Highly diastereoselective synthesis of 1,2-amino alcohols via nucleophilic addition of organocerium reagents to 4- and 5-oxazolidinonecarbaldehydes

Andrew G.H. Wee and Fuxing Tang

Abstract: The reaction of chiral, non-racemic 4- and 5-oxazolidinonecarbaldehydes, **6** and **13**, with organocerium reagents proceeds efficiently with good to excellent diastereoselectivity to give *syn* and *anti* alcohols, respectively. A model to explain the observed diastereoselectivity of the reaction of **6** and **13** is provided. The utility of this method for the synthesis of amino alcohols is exemplified by the synthesis of C-18-D-*ribo*-phytosphingosine from the *anti* alcohol **14f**.

Key words: oxazolidinonecarbaldehydes, organocerium, diastereoselective, amino alcohols, C-18-*ribo*-phytospingosine.

Résumé : La réaction de réactifs organiques du cérium avec les 4- et 5-oxazolidinonecarbaldéhydes chiraux et non racémiques, **6** et **13**, s'effectuent d'une façon efficace, avec des diastéréosélectivités allant de bonnes à excellentes, et elles conduisent aux alcools *syn* et *anti* respectivement. On propose un modèle pour expliquer la diastéréosélectivité de la réaction des produits **6** et **13**. Comme exemple pour démontrer l'utilité de cette méthode pour la synthèse d'aminoalcools, on propose la synthèse de la C-18-D-*ribo*-phytosphingosine à partir de l'alcool *anti*, **14f**.

Mots clés : oxazolidinonecarbaldéhydes, organocérium, diastéréosélectif, aminoalcools, C-18-*ribo*-phytosphingosine.

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Introduction

The 1,2-amino alcohol moiety is a common subunit that is found in many naturally occurring and medicinally important compounds such as sphingolipids (1*a*), hydroxylated alkaloids (1*b*, 1*c*), amino acids (1*d*, 1*e*), HIV-enzyme inhibitors (1*f*, 1*g*), and amino sugars (1*h*). As well, chiral auxiliaries (2*a*) and ligands (2*b*) that are widely employed in asymmetric synthesis possess the 1,2-amino alcohol unit as a key structural feature. Much effort has, therefore, been devoted towards developing new strategies (for reviews, see ref. 3) for the synthesis of 1,2-amino alcohols. The most widely used method involves the nucleophilic addition of C-centred nucleophiles to α-amino aldehydes (3*a*, 3*c)* However, some limitations of the method have been noted; for example, the α-amino aldehyde is prone to racemization under the reaction conditions (3*a*, 4). As well, the diastereoselectivity of the nucleophilic addition reaction is usually not as high as expected although, recently, methods (3*c*) have been devised to overcome this problem.

In comparison, the use of 2-oxazolidinones for the synthesis of 1,2-amino alcohols has not been extensively investigated (5). Two aspects that make them attractive synthetic intermediates are (*a*) the 2-oxazolidinone moiety can be considered as a protected amino alcohol synthon, which can be subsequently unmasked to reveal the 1,2-amino alcohol unit, and (*b*) the reactions carried out on oxazolidinone derivatives are usually highly stereoselective (5).

Herein, we report our studies on the nucleophilic addition of organocerium reagents to chiral, non-racemic 4- and 5-oxazolidinonecarbaldehydes (**6** and **13**, respectively) (for a preliminary communication, see ref. 6). The addition was found to proceed with good to excellent diastereoselectivity to give *syn* or *anti* alcohol products in moderate to good chemical yields. We also developed a procedure for the generation and in situ reaction of 4-oxazolidinonecarbaldehyde **6** with organocerium reagents.

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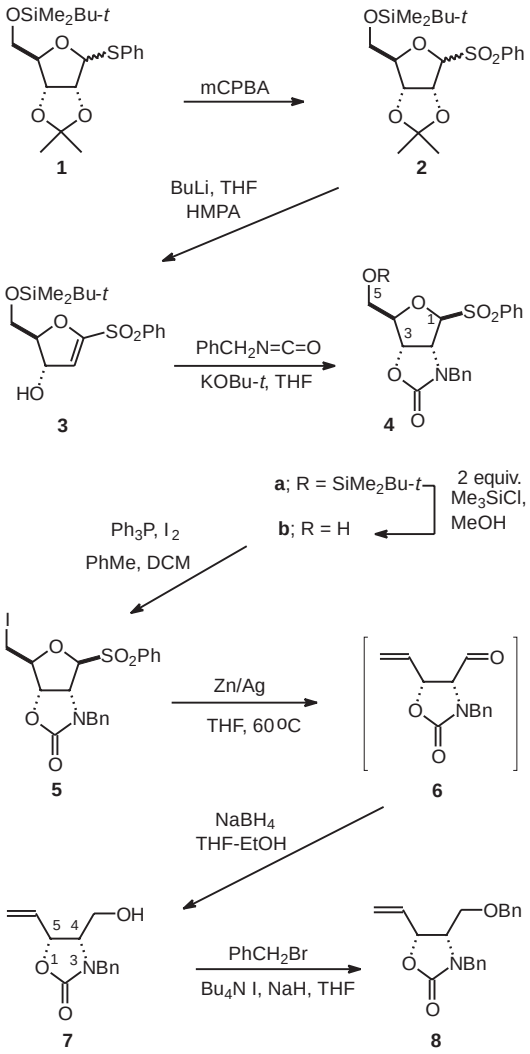
Results and discussion

Preparation of iodophenylsulfone (5) and benzylether (8)

The iodo phenylsulfone **5** serves as a convenient and shelf-stable precursor of the aldehyde **6**. The preparation of **5** is summarized in Scheme 1 and began with the oxidation of the known phenylsulfide **1** (7*a*) (α:β ratio 8.5:1.5 based on integration of H-1) with mCPBA to give a separable mixture of α,β-anomers (8:2)[2,3] of **2**. The slightly light-sensitive **2** were then treated with *n*-butyllithium in the presence of HMPA as a cosolvent to effect 1,2-elimination of a molecule of acetone to give the ene alcohol **3** (for the use of

Scheme 1.



organosulfones in synthesis, see ref. 8). We found it unnecessary to treat α-**2** and β-**2** separately in this elimination reaction since both anomers lead to the same ene alcohol with no loss in yield. Compound **3** was found to be unstable during storage (~ 3 d) and was utilized immediately in the carbamation step. Base-catalyzed reaction of **3** with benzylisocyanate afforded *cis*-bicycle **4a** as a single diastereomer in good yield.

It was found that the use of KOBu-*t* is essential for efficient carbamation. With NaH as the base only a low yield of the **4a** was obtained; the uncyclized urethane, which had resulted from the nucleophilic addition of only the alcohol unit to the benzylisocyanate, was the major product. A likely explanation for the lack of intramolecular Michael addition is that, with NaH, the phenylsulfonyl-stabilized carbanion (8*b*) intermediate is prone to undergo a retro-Michael reaction. This pathway is absent in the *tert*-butoxide-catalyzed reaction because the phenylsulfone-stabilized carbanion is protonated by the *tert*-butyl alcohol that is present.

Desilylation of **4a** to the primary alcohol **4b** was accomplished using Me_3SiCl in MeOH and was followed by reaction of **4b** with $Ph_3P–I_2$ (9) to give the iodo phenylsulfone **5**.

We were not able to ascertain from the ^{1}H NMR spectra of **4a,b** whether the stereochemistry of the 1-phenylsulfonyl group is α or β because of the overlap of the H-1, H-2, and PhCHN resonances. However, the ^{1}H NMR of **5** was better resolved and showed H-1 as a doublet centred at δ 4.82 with a vicinal coupling constant, $J_{1,2}$, of 1.8 Hz. This small *J* value[3] suggests that the 1-phenylsulfonyl group has the β-configuration. This outcome is unexpected when the conversion of **3** to **4a** is considered and it suggests that the phenylsulfone-stabilized carbanion intermediate that is generated during the intramolecular carbamation reaction is protonated from the more hindered, concave side of the bicycle to give **4a**. It should be noted that protonation from the less hindered, convex side of the bicycle should, in principle, be more favoured; however, this would lead to a sterically congested product wherein the α-phenylsulfonyl moiety is engaged in severe nonbonded interactions with the *syn* oxazolidinone moiety.

The next step was the Zn–Ag[4] (10) mediated reductive elimination of **5** in dry THF at 60°C to afford the olefinic aldehyde **6**. Subsequent reduction of **6** with $NaBH_4$ proceeded uneventfully to give crystalline primary alcohol **7** ($[\alpha]_D^{23}$ –15.2 (*c* 0.98, $CHCl_3$))[5] in high yield. Alcohol **7** was then benzylated to give **8**, which served as the precursor for the 5-oxazolidinonecarbaldehyde **13**.

The formation of **6** deserves some comments. The ^{1}H and ^{13}C NMR spectra of the primary alcohol **7** that is derived from **6** are in accord with the assigned structure. The salient feature in the ^{1}H NMR spectrum is the pseudo triplet due to H-5 that was centred at δ 4.92. It has a $J_{4,5}$ of 7.4 Hz[6] that is characteristic of a *cis* stereochemistry (11). This indicates that no epimerization of the aldehyde to the *trans* diastereomer had occurred under the reaction conditions used in the reductive elimination step.

Formation and reaction of 4-oxazolidinonecarbaldehyde (6) with $RCeCl_2$

It is well documented (3*a*, 4) that amino aldehydes (except for a serine-derived aldehyde (12)) are, in general, unstable and are not amenable to isolation. To avoid potential difficulties associated with the isolation of **6**, we decided to investigate its generation and in situ reaction with the preformed organocerium reagent (13*a*, 13*b*) (hereafter referred to as $RCeCl_2$; the exact speciation of the organocerium reagent is not known. See ref. 13*c*) as depicted in eq. [1]. The

[2] Ratio is based on isolated yields. Decoupling of the H-3 multiplet (δ 4.72–4.81) in α-2 simplified the H-1,H-2 multiplet at δ 5.02–5.10; H-2 collapsed to a singlet at δ 5.9. H-1 was observed as a doublet centred at δ 5.7 and has a $J_{1,2}$ of 3.8 Hz.

[3] Typically, H-1 in the α-anomer shows a $J_{1,2}$ in the range 3.8–4.4 Hz, and in the β-anomer $J_{1,2}$ is in the range of 1.8–2.0 Hz (7).

[4] We have also examined other Zn-based methods such as Zn dust, EtOH; Zn/Cu, THF; and $ZnCl_2–C_8K$, THF. These methods either gave low yields of 6 and a substantial amount of the reduced product or decomposition products.

[5] We have prepared ent-**7** from D-mannose and it has $[\alpha]_D^{23}$ = +14.8 (c 1.01, $CHCl_3$).

[6] Decoupling of the alkene methine multiplet at δ 5.99–6.19 collapsed the H-5 "triplet" to a broad doublet centred at δ 4.92. Typically, J_{trans} = 3.3–4.5 Hz and J_{cis} = 6.2–7.5 Hz (11).

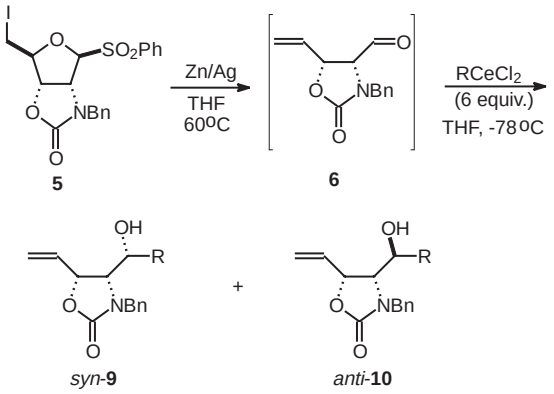
Table 1. Reaction of **6** with $RCeCl_2$ according to method A.

