Strategy for Enantio- and Diastereoselective Syntheses of All Possible Stereoisomers of 1,3-Polyol Arrays Based on a Highly Catalyst-Controlled Epoxidation of α,β-Unsaturated Morpholinyl Amides: Application to Natural Product Synthesis

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Abstract: We describe a new strategy for enantio- and diastereoselective syntheses of all possible stereoisomers of 1,3-polyol arrays. This strategy relies on a highly catalyst-controlled epoxidation of α,β-unsaturated morpholinyl amides promoted by the Sm–BINOL–$Ph_3As{=}O$ (1:1:1) complex, followed by a conversion of morpholinyl amides into ketones and diastereoselective ketone reduction. Highly enantio- (up to >99% *ee*) or diastereoselective (up to >99.5:0.5) epoxidation was achieved using 5–10 mol% of the Sm complex to afford synthetically very useful, nearly optically pure α,β-epoxy morpholinyl amides. Stereoselectivity of the epoxidation was controlled by the chirality of BINOL with overwhelming inherent diastereofacial preference for the substrate. Combination with the *syn*- and *anti*-selective ketone reduction with the highly catalyst-controlled epoxidation allowed for an iterative strategy for the syntheses of all possible stereoisomers of 1,3-polyol arrays. Eight possible stereoisomers of 1,3,5,7-tetraol arrays were synthesized with high to excellent stereoselectivity. Moreover, the efficiency of the present strategy was successfully demonstrated by enantioselective syntheses of several 1,3-polyol/α-pyrone natural products, for example, cryptocaryolone diacetate.

Keywords: asymmetric synthesis · diastereoselectivity · epoxidation · morpholinyl amide · polyols

Introduction

The stereoselective synthesis of 1,3-polyol arrays is one of the most important topics in organic chemistry because of the ubiquity of 1,3-polyols in various biologically active natural products and drugs, such as polyene macrolide antibiotics.[1] Thus, numerous strategies for their synthesis have been developed with great success.[2] The synthesis of 1,3-polyol arrays starts with the introduction of the first chiral center to the molecule. For this purpose, with the majority of chiral pool strategy,[3] a wide variety of synthetic methods are utilized[4] and the following asymmetric reactions are mainly used for 1,3-polyol syntheses: chiral auxiliary controlled aldol reaction,[5] allylboration using chiral borane reagents,[6] catalytic asymmetric epoxidation of allylic alcohols[7] or unfunctionalized olefins,[8] catalytic asymmetric hydrogenation,[9] catalytic asymmetric Mukaiyama type aldol reaction,[10] and catalytic asymmetric dihydroxylation.[11] The second stage of the synthesis is the elongation of 1,3-polyol arrays by stereoselective construction of the next chiral center. Chirality in the vicinity of the substrate reaction site makes this process very challenging and attractive in terms of the diversity of diastereocontrol. Thus, organic chemists have developed a variety of strategies, which can be classified into three approaches according to the structure relation between the chiral source and chiral products: a) substrate control synthesis (employing intramolecular chirality transfer); b) reagent control synthesis (employing stoichiometric amounts of the chiral source); and c) catalyst control synthesis (employing catalytic amounts of the chiral source). The majority of the strategies use the substrate controlled asymmetric induction (category a). Many highly stereocontrolled 1,3-asymmetric induction reactions[12] have been developed that mainly rely on 1,3-*syn*[13]- or *anti*[14]-selective ketone reduction using borane reagents, intramolecular addition of the acetal to olefins,[15] inter- or intramolecular addition of silyl reagents to olefins such as hydrosilylation,[16] and intramolecular allylsilylation to carbonyl groups.[17] In

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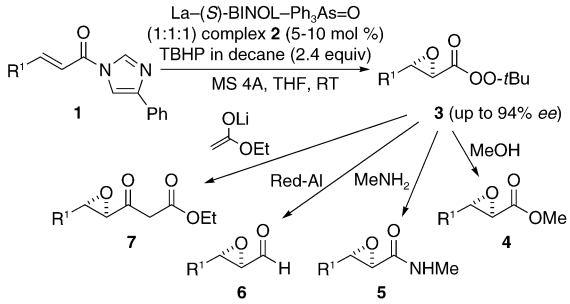
contrast to the diversity of asymmetric reactions that are employed for the introduction of the first chirality, only a few chiral reagents (category b) or chiral catalysts (category c) are applied for stereoselective elongation of 1,3-polyol arrays due to crucial *matched* or *mismatched* effects caused by the substrate chirality. Among the above-mentioned asymmetric reactions, chiral auxiliary controlled aldol reaction (category b),[5,18] allyl addition using chiral borane or titanium reagents (category b),[6,19] and catalytic asymmetric epoxidation of allylic alcohols (category c)[7,20] are commonly used for 1,3-polyol synthesis. Employing these strategies,[21] many polyene macrolide antibiotics, such as amphotericin B,[22] mycoticin A,[23] roxaticin,[24] filipin III,[25] roflamycoin,[26] dermostatin,[27] and 1,3-polyol/α-pyrones[28] were synthesized in a highly stereocontrolled manner.[29]

To synthesize not only 1,3-polyol natural products, but also their analogues, a highly versatile synthetic method that makes all possible stereoisomers freely accessible with the same efficiency is required. To address this issue, catalyst-controlled chiral induction would be more desirable in terms of accessibility to a variety of stereoisomers. In reality, however, chiral induction controlled by an asymmetric catalyst results in low selectivity in a *mismatched* case affected by the chirality in the vicinity of the reaction site.[30] Crucial *mismatched* effects are sometimes observed even in well-established Sharpless' catalytic asymmetric epoxidation.[30] Here, we report a new general strategy for the stereoselective syntheses of all possible stereoisomers of 1,3-polyol arrays based on a highly catalyst-controlled epoxidation of α,β-unsaturated morpholinyl amides and diastereoselective ketone reduction. Syntheses of all possible stereoisomers of 1,3,5,7-tetraol arrays were achieved by repeating the present strategy. Moreover, synthetic application to the enantioselective syntheses of several 1,3-polyol/α-pyrone natural products was successfully demonstrated.

Results and Discussion

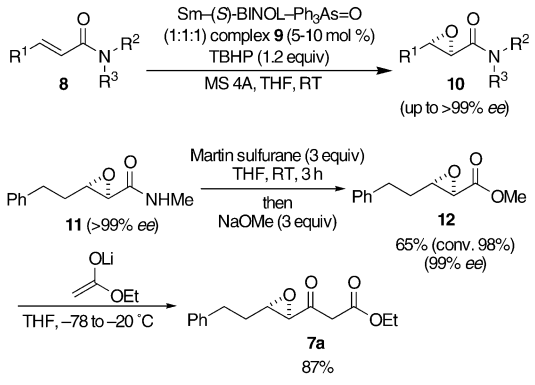
Catalytic asymmetric epoxidation of α,β-unsaturated amides: We previously reported a highly enantioselective catalytic asymmetric epoxidation of α,β-unsaturated carboxylic acid imidazolides **1**[31] promoted by the La–BINOL–Ph_3As=O (1:1:1) complex **2**[32] (Scheme 1). This is the first example of a general catalytic asymmetric epoxidation of α,β-unsaturated carboxylic acid derivatives using a 1,4-addition of hydroperoxide as the initial step. Although a salen–manganese complex[33] or an optically active ketone[34] has been used for catalytic asymmetric epoxidation of α,β-unsaturated esters, our strategy is more desirable in terms of chemoselectivity.[35] Epoxidation of α,β-unsaturated carboxylic acid imidazolides afforded stable chiral α,β-epoxy peroxy esters **3** (up to 94% *ee*)[36] that were efficiently converted to the corresponding chiral α,β-epoxy esters **4**, α,β-epoxy amides **5**, α,β-epoxy aldehydes **6**, and γ,δ-epoxy β-keto esters **7**. Thus, α,β-epoxy peroxy esters **3** are synthetically useful versatile intermediates.[37] In contrast to β-*aryl*-substituted substrates, epoxidation of β-*alkyl*-substituted α,β-unsaturated carboxylic acid imidazolides **1**, however, had lower selectivity even after improvement using the Pr–BINOL–Ph_3As=O (1:1:1) complex (up to 86% *ee*, Scheme 1).[38b]

We recently reported a more general variant of this catalytic asymmetric epoxidation by using simple α,β-unsaturated amides **8** promoted by Sm–BINOL–Ph_3As=O (1:1:1)



Scheme 1. Catalytic asymmetric epoxidation of α,β-unsaturated carboxylic acid imidazolides.

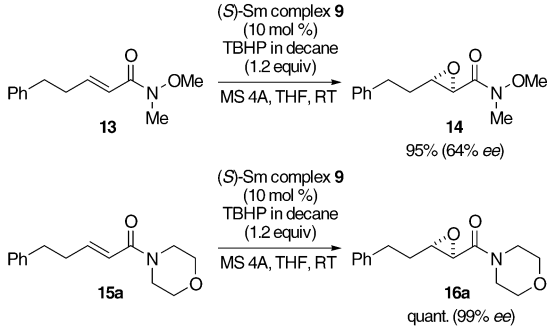
complex **9** (Scheme 2).[38] In this case, the corresponding α,β-epoxy amides **10** were obtained in excellent yield (up to 99%) and in quite high enantiomeric excess (up to >99%) with broad substrate generality (R^1 = alkyl or Ar). For the synthesis of a chiral 1,3-polyol array, γ,δ-epoxy β-keto esters **7** are promising intermediates. In fact, both *syn*- and *anti*-3,5-dihydroxy esters were obtained by a regioselective epoxide opening reaction of **7**, followed by a diastereoselective ketone reduction (see below). γ,δ-Epoxy β-keto esters **7** can also be synthesized from highly optically active α,β-epoxy amides **10** through esterification by Martin sulfurane.[38b,39] The requirement for excess amount of the expensive Martin sulfurane (>3 equiv), however, makes this process difficult to apply to large-scale synthesis.



Scheme 2. Catalytic asymmetric epoxidation of α,β-unsaturated simple amides.

From a synthetic point of view, we examined the catalytic asymmetric epoxidation of α,β-unsaturated Weinreb amide[40] **13** using 10 mol% of (*S*)-Sm complex **9** (Scheme 3). Although the reaction proceeded smoothly, it had exceptionally low enantioselectivity (64% *ee*). Thus, we explored other synthetically useful substrates that can take the place of Weinreb amides. Morpholinyl amides are as

useful as Weinreb amides.[41] A variety of organometallic reagents, such as Grignard reagents, alkyllithiums, and metal hydrides, react with morpholinyl amide through a reaction mechanism similar to that of the Weinreb amide, affording the corresponding ketone or aldehyde in good yield. When α,β-unsaturated morpholinyl amide **15a** was used as a substrate, in sharp contrast to the Weinreb amide **13**, 10 mol% of (*S*)-Sm complex **9** afforded the corresponding α,β-epoxy morpholinyl amide **16a** in quantitative yield and excellent enantiomeric excess (99% *ee*). In a multi-gram scale reaction, the use of 5 mol% of the catalyst also gave satisfactory results (quant., 98% *ee*).



Scheme 3. Catalytic asymmetric epoxidation of α,β-unsaturated Weinreb amide and morpholinyl amide.

Studies towards the selectivity difference between Weinreb amide and morpholinyl amide would lead to a better understanding of the mechanism of the Ln–BINOL–Ph_3As=O complex-promoted catalytic asymmetric epoxidation. Our previous studies utilizing X-ray analysis and laser desorption/ionization time-of-flight mass spectrometry suggest that the active catalyst of epoxidation is a monomeric species.[32b] Moreover, the results of all catalytic asymmetric epoxidations of α,β-unsaturated carbonyl compounds are consistent with our proposed mechanism involving coordination of a carbonyl oxygen to the lanthanide metal in a *syn–s–cis* coordination manner and internal delivery of *tert*-butyl peroxide from a lanthanide metal to the β-carbon of an α,β-unsaturated carbonyl compound (Figure 1, **17**→**18**). When using Weinreb amide **20** or *N*-acyloxazolidinone **19**,[31,42] there should be an unfavorable *anti* coordination, and this bidentate coordination might disturb the favorable manner of the reaction, resulting in unsatisfactory selectivity. On the other hand, asymmetric epoxidation of morpholinyl amide should proceed in the favorable *syn-s-cis* coordination manner **21** because the rotation of the C–N bond to form a bidentate coordination (**21**→**22**) would be prevented by unfavorable energetics, such as orthogonality of the N-lone pair and the carbonyl π-orbitals. Enantiomeric induction in the present system is explained by assuming the transition state shown in Figure 2.

Syntheses of all possible stereoisomers of 3,5,7,9-tetrahydroxy esters based on highly catalyst-controlled epoxidation: Our strategy for the stereoselective synthesis of the 1,3-polyol array relies on a highly catalyst-controlled asymmetric epoxidation of α,β-unsaturated morpholinyl amide, followed by a conversion of morpholinyl amides into ketones and diastereoselective ketone reduction (Scheme 4). An important feature of this epoxidation is that the stereochemical outcome is very predictable, [e.g., (*S*)-catalyst gives (2*R*,3*S*)-epoxides without exception].[31,32,38] In addition, the epoxidation exhibits almost perfect enantioselectivity (99% *ee*) with high substrate generality. Thus, we expect that even when a chiral center is in the vicinity of the β-carbon of an α,β-unsaturated morpholinyl amide, stereoselectivity of the epoxidation will be controlled by the chirality of BINOL with overwhelming inherent diastereofacial preference for the substrate. Incorporation of the established *syn*- and *anti*-selective ketone reduction with the catalyst controlled epoxidation allows for an iterative strategy for the syntheses of all possible stereoisomers of 1,3-polyol arrays.

Syntheses of both *syn*- and *anti*-5,7-dihydroxy α,β-unsaturated morpholinyl amides are described in Scheme 5. Reaction of epoxy morpholinyl amide **16a** with lithium enolate

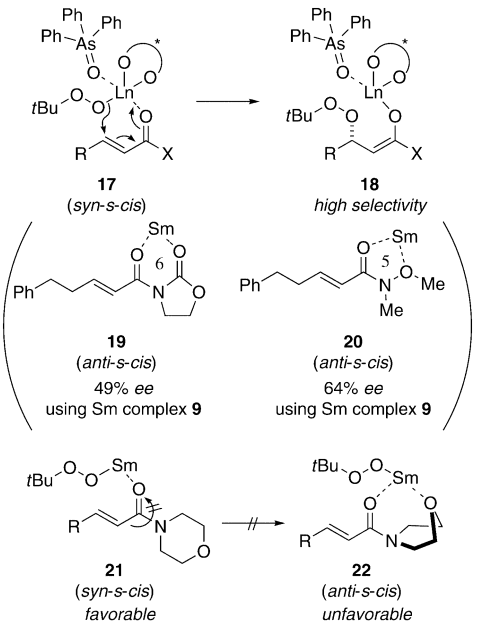


Figure 1. Proposed mechanism for the catalytic asymmetric epoxidation promoted by the Ln–BINOL–Ph_3As=O (1:1:1) complex.

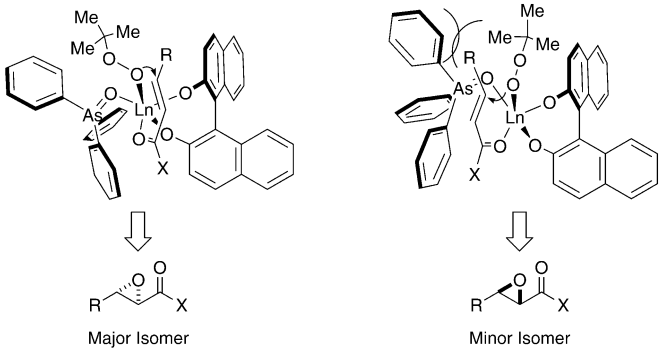
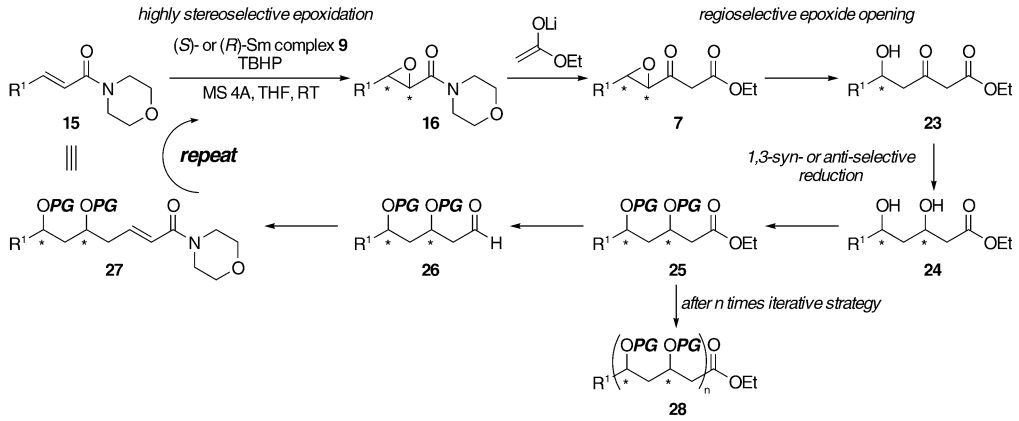


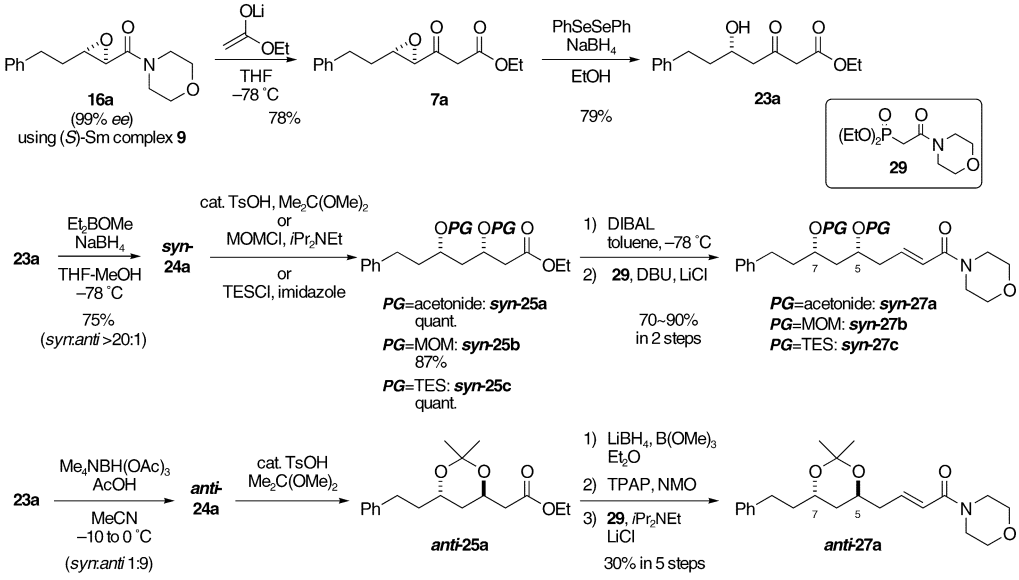
Figure 2. Working transition state model for the catalytic asymmetric epoxidation promoted by the Ln–BINOL–Ph_3As=O (1:1:1) complex.



