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Practical synthesis of *trans*-dihydroxybutyrolactols as chiral C_4 building blocks and their application to the synthesis of polyhydroxylated alkaloids†

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Practical syntheses of *trans*-dihydroxybutyrolactols **2a**, **2b** and **2c** from inexpensive chiral pool compounds L-ascorbic, D- and L-tartaric acid have been achieved on a multigram-scale. The synthetic applications of these chiral building blocks have been demonstrated in the efficient total or formal synthesis of polyhydroxylated alkaloids (+)-lentiginosine and (−)-deacetylanisomycin in concise routes.

Introduction

Structural motifs containing vicinal chiral polyhydroxy groups are ubiquitous and commonly found in natural products with therapeutic significance, exemplified by polyhydroxylated alkaloids. In the past few decades, more than 100 polyhydroxylated alkaloids have been isolated, which can be categorised into pyrrolidines, piperidines, pyrrolizidines, indolizines and nortropanes based on their structural skeletons (Fig. 1). Polyhydroxylated alkaloids have also been classified as iminosugars or azasugars due to their structural similarity to carbohydrates. As a result, these iminosugars have been used as carbohydrate mimics to inhibit various glycosidases in a reversible or competitive manner, as well as tested for anticancer, anti-HIV and immunoregulatory activities.[1] The natural abundance of polyhydroxylated alkaloids and their remarkable, diverse bioactivities have stimulated much interest in the total synthesis of these compounds.[2] However, one of the major challenges of their total syntheses lies in the efficient and stereoselective construction of the contiguous polyhydroxy groups. Despite the significant advancement in the enantio- and diastereoselective construction of polyhydroxy systems, such as asymmetric dihydroxylation and epoxidation reactions, the most common and powerful strategy remains to be the 'chiron' approach in which chiral building blocks (or synthons) generated from readily available, optically pure natural molecules are used as the starting materials.

Among the polyhydroxy chiral synthons, dihydroxybutyrolactols (Scheme 1, **1a–d**) have long been recognized as valuable, versatile building blocks and been widely utilized in the total synthesis of natural products. The general strategy of the synthetic application of dihydroxybutyrolactols includes nucleophilic addition and Wittig reactions on the lactol moiety, which is the equivalent of a masked aldehyde, to enable C–C bond

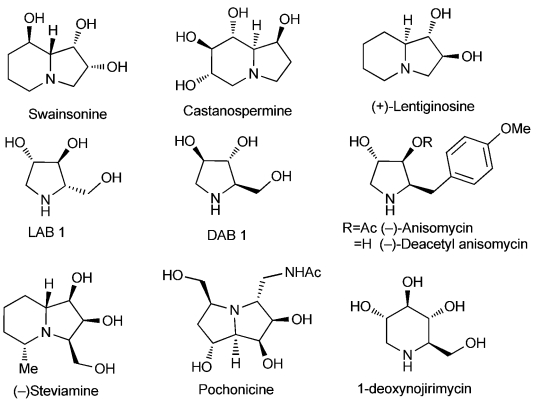
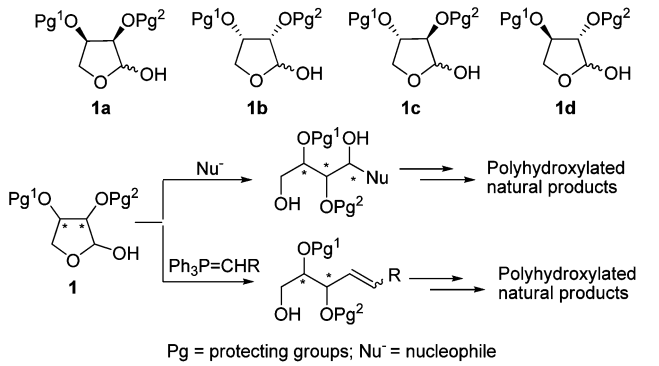


Fig. 1 Representative bioactive naturally occurring polyhydroxylated alkaloids.



Scheme 1 Dihydroxybutyrolactols as building blocks.

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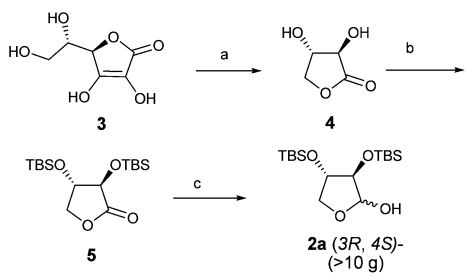
formation and further chemical transformations and functionalisations.[3] However, the successful application of this strategy has mainly been limited to *cis*-dihydroxybutyrolactols whereas that of *trans*-dihydroxybutyrolactols is much less explored.[4] In conjunction with our continuing efforts in the exploration of new synthetic applications of dihydroxybutyrolactols as building blocks,[5] we report herein practical and scalable syntheses of *trans*-dihydroxybutyrolactols (**1c** and **1d**) and their application in the synthesis of polyhydroxylated alkaloids.

Results and discussion

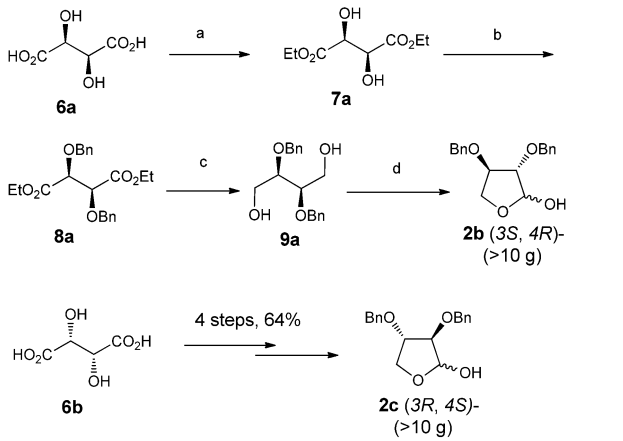
Our study commenced with the development of practical synthetic routes to *trans*-dihydroxybutyrolactols. We first examined the synthesis of lactone **4**, a precursor to lactol **1c**, from L-ascorbic acid (**3**) in a way similar to that for the preparation of D-(−)-erythronolactone from D-ascorbic acid.[6] Although D-(−)-erythronolactone is commercially available and can be readily prepared, the synthesis of its diastereomeric analogue **4** is challenging due to its highly hygroscopic nature. Nevertheless, by modifying Tenji's two-step procedure,[7] notably by addition of sodium chloride to facilitate water removal and extraction after evaporation, we were able to obtain **4** from **3** in near 80% yield in 15 gram scale. Bis-TBS protection followed by DIBAL-H reduction and quenching the reaction at a low temperature (−78 °C) provided the protected *trans*-dihydroxylactol **2a** in nearly 70% overall yield and >10 gram scale from **3** (Scheme 2).

We next investigated the practical synthesis of **2b** which is the enantiomer of **2a** using D-tartaric acid **6a** as the starting material (Scheme 3). Esterification followed by benzyl protection of **6a** afforded **8a** in excellent yield. Reduction of **8a** with KBH_4/LiCl led to 1,4-diol **9a** in 85% yield. Selective oxidation of **9a** by 2-iodoxybenzoic acid (IBX) in DMSO produced the desired lactol **2b** in 87% yield. The lactol **2c**, which is the benzyl protected equivalent of **2a**, was obtained in 64% overall yield in the same sequence from L-tartaric acid **6b**. These short routes provide convenient and practical access to both TBS and benzyl protected *trans*-dihydroxybutyrolactols (**2a–c**) in multigram scales for synthetic applications.

Although the reaction of protected *cis*-dihydroxybutyrolactol with Grignard reagents at low temperature is well known to form *anti* product with high diastereoselectivity,[8] the reaction of



Scheme 2 *Reagents and conditions*: (a) (i) Na_2CO_3, H_2O_2, 5–15 °C then charcoal, 75 °C; (ii) 6 M HCl, pH 1.5, evap. to dry, extract with EtOAc at reflux, 79%; (b) TBSCl, imidazoles, DMF, 0 °C–rt, 93%; (c) DIBAL-H, THF, −78 °C, 1 h then methanol, 1.0 M HCl pH 3, 94%.



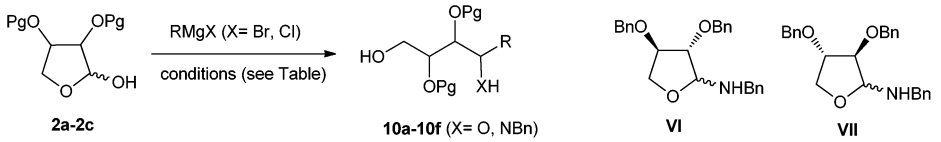
Scheme 3 Synthesis of **2b** and **2c** from tartaric acid. (a) H_2SO_4 (cat. amount), EtOH, reflux, 98%; (b) BnBr, Ag_2O, rt, 48 h, 88%; (c) LiCl, KBH_4, THF, reflux, 85%; (d) IBX, DMSO, rt, 5 h, 87%.

protected *trans*-dihydroxybutyrolactols is much less studied.[4a,9] With the protected *trans*-dihydroxylactols (**2a–c**) in hand, we set out to investigate their reaction with various Grignard reagents (Table 1). The reaction with various organomagnesium reagents under different conditions (Table 1, entry 1–6) afforded the addition products in excellent yields and in modest *syn* selectivity (*ca.* 3.6 : 1) as determined by ^{1}H NMR analysis of the product. This level of selectivity is consistent with those reported in the literature[4a,9] and appeared to be not sensitive to temperature as reactions carried out at both −78 °C and 0 °C gave very similar selectivities (Table 1, entry 3, 4). The stereochemistry of the products was confirmed by ^{1}H NMR spectroscopic correlation of lactones **II** and **III** to known close analogues **IV** and **V** (ref. 10) (Scheme 4). Thus, consecutive oxidation with IBX and Dess–Martin periodinane (DMP) of diastereomeric mixture **10a** (*syn* : *anti* = 3.6 : 1) led to the corresponding lactones (**II** and **III**). ^{1}H NMR spectra analyses revealed that the lactone **II** derived from the major *syn*-diastereomer has a smaller H-4, H-5 coupling constant of 4.8 Hz in agreement with the known **IV** whereas **III** derived from the *anti*-isomer has a larger coupling constant of 6.6 Hz similar to **V**. The *syn* stereochemistry of the major diastereomer was further confirmed in the synthesis of (+)-lentiginosine (Scheme 5, *vide infra*).