Entry	$RCeCl_2$	T,°C/h	*syn*-**9**:*anti*-**10** [b]	Yield (%)
1	**a**; MeLi	–78/5	95:5	85
2	MeLi[a]	–78/5	89:11	35
3	**b**; CH_2=CHMgBr	–78/5	>99:1	85
4	CH_2=CHMgBr[a]	–78/5	83:17	40
5	**c**; CH_2=C(OBu-*t*)O$^-$ Li^+	–78/5	86:14[c]	92
6	**d**; PhC≡CLi	–78/5	>99:1	94
7	**e**; 2-Furanyl Li	–78/5	>99:1	85
8	**f**; PhMgBr	–78/5; 0/1	88:12	52
9	PhMgBr	–78/5	88:12	29

[a]Reaction was performed without $CeCl_3$.
[b]Alcohols were inseparable. Ratio was based on the integration of Me resonance in the ^{1}H NMR of acetate derivatives.
[c]Ratio was based on the integration of the *t*-Bu singlet.

use of dry THF for the reductive elimination step was essential for the success of this procedure.

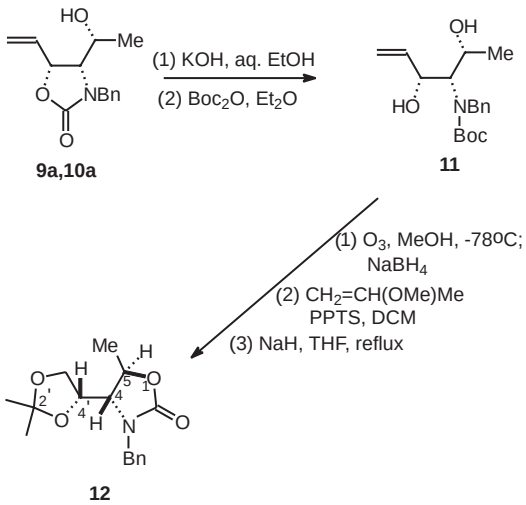
[1]



As shown in Table 1, Grignard-derived and organolithium-derived organocerium reagents reacted well with **6**. The nucleophilic addition reaction produced a crystalline, diastereomeric mixture of alcohols *syn*-**9** and *anti*-**10** in which the former was present as the predominant or exclusive product. For reactions in which Grignard-derived $RCeCl_2$ reagents were used, it was advantageous to warm the reaction mixture to 0°C and to maintain the reaction at 0°C for at least 1 h. Thus, quenching the $PhCeCl_2$ reaction after 5 h at –78°C yielded 29% of a mixture of **9f** and **10f** (entry 9). However, a 52% yield of **9f**, **10f** was obtained when the mixture was warmed to and maintained at 0°C for 1 h (entry 8). For the CH_2=$CHCeCl_2$ reaction, the reaction mixture must be conducted at –78°C because the organocerium reagent is unstable at 0°C (13*b*, 14). The use of Grignard and organolithium reagents alone resulted in lower diastereoselectivity and poorer chemical yields of products (compare entries 1, 2 and 3, 4).

The relative stereochemistry of the hydroxyl group and the benzylamino moiety of the oxazolidinone unit in **9** was assigned as *syn* on the basis of the data obtained from proton decoupling and NOE experiments performed on **12**. Compound **12** was synthesized from **9a,10a** using standard functional group manipulations as summarized in eq. [2]. Decoupling of the C-5 methyl doublet (δ 1.25) in **12** collapsed the H-5 quintet (br, δ 4.42) to a doublet, $J_{5,4}$ = 4.4 Hz. Similarly, irradiation of the H-4′ multiplet (δ 4.00–4.18) simplified the H-4 triplet (δ 3.11) to a doublet, $J_{4,5}$ = 4.4 Hz. Based on this small vicinal coupling constant (11) the relative stereochemistry of the methyl and dioxalanyl groups was, therefore, assigned as *trans*. This result was confirmed by the observation of a strong NOE enhancement (6.7%) for the H-4 proton upon irradiation of the C-5 methyl doublet.

[2]



Formation and reaction of 5-oxazolidinonecarbaldehyde (13) with $RCeCl_2$

Aldehyde **13** was prepared by ozonolysis of the benzyl ether **8** in DCM followed by replacement of the DCM with dry THF. The THF solution of crude **13** was then added to $RCeCl_2$ (4 equiv.) at –78°C (eq. [3]). Again, we found that it

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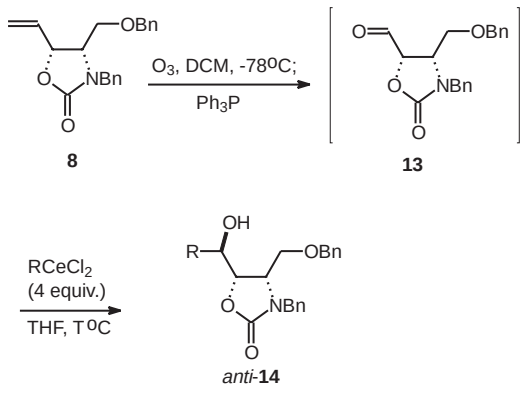


Table 2. Reaction of **13** with $RCeCl_2$ according to method B.

Entry	$RCeCl_2$	T,°C/h	*anti*-**14**	Yield (%)[b]
1	**a**; MeLi	–78/5	>99:1	62
2	MeLi[a]	–78/5	Dec.	0
3	**b**; CH_2=CHMgBr	–78/5	>99:1	59
4	CH_2=CHMgBr[a]	–78/5	>99:1	21
5	**c**; PhC≡CLi	–78/5	>99:1	85
6	**d**; CH_2=C(OBu-*t*)O$^-$ Li^+	–78/5	>99:1	84
7	**e**; 2-Furanyl Li	–78/5	>99:1	64
8	**f**; $C_{14}H_{29}MgBr$	–78/5; 0/1	>99:1	69
9	$C_{14}H_{29}MgBr$	–78/5	>99:1	40

[a]Reaction was performed in the absence of $CeCl_3$.
[b]Isolated yields.

was advantageous to warm the reactions involving Grignard-derived $RCeCl_2$ to 0°C before being quenched (Table 2, entries 8 and 9). In all cases, the alcohol product **14** was obtained as an oil, and in moderate to good overall yields. Only one diastereomer was produced as evidenced by ^1H and ^{13}C NMR analysis of the crude product: the other epimer was not detected.

The use of $CeCl_3$ is essential for the success of the reaction. For example, the use of MeLi only resulted in the complete decomposition of **13** (Table 2, compare entries 1 and 2) and the use of only CH_2=CHMgBr gave a lower yield of **14** (compare entries 3 and 4). The relative stereochemistry between the hydroxyl and the oxygen atom of the oxazolidinone unit was assigned as *anti* on the basis of the conversion of compound **14f** to C-18-D-*ribo*-phytosphingosine **18** (see later).

It was also of interest to examine the diastereoselectivity of nucleophilic addition reaction of **6** and **13** with $MeTi(OPr\text{-}i)_3$. It is well documented (15) that this nucleophilic reagent reacts with α-alkoxy aldehydes in a non-chelation controlled pathway because of the reduced Lewis acidity of the titanium centre. Unfortunately, the reaction of $MeTi(OPr\text{-}i)_3$ with **6** (using the same procedure developed for the conversion of **5** → **9**, **10**) resulted only in decomposition products. On the other hand, the reaction of $MeTi(OPr\text{-}i)_3$ with **13** (eq. [4]) gave a good yield (72%) of the addition product **15**. The ^1H NMR spectrum of **15** was very similar to that of *anti*-**14a**. We therefore prepared the

[4]

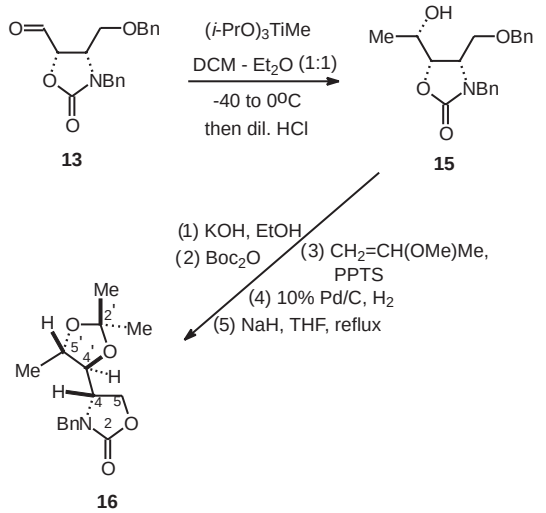
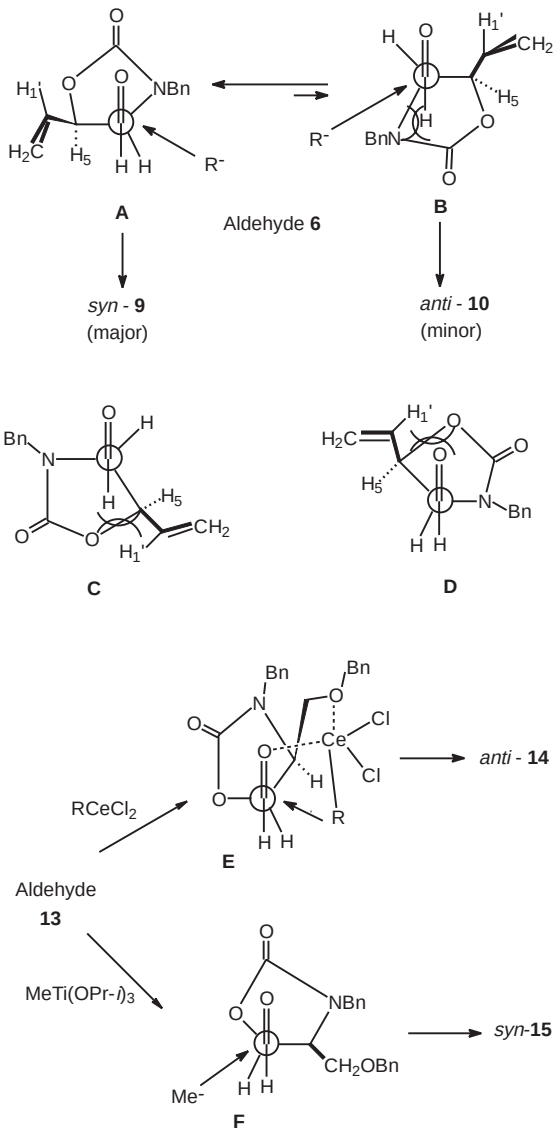
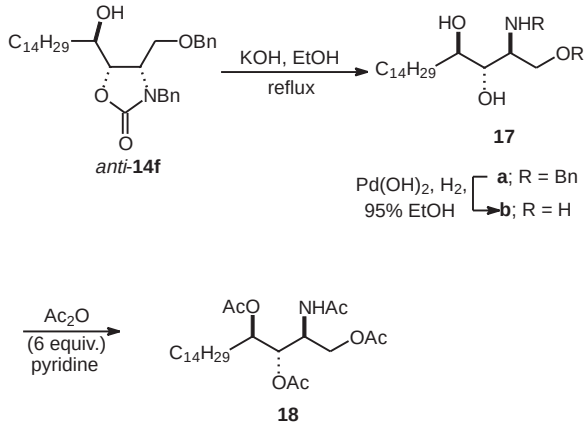


Chart 1.



oxazolidinone derivative **16** (eq. [4]), which was subjected to NOE analysis. In particular, irradiation of the C-5′ methyl doublet centred at δ 1.05 resulted in a 3% enhancement of the H-4′ double doublet centred at δ 4.44. On the basis of this result, the configuration of the newly created carbinol

Scheme 2.



centre was assigned as *S*. That is, the addition reaction has proceeded with *syn* diastereoselectivity.