Scheme 4. New iterative strategy for the syntheses of all possible stereoisomers of 1,3-polyol arrays without stereochemical limitation.

of ethyl acetate at −78 °C afforded γ,δ-epoxy β-keto esters **7a** (78%). A regioselective epoxide opening reaction of **7a** was achieved with Na[(PhSe)B(OEt)$_3$],[43] prepared from PhSeSePh and $NaBH_4$ in ethanol, to afford δ-hydroxy β-keto esters **23a** in 79% yield.[44] After the reaction was complete, PhSeSePh was regenerated, easily recovered by silica gel column chromatography, and reused with the initial efficiency.[43] *syn*-Selective reduction of **23a** was performed with Et_2BOMe and $NaBH_4$ to give the desired *syn*-diol ***syn*-24a** in 75% isolated yield (*syn*:*anti* >20:1).[13,45] *anti*-Diol ***anti*-24a** was synthesized in 80% isolated yield by *anti*-selective reduction with $Me_4NBH(OAc)_3$ (*syn*:*anti* 1:9).[14,45–47] Taking into account the synthetic utility of this strategy, the diols were protected with three types of protecting groups (acetonide ***syn*-25a**, MOM ***syn*-25b**, and TES ***syn*-25c**). The enantiomeric excesses of ***syn*-** and ***anti*-24a** were determined after conversion to acetonides (***syn*-** and ***anti*-25a**), and it was confirmed that no racemization occurred during the process.[48] Then, the protected diol ***syn*-25a** was converted to the corresponding (*E*)-α,β-unsaturated morpholinyl amide ***syn*-27a** by a DIBAL reduction to aldehyde ***syn*-26a** followed by Masamune–Roush-type Horner–Wadsworth–Emmons reaction.[49] In the case of acetonide-protected *anti*-diol ***anti*-25a**, the DIBAL reduction resulted in decomposition of the substrate. Thus, conversion of ***anti*-25a** to aldehyde ***anti*-26a** was conducted with a $LiBH_4$/$B(OMe)_3$ reduction[50] followed by TPAP oxidation.

To elongate the 1,3-polyol array stereoselectively, a second asymmetric epoxidation was investigated. The results are summarized in Table 1. As expected, even when using substrates that have a chirality and several functions in the vicinity of the reaction site, both the (*S*)- and (*R*)-Sm complex promoted the epoxidation with nearly perfect stereoselectivity (entries 1–5, 7, 8).[48,51] Only in the reaction of TES protected (5*R*,7*S*)-diol ***syn*-27c** with the (*R*)-Sm complex was a slightly lower diastereoselectivity observed (92:8) (entry 6).[45] The stereochemistry of epoxide **30** was confirmed by X-ray crystallographic analysis (Figure 3). The stereochemistry of other epoxides was also determined by appropriate derivatization.[42] The results indicated that the



Scheme 5. Syntheses of both *syn*- and *anti*-5,7-dihydroxy α,β-unsaturated molpholinyl amides.

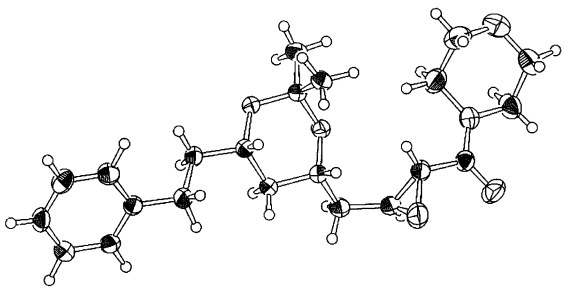


Figure 3. X-ray structure of **30**.

Sm–BINOL–Ph_3As=O complex promotes the asymmetric epoxidation under high catalyst control with overwhelming inherent diastereofacial preference for the substrate.

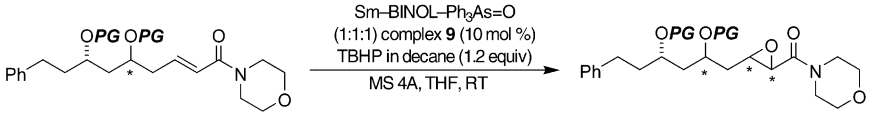
Finally, we demonstrated stereoselective conversion of both *syn*- and *anti*-5,7-dihydroxy 2,3-epoxy amides to 3,5,7,9-tetrahydroxy esters. According to the method shown in Scheme 6, epoxy amides **30**, **31**, **36**, and **37** were successfully converted to all eight possible stereoisomers **40**–**47** in good to excellent stereoselectivity (Table 2).[52] Undoubtedly, enantiomers of all eight stereoisomers can be synthesized by employing the (*R*)-Sm complex for the first asymmetric epoxidation. To the best of our knowledge, this is the first demonstration of the syntheses of all possible stereoisomers of 1,3,5,7-tetraol arrays with high enantio- and diastereoselectivity.[52] The present strategy paves the way for the highly stereoselective syntheses of all possible stereoisomers of 1,3-polyols with broad substrate generality.

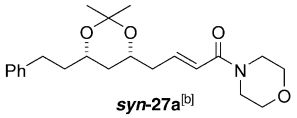
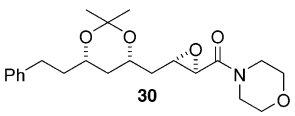
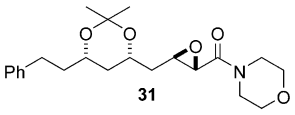
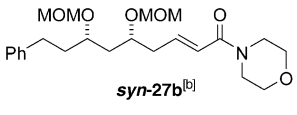
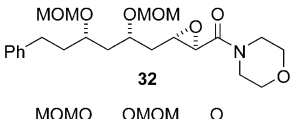
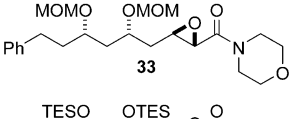
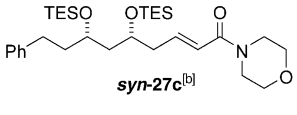
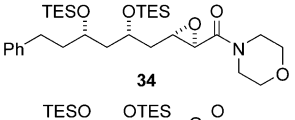
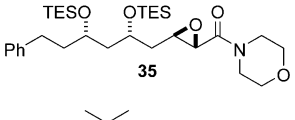
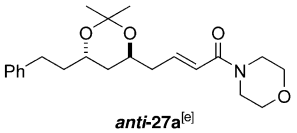
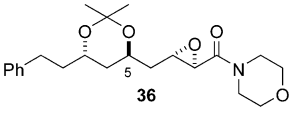
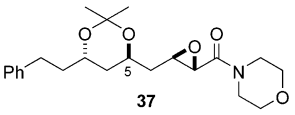
Application to natural product synthesis (1)

Triol synthesis:[38b] Having established stereoselective synthesis of 1,3-polyol arrays, we applied the method to enantioselective synthesis of 1,3-polyol/α-pyrone natural products, which are very attractive target natural products because of their interesting bioactivity, such as antifungal activity and antitumor activity.

Compounds **54** and **55** were isolated from the leaves and bark extract of *Ravensara anisata* by Hostettmann et al. and

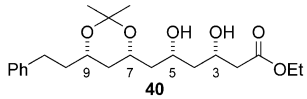
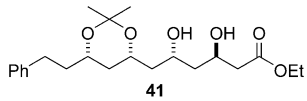
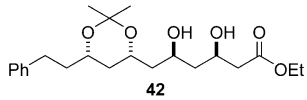
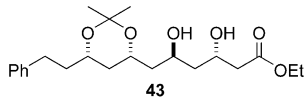
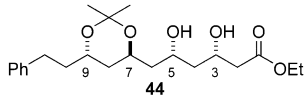
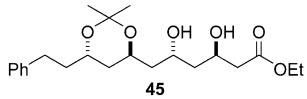
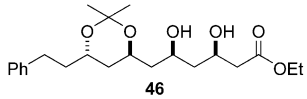
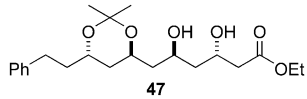
Table 1. The second stereoselective catalytic epoxidation promoted by (*S*)- or (*R*)-Sm complex **9**.



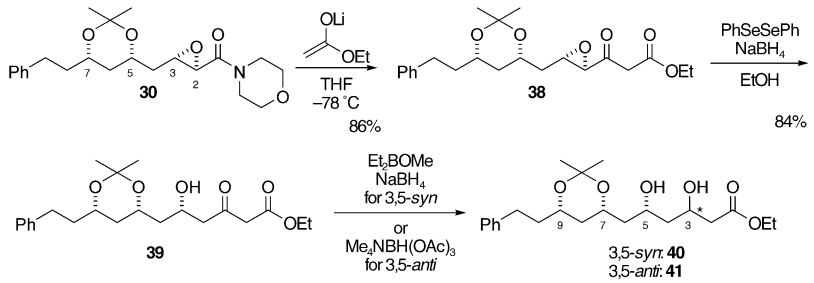
Entry	Substrate	Catalyst	Product	Yield [%][a]	Ratio of Diastereoisomers
1	 ***syn*-27a**[b]	(*S*)-Sm **9**	 **30**	95	**30**:**31** >99:1[c]
2	***syn*-27a**[b]	(*R*)-Sm **9**	 **31**	quant.	**30**:**31** 1:>99[c]
3	 ***syn*-27b**[b]	(*S*)-Sm **9**	 **32**	90	**32**:**33** >99.5:0.5[c]
4	***syn*-27b**[b]	(*R*)-Sm **9**	 **33**	87	**32**:**33** 0.5:>99.5[c]
5	 ***syn*-27c**[b]	(*S*)-Sm **9**	 **34**	81	**34**:**35** >95.5[d]
6	***syn*-27c**[b]	(*R*)-Sm **9**	 **35**	97	**34**:**35** 8:92[d]
7	 ***anti*-27a**[e]	(*S*)-Sm **9**	 **36**	99[f]	**36**:**37** >99:1[g]
8	***anti*-27a**[e]	(*R*)-Sm **9**	 **37**	89[f]	**36**:**37** 1:>99[g]

[a] Isolated yield of the two diastereomers. [b] The diastereomeric ratio of the substrate was >99:1. [c] Determined by HPLC analysis. [d] Determined by ^{1}H NMR analysis. [e] A mixture of diastereomers (*anti*:*syn* 9:1) was used as the substrate. [f] Product included ca. 10% of inseparable C-5 epimer (**30** or **31**). [g] Determined by HPLC analysis. All possible stereoisomers (**30**, **31**, **36**, and **37**) were separable on HPLC.

Table 2. Syntheses of all possible stereoisomers of 3,5,7,9-tetrahydroxy esters.

Entry	Product	Yield [%][a]	Ratio of diastereoisomers[b]
1[c]	 **40**	85	**40**:**41** >99.5:0.5
2[c]	 **41**	75	**40**:**41** 5:>95
3[c]	 **42**	97	**42**:**43** >99:1
4[c]	 **43**	93	**42**:**43** 6:94
5[d]	 **44**	57[e]	**44**:**45** >99:1
6[d]	 **45**	53	**44**:**45** 4:96
7[d]	 **46**	86	**46**:**47** >99.5:0.5
8[d]	 **47**	90[f]	**46**:**47** 2:98

[a] Isolated yield of two diastereomers. [b] Determined by HPLC analysis. [c] Ratio of the first major isomer and the other isomer of the substrate was >99:1. [d] Ratio of the first major isomer and the other isomer (C-7 epimer) of the substrate was 9:1. [e] Product included 8% inseparable C-7 epimer **40**. [f] Product included 7% inseparable C-7 epimer **43**.

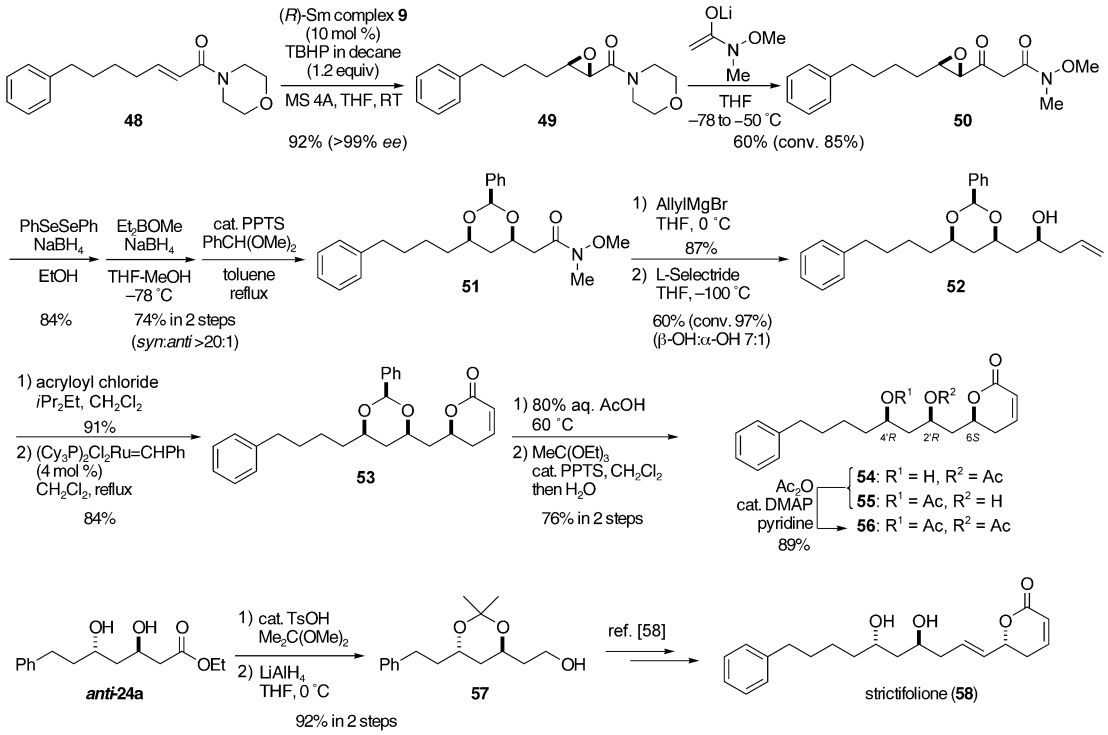


Scheme 6. Representative procedure for the stereoselective syntheses of 3,5,7,9-tetrahydroxy esters.

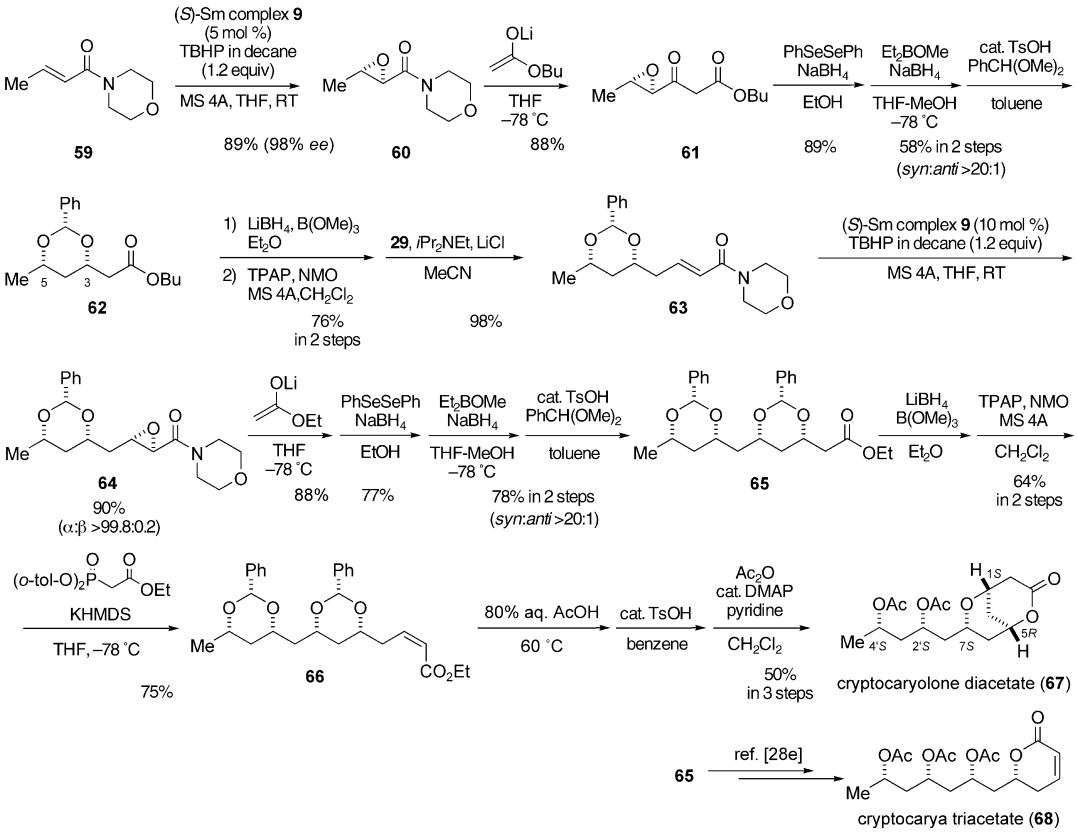
exhibit antifungal activity.[53] The synthetic route to **54** and **55** is outlined in Scheme 7. Catalytic asymmetric epoxidation of α,β-unsaturated morpholinyl amide **48** with 10 mol% Sm–(*R*)-BINOL–Ph_3As=O complex **9** afforded α,β-epoxy amide **49** (92%, >99% *ee*).[48,54] Reaction of epoxy amide **49** with the lithium enolate of the Weinreb amide afforded γ,δ-epoxy β-keto amide **50**. A regioselective epoxide opening reaction followed by *syn*-selective reduction and benzylidene protection furnished protected diol amide **51**. The choice of a diol protecting group was crucial for the diastereoselective ketone reduction at a later stage.[55] Treatment of **51** with allylmagnesium bromide resulted in allyl ketone without C–C double bond migration. Diastereoselective ketone reduction was achieved by the reaction of L-Selectide at −100 °C to afford the desired alcohol **52** (60%, conv. 97%, β-OH:α-OH 7:1).[56] Esterification of **52** with acryloyl chloride proceeded smoothly, and the resulting acryloyl ester was converted into α-pyranone **53** by ring-closing metathesis.[57] In this stage, two diastereomers were separated. Finally, the total syntheses of **54** and **55** were achieved for the first time by removal of the benzylidene group followed by monoacetylation via cyclic ortho ester formation. They were subjected to further acylation with Ac_2O/DMAP to give diacetate **56**. Spectral data of **54**, **55**, and **56** on ^1H NMR and ^{13}C NMR were identical with those reported in the literature.[53] The optical rotation of **54** and **55** ($[\alpha]_D^{25} = -29.7$ ($c = 0.60$ in MeOH)) was opposite to the reported optical rotation ($[\alpha]_D = +35$ ($c = 0.05$ in MeOH)).[53] These results indicate that the absolute stereochemistry of the natural product was 6*R*, 2′*S*, 4′*S*. Moreover, *anti*-3,5-dihydroxy ester ***anti*-24a** was efficiently converted to Aimi's intermediate **57** for the synthesis of strictifolione (**58**) in two steps (92%).[58]

Application to natural product synthesis (2)

Tetraol synthesis: Cryptocaryolone diacetate (**67**) was isolated from the leaves and bark of *Cryptocarya latifolia* by Drewes et al.,[59a] and the first total synthesis of **67** was recently reported by O'Doherty et al.[28e] Although their synthesis was performed in an enantioselective manner, the absolute configuration of cryptocaryolone diacetate (**67**) remains unclear because O'Doherty et al. did not report the optical rotation. Thus, to confirm the absolute configuration and demonstrate the usefulness of the above-mentioned iterative strategy based on stereoselective epoxidation and diastereoselective reduction, we performed enantioselective synthesis of **67** (Scheme 8). Our synthesis of **67** began with the catalytic asymmetric epoxidation of **59**. The use of 5 mol% of (*S*)-Sm complex **9** effectively promoted



Scheme 7. First total synthesis of 1,3-polyol/α-pyrone natural products **54** and **55**.



