Enantiospecific Synthesis of Trisubstituted Butyrolactone Natural Products and Their Analogs

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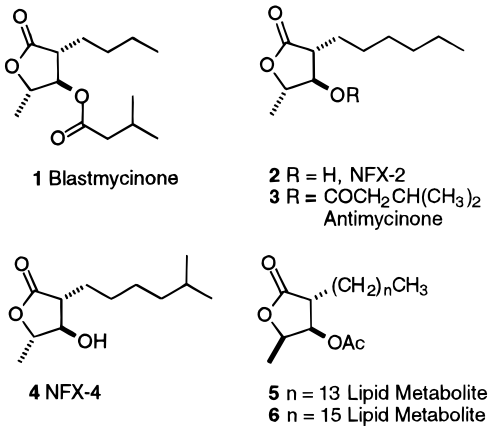
A general methodology for the synthesis of highly substituted butyrolactones in enantiomerically pure form has been developed. The application of this process in a highly efficient synthesis of lactone natural products blastmycinone (**1**), NFX-2 (**2**), antimycinone (**3**), and NFX-4 (**4**) and two lipid metabolites (**5**, **6**) are described. Additionally, the total synthesis of 5-*epi*-blastmycinone (**22**), 5-*epi*-NFX-2 (**21b**), 5-*epi*-NFX-4 (**21c**), and lipid metabolite analogs (**19**, **20**) are also described. The overall yields for the target molecules are the highest reported so far in the literature.

Introduction

Development of new methodologies for the synthesis of butyrolactone natural products has received considerable attention from organic chemists.[2] This can be attributed to the wide and potent biological activity exhibited by many different classes of compounds containing the butyrolactone skeleton. The 3-alkyl-4-hydroxy-5-methyl-2(3*H*)-dihydrofuranone substructure is found in a wide variety of metabolites with a very disparate origin.[3] Polyketide metabolites blastmycinone[4] (**1**), NFX-2[5] (**2**), antimycinone[6] (**3**), and NFX-4[5] (**4**) contain short to medium length carbon chains at the 3-position. The unusual lipid metabolites **5** and **6** isolated from Gorgonian coral *Plexaura flava* are compounds that have long alkyl chains at the 3-position.[3c]

The three contiguous chiral centers embodied in these molecules present a reasonable challenge for the development of new methodologies. Control of the relative as well as absolute stereochemistry of these centers in a general way would be desirable for the efficient synthesis of the targets natural products as well as their analogs for structure−activity studies. Methodologies have been developed for the synthesis of the targets blastmycinone,[7]



5-*epi*-blastmycinone,[7i] antimycinone,[7bb] NFX-2,[8] and NFX-4[7bb] and lipid metabolites.[9] Some of the strategies include transformation of chiral natural products,[10] enzymatic resolution,[11] oxidative heterocyclization,[12] Sharpless oxi-

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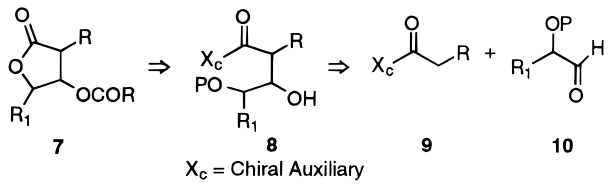
Scheme 1

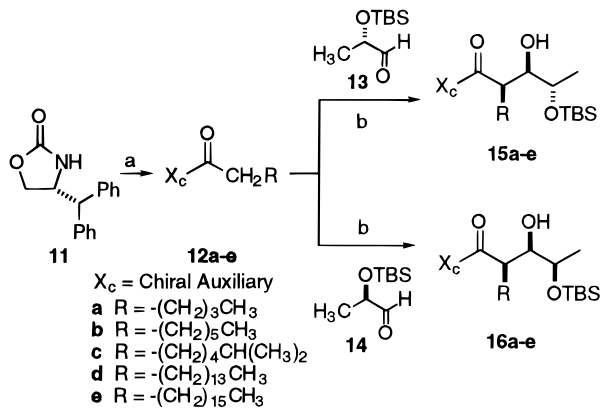


dation,[13] and nitrile oxide cycloaddition.[7d] Of the readily available chiral starting materials, lactic and tartaric acid derivatives have found some interesting application in the synthesis of the stereotriad present in the target natural products. We have been interested in exploring aldol reactions between α-alkoxy aldehydes **10** and chiral *N*-acyloxazolidinones **9** as a method for the establishment of the stereotriad. The relative and absolute stereochemistries of the stereocenters will then be established by the nature of the aldol reaction (*syn* or *anti*) and by the resident chirality of the chiral auxiliary and the α-alkoxy aldehyde (Scheme 1). Joullié *et al.* have used a similar methodology in the preparation of a butyrolactone intermediate for the total synthesis of didemnins A.[14] In this paper we report the enantiospecific synthesis of blastmycinone, NFX-2, antimycinone, and NFX-4 using the methodology shown in Scheme 1. The first enantiospecific synthesis of the lipid metabolites **5** and **6**, 5-*epi*-blastmycinone, 5-*epi*-NFX-2, 5-*epi*-NFX-4, and analogs of the lipid metabolites is also included. The overall yields for the butyrolactone natural products and analogs by our methodology are the highest reported so far in the literature. Additionally, the effect of alkyl chain length and absolute stereochemistry of the α-alkoxy aldehyde on aldol yields is discussed.

Results and Discussion

Our methodology for the synthesis of the butyrolactone natural and unnatural products started with the attachment of the required side chain to (*R*)-4-(diphenylmethyl)-2-oxazolidinone (**11**). The synthesis and application of this new chiral oxazolidinone **11** in aldol, Diels−Alder, and radical reactions have recently been reported from our laboratory.[15] Auxiliary **11** was the substrate of choice for this work for several reasons: the absolute stereochemistry of the starting material translated to the natural configuration of the targets; easy availability from L-serine; easy recovery; crystallinity of the intermediates. Treatment of **11** with *n*-BuLi produced an anion which was quenched with the appropriate acid chlorides to produce the acylated oxazolidinones **12** in very high yields (Scheme 2, Table 1).

Scheme 2[a]



[a] Key: (a) *n*-BuLi, −78 °C, RCH_2COCl; (b) method A, (i) Bu_2BOTf, Et_3N CH_2Cl_2, 0 °C, 1 h, (ii) aldehyde, −78 °C to 0 °C, 24 h, or method B, (i) Bu_2BOTf, Me_2NPh, Et_2O 0 °C, 1 h, (ii) aldehyde, −78 °C to 0 °C, 24 h.

With the desired starting materials in hand, the key aldol reactions relied on methodologies developed in the laboratories of Evans.[16] Treatment of the acyloxazolidinone **12a** with freshly prepared dibutylboron triflate followed by triethylamine furnished the boron enolate. This was quenched with freshly prepared (*S*)-*O*-TBS-protected lactaldehyde **13**[17] to furnish the *syn* aldol product **15a** (Bu_2BOTf, Et_3N, CH_2Cl_2/0 °C/1 h; aldehyde/−78 °C/30 min/0 °C/1 h). The yields for the aldol product from several runs only averaged around 60%. We sought to improve chemical yields by using the modification of the aldol protocol as reported by Boger.[18] Thus, generation of the boron enolate followed by quenching with the aldehyde and warming the reaction from −78 to 0 °C over 24 h (Bu_2BOTf, Et_3N, CH_2Cl_2/0 °C/1 h; aldehyde/−78 °C to 0 °C/24 h, method A) (Table 1, entry 1) furnished the aldol product in 90% yield as a single diastereomer (>99% de, by ^1H 400 MHz NMR of the crude reaction product). In contrast, the use of (*S*)-*O*-benzyl-protected lactaldehyde in place of **13** gave the *syn* aldol product in 64% chemical yield and 94% diastereomeric excess.[19] Thus, for the remainder of the series, the *O*-TBS-protected aldehydes were used in the aldol reactions. Application of method A for the aldol reaction of **12b** with **13**, however, led to a large decrease in chemical yield (Table 1, compare entry 1 with entry 2). A similar trend persisted with increasing chain length for compounds **12c**−**e** (Table 1, entries 3−5 for method A). The *syn* diastereoselectivity was still excellent (>99% de) for all of these substrates.[20]

The large differences in chemical yield with variation in alkyl chain length were puzzling and led us to examine some of the variables in the aldol reaction. These were

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(19) In a similar aldol reaction but using 2-(benzyloxy)-3-methylbutanal, Joullié *et al.* obtained a 17:1 diastereoselectivity for the aldol product. See: ref 14.

