M^+ – Me], 308 (100) [$M^+ - C_2H_5OSiMe_3$], 91 (47) [Bn^+], 73 (16) [Me_3Si^+]. $C_{21}H_{35}NO_5Si$ (409.6): calcd. C 61.58, H 8.61, N 3.42; found C 61.18, H 8.58, N 3.34.

(3*S*,4*R*,5*S*,4′*S*)-2-Benzyl-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-5-hydroxy-4-[(2′′-trimethylsilyl)ethoxy]-3,4,5,6-tetrahydro-2*H*-1,2-oxazine (*epi*-2b): To a solution of **2b** (520 mg, 1.28 mmol) in CH_2Cl_2 (2.5 mL) Dess–Martin periodinane (1.71 g, 4.03 mmol) was added. The mixture was stirred at room temp. for 6 h. Afterwards $Na_2S_2O_3$ solution (satd.; 2.5 mL) was added, and the mixture was stirred for additional 30 min. Then it was diluted with Et_2O (10 mL), washed with H_2O, and the organic layer was dried with Na_2SO_4. After filtration and removal of the solvents in vacuo, the respective 1,2-oxazinone (570 mg, quant.) was isolated as a pale yellow oil. No purification was performed. To a solution of this 1,2-oxazinone (122 mg, 0.299 mmol) in THF (3 mL) L-Selectride (1 M in THF; 450 μL, 0.450 mmol) was added dropwise at –78 °C. The mixture was stirred at this temperature for 3 h and afterwards quenched with H_2O (3 mL). It was warmed to room temp. and extracted with Et_2O. After drying with Na_2SO_4, the solvents were removed in vacuo. The crude product was purified by column chromatography (silica gel; hexane/EtOAc gradient 8:1, 6:1, 4:1). 1,2-Oxazine *epi*-**2b** was obtained as a colourless oil (86 mg, 70%). $[\alpha]_D^{20}$ = –45.3 ($CHCl_3$, c = 0.40). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.01 (s, 9 H, $SiMe_3$), 0.94 (m_c, 2 H, CH_2Si), 1.39, 1.40 (2 s, 3 H each, Me), 2.32 (br. s, 1 H, OH), 3.22 (dd, J = 5.3, 8.4 Hz, 1 H, 3-H), 3.58–3.63 (m, 2 H, OCH_2), 3.72 (t, J = 8.8 Hz, 1 H, 5′-H_A), 3.78 (dd, J = 3.5, 5.4 Hz, 1 H, 4-H), 3.82 (m_c, 1 H, 5-H), 3.87–3.96 (m, 2 H, 6-H), 3.98, 4.32 (2 d, J = 14.9 Hz, 1 H each, NCH_2), 4.09 (d, J = 5.4, 8.8 Hz, 1 H, 5′-H_B), 4.99 (m_c, 1 H, 4′-H), 7.20–7.24, 7.27–7.31, 7.34–7.38 (3 m, 5 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 1.27 (q, $SiMe_3$), 18.7 (t, CH_2Si), 26.5, 27.1 (2 q, Me), 60.5 (t, NCH_2), 64.9 (d, C-3), 66.2 (d, C-5), 67.4 (t, OCH_2), 68.0 (t, C-5′), 72.7 (t, C-6), 73.7 (d, C-4′), 77.8 (d, C-4), 107.7 (s, C-2′), 126.9, 128.2, 128.5, 139.4 (3 d, s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3475 (OH), 3085–3030 (=CH), 2985–2900 (CH) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{21}H_{35}NO_5SiNa$ [M + Na^+] 432.2177; found 432.2180. $C_{21}H_{35}NO_5Si$ (409.6): calcd. C 61.58, H 8.61, N 3.42; found C 61.84, H 6.26, N 3.70.

