Graphical Abstract

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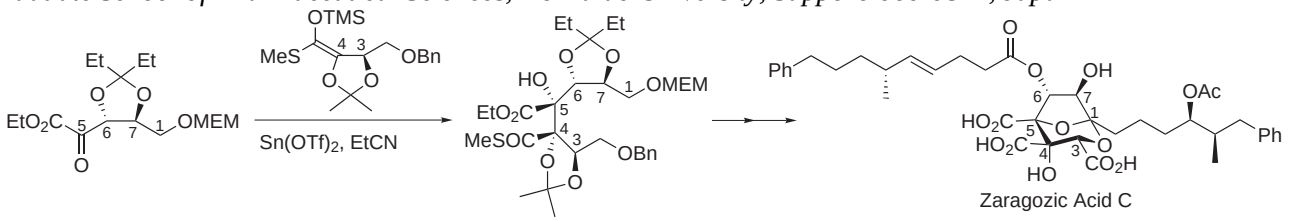

Zaragozic Acid C

Total synthesis of zaragozic acid C by an aldol-based strategy

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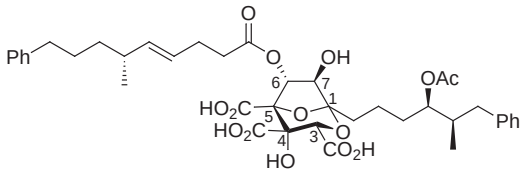
Abstract—A total synthesis of zaragozic acid C by a convergent strategy is described in which the key features include (1) the simultaneous creation of the C4 and C5 quaternary stereogenic centers by a $Sn(OTf)_2$-promoted aldol coupling reaction between an α-keto ester and a silyl ketene thioacetal derived from L- and D-tartaric acids, respectively, (2) the direct introduction of lithium acetylide as the C1 side chain equivalent onto the fully functionalized aldehyde, and (3) construction of the bicyclic core structure by acid-catalyzed internal ketalization under kinetically controlled conditions.

1. Introduction

The zaragozic acids and squalestatins, fungal metabolites isolated and characterized independently by researchers at Merck,[1] Glaxo,[2] and Tokyo Noko University/Mitsubishi Kasei Corporation[3] in 1992, have been shown to be picomolar competitive inhibitors of the enzyme squalene synthase. Consequently, they are considered to be promising lead compounds for the development of new serum cholesterol-lowering drugs.[4] Some members of this family have also been found to display farnesyl–protein transferase inhibitory activity,[1e,5] which has implications in the development of antitumor agents. Structurally, these molecules share a 4,6,7-trihydroxy-2,8-dioxabicyclo[3.2.1]-octane-3,4,5-tricarboxylic acid core with an array of six stereogenic centers including contiguous quaternary ones, and represent considerable variations in the C1 alkyl and C6 acyl side chains. The gross structural similarity between presqualene pyrophosphate (PSPP) and zaragozic acids, i.e. a highly acidic central core with two long lipophilic side chains, has led to the speculation that zaragozic acids inhibit squalene synthase by effectively mimicking the binding of PSPP to the enzyme.[1c,3] Due to the biological activity of these compounds and their novel structural aspects, zaragozic acids (squalestatins) have elicited considerable attention from numerous synthetic chemists.[6,7] Of a variety of approaches to preparing the densely oxygenated 2,8-dioxabicyclo[3.2.1]octane ring system by innovative strategies and tactics, the two research groups of Carreira[8] and Nicolaou[9] accomplished the first total syntheses of zaragozic acid C (**1**) and zaragozic acid A, respectively, in 1994. Since then the Evans[10] and Armstrong[11] groups reported the total syntheses of **1**, while the efforts of the Heathcock,[12] and Tomooka and Nakai[13] groups culminated in the total syntheses of zaragozic acid A. In addition to the six total syntheses, a total synthesis of 6,7-dideoxysqualestatin H5, a less oxygenated congener of the zaragozic acids, has also been reported by Martin and co-workers.[14] All of these approaches involve internal ketalization to construct the core structure; only Heathcock adopted a stepwise approach, wherein the full C1 alkyl side chain was installed after the ketalization event. Our own efforts in this area have led to two total syntheses of zaragozic acid C (**1**) through entirely distinct routes based on an aldol approach[15] and a carbonyl ylide cycloaddition approach,[16] respectively. In this article, we describe the details of the total synthesis of **1** by the aldol-based strategy.



Zaragozic Acid C (**1**)

2. Results and discussion

2.1. Synthetic plan

The main problem in zaragozic acid synthesis is the construction of the highly oxygenated bicyclic core bearing an array of six stereogenic centers, including contiguous quaternary ones. Our retrosynthetic analysis of zaragozic acid C (**1**) originated from the identification of L- and D-tartaric acids in the core structure (Scheme 1).[17] While some concern arose over the formation of the isomeric bicycloketal **4**, we expected that the natural 2,8-dioxabicyclo[3.2.1]octane core structure **3** would be thermodynamically more stable than **4**. We envisioned that the addition of the metalated C1 alkyl side chain equivalent **7** to aldehyde **6**, followed by oxidation, would provide the ketalization precursor **5**. The aldol moiety in **6** allowed the indicated disconnection, defining the tartrate-derived α-keto ester **8** and enolate **9** as potential intermediates. This

Keywords: Zaragozic acids; Aldol reaction; α-Keto ester; Silyl ketene thioacetal; Internal ketalization

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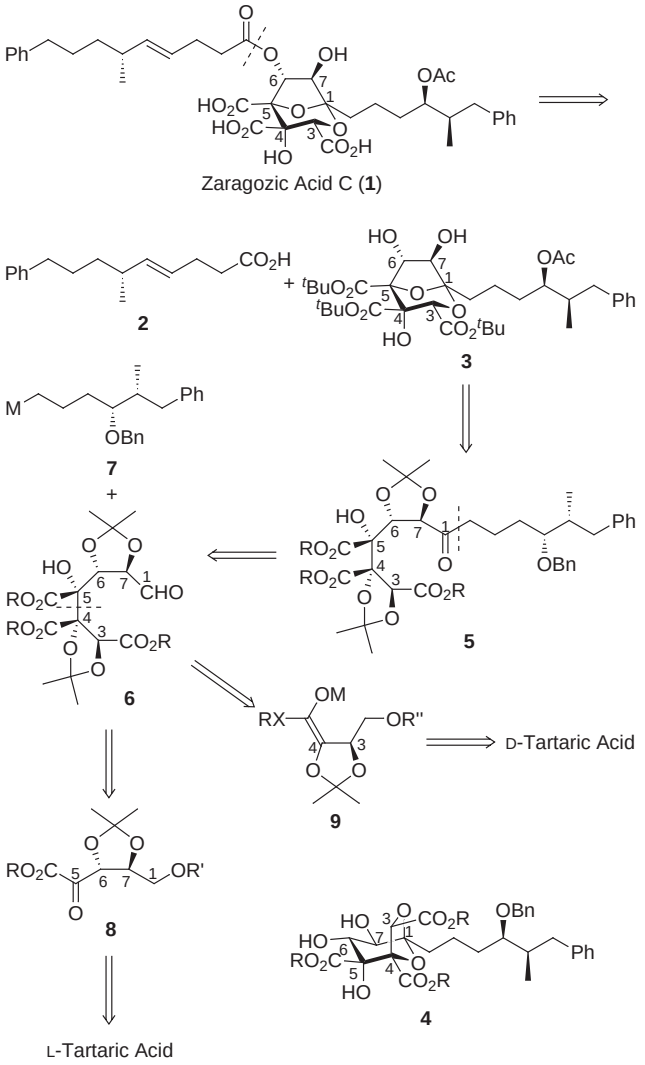
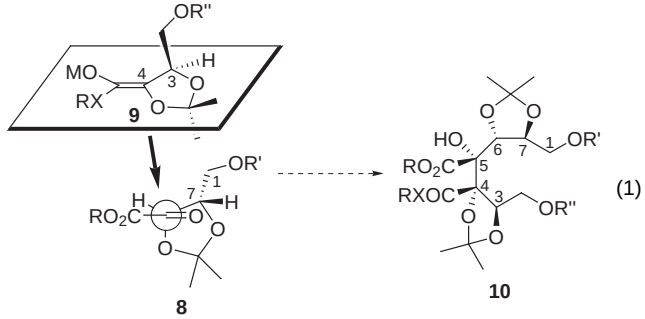


Scheme 1. Retrosynthetic analysis of zaragozic acid C (**1**).

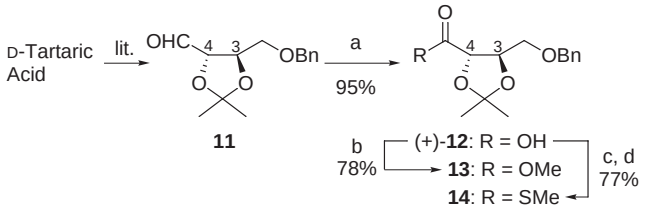
approach has the advantage of minimizing the use of protecting groups and oxidation state manipulation.

With regard to the aldol reactions associated with our scenario, Seebach and co-workers reported that the acetonide derivative of dimethyl L-tartrate could be deprotonated without β-elimination by LDA at –78 °C to provide the corresponding lithium enolate, the reaction of which with acetone took place preferentially from the less hindered face to give a 4:1 mixture of adducts in 60% yield.[18] Provided that the nucleophilic addition of enolate **9** to α-keto ester **8** occurs in accord with the Felkin–Anh model, the formation of the desired stereoisomer **10** with the correct stereochemistry would be expected (Eq. 1).[19]



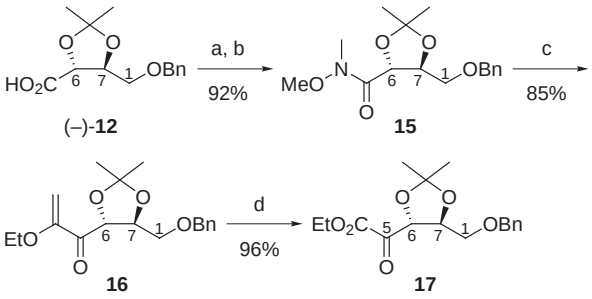
2.2. Preparation of substrates for the aldol coupling

At the outset of our studies, a number of enolate precursors and α-keto esters were prepared to investigate the key aldol reaction. The enolate precursors **13** and **14** were readily available via short synthetic routes depicted in Scheme 2. The known D-tartaric acid-derived aldehyde **11**[20] was subjected to a Pinnick oxidation[21] to give carboxylic acid (+)-**12** in 95% yield. Treatment of (+)-**12** with CH_2N_2 in Et_2O afforded methyl ester **13** in 78% yield, whereas the corresponding thioester **14** could be obtained through the intermediacy of the acid chloride in 77% yield in two steps.



Scheme 2. *Reagents and conditions*: (a) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH–H_2O, 18 h; (b) CH_2N_2, Et_2O, 0 °C, 30 min, then rt, 30 min; (c) $(COCl)_2$, cat. DMF, CH_2Cl_2, 1.5 h; (d) 20% aqueous MeSNa, Bu_4NI, CH_2Cl_2, 0 °C, 10 min.

On the other hand, α-keto ester **17** could be prepared from the L-tartaric acid-derived carboxylic acid (–)-**12** in four steps via the α-keto vinyl ether intermediate **16** (Scheme 3).[22] The reaction of (–)-**12** with $(COCl)_2$, followed by condensation with *N*,*O*-dimethylhydroxylamine hydrochloride, afforded the Weinreb amide **15** in 92% yield,

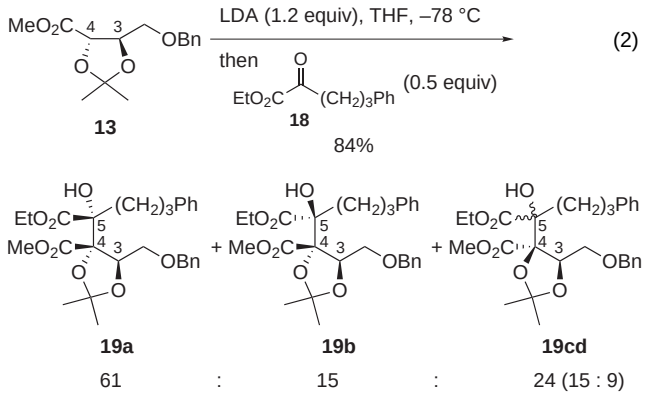


Scheme 3. *Reagents and conditions*: (a) $(COCl)_2$, cat. DMF, CH_2Cl_2, 30 min; (b) MeONHMe·HCl, pyridine, CH_2Cl_2, 0 °C, 1 h; (c) ethyl vinyl ether (EVE), ^{t}BuLi, THF, –78 °C, 3 h; (d) O_3, CH_2Cl_2, –78 °C, 10 min, then Me_2S, –78 °C to rt, 1 h.

which upon treatment with lithiated ethyl vinyl ether gave the α-keto vinyl ether **16** in 85% yield. Ozonolysis of **16** furnished the desired α-keto ester **17** in 96% yield. The synthetic schemes described above proved to be effective for a variety of thioesters and α-keto esters. Since the tartrate-derived α-keto esters were prone to hydration, they were azeotropically dried with benzene prior to use.

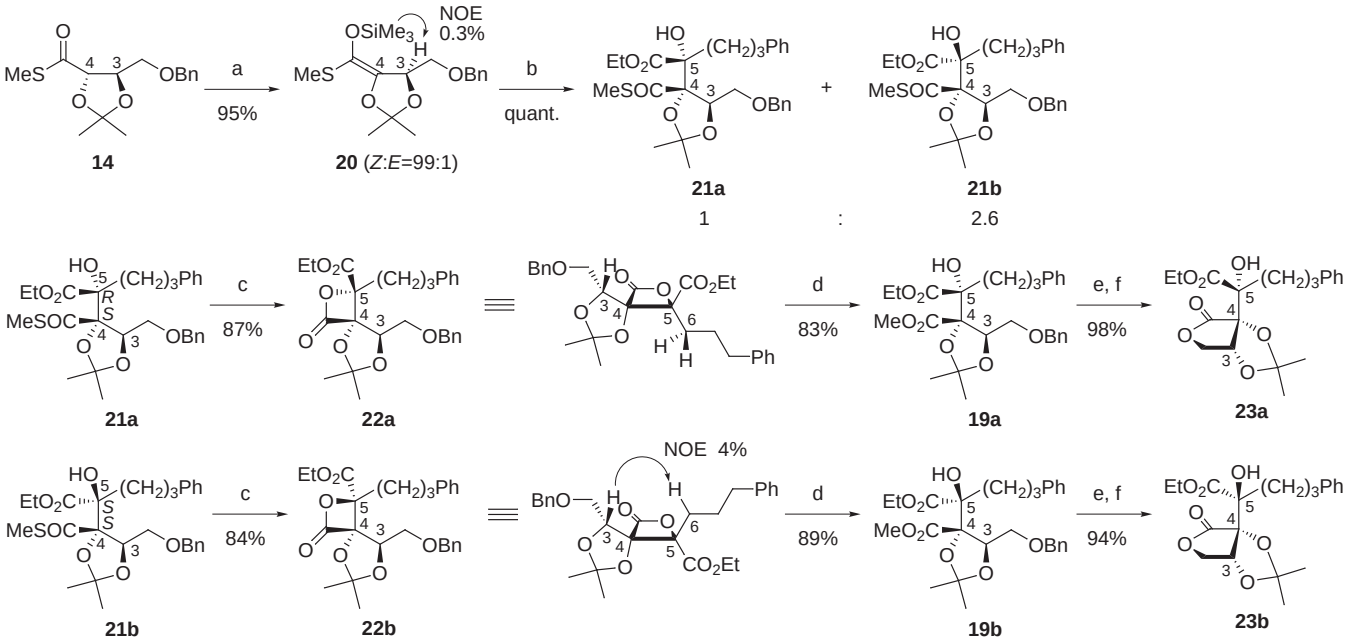
2.3. Aldol reaction

With the enolate precursors and α-keto esters in hand, we then proceeded to investigate the key aldol coupling reaction. Since the simultaneous creation of the consecutive quaternary stereogenic centers by an aldol reaction of α-keto esters is unprecedented in the literature,[23,24] we felt it was prudent to test the viability of the reaction using a simple α-keto ester. The known compound **18**[25] was then chosen as a model substrate for the reaction. We initially explored the reaction of the lithium enolate derived from ester **13** with α-keto ester **18** (Eq. 2). Treatment of ester **13**



with LDA at –78 °C followed by the addition of α-keto ester **18** led to an inseparable mixture of four aldol adducts **19** in 84% combined yield, the ratio of which was determined to be 61:15:15:9 by 270 MHz ^{1}H NMR. The stereochemical assignment of the two isomers **19a** and **19b** will be presented later (vide infra). A similar result (84% yield, dr = 60:17:16:7) was obtained when HMPA was used as a co-solvent. However, under these conditions the reaction with **17** did not proceed beyond a 50% conversion. As a result, we were prompted to investigate the Lewis acid-promoted aldol reaction.

The enolate precursors **13** and **14** could be converted to the corresponding silyl ketene acetals by treatment with LiHMDS at –78 °C followed by the addition of TMSCl (Scheme 4). Although the hydrolysis-prone silyl ketene acetal derived from ester **13** could not be obtained in synthetically useful levels of purity in our hands, silyl ketene thioacetal **20** (*Z*:*E*=99:1), derived from thioester **14** in 95% yield, was more stable than the corresponding ester derivative,[26] and could be purified on Florisil. The stereochemistry of the major isomer was verified by ^{1}H NOE correlation (0.3%) between Si(CH_3)$_3$ and the methine proton in **20**. At the inception of this project, several literature reports appeared documenting the effectiveness of $TiCl_4$ and $Sn(OTf)_2$ as promoters in the Mukaiyama aldol addition to α-keto esters.[23b–g] While $TiCl_4$ had no effect on the reaction of α-keto ester **18** with silyl ketene thioacetal **20**, the use of $Sn(OTf)_2$ in EtCN, a combination developed for aldol reactions of pyruvates by Kobayashi and co-workers,[23e,g,27] resulted in a quantitative reaction, whereby a 1:2.6 mixture of two adducts **21a** and **21b** with the correct stereochemistry at C4 out of the four possible diastereomers was obtained. The absolute stereochemical relationship of each of the easily separable diastereomers was determined based on the C3 stereocenter, the configuration of which was secure. The treatment of each diastereomer with $Hg(OCOCF_3)_2$ in MeCN resulted in the formation of β-lactone,[28] thus affording **22a** and **22b**, respectively, in high yields. The ^{1}H NOE (4%) between C3-H and C6-H confirmed the relative stereochemical relationship between the quaternary stereocenters in **22b**, whereas the absence of an NOE between C3-H and C6-H in **22a** indicated an opposite relationship to that in **22b**. Methanolysis of β-lactones **22a** and **22b** afforded methyl

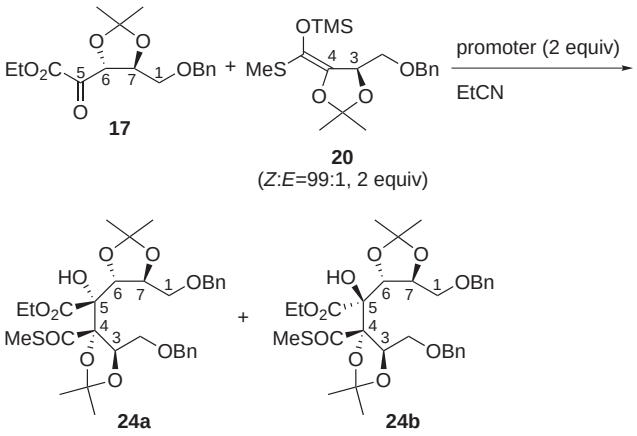


Scheme 4. *Reagents and conditions*: (a) LiHMDS, THF, –78 °C, 30 min, then TMSCl, –78 °C, 1 h, and rt, 15 min; (b) α-keto ester **18**, $Sn(OTf)_2$, EtCN, –78 °C, 30 min; (c) $Hg(OCOCF_3)_2$, MeCN; (d) K_2CO_3, MeOH; (e) H_2, 10% Pd/C, EtOH, 2 h; (f) DMAP, CH_2Cl_2, 1 h.

esters **19a** and **19b**, respectively. Debenzylation of **19a** and **19b** followed by treatment with DMAP effected the γ-lactone formation, insuring the relative stereochemical relationship between C3 and C4. This sequence of experiments established the stereochemistry of **21a**/**19a** and **21b**/**19b** as 4*S*,5*R* and 4*S*,5*S*, respectively. Despite the lack of carbonyl diastereofacial selectivity, it appeared attractive for the present coupling that the $Sn(OTf)_2$-promoted reaction occurred exclusively from the less hindered *si*-face of silyl ketene thioacetal **20** due to the steric demands of the benzyloxymethyl group, thus creating the proper configuration at C4. Following these results, this reaction was applied to the more functionalized substrate **17**.

Under the foregoing conditions, the aldol reaction between α-keto ester **17** and silyl ketene thioacetal **20** (*Z*:*E*=99:1) proceeded to completion within 1.5 h to give a 1:2.2 mixture of aldol adducts **24a** and **24b** in 90% combined yield (Table 1, entry 1). In an effort to reverse the stereochemical outcome of the aldol reaction to give the desired stereoisomer, alternate conditions were investigated. A survey of reaction solvents (EtCN, CH_2Cl_2, toluene, THF, Et_2O) revealed that EtCN was the only solvent that permitted the present coupling to proceed. Of the Lewis acids screened, $Sc(OTf)_3$, TiF_4 and $(^iPrO)_2TiCl_2$ also promoted the formation of aldol adducts (entries 2–4). Although the diastereoselectivity could be improved by employing $(^iPrO)_2TiCl_2$ as a promoter, a much reduced yield (55%) was obtained, even when 5 equivalents of **20** were used (entry 5). Kobayashi and co-workers demonstrated that the *syn*:*anti* stereoselectivity is controlled by the geometry of silyl ketene thioacetals in $Sn(OTf)_2$-promoted aldol additions to pyruvate esters.[23e,g,27] After considerable experimentation, it was found that the dropwise addition of KHMDS to the thioester **14** over a period of 2 h at –78 °C (inverse addition) followed by treatment with TMSCl furnished silyl ketene thioacetal **25** in 87% yield with virtually complete *E*-selectivity (*Z*:*E*=1:99, Scheme 5). Since the preferential formation of (*Z*)-silyl ketene thioacetal (*Z*:*E*=72:28) was observed with KHMDS at –78 °C by the internal quench method,[29] this outcome would be a consequence of thermodynamic control. Disappointingly, however, (*E*)-silyl ketene thioacetal **25** was found to be a less reactive nucleophile compared to the corresponding (*Z*)-isomer **20**, and the $Sn(OTf)_2$-promoted aldol reaction of **25** (*Z*:*E*=1:99) with α-keto ester **17** proceeded slowly at –55 °C to afford adducts in 36% yield with 1:10 stereoselectivity favoring the undesired diastereomer **24b**. These results definitely revealed the advantages of the (*Z*)-silyl ketene thioacetal over its (*E*) counterpart in terms of both yield and ratio of the desired product.

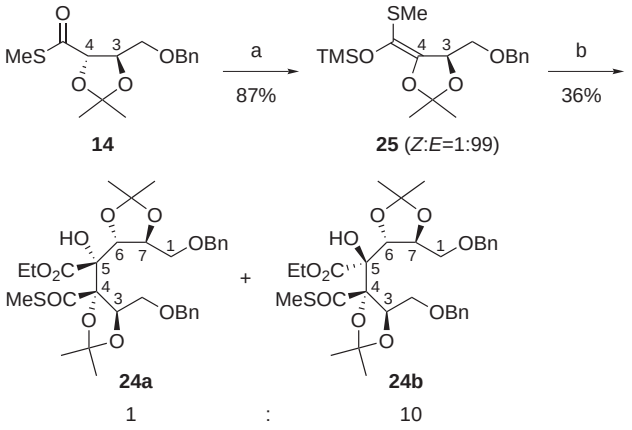
Table 1. Lewis acid-promoted aldol reaction of α-keto ester **17** with (*Z*)-silyl ketene thioacetal **20**.



Entry	Lewis acid	Temp, °C	Time, h	Yield, %	**24a**:**24b**[a]
1	$Sn(OTf)_2$	–70	1.5	90	1:2.2
2	$Sc(OTf)_3$	–45	0.5	31	1:5.3
3	TiF_4	–60	2	70	1:5
4	$(^iPrO)_2TiCl_2$	rt	12	30	1:1.5
5[b]	$(^iPrO)_2TiCl_2$	rt	12	55	1:1.5

[a]The ratio was determined by 270 MHz ^1H NMR analysis of the crude mixture.

[b]The reaction was performed using 5 equiv of silyl ketene thioacetal **20**.

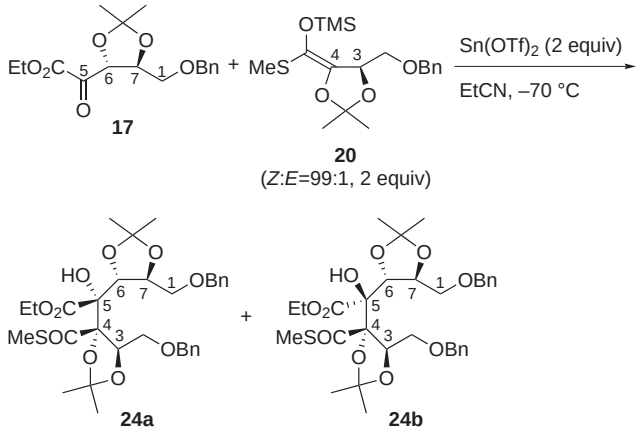


Scheme 5. *Reagents and conditions*: (a) KHMDS (inverse addition), THF, –78 °C, 2.5 h, then TMSCl, –78 °C, 30 min, and rt, 15 min; (b) α-keto ester **17**, $Sn(OTf)_2$, EtCN, –55 °C, 1 h.

These results suggest that $Sn(OTf)_2$ was the optimal Lewis acid and (*Z*)-silyl ketene thioacetal **20** was identified as a suitable coupling partner for this reaction. During the course of these studies, we found that when $Sn(OTf)_2$ was used as a promoter, the product ratio (**24a**:**24b**) changed as the reaction proceeded (Table 2). Although undesired isomer **24b** was exclusively formed during the initial 5-min period of the reaction (entry 1), a 1:2.2 mixture of adducts was obtained on completion of the reaction. Since the isomerization of **24b** to **24a** did not occur under these conditions, these observations suggest that multiple reaction pathways are involved in this coupling.

We next anticipated that the carbonyl π-facial selectivity might be reversed by the judicious choice of protecting groups imparted to each reaction partner. A number of thioesters and α-keto esters were prepared by routes analogous to that illustrated for **14** (Scheme 2) and **17** (Scheme 3), and evaluated as substrates for the $Sn(OTf)_2$-

Table 2. $Sn(OTf)_2$-promoted aldol coupling between α-keto ester **17** and silyl ketene thioacetal **20**.



17

20
(*Z*:*E*=99:1, 2 equiv)

24a **24b**

Entry	Time, min	Yield, %	**24a**:**24b**[a]
1	5	28	0:1
2	15	75	1:3.2
3	90	90	1:2.2

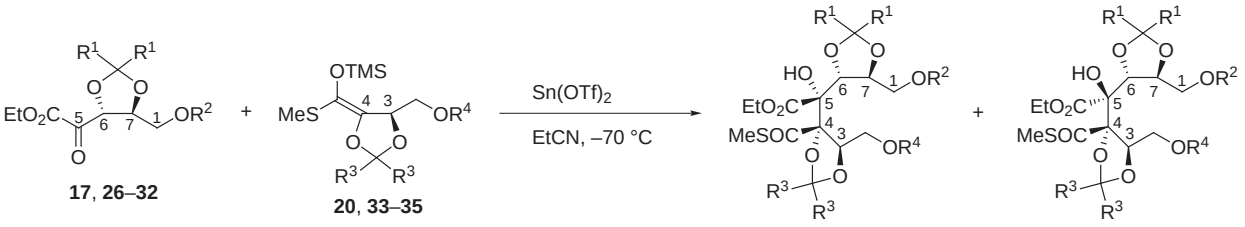
[a]The ratio was determined by 270 MHz ^{1}H NMR analysis of the crude mixture.

promoted aldol reaction. The results of the aldol reactions are shown in Table 3.

While the acetal moiety in the α-keto esters had a little influence on the carbonyl facial selectivity, the ratio of the desired product to the undesired C5 epimer increased slightly when the pentylidene acetal **27** was used (entries 3 vs 1, 2 and 4). With regard to acetal protection in silyl ketene thioacetals, an exceptionally high order of selectivity for the undesired C5 epimer was obtained in the case of methylene acetal **33**, with little variation being observed between isopropylidene and pentylidene acetals **20** and **34** (entries 5 vs 3 and 6). Switching protection of the primary alcohol in **20** or **27** from a benzyl ether to a *tert*-butyldiphenylsilyl ether led to the predominant formation of the undesired isomers **41b** and **42b** (entries 3 vs 7 and 8), suggesting that the chelating ability of the oxygen atoms might be responsible for the desired π-facial selectivity. Of the substituted methyl ethers surveyed for R^2 (entries 9–11), MEM ether proved to be the protecting group of choice for the primary alcohol at C1, providing a mixture of aldol adducts **45a** and **45b** in a ratio of 1.6:1 (entry 11).