Reaction pathway

The diastereoselectivity observed in the reaction of aldehyde **6** can be understood if we consider the two reactive conformers **A** and **B** (Chart 1). In each of the conformers, the preferred orientation of the C-5-vinyl substituent with respect to the rigid, planar oxazolidinone unit is the one in which the vinyl H-1′ hydrogen is aligned antiperiplanar to the oxazolidinone H-5 hydrogen. This arrangement is adopted in order to relieve $A^{1,3}$ strain (16). Conformer **A** (17*a*) is more stable than **B** because in the latter a destabilizing interaction is present. Preferential nucleophilic attack via the sterically less hindered side in **A** leads to the major *syn* diastereomer **9** whereas attack via the sterically encumbered side in **B** results in the minor *anti* diastereomer **10**. The conformers **C** and **D** correspond to the Felkin–Anh-type model (17) but are considered less stable than **A** and **B** because of the presence of destabilizing steric interactions. **C** is destabilized by the steric interaction between the aldehydic hydrogen and the *cis*-vinyl group and especially H-1′. Similarly, steric interaction between the *cis*-vinyl group/H-1′ and the oxygen of the carbonyl function in **D** results in its destabilization.

The involvement of a five-membered chelate intermediate resulting from coordination of the carbonyl oxygen and the nitrogen atom of the NBn moiety to Lewis acidic Ce(III) (13*a*) is not likely because of the reduced basicity of the nitrogen atom resulting from conjugation of the nitrogen lone pair of electrons with the π-bond of the carbonyl group of the oxazolidinone unit.

In the case of **13**, a possible explanation for the unexpectedly high diastereoselectivity is the involvement of a seven-membered Ce(III) chelate **E** (Chart 1) (for the involvement of 7-membered chelates, see ref. 18). Its formation is entropically favoured because of the *cis* relationship of the aldehyde and $BnOCH_2$ moieties. Also, it is well documented that the oxygen atom in benzyl ethers shows a propensity to coordinate to Lewis acids (15*a*). The chelate can also accommodate a Felkin–Anh (17) arrangement. Thus, both chelation control and stereoelectronic effects reinforce one another in controlling the diastereoselectivity of the reaction. Intramolecular or intermolecular delivery of R′ will occur from the less hindered side of the carbonyl function, leading to *anti*-**14**. This line of reasoning is further supported by the result from the reaction of **13** with $MeTi(OPr\text{-}i)_3$. In the absence of any chelation to the titanium centre in the reagent, nucleophilic addition would proceed via **F** to give the *syn* diastereomer **15**.

Synthesis of C-18-D-*ribo*-phytosphingosine.

The oxazolidinone alcohol *anti*-**14f** ($[\alpha]_D^{22}$ +35.0 (*c* 1.50, $CHCl_3$)) was hydrolyzed in alcoholic 2 M aqueous KOH to provide **17a** in 83% yield (Scheme 2). Hydrogenolysis of the N,O-benzyl protecting groups in **17a** using Pearlman's catalyst afforded phytosphingosine **17b** as a powdery solid, which was subsequently peracetylated to give the crystalline tetraacetate derivative **18**. The spectroscopic data and specific rotations of **17b** and **18** are in excellent agreement with those reported (19).

Conclusions

The reactions of oxazolidinonecarbaldehydes **6** and **13** with organocerium reagents were found to proceed efficiently and with good to excellent diastereoselectivity to afford the corresponding secondary alcohol products. Compounds **6** reacted to give *syn* alcohols **9** as the major or exclusive products. With compounds **13**, the *anti* alcohols **14** were formed as the exclusive products. The results suggest that oxazolidinonecarbaldehyde **6** reacted with $RCeCl_2$ in a non-chelation pathway but with **13** a cerium chelate is involved. The method was applied to the synthesis of naturally occurring amino alcohol C18-D-*ribo*-phytosphingosine. Further application of this method and use of chiral, non-racemic 2-oxazolidinonecarbaldehydes in synthesis are in progress.

Experimental

General

Melting points are uncorrected and were measured on a Kofler hot-stage melting point apparatus. Infrared spectra were recorded using a Perkin Elmer 1600FT spectrophotometer: only diagnostic absorptions in the infrared spectrum are reported. ^1H (200 MHz) and ^{13}C (50.3 MHz) NMR spectra were recorded in $CDCl_3$ (unless otherwise stated), using a Bruker 200QNP spectrometer. Tetramethylsilane (δ_H = 0.00) and the $CDCl_3$ resonance (δ_C = 77.0) were used as references. Multiplicities "t", "q", and "quintet" represent pseudo triplet, quartet, and quintet, respectively, and are quoted as they appear in the ^1H NMR spectra. Where applicable, the signals of minor diastereomers are given within square brackets. Proton assignments were made using double irradiation experiments and, where necessary, 2D-COSY-45 experiments. Numberings in compounds **2–5** follow sugar numberings and, in compounds **6** onwards, numberings follow 2-oxazolidinone numberings. Elemental analyses and high-resolution electron impact (70 eV) and chemical ionization mass spectral analyses were performed at the Chemistry Department, University of Saskatchewan. Optical rotations were measured using an Optical Activity AA-5 polarimeter.

Reaction progress was monitored by thin-layer chromatography on Merck silica gel $60F_{254}$ precoated (0.25 mm) on aluminum backed sheets. Air- and moisture-sensitive reactions were conducted under a static pressure of argon. All organic extracts were dried over anhydrous Na_2SO_4. Flash chromatography (20) was performed on Merck silica gel 60 (230–400 mesh). Unless stated otherwise, the eluent is a mixture of petroleum ether:EtOAc in v/v ratio as follows: solvent A, 1:1; solvent B, 2:1; solvent C, 3:1; solvent D, 4:1; solvent E, 5:1. Abbreviations of solvents used: petroleum ether (PE, bp 35–60°C), ethyl acetate (EtOAc), diethyl ether (Et_2O), tetrahydrofuran (THF), and dichloromethane (DCM). THF and Et_2O were distilled from sodium-benzophenone, and DCM was distilled from CaH_2.

Organometallic reagents

Simple Grignard and organolithium reagents were purchased from Aldrich. Tetradecylmagnesium bromide was prepared from tetradecylbromide and magnesium metal as a 0.5 M solution in THF. Lithium phenylacetylide (21*a*), 2-lithiofuran (21*b*), and $CH_2 = C(OBu\text{-}t)O^- Li^+$ (21*c*) were prepared according to literature procedures. Organometallic reagents were standardized before use by titration using either 1,3-diphenylacetone *p*-tosylhydrazone (22*a*) (RLi) or pyreneacetic acid (22*b*) (RMgBr) as indicators.

Phenyl 5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-α,β-D-ribofuranosyl sulfone (2)

The phenylthio furanoside (7 g, 18 mmol) was dissolved in DCM (100 mL) and saturated aqueous $NaHCO_3$ (200 mL) was added. The biphasic mixture was cooled to 0°C in an ice-bath and mCPBA (11 g, 39 mmol, 60% tech.) was added portionwise. Then the mixture was stirred at room temperature (rt) for 20 h. The mixture was recooled to 0°C and 10% aqueous $NaHSO_3$ was added to destroy unreacted mCPBA. The mixture was stirred at rt for 1 h, and the aqueous phase was separated and back-extracted with DCM (50 mL). The combined organic phases were washed with saturated $NaHCO_3$ (2 × 50 mL), dried, filtered, and evaporated. The crude oil was chromatographed (solvent E) to give the desired sulfone (6.2 g, 85%) as a thick, viscous oil. β-**2**: ^{1}H NMR, δ: 0.00 (s, 6H, $SiMe_2$), 0.80 (s, 9H, *t*-Bu), 1.28 (s, 3H, Me), 1.40 (s, 3H, Me), 3.66 (dd, 1H, *J* = 10.3, 7.6 Hz, H-5), 3.76 (dd, 1H, *J* = 10.3, 6.5 Hz, H-5′), 4.23 (dt, 1H, *J* = 6.5, 2.1 Hz, H-4), 4.65 (dd, 1H, *J* = 6.5, 2.1 Hz, H-3), 4.82 (d, 1H, *J* = 2.1 Hz, H-1), 5.24 (dd, 1H, *J* = 6.5, 2.1 Hz, H-2), 7.40–7.62 (m, 3H, PhH), 7.76–7.87 (m, 2H, PhH). α-**2**: ^{1}H NMR, δ: –0.06 (s, 3H, SiMe), –0.02 (s, 3H, SiMe), 0.70 (s, 9H, *t*-Bu), 1.15 (s, 3H, Me), 1.26 (s, 3H, Me), 3.63 (dd, 1H, *J* = 11.4, 2.2 Hz, H-5), 3.75 (dd, 1H, *J* = 11.4, 2.2 H, H-5′), 4.27–4.32 (m, 1H, H-4), 4.72–4.81 (m, 1H, H-3), 5.02–5.13 (m, 2H, H-1, H-2), 7.42–7.62 (m, 3H, PhH), 7.94 (d, 2H, J = 7.5 Hz, PhH). ^{13}C NMR, δ: –5.4, 17.9, 24.2, 25.1, 25.7, 65.0, 81.0, 82.1, 86.1, 96.3, 114.3, 128.5, 129.4, 133.4, 139.1. Anal. calcd. for $C_{20}H_{32}O_6SSi \cdot ¼H_2O$: C 55.46, H 7.57; found: C 55.41, H 7.52.

Phenyl 2-benzylamino-5-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-α-D-ribofuranosyl sulfone (4a)

The phenylsulfone **2** (6.2 g, 14.5 mmol) was dissolved in a mixture of dry THF (77 mL) containing dry HMPA (3.2 mL) under Ar. The solution was cooled to –78°C and *n*-BuLi (10.8 mL, 21.7 mmol, 2.1 M in hexanes) was added dropwise via syringe to the mixture. A deep yellow-orange solution resulted, which was stirred at –78°C for 1 h and then the cooling bath was removed. The mixture was allowed to warm slowly to rt, stirred at rt for 2 h, and then recooled to 0°C. Saturated aqueous NH_4Cl (15 mL) was added, followed by EtOAc (50 mL). The organic layer was removed and the aqueous phase was reextracted with EtOAc (2 × 50 mL). The combined organic phases were washed with saturated aqueous NaCl (70 mL), dried, filtered, and evaporated. The residual yellow oil was chromatographed (solvent C) to give **3** as a pale yellow oil (3.8 g, 71%) that slowly crystallized on standing. The product was found to be unstable and is best kept in the freezer for prolonged storage. IR, ν_{max}: 3575–3275 cm^{-1}. ^{1}H NMR, δ: –0.02 (s, 3H, SiMe), –0.05 (s, 3H, SiMe), 0.78 (s, 9H, *t*-Bu), 2.08–2.20 (br hump, 1H, OH), 3.57 (dd, 1H, *J* = 11.5, 4.8 Hz, H-5), 3.69 (dd, 1H, *J* = 11.5, 4.8 Hz, H-5′), 4.50 (q, 1H, *J* = 4.9 Hz, H-4), 4.92–5.2 (m, 1H, H-3), 5.98 (d, 1H, *J* = 2.6 Hz, H-2), 7.46–7.71 (m, 3H, PhH), 7.92–8.01 (m, 2H, PhH). ^{13}C NMR, δ: –5.4, 18.2, 25.7, 62.5, 74.9, 92.7, 109.6, 128.7, 129.2, 134.3, 137.9, 157.9.