(3*S*,4*R*,5*R*,1′*S*)-4,5-Dihydroxy-3-(1′,2′-dihydroxyethyl)-3,4,5,6-tetrahydro-2*H*-1,2-oxazine (3): A stirred solution of Pd on charcoal (121 mg, 0.114 mmol) in MeOH (8 mL) was saturated with hydrogen for 1 h. Then a solution of 1,2-oxazine **2b** (260 mg, 0.635 mmol) in MeOH (2 mL) was added, and the mixture was stirred under hydrogen at normal pressure and room temp. for 20 min. After filtration through a pad of Celite, the solvent was removed in vacuo. The crude product was purified by chromatography (silica gel; hexane/EtOAc 2:1, then 1:1, then 1:2). The respective debenzylated 1,2-oxazine (170 mg, 84%) was isolated as a colourless oil. $[\alpha]_D^{20}$ = –34.1 (c = 0.75, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, $SiMe_3$), 0.82–0.95 (m, 2 H, CH_2Si), 1.30, 1.35 (2 s, 3 H each, Me), 2.67 (br. s, 1 H, OH), 3.27 (dd, J = 3.3, 9.1 Hz, 1 H, 3-H), 3.32 (br. s, 1 H, 4-H), 3.47–3.53 (m, 1 H, OCH_2), 3.54–3.61 (m, 1 H, OCH_2), 3.62–3.68 (m, 2 H, 6-H_A, 5′-H_A), 3.71 (dt, J = 3.3, 5.7 Hz, 1 H, 5-H), 4.03–4.10 (m, 2 H, 6-H_B, 5′-H_B), 4.24 (br. q, $J \approx$ 7.5 Hz, 1 H, 4′-H), 5.89 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = –1.34 (q, $SiMe_3$), 18.8 (t, CH_2Si), 25.7, 26.9 (2 q, Me), 61.0 (d, C-3), 65.7 (d, C-5), 67.1 (t, C-5′), 68.2 (t, OCH_2), 71.7 (t, C-6), 73.1 (d, C-4′), 76.9 (d, C-4), 109.0 (s, C-2′) ppm. IR (neat): $\tilde{\nu}$ = 3435, 3295 (OH, NH), 2985–2895 (CH) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{14}H_{29}NO_5Si$ [M + Na^+] 342.1707; found 342.1704. $C_{14}H_{29}NO_5Si$ (319.5): calcd. C 52.63, H 9.15, N 4.38; found C 52.37, H 9.03, N 4.43. To a solution of this *N*-debenzylated 1,2-oxazine (160 mg, 0.501 mmol) acidic ion exchange resin DOWEX 50 (640 mg; washed several times with EtOH before usage) was added. The suspension was heated to 50 °C and stirred for 3 d. After filtration and evaporation of the solvent, crude 1,2-oxazine **3** was isolated as an amorphous colourless solid. It was purified by recrystallisation with MeOH and H_2O. Pure tetrahydroxylated 1,2-oxazine **3** (84 mg, 93%) was isolated as colourless crystals. M.p. 183–185 °C. $[\alpha]_D^{20}$ = +19.5 (H_2O, c = 0.21). ^{1}H NMR (500 MHz, D_2O): δ = 3.42 (br. dd, $J \approx$ 1.5, 7.8 Hz, 1 H, 3-H), 3.62 (dd, J = 4.0, 6.9 Hz, 1 H, 2′-H_A), 3.71 (m_c, 1 H, 5-H), 3.69–3.82 (m, 4 H, 4-H, 6-H_A, 1′-H, 2′-H_B), 4.13 (br. dd, $J \approx$ 1.5, 12.8 Hz, 1 H, 6-H_B) ppm. ^{13}C NMR (126 MHz, D_2O): δ = 58.0 (d, C-3), 62.4 (t, C-2′), 65.6 (d, C-4), 67.1 (d, C-5), 70.0 (d, C-1′), 70.1 (t, C-6) ppm. IR (KBr): $\tilde{\nu}$ = 3450, 3365, 3295, 3235, 3200 (OH, NH), 2960–2615 (CH) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_6H_{13}NO_5Na$ [M + Na^+] 202.0686; found 202.0690. $C_6H_{13}NO_5$ (179.2): calcd. C 40.22, H 7.31, N 7.82; found C 40.32, H 7.24, N 7.79.

(3*S*,4*R*,5*S*,1′*S*)-4,5-Dihydroxy-3-(1′,2′-dihydroxyethyl)-3,4,5,6-tetrahydro-2*H*-1,2-oxazine (*epi*-3): By a procedure similar to that of **3**, first 1,2-oxazine *epi*-**2b** (325 mg, 0.794 mmol) was treated with hydrogen and Pd/C (151 mg, 0.142 mmol) in MeOH (5 mL) at room temp. for 20 min. Purification of the crude product by chromatography (silica gel; hexane/EtOAc 2:1, then 1:1, then 1:2) yielded the respective debenzylated 1,2-oxazine (229 mg, 90%). $[\alpha]_D^{20}$ = –47.2 (c = 0.35, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 (s, 9 H, $SiMe_3$), 0.95 (m_c, 2 H, CH_2Si), 1.34, 1.37 (2 s, 3 H each, Me), 2.32 (br. s, 1 H, OH), 3.01 (dd, J = 2.9, 6.0 Hz, 1 H, 3-H), 3.59–3.67 (m, 3 H, 4-H, OCH_2), 3.77 (t, J = 6.0 Hz, 1 H, 5′-H_A), 3.81 (m_c, 1 H, 5-H), 3.86–3.90 (m, 1 H, 6-H), 4.07 (dd, J = 4.4, 6.0 Hz, 1 H, 5′-H_B), 4.67 (m_c, 1 H, 4′-H) ppm; NH signal could not be assigned unambiguously. ^{13}C NMR (126 MHz, $CDCl_3$): δ = –1.27 (q, $SiMe_3$), 19.0 (t, CH_2Si), 25.7, 27.0 (2 q, Me), 62.5 (d, C-3), 66.3 (d, C-5), 67.5 (t, C-5′), 68.6 (d, C-4), 71.9 (t, C-6), 73.6 (d, C-4′), 75.4 (t, OCH_2), 108.7 (s, C-2′) ppm. IR (neat): $\tilde{\nu}$ = 3450, 3295 (OH, NH), 2985–2895 (CH) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{14}H_{29}NO_5Si$ [M + Na]$^+$ 342.1707; found 342.1700. This *N*-debenzylated 1,2-oxazine (184 mg, 0.576 mmol) was then treated with DOWEX 50 (732 mg) in EtOH (5 mL) at 50 °C for 3 d. Crude *epi*-**3** was isolated as a pale yellow oil and purified by precipitation from CH_3CN and MeOH. *epi*-**3** (83 mg, 80%) was isolated as an

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amorphous colourless solid. M.p. 132–134 °C. $[\alpha]_D^{20}$ = +36.4 (H_2O, c = 0.47). ^{1}H NMR (500 MHz, D_2O): δ = 3.16 (dd, J = 1.5, 7.9 Hz, 1 H, 3-H), 3.65 (dd, J = 6.5, 12.6 Hz, 1 H, 6-H_A), 3.68–3.78 (m, 3 H, 1′-H, 2′-H), 3.80–3.86 (m, 2 H, 5-H, 6-H_B), 3.99 (m_c, 1 H, 4-H) ppm. ^{13}C NMR (101 MHz, D_2O): δ = 61.5 (d, C-3), 62.2 (t, C-2′), 65.7 (d, C-4), 66.3 (t, C-6), 68.1 (d, C-5), 69.7 (d, C-1′) ppm. IR (KBr): $\tilde{\nu}$ = 3475, 3430, 3350, 3205, 3165 (OH, NH), 2925–2875 (CH) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_6H_{14}NO_5$ [M + H$^+$]: 180.0867; found 180.0865. $C_6H_{13}NO_5$ (179.2): calcd. C 40.22, H 7.31, N 7.82; found C 39.90, H 6.64, N 7.70.