Scheme 8. Total synthesis of cryptocaryolone diacetate **67**.

the asymmetric epoxidation to afford α,β-epoxy morpholinyl amide **49** (89%, 98% *ee*).[60] Reaction of epoxy morpholinyl amide **60** with the lithium enolate of butyl acetate afforded γ,δ-epoxy β-keto ester **61**.[61] A regioselective epoxide opening reaction with Na[(PhSe)B(OEt)$_3$] followed by *syn*-selective reduction and benzylidene protection furnished protect-

ed 3,5-dihydroxy ester **62**.[62] Conversion of **62** to the corresponding (*E*)-α,β-unsaturated morpholinyl amide **63** was performed with a procedure similar to that described above. The second epoxidation of **63** using 10 mol% of (*S*)-Sm complex **9** afforded **64** in a highly stereocontrolled manner (90%, α:β >99.8:0.2).[48] The sequence from the reaction with the lithium enolate of ethyl acetate to the benzylidene protection provided the known intermediate **65** for the syntheses of **67** and **68**. The spectral analysis data and optical rotation were consistent with the reported values.[28e] After conversion to aldehyde, a highly *Z*-selective Wittig reaction according to Ando's method[63] provided (*Z*)-α,β-unsaturated ester **66** as the sole detectable isomer. Finally, by following the procedure of O'Doherty et al., **66** was successfully converted to cryptocaryolone diacetate (**67**), which was confirmed by spectral data on ^{1}H NMR, ^{13}C NMR, H-H COSY, HMQC, IR, and HR-MS. NMR data for C_6D_6 were consistent with those reported by Drewes et al.[59a] and ^{13}C NMR data for $CDCl_3$ were consistent with those reported by O'Doherty et al.[28e] Since there was a magnitude gap of the optical rotation between synthetic cryptocaryolone diacetate ($[\alpha]_D^{23} = -18.8$ ($c = 0.35$ in $CHCl_3$)), whose purity was elucidated based on ^{13}C NMR analysis,[42] and natural cryptocaryolone diacetate ($[\alpha]_D^{23} = -145$ ($c = 0.27$ in $CHCl_3$)),[59a,64] unfortunately, we have not succeeded in the determination of the absolute configuration of cryptocaryolone diacetate. However, we can conclude that cryptocaryolone diacetate with 1*S*,5*R*,7*S*,2′*S*,4′*S* has the optical rotation ($[\alpha]_D^{23} = -18.8$ ($c = 0.35$ in $CHCl_3$)). Moreover, O'Doherty et al.[28e] succeeded in synthesizing cryptocarya triacetate (**68**),[59] using **65** as an intermediate; this indicates that a formal total synthesis of **68** has been also achieved in our group. The absolute configuration of **68** has been unequivocally determined by the total synthesis.[28b]

Conclusion

In summary, a new strategy for the stereoselective syntheses of all possible stereoisomers of 1,3-polyol arrays was achieved using the Sm–BINOL–Ph_3As=O (1:1:1) complex, which promoted highly enantioselective as well as diastereoselective epoxidation of α,β-unsaturated morpholinyl amides. Even when there is chirality in the vicinity of the β-carbon of an α,β-unsaturated morpholinyl amide, stereoselectivity of the epoxidation can be controlled by the chirality of BINOL with overwhelming inherent diastereofacial preference for the substrate. The resulting chiral α,β-epoxy morpholinyl amides are synthetically very useful and versatile intermediates, that react with a variety of nucleophiles to afford the corresponding chiral carbonyl compounds such as γ,δ-epoxy β-keto esters. The following regioselective epoxide opening reaction and *syn*- or *anti*-selective ketone reduction allows for a highly stereoselective 1,3-diol synthesis. Stereoselective elongation of 1,3-polyol arrays was realized by repeating the above process. The present strategy paves the way for highly stereoselective syntheses of all possible stereoisomers of 1,3-polyol arrays and eight possible stereoisomers of 1,3,5,7-tetraol arrays were successfully demonstrated for the first time. Furthermore, enantioselective syntheses of several 1,3-polyol/α-pyrone natural products such as cryptocaryolone diacetate were achieved using the present strategy. Further applications of this strategy to stereoselective syntheses of 2*n*-substituted 1,3-polyol arrays by regioselective epoxide opening reaction with various nucleophiles are currently in progress.

Experimental Section

General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform IR spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^{1}H NMR and 125.65 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (=0 ppm) for ^{1}H NMR or in the scale relative to $CHCl_3$ (7.26 ppm for ^{1}H NMR) as an internal reference. For ^{13}C NMR, chemical shifts were reported downfield from TMS (=0 ppm) or in the scale relative to $CHCl_3$ (77.00 ppm for ^{13}C NMR) as an internal reference. Chemical shifts in C_6D_6 were reported in the scale relative to C_6H_6 (7.16 ppm for ^{1}H NMR) as an internal reference. For ^{13}C NMR, chemical shifts were reported in the scale relative to C_6H_6 (128.00 ppm for ^{13}C NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. EI mass spectra were measured on JEOL JMS-DX303, JEOL JMS-AX505W or JMS-BU20 GCmate. ESI mass spectra were measured on Waters micromass ZQ or AB Mariner. FAB-HRMS spectra were measured on JEOL S-SX102A. EI-HRMS spectra were measured on JEOL JMS-AX505W. The enantiomeric excess (*ee*) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, 880-PU or PU-980: detector, 875-UV or UV-970. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Ln(O*i*Pr)$_3$ was purchased from Kojundo Chemical Laboratory Co., LTD., 5-1-28, Chiyoda, Sakado-shi, Saitama 350-0214, Japan (fax: +(81)-492-84-1351). MS 4 Å (Molecular Sieve UOP type 4 Å, powder) was purchased from Fluka. Other reagents were purified by the usual methods.

Catalytic asymmetric epoxidation of α,β-unsaturated Weinreb amide and morpholinyl amide

(2*R*,3*S*)-2,3-Epoxy-*N*-methoxy-*N*-methyl-5-phenylpentanamide (14): pale yellow oil; $[\alpha]_D^{21} = -15.1$ ($c = 1.36$, $CHCl_3$, 64% *ee*); IR (neat): $\tilde{\nu}$ = 2938, 1672, 1455, 1386, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.30–7.18 (m, 5H), 3.70–3.66 (m, 4H), 3.23–3.20 (m, 4H), 2.81 (m, 2H), 2.00 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 168.3, 140.6, 128.4, 128.2, 126.0, 61.7, 57.3, 51.9, 33.1, 32.4, 31.8, 30.7; HPLC conditions (column: DAICEL CHIRALPAK AS-H, isopropanol/hexane 1:4, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R [(2*R*,3*S*)-isomer] = 25.0 min, [(2*S*,3*R*)-isomer] = 37.5 min).

4-[(*E*)-1-Oxo-5-phenyl-2-pentenyl]morpholine (15a): Oxalyl chloride (3.2 mL, 36.9 mmol) was added at 4°C to a solution of 5-phenyl-2-pentenoic acid (5 g, 28.4 mmol) in dichloromethane (50 mL). After the addition, the flask was warmed to room temperature and stirred for 2 h. The reaction mixture was evaporated and then THF (20 mL) was added to the residue. The resulting acyl chloride solution was dropped into a solution of morpholine (2.6 mL, 30 mmol) in THF (20 mL) and saturated aqueous $NaHCO_3$ (7 mL). After stirring for 50 min, the reaction mixture was evaporated. The residue was taken up with ethyl acetate, and the organic phase was washed with 1N HCl, and brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography (silica gel, ethyl acetate) to afford **15a** as pale yellow oil (6.53 g, 94%). It solidified upon standing. M.p. 42°C; IR (neat): $\tilde{\nu}$ = 2920, 2855, 1620, 1432, 1115 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 2.59 (td, J=7.5, 7.0 Hz, 2H), 2.84 (t, J=7.5 Hz, 2H), 3.71–3.48 (m, 8H), 6.19 (d, J=15.0 Hz, 1H), 6.94 (dt, J=15.0, 7.0 Hz, 1H), 7.23 (m, 3H), 7.34 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 34.2, 34.6, 42.2, 46.0, 66.8, 120.5, 126.0, 128.3, 128.4, 140.9, 145.3, 165.7; HRMS (FAB+): *m*/*z*: calcd for $C_{15}H_{20}O_2N$: 246.1494, found: 246.1499.

4-[(2*R*,3*S*)-2,3-Epoxy-1-oxo-5-phenylpentyl]morpholine (16a): Sm(O*i*Pr)$_3$ (6.4 mL, 1.28 mmol, 0.2M solution in THF) at room temperature was added to a mixture of (*S*)-BINOL (336 mg, 1.28 mmol), triphenylarsine

oxide (412 mg, 1.28 mmol) and MS 4 Å (25.6 g; MS 4 Å was not dried. 1000 mg per 1 mmol of starting material) in THF (91.6 mL). After stirring for 40 min at the same temperature, *tert*-butyl hydroperoxide (TBHP; 6.14 mL, 30.72 mmol, 5 M solution in decane) was added. After 10 min, a solution of amide **15a** (6.28 g, 25.6 mmol) in THF (30 mL) was added. After stirring for 8 h, the reaction mixture was filtered and the filtrate was diluted with ethyl acetate. The resulting solution was washed with 2% aqueous citric acid, saturated aqueous sodium thiosulfate and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 2:1 to 0:1) to afford **16a** as yellow oil (6.7 g, 25.6 mmol, quant., 98% *ee*). It solidified upon standing. The solid was recrystallized from diethyl ether to afford **16a** with up to 99% *ee*. M.p. 66 °C; $[\alpha]_D^{24} = -28.7$ ($c = 1.56$, $CHCl_3$, 99% *ee*); IR (KBr): $\tilde{\nu} =$ 2918, 2852, 1637, 1468, 1249, 1118 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.92$ (m, 2H), 2.82–2.66 (m, 2H), 3.13 (td, $J = 5.5$, 2.0 Hz, 1H), 3.22 (d, $J = 2.0$ Hz, 1H), 3.26 (m, 1H), 3.40 (m, 1H), 3.59–3.48 (m, 6H), 7.14 (m, 3H), 7.22 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 31.7$, 33.0, 42.2, 45.1, 53.8, 57.6, 66.6, 126.2, 128.3, 128.5, 140.6, 165.9; HRMS (FAB+): calcd for $C_{15}H_{20}O_3N$: 262.1443, found 262.1423; HPLC conditions (column: DAICEL CHIRALPAK AS-H, isopropanol/hexane 1:4, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R [(2*S*,3*R*)-isomer] = 43.5 min, (**16a**) = 62.5 min).

Syntheses of all possible stereoisomers of 3,5,7,9-tetrahydroxy esters based on highly catalyst-controlled epoxidation

Ethyl (4*R*,5*S*)-4,5-epoxy-3-oxo-7-phenylheptanoate (7a): Ethyl acetate (2.2 mL, 23.0 mmol) was added dropwise at −78 °C to a mixture of LHMDS (23.0 mL, 23.0 mmol, 1.0 M solution in THF) and THF (45 mL). After 30 min, **16a** (2 g, 7.65 mmol) in THF (20 mL) was added dropwise and the reaction mixture was stirred for 6 h at −78 °C. The reaction was quenched with saturated aqueous NH_4Cl at −78 °C and warmed to room temperature. The resulting mixture was extracted with ethyl acetate (3×). The combined organic layers were washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 4:1) to afford **7a** as yellow oil (1.56 g, 5.95 mmol, 78%). $[\alpha]_D^{21} = +22.4$ ($c = 0.78$, $CHCl_3$, 99% *ee*). The spectral data were identical to those of an authentic sample.[31b]

Ethyl (5*S*)-5-hydroxy-3-oxo-7-phenylheptanoate (23a):[65] $NaBH_4$ (532 mg, 14.07 mmol) was added portionwise to a mixture of PhSeSePh (2.19 g, 7.03 mmol) in ethanol (20 mL) at room temperature. After 15 min, the reaction mixture was cooled to 0 °C, and then **7a** (1.23 g, 4.69 mmol) in ethanol (5 mL) was added. After stirring for 10 min, the reaction was quenched with saturated aqueous NH_4Cl. The resulting mixture was extracted with ethyl acetate (3×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 5:1 to 2:1) to afford **23a** as yellow oil (0.98 g, 3.7 mmol, 79%). $[\alpha]_D^{23} = +9.35$ (*c* 1.25, $CHCl_3$, 99% *ee*).

Ethyl (3*S*,5*S*)-3,5-dihydroxy-7-phenylheptanoate (*syn*-24a):[65] $BEt_2(OMe)$ (4.2 mL, 4.16 mmol, 1.0 M in THF) was added at −78 °C to a solution of **23a** (1 g, 3.78 mmol) in THF (30 mL) and MeOH (10 mL). After stirring for 1 h, $NaBH_4$ (179 mg, 4.73 mmol) was added portionwise at −78 °C. After 2 h, the reaction was quenched with brine at −78 °C and warmed to room temprature. The resulting mixture was extracted with ethyl acetate (2×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 5:1 to 2:1) to afford ***syn*-24a** as a colorless oil (758 mg, 2.84 mmol, 75%).

Ethyl (3*S*,5*S*)-7-phenyl-3,5-bis(triethylsilyloxy)heptanoate (*syn*-25c): Triethylsilyl chloride (0.99 mL, 5.89 mmol) was added dropwise at room temperature to a stirred solution of ***syn*-24a** (654 mg, 2.46 mmol), imidazole (802 mg, 11.79 mmol) and DMAP (catalytic amount) in DMF (3 mL) and the resulting solution was stirred overnight. The reaction mixture was poured into brine, and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 1:0 to 40:1) to afford ***syn*-25c** as an oil (1.22 g, 2.46 mmol, quant.). $[\alpha]_D^{24} = +10.9$ ($c = 1.00$, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu} = 2954$, 2877, 1737, 1097, 1006 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 0.60$ (m, 12H), 0.95 (m, 18H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.66–1.88 (m, 4H), 2.42 (dd, $J = 7.0$, 14.5 Hz, 1H), 2.49 (dd, $J = 7.0$, 14.5 Hz, 1H), 2.58–2.72 (m, 2H), 3.82 (tt, $J = 5.5$, 11.5 Hz, 1H), 4.11 (m, 2H), 4.24 (tt, $J = 6.0$, 12.5 Hz, 1H), 7.15–7.20 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 4.9$, 5.1, 6.8, 6.9, 14.1, 31.4, 39.2, 43.0, 45.0, 60.3, 66.8, 68.9, 125.7, 128.32, 128.36, 142.4, 171.4; HRMS (FAB+): calcd for $C_{27}H_{51}O_4Si_2$: 495.3326, found 495.3333.

4-[(2*E*,5*R*,7*S*)-1-Oxo-9-phenyl-5,7-bis(triethylsilyloxy)-2-nonenyl]morpholine (*syn*-27c): DIBAL-H (2.4 mL, 2.4 mmol, 1.0 M in toluene) was added dropwise at −78 °C to a solution of ***syn*-25c** (1.0 g, 2.02 mmol) in toluene (25 mL). After stirring for 3 h at the same temperature, the reaction mixture was quenched with methanol. 20% aqueous potassium sodium tartrate was added to the solution and the resulting mixture was extracted with ethyl acetate (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 30:1) to afford an aldehyde as oil (882 mg, 1.96 mmol, 97%). To a stirred mixture of the aldehyde (1.03 g, 2.28 mmol), LiCl (116 mg, 2.74 mmol), 4-(2-diethoxyphosphoryl-1-oxoethyl)morpholine (**29**; 727 mg, 2.74 mmol) in acetonitrile (13 mL) at room temperature was added DBU (0.41 mL, 2.74 mmol). After stirring overnight, The reaction mixture was diluted with ethyl acetate. The resulting mixture was washed with saturated aqueous NH_4Cl, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 1:1) to afford ***syn*-27c** as oil (1.2 g, 2.14 mmol, 94%). $[\alpha]_D^{23} = +1.27$ ($c = 1.10$, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu} = 2954$, 2877, 1737, 1097, 1006 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 0.59$ (m, 12H), 0.96 (m, 18H), 1.62 (m, 1H), 1.66–1.75 (m, 2H), 1.80 (m, 1H), 2.31 (ddd, $J = 6.0$, 7.0, 14.5 Hz, 1H), 2.42 (ddd, $J = 6.0$, 7.0, 14.5 Hz, 1H), 2.60 (m, 1H), 2.67 (m, 1H), 3.50–3.73 (br, 8H), 3.83 (tt, $J = 6.0$, 12.0 Hz, 1H), 3.92 (tt, $J = 6.0$, 12.0 Hz, 1H), 6.22 (d, $J = 15.0$ Hz, 1H), 6.87 (dt, $J = 15.0$, 7.0 Hz, 1H), 7.15–7.20 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 5.0$, 5.1, 6.90, 6.95, 31.5, 39.3, 40.8, 42.1, 44.9, 46.0, 66.7, 66.8, 68.5, 69.0, 121.8, 125.7, 128.2, 128.3, 142.3, 143.0, 165.2; HRMS (FAB+): *m*/*z*: calcd for $C_{31}H_{56}NO_4Si_2$: 562.3748, found 562.3768.

4-[(2*R*,3*S*,5*R*,7*S*)-2,3-Epoxy-1-oxo-9-phenyl-5,7-bis(triethylsilyloxy)nonyl]morpholine (34): $Sm(OiPr)_3$ (0.87 mL, 0.174 mmol, 0.2 M solution in THF) was added at room temperature to a mixture of (*S*)-BINOL (49.7 mg, 0.174 mmol), triphenylarsine oxide (55.9 mg, 0.174 mmol) and MS 4 Å (1.74 g; MS 4 Å was not dried. 1000 mg per 1 mmol of starting material) in THF (4.0 mL). After stirring for 40 min at the same temperature, TBHP (0.42 mL, 2.08 mmol, 5 M solution in decane) was added. Afer stirring for 10 min, ***syn*-27c** (975 mg, 1.74 mmol) in THF (3.8 mL) was added and stirred for 12 h. The reaction mixture was filtered and the filtrate was diluted with ethyl acetate. The resulting mixture was washed with 2% aqueous citric acid, saturated aqueous sodium thiosulfate, and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 4:1 to 2:3) to afford **34** as yellow oil (753 mg, 1.3 mmol, 75%). The diastereomeric ratio of **34** and **35** was over 95:5 (^1H NMR analysis). **34**:**35** >95:5 prepared from ***syn*-27c** (99% *ee*); $[\alpha]_D^{22} = -4.0$ ($c = 1.00$, $CHCl_3$); IR (neat): $\tilde{\nu} = 2954$, 1661, 1456, 1239, 1116 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 0.59$ (m, 12H), 0.96 (m, 18H), 1.70–1.88 (m, 2H), 2.65 (m, 2H), 3.26 (dt, $J = 2.5$, 5.0 Hz, 1H), 3.73 (d, $J = 2.5$ Hz, 1H), 3.57–3.75 (br, 8H), 3.89 (tt, $J = 5.0$, 10.5 Hz, 1H), 4.05 (tt, $J = 6.0$, 12.0 Hz, 1H), 7.15–7.20 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 4.9$, 5.1, 6.90, 6.96, 31.4, 38.9, 39.5, 42.3, 44.0, 45.3, 53.4, 54.8, 66.7, 67.2, 69.0, 125.7, 128.2, 128.3, 142.3, 166.1; HRMS (FAB+): *m*/*z*: calcd for $C_{31}H_{56}NO_5Si_2$: 578.3697, found 578.3712.