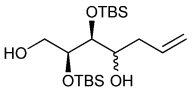
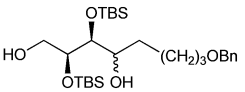
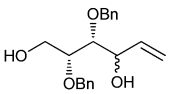
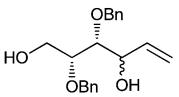
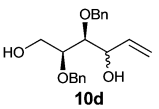
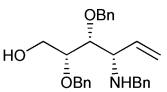
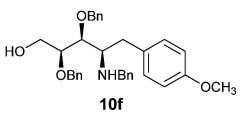
In sharp contrast, the reaction of Grignard reagents with the corresponding *N*,*O*-acetals (**VI** and **VII**) formed *in situ* afforded predominantly (>99 : 1) the *syn* amino alcohols (Table 1, entry 6, 7). The high *syn* selectivity is attributed to the good coordinate probability of imine to form a strong Cram chelation control model.[11]

Despite modest *syn*-selectivity in the Grignard addition reaction, in view of the convenient and scalable access to the chiral lactol building blocks and high yielding of the reaction, we sought to explore their application in the synthesis of natural products. (+)-Lentiginosine, an indolizidine alkaloid with potent and selective amyloglucosidase inhibition activity,[12,13] was selected as an appropriate target for synthetic studies. As depicted in Scheme 5, permesylation of the diastereomeric 1,4-diol mixture **10b** (*syn* : *anti* = 3.6 : 1) obtained from the addition of $BnO(CH_2)_4MgBr$ to **2a** (Table 1, entry 2) led to the

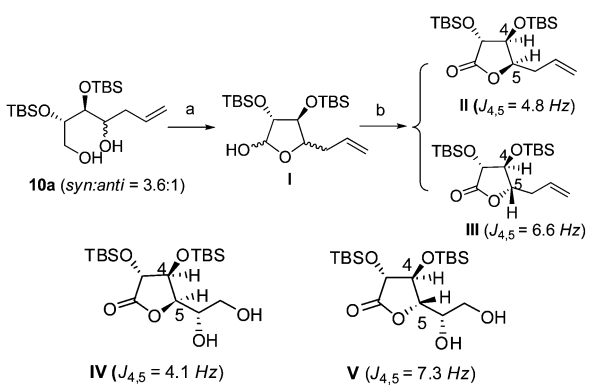
Table 1 Addition reactions to *trans*-dihydroxylactols



2a-2c **10a-10f** (X= O, NBn) **VI** **VII**

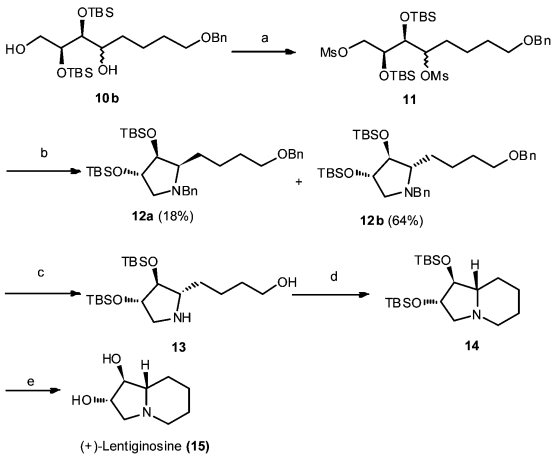
Entry	Substrate	RMgX and conditions	Product	Yield[a] (%)	*Syn* : *anti*[b]
1	**2a**	CH_2=$CHCH_2MgBr$ Et_2O/−78 °C	 **10a**	96	3.6 : 1
2	**2a**	$BnO(CH_2)_4MgBr$ THF/0 °C	 **10b**	93	3.6 : 1
3	**2b**	CH_2=CHMgCl THF/−78 °C	 **10c**	96	3.8 : 1
4	**2b**	CH_2=CHMgCl THF/0 °C	 **10c**	91	3.6 : 1
5	**2c**	CH_2=CHMgCl THF/0 °C	 **10d**	92	3.7 : 1
6	**2b**	(i) Benzylamine, 4 Å MS; (ii) CH_2=CHMgCl THF/0 °C–rt	 **10e**	80	>99 : 1
7	**2c**	(i) Benzylamine, 4 Å MS; (ii) *p*-CH_3O–$C_6H_4CH_2MgCl$ THF/0 °C–rt	 **10f**	83	>99 : 1

[a] Isolated yields. [b] Determined by ^{1}H NMR spectroscopic analysis.



Scheme 4 Stereochemistry confirmation of the Grignard addition products. (a) IBX, DMSO, rt, 5 h; 80%; (b) DMP, CH_2Cl_2, rt, 4 h, 62% for **II** and 17% for **III**.

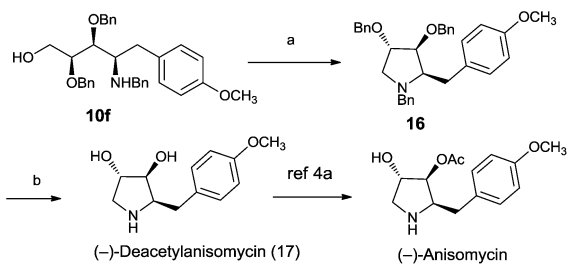
corresponding bismesylate **11**. Treatment of **11** with freshly distilled benzylamine led to the formation of diastereomeric pyrrolidines **12a** and **12b** *via* an efficient one-pot displacement–cyclization sequence. The diastereomeric mixture was fortunately separable by column chromatography, providing pure **12a** and **12b** in 18% and 64% yields respectively. However, removal of the benzyl groups of **12b** proved to be quite difficult. After examining various conditions, we finally found that under hydrogenolysis conditions [$Pd(OH)_2$/C and Pd/C successively, H_2, 1 atm] over four days, alcohol **13** was obtained in 65% yield. Further intramolecular cyclization of **13** *via* a one-pot Appel reaction-cyclization[14] led to TBS-protected (+)-lentiginosine **14** in 88% yield. Final TBS deprotection of **14** using TBAF furnished an efficient total synthesis of (+)-lentiginosine (**15**) in 5 steps and 25% overall yield from TBS protected *trans*-dihydroxylactol **2a**. Comparison of the optical rotation of **15** with the reported value (see Experimental section) confirmed the stereochemistry.



Scheme 5 Total synthesis of (+)-lentiginosine. (a) MsCl, pyridine, 0 °C, 12 h, 80%; (b) $BnNH_2$, 80 °C, 48 h, 18% for **12a**, 64% for **12b**; (c) $Pd(OH)_2/C$, H_2, 2 days then Pd/C, H_2, 4 days, 65%; (d) PPh_3, CCl_4, CH_2Cl_2, Et_3N, 0 °C–rt, 12 h, 88%; (e) TBAF, THF, overnight, 90%.

Having demonstrated the usefulness of the Grignard addition product in alkaloid synthesis, we further explored the synthetic applications of the amino alcohols, such as **10e**/**10f**, resulting from the reaction of *N*,*O*-acetals (**VI** and **VII**) with the Grignard reagents. These would be more advantageous for alkaloid synthesis as an amine moiety has already been installed with much higher stereoselectivity, which would avoid separating the undesired isomer. Envisioning that the amino alcohols **10e**/**10f** are the acyclic precursors of pyrrolidine alkaloids, we anticipated that molecules such as anisomycin (Fig. 1) could be accessed by concise synthetic sequences (Scheme 6).

(−)-Anisomycin is a pyrrolidine antibiotic isolated from the fermentation broths of *Streptomyces griseolus*. It exhibits strong and selective activity against pathogenic protozoa and fungi, and has been used clinically for the treatment of *Trichomonas vaginitis* and amoebic dysentery.[15] In addition, (−)-anisomycin has been shown to exhibit antiviral and antitumor activities.[16] Furthermore, both anisomycin and deacetylanisomycin have been employed as fungicides in the eradication of bean mildew and to inhibit other pathogenic fungi in plants.[17] Taking advantage of the highly stereoselective reaction of the *N*,*O*-acetal (**VII**) with 4-methoxybenzyl magnesium bromide, we envisioned that amino alcohol (**10f**) would provide an efficient synthesis of (−)-deacetylanisomycin[18] and a formal synthesis of (−)-anisomycin. Thus Appel reaction and *in situ* cyclization of **10f** led to perbenzylated pyrrolidine **16** in 90% yield. Global debenzylation by hydrogenolysis provided (−)-deacetylanisomycin (**17**) in 76% yield. Since it is well documented that (−)-anisomycin can be easily obtained from (−)-deacetylanisomycin,[4a] our synthetic route constitutes one of the most concise total syntheses of (−)-deacetylanisomycin and formal synthesis of (−)-anisomycin.