The above ene alcohol (3.8 g, 10.3 mmol) was dissolved in dry THF (37 mL), under Ar. Benzyl isocyanate (1.4 mL, 11.4 mmol) was added and the reaction mixture was cooled to 0°C. Potassium *tert*-butoxide (0.24 g, 2.2 mmol) was added in one portion and the brown reaction mixture was stirred at 0°C for 1 h and at rt for 20 h. Then saturated NH_4Cl (20 mL) and EtOAc (20 mL) were added. The organic phase was separated and the aqueous phase was reextracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (50 mL), dried, filtered, and evaporated. The crude product was chromatographed (solvent E) to give the bicyclic oxazolidinone **4a** (4.6 g, 89%) as a pale yellow, viscous oil. IR, ν_{max}: 1766, 1585 cm^{-1}. ^{1}H NMR, δ: 0.30 (s, 6H, SiMe), 1.10 (s, 9H, *t*-Bu), 4.02 (dd, 1H, *J* = 10.9, 7.7 Hz, H-5), 4.08 (dd, 1H, *J* = 10.9, 6.0 Hz, H-5′), 4.55–4.65 (m, 1H, H-4), 4.57 (d, 1H, *J* = 14.6 Hz, PhCHN), 4.95 (d, 1H, *J* = 14.6 Hz, PhCHN), 4.98–5.05 (m, 2H, H-1, H-2), 5.09–5.18 (m, 1H, H-3), 7.50–8.10 (m, 10H, PhH). ^{13}C NMR, δ: –5.5, 18.1, 25.7, 47.2, 60.3, 62.0, 78.0, 89.1, 97.5, 128.3, 128.9, 129.2, 134.6, 135.0, 135.5, 156.6. Anal. calcd. for $C_{25}H_{33}NO_6SSi$: C 59.62, H 6.60, N 2.78; found: C 59.71, H 6.77, N 2.81.

Phenyl 2-benzylamino-2*N*,3*O*-carbamoyl-2-deoxy-α-D-ribofuranosyl sulfone (4b)

Compound **4a** (6.7 g, 13.4 mmol) was dissolved in dry MeOH (100 mL) under Ar, and the solution was cooled to 0°C. Freshly distilled Me_3SiCl (3.4 mL, 27 mmol) was added dropwise, via syringe, and the mixture was stirred at 0°C for 1 h. During this time, the white, fluffy, alcohol product precipitated out of solution. The solid product was filtered off and the filtrate was concentrated. The residue was triturated with solvent D and the resulting white, fluffy, product was filtered off. The filtrate was concentrated and chromatographed (solvent A) to obtain more product. The combined yield of **4b** was 4.5 g (88%); mp 172–174°C. IR,

ν_{max}: 3565–3307, 1754 cm^{-1}. ^1H NMR, δ: 3.30–3.40 (m, 1H, OH), 3.66–3.84 (m, 1H, H-5′), 3.86–3.99 (m, 1H, H-5), 4.36 (d, 1H, *J* = 14.4 Hz, PhCHN), 4.57–4.63 (m, 1H, H-4), 4.73 (d, 1H, *J* = 14.4 Hz, PhCHN), 4.77–4.87 (m, 2H, H-1, H-2), 5.03–5.12 (m, 1H, H-3), 7.30–7.85 (m, 10H, PhH). ^{13}C NMR, δ: 47.1, 61.2, 62.8, 78.6, 89.9, 98.5, 128.3, 128.7, 128.9, 128.9, 129.4, 134.8, 135.2, 135.5, 156.2. Anal. calcd. for $C_{19}H_{19}NO_6S$: C 58.60, H 4.92, N 3.60; found: C 58.53, H 5.13. N 3.67.

Phenyl 2-benzylamino-2*N*,3*O*-carbamoyl-2,5-dideoxy-5-iodo-α-D-ribofuranosyl sulfone (5)

The alcohol **4b** (2.9 g, 7.5 mmol) was dissolved in a mixture of dry toluene (60 mL), dry DCM (28 mL), and dry pyridine (1.8 mL, 26 mmol), under Ar. In a separate flask, Ph_3P (2.5 g, 9.4 mmol) was dissolved in dry toluene (30 mL) and iodine (2 g, 7.9 mmol) was added. The mixture was heated at 60°C for 30 min and then the temperature was raised to 80°C. The solution of the alcohol was added dropwise, via cannula, to the $Ph_3P–I_2$ mixture. After addition was complete, the mixture was heated at 80°C (oil bath) for 4 h, during which time the reddish brown precipitate was consumed and a white precipitate was formed. The reaction mixture was cooled to rt, filtered through a Florisil pad, and the solid residue was washed with EtOAc (2 × 30 mL). The combined filtrates were evaporated to leave a thick oil. Chromatographic purification (30:1 DCM:acetone) gave the desired iodide **5** (3.6 g, 95%) as a white solid; mp 188–190°C. IR, ν_{max}: 1747, 1584 cm^{-1}. ^1H NMR, δ : 3.43 (dd, 1H, *J* = 10.1, 6.3 Hz, H-5), 3.52 (dd, 1H, *J* = 10.1, 8.2 Hz, H-5′), 4.37 (d, 1H, *J* = 14.6 Hz, PhCH), 4.64 (dq, 1H, *J* = 8.5, 6.1, 2.2 Hz, H-4), 4.71 (d, 1H, *J* = 14.6 Hz, PhCH), 4.82 (d, 1H, *J* = 1.8 Hz, H-1), 4.89 (dd, 1H, *J* = 8.4, 1.8 Hz, H-2), 4.96 (dd, 1H, *J* = 8.4, 2.2 Hz, H-3), 7.30–7.40 (m, 5H, PhH), 7.50–7.80 (m, 3H, PhH), 7.80–7.90 (m, 2H, PhH). ^{13}C NMR, δ: 2.9, 47.5, 60.9, 79.9, 89.4, 97.8, 128.5, 128.9, 129.0, 129.4, 134.7 134.8, 135.1, 155.9. Anal. calcd. for $C_{19}H_{18}INO_5S$: C 45.70, H 3.63, N 2.81; found: C 45.70, H 3.59, N 2.82.

(4*S*,5*R*)-3-Benzyl-4-(hydroxymethyl)-5-vinyl-2-oxazolidinone (7)

Activated Zn dust (0.73g, 0.011 g atoms) was added to a solution of AgOAc (0.29 g, 1.77 mmol) in glacial AcOH (87 mL) at 110°C (oil bath). The mixture was stirred at 110°C for

35–40 s and then was allowed to cool slightly. Glacial AcOH was decanted off and the Zn/Ag couple was washed thoroughly with dry THF (4 × 10 mL) and then was covered with dry THF (10 mL). The slurry of the Zn/Ag couple in dry THF was heated to 60°C and a solution of the iodosulfone **5** (0.250 g, 0.50 mmol) was added dropwise via cannula to the Zn/Ag couple. The reaction mixture was heated at 60°C for 1 h, allowed to cool to rt, and the THF supernatant containing the aldehyde **6** was filtered through glass wool plug into a clean flask. The reaction flask was rinsed with THF (2 × 5 mL) and the washings filtered into the flask. The THF filtrate was cooled to 0°C and 95% ethanol (10 mL) was added, at which time the reaction mixture turned cloudy. Sodium borohydride (0.19 g, 5 mmol) was added, portionwise, to the mixture and the reaction mixture was stirred at 0°C for 2 h and then at rt overnight. The reaction mixture was recooled to 0°C and glacial AcOH (0.5 mL) was carefully added to destroy excess $NaBH_4$. After effervescence had subsided, the reaction mixture was evaporated and the residual oil was taken into EtOAc (15 mL). The organic phase was washed with water (10 mL), saturated aqueous $NaHCO_3$ (3 × 10 mL), and brine and then dried. The filtered solution was evaporated to give the crude crystalline primary alcohol. Chromatographic purification of the alcohol **7** (40:1 DCM:acetone) yielded white, fine needles (106 mg, 90%); mp 138–140°C. IR ν_{max}: 3518–3330, 1724, 1713 cm^{-1}. ^1H NMR, δ ($CDCl_3$-CD_3CN): 2.87 (t, 1H, *J* = 5.1 Hz, OH), 3.50–3.76 (m, 3H, H-4, CH_2O), 4.20 (d, 1H, *J* = 14.4 Hz, PhCH), 4.80 (d, 1H, *J* = 14.4 Hz, PhCH), 4.95 (“t”, 1H, *J* = 8.2 Hz, H-5), 5.32–5.51 (m, 2H, CH_2=), 5.99–6.19 (m, 1H, =CH). ^{13}C NMR, δ ($CDCl_3$-CD_3CN): 45.7, 57.8, 58.1, 77.1, 116.5, 119.8, 127.1, 127.3, 128.1, 131.1, 135.9, 157.9. Anal. calcd. for $C_{13}H_{15}NO_3$: C 66.94, H 6.48, N 6.00; found: C 66.70, H 6.68, N 5.89.

(4*S*,5*R*,)-3-Benzyl-4-(benzyloxymethyl)-5-vinyl-2-oxazolidinone (8)

The primary alcohol **7** (106 mg, 0.455 mmol) was dissolved in dry THF (5 mL), under Ar. The solution was added to a suspension of NaH (66 mg, 50% dispersion in mineral oil) in dry THF (10 mL) containing benzyl bromide (70 µL, 0.59 mmol) at 0°C. The mixture was stirred at 0°C to rt overnight (20 h). Then saturated NH_4Cl (5 mL), followed by saturated NaCl (5 mL) and EtOAc (10 mL), was added. The aqueous phase was separated and reextracted with EtOAc (5 mL). The combined organic phases were washed with water (10 mL), saturated NaCl (10 mL), dried, filtered, and evaporated. The crude oil was chromatographed (solvent C) to give the benzyl ether **8** as a pale yellow oil (127 mg, 86%). $[\alpha]_D^{21}$ –8.8 (*c* 1.70, $CHCl_3$). IR, ν_{max}: 3086, 3063, 3031, 1760 cm^{-1}. ^1H NMR, δ: 3.43 (dd, 1H, *J* = 14.7, 5.3 Hz, CHOBn), 3.51 (dd, 1H, *J* = 14.7, 3.5 Hz, CHOBn), 3.75 (“quintet”, 1H, *J* = 4.4 Hz, H-4), 4.12 (d, 1H, *J* = 14.3 Hz, PhCHN), 4.39 (d, 1H, *J* = 14.1 Hz, PhCHO), 4.47 (d, 1H, *J* = 14.1 Hz, PhCHO), 4.81 (d, 1H, *J* = 14.3 Hz, PhCHN), 4.93 (“t”, 1H, *J* = 8.5 Hz, H-5), 5.30–5.53 (m, 2H, $=CH_2$), 5.87–6.06 (m, 1H, =CH), 7.15–7.45 (m, 10H, PhH). ^{13}C NMR, δ: 46.6, 57.1, 66.6, 73.2, 77.1, 120.3, 127.7, 127.8, 128.0, 126.4, 128.6, 131.1, 136.2, 137.2, 157.9. HRMS, calcd. for $C_{20}H_{21}NO_3(M^+)$: 323.1521; found: 323.1525. Anal. calcd. for $C_{20}H_{21}NO_3$: C 74.28, H 6.55 N 4.33; found: C 73.99, H 6.43, N 4.35.