The stereochemical outcome of each reaction was inferred on the basis of the chemical transformations and NOE data analogous to that illustrated in Scheme 4. For example, isomers **37a** and **37b** were converted to β-lactones **46a** and **46b**, respectively, and the NOE experiments indicated unequivocally relative stereochemical relationships between the quaternary stereocenters for both isomers (Scheme 6). The fact that the methanolysis of β-lactones **46a** and **46b** followed by debenzylation and treatment with DMAP gave γ-lactones **47a** and **47b**, respectively, confirmed a 4*S* configuration. As the work progressed and

Table 3. $Sn(OTf)_2$-promoted aldol coupling between an α-keto ester and a silyl ketene thioacetal.



17, **26**–**32**

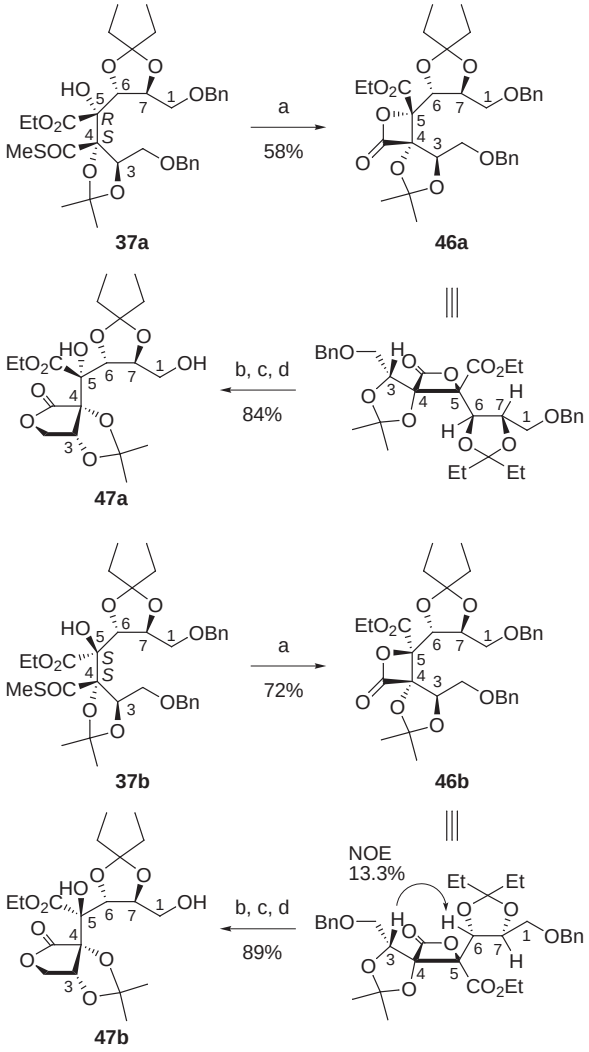
20, **33**–**35**

24a, **36a**–**45a**

24b, **36b**–**45b**

	α-Keto ester			Silyl ketene thioacetal			Aldol adducts		
Entry		R^1	R^2		R^3	R^4		Yield, %	desired:undesired[a]
1	**17**	Me	Bn	**20**	Me	Bn	**24**	90	1:2.2
2	**26**	H	Bn	**20**	Me	Bn	**36**	49	1:2.6
3	**27**	Et	Bn	**20**	Me	Bn	**37**	79	1:1.1
4	**28**	^{n}Pr	Bn	**20**	Me	Bn	**38**	82	1:1.6
5	**27**	Et	Bn	**33**	H	Bn	**39**	67	1:>20
6	**27**	Et	Bn	**34**	Et	Bn	**40**	67	1:1.9
7	**27**	Et	Bn	**35**	Me	TBDPS	**41**	65	1:>20
8	**29**	Et	TBDPS	**20**	Me	Bn	**42**	45	1:5
9	**30**	Et	MOM	**20**	Me	Bn	**43**	79	1.1:1
10	**31**	Et	BOM	**20**	Me	Bn	**44**	90	1:1.6
11	**32**	Et	MEM	**20**	Me	Bn	**45**	83	1.6:1

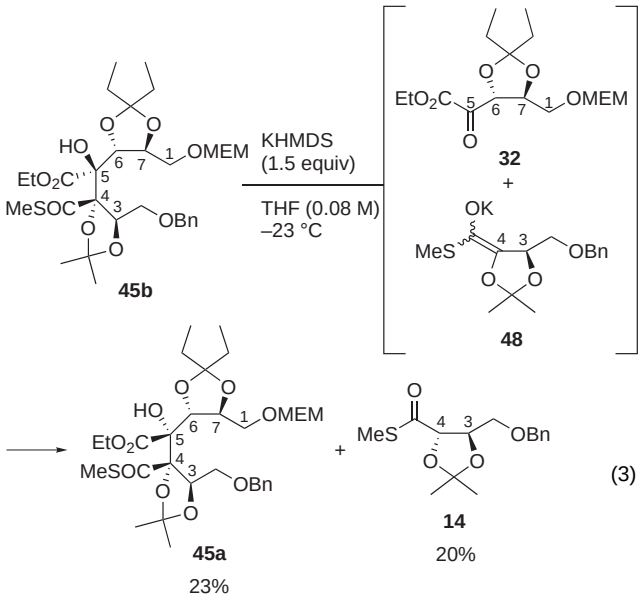
[a]The ratio was determined by 270 MHz ^{1}H NMR analysis of the crude mixture.



Scheme 6. *Reagents and conditions*: (a) $Hg(OCOCF_3)_2$, MeCN, 200 h (for **37a**) or 10 h (for **37b**); (b) K_2CO_3, MeOH, 1.5 h; (c) H_2, 10% Pd/C, MeOH, 1 h; (d) DMAP, MeCN, 1.5 h.

we acquired a library of spectral data, we also noticed that these isomers were readily distinguishable by the ^{1}H NMR signals for the *S*-methyl protons, which were always 0.04–0.1 ppm downfield in the desired product relative to its C5 epimer. It is also noteworthy that the cyclization of undesired isomer **37b** proceeded to completion within 10 h, while extended reaction times (200 h) were required for the complete conversion of **37a** to **46a** under the same reaction conditions.

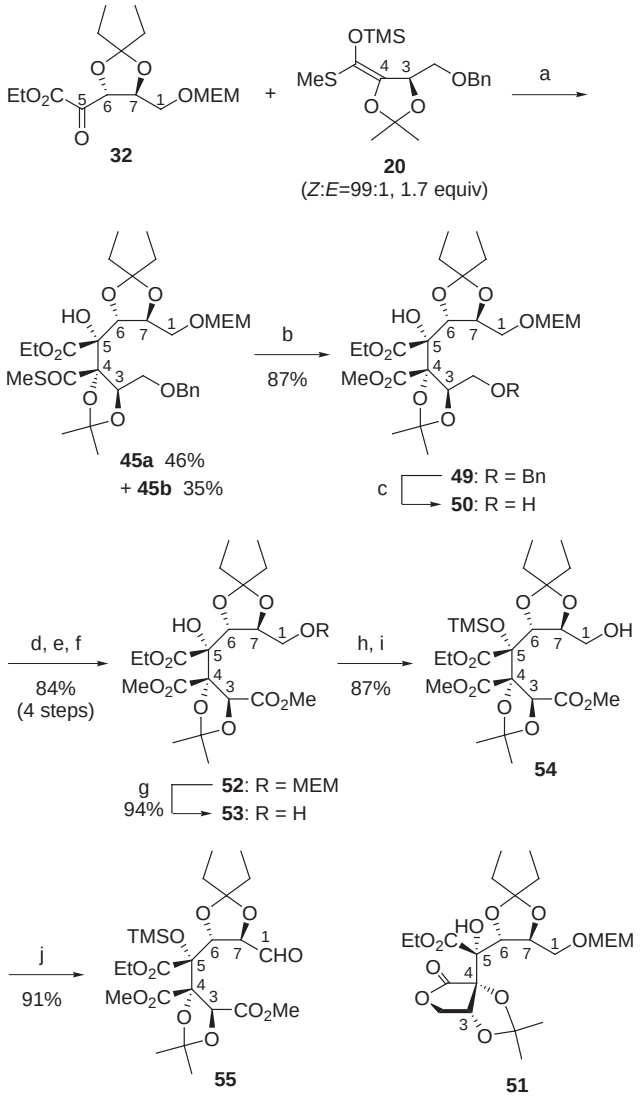
Ironically, the undesired diastereomers **39b** and **41b** were exclusively formed by the proper choice of the protecting groups for each reaction partner; however, it was quite difficult to obtain the desired isomer predominantly by this aldol coupling.[30] Our attention was then directed to recycling the undesired isomer back to the starting α-keto ester and thioester. After considerable experimentation, we found that the treatment of **45b** with KHMDS in THF at temperatures above –23 °C effected a retro-aldol reaction. Surprisingly, when the reaction was performed at substrate concentrations of more than 0.08 M, the undesired isomer **45b** was completely consumed within 2 h and the desired isomer **45a** was formed in 23% yield, along with 20% of thioester **14** (Eq. 3). It is clear that the observed isomeriza-



tion of **45b** to **45a** is the result of an aldol reaction between α-keto ester **32** and potassium enolate **48**, produced by the retro-aldol reaction of **45b**, and that the desired isomer **45a** is thermodynamically more stable than **45b**.[32] The low yield can be attributed to the lability of **32** to base. Despite the low yields of the products, this equilibration/recycling process permitted the undesired isomer **45b** to be productively utilized and therefore enhanced the overall synthetic efficiency.

2.4. Synthesis of internal ketalization precursor

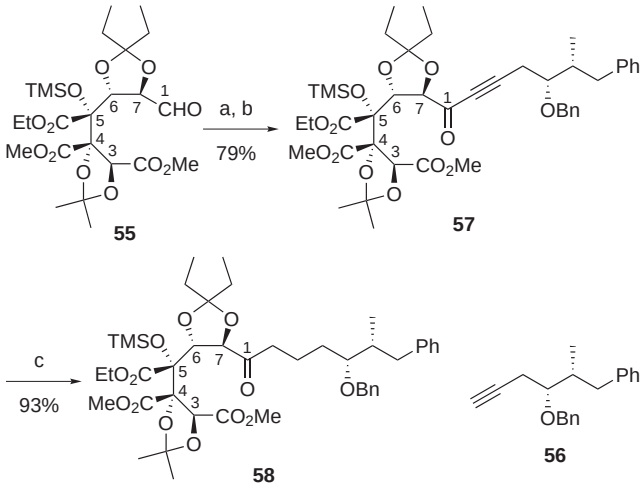
Having accomplished the simultaneous creation of the consecutive quaternary stereogenic centers by a $Sn(OTf)_2$-promoted aldol coupling between an α-keto ester and a silyl ketene thioacetal, we then proceeded to the elaboration of the internal ketalization precursor. The aldol coupling of α-keto ester **32**[33] with 1.7 equiv of silyl ketene thioacetal **20** on a multigram scale proceeded in 81% yield, albeit with a slightly diminished selectivity (**45a**:**45b**=1.3:1, Scheme 7). After separation of the C5 epimer **45b**, thioester **45a** was converted to methyl ester **49** in 87% yield by treatment with $Hg(OCOCF_3)_2$ in refluxing MeOH.[28] Although the hydrogenolysis of **49** over 10% Pd/C in MeOH gave the corresponding alcohol **50**, we found these conditions to be capricious due to the formation of γ-lactone **51** as a byproduct. This side reaction could be minimized by the use of 20% $Pd(OH)_2$/C in AcOEt. The lactonization-prone alcohol **50** was then converted into a carboxylic acid by two successive oxidations (Dess–Martin periodinane;[35] $NaClO_2$), which was subjected to CH_2N_2 to provide triester **52** in 84% overall yield without intervening purification. It should be noted that the application of the



Scheme 7. *Reagents and conditions*: (a) $Sn(OTf)_2$, EtCN, –70 °C, 1.5 h; (b) $Hg(OCOCF_3)_2$, MeOH, reflux, 10 h; (c) H_2, 20% $Pd(OH)_2$/C, AcOEt, 10 h; (d) Dess–Martin periodinane, CH_2Cl_2, 8 h; (e) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, $^tBuOH–H_2O$ (10:3), 2.5 h; (f) CH_2N_2, Et_2O, 0 °C, 10 min; (g) TMSCl, NaI, MeCN, –23 °C, 2 h; (h) MeN(TMS)$COCF_3$, 90 °C, 3 h; (i) 10% aqueous HCl, Et_2O, 1.5 h; (j) Dess–Martin periodinane, CH_2Cl_2, 3.5 h.

standard Swern protocol[36] in place of the Dess–Martin procedure resulted in the significant epimerization at C3. The selective removal of the MEM ether was effected with TMSCl/NaI in MeCN at –23 °C,[37] affording diol **53** in 94% yield. At this juncture, the C5 tertiary alcohol was protected as its TMS ether via a two-step bissilylation–monodesilylation sequence[9b,d] to give alcohol **54** in 87% yield, which, upon treatment with Dess–Martin periodinane, furnished aldehyde **55** in 91% yield.

To install the C1 alkyl side chain, initial attempts to employ Grignard reagent **7** (M=MgBr) resulted in a low yield. We then elected to use alkyne **56**[38] as a C1 alkyl side chain equivalent (Scheme 8). As anticipated, the installation of the C1 alkyl side chain was uneventfully achieved by the

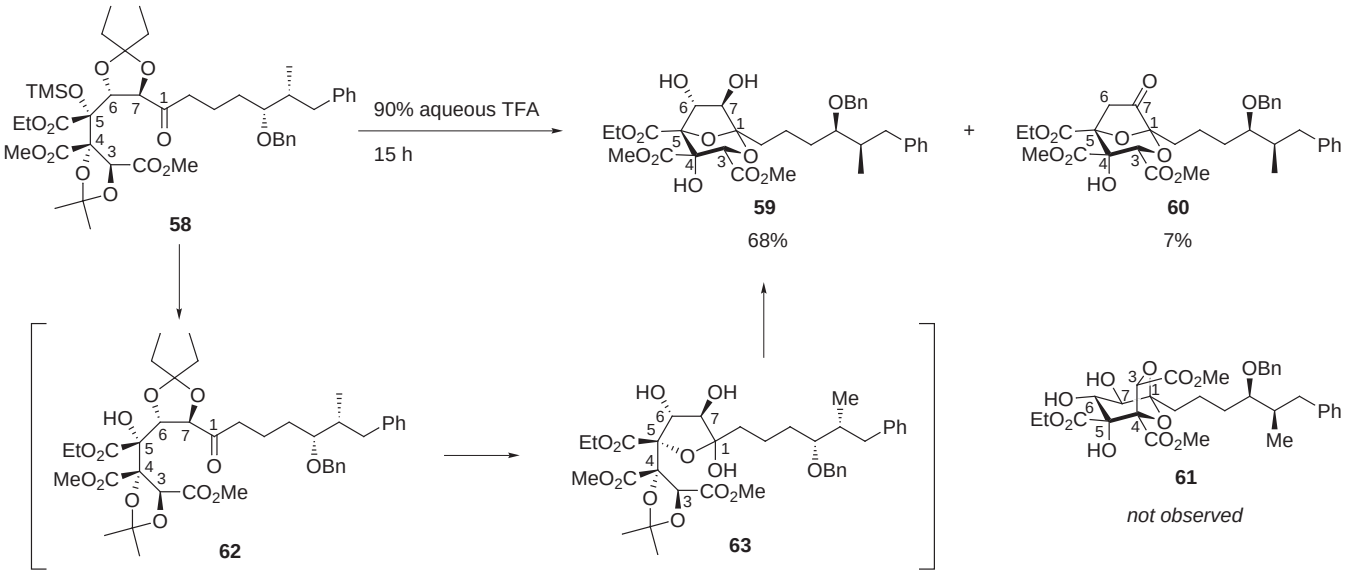


Scheme 8. *Reagents and conditions*: (a) alkyne **56**, BuLi, THF, –78 °C, 45 min, then aldehyde **55**, 30 min; (b) Dess–Martin periodinane, CH_2Cl_2, 11 h; (c) H_2, 10% Pd/C, AcOEt, 10 min.

addition of the lithium acetylide, generated from alkyne **56**, to aldehyde **55**, providing a diastereomeric mixture of coupling products, which, upon treatment with Dess–Martin periodinane, furnished ynone **57** in 79% yield in two steps. Finally, catalytic hydrogenation of the triple bond gave the internal ketalization precursor **58** in 93% yield.

2.5. Internal ketalization

With a viable route to ketone **58** secured, the stage was now set for the crucial internal ketalization. Exposure of **58** to 90% aqueous TFA resulted in the removal of protecting groups and concomitant ketalization, affording bicycloketal **59** in 68% yield (Scheme 9). While the formation of the 6,8-dioxabicyclo[3.2.1]octane isomer **61** was not observed, a minor byproduct **60** arising from dehydration of the C6 hydroxyl group was isolated.[39] When the reaction was quenched after a 10-min period, alcohol **62** and hemiketal **63** were obtained as intermediates in 53% and 29% yields, respectively. Monitoring the internal ketalization by TLC analysis showed that desilylation occurred immediately, forming hydroxyketone **62**, from which the pentylidene ketal was subsequently removed to give the five-membered hemiketal **63** through closure of the C5 hydroxyl group onto the C1 carbonyl. The steric congestion around the acetonide required 15 h for its hydrolytic removal to reach completion, and then the desired bicycloketal **59** was formed as a single stereoisomer. These observations suggest that the selectivity in the internal ketalization process is mainly due to the differential rates of hydrolysis of the protecting groups. Independent of our study, a similar conclusion was reached by Armstrong and co-workers in their total synthesis of zaragozic acid C.[11] The ratio of TFA/H_2O in this reaction is not arbitrary: extended reaction times (48 h) were required for complete conversion with 80% aqueous TFA, lowering the product yield due to the formation of a debenzylated byproduct.



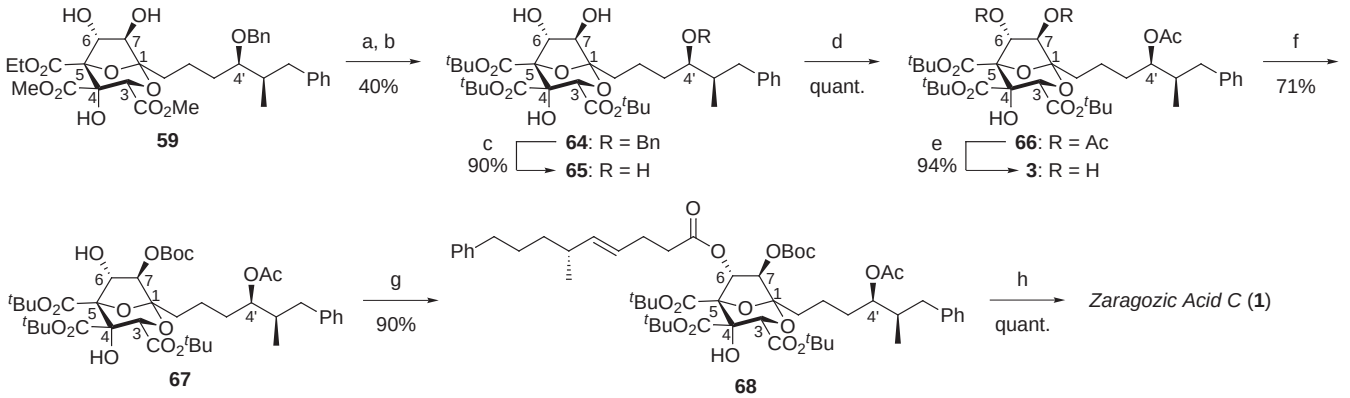
Scheme 9. Internal ketalization

2.6. Completion of the total synthesis

To avoid concomitant hydrolytic cleavage of the C6 acyl side chain at the end of the synthesis, the triesters present in **59** should be hydrolyzed and converted to the corresponding tri(*tert*-butyl) ester at this stage. Although the C4 methyl ester proved to be extremely resistant to hydrolysis, the reaction of **59** with 1N aqueous KOH in dioxane at 100 °C furnished the triacid which, upon treatment with *N,N'*-diisopropyl-*O*-*tert*-butylisourea,[40] gave tri(*tert*-butyl ester) **64** in 40% yield in two steps (Scheme 10). Hydrogenolysis of the C4' benzyl ether provided tetraol **65** in 90% yield, which was acetylated to give triacetate **66** in quantitative yield. The route to **66** constitutes a formal synthesis of zaragozic acid C (**1**) since it intersects the same intermediate employed by Carreira and Du Bois.[8] However, the specific rotation of compound **66** [$[\alpha]_D^{21}$ +17.6° (*c* 0.91, CH_2Cl_2)] was not in agreement with the reported value [$[\alpha]_D$ +69.9° (*c* 0.29, CH_2Cl_2)].[8b] Following the procedure developed by Carreira,[8b] selective removal of the C6 and C7 acetyl groups by treatment with 0.2% K_2CO_3 in MeOH, selective protection of the C7 hydroxyl group by $(Boc)_2O$, esterification with acid **2**,[1f] and global deprotection with TFA gave zaragozic acid C (**1**) in 60% overall yield. The synthetic material **1**, $[\alpha]_D^{23}$ +9.4° (*c* 0.30, EtOH) [lit.,[1b] $[\alpha]_D^{20}$ +9.6° (*c* 0.29, EtOH)], was obtained as a white film and relevant spectroscopic data were identical with those reported for natural zaragozic acid C (IR, ^{1}H NMR, ^{13}C NMR, HRMS).

3. Conclusion

The total synthesis of zaragozic acid C was completed in 30 steps for the longest linear sequence from diethyl L-tartrate and 1.4% overall yield. Although our synthesis incurs a stereochemical problem at C5 in the key fragment assembly aldol process, we found that the contiguous quaternary stereocenters at C4 and C5 could be formed simultaneously in a single operation by a $Sn(OTf)_2$-promoted aldol reaction



Scheme 10. *Reagents and conditions*: (a) 1N aqueous KOH, dioxane, 100 °C, 24 h; (b) ^{i}PrN=C(O^{t}Bu)NH^{i}Pr, CH_2Cl_2, 24 h; (c) H_2, 10% Pd/C, MeOH, 17 h; (d) Ac_2O, DMAP, CH_2Cl_2, 0 °C, 30 min; (e) 0.2% K_2CO_3 in MeOH, 1 h; (f) $(Boc)_2O$, 4-pyrrolidinopyridine, Et_3N, CH_2Cl_2, 0 °C, 12 h; (g) carboxylic acid **2**, DCC, DMAP, CH_2Cl_2, 48 h; (h) TFA, CH_2Cl_2, 16 h.

between an α-keto ester and a silyl ketene thioacetal. We also demonstrate that the selectivity in the internal ketalization process was mainly due to the differential rates of hydrolysis of the protecting groups.

4. Experimental

4.1. General

Melting points were determined on a Büchi 535 digital melting point apparatus and were uncorrected. Optical rotations were recorded on JASCO DIP-370 or P-1030 digital polarimeters. Infrared (IR) spectra were recorded on a JASCO FT/IR-5300 spectrophotometer and absorbance bands are reported in wavenumber (cm^{-1}). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on JEOL EX-270 (270 MHz), JEOL EX-400 (400 MHz) or Bruker ARX500 (500 MHz) spectrometers with tetramethylsilane (δ_H 0.00) as an internal standard. Coupling constants (*J*) are reported in hertz (Hz). Abbreviations of multiplicity are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Data are presented as follows: chemical shift, multiplicity, coupling constants, integration and assignment. Zaragozic acid numbering is used for proton assignments of all intermediates. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on JEOL EX-270 (67.8 MHz), JEOL EX-400 (100.6 MHz) or Bruker ARX500 (125.8 MHz) spectrometers with $CDCl_3$ (δ_C 77.0) as an internal standard. Fast atom bombardment (FAB) mass spectra were recorded on a JEOL JMS-HX110 spectrometer.

Column chromatography was carried out on Merck Kieselgel 60 (63–200 μm or 40–63 μm), Fuji Davison silica gel BW-200 (40–50 μm) or Wakogel C-200 (75–150 μm). Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F_{254} plates. Visualization was accomplished with ultraviolet light and anisaldehyde or phosphomolybdic acid stain, followed by heating.

Reagents and solvents were purified by standard means or used as received unless otherwise noted. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium metal/benzophenone ketyl prior to use. Dichloromethane (CH_2Cl_2), propionitrile (EtCN), acetonitrile (MeCN) and diisopropylamine ($^iPr_2NH$) were distilled from calcium hydride prior to use. Dimethyl sulfoxide (DMSO) was distilled under reduced pressure from calcium hydride.

All reactions were conducted under an argon atmosphere. Ethyl 2-oxo-5-phenylpentanoate,[25] diisopropoxytitanium (IV) dichloride [(^{i}PrO)$_2$TiCl$_2$],[41] Dess–Martin periodinane[42] (4*R*,5*R*)-4-benzyloxy-5-methyl-6-phenyl-1-hexyne (**56**),[38] *N*,*N*'-diisopropyl-*O*-*tert*-butylisourea[40] and (4*E*,6*R*)-6-methyl-9-phenyl-4-nonenoic acid (**2**)[1f] were prepared according to literature procedures.

4.2. Preparation of substrates for the aldol coupling

4.2.1. (2*S*,3*R*)-4-Benzyloxy-2,3-(dimethylmethylenedioxy)butyric acid [(+)-12]. A solution of NaH_2PO_4 (5.8 g, 48.0 mmol) in water (80 mL) was added to a solution of (2*S*,3*R*)-4-benzyloxy-2,3-(dimethylmethylenedioxy)butanal (**11**)[20] (12.0 g, 48.0 mmol) and 2-methyl-2-butene (21 mL, 199 mmol) in *tert*-butyl alcohol (250 mL). $NaClO_2$ (14.8 g, 164 mmol) was added portionwise to the mixture. After stirring at room temperature for 18 h, the mixture was evaporated in vacuo. The residue was dissolved in saturated aqueous $NaHCO_3$ (50 mL) and water (100 mL) and the whole was washed with *n*-hexane (3×30 mL). The aqueous layer was acidified with 10% aqueous HCl (40 mL), saturated with NaCl, and then extracted with AcOEt (3×100 mL). The combined organic extracts were washed with brine (50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 100 g, AcOEt) afforded carboxylic acid (+)-**12** (12.1 g, 95%) as a pale yellow oil: $[\alpha]_D^{24}$ +13.7° (*c* 1.19, $CHCl_3$); IR (film) 3700–2300, 2990, 1734, 1454, 1383, 1215, 1101, 852, 752, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 3H, acetonide C*H*$_3$), 1.42 (s, 3H, acetonide C*H*$_3$), 3.63 (dd, *J* = 5.2, 10.7 Hz, 1H, C*H*OBn), 3.71 (dd, *J* = 3.2, 10.7 Hz, 1H, C*H*OBn), 4.29 (ddd, *J* = 3.2, 5.2, 7.7 Hz, 1H, C3-*H*), 4.36 (d, *J* = 7.7 Hz, 1H, C4-*H*), 4.54 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.57 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 7.17–7.30 (m, 5H, Ar*H*), 9.51 (br s, 1H, CO_2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 25.6 (CH_3), 26.8 (CH_3), 69.6 (CH_2), 73.7 (CH_2), 75.3 (CH), 78.2 (CH), 111.9 (C), 127.7 (CH), 127.8 (CH), 128.4 (CH), 137.6 (C), 174.9 (C=O); FAB-HRMS *m*/*z* calcd for $C_{14}H_{19}O_5$ $(M+H)^+$ 267.1233, found 267.1240.

4.2.2. Methyl (2*S*,3*R*)-4-benzyloxy-2,3-(dimethylmethylenedioxy)butyrate (13). A solution of diazomethane in Et_2O was added to a solution of carboxylic acid (+)-**12** (4.32 g, 16.2 mmol) in Et_2O (30 mL) at 0 °C until a yellow color persisted. After stirring at 0 °C for 30 min and then room temperature for 30 min, the reaction was quenched with AcOH. The resulting mixture was washed successively with water (10 mL), saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 100 g, 6:1 *n*-hexane/AcOEt) afforded methyl ester **13** (3.55 g, 78%) as a pale yellow oil: $[\alpha]_D^{21}$ +19.0° (*c* 1.30, $CHCl_3$); IR (film) 2992, 2938, 1761, 1454, 1381, 1208, 1107, 1024, 853, 740, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 3H, acetonide C*H*$_3$), 1.49 (s, 3H, acetonide C*H*$_3$), 3.68 (dd, *J* = 5.3, 10.7 Hz, 1H, C*H*OBn), 3.75 (dd, *J* = 3.2, 10.7 Hz, 1H, C*H*OBn), 3.76 (s, 3H, CO_2CH_3), 4.35 (ddd, *J* = 3.2, 5.3, 7.6 Hz, 1H, C3-*H*), 4.40 (d, *J* = 7.6 Hz, 1H, C4-*H*), 4.61 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.63 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 7.25–7.37 (m, 5H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 25.7 (CH_3), 26.9 (CH_3), 52.3 (CH_3), 69.8 (CH_2), 73.6 (CH_2), 75.7 (CH), 78.4 (CH), 111.6 (C), 127.6 (CH), 127.7 (CH), 128.4 (CH), 137.9 (C), 171.0 (C=O); FAB-HRMS *m*/*z* calcd for $C_{15}H_{21}O_5$ $(M+H)^+$ 281.1389, found 281.1411.