Scheme 6 Formal synthesis of (−)-anisomycin. (a) PPh_3, CCl_4, CH_2Cl_2, Et_3N, 0 °C–rt, 12 h, 90%; (b) $Pd(OH)_2/C$, H_2, 3 days, 76%.

Conclusion

In conclusion, we have developed two facile synthetic routes to *trans*-dihydroxybutyrolactols from inexpensive and abundant natural chiral starting materials. The overall high yield and simple chemical transformations enabled their large-scale syntheses, highlighting the potential industrial applications of these methodologies. Grignard reactions with these chiral lactols or their aza-analogues provided polyhydroxylated compounds or amino alcohols. The potential application of the Grignard addition products were successfully demonstrated in the concise synthesis of polyhydroxylated alkaloids (+)-lentiginosine and (−)-deacetylanisomycin.

Experimental section

General experimental procedures

Optical rotations were recorded on a Perkin-Elmer 341 automatic polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AV400 spectrometer. Unless otherwise indicated, ^1H NMR spectra were obtained in $CDCl_3$, and chemical shifts are expressed in parts per million (ppm) relative to internal Me_4Si standard. IR spectra were recorded on a Nicolet Avatar 360 FT-IR spectrophotometer using film or KBr pellet techniques. Mass spectra were recorded on Bruker Dalton Esquire 3000 plus LC-MS apparatus. HRMS spectra were recorded on a Bruker APEX-FTMS apparatus. Melting points were determined by a Yanaco MP-500 melting point apparatus and are uncorrected. Anhydrous solvents were obtained according to procedures provided in the literature.[19] Flash column chromatography was performed on silica gel (300–400 mesh, Zhifu Co Ltd, China) eluting with ethyl acetate (EtOAc) in petroleum ether (PE, 60–90 °C) mixture unless otherwise noted.

L-Threonic acid-4-lactone (4)

To a stirred cooled (~5 °C) solution of L-ascorbic acid (28.2 g, 0.16 mol) in water (300 mL) was added Na_2CO_3 (33.9 g, 0.32 mol) in portions. After 30 min, hydrogen peroxide (30% w/w, 35.2 mL) was added at a rate that maintained the reaction temperature at <15 °C. The resulting mixture was warmed to 40 °C and stirred for 30 min before portionwise addition of charcoal (Norite SG, 4.0 g). The temperature of the mixture was gradually raised to 75 °C and stirred until hydrogen peroxide had completely decomposed (negative as tested by starch potassium iodide paper). The mixture was allowed to cool to room temperature and filtered. The filtrate was acidified to pH 1.5 with 6.0 M HCl aqueous solution. Sodium chloride (70 g) was then added and the water was evaporated to dryness under high vacuum. The residue was

extracted with ethyl acetate (500 mL) by heating under reflux and filtered hot through Celite. The filter cake was washed with hot ethyl acetate (3 × 100 mL). The combined filtrates were evaporated under reduced pressure to give **4** (15.0 g, 79%) as a white solid. Mp 62–64 °C (ref. 20), 61–76 °C; $[\alpha]_D^{20}$ +28.3 (*c* 1.2, H_2O),[21] $[\alpha]_D^{20}$ +30.0 (*c* 1.0, H_2O); IR (film, cm^{-1}): 3353, 2916, 1775; ^1H NMR (500 MHz, CD_3COCD_3): δ 3.93 (dd, J = 6.5, 8.0 Hz, 1H, H-4), 4.23 (dd, J = 5.5, 6.5 Hz, 1H, H-2), 4.34–4.42 (m, 2H, H-3, H-4), 4.97 (d, J = 4.0 Hz, 1H, OH), 5.15 (d, J = 5.5 Hz, 1H, OH); ^{13}C NMR (125 MHz, D_2O): δ 69.7, 72.4, 73.3, 177.6.

(2*R*,3*S*)-2,3-Bis(*tert*-butyldimethylsilyloxy)-γ-butyrolactone (5)

To a solution of **4** (5.1 g, 43.6 mmol) in DMF (45 mL) was added imidazole (13.9 g, 203.0 mmol) and DMAP (265 mg). The mixture was stirred and cooled to 0 °C followed by dropwise addition of a solution of TBSCl (18.4 g, 122.0 mmol) in DMF (60 mL) in 60 min. The mixture was allowed to warm to rt and stirred overnight. The resulting mixture was diluted with CH_2Cl_2 (100 mL), washed sequentially with water (5 × 100 mL), and brine. The organic phase dried over anhydrous Na_2SO_4. Evaporation of the solvents under reduced pressure and purification of the crude product by flash chromatography on silica gel (PE : EtOAc = 20 : 1) afforded **5** (14.2 g, 94%) as a white solid. Mp 52–53 °C; $[\alpha]_D^{20}$ +46.9 (*c* 1.1, $CHCl_3$),[22] ***ent*-5** $[\alpha]_D^{20}$ −51.0 (*c* 1.0, $CHCl_3$); IR (film, cm^{-1}): 1801; ^1H NMR (400 MHz, $CDCl_3$): δ 0.09 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.15 (s, 3H, $SiCH_3$), 0.20 (s, 3H, $SiCH_3$), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.93 (s, 9H, $SiC(CH_3)_3$), 4.22 (d, J = 6.3 Hz, 1H, H-2), 4.31–4.37 (m, 2H, H-4), 3.87–3.92 (m, 1H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.0, −4.8, −4.7, −4.6, 17.9, 18.2, 25.6, 70.1, 74.5, 75.0, 173.9; ESI-HRMS calcd for $C_{16}H_{38}O_4NSi_2$ $(M + NH_4)^+$: 364.2334; found: 364.2337.

(2*R*,3*S*)-2,3-Bis(*tert*-butyldimethylsilyloxy)-γ-butyrolactol (2a)

A solution of **5** (11.2 g, 32.4 mmol) in DCM (100 mL) was stirred rapidly at −78 °C while a 1.0 M solution of DIBAL-H in toluene (35.6 mL, 35.6 mmol) was added dropwise under N_2 over a period of 30 min. The resulting reaction mixture was stirred for 1 h at −78 °C before being quenched by dropwise addition of methanol (10 mL) and further addition of a mixture of ethyl acetate and water (1 : 1 mixture, 120 mL). To the resulting mixture was then added 2 M aqueous sulfuric acid until pH 3. The mixture was transferred into a separatory funnel where upon the layers were separated and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with saturated aqueous sodium bicarbonate solution, then dried and evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel with PE : EtOAc (20 : 1) to afford **2a** (11.1 g, 94%) as a colorless oil. $[\alpha]_D^{20}$ +2.0 (*c* 0.5, $CHCl_3$); IR (film, cm^{-1}): 3510, 2955; ^1H NMR (400 MHz, $CDCl_3$) (diastereomixture 1.7 : 1, data of major isomer): δ 0.03–0.15 (m, 12H, $SiCH_3$), 0.89–0.93 (m, 18H, $SiC(CH_3)_3$), 3.68 (d, J = 12.2 Hz, 1H, OH), 3.99–4.05 (m, 3H, H-3, H-4), 4.08–4.13 (m, 1H, H-2), 5.04 (d, J = 12.2 Hz, 1H, H-1); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.0, −4.7, −4.6, 17.9, 18.2, 25.7, 74.9, 77.2, 80.3, 103.7; ESI-HRMS calcd for $C_{16}H_{36}O_4Si_2Na$ $(M + Na)^+$: 371.2044; found: 371.2046.

(2*S*,3*S*)-Diethyl 2,3-bis(benzyloxy)succinate (8a)

To a suspension of L-tartaric acid diethyl ester (16.4 g, 79.6 mmol) and silver oxide (74.0 g, 319.0 mmol) in anhydrous acetonitrile (160 mL) was added dropwise benzyl bromide (28.5 mL, 480 mmol) under mechanically stirring. After completion of the addition, the reaction mixture was stirred at room temperature for 2 days avoiding light. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with PE : EtOAc (20 : 1) to give **8a** (27.2 g, 88%) as a light yellow oil. $[\alpha]_D^{20}$ −101.1 (*c* 0.8, $CHCl_3$); IR (film, cm^{-1}): 2988, 1762, 1731, 1443; ^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.2 Hz, 6H, CH_3), 4.06–4.14 (m, 2H, MeCH_2), 4.19–4.27 (m, 2H, MeCH_2), 4.42 (s, 2H, *CHO*Bn), 4.48 (d, J = 12.0 Hz, 2H, PhCH_2), 4.90 (d, J = 12.0 Hz, 2H, PhCH_2), 7.28–7.36 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.1, 61.3, 73.2, 78.4, 127.9, 128.3, 128.4, 137.0, 169.2.

(2*R*,3*R*)-Diethyl 2,3-bis(benzyloxy)succinate (8b)

Following the procedures for the preparation of **8a**, **8b** was obtained in 87% yield as a white solid. Mp 46–47 °C; $[\alpha]_D^{20}$ +107.9 (*c* 1.0, $CHCl_3$),[23] $[\alpha]_D^{20}$ +105.0 (*c* 1.0, $CHCl_3$); IR (film, cm^{-1}): 2988, 1762, 1731, 1443, 1276, 1205, 742, 692; ^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (t, J = 7.2 Hz, 6H, CH_3), 4.07–4.12 (m, 2H, MeCH_2), 4.21–4.25 (m, 2H, MeCH_2), 4.42 (s, 2H, *CHO*Bn), 4.48 (d, J = 12.0 Hz, 2H, PhCH_2), 4.90 (d, J = 12.0 Hz, 2H, PhCH_2), 7.30–7.34 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 61.3, 73.2, 78.4, 128.0, 128.3, 128.4, 137.0, 169.2.