4-[(2*S*,3*R*,5*R*,7*S*)-2,3-Epoxy-1-oxo-9-phenyl-5,7-bis(triethylsilyloxy)nonyl]morpholine (35): **34**:**35** = 8:92 prepared from ***syn*-27c** (99% *ee*); $[\alpha]_D^{24} = +21.7$ ($c = 1.02$, $CHCl_3$); IR (neat): $\tilde{\nu} = 2954$, 1656, 1459, 1238, 1115 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 0.61$ (m, 12H), 0.96 (m, 18H), 1.66 (m, 2H), 1.70–1.85 (m, 4H), 2.64 (m, 2H), 3.30 (ddd, $J = 2.5$, 6.5, 6.5 Hz, 1H), 3.34 (d, $J = 2.5$ Hz, 1H), 3.55–3.75 (br, 8H), 3.80 (tt, $J = 5.5$, 6.5 Hz, 1H), 4.04 (tt, $J = 5.5$, 6.5 Hz, 1H), 7.15–7.21 (m, 3H), 7.26–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 4.9$, 5.1, 6.8, 6.9, 31.3, 39.4, 39.6, 42.3, 45.3, 54.2, 55.5, 66.6, 67.2, 68.8, 125.7, 128.2, 128.3, 142.2, 165.9; HRMS (FAB+): *m*/*z*: calcd for $C_{31}H_{56}NO_5Si_2$: 578.3697, found 578.3691.

Ethyl (3*S*,5*S*)-3,5-isopropylidenedioxy-7-phenylheptanoate (*syn*-25a): $[\alpha]_D^{23} = -27.4$ (*c* 1.08, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2991, 2940, 1737, 1496, 1455, 1380, 1199, 1167, 1028, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.25 (dt, *J* = 0.6, 7.2 Hz, 3H), 1.40 (s, 3H), 1.43 (s, 3H), 1.72–1.54 (m, 3H), 1.787–1.79 (m, 1H), 2.36 (dd, *J* = 6.3, 15.4 Hz, 1H), 2.52 (dd, *J* = 6.9, 15.4 Hz, 1H), 2.65 (ddd, *J* = 8.0, 8.3, 14.0 Hz, 1H), 2.74 (ddd, *J* = 5.2, 9.0, 14.0 Hz, 1H), 3.84–3.78 (m, 1H), 4.18–4.11 (m, 2H), 4.29–4.24 (m, 1H), 7.19–7.17 (m, 2H), 7.29–7.26 (m, 3H); ^{13}C NMR ($CDCl_3$): δ = 14.2, 19.7, 30.1, 31.0, 36.5, 37.8, 41.5, 60.4, 66.0, 67.6, 98.8, 125.8, 128.3, 128.5, 141.9, 171.0; ESI-MS (ESI+): *m*/*z*: calcd for $C_{18}H_{26}O_4Na$: 329.17288, found: 329.17278 [*M*+Na^+]; HPLC conditions (column: DAICEL CHIRALCEL OJ-H, hexane/isopropanol 99:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (***syn*-25a**) = 17.7 min, [(3*R*,5*R*)-isomer] 14.4 min).

4-(2*E*,5*R*,7S)-5,7-Isopropylidenedioxy-1-oxo-9-phenyl-2-nonenyl]morpholine (*syn*-27a): $[\alpha]_D^{22} = -15.1$ (*c* = 1.27, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2921, 2851, 1660, 1615, 755, 701 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.21 (m, 1H), 1.40 (s, 2×3H), 1.53 (m, 1H), 1.68 (m, 1H), 1.83 (m, 1H), 2.30 (m, 1H), 2.43 (m, 1H), 2.76–2.62 (m, 2H), 3.68–3.50 (m, 8H), 3.76 (m, 1H), 3.92 (m, 1H), 6.26 (d, *J* = 15.0 Hz, 1H), 6.84 (dt, *J* = 15.0, 7.5 Hz, 1H), 7.23–7.17 (m, 3H), 7.31–7.24 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 19.8, 30.2, 31.0, 36.7, 27.8, 39.5, 42.2, 46.1, 66.8, 67.6, 67.9, 98.7, 121.8, 125.7, 128.3, 128.5, 141.9, 142.1, 165.4; HRMS (FAB+): *m*/*z*: calcd for $C_{21}H_{32}O_4N$: 374.2331, found 374.2335.

4-[(2*R*,3*S*,5*R*,7*S*)-2,3-Epoxy-5,7-isopropylidenedioxy-1-oxo-9-phenylnonyl]morpholine (30): **30**:**31** >99:1 prepared from ***syn*-27a** (99% *ee*); $[\alpha]_D^{23} = -19.2$ (*c* = 1.54, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3000, 2920, 2851, 1664, 1467, 1111 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.38 (s, 3H), 1.40 (s, 3H), 1.89–1.66 (m, 3H), 2.76–2.61 (m, 2H), 3.23 (td, *J* = 5.0, 2.0 Hz, 1H), 3.46 (d, *J* = 2.0 Hz, 1H), 3.75–3.60 (m, 8H), 3.78 (m, 1H), 3.96 (m, 1H), 7.19–7.15 (m, 3H), 7.29–7.25 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 19.9, 30.2, 31.0, 36.2, 37.2, 37.7, 42.2, 45.2, 53.5, 54.6, 65.4, 66.7, 67.6, 98.6, 125.8, 128.3, 128.5, 141.8, 166.1; HRMS (FAB+): *m*/*z*: calcd for $C_{21}H_{32}O_5N$ 390.2280, found 390.2264; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 3:1, flow rate: 1.2 mL min^{-1}, detector: 254 nm, t_R (**30**) = 32.2 min, (**31**) = 22.8 min).

Compound **30** was recrystalized from ethyl acetate/hexane at 4°C. Colorless crystal thus obtained was subjected to X-ray crystallographic analysis to confirm the stereochemistry.

4-[(2*S*,3*R*,5*R*,7*S*)-2,3-Epoxy-5,7-isopropylidenedioxy-1-oxo-9-phenylnonyl]morpholine (31): **30**:**31** = 1:>99 prepared from ***syn*-27a** (99% *ee*); $[\alpha]_D^{24} = -4.3$ (*c* = 1.45, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 2993, 2937, 2852, 1671, 1430, 1114 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.38 (s, 3H), 1.42 (s, 3H), 1.86–1.63 (m, 3H), 2.75–2.62 (m, 2H), 3.24 (td, *J* = 5.5, 2.0 Hz, 1H), 3.39 (d, *J* = 2.0 Hz, 1H), 3.75–3.58 (m, 8H), 3.81 (m, 1H), 4.05 (m, 1H), 7.20–7.17 (m, 3H), 7.29–7.24 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 19.9, 30.2, 31.0, 37.2, 37.8, 39.2, 42.3, 45.2, 54.1, 55.4, 66.7, 67.5, 98.7, 125.8, 128.3, 128.5, 141.8, 166.0; HRMS (FAB+): *m*/*z*: calcd for $C_{22}H_{32}O_5N$: 390.2280, found 390.2244; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 3:1, flow rate: 1.2 mL min^{-1}, detector: 254 nm, t_R (**30**) = 32.2 min, (**31**) 22.8 min).

4-(2*E*,5*R*,7*S*)-5,7-Bis(methoxymethyloxy)-1-oxo-9-phenyl-2-nonenyl]morpholine (*syn*-27b): $[\alpha]_D^{25} = -9.8$ (*c* = 1.33, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2926, 1655, 1617, 1436, 1032 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.65 (m, 1H), 1.78–1.95 (m, 3H), 2.42 (m, 1H), 2.51 (m, 1H), 2.64 (m, 1H), 2.73 (m, 2H), 3.34 (s, 3H), 3.40 (s, 3H), 3.50–3.74 (m, 9H), 3.80 (m, 1H), 4.58–4.68 (m, 2H), 6.26 (d, *J* = 15.0 Hz, 1H), 6.91 (ddd, *J* = 7.5, 15.0, 15.0 Hz, 1H), 7.16–7.21 (m, 3H), 7.25–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 31.4, 36.3, 37.8, 39.4, 42.2, 46.0, 55.72, 55.79, 66.7, 66.8, 73.6, 74.2, 95.4, 95.5, 121.9, 125.8, 128.3, 128.4, 142.0, 142.6, 165.1; HRMS (FAB+): *m*/*z*: calcd for $C_{23}H_{36}O_6N$: 422.2543, found 422.2529.

4-(2*R*,3*S*,5*R*,7*S*)-2,3-Epoxy-5,7-bis(methoxymethyloxy)-1-oxo-9-phenylnonyl]morpholine (32): **32**:**33** >99.5:0.5 prepared from ***syn*-27b** (99% *ee*); $[\alpha]_D^{25} = -3.4$ (*c* = 1.00, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2928, 1654, 1454, 1240, 1114, 1032 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.78 (m, 2H), 1.86 (m, 2H), 1.99 (m, 2H), 2.60–2.78 (m, 2H), 3.30 (m, 1H), 3.34 (s, 3H), 3.38–3.40 (m, 4H), 3.57–3.75 (m, 9H), 3.90 (m, 1H), 4.60–4.70 (m, 4H), 7.16–7.21 (m, 3H), 7.25–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 31.4, 36.2, 36.4, 39.1, 42.3, 45.3, 53.4, 55.1, 55.72, 55.77, 66.7, 72.5, 74.4, 95.5, 95.6, 125.8, 128.3, 128.4, 141.9, 165.9; HRMS (FAB+): *m*/*z*: calcd for $C_{23}H_{36}O_7N$: 438.2492, found 438.2477; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 1:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**32**) = 19.7 min, (**33**) = 11.8 min).

4-(2*S*,3*R*,5*R*,7*S*)-2,3-Epoxy-5,7-bis(methoxymethyloxy)-1-oxo-9-phenylnonyl]morpholine (33): **32**:**33** = 0.5:>99.5 prepared from ***syn*-27b** (99% *ee*); $[\alpha]_D^{25} = +19.8$ (*c* = 1.00, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2926, 1654, 1451, 1240, 1114, 1031 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.68 (m, 1H), 1.78 (m, 1H), 1.82–1.92 (m, 3H), 2.00 (m, 1H), 2.62–2.76 (m, 2H), 3.29 (m, 1H), 3.35 (s, 3H), 3.37 (d, *J* = 2.5 Hz, 1H), 3.40 (s, 1H), 3.58–3.74 (m, 9H), 3.90 (m, 1H), 4.62–4.69 (m, 4H), 7.14–7.21 (m, 3H), 7.25–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 31.4, 36.3, 37.3, 39.9, 42.3, 45.3, 54.3, 55.5, 55.7, 55.8, 66.7, 72.6, 74.1, 95.4, 95.8, 125.8, 128.2, 128.4, 141.9, 165.8; HRMS (FAB+): *m*/*z*: calcd for $C_{23}H_{36}O_7N$: 438.2492, found 438.2477; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 1:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**32**) = 19.7 min, (**33**) = 11.8 min).

Ethyl (4*R*,5*S*,7*R*,9*S*)-4,5-epoxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate (38): Prepared from **30** (**30**:**31** >99:1); $[\alpha]_D^{23} = +18.4$ (*c* = 1.01, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2990, 2918, 1743, 1717, 1653, 1380, 1199 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.25–1.32 (m, 4H), 1.33–1.50 (m, 8H), 1.70 (m, 1H), 1.76–1.89 (m, 3H), 2.66 (m, 1H), 2.73 (m, 1H), 3.22–3.42 (m, 3H), 3.78 (m, 1H), 3.98 (m, 1H), 4.20 (m, 2H), 7.14–7.20 (m, 3H), 7.23–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 19.7, 30.1, 31.0, 36.4, 37.7, 37.9, 43.7, 55.0, 58.9, 61.5, 66.0, 67.5, 98.7, 125.7, 128.2, 128.5, 141.8, 166.5, 199.9; HRMS (FAB+): *m*/*z*: calcd for $C_{22}H_{31}O_6$: 391.2121, found 391.2112.

Ethyl (5*S*,7*R*,9*S*)-5-hydroxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate (39): Prepared from **38** mentioned above; $[\alpha]_D^{23} = -0.4$ (*c* = 1.06, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3502, 2990, 2939, 1742, 1716, 1380, 1092 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.20–1.29 (m, 4H), 1.38–1.47 (m, 7H), 1.55–1.73 (m, 3H), 1.82 (m, 1H), 2.60–2.67 (m, 2H), 2.70–2.76 (m, 2H), 3.49 (s, 2H), 3.61 (s, 1H), 3.79 (m, 1H), 4.10 (m, 2H), 4.19 (q, *J* = 7.0 Hz, 2H), 4.26 (m, 1H), 7.15–7.21 (m, 3H), 7.25–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 19.9, 30.1, 30.9, 36.9, 37.7, 42.3, 49.9, 50.0, 61.3, 67.3, 67.5, 69.4, 98.7, 125.7, 128.2, 128.4, 141.8, 167.0, 202.4; HRMS (FAB+): *m*/*z*: calcd for $C_{22}H_{33}O_6$: 393.2277, found 393.2264.

Ethyl (3*S*,5*R*,7*R*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (40): $BEt_2(OMe)$ (0.14 mL, 0.14 mmol, 1.0 M in THF) was added at −78°C to a solution of **39** (50 mg, 0.128 mmol) in THF (1.5 mL) and MeOH (1.5 mL). After stirring for 1 h, $NaBH_4$ (6.1 mg, 0.16 mmol) was added at −78°C. After 4 h, the reaction was quenched with saturated aqueous NH_4Cl at −78°C and warmed to room temperature. The resulting mixture was extracted with ethyl acetate (3×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 3:1) to afford **40** as oil (43 mg, 0.109 mmol, 85% yield, *syn*:*anti* >99.5:0.5).

A mixture of **40** and **41** (**40**:**41** >99.5:0.5); $[\alpha]_D^{23} = -4.5$ (*c* = 1.01, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3404, 2939, 2912, 1733, 1379, 1094 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.21–1.29 (m, 4H), 1.38–1.47 (m, 7H), 1.51–1.59 (m, 2H), 1.60–1.72 (m, 3H), 1.82 (m, 1H), 2.45 (dd, *J* = 5.0, 16.0 Hz, 1H), 2.52 (dd, *J* = 7.5, 16.0 Hz, 1H), 2.64 (m, 1H), 2.73 (m, 1H), 3.79 (m, 1H), 3.94 (brs, 1H), 3.97 (brs, 1H), 4.10 (m, 2H), 4.15 (q, J = 7.0 Hz, 2H), 4.26 (m, 1H), 7.15–7.20 (m, 3H), 7.25–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 19.9, 30.1, 30.9, 37.0, 37.6, 41.7, 42.7, 43.1, 60.5, 67.5, 68.1, 69.7, 71.3, 98.6, 125.7, 128.2, 128.4, 141.8, 172.1; HRMS (FAB+): *m*/*z*: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2418; HPLC conditions (column: YMC-PACK A-003-5-06 S-5 60A SIL 4.6×250 mm, hexane/isopropanol 98:2, flow rate: 1.5 mL min^{-1}, detector: 254 nm, t_R (**40**) = 32.8 min, (**41**) = 36.0 min).

Ethyl (3*R*,5*R*,7*R*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (41): Acetic acid (0.7 mL) was added at room temperature to a mixture of tetramethylammonium triacetoxyborohydride (249 mg, 0.899 mmol) and acetonitrile (0.7 mL). The reaction mixture was stirred for 30 min and then cooled to −5°C. The solution of **39** (50 mg, 0.128 mmol) in acetonitrile (1 mL) was added. After stirring for 4.5 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$, and the resulting mixture was extracted with ethyl acetate (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatogra-

phy (silica gel, hexane/ethyl acetate 1:1) to afford **41** as oil (38 mg, 0.096 mmol, 75% yield, *anti*:*syn* >95:5).

A mixture of **40** and **41** (**40**:**41** = 5:>95); $[\alpha]_D^{23} = -9.9$ (c = 1.01, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3421, 2990, 2940, 1732, 1716, 1379, 1199, 1162, 1095 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.27–1.30 (m, 4H), 1.39–1.48 (m, 7H), 1.50–1.77 (m, 5H), 1.83 (m, 1H), 2.50 (m, 2H), 2.64 (m, 1H), 2.73 (m, 2H), 3.60 (brs, 1H), 3.80 (m, 1H), 3.84 (brs, 1H), 4.03–4.20 (m, 4H), 4.33 (m, 1H), 7.15–7.21 (m, 3H), 7.23–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 19.9, 30.1, 30.9, 37.1, 37.6, 41.6, 42.6, 42.8, 60.5, 65.3, 67.5, 68.9, 70.3, 98.7, 125.7, 128.2, 128.4, 141.8, 172.5; HRMS (FAB+): m/z: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2418; HPLC conditions (column: YMC-PACK A-003-5-06 S-5 60A SIL 4.6×250 mm, hexane/isopropanol 98:2, flow rate: 1.5 mL min^{-1}, detector: 254 nm, t_R (**40**) = 32.8 min, (**41**) = 36.0 min).

Ethyl (4*S*,5*R*,7*R*,9*S*)-4,5-epoxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate: Prepared from **31** (**30**:**31** = 1:>99); $[\alpha]_D^{24} = -30.2$ (c = 1.12, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2991, 2940, 1747, 1716, 1652, 1380, 1199 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.17–1.34 (m, 4H), 1.35–1.54 (m, 9H), 1.69 (m, 1H), 1.77–1.95 (m, 2H), 2.65 (m, 1H), 2.74 (m, 1H), 3.28 (m, 1H), 3.33 (m, 1H), 3.39 (d, J = 9.0 Hz, 1H), 3.80 (m, 1H), 4.04 (m, 1H), 4.20 (m, 2H), 7.16–7.20 (m, 3H), 7.25–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 19.8, 30.1, 30.9, 37.0, 37.7, 39.0, 43.9, 55.3, 59.5, 61.5, 66.4, 67.4, 98.7, 125.7, 128.2, 128.4, 141.8, 166.5, 199.6; HRMS (FAB+): m/z: calcd for $C_{22}H_{31}O_6$: 391.2121, found 391.2119.