General procedure for the preparation of $RCeCl_2$ and reaction with oxazolidinonecarbaldehydes (6) and (13)

Anhydrous $CeCl_3$ (see also ref. 23)

Powdered $CeCl_3 \cdot 7H_2O$ (3 g) was placed in a 100 mL round-bottom flask containing a stir bar. The flask was fitted with an outlet tap and then connected to a high-vacuum pump (0.01–0.015 Torr; 1 Torr = 133.3 Pa). The flask was carefully evacuated, during which time a small amount of water was removed, and the salt had a whitish appearance. The flask was immersed in an oil bath that was heated at between 60 and 70°C and the salt was vigorously stirred. The

salt was heated at 60–70°C for 6 h and then the temperature of the bath was raised to 80–90° C and heating was continued for 2 h. After this period, the temperature was raised slowly, over a period of 1 h, to 140°C and the salt was stirred at this temperature for 18 h. The salt was cooled slowly to rt and then stored under Ar. The salt has an off-white appearance.

Method A: Dry THF (5 mL, at rt) was added to anhydrous $CeCl_3$ (1.2 mmol) under Ar and the mixture was stirred briefly. Then the suspension was sonicated for 1 h and allowed to stir at rt for 18 h. The white suspension was cooled to –78°C and RLi or RMgBr reagent (1.2 mmol) was added slowly. After addition was complete, the mixture assumed a light yellow or yellow-orange colour. The organometallic reagent was allowed to stir at –78°C for 1.5 h before use. The aldehyde **6** was generated from iodosulfone **5** (0.2 mmol) using a Zn/Ag couple (prepared using 292 mg Zn dust and 119 mg AgOAc) in dry THF (5 mL) according to the procedure used in the preparation of **7**. The THF supernatant was filtered (5 mL THF rinse) under Ar into a clean flask. This solution of **6** was transferred via cannula to the $RCeCl_2$ and the mixture was stirred at –78°C for the specified time (see Table 1). Then the mixture was quenched by addition of saturated NH_4Cl (5 mL) and stirred at rt for 20 min. The mixture was filtered through Florisil, and the residue washed with THF (2 × 10 mL). The combined filtrates were concentrated and the aqueous mixture was extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine, dried, filtered, and evaporated. The residual product was purified by chromatography.

Method B: The organocerium reagent was prepared as described in Method A except that 4 mol- equiv. of $RCeCl_2$ (0.62 mmol dry $CeCl_3$ and 0.62 mmol RLi or RMgBr) was used. The aldehyde **13** was generated by ozonolysis of olefin **8** (0.16 mmol) in dry DCM (5 mL) at –78°C. Ph_3P (0.19 mmol) was added and the mixture was slowly warmed to rt, under Ar, and stirred at rt for 18 h. The DCM was removed at rt under high vacuum and dry THF (5 mL) was added under Ar. The THF solution of **13** was added to the organocerium reagent and the mixture was stirred at –78°C for the specified time (see Table 2). The reaction mixture was processed as described in Method A.

(4*S*,5*R*)-3-Benzyl-4-[(1*RS*)-1-(hydroxyethyl)]-5-vinyl-2-oxazolidinone (9a,10a)

Method A: Solvent B: Yield, 85%; mp 95–97°C. IR, ν_{max}: 3600–3250, 1731 cm^{-1}. ^1H NMR, δ: 1.22 (d, *J* = 6.6 Hz, Me) and [1.48, d, *J* = 6.6 Hz, Me](3H), 2.46 (d, 1H, *J* = 5.6 Hz, OH), 3.52 (dd, *J* = 8, 4.8 Hz, H-4) and [3.71, dd, *J* = 8, 2.1 Hz, H-4](1H), 3.85–4.05 (m, 1H, CHOH), 4.41 (d, 1H, *J* = 15.2 Hz, PhCH), 4.85 ("t", 1H, *J* = 7.5 Hz, H-5), 4.93 (d, 1H, *J* = 15.2 Hz, PhCH), 5.36–5.54 (m, 2H, $=CH_2$), 5.90–6.12 (m, 1H, =CH), 7.24–7.42 (m, 5H, PhH). ^{13}C NMR, δ: 21.1, 48.4, 62.3, 66.6, 78.4, 121.0, 127.8, 128.0, 128.9, 131.4, 136.6, 159.3. LRMS-CI, NH_3 (*m*/*z*, rel. intensity): 265 (M + 18, 7.4), 248 (M + 1, 100), 202 (M – MeCHOH, 32), 91 ($PhCH_2^+$, 57). HRMS, calcd. for $C_{14}H_{17}NO_3$ (M^+): 247.1208; found: 247.1207.

(4*S*,5*R*)-3-Benzyl-4-[(1*R*)-1-(hydroxy-2-propenyl)]-5-vinyl-2-oxazolidinone (9b)

Method A: Solvent B: Yield, 85%; mp 157–159°C. IR, ν_{max}: 3471–3213, 1715, 1704 cm^{-1}. ^1H NMR, δ: 2.08 (d, 1H, *J* = 7.7 Hz, OH), 3.70 (dd, 1H, *J* = 8.5, 2.5 Hz, H-4), 4.25 (d, 1H, *J* = 15.4 Hz, PhCHN), 4.27–4.35 (m, 1H, CHOH), 4.90 ("t", 1H, *J* = 8.5 Hz, H-5), 4.95 (d, 1H, *J* = 15.4 Hz, PhCHN), 5.24–5.58 (m, 4H, 2× $=CH_2$), 5.81–6.00 (m, 1H, =CH), 6.08–6.23 (m, 1H, =CH), 7.16–7.40 (m, 5H, PhH). ^{13}C NMR, δ: 47.2, 60.7, 70.5, 78.3, 116.6, 121.1, 127.9, 128.0, 128.8, 131.6, 136.2, 137.9, 158.7. LRMS-CI, NH_3 (*m*/*z*, rel. intensity): 277 (M + 18, 8.4), 260 (M + 1, 100), 202 (M – CH_2=CHCHOH, 45), 91 ($PhCH_2^+$, 70). HRMS, calcd. for $C_{15}H_{18}NO_3$ (M + 1): 260.1286; found: 260.1275.

(4*S*,5*R*)-3-Benzyl-4-[(1*R*,*S*)-2-(*tert*-butyloxycarbonyl)-1-(hydroxyethyl)]-5-vinyl-2-oxazolidinone (9c,10c)

Method A: Solvent C: Yield, 92%; mp: 97–99°C. IR, ν_{max}: 3618–3131, 1726 cm^{-1}. ^1H NMR, δ: 1.40 (s, *t*-Bu) and [1.43, s, *t*-Bu](9H), 2.31 (dd, *J* = 15.4, 3.8 Hz) and 2.40–2.58 (m)(2H, CH_2CO), 3.14 (d, *J* = 5.1 Hz, OH) and [3.49, d, *J* = 5.1 Hz, OH](1H), 3.60 (dd, *J* = 7.7, 5.1 Hz, H-4) and [3.76, dd, *J* = 7.7, 2.3 Hz, H-4], 4.08–4.21 (m, 1H, CHOH), 4.31 (d, *J* = 14.9 Hz, PhCHN) and [4.33, d, *J* = 14.9 Hz, PhCHN](1H), 4.85 ("t", 1H, *J* = 7.7 Hz, H-5), 4.91 (d, 1H, *J* = 14.9 Hz, PhCHN), 5.34–5.55 (m, 2H, $=CH_2$), [5.80–5.97, m, =CH] and 5.98–6.17 (m, =CH)(1H), 7.20–7.35 (m, 5H, PhH). ^{13}C NMR, δ: 28.0, [30.0], [37.0], 39.1, [47.3], 48.0, 60.0, [60.6], 67.0, [68.1], 77.9, [81.2], 82.2, [85.2], [120.6], 120.8, 127.8, 128.0, [128.4], 128.7, 128.8, [128.9], [129.3], [130.6], 131.6, [134.6], 136.2, [157.5], 158.8, 171.5, [172.0]. Anal. calcd. for $C_{19}H_{25}NO_5$: C 65.69, H 7.25, N 4.03; found: C 65.59, H 7.38, N 3.95.

(4*S*,5*R*)-3-Benzyl-4-[(1*R*)-1-hydroxy-(3-phenyl-2-propynyl)]-5-vinyl-2-oxazolidinone (9d)

Method A: Solvent C: Yield, 94%; mp 119–121°C. IR, ν_{max}: 3550–3125, 2212, 1743, 1725, 1595, 1500 cm^{-1}. ^1H NMR, δ: 2.90–3.20 (br hump, 1H, OH), 3.90 (dd, 1H, *J* = 8.2, 3.3 Hz, H-4), 4.60 (d, 1H, *J* = 15.2 Hz, PhCHN), 4.75 (d, 1H, *J* = 3.1 Hz, CHOH), 4.94 ("t", 1H, *J* = 8 Hz, H-5), 5.02 (d, 1H, *J* = 15.2 Hz, PhCHN), 5.38–5.56 (m, 2H, $=CH_2$), 6.10–6.33 (m, 1H, =CH), 7.23–7.44 (m, 10H, PhH). ^{13}C NMR, δ: 47.4, 61.0, 61.2, 78.2, 87.3, 121.8, 128.0, 128.2, 128.5, 128.8, 129.0, 131.2, 131.6, 136.4, 158.4. LRMS-CI, NH_3 (*m*/*z*, rel. intensity): 351 (M + 18, 12), 334 (M + 1, 100), 202 (M – PhCCHOH, 52), 91 ($PhCH_2^+$, 66). HRMS, calcd. for $C_{21}H_{20}NO_3$(M + 1): 334.1443; found: 334.1426.

(4*S*,5*R*)-3-Benzyl-4-[(1*S*)-1-(2-furanyl)-1-(hydroxymethyl)]-5-vinyl-2-oxazolidinone (9e)

Method A: Solvent C: Yield, 85%; mp 137–139°C. IR ν_{max}: 3500–3150, 1715, 1703 cm^{-1}. ^1H NMR, δ (CD_3CN): 3.75 (d, 1H, *J* = 15 Hz, PhCHN), 3.93 (d, 1H, *J* = 6 Hz, OH), 4.08 (dd, 1H, *J* = 7.2, 3.6 Hz, H-4), 4.73 (d, 1H, *J* = 15 Hz, PhCHN), 4.75–4.85 (m, 1H, CHOH), 4.95 ("t", 1H, *J* = 7.2 Hz, H-5), 5.30–5.46 (m, 2H, $=CH_2$), 5.95–6.18 (m, 1H, =CH), 6.28–6.45 (m, 2H, furan-H), 7.05 (dd, 1H, *J* = 6.6,

2.4 Hz, furan-H), 7.20–7.45 (m, 5H, PhH). ^{13}C NMR, δ (CD_3CN): 48.2, 60.7, 67.0, 78.9, 107.9, 112.1, 121.9, 128.2, 128.9, 129.5, 133.0, 143.2, 157.0, 160.6. LRMS-CI, NH_3 (*m/z*, rel. intensity): 300 (M + 1, 100), 202 (M – furan-CHOH, 22), 91 ($PhCH_2^+$, 56). HRMS, calcd. for $C_{17}H_{17}NO_4$ (M^+): 299.1157; found: 299.1152.