(2*R*,3*R*)-2,3-Bis(benzyloxy)butane-1,4-diol (9a)

To a solution of anhydrous lithium chloride (6.4 g, 150 mmol) in THF (90 mL) was added potassium borohydride (8.2 g, 150 mmol) in one portion and the reaction mixture was stirred at rt for 4 h under nitrogen. To this solution was added a solution of **8a** (23.2 g, 60 mmol) in THF (30 mL) and the resulting mixture was stirred under reflux for 2 h. The reaction was quenched by the addition of 10% citric acid at 0 °C, followed by addition of 2 M aqueous NaOH until the solution was clear. The mixture was concentrated under vacuum and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with PE : EtOAc (3 : 2) to provide **9a** (15.9 g, 87%) as a colorless oil. $[\alpha]_D^{20}$ −10.1 (*c* 0.78, $CHCl_3$); IR (film, cm^{-1}): 3435, 2927, 2874, 1450, 1337, 1104; ^1H NMR (400 MHz, $CDCl_3$): δ 2.34 (br, 2H, OH), 3.68–3.74 (m, 4H, CH_2O), 3.82–3.84 (m, 4H, CHO), 4.65 (s, 4H, PhCH_2), 7.29–7.38 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 60.8, 72.6, 78.9, 127.9, 128.0, 128.6, 138.0.

(2*S*,3*S*)-2,3-Bis(benzyloxy)butane-1,4-diol (9b)

Following the above procedures for the preparation of **9a**, **9b** was obtained in 87% yield as a colorless oil. $[\alpha]_D^{20}$ +10.8 (*c* 1.0, $CHCl_3$); IR (film, cm^{-1}): 3435, 2927, 2874, 1450, 1337, 1104; ^1H NMR (400 MHz, $CDCl_3$): δ 2.33 (br, 2H, OH), 3.70–3.74 (m, 4H, CH_2O), 3.82–3.84 (m, 4H, CHO), 4.65 (s, 4H, PhCH_2), 7.26–7.37

(m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 60.8, 72.6, 78.9, 127.9, 128.0, 128.6, 138.0.

(3*S*,4*R*)-3,4-Bis(benzyloxy)tetrahydrofuran-2-ol (2b)

To a solution of **9a** (12.4 g, 41.2 mmol) in acetone (80 mL) was added a solution of IBX (13.6 g, 16.4 mmol) in DMSO (50 mL). After stirred at rt for 5 h, the reaction mixture was quenched by the addition of water (40 mL), then filtered and the filtrate was concentrated under reduced pressure. The residue was partitioned between water and CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with PE : EtOAc (2 : 1) to give **2b** (10.8 g, 87%) as a colorless oil. $[\alpha]_D^{20}$ −12.5 (*c* 1.2, $CHCl_3$); IR (film, cm^{-1}): 3448, 1610, 1455; ^{1}H NMR (400 MHz, CD_3COCD_3) (diastereomixture 1.8 : 1, data of major isomer): δ 3.93 (dd, J = 8.9, 5.1 Hz, 1H, H-4), 3.98–4.00 (m, 1H, H-2), 4.06–4.14 (m, 2H, H-3, H-4), 4.52–4.73 (m, 4H, PhCH_2), 5.07 (d, J = 6.6 Hz, 1H, OH), 5.29 (d, J = 6.6 Hz, 1H, H-1), 7.28–7.43 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.2, 71.9, 73.0, 81.0, 84.9, 101.0, 127.7, 127.9, 128.0, 128.2, 128.5, 128.6, 136.8, 137.4; ESI-HRMS calcd for $C_{18}H_{20}O_4Na$ $(M + Na)^+$: 323.1254; found: 323.1249.

(3*R*,4*S*)-3,4-Bis(benzyloxy)tetrahydrofuran-2-ol (2c)

Following the above procedures for the preparation of **2b**, **2c** was obtained in 87% yield as a colorless oil. $[\alpha]_D^{20}$ +13.5 (*c* 1.3, $CHCl_3$); IR (film, cm^{-1}): 3443, 1606, 1450; ^{1}H NMR (400 MHz, CD_3COCD_3) (diastereomixture 1.8 : 1, data of major isomer): δ 3.93 (dd, J = 8.9, 5.1 Hz, 1H, H-4), 3.97–4.00 (m, 1H, H-2), 4.06–4.14 (m, 2H, H-3, H-4), 4.54–4.70 (m, 4H, PhCH_2), 5.06 (d, J = 5.8 Hz, 1H, OH), 5.29 (dd, J = 5.8, 1.1 Hz, 1H, H-1), 7.28–7.43 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.2, 71.9, 73.0, 81.0, 82.2, 101.0, 127.7, 127.9, 128.0, 128.2, 128.5, 128.6, 136.8, 137.4; ESI-HRMS calcd for $C_{18}H_{20}O_4Na$ $(M + Na)^+$: 323.1254; found: 323.1250.

(2*S*,3*S*)-2,3-Bis(*tert*-butyldimethylsilyloxy)hept-6-ene-1,4-diol (10a)

To a suspension of magnesium turnings (2.2 g, 91.2 mmol) and several crystals of iodine in dry Et_2O (5 mL) wad added a few drops of allyl bromide under nitrogen. After the reaction had initiated, the mixture was cooled to 0 °C and a solution of allyl bromide (1.4 mL, 16.0 mmol) in Et_2O (48 mL) was added slowly during 30 min under vigorously stirring. The resulting mixture was allowed to warm to rt and stirred for 1 h followed by cooling to −78 °C. A solution of **2a** (1.1 g, 3.2 mmol) in Et_2O (4 mL) was added dropwise and stirred for 1 h followed by being warmed to rt and stirred overnight. The reaction was quenched with sat. aq. NH_4Cl, extracted with Et_2O (3 × 10 mL). The combined organic phases were dried and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel with PE : EtOAc (10 : 1) to afford **10a** (1.2 g, 96%) as a colorless oil. $[\alpha]_D^{20}$ −14.6 (*c* 0.85, $CHCl_3$); IR (film cm^{-1}): 3434, 3000; ^{1}H NMR (400 MHz, CD_3COCD_3) (diastereomixture): δ 0.11–0.16 (m, 12H, Si$(CH_3)_2$), 0.86–0.95 (m, 18H, SiC$(CH_3)_3$), 2.10–2.46 (m, 2H, H-5), 2.8 (s, 2H, OH), 3.63–3.96 (m, 5H, H-1, H-2, H-3, H-4), 4.97–5.07 (m, 2H, H-7), 5.91–5.98 (m, 1H, H-6); ^{13}C NMR (100 MHz, CD_3COCD_3): δ −5.7, −5.3, −5.2, −5.1, 17.6, 25.1, 25.2, 38.3, 61.8, 72.1, 74.8, 76.4, 115.3, 136.0; ESI-HRMS calcd for $C_{19}H_{42}O_4Si_2Na$ $(M + Na)^+$: 413.2514; found: 413.2518.

(2*R*,3*R*)-2,3-Bis(benzyloxy)hex-5-ene-1,4-diol (10c)

To a solution of **2b** (0.9 g, 3.0 mmol) in dry THF (6 mL) was added dropwise a solution of vinylmagnesium chloride in THF (15% wt, 4.4 mL, 7.5 mmol) at 0 °C under nitrogen. After addition was complete, the reaction mixture was allowed to stir at rt for 2 h. The reaction mixture was then quenched with saturated aqueous NH_4Cl and filtered. The filtrate was concentrated under reduced pressure and extracted with ethyl acetate (30 mL). The combined organic solvents were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with PE : EtOAc (7 : 3) to give **10c** (0.92 g, 91%) as a colorless oil. $[\alpha]_D^{20}$ −18.5 (*c* 1.3, $CHCl_3$); IR (film, cm^{-1}): 3402, 3030, 1454; ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomixture 3.6 : 1): δ 2.64 (br, 2H, OH), 3.59 (dd, J = 2.5, 5.7 Hz, 1H, H-3), 3.64–3.67 (m, 1H, H-2), 3.72–3.86 (m, 2H, H-1), 4.35–4.43 (m, 1H, H-4), 4.58–4.75 (m, 4H, PhCH_2), 5.17–5.26 (m, 1H, H-6), 5.32–5.42 (m, 1H, H-6), 5.87–5.98 (m, 1H, H-5), 7.28–7.36 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 60.6, 61.4, 71.1, 72.2, 72.5, 72.6, 73.1, 74.5, 79.0, 79.3, 80.7, 80.8, 115.7, 116.5, 127.9, 128.0, 128.1, 128.2, 128.5, 137.4, 137.6, 137.7, 138.8, 138.1, 138.5; ESI-HRMS calcd for $C_{20}H_{24}O_4Na$ $(M + Na)^+$: 351.1567; found: 351.1568.