Table 1. Aldol Reactions with *O*-TBS Protected α-Alkoxy Aldehydes

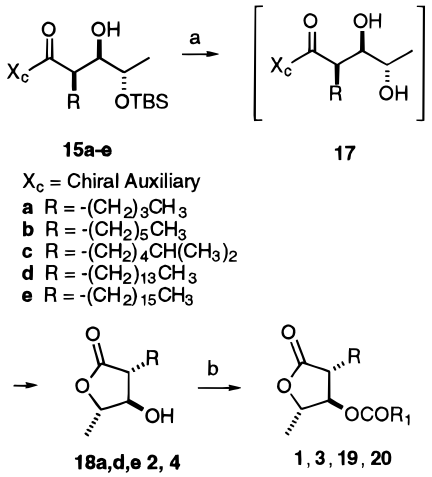
entry	substituent R	acylation yield, %[a]	aldol product[b]	method A yield, %[a,c]	method B yield, %[a,d]	aldol product[e]	method B yield, %[a,c]
1	**12a,** R = $(CH_2)_3CH_3$	96	**15a**	90	88	**16a**	67
2	**12b,** R = $(CH_2)_5CH_3$	99	**15b**	48	70	**16b**	45
3	**12c,** R = $(CH_2)_4CH(CH_3)_2$	97	**15c**	45	61	**16c**	47
4	**12d,** R = $(CH_2)_{13}CH_3$	98	**15d**	50	68	**16d**	43
5	**12e,** R = $(CH_2)_{15}CH_3$	95	**15e**	49	60	**16e**	42

[a] Yields are for isolated and purified materials. [b] Aldol reaction with (*S*)-α-alkoxy aldehyde. [c] Standard Evans aldol protocol and warming to 0 °C over 24 h after aldehyde addition. [d] Aldol reactions using Me_2NPh as the base and ether as the solvent. [e] Aldol reaction with (*R*)-α-alkoxy aldehyde.

the extent of enolate formation, solvent, the base used for enolization, and the nature of the aldehyde partner. The extent of enolate formation was assessed by a deuterium quenching experiment (boron enolate generation followed by quenching with MeOD or CF_3COOD and NMR analysis). Enolate generation using substrate **12a** under Evans conditions and MeOD quenching showed a 90% D incorporation (using CF_3COOD, 89% D). This was consistent with the yield for the aldol reaction. For the longer alkyl chain substrates, compound **12b** was used a model. Enolate generation using **12b** under Evans conditions and MeOD quenching showed a 60% D (±5%) incorporation. The extent of the enolate formation was consistent with the low chemical yield observed for the aldol reaction with **12b**. Several base−solvent combinations were then evaluated for enolate generation with **12b**. Of the different solvents evaluated using triethylamine as a base, CH_2Cl_2 gave 60% D, Et_2O gave 72% D, THF gave 54% D, and toluene gave 0% D. Then several bases were evaluated using Et_2O as a solvent. Of these dimethylethylamine gave 23% D, diisopropylethylamine gave 20% D, 4-(dimethylamino)pyridine gave 15% D, 2,6-lutidine gave 40% D, and *N*,*N*-dimethylaniline gave 88% D. Subsequently, enolate generation for substrates **12a**−**e** and aldol condensation with **13** was carried out using the optimized conditions (Bu_2BOTf, Me_2NPh/Et_2O/0 °C/1 h; aldehyde/−78 °C to 0 °C/24 h, method B) and these results are shown in Table 1, method B column. As can be evidenced from Table 1, modification of the reaction conditions led to a reasonable improvement in chemical yields for the aldol products. The *syn* diastereoselectivity for the aldols was the same using either method A or B. It is interesting to note that the shorter chain substrate **12a** gave the highest yield under all the different reaction conditions employed for the aldol reaction.

Having established the optimal reaction conditions for aldol reactions with lactaldehyde **13**, we turned our attention to reaction with the enantiomeric compound. The enantiomeric (*R*)-*O*-TBS-protected lactaldehyde **14** was prepared from commercially available (*R*)-methyl lactate.[21] The aldol reactions were carried out using method B.[22] Table 1 lists the chemical yields for the aldol products. As can be evidenced from the table, reactions with **14** were generally less efficient than reactions with **13**. However, the *syn* diastereoselectivities were still excellent.

Scheme 3[a]



[a] Key: (a) HOAc/THF/H_2O (3:1:1), rt or 60−65 °C; (b) R_1COCl, DMAP, CH_2Cl_2, or $(R_1CO)_2O$, pyridine, CH_2Cl_2.

Table 2. Conversion of Aldols from (*S*)-Aldehyde to Lactones

entry	substituent R	lactone yield, %[a]	acyl substituent R_1	yield, %[a]
1	**18a**, R = $(CH_2)_3CH_3$	87	**1**, $CH_2CH(CH_3)_2$	86
2	**2**, R = $(CH_2)_5CH_3$	84	**3**, $CH_2CH(CH_3)_2$[b]	84
3	**4**, R = $(CH_2)_4CH(CH_3)_2$	82		
4	**18d**, R = $(CH_2)_{13}CH_3$	81	**19**, CH_3[c]	95
5	**18e**, R = $(CH_2)_{15}CH_3$	89	**20**, CH_3[c]	95

[a] Yields are for isolated and purified materials. [b] Acylation using DMAP. [c] Acetylation using pyridine.

With the aldol reactions successfully completed, the next step was the removal of the *O*-TBS protecting group. Several procedures for the deprotection of the TBS group in **15** were tried.[23] The standard TBAF deprotection procedure was successful; however, a 1:1 diastereomeric mixture (diastereomeric at C-3) of lactone products was obtained. Clean deprotection without any epimerization was achieved under acidic conditions (HOAc/THF/H_2O, rt or heat) (Scheme 3). Deprotection furnished the intermediate **17** cleanly, and it underwent spontaneous lactonization to provide lactones **18**. The overall yields for this two-step one-pot process averaged around 84% (Table 2, entries 1−5). The chiral auxiliary was also recovered in >95% yield. The spectral data of **18a** were identical in all respects to that reported in the literature for blastmycinolactol.[24] A similar reaction using **15b** and **15c** as substrates produced NFX-2 (**2**) and NFX-4 (**4**), respectively, in high yields. The spectral characteristics

(20) The realtive as well as the absolute stereochemsitrry in the *syn*-boron aldols using chiral auxiliary **11** has been previously reported from our laboratory, ref 15a. The stereochemistry of the aldol products in this study is further established by conversion into the known target natural products.

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(22) Aldol reaction of **12a** using either method A or B gave similar yields. For substrates **12b**−**e**, method B gave slightly higher yields.

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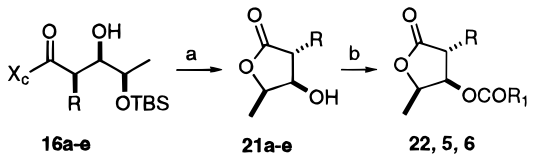
(24) References 7d,j,l,x.

Scheme 4[a]



X_c = Chiral Auxiliary
a R = -$(CH_2)_3CH_3$
b R = -$(CH_2)_5CH_3$
c R = -$(CH_2)_4CH(CH_3)_2$
d R = -$(CH_2)_{13}CH_3$
e R = -$(CH_2)_{15}CH_3$

[a] Key: (a) HOAc/THF/H_2O (3:1:1), rt or 60−65 °C; (b) R_1COCl, DMAP, CH_2Cl_2, or $(R_1CO)_2O$, pyridine, CH_2Cl_2.

Table 3. Conversion of Aldols from (*R*)-Aldehyde to Lactones

entry	substituent R	lactone yield, %[a]	acyl substituent R_1	nat prod yield, %[a]
1	**21a**, R = $(CH_2)_3CH_3$	88	**22**, $CH_2CH(CH_3)_2$[b]	82
2	**21b**, R = $(CH_2)_5CH_3$	84		
4	**21c**, R = $(CH_2)_4CH(CH_3)_2$	86		
4	**21d**, R = $(CH_2)_{13}CH_3$	81	**5**, CH_3[c]	92
5	**21e**, R = $(CH_2)_{15}CH_3$	89	**6**, CH_3[c]	93

[a] Yields are for isolated and purified materials. [b] Acylation using DMAP. [c] Acetylation using pyridine.

of these compounds were identical to those reported in the literature.[9] The overall yields for NFX-2 and NFX-4 were 58% and 49%, respectively. This compares very favorably with the overall yields reported for these two natural products in the literature.[9] The hydroxybutyrolactone **18a** was converted to natural blastmycinone (**1**) by acylation with isovaleryl chloride using a slightly modified procedure in 86% yield. The overall yield for **1** from our methodology is 64% over four steps. This is the highest yield reported for the synthesis of blastmycinone.[25] The spectral and rotation data of **1** were identical in all respects to those reported in the literature.[7x] NFX-2 was converted to antimycinone (**3**) in 86% yield by acylation with isovaleryl chloride. Acetylation of compounds **18d** and **18e** using acetic anhydride and pyridine produced the acetates **19** and **20**, respectively, in excellent yields. Compounds **19** and **20** are diastereomeric analogs of the naturally occurring lipid metabolite **5** and **6**.