(2*R*,3*R*,4*S*,5*S*)-4-Aminohexane-1,2,3,5,6-pentaol (4): To a solution of hydroborated 1,2-oxazine **2b** (300 mg, 0.730 mmol) in CH_2Cl_2 (3 mL) at 0 °C was added BF_3·Et_2O (264 μL, 2.20 mmol), and the resulting solution was stirred at 0 °C for 5 min, then at room temp. for 6 h, and then quenched with H_2O (ca. 3 mL). The two layers were separated, and the aqueous layer was extracted several times with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under vacuum. Column chromatography (silica gel; hexane/EtOAc, 1:5) gave rise to the respective desilylated 1,2-oxazine (221 mg, 98%) as colourless crystals. M.p. 74–76 °C. $[\alpha]_D^{22}$ = +66.3 (c = 0.24, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41, 1.83 (2 s, 3 H each, Me), 2.54, 2.97 (2 br. s, 1 H each, OH), 3.28 (dd, J = 1.9, 7.6 Hz, 1 H, 3-H), 3.56 (m_c, 1 H, 5-H), 3.63 (m_c, 1 H, 4-H), 3.68 (dd, J = 2.0, 12.6 Hz, 1 H, 6-H_B), 3.78 (m_c, 1 H, 5′-H_B), 3.80 (d, J = 15.1 Hz, 1 H, NCH_2Ph), 4.12 (dd, J = 1.6, 12.6 Hz, 1 H, 6-H_A), 4.22 (m_c, 1 H, 5′-H_A), 4.26 (m_c, 1 H, 4′-H), 4.42 (d, J = 15.1 Hz, 1 H, NCH_2Ph), 7.22–7.37 (m, 5 H, Ph) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.4, 26.8 (2 q, Me), 59.8 (t, NCH_2Ph), 63.3 (d, C-3), 66.3 (d, C-4), 66.4 (t, C-5′), 68.0 (d, C-5), 71.7 (t, C-6), 74.9 (d, C-4′), 109.2 (s, C-2′), 126.8, 128.1, 128.4, 138.8 (3 d, s, Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3535–3430 (OH), 2990–2890 (CH) cm^{-1}. MS (EI): m/z (%) = 309 (5) [M$^+$], 294 (4) [M$^+$ – CH_3], 208 (100) [M$^+$ – $C_2H_5OSiMe_3$], 91 (47) [CH_2Ph^+]. HRMS (EI): calcd. for $C_{16}H_{23}NO_5$ [M$^+$] 309.15762; found 309.15933. $C_{16}H_{23}NO_5$ (309.4): calcd. C 62.12, H 7.22, N 4.50; found C 62.46, H 7.22, N 4.27. This desilylated 1,2-oxazine (290 mg, 0.940 mmol) was dissolved in a mixture of AcOH/H_2O (60:40; 18 mL) and THF (9 mL). After stirring at 50 °C overnight, the solvent was co-evaporated with toluene. The crude product was purified by column chromatography (silica gel; CH_2Cl_2/MeOH, 4:1) to give the respective tetrahydroxylated 1,2-oxazine 207 mg (82%) as colourless crystals. M.p. 43–45 °C. $[\alpha]_D^{22}$ = +39.3 (c = 0.40, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 3.28 (dd, J = 2.7, 6.5 Hz, 1 H, 3-H), 3.57–3.61 (m, 2 H, 5-H, 6-H_B), 3.75 (dd, J = 6.3, 11.4 Hz, 1 H, 1-H_B), 3.80 (d, J = 14.4 Hz, 1 H, NCH_2Ph), 3.82 (dd, J = 3.7, 11.4 Hz, 1 H, 1-H_A), 3.88 (dd, J = 2.7, 4.3 Hz, 1 H, 4-H), 3.97 (ddd, J = 3.7, 6.3, 6.5 Hz, 1 H, 2-H), 4.07 (dd, J = 3.7, 13.1 Hz, 1 H, 6-H_A), 4.32 (d, J = 14.4 Hz, 1 H, NCH_2Ph), 7.15–7.39 (m, 5 H, Ph) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 60.2 (t, NCH_2Ph), 65.0 (t, C-2′), 67.1 (d, C-3), 69.3 (d, C-5), 70.0 (d, C-4), 70.2 (t, C-6), 71.9 (d, C-1′), 127.7, 128.9, 129.6, 140.2 (3 d, s, Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3430–3365 (O–H), 3060–3030 (=CH), 2980–2880 (C–H) cm^{-1}. MS (EI): m/z (%) = 270 (14) [M$^+$ + H], 208 (30) [M$^+$ – $C_2H_5O_2$], 91 (62) [CH_2Ph^+]. $C_{13}H_{19}NO_5$ (269.3): C 57.98, H 7.11, N 5.20; C 57.60, H 7.03, N 5.18. A stirred suspension of Pd on charcoal (150 mg, 0.140 mmol) in MeOH (25 mL) was saturated with hydrogen for 1 h. Then a solution of the tetrahydroxylated 1,2-oxazine (100 mg, 0.371 mmol) in MeOH (10 mL) was added, and the mixture was stirred under hydrogen at normal pressure at room temp. for 6 h. Filtration through a pad of Celite and removal of the solvent in vacuo yielded the amino alcohol **4** (76 mg, quant.) as a colourless oil. The product could not be purified. $[\alpha]_D^{22}$ = –66.8 (MeOH, c = 0.33). ^{1}H NMR (500 MHz, CD_3OD): δ = 3.47 (t, J = 4.9 Hz, 1 H, 4-H), 3.60–3.74 (m, 5 H, 1-H, 2-H, 6-H), 3.88 (m_c, 1 H, 5-H), 3.94 (m_c, 1 H, 3-H) ppm. ^{13}C NMR (CD_3OD, 126 MHz): δ = 57.1 (d, C-4), 63.8 (t, C-1), 64.7 (t, C-6), 78.3 (d, C-2, C-3), 81.1 (d, C-5) ppm. IR (neat): $\tilde{\nu}$ = 3435–3355 (OH), 2955–2845 (CH), 1250 (CO) cm^{-1}. MS (EI): m/z (%) = 182 (8) [M$^+$ + H], 164 (2) [M$^+$ + H – H_2O], 132 (12) [$C_5H_{10}NO_3^+$]. HRMS (EI): calcd. for $C_6H_{15}NO_5$ [M$^+$ – 49] 132.0661; found 132.0662.