Ethyl (5*R*,7*R*,9*S*)-5-hydroxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate: $[\alpha]_D^{24} = -17.0$ (c = 1.08, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3489, 2991, 2940, 1742, 1714, 1380, 1265, 1200 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.25–1.35 (m, 4H), 1.37–1.45 (m, 7H), 1.54 (m, 1H), 1.61–1.73 (m, 2H), 1.82 (m, 1H), 2.60–2.76 (m, 4H), 3.22 (d, J = 6.0 Hz, 1H), 3.47 (m, 2H), 3.80 (m, 1H), 4.12 (m, 1H), 4.20 (m, 2H), 4.33 (m, 1H), 7.15–7.21 (m, 3H), 7.23–7.28 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 19.7, 30.2, 31.0, 36.6, 37.7, 41.9, 49.8, 49.9, 61.3, 64.4, 66.4, 67.7, 98.7, 125.7, 128.2, 128.4, 141.9, 166.9, 203.1; HRMS (FAB+): m/z: calcd for $C_{22}H_{32}O_6$: 393.2277, found 393.2262.

Ethyl (3*R*,5*S*,7*R*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (42): A mixture of **42** and **43** (**42**:**43** >99:1); $[\alpha]_D^{24} = -7.6$ (c = 1.00, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3421, 2940, 1732, 1379, 1266, 1199, 1095 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.24–1.29 (m, 4H), 1.36–1.44 (m, 7H), 1.52–1.73 (m, 5H), 1.84 (m, 1H), 2.45 (dd, J = 4.5, 16.0 Hz, 1H), 2.51 (dd, J = 7.5, 16.0 Hz, 1H), 2.65 (m, 1H), 2.73 (m, 1H), 3.76–3.84 (m, 2H), 3.96 (brs, 1H), 4.12–4.19 (m, 4H), 4.29 (m, 1H), 7.16–7.20 (m, 3H), 7.24–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 19.7, 30.2, 31.0, 36.6, 37.7, 41.7, 42.5, 42.6, 60.6, 66.8, 67.7, 68.7, 68.8, 98.7, 125.7, 128.2, 128.5, 141.9, 172.3; HRMS (FAB+): m/z: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2412; HPLC conditions (column: YMC-PACK A-003-5-06 S-5 60A SIL 4.6× 250 mm, hexane/isopropanol 98:2, flow rate: 1.5 mL min^{-1}, detector: 254 nm, t_R (**42**) = 33.0 min, (**3**) = 37.9 min).

Ethyl (3*S*,5*S*,7*R*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (43): A mixture of **42** and **43** (**42**:**43** 6:94); $[\alpha]_D^{24} = +1.0$ (c = 1.00, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3421, 2990, 2940, 1732, 1379, 1266, 1199, 1159, 1094 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.27 (t, J = 7.0 Hz, 1H), 1.36–1.45 (m, 8H), 1.57–1.64 (m, 3H), 1.64–1.76 (m, 2H), 1.84 (m, 1H), 2.50 (m, 2H), 2.65 (m, 1H), 2.74 (m, 1H), 3.38 (d, J = 4.5 Hz, 1H), 3.49 (d, J = 2.5 Hz, 1H), 3.80 (m, 1H), 4.17 (q, J = 7.0 Hz, 2H), 4.24 (m, 1H), 4.34 (m, 1H), 7.15–7.20 (m, 3H), 7.25–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 19.7, 30.2, 31.0, 36.3, 37.7, 41.4, 42.0, 42.3, 60.6, 65.6, 67.8, 98.7, 125.7, 128.2, 128.5, 141.9, 172.7; HRMS (FAB+): m/z: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2410; HPLC conditions (column: YMC-PACK A-003-5-06 S-5 60A SIL 4.6×250 mm, hexane/isopropanol 98:2, flow rate: 1.5 mL min^{-1}, detector: 254 nm, t_R (**42**) = 33.0 min, (**43**) = 37.9 min).

Synthesis of *anti*-27a from 23a: Acetic acid (10 mL) was added at room temperature to a mixture of tetramethylammonium triacetoxyborohydride (3.67 g, 13.24 mmol) and acetonitrile (15 mL). After stirring for 30 min, the mixture was cooled to −10 °C and the solution of **23a** (700 mg, 2.65 mmol, >99% *ee*) in acetonitrile (10 mL) was added. After stirring for 8 h at 0 °C, the reaction mixture was poured into saturated aqueous $NaHCO_3$, and extracted with ethyl acetate (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 4:1 to 2:1) to afford ***anti*-24a** (682 mg).

***anti*-24a** (682 mg) was dissolved in 2,2-dimethoxypropane (10 mL) and $TsOH{\cdot}H_2O$ (10 mg) was added to the mixture. After stirring for 7 h at room temperature, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. After extracting with ethyl acetate (3×), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 5:1) to afford ***anti*-25a** as oil (660 mg).

$LiBH_4$ (84 mg, 3.84 mmol) and trimethoxyborane (0.032 mL, 0.28 mmol) were added at room temperature to a solution of ***anti*-25a** (660 mg) in diethyl ether (30 mL). The reaction mixture was stirred for 1 h at the same temperature and quenched with saturated aqueous $NaHCO_3$. After extracting with ethyl acetate (3×), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford an alcohol as oil (425 mg).

MS 4 Å (800 mg; MS 4 Å not dried), *N*-methylmorpholine-*N*-oxide (282 mg, 2.41 mg) and TPAP (28 mg, 0.08 mmol) were added at room temperature to a solution of the alcohol (425 mg) in acetonitrile (15 mL). The reaction mixture was stirred for 1 h and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 6:1) to afford an aldehyde as oil (250 mg).

N,*N*-Diisopropylethylamine (0.2 mL, 1.14 mmol) was added at room temperature to a stirred mixture of the aldehyde (250 mg, 0.953 mmol), LiCl (48.3 mg, 1.14 mmol), 4-(2-diethoxyphosphoryl-1-oxoethyl)morpholine (**29**; 302 mg, 1.14 mmol) in acetonitrile (8 mL). The reaction mixture was stirred overnight, and diluted with ethyl acetate. The resulting mixture was washed with 2% aqueous citric acid, saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, ethyl acetate) to afford ***anti*-27a** as oil (292 mg, 0.78 mmol, 30% yield, 5 steps). The diasteromeric ratio of *anti*:*syn* acetonide was determined 90:10 by HPLC analysis.

Ethyl (3*R*,5*S*)-3,5-isopropylidenedioxy-7-phenylheptanoate (*anti*-25a): $[\alpha]_D^{22} = +17.4$ (c = 0.70, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2986, 2937, 1738, 1496, 1455, 1380, 1224, 1187, 1025, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.29–7.26 (m, 3H), 7.19–7.16 (m, 2H), 4.29–4.25 (m, 1H), 4.17–4.11 (m, 2H), 3.79–3.75 (m, 1H), 2.77 (ddd, J = 5.5, 9.5, 13.8 Hz, 1H), 2.61 (ddd, J = 7.2, 8.9, 13.8 Hz, 1H), 2.50 (dd, J = 8.3, 15.3 Hz, 1H), 2.41 (dd, J = 5.2, 15.3 Hz, 1H), 1.88–1.82 (m, 1H), 1.76–1.59 (m, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 170.9, 141.9, 128.4, 128.3, 125.8, 100.6, 65.6, 63.5, 60.4, 40.8, 37.9, 37.4, 31.6, 24.7, 24.6, 14.2; EI-MS m/z: 306 [M^+]; HRMS (FAB+): m/z: calcd for $C_{18}H_{27}O_4$: 307.1904, found 307.1902; HPLC conditions (column: DAICEL CHIRALCEL OJ-H, hexane/isopropanol 98:2, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (***anti*-25a**) = 8.7 min, [(3*S*,5*R*)-isomer] 11.6 min).

4-[(2*E*,5*S*,7*S*)-5,7-Isopropylidenedioxy-1-oxo-9-phenyl-2-nonenyl]morpholine (*anti*-27a): A mixture of ***syn*-27a** and ***anti*-27a** (***syn*-27a**:***anti*-27a** 1:9); $[\alpha]_D^{22} = +25.5$ (c = 0.89, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2933, 2857, 1660, 1619, 1432, 1224, 1115 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.33 (s, 3H), 1.36 (s, 3H), 1.62 (m, 2H), 1.74 (m, 1H), 1.83 (m, 1H), 2.33 (m, 1H), 2.41 (m, 1H), 2.60 (m, 1H), 2.75 (m, 1H), 3.55 (br, 2H), 3.68 (br, 6H), 3.76 (m, 1H), 3.93 (m,1H), 6.26 (d, J = 15.0 Hz, 1H), 6.83 (dt, J = 15.0, 7.0 Hz, 1H), 7.16–7.21 (m, 3H), 7.25–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.8, 24.9, 31.5, 37.3, 38.2, 38.6, 42.2, 46.1, 65.5, 65.6, 66.7, 66.8, 100.5, 121.6, 125.7, 128.2, 128.4, 141.8, 142.3, 165.4; HRMS (FAB+): m/z: calcd for $C_{22}H_{32}O_4N$: 374.2331, found 374.2346; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 98:2, flow rate: 1.2 mL min^{-1}, detector: 254 nm, t_R (***anti*-27a**) = 98.9 min, (***syn*-27a**) = 115.1 min).

4-[(2*S*,3*R*,5*S*,7*S*)-2,3-Epoxy-5,7-isopropylidenedioxy-1-oxo-9-phenylnonyl]morpholine (37): A mixture of **37** and **31** (**37**:**31** 9:1); $[\alpha]_D^{24} = -4.3$ (c = 1.45, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2921, 2855, 1655, 1379, 1115 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.34+1.37 (*syn* acetonide) +1.38+1.41 (*anti* acetonide) (s, 2×3H), 1.61–1.79 (m, 3H), 1.80–1.91 (m, 3H), 2.61 (m, 1H), 2.76 (m, 1H), 3.25 (m, 1H), 3.38 (*syn*, d, J = 1.5 Hz, 1H) + 3.45 (*anti*, d, J = 2.5 Hz, 1H), 3.57–3.81 (m, 9H), 3.99 (m, 1H), 7.14–7.20 (m, 3H), 7.25–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.8, 24.9, 31.5, 36.8, 37.3,

37.8, 42.2, 45.2, 53.3, 55.0, 63.3, 65.6, 66.7, 100.4, 125.80, 128.3, 128.4, 141.8, 166.0 (for **37**); HRMS (FAB+): *m/z*: calcd for $C_{22}H_{32}O_5N$: 390.2280, found 390.2282; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 4:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**31**) = 39.6 min, (**37**) = 32.5 min).

4-[(2*R*,3*S*,5*S*,7*S*)-2,3-Epoxy-5,7-isopropylidenedioxy-1-oxo-9-phenylnonyl]morpholine (36): A mixture of **36** and **30** (**36**:**30** 9:1); $[\alpha]_D^{22}$ = +8.2 (*c* = 1.00, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2984, 2920, 2857, 1653, 1240, 1114 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25–1.40 (m, 7H), 1.52–1.90 (m, 5H), 2.62 (m, 1H), 2.76 (m, 1H), 3.24 (m, 1H), 3.37 (*anti* acetonide) + 3.46 (*syn* acetonide) (m, 1H), 3.55–3.83 (m, 9H), 3.96 (*syn* acetonide) + 4.06 (*anti* acetonide) (m, 1H), 7.16–7.22 (m, 3H), 7.25–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.8, 24.9, 31.5, 37.3, 38.4, 38.5, 42.3, 45.2, 54.2, 55.6, 64.0, 65.6, 66.7, 100.5, 125.7, 128.2, 128.4, 141.8, 165.9; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{32}O_5N$: 390.2280, found 390.2278; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 4:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**30**) = 55.3 min, (**36**) = 40.8 min).

Ethyl (4*S*,5*R*,7*S*,9*S*)-4,5-epoxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate: Prepared from a mixture of **37** and **31** (**37**:**31** 9:1); $[\alpha]_D^{23}$ = −14.6 (*c* = 1.04, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2986, 2937, 1743, 1720, 1380, 1224, 1029 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25–1.31 (m, 3H), 1.32–1.44 (m, 6H), 1.60–1.92 (m, 6H), 2.62 (m, 1H), 2.75 (m, 1H), 3.17–3.42 (m, 4H), 3.78 (m, 1H), 3.98 (m, 1H), 4.19 (m, 2H), 7.16–7.21 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 24.6, 24.7, 31.5, 37.2, 37.3, 37.9, 43.7, 55.3, 58.7, 61.5, 63.7, 65.5, 100.5, 125.7, 128.2, 128.4, 141.8, 165.5, 199.8; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{31}O_6$: 391.2121, found 391.2119.

Ethyl (4*R*,5*S*,7*S*,9*S*)-4,5-epoxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate: Prepared from a mixture of **36** and **30** (**36**:**30** 9:1); $[\alpha]_D^{22}$ = +37.9 (*c* = 1.14, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2986, 2937, 1745, 1719, 1380, 1224 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25–1.45 (m, 9H), 1.56–1.93 (m, 6H), 2.62 (m, 1H), 2.76 (m, 1H), 3.13–3.45 (m, 4H), 3.78 (m, 1H), 4.05 (m, 1H), 4.22 (m, 2H), 7.16–7.22 (m, 3H), 7.26–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 24.7, 24.8, 31.5, 37.3, 38.2, 38.4, 43.8, 100.6, 125.8, 128.3, 128.4, 141.8, 166.5, 199.7; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{32}O_6$: 391.2121, found 391.2219.

Ethyl (5*S*,7*S*,9*S*)-5-hydroxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate: A mixture of (7*S*,9*S*)-isomer and (7*R*,9*S*)-isomer ((7*S*,9*S*)-isomer:(7*R*,9*S*)-isomer 9:1); $[\alpha]_D^{21}$ = +30.0 (*c* 1.06, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3446, 2985, 2938, 1741, 1715, 1380, 1223 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.26–1.44 (m, 10H), 1.55–1.78 (m, 4H), 1.84 (m, 1H), 2.62 (m, 1H), 2.71–2.80 (m, 3H), 3.16 (d, *J* = 4.0 Hz, 1H), 3.46–3.50 (m, 2H), 3.76 (m, 1H), 4.10–4.24 (m, 1H), 4.30 (m, 1H), 7.16–7.22 (m, 3H), 7.26–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 24.80, 24.83, 31.6, 37.4, 38.1, 41.4, 49.7, 49.9, 61.4, 63.8, 64.7, 65.8, 100.5, 125.7, 128.2, 128.4, 141.8, 166.9, 203.1; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{33}O_6$: 393.2277, found 393.2262.

Ethyl (5*R*,7*S*,9*S*)-5-hydroxy-7,9-isopropylidenedioxy-3-oxo-11-phenylundecanoate: A mixture of (7*S*,9*S*)-isomer and (7*R*,9*S*)-isomer ((7*S*,9*S*)-isomer:(7*R*,9*S*)-isomer 9:1); $[\alpha]_D^{24}$ = +11.3 (*c* = 1.15, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3461, 2985, 2938, 1742, 1715, 1380, 1224 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.27 (t, *J* = 7.0 Hz, 3H), 1.32 (s, 3H), 1.40 (s, 3H), 1.59–1.76 (m, 5H), 1.83 (m, 1H), 2.61 (m, 2H), 2.74 (m, 2H), 3.49 (s, 2H), 3.60 (s, 1H), 3.76 (m, 1H), 4.10 (m, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 4.25 (m, 1H), 7.16–7.20 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 24.7, 24.9, 31.5, 37.3, 38.5, 41.8, 49.8, 50.1, 61.3, 65.6, 67.0, 67.6, 100.6, 127.7, 128.3, 128.4, 167.0, 202.3; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{31}O_6$: 391.2121, found 391.2119.

Ethyl (3*S*,5*R*,7*S*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (44): A mixture of **44**, **45** and **40** (**44**:**45**:**40** 91:1:8); $[\alpha]_D^{23}$ = +15.9 (*c* = 1.50, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3421, 2985, 2938, 1733, 1379, 1223, 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.27 (t, *J* = 7.0 Hz, 3H), 1.33 (s, 3H), 1.39 (s, 3H), 1.54–1.70 (m, 6H), 1.74 (m, 1H), 1.85 (m, 1H), 2.45 (dd, *J* = 4.6, 16.2 Hz, 1H), 2.51 (dd, *J* = 8.1, 16.2 Hz, 1H), 2.61 (m, 1H), 2.76 (m, 1H), 3.69 (s, 1H), 3.77 (m, 1H), 3.93 (s, 1H), 4.05–4.20 (m, 4H), 4.28 (m, 1H), 7.16–7.19 (m, 3H), 7.24–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 24.8, 24.9, 31.6, 37.4, 38.1, 41.8, 42.1, 42.4, 60.6, 64.1, 65.8, 68.7, 69.1, 100.5, 125.7, 128.3, 128.4, 141.8, 172.3; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2393; HPLC conditions (column: SHISEIDO SILICA SG80 4.6 mm∅ × 250 mm, hexane/isopropanol 98:2, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**40**) = 30.6 min, (**44**) = 34.3 min, (**45**) = 38.5 min).

Ethyl (3*R*,5*R*,7*S*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (45): A mixture of **44** and **45** (**44**:**45** 4:96); $[\alpha]_D^{22}$ = +5.9 (*c* = 1.15, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3421, 2985, 2938, 1732, 1379, 1223, 1163 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.27 (t, *J* = 7.0 Hz, 3H), 1.33 (s, 3H), 1.38 (s, 3H), 1.58 (m, 1H), 1.63 (m, 3H), 1.69–1.78 (m, 3H), 1.84 (m, 1H), 2.50–2.53 (m, 2H), 2.62 (m, 1H), 2.76 (m, 1H), 3.26 (d, *J* = 5.0 Hz, 1H), 3.46 (d, *J* = 4.0 Hz, 1H), 3.77 (m, 1H), 4.07–4.23 (m, 4H), 4.34 (m, 1H), 7.14–7.20 (m, 3H), 7.26–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 24.80, 24.89, 31.6, 37.4, 37.9, 41.4, 41.6, 42.3, 60.6, 64.4, 65.6, 65.8, 65.9, 100.5, 125.7, 128.3, 128.4, 141.8, 172.7; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2394; HPLC conditions (column: SHISEIDO SILICA SG80 4.6 mm∅ × 250 mm, hexane/isopropanol 98:2, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**44**) = 34.3 min, (**45**) = 38.5 min).

Ethyl (3*R*,5*S*,7*S*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (46): A mixture of **46**:**47** (**46**:**47** >99.5:0.5); $[\alpha]_D^{23}$ = +11.7 (*c* 1.30, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3445, 2985, 2938, 1732, 1379, 1223, 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.26 (t, *J* = 7.0 Hz, 3H), 1.33 (s, 3H), 1.41 (s, 3H), 1.50–1.66 (m, 6H), 1.73 (m, 1H), 1.84 (m, 1H), 2.44 (dd, *J* = 4.9, 15.9 Hz, 1H), 2.52 (dd, *J* = 7.7, 15.9 Hz, 1H), 2.60 (m, 1H), 2.75 (m, 1H), 3.77 (m, 1H), 3.94 (s, 2H), 4.04–4.13 (m, 2H), 4.16 (q, *J* = 7.0 Hz, 2H), 4.27 (m, 1H), 7.15–7.20 (m, 3H), 7.25–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 24.7, 25.0, 31.5, 37.3, 38.6, 41.8, 42.6, 42.8, 60.5, 65.6, 67.6, 68.1, 71.8, 100.6, 125.8, 128.3, 128.4, 141.8, 172.2; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2409; HPLC conditions (column: SHISEIDO SILICA SG80 4.6 mm∅ × 250 mm, hexane/isopropanol 98:2, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**46**) = 30.2 min, (**47**) = 34.0 min).