The aldol products from **14** also underwent clean deprotection and lactonization under acidic conditions. Thus, deprotection of **16a**−**e** provides intermediates for the preparation of other targets. The first chiral synthesis of 5-*epi*-blastmycinone is illustrated in Scheme 4. Silyl deprotection of **16a** furnished 5-*epi*-blastmycinolactol **21a** in 88% yield (Table 3). Acylation of the lactol under standard conditions gave 5-*epi*-blastmycinone **22** in 82% yield. The spectral data for the final product are identical to those one reported for racemic material.[7i] The overall yield for **22** over four steps was 47%. Analogs of NFX-2 and NFX-4 (**21b** and **21c**) were readily obtained in 37% and 39% overall yields from aldols **16b** and **16c**, respectively. These compounds have the *epi* configuration at the 5-position as compared to the natural products. Acidic deprotection followed by acetylation of **16d** and **16e** gave the lipid metabolites **5** and **6**, respectively, in their natural configurations. The spectral data of these compounds matched those reported in the literature. The overall yields of **5** and **6** over four steps were 31% and 33%.

In conclusion, we have illustrated a short and efficient method for the preparation of biologically active butyrolactone natural products. The generality of the method allows for the preparation of a variety of natural products and analogs by a simple change in the starting materials. Extension of the methodology for the synthesis of more complex butyrolactone and other natural products is underway.

Experimental Section[26]

General Procedure for the Acylation of (*R*)-4-(Diphenylmethyl)-2-oxazolidinone (11). To a flame-dried 100 mL three-necked flask under N_2 was added a solution of (*R*)-4-(diphenylmethyl)-2-oxazolidinone (**11**) (3.0 g, 11.86 mmol) dissolved in freshly distilled THF (40 mL). The solution was cooled to −78 °C in a dry ice/acetone bath. *n*-BuLi (2.14 M, 5.8 mL, 12.4 mmol) was added in a dropwise fashion *via* syringe over a period of 10 min at −78 °C. During this process, the color of the solution changed from light yellow to orange, and eventually to red. This red solution was further stirred at −78 °C for 10 min. The corresponding acid chloride (13.8 mmol) was added slowly over 5 min. The light yellow solution was stirred at −78 °C for 15 min and at 0 °C for 30 min. The reaction was quenched with saturated NH_4Cl (15 mL) at 0 °C. The solvent was evaporated under reduced pressure, and the residue was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with H_2O (40 mL) and brine (40 mL), dried with anhydrous $MgSO_4$, and filtered, and evaporation of the solvent resulted in a white solid. Recrystallization of the crude product from ethyl acetate and hexane afforded a white crystalline compound. Purification of the mother liquor by flash column chromatography (eluted with 20% EtOAc in hexane) gave another portion of final product. Average yield is 95−99%.

(−)-(*R*)-3-(1-Oxohexyl)-4-(diphenylmethyl)-2-oxazolidinone (12a): from **11** (3.0 g, 11.9 mmol) was obtained **12a** (4.0 g, 11.4 mmol), 96%; mp 95−96.5 °C; R_f 0.35 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.0 Hz, 3H), 1.23−1.33 (m, 3H), 1.50−1.58 (m, 3H), 2.71−2.85 (m, 2H), 4.37 (dd, J = 9.1, 2.7 Hz, 1H), 4.41 (dd, J = 9.1, 6.5 Hz, 1H), 4.68 (d, J = 6.5 Hz, 1H), 5.33 (ddd, J = 6.5, 6.5, 2.7 Hz, 1H), 7.10−7.34 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 153.4, 139.5, 138.1, 129.2, 128.9, 128.6, 128.4, 127.8, 127.1, 65.2, 56.2, 51.1, 35.4, 31.2, 23.9, 22.4, 13.9; IR ($CDCl_3$) 2957, 2872, 1780, 1701, 1501, 1496, 1452, 1388, 1249 cm^{-1}; $[\alpha]^{25}_D$ = −105.4° (*c* 1.06, CH_2Cl_2). Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.57; H, 7.35; N, 3.86.

(−)-(*R*)-3-(1-Oxooctyl)-4-(diphenylmethyl)-2-oxazolidinone (12b): from **11** (3.0 g, 11.9 mmol) was obtained **12b** (4.46 g, 11.8 mmol, 99%); mp 99−100.5 °C; R_f 0.32 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3H), 1.19−1.38 (m, 8H), 1.44−1.62 (m, 2H), 2.70−2.86 (m, 2H), 4.37 (dd, J = 9.4, 2.9 Hz, 1H), 4.41 (dd, J = 9.4, 7.3 Hz, 1H), 4.68 (d, J = 5.9 Hz, 1H), 5.32 (ddd, J = 7.3, 5.9, 2.9 Hz, 1H), 7.10−7.38 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 153.4, 139.5, 138.1, 129.2, 128.8, 128.6, 128.4, 127.8, 127.1, 65.1, 56.2, 51.1, 35.4, 31.6, 28.9, 24.2, 22.6, 14.1; IR ($CDCl_3$) 3088, 3065, 3032, 2955, 2928, 2859, 1782, 1701, 1601, 1497, 1453, 1387, 1337, 1211, 1096 cm^{-1}; $[\alpha]^{25}_D$ = −96.0° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{24}H_{29}NO_3$: C, 75.96; H, 7.70; N, 3.69. Found: C, 75.59; H, 7.80; N, 3.66.

(−)-(*R*)-3-(1-Oxo-7-methyloctyl)-4-(diphenylmethyl)-2-oxazolidinone (12c): from **11** (3.0 g, 11.9 mmol) and the acid

(25) The highest yield for blastmycinone reported so far is 22% over six steps. See ref 7x.

(26) ^{1}H and ^{13}C NMR were recorded on JEOL-GSX instruments. IR spectra were recorded on Mattson Instruments 2020 Galaxy series FT-IR spectrophotometer. Optical rotations were recorded on a JASCO-DIP-370 instrument. For typical experimental protocols, see: Gaboury, J. A.; Sibi, M. P. *J. Org. Chem.* **1993**, *58*, 2173.

chloride[27] was obtained **12c** (4.59 g, 11.53 mmol, 97%); mp 88−90 °C; R_f 0.34 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J = 6.7 Hz, 6H), 1.08−1.20 (m, 2H), 1.20−1.33 (m, 4H), 1.42−1.61 (m, 3H), 2.71−2.84 (m, 2H), 4.37 (dd, J = 9.1, 2.9 Hz, 1H), 4.41 (dd, J = 9.1, 7.8 Hz, 1H), 4.68 (d, J = 6.2 Hz, 1H), 5.32 (ddd, J = 7.8, 6.2, 2.9 Hz, 1H), 7.09−7.39 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 153.4, 139.5, 138.1, 129.2, 128.9, 128.6, 128.4, 127.8, 127.1, 65.1, 56.2, 51.1, 38.7, 35.4, 29.3, 27.9, 27.1, 24.2, 22.6; IR ($CDCl_3$) 2955, 2930, 2868, 1782, 1701, 1601, 1497, 1453, 1385, 1339, 1211, 1034, 702 cm^{-1}; $[\alpha]^{25}_D$ = −98.1° (*c* 1.10, CH_2Cl_2). Anal. Calcd for $C_{25}H_{31}NO_3$: C, 76.30; H, 7.94; N, 3.56. Found: C, 76.14; H, 7.87; N, 3.87.

(−)-(*R*)-3-(1-Oxohexadecyl)-4-(diphenylmethyl)-2-oxazolidinone (12d): from **11** (4.0 g, 15.8 mmol) was obtained **12d** (7.62 g, 15.5 mmol, 98%); mp 71−73 °C; R_f 0.47 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3H), 1.26 (bs, 24 H), 1.47−1.62 (m, 2H), 2.70−2.87 (m, 2H), 4.37 (dd, J = 9.1, 2.7 Hz, 1H), 4.47 (dd, J = 9.1, 7.5 Hz, 1H), 4.68 (d, J = 5.9 Hz, 1H), 5.32 (ddd, J = 7.5, 5.9, 2.7 Hz, 1H), 7.08−7.38 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 153.4, 139.5, 138.1, 129.2, 128.9, 128.6, 128.4, 127.8, 127.0, 65.1, 56.2, 51.1, 35.4, 31.9, 29.7, 29.6, 29.5, 29.3, 29.0, 24.2, 22.7, 14.1; IR ($CDCl_3$) 2928, 2854, 1782, 1699, 1496, 1454, 1397, 1211 cm^{-1}; $[\alpha]^{25}_D$ = −74.9° (*c* 1.01, CH_2Cl_2). Anal. Calcd for $C_{32}H_{45}NO_3$: C, 78.17; H, 9.22; N, 2.85. Found: C, 78.18; H, 9.30; N, 3.01.