(3*S*,4*R*,5*R*,4′*S*)-2-Benzyl-5-benzyloxy-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-4-methoxy-3,4,5,6-tetrahydro-1,2-oxazine (5): A solution of **2a** (0.300 g, 0.928 mmol) in DMF (8 mL) was added to NaH (60% in mineral oil; 0.056 g, 1.39 mmol) at 0 °C. Benzyl bromide (0.198 g, 1.16 mmol) was added and the solution was stirred at room temp. overnight. H_2O (10 mL) was added, the aqueous layer was extracted with Et_2O (3 × 10 mL), and the combined extracts were dried with $MgSO_4$. After filtration, the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel; hexane/EtOAc, 6:1) giving rise to compound **5** as colourless oil (0.346 g, 90%). $[\alpha]_D^{20}$ = +8.0 ($CHCl_3$, c = 1.7). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37, 1.40 (2 s, 3 H each, Me), 3.31 (dd, J = 3.6, 8.1 Hz, 1 H, 3-H), 3.33 (s, 3 H, OMe), 3.40 (m_c, 1 H, 4-H), 3.45 (dt, J = 3.5, 5.4 Hz, 1 H, 5-H), 3.67 (dd, J = 8.3, 9.2 Hz, 1 H, 5′-H_A), 3.75 (dd, J = 5.4, 11.9 Hz, 1 H, 6-H_A), 3.98 (dd, J = 3.5, 11.9 Hz, 1 H, 6-H_B), 4.09 (dd, J = 5.5, 8.3 Hz, 1 H, 5′-H_B), 4.39–4.44 (m, 1 H, 4′-H), 3.84, 4.41 (2 d, J = 14.9 Hz, 1 H each, NCH_2Ph), AB system (δ_A = 4.63 ppm, δ_B = 4.59 ppm, J_{AB} = 12.1 Hz, 2 H, OCH_2Ph), 7.19–7.40 (m, 10 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.2, 26.7 (2 q, Me), 58.0 (q, OMe), 60.2 (t, NCH_2Ph), 65.5 (d, C-3), 66.7 (t, C-5′), 68.8 (t, C-6), 71.8 (t, OCH_2Ph), 68.7, 74.2, 80.1 (3 d, C-4, C-5, C-4′), 108.3 (s, C-2′), 126.5, 127.6, 127.7, 127.9, 128.3, 128.3, 138.2, 139.0 (6 d, 2 s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 2985–2830 (CH) cm^{-1}. MS (EI): m/z (%) = 413 (4) [M$^+$], 398 (2) [M$^+$ – Me], 312 (100) [M$^+$ – $C_5H_9O_2$], 178 (12), 91 (36) [Bn$^+$]. $C_{24}H_{31}NO_5$ (413.5): calcd. C 69.71, H 7.56, N 3.39; found C 69.44, H 7.47, N 3.22.

(4*S*,1′*S*,2′*R*,3′*R*)-4-(1′-Benzylamino-3′-benzyloxy-4′-hydroxy-2′-methoxybut-1′-yl)-2,2-dimethyl-1,3-dioxolane (6): 1,2-Diiodoethane (2.48 g, 8.80 mmol) and samarium (1.65 g, 11.0 mmol) were transferred into a dry flask under argon. THF (50 mL) was added, and the solution was stirred. After the solution had turned blue, the mixture was stirred at room temp. for 2 h. 1,2-Oxazine **5** (0.910 g, 2.20 mmol) was added, and the reaction mixture was stirred at room temp. for 3.5 h, then quenched with $NaHCO_3$ (satd.; 20 mL) solution. The filtrate was decanted from the residue, and the solvent was removed to yield amino alcohol **6** (495 mg, 98%) as pale yellow oil. $[\alpha]_D^{20}$ = –7.8 ($CHCl_3$, c = 1.2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.36, 1.42 (2 s, 3 H each, Me), 3.08 (dd, J = 2.2, 7.5 Hz, 1 H, 1′-H), 3.35 (s, 3 H, OMe), 3.41 (dd, J = 2.2, 6.6 Hz, 1 H, 2′-H), 3.64 (td, J = 4.0, 6.6 Hz, 1 H, 3′-H), 3.72 (d, J = 4.0 Hz, 2 H, 4′-H), 3.77 (dd, J = 7.5, 8.3 Hz, 1 H, 5-H_A), 4.02 (dd, J = 6.3, 8.3 Hz, 1 H, 5-H_B), 3.98, 4.03 (2 d, J = 12.6 Hz, 1 H each, NCH_2Ph), 4.11 (br. s, 2 H, NH, OH), 4.40 (dt, J = 6.3, 7.5 Hz, 1 H, 4-H), 4.59, 4.69 (2 d, J = 11.8 Hz, 1 H each, OCH_2Ph), 7.23–7.35 (m, 10 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.3, 26.5 (2 q, Me), 51.6 (t, NCH_2Ph), 58.0 (d, C-1′), 59.2 (q, OMe), 59.6 (t, C-4′), 67.1 (t, C-5), 71.9 (t, OCH_2Ph), 76.1 (d, C-4), 77.9 (d, C-3′), 81.4 (d, C-2′), 108.9 (s, C-2), 127.3, 127.5, 127.7, 128.2, 128.4, 128.4, 138.2, 138.8 (6 d, 2 s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3340 (NH, OH), 3030–2935 (CH) cm^{-1}. MS (EI): m/z (%) = 415 (< 1) [M$^+$], 400 (3) [M$^+$ – Me], 314 (5) [M$^+$ $C_5H_9O_2$], 220 (50), 91 (100) [Bn$^+$]. $C_{24}H_{33}NO_5$ (415.5): calcd. C 69.37, H 8.00, N 3.37; found C 69.07, H 7.95, N 3.08.