4.2.3. *S*-Methyl (2*S*,3*R*)-4-benzyloxy-2,3-(dimethylmethylenedioxy)butanethioate (14). Oxalyl chloride (1.8 mL, 20.6 mmol) and DMF (0.1 mL, 1.3 mmol) were added to a

solution of carboxylic acid (+)-**12** (4.75 g, 17.8 mmol) in CH_2Cl_2 (50 mL). The mixture was stirred at room temperature for 1.5 h and evaporated in vacuo. The residual oil was dissolved in CH_2Cl_2 (50 mL), and *n*-Bu_4NI (76 mg, 0.2 mmol) and a 20% aqueous solution of MeSNa (7.5 mL, 21.4 mmol) were added at 0 °C. After stirring vigorously at 0 °C for 10 min, the mixture was partitioned between CH_2Cl_2 (50 mL) and water (50 mL). The organic extract was washed successively with water (30 mL) and brine (30 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 100 g, 20:1 *n*-hexane/AcOEt) afforded thioester **14** (4.04 g, 77%) as a pale yellow oil: $[\alpha]_D^{25}$ –8.95° (*c* 1.2, $CHCl_3$); IR (film) 2990, 2930, 1676 (C=O), 1454, 1381, 1215, 1090, 852, 739, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 6H, 2×acetonide C*H*$_3$), 2.28 (s, 3H, SC*H*$_3$), 3.66 (dd, *J* = 5.7, 10.8 Hz, 1H, C*H*OBn), 3.81 (dd, *J* = 2.5, 10.8 Hz, 1H, C*H*OBn), 4.24 (ddd, *J* = 2.5, 5.7, 8.0 Hz, 1H, C3-*H*), 4.35 (d, *J* = 8.0 Hz, 1H, C4-*H*), 4.62 (s, 2H, OC*H*$_2$Ph), 7.25–7.38 (m, 5H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 10.8 (CH_3), 26.0 (CH_3), 27.1 (CH_3), 69.7 (CH_2), 73.6 (CH_2), 78.8 (CH), 81.6 (CH), 112.1 (C), 127.7 (CH), 128.4 (CH), 137.8 (CH), 201.4 (C=O); FAB-HRMS *m*/*z* calcd for $C_{15}H_{21}O_4S$ $(M+H)^+$ 297.1161, found 297.1152; Anal. calcd for $C_{15}H_{21}O_4S$: C, 60.79; H, 6.80; S, 10.82, found: C, 60.63; H, 6.78; S, 11.07.

4.2.4. (2*R*,3*S*)-4-Benzyloxy-2,3-(dimethylmethylenedioxy)-*N*-methoxy-*N*-methylbutanamide (15). Oxalyl chloride (6 mL, 69 mmol) and DMF (0.3 mL, 3.9 mmol) were added to a solution of carboxylic acid (–)-**12** (15.20 g, 57.1 mmol) in CH_2Cl_2 (170 mL). The mixture was stirred at room temperature for 30 min and evaporated in vacuo. The residual oil was dissolved in CH_2Cl_2 (170 mL), and *N*,*O*-dimethylhydroxylamine hydrochloride (6.1 g, 62.5 mmol) and pyridine (12 mL, 148 mmol) were added at 0 °C. After stirring at 0 °C for 1 h, the reaction was quenched with 1N aqueous HCl (100 mL), and the layers were separated. The organic layer was washed successively with 1N aqueous HCl (2×100 mL), saturated aqueous $NaHCO_3$ (80 mL) and brine (80 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 150 g, 3:1→2:1 *n*-hexane/AcOEt) afforded amide **15** (16.28 g, 92%) as a colorless oil: $[\alpha]_D^{25}$ +3.97° (*c* 2.03, $CHCl_3$); IR (film) 2988, 2938, 1780, 1669, 1454, 1381, 1256, 1165, 1092, 997, 910, 855 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 3H, acetonide C*H*$_3$), 1.49 (s, 3H, acetonide C*H*$_3$), 3.20 (s, 3H, NC*H*$_3$), 3.63–3.71 (m, 2H, C1-*H*$_2$), 3.76 (s, 3H, OC*H*$_3$), 4.59 (m, 1H, C7-*H*), 4.60 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.71 (br s, 1H, C6-*H*), 7.25–7.33 (m, 5H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 26.1 (CH_3), 26.7 (CH_3), 32.3 (CH_3), 61.5 (CH_3), 69.8 (CH_2), 73.4 (CH_2), 74.1 (CH), 77.7 (CH), 111.2 (C), 127.6 (CH), 127.8 (CH), 138.0 (CH), 170.3 (C=O); FAB-HRMS *m*/*z* calcd for $C_{16}H_{23}NO_5$ $(M)^+$ 309.1576, found 309.1575.

4.2.5. (4*R*,5*S*)-6-Benzyloxy-4,5-(dimethylmethylenedioxy)-2-ethoxy-1-hexen-3-one (16). *tert*-Butyllithium in pentane (2.13 M, 1.95 mL, 4.15 mmol) was added to a stirred solution of ethyl vinyl ether (0.4 mL, 4.18 mmol) in THF (4 mL) at –78 °C. After stirring at 0 °C for 30 min, the mixture was cooled to –78 °C and a solution of amide **15** (437 mg, 1.41 mmol) in THF (1 mL) was added. After stirring at –78 °C for 3 h, the reaction mixture was poured into a well-stirred mixture of saturated aqueous NH_4Cl (20 mL) and Et_2O (10 mL) at 0 °C. The layers were separated, and the organic layer was washed with brine (8 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 10 g, 10:1→7:1 *n*-hexane/AcOEt) afforded enone **16** (386 mg, 85%) as a colorless oil: $[\alpha]_D^{25}$ –49.9° (*c* 2.03, $CHCl_3$); IR (film) 2986, 2936, 1723, 1610, 1454, 1379, 1285, 1215, 1117, 1092, 976, 853 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.18 (t, *J* = 7.0 Hz, 3H, OCH_2CH_3), 1.43 (s, 3H, acetonide C*H*$_3$), 1.51 (s, 3H, acetonide C*H*$_3$), 3.66 (dd, *J* = 6.0, 10.5 Hz, 1H, C1-*H*), 3.75 (dd, *J* = 3.1, 10.5 Hz, 1H, C1-*H*), 3.76 (q, *J* = 7.0 Hz, 2H, OCH_2CH_3), 4.40 (ddd, *J* = 3.1, 6.0, 6.5 Hz, 1H, C7-*H*), 4.53 (d, *J* = 2.7 Hz, 1H, C*H*=C), 4.60 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.64 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.92 (d, *J* = 6.5 Hz, 1H, C6-*H*), 5.31 (d, *J* = 2.7 Hz, 1H, C*H*=C), 7.26–7.34 (m, 5H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3 (CH_3), 26.7 (CH_3), 27.7 (CH_3), 64.1 (CH_3), 70.8 (CH_2), 73.8 (CH_2), 78.2 (CH), 79.1 (CH), 93.7 (CH), 112.1 (C), 127.9 (CH), 128.6 (CH), 138.2 (CH), 156.6 (CH_2), 194.2 (C=O); FAB-LRMS *m*/*z* 309 $(M–CH_2+H)^+$, 277 $(M–OEt+H)^+$.

4.2.6. Ethyl (3*R*,4*S*)-5-benzyloxy-3,4-(dimethylmethylenedioxy)-2-oxopentanoate (17). A stream of ozone in oxygen was bubbled through a stirred solution of enone **16** (386 mg, 1.21 mmol) in CH_2Cl_2 (7 mL) at –78 °C until the solution turned pale blue. After stirring at –78 °C for 10 min, excess ozone was removed by bubbling a stream of nitrogen, and Me_2S (1 mL) was added. After stirring at room temperature for 1 h, the volatile elements were removed in vacuo. The residue (548 mg) was purified by column chromatography (silica gel 10 g, 4:1→5:2 *n*-hexane/AcOEt) to give α-keto ester **17** (371 mg, 96%) as a colorless oil: $[\alpha]_D^{22}$ –5.39° (*c* 1.6, $CHCl_3$); IR (film) 3449, 2990, 1730, 1454, 1373, 1254, 1217, 1094, 1042, 853, 741, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.40 (s, 3H, acetonide C*H*$_3$), 1.50 (s, 3H, acetonide C*H*$_3$), 3.71 (dd, *J* = 5.3, 10.5 Hz, 1H, C*H*OBn), 3.75 (dd, *J* = 4.2, 10.5 Hz, 1H, C*H*OBn), 4.23–4.36 (m, 2H, $CO_2CH_2CH_3$), 4.43 (ddd, *J* = 4.2, 5.3, 7.0 Hz, 1H, C7-*H*), 4.61 (s, 2H, OC*H*$_2$Ph), 4.85 (d, *J* = 7.0 Hz, 1H, C6-*H*), 7.25–7.38 (m, 5H, Ar*H*); FAB-HRMS *m*/*z* calcd for $C_{17}H_{23}O_6$ $(M+H)^+$ 323.1495, found 323.1508.

Since the tartrate-derived α-keto esters were prone to hydration, they were azeotropically dried with benzene prior to use.

4.3. Aldol reaction

4.3.1. Reaction of α-keto ester 18 with lithium enolate generated from ester 13. Butyllithium in *n*-hexane (1.60 M, 0.35 mL, 0.56 mmol) was added to a solution of ^{i}Pr$_2$NH (0.08 mL, 0.61 mmol) in THF (1.5 mL) at –5 °C. After stirring at –5 °C for 20 min, the solution was cooled to –78 °C, and a solution of ester **13** (129 mg, 0.46 mmol) in

THF (0.6 mL) was added dropwise over 10 min. After stirring at –78 °C for 1 h, a solution of α-keto ester **18** (51 mg, 0.23 mmol) in THF (0.3 mL) was added to the mixture at –78 °C. After stirring at –78 °C for 10 min, the mixture was quenched with saturated aqueous NH_4Cl (3 mL), and the whole was extracted with AcOEt (15 mL). The organic extract was washed with brine (2×5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (168 mg), which was purified by flash column chromatography (silica gel 5 g, 10:1→3:1 *n*-hexane/AcOEt) to give an inseparable mixture of aldol adducts **19** (96 mg, 84%) as a colorless oil. The ratio of the adducts was determined to be 61:15:15:9 by 270 MHz ^{1}H NMR: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.10–1.60 (m, 10H, $CO_2CH_2CH_3$, 2×acetonide CH_3, one of CH_2), 1.70–1.95 (m, 2H, CH_2), 1.95–2.15 (m, 1H, one of CH_2), 2.46–2.71 (m, 2H, PhCH_2), 3.35–3.53 (m, 1H, BnOC*H*), 3.65 (s, 1.83H, OCH_3), 3.67 (s, 0.45H, OCH_3), 3.74 (s, 0.27H, OCH_3), 3.75 (s, 0.45H, OCH_3), 3.82–4.32 (m, 4H, BnOC*H*, $CO_2CH_2CH_3$, O*H*), 4.40–4.75 (m, 3H, C3-*H*, PhCH_2O), 7.25–7.38 (m, 10H, Ar*H*).

4.3.2. (*R*,*Z*)-4-(Benzyloxy)methyl-5-[methylthio(trimethylsilyloxy)methylene]-2,2-dimethyl-1,3-dioxolane (20). Butyllithium in *n*-hexane (1.61 M, 12.7 mL, 20.4 mmol) was added to a stirred solution of 1,1,1,3,3,3-hexamethyldisilazane (4.5 mL, 21.3 mmol) in THF (80 mL) at –5 °C. After stirring at –5 °C for 30 min, the solution was cooled to –78 °C, and a solution of thioester **14** (5.51 g, 18.6 mmol) in THF (15 mL) was added. After stirring at –78 °C for 30 min, TMSCl (2.7 mL, 21.3 mmol) was added, and the resulting mixture was stirred at –78 °C for 1 h. The mixture was allowed to warm to room temperature. After stirring at room temperature for 15 min, the volatile elements were removed in vacuo. The residue was suspended in *n*-hexane and passed through a short plug of Florisil (eluting with AcOEt) to give silyl ketene thioacetal **20** (6.71 g, 95%, *Z*:*E*=99:1) as a yellow oil: $[\alpha]_D^{26}$ +148.7° (*c* 1.16, benzene); IR (film) 2990, 2957, 2865, 1740, 1680, 1454, 1373, 1254, 1213, 1138, 1028, 883, 849, 737 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 0.23 (s, 9H, Si(CH_3)$_3$), 1.33 (s, 3H, acetonide CH_3), 1.53 (s, 3H, acetonide CH_3), 2.12 (s, 3H, SCH_3), 3.74 (dd, *J* = 6.2, 10.6 Hz, 1H, C*H*OBn), 4.04 (dd, *J* = 1.9, 10.6 Hz, 1H, C*H*OBn), 4.52 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.58 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 5.11 (dd, *J* = 1.9, 6.2 Hz, 1H, C3-*H*), 7.08–7.24 (m, 3H, Ar*H*), 7.36 (m, 2H, Ar*H*); ^{13}C NMR (67.8 MHz, C_6D_6) δ 1.0 (CH_3), 16.6 (CH_3), 26.2 (CH_3), 27.1 (CH_3), 71.3 (CH_2), 73.9 (CH_2), 79.0 (CH), 112.1 (C), 123.9 (C), 128.2 (CH), 129.0 (CH), 139.6 (C), 144.7 (C); FAB-LRMS *m*/*z* 369 $(M+H)^+$, 277 $(M–Bn+H)^+$.

4.3.3. Ethyl (3*S*,4*R*)-5-benzyloxy-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonyl-2-(3-phenylpropyl)pentanoate (21). $Sn(OTf)_2$ (566 mg, 1.36 mmol) was added to a stirred solution of α-keto ester **18** (149 mg, 0.68 mmol) and silyl ketene thioacetal **20** (500 mg, 1.36 mmol) in EtCN (14 mL) at –78 °C. After stirring at –78 °C for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL). The mixture was diluted with AcOEt (10 mL) and *n*-hexane (1 mL), and filtered through a Celite pad. The filtrate was extracted with AcOEt (10 mL), and the organic extract was washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (850 mg), which was purified by flash column chromatography (silica gel 20 g, 20:1→15:1 *n*-hexane/AcOEt) to give aldol adducts **21a** (98 mg, 28%) and **21b** (252 mg, 72%) as pale yellow oils. Data for (2*R*,3*S*,4*R*)-isomer (**21a**): $[\alpha]_D^{24}$ –33.5° (*c* 1.81, $CHCl_3$); IR (film) 3499, 2980, 2930, 2866, 1734, 1682, 1454, 1381, 1256, 1113, 1022, 750, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.25 (m, 1H, one of $(CH_2)_2$), 1.50 (s, 3H, acetonide CH_3), 1.68 (m, 1H, one of $(CH_2)_2$), 1.73 (s, 3H, acetonide CH_3), 1.81 (m, 1H, one of $(CH_2)_2$), 2.12 (m, 1H, one of $(CH_2)_2$), 2.15 (s, 3H, COSCH_3), 2.56 (dt, *J* = 10.3, 3.2 Hz, 2H, CH_2Ph), 3.33 (dd, *J* = 8.0, 10.9 Hz, 1H, C*H*OBn), 3.67 (s, 1H, O*H*), 3.86 (dd, *J* = 1.7, 10.9 Hz, 1H, C*H*OBn), 4.00 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.22 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.46 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.65 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.66 (dd, *J* = 1.7, 8.0 Hz, 1H, C3-*H*), 7.11 (m, 2H, Ar*H*), 7.16 (m, 1H, Ar*H*), 7.22–7.31 (m, 3H, Ar*H*), 7.31–7.38 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 11.9 (CH_3), 13.9 (CH_3), 25.2 (CH_2), 26.4 (CH_3), 27.0 (CH_3), 32.5 (CH_2), 35.8 (CH_2), 62.4 (CH_2), 70.2 (CH_2), 73.4 (CH_2), 79.0 (CH), 79.2 (C), 92.4 (C), 111.9 (C), 125.8 (CH), 127.6 (CH), 127.8 (CH), 138.0 (C), 141.8 (C), 172.4 (C=O), 203.0 (C=O); FAB-HRMS calcd for $C_{28}H_{37}O_7S$ $(M+H)^+$ 517.2260, found 517.2252. Data for (2*S*,3*S*,4*R*)-isomer (**21b**): $[\alpha]_D^{23}$ –23.2° (*c* 1.63, $CHCl_3$); IR (film) 3518, 2980, 2932, 2866, 1738, 1678, 1454, 1381, 1254, 1219, 1182, 1089, 1022, 853, 739, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.25 (m, 1H, one of $(CH_2)_2$), 1.40 (s, 3H, acetonide CH_3), 1.74 (s, 3H, acetonide CH_3), 1.78–1.95 (m, 3H, three of $(CH_2)_2$), 2.14 (s, 3H, COSCH_3), 2.54 (ddd, *J* = 2.1, 6.7, 13.7 Hz, 1H, C*H*Ph), 2.63 (ddd, *J* = 3.0, 5.9, 13.7 Hz, 1H, C*H*Ph), 3.39 (dd, *J* = 8.0, 11.1 Hz, 1H, C*H*OBn), 3.54 (s, 1H, O*H*), 3.94 (dd, *J* = 1.8, 11.1 Hz, 1H, C*H*OBn), 4.14 (dq, *J* = 10.9, 7.1 Hz, 1H, CO_2CHCH_3), 4.21 (dq, *J* = 10.9, 7.1 Hz, 1H, CO_2CHCH_3), 4.50 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.67 (dd, *J* = 1.8, 8.0 Hz, 1H, C3-*H*), 7.12 (m, 2H, Ar*H*), 7.16 (m, 1H, Ar*H*), 7.22–7.30 (m, 3H, Ar*H*), 7.30–7.37 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 11.8 (CH_3), 14.0 (CH_3), 25.2 (CH_2), 26.4 (CH_3), 27.3 (CH_3), 32.7 (CH_2), 35.8 (CH_2), 62.3 (CH_2), 70.2 (CH_2), 73.4 (CH_2), 79.4 (CH), 80.9 (C), 91.3 (C), 112.1 (C), 125.8 (CH), 127.6 (CH), 127.7 (CH), 128.3 (CH), 138.0 (C), 141.8 (C), 172.4 (C=O), 203.8 (C=O); FAB-HRMS calcd for $C_{28}H_{37}O_7S$ $(M+H)^+$ 517.2260, found 517.2267.

4.3.4. Ethyl (3*R*,4*S*,8*R*)-8-(benzyloxymethyl)-6,6-dimethyl-1-oxo-3-(3-phenylpropyl)-2,5,7-trioxaspiro[3.4]octane-3-carboxylate (22a). $Hg(OCOCF_3)_2$ (139 mg, 0.325 mmol) was added to a stirred solution of thioester **21a** (80 mg, 0.155 mmol) in MeCN (16 mL). After stirring for 48 h, the reaction mixture was evaporated in vacuo. The residue was suspended in Et_2O (5 mL) and passed through a short plug of silica gel (eluting with Et_2O) to remove insoluble Hg salt. Purification of the crude product (87 mg) by column chromatography (silica gel 10 g, 8:1 *n*-hexane/

AcOEt) afforded β-lactone **22a** (63 mg, 87%) as a colorless oil: $[\alpha]_D^{26}$ +50.3° (*c* 2.01, $CHCl_3$); IR (film) 2931, 1844, 1734, 1509, 1456, 1375, 1094 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.14 (t, *J* = 7.3 Hz, 3H, $CO_2CH_2CH_3$), 1.39 (s, 3H, acetonide CH_3), 1.54 (s, 3H, acetonide CH_3), 1.56 (m, 1H, C7-*H*), 1.87 (m, 1H, C7-*H*), 2.05 (ddd, *J* = 4.8, 11.5, 14.7 Hz, 1H, C6-*H*), 2.14 (ddd, *J* = 5.0, 11.5, 14.7 Hz, 1H, C6-*H*), 2.65 (ddd, *J* = 6.6, 8.8, 13.6 Hz, 1H, C*H*Ph), 2.67 (ddd, *J* = 6.6, 8.8, 13.6 Hz, 1H, C*H*Ph), 3.56 (dd, *J* = 7.3, 9.1 Hz, 1H, C*H*OBn), 3.75 (dd, *J* = 6.3, 9.1 Hz, 1H, C*H*OBn), 3.97 (dq, *J* = 10.9, 7.3 Hz, 1H, CO_2CHCH_3), 4.21 (dq, *J* = 10.9, 7.3 Hz, 1H, CO_2CHCH_3), 4.44 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.50 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.60 (dd, *J* = 6.3, 7.3 Hz, 1H, C3-*H*), 7.13–7.23 (m, 3H, Ar*H*), 7.23–7.40 (m, 7H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.0 (CH_3), 24.9 (CH_2), 25.2 (CH_3), 26.5 (CH_3), 32.9 (CH_2), 35.5 (CH_2), 61.2 (CH_2), 68.7 (CH_2), 73.8 (CH_2), 76.7 (CH), 86.6 (C), 94.6 (C), 112.9 (C), 126.0 (CH), 127.8 (CH), 128.1 (CH), 128.31 (CH), 128.34 (CH), 128.4 (CH), 137.1 (C), 141.3 (C), 168.16 (C=O), 168.23 (C=O); FAB-HRMS *m*/*z* calcd for $C_{27}H_{33}O_7$ $(M+H)^+$ 469.2226, found 469.2243.

4.3.5. Ethyl (2*R*,3*S*,4*R*)-5-benzyloxy-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-methoxycarbonyl-2-(3-phenylpropyl)pentanoate (19a). Potassium carbonate (20 mg, 0.145 mmol) was added to a solution of β-lactone **22a** (52 mg, 0.111 mmol) in MeOH (1 mL). After stirring for 30 min, the mixture was evaporated in vacuo. The residue (75 mg) was purified by column chromatography (silica gel 10 g, 4:1 *n*-hexane/AcOEt) to give methyl ester **19a** (46 mg, 83%) as a colorless oil: $[\alpha]_D^{26}$ –14.8° (*c* 1.07, $CHCl_3$); IR (film) 3501, 3027, 2988, 1732, 1497, 1454, 1373, 1250, 1181, 1105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.19 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.25 (m, 1H, C7-*H*), 1.44 (s, 3H, acetonide CH_3), 1.56 (s, 3H, acetonide CH_3), 1.80 (ddd, *J* = 4.2, 12.1, 13.9 Hz, 1H, C6-*H*), 1.82 (m, 1H, C7-*H*), 2.06 (ddd, *J* = 4.2, 12.1, 13.9 Hz, 1H, C6-*H*), 2.58 (ddd, *J* = 6.5, 8.4, 14.3 Hz, 1H, C*H*Ph), 2.59 (ddd, *J* = 6.5, 8.4, 14.3 Hz, 1H, C*H*Ph), 3.39 (dd, *J* = 7.2, 11.0 Hz, 1H, C*H*OBn), 3.61 (s, 1H, O*H*), 3.64 (s, 3H, CO_2CH_3), 3.85 (dd, *J* = 1.8, 11.0 Hz, 1H, C*H*OBn), 4.06 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.20 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.48 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 4.62 (dd, *J* = 1.8, 7.2 Hz, 1H, C3-*H*), 4.63 (d, *J* = 12.1 Hz, 1H, OC*H*Ph), 7.11 (d, *J* = 7.3 Hz, 2H, Ar*H*), 7.15 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.23–7.32 (m, 3H, Ar*H*), 7.34 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.2 (CH_3), 25.4 (CH_3), 26.8 (CH_3), 27.3 (CH_3), 33.1 (CH_2), 36.0 (CH_2), 52.3 (CH_2), 62.7 (CH_2), 70.4 (CH_2), 73.7 (CH_2), 79.2 (C), 79.6 (C), 89.2 (C), 111.3 (C), 126.1 (CH), 127.9 (CH), 128.1 (CH), 128.56 (CH), 128.59 (CH), 138.2 (CH), 142.0 (C), 171.1 (C=O), 172.8 (C=O); FAB-HRMS *m*/*z* calcd for $C_{28}H_{37}O_8$ $(M+H)^+$ 501.2488, found 501.2497.

4.3.6. Ethyl [2*R*,2(3a*S*,6a*R*)]-2-hydroxy-5-phenyl-2-(tetrahydro-2,2-dimethyl-4-oxofuro[3,4-*d*][1,3]dioxol-3a-yl)-pentanoate (23a). Palladium on carbon (10%, 7 mg) was added to a solution of benzyl ether **19a** (44 mg, 0.088 mmol) in EtOH (1 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 2 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. The crude product (33 mg) thus obtained was used without further purification.

DMAP (43 mg, 0.352 mmol) was added to a solution of the crude γ-hydroxyester (33 mg) in CH_2Cl_2 (1 mL). After stirring for 1 h, the reaction was quenched with saturated aqueous NH_4Cl (6 mL), and the whole was extracted with AcOEt (10 mL). The organic extract was washed with brine (6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (33 mg), which was purified by column chromatography (silica gel 10 g, 5:1 *n*-hexane/AcOEt) to give γ-lactone **23a** (33 mg, 98%) as a colorless oil: $[\alpha]_D^{24}$ –55.9° (*c* 1.02, $CHCl_3$); IR (film) 3486, 2990, 2940, 2866, 1790, 1728, 1456, 1377, 1263, 1117, 1019, 972, 914 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.29 (m, 1H, C7-*H*), 1.32 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.38 (s, 3H, acetonide CH_3), 1.44 (s, 3H, acetonide CH_3), 1.82 (m, 1H, C7-*H*), 2.12 (ddd, *J* = 4.6, 12.3, 13.8 Hz, 1H, C6-*H*), 2.20 (ddd, *J* = 4.6, 12.3, 13.8 Hz, 1H, C6-*H*), 2.60 (ddd, *J* = 6.0, 9.5, 14.0 Hz, 1H, C*H*Ph), 2.66 (ddd, *J* = 6.0, 9.5, 14.0 Hz, 1H, C*H*Ph), 3.76 (s, 1H, O*H*), 4.23 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.32 (d, *J* = 1.7 Hz, 2H, lactone CH_2), 4.36 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.56 (t, *J* = 1.7 Hz, 1H, C3-*H*), 7.13–7.19 (m, 3H, Ar*H*), 7.26–7.28 (m, 2H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3 (CH_3), 25.3 (CH_3), 26.9 (CH_3), 27.4 (CH_2), 32.1 (CH_2), 36.0 (CH_2), 63.3 (CH_2), 71.0 (CH_2), 78.0 (CH), 79.1 (C), 86.4 (C), 114.3 (C), 126.1 (CH), 128.5 (CH), 128.6 (CH), 142.1 (C), 173.3 (C=O), 174.2 (C=O); FAB-HRMS calcd for $C_{20}H_{27}O_7$ $(M+H)^+$ 379.1757, found 379.1753.

4.3.7. Ethyl (3*S*,4*S*,8*R*)-8-(benzyloxymethyl)-6,6-dimethyl-1-oxo-3-(3-phenylpropyl)-2,5,7-trioxaspiro[3.4]octane-3-carboxylate (22b). $Hg(OCOCF_3)_2$ (209 mg, 0.489 mmol) was added to a stirred solution of thioester **21b** (120 mg, 0.233 mmol) in MeCN (23 mL). After stirring for 4 h, the reaction mixture was evaporated in vacuo. The residue was suspended in Et_2O (5 mL) and passed through a short plug of silica gel (eluting with Et_2O) to remove insoluble Hg salt. Purification of the crude product (130 mg) by column chromatography (silica gel 10 g, 8:1 *n*-hexane/AcOEt) afforded β-lactone **22b** (92 mg, 84%) as a colorless oil: $[\alpha]_D^{26}$ –18.1° (*c* 2.06, benzene); IR (film) 2935, 1842, 1757, 1454, 1381, 1271, 1094 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.31 (s, 3H, acetonide CH_3), 1.49 (s, 3H, acetonide CH_3), 1.53 (m, 1H, C7-*H*), 1.74 (m, 1H, C7-*H*), 2.04 (ddd, *J* = 6.8, 8.7, 13.9 Hz, 1H, C6-*H*), 2.15 (ddd, *J* = 6.4, 8.9, 13.9 Hz, 1H, C6-*H*), 2.46 (ddd, *J* = 4.9, 11.3, 13.7 Hz, 1H, C*H*Ph), 2.47 (ddd, *J* = 4.9, 11.3, 13.7 Hz, 1H, C*H*Ph), 3.66 (dd, *J* = 8.7, 9.1 Hz, 1H, C*H*OBn), 3.85 (dd, *J* = 5.1, 8.7 Hz, 1H, C*H*OBn), 4.24 (dq, *J* = 10.9, 7.2 Hz, 1H, CO_2CHCH_3), 4.32 (dq, *J* = 10.9, 7.2 Hz, 1H, CO_2CHCH_3), 4.40 (d, *J* = 11.1 Hz, 1H, OC*H*Ph), 4.50 (d, *J* = 11.1 Hz, 1H, OC*H*Ph), 4.62 (dd, *J* = 5.1, 9.1 Hz, 1H, C3-*H*), 7.07 (d, *J* = 7.2 Hz, 2H, Ar*H*), 7.16 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.20–7.38 (m, 7H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.1 (CH_3), 25.2 (CH_2), 25.4 (CH_3), 26.8 (CH_3), 31.1 (CH_2), 35.3 (CH_2), 62.1 (CH_2), 68.6 (CH_2), 73.8 (CH_2), 75.7 (CH), 87.7 (C), 95.5 (C), 113.1 (C), 125.9 (CH), 128.0 (CH), 128.1 (CH), 128.2

(CH), 128.3 (CH), 128.4 (CH), 137.1 (C), 141.3 (C), 167.9 (C=O), 168.1 (C=O); FAB-HRMS *m*/*z* calcd for $C_{27}H_{33}O_7$ $(M+H)^+$ 469.2226, found 469.2257.