(−)-(*R*)-3-(1-Oxooctadecyl)-4-(diphenylmethyl)-2-oxazolidinone (12e): from **11** (2.70 g, 10.67 mmol) was obtained **12e** (5.26 g, 10.13 mmol), 95%; mp 68−70 °C; R_f 0.45 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3H), 1.08−1.38 (m, 28H), 1.44−1.59 (m, 2H), 2.70−2.86 (m, 2H), 4.37 (dd, J = 9.1, 2.6 Hz, 1H), 4.40 (dd, J = 9.1, 6.9 Hz, 1H), 4.68 (d, J = 5.9 Hz, 1H), 5.33 (ddd, J = 6.9, 5.9, 2.6 Hz, 1H), 7.09−7.37 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 153.4, 139.5, 138.1, 129.2, 128.9, 128.6, 128.4, 127.9, 127.1, 65.1, 56.2, 51.1, 35.4, 31.9, 29.7, 29.6, 29.5, 29.3, 29.1, 24.2, 22.7, 14.1; IR ($CDCl_3$) 2926, 2855, 1784, 1703, 1601, 1496, 1454, 1386, 1249, 1211, 910, 734, 702 cm^{-1}; $[\alpha]^{25}_D$ = −70.8° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{34}H_{49}NO_3$: C, 78.57; H, 9.50; N, 2.69. Found: C, 78.60; H 9.60; N, 2.52.

General Procedure for the Aldol Reaction of (*R*)-*N*-Acyl-4-(diphenylmethyl)-2-oxazolidinone (12a−e) with 2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]propanal (13, 14). Method A. To a flame-dried two-necked 25 mL flask under N_2 was added **12a−e** (2.0 mmol) in CH_2Cl_2 (5 mL), and the solution was cooled to 0 °C in an ice bath. Dibutylboron triflate (2.2 mmol) was added slowly over a period of 5 min, and the resultant brownish solution was stirred for another 5 min. Freshly distilled triethylamine (0.34 mL, 2.6 mmol) was then added dropwise while the temperature was maintained at 0 °C. The pale yellow solution was stirred at 0 °C from 45 min to 1 h. The boron enolate solution was then cooled to −78 °C. Freshly prepared **13** or **14** (0.45 g, 2.40 mmol) in 3 mL of CH_2Cl_2 was added dropwise over 10 min. The reaction mixture was warmed gradually to 0 °C over a period of 24 h. The progress of the reaction was monitored by TLC. The reaction was quenched slowly with pH = 7 buffer (2.0 mL), MeOH (6 mL), and MeOH/30% H_2O_2 = 2/1 (6 mL). The cloudy mixture was stirred at 0 °C for 1 h. The aqueous layer was separated and extracted with CH_2Cl_2 (4 × 15 mL). The combined extracts were dried over Na_2SO_4 and filtered, and the solvent was evaporated to dryness under reduced pressure. Purification of the residue by flash chromatography furnished diastereomerically pure aldol product.

Method B. Same as method A but the reaction was carried out using Me_2NPh (distilled from CaH_2) as a base for enolization and Et_2O as a solvent for the reaction. During the enolization process, substrates partially precipitated out from solvent at 0 °C, but eventually dissolved upon the addition of Bu_2BOTf.

(−)-[3-(2*R*,3*R*,4*S*),4R]-3-[1-Oxo-2-butyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-pentyl]-4-(diphenylmethyl)-2-oxazolidinone (15a): method A (90%), colorless sticky oil; R_f 0.35 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.87−0.89 (m, 12H), 1.07−1.17 (m, 5H), 1.08−1.30 (m, 2H), 1.57−1.67 (m, 2H), 2.73 (d, J = 3.2 Hz, 1H), 3.69 (ddd, J = 5.9, 5.4, 3.2 Hz, 1H), 3.82 (dq, J = 6.4, 5.4 Hz, 1H), 4.00 (ddd, J = 8.4, 5.9, 5.1 Hz, 1H), 4.36 (dd, J = 9.7, 7.5 Hz, 1H), 4.42 (dd, J = 9.7, 1.6 Hz, 1H), 4.78 (d, J = 5.9 Hz, 1H), 5.32 (ddd, J = 7.5, 5.9, 1.6 Hz, 1H), 7.14−7.34 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 152.9, 139.6, 137.9, 129.1, 128.9, 128.7, 128.4, 127.9, 127.1, 74.9, 69.0, 64.7, 56.9, 51.1, 43.6, 28.7, 26.9, 25.8, 23.1, 18.9, 17.9, 13.9, −4.3, −4.9; IR ($CDCl_3$) 3547, 2959, 2931, 2860, 2251, 1784, 1691, 1496, 1464, 1386, 1253, 1207, 1089 cm^{-1}; $[\alpha]^{25}_D$ = −82.5° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{31}H_{45}NO_5Si$: C, 68.98; H, 8.40; N, 2.59. Found: C, 69.11; H, 8.46; N, 2.67.

(−)-[3-(2*R*,3*R*,4*S*),4*R*]-3-[1-Oxo-2-hexyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (15b): method A (48%), method B (70%); R_f 0.08 (90:10 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.87−0.92 (m, 12H), 1.10−1.33 (m, 11H), 1.58−1.72 (m, 2H), 2.71 (d, J = 3.2 Hz, 1H), 3.70 (ddd, J = 5.4, 5.4, 3.2 Hz, 1H), 3.82 (dq, J = 6.2, 5.4 Hz, 1H), 4.00 (ddd, J = 8.6, 5.4, 4.8 Hz, 1H), 4.36 (dd, J = 9.4, 8.3 Hz, 1H), 4.43 (dd, J = 9.4, 2.7 Hz, 1H), 4.78 (d, J = 5.7 Hz, 1H), 5.31 (ddd, J = 8.3, 5.7, 2.7 Hz, 1H), 7.12−7.34 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 152.9, 139.5, 137.9, 129.1, 128.9, 128.7, 128.3, 127.8, 127.1, 74.9, 69.0, 64.6, 56.8, 50.9, 43.6, 31.6, 29.8, 27.2, 26.6, 25.7, 22.7, 18.9, 17.9, 14.1, −4.3, −5.0; IR ($CDCl_3$) 3532 (b), 3088, 3063, 2930, 1952, 1784, 1693, 1601, 1497, 1462, 1386, 1209, 968 cm^{-1}; $[\alpha]^{25}_D$ = −75.6° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{33}H_{49}NO_5Si$: C, 69.80; H, 8.70; N, 2.47. Found: C, 69.43; H, 8.46; N, 2.50.

(−)-[3-(2*R*,3*R*,4*S*),4*R*]-3-[1-Oxo-2-(5-methylhexyl)-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-pentyl]-4-(diphenylmethyl)-2-oxazolidinone (15c): method A (45%), method B (61%), colorless sticky oil; R_f 0.08 (90:10 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.86−0.92 (m, 15H), 1.08−1.38 (m, 10H), 1.48−1.72 (m, 2H), 2.69−2.75 (bs, 1H), 3.69 (dd, J = 5.6, 5.4 Hz, 1H), 3.82 (dq, J = 6.2, 5.6 Hz, 1H), 4.01 (ddd, J = 8.0, 5.4, 4.0 Hz, 1H,), 4.36 (dd, J = 9.4, 8.1 Hz, 1H), 4.43 (dd, J = 9.4, 2.7 Hz, 1H), 4.78 (d, J = 5.6 Hz, 1H,), 5.32 (ddd, J = 8.1, 5.6, 2.7 Hz, 1H), 7.12−7.38 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 153.0, 139.7, 138.0, 129.3, 129.0, 128.9, 128.5, 127.9, 127.2, 75.1, 69.2, 64.8, 56.9, 51.2, 43.8, 31.8, 29.9, 27.4, 26.8, 25.9, 22.8, 19.1, 18.0, 14.2, −4.1, −4.8; IR (neat) 3543 (b), 3088, 3063, 3030, 2951, 1950, 1786, 1693, 1601, 1497, 1454, 1383, 953, 833 cm^{-1}; $[\alpha]^{25}_D$ = −71.0° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{34}H_{51}NO_5Si$: C, 70.18; H, 8.83; N, 2.41. Found: C, 69.98; H, 8.53; N, 2.81.