(2*S*,3*S*)-2,3-Bis(benzyloxy)hex-5-ene-1,4-diol (10d)

Following the above procedures to prepare of **10c**, **10d** were obtained in 92% yield as a colorless oil. $[\alpha]_D^{20}$ +17.8 (*c* 1.1, $CHCl_3$); IR (film, cm^{-1}): 3406, 3030, 1601, 1453; ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomixture 3.7 : 1): δ 2.62 (br, 2H, OH), 3.56–3.61 (m, 1H, H-3), 3.62–3.68 (m, 1H, H-2), 3.72–3.86 (m, 2H, H-1), 4.35–4.44 (m, 1H, H-4), 4.58–4.75 (m, 4H, 2 × PhCH_2), 5.16–5.27 (m, 1H, H-6), 5.31–5.42 (m, 1H, H-6), 5.87–5.98 (m, 1H, H-5), 7.25–7.36 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 60.6, 61.4, 71.1, 72.2, 72.5, 72.6, 73.1, 74.5, 79.0, 80.7, 80.8, 115.7, 116.5, 127.9, 128.0, 128.2, 128.5, 128.6, 137.4, 137.8, 138.8.

(2*S*,3*S*)-8-(Benzyloxy)-2,3-bis(*tert*-butyldimethylsilyloxy) octane-1,4-diol (10b)

To a suspension of magnesium turnings (360.0 mg, 15.0 mmol) and several crystals of iodine in THF (2 mL) wad added dropwise a solution of (4-benzyloxy)butyl bromide (2.4 g, 10.0 mmol) in THF (10 mL). After addition was completed, the resulting mixture was heated to reflux for 30 min, then cooled to 0 °C and a solution of **2a** (0.69 g, 2.0 mmol) in THF (5 mL) was added dropwise. After addition was completed, the resulting mixture was stirred for 2 h at rt, quenched with sat. aq. NH_4Cl, extracted with Et_2O (3 × 10 mL). The combined organic phases were dried and evaporated under reduced pressure, and the residue was purified by flash chromatography on silica gel with PE : EtOAc (10 : 1) to give **10b** (0.95 g, 93%) as a colorless oil. $[\alpha]_D^{20}$ −17.3 (*c* 0.70, CH_2Cl_2); IR (film, cm^{-1}): 3443, 1474; ^{1}H NMR (400 MHz,

$CDCl_3$): δ 0.06–0.15 (m, 12H, $Si(CH_3)_2$), 0.88–0.92 (m, 18H, $SiC(CH_3)_3$), 1.38–1.70 (m, 6H, H-5, H-6, H-7), 2.57 (br, 1H, OH), 2.98 (br, 1H, OH), 3.48 (t, $J = 6.8$ Hz, 2H, H-8), 3.51–3.54 (m, 1H, H-3), 3.59–3.77 (m, 4H, H-1, H-2, H-4), 4.50 (s, 2H, PhCH_2), 7.27–7.34 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.3, −4.2, 17.6, 17.9, 18.0, 22.1, 22.8, 25.7, 25.8, 29.7, 29.9, 34.0, 35.5, 61.8, 62.7, 67.6, 70.3, 70.5, 72.9, 73.0, 73.8, 75.0, 75.3, 76.0, 77.2, 127.5, 127.6, 128.3, 138.6; ESI-HRMS calcd for $C_{27}H_2O_5Si_2Na$ (M + Na)$^+$: 535.3245; found: 535.3245.

(2*R*,3*R*,4*S*)-4-(Benzylamino)-2,3-bis(benzyloxy)hex-5-en-1-ol (10e)

To a solution of **2b** (2.25 g, 7.5 mmol) in dry CH_2Cl_2 (20 mL) was added pulverized 4 Å molecular sieves (3 g), followed by benzylamine (0.99 mL, 9.0 mmol). The resulting mixture was stirred at rt under N_2 for 4 h. The molecular sieves was then removed by filtration and washed with dry CH_2Cl_2. The combined filtrates were evaporated under reduced pressure to provide a pale yellow oil (2.9 g) which was dissolved in dry THF (7.5 mL) and cooled to 0 °C. To the solution was added a solution of vinylmagnesium chloride in THF (15% wt, 17.8 mL, 30.0 mmol). The resulting reaction mixture was warmed to rt and stirred for 3 h, quenched with saturated aqueous NH_4Cl. The solid was removed by filtration and the filtrate was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with brine, dried and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel with PE : EtOA (7 : 3) to afford **10e** (2.5 g, 80%) as a colorless oil. $[\alpha]_D^{20}$ −15.9 (*c* 1.05, $CHCl_3$); IR (film, cm^{-1}): 3316, 3063, 1496, 1453; ^{1}H NMR (400 MHz, CD_3COCD_3): δ 2.8 (br, 2H, OH, *NH*Bn), 3.41 (dd, J = 3.0, 8.6 Hz, 1H, H-4), 3.55 (d, J = 13.0 Hz, 1H, PhCH_2N), 3.68–3.82 (m, 4H, H-1, H-2, H-3), 3.84 (d, $J = 13.0$ Hz, 1H, PhCH_2N), 4.57 (d, $J = 11.7$ Hz, 1H, PhCH_2O), 4.59 (d, $J = 11.7$ Hz, 1H, PhCH_2O), 4.75 (d, J = 11.3 Hz, 2H, PhCH_2O), 5.15–5.26 (m, 2H, CH=CH_2), 5.94 (ddd, J = 8.6, 10.3, 17.2 Hz, 1H, *CH*=CH_2), 7.22–7.36 (m, 15H, Ar-H); ^{13}C NMR (100 MHz, CDCl3): δ 50.9, 57.9, 58.8, 71.1, 73.9, 82.5, 117.8, 127.3, 127.7, 127.9, 128.0, 128.4, 128.6, 128.8, 137.9, 138.2, 138.4, 138.8; ESI-HRMS calcd for $C_{22}H_{29}O_8S_2$ (M + H)$^+$: 418.2377; found: 418.2381.

(2*S*,3*S*,4*R*)-4-(Benzylamino)-2,3-bis(benzyloxy)-5-(4-methoxyphenyl)pentan-1-ol (10f)

To a solution of **2c** (1.2 g, 4.0 mmol) in dry CH_2Cl_2 (20 mL) was added pulverized 4 Å molecular sieves (1.6 g) followed by benzylamine (0.53 mL, 4.8 mmol). The resulting mixture was stirred for 4 h at rt under nitrogen. The solid was then removed by filtration and washed with dry CH_2Cl_2. The combined organic filtrates were concentrated under reduced pressure to provide the corresponding crude *N*,*O*-acetal **(VII)** a pale yellow oil (1.56 g).

To a suspension of magnesium turnings (1.2 g, 48.0 mmol) and iodine (50 mg) in THF (5 mL) wad added dropwise a solution of 4-methoxybenzyl chloride (5.4 mL, 40.0 mmol) in THF (40 mL). The resulting mixture was heated to reflux for 30 min to afford 4-methoxybenzyl magnesium chloride which was then cooled with an ice bath and added a solution of the above *N*,*O*-acetal in dry THF (4 mL). The mixture was stirred for 3 h then quenched with sat. aq. NH_4Cl, extracted with ether (3 × 8 mL). The combined organic layers were washed with brine, dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel with PE : EtOAc (2 : 1) to give **10f** as a colorless oil (1.7 g, 83%). $[\alpha]_D^{20}$ −25.9 (*c* 0.56, $CHCl_3$); IR (film, cm^{-1}): 3332, 3060, 1610, 1511, 1454; ^{1}H NMR (400 MHz, CD_3COCD_3): δ 2.70 (d, J = 13.0, 8.9 Hz, 1H, H-5), 2.82 (br, 2H, OH, *NH*Bn), 3.13–3.24 (m, 2H, H-4, H-5), 3.65–3.71 (m, 3H, H-1, H-2, H-3), 3.74–3.81 (m, 5H, CH_3O, H-1, PhCH_2N), 4.02 (d, $J = 12.5$ Hz, PhCH_2N), 4.38 (d, $J = 12.0$ Hz, PhCH_2O), 4.51 (d, J = 11.6 Hz, PhCH_2O), 4.57 (d, J = 12.0 Hz, PhCH_2O), 4.73 (d, $J = 11.6$ Hz, PhCH_2O), 6.83 (d, $J = 8.7$ Hz, 2H, Ar-H), 7.02 (d, $J = 8.7$ Hz, 2H, Ar-H), 7.14–7.38 (m, 15H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.2, 50.9, 55.3, 56.9, 58.9, 71.2, 72.8, 76.7, 77.9, 114.1, 127.5, 127.7, 128.0, 128.2, 128.3, 128.6, 128.7, 128.8, 130.2, 131.2, 138.2, 138.4, 138.7, 159.2; ESI-HRMS calcd for $C_{20}H_{44}NO_2Si_2$ (M + H)$^+$:512.2795; found: 512.2800.

(3*R*,4*S*,5*R*)-5-Allyl-3,4-bis(*tert*-butyldimethylsilyloxy)-dihydrofuran-2(3*H*)-one (II) and (3*R*,4*S*,5*S*)-5-allyl-3,4-bis(*tert*-butyldimethylsilyloxy)dihydrofuran-2(3*H*)-one (III)

To a solution of **10a** (165.0 mg, 0.42 mmol) in acetone (1 mL) was added a solution of IBX (142.1 mg, 0.51 mmol) in DMSO (0.4 mL). After stirred at rt for 5 h, the reaction mixture was quenched by the addition of water (10 mL), then filtered and the filtrate was concentrated under reduced pressure. The residue was partitioned between water and CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give a crude colorless oil.

To a solution of above oil in CH_2Cl_2 (0.5 mL) was added a solution of DMP (216.0 mg, 0.51 mmol) in CH_2Cl_2 (2 mL) at rt, the result reaction mixture was stirred for 4 h, then diluted with water (2 mL), extracted with CH_2Cl_2 (3 × 5 mL), The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure, purified by column chromatography on silica gel with PE : EtOAc (10 : 1) to give **II** (81.2 mg, 62%) and **III** (22.7 mg, 17%).