Ethyl (3*S*,5*S*,7*S*,9*S*)-3,5-dihydroxy-7,9-isopropylidenedioxy-11-phenylundecanoate (47): A mixture of **47**, **46** and **43** (**47**:**46**:**43** 92:1:7); $[\alpha]_D^{23}$ = +22.8 (*c* = 1.30, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3425, 2984, 2938, 1733, 1379, 1223, 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.26 (t, *J* = 7.0 Hz, 3H), 1.33 (s, 3H), 1.41 (s, 3H), 1.54–1.68 (m, 6H), 1.74 (m, 1H), 1.85 (m, 1H), 2.51 (m, 2H), 2.62 (m, 1H), 2.76 (m, 1H), 3.60 (m, 1H), 3.75–3.82 (m, 2H), 4.07–4.19 (m, 4H), 4.34 (m, 1H), 7.14–7.22 (m, 3H), 7.26–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 24.7, 25.0, 31.5, 37.3, 38.7, 41.7, 42.2, 42.6, 60.5, 65.3, 65.6, 68.0, 69.4, 100.6, 125.8, 128.3, 128.4, 141.7, 172.5; HRMS (FAB+): *m/z*: calcd for $C_{22}H_{35}O_6$: 395.2434, found 395.2408; HPLC conditions (column: SHISEIDO SILICA SG80 4.6 mm∅ × 250 mm, hexane/isopropanol 98:2, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**43**) = 36.4 min, (**46**) = 30.2 min, (**47**) = 34.0 min).

Application to natural product synthesis (1): Triol

4-[(*E*)-1-Oxo-7-phenyl-2-heptenyl]morpholine (48): Pale yellow oil; IR (neat): $\tilde{\nu}$ = 2926, 2855, 1658, 1620, 1432, 1268, 1230, 1116, 975, 749, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.29–7.26 (m, 2H), 7.19–7.15 (m, 3H), 6.89 (dt, *J* = 15.0, 7.0 Hz, 1H), 6.17 (d, *J* = 15.0 Hz, 1H), 3.67–3.39 (m, 8H), 2.62 (t, *J* = 7.5 Hz, 2H), 2.25–2.21 (m, 2H), 1.68–1.62 (m, 2H), 1.54–1.48 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 165.6, 146.9, 142.2, 128.3, 128.2, 125.7, 119.5, 66.8, 46.0, 42.2, 36.7, 32.4, 31.0, 27.8; LRMS (EI+): *m/z*: 273 [M^+]; HRMS (FAB+): *m/z*: calcd for $C_{17}H_{24}O_2N$: 274.1807, found 274.1805.

(2*S*,3*R*)-2,3-Epoxy-1-oxo-7-phenylheptyl]morpholine (49): colorless oil; $[\alpha]_D^{24}$ = +20.0 (*c* = 0.79, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2928, 2857, 1659, 1465, 1274, 1239, 749, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.29–7.26 (m, 2H), 7.19–7.16 (m, 3H), 3.69–3.56 (m, 8H), 3.33 (d, *J* = 2.1 Hz, 1H), 3.15 (ddd, *J* = 6.4, 4.6, 2.1 Hz, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 1.72–1.48 (m, 6H); ^{13}C NMR ($CDCl_3$): δ = 166.1, 142.1, 128.3, 128.3, 125.8, 66.7, 58.2, 53.9, 45.3, 42.3, 35.7, 31.4, 31.0, 25.4; LRMS (EI+): *m/z*: 289 [M^+]; HRMS (FAB+): *m/z*: calcd for $C_{17}H_{24}O_3N$ 290.1756, found 290.1758; HPLC conditions (column: DAICEL CHIRALPAK AS-H, isopropanol/hexane 1:4, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R [(2*S*,3*R*)-isomer] = 32.3 min, [(2*R*,3*S*)-isomer] = 58.1 min).

(4*S*,5*R*)-4,5-Epoxy-*N*-methoxy-*N*-methyl-3-oxo-9-phenylnonanamide (50): LHMDS (0.25 mL, 0.25 mmol, 1.0 M solution in THF) was added at −78 °C to a stirred solution of *N*-methoxy-*N*-methylacetoamide (28 μL, 0.263 mmol) in THF (0.75 mL). After stirring for 20 min, a THF solution of **49** (30.5 mg, 0.105 mmol in 0.4 mL THF) was added to the reaction mixture at the same temperature. The reaction was slowly warmed to

−50 °C over a period of 1 h and stirred for 70 h. The reaction was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate (2×5 mL) and the combined organic layers were washed with brine, and dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 3:1) to give **50** [19.3 mg, 60 % (conv. 85 %)] as a pale yellow oil, with recovery of **49** (8.7 mg, 29 %). $[\alpha]_D^{26} = -21.1$ (*c* = 0.87, $CHCl_3$, 99 % *ee*); IR (neat): $\tilde{\nu}$ =2936, 2858, 1724, 1643, 1454, 1359, 1185, 1009, 749, 701 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.27 (m, 2H), 7.17 (m, 3H), 3.66 (s, 3H), 3.59 (d, *J* = 16 Hz, 1H), 3.41 (d, *J* = 16 Hz, 1H), 3.30 (d, *J* = 1.5 Hz, 1H), 3.20 (s, 3H), 3.15 (m, 1H), 2.62 (t, *J* = 7.5 Hz, 2H), 1.74–1.46 (m, 6H); ^{13}C NMR ($CDCl_3$): δ = 200.9, 167.6, 142.0, 128.34, 128.29, 125.8, 61.3, 59.6, 58.1, 42.3, 35.6, 32.1, 31.6, 30.9, 25.3; LRMS (EI+): *m*/*z*: 305 [M^+]; HRMS (FAB+): *m*/*z*: calcd for $C_{17}H_{24}O_4N$: 306.1705, found 306.1718.

(5*R*)-5-Hydroxy-*N*-methoxy-*N*-methyl-3-oxo-9-phenylnonanamide: PhSeSePh (936 mg, 3.00 mmol) was added at 0 °C to a stirred suspension of $NaBH_4$ (227 mg, 6.00 mmol) in EtOH (5 mL). The reaction was allowed to warm to room temperature, and then stirred for 20 min. A solution of **50** (305 mg, 1.00 mmol) in EtOH (3 mL) was added to the reaction mixture. After stirring for 10 min, the reaction was diluted with ethyl acetate and poured into water. The aqueous layer was extracted with ethyl acetate (2×10 mL) and the combined organic layers were washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 1:2) to give the title compound (259 mg, 84 %) as a pale yellow oil. $[\alpha]_D^{27} = -18.8$ (*c* = 1.21, $CHCl_3$, 99 % *ee*); IR (neat): $\tilde{\nu}$ = 3429, 2934, 1715, 1650, 1454, 1194, 749, 701 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.28 (m, 2H), 7.18 (m, 3H), 4.08 (m, 1H), 3.68 (s, 3H), 3.61 (s, 2H), 3.22 (s, 3H), 2.72–2.62 (m, 4H), 1.68–1.39 (m, 6H); ^{13}C NMR ($CDCl_3$): δ = 204.8, 167.8, 142.5, 128.3, 128.2, 125.6, 67.5, 61.4, 49.8, 48.2, 36.3, 35.8, 32.0, 31.3, 25.1; LRMS (EI+): *m*/*z*: 307 [M^+]; HRMS (FAB+): *m*/*z*: calcd for $C_{17}H_{26}O_4N$: 308.1862, found 308.1874.

(2*R*,4*R*,6*R*)-*N*-Methoxy-*N*-methyl-2-phenyl-6-(4-phenylbutyl)-1,3-dioxane-4-acetamide (51): $BEt_2(OMe)$ (0.45 mL, 0.45 mmol, 1.0 M solution in THF) was added at −78 °C to a stirred solution of (5*R*)-5-hydroxy-*N*-methoxy-*N*-methyl-3-oxo-9-phenylnonanamide (69.1 mg, 0.225 mmol) in THF (1.3 mL) and MeOH (0.44 mL). After stirring for 15 min, $NaBH_4$ (30 mg, 0.79 mmol) was added and stirred for 5 h at the same temperature. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (2×10 mL). The combined organic layers were washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was azeotroped a few times with MeOH to give crude diol. To a solution of the crude diol in toluene (1.0 mL) was added benzaldehyde dimethyl acetal (0.084 mL, 0.563 mmol) and PPTS (2.8 mg, 0.011 mmol) at room temperature, and then the mixture was heated to reflux. After stirring for 10 h, the reaction was diluted with ether and poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with diethyl ether (2×5 mL) and the combined organic layers were washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 5:1) to give **51** (66.2 mg, 74 % in 2 steps) as yellow oil. $[\alpha]_D^{27} = +21.8$ (*c* = 0.92, $CHCl_3$, 99 % *ee*); IR (neat): $\tilde{\nu}$ = 2936, 2857, 1661, 1454, 1343, 1120, 1026, 752, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.48 (m, 2H), 7.36–7.27 (m, 5H), 7.18 (m, 3H), 5.56 (s, 1H), 4.38 (m, 1H), 3.85 (m, 1H), 3.68 (s, 3H), 3.20 (s, 3H), 2.98 (dd, *J* = 17.5, 5.5 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.55 (dd, *J* = 17.5, 6 Hz, 1H), 1.81–1.40 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 171.4, 142.6, 138.7, 128.5, 128.4, 128.2, 128.1, 126.1, 125.6, 100.6, 76.6, 73.5, 61.4, 38.2, 37.0, 35.8, 35.7, 32.0, 31.4, 24.7; LRMS (EI+): *m*/*z*: 397 [M^+]; HRMS (FAB+): *m*/*z*: calcd for $C_{17}H_{24}O_4N$: 398.2331, found 398.2321; HPLC conditions (column: DAICEL CHIRALPAK AD-H, *i*PrOH/hexane 1:9, flow rate: 1.0 mL min^{-1}, detector 254 nm, t_R [(4*S*,6*S*)-isomer] = 7.9 min, [(4*R*,6*R*)-isomer] =) = 10.0 min).

1-[(2*R*,4*R*,6*R*)-2-Phenyl-6-(4-phenylbutyl)-1,3-dioxan-4-yl]-4-penten-2-one: Allylmagnesium bromide (0.39 mL, 0.39 mmol, 1.0 M solution in Et_2O) was added at 0 °C to a stirred solution of **51** (77.9 mg, 0.196 mmol) in THF (1.6 mL). After stirring for 30 min at the same temperature, the reaction was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate (2×4 mL) and the combined organic layers were washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 20:1) to give the title compound (64.2 mg, 87 %) as colorless oil. $[\alpha]_D^{30} = -2.1$ (*c* 1.36, $CHCl_3$, 99 % *ee*); IR (neat): $\tilde{\nu}$ = 2934, 2857, 1715, 1454, 1346, 1128, 1026, 921, 752, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.45 (m, 2H), 7.37–7.29 (m, 5H), 7.18 (m, 3H), 5.92 (ddt, 17.5, 10.5, 7 Hz, 1H), 5.53 (s, 1H), 5.20 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.14 (dd, *J* = 17.5, 1.5 Hz, 1H), 4.32 (m, 1H), 3.83 (m, 1H), 3.24 (ddd, *J* = 7, 1.5, 1.5 Hz, 2H), 2.89 (dd, *J* = 16, 6.5 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.57 (dd, *J* = 16, 6 Hz, 1H), 1.72–1.35 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 206.4, 142.5, 138.5, 130.1, 128.6, 128.4, 128.2, 128.1, 126.0, 125.6, 119.1, 100.5, 76.6, 73.0, 48.8, 48.2, 36.7, 35.8, 35.6, 31.4, 24.6; LRMS (EI+): *m*/*z*: 378 [M^+]; HRMS (FAB+): *m*/*z*: calcd for $C_{25}H_{31}O_3$: 379.2273, found 379.2276.

(α*S*,2*R*,4*S*,6*R*)-2-Phenyl-6-(4-phenylbutyl)-α-2-propenyl-1,3-dioxane-4-ethanol (52): L-Selectride (0.117 mL, 0.117 mmol, 1.0 M solution in THF) was added at −100 °C to a stirred solution of the allylketone prepared above (22.2 mg, 0.0586 mmol) in THF (0.6 mL). After stirring for 2 h at the same temperature, the reaction was quenched with H_2O_2 (30 wt. % solution in water) and 1 M NaOH. The mixture was allowed to warm to room temperature and diluted with Et_2O. The aqueous layer was extracted with Et_2O (2×3 mL) and the combined organic layers were washed with 2 % aqueous $Na_2S_2O_3$, brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 10:1) to give **52** [13.3 mg, 60 % (conv. 97 %), inseparable mixture of *syn*,*syn*- and *syn*,*anti*-diastereomer (7:1)] as colorless oil. $[\alpha]_D^{23} = -0.93$ (*c* = 1.40, $CHCl_3$, 99 % *ee*, 7:1 mixture of *syn*,*syn*- and *syn*,*anti*-diastereomer); IR (neat): $\tilde{\nu}$ = 3522, 2935, 2857, 1454, 1342, 1104, 1026, 914, 752, 698 cm^{-1}; ^1H NMR ($CDCl_3$): *syn*,*syn*-diastereomer: δ = 7.46 (m, 2H), 7.36–7.27 (m, 5H), 7.18 (m, 3H), 5.84 (ddt, *J* = 17.5, 10.5, 7 Hz), 5.55 (s, 1H), 5.12 (m, 2H), 4.08 (m, 1H), 3.97 (m, 1H), 3.82 (m, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.26 (m, 2H), 1.80–1.43 (m, 10H); ^{13}C NMR ($CDCl_3$): *syn*,*syn*-diastereomer: δ = 142.5, 138.3, 134.7, 128.7, 128.4, 128.3, 128.2, 126.0, 125.6, 117.6, 100.6, 77.3, 76.8, 70.4, 42.0, 37.1, 35.8, 35.6, 31.4, 24.6; LRMS (EI+): *m*/*z*: 380 [M^+]; HRMS (FAB+): *m*/*z*: calcd for $C_{25}H_{33}O_3$: 381.2430, found 381.2428.

(*S*)-1-[[(2*R*,4*R*,6*R*)-2-Phenyl-6-(4-phenylbutyl)-1,3-dioxan-4-yl]methyl]-3-butenyl 2-propenoate: Acryloyl chloride (9.0 μL, 0.11 mmol) and *i*Pr_2NEt (20 mL, 0.115 mmol) were added at 0 °C to a stirred solution of **52** (21.1 mg, 0.0554 mmol) in CH_2Cl_2 (0.55 mL). The mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was diluted with Et_2O and poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ether and the combined organic layers were washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 25:1) to give the title compound (21.8 mg, 91 %, inseparable mixture of *syn*,*syn*- and *syn*,*anti*-diastereomer) as a colorless oil. $[\alpha]_D^{23} = +4.6$ (*c* = 1.09, $CHCl_3$, 99 % *ee*, mixture of *syn*,*syn*- and *syn*,*anti*-diastereomer). IR (neat):$\tilde{\nu}$= 2934, 2857, 1721, 1404, 1194, 1026, 699 cm^{-1}; ^1H NMR ($CDCl_3$): *syn*,*syn*-diastereomer: δ = 7.40 (m, 2H), 7.28–7.18 (m, 5H), 7.10 (m, 3H), 6.30 (dd, *J* = 17.5, 1.5 Hz, 1H), 6.01 (dd, *J* = 17.5, 10.5 Hz, 1H), 5.73 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.70 (ddt, *J* = 17.5, 10.5, 7 Hz, 1H), 5.40 (s, 1H), 5.14 (m, 1H), 5.02 (m, 2H), 3.83 (m, 1H), 3.70 (m, 1H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.00 (m, 1H), 1.70 (m, 1H), 1.63–1.29 (m, 8H); ^{13}C NMR ($CDCl_3$): *syn*,*syn*-diastereomer: δ = 165.7, 142.6, 138.7, 133.2, 130.7, 128.6, 128.5, 128.4, 128.2, 128.1, 126.1, 125.6, 118.2, 100.6, 76.6, 74.0, 70.4, 39.8, 38.9, 36.8, 35.8, 35.7, 31.4, 24.7; LRMS (EI+): *m*/*z*: 434 [M^+]; HRMS (FAB+): *m*/*z*: calcd for $C_{28}H_{35}O_4$: 435.2535, found 435.2526.

(6*S*)-5,6-Dihydro-6-[[(2*R*,4*R*,6*R*)-2-phenyl-6-(4-phenylbutyl)-1,3-dioxan-4-yl]methyl]-2*H*-pyran-2-one (53): The acryloyl ester prepared above (19.9 mg, 0.0458 mmol) was dissolved in CH_2Cl_2 (6.5 mL). After degassing, Grubbs' catalyst (1.5 mg, 1.8 μmol) was added to the mixture at room temperature. The reaction was heated to reflux for 9 h. After the solvent being removed, the resulting residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 4:1) to give **53** (15.7 mg, 84 %, a separable mixture of **53** and **6-*epi*-53**) as a colorless oil. The mixture was purified by preparative thin-layer chromatography and **53** and **6-*epi*-53** were isolated as a colorless oil (**53**: 13.0 mg, 70 %; **6-*epi*-53**: 1.5 mg, 8 %). **53**: $[\alpha]_D^{27} = -47.6$ (*c* 1.21, $CHCl_3$, 99 % *ee*); IR (neat): $\tilde{\nu}$ = 2929, 2857, 1730, 1245, 1119, 1026, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.46 (m, 2H), 7.38–7.24 (m, 5H), 7.18 (m, 3H), 6.90 (m, 1H), 6.04 (dd,

$J=10$, 1.5 Hz, 1H), 5.52 (s, 1H), 4.68 (m, 1H), 4.16 (m, 1H), 3.83 (m, 1H), 2.63 (t, $J=7.5$ Hz, 2H), 2.55–2.39 (m, 2H), 2.22 (m, 1H), 1.92 (m, 1H), 1.73–1.43 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 164.3, 145.3, 142.5, 138.6, 128.6, 128.4, 128.2, 128.1, 126.0, 125.6, 121.2, 100.5, 77.2, 74.6, 72.5, 40.3, 36.5, 35.8, 35.7, 31.4, 29.3, 24.7; LRMS (EI+): m/z: 406 [M^+]; HRMS (FAB+): m/z: calcd for $C_{26}H_{31}O_4$: 407.2222, found 407.2220.