(−)-[3-(2*R*,3*R*,4*S*),4*R*]-3-[1-Oxo-2-tetradecyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (15d): method A (50%), method B (68%), colorless sticky oil; R_f 0.12 (90:10 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.85−0.91 (m, 12H), 1.11−1.41 (m, 27H), 1.59−1.80 (m, 2H), 2.72 (d, J = 3.0 Hz, 1H), 3.70 (ddd, J = 5.4, 5.4, 3.0 Hz, 1H), 3.82 (dq, J = 6.2, 5.4 Hz, 1H), 4.00 (ddd, J = 8.1, 5.4, 3.8 Hz, 1H), 4.36 (dd, J = 9.4, 7.5 Hz, 1H), 4.43 (dd, J = 9.4, 2.2 Hz, 1H), 4.78 (d, J = 5.6 Hz, 1H), 5.32 (ddd, J = 7.5, 5.6, 2.2 Hz, 1H), 7.14−7.41 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 152.9, 139.6, 137.9, 129.1, 128.9, 128.7, 128.4, 127.8, 127.1, 74.9, 69.0, 64.7, 56.8, 51.0, 43.7, 39.9, 30.1, 29.7, 29.6, 29.5, 29.4, 27.2, 26.6, 25.7, 22.7, 19.0, 17.9, 14.1, −4.3, −4.9; IR (neat) 3532, 3063, 3030, 2933, 2858, 1788, 1692, 1601, 1464, 1387, 1260, 1208, 1094 cm^{-1}; $[\alpha]^{25}_D$ = −60.3° (*c* 0.98, CH_2Cl_2). Anal. Calcd for $C_{41}H_{65}NO_5Si$: C, 72.41; H, 9.63; N, 2.06. Found: C, 72.51; H, 9.52; N, 1.82.

(−)-[3-(2*R*,3*R*,4*S*),4*R*]-3-[1-Oxo-2-hexadecyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (15e): method A (49%), method B (60%), colorless sticky oil; R_f 0.12 (90:10 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.85−0.90 (b, 12H), 1.12 (d, 6.2 Hz, 3H), 1.13−1.35 (b, 28H), 1.58−1.74 (m, 2H), 2.72 (d, J = 3.2 Hz, 1H), 3.70 (ddd, J = 5.4, 5.4, 3.2 Hz, 1H), 3.82 (dq, J = 6.2, 5.4 Hz, 1H), 4.00

(27) The acid chloride was prepared according to a literature procedure: Kaga, H.; Miura, M.; Orito, K. *Synthesis* **1989**, 864.

(ddd, J = 7.9, 5.4, 3.9 Hz, 1H), 4.36 (dd, J = 9.3, 7.7 Hz, 1H), 4.43 (dd, J = 9.3, 2.8 Hz, 1H), 4.78 (d, J = 5.7 Hz, 1H), 5.32 (ddd, J = 7.7, 5.7, 2.8 Hz, 1H), 7.14−7.35 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 152.9, 139.6, 137.9, 129.1, 129.0, 128.7, 128.4, 127.8, 127.1, 74.9, 69.1, 64.7, 56.9, 51.1, 43.7, 31.9, 30.1, 29.7, 29.6, 29.5, 29.4, 27.2, 26.7, 25.8, 22.7, 19.0, 17.9, 14.1, −4.2, −4.9; IR (neat) 3543 (b), 2926, 2855, 1783, 1693, 1691, 1496, 1464, 1387, 1251, 1205, 1093, 835, 775, 702 cm^{-1}; $[\alpha]^{25}_D = -59.3°$ (c 1.01, CH_2Cl_2). Anal. Calcd for $C_{43}H_{69}NO_5Si$: C, 72.94; H, 9.82; N, 1.98. Found: C, 72.99; H, 9.52; N, 2.27.

(−)-[3-(2*R*,3*R*,4*R*),4*R*]-3-[1-Oxo-2-butyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (16a): method B (67%), R_f 0.65 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.82−0.96 (b, 12H), 1.20−1.40 (m, 6H), 1.42−1.53 (m, 1H), 1.71−1.81 (m, 1H), 2.17−2.28 (m, 1H), 2.41 (d, J = 7.5 Hz, 1H), 3.49 (dd, J = 9.1, 8.1 Hz, 1H), 3.88 (dd, J = 9.1, 2.2 Hz, 1H), 3.96 (dq, J = 5.9, 3.8 Hz, 1H), 4.05 (ddd, J = 7.5, 7.0, 3.8 Hz, 1H), 4.14 (ddd, J = 7.5, 7.0, 3.2 Hz, 1H), 4.78 (d, J = 5.9 Hz, 1H), 5.04 (ddd, J = 8.1, 5.9, 2.2 Hz, 1H), 6.86−7.07 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 152.9, 138.0, 129.1, 128.9, 128.7, 128.4, 127.8, 127.1, 74.5, 69.7, 64.9, 56.7, 51.1, 45.5, 29.7, 28.3, 26.6, 25.7, 23.0, 20.5, 13.9, −4.0, −5.1; IR (neat) 3543 (b), 2926, 2854, 1786, 1694, 1601, 1497, 1464, 1386, 1251, 1205, 1093, 835, 775, 702 cm^{-1}; $[\alpha]^{25}_D$ = −83.6° (c 1.00, CH_2Cl_2). Anal. Calcd for $C_{31}H_{45}NO_5Si$: C, 68.98; H, 8.40; N, 2.59. Found: C, 69.01; H, 8.19; N, 2.57.

(−)-[3-(2*R*,3*R*,4*R*),4*R*]-3-[1-Oxo-2-hexyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (16b): method B (45%), R_f 0.44 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.87−0.94 (m 12H), 1.27−1.39 (m, 10H), 1.49−1.60 (m, 1H), 1.72−1.86 (m, 1H), 2.16−2.30 (m, 1H), 2.43 (d, J = 7.4 Hz, 1H), 3.53 (dd, J = 9.3, 8.5 Hz, 1H), 3.90 (dd, J = 9.3, 2.5 Hz, 1H), 3.96 (dq, J = 6.2, 3.7 Hz, 1H), 4.05 (ddd, J = 7.4, 7.0, 3.7 Hz, 1H), 4.15 (ddd, J = 7.3, 7.0, 2.4 Hz, 1H), 4.81 (d, J = 5.6 Hz, 1H), 5.07 (ddd, J = 8.5, 5.6, 2.5 Hz, 1H), 6.86−7.07 (m, 10H); ^{13}C NMR (100 MHz, C_6D_6) δ 174.1, 153.0, 139.9, 138.4, 129.3, 128.8, 128.6, 127.9, 127.6, 126.9, 74.9, 70.4, 64.2, 56.7, 51.2, 46.0, 32.0, 30.0, 27.6, 26.6, 25.8, 22.9, 20.7, 17.9, 14.1, −4.2, −5.2; IR (neat) 3522 (b), 3063, 3030, 2955, 2858, 1790, 1694, 1601, 1496, 1454, 1387, 1251, 1211, 1089, 968 cm^{-1}; $[\alpha]^{25}_D$ = −81.6° (c 1.15, CH_2Cl_2). Anal. Calcd for $C_{33}H_{49}NO_5Si$: C, 69.80; H, 8.70; N, 2.47. Found: C, 70.03; H, 8.44; N, 2.52.

(−)-[3-(2*R*,3*R*,4*R*),4*R*]-3-[1-Oxo-2-(5-methylhexyl)-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (16c): method B (47%), R_f 0.45 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.87−0.94 (m 15H), 1.18−1.40 (m, 8H), 1.45−1.60 (m, 2H), 1.75−1.88 (m, 1H), 2.18−2.30 (m, 1H), 3.51 (dd, J = 9.0, 8.7 Hz, 1H), 3.90 (dd, J = 9.0, 2.5 Hz, 1H), 3.99 (dq, J = 6.2, 3.5 Hz, 1H), 4.07 (dd, J = 7.0, 3.5 Hz, 1H), 4.16 (ddd, J = 7.4, 7.0, 2.4 Hz, 1H), 4.82 (d, J = 5.7 Hz, 1H), 5.05 (ddd, J = 8.7, 5.7, 2.5 Hz, 1H), 6.84−7.11 (m, 10H); ^{13}C NMR (100 MHz, C_6D_6) δ 174.1, 153.0, 139.9, 138.5, 129.3, 128.8, 128.6, 127.9, 126.9, 74.9, 70.4, 64.2, 56.7, 51.3, 46.0, 39.0, 28.2, 28.1, 27.7, 26.8, 25.8, 25.6, 22.6, 20.7, 17.9, -4.2, −5.2; IR (neat) 3425 (b), 3063, 3030, 2953, 2931, 2856, 1753, 1695, 1601, 1495, 1464, 1386, 1249, 1215, 1060, 835 cm^{-1}; $[\alpha]^{25}_D = -79.8°$ (c 1.01, CH_2Cl_2). Anal. Calcd for $C_{34}H_{51}NO_5Si$: C, 70.18; H, 8.83; N, 2.41. Found: C, 70.39; H, 8.67; N, 2.53.