4.3.8. Ethyl (2*S*,3*S*,4*R*)-5-benzyloxy-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-methoxycarbonyl-2-(3-phenylpropyl)pentanoate (19b). Potassium carbonate (24 mg, 0.175 mmol) was added to a solution of β-lactone **22b** (63 mg, 0.134 mmol) in MeOH (1.3 mL). After stirring for 1 h, the mixture was evaporated in vacuo. The residue (68 mg) was purified by column chromatography (silica gel 10 g, 4:1 *n*-hexane/AcOEt) to give methyl ester **19b** (60 mg, 89%) as a colorless oil: $[\alpha]_D^{26}$ +13.5° (*c* 2.03, $CHCl_3$); IR (film) 3513, 3029, 2986, 1732, 1497, 1454, 1373, 1240, 1101, 1024 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.22 (m, 1H, C7-*H*), 1.29 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.35 (s, 3H, acetonide CH_3), 1.57 (s, 3H, acetonide CH_3), 1.82 (m, 1H, C7-*H*), 1.86 (ddd, *J* = 2.8, 8.2, 12.0 Hz, 1H, C6-*H*), 2.02 (ddd, *J* = 3.4, 8.9, 12.0 Hz, 1H, C6-*H*), 2.53 (ddd, *J* = 6.3, 8.4, 13.6 Hz, 1H, C*H*Ph), 2.61 (ddd, *J* = 4.9, 8.7, 13.6 Hz, 1H, C*H*Ph), 3.47 (dd, *J* = 7.2, 11.1 Hz, 1H, C*H*OBn), 3.66 (s, 3H, CO_2CH_3), 3.68 (s, 1H, O*H*), 3.93 (dd, *J* = 1.8, 11.1 Hz, 1H, C*H*OBn), 4.17 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.28 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.52 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.63 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.66 (dd, *J* = 1.8, 7.2 Hz, 1H, C3-*H*), 7.07 (d, *J* = 7.2 Hz, 2H, Ar*H*), 7.16 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.23–7.35 (m, 7H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3 (CH_3), 25.4 (CH_3), 26.7 (CH_3), 27.2 (CH_3), 33.3 (CH_2), 36.0 (CH_2), 52.4 (CH_2), 62.7 (CH_2), 70.3 (CH_2), 73.8 (CH_2), 79.3 (C), 81.2 (C), 88.3 (C), 111.6 (C), 126.1 (CH), 127.9 (CH), 128.0 (CH), 128.57 (CH), 128.60 (CH), 138.2 (CH), 142.1 (C), 171.1 (C=O), 172.9 (C=O); FAB-HRMS *m*/*z* calcd for $C_{28}H_{37}O_8$ $(M+H)^+$ 501.2488, found 501.2501.

4.3.9. Ethyl [2*S*,2(3a*S*,6a*R*)]-2-hydroxy-5-phenyl-2-(tetrahydro-2,2-dimethyl-4-oxofuro[3,4-*d*][1,3]dioxol-3a-yl)-pentanoate (23b). Palladium on carbon (10%, 7 mg) was added to a solution of benzyl ether **19b** (41 mg, 0.082 mmol) in EtOH (1 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 2 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. The crude product (32 mg) thus obtained was used without further purification.

DMAP (40 mg, 0.328 mmol) was added to a solution of the crude γ-hydroxyester (32 mg) in CH_2Cl_2 (1 mL). After stirring for 1 h, the reaction was quenched with saturated aqueous NH_4Cl (6 mL), and the whole was extracted with AcOEt (10 mL). The organic extract was washed with brine (6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (30 mg), which was purified by column chromatography (silica gel 5 g, 5:1 *n*-hexane/AcOEt) to give γ-lactone **23b** (29 mg, 94%) as a colorless oil: $[\alpha]_D^{26}$ –24.0° (*c* 1.46, $CHCl_3$); IR (film) 3472, 2990, 2938, 1786, 1726, 1497, 1456, 1377, 1256, 1218, 1179, 1101, 1074 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (m, 1H, C7-*H*), 1.32 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.44 (s, 6H, 2×acetonide CH_3), 1.74 (ddd, *J* = 4.4, 12.3, 16.0 Hz, 1H, C6-*H*), 1.82 (m, 1H, C7-*H*), 2.24 (ddd, *J* = 4.4, 12.3, 16.0 Hz, 1H, C6-*H*), 2.63 (ddd, *J* = 6.1, 8.6, 13.7 Hz, 1H, C*H*Ph), 2.65 (ddd, *J* = 6.1, 8.6, 13.7 Hz, 1H, C*H*Ph), 3.72 (s, 1H, O*H*), 4.26 (dd, *J* = 3.8, 10.5 Hz, 1H, one of lactone CH_2), 4.31 (dd, *J* = 3.8, 10.5 Hz, 1H, one of lactone CH_2), 4.34 (dq, *J* = 10.9, 7.2 Hz, 1H, CO_2CHCH_3), 4.35 (dq, *J* = 10.9, 7.2 Hz, 1H, CO_2CHCH_3), 4.82 (t, *J* = 3.8 Hz, 1H, C3-*H*), 7.14–7.19 (m, 3H, Ar*H*), 7.27 (m, 2H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 15.1 (CH_3), 25.6 (CH_3), 27.8 (CH_3), 28.3 (CH_2), 33.9 (CH_2), 36.8 (CH_2), 64.4 (CH_2), 72.2 (CH_2), 78.4 (CH), 79.5 (C), 88.2 (C), 115.5 (C), 127.1 (CH), 129.4 (CH), 129.5 (CH), 142.7 (C), 174.1 (C=O), 175.8 (C=O); FAB-HRMS *m*/*z* calcd for $C_{20}H_{27}O_7$ $(M+H)^+$ 379.1757, found 379.1763.

4.3.10. Typical procedure for the aldol reaction of α-keto esters with silyl ketene thioacetals: ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(dimethylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (24). $Sn(OTf)_2$ (42 mg, 0.10 mmol) was added to a stirred solution of α-keto ester **17** (16.5 mg, 0.051 mmol) and silyl ketene thioacetal **20** (37 mg, 0.10 mmol) in EtCN (1 mL) at –70 °C. After stirring at –70 °C for 1.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL). The mixture was diluted with 1:1 AcOEt/*n*-hexane (10 mL) and filtered through a Celite pad. The layers were separated, and the organic layer was washed successively with saturated aqueous $NaHCO_3$ (3 mL) and brine (3 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (45 mg), whose ^1H NMR revealed a **24a**/**24b** ratio of 1:2.2. Purification by column chromatography (silica gel 5 g, 7:1→4:1 *n*-hexane/AcOEt) afforded aldol adducts **24b** (19.5 mg, 62%) and **24a** (8.9 mg, 28%) as colorless oils. Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**24a**): $[\alpha]_D^{24}$ –12.1° (*c* 0.36, $CHCl_3$); IR (film) 3468, 2928, 1734, 1671, 1456, 1373, 1259, 1219, 1086, 866, 737, 698 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.36 (s, 6H, 2×acetonide CH_3), 1.62 (s, 3H, acetonide CH_3), 1.82 (s, 3H, acetonide CH_3), 2.17 (s, 3H, $COSCH_3$), 3.25 (dd, *J* = 7.8, 10.4 Hz, 1H, C*H*OBn), 3.56 (dd, *J* = 6.4, 10.4 Hz, 1H, C1-*H*), 3.72 (dd, *J* = 3.4, 10.4 Hz, 1H, C1-*H*), 3.83 (dd, *J* = 1.7, 10.4 Hz, 1H, C*H*OBn), 3.98 (s, 1H, O*H*), 3.99 (ddd, *J* = 3.4, 6.4, 8.0 Hz, 1H, C7-*H*), 4.12 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.23 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.41 (d, *J* = 8.0 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.57 (s, 2H, OCH_2Ph), 4.65 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 5.32 (dd, *J* = 1.7, 7.8 Hz, 1H, C3-*H*), 7.21–7.39 (m, 10H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 12.1 (CH_3), 14.1 (CH_3), 26.2 (CH_3), 27.1 (CH_3), 27.3 (CH_3), 27.5 (CH_3), 63.3 (CH_2), 70.7 (CH_2), 72.1 (CH_2), 73.5 (CH_2), 73.6 (CH_2), 76.7 (CH), 77.5 (CH), 78.1 (CH), 79.1 (C), 93.9 (C), 110.9 (C), 112.2 (C), 127.8 (CH), 127.85 (CH), 127.91 (CH), 127.93 (CH), 128.5 (CH), 128.6 (CH), 138.1 (C), 138.5 (C), 170.2 (C=O), 204.3 (C=O); FAB-HRMS *m*/*z* calcd for $C_{32}H_{43}O_{10}S$ $(M+H)^+$ 619.2577, found 619.2588. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**24b**): $[\alpha]_D^{25}$ –30.9° (*c* 0.74, $CHCl_3$); IR (film) 3510, 2930, 1736, 1670, 1381, 1260, 1219, 1148, 1088, 860, 737, 698 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.09 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.42 (s, 3H, acetonide CH_3), 1.49 (s, 3H, acetonide CH_3), 1.68 (s, 3H, acetonide CH_3), 1.82 (s, 3H, acetonide CH_3), 2.08 (s, 3H,

COSCH_3), 3.34 (d, J = 4.5 Hz, 2H, C1-H_2), 3.35 (dd, J = 7.7, 10.8 Hz, 1H, CHOBn), 3.69 (d, J = 0.8 Hz, 1H, OH), 3.75 (dq, J = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.86 (dd, J = 2.2, 10.8 Hz, 1H, CHOBn), 3.90 (dq, J = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.23 (dt, J = 7.5, 4.5 Hz, 1H, C7-H), 4.49 (d, J = 12.5 Hz, 1H, OCHPh), 4.51 (dd, J = 0.8, 7.5 Hz, 1H, C6-H), 4.52 (d, J = 12.5 Hz, 1H, OCHPh), 4.61 (d, J = 12.5 Hz, 2H, 2×OCHPh), 5.37 (dd, J = 2.2, 7.7 Hz, 1H, C3-H), 7.20–7.38 (m, 10H, ArH); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 12.0 (CH_3), 13.9 (CH_3), 26.2 (CH_3), 26.7 (CH_3), 27.79 (CH_3), 27.83 (CH_3), 62.5 (CH_2), 70.4 (CH_2), 71.0 (CH_2), 73.3 (CH_2), 73.6 (CH_2), 76.7 (CH), 77.5 (CH), 79.2 (CH), 80.1 (C), 91.0 (C), 111.2 (C), 113.6 (C), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 128.5 (CH), 128.6 (CH), 138.2 (C), 138.4 (C), 171.2 (C=O), 205.6 (C=O); FAB-HRMS m/z calcd for $C_{32}H_{43}O_{10}S$ $(M+H)^+$ 619.2577, found 619.2571.

4.3.11. (*R*,*E*)-4-(Benzyloxy)methyl-5-[methylthio(trimethylsilyloxy)methylene]-2,2-dimethyl-1,3-dioxolane (25). KHMDS in toluene (0.5 M, 5.0 mL, 2.5 mmol) was added to a stirred solution of thioester **14** (697 mg, 2.35 mmol) in THF (10 mL) at –78 °C over a 2-h period. After stirring at –78 °C for 30 min, TMSCl (0.33 mL, 21.3 mmol) was added, and the resulting mixture was stirred at –78 °C for 30 min. The mixture was allowed to warm to room temperature. After stirring at room temperature for 15 min, the mixture was evaporated in vacuo. The residue was suspended in *n*-hexane and passed through a short plug of Florisil (eluting with AcOEt) to give silyl ketene thioacetal **25** (751 mg, 87%, *Z*:*E*=1:99) as a yellow oil: ^{1}H NMR (500 MHz, C_6D_6) δ 0.36 (s, 9H, Si(CH_3)$_3$), 1.33 (s, 3H, acetonide CH_3), 1.51 (s, 3H, acetonide CH_3), 1.98 (s, 3H, SCH_3), 3.84 (dd, J = 5.6, 10.6 Hz, 1H, CHOBn), 3.94 (dd, J = 2.0, 10.6 Hz, 1H, CHOBn), 4.51 (s, 2H, OCH_2Ph), 5.13 (dd, J = 2.0, 5.6 Hz, 1H, C3-H), 7.07–7.37 (m, 5H, ArH); ^{13}C NMR (67.8 MHz, C_6D_6) δ 1.1 (CH_3), 16.3 (CH_3), 27.2 (CH_3), 27.5 (CH_3), 72.8 (CH_2), 73.9 (CH_2), 78.8 (CH), 112.8 (C), 121.8 (C), 128.2 (CH), 128.9 (CH), 139.5 (C), 141.5 (C).

4.3.12. Sn(OTf)$_2$-promoted aldol reaction between α-keto ester 17 and (*E*)-silyl ketene thioacetal 25. The aldol reaction was performed according to the typical procedure (2 mL EtCN, –55 °C, 1 h) employing α-keto ester **17** (30 mg, 0.093 mmol), (*E*)-silyl ketene thioacetal **25** (69 mg, 0.187 mmol), and Sn(OTf)$_2$ (78 mg, 0.187 mmol). A diastereomeric mixture of aldol adducts **24** (21 mg, 36%, **24a**:**24b**=1:10) was obtained as a colorless oil after flash column chromatography (silica gel 5 g, 8:1 *n*-hexane/AcOEt).

4.3.13. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(methylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (36). The aldol reaction was performed according to the typical procedure (1.2 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **26** (19 mg, 0.063 mmol), silyl ketene thioacetal **20** (50 mg, 0.136 mmol), and Sn(OTf)$_2$ (53 mg, 0.127 mmol). The diastereomeric ratio of the products was determined to be 1:2.6 by ^{1}H NMR of the crude product (43 mg), from which an inseparable mixture of aldol adducts **36** (18 mg, 49%, **36a**:**36b**=1:2.6) was obtained as a colorless oil after flash column chromatography (silica gel 8 g, 5:1→3:1 *n*-hexane/AcOEt): $[\alpha]_D^{26}$ –40.0° (*c* 0.81, $CHCl_3$); IR (film) 3504, 2869, 1734, 1671, 1456, 1383, 1261, 1221, 1094, 737, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) for **36b** δ 1.12 (t, J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.66 (s, 3H, acetonide CH_3), 1.81 (s, 3H, acetonide CH_3), 2.09 (s, 3H, COSCH_3), 3.38 (dd, J = 7.6, 10.8 Hz, 1H, CHOBn), 3.41 (dd, J = 6.0, 10.6 Hz, 1H, C1-H), 3.49 (dd, J = 3.1, 10.6 Hz, 1H, C1-H), 3.72 (d, J = 0.8 Hz, 1H, OH), 3.85 (dq, J = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 3.89 (dd, J = 2.2, 10.8 Hz, 1H, CHOBn), 4.03 (dq, J = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.15 (dt, J = 3.1, 6.0 Hz, 1H, C7-H), 4.52 (d, J = 12.3 Hz, 1H, OCHPh), 4.53 (d, J = 12.3 Hz, 1H, OCHPh), 4.55 (m, 1H, C6-H), 4.59 (d, J = 12.3 Hz, 2H, 2×OCHPh), 5.10 (s, 2H, OCH_2O), 5.40 (dd, J = 2.2, 7.6 Hz, 1H, C3-H), 7.22–7.38 (m, 10H, ArH). The minor isomer (**36a**) had additional signals at 1.22 (t, J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 2.17 (s, 3H, COSCH_3), and 5.40 (dd, J = 1.6, 7.7 Hz, 1H, C3-H). FAB-LRMS m/z 591 $(M+H)^+$.

4.3.14. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (37). The aldol reaction was performed according to the typical procedure (4 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **27** (111 mg, 0.32 mmol), silyl ketene thioacetal **20** (204 mg, 0.055 mmol), and Sn(OTf)$_2$ (269 mg, 0.65 mmol). The diastereomeric ratio of the products was determined to be 1:1.1 by ^{1}H NMR of the crude product (263 mg), from which aldol adducts **37a** (79 mg, 39%) and **37b** (82 mg, 40%) were obtained as colorless oils after flash column chromatography (silica gel 13 g, 8:1→6:1 *n*-hexane/AcOEt). Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**37a**): $[\alpha]_D^{22}$ –13.3° (*c* 0.45, $CHCl_3$); IR (film) 3461, 2930, 1725, 1673, 1455, 1377, 1257, 1221, 1174, 1097, 736, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (t, J = 7.6 Hz, 3H, pentylidene CH_3), 0.91 (t, J = 7.6 Hz, 3H, pentylidene CH_3), 1.22 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.39–1.74 (m, 4H, 2×pentylidene CH_2), 1.63 (s, 3H, acetonide CH_3), 1.82 (s, 3H, acetonide CH_3), 2.17 (s, 3H, COSCH_3), 3.28 (dd, J = 7.8, 10.5 Hz, 1H, CHOBn), 3.57 (dd, J = 6.1, 10.4 Hz, 1H, C1-H), 3.73 (dd, J = 3.5, 10.4 Hz, 1H, C1-H), 3.86 (dd, J = 1.8, 10.5 Hz, 1H, CHOBn), 4.00 (ddd, J = 3.5, 6.1, 8.5 Hz, 1H, C7-H), 4.03 (s, 1H, OH), 4.13 (dq, J = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.19 (dq, J = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.37 (d, J = 8.5 Hz, 1H, C6-H), 4.48 (d, J = 12.5 Hz, 1H, OCHPh), 4.57 (s, 2H, OCH_2Ph), 4.66 (d, J = 12.5 Hz, 1H, OCHPh), 5.35 (dd, J = 1.8, 7.8 Hz, 1H, C3-H), 7.22–7.38 (m, 10H, ArH); FAB-HRMS m/z calcd for $C_{34}H_{47}O_{10}S$ $(M+H)^+$ 647.2890, found 647.2911. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**37b**): $[\alpha]_D^{24}$ –27.7° (*c* 0.51, $CHCl_3$); IR (film) 3515, 2928, 1736, 1671, 1456, 1383, 1261, 1147, 1090, 737, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87 (t, J = 7.3 Hz, 3H, pentylidene CH_3), 0.94 (t, J = 7.5 Hz, 3H, pentylidene CH_3), 1.09 (t, J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.47–1.85 (m, 4H, 2×pentylidene CH_2), 1.69 (s, 3H, acetonide CH_3), 1.82 (s, 3H, acetonide CH_3), 2.09 (s, 3H, COSCH_3), 3.337 (d, J = 4.2 Hz, 2H, C1-H_2), 3.340 (dd, J = 7.9, 10.6 Hz, 1H, CHOBn), 3.66 (s, 1H, OH), 3.73 (dq, J = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.87 (dd, J = 2.0, 10.6

Hz, 1H, C*H*OBn), 3.88 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.24 (dt, *J* = 8.2, 4.2 Hz, 1H, C7-*H*), 4.44 (d, *J* = 8.2 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.50 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.62 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 5.39 (dd, *J* = 2.0, 7.9 Hz, 1H, C3-*H*), 7.21–7.37 (m, 10H, Ar*H*); FAB-HRMS *m*/*z* calcd for $C_{34}H_{47}O_{10}S$ $(M+H)^+$ 647.2890, found 647.2881.

4.3.15. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(dipropylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (38). The aldol reaction was performed according to the typical procedure (1.2 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **28** (21.0 mg, 0.055 mmol), silyl ketene thioacetal **20** (52.1 mg, 0.14 mmol), and $Sn(OTf)_2$ (39.0 mg, 0.094 mmol). The diastereomeric ratio of the products was determined to be 1:1.6 by ^{1}H NMR of the crude product (62 mg), from which aldol adducts **38a** (12.8 mg, 34%) and **38b** (17.8 mg, 48%) were obtained as colorless oils after flash column chromatography (silica gel 8 g, 10:1→8:1→5:1 *n*-hexane/AcOEt). Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**38a**): $[\alpha]_D^{25}$ –13.6° (*c* 0.52, $CHCl_3$); IR (film) 3464, 2961, 1734, 1676, 1456, 1375, 1260, 1219, 1103, 735, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.3 Hz, 3H, heptylidene CH_3), 0.92 (t, *J* = 7.3 Hz, 3H, heptylidene CH_3), 1.22 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.20–1.72 (m, 8H, 4×heptylidene CH_2), 1.62 (s, 3H, acetonide CH_3), 1.82 (s, 3H, acetonide CH_3), 2.17 (s, 3H, COSCH_3), 3.27 (dd, *J* = 7.8, 10.4 Hz, 1H, C*H*OBn), 3.55 (dd, *J* = 6.0, 10.3 Hz, 1H, C1-*H*), 3.72 (dd, *J* = 3.7, 10.3 Hz, 1H, C1-*H*), 3.85 (dd, *J* = 1.5, 10.4 Hz, 1H, C*H*OBn), 3.97 (m, 1H, C7-*H*), 4.03 (s, 1H, O*H*), 4.14 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.19 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.38 (d, *J* = 8.3 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.56 (s, 2H, OCH_2Ph), 4.66 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.33 (dd, *J* = 1.5, 7.8 Hz, 1H, C3-*H*), 7.20–7.40 (m, 10H, Ar*H*); FAB-LRMS *m*/*z* 675 $(M+H)^+$, 631 $(M–C_3H_7)^+$. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**38b**): $[\alpha]_D^{26}$ –25.3° (*c* 0.76, $CHCl_3$); IR (film) 3510, 2961, 1736, 1669, 1456, 1383, 1261, 1148, 1090, 736, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.3 Hz, 3H, heptylidene CH_3), 0.92 (t, *J* = 7.3 Hz, 3H, heptylidene CH_3), 1.09 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.18–1.80 (m, 8H, 4×heptylidene CH_2), 1.68 (s, 3H, acetonide CH_3), 1.82 (s, 3H, acetonide CH_3), 2.09 (s, 3H, COSCH_3), 3.33 (d, *J* = 4.5 Hz, 2H, C1-H_2), 3.34 (dd, *J* = 7.9, 10.7 Hz, 1H, C*H*OBn), 3.67 (d, *J* = 0.8 Hz, 1H, O*H*), 3.74 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.86 (dd, *J* = 2.1, 10.7 Hz, 1H, C*H*OBn), 3.88 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.23 (dt, *J* = 7.9, 4.5 Hz, 1H, C7-*H*), 4.43 (dd, *J* = 0.8, 7.9 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.53 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.59 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.37 (dd, *J* = 2.1, 7.9 Hz, 1H, C3-*H*), 7.20–7.40 (m, 10H, Ar*H*); FAB-LRMS *m*/*z* 675 $(M+H)^+$, 631 $(M–C_3H_7)^+$.

4.3.16. Ethyl [2*S*,2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-2-hydroxy-3,4-(methylenedioxy)-3-(methylthio)carbonylpentanoate (39b). The aldol reaction was performed according to the typical procedure (1.5 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **27** (27.3 mg, 0.078 mmol), silyl ketene thioacetal **33** (53.2 mg, 0.156 mmol), and $Sn(OTf)_2$ (65.0 mg, 0.156 mmol). The diastereomeric ratio of the products was determined to be 1:>20 by ^{1}H NMR of the crude product (83.2 mg), from which aldol adduct **39b** (32.3 mg, 67%) was obtained as a colorless oil after flash column chromatography (silica gel 5 g, 8:1→5:1 *n*-hexane/AcOEt): $[\alpha]_D^{24}$ –3.0° (*c* 0.92, $CHCl_3$); IR (film) 3493, 2975, 1738, 1672, 1454, 1368, 1260, 1150, 1094, 980, 752, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 0.94 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.09 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.60–1.83 (m, 4H, 2×pentylidene CH_2), 2.11 (s, 3H, COSCH_3), 3.31 (d, *J* = 4.2 Hz, 2H, C1-H_2), 3.36 (dd, *J* = 7.8, 10.7 Hz, 1H, C*H*OBn), 3.62 (s, 1H, O*H*), 3.74 (dq, *J* = 10.6, 7.2 Hz, 1H, CO_2CHCH_3), 3.78 (dd, *J* = 2.2, 10.7 Hz, 1H, C*H*OBn), 4.01 (dq, *J* = 10.6, 7.2 Hz, 1H, CO_2CHCH_3), 4.21 (dt, *J* = 8.0, 4.2 Hz, 1H, C7-*H*), 4.44 (d, *J* = 8.0 Hz, 1H, C6-*H*), 4.47 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.52 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.57 (d, *J* = 12.3 Hz, 2H, 2×OC*H*Ph), 5.16 (dd, *J* = 2.2, 7.8 Hz, 1H, C3-*H*), 5.36 (s, 1H, OC*H*O), 5.50 (s, 1H, OC*H*O), 7.22–7.37 (m, 10H, Ar*H*); FAB-LRMS *m*/*z* 619 $(M+H)^+$, 589 $(M–Et)^+$.

4.3.17. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-3,4-(diethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (40). The aldol reaction was performed according to the typical procedure (3 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **27** (62.2 mg, 0.178 mmol), silyl ketene thioacetal **34** (137.3 mg, 0.346 mmol), and $Sn(OTf)_2$ (151.6 mg, 0.364 mmol). The diastereomeric ratio of the products was determined to be 1:1.9 by ^{1}H NMR of the crude product (161.6 mg), from which aldol adducts **40a** (31.3 mg, 26%) and **40b** (49.2 mg, 41%) were obtained as colorless oils after flash column chromatography (silica gel 10 g, 15:1→10:1→8:1 *n*-hexane/AcOEt). Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**40a**): $[\alpha]_D^{29}$ –5.4° (*c* 1.0, $CHCl_3$); IR (film) 3464, 2975, 1723, 1672, 1456, 1366, 1256, 936, 737, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 0.90 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 0.94 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.05 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.25 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.47–1.75 (m, 4H, 2×pentylidene CH_2), 1.86–1.98 (m, 2H, pentylidene CH_2), 2.05–2.20 (m, 2H, pentylidene CH_2), 2.14 (s, 3H, COSCH_3), 3.29 (dd, *J* = 7.2, 10.6 Hz, 1H, C*H*OBn), 3.57 (dd, *J* = 6.0, 10.4 Hz, 1H, C1-*H*), 3.76 (dd, *J* = 3.1, 10.4 Hz, 1H, C1-*H*), 3.86 (dd, *J* = 1.7, 10.6 Hz, 1H, C*H*OBn), 3.93 (s, 1H, O*H*), 4.01 (ddd, *J* = 3.1, 6.0, 8.2 Hz, 1H, C7-*H*), 4.17 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.23 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.39 (d, *J* = 8.2 Hz, 1H, C6-*H*), 4.49 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.57 (s, 2H, OCH_2Ph), 4.61 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.30 (dd, *J* = 1.7, 7.2 Hz, 1H, C3-*H*), 7.22–7.37 (m, 10H, Ar*H*); FAB-HRMS *m*/*z* calcd for $C_{36}H_{51}O_{10}S$ $(M+H)^+$ 675.3203, found 675.3234. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**40b**): $[\alpha]_D^{27}$ –27.0° (*c* 0.68, $CHCl_3$); IR (film) 3512, 2940, 1738, 1667, 1368, 1090, 930, 737, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 0.925 (t, *J* = 7.5 Hz, 3H,

pentylidene CH_3), 0.928 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.04 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.10 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.55–1.82 (m, 4H, 2×pentylidene CH_2), 1.92–2.18 (m, 4H, 2×pentylidene CH_2), 2.07 (s, 3H, COSCH_3), 3.33 (dd, *J* = 6.0, 11.2 Hz, 1H, C1-*H*), 3.37 (dd, *J* = 7.2, 11.2 Hz, 1H, C*H*OBn), 3.40 (dd, *J* = 2.4, 11.2 Hz, 1H, C1-*H*), 3.69 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.74 (s, 1H, O*H*), 3.88 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.89 (dd, *J* = 2.3, 11.2 Hz, 1H, C*H*OBn), 4.22 (ddd, *J* = 2.4, 6.0, 7.8 Hz, 1H, C7-*H*), 4.49 (d, *J* = 7.8 Hz, 1H, C6-*H*), 4.51 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.59 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.60 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.60 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.39 (dd, *J* = 2.3, 7.2 Hz, 1H, C3-*H*), 7.20–7.40 (m, 10H, Ar*H*); FAB-HRMS *m*/*z* calcd for $C_{36}H_{51}O_{10}S$ $(M+H)^+$ 675.3203, found 675.3214.