(2*S*,3*R*,4*R*,4′*S*)-1-Benzyl-4-benzyloxy-2-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-methoxypyrrolidine (7): The crude amino alcohol **6**

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(0.913 g, 2.20 mmol) was dissolved CH_2Cl_2 (40 mL), and mesyl chloride (0.378 g, 3.30 mmol) and triethylamine (1.34 g, 13.2 mmol) were added. After stirring at room temp. for 15 h, H_2O (20 mL) was added. The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL), the combined extracts were dried with $MgSO_4$, and the solvents were removed in vacuo. The crude product **7** was purified by column chromatography (aluminum oxide; hexane/EtOAc, 7:1). Compound **7** was obtained as a colourless oil (0.720 g, 82%). $[\alpha]_D^{20}$ = +91.7 ($CHCl_3$, *c* = 0.96). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35, 1.43 (2 s, 3 H each, Me), 2.25 (dd, *J* = 6.1, 10.2 Hz, 1 H, 5-H_A), 2.92 (dd, *J* = 6.3, 8.0 Hz, 1 H, 2-H), 3.30 (s, 3 H, OMe), 3.31 (dd, *J* = 6.1, 10.2 Hz, 1 H, 5-H_B), 3.42, 4.49 (2 d, *J* = 13.3 Hz, 1 H each, NCH_2Ph), 3.63 (dd, *J* = 2.4, 6.3 Hz, 1 H, 3-H), 3.64 (t, *J* = 8.0 Hz, 1 H, 5′-H_A), 3.92 (dt, *J* = 2.4, 6.1 Hz, 1 H, 4-H), 4.19 (dd, *J* = 6.4, 8.0 Hz, 1 H, 5′-H_B), 4.36 (dt, *J* = 6.4, 8.0 Hz, 1 H, 4′-H), AB system (δ_A = 4.44 ppm, δ_B = 4.43 ppm, J_{AB} = 11.6 Hz, 2 H, OCH_2Ph), 7.21–7.38 (m, 10 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.5, 26.7 (2 q, Me), 57.1 (q, OMe), 57.5 (t, C-5), 59.2 (t, N*C*H_2Ph), 67.5 (t, C-5′), 68.7 (d, C-2), 71.4 (t, O*C*H_2Ph), 80.8 (d, C-4), 86.5 (d, C-3), 108.7 (s, C-2′), 126.7, 127.5, 127.7, 128.0, 128.4, 129.1, 137.8, 139.1 (6 d, 2 s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3030–2820 (CH) cm^{-1}. MS (EI): *m*/*z* (%) = 397 (< 1) [M^+], 382 (3) [M^+ – Me], 296 (100) [$M^+ - C_5H_9O_2$], 91 (39) [Bn^+]. $C_{24}H_{31}NO_4$ (397.5): calcd. C 72.52, H 7.86, N 3.52; found C 72.29, H 7.66, N 3.46.

(2*S*,3*R*,4*R*,4′*S*)-1-Benzyl-4-benzyloxy-2-(1′,2′-dihydroxyethyl)-3-methoxypyrrolidine (8): To a stirred solution of **7** (0.530 g, 1.33 mmol) in MeOH (10 mL) a solution of *p*-toluenesulfonic acid (0.380 g, 2.00 mmol) in MeOH (5 mL) was added. The solution was stirred at room temp. for 2 d, and then aqueous $NaHCO_3$ solution (satd.) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined extracts were dried with $MgSO_4$. After evaporation of the solvent in vacuo, the crude product was purified by column chromatography (silica gel; CH_2Cl_2/MeOH, 9:1) giving rise to pure pyrrolidine **8** (0.470 g, 99%) as a colourless oil. $[\alpha]_D^{20}$ = +15.8 ($CHCl_3$, *c* = 0.48). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.47 (dd, *J* = 6.3, 10.6 Hz, 1 H, 5-H_A), 3.19 (dd, *J* = 5.8, 10.7 Hz, 1 H, 5-H_B), 3.28 (dd, *J* = 4.6, 7.9 Hz, 1 H, 2-H), 3.43 (s, 3 H, OMe), 3.66 (dd, *J* = 5.8, 11.0 Hz, 1 H, 2′-H_A), 3.74 (dd, *J* = 4.6, 11.0 Hz, 1 H, 2′-H_B), 3.87 (td, *J* = 4.6, 5.8 Hz, 1 H, 1′-H), 3.97 (dd, *J* = 5.4, 7.9 Hz, 1 H, 3-H), 3.63, 4.03 (2 d, *J* = 12.9 Hz, 1 H each, NCH_2Ph), 4.06 (br. q, *J* ≈ 5.8 Hz, 1 H, 4-H), AB system (δ_A = 4.51 ppm, δ_B = 4.53 ppm, J_{AB} = 11.7 Hz, 2 H, OCH_2Ph), 7.25–7.35 (m, 10 H, Ph) ppm; the OH signals have not been observed. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 54.8 (t, C-5), 58.5 (q, OMe), 61.6 (t, N*C*H_2Ph), 65.1 (d, C-2), 65.3 (t, C-2′), 68.7 (d, C-1′), 71.9 (t, O*C*H_2Ph), 82.0 (d, C-4), 85.8 (d, C-3), 127.3, 127.4, 127.7, 128.0, 128.4, 128.8, 137.9, 138.2 (6 d, 2 s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3415 (OH), 2930–2830 (CH) cm^{-1}. MS (EI): *m*/*z* (%) = 357 (< 1) [M^+], 326 (6) [M^+ – OMe], 296 (100) [$M^+ - C_2H_5O_2$], 91 (85) [Bn^+]. HRMS (EI): calcd. for $C_{20}H_{24}NO_3$ [M^+ – OMe] 326.1756; found 326.1783.