(−)-[3-(2*R*,3*R*,4*R*),4*R*]-3-[1-Oxo-2-tetradecyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (16d): method B (43%); mp 63−65 °C; R_f 0.65 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.90 (b, 12H), 1.15−1.50 (m, 26H), 1.51−1.68 (m, 1H), 1.76−1.89 (m, 1H), 2.20−2.33 (m, 1H), 2.43 (d, J = 7.5 Hz, 1H), 3.51 (dd, J = 9.3, 6.3 Hz, 1H), 3.89 (dd, J = 9.3, 2.4 Hz, 1H), 4.00 (dq, J = 6.2, 3.4 Hz, 1H), 4.09 (ddd, J = 7.5, 6.9, 3.4 Hz, 1H), 4.19 (ddd, J = 7.6, 6.9, 3.7 Hz, 1H), 4.82 (d, J = 5.5 Hz, 1H), 5.05 (ddd, J = 6.3, 5.5, 2.4 Hz, 1H), 6.85−7.12 (m, 10H); ^{13}C NMR (100 MHz, C_6D_6) δ 174.1, 152.9, 139.9, 138.5, 129.3, 128.8, 128.6, 127.9, 127.6, 126.9, 74.9, 70.4, 64.2, 56.7, 51.2, 46.0, 32.1, 30.4, 30.0, 29.9, 29.8, 29.6, 22.9, 20.7, 17.9, 14.1, −4.2, −5.1; IR (neat) 3543 (b), 2926, 2854, 1786, 1694, 1601, 1497, 1464, 1386, 1251, 1205, 1093, 835, 775, 702 cm^{-1}; $[\alpha]^{25}_D = -72.5°$ (c 1.00, CH_2Cl_2). Anal. Calcd for $C_{41}H_{65}NO_5Si$: C, 72.41; H, 9.63; N, 2.06. Found: C, 72.68; H, 9.30; N, 2.40.

(−)-[3-(2*R*,3*R*,4*R*),4*R*]-3-[1-Oxo-2-hexadecyl-3-hydroxy-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]pentyl]-4-(diphenylmethyl)-2-oxazolidinone (16e): method B (42%); mp 42−44 °C; R_f 0.65 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, C_6D_6) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.89−0.93 (b, 12H), 1.25−1.41 (m, 30H), 1.51−1.70 (m, 1H), 1.74−1.90 (m, 1H), 2.21−2.35 (m, 1H), 2.43 (d, J = 7.5 Hz, 1H), 3.51 (dd, J = 9.4, 6.4 Hz, 1H), 3.89 (dd, J = 9.4, 2.5 Hz, 1H), 3.99 (dq, J = 6.2, 3.3 Hz, 1H), 4.08 (ddd, J = 7.5, 6.7, 3.3 Hz, 1H), 4.17 (ddd, J = 7.6, 6.7, 3.7 Hz, 1H), 4.82 (d, J = 5.6 Hz, 1H), 5.05 (ddd, J = 6.4, 5.6, 2.5 Hz, 1H), 6.85−7.13 (m, 10H); ^{13}C NMR (100 MHz, C_6D_6) δ 174.1, 152.9, 139.9, 138.5, 129.3, 128.8, 128.6, 127.9, 127.6, 126.9, 74.9, 70.4, 64.2, 56.7, 51.2, 46.0, 32.1, 30.4, 30.0, 29.9, 29.8, 29.6, 27.6, 26.7, 25.8, 25.7, 22.9, 20.7, 17.9, 14.1, −4.2, −5.1; IR (neat) 3543, 2925, 2854, 1786, 1693, 1476, 1464, 1387, 1251, 1205, 1093, 836, 775, 702 cm^{-1}; $[\alpha]^{25}_D = -69.3°$ (c 1.00, CH_2Cl_2). Anal. Calcd for $C_{43}H_{69}NO_5Si$: C, 72.94; H, 9.82; N, 1.98. Found: C, 73.35; H, 9.65; N, 2.23.

General Procedure for TBS Deprotection and Lactone Formation. To a 25 mL round bottomed flask under N_2 was added a solution of the aldol product (0.5 mmol) in HOAc (6 mL), THF (2 mL), and H_2O (2 mL). This mixture was stirred at ambient temperature for 24 h or at 60−65 °C for 48 h (for longer alkyl chain substrates). The reaction was diluted with H_2O (10 mL) and neutralized with Na_2CO_3 to pH = 7 at 0 °C. The mixture was taken up with CH_2Cl_2 (15 mL) and H_2O (5 mL) into a separatory funnel. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over Na_2SO_4, and solvent was evaporated under reduced pressure. The resultant TBS-deprotected aldol adduct cyclized to the corresponding lactol in >80% yields during flash column chromatography. The product was eluted with 30% EtOAc in hexane. The chiral auxiliary was recovered (ca. 95%) during the chromatographic purification.

(−)-(3*R*,4*R*,5*S*)-3-Butyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone [(−)-blastmycinolactol] (18a): 15a (0.10 g, 0.185 mmol) gave **18a** (22.7 mg, 0.132 mmol, 87%); mp 49−51 °C; R_f 0.47 (50:50 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 6.9 Hz, 3H), 1.20−1.55 (m, 7H), 1.55−1.69 (m, 1H), 1.81−1.93 (m, 1H), 2.17−2.29 (bs, 1H), 2.57 (ddd, J = 8.6, 7.5, 5.9 Hz, 1H), 3.85 (dd, J = 8.6, 6.9 Hz, 1H), 4.21 (dq, J = 6.9, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 79.9, 79.1, 48.6, 28.9, 28.1, 22.6, 18.2, 13.8; IR (neat) 3441 (b), 2960, 2933, 2874, 1757, 1456, 1388, 1182, 1107, 1057, 856 cm^{-1}; $[\alpha]^{25}_D = -19.4°$ (c 1.01, $CDCl_3$) {lit.[7j] $[\alpha]^{20}_D = -18.4°$ (c 0.98, CD_3OD}.

(−)-(3*R*,4*R*,5*S*)-3-Hexyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone [(−)-NFX-2] (2): 15b (0.2810 g, 0.4966 mmol) gave **2** (0.0831 g, 0.4155 mmol, 84%); mp 56−58 °C; R_f 0.49 (50:50 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3H), 1.20−1.38 (b, 6H), 1.39−1.53 (m, 5H), 1.54−1.65 (m, J = 6.5 Hz, 1H), 1.80−1.90 (m, J = 4.3 Hz, 1H), 2.20−2.50 (b, 1H), 2.57 (ddd, J = 8.6, 6.5, 4.3 Hz, 1H), 3.84 (dd, J = 8.6, 7.3 Hz, 1H), 4.21 (dq, J = 7.3, 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 80.0, 78.9, 48.6, 31.5, 29.2, 28.4, 26.6, 22.5, 18.2, 14.0; IR ($CDCl_3$) 3472 (b), 2931, 2860, 1757, 1458, 1390, 1302, 1184, 1109, 1058, 804, 735 cm^{-1}; $[\alpha]^{25}_D$ = −15.1° (c 1.20, MeOH) {lit.[7bb] $[\alpha]^{25}_D$ = −13.58° (c 1.23, MeOH)}.

(−)-(3*R*,4*R*,5*S*)-3-(5-Methylhexyl)-4-hydroxy-5-methyldihydro-2(3*H*)-furanone [(−)-NFX-4] (4): 15c (0.2232 g, 0.38 mmol) gave **4** (0.0684 d, 0.3123 mmol, 82%); mp 61−63 °C; R_f 0.53 (50:50 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J = 6.7 Hz, 6H), 1.15−1.22 (m, 3H), 1.29−1.38 (m, 2H), 1.40−1.57 (m, 5H), 1.57−1.65 (m, 1H), 1.80−1.91 (m, 1H), 2.20−2.46 (b, 1H), 2.57 (ddd, J = 8.6, 7.7, 5.8 Hz, 1H), 3.84 (dd, J = 8.6, 7.3 Hz, 1H), 4.22 (dq, J = 7.3, 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 80.1, 78.9, 48.6, 38.7, 28.4, 27.8, 27.3, 26.9, 22.6, 18.2; IR ($CDCl_3$) 3453 (b), 2932, 2866,

1759, 1466, 1387, 1321, 1180, 1059, 920, 729, 650 cm^{-1}; $[\alpha]^{25}_D$ = −11.2° (*c* 1.62, MeOH) {lit.[7bb] $[\alpha]^{25}_D$ = −12.12° (*c* 1.825, MeOH)}.

(−)-(3*R*,4*R*,5*S*)-3-Tetradecyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone (18d): 15d (0.4032 g, 0.59 mmol) gave **18d** (0.1529 g, 0.48 mmol, 81%); mp 88−90 °C; R_f 0.21 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.7 Hz, 3H), 1.10−1.38 (b, 22H), 1.39−1.40 (m, 6H), 1.80−1.92 (m, 1H), 2.37 (d, *J* = 4.3 Hz, 1H), 2.57 (ddd, *J* = 8.1, 7.5, 5.4 Hz, 1H), 3.84 (ddd, *J* = 8.1, 7.0, 4.3 Hz, 1H), 4.21 (dq, *J* = 7.0, 5.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 79.9, 79.0, 48.6, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 26.7, 22.7, 18.2, 14.1; IR ($CDCl_3$) 3414 (b), 2955, 2920, 2849, 1734, 1459, 1327, 1058 cm^{-1}; $[\alpha]^{25}_D$ = −12.6° (*c* 1.17, CH_2Cl_2). Anal. Calcd for $C_{19}H_{36}O_3$: C, 73.03; H, 11.61. Found: C, 73.09; H, 11.22.