4.3.18. Ethyl [2*S*,2(1*R*,2*S*),3*S*,4*R*]-2-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-5-(*tert*-butyldiphenylsilyl)oxy-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (41b). The aldol reaction was performed according to the typical procedure (5 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **27** (69.6 mg, 0.199 mmol), silyl ketene thioacetal **35** (209.1 mg, 0.405 mmol), and $Sn(OTf)_2$ (170.6 mg, 0.409 mmol). The diastereomeric ratio of the products was determined to be 1:>20 by ^{1}H NMR of the crude product (284.2 mg), from which aldol adduct **41b** (102.0 mg, 65%) was obtained as a colorless oil after flash column chromatography (silica gel 15 g, 15:1 *n*-hexane/AcOEt): $[\alpha]_D^{23}$ –10.6° (*c* 0.39, $CHCl_3$); IR (film) 3515, 2932, 2884, 2859, 1738, 1667, 1462, 1427, 1375, 1262, 1221, 1111, 1026, 912, 887 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 0.92 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 1.03 (s, 9H, SiC(CH_3)$_3$), 1.07 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.50–1.79 (m, 4H, 2×pentylidene CH_2), 1.69 (s, 3H, acetonide CH_3), 1.79 (s, 3H, acetonide CH_3), 2.01 (s, 3H, COSCH_3), 3.33 (d, *J* = 4.1 Hz, 2H, C1-H_2), 3.54 (dd, *J* = 7.2, 11.2 Hz, 1H, C*H*OTBDPS), 3.69 (s, 1H, O*H*), 3.71 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.85 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.01 (dd, *J* = 2.7, 11.2 Hz, 1H, C*H*OTBDPS), 4.26 (dt, *J* = 8.0, 4.1 Hz, 1H, C7-*H*), 4.41 (d, *J* = 8.0 Hz, 1H, C6-*H*), 4.47 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.62 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.31 (dd, *J* = 2.7, 7.2 Hz, 1H, C3-*H*), 7.23–7.45 (m, 9H, Ar*H*), 7.66–7.73 (m, 6H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 5.4 (CH_3), 6.5 (CH_3), 9.5 (CH_3), 11.4 (CH_3), 17.0 (CH_3), 23.8 (CH_3), 24.5 (CH_3), 25.3 (CH_3), 26.9 (CH_3), 27.9 (CH_2), 59.9 (CH_2), 62.1 (CH_2), 68.5 (CH_2), 71.0 (CH_2), 73.9 (CH_2), 76.9 (CH), 79.5 (C), 88.5 (C), 110.8 (C), 112.7 (C), 125.2 (CH), 125.3 (CH), 125.4 (CH), 125.6 (CH), 126.1 (CH), 127.2 (CH), 128.5 (CH), 133.5 (C), 133.6 (C), 168.9 (C=O), 203.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{43}H_{59}O_{10}SSi$ $(M+H)^+$ 795.3598, found 795.3590.

4.3.19. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-(*tert*-butyldiphenylsilyl)oxy-1,2-(diethylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (42). The aldol reaction was performed according to the typical procedure (1.2 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **29** (28 mg, 0.056 mmol), silyl ketene thioacetal **20** (43 mg, 0.117 mmol), and $Sn(OTf)_2$ (47 mg, 0.113 mmol). The diastereomeric ratio of the products was determined to be 1:5 by ^{1}H NMR of the crude product (57 mg), from which an inseparable mixture of aldol adducts **42** (20 mg, 45%, **42a**:**42b**=1:5) was obtained as a colorless oil after flash column chromatography (silica gel 8 g, 7:1 *n*-hexane/AcOEt): $[\alpha]_D^{23}$ –25.8° (*c* 0.97, $CHCl_3$); IR (film) 3511, 2934, 1736, 1667, 1462, 1429, 1381, 1262, 1219, 1088, 741, 702 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) for **42b** δ 0.91 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 0.95 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.01 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.07 (s, 9H, SiC(CH_3)$_3$), 1.60–1.86 (m, 4H, 2×pentylidene CH_2), 1.72 (s, 3H, acetonide CH_3), 1.83 (s, 3H, acetonide CH_3), 2.09 (s, 3H, COSCH_3), 3.32 (dd, *J* = 4.3, 11.7 Hz, 1H, C1-*H*), 3.36 (dd, *J* = 7.9, 10.6 Hz, 1H, C*H*OBn), 3.56 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.66 (d, *J* = 0.8 Hz, 1H, O*H*), 3.76 (dd, *J* = 1.6, 11.7 Hz, 1H, C1-*H*), 3.87 (dd, *J* = 2.1, 10.6 Hz, 1H, C*H*OBn), 3.92 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.14 (ddd, *J* = 1.6, 4.3, 7.8 Hz, 1H, C7-*H*), 4.51 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.62 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.75 (dd, *J* = 0.8, 7.8 Hz, 1H, C6-*H*), 5.47 (dd, *J* = 2.1, 7.9 Hz, 1H, C3-*H*), 7.21–7.46 (m, 11H, Ar*H*), 7.64–7.75 (m, 4H, Ar*H*). The minor isomer (**42a**) had additional signals at 1.05 (s, 9H, SiC(CH_3)$_3$), 2.16 (s, 3H, COSCH_3), and 5.34 (dd, *J* = 1.6, 7.7 Hz, 1H, C3-*H*). FAB-LRMS *m*/*z* 795 $(M+H)^+$, 765 $(M–Et)^+$.

4.3.20. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[1,2-(diethylmethylenedioxy)-3-(methoxymethoxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)-carbonylpentanoate (43). The aldol reaction was performed according to the typical procedure (1.2 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **30** (18 mg, 0.059 mmol), silyl ketene thioacetal **20** (52 mg, 0.141 mmol), and $Sn(OTf)_2$ (54 mg, 0.13 mmol). The diastereomeric ratio of the products was determined to be 1.1:1 by ^{1}H NMR of the crude product (55 mg), from which aldol adducts **43a** (14.7 mg, 41%) and **43b** (13.5 mg, 38%) were obtained as colorless oils after flash column chromatography (silica gel 8 g, 10:1→6:1→4:1 *n*-hexane/AcOEt). Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**43a**): $[\alpha]_D^{27}$ –12.3° (*c* 0.66, $CHCl_3$); IR (film) 3462, 2930, 1732, 1672, 1458, 1383, 1256, 1219, 1098, 1042, 735, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 0.92 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.22 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.43–1.70 (m, 4H, 2×pentylidene CH_2), 1.65 (s, 3H, acetonide CH_3), 1.83 (s, 3H, acetonide CH_3), 2.17 (s, 3H, COSCH_3), 3.29 (dd, *J* = 7.8, 10.4 Hz, 1H, C*H*OBn), 3.35 (s, 3H, OCH_3), 3.65 (dd, *J* = 6.6, 10.8 Hz, 1H, C1-*H*), 3.83 (dd, *J* = 3.0, 10.8 Hz, 1H, C1-*H*), 3.83 (dd, *J* = 1.7, 10.4 Hz, 1H, C*H*OBn), 3.95 (s, 1H, O*H*), 3.99 (ddd, *J* = 3.0, 6.6, 8.3 Hz, 1H, C7-*H*), 4.13 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.19 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.39 (d, *J* = 8.3 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.64 (s, 2H, OCH_2O), 4.67 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.33 (dd, *J* = 1.7, 7.8 Hz, 1H, C3-*H*), 7.20–7.45 (m, 5H, Ar*H*); FAB-LRMS *m*/*z* 601 $(M+H)^+$, 543 $(M–C_4H_9)^+$. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**43b**): $[\alpha]_D^{27}$ –33.3° (*c* 0.67, $CHCl_3$); IR (film) 3525, 2932, 1736, 1671, 1458, 1383, 1261, 1149, 1096, 1043 cm^{-1}; ^{1}H NMR

(270 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 0.94 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.55–1.86 (m, 4H, 2×pentylidene C*H*$_2$), 1.71 (s, 3H, acetonide C*H*$_3$), 1.83 (s, 3H, acetonide C*H*$_3$), 2.11 (s, 3H, COSC*H*$_3$), 3.34 (s, 3H, OC*H*$_3$), 3.35 (dd, *J* = 7.8, 10.8 Hz, 1H, C*H*OBn), 3.40 (dd, *J* = 6.4, 11.2 Hz, 1H, C1-*H*), 3.50 (dd, *J* = 2.2, 11.2 Hz, 1H, C1-*H*), 3.69 (d, *J* = 0.7 Hz, 1H, O*H*), 3.88 (dd, *J* = 2.2, 10.8 Hz, 1H, C*H*OBn), 4.10 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.19 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.22 (ddd, *J* = 2.2, 6.4, 7.7 Hz, 1H, C7-*H*), 4.46 (dd, *J* = 0.7, 7.7 Hz, 1H, C6-*H*), 4.51 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.61 (s, 2H, OC*H*$_2$O), 4.62 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 5.41 (dd, *J* = 2.2, 7.8 Hz, 1H, C3-*H*), 7.20–7.40 (m, 5H, Ar*H*); FAB-LRMS *m*/*z* 601 $(M+H)^+$.

4.3.21. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxymethoxy-1,2-(diethylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (44). The aldol reaction was performed according to the typical procedure (1.2 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **31** (19.6 mg, 0.052 mmol), silyl ketene thioacetal **20** (51.0 mg, 0.138 mmol), and $Sn(OTf)_2$ (60 mg, 0.144 mmol). The diastereomeric ratio of the products was determined to be 1:1.6 by ^{1}H NMR of the crude product, from which aldol adducts **44a** (12.4 mg, 36%) and **44b** (18.9 mg, 54%) were obtained as colorless oils after flash column chromatography (silica gel 8 g, 6:1 *n*-hexane/AcOEt). Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**44a**): $[\alpha]_D^{27}$ –11.6° (*c* 0.55, $CHCl_3$); IR (film) 3462, 2936, 1734, 1671, 1456, 1380, 1256, 1171, 1096, 1042, 737, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.92 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.21 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.45–1.73 (m, 4H, 2×pentylidene C*H*$_2$), 1.65 (s, 3H, acetonide C*H*$_3$), 1.82 (s, 3H, acetonide C*H*$_3$), 2.17 (s, 3H, COSC*H*$_3$), 3.28 (dd, *J* = 7.8, 10.4 Hz, 1H, C*H*OBn), 3.72 (dd, *J* = 6.5, 10.8 Hz, 1H, C1-*H*), 3.86 (dd, *J* = 1.7, 10.4 Hz, 1H, C*H*OBn), 3.90 (dd, *J* = 3.0, 10.8 Hz, 1H, C1-*H*), 3.92 (s, 1H, O*H*), 4.01 (ddd, *J* = 3.0, 6.5, 8.3 Hz, 1H, C7-*H*), 4.13 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.16 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.43 (d, *J* = 8.3 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.6 Hz, 1H, OC*H*Ph), 4.61 (s, 2H, OC*H*$_2$O), 4.68 (d, *J* = 12.6 Hz, 1H, OC*H*Ph), 4.78 (s, 2H, OC*H*$_2$Ph), 5.34 (dd, *J* = 1.7, 7.8 Hz, 1H, C3-*H*), 7.22–7.39 (m, 10H, Ar*H*); FAB-LRMS *m*/*z* 677 $(M+H)^+$, 647 $(M–Et)^+$. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**44b**): $[\alpha]_D^{27}$ –27.2° (*c* 0.86, $CHCl_3$); IR (film) 3506, 2937, 1736, 1671, 1456, 1383, 1261, 1148, 1090, 1044, 735, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.3 Hz, 3H, pentylidene C*H*$_3$), 0.95 (t, *J* = 7.3 Hz, 3H, pentylidene C*H*$_3$), 1.14 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.55–1.87 (m, 4H, 2×pentylidene C*H*$_2$), 1.72 (s, 3H, acetonide C*H*$_3$), 1.84 (s, 3H, acetonide C*H*$_3$), 2.11 (s, 3H, COSC*H*$_3$), 3.35 (dd, *J* = 8.1, 10.6 Hz, 1H, C*H*OBn), 3.44 (dd, *J* = 6.6, 11.2 Hz, 1H, C1-*H*), 3.58 (dd, *J* = 2.2, 11.2 Hz, 1H, C1-*H*), 3.68 (s, 1H, O*H*), 3.88 (dd, *J* = 2.2, 10.6 Hz, 1H, C*H*OBn), 3.97 (dq, *J* = 10.6, 7.2 Hz, 1H, CO_2CHCH_3), 4.11 (dq, *J* = 10.6, 7.2 Hz, 1H, CO_2CHCH_3), 4.26 (m, 1H, C7-*H*), 4.48 (d, *J* = 8.1 Hz, 1H, C6-*H*), 4.51 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.59 (s, 2H, OC*H*$_2$Ph), 4.63 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.74 (d, *J* = 6.8 Hz, 1H, OC*H*O), 4.77 (d, *J* = 6.8 Hz, 1H, OC*H*O), 5.41 (dd, *J* = 2.2, 8.1 Hz, 1H, C3-*H*), 7.20–7.40 (m, 10H, Ar*H*); FAB-LRMS *m*/*z* 677 $(M+H)^+$, 647 $(M–Et)^+$.

4.3.22. Ethyl [2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[1,2-(diethylmethylenedioxy)-3-[(2-methoxyethoxy)methoxy]propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (45). The aldol reaction was performed according to the typical procedure (1.2 mL EtCN, –70 °C, 1.5 h) employing α-keto ester **32** (24 mg, 0.069 mmol), silyl ketene thioacetal **20** (52 mg, 0.141 mmol), and $Sn(OTf)_2$ (49 mg, 0.118 mmol). The diastereomeric ratio of the products was determined to be 1.6:1 by ^{1}H NMR of the crude product (58 mg), from which aldol adducts **45a** (22.6 mg, 51%) and **45b** (14.2 mg, 32%) were obtained as colorless oils after flash column chromatography (silica gel 8 g, 4:1→7:2 *n*-hexane/AcOEt). Data for [2*R*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**45a**): $[\alpha]_D^{25}$ –13.1° (*c* 1.0, $CHCl_3$); IR (film) 3459, 2938, 1732, 1672, 1462, 1377, 1254, 1175, 1046, 858, 793, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.91 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.22 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.55–1.70 (m, 4H, 2×pentylidene C*H*$_2$), 1.65 (s, 3H, acetonide C*H*$_3$), 1.83 (s, 3H, acetonide C*H*$_3$), 2.17 (s, 3H, COSC*H*$_3$), 3.29 (dd, *J* = 7.8, 10.4 Hz, 1H, C*H*OBn), 3.37 (s, 3H, OC*H*$_3$), 3.52–3.57 (m, 2H, OC*H*$_2$), 3.67 (dd, *J* = 6.4, 10.7 Hz, 1H, C1-*H*), 3.67–3.72 (m, 2H, OC*H*$_2$), 3.87 (dd, *J* = 1.4, 10.4 Hz, 1H, C*H*OBn), 3.88 (dd, *J* = 2.8, 10.7 Hz, 1H, C1-*H*), 3.98 (ddd, *J* = 2.8, 6.4, 8.4 Hz, 1H, C7-*H*), 3.99 (s, 1H, O*H*), 4.13 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.19 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.39 (d, *J* = 8.4 Hz, 1H, C6-*H*), 4.48 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.67 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.72 (s, 2H, OC*H*$_2$O), 5.33 (dd, *J* = 1.4, 7.8 Hz, 1H, C3-*H*), 7.27 (m, 1H, Ar*H*), 7.29–7.37 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8.1 (CH_3), 8.3 (CH_3), 11.8 (CH_3), 13.7 (CH_3), 26.2 (CH_3), 27.2 (CH_3), 29.1 (CH_2), 29.8 (CH_2), 58.9 (CH_3), 63.1 (CH_2), 66.7 (CH_2), 69.3 (CH_2), 70.3 (CH_2), 71.2 (CH_2), 73.1 (CH_2), 76.4 (CH), 77.9 (CH), 78.9 (CH), 79.1 (C), 93.6 (C), 95.4 (CH_2), 111.8 (C), 114.8 (C), 127.5 (CH), 127.6 (CH), 128.2 (CH), 138.3 (C), 170.6 (C=O), 193.7 (C=O); FAB-HRMS *m*/*z* calcd for $C_{31}H_{49}O_{12}S$ $(M+H)^+$ 645.2945, found 645.2916; Anal. calcd for $C_{31}H_{48}O_{12}S$: C, 57.75; H, 7.50; S, 4.97, found: C, 57.47; H, 7.43; S, 4.84. Data for [2*S*,2(1*R*,2*S*),3*S*,4*R*]-isomer (**45b**): $[\alpha]_D^{25}$ –33.5° (*c* 1.5, $CHCl_3$); IR (film) 3459, 2938, 1732, 1672, 1462, 1377, 1254, 1175, 1046, 858, 793, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 0.94 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.58–1.87 (m, 4H, 2×pentylidene C*H*$_2$), 1.71 (s, 3H, acetonide C*H*$_3$), 1.83 (s, 3H, acetonide C*H*$_3$), 2.11 (s, 3H, COSC*H*$_3$), 3.35 (dd, *J* = 7.8, 10.5 Hz, 1H, C*H*OBn), 3.42 (dd, *J* = 6.6, 11.2 Hz, 1H, C1-*H*), 3.38 (s, 3H, OC*H*$_3$), 3.52 (dd, *J* = 2.0, 11.2 Hz, 1H, C1-*H*), 3.52–3.57 (m, 2H, OC*H*$_2$), 3.63–3.72 (m, 2H, OC*H*$_2$), 3.69 (s, 1H, O*H*), 3.88 (dd, *J* = 2.0, 10.5 Hz, 1H, C*H*OBn), 4.09 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.19 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.22 (m, 1H, C7-*H*), 4.45 (d, *J* = 7.9 Hz, 1H, C6-*H*), 4.51 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.69 (d, *J* = 6.8 Hz, 1H, OC*H*O), 4.71 (d, *J* = 6.8 Hz, 1H, OC*H*O), 5.40 (dd, *J* = 2.0, 7.8 Hz, 1H, C3-

H), 7.25 (m, 1H, Ar*H*), 7.29–7.38 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.5 (CH_3), 8.5 (CH_3), 11.8 (CH_3), 13.7 (CH_3), 26.0 (CH_3), 27.4 (CH_3), 29.3 (CH_2), 30.0 (CH_2), 58.9 (CH_3), 62.5 (CH_2), 66.8 (CH_2), 68.1 (CH_2), 70.2 (CH_2), 71.6 (CH_2), 73.1 (CH_2), 76.0 (CH), 76.8 (CH), 79.0 (C), 79.9 (CH), 90.7 (C), 95.5 (CH_2), 113.2 (C), 114.9 (C), 127.4 (CH), 127.5 (CH), 128.2 (CH), 138.1 (C), 170.9 (C=O), 205.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{31}H_{49}O_{12}S$ $(M+H)^+$ 645.2945, found 645.2950.

4.3.23. Ethyl [3*R*,3(1*R*,2*S*),4*S*,8*R*]-3-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-8-(benzyloxymethyl)-6,6-dimethyl-1-oxo-2,5,7-trioxaspiro[3.4]octane-3-carboxylate (46a). $Hg(OCOCF_3)_2$ (133 mg, 0.31 mmol) was added to a stirred solution of thioester **37a** (98 mg, 0.15 mmol) in MeCN (16 mL). After stirring for 200 h, the reaction mixture was evaporated in vacuo. The residue was suspended in Et_2O and passed through a short plug of silica gel (eluting with Et_2O) to remove insoluble Hg salt. Purification of the residue (97 mg) by column chromatography (silica gel 5 g, 11:1 *n*-hexane/AcOEt) afforded β-lactone **46a** (52 mg, 58%) as a colorless oil: $[\alpha]_D^{29}$ +18.6° (*c* 1.15, $CHCl_3$); IR (film) 2978, 1848, 1730, 1456, 1379, 1219, 1103, 1094 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.17 (t, *J* = 7.0 Hz, 3H, $CO_2CH_2CH_3$), 1.35 (s, 3H, acetonide C*H*$_3$), 1.41 (s, 3H, acetonide C*H*$_3$), 1.59–1.72 (m, 4H, 2×pentylidene C*H*$_2$), 3.50 (dd, *J* = 7.9, 8.2 Hz, 1H, C*H*OBn), 3.64 (dd, *J* = 5.5, 10.6 Hz, 1H, C1-*H*), 3.76 (dd, *J* = 6.0, 8.2 Hz, 1H, C*H*OBn), 3.78 (dd, *J* = 5.5, 10.6 Hz, 1H, C1-*H*), 3.96 (dq, *J* = 10.6, 7.0 Hz, 1H, CO_2CHCH_3), 4.27 (dq, *J* = 10.6, 7.0 Hz, 1H, CO_2CHCH_3), 4.37 (m, 1H, C7-*H*), 4.39 (d, *J* = 11.9 Hz, 1H, OC*H*Ph), 4.51 (d, *J* = 11.9 Hz, 1H, OC*H*Ph), 4.60 (s, 2H, OC*H*$_2$Ph), 4.63 (d, *J* = 6.5 Hz, 1H, C6-*H*), 4.81 (dd, *J* = 6.0, 7.9 Hz, 1H, C3-*H*), 7.25–7.37 (m, 10H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 8.0 (CH_3), 8.1 (CH_3), 8.2 (CH_3), 13.9 (CH_3), 24.9 (CH_3), 26.4 (CH_2), 26.5 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 62.1 (CH_2), 68.1 (CH_2), 70.1 (CH_2), 73.4 (CH), 73.8 (CH), 76.4 (CH), 85.6 (C), 94.2 (C), 113.3 (C), 114.6 (C), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.9 (CH), 136.9 (C), 138.1 (C), 166.1 (C=O), 167.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{33}H_{43}O_{10}$ $(M+H)^+$ 599.2856, found 599.2826.

4.3.24. Ethyl [2*R*,2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methoxycarbonyl)pentanoate. Potassium carbonate (15.6 mg, 0.113 mmol) was added to a solution of β-lactone **46a** (51.6 mg, 0.086 mmol) in MeOH (1.5 mL). After stirring for 1.5 h, the mixture was partitioned between AcOEt (10 mL) and brine (7 mL). The organic extract was washed successively with saturated aqueous NH_4Cl (7 mL) and brine (7 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (57.3 mg), which was purified by column chromatography (silica gel 8 g, 7:2 *n*-hexane/AcOEt) to give methyl ester (46.5 mg, 86%) as a colorless oil: $[\alpha]_D^{28}$ –5.20° (*c* 1.0, $CHCl_3$); IR (film) 3464, 2976, 2940, 1732, 1497, 1454, 1372, 1258, 1090, 936 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 0.90 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.24 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.53 (q, *J* = 7.4 Hz, 2H, pentylidene C*H*$_2$), 1.55 (s, 3H, acetonide C*H*$_3$), 1.62 (q, *J* = 7.5 Hz, 2H, pentylidene C*H*$_2$), 1.64 (s, 3H, acetonide C*H*$_3$), 3.40 (dd, *J* = 6.3, 10.6 Hz, 1H, C*H*OBn), 3.60 (dd, *J* = 5.8, 10.3 Hz, 1H, C1-*H*), 3.61 (s, 3H, CO_2CH_3), 3.70 (dd, *J* = 3.9, 10.3 Hz, 1H, C1-*H*), 3.90 (dd, *J* = 1.3, 10.6 Hz, 1H, C*H*OBn), 4.00 (ddd, *J* = 3.9, 5.8, 8.6 Hz, 1H, C7-*H*), 4.14 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.20 (s, 1H, O*H*), 4.24 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.41 (d, *J* = 8.6 Hz, 1H, C6-*H*), 4.51 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 4.57 (s, 2H, OC*H*$_2$Ph), 4.62 (d, *J* = 12.4 Hz, 1H, OC*H*Ph), 5.34 (dd, *J* = 1.3, 6.3 Hz, 1H, C3-*H*), 7.26–7.33 (m, 10H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8.1 (CH_3), 8.2 (CH_3), 13.8 (CH_3), 26.7 (CH_3), 27.2 (CH_3), 29.3 (CH_2), 29.9 (CH_2), 52.2 (CH_3), 62.8 (CH_2), 70.1 (CH_2), 71.5 (CH_2), 73.3 (CH_2), 73.4 (CH_2), 77.6 (CH), 78.8 (CH), 79.2 (C), 89.6 (C), 111.2 (C), 114.4 (C), 127.5 (CH), 127.6 (CH), 127.7 (CH), 128.2 (CH), 128.3 (CH), 137.7 (C), 138.3 (C), 170.5 (C=O), 171.3 (C=O); FAB-HRMS *m*/*z* calcd for $C_{34}H_{47}O_{11}$ $(M+H)^+$ 631.3118, found 631.3139.

4.3.25. Ethyl [2*R*,2(3a*S*,6a*R*),3*R*,4*S*]-3,4-(diethylmethylenedioxy)-2,5-dihydroxy-2-(tetrahydro-2,2-dimethyl-4-oxofuro[3,4-*d*][1,3]dioxol-3a-yl)pentanoate (47a). Palladium on carbon (10%, 10.8 mg) was added to a solution of benzyl ether (46.2 mg, 0.073 mmol) in MeOH (2 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 1 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. The crude product (32.9 mg) thus obtained was used without further purification.

DMAP (38.6 mg, 0.316 mmol) was added to a solution of the crude γ-hydroxyester (32.9 mg) in MeCN (1.5 mL). After stirring for 1.5 h, the reaction was quenched with saturated aqueous NH_4Cl (6 mL), and the whole was extracted with AcOEt (15 mL). The organic extract was washed with brine (6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (36.5 mg), which was purified by column chromatography (silica gel 5 g, 2:1 *n*-hexane/AcOEt) to give γ-lactone **47a** (30.0 mg, 98%) as a colorless oil: $[\alpha]_D^{28}$ –77.5° (*c* 1.01, $CHCl_3$); IR (film) 3480, 2978, 2942, 1790, 1730, 1464, 1377, 1256, 1171, 1090, 976 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.89 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 1.35 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.46 (s, 3H, acetonide C*H*$_3$), 1.50 (s, 3H, acetonide C*H*$_3$), 1.58 (q, *J* = 7.4 Hz, 2H, pentylidene C*H*$_2$), 1.64 (q, *J* = 7.5 Hz, 2H, pentylidene C*H*$_2$), 2.23 (br s, 1H, O*H*), 3.92 (dd, *J* = 4.7, 9.5 Hz, 1H, one of lactone C*H*$_2$), 4.00 (dd, *J* = 9.5, 10.4 Hz, 1H, one of lactone C*H*$_2$), 4.23 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.35 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.36 (dd, *J* = 3.7, 11.2 Hz, 1H, C1-*H*), 4.38 (dd, *J* = 7.9, 11.2 Hz, 1H, C1-*H*), 4.39 (s, 1H, O*H*), 4.48 (ddd, *J* = 3.7, 4.4, 7.9 Hz, 1H, C7-*H*), 4.61 (dd, *J* = 4.7, 10.4 Hz, 1H, C3-*H*), 5.05 (d, *J* = 4.4 Hz, 1H, C6-*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8.1 (CH_3), 8.2 (CH_3), 14.2 (CH_3), 27.1 (CH_3), 27.2 (CH_3), 30.0 (CH_2), 30.2 (CH_2), 63.15 (CH_2), 63.21 (CH_2), 73.1 (CH_2), 76.8 (CH), 77.8 (CH), 79.0 (CH), 79.1 (C), 85.1 (C),

113.4 (C), 114.2 (C), 171.5 (C=O), 176.1 (C=O); FAB-HRMS *m*/*z* calcd for $C_{19}H_{31}O_{10}$ $(M+H)^+$ 419.1917, found 419.1890.