(2*S*,3*R*,4*R*,4′*S*)-2-(1′,2′-Dihydroxyethyl)-3-methoxy-4-hydroxypyrrolidine Hydrochloride (9): A stirred suspension of Pd/C (10%, 0.101 g, 0.095 mmol) in MeOH (10 mL) was saturated with hydrogen for 1 h. Then HCl/MeOH (satd., 0.6 mL) and a solution of pyrrolidine **8** (0.170 g, 0.476 mmol) in MeOH (5 mL) were added, and the mixture was stirred under hydrogen at normal pressure at room temp. for 22 h. Filtration through a pad of Celite and removal of the solvent in vacuo yielded spectroscopically pure hydrochloride **9** (0.130 g, 100% = 0.102 g) as a pale yellow oil. Since the mass of the product isolated is higher than 100%, it probably contains more than 1 equiv. of HCl. $[\alpha]_D^{20}$ = +18.4 (MeOH, *c* = 1.79). ^{1}H NMR (500 MHz, CD_3OD): δ = 3.14 (d, *J* = 12.2 Hz, 1 H, 5-H_A), 3.42 (s, 3 H, OMe), 3.46 (dd, *J* = 3.7, 12.2 Hz, 1 H, 5-H_B), 3.59 (dd, *J* = 4.1, 11.6 Hz, 1 H, 2′-H_A), 3.68 (dd, *J* = 3.5, 11.6 Hz, 1 H, 2′-H_B), 3.80–3.84 (m, 2 H, 2-H, 3-H), 4.01 (td, *J* ≈ 4.0, 8.3 Hz, 1 H, 1′-H), 4.52 (d, *J* = 3.7 Hz, 1 H, 4-H) ppm. ^{13}C NMR (126 MHz, CD_3OD): δ = 52.0 (t, C-5), 58.5 (q, OMe), 64.4 (d, C-2), 64.7 (t, C-2′), 69.0 (d, C-1′), 72.0 (d, C-4), 84.9 (d, C-3) ppm. MS (EI): *m*/*z* (%) = 212 (< 1) [M^+ – H], 177 (1) [M^+ – HCl], 160 (1) [M^+ – HCl – OH], 146 (7) [M^+ – HCl – CH_2OH], 116 (100) [M^+ – HCl – $C_2H_5O_2$], 36 (63) [HCl].

(4*S*,1′*R*,2′*R*,3′*R*)-4-{1′-Benzylamino-3′,4′-dihydroxy-2′-[2-(trimethylsilyl)ethoxy]but-1′-yl}-2,2-dimethyl-1,3-dioxolane (10): By a procedure similar to that for **5**, compound **2b** (500 mg, 1.22 mmol) was treated with samarium diiodide generated from samarium (656 mg, 4.39 mmol) and 1,2-diiodoethane (1.14 g, 4.03 mmol) for 3 h yielding amino alcohol **10** (495 mg, 98%) as a pale yellow oil. This product was not further purified and used directly for the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 (s, 9 H, $SiMe_3$), 0.54 (m_c, 2 H, CH_2Si), 1.32, 1.38 (2 s, 3 H each, Me), 2.90 (dd, *J* = 2.5, 7.4 Hz, 1 H, 1′-H), 3.32 (dd, *J* = 2.5, 5.2 Hz, 1 H, 2′-H), 3.43–3.60 (m, 4 H, 5-H_A, 4′-H_A, OCH_2), 3.76 (d, *J* = 13.7 Hz, 1 H, NCH_2Ph), 3.77 (m_c, 1 H, 3′-H), 3.86 (m_c, 1 H, 4′-H_B), 3.92 (d, *J* = 13.7 Hz, 1 H, NCH_2Ph), 4.03 (dd, *J* = 6.3, 8.4 Hz, 1 H, 5-H_B), 4.34 (dt, *J* = 6.3, 7.4 Hz, 1 H, 4-H), 7.21–7.38 (m, 5 H, Ph) ppm; signal of OH not detected. ^{13}C NMR (126 MHz, $CDCl_3$): δ = –1.5 (q, $SiMe_3$), 18.8 (t, CH_2Si), 25.4, 26.7 (2 q, Me), 51.6 (t, C-4′), 59.0 (d, C-1′), 63.0 (t, CH_2Ph), 67.1 (t, C-5), 68.4 (t, OCH_2), 71.0 (d, C-3′), 77.8 (d, C-4), 79.3 (d, C-2′), 108.8 (s, C-2), 127.9, 129.2, 129.3, 139.0 (3 d, s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3340 (OH), 3090–3030 (=CH), 2980–2890 (CH) cm^{-1}. MS (EI): *m*/*z* (%) = 412 (4) [M^+], 101 (18) [$C_2H_5OSiMe_3^+$], 91 (86) [CH_2Ph^+], 73 (100) [$SiMe_3^+$].