(4*S*,5*R*)-3-Benzyl-4-[(1*R*,*S*)-1-hydroxy-1-phenylmethyl]-5-vinyl-2-oxazolidinone (9f,10f)

Method A: Solvent B: Yield, 52%; mp 142–144°C. IR ν_{max}: 3600–3283, 3075, 3025, 1751 cm^{-1}. ^{1}H NMR, δ: [2.28, d, *J* = 4.4 Hz, OH] and 2.47 (d, *J* = 4.4 Hz, OH)(1H), 3.56 (d, 1H, *J* = 15.4 Hz, PhCHN), 3.90 (dd, 1H, *J* = 8, 2.2 Hz, H-4), 4.80 (d, 1H, *J* = 15.2 Hz, PhCHN), 4.85–5.00 (m, 2H, CHOH, H-5), 5.30–5.70 (m, 2H, $=CH_2$), 6.00–6.27 (m, 1H, =CH), 7.12–7.50 (m, 10H, PhH). ^{13}C NMR, δ: 47.7, [48.1], 60.7, 62.6, 71.3, 78.1, 118.7, 121.3, 125.7, [126.9], 127.8, 128.1, 128.5, 128.6, [128.7], 131.2, 136.2, 140.7, 158.2. LRMS-CI, NH_3 (*m/z*, rel. intensity): 310 (M + 1, 100), 232 (M – Ph, 10), 202 (M – PhCHOH, 30), 91 ($PhCH_2^+$, 90). HRMS, calcd. for $C_{19}H_{20}NO_3$ (M + 1): 310.1443; found: 310.1453.

(4*R*,5*R*)-3-Benzyl-5-methyl-4-[(4*S*)-4-(2,2-dimethyl-1,3-dioxolanyl)]-2-oxazolidinone (12)

Compound **9a,10a** (111 mg. 0.45 mmol) was hydrolyzed using 2 M aqueous KOH (2.6 mL) in 95% EtOH (6.4 mL) at reflux for 20 h. The cooled reaction mixture was evaporated to dryness and distilled water (1 mL) was added followed by DCM (2 mL). The mixture was cooled to 0°C and Boc_2O (108 mg, 0.49 mmol) was added and the mixture was stirred under Ar for 20 h. The DCM layer was separated and saturated aqueous NaCl and solid NaCl were added to the aqueous layer. The mixture was stirred for 1 h and extracted with DCM (2 × 5 mL). The combined organic phases were dried, filtered, and evaporated to give the crude diol as a thick oil. Chromatographic separation (solvent B) gave 81 mg (59%) of diol **11.** IR ν_{max}: 3680–3113, 1690, 1660 cm^{-1}. ^{1}H NMR, δ: 0.80 (d, 3H, *J* = 7 Hz, Me), 1.50 (s, 9H, *t*-Bu), 2.90–3.10 (m, 1H), 3.25–3.42 (m, 1H), 3.95–4.25 (m, 1H), 4.65 (d, 1H, *J* = 12.6 Hz, PhCHN), 4.65–4.78 (m, 1H), 4.95–5.30 (m, 3H), 5.67–5.90 (m, 1H, =CH), 7.15–7.35 (m, 5H, PhH).

The diol **11** (40 mg) was dissolved in dry MeOH (3 mL) and was ozonized at –78°C until the blue color of ozone is visible. Argon was bubbled into the cold mixture and then $NaBH_4$ (25 mg, 0.65 mmol) was added. The mixture was allowed to stir at –78°C for 15 min and then warmed slowly to rt and stirred at rt for 20 h. Glacial AcOH (4 drops) was added to destroy unreacted $NaBH_4$. The mixture was concentrated and saturated aqueous $NaHCO_3$ (5 mL) was added. The mixture was thoroughly extracted with DCM (2 × 10 mL), the combined organic phases were dried, filtered, and evaporated to furnish crude triol (40 mg). Without further purification, the triol was treated with 2,2-dimethoxypropane (20 µL, 0.16 mmol) in dry DCM (2 mL) in the presence of *p*-$TSO_3H\cdot H_2O$ (1 crystal). After reaction was complete, dry Et_3N was added, the mixture was evaporated, and the residue was chromatographed (solvent C) to give the ketal (26 mg, 55%) as an oil. IR, ν_{max}: 3577–3224, 1691, 1675 cm^{-1}. ^{1}H NMR, δ: 1.08 (d, 3H, *J* = 7.1 Hz, Me), 1.25 and [1.32] (s, 3H, Me), 1.35 and [1.42] (s, 3H, Me), 1.49 (s, 9H, *t*-Bu), 3.42–3.95 (m, 3H), 4.05–5.85 (m, 5H), 7.18–7.40 (m, 5H, PhH).

The ketal (26 mg, 0.071 mmol) was dissolved in dry THF (2 mL) and was transferred, via cannula, to a suspension of NaH (2.5 mg, 0.11 mmol, 50% dispersion in mineral oil) in dry THF (2 mL). The mixture was refluxed under Ar for 2 h and then cooled to rt. Saturated NH_4Cl (4 drops) was added and the mixture was concentrated in vacuo. EtOAc (5 mL) and saturated NaCl (4 mL) were added and the organic layer was separated. The aqueous layer was reextracted with EtOAc (3 mL) and the combined organic extracts were dried, filtered, and evaporated to crude ketal oxazolidinone. Chromatographic purification (solvent C) furnished crystalline 2-oxazolidinone **12** (16 mg, 77%); mp 88–90°C. IR, ν_{max}: 1745 cm^{-1}. ^{1}H NMR, δ: 1.25 (s, 3H, Me), 1.27 (d, 3H, *J* = 7.0 Hz, Me), 1.35 (s, 3H, Me), 3.11 (t, 1H, *J* = 4.2 Hz, H-4), 3.51 (dd, 1H, *J* = 7.9, 5.5 Hz, H-4′), 3.90 (br "t", 1H, *J* = 7.9 Hz, H-5′), 4.07 (d, 1H, *J* = 14.3 Hz, PhCHN), 4.06–4.16 (m, 1H, H-5′), 4.42 (br "quintet", 1H, *J* = 4.2 Hz, H-5), 4.82 (d, 1H, *J* = 14.3 Hz, PhCHN), 7.10–7.40 (m, 5H, PhH). Anal. calcd. for $C_{16}H_{21}NO_4$: C 65.96, H 7.27, N 4.81; found: C 66.14, H 7.46, N 4.62.

(4*S*,5*S*)-3-Benzyl-4-benzyloxymethyl-5-[(1*R*)-1-(hydroxyethyl)]-2-oxazolidinone (14a)

Method B: Solvent A: Yield, 62%. IR, ν_{max}: 3450–3000, 1735 cm^{-1}. ^{1}H NMR, δ: 1.32 (d, 3H, *J* = 5.7 Hz, Me), 3.23–3.32 (br hump, 1H, OH), 3.53 (dd, 1H, *J* = 8.9, 4.3 Hz, CHOBn), 3.62 (t, 1H, *J* = 8.9 Hz, CHOBn), 3.78 (td, 1H, *J* = 8.9, 8.9, 4.3 Hz, H-4), 3.70–4.70 (m, 1H, CHOH), 4.00 (d, 1H, *J* = 15.2 Hz, PhCHN), 4.14 (dd, 1H, *J* = 8.9, 6.6 Hz, H-5), 4.51 (s, 2H, OCH_2Ph), 4.76 (d, 1H, *J* = 15.2 Hz, PhCHN), 7.14–7.45 (m, 10H, PhH). ^{13}C NMR, δ: 20.1, 45.5, 55.9, 64.5, 64.6, 73.8, 80.5, 127.9, 128.0, 128.1, 128.4, 128.7, 128.8, 135.4, 136.1, 157.1. Anal. calcd. for $C_{20}H_{23}NO_4\cdot\frac{1}{4}H_2O$: C 69.43, H 6.85, N 4.05; found: C 69.46, H 6.90, N 4.02.

(4*S*,5*S*)-3-Benzyl-4-(benzyloxymethyl)-5-[(1*R*)-(1-hydroxy-2-propenyl)]-2-oxazolidinone (14b)

Method B: Solvent B: Yield, 59%. IR, ν_{max}: 3550–3000, 1727, 1644 cm^{-1}. ^{1}H NMR, δ: 3.24 (d, 1H, *J* = 4.1 Hz, OH), 3.55–3.66 (m, 2H, CH_2OBn), 3.68–3.82 (m, 1H, H-4), 3.99 (d, 1H, *J* = 14.8 Hz, PhCHN), 4.24 (dd, 1H, *J* = 9.1, 6.8 Hz, H-5), 4.33–4.43 (m, 1H, CHOH), 4.45 (d, 1H, *J* = 12.5 Hz, PhCHO), 4.55 (d, 1H, *J* = 12.5 Hz, PhCHO), 4.77 (d, 1H, *J* = 14.8 Hz, PhCHN), 5.22–5.46 (m, 2H, $=CH_2$), 5.87–6.07 (m, 1H, =CH), 7.12–7.45 (m, 10H, PhH). ^{13}C NMR, δ: 45.5, 56.1, 64.8, 69.3, 73.8, 78.6, 117.2, 127.9, 128.1, 128.4, 128.7, 128.9, 136.1, 136.4, 157.5. Anal. calcd. for $C_{21}H_{23}NO_4$: C 71.37, H 6.56, N 3.96; found: C 71.40, H 6.77, N 3.90.

(4*S*,5*S*)-3-Benzyl-4-(benzyloxymethyl)-5-[(1*R*)-1-hydroxy-(3-phenyl-2-propynyl)]-2-oxazolidinone (14c)

Method B: Solvent B: Yield, 85%. IR, ν_{max}: 3575–3175, 3060, 3025, 2212, 1743, 1738, 1581, 1500 cm^{-1}. ^{1}H NMR, δ: 3.69–4.00 (m, 4H, CH_2OBn, OH, H-4), 4.05 (d, 1H, *J* =

15.4 Hz, PhCHN), 4.39 (d, 1H, *J* = 12 Hz, PhCHO), 4.55 (d, 1H, *J* = 12 Hz, PhCHO), 4.62 (dd, 1H, *J* = 7.7, 5.1 Hz, H-5), 4.75 (d, 1H, *J* = 15.4 Hz, PhCHN), 4.92 (dd, 1H, *J* = 7.7, 5.1 Hz, CHO), 7.05–7.45 (m, 15H, PhH). ^{13}C NMR, δ: 46.5, 56.1, 61.7, 65.0, 73.7, 77.4, 86.0, 86.8, 122.0, 127.9, 128.0, 128.1, 128.3, 128.4, 128.7, 128.8, 128.9, 131.7, 131.8, 135.9, 136.4, 157.8. Anal. calcd. for $C_{27}H_{25}NO_4$: C 75.86, H 5.89, N 3.28; found: C 75.78, H 5.95, N 3.20.

(4*S*,5*S*)-3-Benzyl-4-(benzyloxymethyl)-5-[(1*R*)-2-(*tert*-butyloxycarbonyl)-1-(hydroxyethyl)]-2-oxazolidinone (14d)

Method B: Solvent B: Yield, 84%. IR, ν_{max}: 3575–3275, 3075, 3030, 1748, 1731, 1625, 1587, 1520. 1500 cm^{-1}. ^{1}H NMR, δ: 1.50 (s, 9H, *t*-Bu), 2.43 (dd, 1H, *J* = 16.7, 7.5 Hz, $CHCO_2$), 2.79 (dd, 1H, *J* = 16.7, 2 Hz, $CHCO_2$), 3.57–3.84 (m, 4H, H-4, CH_2OBn, OH), 3.95 (d, 1H, *J* = 14.9 Hz, PhCHN), 4.20–4.39 (m, 2H, H-5, CHO), 4.45 (d, 1H, *J* = 11.5 Hz, PhCHO), 4.54 (d, 1H, *J* = 11.5 Hz, PhCHO), 4.78 (d, 1H, *J* = 14.7 Hz, PhCHN), 7.10–7.45 (m, 10H, PhH). ^{13}C NMR, δ: 28.0, 38.8, 46.3, 56.1, 64.8, 65.8, 73.4, 76.9, 81.6, 127.8, 127.9, 127.9, 128.0, 128.5, 128.7, 135.9, 136.9, 157.3, 171.8. Anal. calcd. for $C_{25}H_{31}NO_6$: C 67.99, H 7.08, N 3.17; found: C 67.68, H 7.32, N 3.48.