4.3.26. Ethyl [3*S*,3(1*R*,2*S*),4*S*,8*R*]-3-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-8-(benzyloxymethyl)-6,6-dimethyl-1-oxo-2,5,7-trioxaspiro[3.4]octane-3-carboxylate (46b). $Hg(OCOCF_3)_2$ (155 mg, 0.36 mmol) was added to a stirred solution of thioester **37b** (112 mg, 0.17 mmol) in MeCN (18 mL). After stirring for 10 h, the reaction mixture was evaporated in vacuo. The residue was suspended in Et_2O and passed through a short plug of silica gel (eluting with Et_2O) to remove insoluble Hg salt. Purification of the residue by column chromatography (silica gel 5 g, 8:1 *n*-hexane/AcOEt) afforded β-lactone **46b** (74.5 mg, 72%) as a colorless oil: $[\alpha]_D^{29}$ +6.52° (*c* 1.09, $CHCl_3$); IR (film) 2980, 2939, 2882, 1852, 1762, 1738, 1497, 1454, 1375, 1273, 1204, 1171, 1098, 1026, 937 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.76 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.86 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 1.21 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.38 (s, 3H, acetonide C*H*$_3$), 1.42–1.67 (m, 4H, 2×pentylidene C*H*$_2$), 1.53 (s, 3H, acetonide C*H*$_3$), 3.46 (dd, *J* = 6.6, 11.0 Hz, 1H, C1-*H*), 3.58 (dd, *J* = 3.2, 11.0 Hz, 1H, C1-*H*), 3.72 (dd, *J* = 8.7, 9.7 Hz, 1H, C*H*OBn), 3.87 (dd, *J* = 2.0, 9.7 Hz, 1H, C*H*OBn), 4.09 (ddd, *J* = 3.2, 6.6, 8.1 Hz, 1H, C7-*H*), 4.10 (q, *J* = 7.2 Hz, 2H, $CO_2CH_2CH_3$), 4.49 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.52 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.56 (d, *J* = 12.5 Hz, 1H, OC*H*Ph), 4.61 (d, *J* = 8.1 Hz, 1H, C6-*H*), 4.68 (d, *J* = 12.0 Hz, 1H, OC*H*Ph), 4.94 (dd, *J* = 2.0, 8.7 Hz, 1H, C3-*H*), 7.26–7.38 (m, 10H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.8 (CH_3), 7.9 (CH_3), 13.9 (CH_3), 25.8 (CH_3), 27.2 (CH_3), 29.6 (CH_2), 29.9 (CH_2), 62.5 (CH_2), 69.2 (CH_2), 70.6 (CH_2), 73.6 (CH_2), 73.7 (CH_2), 75.2 (CH), 76.2 (CH), 79.0 (CH), 85.7 (CH), 96.4 (C), 113.7 (C), 114.5 (C), 127.65 (C), 127.70 (CH), 127.74 (CH), 128.0 (CH), 128.35 (CH), 128.37 (CH), 137.70 (C), 137.73 (C), 165.3 (C=O), 166.6 (C=O); FAB-HRMS *m*/*z* calcd for $C_{33}H_{43}O_{10}$ $(M+H)^+$ 599.2856, found 599.2830.

4.3.27. Ethyl [2*S*,2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[3-benzyloxy-1,2-(diethylmethylenedioxy)propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methoxycarbonyl)pentanoate. Potassium carbonate (22.0 mg, 0.159 mmol) was added to a solution of β-lactone **46b** (74.5 mg, 0.124 mmol) in MeOH (1.5 mL). After stirring for 1.5 h, the mixture was partitioned between AcOEt (10 mL) and brine (7 mL). The organic extract was washed successively with saturated aqueous NH_4Cl (7 mL) and brine (7 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (85.3 mg), which was purified by column chromatography (silica gel 8 g, 5:1 *n*-hexane/AcOEt) to give methyl ester (78.3 mg, quant.) as a colorless oil: $[\alpha]_D^{30}$ +6.76° (*c* 1.0, $CHCl_3$); IR (film) 3513, 2978, 2942, 1738, 1496, 1454, 1372, 1262, 1221, 1093, 932 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 0.94 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.09 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.61 (s, 3H, acetonide C*H*$_3$), 1.66 (s, 3H, acetonide C*H*$_3$), 1.73 (m, 2H, pentylidene C*H*$_2$), 1.77 (m, 2H, pentylidene C*H*$_2$), 3.26 (dd, *J* = 2.5, 10.7 Hz, 1H, C1-*H*), 3.35 (dd, *J* = 6.4, 10.7 Hz, 1H, C1-*H*), 3.42 (dd, *J* = 6.8, 11.0 Hz, 1H, C*H*OBn), 3.56 (s, 3H, CO_2CH_3), 3.63 (s, 1H, O*H*), 3.74 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 3.84 (dd, *J* = 2.3, 11.0 Hz, 1H, C*H*OBn), 3.93 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.29 (ddd, *J* = 2.5, 6.4, 8.1 Hz, 1H, C7-*H*), 4.40 (d, *J* = 8.1 Hz, 1H, C6-*H*), 4.47 (d, *J* = 12.6 Hz, 1H, OC*H*Ph), 4.55 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.59 (d, *J* = 12.2 Hz, 1H, OC*H*Ph), 4.62 (d, *J* = 12.6 Hz, 1H, OC*H*Ph), 5.30 (dd, *J* = 2.3, 6.8 Hz, 1H, C3-*H*), 7.22–7.36 (m, 10H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8.7 (CH_3), 9.7 (CH_3), 14.9 (CH_3), 27.6 (CH_3), 28.4 (CH_3), 30.5 (CH_2), 31.4 (CH_2), 53.1 (CH_3), 63.3 (CH_2), 71.0 (CH_2), 71.9 (CH_2), 74.4 (CH_2), 74.5 (CH_2), 77.0 (CH), 78.4 (CH), 78.7 (CH), 79.8 (CH), 80.8 (C), 87.7 (C), 113.9 (C), 115.8 (C), 128.6 (CH), 128.75 (CH), 128.79 (CH), 129.0 (CH), 129.1 (CH), 129.2 (CH), 129.4 (CH), 129.5 (CH), 139.1 (C), 139.2 (C), 173.1 (C=O), 173.8 (C=O); FAB-HRMS *m*/*z* calcd for $C_{34}H_{47}O_{11}$ $(M+H)^+$ 631.3118, found 631.3152.

4.3.28. Ethyl [2*S*,2(3a*S*,6a*R*),3*R*,4*S*]-3,4-(diethylmethylenedioxy)-2,5-dihydroxy-2-(tetrahydro-2,2-dimethyl-4-oxofuro[3,4-*d*][1,3]dioxol-3a-yl)pentanoate (47b). Palladium on carbon (10%, 11.7 mg) was added to a solution of benzyl ether (78.3 mg, 0.124 mmol) in MeOH (2 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 1 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. The crude product (64.3 mg) thus obtained was used without further purification.

DMAP (76.4 mg, 0.625 mmol) was added to a solution of the crude γ-hydroxyester (64.3 mg) in MeCN (1 mL). After stirring for 1.5 h, the reaction was quenched with saturated aqueous NH_4Cl (6 mL), and the whole was extracted with AcOEt (10 mL). The organic extract was washed with brine (6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (68 mg), which was purified by column chromatography (silica gel 5 g, 2:1 *n*-hexane/AcOEt) to give γ-lactone **47b** (46.2 mg, 89%) as a colorless oil: $[\alpha]_D^{28}$ –49.9° (*c* 1.5, $CHCl_3$); IR (film) 3459, 2978, 2942, 2883, 1782, 1730, 1462, 1377, 1206, 1022, 928, 907 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.91 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.40 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.43 (s, 3H, acetonide C*H*$_3$), 1.48 (s, 3H, acetonide C*H*$_3$), 1.67 (q, *J* = 7.5 Hz, 2H, pentylidene C*H*$_2$), 1.71 (q, *J* = 7.5 Hz, 2H, pentylidene C*H*$_2$), 1.97 (br s, 1H, O*H*), 3.38 (dd, *J* = 3.3, 12.2 Hz, 1H, one of lactone C*H*$_2$), 3.72 (dd, *J* = 1.6, 12.2 Hz, 1H, one of lactone C*H*$_2$), 4.11 (m, 2H, C1-*H*$_2$), 4.32 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.35 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.37 (s, 1H, O*H*), 4.40 (ddd, *J* = 3.6, 3.9, 8.1 Hz, 1H, C7-*H*), 4.49 (d, *J* = 8.1 Hz, 1H, C6-*H*), 5.51 (dd, *J* = 1.6, 3.3 Hz, 1H, C3-*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.8 (CH_3), 8.2 (CH_3), 13.9 (CH_3), 26.5 (CH_3), 27.4 (CH_3), 29.6 (CH_2), 29.9 (CH_2), 61.9 (CH_2), 63.6 (CH_2), 71.5 (CH_2), 76.1 (CH), 76.5 (CH), 77.1 (CH), 78.5 (C), 85.9 (C), 114.0 (C), 114.3 (C), 170.8 (C=O), 175.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{19}H_{31}O_{10}$ $(M+H)^+$ 419.1917, found 419.1925.

4.3.29. Isomerization of 45b to 45a. KHMDS in toluene (0.5 M, 1.54 mL, 0.77 mmol) was added to a solution of

undesired isomer **45b** (332 mg, 0.51 mmol) in THF (5 mL) at –78 °C under an argon atmosphere, and the resulting mixture was stirred at –23 °C for 2 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the whole was extracted with AcOEt (20 mL). The organic extract was washed with brine (2×5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (308 mg), which was purified by flash column chromatography (silica gel 10 g, 15:1→3:1 *n*-hexane/AcOEt) to give desired isomer **45a** (77 mg, 23%) as a colorless oil, along with thioester **14** (30 mg, 20%) as a pale yellow oil.

4.3.30. Aldol reaction of α-keto ester 32 with potassium enolate 48 generated from thioester 14. A solution of thioester **14** (34 mg, 0.115 mmol) in THF (0.2 mL) was added to a 0.6 M solution of KHMDS in toluene (0.23 mL, 0.137 mmol) at –78 °C. After stirring at –78 °C for 30 min, a solution of α-keto ester **32** (20 mg, 0.057 mmol) in THF (0.2 mL) was added. After stirring at –23 °C for 1 h, the reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the whole was extracted with AcOEt (15 mL). The organic extract was washed with brine (8 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (62 mg), whose ^{1}H NMR revealed a **45a**/**45b** ratio of 2:1. Purification by column chromatography (silica gel 8 g, 4:1→7:2 *n*-hexane/AcOEt) afforded aldol adducts **45a** (8.9 mg, 23%) and **45b** (4.4 mg, 12%) as colorless oils.

4.4. Synthesis of internal ketalization precursor

4.4.1. Diethyl (4*R*,5*R*)-2,2-diethyl-1,3-dioxolane-4,5-dicarboxylate. *p*-Toluenesulfonic acid (202 mg, 1.6 mmol) was added to a stirred solution of diethyl L-(+)-tartrate (26.2 g, 0.127 mol) and 3,3-dimethoxypentane (25.1 g, 0.190 mol) in benzene (200 mL). The flask was fitted with a Soxhlet extractor and reflux condenser, and a thimble containing freshly activated 4Å molecular sieves (11 g) was placed in the Soxhlet extractor. The whole was refluxed for 3 h, during which time the thimble was recharged with fresh sieves every 1 h. The reaction mixture was cooled to room temperature, and anhydrous K_2CO_3 (400 mg) was added. After stirring at room temperature for 10 min, the mixture was filtered, and the filtrate was evaporated in vacuo. The residue was partitioned between AcOEt (150 mL) and water (50 mL). The organic extract was washed successively with water (50 mL), saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by distillation under reduced pressure afforded the title compound (19.59 g, 96%) as a pale yellow oil: bp 124–125 °C (0.1 mmHg); $[\alpha]_D^{22}$ –20.2° (*c* 1.3, $CHCl_3$); IR (film) 2980, 2943, 1757, 1466, 1200, 1113 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.5 Hz, 6H, 2×pentylidene C*H*$_3$), 1.32 (t, *J* = 7.1 Hz, 6H, 2×$CO_2CH_2CH_3$), 1.74 (q, *J* = 7.5 Hz, 4H, 2×pentylidene C*H*$_2$), 4.28 (q, *J* = 7.1 Hz, 4H, 2×$CO_2CH_2CH_3$), 4.71 (s, 2H, 2×C*H*CO_2Et); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 7.8 (CH_3), 14.1 (CH_2), 29.6 (CH_2), 61.8 (CH_2), 77.4 (CH), 117.8 (C), 169.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{13}H_{23}O_6$ $(M+H)^+$ 275.1495, found 275.1506; Anal. calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08, found: C, 56.72; H, 8.01.

4.4.2. (2*S*,3*S*)-2,3-(Diethylmethylenedioxy)butane-1,4-diol. A solution of the diester (30.2 g, 0.11 mol) in THF (50 mL) was added dropwise over a 50-min period to a stirred suspension of $LiAlH_4$ (8.3 g, 0.22 mol) in THF (200 mL) at 0 °C. After stirring at 0 °C for 40 min, the reaction was quenched by dropwise addition of water (8 mL) followed by 15% aqueous NaOH (8 mL) and water (24 mL). The mixture was stirred vigorously for 10 min, and then anhydrous $MgSO_4$ was added. After stirring at room temperature for additional 1 h, the suspension was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the residue by column chromatography (silica gel 60 g, 2:1→1:2 *n*-hexane/AcOEt) afforded the title compound (19.0 g, 91%) as a white solid: mp 39.5–41.5 °C; $[\alpha]_D^{22}$ +5.05° (*c* 5.00, $CHCl_3$); IR (film) 3410 (br), 2934, 1464, 1201, 1172, 1053 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.5 Hz, 6H, 2×pentylidene C*H*$_3$), 1.67 (q, *J* = 7.5 Hz, 4H, 2×pentylidene C*H*$_2$), 2.44 (br s, 2H, O*H*), 3.67–3.85 (m, 4H, 2×C*H*$_2$OH), 3.97 (m, 2H, 2×OC*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 8.0 (CH_3), 30.4 (CH_2), 61.2 (CH_2), 78.4 (CH), 113.0 (C); FAB-HRMS *m*/*z* calcd for $C_9H_{19}O_4$ $(M+H)^+$ 191.1285, found 191.1290.

4.4.3. (2*S*,3*S*)-2,3-Diethylmethylenedioxy-4-[(2-methoxyethoxy)methoxy]-1-butanol. A solution of the diol (2.00 g, 10.5 mmol) in THF (6 mL) was added dropwise to a suspension of NaH (60% in oil, 430 mg, 10.8 mmol) in THF (40 mL). After stirring at room temperature for 1 h, the mixture was cooled to 0 °C, and MEMCl (1.82 mL, 10.5 mmol) was added. After stirring at 0 °C for 1.5 h, the mixture was poured into brine (100 mL), and the whole was extracted with AcOEt (2×50 mL). The combined organic extracts were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 50 g, 1:1 *n*-hexane/AcOEt) afforded the title compound (2.72 g, 93%) as a colorless oil: $[\alpha]_D^{25}$ –7.16° (*c* 1.0, EtOH); IR (film) 3472 (br), 2973, 2938, 2882, 1464, 1202, 1175, 1092, 1046, 982, 934, 849 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.92 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.60–1.73 (m, 4H, 2×pentylidene C*H*$_2$), 2.25 (br s, 1H, O*H*), 3.39 (s, 3H, OC*H*$_3$), 3.53–3.60 (m, 2H, OC*H*$_2$), 3.65–3.83 (m, 6H, 3×OC*H*$_2$), 3.91 (dt, *J* = 8.5, 4.2 Hz, 1H, OC*H*), 4.03 (dt, *J* = 8.5, 5.2 Hz, 1H, OC*H*), 4.75 (s, 2H, OC*H*$_2$O); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8.0 (CH_3), 30.36 (CH_2), 30.41 (CH_2), 59.0 (CH_3), 62.6 (CH_2), 67.0 (CH_2), 68.1 (CH_2), 71.7 (CH_2), 76.8 (CH), 79.6 (CH), 97.5 (CH_2), 113.2 (C); FAB-HRMS *m*/*z* calcd for $C_{13}H_{27}O_6$ $(M+H)^+$ 279.1808, found 279.1795.

4.4.4. (2*R*,3*S*)-2,3-(Diethylmethylenedioxy)-4-[(2-methoxyethoxy)methoxy]butyric acid. A solution of DMSO (1.1 mL, 15.5 mmol) in CH_2Cl_2 (3 mL) was added to a stirred solution of oxalyl chloride (1.1 mL, 12.6 mmol) in CH_2Cl_2 (40 mL) at –78 °C. After 15 min, a solution of the alcohol (2.00 g, 10.5 mmol) in CH_2Cl_2 (7 mL) was added, and the mixture was stirred for 15 min. Et_3N (15 mL, 110 mmol) was added, and the resulting mixture was stirred at

–40 °C for 15 min. The reaction mixture was poured into pH 7 phosphate buffer (100 mL), and the whole was extracted with Et_2O (50 mL). The aqueous layer was saturated with NaCl and extracted with Et_2O (3×30 mL). The combined organic extracts were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.77 g), which was used without further purification for the next reaction.

A solution of NaH_2PO_4 (1.30 g, 10.8 mmol) in water (12 mL) was added to a solution of the crude aldehyde (2.77 g) and 2-methyl-2-butene (7 mL, 66 mmol) in *tert*-butyl alcohol (50 mL). $NaClO_2$ (4.70 g, 40.5 mmol) was added portionwise to the mixture. After stirring at room temperature for 8 h, the mixture was evaporated in vacuo. The residue was dissolved in 10% aqueous NaOH (5 mL) and water (30 mL), and the whole was washed with 1:1 *n*-hexane/Et_2O (3×20 mL). The aqueous layer was acidified with 10% aqueous HCl (8 mL), saturated with NaCl, and extracted with AcOEt (3×50 mL). The combined organic extracts were washed with brine (3×50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 25 g, 10:1 $CHCl_3$/MeOH) afforded the title compound (2.26 g, 79%) as a colorless oil: $[\alpha]_D^{23}$ –8.26° (*c* 2.0, $CHCl_3$); IR (film) 3700–3300 (br), 2940, 1736, 1462, 1175, 1107, 1044, 982, 928, 849 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 0.95 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 1.71 (q, *J* = 7.4 Hz, 4H, 2×pentylidene C*H*$_2$), 3.40 (s, 3H, OC*H*$_3$), 3.56–3.61 (m, 2H, OC*H*$_2$), 3.70–3.75 (m, 2H, OC*H*$_2$), 3.77 (dd, *J* = 5.3, 11.1 Hz, 1H, C1-*H*), 3.93 (dd, *J* = 2.9, 11.1 Hz, 1H, C1-*H*), 4.31 (ddd, *J* = 2.9, 5.3, 8.4 Hz, 1H, C7-*H*), 4.40 (d, *J* = 8.4 Hz, 1H, C6-*H*), 4.78 (d, *J* = 6.8 Hz, 1H, OC*H*O), 4.80 (d, *J* = 6.8 Hz, 1H, OC*H*O), 8.5 (br s, 1H, COO*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.5 (CH_3), 8.2 (CH_3), 29.7 (CH_2), 29.8 (CH_2), 58.9 (CH_3), 66.9 (CH_2), 67.1 (CH_2), 71.7 (CH_2), 75.5 (CH), 78.4 (CH), 95.8 (CH_2), 115.9 (C), 173.7 (C=O); FAB-HRMS *m*/*z* calcd for $C_{13}H_{25}O_7$ $(M+H)^+$ 293.1600, found 293.1619.

4.4.5. (2*R*,3*S*)-2,3-(Diethylmethylenedioxy)-*N*-methoxy-4-[(2-methoxyethoxy)methoxy]-*N*-methylbutanamide. To a solution of the carboxylic acid (199 mg, 0.682 mmol) in DMF (5 mL) at 0 °C was added *N*,*O*-dimethylhydroxylamine hydrochloride (110 mg, 1.13 mmol), followed by addition of diethyl cyanophosphonate (DEPC, 0.12 mL, 0.791 mmol) and Et_3N (0.26 mL, 1.87 mmol). After stirring at room temperature for 1.5 h, the reaction was quenched with 1N aqueous HCl (5 mL), and the whole was extracted with AcOEt (2×15 mL). The combined organic extracts were washed successively with brine (8 mL), saturated aqueous $NaHCO_3$ (10 mL) and brine (8 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (267 mg), which was purified by column chromatography (silica gel 10 g, 3:2 *n*-hexane/AcOEt) to give the title compound (203 mg, 89%) as a colorless oil: $[\alpha]_D^{24}$ –17.1° (*c* 2.0, benzene); IR (film) 2940, 1672, 1464, 1175, 1098, 1046, 993, 932, 846 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.926 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.931 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.65–1.79 (m, 4H, 2×pentylidene C*H*$_2$), 3.24 (s, 3H, NC*H*$_3$), 3.39 (s, 3H, OC*H*$_3$), 3.53–3.59 (m, 2H, OC*H*$_2$), 3.65–3.74 (m, 3H, OC*H*$_2$, C1-*H*), 3.75 (s, 3H, NOC*H*$_3$), 3.82 (dd, *J* = 3.2, 10.8 Hz, 1H, C1-*H*), 4.48–4.68 (m, 2H, C6-*H*, C7-*H*), 4.76 (d, *J* = 6.8 Hz, 1H, OC*H*O), 4.78 (d, *J* = 6.8 Hz, 1H, OC*H*O); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.6 (CH_3), 8.2 (CH_3), 29.5 (CH_2), 29.9 (CH_2), 32.2 (CH_3), 58.8 (CH_3), 61.6 (CH_3), 66.8 (CH_2), 67.2 (CH_2), 71.6 (CH_2), 74.1 (CH), 77.5 (CH), 95.7 (CH_2), 114.9 (C), 169.9 (C=O); FAB-HRMS *m*/*z* calcd for $C_{15}H_{30}NO_7$ $(M+H)^+$ 336.2022, found 336.2016.

4.4.6. (4*R*,5*S*)-4,5-(Diethylmethylenedioxy)-2-ethoxy-6-[(2-methoxyethoxy)methoxy]-1-hexen-3-one. *tert*-Butyllithium in pentane (2.13 M, 6.0 mL, 12.8 mmol) was added to a stirred solution of ethyl vinyl ether (1.4 mL, 14.7 mmol) in THF (18 mL) at –78 °C. After stirring at 0 °C for 30 min, the mixture was added to a stirred solution of the amide (1.38 g, 4.12 mmol) in THF (30 mL) at –78 °C via cannula over a 20-min period. After stirring at –78 °C for 30 min, the reaction was quenched with saturated aqueous NH_4Cl (50 mL), and the whole was partitioned between AcOEt (100 mL) and water (30 mL). The organic extract was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 15 g, 4:1 *n*-hexane/AcOEt) afforded the title compound (1.29 g, 90%) as a colorless oil: $[\alpha]_D^{23}$ –35.1° (*c* 1.0, $CHCl_3$); IR (film) 2976, 2940, 1732, 1611, 1462, 1366, 1287, 1175, 1098, 1046, 978, 851 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.4 Hz, 6H, 2×pentylidene C*H*$_3$), 1.40 (t, *J* = 7.0 Hz, 3H, OCH$_2$C*H*$_3$), 1.66 (q, *J* = 7.4 Hz, 2H, pentylidene C*H*$_2$), 1.73 (q, *J* = 7.4 Hz, 2H, pentylidene C*H*$_2$), 3.39 (s, 3H, OC*H*$_3$), 3.52–3.60 (m, 2H, OC*H*$_2$), 3.68–3.77 (m, 3H, OC*H*$_2$, C1-*H*), 3.85 (q, *J* = 7.0 Hz, 2H, OC*H*$_2$CH$_3$), 3.92 (dd, *J* = 3.0, 10.9 Hz, 1H, C1-*H*), 4.35 (ddd, *J* = 3.0, 6.4, 7.3 Hz, 1H, C7-*H*), 4.60 (d, *J* = 2.8 Hz, 1H, C=C*H*), 4.77 (d, *J* = 6.8 Hz, 1H, OC*H*O), 4.79 (d, *J* = 6.8 Hz, 1H, OC*H*O), 4.84 (d, *J* = 7.3 Hz, 1H, C6-*H*), 5.35 (d, *J* = 2.8 Hz, 1H, C=C*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 7.7 (CH_3), 8.3 (CH_3), 14.2 (CH_3), 29.6 (CH_2), 30.1 (CH_2), 59.0 (CH_3), 63.9 (CH_2), 66.9 (CH_2), 68.1 (CH_2), 71.7 (CH_2), 77.7 (CH), 78.7 (CH), 93.8 (CH_2), 95.8 (CH_2), 115.5 (C), 156.5 (CH_2), 193.7 (C=O); FAB-HRMS *m*/*z* calcd for $C_{17}H_{31}O_7$ $(M+H)^+$ 347.2070, found 347.2044.

4.4.7. Ethyl (3*R*,4*S*)-3,4-(diethylmethylenedioxy)-5-[(2-methoxyethoxy)methoxy]-2-oxopentanoate (32). A stream of ozone in oxygen was bubbled through a stirred solution of the enone (1.27 g, 3.67 mmol) in CH_2Cl_2 (15 mL) at –78 °C until the solution turned pale blue. After stirring at –78 °C for 10 min, excess ozone was removed by bubbling a stream of nitrogen, and Me_2S (3 mL) was added. After stirring at room temperature for 1 h, the volatile elements were removed in vacuo. The residue was purified by column chromatography (silica gel 20 g, 4:1 *n*-hexane/AcOEt) to give α-keto ester **32** (1.10 g, 86%) as a colorless oil: $[\alpha]_D^{24}$ +7.71° (*c* 2.0, $CHCl_3$); IR (film) 2976, 2940, 1732, 1611, 1462, 1366, 1287, 1175, 1098, 1046, 978, 851 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.5 Hz,

3H, pentylidene CH_3), 0.92 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.38 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.57–1.76 (m, 4H, 2×pentylidene CH_2), 3.40 (s, 3H, OCH_3), 3.52–3.60 (m, 2H, OCH_2), 3.67–3.76 (m, 2H, OCH_2), 3.78 (dd, *J* = 5.4, 10.8 Hz, 1H, C1-*H*), 3.88 (dd, *J* = 5.4, 10.8 Hz, 1H, C1-*H*), 4.36 (q, *J* = 7.2 Hz, 2H, $CO_2CH_2CH_3$), 4.42 (m, 1H, C7-*H*), 4.73–4.81 (m, 3H, C6-*H*, OCH_2O); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 7.5 (CH_3), 8.2 (CH_3), 13.9 (CH_3), 29.3 (CH_2), 29.8 (CH_2), 58.9 (CH_3), 62.5 (CH_2), 66.9 (CH_2), 67.2 (CH_2), 71.6 (CH_2), 77.3 (CH), 80.0 (CH), 95.7 (CH_2), 116.0 (C), 162.0 (C), 193.0 (C=O); FAB-HRMS *m*/*z* calcd for $C_{16}H_{29}O_8$ $(M+H)^+$ 349.1863, found 349.1850.

4.4.8. Ethyl [2*R*,2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[1,2-(diethylmethylenedioxy)-3-[(2-methoxyethoxy)methoxy]propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methylthio)carbonylpentanoate (45a). A solution of α-keto ester **32** (3.62 g, 10.4 mmol) and silyl ketene thioacetal **20** (6.71 g, 17.7 mmol) in EtCN (15 mL) was added to a solution of $Sn(OTf)_2$ (7.08 g, 17.0 mmol) in EtCN (60 mL) at –70 °C. After stirring at –70 °C for 1.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (50 mL). The mixture was diluted with AcOEt (300 mL) and *n*-hexane (30 mL), and filtered through a Celite pad. The layers were separated and the organic layer was washed successively with saturated aqueous $NaHCO_3$ (100 mL) and brine (2×100 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (9.98 g), which was purified by flash column chromatography (silica gel 360 g, 4:1→7:2 *n*-hexane/AcOEt) to give aldol adducts **45a** (3.09 g, 46%) and **45b** (2.37 g, 35%) as colorless oils.

4.4.9. Ethyl [2*R*,2(1*R*,2*S*),3*S*,4*R*]-5-benzyloxy-2-[1,2-(diethylmethylenedioxy)-3-[(2-methoxyethoxy)methoxy]propyl]-3,4-(dimethylmethylenedioxy)-2-hydroxy-3-(methoxycarbonyl)pentanoate (49). $Hg(OCOCF_3)_2$ (4.06 g, 9.52 mmol) was added to a stirred solution of thioester **45a** (3.06 g, 4.75 mmol) in MeOH (120 mL). The mixture was refluxed for 10 h and evaporated in vacuo. The residue was suspended in Et_2O (30 mL) and passed through a short plug of silica gel (eluting with Et_2O) to remove insoluble Hg salt. Purification by column chromatography (silica gel 150 g, 2:1→3:2 *n*-hexane/AcOEt) afforded methyl ester **49** (2.59 g, 87%) as a colorless oil: $[\alpha]_D^{23}$ +5.58° (*c* 3.4, benzene); IR (film) 3461 (br), 2942, 1730, 1456, 1372, 1252, 1175, 1096, 935, 864, 739, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 0.90 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.24 (t, *J* = 7.3 Hz, 3H, $CO_2CH_2CH_3$), 1.57 (s, 3H, acetonide CH_3), 1.65 (s, 3H, acetonide CH_3), 1.48–1.65 (m, 4H, 2×pentylidene CH_2), 3.37 (s, 3H, OCH_3), 3.40 (dd, *J* = 6.3, 10.6 Hz, 1H, C*H*OBn), 3.54 (m, 2H, OCH_2), 3.62 (s, 3H, CO_2CH_3), 3.68 (m, 2H, OCH_2), 3.69 (dd, *J* = 6.2, 10.6 Hz, 1H, C1-*H*), 3.86 (dd, *J* = 3.1, 10.6 Hz, 1H, C1-*H*), 3.89 (dd, *J* = 1.9, 10.6 Hz, 1H, C*H*OBn), 3.99 (ddd, *J* = 3.1, 6.2, 8.4 Hz, 1H, C7-*H*), 4.12 (br s, 1H, O*H*), 4.15 (dq, *J* = 10.9, 7.3 Hz, 1H, CO_2CHCH_3), 4.23 (dq, *J* = 10.9, 7.3 Hz, 1H, CO_2CHCH_3), 4.42 (d, *J* = 8.4 Hz, 1H, C6-*H*), 4.51 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.63 (d, *J* = 12.3 Hz, 1H, OC*H*Ph), 4.73 (s, 2H, OCH_2O), 5.32 (dd, *J* = 1.9, 6.3 Hz, 1H, C3-*H*), 7.25–7.35 (m, 5H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 8.1 (CH_3), 8.2 (CH_3), 13.8 (CH_3), 26.7 (CH_3), 27.2 (CH_3), 29.3 (CH_2), 29.9 (CH_2), 52.2 (CH_3), 58.9 (CH_3), 63.0 (CH_3), 66.8 (CH_2), 69.2 (CH_2), 70.0 (CH_2), 71.7 (CH_2), 73.3 (CH_2), 77.0 (CH), 77.7 (CH), 78.8 (CH), 79.2 (C), 89.7 (C), 95.5 (CH_2), 111.3 (C), 114.5 (C), 127.5 (CH), 127.6 (CH), 128.2 (CH), 138.3 (C), 170.6 (C=O), 171.3 (C=O); FAB-HRMS *m*/*z* calcd for $C_{31}H_{49}O_{13}$ $(M+H)^+$ 629.3173, found 629.3203; Anal. calcd for $C_{31}H_{48}O_{13}$: C, 59.22; H, 7.70, found: C, 59.04; H, 7.65.