(6*S*)-6-[(2*R*,4*R*)-2-Acetoxy-4-hydroxy-8-phenyloctyl]-5,6-dihydro-2*H*-pyran-2-one (54), (6*S*)-6-[(2*R*,4*R*)-4-acetoxy-2-hydroxy-8-phenyloctyl]-5,6-dihydro-2*H*-pyran-2-one (55): Compound **53** (9.0 mg, 0.022 mmol) was dissolved in an 80% solution of AcOH (0.5 mL) and the solution was heated to 60°C. After stirring for 5 h, the reaction was diluted with ethyl acetate and then poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, and then dried over Na_2SO_4. After concentration in vacuo, crude diol was obtained. To a stirred solution of the crude diol in CH_2Cl_2 (0.2 mL) was added triethyl orthoacetate (10 μL, 0.055 mmol) and PPTS (0.5 mg, 2 μmol) at room temperature. After the reaction being stirred until all of the starting material was consumed (1 h), water (1 μL) was added to the reaction and the mixture was stirred for 1 h. The reaction mixture was directly purified by flash column chromatography (silica gel, hexane/ethyl acetate 1:1) to give a mixture of **54** and **55** (6.0 mg, 76% in 2 steps) as a yellow oil. $[\alpha]_D^{26} = -29.7$ (c = 0.60, MeOH, 99% *ee*, a mixture of synthetic **54** and **55**) (lit.[53]: $[\alpha]_D = +35$ (c = 0.05, MeOH) for **54** and $[\alpha]_D = +35$ (c = 0.05, MeOH) for **55**); IR (neat): $\tilde{\nu}$ = 3453, 2933, 1730, 1375, 1246, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$): **54**: δ = 7.27 (m, 2H), 7.18 (m, 3H), 6.89 (m, 1H), 6.02 (d, $J=9.5$ Hz, 1H), 4.95 (m, 1H), 4.65 (m, 1H), 3.89 (m, 1H), 2.61 (t, $J=7.5$ Hz, 2H), 2.41 (m, 2H), 2.20–1.31 (m, 10H), 2.04 (s, 3H); ^{13}C NMR ($CDCl_3$): **54**: δ = 171.3, 163.8, 145.2, 142.3, 128.4, 128.3, 125.7, 121.3, 76.7, 72.4, 67.1, 42.3, 41.7, 35.7, 34.6, 31.1, 29.4, 24.8, 21.3; ^{1}H NMR ($CDCl_3$): **55**: δ = 7.27 (m, 2H), 7.18 (m, 3H), 6.89 (m, 1H), 6.02 (d, $J=9.5$ Hz, 1H), 5.23 (m, 1H), 4.51 (m, 1H), 3.70 (m, 1H), 2.62 (t, $J=7.5$ Hz, 2H), 2.42–2.22 (m, 2H), 2.20–1.31 (m, 10H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$): **55**: δ = 171.3, 163.8, 144.7, 142.3, 128.4, 128.3, 125.7, 121.4, 75.1, 69.2, 69.0, 41.7, 39.3, 37.7, 35.8, 31.3, 29.2, 25.0, 21.3; LRMS (EI+): m/z: 360 [M^+]; HRMS (FAB+): m/z: calcd for $C_{21}H_{28}O_5$: 361.2015, found 361.2019.

(6*S*)-6-[(2*R*,4*R*)-2,4-Diacetoxy-8-phenyloctyl]-5,6-dihydro-2*H*-pyran-2-one (56): Ac_2O (2.5 μL, 0.027 mmol) and catalytic amount of DMAP were added to a stirred solution of a mixture of **54** and **55** (2.4 mg, 6.7 μmol) in pyridine (0.1 mL). After stirring for 30 min, the reaction mixture was diluted with ethyl acetate and the solution was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with 1N HCl, brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by preparative thin-layer chromatography (silica gel, hexane/ethyl acetate 1:2) to give **56** (2.4 mg, 89%) as a yellow oil. $[\alpha]_D^{22} = -31.5$ (c = 0.33, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2931, 1730, 1372, 1240, 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.27 (m, 2H), 7.18 (m, 3H), 6.88 (m, 1H), 6.01 (dd, $J=9.75$, 2 Hz, 1H), 5.04 (m, 1H), 4.93 (m, 1H), 4.48 (m, 1H), 2.60 (t, $J=7.5$ Hz, 2H), 2.45–2.27 (m, 2H), 2.06 (s, 3H), 2.04 (s, 3H), 2.16–1.78 (m, 4H), 1.62 (m, 4H), 1.34 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 170.8, 170.7, 163.8, 144.7, 142.3, 128.4, 128.3, 125.7, 121.4, 74.9, 70.8, 67.9, 39.0, 39.0, 35.7, 34.1, 31.1, 29.1, 24.7, 21.2, 21.2; LRMS (EI+): m/z: 402 [M^+]; HRMS (FAB+): m/z: calcd for $C_{23}H_{31}O_6$: 403.2121, found 403.2108.

In confirmation of the stereochemistry, minor isomer **6-*epi*-53** was also converted to the corresponding diacetate **6-*epi*-56** by the same procedure.

(6*R*)-5,6-Dihydro-6-[[(2*R*,4*R*,6*R*)-2-phenyl-6-(4-phenylbutyl)-1,3-dioxan-4-yl]methyl]-2*H*-pyran-2-one (6-*epi*-53): $[\alpha]_D^{27} = -2.1$ (c = 0.28, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2930, 2857, 1724, 1248, 1120, 1026, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.46 (m, 2H), 7.37–7.27 (m, 5H), 7.19 (m, 3H), 6.88 (ddd, $J=10$, 5.5, 3 Hz, 1H), 6.03 (dd, $J=10$, 1.5 Hz, 1H), 5.50 (s, 1H), 4.80 (m, 1H), 4.23 (m, 1H), 3.82 (m, 1H), 2.63 (t, $J=7.5$ Hz, 2H), 2.36 (m, 2H), 1.94 (m, 1H), 1.86 (m, 1H), 1.73–1.37 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 164.4, 145.1, 142.6, 138.7, 128.6, 128.4, 128.3, 128.2, 126.1, 125.6, 121.4, 100.4, 76.7, 74.0, 72.0, 41.6, 37.2, 35.8, 35.7, 31.4, 30.0, 24.7; LRMS (EI+): m/z: 406 [M^+]; HRMS (FAB+): m/z: calcd for $C_{26}H_{30}O_4$: 407.2222, found 407.2213.

(6*R*)-6-[(2*R*,4*R*)-2,4-Diacetoxy-8-phenyloctyl]-5,6-dihydro-2*H*-pyran-2-one (6-*epi*-56): $[\alpha]_D^{22} = +17.8$ (c = 0.18, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2931, 1731, 1373, 1240, 1023 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 7.27 (m, 2H), 7.19 (m, 3H), 6.85 (ddd, $J=10$, 5.5, 3 Hz, 1H), 6.02 (dd, $J=10$, 1.5 Hz, 1H), 5.14 (m, 1H), 4.92 (m, 1H), 4.48 (m, 1H), 2.60 (t, $J=7.5$ Hz, 2H), 2.35–2.31 (m, 2H), 2.10–1.78 (m, 4H), 2.04 (s, 3H), 1.60 (m, 4H), 1.32 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 170.8, 170.3, 163.6, 144.5, 142.3, 128.4, 128.3, 125.7, 121.6, 74.5, 70.7, 68.0, 39.4, 38.8, 35.7, 34.0, 31.1, 29.6, 24.7, 21.2, 21.2; LRMS (EI+): m/z: 402 [M^+]; HRMS (FAB+): m/z: calcd for $C_{23}H_{31}O_6$: 403.2121, found 403.2108.

(3*S*,5*S*)-3,5-Isopropylidenedioxy-7-phenyl-1-heptanol (57): TsOH·H_2O (1.6 mg, 0.008 mmol) was added at room temperature to a stirred solution of ***anti*-24a** (22.8 mg, 0.086 mmol) in dimethoxypropane (0.6 mL). After 2 h, the reaction was diluted with ethyl acetate (10 mL). The solution was washed with saturated aqueous $NaHCO_3$ and brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 30:1) to give ***anti*-25a** (25.2 mg, 96%). To a suspension of lithium aluminum hydride (6.6 mg, 0.175 mmol) in THF (0.3 mL) was added a solution of ***anti*-25a** (22.4 mg, 0.073 mmol) in THF (0.7 mL) at 0°C. After stirring for 1 h, the reaction was quenched with excess MeOH, and diluted with ethyl acetate. The mixture was washed with 0.1N aqueous HCl, saturated aqueous $NaHCO_3$, brine, and then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by flash column chromatography (silica gel, hexane/ethyl acetate 2:1) to give alcohol **57** as a colorless oil (18.6 mg, 96%).

The spectral data were identical to the reported data.[58] $[\alpha]_D^{23} = +23.1$ (c = 1.07, $CHCl_3$, 99% *ee*) (lit.[58] $[\alpha]_D^{25} = +24.9$ (c = 1.70, $CHCl_3$)).

Application to natural product synthesis (2): Tetraol

4-[(2*R*,3*S*)-2,3-Epoxy-1-oxobutyl]morpholine (60): $Sm(OiPr)_3$ (2.1 mL, 0.42 mmol, 0.2M in THF) was added at room temperature to a mixture of (*S*)-BINOL (120 mg, 0.42 mmol), triphenylarsine oxide (135 mg, 0.42 mmol) and MS 4 Å (8.38 g; MS 4 Å was not dried. 1000 mg per 1 mmol of starting material) in THF (32 mL). After stirring for 40 min at the same temperature, TBHP (2.0 mL, 10.1 mmol, 5M in decane) was added. After 10 min, **59** (1.3 g, 8.38 mmol) in THF (8 mL) was added. The reaction mixture was stirred for 8 h at the same temperature, and the reaction mixture was filtered and the filtrate was diluted with ethyl acetate (80 mL). The resulting mixture was washed with 2% aqueous citric acid, saturated aqueous sodium thiosulfate and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 1:1 to 0:1) to afford **60** as white foam (1.28 g, 7.47 mmol, 89%). $[\alpha]_D^{22} = -15.9$ (c = 0.98, $CHCl_3$, 98% *ee*); IR (neat): $\tilde{\nu}$ = 2860, 1650, 1244, 1113 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.41 (d, $J=5.1$ Hz, 3H), 3.24 (dq, $J=2.2$, 5.1 Hz, 1H), 3.31 (d, $J=2.2$ Hz, 1H), 3.19–3.76 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 17.2, 42.3, 45.4, 54.3, 54.9, 66.7, 166.0; HRMS (EI+): m/z: calcd for $C_8H_{13}O_3N$: 171.0895, found 171.0894.

4-[(2*S*,3*R*)-2,3-Epoxy-1-oxobutyl]morpholine (*ent*-60): $[\alpha]_D^{22} = +13.8$ (c = 1.09, $CHCl_3$, 99% *ee*); IR (neat): $\tilde{\nu}$ = 2862, 1643, 1246, 1111 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.41 (d, $J=5.1$ Hz, 3H), 3.24 (dq, $J=2.2$, 5.1 Hz, 1H), 3.31 (d, $J=2.2$ Hz, 1H), 3.19–3.76 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 17.2, 42.3, 45.4, 54.3, 54.9, 66.7, 166.0; HRMS (EI+): m/z: calcd for $C_8H_{13}O_3N$: 171.0895, found 171.0897.

(3*R*,4*S*)-3,4-Epoxy-1-phenyl-2-pentanone: Benzylmagnesium chloride (0.23 mL, 2M in THF) was added dropwise at 4°C to a solution of **60** (40 mg, 0.233 mmol) in THF (3 mL). The reaction mixture was quenched with saturated aqueous NH_4Cl. After extracting with ethyl acetate (3×), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 8:1) to afford the benzyl ketone as oil (25 mg, 0.142 mmol, 60% yield, 98% *ee*). $[\alpha]_D^{22} = +53.5$ (c = 0.77, $CHCl_3$, 98% *ee*); IR (neat): $\tilde{\nu}$ = 1718, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.37 (d, $J=5.2$ Hz, 3H), 3.12 (dq, $J=1.9$, 5.2 Hz, 1H), 3.24 (d, $J=1.9$ Hz, 1H), 3.63 (d, $J=15.5$ Hz, 1H), 3.72 (d, $J=15.5$ Hz, 1H), 7.20 (m, 2H), 7.26 (m, 1H), 7.32 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 17.4, 44.2, 54.5, 60.3, 127.1, 128.6, 129.5, 132.8, 204.6; HRMS (EI+): m/z: calcd for $C_{11}H_{12}O_2$: 176.0837, found 176.0830; HPLC conditions (column: DAICEL CHIRALPAK AD-H, hexane/isopropanol 99:1, flow rate:

0.8 mL min^{-1}, detector: 254 nm, t_R [(3*R*,4*S*)] = 28.5 min, [(3S,4*R*)] = 33.5 min).

Butyl (4*R*,5*S*)-4,5-epoxy-3-oxohexanoate (61): *n*-Butyl acetate (1.45 mL, 11.0 mmol) was added dropwise at −78 °C to a mixture of LHMDS (11.0 mL, 10.6 mmol, 1.0 M solution in THF) and THF (50 mL). After stirring for 30 min, a solution of **60** (628 mg, 3.67 mmol) in THF (10 mL) was added dropwise and the reaction mixture was stirred for 6 h at −78 °C. The reaction was quenched with saturated aqueous NH_4Cl at −78 °C and warmed to room temperature. The aqueous layer was extracted with ethyl acetate (3×) and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 9:1) to afford **61** as colorless oil (644 mg, 3.2 mmol, 88 %). $[\alpha]_D^{21}$ = +54.9 (*c* = 0.99, $CHCl_3$, 98 % *ee*); IR (neat): $\tilde{\nu}$ = 2961, 1742, 1718 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.92 (t, *J* = 7.3 Hz, 3H), 1.38 (tq, *J* = 7.6, 7.3 Hz, 2H), 1.42 (d, *J* = 4.9 Hz, 3H), 1.62 (tt, *J* = 6.4, 7.6 Hz, 2H), 3.23 (m, 1H), 3.26 (s, 2H), 3.37 (s, 3H), 4.13 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.5, 17.2, 18.9, 30.3, 43.6, 54.3, 60.4, 65.3, 166.6, 200.1; HRMS (FAB+): *m*/*z*: calcd for $C_{10}H_{17}O_4$: 201.1127, found 201.1139.

Butyl (*S*)-5-hydroxy-3-oxohexanoate: $NaBH_4$ (387 mg, 10.24 mmol) was added portionwise at room temperature to a mixture of PhSeSePh (1.6 g, 5.12 mmol) in ethanol (8 mL). After stirring for 15 min, the reaction mixture was cooled to 0 °C, and then a solution of **61** (644 mg, 3.2 mmol) in ethanol (5 mL) was added. After stirring for 5 min at the same temperature, the reaction was quenched with saturated aqueous NH_4Cl. The resulting mixture was extracted with ethyl acetate (3×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 20:1, 10:1, 2:1 to 1:1) to afford the ketoester as yellow oil (574 mg, 2.83 mmol, 89 %). $[\alpha]_D^{22}$ = +36.0 (*c* = 1.15, $CHCl_3$, 98 % *ee*); IR (neat): $\tilde{\nu}$ = 2964, 1738, 1713 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.93 (t, *J* = 6.9 Hz, 3H), 1.21 (d, *J* = 5.8 Hz, 3H), 1.37 (m, 2H), 1.63 (m, 2H), 2.65 (dd, *J* = 8.5, 17.4 Hz, 1H), 2.73 (d, *J* = 17.4 Hz, 1H), 2.81 (s, 3H), 3.46 (s, 2H), 4.14 (t, *J* = 6.4 Hz, 2H), 4.26 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.5, 18.9, 22.3, 30.3, 49.7, 51.0, 63.6, 65.3, 166.9, 203.5; LRMS (FAB+): *m*/*z*: calcd for $C_{10}H_{19}O_4$: 203, found 203; HRMS (FAB+): *m*/*z*: calcd for $C_{10}H_{19}O_4$: 203.1283, found 203.1287.

Butyl (2*S*,4*S*,6*S*)-6-methyl-2-phenyl-1,3-dioxane-4-acetate (62): $BEt_2(OMe)$ (3.11 mL, 3.11 mmol, 1.0 M in THF) was added at −78 °C to a solution of the δ-hydroxy β-ketoester (574 mg, 2.83 mmol) in THF (4 mL) and MeOH (4 mL). After stirring for 1 h, $NaBH_4$ (134 mg, 3.54 mmol) was added and stirred for 5.5 h at the same temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl at −78 °C and then warmed to room temperature. The resulting mixture was extracted with ethyl acetate (3×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. To the obtained residue (653 mg) in toluene (20 mL) at room temperature was added benzaldehyde dimethyl acetal (0.85 mL, 5.66 mmol) and $TsOH\cdot H_2O$ (10 mg). After stirring overnight, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with ethyl acetate (3×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 30:1, 10:1 to 4:1) to afford **62** as yellow oil (496 mg, 1.7 mmol, 60 %). $[\alpha]_D^{22}$ = +11.3 (*c* 1.15, $CHCl_3$, 98 % *ee*); IR (neat): $\tilde{\nu}$ = 2960, 1735, 1176, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, *J* = 7.3 Hz, 3H), 1.31 (d, J = 6.1 Hz, 1H), 1.36 (tq, *J* = 7.6, 7.3 Hz, 2H), 1.44 (ddd, *J* = 11.3, 12.0, 12.8 Hz, 1H), 1.61 (tt, *J* = 6.8, 7.6 Hz, 2H), 1.73 (ddd, *J* = 2.2, 2.3, 12.8 Hz, 1H), 2.50 (dd, *J* = 6.1, 15.5 Hz, 1H), 2.72 (dd, *J* = 7.3, 15.5 Hz, 1H), 3.99 (m, 1H), 4.10 (t, *J* = 6.8 Hz, 2H), 4.30 (m, 1H), 5.55 (s, 1H), 7.29–7.37 (m, 3H), 7.48–7.52 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.6, 19.0, 21.5, 30.5, 38.1, 40.9, 64.4, 72.7, 73.2, 100.7, 126.0, 128.1, 128.5, 138.4, 170.8; HRMS (EI+): *m*/*z*: calcd for $C_{17}H_{24}O_4$: 292.1675, found 292.1680.

Synthetic route to 63: $LiBH_4$ (26 mg, 1.19 mmol) and trimethoxyborane (0.013 mL, 0.119 mmol) were added successively at room temperature to a solution of **62** (316 mg) in diethyl ether (20 mL). After stirring for 1 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and the resulting mixture was extracted with ethyl acetate (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford an alcohol as oil (260 mg).

To a mixture of the alcohol (260 mg), MS 4 Å (400 mg; MS 4 Å not dried), *N*-methylmorpholine-*N*-oxide (193 mg, 1.65 mmol) and dichloromethane (20 mL) at room temperature was added TPAP (19 mg, 0.055 mmol). The reaction mixture was stirred for 1 h and concentrated in vacuo. The resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate 3:1) to afford an aldehyde as oil (180 mg).

To a stirred mixture of the aldehyde (156 mg, 0.708 mmol), LiCl (36 mg, 0.85 mmol), 4-(2-diethoxyphosphoryl-1-oxoethyl)morpholine (**29**; 225 mg, 0.85 mmol) in acetonitrile (45 mL) at room temperature was added *N*,*N*-diisopropylethylamine (0.15 mL, 0.85 mmol). After stirring overnight, the reaction mixture was diluted with ethyl acetate. The resulting mixture was washed with 2 % aqueous citric acid, saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, ethyl acetate) to afford **63** as oil (230 mg, 0.69 mmol, 74 %, 3 steps).