(−)-(3*R*,4*R*,5*S*)-3-Hexadecyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone (18e): 15e (0.1380 g, 0.19 mmol) gave **18e** (0.0582 g, 0.17 mmol, 89%); mp 91−93 °C; R_f 0.62 (50:50 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.9 Hz, 3H), 1.19−1.30 (b, 26H), 1.40−1.67 (m, 6H), 1.83−1.93 (m, 1H), 2.12 (d, *J* = 5.1 Hz, 1H), 2.56 (ddd, *J* = 8.6, 7.4, 5.8 Hz, 1H), 3.85 (ddd, *J* = 8.6, 7.3, 5.1 Hz, 1H), 4.21 (dq, *J* = 7.3, 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 79.8, 79.1, 48.6, 31.9, 29.7, 29.6, 29.3, 28.5, 26.8, 22.7, 18.3, 18.2, 14.1; IR ($CDCl_3$) 3414, 2920, 2849, 1734, 1471, 1327, 1286, 1057, 972, 864 cm^{-1}; $[\alpha]^{25}_D$ = −10.7° (*c* 0.85, CH_2Cl_2) {lit.[3b] $[\alpha]^{24}_D$ = −9.6° (dioxane)}.

(+)-(3*R*,4*R*,5*R*)-3-Butyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone [(+)-5-*epi*-blastmycinolactol] (21a): 16a (0.1235 g, 0.2291 mmol) gave **21a** (0.0347 g, 0.2017 mmol, 88%); R_f 0.48 (50:50 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3H), 1.20−1.63 (m, 8H), 1.65−1.78 (m, 1H), 2.55 (ddd, *J* = 8.2, 6.6, 3.2 Hz, 1H), 2.63 (d, *J* = 4.3 Hz, 1H), 4.21 (ddd, *J* = 4.8, 4.3, 3.2 Hz, 1H), 4.65 (dq, *J* = 6.7, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 78.6, 73.9, 49.2, 29.3, 28.1, 22.4, 13.9, 13.8; IR (neat) 3443 (b), 2959, 2936, 2874, 1757, 1458, 1383, 1341, 1230, 1186, 1138, 1055, 995, 949, 825, 732, 663 cm^{-1}; $[\alpha]^{25}_D$ = +59.8° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 63.05; H, 9.10.

(+)-(3*R*,4*R*,5*R*)-3-Hexyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone [(+)-5-*epi*-NFX-2] (21b): 16b (0.2689 g, 0.4744 mmol) gave **21b** (0.0797 g, 0.3985 mmol, 84%); R_f 0.48 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 6.9 Hz, 3H), 1.20−1.34 (m, 6H), 1.37 (d, *J* = 6.6 Hz, 3H), 1.40−1.59 (m, 3H), 1.61−1.74 (m, 1H), 2.52 (ddd, *J* = 8.0, 6.5, 3.3 Hz, 1H), 2.82 (b, 1H), 4.16 (dd, *J* = 4.8, 3.3 Hz, 1H), 4.61 (dq, *J* = 6.6, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 78.9, 73.9, 49.4, 31.6, 29.1, 28.5, 27.6, 22.6, 14.1, 13.9; IR (neat) 3448 (b), 2953, 2933, 1765, 1465, 1340 cm^{-1}; $[\alpha]^{25}_D$ = +47.4° (*c* 0.93, CH_2Cl_2). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 66.14; H, 9.88.

(+)-(3*R*,4*R*,5*R*)-3-(5-Methylhexyl)-4-hydroxy-5-methyldihydro-2(3*H*)-furanone [(+)-5-*epi*-NFX-4] (21c): 16c (0.2898 g, 0.509 mmol) gave **21c** (0.0959 g, 0.4378 mmol, 86%); R_f 0.45 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.6 Hz, 6H), 1.12−1.20 (m, 2H), 1.22−1.36 (m, 2H), 1.39 (d, *J* = 6.6 Hz, 3H), 1.42−1.61 (m, 4H), 1.62−1.77 (m, 1H), 2.07−2.77 (b, 1H), 2.53 (ddd, *J* = 8.1, 6.5, 3.3 Hz, 1H), 4.19 (dd, *J* = 5.5, 3.3 Hz, 1H), 4.62 (dq, *J* = 6.6, 5.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 77.4, 77.1, 49.3, 38.7, 28.5, 28.0, 27.6, 27.2, 22.7, 22.6, 14.0; IR (neat) 3449 (b), 2953, 2933, 2865, 1764, 1465, 1385, 1341 cm^{-1}; $[\alpha]^{25}_D$ = +45.5° (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.45; H, 10.21.

(+)-(3*R*,4*R*,5*R*)-3-Tetradecyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone (21d): 16d (0.1793 g, 0.26 mmol) gave **21d** (0.0640 g, 0.21 mmol, 81%); mp 66−68 °C; R_f 0.26 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.7 Hz, 3H), 1.19−1.62 (m, 28H), 1.66−1.78 (m, 1H), 2.18−2.42 (b, 1H), 2.55 (ddd, *J* = 8.1, 6.2, 3.2 Hz, 1H), 4.20 (dd, *J* = 4.8, 3.2 Hz, 1H), 4.64 (dq, *J* = 6.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 78.4, 73.9, 49.3, 31.9, 29.7, 29.6, 29.5, 29.3, 28.4, 27.3, 22.7, 14.1, 13.9; IR ($CDCl_3$) 3528 (b), 2920, 2852, 1759, 1736, 1454, 1267, 1236, 1051 cm^{-1}; $[\alpha]^{25}_D$ = +31.4° (*c* 1.15, CH_2Cl_2). Anal. Calcd for $C_{19}H_{36}O_3$: C, 73.03; H, 11.61. Found: C, 73.37; H, 11.26.

(+)-(3*R*,4*R*,5*R*)-3-Hexadecyl-4-hydroxy-5-methyldihydro-2(3*H*)-furanone (21e): 16e (0.1776 g, 0.25 mmol) gave **21e** (0.0689 g, 0.203 mmol, 81%); mp 73−75 °C; R_f 0.23 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.15−1.62 (m, 32H), 1.67−1.76 (m, 1H), 2.30 (b, 1H), 2.54 (ddd, *J* = 7.9, 6.6, 3.2 Hz, 1H), 4.20 (dd, *J* = 4.8, 3.2 Hz, 1H), 4.64 (dq, *J* = 6.7, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 78.4, 74.0, 49.3, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 28.4, 27.3, 22.7, 14.1, 13.9; IR ($CDCl_3$) 3429, 2920, 2852, 1759, 1736, 1454, 1267, 1236, 1136, 1084, 1051, 877, 732, 597 cm^{-1}; $[\alpha]^{25}_D$ = +39.8° (*c* 1.42, dioxane). Anal. Calcd for $C_{21}H_{40}O_3$: C, 74.07; H, 11.84. Found: C, 74.16; H, 11.49.

General Procedure for the Preparation of 4-(Acyloxy)-butyrolactones. Method A. To a solution of isovaleryl chloride (3 mmol) in CH_2Cl_2 (2 mL) in a 10 mL round bottomed flask at ambient temperature was added the hydroxy lactone (0.50 mmol) and DMAP (2 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at rt for 24 h. The reaction was quenched with H_2O (1 mL) and 10% citric acid (1 mL). The residue was taken up with CH_2Cl_2 (10 mL) and H_2O (5 mL) into a separatory funnel. The aqueous layer was separated and extracted with CH_2Cl_2 (4 × 10 mL). The combined organic extracts were washed with H_2O (15 mL) and brine (20 mL) and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. Purification of the residue by flash column chromatography (eluted with 10% EtOAc in hexane) furnished the butyrolactones.

Method B. A solution of hydroxy lactone (0.5 mmol) and acetic anhydride (7.5 mmol) in pyridine (3 mL) was stirred at rt for 24 h. The solvent was evaporated under vacuum. The residue was taken up with CH_2Cl_2 (10 mL) into a separatory funnel, and the organic layer was washed with 10% citric acid (10 mL), H_2O (10 mL), and brine (10 mL) and dried over $MgSO_4$. Flash column chromatography using silica gel gave the acetylated butyrolactones.