4.4.10. 3-Ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*S*)-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-3-hydroxy-6-[(2-methoxyethoxy)methoxy]hexane-1,2,3-tricarboxylate (52). Palladium hydroxide on carbon (20%, 240 mg) was added to a solution of benzyl ether **49** (2.39 g, 3.81 mmol) in AcOEt (20 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 10 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo to furnish the crude product (2.47 g) as a colorless oil.

Dess–Martin periodinane (4.36 g, 10.3 mmol) was added to a solution of the crude alcohol **50** (2.47 g) in CH_2Cl_2 (30 mL). After stirring at room temperature for 8 h, the mixture was diluted with Et_2O (40 mL) and poured into an ice-cooled saturated aqueous $NaHCO_3$ (100 mL) containing $Na_2S_2O_3{\cdot}5H_2O$ (15 g). The layers were separated, and the organic layer was washed successively with saturated aqueous $NaHCO_3$ (2×50 mL), water (40 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo gave the crude product (2.14 g), which was used without further purification.

A solution of NaH_2PO_4 (915 mg, 7.62 mmol) in water (10 mL) was added to a solution of the crude aldehyde (2.14 g) and 2-methyl-2-butene (10 mL, 95 mmol) in *tert*-butyl alcohol (50 mL), followed by addition of a solution of $NaClO_2$ (1.10 g, 9.52 mmol) in water (5 mL). After stirring at room temperature for 2.5 h, the mixture was evaporated in vacuo, and the residue was partitioned between AcOEt (120 mL) and 1N HCl (60 mL). The aqueous layer was saturated with NaCl and extracted with AcOEt (2×40 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.31 g), which was used without further purification.

A solution of diazomethane in Et_2O was added to a solution of the crude carboxylic acid (2.31 g) in Et_2O (20 mL) at 0 °C until a yellow color persisted. The mixture was evaporated in vacuo to furnish the crude product (2.28 g), which was purified by column chromatography (silica gel 50 g, 2:1→1:1 *n*-hexane/AcOEt) to give methyl ester **52** (1.81 g, 84% for 4 steps) as a colorless oil: $[\alpha]_D^{26}$ –9.39° (*c* 2.1, benzene); IR (film) 3463 (br), 2978, 2944, 2884, 1738, 1462, 1441, 1383, 1254, 1209, 1177, 1117, 982, 937, 756 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 0.90 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 1.34 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.58 (s, 3H, acetonide CH_3), 1.68 (s, 3H, acetonide CH_3), 1.45–1.71 (m, 4H, 2×pentylidene CH_2), 3.38 (s, 3H, OCH_3), 3.52–3.59 (m,

2H, OCH_2), 3.69 (dd, *J* = 6.1, 10.8 Hz, 1H, C1-*H*), 3.65–3.74 (m, 2H, OCH_2), 3.75 (s, 3H, CO_2CH_3), 3.76 (s, 3H, CO_2CH_3), 3.89 (dd, *J* = 3.0, 10.8 Hz, 1H, C1-*H*), 4.09 (s, 1H, O*H*), 4.12 (ddd, *J* = 3.0, 6.1, 8.5 Hz, 1H, C7-*H*), 4.28 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.35 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.38 (d, *J* = 8.5 Hz, 1H, C6-*H*), 4.75 (s, 2H, OCH_2O), 5.73 (s, 1H, C3-*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 8.0 (CH_3), 8.1 (CH_3), 13.6 (CH_3), 26.7 (CH_3), 26.9 (CH_3), 29.5 (CH_2), 30.0 (CH_2), 52.4 (CH_3), 52.6 (CH_3), 58.9 (CH_3), 63.0 (CH_3), 66.8 (CH_2), 69.0 (CH_2), 71.7 (CH_2), 76.5 (CH), 77.6 (CH), 79.1 (C), 79.3 (CH), 91.2 (C), 95.5 (CH_2), 114.2 (C), 114.4 (C), 169.4 (C=O), 170.5 (C=O), 170.8 (C=O); FAB-HRMS *m*/*z* calcd for $C_{25}H_{43}O_{14}$ $(M+H)^+$ 567.2653, found 567.2664; Anal. calcd for $C_{25}H_{42}O_{14}$: C, 53.00; H, 7.47, found: C, 53.24; H, 7.48.

Data for ethyl [2*R*,2(3a*S*,6a*R*),3*R*,4*S*]-3,4-(diethylmethylenedioxy)-2-hydroxy-5-[(2-methoxyethoxy)methoxy]-2-(tetrahydro-2,2-dimethyl-4-oxofuro[3,4-*d*][1,3]dioxol-3a-yl)pentanoate (**51**): $[\alpha]_D^{25}$ –59.2° (*c* 2.2, $CHCl_3$); IR (film) 3478 (br), 2976, 2942, 2883, 1790, 1761, 1730, 1462, 1375, 1248, 1173, 1096, 1046 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 0.87 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 1.33 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.46 (s, 3H, acetonide CH_3), 1.50 (s, 3H, acetonide CH_3), 1.54–1.66 (m, 4H, 2×pentylidene CH_2), 3.39 (s, 3H, OCH_3), 3.57 (t, *J* = 4.5 Hz, 2H, OCH_2), 3.75 (dd, *J* = 4.9, 10.3 Hz, 1H, one of lactone CH_2), 3.76 (t, *J* = 4.5 Hz, 2H, OCH_2), 4.05 (dd, *J* = 2.1, 10.5 Hz, 1H, C1-*H*), 4.22 (dq, *J* = 10.9, 7.2 Hz, 1H, CO_2CHCH_3), 4.31 (s, 1H, O*H*), 4.32 (dd, *J* = 8.3, 10.5 Hz, 1H, C1-*H*), 4.33 (dq, *J* = 10.9, 7.2 Hz, 1H, CO_2CHCH_3), 4.38 (dd, *J* = 10.3, 10.5 Hz, 1H, one of lactone CH_2), 4.60 (ddd, *J* = 2.1, 4.7, 8.3 Hz, 1H, C7-*H*), 4.65 (dd, *J* = 4.9, 10.5 Hz, 1H, C3-*H*), 4.79 (d, *J* = 8.9 Hz, 1H, OC*H*O), 4.81 (d, *J* = 8.9 Hz, 1H, OC*H*O), 5.15 (d, *J* = 4.7 Hz, 1H, C6-*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 8.08 (CH_3), 8.13 (CH_3), 14.2 (CH_3), 27.0 (CH_3), 27.3 (CH_3), 30.0 (CH_3), 30.3 (CH_2), 59.2 (CH_2), 63.0 (CH_2), 66.9 (CH_2), 68.8 (CH_2), 72.0 (CH_2), 73.5 (CH_2), 75.9 (CH_2), 77.5 (CH), 78.8 (CH), 79.3 (CH), 85.0 (C), 96.0 (C), 113.8 (C), 114.0 (C), 171.5 (C=O), 176.2 (C=O); FAB-HRMS *m*/*z* calcd for $C_{23}H_{39}O_{12}$ $(M+H)^+$ 507.2442, found 507.2453.

4.4.11. 3-Ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*S*)-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-3,6-dihydroxyhexane-1,2,3-tricarboxylate (53). To a solution of MEM ether **52** (1.23 g, 2.18 mmol) in MeCN (25 mL) was added sodium iodide (3.27 g, 21.8 mmol) followed by addition of chlorotrimethylsilane (2.35 g, 21.7 mmol) at –23 °C. After stirring at –23 °C for 2 h, the mixture was poured into brine (30 mL), and the whole was partitioned between AcOEt (30 mL) and water (10 mL). The organic layer was washed successively with saturated aqueous $Na_2S_2O_3$ (3×20 mL) and brine (15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.16 g), which was purified by column chromatography (silica gel 30 g, 1:1 *n*-hexane/AcOEt) to give diol **53** (978 mg, 94%) as a colorless oil: $[\alpha]_D^{24}$ +4.19° (*c* 3.1, $CHCl_3$); IR (film) 3468 (br), 2978, 2946, 2884, 1748, 1462, 1441, 1381, 1256, 1221, 1177, 1092, 935 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 0.90 (t, *J* = 7.4 Hz, 3H, pentylidene CH_3), 1.34 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.58 (s, 3H, acetonide CH_3), 1.67 (s, 3H, acetonide CH_3), 1.50–1.70 (m, 4H, 2×pentylidene CH_2), 2.07 (t, *J* = 6.1 Hz, 1H, C1-O*H*), 3.76 (s, 6H, 2×CO_2CH_3), 3.77 (ddd, *J* = 5.0, 6.1, 11.7 Hz, 1H, C1-*H*), 3.88 (ddd, *J* = 3.7, 6.1, 11.7 Hz, 1H, C1-*H*), 4.02 (s, 1H, C5-O*H*), 4.07 (ddd, *J* = 3.7, 5.0, 8.4 Hz, 1H, C7-*H*), 4.30 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.35 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.44 (d, *J* = 8.4 Hz, 1H, C6-*H*), 5.67 (s, 1H, C3-*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 8.0 (CH_3), 8.1 (CH_3), 13.6 (CH_3), 26.7 (CH_3), 26.9 (CH_3), 29.6 (CH_2), 30.0 (CH_2), 52.4 (CH_3), 52.7 (CH_3), 58.9 (CH_3), 63.2 (CH_2), 63.7 (CH_2), 76.4 (CH), 78.5 (CH), 79.1 (C), 79.2 (CH), 91.1 (C), 114.1 (C), 114.3 (C), 169.3 (C=O), 170.6 (C=O), 170.9 (C=O); FAB-HRMS *m*/*z* calcd for $C_{21}H_{35}O_{12}$ $(M+H)^+$ 479.2129, found 479.2144.

4.4.12. 3-Ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*S*)-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-6-hydroxy-3-(trimethylsilyloxy)hexane-1,2,3-tricarboxylate (54). A mixture of diol **53** (978 mg, 2.04 mmol) and *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (3.0 mL, 16.2 mmol) was heated at 90 °C for 3 h. After cooling to room temperature, the mixture was evaporated in vacuo to provide a crude product (1.42 g), which was used without further purification.

To a solution of the crude bis(trimethylsilyl) ether in Et_2O (15 mL) was added 10% aqueous HCl (2 mL), and the biphasic mixture was stirred vigorously at room temperature for 1.5 h. The reaction was quenched by addition of solid $NaHCO_3$ at 0 °C, and the layers were separated. The organic layer was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.16 g), which was purified by column chromatography (silica gel 30 g, 4:1 *n*-hexane/AcOEt) to give alcohol **54** (975 mg, 87%) as a white solid: mp 105–106 °C (colorless prisms from *n*-hexane); $[\alpha]_D^{24}$ –12.6° (*c* 1.1, $CHCl_3$); IR (nujol) 3526 (br), 2978, 1738, 1437, 1375, 1252, 846, 758 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.15 (s, 9H, Si(CH_3)$_3$), 0.85 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene CH_3), 1.30 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.54 (s, 3H, acetonide CH_3), 1.64 (s, 3H, acetonide CH_3), 1.44–1.67 (m, 4H, 2×pentylidene CH_2), 2.01 (t, *J* = 6.5 Hz, 1H, O*H*), 3.70 (ddd, *J* = 4.8, 6.5, 11.8 Hz, 1H, C1-*H*), 3.73 (s, 3H, CO_2CH_3), 3.76 (s, 3H, CO_2CH_3), 3.90 (ddd, *J* = 2.8, 6.5, 11.8 Hz, 1H, C1-*H*), 4.22 (ddd, *J* = 2.8, 4.8, 8.5 Hz, 1H, C7-*H*), 4.17 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.29 (dq, *J* = 10.7, 7.1 Hz, 1H, CO_2CHCH_3), 4.42 (d, *J* = 8.5 Hz, 1H, C6-*H*), 5.49 (s, 1H, C3-*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 2.7 (CH_3), 8.0 (CH_3), 8.1 (CH_3), 13.8 (CH_3), 26.7 (CH_3), 27.2 (CH_3), 29.7 (CH_2), 30.2 (CH_2), 52.3 (CH_3), 52.4 (CH_3), 61.9 (CH_3), 63.8 (CH_2), 76.2 (CH), 78.4 (CH), 79.6 (CH), 89.3 (C), 91.3 (C), 113.7 (C), 169.4 (C=O), 169.7 (C=O), 169.9 (C=O); FAB-HRMS *m*/*z* calcd for $C_{24}H_{43}O_{12}Si$ $(M+H)^+$ 551.2524, found 551.2549; Anal. calcd for $C_{24}H_{42}O_{12}Si$: C, 52.35; H, 7.69, found: C, 52.30; H, 7.53.

4.4.13. 3-Ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*R*)-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-5-formyl-3-(trimethylsilyloxy)pentane-1,2,3-tricarboxylate (55). A solution of alcohol **54** (425 mg, 0.771 mmol) in CH_2Cl_2 (1.5 mL) was added to a suspension of Dess–Martin periodinane (890 mg, 2.10 mmol) in CH_2Cl_2 (4 mL). After stirring at room temperature for 3.5 h, the mixture was diluted with Et_2O (10 mL) and poured into an ice-cooled saturated aqueous $NaHCO_3$ (60 mL) containing $Na_2S_2O_3{\cdot}5H_2O$ (10 g). The layers were separated, and the organic layer was washed successively with saturated aqueous $NaHCO_3$ (2×20 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (436 mg), which was purified by column chromatography (silica gel 8 g, 4:1 *n*-hexane/AcOEt) to give aldehyde **55** (387 mg, 91%) as a white solid: mp 104.5–105.5 °C (colorless prisms from *n*-hexane); $[\alpha]_D^{25}$ –12.5° (*c* 2.0, $CHCl_3$); IR (nujol) 2978, 2953, 1740, 1462, 1439, 1375, 1252, 1175, 1132, 849, 758 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.14 (s, 9H, Si(C*H*$_3$)$_3$), 0.89 (t, *J* = 7.6 Hz, 3H, pentylidene C*H*$_3$), 0.90 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 1.32 (t, *J* = 7.3 Hz, 3H, $CO_2CH_2CH_3$), 1.51 (s, 3H, acetonide C*H*$_3$), 1.63 (s, 3H, acetonide C*H*$_3$), 1.48–1.72 (m, 4H, 2×pentylidene C*H*$_2$), 3.74 (s, 3H, CO_2CH_3), 3.76 (s, 3H, CO_2CH_3), 4.21 (dq, *J* = 10.9, 7.3 Hz, 1H, CO_2CHCH_3), 4.30 (dq, *J* = 10.9, 7.3 Hz, 1H, CO_2CHCH_3), 4.63 (dd, *J* = 1.0, 6.9 Hz, 1H, C7-*H*), 4.76 (d, *J* = 6.9 Hz, 1H, C6-*H*), 5.49 (s, 1H, C3-*H*), 9.72 (d, *J* = 1.0 Hz, 1H, C*H*O); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 2.6 (CH_3), 8.0 (CH_3), 8.2 (CH_3), 13.8 (CH_3), 26.7 (CH_3), 27.0 (CH_3), 28.5 (CH_2), 29.0 (CH_2), 52.4 (CH_3), 62.1 (CH_3), 77.7 (CH), 79.4 (CH), 80.9 (CH), 82.8 (C), 90.8 (C), 113.5 (C), 116.2 (C), 169.0 (C=O), 169.2 (C=O), 169.8 (C=O), 198.6 (C=O); FAB-HRMS *m*/*z* calcd for $C_{24}H_{41}O_{12}Si$ $(M+H)^+$ 549.2368, found 549.2350; Anal. calcd for $C_{24}H_{40}O_{12}Si$: C, 52.54; H, 7.35, found: C, 52.44; H, 7.28.

4.4.14. 3-Ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*R*,10*R*,11*R*)-10-benzyloxy-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-11-methyl-6-oxo-12-phenyl-3-(trimethylsilyloxy)-7-dodecyne-1,2,3-tricarboxylate (57). Butyllithium in *n*-hexane (1.54 M, 0.91 mL, 1.40 mmol) was added to a solution of alkyne **56** (440 mg, 1.58 mmol) in THF (5 mL) at –78 °C. After stirring at –78 °C for 45 min, a solution of aldehyde **55** (387 mg, 0.705 mmol) in THF (2 mL) was added. After stirring at –78 °C for 30 min, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the whole was extracted with AcOEt (2×15 mL). The combined organic extracts were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (888 mg), which was purified by column chromatography (silica gel 8 g, 20:1→6:1 *n*-hexane/AcOEt) to give a diastereomeric mixture of coupling products (565 mg, 97%) as a colorless viscous oil, along with recovered alkyne **56** (261 mg) as a colorless oil.

A solution of the coupling product (565 mg) in CH_2Cl_2 (2 mL) was added to a suspension of Dess–Martin periodinane (727 mg, 1.71 mmol) in CH_2Cl_2 (5 mL). After stirring at room temperature for 11 h, the mixture was diluted with Et_2O (20 mL) and poured into an ice-cooled saturated aqueous $NaHCO_3$ (20 mL) containing $Na_2S_2O_3{\cdot}5H_2O$ (1 g). The layers were separated, and the organic layer was washed successively with saturated aqueous $NaHCO_3$ (2×5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 23 g, 8:1 *n*-hexane/AcOEt) afforded ynone **57** (461 mg, 82%) as a colorless oil: $[\alpha]_D^{25}$ –8.31° (*c* 1.2, $CHCl_3$); IR (film) 2976, 2211, 1748, 1682, 1456, 1373, 1250, 1098, 849, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.12 (s, 9H, Si(C*H*$_3$)$_3$), 0.87 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.91 (t, *J* = 7.4 Hz, 3H, pentylidene C*H*$_3$), 0.96 (d, *J* = 6.8 Hz, 3H, C5′-C*H*$_3$), 1.33 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.56 (s, 3H, acetonide C*H*$_3$), 1.67 (s, 3H, acetonide C*H*$_3$), 1.45–1.77 (m, 4H, 2×pentylidene C*H*$_2$), 2.19 (m, 1H, C5′-*H*), 2.51 (dd, *J* = 8.8, 13.5 Hz, 1H, C6′-*H*), 2.66 (dd, *J* = 6.6, 17.4 Hz, 1H, C3′-*H*), 2.79 (dd, *J* = 6.2, 17.4 Hz, 1H, C3′-*H*), 2.84 (dd, *J* = 6.2, 13.5 Hz, 1H, C6′-*H*), 3.63 (m, 1H, C4′-*H*), 3.75 (s, 3H, CO_2CH_3), 3.77 (s, 3H, CO_2CH_3), 4.22 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.31 (dq, *J* = 10.8, 7.2 Hz, 1H, CO_2CHCH_3), 4.54 (d, *J* = 11.6 Hz, 1H, OC*H*Ph), 4.65 (d, *J* = 5.7 Hz, 1H, C6-*H*), 4.73 (d, *J* = 11.6 Hz, 1H, OC*H*Ph), 5.09 (d, *J* = 5.7 Hz, 1H, C7-*H*), 5.67 (s, 1H, C3-*H*), 7.15 (m, 2H, Ar*H*), 7.20 (m, 1H, Ar*H*), 7.26–7.35 (m, 3H, Ar*H*), 7.37–7.42 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 2.5 (CH_3), 8.0 (CH_3), 8.5 (CH_3), 13.6 (CH_3), 13.8 (CH_3), 22.6 (CH_2), 26.7 (CH_3), 26.9 (CH_3), 28.1 (CH_2), 28.7 (CH_2), 38.7 (CH), 39.6 (CH_2), 52.3 (CH_3), 62.0 (CH_3), 72.3 (CH_2), 77.5 (CH), 79.4 (CH), 81.4 (C), 81.8 (CH), 82.8 (C), 90.9 (C), 95.1 (C), 113.7 (C), 116.4 (C), 125.9 (CH), 127.6 (CH), 127.7 (CH), 128.3 (CH), 128.4 (CH), 129.1 (CH), 138.3 (C), 140.6 (C), 169.3 (C=O), 169.5 (C=O), 170.0 (C=O), 184.8 (C=O); FAB-HRMS *m*/*z* calcd for $C_{44}H_{61}O_{13}Si$ $(M+H)^+$ 825.3882, found 825.3849.

4.4.15. 3-Ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*R*,10*R*,11*R*)-10-benzyloxy-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-11-methyl-6-oxo-12-phenyl-3-(trimethylsilyloxy)dodecane-1,2,3-tricarboxylate (58). Palladium on carbon (10%, 240 mg) was added to a solution of alkyne **57** (461 mg, 0.559 mmol) in AcOEt (15 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 10 min. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the residue by column chromatography (silica gel 20 g, 7:1 *n*-hexane/AcOEt) afforded ketone **58** (432 mg, 93%) as a colorless oil: $[\alpha]_D^{27}$ –2.97° (*c* 3.2, EtOH); IR (film) 2951, 1740, 1456, 1375, 1252, 1209, 1111, 910, 847, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.08 (s, 9H, Si(C*H*$_3$)$_3$), 0.81 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 0.87 (d, *J* = 6.8 Hz, 3H, C5′-C*H*$_3$), 0.89 (t, *J* = 7.5 Hz, 3H, pentylidene C*H*$_3$), 1.31 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.54 (s, 3H, acetonide C*H*$_3$), 1.63 (s, 3H, acetonide C*H*$_3$), 1.37–1.81 (m, 8H, 2×pentylidene C*H*$_2$, C2′-*H*$_2$, C3′-*H*$_2$), 2.05 (m, 1H, C5′-*H*), 2.34 (dd, *J* = 9.8, 13.3 Hz, 1H, C6′-*H*), 2.62 (m, 1H, C1′-*H*), 2.77 (m, 1H, C1′-*H*), 2.90 (dd, *J* = 4.9, 13.3 Hz, 1H, C6′-*H*), 3.32 (m, 1H, C4′-*H*), 3.72 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 4.19 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.28 (dq, *J* = 10.8, 7.1 Hz, 1H, CO_2CHCH_3), 4.56 (s, 2H, OC*H*$_2$Ph), 4.58 (d, *J* = 5.7 Hz, 1H, C6-*H*), 5.03 (d, *J* = 5.7

Hz, 1H, C7-*H*), 5.61 (s, 1H, C3-*H*), 7.11 (m, 2H, Ar*H*), 7.17 (m, 1H, Ar*H*), 7.22–7.30 (m, 3H, Ar*H*), 7.31–7.41 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 2.4 (CH_3), 8.1 (CH_3), 8.5 (CH_3), 13.8 (CH_3), 14.4 (CH_3), 19.9 (CH_2), 26.7 (CH_3), 26.8 (CH_3), 27.8 (CH_2), 28.6 (CH_2), 30.1 (CH_2), 37.9 (CH), 38.7 (CH_2), 40.3 (CH_2), 52.3 (CH_3), 61.9 (CH_3), 71.7 (CH_2), 77.2 (CH), 79.4 (CH), 80.6 (CH), 82.4 (CH), 82.9 (CH), 90.9 (C), 113.7 (C), 115.7 (C), 125.7 (CH), 127.4 (CH), 127.6 (CH), 128.2 (CH), 128.3 (CH), 129.1 (CH), 139.1 (C), 141.6 (C), 169.4 (C=O), 169.5 (C=O), 170.0 (C=O), 207.6 (C=O); FAB-HRMS *m*/*z* calcd for $C_{44}H_{65}O_{13}Si$ $(M+H)^+$ 829.4195, found 829.4153; Anal. calcd for $C_{44}H_{64}O_{13}Si$: C, 63.74; H, 7.78, found: C, 63.59; H, 7.79.

4.5. Internal ketalization

4.5.1. 5-Ethyl 3,4-dimethyl [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-1-(4-benzyloxy-5-methyl-6-phenylhexyl)-4,6,7-trihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (59). A solution of ketone **58** (95 mg, 0.115 mmol) in 90% aqueous trifluoroacetic acid (10 mL) was stirred at room temperature for 15 h. The reaction mixture was evaporated in vacuo, and the crude product was concentrated from toluene (2×20 mL) to remove residual trifluoroacetic acid. Purification of the residue by column chromatography (silica gel 10 g, 1:1→1:2 *n*-hexane/AcOEt) afforded bicyclic compound **59** (49.5 mg, 68%) as a colorless oil, along with ketone **60** (4.9 mg, 7%) as a colorless oil: $[\alpha]_D^{24}$ +3.30° (*c* 3.0, acetone); IR (film) 3493, 2975, 2870, 1748, 1495, 1441, 1373, 1279, 1117, 958, 833, 747 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.9 Hz, 3H, C5′-C*H*$_3$), 1.27 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.52–1.75 (m, 4H, C2′-*H*$_2$, C3′-*H*$_2$), 1.90–2.00 (m, 2H, C1′-*H*$_2$), 2.07 (m, 1H, C5′-*H*), 2.31 (dd, *J* = 10.0, 13.2 Hz, 1H, C6′-*H*), 2.90 (dd, *J* = 4.4, 13.2 Hz, 1H, C6′-*H*), 3.15 (br s, 1H, O*H*), 3.26–3.40 (m, 2H, O*H*, C4′-*H*), 3.72 (s, 3H, CO_2CH_3), 3.83 (s, 1H, C4-O*H*), 3.89 (s, 3H, CO_2CH_3), 4.13 (m, 1H, C7-*H*), 4.25 (q, *J* = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 4.55 (d, *J* = 11.7 Hz, 1H, OC*H*Ph), 4.58 (d, *J* = 11.7 Hz, 1H, OC*H*Ph), 5.06 (m, 1H, C6-*H*), 5.18 (s, 1H, C3-*H*), 7.11 (m, 2H, Ar*H*), 7.17 (m, 1H, Ar*H*), 7.22–7.31 (m, 3H, Ar*H*), 7.31–7.41 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.0 (CH_3), 14.7 (CH_3), 19.6 (CH_2), 29.7 (CH_2), 35.2 (CH_2), 37.7 (CH), 38.3 (CH_2), 52.6 (CH_3), 53.5 (CH_3), 62.5 (CH_2), 71.6 (CH_2), 74.8 (C), 75.5 (CH), 78.4 (CH), 82.2 (CH), 82.5 (CH), 91.1 (C), 106.4 (C), 125.7 (CH), 127.6 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 129.1 (CH), 138.9 (C), 141.6 (C), 166.4 (C=O), 167.2 (C=O), 169.9 (C=O); FAB-HRMS *m*/*z* calcd for $C_{33}H_{43}O_{12}$ $(M+H)^+$ 631.2754, found 631.2758.

Data for 5-ethyl 3,4-dimethyl [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*]-1-(4-benzyloxy-5-methyl-6-phenylhexyl)-4-hydroxy-7-oxo-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (**60**): IR ($CHCl_3$) 3543, 1772, 1741, 1263, 1228, 1150 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.9 Hz, 3H, C5′-C*H*$_3$), 1.30 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.40–1.69 (m, 4H, C2′-*H*$_2$, C3′-*H*$_2$), 1.93 (m, 1H, C1′-*H*), 1.97–2.07 (m, 2H, C1′-*H*, C5′-*H*), 2.34 (dd, *J* = 9.7, 13.3 Hz, 1H, C6′-*H*), 2.68 (d, *J* = 18.8 Hz, 1H, C6-*H*), 2.88 (dd, *J* = 4.4, 13.3 Hz, 1H, C6′-*H*), 3.31 (m, 1H, C4′-*H*), 3.55 (d, *J* = 18.8 Hz, 1H, C6-*H*), 3.75 (s, 3H, CO_2CH_3), 3.90 (s, 1H, C4-O*H*), 3.91 (s, 3H, CO_2CH_3), 4.28 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.30 (dq, *J* = 10.7, 7.2 Hz, 1H, CO_2CHCH_3), 4.54 (s, 2H, OC*H*$_2$Ph), 4.88 (s, 1H, C3-*H*), 7.10–7.40 (m, 10H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 13.9 (CH_3), 14.5 (CH_3), 18.9 (CH_2), 30.3 (CH_2), 31.3 (CH_2), 37.8 (CH), 38.7 (CH_2), 41.7 (CH_3), 52.9 (CH_3), 53.7 (CH_3), 62.8 (CH_2), 71.6 (CH_2), 74.9 (C), 75.8 (CH), 82.2 (CH), 83.8 (C), 101.9 (C), 125.7 (CH), 127.4 (CH), 127.7 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 129.1 (CH), 139.2 (C), 141.6 (C), 166.3 (C=O), 166.8 (C=O), 169.4 (C=O), 205.4 (C=O); FAB-HRMS *m*/*z* calcd for $C_{33}H_{41}O_{11}$ $(M+H)^+$ 613.2649, found 613.2653.