(4*S*,5*S*)-3-Benzyl-4-(benzyloxymethyl)-5-[(1*S*)-1-(2-furanyl)-1-(hydroxymethyl)]-2-oxazolidinone (14e)

Method B: Solvent B: Yield, 64%. IR, ν_{max}: 3637–3125, 3100, 3050, 1731, 1606, 1581, 1500 cm^{-1}. ^{1}H NMR, δ: 3.43 (d, 1H, *J* = 5.6 Hz, OH), 3.64 ("d" 2H, *J* = 4.3 Hz, CH_2OBn), 3.82 (dt, 1H, *J* = 7.5, 4.1 Hz, H-4), 3.96 (d, 1H, *J* = 15 Hz, PhCHN), 4.45 (d, 1H, *J* = 11.6 Hz, PhCHO), 4.55 (d, 1H, *J* = 11.6 Hz, PhCHO), 4.78 ("t", 1H, *J* = 7.5 Hz, H-5), 4.78 (d, 1H, *J* = 15 Hz, PhCHN), 4.98 (dd, 1H, *J* = 8.5, 5.6 Hz, CHO), 6.31–6.39 (m, 2H, furan-H), 7.12–7.45 (m, 11H, PhH, furan-H). ^{13}C NMR, δ: 45.3, 56.0, 64.6, 65.2, 73.6, 76.5, 108.5, 110.4, 127.9, 128.1, 128.3, 128.7, 128.8, 135.9, 136.1, 142.6, 152.2, 157.4. Anal. calcd. for $C_{23}H_{23}NO_5$: C 70.21, H 5.89, N 3.56; found: C 69.97, H 6.02, N 3.51.

(4*S*,5*S*)-3-Benzyl-4-(benzyloxymethyl)-5-[(1*R*)-1-(hydroxytetradecyl)]-2-oxazolidinone (14f)

Method B: Solvent D: Yield, 69%. IR, ν_{max}: 3600–3150, 1737, 1500 cm^{-1}. ^{1}H NMR, δ: 0.90 (t, 3H, *J* = 6.5 Hz, Me), 1.12–1.55 (m, 25H, CH_2), 1.65–1.85 (m, 1H, CH), 3.23 (d, 1H, *J* = 3.6 Hz, OH), 3.52 (dd, 1H, *J* = 9.7, 3.4 Hz, CHOBn), 3.60 ("t", 1H, *J* = 9.7 Hz, CHOBn), 3.70–3.85 (m, 2H, H-4, CHO), 3.99 (d, 1H, *J* = 15.4 Hz, PhCHN), 4.17 (dd, 1H, *J* = 9.5, 6.8 Hz, H-5), 4.46 (d, 1H, *J* = 12 Hz, PhCHO), 4.55 (d, 1H, *J* = 12 Hz, PhCHO), 4.75 (d, 1H, *J* = 15.4 Hz, PhCHN), 7.15–7.40 (m, 10H, PhH). ^{13}C NMR, δ: 14.1, 22.6, 24.8, 29.3, 29.6, 29.6, 31.9, 33.5, 46.4, 56.0, 64.5, 68.1, 73.8, 79.1, 127.6, 127.9, 128.0, 128.1, 128.4, 128.7, 128.8, 135.9, 136.1, 157.4. Anal. calcd. for $C_{33}H_{49}NO_4$: C 75.60, H 9.44, N 2.68; found: C 75.68, H 9.59, N 2.94.

(4*S*,5*S*)-3-Benzyl-4-(benzyloxymethyl)-5-[(1*S*)-1-(hydroxyethyl)]-2-oxazolidinone (15)

The MeTi(OPr-i)$_3$ reagent was prepared by treatment of ClTi(OPr-i)$_3$ (0.22 mL, 0.90 mmol) with MeLi (0.90 mL, 0.90 mmol) in dry ether (5 mL) at –40°C. Then the mixture was warmed slowly to rt and stirred at rt for 1.5 h. The mixture turned cloudy and a yellow precipitate was formed. In a separate flask the olefin **8** was dissolved in dry DCM (5 mL) and then oxidized (O_3; Pah_3) as described in Method B to provide **13**. The solution of **13** was added to the ethereal solution of MeTi(OPr-i)$_3$ at –40°C and the mixture was stirred at –40°C for 1 h. After this time, the reaction mixture was warmed slowly to rt and stirred at rt for 1.5 h. The reaction mixture was quenched by addition of aqueous 1 M HCl (10 mL) followed by DCM (10 mL). The aqueous phase was separated and reextracted with DCM (10 mL). The combined organic extracts were washed with brine, dried, filtered, and evaporated. Chromatographic purification (solvent B) of the residual oil gave **15** (57 mg, 74%). IR, ν_{max}: 3450–3050, 1735 cm^{-1}. ^{1}H NMR, δ: 1.29 (d, 3H, *J* = 5.7 Hz, Me), 3.34 (d, 1H, *J* = 8.5, 3.6 Hz, CHOBn), 3.62 (t, 1H, *J* = 8.5 Hz, CHOBn), 3.78 (td, *J* = 8.5, 8.5, 3.6 Hz, H-4), 3.92–4.06 (m, 1H, CHOH), 3.99 (d, 1H, *J* = 15.4 Hz, PhCHN), 4.14 (dd, 1H, *J* = 8.5, 6.8 Hz, H-5), 4.50 (s, 2H, OCH_2Ph), 4.76 (d, 1H, *J* = 15.4 Hz, PhCHN), 7.10–7.48 (m, 10H, PhH). ^{13}C NMR, δ: 20.1, 46.4, 55.9, 64.5, 64.6, 73.8, 80.5, 127.9, 127.9, 128.0, 128.4, 128.7, 128.8, 135.8, 136.1, 157.4. Anal. calcd. for $C_{20}H_{23}NO_4$: C 70.36, H 6.79, N 4.10; found: C 70.17, H 7.00, N 3.90.

(4*R*)-3-Benzyl-4-[(4*S*,5*R*)-4-(2,2,5-trimethyl-1,3-dioxolanyl)]-2-oxazolidinone (16)

2-Oxazolidinone **15** (33 mg, 0.097 mmol) was dissolved in a mixture of 95% EtOH (5 mL) and 2 M aqueous KOH (2 mL). The mixture was refluxed under Ar for 20 h. The cooled reaction mixture was evaporated to dryness and distilled water (2 mL) was added. Then Et_2O (4 mL) and Boc_2O (25 mg, 0.12 mmol) were added and the mixture stirred at rt, under Ar, for 4 h. The aqueous phase was removed and solid NaCl (1 g) was added. The mixture was stirred for 1 h; the aqueous phase was removed and then back-extracted with Et_2O (3 × 5 mL). The combined ether extracts were dried, filtered, and evaporated to leave crude diol as an oil (34 mg). Without further purification, the diol (34 mg) was dissolved in dry DCM (3 mL), and PPTS (11 mg) and 2-methoxypropene (0.2 mL) were added. The mixture was stirred under Ar for 3 h and then dry Et_3N (0.5 mL) was added. The mixture was evaporated to dryness and the crude residue was chromatographed (PE:EtOAc, 10:1) to give the ketal (30 mg).

The ketal (30 mg) was dissolved in dry MeOH (2 mL) and was hydrogenated (H_2, 1 atm (101.3 kPa), balloon) over 10% Pd/C (15 mg) for 4 h. The mixture was filtered through a Celite pad, the residue washed with dry MeOH (4 mL), and the combined filtrate was evaporated to leave an oil. The crude oil was dried under high vacuum for 2 h and then dissolved in dry THF (2 mL). The solution was added to a suspension of hexane-washed NaH (7 mg, 50% dispersion in mineral oil) in dry THF (2 mL). The mixture was refluxed for 45 min, cooled, and saturated NH_4Cl (4 drops) was added. The mixture was evaporated, and EtOAc (5 mL) and

saturated aqueous NaCl were added. The aqueous phase was separated and reextracted with EtOAc (4 mL). The combined organic phases were dried, filtered, and evaporated to give crude **16**. Chromatographic purification (solvent C) gave crystalline **16** (17 mg, 89%); mp 134–135°C. IR, ν_{max}: 1748 cm^{-1}. ^1H NMR, δ: 1.05 (d, 3H, *J* = 6.3 Hz, Me), 1.34 (s, 3H, Me), 1.50 (s, 3H, Me), 3.57 (dq, 1H, *J* = 8.9, 5.6, 2.1 Hz, H-4), 4.13 (d, 1H, *J* = 15.9 Hz, PhCHN), 4.25 ("t", 1H, *J* = 8.2 Hz, H-5), 4.27 (dd, 1H, *J* = 8.2, 2.1 Hz, H-5), 4.37 ("q", 1H, *J* = 6.3 Hz, H-5′), 4.44 (dd, 1H, *J* = 8.9, 5.2 Hz, H-4′), 4.93 (d, 1H, *J* = 15.9 Hz, PhCHN), 7.25–7.50 (m, 5H, PhH). ^{13}C NMR, δ: 15.2, 24.48, 26.4, 45.7, 54.8, 63.0, 71.6, 73.3, 108.4, 127.8, 127.9, 128.9, 135.7, 158.5. Anal. calcd. for $C_{16}H_{21}NO_4$: C 65.96, H 7.27, N 4.81; found: C 65.97, H 7.40, N 4.60.

(2*S*,3*S*,4*R*)-2-Benzylamino-1,3,4-dihydroxyoctadecane (17a)

The 2-oxazolidinone **14f** (270 mg, 0.528 mmol) was dissolved in 95% EtOH (10 mL) and aqueous 2 M KOH (4 mL) was added. The mixture was refluxed under Ar for 20 h, then cooled to rt, at which time a fluffy white precipitate was formed. The reaction mixture was concentrated and saturated NaCl (10 mL) was added. The mixture was thoroughly extracted with DCM (3 × 10 mL), the combined organic extracts were dried, filtered, and evaporated. The crude solid was chromatographed (DCM:MeOH, 190:2) to give crystalline **17a** (256 mg, 83%); mp 75–77°C. $[\alpha]_D^{23}$ +21.4 (*c* 1.75, $CHCl_3$). IR, ν_{max}: 3154–3448 cm^{-1}. ^1H NMR, δ: 0.90 (t, 3H, *J* = 6.5 Hz, Me), 1.15–1.75 (m, 26H, CH_2), 2.92 (dt, 1H, *J* = 6.8, 4 Hz), 3.10–3.30 (br hump, 3H), 3.47 ("t", 1H, *J* = 6.8 Hz), 3.55–3.85 (m, 5H), 4.49 (d, 1H, *J* = 13 Hz, PhCHO), 4.56 (d, 1H, *J* = 13 Hz, PhCHO), 7.20–7.42 (m, 10H, PhH). ^{13}C NMR, δ: 14.1, 22.7, 25.3, 29.3, 29.7, 29.8, 31.9, 33.9, 51.3, 60.3, 67.1, 72.1, 73.3, 74.4, 76.4, 77.0, 77.6, 127.3, 127.8, 127.9, 128.2, 128.5, 137.7, 139.1. HRMS, calcd. for $C_{32}H_{51}NO_3$ (M^+): 497.3869; found: 497.3868.