(+)-(3*R*,4*R*,5*S*)-3-Butyl-5-methyl-4-((3-methylbutyryl)-oxy)-5-methyldihydro-2(3*H*)-furanone [(+)-blastmycinone] (1): method A; **18a** (0.0740 g, 0.43 mmol) furnished **1** as a colorless oil (0.0948 g, 0.37 mmol, 86%); R_f 0.31 (90:10 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 6H), 1.25−1.57 (m, 7H), 1.59−1.70 (m, 1H), 1.82−1.92 (m, 1H), 2.11 (m, 1H), 2.23 (d, *J* = 7.0 Hz, 2H), 2.69 (ddd, *J* = 8.6, 5.9, 5.4 Hz, 1H), 4.37 (dq, *J* = 6.5, 4.3 Hz, 1H), 4.95 (dd, *J* = 5.4, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 172.4, 79.4, 78.3, 46.4, 43.1, 29.0, 28.9, 25.7, 22.3, 22.2, 19.4, 13.7; IR (neat) 2959, 2936, 2874, 1784, 1745, 1465, 1369, 1294, 1253, 1176, 1118, 1039, 958 cm^{-1}; $[\alpha]^{25}_D$ = +11.3° (*c* 1.18, $CHCl_3$) {lit.[7j] $[\alpha]^{20}_D$ = +11.0° (*c* 2.43, $CDCl_3$)}.

(+)-(3*R*,4*R*,5*S*)-3-Hexyl-4-((3-methylbutyryl)oxy)-5-methyldihydro-2(3*H*)-furanone [(+)-antimycinone] (3): method A; **2** (0.0525 g, 0.26 mmol) yielded **3** (0.0630 g, 0.22 mmol, 84%) as a colorless oil; R_f 0.58 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 6H), 1.20−1.36 (b, 6H), 1.37−1.50 (m, 5H), 1.58−1.68 (m, *J* = 8.3 Hz, 1H), 1.80−1.91 (m, *J* = 5.6 Hz, 1H), 2.11 (m, 1H), 2.23 (d, *J* = 6.7 Hz, 2H), 2.69 (ddd, *J* = 8.3, 5.6, 5.6 Hz, 1H), 4.37 (dq, *J* = 6.8, 4.6 Hz, 1H), 4.94 (dd, *J* = 5.6, 4.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 172.4, 79.4, 78.3, 46.4, 43.1, 31.5, 29.3, 28.9, 26.7, 25.7, 22.5, 22.3, 19.4, 14.0; IR (neat) 2958.9, 2933.9, 2872.2, 1788.1, 1745.6, 1465.9, 1369.5, 1292.4, 1251.9, 1174.7, 1118.8, 1039.7, 968.3 cm^{-1}; $[\alpha]^{25}_D$ = +10.8° (*c* 0.50, $CHCl_3$) {lit.[7z] $[\alpha]^{21}_D$ = +8° (*c* 0.50, $CHCl_3$)}. Anal. Calcd for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. Found: C, 67.61; H, 9.78.

(+)-(3*R*,4*R*,5*S*)-3-Tetradecyl-4-*O*-acetyl-5-methyldihydro-2(3*H*)-furanone (19): method B; **18d** (0.0697 g, 0.22 mmol) furnished **19** (0.0752 g, 0.21 mmol, 95%); mp 48−50 °C; R_f 0.48 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.20−1.36 (m, 22H), 1.36−1.52 (m, 5H), 1.57−1.70 (m, 1H), 1.80−1.90 (m, 1H), 2.11 (s, 3H), 2.69 (ddd, *J* = 8.1, 5.9, 5.4 Hz, 1H), 4.39 (dq, *J* = 6.5, 4.3 Hz, 1H), 4.92 (dd, *J* = 5.4, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 170.3, 79.4, 78.6, 46.4, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 26.8, 22.7, 20.9, 19.4, 14.1; IR ($CDCl_3$) 2855, 2926, 1777,

1742, 1466, 1367, 1238, 1180, 1059, 966, 912, 737 cm^{-1}; $[\alpha]^{25}_D = +6.8°$ (*c* 1.90, CH_2Cl_2). Anal. Calcd for $C_{21}H_{38}O_4$: C, 71.15; H, 10.80. Found: C, 71.33; H, 10.53.

(+)-(3*R*,4*R*,5*S*)-3-Hexadecyl-4-*O*-acetyl-5-methyldihydro-2(3*H*)-furanone (20): method B; **18e** (0.0270 g, 0.079 mmol) gave **20** (0.0289 g, 0.75 mmol, 95%); mp 54−56 °C; R_f 0.47 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, J = 6.8 Hz, 3H), 1.21−1.30 (b, 28H), 1.45 (d, J = 6.6 Hz, 3H), 1.57−1.66 (m, 1H), 1.79−1.88 (m, 1H), 2.10 (s, 3H), 2.68 (ddd, J = 8.3, 5.6, 5.4 Hz, 1H), 4.37 (dq, J = 6.6, 4.5 Hz, 1H), 4.91 (dd, J = 5.4, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 170.3, 79.5, 78.9, 46.5, 32.0, 29.8, 29.7, 29.6, 29.4, 26.9, 22.8, 20.9, 19.5, 14.2; IR ($CDCl_3$) 2928, 2854, 1777, 1742, 1468, 1367, 1317, 1240, 1182, 1083, 910, 734 cm^{-1}; $[\alpha]^{25}_D = +6.0°$ (*c* 1.00, CH_2Cl_2).

(+)-(3*R*,4*R*,5*R*)-3-Butyl-5-methyl-4-((3-methylbutyryl)-oxy)-5-methyldihydro-2(3*H*)-furanone [(+)-5-*epi*-blastmycinone] (22): method A; **21a** (34 mg, 0.198 mmol) furnished colorless oil **22** (42 mg, 0.163 mmol, 82%); R_f 0.47 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 7.3 Hz, 3H), 0.97 (d, J = 6.7 Hz, 6H), 1.34 (d, J = 6.5 Hz, 3H) 1.25−1.41 (m, 2H), 1.42−1.54 (m, 2H), 1.55−1.69 (m, 1H), 1.62−1.84 (m, 1H), 2.11 (m, 1H), 2.23 (s, 1H), 2.25 (d, 1H), 2.59 (ddd, J = 8.6, 5.9, 2.7 Hz, 1H), 4.77 (dq, J = 6.5, 4.8 Hz, 1H), 5.18 (dd, J = 4.8, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 172.2, 76.7, 75.2, 47.2, 43.0, 29.1, 28.2, 25.6, 22.3, 14.3, 13.7; $[\alpha]^{25}_D = +48.9°$ (*c* 1.00, CH_2Cl_2). Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.78; H, 9.11.

(+)-(3*R*,4*R*,5*R*)-3-Tetradecyl-4-*O*-acetyl-5-methyldihydro-2(3*H*)-furanone (5): Method B; **21d** (0.0454 g, 0.1455 mmol) yielded **5** (0.0475 g, 0.1339 mmol, 92%); mp 31−33 °C; R_f 0.51 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3H), 1.20−1.30 (b, 22H), 1.34 (d, J = 6.4 Hz, 3H), 1.40−1.52 (m, 2H), 1.57−1.67 (m, 1H), 1.70−1.81 (m, 1H), 2.12 (s, 3H), 2.61 (ddd, J = 8.3, 6.5, 2.7 Hz, 1H), 4.76 (dq, J = 6.4, 4.8 Hz, 1H), 5.17 (dd, J = 4.8, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 170.1, 76.7, 75.5, 47.1, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 28.5, 26.9, 22.7, 20.7, 14.2, 14.1; IR ($CDCl_3$) 2926, 2854, 1778, 1743, 1460, 1375, 1231, 1192, 1057, 1020 cm^{-1}; $[\alpha]^{25}_D = +37.4°$ (*c* 1.92, CH_2Cl_2) {lit.[3c] $[\alpha]^{20}_D = +36.1°$ (*c* 1.9, CH_2Cl_2)}.

(+)-(3*R*,4*R*,5*R*)-3-Hexadecyl-4-*O*-acetyl-5-methyldihydro-2(3*H*)-furanone (6): method B; treatment of **21e** (0.0521 g, 0.15 mmol) yielded **6** (0.0546 g, 0.14 mmol, 93%); mp 42−44 °C; R_f 0.51 (80:20 hexane:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3H), 1.20−1.32 (b, 26H), 1.34 (d, J = 6.5 Hz, 3H), 1.41−1.52 (m, 2H), 1.57−1.68 (m, 1H), 1.70−1.81 (m, 1H), 2.12 (s, 3H), 2.61 (ddd, J = 8.3, 6.5, 2.7 Hz, 1H), 4.76 (dq, J = 6.5, 4.8 Hz, 1H), 5.17 (dd, J = 4.8, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 170.1, 76.7, 75.5, 47.1, 31.9, 29.7, 29.6, 29.5, 29.3, 29.2, 28.5, 27.0, 22.7, 20.7, 14.2, 14.1; IR ($CDCl_3$) 2926, 2854, 1778, 1744, 1460, 1375, 1192, 1235, 1057, 1020, 835 cm^{-1}; $[\alpha]^{25}_D = +31.5°$ (*c* 1.30, CH_2Cl_2) {lit.[3c] $[\alpha]^{20}_D = +31.9°$ (*c* 1.30, CH_2Cl_2)}.

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