II: $[\alpha]_D^{20}$ +60.5 (*c* 0.77, $CHCl_3$); IR (film, cm^{-1}): 2954, 1793; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.13 (s, 3H, $Si(CH_3)_2$), 0.14 (s, 3H, $Si(CH_3)_2$), 0.17 (s, 3H, $Si(CH_3)_2$),0.18 (s, 3H, $Si(CH_3)_2$), 0.92 (s, 18H, 2 × $SiC(CH_3)_3$), 2.47–2.50 (m, 2H, CH_2CH=CH_2), 4.14 (d, $J = 4.4$ Hz, 1H, H-3), 4.21 (*pseudo*-t, $J = 4.8$, 4.6 Hz, H-4), 4.56–4.61 (m, 1H, H-5), 5.15–5.24 (m, 2H, CH=CH_2), 5.82–5.93 (m, 1H, *CH*=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.1, −4.9, −4.7, −4.6, 17.9, 18.1, 25.6, 25.7, 33.4, 74.7, 75.4, 81.3, 118.5, 133.0, 178.8; ESI-HRMS calcd for $C_{19}H_{38}O_4Si_2Na$ (M + Na)$^+$: 409.2206; found: 409.2210.

III: $[\alpha]_D^{20}$ +4.4 (*c* 0.27, $CHCl_3$); IR (film, cm^{-1}): 2960, 1795; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.13 (s, 3H, $Si(CH_3)_2$), 0.14 (s, 3H, $Si(CH_3)_2$), 0.19 (s, 3H, $Si(CH_3)_2$), 0.21 (s, 3H, $Si(CH_3)_2$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.92 (s, 9H, $SiC(CH_3)_3$), 2.38–2.42 (m, 1H, CH_2CH=CH_2), 2.55–2.53 (m, 1H, CH_2CH=CH_2), 3.98 (*pseudo*-t, $J = 6.5$ Hz, H-4), 4.10–4.16 (m, 1H, H-5), 4.26 (d, $J = 6.6$ Hz, 1H, H-3), 5.15–5.22 (m, 2H, CH=CH_2), 5.77–5.88 (m, 1H, *CH*=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.8, −4.5, −4.4, −4.0, 17.8, 18.2, 25.6, 25.7, 36.1, 76.0, 77.9, 81.5, 118.9, 132.1, 173.4; ESI-HRMS calcd for $C_{19}H_{38}O_4Si_2Na$ (M + Na)$^+$: 409.2206; found: 409.2209.

(2*S*,3*S*)-8-(Benzyloxy)-2,3-bis(*tert*-butyldimethylsilyloxy)-1,4-bis(methansulfonyloxy)octane (11)

To a stirred solution of 4-(dimethylamino)pyridine (DMAP) (61.0 mg, 0.05 mmol) and MsCl (0.77 μL, 1.00 mmol) in pyridine (0.5 mL) cooled to 0 °C was added dropwise a solution of **10b** (128.5 mg, 0.25 mmol) in pyridine (0.25 mL). The resulting reaction mixture was stirred at 0 °C for 12 h, then poured into ice water (5 mL) and extracted with Et_2O (3 × 1 mL). The combined organic phases were washed with saturated aqueous $CuSO_4$, dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel by gradient elution with PE : EtOAc (20 : 1 to 10 : 1) to give **11** (134 mg, 80%) as a colorless oil. $[\alpha]_D^{20}$ −21.4 (*c* 0.98, CH_2Cl_2); IR (film, cm^{-1}): 1598, 1458; ^1H NMR (400 MHz, $CDCl_3$) (diastereomixture 3.7 : 1, data of major isomer): *δ* 0.09 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$), 0.91 (s, 9H, $SiC(CH_3)_3$), 0.92 (s, 9H, $SiC(CH_3)_3$), 1.40–1.43 (m, 2H, H-6), 1.62–1.67 (m, 2H, H-7), 1.82–1.97 (m, 2H, H-7), 2.99 (s, 3H, CH_3SO_2), 3.02 (s, 3H, CH_3SO_2), 3.47 (t, *J* = 6.3 Hz, 2H, CH_2OBn), 3.81 (dd, *J* = 2.3, 5.4 Hz, 1H, H-3), 4.02–4.07 (m, 1H, H-2), 4.36 (dd, *J* = 8.1, 10.2 Hz, 1H, H-1), 4.46–4.52 (m, 3H, PhCH_2, H-1′), 4.91–4.93 (m, 1H, H-4), 7.27–7.36 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, CDCl3): *δ* −4.9, −4.7, 17.8, 18.0, 22.2, 25.3, 25.6, 25.7, 29.3, 30.7, 36.7, 39.4, 69.6, 70.9, 72.1, 72.8, 79.5, 84.2, 127.4, 127.5, 128.2, 138.4; ESI-HRMS calcd for $C_{29}H_{60}O_9NS_2Si_2$ $(M + NH_4)^+$: 686.3243; found: 686.3235.

(2*R*,3*S*,4*S*)-Benzyl-2-(4-(benzyloxy)butyl)-3,4-bis(*tert*-butyldimethylsilyloxy)pyrrolidine (12a) and (2*S*,3*S*,4*S*)-1-benzyl-2-(4-(benzyloxy)butyl)-3,4-bis(*tert*-butyldimethylsilyloxy)pyrrolidine (12b)

To freshly distilled benzyl amine (0.5 mL) was added **11** (146.0 mg, 0.22 mmol), the resulting reaction mixture was stirred at 80 °C for 2 days, then cooled and diluted with diethyl ether (3 mL). The solid was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with PE : EtOAc (10 : 1) to afford **12a** (21.6 mg, 18%) and **12b** (77.7 mg, 64%) as colorless oils.

12a: $[\alpha]_D^{20}$ −14.9 (*c* 0.94, CH_2Cl_2); IR (film, cm^{-1}): 1598, 1466, 1361, 1248; ^1H NMR (400 MHz, $CDCl_3$): *δ* 0.08 (s, 3H, $SiCH_3$), 0.09 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.95 (s, 9H, $SiC(CH_3)_3$), 1.44–1.71 (m, 6H, H-6, H-7, H-8), 2.27–2.31 (m, 1H, H-2), 2.83–2.85 (m, 1H, H-5), 3.19 (dd, *J* = 10.4, 4.3 Hz, 1H, H-5), 3.51 (t, *J* = 6.7 Hz, 2H, CH_2OBn), 3.57 (d, *J* = 13.4 Hz, 1H, PhCH_2N), 3.95–4.01 (m, 3H, H-3, H-4, PhCH_2N), 4.55 (s, 2H, PhCH_2O), 7.27–7.38 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* −4.7, −4.6, −4.5, −4.2, 17.9, 18.1, 23.5, 25.8, 25.9, 28.6, 30.3, 58.9, 60.4, 66.6, 70.5, 72.8, 77.7, 79.3, 126.6, 127.4, 127.6, 128.1, 128.3, 128.7, 138.7, 140.2; HRMS calcd for $C_{34}H_{58}NO_3Si_2$ $(M + H)^+$: 584.3950; found: 584.3945.

12b: $[\alpha]_D^{20}$ +40.4 (*c* 0.55, CH_2Cl_2); IR (film, cm^{-1}): 1598, 1466, 1361, 1248; ^1H NMR (400 MHz, $CDCl_3$): *δ* 0.08 (s, 3H, $SiCH_3$), 0.09 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.95 (s, 9H, $SiC(CH_3)_3$), 1.50–1.75 (m, 6H, H-6, H-7, H-8), 2.49–2.52 (m, 1H, H-2), 2.57 (dd, *J* = 5.2, 10.3 Hz, 1H, H-5), 2.82 (d, *J* = 10.3 Hz, 1H, H-5), 3.36 (d, *J* = 13.6 Hz, 1H, PhCH_2N), 3.52 (t, *J* = 6.6 Hz, 2H, CH_2OBn), 3.87 (dd, *J* = 2.2, 3.6 Hz, 1H, H-3), 3.95–3.96 (m, 1H, H-4), 4.03 (d, *J* = 13.6 Hz, 1H, PhCH_2N), 4.54 (s, 2H, PhCH_2O), 7.28–7.40 (m, 10H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* −4.7, −4.6, −4.4, −4.2, 17.9, 18.0, 22.1, 25.8, 30.2, 31.2, 59.1, 59.7, 70.5, 71.3, 72.9, 78.3, 83.1, 126.6, 127.4, 127.6, 128.1, 128.3, 128.5, 138.7, 140.0; HRMS calcd for $C_{34}H_{58}NO_3Si_2$ $(M + H)^+$: 584.3950; found: 584.3957.