(2*S*,3*R*,4*R*,4′*S*)-1-Benzyl-2-(2′,2′-dimethyl-1′,3′-dioxolan-4-yl)-3-[2-(trimethylsilyl)ethoxy]-4-methylsulfonyloxypyrrolidine (11): By a procedure similar to that for **6**, crude **10** (500 mg, 1.21 mmol) was treated with mesyl chloride (261 mg, 2.38 mmol) and triethylamine (370 mg, 3.66 mmol) in CH_2Cl_2 (30 mL) for 1 d. Purification was performed by column chromatography (silica gel; hexane/EtOAc, 3:1) to yield mesylate **11** (340 mg, 60%) as colourless crystals. M.p. 55–57 °C. $[\alpha]_D^{22}$ = +67.5 ($CHCl_3$, *c* = 0.35). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 (s, 9 H, $SiMe_3$), 0.89 (m_c, 2 H, CH_2Si), 1.37, 1.42 (2 s, 3 H each, Me), 2.43 (dd, *J* = 5.2, 11.1 Hz, 1 H, 5-H_A), 2.91 (s, 3 H, Ms), 2.97 (dd, *J* = 6.4, 7.8 Hz, 1 H, 2-H), 3.36–3.45 (m, 2 H, OCH_2, 5-H_B), 3.54 (d, *J* = 13.5 Hz, 1 H, NCH_2Ph), 3.63 (t, *J* ≈ 8.0 Hz, 1 H, 5′-H_A), 3.70 (m_c, 1 H, OCH_2), 3.91 (dd, *J* = 2.6, 6.4 Hz, 1 H, 3-H), 4.16 (dd, *J* = 6.4, 8.0 Hz, 1 H, 5′-H_B), 4.34 (dt, *J* = 6.4, 7.8 Hz, 1 H, 4′-H), 4.39 (d, *J* = 13.5 Hz, 1 H, NCH_2Ph), 4.93 (ddd, *J* = 2.6, 5.2, 6.3 Hz, 1 H, 4-H), 7.22–7.39 (m, 5 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = –1.2 (q, $SiMe_3$), 18.2 (t, CH_2Si), 26.2, 27.0 (2 q, Me), 38.3 (q, Ms), 56.1 (t, C-5), 59.0 (t, NCH_2Ph), 72.3 (d, C-2), 72.4 (t, C-5′), 72.6 (t, OCH_2), 77.5 (d, C-4′), 81.2 (d, C-4), 83.3 (d, C-3), 108.0 (s, C-2′), 126.9, 128.2, 129.0, 138.7 (3 d, s, Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3025–2950 (=CH), 2895–2805 (CH), 1030 (SO_2) cm^{-1}. MS (EI): *m*/*z* (%) = 471 (< 1) [M^+], 456 (2) [$M^+ - CH_3$], 370 (100) [$M^+ - C_2H_5OSiMe_3$], 101 (5) [$C_2H_5OSiMe_3^+$], 91 (75) [$C_7H_7^+$], 73 (32) [Me_3Si^+]. HRMS (EI): calcd. for $C_{22}H_{37}NO_6SSi$ [M^+] 471.2111; found 471.2144.

(2*S*,3*R*,4*R*,4′*S*)-1-Benzyl-2-(2′,2′-dimethyl-1′,3′-dioxolan-4-yl)-4-hydroxy-3-[2-(trimethylsilyl)ethoxy]pyrrolidine (12): *n*BuLi (2.0 M in hexanes, 0.210 mL, 0.410 mmol) was added to diisopropylamine (0.060 mL, 0.410 mmol) in THF (1 mL) at –78 °C. At this temperature mesylated pyrrolidine derivative **11** (120 mg, 0.257 mmol) was added to the previously generated LDA solution. The reaction mix-

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ture was stirred at –78 °C and then at room temp. for 7 h and then quenched with NH_4Cl solution (satd.) followed by addition of EtOAc. The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried, filtered and concentrated to yield pyrrolidine derivative **12** (91 mg, 90%) as colourless oil. $[a]_D^{22}$ = +61.6 ($CHCl_3$, *c* = 0.35). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.00 (s, 9 H, $SiMe_3$), 0.90 (m_c, 2 H, CH_2Si), 1.37, 1.42 (2 s, 3 H each, Me), 2.19 (dd, *J* = 6.0, 10.2 Hz, 1 H, 5-H_A), 2.98 (dd, *J* = 7.1, 8.0 Hz, 1 H, 2-H), 3.24 (dd, *J* = 6.2, 10.2 Hz, 1 H, 5-H_B), 3.39 (ddd, *J* = 5.5, 9.4, 10.7 Hz, 1 H, OCH_2), 3.54 (d, *J* = 13.5 Hz, 1 H, NC*H*$_2$Ph), 3.58 (m_c, 1 H, OCH_2), 3.60 (dd, *J* = 3.4, 6.6 Hz, 1 H, 5′-H_A), 3.63 (d, *J* = 8.0 Hz, 1 H, 3-H), 4.17 (m_c, 2 H, 4-H, 5′-H_B), 4.35 (m_c, 1 H, 4′-H), 4.36 (d, *J* = 13.5 Hz, 1 H, NC*H*$_2$Ph), 7.22–7.39 (m, 5 H, Ph) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = –1.4 (q, $SiMe_3$), 18.6 (t, CH_2Si), 25.4, 26.8 (2 q, Me), 59.2 (t, C-5), 59.3 (t, NC*H*$_2$Ph), 67.3 (t, OCH_2), 67.7 (t, C-5′), 68.0 (d, C-2), 74.8 (d, C-4), 78.2 (d, C-4′), 86.2 (d, C-3), 108.6 (s, C-2′), 126.7, 128.0, 129.1, 138.7 (3 d, s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3435 (OH), 3085–3025 (=CH), 2895–2805 (CH), 1250 (CO) cm^{-1}. MS (EI): *m*/*z* (%) = 393 (1) [M^+], 378 (2) [$M^+ - CH_3$], 350 (1) [$M^+ - SiMe_3$], 292 (82) [$M^+ - C_2H_5O_2$], 91 (100) [$C_7H_7^+$], 73 (49) [Me_3Si^+]. HRMS (EI): calcd. for $C_{21}H_{35}NO_4Si$ [M^+]: 393.2336; found 393.2353.