4-[(*E*)-4-[(2*S*,4*R*,6*S*)-6-Methyl-2-phenyl-1,3-dioxan-4-yl]-1-oxo-2-butenyl]morpholine (63): $[\alpha]_D^{21}$ = +8.4 (*c* 1.00, $CHCl_3$, 98 % *ee*); IR (neat): $\tilde{\nu}$ = 2854, 1659, 1617, 1434, 1113 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.31 (d, *J* = 6.1 Hz, 3H), 1.42 (ddd, *J* = 11.3, 11.3, 12.8 Hz, 1H), 1.65 (ddd, *J* = 2.1, 2.3, 12.8 Hz, 1H), 2.44 (ddd, *J* = 7.3, 7.3, 10.4 Hz, 1H), 2.58 (ddd, *J* = 7.3, 7.3, 14.5 Hz, 1H), 3.50–3.75 (br, 8H), 3.96 (m, 2H), 5.51 (s, 1H), 6.30 (d, *J* = 15.3 Hz, 1H), 6.89 (dt, *J* = 15.3, 7.3 Hz, 1H), 7.29–7.38 (m, 3H), 7.46–7.51 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 21.6, 38.2, 38.8, 42.1, 46.1, 66.6, 66.8, 72.8, 75.3, 100.7, 122.4, 126.1, 128.1, 128.6, 138.5, 141.4, 165.4; HRMS (FAB+): *m*/*z*: calcd for $C_{19}H_{26}O_4N_1$: 332.1862, found 332.1872.

4-[(2*S*,3*R*)-2,3-Epoxy-4-[(2*S*,4*R*,6*S*)-6-methyl-2-phenyl-1,3-dioxan-4-yl]-1-oxobutyl]morpholine (64′): A mixture of **64**′ and **64** (**64**′:**64** >99:1) prepared from **63** (98 % *ee*); $[\alpha]_D^{22}$ = +29.3 (*c* = 1.50, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2856, 1654, 1240, 1116 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.30 (d, *J* = 6.4 Hz, 3H), 1.46 (ddd, *J* = 12.2, 13.1, 24.1 Hz, 1H), 1.65 (ddd, *J* = 2.1, 2.3, 13.1 Hz, 1H), 1.79 (ddd, *J* = 6.8, 10.0, 14.2 Hz, 1H), 1.98 (ddd, *J* = 2.8, 4.1, 14.2 Hz, 1H), 3.10–3.30 (m, 4H), 3.35–3.44 (m, 2H), 3.46–3.65 (m, 4H), 3.98 (m, 1H), 4.07 (m, 1H), 5.51 (s, 1H), 7.34–7.40 (m, 3H), 7.46–7.49 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 21.5, 38.7, 38.8, 42.2, 44.9, 54.1, 55.4, 66.2, 66.5, 72.9, 73.7, 101.3, 126.4, 128.3, 129.1, 138.5, 165.9; HRMS (FAB+): *m*/*z*: calcd for $C_{19}H_{26}O_5N_1$: 348.1811, found 348.1811; HPLC conditions (column: AS-H(DAICEL), hexane/isopropanol 3:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**64**′) = 68.9 min, (**64**) = 91.6 min).

4-[(2*R*,3*S*)-2,3-Epoxy-4-[(2*S*,4*R*,6*S*)-6-methyl-2-phenyl-1,3-dioxan-4-yl]-1-oxobutyl]morpholine (64): $Sm(OiPr)_3$ (0.62 mL, 0.124 mmol, 0.2 M in THF) was added at room temperature to a mixture of (*S*)-BINOL (35.5 mg, 0.124 mmol), triphenylarsine oxide (39.9 mg, 0.124 mmol) and MS 4 Å (1.24 g; MS 4 Å was not dried. 1000 mg per 1 mmol of starting material) in THF (2.5 mL). After stirring for 30 min, TBHP (2.0 mL, 10.1 mmol, 5 M in decane) was added. After stirring for 10 min, **63** (412 mg, 1.24 mmol) in THF (3 mL) was added and the reaction mixture was stirred for 8 h at the same temprerature. The reaction mixture was filtered and the filtrate was diluted with ethyl acetate (40 mL). The resulting mixture was washed with 2 % aqueous citric acid, saturated aqueous sodium thiosulfate, and brine. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 3:1 to 0:1) to afford **64** as yellow oil (387 mg, 1.11 mmol, 90 %).

A mixture of **64** and **64**′ (**64**:**64**′ 99.8:0.2) prepared from **63** (98 % *ee*); $[\alpha]_D^{24}$ = −3.0 (*c* = 1.11, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2856, 1655, 1240, 1115, 1017 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.32 (d, *J* = 6.1 Hz, 3H), 1.52 (m, 1H), 1.64 (ddd, *J* = 2.2, 2.4, 13.2 Hz, 1H), 2.00 (ddd, *J* = 4.1, 4.3, 15.0 Hz, 1H), 2.12 (ddd, *J* = 4.6, 5.8, 15.0 Hz, 1H), 3.23–3.33 (m, 3H), 3.37 (m, 2H), 3.50–3.63 (m, 5H), 3.98 (m, 2H), 5.51 (s, 1H), 7.32–7.38 (m, 3H), 7.45–7.49 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 21.4, 36.3, 37.5, 42.0, 44.9, 53.3, 54.2, 66.2, 66.4, 72.4, 72.9, 100.7, 126.0, 128.1, 128.8, 138.3, 165.9; HRMS (FAB+): *m*/*z*: calcd for $C_{19}H_{26}O_5N_1$: 348.1811, found 348.1813; HPLC conditions (column: DAICEL CHIRALPAK AS-H, hexane/isopropanol 3:1, flow rate: 1.0 mL min^{-1}, detector: 254 nm, t_R (**64**′) = 68.9 min, (**64**) = 91.6 min).

Ethyl (4*R*,5*S*)-4,5-epoxy-6-[(2*S*,4*R*,6*S*)-6-methyl-2-phenyl-1,3-dioxan-4-yl]-3-oxohexanoate: Ethyl acetate (0.31 mL, 3.2 mmol) was added dropwise at −78 °C to a mixture of LHMDS (3.2 mL, 3.2 mmol, 1.0 M solution in THF) and THF (4 mL). After stirring for 25 min at the same tempera-

ture, a solution of **64** (370 mg, 1.07 mmol) in THF (4 mL) was added dropwise and the reaction mixture was stirred for 4 h at −78 °C. The reaction was quenched with saturated aqueous NH_4Cl at −78 °C and warmed to room temperature. After extracting with ethyl acetate (3×), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 4:1 to 3:1) to afford the epoxy ketoester as pale yellow oil (328 mg, 0.94 mmol, 88 %). The title compound was prepared from **64** (a mixture of **64**:**64′** (**64**:**64′** 99.8:0.2)); $[\alpha]_D^{21} = +50.6$ (c = 1.04, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2976, 1742, 1718, 1118 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.25 (d, J=7.3 Hz, 3H), 1.33 (d, J= 6.4 Hz, 3H), 1.55–1.68 (m, 2H), 1.92–2.05 (m, 2H), 3.30–3.45 (m, 4H), 4.00 (m, 2H), 4.15–4.24 (m, 2H), 5.54 (s, 1H), 7.31–7.38 (m, 3H), 7.44–7.53 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 21.5, 37.6, 37.9, 43.8, 55.0, 59.0, 61.5, 72.9, 73.5, 100.7, 126.1, 128.2, 128.7, 138.3, 166.5, 199.8; HRMS (FAB+): m/z: calcd for $C_{19}H_{25}O_6$: 349.1651, found 349.1641.

Ethyl (*S*)-5-hydroxy-6-[(2*S*,4*R*,6*S*)-6-methyl-2-phenyl-1,3-dioxan-4-yl]-3-oxohexanoate: $NaBH_4$ (114 mg, 3.0 mmol) was added portionwise at room temperature to a mixture of PhSeSePh (311 mg, 1.0 mmol) in ethanol (4 mL). After stirring for 5 min, the epoxy ketoester (328 mg, 0.94 mmol) prepared above in ethanol (4 mL) was added. After stirring for 5 min at the same temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl. After extracting with ethyl acetate (3×), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 4:1, 2:1 to 2:3) to afford the hydroxy ketoester as yellow oil (252 mg, 0.72 mmol, 77 %). $[\alpha]_D^{24} = +27.1$ (c = 1.07, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3447, 2974, 1740, 1715, 1111, 1025 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.26 (d, J=7.0 Hz, 3H), 1.31 (d, J= 6.1 Hz, 3H), 1.46 (ddd, J=10.9, 11.3, 13.1 Hz, 1H), 1.64 (ddd, J=2.3, 2.4, 13.1 Hz, 1H), 1.72 (ddd, J=3.5, 3.7, 14.4 Hz, 1H), 1.84 (ddd, J=8.9, 8.9, 14.4 Hz, 1H), 2.65 (dd, J=4.6, 16.8 Hz, 1H), 2.78 (dd, J=7.7, 16.8 Hz, 1H), 3.37 (d, J=1.9 Hz, 1H), 3.47 (s, 2H), 3.98 (m, 1H), 4.11–4.22 (m, 3H), 4.37 (m, 1H), 5.55 (s, 1H), 7.30–7.37 (m, 3H), 7.44–7.48 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 21.5, 38.4, 41.8, 49.7, 49.9, 61.3, 66.6, 72.9, 76.1, 100.8, 126.0, 128.2, 128.7, 138.2, 166.9, 202.6; HRMS (FAB+): m/z: calcd for $C_{19}H_{27}O_6$: 351.1808, found 351.1818.

Ethyl (2*S*,4*S*,6*S*)-6-[[(2*S*,4*S*,6*S*)-6-methyl-2-phenyl-1,3-dioxan-4-yl]methyl]-2-phenyl-1,3-dioxane-4-acetate (65): To a solution of the δ-hydroxy β-ketoester (252 mg, 0.72 mmol) prepared above, in methanol (1 mL) and THF (3 mL) at −78 °C was added dropwise $Et_2B(OMe)$ (0.79 mL, 1.0 M in THF). After stirring for 1 h, $NaBH_4$ (34 mg, 0.9 mmol) was added one portion. The resulting mixture was stirred for 6 h at −78 °C and then for 2 h at −40 °C. The reaction was quenched with saturated aqueous NH_4Cl at −40 °C. The resulting mixture was extracted with ethyl acetate (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to give a crude product. To a solution of the crude product in toluene (10 mL) at room temperature were added benzaldehyde dimethyl acetal (0.16 mL, 1.08 mmol) and $TsOH\cdot H_2O$ (10 mg). After stirring overnight at the same temperature, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with ethyl acetate (3×), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 10:1 to 4:1) to afford **65** as colorless oil (246 mg, 0.56 mmol, 78 %). $[\alpha]_D^{26} = +7.9$ (c 1.06, $CHCl_3$), $[\alpha]_D^{25} = +17.9$ (c 0.98, EtOH) (lit.[28e] $[\alpha]_D^{21} = +15.7$ (c 0.99, EtOH)); IR (neat): $\tilde{\nu}$ = 1734, 1375, 1341, 1113, 1025, 755 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.26 (t, J=7.0 Hz, 3H), 1.32 (d, J=6.1 Hz, 3H), 1.45–1.57 (m, 2H), 1.68 (d, J=13.1 Hz, 1H), 1.73–1.81 (m, 2H), 2.14 (ddd, J=7.0, 7.0, 14.0 Hz, 1H), 2.52 (dd, J=6.5, 15.5 Hz, 1H), 2.73 (dd, J=7.0, 15.5 Hz, 1H), 3.97 (m, 1H), 4.05–4.15 (m, 2H), 4.16 (q, J=7.0 Hz, 2H), 4.33 (m, 1H), 5.53 (s, 1H), 5.57 (s, 1H), 7.30–7.39 (m, 6H), 7.44–7.52 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 21.6, 36.3, 38.4, 41.0, 41.6, 60.5, 72.9, 73.0, 73.2, 100.5, 100.7, 126.0, 126.1, 128.1, 128.2, 128.64, 128.66, 138.4, 138.7, 170.6; HRMS (FAB+): m/z: calcd for $C_{26}H_{33}O_6$: 441.2277, found 441.2274.

Ethyl (*Z*)-4-[(2*R*,4*R*,6*R*)-6-[[(2*S*,4*S*,6*S*)-6-methyl-2-phenyl-1,3-dioxan-4-yl]methyl]-2-phenyl-1,3-dioxan-4-yl]-2-butenoate (66): $LiBH_4$ (4.4 mg, 0.198 mmol) and trimethoxyborane (2.2 μL, 0.02 mmol) were added successively at room temperature to a solution of **65** (80 mg, 0.18 mmol) in diethyl ether (2 mL). After stirring for 20 min at the same temperature, the reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate. The resulting mixture was extracted with ethyl acetate twice, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to afford an alcohol.

To a mixture of the alcohol, and *N*-methylmorpholine-*N*-oxide (32 mg, 0.27 mmol) and MS 4 Å (80 mg; MS 4 Å not dried) in dichloromethane (1 mL) at room temperature was added TPAP (3.2 mg, 0.009 mmol). After stirring for 30 min at the same temperature, the reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 4:1) to afford an aldehyde as oil (46 mg, 0.116 mmol, 64 %).

To a stirred solution of di-*o*-tolylphosphonoacetic acid ethyl ester (35 mg, 0.1 mmol) in THF (1 mL) at −78 °C was added dropwise KHMDS (0.2 mL, 0.1 mmol, 0.5 M in toluene). After stirring for 1 h at the same temperature, a solution of the aldehyde (25 mg, 0.063 mmol) in THF (1 mL) was added dropwise and the resulting solution was stirred for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and the resulting mixture was extracted with ethyl acetate 311times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 1:0 to 4:1) to afford **66** as oil (22 mg, 0.047 mmol, 75 %). $[\alpha]_D^{24} = +27.8$ (c 1.10, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2865, 1715, 1340, 1189, 1118, 1025 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.29 (t, J=7.0 Hz, 3H), 1.32 (d, J=6.4 Hz, 3H), 1.45–1.59 (m, 2H), 1.66–1.77 (m, 3H), 2.14 (ddd, J=7.0, 7.2, 14.0 Hz, 1H), 2.91 (ddd, J=7.0, 14.0, 15.9 Hz, 1H), 3.10 (m, 1H), 3.98 (m, 2H), 4.09 (m, 2H), 4.18 (q, J= 7.0 Hz, 2H), 5.53 (s, 1H), 5.54 (s, 1H), 5.88 (d, J=11.6 Hz, 1H), 6.46 (ddd, J=7.0, 7.2, 11.6 Hz, 1H), 7.31–7.41 (m, 6H), 7.49–7.55 (m, 4H); ^{13}C NMR ($CDCl_3$): δ = 14.2, 21.6, 35.0, 36.3, 38.5, 41.7, 59.8, 72.9, 73.0, 73.1, 75.9, 100.6, 100.7, 121.3, 126.0, 126.1, 128.16, 128.19, 128.61, 128.64, 138.65, 138.79, 145.35, 166.31; HRMS (FAB+): m/z: calcd for $C_{28}H_{35}O_6$: 467.2434, found 467.2436.

Cryprocaryolone diacetate (67): Compound **66** (20 mg, 0.0428 mmol) was dissolved in 80 % aq. acetic acid (1.5 mL) and the solution was heated to 60 °C. After stirring for 80 min at the same temperature, the reaction mixture was cooled to room temperature. The resulting solution was dried over Na_2SO_4, filtered, and concentrated in vacuo. To a solution of the crude product in benzene (1 mL) was added $TsOH\cdot H_2O$ (3 mg), and the resulting mixture was stirred at room temperature for 36 h. The reaction mixture was neutralized with saturated aqueous $NaHCO_3$ and diluted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. To a solution of the crude product in dichloromethane (1 mL) at room temperature were added pyridine (5 μL), DMAP (1 mg) and Ac_2O (50 μL). After stirring for 5 h at the same temperature, the reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate. The resulting mixture was extracted with ethyl acetate, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate 2:1, 1:1 to 1:2) to afford **67** as oil (7 mg, 0.021 mmol, 50 % yield, three steps). $[\alpha]_D^{23} = -18.8$ (c = 0.35, $CHCl_3$) (lit.[59a] $[\alpha]_D^{23} = -145$ (c = 0.27, $CHCl_3$)); IR (neat): $\tilde{\nu}$ = 2924, 1732, 1240, 1075 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.22 (d, J=6.4 Hz, 3H, H-5′), 1.56 (ddd, J=2.1, 14.0, 15.2 Hz, 1H, H-8a), 1.67 (ddd, J=4.3, 5.5, 14.4 Hz, 1H, H-1a′), 1.72 (ddd, J=5.5, 5.8, 14.4 Hz, 1H, H-3a′), 1.85 (dd, J=7.4, 14.7 Hz, 1H, H-1′b), 1.85–2.40 (m, 10H, H-9a, H-9b, H-3′b, H-8b, 2.01, 2.02 (2s, 2×3H, 2AcO), 2.75 (dd, J=5.2, 19.3 Hz, 1H, H-4a), 2.86 (d, J=19.3 Hz, 1H, H-4b), 3.88 (ddd, J=4.3, 7.6, 15.2 Hz, 1H, H-7), 4.32 (m, 1H, H-5), 4.87 (m, 1H, H-1), 4.95 (dq, J=14.4, 6.4 Hz, 1H, H-4′), 5.08 (ddd, J=5.5, 7.4, 12.7 Hz, 1H, H-2′); ^{13}C NMR ($CDCl_3$): δ = 20.0 (C-5′), 21.2 (*C*H_3CO-), 21.3 (*C*H_3CO-), 29.3 (C-9), 36.3 (C-4), 37.0 (C-8), 40.0 (C-1′), 40.4 (C-3′), 63.2 (C-7), 66.0 (C-5), 67.7 (C-4′), 68.2 (C-2′), 72.1 (C-1), 168.0, 169.7, 169.8; ^1H NMR (C_6D_6): δ = 0.94–0.99 (m, 2H, H-8a, H-9a), 1.12 (d, J=6.1 Hz, 3H, H-5′), 1.14 (m, 1H, H-9b), 1.35 (ddd, J=4.9, 4.9, 14.1 Hz, 1H, H-1′a), 1.51 (ddd, J=5.5, 5.8, 14.1 Hz, 1H, H-3′a), 1.55 (m, 1H, H-8b), 1.67–1.76 (m, 7H, H-1′b, 1.68, 1.71 (2s, 2×3H, 2AcO), 1.84 (ddd, J=7.3, 7.3, 14.1 Hz, 1H, H-3′b), 2.09 (dd, J=5.2, 18.9 Hz, 1H, H-4a), 2.63 (d, J=18.9 Hz, 1H, H-4b), 3.56 (brs, 1H, H-5), 3.80 (ddd, J=4.0, 11.3, 14.1 Hz, 1H, H-7), 4.11 (brs, 1H, H-1), 5.11 (dq, J=5.8, 6.1 Hz, 1H, H-4′), 5.20 (dddd, J=4.9, 5.3, 7.3, 12.8 Hz, 1H, H-2′); ^{13}C NMR (C_6D_6): δ = 20.1 (C-5′), 20.6 (*C*H_3CO-), 20.8 (*C*H_3CO-), 29.6 (C-9), 36.1 (C-4), 36.9 (C-8), 39.7

(C-1′), 39.9 (C-3′), 63.0 (C-7), 65.8 (C-5), 67.8 (C-4′), 68.3 (C-2′), 72.8 (C-1), 169.4, 170.44, 170.47; HRMS (FAB+): *m/z*: calcd for $C_{16}H_{25}O_7$: 329.1600, found 329.1588.

CCDC-223952 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

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