4-[(2*S*,3*S*,4*S*)-3,4-Bis(*tert*-butyldimethylsilyloxy)pyrrolidin-2-yl]-butan-1-ol (13)

To a solution of **12b** (240.0 mg, 0.41 mmol) in MeOH (5 mL) was added $Pd(OH)_2/C$ (200.0 mg) and the resulting mixture was stirred under H_2 (balloon, 1 atm) for 2 days. The catalyst was filtered and to the filtrate was added Pd/C (200 mg). The resulting mixture was stirred for an additional 4 days under H_2 (balloon, 1 atm). The solid was filtered and the filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel with PE : EtOAc (1 : 2) to give **13** (108.0 mg, 65%) as a colorless oil. $[\alpha]_D^{20}$ +18.5 (*c* 1.82, CH_2Cl_2); IR (film, cm^{-1}): 3342; ^1H NMR (400 MHz, CD_3COCD_3): *δ* 0.08 (s, 3H, $Si(CH_3)$), 0.09 (s, 3H, $Si(CH_3)$), 0.11 (s, 3H, $Si(CH_3)$), 0.12 (s, 3H, $Si(CH_3)$), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.91 (s, 9H, $SiC(CH_3)_3$), 1.48–1.58 (m, 6H, H-6, H-7, H-8), 2.06–2.09 (m, 1H, H-2), 2.23 (br, 2H, OH, NH), 2.54 (dd, *J* = 6.4, 10 Hz, 1H, H-5), 2.87 (dt, *J* = 10, 0.8 Hz, 1H, H-5), 3.54 (t, *J* = 6.4 Hz, 2H, PhCH_2O), 3.83 (dd, *J* = 2.0, 4.8 Hz, 1H, H-3), 3.97 (dd, *J* = 2.0, 5.6 Hz, 1H, H-4); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* −4.7, −4.6, −4.3, −4.2, 17.8, 18.0, 21.7, 25.8, 25.9, 30.7, 33.0, 62.4, 63.1, 73.7, 78.5, 83.6; ESI-HRMS calcd for $C_{20}H_{46}NO_3Si_2$ $(M + H)^+$: 404.3016; found: 404.3014.

(1*S*,2*S*,8a*S*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-octahydroindolizine (14)

To cooled (0 °C) solution of **13** (80.4 mg, 0.2 mmol) and PPh_3 (104.8 mg, 0.4 mmol) in dry CH_2Cl_2 (1 mL) was added dropwise fresh distilled CCl_4 (38.8 μL, 0.4 mmol). The resulting mixture was warmed to rt and stirred for 1 h followed by addition Et_3N (56 μL, 0.4 mmol). The resulting reaction mixture was stirred for 12 h followed by evaporation of the solvent. The crude product was purified by flash chromatography on silica gel with PE : EtOAc (10 : 1) to give **14** (77.2 mg, 88%) as colorless oil. $[\alpha]_D^{20}$ +8.9 (*c* 0.80, $CHCl_3$); IR (film, cm^{-1}): 2933, 2855; ^1H NMR (400 MHz, $CDCl_3$): *δ* 0.03 (s, 3H, $Si(CH_3)$), 0.05 (s, 3H, $Si(CH_3)$), 0.06 (s, 3H, $Si(CH_3)$), 0.08 (s, 3H, $Si(CH_3)$), 0.87–0.91 (m, 18H, $SiC(CH_3)_3$), 1.16–1.27 (m, 2H, H-6, H-7), 1.53–1.61 (m, 2H, H-6, H-7), 1.72–1.95 (m, 4H, H-5, H-8, H-8a), 2.52 (dd, *J* = 7.9, 10.1 Hz, 1H, H-3), 2.84 (dd, *J* = 2.1, 10.1 Hz, 1H, H-3), 2.91 (dt, *J* = 3.2, 10.8 Hz, 1H, H-5), 3.72 (dd, *J* = 4.1, 8.5 Hz, 1H, H-1), 3.98 (ddd, *J* = 2.1, 4.1, 7.9 Hz, 1H, H-2); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* −4.7, −4.2, −4.1, 17.9, 18.0, 24.0, 24.9, 25.9, 26.0, 28.7, 53.4, 62.1, 68.4, 78.1, 85.2; ESI-HRMS calcd for $C_{20}H_{44}NO_2Si_2$ $(M + H)^+$: 386.2910; found: 386.2905.

(+)-Lentiginosine (15)

To a solution of **14** (38.6 mg, 0.1 mmol) in dry THF (0.5 mL) was added TBAF (1 M in THF, 0.4 mL) and the resulting mixture was stirred overnight at rt. The solvent was evaporated under

reduced pressure and the crude product was purified by flash chromatography on silica gel with CH_2Cl_2 : MeOH : $NH_3 \cdot H_2O$ (85 : 15 : 1) to give (+)-lentiginosine as a white solid (14.1 mg, 90%). Mp 105–106 °C,[24] 106–107 °C; $[\alpha]_D^{20}$ +3.1 (*c* 0.28, MeOH),[24] $[\alpha]_D^{20}$ +3.1 (*c* 0.31, MeOH); IR (KBr, cm^{-1}): 3405; ^1H NMR (400 MHz, D_2O): δ 1.24–1.34 (m, 2H, H-6, H-7), 1.42–1.54 (m, 1H, H-7), 1.62–1.72 (m, 1H, H-6), 1.78–1.88 (m, 1H, H-8), 1.92–2.04 (m, 2H, H-5, H-8a), 2.10 (td, J = 11.9, 3.0 Hz, 1H, H-8), 2.68 (dd, J = 11.3, 7.5 Hz, 1H, H-3), 2.87 (dd, J = 11.3, 1.6 Hz, H-3), 2.98 (br d, J = 11.1 Hz, H-5), 3.68 (dd, J = 3.9, 8.8 Hz, 1H, H-1), 4.09 (ddd, J = 1.8, 3.9, 7.5 Hz, 1H, H-2); ^{13}C NMR (100 MHz, D_2O): δ 24.8, 25.8, 29.3, 54.5, 62.0, 70.4, 77.4, 84.7.

(2*R*,3*S*,4*S*)-2-(4-Methoxybenzyl)-1-benzyl-3,4-bis(benzyloxy)-pyrrolidine (16)

To a solution of **10f** (1.2 g, 2.3 mmol) and PPh_3 (1.2 g, 4.7 mmol) in DMF (12 mL) was added CCl_4 (0.46 mL, 4.7 mmol) dropwise at 0 °C. After 30 min, the resulting mixture was warmed to rt, followed by dropwise addition of Et_3N (0.66 mL, 4.7 mmol). The mixture was stirred overnight, filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with PE : EtOAc (1 : 2) to give **16** (1.0 g, 90%) as a colorless oil. $[\alpha]_D^{20}$ −66.7 (*c* 0.39, $CHCl_3$); IR (film, cm^{-1}): 1511, 1454; ^1H NMR (400 MHz, $CDCl_3$): δ 2.29 (dd, J = 5.0, 10.4 Hz, 1H, H-5), 2.83–2.91 (m, 1H, H-5), 2.95–3.05 (m, 1H, (MeO)PhCH_2), 3.32–3.38 (m, 2H, H-2, PhCH_2N), 3.72 (br d, J = 13.2 Hz, 1H, H-3), 3.78 (s, 3H, CH_3O), 3.92–2.98 (m, 1H, H-4), 4.04 (d, J = 13.0 Hz, 1H, PhCH_2N), 4.32–4.42 (m, 3H, PhCH_2O), 4.50 (d, J = 11.8 Hz, 1H, PhCH_2O), 6.78 (d, J = 8.5 Hz, 2H, Ar-H), 7.11 (d, J = 8.5 Hz, 2H, Ar-H), 7.21–7.35 (m, 15H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.9, 55.3, 58.1, 59.0, 68.4, 71.3, 71.7, 81.2, 83.5, 113.7, 126.9, 127.6, 127.7, 128.0, 128.3, 128.4, 129.1, 130.2, 132.0, 138.1, 138.3, 138.7, 157.8; ESI-HRMS calcd for $C_{20}H_{42}NOSi_2$ $(M + H)^+$: 494.2690; found: 494.2698.

(2*R*,3*S*,4*S*)-2-(4-Methoxybenzyl)pyrrolidine-3,4-diol [(−)-deacetylanisomycin] (17)

To a solution of **16** (493.6 mg, 1.0 mmol) in EtOH (5 mL) was added $Pd(OH)_2/C$ (200.0 mg) and the mixture was stirred under hydrogen atmosphere (1 atm) at rt for 3 days. The mixture was filtered and the filtrate concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel with PE : EtOAc (1 : 2) to give (−)-deacetylanisomycin (169.0 mg, 76%) as a white solid. Mp 174–175 °C,[4a] 176–177 °C,[25] 173–174 °C; $[\alpha]_D^{20}$ −21.0 (*c* 0.39, MeOH),[26] $[\alpha]_D^{20}$−22.5 (*c* 0.84, MeOH); ^1H NMR (400 MHz, $CDCl_3$): δ 2.76–2.83 (m, 2H, (MeO) $PhCH_2$), 2.98 (dd, J = 6.5, 12.9 Hz, 1H, H-5), 3.37 (dd, J = 5.4, 12.9 Hz, 1H, H-5), 3.51–3.57 (m, 1H, H-2), 3.82 (s, 3H, CH_3O), 3.97–4.01 (m, 1H, H-3), 4.23–4.28 (m, 1H, H-4), 6.98 (d, J = 8.7 Hz, 2H, Ar-H), 7.29 (d, J = 8.7 Hz, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.2, 51.0, 55.3, 62.5, 76.2, 76.5, 114.2, 130.1, 131.1, 157.4.