Synthetic (2*S*,3*S*,4*R*)-2-Amino-1,2,3-trihydroxyoctadecane (phytosphingosine) (17b)

The amino alcohol **17a** (256 mg) was dissolved in 95% EtOH (15 mL) and $Pd(OH)_2$ (281 mg) was added. The mixture was hydrogenated (H_2 at 50 psi (1 psi = 6.9 kPa)) for 16 h using a Parr apparatus. The mixture was filtered through Celite and the residue washed with 95% EtOH (3 × 2 mL). The combined filtrate was concentrated to about 8 mL, distilled water was added until the mixture was slightly turbid, and the mixture was placed in the freezer. The white powdery solid was filtered off and dried. Yield of **17b** was 130 mg (80%); mp 99–100°C (lit. (19*b*) mp 98–100°C; (19*c*) mp 103°C). $[\alpha]_D^{21}$ +8.3 (*c* 1.2, pyridine) (lit. (19*a*) $[\alpha]_D^{24}$ +8.7 (*c* 0.80, pyridine); (19*c*) $[\alpha]_D^{20}$ +7.9 (*c* 1.0, pyridine)). ^1H NMR, δ (DMSO-d_6): 0.85 (t, 3H, *J* = 6.5 Hz, Me), 1.15–1.35 (m, 24H, CH_2), 1.40–1.65 (m, 2H, CH_2), 2.60–2.75 (m, 1H, CHO), 3.05 (t, 1H, *J* = 6.7 Hz, CHO), 3.20–3.40 (m, 5H), 3.52 (dd, 1H, *J* = 9.6, 3.6 Hz), 4.40–4.60 (m, 1H).

Synthetic phytosphingosine tetraacetate (18)

Phytosphingosine **17b** (84 mg, 0.27 mmol) was dissolved in dry pyridine (2 mL) containing DMAP (30 mg), and Ac_2O (150 μL, 1.60 mmol) was added. The mixture was kept at rt for 18 h and then diluted with EtOAc (15 mL). The organic layer was washed twice with aqueous 1 N H_2SO_4 (10 mL), water (10 mL), and saturated $NaHCO_3$, then dried, filtered, and evaporated. The crude product was chromatographed (solvent B) to give **18** (126 mg, 98%); mp 46–48°C (lit. (19*c*) mp 48°C; (19*a*) mp 34–37°C).$[\alpha]_D^{21}$ +28.9 (*c* 0.95, $CHCl_3$), $[\alpha]_D^{21}$ +4 (*c* 1.25, DMF) (lit. (19*a*) $[\alpha]_D^{24}$ +28 (*c*, 1.30, $CHCl_3$); (19*b*) $[\alpha]_D^{30}$ +4.4 (*c* 1.12, DMF)). IR, ν_{max}: 3236–3342, 1746, 1660 cm^{-1}. ^1H NMR, δ: 0.87 (t, 3H, *J* = 6.8 Hz, Me), 1.18–1.33 (m, 24H, CH_2), 1.55–1.75 (m, 2H, CH_2), 2.20 (s, 3H, OAc), 2.50 (s, 6H, OAc), 2.80 (s, 3H, OAc), 4.00 (dd, 1H, *J* = 10.9, 2.8 Hz, CHOAc), 4.29 (dd, 1H, *J* = 10.9, 4.2 Hz, CHOAc), 4.40–4.55 (m, 1H), 4.94 (dt, 1H, *J* = 8.3, 3.4 Hz), 5.11 (dd, 1H, *J* = 8.0, 3.1 Hz), 6.05 (d, 1H, *J* = 8.3 Hz). ^{13}C NMR, δ: 14.1, 20.6, 20.7, 21.0, 22.6, 23.2, 25.5, 28.1, 29.2, 29.3, 29.4, 29.5, 29.6, 29.6, 31.9, 47.5, 62.8, 71.9, 72.9, 76.4, 76.9, 77.6, 169.7, 170.0, 170.8, 171.1. HRMS, calcd. for $C_{23}H_{42}NO_5$ (M – CH_2OAc): 412.3063; found: 412.3056.

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References

1. Sphingolipids: (*a*) C.C. Sweeley. *In* Biochemistry of lipids and membranes. *Edited by* D.E. Vance and J.E. Vance. Benjamin/Cummings, Menlo Park, Calif. 1985. Chap. 12. Hydroxylated alkaloids: (*b*) G.R. Cook, L.G. Beholz, and J.R. Stille. J. Org. Chem. **59**, 3575 (1994), and references cited; (*c*) G.W.J. Fleet and D.R. Witty. Tetrahedron: Asymmetry, **1**, 119 (1990). Amino acids: (*d*) R. Duthaler. Tetrahedron, **50**, 1539 (1994); (*e*) C.N.C. Drey. *In* Chemistry and biochemistry of the amino acids. HIV protease inhibitors. *Edited by* G.C. Barrett. Chapman and Hall, New York. 1985.Chap. 3: HIV protease inhibitors; (*f*) P. Remuzon, C. Dussy, J.-P. Jacquet, P. Roty, and D. Bouzard. Tetrahedron: Asymmetry, **7**, 1181 (1996); (*g*) M.A. Schwindt, D.T. Belmont, M. Carlson, L.C. Franklin, V.S. Hendrickson, G.L. Farrick, R.W. Poe, D.M. Sobieray, and J. Van De Vusse. J. Org. Chem. **61**, 9564 (1996). Amino sugars: (*h*) F.M. Hauser and S.R. Ellenberger. Chem. Rev. **86**, 35 (1986).
2. (*a*) Oxazolidinone-based chiral auxiliaries: D.J. Ager, I. Prakash, and D.R. Schaad. Chem. Rev. **96**, 835 (1996). (*b*) Chiral oxazoline ligands: A.V. Bedekar, E.B. Koroleva, and P.G. Andersson. J. Org. Chem. **62**, 2518 (1997), and refs. cited.
3. (*a*) J. Jurczak and A. Golebiowski. Chem. Rev. **89**, 149 (1989); (*b*) G. Cardillo and M. Orena. Tetrahedron, **46**, 3321 (1990); (*c*) M.T. Reetz. Angew. Chem. Int. Ed. Engl. **30**, 1531 (1991); (*d*) A. Dondoni and D. Perrone. Aldrichimica Acta, **30**, 35 (1997). Recent approaches: (*e*) D.R. Williams, M.H. Osterhout, and J.P. Reddy. Tetrahedron Lett. **34**, 3271 (1993);

(*f*) R. Muller, T. Leibold, M. Patzel, and V. Jager. Angew. Chem. Int. Ed. Engl. **33**, 1295 (1994); (*g*) H.Y. Chang and K.B. Sharpless. Tetrahedron Lett. **37**, 3219 (1996); (*h*) A.G.M. Barrett, M.A. Seefeld, A.J.P. White, and D.J. Williams. J. Org. Chem. **61**, 2677 (1996).

4. (*a*) J.S. Ng, C.A. Przybyla, C. Liu, J.C. Yen, F.W. Muellner, and C.L. Weyker. Tetrahedron, **51**, 6397 (1995); (*b*) R. Polt, M.A. Peterson, and L. De Young. J. Org. Chem. **57**, 5469 (1992).
5. (*a*) Review: T. Yokomatsu, Y. Yuasa, and S. Shibuya. Heterocycles, **33**, 1051 (1992); (*b*) R.W. Friesen and A.E. Kolaczewska. J. Org. Chem. **56**, 4888 (1991); (*c*) M. Kimura, K. Fugami, S. Tanaka, and Y. Tamaru. J. Org. Chem. **57**, 6377 (1992); (*d*) T. Ishizuka, S. Ishibushi, and T. Kuneida. Tetrahedron, **49**, 1841 (1993); (*e*) M.P. Sibi, D. Rutherford, and R. Sharma. J. Chem. Soc. Perkin Trans. 1, 1675 (1994); (*f*) J.C. Carretero and E. Dominguez. Tetrahedron Lett. **35**, 4603 (1994); (*g*) A.B. Bueno, M.C. Carreno, J.L.G. Ruano, R.G. Arrayas, and M.M. Zarzuelo. J. Org. Chem. **6**2 2139 (1997); (*h*) S.C. Bergmeier and D.M. Stachina. J. Org. Chem. **62**, 4449 (1997).
6. A.G.H. Wee and F. Tang. Tetrahedron Lett. **37**, 6677 (1996).
7. (*a*) A. Furstner. Liebigs Ann. Chem. 1211 (1993); (*b*) P.M. Collins and B.R. Whitton. Carbohydr. Res. **36**, 293 (1974).
8. (*a*) N.S. Simpkins. Tetrahedron, **46**, 6951 (1990); (*b*) B.M. Trost. Bull. Soc. Chem. Jpn. **61**, 107 (1988).
9. R.S. Coleman and A.J. Carpenter. J. Org. Chem. **57**, 5813 (1992).
10. J.M. Denis, C. Girard, and J.M. Conia. Synthesis, 549 (1972).
11. T. Tsunada, K. Fujiwara, Y. Yamamoto, and S. Ito. Tetrahedron Lett. **32**, 1975 (1991).
12. P. Garner and J.M. Park. J. Org. Chem. **52**, 2361 (1987).
13. (*a*) T. Imamoto *In* Comprehensive organic chemistry. Vol. 1. *Edited by* B.M. Trost and I. Fleming. Pergamon Press, New York. 1991. Chap. 1.8. p. 231; (*b*) T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, and T. Kanuya. J. Am. Chem. Soc. **111**, 4392 (1989); (*c*) P.M.J. Jung, A. Burger, and J.F. Biellmann. J. Org. Chem. **62**, 8309 (1997), and refs. cited
14. T. Imamoto, T. Hatajima, and K. Ogata. Tetrahedron Lett. **32**, 2787 (1991).
15. (*a*) M.T. Reetz. Angew. Chem. Int. Ed. Engl. **23**, 556 (1984); (*b*) M.T. Reetz, J. Westermann, R. Steinbach, B. Wenderoth, R. Peter, R. Ostanek, and S. Maus. Chem. Ber. **118**, 1421 (1985).
16. T. Ibuka, K. Suzuki, H. Habashita, A. Otaka, H. Tamamura, N. Mimura, Y. Miwa, T. Taga, and N. Fujii. Chem. Commun. 2151, (1994).
17. (*a*) M. Cherest, H. Felkin, and N. Prudent. Tetrahedron Lett. 2199 (1968); (*b*) N.T. Anh. Top. Curr. Chem. **88**, 145 (1980).
18. P. Munier, A. Krusinski, D. Picq, and D. Anker. Tetrahedron, **51**, 1229 (1995).
19. (*a*) T. Murakami, H. Minamikawa, and M. Hato. Tetrahedron Lett. **35**, 745 (1994); (*b*) A. Dondoni, G. Fantin, M. Fogagnolo, and P. Pedrini. J. Org. Chem. **55**, 1439 (1990); (*c*) J. Mulzer and C. Brand. Tetrahedron, **42**, 5961 (1986).
20. W.C. Still, M. Kahn, and A. Mitra. J. Org. Chem. **43**, 2923 (1978).
21. (*a*) J. Wardell. *In* Inorganic reactions and methods. Vol 11. *Edited by* J.J. Zuckerman. VCH, New York. 1988. p. 107; (*b*) V. Ramanathan and R. Levine. J. Org. Chem. **27**, 1316 (1962); (*c*) M.W. Rathke and D.F. Sullivan. J. Am. Chem. Soc. **75**, 3050 (1973).
22. (*a*) M.F. Lipton, C.M. Sorenson, A.C. Sadler, and R.H. Shapiro. J. Organomet. Chem. **186**, 155 (1980); (*b*) H. Kiljunen and T.H. Hase. J. Org. Chem. **56**, 6950 (1991).
23. V. Dimitrov, K. Kostova, and M. Genov. Tetrahedron Lett. **37**, 6787 (1996), and refs. cited.