4.5.2. Isolation of the cyclization intermediates 62 and 63. Aqueous trifluoroacetic acid (90%, 5 mL) was added to ketone **58** (113 mg, 0.136 mmol) at 0 °C. After stirring at room temperature for 10 min, the reaction mixture was diluted with toluene (10 mL) and evaporated in vacuo. The residue was azeotropically dried with toluene (2×10 mL) and purified by flash column chromatography (silica gel 7.5 g, 4:1→2:1→1:1→1:2 *n*-hexane/AcOEt) to give hydroxyketone **62** (55 mg, 53%) and hemiketal **63** (28 mg, 29%) as white foams.

Data for 3-ethyl 1,2-dimethyl (1*S*,2*S*,3*R*,4*R*,5*R*,10*R*,11*R*)-10-benzyloxy-4,5-(diethylmethylenedioxy)-1,2-(dimethylmethylenedioxy)-3-hydroxy-11-methyl-6-oxo-12-phenyldodecane-1,2,3-tricarboxylate (**62**): $[\alpha]_D^{26}$ –5.27° (*c* 1.1, $CHCl_3$); IR (film) 3472, 2942, 1732, 1454, 1375, 1254, 1096, 932, 741 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.6 Hz, 3H, C5′-C*H*$_3$), 0.88 (t, *J* = 7.3 Hz, 6H, 2×pentylidene C*H*$_3$), 1.33 (t, *J* = 7.3 Hz, 3H, $CO_2CH_2CH_3$), 1.53 (s, 3H, acetonide C*H*$_3$), 1.65 (s, 3H, acetonide C*H*$_3$), 1.50–1.80 (m, 8H, 2×pentylidene C*H*$_2$, C2′-*H*$_2$, C3′-*H*$_2$), 2.04 (m, 1H, C5′-*H*), 2.33 (dd, *J* = 9.9, 13.2 Hz, 1H, C6′-*H*), 2.68 (t, *J* = 6.6 Hz, 2H, C1′-*H*$_2$), 2.89 (dd, *J* = 5.3, 13.2 Hz, 1H, C6′-*H*), 3.30 (m, 1H, C4′-*H*), 3.736 (s, 3H, CO_2CH_3), 3.743 (s, 3H, CO_2CH_3), 4.13 (s, 1H, O*H*), 4.26–4.37 (m, 2H, $CO_2CH_2CH_3$), 4.49 (d, *J* = 6.6 Hz, 1H, C6-*H*), 4.55 (s, 2H, OC*H*$_2$Ph), 4.83 (d, *J* = 6.6 Hz, 1H, C7-*H*), 5.58 (s, 1H, C3-*H*), 7.11 (m, 2H, Ar*H*), 7.18 (m, 1H, Ar*H*), 7.22–7.33 (m, 3H, Ar*H*), 7.34–7.40 (m, 4H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 7.9 (CH_3), 8.4 (CH_3), 13.7 (CH_3), 14.4 (CH_3), 19.7 (CH_2), 26.6 (CH_3), 26.8 (CH_3), 29.09 (CH_2), 29.15 (CH_2), 29.9 (CH_2), 37.8 (CH), 38.7 (CH_2), 39.7 (CH_2), 52.4 (CH_3), 52.6 (CH_3), 62.9 (CH_2), 71.6 (CH_2), 76.7 (CH), 79.0 (CH), 79.2 (C), 81.0 (CH), 82.3 (CH), 90.7 (C), 114.0 (C), 116.0 (C), 125.6 (CH), 127.4 (CH), 127.6 (CH), 128.2 (CH), 128.3 (CH), 129.1 (CH), 139.1 (C), 141.5 (C), 169.1 (C=O), 170.0 (C=O), 170.1 (C=O), 208.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{41}H_{57}O_{13}$ $(M+H)^+$ 757.3799, found 757.3790.

Data for dimethyl [4*S*,4[2*R*,3*R*,4*R*,5(4*R*,5*R*)],5*S*]-4-[5-(4-benzyloxy-5-methyl-6-phenylhexyl)-2-ethoxycarbonyl-3,4,5-trihydroxytetrahydrofuran-2-yl]-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (**63**): $[\alpha]_D^{24}$ +16.5° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3543, 3028, 2955, 1738, 1439, 1373, 1260, 1109, 1055 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (d, *J* = 6.9 Hz, 3H, C5′-C*H*$_3$), 1.26 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.45 (s, 3H, acetonide C*H*$_3$), 1.51–1.76 (m,

4H, C2′-H_2, C3′-H_2), 1.66 (s, 3H, acetonide CH_3), 1.88–2.03 (m, 2H, C1′-H_2), 2.10 (m, 1H, C5′-*H*), 2.30 (dd, *J* = 9.9, 13.2 Hz, 1H, C6′-*H*), 2.52 (d, *J* = 8.2 Hz, 1H, C7-O*H*), 2.92 (dd, *J* = 4.5, 13.2 Hz, 1H, C6′-*H*), 3.38 (m, 1H, C4′-*H*), 3.68 (d, *J* = 2.6 Hz, 1H, C6-O*H*), 3.77 (s, 3H, CO_2CH_3), 3.83 (s, 3H, CO_2CH_3), 4.09 (s, 1H, C1-O*H*), 4.11–4.19 (m, 2H, C7-*H*, CO_2CHCH_3), 4.25 (dq, *J* = 10.9, 7.1 Hz, 1H, CO_2CHCH_3), 4.52 (d, *J* = 11.7 Hz, 1H, OC*H*Ph), 4.62 (d, *J* = 11.7 Hz, 1H, OC*H*Ph), 4.73 (dd, *J* = 2.6, 8.7 Hz, 1H, C6-*H*), 5.37 (s, 1H, C3-*H*), 7.12 (m, 2H, Ar*H*), 7.19 (m, 1H, Ar*H*), 7.22–7.40 (m, 7H, Ar*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 14.0 (CH_3), 14.7 (CH_3), 19.8 (CH_2), 26.5 (CH_3), 26.9 (CH_3), 30.0 (CH_2), 37.8 (CH), 38.1 (CH_2), 38.3 (CH_2), 52.8 (CH_3), 53.2 (CH_3), 61.9 (CH_2), 71.7 (CH_2), 77.1 (CH), 78.2 (CH), 79.0 (CH), 82.9 (CH), 87.7 (C), 89.0 (C), 102.2 (C), 114.1 (C), 125.7 (CH), 127.6 (CH), 127.8 (CH), 128.2 (CH), 128.4 (CH), 129.0 (CH), 138.7 (C), 141.5 (C), 169.3 (C=O), 169.5 (C=O), 173.7 (C=O); FAB-HRMS *m*/*z* calcd for $C_{36}H_{49}O_{13}$ $(M+H)^+$ 689.3173, found 689.3198.

4.6. Completion of the total synthesis

4.6.1. Tri(*tert*-butyl) [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-1-(4-benzyloxy-5-methyl-6-phenylhexyl)-4,6,7-trihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (64). A 1N aqueous KOH (1.5 mL, 1.5 mmol) was added to a solution of triester **59** (49 mg, 0.078 mmol) in 1,4-dioxane (3 mL), and the whole was heated at 100 °C for 24 h. After cooling, 1N aqueous HCl (2 mL) was added, and the mixture was evaporated in vacuo. The crude mixture thus obtained was suspended in CH_2Cl_2 (5 mL), and *N*,*N*′-diisopropyl-*O*-*tert*-butylisourea (505 mg, 2.53 mmol) was added. After stirring at room temperature for 24 h, the mixture was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the residue by column chromatography (silica gel 8 g, 3:2→1:1 *n*-hexane/AcOEt) afforded tri(*tert*-butyl) ester **64** (23 mg, 40%) as a colorless oil: $[\alpha]_D^{23}$ –2.90° (*c* 1.5, EtOH); IR (film) 3486 (br), 2932, 1732, 1456, 1370, 1157, 843, 739, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.8 Hz, 3H, C5′-CH_3), 1.44 (s, 9H, $CO_2C(CH_3)_3$), 1.48 (s, 9H, $CO_2C(CH_3)_3$), 1.52–1.73 (m, 4H, C2′-H_2, C3′-H_2), 1.59 (s, 9H, $CO_2C(CH_3)_3$), 1.86–1.99 (m, 2H, C1′-H_2), 2.05 (m, 1H, C5′-*H*), 2.35 (dd, *J* = 9.7, 13.3 Hz, 1H, C6′-*H*), 2.50 (br s, 2H, 2×O*H*), 2.88 (dd, *J* = 4.8, 13.3 Hz, 1H, C6′-*H*), 3.32 (m, 1H, C4′-*H*), 3.90 (s, 1H, C4-O*H*), 4.07 (br s, 1H, C7-*H*), 4.55 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.56 (d, *J* = 11.8 Hz, 1H, OC*H*Ph), 4.92 (s, 1H, C3-*H*), 5.02 (br s, 1H, C6-*H*), 7.11 (d, *J* = 7.3 Hz, 2H, Ar*H*), 7.17 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.23–7.31 (m, 3H, Ar*H*), 7.32–7.41 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.5 (CH_3), 19.6 (CH_2), 28.0 (CH_3), 28.1 (CH_3), 28.2 (CH_3), 29.9 (CH_2), 35.4 (CH_2), 37.7 (CH), 38.7 (CH_2), 71.6 (CH_2), 74.3 (C), 75.1 (CH), 78.8 (CH), 82.1 (CH), 82.4 (CH), 83.1 (C), 84.2 (C), 85.0 (C), 91.2 (C), 105.2 (C), 125.6 (CH), 127.5 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 129.1 (CH), 139.1 (C), 141.7 (C), 165.9 (C=O), 166.5 (C=O), 168.5 (C=O); FAB-HRMS *m*/*z* calcd for $C_{41}H_{59}O_{12}$ $(M+H)^+$ 743.4007, found 743.3984.

4.6.2. Tri(*tert*-butyl) [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-4,6,7-trihydroxy-1-(4-hydroxy-5-methyl-6-phenylhexyl)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (65). Palladium on carbon (10%, 28.6 mg) was added to a solution of benzyl ether **64** (57.7 mg, 0.077 mmol) in MeOH (2 mL), and the mixture was vigorously stirred under 1 atm of hydrogen for 17 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the residue (55.1 mg) by column chromatography (silica gel 8 g, 1:1→1:2 *n*-hexane/AcOEt) afforded tetraol **65** (46 mg, 90%) as a white foam: $[\alpha]_D^{23}$ +4.69° (*c* 1.3, EtOH); IR (film) 3481 (br), 2980, 2932, 1732, 1370, 1262, 1155, 739, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.8 Hz, 3H, C5′-CH_3), 1.44 (s, 9H, $CO_2C(CH_3)_3$), 1.48 (s, 9H, $CO_2C(CH_3)_3$), 1.50–1.85 (m, 4H, C2′-H_2, C3′-H_2), 1.59 (s, 9H, $CO_2C(CH_3)_3$), 1.86–2.03 (m, 3H, C1′-H_2, C5′-*H*), 2.41 (dd, *J* = 9.0, 13.3 Hz, 1H, C6′-*H*), 2.80 (dd, *J* = 5.9, 13.3 Hz, 1H, C6′-*H*), 3.10 (br s, 1H, O*H*), 3.50–3.60 (m, 2H, C4′-*H*, O*H*), 3.99 (s, 1H, C4-O*H*), 4.14 (br s, 1H, C7-*H*), 4.97 (s, 1H, C3-*H*), 5.01 (br s, 1H, C6-*H*), 7.13–7.20 (m, 3H, Ar*H*), 7.23–7.29 (m, 2H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 11.4 (CH_3), 19.7 (CH_2), 28.0 (CH_3), 28.1 (CH_3), 28.2 (CH_3), 33.9 (CH_2), 35.1 (CH_2), 39.8 (CH_2), 40.6 (CH), 74.2 (CH), 74.3 (C), 75.1 (CH), 78.8 (CH), 82.5 (CH), 83.4 (C), 84.2 (C), 85.0 (C), 91.3 (C), 105.3 (C), 125.7 (CH), 128.2 (CH), 129.2 (CH), 141.2 (C), 166.2 (C=O), 166.4 (C=O), 168.7 (C=O); FAB-HRMS *m*/*z* calcd for $C_{34}H_{53}O_{12}$ $(M+H)^+$ 653.3537, found 653.3527.

4.6.3. Tri(*tert*-butyl) [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-6,7-diacetoxy-1-(4-acetoxy-5-methyl-6-phenylhexyl)-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (66). To a solution of tetraol **65** (45.7 mg, 0.070 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added 4-*N*,*N*-dimethylaminopyridine (86 mg, 0.705 mmol) followed by addition of acetic anhydride (0.035 mL, 0.37 mmol). After stirring at 0 °C for 30 min, the reaction was quenched with 1N aqueous KH_2PO_4 (5 mL) and the mixture was extracted with 10:1 Et_2O/*n*-hexane (11 mL). The organic extract was washed with brine (2×4 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (59.8 mg), which was purified by column chromatography (silica gel 5 g, 7:3 *n*-hexane/AcOEt) to give triacetate **66** (54 mg, quant.) as a white foam: $[\alpha]_D^{21}$ +17.6° (*c* 0.91, CH_2Cl_2) [lit.[8b] $[\alpha]_D$ +69.9° (*c* 0.29, CH_2Cl_2)]; IR (film) 3453 (br), 2978, 2934, 1759, 1732, 1477, 1456, 1372, 1236, 1154, 1119, 1040, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.8 Hz, 3H, C5′-CH_3), 1.460 (s, 9H, $CO_2C(CH_3)_3$), 1.464 (s, 9H, $CO_2C(CH_3)_3$), 1.51–1.71 (m, 4H, C2′-H_2, C3′-H_2), 1.62 (s, 9H, $CO_2C(CH_3)_3$), 1.88–2.12 (m, 3H, C1′-H_2, C5′-*H*), 2.05 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 2.15 (s, 3H, $COCH_3$), 2.30 (dd, *J* = 9.7, 13.4 Hz, 1H, C6′-*H*), 2.76 (dd, *J* = 4.9, 13.4 Hz, 1H, C6′-*H*), 4.07 (s, 1H, C4-O*H*), 4.88 (m, 1H, C4′-*H*), 4.88 (s, 1H, C3-*H*), 5.09 (d, *J* = 1.8 Hz, 1H, C7-*H*), 6.34 (d, *J* = 1.8 Hz, 1H, C6-*H*), 7.13 (m, 2H, Ar*H*), 7.17 (m, 1H, Ar*H*), 7.23–7.31 (m, 2H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3, 20.1, 20.5, 20.7, 21.1, 28.4, 28.5, 32.3, 36.5, 39.7, 40.6, 75.6, 76.9, 77.9, 81.6, 85.0, 85.4, 86.4, 91.2, 105.6, 127.0, 129.3, 130.2, 142.0, 165.6,

167.4, 168.8, 170.2, 171.1, 173.0; FAB-HRMS *m*/*z* calcd for $C_{40}H_{59}O_{15}$ $(M+H)^+$ 779.3853, found 779.3823.

4.6.4. Tri(*tert*-butyl) [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-1-(4-acetoxy-5-methyl-6-phenylhexyl)-4,6,7-trihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (3). A 0.2% solution of potassium carbonate in MeOH (1.5 mL) was added to triacetate **66** (50.7 mg, 0.065 mmol) at 0 °C. After stirring at room temperature for 1 h, the reaction was quenched with 0.3N aqueous KH_2PO_4 (1 mL), and the whole was partitioned between AcOEt (10 mL) and brine (4 mL). The organic layer was washed with brine (4 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 5 g, 3:2 *n*-hexane/AcOEt) afforded triol **3** (42.5 mg, 94%) as a white foam: $[\alpha]_D^{23}$ +7.58° (*c* 1.0, CH_2Cl_2); IR (film) 3482, 2980, 2932, 1733, 1456, 1393, 1372, 1258, 1156, 965, 845, 701 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 0.87 (d, *J* = 6.9 Hz, 3H, C5′-C*H*$_3$), 1.45 (s, 9H, $CO_2C(CH_3)_3$), 1.46 (s, 9H, $CO_2C(CH_3)_3$), 1.52–1.65 (m, 2H, C2′-*H*$_2$), 1.60 (s, 9H, $CO_2C(CH_3)_3$), 1.66–1.75 (m, 2H, C3′-*H*$_2$), 1.79–1.93 (m, 2H, C1′-*H*$_2$), 2.05 (m, 1H, C5′-*H*), 2.06 (s, 3H, COC*H*$_3$), 2.36 (dd, *J* = 9.1, 13.4 Hz, 1H, C6′-*H*), 2.74 (dd, *J* = 5.6, 13.4 Hz, 1H, C6′-*H*), 4.00 (d, *J* = 1.8 Hz, 1H, C7-*H*), 4.87 (m, 1H, C4′-*H*), 4.96 (d, *J* = 1.8 Hz, 1H, C6-*H*), 4.97 (s, 1H, C3-*H*), 7.12–7.18 (m, 3H, Ar*H*), 7.21–7.27 (m, 2*H*, Ar*H*); ^{13}C NMR (125.8 MHz, CD_3OD) δ 14.2, 20.1, 21.1, 28.4, 28.5, 28.7, 32.5, 36.6, 39.5, 40.6, 76.0, 76.8, 78.3, 79.9, 84.2, 84.3, 84.5, 93.2, 106.4, 126.9, 129.3, 130.2, 142.0, 167.4, 168.3, 169.8, 173.0; FAB-HRMS *m*/*z* calcd for $C_{36}H_{55}O_{13}$ $(M+H)^+$ 695.3643, found 695.3670.

4.6.5. Tri(*tert*-butyl) [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,7*R*]-1-(4-acetoxy-5-methyl-6-phenylhexyl)-7-(*tert*-butoxycarbonyl)oxy-4,6-dihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (67). A 0.1M solution of di-*tert*-butyl dicarbonate in CH_2Cl_2 (0.84 mL, 0.084 mmol) was added to a solution of triol **3** (14.5 mg, 0.0209 mmol), 4-pyrrolidinopyridine (4.9 mg, 0.033 mmol) and Et_3N (12 μL, 0.086 mmol) in CH_2Cl_2 (2.5 mL) at 0 °C. After stirring at 0 °C for 12 h, the mixture was diluted with 1:1 *n*-hexane/Et_2O (12 mL) and quenched with 1M aqueous K_2HPO_4 (3 mL). The layers were separated, and the organic layer was washed with brine (3 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 8 g, 3:1 *n*-hexane/AcOEt) afforded *tert*-butyl carbonate **67** (11.8 mg, 71%) as a colorless foam: $[\alpha]_D^{21}$ +23.8° (*c* 0.59, EtOH) [lit. $[\alpha]_D$ +43.3° (*c* 0.25, CH_2Cl_2),[8b] $[\alpha]_D^{27}$ +25.8° (*c* 0.47, CH_2Cl_2)[11b]]; IR (film) 3459 (br), 2980, 2933, 1733, 1456, 1395, 1371, 1278, 1257, 1159, 1121, 967, 845, 743 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.9 Hz, 3H, C5′-C*H*$_3$), 1.45 (s, 9H, $CO_2C(CH_3)_3$), 1.49 (s, 9H, $CO_2C(CH_3)_3$), 1.50 (s, 9H, $CO_2C(CH_3)_3$), 1.58 (s, 9H, $CO_2C(CH_3)_3$), 1.54–1.73 (m, 4H, C2′-*H*$_2$, C3′-*H*$_2$), 1.87–2.12 (m, 3H, C1′-*H*$_2$, C5′-*H*), 2.06 (s, 3H, COC*H*$_3$), 2.31 (dd, *J* = 9.6, 13.4 Hz, 1H, C6′-*H*), 2.75 (dd, *J* = 4.9, 13.4 Hz, 1H, C6′-*H*), 2.85 (d, *J* = 3.5 Hz, 1H, C6-O*H*), 3.94 (s, 1H, C4-O*H*), 4.64 (d, *J* = 1.8 Hz, 1H, C7-*H*), 4.72 (s, 1H, C3-*H*), 4.88 (m, 1H, C4′-*H*), 5.11 (br s, 1H, C6-*H*), 7.13 (m, 2H, Ar*H*), 7.17 (m, 1H, Ar*H*), 7.23–7.29 (m, 2H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 13.8, 18.9, 21.2, 27.7, 27.8, 28.0, 28.1, 30.9, 35.5, 37.9, 39.4, 74.0, 75.3, 76.9, 77.0, 83.2, 83.8, 84.0, 85.0, 85.5, 90.7, 103.8, 125.8, 128.2, 129.1, 140.7, 153.7, 165.2, 165.8, 168.5, 170.9; FAB-HRMS *m*/*z* calcd for $C_{41}H_{62}O_{15}Na$ $(M+Na)^+$ 817.3986, found 817.3989.

4.6.6. Tri(*tert*-butyl) [1*S*,1(4*R*,5*R*),3*S*,4*S*,5*R*,6*R*,6(4*E*,6*R*),7*R*]-1-(4-acetoxy-5-methyl-6-phenylhexyl)-7-(*tert*-butoxycarbonyloxy)-4-hydroxy-6-(6-methyl-9-phenyl-4-nonenoyl)oxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (68). DCC (31 mg, 0.150 mmol) was added to a solution of carboxylic acid **2** (37 mg, 0.150 mmol) in CH_2Cl_2 (1.5 mL), and the mixture was stirred at room temperature for 15 min. The solution of DCC–carboxylic acid **2** in CH_2Cl_2 (0.5 mL) was added to a solution of diol **67** (11.8 mg, 0.0149 mmol) and DMAP (14.5 mg, 0.119 mmol) in CH_2Cl_2 (2 mL). After stirring at room temperature for 48 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (6 mL), and the whole was extracted with 3:1 Et_2O/*n*-hexane (8 mL). The organic extract was washed successively with saturated aqueous $NaHCO_3$ (3 mL) and brine (3 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by column chromatography (silica gel 8 g, 5:1 *n*-hexane/AcOEt) afforded ester **68** (13.7 mg, 90%) as a colorless oil: $[\alpha]_D^{23}$ +8.4° (*c* 0.38, CH_2Cl_2) [lit. $[\alpha]_D$ +8.5° (*c* 0.27, CH_2Cl_2),[8b] $[\alpha]_D^{23}$ +9.0° (*c* 0.27, CH_2Cl_2)[11b]]; IR (film) 3452 (br), 2978, 2932, 1748, 1456, 1395, 1372, 1281, 1256, 1159, 1119, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.8 Hz, 3H, C5′-C*H*$_3$), 0.93 (d, *J* = 6.7 Hz, 3H, C6″-C*H*$_3$), 1.29 (q, *J* = 7.7 Hz, 2H, C7″-*H*$_2$), 1.44 (s, 9H, $CO_2C(CH_3)_3$), 1.45 (s, 9H, $CO_2C(CH_3)_3$), 1.47 (s, 9H, $CO_2C(CH_3)_3$), 1.61 (s, 9H, $CO_2C(CH_3)_3$), 1.50–1.72 (m, 6H, C2′-*H*$_2$, C3′-*H*$_2$, C8″-*H*$_2$), 1.89–2.13 (m, 4H, C1′-*H*$_2$, C5′-*H*, C6″-*H*), 2.04 (s, 3H, COC*H*$_3$), 2.24–2.43 (m, 5H, C6′-*H*, C2″-*H*$_2$, C3″-*H*$_2$), 2.57 (t, *J* = 7.7 Hz, 2H, C9″-*H*$_2$), 2.76 (dd, *J* = 4.7, 13.4 Hz, 1H, C6′-*H*), 4.06 (s, 1H, C4-O*H*), 4.86 (d, *J* = 1.7 Hz, 1H, C7-*H*), 4.87 (m, 1H, C4′-*H*), 4.91 (s, 1H, C3-*H*), 5.28–5.40 (m, 2H, C4″-*H*, C5″-*H*), 6.40 (d, *J* = 1.7 Hz, 1H, C6-*H*), 7.10–7.20 (m, 6H, Ar*H*), 7.23–7.30 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 13.9, 18.9, 20.6, 21.2, 27.68, 27.71, 27.9, 28.0, 28.1, 29.2, 30.9, 34.1, 35.8, 36.1, 36.5, 36.6, 38.0, 39.4, 74.0, 75.3, 76.2, 77.0, 83.1, 83.3, 83.4, 83.9, 86.1, 89.8, 103.8, 125.6, 125.8, 126.1, 128.20, 128.23, 128.4, 129.1, 137.6, 140.8, 142.8, 152.4, 164.0, 165.6, 168.6, 170.7, 170.8; FAB-HRMS *m*/*z* calcd for $C_{57}H_{82}O_{16}Na$ $(M+Na)^+$ 1045.5500, found 1045.5450.

4.6.7. Zaragozic acid C (1). Trifluoroacetic acid (2.2 mL) was added to a solution of compound **68** (13.5 mg, 0.0132 mmol) in CH_2Cl_2 (6.5 mL). After stirring at room temperature for 16 h, the mixture was evaporated in vacuo, and the crude product was concentrated from toluene (10 mL) to remove residual trifluoroacetic acid. Trituration of the residue with petroleum ether provided zaragozic acid C (**1**) (10.1 mg, quant.) as a white film: $[\alpha]_D^{23}$ +9.4° (*c* 0.30, EtOH) [lit. $[\alpha]_D^{20}$ +9.6° (*c* 0.29, EtOH),[1b] $[\alpha]_D$ +9.0° (*c* 0.23, EtOH),[8b] $[\alpha]_D^{24}$ +9.6° (*c* 1.0, EtOH)[11b]]; IR (film) 3453 (br), 2928, 1732, 1495, 1454, 1375, 1250, 1148, 1026, 970, 745, 700 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 0.86 (d, *J* = 6.8

Hz, 3H, C5′-CH_3), 0.93 (d, J = 6.7 Hz, 3H, C6″-CH_3), 1.19–1.37 (m, 2H, C7″-H_2), 1.50–1.64 (m, 4H, C2′-H_2, C8″-H_2), 1.64–1.73 (m, 2H, C3′-H_2), 1.82–1.94 (m, 2H, C1′-H_2), 1.97–2.12 (m, 2H, C5′-*H*, C6″-*H*), 2.05 (s, 3H, COCH_3), 2.22–2.30 (m, 2H, C3″-H_2), 2.30–2.39 (m, 3H, C6′-*H*, C2″-H_2), 2.50–2.61 (m, 2H, C9″-H_2), 2.73 (dd, J = 5.6, 13.3 Hz, 1H, C6′-*H*), 4.00 (d, J = 1.6 Hz, 1H, C7-*H*), 4.90 (m, 1H, C4′-*H*), 5.22 (s, 1H, C3-*H*), 5.31 (dd, J = 7.6, 15.3 Hz, 1H, C5″-*H*), 5.37 (dt, J = 15.3, 6.2 Hz, 1H, C4″-*H*), 6.23 (br s, 1H, C6-*H*), 7.09–7.17 (m, 6H, Ar*H*), 7.19–7.27 (m, 4H, Ar*H*); ^{13}C NMR (125.8 MHz, CD_3OD) δ 14.3, 20.2, 21.1, 21.3, 28.8, 30.5, 32.5, 35.4, 36.3, 36.9, 37.6, 37.8, 39.7, 40.5, 75.7, 76.7, 78.2, 81.3, 82.3, 91.1, 107.2, 126.6, 126.9, 127.6, 129.26, 129.28, 129.4, 130.2, 138.8, 142.0, 143.9, 168.7, 170.3, 172.6, 173.1, 173.2; FAB-HRMS *m/z* calcd for $C_{40}H_{50}O_{14}Na$ $(M+Na)^+$ 777.3098, found 777.3049.

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33. α-Keto ester **32** was prepared in 44% overall yield from diethyl L-tartrate by a slight modification of the route illustrated for **17** (Scheme 3), in which the chemical yield was improved by the use of DEPC[34] as a condensation agent: (1) $Et_2C(OMe)_2$, TsOH, benzene, reflux, 3 h, 96%; (2) $LiAlH_4$, THF, 0 °C, 1.5 h, 91%; (3) NaH, THF, 1 h, then MEMCl, 0 °C, 1.5 h, 93%; (4) $(COCl)_2$, DMSO, CH_2Cl_2, –78 °C, 15 min, then Et_3N, –40 °C, 15 min; (5) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH–H_2O (4:1), 8 h, 79% (2 steps); (6) MeONHMe·HCl, DEPC, Et_3N, DMF, 1.5 h, 89%; (7) EVE, ^{t}BuLi, THF, –78 °C, 50 min, 90%; (8) O_3, CH_2Cl_2, –78 °C, 10 min, then Me_2S, –78 °C to rt, 1 h, 86%.

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