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Notes and references

1 I. S. Kim and Y. H. Jung, *Heterocycles*, 2011, **83**, 2489, and references therein.

2 For reviews, see: (*a*) H. Yoda, *Curr. Org. Chem.*, 2002, **6**, 223; (*b*) M. D. Lopez, J. Cobo and M. Nogueras, *Curr. Org. Chem.*, 2008, **12**, 718; (*c*) *Iminosugars: From Synthesis to Therapeutic Applications*, ed. P. Compain and O. R. Martin, Wiley-VCH, Weinheim, 2007; (*d*) B. L. Stocker, E. M. Dangerfield, A. L. Win-Mason, G. W. Haslett and M. S. M. Timmer, *Eur. J. Org. Chem.*, 2010, 1615; (*e*) R. Lahiri, A. A. Ansari and Y. D. Vankar, *Chem. Soc. Rev.*, 2013, **42**, 5102; (*f*) D. J. Wardrop and S. L. Waidyarachchi, *Nat. Prod. Rep.*, 2010, **27**, 1431; (*g*) T. Ritthiwigrom, C. W. G. Au and S. G. Pyne, *Curr. Org. Synth.*, 2012, **9**, 583.

3 For selected examples, see: (*a*) N. G. Argyropoulos, P. Gkizis and E. Coutouli-Argyropoulou, *Tetrahedron*, 2008, **64**, 8752; (*b*) S. Cicchi, M. Marradi, P. Vogel and A. Goti, *J. Org. Chem.*, 2006, **71**, 1614; (*c*) K. P. Kaliappan, V. Ravikumar and S. A. Pujari, *Tetrahedron Lett.*, 2006, **47**, 981; (*d*) A. E. Koumbis and D. D. Chronopoulos, *Tetrahedron Lett.*, 2005, **46**, 4353; (*e*) X. M. Yu, G. Shen and B. S. J. Blagg, *J. Org. Chem.*, 2004, **69**, 7375; (*f*) U. M. Krishna, K. D. Deodhar and G. K. Trivedi, *Tetrahedron*, 2004, **60**, 4829; (*g*) A. Trabocchi, G. Menchi, M. Rolla, F. Machetti, I. Bucelli and A. Guarna, *Tetrahedron*, 2003, **59**, 5251; (*h*) A. E. Koumbis, K. M. Dieti, M. G. Vikentiou and J. K. Gallos, *Tetrahedron Lett.*, 2003, **44**, 2513; (*i*) A. Furstner, K. Radkowski, C. Wirtz, R. Goddard, C. W. Lehmann and R. Mynott, *J. Am. Chem. Soc.*, 2002, **124**, 7061; (*j*) A. G. Myers and S. D. Goldberg, *Angew. Chem., Int. Ed.*, 2000, **39**, 2732; (*k*) K. Burgess and I. Henderson, *Tetrahedron Lett.*, 1990, **31**, 6949; (*l*) D. R. Williams and F. D. Klingler, *J. Org. Chem.*, 1988, **53**, 2134.

4 (*a*) H. Iida, N. Yamazaki and C. Kibayashi, *J. Org. Chem.*, 1986, **51**, 1069. Similar synthesis and applications, see: (*b*) D. Vina, T. F. Wu, M. Renders, G. Laflamme and P. Herdewijn, *Tetrahedron*, 2007, **63**, 2634; (*c*) T. F. Wu, M. Froeyen, V. Kempeneers, C. Pannecouque, J. Wang, R. Busson, E. De Clercq and P. Herdewijn, *J. Am. Chem. Soc.*, 2005, **127**, 5056; (*d*) K.-U. Schöning, P. Scholz, X. L. Wu, S. Guntha, G. Delgado, R. Krishnamurthy and A. Eschenmoser, *Helv. Chim. Acta*, 2002, **85**, 4111; (*e*) K.-U. Schöning, P. Scholz, S. Guntha, X. Wu, R. Krishnamuthy and A. Eschnmoser, *Science*, 2000, **290**, 1347; (*f*) A. B. Smith III, G. A. Sulikowski and K. Fujimoto, *J. Am. Chem. Soc.*, 1989, **111**, 8041.

5 (*a*) J. J. Zhuang, J. L. Ye, H. K. Zhang and P. Q. Huang, *Tetrahedron*, 2012, **68**, 1750; (*b*) N. Q. Vu, C. L. L. Chai, K. P. Lim, S. C. Chia and A. Chen, *Tetrahedron*, 2007, **63**, 7053.

6 (*a*) A. Gypser, M. Peterek and H. D. Scharf, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1013; (*b*) N. Cohen, B. Banner, R. Lopresti, F. Wong, M. Rosenberger, Y. Liu, E. Thom and A. Liebman, *J. Am. Chem. Soc.*, 1983, **105**, 3661.

7 C. C. Wei, S. D. Bernardo and J. P. Tengi, *J. Org. Chem.*, 1985, **50**, 3462.

8 B. Mekki, G. Singh and R. H. Wightman, *Tetrahedron Lett.*, 1991, **32**, 5143.
9 Other literatures on Grignard reaction of *trans*-dihydroxylactol analogues, see: (*a*) A. Almelund and R. Madsen, *J. Org. Chem.*, 2005, **70**, 8248; (*b*) M. Seepersaud and Y. Al-Abed, *Tetrahedron Lett.*, 2000, **41**, 7801; (*c*) W. H. Pearson and E. J. Hembre, *J. Org. Chem.*, 1996, **61**, 5546.
10 T. M. Krülle, C. de la Fuente, L. Pickering, R. T. Aplin, K. E. Tsitsanou, S. E. Zographos, N. G. Oikonomakos, R. J. Nash, R. C. Griffiths and G. W. J. Fleet, *Tetrahedron: Asymmetry*, 1997, **8**, 3807.
11 (*a*) A. Eniade and O. R. Martin, *Carbohydr. Res.*, 2002, **337**, 273; (*b*) L. Cipolla, L. Lay, F. Nicotra, C. Pangrazio and L. Panza, *Tetrahedron*, 1995, **51**, 4679; (*c*) M. Nagai, J. J. Gaudino and C. S. Wilcox, *Synthesis*, 1992, 163.
12 I. Pastuszak, R. J. Molyneux, L. F. James and A. D. Elbein, *Biochemistry*, 1990, **29**, 1886.
13 For synthetic reviews, see: (*a*) F. Cardona, A. Goti and A. Brandi, *Eur. J. Org. Chem.*, 2007, 1551. For selected recent examples, see: (*b*) K. L. Chandra, M. Chandrasekhar and V. K. Singh, *J. Org. Chem.*, 2002, **67**, 4630; (*c*) R. Lahiri, H. P. Kokatla and Y. D. Vankar, *Tetrahedron Lett.*, 2011, **52**, 781; (*d*) T. M. Shaikh and A. Sudalai, *Tetrahedron: Asymmetry*, 2009, **20**, 2287; (*e*) M. A. Alam and Y. D. Vankar, *Tetrahedron Lett.*, 2008, **49**, 5534; (*f*) See also ref 5*a*.
14 R. Appel, *Angew. Chem., Int. Ed.*, 1975, **14**, 801.
15 (*a*) B. A. Sobin and F. W. Tanner, *J. Am. Chem. Soc.*, 1954, **76**, 4053; (*b*) Y. Hosoya, T. Kameyama, H. Naganawa, Y. Okami and T. J. Takeuchi, *J. Antibiot.*, 1993, **46**, 1300; (*c*) T. Korzybski, Z. Kowszyk-Gindifer and W. Kurytowicz, in *Antibiotics*, American Society of Microbiology, Washington, DC, 1978, vol. 1, pp. 343–346.
16 (*a*) T. A. Stadheim and G. L. Kucera, *Leuk. Res.*, 2002, **26**, 55; (*b*) B. Torocsik and J. Szeberenyi, *Biochem. Biophys. Res. Commun.*, 2000, **278**, 550; (*c*) Y. S. Lee and R. D. Wurster, *Cancer Lett.*, 1995, **93**, 157.
17 M. Windholtz, *The Merck Index*, Merck, Whitehouse Station, NJ, 12th edn, 1996, p. 710.
18 For recent synthetic examples, see: (*a*) J. E. Joo, K. Y. Lee, V. T. Pham, Y. S. Tian and W. H. Ham, *Org. Lett.*, 2007, **9**, 3627; (*b*) P. V. Chouthaiwale, S. P. Kotkar and A. Sudalai, *ARKIVOC*, 2009, 88; (*c*) J. H. Kim, M. J. Crutis-Long, W. D. Seo, Y. B. Ryu, M. S. Yang and K. H. Park, *J. Org. Chem.*, 2005, **70**, 4082; (*d*) A. N. Hulme and E. M. Rosser, *Org. Lett.*, 2002, **4**, 265, and references therein.
19 W. L. F. Armarego and C. L. L. Chai, *Purification of Laboratory Chemicals*, Butterworth-Heinemann, 6th edn, 2009.
20 (*a*) E. Hardegger, K. kreis and H. EI Khadem, *Helv. Chim. Acta*, 1951, **34**, 2343; (*b*) K. Ernst, K.-L. katarina and D. Max, *Helv. Chim. Acta*, 1980, **61**, 1143; (*c*) D. J. Hwang, J. K. Dong and J. H. Choi, *Bioorg. Med. Chem.*, 2001, **9**, 1429.
21 M. L. Wolfrom and R. B. Bennett, *J. Org. Chem.*, 1965, **30**, 458.
22 C. Rene, K. Martin and S. Dieter, *Tetrahedron*, 1997, **53**, 1311.
23 D. Dubreuil, J. Cleophax and A. Loupy, *Carbohydr. Res.*, 1994, **252**, 149.
24 M. O. Rasmussen, P. Delair and A. E. Green, *J. Org. Chem.*, 2001, **66**, 5438.
25 P. Hutin, M. Haddad and M. Larchevêque, *Tetrahedron: Asymmetry*, 2000, **11**, 2547.
26 S. Chandrasekhar, T. Ramachandar and M. N. Reddy, *Synthesis*, 2002, 1867.