(2*S*,3*R*,4*R*,2′*S*)-2-(1,2-Dihydroxyethyl)pyrrolidine-3,4-diol Hydrochloride (13): To a solution of pyrrolidine derivative **12** (70 mg, 0.180 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added $BF_3{\cdot}Et_2O$ (63 µL, 0.590 mmol), and the resulting solution was stirred at 0 °C for 5 min, then at room temp. for 6 h, and then quenched with H_2O (ca. 1 mL). The two layers were separated, and the aqueous layer was extracted several times with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under vacuum to yield the respective *O*-deprotected compound (41 mg, 90%) as colourless oil. $[a]_D^{22}$ = +10.0 (*c* = 0.90, MeOH). ^1H NMR (500 MHz, CD_3OD): δ = 3.22 (dd, *J* = 1.6, 12.5 Hz, 1 H, 5-H_B), 3.48 (dd, *J* = 3.0, 12.5 Hz, 1 H, 5-H_A), 3.69 (dd, *J* = 3.8, 11.7 Hz, 1 H, 1′-H_B), 3.79 (dd, *J* = 3.2, 11.7 Hz, 1 H, 1′-H_A), 3.95 (dd, *J* = 3.8, 10.1 Hz, 1 H, 2-H), 4.21 (d, *J* = 12.6 Hz, 1 H, NC*H*$_2$Ph), 4.24 (dd, *J* = 1.6, 3.0 Hz, 1 H, 4-H), 4.30 (m_c, 2 H, 3-H, 2′-H), 4.99 (d, *J* = 12.6 Hz, 1 H, NC*H*$_2$Ph), 7.46–7.54 (m, 5 H, Ph) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 57.6 (t, C-5), 64.7 (t, C-1′), 65.0 (t, NC*H*$_2$Ph), 70.2 (d, C-2′), 74.5 (d, C-2), 75.1 (d, C-3), 76.6 (d, C-4), 130.3, 131.0, 131.9, 139.4 (3 d, s, Ph) ppm. IR (neat): $\tilde{\nu}$ = 3475, 3445 (O–H), 3090–3030 (=C–H), 2960–2855 (C–H) cm^{-1}. MS (FAB): *m*/*z* (%) = 254 (64) [$M^+ + H$], 236 (6) [$M^+ - OH$], 91 (100) [$C_7H_7^+$]. $C_{13}H_{19}NO$ (253.3): C 61.64, H 7.56, N 5.53; C 60.97, H 7.31, N 5.43. A stirred solution of Pd on charcoal (12 mg, 0.060 mmol) in MeOH (2 mL) was saturated with hydrogen for 1 h. Then a solution of the *O*-deprotected compound (21 mg, 0.083 mmol) in MeOH (2 mL) was added followed by addition of a methanolic HCl solution (1 mL), and the mixture was stirred under hydrogen at normal pressure at room temp. for 1 d. Filtration through a pad of Celite and removal of the solvent in vacuo yielded hydrochloride **13** in (17 mg, quant.) as pale yellow crystals. M.p. 153–155 °C. $[a]_D^{20}$ = +3.7 (MeOH, *c* = 0.40) {ref.[25] 157–158 °C; $[a]_D^{22}$ = +1.95 (H_2O, *c* = 3)}. ^1H NMR (500 MHz, CD_3OD): δ = 3.11 (d, *J* = 12.5 Hz, 1 H, 5-H_A), 3.52 (d, *J* = 12.5 Hz, 1 H, 5-H_B), 3.62 (d, *J* = 11.3 Hz, 1 H, 1′-H_A), 3.70 (d, *J* = 11.3 Hz, 1 H, 1′-H_B), 3.75 (d, *J* = 7.6 Hz, 1 H, 2-H), 4.03 (m_c, 1 H, 2′-H), 4.13 (m_c, 1 H, 3-H), 4.29 (m_c, 1 H, 4-H) ppm. ^{13}C NMR (126 MHz, CD_3OD): δ = 52.2 (t, C-5), 64.7 (d, C-2), 65.1 (t, C-1′), 69.6 (d, C-2′), 75.8 (d, C-3), 76.3 (d, C-4) ppm. IR (KBr): $\tilde{\nu}$ = 3445 (OH), 2895–2805 (CH), 1250 (CO) cm^{-1}. MS (EI): *m*/*z* (%) = 163 (21) [M^+ – HCl], 36 (100) [HCl^+]. MS (FAB): *m*/*z* = 164 (100) [M^+ – Cl].

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